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Investigation of a Metal Complexing Route to Arene Trans-Dihydrodiols

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Investigation of a Metal Complexing Route to Arene *trans*-Dihydrodiols

By

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A Thesis submitted to the Dublin Institute of Technology
for the Degree of MPhil

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For Mum and Dad

"Nothing shocks me, I'm a Scientist."

Indiana Jones
(Indiana Jones and the Temple of Doom)

Abstract

In this work, a route for the conversion of arene *cis*-dihydrodiols to their *trans* isomers was examined. Arene *trans*-dihydrodiols are potentially important chiral building blocks in synthetic chemistry and are more stable than their *cis* analogues. While the *cis*-arene dihydrodiols can be produced on a relatively large scale by fermentation, their *trans* isomers cannot. The principal aim of this work was to carry out studies in tandem to inform the development of the synthetic pathway to convert arene *cis*-dihydrodiols to their *trans* isomers by (a) the synthesis of organometallic intermediates and (b) investigation of their reactivity by means of kinetic and equilibrium studies. A number of analogues based on seven-membered ring systems instead of six were also investigated as a comparison.

The four-step synthetic route being investigated involved formation of a tricarbonyl iron complex of the arene *cis*-dihydrodiol substrate, followed by reaction in acid to form a carbocation intermediate. This cation complex is trapped stereoselectively using hydroxide to give a *trans* isomer and decomplexation to remove the iron tricarbonyl moiety is the final step. Two substrates were examined, 3-bromocyclohexa-3,5-diene-1,2-diol and 3-trifluoromethylcyclohexa-3,5-diene-1,2-diol. The first three steps in the route were successfully performed on each compound in yields of 52 % and 43 % overall for the 3-bromo and 3-trifluoromethyl starting materials respectively. The final decomplexation step was not successful however and will require optimisation of the conditions. The ionisation of the tricarbonyl iron *cis*-dihydrodiol intermediates was investigated kinetically in strong acid, and the corresponding rate constant for the bromo substituted complex was determined to be 8.0×10^{-8} M^{-1} s^{-1} showing a significant lack of reactivity towards cation complex formation. This is expected based on previous work that reports low reactivity towards ionisation for any complexes that have hydroxyl groups *endo* to the iron centre, as is the case here. The reverse reaction, hydrolysis of the bromo-substituted cation, was too fast to measure but a pK_R of 0.5 was estimated.

It can be concluded that ionisation of the coordinated *endo* (i.e. *cis*-) diol to form the corresponding cation is the difficult step in the route to convert arene *cis*-dihydrodiols to their *trans* isomers.

Among the seven-membered ring complexes synthesised were salts of the cation species, tricarbonyl (η^5-cyclohepta-1,3-dienyl) iron and tricarbonyl (η^7-cycloheptatrienyl) chromium. Rate constants for the nucleophilic reaction of the former cation complex with water to give tricarbonyl (η^5-cyclohepta-2,4-diene-1-ol iron) and conversion of this complex back to the cation were measured, allowing a pH profile (log *k* versus pH) to be constructed. From this, an equilibrium constant, pK_R, = 4.2 was determined for the interconversion between the cycloheptadienyl complex [R^+] and the corresponding hydrolysis product [ROH] in which the hydroxyl group is *exo* to the iron centre.

Comparison of this equilibrium constant to that reported for the uncoordinated cycloheptadienyl cation shows that the iron tricarbonyl moiety is highly stabilising (ΔpK_R = 15.8). The uncoordinated tropylium (or cycloheptatrienyl) ion however shows a similar stability to tricarbonyl (η^5-cyclohepta-1,3-dienyl) iron due to aromatic stabilisation. The effect of having one less methylene group in the ring was found to be negligible as $\Delta p K_R$ = 0.4 for the coordinated cycloheptadienyl and cyclohexadienyl cations.

It is proposed that, in weak base, the tricarbonyl cycloheptatrienyl chromium complex gives a zwitterionic complex in which a carbonyl ligand is converted to a carboxylate ion. Equilibrium between this zwitterion and a cationic form in which the carboxylate has been protonated to give the carboxylic acid is postulated to occur in weakly acid solutions. An acid dissociation constant, pK_a of 4.8 was determined for this equilibrium spectrophotometrically.

Declaration

I certify that this thesis which I now submit for the award of an MPhil is entirely my own work and has not been taken from the work of others save and to the extent that such work has been cited and acknowledged within the text of my own work.

This thesis was prepared according to the Regulations for Postgraduate Study by Research of the Dublin Institute of Technology and has not been submitted in whole or in part for an award of any other Institute or University.

The work reported on in this thesis conforms to the principles and requirements of the Institute's guidelines for ethics in research.

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Signature_____ **Date**_____

Candidate

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I would first like to thank my supervisors Dr. Claire McDonnell and Prof. Rory More O'Ferrall for all their help and guidance throughout my studies. Their time and effort is very much appreciated.

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A huge thanks to my best friends Aoife and Krystle who have supported me over the past 15 years and hopefully will never mention the word thesis again under threat of torture.

Finally, I would like to give the biggest thanks to my family, especially to my parents for all their encouragement. To my brothers and sister, and to my nieces and nephews, especially Ryan who always acted interested when his Auntie Crystal started talking about that science stuff.

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Abbreviations and Symbols

A	absorbance
Ac	acetyl
Ac_2O	acetic anhydride
AcO	acetoxy
Apt	apparent
B	buffer base
Bda	benzylideneacetone
BH	buffer acid
BOC	dibutyl dicarbonate
br	broad
COSY	correlation spectroscopy
^{13}C NMR	carbon 13 nuclear magnetic resonance
δ	chemical shift
^{o}C	degrees celsius
d	doublet
DCM	dichloromethane
dd	doublet of doublets
ddd	doublet of doublet of doublets
DME	dimethoxyethane
DMSO	dimethylsulfoxide
Et	ethyl
equiv	equivalents
FTIR	Fourier transform infrared spectroscopy
g	gram(s)
hr(s)	hour(s)
^{1}H NMR	proton nuclear magnetic resonance
Hz	hertz
IR	infrared
J	coupling constant

k	rate constant
K_a	acid dissociation constant
K_R	equilibrium constant
KHz	kilohertz
KBr	potassium bromide
λ	wavelength
l	litre(s)
lit.	literature value
log	logarithm
M	moles/litre
m	multiplet
Me	methyl
ml	millilitre(s)
µl	microlitres
mmol	millimole(s)
m.p.	melting point
MHz	megahertz
NMR	nuclear magnetic spectroscopy
PAH(s)	polycyclic aromatic hydrocarbon(s)
Ph	phenyl
ppm	parts per million
R	alkyl substituent or buffer ratio
R_f	retention factor
s	seconds or singlet
temp	temperature
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
t	triplet
UV	ultraviolet
Vis	visible

X	excess acidity function

Chapter 1

Introduction

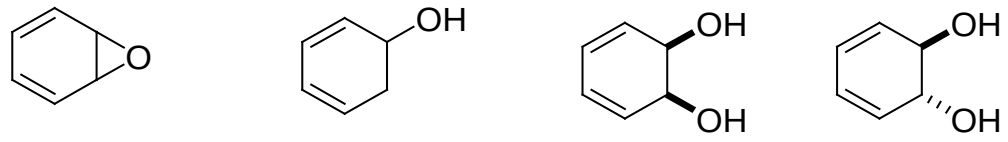
Chapter 1 Introduction.

Oxidative products of aromatic hydrocarbons and the study of organometallic compounds are two areas of significant interest in organic chemistry. Oxidative products have potential as starting materials for the synthesis of industrial and pharmaceutical target molecules and the use of organometallic complexes in organic synthesis can provide access to molecules that are not otherwise readily available. In the work described in this thesis, aspects of both areas are examined, as the compounds studied are iron complexes of oxidative metabolites of aromatic hydrocarbons, iron complexes of analogous ring systems and chromium complexes of seven-membered ring systems. This chapter provides background information on this research and a summary of relevant previous work.

The work carried out for this project was part of a larger study which investigated efficient methods for the conversion of arene *cis*-dihydrodiols to industrially important products such as catechols, phenols and arene *trans*-dihydrodiols.[1] This thesis describes optimisation of a synthetic route for the conversion of arene *cis*-dihydrodiols to arene *trans*-dihydrodiols using tricarbonyl iron intermediates. Syntheses of seven-membered ring system complexes were also investigated and kinetic studies were carried out on some complexes.

1.1 Oxidative Metabolites of Aromatic Hydrocarbons.

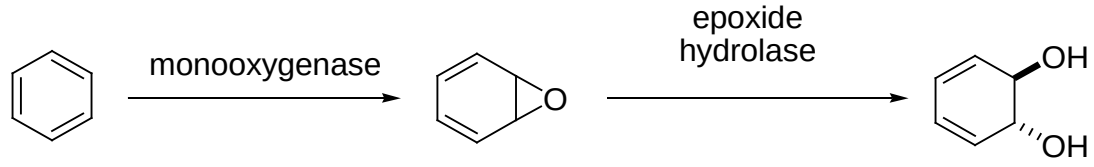
Oxidative metabolites are formed as a result of reactions of mono- and di-oxygenase enzymes with aromatic and dihydroaromatic molecules. There are four possible products: arene oxides **(1)**, arene hydrates **(2)**, arene *cis*-dihydrodiols **(3)** and arene *trans*-dihydrodiols **(4)**. The metabolites obtained when benzene is the aromatic substrate are shown in Chart 1.1.



(1) **(2)** **(3)** **(4)**

Chart 1.1 Oxidative metabolites of benzene.

In animals, plants and fungi (eukaryotes), oxidation of aromatic hydrocarbons involves the action of monooxygenase and epoxide hydrolase enzymes and yields an arene oxide **(1)** intermediate, which is converted to an arene *trans*-dihydrodiol **(4)** by enzyme hydrolysis, as shown in Scheme 1.1. Monooxygenases are a class of enzymes which insert one atom of an oxygen molecule into the substrate while the other atom is reduced to water. Epoxide hydrolase enzymes have the ability to cleave epoxide rings by catalysing the addition of a water molecule in a hydrolysis reaction to give a 1,2-diol.[2]



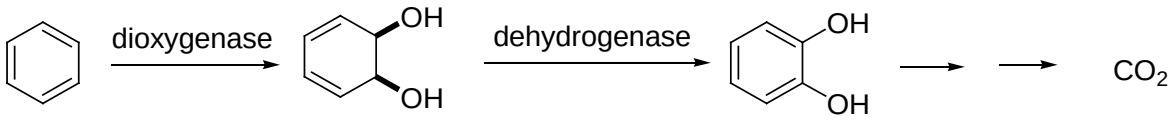
(1) **(4)**

Scheme 1.1 Oxidative metabolism of aromatic hydrocarbons in eukaryotes.

Oxidative metabolism is the main process by which aromatic hydrocarbons are degraded in mammals. This process occurs in the liver where water-soluble polar derivatives are formed which can then be excreted from the body. *Trans*-dihydrodiols can be further metabolised to their corresponding epoxy dihydrodiols; however, these compounds are potentially carcinogenic.[3]

In bacteria (prokaryotes), oxidation of aromatic substrates yields arene *cis*-dihydrodiols **(3)** rather than their *trans* analogues. This occurs by dioxgenase-catalysed oxidation of arenes to initially form *cis*-dihydrodiols **(3)**,[4] which then

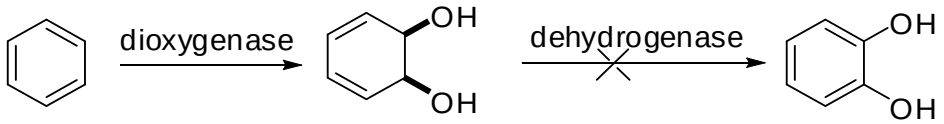
undergo enzymatic dehydrogenation to form catechols **(5)**. Further degradation of the catechol gives carbon dioxide as shown in Scheme 1.2. Dioxygenase enzymes are multicomponent enzymes that incorporate both atoms of an oxygen molecule into the substrate and for this example they are members of a family of aromatic ring-hydroxylating dioxygenase enzymes.[5] Dehydrogenase enzymes catalyse the removal of two hydrogen atoms on neighbouring carbons causing the formation of a double bond resulting in dehydrogenation.



(3) **(5)**

Scheme 1.2 Oxidative metabolism of aromatic hydrocarbons in prokaryotes.

If the bacteria lack the diol dehydrogenase enzyme, degradation to the corresponding catechol **(5)** cannot occur and the *cis*-dihydrodiol is isolated. One such type of bacterium is a mutant strain (UV4) of *Pseudomonas putida*. A mutation such as this is a modification of the base sequence in the bacterium's DNA which results in an alteration in the protein encoded by the gene. It disrupts the normal metabolic pathway of these bacteria as shown in Scheme 1.3.[6]



(3) **(5)**

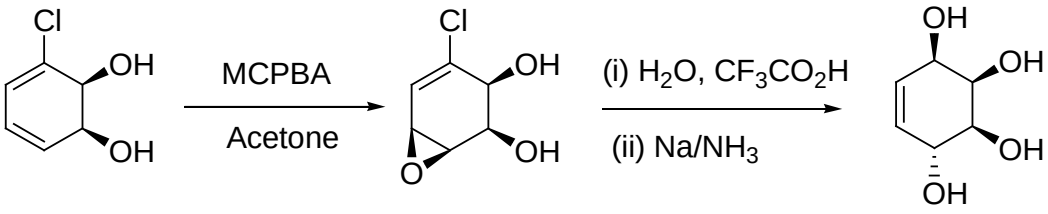
Scheme 1.3 Formation of benzene *cis*-dihydrodiol from the action of a mutant strain (UV4) of *Pseudomonas putida* on benzene.

Arene *cis*-dihydrodiols and arene *trans*-dihydrodiols will now be discussed in more detail.

1.1.1 Arene *Cis*- and *Trans*-Dihydrodiols.

Aromatic hydrocarbons undergo oxidatitive metabolism in mammals to form arene *trans*-dihydrodiols as was already shown in Scheme 1.1. Oxidatitive metabolism of aromatic compounds in bacteria affords arene *cis*-dihydrodiols. Arene *cis*-dihydrodiols can be produced in relatively large quantities by biotransformations using the UV4 mutant strain of *Pseudomonas putida* (see Scheme 1.3).

The isolation of *cis*-dihydrodiols from the action of *Pseudomonas putida* on benzene was first reported by Gibson *et al.* in 1968.[7] More recently, optimised biotransformations using the *Pseudomonas putida* (UV4) bacteria have allowed commercial quantities of a range of arene *cis*-dihydrodiols to be produced.[4,8] These arene *cis*-dihydrodiols have a wide application in industry and have the potential to be used as chiral precursors for the synthesis of pharmaceuticals and natural products.[9] An example of this is the preparation of conduritols, which have potential to be used as glycosidase inhibitors. An example of a conduritol derived from a *cis*-dihydrodiol is (-)-conduritol. This synthesis involves microbial oxidation of chlorobenzene to give a *cis*-arene dihydrodiol **(6)**, as shown in Scheme 1.4 which is then converted to the vinylic epoxide **(7)**. Ring opening of this intermediate gives chloroconduritol which is then converted to (-)-conduritol C **(8)**.[10]

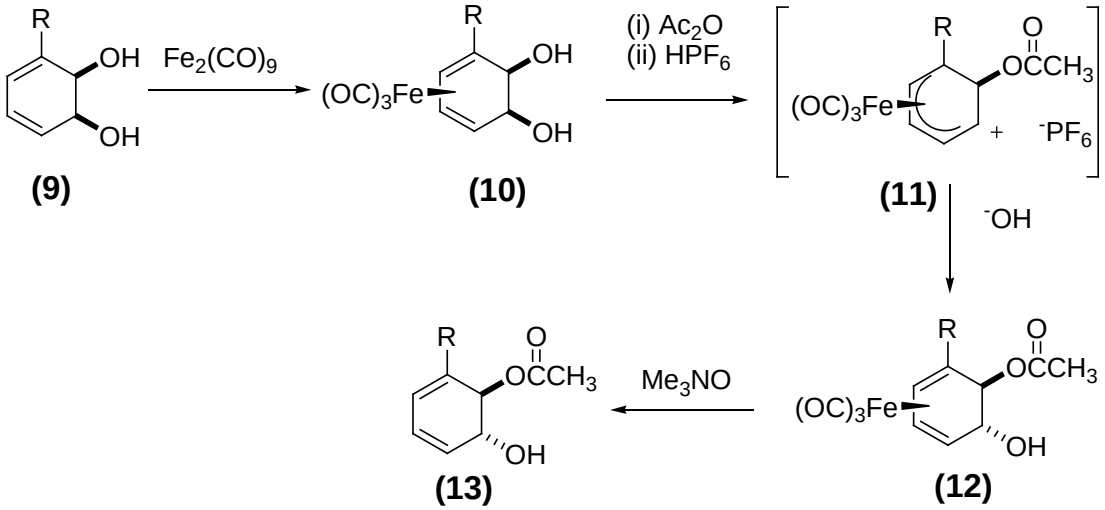


(6) **(7)** **(8)**

Scheme 1.4 Synthesis of (-)-conduritol C (8) by a 4-step pathway from chlorobenzene.

Another example of a pharmaceutical that can be synthesised from a *cis*-dihydrodiol precursor is the antiviral drug Tamiflu which is used to treat influenza viruses types A and B.[11] However, while arene *cis*-dihydrodiols are more accessible, the *trans*-dihydrodiols are more stable. This increased stability gives the *trans* isomers the potential to be more useful as chiral building blocks and has led to an interest in converting the readily available arene *cis*-dihydrodiols to their *trans* isomers. A review from Boyd and Sharma in 2002 summarised a number of possible routes to the *trans*-dihydrodiols.[12] In addition, a seven step synthetic route for the conversion of arene *cis*-dihydrodiols to arene *trans*-dihydrodiols was reported in 2007.[13]

One proposed chemoenzymatic route involved the formation of tricarbonyl iron intermediate complexes and was based on original research by Stephenson *et al.*[14] This pathway is shown in Scheme 1.5 and involves initial complexation of a tricarbonyl iron fragment to the arene *cis*-dihydrodiol. This is then reacted with hexafluorophosphoric acid and acetic anhydride to give a coordinated cyclohexadienyl cation **(11)** intermediate. Nucleophilic attack of a hydroxyl group *anti* to the metal provides the *trans* complex **(12)**. Decomplexation using trimethylamine-*N*-oxide yields the *trans* product **(13)** shown in Scheme 1.5.



Scheme 1.5 Synthetic route for the conversion of arene *cis*-dihydrodiols to their *trans*-isomers.[12]

A significant part of the work in this study involved optimising this route for the conversion of arene *cis*-dihydrodiols with bromo- or trifluoromethyl- substituents at position 3 to their *trans* isomers, represented by the R group in Scheme 1.5. The stereochemistry in these *cis* and *trans* arene dihydrodiols is relative in all cases and thus they are mixtures of the two possible enantiomeric forms as shown in Chart 1.2.

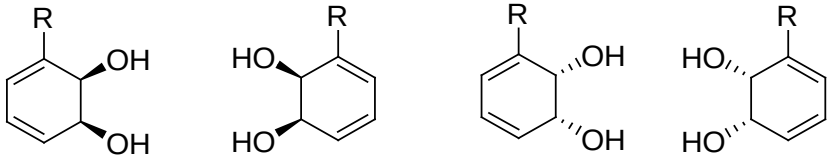


Chart 1.2 *cis* and *trans* enantiomers of substutited arene-dihydrodiols.

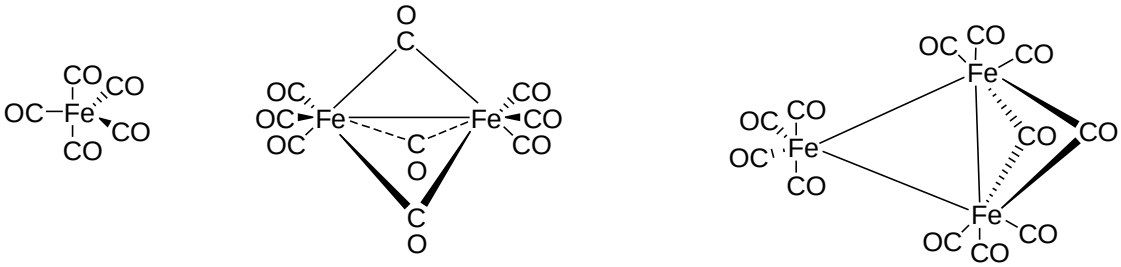
1.2 Organometallic Chemistry.

Since the discovery of ferrocene in 1951 by Kealy and Pauson,[15] a rapid development in the area of organometallic chemistry has occurred. Although a number of metal complexes have been known since 1827 when Zeise synthesied the first organometallic compound,[16] it is only since the second half of the 20th century that technology, such as X-ray crystallography and NMR spectroscopy, has been available to aid in the characterisation and structure determination of these compounds.

A number of transition metals such as palladium, manganese and rhodium have been used to prepare complexes. This review will be restricted to organoiron and organochromium complexes only as the research in this work involved the use of iron and chromium complexes.

1.2.1 Organoiron Chemistry.

Iron carbonyls are the most common class of organoiron complexes. There are three known stable compounds, iron pentacarbonyl, diironnonacarbonyl and triirondodecacarbonyl. Iron pentacarbonyl, $Fe(CO)_5$ **(14)**, is obtained from the reaction of carbon monoxide on iron. Diironnonacarbonyl, $Fe_2(CO)_9$ **(15)**, is prepared from photolysis of pentacarbonyl iron in ethanoic acid using a mercury lamp, and triirondodecacarbonyl, $Fe_3(CO)_{12}$ **(16)**, can be prepared in a number of ways.[17] All three carbonyls were encountered during this study, either as reactants or as side-products, and are shown in Chart 1.3.

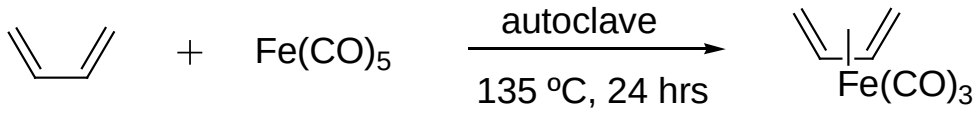


(14) **(15)** **(16)**

Chart 1.3 Structures of iron pentacarbonyl (14), diironnonacarbonyl (15) and triirondodecacarbonyl (16).

1.2.1.1 Initial Synthesis of Tricarbonyl Iron Complexes.

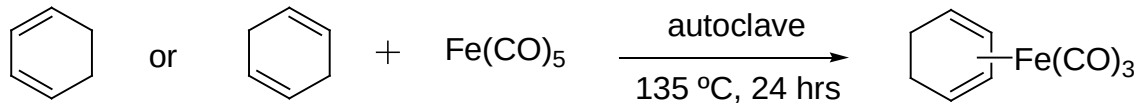
The first tricarbonyl iron complex was synthesised in 1930 by Reihlen *et al.* when they isolated tricarbonyl (η^4-buta-1,3-diene) iron **(18)** from heating iron pentacarbonyl with buta-1,3-diene **(17)** as shown in Scheme 1.6.[18]



(17) **(18)**

Scheme 1.6 Synthesis of tricarbonyl (η^4-buta-1,3-diene) iron (18).

Since this procedure was developed, a wide range of tricarbonyl butadiene iron complexes have been synthesised. This study was then extended further in 1958 by Hallam and Pauson when they prepared tricarbonyl (η^4-cyclohexa-1,3-diene) iron **(21)** using direct complexation with iron pentacarbonyl with cyclohexa-1,3-diene **(19)** as shown in Scheme 1.7.[19]



(19) **(20)** **(21)**

Scheme 1.7 Synthesis of tricarbonyl (η^4-cyclohexa-1,3-diene) iron (21) from either structural isomer of cyclohexadiene.

When the further reactions of these complexed dienes were investigated by Hallam and Pauson, it was found that they resisted hydrogenation and Diels-Alder type reactions, which are typical reactions of dienes. This lack of reactivity led to the conclusion that when the tricarbonyl iron moiety is coordinated to the organic ligand, it stabilises it and acts as a protecting group.[20]

In 1961, it was discovered by Arnet and Pettit that treatment of a non-conjugated diene with iron pentacarbonyl resulted in a rearrangement to give a conjugated isomer.[21] Thus, cyclohexa-1,4-diene **(20)**, when reacted with iron pentacarbonyl gave concomitant isomerisation of the diene to furnish complex **(21)** as shown above in Scheme 1.7. A range of substituted cyclohexa-1,4-dienes are available by a Birch reduction of the corresponding benzene derivatives.[22] It therefore became possible to synthesise a broad range of tricarbonyl (η^4-cyclohexa-1,3-diene) iron complexes.

