Transition Metal Mediated Cleavage of C-C Bonds in Aromatic Rings

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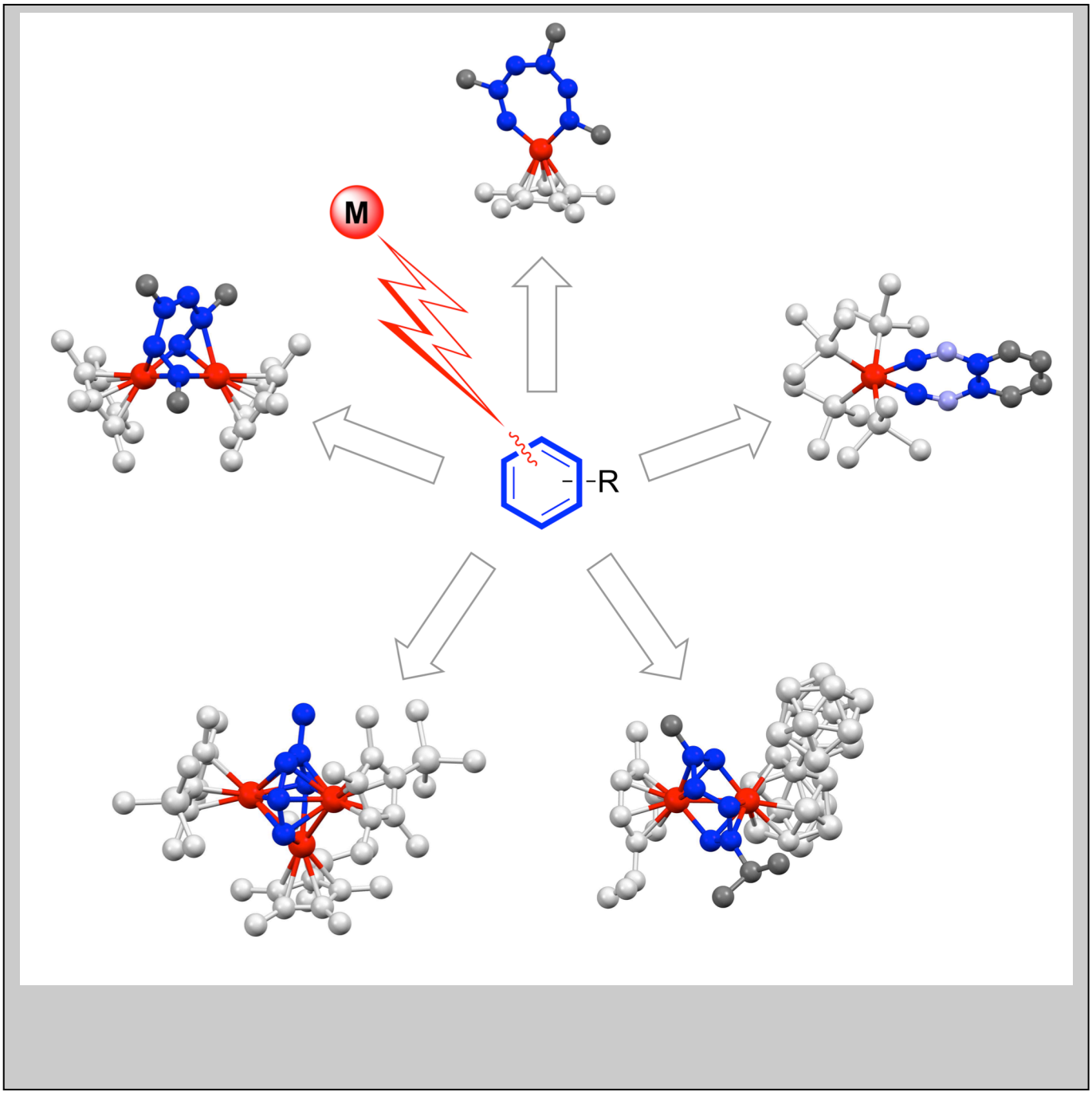

Abstract: Metal-mediated cleavage of aromatic C-C bonds has a range of potential synthetic applications: from direct coal liquefaction to synthesis of natural products. However, in contrast to the activation of aromatic C-H bonds, which has already been widely studied and exploited in diverse set of functionalization reactions, cleavage of aromatic C-C bonds is still *Terra Incognita*. This focus review summarizes the recent progress in this field and outlines key challenges to be overcome to develop synthetic methods based on this fundamental organometallic transformation.

1. Introduction

1.1. Background and scope of this review

Many organic reactions involve formation of new C-C bonds to make a range of aromatic and heteroaromatic molecules found in many pharmaceuticals, natural compounds, materials and precursors for the synthesis of more complex molecules.[1] While the current organic synthesis demonstrates the numerous possibilities of forming large and complex structures through making aromatic C-C bonds, cleaving these bonds has been out of limelight. In the same time, the ability to control cleavage of aromatic C-C bonds is valuable for a number of reasons. First, generation of value-added chemicals from fossil fuel often requires cleavage of large aromatic molecules into smaller, synthetically useful units through C-C scission. For example, direct liquefaction of coal, or conversion of coal into smaller hydrocarbons, involves catalytic cleavage of aromatic C-C bonds.[2] Our chemical industry currently relies on gas and petroleum as major sources of organic chemicals, but with depleting of these natural resources more attention is paid to coal as a potential feedstock for production of chemicals. In this context development of mild coal liquefaction is an attractive goal. Second, mild scission of aromatic rings is critical for cleaner valorization of lignocellulosic biomass.[3] In terms of lab scale synthesis, activation of arene ring C-C bonds underpins the design of novel arene functionalizations via ring expansion and ring opening reactions valuable for the synthesis of natural products and pharmaceuticals.[4] From the other hand, cleavage of arene rings also plays a deleterious role being involved in decomposition pathways of homogeneous catalysts.[5]

In this focus review we will discuss the scope and applications of metal mediated cleavage of aromatic ring C-C bonds by looking at transformations of the most common aromatic entities found in organometallic systems and catalysis, namely, arene and cyclopentadienyl ligands. Among these reactions, we will focus on non-oxidative metal induced scissions of arene ring C-C bonds. Oxidative scissions of aromatic C-C bonds, which are of particular importance in variety of biochemical processes, are reviewed elsewhere.[6] This review will compliment a number of excellent reviews on metal-mediated cleavage of single C-C bonds.[7]

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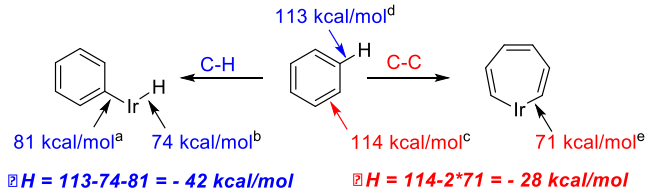
1.2. Challenges in metal mediated cleavage of aromatic C-C bonds

In contrast to activation of aromatic C-H bonds, which is now widely used in organic synthesis, activation of aromatic C-C bonds is still a challenging and largely unexplored area.[1, 8] Activation of strong aromatic C-C bonds requires harsh reaction conditions, and occurs with poor chemoselectivity (C-H bonds are activated preferentially) and regioselectivity (different kinds of aromatic C-C bonds can be activated indiscriminately), which limits synthetic applications of this promising transformation. The poor reactivity and selectivity result from thermodynamic and kinetic limitations for aromatic C-C activation, which are of similar kind to those for activation of aliphatic C-C bonds, but the situation is exacerbated by a higher bond dissociation energy of aromatic C-C bonds (114 kcal/mol in benzene[9] vs 90 kcal/mol in ethane[10]).

