The Calculation of Proton Chemical Shifts in Aromatics, Carbonitriles, Acetylenes and Hetero-aromatics

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By

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Publications

"Proton chemical shifts in NMR. Part 14. Proton chemical shifts, ring currents and π-electron effects in condensed aromatic hydrocarbons and substituted benzenes."

R.J.Abraham, M.Canton, M.Reid and L.Griffiths, *J.Chem.Soc., Perkin Trans. 2*, 2000, **4**, 803.

"Proton chemical shifts in NMR. Part 15. Proton chemical shifts in nitriles and the electric field and π-electron effects of the cyano group."

R.J.Abraham and Matthew Reid, *Magn.Res.Chem.*, 2000, **38**, 570.

"Proton chemical shifts in NMR. Part 16. Proton chemical shifts in acetylenes and the anisotropic and steric effects of the acetylene group."

R.J.Abraham and Matthew Reid, *J.Chem.Soc., Perkin Trans.2*, 2001, 1195.

Abstract

The Calculation of Proton Chemical Shifts in Aromatics, Carbonitriles, Acetylenes and Hetero-aromatics

By Matthew Simon Reid

A semi-empirical calculation of the partial atomic charges in organic molecules based on molecular dipole moments (CHARGE3) has developed into a model capable of predicting the proton chemical shifts in a variety of organic molecules to a good degree of accuracy.

The model has subsequently been modified to incorporate condensed aromatic hydrocarbons, substituted benzenes, carbonitriles, acetylenes and hetero-aromatics. In the aromatic and hetero-aromatic compounds the influence of π-electron densities, ring current effects and electronic effects (α, β and γ-effects). The model gives the first comprehensive calculation of the proton chemical shifts in aromatic and hetero-aromatic compounds and the proton chemical shifts (SCS) in substituted benzenes. For condensed aromatics and hetero-aromatics with data sets of 55 and 215 proton chemical shifts respectively spanning a range of 1.9 to 9.4ppm, rms. errors of the observed vs. calculated shifts were ca.0.120 and 0.096ppm respectively.

Then model has been developed to calculate the proton chemical shifts for a range of cyanides, calculating the linear electric field and electronic effects of the cyano group. For a data set of 95 proton chemical shifts spanning a range of ca.0.70 to 9.00ppm an rms error of 0.087ppm is calculated.

The model has also been applied to a range of acetylene compounds, calculating the anisotropy, steric and electronic effects of the acetylene group. The proton chemical shifts of all acetylene compounds and their derivatives are composed of 102 data points spanning a range of ca.0.70. to 9ppm and are predicted with an rms error of 0.114ppm.

Abbreviations

SCS	Substituent chemical shift
PNMR	Proton nuclear magnetic resonance
TMS	Tetramethylsilane
$CDCl_3$	Deuterated chloroform
Eqtn.	Equation
ppm	Parts per million
GIAO	Gauge invarient atomic orbitals
GSEF	Gamma substituents effect
BSEF	Beta substituents effect
CCl_4	Carbontetrachloride
HMQC	Heteronuclear quantum correlation
HMBC	Heteronuclear bond correlation
COSY	Correlated spectroscopy
NOE	Nuclear overhauser effect
HETCOR	Heteronuclear correlation
ΔG	Gibbs free energy
MP2	Moller-Plessat
DFT	Density functional theory
RMS	Root mean square
PC	Personal computer
Å	Angstrom

Chapter One.

Proton chemical shifts in nuclear magnetic resonance spectroscopy.

Chapter One. Proton chemical shifts in nuclear magnetic resonance spectroscopy.

1.1. Introduction-Proton nuclear magnetic resonance spectroscopy and substituent chemical shift (SCS).

In high-resolution nuclear magnetic resonance spectroscopy the proton chemical shift is the single most important parameter. This was illustrated by Arnold, Dharmatti and Packard[1] in 1951 in their analysis of ethanol. The three separate proton resonances illustrated clearly the massive potential of proton nuclear magnetic resonance (PNMR) in structural organic chemistry. Since this initial discovery PNMR has become the most common and vital tool of the research scientist in industry and academia and is vital in the characterisation and structure elucidation of chemical compounds. Although NMR and in particular PNMR has become as essential analytical tool there is still no semi-empirical or theoretical calculation capable of predicting ^1H chemical shifts of organic compounds to a degree of accuracy that is of practical use to the analytical chemist. As a result many attempts into the calculation of ^1H chemical shifts have been conducted over many years, with attempts generally focusing on particular families of chemicals rather than a whole range of chemical compounds.

As most chemists are familiar, ^1H chemical shifts are usually measured on the δ scale or in ppm and measured from an internal reference, usually TMS ($SiMe_4$). In organic PNMR the range of ^1H chemical shifts is usually 0-10ppm and with today's modern spectrometers with operating fields of up to 900MHz shifts can be measured to great accuracy (0.01ppm or better). However, due to other interactions the absolute accuracy of the ^1H chemical shift is accurate to 0.001ppm. Solvent effects in PNMR are often very significant[2], the ^1H chemical shift variation of acetone[3, 4] in various solvents being an example. In order to minimise these effects all ^1H chemical shifts given in this work are recorded in dilute solutions in $CDCl_3$. Other conditional variations such as changes in concentration and temperature can have marked effects on the chemical shift.

The influence of any substituent X, on the chemical shift of any proton is termed the substituent chemical shift (SCS) and is defined as:

$$\mathbf{SCS = \delta(RX) - \delta(RH)}$$

In order to simplify the SCS we may break it down into three separate parts. There is a one-bond or α-effect (H-X), a two-bond or β-effect (H-C-X), a three-bond or γ-effects (H-C-C-X) and long-range effects (more than three bonds). The one bond effect is of little practical value as in organic compounds the ^1H chemical shifts are of protons attached to carbon atoms and hence it is of only theoretical interest. The chemical shifts of protons attached directly to other atoms such as OH, NH, SH, etc., undergo large shift changes due to concentration and solvent effects and are hence of little use to the structural chemist.

Many researchers have not offered comprehensive investigations into the analysis of chemical shifts over a whole molecule and have concentrated on two-bond (β) effects or been limited because of poor instrumentation or lack of suitable compounds for analysis. This chapter will give a brief account of the work undertaken by various researchers into the analysis of ^1H chemical shifts and the methodologies used and will focus on those studies that are more relevant to this work.

1.2. Analysis of proton chemical shifts.

a) Semi-empirical calculations.

Daily and Shoolery[5] and subsequently Allred and Rochow[6] investigated the two-bond effect of substituents on ^{1}H chemical shifts. By examining the chemical shifts of methyl derivatives (CH_3-X) they discovered a linear relationship between the chemical shifts and the electronegativity of the substituent, X. This is illustrated in **table 1.1**.

Table 1.1. ^{1}H chemical shifts (δ) of CH_3-X compounds vs. electronegativity of X[a].

X	δ_H	E_X
$SiMe_3$	0.0	1.90
H	0.22	2.20
Me	0.86	*2.60*
Et	0.90	*2.60*
CCl_3	2.75	*2.60*
CN	1.98	*2.60*
CO.Me	2.17	*2.60*
SMe	2.08	*2.60*
I	2.16	2.65
NH_2	2.46	3.05
Br	2.68	2.95
Cl	3.05	3.15
OH	3.38	3.50
F	4.26	3.90

[a]Pauling electronegativity, see Ref[7].

When we examine **table 1.1** we observe that for multivalent atoms the chemical shift of the methyl protons are influenced by the γ substituent. If we examine X=Me vs. CCl_3, CN and CO.Me we observe that effects other than electronegativity must be influencing the ^{1}H chemical shift. Dailey and Schoolery[5] also observed that the effects of a substituent in a position γ to the proton in question were different to the β-effects. From **table 1.1** it can be seen that the β-effect of the methyl group is 0.64ppm (ethane vs.

methane) and the γ-effect of the methyl group is 0.04ppm (propane vs. ethane). It can also be observed that the γ-effect is more than a function of electronegativity for the substituent. This is again illustrated by the methyl group in ethyl chloride having a larger value than that of ethanol, 1.49 vs. 1.24δ. This is despite the fact that the electronegativities of the chlorine and hydroxyl group are in reverse order. These observations led researchers to conclude that other factors must be influencing the chemical shifts of protons with a γ-substituent, such as electric field and magnetic anisotropy effects.

The relationship between electronegativity and chemical shifts determined by Shoolery is given using Shoolery's rule[8], enabling the prediction of the chemical shift of any CH_2XY and CHXYZ protons by use of the **eqtn.1.1**.

$$\delta_H = b + \Sigma\sigma_{eff} \qquad \textbf{(Eqtn.1.1)}$$

Where:

b is a base value and $\Sigma\sigma_{eff}$ is the sum of the contributions of the substituents.

This linear relationship was only applied to substituents α to the proton under investigation. Another limitation was the fact that for more heavily substituted systems, the additivities gave inaccurate answers.

In a subsequent investigation Bell et al[9] further studied the use of additive parameters for the prediction of ^1H chemical shifts using a larger data set with a more varied range of substituents. They studied the chemical shifts of methine protons using multiple linear regression analysis and Simplex function minimization in order to determine under what limiting circumstances the additivity of shift parameters can apply. They examined a range of compounds comprising 441 chemical shifts and involving 31 different substituents and determined a value of b of 2.50. A standard error for the calculated shifts of 0.2ppm was obtained for a proton range of 3.00 - 7.75ppm.

In the studies by Bell et al the effects of β substituents were also included. An example of this is in the predicted chemical shift of $CHCl_3$. The base value (2.50) plus the contributions for three chlorine substituents (3 x 1.56) produces a calculated chemical shift of 7.18 ppm. This is in good agreement with the observed value of 7.25 ppm. This is an enhancement on the value determined by Shoolery of 7.67 ppm.

b) The influence of functional groups on distant protons.

Zurcher[12] conducted an interesting and thorough investigation of the effects of substituent groups on distant protons in various saturated compounds. All subsequent investigations into long-range effects have been based on Zurcher's analysis. Zurcher's model proposed that the influence of a distant group on the chemical shift of a proton under investigation may be broken down into separate contributions, which can be seen below.

i) Steric or Van der Waals effects due to the proximity of the proton and the substituent ($\delta\Delta_{ster}$)

ii) The difference between the electric dipole moments of the C-X bond and of the C-H_X (H_X-proton replaced by the substituent X) bond in the unsubstituted molecule ($\delta\Delta_{el}$).

iii) Magnetic anisotropy of the substituents ($\delta\Delta_{anis}$)

By unifying present theories on the above long range effects Zurcher was able to investigate the influence of a number of substituents on proton chemical shifts and hence determine the substituent SCS, given in **eqtn.1.2**.

$$\Delta\delta = \Delta\delta_{el} + \Delta\delta_{ster} + \Delta\delta_{anis} + \Delta\delta_{solv} \qquad \textbf{(Eqtn.1.2)}$$

Please note ^{1}H chemical shifts of solutes in dilute solutions in $CDCl_3$ are considered here and we assume that solvent effect contributions are negligible under these conditions.

Zurcher incorporated McConnell and Pople's model of magnetic anisotropy, based on the anisotropy of the magnetic susceptibility of the substituent[13, 14] in his calculations. Buckingham[15] amongst others, based his model on the electric dipole moment of the substituent, and Bothner-By based his on the London-Van der Waals interaction between the substituent and the hydrogen atom[16]. These were also incorporated into Zurcher's calculations.

In his investigation Zurcher used conformationally fixed systems to analyse substituents such as Cl, OH, CN and CO. Unfortunately because of limitations in instrumentation at the time only methyl protons at various ring positions could be examined. The SCS for Cl, OH and CN were satisfactorily explained in terms of the electric field term only, with the need to include electric field and anisotropic terms for the carbonyl group.

Zurcher also attempted to calculate the ^1H chemical shift of protons in α positions relative to the substituent in substituted methanes, ethanes, n-propanes and iso-propanes. The poor correlation between calculated and observed chemical shifts for Cl, OH and CN substituents illustrated that effects other than the linear electric field effect must be operating at such short distances. Some of these results can be seen in **table 1.2**.

Table 1.2. Observed vs. calculated chemical shifts ($\Delta\delta_{obs}$ and $\Delta\delta_{calc}$) of protons in α-positions.

Substituent	**Methane** $\Delta\delta_{obs}$	**Ethane** $\Delta\delta_{obs}$	**n-Propane** $\Delta\delta_{obs}$	**Iso-Propane** $\Delta\delta_{obs}$	$\Delta\delta_{calc}$
Cl	2.83	2.62	2.57	2.80	2.83
OH	3.17	2.73	2.58	2.60	1.61
CN	1.75	1.48	1.38	1.33	1.19

*Note $\Delta\delta = \delta_s - \delta_{us}$ where δ_s and δ_{us} are the observed chemical shifts of the proton under examination in the molecule with and without the substituent.

Zurcher's investigation into long range ^1H chemical shifts still did not provide a definitive model for the calculation of ^1H chemical shifts as no molecules containing protons that were β or γ to the substituent were considered.

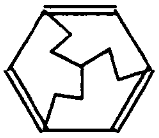
c) *The use of ^1H and ^{13}C databases in NMR prediction.*

The database approach to the prediction of ^{1}H chemical shifts has not been widely used in the past but is a fast growing method with a range of companies developing packages that contain a vast range of organic compounds. In the past, only limited examples of the database approach can be found in the literature which have been employed in particular systems such as steroids[17] or adamantanes[18], among others.

The database approach is still an unreliable tool for the prediction of ^{1}H chemical shifts and has some very significant problems. However some success has been achieved in the prediction of carbon chemical shifts. For ^{1}H chemical shift prediction to work effectively the database package must include a vast range of organic molecules with every conceivable combination of substituents. One such ^{1}H database package in existence is ACD-Labs[19] and this has been presented as the ultimate data base approach. The package is used to elucidate the structure of unknown compounds under investigation by inputting analytical data (1D/2D-^{1}H/^{13}C NMR, IR, MS) into a sub structure database. Structure fragment "hits" are produced which correspond to the experimental analytical data, which go on further to give a possible complete chemical structure. The program then displays a series of compounds, which may be the one under examination.

The package can also be used to predict the ^{1}H chemical shifts of known compounds. This can be useful but three-dimensional (stereo-specific) effects exist in NMR so compounds can display chemical shifts that are not expected. To illustrate this deficiency we may examine the case of the tri-bridged cyclophane seen in **fig.1.1**, where a proton lies directly above an aromatic ring.

Figure 1.1. Tri-bridged cyclophane.



The observed chemical shift for this proton is ca.-4ppm. The ACD package in this case predicted a shift of ca. 2ppm, which is a poor correlation. The way ACD overcame this problem was to simply add the observed shifts of this compound to their database, so when the shifts for this compound are calculated again it gives a perfect match. This gives a clear example of how a database package is not enough when trying to predict ^{1}H NMR, unless the researcher has a huge database of the chemical shifts of related structures and is constantly adding to the database.

Another problem is that many ^{1}H NMR database packages rely on experimental data from the literature. Many researchers will confirm that the literature can be far from reliable and in many cases one compound can have three references for its ^{1}H NMR in the same solvent but each reference states different chemical shifts!

d) The quantum mechanical approach to chemical shift prediction.

Quantum mechanical molecular orbital theory plays a major role in the study of inorganic and organic chemicals. Molecular orbital theory has played a major role and is used for the calculations of magnetic shielding constants and chemical shifts to the calculation of minimum energy molecular geometries, electron densities, dipole moments and the relationships between electronic structure and reactivity. With the technology available today packages such as Gaussian98W[20] can be utilised to calculate the chemical shifts of nuclei such as ^{13}C, ^{15}N, ^{17}O, ^{19}F, ^{31}P and heavier nuclei such as transition metals with a good accuracy.

Ellis et al[21] used gauge-invariant atomic orbitals (GIAO) to develop the SCF molecular orbital theory of nuclear magnetic shielding constants. The resulting equations were applied to the INDO calculation of ^{13}C shielding for a set of hydrocarbons. A resulting set of INDO parameters along with the London overlap approximation lead to a good correlation of calculated ^{13}C chemical shift with the experimental values. Hehre et al[22] attempted to correlate ^{13}C chemical shift with π electron densities using the STO-3G basis set. They illustrated that the ^{13}C SCS could be interpreted on the basis of calculated electron densities. However this was not the case for the ^{1}H SCS and this will be discussed later (Chapter six).

We should in theory therefore, be able to utilise quantum mechanics to successfully calculate ^{1}H chemical shifts. However this has been done with very limited success and only the calculations of the chemical shifts of heavier nuclei has proved fruitful. As we have seen, the gauge independent GIAO calculations have been successfully applied to calculate chemical shifts of heavier nuclei[23].

e) *Partial atomic charges and the development of the CHARGE model.*

The semi-empirical calculations of partial atomic charges in molecules have given good correlations with ^1H chemical shifts and this has been the area of most success in approaches to the prediction of ^1H chemical shifts in organic molecules. Gasteiger and Marsili[24-27] illustrated that the partial atomic charges calculated by their electronegativity equalisation approach gave a good correlation of ^1H chemical shifts for a variety of substituted simple alkanes. Partial atomic charges were calculated through iterative partial equalisation of orbital electronegativity[24]. The orbital electronegativity was considered to be dependent on total charge, Q, irrespective of whether the charge lies in the orbital under consideration or in others.

In subsequent work Gasteiger and Marsili[27] determined a relationship between the chemical shift and the corresponding charge of a proton under investigation. This relationship is given by **eqtn.1.2** below.

$$\delta = 106.4\, q_H - 1.347 \qquad \textbf{(Eqtn.1.2)}$$

Where q_H is the charge on the proton in question.

They found that the charges they defined by the iterative procedure above gave good correlation between the chemical shift and the charge on the proton under examination. However, they made the conclusion that since there was no correlation between charges on carbon and hydrogen atoms, no correlation could be drawn between ^1H chemical shifts and charge density on carbon atoms. Some results may be seen in **table 1.3.**

Table 1.3. Atomic charges, q_H(me) and observed vs. calculated chemical shifts (δ_{obs} and δ_{calc}) for various protons in hydrocarbons and substituted hydrocarbons[27].

Compound	**q_H (me)**	$\delta_{obs.}$	$\delta_{calc.}$
CH_4	19.0	0.23	0.67
$CH_3CH_2CH^*_3$	23.0	0.91	1.10
$(CH^*_3)_3CH$	23.2	0.89	1.12
$CH_2{=}CH_2$	52.9	5.28	4.26
CH_3F	49.8	4.27	3.95
$CH^*_3CH_2F$	24.9	1.24	1.30
CH_3 CH^*_2F	53.1	4.36	4.30
CH_3Cl	41.1	3.06	3.03
CH_3Br	38.6	2.69	2.76
CH_3I	33.7	2.16	2.24
CH_3OH	42.2	3.39	3.14
CH_3OCH_3	42.4	3.24	3.16
HCHO	98.8	9.60	9.50
$CH^*_3NH_2$	38.6	2.47	2.76

Note * denotes the proton under examination.

Abraham et al[28-31] modified a computer program capable of predicting dipole moments (CHARGE) into a model capable of predicting the ^1H chemical shifts of organic compounds based on the calculation of partial atomic charges. This model has subsequently been developed into a model capable of predicting the ^1H chemical shifts and dipole moments in a wide range of organic compounds. Throughout the years of its development the CHARGE scheme has been modified to incorporate the influence of functional groups on ^1H chemical shifts and as a result effectively predicts the ^1H chemical shifts for compounds containing a number of substituents. Details of the development of CHARGE can be seen in a review[32].

The objective of this research was to add to the development of the CHARGE scheme in order to be able to calculate the ^1H chemical shifts in aromatics and hetero-aromatics and to investigate the influence of cyanide and acetylene substituents on the ^1H

chemical shifts of compounds containing these functional groups. The CHARGE model was to be parameterised in order to calculate the chemical shifts for the above functionalilies.

1.3. References.

1. J.T.Arnold, S.S.Dharmatti and M.E.Packard, *J.Chem.Phys.*, 1951, **19**, 507.
2. P.Laszlo, *Prog.Nuc.Mag.Res.Spect.*, 1967, **3**, 231.
3. G.V.D.Tiers, in: J.W.Emsley, J.Feeney and L.H.Sutcliffe (Eds.), Appendix B, High Resolution NMR Spectrscopy, 2, Pergamon Press, Oxford, 1966.
4. GlaxoWellcome, NMR chemical shifts for solvents, brochure.
5. B.P.Dailey, J.N.Shoolery, *J.Am.Chem.Soc*, 1956, **77**, 3977.
6. A.L.Allred, E.G.Rochow, *J.Am.Chem.Soc*, 1957, **79**, 5361.
7. M.L.Higgins, *J.Am.Chem.Soc.*, 1957, **79**, 3977.
8. J.N. Shoolery, *J. Am. Chem. Soc*, **21**, (1953), 1899.
9. a) HM Bell, DB Bowles, F Senese, *Org.Mag.Res*, 16, (1981), 285.

   b) HM Bell, LK Berry, EA Madigan, *Org.Mag.Res*, 22, (1984), 293.
10. E Pretsch, C Arnold, RB Schaller, *Anal.Chim.Acta*, **312**, (1995), 95.
11. A Gloor, M Cadisch, RB Schaller, M Farkas, T Kocsis, JT Clerc, E Pretsch, R.Aeschimann, M Badertscher, T Brodmeier, A Furst, HJ Heidiger, M Junghans, H Kubinyi, ME Munk, H Schriber and D Wegman, *Chemical Concepts*, GmbH, Weinheim (1994).
12. R.F.Zürcher, *Progress in Nuclear Magnetic Resonance Spectroscopy*, 1967, **2**, 205.
13. H.M.McConnell, *J.Chem.Phys.*, 1957, **27**, 226.
14. J.A.Pople, *Proc.Roy.Soc.*, 1957, **A239**, 550.
15. A.D.Buckingham, *Can.J.Chem.*, 1960, **38**, 300.
16. a) A.A.Bothner-By, *J.Mol.Spect.*, 1960, **5**, 52.

    b) A.A.Bothner-By and C.Naar-Colin, *J.Am.Chem.Soc.*, 1961, **83**, 231.
17. N.S.Bhacca and D.H.Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, Holden-Day, 1964.
18. R.C.Fort, P.Von and R.Schleyer, *J.Org.Chem.*, 1965, **30**, 789.
19. A.Williams, S.Bakulin and S.Golotvin, NMR Prediction Software, Advanced Chemistry Development Inc., Toronto, Ontario, 1998-1999.
20. GAUSSIAN 98, Revision.A9, Gaussian Inc., Pittsburgh PA, 1998.

    M.J.Frisch, G.W.Trucks, H.B.Schlegel, G.E.Scuseria, M.A.Robb, J.R.Cheeseman, V.G.Zakrzewski, J.A.Montgomery, Jnr., R.E.Stratmann, J.C.Burant, S.Dapprich, J.M.Millam, A.D.Daniels, K.N.Kudin, M.C.Strain, O.Farkas, J.Tomasi, V.Barone, M.Cossi, R.Cammi, B.Mennucci, C.Pomelli, C.Adamo, S.Clifford, J.Ochterski, G.A.Petersson, P.Y.Ayala, Q.Cui, K.Morokuma, D.K.Malick, A.D.Rabuck, K.Raghavachari, J.B.Foresman, J.Cioslowski, J.V.Ortiz, A.G.Baboul, B.B.Stefanov, G.Liu, A.Liashenko, P.Piskorz, I.Komaromi, R.Gomperts, R.L.Martin, D.J.Fox, T.Keith, M.A.Al-Laham, C.Y.Peng, A.Nanayakkara, M.Challacombe, P.M.W.Gill, B.Johnson, W.Chen, M.W.Wong, J.L.Andres, C.Gonzalez, M.Head-Gordon, E.S.Replogle and J.A.Pople.

21. P.D.Ellis, G.E.Maciel and J.W.McIver, Jnr., *J.Am.Chem.Soc.*, 1972, **94**, 4069.
22. W.J.Hehre, R.W.Taft and R.D.Topsom, *Prog.Phys.Org.Chem.*, **12**, 159.
23. H.M.Sulzbach, P.V.R.Schleyer and H.F.Schaefer, *J.Am.Chem.Soc.*, 1994, **116**, 3967.
24. J.Gasteiger and M.Marsili, *Tetrahedron Lett.*, 1978, 3181.
25. J.Gasteiger and M.Marsili, *Tetrahedron*, 1980, **36**, 3219.
26. J.Gasteiger and M.Marsili, *Croat.Chem.Acta*, 1980, **53**, 601.
27. J.Gasteiger and M.Marsili, *Org. Magn. Reson.*, 1981, **15**, 360.
28. R.J.Abraham, L.Griffiths and P.Loftus, *J.Comp.Chem.*, 1982, **3**, 407.
29. R.J.Abraham and B.Hudson, *J.Comp.Chem.*, 1984, **5**, 562.
30. R.J.Abraham and B.Hudson, *J.Comp.Chem,*, 1985, **6**, 173.
31. R.J.Abraham and P.E.Smith, *J.Comp.Chem.*, 1987, **9**, 288.
32. R.J.Abraham, *Prog.Nucl.Magn.Reson.Spec.*, 1999, **35**, 85.

Chapter Two.

The theory behind the CHARGE model.

Chapter Two. The theory behind the CHARGE model.

2.1. Introduction.

As we have seen previously (chapter one) the CHARGE programme was initially developed for use in molecular mechanics calculations for the prediction of partial atomic charges in organic molecules. It has subsequently been developed into a model capable of predicting proton chemical shifts in a wide range of molecules. The model uses the partial atomic charges for short-range effects and the principles applied by Zurcher[1] for the long-range effects (more than three bonds). The model has been successfully applied to a range of saturated and unsaturated hydrocarbons, haloalkanes, ethers, ketones and aromatic compounds.

A brief account of the theory for the latest version (CHARGE7) will be given here as it has been given extensively in previous accounts[2, 3]. The theory distinguishes between substituent effects over one, two and three bonds, which are attributed to the electronic effects of the substituents and longer-range effects due to the electric fields, steric effects and anisotropy of the substituents.

2.2. The theory of the CHARGE model.

The CHARGE model calculates the effects of atoms on the partial atomic charge of the atom under consideration, based upon classical concepts of inductive and resonance contributions. If we consider an atom I in a four atom fragment I-J-K-L the partial atomic charge on I is due to three effects. There is a α effect from atom J given by the difference in the electronegativity of atoms I and J. This is given by **eqtn 2.1**.

$$q_i(\alpha) = (E_J - E_I) / A_{(I,J)} \qquad \textbf{(Eqtn.2.1)}$$

Where:

$q_i(\alpha)$ is the partial atomic charge on the atom I due to the α effect.

E_J-E_I is the electronegativity difference between atoms J and I.

$A_{(I,J)}$ is a proportionality constant that is a function of the exchange and overlap integrals for the bond I-J.

A β-effect from atom K proportional to both the electronegativity of atom K and the polarisability of atom I is given in **eqtn 2.2**.

$$q_i(\beta) = (E_K - E_H) * P_I / c \qquad \textbf{(Eqtn.2.2)}$$

Where:

$q_i(\beta)$ is the Partial atomic charge on atom I due to the β-effect.

c is a constant.

To account for the variation of polarisability with charge, calculation of the β-effect is performed by iteration. This is done according to **eqtn.2.3**.

$$P_i = P^o_i\,(1.0 + 3.0\,(q^o_i - q_i)) \qquad \textbf{(Eqtn.2.3)}$$

Where:

P_i is the polarisability of atom I with charge q_i.

P^o_i and q^o_i are the corresponding initial values.

A γ-effect (GSEF) from atom L also exists and is given by the product of the atomic polarisabilities of atoms I and L for I = H and L = F, Cl, Br, I, S. This is given in **eqtn.2.4**.

$$q_i(\gamma) = 0.005\, P_I\, P^o_L \qquad \textbf{(Eqtn.2.4)}$$

Where:

$q_i(\gamma)$ is the partial atomic charge on the atom I due to the γ-effect.

P_I is the polarisability of atom I and P^o_L is a literature value for the polarisability of atom L.

However for the second row atoms (C, O, etc.) the γ-effect (i.e. C.C.C.H) is parameterised separately. This is given by **eqtn.2.5**.

$$\begin{aligned} \text{GSEF} &= A+B_1\cos\theta & 0^0 \leq \theta \leq 90^0 \\ &= A+B_2\cos\theta & 90^0 \leq \theta \leq 180^0 \end{aligned} \qquad \textbf{(Eqtn.2.5)}$$

Where:

θ is the C.C.C.H dihedral angle and A and B empirical parameters.

Routines for the methyl γ-effect and for the decrease in the γ-effect of the electronegative oxygen and fluorine atoms for CX_2 and CX_3 groups also exist. The total charge is given by summing these effects and the partial atomic charges (q) converted to shift values using **eqtn.2.6.**

$$\delta_{\text{charge}} = 160.84q - 6.68 \qquad \textbf{(Eqtn.2.6)}$$

The effects of more distant atoms on the proton chemical shifts are due to steric, anisotropic and electric field contributions. These follow the principles of Zurchers work[1]. As we have seen previously (chapter one) we neglect solvent effects.

H..H steric interactions in alkanes were found to be shielding and X..H (X = C, O, F, Cl, Br, I) interactions deshielding, according to a simple r^{-6} dependence (**eqtn.2.7**).

$$\delta_{\text{steric}} = a_S / r^6 \qquad \textbf{(Eqtn.2.7)}$$

Furthermore any X..H steric contribution on a methylene or methyl proton resulted in a push-pull effect (shielding) on the other proton(s) on the attached carbon.

The effects of the electric field of the C-X bonds (X= H,F,Cl,Br,I,O) were calculated from **eqtn.2.8**.

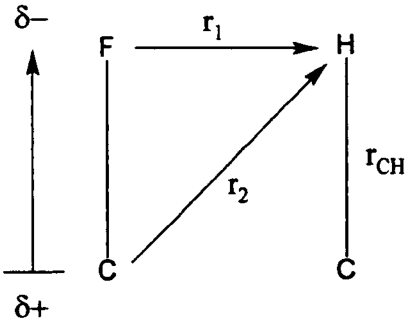
$$\delta_{el} = A_Z.E_Z \qquad \textbf{(Eqtn.2.8)}$$

Where:

A_Z was determined as $3.67\text{x}10^{-12}$ esu (63 ppm au) and E_Z is the component of the electric field along the C-H bond.

The electric field for a univalent atom (e.g. fluorine) is calculated as being due to the charge on the fluorine atom and an equal and opposite charge on the attached carbon atom. The vector sum gives the total electric field at the proton concerned (**figure 2.1**) and the component of the electric field along the C-H bond considered is E_Z in **eqtn.2.8**. This procedure is both simpler and more accurate than the alternative calculation using bond dipoles.

Figure 2.1. Model used to calculate electric field effects.



The magnetic anisotropy effect depends on the symmetry of the substituent in question. The magnetic anisotropy of a bond with cylindrical symmetry such as C≡C was obtained using the McConnell equation[4] (**eqtn.2.9**).

$$\delta_{an} = \Delta\chi^{C\equiv C}(3\cos^2\varphi - 1)/\ 3R^3 \qquad \textbf{(Eqtn.2.9)}$$

Where:

R is the distance from the perturbing group to the nucleus of interest in Å.

φ is the angle between the vector R and the symmetry axis.

$\Delta\chi^{C\equiv C}$ the molar anisotropy of the C≡C bond. ($\Delta\chi^{C\equiv C} = \chi^{C\equiv C}_{parl} - \chi^{C\equiv C}_{perp}$, where $\chi^{C\equiv C}_{parl}$ and $\chi^{C\equiv C}_{perp}$ are the susceptibilities parallel and perpendicular to the symmetry axis respectively). This is illustrated in **figure 2.2.**

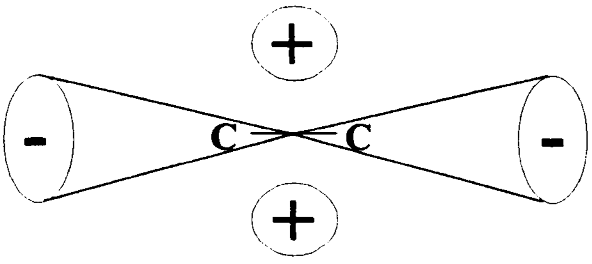


Figure 2.2. Representation of the anisotropic shielding (Δδ) in an axially symmetric molecule such as acetylene.

For non-symmetrical groups such as the carbonyl group, **eqtn.2.9** is replaced by the full McConnell equation (**Eqtn.2.10**).

$$\delta_{an} = [\Delta\chi_1 (3\cos^2\theta_1 - 1) + \Delta\chi_2 (3\cos^2\theta_2 - 1)]/3\ R^3 \qquad \textbf{(Eqtn.2.10)}$$

The C=O group has different magnetic susceptibilities (χ_1, χ_2 and χ_3) along the axes (X_1, X_2 and X_3) and thus two anisotropy terms are required.

Aromatic Compounds.

For aromatic compounds it is necessary to include the shifts due to the aromatic ring current and the π-electron densities in the aromatic ring. The aromatic ring current density is calculated in CHARGE from the Pauling theory and the equivalent dipole approximation is then used to calculate the ring current shifts[2]. This treatment reproduces the proton chemical shifts of a wide range of aromatic hydrocarbons and is incorporated unchanged here.

The π-electron densities are calculated from Huckel theory[5, 6]. The standard coulomb and resonance integrals for the Huckel routine are given by **eqtn.2.11.**

$$\alpha_r = \alpha_0 + h_r\beta_0 \qquad \textbf{(Eqtn.2.11)}$$
$$\beta_{rs} = k_{rs}\beta_0$$

Where:

α_0 and β_0 are the coulomb and resonance integrals for a carbon $2p_Z$ atomic orbital.

h_r and k_{rs} the factors modifying these integrals for orbitals other than sp^2 carbon.

For alternant aromatic hydrocarbons this gives π-electron densities at every carbon equal 1.0 as in benzene and this agrees with the results of more sophisticated calculations[7].

For substituted aromatics the appropriate values of the coefficients h_r and k_{rs} in **eqtn.2.11** for the orbitals involving heteroatoms have to be found. These are now obtained in CHARGE so that the π-electron densities calculated from the Huckel routine reproduce the π-electron densities given from ab initio calculations.

The effect of the excess π-electron density at a given carbon atom on the proton chemical shifts of the neighbouring protons is given in CHARGE by **eqtn.2.12.** Δq_α and Δq_β are the excess π-electron density at the α and β carbon atoms and the values of the coefficients a_1 and a_2 were found to be 10.0 and 2.0 ppm/electron$^{2.}$

$$\Delta\delta = a_1\Delta q_\alpha + a_2\Delta q_\beta \qquad \textbf{(Eqtn.2.12)}$$

The above contributions are added to the shifts of **eqtn.2.6** to give the calculated shift of **eqtn.2.13**.

$$\delta_{total} = \delta_{charge} + \delta_{steric} + \delta_{anisotropy} + \delta_{el} + \delta_{\pi} \qquad \textbf{(Eqtn.2.13)}$$

2.3. References.

1. R. F. Zürcher, *Progress in Nuclear Magnetic Resonance Spectroscopy*, 1967, **2**, 205.
2. M.Canton, M.Reid and L.Griffiths, *J.Chem.Soc.Perkin Trans.2, 2000, 803.*
3. R.J.Abraham, *Progress in NMR Spectroscopy*, 1999, **35**, 85.
4. H.M.McConnell, *J.Chem.Phys.*, 1957, **27**, 226.
5. R.J.Abraham and P.E.Smith, *J.Comp.Chem.*, 1987, **9**, 288.
6. R.J.Abraham and P.E.Smith, *J.Comp.Aid.Molec.Design*, 1989, **3**, 175.
7. Part 15, R.J.Abraham and M.Reid, *Mag.Reson.Chem.*, 2000, **38**, 570.

Chapter Three.

Condensed aromatic hydrocarbons and substituted benzenes.

Chapter Three. Condensed aromatic hydrocarbons and substituted benzenes.

3.1. Introduction[‡].

The influence of the π-electron densities and ring currents of aromatic compounds on their proton chemical shifts have been investigated since the beginning of proton NMR spectroscopy[1]. Thus it is all the more surprising that despite this wealth of investigation there is still no authoritative calculation (even a semi-empirical one) of the proton chemical shifts of aromatic compounds and the structural chemist still has to rely on proton data banks for the identification of aromatic compounds by NMR.

Pauling[2] introduced the concept of an aromatic ring current to explain the diamagnetic anisotropy of crystalline benzene. Using quantum-mechanical perturbation theory he calculated the diamagnetic susceptibility of benzene and applied this theory in condensed aromatic molecules. Pople[3] extended this theory to explain the difference in the chemical shifts of benzene and ethylene and illustrated that the equivalent dipole model of this ring current accounted well for this difference.

More sophisticated ring current models for benzene were then developed. The classical double-loop[4] and double dipole models[5] mimic the π-electron circulation by placing the current loops (and equivalent dipoles) above and below the benzene ring plane. A value of ±0.64 Å between the loops was found to be most appropriate. The equations of Haigh and Mallion[6] give the shielding ratios directly from quantum mechanical theory. Schneider et al[7] have recently presented a detailed experimental examination of the double-loop and Haigh and Mallion ring current models, though not the simple equivalent dipole model. The calculations gave good agreement with the experimental data, thus the effect of the benzene ring current on the chemical shifts of neighbouring protons is reasonably well understood.

However, the proton chemical shifts in condensed aromatic compounds and substituted benzenes have not yet been well calculated and this is the subject of this investigation. Bernstein et al[8] in their initial calculations of the proton chemical shifts of condensed aromatic compounds assumed the same ring current for each benzenoid ring but this was subsequently considered to be an oversimplification. Thus it is first necessary

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[‡] Part of this introduction reproduced from Ref.47 with permission.

to calculate the π-electron current density for each benzenoid ring and then to calculate the effects of these currents on the chemical shifts of the ring protons. The quantum mechanical method for calculating the π-electron current intensities was first given by Pople[9] and McWeeny[10] subsequently extended the London-Pople theory. McWeeny's work gives not only the circulating current density but also the effect of this circulating current at the proton in question. It should be noted that all these theories were based on simple Hückel theory.

Early experimental investigations to test these theories were not helped by the complex proton spectra of many condensed aromatic hydrocarbons at the low applied magnetic fields then in use and also by the quite large concentration effects on the proton chemical shifts due to the propensity of these large planar rings to stack in solution. However three systematic investigations attempted to overcome these difficulties. Jonathan et al[11] analysed the proton spectra of several condensed aromatics at infinite dilution in CCl_4 or CS_2. They then used the London-Pople theory to calculate the current intensity in the benzenoid rings and the Johnson-Bovey tables[4] to obtain the ring current shifts. They noted that other interactions were affecting the proton shifts and in particular noted a high frequency shift for close protons, which was suggested to be due to Van der Waals contact but did not attempt to quantify this.

Subsequently Cobb and Memory[12] and Haigh and Mallion[6] performed two similar but more extensive investigations. The proton spectra of several condensed aromatic compounds in dilute solution were analysed and the McWeeny equation used to obtain the ring current densities and shielding ratios. They both ignored σ bond anisotropies in this calculation. Both investigations obtained reasonable correlations for "non overcrowded protons" between the observed proton shifts and the ratio of the π-electron shielding for a given proton compared to benzene (H'/H'_b in the nomenclature of ref.6). The more comprehensive data of ref.6 when converted to the δ scale may be written as $\delta_{obs}=1.56\,(H'/H'_b) + 5.66$ with an rms error of 0.06 ppm over a range of *ca.*1.6 ppm. However the differences between the calculated and observed data for the "crowded" protons were *ca.* 0.5-0.7 ppm with one of 1.2 ppm, all to high frequency of the calculated value. Again they attributed these shifts to steric effects but did not quantify or define these effects.

More recently Westermayer et al[13] used a double dipole model to test the observed shifts. They correlated the resulting geometric factors with the observed shifts to obtain a value for the benzene diamagnetic susceptibilty anisotropy. They stated that superior results for the sterically crowded protons were obtained but it is not clear why should be the case as no steric term was introduced.

Although it is obvious which protons are crowded it is not obvious whether this interaction is also present in the other "less crowded" protons. Thus the simple question of whether the difference between the α and the β proton chemical shifts in naphthalene is due to ring currents, π-electron densities or steric effects has still not been satisfactorily answered. Although Pople in his original studies[9] calculated the ring current intensities in the five- and seven-membered rings of azulene, to our knowledge there has not been any calculation of the proton chemical shifts in non-alternant hydrocarbons.

The influence of the substituents on the proton chemical shifts in the benzene ring has also been investigated for many years and again there is still no-quantitative calculation of these effects. Following the classic work of Castellano et al[14] and Hayamizu and Yamamoto[15], who completely analysed the complex proton spectra of a wide range of monosubstituted benzenes in dilute solution in CCl_4, the proton substituent chemical shifts (SCS) are known accurately, and tables of these SCS are an integral part of any text on NMR spectroscopy[16-18]. The theoretical interpretations of these effects have concentrated on the correlation between the SCS and the calculated π (and also σ) electron densities on the adjacent carbon atoms following the excellent correlation found between the ^{13}C SCS and the π-electron densities at the *para* carbon atom in monosubstituted benzenes[19].

Correlations with π-electron densities calculated by various methods have been reported, the most recent being the *ab initio* calculations of Hehre et al[20], which will be considered in depth in chapter six. They used the STO-3G basis set and showed that the ^{13}C SCS could be well interpreted on the basis of calculated electron densities but this was not the case for the proton SCS. The *para* proton SCS could be correlated with the total charge density at the *para* carbon atom but the *meta* proton SCS did not correlate well with the calculated *meta* carbon charge densities but with the sum of the charges at the hydrogen an attached carbon atoms. They stated that "this lack of consistency indicates either that the calculations are unrealistic or that the ^{1}H SCS depend to a very significant extent on factors other than electron densities at the H and attached C atoms". They omitted the *ortho* proton SCS presumably on the grounds that these other effects are even more important at these protons. They also noted that strongly electronegative substituents caused polarisation of the π system without charge transfer, leading to changes in the π-electron densities around the ring and this is termed the π-inductive effect. They also found various correlations between the calculated charge densities and the Taft σ_I and σ_R values. This reflects the results of other investigations, which have attempted to correlate substituent parameters with the proton SCS[15, 21 & 22]. Despite all these endeavours there is still no calculation of proton SCS in substituted benzenes reliable enough to be of use to the structural chemist.

We give here the proton chemical shifts of a selection of condensed aromatic compounds in $CDCl_3$ and show that these differ by a small but significant amount from the earlier data in CCl_4 solution. These provide sufficient data for an analysis of the proton chemical shifts based on the CHARGE model for calculating proton chemical shifts. CHARGE has been applied successfully to a variety of saturated hydrocarbons[23], haloalkanes[24], ethers[25] and ketones[26]. We shall show that this model can be extended to provide a quantitative calculation of the proton shifts in condensed aromatic compounds, including two non-alternant hydrocarbons and the SCS of monosubstituted benzenes.

We give two alternative calculations of the ring current intensity in the benzenoid rings together with a dipole model of the benzene ring current. In model A the ring current intensity in the individual benzenoid rings is a function of the number of adjoining rings whereas in the model B the molecular ring current is given by the classical Pauling treatment as proportional to the molecular area divided by the molecular perimeter. All the protons in the condensed aromatic compounds are considered and the “crowded” proton chemical shifts reproduced by a simple steric effect. The effects of substituents in monosubstituted benzenes are well reproduced for the *ortho*, *meta* and *para* protons on the basis of calculated π-electron densities plus the steric, anisotropic and electric field effects of the substituents. We show also that the model reproduces the high field shifts of protons situated over the benzene ring thus providing a general calculation of proton chemical shifts of condensed aromatic compounds.

3.2. Application of the theory to aromatic compounds.

A detailed account of the CHARGE[27] theory can be seen previously (chapter two).

a) Identifying aromatic systems.

A new subroutine was added to CHARGE model in order to take into account the whole range of aromatic compounds. Only a few monosubstituted benzenes were in the model at that moment. Therefore it was necessary to include five-membered rings, condensed aromatic hydrocarbons and to increase the range of substituted aromatic compounds.

In a first attempt we considered that the single bond length between two double bonds could identify an aromatic ring. The geometries for benzene and *e*-butadiene were then calculated using GAUSSIAN94 programme[32] at the MP2/6-31G* level. The calculated bond length for benzene was 1.397 Å and 1.458 Å for *e*-butadiene. Thus we assumed that bond lengths greater than 1.40 Å did not belong to an aromatic bond. However some of the aromatic molecules were not identified as aromatics in this subroutine. A closer look at these molecules showed that not all the aromatic bond lengths are less than 1.40 Å. Allinger *et al*[28] investigated the structures of hydrocarbons containing delocalised electronic systems by molecular mechanics. They found aromatic bond lengths greater than 1.40 Å (*e.g.* 1.471 Å for one of the bond lengths in perylene).

Thus a new subroutine was used to identify the aromatic compounds. The subroutine is divided into two different sections to distinguish between five- and six-membered rings (see the coding of the subroutine in appendix one). Each ring is identified individually. Thus the subroutine identifies each ring at a time for condensed aromatic compounds.

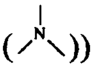
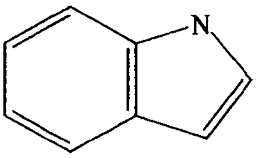
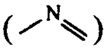
Within five-membered rings, the heteroatom (oxygen, sulphur or nitrogen sp^2 ()) or a carbon sp^2, such as in indole (see **Figure 3.1**), is the first detected atom. After its detection, the model begins to find the connectivities (α atoms), starting from the heteroatom. Therefore it must find four more atoms attached to each other, and the last atom must be attached to either the hetero-atom or the carbon sp^2.

Figure 3.1. Indole.



On the other hand, within six-membered rings, the first detected atom is either an sp^2 carbon or nitrogen sp^2 (). Subsequently the model finds the other five atoms, having in consideration that the last atom must be attached to the first one.

b) *Ring Currents.*

In order to calculate the aromatic ring currents a number of modifications were made to the CHARGE model. The aromatic ring current at any proton was then calculated from the equivalent dipole moment (**Eqtn.3.1**).

$$\delta_{rc} = fc\,\mu\,(3\cos^2\theta - 1)\,/\,R^3 \qquad \textbf{(Eqtn.3.1)}$$

Where:

δ_{rc} is the chemical shift due to the aromatic ring current.

R is the distance of the proton from the benzene ring centre.

θ the angle of the R vector from the benzene ring symmetry axis.

μ is the equivalent dipole of the benzene ring.

fc is the π-electron current intensity for the benzenoid ring, being equal to 1.0 for benzene.

In order to calculate the value of fc for the compound under investigation two alternative methods were implemented. The first method (model A) was based on inspection of the calculated ring current intensities of refs.6 and 11. Haig and Mallion[6] did not publish the calculated ring current intensities for the common aromatic compounds, but a selection of their calculated values for some less common condensed aromatic compounds is given in **Table 3.1**.

Closer examination of this data shows that the changes in the ring current are due to the number and orientation of the rings attached to the benzenoid ring. In model A we assume that the ring current intensity is only a function of the number and orientation of the rings attached to the benzenoid ring in question. This may be quantified by the number and the orientation of the substituent sp^2 carbon atoms attached to the ring in question (R_o). Thus we must define:

i) The number of attached sp^2 carbons on each carbon of the ring.

ii) The relative position of these attached atoms in the benzene ring.

Thus for benzene each carbon atom has two sp^2 carbon atoms attached to it which means R_o=12. For either ring in naphthalene two of the carbon atoms have three carbon neighbours and hence R_o=14. The middle rings of anthracene and phenanthrene both have R_o=16 but the relative positions of the substituent carbons differ in the two cases. These are defined as R_o=16a and 16b. This analysis gives seven different systems (**table 3.1**) of which six are present in the molecules indicated in **Figure 3.2.**

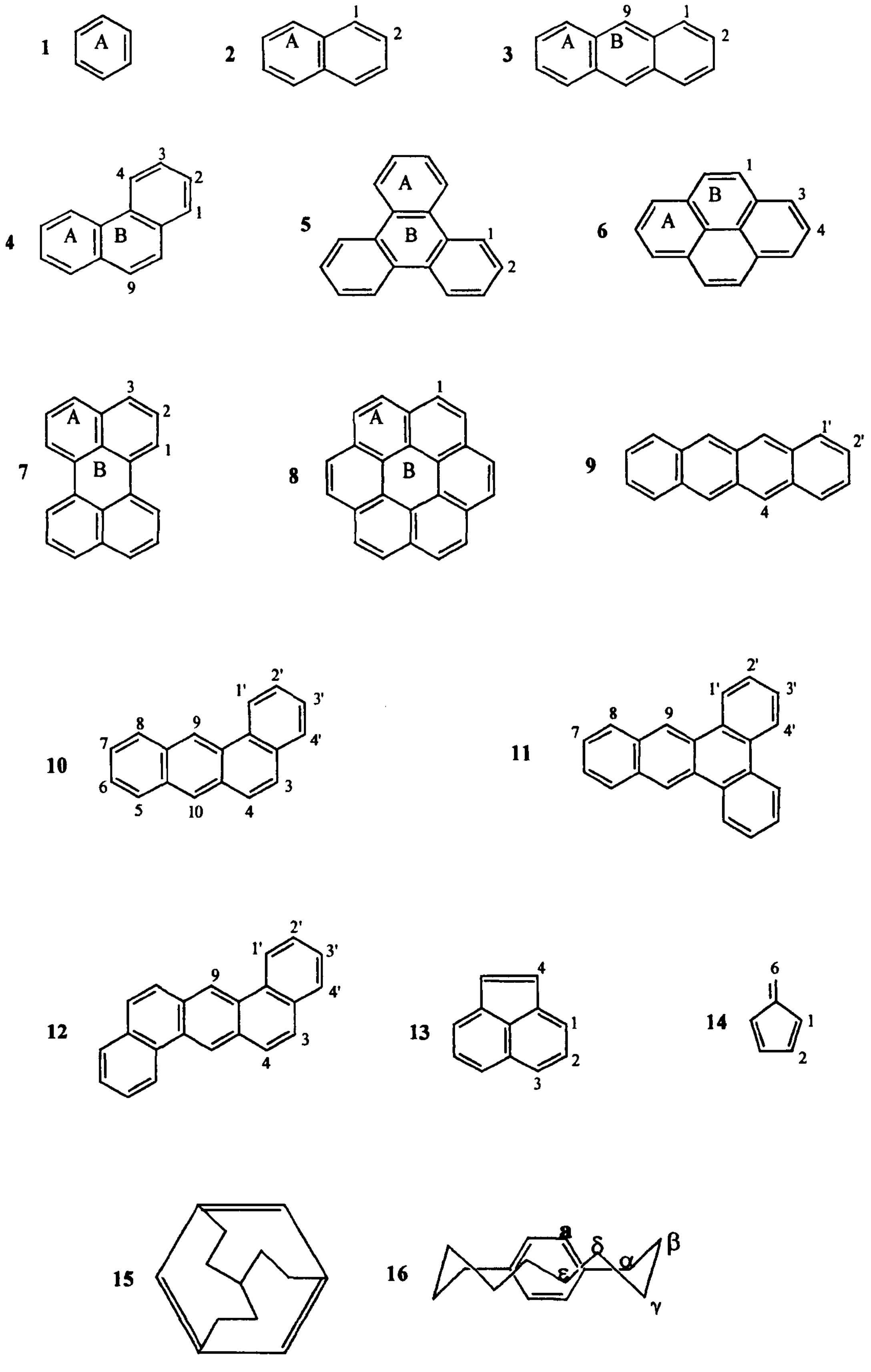
Closer examination of **table 3.1** shows that with few exceptions the separation of the ring current densities into the different ring types gives a reasonably constant value for each ring type. The only serious exception is the calculated values for ring type 18 of ref.11 which are very different for perylene and coronene. It would be possible to average the calculated values of ref.6 for each ring current and use these averages in our calculation. In view of the approximations inherent in these calculations it was decided to parameterise the current intensity for each ring type separately to obtain the best agreement with the observed shifts.

Table 3.1. Calculated ring current intensities in condensed aromatic hydrocarbons.

Molecule	Ring type[a]	(R_o)	Ring Current Intensity (*fc*)			
			[b]	[c]	Model A	Model B[d]
Benzene (1)		12	1.00	1.00	1.00	1.00
Naphthalene (2)		14	1.093	1.048[e], 1.094[f], 1.121[g]	0.95	0.925
Anthracene (3)	Ring A	14	1.085	1.119[h], 1.197[i], 1.104[j]		0.943
	Ring B	16a	1.280	1.291[e], 1.311[f], 1.299[g], 1.298[h], 1.170[j]	0.818	
Phenanthrene (4)	Ring A	14	1.133			0.876
	Ring B	16b	0.975	0.877[g], 0.876[h]	0.745	
Triphenylene (5)	Ring A	14	1.111			
	Ring B	18	0.747			
Pyrene (6)	Ring A	15	1.329	1.337[i], 1.292[k]	0.786	0.878
	Ring B	16b	0.964			
Perylene (7)	Ring A	15	0.979			0.681
	Ring B	18	0.247	0.603[f], 0.606[l]	0.173	
Coronene (8)	Ring A	16b	1.460		1.06[a]	1.008
	Ring B	18	1.038	0.745[m], 0.684[k]		
		17	-	1.297[i], 1.226[l], 1.310[i]		

[a] See text. [b]Ref.11. [c]Ref.6. [d]this work. [f]Dibenzo[*a,c*]naphthacene. [g]Dibenzo[*a,j*]naphthacene. [h]Dibenzo[*a,l*]naphthacene. [i]Dibenzo[*def,mno*]chrysene. [j]Benzno[*h*]pentaphene. [k]Benzo[*ghi*]perylene. [l]Naphtho[1,2,3,4-*def*]crysene. [m]Dibenzo[*b,def*]crysene.

Figure 3.2. Molecules studied and their nomenclature.



An alternative method of calculating the aromatic ring current is to use the Pauling model[2] (model B) in which the carbon skeleton is considered as a conducting electrical network in which for any current loop the emf is proportional to the area[2]. In other words, if the condensed aromatics are considered to be made up of a number of regular hexagons the ring current for any molecule is simply proportional to the number of hexagons in the molecule divided by the number of bonds in the perimeter of the molecule. For example, the ring current ratio for benzene is 1/6, for naphthalene is 2/10 and for anthracene is 3/14. The Pauling model gives too large a value for the diamagnetic anisotropy of condensed aromatics[5a] so that as in method A the Pauling model was used to separate the various molecular types and the ring current for each molecular type was parametrised against the experimental data Although the same experimental data are used in both models the different selectivities give different answers. As an example, in model B anthracene and phenanthrene have identical ring currents, which is not the case in model A.

c) *π-electron densities.*

The π-electron densities are calculated in the CHARGE model from Hückel theory[29]. The standard coulomb and resonance integrals for the Hückel routine are given by **eqtn.2.11.**

$$\alpha_r = \alpha^0 + h_r \beta^0 \qquad \textbf{(Eqtn.2.11)}$$
$$\beta_{rs} = k_{rs} \beta^0$$

Where α^0 and β^0 are the coulomb and the resonance integrals for a carbon $2p_z$ atomic orbital and h_r and k_{rs} the factors modifying these integrals for orbitals other than sp^2 carbon. The Huckel technique was modified by the ω technique to model the very polar π systems of the nucleic acid bases[30]. The ω technique involves varying the coulomb integral for each atom according to the charge on that atom. This is shown in **eqtn.3.2** where α_r is the coulomb integral, α_r^0 the initial coulomb integral, q_r the excess π charge on atom r and ω a constant.

$$\alpha_r = \alpha_r^0 - q_r\omega \qquad \textbf{(Eqtn.3.2)}$$

Eqtn.3.2 "cuts in" at a given value of the excess π charge on atom r. For the nucleic acid bases the value of ω was 1.40 and the cut-in threshold 0.2 electrons.

For alternant aromatic hydrocarbons this calculations gives π-electron densities at every carbon equal to 1.0 as in benzene. Thus the excess π density is zero. This is in agreement with the results of more sophisticated calculations. For example, the excess π-electron densities at the α and β carbons of naphthalene are calculated as –0.8 and –4.1 me (millielectrons) from *ab initio* calculations with the 6-31G* basis set.

For the non-alternant hydrocarbons fulvene and acenaphthylene the Hückel routine gives large excess π-electron densities at certain carbon atoms, which are much larger than those calculated by *ab initio* methods in which iteration procedures restrict the tendency in the Hückel routine to separate the π charges. Therefore the ω tecnique was modified to correct this by decreasing the "cut in" point of **eqtn.3.2** from 0.2 to 0.01 electrons and increasing the value of ω to 6.0. This modification gave acceptable results for these two compounds, though the dipole moments are higher than the observed values. As these hydrocarbons have quite different π-electron densities and geometries, both ring currents of the five-membered and the ring current intensity of the attached six-membered ring were parameterised separately.

For the substituted benzenes the appropriate values of the coefficients h_r and k_{rs} in **eqtn.2.11** for the orbitals involving heteroatoms have to be found. In ref.29 two procedures were considered. One was to obtain those values that gave the best agreement with the experimental dipole moments of the compounds studied. The other procedure was to consider the values that gave the best agreement with the π-electron densities obtained by *ab initio* calculations. We began by using the first procedure as the simplest method of obtaining dipole moments of unsaturated compounds. However later developments showed that the π-electron densities calculated from *ab initio* calculations were a more flexible method. We now use the latter set so that the π densities calculated from the Huckel routine reproduce those given from *ab initio* calculations.

The other modification to the Hückel routine concerns the effect of saturated substituents (*e.g.* CH_3) on the π-electron densities in the benzene ring, which is usually termed hyperconjugation. In this case an equation corresponding to **eqtn.3.2** was used to vary the coulomb integral of the aromatic carbon connected to an sp^3 carbon. In this way changes to the π-electron density of the benzene ring due to both electron-donating substituents such as CH_3 and electron withdrawing substituents such as CF_3 can be handled by the same procedure.

Having obtained the π-electron density in the benzene ring it is then necessary to determined the effect of the π-electron density at a given carbon atom on the proton chemical shifts. Gunther et al[31] measured the proton chemical shifts of a variety of cyclic charged molecules (tropylium cation, cyclopentadienyl anion, etc) and compared them with benzene. From this data they obtained a value of the coefficient a_1 (**Eqtn.2.12**) of 10.0 between the proton shift $\Delta\delta$ and the excess π charge Δq_α on the attached carbon atom.

$$\Delta\delta = a_1\,\Delta q_\alpha + a_2\,\Delta q_\beta \qquad \textbf{(Eqtn.2.12)}$$

It has also been recognised that there is an influence of the excess π charge on the carbon atom β to the proton considered. Considering this, in aromatic compounds in which the CH bond is orthogonal to the π orbital, θ is 90° and the value of a_2 in **eqtn.2.12** is negative and ca. 1/5th of a_1, i.e. -2.0.

These modifications were the only ones needed to apply the CHARGE model to aromatic compounds. However, it is still necessary to calculate the charge densities at the aromatic protons in CHARGE and thus to quantify the appropriate α, β and γ-effects. Also the long-range interactions present in the aliphatic molecules must also be included and where necessary evaluated. These will be considered subsequently.

d) Long-range effects.

As discussed earlier the long-range effects of the aromatic ring are due to steric plus magnetic anisotropy (i.e. ring current) effects. There is also a small electric field effect due to the C-H dipoles and this is calculated directly by CHARGE from the partial atomic charges as the coefficient A_Z in **eqtn.2.8** has been previously determined.

The steric effect of all non-hydrogen atoms for substituted alkanes investigated in previous versions of CHARGE was deshielding on the near protons, with a shielding effect observed for proton-proton interactions. This is in contrast to the results of previous investigations[6, 12] and the data presented here shows that proton-proton interactions in the aromatic systems considered give rise to deshielding effects on the proton chemical shifts.

To confirm that steric effects on proton chemical shifts in aromatic and saturated systems are different we can examine the proton chemical shift of the unique CH proton in the cyclophane (**15**). This proton occupies a position along the symmetry axis of the benzene ring and occurs at -4.03δ. It is a good test of any ring current theory because of its proximity to the benzene ring plane and was used by Schneider et al[7] in a separate investigation of different ring current models. This proton is in close proximity to the benzene ring carbon atoms, the average C-H distance is *ca.* 2.20 Å. Any deshielding effect from the aromatic carbon atoms comparable to that found for saturated carbon atoms would have a pronounced deshielding effect on this proton. For example using the steric coefficient found for saturated carbon atoms would give a value for the CH proton chemical shift of +6.0 δ. Clearly there is no significant deshielding steric effect from the aromatic carbon atoms at this proton. Schneider et al[7] termed this a "soft" steric effect in contrast to the "hard" steric effect of proton-proton interactions. This result was adopted in the CHARGE routine so that there is no steric effect on the proton chemical shifts from any aromatic carbon atom.

3.3. Experimental.

Ethylene, benzene, toluene, d^8-toluene, tert-butylbenzene, naphthalene, anthracene, phenanthrene, pyrene, triphenylene, 1,2-benzanthracene, 1,2:3,4-dibenzanthracene, 1,2:5,6-dibenzanthracene, acenaphthylene, fulvene and the $CDCl_3$ solvent were obtained commercially (Aldrich Chem. Co.). The solvent was stored over molecular sieves and used without further purification.

^{1}H and ^{13}C NMR spectra were obtained on a Bruker AMX400 spectrometer operating at 400.14 MHz for proton and 100.63 MHz for carbon. Spectra were recorded in 10 mg cm^{-3} solutions (^{1}H) and *ca.* 50mg cm^{-3} (^{13}C) with a probe temperature of *ca.* 25°C in $CDCl_3$ and referenced to TMS unless otherwise stated. Typical ^{1}H conditions were 128 transients, spectral width 3300 Hz, 32 k data points, giving an acquisition time of 5s and zero-filled to 128k to give a digital resolution of 0.025 Hz.

The geometries of the compounds were obtained by optimisations using the GAUSSIAN94[32] programme at the RHF/6-31G* level. For molecules too large to be handled by GAUSSIAN at the 6-31G* level, *e.g.* perylene, smaller basis set were used, *e.g.* 3-21G. For the largest molecules, *e.g.* coronene, the molecular mechanics PCMODEL programme was used[33]. The geometry and CHARGE computations were performed on a PC.

The ^{1}H NMR spectra for 1,2-benzanthracene, 1,2:3,4-dibenzanthracene, 1,2:5,6-dibenzanthracene can be seen in **figures 3.3, 3.4** and **3.5**. The proton spectrum for ethylene, benzene, tert-butylbenzene, toluene and d^8-toluene were also measured and simply assigned[‡].

[‡] The remaining compounds were measured in the same way by M. Canton.

Figure 3.3. ^{1}H NMR spectrum of 1,2-benzanthracene.

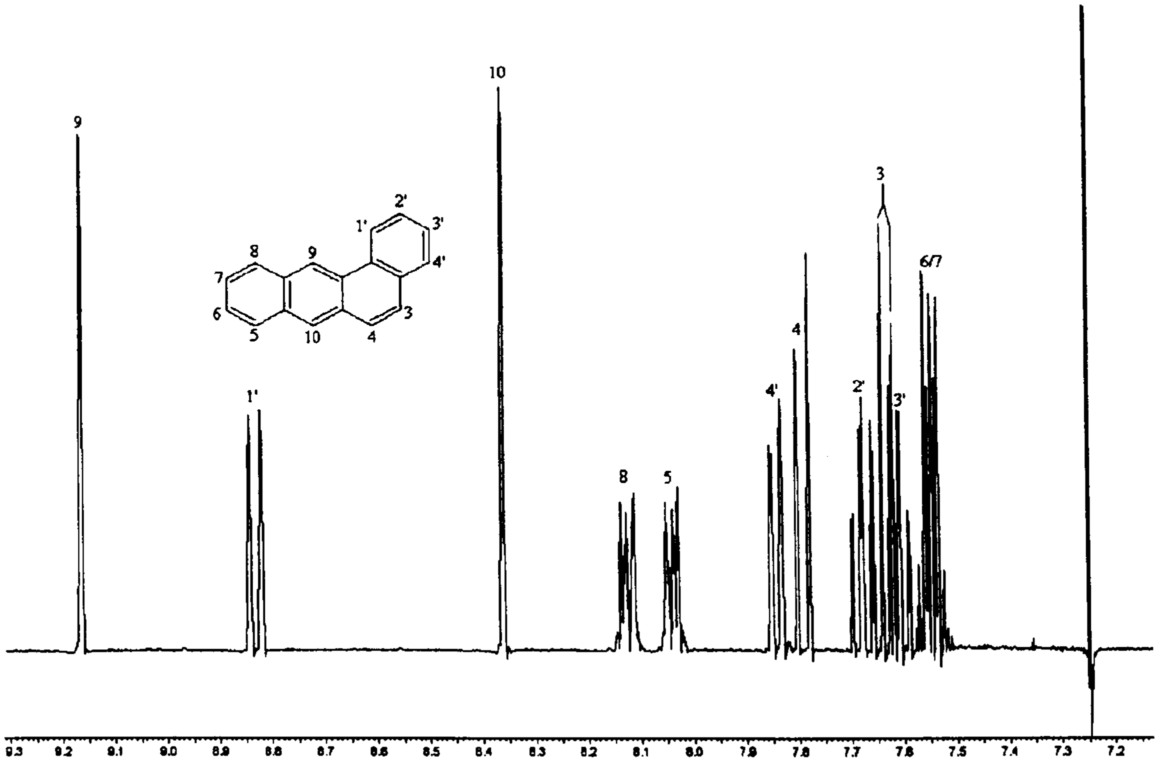


Figure 3.4. ^{1}H NMR spectrum of 1,2:3,4-dibenzanthracene.

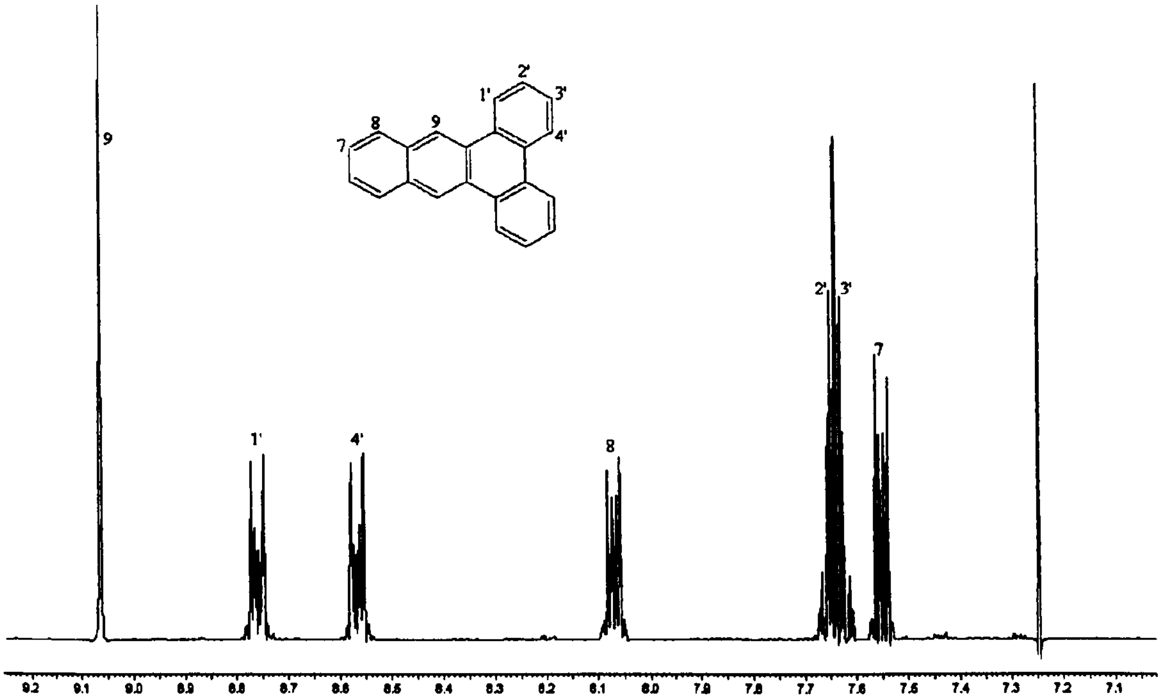
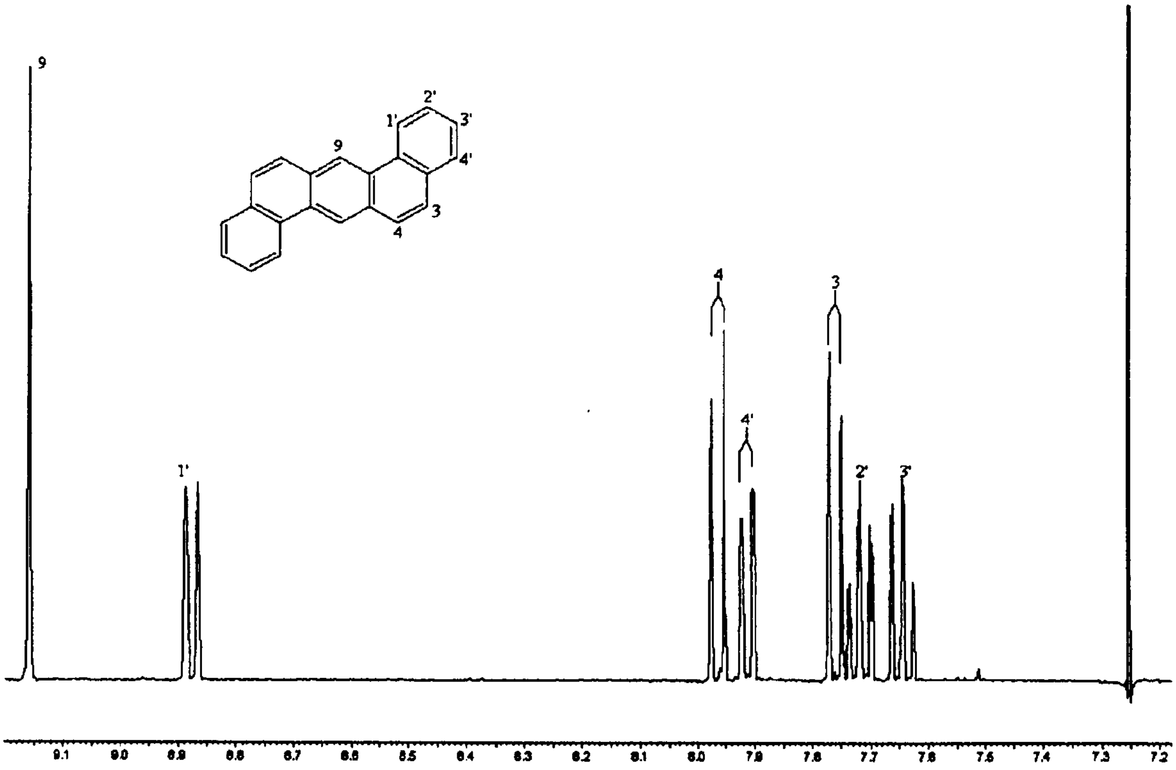


Figure 3.5. ^{1}H NMR spectrum of 1,2:5,6-dibenzanthracene.

Figure 3.5. ^{1}H NMR spectrum of 1,2:5,6-dibenzanthracene.



3.4. Results.

The proton spectra of the compounds all consisted of well separated peaks at 400MHz (except for toluene) thus the proton chemical shifts could be obtained immediately and the assignments of the compounds followed previous investigations. For toluene the proton spectrum of toluene-d_8 was first obtained. The dilute ^{1}H spins only couple to the ^{2}D nuclei and the spectrum consists of three broad singlets at 7.165, 7.170 and 7.254δ. This gave sufficient information to identify the coupling patterns in the ^{1}H spectrum of toluene and hence the slightly more accurate proton chemical shifts given in **table 3.2.**

The data obtained in $CDCl_3$ solution are given and compared with that of previous investigations in CCl_4 solution in **table 3.2.** In ref.11 the authors only reported the shift differences from benzene and we have added 7.27ppm (the benzene value in CCl_4) to them.

Table 3.2. Observed and calculated proton chemical shifts (δ) for aromatic compounds.

Compound	Proton	Observed			Calculated		
		$CDCl_3$[a]	CCl_4[b,c]		Model A		Model B
Ethylene		5.405	5.352[d]	-	5.407		
Benzene (1)		7.341	7.27[b]	7.27[c]	7.331		7.342
Naphthalene (2)	1	7.844	7.73	7.81	7.931		7.829
	2	7.477	7.38	7.46	7.524		7.493
Anthracene (3)	1	8.009	7.93	8.01	7.948		8.009
	2	7.467	7.39	7.39	7.524		7.577
	9,10	8.431	8.36	8.31	8.495		8.485
Phenanthrene (4)	1	7.901	7.80	Un	7.930		7.968
	2	7.606	7.51	Un	7.509		7.544
	3	7.666	7.57	Un	7.566		7.600
	4,5	8.702	8.62	8.51	8.455		8.433
	9,10	7.751	7.65	7.71	7.839		8.085
Triphenylene (5)	1	8.669	8.61	8.56	8.587		8.707
	2	7.669	7.58	7.61	7.613		7.654
Pyrene (6)	1	8.084	8.00	8.06	7.976		8.253
	3	8.190	8.10	8.16	7.930		8.156
	4	8.010	7.93	7.99	7.546		7.785
Perylene (7)	1	8.196	8.11	8.09	8.361		8.250
	2	7.466	7.38	7.41	7.515		7.404
	3	7.656	7.57	7.60	7.845		7.630
Coronene (8)	1	8.90[e]	8.82	8.84			8.900
1,2-benzanthracene (9)	1’	8.840	8.77		8.698		8.553
	2’	7.685	7.59		7.708		7.627
	3’	7.651	7.525		7.638		7.557
	4’	7.849	7.755		8.102		8.004
	3	7.616	7.55		7.987		8.117
	4	7.800	7.72		8.027		8.200
	5	8.048	8.03		8.101		7.977
	6	7.540	7.465		7.637		7.544
	7	7.564	7.47		7.647		7.553
	8	8.133	8.03		8.169		8.038
	9	9.174	9.08		9.125		9.052
	10	8.370	8.28		8.561		8.572
2,3-benzanthracene (10)	1’	8.00[f]			8.082		7.947
	2’	7.39			7.619		7.522
	4	8.67			8.581		8.546
1,2:3,4-dibenzanthracene (11)	1’	8.791	8.675		8.685		8.758
	2’	7.670	7.54		7.649		7.634
	3’	7.651	7.53		7.636		7.618
	4’	8.592	8.475		8.637		8.674
	7	7.568	7.455		7.641		7.521
	8	8.097	7.965		8.134		8.008
	9	9.097	9.075		9.103		9.238
1,2:5,6-dibenzanthracene (12)	1’	8.874	8.805		8.708		8.502
	2’	7.719	7.625		7.721		7.583
	3’	7.646	7.55		7.649		7.511

	4'	7.914	7.82		8.113		7.944
	3	7.760	7.67		8.016		8.077
	4	7.963	7.88		8.121		8.230
	10	9.155	9.075		9.170		9.107
Acenaphthylene (**13**)	1	7.812			7.829		7.826
	2	7.548			7.474		7.519
	3	7.692			7.708		7.701
	5,6	7.083			7.070		7.024
Fulvene (**14**)	1,4	6.228[g]			6.384		6.317
	2,3	6.531			6.421		6.404
	6	5.892			6.015		5.960
Toluene	*ortho*	7.180	7.061[h]		7.080		
	meta	7.260	7.140		7.284		
	para	7.165	7.042		7.172		
	Me	2.343	2.337[i]		2.343		
tert-Butylbenzene	*ortho*	7.390	7.281[h]		7.279		
	meta	7.297	7.180		7.358		
	para	7.165	7.052		7.218		
	Me	1.325	1.319[i]		1.332		

[a]This work, [b]Ref.6, [c]Ref.11, [d]Ref.34, [e]Ref.35, [f]Ref.36, [g]Ref.37, [h]Ref.15
[i]Ref.1, vol.2, Appendix B. un=unresolved.

The shift values in **table 3.2** are of interest. There is generally good agreement between the data sets but it is noteworthy that there is a small but almost constant difference in the proton chemical shifts in $CDCl_3$ solution compared to CCl_4. Averaging over all the aromatic compounds in **table 3.2** gives a value of 0.086ppm (± 0.01) to low field in $CDCl_3$ solution. This is also the case for ethylene but here the difference is slightly less. The aliphatic protons of the methyl groups in toluene and tert-butylbenzene do not show this effect but have the same shifts in the two solvents. The constant value of this difference means that data in CCl_4 solution can be converted directly to $CDCl_3$ solution by merely relating the shifts to benzene. Furthermore this suggests that the accurate SCS values reported earlier for the monosubstituted benzenes in CCl_4 solution may be used with confidence to investigate the application of the CHARGE model to these compounds and this data is reproduced in **table 3.3**. Also given in **table 3.3** are the SCS values obtained in our laboratory for selected compounds in dilute $CDCl_3$ solution. The excellent agreement between the sets of SCS values confirms this assumption.

The data collected in **tables 3.2 and 3.3** provide a rigorous test of the application of both the CHARGE model and also of present ring current theories to these compounds. The compounds listed in the tables are all of fixed conformation. The GAUSSIAN94 (6-31G*/3-21G) and the PCMODEL calculations gave molecular geometries for the aromatic hydrocarbons in excellent agreement with the experimental geometries, where known. E.g. benzene C.C 1.397 Å, C.H 1.087Å (MP2/6-31G*), vs. 1.395Å and 1.087Å (PCMODEL) and 1.396Å and 1.083Å (experimental)[38], etc.

In the CHARGE model the α, β and γ-effects of the substituents are considered to be due to electronic effects and therefore they are modelled on a simple empirical basis. The α-effect of an sp^2 carbon is given from the difference in the electronegativities of the carbon and hydrogen atoms divided by the appropriate exchange integral. The value of this integral was chosen to reproduce the observed chemical shift of ethylene (**table 3.2**). This gives a partial atomic charge for the ethylene protons of +0.075e, which corresponds to a C-H bond dipole of 0.4D. This is in reasonable agreement with the usual quoted range (ca 0.6 - 0.7D)[39].

The β-effect is calculated directly from the carbon electronegativity and proton polarisability[27] thus the only other electronic effect to be considered is the γ-effect (H.C.C.C) of the unsaturated carbon atoms in the aromatic compounds. For the analysis of the γ-effect of any nucleus, a simple angular function ($A+B\cos\theta$) may be utilised. The coefficients A and B are obtained from the observed data. This approach was implemented in all our investigations.

Table 3.3. Observed[a] vs. calculated proton SCS ($\Delta\delta_H$) of substituted benzenes.

	Proton substituent chemical shifts ($\Delta\delta_H$)					
Substituent	**ortho**		**meta**		**para**	
	Obs	*Calc*	*Obs*	*Calc*	*Obs*	*Calc*
H	0.00	0.00	0.00	0.00	0.00	0.00
CH_3	-0.20	-0.27	-0.12	-0.06	-0.22	-0.17
	-0.16		-0.08		-0.18[b]	
t-Bu	0.02	-0.06	-0.08	0.02	-0.21	-0.12
	0.05		-0.04		-0.19[b]	
F	-0.29	-0.23	-0.02	0.02	-0.23	-0.21
Cl	0.03	-0.04	-0.02	0.07	-0.09	-0.08
Br	0.18	0.07	-0.08	0.09	-0.04	-0.02
I	0.39	0.18	-0.21	0.08	0.00	0.01
OH	-0.56	-0.53	-0.12	-0.13	-0.45	-0.42
OCH_3	-0.48	-0.44	-0.09	-0.12	-0.44	-0.41
NH_2	-0.75	-0.62	-0.25	-0.24	-0.65	-0.65
CF_3	0.32	0.28	0.14	0.18	0.20	0.20
	0.29		0.14		0.21[c]	
CHO	0.56	0.54[d]	0.22	0.20[d]	0.29	0.26
$CO.CH_3$	0.62	0.61[d]	0.14	0.21[d]	0.21	0.28
$CO.OCH_3$	0.71	0.91[d]	0.11	0.21[d]	0.21	0.26
CN	0.36	0.35	0.18	0.21	0.28	0.24
	0.32		0.14		0.27[e]	
NO_2	0.95	0.81	0.26	0.23	0.38	0.25

a) ref.15 unless stated otherwise, b) this work ($CDCl_3$ soln.), c) ref 40, d) averaged e) ref 41.

The only parameters to be determined from the observed results in **table 3.2** are the coefficients A and B for the carbon γ-effect, the appropriate H.H steric coefficient (**eqtn.2.7**), the ring current equivalent dipole μ (**eqtn.3.1**) and the factors fc (**eqtn.3.1**) for the condensed rings, a total of 10 parameters. The values of the unknown parameters were achieved using a non-linear least mean squares programme (CHAP8)[42] to give the best fit with the observed data. These iterations were performed using model A and model B. The data set used comprises all the condensed aromatics of **table 3.2**, a total of 57 proton shifts thus the iteration is over-determined. The initial iteration for model A clearly showed that coronene was an exception and this was removed from the subsequent iteration. With this amendment the programme iterated satisfactorily with reasonable rms. error and definition. For model B coronene was parameterised separately and the iteration performed satisfactorily. The iteration gave A = -0.107, B = 0.143, the H..H steric ceoefficient a_S = +24.55ppm Å^6, μ = 26.2ppm Å^3 and the *fc* values in **table 3.1**. In fulvene and acenaphthylene both the ring current of the five-membered ring (μ_p) and also the factors (*fc*) for the benzenoid rings in acenaphthylene were parameterised separately. This gave μ_p = 11.6ppm Å^3 and *fc* = 0.81. These iterations are for two unknowns and seven observed shifts.

The determination of these unknown parameters also allows the calculation of the proton SCS of the monosubstituted benzenes in **table 3.3** as the electric field and anisotropic effects of the substituents have already been determined previously. The appropriate values of the coefficients in **eqtn.3.2** needed to model the effect of the alkyl substituents on the π densities were $\alpha_r^o = \alpha_r + 0.15$, $\omega = -0.50$. The only additional requirement is the steric effects of the side-chain protons, which in some cases affect the ortho protons. The steric effect of alkane protons on olefinic protons was determined from a general investigation involving a variety of olefinic molecules[40] and found to be deshielding and this result was used here. The steric effect of the OH and NH protons in alcohols and amines has been shown to be zero[43] and again this result was incorporated into the present calculations. The influence of the substituents on the π-electron densities within these molecules has also been determined (see chapter four for cyanobenzene) as have the electronic effects or γ-effects. This allowed the determination of the proton SCS of all the monosubstituted benzenes of **table 3.3** and these results are given with the observed data in the table.

It was also of interest to determine whether the equivalent dipole ring current calculation given here could be used to determine the benzene ring current effect for protons at the side and over the benzene ring. This data was used by Schneider[7] in determining the accuracy of the various ring current models. We consider here two illustrative examples; the unique CH proton in the tribridged cyclophane (**15**)[7] and the protons in [10]-para cyclophane (**16**)[44]. The proton chemical shifts for both compounds have been recorded in dilute $CDCl_3$ solution. The geometries of both compounds were modelled by PCMODEL and GAUSSIAN94. (**15**) is a rigid strained molecule but in (**16**) the methylene chain exists in two equivalent rapidly interconverting staggered conformations. The two protons on each methylene group in the alkyl chain have the same observed shift and the calculated shifts have to be averaged over each methylene group. The calculations were performed routinely using **eqtn.3.1** to determine the ring current shifts with the value of the equivalent dipole found from the results of **table 3.2**. The CH proton of (**15**) is observed at -4.03δ (calc. -4.03δ) and the corresponding data for (**16**) is given in **table 3.4**.

Table 3.4. Observed vs. calculated proton chemical shifts (δ) in [10]-paracyclophane **16**).

Proton	Observed	Calculated	(average)
α	2.62	2.453 2.759	2.606
β	1.54	1.806 1.592	1.699
γ	1.08	1.631 0.909	1.270
δ	0.73	1.133 0.655	0.894
ε	0.51	0.626 0.424	0.525
Aromatic	7.04	7.102 7.074	7.088

3.5. Discussion

The general agreement of the observed vs. calculated shifts in **tables 3.2** and **3.4** and the observed vs. calculated SCS of **table 3.3** is very good. Although the calculated values for models A and models B for the individual protons vary appreciably (**table 3.2**), the overall agreement for both models is similar. For the 57 data points of **table 3.2** the rms. error (obs vs. calc shifts) is 0.13ppm (model A) and 0.12ppm (model B) over a range of 3.3ppm. The analogous calculation using only the benzene ring current (i.e. all fc values =1.0) gives much poorer agreement (rms = 0.28ppm) showing that it is necessary to take account of the variation in the ring current intensity for a proper description of the proton chemical shifts. Although for convenience the SCS are given in **table 3.3**, as the proton chemical shift of benzene is calculated accurately (**table 3.2**) obviously the actual chemical shifts of all the substituted benzenes are calculated to the same accuracy as the SCS values in **table 3.3**. It can be seen that the great majority of the observed shifts are reproduced to < 0.1ppm, although there are some exceptions.