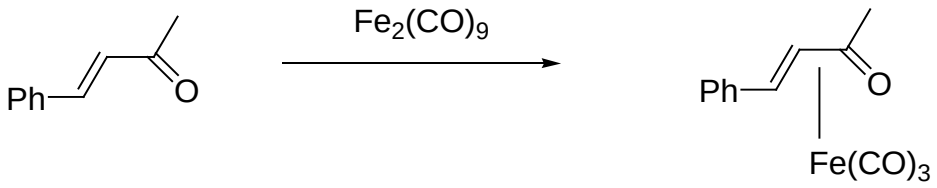
A number of experimental methods for complexing dienes have since been developed. The most common procedure used was developed by Cais and Maoz and involves the direct reaction of a diene with iron pentacarbonyl by refluxing in di-n-butylether.[23] Other sources of the tricarbonyl iron moiety are diironnonacarbonyl and triirondodecacarbonyl. Diironnonacarbonyl is limited to reactions with 1,3-dienes only,[20] but the advantage is that it can be used under milder conditions than iron pentacarbonyl.

The yields for complexation reactions using any of the iron carbonyl species are quite moderate (30 – 50 %) and a large excess of the iron carbonyl is generally required. This can result in the formation of pyrophoric iron which is hazardous during work-up.[20] However, complexation can usually be achieved under milder conditions and with greater selectivity by using a tricarbonyl iron transfer reagent.[20]

1.2.2 Tricarbonyl Iron Complexation Using Tricarbonyl Iron Transfer Reagents.

The use of tricarbonyl iron transfer reagents provides an alternative synthetic approach for complexation of dienes to tricarbonyl iron.

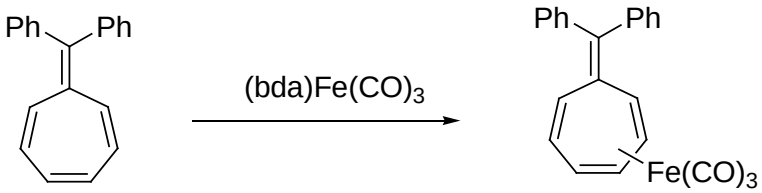
In 1964, complexes of tricarbonyl (η^4-1-oxabuta-1,3-diene) iron were first reported by Weiss,[24] and later introduced as transfer reagents in 1972 by Lewis.[25] It was found that tricarbonyl (η^4-benzylideneacetone) iron, (bda)$Fe(CO)_3$ **(22)**, was very efficient as a transfer reagent for the synthesis of tricarbonyl iron diene complexes. It is synthesised when benzylideneacetone **(23)** is reacted with diironnonacarbonyl as shown in Scheme 1.8.[26]



(23) **(22)**

Scheme 1.8 Synthesis of (bda)$Fe(CO)_3$ (22).

This transfer reagent reacts under mild conditions and can be useful for sensitive dienes or when the iron carbonyl reagents are unsatisfactory.[27] An example of its application as a transfer reagent is the synthesis of tricarbonyl (8,8-diphenylheptafulvene) iron **(24)**, where the heptafulvene **(25)** is reacted with a small excess of the (bda)$Fe(CO)_3$ to give a yield of 70 % as shown in Scheme 1.9. The synthesis of this product was not possible before the development of iron transfer reagents as the starting material is both heat and UV light sensitive, which excludes the use of $Fe(CO)_5$ and $Fe_3(CO)_{12}$ as reagents, and reaction with $Fe_2(CO)_9$ gave an unstable hexacarbonyl diiron complex.[25]

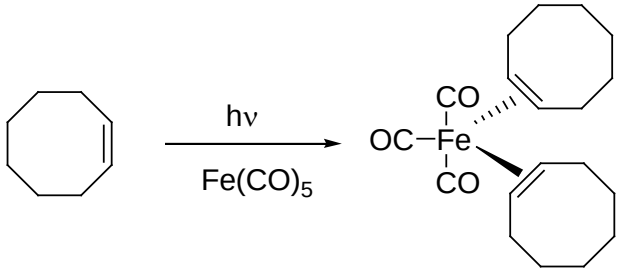


(25) **(24)**

Scheme 1.9 Synthesis of tricarbonyl (η^4-8,8-diphenylheptafulvene) iron (24) using the tricarbonyl iron transfer reagent (bda)$Fe(CO)_3$.

1.2.2.1 Grevels' Reagent.

In 1984, another transfer reagent was synthesised by Grevels.[28] Known as Grevels' reagent **(26)**, it was isolated following photolysis of iron pentacarbonyl using an excess of *cis*-cyclooctene **(27)** as shown in Scheme 1.10.



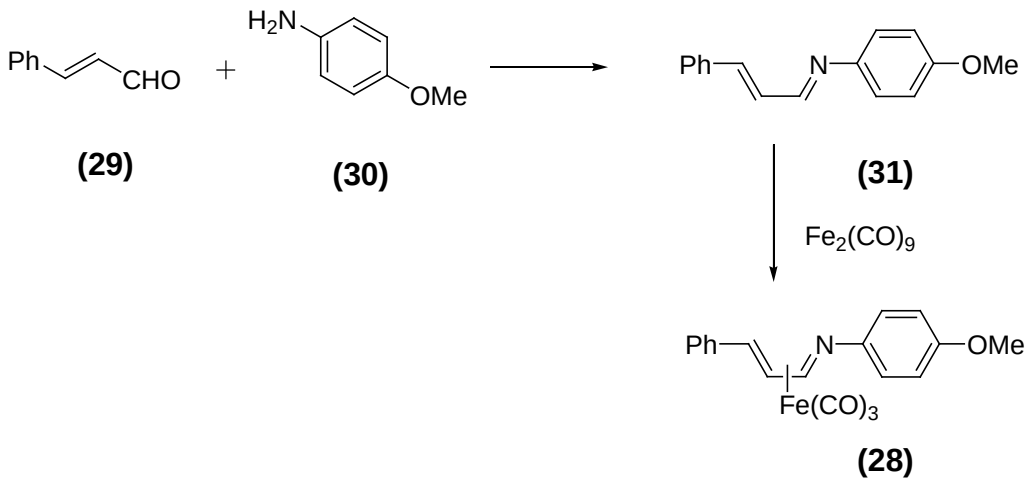
(27) **(26)**

Scheme 1.10 Synthesis of Grevels' reagent (26)

The reactivity of Grevels' reagent was examined by Fleckner *et al.*[28] It was found to be useful in reactions with heterodienes, cyclic dienes, and vinyl and substituted aromatic compounds. Grevels' reagent can react at low temperatures, below 0 °C, and can complex 1,4-dienes with concomitant isomerisation to the 1,3-diene, which is an advantage over (bda)$Fe(CO)_3$ which can only react with conjugated dienes.[20]

1.2.2.2 1-Azabuta-1,3-dienes.

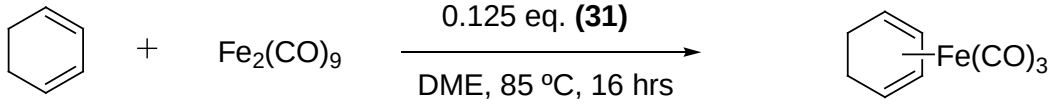
Another group of tricarbonyl iron transfer reagents, complexes of 1-azabuta-1,3-dienes, were first reported by Otsuka[29] and Lewis[30] in the late 1960's. Following investigations by Knölker *et al.*, tricarbonyl (η^4-1-azabuta-1,3-diene) iron complexes were found to be the most efficient tricarbonyl iron transfer reagents.[20,26,31] Various methods have been reported for their synthesis. The most convenient method is outlined in Scheme 1.11 for the example of tricarbonyl [η^4-1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene] iron **(28)**, which was found to be the most efficient of the series of transfer reagents prepared by Knölker.[26,32] A condensation of *trans*-cinnamaldehyde **(29)** with *p*-anisidine **(30)** gives 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene **(31)**, and a further reaction of this diene with diironnonacarbonyl affords the transfer reagent **(28)**.



(29) **(30)** **(31)** **(28)**

Scheme 1.11 Synthesis of the tricarbonyl iron transfer reagent, tricarbonyl [η^4-1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene] iron (28).

Knölker complexed 1,3-cyclohexadiene **(19)** to tricarbonyl iron by generating the 1-azabuta-1,3-diene complex **(28)** *in situ*, to produce tricarbonyl cyclohexa-1,3-diene iron **(21)** in a yield of 98% as shown in Scheme 1.12.[32]



(98 %)

(19) **(21)**

Scheme 1.12 One-step synthesis of tricarbonyl (η^4-cyclohexa-1,3-diene) iron (21) using the tricarbonyl iron transfer reagent 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (31).

Prior to the application of the 1-azabuta-1,3-diene family of catalysts to the synthesis of complex **(21)**, the reaction was carried out by direct complexation of cyclohexadiene with iron pentacarbonyl, diironnonacarbonyl or tri-irondodecacarbonyl resulting in low yields between 21 and 77 %.[26] With the use of

a range of tricarbonyl (η^4-1-azabuta-1,3-diene) iron complexes in the one-step procedure shown above in Scheme 1.12, the product yields have increased to between 70 and 90 %. The tricarbonyl azabutadiene iron complexes offer a number of advantages as iron tricarbonyl transfer reagents over (bda)$Fe(CO)_3$ and Grevels' reagent which were mentioned in Sections 1.2.2 and 1.2.2.1 respectively. A major advantage is that coordination of cyclohexa-1,3-diene can be performed in a one step procedure as shown in Scheme 1.12.[31] In addition, an excess of iron carbonyl reagent is not required when azabutadiene is employed.[31] A limiting factor for tricarbonyl azabutadiene iron complexes is that they do not undergo complexation reactions with non-conjugated dienes.

It has also been established that tricarbonyl (η^4-1-azabuta-1,3-diene) iron complexes can be used in the preparation of enantiopure tricarbonyl iron complexes. The first asymmetric catalytic complexation of prochiral dienes was performed by Knölker *et al.* and involved using chiral camphor derivatives of 1-azabutadienes as catalysts.[33] The enantiopure compounds formed have been used as building blocks in the stereoselective synthesis of spirocyclic compounds.[20,34]

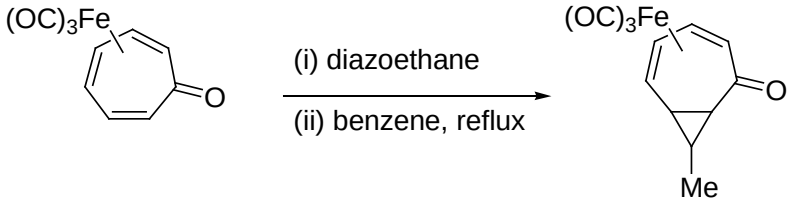
1.2.3 Synthetic Applications of Tricarbonyl Iron Complexes.

Tricarbonyl iron complexes have found many useful applicatons in organic synthesis due to the properties displayed by the tricarbonyl iron group. These properties include the potential to be used as protecting groups, activating groups and stereochemical controllers. An outline of these applications is given in the following sections.

1.2.3.1 The Tricarbonyl Iron Fragment as a Protecting Group.

As discussed in Section 1.2.1.1, Hallam and Pauson were the first to observe that when the tricarbonyl iron moiety was complexed to organic compounds, it

conferred properties upon them which were different from before complexation. The tricarbonyl iron fragment acts as a protecting group by reducing the reactivity of the diene as stable η^4 complexes are formed.[35] An example which demonstrates this is the ability of tricarbonyl iron to block unwanted carbon-carbon bond forming reactions in the cyclopropanation of tropone-$Fe(CO)_3$ with diazoethane as reported by Franck-Neumann and Martina.[36] This selective cyclopropanation can be seen in Scheme 1.13. Without the tricarbonyl iron as a protecting group, cyclopropanation could occur at any of the carbon-carbon double-bonds.[36]



(32)

Scheme 1.13 Cyclopropanation of the tropone-$Fe(CO)_3$ complex (32).

1.2.3.2 Stereochemical Control Using the Tricarbonyl Iron Group.

Stereochemical control can be achieved by the use of tricarbonyl iron complexes. An example of this has been reported by Pearson and Srinivasan in which unwanted reactions are prevented during the synthesis of hepitol derivatives.[37] In this case a tricarbonyl tropone iron complex **(32)** is reduced using sodium borohydride to give a key intermediate as a single diastereoisomer. This occurs due to the stereodirecting effect of the bulky tricarbonyl iron fragment forcing the addition of the hydride to the organic ligand on the opposite face to the iron.[37]

1.2.3.3 Tricarbonyl Iron as an Activating Group.

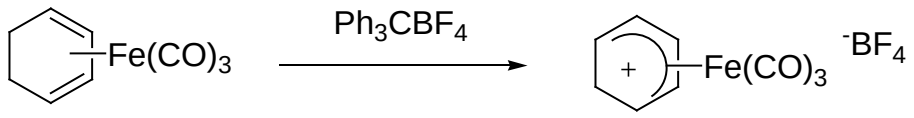
Tricarbonyl iron can be used as an activating group to facilitate nucleophilic addition reactions which do not occur under normal circumstances. These reactions are possible due to the strong electron-withdrawing effect of the iron.[38] Electron-rich unsaturated organic compounds such as alkenes, alkynes and arenes are unreactive towards nucleophiles. However, when coordinated to electron deficient metals such as iron, their reactivity changes as their electron-density decreases. They then become reactive towards nucleophilic attack. Neutral tricarbonyl iron complexes only undergo direct reactions with a limited number of nucleophiles. However, converting these complexes to the corresponding cations allows reaction with a virtually unlimited range of nucleophiles as will be discussed in Section 1.2.3.6 on page 18.

1.2.3.4 Stabilising Ability of the Tricarbonyl Iron Unit.

Tricarbonyl iron can be used to stabilise cyclohexadienone, a tautomer of phenol.[22] Uncomplexed cyclohexadienone undergoes tautomerisation to phenol but, when coordinated to tricarbonyl iron, the complex remains in its keto form and can be used in subsequent reactions.[17]

1.2.3.5 Tricarbonyl Cyclohexadienyl Iron Complexes.

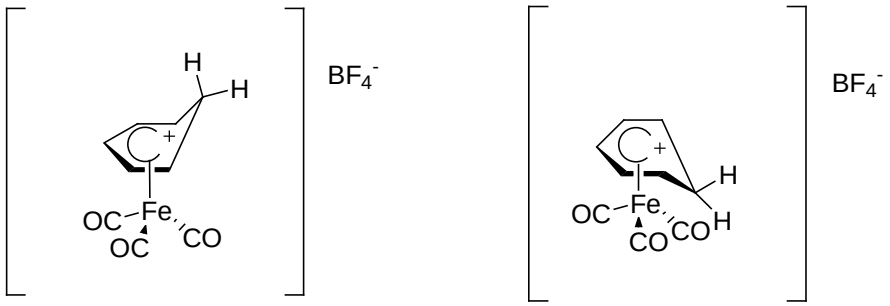
In 1960, Fischer and Fischer reported hydride abstraction from tricarbonyl (η^4-cyclohexa-1,3-diene) iron **(21)** using triphenylcarbenium tetrafluoroborate.[39] The complex **(21)** was converted into its stable salt, tricarbonyl (η^5-cyclohexadienyl) iron tetrafluoroborate **(33)**, shown in Scheme 1.14. The tricarbonyl iron moiety activates the allylic C-H bonds thus enabling the hydride abstraction.



(21) **(33)**

Scheme 1.14 Fischer and Fischer synthesis of tricarbonyl (η^5-cyclohexadienyl) iron tetrafluoroborate (33).

The cyclohexadienyl complexes that form are not completely planar. The iron is bonded to five sp^2 carbons that are all planar, but the unbonded sixth carbon is sp^3 hybridised and can occupy a position above (*exo*) **(34)** or below (*endo*) **(35)** the plane, as shown in Chart 1.4. It was found that the more stable configuration is the *exo* **(34)**, and this is due to the repulsive interaction with the metal that occurs in the other configuration **(35)**.[40,41]

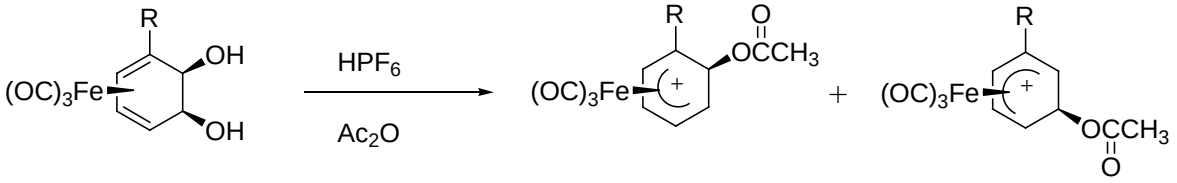


(34) **(35)**

Chart 1.4 The sp^3 carbon in the tricarbonyl (η^5-cyclohexadienyl) iron tetrafluoroborate complex occupying a position above **(34)** and below **(35)** the plane.

Reactions of dienyl complexes have been found to be highly regioselective as nucleophilic attack on the ring occurs on the opposite face (*anti*) to the metal and at the dienyl terminus.[42]

Stephenson *et al.* have reported regioselectivity for the cation formation of mono-substituted tricarbonyl cyclohexadiene-1,2-diol iron complexes when electron-withdrawing substituents were present.[14] In diene complexes with a chloro **(10a)** or methoxy **(10b)** substituent, for example, one structural isomer, **(11a)** or **(11b)** is formed over another, **(36a)** or **(36b)** in ratios of 7:2 and 2:1 respectively. In comparison, the more electron-withdrawing substituent, trifluoromethyl, provided complete regiocontrol to give exclusively **(11c)** (see Scheme 1.15).



(10 a-c) **(11 a-c)** **(36 a-c)**

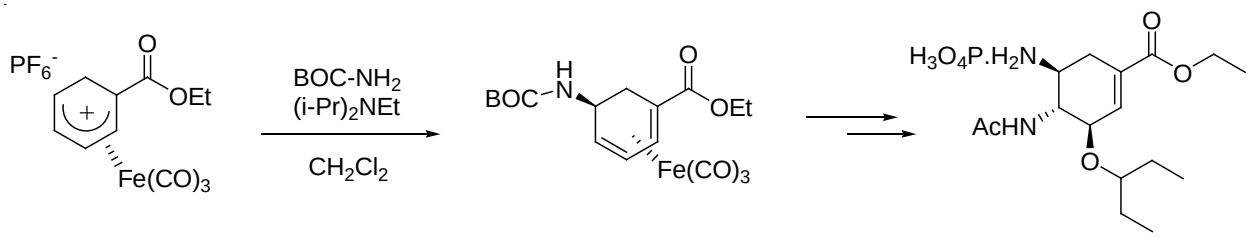
(a) R = Cl
(b) R = OCH_3
(c) R = CF_3

Scheme 1.15 **Substituent effect on the formation of tricarbonyl (η^5-cyclohexadienyl) iron complexes.**

1.2.3.6 Synthetic Applications of Tricarbonyl Cyclohexadienyl Iron Complexes.

Tricarbonyl cyclohexadienyl iron complexes have the ability to react with a virtually unlimited range of nucleophiles.[42] High regio- and stereo- selectivity are also

usually observed in their reactions. For example, in 2007 Kann *et al.* reported the use of tricarbonyl cyclohexadienyl iron as an intermediate in the synthesis of oseltamivir, which is marketed as Tamiflu®.[43] Tamiflu is an influenza neuraminidase inhibitor and has been used in the treatment of influenza strains such as H1N1 (swine flu) and H5N1 (avian flu). As part of the twelve-step synthesis reported, a tricarbonyl cyclohexadienyl iron complex **(37)** is reacted with a BOC-amine to provide **(38)** which is then decomplexed and reacted further to give oseltamivir phosphate **(39)** as one stereoisomer only as shown in Scheme 1.16.



(37) **(38)** **(39)**

Scheme 1.16 **Synthesis of oseltamivir phosphate utilising tricarbonyl cyclohexadienyl iron complexed intermediates.**

The use of tricarbonyl cyclohexadiene iron analogues can provide a diverse range of oseltamivir analogues which can be useful if resistance becomes prevalent.

1.2.3.7 Ligand Exchange of a Carbonyl Ligand for a Triphenylphosphine Ligand.

When a transition metal is bonded to a ligand, bonds arise from both forward and back-donation of electrons. When a carbonyl ligand donates a pair of electrons to a

vacant *d* orbital of the metal, a sigma bond (σ) is formed. Back-donation, or back-bonding, occurs when electrons are accepted into an *anti*-bonding (π*) orbital of the ligand from a filled metal orbital.[44] The replacement of one of the carbonyl ligands on the iron with triphenylphosphine (PPh_3) has a marked effect on the reactivity of the tricarbonyl cyclohexadienyl iron complexes. This is caused by a change in the electron density around the metal. Back-bonding between the metal and the ligand is reduced upon replacement of a carbonyl ligand with triphenylphosphine. This causes a decrease in the reactivity of the carbonyl ligands towards nucleophiles and their ability to accept electrons decreases.[45]

There are various methods of ligand exchange, but the most common for triaryl and trialkyl phosphines is reported by Pearson *et al.*[46] It involves the reflux of the diene complex in cyclohexanol with the triaryl or trialkyl phosphine ligand at 160 ºC. However, the yields to these reactions are, on average, 40 %. It has been reported that varying substituents on the cyclohexadiene ring can increase the yield.[47]

1.2.3.8 Decomplexation of Tricarbonyliron Complexes.

For the tricarbonyl iron fragment to be of use synthetically, it is important that it can be removed easily and in high yields. This is usually achieved using oxidising agents such as ferric chloride, trimethylamine-*N*-oxide, ceric ammonium nitrate (CAN), or copper (II) chloride.[48] Trimethylamine-*N*-oxide is by far the most widely used decomplexation agent and is preferred due to the mild reaction conditions required. Since it does not generate acidic conditions, it is suitable for use with compounds that have acid-sensitive functional groups.[17]

1.2.4 Organochromium Chemistry.

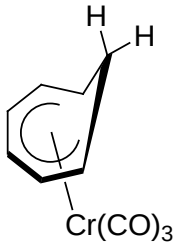
While tricarbonyl iron can only coordinate to two double bonds (4 π electrons), tricarbonyl chromium is able to complex to ligands with three double bonds (6 π

electrons), due to the 18 electron rule.[44] Tricarbonyl chromium complexes of benzene compounds have been studied to a greater extent than cycloheptatriene compounds.[49]

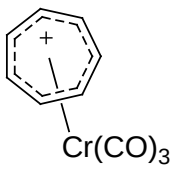
1.2.4.1 Synthesis of Tricarbonyl Chromium Complexes of Seven-Membered Ring Systems.

In 1958, Abel *et al.* reported the coordination of tricarbonyl chromium to cycloheptatriene.[50] It was found that while in its solid state, the tricarbonyl cycloheptatriene chromium can be stored indefinitely. In solution, it decomposes in air and light and this reaction is especially rapid in alcohol or acetone.

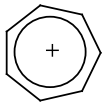
Munro and Pauson reported an effective method for the complexation of tricarbonyl chromium to cycloheptatriene and subsequent conversion to its corresponding cation.[51] This was carried out by refluxing hexacarbonyl chromium with cycloheptatriene in diethylene glycol dimethyl ether at 160 ºC under anhydrous conditions to give tricarbonyl cycloheptatriene chromium **(40)**. As with the iron complexes, it can be seen that the more stable conformation is that in which the sp^3 carbon is above the plane of the hydrocarbon ring anti to the metal, as shown in Chart 1.5. Due to the instability of the resulting complex in solution, it is then converted to the corresponding cation **(41)**. This is because the cation ring system becomes aromatic and is much more stable than the neutral complex.



(40)



(41)



(42)

Chart 1.5 Structures of tricarbonyl cycloheptatriene chromium complexes and tropylium.

1.2.4.2 Reactions of Tricarbonyl Tropylium Chromium Complexes.

The reactions of the tropylium cation complex **(41)** with anions were investigated by Munro and Pauson.[51] The cation complex was expected to react in two ways as shown in Equations 1.1 and 1.2.

$$[C_7H_7Cr(CO)_3]^+ + X^- \longrightarrow XC_7H_7Cr(CO)_3 \quad (1.1)$$

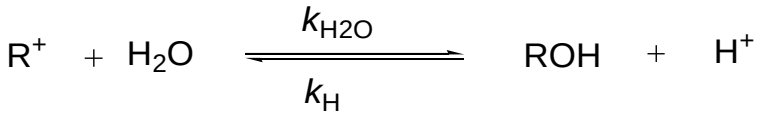
$$[C_7H_7Cr(CO)_3]^+ + X^- \longrightarrow C_7H_7Cr(CO)_2X + CO \quad (1.2)$$

Equation 1.1 assumes that the positive charge resides mainly on the ring and that anions add to the ring. This was found to be the most common reaction observed. Equation 1.2 assumes that the positive charge lies mainly on the metal and the reactions occur on the metal rather than on the organic ligand.

