UNIVERSITY OF LIVERPOOL

Towards a Low Temperature, Liquid Phase Methyl Methacrylate Process through Mechanism-Guided Process Design

Thesis submitted in accordance with the requirements of the University of Liverpool

for the degree of Doctor in Philosophy

By

Michael Beaumont

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Declaration

The research contained within this thesis was conducted solely by the author, unless clearly stated. The research was carried out under the supervision of Dr. Jonathan A. Iggo at the University of Liverpool between September 2011 and September 2015.

This PhD. studentship has been funded by Lucite International UK Ltd., who own the commercial rights to any research contained within this thesis. A patent has been submitted to cover this work.

Michael Beaumont

University of Liverpool

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Abstract

A liquid (slurry) phase, base-catalysed process for the production of methyl methacrylate from methyl propanoate and formaldehyde has been developed, that runs at temperatures around 200 °C below the current, heterogeneous process (160-180 °C vs. 330-360 °C) running at ALPHA-1, a commercial, methyl methacrylate-producing chemical plant.

Initially, caesium carbonate was used as the base, however fast deactivation of this base, producing hydroxide, results in the formation of inactive bases, caesium propanoate and caesium methacrylate from methyl esters. Through understanding of the mechanism of base deactivation, a new base catalyst, caesium methylcarbonate, was developed that does not act as a source of hydroxide.

Understanding of the mechanisms of the condensation reaction, base deactivation and formaldehyde decomposition has allowed a system to be developed that achieves high conversions of methyl propanoate with excellent selectivity (up to 43 % conversion with up to 99.5 % selectivity on methyl propanoate, compared with 18 % conversion at 93 % selectivity in the current process). The system requires a polar, aprotic solvent to increase the activity of the base catalyst and high temperature addition is essential for high selectivity on formaldehyde.

The caesium methylcarbonate is slowly deactivated through reaction of methyl esters with water, the co-product of the condensation reaction, to caesium propanoate and caesium methacrylate. For this reason, systems for the recycling to these methyl esters and caesium methylcarbonate have been developed so that multiple turnovers on caesium can be achieved through reaction-regeneration cycles. Regeneration of the active base can be achieved in a separate process step using carbon dioxide and methanol, to effectively reverse the equilibrium by which hydrolysis occurs, or with an *in situ* method using dimethyl carbonate as a sacrificial scavenger.

A patent has been submitted to cover the work in this thesis and work on this project is continuing at Lucite International, the sponsors of this PhD studentship. This process is under active consideration for scale up and commercialization.

List of Abbreviations

ACH	Acetone cyanohydrin
BMIM	1-Butyl-3-methylimidazolium
$CDCl_3$	Deuterochloroform
CO_2	Carbon dioxide
Cs_2CO_3	Caesium carbonate
CsMA	Caesium methacrylate
CsMC	Caesium methylcarbonate
CsOH	Caesium hydroxide
CsP	Caesium propanoate
D_2O	Deuterium oxide
DMAc	*N*,*N*-Dimethylacetamide
DMC	Dimethyl carbonate
DMEU	1,3-Dimethyl-2-imidazolidinone
DMF	*N*,*N*-dimethylformamide
DMSO	Dimethyl sulphoxide
DMPU	1,3-Dimethyl-3,4,5,6-tetrahydro-2-pyrimidinone
GC	Gas chromatography
GC-MS	Gas chromatography-mass spectrometry
h	Hours
HCHO	Formaldehyde
IR	Infra-red
J	Coupling constant
K	Kelvin
KMC	Potassium methylcarbonate
KP	Potassium propanoate
M	Molar concentration (moles per litre)
Me	Methyl
MeIm	1-Methylimidazole
MeOD	Deuteromethanol

MeOH	Methanol
MeP	Methyl propanoate
mins	Minutes
MMA	Methyl methacrylate
mol %	Mole percent
NaMC	Sodium methylcarbonate
NaP	Sodium propanoate
NMP	*N*-Methyl-2-pyrrolidinone
NMR	Nuclear Magnetic Resonance
PA	Propanoic acid
RbMC	Rubidium methylcarbonate
RbP	Rubidium propanoate
ppm	Parts per million
T_1	Spin-lattice relaxation time

Contents

List of Figures

List of Tables

Chapter One

Introduction

1. Introduction

1.1 Methyl methacrylate

Methyl methacrylate (MMA, methyl 2-methylpropenoate, $C_5H_8O_2$), figure 1.1, is a commodity chemical, with a global demand of over 3.6 million tonnes annually and growing.[1] Methyl methacrylate has a range of uses, including in acrylic sheet, moulding compounds, surface coatings and emulsion polymers, that are used in a number of industries.[2,3] The principle use of methyl methacrylate is as a monomer for the production of a range of homo- and co-polymers. Poly(methyl methacrylate) is traded under the trade names Perspex® (or Lucite® in North America) and Plexiglas® and is used as a lightweight, shatterproof alternative to glass.[4]

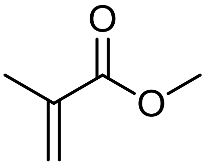


Figure 1.1: Methyl methacrylate (MMA).

Lucite International is the global leader in the manufacture of methyl methacrylate, with over 35 % market share. Lucite International holds a unique position in that it has access to all commercial technologies for the production of methyl methacrylate and it owns a number of methyl methacrylate production sites across Europe, Asia, the Middle East and North America.[4,5] With high and growing demand for methyl methacrylate, and to maintain its competitive advantage, Lucite International invests heavily in research and development into new methyl methacrylate producing technologies and towards improvements in efficiency in its current processes. As part of its commitment to the sustainable development of its business, Lucite

International reduced the amount of energy used per tonne of methyl methacrylate produced by 10 % between 2005 and 2010.[6]

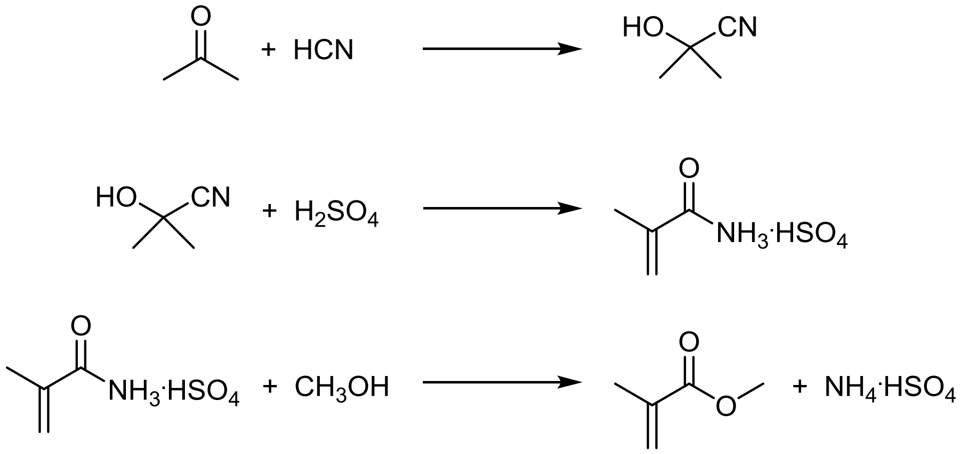
1.2 Commercial processes for the manufacture of methyl methacrylate

There are currently only a few commercially viable processes for the manufacture of methyl methacrylate and until recent advancements, the processes used have been unsustainable, producing large amounts of waste.

Very recently, some routes to methyl methacrylate from bio-derived feedstocks have been developed or are under development.[7–9] However, at this stage bio-derived methyl methacrylate production is uncompetitive economically and can only be done on a very small scale. The production of methyl methacrylate from non-edible natural/biological sources is a significant intellectual and technical challenge for the future. Almost all of the methyl methacrylate produced commercially is from petrochemical feedstocks and is based on old, well-established chemical methods with little scope for improvements in efficiencies or process economics.

1.2.1 Acetone-cyanohydrin (ACH) Route

The first commercial route to methyl methacrylate, the ACH route, is the process by which around 70 % of the world's methyl methacrylate was produced in 2009.[1] The ACH route was developed in the 1930's by Rohm and Haas chemical company.[2] The route combines acetone and hydrogen cyanide to the intermediate acetone cyanohydrin, which is then converted to methacrylamide acid sulphate with excess concentrated sulphuric acid. Esterification with methanol gives methyl methacrylate and ammonium bisulphate waste, scheme 1.1. There are a number of drawbacks of this process, including the cost, availability and safe handling of the raw materials, the use of excess corrosive concentrated sulphuric acid and the production of stoichiometric waste products.



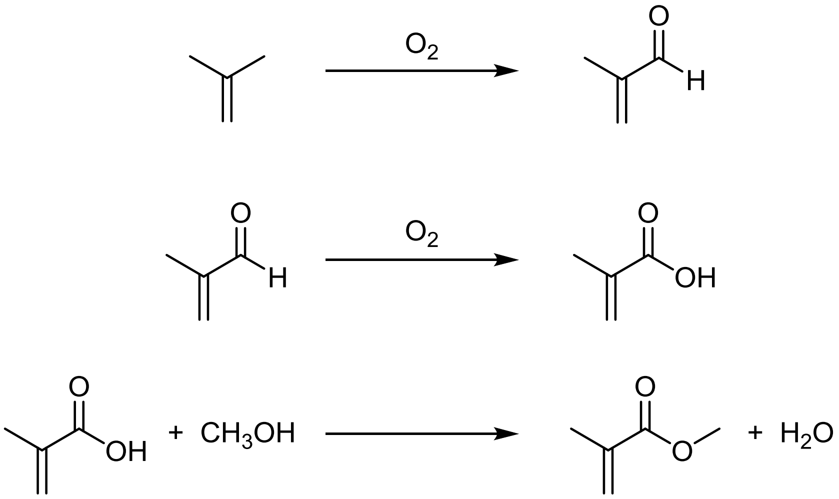
Scheme 1.1: The acetone cyanohydrin (ACH) process, developed in the 1930's is still the route by which most methyl methacrylate is produced in the world today.

The cheapest supply of both acetone and hydrogen cyanide are as by-products in the manufacture of other commodity chemicals, which means that their availability and cost is heavily dependent on demand for these commodity chemicals. Most acetone is produced in the cumene process for the production of phenol [10] and 30 % of the world's supply of hydrogen cyanide is from the acrylonitrile process;[11] other hydrogen cyanide production processes are economically unfavourable. Technological improvements in the acrylonitrile production process means that less hydrogen cyanide is produced in this process, further limiting availability.[1] Hydrogen cyanide is extremely toxic, adding costs associated with its containment and also limits the scale of ACH plants to around 100,000 tonnes per year.

Because of the requirement for excess sulphuric acid to convert the acetone cyanohydrin to methacrylamide acid sulphate, 300,000 tonnes of spent sulphuric acid must be reprocessed for a 100,000 tonnes per year ACH methyl methacrylate plant. As sulphuric acid is corrosive, special alloys are required for the reactors, further increasing costs. For every tonne of methyl methacrylate produced in this process, 1.6 tonnes of low value ammonium bisulphate waste is produced. Processes for the recycling of this waste back to sulphuric acid have been developed [12,13] but this still produces waste and increases the overall energy demand of the process. Even with more than 80 years of development, the overall yield of methyl methacrylate from cyanohydrin is around 87 % and the E factor for the process is still poor.

1.2.2 C4 Processes

In the 1980's, new processes for the manufacture of methyl methacrylate based on C4 feedstocks (mostly isobutene, although butanol can be used) were developed, firstly by Nippon Shokubai and Mitsubishi Rayon.[2] The C4 process involves two successive oxidations, from isobutene to methacrylic acid, *via* methacrolein, followed by esterification to methyl methacrylate, scheme 1.2. The overall yield of methyl methacrylate from isobutene is around 70 % owing to the low selectivity of the oxidation steps.[1] There are a number of chemical plants using this technology in Asia, however owing to low availability of feedstocks, no production facilities in other areas of the world use this technology.

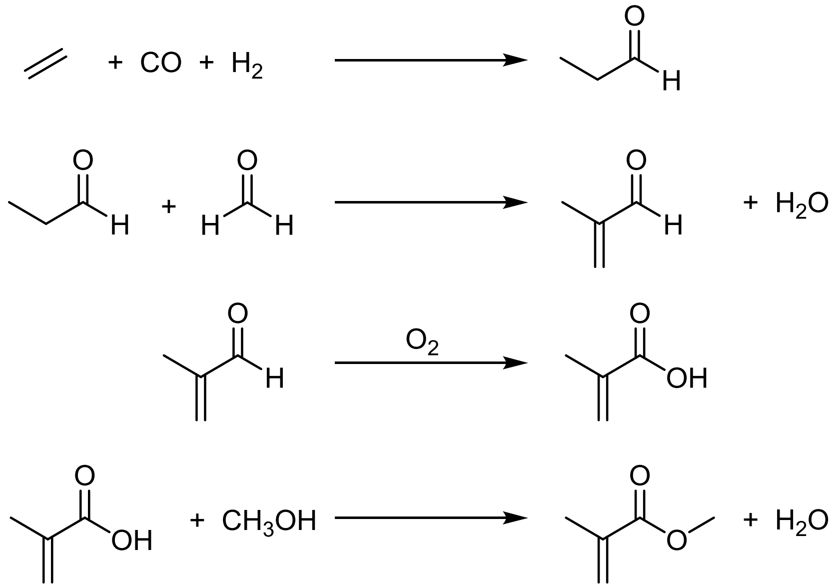


Scheme 1.2: The C4 route to methyl methacrylate is used in Asia but it suffers from low selectivity for methyl methacrylate and low feedstock availability elsewhere.

The major drawbacks of the C4 route is the cost and limited availability of feedstocks, especially outside of Asia, limiting C4 plants to a maximum of 90,000 to 100,000 tonne per year in size and the low selectivity for methyl methacrylate.

1.2.3 BASF’s C2 Route

In 1990, BASF built a 40,000 tonne per year methyl methacrylate plant at its Verbund site in Ludwigshafen where methacrolein was produced as an intermediate through hydroformylation of ethene to propanal, followed by condensation with formaldehyde.[1] Methacrolein could then be converted to methyl methacrylate in the same manner as the C4 route, scheme 1.3. The BASF methyl methacrylate plant at Ludwigshafen is relatively small scale and no new plants based on this chemistry have been built.

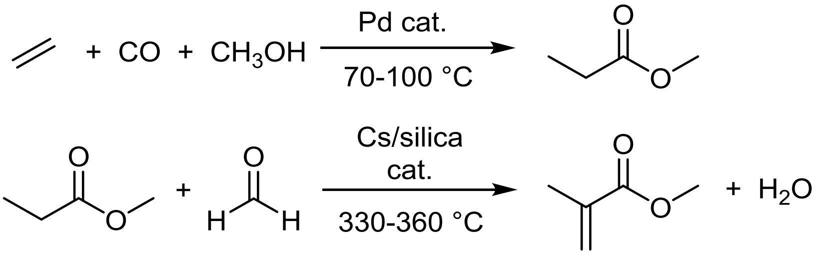


Scheme 1.3: The BASF C2 route to methyl methacrylate.

The competitive longevity of the ACH process highlights the difficulty in producing methyl methacrylate in an economically competitive manner. Methyl methacrylate is not a simple molecule to make, as a result of it being branched and very reactive. Other chemical routes to methyl methacrylate have been developed, such as propyne carbonylation [14] and propene hydrocarbonylation [3] but have, so far, not reached commercial viability.

1.2.4 The ALPHA Process

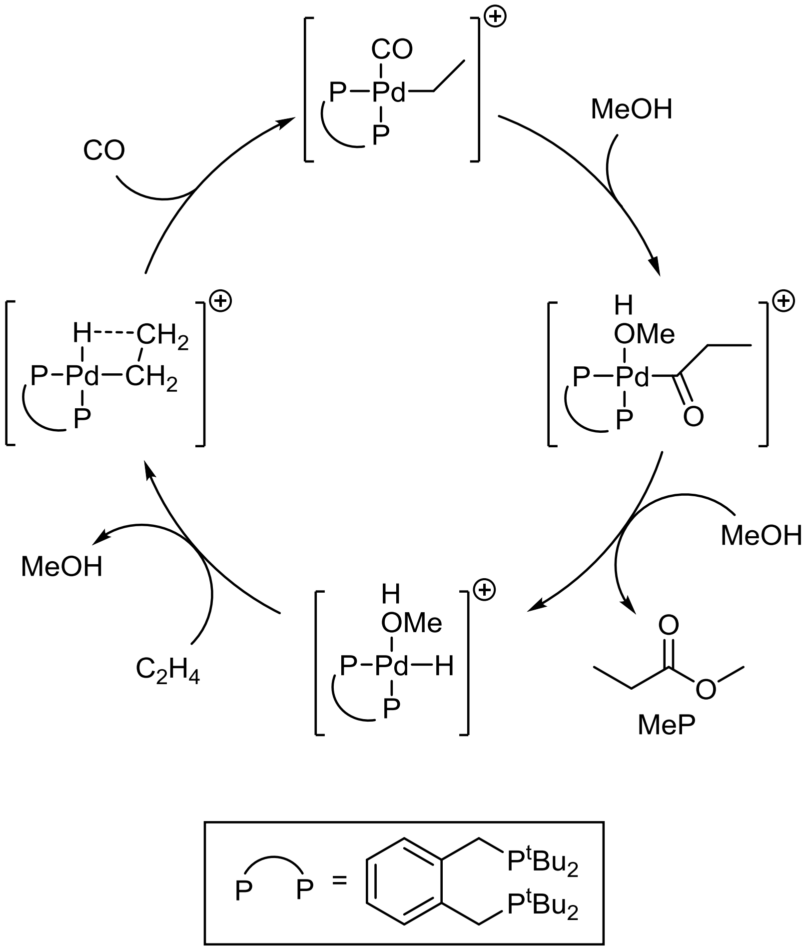
A step change in methyl methacrylate production technology came in 2007 when Lucite International successfully commercialized a new, more efficient, more sustainable, two-step route to methyl methacrylate based on entirely new chemistry, utilizing cheap, readily available raw materials through the intermediate methyl propanoate (MeP), scheme 1.4. ALPHA-1, the first production facility was built, on budget and on time, in Singapore with a nameplate capacity of 100,000 tonnes per year. It produces 135,000 tonnes of methyl methacrylate per year presently with a cost benefit of 30-40 % compared with other methyl methacrylate production processes.[5] A new ALPHA chemical plant that will produce 250,000 tonnes per year of methyl methacrylate is currently being built in the Kingdom of Saudi Arabia, where the raw materials are cheaper.



Scheme 1.4: The ALPHA Process: a new, more efficient route for the manufacture of methyl methacrylate.

1.2.4.1 The ALPHA Process: Stage One

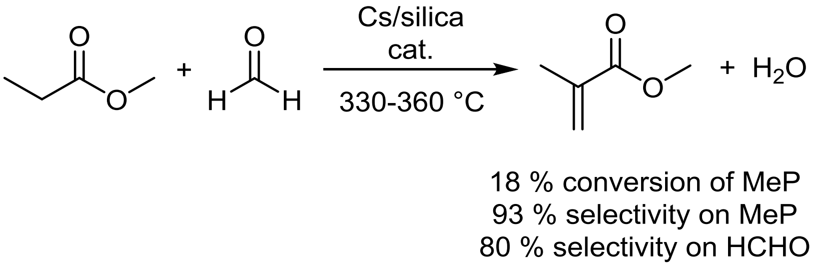
The first stage of the ALPHA process is the methoxycarbonylation of ethene using a palladium diphosphine catalyst. The design of the ligand has a major impact on the selectivity for methyl propanoate,[15] and the catalyst used in the process gives enzyme-like selectivity of 99.996 % with high turnover frequency at 70-100 °C and high turnover number. Academic and industrial collaboration determined the mechanism of the reaction,[16–18] scheme 1.5, which had a direct impact on reactor design and how the process is run.



Scheme 1.5: The mechanism for the palladium diphosphine-catalysed methoxycarbonylation of ethene to methyl propanoate, Stage One of the ALPHA process. Figure adapted from Iggo et al.[16]

1.2.4.2 The ALPHA Process: Stage Two

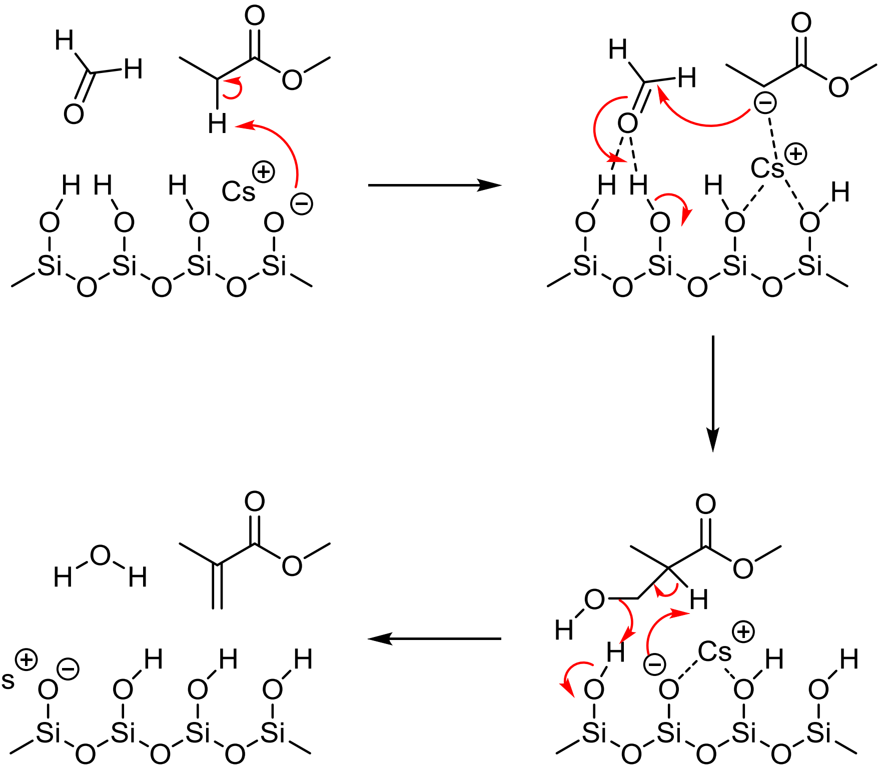
Stage Two of the ALPHA process, the condensation of methyl propanoate with formaldehyde, is by comparison, less efficient and much more energy intensive. The reaction is run at 330-360 °C with gaseous reactants and a solid caesium on silica catalyst.[19,20] The reaction conditions used are severe to attain reasonable conversion, with around 18 % conversion of methyl propanoate achieved with 93 % selectivity for methyl methacrylate. Selectivity on formaldehyde is around 80 % owing to its extremely high reactivity. Water, a stoichiometric by-product in the condensation reaction also causes hydrolysis of the methyl propanoate and methyl methacrylate to acids and methanol. To reduce the extent of hydrolysis, feed with the minimum amount of water possible is required.



Scheme 1.6: Stage Two of the ALPHA process is energy intensive and far less selective than Stage One.

The low single pass conversions means that unreacted starting material must be purified from products and by-products and then recycled back through the reactor. The harsh conditions used with low single pass conversion and the large temperature swings (hot reaction-cool purification-hot reaction) result in the process being very energy intensive.

Condensation reactions of this type can either be acid- or base-catalysed, through the formation of either an enol or enolate intermediate.[21] The catalyst contains strongly basic caesium oxide sites and weakly acidic silanol groups and it is postulated that both types of site play a role in the catalysis. The proposed mechanism, scheme 1.7, involves coordination of the gaseous reactants on the surface followed by deprotonation of methyl propanoate at one of the strongly basic sites. The most acidic protons of methyl propanoate are α to the carbonyl group as deprotonation here gives a resonance stabilized carbanion/enolate species. The carbanion is nucleophilic and can attack the very electrophilic formaldehyde carbon, which may be activated by the silanol protons. This bond forming reaction gives a β-hydroxy ester intermediate that is unstable and dehydrates to give methyl methacrylate and water.



Scheme 1.7: The proposed mechanism of the condensation of methyl propanoate with formaldehyde over a caesium on silica catalyst is through cooperative strong base/weak acid catalysis. The solid support is represented as repeating Si-O units with the fourth Si-O bond omitted for clarity.

Using formaldehyde as a reactant presents a significant chemical engineering challenge due to its high reactivity and lack of stability. Formalin solution, the commercially available formaldehyde feedstock, is a mixture of approximately 37 weight percent formaldehyde, 10-15 weight percent methanol and the remainder water. In solution formaldehyde forms a complex mixture of methylene glycols and oligomers.[22] Lucite International have developed ways to remove water from formalin solution, forming essentially water-free methanolic formaldehyde.[23] Methanolic formaldehyde is a mixture of hemiformals,[24] figure 1.2.

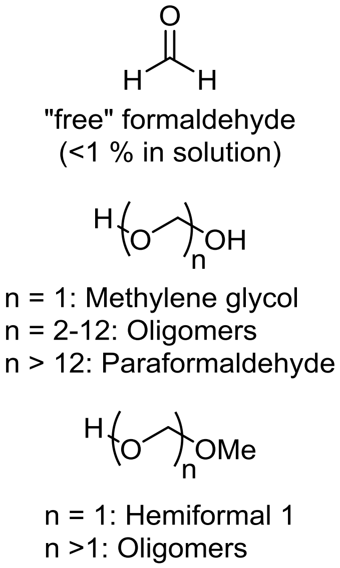


Figure 1.2: Formaldehyde in solution exists as a complex mixture of methylene glycols and hemiformals, depending on the co-solvent(s).

The high reactivity of formaldehyde and methyl methacrylate means a number of by-products, including reduction products and dimers formed through Claisen ester condensation are produced as a result of the relatively harsh reaction conditions and the mixture of active sites on the catalyst. A small amount of non-volatile coke is formed on the surface of the catalyst, which causes a loss of activity and selectivity for methyl methacrylate. High temperature calcination regenerates the catalyst and so two reaction columns are required on the chemical plant allowing for continuous production of methyl methacrylate through parallel reaction-regeneration cycles between each column.

After a number of distillations, the methyl methacrylate produced is of higher purity than for other processes and the selectivity for methyl methacrylate from starting materials is greater than the other commercialized processes, above 90 % compared with 87 % for ACH and 70 % for C4 processes. In large scale industrial processes, the selectivity of a particular reaction or process is an important consideration, for example if a by-product is produced at 5 % for a process that manufactures 0.75 M tonne per annum of product (the combined projected output of ALPHA1-3), this equates to over 37,500 tonnes that has to be removed from the product and disposed of, adding significant further costs and contributing to the sustainability (or "green credentials") of a process.

The economic advantage of the ALPHA process comes mostly from Stage One, with its high reaction rate and near perfect selectivity. While Stage Two has been optimized to be good enough to make the process competitive, it is still the weaker part of the whole process. Any improvement in the energy efficiency and/or selectivity of this reaction through improved catalysis at lower temperatures could result in significant cost reductions and a further improvement in the sustainability of the ALPHA process, by further adhering to one of the twelve principles of green chemistry,[25–27] regarding maximizing energy efficiency in chemical processes.

A survey of the literature on the condensation reaction of methyl propanoate with formaldehyde to methyl methacrylate shows all attempts at this reaction have used heterogeneous conditions, with a solid catalyst and reactants in the gas phase at around 300-400 °C, table 1.1.[28-33] The related condensation of propanoic acid with formaldehyde has also received much attention, again using heterogeneous catalysis.[28–31]

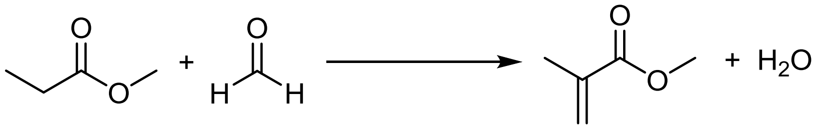


Table 1.1: Focus on the condensation of methyl propanoate with formaldehyde in the literature has been on heterogeneous catalysis with high temperature conditions. N.R = not reported

Entry	**Catalyst**	**Conditions**	**Conversion of MeP / %**	**Selectivity on MeP / %**	**Selectivity on HCHO / %**
1	ALPHA catalyst	330-360 °C, water-free formaldehyde [19,20]	18	93	80
2	V-Si-P ternary oxides	300 °C, trioxane [32]	4.83 (yield)	N.R	22.2 (yield)
3	CsOH on silica	320-380 °C, formalin [33]	14.05	91.5	86.5
4	Cs-Zr-Mg/SiO_2	360 °C, methanol + paraformaldehyde [34]	55.4	76.6	N.R
5	Zr-Fe-Cs on SBA15 (silica)	320 °C, methanol + paraformaldehyde [35]	26.0	93.6	N.R
6	15 % CsOAc on silica	330-390 °C, various HCHO sources [36]	22.78	N.R	N.R
7	Supported barium phosphates	300-360 °C, dimethoxymethane [37]	3.2 (yield)	95.9	N.R

While there are a number of reports of heterogeneous catalysts and conditions for the condensation of methyl propanoate with formaldehyde, only one report, a patent in Chinese, could be found of a homogeneous-type reaction system that pre-dates the start of this work.[38] In this report, ionic liquids based on imidazolium cations with basic anions were used as catalysts or solvents at 103-213 °C. Work based around this system is covered in chapter 5.

1.3 Project aims

The condensation reaction of methyl propanoate with formaldehyde is similar to a crossed-aldol condensation reaction, which is often run under mild, homogeneous conditions with an acid or base catalyst.[21] An advantage of homogeneous catalysis is that, very often, relatively high activity can be achieved under milder conditions compared with heterogeneous catalysis. All the active sites in a homogeneous catalyst are in solution (and so, are active) and the active sites are uniform (there is usually only one type of active site on a homogeneous catalyst), where unwanted side-reactions can occur at different sites on a solid catalyst, for example at acidic silanol sites on the basic caesium oxide on silica catalyst.

For these reasons, Lucite International investigated the possibility of a homogeneous-type system using simple, mild organic or inorganic bases. The work contained in this thesis is a continuation of one of the promising candidates for such a system, using caesium carbonate as a base under mild conditions at 160 °C. An advantage of using alkali metal salts is their non-volatility, which allows for simple separation of products and unreacted starting materials from the base catalyst through distillation, which is often a difficulty with homogeneous catalysis.[39,40] Some activity, around 11 % conversion of methyl propanoate to methyl methacrylate, could be achieved (see chapter 2, section 2.1) under much milder conditions than the current, heterogeneous ALPHA Stage Two catalyst.

The milder reaction conditions are favourable both because this adheres to the principles of green chemistry and because unwanted, high energy barrier side-reactions of both reactants and products can be reduced, potentially resulting in higher selectivity and reduced waste formation. This could result in significant cost savings and a more efficient and sustainable process through reducing both the energy demand of the process and the amount of waste produced.

Reaction monitoring and mechanistic understanding are easier to obtain in homogeneous catalysis, compared with heterogeneous catalysis, with a range of techniques available to aid understanding of the chemistry involved during the reaction. This knowledge can potentially be used for iterative, mechanism-guided reaction optimization and process design. For this reason, a key first aim of the project was to fully understand the chemistry occurring in the reaction conditions, with a view to optimizing the conversion and selectivity for methyl methacrylate and the catalyst lifetime in the system.

During all of this work, a key driver has been to maximize the possibility of this work becoming economically competitive with the current ALPHA Stage Two process, with a view to potential scale-up and replacement of the current system used in the manufacturing process. This has meant that the catalysts and additives used have had to be relatively cheap and readily available in large quantities and that regeneration and recycling of materials has been a crucial consideration throughout the development of this project.

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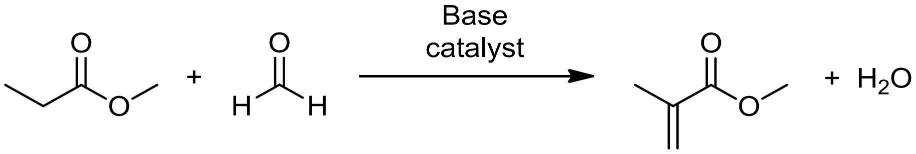
Chapter Two

A low temperature, caesium carbonate-promoted condensation of methyl propanoate with formaldehyde

2. A low temperature, caesium carbonate-promoted condensation of methyl propanoate with formaldehyde

2.1 Introduction

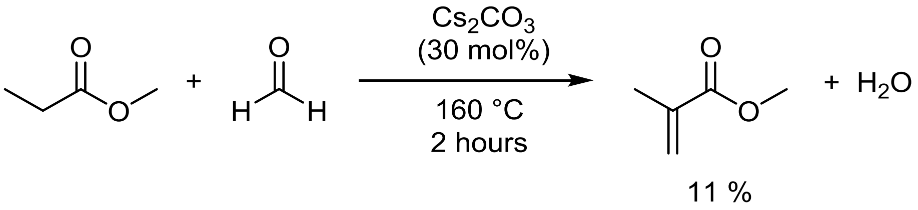
The condensation reaction of methyl propanoate with formaldehyde to form methyl methacrylate, scheme 2.1, is currently performed at high temperatures (330-360 °C) with the reagents in the gas phase with a solid caesium on silica catalyst. Low single pass conversions (around 18 % of the methyl propanoate is converted at 93 % selectivity) are achieved meaning large temperature swings are required to recover starting material through distillation for recycling back into the process. This makes the whole process very energy intensive. A system where the condensation reaction is run at lower temperatures would mean reduced temperature swings and reduced energy consumption.