Thermodynamic limitations indicate that arene C-C cleavage is less favorable as compared to arene C-H cleavage (Scheme 1). Estimated bond dissociation energy (BDE) of benzene ring C-C bond is relatively high (114 kcal/mol)[9], but comparable to BDE of benzene ring C-H bond (113 kcal/mol)[11]. Metal insertion into the aromatic C-C bonds is thermodynamically favorable, but less exothermic than the insertion into aromatic C-H bonds as illustrated for the insertion of a Cp*Ir(PMe_3) fragment into the C-H and C-C bonds of benzene (Scheme 1). More favorable thermodynamics for insertion into aromatic C-H bonds is explained by formation of stronger [Ir]-H (74 kcal/mol)[12] and [Ir]-Ph (81 kcal/mol)[12] bonds as compared to two [Ir]-vinyl bonds (2x71 kcal/mol)[13]. However, care must be taken for making generalizations on thermodynamics of metal insertion based on BDE as the latter heavily depends on the metal center, its oxidation state and ancillary ligands.



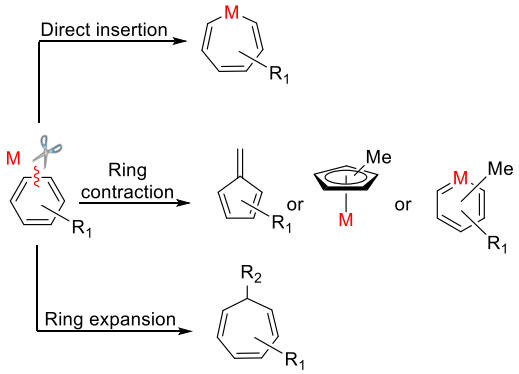
[a] Cp*Ir(**Ph**)(H)(PMe_3), Ref 12; [b] Cp*Ir(**H**)(H)(PMe_3), Ref 12; [c] Ref 9; [d] Ref 11; [e] Cp*Ir(**$CH=CH_2$**)($CH=CH_2$)(PMe_3), Ref 13.

Scheme 1. Literature bond dissociation energies pertinent to oxidative addition of C-H and C-C bonds to an iridium (I) complex.

Kinetic limitations. Similar to metal insertion into aliphatic C-C bonds, metal insertion into aromatic C-C bonds is hampered by lower steric accessibility of aromatic C-C bonds and more directional character of these bonds as compared to C-H bonds.[7b, 14] The latter bonds are also generally more abundant in alkyl benzenes and hence their activation is statistically more likely.[7b, 14-15]

2. Metal mediated C-C scission in arenes and heteroarenes

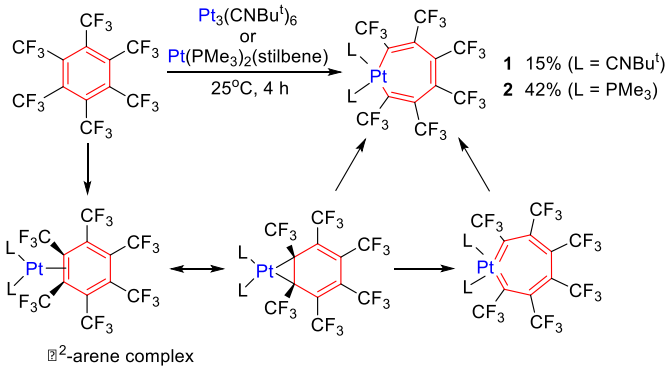
Like the cleavage of aliphatic C-C bonds, cleavage of aromatic C-C bonds can be facilitated using the following general strategies: creation of a ring strain and the use of directing groups. In this context, all examples involving C-C scissions in arenes can be divided into three major classes: direct metal insertion into the ring, metal-induced ring contraction and ring expansion (Scheme 2). These classes of reactivity will be discussed below.



Scheme 2. General types of metal mediated cleavage of arene ring C-C bonds.

2.1 Direct metal insertion into arene ring

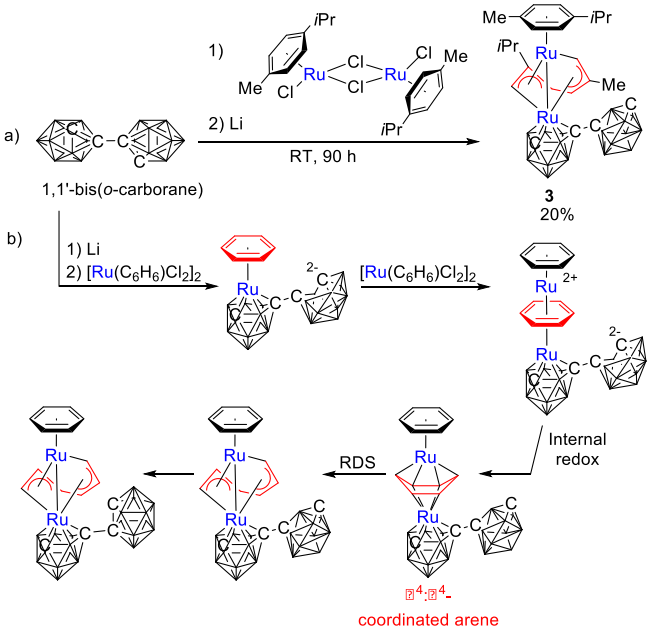
First example of a direct metal insertion into aromatic ring was reported by Stone *et al.* in 1975.[16] The reaction of isonitrile platinum complex *triangulo*-[$Pt_3(CNBu^t)_6$] with hexakis(trifluoromethyl)benzene at room temperature led to an unexpected metallacycle **1** in 15% yield (Scheme 3). When a phosphine complex $Pt(PMe_3)_2$(stilbene) was used instead the insertion occurred with a higher yield of 42%.



Scheme 3. First example of a metal insertion into an arene ring.