The calculation provides an insight into the interpretation of these proton chemical shifts as the different interactions responsible for the calculated values are separately identified and quantified in the CHARGE programme. The ring current calculations provide further evidence for the accuracy of the simple equivalent dipole model of the benzene ring current. The value of μ (**eqtn.3.1**) is given from the iteration as 26.2ppm Å^3. This is very similar to that obtained from the classical circulating current model (27.6)[16, 45]. The calculations also confirm previous studies[45] in demonstrating that the ring current effect is not the only factor responsible for the difference between the ethylene and benzene proton shifts. The experimental difference of 1.93ppm (**table 3.2**) is made up of 1.77ppm from the ring current and 0.17ppm from the electronic effects of the β and γ carbon atoms of benzene. This was allowed for in some previous ring current calculations by using cyclohexadiene rather than ethylene as the appropriate olefinic model[45] and the above calculations support this approach. It is of great interest to note the excellent agreement obtained with the simple equivalent dipole model. On this basis the use of the more complex double dipole and double loop models does not appear to be justified. Interestingly Mallion[46] came to exactly the same conclusion many years ago.

The values of the separate ring current factors (*fc* of **eqtn.3.1**) are given in **table 3.1** for comparison with the values obtained previously[6, 11]. In general the trends are similar supporting the original compartmentalisation of these factors though the values obtained here are mostly much nearer to the benzene value (fc=1) than the previous calculations. This is exactly to be expected as Huckel theory usually over estimates any electron separation. The only exception is the value for coronene. In model A the outer rings are of type 16β (i.e. analogous to the middle ring of phenanthrene) but this value of the ring current intensity (0.745, **table 3.1**) gives a much too low value for the proton chemical shift. A value of fc of 1.06 reproduces the experimental proton chemical shift. In model B this problem does not arise as coronene is a separate case, and the iteration gives a value of fc = 1.008 very close to the benzene value and the Huckel calculated value.

It is encouraging that the calculated shifts for the non-alternant hydrocarbons of fulvene and acenaphthylene are in very good agreement with the observed shifts (**table 3.2**) as this suggests that the approach adopted here can be extended to these systems. The ring current of the five-membered ring was parametrised separately to give a value of μ of 11.6ppm $Å^3$. The equivalent dipole $\mu = iA$ where A is the area of the current loop. After allowing for the area of the five-membered ring compared to benzene this gives a current intensity of $0.63i_b$, much less than benzene. More data on similar systems would be necessary to confirm this result.

3.6. Conclusions.

The agreement of the observed *vs.* calculated proton chemical shifts in **tables 3.2**, and **3.4** and the observed *vs.* calculated SCS of **table 3.3** are very good. The addition of a new subroutine in CHARGE allows us to calculate successfully the proton chemical shifts of a range of aromatic compounds with a good degree of accuracy. The ring current calculations provide further evidence for the accuracy of the simple equivalent dipole model of the benzene ring current. The calculations also demonstrate that the ring current effect is not the only factor responsible for the difference between the ethylene and benzene proton shifts.

It is encouraging that the calculated shifts for a non-alternant hydrocarbons of fulvene and acenaphthylene are in very good agreement with the observed shifts (**table 3.2**) as this suggests that the approach adopted here can be extended to these systems. This quantitative calculation can be applied with confidence to the prediction of the proton chemical shifts of virtually any substituted benzenoid compound.

3.7. References.

1.a) J.W.Emsley, J.Feeney and L.H.Sutcliffe, *High Resolution NMR Spectroscopy*, Pergamon Press, Oxford, 1965.

b) R.C.Haddon, V.R. Haddon and L. M. Jackman, *Top.Curr.Chem.*, 1971, **16**, 103.

2. L.Pauling, *J.Chem.Phys.*, 1936, **4**, 673.

3. J.A.Pople, *J.Chem.Phys.*, 1956, **24**, 1111.

4.a) J.S.Waugh and R.W.Fessenden, *J.Am.Chem.Soc.*, 1957, **79**, 846.

b) C.E.Johnson and F.A.Bovey, *J.Chem.Phys.*, 1958, **29**, 1012.

5.a) R.J.Abraham, *Mol.Phys.*, 1961, **4**, 145.

b) R.J.Abraham and C.J.Medforth, *Mag.Reson.Chem.*, 1987, **25**, 432.

6.a) C.W.Haigh and R.B.Mallion, *Mol. Phys.*, 1970, **18**, 737 and 767.

b) C.W.Haigh, R.B.Mallion and E.A.G.Armour, *Mol.Phys.*,1970, **18**, 751.

7. H.J.Schneider, V.Rudiger and U.Cuber, *J.Org.Chem.*, 1995, **60**, 996.

8. H.J.Berstein, W.G.Schneider and J.A.Pople, *Proc.R.Soc.London*, Ser., 1956, **236**, 515.

9. J.A.Pople, *Mol.Phys.*, 1958, **1**, 175.

10. R.McWeeny, *Mol.Phys.*, 1958, **1**, 311.

11. N.Jonatham, S.Gordon and B.P.Dailey, *J.Chem.Phys.*, 1962, **36**, 2443.

12. T.B.Cobb and J.D.Memory, *J.Chem.Phys.*, 1967, **47**, 2020.

13. M.Westermayer, G.Hafelinger and C.Regelmann, *Tetrahedron*, 1984, **40**, 1845.

14.a) S.Castellano and C.Sun, *J.Am.Chem.Soc.*,1066, **88**, 4741.

b) S.Castellano, C.Sun and R.Kostelnik, *Tetrahedron Lett.*, 1967, **46**, 4635 and 1967, **51**, 5205.

c) M.P.Williamson, R.J.Kostelnik and S.M.Castellano, *J.Chem.Phys.*, 1968, **49**, 2218.

15. K.Hayamizu and O.Yamamoto, *J.Mol.Spectrosc.*, 1968, **28**, 89 and 1969, **29**, 183.

16. R.J.Abraham, J.Fisher and P.Loftus, *Introduction to NMR Spectroscopy*, J. Wiley, New York, 1988.

17. J.B.Lambert, H.B.Shurvell, D.A.Kightner and R.G.Cooks, *Organic Structural Spectroscopy*, Prentice-Hall, New Jersey, 1998.

18. E.Pretsch, J.Seibl, T.Clerc and W.Simon, *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd. Edn., Springer-Verlag, Berlin, 1989.

19. G.C.Levy and G.L.Nelson, *Carbon 13 NMR for Organic Chemists*, J.Wiley, New York, 1972.
20. W.J.Hehre, R.W.Taft and R.D.Topsom, *Prog.Phys.Org.Chem.*, 1976, **12**, 159.
21. R.T.C.Brownlee and R.W.Taft, *J.Am.Chem.Soc.*, 1970, **92**, 7007.
22. G.K.Hamer, I.R.Peat and W.F.Reynolds, *Can.J.Chem.*, 1973, **51**,, 897 and 915.
23. R.J.Abraham, L.Griffiths and M.A.Warne, *J.Chem.Soc., Perkin Trans.2*, 1997, 31.
24. R.J.Abraham, L.Griffiths and M.A.Warne, *J.Chem.Soc., Perkin Trans.2*, 1997, 203, 881.
25. R.J.Abraham, L.Griffiths and M.A.Warne, *J.Chem.Soc., Perkin Trans.2*, 1998, 1751.
26. R.J.Abraham and N.Ainger, *J.Chem.Soc.Perlin Trans.2,* 1999, 441
27. R.J. Abraham, L.Griffiths and M.A.Warne, *Magn.Reson.Chem.*, 1998, **S179**, 36.
28. N.L.Allinger and J.T.Sprague, *J.Am.Chem.Soc.*, 1973, **95**, 3893.
29.a) R.J.Abraham and P.E.Smith, *J.Comp.Chem*, 1987, **9**, 288.
b) R.J.Abraham and P.E.Smith, *J.Computer Aided Molecular Design*, 1989, **3**, 175.
30. R.J.Abraham and P.E.Smith, *Nucleic Acids Research*, 1988, **16**, 2639.
31. H.Gunther, *NMR Spectroscopy*, 2nd Ed., p 71, J.Wiley, Chichester, 1995.
32. Gaussian 94, Gaussian Inc., Pittsburgh PA, 1994. M.J.Frisch, G.W.Trucks, M.Head-gordon, P.M.W.Gill, M.W.Wong, J.B.Foresman, B.G.Johnson, H.B.Schlegel, M.A.Robb, E.S.Replogle, R.Gomperst, J.L.Andres, K.Raghavachari, J.S.Binkley, C.Gonzalez, R.L.Martin, D.J. Fox, D.J.Defrees, J.Baker, J.J.P.Stewart and J.A.Pople.
33. PC Model Version 7.0, Serena Software Ltd., PO BOX 3076, Bloomington, Indiana, 1998.
34. U.E.Matter, C.Pascual, E.Prestsch, A.Pross, W.Simon and S.Sternell, *Tetrahedron*, 1969, **25**, 691.
35. C.J.Puchert and J.Behnke, *Aldirch Library of ^{13}C and ^{1}H FT NMR Spectra*, Aldrich Chemical Company Inc., Milwaukee, USA, (1993).
36. J.Netka, S.L.Crump and B.Rickborn, *J.Org.Chem.*, 1986, **51**, 1189.
37. U.Nuchter, G.Zimmerman, V.Francke and H.Hopf, *Liebigs Ann.Rec.*, 1997, 1505.
38. Landholt-Bornstein, Vol 7, *Structure Data of Free Polyatomic Molecules*, Ed. K.H.Hellwege and A.M.Hellwege, Springer, NY, 1976.

39.a) O.Exner, *Dipole Moments in Organic Chemistry*, George Thieme Pub., Stuttgart, 1975.

b) V.I.Minkin, O.A.Osipov and Y.A.Zhdanov, *Dipole Moments in Organic Chemistry,* Plenum Press, NY, 1970.

40. R.J.Abraham and M.Canton, *MagRes.Chem.,* 2000, **39**, 421.

41. R.J.Abraham and M.Reid, *Mag.Reson.Chem.,* 2000, **38**, 570-579.

42. S.S.Kuo, *Computer Applications of Numerical Methods*, ch.8, Addison-Wesley, London, 1972.

43. R.J.Abraham, unpublished work.

44. A.Argawal, J.A.Barnes, J.L.Fletche, M.J.McGlinchey and B.G.Sayer, *Can.J.Chem*, 1973, **51**, 897.

45. R.J.Abraham and W.A.Thomas, *J. Chem. Soc. B*, 1966, 127.

46. R.B.Mallion, *J.Chem.Phys.*, 1980, **75**, 793.

47. R.J.Abraham, M.Canton, M.Reid and L.Griffiths, *J.Chem.Soc., Perkin Trans.2*, 2000, **4**, 803.

Chapter Four.

Proton chemical shifts in carbonitriles and the electric field, electronic and π-electron effects of the carbonitrile group.

Chapter Four. Proton chemical shifts in carbonitriles and the electric field, electronic and π-electron effects of the carbonitrile group.

4.1. Introduction.

In organic chemistry, nitriles are of great importance as they are both versatile synthetic intermediates and important compounds per se (see ref.1). As a consequence the proton nuclear magnetic resonance spectra of nitriles has been studied since the beginning of NMR spectroscopy. There is however significant argument over the causes of the SCS of the cyano (CN) group. The CN group is strongly polar and anisotropic and as a result these factors have been proposed to account for the carbonitrile SCS.

Many investigations into the influence of the CN group on proton chemical shifts have been undertaken over many years. The description of the magnetic anisotropy of the carbonyl and acetylene groups has been well documented[2] and the magnetic anisotropy of the CN group is considered in the same way as the acetylene group. There have been numerous investigations into the prediction of ^1H chemical shifts in various cyano compounds. However, these have often been limited to predicting the chemical shifts of methyl protons and protons in an alpha position. Studies have been undertaken into the long range shielding effects of the CN group but these have often been limited to 2-cyanonorbornenes. Therefore, there has been no definitive investigation into the influence of the CN group on a wide range of compounds where all the protons in the system were considered.

Much of the early work on the CN group concentrated on the long range shielding effects of the CN group. ApSimon, Beierbeck and Todd[3] concluded that methyl proton chemical shifts in various steroids were entirely due to the electric field effects of the CN and felt that little was to be gained by including the magnetic anisotropy of the CN in their calculations. The CN anisotropy was calculated by modification of the McConnell equation[4].

Cross and Harrison[5] used a value of CN anisotropy calculated by Reddy and Goldstein[6] to calculate the shifts of the C-19 methyl groups in some 5α and 5β–cyano steroids. The predicted shifts were in the wrong direction and were rationalised in terms of conformational changes. In contrast to other research, Reddy and Goldstein concluded that the long range shielding effect of the CN was due to its magnetic anisotropy. They conducted work on aliphatic nitriles, where the magnetic anisotropy of the CN group was determined by its analogy to the acetylene group. The anisotropy of the acetylene group was calculated by use of a relationship between proton chemical shifts and ^{13}C-H coupling constants and agreed well with the theoretical estimate of Pople[2]. These calculated values of the CN anisotropy were included in their calculations of the proton chemical shifts. It was assumed that the geometrical centre of the CN was in the centre of the triple bond, although the π-electron system may be more or less displaced towards the more electronegative atom. Nevertheless, the results obtained indicated that this did not need to be taken into consideration.

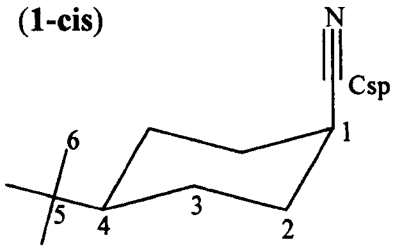
Zurcher[7] gave a more detailed analysis of CN-SCS. An investigation into the methyl proton chemical shifts in various steroids and also into the chemical shifts of α-protons was conducted in a limited number of straight and branched chained substituted alkanes, along with an investigation into the β-protons in cyanonorbornanes, norbornenes and adamantanes. Zurcher generally found a good correlation for the methyl proton resonances in the cyano-steroids. Zurcher concluded that the chemical shifts were mainly a result of the electric field effects and the magnetic anisotropy of the CN group was small and had a minimal contribution to the proton chemical shifts. Zurcher used the McConnell equation to calculate the magnetic anisotropy of the CN and the CN dipole to calculate the electric field effect. Zurcher did not find it necessary to incorporate any steric effects of the CN group in his calculations.

When extending his work to predict the chemical shifts of α-protons in various ethyl derivatives, Zurcher found a great variation between calculated and observed proton chemical shifts. These calculations were performed using the electric field only for the CN. It was concluded that there must be other factors beside the linear electric field affecting the proton chemical shifts.

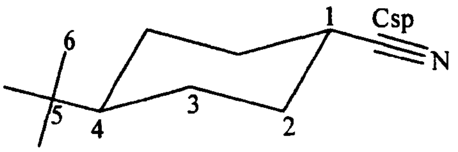
In this work a complete analysis of CN-SCS is presented using a large data set of conformationally rigid molecules with fully assigned ^{1}H NMR spectra. Presented here is the complete assignment of the ^{1}H NMR spectra of a range of aliphatic and aromatic nitriles of fixed conformation. The aliphatic nitriles investigated are cis and trans-4-t-butylcyclohexanecarbonitrile (**1-cis/1-trs**), axial and equatorial-cyclohexanecarbonitrile (**2-ax/2-eq**) and axial-axial and equatorial-equatorial-1, 4-dicyanocyclohexane (**3-ax- ax/3-eq-eq**). Also included are the ^{1}H NMR spectra of 2-exo and 2-endo-norbornanecarbonitrile (**4-ex/4-en**) and 1-adamantanecarbonitrile (**5**) which have been recorded previously[8] and acetonitrile (**6**), propionitrile (**7**), isobutyronitrile (**8**) and trimethylacetonitrile (**9**), the ^1H chemical shifts of which were obtained from the Aldrich catalogue[9]. The aromatic nitriles included in this investigation are benzonitrile (**10**), o, m and p-dicyanobenzene (**11, 12, 13**), 1 and 2-cyanonaphthalene (**14, 15**) and 9-cyanoanthracene (**16**). Acrylonitrile (**17**) was also analysed and assigned. Compounds **1-17** can be seen in **figure 4.1.**

Figure 4.1. Molecules studied and their nomenclature.

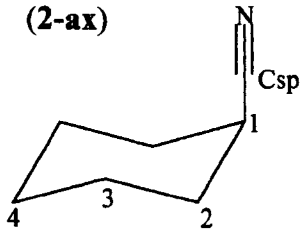
(1-cis)



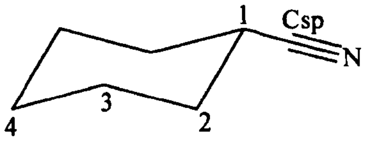
(1-trs)



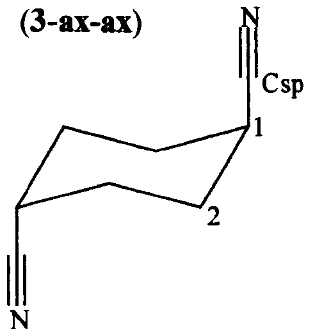
(2-ax)



(2-eq)



(3-ax-ax)



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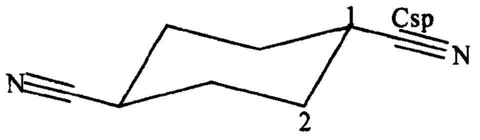
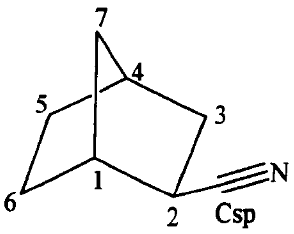


(4-ex)



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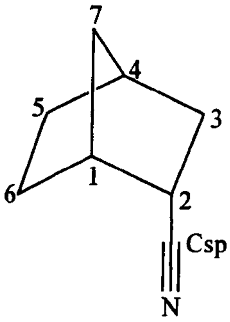

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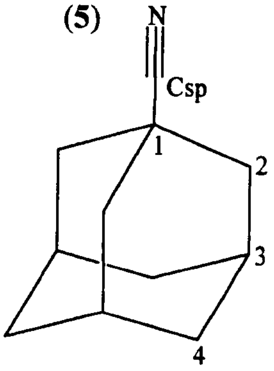

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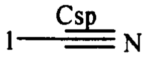

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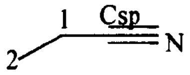

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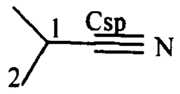

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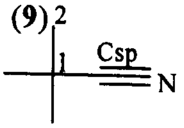

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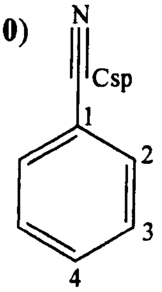

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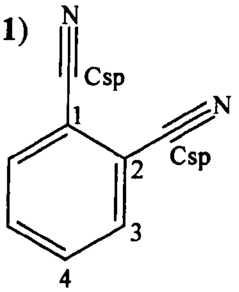

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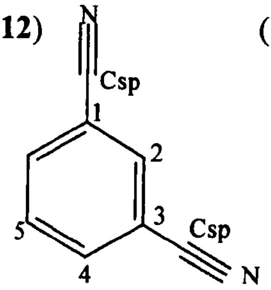

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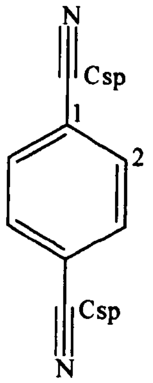

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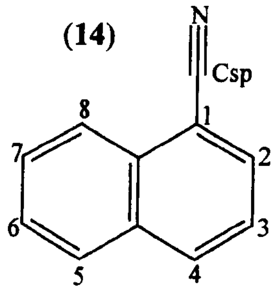

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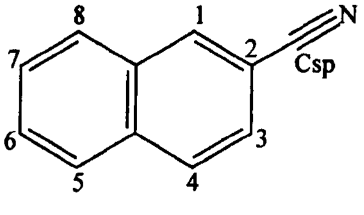
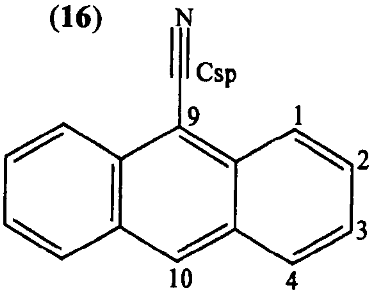
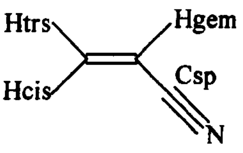


(16)



(17)



The chemical shift data above provides a sufficient amount of data for a quantitative analysis of CN-SCS using the CHARGE model. Here the model is be used to perform a quantitative analysis of CN-SCS and we show that they are due primarily to electric field effects (>3 bonds away) and electronic effects (3 bonds or less away). The anisotropic and steric effects of the CN group are shown to be negligible as far as the proton substituent chemical shifts are concerned.

4.2. Application of the theory to carbonitrile compounds.

A detailed account of the CHARGE theory can be seen previously (chapter two).

The CN group has in principle steric, electric field and anisotropic effects on protons more than three bonds away plus for aromatics a large effect on the π-electron densities. All these have to be incorporated into the model. The electric field of the CN group is calculated in an identical manner to any other C-X bond. The electric field is calculated as being due to the charge on the nitrogen atom of the CN and an equal and opposite charge on the carbon atom of the CN bond. The charge on the nitrogen atom is already calculated in the CHARGE model and the coefficient in **eqtn.2.8** (chapter two) is known so the electric field is given without any further parameterisation.

This of course assumes that the charges used in **eqtn.2.8** (chapter two) provide a reasonable measure of the electric field of the CN group. The partial atomic charges obtained in the CHARGE programme have been derived from the observed molecular dipole moments and the extent of the agreement provides one check on the electric field calculation. The calculated vs. observed (in parenthesis) dipole moments[10] (in debye) of acetonitrile, propionitrile, iso-butyronitrile, t-butylcarbonitrile, **1-cis**, **1-trs**, acrylonitrile and benzonitrile are 3.94 (3.97), 3.95 (4.02), 4.00 (3.76), 4.06 (3.95), 3.89 (3.82), 4.13 (3.76), 4.38 (3.89) and 4.38 (4.14) and the good agreement provides strong support for the electric field calculation. Note that all the dipole moments are gas phase microwave measurements except for **1-cis/trs** which are measured in benzene solution.

The CN group has cylindrical symmetry and **eqtn.2.9** (chapter two) may be used to calculate the contribution of the anisotropy to the proton chemical shifts. The steric effects of the CN group are calculated by use of **eqtn.2.7** (chapter two). The unknowns to be obtained are therefore the molar anisotropy of the CN bond, $\Delta\chi^{CN}$ and the steric coefficient a_s^{CN}.

For protons of three bonds or less from the CN group it is necessary to determine the orientational dependence of the γ proton chemical shift with respect to the carbonitrile carbon. This is simulated by a γ substituent effect (GSEF) from the carbonitrile carbon following **eqtn.2.5** in which the coefficients A and B may differ for the CN group in aromatic vs. saturated compounds. There is also a possible effect from the nitrogen atom, which affects the β protons, and since this has no orientation dependence it may be considered as dependent only on the polarisability of the nitrogen atom.

For the aromatic cyanides it is first necessary to obtain the appropriate values of the factors h_r and k_{rs}, which give the Huckel integrals for the CN group (**eqtn.2.11**, chapter two). An iterative least mean square programme, CHAP8[11] was used to obtain the best-fit values of these parameters from π-electron densities obtained from GAUSSIAN94[12] calculations. The π-electron densities and dipole moments from these *ab initio* calculations are very dependent on the basis set used. As the 3-21G basis set gave the best agreement with the observed dipole moment, the π-electron densities from this basis set were used to parameterise the Huckel calculations. Values of h_r of 0.12 and 0.30 for C(sp) and N(sp) and of k_{rs} of 1.05 for (Csp^2-Csp) and 1.20 for (Csp-Nsp) gave π-electron densities for the aromatic nitriles in reasonable agreement with those from the ab initio calculations. The electron densities (total and π) and dipole moments calculated for benzonitrile and acetonitrile by the CHARGE model and GAUSSIAN94 can be seen in **table 4.1**.

Table 4.1. Total and π (in parenthesis) charges (me), and dipole moments for benzonitrile.

Atom	Method				
	STO-3G	**3-21G**	**6-31G**	**CHARGE**	**Obs**
N (sp)	-200 (-49)	-504 (-87)	-273 (-63)	-525 (-60)	
C (sp)	73 (26)	338 (31)	21 (52)	428 (30)	
C_1	2 (-56)	-58 (-77)	10 (-76)	19 (-3)	
C_o	-42 (24)	-194 (37)	-148 (37)	-48 (12)	
C_m	-58 (2)	-232 (0)	-212 (1)	-72 (-0.3)	
C_p	-49 (28)	-227 (36)	-180 (34)	-66 (10)	
μ (D)	*3.65*	*4.55*	*4.82*	*4.38*	*4.14*

Table 4.2. Total and π (in parenthesis) charges (me), and dipole moments for acetonitrile.

Atom	Method				
	STO-3G	**3-21G**	**6-31G**	**CHARGE**	**Obs**
N(sp)	-195 (-52)	-511 (-54)	-333 (-80)	-535 (-64)	
C(sp)	76 (37)	312 (37)	135 (61)	433 (64)	
C_1	-184 (-54)	-611 (-169)	-470 (-143)	-61 (0)	
μ (D)	*3.07*	*3.92*	*4.16*	*3.93*	*3.97*

4.3. Experimental.

Cis/trans-4-t-butylcyclohexanecarbonitrile (**1-cis/1-trs**) was synthesised by dehydration of the amide by reaction with phosphorus oxychloride[13].

General procedure: *Synthesis of cis/trans-4-t-butylcyclohexanecarbonitrile* (**1**).

6.7g (0.036mol) of 4-t-butylcyclohexanecarboxylicacid (99%cis/trans) was added to 3ml (0.042mol) of thionylchloride and stirred overnight. The excess thionyl chloride was removed by rotary evaporation to yield the acylchloride.

The acylchloride was allowed to cool and 60ml of 30% ammoniumhydroxide added rapidly to give a white slurry. This mixture was heated slowly and the solid residue filtered off. The solid material was then dissolved in hot methanol and filtered hot. Water was then added drop-wise to clouding point and the mixture cooled. The resulting carboxamide was subsequently recrystallised from ethanol to give cis/trans-4-t-butylcyclohexanecarboxamide as pure white crystals (3.25g/48.8%): mp 152-154°C; IR (nujol) 3400-3200(m, NH), 2900(s, CH), 1680(s, C=O); MS *m/z* (rel.int.) 184(M+, 2), 126(100), 72(41), 57(45); NMR (750MHz, ^1H, $CDCl_3$) δ2.54(1H), δ2.13(2H), δ2.08(1H), δ2.00(2H), δ1.86(2H), δ1.65(2H), δ1.53(2H), δ1.42(2H), δ1.21(2H), δ1.10(4H), δ0.85(9H), δ0.83(9H).

2.0g (0.011mol) of 4-t-butylcyclohexanecarboxamide were added to 5.7ml of phosphorus oxychloride and the mixture refluxed for 1.5hrs. 10ml of dichloromethane and 50ml of water were then added and the mixture extracted. Another portion of dichloromethane was used to extract the aqueous phase and the organic extracts combined. The organic extracts were then washed with water and the dichlormethane removed by rotary evaporation. After cooling the mixture was neutralised with dilute sodium hydroxide and the organic phase separated and dried to yield the 4-t-butylcyclohexanecarbonitrile as a clear oily liquid (1.05g/58.2%): IR (nujol) 2200-2250(w, $C\equiv N$), 2800-2900(s, CH).

Cyclohexanecarbonitrile (**2**), 1, 4-dicyanocyclohexane (**3**), 2-norbornanecarbonitrile (**4**), 1-adamantanecarbonitrile (**5**), acetonitrile (**6**), benzonitrile (**10**), o, m and p-dicyanobenzene (**11, 12, 13**), 1 and 2-naphthalenecarbonitrile (**14, 15**), 9-anthracenecarbonitrile (**16**) and acrylonitrile (**17**) were obtained commercially[14], [15].

^1H and ^{13}C NMR were obtained on a Bruker AMX400 spectrometer operating at 400MHz for proton and 100.63MHz for carbon. The spectra for **1-cis** and **1-trs** were recorded on a Varian 750MHz spectrometer at GlaxoWellcome[16]. Here HMQC, HMBC and NOE experiments were conducted.

The spectra were generally recorded in 10mg cm^{-3} solutions (^1H) and ca.50mg cm^{-3} (^{13}C) with a probe temperature of ca.25°C in $CDCl_3$ and referenced to TMS unless indicated otherwise. Typical running conditions of the spectrometers were 128 transients, spectral width 3300Hz and 32k data points. This gave an acquisition time of 5s and zero-filled to 128K to give a digital resolution of 0.025Hz.

The 2D experiments were conducted using the Bruker AMX400 and Varian 750MHz machines using the standard Bruker COSY-DQF and HXCO-BI and the standard Varian HMQC and GHMQC-DA pulse sequences[17, 18]. The geometry of the compounds investigated was obtained by use of the program PC MODEL Version 7.0[19]. Geometry's were also optimised using the GAUSSIAN 94W programme at the RHF/6-31G* and MP2/6-31G* levels[12]. The GAUSSIAN 94W and CHARGE calculations were carried out using a PC.

4.4. Spectral Analysis.

The full ^1H NMR assignments of compounds **1-9** can be seen in **tables 4.4-4.7**, along with the calculated ^1H chemical shifts from the CHARGE model.

The full ^1H NMR assignments of compounds **10-17** can be seen in **tables 4.11-4.13**, along with the calculated ^1H chemical shifts from the CHARGE model. The full analysis and assignment of benzonitrile (**10**) and ortho (**11**) and meta (**12**) dicyanobenzene have been given previously[23] and our analyses follow these assignments. The ^1H chemical shifts for propionitrile (**7**), iso-butyronitrile (**8**), trimethylacetonitrile (**9**) and acrylonitrile (**17**) were measured directly from the Aldrich ^1H NMR catalogue[9].

Acetonitrile (6)

The ^1H NMR spectrum of acetonitrile can be seen as a singlet occurring at 2.03ppm.

Cis and trans-isomers of 4-t-butylcyclohexanecarbonitrile (1-cis/1-trs)

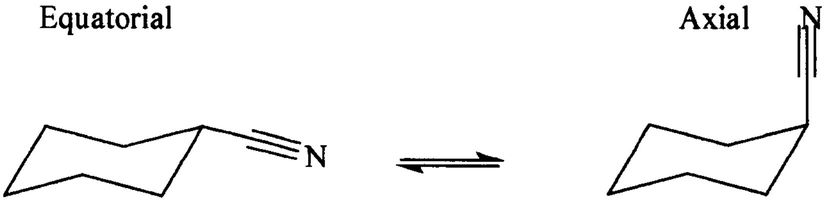
The ^1H (**fig.4.2**), ^{13}C, 2-D and NOE spectra for these isomers were recorded at both 400 and 750MHz. The spectra for both the cis and trans isomers were recorded as a mixture because they were not separated. However, this does not present any problem as all the resonances are well resolved and may be distinguished from each other.

(1-cis). The ^1H NMR spectrum of this compound consists of six proton resonances including the methyl resonances. Protons 1e, 2e and 2a are readily assigned. H-1e is readily identified as a quintet at ca. 3.05ppm. H-2e and H-2a were then easily identified from a ^{1}HCOSY spectrum by examining the couplings to H-1e. 2-D and NOE experiments were utilised to assign protons 3e, 3a and 4a. The strong couplings to H-2e and H-2a identified H-3e and H-3a. H-4a is readily assigned by its strong coupling to H-3a in the ^1H COSY plot. This assignment was further confirmed by examination of a $^1H/^{13}C$ 2D HETCOR and the known ^{13}C spectral assignment[20], and also by examination of NOE spectra.

(1-trs). The ^1H spectrum of this isomer again consisted of six proton resonances and was readily assigned in the same way as **1-cis**, using H-1a, which existed as a triplet of triplets as a starting point. By examination of a ^1H COSY plot H-2e and H-2a were readily identified by their strong coupling to H-1a. H-3e and H-3a were assigned in the same way by their strong couplings to H-2e and H-2a. Again, this assignment was further confirmed by examination of a $^{1}H/^{13}C$ 2D HETCOR and the known ^{13}C spectral assignment[20] and also by examination of NOE spectra. H-1a was found to have a strong NOE to H-3a.

Axial and equatorial-cyclohexanecarbonitrile (2-ax, 2-eq)

The spectra of the separate conformers were obtained by recording the spectra at -60°C. The integrals (n) taken for protons 1e and 1a in the axial and equatorial conformers are 0.59 and 1.13 respectively. By use of **eqtn.4.1** we are able to determine that the equatorial conformer is the more favoured, with ΔG (eq-ax) = 0.28 Kcal mol^{-1}. This value is in agreement with the literature value[21] of 0.20 kcal mol^{-1}.



$$n(eq)/n(ax) = e\text{-}(\Delta G/RT) \qquad \textbf{(Eqtn.4.1)}$$

Where:

n(ax) and n(eq) are the integral values of H-axial and H-equatorial.

A ^{1}HCOSY spectrum was recorded at -60°C to fully assign the two conformations. However, because of the number of different protons within these conformers, the exact chemical shifts can only be approximated, as there is great deal of overlapping of resonances.

(**2-ax**). The ^{1}H NMR spectrum of this conformer consists of seven different proton resonances. H-1e is readily identified as an unresolved quintet and from the ^{1}HCOSY H-2e and H-2a were easily identified from their couplings to H-1e. From the ^{1}HCOSY plot, H-3e and H-3a were assigned from their couplings to H-2e and H-2a. However, because of the large overlapping of resonances in the ^{1}H NMR of the two conformers it is only possible to estimate the exact chemical shifts of H-4e and H-4a.

(**2-eq**). This conformer was assigned in the same way as **2-ax**, this time using a ^{1}HCOSY to identify all the protons, starting with H-1a, which exists as a triplet of triplets.

Ax-ax and eq-eq trans-1, 4-dicyanocyclohexane (3-ax-ax/ 3-eq-eq)

The 1,4-dicyanocyclohexane was found to exist in the trans form, with the CN groups occupying either 1,4-di-equatorial positions or 1,4-di-axial positions. This was confirmed by determining the melting point of the compound, which was found to be 140-141°C. Literature data[22] stated that the melting point of the trans compound was 139-140°C. This could be further confirmed by the fact that the trans conformer has three distinct signals at room temperature and each conformer has three distinct signals at low temperature. The cis conformer has three separate signals at room temperature but the single low energy conformer has six signals at low temperature. Therefore we are able to distinguish between the cis and trans conformers at low temperature.

The ^1H spectrum (**fig.4.3**) for both the (axial-axial/equatorial-equatorial) trans-dicyano conformers was recorded at ca. -60°C. The -60°C spectrum was assigned by recording spectra every 20°C and following the coalescence of the peaks and finally the emergence of the individual conformers at -60°C. By examining the ratio of the integrals between H-1e of the ax-ax and H-1a of the eq-eq conformers (ratio of 1.5/1.0) it was possible to determine the free energy difference between the two conformers. A value of $\Delta E = 0.17$ Kcal mol^{-1} was calculated with the di-equatorial conformer the most stable.

H-1e and H-1a were readily identified as an unresolved quintet and triplet of triplets respectively. Examining their integrals readily identifies H-2e and H-2a for both conformers. It was found that H-2e and H-2a for the di-axial conformer gave an AB pattern.

We must note that for compounds **2** and **3** we recorded the spectra at –60°C. It was therefore of interest to determine whether the chemical shifts displayed an intrinsic temperature dependence. By measuring the spectra of compound **1** at various temperatures we could examine if there was any temperature dependence of the chemical shift. The results can be observed in table **4.3**. As we can see the only protons undergoing any significant change in chemical shift with varying temperature are H-1e ($\Delta\delta$ of 0.098ppm) and H-1a ($\Delta\delta$ of 0.074ppm) in compounds **1-cis** and **1-trs**. Because of this phenomenon the difference between the chemical shifts of these protons in the **1-cis** and **1-trs** conformations of this compound at -60°C and room temperature was used as a correctional factor for the α protons in compounds **2** and **3**.

Table 4.3. ^1H chemical shifts (δ) for cis and trans-4-t-butyl-cyclohexanecarbonitrile (**1-cis, 1-trs**) as a function of temperature.

^1H Number	**Cis**			**Trans**		
	R.T	**-20°C**	**-60°C**	**R.T**	**-20°C**	**-60°C**
1e	2.921	2.973	3.019	-----------	-----------	-----------
1a	-----------	-----------	-----------	2.314	2.347	2.388
2e	2.037	2.059	2.077	2.161	2.179	2.192
2a	1.516	1.520	1.528	1.529	1.535	1.550
3e	1.771	1.782	1.794	1.855	1.856	1.862
3a	1.367	1.341	1.324	0.981	0.985	0.990
4a	0.986	0.986	0.987	1.023	1.026	1.030

Figure 4.2. ^{1}H NMR spectrum of *cis* and trans-4-t-butylcyclohexanecarbonitrile (1-*cis*/1-trs).

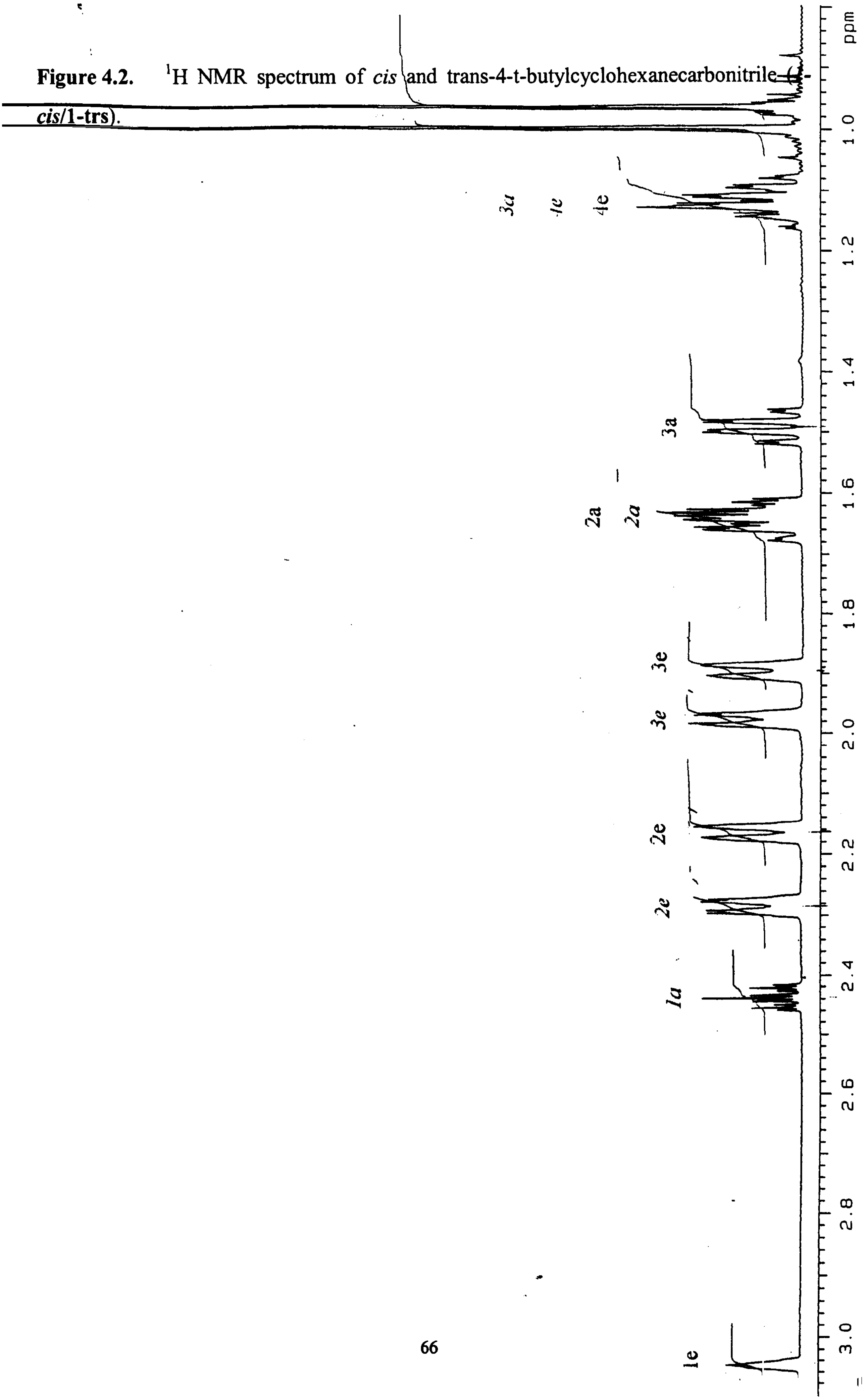
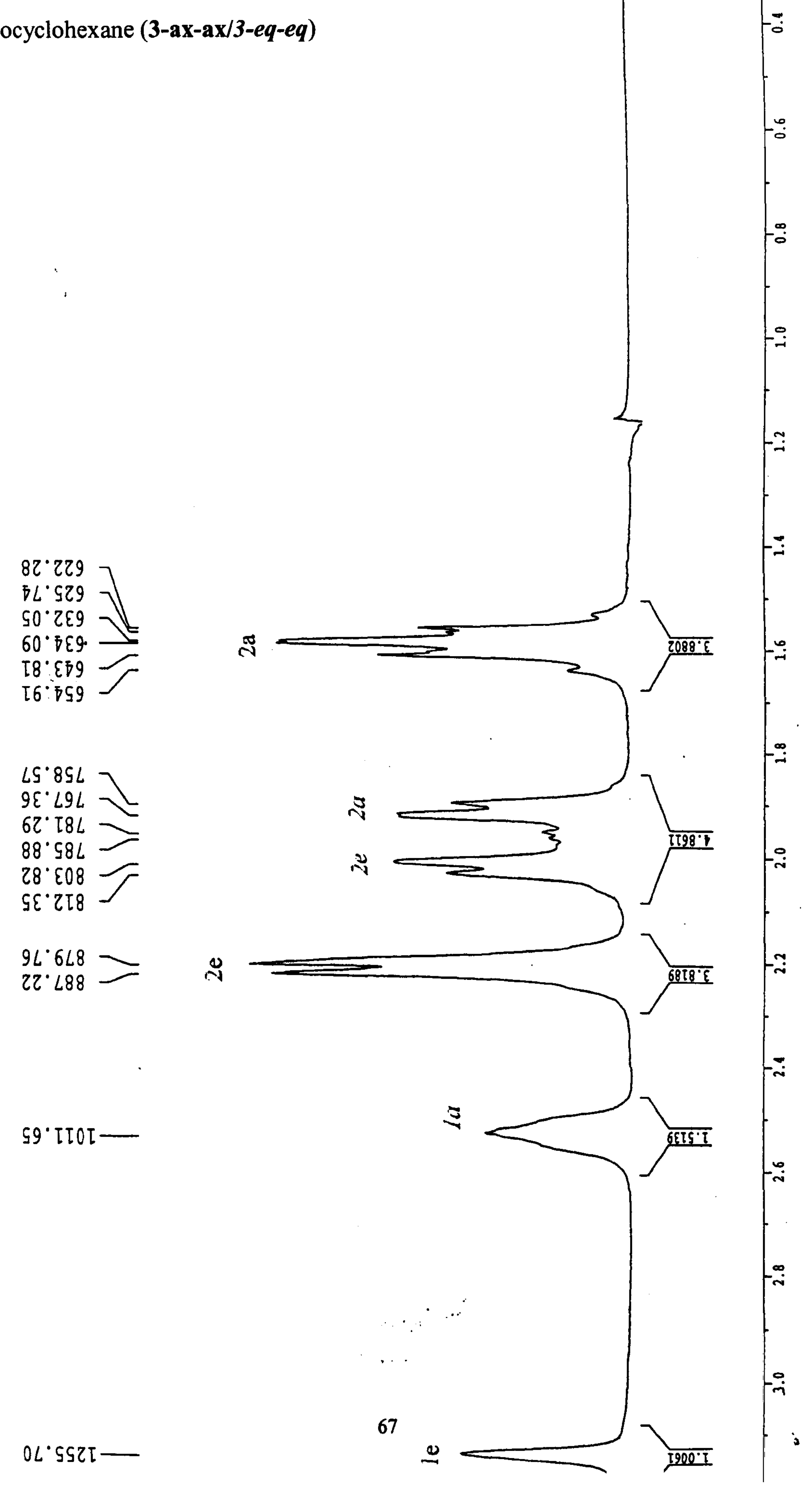


Figure 4.3. ^{1}H NMR spectrum at –60°C of Ax-ax and *eq-eq* trans-1, 4-dicyanocyclohexane (**3-ax-ax/*3-eq-eq***)



1-adamantanecarbonitrile (5)

The ^{1}H spectrum for this compound consists of two different proton resonances occurring at ca.2.0 and 1.7ppm. Since there is reliable literature[8], which documents all ^{1}H chemical shifts, the resonances were readily assigned.

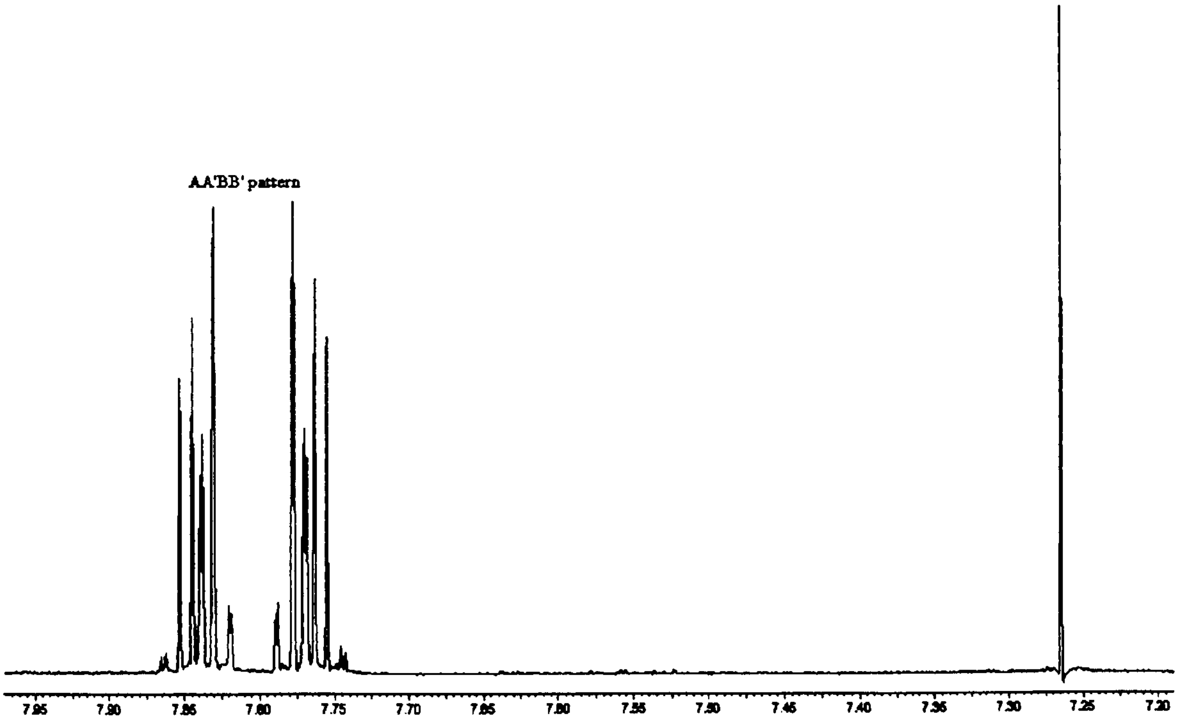
Benzonitrile (10)

The ^{1}H spectrum for benzonitrile consists of three different proton resonances. H-4 is easily identified as a single proton occuring at ca. 7.61ppm. H-2, 6 and H-3, 5 were assigned by simply referring to previous analysis[23]. Accurate chemical shifts for all the protons were acquired by use of the LAOCOON programme[24]. From this analysis it was found that H-2, 6 and H-3, 5 occur at ca.7.67 and 7.49ppm respectively.

o-dicyanobenzene (11)

The ^{1}H spectrum (**fig.4.4**) consists of an AA'BB' pattern occurring between ca.7.85 and 7.78ppm. Accurate chemical shifts were obtained for these protons by use of the LAOCOON programme. H-3, 6 were assumed to occur at lower field than H-4, 5.

Figure 4.4. ^{1}H NMR spectrum of ortho-dicyanobenzene (**11**).



m-dicyanobenzene (12)

The ^1H spectrum for m-dicyanobenzene consists of three different proton resonances. H-4/6 exists as a doublet of doublets at ca.7.9ppm. We observe H-5 occuring at ca.7.7ppm as a triplet of doublets. We can confirm this assignment by the fact that H-5 has a large coupling of ca.9.7Hz with H-4, 6, which H-2 does not display. Therefore we know that H-2 is the triplet of doublets occurring at ca.7.97ppm. This assignment can be confirmed by analysis of previously recorded ^1H NMR data found in the literature[23].

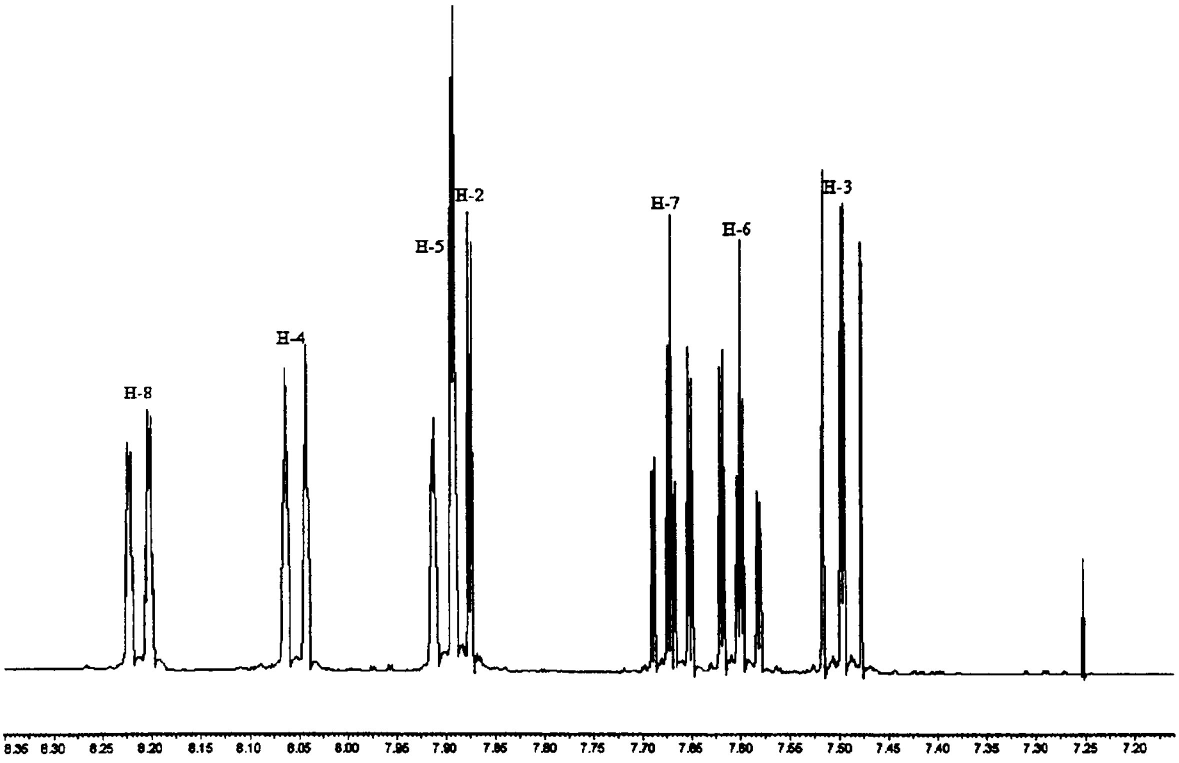
p-dicyanobenzene (13)

The ^1H spectrum for p-dicyanobenzene consists of one proton resonance occurring at ca. 7.87ppm.

1-Naphthalenecarbonitrile (14)

The ^1H spectrum for 1-naphthalenecarbonitrile (**fig.4.5**) consists of seven different proton resonances. An $^1H/^{13}C$ 2D HETCOR spectrum, along with the full ^{13}C literature assignment[20] gave a comprehensive assignment of this molecule. The assignment was further confirmed by recording a ^1HCOSY spectrum. From this plot we observe a coupling of H-2, occurring at ca.7.9ppm, with the resonances at ca.7.5ppm and 8.08ppm, thus assigning H-3 and H-4. H-8, occurring at ca.8.2ppm, has a large coupling to the resonance at ca.7.7ppm thus assigning H-7. This in turn has a large coupling to the resonance at ca.7.56ppm and a much smaller coupling to the resonance at ca. 7.90ppm, assigning H-6 and H-5 respectively.

Figure 4.5. ^{1}H NMR spectrum of 1-naphthalenecarbonitrile (**14**)



2-napthalenecarbonitrile (15)

The ^{1}H spectrum for 2-naphthalenecarbonitrile consists of seven overlapping proton resonances. From the ^{1}H spectrum we observe a singlet at ca.8.25ppm clearly assigned to H-1. However, the remaining resonances cannot be assigned by examination of the ^{1}H spectrum and a ^{1}HCOSY plot yields no useful information so we rely on a ^{1}H/^{13}C 2D HETCOR spectrum, along with the full ^{13}C literature assignment[20] to obtain a comprehensive assignment for this molecule.

9-anthracenecarbonitrile (16)

The ^{1}H spectrum for 9-anthracenecarbonitrile consists of five proton resonances. H-10 is immediately identified as a singlet with an integral half the size of all the other resonances, occurring at ca.8.7ppm. H-1 and H-4 can each be seen as a doublet of quartets occurring at ca. 8.45 and 8.05ppm respectively. H-2 and H-3 can each be seen as a doublet of doublets, occurring at ca.7.75 and 7.6ppm respectively. Although the ^{1}HCOSY yielded little information as to which resonances could be assigned to H-1 and H-4, H-2 and H-3, it was not necessary to record a ^{1}H/^{13}C 2D HETCOR spectrum as there was reliable literature[25], which documented all ^{1}H and ^{13}C chemical shifts in this molecule to which comparison could be made with our data and thus assign the proton and carbon chemical shifts.

Acrylonitrile (17)

The ^{1}H spectrum of acrylonitrile consists of three proton resonances. H_{trs} and H_{cis} can be easily identified as the resonances occurring at ca. 6.24and 6.10ppm respectively, both having a geminal coupling to each other of ca.0.8Hz. The resonance at 6.24ppm can be identified identified as H_{cis} by its large trans coupling to H_{gem} of 18Hz. H_{trs} displays a much smaller coupling to H_{gem} of 10Hz.

4.5. Results.

The data for the aromatic nitriles obtained here in dilute $CDCl_3$ solution is in excellent agreement with the earlier data obtained in CCl_4 solution[23b]. For example the ortho, meta and para proton shifts in benzonitrile in $CDCl_3$ and in CCl_4 solution (in parentheses) are 7.660 (7.631), 7.482 (7.452) and 7.559 (7.552). As found previously for the aromatic hydrocarbons[26] there is a small almost constant shift to higher δ values in $CDCl_3$ compared to CCl_4. Thus the proton SCS for the CN group obtained by earlier investigations may be used unchanged for the $CDCl_3$ solutions used here.

The experimental data set obtained in this study combined with the proton chemical shifts of the parent compounds given previously[26, 27] allow the ^1H chemical shifts and carbonitrile substituent chemical shifts (CN-SCS) to be determined in these compounds. The ^1H chemical shifts and CN-SCS have also been calculated using the CHARGE model. Using the calculated proton chemical shifts of the parent compounds and subtracting these from the calculated proton chemical shifts of the cyano molecules gave the calculated CN-SCS. The factors influencing the proton chemical shifts were also determined by a conducting a series of iterations on the experimental data.

The short-range effects of the CN group (3 bonds or less) will be explained in terms of electronic effects (α, β and γ-effects) in both aliphatic and unsaturated nitriles. There is also a possible γ-effect from the carbonitrile nitrogen, which is considered to be a polarisability effect. The long-range effects of the CN are small and extend over the whole system. These will be explained in terms of electric field, anisotropic and steric effects of the CN group if any exist at all. We therefore have to determine the steric coefficient, $a_S^{C\equiv N}$, magnetic anisotropy, $\Delta\chi^{C\equiv N}$ and γ-effects that exist for aliphatic and unsaturated nitriles.

Iterations were carried out on five unknowns, the steric term, anisotropy term, the nitrogen polarisability and the γ-effect coefficients **A** and **B**. These iterations were conducted using the anisotropy and steric term together, the anisotropy alone, the steric term alone and and with no anisotropic or steric term. The nitrogen atom was considered to be of a sufficient distance from the protons within the system so as to have no noticeable steric interaction with them. Iterations were carried out on a dataset made up of 93 proton chemical shifts to determine the best-fit values of all the unknown parameters using a non-linear mean squares programme (CHAP8[11]).

The anisotropy of the CN bond χ^{CN} was taken from the centre of the CN bond and the steric effect of the CN group from the sp carbon of the CN group. All iterations performed yielded no enhancement of the calculated chemical shifts than those calculations performed with no anisotropic or steric term. The major influence on the long-range proton chemical shifts was the electric field effect. The short-range γ-effects were found to significantly enhance the calculated chemical shifts in both aliphatic and unsaturated nitriles (see later).

a) Aliphatic nitriles.

The CN-SCS of compounds **1-cis/1-trs, 2-ax/2-eq** and **4-ex/4-en** can be seen in **tables 4.8** and **4.9.** The CN-SCS of the cyclohexane derivatives is of great interest. We may observe from the table that generally we have an excellent agreement of observed vs. calculated CN-SCS. We may see that all the protons in compounds **1-cis/1-trs, 2-ax/2-eq** and **4-ex/4-en** are deshielded.

By examination of **tables 4.8** and **4.9** we note that the SCS on the β protons (H.C.CN) is more or less constant at ca.1.24ppm. We also observe that the γ–effect of the CN group has little orientational dependence. For example, the 2-eq and 2-ax protons in **1-cis** and **1-trs** and the 3-exo and 3-endo protons in **4-ex** and **4-en** all give an SCS of ca.0.41ppm.

In trans-4-tert-butyl-cyclohexanecarbonitrile and equatorial-cyclohexanecarbonitrile we observe that the CN-SCS decreases with increasing distance of the proton from the CN, with the equatorial protons generally displaying a greater CN-SCS than the axial protons. However for the cis-4-t-butyl-cyclohexanecarbonitrile and axial-cyclohexanecarbonitrile we see that the CN-SCS for H-3a is very large. A similar effect can be observed in the CN-SCS of the 7s proton in 2-exonorbornanecarbonitrile and the 6x proton in 2-endonorbornanecarbonitrile. In this instance the C-CN bond is parallel to the C-H bond of H-3a and a large deshielding effect on the proton exists, resulting in a larger downfield shift.

As we have discussed, the CN-SCS may be due to the CN anisotropy or electric field. However, the CN-SCS is deshielding for H-3a and H-3e in **1-trs** and H-7s in **4-en.** This would not be the case if the SCS were primarily due to the anisotropy of the CN group.

Table 4.4. Observed vs. calculated ^1H chemical shifts (δ) for trans/cis 4-t-butylcyclohexanecarbonitrile (**1-cis/1-trs**), axial/equatorial-cyclohexanecarbonitrile (**2-ax/2-eq**) and ax-ax and eq-eq trans-1, 4-dicyanocyclohexane (**3ax/ax, 3-eq/eq**).

^1H no.	**1-cis**		**1-trs**		**2-ax[a]**		**2-eq[a]**		**3-ax-ax[a]**		**3-eq-eq[a]**	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
1e	2.921	2.926	------	------	2.960	2.860	------	------	3.040	3.011	------	------
1a	------	------	2.314	2.447	------	------	2.386	2.337	------	------	2.445	2.442
2e	2.037	2.092	2.161	2.083	2.000	2.056	2.076	2.055	2.009	2.230	2.208	2.217
2a	1.516	1.656	1.529	1.655	1.538	1.591	1.521	1.589	1.918	2.016	1.582	1.701
3e	1.771	1.852	1.855	1.833	1.700	1.815	1.760	1.801	------	------	------	------
3a	1.367	1.305	0.981	0.983	1.500	1.588	1.220	1.282	------	------	------	------
4e	------	------	------	------	1.700	1.788	1.700	1.752	------	------	------	------
4a	0.986	1.077	1.023	1.094	1.200	1.252	1.220	1.274	------	------	------	------

[a]In $CDCl_3$ at -60°C.

Table 4.5. Observed vs. calculated ^1H chemical shifts (δ) for 2-exo/endo-norbornanecarbonitrile (**4ex/4-en**).

^1H Number	**4-ex[a]**		**4-en[a]**	
	Observed	**Calculated**	**Observed**	**Calculated**
1	2.599	2.584	2.520	2.555
2x	-----------------	-----------------	2.694	2.914
2n	2.360	2.518	-----------------	-----------------
3x	1.810	1.957	1.982	1.938
3n	1.697	1.631	1.458	1.588
4	2.397	2.350	2.348	2.329
5x	1.528	1.649	1.619	1.654
5n	1.171	1.272	1.356	1.376
6x	1.570	1.625	1.505	1.644
6n	1.225	1.361	1.814	1.785
7s	1.621	1.495	1.308	1.238
7a	1.381	1.303	1.417	1.277

[a]Ref[8]

Table 4.6. Observed vs. calculated ^{1}H chemical shifts (δ) for 1-adamantanecarbonitrile (**5**).

^{1}H Number	5^{a}	
	Observed	Calculated
2	2.042	1.963
3	2.042	2.064
4e	1.735	1.760
4a	1.735	1.749

^{a}Ref^{8}

Table 4.7. Observed vs. calculated ^{1}H chemical shifts (δ) for acetonitrile (**6**), propionitrile (**7**), iso-butyronitrile (**8**) and trimethylacetonitrile (**9**).

^{1}H No.	6		7		8		9	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
1	2.030	1.995	2.470	2.433	2.780	2.849	--------	--------
2	--------	--------	1.300	1.222	1.350	1.294	1.400	1.357

The data collected in **tables 4.4-4.7** provides a thorough examination of the application of the CHARGE model and the theories about the influence of the carbonitrile group on proton chemical shifts. The majority of the compounds listed are of fixed geometry with the exception of the 1,4-dicyanocyclohexane and cyclohexane carbonitrile. Fortunately these compounds exist as two conformers, which can be easily 'frozen out' and examined. All the cyclohexane derivatives exist in the chair form, with the norbornane occupying its own unique geometry. The minimum energy geometry's were obtained by conducting molecular mechanics calculations using GAUSSIAN 94W.

By examining the data in the above tables we observe a good agreement between observed and calculated ^{1}H chemical shifts. There is generally a good agreement between the observed versus calculated shifts and the calculated shifts are generally within 0.1ppm of the observed values. There are however still large errors for some of the protons in the norbornane systems. Protons 2n and 2x in both **7-ex** and **7-en** compounds were larger than the observed values. This could possibly be due to either solvent interactions or inaccurate geometry's. Use of GAUSSIAN 94W at the MP2/6-31G* level geometry may rectify this problem.

In the CHARGE model the γ-effects are modelled on a semi-empirical basis and we therefore look at the γ-effect as being due to electronic effects as seen previously (see chapter two). For these calculations the electronic γ-effects of the carbonitrile carbon displays an orientational dependence with respect to the protons in question.

The value of the coefficients **A** and **B** were determined from the observed chemical shifts to give **eqtn.4.2** for the carbonitrile carbon GSEF:

$$\mathrm{GSEF} = 0.090 - 0.056\cos\theta \qquad \textbf{(Eqtn.4.2)}$$

The orientational dependence of the γ CN effect (H.C.C.CN) is very small. The γ-effect from the nitrogen atom, found to be dependent on the nitrogen polarisability, was determined to be 0.47. As stated previously, the long-range effects of the CN were found to consist of electric field effect only. The final parameterisation of the CN group in aliphatics therefore included electronic effects for protons 2 or 3 bonds away from the CN and electric field effects operating on all protons within the molecule.

Table 4.8. Observed vs. calculated CN-SCS for cis/trans-4-t-butylcyclohexanecarbonitrile (**1-cis/1-trs**) and axial/equatorial-cyclohexanecarbonitrile (**2-ax/2-eq**).

Molecule	^{1}H Number	Observed	Calculated
	1a	1.281	1.237
	2e	0.287	0.408
1-cis	2a	0.326	0.422
	3e	0.021	0.170
	3a	0.457	0.413
	4a	0.046	0.073
	1e	1.234	1.201
	2e	0.411	0.413
1-trs	2a	0.339	0.413
	3e	0.105	0.153
	3a	0.071	0.108
	4a	0.083	0.090
	1e	1.280	1.144
	2e	0.320	0.411
	2a	0.348	0.389
2-ax	3e	0.020	0.164
	3a	0.310	0.377
	4e	0.020	0.139
	4a	0.010	0.056
	1a	1.196	1.144
	2e	0.396	0.410
	2a	0.331	0.393
2-eq	3e	0.080	0.152
	3a	0.030	0.086
	4e	0.020	0.106
	4a	0.030	0.079

Table 4.9. Observed vs. calculated CN-SCS for 2-exo/endo-norbornanecarbonitrile (**4ex**/**4-en**).

Molecule	^{1}H Number	Observed	Calculated
	1	0.41	0.43
	2n	1.20	1.34
	3x	0.34	0.43
	3n	0.54	0.46
	4	0.21	0.20
4-ex	5x	0.06	0.12
	5n	0.01	0.10
	6x	0.10	0.10
	6n	0.07	0.19
	7a	0.20	0.13
	7s	0.44	0.32
	1	0.33	0.40
	2x	1.22	1.38
	3x	0.51	0.41
	3n	0.30	0.41
	4	0.16	0.18
4-en	5x	0.15	0.12
	5n	0.20	0.20
	6x	0.04	0.11
	6n	0.65	0.61
	7a	0.24	0.11
	7s	0.13	0.07

Table 4.10. Observed vs. calculated CN-SCS with the C-CN/C-H electric field and C/H-steric contributions for cis/trans-4-t-butylcyclohexanecarbonitrile (**1-cis/1-trs**) and axial/equatorial-cyclohexanecarbonitrile (**2-ax/2-eq**).

Compound	^{1}H Number	Obs.	Calc.	C-CN Electric field	C-H Electric field	C-Steric	H-Steric
1-cis	2e	0.287	0.408	0.344	-0.001	0.000	0.000
	2a	0.326	0.422	0.262	-0.001	0.000	0.000
	3e	0.021	0.170	0.153	0.005	0.000	0.012
	3a	0.457	0.413	0.270	0.040	0.000	0.103
	4a	0.046	0.073	0.070	-0.005	0.000	0.009
1-trs	2e	0.411	0.413	0.332	-0.001	0.000	0.000
	2a	0.339	0.413	0.336	-0.001	0.000	0.000
	3e	0.105	0.153	0.120	0.027	0.000	0.006
	3a	0.071	0.108	0.079	0.017	0.000	0.012
	4a	0.083	0.090	0.061	0.022	0.000	0.007
2-ax	2e	0.320	0.411	0.335	0.000	0.000	-0.001
	2a	0.348	0.389	0.257	-0.003	0.002	-0.012
	3e	0.020	0.164	0.148	0.006	0.000	0.011
	3a	0.310	0.377	0.245	0.039	0.000	0.096
	4e	0.020	0.139	0.125	0.010	0.002	0.005
	4a	0.010	0.056	0.076	-0.005	0.001	-0.010
2-eq	2e	0.396	0.410	0.330	0.000	0.000	-0.001
	2a	0.331	0.393	0.332	-0.002	0.002	-0.013
	3e	0.080	0.152	0.120	0.028	0.000	0.004
	3a	0.003	0.086	0.079	0.016	0.002	-0.004
	4e	0.020	0.106	0.087	0.018	0.000	0.001
	4a	0.003	0.079	0.070	0.021	0.001	-0.008

It is of great interest to consider the actual magnitudes of the contributions to the CN-SCS. **Table 4.10** gives the observed vs. calculated CN-SCS for the cyclic carbonitriles along with the calculated electric field and steric contributions.

We can see from the data presented in **table 4.10** the magnitudes of the various contributions to the CN-SCS. The table illustrates that the C-CN electric field, C-H electric field and C/H-steric effects are important in determining the CN-SCS. We may observe that the contributions due to C/H-steric interactions are effectively zero. Exceptions are the H-steric effects for the H-3a protons in compounds where the CN is in an axial position. We have a significant contribution to the overall CN-SCS for these protons because they are in close proximity to the CN and there is a likely steric interaction between them.

It can be noted from **table 4.10** that the major contribution to the CN-SCS is the CN electric field effect. For protons that are 3 bonds or more away from the CN we can observe that the sum of all the components contributing to the CN-SCS gives us approximately the total CN-SCS that has been calculated. However, for the H-2e/H-2a protons in all the compounds investigated in we observe that the components do not add up to give us our calculated value of CN-SCS. This is due to the electronic effects, i.e. γ-effects, which are calculated separately and which affect protons that are 3 bonds or less away from the CN.

The results for the non-cyclic molecules provide a rigorous test for the CHARGE model. Zurcher found he could not accurately predict the α-proton chemical shifts in compounds (**6**), (7) and (**8**). We may observe from **table 4.7** the calculated chemical shift for the α protons are excellent.

Zurcher calculated the chemical shifts of the α-protons in acetonitrile, propionitrile, n-butyro and iso-butyrocarbonitrile and norbornenecarbonitrile by using the electric field effects of the CN only in his calculations. He calculated a value of 1.19ppm for all the compounds and concluded that other effects besides the linear electric field effect must be operating to different degrees in each compound. He suggested the different steric environments of particular protons and their interactions with the solvent molecules. We must also note that Zurcher did not use calculations that were specific for short-range protons and long-range protons. His calculation for the effect of the electric field on proton chemical shifts was a general term for all protons over the whole molecule, and thus no α, β or γ-effects were calculated.

In this investigation we have included a γ-effect from the carbonitrile nitrogen, which is obviously vital in calculating the chemical shifts of α protons. This as we now know is dependent on the polarisability of the terminal nitrogen and it was found that if we optimised the polarisability of the nitrogen we arrived at excellent agreement of observed and calculated chemical shifts for the α protons. We do not however optimise the polarisibility of the cyano carbon (Csp) because this carbon is to be used in acetylenes (chapter five), and its polarisibility in this functional group may be different to that of nitriles.

b) *Aromatic nitriles.*

The data for the unsaturated nitriles consists of 31 data points, which can be seen in **tables 4.11-4.13**. The CN-SCS can be seen for compounds **10-17** can be seen in **table 4.14**. We observe from **table 4.14** that we have good agreement between the observed and calculated CN-SCS and we observe that all the protons in the aromatic nitriles are deshielded. Even though the observed and calculated shifts do not correspond completely accurately we observe a good correlation.

There is no general trend to the magnitude of the CN-SCS throughout the molecules in the aromatics and we must therefore take into consideration the π-electron effects in the olefinic hydrogen atoms on the chemical shifts of the protons. We also observe a ring current in the aromatic systems, which contributes very significantly to the overall proton chemical shift, although it is a constant value and does not depend on whether the molecule has any substituents present. We also observe field and resonance effects due to the CN, which are delocalised over the molecule and these will be discussed in chapter six.

Table 4.11. Observed vs. calculated ^1H chemical shifts (δ) for benzonitrile (**10**), o, m and p- dicyanobenzene (**11,12,13**).

^1H Number	10		11		12		13	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
2	7.660	7.662	--------	--------	7.971	7.995	7.806	7.866
3	7.482	7.558	7.850	7.876	--------	--------	7.806	7.866
4	7.615	7.579	7.782	7.788	7.916	7.898	--------	--------
5	7.482	7.558	7.782	7.788	7.671	7.777	7.806	7.866
6	7.660	7.662	7.850	7.876	7.916	7.898	7.806	7.866

Table 4.12. Observed vs. calculated ^1H chemical shifts (δ) for 1 and 2-naphthalenecarbonitrile (**14**, **15**) and 9-anthracenecarbonitrile (**16**).

^1H Number	**14**		**15**		**16**	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
1	----------	----------	8.245	8.224	8.431	8.349
2	7.900	7.866	----------	----------	7.728	7.724
3	7.512	7.716	7.611	7.745	7.596	7.638
4	8.069	8.119	7.925	8.020	8.089	8.134
5	7.916	7.931	7.908	7.895	----------	----------
6	7.612	7.552	7.663	7.553	----------	----------
7	7.685	7.616	7.610	7.534	----------	----------
8	8.226	8.161	7.907	7.937	----------	----------
10	----------	----------	----------	----------	8.691	8.839

Table 4.13. Observed vs. calculated ^1H chemical shifts (δ) for acrylonitrile (**17**).

^1H Number	**17**	
	Observed	**Calculated**
H_{trs}	6.100	6.089
H_{cis}	6.240	6.052
H_{gem}	5.660	5.672

Table 4.14. CN-SCS for aromatic nitriles (**10-16**) and acrylonitrile (**17**).

Molecule	^{1}H Number	Experimental	Calculated
Benzonitrile	2,6	0.319	0.347
	3,5	0.141	0.213
	4	0.274	0.239
o-dicyanobenzene	3,6	0.509	0.525
	4,5	0.441	0.428
m-dicyanobenzene	2	0.630	0.663
	4,6	0.575	0.553
	5	0.330	0.411
p-dicyanobenzene	2,3,5,6	0.465	0.512
1-Naphthalene carbonitrile	2	0.423	0.404
	3	0.035	0.228
	4	0.225	0.283
	5	0.072	0.099
	6	0.135	0.071
	7	0.208	0.131
	8	0.382	0.304
2-Naphthalene carbonitrile	1	0.401	0.416
	3	0.134	0.286
	4	0.081	0.183
	5	0.064	0.066
	6	0.186	0.073
	7	0.133	0.055
	8	0.063	0.106
9-Anthracene carbonitrile	1	0.422	0.416
	2	0.261	0.226
	3	0.129	0.146
	4	0.080	0.235
	10	0.260	0.549
Acrylonitrile	H_{trs}	0.695	0.570
	H_{cis}	0.835	0.664
	H_{gem}	0.255	0.346

The data provided in **tables 4.11-4.13** provides us with a thorough examination of the application of the CHARGE model and about the influence of the CN group on aromatic protons chemical shifts. Like the aliphatic compounds, the compounds listed above are of fixed rigid geometry. All the minimum energy geometry's for use in CHARGE were obtained from GAUSSIAN 94W in the same manner as the cyclic and aliphatic nitriles. The geometry's were calculated at the MP2/6-31G* level.

The observed versus calculated proton chemical shifts are given in **tables 4.11-4.13**. There is a good agreement between the observed and calculated shifts and they are generally within 0.10ppm of each other. However, we do notice some discrepancies with some of the protons. H-3 in 1-naphthalenecarbonitrile and H-10 in 9-anthracenecarbonitrile are 0.204 and 0.148ppm higher than the observed chemical shifts. This is an interesting anomaly and there is no general explanation for it.

If we examine the observed CN-SCS for the meta proton in benzonitrile we see that it is 0.141ppm compared to 0.035ppm for 1-naphthalenecarbonitrile. We would expect them to be similar in magnitude and we see that in the calculated CN-SCS values from the CHARGE model for these protons. We may therefore conclude that the CN-SCS operates to different magnitudes in naphthalene and benzene. In acrylonitrile we also observe that the calculated chemical shift is 0.188ppm lower than the observed value.

As in aliphatic nitriles, the short-range effects of the CN group consist of electronic effects. A γ-effect was calculated for aromatics. For these calculations the γ-effect of the nitrile carbon displays an orientational dependence with respect to the protons in question.

The value of the coefficients A and B can be seen below in **eqtn.4.3**.

$$\mathrm{GSEF} = -0.132 + 0.076\cos\theta \qquad \textbf{(Eqtn.4.3)}$$

Again, the orientational dependence of the γ CN effect (H.C.C.CN) is very small. The nitrogen polarisability is the same value as that obtained for the aliphatic nitriles.

For the long range aromatic nitrile proton chemical shifts the electric field effects are the major influence. Therefore, the final parameterisation of the nitrile group in aromatics included electronic effects for protons 2 or 3 bonds away and electric field effects operating on all protons within the molecule.

The results for the aromatic nitriles provide us with a rigorous test for the CHARGE model. Along with the parameterisation of the CN contribution we also need the model to accurately calculate the contribution to the proton chemical shifts of the aromatic ring current and the π-electron density in the aromatic protons. This has been done by parameterisation of the model for these two factors on the parent aromatic molecules. With this done we see realistically calculated proton chemical shifts for the aromatic nitriles.

It is again of interest to consider the individual contributions to the CN-SCS. **Table 4.15** gives the observed versus calculated CN-SCS for selected molecules, along with the electric field, ring current and π-shift contributions.

Table 4.15. Calculated and observed CN-SCS (δ) with C-CN, C-H electric field, ring current and π-shift contributions for benzonitrile (**10**) and 1/2-naphthalenecarbonitrile (**14** and **15**).

Compound	1H Number	Observed	Calculated	C-CN Electric field	C-H Electric field	Ring Current	π-shift
10	2,6	0.319	0.347	0.370	0.000	0.000	0.116
	3,5	0.141	0.213	0.127	0.046	0.000	0.044
	4	0.274	0.239	0.096	0.036	0.000	0.107
14	2	0.423	0.404	0.375	0.000	0.000	0.169
	3	0.035	0.228	0.126	0.046	0.000	0.059
	4	0.225	0.283	0.096	0.035	0.000	0.154
	5	0.072	0.099	0.058	0.014	0.000	0.028
	6	0.135	0.071	0.054	0.010	0.000	0.008
	7	0.208	0.131	0.089	0.012	0.000	0.032
	8	0.382	0.304	0.333	0.074	0.000	0.001
15	1	0.401	0.416	0.376	0.000	0.000	0.180
	3	0.134	0.286	0.367	0.000	0.000	0.059
	4	0.081	0.183	0.127	0.046	0.000	0.014
	5	0.064	0.066	0.040	0.013	0.000	0.012
	6	0.186	0.073	0.035	0.000	0.000	0.037
	7	0.133	0.055	0.039	0.000	0.000	0.015
	8	0.063	0.106	0.050	0.021	0.000	0.037

From the data above we observe that the C-CN electric field and π-shift contributions are very important in determining the CN-SCS for all the protons in an aromatic system. We can see that the C-CN electric field is larger for protons in closer proximity to the CN. We can also observe the large deshielding effect it has on H-8 in compound **14**, which is parallel to the C-CN bond.

We can also observe that the ring current makes no contribution to the CN-SCS. For mono or disubstituted benzenes we observe that the ring current is calculated from the parent molecule, i.e. all protons in benzene are equivalent so the ring current is a constant for all protons in the benzonitrile. In the naphthalene and anthracene we have different ring currents for the chemically unequivalent protons. However this ring current remains constant regardless of any substituents, which may be added to the aromatic system. In contrast, if we look at the π-shift we see that the magnitude of the contribution is dependent on the position of the proton with respect to the CN group. The magnitude of this contribution is dependent on the magnitude of field and resonance effects operating in the molecule.

To explain the proton chemical shift in these aromatic molecules, we have to consider various effects and the nature of the substituent, i.e., its effect on the electron distribution throughout the aromatic system. This topic will be explored in detail in chapter six.

4.6. Conclusions.

The proton chemical shifts of the carbonitrile compounds are composed of 95 proton chemical shifts spanning a range of ca.0.70 to 9.00ppm and are predicted with an rms error of 0.087ppm. We may conclude that the CN-SCS over more than three bonds is determined by linear electric field effects only, without the need to include any steric or anisotropic effects of the CN. The short-range protons (<3bonds) require the inclusion of a γ-effect from both the carbon and nitrogen of the CN substituent and these contributions are used to calculate the chemical shifts β and α protons respectively. The γ-effect of the carbonitrile carbon atom is found to have an orientational dependence, whereas the γ-effect of the nitrogen is found to be dependant on the polarisability of the nitrogen.

4.7. References.

1. S.Patai and Z.Rappoport (eds), *The Chemistry of Triple-bonded Functional Groups,* J.Wiley & Sons, Chichester, 1983.
2. A.A.Bothner-By and J.A.Pople, *Ann.Rev.Phys.Chem.*, 1965, **16**, 43.
3. J.W.ApSimon, H.Bieirbeck and D.K.Todd, *Can.J.Chem.*, 1972, **50**, 2351.
4. H.M.McConnell, *J.Chem.Phys.*, 1957, **27**, 226.
5. A.D.Cross and I.T.Harrison, *J.Am.Chem.Soc.*, 1963, **85**, 3223.
6. G.S.Reddy and J.H.Goldstein, *J.Chem.Phys.*, 1963, **39**, 12, 3509.
7. R.F.Zurcher, *Prog.Nuclear.Mag.Res.Spec*, 1967, **2**, 205.
8. R.J.Abraham and J.Fisher, *Mag.Res.Chem.*, 1986, **24**, 451.
9. C.J.Puchert and J.Behnke, *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, Aldrich Chemical Company Inc. Milwaukee, USA, 1993.
10. A.L.McClellan, *Tables of Experimental Dipole Moments,* vols 1-3, Rahara Enterprises, Ca., 1989.
11. S.S.Kuo, *Computer Applications of Numerical Methods,* ch. 8, Addison-Wesley, London, 1972.
12. Gaussian 94, Gaussian Inc., Pittsburgh PA, 1994.
    M.J.Frisch, G.W.Trucks, M.Head-Gordon, P.M.W.Gill, M.W.Wong, J.B.Foresman, B.G.Johnson, H.B.Schlegel, M.A.Robb, E.S.Replogle, R.Gomperts, J.L.Andres, K. Raghavachari, J.S.Binkley, C.Gonzalez, R.L.Martin, D.J.Fox, D.J.Defrees, J.Baker, J.J.P.Stewart and J.A.Pople.
13. N.L.Allinger and W.Szkrybalo, *J.Org.Chem.*, 1962, **27**, 4601.
14. Aldrich Chem. Co., Eastman Kodak Co., Rochester, USA.
15. Lancaster Synthesis Ltd., Eastgate, White Lund, Morecambe, Lancs., LA3 3DY.
16. GlaxoWellcome R&D, Gunnelswood Rd., Stevenage, Herts., SG1 2NY.
17. Bruker UXNMR version 010892, Bruker AM, Silbersteifen, D-7512 Germany.
18. Varian Associates, Palo Alta, Ca, USA.
19. PC Model Version 7.0., Serena Software, Box 3076, Bloomington, IN, USA.
20. W.F.Bailey and A.Cioffi, *Magn.Reson.Chem.*, 1987, **25**, 181.
21. E.L.Eliel and S.H.Wilen, *Stereochemistry of Organic Compounds*, J.Wiley, NY, 1994.

22. H.Süess and M.Hesse, *Helv.Chem.Acta.*, 1979, **62**, 1040.

23.a) H.Burgess and J.A.Donnelly, *Tetrahedron*, 1991, **47**, 1, 111-120

b) S.Castellano and C.Sun, *J.Am.Chem.Soc.*, 1966, **88**, 4741.

c) K.Hayamizu and O.Yamamoto, *J.Mol.Spect.*, 1968, **28**, 89 and 1969, **29**, 183.

24. S.Castellano and A.A.Bothner-By, *J.Chem.Phys.*, 1964, **41**, 3863.

25. M.Nir, R.E.Hoffman, I.O.Shapiro and M.Rabinovitz, *J.Chem.Soc.Perkin Trans.2*, 1995, 1433.

26. R.J.Abraham, M.Canton, M.Reid and L.Griffiths, *J.Chem.Soc., Perkin Trans.2*, 2000, **4**, 803.

27. Part 12, R.J.Abraham, L.Griffiths and M.A.Warne, *J.Chem.Soc.Perkin Trans.2*, 1998, **31**, 1751.

Chapter Five.

Proton chemical shifts in acetylenes and the electronic, anisotropic, steric and π-electron effects of the acetylene group.

Chapter Five. Proton chemical shifts in acetylenes and the electronic, anisotropic, steric and π-electron effects of the acetylene group.