Rigby *et al.* found that tricarbonyl cycloheptatriene chromium could be used as an efficient catalyst for room temperature [6π + 2π] cycloaddition reactions.[52]

1.3 Stability of Coordinated Cyclohexadienyl Cations.

The stability of coordinated cyclohexadienyl cations can be determined by measurement of K_R, the equilibrium constant for the conversion of the coordinated cyclohexadienyl carbocation (R^+) to the coordinated arene hydrate (ROH), based on the reaction shown in Scheme 1.17. This approach can also be applied to coordinated cycloheptadienyl and cycloheptatrienyl cations.



Scheme 1.17 Formation of a coordinated arene hydrate (ROH) from a coordinated cyclohexadienyl cation (R^+).

In Scheme 1.17, k_{H2O} is the rate constant for the reaction of the coordinated cyclohexadienyl cation in water. The rate constant, k_H, refers to the acid catalysed ionisation of the coordinated arene hydrate to form the coordinated cyclohexadienyl cation. This type of equilibrium is sometimes refered to as a pseudobase equilibrium. The equilibrium constant, K_R, can be expressed in terms of its negative logarithm defined as pK_R (pK_R = -log K_R). A larger K_R signifies a less stable cation species.

In principle, there are two methods by which the constant K_R can be determined. They are:

1 By a direct measurement of the equilibrium concentrations of the tricarbonyl arene hydrate iron complex combined with the tricarbonyl cyclohexadienyl iron carbocation.

2 By kinetic measurement of the forward and reverse rates of ionisation of the tricarbonyl arene hydrate iron complex and hydrolysis of the tricarbonyl cyclohexadienyl iron carbocation complex respectively, under the same conditions.

1.3.1 Direct Equilibrium Measurements.

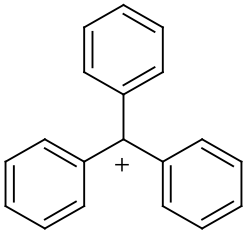
The relationship between the concentrations of reactants and products for direct equilibrium measurements of the equilibrium constants K_R, from Scheme 1.17, is

given by Equation 1.3. The solvent, H_2O, has been omitted from this equation as is common with K_a equilibria.

$$K_R = \frac{[ROH][H^+]}{[R^+]} \qquad (1.3)$$

UV-Vis spectroscopy is commonly used to carry out direct determinations of K_R. This is achieved by determining the relative concentrations of the carbocation and the neutral complex being studied at equilibrium at particular acid concentrations. An appreciable change in spectrum is required between the fully ionised and fully neutral species and both species must be sufficiently stable to be directly observable. An example of a cation that is stable enough to allow equilibrium measurements in dilute acid solutions is the tropylium cation **(42)**[53] as shown in Chart 1.6.

(42)



(43)

Chart 1.6 Tropylium **(42)** and triphenylmethyl **(43)** cations.

For cations such as the triphenylmethyl cation **(43)**, measurements were carried out in more concentrated acid solutions.[54,55] As a result of medium effects, the K_R value must be extrapolated to water by using the acidity function method. By use of reference reactions, a plot of log K_R versus the acidity function, X_0, can be obtained and the value of K_R is determined in the absence of acid by extrapolating to pure water for which $X_0 = 0$ is determined.[56,57]

In practice, concentrated strong acid mixtures lead to large medium effects which affect protonation equilibria. Much work has been carried out on measuring the medium effect on the protonation equilibria in sulphuric acid, hydrochloric acid and

perchloric acid. This effect may be expressed by the relationship shown in Equation 1.4, where K is the equilibrium constant at various acid concentrations, and K_{H2O} is the equilibrium constant in water, and m* is the slope of this relationship.

$$\log \frac{K}{K_{H2O}} = m^* X_0 \qquad (1.4)$$

The acidity function, X_0 is defined by Cox and Yates as $\log(K / K_{H2O})$, where K and K_{H2O} refer to equilibrium constants for a reference acid-base reaction.[58]

1.3.2 Kinetic Measurements.

An alternative to employing UV-Vis equilibrium measurements to determine K_R is the use of kinetic measurements. In this approach, the equilibrium constant is obtained by combining the forward and reverse reaction rates, k_H and k_{H2O} respectively, as shown in Equation 1.5.

$$K_R = \frac{k_{H2O}}{k_H} \qquad (1.5)$$

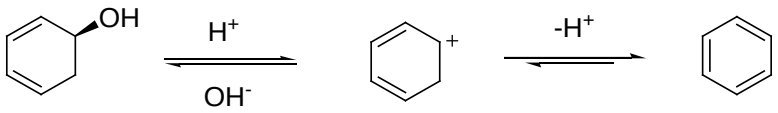
For uncoordinated carbocations, k_{H2O} can be difficult to measure as, in the case of very reactive carbocations, the reaction of the carbocation with water occurs rapidly and the reactive species are difficult to isolate as reactants.

The stabilising ability of the tricarbonyl iron fragment allows the rate constant, k_{H2O}, to be measured directly in the case of the reaction of the tricarbonyl cyclohexadienyl iron cation to give the corresponding arene hydrate complex. The rate constant, k_H, for carbocation formation from alcohols has been determined by various methods. For the coordinated cycloheptadienyl and cycloheptatrienyl cations being examined in this work, k_H can be measured by first allowing the

coordinated cation to react fully to form the complementary hydrate complex and subsequently quenching this hydrate into a solution of sufficiently lower pH that will allow the formation of the cation to be observed.

1.3.3 Relevant Complexes Studied Previously.

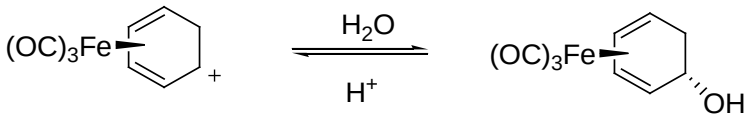
The pK_a and the pK_R for the uncoordinated benzenonium ion **(44)** have been determined and these equilibria are shown in Scheme 1.18. It was calculated that in one molar acid, less than one molecule per mole of benzene exists in the protonated cyclohexadienyl cation **(44)** form and, in aqueous solution, it is deprotonated at a rate close to the limiting rate of relaxation of the solvent.[59]



(2) **(44)**

Scheme 1.18 **Equilibrium reactions for the uncoordinated benzenonium ion (44).**

The pK_R for the tricarbonyl cyclohexadienyl iron cation **(45)** has been determined previously in this group and the equilibrium reaction is shown in Scheme 1.19.[60] Studies of the equilibrium between the coordinated cyclohexadienyl cation and its corresponding *exo* hydrate **(46)** allowed a rate constant, k_H, for ionisation of this isomer of 7.2 x 10^3 M^{-1} s^{-1} to be estimated.[60] As mentioned previously, it is know that the nucleophile will add *anti* to the tricarbonyl iron moiety in such a reaction.[17]

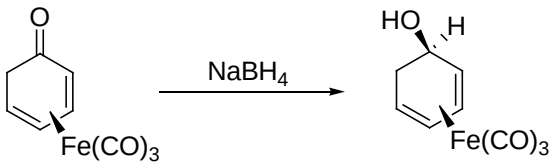


(45) **(46)**

Scheme 1.19 Nucleophilic attack of hydroxide on tricarbonyl cyclohexadienyl iron.

A contrast to the benzenonium cation is observed for the tricarbonyl cyclohexadienyl iron cation as it is readily isolated in its tetrafluoroborate (BF^-_4) and hexafluorophosphate (PF^-_6) salts, and is stable at mild acidic pH and can be recrystallised from water.[22] In the presence of bases, deprotonation does not occur. Instead, nucleophilic substitution occurs to give the corresponding *exo* arene hydrate **(46)** as shown above in Scheme 1.19. This is evidence to support the fact that the stability of the cyclohexadienyl cations and their analogues is greatly increased when coordinated to tricarbonyl iron.

The *endo* isomer of this complex has been prepared by Birch *et al.* by sodium borohydride reduction of the tricarbonyl iron-coordinated keto complex (47) as shown in Scheme 1.20.[22]



(47) **(48)**

Scheme 1.20 Synthesis of tricarbonyl *endo*-cyclohexadienol iron (48)

The two isomers are distinguished by NMR spectroscopy. The rate constant for the acid catalysed conversion of the *endo*-substituted coordinated complex **(48)** to the corresponding cyclohexadienyl cation complex **(46)** was measured[61] and was found to be 2.0×10^{-3} M^{-1} s^{-1}, which is 10^7 times less than the rate constant for the corresponding *exo* hydrate.[60,61] This would indicate that the *endo* isomer is less reactive than the *exo* analogue. A possible explanation for this low reactivity of the *endo* isomer would be that a favourable interaction between the tricarbonyl iron moiety and the *endo* hydroxyl group has a stabilising effect.[60]

1.4 Organometallic Coordination of Oxidative Metabolites of Aromatic Hydrocarbons – Aims of This Study.

As discussed in Section 1.1, arene *cis*-dihydrodiols can be produced in large quantities from biotransformations using mutant strains of bacteria and have found many uses as chiral precursors for the formation of products of synthetic and industrial importance. The corresponding *trans* analogues are potentially important chiral synthons as they are more stable than their *cis* isomers. The *trans* isomers are as yet not accessible on a commercial scale, but a number of pathways that could be used to synthesise substituted arene *trans* dihydrodiols from their *cis* isomers have been described in a review by Boyd and Sharma.[62] One of the most promising of these routes was outlined in Scheme 1.5 and involves coordination of the tricarbonyl iron moiety to arene *cis* dihydrodiols and this synthetic route is investigated in this project. Since the synthesis involves the formation of tricarbonyl iron intermediates, it was decided to study the reactivity of these tricarbonyl iron complexes and some related complexes to allow the synthetic route to be optimised.

Thus the aims of this project are:

- To carry out and optimise the metal coordination route proposed for the conversion of arene *cis* dihydrodiols to their *trans* isomers on a number of substrates.
- To investigate the steps of this synthetic pathway using kinetic and equilibrium studies to provide information to optimise the route and in so doing add to the existing knowledge of the relatively unexplored organometal complexes involved.
- To synthesise tricarbonyl iron and tricarbonyl chromium complexes of seven- membered ring systems and perform kinetic and equilibrium studies on a number of them to provide a comparison to complexes previously studied within the group.

Chapter 2

Results

Chapter 2 Results.

The results are presented in two sections which entail (a) synthesis of organic and organometallic compounds, (b) investigation of some of the complexes using kinetic studies and, in some cases, using ^{1}H NMR spectroscopy.

2.1 Synthesis of Organic and Organometallic Compounds.

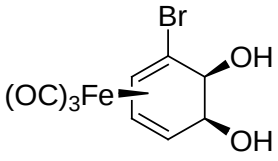
This section outlines the synthesis performed in this study and gives information on the organic and organometallic compounds produced. Tables of results summarise the reaction conditions and yields obtained.

2.1.1 Tricarbonyl Iron Complexes of Substituted Benzene *cis*-Dihydrodiols.

Bromo- and trifluoromethyl- substituted benzene *cis*-dihydrodiols were coordinated to tricarbonyl iron using a direct complexation procedure by reaction with diironnonacarbonyl (3 equiv.) in tetrahydrofuran in a similar procedure to that reported by Suemune *et al.*[63] to give complexes **(49)** and **(50)** as shown in Chart 2.1. The large excess of diironnonacarbonyl required limits the scale of the reactions. This is due to toxicity of a side product, ironpentacarbonyl, and 5 g of diironnonacarbonyl is the maximum amount that can be used with the apparatus available.

Percentage yields for the reaction were in a range of 60 - 66% for complex **(49)** and 52-91% for complex **(50)** as shown in Table 2.1.[i]

[i] The wide yield range depended on the quality of the starting material



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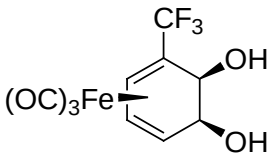


(50)

Chart 2.1

Table 2.1 Reaction conditions and yields for the preparation of tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** and tricarbonyl (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)**.

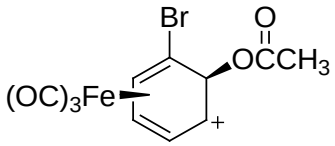
Compound	Scale (mmol)	Equivalents of $Fe_2(CO)_9$	Reaction time (hours)	R_f[i]	% Yield	% Yield Lit
(49)	1.13	3	3	0.35	60 – 66	-
(50)	1.14	3	3-4	0.38	52 - 91	68[64]

2.1.2 Tricarbonyl Iron-Substituted Cyclohexadienyl Cation Complexes.

The *cis* complexes, tricarbonyl (η^4-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** and tricarbonyl (η^4-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)** were treated with acetic anhydride and hexafluorophosphoric acid in dichloromethane in a similar procedure to that proposed by Pearson *et al.*[64] to form their corresponding substituted cyclohexadienyl cations shown in Chart 2.2. The cations were isolated by adding the reaction mixture dropwise to diethyl ether to form a yellow precipitate, the solvent was then decanted and the solid washed with ether. The

[i] The solvent system used to monitor the reaction by TLC and for flash chromatography was 1:1 cyclohexane:ethyl acetate.

yields are not reported as purification proved difficult due to the cations undergoing decomposition. The cations were used directly in the next step of the synthetic route and yields of 100% were assumed. Reaction conditions are shown in Table 2.2. The decomposition of these complexes was monitored by ^{1}H NMR spectroscopy. Cation **(51)** was found to decompose to bromobenzene, with 50% conversion having occurred within 24 hours. Cation **(52)** had undergone complete conversion to trifluoromethyl benzene within the same time span.



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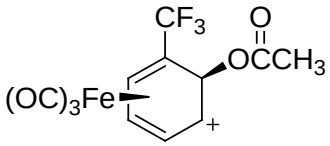


(52)

Chart 2.2

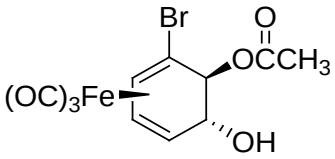
Table 2.2 Reaction conditions for the synthesis of tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron (0) hexafluorophosphate **(51)** and tricarbonyl (η^5-1-acetoxy-2-trifluoromethylcyclohexadienyl) iron (0) hexafluorophosphate **(52)**.

Compound	Scale (mmol)	Equivalents of HPF_6	Reaction conditions	R_f[i]
(51)	0.39	4	2 hrs, 0 ºC	0.50
(52)	0.28	4	4 hrs, 0 ºC	0.58

[i] The solvent system used to monitor the reaction was 1:1 cyclohexane:ethyl acetate.

2.1.3 Tricarbonyl Iron Complexes of Substituted Benzene *trans*-Dihydrodiol Monoacetate Derivatives.

The cyclohexadienyl cations **(51)** and **(52)** were dissolved in acetonitrile, cooled and added dropwise to a buffer. Originally aqueous sodium hydrogen carbonate was used,[64] but it was found that milder base, aqueous sodium acetate, also worked well. The corresponding *trans*-products **(53)** and **(54)** shown in Chart 2.3 are formed in yields of 79% and 47% respectively as shown in Table 2.3.



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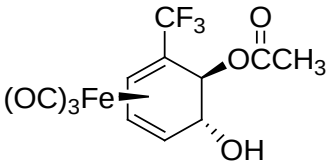


(54)

Chart 2.3

Table 2.3 Reaction conditions and yields for the preparation of tricarbonyl (η^4-*trans*-2-acetoxy-3-bromocyclohexa-3,5-diene-1-ol) iron **(53)** and tricarbonyl (η^4-*trans*-2-acetoxy-3-trifluoromethylcyclohexa-3,5-diene-1-ol) iron **(54)**.

Compound	Scale (mmol)[i]	Equiv. of base	Reaction conditions	R_f[ii]	% Yield[iii]	% Yield Lit
(53)	0.28	4	1hr, 0 ºC	0.30	79	-
(54)	0.94	4	1 hr, 0 ºC	0.39	47	83[64]

[i] Based on crude weight from previous cation reaction.
[ii] The solvent system used to monitor the reaction by TLC was 1:1 cyclohexane:ethyl acetate.
[iii] A side product was observed in the ^{1}H NMR spectrum of both complexes amounting to approximately 25% for **(53)** and 3% for **(54)** based on integration.

2.1.4 Tricarbonyl Iron Complexes of Substituted Benzene *trans*-Dihydrodiols.

In order to try to characterize the side products observed in the NMR spectra of the *trans* complexes **(53)** and **(54),** they were deprotected to give their corresponding diols. This was done to compare with the NMR spectra of the complexed *cis*-diols to determine is any *cis* was present in the product. This was achieved by dissolving them in 1:1 methanol: dichloromethane and reacting with a catalytic amount of finely crushed potassium carbonate to form the *trans* dihydrodiols **(55)** and **(56)** as shown in Chart 2.4. Reaction conditions and yields obtained are shown in Table 2.4.

(55) **(56)**

Chart 2.4

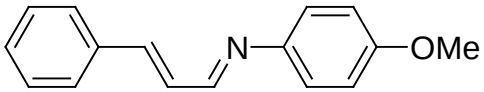
Table 2.4 Reaction conditions and yields for the preparation of tricarbonyl (η^4-*trans*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(55)** and tricarbonyl (η^4-*trans*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(56)**.

Compound	Scale (mmol)	Equivalents of K_2CO_3	Reaction conditions	R_f[i]	% Yield
(55)	0.16	0.08	Overnight /rt	0.33	97
(56)	0.11	0.10	Overnight /rt	0.35	86

[i] The solvent system used to monitor the reaction by TLC was 1:1 cyclohexane:ethyl acetate.

2.1.5 Synthesis of Azabutadiene Iron Transfer Catalysts.

The complexation of tricarbonyl iron to other compounds required the use of a transfer catalyst. The catalyst used, 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene **(31)**, shown in Chart 2.5 was synthesized by the reaction of *trans*-cinnamaldehyde with *p*-anisidine in the presence of magnesium sulfate in ethyl acetate.[26] It is then either used *in situ* during a complexation or, in some cases, it has been complexed to tricarbonyl iron and then reacted with the substrate. The complexation of the transfer catalyst to tricarbonyl iron to form tricarbonyl 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene iron **(28)** is achieved by sonication with diironnonacarbonyl in tetrahydrofuran at 40 kHz.[26] Reaction conditions and yields are shown in Table 2.5.



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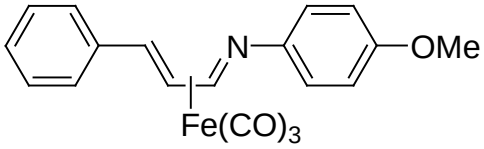

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Chart 2.5

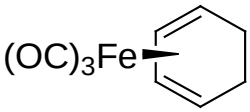
Table 2.5 Reaction conditions and yields for the preparation of 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene **(31)** and tricarbonyl 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene iron **(28)**.

Compound	Scale (mmol)	Reaction Conditions	Solvent	R_f[i]	% Yield	% Yield Lit[26]
(31)	84	N_2 atmosphere	ethyl acetate	0.14	42	100
(28)	2.19	N_2 atmosphere, sonication	THF	0.40	50	88

[i] The solvent system used to monitor the reaction by TLC was 9:1 pentane:diethyl ether.

2.1.6 Tricarbonyl Cyclohexa-1,3-diene Iron (21) and Dicarbonyl Cyclohexa-1,3-diene Triphenylphosphine Iron (57).

Cyclohexa-1,3-diene was complexed to tricarbonyl iron using the azabutadiene catalyst **(31)** and diironnonacarbonyl in dimethoxyethane as described by Knölker *et al.*[35] to give tricarbonyl cyclohexa-1,3-diene iron **(21)** as shown in Chart 2.6, in yield of 49%. This was then reacted with triphenylphosphine in cyclohexanol. Vacuum distillation of the cyclohexanol as described by Pearson *et al.*[65] gave the ligand exchange product dicarbonyl cyclohexa-1,3-diene triphenylphosphine iron **(57)** in yield of 17%. Reaction conditions are shown in Table 2.6. The yields were calculated based on the diironnonacarbonyl.



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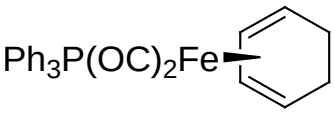

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Chart 2.6

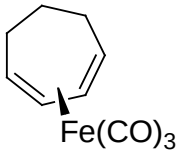
Table 2.6 Reaction conditions and yields for the synthesis of tricarbonyl (η^4-cyclohexa-1,3-diene) iron **(21)** and dicarbonyl (η^4-cyclohexa-1,3-diene) triphenylphosphine iron **(57)**.

Compound	Scale (mmol)	Equiv. of Reagents	Reaction Conditions	R_f	% Yield	% Yield Lit
(21)	38	11 % catalyst, 0.33 equiv. $Fe_2(CO)_9$,	82 ºC, 24 hrs	0.60[i]	49	98[35]
(57)	4.62	1.1 equiv. PPh_3	168 ºC, 24 hrs	0.50[ii]	17	62[65]

[i] The solvent system used to monitor the reaction by TLC was 9:1 pentane:ethyl acetate.
[ii] The solvent system used to monitor the reaction by TLC was 9:1 petroleum ether:ethyl acetate.

2.1.7 Tricarbonyl (η^4-Cyclohepta-1,3-diene) Iron (58) and Tricarbonyl (η^4-Cyclohepta-1,3,5-triene) Iron (59).

Tricarbonyl (η^4-cyclohepta-1,3-diene) iron **(58)**, as shown in Chart 2.7, was synthesised by two different methods. The first involved reacting the azabutadiene catalyst **(31)** and diironnonacarbonyl with cycloheptadiene to give the product in a yield of 68%, and the second method was the reduction of the less expensive starting material cycloheptatriene with sodium borohydride followed by coordination with iron pentacarbonyl to give the product **(58)** in a yield of 44%. The synthesis of tricarbonyl (η^4-cyclohepta-1,3,5-triene) iron **(59)** was also attempted using two methods, the first reacting the catalyst **(31)** and diironnonacarbonyl with cycloheptatriene which gave the product in a yield of 28%. The second entailed reacting the complexed catalyst **(28)** directly with cycloheptatriene; however the desired product was not isolated. Reaction conditions for the successful synthesis are shown in Table 2.7.



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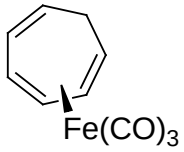

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Chart 2.7

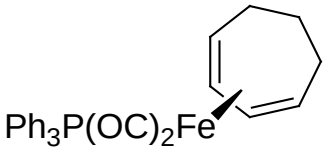
Table 2.7 Reaction conditions and yields for the synthesis of tricarbonyl (η^4-cyclohepta-1,3-diene) iron **(58)** and tricarbonyl (η^4-cyclohepta-1,3,5-triene) iron **(59)**.

Compound	Scale (mmol)	Reaction Conditions	R_f[i]	% Yield	% Yield Lit
(58)	(i) 15.70	(i) 1 equiv. $Fe_2(CO)_9$, 33% catalyst **(31)**, 9 equiv. cycloheptadiene.	0.60	(i) 68	84[35]
	(ii) 7.20	(ii) 1 equiv. cycloheptatriene, 3 equiv. $Fe(CO)_5$, 0.2 equiv. $NaBH_4$		(ii) 44	90[66]
(59)	40	1 equiv. $Fe_2(CO)_9$, 33% catalyst **(31)**, 3 equiv. cycloheptatriene.	0.60	28	-

2.1.8 Dicarbonyl (η^4-Cyclohepta-1,3-diene) Triphenylphosphine Iron (60) and Dicarbonyl (η^4-Cyclohepta-1,3,5-triene) Triphenylphosphine Iron (61).

A ligand exchange with triphenylphosphine was carried out on complexes **(58)** and **(59)**. The coordinated cycloheptadiene and cycloheptatriene were dissolved in di-*n*-butyl ether and reacted with triphenylphosphine at 150 ºC in a similar procedure to that reported by Pearson *et al.*[67] to form the products **(60)** and **(61)** shown in Chart 2.8 in yields of 35% and 16% respectively as shown in Table 2.8.

[i] The solvent system used to monitor the reaction by TLC was 9:1 hexane:ethyl acetate.



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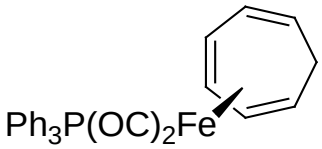


(61)

Chart 2.8

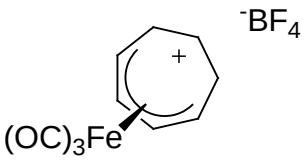
Table 2.8 Reaction conditions and yields for the synthesis of dicarbonyl (η^4-cyclohepta-1,3-diene) triphenylphosphine iron **(60)** and dicarbonyl (η^4-cyclohepta-1,3,5-triene) triphenylphosphine iron **(61)**.

Compound	Scale (grams)	Equiv of PPh_3	Reaction Conditions	R_f[i]	% Yield	% Yield Lit
(60)	0.94	1	150 ºC, 44 hrs	0.45	35	94[67]
(61)	2.19	1	150 ºC, 48 hrs	0.33	16	-

2.1.9 Tricarbonyl (η^5-Cycloheptadienyl) Iron Tetrafluoroborate Salt (62) and Dicarbonyl (η^5-Cycloheptadienyl) Triphenylphosphine Iron Tetrafluoroborate Salt (63).