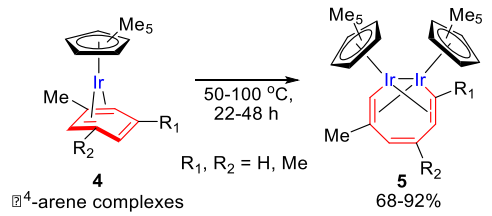
However, replacement of PMe_3 for PEt_3 in the starting complex led to an η^2-arene complex $Pt(\eta^2\text{-}C_6(CF_3)_6)(PEt_3)_2$, which did not undergo C-C cleavage even upon heating at 140 °C for 14 h. The XRD structure of $Pt(\eta^2\text{-}C_6(CF_3)_6)(PEt_3)_2$ indicated that the complex can be better described as a substituted metallacyclopropane due to a combination of strong π-donating properties of the platinum center and π-accepting properties of the electron poor arene.[17] On the basis of these observations, the authors suggested that the insertion reaction occurs via initial formation of an η^2-arene complex, which then undergoes ring expansion to relieve the ring strain and give the corresponding metallacycle **1** or **2**. The ring expansion here can proceed via a direct insertion of Pt into a weakened single C-C bond in a strained metallacylopropane or via electrocyclic ring opening as in norcaradiene cycloheptatriene-isomerization[18], given isolobal analogy of PtL_2 and carbene fragment.[19] Thus, the success of this arene ring C-C bond scission is the result of a combination of a metal induced ring strain that promoted C-C scission and the use of H-free arene that helped to avoid competing C-H activation.

First example of a metal insertion into the aromatic ring of an alkylarene was reported by Welch, MacGregor *et al* (Scheme 4).[20] [$(Ru(p\text{-cymene})Cl_2)_2$] was treated with a mixture of 1,1'-bis(*o*-carborane) and excess of lithium at room temperature to give complex **3** in 20% yield. Complex **3** resulted from insertion of two ruthenium atoms into the least substituted arene ring C-C bond of *p*-cymene (Scheme 4a). The two ruthenium atoms are linked by a single metal-metal bond and a S-shaped η^3: η^3-hydrocarbon chain resulted from the cleavage of the aromatic ring. To propose a potential mechanism, the authors conducted DFT calculations for a simpler cleavage of more symmetrical arene (Scheme 4b). The calculations suggested that the rate determining step is the C-C bond cleavage in the distorted η^4:η^4-coordinated arene clutched between two Ru atoms.



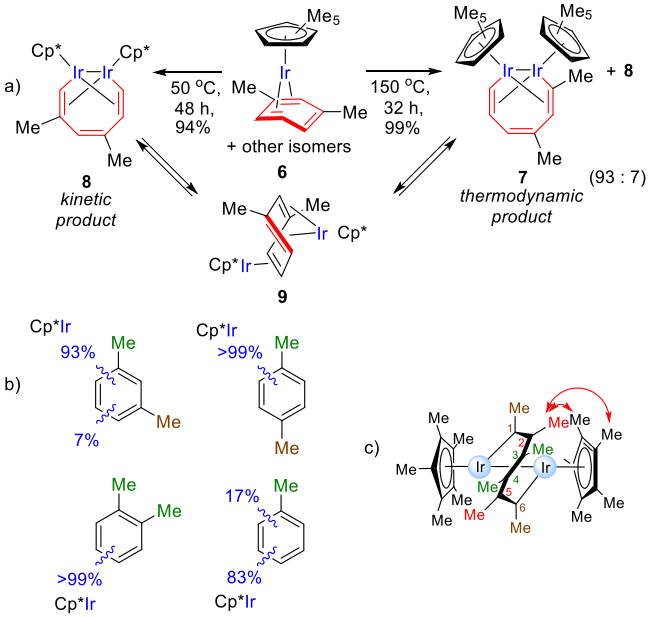
Scheme 4. Cleavage of coordinated cymene by ruthenium bearing biscarborane ligands: a) reaction scheme; b) DFT mechanism for cleavage of benzene.

A different approach for activation of aromatic C-C bonds was proposed by our group.[21] To facilitate metal insertion into aromatic ring C-C bonds, we used simple Cp*Ir-containing complexes **4** with η^4-coordinated arene rings (Scheme 5). In these complexes the aromatic ring is bonded to the metal center through four carbon atoms and the remaining two carbon atoms make up an uncoordinated C-C double bond. This coordination mode leads to distortion of the aromatic ring thus making the coordinated arene undergo reactions typical for strained cycloalkenes. This approach was inspired by work of the Gladysz group who demonstrated that η^4-coordinated benzene in a CpIr complex undergoes ring opening polymerization in the presence of Grubbs II catalyst.[4b] We found that [Cp*Ir(η^4-arene)] complexes of mesitylene, *m*-xylene and toluene (**4**) undergo clean insertion of two iridium fragments into the aromatic ring C-C bonds to form eight membered metallacycles **5** with excellent yields (Scheme 5). The reaction occurred without observable formation of products of C-H activation and required relatively mild conditions (50-100 °C). The likely reason for the observed unusual arene cleavage is the ring strain that enhanced the reactivity of the ring C-C bonds with respect to the corresponding C-H bonds. Intriguingly, the relative reactivity of coordinated methyl arenes increased with increase in the number of Me substituents, while the least substituted benzene complex did not undergo the C-C cleavage.



Scheme 5. Cleavage of coordinated alkyl benzene in η^4-arene complexes.

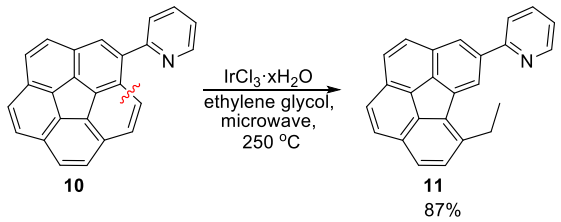
The scope of the methyl arenes undergoing this C-C cleavage was further expanded to all xylenes (Scheme 6).[22] While regioselectivity of the insertion into xylenes and toluene was modest to good at 50-100 °C, it increased with temperature, exceeding 93% selectivity for most substrates at 150 °C (Scheme 6a). Moreover, the regioselectivity of Ir insertion into *m*-xylene in complex **6** was completely switched by changing the reaction temperature from 50 to 150 °C to give predominantly regioisomer **7** over **8** (Scheme 6b). The observed regioselectivity at higher temperatures is counterintuitive and cannot be predicted on the basis of steric accessibility of the ring C-C bonds. Kinetic and DFT studies revealed that the observed regioselectivity results from a reversible insertion of iridium into the aromatic ring C-C bonds. At elevated temperatures initially formed diiridium metallacycles undergo equilibration via formation and cleavage of the aromatic ring through a triple-decker intermediate **9**. The observed regioselectivity is controlled by the different stability of the regioisomeric metallacycles products due to steric repulsion of Me groups on the cleaved arene backbone and Cp* ligands (Scheme 6c). A simple empirical rule was proposed to predict stability and hence the regioselectivity of the C-C cleavage.



Scheme 6. Reversible insertion of iridium into the arene ring of toluene and xylenes. a) Reversible cleavage of arene C-C bonds in the coordinated *m*-xylene. b) Selectivity of the arene ring cleavage under thermodynamic conditions. c) General structure of the metallacycle product with key repulsive interactions.