5.1. Introduction.

Many investigations into the influence of the acetylene group on proton chemical shifts have been undertaken over many years. However, there have not been many investigations into the prediction of ^1H chemical shifts in acetylene compounds, though many calculations to determine the anisotropy of the C≡C bond have been well documented.

Pople and Bothner-By[1] first proposed that the magnetic anisotropy of the acetylene group could explain the high-field shift of the acetylene proton compared to that of ethylene. An independent electron molecular orbital theory for the diamagnetic behaviour of electrons in the presence of an applied magnetic field was developed. The molecular orbitals are written as linear combinations of gauge invariant atomic orbitals, with the dependence of the coefficients on the magnetic field being studied by perturbation theory. Although no examination of this theory will be given here, a brief description may be given. By making a systematic set of approximations, a general expression was derived for the diamagnetic susceptibility tensor as a sum of atomic contributions. The theory provides a simple basis for interpretation of the Pascal constants used for empirical calculations of diamagnetic susceptibilities of large molecules and is able to make a number of predictions about diamagnetic anisotropies. A value for the magnetic anisotropy ($\Delta\chi^{C\equiv C}$) of -19.4×10^{-6} cm^3 mol^{-1} was calculated.

Other researchers have also determined other values of $\Delta\chi^{C\equiv C}$. Early work on determining the acetylene group anisotropy was undertaken by Reddy and Goldstein[2]. They determined the C≡C anisotropy by use of a simple method based upon the linear relationship found to exist between proton shifts and the corresponding ^{13}C-^1H coupling constants in series of compounds where the anisotropic effects were negligible or reasonably constant. Anisotropic effects of other groups could then be estimated by use of these linear plots. The anisotropy of the C≡C group was obtained by observations on a range of acetylenic compounds and a linear relationship between chemical shifts and ^{13}C-^1H coupling constants for acetylenic protons was established.

Work has been undertaken into examining the relationship between the magnetic anisotropy of a functional group on the chemical shifts in NMR. Zeil and Buchert[3] examined the proton chemical shifts in a variety of ethyl- and iso-propylacetylenes, haloacetylenes and nitriles. They assumed that the proton chemical shifts were linearly dependent on the electronegativity of the substituent and had shifts arising from the diamagnetic anisotropy of the substituents, which were constant from one compound to another. By taking appropriate differences to eliminate the effect of electronegativity they calculated $\Delta\chi^{C\equiv C}$ in all compounds investigated to be approximately $-36\text{x}10^{-6}$ cm^3 mol^{-1}.

Shoemaker and Flygare[4] have also investigated the anisotropy of the acetylene group. The method they used involved examining the high-field Zeeman effect in the microwave spectra of methylacetylene and its isotopic species. By examining the second-order Zeeman effects, values of the anisotropy of the magnetic susceptibility were determined (see later).

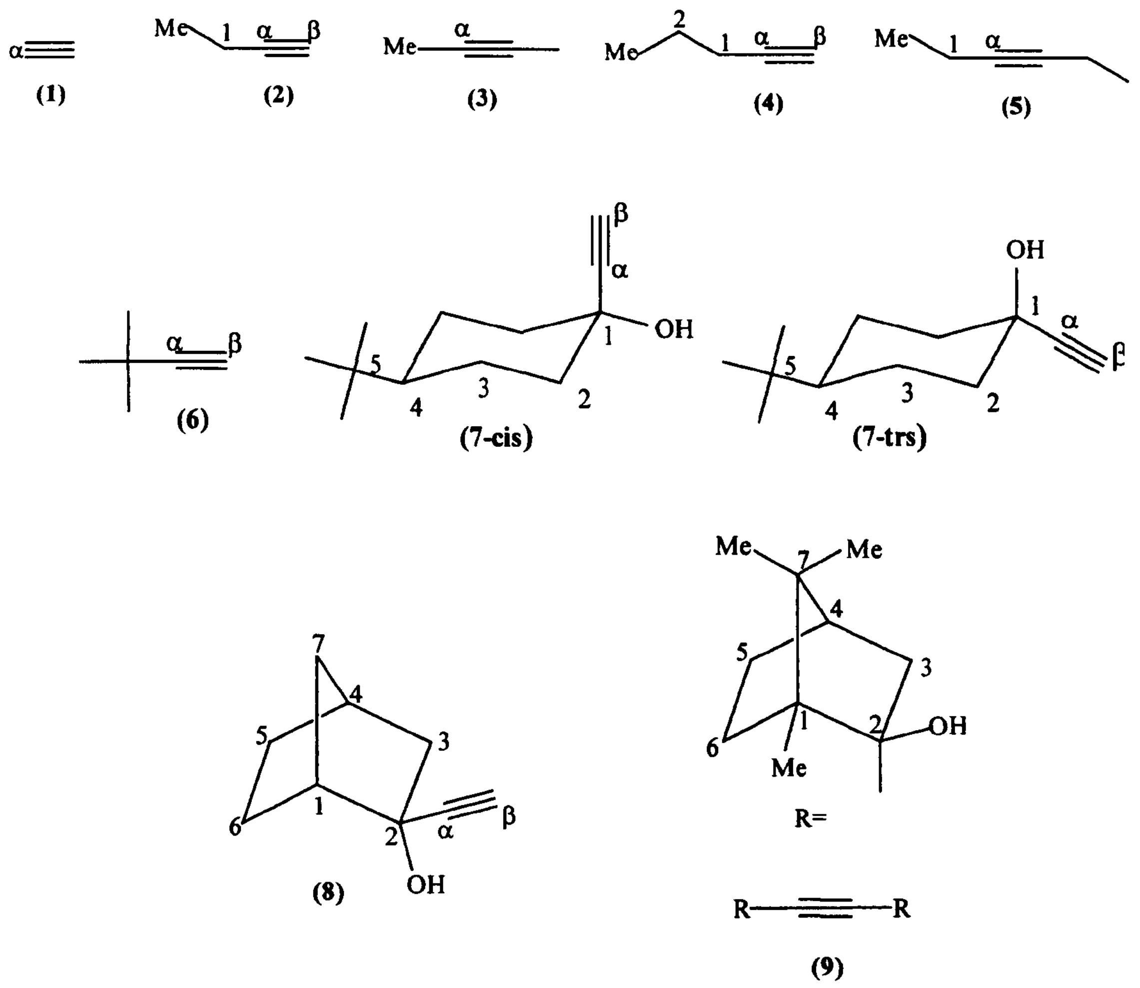
Mallory and Baker[5] noted the existence of regions of deshielding alongside carbon-carbon triple bonds. They confirmed experimentally that regions of magnetic deshielding exist by the observation of low-field proton NMR chemical shifts in various aromatic compounds. The theory is that due to the negative sign of the magnetic anisotropy, $\Delta\chi^{C\equiv C}$, the acetylenic proton of a terminal acetylene that is tumbling in an external magnetic field finds itself in regions of magnetic shielding. As a consequence, regions of magnetic deshielding are predicted to exist alongside the C≡C bond. They found that the protons in question within the molecules they were studying were deshielded and that the magnitude of deshielding fell off with distance, although no reliable estimation of distance dependence of the deshielding effect was obtained. They did however conclude that the deshielding effect of the C≡C bond fell off approximately as $1/r^3$. Compounds investigated were 4-ethynylphenanthrene, 5-ethynyl-1, 4-dimethylnaphthalene and 5-ethynyl-1, 4-diethylnaphthalene.

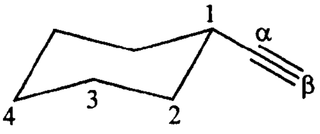
No attempt has yet been made to calculate the proton chemical shifts of acetylenic compounds and in this is the subject of this chapter. Here is presented the complete ^1H NMR assignment of a range of conformationally rigid aliphatic and aromatic acetylene molecules. The aliphatic acetylenes investigated are acetylene (**1**), ethynylcylohexane (**10-eq/10-ax**) at -60°C, 1,4-di-(adamantyl-(1))-diacetylene (**11**), cis/trans-1-ethynyl-4-t-butylcyclohexan-1-ol (**7-cis/7-trs**), 2-ethynyl-endo-norbornan-2-ol (**8**) and 1,7,7,1',7',7'-

hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol (**9**). ^{1}H NMR chemical shifts of but-1-yne (**2**), but-2-yne (**3**), pent-1-yne (**4**), hex-3-yne (**5**), tert-butylacetylene (**6**) were obtained from the Aldrich catalogue[6]· The aromatic acetylenes included in this investigation are phenylacetylene (**12**), o-ethynyltoluene (**13**), 2-ethynylnaphthalene (**16**) and 9-ethynylanthracene (**17**). Also included are p-ethynyltoluene (**14**) and 2-ethynylpropenepropene (**18**)[6]. The data for 1-ethynylnaphthalene (**15**) was obtained from ref.7. Compounds **1-17** can be seen in **figure 5.1.**

The data above provides a sufficient amount of data for a quantitative analysis of acetylene SCS using the CHARGE model. We shall use this model to perform a quantitative analysis of C≡C-SCS and show that both short and long-range chemical shifts are influenced by the magnetic anisotropy and steric of the acetylene group.

Figure 5.1. Molecules studied and their nomenclature.





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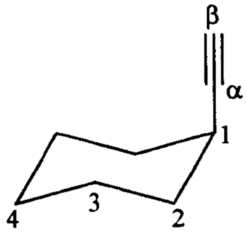

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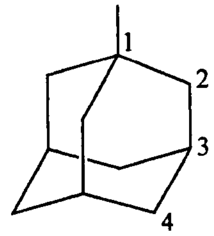

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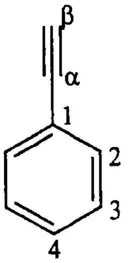

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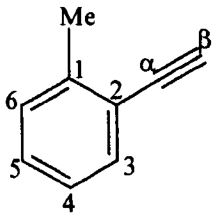

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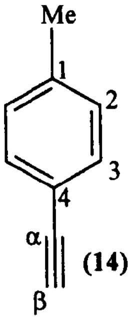

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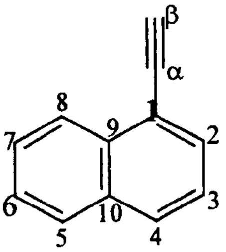

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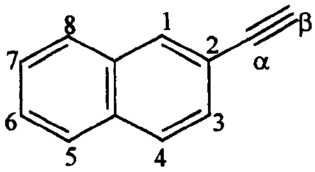

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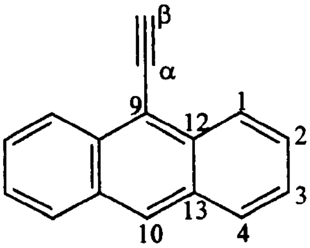

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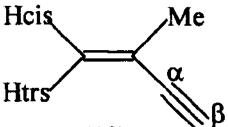

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5.2. Application of the theory to the acetylene group.

A detailed account of the CHARGE theory can be seen previously (chapter two).

The acetylene group has in principle steric, electric field and anisotropic effects on protons more than three bonds away plus for aromatics an effect on the π electron densities. All these have to be incorporated into the model. The major electric field of the acetylene group is due to the ≡C.H bond as the C≡C bond is non-polar. The C≡C group has cylindrical symmetry and **eqtn.2.9** (chapter two) may be used to calculate the contribution of the anisotropy to the proton chemical shifts. There is also a possible steric effect of the acetylene group on the neighbouring protons and a possible steric effect of the near aliphatic protons on the acetylene proton. These are both given by **eqtn.2.7** (chapter two) with different steric coefficients a_S which may be of either sign. Thus the unknowns to be obtained are $\Delta\chi$, the molar anisotropy of the C≡C bond and the steric coefficient, a_S.

For protons of three bonds or less from the C≡C group it is necessary to determine the orientational dependence of the γ proton chemical shift w.r.t the α acetylene carbon. This is simulated by a γ substituent effect (GSEF) from the acetylene carbon (H.C.C.C≡) following **eqtn.2.5** (chapter two), in which the coefficients **A** and **B** may differ for the C≡C group in aromatic vs. saturated compounds. Also in CHARGE the β-effect is given by a simple general equation, which was sufficient for the calculation of charge densities but not sufficiently accurate to reproduce the proton chemical shifts. Thus the β-effect from the acetylene carbon atom (H.C.C≡) needs to be obtained. As there is no orientation dependence in this case only one coefficient, **C** is required.

There is also a possible γ-effect on the acetylene proton from the aliphatic and aromatic carbon atoms attached to the C≡C bond (C.C≡.C.H, =C.C≡.C.H). These display no orientational dependence so we have coefficients **D** and **E** to determine.

For the aromatic acetylenes it is necessary to obtain the appropriate values of the factors h_r and k_{rs}, which are the Huckel integrals for the C≡C group (**eqtn.2.20**, chapter two). The π-electron densities and dipole moments from *ab initio* calculations are very dependent on the basis set used. The 3-21G basis set gave the best agreement with the observed dipole moments (**table 5.1**) and the π-electron densities from this basis set were used to parameterise the Huckel calculations. The CN group contains an sp hybridised carbon atom and the parameters for this group have already been derived as seen in chapter four. Thus the value of h_r (Csp) and k_{rs} (Csp^2-Csp) calculated for nitriles was implemented for the acetylene calculations as the Huckel integrals for Csp operates for both of these functional groups. The value of h_r of 0.12 for C(sp) and k_{rs} of 1.05 (Csp^2-Csp) used for nitriles were used for the acetylene calculations. A value of k_{rs} of 1.60 (Csp-Csp) gave π-electron densities for the aromatic acetylenes in reasonable agreement with those from the ab initio calculations.

The accuracy of the π-electron densities calculated in the CHARGE model can be examined by calculating the dipole moments of various acetylene molecules. The calculated vs. observed (in parenthesis) dipole moments[7] (in debye) of propyne, But-1-yne, tert-butylacetylene, phenylacetylene, para-ethynyltoluene are 0.50(0.75), 0.50 (0.81), 0.52 (0.66), 0.36 (0.72) and 1.26 (1.02) and the reasonably good agreement provides support for the π-electron density calculations. The electron densities (total and π) and dipole moments calculated for phenylacetylene and methylacetylene by CHARGE and GAUSSIAN94 are given in **tables 5.1** and **5.2**.

Table 5.1. Total and π (in parenthesis) charges (me), and dipole moments for phenylacetylene (**12**).

Atom	**Method**				
	STO-3G	**3-21G**	**6-31G**	**CHARGE**	**Observed**
C_β	-125 (-5.1)	-363 (-14.2)	-531 (-16.5)	-83(-10.6)	
C_α	-40 (-0.9)	-60 (-0.1)	-155 (2.4)	-46 (-0.7)	
C_1	2 (-21.0)	-44 (-32.6)	-156 (-26.7)	-24 (-0.6)	
C_2	-54 (8.6)	-215 (18.5)	-148 (14.9)	-57 (4.5)	
C_3	-63 (0.3)	-230 (-1.3)	-209 (0.1)	-72 (-0.3)	
C_4	-59 (9.1)	-237 (12.6)	-188 (10.8)	-73 (3.6)	
μ (D)	*0.50*	*0.65*	*0.64*	*0.36*	*0.72*

Table 5.2. Total and π (in parenthesis) charges (me), and dipole moments for methylacetylene.

Atom	Method				
	STO-3G	**3-21G**	**6-31G**	**CHARGE**	**Observed**
C_β	-136 (-21.7)	-419 (-22.0)	-488 (-24.7)	-106(-22.4)	
C_α	-37 (11.3)	-47 (12.2)	-29 (13.9)	-62 (22.4)	
μ (D)	*0.50*	*0.69*	*0.68*	*0.50*	*0.75*

Values of h_r for various atoms have been determined along with k_{rs} for X-Csp for a number of different substituents X, on a triple bond. The best-fit values of h_r for fluorine, chlorine, oxygen were obtained from π-electron densities and dipole moments obtained from GAUSSIAN94W calculations at the 3-21G level for a range of olefinic compounds[8]. These were left unchanged and the appropriate values of k_{rs} were determined. Values of 0.74 (Csp-F), 0.57 (Csp-Cl) and 1.00 (Csp-O) gave π electron densities in reasonable agreement with those calculated from GAUSSIAN94W. The corresponding (Csp-Csp_2) value for propynal was taken directly from phenylacetylene.

Again, the accuracy of the π-electron densities calculated in the CHARGE program can be examined by calculating the dipole moments of various acetylene molecules. The calculated vs. observed (in parenthesis) dipole moments of fluoroacetylene, chloroacetylene, propynal and methoxyacetylene are 0.79 (0.75), 0.74 (0.44), 2.56 (2.46), and 1.62 (1.93). Also, the ^1H chemical shift of the acetylene proton in fluoroacetylene, chloroacetylene and propynal (no literature data for methoxyacetylene) has been calculated. The calculated vs. observed (in parenthesis) proton chemical shifts are 1.33 (1.63), 1.95 (1.80) and 3.61 (3.47). The good agreement of the calculated vs. observed chemical shifts for these molecules is strong support for the above treatment.

5.3. Experimental.

Acetylene (**1**), cyclohexylacetylene (**10**), 1,4-di-(adamantyl-(1))-diacetylene(**11**) and phenylacetylene(**12**) were obtained commercially[9, 10, 11, 12]. Ortho-ethynyltoluene (**13**) and 2-Ethynylnaphthalene (**16**) were synthesised by double elimination of 1-(1,2-dibromo-ethyl)-2-methylbenzene and 1-(1-naphthyl)-1,2-dibromo-ethane[13]. 9-Ethynylanthracene (**17**) was synthesised by Sonogashira coupling[14] of 9-bromoanthracene and trimethylsilylyacetylene.

Cis/trans-1-ethynyl-4-t-butylcyclohexane-1-ol (**7-cis/7-trs**), 2-exo-ethynylnorbornan-2-ol (**8**) and 1,7,7,1',7',7'-hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol (**9**) were synthesised by the addition of ethynylmagnesiumbromide to the corresponding ketones in THF[15]. The conformations of these compounds were determined by x-ray crystallography[16] and lanthanide induced shift NMR experiments.

General procedure: ***Synthesis of 9-ethynylanthracene*** **(17)**

A de-aerated solution of 0.75g (2.92mmol) of 9-bromoanthracene and 0.443g (4.52mmol) of ethynyltrimethylsilane in anhydrous diethylamine (40ml) was treated with 0.041g(0.058mmol) of bis-(triphenylphosphine) palladiumdichloride and 0.003g of copper$^{(II)}$iodide. The mixture was allowed to react for 5 days under an argon atmosphere. The dark orange/brown solution was filtered, the filtrate concentrated and purified by column chromatography (alumina; n-hexane), giving anthracen-9-ylethynyl-trimethyl-silane as fine yellow/brown crystals (0.29g, 34.7%): mp 61-62°C; IR (nujol) 3300(C≡C-H), 3070(Ar-H), 2100(C≡C), 1250(Si-CH_3); MS *m/z* (rel.int.) 274 (M+, 1), 202 (10), 176 (78), 88 (79); NMR (400MHz, ^{1}H, $CDCl_3$) δ0.49(9H), δ7.50(2H), δ7.59(2H), δ8.00(2H), δ8.42(1H), δ8.56(2H).

0.20g (7.09mmol) of anthracen-9-ylethynyl-trimethyl-silane was directly converted into 9-ethynylanthracene by treatment with 0.04g of anhydrous K_2CO_3 in methanol (20ml) at room temperature for 5 hrs. The methanol was removed and the mixture worked up by extraction with dichloromethane (3x30ml), followed by washing with aqueous sodiumbicarbonate (2x20ml). The pure compound was obtained as yellow crystals (0.122g, 85.2%): mp 58-60°C; IR (nujol) 3300(C≡C-H), 3070(Ar-H), 2100(C≡C); MS *m/z* (rel.int.) 202(M+, 0.8), 176(56), 88(90).

General procedure: ***Synthesis of cis/trans-1-ethynyl-4-t-butylcyclohexan1-ol*** **(7)**

1.5g (0.097mol) of 4-t-butylcyclohexanone was dissolved in 20ml of THF and placed in a two necked round bottomed flask equipped with a reflux condenser. 3.78g (0.029mol) of ethynylmagnesiumbromide were then added slowly and the resulting orange/brown mixture refluxed with stirring for 4 hrs. Normal acidic work-up yielded the desired alcohols. The product was recrystallised from n-pentane in to give a pale yellow solid (1.07g, 61%): mp 96-98°C; IR (nujol) 3500(w, OH), 3210(w, C≡C-H), 2060(w, C≡C) cm^{-1}; MS *m/z* (rel.int.) 180(M+, 7), 137(9), 91(61), 57(100).

2-exo-ethynylnorbornan-2-ol **(8)**: white solid (0.79g, 64%); recrystallised form n-pentane; mp 42-44°C; IR (nujol) 3400(s, OH), 3320(s, C≡C-H), 2120(w, C≡C) cm^{-1}; MS *m/z* (rel.int.) 136(M+, 0.9), 107(44), 93(32), 67(100).

1,7,7,1',7',7'-hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol **(9)**: white solid (0.76g, 35%); recrystallised from n-pentane; mp 196-198°C; IR (nujol) 3330(m, OH), 2180(w, C≡C) cm^{-1}; MS *m/z* (rel.int.) 330(M+,0.1), 203(9), 159(7), 109(36), 95(100).

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX400 spectrometer operating at 400MHz for proton and 100.63MHz for carbon. The spectra for **7-trs/7-cis**, **8** and **9** were recorded on a Varian 750MHz spectrometer at GlaxoWellcome[16]. Here HMQC, HMBC and NOE experiments were conducted.

The spectra were generally recorded in 10mg cm^{-3} solutions (^{1}H) and ca.50mg cm^{-3} (^{13}C) with a probe temperature of ca.25°C in $CDCl_3$ and referenced to TMS unless indicated otherwise. Typical running conditions of the spectrometers were 128 transients, spectral width 3300Hz and 32k data points. This gave an acquisition time of 5s and zero-filled to 128k to give a digital resolution of 0.025Hz.

The 2D experiments were conducted using the Bruker AMX400 and Varian 750MHz machines using the standard Bruker COSY-DQF and HXCO and the standard Varian HMQC and GHMQC-DA pulse sequences[17, 18]. The geometry's of the compounds investigated were obtained using GAUSSIAN 94W at the RHF/6-31G* and MP2/6-31G* levels[19a] and later using GAUSSIAN98W[19b] at the DFT/B3LYP/6-31G** level. All calculations were carried out using a PC.

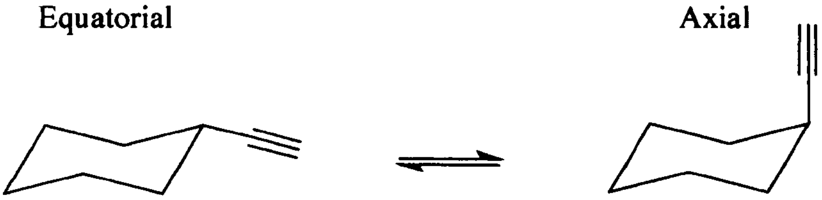
5.4. Spectral analysis.

The ^{1}H NMR assignments of all the compounds investigated are given in **tables 5.3, 5.4, 5.6, 5.7, 5.9, 5.10** and **5.12** together with the calculated proton chemical shifts.

The ^{1}H NMR data for but-1-yne (**2**), but-2-yne (**3**), pent-1-yne (**4**), hex-3-yne (**5**), t-butylacetylene (**6**), para-ethynyltoluene (**14**), and 2-ethynylpropene (**18**) were taken from ref.6 and from ref.13. for 1-ethynylnaphthalene (**15**).

Equatorial and axial ethynylcyclohexane (10-eq, 10-ax)

The ^{1}H and ^{13}C spectra of the separate conformers were obtained by recording the spectra at –60°C (**figs.5.2** and **5.3**). The integrals (n) taken for protons 1e and 1a were 1 and 6.2 respectively. By using **eqtn.5.1** we are able to determine that the equatorial conformer is the more favoured, with ΔG (eq-ax) = 0.77 KCal mol^{-1}.



$$n(eq)/n(ax) = e\text{-}(\Delta G/RT) \qquad \textbf{(Eqtn.5.1)}$$

Where:

n(ax) and n(eq) are the integral values of H-axial and H-equatorial

This value is in reasonable agreement with previous measurements of ΔG (eq-ax). Eliel[20] quotes 0.41-0.52 kcal mol^{-1}. Schneider and Hoppen[21] determined a value of ΔG for ethynylcyclohexane by dynamic ^{13}C NMR spectroscopy. They calculated a lower ΔG value of 0.52 Kcal mol^{-1} using 20% in $CFCl_3$ with 5%Me_4Si. Jensen and Bushweller[22] also calculated a ΔG value of 0.41 Kcal mol^{-1}. This was calculated by examining the integrals of protons in the low temperature ^{1}H NMR using 20% in CS_2 at 190-200K.

(**10-eq**). 2D ^{1}H COSY and ^{1}H/^{13}C HETCOR spectra were recorded at –60°C to fully assign the equatorial conformer. For **10-eq**, proton 1a is readily identified as a quintet. From correlations to H-1a, H-2e and 2a are readily assigned by examination of the ^{1}H COSY by way of their couplings to H-1a. Further examination of the ^{1}HCOSY and ^{1}H/^{13}C 2D HETCOR plots plus the integrals of the ^{1}H spectrum gave the assignments of the remaining protons.

(**10-ax**). For **10-ax** only protons 1e, 2e and 2a were assigned by examination of the ^{1}HCOSY, with H-1e occurring as a triplet of triplets. The remaining protons were hidden underneath the resonances of the protons in **10-eq** and could only be assigned by use of a ^{1}H/^{13}C 2D HETCOR plot.

Figure 5.2. Variable temperature ^{1}H NMR spectra for 1-ethynylcyclohexane (10-eq).

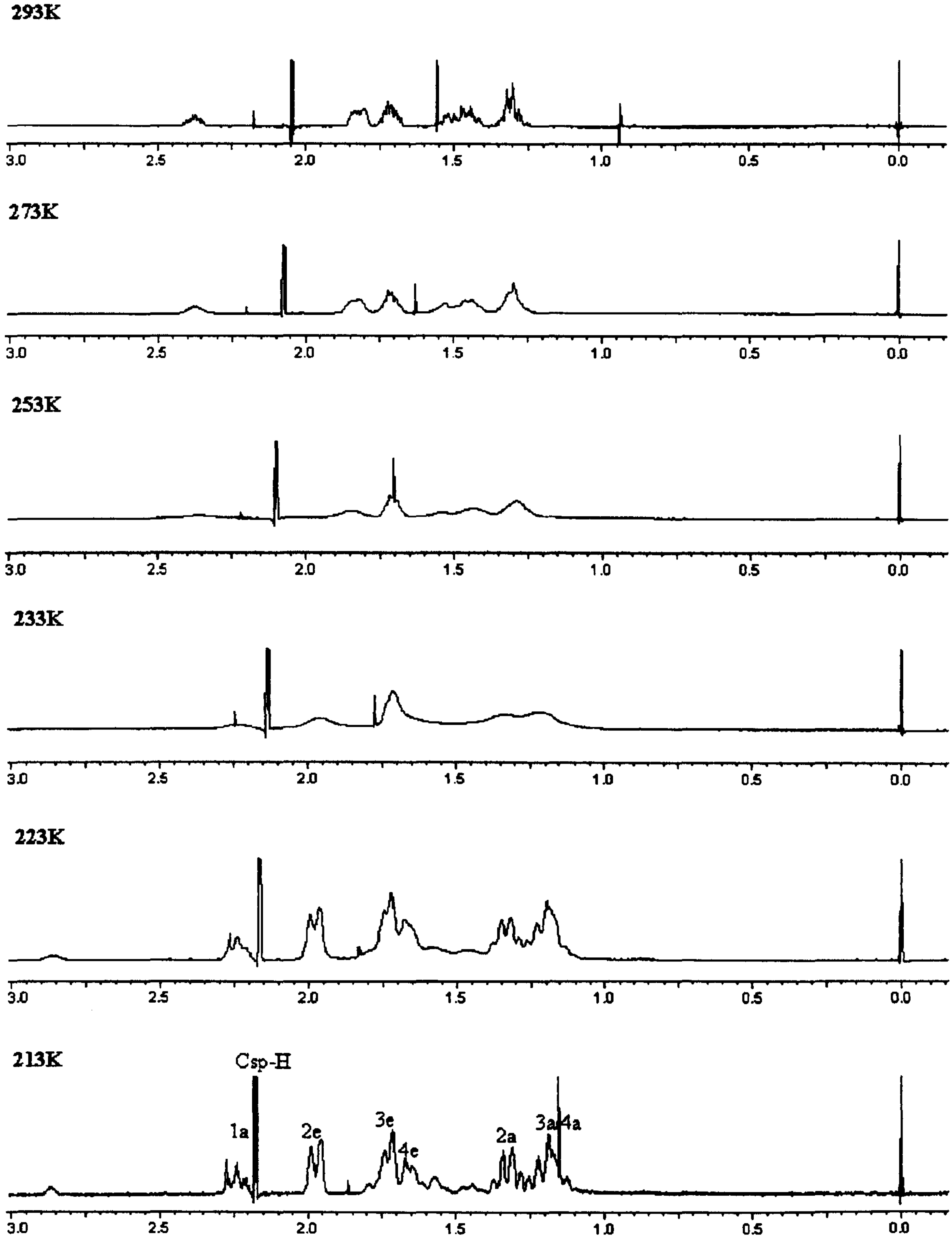
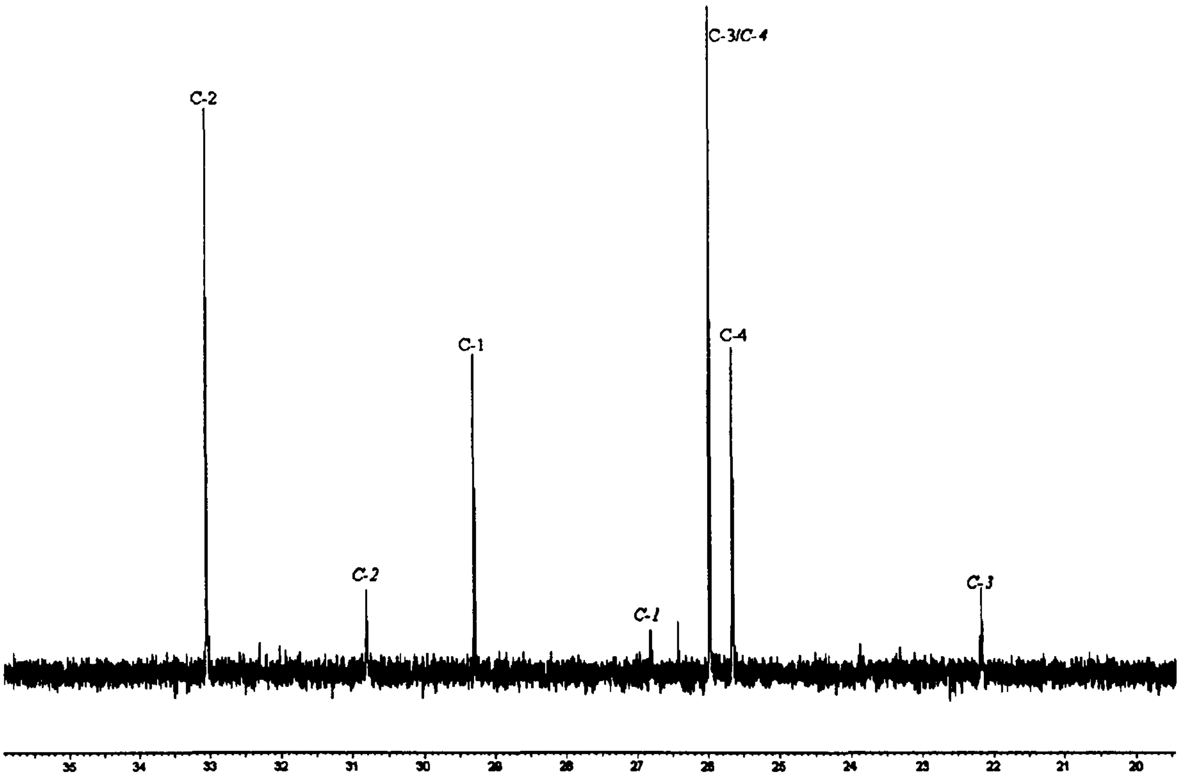


Figure 5.3. ^{13}C NMR spectra for 1-ethynylcyclohexane (10-eq/*10-ax*) at -60°C.



1,4-Di-(adamantyl-(1))-diacetylene (11)

The ^{1}H spectrum of **11** consists 4 different proton resonances and was readily assigned. By examining the integrals H-δ was easily identified at ca.1.94ppm. H-γ was identified as a doublet with a coupling of ca.4.5Hz to H-δ, occurring at ca.1.86ppm. H-e and H-a were seen as a single resonance at ca.1.67ppm.

Cis and trans-1-ethynyl-4-t-butylcyclohexan-1-ol (7-cis, 7-trs)

The ^{1}H, ^{13}C and 2-D spectra for these isomers were recorded at 750MHz. The spectra for the pure trans isomer were recorded, but the spectra for the cis isomer were recorded from a mixture of the cis and trans conformers. This was not a problem as the resonances were easily separated.

(7-cis). The ^{1}H NMR spectrum consists of five separate resonances including the methyl resonances. These were assigned by use of a ^{1}H COSY. H2e and H3e were easily distinguished as only H3e displayed a coupling to H4a. H3a and H2a were identified by examination of the splitting pattern of the resonances. This assignment was further confirmed by examination of a $^1H/^{13}C$ 2D HETCOR plot and the known ^{13}C spectral assignment[23].

(**7-trs**). The ^1H spectrum of this isomer again consists of five resonances and was readily assigned in the same way as **7-cis**.

A lanthanide induced shift experiment using $Yb(fod)_3$[‡] was conducted on the sample of the pure trans isomer to confirm that the configuration in **figure 5.1** was correct. $Yb(fod)_3$ is known to bind to the OH group and therefore downfield shifts in the ^1H spectrum would be expected to be observed on H2e and H2a, as they are in close proximity to the $Yb(fod)_3$. This was indeed observed and confirmed the characterisation of this isomer.

2-Ethynyl-endo-norbornan-2-ol (8)

The ^1H, ^{13}C, 2-D and NOE spectra for this compound were recorded at 750MHz. An x-ray crystal structure[16] of this compound (**fig.5.4**) was recorded to confirm its configuration at C-2, thus enabling an unambiguous assignment of the ^1H NMR.

The ^1H spectrum for this compound (**fig.5.5**) consists of 10 proton resonances. H-1 and H-4 were readily identifiable by examination of their splitting patterns, H-1 appearing as a doublet, H-4 as a triplet. The other proton groups were elucidated by examination of a $^1H/^{13}C$ 2D HETCOR plot plus known ^{13}C spectra[24]. By examination of the ^{1}HCOSY H-5x and H-6x were identified by their strong coupling to H-4 and H-1 respectively. H-3x was identified by its strong coupling to H-4 and H-5x. H-7s was identified by ^{1}HCOSY, HMBC and NOE experiments. H-7s displays a W-coupling to H-6n and H-5n and a strong 3-bond HMBC coupling is also observed to C-6 and C-5, which is much less intense in H-7-a. An NOE performed on H-3x (**fig.5.6**) also helped to elucidate H-7s.

With these assignments at our disposal it was possible to assign the geminal partners of H-3x, 5x, 6x and 7s by examination of a $^1H/^{13}C$ 2D HETCOR spectrum. The assignments of these protons were confirmed by ^{1}HCOSY, NOE and HMBC experiments.

[‡] The IUPAC name for fod is 6, 6, 7, 7, 8, 8, 8-heptafluoro-2, 2-dimethyl-3, 5-octanedionato.

Fig.5.4. X-ray structure of 2-ethynyl-endo-nobornan-2-ol (**8**).

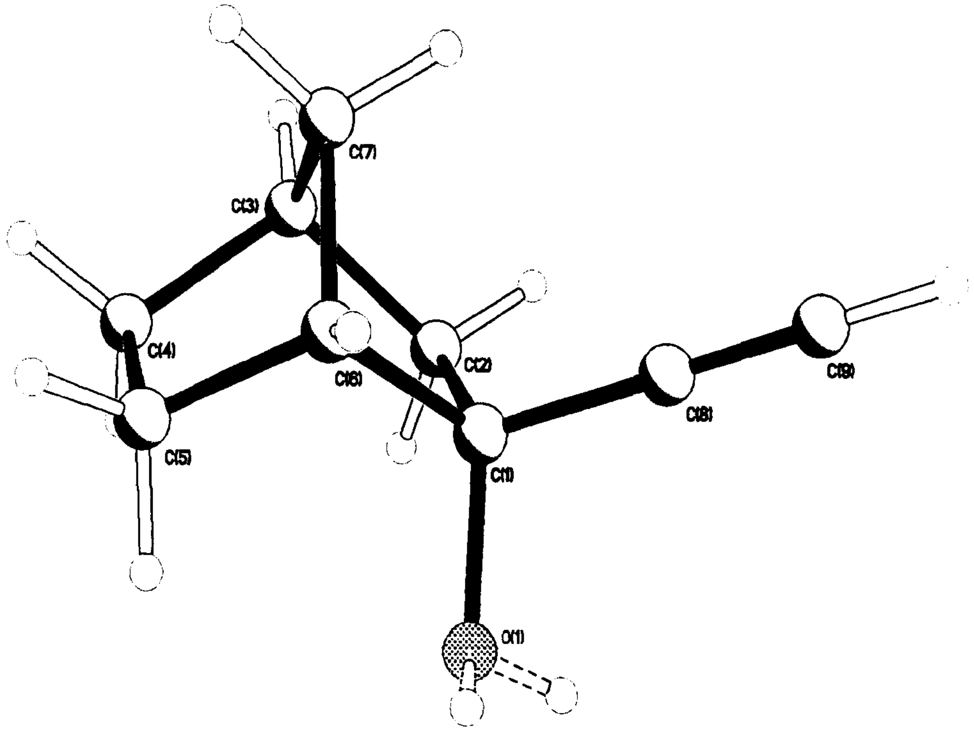


Figure 5.5. ^{1}H NMR spectrum of 2-Ethynyl-endo-norbornan-2-ol (**8**)

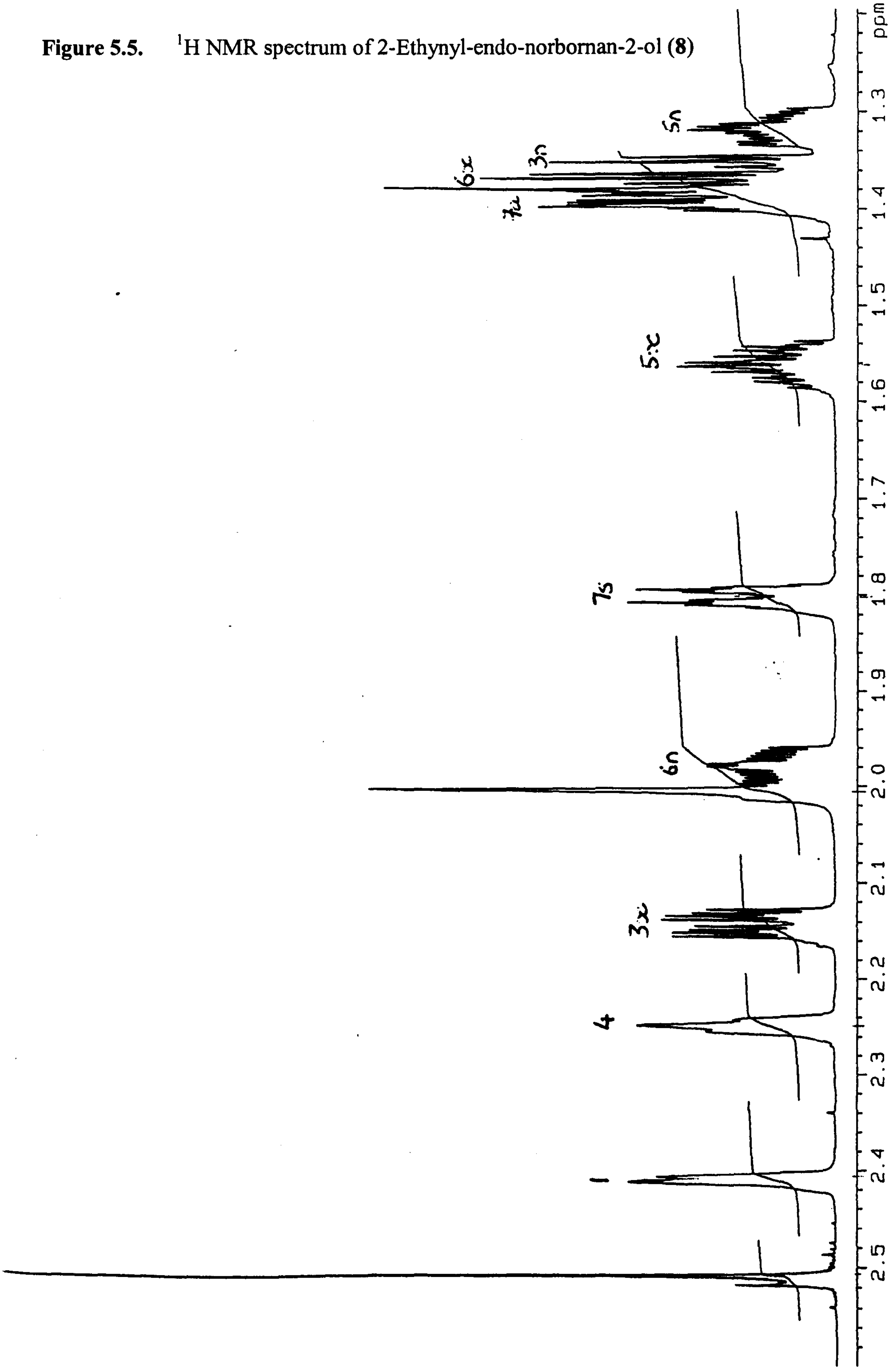
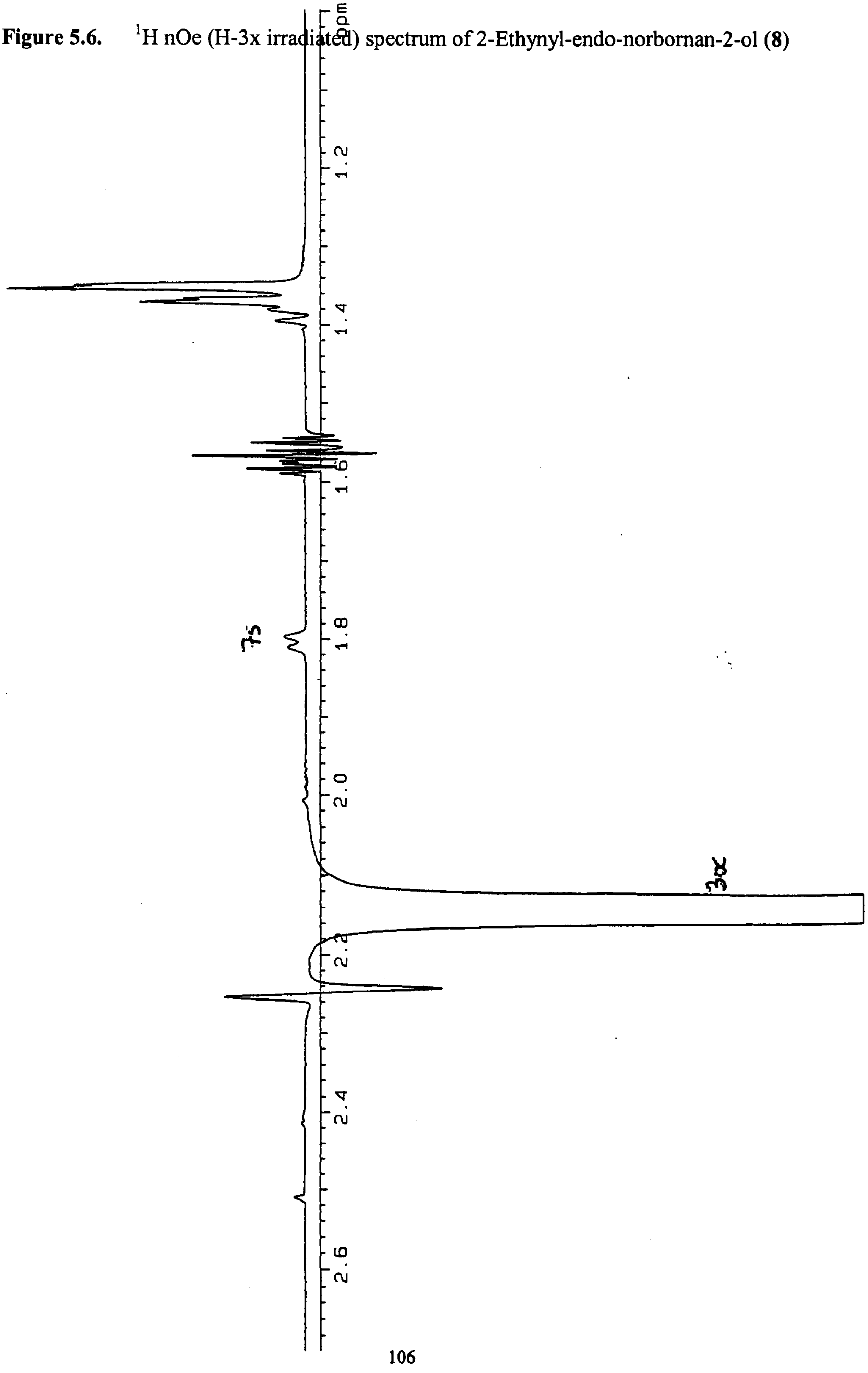


Figure 5.6. ^{1}H nOe (H-3x irradiated) spectrum of 2-Ethynyl-endo-norbornan-2-ol (**8**)



1,7,7,1',7',7'-hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol (9)

The ^{1}H, ^{13}C, 2-D and NOE spectra for this compound were recorded at 750MHz. An x-ray crystal structure[16] of this compound was recorded (**fig.5.7**) to confirm its configuration at C-2. The compound was found to exist as a dimer, as seen in the x-ray structure.

The ^{1}H spectrum of this compound (**fig.5.8**) consists of seven resonances including three methyl resonances. H-3x and H-3n were readily identified by examination of their splitting patterns, H-3x is a doublet of triplets and H-3n a doublet with a large coupling to H-3x. H-4 was easily identifiable by examination of the ^{1}HCOSY. Large couplings to H-3x and H-5x were observed giving the expected triplet. H-5x was identified from the ^{1}HCOSY as large couplings are seen to H-3x and H-4. H-5n was assigned by examination of a ^{1}H/^{13}C 2D HETCOR (**fig.5.9**) plot plus the known assignment of the ^{13}C spectra[24] and this was confirmed by NOE experiments conducted on H-5x and H-3n.

H-6x was assigned from the ^{1}HCOSY, with a large coupling observed to H-5x. HMBC spectra also reveal a large 3-bond coupling from H-6x to the 1-methyl carbon atom. H-6n was then assigned from the ^{1}H/^{13}C 2D HETCOR plot and confirmed by an NOE experiment on H-6x.

The methyl's in the 7a and 7s positions are easily assigned by NOE experiments. The 7a methyl gave NOE's to H-5x, H-6x and H-4 and the 7s methyl gave NOE's to H-3x, H-3n and H-4. The C-1 methyl is then immediately assigned.

Fig.5.7. 1,7,7,1',7',7'-hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol (**9**).

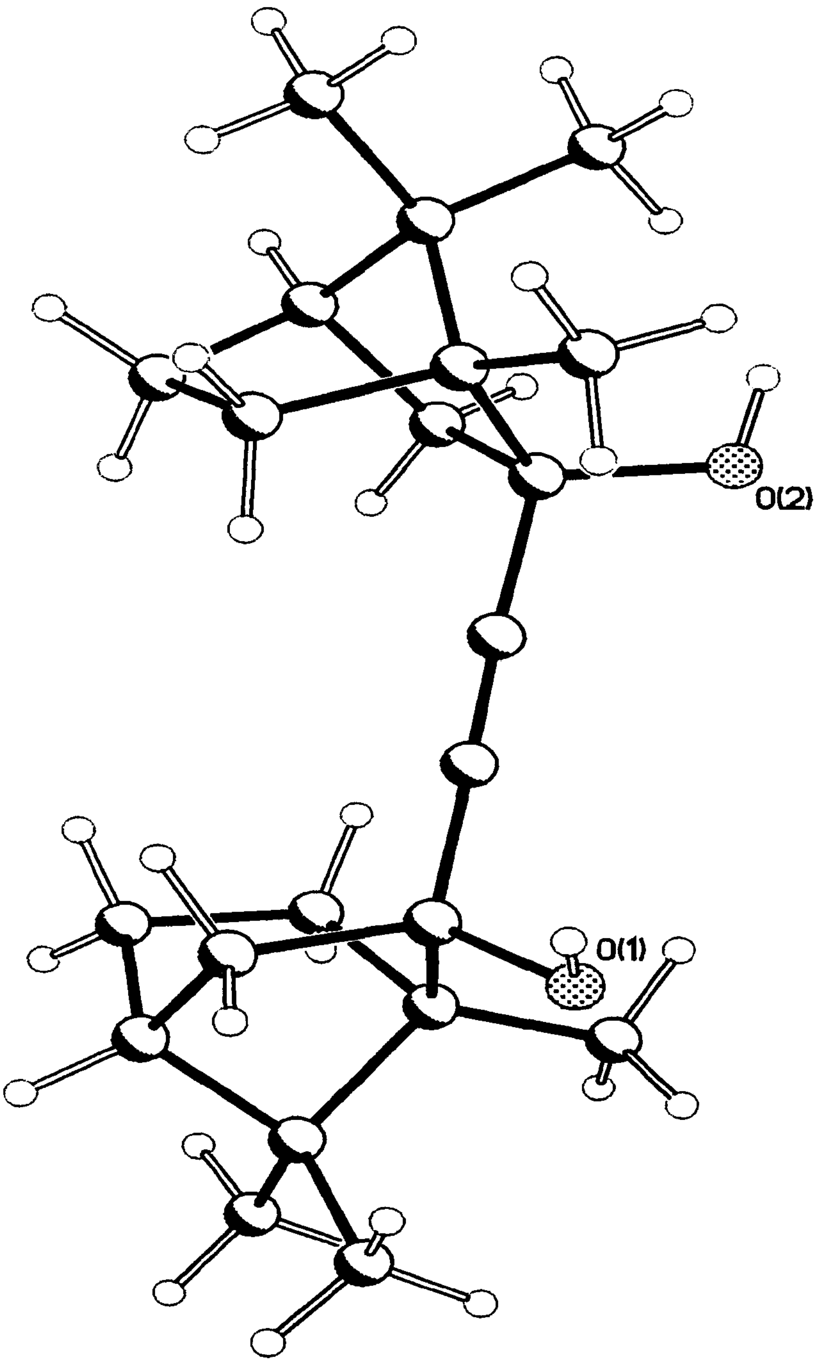
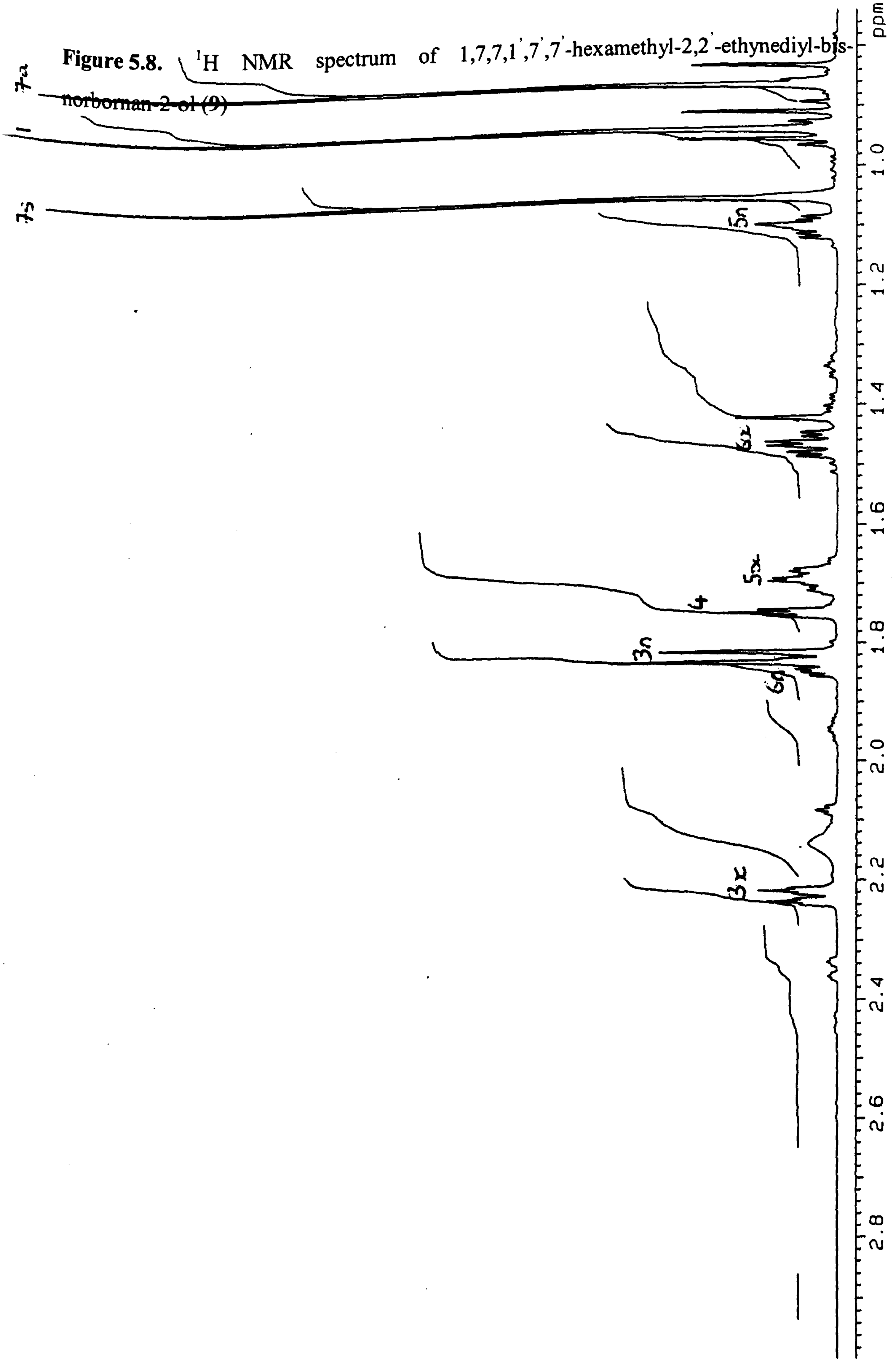


Figure 5.8. ^{1}H NMR spectrum of 1,7,7,1',7',7'-hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol (**9**)

Figure 5.8. ^1H NMR spectrum of 1,7,7,1',7',7'-hexamethyl-2,2'-ethynediyl-bis-norbornan-2-ol (9)



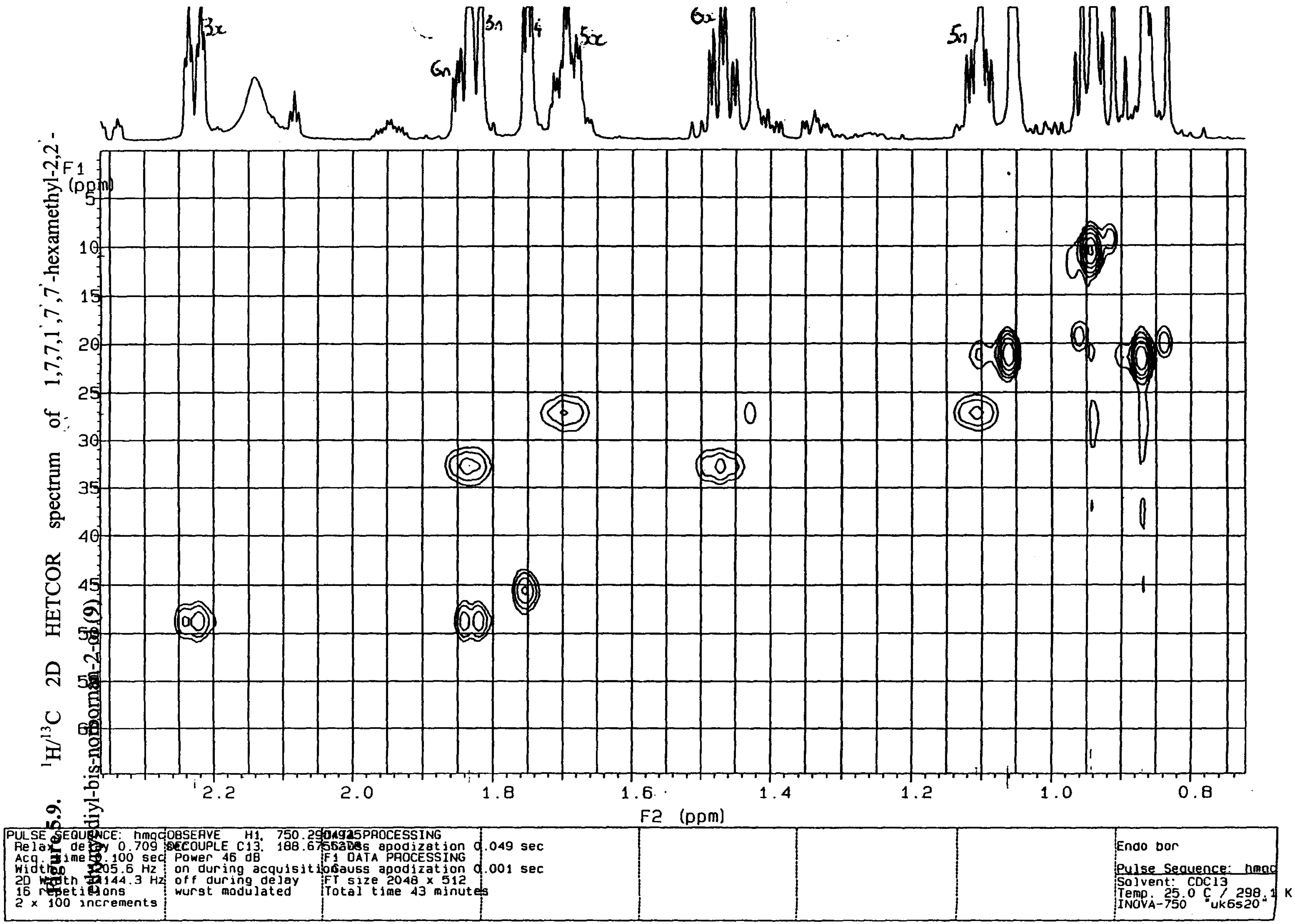
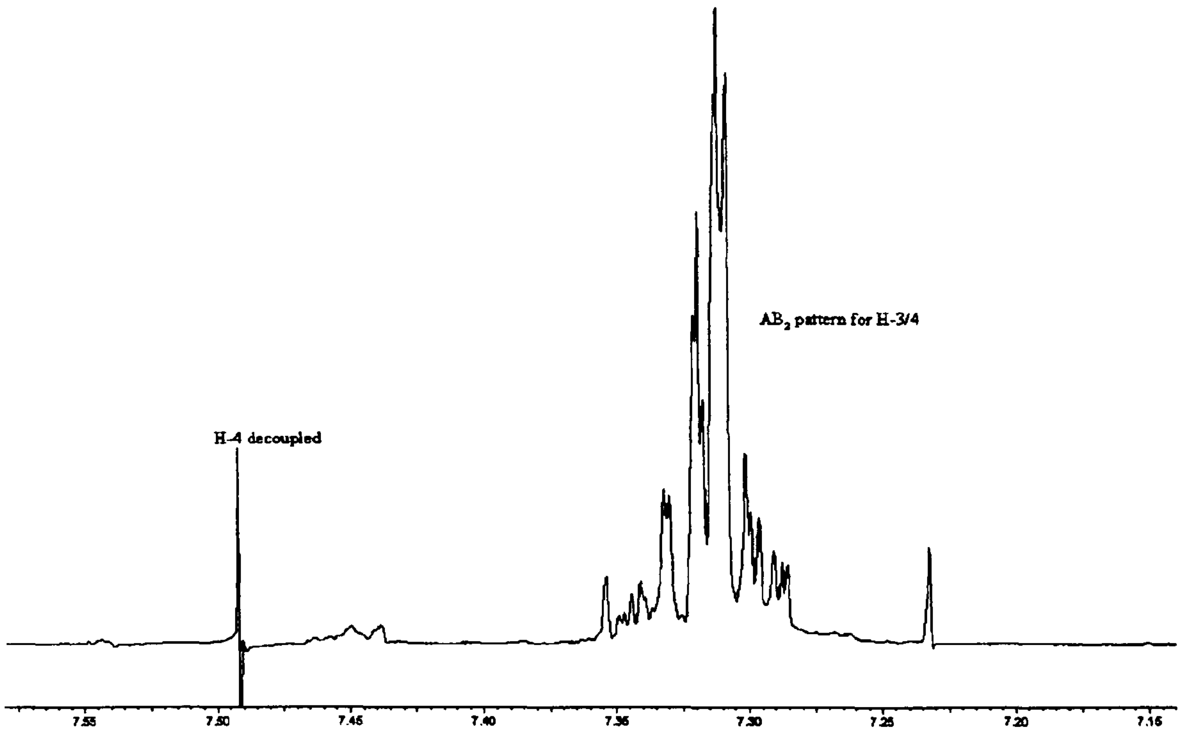


Figure 5.9. $^1H/^{13}C$ 2D HETCOR spectrum of 1,7,7,1',7',7'-hexamethyl-2,2'-[illegible]diyl-bis-norbornan-2-ol (9)

Figure 5.11. ^1H NMR spectrum of phenylacetylene (**12**) with H-2 decoupled.



Ortho-ethynyltoluene (13)

The ^1H spectrum for ortho-ethynyltoluene consists of 4 proton resonances. H-3 and H-6 can be seen as two doublets of doublets with H-6 split further by its coupling to the methyl protons. H-4 and H-5 are triplets easily identified by their roofing patterns.

2-Ethynylnaphthalene (16)

The ^1H spectrum for 2-ethynylnaphthalene consists of 7 proton resonances. The singlet at ca. 8.02ppm is identified immediately as H-1. H-3 and H-4 are easily identified at ca.7.77 and 7.53ppm as a doublet of doublets and a doublet respectively. H-6 and H-7 can be seen as an AB system at ca.7.50ppm, H-5 and H-8 can be seen as a multiplet at ca.7.82ppm. A HMQC plot confirmed this assignment in conjunction with the known ^{13}C assignment of this compound from the literature[25].

9-Ethynylanthracene (17)

The ^{1}H spectrum for this compound (**fig.5.12**) consists of 5 proton resonances. H-10 is readily identified as the singlet occurring at ca.8.43ppm. Since the ^{13}C assignment for this compound is not known a ^{13}C/^{1}H-undecoupled spectrum was recorded to assign C-1 and C-4, hence the ^{13}C spectrum (**fig.5.13**). C-4 has a ^{1}JCH coupling to H-4 (ca.160Hz) and two ^{3}JCH to H-2 and H-10 (ca.6Hz) to give a doublet of triplets. This can be seen in the spectra as two large triplets occurring at ca.129.4 and 127.8ppm. C-1 has one ^{1}JCH coupling to H-1 (ca.160Hz) and one ^{3}JCH coupling to H-3 (ca.6Hz) to give two doublets of triplets occurring at ca.128.4 and 125.2ppm. The assignment of C-1 and C-4 allows the assignment of H-1 and H-4 in the proton spectra from a 2D ^{13}C/^{1}H HETCOR plot.

A ^{1}HCOSY identifies H-2 and H-3 from their couplings to H-1 and H-4 respectively and the assignment of C-2 and C-3 followed from a ^{1}H/^{13}C HETCOR plot. The ^{1}H and ^{13}C assignments for compounds **16** and **17** can be seen in **table's 5.10** and **5.11.**

Figure 5.12. ^{1}H NMR spectrum of 9-ethynylanthracene (**17**).

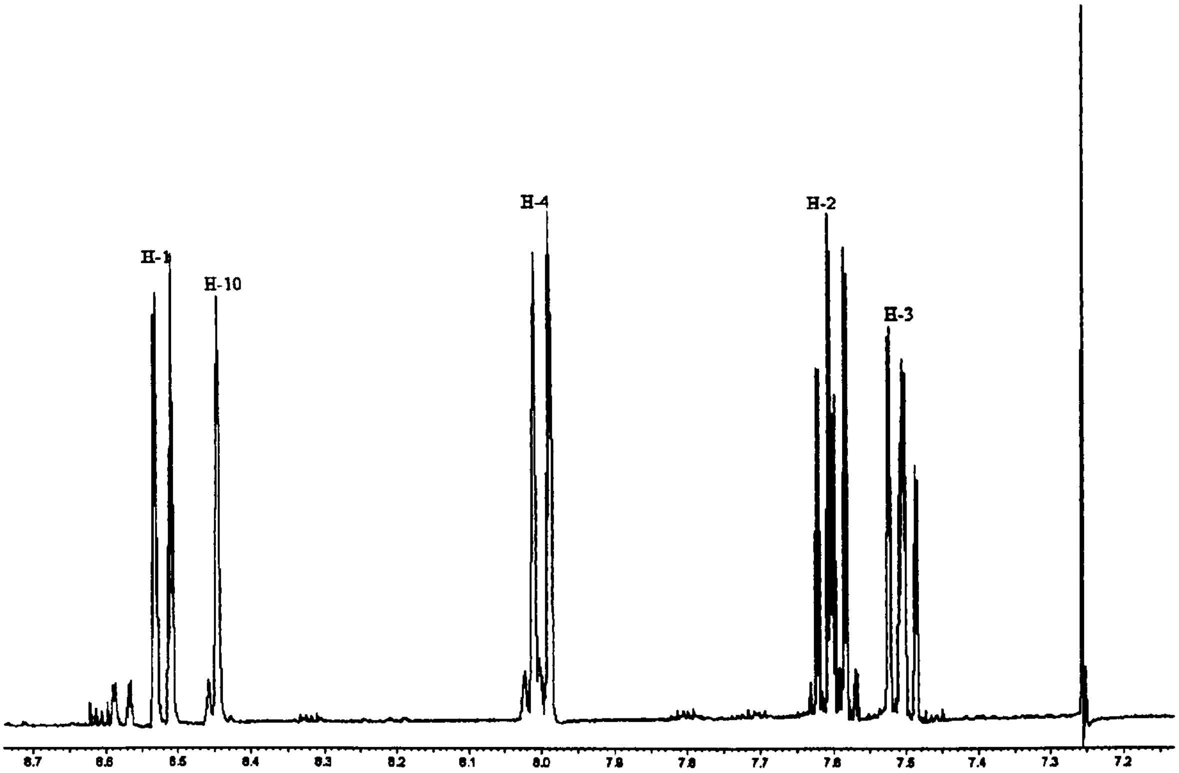
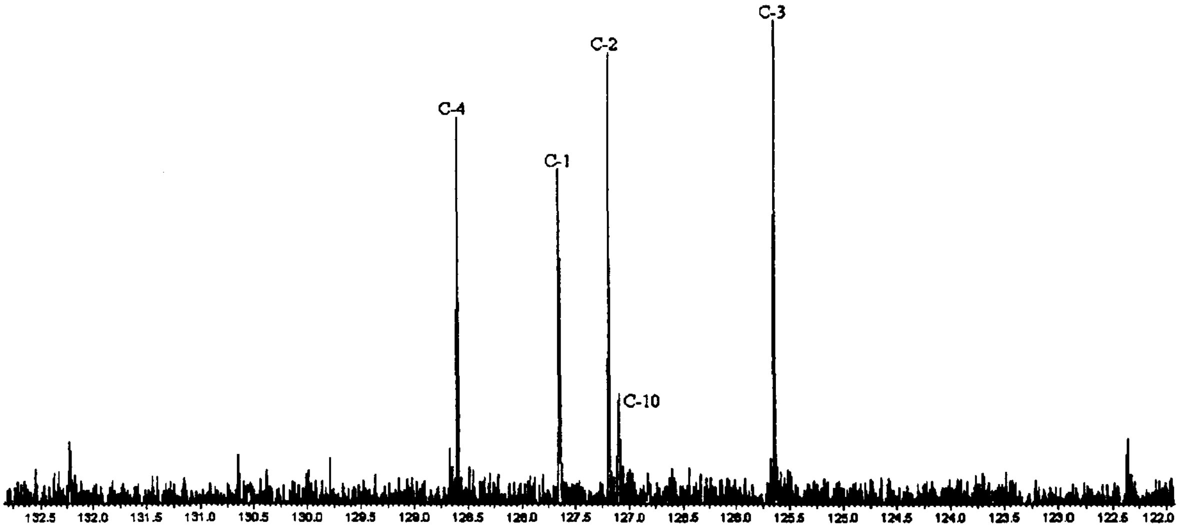


Figure 5.13. ^{13}C NMR spectrum of 9-ethynylanthracene (**17**).



5.5. Results.

The data for the acetylenes obtained here in dilute $CDCl_3$ solution are in excellent agreement with the earlier data obtained in various solvents. The value for acetylene (1.912δ) compares with previous literature values of 1.80 (CCl_4)[26] and 1.91 (CD_2Cl_2)[27]. The proton chemical shift of benzene in $CDCl_3$ is 7.341 and this gives the ortho, meta and para proton SCS in phenylacetylene in $CDCl_3$ from the above data as 0.151, -0.030 and 0.000 ppm. These agree exactly with the comparable values in CCl_4 solution of 0.15, -0.02 and -0.01[26]. As found previously for other aromatic compounds[28] there is a small almost constant shift to higher δ values in $CDCl_3$ compared to CCl_4 but the proton SCS for substituted benzenes obtained by earlier investigations may be used unchanged for the $CDCl_3$ solutions.

The data obtained here for the acetylenes may be combined with the proton chemical shifts of the parent compounds given previously[28, 29] to allow the ^1H chemical shifts and acetylene substituent chemical shift (C≡C-SCS) to be obtained in these compounds. The ^1H chemical shifts and C≡C-SCS have also been calculated using the CHARGE model. Using the calculated proton chemical shifts of the parent compounds and subtracting these from the calculated proton chemical shifts of the acetylene molecules gave the calculated C≡C-SCS.

The short-range effects of the C≡C (3 bonds or less) are explained in terms of anisotropic, steric and electronic effects (β/γ-effects) in both aliphatic and aromatic acetylenes. The long-range effects of the C≡C are small and extend over the whole system. These are explained in terms of anisotropic and steric effects of the acetylene group. The unknowns to determine are therefore the steric coefficient $a_S^{C\equiv C}$, the magnetic anisotropy $\Delta\chi^{C\equiv C}$ and γ-effects that exist for aliphatic and aromatic acetylenes. A second coefficient to determine the steric effect of neighbouring sp_3/sp_2 carbon atoms on the acetylene proton may also exist.

The position of the acetylene magnetic anisotropy on the C≡C bond must also be determined. Iterations were carried out on a large diverse data set incorporating both aromatic and aliphatic acetylenes. The iterations were carried out on the observed chemical shift data of all protons by use of the non-linear mean squares programme (CHAP8[30]). Iterations were carried out on all protons except the acetylenic protons in aliphatic and aromatic compounds.

These calculations were carried out when the magnetic anisotropy of the acetylene group was:

a) at the centre of the C≡C bond and

b) operating from each carbon of the C≡C bond.

The chemical shift calculation for the acetylenic protons was treated separately to all the rest of the protons in the acetylene molecules. The acetylenic chemical shifts could be reproduced in the CHARGE model by finding the appropriate values of the integral for the H.C≡ bond. The near effects of anisotropic bonds have been calculated in this manner previously. This is because it is not feasible to calculate anisotropic effects by means of simple geometric functions at such short distances. If we do attempt this method of calculation the charge on the acetylene proton would be approximately equal to that in ethane which is certainly not the case in reality as the acetylene proton is more acidic and the CH bond more polar.

The procedure that was adopted was that the values of $\Delta\chi^{C\equiv C}$ and the steric coefficient together with the coefficients for the β/γ-effects were obtained from iterations on all but the acetylene protons. Calculations to determine the appropriate parameters for the acetylene protons were then subsequently conducted.

The iterations performed yielded enhanced results when the anisotropy was operating from each carbon of the C≡C bond. The steric effect of the sp carbon atoms was taken as usual from the atom considered. It was concluded that anisotropy and steric effects of the acetylene group were the major factors influencing both the short and long-range proton chemical shifts in the acetylene compounds. γ and β- effects were also found to exist in both aliphatic and aromatic acetylenes (see later). It was also found that the values of the anisotropy, steric coefficient and the coefficients **A** and **B** **(eqtn.5.2)** for the γ-effects were identical when the iterations were performed with either the aliphatic compounds alone or the aromatic compounds, thus the final iteration was performed including all the compounds.

a) *Aliphatic acetylenes.*

The experimental data seen above combined with the proton chemical shifts of the aliphatic parent compounds given previously allow the ^1H chemical shifts and C≡C-SCS to be obtained in these compounds. The ^1H chemical shifts and C≡C-SCS have also been calculated using the CHARGE model. The C≡C-SCS of compounds **10-eq/10-ax**, **11**, **7-cis/7-trs**, and **8**, **9** can be seen in **table's 5.5-5.7**. The C≡C-SCS of the cyclohexane derivatives are of great interest. Unfortunately, 1-ethynyl-4-t-butylcyclohexane is not commercially available and the ^1H chemical shifts for this compound are not in the literature. Therefore, because of the general difficulty in its synthesis, derivatives **7-cis** and **7-trs** were synthesised. The parameterisation of alcohols in the CHARGE model is ongoing and therefore, examining their C≡C-SCS only parameterised the ethynyl-alcohol compounds. The C≡C-SCS was calculated for the ethynyl-alcohols by simply subtracting the ^1H chemical shift of the parent molecules (in this case 4-t-butylcyclohexanol, endo-norborneol and isoborneol[31]) from the ^1H chemical shifts of the ethynyl-alcohols. This data can be seen in **table's 5.6a/b** and **5.7**.

From the tables we see that we generally have an excellent agreement of experimental vs. calculated C≡C-SCS. The SCS are both shielding and deshielding. The γ-effect from the α carbon of the acetylene group is also deshielding and for the saturated acetylenes displays a significant orientational dependence. This dependence shows no particular pattern. However, the γ SCS of the norbornane and bornane derivatives **8** and **9** is greater for the 120° orientation than for the eclipsed orientation for both the exo and endo compound. This is a very interesting observation and has been noted for all norbornane substituents so far studied[32, 33].

For protons that are in a parallel position to the C≡C, i.e., H-3a in compound **7-cis**, we observe a large di-axial interaction resulting in a large downfield shift. This relationship of the acetylene group to protons in parallel positions can also be observed in H-7s in compound **8**, H-5n/6n in compound **9** and H-3a in **10-ax**. Since there is no electric field effect this observation is due to the anisotropy or steric effect of the C≡C group or both. Another interesting observation is that for protons in a position along the C≡C bond (H-3a and H-3e in **10-eq**, H-7s in **9**) the SCS is always deshielding. If the C≡C-SCS were solely due to the C≡C anisotropy this would not be the case.

In **table 5.6a** we observe that the experimental vs. calculated C≡C-SCS is generally in very good agreement. We do note however that for H-2e in compound **7-cis** and **10-ax** the observed values of 0.033ppm and 0.095ppm compared to the calculated values of 0.264ppm and 0.239ppm respectively. It was thought that because H-2e in compound **7-cis** is in an environment with a hydroxyl group, the OH group and the C≡C group may have some significant interaction that affects the influence of the acetylene group on proton in close proximity. However by examination of the C≡C-SCS for H-2e in compound **10-ax** it seems this is not a legitimate conclusion to make.

Table 5.3. Observed vs. calculated ^{1}H chemical shifts (δ) for equatorial/axial-ethynylcyclohexane (**10-eq**/**10-ax**) and 1-ethynyladamantane (**11**).

^{1}H Number	**10-eq**		**10-ax**		**11**	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
1e	-------------	-------------	2.871	2.667	-------------	-------------
1a	2.246	2.094	-------------	-------------	-------------	-------------
2e	1.977	1.877	1.775	1.863	-------------	-------------
2a	1.335	1.408	1.481	1.519	-------------	-------------
3e	1.734	1.617	1.660	1.630	-------------	-------------
3a	1.200	1.084	1.511	1.630	-------------	-------------
4e	1.666	1.600	1.715	1.641	-------------	-------------
4a	1.170	1.138	1.176	1.111	-------------	-------------
γ	-------------	-------------	-------------	-------------	1.861	1.810
δ	-------------	-------------	-------------	-------------	1.941	1.943
e	-------------	-------------	-------------	-------------	1.681	1.646
a	-------------	-------------	-------------	-------------	1.681	1.639
C≡C-H	2.182	2.100	2.278	2.137	-------------	-------------

Table 5.4. Observed vs. calculated ^{1}H chemical shifts (δ) for acetylene (**1**), but-1-yne (**2**), but-2-yne (**3**), pent-1-yne (**4**), hex-3-yne (**5**) and tert-butylacetylene (**6**).

^{1}H Number	**2**		**3**		**4**		**5**		**6**	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
1	2.25	2.18	1.75	1.82	2.18	2.02	2.15	2.22	1.24	1.24
2	1.18	1.10	------	------	1.57	1.55	1.11	1.13	------	------
3	------	------	------	------	1.00	0.77	------	------	------	------
C≡C-H	1.97	2.04	------	------	1.95	2.05	------	------	2.07	2.10

Note. The experimental and calculated value for acetylene itself is 1.912 and 1.913 respectively.

Table 5.5. Observed vs. calculated C≡C-SCS for equatorial and axial-ethynylcyclohexane (**10-eq**, **10-ax**) and 1-ethynyladamantane (**11**).

Molecule	^{1}H Number	Experimental	Calculated
	1a	1.056	0.906
	2e	0.297	0.253
	2a	0.145	0.220
10-eq	3e	0.054	-0.007
	3a	0.011	-0.104
	4e	-0.014	-0.024
	4a	-0.020	-0.050
	1e	1.231	1.043
	2e	0.095	0.239
	2a	0.291	0.331
10-ax	3e	-0.020	0.006
	3a	0.352	0.442
	4e	0.035	0.017
	4a	0.017	-0.077
	γ	0.111	0.131
	δ	0.071	-0.019
11	e	0.069	-0.032
	a	0.069	-0.039

Tables 5.6a/b and 5.7. Observed vs. calculated C≡C-SCS for cis/trans-1-ethynyl-4-t-butylcyclohexan-1-ol (**7-cis**, **7-trs**) calculated from trans/cis 4-t-butylcyclohexan-1-ol (**22a**, **22b**).

Table 5.6a. δH (chemical shift) for cis-1-ethynyl-4-t-butylcyclohexan-1-ol (**7-cis**) and trans-4-t-butylcyclohexan-1-ol (**22a**) and observed vs. calculated C≡C-SCS for **7-cis**.

^{1}H Number	δH for 7-cis	δH for 22a	C≡C-SCS for 7-cis	
	Obs.	Obs.	Obs.	Calc.
2e	2.040	2.007	0.033	0.264
2a	1.514	1 .217	0.297	0.344
3e	1.762	1.782	-0.020	0.050
3a	1.367	1.046	0.321	0.542
4a	1.000	0.965	0.035	0.0

Table 5.6b. δH (chemical shift) for trans-1-ethynyl-4-t-butylcyclohexan-1-ol (**7-trs**) and cis-4-t-butylcyclohexan-1-ol (**22b**) and observed vs. calculated C≡C-SCS for **7-trs**.

^{1}H Number	δH for 7-trs	δH for 22b	C≡C-SCS for 7-trs	
	Obs.	Obs.	Obs.	Calc.
2e	2.037	1.833	0.204	0.230
2a	1.705	1.489	0.216	0.264
3e	1.596	1.548	0.048	0.054
3a	1.379	1.359	0.020	-0.057
4a	1.010	0.993	0.017	0.026

Table 5.7. δH (chemical shift) and observed vs. calculated C≡C-SCS for 2-ethynyl-endo-norbornan-2-ol (**8**) and 2-ethynyl-exo-bornan-2-ol (**9**).

Compound	**^{1}H Number**	**Observed chemical shift (δH)**	**C≡C-SCS**	
			Obs.	**Calc.**
8	1	2.407	0.155	0.229
	3x	2.140	0.269	0.255
	3n	1.360	0.334	0.406
	4	2.250	0.079	0.022
	5x	1.561	-0.009	-0.018
	5n	1.318	-0.017	-0.082
	6x	1.380	-0.002	0.019
	6n	1.979	0.109	-0.143
	7s	1.802	0.462	0.484
	7a	1.389	0.099	-0.058
9	3x	2.228	0.489	0.356
	3n	1.822	0.083	0.236
	4	1.750	0.029	-0.018
	5x	1.695	0.020	0.007
	5n	1.180	0.222	0.164
	6x	1.468	-0.037	0.080
	6n	1.835	0.827	1.152
	Me (1)	0.940	0.034	0.110
	Me (7s)	1.057	0.039	-0.057
	Me (7a)	0.870	0.042	-0.016

The data collected in **table's 5.3-5.7** provides a thorough examination of the application of the CHARGE model and the theories about the influence of the acetylene group on proton chemical shifts. The majority of the compounds listed are of fixed geometry with the exception of the ethynylcyclohexane. Fortunately this compound exists as two conformers, which can be easily 'frozen out' and examined. All the cyclohexane derivatives exist in the chair form, with the norbornane and bornane compounds occupying their own unique geometry's. The minimum energy geometry's were obtained by conducting molecular mechanics calculations using GAUSSIAN 98W.

The *ab initio* geometries calculated are of some interest. GAUSSIAN94 at the MP2/6-31G* level gave H.C≡ and C≡C bond lengths of 1.06 and 1.203 Å in acetylene. This is in agreement with experimental values of 1.061 and 1.203Å[34]. However, for phenylacetylene and para-ethynyltoluene we get contrasting values of 1.057, 1.188 Å and 1.067, 1.223 Å respectively. The large change on the introduction of a para methyl seemed a strange anomaly and poor results were obtained in the charge model, in particular the chemical shift of the acetylene proton in this molecule. By using the DFT/B3LYP[19c] routine with the 6-31G** basis set in GAUSSIAN98 we calculate bond lengths of 1.065 and 1.210 Å. These values were then used as standard for all the aromatic molecules.

We can see from the above data that we have a good agreement between the observed and calculated proton chemical shifts. However we do observe a few discrepancies in our calculated values of chemical shifts. H-1e in compound **10-ax** and H-1a in **10**-eq are 0.204ppm and 0.152ppm lower than the observed values respectively. It is interesting to note that these are methane protons further investigation into methane proton chemical shifts would be of interest. The observed vs. calculated C≡C-SCS for H-2e in both **10-ax** and **7-cis** are also much higher than the calculated value.

By examining the data in **table's 5.6a/b** and **5.7** we can see that there is a reasonable agreement between the observed and calculated C≡C-SCS. The large discrepancies between the observed and calculated C≡C-SCS for the H-3x/3n protons in compound **9** and H-6n in compounds **8** and **9** can be accounted for by the fact that the parent alcohol parameterisation is ongoing in the CHARGE model and as mentioned earlier, there may be a possible interaction between the OH and C≡C which affects the protons in a different way than that expected if these compounds had an acetylene group only. We may also note that in these hydroxyl compounds the acetylene group is sterically hindered and this may be of some significance. For the remaining protons we generally see a good agreement of experimental and observed C≡C-SCS.

For the protons in a parallel position to the C≡C bond we observe a large downfield shift. This is observed in H-3a in **7-cis**, H-7s in **8** and H-6n/5n in **9**. This large downfield shift clearly demonstrates that there is a large steric effect due to acetylene triple bond and also a significant positive anisotropy contribution.

As we have seen in the theory the γ-effects are modelled on a semi-empirical basis and the γ-effects of the α acetylene carbon (H.C.C.C≡) display an orientational dependence with respect to the protons in question. An A + Bcosθ term was incorporated into the CHARGE model to calculate the γ-effect of this carbon. A β effect from the α acetylene carbon with no orientational dependence atom was also incorporated into the CHARGE model. It was found that both these effects gave a significantly enhanced correlation of the protons in a γ position to the α sp-carbon and those protons in a β position to the α sp-carbon with the experimental chemical shifts.