Tricarbonyl (η^4-cyclohepta-1,3-diene) iron and dicarbonyl (η^4-cyclohepta-1,3-diene) triphenylphosphine iron were treated with triphenylcarbenium tetrafluoroborate in dichloromethane to form the salts tricarbonyl cycloheptadienyl iron tetrafluoroborate **(62)** and dicarbonyl cycloheptadienyl triphenylphosphine iron tetrafluoroborate **(63)** shown in Chart 2.9 in yields of 85% and 96% respectively as summarized in Table 2.9.

[i] The solvent system used to monitor the reaction by TLC was 3:2 hexane:diethyl ether.



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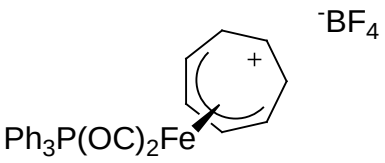


(63)

Chart 2.9

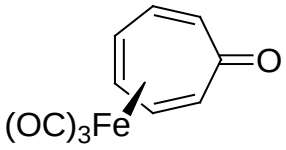
Table 2.9 Reaction conditions and yields for the synthesis of tricarbonyl (η^5-cyclohepta-1,3-dienyl) iron tetrafluoroborate **(62)** and dicarbonyl (η^5-cyclohepta-1,3-dienyl) triphenylphosphine iron tetrafluoroborate **(63)**.

Compound	Scale (mmol)	Equiv. of Ph_3C^+ $^{-}BF_4$	Reaction Conditions	R_f[i]	% Yield	% Yield Lit
(62)	1.00	1.2	Ar atmosphere, 0 ºC, 24 hrs	0.37	85	92[68]
(63)	0.32	1.4	Ar atmosphere, 0 ºC, 1 hr	0.50	96	76[69]

2.1.10 Tricarbonyl Iron and Dicarbonyl Triphenylphosphine Iron Complexes of Cycloheptatrienone.

Cycloheptatrienone was coordinated to tricarbonyl iron using a direct complexation procedure with diironnonacarbonyl to give tricarbonyl cycloheptatrienone iron **(32)** shown in Chart 2.10 in a yield of 89%. A ligand exchange was then performed using triphenylphosphine and trimethylamine-*N*-oxide to give the product dicarbonyl cycloheptatrienone triphenylphosphine iron **(64)** in a yield of 50%. This was then reacted further with cerium (III) chloride and sodium borohydride to form the new compound dicarbonyl cyclohepta-2,4,6-triene-1-ol triphenylphosphine iron **(65)** in yield of 73%. Reaction conditions and yields are presented shown in Table 2.10.

[i] The solvent system used to monitor the reaction by TLC was 1:1 cyclohexane:ethyl acetate



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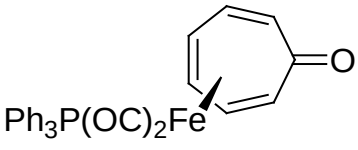

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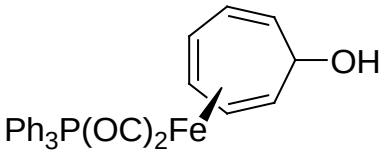


(65)

Chart 2.10

Table 2.10 Reaction conditions and yields for the synthesis of tricarbonyl (η^4-cycloheptatrienone) iron **(32)**, dicarbonyl (η^4-cycloheptatrienone) triphenylphosphine iron **(64)** and dicarbonyl (η^4-cyclohepta-2,4,6-triene-1-ol) triphenylphosphine iron **(65)**.

Compound	Scale (mmol)	Reaction Conditions	Solvent	R_f	% Yield	% Yield Lit
(32)	6.00	2.3 eq. $Fe_2(CO)_9$, in dark	Toluene	0.60[i]	89	79[70]
(64)	4.00	1.5 eq. PPh_3, 1.7 eq. Me_3NO	Acetone	0.40[ii]	50	61[71]
(65)	0.42	11 eq. $CeCl_3.7H_2O$, 19 eq. $NaBH_4$	Methanol	0.68[iii]	73	-

[i] The solvent system used to monitor the reaction by TLC was 3:2 diethyl ether:dichloromethane on alumina plates.
[ii] The solvent system used to monitor the reaction by TLC was 1:1 petroleum ether:ethyl acetate on alumina plates.
[iii] The solvent system used to monitor the reaction by TLC was 1:1 cyclohexane:ethyl acetate on alumina plates.

2.1.11 Tricarbonyl Chromium Complexes of Cycloheptatriene.

Cycloheptatriene was coordinated to tricarbonyl chromium using direct complexation with chromium hexacarbonyl to give tricarbonyl cyclohepta-1,3,5-triene chromium **(40)** as described by Munro and Pauson.[72] This compound decomposes upon exposure to air and light and is used directly in the next reaction without purification. The crude compound was reacted with triphenylcarbenium tetrafluoroborate to form the stable aromatic cation tricarbonyl cycloheptatrienyl chromium tetrafluoroborate **(41)** in a yield of 10%. The low yield is due to the instability of the neutral complex precursor **(40)**. Reaction conditions are shown in Table 2.11.

(40) **(41)**

Chart 2.11

Table 2.11 Reaction conditions and yields for the synthesis of tricarbonyl (η^6-cycloheptatriene) chromium **(40)** and tricarbonyl (η^7-cycloheptatrienyl) chromium tetrafluoroborate **(41)**.

Compound[i]	Scale (mmol)	Reaction Conditions	Solvent	% Yield	% Yield Lit[72]
(40)	26.2	2.8 eq. cycloheptatriene, 1 eq. $Cr(CO)_6$, 162 ºC, 24 hrs, in dark, N_2 atmosphere	Diglyme[ii]	not determined	64
(41)	2.27	0.88 eq. Ph_3C^+ BF_4^- N_2 atmosphere	DCM	10	99

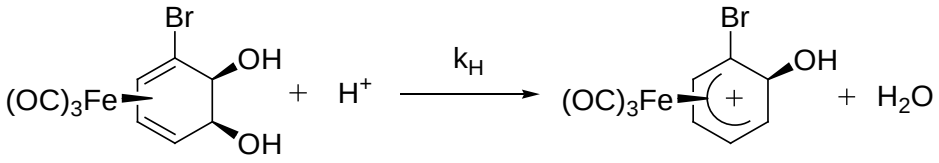
[i] Due to the instability of complex **(40)**, these reactions were not followed by TLC analysis.
[ii] Diethylene glycol dimethyl ether.

2.2 Kinetic and Equilibrium Measurements on Organometallic Compounds.

2.2.1 UV-Vis Studies on Tricarbonyl Bromo-Substituted Arene *cis*-Dihydrodiol Iron Complexes.

2.2.1.1 Ionisation of Bromo-Substituted Arene *cis*-Dihydrodiol Complex.

Studies of the ionisation of tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** to form the cation complex **(66)**, shown in Scheme 2.1, allowed the rate constant to be measured for the reaction. This was determined spectrophotometrically in concentrated aqueous perchloric acid solutions at 25 ºC, by measuring the UV absorption change.



(49) **(66)**

Scheme 2.1

A solution of tricarbonyl (η^4-*cis*-3-bromo-cyclohexa-3,5-diene-1,2-diol) iron **(49)** was prepared by dissolving it in acetonitrile to give a final concentration of 6.0 x 10^{-3} M. The cation **(66)** was generated by injecting 50 µL of this solution into 2 mL of 6.05 M $HClO_4$ in a 1 cm quartz cuvette. Repetitive UV-Vis scans collected at regular intervals were used to follow the progress of the reaction of the iron complex in acid, shown in Scheme 2.1, to determine the wavelength to use for

kinetic studies. This reaction exhibits a decrease in absorption occurring in the range 200 to 230 nm.

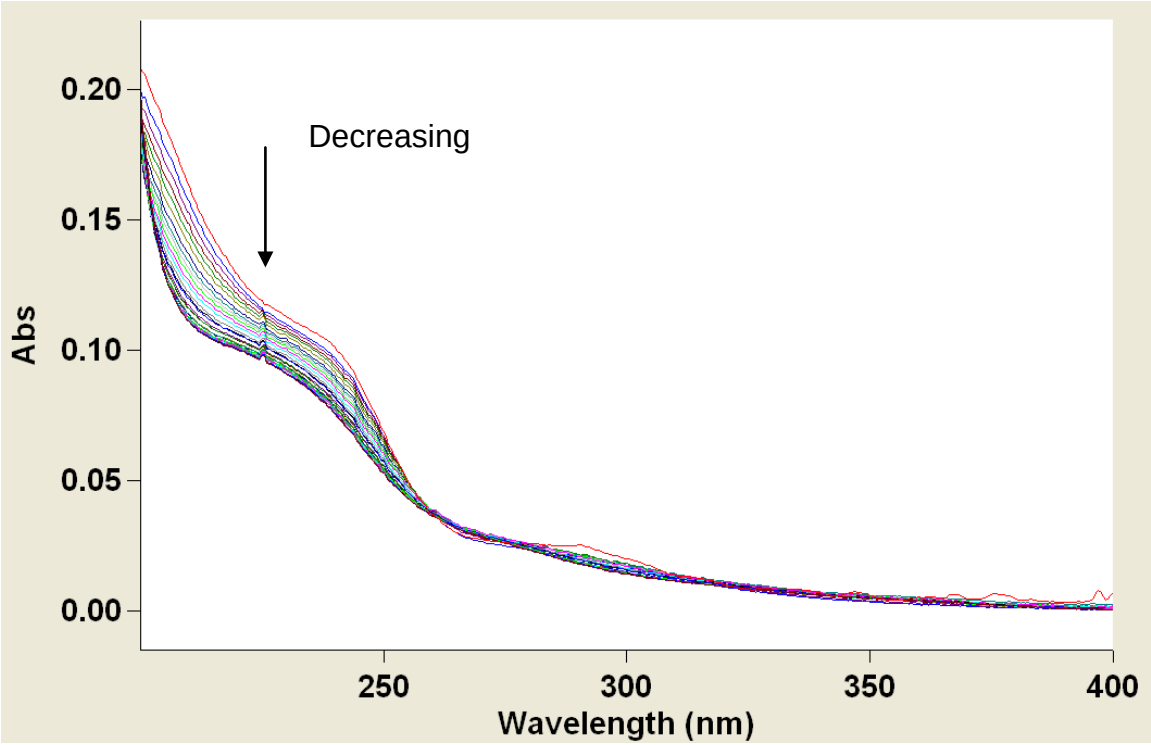


Figure 2.1 UV-Vis repetitive scan for the ionisation of tricarbonyl η^4-*cis*-(3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** in 6.05 M perchloric acid (cycle time 10 minutes) at 25 ºC, and a substrate concentration of 1.5×10^{-4} M.

The rate constant for ionisation of the bromo *cis*-diol complex **(49)** was determined by measuring the decrease in substrate absorbance over time at 210 nm in a range of aqueous concentrated perchloric acid solutions. This wavelength was selected because the greatest change in absorbance between the reactant and product UV spectra occurred there. Figure 2.2 shows a representative kinetic scan recorded at 210 nm and the first and second order rate constants determined in a range of concentrated perchloric acid solutions are presented in Table 2.12. In the strongly acidic solutions used for the kinetic measurements, we are no longer dealing with ideal aqueous solutions.[73] Since

the ionisation reactions were carried out in concentrated perchloric acid, values of $k_{obs}/[H^+]$ were not constant and increased with acid concentration. It was therefore necessary to extrapolate the measured rate constants to dilute acid solution. This was done by using the acidity parameter, X_0, which was discussed in the Introduction on page 24[57,74] instead of pH. Values of $\log(k_{obs}/[H^+])$ were plotted against X_0 to obtain a linear correlation shown in Figure 3.1 (page 85). By extrapolating to $X_0 = 0$, the log of the second order rate constant in dilute acid solutions was found to be log k_2 = -7.09 which corresponds to $k_2 = 8.0 \times 10^{-8}$ M^{-1} s^{-1}.

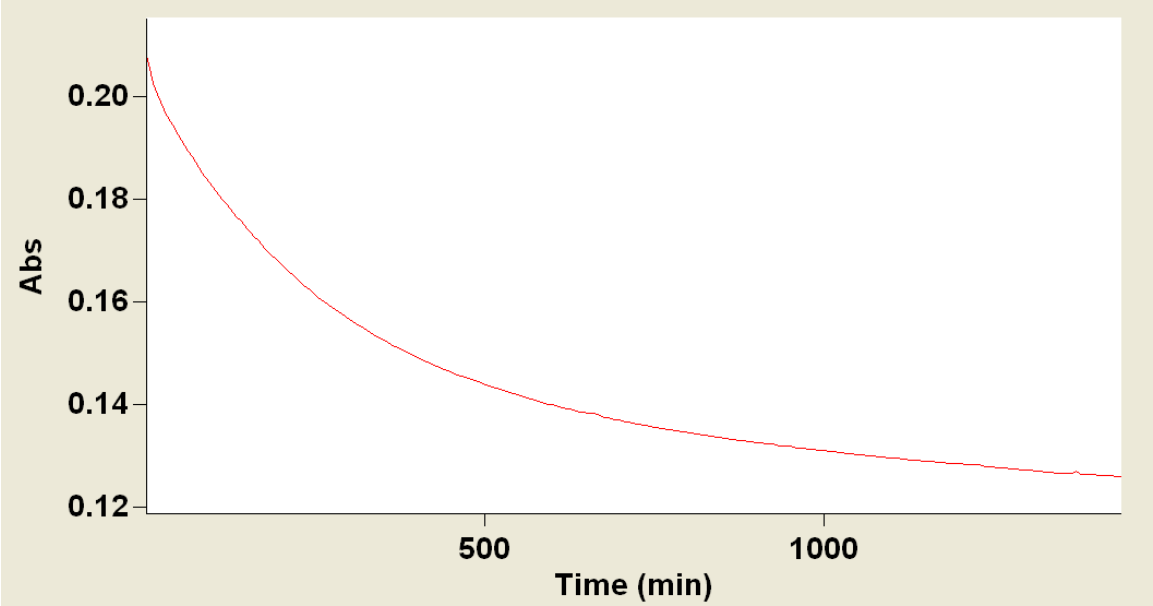


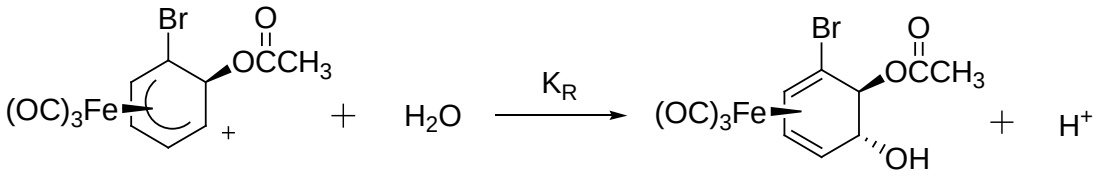
Figure 2.2 Kinetic measurement at 210 nm for the ionisation of tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** in 6.05 M perchloric acid at 25 ºC and a substrate concentration of 1.5×10^{-4} M.

Table 2.12 First and second order rate constants for the ionisation of tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** in aqueous acid solutions at 25 ºC, measured at 210 nm and a substrate concentration of 1.5 x 10^{-4} M.

$[HClO_4]$ (M)	X_0	10^5 k_{obs} (s^{-1})	10^6 $k_{obs}/[H^+]$ ($M^{-1}s^{-1}$)	$\log(k_{obs}/[H^+])$
6.66	2.4	27.2	40.8	-4.38
6.06	2.0	11.0	18.0	-4.74
5.45	1.75	5.83	10.7	-4.97
5.00	1.5	3.33	6.66	-5.77
4.84	1.45	9.97	2.06	-5.68

2.2.1.2 Nucleophilic Attack on Bromo-Cation Complex to form the *trans* Complex.

Studies were then carried out on the cation species tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)**. Conversion to *trans* complex **(53)** as shown in Scheme 2.2 was monitored by UV-Vis spectroscopy.



(51) **(53)**

Scheme 2.2

A solution of the cation complex **(51)** in acetonitrile was injected into water, acetonitrile and various concentrations of perchloric acid and an overlay of the

spectra obtained is presented in Figure 2.3. Kinetic studies were attempted using a fast-mixing apparatus, however the reaction was found to be too fast to measure. It can be estimated from the UV-Vis spectra recorded that the equilibrium constant for the hydrolysis of the cation **(51)**, pK_R, is approximately 0.2 – 0.5.

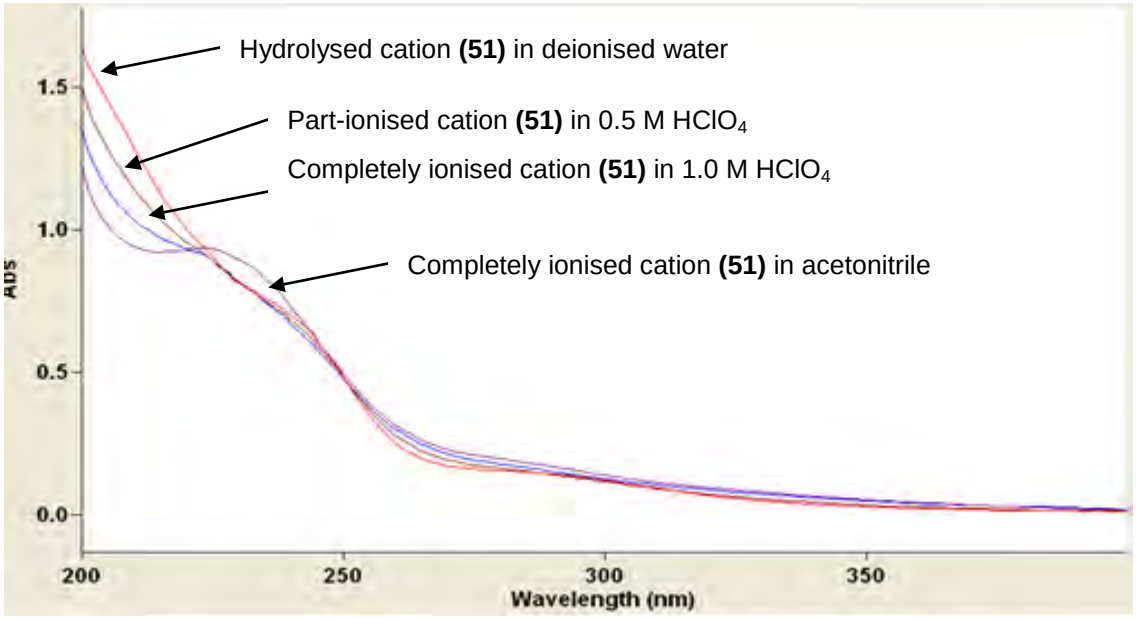
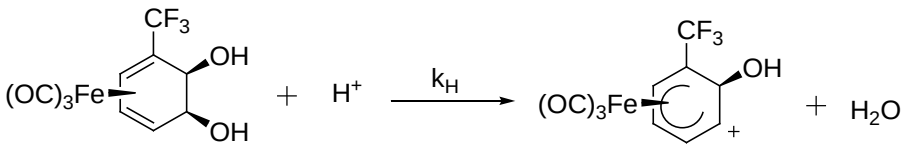


Figure 2.3 Overlay of UV-Vis spectra of tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)** in a range of solutions at 25 ºC.

2.2.2 Ionisation of Tricarbonyl Trifluoromethyl Diol Iron Complexes.

Studies of the ionisation of tricarbonyl (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)** to form the cation complex **(67)**, shown in Scheme 2.3 were performed in a range of concentrated perchloric acid solutions spectrophotometrically at 25 ºC, by measuring the UV absorption change.



(50) **(67)**

Scheme 2.3

A solution of tricarbonyl (η^4-*cis*-3-trifluoromethyl-cyclohexa-3,5-diene-1,2-diol) iron **(50)** was prepared by dissolving it in acetonitrile to give a final concentration of 3.17 x 10^{-3} M. The cation **(67)** was generated by injecting 50µL of this solution into 2 mL of 6.66 M $HClO_4$ in a 1 cm quartz cuvette. Repetitive UV-Vis scans collected at regular intervals allowed the progress of the reaction of the iron complex in acid to be followed (see Scheme 2.3) and the selection of a suitable monitoring wavelength for kinetic studies.

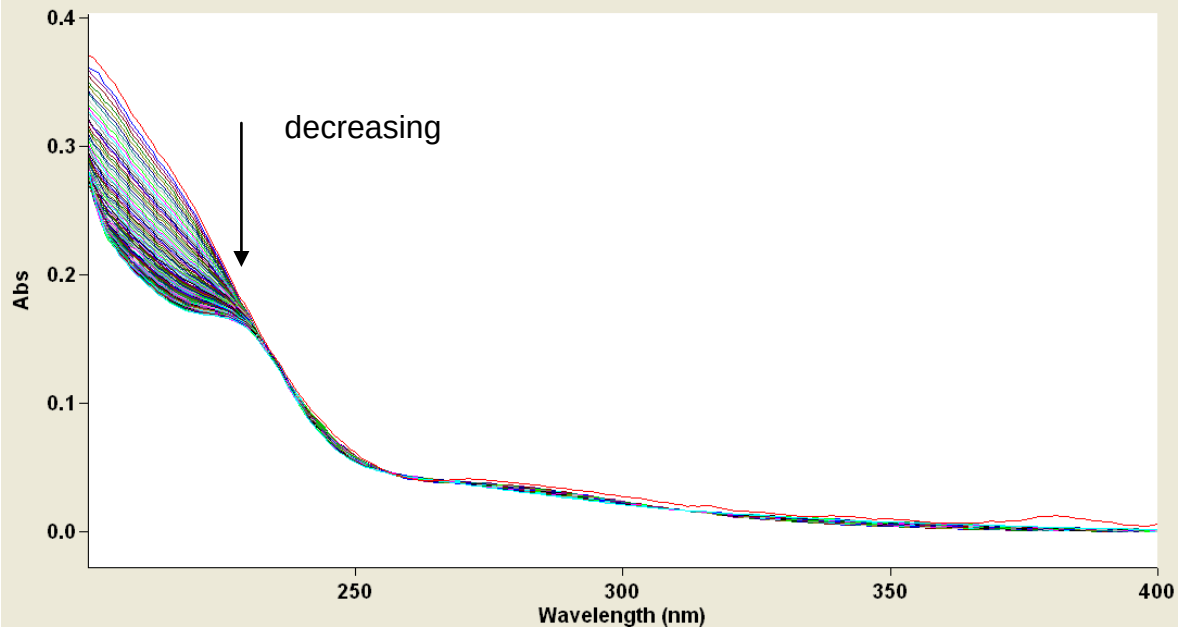


Figure 2.4 UV-Vis repetitive scan of tricarbonyl (η^4-*cis*-3-trifluoromethyl-3,5-diene-1,2-diol) iron **(50)** in 6.66 M perchloric acid (cycle time 10 minutes) at 25 °C, and a substrate concentration of 7.91 x 10^{-5} M.

The decrease in absorbance of the trifluoromethyl *cis*-diol complex **(50)** was measured at 215 nm in a range of aqueous perchloric acid solutions. However, difficulties arose when measuring a rate constant, as rates were too fast to be measured in acid concentration higher than 6.66 M and concentrations below 5.0 M showed no reaction. Rate determinations between these concentrations gave inconsistent results in some cases however and only three rate measurements were obtained. Figure 2.5 shows a typical kinetic scan recorded at 215 nm. There is evidence of a slower reaction occuring and this contributed to the difficulty in determining rate constants. In Table 2.13, the first and second order rate constants determined in the narrow range of concentrated perchloric acid solutions over which consistent rates were determined are presented. As these rates were measured in concentrated acid solutions, the acidity function value, X_0,[57,74] is used instead of pH.