The detailed investigation of the mechanism of initial C-C cleavage in η^4-complexes is needed to elucidate the unusual order of reactivity of methyl arenes and the role of methyl substituents in the process. Attempts towards this direction were made by, Li *et al.* who conducted DFT calculations of related arene ring C-C cleavage on Cp*Ir-derived clusters and proposed that the higher reactivity of more substituted arenes could be attributed to steric effects.[23]

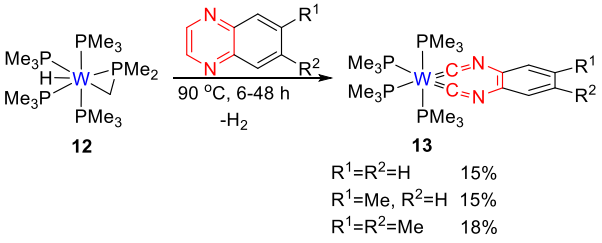
In the above examples, scission of aromatic C-C bonds was facilitated by metal-induced ring strain in starting or intermediate arene complexes. An alternative strategy for cleavage of aromatic C-C bonds involves the use of inherently strained polycyclic aromatic hydrocarbons. Shionoya *et al.* reported $IrCl_3$ catalyzed site-selective reductive cleavage of a strained aromatic C-C bond in a bowl-shaped corannulene **10** to give flat benzo[*ghi*]fluoranthene **11** (Scheme 7).[24] The reaction required the presence of a 2-pyridyl directing group, as no C-C scission occurs in the unsubstituted corannulene. Remarkably, iridium (III) chloride showed the highest activity as compared to salts of other metals including Rh, Fe, Co, Ni, Cu, Ru, Pd, Ag, Pt, Au. The proposed mechanism includes directed insertion of iridium into the aromatic C-C bond of **10** to relieve ring strain in the curved corannulene core followed by hydrogenolysis of the resulting metallacycle and hydrogenation of the vinyl group with ethylene glycol as a hydrogen source to give **11**.



Scheme 7. Iridium-catalyzed directed reductive cleavage of a C-C bond in a substituted corannulene.

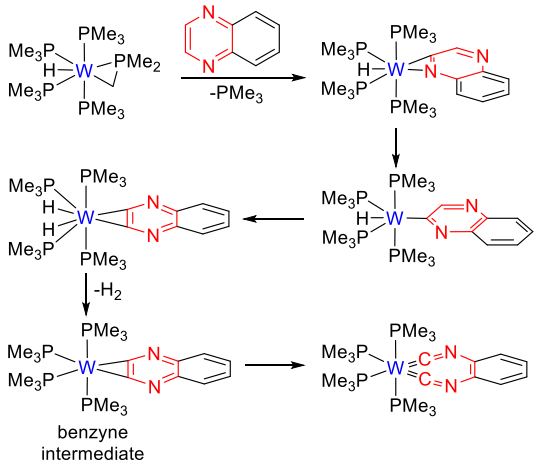
2.1. Metal insertion into arene ring with prior chemical modification

Scission of non-strained aromatic C-C bonds is often preceded by activation of more accessible aromatic C-H bonds. An example of this reactivity was shown by Parkin and Sattler who reported directed metal insertion of tungsten into the aromatic ring of quinoxaline (Scheme 8).[25] The reaction of trimethylphosphine tungsten complex **12** with quinoxalines gave diisonitrile complexes **13** in 15-18% yields.



Scheme 8. Directed insertion of tungsten into the aromatic ring of quinoxaline.

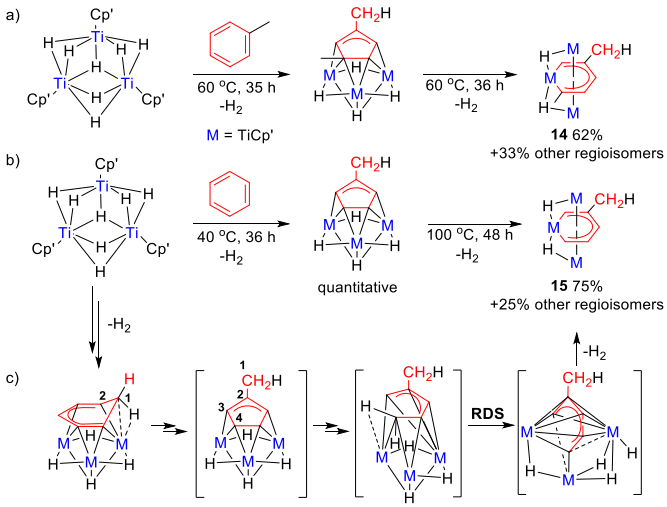
The insertion was proposed to occur via a directed double C-H activation and reductive elimination to form a benzyne intermediate that undergoes metal insertion (Scheme 9).



Scheme 9. Mechanism for dehydrogenative insertion of tungsten into quinoxaline.

General details of the proposed mechanism were confirmed by DFT calculations of Miscioni and Bottoni *et al.*[26] The calculations suggest that the likely driving force for C-C scission is the formation of a strained benzyne complex that undergoes metal insertion to relieve the ring strain. This C-C insertion is the rate determining step with the overall barrier of 32.6 kcal/mol. However, such activation energy is quite high for the observed reaction conditions (90 °C, 24 h). A variation of this mechanism was reported by Yoshizawa *et al.*[27] with much lower barrier of 17.2 kcal/mol corresponding to reductive elimination of dihydrogen. In a competing paper, Zhang *et al.* proposed an alternative mechanism that involves a C-H activation, rate-determining insertion into the ring C-C bond, second C-H activation and elimination of dihydrogen. The overall energy barrier (28.5 kcal/mol), however, was higher than that reported by Yoshizawa *et al.*[28] This reported C-C scission is particularly intriguing in the view of earlier results on metal-mediated cleavage of pyridine ring that occurred via breaking the ring C-N bond.[29]

Arene cleavage also occurs on some heterogeneous metal catalysts and may involve dehydrogenation prior to the C-C scission step.[30] As shown by Somoraj *et al.*, benzene cleavage on metal surface could occur under relatively mild conditions via synergetic effect of several metal centers, although the resulting products are not well defined species.[31] An appealing idea is to probe this effect through the use of well-defined metal clusters as a platform for C-C scission of arenes. This idea was successfully realized by Hou *et al.* who employed a highly reactive trinuclear titanium hydride cluster for cleavage of toluene and benzene under relatively mild conditions (Scheme 10).[32] The cleavage leads to formation of titanabenzene products **14** and **15**, respectively. Notably, the reaction with toluene (60 °C, 36 h) occurred under milder conditions with respect to benzene (100 °C, 48 h). The process occurs via cyclopentadienyl intermediates: methylcyclopentadienyl in case of benzene and 1,3-dimethylcyclopentadienyl in case of toluene.



Scheme 10. Cleavage of benzene and toluene on trinuclear titanium cluster: a-b) Experimental results; c) Proposed mechanism (M=TiCp').