The value of the coefficients **A** and **B** were determined from the observed chemical shifts by an iterative mean squares calculation to give **eqtn.5.2** for the α acetylene carbon GSEF:

$$\mathrm{GSEF} = 0.423 - 0.177\cos\theta \qquad \textbf{(Eqtn.5.2)}$$

The non-orientational β-effect (**C**) from the α acetylene carbon (H.C.C≡) was also incorporated into the CHARGE model and can be seen in **eqtn.5.3**.

$$\mathrm{BSEF} = 1.37 \qquad \textbf{(Eqtn.5.3)}$$

A γ-effect from the Csp_3 carbon attached directly to the acetylene (H.C≡C.C) group influencing the ^1H chemical shift of the acetylene protons was also determined. The coefficient **D** can be seen in **eqtn.5.4**.

$$\mathrm{GSEF} = 0.223/160.84 \qquad \textbf{(Eqtn.5.4)}$$

For the acetylenic protons in the aliphatic acetylenes, a value of the steric coefficient ($H.Csp_3.C\equiv.H$) of 46.5 was also determined. In addition to this a value of 42.8 for the Csp.H exchange integral for all acetylenic protons was determined.

As stated previously, the steric coefficient, $a_S^{C\equiv C}$, and magnetic anisotropy, $\Delta\chi^{C\equiv C}$, were determined by performing iterations on the chemical shift of all non-acetylenic protons of both aromatic and aliphatic molecules. For the aliphatic molecules all iterations performed yielded a greater improvement of the calculated chemical shifts when the steric and anisotropy terms were included and operated from each sp-carbon atom. The anisotropy coefficient and steric coefficient calculated can be seen below.

$$\Delta\chi^{C\equiv C} = -11.56 \times 10^{-6}\ \text{cm}^3\ \text{mol}^{-1}$$

$$a_S^{C\equiv C} = 56.59\ \text{Å}^6\ \text{atom}^{-1}$$

It was therefore concluded that the steric and anisotropy terms of the acetylene group are the only major factor influencing the long-range proton chemical shifts. The final parameterisation of the acetylene group in aliphatics therefore included electronic effects for protons 2 or 3 bonds away from the C≡C and steric and anisotropy effects operating on all protons within the molecules.

It is of great interest to consider the actual magnitudes of the contributions to the C≡C-SCS. **Table 5.8** gives the observed vs. calculated C≡C-SCS for the cyclic acetylenes along with the calculated C≡C-anisotropy, C≡C-steric, electric field and H/C-steric contributions.

Table 5.8. Observed vs. calculated C≡C-SCS with the C-H electric field, C/H-steric, C≡C-anisotropy and C≡C-steric contributions for equatorial/axial-ethynylcyclohexane (**10-eq**/**10-ax**) and 1-ethynyladamantane (**11**).

Cpd.	Proton No.	Obs.	Calc.	C-H Electric field	C≡C-Anis.	C≡C-steric	C-Steric	H-Steric	π- Shift
10-eq	1a	1.056	0.906	-0.053	-0.590	0.0	0.016	-0.046	
	2e	0.297	0.245	-0.019	-0.074	0.027	0.0	0.0	
	2a	0.145	0.225	-0.025	-0.072	0.028	0.005	-0.023	
	3e	0.054	-0.024	0.028	-0.059	0.007	0.0	0.004	
	3a	0.011	-0.110	0.011	-0.011	0.014	0.004	-0.019	
	4e	-0.014	-0.041	0.016	-0.056	0.002	-0.001	0.002	
	4a	-0.020	-0.057	0.016	-0.062	0.009	0.001	-0.010	
	C≡C-H	------	------	-0.027	-5.556	0.0	0.050	0.031	-0.169
10-ax	1e	1.231	1.043	-0.045	-0.560	0.0	0.001	0.0	
	2e	0.095	0.239	-0.019	-0.072	0.028	-0.001	-0.001	
	2a	0.291	0.332	-0.033	-0.174	0.007	0.008	-0.034	
	3e	-0.020	0.006	-0.016	-0.008	0.018	0.0	0.012	
	3a	0.352	0.442	0.040	0.125	0.185	0.002	0.098	
	4e	0.035	0.017	-0.008	0.008	0.011	-0.001	0.006	
	4a	0.017	-0.077	-0.014	-0.054	0.011	-0.001	-0.011	
	C≡C-H	------	------	-0.064	-5.550	0.0	0.098	0.052	-0.170
11	γ	0.111	0.137	-0.024	-0.071	0.028	0.001	-0.005	
	δ	0.071	-0.012	0.028	-0.059	0.008	-0.001	0.006	
	e	0.069	-0.036	0.017	-0.062	0.009	-0.002	0.006	
	a	0.069	-0.042	0.015	-0.056	0.002	-0.001	0.002	

The data presented in **table 5.8** illustrates the magnitudes of the various contributions to the C≡C-SCS. The contributions due to C-H electric field and C/H-steric interactions are very small but of some significance. The major contribution to the chemical shifts in the alkyl acetylenes is the anisotropy, with the steric effect of the acetylene group to a slightly lesser extent. However we may note the large deshielding steric effect of the C≡C group on protons in a parallel position. This is seen in the H-3a in **10-ax** and H-3a in **7-cis**. For protons in this parallel position the major contribution to the SCS is the steric effect of the acetylene group as seen in **table 5.8**.

The chemical shifts of the acetylenic protons are also of interest. In **10-eq** a partial atomic charge on the acetylene proton is calculated at 0.090 electrons. By use of **eqtn.2.6** we calculate a shift of 7.76ppm. From **table 5.8** we observe that the difference between the calculated shift of 2.10ppm is almost solely due to the anisotropy contribution of the acetylene group (-5.56ppm). We may also observe the significant π-electron contribution to the chemical shift of the acetylene protons.

For protons that are 3 bonds or more away from the C≡C we can observe that the sum of all the components contributing to the C≡C-SCS gives us approximately the total C≡C-SCS that has been calculated. However, for the H-2e/H-2a protons in all the compounds investigated in **table 5.3** we observe that the components do not add up to give us our calculated value of C≡C-SCS. This is due to the electronic effects, i.e. γ-effects, which are calculated separately and which affect protons that are 3 bonds or less away from the C≡C.

b) *Aromatic acetylenes.*

The C≡C-SCS of compounds **12-18** can be seen in **table 5.9**. From this table we can observe the good agreement of observed vs. calculated C≡C-SCS. Even though the observed and calculated shifts are not completely accurate we see a general trend between the two. We observe that all the γ protons in the aromatics are deshielded.

There is no general trend to the magnitude of the C≡C-SCS throughout the molecules in the aromatics and we must now take into consideration the π-electron excess in the olefinic hydrogen atoms on the chemical shifts of the protons. We also observe a ring current in the aromatic systems that contributes very significantly to the overall proton chemical shift, although it is a constant value and does not depend on whether the molecule has any substituent present. We also observe possible field and resonance effects due to the C≡C, which are delocalised over the molecule and these will be discussed in a chapter six.

Table 5.9. Observed vs. calculated ^{1}H chemical shifts (δ) for phenylacetylene (**12**), o-ethynyltoluene and p-ethynyltoluene (**13, 14**).

^{1}H Number	12		13		14	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
2	7.492	7.544	---------	---------	7.100	7.016
3	7.311	7.337	7.460	7.484	7.400	7.496
4	7.341	7.343	7.138	7.155	--------	--------
5	7.311	7.337	7.245	7.289	7.400	7.496
6	7.492	7.545	7.202	7.005	7.100	7.016
Me	--------	--------	2.454	2.494	2.340	2.251
C≡C-H	3.069	3.191	3.271	3.156	3.020	3.124

Table 5.10. Observed vs. calculated ^1H chemical shifts (δ) for 1 and 2-ethynylnaphthalene (**15**, **16**) and 9-ethynylanthracene (**17**).

1H Number	**(15)**		**(16)**		**(17)**	
	Observed	**Calc.**	**Observed**	**Calc.**	**Observed**	**Calc.**
1	-----------	-----------	8.028	8.067	8.522	8.478
2	7.700	7.692	-----------	-----------	7.602	7.598
3	7.340	7.478	7.524	7.652	7.504	7.546
4	7.760	7.856	7.788	7.810	8.001	8.003
5	7.760	7.814	7.810	7.803	-----------	-----------
6	7.440	7.478	7.500	7.467	-----------	-----------
7	7.530	7.515	7.500	7.462	-----------	-----------
8	8.350	8.340	7.810	7.832	-----------	-----------
10	-----------	-----------	-----------	-----------	8.447	8.410
C≡C-H	3.430	3.298	3.142	3.225	3.990	3.594

Table 5.11. Observed ^{13}C chemical shifts (δ) for 2-ethynylnaphthalene (**16**) and 9-ethynylanthracene (**17**).

^{13}C Number	**16**	**17**
1	132.30	127.65
2	119.30	127.18
3	128.55	125.63
4	128.01	128.59
5	127.78	------------------------------
6	126.89	------------------------------
7	126.60	------------------------------
8	127.76	------------------------------
9	132.70	115.97
10	132.90	127.08
12	------------------------------	130.64 (132.21)
13	------------------------------	132.21 (130.64)
C_β	84.00	80.36
C_α	77.50	88.17

Table 5.12. Observed vs. calculated ^{1}H chemical shifts (δ) for 2-ethynylpropene (**18**).

^{1}H Number	**(18)**	
	Observed	**Calculated**
H_{trans}	5.300	5.233
H_{cis}	5.390	5.479
Methyl	1.900	1.788
C≡C-H	2.870	3.164

Table 5.13. Observed vs. calculated C≡C-SCS for aromatic acetylenes (**12-18**).

Molecule	^1H Number	Observed C≡C-SCS	Calculated C≡C-SCS
Phenylacetylene	2, 6	0.151	0.207
	3, 5	-0.030	0.000
	4	0.000	0.006
o-ethynyltoluene	3	0.200	0.178
	4	-0.027	-0.041
	5	-0.015	-0.017
	6	0.022	-0.022
	Me	0.111	0.252
p-ethynyltoluene	2, 6	-0.080	-0.011
	3, 5	0.140	0.190
	Me	-0.003	-0.033
1-Ethynyl naphthalene	2	0.223	0.216
	3	-0.137	0.002
	4	-0.084	0.031
	5	-0.084	-0.011
	6	-0.037	0.002
	7	0.053	0.039
	8	0.506	0.515
2-Ethynyl naphthalene	1	0.184	0.242
	3	0.047	0.176
	4	-0.056	-0.015
	5	-0.034	-0.022
	6	0.023	-0.009
	7	0.023	-0.014
	8	-0.034	0.007
9-Ethynylanthracene	1	0.513	0.475
	2	0.135	0.043
	3	0.037	-0.009
	4	-0.008	0.0
	10	0.016	-0.022
2-Ethynylpropene	H_{trans}	0.359	0.337
	H_{cis}	0.359	0.553
	Methyl	0.175	0.149

The data provided in **tables 5.9-5.12** again provides us with a thorough examination of the application of the CHARGE model and about the influence of the acetylene group on aromatic protons chemical shifts. The compounds listed above are of fixed rigid geometry. All the minimum energy geometry's for use in CHARGE were obtained from GAUSSIAN98W. The geometry's were calculated at the B3LYP/6-31G** level.

The observed versus calculated proton chemical shifts are given in **tables 5.9, 5.10** and **5.12**. There is good agreement between the chemical shifts and they are generally within 0.1ppm of each other. We do however notice discrepancies with some of the protons. From **table 5.13** we see that the observed C≡C-SCS for H-3 in 1-ethynylnaphthalene is -0.137. The difference between the observed and calculated value for H-3 is 0.139ppm. There is no general explanation for this and it is an interesting anomaly. The observed value for the meta proton in phenylacetylene is much larger at – 0.030ppm. We would however expect them to be similar in magnitude and that is what we see in the calculated C≡C-SCS values for these protons from the CHARGE model. We may therefore conclude that the C≡C-SCS operates to different magnitudes in naphthalene and benzene.

Large discrepancies exist in the calculated chemical shift of the acetylene protons. In most of the aromatics we observe good agreement but we observe an average difference of ca. 0.36ppm in 9-ethynylanthracene and 2-ethynlpropene.

Again, it is of interest to examine the large deshielding due to the steric and anisotropic effects of the group. H-8 in 1-ethynylnaphthalene and H-1 in 9-ethynylanthracene occupy a parallel position to the C≡C and downfield shifts ca. 8.3 and 8.5ppm respectively are observed. The C≡C-SCS for these protons from **table 5.13** also illustrates this large deshielding effect.

As discussed previously, the γ-effect calculated from the α acetylene carbon for the aromatics is identical to that in the aliphatics. A γ-effect from the sp^2 carbon atom of an unsaturated system attached directly to the acetylene ($H.C{\equiv}C.Csp_2$) group influencing the ^1H chemical shift of the acetylene proton was determined. This non-orientational γ-effect was incorporated into the CHARGE model:

$$GSEF = 1.20/160.84 \qquad \textbf{(Eqtn.5.5)}$$

For the long-range protons the steric and anisotropy terms of the acetylene group are the major influence. For the aromatic molecules all iterations performed yielded a greater improvement of the calculated chemical shifts when the steric and anisotropy terms were included and operated from each sp-carbon atom and also when the γ–effect was included.

The final parameterisation of the acetylene group in aromatics included electronic effects for protons 2 or 3 bonds away from the C≡C and steric and anisotropy effects operating on all protons within the molecules.

The aromatic acetylenes have other mechanisms that may affect the proton chemical shifts, in particular, the ring current and π-electron effects. The CHARGE model assumes that the introduction of the acetylene group has no effect on the parent aromatic ring current and the good correlation between calculated and observed chemical shifts justifies this assumption. In contrast the introduction of the C≡C group has a very significant effect on aromatic π-electron densities, hence a significant effect on the C≡C-SCS.

To explain the proton chemical shift in these aromatic molecules, we have to consider various effects and the nature of the substituent, i.e., its effect on the electron distribution throughout the aromatic system. This will be discussed in chapter six.

It is again of interest to consider the magnitude of the factors, which contribute to the C≡C-SCS. **Table 5.14** gives the observed versus calculated C≡C-SCS for selected molecules, along with the electric field, ring current and π-electron contributions.

Table 5.14. Calculated and observed C≡C-SCS, with C≡C steric, C≡C anisotropy, C-H electric field, ring current and π-electron contributions for phenylacetylene (**12**) and 1/2-ethynylnaphthalene (**15** and **16**).

Compound	^{1}H Number	Obs. C≡C-SCS	Calc. C≡C-SCS	C≡C-Steric	C≡C-Anis.	C-H Electric Field	Ring Current	π-shift
12	2,6	0.151	0.207	0.029	-0.072	-0.020	0.004	0.043
	3,5	-0.030	0.0	0.008	-0.068	0.045	0.005	0.013
	4	0.0	0.006	0.002	-0.063	0.033	-0.001	0.035
	C≡C-H	------	------	0.0	-5.582	-0.004	0.196	-0.108
15	2	0.223	0.216	0.029	-0.080	-0.020	0.0	0.065
	3	-0.137	0.002	0.008	-0.070	0.046	0.0	0.023
	4	-0.084	0.031	0.002	-0.062	0.034	0.0	0.058
	5	-0.084	-0.011	0.0	-0.036	0.014	0.0	0.010
	6	-0.037	0.002	0.0	-0.010	0.010	0.0	0.003
	7	0.053	0.039	0.007	0.023	0.0	0.0	0.012
	8	0.506	0.515	0.326	0.210	0.084	0.0	0.0
	C≡C-H	------	------	0.0	-5.581	0.009	0.318	-0.136
16	1	0.184	0.242	0.032	-0.061	-0.021	0.0	0.068
	3	0.047	0.176	0.027	-0.078	-0.020	0.0	0.024
	4	-0.056	-0.015	0.007	-0.069	0.045	0.0	0.006
	5	-0.034	-0.022	0.0	-0.038	0.012	0.0	0.004
	6	0.023	-0.009	0.0	-0.022	-0.001	0.0	0.013
	7	0.023	-0.014	0.0	-0.019	-0.001	0.0	0.006
	8	-0.034	0.007	0.005	-0.029	0.018	0.0	0.014
	C≡C-H	------	------	0.0	-5.581	-0.004	0.246	-0.123

From the data above we observe that the C≡C steric and anisotropy are very important in determining the C≡C-SCS for all the protons in an aromatic system. We can see that the C≡C shielding is larger for protons in closer proximity to the C≡C. As stated earlier the shielding contribution is proportional to $1/r^6$. We may observe the large deshielding effect on H-8 in compound **15**, which is parallel to the C≡C bond. It is again of interest to note that this SCS is due in large to the steric effect of the C≡C group.

For the aromatic acetylenes the ring current is calculated from the parent molecules, i.e. only two protons in naphthalene are different so the ring current is the same for these protons in the ethynylnaphthalenes. If we examine the π-electron contributions we see that the magnitude of the contribution is dependent on the position of the proton with respect to the C≡C group. The magnitude of this contribution is dependent on the magnitude of field and resonance effects operating in the molecule.

5.6. Discussion.

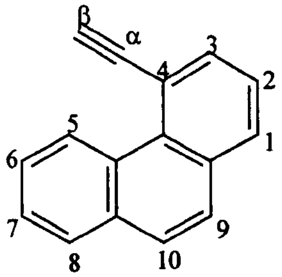
The results for the non-cyclic molecules provide a rigorous test for the CHARGE model. Unfortunately, few studies have been undertaken into calculating proton chemical shifts in acetylene compounds. As stated previously, various authors have undertaken calculations of the diamagnetic anisotropy of the acetylene group and these will be discussed.

Reddy and Goldstein calculated a value for the acetylene anisotropy of -16.5×10^{-6} $cm^3\ mol^{-1}$. ^{13}C-H coupling constants were used as a measure of s-character. This therefore gave a measure of hybridisation and local shielding in a C-H bond. Vertical lines were obtained when plots of observed chemical shifts vs. ^{13}C-H coupling constants were made for compounds of similar structure. In order to obtain the effect of C≡C anisotropy on the acetylenic proton, the anisotropy shift of the CH_3 in methylacetylene (the chemical shift of methyl protons in methane was subtracted from that of methyl acetylene) was determined from one of the plots and the value of $\Delta\chi^{C\equiv C}$ determined from the McConnell equation. The value of anisotropy calculated by Reddy and Goldstein is higher than the value calculated in this work. Our value of -11.56×10^{-6} $cm^3\ mol^{-1}$ is a little smaller than that calculated by Reddy and Goldstein. Unfortunately, the value calculated by these authors was calculated by considering the acetylene protons only. Therefore it cannot be concluded that this value is acceptable for use in calculating the chemical shift of protons in molecules of different structure (i.e., ring systems and aromatics) or for protons more than three bonds away.

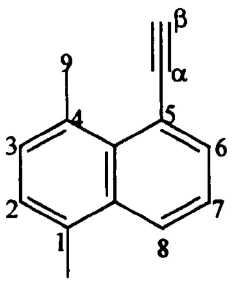
Shoemaker and Flygare also calculated a value for the magnetic anisotropy of the acetylene group by use of the method discussed in the introduction. Although the authors considered no influence of the acetylene group in NMR, it is interesting to note the value of anisotropy calculated. The theory behind Shoemaker and Flygare's calculations will not be discussed here, but the value of -7.70×10^{-6} $cm^3\ mol^{-1}$ was calculated. This value is a lot lower than that calculated by Pople (-19.4×10^{-6} $cm^3\ mol^{-1}$), Reddy and Goldstein (-

16.5x10^{-6} cm^{3} mol^{-1}), and Zeil and Buchert (-36x10^{-6} cm^{3} mol^{-1}). This stark contrast is interesting because even though the value calculated by Shoemaker and Flygare is by a method unrelated to NMR, it is very comparable to the value calculated by the CHARGE model.

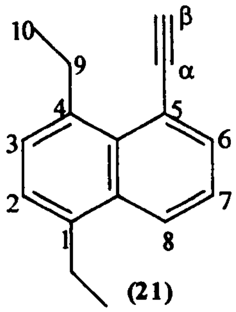
Many authors have investigated the magnetic anisotropy of the acetylene group but very few have examined the possibility of deshielding regions alongside the C≡C bond. Mallory and Baker confirmed that regions of deshielding existed alongside the C≡C bond by examining the proton NMR of 4-ethynylphenanthrene (**19**), 5-ethynyl-1, 4-dimethylnaphthalene (**20**) and 5-ethynyl-1, 4-diethylnaphthalene (**21**).



(19)



(20)



(21)

By examining the proton NMR of protons that exist in a parallel position to the C≡C group, i.e., H-5 in **19**, the methyl protons in **20** and the methylene protons in **21**, they observed unusually large downfield shifts, which results from the deshielding effect of the C≡C group.

A large deshielding of H-5 in **19** (1.63ppm downfield from H-5 in parent molecule) was observed. In **20** the shielding of the protons in the C-4 methyl group (0.49ppm) were considerable but less than that of H-5 in **19** because of rotational averaging. The methylene protons in the C-4 ethyl group of **21** are slightly closer to the triple bond than the methyl protons in **20** and were found to be deshielded by 0.55ppm. Mallory and Baker made an assumption on the distance dependence of this deshielding steric effect of the acetylene group because the distances they used from the protons in question to the centre of the acetylene bond are from Dreiding models and only provide a hint to any distance dependence. The ^{1}H chemical shifts calculated by the CHARGE model for the proton on C-4 in **19** and for the methyl and ethyl protons in **20** and **21** can be seen in **table 5.15.**

Table 5.15. Observed vs. calculated ^1H chemical shifts (δ) for selected protons in molecules **19**, **20** and **21**.

Compound	**^{1}H Number**	**^{1}H chemical shift**	
		Obs.	**Calc.**
19	5	10.340	9.409
20	Methyl	3.010	2.946
21	CH_2	3.620	3.419

If we examine **table 5.15** we observe a good correlation between the observed and calculated shifts for the methyl and CH2 in compounds **20** and **21**. However, when we look at H-5 in **19** we observe a very large of ca.0.96ppm difference between the observed and calculated value. This is not a cause for concern however as H-5 occupies a very unique geometry and is in very close proximity to the triple bond. The accuracy of the minimum geometry calculated by GAUSSIAN98W at the B3LYP/6-31G** level may not be absolutely correct and since very small changes in bond lengths and angles have a very significant influence on the calculated proton chemical shifts it would be best to try and obtain an absolute geometry from x-ray crystal data and input this into charge.

The distance between the centre of the triple bond and H-5 in 19 calculated from G98 is 2.208Å. This compares with the value of 1.55Å measured from Dreiding models and also 2.408 calculated by PC Model[35]. If we calculate the chemical shift of H-5 in **19** by having the anisotropy in the middle of the double bond we observe no improvement in the calculated chemical shift.

Mallory and Baker predicted a distance dependence on the magnitude of the acetylene shielding as proportional to $1/r^3$ and that the shielding was from the centre of the triple bond. In the CHARGE model the shielding falls off at $1/r^6$ and is calculated at each carbon atom in the acetylene bond. However, a $1/r^3$ fall off point was incorporated into the CHARGE model, the rms. error of the calculated proton chemical shifts in the molecules investigated increases.

5.7. Conclusions.

The proton chemical shifts of all the acetylene only compounds are composed of 72 data points spanning a range of ca.0.70 to 9.00ppm and are predicted with an rms error of 0.074ppm. The C≡C-SCS of all acetylene compounds and their derivatives are composed of 102 data points spanning a range of ca.0.70. to 9ppm and are predicted with an rms error of 0.114ppm.

We may conclude that the C≡C-SCS long-range protons determined by magnetic anisotropy and steric effects only for both aliphatic and aromatic compounds, with the steric effect having a greater influence on chemical shifts. The short-range protons (<3bonds) also require the inclusion of magnetic anisotropy and steric effects for aliphatic and aromatic compounds. The inclusion of a γ-effect from the α acetylene carbon in both aliphatic and aromatic acetylenes is needed to calculate the chemical shifts of protons 3 bonds away from the α sp-carbon. This γ-effect of the acetylene carbon atom is found to have an orientational dependence and operates for both aliphatic and aromatic acetylenes. A non-orientation dependent β-effect from the acetylene α carbon in aliphatic acetylenes has also been incorporated into the CHARGE model, as has a γ-effect from sp3 and sp2 carbons on the acetylene proton chemical shift.

5.8. References.

1. A.A.Bothner-By and J.A.Pople, *Ann.Rev.Phys.Chem.*, 1965, **16**, 43.
2. G.S.Reddy and J.H.Goldstein, *J.Chem.Phys.*, 1963, **39**, 12, 3509.
3. W.Zeil and H.Buchert, *Z.Physik.Chem.*, 1963, **38**, 47.
4. R.L.Shoemaker and W.H.Flygare, *J.Am.Chem.Soc.*, 1969, **91:20**, 5417-5421.
5. F.B.Mallory and M.B.Baker, *J.Org.Chem.*, 1984, **49:8**, 1323-1326.
6. C.J.Puchert and J.Behnke, *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, Aldrich Chemical Company Inc. Milwaukee, USA, 1993.
7. A.L.McClellan, *Tables of Experimental Dipole Moments*, vols. 1-3, Rahara Enterprises, Ca., 1989.
8. R.J.Abraham and M.Canton, *MagRes.Chem.*, 2000, **39**, 421.
9. Univesity of Liverpool Chemistry Workshop, Chemistry Department, The University of Liverpool, P.O.Box 147, Liverpool L69 3BX.
10. Chemsampco, Inc. 40 Enterprise Avenue, Trenton, NJ 08638, USA.
11. Sigma-Aldrich Library of Rare Chemicals.
12. Aldirch Chemical Company, The Old Brickyard Road, New Road, Gillingham, U.K.
13. J.C.Hanekamp and P.A.A.Klusener, *Synth.Comms.*, 1989, **19:15**, 2677-2682.
14. An offprint from: Transition Metals in Organic Synthesis-A Practical Approach-Edited by S.E.Gibson, 1997. Dept. of Chemistry, Imperial College of Science, Technology and Medicine, London, U.K.
15. D.G.Garratt, P.L.Beaulieu and V.M.Morisset, *Can.J.Chem.*, 1981, **59**, 927-934.
16. GlaxoWellcome R&D, Gunnelswood Rd., Stevenage, Herts., SG1 2NY.
17. Bruker UXNMR version 010892, Bruker AM, Silbersteifen, D-7512 Germany.
18. Varian Associates, Palo Alta, Ca., USA.
19. a) GAUSSIAN 94, Gaussian Inc., Pittsburgh PA, 1994.
    M.J.Frisch, G.W.Trucks, M.Head-Gordon, P.M.W.Gill, M.W.Wong, J.B.Foresman, B.G.Johnson, H.B.Schlegel, M.A.Robb, E.S.Replogle, R.Gomperts, J.L.Andres, K.Raghavachari, J.S.Binkley, C.Gonzalez, R.L.Martin, D.J.Fox, D.J.Defrees, J.Baker, J.J.P.Stewart and J.A.Pople.
    b) GAUSSIAN 98, Revision.A9, Gaussian Inc., Pittsburgh PA, 1998.

M.J.Frisch, G.W.Trucks, H.B.Schlegel, G.E.Scuseria, M.A.Robb, J.R.Cheeseman, V.G.Zakrzewski, J.A.Montgomery, Jr., R.E.Stratmann, J.C.Burant, S.Dapprich, J.M.Millam, A.D.Daniels, K.N.Kudin, M.C.Strain, O.Farkas, J.Tomasi, V.Barone, M.Cossi, R.Cammi, B.Mennucci, C.Pomelli, C.Adamo, S.Clifford, J.Ochterski, G.A.Petersson, P.Y.Ayala, Q.Cui, K.Morokuma, D.K.Malick, A.D.Rabuck, K.Raghavachari, J.B.Foresman, J.Cioslowski, J.V.Ortiz, A.G.Baboul, B.B.Stefanov, G.Liu, A.Liashenko, P.Piskorz, I.Komaromi, R.Gomperts, R.L.Martin, D.J.Fox, T.Keith, M.A.Al-Laham, C.Y.Peng, A.Nanayakkara, M.Challacombe, P.M.W.Gill, B.Johnson, W.Chen, M.W.Wong, J.L.Andres, C.Gonzalez, M.Head-Gordon, E.S.Replogle and J. A. Pople.

c) J.B.Foresman and A.Frisch, "Exploring Chemistry with Electronic Structure Methods", 2nd Edn, Gaussian Inc., 1997.

20. E.L.Eliel and S.H.Wilen, *Stereochemistry of Organic Compounds*, J.Wiley, New York, 1994.

21. H.S.Schneider and V.Hoppen, *J.Org.Chem.*, 1978, **43**, 20, 3866-3873.

22. F.R.Jensen and C.H.Bushweller, *Adv.Alicycl.Chem.*, 1971, **3**, 139.

23. M.Manoharan and E.L.Eliel, *Mag.Res.Chem.*, 1985, **23**, 4, 225.

24. E.Djuardi, P.Bovonsombat and E.McNelis, *Tetrahedron*, 1994, **50**, 41, 11793.

25. C.F.Wilcox and K.A.Weber, *Tetrahedron*, 1985, **41:20**, 4425-4436.

26. P.D.Pretsch, T.Clerc, J.Seibl and W.Simon, *Spectral Data for Structure Determination of Organic Compounds*, 2nd Edn., Springer-Verlag, NY, 1989.

27. L.Luan, J.S.Song and R.M.Bullock, *J.Org.Chem.*, 1995, 60, **22**, 7170.

28. R.J.Abraham, M.Canton, M.Reid and L.Griffiths, *J.Chem.Soc., Perkin Trans.2*, 2000, 4, 803.

29. R.J.Abraham, *Progress in NMR Spectroscopy*, 1999, **35**, 85.

30. S.S.Kuo, *Computer Applications of Numerical Methods*, ch.8, Addison-Wesley, London, 1972.

31. Part 4, R.J.Abraham, A.P.Barlow and A.E.Rowan, *Mag.Reson.Chem.*, 1989, **27**, 1074.

32. R.J.Abraham, L.Griffiths and M.A.Warne, *J.Chem.Soc.Perkin Trans.2*, 1997, **203**, 881.

33. Part 12, R.J.Abraham, L.Griffiths and M.A.Warne, *J.Chem.Soc.Perkin Trans.2,* 1998, **31**, 1751.

34. W.J.Lafferty and R.J.Thibault, *J.Mol.Spectry.,* 1964, **14**, 79.

35. PC Model Version 7.0 Serena Software, Box 3076, Bloomington, IN, USA.

Chapter Six.

Field and resonance effects in substituted aromatic compounds.

Chapter Six. Field and resonance effects in substituted aromatic compounds.

6.1. Introduction.

The influence of a substituent on the protons in the benzene ring has been a source of investigation for a number of years. However, there is still no quantitative calculation of these effects. Work by Castellano et al[1] and Hayamizu and Yamamoto[2] involved the analysis of the proton spectra of a wide range mono substituted benzenes in dilute solution in CCl_4. The thorough analysis carried out allowed the accurate determination of the proton substituent chemical shift (SCS) and tables of the SCS are now an important part of NMR text[3, 4 & 5]. Many researchers have attempted to theoretically interpret this data, concentrating mainly on the correlation of the substituent SCS and the calculated π (and σ) electron densities on the carbon atoms adjacent to the proton under investigation. These investigations were motivated by the very good correlations between ^{13}C substituent SCS and the π-electron densities at the para carbon atom in mono-substituted benzenes[6].

Hehre[7] et al conducted research into the correlation of substituent chemical shift with π-electron densities, using *ab initio* calculations. Using the STO-3G basis set they illustrated that the ^{13}C SCS could be interpreted on the basis of calculated electron densities. However, this was not the case for the proton SCS. Later investigations[2, 8 & 9] have attempted to correlate the ^1H SCS with substituent parameters.

In this chapter we will examine the attempts of authors to account for the substituent chemical shift of the carbonitrile and acetylene group in mono and di-substituted benzenes and larger aromatic systems.

6.2. Correlation of π (and σ) electron densities with substituent chemical shift.

To explain proton chemical shifts in substituted aromatic molecules, we have to consider various effects and the nature of the substituent, i.e., its effect on the electron distribution throughout the aromatic system. As stated above, work by Hehre et al examined how the substituent may disturb the electron distribution within a molecule and thus affect proton chemical shifts. Hehre et al conducted work on a range of substituted benzenes and considered the effect of the substituent on the meta and para carbons and protons, since these are the most perturbed atoms in these molecules. They omitted the ortho proton SCS presumably on the grounds that these "other" effects are even more important at these protons. They also noted that strongly electronegative substituents caused polarisation of the π system without charge transfer, leading to changes in the π densities around the ring and this is termed the π-inductive effect.

Hehre et al published π-electron distributions for all the ring carbons for a series of monosubstituted carbons and found that they reflected the many of the ideas of classical organic chemistry. Therefore groups such as CN, NO_2, CO_2, etc., that are capable of conjugation with the *2p* orbitals on the aromatic ring carbons lead to π-electron disturbance at ortho and para positions and π charge transfer between the substituent and the ring. Various *ab initio* calculations at the STO-3G level were carried out to determine the change in the electron populations of the π and σ orbitals relative to benzene for meta and para carbon atoms and for the attached hydrogens.

An attempt was made to establish a link between the electron densities at the proton and at the carbon to which it is attached and the chemical shift of this proton. It was concluded that in terms of calculated charge densities, the chemical shift of the meta proton could be approximated with the combination of the σ-charges at the hydrogen atom and at the attached carbon. The proton chemical shift of the para proton could be correlated with the total charge at the carbon atom but displayed very minimal dependence on the charges at the hydrogen. These correlations can be seen in **figures 6.1 and 6.2**.

Fig.6.1. Plot of meta proton SCS vs. sum of the meta-proton and meta-carbon σ-electron charges for monosubstituted benzenes.

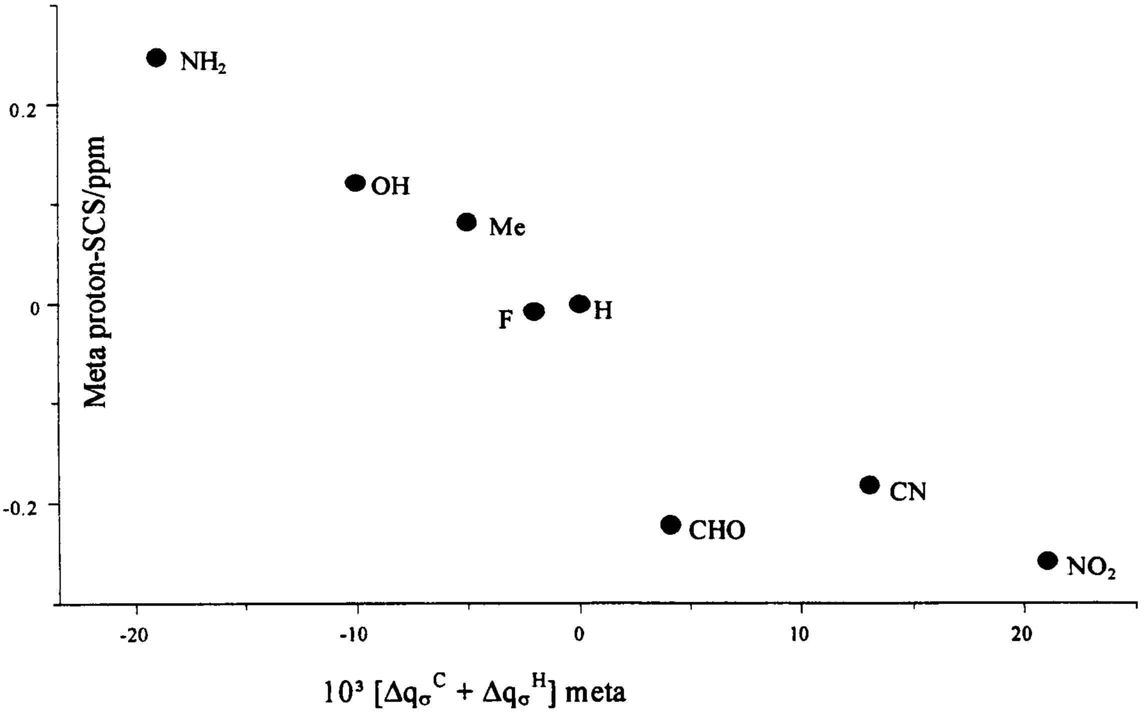
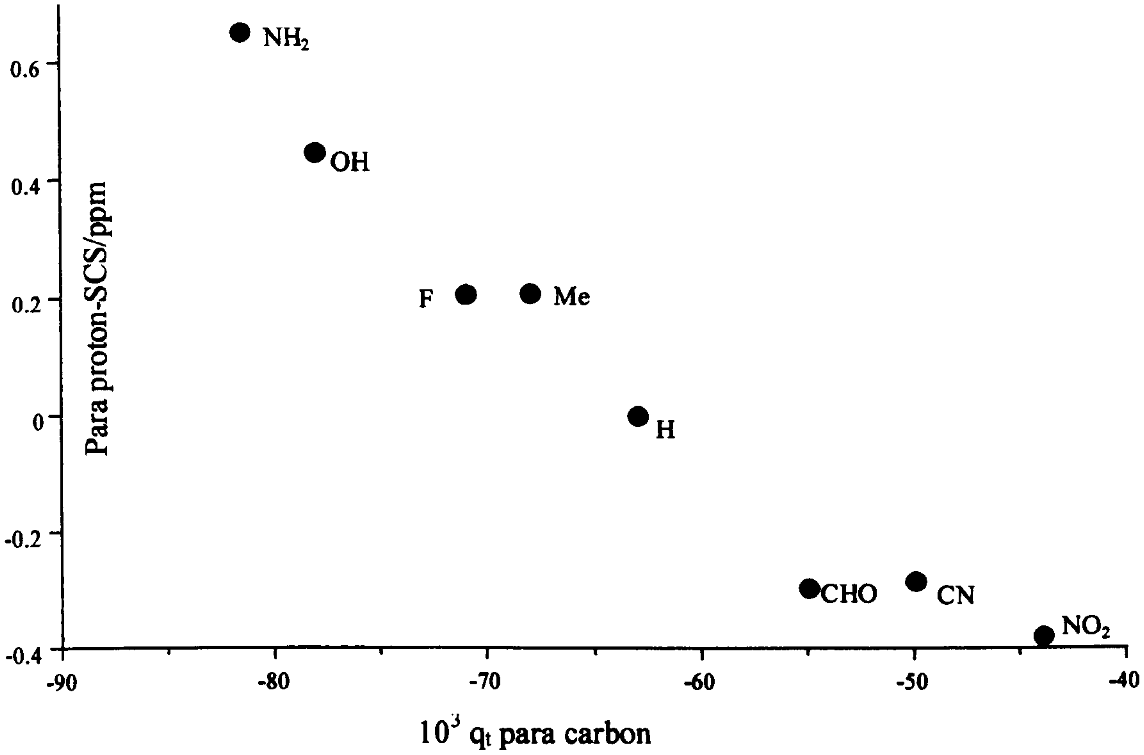


Fig.6.2. Plot of para proton SCS vs. para carbon total charge density for mono-substituted benzenes.



It was therefore permissible to say that the proton chemical shifts depend on factors other than electron densities at the hydrogen atom and adjoining carbon atom. As calculated in this work, these other factors include ring current effects, which are proportional to the substituent resonance interaction and inductive effects.

Hehre et al concluded that the chemical shifts of protons in meta and para positions were much more dependent on the resonance contribution than the calculated charge densities at their respective hydrogen atoms. It was found that an approximate correlation of chemical shifts for meta and para protons can be achieved by a combination of change in the electron populations at the hydrogen and the total π-charge transfer to or from the substituent and the benzene ring. This π-charge transfer was assumed to account for the ring current effects. This combination was deemed acceptable as long as a correction term for the π-electron ring current effects was included. The can be seen in **eqtn.6.1.**

$$\Delta q^H - 0.14\,(\Sigma\Delta q_\pi) \qquad \textbf{(Eqtn.6.1)}$$

Where:

Δq^H is the change in the electron density at the hydrogen.

$\Sigma\Delta q_\pi$ is the total π-charge transfer to or from the substituent and the benzene ring.

When this term was plotted against the SCS for the meta and para protons for a range of substituents a good correlation was obtained. However, this term seems to be of no use at all. By using this plot alone we cannot deduce why the para proton in the molecule of interest in this work, benzonitrile, is shifted 0.1ppm more downfield than the meta proton, because Hehre et al determined that Δq^H and $\Sigma\Delta q_\pi^C$ are effectively the same for meta and para carbons and protons. What we do notice is that for the para carbon in benzonitrile we have a decrease in electron density at the π orbital (Δq_π^C) and a slight increase in electron density at the σ orbital (Δq_σ^C) with respect to benzene. This relationship is not displayed in the meta position where the electron density at the π orbital remains effectively the same as in benzene but the σ electron density at the carbon increases. Therefore what we may conclude is that Hehre et al could establish no direct link between the electron densities at the specific atoms and the proton chemical shifts related to them.

6.3. Field (*F*) and resonance (*R*) effects on substituent chemical shifts in substituted aromatics.

a) The carbonitrile group (C≡N).

Although no direct work was undertaken with respect to ^{1}H chemical shifts, Swain and Lupton[10] calculated the field and resonance components (***F*** and ***R***) of substituent effects in the hope that they may provide more accurately defined and more physically significant independent variables for predicting substituent effects on physical properties (we note that pure field [through space] and inductive effects [through bond polarisation] are joined together to under the name field effect). They concluded that the CN group had ***F*** and ***R*** effects operating to different degrees for different positions in an aromatic ring (benzonitrile). The CN group was found to be a very good electron acceptor by resonance but it was determined that the CN group had a much larger positive field effects than resonance effects. In terms of position of atoms with respect to the CN, it was found that the sensitivity to resonance effects is much greater for para subsituents (in this case carbon and hydrogen). However, even though conjugation is not as complete for a meta substituent it cannot be neglected.

Field effects for the CN group are more of an unknown in aromatics and we do not know whether they or resonance effects are more important for meta substituents, although we know resonance effects are not as complete for meta substituents. However, we can estimate the significance of field and resonance effects on the substituent chemical shift. This can be done by implementing **eqtn.6.11**, used by Swain and Lupton to determine the substituent constant, σ:

$$\sigma = fF + rR \qquad \textbf{(Eqtn.6.11)}$$

Where:

σ is the substituent constant and f and r are weighting factors or empirical sensitivities.

To establish how the substituent chemical shift depends on or is influenced by ***F*** and ***R*** effects we can simply replace σ with the SCS for different substituents on benzene for protons in the meta and para positions of the benzene ring. Therefore we may write equations **6.3** and **6.4**.

$$\Delta^{m\text{-}X} = fF + rR \qquad \textbf{(Eqtn.6.3)}$$

and

$$\Delta^{p\text{-}X} = fF + rR \qquad \textbf{(Eqtn.6.4)}$$

Where:

$\Delta^{m\text{-}X}$ / $\Delta^{p\text{-}X}$ is the SCS for protons in para and meta positions of substituted benzene.

With the SCS for protons in the meta and para positions at our disposal we may use a non-linear mean squares calculation to determine the coefficients ***f*** and ***r***. The values of ***F*** and ***R*** have been determined for a range of substituents by Hansch, Leo and Taft[11], which are very similar to values determined by Swain and Lupton but covering a wider range of substituent groups. These values of ***F*** and ***R*** can be seen in **table 6.1**.

Table 6.1. Substituent field (***F***) and resonance (***R***) effects and the SCS for meta and para protons in mono-substituted benzene.

Substituent	**Component**		**Substituent chemical shift/ppm**	
	Field effect (*F*)	**Resonance effect (*R*)**	**Meta-proton**	**Para-proton**
NH_2	0.08	-0.74	-0.25	-0.65
OH	0.33	-0.70	-0.12	-0.45
F	0.45	-0.39	-0.02	-0.23
CH_3	0.01	-0.18	-0.12	-0.22
H	0.00	0.00	0.00	0.00
C≡N	0.51	0.15	0.18	0.28
NO_2	0.65	0.13	0.26	0.38
$-CO.CH_3$	0.33	0.17	0.14	0.21
$-OCO.CH_3$	0.42	-0.11	0.03	-0.13
Cl	0.42	-0.19	-0.02	-0.09
Br	0.45	-0.22	-0.08	-0.04
I	0.42	-0.24	-0.21	0.00
$-OCH_3$	0.29	-0.56	-0.09	-0.44
C≡C	0.22	0.01	0.025	0.00

Note that -ve values of SCS indicate upfield shifts from benzene

The calculated values of ***f*** and ***r*** can be seen below for the m and p protons:

i) *Meta proton*

$$\Delta^{m\text{-}X} = 0.184\boldsymbol{F} + 0.363\boldsymbol{R} \qquad \textbf{(Eqtn.6.5)}$$

The values of ***f*** and ***r*** were determined with an rms error of 0.072 and average error of 0.050. We can see from this equation that the resonance effect seems to play a greater part in influencing the chemical shift of the meta proton of substituted benzenes. However the value of the coefficients do not differ by a huge amount and we cannot say that the dependence of proton chemical shifts upon the resonance effects of the substituent group is greater than the dependence on field effects.

ii) *Para proton*

$$\Delta^{p\text{-}X} = 0.286F + 0.881R \qquad \textbf{(Eqtn.6.6)}$$

The values for f and r were determined with an rms. error of 0.064 and average error of 0.050. We can clearly see that the dependence of the SCS on resonance effects is far greater than the dependence on field effects. This is to be expected since resonance is greater for para substituents. Plots of m and p-SCS vs. F and R components can be seen in **figures 6.3** and **6.4.**

Figure 6.3. Meta proton SCS vs. field and resonance components for various functional groups in mono-substituted benzene.

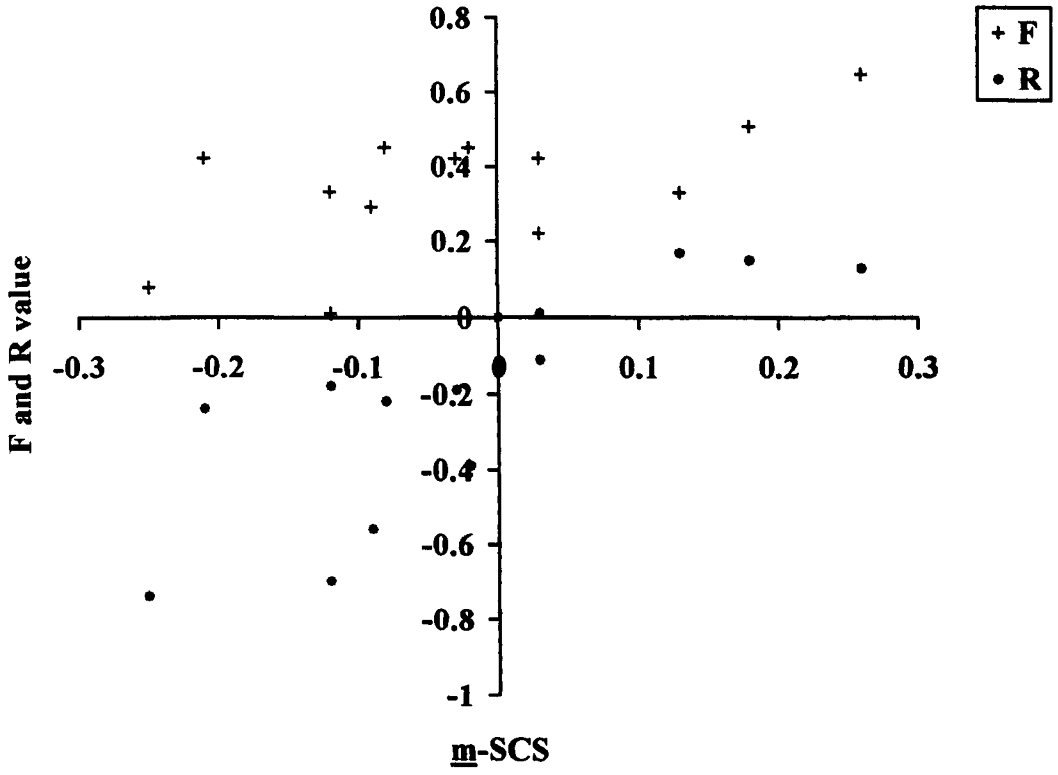
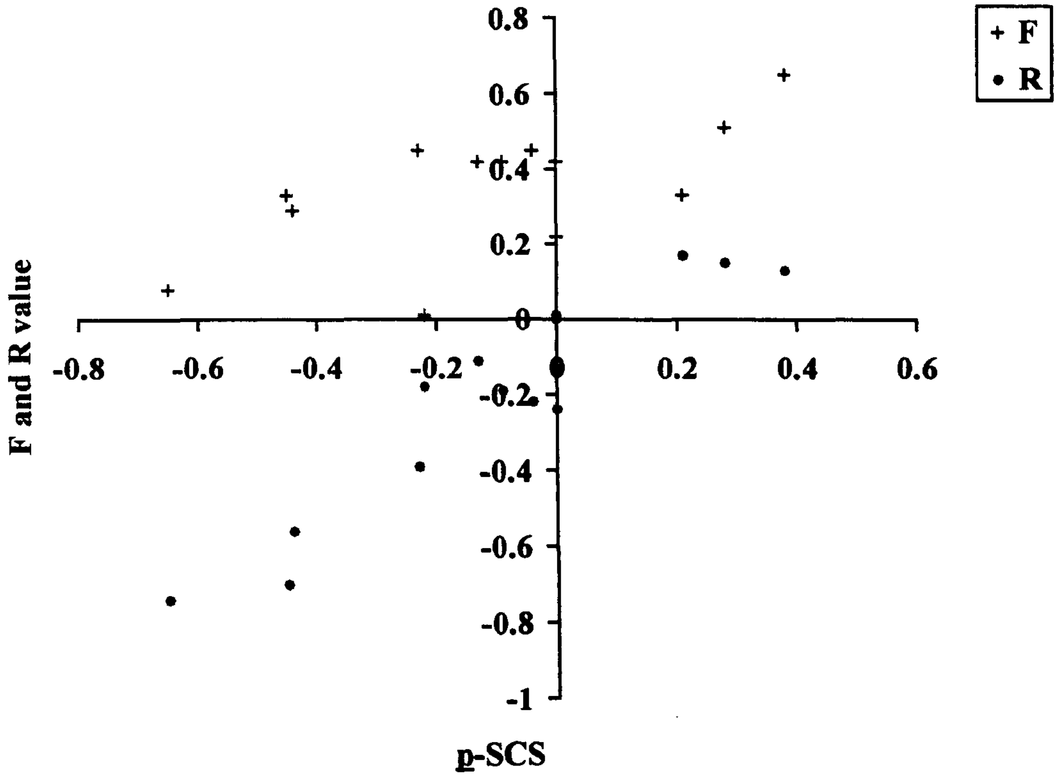


Figure 6.4. Para proton SCS vs. field and resonance components for various functional groups in mono-substituted benzene.



From **figures 6.3** and **6.4** we can clearly observe the greater correlation of SCS with F and R components for the para proton in mono-substituted benzene.

The field and resonance contributions to the proton SCS (***fF*** and ***rR***) in benzonitrile are thus given from **eqtn's. 6.5** and **6.6** as 0.094 and 0.055 for the meta protons and 0.146 and 0.132 for the para protons. It is of some interest to compare these values with the calculated contributions to the proton SCS in benzonitrile in table 10 of chapter five. For benzonitrile the meta proton SCS has electric field and π charge contributions of 0.121 and 0.044 res. and for the para proton SCS the calculated contributions are 0.092 and 0.107 res. These values are in good agreement with the values obtained by the Swain and Lupton treatment although they are based on a totally different conceptual treatment and this gives strong support for the model used in these calculations.

The ^{1}H chemical shifts and CN-SCS for the dicyanobenzenes has been calculated to a good degree of accuracy (**table 4.11** [chapter four]). Again we observe contributions to the ^{1}H chemical shift from electric field effects and ring current effects. However contributions that arise from resonance and field effects cannot be easily quantified because of di-substitution. For example, in ortho-dicyanobenzene protons 4 and 5 are in meta and para positions to the two cyanides and protons 3 and 6 are in ortho and meta positions to the cyanides. Thus, it is difficult to say to what degree field and resonance contributions operate on the protons. The same can be said for all the dicyanobenzenes.

The ^{1}H chemical shifts of the 1/2-naphthonitriles and 9-anthracenecarbonitrile are also calculated to a good degree of accuracy but there are a few large discrepancies. From **table 4.12** (chapter four), we observe that the calculated chemical shift of H-3 in 1-naphthalenecarbonitrile is a large ca.0.203ppm from the observed value. We would expect this proton meta to the CN group to exhibit similar behaviour to that of the meta proton in the benzonitrile and dicyanobenzenes and display a similar CN-SCS or significant CN-SCS. However, we actually observe a negligible CN-SCS (**table 4.14** [chapter four]). This behaviour must indicate that the presence of two aromatic rings must significantly alter the behaviour of all the protons in the system.

We also see a large discrepancy in 9-anthracenecarbonitrile. From **table 4.12** (chapter four) the calculated chemical shift of H-10 is ca.0.26ppm downfield from the observed value. The ring system must possess complex electronic properties and hence field and resonance effects must operate all over the system.

b) *The acetylene group* (C≡C).

Unlike the carbonitrile group, correlation of π (and σ) electron densities with the substituent chemical shift of the acetylene group was not included by Hehre et al in their investigation. In this work, GAUSSIAN98W and CHARGE calculations have shown that the π-electron density at the para carbon is less than that at the meta carbon indicating that resonance effects withdraw the π-electron density to a greater extent in the para carbon. The σ-electron density remains roughly the same for the meta and para carbons so it is possible to say that this smaller π-electron density at the para carbon plays a significant role influencing the chemical shift of the para proton. However, the C≡C-SCS for this proton is only slightly more upfield than the meta proton. Therefore for the acetylene group, equating the C≡C-SCS of a particular proton and π-electron density at the connecting carbon atom can really lead to no significant conclusions.

Following on from the "Swain and Lupton" treatment into the influence of field and resonance effects on carbonitrile SCS in substituted aromatics, the same procedure was performed for the acetylene group. We have already calculated the values of ***f*** and ***r*** for substituted benzenes from **eqtns.6.3 and 6.4**. Therefore all we need to calculate is the field and resonance contributions to the proton SCS (***fF*** and ***rR***) in phenylacetylene using **eqtns.6.5** and **6.6**. Thus, values of 0.005 and 0.009 for the meta protons and 0.0 for the para protons are calculated. It is again of interest to compare these values with the calculated contributions to the proton SCS in phenylacetylene in **table 5.9** (chapter five). For phenylacetylene, the meta proton SCS has electric field and π charge contributions of 0.0 and 0.013 res. and for the para proton SCS the calculated contributions are 0.0 and 0.035 res. Again, these values are in reasonable agreement with the values obtained by the Swain and Lupton treatment.

The ^{1}H chemical shifts of the 1/2-ethynylnaphthalenes and 9-ethynylanthracene are calculated to a good degree of accuracy but there are a few large discrepancies. From **table 5.13** (chapter five) we observe that the experimental C≡C-SCS of H-3 (meta) in 1-ethynylnaphthalene is -0.137ppm. We would expect this proton to exhibit similar behaviour to that of the meta proton in the phenylacetylene, or the meta protons in ortho and para-ethynyltoluene and display a similar C≡C-SCS. However, we actually observe C≡C-SCS of ca.0.0ppm for the phenylacetylene and ortho and para-ethynyltoluenes. This behaviour may indicate that the presence of two aromatic rings must significantly alter the behaviour of all the protons in the system, as we have seen above in the carbonitriles.

An interesting observation in the aromatic acetylenes is the very similar calculated and observed C≡C-SCS for the para protons in phenylacetylene, 1-ethynylnaphthalene and 9-ethynylanthracene. From the studies on the aromatic carbonitriles above it was noted that the para proton CN-SCS in benzonitrile and 1-cyanonaphthalene varied greatly to that in 9-cyanoanthracene. It was concluded that the 9-cyanoanthracene must have complex electronic properties and so field and resonance effects must operate all over the system. However, it is quite clear from **table 5.13** (chapter five) that in 9-ethynylanthracene the field and resonance effect must be operating to a much lesser extent over the three ring system, or even the two ring system of 1-ethynlnaphthalene as all the C≡C-SCS values for the para protons are approximately zero. This suggests that the carbonitrile group has significantly different field and resonance effects in aromatic systems than the acetylene group when we have different numbers of aromatic rings in the molecules.

6.4. Conclusions.

We have seen from the work by Hehre et al that equating the substituent chemical shift of meta and para protons in substituted benzenes with electron densities, provides no direct link between electron densities at the specific atoms and the proton chemical shifts. They concluded that the proton SCS depends on factors other than the electron densities at the hydrogen atom and adjoining carbon atom. It is unfortunate that these investigations did not attempt to correlate the proton SCS with the π-electron charge density at both the attached and neighbouring carbon atoms (**eqtn.2.12** [chapter two]) as this approach has been successful for both the cyano derivatives studied in chapter four and a range of monosubstituted benzenes (chapter three).

The analysis using the "Swain and Lupton" treatment indicates how field and resonance effects operate to different degrees in monosubstituted benzenes. Equations **6.5** and **6.6** illustrate that the dependence of proton chemical shifts on ***F*** and ***R*** effects operate to approximately the same degree for meta protons and that resonance effects operate to a greater degree for para protons.

The main problem of using correlations such as those in **eqtn.6.3** and **6.4** is that they do not take into account the large differences in the SCS components of the various groups, which need to be considered individually. Earlier work[12] has shown for example, that the OH group has no anisotropic or steric effect and both the meta and para SCS are dominated by the π-electron shift. This is much greater in the para position but the meta SCS is still dominated by the π-effect. In contrast, in benzaldehyde the electric field and anisotropy contributions equal the π-shift for the meta proton and are a significant but minor contribution for the para proton. In addition, the nitro and cyano groups differ from both these in that they have no anisotropic effect but the electric field effect is predominant at the meta proton and equal to the π shift at the para proton. This shows that each substituent group must be considered separately in order to calculate the separate steric, electric and anisotropic contributions at the various protons.

6.5. References.

1.a) S.Castellano and C.Sun, *J.Am.Chem.Soc.*, 1966, **88**, 4741.

b) S.Castellano, C.Sun and R.Kostelnik, *Tetrahedron Letters*, 1967, **46**, 4635 and **51**, 5205.

c) M.P.Williamson, R.J.Kostelnik and S.M.Castellano, *J.Chem.Phys.*, 1968, **49**, 2218.

2. K.Hayamizu and O.Yamamoto, *J.Mol.Spect.*, 1968, **28**, 89 and 1969, **29**, 183.

3. R.J.Abraham, J.Fisher and P.Loftus, *Introduction to NMR Spectroscopy*, J.Wiley 1988.

4. J.B.Lambert, H.B.Shurvell, D.A.Kightner and R.G.Cooks, *Organic Structural Spectroscopy*, Prentice-Hall, New Jersey, 1998.

5. E.Pretsch, J.Seibl, T.Clerc and W.Simon, *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd Edn., Springer-Verlag, Berlin, 1989.

6. G.C.Levy and G.L.Nelson, *Carbon-13 NMR for Organic Chemists*, J.Wiley, NY, 1972.

7. W.J.Hehre, R.W.Taft and R.D.Topsom, *Prog.Phys.Org.Chem.*, 1976, **12**,159.

8. R.T.C.Brownlee and R.W.Taft, *J.Am.Chem.Soc.*, 1970, **92**, 7007.

9. G.K.Hamer, I.R.Peat and W.F.Reynolds, *Can.J.Chem.*, 1973, **51**, 897 and 915.

10. C.G.Swain and E.P.Lupton, *J.Am.Chem.Soc.*, 1968, **90**, 4328.

11. C.Hansch, A.Leo and R.W Taft, *Chem.Rev.*, 1991, **91**, 165.

12. R.J.Abraham, M.Canton, M.Reid and L.Griffiths, *J.Chem.Soc., Perkin Trans.2*, 2000, **4**, 803.

Chapter Seven.

Proton chemical shifts, ring currents and π-electron effects in hetero-aromatics.

Chapter Seven. Proton chemical shifts, ring currents and π-electron effects in hetero-aromatics.

7.1. Introduction

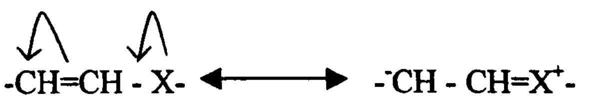
Investigations into the chemical shifts of hetero-aromatics are of considerable interest and importance in organic chemistry, since hetero-aromatic are a vital component in a range of chemical compounds[1]. We have examined the condensed aromatic hydrocarbons in great details in chapter three and now we need to apply the same theories to hetero-aromatic compounds. As stated previously (chapter three), the influence of π-electron densities and ring currents on aromatic proton chemical shifts has been the subject of limited investigations over the years. There is still no authoritative calculation (even a semi-empirical one) of the proton chemical shifts of aromatic compounds and the structural chemist still has to rely on proton data banks for the identification of aromatic compounds by NMR. This also applies for hetero-aromatic compounds and hence a comprehensive investigation into the proton chemical shifts of hetero-aromatics has been conducted here.

A very limited amount of research into proton chemical shifts in heteroaromatic compounds has been carried over the years. Abraham and Thomas[2] calculated the ring currents in a range of five membered hetero-aromatic compounds under investigation. The method used to calculate the effect of the ring current on the chemical shifts of ring protons or methyl groups was to compare the shifts in aromatic molecules with those for similarly bonded molecules where no ring current was possible. For example, benzene should be compared with cyclohexa-1, 3-diene. The contributions to the chemical shift other than the ring current contributions should be cancelled out by use of this method.

By use of this method it was possible to estimate the ring current shift in furan, thiophene, thiazole and imidazole and determine the ratio of ring currents in these molecules with respect to benzene. This was performed by comparing the proton chemical shifts of the aromatic compounds with those of similarly constituted protons in the 4,5-dihydro-compounds. It was thought that the only effect influencing the chemical shift of H-2 in the aromatic ring would be the introduction of a second double bond. Hence, the difference between the shifts is due to the ring current. The ring current was modified in order to obtain a calculated value of ΔδH-2, the difference in chemical shift between H-2 in the aromatic and 4, 5-dihydro compounds, matching the observed value. 2-Methyl substituted aromatics were also used, with comparison being made to the methyl shift in the dihydro compound.

The chemical shift of proton and methyl groups on C-2 in the compounds investigated were used because of mesomeric effects that occur on H-3 in the dihydro form (**fig.7.1**), resulting in a shielding effect on H-3 and hence high field shift. Therefore H-3 should not be used in studying ring current effects. This above method was used in this investigation to calculate the ring currents of various five membered hetero-aromatics compounds and will be discussed in more details later.

Figure 7.1. Mesomeric forms in the dihydro compounds.



$$\text{-CH=CH - X-} \longleftrightarrow \text{-}{}^{-}\text{CH - CH=X}^{+}\text{-}$$

(X=O, S or N)

The results of the investigation by Abraham and Thomas showed good agreement of calculated and observed chemical shift for H-2. However, there is some controversy surrounding the use of dihydro compounds as a non-aromatic model. Corrections for the missing double bond, the heteroatom (which has a large inductive effect) and mesomeric effects must be considered. There are also possible conformational changes between the aromatic and dihydro compounds, and the effect of change in hybridisation state of the heteroatom, which may affect the accuracy of results. Because of these considerations, only methyl shifts in the C-2 position of the compounds investigated were used in determining the ring current in this investigation because all of the above considerations are much smaller when considering the chemical shift of the methyl. However, this was dependent on the availability of non-aromatic model compounds containing a methyl group in the appropriate position.

Because of the concerns over the use of dihydro compounds as a non-aromatic model, various authors have criticised their use. Elvidge[3] proposed other non-aromatic models for comparison with furan, etc. He compared the methyl shift of a 'in chain' methyl group in a polyene with toluene, arguing that bond alternation is minimal in this system. The assumption was that the shielding effect of the double bonds in the polyene was equivalent to that of two double bonds in methylcyclohexatriene. However, this method does not take into consideration the different geometry's of the two systems, the double bonds in the polyene being s-trans and in the ring s-cis. This seems to suggest that this method is less reliable for use as a model for ring current calculations.

De Jongh and Wynberg[4] used the same method as Abraham and Thomas but instead of ignoring H-3 shifts they averaged the shifts of H-2 and H-3 in the dihydro compounds. They also made a comparison of benzene to cyclohexane to have some consistency with their furan to dihydrofuran shifts. By doing this they assume that in the cases of dihydrofuran and cyclohexane the effect of a second double will be the same, which is known to be incorrect.

In this investigation we shall see how the implementation of the method used by Abraham and Thomas enabling us to calculate the ring current in the hetero-aromatics investigated. This provides us with an excellent account of the influence of the ring current on proton chemical shifts. The use of the non-aromatic model proposed by Abraham et al is subject to some debate but it is still the least prone to error of all the models proposed and is implemented where appropriate in these calculations.

We give here the proton chemical shifts of a selection of condensed hetero-aromatic compounds in $CDCl_3$. These provide sufficient data for an analysis of the proton chemical shifts in hetero-aromatics based on the CHARGE model. In this investigation we shall use model B for the calculation of the ring current intensities for various hetero-aromatic compounds (see chapter two). The effects of the heteroatom are well reproduced for all the protons on the basis of calculated π-electron densities. It was also necessary to calculate the charge densities at the aromatic protons to quantify the appropriate α, β and γ-effects if any exist and this will be discussed in detail later.

In this work a complete analysis of the ^1H chemical shifts in hetero-aromatic compounds is presented using a large data set of conformationally rigid molecules with fully assigned ^1H NMR spectra. These include phenol (**2**), anisole (**3**), benzofuran (**10**), thionaphthene (**19**), indole (**26**) and N-methyl (**27**), 2-methyl (**28**), 3-methyl (**29**) and 7-methylindoles (**30**), aniline (**31**), pyridine (**32**), 2-picoline (**33**), 3-picoline (**34**), quinoline (**36**), 2-methyl (**37**), 3-methyl (**39**), 4-methyl (**40**) and 6-methylquinolines (**41**) and isoquinoline (**42**). This data together with previous literature data for vinylmethylether (**1**), furan (**4**), 4, 5-dihydrofuran (**5**), 2-methylfuran (**6**), 2-methyl-4, 5-dihydrofuran (**7**), 2, 5-

dimethylfuran (**8**), 3-methylfuran (**9**), vinylmethylsulfide (**11**), thiophenol (**12**), thiophene (**13**), 4, 5-dihydrothiophene (**14**), 2-methylthiophene (**15**), 2-methyl-4, 5-dihydrothiophene (**16**), 2,5-dimethylthiophene (**17**), 3-methylthiophene (**18**), pyrrole (**20**), N-methylpyrrole (**21**), 2-methylpyrrole (**22**), 2, 5-dimethylpyrrole (**23**), 1, 2, 5-trimethylpyrrole (**24**), 3-methylpyrrole (**25**), 4-picoline (**35**), 2-Methyl-3, 4-dihydroquinoline (**38**), 1-methylisoquinoline (**42**), 1-methyl-3, 4-dihydroisoquinoline (**44**) and 3-methylisoquinoline (**45**) allowed the calculation of the ^{1}H chemical shifts for these molecules. Molecules with two heteroatoms were also considered. These were the diazbenzenes as pyrimidine (**46**), pyrazine (**47**), pyridazine (**48**). Also considered was imidazole (**49**), 2-methylimidazole (**50**), 2-methyl-4, 5-dihydroimidazole (**51**), thiazole (**52**), 2-methylthiazole (**53**), 2-methyl-4, 5-dihydroithiazole (**54**) and oxazole (**55**). Compounds **8, 12, 17, 18, 20-24, 35, 42** and **45-48** were obtained from the Aldrich library of chemical shifts[5]. Compounds **4-7, 13-16** and **50-54** were obtained from ref.2. Vinylmethylether (**1**), 3-methylfuran (**9**), vinylmethylsulfide (**11**), 2-methylpyrrole (**22**), imidazole (**49**), 2-methyl-3, 4-dihydroquinoline (**38**) and oxazole (**55**) were obtained from refs.6-12 respectively. The molecules examined and their nomenclature can be seen in **figures 7.2-7.8.**

Figure 7.2. Oxygen containing hetero-aromatic molecules.

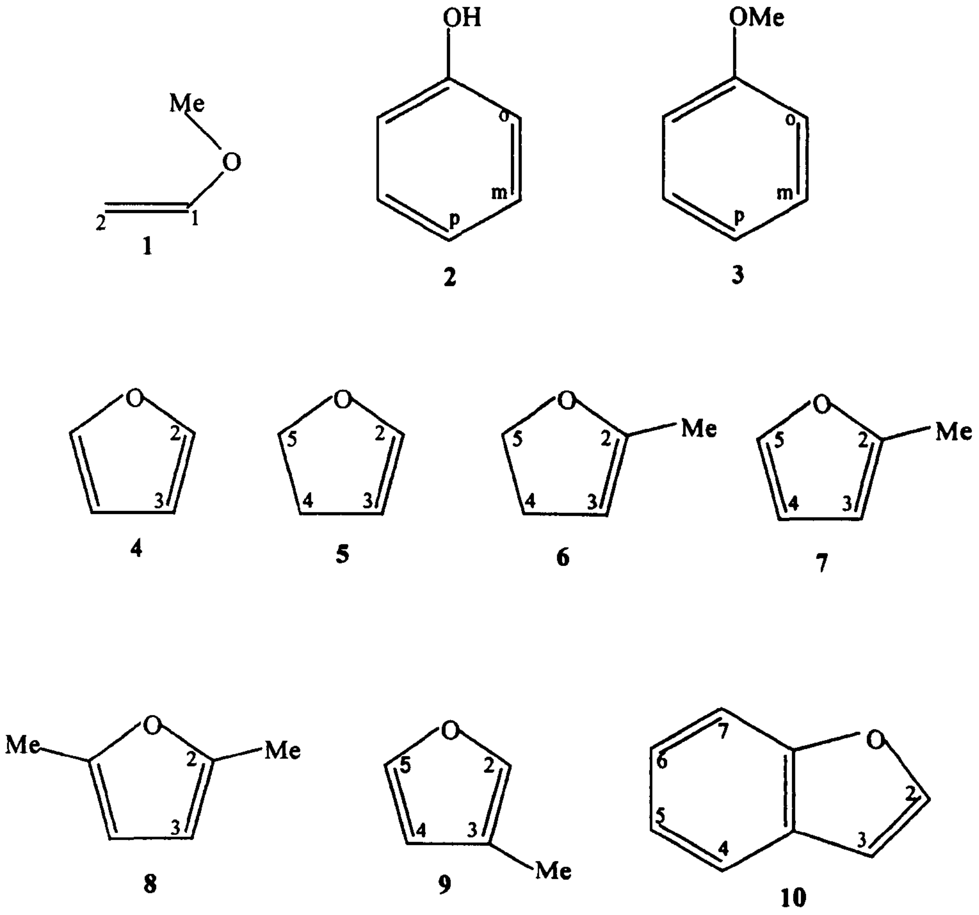
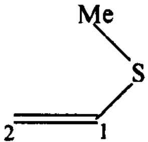


Figure 7.3. Sulphur containing hetero-aromatic molecules.



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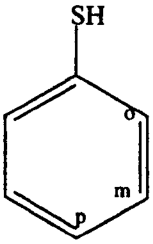

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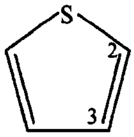

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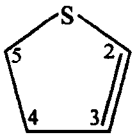

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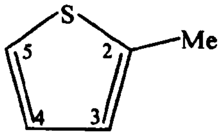

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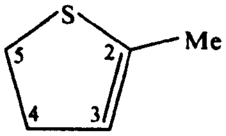

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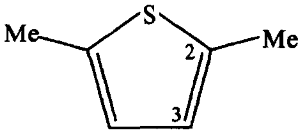

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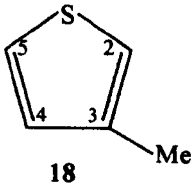

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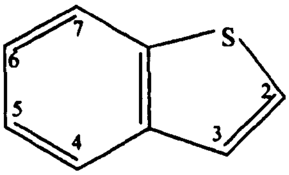

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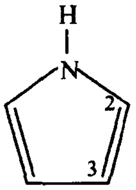
Figure 7.4. Pyrroles.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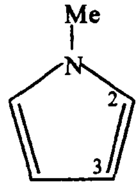
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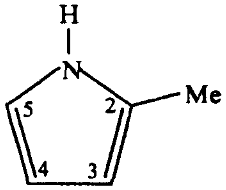
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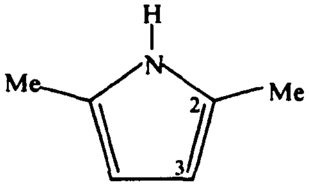
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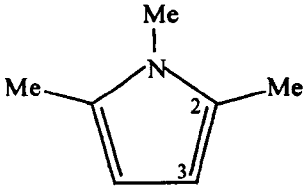
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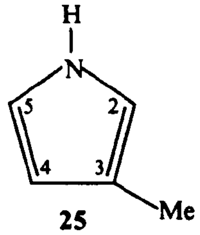
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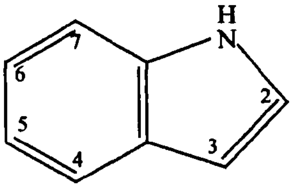
Figure 7.5. Indoles.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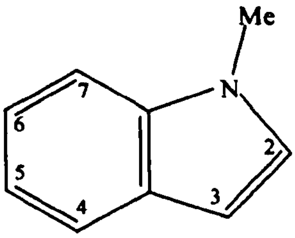
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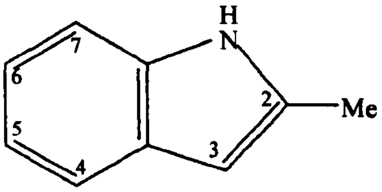
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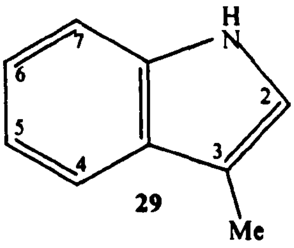
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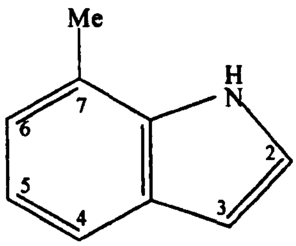
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Figure 7.6. Aniline, pyridines and diazabenzenes

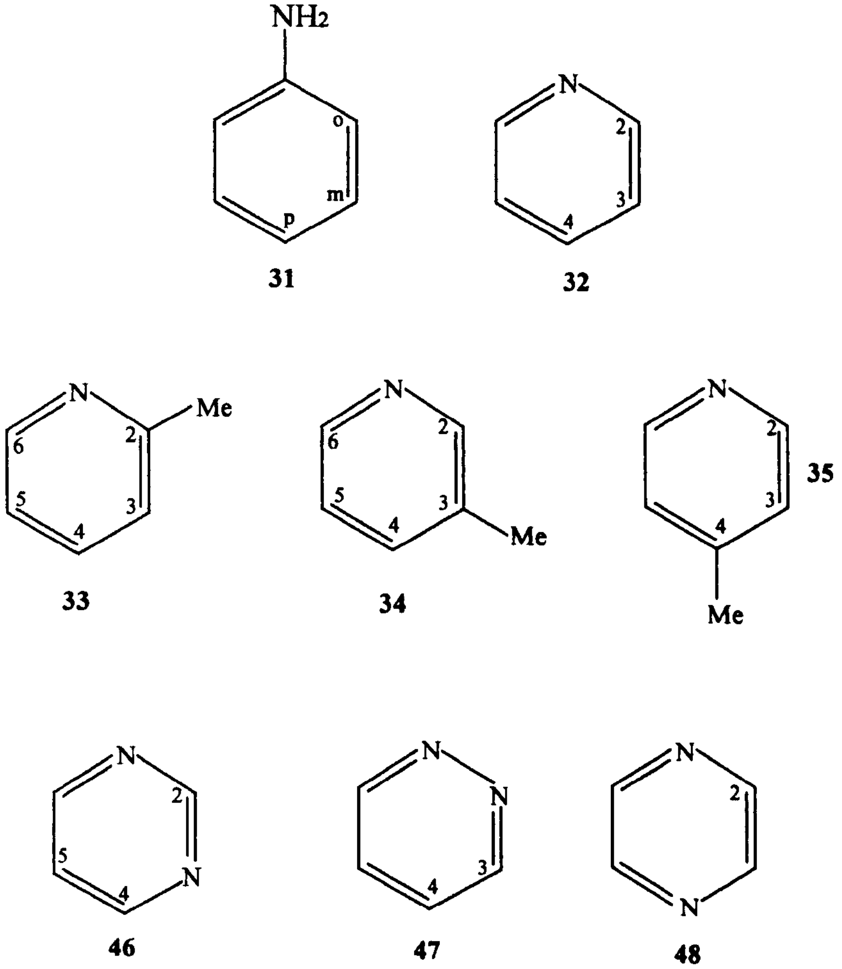
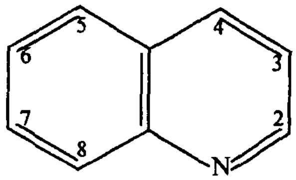


Figure 7.7. Quinolines and iso-quinolines.



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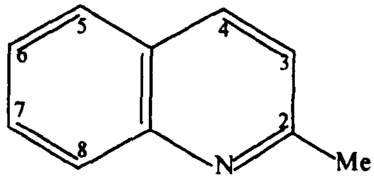

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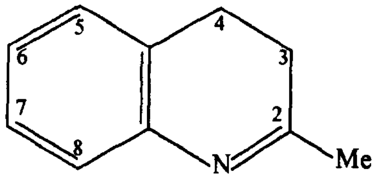

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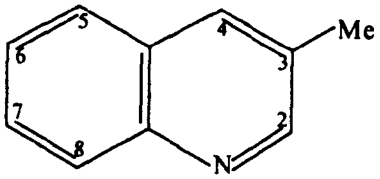

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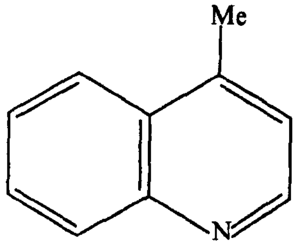

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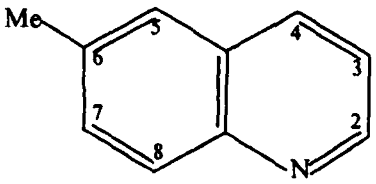

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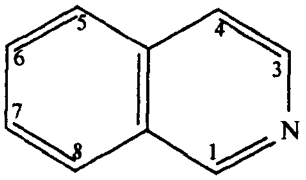

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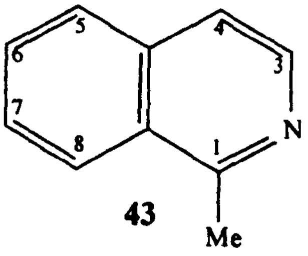

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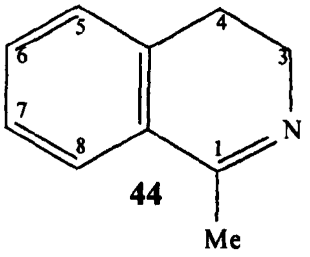

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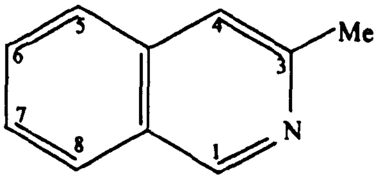

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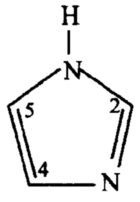
Figure 7.8. Imidazoles, Thiazoles and Oxazole.



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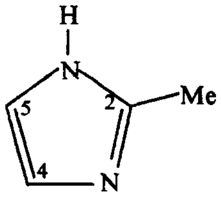

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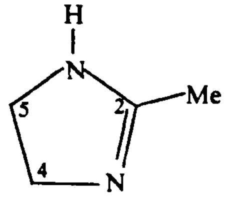

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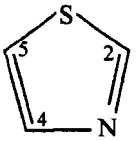

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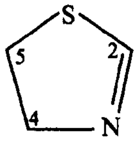

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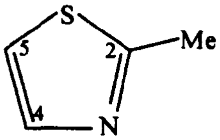

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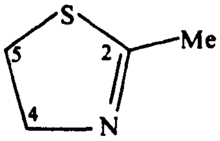

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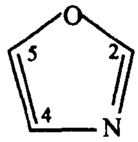

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7.2. Application of the theory to hetero-aromatic compounds.

A detailed account of the CHARGE theory can be seen previously (chapter two).

a) *Identifying aromatic systems.*

The major contributions to the proton chemical shifts in hetero-aromatic compounds are ring current and π-electron effects, with smaller contributions due to charge densities, hence α, β and γ-effects and the long-range contributions. It was therefore necessary to determine the π-electron densities at each atom and the ring currents in the compounds investigated. These will be discussed in depth below. As discussed in chapter two, subroutines were added to the CHARGE model in order to take into account a range of aromatic systems, with its capabilities extended to incorporate systems such as benzofuran, quinoline and systems containing two heteroatoms. With this done, it was necessary to parameterise the ring currents, π-electron effects and electronic effects in hetero-aromatic compounds.

b) *Ring Currents.*

As we have seen in chapter three, the CHARGE model was modified to be able to determine the aromatic ring current at a given proton in a number of aromatic compounds from the equivalent dipole model, **eqtn.3.1**.

$$\delta_{rc} = fc\,\mu\,(3\cos^2\theta - 1) / R^3 \qquad \textbf{(Eqtn.3.1)}$$

Where:

δ_{rc} is the chemical shift due to the aromatic ring current.

R is the distance of the proton from the benzene ring centre.

θ the angle of the *R* vector from the benzene ring symmetry axis.

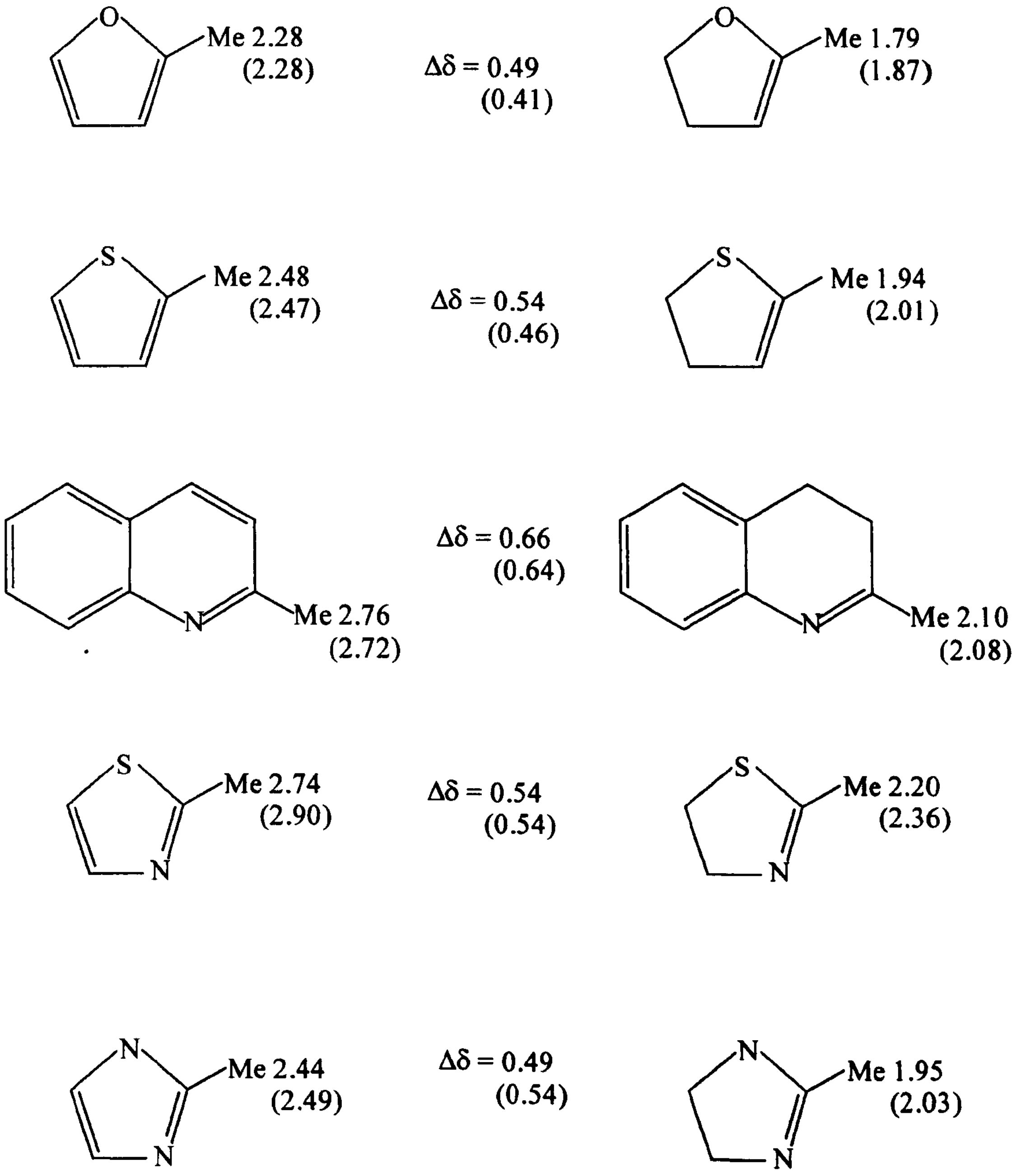
μ is the equivalent dipole of the benzene ring.

fc is the π-electron current density for the benzenoid ring, being equal to 1.0 for benzene.