Scheme 2.1: The condensation of methyl propanoate with formaldehyde, which comprises the second stage of the ALPHA Process.

This chapter examines the caesium carbonate-promoted condensation reaction of methyl propanoate with formaldehyde at 160 °C, with a view to a low temperature, liquid phase process as a potential alternative to the current process for Stage Two of the ALPHA Process.

Prior to the work described herein, Lucite International, following a patent by Du Pont,[1] had shown that methyl propanoate was a much less reactive ester than γ-butyrolactone in the base catalysed reaction with methanolic formaldehyde (a 55 weight % solution of formaldehyde, known as methyl alcoform).[2] 74 % conversion of γ-butyrolactone to the α-methylene-γ-butyrolactone was achieved using caesium carbonate as a catalyst, whereas only 11 % conversion of methyl propanoate was achieved under the same conditions, scheme 2.2. Lucite International had also screened various bases as potential catalysts and shown caesium carbonate to be the most promising base for a low temperature, liquid phase process. Other commercially available basic alkali metal salts or organic amines either gave poorer conversions or unwanted side-reactions resulting in poor selectivity.



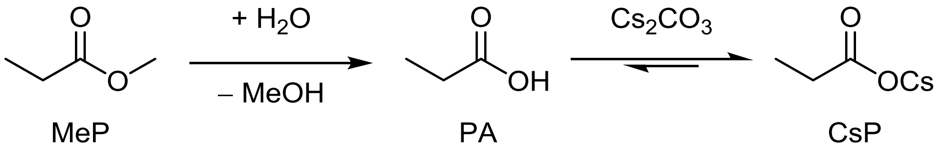
Scheme 2.2: The caesium carbonate-promoted condensation of methyl propanoate with formaldehyde, developed at Lucite International and used as the starting point for this work.

Although a two molar excess of formaldehyde (relative to methyl propanoate) was used, little or no formaldehyde is detected in exit mixtures from these reactions, as a significant amount of formaldehyde decomposition occurs by parallel reactions. The condensation reaction stops when no formaldehyde remains and no further increase in conversion of methyl propanoate could be achieved with longer reaction times. A large pressure increase during the experiment was observed and attributed to the Cannizzaro reaction of two formaldehyde molecules giving gaseous products. This reaction and other formaldehyde decomposition reactions are considered in more detail in chapter 4.

The proposed mechanism for the condensation reaction is similar to that of the heterogeneous process outlined in chapter 1, section 1.2.4, with the absence of the acidic sites of the silanol groups. First, methyl propanoate is deprotonated at the *α*-position to the carbonyl group (pK_a = ca. 25)[3] by the carbonate, forming a delocalised carbanion/enolate species. This negatively charged intermediate is nucleophilic and attacks the electrophilic carbonyl carbon of formaldehyde to give an alkoxide which, on protonation, gives a postulated *β*-hydroxy carbonyl compound. The condensation process is completed through base catalysed dehydration of the postulated *β*-hydroxy carbonyl compound to the *α,β*-unsaturated carbonyl compound, methyl methacrylate and water.

Basic caesium salts such as caesium carbonate have been reported to have synthetic utility, affording enhanced yields and rates of reaction compared with the other alkali metal salts, sometimes termed “the caesium effect”.[4–7] A “caesium effect” was encountered in this reaction: use of sodium or potassium carbonates results in lower conversions. The caesium effect is a periodic trend. As group 1 is descended, the alkali metal cations become larger, with reduced charge density resulting in weaker ion pairing interactions between cation and anion giving more soluble salts (for example, caesium carbonate is at least ten times more soluble than potassium carbonate in polar aprotic solvents)[8] and less well stabilized, more reactive anionic species (more basic, more nucleophilic).[5,9]

Water is a stoichiometric by-product in the reaction and so the exit mixtures should contain equimolar amounts of water and methyl methacrylate. However, Karl-Fischer analysis of the exit mixture shows there is significantly less water present than is expected.[2] Caesium propanoate was identified as a by-product, and its formation was attributed, incorrectly, to be only through reaction of methyl propanoate with the water produced in the condensation reaction, forming propanoic acid (PA) and methanol. Under the basic conditions the carboxylic acid is deprotonated to the carboxylate salt, caesium propanoate (CsP). Hydrolysis occurs throughout the reaction and is problematic, leading to much weaker base species that are less active catalysts for the condensation reaction of methyl propanoate with formaldehyde.



Scheme 2.3: Hydrolysis of methyl propanoate produces caesium propanoate as the initial product, propanoic acid, is deprotonated under the basic conditions.

The turnover number on carbonate achieved in the Lucite study was sub-stoichiometric (11 % conversion at 30 mol% loading of caesium carbonate) and the formation of inactive or only weakly active caesium propanoate meant the caesium carbonate catalyst was not recyclable, limiting the commercial viability of the system since each batch of carbonate would have to be reusable for many runs of the condensation reaction.

In this chapter, catalyst performance testing has been combined with mechanistic studies to obtain insight and further understanding of the reaction pathways in order to develop strategies for optimization of the reaction to assist the development of a new, low temperature, homogeneous alternative to the current high temperature, heterogeneous process. This has resulted in a four-fold improvement in conversion with excellent selectivity on methyl propanoate, over 97 %.

2.2 Results and Discussion

2.2.1 Caesium carboxylate formation from caesium carbonate and methyl esters

Initial mechanistic studies sought to quantify more accurately the extent of the hydrolysis of methyl esters (methyl propanoate and methyl methacrylate) to caesium carboxylates. Catalyst testing with the experimental protocol developed by Lucite was used, however NMR spectroscopy was chosen as the preferred analytical technique as this gives information about both the volatile and non-volatile components of the crude exit mixture. Previously, vacuum distilled exit mixtures were analysed by gas chromatography (GC), however this analysis does not give information on the composition of the (non-volatile) caesium salts.

The crude exit mixture from these experiments is a thick brown liquid (a brown oil is formed through formaldehyde decomposition). The mixture was diluted with methanol to ensure full dissolution of the caesium salts. Methanol was chosen as the work up solvent as there was already some methanol in the exit mixture and because at this stage methanol was (incorrectly) thought to be an innocent, unreactive solvent in the reaction.

The ^{1}H NMR spectrum of the crude exit mixture of a condensation reaction experiment, figure 2.1, confirms that NMR spectroscopy allows for observation of both volatile material and non-volatile material. A fourth methyl propanoate-derived compound, caesium methacrylate (CsMA), formed through hydrolysis of methyl methacrylate and subsequent deprotonation, was detected in the ^{1}H and $^{13}C\{^{1}H\}$ spectra.

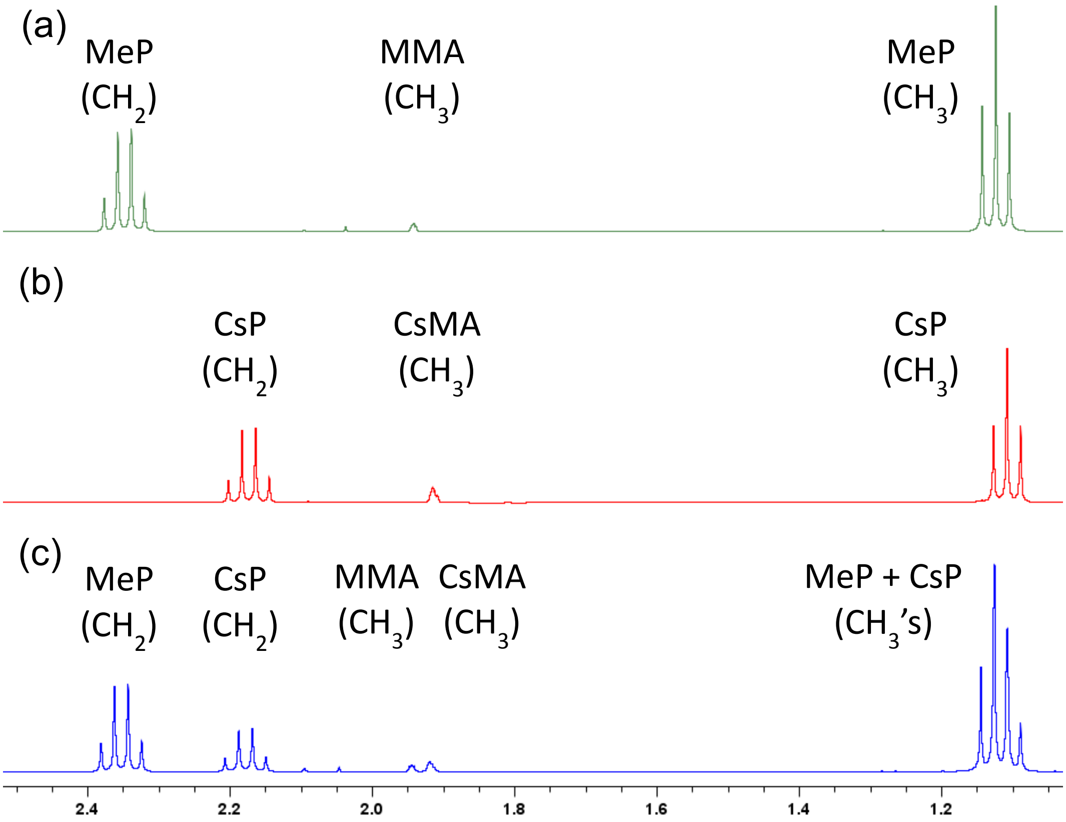


Figure 2.1: Selected ^{1}H NMR spectra from the caesium carbonate-promoted condensation reaction. (a) Collection of the volatile species by vacuum distillation. (b) The remaining non-volatile salts from the vacuum distillation, dissolved in methanol. (c) The crude exit mixture, dissolved in methanol.

After correcting for the difference in multiplicity of the methylene (CH_2) resonances of methyl propanoate and caesium propanoate and the methyl (CH_3) resonances of methyl methacrylate and caesium methacrylate, the integrations of these resonances can be used to determine the relative amounts of these species (see section 7.4) as: MeP 66 %; CsP 28 %; MMA 2 %; CsMA 4 %. A greater proportion of the methyl methacrylate produced is hydrolysed to caesium methacrylate than the proportion of methyl propanoate that is hydrolysed to caesium propanoate. In all cases of catalyst testing that follow, this relationship is observed and is attributed to the greater acidity of methacrylic acid compared with propionic acid; so the greater stabilization of the methacrylate anion by the caesium cation makes hydrolysis of methyl methacrylate more favourable.[2]

It is not immediately obvious how 32 % of the methyl esters can be hydrolysed to caesium carboxylates when the stoichiometry of the condensation reaction only allows for 6 %. Clearly there must be other source(s) of water in the reaction system. Although caesium carbonate is hygroscopic, the extent of excess hydrolysis observed is too great to be attributed to contamination of the reaction by water from this source. An understanding of the mechanism of this hydrolysis is, therefore, required due to its role in deactivating the catalyst and limiting the turnover number achievable.

2.2.2 Mechanisms of hydrolysis of methyl esters with caesium carbonate

$^{13}C\{^1H\}$ NMR spectroscopic analysis of the non-volatile salts revealed that the caesium carbonate is completely consumed in the reaction (no resonance at $\delta = 168.8$ ppm), figure 2.2. In addition to the expected resonances of caesium propanoate and caesium methacrylate, resonances at 160.0 and 55.0 ppm, attributed to caesium methylcarbonate are present, assigned by comparison with the chemical shifts of sodium methylcarbonate, in the report by Kunert et al.[10] A resonance in the ^1H NMR spectrum at 3.54 ppm ($CsOC(O)OC\mathbf{H_3}$) is also present, confirming the assignment of these resonances to caesium methylcarbonate.

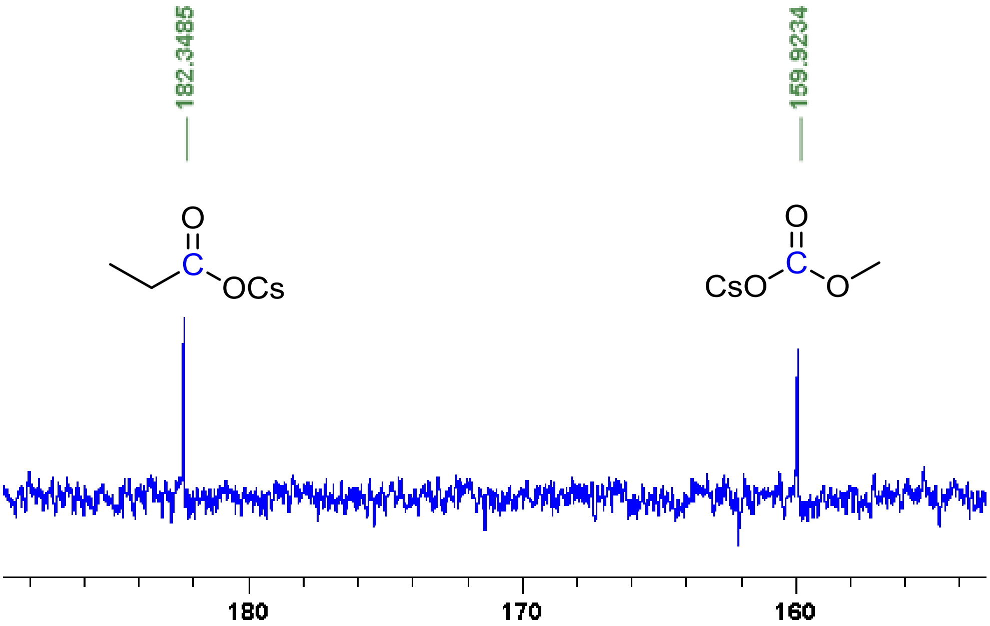


Figure 2.2: The carbonyl region of the $^{13}C\{^{1}H\}$ NMR spectrum of the non-volatile salts in methanol contains two resonances; 182.3 ppm (caesium propanoate) and 160.0 ppm (caesium methylcarbonate).

Potential mechanisms for the formation of caesium methylcarbonate and caesium carboxylates (caesium propanoate or caesium methacrylate) from methyl esters and caesium carbonate can be proposed, e.g. (1) nucleophilic attack by the carbonate on the carbonyl carbon of methyl propanoate forming a 6-membered transition state, breaking the carbonyl carbon-methoxy (C-O) bond, the $B_{AC}2$ mechanism or (2) direct methyl transfer through nucleophilic attack of the carbonate on the methyl group breaking the O-C bond of the methoxy group, the $B_{AL}2$ mechanism, figure 2.3. In the case of hydrolysis of esters with hydroxide, the $B_{AC}2$ mechanism is usually more favoured, with the $B_{AL}2$ mechanism generally only observed for esters that are sterically hindered at the carbonyl group.[11–14]

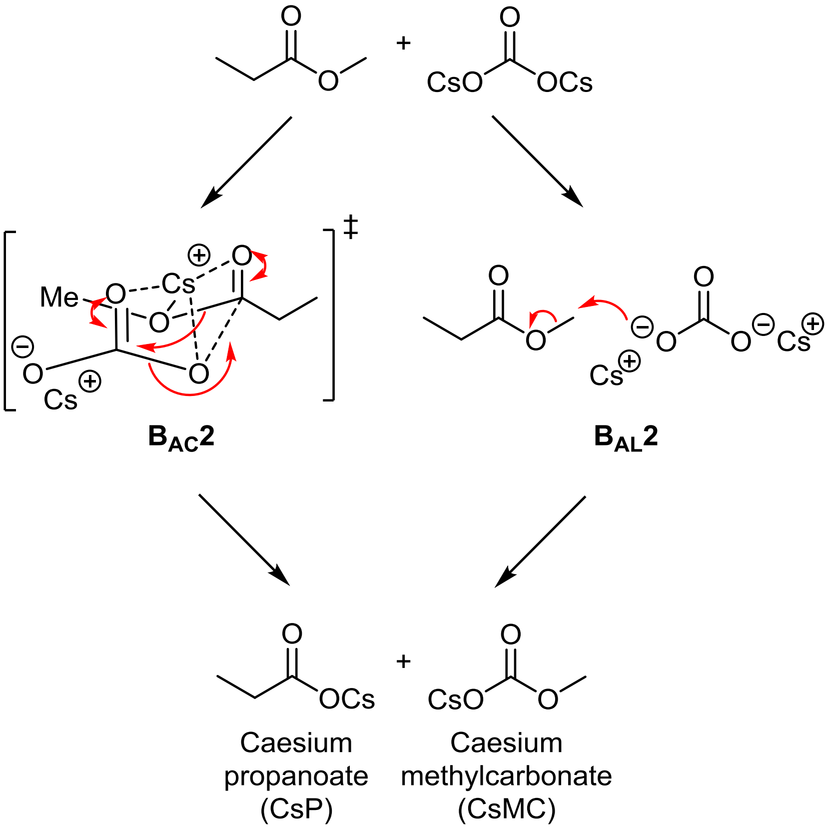
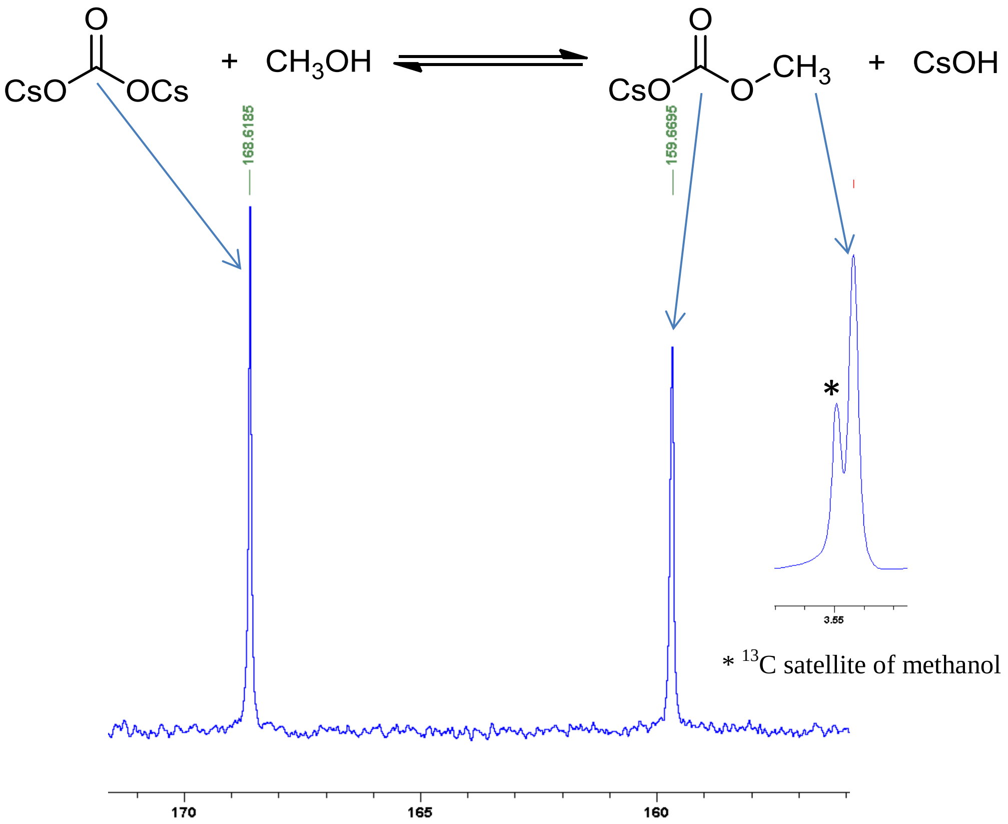


Figure 2.3: $B_{AC}2$ or $B_{AL}2$ type mechanisms could explain the formation of caesium propanoate and caesium methylcarbonate from methyl propanoate and caesium carbonate.

However, caesium methylcarbonate formation is only observed when methanol is present, militating against the mechanistic proposals of figure 2.3, neither of which require methanol. To investigate the role of methanol in the base deactivation, caesium carbonate was dissolved in methanol and the resulting mixture analysed by ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy. The methoxy resonance of caesium methylcarbonate is observed in the ^{1}H NMR spectrum and the resonances of both caesium carbonate and caesium methylcarbonate are observed in the $^{13}C\{^{1}H\}$ NMR spectrum, figure 2.4.



* ^{13}C satellite of methanol

Figure 2.4: $^{13}C\{^{1}H\}$ NMR spectroscopy shows a mixture of caesium carbonate and caesium methylcarbonate is produced when the former is dissolved in methanol. Insert, ^{1}H NMR spectrum.

The relative intensities of the carbonate and methylcarbonate resonances do not change over time, suggesting an equilibrium is quickly established between caesium carbonate and caesium methylcarbonate. As the concentration of the caesium cations in solution is reduced with addition of further methanol, the carbonate resonance is reduced in intensity relative to the methylcarbonate resonance in the $^{13}C\{^{1}H\}$ NMR spectrum, figure 2.5. Thus, at high caesium concentrations the carbonate resonance has a similar intensity to the methylcarbonate resonance but below 0.6 M caesium cation concentration, the carbonate resonance is no longer visible above the baseline consistent with the equilibrium being pushed in favour of methylcarbonate in accordance with Le Chatelier’s Principle.

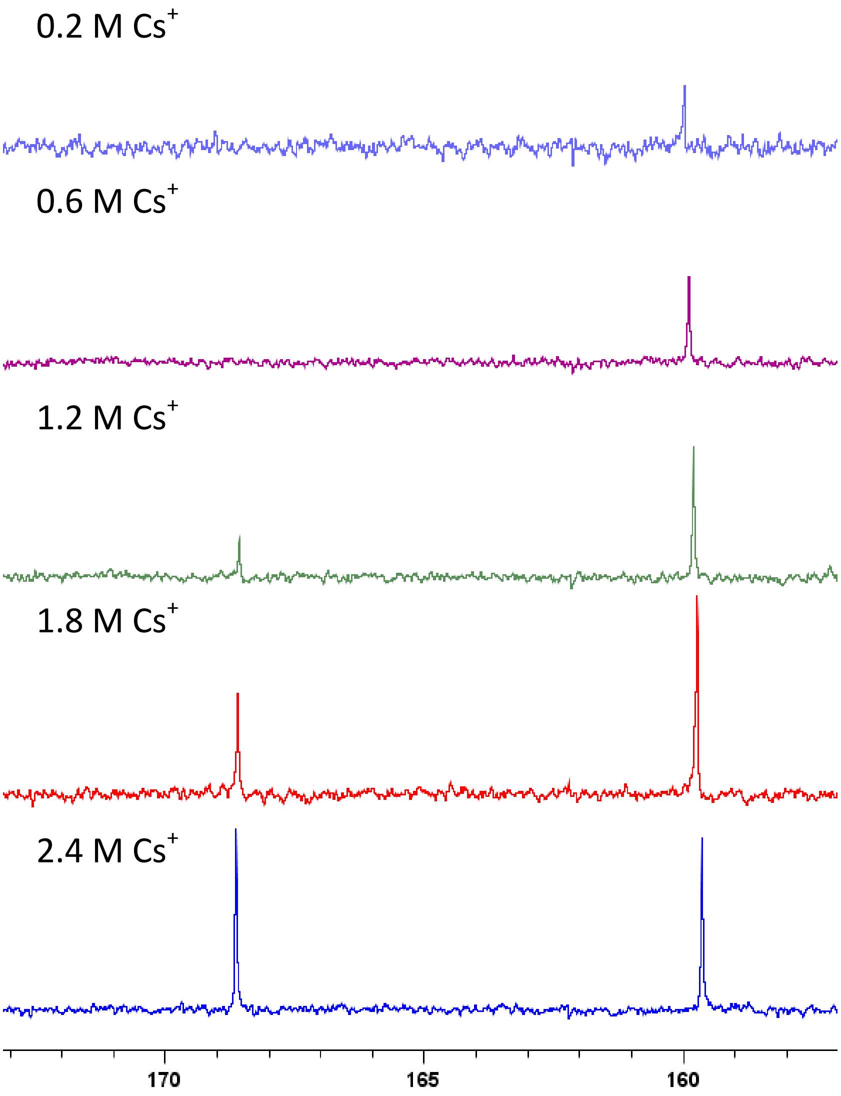
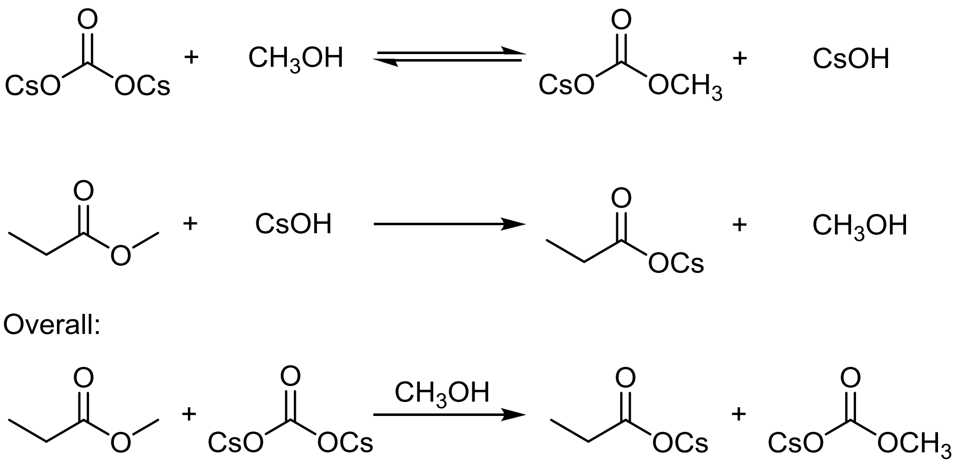


Figure 2.5: The $^{13}C\{^{1}H\}$ NMR spectra of caesium carbonate mixtures in methanol. On dilution with further methanol, the carbonate resonance (δ = 168.8 ppm) is decreased in intensity relative to the methylcarbonate resonance (δ = 159.9 ppm).

The other product in this reaction must be caesium hydroxide, scheme 2.4. Although this has not been directly verified experimentally, the presence of caesium hydroxide is strongly suggested by the observation that addition of methyl propanoate to a caesium carbonate / caesium methylcarbonate mixture in methanol results in the formation of caesium propanoate, figure 2.6.



Scheme 2.4: Consumption of caesium hydroxide through reaction with methyl propanoate pulls the caesium carbonate/methylcarbonate equilibrium towards stoichiometric (on carbonate) conversion of methyl propanoate to caesium propanoate.

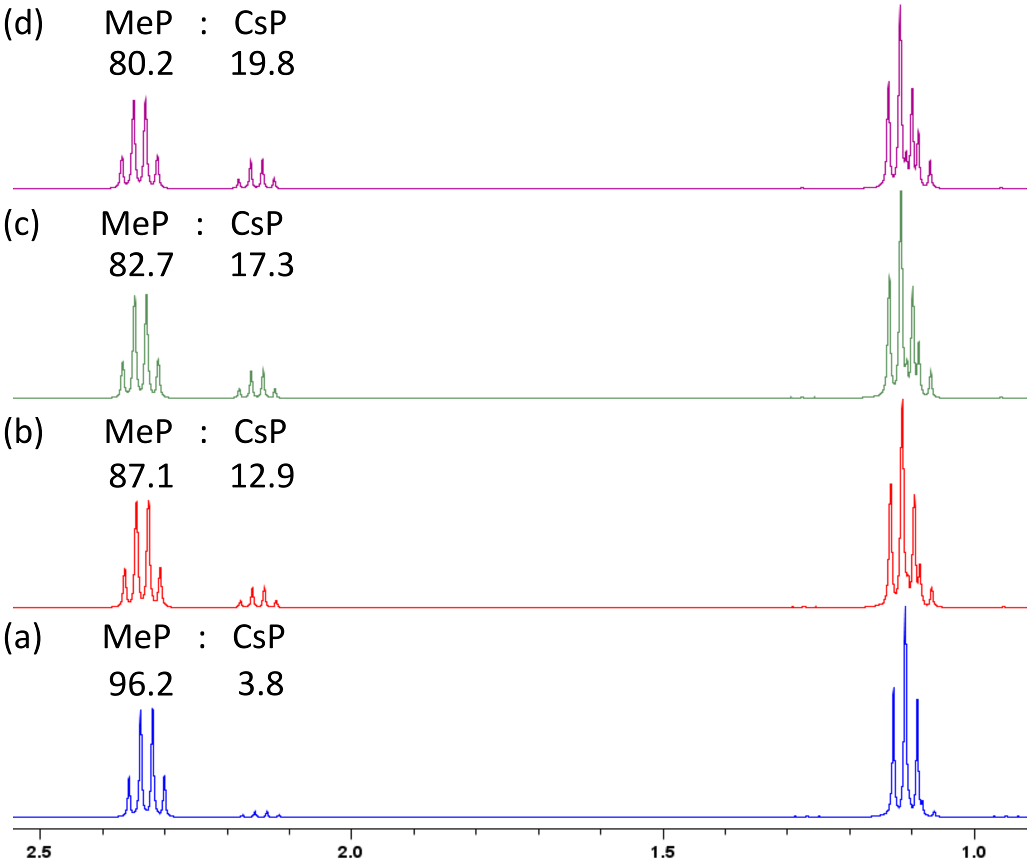


Figure 2.6: The caesium hydroxide co-produced in the formation of caesium methylcarbonate causes hydrolysis of methyl propanoate affording caesium propanoate, as observed in the ^{1}H NMR spectra of the mixture over time. 5 equivalents of methyl propanoate relative to starting caesium carbonate was added. (a) mixture after 10 minutes (time taken to set up experiment); (b) 1 hour 10 minutes; (c) 2 hours 10 minutes; (d) 3 hours 10 minutes.

Attack of caesium hydroxide on methyl propanoate is strongly favoured, resulting in essentially complete conversion of the hydroxide. As a result, the caesium carbonate resonance in the $^{13}C\{^{1}H\}$ NMR spectrum completely disappears, figure 2.7. This is consistent with consumption of caesium hydroxide driving the position of the carbonate/methylcarbonate equilibrium to the right according to Le Chatelier's Principle.

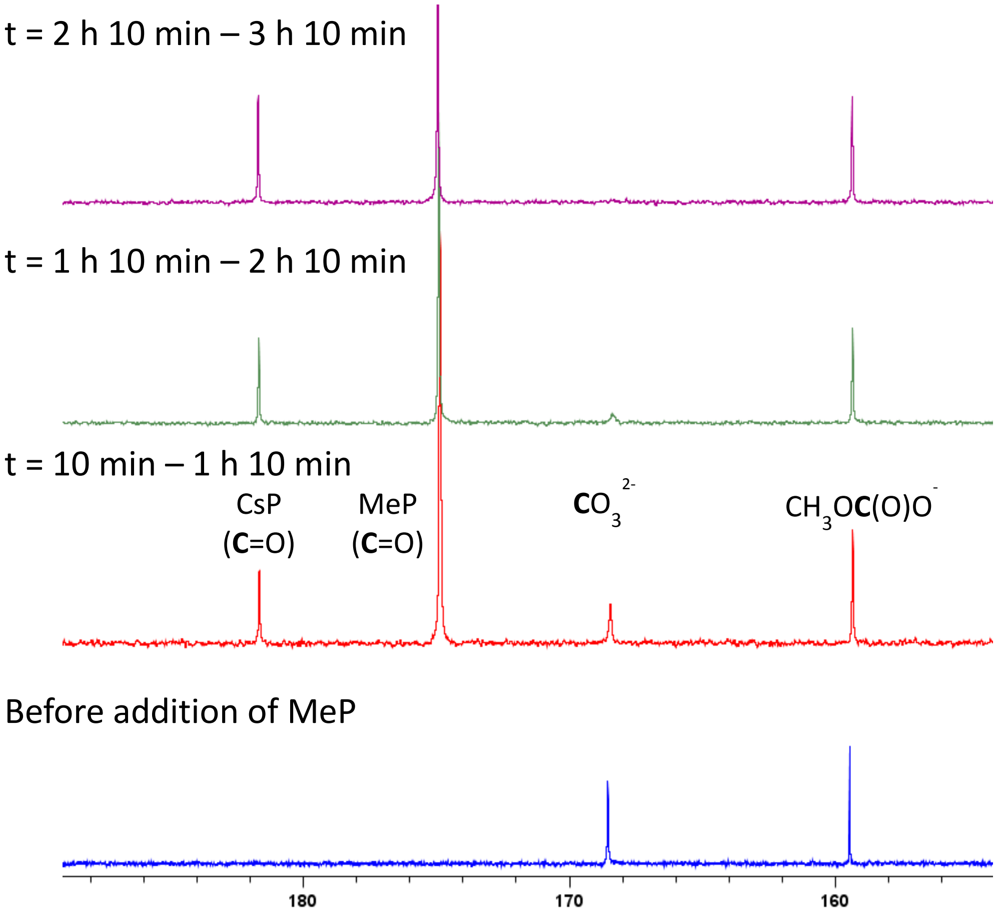
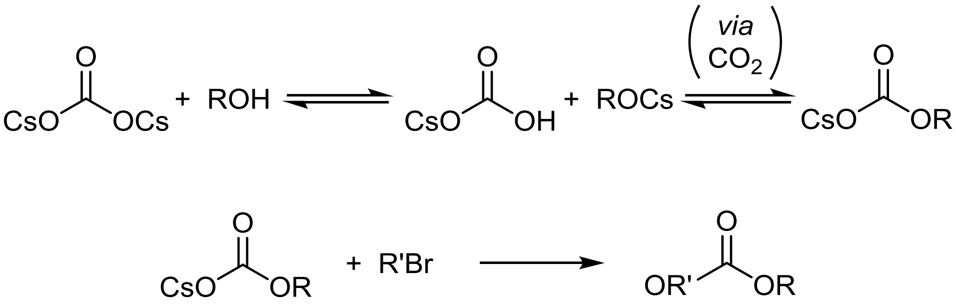


Figure 2.7: Reaction of caesium hydroxide with methyl propanoate giving caesium propanoate drives the carbonate/methylcarbonate equilibrium towards methylcarbonate, the carbonate resonance in the $^{13}C\{^{1}H\}$ NMR spectrum decreases in intensity until it is no longer visible above the baseline.