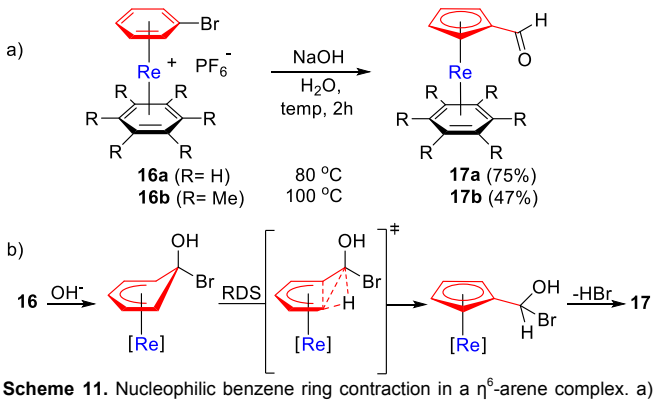
Intriguingly, the regioselectivity of metal insertion into the substituted Cp rings does not correlate with steric accessibility of the C-C bonds (Scheme 10a-b).

The same group reported DFT studies of the process, [33] which suggest that the mechanism involves coordination of arene with reductive elimination of H_2, hydrometallation, ring contraction to form the methylcyclopentadienyl ligands, and insertion of Ti into the C-C ring bond of MeCp. Overall, the mechanism of this complex process involves two C-C insertions, and four C-H activations. The rate-determining step was found to be C-H activation leading to the penultimate intermediate with the barrier of 30.7 kcal/mol. In the same time, Guan and Su described a similar mechanism highlighting the importance of cooperative effect of several metal centers for success of the process.[34] The origin of the observed intriguing regioselectivity, however, remains to be addressed.

2.3 Scission of arene ring without metal insertion into aromatic ring

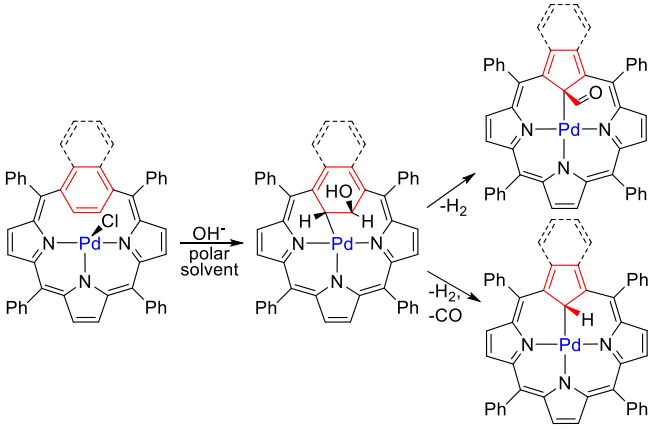
2.3.1. Contraction of arene ring

An excellent example of contraction of an arene ring to a cyclopentadienyl moiety was observed by Hou *et al.* in titanium-mediated scission of benzene and toluene and discussed above (Scheme 10).[32] Alberto *et al.* reported a simpler ring contraction reaction that occurred in a classical cationic arene complex **16** (Scheme 11a). When **16** was treated with aqueous NaOH, the coordinated bromobenzene underwent ring contraction to give a formyl cyclopentadienyl ligand in **17**.[35] The authors suggested a mechanism that involves attack of OH- on the *ipso* carbon atom of the bromobenzene, followed by rate-determining rearrangement and the loss of HBr (Scheme 11a). The overall barrier (35.7 kcal/mol) computed for the conversion of **16a** to **17a** is, however, too high for a reaction occurring at 80 °C for 2 h. Notably, the corresponding reaction conducted with the corresponding Tc complexes does not lead to the ring contraction product, but gives a phenol complex. The latter reactivity is common for transition metal π-complexes of haloarenes.[36]



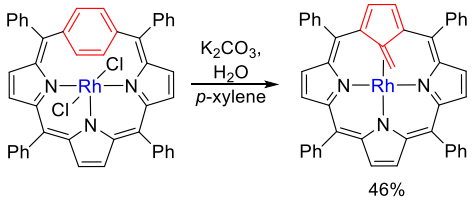
Scheme 11. Nucleophilic benzene ring contraction in a η^6-arene complex. a) Experimental results; b) Proposed mechanism for ring contraction in **16a**. [Re]=Re(η^6-C_6R_6)

Related nucleophile-induced benzene ring contraction in palladium complexes of porphyrins was reported by Latos-Grazynski (Scheme 12).[37] Analogous Au(III) complexes of *p*- and *m*-benziporphyrins underwent benzene ring contraction with the loss of one carbon atom (possibly via expulsion of CO).[38]



Scheme 12. Nucleophilic benzene ring contraction in Pd porphyrin complexes.

A different kind of ring contraction was observed in rhodium (III) *p*-benziporphyrin complexes that were allowed to react under basic conditions.[39] The reaction led to isomerization of the benzene ring into a coordinated fulvene. The mechanism of this ring remarkable contraction is currently not clear.



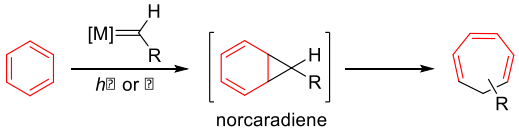
Scheme 13. Benzene to fulvene ring contraction in Rh benziporphyrin.

Similar fulvene derivatives are also obtained from rhodium(III) *m*-benziporphyrin complexes, which undergo ring contraction upon contact with basic alumina in the presence of CH_2Cl_2 solvent.[40] Although the detailed mechanism has yet to be elucidated, the authors suggested that the ring contraction occurs via a strained bicyclic cyclopropanol intermediate that can undergo carbene expulsion or ring opening isomerization to give a five membered ring.

Additionally, the same group has recently shown that this type of arene ring transformations can be extended to a ring contraction of azulene in a hexaphyrin.[41]

2.3.2. Expansion of arene ring

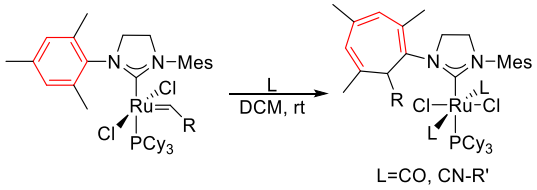
A number of arene ring expansion reactions occur in the presence of a transition metal catalyst and carbine precursors (Scheme 14). Particularly useful among these is the Buchner reaction, which was reviewed elsewhere and therefore will be discussed only briefly.[42]



Scheme 14. Arene ring expansion via metal mediated carbene and nitrene insertion into the aromatic ring.