In this investigation it was therefore necessary to determine the ring current density *fc*, for the different hetero-aromatic ring systems under investigation. As has been stated previously, the CHARGE model calculates the molecular ring current by use of method B in chapter two, using the Pauling model[13]. The method implemented for the parameterisation of the ring currents was that utilised in earlier work by Abraham and Thomas as discussed in the introduction. For the furans, thiophenes, imdazoles and thiazoles the ring current was calculated by examining the proton chemical shift of methyl groups in the C-2 position of the ring in the aromatic and dihydro compounds. Hence, the ring current was modified in order to obtain a calculated value of $\Delta\delta CH_3$, the difference in chemical shift between the CH_3 in the aromatic and 4, 5-dihydro compound, which matched the experimental value of $\Delta\delta CH_3$. This value of $\Delta\delta CH_3$ represents the chemical shift change of the methyl group due to the ring current. This method was also used to determine the ring current in the hetero-aromatic ring of quinoline and isoquinoline, using the 2-methylquinoline/2-methyl-3, 4-dihydroquinoline and 1-methylisoquinoline/1methyl-3, 4-isoquinoline.

In **figure 7.9** is the experimental vs. calculated chemical shift of the methyl protons and the $\Delta\delta$ values in the following aromatics.

Figure 7.9. Observed vs. calculated (in parenthesis) chemical shifts and Δδ values for methyl protons in aromatic and dihydro derivatives. (All values in ppm).



In order to calculate *fc* in the remaining compounds, all of the proton chemical shifts in the ring systems were included in the parameterisation. 4, 5-dihydropyrrole compounds decompose rapidly and as a result relevant chemical shift data could not be obtained. The same may be said for pyridine and its methyl derivatives (2, 3 and 4-picoline) and also the diazabenzenes. No data for 2-methyloxazole could be found in the literature and as a result all protons in the ring must be considered in this system.

Table 7.3. Calculated ring current intensities in various hetero-aromatic families.

Molecule	Ring current intensity (*fc*)
Furans	0.67
Pyrroles	0.72
Thiophenes	0.83
Pyridines	0.85
Diazabenzenes	0.72
Quinolines/Isoquinolines	0.75
Imidazoles	0.61
Thiazoles	0.76
Oxazoles	0.67

Inspection of **table 7.3** shows the calculated values of *fc* for all the ring systems investigated. These calculated values give the best fit with the observed chemical shift data. These optimised values will be considered in detail later.

c) π-electron densities.

The π systems in the range of hetero-aromatic compounds investigated are varied and often complex, ranging from systems such as that in furans and vinylethers to benzofurans and quinolines. Because of the nature of these compounds it was necessary for the CHARGE model to differentiate the various π systems encountered. For example, the non-aromatic π system of vinylmethylether may be quite different to that of furan and phenol as the influence of a substituent on a aromatic sp_2 carbon may be different to that on a non-aromatic sp_2 carbon and therefore it was necessary to treat these compounds separately. It was also important to consider that the π systems in five and six membered hetero-aromatic rings may differ.

To overcome this problem routines were added to the CHARGE model in order to calculate the π-electron densities in the various hetero-aromatic systems, treating compounds containing oxygen, sulphur and nitrogen as separate entities, and breaking these down to calculate the π-electron densities in unsaturated non-aromatic, five membered, six membered and the two ring systems (e.g. quinoline and indole). It was also necessary to differentiate the different types of nitrogen atoms present in these compounds. The nitrogen atom in aniline, labelled $N_{(1)}$, is in a different hybridisation state to that of the nitrogen atom in pyrrole $N_{(2)}$ and pyridine $N_{(3)}$.

From the theory (chapter two) we have seen that the CHARGE model calculates π-electron densities from Huckel theory using **eqtn. 2.11**.

$$\alpha_r = \alpha_0 + h_r\beta_0 \qquad \textbf{(Eqtn.2.11)}$$

$$\beta_{rs} = k_{rs}\beta_0$$

Where:

α_0 and β_0 are the coulomb and resonance integrals for a carbon $2p_Z$ atomic orbital.

As a result it was necessary to determine the values of the atomic orbital coefficients h_r and k_{rs} which are the Huckel integrals for Csp_2-X, where X = O, S, N. These were calculated for the five membered hetero-aromatics, six membered hetero-aromatics, five attached to six membered ring heteroaromatics, quinolines and isoquinoline systems and the non-aromatic vinyl ethers.

The π-electron densities were reproduced from those calculated using GAUSSIAN98W[14]. As we have seen in previous chapters the results from the *ab initio* calculations are very dependent on the basis set used and different values of dipole moments and π-electron densities may be obtained from using different basis sets. It was found that using the 3-21G basis set at the B3LYP level gave the best values of dipole moment for the compounds investigated and as a result the π-electron densities from this basis set were used to parameterise the Huckel calculations.

The accuracy of the π-electron densities calculated in the CHARGE scheme may be examined by calculating the dipole moments of some hetero-aromatic systems. The calculated vs. observed (in parenthesis) dipole moments[15] (D) of vinylmethylether, furan, thiophene, pyrrole, phenol, indole and quinoline are 0.94(1.11), 0.88(0.72), 0.70(0.53), 1.59(1.74), 1.56(1.50), 1.78(2.09) and 2.20(1.94). This general agreement demonstrates support for π-electron density calculations and the electron densities (π) and dipole moments calculated for a range of compounds by the CHARGE model and GAUSSIAN98W are given in **table 7.1.**

Table 7.1. π charges (milli-electrons), and dipole moments μ (D), for methylvinylether, furan, thiophene, pyrrole, pyridine and indole.

Compound	**Atom**	**Method**				
		STO-3G	**3-21G**	**6-31G**	**CHARGE**	**Observed**
Vinylmethyl ether	C_1	-58	-156	-11	-76	
	C_2	-132	-18	-137	2	
	O	216	236	193	74	
	μ	***1.46***	***1.09***	***1.319***	***0.94***	***1.23***
Furan	C_2	-130	-107	-94	-48	
	C_3	-72	-75	-68	-33	
	O	404	364	323	162	
	μ	***0.17***	***0.71***	***0.97***	***0.88***	***0.72***
Thiophene	C_2	-113	-130	-133	-61	
	C_3	-58	-35	-32	-18	
	S	342	330	331	157	
	μ	***0.57***	***0.72***	***0.82***	***0.70***	***0.53***
Pyrrole	C_2	-129	-125	-92	-75	
	C_3	-88	-93	-87	-57	
	N	434	436	394	264	
	μ	***2.00***	***2.03***	***1.93***	***1.59***	***1.74***
Pyridine	C_2	4	22	36	47	
	C_3	7	-3	-2	3	
	C_4	24	39	41	30	
	N	-47	-78	-110	-119	
	μ	***2.00***	***2.25***	***2.49***	***2.02***	***2.15***
Indole	C_2	-83	-76	-66	-48	
	C_3	-97	-106	-102	-70	
	C_4	-13	-11	-13	-9	
	C_5	-29	-37	-36	-21	
	C_6	-18	-22	-21	-13	
	C_7	-52	-57	-55	-21	
	N	392	394	347	234	
	μ	***2.15***	***2.26***	***2.16***	***1.78***	***2.09***

Note that π-electron densities for phenol, thiophenol and aniline have been calculated in previous work.

Values of k_{rs} and h_r for Csp_2-X gave π-electron densities in reasonable agreement with those calculated from *ab initio* calculations. These values can be seen in **table 7.2.**

Table 7.2. Values of k_{rs} and h_r for Csp_2-X where X = O, S, N in a range of hetero-aromatic, substituted and non-aromatic compounds.

Compound	**k_{rs}**	**h_r**
Phenol	1.45	0.90
Furan	1.69	0.59
Vinylmethylether	1.13	0.59
Benzofuran	1.223	0.59
Thiophenol	1.27	0.66
Vinylmethylsulfide	0.97	0.40
Thiophene	1.27	0.47
Benzothiophene	0.79	0.47
Pyrrole	1.60	1.28
Indole	1.50	1.28
Pyridine	0.30	1.00
Imidazole (Csp_2-N=Csp_2)	0.16	1.00
Imidazole (Csp_2-NH-Csp_2)	1.60	1.28

d) Electronic effects (α, β and γ-effects).

As we have seen in previous chapters of this work, the α, β, and γ-effects of the substituents are due to electronic effects and are modelled on a semi-empirical basis. The α-effect has been determined previously in chapter three and hence only the β and γ-effects must be determined. The β-effect is calculated directly from the heteroatom electronegativity and proton polarisability. There are a significant number of γ-effects (GSEF) to calculate and these will be discussed in more details later.

e) Long-range effects.

The long-range effects in aromatic compounds have been analysed previously (chapter three) and as a result no further parameterisation is required. The electric field effects due to the C-H and C-X (where X=O, S, Nsp_3, N-pyrrole and N-pyridine) are calculated by CHARGE directly from partial atomic charges as the coefficient A_Z in **eqtn.2.8.** has already been determined. The steric effects for aromatic protons have also been previously determined in chapter three and there are no steric effect on any aromatic protons from the heteroatoms in this investigation.

7.3. Experimental.

Phenol (**2**), anisole (**3**), benzofuran (**10**), thionaphthene (**19**), indole (**26**) and N-methyl (**27**), 2-methyl (**28**), 3-methyl (**29**) and 7-methylindoles (**30**), aniline (**31**), pyridine (**32**), 2-picoline (**33**), 3-picoline (**34**), quinoline (**36**), 2-methyl (**37**), 3-methyl (**39**), 4-methyl (**40**) and 6-methylquinolines (**41**) and isoquinoline (**42**) were obtained commercially[17], [18].

^1H and ^{13}C NMR were obtained on a Bruker Avance spectrometer operating at 400.13MHz for proton and 100.63MHz for carbon. HMQC, HMBC and NOE experiments were also conducted.

The spectra were generally recorded in 10mg cm^{-3} solutions (^1H) and ca.50mg cm^{-3} (^{13}C) with a probe temperature of ca.25°C in $CDCl_3$ and referenced to TMS unless indicated otherwise. Typical running conditions of the spectrometers were 128 transients, spectral width 3300Hz and 32k data points. This gave an acquisition time of 5s and zero-filled to 128k to give a digital resolution of 0.025Hz.

The 2D experiments were conducted using the standard Bruker COSY-DQF and HMQC pulse sequences[19]. The geometry's of the compounds investigated were obtained by use of the program PC MODEL Version 7.0[20]. The molecular geometry's of the compounds investigated were optimised using the GAUSSIAN98 programme at the B3LYP/6-31G** levels[14]. The GAUSSIAN98 and CHARGE calculations were carried out using a PC.

7.4. Spectral Analysis.

The ^{1}H NMR assignments of compounds of all the compounds investigated can be seen in **tables 7.4-7.15**, along with the calculated ^{1}H chemical shifts from the CHARGE model.

Phenol (2)

The ^{1}H spectrum of **2** consists of 3 different proton resonances.

Anisole (3)

The ^{1}H spectrum of **3** consists of 3 resonances. By examination of the integrals H-4 is immediately identified as a triplet of triplets half the size of the two other resonances. H-2 and H-3 are identified as a doublet and doublet of doublets respectively.

Benzofuran (10)

The ^{1}H spectrum of **10 (fig 7.10)** consists of 7 resonances. H-2 is immediately identified as a doublet occurring at ca.7.60δ. A ^{1}HCOSY identified H-3 from its strong coupling to H-2. A 2D ^{1}H/^{13}C HMQC spectrum was then recorded to assign C-2 and C-3 from correlations to the respective protons. H-4 then was assigned by its correlation to C-3 in a 2D ^{1}H/^{13}C HMBC plot **(fig.7.11)**. The remaining protons were then assigned from the ^{1}HCOSY. H-5 can be seen to have a large coupling to H-4, H-6 a large coupling to H-5 and H-7 a large coupling to H-7. This assignment was confirmed from the 2D ^{1}H/^{13}C HMQC and HMBC experiments.

Fig.7.10. ^{1}H spectrum of benzofuran.

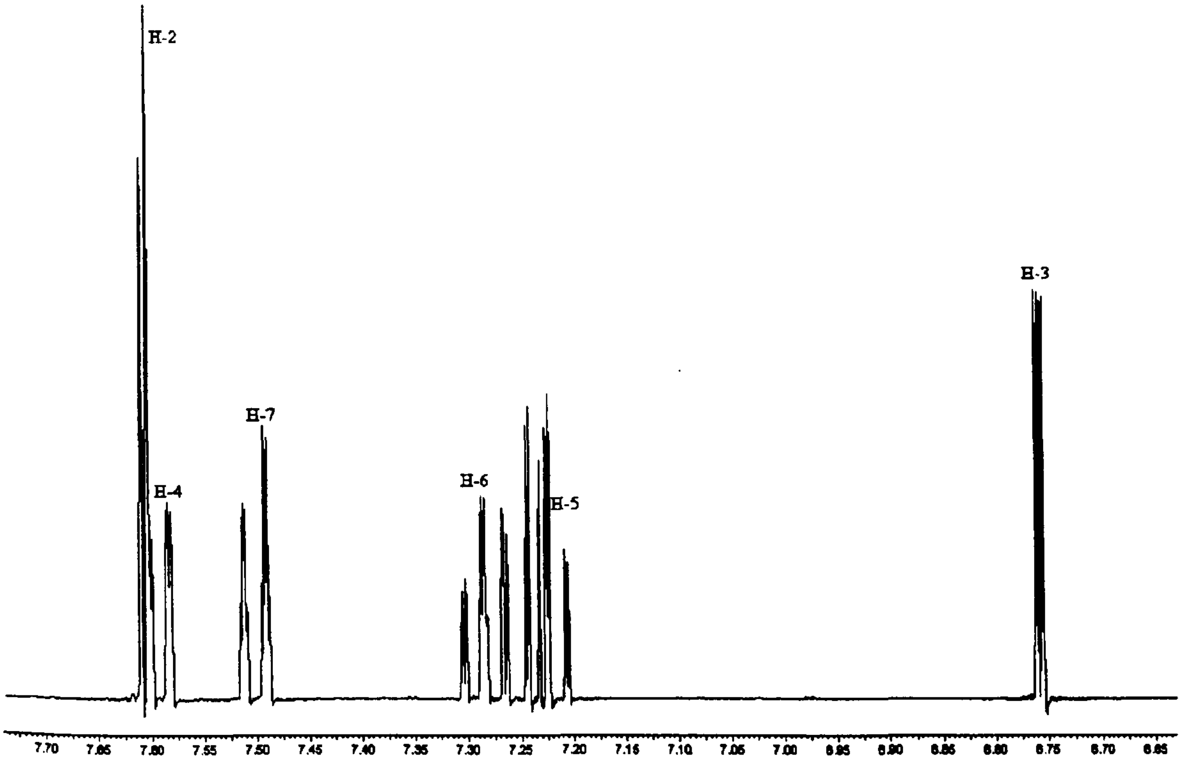
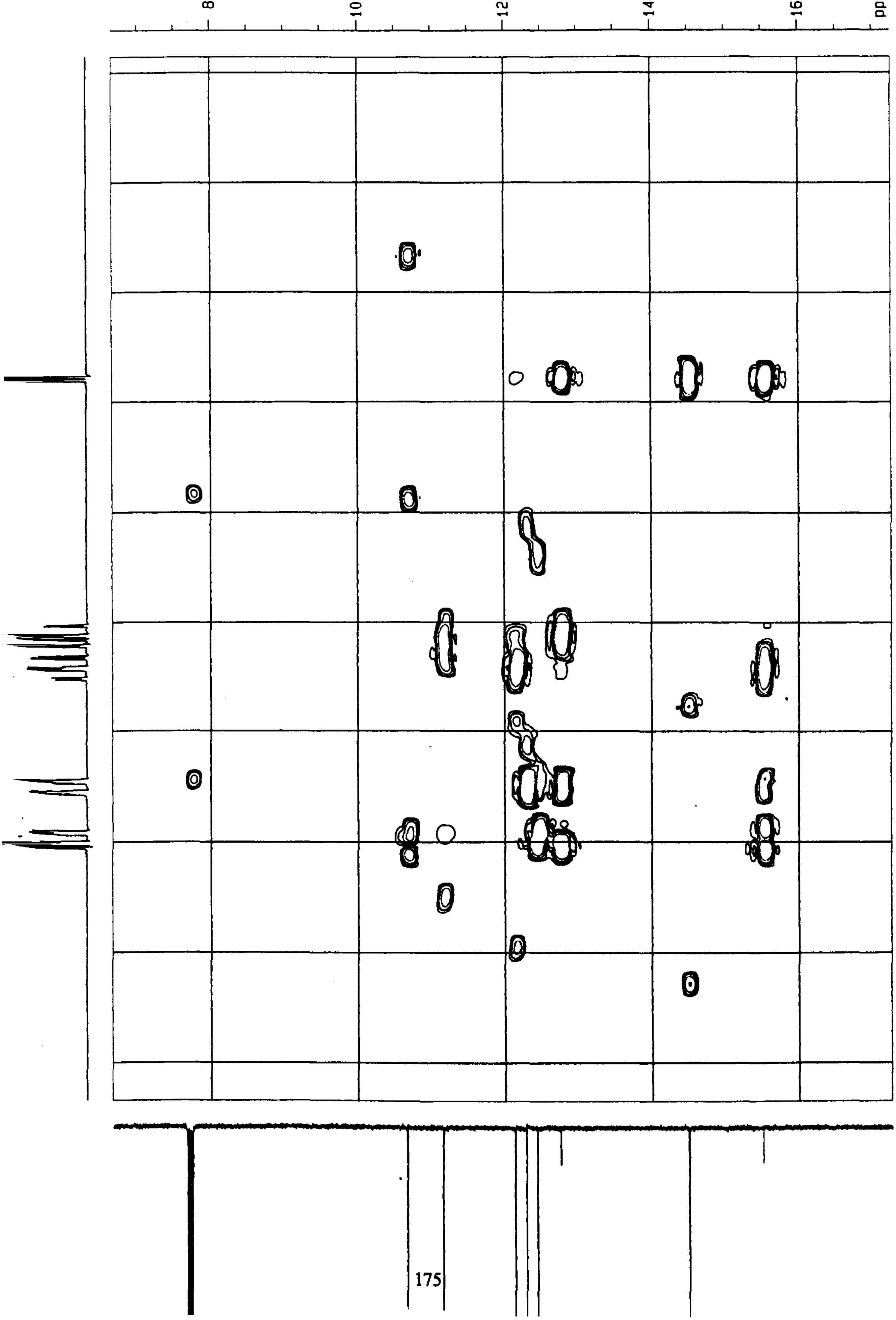


Fig.7.11. $^1H/^{13}C$ HMBC spectrum of benzofuran



Thionaphthene (19)

The ^{1}H spectrum of **19** consists of 7 resonances. H-2 is immediately identified as a large doublet occurring at ca.7.42δ. By examination of a ^{1}HCOSY, H-3 was readily assigned from its coupling to H-2. Performing an NOE experiment on the suspected H-4 resonances and observing an NOE on H-3 identified H-4. The remaining protons were then assigned from the ^{1}HCOSY. H-5 can be seen to have a large coupling to H-4, H-6 a large coupling to H-5 and H-7 a large coupling to H-7. This assignment was confirmed by performing 2D ^{1}H/^{13}C HMQC and HMBC experiments.

Indole (26)

The ^{1}H spectrum of **26** consists of 7 resonances. H-3 is immediately identified as the multiplet occurring at ca.6.55δ. By examination of a ^{1}HCOSY, H-2 was readily identified by its strong coupling to H-3. A 2D ^{1}H/^{13}C HMQC spectrum was then recorded to assign C-2 and C-3 from correlations to the respective protons. H-4 was then assigned by its correlation to C-3 in a 2D ^{1}H/^{13}C HMBC plot. By performing an NOE experiment on H-3, H-4 was identified as the doublet of quartets occurring at ca.7.65δ. The remaining resonances were assigned by use of the ^{1}HCOSY plot.

N-methylindole (27)

The ^{1}H spectrum of **27** consists of 6 well separated resonances including the methyl resonance. H-2 is immediately identified as a doublet occurring at ca.7.00δ. By examination of a ^{1}HCOSY plot H-3 is assigned from its coupling to H-2. An NOE experiment performed on H-3 allowed us to assign H-4 and the remaining protons were assigned by examination of the ^{1}HCOSY plot.

2-Methylindole (28)

The ^{1}H spectrum of **28** consists of 5 well separated resonances including the methyl resonance. H-3 is immediately assigned as the multiplet occurring at ca.6.20δ. This can be confirmed by examination of a ^{1}HCOSY plot. H-3 can be seen to have a coupling with the methyl group. A 2D ^{1}H/^{13}C HMQC spectrum was then recorded to assign C-3 from correlation to the H-3. H-4 was then assigned by its correlation to C-3 in a 2D

$^1H/^{13}C$ HMBC plot. The remaining protons were assigned by examination of the ^{1}HCOSY plot.

3-Methylindole (29)

The ^1H spectrum of **29** consists of 5 well separated resonances including the methyl resonance. H-2 is immediately assigned as the multiplet occurring at ca.6.95δ. This can be further confirmed by examination of a ^{1}HCOSY plot. H-2 can be seen to have a coupling with the methyl group. H-4 is readily assigned by performing an NOE experiment on the methyl group. The remaining resonances can then be assigned by examination of the ^{1}HCOSY plot.

7-Methylindole (30)

The ^1H spectrum of **30** consists of 5 well separated resonances including the methyl resonance. H-5 is immediately assigned as the quartet, with coupling to H-6 and H-4 (ca.6Hz). H-6 can be seen a two complex doublets, coupling with the methyl group. This is further confirmed by performing an NOE experiment on the methyl group. H-4 is assigned from its coupling to H-5. H-3 is assigned by performing an NOE experiment on H-4 and H-2 is subsequently assigned form the ^{1}HCOSY plot from its coupling to H-3.

Aniline (31)

The ^1H spectrum of **31** consists of 3 different resonances. By examination of the integrals H-4 is immediately identified as a triplet of triplets half the size of the two other resonances. H-2 and H-3 are identified as a doublet and doublet of doublets respectively.

Pyridine (32)

The ^1H spectrum of **32** consists of 3 different resonances. By examination of the integrals H-4 is immediately identified as a triplet of triplets half the size of the two other resonances. H-2 and H-3 are identified as a doublet and doublet of doublets respectively.

2-Picoline (33)

The ^1H spectrum of **33** consists of 4 different resonances. H-3 is immediately identified as a doublet occurring at ca.7.10δ. By examination of a ^{1}HCOSY plot H-4 is immediately assigned from its large coupling to H-3. H-5 and H-6 are subsequently assigned from large couplings to H-4 and H-5 respectively.

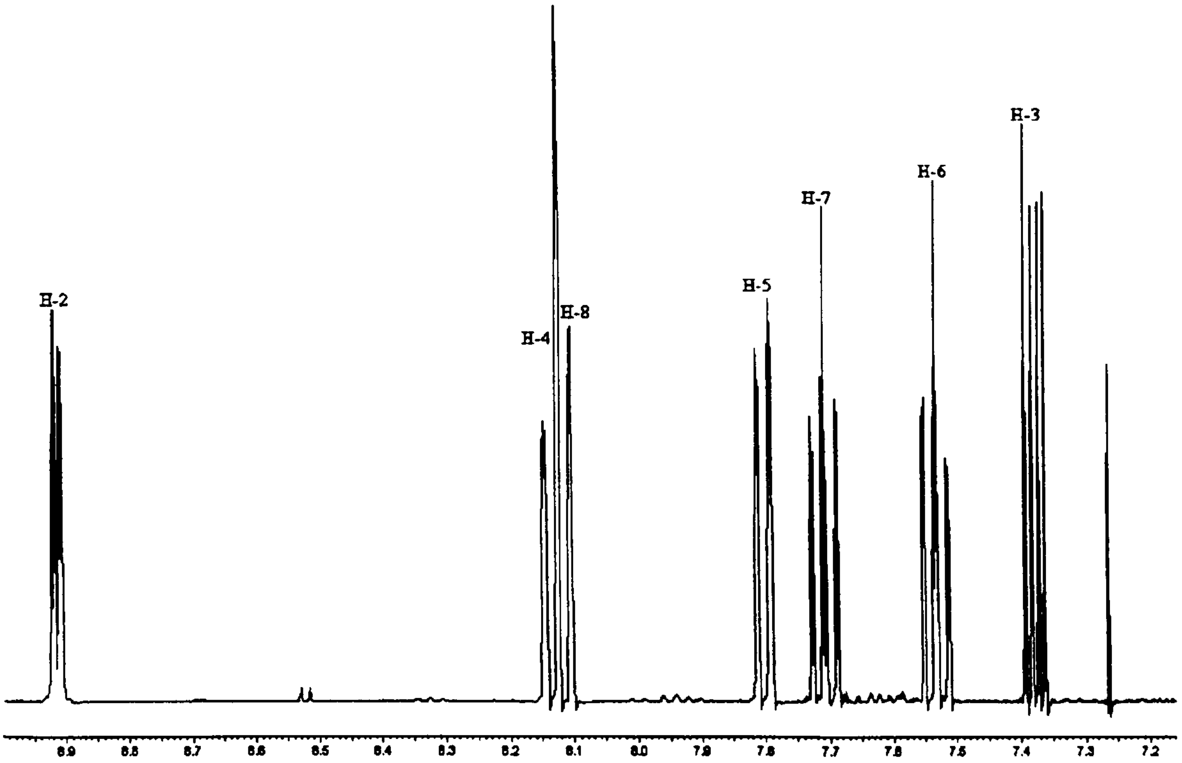
3-Picoline (34)

The ^{1}H spectrum of **34** consists of 4 different resonances. H-2 is immediately identified as a singlet occurring at ca.8.45δ. H-4 is identified as a doublet which is split further by its coupling to the methyl group. By examination of a ^{1}HCOSY plot H-5 is immediately assigned from its large coupling to H-4. H-6 is assigned from large couplings to H-5.

Quinoline (36)

The ^{1}H spectrum of **36 (fig.7.12)** consists of 7 well separated resonances. H-3 is immediately assigned as quartet, with couplings to H-2 and H-4. By examination of a ^{1}HCOSY plot H-2 and H-4 are identified from large couplings to H-3, with H-2 shifted downfield due to the close proximity of the nitrogen atom. By performing a 2D ^{1}H/^{13}C HMQC plot the ^{13}C assignment of C-2, C-3 and C-4 were made by correlations to the respective protons. H-5 was then assigned on the basis of a HMBC correlation to C-4. With the assignment of H-5 made, H-6, H-7 and H-8 were made by examination of the ^{1}HCOSY plot.

Fig.7.12. ^1H spectrum of quinoline.



2-Methylquinoline (37)

The ^1H spectrum of **37** consists of 6 well separated resonances plus the methyl resonance. H-3 is immediately identified as a doublet occurring at ca.7.25δ. By examination of a ^{1}HCOSY plot H-4 is assigned from its strong coupling to H-3. By performing a 2D $^1H/^{13}C$ HMQC plot the ^{13}C assignment of C-3 and C-4 were made by correlations to the respective protons. H-5 was then assigned on the basis of a HMBC correlation to C-4. With the assignment of H-5 made, H-6, H-7 and H-8 were made by examination of the ^{1}HCOSY plot.

3-Methylquinoline (39)

The ^1H spectrum of **39** consists of 6 well separated resonances including the methyl resonance. H-2 and H-4 are immediately assigned as two doublets with a small coupling (ca.2.3Hz). H-2 occurs is shifted downfield due to the proximity of the nitrogen atom. The same procedure as used in the cases of quinoline and 2-methylquinoline was undertaken to assign H-5, H-6, H-7 and H-8.

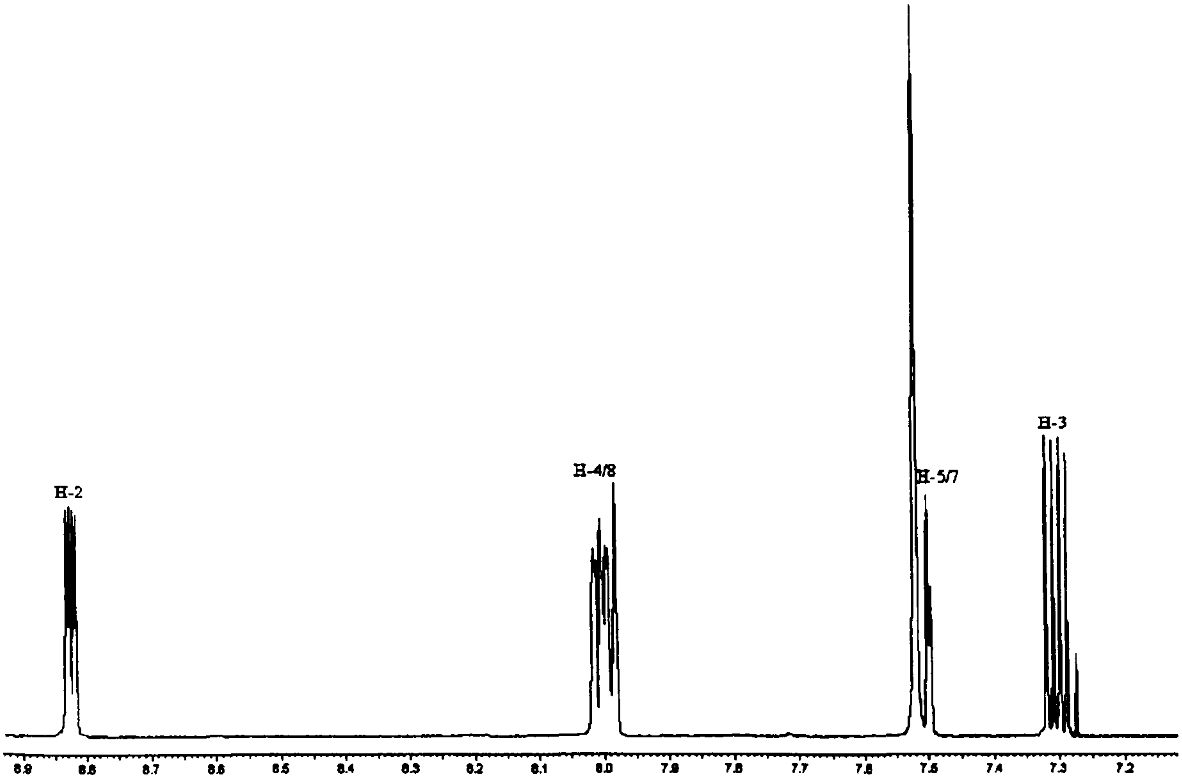
4-Methylquinoline (40)

The ^{1}H spectrum of **40** consists of 6 well separated resonances including the methyl resonance. H-2 and H-3 are immediately assigned as doublets, with H-2 shifted downfield due to the proximity of the nitrogen atom. H-5 was assigned by performing an NOE experiment on the methyl group. Using a ^{1}HCOSY plot, H-6, H-7 and H-8 were subsequently assigned from correlations starting from H-5.

6-Methylquinoline (41)

The ^{1}H spectrum of **41** (**fig.7.13**) consists of 6 different protons including the methyl resonance. From examination of the integrals, two resonances, each made up of two protons are seen to occur at ca. 8.00 and 7.50δ. H-5 is immediately assigned as the singlet occurring at ca.7.50δ. H-2 is seen as a doublet of doublets occurring downfield at ca.8.80δ due to the proximity of the nitrogen atom. By examination of a ^{1}HCOSY plot H-3 and H-4 are subsequently assigned, with H-3 seen to have a large coupling to H-2. By performing a 2D ^{1}H/^{13}C HMQC plot the ^{13}C assignment of C-5 was made by correlation to H-5. H-7 was then assigned on the basis of a HMBC correlation to C-5. With the assignment of H-7 made (occurring at 7.50δ), H-8 was the only remaining resonance unaccounted for, the doublet overlapping with the resonance from H-4 at ca.8.00δ.

Fig.7.13. ^1H spectrum of 6-methylquinoline.

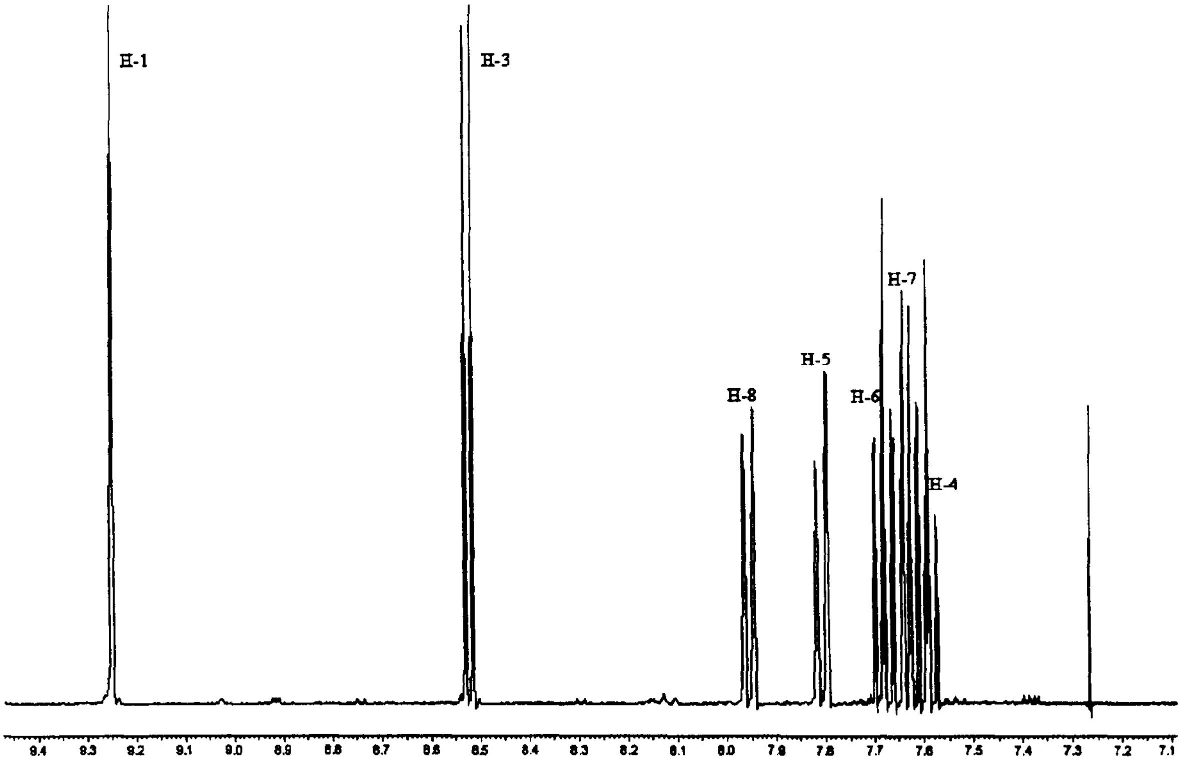


Isoquinoline (42)

The ^1H spectrum of **42** (**fig.7.14**) consists of 7 different proton resonances. H-1 is immediately identified as the singlet occurring at ca.9.25δ. Examination of a ^{1}HCOSY plot indicates two resonances (both doublets occurring at ca.8.50 and 7.65δ respectively) displaying only one coupling, that being a coupling to eachother. This clearly indicated that these resonances belong to H-3 and H-4. By performing a 2D $^1H/^{13}C$ HMQC plot the ^{13}C assignment of C-1 was made by correlation to H-1. H-3 was then assigned on the basis of a HMBC correlation to C-1. With the assignment of H-3 made (occurring at 8.50δ), H-4 was the other doublet occurring at 7.65δ.

By examination of the HMQC plot the ^{13}C assignments of C-3 and C-4 were made by correlations to the respective protons. H-5 was then assigned on the basis of a HMBC correlation to C-4. With the assignment of H-5 made, H-6, H-7 and H-8 were made by examination of the ^{1}HCOSY plot.

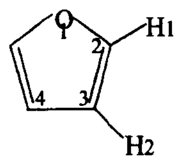
Fig.7.14. ^{1}H spectrum of isoquinoline.



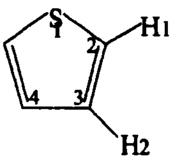
7.5. Results.

The data collected in **table's 7.4-7.15** provide a rigorous test of the CHARGE model and also the present ring current theories that have previously been applied to aromatic hydrocarbons (chapter three). The compounds examined in this work are all of fixed conformation with the exception of the imidazoles, which exist in a tautomeric equilibrium. The GAUSSIAN98W (B3LYP/6-31G**) and the PCMODEL calculations gave molecular geometries for the hetero-aromatics in excellent agreement with the experimental geometries, where known. For example, observed vs. calculated (obtained using G98W) bond lengths furan, thiophene, pyrrole and pyridine can be seen in **figure 7.15**.

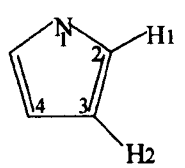
Figure 7.15. Experimental[21] and (calculated) bond length (Å) for furan, thiophene, pyrrole and pyridine.



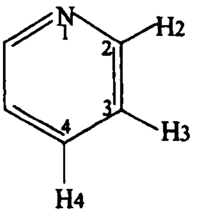
O_1-C_2 = 1.362 (1.364)
C_2-C_3 = 1.361 (1.361)
C_3-C_4 = 1.431 (1.436)
C_2-H_1 = 1.075 (1.079)
C_3-H_2 = 1.077 (1.080)



S_1-C_2 = 1.714 (1.736)
C_2-C_3 = 1.370 (1.367)
C_3-C_4 = 1.423 (1.430)
C_2-H_1 = 1.078 (1.081)
C_3-H_2 = 1.081 (1.084)



N_1-C_2 = 1.370 (1.375)
C_2-C_3 = 1.382 (1.378)
C_3-C_4 = 1.417 (1.425)
C_2-H_1 = 1.076 (1.080)
C_3-H_2 = 1.077 (1.081)



N_1-C_2 = 1.338 (1.339)
C_2-C_3 = 1.394 (1.396)
C_3-C_4 = 1.392 (1.394)
C_2-H_2 = 1.087 (1.089)
C_3-H_3 = 1.088 (1.086)
C_4-H_4 = 1.082 (1.086)

From the data above we may observe the excellent agreement of the G98W calculated bond lengths with the experimental values.

The β-effect is calculated directly from the carbon electronegativity and proton polarisability. Thus the only other electronic effect to be considered is the γ-effects (H.C.X.Y) of the unsaturated carbon atoms and heteroatoms in the aromatic compounds. For the analysis of the γ-effect of any nucleus, a simple angular function (A+Bcosθ) may be utilised. This approach has been implemented in all the investigations in this work. The coefficients **A** and **B** are obtained from the observed data.

a) Oxygen containing unsaturated and hetero-aromatic compounds.

The experimental data for the oxygen containing compounds provides us with an extensive data set, which allows us to calculate the chemical shifts in these compounds using the CHARGE model.

Table 7.4. Observed vs. calculated ^{1}H chemical shifts (δ) for compounds **1-10**.

Compound	^{1}H Number	Observed	Calculated
Vinylmethylether (**1**)	1-gem	6.530	6.616
	2-cis	4.160	4.190
	2-trans	4.000	4.024
Phenol (**2**)	o	6.781	6.877
	m	7.321	7.212
	p	6.891	6.926
Anisole (**3**)	o	6.897	6.861
	m	7.277	7.239
	p	6.934	6.926
	Me	3.789	3.738
Furan (**4**)	2	7.420	7.415
	3	6.380	6.360
4, 5-dihydrofuran (**5**)	2	6.310	6.160
	3	4.950	4.902
	4	2.580	2.384
	5	4.310	4.224
2-Methylfuran (**6**)	3	5.940	5.923
	4	6.230	6.289
	5	7.270	7.189
	Me	2.280	2.278
2-Methyl-4, 5-dihydrofuran (**7**)	3	4.570	4.458
	4	2.580	2.432
	5	4.310	4.273
	Me	1.790	1.867
2, 5-Dimethylfuran (**8**)	3	5.810	5.848
	Me	2.220	2.295
3-Methylfuran (**9**)	2	7.160	6.917
	4	6.220	6.193
	5	7.290	7.450
	Me	2.030	2.172
Benzofuran (**10**)	2	7.607	7.807
	3	6.758	6.671
	4	7.593	7.514
	5	7.225	7.239
	6	7.285	7.312
	7	7.502	7.400

From **table 7.4**, we observe a very good agreement between observed and calculated chemical shifts. However we do notice that there are some discrepancies in the calculated data. In the case of 3-methylfuran we observe that H-2 and H-5 are ca.0.15ppm lower and larger than the observed chemical shifts respectively. It seems that in the case of the 2 and 3-methylfurans the position of the methyl group has a significant influence on the chemical shifts.

We also observe that H-2 in benzofuran is 0.2ppm larger than the observed value. In benzofuran the six-membered ring may have a significant effect on the electron distribution and ring current within the whole system and this may account for the downfield shifts of H-2 and H-3 with respect to furan.

From the observed data in **table 7.4** it is very interesting to note the influence of an additional double bond. We see the ring current shift of H-2 and the C-2 methyl in going from the dihydro to the aromatic furan of ca.1.10 and 0.41ppm respectively. It is also interesting to note the influence of the introduction of a methyl group to protons in the furan ring. We observe that all the protons in 2-methyl and 3-methylfuran are shifted upfield with respect to unsubstituted furan, especially protons that are γ to the methyl group. The electron donating methyl groups are pushing electron density onto the ring protons, hence the upfield shift.

The parameters to be determined from the results in **table 7.4** are the ring current intensity for furan *fc*, and the γ-effects. The β-effect of the oxygen atom has been previously determined and requires no further parametrisation. In this investigation we include the molecules methylvinylether and phenol. We must note that only the parameterisation of γ-effects is needed for these molecules.

As we have discussed previously, the ring current for furan is calculated by examining the proton chemical shift of the methyl groups in the C-2 position of the ring in the aromatic and 4, 5-dihydro furans, in order to obtain a calculated value of $\Delta\delta CH_3$, the difference in chemical shift between the CH_3 in the aromatic and 4, 5-dihydro compound, which gave good agreement with the experimental value of $\Delta\delta CH_3$. A value of *fc* of 0.67 gave a value of $\Delta\delta CH_3$ of 0.41ppm, which compares with the observed value of 0.49ppm.

The γ-effects that must be parameterised are from the heteroatom atom to the γ proton ($X.Csp_2.Csp_2.H$ and $X.Csp_2.Csp_3.H$) and from an sp_2 and sp_3 carbon atom through the heteroatom ($Csp_2.X.Csp_2.H$ and $C.sp_3.X.Csp_2.H$). Note that the parameterisations of γ-effects on methyl hydrogen atoms ($X.Csp_2.Csp_3.H$) are treated separately from methine and methylene protons. Hence only γ-effects on methyl protons and not on H-4 and H-5 protons in any of the dihydro compounds are determined in this investigation.

We must also note that the gamma substituents effect (GSEF) $X.Csp_2.Csp_2.H$ must be determined for three separate systems when appropriate, them being the non-aromatic (e.g.methylvinylether, 4, 5-dihydrofuran), phenol/aniline systems and the hetero-aromatic systems (e.g.furan, pyridine, etc). In the case of the oxygen containing compounds, phenol and anisole display only one GSEF (O.Cps2.Csp2.H), which needs to be determined. This was found to display no orientational dependence and a value of the coefficient of 0.032 was calculated. The remaining unknowns were achieved by using the non-linear least mean squares programme (CHAP8)[16] to give the best fit with the observed data from **table 7.4**, excluding the phenol and anisole data. A total of 26 proton chemical shifts were included in the iteration spanning a range of ca.1.8 to 7.6ppm and were calculated with an rms. error of 0.073ppm.

The GSEF $O.Csp_2.Csp_2.H$ was found to display an orientational dependence with respect to the protons in question and an A + Bcosθ term was incorporated into the CHARGE model. It was found that only one term was needed for both the non-aromatic systems and the aromatic furans. Values of the coefficients **A** and **B** were determined and can be seen in **eqtn.7.1**.

$$\mathrm{GSEF} = -0.554 - 0.085\cos\theta \qquad \textbf{(Eqtn.7.1)}$$

The GSEF $O.Csp_2.Csp_3.H$ displays no orientational dependence and the coefficient C, was determined.

$$\mathrm{GSEF}\ (O.Csp_2.Csp_3.H) = 0.20/160.84 \qquad \textbf{(Eqtn.7.2)}$$

The GSEF's ($Csp_2.O.Csp_2.H$ and $C.sp_3.O.Csp_2.H$) displayed no orientational dependence and the coefficients **D** and **E** were determined.

$$\text{GSEF } (Csp_2.O.Csp_2.H) = 0.428/160.84 \qquad \textbf{(Eqtn.7.3)}$$

$$\text{GSEF } (C.sp_3.O.Csp_2.H) = 0.563/160.84 \qquad \textbf{(Eqtn.7.4)}$$

Therefore the final parameterisation for the oxygen containing compounds included π-electron densities, ring current and electronic effects operating on all protons within molecules.

It is of interest to examine the individual contributions to the chemical shift in the furans. **Table 7.5** gives the observed versus calculated chemical shifts for selected molecules, along with the electric field, ring current and π-shift contributions.

Table 7.5. Calculated and observed chemical shift (δ) with C-H electric field, ring current and π-shift contributions for furan (**4**), 2-methyl (**6**)/3-methylfuran (**9**) and benzofuran (**10**).

Compound	**^{1}H Number**	**Observed**	**Calculated**	**C-H Electric field**	**Ring current**	**π-shift**
4	2	7.420	7.415	-0.110	1.600	-0.549
	3	6.380	6.360	-0.057	1.507	-0.487
6	3	5.940	5.923	-0.126	1.514	-0.733
	4	6.230	6.289	-0.024	1.503	-0.585
	5	7.270	7.189	-0.077	1.595	-0.799
	Me	2.280	2.278	-0.054	0.500	0.000
9	2	7.160	6.917	-0.180	1.596	-0.855
	4	6.220	6.193	-0.121	1.513	-0.464
	5	7.290	7.450	-0.082	1.607	-0.534
	Me	2.030	2.172	-0.077	0.466	0.000
10	2	7.607	7.807	-0.030	1.905	-0.536
	3	6.758	6.671	-0.079	1.958	-0.664
	4	7.593	7.514	-0.151	1.967	-0.175
	5	7.225	7.239	-0.060	1.771	-0.250
	6	7.285	7.312	-0.046	1.762	-0.184
	7	7.502	7.400	-0.121	1.985	-0.246

From the above data we observe the very significant ring current and π-shift contributions to the proton chemical shift. We can see clearly the influence the introduction of a methyl group has on the π-electron density in the furan ring and thus the chemical shifts. We also observe significant π-shifts in benzofuran. Here we observe a small but significant difference in H-2 and H-3 compared to that in furan, indicating the difference between the two types of ring system. We may also observe the larger ring current contribution to the shifts of H-2 and H-3 in benzofuran compared to furan, indicating how the presence of an adjoining six membered ring on the furan ring has a significant effect on the ring current contribution to the shift of H-2 and H-3 in benzofuran. We also note that the C-H electric field, ring current and pi-shift contributions do not add up to the calculated value in the table. The remaining contributions are the charge effects (α, β and γ-effects).

b) *Sulphur containing unsaturated and hetero-aromatic compounds.*

The experimental data for the sulphur containing compounds provides us with an extensive data set, which allows us to calculate the chemical shifts in these compounds using the CHARGE model.

Table 7.6. Observed vs. calculated ^{1}H chemical shifts (δ) for compounds **11-19**.

Compound	**^{1}H Number**	**Observed**	**Calculated**
Vinylmethylsulfide (**11**)	gem	6.460	6.549
	cis	5.200	5.189
	trans	4.970	4.833
Thiophenol (**12**)	o	7.230	7.316
	m	7.190	7.276
	p	7.110	7.081
Thiophene (**13**)	2	7.310	7.263
	3	7.090	7.044
4, 5-dihydrothiophene (**14**)	2	6.170	6.076
	3	5.630	5.717
	4	2.740	2.592
	5	3.220	3.169
2-Methylthiophene (**15**)	3	6.720	6.598
	4	6.870	6.970
	5	7.040	7.017
	Me	2.480	2.470
2-Methyl-4, 5-dihydrothiophene (**16**)	3	5.250	5.248
	4	2.790	2.657
	5	3.260	3.195
	Me	1.940	2.009
2, 5-Dimethylthiophene (**17**)	3	6.560	6.520
	Me	2.400	2.481
3-Methylthiophene (**18**)	2	6.870	6.766
	4	6.870	6.866
	5	7.190	7.305.
	Me	2.280	2.214
Thionaphthene (**19**)	2	7.422	7.523
	3	7.325	7.347
	4	7.780	7.642
	5	7.330	7.302
	6	7.310	7.340
	7	7.860	7.996

From **table 7.6**, we observe a very good agreement between observed and calculated chemical shifts. Like in the furan family we do notice that there are some discrepancies in the calculated data. Like in the case of 3-methylfuran, H-2 and H-5 in 3-methylthiophene are ca.0.12ppm lower and larger than the observed chemical shifts respectively. In the case of 2-methylthiophene we observe that H-3 is ca.0.12ppm lower than the observe value. As seen in the furans, the position of the methyl group in the 2 and 3-methylthiophenes has a significant influence on the chemical shifts.

We observe an excellent agreement between the observed and calculated chemical shift in thionapthene, with the observed chemical shifts of H-2 and H-3 significantly larger than in thiophene itself. Again, the six-membered ring may have a significant effect on the electron distribrution and ring current of the thiophene ring and this may account for the downfield shift of H-2 and H-3 with respect to thiophene.

It is again interesting to note the influence of an additional double bond. We observe the ring current shift of H-2 and the C-2 methyl in going from the dihydro to the aromatic thiophene of ca.1.14 and 0.54ppm respectively. We again make the observation that on the introduction of a methyl group to the thiophene ring the protons are shifted upfield with respect to thiophene, especially protons that are γ to the methyl group.

The parameters to be determined from **table 7.6** are exactly the same as those in the oxygen containing compounds and are determined in the same way. The ring current intensity for thiophene *fc*, and the γ-effects must be determined. The β-effect of the sulphur atom has been previously determined and requires no further parametrisation.

The ring current for thiophene was calculated in the same way as furan and a value of *fc* of 0.83 was determined and gave a value of $\Delta\delta CH_3$ of 0.46ppm, which compares with the observed value of 0.54ppm.

The γ-effects to parameterise are the same as in the oxygen compounds and the following unknowns were determined. For thiophenol only one GSEF (S.Cps2.Csp2.H) needed to be determined and the values of the coeffiecients **A** and **B** were determined as 0.064 and –0.249. The remaining unknowns were achieved by using the CHAP8 programme to give the best fit with the observed data from **table 7.6**, excluding thiophenol. A total of 25 proton chemical shifts were included in the iteration spanning a range of ca.1.9 to 7.9ppm and were calculated with an rms. error of 0.059ppm.

The GSEF S.Csp$_2$.Csp$_2$.H displayed an orientational dependence with respect to the protons in question and an A + Bcosθ term was incorporated into the CHARGE model. It was found that separate terms were needed for the non-aromatic systems and the aromatic thiophenes. Values of the coefficients **A** and **B** were determined for non-aromatic and aromatic systems and can be seen in **eqtn.7.5** and **7.6**.

$$\mathrm{GSEF} = 0.092 - 0.434\cos\theta \qquad \textbf{(Eqtn.7.5)}$$

$$\mathrm{GSEF} = -0.141 - 0.180\cos\theta \qquad \textbf{(Eqtn.7.6)}$$

The GSEF S.Csp$_2$.Csp$_3$.H displays no orientational dependence and the coefficient **C**, was determined.

$$\mathrm{GSEF\ (S.Csp_2.Csp_3.H)} = 0.36/160.84 \qquad \textbf{(Eqtn.7.7)}$$

The GSEF's (Csp$_2$.S.Csp$_2$.H and C.sp$_3$.S.Csp$_2$.H) displayed no orientational dependence and coefficients **D** and **E** were determined.

$$\mathrm{GSEF\ (Csp_2.S.Csp_2.H)} = -0.159/160.84 \qquad \textbf{(Eqtn.7.8)}$$

$$\mathrm{GSEF\ (C.sp_3.S.Csp_2.H)} = 0.157/160.84 \qquad \textbf{(Eqtn.7.9)}$$

The final parameterisation for the sulphur containing compounds therefore included π-electron densities, ring current and electronic effects operating on all protons within molecules.

It is again of interest to examine the individual contributions to the chemical shift in the thiophenes. **Table 7.7** gives the observed versus calculated chemical shifts for selected molecules, along with the electric field, ring current and π-shift contributions.

Table 7.7. Calculated and observed chemical shift (δ) with C-H electric field, ring current and π-shift contributions for thiophene (**13**), 2-methyl (**15**), 3-methylthiophene (**18**) and benzothiophene (**19**).

Compound	^{1}H Number	Observed	Calculated	C-H Electric field	Ring current	π-shift
13	2	7.310	7.263	-0.095	1.679	-0.641
	3	7.090	7.044	-0.052	1.764	-0.333
15	3	6.720	6.598	-0.130	1.775	-0.588
	4	6.870	6.970	-0.023	1.761	-0.430
	5	7.040	7.017	-0.068	1.667	-0.898
	Me	2.480	2.470	-0.045	0.542	0.000
18	2	6.870	6.886	-0.171	1.692	-0.620
	4	6.870	6.866	-0.122	1.773	-0.303
	5	7.190	7.305.	-0.065	1.676	-0.620
	Me	2.280	2.214	-0.072	0.564	0.000
19	2	7.422	7.523	-0.026	1.934	-0.702
	3	7.325	7.347	-0.089	2.235	-0.545
	4	7.780	7.642	-0.162	2.095	-0.122
	5	7.330	7.302	-0.061	1.786	-0.172
	6	7.310	7.340	-0.046	1.778	-0.140
	7	7.860	7.996	-0.115	2.058	-0.175

From the above data we observe the very significant ring current and π-shift contributions to the proton chemical shifts and we observe the same trends as in the furan family. We again observe the influence the introduction of a methyl group has on the π-electron density in the thiophene ring and thus the chemical shifts. We also observe a significant π-shift in thionaphthene. Like in the furans we observe a small but significant difference in H-2 and H-3 compared to that in thiophene, indicating the difference between the two types of ring system. We also observe the larger ring current contribution to the shifts of H-2 and H-3 in thionaphthene compared to thiophene. It will be interesting to compare the magnitude of these contributions in different 5-membered hetero-aromatics families and this will be discussed later.

c) *Aniline, pyrroles and indoles.*

The experimental data for aniline, pyrroles and indole compounds provides us with an extensive data set, which allows us to calculate the chemical shifts in these compounds using the CHARGE model.

Table 7.8. Observed vs. calculated ^{1}H chemical shifts (δ) for compounds **31** and **20-25**.

Compound	**^{1}H Number**	**Observed**	**Calculated**
Aniline (**31**)	o	6.650	6.609
	m	7.136	7.132
	p	6.740	6.676
Pyrrole (**20**)	2	6.710	6.708
	3	6.230	6.187
N-methylpyrrole (**21**)	2	6.670	6.590
	3	6.110	6.155
	N-Me	3.600	3.513
2-Methylpyrrole (**22**)	3	5.890	5.784
	4	6.110	6.112
	5	6.640	6.508
	Me	2.270	2.285
2, 5-Dimethylpyrrole (**23**)	3	5.720	5.704
	Me	2.200	2.300
1, 2, 5-Trimethylpyrrole (**24**)	3	5.750	5.677
	Me	2.190	2.254
	N-Me	3.330	3.586
3-Methylpyrrole (**25**)	2	6.530	6.264
	4	6.020	5.988
	5	6.650	6.722
	Me	2.090	2.153

Table 7.9. Observed vs. calculated ^{1}H chemical shifts (δ) for compounds **26-30**.

Compound	^{1}H Number	Observed	Calculated
Indole (**26**)	2	7.207	7.321
	3	6.558	6.643
	4	7.647	7.489
	5	7.115	7.212
	6	7.185	7.263
	7	7.396	7.358
N-methylindole (**27**)	2	7.001	7.204
	3	6.466	6.611
	4	7.615	7.488
	5	7.092	7.211
	6	7.204	7.258
	7	7.292	7.330
	N-Me	3.742	3.813
2-Methylindole (**28**)	3	6.216	6.189
	4	7.508	7.443
	5	7.059	7.186
	6	7.104	7.202
	7	7.282	7.347
	Me	2.445	2.469
3-Methylindole (**29**)	2	6.964	6.832
	4	7.584	7.496
	5	7.121	7.212
	6	7.189	7.264
	7	7.301	7.370
	Me	2.335	2.427
7-Methylindole (**30**)	2	7.207	7.326
	3	6.563	6.654
	4	7.498	7.276
	5	7.031	7.143
	6	6.994	6.893
	Me	2.502	2.620

From **table's 7.8** and **7.9**, we observe a very good agreement between observed and calculated chemical shifts. Like in the previous hetero-aromatic families we notice that there are some discrepancies in the calculated data. For H-2 in 3-methylpyrrole the calculated chemical shift is ca.0.27ppm lower than the observed value. We also note that the calculated chemical shifts for H-4 in the indole's is consistently lower than the observed shifts by a substantial amount. We also observe an error in the case of H-2 and H-5 in 2-methylpyrrole, which are ca.0.11ppm lower than the observed chemical shifts.

From the tables we observe an excellent agreement between the observed and calculated chemical shift in indole, with the observed chemical shifts of H-2 and H-3 significantly larger than in pyrrole itself. For all N-, 2- and 3-methyl substituted indoles the chemical shifts of H-2 and H-3 are at higher field than those in indole itself, confirming the influence of the methyl group on the chemical shifts.

The parameters to be determined from **table's 7.8** and **7.9** are again the same as those in the previous studies. However, because of the chemical instability of non-aromatic pyrrole models we cannot determine the ring current intensity *fc* in the same way as has been seen for furan and thiophene. Therefore all the unknowns are determined by performing iterations on all the observed chemical shifts. The γ-effects in these compounds must be determined, with the β-effect of the nitrogen atom having been determined in a previous investigation.

As stated previously the nitrogen atoms in aniline, pyrroles/indoles and pyridines/quinolines are treated as different and as a result γ-effects from or through these nitrogen atoms must be parameterised separately. For aniline the γ-effect has been determined in a previous investigation and no further parameterisation is required. The unknowns including the ring current intensity *fc*, were achieved by using the CHAP8 program to give the best fit with the observed data from **table's 7.8** and **7.9**. A total of 49 proton chemical shifts were included in the iteration spanning a range of ca.2.0 to 7.7ppm and were calculated with an rms. error of 0.107ppm.

A value of the ring current intensity of 0.72 for the pyrroles and indoles was determined along with the various GSEF's. The GSEF $N_{(2)}.Csp_2.Csp_2.H$ displayed an orientational dependence with respect to the protons in question and an A + Bcosθ term was incorporated into the CHARGE model. Values of the coefficients **A** and **B** can be seen in **eqtn.7.10** and **7.11**.

$$\text{GSEF} = 0.300 - 0.293\cos\theta \qquad \textbf{(Eqtn.7.10)}$$

The GSEF $N_{(2)}.Csp_2.Csp_3.H$ displays no orientational dependence and the coefficient C, was determined.

$$\text{GSEF } (N_{(2)}.Csp_2.Csp_3.H) = 0.19/160.84 \qquad \textbf{(Eqtn.7.11)}$$

The GSEF's ($Csp_2.N_{(2)}.Csp_2.H$ and $C.sp_3.N_{(2)}.Csp_2.H$) displayed no orientational dependence and coefficients **D** and **E** were determined.

$$\mathrm{GSEF}\ (Csp_2.N_{(2)}.Csp_2.H) = 0.188/160.84 \qquad \textbf{(Eqtn.7.12)}$$

$$\mathrm{GSEF}\ (C.sp_3.N_{(2)}.Csp_2.H) = -0.070/160.84 \qquad \textbf{(Eqtn.7.13)}$$

The final parameterisation for aniline, pyrroles and indoles therefore included π-electron densities, ring current and electronic effects operating on all protons within molecules.

It is again of interest to examine the individual contributions to the chemical shift in the thiophenes. **Table 7.10** gives the observed versus calculated chemical shifts for selected molecules, along with the electric field, ring current and π-shift contributions.

Table 7.10. Calculated and observed chemical shift (δ) with C-H electric field, ring current and π-shift contributions for pyrrole (**20**), 2-methyl (**22**)/3-methylpyrrole (**25**) and indole (**26**).

Compound	^{1}H Number	Observed	Calculated	C-H Electric field	Ring current	π-shift
20	2	6.710	6.708	-0.105	1.645	-0.865
	3	6.230	6.187	-0.054	1.633	-0.830
22	3	5.890	5.784	-0.125	1.641	-1.043
	4	6.110	6.112	-0.023	1.628	-0.928
	5	6.640	6.508	-0.075	1.640	-1.088
	Me	2.270	2.285	-0.051	0.510	0.000
25	2	6.530	6.264	-0.176	1.652	-1.117
	4	6.020	5.988	-0.120	1.639	-0.839
	5	6.650	6.722	-0.077	1.641	-0.872
	Me	2.090	2.153	-0.073	0.503	0.000
26	2	7.207	7.321	-0.029	1.938	-0.618
	3	6.558	6.643	-0.081	2.083	-0.866
	4	7.647	7.489	-0.153	2.016	-0.196
	5	7.115	7.212	-0.060	1.775	-0.254
	6	7.185	7.263	-0.046	1.767	-0.212
	7	7.396	7.358	-0.118	2.002	-0.272

From the above data we observe the trends identified in the furan and thiophene families. Again we observe very significant ring current and π-shift contributions to the proton chemical shifts. The introduction of a methyl group again has a significant effect on the π-electron densities in the pyrrole ring. The chemical shifts of H-2 and H-3 in indole are more downfield than the corresponding protons in pyrrole, indicating the difference between the two types of ring system.

d) Pyridines, diazabenzenes, quinolines and isoquinolines.

The experimental data for the pyridines, diazabenzenes, quinolines and isoquinolines provides us with a comprehensive and extensive data set, which allows us to calculate the chemical shifts in these compounds using the CHARGE model.

Table 7.11. Observed vs. calculated ^{1}H chemical shifts (δ) for pyridine (**32**), 2-picoline (**33**), 3-picoline (**34**) and 4-picoline (**35**).

^{1}H Number	32		33		34		35	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
2	8.609	8.577	--------	--------	8.440	8.331	8.440	8.584
3	7.266	7.279	7.014	7.027	--------	--------	7.080	7.027
4	7.657	7.574	7.571	7.574	7.465	7.319	--------	--------
5	7.266	7.279	7.195	7.213	7.159	7.268	7.080	7.027
6	8.609	8.577	8.599	8.597	8.407	8.500	8.440	8.584
Me	--------	--------	2.547	2.608	2.320	2.319	2.320	2.310

Table 7.12. Observed vs. calculated ^{1}H chemical shifts (δ) for quinoline (**36**), 2-methylquinoline (**37**), 2-methyl-3, 4-dihydroquinoline (**38**), 3-methylquinoline (**39**) and 4-methylquinoline (**40**) and 6-methylquinoline (**41**).

^{1}H Number	36		37		38		39		40		41	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
2	8.915	8.865	——	——	——	——	8.760	8.662	8.770	8.865	8.825	8.836
3	7.377	7.429	7.295	7.215	——	——	——	——	7.212	7.147	7.303	7.419
4	8.139	8.122	8.055	8.141	——	——	7.876	7.822	——	——	8.005	8.109
5	7.803	7.841	7.778	7.844	——	——	7.714	7.827	7.985	7.822	7.522	7.546
6	7.533	7.509	7.485	7.482	——	——	7.489	7.500	7.552	7.499	——	——
7	7.709	7.571	7.561	7.627	——	——	7.627	7.542	7.697	7.569	7.512	7.367
8	8.114	8.060	8.024	8.050	——	——	8.066	8.062	8.104	8.067	7.995	8.071
Me	——	——	2.757	2.716	2.100	2.083	2.482	2.416	2.692	2.531	2.501	2.416

Table 7.13. Observed vs. calculated ^{1}H chemical shifts (δ) for isoquinoline (**42**) and 1-methylisoquinoline (**43**), 1-methyl-3, 4-dihydroisoquinoline (**44**) and 3-methylisoquinoline (**45**).

^{1}H Number	42		43		44		45	
	Obs.	**Obs.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
1	9.251	9.177	------	------	------	------	9.150	9.207
3	8.522	8.539	8.370	8.556	3.670	------	------	------
4	7.635	7.621	7.440	7.538	2.710	------	7.410	7.329
5	7.808	7.800	7.730	7.817	7.180	7.210	7.680	7.793
6	7.680	7.596	7.600	7.595	7.360	7.553	7.590	7.588
7	7.594	7.533	7.510	7.526	7.300	7.360	7.480	7.507
8	7.955	7.915	8.040	7.897	7.480	7.394	7.880	7.918
Me	------	------	2.910	2.851	2.400	2.428	2.690	2.707

Table 7.14. Observed vs. calculated ^{1}H chemical shifts (δ) pyrimidine (**46**), pyrazine (**47**) and pyridazine (**48**).

^{1}H Number	46		47		48	
	Obs.	**Calc.**	**Obs.**	**Calc.**	**Obs.**	**Calc.**
2	9.250	9.248	----------	----------	8.600	8.476
3	----------	----------	9.220	9.316	8.600	8.476
4	8.770	8.856	7.560	7.646	----------	----------
5	7.270	7.245	7.560	7.646	8.600	8.476
6	8.770	8.856	9.220	9.316	8.600	8.476

From **table's 7.11-7.14**, we observe a good agreement between observed and calculated chemical shifts, in particular the correlation in quinoline and isoquinoline. Again, there are a number of discrepancies in the calculated data but overall an excellent agreement can be seen. H-2 in 4-picoline is ca.1.4ppm larger than the observed chemical shift and H-5/H-7 in 4-methylquinoline are some ca.1.4ppm smaller than the observed shifts. We again also note that the introduction of a methyl group to an aromatic system has a significant effect on the proton chemical shifts.

We notice from the table's the significant difference in the chemical shifts of H-2, H-3 and H-4 in pyridine and quinoline, again indicating that the adjoining six-memebered ring has a significant effect on the electron distribrution and ring current in the quinolines and isoquinolines.

We again note the influence of an additional double bond. In the case of 2-methylquinoline and 1-methylisoquinoline we observe the ring current shift of the 2 and 1-

methyl groups in going from the dihydro to the aromatic compounds of ca.0.65 and 0.51ppm respectively.

The parameters to be determined from the tables are the ring current intensity for pyridines, diazabenzenes and the quinolines/isoquinolines. The β-effects of the $N_{(3)}$ atom have been previously determined and require no further parametrisation, with the exception of the beta effect on H-2 in pyrimidine, which has two β nitrogen atoms. A non-orientational dependent BSEF was added to the CHARGE model and a value of coefficient of 0.83 was determined for this one proton.

Aside from this one BSEF only the γ-effects need to be determined. The ring current intensities for the pyridines and diazabenzenes must be determined by performing iterations on all the data since no non-aromatic model exists for these compounds. In the case of the quinolines/isoquinolines we implement the method used for the ring current calculations of furan and thiophene. A value of *fc* of 0.75 was calculated for quinoline and isoquinoline. This gave calculated values of $\Delta\delta CH_3$ of 0.63 and 0.42ppm, which compare with the observed values of 0.55 and 0.51ppm.

Values of the ring current intensities of 0.85 and 0.72 for the pyridines and diazabenzenes were determined along with the various GSEF's by performing iterations on the observed data using the CHAP8 program. A total of 84 proton chemical shifts were included in the iteration spanning a range of ca.2.0 to 9.4ppm and were calculated with an rms. error of 0.088ppm.

The GSEF $Csp_2.N_{(3)}.Csp_2H$ has been determined in a previous investigation and does not require parameterisation. The GSEF $N_{(3)}.Csp_2.Csp_2.H$ displayed an orientational dependence with respect to the protons in question and an A + Bcosθ term was incorporated into the CHARGE model. Values of the coefficients **A** and **B** were determined for non-aromatic and aromatic systems and can be seen in **eqtn.7.14**.

$$GSEF = 0.093 - 0.326\cos\theta \qquad \textbf{(Eqtn.7.14)}$$

The GSEF $N_{(3)}.Csp_2.Csp_3.H$ displays no orientational dependence and the coefficient C, was determined.

$$GSEF\ (N_{(3)}.Csp_2.Csp_3.H) = 0.50/160.84 \qquad \textbf{(Eqtn.7.15)}$$

The final parameterisation for the pyridines, diazbenzenes and quinolines/isoquinloines therefore included π-electron densities, ring current intensities and electronic effects operating on all protons within molecules.

e) *Imidazoles, thiazoles and oxazoles.*

The experimental data for the imidazoles, thiazoles and oxazole is not extensive but gives us enough data to calculate the chemical shifts using the CHARGE model and thus quantify the ring current intensities, π-electron effects and electronic effects in these compounds.

Table 7.15 Observed vs. calculated ^{1}H chemical shifts (δ) imidazole (**49**), 2-methylimidazole (**50**), 2-methyl-3, 4-dihydroimidazole (**51**), thiazole (**52**), 2-methylthiazole (**53**), 2-methyl-3, 4-dihydrothiazole (**54**) and oxazole (**55**).

^{1}H No.	49		50		51		52		53		54		55	
	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc
2	7.74	7.78	—	—	—	—	8.88	8.84	—	—	—	—	7.90	7.92
4	7.13	6.87	6.97	6.77	3.60	—	7.98	8.08	7.64	8.10	3.32	—	7.68	7.59
5	7.13	6.87	6.97	6.77	3.60	—	7.41	7.16	7.17	6.93	4.22	—	7.15	7.44
Me	—	—	2.44	2.49	1.95	2.03	—	—	2.74	2.83	2.20	2.29	—	—

From **table 7.15**, we observe a good agreement between observed and calculated chemical shifts but we do notice some substantial differences between the calculated and observed data. From the table we see the large discrepancies in the calculated shifts of H-4/5 in imidazole and 2-methylimidazole, H-5 in thiazole and oxazole and H-4 in 2-methylthiazole.

We again note the influence of an additional double bond. In the case of 2-methylimidazole and 2-methylthiazole we observe the ring current shift of the 2-methyl groups in going from the dihydro to the aromatic compounds of ca.0.49 and 0.54ppm respectively.

The parameters to be determined from the tables are the ring current intensities and a number of β-effects for the imidazole, thiazole and oxazole. The β-effects to parameterise are on H-2 and both adjacent heteroatoms influence the chemical shift, hence three separate effects need to be parameterised. The ring current intensities for imdazole and thiazole are determined in the same way as in furan, with the value of *fc* for oxazole determined from the three available proton shifts.

Values of *fc* of 0.61 and 0.76 were calculated for imidazole and thiazole. This gave calculated values of $\Delta\delta CH_3$ of 0.49 and 0.54ppm, which compare with the observed values of 0.54 and 0.54ppm.

A value of *fc* of 0.67 was determined for oxazole along with the various BSEF's by performing iterations on the observed data using the CHAP8 program. A total of 11 proton chemical shifts were included in the iteration spanning a range of ca.2.0 to 9.4ppm and were calculated with an rms. error of 0.132ppm.

The values of the coefficients for the BSEF on H-2 in imdazole, thiazole and oxazole were calculated as 0.60, 1.12 and 0.34 respectively.

The final parameterisation for the imidazoles, thiazoles and oxazole therefore included π-electron densities, ring current intensities and electronic effects operating on all protons within molecules.

7.6. Discussion.

The observed vs. calculated chemical shifts in the tables is in good agreement. For the 215 data points of the above tables the rms. error (obs. vs. calc. shifts) is 0.096ppm over a range of 1.9 to 9.4ppm. The calculation provides an insight into the interpretation of these proton chemical shifts as the different interactions responsible for the calculated values are separately identified and quantified in the CHARGE model. We have seen that it is necessary to take into account the variation of ring current intensity in these hetero-aromatics to give an adequate account for the proton chemical shifts.

The ring current calculations again provide evidence for the accuracy of the simple equivalent dipole model of the benzene ring current, which has been determined in chapter three. The calculations performed also confirm that the ring current is not the only factor in accounting for the difference between the H-2 and H-3 protons in aromatic heterocycles (furan, thiophene, etc) and their non-aromatic derivatives. The difference in the experimental chemical shift of H-2 in furan and 4, 5-dihydrofuran is 1.11ppm. This is made up of 1.60ppm from the ring current with the remainder made up from π-electron and electronic effects. As seen in chapter three this has been allowed for in previous studies[22] and the above calculations again support this approach.

It is of great interest to compare the shifts of the protons in the 5-membered hetero-aromatic compounds. By examination of table's **7.4**, **7.6** and **7.8** we can see the difference in chemical shift of the protons as the heteroatom in the ring varies from oxygen, sulphur and nitrogen. The shifts of H-2 and H-3 in the aromatic 5-membered systems vary significantly. The ring current contributions to the shifts of H-2 and H-3 remain fairly constant throughout each hetero-aromatic family but we observe very different π-shift contributions, illustrating the effect the different heteroatoms must have on the π-electron density in each hetero-aromatic family. We also note the variation in the γ-effects in the furan, thiophene and pyrrole. These γ-effects vary quite considerably and illustrate the different electronic effects operating in these systems.

In the benzofuran, thionaphthene and indole we again observe the same pattern as in furan, thiophene and pyrrole. The adjoining benzenoid ring in these molecules has a significant effect on the π-electron densities on the proton chemical shifts of H-2 and H-3. We do note that we have fairly consistent ring current contributions to the chemical shifts. The same can be said for the pyridine and quinloine/isoquinolines. We observe the larger downfield shifts of protons 2/3 and 4 in quinoline compared to those in pyridine. The ring current and π-shift contributions remain relatively constant apart from H-4, which lies in a position para to the nitrogen atom. Here the ring current contribution is significantly larger in the case of quinoline.

The chemical shifts of imidazole, thiazole and oxazole are of great interest to consider. We observe a downfield shift of ca.1.0ppm for H-2 in thiazole (8.8ppm) compared to that in imidazole and oxazole. When we examine the contributions we observe that the ring current effect on H-2 is similar throughout these three systems and there is a very small pi-shift contribution to the shift of H-2 in thiazole and oxazole. The main contribution to the large downfield shift of H-2 in the case of thiazole seems to be due to electronic effects and a large β-effect is observed.

The ring current in the hetero-aromatic rings may be given by **eqtn.7.16**.

$$\mu = i\,A \qquad \textbf{(Eqtn.7.16)}$$

Where:

μ is the aromatic ring current.

A is the molecular area.

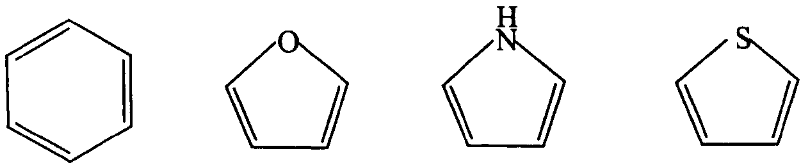
i is the equivalent dipole.

Therefore, since the observed chemical shift difference is produced by the magnetic field of the dipole, the ratio of the ring currents of a molecule in question and benzene for example can be given by the simple equation below

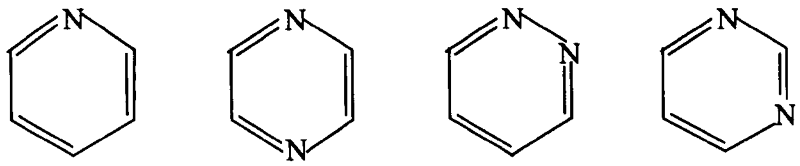
$$i/iB = \mu/\mu B * AB/A \qquad \textbf{(Eqtn.7.17)}$$

By this method we may determine the relative ring currents as a ratio of the ring current in benzene. The ring current ratios for a range of hetero-aromatics with benzene and naphthalene can be seen below in **figure 7.16.**

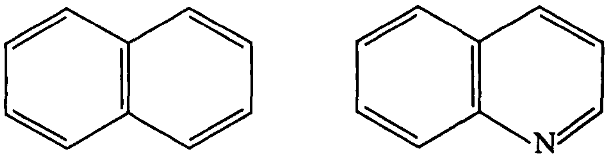
Figure 7.16. Ratio of ring currents for various hetero-aromatics with benzene and naphthalene.



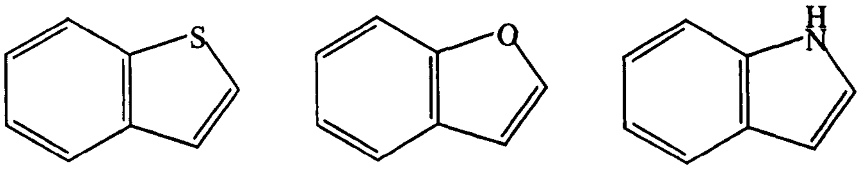
Ring current (i/iB) (i/iB = μ/μB * AB/A)	1.00	:	1.04	:	1.03	:	1.08
Equivalent dipole, μ	26.2	:	17.6	:	19.0	:	21.8



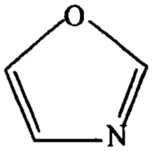
Ring current (i/iB) (i/iB = μ/μB * AB/A)	0.85	:	0.74	:	0.74	:	0.74
Equivalent dipole, μ	22.2	:	19.2	:	19.2	:	19.2

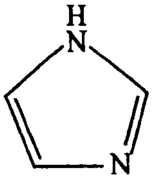


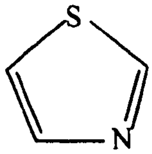
Ring current (i/iN) (i/iN = μ/μN * AN/A)	1.00	:	0.81
Equivalent dipole, μ	24.4	:	19.7



Ring current (i/iN) (i/iN = μ/μN * AN/A)	0.88	:	0.79	:	0.87
Equivalent dipole, μ	21.8	:	17.6	:	19.0







Ring current (i/iB) ($i/i_B = \mu/\mu_B * A_B/A$)	1.00	:	0.89	:	0.95
Equivalent dipole, μ	17.6	:	16.0	:	20.0

Where:

i, A & μ are the ring current, molecular area and equivalent dipole of the compound in question.

$i_{B/N}$, $A_{B/N}$, & $\mu_{B/N}$ are the ring current, molecular area and equivalent dipole of benzene and naphthalene respectively.

The areas for benzene, furan and thiophene were taken from ref.2. The program PC Model was used to calculate the areas of the remaining compounds. The results from **figure 7.16** are very interesting to consider. We see from the data that the ring currents in benzene, furan, pyrrole and thiophene are effectively the same as in benzene. The same can be said for imidazole, thiazole and oxazole. It is interesting to note that pyridine and the diazabenzenes have a smaller ring current than benzene and the benzofuran, benzothiophene, indole and pyridine have s smaller ring current than naphthalene.

In the work performed by Elvidge, the end chain of a long polyene was used and the contribution of the heteroatoms deducted. Compounds with pure σ bonds were used to determine the paramagnetic contributions in his work. Low field shifts were determined by subtracting the shift of the substituted ether ($CH_3.X.CH_3$, X = O, S and N) from that of ethane. Shift differences were thus calculated as 7.59, 8.73 and 8.78ppm for O, S and N respectively. By subtracting these values from the chemical shift of an end chain methyl group in his polyene gives the H-2 chemical shifts for furan, thiophene and pyrrole. Shifts of 0.15, 0.50 and 1.23 were determined and these are the aromaticity shifts for O, S and N. By examination of our results we see that these are very poor. It seems that the paramagnetic contribution of an oxygen atom next to a double bond as determined by Elvidge is less than that of one in a saturated system! We have seen earlier the method used by De Jongh and Wynberg and the results obtained in this investigation justifies the methods used.

7.7. Conclusions.

The agreement of the observed *vs.* calculated proton chemical shifts in the **tables** are very good. As stated previously, the ring current calculations provide further evidence for the accuracy of the simple equivalent dipole model of the benzene ring current and also demonstrates that the ring current effect is not the only factor responsible for the difference between the chemical shifts in the aromatic and non-aromatic heteroaromatic compounds.

Although the non-aromatic model is rather approximate, the use of the dihydro compounds as a non-aromatic model has been seen to be effective and less prone to error than other methods.

7.8. References

1. D.T.Davies, Aromatic Heterocyclic chemistry, 1992, Oxford University Press, Oxford
2. W.A.Thomas, PhD Thesis, University of Liverpool.
3. Elvideg, *Chem.Comm.,* 1965, 160.
4. De Jongh and Wynberg, *Tetrahedron,* 1965, **21**, 515.
5. C.J.Puchert and J.Behnke, *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra,* Aldrich Chemical Company Inc. Milwaukee, USA, 1993.
6. E.Taskien, *Mag.Res.Chem.,* 1995, **33**, **4**, 256.
7. K.Yoshida and T.Fueno, *Bul.Chem.Soc.Jpn.,* 1987, **60**, 229.
8. R.A.Aitken, J.M.Armstrong, M.J.Drysdale, F.C.Rossi and B.M.Ryan, *J.Chem.Soc.Perkin Trans.1*, 1999, 593.
9. P.M.Hatton and S.Sternhell, *J.Het.Chem.,* 1992, **29**, 933.
10. I.I.Padialla-Martinez, A.Ariza-Castolo and R.Contreras, *Mag.Res.Chem.,* 1993, **31**, 189.
11. G.Adam, J.Andrieux and M.M.Plat, *Tetrahedron Lett., 1983, **24**, 34, 3609.*
12. C.M.Shafer and T.F.Molinsk, *Heterocycles,* 2000, **53**, 5, 1167.
13. L.Pauling, *J.Chem.Phys.*, 1936, **4**, 673.

14.a) GAUSSIAN 94, Gaussian Inc., Pittsburgh PA, 1994.
M.J.Frisch, G.W.Trucks, M.Head-Gordon, P.M.W.Gill, M.W.Wong, J.B.Foresman, B.G.Johnson, H.B.Schlegel, M.A.Robb, E.S.Replogle, R.Gomperts, J.L.Andres, K.Raghavachari, J.S.Binkley, C.Gonzalez, R.L.Martin, D.J.Fox, D.J.Defrees, J.Baker, J.J.P.Stewart and J.A.Pople.

b) GAUSSIAN 98, Revision.A9, Gaussian Inc., Pittsburgh PA, 1998.
M.J.Frisch, G.W.Trucks, H.B.Schlegel, G.E.Scuseria, M.A.Robb, J.R.Cheeseman, V.G.Zakrzewski, J.A.Montgomery, Jr., R.E.Stratmann, J.C.Burant, S.Dapprich, J.M.Millam, A.D.Daniels, K.N.Kudin, M.C.Strain, O.Farkas, J.Tomasi, V.Barone, M.Cossi, R.Cammi, B.Mennucci, C.Pomelli, C.Adamo, S.Clifford, J.Ochterski, G.A.Petersson, P.Y.Ayala, Q.Cui, K.Morokuma, D.K.Malick, A.D.Rabuck, K.Raghavachari, J.B.Foresman, J.Cioslowski, J.V.Ortiz, A.G.Baboul, B.B.Stefanov, G.Liu, A.Liashenko, P.Piskorz, I.Komaromi, R.Gomperts, R.L.Martin, D.J.Fox, T.Keith,

M.A.Al-Laham, C.Y.Peng, A.Nanayakkara, M.Challacombe, P.M.W.Gill, B.Johnson, W.Chen, M.W.Wong, J.L.Andres, C.Gonzalez, M.Head-Gordon, E.S.Replogle and J. A. Pople.

c) J.B.Foresman and A.Frisch, "Exploring Chemistry with Electronic Structure Methods", 2nd Edn, Gaussian Inc., 1997.

15. A.L.McClellan, *Tables of Experimental Dipole Moments,* vols 1-3, Rahara Enterprises, Ca., 1989.
16. S.S.Kuo, *Computer Applications of Numerical Methods*, ch.8, Addison-Wesley, London, 1972.
17. Lancaster Synthesis Ltd., Eastgate, White Lund, Morecambe, Lancs.,
    LA3 3DY.
18. Aldrich Chem. Co., Eastman Kodak Co., Rochester, USA.
19. Bruker XWINNMR version 3.0, Bruker AM, Silbersteifen, D-7512 Germany.
20. PC Model Version 7.0 Serena Software, Box 3076, Bloomington, IN, USA.
21. K.H.Hellwege and A.M.Hellwege, *Landolt-Bornstein Structure Data of Free Polyatomic Molecules*, Vol.15, 1987.
22. R.B.Mallion, *J.Chem.Phys.*, 1980, **75**, 793.