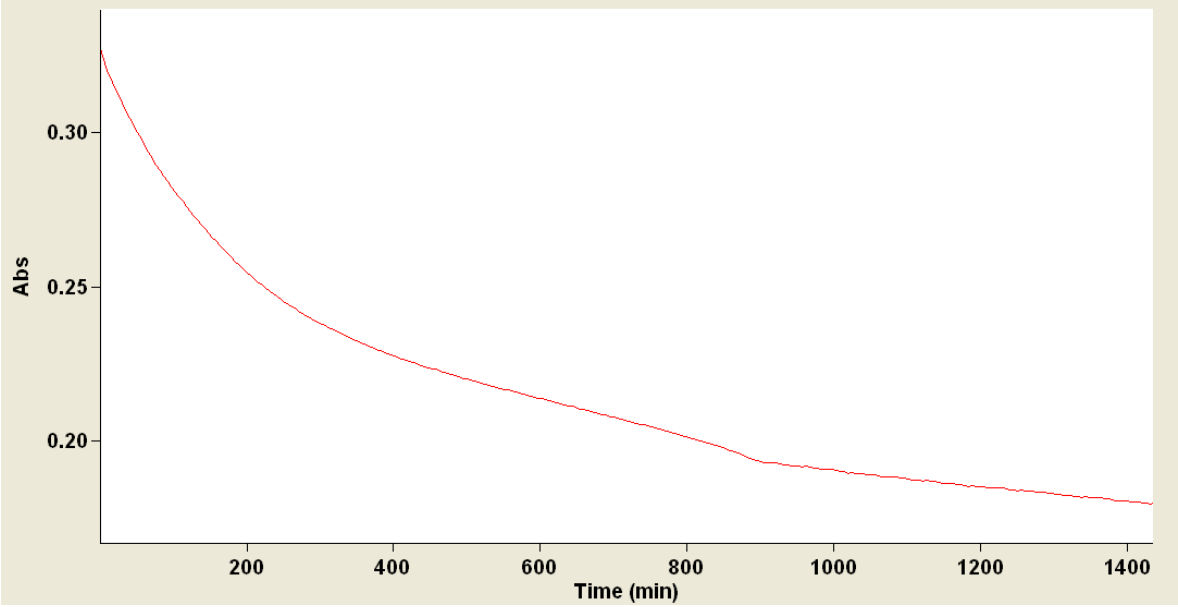


Figure 2.5 Kinetic measurement at 215 nm for the ionisation of tricarbonyl (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)** in 6.05 M perchloric acid at 25 ºC and a substrate concentration of 7.91 x 10^{-5} M.

Table 2.13 First and second order rate constants for the ionisation of tricarbonyl (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)** in aqueous acid solution at 25 ºC, measured at 215 nm and a substrate concentration of 7.91 x 10^{-5} M.

$[HClO_4]$ (M)	X_0	10^4 k_{obs} (s^{-1})	10^4 $k_{obs}/[H^+]$ ($M^{-1}s^{-1}$)	$\log(k_{obs}/[H^+])$
6.66	2.4	83.3	12.5	-2.90
5.45	1.75	89.9	1.65	-3.78
5.00	1.5	3.00	0.60	-4.22

Studies on the hydrolysis of the tricarbonyl (η^5-1-acetoxy-2-trifluoromethylcyclo-hexadienyl) iron **(52)** complex were attempted but the cation **(52)** was much more reactive than the corresponding bromo cation complex **(51)** and rapidly decomposes to trifluoromethylbenzene.

Brief studies were carried out on the ionisation of tricarbonyl (η^4-*trans*-2-acetoxy-3-trifluoromethylcyclohexa-4,5-diene-1-ol) iron **(54)** complex. However on examination of the UV-Vis spectra it was found that there was more than one reaction occuring and the reaction was not investigated further.

2.2.3 Investigation of the Decomposition of Bromo- and Trifluoromethyl- Substituted Arene Dihydrodiol Cations by ^{1}H NMR Spectroscopy.

During the investigation of the synthetic route from *cis* to t*rans* dihydrodiols, it was found that the cations tricarbonyl (1-acetoxy-2-bromocyclohexadienyl) iron **(51)** and tricarbonyl (1-acetoxy-2-trifluoromethylcyclohexadienyl) iron **(52)** were unstable and readily decomposed even when stored at -18 ºC. This

decomposition was monitored by ^{1}H NMR spectroscopy. It was found that the bromo-substituted cation **(51)** began to decompose after 24 hours and had significantly decomposed after 7 days. The ^{1}H NMR spectrum of the product that formed was compared to possible decomposition products and was found to match that of bromobenzene. Figures 2.6 – 2.8 show ^{1}H NMR spectra which track the stages of decompostion of tricarbonyl (1-acetoxy-2-bromocyclohexadienyl) iron **(51)**.

On monitoring the decomposition of tricarbonyl (1-acetoxy-2-trifluoromethylcy-clohexadienyl) iron **(52)**, it was found that it almost fully decomposed to the corresponding aromatic compound trifluoromethylbenzene in under 24 hours. This implies that the trifluoromethyl complex is considerably more reactive than the bromo complex.

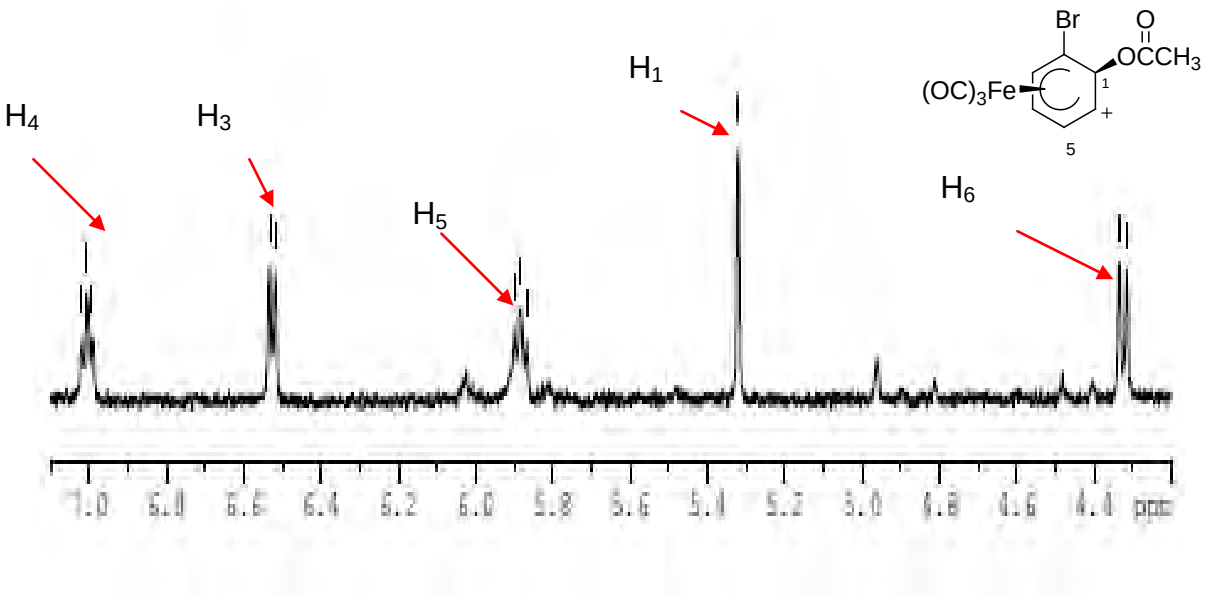


Figure 2.6 Expansion of the ^{1}H-NMR spectrum of freshly prepared tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)** in deuterated aceto-nitrile.[i]

[i] The entire spectra for Figures 2.6, 2. 7 and 2.8 are included in Appendix C.

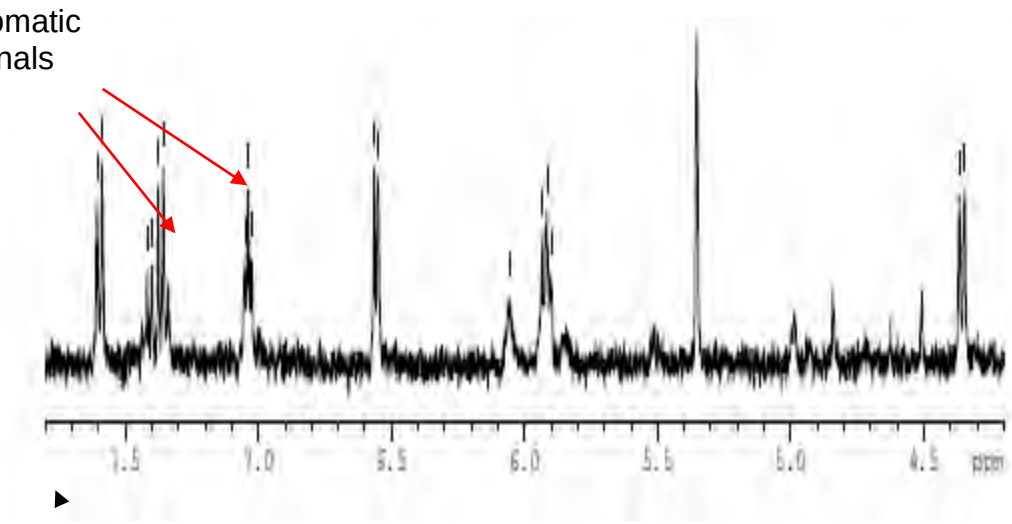


Figure 2.7 Expansion of ^{1}H-NMR spectrum of tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)** in deuterated acetonitrile after one day, showing the appearance of aromatic signals.

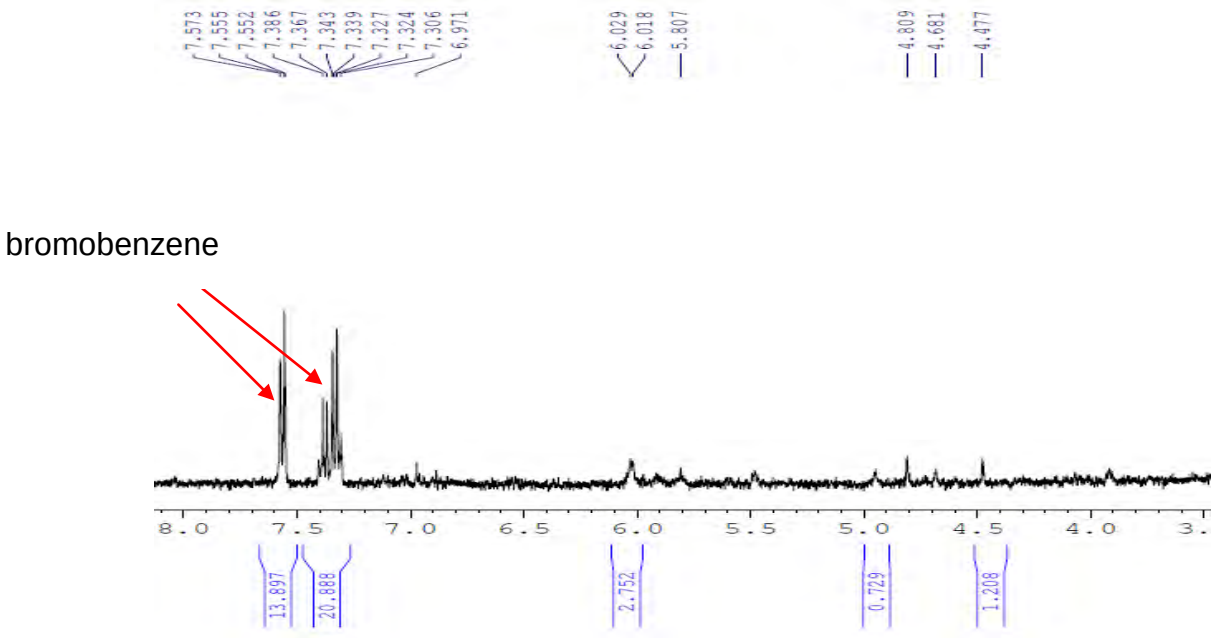
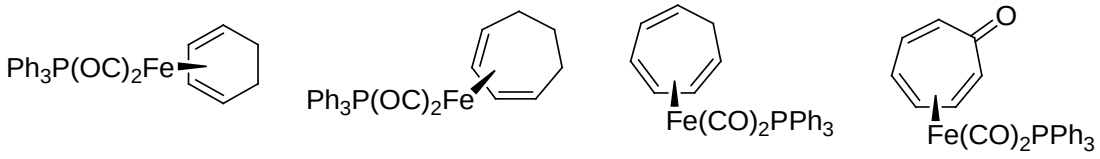


Figure 2.8 Expansion of ^{1}H-NMR spectrum of tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)** in deuterated acetonitrile after seven days, showing approximately 85% decomposition to bromobenzene.

2.2.4 Studies on Dicarbonyl Triphenylphosphine Iron Complexes of Unsaturated 6- & 7- Membered Rings.

Initial kinetic studies were carried out on the dicarbonyl triphenylphosphine iron complexes: dicarbonyl cyclohexadiene triphenylphosphine iron **(57)**, dicarbonyl cycloheptadiene triphenylphosphine iron **(60)**, dicarbonyl cycloheptatriene triphenylphosphine iron **(61)** and dicarbonyl cycloheptatrienone triphenylphosphine iron **(64)** shown in Chart 2.12.



(57) **(60)** **(61)** **(64)**

Chart 2.12

It was found that these complexes were undergoing a reaction in aqueous solutions. An example of a repetitive scan recorded of dicarbonyl cyclohexadiene triphenylphosphine iron **(57)** is shown in Figure 2.9 and is representative of what was observed for all of these compounds. This reactions occurred with both methanol and acetonitrile stock solutions.

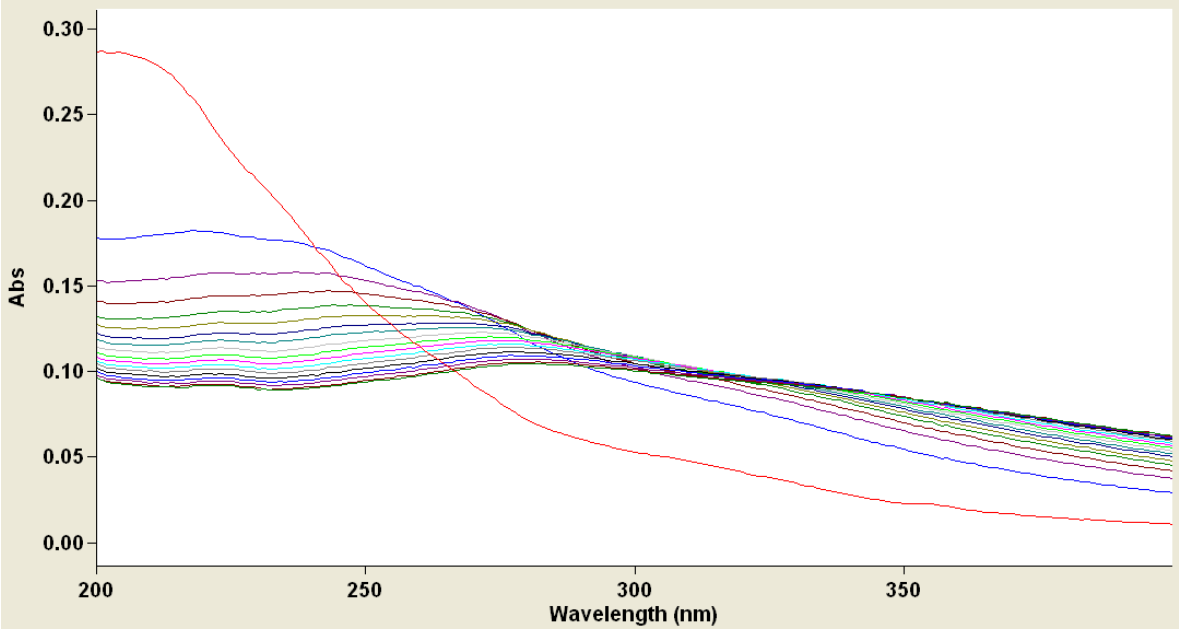


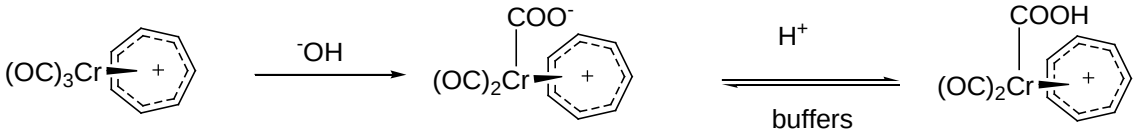
Figure 2.9 UV-Vis repetitive scan of dicarbonyl (η^4-cyclohexadiene) tri-phenylphosphine iron **(57)** (methanol stock solution) in 20 % aqueous methanol (cycle time 5 minutes) at 25 ºC, and a substrate concentration of 4.40 x 10^{-6} M.

It was found that this reaction did not occur in solutions containing over 90% methanol.

2.2.5 Tricarbonyl η^7-Cycloheptatrienyl Chromium Tetrafluoroborate (41) Species in Acidic and Basic Conditions.

UV-Vis studies were carried out on the tricarbonyl (η^7-cycloheptatrienyl) chromium cation complex **(41)**. The reversibility of the reactions of this complex in aqueous base and acid solutions was investigated. Scheme 2.4 shows the initial reaction of the cation (acidic form) with base which is believed to involve attack at a carbonyl ligand to give a zwitterion (neutral form). This neutral species can undergo a second reaction with base at a higher pH which probably

corresponds to addition of the hydroxide ion to the ring forming the corresponding hydrate of the neutral species (basic form).



(41) **(68)** **(69)**

Cation Zwitterion

Scheme 2.4

A solution of the tricarbonyl (η^7-cycloheptadienyl) chromium tetrafluoroborate substrate **(41)** was prepared by dissolving it in methanol to give a concentration of 6.37 x 10^{-3} M. 40 µL of this solution was then injected into 2 mL of water. Quantities of 0.10 M solutions of sodium hydroxide followed by perchloric acid were then added dropwise in succession to alter the pH from basic to acidic, repetitive UV spectra were recorded and showed that no further reaction was occuring. Figure 2.10 shows the UV spectra of the acid and base species observed to form. Having shown that the conversion was reversible sodium acetate was used to return the complex to its neutral form from its acidic form.

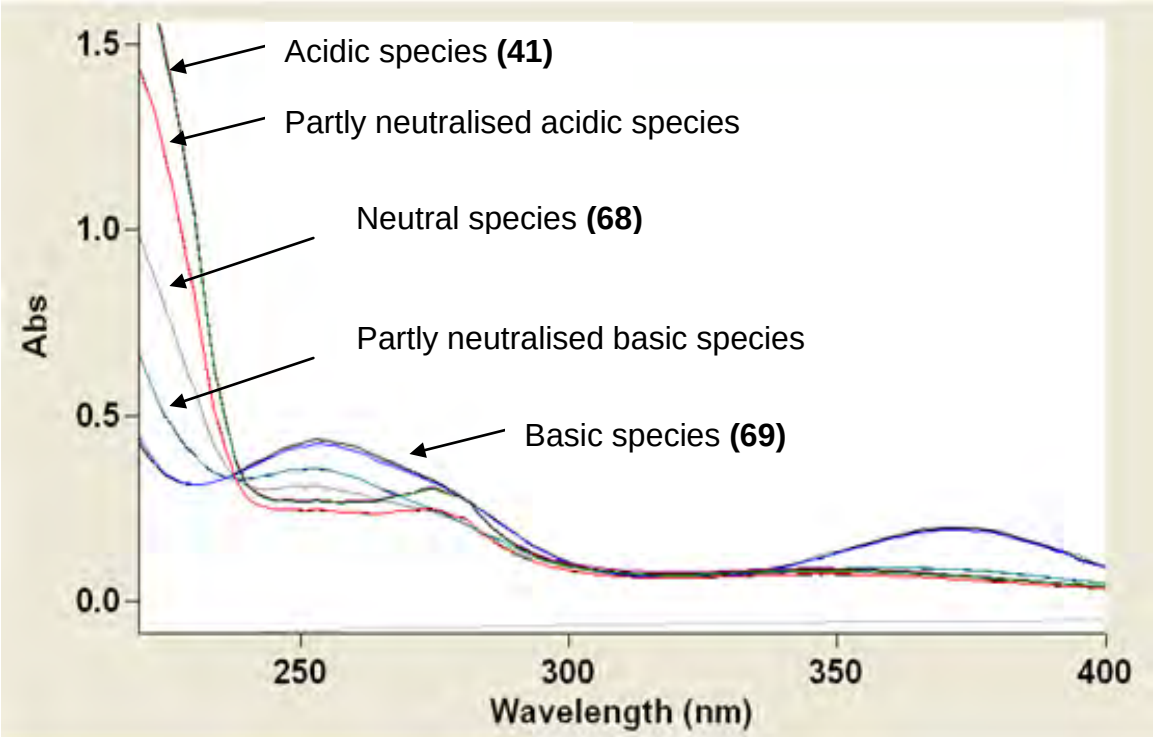


Figure 2.10 UV-Vis scans of tricarbonyl (η^7-cycloheptatrienyl) chromium **(41)** after alternate addition of 0.10 M perchloric acid, 0.10 M sodium hydroxide and 0.20 M sodium acetate (cycle times 2 minutes) at 25 ºC, and a substrate concentration of 6.37 x 10^{-5} M.

2.2.5.1 Ionisation Constant for Conversion from Tricarbonyl (η^7-Cycloheptatrienyl Chromium Tetrafluoroborate (41) to Neutral Species.

The pK_R of the cation **(41)** was then measured by first quenching 20 µL of the chromium cation into 1 mL of 0.2 M aqueous sodium acetate solution. This was left to react for 24 hours after which time it was believed to be completely converted to the zwitterion **(68)**. A further 1 mL aliquot was then added either to water or to perchloric acid of concentration less than 0.2 M to generate an acetic acid buffer. UV spectra were then recorded and the pH of each solution was measured. The spectra obtained are presented in Figure 2.11. Table 2.14

lists absorbance measurements made at 223 nm and 251 nm over the range of pH's examined.

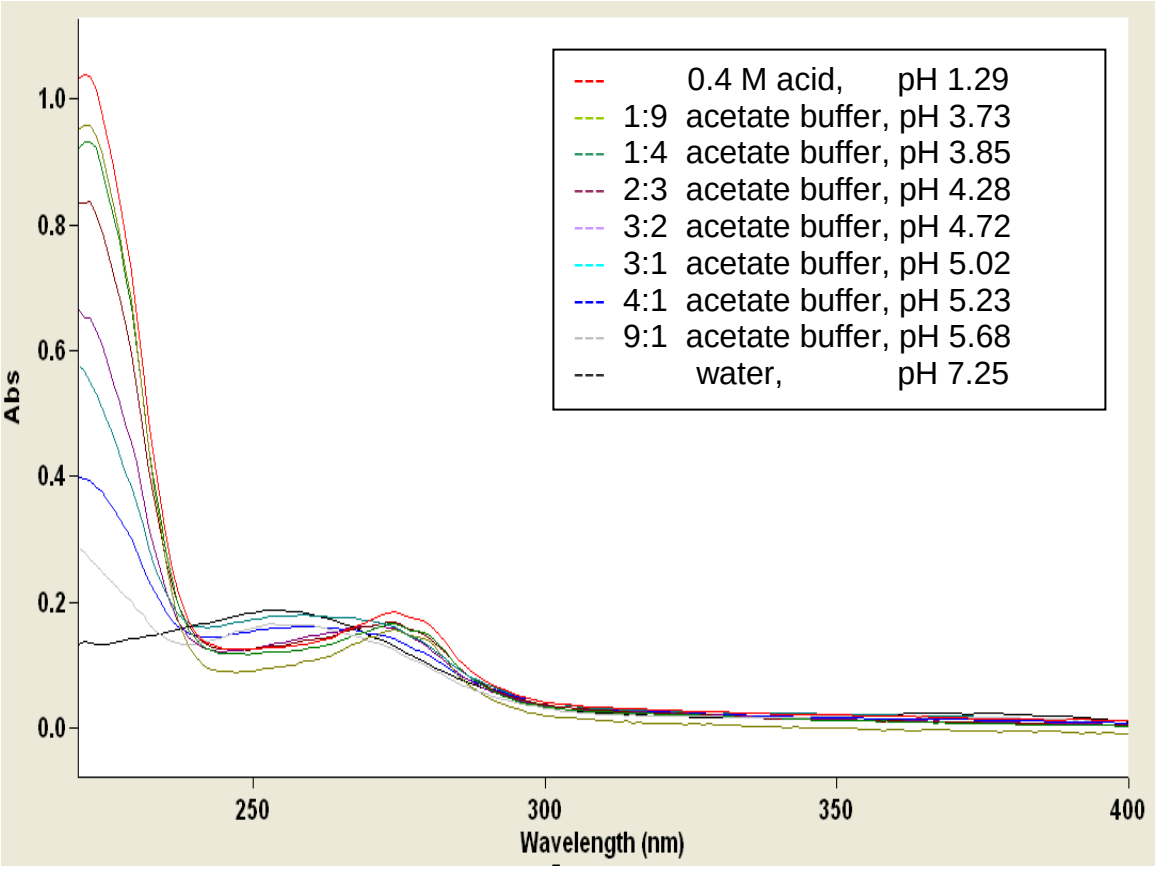


Figure 2.11 Overlay of UV-Vis spectra of tricarbonyl (η^7-cycloheptadienyl) chromium **(41)** in water, perchloric acid and a range of 0.2 M acetate buffer solutions at 25 ºC, and a substrate concentration of 1.27 x 10^{-4} M.

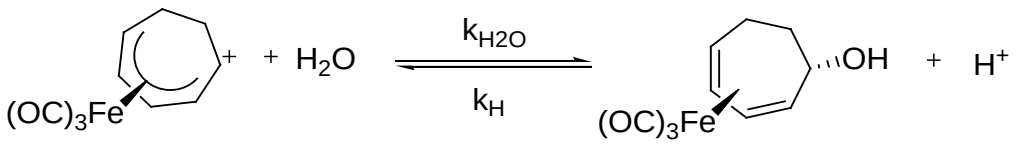
Table 2.14 Absorbance measurements for tricarbonyl (η^7-cycloheptadienyl) chromium **(41)** in perchloric acid and 0.2 M sodium acetate buffered solutions at 25 ºC.