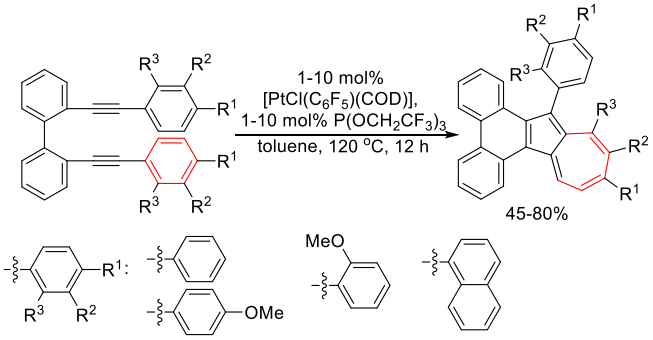
Buchner reaction involves cyclopropanation of arene ring by a carbene species to give a bicyclic norcaradiene, which undergoes ring expansion via electrocyclic isomerization. The reaction typically occurs with an arene and a diazoester and facilitated in the presence Cu or Rh catalysts.[42b] The role of the metal is to generate active carbenoid species and enable cyclopropanation of the aromatic ring. The subsequent electrocyclic ring expansion occurs without participation of a metal. Buchner reaction typically requires electron-rich or electron-neutral arenes and electron poor diazocompounds, and is often complicated by competitive carbene insertion into C-H bonds. The regioselectivity of the ring expansion is relatively poor and mixtures of regioisomers are often formed. However, selectivity of an intramolecular Buchner reaction can be sufficiently high for to be applied for the synthesis of pharmaceuticals and natural products.[42-43]

Buchner-type ring expansion was also observed in Grubbs catalysts[44] and was identified as one of potential catalyst decomposition pathways in alkene metathesis (Scheme 15).[5]



Scheme 15. Arene ring expansion in Grubbs catalysts.

Alternatively, benzene ring expansion can be triggered by electron-poor metal complexes. Matsuda and Murakami *et al.* have shown that heating of dialkynyl biaryls with a Pt(II) complex ligated with a phosphite ligand yields substituted azulenes (Scheme 16). $PtCl_2$ and a cationic Au(I) catalyst demonstrated comparable performance.[45] Although the mechanism is unknown, the ring expansion is likely to occur via electrophilic rearrangement with a transition metal catalyst acting as a Lewis acid. Indeed, it was shown that $AlCl_3$ mediates related benzene ring expansion in diphenylacetylene.[46]

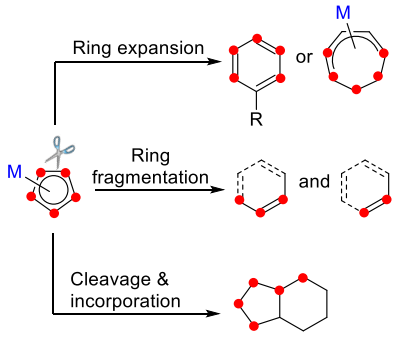


Scheme 16. Benzene ring expansion in dialkynyl biaryls.

3. Metal mediated C-C scission in cyclopentadiene ligands

While cleavage of aromatic C-C bonds is rare, more common is the scission of ring C-C bonds in aromatic cyclopentadienyl ligands, which are one of the most versatile and widely used ligands in transition metal catalysis. For example, the cyclopentadienyl (Cp) ligand and its substituted analogues are usually considered as innocent spectator ligands.[47] However, in the last three decades there have been some reported cases where the stability of the C5-core has been put into question and furthermore, it has been shown that the aromatic C-C bond in Cp-systems can be remarkably reactive towards cleavage (Scheme 17).

In particular, cyclopentadienyl ligands undergo ring expansion reactions via formal insertion of one or two atom fragments, ring scission to form 3 and 2 carbon fragments or consecutive linear chains embedded in bicyclic ring structures. All these reaction types are reviewed in the following sections.

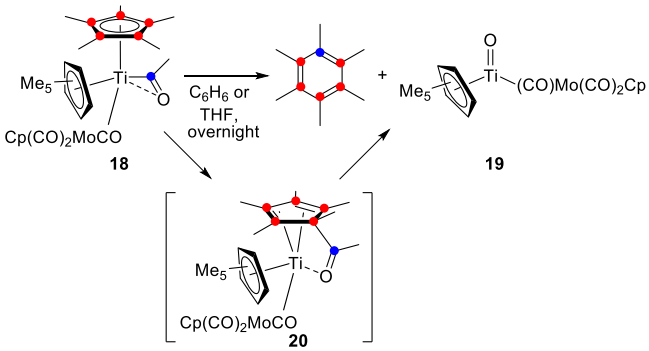


Scheme 17. General types of metal mediated cleavage of aromatic C-C bonds in cyclopentadienyl ligands.

3.1. Cp ring expansion to form six and seven membered rings

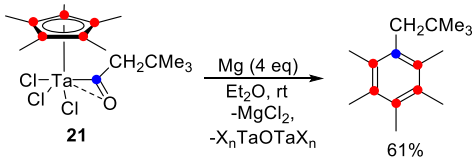
De Boer and de With reported the first example of ring expansion in a cyclopentadienyl ligand through formal insertion

of a methylcarbyne fragment into a Cp* in a Ti-Mo acyl complex **18** (Scheme 18).[48] A two-step mechanism was suggested to account for the peculiar formation of C_6Me_6 and complex **19**. In the first step acylation of one of the Cp* ligands takes place, presumably via $\eta^5 \rightarrow \eta^3$ hapticity change of the Cp* ligand followed by a reductive elimination. The resulting complex **20** undergoes an acyl C-O bond scission by the oxophilic titanium centre[49] and the resulting carbene species undergo ring expansion yielding hexamethylbenzene.



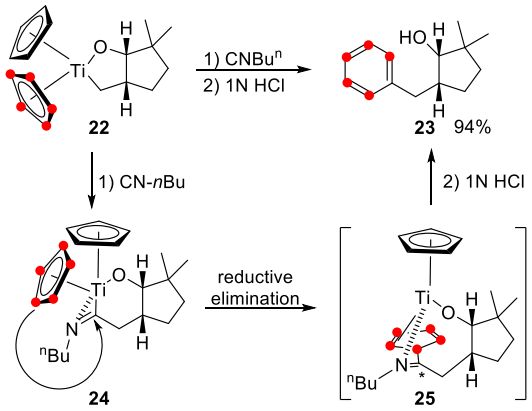
Scheme 18. Ring expansion of Cp* to hexamethylbenzene in a titanium acyl complex.

Related Cp* ring expansion takes place upon reduction of tantalum acyl complex **21** with magnesium (Scheme 19).[50] Although exact mechanism is unknown, the reaction may occur via generation and insertion of carbenoid species in a similar manner to the above example.



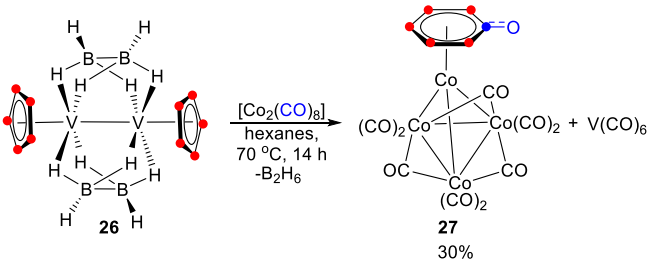
Scheme 19. Ring expansion of Cp* in a tantalum acyl complex.