Transformation of alkali metal carbonates to alkali metal methylcarbonates and alkali metal propanoates in the presence of methanol and methyl propanoate is also observed for rubidium, potassium and sodium, see section 7.5.3. The rate of alkali metal propanoate formation on addition of methyl propanoate to methanolic alkali metal carbonate solutions increases as the group is descended, presumably because the anion is more reactive as it forms a less strongly bound ion pair with the cation.

The presence, even transiently, of the strong base caesium hydroxide in the solution makes caesium hydroxide, rather than caesium carbonate a candidate for the active species in the base catalysed condensation of methyl propanoate with formaldehyde, as it is the strongest base present during the experiment. However, when the commercially available caesium hydroxide monohydrate is used as the base, only 1 % conversion of methyl propanoate to caesium methacrylate (no methyl methacrylate is detected by ^{1}H NMR spectroscopy) was observed with 59 % of the methyl esters converted to caesium carboxylates at 60 molar % loading of caesium hydroxide monohydrate. This suggests that caesium hydroxide is a short-lived species that is consumed by the formation of caesium propanoate from methyl propanoate and is not catalytically active in the condensation reaction.

While the reaction of caesium carbonate with methanol in this system was unexpected, several examples of the alkylation of carbonates with alcohols exist in the literature.[15–24] For example, Jung et al. synthesized mixed alkylcarbonates from caesium carbonate, alcohols and alkyl bromides.[15] In this synthesis, caesium carbonate acts both as a base and as the carbonate source. The authors' mechanistic proposal is that carbon dioxide is formed from collapse of caesium carbonate or caesium bicarbonate and is then attacked by an alkoxide to form a caesium alkylcarbonate intermediate, scheme 2.5. Alkylation of the caesium alkylcarbonate with the alkyl halide pulls the equilibrium towards the unsymmetrical alkylcarbonate products. The formation of this caesium alkylcarbonate intermediate provides precedent for the observed caesium methylcarbonate formation from caesium carbonate and methanol.



Scheme 2.5: Jung et al.'s mechanistic proposal for the synthesis of mixed alkylcarbonates *via* a caesium alkylcarbonate intermediate formed through the reaction of caesium carbonate with an alcohol.[15]

During the condensation reaction experiment, the active caesium carbonate catalyst is converted to the inactive caesium propanoate and caesium methacrylate, meaning that the base is non-recyclable. For a process based on this chemistry to be viable, either the formation of caesium propanoate has to be blocked or the activity of caesium propanoate to promote the condensation reaction of methyl propanoate with formaldehyde has to be significantly increased. These two strategies were explored and are discussed below.

2.2.3 Strategies to prevent the formation of caesium carboxylates

2.2.3.1 Exclusion of methanol

To prevent caesium propanoate formation in the condensation reaction system using caesium carbonate as the promoter requires the complete exclusion of methanol from the system and removal of water as soon as it is produced in the reaction. The addition of activated 3 Å molecular sieves to remove water and prevent hydrolysis did not improve the conversion to methacrylates or decrease the amount of caesium carboxylates formed during the experiment, possibly because the sieves were ground up by the mechanical stirrer, chemically decomposed by the reaction mixture or because the molecular sieves are not sufficiently efficient water scavengers at the relatively high temperatures of the reaction.

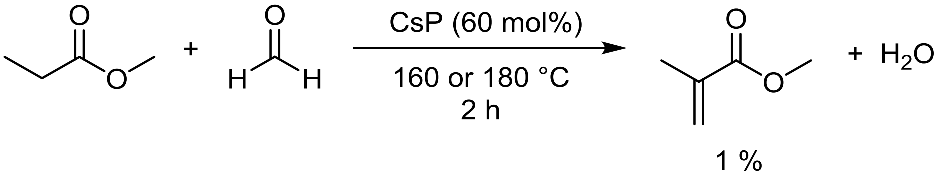
Although it is not possible to exclude methanol completely from the reaction system, as it is an inevitable by-product formed in the Cannizzaro decomposition of formaldehyde, strategies for reducing the methanol concentration in the experiment were investigated to discover if kinetic control of the caesium methylcarbonate formation could afford a viable process.

An alternative formaldehyde source was required as methyl alcoform contains around 45 weight percent methanol. Paraformaldehyde was used as the formaldehyde source in some experiments but lower conversions of methyl propanoate to methacrylates were achieved, presumably because this formaldehyde source has a different (reduced in the manner required) reactivity and/or because some methanol is required in the reaction system to aid the dissolution of the caesium salts. Other formaldehyde sources were considered, including trioxane, dimethoxymethane or gaseous formaldehyde (through design of new equipment) but these formaldehyde sources were not tested due to time constraints.

2.2.3.2 Caesium propanoate as a catalyst for the condensation reaction

As caesium propanoate is formed during the course of the condensation reaction experiments, another strategy to achieve a viable process would be to adjust the process conditions to enhance the activity of caesium propanoate as a base catalyst for the condensation reaction. Coetzee et al. have previously used deuterium scrambling from d_1-methanol into the α-position of methyl propanoate to show that commercially available sodium propanoate is effective in deprotonating methyl propanoate at 160 °C.[25] However, under the same conditions, or at higher temperatures (180 or 220 °C),[2] sodium propanoate is inactive as a base in the condensation reaction of methyl propanoate with formaldehyde; presumably the sodium enolate/carbanion produced from the deprotonation of methyl propanoate is only very weakly nucleophilic because of strong ion pairing between the small sodium cation and the anion.

To determine if the reduced ion pairing expected with caesium would increase the activity of the propanoate base, caesium propanoate was prepared and used in place of caesium carbonate in the base catalysed condensation of methyl propanoate with formaldehyde; minimal activity was observed under the conditions described above, with 1 % of the methyl propanoate converted to methacrylates.



Scheme 2.6: Caesium propanoate is an inactive base in the condensation of methyl propanoate with formaldehyde under the same conditions as with the caesium carbonate-promoted reaction.

The low activity of caesium propanoate in the condensation reaction despite its ability to deprotonate methyl propanoate at the α-carbon implies the active basic species in the reactions described in section 2.2.1 must be either or both caesium carbonate and caesium methylcarbonate. Two reaction pathways can then be proposed: (i) caesium carbonate is highly active but is short-lived, being converted rapidly into inactive caesium propanoate and caesium methylcarbonate; or (ii) both carbonate and methylcarbonate are active catalysts for the reaction. The catalytic activity of caesium methylcarbonate is explored in chapter 3, where it is shown to be an active base in the reaction.

The remainder of this chapter describes the author's work to optimize the caesium carbonate-promoted reaction. If high conversions of methyl propanoate to methacrylates could be achieved, it might be possible to design a viable process if additionally an efficient catalyst recycling method was developed. Knowledge of the maximum single pass conversion of methyl propanoate to methacrylates that can be achieved would allow process cost estimates to be made to determine whether further research into this chemistry and into developing a recycling process was worthwhile. If no major improvement in the conversion of methyl propanoate to methyl methacrylate was possible, then an alternative route, for example using a different base, would have to be sought.

2.2.4 Optimization of the caesium carbonate-promoted condensation of methyl propanoate and formaldehyde

Two issues must be addressed in achieving high conversion of methyl propanoate to methacrylates in this system: (i) the decomposition of formaldehyde which removes an essential substrate from the reaction mixture and (ii) maintaining the base catalyst in the most active form for as long as possible at reaction temperature.

2.2.4.1 Injection of methyl alcoform at high temperature

The experimental protocol used up to this point involved charging the base and reagents into the cold autoclave and then heating them to reaction temperature. Two unwanted reactions occur during the heating phase of the experiment: (i) decomposition of formaldehyde, which is favoured over condensation with methyl propanoate at lower temperatures because the activation barrier for the former reaction is lower than for the latter and (ii) reaction of caesium carbonate, methanol (in the methyl alcoform) and methyl propanoate to give caesium methylcarbonate and caesium propanoate which converts, at least partially, the caesium carbonate to milder bases before reaction temperature is reached.

Ideally, the methyl alcoform solution should be introduced at reaction temperature to minimize decomposition of formaldehyde and the formation of caesium methylcarbonate and caesium propanoate prior to onset of the desired condensation reaction. For this reason, a high pressure injector was designed, constructed and used to inject the methyl alcoform after the autoclave containing the other components of the reaction had been heated. This revised reaction protocol ensured that, (i) the caesium carbonate base did not come into contact with methanol during heating and (ii) the formaldehyde came into contact with hot, reactive methyl propanoate and base, thereby preserving a higher concentration of formaldehyde at reaction temperature.

High temperature injection of methyl alcoform was, however, not without issues. On injection of the methyl alcoform into a mixture of caesium carbonate and methyl propanoate at 160 °C, after a brief decrease in temperature as a result of the cold methyl alcoform contacting the hot mixture, a large temperature spike, up to 209 °C, and pressure increase was observed. The temperature spike was caused by the reaction of methanol (in the methyl alcoform) with caesium carbonate and formaldehyde decomposition, both of which are exothermic and results in poor conversions of methyl propanoate to (methyl and caesium) methacrylates.

The autoclave did not allow for *in situ* cooling of the reaction mixture. In all injection experiments, including in section 2.2.4.2 and chapter 3, when the temperature spike on injection caused the temperature to increase substantially above 160 °C, poorer conversions of methyl propanoate to methacrylates were observed and the exit mixtures contained a thick, black tar. Therefore a lower injection temperature was used to ensure the temperature of the reaction, as measured by an internal thermocouple, did not increase substantially above 160 °C.

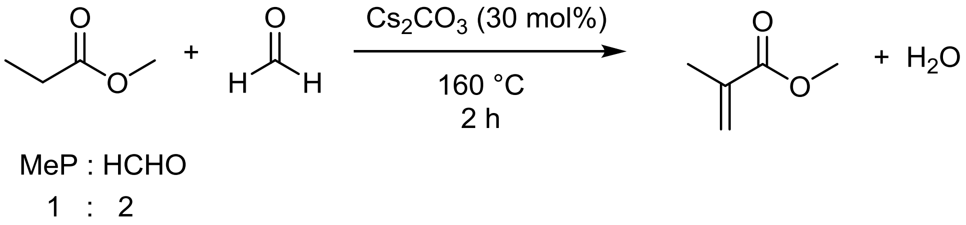


Table 2.1: Controlling the temperature spike on injection of methyl alcoform results in improved conversion of methyl propanoate to methacrylates compared with loading at room temperature.

Entry	Injection temperature / °C	Temperature spike maximum / °C	Conversion to MMA and CsMA / %
1	Loaded at RT	-	6
2	110	128	8
3	128	170	9
4	160	209	4

Injection of the methyl alcoform at 110 or 128 °C results in a reduced temperature spike (compared with injection at 160 °C), affording 8 or 9 % conversion of methyl propanoate to methacrylates, respectively, representing an improvement of 50 % in terms of conversion when both reactants are loaded in at room temperature, compare table 2.1, entries 1-3. This improved conversion is attributed to a higher concentration of formaldehyde at the reaction temperature as a result of reduced formaldehyde decomposition and reduced formation of caesium propanoate during the heating phase of the experiment. High temperature addition of methyl alcoform is essential for improved formaldehyde selectivity, and this issue is addressed further in chapter 4.

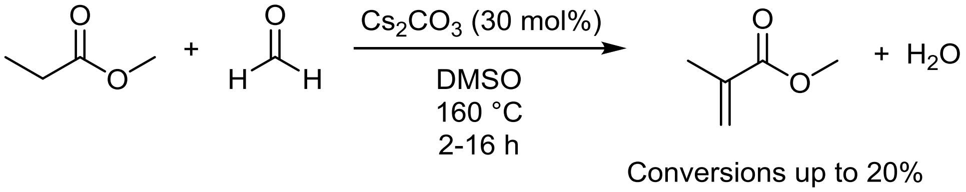
2.2.4.2 Increasing the activity of the base: choice of solvent

Next, attention turned to increasing the reactivity of the base. Caesium carbonate is almost insoluble in methyl propanoate and the reaction mixture is a slurry at the start of the experiment, with the caesium salts becoming more soluble as more methanol, a better solvent for caesium salts, is produced through formaldehyde decomposition. Solvation of the dissolved ions was expected to have a significant impact on the kinetics, selectivity and yield of the reaction.[26–29] Selection of a solvent to solubilize caesium carbonate and to disrupt ion pair formation was identified as an opportunity to increase the concentration and activity of dissolved caesium salts in the reaction mixture.

A polar, aprotic solvent was expected to be the most desirable for this reaction because such solvents are effective cation solvators but poor anion solvators, resulting in reduced ion pairing and less well stabilized, and therefore more reactive (more basic and more nucleophilic) anions.[30] Thus, Bordwell showed that the pK_{aH} of the methoxide anion is 29.0 in dimethyl sulfoxide (DMSO), whereas the calculated pK_{aH} in water is only 15.5,[30,31] demonstrating the large effect that choice of solvent can have on the effective strength of the base. The pK_{aH} values of bases in other polar, aprotic solvents including *N*-methyl-2-pyrrolidone (NMP) and *N*,*N*-dimethylformamide (DMF) were found to be comparable to that in DMSO.[32]

Furthermore, the enolate species produced through deprotonation of methyl propanoate will be more nucleophilic in a polar, aprotic solvent. For example, Zaugg showed that the rate of alkylation of a pre-prepared enolate species was increased by 970 times in DMF and by 1420 times in DMSO compared with that when the reaction was performed in benzene.[29,30]

DMSO, which is the polar, aprotic solvent of choice for many reactions,[30] was the first polar, aprotic solvent tested and afforded promising results, scheme 2.7. The formaldehyde lifetime and/or catalyst activity was significantly enhanced, with up to 20 % conversion of methyl propanoate to methacrylates achieved.



Scheme 2.7: Improved conversions of methyl propanoate to methacrylates could be achieved when DMSO was used as a polar, aprotic solvent.

However, inconsistent results were obtained with different batches of DMSO giving widely varying conversions. This was attributed to the highly hygroscopic nature of DMSO, resulting in varying amounts of hydrolysis of methyl esters, and to varying concentrations of other impurities, which are known to have a great impact on the properties, stability and reactivity of DMSO.[33]

The exit mixtures of reactions in DMSO always smelled strongly sulphurous, indicating solvent decomposition occurs during the experiment. While pure DMSO is stable up to or slightly above its boiling point of 189 °C,[34] autocatalytic exothermic decomposition reactions are known to occur at higher temperatures. The presence of acids, bases or halides in the reaction mixtures all reduce the temperature of the onset of these autocatalytic decomposition reactions.[33,35,36]

Furthermore, it is known that DMSO can be deprotonated by strong bases [37,38] and that the dimethylsulfinyl anion is less stable than DMSO.[39] To probe if the DMSO was being deprotonated under reaction conditions, an experiment was performed in d_6-DMSO, inspired by a similar study by Clark et al.[40] ^{2}H NMR showed that the label is scrambled into the methylene groups of both methyl propanoate and caesium propanoate as well as the hydroxyl group of methanol ($CH_3O\mathbf{D}$) confirming that DMSO is deprotonated under reaction conditions. For these reasons, an alternative polar, aprotic solvent was sought that would be more stable and safer in use. *N*,*N*-dimethylformamide (DMF) was also discounted as a result of concerns about its stability of under basic conditions[41] and exothermic runaway reactions with strong bases.[42]

Of other polar, aprotic solvents, *N*,*N*-dimethylacetamide (DMAc or DMA) is commonly used [27] and there is a recent report in which *N*,*N*-dimethylacetamide has been used as a solvent at 150 °C in the presence of potassium carbonate and no solvent decomposition was noted.[43] Furthermore, Clark et al. reported that *N*,*N*-dimethylacetamide is a preferable solvent for reactions when using tetramethylammonium fluoride compared with DMSO, effectively breaking up ion pairs, obtaining improved yields in their reactions and improved solvent stability,[44] although they did note deprotonation of *N*,*N*-dimethylacetamide by tetramethylammonium fluoride or potassium hydroxide in other reports, as well as by-products formed from nucleophilic attack of the solvent on other reaction components.[38] These reports encouraged us to investigate the condensation reaction in *N*,*N*-dimethylacetamide, table 2.2.

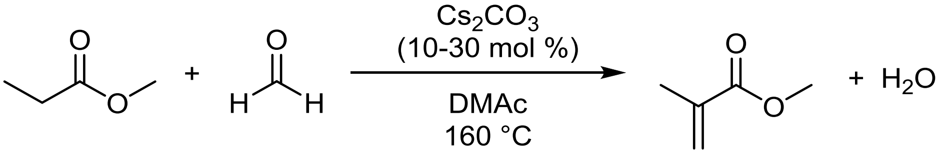


Table 2.2: Conversion of methyl propanoate to methacrylates using DMAc as solvent. *Propanoic acid (PA) is produced when all caesium cations are coordinated to propanoate or methacrylate anions.

Entry	Cs_2CO_3 loading / mol%	Reaction time / hours	Conversion to methacrylates by ^{1}H NMR / %	CsP + CsMA formed from MeP + MMA / %
1	30	2	14	31
2	20	2	11	26
3	20	4	19	24
4	20	16	25	40 (+3% PA*)
5	10	2	6	16
6	40% CsP as base	2	4	N.D

N,N-dimethylacetamide proved to be a useful solvent affording improved conversion of methyl propanoate to methacrylates to 14 %, compared with 9 % under solvent-free conditions, compare table 2.1, entry 2 with table 2.2, entry 1. Dilution of the reaction mixture also reduced the temperature spike on injection allowing the reactants to be injected at higher temperatures (injection at 140 °C was possible without the temperature spike increasing above 160 °C). The reduced temperature spike on dilution can be attributed better heat dissipation through the mixture because of the high heat capacity of the *N,N*-dimethylacetamide.

The initial reaction rate is affected by base loading, compare table 2.2, entries 1, 2 and 5. However, experiments with either 30 mol% or 20 mol% (relative to methyl propanoate) caesium carbonate loading result in similar conversion of methyl propanoate to methacrylates. Further reduction in base loading led to a very low initial rate of reaction, table 2.2, entry 5.

The addition of solvent to the reaction mixture also resulted in increased formaldehyde lifetime, allowing longer productive reaction times, with up to 19 % conversion of methyl propanoate to methacrylates being achieved when the reaction time was doubled from 2 to 4 hours, table 2.2, entries 2 and 3.

With long reaction time, greater than stoichiometric conversions on carbonate loading was achieved; 25 % conversion of methyl propanoate at 20 mol% caesium carbonate loading, table 2.2, entry 4. Whilst the turnover number on carbonate is still low, this was the first time that a turnover number greater than one on carbonate, i.e. the first time that “catalytic conversions” were achieved.

A third set of propanoate resonances were present in the ^{1}H NMR spectrum of the exit mixture, characterized as propanoic acid. As all of the caesium cations were coordinated to propanoate and methacrylate anions at 40 % hydrolysis (the caesium cation loading), any further hydrolysis results in the formation of carboxylic acids. Surprisingly, proton exchange in these mixtures is sufficiently slow that the propanoic acid resonances are separated from the caesium propanoate resonances in the ^{1}H NMR spectrum. In this experiment, the caesium carbonate is fully converted to caesium propanoate and caesium methacrylate, with no other caesium salts in the exit mixture.

The activity of caesium propanoate is enhanced under these optimized, solvent assisted conditions, affording 4 % conversion of methyl propanoate to methacrylates, table 2.2, entry 6. The activity enhancement for caesium propanoate is insufficient to make caesium propanoate a viable catalyst candidate for this process.

2.2.4.3 Stability of *N*,*N*-dimethylacetamide under reaction conditions

Under the relatively harsh reaction conditions used, *N*,*N*-dimethylacetamide is deprotonated and reacts with formaldehyde in an analogous manner to methyl propanoate, affording the *α*,*β*-unsaturated *N*,*N*-dimethylacrylamide (dimethyl prop-2-enamide) which has been characterized by comparison of its ^{1}H NMR spectrum with the literature,[45] figure 2.8. Approximately 1% of the *N*,*N*-dimethylacetamide reacted in this way, showing that methyl propanoate is more reactive than *N*,*N*-dimethylacetamide as would be expected (protons in the *α*-position to amides are less acidic than those of esters).

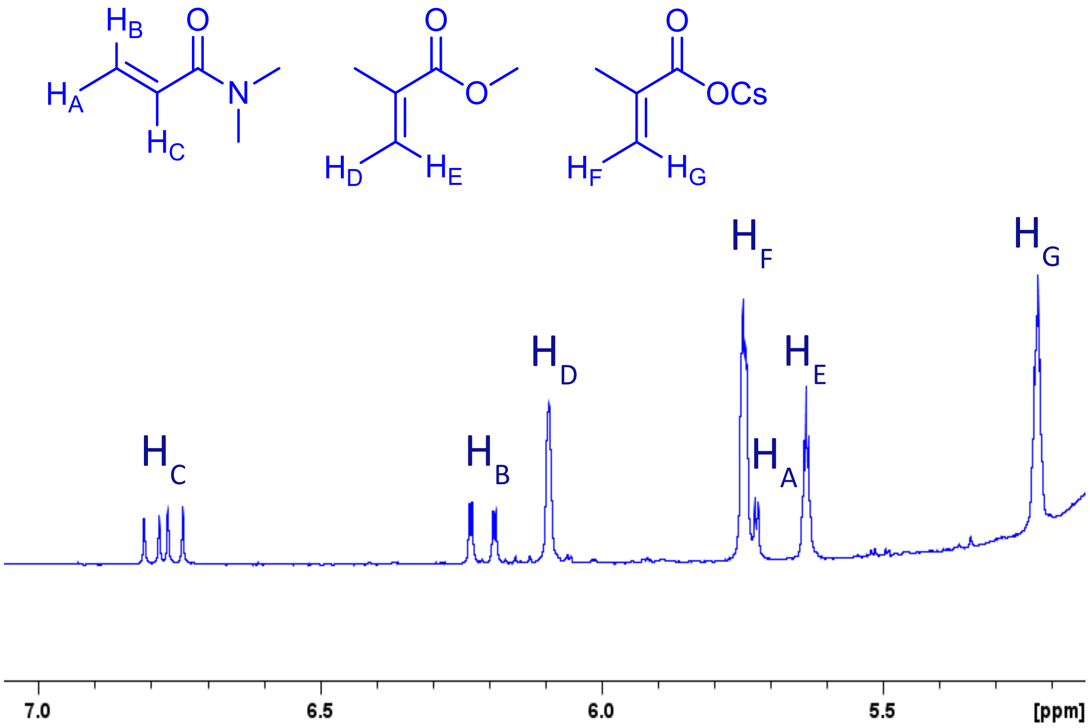


Figure 2.8: New resonances (H_A, H_B, H_C) are observed in the olefinic region of the ^{1}H NMR spectrum when DMAc is used as a solvent, as a result of condensation of DMAc with formaldehyde.

A small amount of methyl acetate, formed through reaction of *N*,*N*-dimethylacetamide with methanol and a minor amount of caesium acetate, formed through hydrolysis and subsequent deprotonation was also detected in these reactions, figure 2.9.

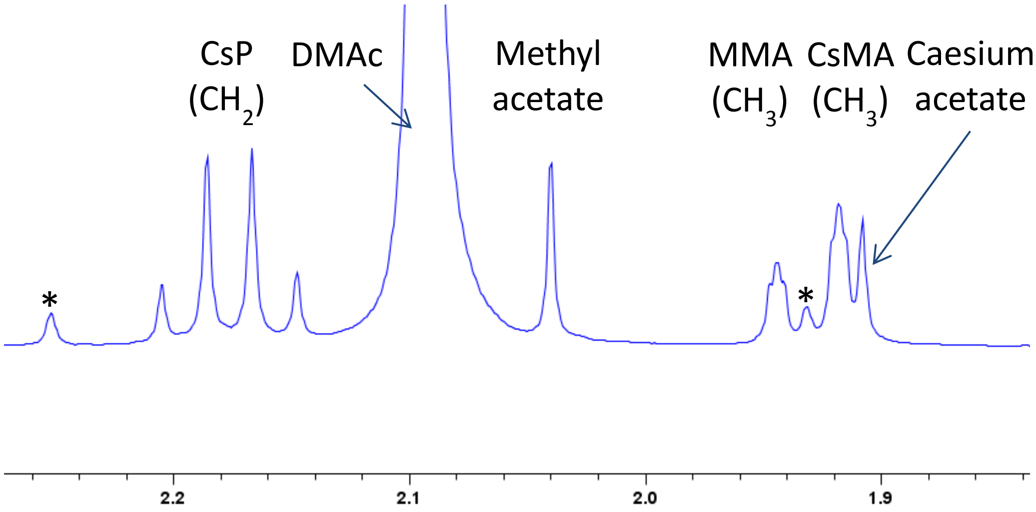


Figure 2.9: Hydrolysis of DMAc to caesium acetate (1.91 ppm) and esterification with methanol to methyl acetate (2.04 ppm) is observed. * ^{13}C satellites of the DMAc peak at 2.09 ppm.

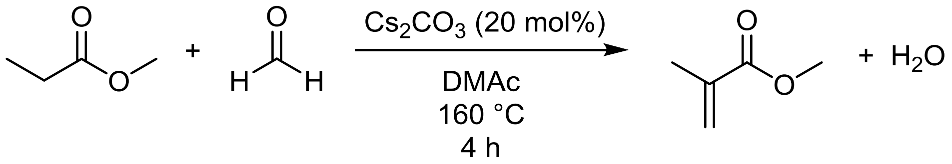
With the exception of these three minor side-reactions *N*,*N*-dimethylacetamide is stable under the reaction conditions (unlike DMSO) and the improvement in conversions achieved is significant. *N*,*N*-dimethylacetamide, however, is not an attractive solvent for industrial processes; it is a mutagen and is listed as 'hazardous' in a recent survey of various pharmaceutical companies solvent selection guides (its classification ranges from 'problematic' by Astra Zeneca to 'substitution required' by Sanofi).[46] However owing to the reproducibility of the catalytic activity with new batches of *N*,*N*-dimethylacetamide (in contrast to DMSO), it was taken forward as the solvent of choice at this stage and attention turned to other parts of the project. For any process based on this chemistry to be viable, the choice of solvent would have to be re-visited to find an alternative, more benign solvent. This issue is addressed in chapter 5.

2.2.5 Selectivity on methyl propanoate

With optimized conversions of methyl propanoate, the selectivity on methyl propanoate for methyl methacrylate was determined. Samples were vacuum distilled and analysed by GC-MS at Lucite International. Only the volatile material was collected by this method so the formation of non-volatile by-products (e.g. carboxylate compounds bound to caesium) was only determined by NMR spectroscopy.

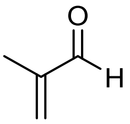
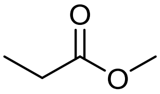
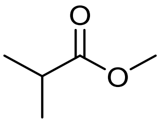
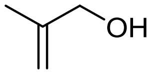
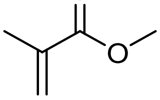
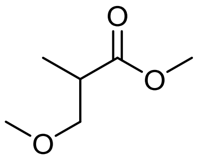
The caesium carbonate-promoted condensation reaction of methyl propanoate and formaldehyde with *N*,*N*-dimethylacetamide as the solvent is remarkably clean, table 2.3. The selectivity for methyl methacrylate from methyl propanoate is 96.8 % (excluding caesium propanoate, caesium methacrylate, which can be recycled back to either methyl propanoate or methyl methacrylate, see chapter 3), with only four by-products detected: methacrolein (0.05 % vs MMA), 2-methyl propenol (0.14 %), methyl isobutyrate (0.10 %) and methyl 3-methoxy-2-methyl propionate (2.90 %).

Methyl-3-methoxy-2-methyl propionate, which corresponded to over 90 % of the volatile by-products, is formed from addition of methanol across the double bond of methyl methacrylate, a reaction that can be reversed under the right conditions to give methyl methacrylate.[2] Thus the overall selectivity on methyl propanoate in this system approaches 99.7 %. This compares very favourably with the selectivity of the current heterogeneous process of around 93 %.



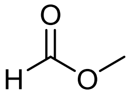
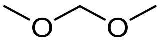
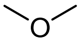
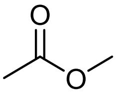
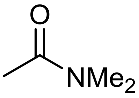
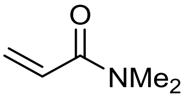
19 % conversion to methacrylates
99.7 % selectivity on methyl propanoate

Table 2.3: Volatile methyl propanoate-derived species from the caesium carbonate-promoted condensation reaction of methyl propanoate and formaldehyde with DMAc as the solvent.

Entry	Compound	Chemical structure	Source	Amount / mol%
1	Methacrolein		Reduction of MeP then condensation with formaldehyde	0.05
2	Methyl propanoate		Starting material	81.31
3	Methyl isobutyrate		Reduction of MMA	0.10
4	2-Methyl propenol		Reduction of methacrolein	0.14
5	Methyl methacrylate		Product	15.5
6	Methyl 3-methoxy-2-propionate		Michael addition of methanol to MMA	2.90

The other compounds produced from the methyl propanoate feed contribute 0.29 %. Methacrolein is produced through reduction of methyl propanoate (possibly through hydride transfer during Cannizzaro formaldehyde decomposition) and subsequent condensation of the propanal intermediate with formaldehyde. 2-methyl propenol can then be formed through further reduction at the aldehyde of methacrolein. Methyl isobutyrate can be formed through reduction of the C=C double bond of methyl methacrylate, again through a hydride transfer reaction. Another possibility for the formation of this by-product is through a methylation of methyl propanoate with methanol, although this seems very unlikely.

Table 2.4: Compounds detected by GC that do not originate from methyl propanoate. [a] The amount of each compound present was calculated as a molar percentage compared to methyl methacrylate.

Entry	**Compound**	**Structure**	**Source**	**Amount in sample [a] / %**
1	Methyl formate		Cannizzaro formaldehyde decomposition intermediate	N.D
2	Dimethoxymethane		Condensation of hemiformal with methanol	0.25
3	Dimethyl ether		Condensation of two methanol molecules	0.13
4	Methyl acetate		DMAc methanolysis	1.95
5	*N*,*N*-Dimethylacetamide		Solvent	N.D
6	*N*,*N*-Dimethylacrylamide		DMAc condensation with formaldehyde	N.D
7	Other unidentified compounds			< 0.26

Other compounds, not derived from methyl propanoate that were identified in the GC and GC-MS traces of the volatile material, include methyl formate (an intermediate in the Cannizzaro reaction of formaldehyde), *N,N*-dimethylacetamide, *N,N*-dimethyl acrylamide (formed from reaction of *N,N*-dimethylacetamide with formaldehyde), methyl acetate (methanolysis of *N,N*-dimethylacetamide), dimethoxymethane (condensation of methanol with formaldehyde) and dimethyl ether (condensation of two methanol molecules), table 2.4. As none of these compounds were formed from methyl propanoate or methyl methacrylate, they can be discounted in the calculation of selectivity on methyl propanoate.