$[H^+]$ (M)	pH	Absorbance at 223 nm	Absorbance at 251 nm
0.40	1.29	1.011	0.124
0.18	3.73	0.923	0.095
0.16	3.85	0.896	0.122
0.12	4.28	0.791	0.129
0.08	4.72	0.608	0.131
0.05	5.02	0.507	0.174
0.04	2.23	0.377	0.156
0.02	5.68	0.251	0.162
water	7.25	0.133	0.188

A spectrophotometric titration curve in which absorbance is plotted against pH is shown in Figure 3.2 (page 90).

2.2.6 pK_R for Tricarbonyl (η^5-Cycloheptatrienyl) Iron Tetrafluoroborate (62).

Studies were carried out on the ionisation and hydrolysis reactions of the tricarbonyl (η^5-cycloheptadienyl) iron cation **(62)** as shown in Scheme 2.5.



(62) **(70)**

Scheme 2.5

A solution of tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)** was prepared by dissolving it in acetonitrile to give a concentration of 6.25 x 10^{-3} M. Ten µL of substrate solution was injected into 0.10 M perchloric acid and 0.10 M sodium hydroxide. UV-Vis repetitive scans collected at regular intervals were used to follow the progress of the reaction of the iron complex in acid and in base to determine the wavelength to use for kinetic studies. The final scans were recorded and are shown in Figure 2.12.

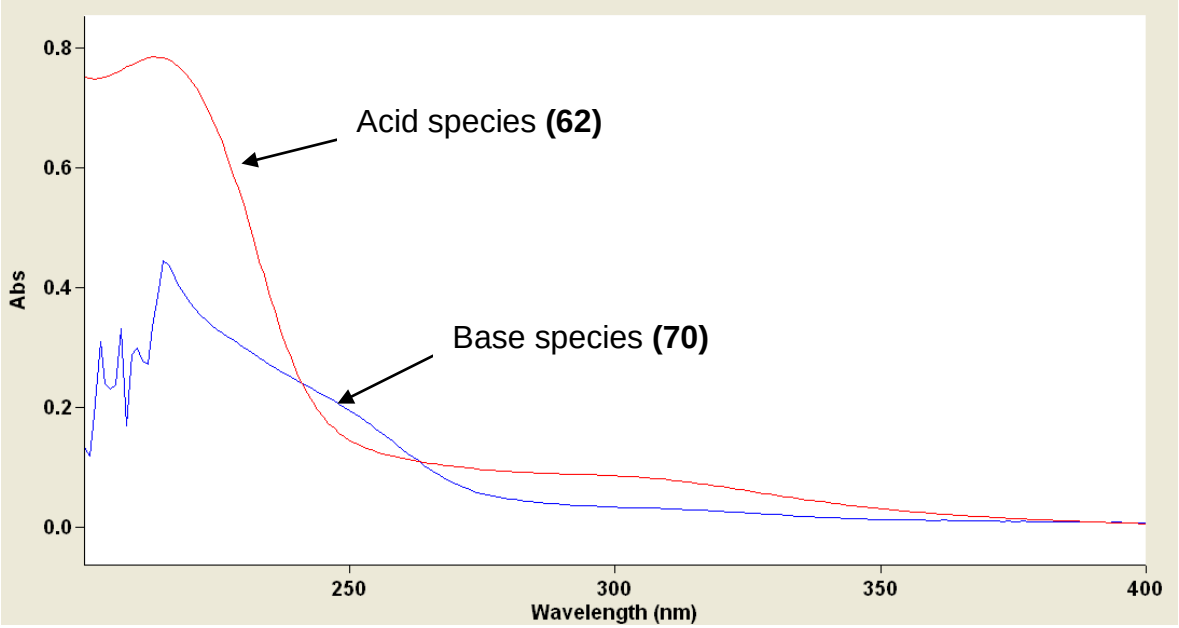


Figure 2.12 Overlay of UV-Vis final scans of tricarbonyl (η^5-cycloheptadienyl) iron **(62)** in 0.1M sodium hydroxide and 0.1 M perchloric acid at 25 ºC, and a substrate concentration of 3.12 x 10^{-5} M.

Kinetic studies for ionisation and hydrolysis of the cycloheptadienyl complex were performed by measuring the change in substrate absorbance over time at 220 nm in a range of aqueous buffer solutions. This wavelength was selected because the greatest change in absorbance between the reactant and product UV spectra occurred there. As these reactions were too fast to measure by injecting the substrate into a UV cell containing aqueous buffer and monitoring

the absorbance change, the rates were determined using a rapid mixing accessory. Kinetic data was obtained in aqueous chloroacetate, acetate and cacodylate buffers as well as perchloric acid solutions. The substrate injection syringe on the fast mixing accessory was filled with a solution of 75 µL of the cation stock (10 mg made up in 5 mL acetonitrile) in either 5 mL dilute acid to ensure the substrate remained in its cationic form in the case of measuring rates for the hydrolysis reaction in cacodylate buffers, or in 5 mL of 1 M NaCl to generate the corresponding alcohol for the ionisation reactions with chloroacetate, acetate and perchloric acid. The second syringe contained the buffer solution.

A pH profile has been constructed from this data and is presented in the Discussion (Section 3.3, pg 94).

2.2.6.1 Ionisation Reaction in Chloroacetate Buffers.

The cation **(62)** was first injected into 5 mL of 1 M NaCl solution and left to react for twenty minutes to hydrolyse to its corresponding alcohol. The observed rate constants for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in a range of aqueous chloroacetate buffers are presented in Table 2.15. A check for buffer catalysis was carried out and a plot of observed rate constants against total buffer concentration is shown in Figure 2.14 and an example of a kinetic scan observed is shown in Figure 2.13. Rates measured at the lowest buffer concentration for the two most acidic buffers (R = 0.11 and R = 0.25) were not included in the plots in Figure 2.14 as they were likely to be subject to buffer breakdown.

Table 2.15 First order rate constants for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous chloroacetate buffer solutions at 25 ºC.[i]

pH	R[ii]	10^2 [$ClCH_2CO_2^-$] /M	10^2 [$ClCH_2COOH$] /M	10^2 k_{obs} (s^{-1})[iii]
2.01	0.11	0.125	1.125	147.31 ± 5.0
2.00	0.11	0.0625	0.5625	121.36 ± 0.3
2.02	0.11	0.050	0.450	106.91 ± 3.0
1.99	0.11	0.025	0.225	79.81 ± 1.0[iv]
2.32	0.25	0.250	1.000	131.08 ± 2.0
2.34	0.25	0.125	0.500	87.56 ± 11.0
2.34	0.25	0.100	0.400	94.29 ± 4.0
2.32	0.25	0.050	0.200	61.11 ± 2.0[iv]
2.75	1.0	0.938	0.938	47.49 ± 3.0
2.78	1.0	0.625	0.625	56.03 ± 3.0
2.77	1.0	0.313	0.313	46.18 ± 3.0
2.76	1.0	0.250	0.250	48.47 ± 2.0
3.30	4.0	1.000	0.250	26.00 ± 2.0
3.32	4.0	0.500	0.125	26.29 ± 2.0
3.31	4.0	0.400	0.100	24.15 ± 1.0
3.32	4.0	0.200	0.050	15.74 ± 3.0
3.76	9.0	1.125	0.125	14.40 ± 1.0
3.77	9.0	0.5625	0.0625	12.23 ± 0.9
3.75	9.0	0.450	0.050	11.84 ± 0.3
3.77	9.0	0.225	0.025	6.40 ± 0.4

[i] All measurements were carried out at 220 nm and a substrate concentration of 4.69 x 10^{-5} M and ionic strength 0.1 M with a fast-mixing apparatus.
[ii] Ratio of [buffer base]/[buffer acid].
[iii] All rates measured are the average of three kinetic runs.
[iv] Points omitted as evidence of buffer breakdown apparent.

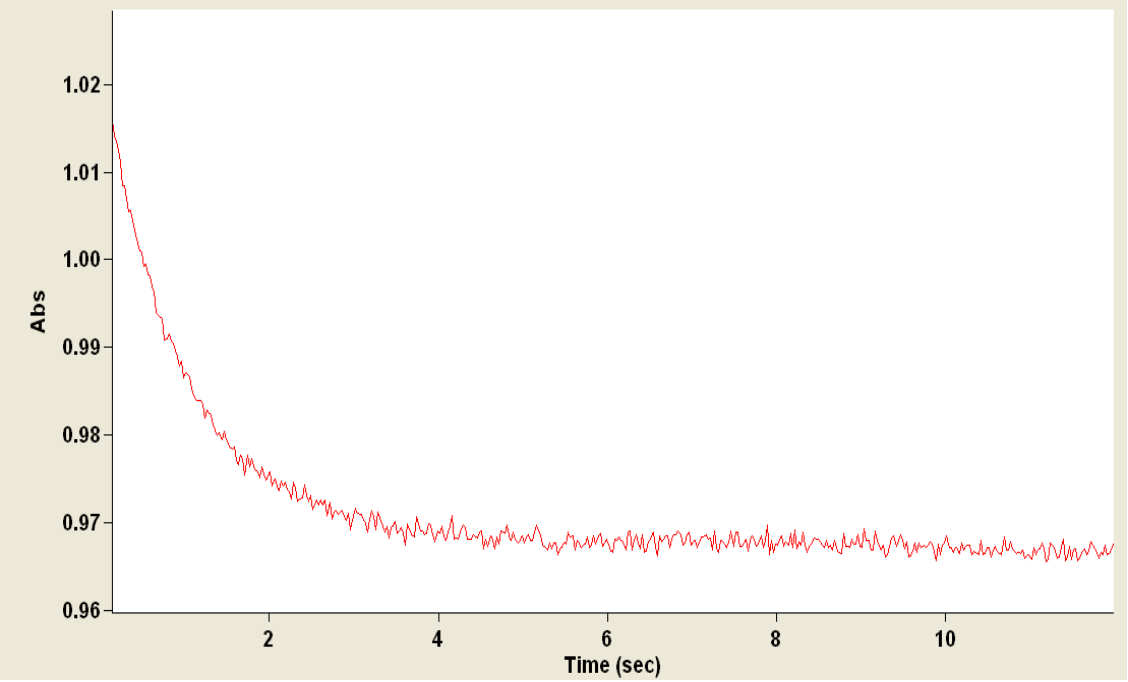


Figure 2.13 Kinetic measurement at 220 nm for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous chloroacetate at a final buffer concentration of 0.005 M and a substrate concentration of 4.69 x 10^{-5} M using a fast-mixing apparatus.

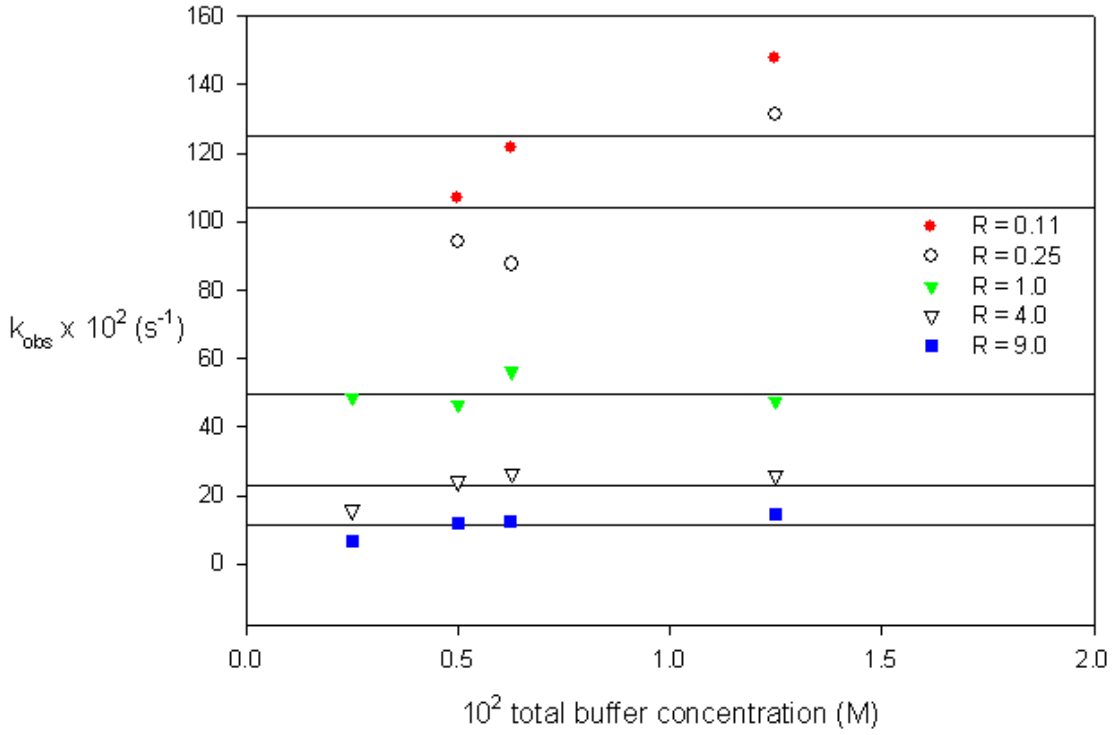


Figure 2.14 Plot of first order rate constants against total buffer concentrations at fixed buffer ratios for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous chloroacetate buffers at 25 ºC.

It can be seen from the plots in Figure 2.14 that general acid catalysis is not observed in the buffer solutions. The equation below describes the reaction and, since there is no buffer catalysis, k_{obs} is equal to the pH-independent reaction of water (k_o) which corresponds to the intercept value for each buffer ratio.

$$k_{obs} = k[CH_2ClCOOH] + k_o \qquad (2.1)$$

The values of these rate constants measured for each buffer ratio are listed below;

(R = 9.0) $k_{obs} = k_o = (11.22 \pm 3.40) \times 10^{-2}\ s^{-1}$

(R = 4.0) $k_{obs} = k_o = (23.05 \pm 4.96) \times 10^{-2}\ s^{-1}$

(R = 1.0) $k_{obs} = k_o = (49.54 \pm 4.43) \times 10^{-2}\ s^{-1}$

(R = 0.25) $k_{obs} = k_o = (104.31 \pm 23.43) \times 10^{-2}\ s^{-1}$

(R = 0.11) $k_{obs} = k_o = (125.19 \pm 20.47) \times 10^{-2}\ s^{-1}$

2.2.6.2 Ionisation Reaction in Acetate Buffers.

The cation **(62)** was first injected into 5 mL of 1 M NaCl solution and left to react for twenty minutes to hydrolyse to its corresponding alcohol. The observed rate constants measured for the ionisation of tricarbonyl cycloheptadienol iron tetrafluoroborate **(70)** in a range of aqueous acetate buffers are presented in Table 2.16. A check for buffer catalysis was carried out and a plot of observed rate constants against total buffer concentration is shown in Figure 2.16. Rates measured at the lowest buffer concentration for the two most acidic buffers (R = 0.11 and R = 0.25) were not included in the plots in Figure 2.16 as they were likely to be subject to buffer breakdown. An example of a typical kinetic scan observed is shown in Figure 2.15.

Table 2.16 First order rate constants for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous acetate buffer solutions at 25 ^{o}C.[i]

pH	R[ii]	10^2 [$CH_3CO_2^-$] /M	10^2 [CH_3COOH] /M	10^2 k_{obs} (s^{-1})[iii]
3.65	0.11	0.125	1.125	12.07 ± 0.2
3.67	0.11	0.0625	0.5625	11.31 ± 0.1
3.66	0.11	0.050	0.450	10.74 ± 0.01
3.65	0.11	0.025	0.225	9.36 ± 0.5[iv]
4.02	0.25	0.250	1.000	7.53 ± 0.1
4.00	0.25	0.125	0.500	7.29 ± 0.2
4.01	0.25	0.100	0.400	6.98 ± 0.1
4.03	0.25	0.050	0.200	6.49 ± 0.2[iv]
4.67	1.0	0.625	0.625	3.54 ± 0.3
4.66	1.0	0.3125	0.3125	3.29 ± 0.3
4.67	1.0	0.250	0.250	3.29 ± 0.5
4.65	1.0	0.125	0.125	3.25 ± 0.5
5.20	4.0	1.000	0.250	2.48 ± 0.1
5.21	4.0	0.500	0.125	2.72 ± 0.3
5.22	4.0	0.400	0.100	2.52 ± 0.3
5.20	4.0	0.200	0.050	2.56 ± 0.7
5.62	9.0	1.125	0.125	3.10 ± 1.0
5.61	9.0	0.5625	0.0625	2.89 ± 0.7
5.62	9.0	0.450	0.050	2.50 ± 0.8
5.62	9.0	0.225	0.025	2.21 ± 0.6

[i] All measurements were carried out at 220 nm and a substrate concentration of 4.69 x 10^{-5} M and ionic strength 0.1 M with a fast-mixing apparatus.
[ii] Ratio of [buffer base]/[buffer acid].
[iii] All rates measured are the average of three kinetic runs.
[iv] Points omitted as evidence of buffer breakdown apparent.

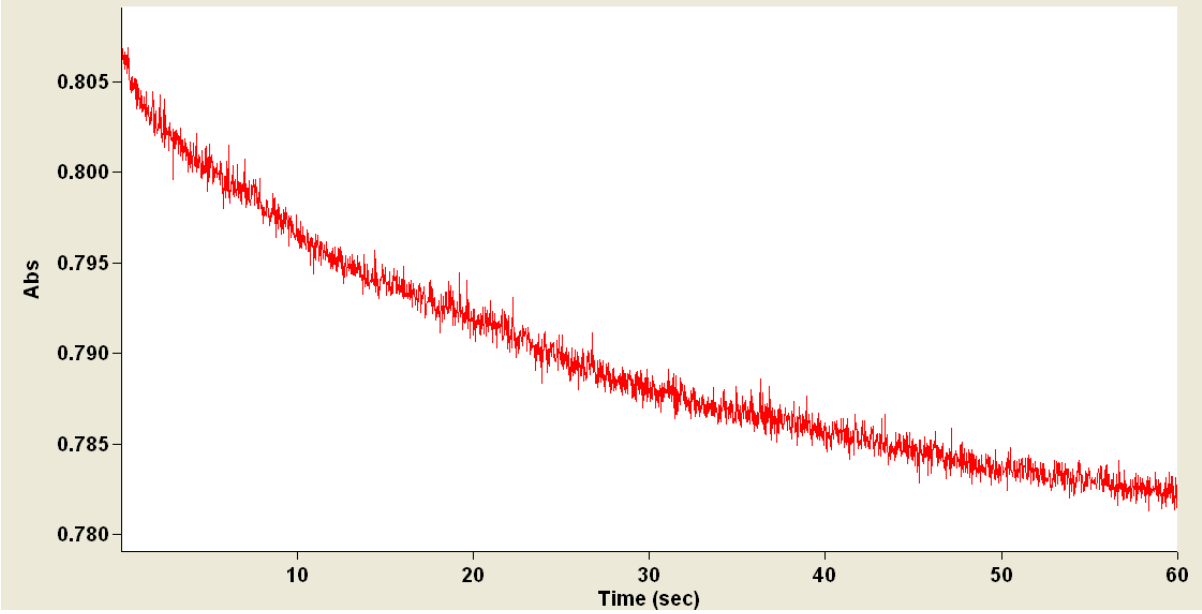


Figure 2.15 Kinetic measurement at 220 nm for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous acetate at a final buffer concentration of 0.005 M and a substrate concentration of 4.69 x 10^{-5} M using a fast-mixing apparatus.

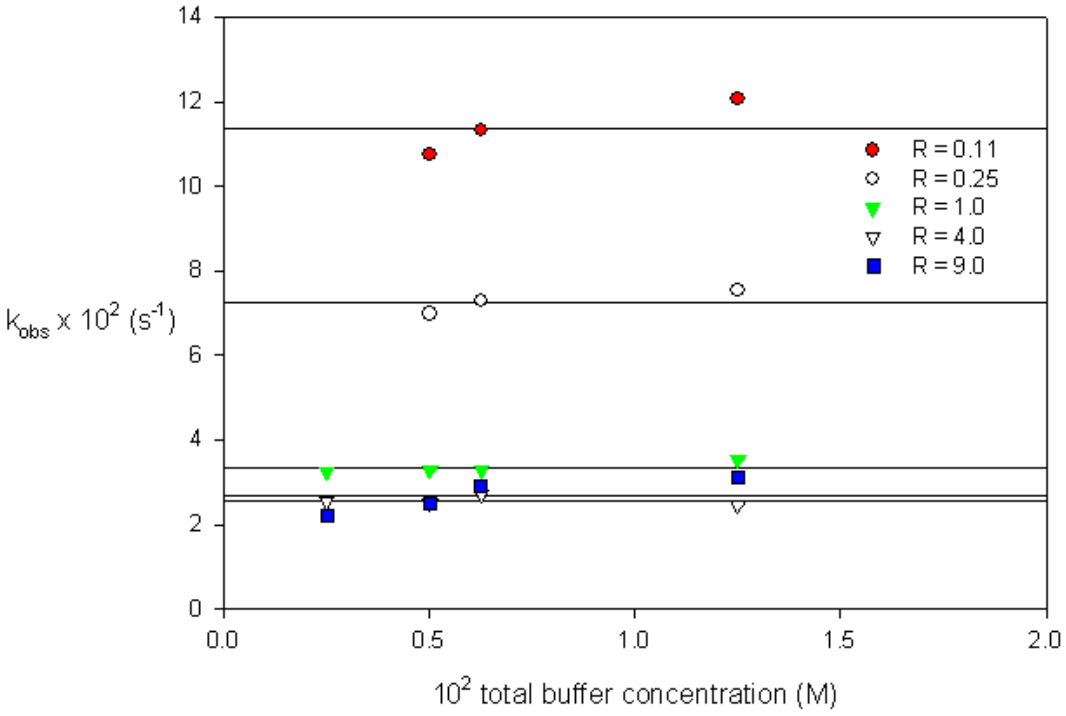


Figure 2.16 Plot of first order rate constants against total buffer concentrations at fixed buffer ratios for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous acetate buffers at 25 ºC.

The equation below describes the reaction which has a contribution from an acid catalysed reaction (k[CH_3COOH]) and the pH independent reaction of water (k_o).

$$k_{obs} = k[CH_3COOH] + k_o \qquad (2.2)$$

It can be seen from the plots in Figure 2.16 however that general acid catalysis is not observed as lines of slope zero are obtained. The intercepts of these plots represent the pH-independent rate constant, k_o, which is also the observed rate constant in this case. The values of these rate constants measured for each buffer ratio are listed below;

(R = 9.0) $k_{obs} = k_o = (2.68 \pm 0.40) \times 10^{-2}\ s^{-1}$

(R = 4.0) $k_{obs} = k_o = (2.57 \pm 0.11) \times 10^{-2}\ s^{-1}$

(R = 1.0) $k_{obs} = k_o = (3.34 \pm 0.13) \times 10^{-2}\ s^{-1}$

(R = 0.25) $k_{obs} = k_o = (7.27 \pm 0.28) \times 10^{-2}\ s^{-1}$

(R = 0.11) $k_{obs} = k_o = (11.37 \pm 0.67) \times 10^{-2}\ s^{-1}$

2.2.6.3 Ionisation Reaction in Dilute Perchloric Acid.

The cation **(62)** was first injected into 5 mL of 1 M NaCl solution and left to react for twenty minutes to hydrolyse to its corresponding alcohol. The observed rate constants measured for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in a range of dilute perchloric acid solutions are presented in Table 2.17. A plot of observed rate constants against acid concentration is shown in Figure 2.18 and an example of a typical kinetic measurement is shown in Figure 2.17.