APPENDIX ONE

Appendix One

```
   SUBROUTINE ARINGS
C
   PARAMETER (NAT=70)
   COMMON /GEOM/ ANU(NAT),AN(NAT),BL(NAT),ALPHA(NAT),BETA(NAT),
  * Z(NAT,4),CHARGE(NAT),SHIFT(NAT),C(NAT,3),DIST(NAT,NAT),NUMBAR,

*CRING(30,2),ALFS(NAT,5),BETS(NAT,13),GAMS(NAT,37),CONVRT,NUMHET,
*PI,NATOMS,NRINGS,NOSUB(NAT),MRING(10,6),MARING(10,6),RINGC(NAT),
  * IEQ(10,2),NEQUIV,JEMC(NAT),JEMN(NAT),JEMO(NAT),JEMCN(NAT),
  * JEMCO(NAT),JEMCCO(NAT)
   INTEGER Z,ANU,AN,CRING,ALFS,BETS,GAMS
C
   COMMON/CHAR/ HUCK(NAT,NAT),AK(80,80),FACTOR(80,80),IAROM(80),
  * PIEXS(NAT),PIELEC(NAT),AH(80),P(80),E(80),NEX(30),EXS(30),
  * MEUX,MEUY,MEUZ,DIPMO,CONS,VALUE,NCHRG,NELEC,NPYR
   REAL MEUX,MEUY,MEUZ
C
C  Recognises aromatic rings.
C  For 5-membered ring,finds alpha connections ISUB-NA1-NB1-NC1-ND1
C  and closes ring ISUB-ND1,for six-membered same routine with
C  ISUB-NA1-NB1-NC1-ND1-NE1 and closes ISUB-NE1.
C  NUMBAR = number of six-membered aromatic rings
C  NUMHET = number of five-membered aromatic rings
C  Identity of aromatic atoms stored in arrays MARINGS (5-membered)
C  and MRINGS (6-membered)
C
     NUMBAR=0
     NUMHET=0
C
     DO 600 ISUB=1,NATOMS
C
     IF(AN(ISUB).EQ.8.OR.AN(ISUB).EQ.16.OR.AN(ISUB).EQ.55.
  *   OR.AN(ISUB).EQ.57) THEN
C
      DO 430 J=1,NUMHET
      DO 430 K=1,6
      IF (ISUB.EQ.MARING(J,K)) GOTO 510
430      CONTINUE

     DO 500 J0=2,5
     NA1=0
     IALFS=ALFS(ISUB,J0)
     IF (IALFS.EQ.0) GOTO 500
     IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NA1=IALFS
     IF(NA1.EQ.0) GOTO 500
```

```
C
      DO 501 J1=2,5
      NB1=0
      IALFS=ALFS(NA1,J1)
      IF (IALFS.EQ.0.OR.IALFS.EQ.ISUB) GOTO 500
      IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NB1=IALFS
      IF(NB1.EQ.0) GOTO 501
C
      DO 502 J2=2,5
      NC1=0
      IALFS=ALFS(NB1,J2)
      IF (IALFS.EQ.0.OR.IALFS.EQ.NA1) GOTO 502
      IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NC1=IALFS
      IF(NC1.EQ.0) GOTO 502
C
      DO 503 J3=2,5
      ND1=0
      IALFS=ALFS(NC1,J3)
      IF(IALFS.EQ.0.OR.IALFS.EQ.NB1) GOTO 503
      IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) ND1=IALFS
      IF(ND1.EQ.0) GOTO 503
C
      DO 504 J4=2,5
      NE1=0
      IALFS=ALFS(ND1,J4)
      IF(IALFS.EQ.0.OR.IALFS.EQ.NC1) GOTO 504
      IF(AN(IALFS).EQ.8.OR.AN(IALFS).EQ.16.OR.AN(IALFS).EQ.55.
     * OR.AN(IALFS).EQ.57) NE1=IALFS
      IF(NE1.EQ.0) GOTO 504
C
      IF (NE1.NE.ISUB) GOTO 504
C
      NUMHET=NUMHET+1
C
       IF (NUMHET.GT.1) THEN
        IF(ISUB.EQ.MARING((NUMHET-1),1)) THEN
        NUMHET=NUMHET-1
        GOTO 510
        ENDIF
       ENDIF
C
C        WRITE(6,588) ISUB,NA1,NB1,NC1,ND1,NUMHET
C 588    FORMAT(6I5)
C
      MARING(NUMHET,1)=ISUB
      MARING(NUMHET,2)=NA1
      MARING(NUMHET,3)=NB1
      MARING(NUMHET,4)=NC1
```

```
      MARING(NUMHET,5)=ND1
C
 504   CONTINUE
 503   CONTINUE
 502   CONTINUE
 501   CONTINUE
 500   CONTINUE
 510   CONTINUE
       ENDIF
 600   CONTINUE
C
      DO 900 ISUB=1,NATOMS
       IF(AN(ISUB).EQ.55.OR.AN(ISUB).EQ.58) THEN
C
C        WRITE(6,*) 'NUMBAR=',NUMBAR
C
        DO 30 J=1,NUMBAR
        DO 30 K=1,6
        IF (ISUB.EQ.MRING(J,K)) GOTO 101
30       CONTINUE
C
       DO 700 J0=2,5
       NA1=0
       IALFS=ALFS(ISUB,J0)
       IF (IALFS.EQ.0) GOTO 700
       IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NA1=IALFS
       IF(NA1.EQ.0) GOTO 700
C
       DO 701 J1=2,5
       NB1=0
       IALFS=ALFS(NA1,J1)
       IF (IALFS.EQ.0.OR.IALFS.EQ.ISUB) GOTO 700
       IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NB1=IALFS
       IF(NB1.EQ.0) GOTO 701
C
        DO 702 J2=2,5
        NC1=0
        IALFS=ALFS(NB1,J2)
        IF (IALFS.EQ.0.OR.IALFS.EQ.NA1) GOTO 702
        IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NC1=IALFS
        IF(NC1.EQ.0) GOTO 702
C
        DO 703 J3=2,5
        ND1=0
        IALFS=ALFS(NC1,J3)
        IF(IALFS.EQ.0.OR.IALFS.EQ.NB1) GOTO 703
        IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) ND1=IALFS
        IF(ND1.EQ.0) GOTO 703
```

```
C
      DO 704 J4=2,5
      NE1=0
      IALFS=ALFS(ND1,J4)
      IF(IALFS.EQ.0.OR.IALFS.EQ.NC1) GOTO 704
      IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NE1=IALFS
      IF(NE1.EQ.0) GOTO 704
C
      DO 710 J5=2,5
      NG1=0
      IALFS=ALFS(NE1,J5)
      IF(IALFS.EQ.0.OR.IALFS.EQ.ND1) GOTO 710
      IF(AN(IALFS).EQ.55.OR.AN(IALFS).EQ.58) NG1=IALFS
      IF(NG1.EQ.0) GOTO 710
      IF (NG1.NE.ISUB) GOTO 710
C
      NUMBAR=NUMBAR+1
C
       IF (NUMBAR.GT.1) THEN
        IF(ISUB.EQ.MRING((NUMBAR-1),1)) THEN
        NUMBAR=NUMBAR-1
        GOTO 101
        ENDIF
       ENDIF
C
      MRING(NUMBAR,1)=ISUB
      MRING(NUMBAR,2)=NA1
      MRING(NUMBAR,3)=NB1
      MRING(NUMBAR,4)=NC1
      MRING(NUMBAR,5)=ND1
      MRING(NUMBAR,6)=NE1
C
C       WRITE(6,986) ISUB,NA1,NB1,NC1,ND1,NE1,NUMBAR
C 986     FORMAT(7I5)
C
 710    CONTINUE
 704    CONTINUE
 703    CONTINUE
 702    CONTINUE
 701    CONTINUE
 700    CONTINUE
 101    CONTINUE
      ENDIF
C
C       WRITE(6,988) ISUB,NUMBAR,RINGSH,RINGC(I)
C 988     FORMAT(2I5,2F10.3)
C
  900   CONTINUE
```

```
C
C   Defines aromatic carbons from MRING and MARING
C   14/3/01 defines all aromatic atoms from MRING and MARING
C
      DO 90 I=1,NATOMS
C        IF(AN(I).EQ.55) THEN
       DO 82 J =1,10
       DO 82 K =1,6
       IF(I.EQ.MRING(J,K)) IAROM(I) = 6
       IF(I.EQ.MARING(J,K)) IAROM(I) =5
 82    CONTINUE
C        ENDIF
 90    CONTINUE
C
C          DO 999 I=1,NUMBAR
C          WRITE (6,988) (MRING(I,J),J=1,6)
C 988      FORMAT(6I5)
C 999      CONTINUE
       RETURN
       END
C
C
      SUBROUTINE RINCUR
C
      PARAMETER (NAT=70)
      COMMON /GEOM/ ANU(NAT),AN(NAT),BL(NAT),ALPHA(NAT),BETA(NAT),
     * Z(NAT,4),CHARGE(NAT),SHIFT(NAT),C(NAT,3),DIST(NAT,NAT),NUMBAR,

*CRING(30,2),ALFS(NAT,5),BETS(NAT,13),GAMS(NAT,37),CONVRT,NUMHET,

*PI,NATOMS,NRINGS,NOSUB(NAT),MRING(10,6),MARING(10,6),RINGC(NAT),
     * IEQ(10,2),NEQUIV,JEMC(NAT),JEMN(NAT),JEMO(NAT),JEMCN(NAT),
     * JEMCO(NAT),JEMCCO(NAT)

      INTEGER Z,ANU,AN,CRING,ALFS,BETS,GAMS
C
      COMMON/CHAR/ HUCK(NAT,NAT),AK(80,80),FACTOR(80,80),IAROM(80),
     * PIEXS(NAT),PIELEC(NAT),AH(80),P(80),E(80),NEX(30),EXS(30),
     * MEUX,MEUY,MEUZ,DIPMO,CONS,VALUE,NCHRG,NELEC,NPYR
      REAL MEUX,MEUY,MEUZ
C
      DIMENSION CENTER(3),R(3),RA(3),S(3),
     * UR(3),URA(3),US(3),UT(3)
C
C   Calculates ring current shifts using MARING (5-memb)
C   and MRING (6-memb) from ARING.
C   NUMBAR = number of six-membered aromatic rings
C   NUMHET = number of five-membered aromatic rings
```

```
C
C   Searches MRING and MARING for common atoms
C
      KOMONA =0
      KOMONH =0
     DO 6 I=1,NUMBAR
     DO 6 J=1,NUMBAR
      IF(I.EQ.J) GOTO 6
     DO 5 KA=1,6
     DO 5 KB=1,6
     IF(MRING(I,KA).EQ.MRING(J,KB)) KOMONA=KOMONA+1
 5    CONTINUE
 6    CONTINUE
C
     DO 10 I=1,NUMBAR
     DO 10 J=1,NUMHET
     DO 10 KA=1,6
     DO 10 KB=1,6
     IF(MRING(I,KA).EQ.MARING(J,KB)) KOMONH=KOMONH+1
10    CONTINUE
C
C    NCARB = the number of quaternary carbon atoms in the molecule
C    i.e. with only aromatic carbons as beta atoms
C
      NCARB  = 0
      DO 40 I=1,NATOMS
      IF(AN(I).EQ.55.AND.IAROM(I).GT.0) THEN
       NBA=BETS(I,1)
       IF(NBA.EQ.0) GOTO 30
       NUMBET = 0
       DO 20 J=2,NBA+1
       IBET=BETS(I,J)
       IF(AN(IBET).EQ.55.AND.IAROM(IBET).GT.0)
     *   NUMBET = NUMBET + 1
 20    CONTINUE
       IF(NUMBET.EQ.6) NCARB=NCARB+1
 30    CONTINUE
      ENDIF
 40    CONTINUE
C
      FACT = 1.0
C
      IF (NUMBAR.EQ.2) FACT = 0.93
      IF (NUMBAR.EQ.3) FACT = 0.94
      IF (NUMBAR.EQ.4.AND.NCARB.EQ.0) FACT = 0.88
      IF (NUMBAR.EQ.4.AND.NCARB.EQ.2) FACT = 0.88
      IF (NUMBAR.EQ.5.AND.NCARB.EQ.0) FACT = 0.85
      IF (NUMBAR.EQ.5.AND.NCARB.EQ.2) FACT = 0.68
```

```
      IF (NUMBAR.EQ.7.AND.NCARB.EQ.6) FACT = 1.01
      IF (NUMBAR.EQ.2.AND.NUMHET.EQ.1.AND.NCARB.EQ.1) FACT = 0.83
      IF(NUMBAR.EQ.1.AND.NUMHET.EQ.1.AND.KOMONH.EQ.2) FACT = 0.90
      IF(KOMONA.EQ.0.AND.NUMHET.EQ.0) FACT = 1.0
C
C       WRITE(6,*)'FACT =',FACT
C
      IF (NUMHET.EQ.0) GOTO 590
       DO 580 NUM=1,NUMHET
        ISUB= MARING(NUM,1)
        NA1 = MARING(NUM,2)
        NB1 = MARING(NUM,3)
        NC1 = MARING(NUM,4)
        ND1 = MARING(NUM,5)
C
C   Calculate co-ords of center of ring,find axis normal
C   to the ring plane and calculate ring current shift
C
      DO 506 J=1,3
      CENTER(J) = (C(ISUB,J)+C(NA1,J)+C(NB1,J)
     * +C(NC1,J)+C(ND1,J))/5.0
 506   CONTINUE
C
      DO 570 I=1,NATOMS
       IF(AN(I).NE.1) GOTO 570
       RINGSH=0.0
C
      DO 507 J =1,3
       R(J)  = CENTER(J)-C(ISUB,J)
       RA(J) = CENTER(J)-C(NB1,J)
       S(J)  = CENTER(J)-C(I,J)
 507   CONTINUE
C
      CALL UNIVEC(UR,R)
      CALL UNIVEC(URA,RA)
      CALL UNIVEC(US,S)
      CALL VECPRD(UT,UR,URA)
      CALL SCLPRD(UT,US,CAL)
      DISTAN=0.0
      DO 508 J=1,3
      DISTAN=DISTAN+(C(I,J)-CENTER(J))**2
 508   CONTINUE
C
       GEOM = (1.0-3.0*CAL**2)/(DISTAN**1.5)
C
C    Counts number of C=O and N= atoms in ring
C
        NCO=0
```

```
       NPYR =0
       DO 510 J=1,5
       IF(JEMCO(MARING(NUM,J)).EQ.1) NCO=NCO+1
       IF(AN(MARING(NUM,J)).EQ.58) NPYR=NPYR+1
 510    CONTINUE
C
      IF(AN(ISUB).EQ.8) THEN
       IF(NPYR.EQ.0) EQDIP=17.6
       IF(NPYR.EQ.1) EQDIP=17.6
      ENDIF
      IF(AN(ISUB).EQ.16) THEN
       IF(NPYR.EQ.0) EQDIP=21.8
       IF(NPYR.EQ.1) EQDIP=20.0
      ENDIF
      IF(AN(ISUB).EQ.57) THEN
       IF(NPYR.EQ.0) EQDIP=19.0
       IF(NPYR.EQ.1) EQDIP=16.0
      ENDIF
      IF(AN(ISUB).EQ.55) THEN
       IF(NCO.EQ.0) EQDIP=11.57
       IF(NCO.EQ.1) EQDIP= 0.0
      ENDIF
C
       RINGSH=EQDIP*GEOM
       RINGC(I) = RINGC(I) + RINGSH
C
 570   CONTINUE
 580   CONTINUE
 590   CONTINUE
C
      IF (NUMBAR.EQ.0) GOTO 790
       DO 780 NUM=1,NUMBAR
        ISUB= MRING(NUM,1)
        NA1 = MRING(NUM,2)
        NB1 = MRING(NUM,3)
        NC1 = MRING(NUM,4)
        ND1 = MRING(NUM,5)
        NE1 = MRING(NUM,6)
C
C   Counts number of CO and pyridine atoms in the aromatic rings
C    NPYR = the no.of pyridine N atoms.
C    NCO  = no. of CO atoms
C
      NCO=0
      NPYR = 0
      DO 610 J=1,6
        IF(JEMCO(MRING(NUM,J)).EQ.1) NCO=NCO+1
        IF(AN(MRING(NUM,J)).EQ.58) NPYR=NPYR+1
```

```
 610   CONTINUE
C
C   Calculate co-ords of center of benzene ring,find axis normal
C   to the ring plane and calculate ring current shift
C
      DO 706 J=1,3
      CENTER(J) = (C(ISUB,J)+C(NA1,J)+C(NB1,J)
     * +C(NC1,J)+C(ND1,J)+C(NE1,J))/6.0
 706   CONTINUE
C
      DO 770 I=1,NATOMS
       IF(AN(I).NE.1) GOTO 770
       RINGSH=0.0
C
      DO 707 J =1,3
       R(J)  = CENTER(J)-C(ISUB,J)
       RA(J) = CENTER(J)-C(NB1,J)
       S(J)  = CENTER(J)-C(I,J)
 707   CONTINUE
C
      CALL UNIVEC(UR,R)
      CALL UNIVEC(URA,RA)
      CALL UNIVEC(US,S)
      CALL VECPRD(UT,UR,URA)
      CALL SCLPRD(UT,US,CAL)
      DISTAN=0.0
      DO 708 J=1,3
      DISTAN=DISTAN+(C(I,J)-CENTER(J))**2
 708   CONTINUE
C
       GEOM = (1.0-3.0*CAL**2)/(DISTAN**1.5)
C
       EQDIP = 26.23*FACT
      IF (NPYR.EQ.1) EQDIP = 22.22
      IF (NPYR.EQ.1.AND.NUMBAR.EQ.2) EQDIP = 19.70
      IF (NPYR.EQ.2) EQDIP = 18.83
C
C      WRITE(6,*)'FACT =',FACT
C
       RINGSH=EQDIP*GEOM
       RINGC(I) = RINGC(I) + RINGSH
 770   CONTINUE
 780   CONTINUE
 790   CONTINUE
      RETURN
      END
```

APPENDIX TWO

PERKIN 2

Proton chemical shifts in NMR. Part 14.[1] Proton chemical shifts, ring currents and π electron effects in condensed aromatic hydrocarbons and substituted benzenes

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The proton resonance spectra of a variety of condensed aromatic compounds including benzene, naphthalene, anthracene, phenanthrene, pyrene, acenaphthylene and triphenylene were obtained in dilute $CDCl_3$ solution. Comparison of the proton chemical shifts obtained with previous literature data for CCl_4 solution shows small but significant differences. A previous model (CHARGE6) for calculating the proton chemical shifts of aliphatic compounds was extended to aromatic compounds. This was achieved by including an automatic identification of both five- and six-membered aromatic rings based on atomic connectivities plus a dipole calculation of the aromatic ring current. The ring current intensity in the molecules was calculated by two alternative methods. a) The ring current intensity in the individual benzenoid rings was a function of the number of adjoining rings and b) the molecular ring current was proportional to the molecular area divided by the molecular perimeter. This, plus the inclusion of deshielding steric effects for the crowded protons in these molecules, gave a good account of the observed chemical shifts. The model was also applied successfully to the non-alternant hydrocarbons of fulvene and acenaphthylene and to the aliphatic protons near to and above the benzene ring in tricyclophane and [10]cyclophane.

The Huckel calculation of the π electron densities in CHARGE6 was used to calculate the π electron densities in substituted benzenes. The π-inductive effect was used to simulate the effect of CX_3 groups (X = H, Me, F) on the benzene ring. These together with the long range effects of the substituent groups identified previously allowed a precise calculation of the SCS of a variety of substituents on all the benzene ring protons.

The model gives the first accurate calculation of the proton chemical shifts of condensed aromatic compounds and of the proton SCS in the benzene ring. For the data set of 55 proton chemical shifts spanning 3 ppm the rms error of the observed *vs.* calculated shifts was *ca.* 0.1 ppm. The model also allows the interpretation of the shifts in terms of the separate interactions calculated in the programme, *i.e.* π electron densities and steric, anisotropic and electric field effects. Previous correlations of the proton SCS with π electron densities and substituent parameters are shown to be over simplified. The relative proportions of these different interactions are very different for each substituent and for each ring proton.

Introduction

The influence of the π electron densities and ring currents of aromatic compounds on their proton chemical shifts have been investigated since the beginning of proton NMR spectroscopy.[2] Thus it is all the more surprising that despite this wealth of investigation there is still no authoritative calculation (even a semi-empirical one) of the proton chemical shifts of aromatic compounds and the structural chemist still has to rely on proton data banks for the identification of aromatic compounds by NMR.

Pauling[3] introduced the concept of an aromatic ring current to explain the diamagnetic anisotropy of crystalline benzene. Pople[4] later extended this to explain the difference in the proton chemical shifts of benzene and ethylene and he further showed that the equivalent dipole model of this ring current gave a surprisingly good account of this difference. More sophisticated ring current models for benzene were then developed. The classical double-loop[5] and double dipole models[6] mimic the π electron circulation by placing the current loops (and equivalent dipoles) above and below the benzene ring plane. A value of ±0.64 Å was found to be most appropriate. The equations of Haigh and Mallion[7] give the shielding ratios directly from quantum mechanical theory. Schneider *et al.*[8] have recently presented a detailed experimental examination of the double-loop and Haigh and Mallion ring current models, though not the simple equivalent dipole model (see later). The calculations gave good agreement with the experimental data, thus the effect of the benzene ring current on the chemical shifts of neighbouring protons is reasonably well understood.

However, the proton chemical shifts in condensed aromatic compounds and substituted benzenes have not yet been well calculated and this is the subject of this investigation. Bernstein *et al.*[9] in their initial calculations of the proton chemical shifts of condensed aromatic compounds assumed the same ring current for each benzenoid ring but this was subsequently considered to be an over simplification. Thus it is first necessary to calculate the π electron current density for each benzenoid ring and then to calculate the effects of these currents on the chemical shifts of the ring protons. The quantum mechanical method for calculating the π electron current densities was first given by Pople[10] and McWeeny[11] subsequently extended the London–Pople theory. McWeeny's work gives not only the circulating current density but also the effect of this circulating current at the proton in question. It should be noted that all these theories were based on simple Huckel theory.

Early experimental investigations to test these theories were not helped by the complex proton spectra of many condensed aromatic hydrocarbons at the low applied magnetic fields then in use and also by the quite large concentration effects on the proton chemical shifts due to the propensity of these

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large planar rings to stack in solution. However three systematic investigations attempted to overcome these difficulties. Jonathan *et al.*[12] analysed the proton spectra of several condensed aromatics at infinite dilution in CCl_4 or CS_2. They then used the Pople–London theory to calculate the current intensity in the benzenoid rings and the Johnson–Bovey tables[5] to obtain the ring current shifts. They also estimated C–C and C–H anisotropic effects and found that these could be ignored. They obtained "only fair agreement" with the observed shifts. Varying the separation of the π-electron loops gave a poorer fit with the observed shifts. They noted that other interactions were affecting the proton shifts and in particular noted a high frequency shift for close protons which was suggested to be due to van der Waals contact but did not attempt to quantify this.

Subsequently Cobb and Memory[13] and Haigh and Mallion[7] performed two similar but more extensive investigations. The proton spectra of several condensed aromatic compounds in dilute solution were analysed and the McWeeny equation used to obtain the ring current densities and shielding ratios. They both ignored σ bond anisotropies in this calculation. Both investigations obtained reasonable correlations for "non overcrowded protons" between the observed proton shifts and the ratio of the π electron shielding for a given proton compared to benzene (H'/H'_b in the nomenclature of ref. 7). The more comprehensive data of ref. 7 when converted to the δ scale may be written as $\delta_{obs} = 1.56\ (H'/H'_b) + 5.66$ with an rms error of 0.06 ppm over a range of *ca.* 1.6 ppm. However the differences between the calculated and observed data for the "crowded" protons were *ca.* 0.5–0.7 ppm with one of 1.2 ppm, all to high frequency of the calculated value. Again they attributed these shifts to steric effects but did not quantify or define these effects.

More recently Westermayer *et al.*[14] used a double dipole model to test the observed shifts. They correlated the resulting geometric factors with the observed shifts to obtain a value for the benzene diamagnetic susceptibility anisotropy. They stated that superior results for the sterically crowded protons were obtained but it is not clear why this should be the case as no steric term was introduced.

Although it is obvious which protons are crowded (*e.g.* H4,5 in phenanthrene) it is not obvious whether this interaction is also present in the other "less crowded" protons. Thus the simple question of whether the difference between the α and β proton chemical shifts in naphthalene is due to ring currents, π-electron densities or steric effects has still not been satisfactorily answered. Although Pople in his original studies[10] calculated the ring current intensities in the five- and seven-membered rings of azulene, to our knowledge there has not been any calculation of the proton chemical shifts in non-alternant hydrocarbons.

The influence of the substituents on the proton chemical shifts in the benzene ring has also been investigated for many years and again there is still no quantitative calculation of these effects. Following the classic work of Castellano *et al.*[15] and Hayamizu and Yamamoto[16] who completely analysed the complex proton spectra of a wide range of monosubstituted benzenes in dilute solution in CCl_4 the proton substituent chemical shifts (SCS) are known accurately and tables of these SCS are an integral part of any text on NMR spectroscopy.[17–19] The theoretical interpretations of these effects have concentrated on the correlation between the SCS and the calculated π (and also σ) electron densities on the adjacent carbon atoms following the excellent correlation found between the ^{13}C SCS and the π electron densities at the *para* carbon atom in monosubstituted benzenes.[20] Correlations with π electron densities calculated by various methods have been reported, the most recent being the *ab initio* calculations of Hehre *et al.*[21] They used the STO-3G basis set and showed that the ^{13}C SCS could be well interpreted on the basis of calculated electron densities but this was not the case for the proton SCS. The *para* proton SCS could be correlated with the total charge density at the *para* carbon atom but the *meta* proton SCS did not correlate well with the calculated *meta* carbon charge densities but with the sum of the charges at the hydrogen and attached carbon atoms. They stated that "this lack of consistency indicates either that the calculations are unrealistic or that the ^1H SCS depend to a very significant extent on factors other than electron densities at the H and attached C atoms". They omitted the *ortho* proton SCS presumably on the grounds that these other effects are even more important at these protons. They also noted that strongly electronegative substituents caused polarisation of the π system without charge transfer, leading to changes in the π densities around the ring and this is termed the π-inductive effect. They also found various correlations between the calculated charge densities and the Taft σ_I and σ_R values. This reflects the results of other investigators who have attempted to correlate substituent parameters with the proton SCS.[16,22,23] Despite all these endeavours there is still no calculation of proton SCS in substituted benzenes reliable enough to be of use to the structural chemist.

We give here the proton chemical shifts of a selection of condensed aromatic compounds in $CDCl_3$ and show that these differ by a small but significant amount from the earlier data in CCl_4 solution. These provide sufficient data for an analysis of the proton chemical shifts based on the CHARGE model for calculating proton chemical shifts.[1] In previous parts of this series this model has been applied successfully to a variety of saturated hydrocarbons,[24] haloalkanes,[25] ethers[26] and ketones.[1] We shall show that this model can be extended to provide a quantitative calculation of the proton shifts in condensed aromatic compounds, including two non-alternant hydrocarbons and the SCS of monosubstituted benzenes. We give two alternative calculations of the ring current intensity in the benzenoid rings together with a dipole model of the benzene ring current. In model A the ring current intensity in the individual benzenoid rings is a function of the number of adjoining rings whereas in model B the molecular ring current is given by the classical Pauling treatment as proportional to the molecular area divided by the molecular perimeter. All the protons in the condensed aromatic compounds are considered and the "crowded" proton chemical shifts reproduced by a simple steric effect. The effects of substituents in monosubstituted benzenes are well reproduced for the *ortho*, *meta* and *para* protons on the basis of calculated π electron densities plus the steric, anisotropic and electric field effects of the substituents. We show also that the model reproduces the high field shifts of protons situated over the benzene ring thus providing a general calculation of proton chemical shifts of condensed aromatic compounds. A preliminary account of this work has been presented.[27]

Theory

As the theory has been detailed previously only a brief summary of the latest version (CHARGE6)[28] is given here. The theory distinguishes between substituent effects over one, two and three bonds which are attributed to the electronic effects of the substituents and longer range effects due to the electric fields, steric effects and anisotropy of the substituents. The CHARGE scheme calculates the effects of atoms on the partial atomic charge of the atom under consideration, based upon classical concepts of inductive and resonance contributions.

If we consider an atom I in a four atom fragment I–J–K–L the partial atomic charge on I is due to three effects. There is an α effect from atom J given by the difference in the electronegativity of atoms I and J and a β effect from atom K proportional to both the electronegativity of atom K and the polarisability of atom I. There is also a general γ effect from atom L given by the product of the atomic polarisabilities of atoms I and L. For the second row atoms (C, O, *etc.*) the γ effect (*i.e.* C–C–C–H) is parameterised separately and is given by eqn. (1) where θ is the C–C–C–H dihedral angle and *A* and *B* empirical parameters.

$$\begin{aligned}\mathrm{GSEF} &= A + B_1\cos\theta \qquad 0° \le \theta \le 90° \\ &= A + B_2\cos\theta \qquad 90° \le \theta \le 180°\end{aligned} \tag{1}$$

There are also routines for the methyl γ effect and for the decrease in the γ effect of the electronegative oxygen and fluorine atoms for CX_2 and CX_3 groups.

The total charge is given by summing these effects and the partial atomic charges (q) converted to shift values using eqn. (2).

$$\delta = 160.84q - 6.68 \tag{2}$$

The effects of more distant atoms on the proton chemical shifts are due to steric, anisotropic and electric field contributions. H···H steric interactions in alkanes were found to be shielding and X···H (X = C, F, Cl, Br, I) interactions deshielding according to a simple r^{-6} dependence [eqn. (3)].

$$\delta_{\mathrm{steric}} = a_S/r^6 \tag{3}$$

Furthermore any X···H steric contributions on a methylene or methyl proton resulted in a push-pull effect (shielding) on the other proton(s) on the attached carbon.

The effects of the electric field of the C–X bonds (X = H, F, Cl, Br, I, O) were calculated from eqn. (4) where A_Z was

$$\delta_{\mathrm{el}} = A_Z E_Z \tag{4}$$

determined as 3.67×10^{-12} esu (63 ppm au) and E_Z is the component of the electric field along the C–H bond. The electric field for a univalent atom (*e.g.* fluorine) is calculated as due to the charge on the fluorine atom and an equal and opposite charge on the attached carbon atom. The vector sum gives the total electric field at the proton concerned and the component of the electric field along the C–H bond considered is E_Z in eqn. (4). This procedure is both simpler and more accurate than the alternative calculation using bond dipoles.

The magnetic anisotropy of a bond with cylindrical symmetry (*e.g.* CN) was obtained using the McConnell equation [eqn. (5)], where R is the distance from the perturbing group to

$$\delta_{\mathrm{an}} = \Delta\chi^{\mathrm{CN}}(3\cos^2\varphi - 1)/3R^3 \tag{5}$$

the nucleus of interest in Å, φ is the angle between the vector R and the symmetry axis and $\Delta\chi^{\mathrm{CN}}$ the molar anisotropy of the CN bond. ($\Delta\chi^{\mathrm{CN}} = \chi^{\mathrm{CN}}{}_{\mathrm{parl}} - \chi^{\mathrm{CN}}{}_{\mathrm{perp}}$) where $\chi^{\mathrm{CN}}{}_{\mathrm{parl}}$ and $\chi^{\mathrm{CN}}{}_{\mathrm{perp}}$ are the susceptibilities parallel and perpendicular to the symmetry axis respectively.

For a non-cylindrically symmetric group such as a carbonyl group eqn. (5) is replaced by the full McConnell eqn. (6). The

$$\delta_{\mathrm{an}} = [\Delta\chi_1(3\cos^2\theta_1 - 1) + \Delta\chi_2(3\cos^2\theta_2 - 1)]/3R^3 \tag{6}$$

C=O group has different magnetic susceptibilities (χ_1, χ_2 and χ_3) along the principal axes (X_1, X_2 and X_3) and thus two anisotropy terms are required.

In eqn. (6) θ_1 and θ_2 are the angles between the radius vector R and χ_1 and χ_3 respectively and $\Delta\chi_1$ $(\chi_1 - \chi_2)$ and $\Delta\chi_2$ $(\chi_3 - \chi_2)$ are the two anisotropies for the C=O bond which may be termed the parallel and perpendicular anisotropy respectively.

These contributions were added to the shifts of eqn. (2) to give the calculated shift of eqn. (7).

$$\delta_{\mathrm{total}} = \delta_{\mathrm{charge}} + \delta_{\mathrm{steric}} + \delta_{\mathrm{anisotropy}} + \delta_{\mathrm{el}} \tag{7}$$

Application to aromatic compounds

Ring current shifts. There are a number of modifications to be made to CHARGE6 to calculate the proton shifts of aromatic compounds. It was necessary to include the effect of the aromatic ring current and for this to be achieved the programme has to automatically recognise an aromatic ring. A routine was written based on the atomic connectivities in the rings and the programme now recognises both five- and six-membered aromatic rings including the heterocyclic rings of pyrrole, furan and thiophene. The aromatic ring current at any proton was then calculated from the equivalent dipole model [eqn. (8)].

$$\delta_{\mathrm{rc}} = fc\mu(3\cos^2\theta - 1)/R^3 \tag{8}$$

In eqn. (8) R is the distance of the proton from the benzene ring centre, θ the angle of the R vector from the benzene ring symmetry axis, μ is the equivalent dipole of the benzene ring and fc the π electron current density for the benzenoid ring. (For benzene $fc = 1$.)

It was next necessary to calculate the value of fc for any given compound and two alternative methods are presented. The first method (model A) was based on inspection of the calculated ring current intensities of refs. 7 and 12. Haigh and Mallion[7] did not publish the calculated ring current intensities for the common aromatic compounds, but a selection of their calculated values for some less common condensed aromatic compounds is given in Table 1.

Inspection of this data shows that the changes in the ring current intensity are a function of the number and orientation of the rings attached to the benzenoid ring. In model A the ring current intensity in any given benzenoid ring is assumed to be only a function of the number and orientation of the rings attached to the benzenoid ring considered. This may be quantified by the number and orientation of the substituent sp^2 carbon atoms attached to the ring in question (R_0). Thus we define a) the number of attached sp^2 carbons on each ring carbon atom and b) the relative position of these attached atoms in the benzene ring. Thus for benzene each carbon atom has two carbon neighbours thus $R_0 = 12$. For either ring in napthalene two of the carbon atoms have three carbon neighbours thus $R_0 = 14$. The middle rings of anthracene and phenanthrene both have $R_0 = 16$ but the relative positions of the substituent carbons differ in the two cases. These are defined as R_0 equals 16a and 16b. This analysis gives seven different ring systems (Table 1) of which six are present in the molecules indicated in Fig. 1. Only the molecules with the rings itemised A, B in Fig. 1 are included in Table 1 as these are the only molecules for which the ring current intensities were given in ref. 7. However all the molecules measured were included in the iteration (see later).

Inspection of Table 1 shows that with few exceptions the separation of the ring current densities into the different ring types gives a reasonably constant value for each ring type. The only serious exception is the calculated values for ring type 18 (*i.e.* all substituted carbons) of ref. 12 which are very different for perylene and coronene. The values from ref. 7 for the similar molecules benzo[*ghi*]perylene and naphtho[1,2,3,4-*def*]chrysene are much more consistent.

It would be possible to average the calculated values of ref. 7 for each ring type and use these averages in our calculation. In view of the approximations inherent in these calculations it was decided to parametrise the current density for each ring type separately to obtain the best agreement with the observed shifts. These optimised values are given in Table 1 (column 5) and will be considered later.

An alternative method of calculating the molecular ring current (model B) is to use the Pauling model[3] in which the carbon skeleton is considered as a conducting electrical network in which for any current loop the emf is proportional to the area enclosed and the resistance proportional to the number of bonds. On this basis if the condensed aromatics are considered to be made up of a number of regular hexagons the ring current for any molecule is simply proportional to the number of hexagons in the molecule divided by the number of bonds in the

Table 1 Calculated ring current intensities in condensed aromatic hydrocarbons

			Ring current intensity (*fc*)			
Molecule	Ring type[a]	(R_0)	[b]	[c]	Model A	Model B[d]
Benzene (**1**)		12	1.00	1.00	1.00	1.00
Naphthalene (**2**)		14	1.093	1.048,[e] 1.094,[f] 1.121[g]	0.950	0.925
Anthracene (**3**)	Ring A	14	1.085	1.119,[h] 1.197,[i] 1.104[j]		0.943
	Ring B	16a	1.280	1.291,[e] 1.311,[f] 1.299,[g] 1.298,[h] 1.170[j]	0.818	
Phenanthrene (**4**)	Ring A	14	1.133			0.943
	Ring B	16b	0.975	0.877,[g] 0.876[h]	0.745	
Triphenylene (**5**)	Ring A	14	1.111			0.876
	Ring B	18	0.747			
Pyrene (**6**)	Ring A	15	1.329	1.337,[k] 1.292[l]	0.786	0.878
	Ring B	16b	0.964			
Perylene (**7**)	Ring A	15	0.979			0.681
	Ring B	18	0.247	0.603,[f] 0.606[m]	0.173	
Coronene (**8**)	Ring A	16b	1.460		1.06[a]	1.008
	Ring B	18	1.038	0.745,[n] 0.684[l]		
		17	—	1.297,[k] 1.226,[m] 1.310[i]		

[a] See text. [b] Ref. 12. [c] Ref. 7. [d] This work. [e] Hexacene. [f] Dibenzo[*a,c*]naphthacene. [g] Dibenzo[*a,j*]naphthacene. [h] Dibenzo[*a,l*]naphthacene. [i] Dibenzo[*def,mno*]chrysene. [j] Benzo[*h*]pentaphene. [k] Dibenzo[*def,mno*]chrysene. [l] Benzo[*ghi*]perylene. [m] Naphtho[1,2,3,4-*def*]chrysene. [n] Dibenzo[*b,def*]chrysene.

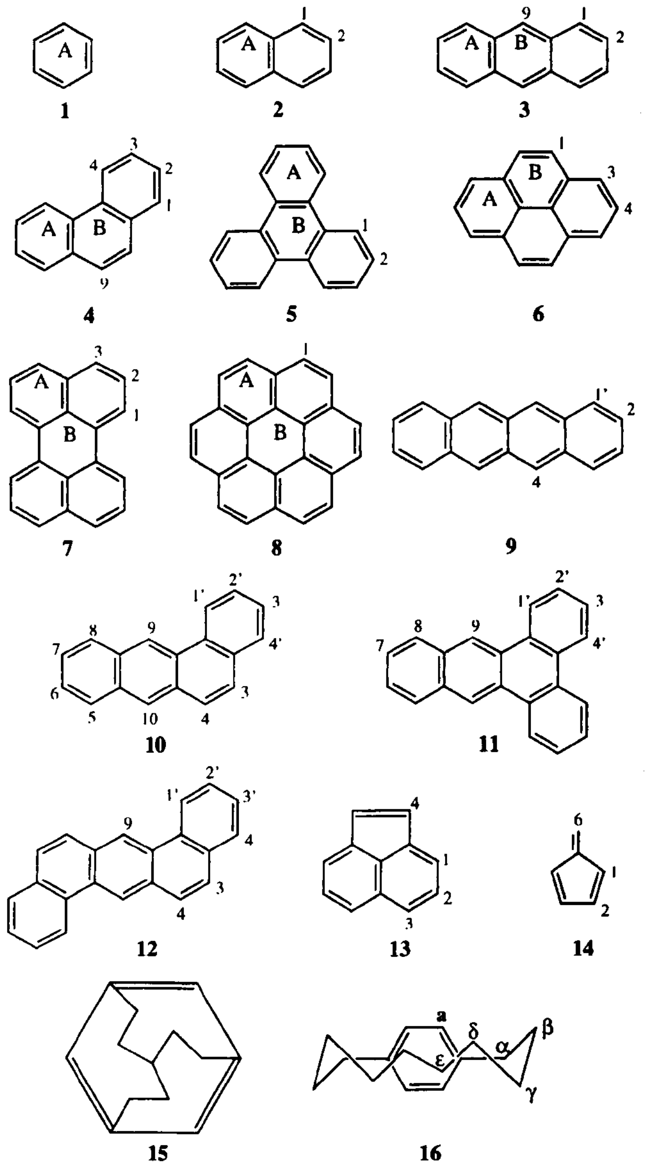

Fig. 1 . Molecules studied and their nomenclature.

perimeter of the molecule. Thus for benzene, naphthalene and anthracene the ring current ratio is 1:6/5:9/7. The Pauling model gives too large a value for the diamagnetic anisotropy of condensed aromatics[6a] so that as in method A the Pauling model was used to separate the various molecular types and the ring current for each molecular type was parametrised against the experimental data. Although the same experimental data are used in both models the different selectivities give different answers. For example in model B anthracene and phenanthrene have identical ring currents which is not the case in model A.

Conversely in model A the fully substituted benzenoid rings in perylene (**7**) and coronene (**8**) have identical ring currents whereas in model B they differ as the molecular area/perimeter ratio differs for the two compounds.

π Electron densities. The π electron densities are calculated in the CHARGE programme from Huckel theory.[29] The standard coulomb and resonance integrals for the Huckel routine are given by eqn. (9), where α_0 and β_0 are the coulomb and

$$\begin{aligned} \alpha_r &= \alpha_0 + h_r\beta_0 \\ \beta_{rs} &= k_{rs}\beta_0 \end{aligned} \tag{9}$$

resonance integrals for a carbon $2p_Z$ atomic orbital and h_r and k_{rs} the factors modifying these integrals for orbitals other than sp^2 carbon. The Huckel routine was modified by the ω technique to model the very polar π systems of the nucleic acid bases.[30] The ω technique involves varying the coulomb integral for each atom according to the charge on that atom. This is shown in eqn. (10) where α_r is the coulomb integral, α_r^0 the

$$\alpha_r = \alpha_r^0 - q_r\,\omega \tag{10}$$

initial coulomb integral, q_r the excess π charge on atom r and ω a constant. Eqn. (10) "cuts in" at a given value of the excess π charge on atom r. For the nucleic acid bases the appropriate value of ω was 1.40 and and the cut-in threshold 0.2 electrons.[30]

For alternant aromatic hydrocarbons this calculation gives π electron densities at every carbon equal to 1.0 as in benzene. Thus the excess π electron density is zero. This is in agreement with the results of more sophisticated calculations. *E.g.* the excess π electron densities at the α and β carbons of naphthalene are calculated as −0.8 and −4.1 me (millielectrons) from *ab initio* calculations with the 6-31G* basis set.

For the non-alternant hydrocarbons fulvene and acenaphthylene the Huckel routine gives large excess π densities at certain carbon atoms which are much larger than those calculated by *ab initio* methods in which iteration procedures restrict the tendency in the Huckel routine to separate the π charges. The ω technique was modified to correct this by decreasing the "cut in" point of eqn. (10) from 0.2 electrons to 0.01 electrons and increasing the value of ω to 6.0. This simple modification gave reasonable results for these two compounds, though the dipole moments are still on the high side (*e.g.* fulvene 0.92 D (calc.) *vs.* 0.44 D (obs.)[31] and acenaphthylene 0.93 D (calc.) *vs.* 0.3 D (obs.)[31]). As these hydrocarbons have quite different π densities and geometries from the alternant hydrocarbons both the ring current of the five-membered ring and the ring current density of the attached six-membered ring were parametrised separately.

For the substituted benzenes the appropriate values of the coefficients h_r and k_{rs} in eqn. (9) for the orbitals involving hetero atoms have to be found. In ref. 29 two procedures were considered. One was to obtain those values which gave the best agreement with the experimental dipole moments of the compounds investigated, the alternative was to find values which best reproduced the π densities obtained by *ab initio* calculations. Both sets of coefficients were given, but the first set was adopted in the CHARGE programme as the simplest method of obtaining reasonable dipole moments of unsaturated compounds. However later developments of the CHARGE method, in which a more flexible method of reproducing observed dipole moments was adopted, meant that the dipole moments of unsaturated compounds could be reproduced with either set of Huckel parameters. We now use the later set so that the π densities calculated from the Huckel routine reproduce the π densities given from *ab initio* calculations.

The only other modification necessary to the Huckel routine concerns the effect of saturated substituents (*e.g.* CX_3) on the π electron densities in the benzene ring which is usually termed hyperconjugation. It is simple to reproduce this effect in a Huckel calculation if it is regarded as an example of the π-inductive effect mentioned earlier. In this case an equation corresponding to eqn. (10) was used to vary the Coulomb integral of the aromatic carbon atom connected to an sp^3 carbon. In this way changes to the π electron density of the benzene ring due to both electron donating substituents such as CH_3 and electron withdrawing substituents such as CF_3 can be handled by the same procedure.

Having obtained the π electron density in the benzene ring it is then necessary to determine the effect of the π electron density at a given carbon atom on the proton chemical shifts. An experimental determination of this factor is due to Gunther *et al.*[32] They measured the proton chemical shifts of a variety of cyclic charged molecules (tropylium cation, cyclopentadienyl anion, *etc.*) and compared them with benzene. From this data they obtained a value of the coefficient a_1 [eqn. (11)] of 10.0

$$\Delta\delta = a_1\Delta q_\alpha + a_2\Delta q_\beta \qquad (11)$$

between the proton shift $\Delta\delta$ and the excess π charge Δq_α on the attached carbon atom.

It has also been recognised that there is an influence of the excess π charge on the carbon atom β to the proton considered and a related effect gives rise to the phenomenon of negative spin density in EPR spectroscopy.[33] The hyperfine couplings to the α and β protons in alkyl radicals, in which the radical carbon atom is planar and sp^2 hybridised, are quoted as $a^{H}_{\alpha} = -22$ G and $a^{H}_{\beta} = 4 + 50\cos^2\theta$ where θ is the dihedral angle between the free radical 2p-orbital and the proton considered.[33] These considerations suggest that in aromatic compounds in which the CH bond is orthogonal to the π orbital, θ is 90° and the value of a_2 in eqn. (11) is negative and *ca.* 1/5th of a_1, *i.e.* −2.0.

These modifications were the only ones needed to apply the CHARGE routine to aromatic compounds. However it is still necessary to calculate the charge densities at the aromatic protons in CHARGE and thus to quantify the appropriate α, β and γ effects. Also the long range interactions present in the aliphatic molecules (*i.e.* steric, electric and anisotropic) must also be included and where necessary evaluated. These will be considered subsequently.

The steric effects of both the aromatic carbon and hydrogen atoms are not known and must be determined. We shall show (see later for a full discussion) that an aromatic carbon atom has no steric effect on a close aromatic proton but that an aromatic proton has a *de*shielding effect on a close aromatic proton. We assume that this can be represented by a simple r^{-6} term [eqn. (3)] thus only the appropriate value of a_S in eqn. (3) for the aromatic proton to proton steric shift needs to be obtained. The electric field and anisotropies of the polar and anisotropic groups involved are calculated in an identical manner to that for any aliphatic C–H bond and thus no further parameterisation is necessary.

Experimental

Ethylene, benzene, toluene, *tert*-butylbenzene, naphthalene, anthracene, phenanthrene, pyrene, triphenylene, benz[*a*]anthracene, benzo[*b*]triphenylene and dibenzo[*ah*]anthracene and the $CDCl_3$ solvent were obtained commercially (Aldrich Chem. Co.). The solvent was stored over molecular sieves and used without further purification.

^1H NMR spectra were obtained on a Bruker AMX400 spectrometer operating at 400.14 MHz. Spectra were recorded in 10 mg cm^{-3} solutions (^1H) with a probe temperature of *ca.* 25 °C in $CDCl_3$ and referenced to TMS. Typical ^1H conditions were 128 transients, spectral width 3300 Hz, 32K data points, giving an acquisition time of 5 s and zero-filled to 128K to give a digital resolution of 0.025 Hz.

The geometries of the compounds were obtained by optimisations using the GAUSSIAN94 programme at the RHF/6-31G* level.[34] For molecules too large to be handled conveniently by GAUSSIAN at the 6-31G* level, *e.g.* perylene, smaller basis sets were used, *e.g.* 3-21G. For the largest molecules, *e.g.* coronene and the two cyclophanes (**15**) and (**16**), the molecular mechanics PCMODEL programme was used.[35] The geometry and CHARGE computations were performed on a PC.

Results

The proton spectra of the compounds all consisted of well separated peaks at 400 MHz (except for toluene) thus the proton chemical shifts could be obtained immediately and the assignments of the compounds followed previous investigations. For toluene the proton spectrum of toluene-d_8 was first obtained. The dilute ^1H spins only couple to the ^2D nuclei and the spectrum consists of three broad singlets at 7.165, 7.170 and 7.254 δ. This gave sufficient information to identify the coupling patterns in the ^1H spectrum of toluene and hence the slightly more accurate proton chemical shifts given in Table 2.

The data obtained in $CDCl_3$ solution are given and compared with that of previous investigations in CCl_4 solution in Table 2. In ref. 12 the authors only reported the shift differences from benzene and we have added 7.27 ppm (the benzene value in CCl_4) to them. The shift values in Table 2 are of interest. There is generally good agreement between the data sets but it is noteworthy that there is a small but almost constant difference in the proton chemical shifts in $CDCl_3$ solution compared to CCl_4. Averaging over all the aromatic compounds in Table 2 gives a value of 0.086 ppm (±0.01) to low field in $CDCl_3$ solution. This is also the case for ethylene but here the difference is slightly less. The aliphatic protons of the methyl groups in toluene and *tert*-butylbenzene do not show this effect but have the same shifts in the two solvents. The constant value of this difference means that data in CCl_4 solution can be converted directly to $CDCl_3$ solution by merely relating the shifts to benzene. Furthermore this suggests that the accurate SCS values reported earlier for the monosubstituted benzenes in CCl_4 solution may be used with confidence to investigate the application of the CHARGE model to these compounds and

Table 2 Observed and calculated proton chemical shifts (δ) for aromatic compounds

		Observed			Calculated	
Compound	Proton	$CDCl_3$[a]	CCl_4[b,c]		Model A	Model B
Ethylene		5.405	5.352[d]	—	5.407	
Benzene (**1**)		7.341	7.27[b]	(7.27)[c]	7.331	7.342
Naphthalene (**2**)	1	7.844	7.73	7.81	7.931	7.829
	2	7.477	7.38	7.46	7.524	7.493
Anthracene (**3**)	1	8.009	7.93	8.01	7.948	8.009
	2	7.467	7.39	7.39	7.524	7.577
	9,10	8.431	8.36	8.31	8.495	8.485
Phenanthrene (**4**)	1	7.901	7.80	un	7.930	7.968
	2	7.606	7.51	un	7.509	7.544
	3	7.666	7.57	un	7.566	7.600
	4,5	8.702	8.62	8.51	8.455	8.433
	9,10	7.751	7.65	7.71	7.839	8.085
Triphenylene (**5**)	1	8.669	8.61	8.56	8.587	8.707
	2	7.669	7.58	7.61	7.613	7.654
Pyrene (**6**)	1	8.084	8.00	8.06	7.976	8.253
	3	8.190	8.10	8.16	7.930	8.156
	4	8.010	7.93	7.99	7.546	7.785
Perylene (**7**)	1	8.196	8.11	8.09	8.361	8.250
	2	7.466	7.38	7.41	7.515	7.404
	3	7.656	7.57	7.60	7.845	7.630
Coronene (**8**)	1	8.90[e]	8.82	8.84		8.900
Benz[*a*]anthracene (**9**)	1′	8.840	8.77		8.698	8.553
	2′	7.685	7.59		7.708	7.627
	3′	7.651	7.525		7.638	7.557
	4′	7.849	7.755		8.102	8.004
	3	7.616	7.55		7.987	8.117
	4	7.800	7.72		8.027	8.200
	5	8.048	8.03		8.101	7.977
	6	7.540	7.465		7.637	7.544
	7	7.564	7.47		7.647	7.553
	8	8.133	8.03		8.169	8.038
	9	9.174	9.08		9.125	9.052
	10	8.370	8.275		8.561	8.572
Benz[*b*]anthracene (**10**)	1′	8.00[f]			8.082	7.947
	2′	7.39			7.619	7.522
	4	8.67			8.581	8.546
Benzo[*b*]triphenylene (**11**)	1′	8.791	8.675		8.685	8.758
	2′	7.670	7.54		7.649	7.634
	3′	7.651	7.53		7.636	7.618
	4′	8.592	8.475		8.637	8.674
	7	7.568	7.455		7.641	7.521
	8	8.097	7.965		8.134	8.008
	9	9.097	9.075		9.103	9.238
Dibenzo[*ah*]anthracene (**12**)	1′	8.874	8.805		8.708	8.502
	2′	7.719	7.625		7.721	7.583
	3′	7.646	7.55		7.649	7.511
	4′	7.914	7.82		8.113	7.944
	3	7.760	7.67		8.016	8.077
	4	7.963	7.88		8.121	8.230
	10	9.155	9.075		9.170	9.107
Acenaphthylene (**13**)	1	7.812			7.829	7.826
	2	7.548			7.474	7.519
	3	7.692			7.708	7.701
	5,6	7.083			7.070	7.024
Fulvene (**14**)	1,4	6.228[g]			6.384	6.317
	2,3	6.531			6.421	6.404
	6	5.892			6.015	5.960
Toluene *ortho*		7.180	7.061[h]		7.080	
meta		7.260	7.140		7.284	
para		7.165	7.042		7.172	
Me		2.343	2.337[i]		2.343	
tert-Butylbenzene *ortho*		7.390	7.281[h]		7.279	
meta		7.297	7.180		7.358	
para		7.165	7.052		7.218	
Me		1.325	1.319[i]		1.332	

[a] This work except where stated. [b] Ref. 7. [c] Ref. 12. [d] Ref. 36. [e] Ref. 37. [f] Ref. 38. [g] Ref. 39. [h] Ref. 16. [i] Ref. 2, vol. 2, Appendix B. un = unresolved.

these data are reproduced in Table 3. Also given in Table 3 are the SCS values obtained in our laboratory for selected compounds in dilute $CDCl_3$ solution. The excellent agreement between the sets of SCS values confirms this assumption.

The data collected in Tables 2 and 3 provide a rigorous test of the application of both the CHARGE model and also of present ring current theories to these compounds. The compounds listed in the tables are all of fixed conformation. The GAUSSIAN94 (6-31G*/3-21G) and the PCMODEL calculations gave molecular geometries for the aromatic

	Proton substituent chemical shifts ($\Delta\delta_H$)					
	ortho		*meta*		*para*	
Substituent	Obs	Calc	Obs	Calc	Obs	Calc
H	0.00	0.00	0.00	0.00	0.00	0.00
CH_3	−0.20	−0.27	−0.12	−0.06	−0.22	−0.17
	−0.16		−0.08		−0.18[b]	
t-Bu	0.02	−0.06	−0.08	0.02	−0.21	−0.12
	0.05		−0.04		−0.19[b]	
F	−0.29	−0.23	−0.02	0.02	−0.23	−0.21
Cl	0.03	−0.04	−0.02	0.07	−0.09	−0.08
Br	0.18	0.07	−0.08	0.09	−0.04	−0.02
I	0.39	0.18	−0.21	0.08	0.00	0.01
OH	−0.56	−0.53	−0.12	−0.13	−0.45	−0.42
OCH_3	−0.48	−0.44	−0.09	−0.12	−0.44	−0.41
NH_2	−0.75	−0.62	−0.25	−0.24	−0.65	−0.65
CF_3	0.32	0.28	0.14	0.18	0.20	0.20
	0.29		0.14		0.21[c]	
CHO	0.56	0.54[d]	0.22	0.20[d]	0.29	0.26
$C(O)CH_3$	0.62	0.61[d]	0.14	0.21[d]	0.21	0.28
$C(O)OCH_3$	0.71	0.91[d]	0.11	0.21[d]	0.21	0.26
CN	0.36	0.35	0.18	0.21	0.28	0.24
	0.32		0.14		0.27[e]	
NO_2	0.95	0.81	0.26	0.23	0.38	0.25

[a] Ref. 16 unless stated otherwise. [b] This work ($CDCl_3$ soln.). [c] Ref. 42. [d] Averaged, see Table 5 and text. [e] Ref. 43.

hydrocarbons in excellent agreement with the experimental geometries, where known (*e.g.* benzene C–C 1.397, C–H 1.087 Å (MP2/6-31G*), *vs.* 1.395 and 1.087 Å (PCMODEL) and 1.396 and 1.083 Å (experimental)[40]).

In the CHARGE model the α, β and γ effects of the substituents are considered to be due to electronic effects and therefore they are modelled on a simple empirical basis. The α effect of an sp^2 carbon is given from the difference in the electronegativities of the carbon and hydrogen atoms divided by the appropriate exchange integral. The value of this integral was chosen to reproduce the observed chemical shift of ethylene (Table 2). This gives a partial atomic charge for the ethylene protons of +0.075 e which corresponds to a C–H bond dipole of 0.4 D. This is in reasonable agreement with the usual quoted range (*ca.* 0.6–0.7 D).[41] The β effect is calculated directly from the carbon electronegativity and proton polarisability,[28] thus the only other electronic effect to be considered is the γ effect (H–C–C–C) of the unsaturated carbon atoms in the aromatic compounds. For the condensed aromatic compounds considered here the only values of the CCCH dihedral angle θ are 0° and 180° (Table 2) and thus eqn. (1) may be simplified to $A + B\cos\theta$ with the coefficients A and B to be obtained from the observed data.

Long-range effects

The interactions considered to be responsible for the long range effects of the aromatic ring have been documented earlier as steric plus magnetic anisotropy (*i.e.* ring current) effects. (There is also a small electric field effect due to the C–H dipoles. This is calculated by CHARGE directly from the partial atomic charges as the coefficient A_Z in eqn. (4) has already been determined). Thus we are now in a position to test the theoretical treatment given earlier against the observed data presented in the tables.

Table 4 Observed *vs.* calculated proton chemical shifts (δ) in [10]paracyclophane (**16**)

Carbon atom (CH_2)	Observed (CH_2)	Calculated (average)	
α	2.62	2.453	2.606
		2.759	
β	1.54	1.806	1.699
		1.592	
γ	1.08	1.631	1.270
		0.909	
δ	0.73	1.133	0.894
		0.655	
ε	0.51	0.626	0.525
		0.424	
Aromatic	7.04	7.102	7.088
		7.074	

In previous investigations in this series which were concerned with substituted alkanes the steric effect of all non-hydrogen atoms was deshielding on the near protons, but proton–proton interactions gave a shielding effect. This was confirmed both experimentally and theoretically. In contrast it is immediately obvious from both the results of previous investigations[7,13] and the data presented here that proton–proton steric interactions in the aromatic systems considered here give rise to *de*shielding effects on the proton chemical shifts. A further unambiguous demonstration that steric effects on proton chemical shifts in aromatic systems are totally different from those in saturated systems came from the observation of the proton chemical shift of the unique CH proton in the cyclophane (**15**). This proton occupies a position along the symmetry axis of the benzene ring and occurs at −4.03 δ. Because of its proximity to the benzene ring plane (it is *ca.* 1.9 Å above the ring plane) it is an excellent test of any ring current theory and was used by Schneider *et al.* in their investigation of the different ring current models.[8] It is also in close proximity to the benzene ring carbon atoms, the average C ··· H distance being *ca.* 2.20 Å. Any deshielding effect from the aromatic carbon atoms comparable to that found for saturated carbon atoms would have a pronounced deshielding effect on this proton. For example using the steric coefficient found previously for saturated carbon atoms (a_s in eqn. (3) = 220.0 ppm Å^6) would give a value for the CH proton chemical shift of +6.0 δ! Clearly there is no significant deshielding steric effect from the aromatic carbon atoms at this proton. Schneider *et al.*[8] termed this a "soft" steric effect in contrast to the "hard" steric effect of proton–proton interactions. This is supported by the results for [10]paracyclophane (Table 4) in which there is good agreement between the observed and calculated shifts again with no sp^2 carbon steric effect. This result was adopted in the CHARGE routine so that there is no steric effect on the proton chemical shifts from any aromatic carbon atom. Note that this may not be the case for olefinic carbon atoms and work is currently in place in our laboratory to further define this interesting result.[42]

Thus the parameters to be determined from the observed results in Table 2 are the coefficients A and B for the carbon γ effect [eqn. (1)], the appropriate H···H steric coefficient [eqn. (3)], the ring current equivalent dipole μ [eqn. (8)] and the factors *fc* [eqn. (8)] for the condensed rings. There are six factors for both model A and model B (Table 1) making a total of 10 unknown parameters. The values of the unknown parameters were achieved using a non-linear least mean squares programme (CHAP8)[44] to give the best fit with the observed data. The data set used comprises all the condensed aromatics of Table 2, a total of 57 proton shifts thus the iteration is over-determined. The initial iteration for model A clearly showed that coronene was an exception and this was removed from the subsequent iteration. With this amendment the programme iterated satisfactorily with reasonable rms error and definition. For model B coronene is a separate case and the iteration performed satisfactorily. The iteration gave $A = -0.107$, $B = 0.143$, the H···H steric coefficient a_S [eqn. (3)] = +24.55 ppm Å^6, μ [eqn. (8)] = 26.2 ppm Å^3 and the *fc* values in Table 1. In fulvene and acenaphthylene both the ring current of the five-membered ring (μ_P) and also the factors (*fc*) for the benzenoid rings in acenaphthylene were parametrised separately. This gave $\mu_P = 11.6$ ppm Å^3 and $fc = 0.81$. These iterations are for two unknowns and seven observed shifts, thus the iterations are still overdetermined.

The determination of these unknown parameters also allows the calculation of the proton SCS of the monosubstituted benzenes in Table 3 as the electric field and anisotropic effects of the substituents have already been determined previously. The appropriate values of the coefficients in eqn. (10) needed to model the effect of the alkyl substituents on the π densities were $a_r^0 = a_r + 0.15$, $\omega = -0.50$. The only other effect to consider is the steric effect of the side-chain protons on the *ortho* protons of the benzene ring. The steric effect of alkane protons on olefinic protons was determined from a general investigation involving a variety of olefinic molecules[42] to be deshielding and this result was used here. The steric effect of the OH and NH protons in alcohols and amines has been shown to be zero[45] and again this result was incorporated into the present calculations. This allowed the determination of the proton SCS of all the monosubstituted benzenes of Table 3 and these results are given with the observed data in the table. There is generally excellent agreement between the observed and calculated shifts in Table 3 and this good agreement allows the SCS in the benzene ring to be analysed further in terms of the constituent interactions (see discussion).

Finally it was felt to be of interest to determine whether the equivalent dipole ring current calculation given here could be used to determine the benzene ring current effect for protons at the side and over the benzene ring. This data was used by Schneider[8] in determining the accuracy of the various ring current models. We consider here two illustrative examples: the unique CH proton in the tribridged cyclophane (**15**)[8] and the protons in [10]paracyclophane (**16**).[46] The proton chemical shifts for both compounds have been recorded in dilute $CDCl_3$ solution. The geometries of both compounds were modelled by PCMODEL and GAUSSIAN. **15** is a rigid strained molecule but in **16** the methylene chain exists in two equivalent rapidly interconverting staggered conformations. Thus the two protons on each methylene group in the alkyl chain have the same observed shift and the calculated shifts for the two methylene protons have to be averaged. The calculations used eqn. (8) to determine the ring current shifts with the value of the equivalent dipole obtained above. The CH proton of **15** is observed at $-4.03\,\delta$ (calc. $-4.03\,\delta$) and the corresponding data for **16** are given in Table 4.

Discussion

The general agreement of the observed *vs.* calculated shifts in Tables 2 and 4 and the observed *vs.* calculated SCS of Table 3 is very good. Although the calculated values for models A and models B for the individual protons vary appreciably (Table 2), the overall agreement for both models is similar. For the 57 data points of Table 2 the rms error (obs. *vs.* calc. shifts) is 0.13 ppm (model A) and 0.12 ppm (model B) over a range of 3.3 ppm. The analogous calculation using only the benzene ring current (*i.e.* all *fc* values = 1.0) gives much poorer agreement (rms = 0.28 ppm) showing that it is necessary to take account of the variation in the ring current density for a proper description of the proton chemical shifts. Although for convenience the SCS are given in Table 3, as the proton chemical shift of benzene is calculated accurately (Table 2) obviously the actual chemical shifts of all the substituted benzenes are calculated to the same accuracy as the SCS values in Table 3. It can be seen that the great majority of the observed shifts are reproduced to <0.1 ppm, though there are some exceptions (see later). This is the first quantitative calculation of this data and it implies that the latest CHARGE programme (CHARGE7) can be applied with some confidence to the prediction of the proton chemical shifts of virtually any substituted benzenoid compound.

The calculation also provides new insight into the interpretation of these proton chemical shifts as the different interactions responsible for the calculated values are separately identified and quantified in the CHARGE programme. The ring current calculations provide further evidence for the accuracy of the simple equivalent dipole model of the benzene ring current. The value of μ of 26.2 ppm Å^3 is very similar to that obtained from the classical circulating current model (27.6).[17,47] The calculations also confirm previous studies[47] in demonstrating that the ring current effect is not the only factor responsible for the difference between the ethylene and benzene proton shifts. The experimental difference of 1.93 ppm (Table 2) is made up of 1.77 ppm from the ring current and 0.17 ppm from the electronic effects of the β and γ carbon atoms of benzene. This was allowed for in some previous ring current calculations by using cyclohexadiene rather than ethylene as the appropriate olefinic model[47] and the above calculations support this approach. It is also pertinent to note the excellent agreement obtained with the simple equivalent dipole model. On this basis the use of the more complex double dipole and double-loop models does not appear to be justified. Interestingly Mallion[48] came to exactly the same conclusion many years ago.

It is of interest to compare the values of the separate ring current factors (*fc*) in Table 1 with the values obtained previously.[7,12] The trends are similar, supporting the original compartmentalisation of these factors, though the values obtained here are mostly much nearer to the benzene value ($fc = 1$) than the previous calculations. This is exactly to be expected as Huckel theory usually over estimates any electron separation. The only exception is the value for coronene. In model A the outer rings are of type 16b (*i.e.* analogous to the middle ring of phenanthrene) but this value of the ring current density (0.745, Table 1) gives a much too low value for the proton chemical shift. A value of *fc* of 1.06 reproduces the experimental proton chemical shift. In model B this problem does not arise as coronene is a separate case, and the iteration gives a value of $fc = 1.008$, very close to the benzene value and the Huckel calculated value.

It is encouraging that the calculated shifts for the non-alternant hydrocarbons of fulvene and acenaphthylene are in very good agreement with the observed shifts (Table 2) as this suggests that the approach adopted here can be extended to these systems. The value of the ring current of the five-membered ring obtained here (11.6 ppm Å^3) may be used to obtain the current density in the five-membered ring as the equivalent dipole $\mu = iA$ where A is the area of the current loop.

Substituent			Calculated contribution				
			γ-Effect	Steric	Anisotropic	Electric field	π Shift
CH_3	*ortho*		−0.144	—	—	—	−0.064
	meta		—	—	—	—	−0.132
	para		—	—	—	—	−0.183
F	*ortho*		0.128	—	—	—	−0.360
	meta		—	—	—	0.115	−0.137
	para		—	—	—	0.088	−0.332
OH	*ortho*		−0.128	—	—	—	−0.494
	meta		—	0.011	—	—	−0.188
	para		—	0.005	—	—	−0.456
CHO	*ortho*	H-2	0.144	—	−0.125	0.360	0.195
		H-6	0.144	—	0.767	0.153	0.195
	meta	H-3	—	—	−0.043	0.062	0.073
		H-5	—	—	0.107	0.069	0.073
	para		—	—	0.010	0.049	0.181
CN	*ortho*		−0.230	—	—	0.372	0.151
	meta		—	—	—	0.127	0.056
	para		—	—	—	0.097	0.138
NO_2	*ortho*		0.096	—	—	0.606	0.105
	meta		—	—	—	0.143	0.043
	para		—	—	—	0.105	0.115

After allowing for the area of the five-membered ring compared to benzene this gives a current density of $0.63i_b$, much less than benzene. More data on similar systems would be necessary to confirm this result.

Proton SCS in substituted benzenes

The good agreement between the observed and calculated SCS in Table 3 together with the separation of the different interactions in CHARGE allows us to determine these interactions for the different substituents and Table 5 gives the contributions to the proton SCS for selected substituents in Table 3.

In Table 5 for the anisotropic substituents (*e.g.* C=O) the contributions are given for each separate proton (*e.g.* H2 and H6) although these are averaged in Table 3 to compare with the observed (averaged) data. The large effect of the carbonyl anisotropy is clearly apparent in these figures. The orientation of the carbonyl is such that the oxygen atom is *syn* to H6. The calculations are supported by and also show very clearly the origin of the large *ortho* proton deshielding in *o*-methoxybenzaldehyde (H6 7.82 δ)[37] compared to *o*-hydroxybenzaldehyde (H6 7.50 δ) where the carbonyl group is now hydrogen bonded to the hydroxy group.

Table 5 also shows that the carbonyl anisotropy is the major factor in the *meta* proton SCS of benzaldehyde (*cf.* H3 and H5). This demonstrates the importance of these "other" effects, which are of course not included in any of the correlations of electron densities *etc.* with the proton SCS. Indeed it is important to stress the difference between the present calculations and the correlations with Hammett σ,[22] the Swain–Lupton *F* and *R* values[49] *etc.* The CHARGE calulations are ground state calculations whilst the other parameters are derived from pH and rate constants and therefore reflect energy differences between the anion or the transition state and the ground state of the molecule, a totally different quantity.

Nevertheless in view of the numerous correlations of these quantities with the proton SCS it is useful to consider these correlations together with the present calculations. The correlation between the proton SCS and Hammett σ_I and $\sigma_R{}^0$ values was given as eqn. (12)[21] for a similar set of substituents to those

$$\begin{aligned} \text{SCS } (para) &= 0.27\sigma_I + 1.25\sigma_R{}^0 \\ \text{SCS } (meta) &= 0.24\sigma_I + 0.446\sigma_R{}^0 \end{aligned} \qquad (12)$$

in Table 5 and a similar analysis of the SCS in terms of the Swain–Lupton *F* and *R* values gives eqn. (13).

$$\begin{aligned} \text{SCS } (para) &= 0.142F + 0.926R \\ \text{SCS } (meta) &= 0.098F + 0.376R \end{aligned} \qquad (13)$$

These equations are reasonably consistent implying in general a much greater resonance effect on the *para* proton SCS than on the *meta* proton SCS. Inspection of the data in Table 5 shows a much more diverse pattern. Indeed the major disadvantage of such correlations is that they obscure the large differences in the SCS components of the various groups which all need to be considered individually. *E.g.* the OH group has no anisotropic or steric effect and both the *meta* and *para* SCS are dominated by the π electron shift. This is much greater in the *para* position but the *meta* SCS is still dominated by the π effect. In contrast, in benzaldehyde the electric field and anisotropy contributions equal the π shift for the *meta* proton and are a significant but minor contribution for the *para* proton. The nitro and cyano groups differ from both of these in that they appear to have no anisotropic effect but the electric field effect is predominant at the *meta* proton and equal to the π shift at the *para* proton. Further investigations in our laboratory have confirmed this result for the cyano group[43] and it would be of interest to perform similar investigations for the nitro group. Clearly each substituent group must be considered separately in order to evaluate the separate steric, electric and anisotropic contributions at the various protons.

Finally it is of interest to consider the discrepancies in the observed *vs.* calculated data of Table 3. The most interesting systematic deviation is that due to Br and I. The calculated values for the *para* SCS for all the halogens are in excellent agreement with the observed data and the *ortho* and *meta* SCS for F and Cl are in reasonable agreement. However the *ortho* SCS for Br and I are more deshielding than calculated and the *meta* SCS much more shielding than calculated. The *ortho* SCS are given by the γ effect, which is a function of the polarisability of the γ atom *i.e.* the halogen. The value of the polarisability was taken from data on alkyl halides[24] thus this may not be appropriate for substituted benzenes. In contrast the *meta* SCS are of interest as similar exceptional behaviour was observed for the 3-protons in equatorial halocyclohexanes.[50] Again there is a large deviation from the calculated value for the Br and I substituents. The equatorial proton is in a similar W orientation to the halogen atom as the *meta* proton in the substituted benzenes and it may be that there is an additional long range (four bond) mechanism for the halogen atoms in this specific orientation. Further studies would be necessary to confirm this.

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References

1 Part 13, R. J. Abraham and N. J. Ainger, *J. Chem. Soc., Perkin Trans. 2*, 1999, 441.

2 (*a*) J. W. Emsley, J. Feeney and L. H. Sutcliffe, *High Resolution NMR Spectroscopy*, Pergamon Press, Oxford, 1965; (*b*) R. C. Haddon, V. R. Haddon and L. M. Jackman, *Top. Curr. Chem.*, 1971, **16**, 103.

3 L. Pauling, *J. Chem. Phys.*, 1936, **4**, 673.

4 J. A. Pople, *J. Chem. Phys.*, 1956, **24**, 1111.

5 (*a*) J. S. Waugh and R. W. Fessenden, *J. Am. Chem. Soc.*, 1957, **79**, 846; (*b*) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012.

6 (*a*) R. J. Abraham, *Mol. Phys.*, 1961, **4**, 145; (*b*) R. J. Abraham and C. J. Medforth, *Magn. Reson. Chem.*, 1987, **25**, 432.

7 (*a*) C. W. Haigh and R. B. Mallion, *Mol. Phys.*, 1970, **18**, 737 and 767; (*b*) C. W. Haigh, R. B. Mallion and E. A. G. Armour, *Mol. Phys.*, 1970, **18**, 751.

8 H. J. Schneider, V. Rudiger and U. Cuber, *J. Org. Chem.*, 1995, **60**, 996.

9 H. J. Bernstein, W. G. Schneider and J. A. Pople, *Proc. R. Soc. London, Ser. A*, 1956, **236**, 515.

10 J. A. Pople, *Mol. Phys.*, 1958, **1**, 175.

11 R. McWeeny, *ibid.*, 1958, **1**, 311.

12 N. Jonathan, S. Gordon and B. P. Dailey, *J. Chem. Phys.*, 1962, **36**, 2443.

13 T. B. Cobb and J. D. Memory, *J. Chem. Phys.*, 1967, **47**, 2020.

14 M. Westermayer, G. Hafelinger and C. Regelmann, *Tetrahedron*, 1984, **40**, 1845.

15 (*a*) S. Castellano and C. Sun, *J. Am. Chem. Soc.*, 1966, **88**, 4741; (*b*) S. Castellano, C. Sun and R. Kostelnik, *Tetrahedron Lett.*, 1967, **46**, 4635 and **51**, 5205; (*c*) M. P. Williamson, R. J. Kostelnik and S. M. Castellano, *J. Chem. Phys.*, 1968, **49**, 2218.

16 K. Hayamizu and O. Yamamoto, *J. Mol. Spectrosc.*, 1968, **28**, 89 and 1969, **29**, 183.

17 R. J. Abraham, J. Fisher and P. Loftus, *Introduction to NMR Spectroscopy*, J. Wiley, New York, 1988.

18 J. B. Lambert, H. B. Shurvell, D. A. Kightner and R. G. Cooks, *Organic Structural Spectroscopy*, Prentice-Hall, New Jersey, 1998.

19 E. Pretsch, J. Seibl, T. Clerc and W. Simon, *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd Edn., Springer-Verlag, Berlin, 1989.

20 G. C. Levy and G. L. Nelson, *Carbon-13 NMR for Organic Chemists*, J. Wiley, New York, 1972.

21 W. J. Hehre, R. W. Taft and R. D. Topsom, *Prog. Phys. Org. Chem.*, 1976, **12**, 159.

22 R. T. C. Brownlee and R. W. Taft, *J. Am. Chem. Soc.*, 1970, **92**, 7007.

23 G. K. Hamer, I. R. Peat and W. F. Reynolds, *Can. J. Chem.*, 1973, **51**, 897 and 915.

24 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 31.

25 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 203, 881.

26 R. J. Abraham, L. Griffiths and M. A. Warne, *ibid.*, 1998, 1751.

27 13th International NMR Conference, Edinburgh, July, 1999.

28 R. J. Abraham, L. Griffiths and M. A. Warne, *Magn. Reson. Chem.*, 1998, **S179**, 36.

29 (*a*) R. J. Abraham and P. E. Smith, *J. Comput. Chem.*, 1987, **9**, 288; (*b*) R. J. Abraham and P. E. Smith, *J. Comput. Aided Mol. Des.*, 1989, **3**, 175.

30 (*a*) R. J. Abraham and P. E. Smith, *Nucleic Acids Res.*, 1988, **16**, 2639; (*b*) A. Streitweiser, *Molecular Orbital Theory for Organic Chemists*, J. Wiley, New York, 1961.

31 A. L. McClellan, *Tables of Experimental Dipole Moments*, vol. 1, Freeman, London, 1963; vols. 2 and 3 Rahara Enterprises, California, vol. 2, 1974, vol. 3, 1989.

32 H. Gunther, *NMR Spectroscopy*, 2nd edn., J. Wiley, Chichester, 1995, p. 71.

33 P. B. Ayscough, *Electron Spin Resonance in Chemistry*, Methuen, London, 1967.

34 GAUSSIAN94, Gaussian Inc., Pittsburgh, PA, 1994; J. Frisch, G. W. Trucks, M. Head-Gordon, P. M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzalez, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart and J. A. Pople.

35 PCMODEL version 7, Serena Software Ltd., PO Box 3076, Bloomington, Indiana, 1998.

36 U. E. Matter, C. Pascual, E. Pretsch, A. Pross, W. Simon and S. Sternhell, *Tetrahedron*, 1969, **25**, 691.

37 C. J. Puchert and J. Behnke, *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, Aldrich Chemical Company Inc., Milwaukee, USA, 1993.

38 J. Netka, S. L. Crump and B. Rickborn, *J. Org. Chem.*, 1986, **51**, 1189.

39 U. Nuchter, G. Zimmermann, V. Francke and H. Hopf, *Liebigs Ann. Rec.*, 1997, 1505.

40 Landholt-Bornstein, vol. 7, *Structure Data of Free Polyatomic Molecules*, ed. K. H. Hellwege and A. M. Hellwege, Springer, New York, 1976.

41 (*a*) O. Exner, *Dipole Moments in Organic Chemistry*, George Thieme Pub., Stuttgart, 1975; (*b*) V. I. Minkin, O. A. Osipov and Y. A. Zhdanov, *Dipole Moments In Organic Chemistry*, Plenum Press, New York, 1970.

42 R. J. Abraham and M. Canton, unpublished work.

43 R. J. Abraham and M. Reid, *Magn. Reson. Chem.*, in the press.

44 S. S. Kuo, *Computer Applications of Numerical Methods*, ch. 8, Addison-Wesley, London, 1972.

45 R. J. Abraham, unpublished work.

46 A. Agarwal, J. A. Barnes, J. L. Fletche, M. J. McGlinchey and B. G. Sayer, *Can. J. Chem.*, 1973, **51**, 897.

47 R. J. Abraham and W. A. Thomas, *J. Chem. Soc. B*, 1966, 127.

48 R. B. Mallion, *J. Chem. Phys.*, 1980, **75**, 793.

49 C. G. Swain and E. P. Lupton, *J. Am. Chem. Soc.*, 1968, **90**, 4328.

50 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 2151.

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Proton chemical shifts in NMR. Part 14.[1] Proton chemical shifts, ring currents and π electron effects in condensed aromatic hydrocarbons and substituted benzenes

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The proton resonance spectra of a variety of condensed aromatic compounds including benzene, naphthalene, anthracene, phenanthrene, pyrene, acenaphthylene and triphenylene were obtained in dilute $CDCl_3$ solution. Comparison of the proton chemical shifts obtained with previous literature data for CCl_4 solution shows small but significant differences. A previous model (CHARGE6) for calculating the proton chemical shifts of aliphatic compounds was extended to aromatic compounds. This was achieved by including an automatic identification of both five- and six-membered aromatic rings based on atomic connectivities plus a dipole calculation of the aromatic ring current. The ring current intensity in the molecules was calculated by two alternative methods. a) The ring current intensity in the individual benzenoid rings was a function of the number of adjoining rings and b) the molecular ring current was proportional to the molecular area divided by the molecular perimeter. This, plus the inclusion of deshielding steric effects for the crowded protons in these molecules, gave a good account of the observed chemical shifts. The model was also applied successfully to the non-alternant hydrocarbons of fulvene and acenaphthylene and to the aliphatic protons near to and above the benzene ring in tricyclophane and [10]cyclophane.

The Huckel calculation of the π electron densities in CHARGE6 was used to calculate the π electron densities in substituted benzenes. The π-inductive effect was used to simulate the effect of CX_3 groups (X = H, Me, F) on the benzene ring. These together with the long range effects of the substituent groups identified previously allowed a precise calculation of the SCS of a variety of substituents on all the benzene ring protons.

The model gives the first accurate calculation of the proton chemical shifts of condensed aromatic compounds and of the proton SCS in the benzene ring. For the data set of 55 proton chemical shifts spanning 3 ppm the rms error of the observed *vs.* calculated shifts was *ca.* 0.1 ppm. The model also allows the interpretation of the shifts in terms of the separate interactions calculated in the programme, *i.e.* π electron densities and steric, anisotropic and electric field effects. Previous correlations of the proton SCS with π electron densities and substituent parameters are shown to be over simplified. The relative proportions of these different interactions are very different for each substituent and for each ring proton.

Introduction

The influence of the π electron densities and ring currents of aromatic compounds on their proton chemical shifts have been investigated since the beginning of proton NMR spectroscopy.[2] Thus it is all the more surprising that despite this wealth of investigation there is still no authoritative calculation (even a semi-empirical one) of the proton chemical shifts of aromatic compounds and the structural chemist still has to rely on proton data banks for the identification of aromatic compounds by NMR.

Pauling[3] introduced the concept of an aromatic ring current to explain the diamagnetic anisotropy of crystalline benzene. Pople[4] later extended this to explain the difference in the proton chemical shifts of benzene and ethylene and he further showed that the equivalent dipole model of this ring current gave a surprisingly good account of this difference. More sophisticated ring current models for benzene were then developed. The classical double-loop[5] and double dipole models[6] mimic the π electron circulation by placing the current loops (and equivalent dipoles) above and below the benzene ring plane. A value of ±0.64 Å was found to be most appropriate. The equations of Haigh and Mallion[7] give the shielding ratios directly from quantum mechanical theory. Schneider *et al.*[8] have recently presented a detailed experimental examination of the double-loop and Haigh and Mallion ring current models, though not the simple equivalent dipole model (see later). The calculations gave good agreement with the experimental data, thus the effect of the benzene ring current on the chemical shifts of neighbouring protons is reasonably well understood.

However, the proton chemical shifts in condensed aromatic compounds and substituted benzenes have not yet been well calculated and this is the subject of this investigation. Bernstein *et al.*[9] in their initial calculations of the proton chemical shifts of condensed aromatic compounds assumed the same ring current for each benzenoid ring but this was subsequently considered to be an over simplification. Thus it is first necessary to calculate the π electron current density for each benzenoid ring and then to calculate the effects of these currents on the chemical shifts of the ring protons. The quantum mechanical method for calculating the π electron current densities was first given by Pople[10] and McWeeny[11] subsequently extended the London–Pople theory. McWeeny's work gives not only the circulating current density but also the effect of this circulating current at the proton in question. It should be noted that all these theories were based on simple Huckel theory.

Early experimental investigations to test these theories were not helped by the complex proton spectra of many condensed aromatic hydrocarbons at the low applied magnetic fields then in use and also by the quite large concentration effects on the proton chemical shifts due to the propensity of these

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large planar rings to stack in solution. However three systematic investigations attempted to overcome these difficulties. Jonathan *et al.*[12] analysed the proton spectra of several condensed aromatics at infinite dilution in CCl_4 or CS_2. They then used the Pople–London theory to calculate the current intensity in the benzenoid rings and the Johnson–Bovey tables[5] to obtain the ring current shifts. They also estimated C–C and C–H anisotropic effects and found that these could be ignored. They obtained "only fair agreement" with the observed shifts. Varying the separation of the π-electron loops gave a poorer fit with the observed shifts. They noted that other interactions were affecting the proton shifts and in particular noted a high frequency shift for close protons which was suggested to be due to van der Waals contact but did not attempt to quantify this.