2.2.6 Selectivity on formaldehyde

Whilst the selectivity on methyl propanoate for methyl methacrylate was extremely high, the selectivity based on formaldehyde was significantly less than the current ALPHA Stage Two process. Formaldehyde conversion in the reactions reported above was essentially 100 %, corresponding to a maximum selectivity on formaldehyde of around 12.5 % (as two molar equivalents of formaldehyde were fed into the reaction and 25 % conversion of methyl propanoate was achieved). Clearly, for any process based on this chemistry to be viable, the selectivity on formaldehyde must be improved. The author’s work to address formaldehyde selectivity is reported in chapter 4.

2.3 Conclusions

A low temperature system for the production of methyl methacrylate and caesium methacrylate from methyl propanoate and formaldehyde, promoted by caesium carbonate has been developed, giving excellent selectivity for methacrylates from methyl propanoate (excluding hydrolysis of methyl esters). Conditions have been optimized to achieve conversions of methyl propanoate of up to 25 %, through injection of both methyl propanoate and methyl alcoform into a hot mixture of caesium carbonate and *N*,*N*-dimethylacetamide. Use of this polar, aprotic solvent aids dissolution of the caesium salts into the reaction mixture and breaks up ion pairing. The cations are well solvated by the solvent; however the anions are not well solvated providing more active anionic species increasing the activity of the anions in the catalysis.

An additional benefit of the diluting solvent is a reduction in the temperature spike that occurs on injection of the reactants into the reactor. The temperature spike is caused in part by the methanol in the methyl alcoform, which reacts exothermically with caesium carbonate to give caesium methylcarbonate and by exothermic formaldehyde decomposition reactions. Two further process benefits result from injection of reactants: the lifetime of the carbonate at reaction temperature is increased since formation of caesium methylcarbonate and caesium propanoate during the heating phase of the reaction is avoided and formaldehyde decomposition during heating is prevented.

Methanol is an unavoidable component in the reaction mixture. Its reaction with caesium carbonate produces an equilibrium mixture of carbonate and its methyl ester, caesium methylcarbonate along with caesium hydroxide. This reaction occurs even at room temperature. The caesium hydroxide formed is responsible for the formation of caesium propanoate and methanol from methyl propanoate. More caesium propanoate and caesium methacrylate are formed in these experiments than the stoichiometry of the condensation reaction allows. The reason for this is the reaction of methanol with caesium carbonate acting as a source of hydroxide, leading to base deactivation.

Caesium propanoate has been shown to be very weakly active as a base catalyst for the condensation reaction, even under optimized conditions. Caesium propanoate and caesium methacrylate formation means that caesium carbonate in this system is a non-recyclable base – the exit non-volatiles cannot be re-used for another cycle of reaction. An important pre-requisite for any process to be commercially viable is that the catalyst can be recycled for a number of runs. To make this possible with this system, a base recycling reaction has to be developed that could convert these inactive bases into more active bases. The author’s work towards a recycling process is discussed in chapter 3.

The improved selectivity on methyl propanoate compared with the current high temperature, heterogeneous ALPHA Stage Two process is attributed to the milder conditions used and as this catalyst system contains no acidic sites, compared with the solid catalyst used where additional chemical transformations can take place at the acidic silanol sites. Whilst the selectivity for methyl methacrylate based on the methyl propanoate feed was excellent, the selectivity on formaldehyde was poor. The maximum formaldehyde selectivity was 12.5 % (100 % conversion of formaldehyde with two molar equivalents of formaldehyde fed in the experiment) and would need to be improved further for a commercially viable process to be achieved. The author's work on this is discussed in chapter 4.

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Chapter Three

Caesium methylcarbonate as an active and recyclable base in the condensation of methyl propanoate with formaldehyde

3. Caesium methylcarbonate as an active and recyclable base in the condensation of methyl propanoate with formaldehyde

3.1 Introduction

The previous chapter showed there are two mechanisms by which caesium propanoate and caesium methacrylate are produced during the caesium carbonate-promoted condensation of methyl propanoate with formaldehyde:

1. As a result of reaction with the caesium hydroxide co-product in the reaction of caesium carbonate and methanol.
2. Through base-catalysed hydrolysis from water produced in the condensation reaction.

This means caesium carbonate is a non-recyclable base in this system as it is converted to inactive bases during the experiment. For any process based on the chemistry developed in the previous chapter to be practical, the formation of caesium carboxylate waste has to be prevented, or a method for recycling caesium propanoate and caesium methacrylate back to an active base must be developed. As prevention of base decomposition in this system is not possible, methods for regeneration of an active base have been developed. As well effecting a base reactivation, the regeneration should convert the caesium propanoate and caesium methacrylate to their methyl esters as the loss of propanoate and methacrylate materials as waste is not acceptable.

Caesium methylcarbonate was chosen as the most attractive target molecule for base regeneration because use of this base effectively removes a source of hydroxide from the reaction system compared with caesium carbonate, but is sufficiently basic to act as a catalyst in the condensation reaction of methyl propanoate and formaldehyde under the preferred reaction conditions, whereas caesium propanoate and caesium methacrylate are not. The intermediate base strength of caesium methylcarbonate is an important advantage because it means that the regeneration of the base from caesium propanoate and caesium methacrylate is relatively straightforward but the high activity and extremely high selectivity in the condensation of methyl propanoate with formaldehyde is maintained.

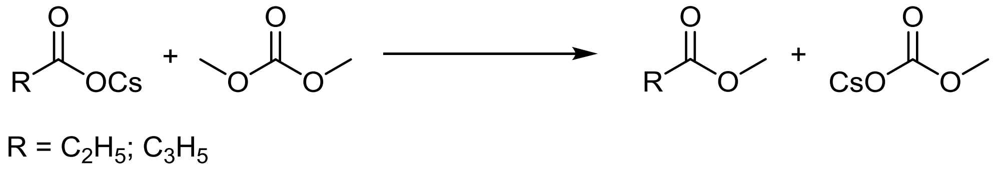
Methylcarbonate salts have been reported only in a limited number of cases. A report from 1973 described the synthesis of a range of alkali metal methylcarbonates (Li, Na, K, Rb, Cs, Tl) through reaction of alkali metal methoxides with carbon dioxide.[1] Sodium[2] and potassium methylcarbonates[3] have since been characterized by X-ray crystallography and lithium methylcarbonate has been synthesized by the same method and characterized by NMR spectroscopy.[4] More recently, a number of methylcarbonate ionic liquid salts have been reported.[5–8] However, no reports of the use of alkali metal methylcarbonates as basic catalysts could be found. Only one report where caesium methylcarbonate is proposed as a catalytic intermediate was found.[9]

This chapter describes the development of two new synthetic routes to these alkali metal methylcarbonates and investigations into the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde.

3.2 Results and Discussion

3.2.1 Methylation of caesium carboxylates with dimethyl carbonate

The most atom efficient method for the esterification of caesium propanoate and caesium methacrylate to methyl propanoate and methyl methacrylate with co-production of caesium methylcarbonate is through direct methyl transfer with dimethyl carbonate, scheme 3.1.

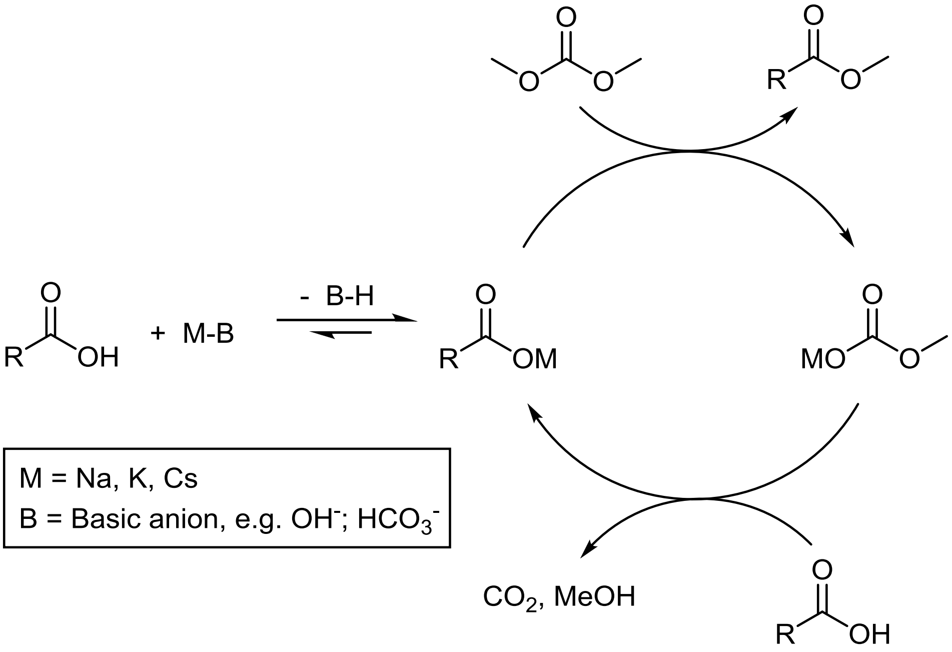


Scheme 3.1: Direct methyl transfer of dimethyl carbonate onto caesium propanoate or methacrylate.

Dimethyl carbonate is a readily available “green”, non-toxic compound.[10,11] It has a tuneable reactivity, behaving as a methoxycarbonylating reagent with some nucleophiles at temperatures around its boiling point (90 °C) or as a methylating reagent, usually at higher temperatures.[12] Traditionally prepared from phosgene, it is now prepared from carbon monoxide and methanol in a catalytic oxidative carbonylation reaction.[13]

A number of studies have shown base-catalysed methyl esterification of (deprotonated) carboxylic acids using dimethyl carbonate is possible under a wide variety of conditions, usually run with stoichiometric loadings of base at high temperatures (130-250 °C in autoclaves).[9,14–21]

In a recent paper, Gorin et al. have used catalytic loadings of basic alkali metal salts as catalysts for the esterification of various carboxylic acids with dimethyl carbonate under mild conditions (90 °C), with the aid of DMSO as a polar, aprotic solvent.[22] An ^{18}O labelling study suggested the esterification occurred by direct methyl transfer from dimethyl carbonate (the dimethyl carbonate acts as a methylating reagent, rather than a methoxycarbonylating reagent).

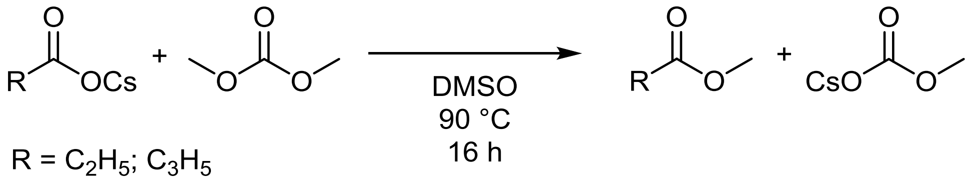


Scheme 3.2: Proposed catalytic cycle for the alkali metal salt catalysed esterification of carboxylic acids with dimethyl carbonate.[22]

Our mechanistic proposal is that the basic salts act as pre-catalysts. Deprotonation of the carboxylic acid with the basic alkali metal salt acts as a pre-equilibrium to the catalytic cycle, forming an alkali metal carboxylate, scheme 3.2. Methylation of the alkali metal carboxylate with dimethyl carbonate produces methyl ester and an alkali metal methylcarbonate. Under acidic conditions (excess carboxylic acid is used), the methylcarbonate salt is protonated to the conjugate acid, hydrogen methylcarbonate.

Hydrogen methylcarbonate has been shown to be unstable to acidic conditions and decomposes to carbon dioxide and methanol.[23,24] Once the excess acid is converted to ester, the alkali metal methylcarbonate is the inorganic salt left at the end of the experiment.

We recognized the system above could be used to convert caesium propanoate and caesium methacrylate (pre-formed alkali metal carboxylates) to methyl esters and caesium methylcarbonate in the absence of carboxylic acid, scheme 3.3. Mimicking the conditions used by Gorin, but using caesium propanoate as base and excluding acidic species, caesium methylcarbonate and methyl propanoate can be prepared.



Scheme 3.3: Caesium methylcarbonate and methyl ester can be formed from pre-formed caesium carboxylates and dimethyl carbonate using the conditions used by Gorin et al.[22]

However, using DMSO as the solvent, a brown non-volatile oil forms through decomposition of DMSO during the experiment and remains with the caesium methylcarbonate after removal of the volatile material by vacuum distillation, contaminating the caesium methylcarbonate. A polar, aprotic solvent is a vital reaction component, effectively increasing the reactivity of the caesium carboxylate. No conversion of caesium propanoate to caesium methylcarbonate and methyl propanoate is observed in the absence of polar, aprotic solvent or with methanol as solvent. Caesium propanoate is the only salt recovered from experiments run in the absence of a polar, aprotic solvent.

Oil formation can be avoided by using *N*,*N*-dimethylacetamide as the solvent. Owing to the lower solubility of these salts in *N*,*N*-dimethylacetamide compared with DMSO, the reaction is heterogeneous in this solvent, making the isolation of the salts simpler as caesium methylcarbonate can be collected through filtration of the cooled exit mixture. Because caesium propanoate is more soluble than caesium methylcarbonate in the reaction mixture, the purity of the isolated salts increases using this isolation method from around 95:5 caesium methylcarbonate : caesium propanoate to greater than 98:2.

Caesium methylcarbonate can also be prepared from caesium methacrylate or a mixture of caesium propanoate and caesium methacrylate (representative of the exit non-volatile salts from the condensation reaction of methyl propanoate with formaldehyde) with no significant decrease in the yield or purity, table 3.1, entry 2.

Potassium or rubidium methylcarbonates can also be prepared by this procedure in similar purities, table 3.1. Sodium methylcarbonate was also prepared by this method; however, its extremely low solubility in methanol meant the purity of the product could not be determined by the NMR spectroscopic assay used.

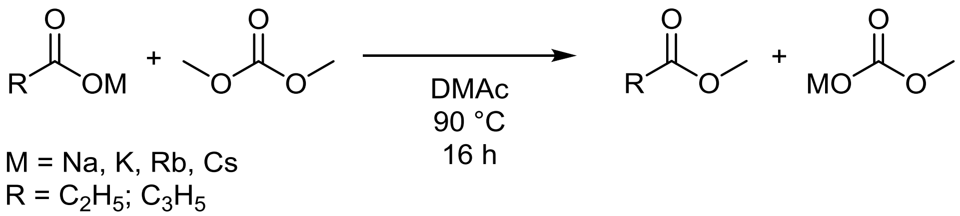


Table 3.1: Alkali metal methylcarbonates can be prepared through the methylation of the corresponding propanoate or methacrylate salts. A 20-fold excess of dimethyl carbonate (relative to alkali metal carboxylate) was used. N.D = not determined due to the low solubility of the sodium salt in methanol.

Entry	**Starting material**	**Yield / %**	**Methylcarbonate purity (vs carboxylate) / %**
1	CsP	62.9	99.8
2	CsMA	65.1	98.0
3	RbP	72.3	>99.9
4	KP	65.0	99.1
5	NaP	70.4	N.D

The filtrate can be re-used several times without a noticeable reduction in yield or purity of the caesium methylcarbonate. A pale yellow colour develops in the liquid phase after several runs but makes no difference to the reaction and can be washed from the solid during filtration with a suitable solvent such as methyl propanoate or ethyl acetate. The methylation of caesium propanoate with dimethyl carbonate could be progressively scaled up from a 6 g scale to 96 g.

Although the caesium methylcarbonate produced using this protocol was not analytically pure – caesium propanoate was always detectable in the ^{1}H NMR spectrum of the salt (usually at less than 2 % of the total caesium salts), removal of trace amounts of caesium propanoate, caesium methacrylate or caesium hydroxide is not required since these will have negligible effect on the catalytic reaction and any process based on the use of caesium methylcarbonate as a base would have to be robust enough to tolerate small amounts of these impurities in the catalyst sample.

3.2.2 Caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde

Caesium methylcarbonate is a more preferable base in the condensation of methyl propanoate and formaldehyde than caesium carbonate. At the same caesium cation loading (the same number of basic sites), at least equal conversion of methyl propanoate to methacrylates is achieved, with less caesium propanoate and caesium methacrylate produced, table 3.2, as a source of caesium hydroxide (from caesium carbonate) is removed from the system.

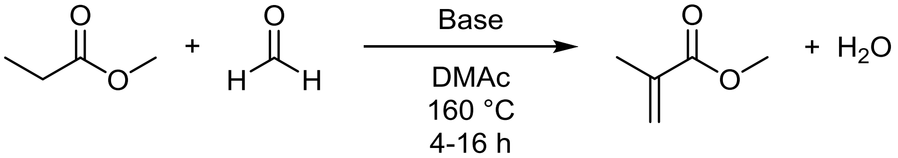


Table 3.2: Using caesium methylcarbonate as the base results in reduced hydrolysis of methyl esters in the condensation of methyl propanoate with formaldehyde, compared with caesium carbonate.

Entry	Base	Reaction time / hours	Conversion to methacrylates / %	CsP + CsMA formed / %	Selectivity on MeP (by GC) / %
1	Cs_2CO_3 (20 mol%)	4	19	24	96.80
2	CsMC (40 mol%)	4	21	18	99.25
3	Cs_2CO_3 (20 mol%)	16	25	43	N.D
4	CsMC (40 mol%)	16	25	37	N.D

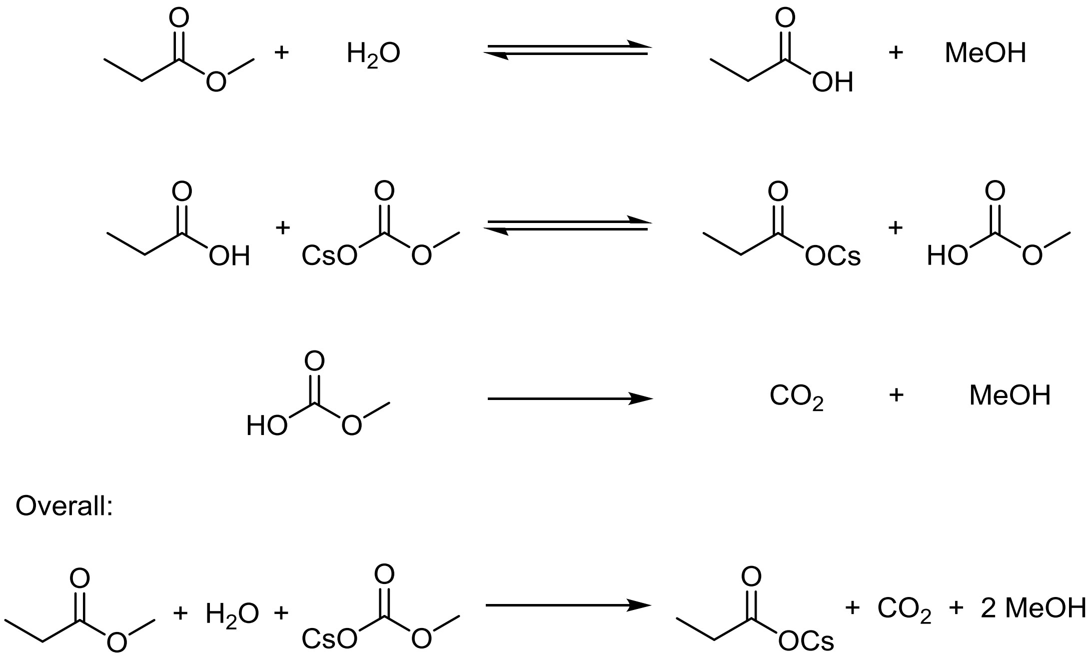
The selectivity on methyl propanoate is increased from 96.8 % to 99.25 % with caesium methylcarbonate compared with caesium carbonate, table 3.2 entries 1 and

2. Three of the four by-products (methacrolein, methyl isobutyrate and 2-methyl propenol) are observed at similar levels in both systems but less methyl 3-methoxy-2-propionate is formed in the caesium methylcarbonate system.

Hydrolysis of methyl propanoate and methyl methacrylate is still observed as a result of base-catalysed hydrolysis with the water co-product of the condensation reaction. The consumption of the water co-product is strongly favoured. In the 16 hour experiment with caesium methylcarbonate and in some experiments in chapters 4 and 5, the amount of hydrolysis is greater than the stoichiometry of the condensation allows (i.e. there is more hydrolysis of methyl esters than conversion of methyl propanoate to methacrylates).

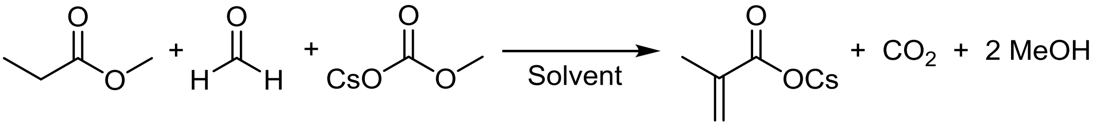
Around 4-5 % of the *N*,*N*-dimethylacetamide reacts with formaldehyde to form *N*,*N*-dimethylacrylamide and water (see section 2.2.4.3) in the 16 hour experiment, table 3.2, entry 4. This extra water produced (the molar ratio of *N*,*N*-dimethylacetamide to methyl propanoate is 2.2:1), along with small amounts of water produced through dimethyl ether and dimethoxymethane formation explains the extra hydrolysis observed. An explanation for why the consumption of water is so strongly favoured is required and so the consequences of base-catalysed hydrolysis were considered, scheme 3.4.

Base-catalysed hydrolysed of methyl esters results, initially, in the formation of the corresponding carboxylic acid, scheme 3.4. Deprotonation of the acid with caesium methylcarbonate is strongly favoured, yielding the caesium carboxylate (caesium propanoate or caesium methacrylate) and hydrogen methylcarbonate. Hydrogen methylcarbonate decomposes to carbon dioxide and methanol,[23,24] acting as an entropic driving force for hydrolysis in the caesium methylcarbonate system; four molecules are produced from three in the forwards direction. As a result, essentially 100 % of the water produced in the condensation reactions is consumed through hydrolysis of methyl propanoate and methyl methacrylate.



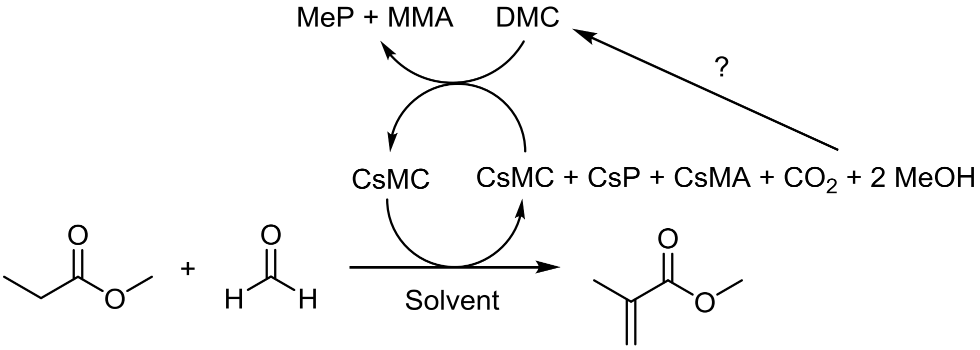
Scheme 3.4: Hydrolysis of methyl esters is entropically favoured as a result of hydrogen methylcarbonate decomposition to carbon dioxide and methanol.

The consumption of caesium methylcarbonate through hydrolysis of the methyl esters to caesium carboxylates effectively makes it a stoichiometric promoter rather than a catalyst, scheme 3.5, even though the condensation reaction mechanism, as drawn is catalytic in base. So long as the caesium methylcarbonate could be regenerated from the caesium carboxylates, multiple turnovers on caesium could be achieved through reaction-regeneration cycles, an important pre-requisite for a process to be commercially viable.



Scheme 3.5: Caesium methylcarbonate behaves more as a stoichiometric promoter of the condensation reaction as a result of hydrolysis of methyl esters with the water co-product. N.B. a mixture of caesium propanoate and caesium methacrylate are formed.

The caesium carboxylates formed in the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde through base-catalysed hydrolysis could be recycled back to caesium methylcarbonate and methyl esters using excess dimethyl carbonate, using the system developed in 3.2.1. This means a process based on this chemistry that allows for multiple turnovers on caesium can be designed, scheme 3.6.



Scheme 3.6: Recycling of the caesium methylcarbonate promoter is possible, allowing a process to be proposed based on this chemistry.

Two issues arise from this proposed process, however: (1) the process as drawn would require three steps (i) dimethyl carbonate production, (ii) condensation reaction, (iii) caesium methylcarbonate regeneration, introducing extra process steps and complexity and (2) conversion of (excess) relatively high value dimethyl carbonate to the low value greenhouse gas, carbon dioxide during the process. Preferably, the process would produce dimethyl carbonate from carbon dioxide, which has been recently reviewed,[25] although no commercially viable process for this reaction has been developed yet.

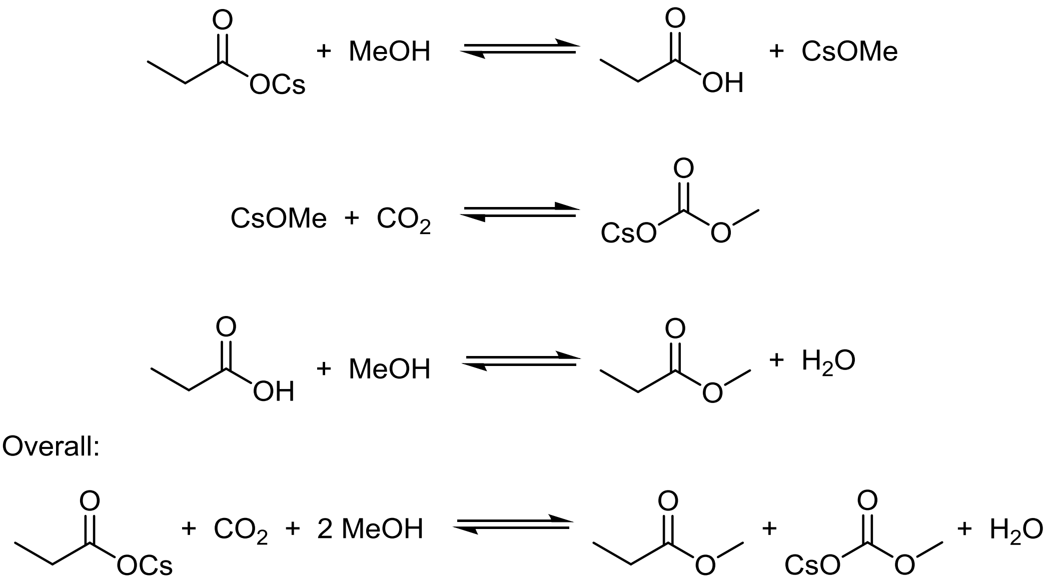
Without significant improvements to the dimethyl carbonate promoted regeneration, which is re-visited in chapter 5, section 5.2.4, this process is very unlikely to be economically attractive. For this reason, an alternative caesium methylcarbonate regeneration process, utilising cheaper raw materials was investigated.

3.2.3 Caesium methylcarbonate formation from carbon dioxide and methanol

The hydrolysis of methyl propanoate and methyl methacrylate in the caesium methylcarbonate-promoted condensation reaction involves three equilibria (see scheme 3.4, above): (i) hydrolysis of the ester with water (ii) deprotonation of the formed carboxylic acid with caesium methylcarbonate (iii) decomposition of hydrogen methylcarbonate to carbon dioxide and methanol.

The increase in entropy in the decomposition of hydrogen methylcarbonate acts as a driving force for the equilibria, resulting in complete or almost complete consumption of water in the system. However, Le Chatelier's principle allows for the equilibria to be reversed, to produce caesium methylcarbonate and methyl esters (methyl propanoate and methyl methacrylate) from dilute solutions of caesium carboxylates in methanol by applying a high pressure of carbon dioxide, scheme 3.7.

The main advantage of a process based on this idea is the use of carbon dioxide as a cheap, readily available raw material, the consumption of which through chemical synthesis is a highly desirable goal.[26–29] As the caesium methylcarbonate promoted condensation reaction of methyl propanoate with formaldehyde produces carbon dioxide (through decomposition of caesium methylcarbonate), a process based on this regeneration system would neither produce or consume carbon dioxide.



Scheme 3.7: Mechanistic proposal for the regeneration of caesium methylcarbonate and methyl propanoate using carbon dioxide.

An alternative mechanistic proposal for regeneration of caesium methylcarbonate considered is nucleophilic attack of the caesium carboxylate on carbon dioxide, to form an anhydride intermediate. Methanolysis at the alkyl ester end of this intermediate would produce the methyl ester and caesium bicarbonate which, in methanol, is unstable with respect to caesium methylcarbonate and water formation, as shown in the previous chapter. While this mechanism cannot be ruled out, no anhydride intermediate has been observed experimentally.

At high temperature under pressure, the equilibria could be manipulated to afford methyl propanoate and caesium methylcarbonate. In these experiments, the caesium methylcarbonate to methyl ester (methyl propanoate and/or methyl methacrylate) ratio was always essentially 1:1, as predicted by the stoichiometry of the proposed reaction. In the absence of carbon dioxide, no caesium methylcarbonate was formed and essentially no esterification of caesium propanoate to methyl propanoate was observed, showing carbon dioxide, acting as a Lewis acid, is required to promote the esterification of the caesium carboxylate.

Screening of the conditions required for caesium methylcarbonate regeneration with carbon dioxide was undertaken, to gain an understanding of the influence of various variables, including temperature, time and carbon dioxide pressure, as well as the difference in reactivity of caesium propanoate and caesium methacrylate, table 3.3.

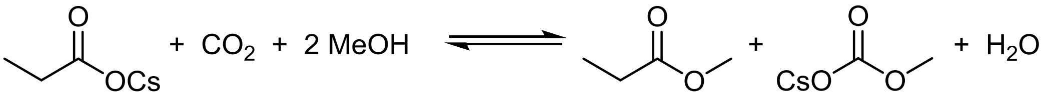


Table 3.3: Esterification of caesium carboxylates with co-production of caesium methylcarbonate is achieved using high pressures of carbon dioxide and high temperatures. [*]

Entry	**Starting salt**	**Time / hours**	**Temperature / °C**	**Pressure [a] / bar**	**Unreacted Cs carboxylate / %**	**Conversion to methyl esters / %**
1	CsP	2	160	15	63	37
2	CsP	18	160	15	45	55
3	CsP	44	160	15	16	84
4	CsP	2	160	40	58	42
5	CsP	2	180	40	30	70
6	CsP	2	200	40	13	87
7	CsMA	2	200	40	37	63
8	CsP / CsMA (1:1)	2	160	40	15 (CsP) 36 (CsMA)	35 (MeP) 14 (MMA)

[a] Pressure charged into the autoclave prior to heating.

High conversions of caesium propanoate to methyl propanoate and caesium methylcarbonate could be achieved with long reaction times at 160 °C with an initial carbon dioxide pressure at room temperature of 15 bar (the pressure at reaction temperature was approximately 25 bar and did not change significantly during the time at 160 °C), table 3.3, entries 1-3. Slightly higher conversion to methyl propanoate and caesium methylcarbonate is achieved with higher pressure of carbon dioxide, the conversion of caesium propanoate to methyl propanoate increasing after 2 hours at 160 °C from 37 % to 42 % with an increase in pressure at room temperature from 15 bar to 40 bar, table 3.3, entry 1 vs 4.

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[*] Preliminary studies revealed a preferred concentration of caesium carboxylate of 0.54 M for the regeneration reaction; higher caesium concentration resulted in some yellow/orange colouration of the exit mixture whilst dilution below 0.54 M resulted in inconveniently slower conversion of caesium carboxylate to methyl ester and caesium methylcarbonate.

Higher conversions to methyl propanoate and caesium methylcarbonate are also achieved with increased reaction temperature, increasing from 42 % to 87 % in 2 hours when the reaction temperature is increased from 160 to 200 °C, table 3.3, entries 4-6, although whether this is for kinetic reasons or because the position of equilibrium is shifted is, at this stage, unclear.

As expected, the esterification of caesium methacrylate is less favoured than that of caesium propanoate (for the same reason that hydrolysis of methyl methacrylate is more favoured than methyl propanoate) and so lower conversions are observed; 63 % of the caesium methacrylate is converted to methyl methacrylate after 2 hours at 200 °C compared with 87 % of the caesium propanoate converted to methyl propanoate under the same conditions, table 3.3, entry 6 vs 7. Consequently, on feeding a mixture of caesium propanoate and caesium methacrylate (more like the non-volatile salts from the exit mixture of a condensation reaction run) to the reactor, around 70 % of the caesium propanoate and around 28 % of the caesium methacrylate are converted to the methyl esters, table 3.3, entry 8.