Analogous iminoacyl complexes also undergo C-C scission of Cp ligands as shown by Crowe and Vu (Scheme 20).[51] Thus, treatment of titanacene **22** with isonitrile $CNBu^n$ followed by acidification yields a monosubsituted arene **23**, with aromatic ring made up from five carbon atoms of the cleaved Cp-ring and one carbon atom of the isonitrile. The proposed mechanism involves insertion of isonitrile in **22** to give an observed iminoacyl complex **24**, which reductive eliminates the product of Cp iminoacylation **25**. The latter undergoes facile ring expansion and after protonation releases the final product. The authors suggest that the isomerization may occur through a carbocationic intermediate generated upon protonation of the imine nitrogen.



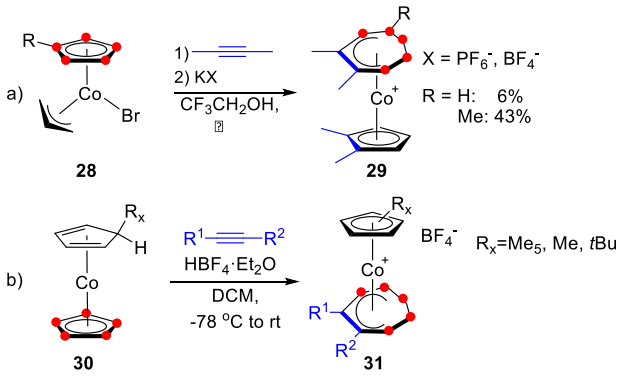
Scheme 20. Ring expansion of a titanocene complex.

A rare example of carbon monoxide insertion into an cyclopentadienyl ligand was described by Ghosh *et al*. Heating of divanadium complex **26** with dicobalt octacarbonyl gave pentanuclear complex cluster **27** with η^6-C_6H_5O ligand (Scheme 21).[52]



Scheme 21. Cobalt-mediated CO insertion into a Cp ligand.

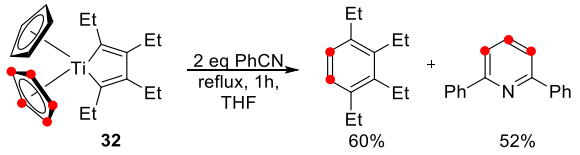
Cyclopentadienyl ligands may also undergo insertion of alkynes into the aromatic ring as demonstrated by Stryker *et al* (Scheme 22).[53] Treatment of Co(III) cyclopentadienyl allyl complex **28** with dimethylacetylene yields the ring expansion product **29** with 6% yield, whereas introduction of a methyl substituent in the Cp ring boosts the yield to 43% (Scheme 22a).[53a] Permethyllated Cp ring is, however, inert towards the insertion.[53a] Later, the same group reported a new ring expansion reaction inspired by their previous results (Scheme 22b).[53b] In the presence of excess of alkyne and $HBF_4 \cdot Et_2O$ complex CpCo(η^4-CpR) **30** undergoes alkyne insertion into the Cp ring to form cycloheptadienyl complexes **31** in 66-94% yield. It should be noted that the reaction proceeds with remarkable regioselectivity as only the less substituted η^5-cyclopentadienyl ligands are being activated towards the alkyne insertion.



Scheme 22. Cobalt-mediated alkyne insertion into a Cp ligand.

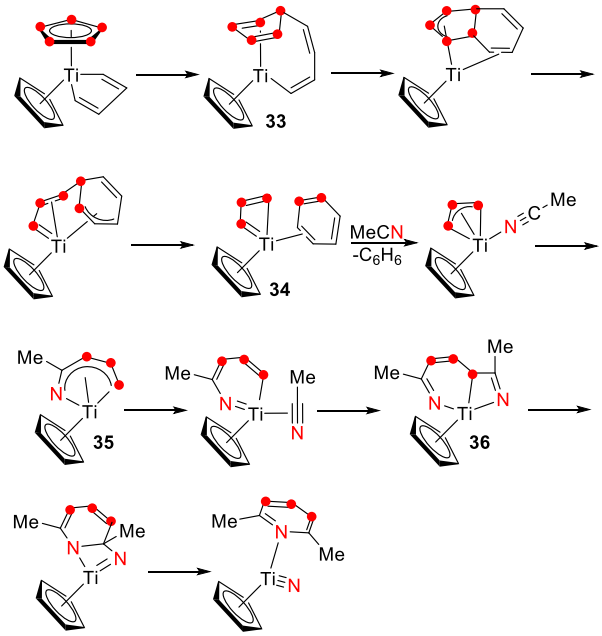
3.1. Cp ring fragmentation

A completely different type of C-C cleavage in a Cp ligand was demonstrated in 2003 by Takahashi and coworkers, who reported an unprecedented cleavage of two ring C-C bonds of the Cp ligand in a titanium complex.[54] In this reaction starting titanacyclopentadiene **32** reacts with two equivalents of PhCN to give 1,2,3,4-tetraethylbenzene and pyridine derivative as organic products (see Scheme 23). These products are assembled from C_2 and C_3 pieces resulted from scission of one of the Cp ligands. The C_2 fragment combines with the butadiendiyl ligand to give the 1,2,3,4-tetraethylbenzene, while the C_3 fragment couples with two equivalents of PhCN to form pyridine derivative. The remaining N-atom from PhCN is likely a part of the nitride complex [$(CpTiN)_4$] as a main organometallic product.[55]



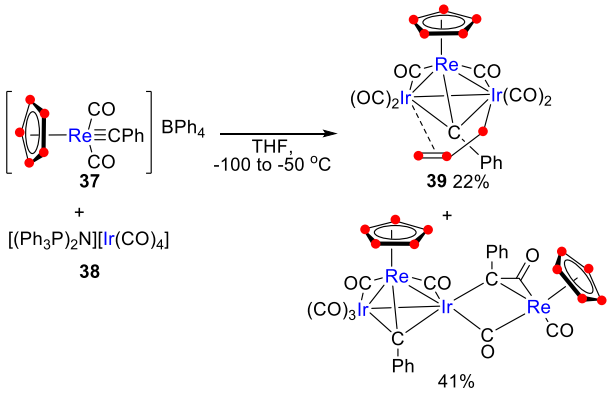
Scheme 23. Benzonitrile triggered C-C scission in a titanium metallocene.

The mechanism of this unusual transformation was probed by DFT (Scheme 24).[56] The reaction starts with the rate-determining C-C bond forming reductive elimination to give **33**, which after migratory insertion and β-carbon elimination produces titanacyclobutadiene with coordinated benzene **34**. Subsequent substitution of the arene ligand for acetronitrile and reductive coupling yields azametallacycle **35**, which after reductive coupling with a second molecule of acetonitrile gives bismetallacycle **36**. Finally, **36** undergoes C-N bond forming ring closure and generation of stable pyridine and nitride ligands. The authors also suggested an alternative pathway for formation of 2,6-dimethylpyridine from **36** involving participation of third molecule of acetonitrile.