Subsequently Cobb and Memory[13] and Haigh and Mallion[7] performed two similar but more extensive investigations. The proton spectra of several condensed aromatic compounds in dilute solution were analysed and the McWeeny equation used to obtain the ring current densities and shielding ratios. They both ignored σ bond anisotropies in this calculation. Both investigations obtained reasonable correlations for "non overcrowded protons" between the observed proton shifts and the ratio of the π electron shielding for a given proton compared to benzene (H'/H'_b in the nomenclature of ref. 7). The more comprehensive data of ref. 7 when converted to the δ scale may be written as $\delta_{obs} = 1.56\ (H'/H'_b) + 5.66$ with an rms error of 0.06 ppm over a range of *ca.* 1.6 ppm. However the differences between the calculated and observed data for the "crowded" protons were *ca.* 0.5–0.7 ppm with one of 1.2 ppm, all to high frequency of the calculated value. Again they attributed these shifts to steric effects but did not quantify or define these effects.

More recently Westermayer *et al.*[14] used a double dipole model to test the observed shifts. They correlated the resulting geometric factors with the observed shifts to obtain a value for the benzene diamagnetic susceptibility anisotropy. They stated that superior results for the sterically crowded protons were obtained but it is not clear why this should be the case as no steric term was introduced.

Although it is obvious which protons are crowded (*e.g.* H4,5 in phenanthrene) it is not obvious whether this interaction is also present in the other "less crowded" protons. Thus the simple question of whether the difference between the α and β proton chemical shifts in naphthalene is due to ring currents, π-electron densities or steric effects has still not been satisfactorily answered. Although Pople in his original studies[10] calculated the ring current intensities in the five- and seven-membered rings of azulene, to our knowledge there has not been any calculation of the proton chemical shifts in non-alternant hydrocarbons.

The influence of the substituents on the proton chemical shifts in the benzene ring has also been investigated for many years and again there is still no quantitative calculation of these effects. Following the classic work of Castellano *et al.*[15] and Hayamizu and Yamamoto[16] who completely analysed the complex proton spectra of a wide range of monosubstituted benzenes in dilute solution in CCl_4 the proton substituent chemical shifts (SCS) are known accurately and tables of these SCS are an integral part of any text on NMR spectroscopy.[17–19] The theoretical interpretations of these effects have concentrated on the correlation between the SCS and the calculated π (and also σ) electron densities on the adjacent carbon atoms following the excellent correlation found between the ^{13}C SCS and the π electron densities at the *para* carbon atom in monosubstituted benzenes.[20] Correlations with π electron densities calculated by various methods have been reported, the most recent being the *ab initio* calculations of Hehre *et al.*[21] They used the STO-3G basis set and showed that the ^{13}C SCS could be well interpreted on the basis of calculated electron densities but this was not the case for the proton SCS. The *para* proton SCS could be correlated with the total charge density at the *para* carbon atom but the *meta* proton SCS did not correlate well with the calculated *meta* carbon charge densities but with the sum of the charges at the hydrogen and attached carbon atoms. They stated that "this lack of consistency indicates either that the calculations are unrealistic or that the ^1H SCS depend to a very significant extent on factors other than electron densities at the H and attached C atoms". They omitted the *ortho* proton SCS presumably on the grounds that these other effects are even more important at these protons. They also noted that strongly electronegative substituents caused polarisation of the π system without charge transfer, leading to changes in the π densities around the ring and this is termed the π-inductive effect. They also found various correlations between the calculated charge densities and the Taft σ_I and σ_R values. This reflects the results of other investigators who have attempted to correlate substituent parameters with the proton SCS.[16,22,23] Despite all these endeavours there is still no calculation of proton SCS in substituted benzenes reliable enough to be of use to the structural chemist.

We give here the proton chemical shifts of a selection of condensed aromatic compounds in $CDCl_3$ and show that these differ by a small but significant amount from the earlier data in CCl_4 solution. These provide sufficient data for an analysis of the proton chemical shifts based on the CHARGE model for calculating proton chemical shifts.[1] In previous parts of this series this model has been applied successfully to a variety of saturated hydrocarbons,[24] haloalkanes,[25] ethers[26] and ketones.[1] We shall show that this model can be extended to provide a quantitative calculation of the proton shifts in condensed aromatic compounds, including two non-alternant hydrocarbons and the SCS of monosubstituted benzenes. We give two alternative calculations of the ring current intensity in the benzenoid rings together with a dipole model of the benzene ring current. In model A the ring current intensity in the individual benzenoid rings is a function of the number of adjoining rings whereas in model B the molecular ring current is given by the classical Pauling treatment as proportional to the molecular area divided by the molecular perimeter. All the protons in the condensed aromatic compounds are considered and the "crowded" proton chemical shifts reproduced by a simple steric effect. The effects of substituents in monosubstituted benzenes are well reproduced for the *ortho*, *meta* and *para* protons on the basis of calculated π electron densities plus the steric, anisotropic and electric field effects of the substituents. We show also that the model reproduces the high field shifts of protons situated over the benzene ring thus providing a general calculation of proton chemical shifts of condensed aromatic compounds. A preliminary account of this work has been presented.[27]

Theory

As the theory has been detailed previously only a brief summary of the latest version (CHARGE6)[28] is given here. The theory distinguishes between substituent effects over one, two and three bonds which are attributed to the electronic effects of the substituents and longer range effects due to the electric fields, steric effects and anisotropy of the substituents. The CHARGE scheme calculates the effects of atoms on the partial atomic charge of the atom under consideration, based upon classical concepts of inductive and resonance contributions.

If we consider an atom I in a four atom fragment I–J–K–L the partial atomic charge on I is due to three effects. There is an α effect from atom J given by the difference in the electronegativity of atoms I and J and a β effect from atom K proportional to both the electronegativity of atom K and the polarisability of atom I. There is also a general γ effect from atom L given by the product of the atomic polarisabilities of atoms I and L. For the second row atoms (C, O, *etc.*) the γ effect (*i.e.* C–C–C–H) is parameterised separately and is given by eqn. (1) where θ is the C–C–C–H dihedral angle and *A* and *B* empirical parameters.

$$= A + B_2\cos\theta \qquad 90^\circ \le \theta \le 180^\circ \qquad (\text{[illegible]})$$

There are also routines for the methyl γ effect and for the decrease in the γ effect of the electronegative oxygen and fluorine atoms for CX_2 and CX_3 groups.

The total charge is given by summing these effects and the partial atomic charges (q) converted to shift values using eqn. (2).

$$\delta = 160.84q - 6.68 \qquad (2)$$

The effects of more distant atoms on the proton chemical shifts are due to steric, anisotropic and electric field contributions. H···H steric interactions in alkanes were found to be shielding and X···H (X = C, F, Cl, Br, I) interactions deshielding according to a simple r^{-6} dependence [eqn. (3)].

$$\delta_{\text{steric}} = a_S/r^6 \qquad (3)$$

Furthermore any X···H steric contributions on a methylene or methyl proton resulted in a push-pull effect (shielding) on the other proton(s) on the attached carbon.

The effects of the electric field of the C–X bonds (X = H, F, Cl, Br, I, O) were calculated from eqn. (4) where A_Z was

$$\delta_{\text{el}} = A_Z E_Z \qquad (4)$$

determined as 3.67×10^{-12} esu (63 ppm au) and E_Z is the component of the electric field along the C–H bond. The electric field for a univalent atom (*e.g.* fluorine) is calculated as due to the charge on the fluorine atom and an equal and opposite charge on the attached carbon atom. The vector sum gives the total electric field at the proton concerned and the component of the electric field along the C–H bond considered is E_Z in eqn. (4). This procedure is both simpler and more accurate than the alternative calculation using bond dipoles.

The magnetic anisotropy of a bond with cylindrical symmetry (*e.g.* CN) was obtained using the McConnell equation [eqn. (5)], where R is the distance from the perturbing group to

$$\delta_{\text{an}} = \Delta\chi^{\text{CN}}\,(3\cos^2\varphi - 1)/3R^3 \qquad (5)$$

the nucleus of interest in Å, φ is the angle between the vector R and the symmetry axis and $\Delta\chi^{\text{CN}}$ the molar anisotropy of the CN bond. ($\Delta\chi^{\text{CN}} = \chi^{\text{CN}}{}_{\text{parl}} - \chi^{\text{CN}}{}_{\text{perp}}$) where $\chi^{\text{CN}}{}_{\text{parl}}$ and $\chi^{\text{CN}}{}_{\text{perp}}$ are the susceptibilities parallel and perpendicular to the symmetry axis respectively.

For a non-cylindrically symmetric group such as a carbonyl group eqn. (5) is replaced by the full McConnell eqn. (6). The

$$\delta_{\text{an}} = [\Delta\chi_1(3\cos^2\theta_1 - 1) + \Delta\chi_2(3\cos^2\theta_2 - 1)]/3R^3 \qquad (6)$$

C=O group has different magnetic susceptibilities (χ_1, χ_2 and χ_3) along the principal axes (X_1, X_2 and X_3) and thus two anisotropy terms are required.

In eqn. (6) θ_1 and θ_2 are the angles between the radius vector R and χ_1 and χ_3 respectively and $\Delta\chi_1$ ($\chi_1 - \chi_2$) and $\Delta\chi_2$ ($\chi_3 - \chi_2$) are the two anisotropies for the C=O bond which may be termed the parallel and perpendicular anisotropy respectively.

These contributions were added to the shifts of eqn. (2) to give the calculated shift of eqn. (7).

$$\delta_{\text{total}} = \delta_{\text{charge}} + \delta_{\text{steric}} + \delta_{\text{anisotropy}} + \delta_{\text{el}} \qquad (7)$$

Application to aromatic compounds

Ring current shifts. There are a number of modifications to be made to CHARGE6 to calculate the proton shifts of aromatic compounds. It was necessary to include the effect of the aromatic ring current and this necessitated a routine which has to automatically recognise an aromatic ring. A routine was written based on the atomic connectivities in the rings and the programme now recognises both five- and six-membered aromatic rings including the heterocyclic rings of pyrrole, furan and thiophene. The aromatic ring current at any proton was then calculated from the equivalent dipole model [eqn. (8)].

$$\delta_{\text{rc}} = fc\mu(3\cos^2\theta - 1)/R^3 \qquad (8)$$

In eqn. (8) R is the distance of the proton from the benzene ring centre, θ the angle of the R vector from the benzene ring symmetry axis, μ is the equivalent dipole of the benzene ring and fc the π electron current density for the benzenoid ring. (For benzene $fc = 1$.)

It was next necessary to calculate the value of fc for any given compound and two alternative methods are presented. The first method (model A) was based on inspection of the calculated ring current intensities of refs. 7 and 12. Haigh and Mallion[7] did not publish the calculated ring current intensities for the common aromatic compounds, but a selection of their calculated values for some less common condensed aromatic compounds is given in Table 1.

Inspection of this data shows that the changes in the ring current intensity are a function of the number and orientation of the rings attached to the benzenoid ring. In model A the ring current intensity in any given benzenoid ring is assumed to be only a function of the number and orientation of the rings attached to the benzenoid ring considered. This may be quantified by the number and orientation of the substituent sp^2 carbon atoms attached to the ring in question (R_0). Thus we define a) the number of attached sp^2 carbons on each ring carbon atom and b) the relative position of these attached atoms in the benzene ring. Thus for benzene each carbon atom has two carbon neighbours thus $R_0 = 12$. For either ring in napthalene two of the carbon atoms have three carbon neighbours thus $R_0 = 14$. The middle rings of anthracene and phenanthrene both have $R_0 = 16$ but the relative positions of the substituent carbons differ in the two cases. These are defined as R_0 equals 16a and 16b. This analysis gives seven different ring systems (Table 1) of which six are present in the molecules indicated in Fig. 1. Only the molecules with the rings itemised A, B in Fig. 1 are included in Table 1 as these are the only molecules for which the ring current intensities were given in ref. 7. However all the molecules measured were included in the iteration (see later).

Inspection of Table 1 shows that with few exceptions the separation of the ring current densities into the different ring types gives a reasonably constant value for each ring type. The only serious exception is the calculated values for ring type 18 (*i.e.* all substituted carbons) of ref. 12 which are very different for perylene and coronene. The values from ref. 7 for the similar molecules benzo[*ghi*]perylene and naphtho[1,2,3,4-*def*]chrysene are much more consistent.

It would be possible to average the calculated values of ref. 7 for each ring type and use these averages in our calculation. In view of the approximations inherent in these calculations it was decided to parametrise the current density for each ring type separately to obtain the best agreement with the observed shifts. These optimised values are given in Table 1 (column 5) and will be considered later.

An alternative method of calculating the molecular ring current (model B) is to use the Pauling model[3] in which the carbon skeleton is considered as a conducting electrical network in which for any current loop the emf is proportional to the area enclosed and the resistance proportional to the number of bonds. On this basis if the condensed aromatics are considered to be made up of a number of regular hexagons the ring current for any molecule is simply proportional to the number of hexagons in the molecule divided by the number of bonds in the

Table 1 Calculated ring current intensities in condensed aromatic hydrocarbons

Molecule	Ring type[a]	(R_0)	Ring current intensity (*fc*)			
			[b]	[c]	Model A	Model B[d]
Benzene (**1**)		12	1.00	1.00	1.00	1.00
Naphthalene (**2**)		14	1.093	1.048,[e] 1.094,[f] 1.121[g]	0.950	0.925
Anthracene (**3**)	Ring A	14	1.085	1.119,[h] 1.197,[i] 1.104[j]		0.943
	Ring B	16a	1.280	1.291,[e] 1.311,[f] 1.299,[g] 1.298,[h] 1.170[j]	0.818	
Phenanthrene (**4**)	Ring A	14	1.133			0.943
	Ring B	16b	0.975	0.877,[g] 0.876[h]	0.745	
Triphenylene (**5**)	Ring A	14	1.111			0.876
	Ring B	18	0.747			
Pyrene (**6**)	Ring A	15	1.329	1.337,[k] 1.292[l]	0.786	0.878
	Ring B	16b	0.964			
Perylene (**7**)	Ring A	15	0.979			0.681
	Ring B	18	0.247	0.603,[f] 0.606[m]	0.173	
Coronene (**8**)	Ring A	16b	1.460		1.06[a]	1.008
	Ring B	18	1.038	0.745,[n] 0.684[l]		
		17	—	1.297,[k] 1.226,[m] 1.310[l]		

[a] See text. [b] Ref. 12. [c] Ref. 7. [d] This work. [e] Hexacene. [f] Dibenzo[*a*,*c*]naphthacene. [g] Dibenzo[*a*,*j*]naphthacene. [h] Dibenzo[*a*,*l*]naphthacene. [i] Dibenzo[*def*,*mno*]chrysene. [j] Benzo[*h*]pentaphene. [k] Dibenzo[*def*,*mno*]chrysene. [l] Benzo[*ghi*]perylene. [m] Naphtho[1,2,3,4-*def*]chrysene. [n] Dibenzo[*b*,*def*]chrysene.

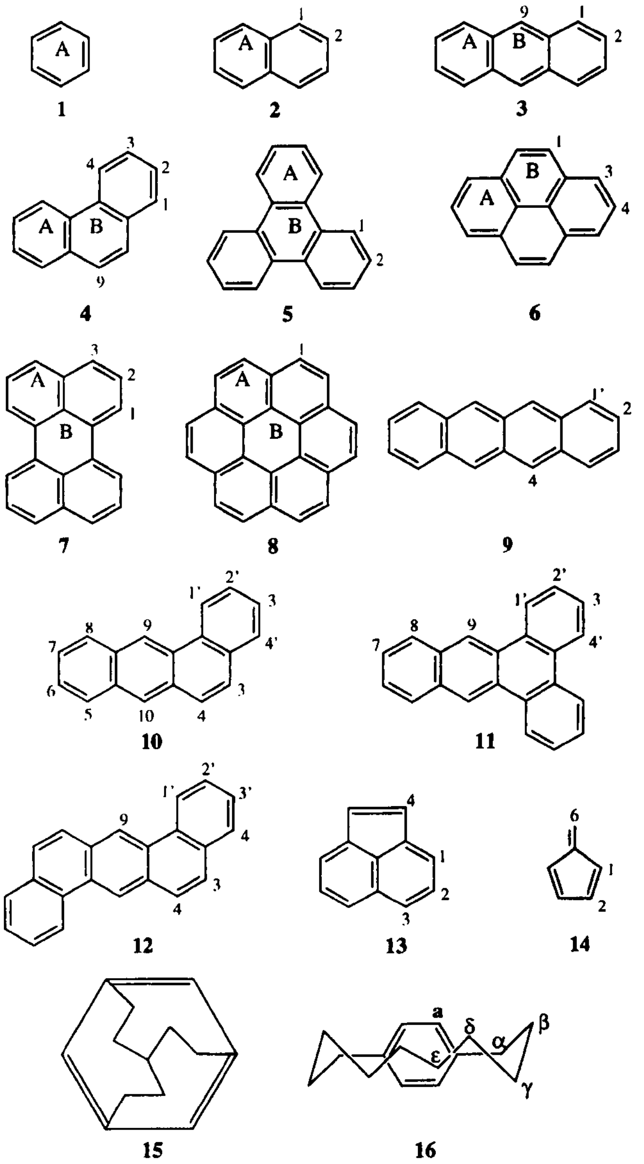

Fig. 1 . Molecules studied and their nomenclature.

perimeter of the molecule. Thus for benzene, naphthalene and anthracene the ring current ratio is 1:6/5:9/7. The Pauling model gives too large a value for the diamagnetic anisotropy of condensed aromatics[6a] so that as in method A the Pauling model was used to separate the various molecular types and the ring current for each molecular type was parametrised against the experimental data. Although the same experimental data are used in both models the different selectivities give different answers. For example in model B anthracene and phenanthrene have identical ring currents which is not the case in model A.

Conversely in model A the fully substituted benzenoid rings in perylene (**7**) and coronene (**8**) have identical ring currents whereas in model B they differ as the molecular area/perimeter ratio differs for the two compounds.

π Electron densities. The π electron densities are calculated in the CHARGE programme from Huckel theory.[29] The standard coulomb and resonance integrals for the Huckel routine are given by eqn. (9), where α_0 and β_0 are the coulomb and

$$\alpha_r = \alpha_0 + h_r\beta_0 \qquad (9)$$
$$\beta_{rs} = k_{rs}\beta_0$$

resonance integrals for a carbon $2p_Z$ atomic orbital and h_r and k_{rs} the factors modifying these integrals for orbitals other than sp^2 carbon. The Huckel routine was modified by the ω technique to model the very polar π systems of the nucleic acid bases.[30] The ω technique involves varying the coulomb integral for each atom according to the charge on that atom. This is shown in eqn. (10) where α_r is the coulomb integral, α_r^0 the

$$\alpha_r = \alpha_r^0 - q_r\,\omega \qquad (10)$$

initial coulomb integral, q_r the excess π charge on atom r and ω a constant. Eqn. (10) "cuts in" at a given value of the excess π charge on atom r. For the nucleic acid bases the appropriate value of ω was 1.40 and and the cut-in threshold 0.2 electrons.[30]

For alternant aromatic hydrocarbons this calculation gives π electron densities at every carbon equal to 1.0 as in benzene. Thus the excess π electron density is zero. This is in agreement with the results of more sophisticated calculations. *E.g.* the excess π electron densities at the α and β carbons of naphthalene are calculated as −0.8 and −4.1 me (millielectrons) from *ab initio* calculations with the 6-31G* basis set.

For the non-alternant hydrocarbons fulvene and acenaphthylene the Huckel routine gives large excess π densities at certain carbon atoms which are much larger than those calculated by *ab initio* methods in which iteration procedures restrict the tendency in the Huckel routine to separate the π charges. The ω technique was modified to correct this by decreasing the "cut in" point of eqn. (10) from 0.2 electrons to 0.01 electrons and reasonable results for these two compounds, though the dipole moments are still on the high side (*e.g.* fulvene 0.92 D (calc.) *vs.* 0.44 D (obs.)[31] and acenaphthylene 0.93 D (calc.) *vs.* 0.3 D (obs.)[31]). As these hydrocarbons have quite different π densities and geometries from the alternant hydrocarbons both the ring current of the five-membered ring and the ring current density of the attached six-membered ring were parametrised separately.

For the substituted benzenes the appropriate values of the coefficients h_r and k_{rs} in eqn. (9) for the orbitals involving hetero atoms have to be found. In ref. 29 two procedures were considered. One was to obtain those values which gave the best agreement with the experimental dipole moments of the compounds investigated, the alternative was to find values which best reproduced the π densities obtained by *ab initio* calculations. Both sets of coefficients were given, but the first set was adopted in the CHARGE programme as the simplest method of obtaining reasonable dipole moments of unsaturated compounds. However later developments of the CHARGE method, in which a more flexible method of reproducing observed dipole moments was adopted, meant that the dipole moments of unsaturated compounds could be reproduced with either set of Huckel parameters. We now use the later set so that the π densities calculated from the Huckel routine reproduce the π densities given from *ab initio* calculations.

The only other modification necessary to the Huckel routine concerns the effect of saturated substituents (*e.g.* CX_3) on the π electron densities in the benzene ring which is usually termed hyperconjugation. It is simple to reproduce this effect in a Huckel calculation if it is regarded as an example of the π-inductive effect mentioned earlier. In this case an equation corresponding to eqn. (10) was used to vary the Coulomb integral of the aromatic carbon atom connected to an sp^3 carbon. In this way changes to the π electron density of the benzene ring due to both electron donating substituents such as CH_3 and electron withdrawing substituents such as CF_3 can be handled by the same procedure.

Having obtained the π electron density in the benzene ring it is then necessary to determine the effect of the π electron density at a given carbon atom on the proton chemical shifts. An experimental determination of this factor is due to Gunther *et al.*[32] They measured the proton chemical shifts of a variety of cyclic charged molecules (tropylium cation, cyclopentadienyl anion, *etc.*) and compared them with benzene. From this data they obtained a value of the coefficient a_1 [eqn. (11)] of 10.0

$$\Delta\delta = a_1\Delta q_\alpha + a_2\Delta q_\beta \qquad (11)$$

between the proton shift $\Delta\delta$ and the excess π charge Δq_α on the attached carbon atom.

It has also been recognised that there is an influence of the excess π charge on the carbon atom β to the proton considered and a related effect gives rise to the phenomenon of negative spin density in EPR spectroscopy.[33] The hyperfine couplings to the α and β protons in alkyl radicals, in which the radical carbon atom is planar and sp^2 hybridised, are quoted as $a^H_\alpha = -22$ G and $a^H_\beta = 4 + 50\cos^2\theta$ where θ is the dihedral angle between the free radical 2p-orbital and the proton considered.[33] These considerations suggest that in aromatic compounds in which the CH bond is orthogonal to the π orbital, θ is 90° and the value of a_2 in eqn. (11) is negative and *ca.* 1/5th of a_1, *i.e.* -2.0.

These modifications were the only ones needed to apply the CHARGE routine to aromatic compounds. However it is still necessary to calculate the charge densities at the aromatic protons in CHARGE and thus to quantify the appropriate α, β and γ effects. Also the long range interactions present in the aliphatic molecules (*i.e.* steric, electric and anisotropic) must also be included and where necessary evaluated. These will be considered subsequently.

atoms are not known and must be determined. We shall show (see later for a full discussion) that an aromatic carbon atom has no steric effect on a close aromatic proton but that an aromatic proton has a *de*shielding effect on a close aromatic proton. We assume that this can be represented by a simple r^{-6} term [eqn. (3)] thus only the appropriate value of a_S in eqn. (3) for the aromatic proton to proton steric shift needs to be obtained. The electric field and anisotropies of the polar and anisotropic groups involved are calculated in an identical manner to that for any aliphatic C–H bond and thus no further parameterisation is necessary.

Experimental

Ethylene, benzene, toluene, *tert*-butylbenzene, naphthalene, anthracene, phenanthrene, pyrene, triphenylene, benz[*a*]anthracene, benzo[*b*]triphenylene and dibenzo[*ah*]anthracene and the $CDCl_3$ solvent were obtained commercially (Aldrich Chem. Co.). The solvent was stored over molecular sieves and used without further purification.

^1H NMR spectra were obtained on a Bruker AMX400 spectrometer operating at 400.14 MHz. Spectra were recorded in 10 mg cm^{-3} solutions (^1H) with a probe temperature of *ca.* 25 °C in $CDCl_3$ and referenced to TMS. Typical ^1H conditions were 128 transients, spectral width 3300 Hz, 32K data points, giving an acquisition time of 5 s and zero-filled to 128K to give a digital resolution of 0.025 Hz.

The geometries of the compounds were obtained by optimisations using the GAUSSIAN94 programme at the RHF/6-31G* level.[34] For molecules too large to be handled conveniently by GAUSSIAN at the 6-31G* level, *e.g.* perylene, smaller basis sets were used, *e.g.* 3-21G. For the largest molecules, *e.g.* coronene and the two cyclophanes (**15**) and (**16**), the molecular mechanics PCMODEL programme was used.[35] The geometry and CHARGE computations were performed on a PC.

Results

The proton spectra of the compounds all consisted of well separated peaks at 400 MHz (except for toluene) thus the proton chemical shifts could be obtained immediately and the assignments of the compounds followed previous investigations. For toluene the proton spectrum of toluene-d_8 was first obtained. The dilute ^1H spins only couple to the ^2D nuclei and the spectrum consists of three broad singlets at 7.165, 7.170 and 7.254 δ. This gave sufficient information to identify the coupling patterns in the ^1H spectrum of toluene and hence the slightly more accurate proton chemical shifts given in Table 2.

The data obtained in $CDCl_3$ solution are given and compared with that of previous investigations in CCl_4 solution in Table 2. In ref. 12 the authors only reported the shift differences from benzene and we have added 7.27 ppm (the benzene value in CCl_4) to them. The shift values in Table 2 are of interest. There is generally good agreement between the data sets but it is noteworthy that there is a small but almost constant difference in the proton chemical shifts in $CDCl_3$ solution compared to CCl_4. Averaging over all the aromatic compounds in Table 2 gives a value of 0.086 ppm (±0.01) to low field in $CDCl_3$ solution. This is also the case for ethylene but here the difference is slightly less. The aliphatic protons of the methyl groups in toluene and *tert*-butylbenzene do not show this effect but have the same shifts in the two solvents. The constant value of this difference means that data in CCl_4 solution can be converted directly to $CDCl_3$ solution by merely relating the shifts to benzene. Furthermore this suggests that the accurate SCS values reported earlier for the monosubstituted benzenes in CCl_4 solution may be used with confidence to investigate the application of the CHARGE model to these compounds and

Table 2 Observed and calculated proton chemical shifts (δ) for aromatic compounds

		Observed			Calculated	
Compound	Proton	$CDCl_3$[a]	CCl_4[b,c]		Model A	Model B
Ethylene		5.405	5.352[d]	—	5.407	
Benzene (**1**)		7.341	7.27[b]	(7.27)[c]	7.331	7.342
Naphthalene (**2**)	1	7.844	7.73	7.81	7.931	7.829
	2	7.477	7.38	7.46	7.524	7.493
Anthracene (**3**)	1	8.009	7.93	8.01	7.948	8.009
	2	7.467	7.39	7.39	7.524	7.577
	9,10	8.431	8.36	8.31	8.495	8.485
Phenanthrene (**4**)	1	7.901	7.80	un	7.930	7.968
	2	7.606	7.51	un	7.509	7.544
	3	7.666	7.57	un	7.566	7.600
	4,5	8.702	8.62	8.51	8.455	8.433
	9,10	7.751	7.65	7.71	7.839	8.085
Triphenylene (**5**)	1	8.669	8.61	8.56	8.587	8.707
	2	7.669	7.58	7.61	7.613	7.654
Pyrene (**6**)	1	8.084	8.00	8.06	7.976	8.253
	3	8.190	8.10	8.16	7.930	8.156
	4	8.010	7.93	7.99	7.546	7.785
Perylene (**7**)	1	8.196	8.11	8.09	8.361	8.250
	2	7.466	7.38	7.41	7.515	7.404
	3	7.656	7.57	7.60	7.845	7.630
Coronene (**8**)	1	8.90[e]	8.82	8.84		8.900
Benz[*a*]anthracene (**9**)	1′	8.840	8.77		8.698	8.553
	2′	7.685	7.59		7.708	7.627
	3′	7.651	7.525		7.638	7.557
	4′	7.849	7.755		8.102	8.004
	3	7.616	7.55		7.987	8.117
	4	7.800	7.72		8.027	8.200
	5	8.048	8.03		8.101	7.977
	6	7.540	7.465		7.637	7.544
	7	7.564	7.47		7.647	7.553
	8	8.133	8.03		8.169	8.038
	9	9.174	9.08		9.125	9.052
	10	8.370	8.275		8.561	8.572
Benz[*b*]anthracene (**10**)	1′	8.00[f]			8.082	7.947
	2′	7.39			7.619	7.522
	4	8.67			8.581	8.546
Benzo[*b*]triphenylene (**11**)	1′	8.791	8.675		8.685	8.758
	2′	7.670	7.54		7.649	7.634
	3′	7.651	7.53		7.636	7.618
	4′	8.592	8.475		8.637	8.674
	7	7.568	7.455		7.641	7.521
	8	8.097	7.965		8.134	8.008
	9	9.097	9.075		9.103	9.238
Dibenzo[*ah*]anthracene (**12**)	1′	8.874	8.805		8.708	8.502
	2′	7.719	7.625		7.721	7.583
	3′	7.646	7.55		7.649	7.511
	4′	7.914	7.82		8.113	7.944
	3	7.760	7.67		8.016	8.077
	4	7.963	7.88		8.121	8.230
	10	9.155	9.075		9.170	9.107
Acenaphthylene (**13**)	1	7.812			7.829	7.826
	2	7.548			7.474	7.519
	3	7.692			7.708	7.701
	5,6	7.083			7.070	7.024
Fulvene (**14**)	1,4	6.228[g]			6.384	6.317
	2,3	6.531			6.421	6.404
	6	5.892			6.015	5.960
Toluene *ortho*		7.180	7.061[h]		7.080	
meta		7.260	7.140		7.284	
para		7.165	7.042		7.172	
Me		2.343	2.337[i]		2.343	
tert-Butylbenzene *ortho*		7.390	7.281[h]		7.279	
meta		7.297	7.180		7.358	
para		7.165	7.052		7.218	
Me		1.325	1.319[i]		1.332	

[a] This work except where stated. [b] Ref. 7. [c] Ref. 12. [d] Ref. 36. [e] Ref. 37. [f] Ref. 38. [g] Ref. 39. [h] Ref. 16. [i] Ref. 2, vol. 2, Appendix B. un = unresolved.

these data are reproduced in Table 3. Also given in Table 3 are the SCS values obtained in our laboratory for selected compounds in dilute $CDCl_3$ solution. The excellent agreement between the sets of SCS values confirms this assumption.

The data collected in Tables 2 and 3 provide a rigorous test of the application of both the CHARGE model and also of present ring current theories to these compounds. The compounds listed in the tables are all of fixed conformation. The GAUSSIAN94 (6-31G*/3-21G) and the PCMODEL calculations gave molecular geometries for the aromatic

	Proton substituent chemical shifts ($\Delta\delta_H$)					
	ortho		*meta*		*para*	
Substituent	Obs	Calc	Obs	Calc	Obs	Calc
H	0.00	0.00	0.00	0.00	0.00	0.00
CH_3	−0.20	−0.27	−0.12	−0.06	−0.22	−0.17
	−0.16		−0.08		−0.18[b]	
t-Bu	0.02	−0.06	−0.08	0.02	−0.21	−0.12
	0.05		−0.04		−0.19[b]	
F	−0.29	−0.23	−0.02	0.02	−0.23	−0.21
Cl	0.03	−0.04	−0.02	0.07	−0.09	−0.08
Br	0.18	0.07	−0.08	0.09	−0.04	−0.02
I	0.39	0.18	−0.21	0.08	0.00	0.01
OH	−0.56	−0.53	−0.12	−0.13	−0.45	−0.42
OCH_3	−0.48	−0.44	−0.09	−0.12	−0.44	−0.41
NH_2	−0.75	−0.62	−0.25	−0.24	−0.65	−0.65
CF_3	0.32	0.28	0.14	0.18	0.20	0.20
	0.29		0.14		0.21[c]	
CHO	0.56	0.54[d]	0.22	0.20[d]	0.29	0.26
$C(O)CH_3$	0.62	0.61[d]	0.14	0.21[d]	0.21	0.28
$C(O)OCH_3$	0.71	0.91[d]	0.11	0.21[d]	0.21	0.26
CN	0.36	0.35	0.18	0.21	0.28	0.24
	0.32		0.14		0.27[e]	
NO_2	0.95	0.81	0.26	0.23	0.38	0.25

[a] Ref. 16 unless stated otherwise. [b] This work ($CDCl_3$ soln.). [c] Ref. 42. [d] Averaged, see Table 5 and text. [e] Ref. 43.

hydrocarbons in excellent agreement with the experimental geometries, where known (*e.g.* benzene C–C 1.397, C–H 1.087 Å (MP2/6-31G*), *vs.* 1.395 and 1.087 Å (PCMODEL) and 1.396 and 1.083 Å (experimental)[40]).

In the CHARGE model the α, β and γ effects of the substituents are considered to be due to electronic effects and therefore they are modelled on a simple empirical basis. The α effect of an sp^2 carbon is given from the difference in the electronegativities of the carbon and hydrogen atoms divided by the appropriate exchange integral. The value of this integral was chosen to reproduce the observed chemical shift of ethylene (Table 2). This gives a partial atomic charge for the ethylene protons of +0.075 e which corresponds to a C–H bond dipole of 0.4 D. This is in reasonable agreement with the usual quoted range (*ca.* 0.6–0.7 D).[41] The β effect is calculated directly from the carbon electronegativity and proton polarisability,[28] thus the only other electronic effect to be considered is the γ effect (H–C–C–C) of the unsaturated carbon atoms in the aromatic compounds. For the condensed aromatic compounds considered here the only values of the CCCH dihedral angle θ are 0° and 180° (Table 2) and thus eqn. (1) may be simplified to $A + B\cos\theta$ with the coefficients A and B to be obtained from the observed data.

Long-range effects

The interactions considered to be responsible for the long range effects of the aromatic ring have been documented earlier as steric plus magnetic anisotropy (*i.e.* ring current) effects. (There is also a small electric field effect due to the C–H dipoles. This is calculated by CHARGE directly from the partial atomic charges as the coefficient A_Z in eqn. (4) has already been determined). Thus we are now in a position to test the theoretical treatment given earlier against the observed data presented in the tables.

Table 4 Observed *vs.* calculated proton chemical shifts (δ) in [10]paracyclophane (**16**)

Carbon atom (CH_2)	Observed (CH_2)	Calculated (average)	
α	2.62	2.453 2.759	2.606
β	1.54	1.806 1.592	1.699
γ	1.08	1.631 0.909	1.270
δ	0.73	1.133 0.655	0.894
ε	0.51	0.626 0.424	0.525
Aromatic	7.04	7.102 7.074	7.088

In previous investigations in this series which were concerned with substituted alkanes the steric effect of all non-hydrogen atoms was deshielding on the near protons, but proton–proton interactions gave a shielding effect. This was confirmed both experimentally and theoretically. In contrast it is immediately obvious from both the results of previous investigations[7,13] and the data presented here that proton–proton steric interactions in the aromatic systems considered here give rise to *de*shielding effects on the proton chemical shifts. A further unambiguous demonstration that steric effects on proton chemical shifts in aromatic systems are totally different from those in saturated systems came from the observation of the proton chemical shift of the unique CH proton in the cyclophane (**15**). This proton occupies a position along the symmetry axis of the benzene ring and occurs at −4.03 δ. Because of its proximity to the benzene ring plane (it is *ca.* 1.9 Å above the ring plane) it is an excellent test of any ring current theory and was used by Schneider *et al.* in their investigation of the different ring current models.[8] It is also in close proximity to the benzene ring carbon atoms, the average C···H distance being *ca.* 2.20 Å. Any deshielding effect from the aromatic carbon atoms comparable to that found for saturated carbon atoms would have a pronounced deshielding effect on this proton. For example using the steric coefficient found previously for saturated carbon atoms (a_s in eqn. (3) = 220.0 ppm Å^6) would give a value for the CH proton chemical shift of +6.0 δ! Clearly there is no significant deshielding steric effect from the aromatic carbon atoms at this proton. Schneider *et al.*[8] termed this a "soft" steric effect in contrast to the "hard" steric effect of proton–proton interactions. This is supported by the results for [10]paracyclophane (Table 4) in which there is good agreement between the observed and calculated shifts again with no sp^2 carbon steric effect. This result was adopted in the CHARGE routine so that there is no steric effect on the proton chemical shifts from any aromatic carbon atom. Note that this may not be the case for olefinic carbon atoms and work is currently in place in our laboratory to further define this interesting result.[42]

Thus the parameters to be determined from the observed results in Table 2 are the coefficients A and B for the carbon γ effect [eqn. (1)], the appropriate $H \cdots H$ steric coefficient [eqn. (3)], the ring current equivalent dipole μ [eqn. (8)] and the factors fc [eqn. (8)] for the condensed rings. There are six factors for both model A and model B (Table 1) making a total of 10 unknown parameters. The values of the unknown parameters were achieved using a non-linear least mean squares programme (CHAP8)[44] to give the best fit with the observed data. The data set used comprises all the condensed aromatics of Table 2, a total of 57 proton shifts thus the iteration is overdetermined. The initial iteration for model A clearly showed that coronene was an exception and this was removed from the subsequent iteration. With this amendment the programme iterated satisfactorily with reasonable rms error and definition. For model B coronene is a separate case and the iteration performed satisfactorily. The iteration gave $A = -0.107$, $B = 0.143$, the $H \cdots H$ steric coefficient a_S [eqn. (3)] = +24.55 ppm Å^6, μ [eqn. (8)] = 26.2 ppm Å^3 and the fc values in Table 1. In fulvene and acenaphthylene both the ring current of the five-membered ring (μ_P) and also the factors (fc) for the benzenoid rings in acenaphthylene were parametrised separately. This gave $\mu_P = 11.6$ ppm Å^3 and $fc = 0.81$. These iterations are for two unknowns and seven observed shifts, thus the iterations are still overdetermined.

The determination of these unknown parameters also allows the calculation of the proton SCS of the monosubstituted benzenes in Table 3 as the electric field and anisotropic effects of the substituents have already been determined previously. The appropriate values of the coefficients in eqn. (10) needed to model the effect of the alkyl substituents on the π densities were $a_r^0 = a_r + 0.15$, $\omega = -0.50$. The only other effect to consider is the steric effect of the side-chain protons on the *ortho* protons of the benzene ring. The steric effect of alkane protons on olefinic protons was determined from a general investigation involving a variety of olefinic molecules[42] to be deshielding and this result was used here. The steric effect of the OH and NH protons in alcohols and amines has been shown to be zero[45] and again this result was incorporated into the present calculations. This allowed the determination of the proton SCS of all the monosubstituted benzenes of Table 3 and these results are given with the observed data in the table. There is generally excellent agreement between the observed and calculated shifts in Table 3 and this good agreement allows the SCS in the benzene ring to be analysed further in terms of the constituent interactions (see discussion).

Finally it was felt to be of interest to determine whether the equivalent dipole ring current calculation given here could be used to determine the benzene ring current effect for protons at the side and over the benzene ring. This data was used by Schneider[8] in determining the accuracy of the various ring current models. We consider here two illustrative examples: the unique CH proton in the tribridged cyclophane (**15**)[8] and the protons in [10]paracyclophane (**16**).[46] The proton chemical shifts for both compounds have been recorded in dilute CDCl$_3$ solution. The geometries of both compounds were modelled by PCMODEL and GAUSSIAN. **15** is a rigid strained molecule but in **16** the methylene chain exists in two equivalent rapidly interconverting staggered conformations. Thus the two protons on each methylene group in the alkyl chain have the same observed shift and the calculated shifts for the two methylene protons have to be averaged. The calculations used eqn. (8) to determine the ring current shifts with the value of the equivalent dipole obtained above. The CH proton of **15** is observed at $-4.03\,\delta$ (calc. $-4.03\,\delta$) and the corresponding data for **16** are given in Table 4.

Discussion

The general agreement of the observed *vs.* calculated shifts in Tables 2 and 4 and the observed *vs.* calculated SCS of Table 3 is very good. Although the calculated values for models A and models B for the individual protons vary appreciably (Table 2), the overall agreement for both models is similar. For the 57 data points of Table 2 the rms error (obs. *vs.* calc. shifts) is 0.13 ppm (model A) and 0.12 ppm (model B) over a range of 3.3 ppm. The analogous calculation using only the benzene ring current (*i.e.* all fc values = 1.0) gives much poorer agreement (rms = 0.28 ppm) showing that it is necessary to take account of the variation in the ring current density for a proper description of the proton chemical shifts. Although for convenience the SCS are given in Table 3, as the proton chemical shift of benzene is calculated accurately (Table 2) obviously the actual chemical shifts of all the substituted benzenes are calculated to the same accuracy as the SCS values in Table 3. It can be seen that the great majority of the observed shifts are reproduced to <0.1 ppm, though there are some exceptions (see later). This is the first quantitative calculation of this data and it implies that the latest CHARGE programme (CHARGE7) can be applied with some confidence to the prediction of the proton chemical shifts of virtually any substituted benzenoid compound.

The calculation also provides new insight into the interpretation of these proton chemical shifts as the different interactions responsible for the calculated values are separately identified and quantified in the CHARGE programme. The ring current calculations provide further evidence for the accuracy of the simple equivalent dipole model of the benzene ring current. The value of μ of 26.2 ppm Å^3 is very similar to that obtained from the classical circulating current model (27.6).[17,47] The calculations also confirm previous studies[47] in demonstrating that the ring current effect is not the only factor responsible for the difference between the ethylene and benzene proton shifts. The experimental difference of 1.93 ppm (Table 2) is made up of 1.77 ppm from the ring current and 0.17 ppm from the electronic effects of the β and γ carbon atoms of benzene. This was allowed for in some previous ring current calculations by using cyclohexadiene rather than ethylene as the appropriate olefinic model[47] and the above calculations support this approach. It is also pertinent to note the excellent agreement obtained with the simple equivalent dipole model. On this basis the use of the more complex double dipole and double-loop models does not appear to be justified. Interestingly Mallion[48] came to exactly the same conclusion many years ago.

It is of interest to compare the values of the separate ring current factors (fc) in Table 1 with the values obtained previously.[7,12] The trends are similar, supporting the original compartmentalisation of these factors, though the values obtained here are mostly much nearer to the benzene value ($fc = 1$) than the previous calculations. This is exactly to be expected as Huckel theory usually over estimates any electron separation. The only exception is the value for coronene. In model A the outer rings are of type 16b (*i.e.* analogous to the middle ring of phenanthrene) but this value of the ring current density (0.745, Table 1) gives a much too low value for the proton chemical shift. A value of fc of 1.06 reproduces the experimental proton chemical shift. In model B this problem does not arise as coronene is a separate case, and the iteration gives a value of $fc = 1.008$, very close to the benzene value and the Huckel calculated value.

It is encouraging that the calculated shifts for the non-alternant hydrocarbons of fulvene and acenaphthylene are in very good agreement with the observed shifts (Table 2) as this suggests that the approach adopted here can be extended to these systems. The value of the ring current of the five-membered ring obtained here (11.6 ppm Å^3) may be used to obtain the current density in the five-membered ring as the equivalent dipole $\mu = iA$ where A is the area of the current loop.

		Calculated contribution				
Substituent		γ-Effect	Steric	Anisotropic	Electric field	π Shift
CH_3	*ortho*	−0.144	—	—	—	−0.064
	meta	—	—	—	—	−0.132
	para	—	—	—	—	−0.183
F	*ortho*	0.128	—	—	—	−0.360
	meta	—	—	—	0.115	−0.137
	para	—	—	—	0.088	−0.332
OH	*ortho*	−0.128	—	—	—	−0.494
	meta	—	0.011	—	—	−0.188
	para	—	0.005	—	—	−0.456
CHO	*ortho* H-2	0.144	—	−0.125	0.360	0.195
	H-6	0.144	—	0.767	0.153	0.195
	meta H-3	—	—	−0.043	0.062	0.073
	H-5	—	—	0.107	0.069	0.073
	para	—	—	0.010	0.049	0.181
CN	*ortho*	−0.230	—	—	0.372	0.151
	meta	—	—	—	0.127	0.056
	para	—	—	—	0.097	0.138
NO_2	*ortho*	0.096	—	—	0.606	0.105
	meta	—	—	—	0.143	0.043
	para	—	—	—	0.105	0.115

After allowing for the area of the five-membered ring compared to benzene this gives a current density of $0.63i_b$, much less than benzene. More data on similar systems would be necessary to confirm this result.

Proton SCS in substituted benzenes

The good agreement between the observed and calculated SCS in Table 3 together with the separation of the different interactions in CHARGE allows us to determine these interactions for the different substituents and Table 5 gives the contributions to the proton SCS for selected substituents in Table 3.

In Table 5 for the anisotropic substituents (*e.g.* C=O) the contributions are given for each separate proton (*e.g.* H2 and H6) although these are averaged in Table 3 to compare with the observed (averaged) data. The large effect of the carbonyl anisotropy is clearly apparent in these figures. The orientation of the carbonyl is such that the oxygen atom is *syn* to H6. The calculations are supported by and also show very clearly the origin of the large *ortho* proton deshielding in *o*-methoxybenzaldehyde (H6 7.82 δ)[37] compared to *o*-hydroxybenzaldehyde (H6 7.50 δ) where the carbonyl group is now hydrogen bonded to the hydroxy group.

Table 5 also shows that the carbonyl anisotropy is the major factor in the *meta* proton SCS of benzaldehyde (*cf.* H3 and H5). This demonstrates the importance of these "other" effects, which are of course not included in any of the correlations of electron densities *etc.* with the proton SCS. Indeed it is important to stress the difference between the present calculations and the correlations with Hammett σ,[22] the Swain–Lupton F and R values[49] *etc.* The CHARGE calulations are ground state calculations whilst the other parameters are derived from pH and rate constants and therefore reflect energy differences between the anion or the transition state and the ground state of the molecule, a totally different quantity.

Nevertheless in view of the numerous correlations of these quantities with the proton SCS it is useful to consider these correlations together with the present calculations. The correlation between the proton SCS and Hammett σ_I and $\sigma_R{}^0$ values was given as eqn. (12)[21] for a similar set of substituents to those

$$\begin{aligned}\text{SCS }(para) &= 0.27\sigma_I + 1.25\sigma_R{}^0\\ \text{SCS }(meta) &= 0.24\sigma_I + 0.446\sigma_R{}^0\end{aligned}\qquad(12)$$

in Table 5 and a similar analysis of the SCS in terms of the Swain–Lupton F and R values gives eqn. (13).

$$\begin{aligned}\text{SCS }(para) &= 0.142F + 0.926R\\ \text{SCS }(meta) &= 0.098F + 0.376R\end{aligned}\qquad(13)$$

These equations are reasonably consistent implying in general a much greater resonance effect on the *para* proton SCS than on the *meta* proton SCS. Inspection of the data in Table 5 shows a much more diverse pattern. Indeed the major disadvantage of such correlations is that they obscure the large differences in the SCS components of the various groups which all need to be considered individually. *E.g.* the OH group has no anisotropic or steric effect and both the *meta* and *para* SCS are dominated by the π electron shift. This is much greater in the *para* position but the *meta* SCS is still dominated by the π effect. In contrast, in benzaldehyde the electric field and anisotropy contributions equal the π shift for the *meta* proton and are a significant but minor contribution for the *para* proton. The nitro and cyano groups differ from both of these in that they appear to have no anisotropic effect but the electric field effect is predominant at the *meta* proton and equal to the π shift at the *para* proton. Further investigations in our laboratory have confirmed this result for the cyano group[43] and it would be of interest to perform similar investigations for the nitro group. Clearly each substituent group must be considered separately in order to evaluate the separate steric, electric and anisotropic contributions at the various protons.

Finally it is of interest to consider the discrepancies in the observed *vs.* calculated data of Table 3. The most interesting systematic deviation is that due to Br and I. The calculated values for the *para* SCS for all the halogens are in excellent agreement with the observed data and the *ortho* and *meta* SCS for F and Cl are in reasonable agreement. However the *ortho* SCS for Br and I are more deshielding than calculated and the *meta* SCS much more shielding than calculated. The *ortho* SCS are given by the γ effect, which is a function of the polarisability of the γ atom *i.e.* the halogen. The value of the polarisability was taken from data on alkyl halides[24] thus this may not be appropriate for substituted benzenes. In contrast the *meta* SCS are of interest as similar exceptional behaviour was observed for the 3-protons in equatorial halocyclohexanes.[50] Again there is a large deviation from the calculated value for the Br and I substituents. The equatorial proton is in a similar W orientation to the halogen atom as the *meta* proton in the substituted benzenes and it may be that there is an additional long range (four bond) mechanism for the halogen atoms in this specific orientation. Further studies would be necessary to confirm this.

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References

1 Part 13, R. J. Abraham and N. J. Ainger, *J. Chem. Soc., Perkin Trans. 2*, 1999, 441.

2 (*a*) J. W. Emsley, J. Feeney and L. H. Sutcliffe, *High Resolution NMR Spectroscopy*, Pergamon Press, Oxford, 1965; (*b*) R. C. Haddon, V. R. Haddon and L. M. Jackman, *Top. Curr. Chem.*, 1971, **16**, 103.

3 L. Pauling, *J. Chem. Phys.*, 1936, **4**, 673.

4 J. A. Pople, *J. Chem. Phys.*, 1956, **24**, 1111.

5 (*a*) J. S. Waugh and R. W. Fessenden, *J. Am. Chem. Soc.*, 1957, **79**, 846; (*b*) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012.

6 (*a*) R. J. Abraham, *Mol. Phys.*, 1961, **4**, 145; (*b*) R. J. Abraham and C. J. Medforth, *Magn. Reson. Chem.*, 1987, **25**, 432.

7 (*a*) C. W. Haigh and R. B. Mallion, *Mol. Phys.*, 1970, **18**, 737 and 767; (*b*) C. W. Haigh, R. B. Mallion and E. A. G. Armour, *Mol. Phys.*, 1970, **18**, 751.

8 H. J. Schneider, V. Rudiger and U. Cuber, *J. Org. Chem.*, 1995, **60**, 996.

9 H. J. Bernstein, W. G. Schneider and J. A. Pople, *Proc. R. Soc. London, Ser. A*, 1956, **236**, 515.

10 J. A. Pople, *Mol. Phys.*, 1958, **1**, 175.

11 R. McWeeny, *ibid.*, 1958, **1**, 311.

12 N. Jonathan, S. Gordon and B. P. Dailey, *J. Chem. Phys.*, 1962, **36**, 2443.

13 T. B. Cobb and J. D. Memory, *J. Chem. Phys.*, 1967, **47**, 2020.

14 M. Westermayer, G. Hafelinger and C. Regelmann, *Tetrahedron*, 1984, **40**, 1845.

15 (*a*) S. Castellano and C. Sun, *J. Am. Chem. Soc.*, 1966, **88**, 4741; (*b*) S. Castellano, C. Sun and R. Kostelnik, *Tetrahedron Lett.*, 1967, **46**, 4635 and **51**, 5205; (*c*) M. P. Williamson, R. J. Kostelnik and S. M. Castellano, *J. Chem. Phys.*, 1968, **49**, 2218.

16 K. Hayamizu and O. Yamamoto, *J. Mol. Spectrosc.*, 1968, **28**, 89 and 1969, **29**, 183.

17 R. J. Abraham, J. Fisher and P. Loftus, *Introduction to NMR Spectroscopy*, J. Wiley, New York, 1988.

18 J. B. Lambert, H. B. Shurvell, D. A. Kightner and R. G. Cooks, *Organic Structural Spectroscopy*, Prentice-Hall, New Jersey, 1998.

19 E. Pretsch, J. Seibl, T. Clerc and W. Simon, *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd Edn., Springer-Verlag, Berlin, 1989.

20 G. C. Levy and G. L. Nelson, *Carbon-13 NMR for Organic Chemists*, J. Wiley, New York, 1972.

21 W. J. Hehre, R. W. Taft and R. D. Topsom, *Prog. Phys. Org. Chem.*, 1976, **12**, 159.

22 R. T. C. Brownlee and R. W. Taft, *J. Am. Chem. Soc.*, 1970, **92**, 7007.

23 G. K. Hamer, I. R. Peat and W. F. Reynolds, *Can. J. Chem.*, 1973, **51**, 897 and 915.

24 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 31.

25 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 203, 881.

26 R. J. Abraham, L. Griffiths and M. A. Warne, *ibid.*, 1998, 1751.

27 13th International NMR Conference, Edinburgh, July, 1999.

28 R. J. Abraham, L. Griffiths and M. A. Warne, *Magn. Reson. Chem.*, 1998, **S179**, 36.

29 (*a*) R. J. Abraham and P. E. Smith, *J. Comput. Chem.*, 1987, **9**, 288; (*b*) R. J. Abraham and P. E. Smith, *J. Comput. Aided Mol. Des.*, 1989, **3**, 175.

30 (*a*) R. J. Abraham and P. E. Smith, *Nucleic Acids Res.*, 1988, **16**, 2639; (*b*) A. Streitweiser, *Molecular Orbital Theory for Organic Chemists*, J. Wiley, New York, 1961.

31 A. L. McClellan, *Tables of Experimental Dipole Moments*, vol. 1, Freeman, London, 1963; vols. 2 and 3 Rahara Enterprises, California, vol. 2, 1974, vol. 3, 1989.

32 H. Gunther, *NMR Spectroscopy*, 2nd edn., J. Wiley, Chichester, 1995, p. 71.

33 P. B. Ayscough, *Electron Spin Resonance in Chemistry*, Methuen, London, 1967.

34 GAUSSIAN94, Gaussian Inc., Pittsburgh, PA, 1994, J. Frisch, G. W. Trucks, M. Head-Gordon, P. M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzalez, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart and J. A. Pople.

35 PCMODEL version 7, Serena Software Ltd., PO Box 3076, Bloomington, Indiana, 1998.

36 U. E. Matter, C. Pascual, E. Pretsch, A. Pross, W. Simon and S. Sternhell, *Tetrahedron*, 1969, **25**, 691.

37 C. J. Puchert and J. Behnke, *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, Aldrich Chemical Company Inc., Milwaukee, USA, 1993.

38 J. Netka, S. L. Crump and B. Rickborn, *J. Org. Chem.*, 1986, **51**, 1189.

39 U. Nuchter, G. Zimmermann, V. Francke and H. Hopf, *Liebigs Ann. Rec.*, 1997, 1505.

40 Landholt-Bornstein, vol. 7, *Structure Data of Free Polyatomic Molecules*, ed. K. H. Hellwege and A. M. Hellwege, Springer, New York, 1976.

41 (*a*) O. Exner, *Dipole Moments in Organic Chemistry*, George Thieme Pub., Stuttgart, 1975; (*b*) V. I. Minkin, O. A. Osipov and Y. A. Zhdanov, *Dipole Moments In Organic Chemistry*, Plenum Press, New York, 1970.

42 R. J. Abraham and M. Canton, unpublished work.

43 R. J. Abraham and M. Reid, *Magn. Reson. Chem.*, in the press.

44 S. S. Kuo, *Computer Applications of Numerical Methods*, ch. 8, Addison-Wesley, London, 1972.

45 R. J. Abraham, unpublished work.

46 A. Agarwal, J. A. Barnes, J. L. Fletche, M. J. McGlinchey and B. G. Sayer, *Can. J. Chem.*, 1973, **51**, 897.

47 R. J. Abraham and W. A. Thomas, *J. Chem. Soc. B*, 1966, 127.

48 R. B. Mallion, *J. Chem. Phys.*, 1980, **75**, 793.

49 C. G. Swain and E. P. Lupton, *J. Am. Chem. Soc.*, 1968, **90**, 4328.

50 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 2151.

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Proton chemical shifts in NMR. Part 15†—proton chemical shifts in nitriles and the electric field and π-electron effects of the cyano group‡

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ABSTRACT: The proton resonance spectra of a number of nitriles of fixed geometry were recorded in dilute CDCl$_3$ solution and assigned. These were *trans*- and *cis*-4-tert-butylcylohexanecarbonitrile, axial and equatorial cyclohexanecarbonitrile and ax–ax- and eq–eq-*trans*-1,4-dicyanocyclohexane, the latter compounds at −60 °C. The aromatic nitriles measured were benzonitrile, *o*-, *m*- and *p*-dicyanobenzene, 1- and 2-cyanonaphthalene and 9-cyanoanthracene. This plus previous literature data allowed the determination of the cyano substituent chemical shifts (SCS) in a variety of molecules. These SCS were analysed in terms of the CN electric field, magnetic anisotropy and steric effects for protons more than three bonds removed together with a model (CHARGE7) for the calculation of the two- and three-bond SCS. For the aromatic nitriles ring current and π-electron effects were included. The anisotropic and steric effects of the cyano group were negligible in all the compounds investigated and in the aliphatic nitriles the SCS were due only to the CN electric field plus for near protons electronic effects. For the aromatic nitriles the π-electron effects were calculated from Hückel theory with the values of the exchange and resonance integrals adjusted to give π-electron densities in agreement with those obtained by *ab initio* calculations. The ring current shifts of the cyano derivatives were assumed to be the same as those of the parent hydrocarbons. The model gives the first comprehensive calculation of the SCS of the cyano group. For the data set of 93 proton chemical shifts from 1 to 9δ, the r.m.s. error (observed vs calculated shifts) was 0.088 ppm. The breakdown of the CN SCS in the aromatic nitriles showed good agreement with the Swain and Lupton field and resonance (*F* and *R*) components of substituent effects. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ^{1}H NMR; proton chemical shifts; nitriles; electric field; π-electron densities

INTRODUCTION

Nitriles are of considerable importance in all branches of chemistry. They are both versatile synthetic intermediates and important compounds *per se* (see Ref. 2 for a comprehensive treatment) and in consequence the proton resonance spectra of nitriles have been studied since the beginning of NMR spectroscopy. Despite this, there is still some controversy and uncertainty over the causes of the substituent chemical shifts (SCS) of the cyano group. The cyano group is both strongly polar and also anisotropic and both of these factors have been proposed to account for cyano SCS. Early workers suggested that the CN magnetic anisotropy should be similar to that of the analogous C≡C bond and Reddy and Goldstein[3] using a correlation between C^{13}–H couplings and the proton chemical shift estimated $\Delta\chi$ as -16.5×10^{-6} cm^3 mol^{-1} for both the CN and the C≡C bond. Cross and Harrison[4] used the value of the CN anisotropy obtained by Reddy and Goldstein to calculate the shifts of the C-19 methyl groups in some 5α- and 5β-cyano steroids. They found that the shifts were opposite to those predicted from the anisotropy and suggested that the CN electric field could be responsible. This early work has been well reviewed by Bothner-By and Pople.[5]

Subsequently, Zurcher[6] and ApSimon *et al.*[7] conducted more detailed analyses of the CN SCS. They both used the McConnell equation[8] to calculate the magnetic anisotropy of the cyano group and the CN dipole to calculate the electric field. They did not consider any steric effects of the CN group in their calculations. They also assumed that the CN anisotropy could be calculated from the centre of the triple bond, although the π-electron system may be more or less displaced towards the more electronegative atom. Both studies came to the conclusion that the electric field effect was predominant. However, both of these studies used mainly the methyl groups of steroids to determine the SCS. When they extended their calculations to include nearer protons, large differences between the observed and calculated shifts were found.

What is required for a definitive analysis is a sufficient data set of CN SCS using conformationally rigid molecules with fully assigned proton spectra. We present the complete assignment of the PMR spectra of both aliphatic and aromatic nitriles of fixed conformation. The aliphatic nitriles analysed are *trans*- and *cis*-4-*tert*-butylcyclohexanecarbonitrile (**1a** and **b**), axial and equatorial

† This paper is dedicated to Professor Dr Harald Günther on the occasion of his 65th birthday.

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† For Part 14, see Ref. 1.

cyclohexanecarbonitrile (**2a** and **b**) and ax–ax- and eq–eq-*trans*-1,4-dicyanocyclohexane (**3a** and **b**). Included also in the analysis are the PMR spectra of 2-*exo*- and 2-*endo*-norbornanecarbonitrile (**4a** and **b**) and 1-adamantanecarbonitrile (**5**), recorded previously,[9] and the proton shifts of acetonitrile (**6**), propionitrile (**7**), isobutyrocarbonitrile (**8**) and trimethylacetonitrile (**9**) from the Aldrich catalogue.[10] The aromatic nitriles recorded here are benzonitrile (**10**), *o*-, *m*- and *p*-dicyanobenzene (**11–13**), 1- and 2-cyanonaphthalene (**14** and **15**) and 9-cyanoanthracene (**16**). The proton chemical shifts of acrylonitrile (**17**) were obtained from the Aldrich catalogue.[10]

These results provide sufficient data for an analysis of cyano SCS using a previous model of proton chemical shifts.[1,11] In previous parts of this series, this model, which is based on simple charge calculations over one, two and three bonds and steric, electric field and anisotropic contributions over more than three bonds, was applied successfully to a variety of saturated hydrocarbons,[12,13] haloalkanes,[14] ethers[15] and ketones.[16] We shall show that this model provides a quantitative treatment for cyano SCS and that these are due solely to the CN electric field. The anisotropic and steric effects of the cyano group are negligible as far as the proton SCS are concerned.

THEORY

A detailed account of the theory behind the model CHARGE can be seen in past references.[1,11] A brief account of the latest model (CHARGE7) will be given here. The theory distinguishes between substituent effects over one, two and three bonds which are attributed to the electronic effects of the substituents and longer range effects due to the electric fields, steric effects and anisotropy of the substituents. The CHARGE scheme calculates the effects of atoms on the partial atomic charge of the atom under consideration, based upon classical concepts of inductive and resonance contributions.

If we consider an atom I in a four atom fragment I—J—K—L, the partial atomic charge on I is due to three effects. There is an α effect from atom J given by the difference in the electronegativity of atoms I and J. A β effect from atom K proportional to both the electronegativity of atom K and the polarizability of atom I. There is also a γ effect from atom L given by the product of the atomic polarizabilities of atoms I and L. This was shown to be true for I = H and L = F, Cl, Br, I and S. However, for the second-row atoms (C, O, etc.) the γ effect (i.e. C—C—C—H) is parameterized separately and is given by Eqn (1):

$$\begin{aligned} \mathrm{GSEF} &= A + B_1 \cos\theta \qquad 0^\circ \le \theta \le 90^\circ \\ &= A + B_2 \cos\theta \qquad 90^\circ \le \theta \le 180^\circ \end{aligned} \tag{1}$$

where θ is the C—C—C—H dihedral angle and A and B are empirical parameters. There are also routines for the methyl γ effect and for the decrease in the γ effect of the electronegative oxygen and fluorine atoms for CX_2 and CX_3 groups.

The total charge is given by summing these effects and the partial atomic charges (q) converted to shift values using the equation

$$\delta = 160.84q - 6.68 \tag{2}$$

The effects of more distant atoms on the proton chemical shifts are due to steric, anisotropic and electric field contributions. H···H steric interactions in alkanes were found to be shielding and X···H (X = C, F, Cl, Br, I) interactions deshielding according to a simple r^{-6} dependence:

$$\delta_{\mathrm{steric}} = a_s / r^6 \tag{3}$$

Furthermore, any X···H steric contributions on a methylene or methyl proton resulted in a push–pull effect (shielding) on the other proton(s) on the attached carbon.

The effects of the electric field of the C—X bonds (X = H, F, Cl, Br, I, O) were calculated from the equation

$$\delta_{\mathrm{el}} = A_z E_z \tag{4}$$

where A_z was determined as 3.67×10^{-12} esu (63 ppm au) and E_z is the component of the electric field along the C—H bond. The electric field for a univalent atom (e.g. fluorine) is calculated as due to the charge on the fluorine atom and an equal and opposite charge on the attached carbon atom. The vector sum gives the total electric field at the proton concerned and the component of the electric field along the C—H bond considered is E_z in Eqn (4). This procedure is both simpler and more accurate than the alternative calculation using bond dipoles.

The magnetic anisotropy of a bond with cylindrical symmetry such as CN is obtained from the equation

$$\delta_{\mathrm{an}} = \Delta\chi^{\mathrm{CN}}(3\cos^2\varphi - 1)/3R^3 \tag{5}$$

where R is the distance from the perturbing group to the nucleus of interest in Å, φ is the angle between the vector R and the symmetry axis and $\Delta\chi^{\mathrm{CN}}$ is the molar anisotropy of the CN bond. ($\Delta\chi^{\mathrm{CN}} = \chi^{\mathrm{CN}}_{\mathrm{parl}} - \chi^{\mathrm{CN}}_{\mathrm{perp}}$) where $\chi^{\mathrm{CN}}_{\mathrm{parl}}$ and $\chi^{\mathrm{CN}}_{\mathrm{perp}}$ are the susceptibilities parallel and perpendicular to the symmetry axis, respectively. This is illustrated in Fig. 1.

Aromatic compounds

For aromatic compounds it is necessary to include the shifts due to the aromatic ring current and the π-electron densities in the aromatic ring. The aromatic ring current density is calculated in CHARGE from the Pauling theory and the equivalent dipole approximation is then used

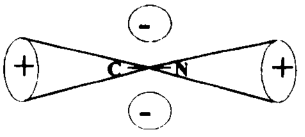


Figure 1. Representation of the anisotropy in an axially symmetric molecule.

to calculate the ring current shifts.[1] This treatment reproduces the proton chemical shifts of a wide range of aromatic hydrocarbons and is incorporated unchanged here.

The π-electron densities are calculated from Hückel theory.[17] The standard coulomb and resonance integrals for the Hückel routine are given by

$$\alpha_r = \alpha_0 + h_r\beta_0$$
$$\beta_{rs} = k_{rs}\beta_0 \qquad (6)$$

where α_0 and β_0 are the coulomb and resonance integrals for a carbon $2P_z$ atomic orbital and h_r and k_{rs} are the factors modifying these integrals for orbitals other than sp^2 carbon. For alternant aromatic hydrocarbons this calculation gives π-electron densities at every carbon equal to 1.0 as in benzene and this is in agreement with the results of more sophisticated calculations.[1]

For substituted aromatics the appropriate values of the coefficients h_r and k_{rs} in Eqn (6) for the orbitals involving heteroatoms have to be found. These are now obtained in CHARGE so that the π-electron densities calculated from the Hückel routine reproduce the those given by *ab initio* calculations.

The effect of the excess π-electron density at a given carbon atom on the proton chemical shifts of the neighbouring protons is given in CHARGE by the equation

$$\Delta\delta = a_1\Delta q_\alpha + a_2\Delta q_\beta \qquad (7)$$

where Δq_α and Δq_β are the excess π-electron density at the α and β carbon atoms, respectively and the values of the coefficients a_1 and a_2 were found to be 10.0 and -2.0 ppm per electron, respectively.[1]

The above contributions are added to the shifts of Eqn (1) to give the calculated shift of Eqn (8):

$$\delta_{\text{total}} = \delta_{\text{charge}} + \delta_{\text{steric}} + \delta_{\text{anisotropy}} + \delta_{\text{el}} + \delta_\pi \qquad (8)$$

Application to the cyano group

The cyano group has in principle steric, electric field and anisotropic effects on protons more than three bonds away plus for aromatics a large effect on the π-electron densities. All these have to be incorporated into the model. The electric field of the cyano group is calculated in an identical manner to any other C—X bond. The electric field is calculated as being due to the charge on the nitrogen atom of the CN and an equal and opposite charge on the carbon atom of the CN bond. The charge on the nitrogen atom is already calculated in CHARGE and the coefficient in Eqn (4) is known so the electric field is given without any further parameterization.

This, of course, assumes that the charges used in Eqn (4) provide a reasonable measure of the electric field of the cyano group. The partial atomic charges obtained in the CHARGE program have been derived from the observed molecular dipole moments and the extent of the agreement provides one check on the electric field calculation. The calculated vs observed (in parentheses) dipole moments (in debye) of acetonitrile, propionitrile, *tert*-butylcarbonitrile, **1a**, **1b**, acrylonitrile and benzonitrile are 3.81 (3.97), 3.77 (4.02), 3.82 (3.95), 3.87 (3.82), 3.65 (3.72), 4.11 (3.89) and 4.25 (4.14) and the good agreement provides strong support for the electric field calculation. All the dipole moments are gas-phase microwave measurements, except for **1a** and **b**, which were measured in benzene solution.[18]

The CN group has cylindrical symmetry and Eqn (5) may be used to calculate the contribution of the anisotropy to the proton chemical shifts. The steric effects of the CN group are calculated by use of Eqn (3). The unknowns to be obtained are $\Delta\chi$, the molar anisotropy of the CN bond and the steric coefficient a_s.

For protons three bonds or less from the CN group it is necessary to determine the orientational dependence of the γ proton chemical shift with respect to the cyano carbon. This is simulated by a γ substituent effect (GSEF) from the cyano carbon following Eqn (1), in which the coefficients A and B may differ for the CN group in aromatic vs saturated compounds. There is also a possible effect from the nitrogen atom which affects the β protons and as this has no orientation dependence it may be considered as dependent only on the polarizability of the nitrogen atom.

For the aromatic cyanides it is first necessary to obtain the appropriate values of the factors h_r and k_{rs}, which give the Hückel integrals for the CN group [Eqn (6)]. An iterative least mean square program (CHAP8)[19] was used to obtain the best fit values of these parameters from π-electron densities obtained from Gaussian 94[20] calculations. The π-electron densities and dipole moments from these *ab initio* calculations are very dependent on the basis set used. As the 3–21G basis set gave the best agreement with the observed dipole moment, the π-electron densities from this basis set were used to parameterize the Hückel calculations. Values of h_r of 0.12 and 0.19 for C(sp) and N(sp) and of k_{rs} of 1.05 for C(sp^2)–C(sp) and 1.20 for C(sp)–N(sp) gave π-electron densities for the aromatic nitriles in reasonable agreement with those from the *ab initio* calculations. The electron densities (total and π) and dipole moments calculated for benzonitrile by CHARGE and Gaussian 94 are given in Table 1.

EXPERIMENTAL

trans and *cis*-4-*tert*-butylcyclohexanecarbonitrile (**1a** and **b**) were synthesized by dehydration of the corresponding amide by reaction with phosphorus oxychloride.[21] Cyclohexanecarbonitrile (**2**), *trans*-1,4-dicyanocyclohexane (**3**), acetonitrile (**6**), benzonitrile (**10**), *o*-, *m*- and *p*-dicyanobenzene (**11–13**), 1- and 2-naphthalenecarbonitrile (**14** and **15**) and 9-anthracenecarbonitrile (**16**) were obtained commercially (Aldrich Chemical, Eastman Kodak, Rochester, NY, USA; Lancaster Synthesis, Movecambe, Lancs., UK).

^{1}H and ^{13}C NMR were obtained on a Bruker AMX400 spectrometer operating at 400 MHz for proton and

Table 1. Total and π (in parentheses) charges (me) and dipole moments for benzonitrile

	Method				
Atom	STO-3G	3–21G	6–31G	CHARGE	Observed
N(sp)	−200 (−49)	−504 (−67)	−273 (−63)	−524 (−60)	
C(sp)	73 (26)	338 (31)	21 (52)	445 (30)	
C-1	2 (−56)	−58 (−77)	10 (−76)	3 (−3)	
C-σ	−42 (24)	−194 (37)	−148 (37)	−47 (14)	
C-m	−58 (2)	−232 (0)	−212 (1)	−72 (−1)	
C-p	−49 (28)	−227 (36)	−180 (34)	−66 (11)	
μ (D)	3.65	4.55	4.82	4.25	4.14

100.63 MHz for carbon. The spectra for **1a** and **b** were recorded on a Varian 750 MHz spectrometer at Glaxo Wellcome (Stevenage, Herts., UK). HMQC, HMBC and NOE experiments were also performed with this spectrometer.

The spectra were recorded in 10 mg cm^{-3} solutions (^{1}H) and ca 50 mg cm^{-3} solutions (^{13}C) with a probe temperature of ca 25 °C in $CDCl_3$ and referenced to TMS. Typical running conditions of the spectrometers were 128 transients, spectral width 3300 Hz and 32 K data points to give an acquisition time of 5 s. The FID were zero-filled to 128 K to give a digital resolution of 0.025 Hz.

The 2D experiments were conducted using the Bruker AMX400 and Varian 750 MHz instruments using the standard Bruker COSY-DQF and HXCO-BI (Bruker UXNMR Version 010892, Bruker, Silbersteifen, Germany) and the standard Varian (Palo Alto, CA, USA) HMQC and GHMQC-DA pulse sequences. The geometries of the compounds investigated were obtained by use of the program PC MODEL Version 7.0 (Serena Software, Bloomington, IN, USA) and were also optimized using the Gaussian 94W program at the RHF/6–31G* and MP2/6–31G* levels.[20] The Gaussian 94W and CHARGE calculations were performed on a PC.

SPECTRAL ASSIGNMENTS

The spectral assignments of the compounds examined are given in Tables 3–7 along with the calculated values from the CHARGE7 model.

trans- and *cis*-4-*tert*-butylcyclohexanecarbonitrile (1a and b)

The ^{1}H, ^{13}C, 2-D and NOE spectra for the 4-*tert*-butylcyclohexanes were recorded at both 400 and 750 MHz. The *cis* and *trans* isomers were not separated and the spectra were recorded together. This was not a problem as the spectra are well resolved and all the resonances may be distinguished from each other.

Compound 1a. The 750 MHz ^{1}H NMR spectrum of **1a** consists of six proton resonances, excluding the methyl resonances. The 1a, 2e and 2a protons are readily assigned but the resonances at ca 1.50δ and 1.0δ contain two and three protons, respectively, and it was necessary to perform 2-D and NOE experiments. By examination of the ^{1}H COSY spectrum, the resonance at ca 1.5 ppm is shown to contain the H-2a proton, and this was confirmed by NOE experiments. Further NOE experiments assigned H-3e, H-3a and H-4a. A HETCOR plot plus the known assignments of the ^{13}C spectra for the *cis* and *trans* compounds[22] further confirmed these assignments.

Compound 1b. The ^{1}H NMR spectrum for **1b** was easy to assign as all the proton resonances are separate. The only uncertainty was for H-2a (ca 1.52δ) and H-4a (ca 0.9δ), which overlap with the H-3a and H-4a protons of the *trans* compound. These were assigned from the ^{1}H COSY spectrum and NOE experiments on H-1e, H-2e and H-3e confirmed these assignments.

Axial and equatorial cyclohexanecarbonitrile (2a and b)

The spectra of the separate conformers were obtained by obtaining the spectra at −60 °C. The equatorial conformer was the more favoured with ΔE(ax−eq) = 0.27 kcal mol^{-1} (1 kcal = 4.184 kJ), in agreement with literature values (0.2 kcal mol^{-1}).[23] A ^{1}H COSY spectrum was recorded at −60 °C to assign the two conformations fully. Because of the number of different protons within these conformers, the exact chemical shifts could only be approximated owing to much overlapping of the resonances.

Compound 2a. Protons 1e and 2e are easily assigned and inspection of the ^{1}H COSY spectrum plus the integrals of the ^{1}H spectrum gave the assignments of the remaining protons, but owing to much overlapping of the resonances the exact chemical shifts can only be approximated.

Compound 2b. The same can be said for the equatorial conformer. H-1a and H-2e can be clearly identified and also H-2a, H-3e and H-3a from the COSY plot. However, as with the axial carbonitrile, the chemical shifts of the H-4 protons are less accurate.

ax–ax-and eq–eq-*trans*-1, 4-dicyanocyclohexane (3a and b)

The commercial sample of 1,4-dicyanocyclohexane was identified as the *trans* isomer from the melting-point of

140–141 °C (lit.[24] 139–140 °C). This was further confirmed by the PMR spectrum. The spectrum has three distinct signals at room temperature and each conformer has three distinct signals at low temperature. The *cis* conformer would be expected to show three separate resonances at room temperature and six resonances from the one conformer at low temperature.

The −60 °C spectrum was assigned by recording spectra every 20 °C and following the coalescence of the peaks and finally the emergence of the individual conformers at −60 °C. From these experiments and the integration of the peaks, the low-temperature spectrum was assigned as there are only three inequivalent protons in each conformer. The diequatorial conformer was the more stable (1.5 : 1.0 ratio) with ΔE(ax–eq) = 0.17 kcal mol^{-1}.

The proton chemical shifts of the individual conformers of **2** and **3** were measured at low temperature (−60 °C). Hence it was of interest to determine whether there was an intrinsic temperature dependence of their chemical shifts. This was achieved by measuring the spectra of **1a** and **1b** at various temperatures and the results are shown in Table 2. It can be seen that the only protons experiencing a significant (>0.05δ) change in their chemical shifts on going from room temperature to −60 °C are the H-1 protons in both **1a** and **1b**. δ (H1eq) changes by 0.098δ and δ (H1ax) changes by 0.072δ and the corresponding protons in **2** and **3** are corrected by these amounts subsequently.

Aromatic nitriles

The full analysis and assignment of benzonitrile (**10**), *o*-dicyanobenzene (**11**) and *m*-dicyanobenzene (**12**) have been given previously[25,26] and our analyses follow these assignments. The 400 MHz PMR spectra of **10** and **11** were analysed using the LAOCOON program[27] to give accurate chemical shifts. The PMR spectrum of **12** is first order and that of *p*-dicyanobenzene is a single line. The PMR spectra of 1- and 2-naphthalenecarbonitrile (**14** and **15**) have not been analysed previously. The spectrum of both **14** and **15** at 400 MHz consist of seven well separated resonances and both assignments were made with the help of COSY and particularly HETCOR plots together with the known assignments of the ^{13}C spectra.[22]

The assignment of both the proton and ^{13}C spectrum of 9-anthracenecarbonitrile (**16**) has been given previously[28] and our analysis confirmed this assignment. The proton chemical shifts for propionitrile (**7**), isobutyronitrile (**8**), trimethylacetonitrile (**9**) and acrylonitrile (**17**) were obtained directly from the Aldrich ^{1}H NMR catalogue.[10] The proton chemical shifts for **16** in the Aldrich catalogue were all to lower δ than our measurements and for H-9 this was ca 0.2 ppm, a significant shift. There is now agreement (J. Behnke, personal communication) that this was due to the higher concentrations used in the Aldrich catalogue. For large condensed aromatic compounds such as **16**, stacking complexes at high concentrations would give high-field shifts as observed.

Table 2. Proton chemical shifts (δ) of *trans*-and *cis*-4-*tert*-butylcyclohexanecarbonitrile (**1a** and **b**) as a function of temperature

	trans			*cis*		
Proton	R.T.	−20 °C	−60 °C	R.T.	−20 °C	−60 °C
1e	—	—	—	2.921	2.973	3.019
1a	2.314	2.347	2.388	—	—	—
2e	2.161	2.179	2.192	2.037	2.059	2.077
2a	1.529	1.535	1.550	1.516	1.520	1.528
3e	1.855	1.856	1.862	1.771	1.782	1.794
3a	0.981	0.985	0.990	1.367	1.341	1.324
4a	1.023	1.025	1.030	0.986	0.986	0.987

RESULTS

The data for the aromatic nitriles obtained here in dilute $CDCl_3$ solution are in excellent agreement with those obtained earlier in CCl_4 solution.[26] For example, the *ortho*, *meta* and *para* proton shifts in benzonitrile in $CDCl_3$ and in CCl_4 solution (in parentheses) are 7.660 (7.631), 7.482 (7.452) and 7.559 (7.552). As found previously for the aromatic hydrocarbons, there is a small, almost constant shift to higher δ values in $CDCl_3$ than in CCl_4. Hence the proton SCS for the cyano group obtained in earlier investigations may be used unchanged for the $CDCl_3$ solutions used here.

The data obtained for the cyano compounds may be combined with the proton chemical shifts of the parent compounds given previously[1,12] to give the cyano SCS in these compounds. These are shown in Fig. 2 for the 4-*tert*-butylcyclohexanecarbonitriles (**1a** and **b**) and 1- and 2-cyanonaphthalene (**14** and **15**), together with the corresponding SCS found earlier for 2-*exo*-and 2-*endo*-norbornane (**4a** and **b**) and are of some interest. The SCS are invariably deshielding. The SCS on the β protons (H—C—CN) is almost constant at 1.24(±0.04) ppm. The γ effect of the CN group (i.e. H—C—C—CN) is also deshielding with, for the saturated nitriles, little orientational dependence. The γ SCS of the cyano norbornanes **4a** and **b** are of interest in that the SCS is greater for the 120° orientation than for the eclipsed orientation for both the *exo*- and *endo*-norbornanes. This was observed previously for other norbornane substituents.[14,15]

The long-range (more than three bonds) effects of the cyano group are also large and extend over both the cyclohexane and bicycloheptene system. For **1a** the CN SCS decreases with increasing distance of the proton from the CN, with the equatorial protons generally displaying a greater CN SCS than the axial protons. However, for **1b** the SCS of H-3a is very large. Similar large effects are observed at the 7-*syn* protons in **4a** and the 6-*endo* protons in **4b**. All these protons are in a similar environment to the cyano group, i.e. essentially orthogonal to the CN bond. Although these SCS can be due to either the CN anisotropy or electric field, significantly the CN SCS at protons situated along the CN bond (e.g. the 3ax and 3eq protons in **1a**, the 7-*syn* protons in **4b**, etc.) is also deshielding which would not be the case if the SCS were primarily due to the CN anisotropy. This suggestion will

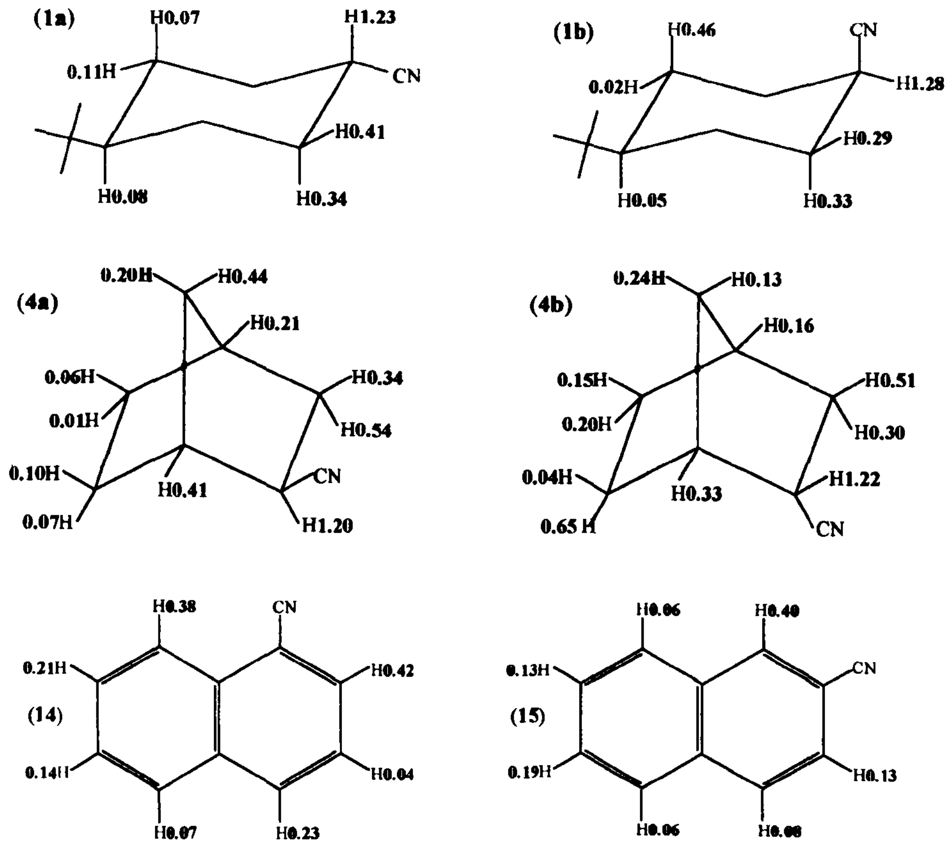


Figure 2. Cyano SCS in aliphatic and aromatic molecules.

be shown to be verified by the detailed analysis in terms of the CHARGE model. Similar CN SCS are observed for the aromatic nitriles **14** and **15** although in these compounds π-electron effects will be present. Again, all the SCS are deshielding and they are considerable even for the protons in the non-substituted aromatic ring.

The data in Tables 3–7 provide a rigorous test of the application of both the CHARGE model and also of present theories of cyano SCS. All the molecules considered are of fixed conformation and the geometries were calculated by *ab initio* calculations, hence the only empirical parameters to be determined are those required for the model. These have been given earlier and are the anisotropy and steric coefficient of the cyano group and the factors involved in the γ effect [Eqn (1)]. The anisotropy of the CN bond, $\Delta\chi^{CN}$, was taken from the centre of the CN bond and the steric effect of the sp carbon atom from the atom considered. The nitrogen atom was considered to be of a sufficient distance from the protons of the molecules considered here to have no noticeable steric interaction with them. There is, however, a possible γ effect from the nitrogen of the CN group (i.e. H—C—CN) which was considered as a polarizability effect (see Theory).