Proper kinetic analysis was not undertaken at this stage but preliminary analysis of the data suggests kinetic analysis will not be straightforward. Plotting conversion to methyl propanoate against time, figure 3.1, gives a straight line that does not pass through the origin. The reaction time is actually the time at 160 °C and does not factor in the heating (1 hour) and cooling (approximately 40 minutes) phases of the experiment. However, even accounting for this extra time, the straight line does not pass through the origin. This suggests there is a fast phase of the reaction, up to around 30-35 % conversion. That the three points fall on a straight line may mean that the reaction becomes zero order on caesium propanoate (the rate is not affected by a reduction in caesium propanoate concentration) or that some other reaction component (perhaps carbon dioxide or methanol) is in essentially constant concentration and is controlling the reaction rate.

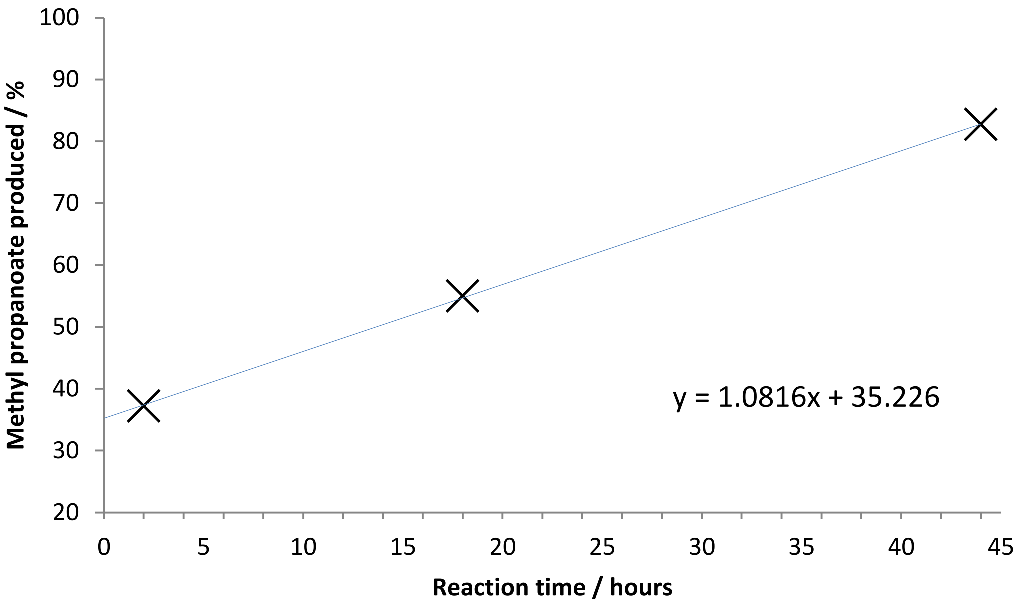


Figure 3.1: Plotting the conversion of caesium propanoate to methyl propanoate against time in the carbon dioxide-promoted regeneration gives a straight line. Data taken from table 3.3, entries 1-3. N.B. The reaction time is the time at 160 °C and does not factor in heating and cooling time.

The other possibility is that the reaction is heterogeneous, especially as more of the strong anti-solvent methyl propanoate is produced, effectively limiting the caesium propanoate concentration. Further experiments, preferably with equipment set up for liquid sampling throughout the experiment, are required to further understand the kinetics of the reaction, which will be a very important factor for the project going forward as an understanding of the kinetics is required for further optimization of the process.

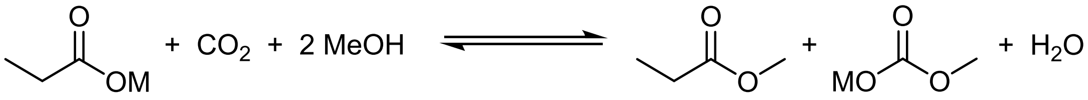


Table 3.4: Alkali metal methylcarbonates and methyl propanoate can be produced from alkali metal propanoates with carbon dioxide and methanol. Reaction conditions: 200 °C, 2 hours, 40 bar CO_2.

Entry	**Starting salt**	**Alkali metal propanoate in exit mixture / %**	**MeP in exit mixture / %**
1	CsP	15	87
2	RbP	18	80
3	KP	11	89

The reaction methodology can be generally applied to the preparation of methyl propanoate and the corresponding alkali metal methylcarbonate from rubidium and potassium propanoates with broadly comparable conversions being observed; 87 % for caesium, 80 % for rubidium and 89 % for potassium, table 3.4. Sodium propanoate was not studied owing to the low solubility of this salt in methanol.

3.2.4 Recycling of caesium methylcarbonate using carbon dioxide regeneration

Moderate single pass conversions of caesium propanoate and caesium methacrylate to caesium methylcarbonate are achieved in relatively short reaction times. Attainment of higher conversions to caesium methylcarbonate can be achieved more quickly by regeneration reaction-distillation cycles with fresh methanol by taking advantage of the fast initial phase of the reaction and effectively shifting the equilibrium to favour caesium methylcarbonate through removal of the other products of the reaction in the forwards direction.

The exit mixture of non-volatile salts from a condensation reaction (containing approximately 57 % caesium propanoate, 22 % caesium methacrylate and 21 % caesium methylcarbonate) could be converted to methyl esters and 93 % caesium methylcarbonate in four 2 hour regeneration reaction-distillation cycles (conditions: 180 °C, 40 bar starting pressure of carbon dioxide), showing that the non-volatile salts could be converted to caesium methylcarbonate using this method, table 3.5. Caesium methacrylate esterification is slower than for caesium propanoate and so methyl propanoate is produced more quickly and after 4 regeneration runs, some caesium methacrylate remained in the sample and was difficult to remove.

Table 3.5: The approximate composition of the non-volatile salts during a caesium methylcarbonate recycling run using 2 hour regeneration runs at 180 °C with 40 bar carbon dioxide.

Entry		**Caesium methylcarbonate / %**	**Caesium propanoate / %**	**Caesium methacrylate /%**
1	Non-volatiles at the end of a reaction	21	57	22
2	End of regeneration run 1	64	17	20
3	End of regeneration run 2	81	5	14
4	End of regeneration run 3	87	1	12
5	End of regeneration run 4	93	trace	7

Alternatively, from a condensation reaction where essentially all of the caesium methylcarbonate had been decomposed to caesium propanoate and caesium methacrylate (40 % hydrolysis of methyl esters at 40 mol% caesium methylcarbonate loading), caesium methylcarbonate could be prepared in high purity with two long regeneration-distillation cycles (a 24 hour regeneration run followed by distillation and a further 12 hour run), table 3.6.

Table 3.6: With longer regeneration reaction times, caesium methylcarbonate could be produced from the exit non-volatiles of a condensation reaction. Conditions as for table 3.5. Regeneration reaction 1 time = 24 hours. Regeneration reaction 2 time = 12 hours.

Entry		Caesium methylcarbonate / %	Caesium propanoate / %	Caesium methacrylate / %
1	Non-volatiles at the end of a reaction	0	67	35
2	End of regeneration run 1	83	7	10
3	End of regeneration run 2	97	trace	3

The caesium methylcarbonate produced in this regeneration procedure from non-volatile salts from a condensation reaction had comparable activity to that produced using the dimethyl carbonate method from freshly prepared caesium propanoate, attaining 15 % conversion compared with 17 % under the same conditions, table 3.7, entries 1 and 2. A second carbon dioxide-promoted regeneration of the exit non-volatiles from table 3.7, entry 2 gave a caesium methylcarbonate sample that gave 15 % conversion of methyl propanoate to methacrylates showing that activity could be maintained over 2 recycles, table 3.7, entry 3.

Around 40 % more hydrolysis (19 % hydrolysis versus 28 %) was observed when the caesium methylcarbonate was prepared using the carbon dioxide method for regeneration of exit non-volatiles, rather than the dimethyl carbonate methylation of caesium propanoate, possibly because some caesium hydroxide or bicarbonate is produced in the regeneration reaction.

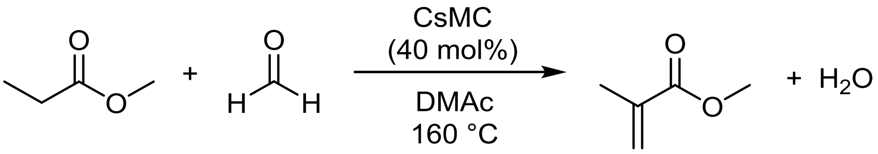


Table 3.7: Caesium methylcarbonate formed through the carbon dioxide regeneration is active in the condensation reaction of methyl propanoate with formaldehyde. For condensation reaction conditions used, see chapter 4, table 4.1, entry 1.

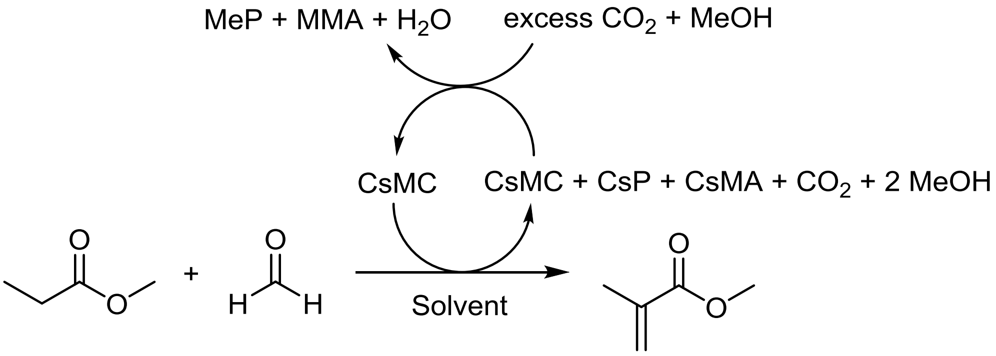
Entry	**CsMC regeneration method**	**CsMC : CsP in starting sample**	**Conversion to methacrylates / %**	**CsP + CsMA formed / %**
1	DMC	98:2	17	19
2	CO_2	97:3	15	28
3	CO_2, second cycle	95:5	15	33

The carbon dioxide regeneration of caesium methylcarbonate from caesium propanoate and caesium methacrylate is the most attractive for use as a process as the raw materials are cheap. However, thus far this regeneration reaction is a lot slower than the condensation reaction (chapter 4 shows that the condensation reaction between methyl propanoate and formaldehyde is fast, under the right conditions). For this reason, further optimization of the carbon dioxide regeneration is required. It may be possible to not run the regeneration to caesium methylcarbonate to completion but operate with intermediate conversions (e.g. ca. 80

% caesium methylcarbonate with the remainder as inactive caesium propanoate and caesium methacrylate).

3.3 Conclusions

Caesium methylcarbonate is an active, highly selective, and regenerable base promoter for the condensation of methyl propanoate with formaldehyde to give methyl methacrylate. Caesium methylcarbonate is a more desirable base for the condensation reaction of methyl propanoate and formaldehyde than caesium carbonate because the methyl group prevents the formation of increased levels of caesium hydroxide from caesium carbonate, resulting in less caesium propanoate and caesium methacrylate being formed from their methyl esters. However, hydrolysis in the system is not completely blocked and is strongly entropically favoured because hydrolysis causes the production of carbon dioxide and methanol from the protonated methylcarbonate anion. For this reason, a regeneration procedure is required for a process based on this chemistry, scheme 3.8.



Scheme 3.8: The chemistry developed in this chapter could allow for multiple turnovers on caesium through reaction-regeneration cycles.

In mechanistic terms the condensation reaction is catalytic in caesium methylcarbonate (the base is chemically unchanged through the mechanism of the reaction), however the methylcarbonate is decomposed during the experiment through reaction of the methyl esters with water, which is co-produced in the condensation reaction; turnover numbers are generally less than one. Caesium methylcarbonate is a catalyst that is decomposed by the co-product of the reaction it catalyses and as such, it behaves as a stoichiometric reagent. While not ideal, a process based on a stoichiometric reaction promoter can be competitive economically, so long as the regeneration process is relatively fast and cheap and as long as the promoter is highly active and selective, allowing for multiple turnovers on caesium to be achieved.

While caesium methylcarbonate can be prepared from caesium propanoate and caesium methacrylate using dimethyl carbonate and a polar, aprotic solvent at 90 °C, this regeneration procedure is unlikely to be commercially viable owing to the use of excess of the relatively expensive dimethyl carbonate. However, this procedure has provided a useful lab-scale preparative procedure for caesium methylcarbonate and scale-up has shown large amounts of caesium methylcarbonate can be produced using this method.

Using mechanistic understanding of the driving force for hydrolysis of methyl esters in the reaction system, the hydrolysis equilibrium can be reversed to favour methyl esters and caesium methylcarbonate under high pressures of carbon dioxide with excess methanol. High temperatures are required to increase the rate of the reaction towards the equilibrium under these conditions and there is an advantage to running at higher pressure of carbon dioxide although higher pressures will also mean thicker reactor walls would be required in a chemical plant using this process, so a trade-off would be necessary.

Greater than 97 % caesium methylcarbonate (<3 % caesium methacrylate) can be obtained through multiple regeneration reaction-distillation cycles to drive the equilibrium towards the desired salt, allowing for a process that converts caesium propanoate and caesium methacrylate to caesium methylcarbonate over multiple cycles. The regenerated caesium methylcarbonate sample has comparable activity for methacrylate production over 3 runs of reaction-regeneration cycles.

An understanding of the kinetics of the reaction and further optimization are required to determine if the carbon dioxide regeneration process is or can be sufficiently fast to make the whole process competitive. However, as caesium methylcarbonate is a highly active base that achieves excellent selectivity on methyl propanoate, attention turned to optimizing the conditions in the methyl methacrylate forming reaction. Up until this point, the selectivity on formaldehyde was poor with either caesium carbonate or caesium methylcarbonate as the base (the highest formaldehyde selectivity was around 12.5 %). Such low formaldehyde selectivity would result in the formation of large quantities of waste and make the process economically unattractive.

The next chapter examines the issues affecting formaldehyde selectivity and this understanding allowed for significant improvements to be made in the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde.

3.4 References

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Chapter Four

Improved formaldehyde selectivity by high temperature addition in the caesium methylcarbonate-promoted condensation with methyl propanoate

4. Improved formaldehyde selectivity by high temperature addition in the caesium methylcarbonate-promoted condensation with methyl propanoate

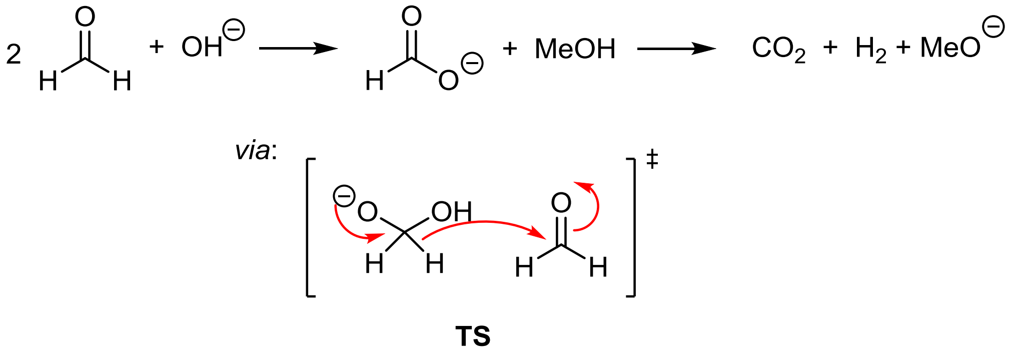
4.1 Introduction

In the preceding chapter, it was demonstrated that caesium methylcarbonate is an active and recyclable base in the condensation of methyl propanoate and formaldehyde, achieving respectable conversion of methyl propanoate to methyl methacrylate and caesium methacrylate with excellent selectivity on methyl propanoate. However, the selectivity on formaldehyde was poor, ranging from around 3-12.5 %, which is very unfavourable compared with the current ALPHA Stage Two process. Three formaldehyde reaction pathways that compete with the methyl methacrylate-forming reaction were identified:

1. Cannizzaro/Tishchenko disproportionation of formaldehyde to give gaseous products, which explains the pressure increase during the experiments.
2. Cyclization of multiple formaldehyde molecules to formaldehyde sugars.
3. Condensation of formaldehyde with *N*,*N*-dimethylacetamide to form *N*,*N*-dimethylacrylamide and water.

4.1.1 Cannizzaro and Tishcenko reactions of formaldehyde

The Cannizzaro reaction is the disproportionation of two aldehyde molecules in the presence of water or hydroxide, forming a carboxylic acid and an alcohol.[1–3] The reaction involves a hydride transfer from one aldehyde to another and is catalysed by base. In the case of formaldehyde, formic acid and methanol are produced, scheme 4.1. Decomposition of formic acid to carbon dioxide and hydrogen is then expected.[4]



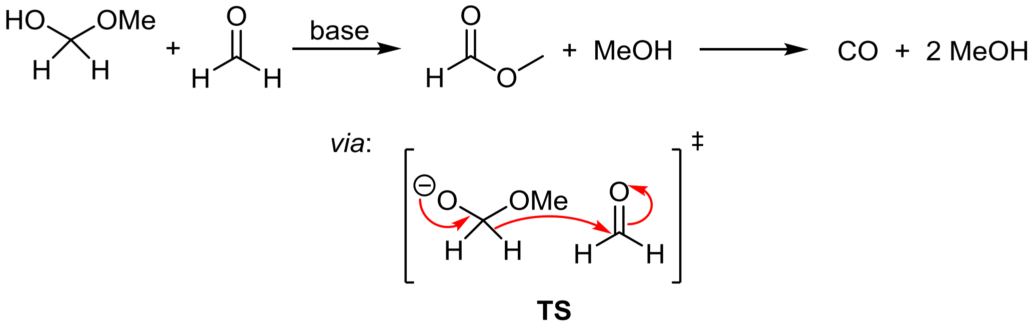
Scheme 4.1: Cannizzaro decomposition of formaldehyde produces methanol and formic acid, which can decompose to carbon dioxide and hydrogen.

The rate of the Cannizzaro reaction is second order on formaldehyde (as the rate-limiting step involves hydride transfer from one formaldehyde molecule to another).[1] The order on base is dependent on the concentration of base; at high concentrations of base the transition state (TS) is doubly deprotonated. At low base concentration the methylene glycol is mono-deprotonated (as drawn) and the reaction is first order on base.

$$\text{Rate} = k\,[\text{HCHO}]^2\,[\text{base}] + k'\,[\text{HCHO}]^2\,[\text{base}]^2$$

Equation 4.1: The rate equation of the Cannizzaro-type decomposition of formaldehyde is the sum of two terms and is second order on formaldehyde concentration.

In alcoholic conditions, another variant of the Cannizzaro reaction takes place, known as the Tishchenko reaction.[5,6] In this case the intermediate is a deprotonated hemiformal and the product is an ester. The Tishchenko reaction of formaldehyde in methanol produces methyl formate and methanol, scheme 4.2. Some methyl formate is observed in the exit mixtures in this work but decomposition of methyl formate to gaseous products is also likely. The energetics of methyl formate decomposition have recently been investigated by high-level ab initio calculations and formation of carbon monoxide and methanol was shown to be the most favoured decomposition pathway.[7] The kinetics of the Tishchenko reaction is likely to be similar to that of the Cannizzaro reaction.



Scheme 4.2: Tishchenko reaction of hemiformal (methanolic formaldehyde) produces methyl formate that can decompose to carbon monoxide and methanol.

Analysis of the gaseous products from an experiment using caesium carbonate as the base with methyl alcoform charged into the autoclave at the start of the experiment (mimicking the starting conditions from chapter 2) showed that both carbon dioxide and carbon monoxide were present, in a ratio of around 1:0.8. This suggests both Cannizzaro and Tishchenko mechanisms are possible in this system, although carbon dioxide can also be produced as a result of caesium carbonate and caesium methylcarbonate decomposition. Cannizzaro decomposition of formaldehyde may also be more favoured in this system than in the caesium methylcarbonate system as hydroxide is a co-product in the caesium methylcarbonate forming reaction from caesium carbonate.

4.1.2 Formaldehyde sugar formation

Brown, sweet-smelling, sugar-like, heavies, known as “formaldehyde sugars” are formed in the current, heterogeneous ALPHA Stage Two process.[8–10] They are cyclic formaldehyde oligomers. The brown oil formed during this work was assumed to be these species. The rate of formation of the heavies can be assumed to be at least second order on formaldehyde concentration. Separation of these sugars from the spent catalyst (the caesium salts in this system) is likely to be more difficult than in the heterogeneous system and so the production of these species must be kept to a minimum.

4.1.3 Condensation of formaldehyde with *N*,*N*-dimethylacetamide

The condensation of formaldehyde with *N*,*N*-dimethylacetamide is expected to follow a similar mechanism to the condensation of formaldehyde with methyl propanoate and so the kinetic regime of these reactions are likely to be similar (see below).

4.1.4 Expected kinetics of the condensation of methyl propanoate with formaldehyde

Two potential kinetic regimes for the condensation reaction of methyl propanoate with formaldehyde must be considered. In the first, the rate-limiting step is the deprotonation of methyl propanoate by the weak base as this requires the breaking of a C-H bond. In the second regime, the rate-limiting step is attack of the enolate species on formaldehyde. In the first regime, the rate equation will be first order on methyl propanoate and on base. In the second regime, the rate should be first order on enolate (so first order on methyl propanoate and first order on base) and first order on formaldehyde. This is much like the self-aldol reaction of acetaldehyde, where the concentration of base affects the rate-limiting step and therefore, the kinetics of the reaction.[1]

In either kinetic regime the maximum order on formaldehyde is one. This is a significant kinetic difference between the formaldehyde decomposition reactions (second order on formaldehyde concentration) and the condensation of formaldehyde with methyl propanoate (maximum first order on formaldehyde concentration) and suggests a “process engineering” approach to address the low selectivity on formaldehyde.

Because formaldehyde decomposition reactions have a higher order on formaldehyde than the condensation reaction, a reduction in formaldehyde concentration should have a larger effect on the rate of the decomposition reactions than on the condensation reaction. For this reason the formaldehyde selectivity is expected to improve when the formaldehyde concentration is reduced. Preliminary formaldehyde lean experiments showed that at very low loadings the formaldehyde selectivity does indeed improve, but at the expense of overall rate resulting in very low conversions of methyl propanoate (only at 0.2 and 0.1 equivalents of formaldehyde relative to methyl propanoate is formaldehyde selectivity improved).

This chapter describes a method for the addition of methyl alcoform solution to the reaction mixture at a slow rate so that the formaldehyde concentration is always as low as possible. Preferably the feed rate should be comparable to the rate of the condensation reaction so that the rate of the formaldehyde decomposition reactions is the minimum possible, hence allowing for high formaldehyde selectivity.

Formaldehyde selectivity is indeed found to improve significantly when controlled addition of formaldehyde to the hot reaction mixture is used. With conditions optimized, experiments were run to determine some preliminary kinetic models for the system. Under these optimized conditions, the effect of base loading and the effect of the alkali metal cation of the methylcarbonate salt were also investigated. Finally, the development of a new process is described in which caesium methylcarbonate is regenerated *in situ* from caesium propanoate and caesium methacrylate allowing for the two step condensation reaction – regeneration reaction system to become a one step process.

4.2 Results and Discussion

4.2.1 Slow addition of methyl alcoform at reaction temperature

Controlled, slow addition of formaldehyde to the other reaction components (base, solvent, methyl propanoate) at reaction temperature was possible with the use of a Gilson pump. The slowest, reproducible and accurate feed rate of the Gilson pump head used was 0.05 mL min^{-1} corresponding to the addition of 1 equivalent of formaldehyde in 33 minutes. Under these conditions no temperature spike (attributed previously to formaldehyde decomposition) was observed during methyl alcoform addition. Although the aim of matching the feed rate of methyl alcoform to the rate of consumption of formaldehyde was not achieved – large amounts of formaldehyde remained in the exit mixture at the end of the experiment – significantly improved formaldehyde selectivity, up to 73.7 % was observed, table 4.1, entry 1.

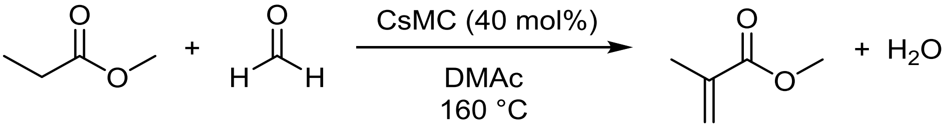


Table 4.1: Addition of methyl alcoform to the hot reaction mixture results in increased formaldehyde selectivity and increased conversion of methyl propanoate.

Entry	Time / hours	MeP conversion to methacrylates [a] / %	Hydrolysis to CsP + CsMA [a] / %	Formaldehyde conversion [b] / %	Formaldehyde selectivity [b] / %
1	33 mins	17	19	25.0	73.7
2	1	22	25	N.D	N.D
3	2	32	31	71.9	43.6
4	3	34	37	91.9	32.4
5	4	38	38	72.2	55.0

[a] Conversion and hydrolysis determined by ^{1}H NMR spectroscopy. [b] Formaldehyde conversion determined by formaldehyde titration of the vacuum distillate by Lucite International. N.D = not determined.

With significant quantities of formaldehyde left at the end of the experiment, the reaction time after the addition of methyl alcoform was increased up to 4 hours, table 4.1, entries 2-5. These experiments reveal that there is a fast initial phase of reaction to methacrylates (methyl methacrylate and caesium methacrylate, as determined by ^{1}H NMR spectroscopy), presumably as there is a high abundance of caesium methylcarbonate. However, as base-catalysed hydrolysis of methyl esters with water produced in the methyl methacrylate-forming reaction (and other condensation reactions, see section 3.2.2) increases, forming more caesium propanoate and caesium methacrylate, the condensation reaction becomes slower. The amount of hydrolysis closely follows the conversion to methacrylates, again showing the conversion of water in the system is close to 100 %.

The exit mixtures from these experiments all contain formaldehyde. Vacuum distilled samples were sent to Lucite International for analysis of formaldehyde conversion and formaldehyde selectivity for methacrylates was determined, by Lucite International, using their protocol. As would be expected, the formaldehyde selectivity decreases over time as the condensation reaction to methacrylates becomes slower. However, the error in these data appears fairly large, with the 4 hour experiment seemingly having higher formaldehyde selectivity for methacrylates than the 2 and 3 hour experiments, compare entries 3-5. This is likely to be as a result of the crude samples standing for varying amounts of time, with formaldehyde decomposition occurring in the presence of base even at room temperature.

As well as increased formaldehyde selectivity with slow addition of formaldehyde at reaction temperature, the conversions achieved were greater than for the other formaldehyde addition methods (injection or loading at room temperature). For a fair comparison, experiments using these formaldehyde addition methods were repeated with caesium methylcarbonate and with 1 molar equivalent of formaldehyde (in previous chapters 2 equivalents of formaldehyde were required for high conversions), table 4.2. The conversion of methyl propanoate to methacrylates is almost doubled in the same time at 160 °C when methyl alcoform is added by controlled high temperature addition compared with addition at room temperature, compare entry 1 and 2.

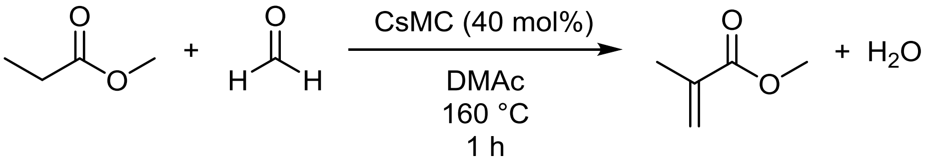


Table 4.2: The methyl alcoform addition method has a major influence on the initial rate of the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde.

Entry	**Methyl alcoform addition method**	**Conversion to methacrylates by ^{1}H NMR / %**	**Hydrolysis to CsP + CsMA / %**
1	Addition at room temperature	13	10
2	Injection at 140 °C	19	25
3	Gilson pump addition at 160 °C	22	25

High temperature addition of methyl alcoform results in a higher concentration of formaldehyde at reaction temperature, as formaldehyde decomposition is much faster than the condensation reaction throughout the addition and heating phases of the experiment. The increased conversions with high temperature addition suggests the rate equation for the condensation reaction has a dependence on formaldehyde, as the initial rate of the reaction is faster with increased formaldehyde concentration. This suggests the order on formaldehyde for this reaction is greater than zero and so the second kinetic regime, outlined in section 4.1.4, is more likely.

4.2.2 Influence of temperature on the reaction

The competing formaldehyde reactions (condensation and decomposition) will have different thermodynamic parameters and activation barriers; therefore a change in temperature is likely to affect the competition between productive reaction (condensation of formaldehyde with methyl propanoate) and the decomposition of formaldehyde. Using the Gilson pump, the reaction is initiated at reaction temperature by addition of methyl alcoform (i.e. the heating time and rate does not affect the experiment), this allowed experiments to be performed at different temperatures to determine the formaldehyde selectivity as a function of temperature.

The formaldehyde selectivity improves as reaction temperature is increased, from 9.8 % in 3 hours at 100 °C to 52.9 % in the same time at 180 °C, figure 4.1. This suggests that the activation barrier for condensation of formaldehyde with methyl propanoate is higher than for decomposition of formaldehyde. This is consistent with the improvement in productivity observed on addition of formaldehyde at high temperature (as in these experiments) compared with addition of formaldehyde at low temperature before heating as the rate of the condensation reaction only becomes significant above 130 °C.

Further analysis of these data by Lucite International predicts the conversion of methyl propanoate at 6 minutes (t = 0.1 h) to provide an initial rate of reaction at the various reaction temperatures[9] which could be fitted to kinetic models to predict the activation energies of the competing reactions. The activation barrier was predicted to be 60 kJ mol^{-1} higher for the methacrylate forming reaction compared with the formaldehyde decomposition reaction.

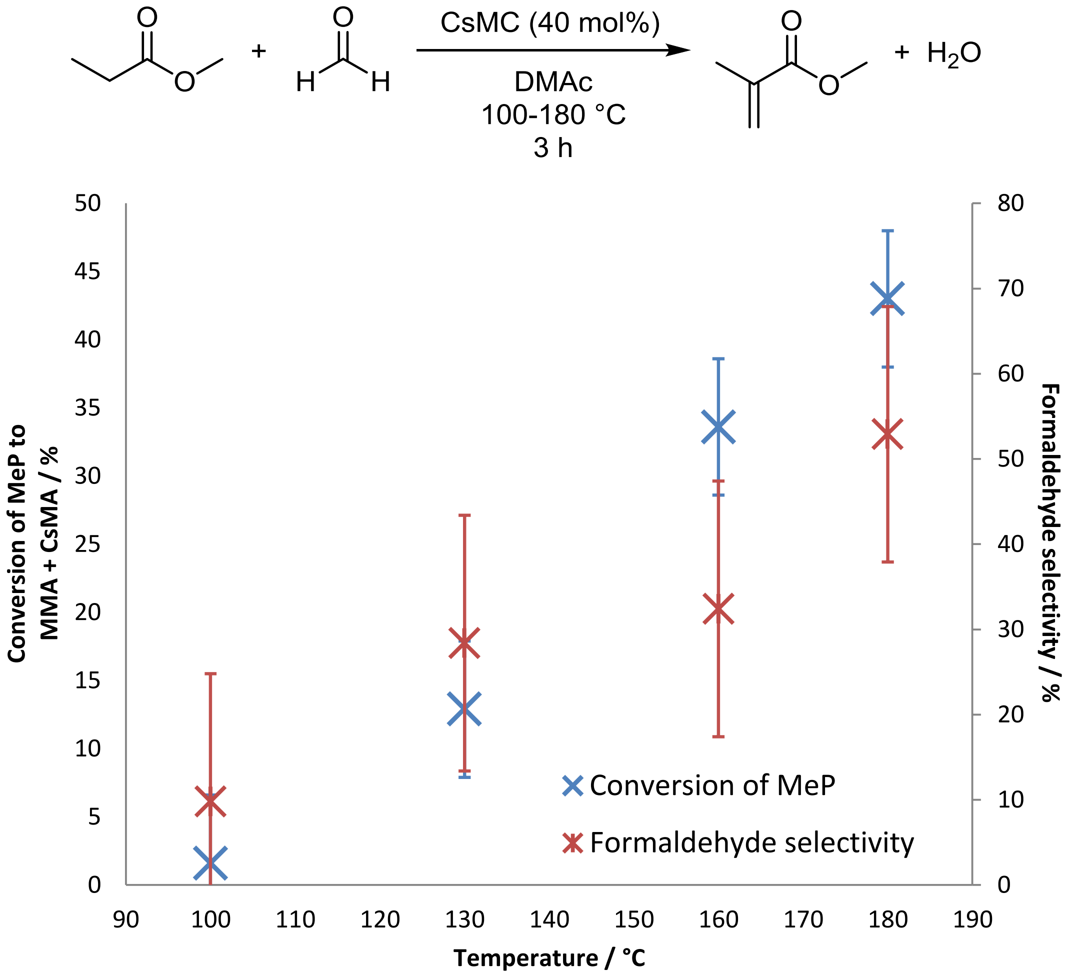


Figure 4.1: Higher temperature results in increased conversion of methyl propanoate and increased formaldehyde selectivity as the condensation reaction with methyl propanoate becomes more favoured over formaldehyde decomposition.