Table 2.17 First and second order rate constants for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous perchloric acid solutions at 25 °C.[i]

10^3 [H^+] /M	pH	k_{obs} (s^{-1})[ii]	$k_{obs}/[H^+]$ ($M^{-1}s^{-1}$)	$\log(k_{obs}/[H^+])$
0.5	3.30	0.29 ± 0.02	580.0	2.76
1.5	3.82	0.85 ± 0.02	566.7	2.75
2.5	2.60	1.39 ± 0.11	556.0	2.75

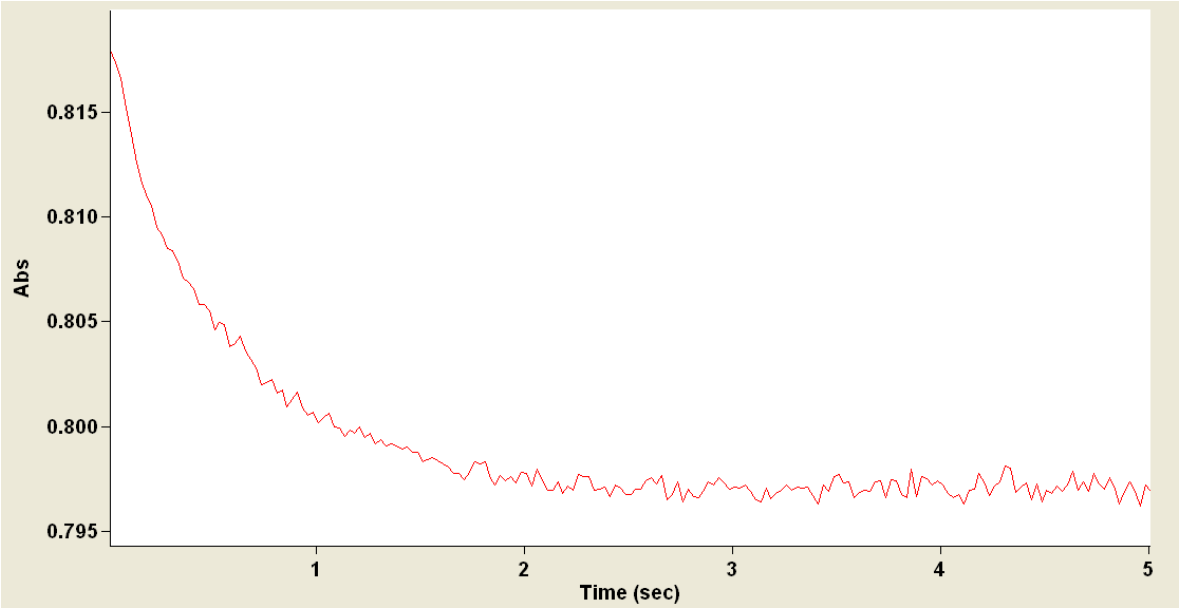


Figure 2.17 Kinetic measurements at 220 nm for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in aqueous perchloric acid at a final concentration of 0.0025 M and a substrate concentration of 4.69 x 10^{-5} M using a fast-mixing apparatus.

[i] All measurements were carried out at 220 nm and a substrate concentration of 4.69 x 10^{-5} M and ionic strength 0.1 M with a fast mixing apparatus.
[ii] All rates reported are the average of 3 kinetic runs.

The measured first order rate constants are shown plotted against acid concentration in Figure 2.18. These rate constants correspond to the sum of the rate constants for forward and reverse reactions for the hydrolysis reaction shown in Equation 2.3 and Scheme 2.5 (page 58). In principle, the two rate constants may be obtained from the slope and the intercept of the straight line plot in Figure 2.18 as summarised in Equation 2.4 based on Equation 2.3.

$$k_{obs} = k_H[H^+] + k_{H2O} \qquad (2.2)$$

$$k_{obs} = 550 \pm 5.77\ M^{-1}s^{-1}\ [H^+] + 0.0183 \pm 0.010\ s^{-1} \qquad (2.3)$$

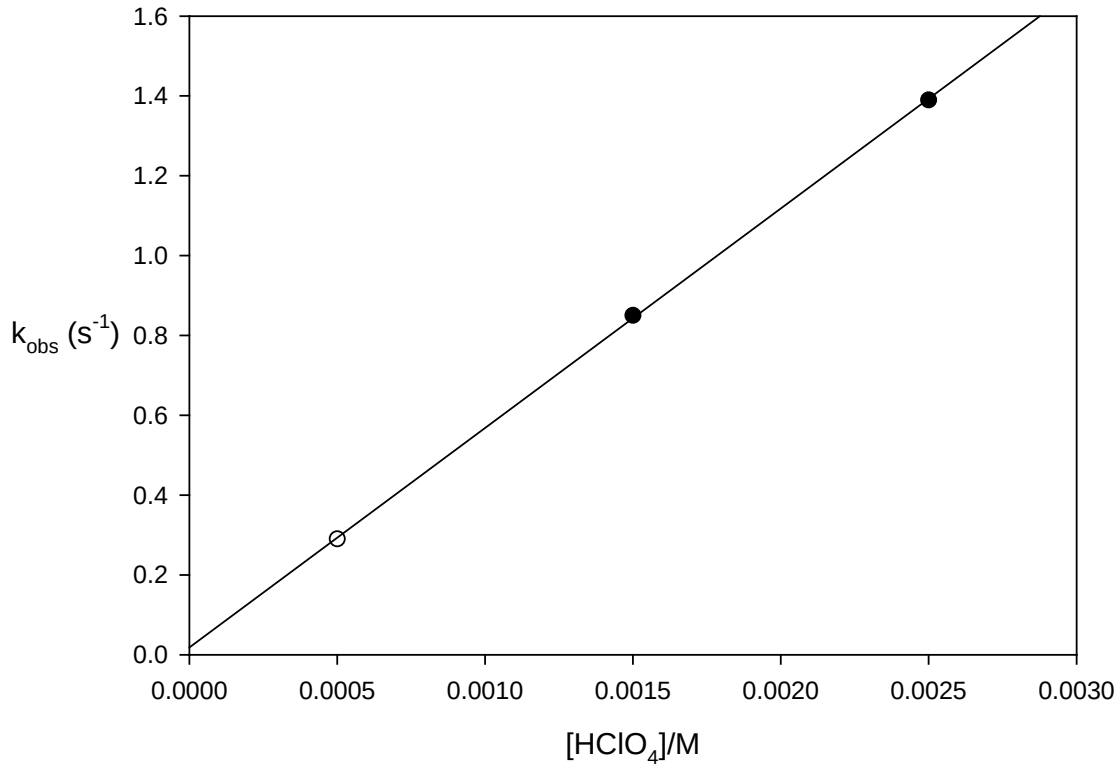


Figure 2.18 Plot of first order rate constants against acid concentrations for the ionisation of tricarbonyl cycloheptadienol iron **(70)** in perchloric acid solutions at 25 ºC.

However, in practice, the intercept from the plot in Figure 2.18 is too small to determine precisely and a more accurate value of the rate constant, k_{H2O}, was taken from the direct measurement of the reaction of the cation complex in more basic buffer solutions. This gives a value of 0.203 ± 0.54 s^{-1} based on rates measured above pH 5.0 in acetate and cacodylate buffers presented in Tables 2.16 and 2.18. Combination of this rate constant with k_H, from Equation 2.4, gives the equilibrium constant K_R as k_{H2O} / k_H. Thus, K_R = 2.03 x 10^{-2} s^{-1} / 550 M^{-1} s^{-1} = 3.69 x 10^{-5} M^{-1}. This corresponds to a value of pK_R = - logK_R = 4.4. This result is based on a k_H value determined based on only three points however and is calculated as a confirmatory check on the value of pK_R obtained from the pH profile constructed in Figure 3.3 in the Discussion.

2.2.6.4 Hydrolysis Reaction in Cacodylate Buffers.

The cation **(62)** was injected into 5 mL of 0.001 M perchloric acid to ensure that it stayed in its cationic form. The observed rate constants for the hydrolysis of tricarbonyl cycloheptadienyl iron tetrafluoroborate **(62)** in a range of aqueous cacodylate buffers is presented in Table 2.18. A check for buffer catalysis was carried out and a plot of observed rate constants against total buffer concentration is shown in Figure 2.20. An example of a typical kinetic scan measurement is shown in Figure 2.19.

Table 2.18 First order rate constants for the hydrolysis of tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)** in aqueous cacodylate buffer solutions at 25 ºC.[i]

pH	R[ii]	10^2 $[(CH_3)_2AsO_2^-]$ /M	10^2 $[(CH_3)_2AsOOH]$ /M	10^2 k_{obs} (s^{-1})[iii]
5.41	0.25	0.500	2.000	1.57 ± 0.06
5.39	0.25	0.375	1.500	1.64 ± 0.02
5.38	0.25	0.250	1.000	1.52 ± 0.1
5.38	0.25	0.125	0.500	1.68 ± 0.03
5.35	0.25	0.100	0.400	1.75 ± 0.2
5.24	0.25	0.050	0.200	1.81 ± 00.1
5.83	1.0	1.250	1.250	1.65 ± 0.3
5.84	1.0	0.9375	0.9375	1.68 ± 0.3
5.84	1.0	0.625	0.625	1.65 ± 0.1
5.85	1.0	0.3125	0.3125	1.51 ± 0.1
5.84	1.0	0.250	0.250	1.59 ± 0.06
6.73	9.0	2.250	0.250	1.68 ± 0.04
6.75	9.0	1.6875	0.1875	1.67 ± 0.04
6.71	9.0	1.125	0.125	1.59 ± 0.08
6.71	9.0	0.5625	0.0625	1.63 ± 0.04
6.73	9.0	0.450	0.050	1.57 ± 0.08
6.72	9.0	0.225	0.025	1.59 ± 0.02

[i] All measurements were carried out at 220 nm and a substrate concentration of 4.69×10^{-5} M and ionic strength 0.1 M with a fast mixing apparatus.
[ii] Ratio of [buffer base]/[buffer acid].
[iii] All rates measured are the average of four kinetic runs.

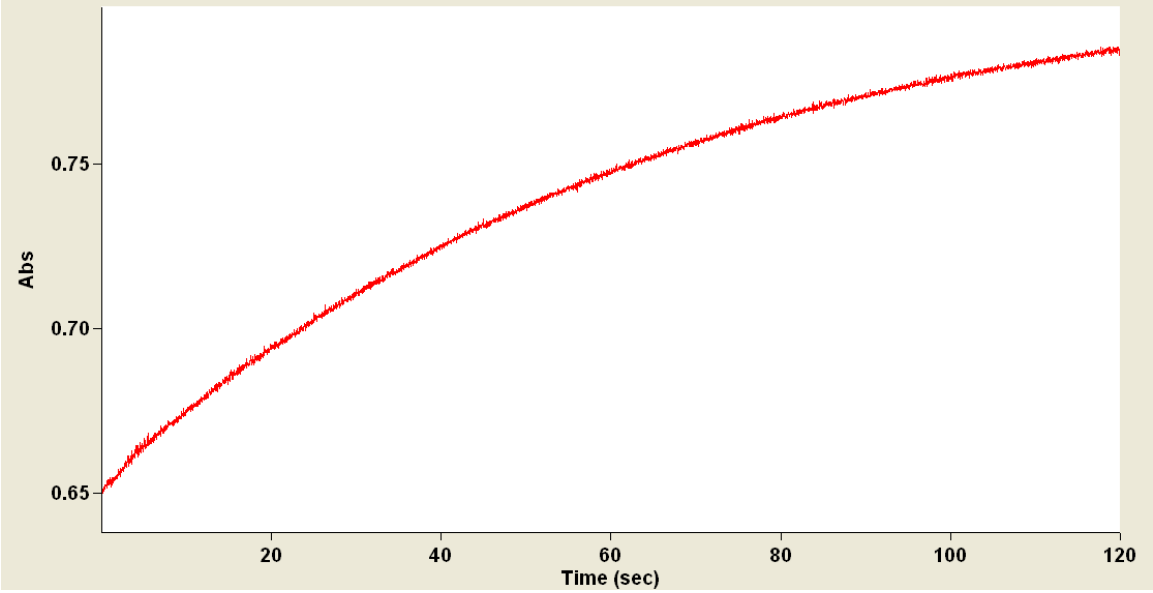


Figure 2.19 Kinetic measurement at 220 nm for the hydrolysis of tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)** in aqueous cacodylate at a final buffer concentration of 0.005 M and a substrate concentration of 4.69 x 10^{-5} M using a fast-mixing apparatus.

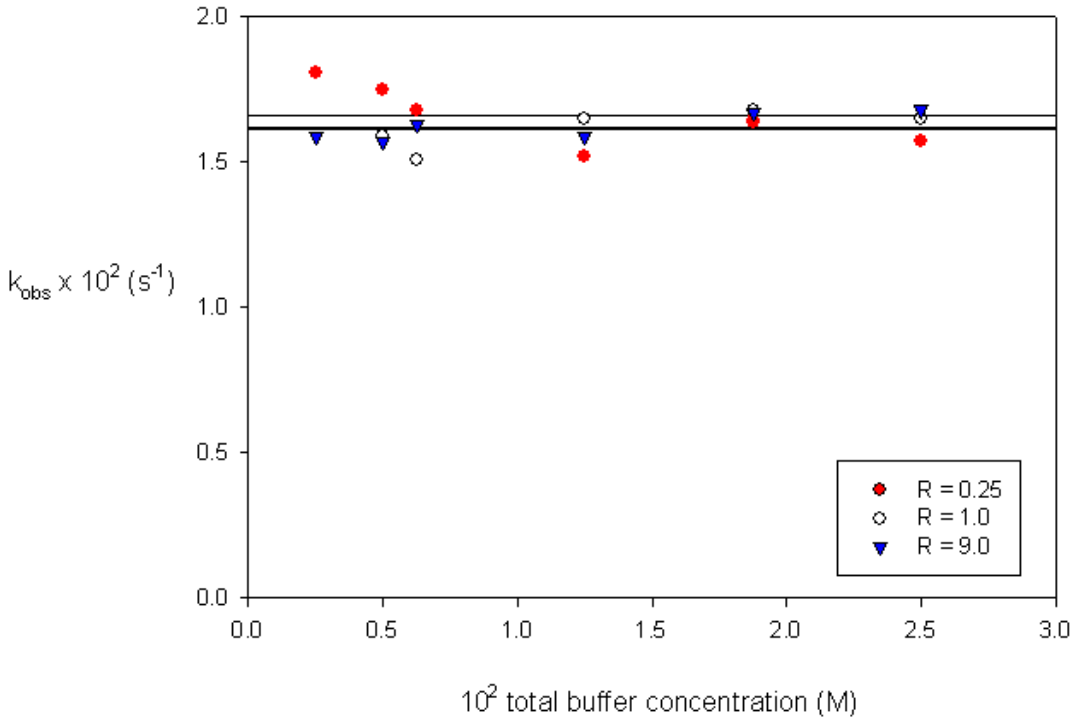


Figure 2.20 Plot of first order rate constants against total buffer concentrations at fixed buffer ratios for the hydrolysis of tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)** in aqueous cacodylate buffers at 25 ºC.

It can be seen from the plots in Figure 2.20 that general acid catalysis is not observed in the buffer solutions. The equation below describes the reaction and, since there is no buffer catalysis, k_{obs} is equal to the pH-independent reaction of water (k_o) which corresponds to the intercept value for each buffer ratio.

$$k_{obs} = k[(CH_3)_2AsO_2^-] + k_o \qquad (2.4)$$

The values of these pH-independent rate constants measured for each buffer ratio are listed below;

$$(R = 9.0)\ k_{obs} = k_o = 1.62 \pm 0.05 \times 10^{-2}\ s^{-1}$$

$$(R = 1.0)\ k_{obs} = k_o = 1.62 \pm 0.07 \times 10^{-2}\ s^{-1}$$

$$(R = 0.25)\ k_{obs} = k_o = 1.66 \pm 0.11 \times 10^{-2}\ s^{-1}$$

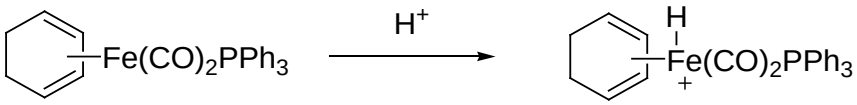
2.3 ^{1}H NMR Spectroscopic Studies.

2.3.1 Investigation of the Reaction of Dicarbonyl (η^4-Cyclohepta-1,3-diene) Triphenylphosphine Iron (60) in Acid.

A ^{1}H-NMR study was undertaken to compare dicarbonyl (η^4-cyclohepta-1,3-diene) triphenylphosphine iron **(60)** with a complex previously studied in the group, dicarbonyl (η^4-cyclohexa-1,3-diene) triphenylphosphine iron **(57)**.[60]

The original investigation involved montoring the reaction of acid with the cyclohexadiene complex **(57)** by ^{1}H NMR spectroscopy.[60] This procedure was repeated as described below to provide a comparison for the work undertaken for this project on the cycloheptadiene complex **(60)**.

Dicarbonyl (η^4-cyclohexa-1,3-diene) triphenylphoshine iron **(57)** was dissolved in deuterated methanol or acetonitrile and a ^{1}H-NMR spectrum was recorded, as shown in Figure 2.21. A drop of trifluoroacetic acid (TFA) was then added to the sample and it was mixed well. The spectrum was recorded and a new signal appeared at - 6.43 ppm as shown in Figure 2.22. This peak corresponds to a metal-hydride signal, in this instance an Fe-H signal. This shows that the initial reaction with an acid for this complex results in the formation of the complex **(71)** as shown in Scheme 2.6.



(57) **(71)**

Scheme 2.6

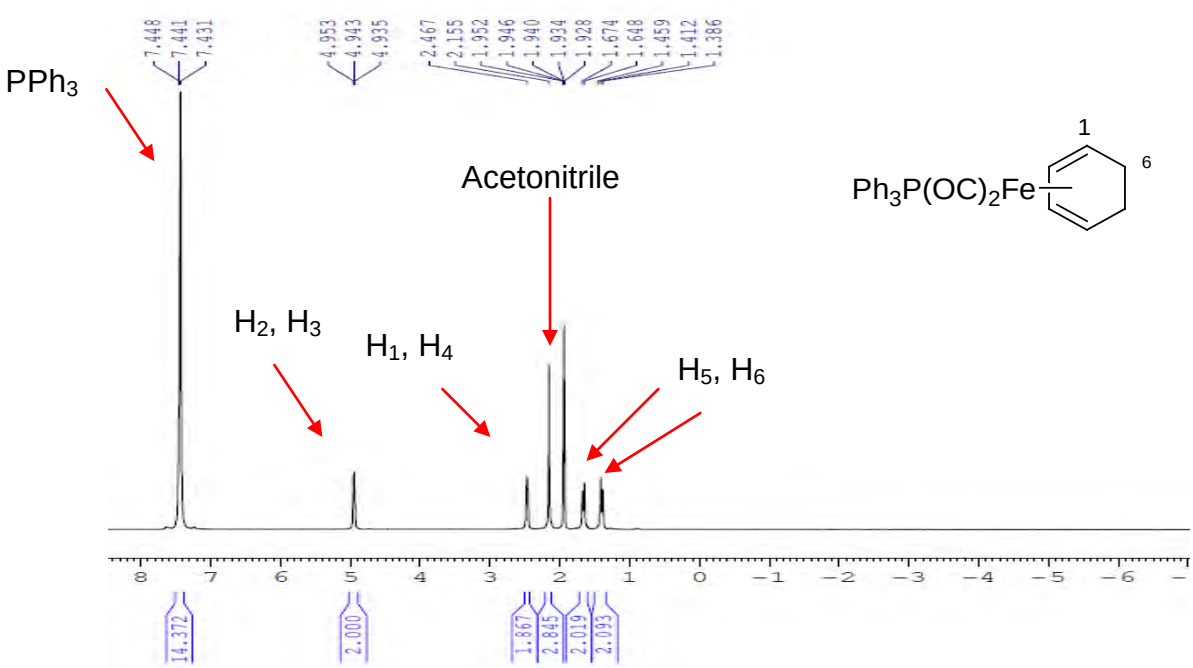


Figure 2.21 ^{1}H NMR spectrum of dicarbonyl (η^{4}-cyclohexa-1,3-diene triphenylphosphine) iron **(57)** in deuterated acetonitrile.

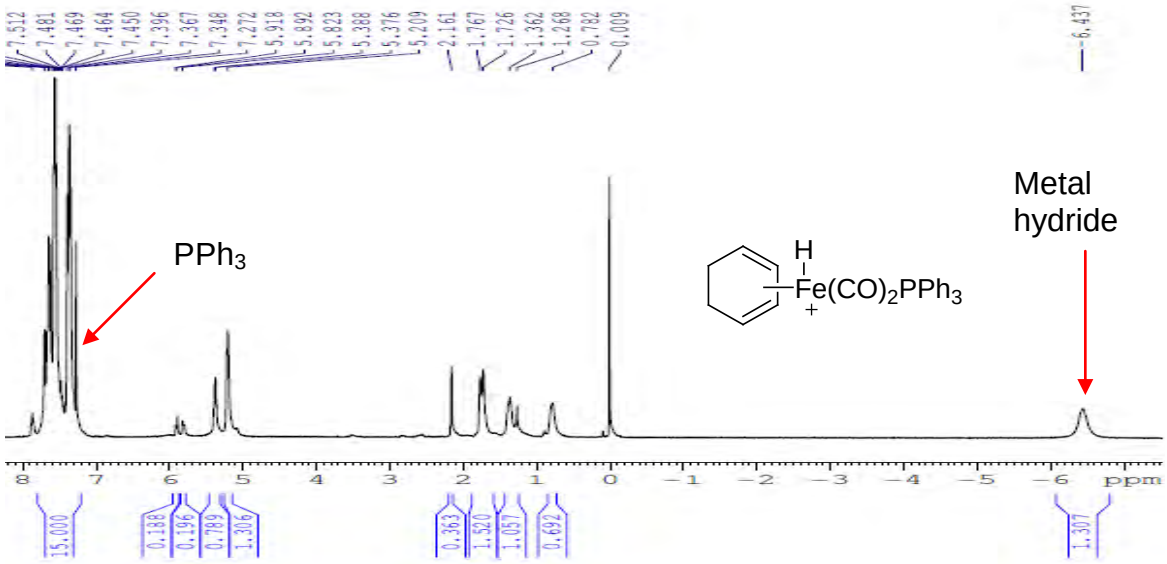
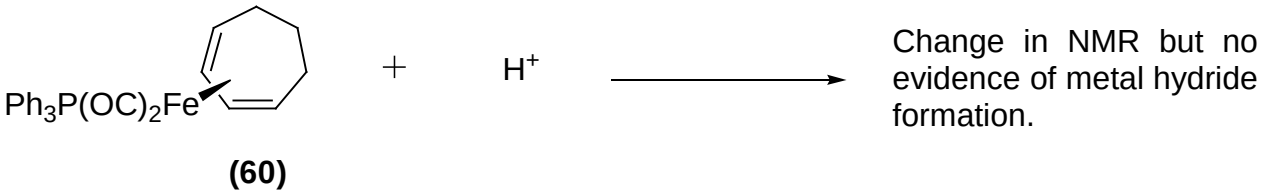


Figure 2.22 ^{1}H NMR spectrum of dicarbonyl (η^{4}-cyclohexa-1,3-diene) triphenylphosphine iron **(57)** in deuterated acetonitrile and 1 drop TFA.

This procedure was repeated with the dicarbonyl (η^4-cyclohepta-1,3-diene) triphenylphosphine iron **(60)**. However, upon repetitive additions of TFA (approximately 5 drops) to a solution of **(60)** in deuterated chloroform, although some changes occurred in the ^{1}H NMR spectrum, none were observed that corresponded to the appearance of a metal hydride signal (see Scheme 2.7) as shown in Figures 2.23 and 2.24.



(60)

Scheme 2.7

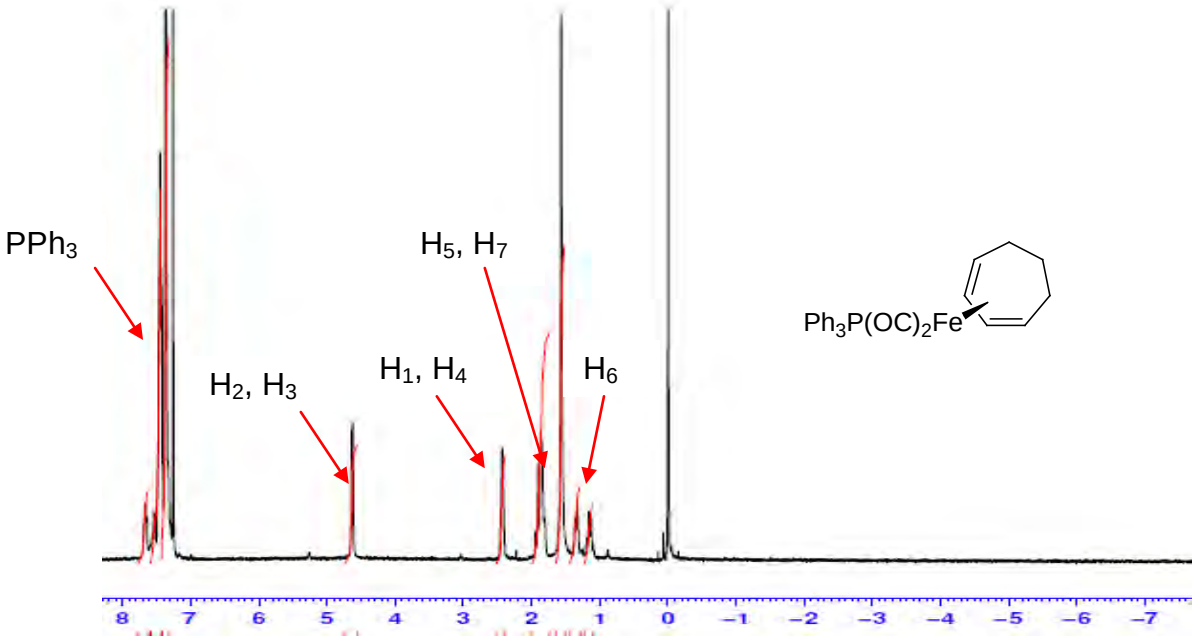


Figure 2.23 ^{1}H NMR spectrum of dicarbonyl (η^{4}-cyclohepta-1,3-diene) triphenylphosphine iron **(60)** in deuterated chloroform.