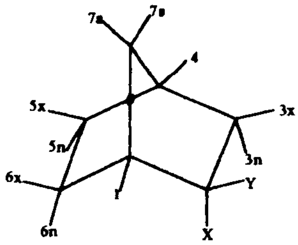
Thus the entire data set of Tables 3–7 is calculated with a total of seven possible parameters which are the anisotropy of the CN bond, the carbon steric effect, the γ effect of the sp carbon atom [coefficients A and B, Eqn (1)] which may differ for aliphatic and aromatic nitriles and the nitrogen polarizability.

Table 3. Observed vs calculated proton chemical shifts (δ) in *trans*- and *cis*-4-*tert*-butylcyclohexanecarbonitrile (**1a** and **2b**), axial and equatorial cyclohexanecarbonitrile (**2a** and **2b**) and ax–ax and eq–eq *trans*-1,4-dicyanocyclohexane (**3a** and **3b**)

	1a		1b		2a[a]		2b[a]		3a[a]		3b[a]	
Proton	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
1e	—	—	2.921	2.886	2.960	2.859	—	—	3.040	2.999	—	—
1a	2.314	2.416	—	—	—	—	2.386	2.342	—	—	2.445	2.440
2e	2.161	2.067	2.037	2.076	2.000	2.035	2.076	2.034	2.009	2.196	2.208	2.184
2a	1.529	1.646	1.516	1.641	1.538	1.587	1.521	1.591	1.918	1.990	1.582	1.695
3e	1.855	1.807	1.771	1.824	1.700	1.788	1.760	1.776	—	—	—	—
3a	0.981	0.985	1.367	1.290	1.500	1.575	1.220	1.284	—	—	—	—
4e	—	—	—	—	1.700	1.763	1.700	1.730	—	—	—	—
4a	1.023	1.095	0.986	1.078	1.200	1.254	1.220	1.277	—	—	—	—

[a] −60 °C; protons 1e and 1a have been corrected by 0.098 and 0.072 ppm, respectively.

Table 4. Observed vs calculated proton chemical shifts (δ) for 2-*exo*- (**4a**) and 2-*endo*-norbornanecarbonitrile, (**4b**)

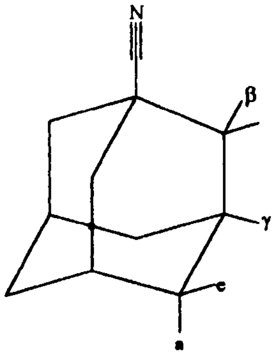


4a: X = H, Y = CN (*exo*)
4b: X = CN, Y = H (*endo*)

Proton	4a		4b	
	Obs.[a]	Calc.	Obs.[a]	Calc.
1	2.599	2.402	2.520	2.373
2x	—	—	2.694	2.873
2n	2.360	2.539	—	—
3x	1.810	1.947	1.982	1.928
3n	1.697	1.664	1.458	1.631
4	2.397	2.204	2.348	2.182
5x	1.528	1.643	1.619	1.641
5n	1.171	1.328	1.356	1.400
6x	1.570	1.620	1.505	1.639
6n	1.225	1.402	1.814	1.835
7s	1.621	1.533	1.308	1.290
7a	1.381	1.356	1.417	1.335

[a] Ref. 9

Table 5. Observed vs calculated proton chemical shifts (δ) for 1-adamantanecarbonitrile (**5**) and acyclic nitriles



(**5**)

Compound	Obs.[a]	Calc.	Compound	Obs.[b]	Calc.
5:					
β	2.04	1.97	CH_3CN	2.03	2.07
γ	2.04	2.12	CH_3CH_2CN:		
e	1.74	1.76	Me	1.30	1.22
a	1.74	1.77	CH_2	2.47	2.44
Acrylonitrile:			Me_2CHCN:		
gem	5.66	5.86	Me	1.35	1.28
cis	6.24	6.09	CH	2.78	2.80
trans	6.10	5.94	*t*-BuCN:		
			Me	1.40	1.33

[a] Ref. 9.
[b] Ref. 10.

Table 6. Observed vs calculated proton chemical shifts (δ) of benzonitrile (**10**) and *o*-, *m*- and *p*-dicyanobenzene (**11, 12, 13**)

Proton	10		11		12		13	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
2	7.660	7.684	—	—	7.971	8.042	7.806	7.876
3	7.482	7.550	7.850	7.888	—	—	7.806	7.876
4	7.615	7.576	7.782	7.775	7.916	7.916	—	—
5	7.482	7.550	7.782	7.775	7.671	7.760	7.806	7.876
6	7.660	7.684	7.850	7.888	7.916	7.916	7.806	7.876

Table 7. Observed vs calculated proton chemical shifts (δ) for 1- and 2-naphthalenecarbonitrile (**14** and **15**) and 9-anthracenecarbonitrile (**16**)

Proton	14		15		16	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
1	—	—	8.245	8.245	8.431	8.316
2	7.900	7.897	—	—	7.728	7.732
3	7.512	7.721	7.611	7.779	7.596	7.652
4	8.069	8.112	7.925	8.012	8.089	8.129
5	7.916	7.928	7.908	7.895	—	—
6	7.612	7.564	7.663	7.566	—	—
7	7.685	7.624	7.610	7.548	—	—
8	8.226	8.133	7.907	7.935	—	—
10	—	—	—	—	8.691	8.867

An iterative program (CHAP8[19]) was used to determine the best fit values of all these parameters using all the above data, a total of 93 shifts. Iterations were carried out including both the steric and anisotropy terms, the anisotropy alone and the steric term alone. All iterations performed yielded little or no improvement of the calculated chemical shifts over those calculations performed with no steric or anisotropic terms present. It was therefore concluded that the steric and anisotropic terms of the cyano group were negligible and the major factor influencing the long range proton chemical shifts was the electric field effect. The final parameterization of the cyano group therefore included electronic effects for protons two or three bonds removed and the electric field effect for protons three or more bonds away. It was found that Eqn (1) could be further simplified with $B_1 = B_2$. Hence the entire data set was reproduced with only five parameters. The values of the coefficients A and B in Eqn (1) were obtained as 0.110 and −0.047 for the saturated nitrilles and −0.185 and 0.030 for the unsaturated nitriles. The orientation dependence of the γ CN effect (H—C—C—CN) is very small in both the saturated and unsaturated compounds. The nitrogen polarizability was obtained as 0.19, lower than the value used previously (0.44).

DISCUSSION

Aliphatic nitriles

The 62 proton chemical shifts of the saturated nitriles in Tables 3–5 range from ca 0.70 to 3.50δ and are predicted with an r.m.s. error of 0.087 ppm and the generally good agreement between the observed and calculated shifts can be seen from the tables. The agreement for the cyclohexane derivatives shown in Table 3 is excellent with the largest error ca 0.15 ppm and the great majority of shifts reproduced to <0.1 ppm.

The agreement for the norbornanes (Table 4) is not as good, owing to the larger errors in the observed vs calculated shifts in the parent compounds than for the cyclohexanes owing to the difficulty of reproducing the proton shifts in these highly strained molecules with a simple model. This is confirmed by the much better agreement between the observed and calculated SCS for these compounds (Table 8).

In particular, the SCS for H-1, H-2 and H-4 are in good agreement with the observed SCS, confirming that the calculations of the CN SCS given are accurate even for these systems. The large deshielding of the H-6*endo* in **4b** is particularly well reproduced, showing that this simple electric field model gives excellent agreement with the observed SCS.

The calculated chemical shifts for the acyclic molecules (Table 5) are also in good agreement with the observed shifts. This is of some interest as Zurcher[6] could not predict the α-proton chemical shifts in these compounds (H—C—CN) or in norbornenecarbonitrile using only the electric field effects of the CN and concluded that other effects besides the linear electric field effect must be present. Zurcher also found that the calculated chemical shifts of protons three bonds from the CN group (H—C—C—CN) in 2-*endo*- and 2-*exo*-norbornenecarbonitrile and 1-adamantanecarbonitrile were very different from the observed chemical shifts and again suggested that factors other than linear electric field effects must be present. He suggested the different steric environments of particular protons and their interactions with the solvent molecules.

ApSimon *et al.*[7] came to similar conclusions. They examined the long-range shielding effects of the CN group on methyl protons in several cyano steroids and also on the ring protons in 2-*endo*- and 2-*exo*-norbornenecarbonitrile. They obtained a poor correlation between the observed and calculated shifts and they also concluded that a modification of the solvent–solute interaction may be responsible for the poor correlation of some protons.

However, it is clear from the present analysis that all these effects can be quantitatively explained in terms of the carbon and nitrogen γ effects outlined above. It is of interest to consider the actual magnitudes of the contributions to the cyano SCS and Table 9 gives the observed vs calculated CN SCS for **1a** and **b** with the calculated electric field and steric contributions. The contributions to the CN SCS include effects due to the removal of the hydrogen in forming the CN derivative. These are the C—H electric field and the steric effect of the hydrogen. However the dominant effect for all long range protons can be seen to be the CN electric field effect.

For protons that are more than three bonds away from the cyano group, the sum of the components gives the total calculated SCS. For the H-2e and H-2a protons the components do not add up to give the calculated value of the CN SCS as these protons experience γ-electron effects [Eqn (1)]. Even in these cases the electric field effect is the major effect.

Aromatic nitriles

The aromatic nitriles have other mechanisms which may affect the proton chemical shifts, in particular the ring current and π-electron effects. The ring currents in the aromatic hydrocarbons are calculated in CHARGE on the basis of the Pauling theory in which the e.m.f. of a current loop is proportional to the area enclosed and the resistance proportional to the number of bonds in the circumference.[1] In this treatment the ring current intensity of the naphthalene, anthracene and benzene rings are all different. The further assumption is made here that the introduction of the cyano group has no effect on the parent hydrocarbon ring current. Hence there are no ring current effects on the CN SCS. In contrast, the CN group does affect the π-electron densities and this has a significant effect on the CN SCS.

The observed versus calculated proton chemical shifts for the aromatic nitriles are given in Tables 6 and 7

Table 8. Observed vs calculated SCS for 2-*exo*- (**4a**) and 2-*endo*-norbornanecarbonitrile (**4b**)

	4a		4b	
Proton	Obs.	Calc.	Obs.	Calc.
1	0.41	0.43	0.33	0.40
2x	—	—	1.22	1.34
2n	1.20	1.30	—	—
3x	0.40	0.41	0.51	0.39
3n	0.54	0.42	0.30	0.45
4	0.21	0.23	0.16	0.21
5x	0.06	0.11	0.15	0.11
5n	0.01	0.09	0.19	0.16
6x	0.10	0.09	0.09	0.10
6n	0.06	0.16	0.65	0.60
7s	0.44	0.30	0.13	0.06
7a	0.20	0.12	0.24	0.10

Table 9. Observed vs calculated CN SCS with the C—CN/C—H electric field and H-steric contributions for *trans*-(**1a**) and *cis*-4-*tert*-butylcyclohexanecarbonitrile (**1b**)

Compound	Proton	Obs. SCS	Calc. SCS	C—CN electric field	C—H electric field	H-steric
1a	2e	0.411	0.413	0.332	−0.001	0.000
	2a	0.339	0.413	0.336	−0.001	0.000
	3e	0.105	0.153	0.120	0.027	0.006
	3a	0.071	0.108	0.079	0.017	0.012
	4a	0.083	0.090	0.061	0.022	0.007
1b	2e	0.287	0.408	0.344	−0.001	0.000
	2a	0.326	0.422	0.262	−0.001	0.000
	3e	0.021	0.170	0.153	0.005	0.012
	3a	0.457	0.413	0.270	0.040	0.103
	4a	0.046	0.073	0.070	−0.005	0.009

Table 10. Observed vs calculated CN SCS ($\Delta\delta$ ppm) with the electric field and π-electron contributions for benzonitrile (**10**), 1- and 2-cyanonaphthalene (**14** and **15**) and 9-cyanoanthracene (**16**)

Compound	Proton	Obs.	Calc.	C—CN electric field	C—H electric field	π shift
10	2, 6	0.319	0.347	0.370	0.000	0.116
	3, 5	0.141	0.213	0.127	0.046	0.044
	4	0.274	0.239	0.096	0.036	0.107
14	2	0.423	0.404	0.375	0.000	0.169
	3	0.035	0.228	0.126	0.046	0.059
	4	0.225	0.283	0.096	0.035	0.154
	5	0.072	0.099	0.058	0.014	0.028
	6	0.135	0.071	0.054	0.010	0.008
	7	0.208	0.131	0.089	0.012	0.032
	8	0.382	0.304	0.333	0.074	0.001
15	1	0.401	0.416	0.376	0.000	0.180
	3	0.134	0.286	0.367	0.000	0.059
	4	0.081	0.183	0.127	0.046	0.014
	5	0.064	0.066	0.040	0.013	0.012
	6	0.186	0.073	0.035	0.000	0.037
	7	0.133	0.055	0.039	0.000	0.015
	8	0.063	0.106	0.050	0.021	0.037
16	1	0.422	0.307	0.339	0.076	0.000
	2	0.261	0.155	0.091	0.013	0.055
	3	0.129	0.075	0.054	0.010	0.011
	4	0.080	0.120	0.058	0.015	0.048
	10	0.260	0.436	0.097	0.035	0.252

and the observed vs calculated SCS for benzonitrile (**10**), 1- and 2-naphthalenecarbonitrile (**14** and **15**) and 9-cyanoanthracene (**16**) in Table 10 together with the calculated contributions to the CN SCS.

There is again generally good agreement between the observed and calculated shifts with the majority of shifts predicted to 0.1 ppm and the majority of SCS to <0.05 ppm. The large deshielding of the *peri* protons H-8 in **14** and H-1 in **16** is well predicted, again demonstrating the accuracy of the electric field calculation even at these short interatomic distances. There are also some discrepancies. The difference between the observed and calculated shifts for H-3 in **14** is 0.21 ppm whereas the corresponding *meta* proton in benzonitrile is predicted fairly well (7.48 vs 7.55).

Table 10 shows that the observed SCS for H-3 in benzonitrile is 0.14 ppm whereas that in **14** is 0.04 ppm. The calculated SCS for these protons are very similar, as would be expected. It would appear that the CN SCS differ significantly in the naphthalene and benzene rings, an interesting effect. The calculated shift of the H-10 proton in **16** is also too large by 0.18 ppm and Table 10 shows that this error is due to the calculated SCS for this proton. This is probably due to the approximations in the Hückel treatment used, which tends to overestimate the π-electron changes in substituted condensed aromatics such as anthracene.

A number of investigators have attempted to explain the proton SCS in aromatic molecules in terms of the π and σ effects of the substituent groups and it is of some interest to consider their results in the light of the above calculations. Hehre *et al.*[29] reviewed the early work in this area and attempted to interpret proton and carbon SCS in substituted benzenes in terms of the charge distributions as calculated by *ab initio* theory. They, like other investigators, considered only the *meta* and *para* protons as the *ortho* protons 'are subject to other effects.'

The *para* carbon in benzonitrile had a decreased π-electron density (with respect to benzene) and a slight increase in the σ electron density. For the *meta* carbon, in contrast the π-electron density is the same as in benzene but the σ-electron density increases. They correlated the chemical shift of the *meta* proton with the sum of the σ charges at the proton and at the attached carbon. The chemical shift of the *para* proton was correlated with the total charge density at the carbon atom but displayed little dependence on the charges at the hydrogen atom. They also found that the proton SCS could be approximately correlated with the hydrogen atom charge densities plus a term in the total π charge density transferred from the substituent to the benzene ring. This π charge transfer was presumed to account for the ring current effects.

These investigators could not find any direct link between the electron densities at the specific atoms and the proton chemical shifts. They concluded that the proton SCS depend on factors other than the electron densities at the hydrogen atom and adjoining carbon atom. It is a pity that they did not attempt to correlate the proton SCS with the π charge density at both the attached and neighbouring carbon atoms [cf. Eqn (7)] as this approach has been successful for both the cyano derivatives studied here and a range of monosubstituted benzenes.[1]

An alternative investigation of proton SCS in benzenes is by the use of the field and resonance components of substituent effects (F and R) obtained by Swain and Lupton.[30] The proportions of field and resonance effects on the CN SCS at any proton can be obtained from the equation used by Swain and Lupton to determine the substituent constant, σ:

$$\sigma = fF + rR \tag{11}$$

where σ is the substituent constant and f and r are weighting factors. Replacing σ with the proton SCS and using the values of F and R for the CN group of 0.847 and 0.184 from Ref. 30 allows the determination of the coefficients f and r. This was done by an iterative least means square analysis using all the data in Tables 5 and 6. This gave values of 0.098 and 0.376 ppm for the *meta* proton SCS and 0.142 and 0.926 ppm for the *para* proton SCS. The field and resonance contributions to the proton SCS (fF and rR) are thus obtained from Eqn (11) as 0.083 and 0.069 ppm for the *meta* protons and 0.120 and 0.174 ppm for the *para* protons.

It is of interest to compare these values with the calculated contributions to the proton SCS in Table 10. For benzonitrile the *meta* proton SCS has electric field and π charge contributions of 0.121 and 0.044 ppm and for the *para* proton SCS the calculated contributions are 0.092 and 0.107 ppm. These values are in very good agreement with the values obtained by the Swain and Lupton treatment although they are based on a totally different conceptual treatment, and this gives strong support for the model used in these calculations.

CONCLUSION

The cyano SCS over more than three bonds are determined by linear electric field effects only, with no significant steric or anisotropic effects. The cyano SCS over three bonds or less is due to γ effects from both the carbon and nitrogen of the CN substituent and these contributions plus the electric field effect for the γ protons (H—C—C—CN) are used to calculate the chemical shifts of the α and β protons, respectively. The γ effect of the cyano carbon atom has a very small orientational dependence. The γ effect of the nitrogen (H—C—CN) which cannot have an orientation dependence is modelled by adjusting the nitrogen polarizability. In the aromatic nitriles the field effect of the cyano group is much larger than the resonance (π-electron) effects at the *ortho* and *meta* protons but the two effects are almost equal at the *para* protons.

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We thank Drs Richard Upton and John Hollerton for their continuing support during this work and for the 750 MHz spectra of **1a** and **b** and the NOE, HMBC and HMQC plots. We thank Dr Jackie Behnke (Aldrich Chemical) for her assistance in determining the concentration dependance of the proton chemical shifts of **16**. M.R. acknowledges a CASE research studentship (BBSRC and Glaxo-Wellcome).

REFERENCES

1. Abraham RJ, Canton M, Reid M, Griffiths L. *J. Chem. Soc., Perkin Trans. 2* 2000; 803.
2. Patai S, Rappoport Z (eds). *The Chemistry of Triple-Bonded Functional Groups*. Wiley: Chichester, 1983.
3. Reddy GS, Goldstein JH. *J. Chem. Phys.* 1963; **39**: 3509.
4. Cross AD, Harrison IT. *J. Am. Chem. Soc.* 1963; **85**: 3223.
5. Bothner-By AA, Pople JA. *Annu. Rev. Phys. Chem.* 1965; **16**: 43.
6. Zurcher RF. *Prog. Nucl. Magn. Reson. Spectrosc.* 1967; **2**: 205.
7. ApSimon JW, Beirbeck H, Todd DK. *Can. J. Chem.* 1972; **50**: 2351.
8. McConnell HM. *J. Chem. Phys.* 1957; **27**: 226.
9. Abraham RJ, Fisher J. *Magn. Reson. Chem.* 1986; **24**: 451.
10. Puchert CJ, Behnke J. *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*. Aldrich Chemical: Milwaukee, WI, 1993.
11. Abraham RJ. *Prog. Nucl. Magn. Reson. Spectrosc.* 1999; **35**: 85.
12. Abraham RJ, Griffiths L, Warne MA. *J. Chem. Soc., Perkin Trans 2* 1997; 31, 1751.
13. Abraham RJ, Griffiths L, Warne MA. *Magn. Reson. Chem.* 1998; **36**: S179.
14. Abraham RJ, Griffiths L, Warne MA. *J. Chem. Soc., Perkin Trans 2* 1997; 203, 881.
15. Abraham RJ, Griffiths L, Warne MA. *J. Chem. Soc., Perkin Trans 2* 1998; 1751.
16. Abraham RJ, Ainger N. *J. Chem. Soc., Perkin Trans 2* 1999; 441.
17. (a) Abraham RJ, Smith PE. *J. Comput. Chem.* 1987; **9**: 288; (b) Abraham RJ, Smith PE. *J. Comput.-Aided Mol. Desi.* 1989; **3**: 175.
18. McClellan AL. *Tables of Experimental Dipole Moments*. vols 1–3. Rahara Enterprises: El Cerrito, CA, 1989.
19. Kuo SS. *Computer Applications of Numerical Methods*. Addison-Wesley: London, 1972; Chapt. 8.
20. Frisch MJ, Trucks GW, Head-Gordon M, Gill PMW, Wong MW, Foresman JB, Johnson BG, Schlegel HB, Robb MA, Replogle ES, Gomperts R, Andres JL, Raghavachari K, Binkley JS, Gonzalez C, Martin RL, Fox DJ, Defrees DJ, Baker J, Stewart JJP, Pople JA. *Gaussian 94*. Gaussian: Pittsburgh, PA, 1994.
21. Allinger NL, Szkrybalo W. *J. Org. Chem.* 1962; **27**: 4601.
22. Bailey WF, Cioffi A. *Magn. Reson. Chem.* 1987; **25**: 181.
23. Eliel EL, Wilen SH. *Stereochemistry of Organic Compounds*. Wiley: New York, 1994.
24. Süess H, Hesse M. *Helv. Chim. Acta* 1979; **62**: 1040.
25. Burgess H, Donnelly JA. *Tetrahedron* 1991; **47**: 111.
26. (a) Castellano S, Sun C. *J. Am. Chem. Soc.* 1966; **88**: 4741; (b) Hayamizu K, Yamamoto O. *J. Mol. Spectrosc.* 1968; **28**: 89; 1969; **29**: 183.
27. Castellano S, Bothner-By AA. *J. Chem. Phys.* 1964; **41**: 3863.
28. Nir M, Hoffman RE, Shapiro IO, Rabinovitz M. *J. Chem. Soc., Perkin Trans 2* 1995; 1433.
29. Hehre WJ, Taft RW, Topsom RD. *Prog. Phys. Org. Chem.* **12**: 159.
30. Swain CG, Lupton EC Jr. *J. Am. Chem. Soc.* 1963; **90**: 1751.

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Proton chemical shifts in NMR. Part 16.[1] Proton chemical shifts in acetylenes and the anisotropic and steric effects of the acetylene group

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The proton resonance spectra of a number of acetylenes of fixed geometry were recorded in dilute $CDCl_3$ solution and assigned. These were acetylene, equatorial- and axial-cyclohexylacetylene at −60 °C, 1,4-di-1-adamantylbutadiyne, 1-ethynyl-*t*- and -*c*-4-*tert*-butylcyclohexan-*r*-1-ol, 2-*exo*-ethynylnorbornan-2-ol † and 2,2′-ethyne-1,2-diyldibornan-2-ol. The aromatic acetylenes measured were phenylacetylene, *o*-ethynyltoluene, 2-ethynylnaphthalene and 9-ethynylanthracene. This data together with previous literature data for but-1-yne, but-2-yne, pent-1-yne, *tert*-butylacetylene, *p*-ethynyltoluene, 1-ethynylnaphthalene and 2-ethynylpropene allowed the determination of the acetylene substituent chemical shifts (SCS) in a variety of molecules. These SCS were analysed in terms of the magnetic anisotropy and steric effects of the acetylene group together with a model (CHARGE7) for the calculation of the two-bond and three-bond electronic effects. For the aromatic acetylenes ring current and π electron effects were included.

Analysis of the SCS showed that the acetylene SCS were due to anisotropic and steric effects plus electronic effects for near protons. A value of $\Delta\chi^{C\equiv C}$ of -11.1×10^{-6} cm^3 mol^{-1} was obtained together with a steric coefficient of 56.6 Å^6. Better results were obtained with both effects operating from the carbon atoms.

The model gives the first comprehensive calculation of the SCS of the acetylene group. For the data set considered of 88 proton chemical shifts spanning *ca.* 8.0 ppm the rms error of observed *vs.* calculated shifts was 0.074 ppm.

Introduction

The magnetic anisotropy of the C≡C bond was first proposed by Pople to explain the high-field shift of the acetylene proton compared to that of ethylene. He subsequently obtained an estimate of $\Delta\chi^{C\equiv C}$ of -19.4×10^{-6} cm^3 mol^{-1} from approximate MO theory. In a review of the early investigations Bothner-By and Pople[2] noted other values of $\Delta\chi^{C\equiv C}$. Reddy and Goldstein[3] obtained a value of -16.5×10^{-6} using the linear relationship they found between proton shifts and the corresponding ^{13}C–^{1}H couplings in compounds where the anisotropic effects were negligible. The anisotropic effects of other groups including the C≡C group were then extrapolated from these linear plots. In a similar manner Zeil and Buchert[4] examined the proton chemical shifts of a variety of acetylenes and nitriles. Assuming that the proton chemical shifts were linearly dependent on the substituent electronegativity plus a constant shift arising from the diamagnetic anisotropy gave a value of -36×10^{-6}. Subsequently Shoemaker and Flygare[5] obtained a value of the anisotropy of the acetylene group as -7.7×10^{-6} from the second-order Zeeman effect in the microwave spectra of propyne and its isotopic species.

Mallory and Baker[6] showed that regions of deshielding existed alongside C≡C bonds by the observation of low-field proton NMR chemical shifts in the aromatic compounds 4-ethynylphenanthrene, 5-ethynyl-1,4-dimethylnaphthalene and 5-ethynyl-1,4-diethylnaphthalene. They concluded that the deshielding effect of the C≡C bond fell off approximately as $1/r^3$.

No systematic attempt has yet been made to calculate the proton chemical shifts of acetylenic molecules and this is the subject of this investigation. We present the complete assignment of the proton spectra of a variety of aliphatic and aromatic acetylenes. This provides a sufficient amount of data for a quantitative analysis of acetylene SCS using a previous model for the calculation of proton chemical shifts. This model is based on simple charge calculations over one, two and three bonds and on steric, anisotropic and electric field contributions for protons greater than three bonds away from the substituent in question. The model has successfully been applied to a variety of saturated hydrocarbons,[7a,b] haloalkanes,[8] ethers,[9] ketones[10] and aromatic compounds.[11] We shall use this model to perform a quantitative analysis of C≡C SCS and show that the proton chemical shifts are influenced by both the magnetic anisotropy and steric effects of the acetylene group.

Theory

As the theory has been given previously[11,12] only a brief summary of the latest version (CHARGE7) will be given here. The theory distinguishes between substituent effects over one, two and three bonds, which are attributed to the electronic effects of the substituents and longer-range effects due to the electric fields, steric effects and anisotropy of the substituents.

The CHARGE scheme calculates the effects of atoms on the partial atomic charge of the atom under consideration, based upon classical concepts of inductive and resonance contributions. If we consider an atom I in a four atom fragment I–J–K–L the partial atomic charge on I is due to three effects. There is an α effect from atom J given by the difference in the electronegativity of atoms I and J. There is a β effect from atom K proportional to both the electronegativity of atom K and the polarisability of atom I. There is also a γ effect (GSEF) from atom L given by the product of the atomic polarisabilities of atoms I and L for I = H and L = F, Cl, Br, I, S. However for the second row atoms (C, O, *etc.*) the γ effect (*i.e.* C–C–C–H) is

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† The IUPAC name for norbornane is bicyclo[2.2.1]heptane.

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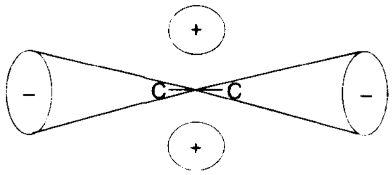

Fig. 1 Representation of the anisotropic shielding ($\Delta\delta$) in an axially symmetric molecule such as acetylene.

parametrised separately and is given by eqn. (1) where θ is the C–C–C–H dihedral angle and A and B empirical parameters.

$$\begin{aligned} \mathrm{GSEF} &= A + B_1\cos\theta \quad 0° \le \theta \le 90° \\ &= A + B_2\cos\theta \quad 90° \le \theta \le 180° \end{aligned} \qquad (1)$$

There are also routines for the methyl γ effect and for the decrease in the γ effect of the electronegative oxygen and fluorine atoms for CX_2 and CX_3 groups. The total charge is given by summing these effects and the partial atomic charges (q) converted to shift values using eqn. (2).

$$\delta_{\mathrm{charge}} = 160.84q - 6.68 \qquad (2)$$

The effects of more distant atoms on the proton chemical shifts are due to steric, anisotropic and electric field contributions. H···H steric interactions in alkanes were found to be shielding and X···H (X = C, O, F, Cl, Br, I) interactions deshielding, according to a simple r^{-6} dependence (eqn. (3)).

$$\delta_{\mathrm{steric}} = a_S/r^6 \qquad (3)$$

Furthermore any X···H steric contribution on a methylene or methyl proton resulted in a push–pull effect (shielding) on the other proton(s) on the attached carbon.

The effects of the electric field of the C–X bonds (X = H, F, Cl, Br, I, O) were calculated from eqn. (4) where A_Z was determined as 3.67×10^{-12} esu units (63 ppm au) and E_Z is the component of the electric field along the C–H bond. The electric field for a univalent atom (*e.g.* fluorine) is calculated as due to the charge on the fluorine atom and an equal and opposite charge on the attached carbon atom. The vector sum gives the total electric field at the proton concerned and the component of the electric field along the C–H bond considered is E_Z in eqn. (4). This procedure is both simpler and more accurate than the alternative calculation using bond dipoles.

$$\delta_{\mathrm{el}} = A_Z E_Z \qquad (4)$$

The magnetic anisotropy of a bond with cylindrical symmetry such as C≡C was obtained using the McConnell equation[13] (eqn. (5)), where R is the distance from the perturbing group to the nucleus of interest in Å, ϕ is the angle between the vector R and the symmetry axis and $\Delta\chi^{\mathrm{C{\equiv}C}}$ the molar anisotropy of the C≡C bond. ($\Delta\chi^{\mathrm{C{\equiv}C}} = \chi^{\mathrm{C{\equiv}C}}_{\mathrm{parl}} - \chi^{\mathrm{C{\equiv}C}}_{\mathrm{perp}}$) where $\chi^{\mathrm{C{\equiv}C}}_{\mathrm{parl}}$ and $\chi^{\mathrm{C{\equiv}C}}_{\mathrm{perp}}$ are the susceptibilities parallel and perpendicular to the symmetry axis respectively. This is illustrated in Fig. 1.

$$\delta_{\mathrm{anisotropy}} = \Delta\chi^{\mathrm{C{\equiv}C}}(3\cos^2\phi - 1)/3R^3 \qquad (5)$$

Aromatic compounds

For aromatic compounds it is necessary to include the shifts due to the aromatic ring current and the π electron densities in the aromatic ring. The aromatic ring current density is calculated in CHARGE from the Pauling theory and the equivalent dipole approximation is then used to calculate the ring current shifts.[11] This treatment reproduces the proton chemical shifts of a wide range of aromatic hydrocarbons and is incorporated unchanged here.

The π electron densities are calculated from Hückel theory.[14,15] The standard coulomb and resonance integrals for the Hückel routine are given by eqn. (6), where α_0 and β_0 are the coulomb and resonance integrals for a carbon $2p_z$ atomic orbital and h_r and k_{rs} the factors modifying these integrals for orbitals other than sp^2 carbon. For alternant aromatic hydrocarbons this gives π electron densities at every carbon equal 1.0 as in benzene and this agrees with the results of more sophisticated calculations.[1]

$$\begin{aligned} \alpha_r &= \alpha_0 + h_r\beta_0 \\ \beta_{rs} &= k_{rs}\beta_0 \end{aligned} \qquad (6)$$

For substituted aromatics the appropriate values of the coefficients h_r and k_{rs} in eqn. (6) for the orbitals involving hetero atoms have to be found. These are now obtained in CHARGE so that the π densities calculated from the Hückel routine reproduce the π densities given from *ab initio* calculations.

The effect of the excess π electron density at a given carbon atom on the proton chemical shifts of the neighbouring protons is given in CHARGE by eqn. (7). Δq_α and Δq_β are the excess π electron density at the α and β carbon atoms and the values of the coefficients a_1 and a_2 were found to be 10.0 and 2.0 ppm per electron.[11]

$$\Delta\delta = a_1\Delta q_\alpha + a_2\Delta q_\beta \qquad (7)$$

The above contributions are added to the shifts of eqn. (2) to give the calculated shift of eqn. (8).

$$\delta_{\mathrm{total}} = \delta_{\mathrm{charge}} + \delta_{\mathrm{steric}} + \delta_{\mathrm{anisotropy}} + \delta_{\mathrm{el}} + \delta_{\pi} \qquad (8)$$

Application to the acetylene group

The acetylene group has in principle steric, electric field and anisotropic effects on protons more than three bonds away plus for aromatics an effect on the π electron densities. All these have to be incorporated into the model.

The major electric field of the acetylene group is due to the C–H bond as the C≡C bond is non-polar. The electric field calculation for any C–H bond is automatically included in the model. The C≡C group has cylindrical symmetry and eqn. (5) is used to calculate the anisotropy contribution. There is a possible steric effect of the acetylene group on the neighbouring protons and a possible steric effect of the near aliphatic protons on the acetylene proton. These are both given by eqn. (3) with different steric coefficients a_S which may be of either sign. Thus the unknowns to be obtained are $\Delta\chi$, the molar anisotropy of the C≡C bond and the steric coefficients a_S.

For protons of three bonds or less from the C≡C group it is necessary to determine the orientational dependence of the γ proton chemical shift with respect to the α acetylene carbon due to electronic effects. This is simulated by a γ substituent effect from the acetylene carbon (H–C–C–C≡) following eqn. (1), in which the coefficients A and B may differ for the C≡C group in aromatic *vs.* saturated compounds. Also in CHARGE the β effect is given by a simple general equation which was sufficient for the calculation of charge densities but not sufficiently accurate to reproduce the proton chemical shifts. Thus the β effect from the acetylene carbon atom (H–C–C≡) needs to be obtained. As there is no orientation dependence in this case only one coefficient is required.

For the aromatic acetylenes it is necessary to obtain the appropriate values of the factors h_r and k_{rs}, which are the Hückel integrals for the C≡C group (eqn. (6)). The π electron densities and dipole moments from *ab initio* calculations are very dependent on the basis set used. The 3-21G basis set gave the best agreement with the observed dipole moments (Table 1)

Table 1 Total and π (in parentheses) charges (*me*), and dipole moments (D) for propyne and phenylacetylene

Atom	Method STO-3G	3-21G	6-31G	CHARGE	Observed
Propyne					
C_β	−136 (−21.7)	−419 (−22.0)	−488 (−24.7)	−106 (−22.4)	
C_α	−37 (11.3)	−47 (12.2)	−29 (13.9)	−62 (22.4)	
μ/D	0.50	0.69	0.68	0.50	0.75
Phenylacetylene					
C_β	−125 (−5.1)	−363 (−14.2)	−531 (−16.5)	−83 (−10.6)	
C_α	−40 (−0.9)	−60 (−0.1)	−155 (2.4)	−46 (−0.7)	
C-1	2 (−21.0)	−44 (−32.6)	−156 (−26.7)	−24 (−0.6)	
C-2	−54 (8.6)	−215 (18.5)	−148 (14.9)	−57 (4.5)	
C-3	−63 (0.3)	−230 (−1.3)	−209 (0.1)	−72 (−0.3)	
C-4	−59 (9.1)	−237 (12.6)	−188 (10.8)	−73 (3.6)	
μ/D	0.50	0.65	0.64	0.36	0.72

and the π densities from this basis set were used to parametrise the Hückel calculations. The CN group contains an sp hybridised carbon atom and the parameters for this group have already been derived.[1] Thus the values of h_r(Csp) and k_{rs}(Csp^2–Csp) used for nitriles were used for the acetylene calculations as the Hückel integrals for Csp operate for both of these functional groups. A value of k_{rs} of 1.60 (Csp–Csp) gave π electron densities for the aromatic acetylenes in reasonable agreement with those from the *ab initio* calculations.

The accuracy of the π densities calculated in the CHARGE program can be examined by calculating the dipole moments of some acetylenes. The calculated *vs.* observed (in parentheses) dipole moments[16] (D) of propyne, but-1-yne, *tert*-butylacetylene, phenylacetylene and *p*-ethynyltoluene are 0.50 (0.75), 0.50 (0.81), 0.52 (0.66), 0.36 (0.72) and 1.26 (1.02) and the general agreement is support for the π density calculations. The electron densities (total and π) and dipole moments calculated for propyne and phenylacetylene by CHARGE and GAUSSIAN94 are given in Table 1.

Values of h_r and k_{rs} for X–Csp have been determined for a number of different substituents C≡C–X. Values of h_r for F, Cl and O for olefins (C=C–X) were obtained previously from π electron densities calculated from GAUSSIAN94W at the 3-21G level for a range of olefinic compounds.[17]

These were left unchanged for the acetylenes and the values of k_{rs} for the ≡C–X bond varied for the best agreement with the *ab initio* π electron densities. Values of 0.74 (Csp–F), 0.57 (Csp–Cl) and 1.00 (Csp–O) gave reasonable agreement with those calculated from GAUSSIAN94W. Again, the accuracy of the calculated charges can be examined by calculating the dipole moments of these molecules. The calculated *vs.* observed (in parentheses) dipole moments (D) of fluoroacetylene, chloroacetylene, propynal and methoxyacetylene are 0.79 (0.75), 0.74 (0.44), 2.56 (2.46), and 1.62 (1.93). Note that the value of k_{rs} for the Csp–Csp^2 bond is already known from the phenylacetylene data. Also, the calculated *vs.* observed (in parentheses) chemical shifts of the acetylene proton in fluoroacetylene, chloroacetylene and propynal are 1.33 (1.63), 1.95 (1.80) and 3.61 (3.47). The good agreement of the calculated *vs.* observed chemical shifts for these molecules is strong support for the above treatment.

Experimental

The molecules studied here with the atom numbering are shown in Fig. 2.

Acetylene (**1**), cyclohexylacetylene (**10**), 1,4-di-1-adamantylbutadiyne (**11**) and phenylacetylene (**12**) were obtained commercially.[18–21] *o*-Ethynyltoluene (**13**) and 2-ethynylnaphthalene (**16**) were synthesised by double elimination of 1-(1,2-dibromoethyl)-2-methylbenzene and 1-(1-naphthyl)-1,2-dibromoethane.[22] 9-Ethynylanthracene (**17**) was synthesised by Sonogashira coupling[23] of 9-bromoanthracene and trimethylsilylacetylene. 1-Ethynyl-*t*- and -*c*-4-*tert*-butylcyclohexan-*r*-1-ol (**7**-*trans*, **7**-*cis*), 2-*exo*-ethynylbicyclo[2.2.1]heptan-2-ol (**8**) and 2,2′-ethyne-1,2-diylbis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol) (**9**) were synthesised by the addition of ethynylmagnesium bromide to the corresponding ketones in THF.[24]

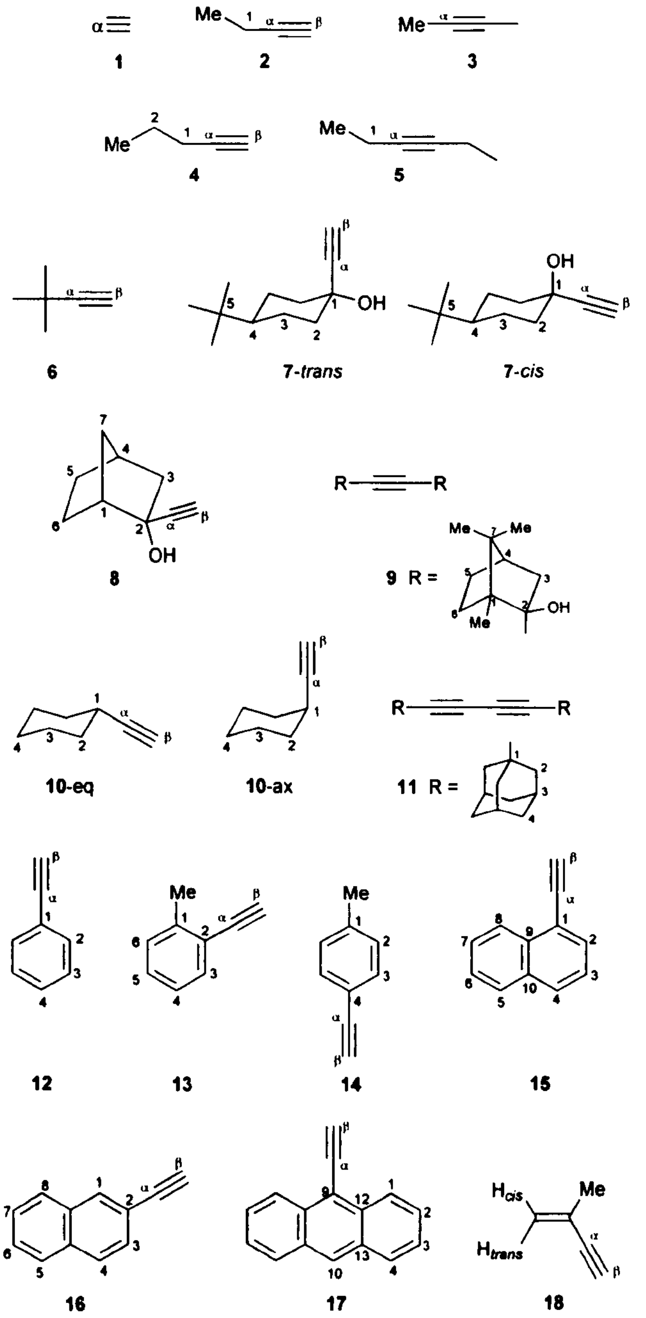

Fig. 2 Molecules studied and their numbering.

Table 2 Observed *vs.* calculated proton chemical shifts (δ) for acetylene[a] (**1**), but-1-yne (**2**), but-2-yne (**3**), pent-1-yne (**4**), *n*-hex-3-yne (**5**) and ***tert***-butylacetylene (**6**)

	2		**3**		**4**		**5**		**6**	
Proton	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
H-1	2.25	2.18	—	—	2.18	2.02	2.15	2.23	—	—
H-2	—	—	—	—	1.57	1.55	—	—	—	—
Me	1.18	1.10	1.75	1.82	1.00	0.77	1.11	1.13	1.24[b]	1.24
C≡C–H	1.97	2.04	—	—	1.95	2.05	—	—	2.07	2.10

[a] Acetylene, obs. 1.91, calc. 1.91. [b] *tert*-Butyl.

^{1}H and ^{13}C NMR were obtained on a Bruker AMX400 spectrometer operating at 400 MHz for proton and 100.63 MHz for carbon. The spectra for **7**-*trans*, **7**-*cis*, **8** and **9** were recorded on a Varian 750 MHz spectrometer at Glaxo-Wellcome[25] which was used for the HMQC, HMBC and NOE experiments.

The spectra were recorded in 10 mg cm^{-3} (^{1}H) and *ca.* 50 mg cm^{-3} (^{13}C) solutions with a probe temperature of *ca.* 25 °C in $CDCl_3$ and referenced to TMS. Typical running conditions of the spectrometers were 128 transients, spectral width 3300 Hz and 32 k data points. This gave an acquisition time of 5 s and zero-filled to 128 k to give a digital resolution of 0.025 Hz.

The 2D experiments were conducted using the Bruker COSY-DQF and HXCO and the Varian HMQC and GHMQC-DA pulse sequences.[26,27] The geometry of the compounds investigated was obtained initially using GAUSSIAN94W at the RHF/6-31G* and MP2/6-31G* levels[28a] and later using GAUSSIAN98W[28b] at the DFT/B3LYP/6-31G** level. All the calculations were carried out using a PC.

Spectral assignments

The assignments of all the compounds investigated are given in Tables 2–6 together with the calculated proton chemical shifts. Letters e, a, x, n and s denote equatorial, axial (or *anti*), *exo*, *endo* and *syn* respectively.

The ^{1}H NMR data for but-1-yne (**2**), but-2-yne (**3**), pent-1-yne (**4**), hex-3-yne (**5**), *tert*-butylacetylene (**6**), *p*-ethynyltoluene (**14**), and 2-ethynylpropene (**18**) were from ref. 29 and that for 1-ethynylnaphthalene (**15**) from ref. 22.

Cyclohexylacetylene (10). The spectra of the separate conformers were obtained by recording the spectra at −60 °C at which temperature the rate of interconversion of the conformers was slow on the NMR time scale. The integral ratio for protons 1e and 1a was 1 : 6.2 with the equatorial conformer more favoured to give ΔG (eq–ax) 0.70 kcal mol^{-1}, in fair agreement with previous measurements of ΔG (eq–ax). Eliel[30] quotes 0.41–0.52 kcal mol^{-1}.

A ^{1}H COSY spectrum was recorded at −60 °C to fully assign the equatorial conformer. For **10**-eq protons 1a, 2e and 2a are readily assigned and examination of the ^{1}H COSY spectrum plus the integrals of the ^{1}H spectrum gave the assignments of the remaining protons. For **10**-ax only protons 1e, 2e and 2a were assigned by examination of the ^{1}H COSY spectrum. The remaining protons were hidden underneath the resonances of the protons in **10**-eq.

1,4-Di-1-adamantylbutadiyne (11). The ^{1}H spectrum of **11** was assigned from the integrals and fine structure. H-δ was easily identified at *ca.* 1.94 ppm, H-γ as a doublet with a coupling of *ca.* 4.5 Hz to H-δ at *ca.* 1.86 ppm. H-e and H-a with respect to the acetylene group were a single broad resonance at *ca.* 1.67 ppm.

1-Ethynyl-*t*- and -*c*-4-*tert*-butylcyclohexan-*r*-1-ol (7-*trans*, 7-*cis*). The ^{1}H, ^{13}C and 2D spectra for these isomers were recorded at 750 MHz. The spectra for the pure *trans* isomer were recorded, but the spectra for the *cis* isomer were recorded from a mixture of the *cis* and *trans* conformers. This was not a problem as the resonances were easily distinguished.

7-*trans*. The ^{1}H spectrum consists of five separate resonances including the methyl resonances. These were assigned by use of a ^{1}H COSY spectrum. H-2e and H-3e were easily distinguished as only H-3e displayed a coupling to H-4a. H-3a and H-2a were identified by examination of the splitting pattern of the resonances. This assignment was further confirmed by examination of a HETCOR spectrum and the known ^{13}C spectral assignment.[31]

7-*cis*. The ^{1}H spectrum of this isomer again consisted of five resonances and was readily assigned in the same way as **7**-***trans***.

A lanthanide induced shift experiment using $Yb(fod)_3$‡ was conducted on the sample of the pure *trans* isomer to confirm that the configuration of Fig. 2 was correct. $Yb(fod)_3$ is known to bind to the OH group and therefore downfield shifts in the ^{1}H spectrum would be expected to be observed on H2e and H2a, as they are in close proximity to the $Yb(fod)_3$. This was observed and confirmed the characterisation of this isomer.

2-*exo*-Ethynylbicyclo[2.2.1]heptan-2-ol (8). The ^{1}H, ^{13}C, 2D and NOE spectra for this compound were recorded at 750 MHz. An X-ray crystal structure[25] of this compound was obtained which confirmed the configuration at C-2 (Fig. 2). The ^{1}H spectrum for this compound consisted of ten resonances. H-1 and H-4 were readily identifiable by examination of their splitting patterns, H-1 appearing as a doublet, H-4 as a triplet. The other proton groups were elucidated by examination of a HETCOR plot together with the known assignment of the ^{13}C spectrum.[32] By examination of the ^{1}H COSY spectrum H-5x and H-6x were identified by their strong coupling to H-4 and H-1 respectively. H-3x was identified by its strong coupling to H-4 and H-5x. H-7s was identified by ^{1}H COSY, HMBC and NOE experiments. H-7s has a W-coupling to H-6n and H-5n. A strong 3-bond HMBC coupling is also observed to C-6 and C-5, which is much less intense in H-7-anti. An NOE performed on H-3x also helped to elucidate H-7s.

With these assignments it was possible to assign the geminal partners of H-3x, 5x, 6x and 7s from the HETCOR plot. The assignments of these protons were confirmed by NOE and HMBC experiments.

2,2′-Ethyne-1,2-diylbis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol) (9). The ^{1}H, ^{13}C, 2D and NOE spectra for this compound were recorded at 750 MHz. An X-ray crystal structure[25] of this compound was obtained to confirm the configuration at C-2. This showed that the compound was as shown in Fig. 2.

The ^{1}H spectrum of this compound consisted of seven resonances plus the three methyl resonances. H-3x and H-3n were readily identified by examination of their splitting patterns, H-3x is a doublet of triplets and H-3n a doublet. H-4 was identified by examination of the ^{1}H COSY. Large couplings to H-3x and H-5x were observed giving the expected triplet pattern.

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‡ The IUPAC name for fod is 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato.

Table 3 Observed *vs.* calculated proton chemical shifts (δ) for equatorial and axial ethynylcyclohexane (**10**-eq, **10**-ax) and 1,4-di-1-adamantylbutadiyne (**11**)

Compound	Proton	Obs.	Calc.
10-eq	1a	2.246	2.094
	2e	1.977	1.877
	2a	1.355	1.408
	3e	1.734	1.617
	3a	1.200	1.084
	4e	1.666	1.600
	4a	1.170	1.138
	C≡C–H	2.182	2.100
10-ax	1e	2.871	2.667
	2e	1.775	1.877
	2a	1.481	1.519
	C≡C–H	2.278	2.137
11	γ	1.861	1.810
	δ	1.941	1.943
	e	1.681	1.646
	a	1.681	1.639

Table 4 Observed proton chemical shift (δ) for 1-ethynyl-*t*- and -*c*-4-*tert*-butylcyclohexan-*r*-1-ol (**7**-*trans*, **7**-*cis*) and observed *vs.* calculated C≡C SCS

			SCS	
Compound	Proton	δ(Obs.)	Obs.	Calc.
7-*trans*	2e	2.040	0.033	0.293
	2a	1.514	0.297	0.328
	3e	1.762	-0.020	0.051
	3a	1.367	0.321	0.543
	4a	1.000	0.035	0.0
7-*cis*	2e	2.037	0.204	0.222
	2a	1.705	0.216	0.263
	3e	1.596	0.048	0.047
	3a	1.379	0.020	-0.038
	4a	1.010	0.017	0.026

Table 5 Proton chemical shifts (δ) for (**8**) and (**9**) and observed *vs.* calculated C≡C SCS

			SCS	
Compound	Proton	δ(Obs.)	Obs.	Calc.
8	1	2.407	0.155	0.229
	3x	2.140	0.269	0.255
	3n	1.360	0.334	0.406
	4	2.250	0.079	−0.006
	5x	1.561	−0.009	−0.003
	5n	1.318	−0.017	−0.091
	6x	1.380	−0.002	0.003
	6n	1.979	0.109	−0.142
	7s	1.802	0.462	0.493
	7a	1.389	0.099	−0.055
9	3x	2.228	0.489	0.336
	3n	1.822	0.083	0.195
	4	1.750	0.029	−0.059
	5x	1.695	0.020	0.056
	5n	1.180	0.222	0.159
	6x	1.468	−0.037	0.134
	6n	1.835	0.827	1.153
	Me (1)	0.940	0.034	0.110
	Me (7s)	1.057	0.039	−0.057
	Me (7a)	0.870	0.042	−0.016

H-5x was also identified from the ^{1}H COSY as large couplings are seen to H-3x and H-4. H-5n was assigned by examination of a HETCOR plot plus the known assignment of the ^{13}C spectrum[32] and this was confirmed by an NOE with H-5x.

H-6x was assigned from the ^{1}H COSY spectrum, with a large coupling to H-5x. HMBC spectra also revealed a large 3-bond coupling from H-6x to the 1-methyl carbon atom. H-6n was then assigned from the HETCOR plot and confirmed by an NOE to H-6x.

The methyls in the 7a and 7s positions were easily assigned by NOE experiments. The 7a methyl gave NOEs to H-5x, H-6x and H-4 and the 7s methyl gave NOEs to H-3x, H-3n and H-4. The C-1 methyl is then immediately assigned.

Phenylacetylene (12). Even at 400 MHz H-3 and H-4 are a strongly coupled multiplet. Decoupling H-2 gave an AB$_2$ pattern for H-3 and H-4 which was routinely analysed.

***o*-Ethynyltoluene (13).** The ^{1}H spectrum for *o*-ethynyltoluene consists of four aromatic resonances. H-3 and H-6 are doublets of doublets with H-6 split further by its coupling to the methyl protons. H-4 and H-5 are triplets easily identified by their roofing patterns.

2-Ethynylnaphthalene (16). The aromatic spectrum for 2-ethynylnaphthalene consists of seven resonances. The singlet at 8.02 is identified as H-1. H-3 and H-4 are also easily identified as a doublet of doublets and a doublet respectively. As the ^{13}C assignment of this compound is known,[33] a ^{13}C–^{1}H HETCOR spectrum confirmed the ^{1}H assignment.

9-Ethynylanthracene (17). The aromatic spectrum for this compound consists of five resonances. H-10 is easily identified as the singlet occurring at *ca.* 8.43 ppm. A ^{13}C–^{1}H-undecoupled spectrum was recorded to assign C-1 and C-4, as C-4 has a $^1J_{CH}$ coupling to H-4 (*ca.* 160 Hz) and two $^3J_{CH}$ couplings to H-2 and H-10 (*ca.* 6 Hz) to give a doublet of triplets. C-1 has one $^1J_{CH}$ coupling to H-1 and one $^3J_{CH}$ coupling to H-3 to give two doublets of triplets. The assignment of C-1 and C-4 allows the assignment of H-1 and H-4 in the proton spectra from a HETCOR plot.

A ^{1}H COSY spectrum identified H-2 and H-3 from their couplings to H-1 and H-4 respectively and the assignment of C-2 and C-3 followed from a ^{1}H–^{13}C HETCOR plot. The ^{13}C assignments are as follows. C-1 127.65, C-2 127.18, C-3 125.63, C-4 128.59, C-9 115.97, C-10 127.08, C-12 130.64, C-13 132.21, C-α 77.50, C-β 84.00.

Further details of all the assignments and spectra are given in ref. 34.

Results

The data for the acetylenes obtained here in dilute CDCl$_3$ solution is in excellent agreement with the earlier data obtained in various solvents. The value for acetylene (1.91 ppm) compares with previous literature values of 1.80 (CCl$_4$)[35] and 1.91 (CD$_2$Cl$_2$).[36] The proton chemical shift of benzene in CDCl$_3$ is 7.341 and this gives the *ortho*, *meta* and *para* proton SCS in phenylacetylene in CDCl$_3$ from the above data as 0.151, −0.030 and 0.000 ppm. These agree exactly with the comparable values in CCl$_4$ solution of 0.15, −0.02 and −0.01.[35] As found previously for other aromatic compounds[11] there is a small, almost constant shift to higher δ values in CDCl$_3$ compared to CCl$_4$ but the proton SCS for substituted benzenes obtained by earlier investigations may be used unchanged for the CDCl$_3$ solutions.

The data obtained here for the acetylenes may be combined with the proton chemical shifts of the parent compounds given previously[11,12] to give the acetylene SCS in these compounds. These are shown in Fig. 3 for eq-cyclohexylacetylene (**10**-eq), 1-ethynyl-*t*-4-*tert*-butylcyclohexan-*r*-1-ol (**7**-*trans*), 1- and 2-ethenylnaphthalene (**15**, **16**) and the norbornane (**8**) and bornane (**9**) derivatives. The SCS for **7**-*trans*, **8** and **9** are obtained as the chemical shifts for **7**, **8** and **9** minus the proton shifts of *t*-4-*tert*-butylcyclohexan-*r*-1-ol, *endo*-norborneol and isoborneol.[37] These SCS are of some interest. The SCS are both shielding and deshielding but the larger SCS are always deshielding. The γ effect of the C≡C group (*i.e.* H–C–C–C≡C) is

Table 6 Observed *vs.* calculated proton chemical shifts (δ) and observed *vs.* calculated C≡C SCS for acetylenes (**12**–**18**)

Compound	Proton	δ(Obs.)	δ(Calc.)	SCS(Obs.)	SCS(Calc.)
Phenylacetylene (**12**)	2,6	7.492	7.544	0.151	0.207
	3,5	7.311	7.337	−0.030	0.000
	4	7.341	7.343	0.0	0.006
	C≡C–H	3.069	3.191		
o-Ethynyltoluene (**13**)	3	7.460	7.484	0.200	0.178
	4	7.138	7.155	−0.027	−0.041
	5	7.245	7.289	−0.015	−0.017
	6	7.202	7.005	0.022	−0.022
	Me	2.454	2.494	0.111	0.252
	C≡C–H	3.271	3.156		
p-Ethynyltoluene (**14**)	2,6	7.100	7.016	−0.080	−0.011
	3,5	7.400	7.496	0.140	0.190
	Me	2.340	2.251	−0.003	−0.033
	C≡C–H	3.020	3.124		
1-Ethynylnaphthalene (**15**)	2	7.700	7.692	0.223	0.216
	3	7.340	7.478	−0.137	0.002
	4	7.760	7.856	−0.084	0.031
	5	7.760	7.814	−0.084	−0.011
	6	7.440	7.478	−0.037	0.002
	7	7.530	7.515	0.053	0.039
	8	8.350	8.340	0.506	0.515
	C≡C–H	3.430	3.298		
2-Ethynylnaphthalene (**16**)	1	8.028	8.067	0.184	0.242
	3	7.524	7.652	0.047	0.176
	4	7.788	7.810	−0.056	−0.015
	5	7.810	7.803	−0.034	−0.022
	6	7.500	7.467	0.023	−0.009
	7	7.500	7.462	0.023	−0.014
	8	7.810	7.832	−0.034	0.007
	C≡C–H	3.142	3.225		
9-Ethynylanthracene (**17**)	1	8.522	8.478	0.513	0.475
	2	7.602	7.598	0.135	0.043
	3	7.504	7.546	0.037	−0.009
	4	8.001	8.003	−0.008	0.0
	10	8.447	8.410	0.016	−0.022
	C≡C–H	3.990	3.594		
2-Ethynylpropene (**18**)	H_{trans}	5.300	5.233	0.359	0.337
	H_{cis}	5.390	5.479	0.359	0.553
	Methyl	1.900	1.788	0.175	0.149
	C≡C–H	2.870	3.164		

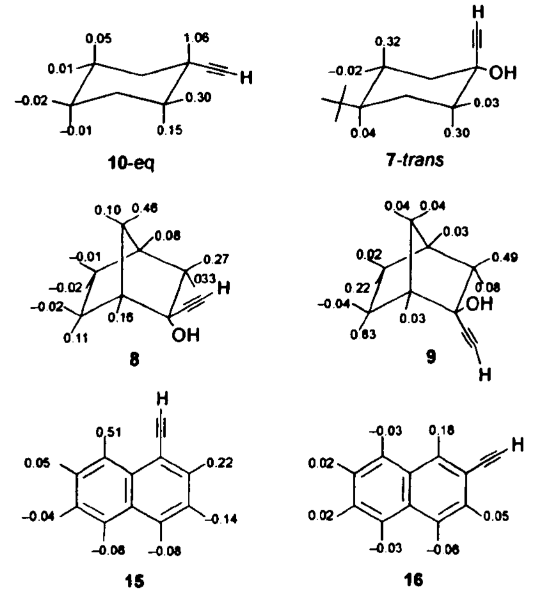


Fig. 3 Observed ethynyl SCS in aliphatic and aromatic molecules.

also deshielding with for the saturated compounds considerable orientational dependence without any obvious pattern, except that the γ SCS of the norbornane and bornane derivatives **8** and **9** is greater for the 120° orientation than for the eclipsed orientation for both the *exo* and *endo* compounds. This intriguing observation is valid for all norbornane substituents so far studied.[8,9]

The long range (>3 bonds) effects of the C≡C group are large but decrease rapidly with distance. For **10**-eq the C≡C SCS is almost zero for all long range protons. There is a large 1,3-diaxial interaction of the acetylene and H-3a in **7**-*trans*. Similar large effects are observed at the 7s protons in **8** and the 6n protons in **9**. All these protons are in a similar environment to the triple bond, *i.e.* essentially orthogonal to the C≡C bond. As there is no electric field effect of the C≡C bond these SCS can be due to either the C≡C anisotropy or a steric effect or both. Significantly the C≡C SCS at protons situated along the C≡C bond (*e.g.* the 3a and 3e protons in **10**-eq, the 7s proton in **9** *etc.*) is small but always deshielding. This would not be so if the SCS were solely due to the C≡C anisotropy. This suggestion will be shown to be verified by the detailed analysis in terms of the CHARGE model. Similar C≡C SCS are observed for the aromatic acetylenes **15** and **16** though in these compounds π electron effects will be present. Again the SCS are of either sign but the large effects are always deshielding, the largest being again due to the *peri* interaction in **15**.

The data in Tables 2–6 provide a rigorous test of the application of both the CHARGE model and also present theories of C≡C SCS. All the molecules considered are of fixed conformation and the geometries calculated by *ab initio* calculations, thus the only empirical parameters to be determined are those required for the model.

The *ab initio* geometries obtained were of some interest. GAUSSIAN94 at the MP2/6-31G* level gave values of the H–C≡ and C≡C bond lengths in acetylene of 1.061 and 1.203 Å respectively in complete agreement with the experimental values (1.061 and 1.203 Å).[38] The same basis set gave corresponding values for phenylacetylene of 1.057 and 1.188 Å, but for *p*-tolylacetylene the values were 1.067 and 1.223 Å. This large change on the introduction of a *p*-methyl group seemed odd and these geometries did not give good results when used in CHARGE. In particular the acetylene proton shift is identical in these aromatic compounds (Table 6) but was not calculated to be so with these geometries. Using the recommended DFT/B3LYP[28c] routine with the 6-31G** basis set in GAUSSIAN98 gave bond lengths of 1.065 and 1.210 Å for both compounds and these values were used as standard for all the aromatic acetylenes. It is well known[28c] that the DFT technique treats electron correlation much better than the MP2 routine and this could be the explanation of the above result.

It is first necessary to consider how the acetylene (H–C≡) protons will be calculated. These could be reproduced in CHARGE by the appropriate values of the integral for the H–Csp bond. The near effects of anisotropic (or polar) bonds have been reproduced in this manner in previous parts of this series as attempting to calculate anisotropic (or polar) effects at such short distances by means of simple geometric functions (eqns. (3)–(5)) is not a feasible option. However if this procedure was adopted here the charge on the acetylene proton would be *ca.* equal to that in ethane, reflecting the near equality of their chemical shifts. This is obviously not the case as the acetylene proton is more acidic and the C–H bond more polar than even the olefinic proton. Thus the anisotropic contribution has been included in the chemical shift calculation for these protons. The procedure adopted was that the values of $\Delta\chi^{C\equiv C}$ and the steric coefficient together with the coefficients of the γ effects were obtained from the shifts of all the protons except the acetylene protons. The appropriate parameters for these protons were then included. This gave the correct chemical shift for the acetylene protons and an acceptable value of the proton charge (see later).

The parameters required for the calculations are the anisotropy of the C≡C bond, the sp carbon steric coefficient $a_S^{C\equiv C}$, the γ effect of the sp carbon atom *i.e.* H–C–C–C≡ (coefficients *A* and *B* eqn. (1)) and the β effect of the β acetylene carbon *i.e.* H–C–C≡. The γ effects may differ for aliphatic and aromatic acetylenes. This gives a total of five parameters for the aliphatic series plus a possible three more for the aromatic compounds. The acetylene proton chemical shifts were then fitted by the appropriate values of the ≡C–H exchange integral and the γ effect H–C≡C–X plus a second steric parameter a_S for the steric effect of neighbouring sp^3 protons on this proton.

The iterations were carried out on the observed chemical shift data of all protons by use of the non-linear mean squares programme (CHAP8[39]). The anisotropy of the C≡C bond was taken from both the centre of the C≡C bond and from each carbon atom, but the steric effect of the sp carbon atoms was taken as usual from the atom considered. The iterations gave better results when the anisotropy was taken from each carbon of the C≡C bond. Also both the values of the anisotropy, steric coefficent and the coefficients *A* and *B* (eqn. (1)) for the γ effects were identical when the iterations were performed with either the aliphatic compounds alone or the aromatic compounds, thus the final iteration was performed including all the compounds and using only five parameters. The values of these parameters were as follows. The anisotropy was −9.18 ppm Å^3 at each carbon atom, *i.e.* $\Delta\chi^{C\equiv C} = -18.36$ ppm Å^3 per molecule, *i.e.* -11.1×10^{-6} cm^3 mol^{-1}. The steric coefficient $a_S^{C\equiv C} = 56.6$ Å^6. The coefficients for the γ effects (H–C–C–C≡), (eqn. (1)), were *A* 0.423 and *B* −0.177 ppm. and the enhanced β effect (H–C–C≡) was 1.37. The acetylene protons were then considered. For these protons the iteration gave values of the C–H exchange integral of 42.8 (*cf.* 41.4), the γ effect (H–C≡C–C) coefficients were 0.22 and 1.20 for sp^3 and sp^2 carbons respectively and the steric coefficient (H–Csp^3 to H–C≡) was 46.5.

The iteration was over 124 chemical shift values of the compounds discussed previously excepting the acetylene alcohols as the parametrisation of the OH group has not been finalised in CHARGE. The rms error of the observed–calculated shifts was 0.074 ppm over a chemical shift range from *ca.* 1–8.5 ppm, a very satisfying result.

Discussion

The data of Tables 2–6 provide an examination of both the application of the CHARGE model to alkynes and of the influence of the acetylene group on proton chemical shifts. There is generally very good agreement between the observed and calculated proton chemical shifts. In the aliphatic compounds the model reproduces very well the sizeable low field shifts of protons situated at the side of the acetylene group; *e.g.* H-3a in axial cyclohexanes SCS (**7**-*trans*), obs. 0.32, calc. 0.43 ppm, H-7s in *exo*-ethynylnorbornanes (**8**), obs. 0.46, calc. 0.49 ppm, and H-6n in *endo*-ethynylbornanes (**9**), obs. 0.83, calc. 1.15 ppm (Fig. 2). The calculated values are due to both anisotropy and steric effects (see later). The smaller γ effects are again mostly to low-field and are also well reproduced by the combination of the anisotropy and the γ effect of eqn. (1).

In the aromatic acetylenes again the large SCS of the acetylene group due to the analogous periplanar interactions are also well reproduced; *e.g.* H-8 in 1-ethynylnaphthalene (**16**), obs. 0.51, calc. 0.51 ppm, H-1,5 in 9-ethynylanthracene (**17**), obs. 0.51, calc. 0.48 ppm. The other major SCS in the aromatic compounds are at the *ortho* protons and again these effects are due to the anisotropy plus γ effects. The SCS at the other ring protons due mainly to π effects are much smaller, reflecting the small interaction between the acetylene and the aromatic π systems.

There are some discrepancies in the calculated values of chemical shifts. Both the 1e proton in **10**-ax and the 1a proton in **10**-eq are *ca.* 0.2 ppm larger than the observed values (Table 3). These are the only methine (HC–C≡) protons in the data set and this may be a general result. Further data would be necessary to test this.

The observed and calculated shifts for H-2e in **10**-ax are in reasonable agreement (Table 3) as are the values for H-2e in **7**-*cis* (Table 4). In the analogous compound **7**-*trans* the corresponding SCS are obs. 0.03, calc. 0.29 ppm. It may be that in **7**-*trans* there is an interaction between the geminal hydroxy and acetylene groups. In this case the SCS for each group cannot be obtained simply by subtracting the shifts in this compound from those of the parent alcohol (or acetylene). There is a similar anomaly in the obs. *vs.* calc. SCS for H-3x and -3n in **9** but not for **8**. It is of interest that the anomalous results occur for compounds in which the acetylene group is sterically hindered. This intriguing possibility could be further tested once the OH group is included in the CHARGE parametrisation.

In the aromatic compounds an interesting anomaly occurs with H-3 in 1-ethynylnaphthalene (**15**). The observed SCS (−0.137 ppm) contrasts with the calculated value (0.002 ppm). The calculated SCS at this proton is as expected the same as the SCS for the *meta* proton in phenylacetylene and this agrees exactly with the observed value for this proton. An exactly similar effect was found for the cyano group. It would appear that both the C≡C and CN SCS operate differently in naphthalene and benzene.

There is generally very good agreement between observed and calculated shifts for the acetylene protons but the model does not fully account for the value in 9-ethynylanthracene (**17**), *cf.* obs. 3.99, calc. 3.59 ppm. This may be due to enhanced π effects at this position or to H (aromatic)–H (acetylene) steric effects which would be expected to give a low-field shift. As no other molecule in the data set experiences these interactions it was not felt necessary to include them.

It is of interest to consider the actual magnitudes of the contributions to the acetylene SCS. The acetylene proton has a partial atomic charge of +0.088 electrons which corresponds to

Table 7 Observed *vs.* calculated C≡C SCS with the electric field, steric and anisotropic contributions for equatorial- and axial-ethynylcyclohexane (**10**-eq and **10**-ax) and 1,4-di-1-adamantylbutadiyne (**11**)

Compound	Proton	Obs.	Calc.	C–H Electric field	C≡C-Anisotropy	C≡C-Steric	C-Steric	H-Steric	π-Shift
10-eq	1a	1.056	0.906	−0.053	−0.590	0.0	0.016	−0.046	
	2e	0.297	0.245	−0.019	−0.074	0.027	0.0	0.0	
	2a	0.145	0.225	−0.025	−0.072	0.028	0.0	−0.023	
	3e	0.054	−0.024	0.028	−0.059	0.0	0.0	0.0	
	3a	0.011	−0.110	0.011	−0.011	0.014	0.0	−0.019	
	4e	−0.014	−0.041	0.016	−0.056	0.0	0.0	0.0	
	4a	−0.020	−0.057	0.016	−0.062	0.0	0.0	−0.01	
	C≡C–H	—	—	−0.027	−5.556	0.0	0.05	0.031	−0.169
10-ax	1e	1.231	1.029	−0.045	−0.560	0.0	0.0	0.0	
	2e	0.095	0.244	−0.019	−0.072	0.028	0.0	0.0	
	2a	0.291	0.332	−0.033	−0.174	0.0	0.0	−0.034	
	C≡C–H	—	—	−0.064	−5.550	0.0	0.098	0.052	−0.170
11	γ	0.111	0.137	−0.024	−0.071	0.028	0.0	0.0	
	δ	0.071	−0.012	0.028	−0.059	0.0	0.0	0.0	
	e	0.069	−0.036	0.017	−0.062	0.0	0.0	0.0	
	a	0.069	−0.042	0.015	−0.056	0.0	0.0	0.0	

Table 8 Observed *vs.* calculated C≡C SCS, with the steric, anisotropy, electric field, ring current and π-shift contributions for phenylacetylene (**12**) and 1- and 2-ethynylnaphthalene (**15** and **16**)

Compound	Proton	Obs.	Calc.	C≡C-Steric	C≡C-Anisotropy	C–H Electric field	Ring current	π-Shift
12	2,6	0.151	0.207	0.029	−0.072	−0.020	−0.004	0.043
	3,5	−0.030	0.0	0.008	−0.068	0.045	0.005	0.013
	4	0.0	0.006	0.002	−0.063	0.033	−0.001	0.035
	C≡C–H	—	—	0.0	−5.582	−0.004	−0.108	
15	2	0.223	0.216	0.029	−0.080	−0.020	0.0	0.065
	3	−0.137	0.002	0.008	−0.070	0.046	0.0	0.023
	4	−0.084	0.031	0.002	−0.062	0.34	0.0	0.058
	5	−0.084	−0.011	0.0	−0.036	0.014	0.0	0.010
	6	−0.037	0.002	0.0	−0.010	0.010	0.0	0.003
	7	0.053	0.039	0.007	0.023	0.00	0.00	0.012
	8	0.506	0.515	0.326	0.210	0.084	0.0	0.0
	C≡C–H	—	—	0.0	−5.581	0.009	0.318	−0.136
16	1	0.184	0.242	0.032	−0.061	0.021	0.0	0.068
	3	0.047	0.176	0.027	−0.078	−0.020	0.0	0.024
	4	−0.056	−0.015	0.007	−0.069	0.045	0.0	0.006
	5	−0.034	−0.022	0.0	−0.038	0.012	0.0	0.004
	6	0.023	−0.009	0.0	−0.022	−0.001	0.0	0.013
	7	0.023	−0.014	0.0	−0.019	−0.001	0.0	0.006
	8	−0.034	0.007	0.005	−0.029	0.018	0.0	0.014
	C≡C–H	—	—	0.0	−5.581	−0.004	0.246	−0.123

a ≡C–H dipole moment of 0.45 D. This charge gives rise from eqn. (2) to a chemical shift of 7.47 ppm. Thus as expected the acetylene proton is more "acidic" than olefinic or aromatic protons. The difference between this value and the calculated shift (1.90 ppm) is due entirely to the C≡C anisotropic contribution (−5.65 ppm). In the other compounds other effects are present and Tables 7 and 8 give the observed *vs.* calculated C≡C SCS for the aliphatic and aromatic acetylenes respectively together with the calculated anisotropic, steric and electric field contributions.

For the alkylacetylenes (Table 7) the major contribution for the α and β protons is the C≡C anisotropy. All the other contributions (C–H electric field, C≡C steric, C-steric and H-steric) are very small for the compounds given with the exception of the acetylene protons in which there is a significant π-shift. (Note that this does not appear in acetylene itself as there is no π excess in acetylene.)

Note that in the SCS of the H-2e and H-2a protons of all the compounds in Table 7 the components do not add up to give the calculated value of the SCS. This is due to the electronic γ effects which are calculated separately and which affect protons that are three bonds or less from the C≡C group.

The large SCS for H-3a in axial-ethynylcyclohexane has been estimated from compound **7**-*trans* as 0.32 (obs.) and 0.43 ppm (calc.). The calculated SCS is made up of a C≡C steric contribution of 0.185 ppm plus an anisotropic contribution of 0.125 ppm plus some other very small contributions. For the other protons with large SCS a similar pattern is found; *e.g.* for H-7s in **8** the calculated SCS of 0.49 ppm is made up of 0.37 (steric) and −0.11 ppm (anisotropy) and for H-6n in **9** the corresponding values are 1.153, 0.57 and 0.27 ppm. The results show categorically that the largest contribution to these SCS is due to the C≡C steric term and not the C≡C anisotropy. Amazingly the C≡C steric term has not been considered in any previous investigation.

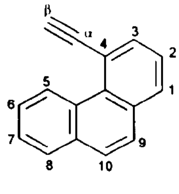
The aromatic acetylenes have other mechanisms which may affect the proton chemical shifts, in particular, the ring current and π electron effects and Table 8 gives the observed *vs.* calculated SCS for selected molecules with the electric field, ring current and π-shift contributions.

We have assumed in this investigation that the introduction of the acetylene group has no effect on the parent hydrocarbon ring current and thus there are no ring current effects on the C≡C SCS. The agreement obtained here is strong support for this assumption. In contrast the C≡C group does affect the π electron densities and this has a significant effect on the SCS.

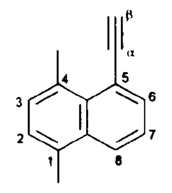
The data of Table 8 show the similarities between the aromatic and aliphatic acetylenes. In particular the large peri-planar interaction between the 1-acetylene and H-8 in **15** giving a calculated SCS of 0.49 ppm is predominantly due to the steric contribution (0.415 ppm) with only a small anisotropic term (0.10 ppm). The remaining SCS for the ring protons are quite small with the π-shifts and electric field effects roughly comparable. The ring current contribution to the SCS of the aromatic protons is as stated above zero but Table 8 includes the actual ring current shift at the acetylene protons and the π-shifts which are both significant.

As stated previously, various values of the C≡C diamagnetic anisotropy have been given ranging from -7.7×10^{-6} to -36×10^{-6} cm^3 mol^{-1}. The value found here of -11.1×10^{-6} cm^3 mol^{-1} is a middle value which is in reasonable agreement with both Pople's original estimate of −19.4 and the value of −7.7 of Shoemaker and Flygare.

It is of some interest to see whether the large low-field shifts observed by Mallory and Baker in the proton NMR of 4-ethynylphenanthrene (**19**), 5-ethynyl-1,4-dimethylnaphthalene (**20**) and 5-ethynyl-1,4-diethylnaphthalene (**21**) are predicted by our model.



19



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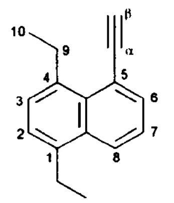

21

They observed large low-field shifts for H-5 in **19** (1.63 ppm from H-5 in phenanthrene), the 4-methyl protons in **20** (0.49 ppm) and the methylene protons of the C-4 ethyl group of **21** (0.55 ppm) due to the deshielding effect of the C≡C group.

The calculated (CHARGE7) proton shifts *vs.* the observed δ values (in parentheses) for H-5 in **19**, the methyl protons in **20** and for the CH_2 protons in **21** are 9.38 (10.34), 2.90 (3.01) and 3.39 (3.62).

There is excellent agreement between the observed and calculated shifts for the methyl and methylene protons in **20** and **21**, but the calculated value for H-5 in **19** is too small by almost 1 ppm. This proton is in very close proximity to the triple bond. The distance between the center of the triple bond and H-5 is calculated as 2.208 Å from GAUSSIAN98. This compares with the values of 1.55 Å from Dreiding models and 2.408 Å from PC Model.[40] The GAUSSIAN98 geometry calculated at the B3LYP/6-31G** level may not be absolutely correct and small changes in bond lengths and angles at this close distance will have a very significant influence on the calculated proton chemical shifts. It would be of interest to obtain the crystal geometry and input this into CHARGE. However the simple eqns. (3) and (5) for the shielding and anisotropy of the C≡C bond are also likely to be less accurate for the close distances observed in this case. The major contribution to the low-field shift of this proton is again the steric term (0.71 *vs.* 0.34 ppm for the anisotropy) and a simple r^{-6} term would not be expected to be very accurate at these short internuclear distances.

Mallory and Baker concluded that the C≡C shielding was proportional to r^{-3} and that the shielding was from the centre of the triple bond. In the CHARGE scheme the steric term is proportional to r^{-6} but the anisotropy is proportional to r^{-3} and both terms are calculated at each carbon atom. Placing the anisotropy in the middle of the acetylene bond and using an r^{-3} steric term both gave poorer agreement for the data set considered here.

Conclusions

The proton chemical shifts of all the protons in the data set considered of 71 data points spanning a range of *ca.* 0.70 to 9.00 ppm are predicted with an rms error of 0.074 ppm. We may conclude that the C≡C SCS over more than three bonds is determined largely by the C≡C bond anisotropy and steric effect for both aliphatic and aromatic compounds. In all the compounds considered here the large SCS effects are due mainly to the steric term. The anisotropy is a significant, but smaller contribution. The protons <3 bonds from the triple bond require in addition the inclusion of electronic β and γ effects from the acetylene carbons in both aliphatic and aromatic acetylenes. The γ effect of the acetylene carbon atom has an orientational dependence.

References

1 Part 15. R. J. Abraham and M. Reid, *Magn. Reson. Chem.*, 2000, **38**, 570.
2 A. A. Bothner-By and J. A. Pople, *Annu. Rev. Phys. Chem.*, 1965, **16**, 43.
3 G. S. Reddy and J. H. Goldstein, *J. Chem. Phys.*, 1963, **39**, 12; G. S. Reddy and J. H. Goldstein, *J. Chem. Phys.*, 1963, **39**, 3509.
4 W. Zeil and H. Buchert, *Z. Phys. Chem.*, 1963, **38**, 47.
5 R. L. Shoemaker and W. H. Flygare, *J. Am. Chem. Soc.*, 1969, **91**, 5417.
6 F. B. Mallory and M. B. Baker, *J. Org. Chem.*, 1984, **49**, 1323.
7 (*a*) R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 31; (*b*) R. J. Abraham, L. Griffiths and M. A. Warne, *Magn. Reson. Chem.*, 1998, S179, 36.
8 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1997, 881.
9 R. J. Abraham, L. Griffiths and M. A. Warne, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1751.
10 R. J. Abraham and N. Ainger, *J. Chem. Soc., Perkin Trans. 2*, 1999, 441.
11 M. Canton, M. Reid and L. Griffiths, *J. Chem. Soc., Perkin Trans. 2*, 2000, 803.
12 R. J. Abraham, *Prog. Nucl. Magn. Reson. Spectrosc.*, 1999, **35**, 85.
13 H. M. McConnell, *J. Chem. Phys.*, 1957, **27**, 226.
14 R. J. Abraham and P. E. Smith, *J. Comput. Chem.*, 1987, **9**, 288.
15 R. J. Abraham and P. E. Smith, *J. Comput. Aided Mol. Des.*, 1989, **3**, 175.
16 A. L. McClellan, *Tables of Experimental Dipole Moments*, vols. 1–3, Rahara Enterprises, El Cerrito, CA, USA, 1989.
17 M. Canton, PhD Thesis.
18 University of Liverpool Chemistry Workshop, Chemistry Department, The University of Liverpool, PO Box 147, Liverpool L69 3BX.
19 Chemsampco, Inc., 40 Enterprise Avenue, Trenton, NJ 08638, USA.
20 Sigma-Aldrich Library of Rare Chemicals.
21 Aldrich Chemical Company, The Old Brickyard Road, New Road, Gillingham, UK.
22 J. C. Hanekamp and P. A. A. Klusener, *Synth. Commun.*, 1989, **19**, 2677.
23 An offprint from: *Transition Metals in Organic Synthesis—A Practical Approach*, ed. S. E. Gibson, 1997, Dept. of Chemistry, Imperial College of Science, Technology and Medicine, London, UK.
24 D. G. Garratt, P. L. Beaulieu and V. M. Morisset, *Can. J. Chem.*, 1981, **59**, 927.
25 CCDC reference numbers 163145 and 163146. See http://www.rsc.org/suppdata/p2/b0/b009321l/ for crystallographic files in .cif or other electronic format.
26 Bruker UXNMR version 010892, Bruker AM, Silbersteifen, D-7512 Germany.
27 Varian Associates, Palo Alta, CA, USA.
28 (*a*) M. J. Frisch, G. W. Trucks, M. Head-Gordon, P. M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzalez, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart and J. A. Pople, GAUSSIAN94, Gaussian Inc., Pittsburgh, PA, 1994; (*b*) M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, GAUSSIAN98, Revision A9, Gaussian Inc., Pittsburgh, PA, 1998; (*c*) J. B. Foresman and A. Frisch, Exploring Chemistry with Electronic Structure Methods, 2nd edn., Gaussian Inc., 1997.

29 C. J. Puchert and J. Behnke, *Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, Aldrich Chemical Company Inc., Milwaukee, USA, 1993.

30 E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley, New York, 1994.

31 M. Manoharan and E. L. Eliel, *Magn. Reson. Chem.*, 1985, **23**, 4; M. Manoharan and E. L. Eliel, *Magn. Reson. Chem.*, 1985, **23**, 225.

32 E. Djuardi, P. Bovonsombat and E. McNelis, *Tetrahedron*, 1994, **50**, 41; E. Djuardi, P. Bovonsombat and E. McNelis, *Tetrahedron*, 1994, **50**, 11793.

33 C. F. Wilcox and K. A. Weber, *Tetrahedron*, 1985, **41**, 4425.

34 M. Reid, PhD in progress.

35 P. D. Pretsch, T. Clerc, J. Seibl and W. Simon, *Spectral Data for Structure Determination of Organic Compounds*, 2nd edn., Springer-Verlag, NY, 1989.

36 L. Luan, J. S. Song and R. M. Bullock, *J. Org. Chem.*, 1995, **22**, 60; L. Luan, J. S. Song and R. M. Bullock, *J. Org. Chem.*, 1995, **22**, 7170.

37 Part 4. R. J. Abraham, A. P. Barlow and A. E. Rowan, *Magn. Reson. Chem.*, 1989, **27**, 1074.

38 W. J. Lafferty and R. J. Thibault, *J. Mol. Spectrosc.*, 1964, **14**, 79.

39 S. S. Kuo, *Computer Applications of Numerical Methods*, ch. 8, Addison-Wesley, London, 1972.

40 PC Model Version 7.0, Serena Software, Box 3076, Bloomington, IN, USA.