4.2.3 The “caesium effect” with alkali metal methylcarbonates

The “caesium effect” is commonly invoked to explain the apparent greater activity of caesium salts in base catalysed reactions when compared to salts of other group 1 metals. The methylcarbonate salts of sodium, potassium and rubidium were, therefore, screened to determine the extent of this periodic trend in the condensation reaction of methyl propanoate and formaldehyde; the expected increase in conversion of methyl propanoate to methacrylates was observed, table 4.3.

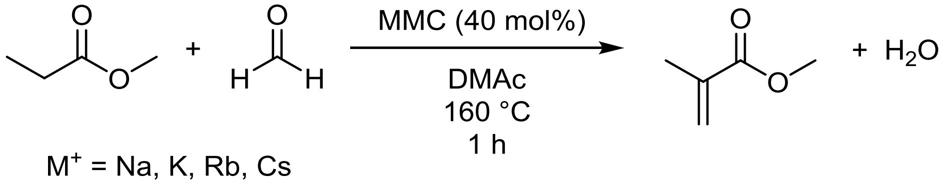


Table 4.3: As group 1 is descended, alkali metal methylcarbonates become more active bases in the condensation of methyl propanoate with formaldehyde.

Entry	Base	MeP conversion to methacrylates by ^{1}H NMR / %	Hydrolysis to propanoate and methacrylate salts / %
1	NaMC	<1	9
2	KMC	12	15
3	RbMC	19	25
4	CsMC	22	25

Potassium methylcarbonate has around half the initial activity of caesium methylcarbonate under these conditions (12 % conversion versus 22 %) and rubidium methylcarbonate has intermediate activity (19 %). Sodium methylcarbonate was not active to any extent (a small methyl methacrylate resonance was observed just above the baseline in the ^{1}H NMR spectrum of the crude exit mixture). The inactivity of sodium methylcarbonate may be due to the expected trend or may be as a result of low purity of the sodium methylcarbonate sample which, owing to the low solubility of sodium methylcarbonate in methanol (or any other solvent) could not be effectively determined.

4.2.4 Caesium methylcarbonate as a stoichiometric reagent

Caesium methylcarbonate effectively acts as a stoichiometric reagent rather than as a catalyst in these reactions: the base is effectively poisoned through hydrolysis of methyl esters. Experiments were therefore performed with stoichiometric loadings of caesium methylcarbonate on methyl propanoate and formaldehyde to determine if higher conversions of methyl propanoate could be achieved with a higher base loading as the concentration of active base should always be high with high loadings.

Halving caesium methylcarbonate loading to 20 mol% results in a slower initial rate of reaction and all of the methylcarbonate base is consumed during the reaction, table 4, entry 1, hinting that higher loadings of base would result in improved conversion of methyl propanoate to methacrylates. At short reaction times, the rate of the condensation reaction is only improved slightly with stoichiometric base loading, table 4.4, entry 3, possibly because the solution is saturated with base even with the 40 mol % caesium methylcarbonate loading. Stoichiometric loadings of caesium methylcarbonate did not result in increased hydrolysis of methyl esters, suggesting the base used contained little water or hydroxide.

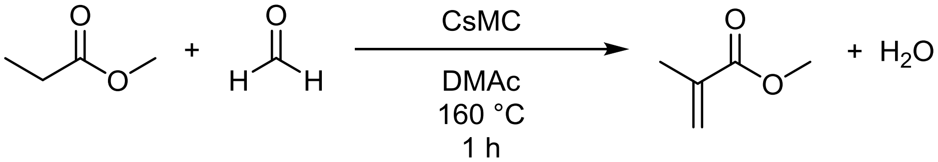


Table 4.4: Caesium methylcarbonate loading in the condensation of methyl propanoate and formaldehyde was briefly investigated.

Entry	**CsMC loading**	**MeP conversion to methacrylates / %**	**Hydrolysis to CsP + CsMA / %**
1	0.2	14	20
2	0.4	22	25
3	1	25	25

As stoichiometric base loading did not improve the conversion of methyl propanoate by much, 40 mol % caesium methylcarbonate loading was maintained as the optimum. Further experiments to determine the optimum base loading were not carried out at this stage. Rather, the possibility of combining the drip feed of formaldehyde with an *in situ* regeneration of the base by further developing the methylation of caesium carboxylates with dimethyl carbonate, from section 3.2.1, was investigated.

4.2.5 Suppression of hydrolysis of methyl esters

4.2.5.1 Water scavenging with trimethyl orthoformate

As an alternative to using higher base loadings, the amount of caesium methylcarbonate available during the reaction could be maintained by removing the water co-product from the reaction system or by regenerating the base *in situ*. Trimethyl orthoformate was screened as a sacrificial water scavenger, however hydrolysis of the methyl esters (methyl propanoate and methyl methacrylate) is still observed indicating that this drying agent is not sufficiently active to block the methyl propanoate and methyl methacrylate hydrolysis reactions.

4.2.5.2 *In situ* regeneration of caesium methylcarbonate

Dimethyl carbonate can act as both a water scavenger or can methylate caesium propanoate and caesium methacrylate to produce methyl esters and caesium methylcarbonate. This would provide a one-pot process with an *in situ* regeneration procedure. The advantage of such a process would be that the exit non-volatile salts could be re-used in the condensation reaction without the need for a separate regeneration procedure. For this reason, *in situ* regeneration of caesium methylcarbonate using dimethyl carbonate was investigated.

Addition of 0.4 equivalents of dimethyl carbonate (the same number of moles as the caesium methylcarbonate) at the start of the experiment effectively inhibited the hydrolysis reactions, only 1 % of the methyl propanoate and methyl methacrylate were hydrolysed to their caesium salts, compared with 25 % of the esters hydrolysed in the absence of dimethyl carbonate additive, compare table 4.5, entry 1 and 2. The remaining non-volatile salt in the exit mixture was caesium methylcarbonate.

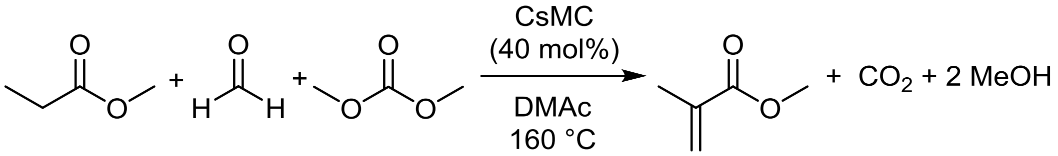


Table 4.5: *In situ* regeneration of caesium methylcarbonate with dimethyl carbonate results in no caesium propanoate or methacrylate in the exit mixture. * Experiment run with less DMAc solvent so that the overall volume of the reaction mixture was the same as for entry 1.

Entry	DMC loading	Time / hours	MeP conversion to methacrylates / %	Hydrolysis to CsP + CsMA / %	DMC conversion / %
1	0	1	22	25	N/A
2	0.4	1	17	1	51.0
3	1	1	15	0	27.5
4	1*	1	16	0	31.5
5	1	4	31	0	53.8
6	1	18	40	0	72.6

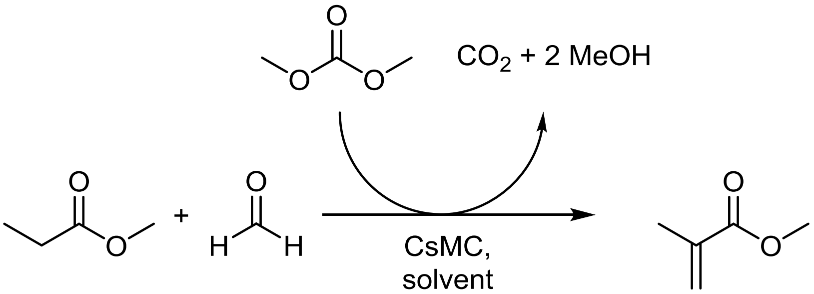
Increasing the dimethyl carbonate in the feed to 1:1 (with respect to methyl propanoate) resulted in complete inhibition of hydrolysis of methyl propanoate or methyl methacrylate, i.e. the only caesium salt observed in the ^{1}H NMR spectrum of the exit solution was caesium methylcarbonate. The selectivity on methyl propanoate was comparable with reactions run in the absence of dimethyl carbonate suggesting there were no undesired reactions of dimethyl carbonate with methyl propanoate or methyl methacrylate.

With dimethyl carbonate as an additive, the conversion of methyl propanoate to methyl methacrylate was reduced from 22 % to 17 % with 0.4 equivalents of dimethyl carbonate added and further reduced to 15 % with 1 equivalent of dimethyl carbonate added, table 4.5, entries 1-3. Addition of dimethyl carbonate to the reaction mixture results in a reduction in the polarity of the solvent mixture and in dilution of the mixture.

In an experiment in which the volume of *N*,*N*-dimethylacetamide used was reduced to correct for the addition of dimethyl carbonate, the conversion of methyl propanoate to methyl methacrylate increased only slightly compared with the more dilute reaction, and the conversion was still reduced compared with the additive-free experiment indicating the changing nature of the solvent decreases the efficacy of the caesium methylcarbonate base. Conversion of methyl propanoate to methyl methacrylate increases with longer reactions times, and with no caesium propanoate or caesium methacrylate in the exit mixture.

To reduce the negative effect on solvent polarity, the dimethyl carbonate could have been added in combination with the methyl alcoform using the drip feed method so that the initial activity (with a high polarity solvent mixture) could be achieved. Experiments using this method were not performed due to time constraints.

Dimethyl carbonate is expected to be consumed when water is produced in the system. However, the number of moles of dimethyl carbonate consumed during the experiment was around double the number of moles of methyl propanoate converted to methyl methacrylate, suggesting there was some dimethyl carbonate decomposition under the reaction conditions. Slow thermal decomposition of dimethyl carbonate in the presence of base at temperatures of 160 °C and above has recently been investigated.[11] To determine the stability of dimethyl carbonate under the reaction conditions, an experiment was run in the absence of methyl alcoform and in 1 hour at 160 °C, 11 % of the dimethyl carbonate was consumed when 1 equivalent of dimethyl carbonate (relative to methyl propanoate) was added to a mixture of caesium methylcarbonate (0.4 equivalents), methyl propanoate and *N*,*N*-dimethylacetamide showing dimethyl carbonate slowly decomposes under the reaction conditions.



Exit salt is CsMC
No separate regeneration step required
Carbon dioxide and methanol produced by hydrolysis of MeP and MMA
Subsequent methylation with DMC reproduces CsMC

Scheme 4.3: An alternative system was developed where *in situ* regeneration with dimethyl carbonate reproduces caesium methylcarbonate making the system a one step process.

A process based on this chemistry could continuously produce methyl methacrylate through reaction-distillation cycles, without the need for a separate regeneration step as the exit caesium salt is caesium methylcarbonate, scheme 4.3. This would simplify process design and the chemical engineering of any process using this chemistry but would require a chemical plant producing dimethyl carbonate to be built next to the methyl methacrylate producing chemical plant.

However, for this alternative process to be economically competitive, the cost for the production of dimethyl carbonate would have to be less than the overall cost of the separate carbon dioxide regeneration process developed in section 3.2.3. A number of potential dimethyl carbonate producing processes were considered, such as the oxidative carbonylation of methanol (first commercialised by EniChem),[12–14] the esterification of urea [15] or the condensation of carbon dioxide with methanol. At this stage, it's unlikely that any of the dimethyl carbonate producing processes are sufficiently cost effective to make the *in situ* regeneration route commercially viable. Clearly, a breakthrough in the manufacture of dimethyl carbonate may make this one-pot, *in situ* regeneration of caesium methylcarbonate chemistry more attractive.

4.3 Conclusions

Selectivity for methacrylates based on the formaldehyde feed is an important consideration for a low temperature process for the production of methyl methacrylate from methyl propanoate, both because of the cost of purchasing and removing water from the feed and because of the production of waste products. Separation of the formaldehyde sugars from the non-volatile caesium salts is also not trivial, adding a further incentive to minimize the production of this waste material.

The selectivity on formaldehyde is improved by more than six-fold, from around 12.5 % to 73.7 %, when 1 equivalent of formaldehyde is added as methyl alcoform solution with a slow, continuous feed with the remaining reaction components at reaction temperature, compared with injection of reactants at intermediate temperature, the previous best system. This increase in formaldehyde selectivity makes the low temperature process more competitive with the current, heterogeneous ALPHA Stage Two process and further increases in selectivity in the low temperature process are expected with reduced loading of formaldehyde relative to methyl propanoate because formaldehyde decomposition reactions are at least second order on formaldehyde concentration where the condensation reaction is first order on formaldehyde.

At temperatures lower than 160 °C, formaldehyde decomposition reactions are much faster than the condensation reaction as these reactions have a lower energy barrier. However, at higher temperatures the condensation reaction becomes more favoured meaning higher formaldehyde selectivity is possible at higher temperature. Experiments at higher temperatures than 180 °C were not performed due to time constraints.

A “caesium effect” is observed in the reaction: as group 1 of the periodic table is descended, a steady increase in the initial activity of alkali metal methylcarbonates is observed. Caesium methylcarbonate is the most active methylcarbonate salt tested. The loading of caesium methylcarbonate was briefly investigated but not fully optimized. Increasing the caesium methylcarbonate loading to 1 equivalent relative to both methyl propanoate and formaldehyde does not lead to a large increase in initial activity in the condensation reaction.

Conditions in the condensation reaction of methyl propanoate with formaldehyde were improved such that the main disadvantage of this system over the current high temperature process was the hydrolysis, which results in base deactivation making base regeneration a requirement after each run for a process to work. To circumvent the requirement of a separate regeneration step, a new system involving *in situ* base regeneration using dimethyl carbonate was developed. In this system, any caesium propanoate or caesium methacrylate produced during the experiment undergoes a methylation reaction, re-producing methyl esters and caesium methylcarbonate. This means a process based on this chemistry would be a one-step process where the exit non-volatile salt can be re-used with no regeneration step. The disadvantage of such a system is that dimethyl carbonate would have to be purchased or, more likely, produced which may make the overall process uncompetitive economically.

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Chapter Five

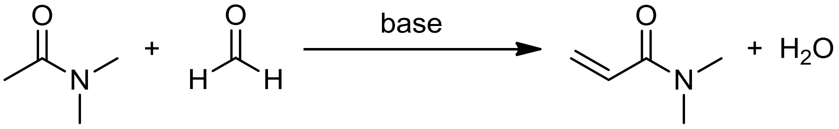
Solvent screening study for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde

5. Solvent screening study for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde

5.1 Introduction

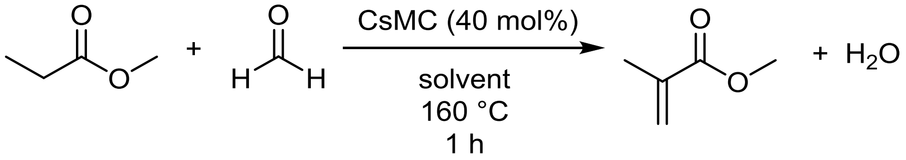
It has been argued that “the best solvent for any chemical process is no solvent at all”.[1] However, it is well established that a solvent can sometimes positively impact a chemical reaction. The considerable impact of the use of *N*,*N*-dimethylacetamide as a solvent for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde has shown that a “non-innocent” solvent is required to achieve high conversions in this reaction.

N,*N*-dimethylacetamide is not an industrially attractive solvent as a result of environmental, health and safety concerns. Also, the parallel reaction of *N*,*N*-dimethylacetamide with formaldehyde, scheme 5.1, has a detrimental effect on the formaldehyde selectivity for methacrylates since up to 10 % of the formaldehyde is consumed through this unwanted side reaction. Furthermore, the associated production of water results in more hydrolysis of methyl esters to caesium carboxylates.



Scheme 5.1: The side reaction condensation of formaldehyde with DMAc results in reduced formaldehyde selectivity for methacrylates and the production of water that leads to further hydrolysis of methyl esters.

It was therefore necessary to investigate the requirement for the solvent to be in the polar, aprotic class and the influence of polarity of the solvent on the reaction in order to identify the optimal solvent for the proposed industrial process. To begin to address this challenge, a solvent screening study using the optimized conditions from chapter 4 was undertaken, scheme 5.2.



Scheme 5.2: The conditions used for the solvent screening study involved addition of 1 equivalent of methyl alcoform at 0.05 mL min^{-1} at reaction temperature.

A number of requirements for the solvent can be identified: it must be stable to the reaction conditions, including high thermal stability and stability towards base, water and formaldehyde. Preferably the solvent should be of low environmental, health and safety concern and should be relatively cheap (although, if the solvent was stable to the reaction conditions indefinitely, an expensive, designer solvent would not be unworkable). Finally, the solvent must confer the increased reactivity observed using *N,N*-dimethylacetamide.

This chapter details work towards finding a suitable solvent. A range of solvents with varying polarities and solvent properties were identified for screening and grouped into five categories, figure 5.1. It was predicted that the caesium salts used would be most reactive in polar, aprotic solvents and solvents capable of disrupting ion pairs with oxygen and/or nitrogen donors.

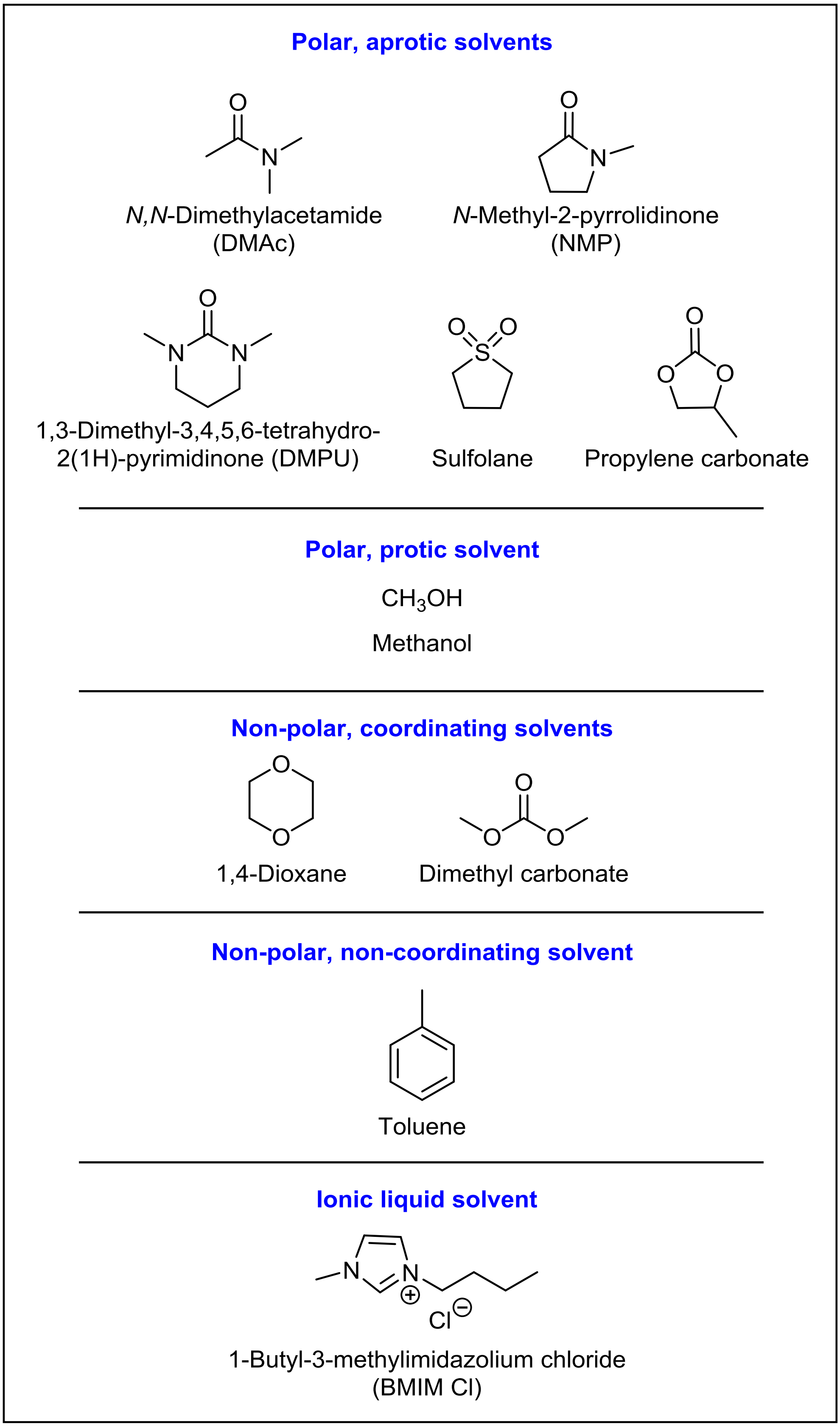


Figure 5.1: The solvents selected for the solvent screening study.

5.2 Results and Discussion

5.2.1 Polar solvents for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde

Table 5.1 reports the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde in several polar solvents and in the absence of an added solvent (i.e. methyl propanoate and methyl alcoform were the only liquids charged into the autoclave). In the absence of a solvent, the conversion of methyl propanoate to methacrylates was 4 %, whilst in the presence of polar, aprotic solvents a six-fold increase in conversion is observed, compare table 5.1, entry 1 with entries 3-5. With the polar, aprotic solvents the reaction is almost certainly a slurry due to the low solubility of caesium methylcarbonate in these solvents.

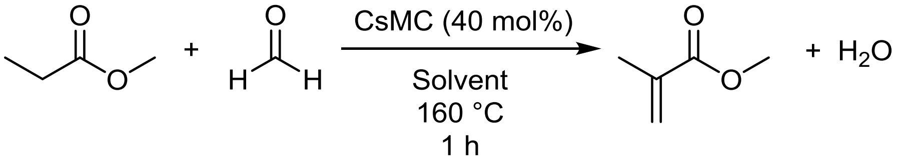


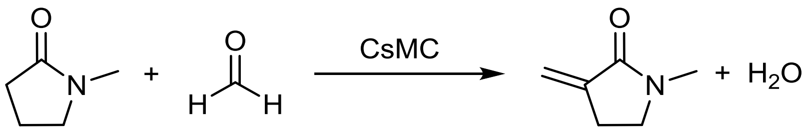
Table 5.1: Polar solvents in the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde.

Entry	Solvent	Dipole moment, μ[2]/ 10^{-30} Cm	MeP conversion to methacrylates (^{1}H NMR) / %	Hydrolysis to CsP + CsMA / %
1	No additional solvent	N/A	4	5
2	Methanol	9.6	4	23
3	*N*,*N*-Dimethylacetamide	12.4	22	25
4	*N*-Methyl-2-pyrrolidinone	13.6	24	26
5	DMPU	14.1	26	19
6	Sulfolane*	16.0	7	N.D
7	Propylene carbonate*	16.5	23	N.D

* Experiments run with injection of reactants.

The improved conversion with polar, aprotic solvents is consistent with the studies of Zaugg, where the rate of alkylation of enolates was significantly increased when polar, aprotic solvents were employed.[3] The effect is attributed to an increase in the base strength of the methylcarbonate base and increased nucleophilicity of the enolate species by solvating the caesium cations, leaving less-well stabilized, more reactive anions.

Both *N*,*N*-dimethylacetamide and *N*-methyl-2-pyrrolidinone react with formaldehyde. *N*-methyl-2-pyrrolidinone has protons in the *α*-position to the carbonyl group and so this solvent reacts with formaldehyde to give *N*-methyl-3-methylenepyrrolidin-2-one, scheme 5.3. The condensation product with *N*-methyl-2-pyrrolidinone is barely detectable by ^{1}H NMR spectroscopy, compared with 4 % of the formaldehyde reacting with *N*,*N*-dimethylacetamide under the same conditions – perhaps because of statistical reasons; *N*-methyl-2-pyrrolidinone has fewer protons in the *α*-position. DMPU, a cyclic urea (or carbamide) has no protons *α* to the carbonyl, hence no reaction between formaldehyde and DMPU is observed, resulting in less water production and less hydrolysis of methyl esters during the reaction. No other products from solvent side-reactions are observed with DMPU.



Scheme 5.3: Condensation of NMP with formaldehyde to form *N*-methyl-3-methylenepyrrolidin-2-one is detected by ^{1}H NMR spectroscopy, although to a reduced level compared with DMAc.

Sulfolane (a popular polar aprotic solvent for industrial process chemistry)[4] and propylene carbonate were not tested as the solvent under optimized conditions as experiments under unoptimized conditions showed that these solvents are not stable to the reaction conditions. The exit mixture from experiments using sulfolane had a strongly sulphurous smell and when propylene carbonate was used as solvent, large pressure increases during the experiments (up to 70.5 bar) were observed due to solvent decomposition.

Although the caesium salts are most soluble in methanol, no improvement in conversion was observed in this solvent, table 5.1, entry 2, confirming that solvent polarity and solubility of the caesium salts are not the only factors to be considered in solvent choice for the reaction. Protic solvents, such as methanol, are likely to result in poorer conversions as the deprotonation equilibrium involved in the mechanism of the condensation reaction of methyl propanoate with formaldehyde becomes even less favoured as there is a higher concentration of protons available for re-protonation of the enolate, resulting in a lower concentration of enolate species and so a slower reaction.

Furthermore, more hydrolysis of the esters to caesium propanoate and caesium methacrylate is observed when methanol is used as the solvent, possibly as a result of adventitious water in the methanol sample or as a result of increased levels of parallel condensation reactions of methanol to dimethoxymethane and/or dimethyl ether producing more water in the system.

5.2.2 Low polarity solvents for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde

Solvents of intermediate polarity were not tested due to time constraints. However, several solvents of low polarity were explored. Comparing the data in tables 5.1 and 5.2 it is clear that the reaction is strongly influenced by solvent polarity.

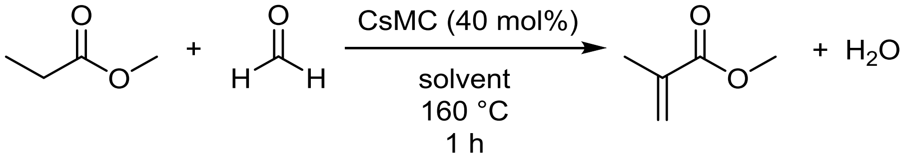


Table 5.2: Low polarity solvents result in poorer conversions of methyl propanoate to methacrylates.

Entry	Solvent	Dipole moment, μ[2] / 10^{-30} Cm	MeP conversion to methacrylates (^{1}H NMR) / %	Hydrolysis to CsP + CsMA / %
1	No added solvent	N/A	4	5
2	Toluene	1.0	0	0
3	1,4-Dioxane	1.5	3	2
4	Dimethyl carbonate	3.0*	13	0

* The dipole moment of dimethyl carbonate was converted from 0.91 D [5] to coulomb meters.

Solvents of the lowest polarity gave significantly poorer conversions of methyl propanoate to methacrylates than did the polar, aprotic solvents, or indeed the “solvent-less” reaction, table 5.2. This is attributed to the tighter ion pairing of the salts in these solvents resulting in a very weakly active methylcarbonate anion. Although 1,4-dioxane is capable of coordinating to caesium cations through the lone pairs on oxygen and this might have been expected to allow caesium methylcarbonate to exhibit some activity in the condensation reaction, a lower conversion was observed than in solvent-free conditions, table 5.2, entry 3. No methyl methacrylate or caesium methacrylate could be detected by ^{1}H NMR spectroscopy in the exit mixtures of experiments performed in toluene, presumably due to the formation of tightly held ion pairs reducing the activity of the methylcarbonate anion. Instead, the only species identified by ^{1}H NMR spectroscopy, other than the solvent were methyl propanoate, caesium methylcarbonate and formaldehyde.

Dimethyl carbonate is of intermediate polarity and affords moderate conversion of methyl propanoate to methacrylates and has the advantage that any caesium propanoate or caesium methacrylate formed is methylated back to the methyl ester and caesium methylcarbonate – a number of studies have shown that dimethyl carbonate can act as a methylating agent in the absence of polar, aprotic solvents at temperatures higher than its boiling point.[6–8] As noted in section 4.2.5, the disadvantage of this solvent is that around 3 dimethyl carbonate molecules are consumed for every methyl methacrylate molecule produced, either *via* the methylation reaction or through thermal decomposition.

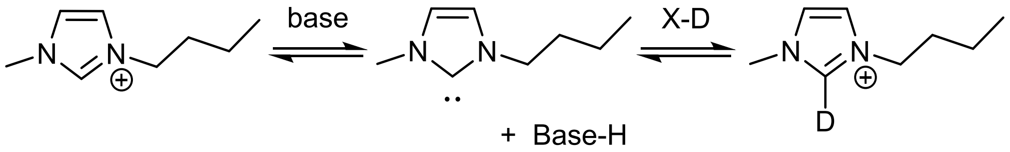
5.2.3 Stability of 1-butyl-3-methylimidazolium ionic liquids under condensation reaction conditions

Ionic liquids are interesting new solvents that are made up of ions, usually an organic cation (such as a quaternary alkyl ammonium) and an inorganic anion.[9–12] In some circumstances, the activity and/or reactivity of some systems is enhanced by the use of ionic liquids as solvents compared with conventional solvents,[13] and the use of these non-volatile solvents can have some processing advantages, so these solvents have found some industrial, large scale applications.[14] A patent has recently claimed that the condensation of methyl propanoate with formaldehyde to methyl methacrylate can be catalysed by basic imidazolium ionic liquids (that is, ionic liquids with anions that are basic).[15]

For this reason, ionic liquids were investigated as potential solvents and/or catalysts in the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde. Much of the work in the literature has focused on the use of imidazolium ionic liquids, and so the ionic liquid 1-butyl-3-methylimidazolium (BMIM) chloride was included in the solvent screening study. The low volatility of these compounds has led some to claim they are "green" solvents,[16,17] even though, for example, BMIM chloride is toxic to aquatic life with long lasting effects.

5.2.3.1 1-Butyl-3-methylimidazolium chloride stability at room temperature

While some reports have claimed imidazolium ionic liquids are stable under basic conditions or with basic anions,[18,19] a number of studies have shown that the C(2)-position of the imidazolium heterocycle is acidic.[20,21] The pK_a of this proton is relatively high, in the range of 21-24, depending on the solvent,[22,23] however H/D exchange reactions have shown that this proton is exchanging *via* a carbene species even at room temperature in the presence of mild bases such as tertiary amines [24] and inorganic carbonates and hydroxides,[25,26] scheme 5.4. Preparation of organometallic carbene complexes through deprotonation of an imidazolium salt with mild bases followed by salt metathesis is becoming increasingly popular,[26–29] and further confirms that the carbene species are present even under mild conditions.



Scheme 5.4: H/D exchange at the C(2)-position of the BMIM cation occurs *via* a highly reactive carbene species.

Deuterium exchange at the C(2)-position of imidazolium ionic liquids in deuterated “protic” solvents (e.g. D_2O, MeOD) occurs even in the absence of base,[21] resulting in a reduction in the intensity of the resonance for the proton at the C(2)-position in the ^1H NMR spectrum. In deuterochloroform ($CDCl_3$), in the absence of base, no deuterium exchange into the C(2)-position of BMIM chloride is observed.[21] However, on addition of caesium methylcarbonate to this solution, ^1H and ^2H NMR spectroscopic analysis shows H/D exchange occurs, causing a reduction in intensity of the C(2)-proton in the ^1H NMR spectrum to 0.2 relative to the other protons of BMIM chloride after 10 minutes at room temperature, figure 5.2. Resonances for 1-methylimidazole (MeIm) are present in the ^1H NMR spectrum suggesting dequarterization of the imidazolium cation occurs in the presence of base.