Scheme 24. DFT mechanism for the Cp cleavage shown in Scheme 23.

An intriguing C-C scission in Cp ligand occurs upon mixing carbyne rhenium complex **37** with iridium carbonylate **38** (Scheme 25). The reaction leads to two Re-Ir clusters, one of which (**39**) has an allyl ligand presumably inherited from the cleaved Cp.[57] Formation of the allyl fragment from phenyl groups of BPh_4^- or $(Ph_3P)N^+$ ions could be excluded through isotope labeling studies. Notably, the process is sensitive to the identity of both metal centres: replacement of Re for Mn in a carbyne complex or Ir for Ru in a carbonylate does not lead to the C-C scission.

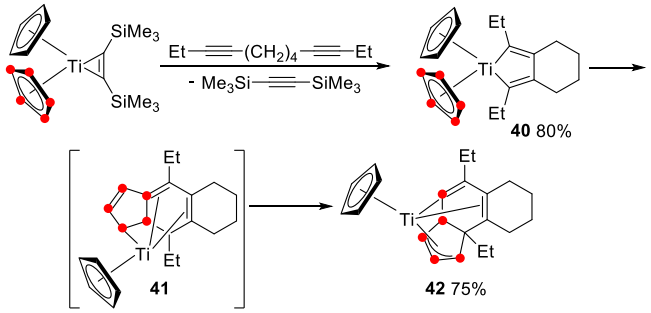


Scheme 25. Iridium-mediated scission of a Cp ligand.

3.3. Cp ring scission with incorporation into a polycyclic systems

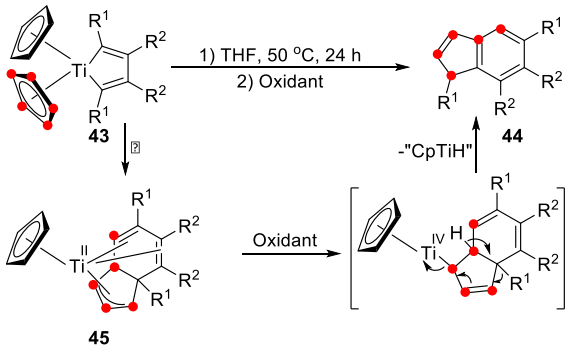
C-C scission in Cp ligands can lead to products with embedded framework of the cleaved aromatic ring into a cyclic framework

of di- or tricyclic system. The first example of such cleavage was reported by Tillack, Rosenthal *et al* (Scheme 26).[58] They showed that dicyclopentadiene complex **40** obtained from the corresponding Cp_2Ti precursor and dialkyne undergoes an unexpected rearrangement that involves cleavage of one of the Cp ligands. The rearrangement is likely to involve change of the coordination mode of the Cp ligand from η^5 to η^3 or η^1 followed by 2+4 cycloaddition to give indenyl complex **41**, which then isomerized into the final product **42**.



Scheme 26. Scission of a Cp ligand via cycloaddition and isomerization in a titanium complex.

A similar strategy was used by Takahashi *et al.* to synthesize substituted indene derivatives by incorporation of a diene moiety in **43** into a Cp ring (Scheme 27).[59] The resulting indene derivative **44** has one alkyl group R^1 unexpectedly relocated to the neighboring carbon atom. Mechanistic experiments suggested that this Cp cleavage occurs via an initial formation of intermediate **45** reported by Rosenthal and Tillack. Oxidation of **45** leads to the final product via elimination of a "CpTiH" fragment, which triggers migration of the Et group at a bridgehead position driven by aromatization[60] of the cyclohexadiene fragment. The rich chemistry of **45** type complexes was further explored by the Takahashi group.[61]



Scheme 27. Formation of indolines via Cp scission involving cycloaddition and and oxidative isomerization.

All the discussed examples involve scission of C-C bonds in Cp ligands triggered by carbene or carbocation species or cycloaddition with subsequent isomerization. A rare example of direct metal insertion into aromatic ring of a cyclopentadienyl ligand was described by Hou *et al.* (Scheme 10)[32] and insertion into a cyclopentadiene ligand has been documented as well.[62] In both cases the insertion occurred on trinuclear hydride clusters of Ti and Ru respectively.[32, 62]

Summary and perspective

Considerable progress has been achieved in metal-mediated scission of strong aromatic C-C bonds in arene and Cp ligands. Feasibility of cleavage of aromatic C-C under mild conditions has been demonstrated and in few cases high yields and selectivities were obtained. In this respect, the activation of aromatic C-C bonds in arenes seems particularly intriguing as it offers a completely new mode of functionalization of arenes that would complement the existing methods relied on activation of aromatic C-H bonds.

However, to translate this highly promising reactivity into useful synthetic applications, problems of competing C-H activation, which triggers unwanted side reactions, and poor regioselectivity should be first addressed. Particularly useful here would be more detailed mechanistic studies of the reported C-C activations to reveal how the identity of the metal center, ancillary ligand and arene affects the reactivity of metal complexes towards cleavage of aromatic C-C bonds. In this context, the idea of metal-induced arene ring strain seems particularly promising for enhancing the reactivity of arene ring C-C bonds and suppressing the undesirable activation of C-H bonds. Ways to improve the regioselectivity of aromatic C-C bond scission can be explored through the use of directing groups, or steric control in the starting aromatic compounds (under kinetic conditions) or in the metallacycle products (under thermodynamic conditions). Finally, discovery of appropriate combinations of arene ring scissions with subsequent functionalizations of resulting metallacycles or π-complexes would open new avenues for arene ring functionalizations through ring opening, contraction or expansion.

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Keywords: C-C activation • cleavage reactions • arenes • arene ligands • cyclopentadienyl ligands • transition metals.

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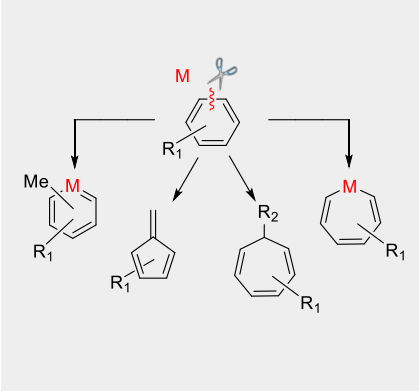
Entry for the Table of Contents

FOCUS REVIEW

Metal mediated cleavage of aromatic C-C bonds offers a unique approach for novel functionalizations of arenes through ring opening, contraction and expansion. Until recently, this fundamental, yet challenging organometallic transformation remained relatively unexplored. This focus review highlights recent progress in this quickly growing and highly promising research field.



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Page No. – Page No.

Transition Metal Mediated Cleavage of C-C Bonds in Aromatic Rings