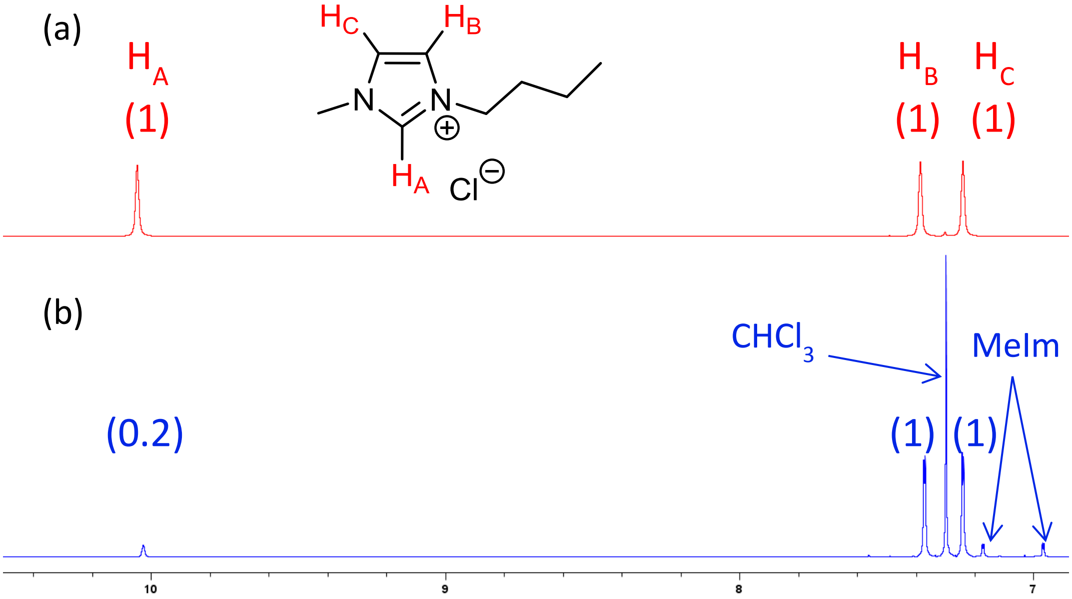
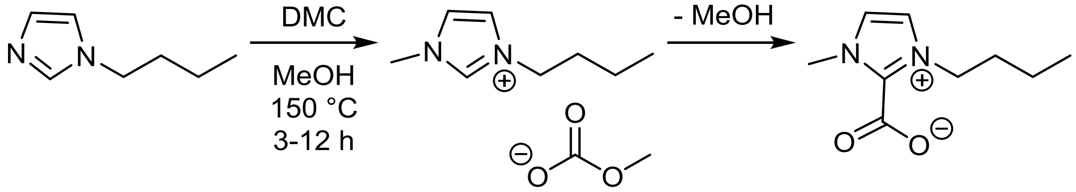


Figure 5.2: ^{1}H NMR spectra of BMIM chloride (a) before and (b) after addition of caesium methylcarbonate. In the presence of base, H/D exchange and some BMIM chloride decomposition occurs in deuterochloroform. Numbers in brackets = relative integrations.

Carbene species are highly reactive [30] and the formation, even transiently, of these free carbene species can have a dramatic influence on reactions involving ionic liquids.[23] Competitive consumption of a reactant through nucleophilic attack of the carbene on an electrophilic centre, such as an aldehyde in the base-catalysed Baylis-Hillman reaction results in poor yields of the desired product.[24] In some cases, nucleophilic attack of the carbene on a reactant can have a positive influence on a reaction, through the formation of a catalytic intermediate, such as a Breslow intermediate.[31]

Addition of a methanolic caesium methylcarbonate solution to BMIM chloride in deuteromethanol at room temperature results in a salt metathesis reaction, forming caesium chloride as a precipitate. This shows that the ionic liquid does not aid solubility of the caesium methylcarbonate, but rather forms a methylcarbonate ionic liquid. With excess ionic liquid (relative to the base), as in the case of the solvent test that follows, a mixture of BMIM chloride and methylcarbonate ionic liquids is formed with insoluble caesium chloride a spectator.

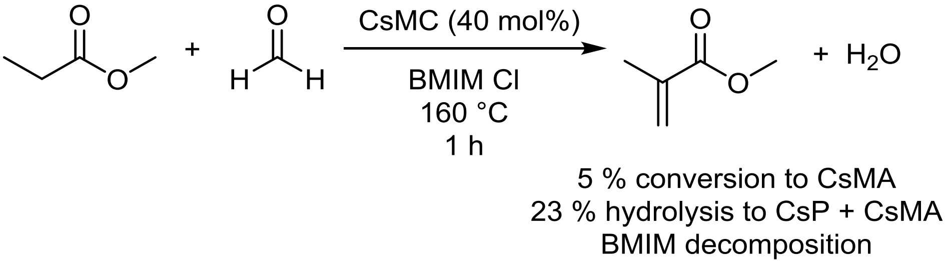
BMIM methylcarbonate is a known compound,[32] and was formed as a mixture through high temperature microwave synthesis from 1-butylimidazole and dimethyl carbonate. The other product of this synthesis is the zwitterionic 1-butyl-3-methylimidazolium-2-carboxylate, scheme 5.5. This species is formed through deprotonation of BMIM at the C(2)-position with the methylcarbonate anion, forming the carbene and hydrogen methylcarbonate, followed by decomposition of the hydrogen methylcarbonate to methanol and carbon dioxide, which is trapped by the carbene.



Scheme 5.5: High temperature synthesis of BMIM methylcarbonate [32] also produces 1-butyl-3-methylimidazolium-2-carboxylate.

5.2.3.2 1-Butyl-3-methylimidazolium chloride as a solvent for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde

BMIM chloride decomposes when it is used as the solvent in the caesium methylcarbonate-promoted condensation of methyl propanoate and formaldehyde. Also, only 5 % of the methyl propanoate is converted to caesium methacrylate (no methyl methacrylate is detected in the exit mixture) and 18 % of the methyl propanoate is converted to caesium propanoate, probably as a result of water being present in the highly hygroscopic ionic liquid.



Scheme 5.6: BMIM chloride is not a suitable solvent for the condensation of methyl propanoate with formaldehyde.

BMIM hydroxide was prepared [18] and used as in catalytic quantities in an attempt to mimic the conditions of the basic ionic liquid-promoted condensation of methyl propanoate with formaldehyde patent (above).[15] No conversion of methyl propanoate to methacrylates was observed. Instead, hydrolysis of methyl propanoate and ionic liquid decomposition were noted.

5.2.3.3 1-Butyl-3-methylimidazolium stability under reaction conditions

Comparison of the ^{1}H and ^{13}C{^{1}H} NMR spectra of the starting ionic liquid and of the crude exit mixture shows a significant proportion of the ionic liquid is decomposed, figure 5.3. Both 1-butyl-3-methylimidazolium-2-carboxylate, formed through high temperature decomposition of 1-butyl-3-methylimidazolium methylcarbonate,[32] as shown in scheme 5.5 (above), and 1-methylimidazole, as observed in section 5.2.3.1 are formed. Other small, unidentified resonances are present, presumably as a result of other BMIM decomposition reactions.

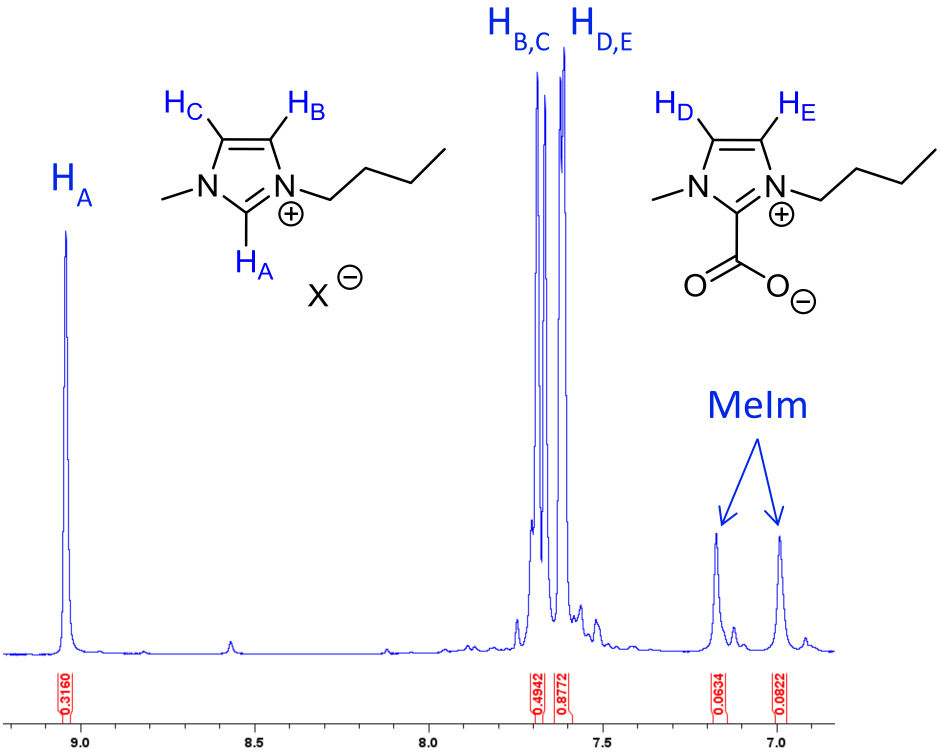


Figure 5.3: The ^{1}H NMR spectrum of the exit mixture shows the BMIM cation is decomposed during the condensation reaction experiment to a number of imizadole species, including 1-butyl-3-methylimidazolium-2-carboxylate.[32] X = Cl or methylcarbonate.

Consumption of the methylcarbonate base through the formation of 1-butyl-3-methylimidazolium-2-carboxylate, which is likely to be weakly basic with a $pK_{a\text{-}H}$ similar to caesium propanoate, may be the reason for the low conversion of methyl propanoate to methacrylates.

Owing to the low stability of BMIM and, presumably, other imidazolium ionic liquids, work was not continued with these solvents. Other base-stable ionic liquids with different cations have been identified in the literature, such as phosphonium,[33] simple tetra-alkyl ammonium [34] and heterocyclic ammonium [35] ionic liquids. When imidazolium cations are alkylated at the 2-position (for example with methyl or isopropyl groups), the stability towards base is increased, although some exchange is still observed with these trialkylimidazoliums.[36,37] An imidazolium with a phenyl group in the 2-position is stable in the presence of strong bases such as quinuclidine and Grignard reagents.[38] Owing to time constraints, further studies with these base-stable ionic liquids as solvents for the condensation of methyl propanoate with formaldehyde were not undertaken.

5.3 Conclusions

The caesium methylcarbonate-promoted condensation reaction of methyl propanoate and formaldehyde to methacrylates is strongly influenced by the polarity of the solvent used. More polar solvents partially aid dissolution of the caesium methylcarbonate (although the reaction mixture is still almost certainly a slurry) and reduce ion pairing, making the base more active. Solvents of very low polarity result in lower conversions than solvent-free conditions as the ions are more tightly paired as they are not stabilized by solvent interaction.

Solubility and disruption of ion pairing are not the only factors that must be considered in choice of the optimal solvent for the condensation reaction. Although caesium methylcarbonate is most soluble in methanol and the high polarity of the solvent should break up ion pairs, low conversions of methyl propanoate to methacrylates are achieved in methanol as the high concentration of relatively acidic protons solvates the methylcarbonate anion, making it less basic and the methyl propanoate deprotonation equilibrium becomes even less favourable as re-protonation of the enolate/carbanion intermediate becomes more favoured.

Solvent stability must also be considered: sulfolane and propylene carbonate decomposed during the experiments and so work with these solvents was abandoned. Dimethyl carbonate also decomposes slowly but has the advantage of returning caesium methylcarbonate to the reaction as caesium propanoate and caesium methacrylate are methylated back to the free esters (see chapter 4). Both of the amides with protons in the α-position, *N,N*-dimethylacetamide and *N*-methyl-2-pyrrolidinone, condense with formaldehyde, reducing the formaldehyde selectivity for methacrylates. Imidazolium ionic liquids are not stable under basic conditions and so are not viable solvents for this process. Other, base-stable ionic liquids were not tested due to time constraints.

The best solvent tested, in terms of stability and enhancement of the activity caesium methylcarbonate in the condensation reaction of methyl propanoate with formaldehyde is DMPU as it has a high dipole moment giving an enhancement of the reactivity of caesium methylcarbonate while the absence of protons in the *α*-position precludes side reaction with formaldehyde; no by-products as a result of reaction of the solvent with any of the reaction components were identified. Other solvents with similar properties can be identified, such as 1,3-dimethyl-2-imidazolidinone (DMEU or DMI) and 3-methyl-2-oxazolidinone, figure 5.4, however, owing to time constraints, these solvents were not tested.

1,3-dimethyl-2-imidazolidinone
dipole moment = $13.6\ 10^{-30}$ Cm

3-methyl-2-oxazolidinone
dipole moment = $13.7\ 10^{-30}$ Cm

Figure 5.4: Cyclic carbamides and carbamates identified as potential solvents for the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde.

In terms of environmental, health and safety issues, DMPU and DMEU are not attractive as they are both mutagenic (as are both *N*,*N*-dimethylacetamide and *N*-methyl-2-pyrrolidinone). Proper containment and disposal of these solvents would be required which would add significant extra costs to any process based on this chemistry. 3-Methyl-2-oxazolidinone is classified as a non-hazardous substance according to Regulation (EC) No. 1272/2008 and as not dangerous according to Directive 67/548/EEC,[39] but is expensive. However, if a cheap method for the production of this solvent were possible (e.g. by methylation of 2-oxazolidinone, perhaps with dimethyl carbonate), it might be the most attractive solvent for a process for the manufacture of methyl methacrylate using caesium methylcarbonate.

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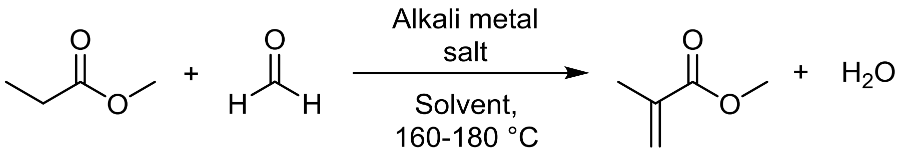
Chapter Six

Conclusions and future work

6. Conclusions and future work

The low temperature condensation of methyl propanoate and formaldehyde to methacrylates can be achieved with basic alkali metal salts. Compared with the current gas/solid caesium on silica catalysed ALPHA Stage Two Process and other literature systems that are run at over 300 °C, increased conversions to methacrylates with far greater selectivity on methyl propanoate are achieved at 160-180 °C. The homogeneous-like alkali metal salt process gives greater selectivity as a result of the mild conditions used and because the catalyst contains only basic sites compared with a mixture of basic and acidic sites on a metal on silica catalyst, allowing for acid catalysed transformations to take place resulting in more side-reactions to by-products.

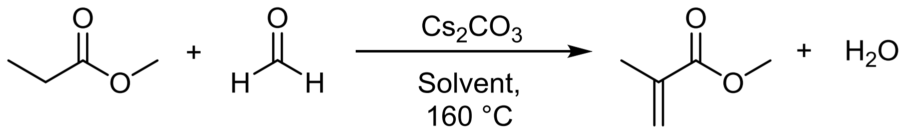


Lower temperatures than current process
Higher conversions to methacrylates with far greater selectivity on methyl propanoate

Scheme 6.1: The low temperature process developed using basic alkali metal salts and a solvent achieves high conversions with excellent selectivity.

NMR spectroscopic analysis is the preferred analytical technique for analysis of this system, allowing the non-volatile caesium salts to be observed along with the volatile material. Even though minor by-products could not be observed by NMR spectroscopy, these were accounted for by subsequent GC analysis.

Caesium carbonate can be used essentially as a pre-catalyst for the reaction, as it is converted to caesium methylcarbonate through reaction with methanol, scheme 6.2. The methylcarbonate-forming reaction is fast and so caesium methylcarbonate is likely to be the active species in this system. Using caesium carbonate brings the disadvantage that caesium hydroxide is inevitably produced by the methylcarbonate-forming reaction, resulting in the formation of more caesium propanoate and caesium methacrylate from methyl esters and thus lowering the overall efficiency of the process. The transformation of carbonates to methylcarbonate and hydroxide in methanol was found to be common to the group 1 carbonates. No method for the recycling of these carboxylates to carbonates was developed.

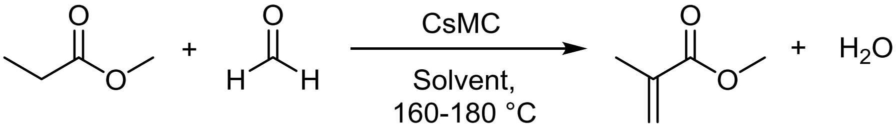


Up to 25 % conversion of methyl propanoate to methacrylates
Complete consumption of the Cs_2CO_3 base
CsP and CsMA are formed through the experiment and are
only very weakly active as base catalysts

Scheme 6.2: Caesium carbonate can be used as a pre-catalyst for the condensation reaction but more caesium propanoate and caesium methacrylate are formed as a result of base deactivation.

Caesium propanoate and caesium methacrylate have some very weak activity for the condensation of methyl propanoate with formaldehyde under the conditions used during the development of this project. However, the activity is significantly less than caesium carbonate or caesium methylcarbonate, even though the difference in base strength between these salts is relatively small. Because of the very weak activity, caesium propanoate and caesium methacrylate are not suitable bases for this reaction. Caesium hydroxide, a strong base, is also not a suitable base catalyst for this condensation reaction as conversion of methyl propanoate to caesium propanoate is faster than the condensation reaction.

Understanding of the mechanisms of base deactivation has allowed for a better base, caesium methylcarbonate, to be designed and for regeneration reactions to be developed. Caesium methylcarbonate is the most active base used, achieving up to 43 % conversion of methyl propanoate to methacrylates with selectivity on methyl propanoate of up to 99.5 %, compared with 18 % conversion at 93 % selectivity in the current ALPHA Stage Two process. Rubidium and potassium methylcarbonates are also active base promoters for the reaction but achieve reduced conversions as a result of increased ion pairing.



Up to 43 % conversion of methyl propanoate to methacrylates
Up to 99.5 % selectivity on methyl propanoate
Up to 73.7 % selectivity on formaldehyde

Scheme 6.3: Caesium methylcarbonate is a highly active base promoter for the condensation of methyl propanoate with formaldehyde, giving excellent selectivity for methacrylates.

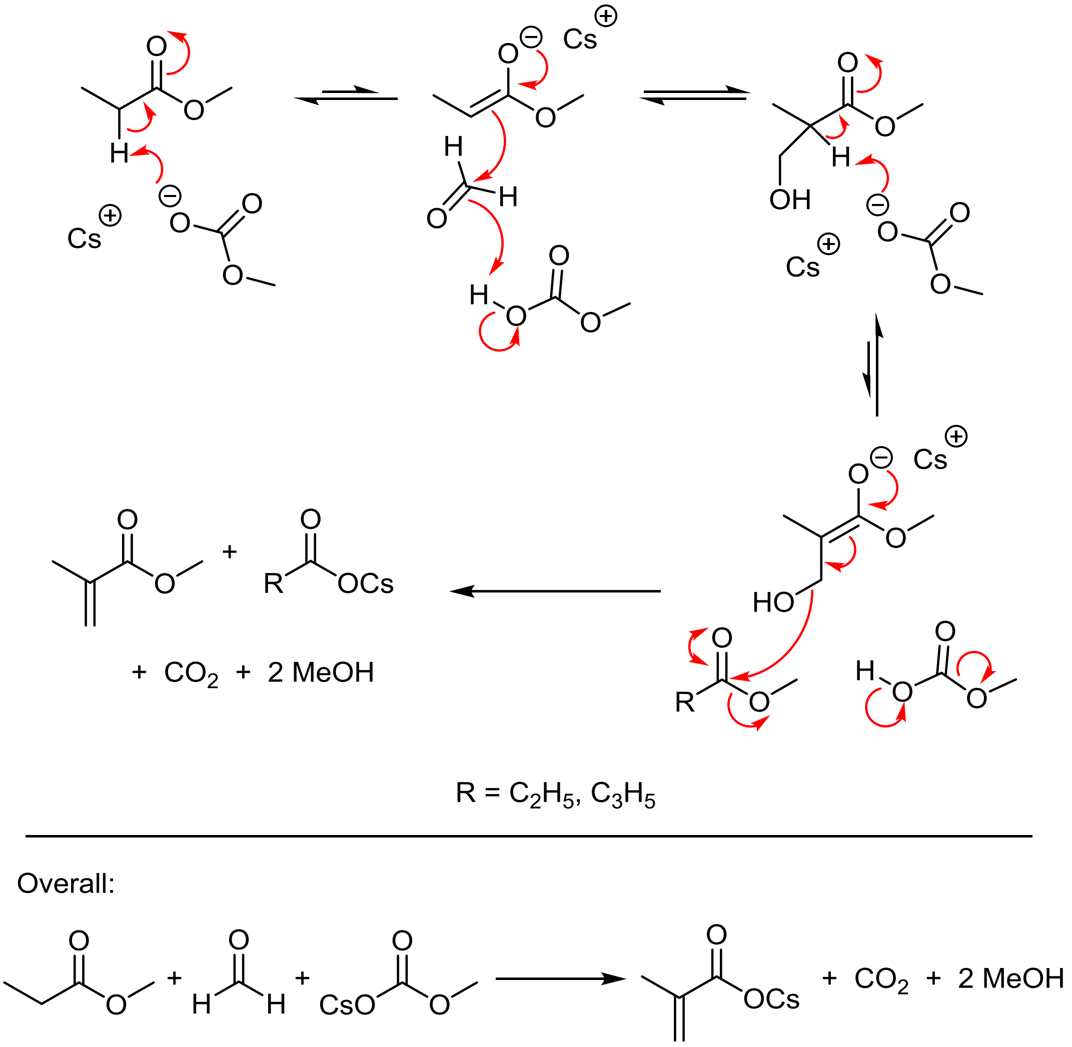
Only three by-products that are derived from methyl propanoate (methacrolein, methyl isobutyrate and 2-methyl propenol) that cannot be recycled are detected in this system. Methods for the recycling of caesium propanoate and caesium methacrylate have been developed and methyl 3-methoxy-2-propionate can also be recycled to methyl methacrylate.

There is a marked solvent effect in this low temperature system for the condensation of methyl propanoate with formaldehyde. A polar, aprotic solvent is crucial to achieving high activity in the system; conversions of up to 26 % in one hour can be achieved with polar, aprotic solvents compared with only 4 % in the absence of solvent or with other classes of solvent under the same conditions. The best solvent tested was 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU). 1,3-dimethyl-2-imidazolidinone and 3-methyl-2-oxazolidinone are also candidates for solvents for the reaction but have not been tested due to time constraints. Imidazolium-based ionic liquids are not suitable solvents for this reaction due to their low stability under basic conditions.

High temperature addition of formaldehyde is essential for high selectivity on formaldehyde, as formaldehyde decomposition reactions (Cannizzaro/Tishchenko reactions and formaldehyde sugar forming reactions) are more favoured at low temperature. The formaldehyde selectivity has been increased to 73.7 %, which is comparable to the current high temperature ALPHA Stage Two process. Selectivity on formaldehyde is increased at higher temperatures, with the best selectivity at the highest temperature tested, 180 °C. Reactions were not run at higher temperatures due to time constraints but investigation of this reaction at higher temperatures is necessary as increased formaldehyde selectivity is expected. Other variables, such as formaldehyde addition rate and dilution with further solvent were not properly investigated, also due to time constraints. Further increases in formaldehyde selectivity are expected with the use of sub-stoichiometric loadings of formaldehyde as this will reduce the formaldehyde concentration, further reducing the rate of formaldehyde decomposition reactions. Sub-stoichiometric formaldehyde loading experiments would also aid the development of the kinetic models used to predict the kinetics of the reaction, which is also necessary for the project moving forward.

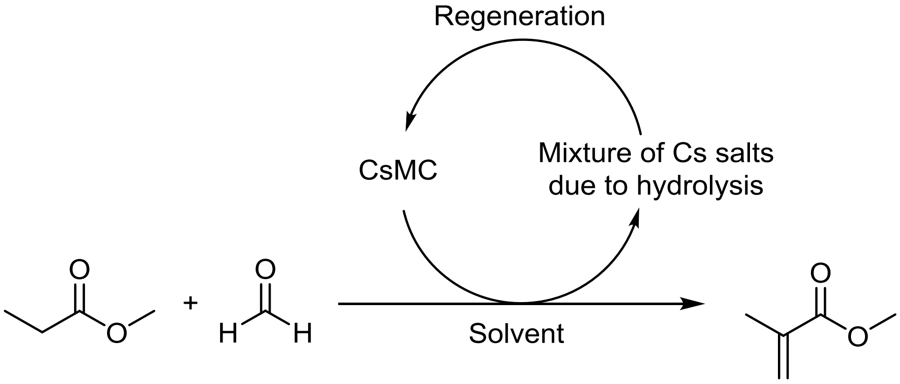
The main issue in this system is hydrolysis of methyl esters with water, of which there are a number of sources in the system, principally as the co-product of the reaction of methyl propanoate and formaldehyde, but water is also produced through condensation of hemiformal with methanol to dimethoxymethane and condensation of two methanol molecules to dimethyl ether, as well as condensation of formaldehyde with some of the solvents used.

Water (or hydroxide) is a short-lived species in the system and the consumption of water within the system through hydrolysis is entropically favoured. Hydroxide can be produced through collapse of the β-hydroxy intermediate formed in the mechanistic proposal from methyl propanoate and formaldehyde, scheme 6.4. This hydroxide could immediately hydrolyse a methyl ester (methyl propanoate or methyl methacrylate) through a $B_{AC}2$ mechanism, producing the caesium carboxylate and methanol. This hydrolysis would result in hydrogen methylcarbonate decomposition to carbon dioxide and another methanol molecule, leading to a maximum turnover per pass of one on caesium methylcarbonate. For this reason, caesium methylcarbonate is a stoichiometric promoter of the reaction, rather than a catalyst.



Scheme 6.4: Mechanistic proposal for the caesium methylcarbonate promoted condensation of methyl propanoate with formaldehyde. Hydroxide is produced from the β-hydroxy intermediate and immediately hydrolyses a methyl ester through the $B_{AC}2$ mechanism, causing hydrogen methylcarbonate decomposition.

Caesium propanoate and caesium methacrylate can be recycled back to caesium methylcarbonate and methyl esters, allowing for a process where the base is constantly recycled allowing for multiple turnovers on caesium through reaction-regeneration cycles, scheme 6.5. A suitable regeneration procedure to attain multiple recycles of caesium methylcarbonate is essential for any process based on this chemistry to become commercially viable.



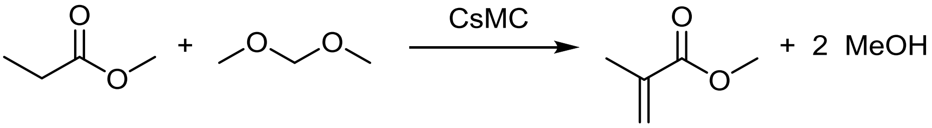
Scheme 6.5: Regeneration cycles are required for multiple turnovers on caesium, which is a pre-requisite for any commercial process based on this chemistry.

Two methods for this recycling have been developed; (i) *in situ* methylation of the caesium carboxylates with dimethyl carbonate and (ii) esterification of the caesium carboxylates with carbon dioxide and methanol, co-producing caesium methylcarbonate. The *in situ* method allows for a one step production process, with a potentially simpler purification procedure, allowing for distillation of reactants and products from caesium methylcarbonate and solvent. However, owing to the cost of dimethyl carbonate and the reduced conversions achieved as a result of the reduced polarity of the solvent system, this system is unlikely to be commercially competitive.

The carbon dioxide-promoted regeneration reaction can be run at the same or similar temperatures to the condensation reaction conditions, negating the need for large temperature swings during the proposed process (unlike the current heterogeneous process). While an understanding of the conditions required to achieve regeneration of caesium carboxylates to methyl esters and caesium methylcarbonate has begun (high temperature and high pressure of carbon dioxide increase the conversion), further work is required to understand this reaction fully to allow for further optimization of the conditions.

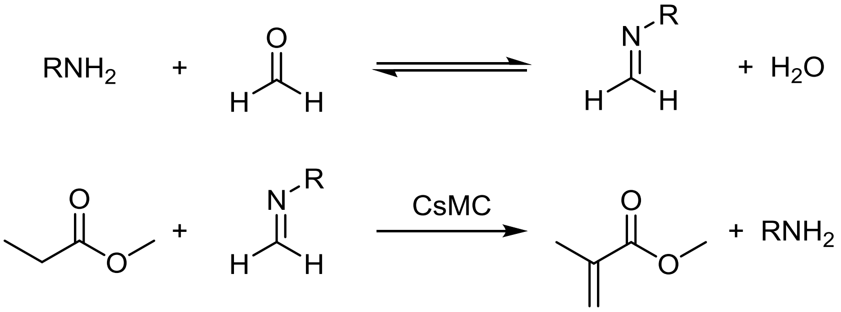
Regeneration to pure caesium methylcarbonate is significantly slower than the condensation reaction and requires a larger volume and increased pressure, effectively making the major part of the process (in terms of energy and space usage) the regeneration, rather than the condensation reaction. For this reason, further work to understand the regeneration reaction kinetics, as well as the requirement for excess methanol, is required. It is likely that full conversion of caesium carboxylates to caesium methylcarbonate will not be feasible under process conditions and so an acceptable regeneration target will also have to be found.

Alternatively, hydrolysis to caesium propanoate and caesium methacrylate must be prevented in the reaction system. *In situ* regeneration with high pressures of carbon dioxide during the condensation reaction may help to disfavour hydrolysis, although this was not tested. Dimethyl carbonate can be used effectively as a sacrificial water scavenger, and has the advantage of regenerating caesium methylcarbonate, there are other, alternative approaches to preventing hydrolysis that could be employed. For example, other reagents capable of acting as methylene sources could be used to instead produce co-products other than water. For example, if dimethoxymethane is used as a methylene source, two methanol molecules are co-produced with every methyl methacrylate molecule, scheme 6.6.



Scheme 6.6: Using dimethoxymethane as a methylene source instead of formaldehyde results in a "water-free" system for the production of methyl methacrylate.

Mannich-type chemistry, using imine or iminium species as methylene sources, scheme 6.7, could be used to co-produce amines that could be recycled through a separate condensation reaction with formaldehyde. In both cases, hydrolysis would be expected to be blocked as the water content of such systems should be zero. However, owing to time constraints, these systems were not investigated.



Scheme 6.7: Mannich-type chemistry allows for removal of water in a separate stage, keeping the methyl methacrylate-forming reaction "water-free".

Further work is continuing at Lucite International on the caesium methylcarbonate-promoted condensation of methyl propanoate with formaldehyde and the research detailed in this PhD thesis has formed the basis of a patent that has been submitted. A process based on this work is under active consideration for commercialization. Work towards process flow diagrams are in progress by chemical engineers at Lucite International with the aim of providing further guidance to determine if the process can be competitive with the current, high temperature ALPHA Stage Two process is underway.

Chapter Seven

Experimental

7. Experimental

7.1 General information

Caesium carbonate (99 % metals basis) was purchased from Sigma-Aldrich, Acros Organics or Alfa Aesar, with no noticeable difference in activity between each sample. Methyl propanoate and methyl alcoform were provided by Lucite International. Methyl alcoform was stored over activated 3 Å molecular sieves. All other reagents were purchased from Sigma-Aldrich or Acros Organics and used as received unless otherwise stated. Alkali metal salts and solvents were stored in a nitrogen-filled glovebox. *N*,*N*-Dimethylacetamide was distilled under vacuum over calcium hydride and stored over activated 3 Å molecular sieves in a nitrogen-filled glovebox.[1] Methanol and toluene were distilled according to literature methods.[2] Other solvents were purchased as >99 % purity grade or stored over activated 3 Å molecular sieves in a nitrogen-filled glovebox.[3]

NMR experiments were performed on a Bruker AVII-400 spectrometer or DPX-400 spectrometer, both operating at 400.13 MHz (^{1}H) and 100.61 MHz (^{13}C). Chemical shifts are reported in ppm and are referenced to the residual solvent peaks. Coupling constants are reported in Hz. ^{133}Cs NMR experiments were run on a Bruker AvIII-500 spectrometer at 65.59 MHz. IR spectra were recorded on a Bruker ALPHA FTIR Spectrometer with platinum ATR sample assembly.

Catalyst testing (condensation reaction) experiments were performed in duplicate and the average conversion and hydrolysis data are reported. The carbon dioxide regeneration experiments were mostly run once each due to time constraints. Catalyst testing experiments in chapters 2 and 3 used excess formaldehyde (2 molar equivalents) relative to methyl propanoate, as per the preliminary work. Catalyst testing experiments in chapters 4 and 5 used a 1:1 molar ratio of methyl propanoate and formaldehyde.

7.2 Autoclave set up

A 25 mL Parr Series 4590 pressure reactor [4] was fitted with Kalrez 4079 o-rings, supplied by Dichtomatik (methyl propanoate corrodes standard o-rings, which could be used disposably, if necessary). The autoclave contained an internal thermocouple and a magnetic stirrer drive that averaged approximately 500-600 rpm. A tap was fitted as an inlet for injection/dropwise addition. A REX-P90 series digital program controller was used for heating control. A 200 bar rated Druck PDCR 91 pressure transducer, attached to a Druck DPI 280 Digital Process Indicator was fitted.

7.3 Generic catalyst testing experimental procedure

The autoclave was charged with base, methyl propanoate (2.65 g, 30 mmol), methyl alcoform (3.3 mL, 60 mmol formaldehyde) and (if used) solvent (6 mL). The mixture was heated to 160 °C over 50 minutes and then the temperature was maintained at 160 °C for the experiment time before cooling to room temperature by carefully placing the hot autoclave into a large bucket of ice. Any residual pressure was released slowly and the exit mixture was dissolved in methanol. A sample was added to d_4-methanol for NMR (^{1}H and ^{13}C{^{1}H}) spectroscopic analysis.

Table 7.1: NMR data for reactants, products and bases used throughout the thesis.

Compound	**^{1}H (400 MHz, d_4-MeOD, ppm) δ**	**^{13}C{^{1}H} (100 MHz, d_4-MeOD, ppm) δ**
Methyl propanoate	3.66 (s, 3H, $\mathrm{OC}\mathbf{H_3}$), 2.34 (q, ^3J = 7.7 Hz, 2H, $\mathrm{C}\mathbf{H_2}$), 1.17 (t, ^3J = 7.7 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	174.8 (**C**(O)), 50.7 ($\mathrm{O}\mathbf{C}\mathrm{H_3}$), 26.7 ($\mathbf{C}\mathrm{H_2}$), 8.2 ($\mathbf{C}\mathrm{H_3}$).
Methyl methacrylate	6.06 (m, 1H, C**H**), 5.58 (m, 1H, C**H**), 3.73 (s, 3H, $\mathrm{OC}\mathbf{H_3}$), 1.92 (dd, ^4J = 1.3, 1.6 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	167.3 (**C**(O)), 136.3 (**C**H), 124.6 (**C**H), 51.0 ($\mathrm{O}\mathbf{C}\mathrm{H_3}$), 17.4 ($\mathbf{C}\mathrm{H_3}$).
Caesium propanoate	2.19 (q, ^3J = 7.6 Hz, 2H, $\mathrm{C}\mathbf{H_2}$), 1.12 (t, ^3J = 7.6 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	182.4 (**C**(O)), 30.8 ($\mathbf{C}\mathrm{H_2}$), 10.0 ($\mathbf{C}\mathrm{H_3}$).
Caesium methacrylate	5.76 (m, 1H, C**H**), 5.25 (m, 1H, C**H**), 1.94 (dd, ^4J = 1.1, 1.3 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	175.3 (**C**(O)), 143.5 (**C**H), 118.4 (**C**H), 18.9 ($\mathbf{C}\mathrm{H_3}$).
Rubidium propanoate	2.18 (q, ^3J = 7.7 Hz, 2H, $\mathrm{C}\mathbf{H_2}$), 1.07 (t, ^3J = 7.7 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	181.1 (**C**(O)), 29.8 ($\mathbf{C}\mathrm{H_2}$), 9.6 ($\mathbf{C}\mathrm{H_3}$).
Potassium propanoate	2.16 (q, ^3J = 7.7 Hz, 2H, $\mathrm{C}\mathbf{H_2}$), 1.08 (t, ^3J = 7.7 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	181.8 (**C**(O)), 30.2 ($\mathbf{C}\mathrm{H_2}$), 9.7 ($\mathbf{C}\mathrm{H_3}$).
Sodium propanoate	2.15 (q, ^3J = 7.7 Hz, 2H, $\mathrm{C}\mathbf{H_2}$), 1.08 (t, ^3J = 7.7 Hz, 3H, $\mathrm{C}\mathbf{H_3}$).	182.5 (**C**(O)), 30.6 ($\mathbf{C}\mathrm{H_2}$), 9.9 ($\mathbf{C}\mathrm{H_3}$).
Caesium carbonate	-	168.8 ($\mathbf{C}\mathrm{O_3^{2-}}$).
Caesium methylcarbonate	3.53 (s, 3H, $\mathrm{-OC}\mathbf{H_3}$).	160.1 (**C**(O)), 52.0 ($\mathrm{-O}\mathbf{C}\mathrm{H_3}$).
Rubidium methylcarbonate	3.50 (s, 3H, $\mathrm{-OC}\mathbf{H_3}$).	159.9 (**C**(O)), 51.9 ($\mathrm{-O}\mathbf{C}\mathrm{H_3}$).
Potassium methylcarbonate	3.50 (s, 3H, $\mathrm{-OC}\mathbf{H_3}$).	159.9 (**C**(O)), 51.9 ($\mathrm{-O}\mathbf{C}\mathrm{H_3}$).
Sodium methylcarbonate (MeP, MeOH, Na_2CO_3 mixture)	3.50 (s, 3H, $\mathrm{-OC}\mathbf{H_3}$).	160.0 (**C**(O)), 51.9 ($\mathrm{-O}\mathbf{C}\mathrm{H_3}$).

Table 7.2: IR bands of alkali metal salts used with relative intensities (br = broad, s = strong, m = medium, w = weak).

Compound	**ṽ / cm^{-1}**
Caesium propanoate	2970 (w), 2936 (w), 2877 (w), 1636 (m), 1560 (s), 1459 (w), 1374 (m), 1359 (m), 1290 (m), 1071 (m), 998 (m), 850 (s), 812 (s), 631 (m), 482 (m).
Caesium methacrylate	3087 (w), 2971 (w), 2922 (w), 1690 (m), 1626 (w), 1552 (s), 1451 (m), 1432 (m), 1397 (s), 1372 (s), 1235 (m), 997 (m), 929 (s), 878 (m), 834 (s), 815 (m), 660 (m), 591 (s), 536 (m), 506 (m).
Rubidium propanoate	3291 (br), 2969 (m), 2933 (w), 2875 (w), 1646 (w), 1560 (s), 1460 (m), 1398 (s), 1360 (s), 1291 (s), 1072 (m), 1001 (w), 865 (m), 811 (m), 639 (w), 491 (m).
Potassium propanoate	2968 (m), 2921 (w), 2875 (w), 1700 (w), 1561 (s), 1462 (m), 1408 (s), 1363 (s), 1293 (s), 1269 (m), 1072 (m), 1001 (m), 869 (m), 810 (m), 639, 577 (w), 499 (m).
Sodium propanoate	3363 (br), 2971 (m), 2937 (w), 2874 (w), 1554 (s), 1461 (s), 1443 (s), 1413 (s), 1367 (s), 1295 (s), 1075 (m), 1002 (w), 877 (m), 812 (s), 642 (s), 580 (m), 504 (s).
Caesium carbonate	2967 (w), 1715 (w), 1562 (w), 1439 (w), 1326 (s), 1040 (w), 875 (m), 709 (w), 673 (w).
Caesium methylcarbonate	2978 (w), 2946 (w), 2841 (w), 1652 (s), 1570 (w), 1474 (w), 1436 (m), 1355 (w), 1297 (s), 1185 (w), 1071 (s), 892 (s), 823 (m), 678 (w), 662 (w), 588 (m).
Rubidium methylcarbonate	3272 (br), 2496 (br), 1628 (m), 1437 (w), 1292 (m), 1181 (m), 1070 (m), 1016 (m), 886 (m), 864 (m), 844 (s), 823 (m), 702 (w), 632 (s), 582 (m).
Potassium methylcarbonate	2994 (w), 2966 (w), 2846 (w), 1668 (m), 1563 (m), 1474 (m), 1435 (m), 1394 (m), 1363 (m), 1294 (s), 1182 (m), 1070 (s), 890 (s), 870 (m), 823 (s), 705 (w), 685 (w), 672 (w), 583 (m).

7.4 Determination of conversion, hydrolysis and selectivity

The ^1H T_1 relaxation constants for the reaction components of interest were estimated using Bruker's T1ir pulse program using the zero (null)-crossing estimate method.[5]

T_1 relaxation constants of pure samples (methyl propanoate, methyl methacrylate, caesium propanoate and caesium methacrylate) in methanol and in the crude exit mixture were measured, table 7.3. The T_1 relaxation constants of the four reaction components were significantly shortened in the exit mixtures compared with the pure samples owing to differences in concentration, change in solvent composition and the presence of formaldehyde sugars.

Table 7.3: T_1 relaxation constants of the four reaction components of interest, as estimated by the zero (null) crossing experiment using the t1ir1d pulse program.

Reaction component	T_1 measured with "pure" sample in methanol / seconds	T_1 measured in crude exit mixture / seconds
Methyl propanoate (CH_2)	4.48	1.40-2.10
Caesium propanoate (CH_2)	1.54	0.84-1.40
Methyl methacrylate (CH_3)	2.38	0.84-1.40
Caesium methacrylate (CH_3)	2.10	0.84-1.40

The d1 delay time in the ^1H NMR experiments used was 15 seconds minimum with a 5 second acquisition time, with 64-160 scans.

The methyl (CH_3) resonances of methyl methacrylate and caesium methacrylate and the methylene (CH_2) resonances of methyl propanoate and caesium propanoate in the ^1H NMR spectrum were used for determination of conversion and hydrolysis. The methyl resonances of methyl propanoate and caesium propanoate overlap so were not used. The methylene integrations were corrected (x 3/2) to allow for comparison with the methyl resonances.

Conversion to methacrylates was determined as:

$$Conversion\ to\ methacrylates = \frac{MMA + CsMA}{MeP + CsP + MMA + CsMA} \times 100\ \%$$

Hydrolysis was determined as:

$$Hydrolysis = \frac{CsP + CsMA}{MeP + CsP + MMA + CsMA} \times 100\ \%$$

The conversion determined by ^{1}H NMR spectroscopy fits well with the GC data acquired at Lucite International on vacuum distilled samples, suggesting the NMR spectroscopic assay is adequate.

Selectivity on methyl propanoate and formaldehyde were calculated by Lucite International according to their own protocols.

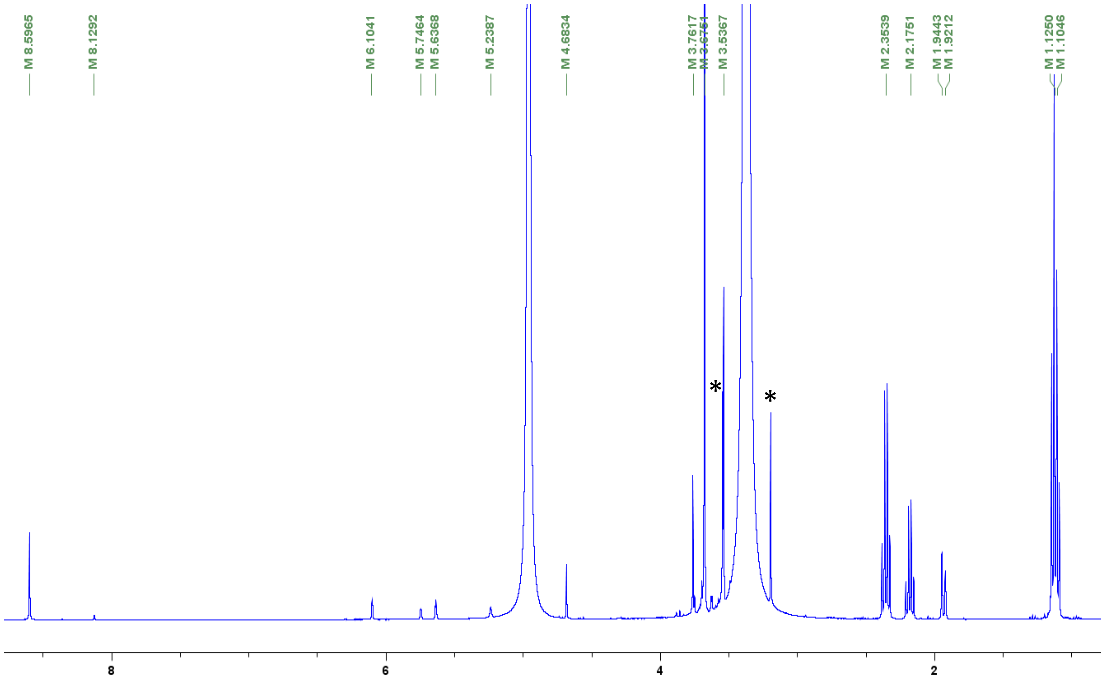


Figure 7.1: Example ^{1}H NMR spectrum of an exit mixture from a condensation reaction catalyst testing experiment. * ^{13}C satellites of methanol.

Table 7.4: Assignment of compounds present (figure 7.1).

Entry	Compound	Chemical shift(s) / ppm
1	Methyl propanoate	3.68, 2.35, 1.13
2	Caesium propanoate	2.18, 1.10
3	Methyl methacrylate	6.10, 5.64, 3.76 1.94
4	Caesium methacrylate	5.75, 5.24, 1.92
5	Methanol	4.95, 3.34
6	Caesium methylcarbonate	3.54
7	Unreacted formaldehyde	4.68
8	Caesium formate	8.60
9	Methyl formate	8.13, 3.75

All NMR data for catalyst testing experiments and regeneration reactions can be found on the supplementary CD.

7.5 Experimental section for chapter 2

7.5.1 Caesium carbonate/methylcarbonate NMR experiments

Method 1: Caesium carbonate was dissolved in a methanol/d_4-methanol (ca. 80:20) mixture at the desired concentrations (5 different samples) and NMR experiments were then performed.

Method 2: Caesium carbonate was dissolved in the methanol/d_4-methanol mixture for NMR spectroscopic analysis followed by subsequent dilution with more methanol.

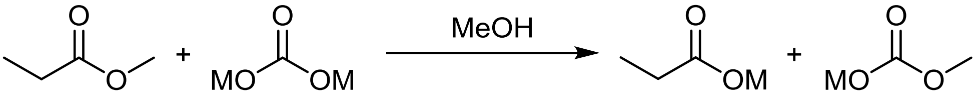
See section 2.2.2 for stack plot of $^{13}C\{^1H\}$ NMR spectra. The NMR data can be found on the supplementary CD at mike\Alkali metal salts\Caesium\Cs2CO3 + MeOH study.

7.5.2 Methyl propanoate hydrolysis NMR experiments

To the 1.2 M caesium solution (from above), methyl propanoate (5 equivalents relative to starting caesium carbonate) was added. After shaking, the mixture was still heterogeneous. The mixture was placed into the NMR spectrometer probe and heated to 313 K, causing dissolution of the solid. A multizg NMR experiment was started where alternating ^1H and $^{13}C\{^1H\}$ experiments were performed for approximately 12 hours. The supplementary CD contains all the NMR files in the folder: mike\Alkali metal salts\Caesium\Cs2CO3 + MeOH + MeP study.

7.5.3 Methyl propanoate hydrolysis with alkali metal carbonates

Methanol (6 mL) was added to alkali metal carbonate (Cs, Rb, K, Na) (0.6 mmol) and stirred for 3 hours. Methyl propanoate (0.54 g, 6 mmol, 10 equivalents) was added. After 1 hour a sample of the caesium and rubidium samples were taken (potassium and sodium samples were heterogeneous) and added to d_4-methanol for ^{1}H and ^{13}C{^{1}H} NMR spectroscopic analysis. After 3 days, the potassium sample had dissolved and a sample was taken. In the case of sodium, extra methanol (10 mL) was added but full dissolution still did not occur in several weeks and so the solid was allowed to settle at the bottom of the vial and a sample of the solution was taken.



M = Na, K, Rb, Cs

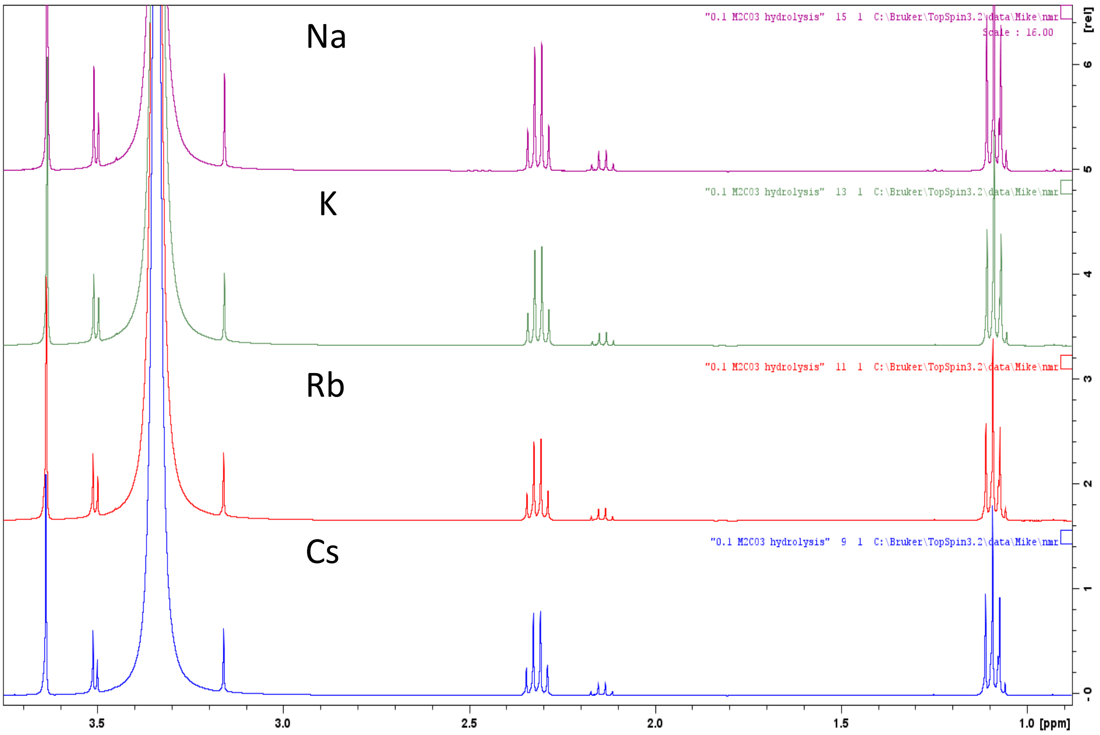
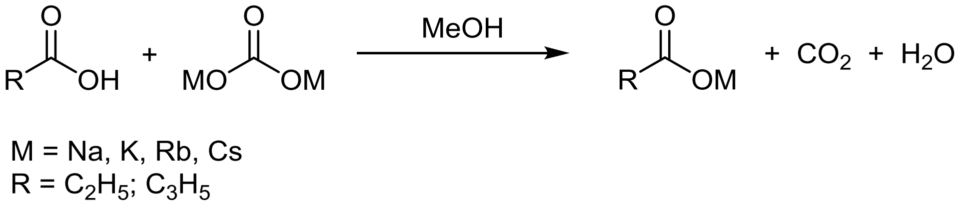


Figure 7.2: Alkali metal propanoates are formed from methyl propanoate with alkali metal carbonates in methanol.

7.5.4 Preparation of alkali metal carboxylates (propanoate and methacrylate)



Scheme 7.1: Preparation of alkali metal propanoate and methacrylate salts

Caesium propanoate was prepared according to literature methods [6] and scaled up to 28.5 g scale. The procedure was modified for the preparation of other alkali metal propanoates and caesium methacrylate (addition of methacrylic acid, rather than caesium propanoate) and for other alkali metal salts.

Alkali metal carbonate (87.4 mmol) was dissolved in methanol (500 mL). Propanoic acid (14.2 g, 192.3 mmol, 2.2 equivalents) was added slowly, causing bubbling. After 1 hour the volatiles were removed *in vacuo* giving a white gel that was washed with diethyl ether (3x 100 mL) and the solid was dried under high vacuum giving a semi-crystalline white powder that was stored in the nitrogen-filled glovebox.

7.5.5 Catalyst testing experiments with injection of reactants

The autoclave was charged with base, methyl propanoate (2.65 g, 30 mmol) and (if used) solvent (6 mL). The mixture was heated to 135 °C over 40 minutes and then methyl alcoform (3.3 mL, 60 mmol formaldehyde) was injected into the autoclave using 15 bar pressure of nitrogen. The tap was closed once the pressure inside the autoclave had reached the set pressure on the nitrogen feed line. The mixture was then heated to 160 °C over 10 minutes and the experiment was then continued in the same way as section 7.3.

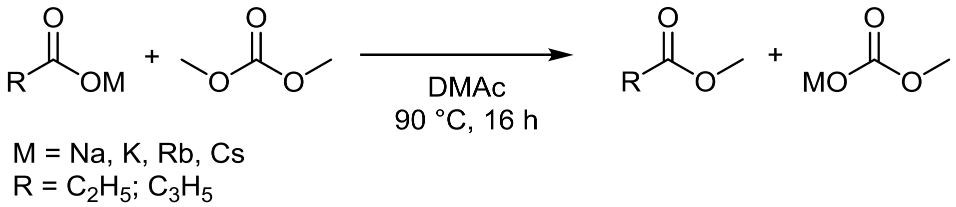
Or, the autoclave was charged with base and solvent before heating to injection temperature. Both methyl propanoate and methyl alcoform were injected with nitrogen. CAUTION: methyl propanoate swells o-rings in the tap and these must be inspected and replaced regularly. The tap leaks when the o-ring is perished, potentially releasing gaseous formaldehyde.

The supplementary CD contains movies recorded during injection of methyl propanoate and methyl alcoform, showing the temperature spike and pressure increase on injection. mike\Chapter 2 Cs2CO3 promoted condensation\Section 2.2.4.1 Injection.

Figure 7.3: Autoclave controller before injection: Green temperature (109 °C) = temperature inside the autoclave according to the internal thermocouple; red temperature (113 °C) = desired temperature according to the heater program; pressure indicator reads 2.44 bar.

7.6 Experimental section for chapter 3

7.6.1 Methylation of alkali metal carboxylates with dimethyl carbonate



Scheme 7.2: Methylation of alkali metal carboxylates with dimethyl carbonate.

Alkali metal propanoate (1 mmol), *N*,*N*-dimethylacetamide (50 mL) and dimethyl carbonate (18 mL, 20 mmol, 20 equivalents) were heated to 90 °C under a nitrogen environment with vigorous stirring for 16 hours. The stirring was stopped and the mixture cooled to room temperature. The off-white solid was collected by filtration and the pale yellow filtrate was stored under nitrogen. The solid was washed with methyl propanoate or ethyl acetate (3x 30 mL) and then dried under vacuum giving clumps of a fluffy white solid that was transferred into the glovebox and crushed with a pestle and mortar.

Caesium methylcarbonate: scale up to 96 g (0.47 moles) with 1 L *N*,*N*-dimethylacetamide and 1 L dimethyl carbonate.

7.6.2 Caesium methylcarbonate regeneration from caesium propanoate or methacrylate with carbon dioxide

Caesium carboxylate (4.85 mmol) was dissolved in methanol (9 mL) and charged into the autoclave. The autoclave was pressurized slowly with carbon dioxide to the desired pressure and then sealed. The mixture was heated to reaction temperature for the desired time and then cooled to room temperature. The residual pressure was released slowly. The exit mixture was taken for ^{1}H and ^{13}C{^{1}H} NMR spectroscopy in d$_4$-methanol.

An improved method was developed for future experiments: The autoclave was pressurized to the desired pressure with carbon dioxide and heated to the reaction temperature. A solution of alkali metal carboxylate in methanol was added using the Gilson pump. Owing to time constraints, regeneration experiments were not repeated with this improved method.

7.7 Experimental section for chapter 4

7.7.1 Condensation reaction experiments with a drip feed of methyl alcoform at reaction temperature

The autoclave was charged with caesium methylcarbonate (2.5 g, 12 mmol), methyl propanoate (2.65 g, 30 mmol) and solvent (6 mL). The mixture was heated to reaction temperature. Methyl alcoform was filtered and added to the hot reaction mixture at 0.05 mL min^{-1} using a Gilson 305 pump with a 5SC-type pump head (33 minutes, 1.65 g, 30 mmol, 1 of equivalent formaldehyde). After the addition, the pump was stopped and the tap closed. The experiment was then continued in the same way as section 7.3. The start of the reaction time was defined as at the onset of methyl alcoform addition.

7.7.2 *In situ* regeneration of caesium methylcarbonate using dimethyl carbonate

The autoclave was charged with caesium methylcarbonate (2.5 g, 12 mmol), methyl propanoate (2.65 g, 30 mmol), dimethylcarbonate (2.71 g, 30 mmol) and *N*,*N*-dimethylacetamide (6 mL). The mixture was heated to the reaction temperature.

Methyl alcoform was filtered and added to the hot reaction mixture at 0.05 mL min^{-1} using the Gilson pump (33 minutes, 1.65 g, 1 equivalent of formaldehyde).

7.8 Experimental section for chapter 5

7.8.1 Solubility study of caesium methylcarbonate in *N*-methyl-2-pyrrolidinone and 1,3-dimethyl-3,4,5,6-tetrahydro-2-pyrimidinone

A thick-walled Carius tube was charged with caesium methylcarbonate (1 g) and solvent (10 mL). The mixture was heated with stirring at 160 °C. The mixtures were visually inspected. In both cases, almost all of the solid remained undissolved at high temperature. The mixtures were cooled to room temperature. Small crystals formed after cooling suggesting there is some solubility at high temperature.

7.8.2 1-Butyl-3-methylimidazolium chloride stability experiments

Stability in chloroform:

1-Butyl-3-methylimidazolium chloride (0.2 g, 1.1 mmol) was dissolved in $CDCl_3$ (0.6 mL) and stored for 24 hours before ^{1}H, ^{2}H and $^{13}C\{^1H\}$ NMR experiments were run.

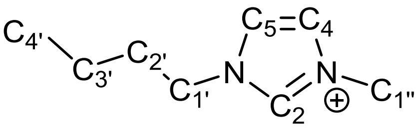


Figure 7.4: 1-Butyl-3-methylimidazolium cation with numbering used for reporting NMR data, analogous to the numbers used in the literature.[7,8]

^{1}H (400 MHz, $CDCl_3$, ppm) δ: 10.05 (br, s, 1H, C_2-**H**), 7.38 (s, 1H, C_5-**H**), 7.24 (s, 1H, C_4-**H**), 3.87 (t, ^3J = 7.5 Hz, 2H, $C_{1'}$-$\mathbf{H_2}$), 3.64 (s, 3H, $C_{1''}$-$\mathbf{H_3}$), 1.42 (quin, ^3J =

7.5 Hz, 2H, $C_{2'}$-$\mathbf{H_2}$), 0.88 (sex, ^{3}J = 7.5 Hz, 2H, $C_{3'}$-$\mathbf{H_2}$), 0.45 (t, ^{3}J = 7.5 Hz, 3H, $C_{4'}$-$\mathbf{H_3}$).[7]

^{2}H (60 MHz, $CDCl_3$, ppm) δ: 7.24 (C**D**Cl_3).

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$, ppm) δ: 137.0 (C_2), 123.5 (C_5), 121.9 (C_4), 49.2 ($C_{1'}$), 36.0 ($C_{1''}$), 31.7 ($C_{2'}$), 18.9 ($C_{3'}$), 13.0 ($C_{4'}$).

The sample was then poured over caesium methylcarbonate (0.12 g, 0.57 mmol, 0.5 equivalents) After 5 minutes at room temperature, the sample was filtered for NMR spectroscopic analysis.

^{1}H (400 MHz, $CDCl_3$, ppm) δ: As above, except: C_2-**H** 10.02, integration = 0.1284 H relative to other BMIM resonances and new resonances present (corresponding to 10 % relative to the $BMIM^{+}$ resonances): 1-methyl imidazole 7.28 (C_2-**H** overlapping with $CHCl_3$) 7.17 (d, ^{3}J = 1.9 Hz, C_5-**H**), 6.97 (d, ^{3}J = 1.9 Hz, C_4-**H**), 3.69 (s, $C_{1''}$-$\mathbf{H_3}$), new butyl species 4.13 (t, ^{3}J = 7.4 Hz), 1.37 (quin, ^{3}J = 7.4 Hz), 0.90 (sex, overlapping), 0.45 (t, overlapping).

^{2}H (60 MHz, $CDCl_3$, ppm) δ: 10.00 (C_2-**D**), 7.24 (C**D**Cl_3).

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$): As above, with a number of small resonances and at 137.1 ppm there is a mixture of two resonances: a singlet ($\mathbf{C_2}$-H) and a 1:1:1 triplet ($\mathbf{C_2}$-D) ($^{1}J_{13C\text{-}2H}$ = 33.2 Hz, upfield-most line of triplet overlaps with singlet).

Stability in methanol:

1-Butyl-3-methylimidazolium chloride (0.2 g, 1.1 mmol) was dissolved in d_4-methanol (0.6 mL) and stored for 6 hours before ^{1}H, ^{2}H and ^{13}C{^{1}H} NMR experiments were run.

^{1}H (400 MHz, d_4-MeOD, ppm) δ: 9.22 (br, s, C_2-**H**, integration = 0.79 relative to 1-methyl group = 3), 7.81 (br, s, 1H, C_5-**H**), 7.73 (br, s, 1H, C_4-**H**), 4.34 (t, ^3J = 7.5 Hz, 2H, $C_{1'}$-$\mathbf{H_2}$), 4.04 (s, 3H, $C_{1''}$-$\mathbf{H_3}$), 1.94 (quin, ^{3}J = 7.5 Hz, 2H, $C_{2'}$-$\mathbf{H_2}$), 1.43 (sex, ^3J = 7.5 Hz, 2H, $C_{3'}$-$\mathbf{H_2}$), 1.01 (t, ^3J = 7.5 Hz, 3H, $C_{4'}$-$\mathbf{H_3}$).

^{2}H (60 MHz, d_4-MeOD, ppm) δ: 9.22 (C_2-**D**), 4.68 (CD_3O**D**), 3.31 (C$\mathbf{D_3}$OD).

^{13}C{^{1}H} (100 MHz, d_4-MeOD, ppm) δ: 136.6 (C_2), 123.7 (C_5), 122.4 (C_4), 49.2 ($C_{1'}$), 35.4 ($C_{1''}$), 31.9 ($C_{2'}$), 19.1 ($C_{3'}$), 12.6 ($C_{4'}$).

Caesium methylcarbonate (0.24 g, 1.1 mmol) dissolved in methanol (2 mL) was added to the 1-butyl-3-methylimidazolium chloride solution, causing a white precipitate to form. The solid was collected by filtration. The filtrate was analysed by NMR spectroscopy. The solid was dissolved in D_2O and analysed by NMR spectroscopy (^{1}H, ^{13}C{^{1}H} and ^{133}Cs) and the aqueous silver nitrate test for halide ions.

Filtrate (1-butyl-3-methylimidazolium methylcarbonate):

^{1}H (400 MHz, d_4-MeOD, ppm) δ: 9.04 (br, s, C_2-$\mathbf{H}$, integration = 0.40 relative to 1-methyl group = 3), 7.68 (d, ^3J = 1.7 Hz, 1H, C_5-$\mathbf{H}$), 7.61 (d, ^3J = 1.7 Hz, 1H, C_4-$\mathbf{H}$), 4.25 (t, ^3J = 7.5 Hz, 2H, $C_{1'}$-$\mathbf{H_2}$), 3.96 (s, 3H, $C_{1''}$-$\mathbf{H_3}$), 3.52 (s, C$\mathbf{H_3}$OC(O)O$^-$), 1.89 (quin, ^3J = 7.5 Hz, 2H, $C_{2'}$-$\mathbf{H_2}$), 1.39 (sex, ^{3}J = 7.5 Hz, 2H, $C_{3'}$-$\mathbf{H_2}$), 1.00 (t, ^3J = 7.5 Hz, 3H, $C_{4'}$-$\mathbf{H_3}$).

^{13}C{^{1}H} (100 MHz, d_4-MeOD, ppm) δ: 159.8 ($CH_3O\mathbf{C}(O)O^-$), 136.6 (C_2), 123.6 (C_5), 122.3 (C_4), 51.9 ($\mathbf{C}H_3OC(O)O^-$), 49.2 ($C_{1'}$), 35.1 ($C_{1''}$), 31.7 ($C_{2'}$), 19.1 ($C_{3'}$), 12.4 ($C_{4'}$).

Solid (CsCl):

^{1}H (400 MHz, D_2O, ppm): Solvent resonance only.

^{13}C{^{1}H} (100 MHz, D_2O, ppm): No resonances (sample does not contain bmim$^+$ or methylcarbonate ions).

^{133}Cs (65.59 MHz, D_2O, ppm) δ: 0.09 (s).

^{133}Cs NMR chemical shifts are solvent, temperature and concentration dependent. The ^{133}Cs NMR chemical shift of caesium chloride in water at 298 K is expected to be in the range of +0.5 to -3.0 ppm in the concentration range 0 to 0.25 M.[9]

Addition of the precipitate dissolved in D_2O to aqueous silver nitrate results in the immediate formation of a white precipitate showing the sample contains chloride ions.

7.9 References

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