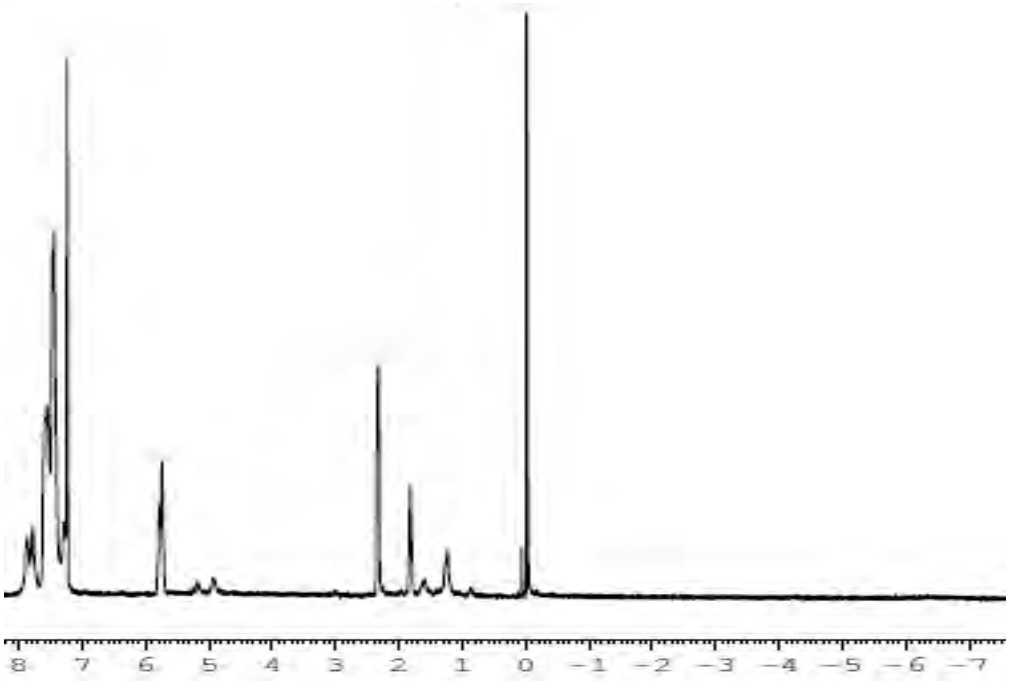
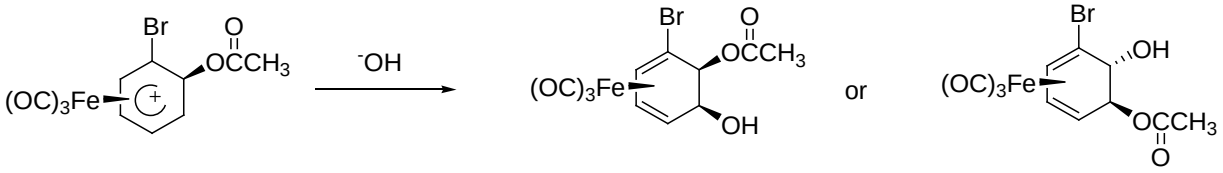


Figure 2.24 ^{1}H NMR spectrum of dicarbonyl (η^{4}-cyclohepta-1,3-diene) triphenylphosphine iron **(60)** in deuterated chloroform and 5 drops TFA.

2.3.2 Attempt to Identify the Side Product Observed in ^{1}H NMR Spectra of Monoester Derivatives of Arene *trans*-Dihydrodiol Complexes.

As mentioned in Section 2.1.3, a contaminant was observed in the ^{1}H NMR spectra of tricarbonyl (η^4-*trans*-2-acetoxy-3-bromocyclohexa-3,5-diene-1-ol) iron **(53)** and tricarbonyl (η^4-*trans*-2-acetoxy-3-trifluoromethyl-3,5-diene-1-ol) iron **(54)** at levels of up to 25 % for the bromo-substituted complex and 3 % for the trifluoromethyl complex. These side products had the same R_f value as the desired products and thus were not removed by column chromatography. It was considered likely that the contaminant was either the *cis* complex resulting from *syn* addition of hydroxide nucleophile to the cation complex [**(49)** or **(50)**] or the other regioisomer of the *trans* complex in which the positions of the acetate and hydroxyl groups were reversed. This regioisomer would form if one of the other possible regioisomers of the cation was produced in the previous step. Scheme 2.8 shows the two possible side products formed.



Scheme 2.8

In order to try to determine what this side product was, a hydrolysis reaction was carried out on the monoester derivatives of the arene *trans* dihydrodiol complexes **(53)** and **(54)** to form their corresponding diols. In this way, the ^{1}H NMR signals present due to the hydrolysed side products could be compared directly with those observed for the previously prepared arene *cis* dihydrodiol complexes **(49)** and **(50)**. Due to the availability of only a small amount of substrate to react (less than 60 mg), the resolution in the ^{1}H NMR spectra recorded of the resulting coordinated *trans* diol products, tricarbonyl (η^4-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(55)**

and tricarbonyl (η^4-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(56)**, was quite poor. A segment from the ^{1}H NMR spectrum recorded for the bromo complex after hydrolysis is shown in Figure 2.25. A comparison was attempted but analysis was only feasible for the bromo-substituted complex as the amount of the side product present for the trifluoromethyl complex was only 3 %. It was found that it was not possible to be certain whether the side product present was or was not the *cis*-diol **(49)** due to the poor resolution obtained and the occurrence of some signals for the main product in regions where *cis*-diol signals were expected and thus further investigation is necessary.

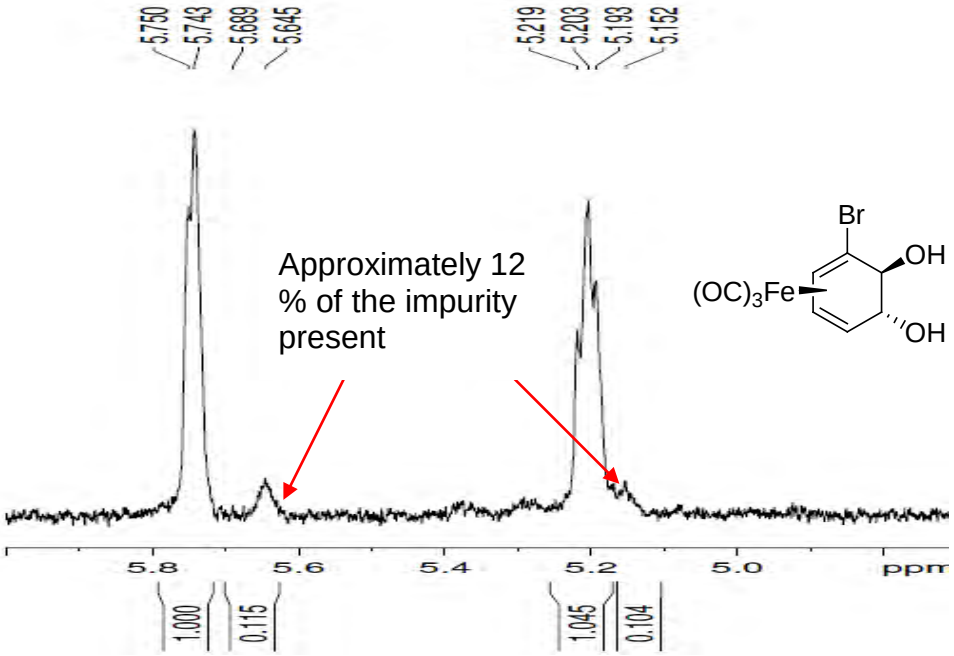


Figure 2.25 Segment of ^{1}H NMR spectrum of tricarbonyl (η^4-*trans*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(55)** formed by hydrolysis of the monoacetate derivative of the bromo-substituted arene *trans* dihydrodiol complex **(53)** in deuterated chloroform.

Chapter 3

Discussion

Chapter 3 Discussion.

The original aim of this study was to investigate a viable route for the conversion of arene *cis*-dihydrodiols to their corresponding *trans*-isomers *via* tricarbonyl iron complexes. The arene dihydrodiols used were (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol **(72)** and (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol **(73)**. The synthesis of the tricarbonyl iron-complexed *trans* analogues of these dihydrodiols was completed successfully. The trifluoromethyl-substituted complex had previously been prepared by another member of the research group[75] and has previously been reported[14] while the synthesis of the bromo-substituted complex was achieved as part of this project. A significant amount of a side product (up to 25%) was present in this bromo-substituted *trans* complex **(53)**. Further work on the optimisation of the synthesis of both of these *trans*-complexes has been carried out; however difficulties arose when it was then attempted to decomplex them. The reactivity of the intermediates tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol iron **(49)** and tricarbonyl (η^4-*cis*-3-trifluoromethyl-3,5-diene-1,2-diol iron **(50)** were examined and kinetic measurements were performed on them.

In an extension of this work, metal complexes of seven-membered diene and triene ring systems were also investigated. The compounds examined were tricarbonyl iron, dicarbonyl triphenylphosphine iron or tricarbonyl chromium complexes of cycloheptadiene, cycloheptatriene or cycloheptatrienone as well as some of their corresponding cations. As part of this study, a previously unreported complex, dicarbonyl cycloheptatrienol iron triphenylphosphine **(65)**, was synthesised and characterised. Kinetic measurements were also performed on the complexed cation, tricarbonyl cycloheptadienyl iron tetrafluoroborate **(62)**.

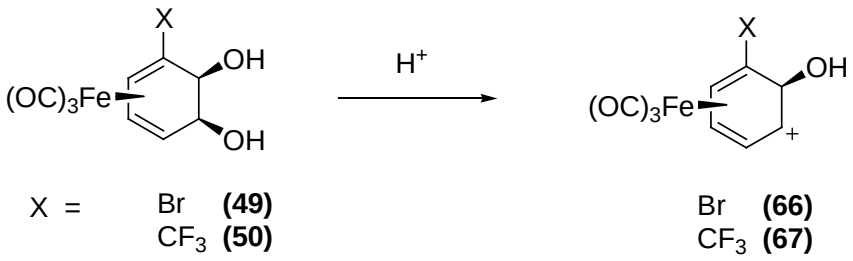
In Section 3.1 in this chapter, measurements of rate constants for cation formation from tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** will be discussed. Section 3.2 examines investigations into the reactivity of tricarbonyl η^7-cycloheptatrienyl chromium **(41)** in aqueous base. In the next section (3.3), a pH-

rate profile constructed for the hydrolysis of the tricarbonyl η^5-cycloheptadienyl iron cation **(62)** which led to the evaluation of the pK_R will be described and analysed. Kinetic and equilibrium data are then compared in Section 3.4. This is followed by a discussion (Section 3.5) on the synthesis of organic and organometallic substrates prepared in this work. Section 3.6 examines the implications of the synthesis and kinetic measurements undertaken or the *cis* to *trans* synthesis route and the final section in the chapter (3.7) summarises the main findings.

3.1 Studies on *cis*-Arene Dihydrodiol Complexes.

3.1.1 Rates of Ionisation.

The bromo and trifluoromethyl cations **(66)** and **(67)** were produced by ionisation of tricarbonyl (η^4-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** and tricarbonyl (η^4-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)** as shown in Scheme 3.1.



Scheme 3.1

The ionisation of the bromo complex **(49)** was accompanied by an absorbance change at 210 nm in the UV spectrum, which was used for kinetic measurements. Since the reaction was very slow, the measurements were carried out in concentrated perchloric acid solutions and the values for the second order rate constants were extrapolated to water using the *X*-acidity function, X_0.[56,57] Figure 3.1 shows a plot of the logarithms of second order rate constants against X_0 for

acid concentrations in the range from 4.84 to 7.26 M. Extrapolation to $X_0 = 0$ yields a rate constant in aqueous solution of ~ 8.0 x 10^{-8} M^{-1} s^{-1}. Table 3.1 on page 97 provides a comparison between this rate constant and those reported for ionisation of other related compounds.

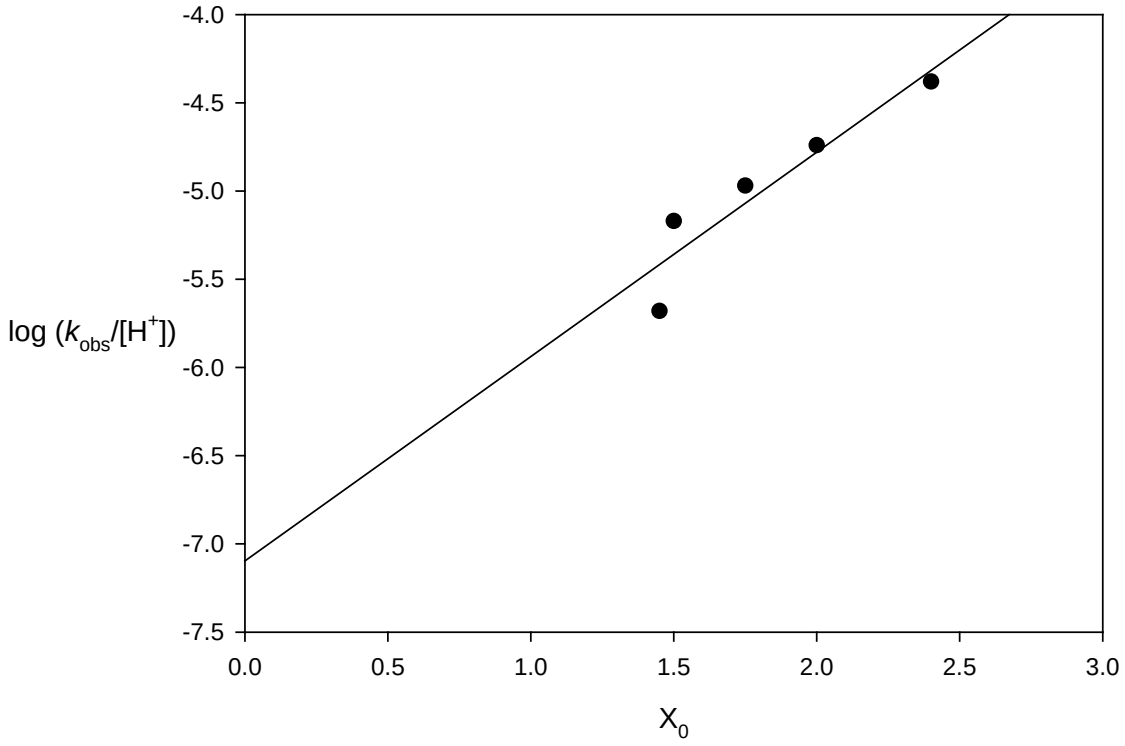


Figure 3.1 Plot of the logarithms of second order rate constants against X_0 for the ionisation of tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** in perchloric acid solutions at 25 °C.

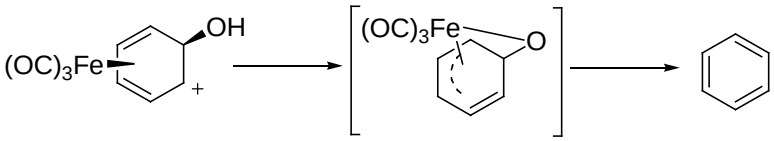
The ionisation of the trifluoromethyl complex **(50)** was accompanied by an absorbance change at 215 nm which was used for kinetic measurements. Since this reaction was also very slow, the measurements were carried out in concentrated perchloric acid solutions. It was found that at acid concentrations greater than 6.66 M the reaction was too fast to be measured, and for concentrations below 5.0 M, it was too slow. For the concentrations between these limits, inconsistent results were obtained due to a second slower reaction,

presumed to be decomposition of the cation to give trifluoromethylbenzene, interfering.

Comparison of the rates that were measured for the trifluoromethyl-substituted complex **(50)** with those measured for the bromo-substituted analogue **(49)** show that the trifluoromethyl complex reacts more quickly in strong acid by a factor of between 10 and 30 (see Section 2.2).

3.1.2 Decomposition of Intermediate Cation Complexes.

The decomposition observed for the CF_3- and Br- substituted cations which were prepared as intermediates in the *cis* to *trans* conversion route for arene dihydrodiols was investigated in more detail. These cations have an acetate group instead of a hydroxyl substituent due to the conditions employed in the synthetic step involved. The decomposition of these α-acetoxy cyclohexadienyl cations, **(51)** and **(52)**, was followed using ^{1}H NMR spectroscopy (see Section 2.3, page 80). It had been reported by Berchtold *et al.* that an α-hydroxy coordinated carbocation **(74)** in methanol or moist acetone can spontaneously form benzene.[76] The decomposition of **(74)** has been proposed to occur *via* the intermediate **(75)** as shown in Scheme 3.2.[76]



(74) **(75)**

Scheme 3.2

This decomposition was reported to occur in under an hour. In this work, when the hydroxy group was replaced by an acetoxy group, it was found that the

trifluoromethyl-substituted cation **(52)** decomposes to trifluoromethylbenzene within 24 hours, and the bromo cation **(51)** takes over a week to decompose substantially to its corresponding bromobenzene.

3.1.3 Hydrolysis of Intermediate Cation Complexes.

At lower acid concentrations, the bromo and trifluoromethyl cations are subject to hydrolysis. A kinetic study of this reaction for the bromo cation **(51)** was attempted using a fast mixing apparatus. The reaction was found to be too fast to be measured. However, an equilibrium constant, pK_R, for the hydrolysis could be estimated from the UV-Vis spectra recorded in a range of aqueous solutions as described in Section 2.2.1.2 (pg 46). The estimated pK_R value is 0.5.

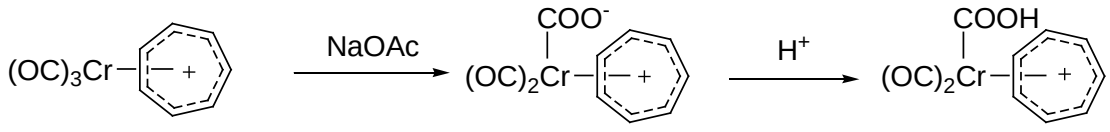
3.2 Reactivity of Tricarbonyl (η^7-Cycloheptatrienyl) Chromium.

Studies on the tricarbonyl (η^7-cyclohepatrienyl) chromium cation **(41)** were previously performed by Watts *et al.* in 1988.[77] It was reported that nucleophilic addition of water to the cation does not occur in solutions of pH < 6. Studies were also carried out in aqueous sodium hydroxide and sodium bicarbonate solutions, and it was found that the ditropyl compounds shown in Chart 3.1 were formed in concentrated base solutions (0.1 M).

Chart 3.1 Complexes formed from reaction of tricarbonyl cycloheptatrienyl chromium cation **(41)** with strong base.[77]

In this present study, the reaction of the cation **(41)** was investigated over a lower pH range and at much lower concentrations of cation at which formation of these ditropyl compounds was not observed.

A species which is postulated to be the cycloheptatrienyl-complexed zwitterion **(68)** was generated by adding 20 µL of a stock solution of tricarbonyl (η^7-cycloheptadienyl) chromium tetrafluoroborate **(41)** in acetonitrile to 1.0 mL of aqueous sodium acetate. Sufficient time was allowed for the cation to be fully converted to the zwitterion, and then the pH was reduced by adding acid leading to conversion to another species with a UV-Visible spectrum that was different to that of the original cation **(41)**. It is proposed that this new species was the cation **(69)** shown in Scheme 3.3, which would be formed as a result of protonation of the carboxylate ligand of the zwitterion **(68)**.



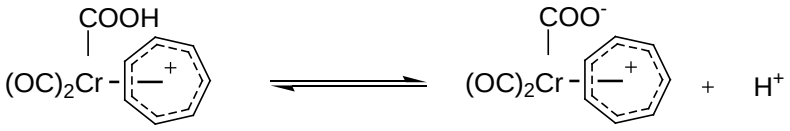
(41) **(68)** **(69)**

Scheme 3.3

Various amounts of perchloric acid were added to the equilibrated solution of the zwitterion species **(68)** in sodium acetate to generate acetic acid buffer solutions

over a pH range from 3.73 to 5.68. UV-Vis spectra were recorded for the carboxylate protonation reaction of the zwitterion **(68)**.

A titration curve was constructed for this reaction in which the absorbance at 233 nm is plotted against pH as shown in Figure 3.2. This allows the pK_a value for the protonation equilibrium (Scheme 3.4) to be estimated. A value of 4.8 was obtained.



(69) **(68)**

Scheme 3.4

The best fit line to the data points was obtained using Equation 3.1 below, which allowed the pK_a value to be estimated.

$$A_{obs} = \{K_a A_{A^-} + A_H[H^+]\} / \{K_a + [H^+]\} \qquad (3.1)$$

In this equation, A is the measured absorbance at the acid concentration indicated and A_{A^-} and A_{AH} are limiting absorbances for the neutral and cationic chromium species **(68)** and **(69)** respectively. Equation 3.1 is derived from rearrangement of the normal expression for spectrophotometric evaluation of K_a shown in Equation 3.2.

$$K_a = [A^-]\,[H^+] / [AH] \qquad (3.2)$$

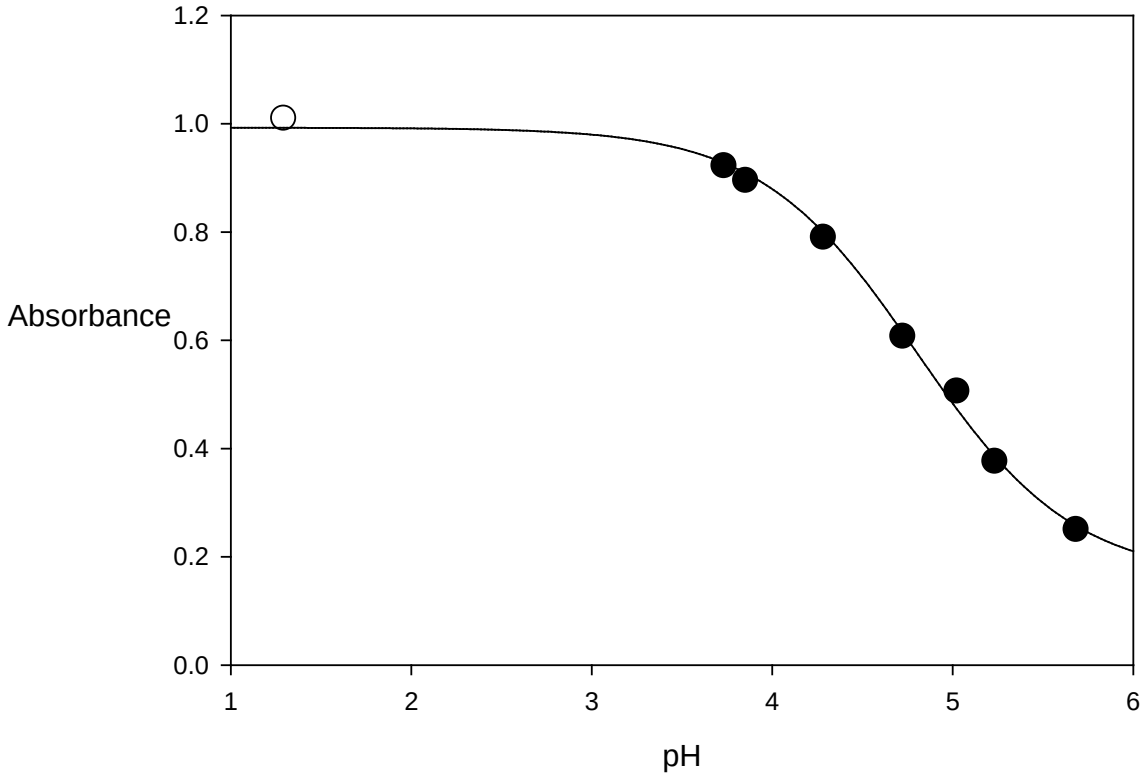
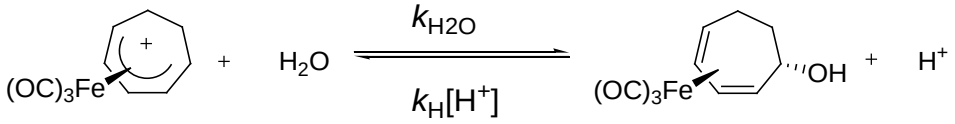


Figure 3.2 Plot of absorbance at 223 nm against pH for the reaction of tricarbonyl (η^7-cycloheptadienyl) chromium **(41)** in perchloric acid and in acetate buffer solutions at 25 ºC.

The pK_a for this species can be compared with that of a simple carboxylic acid, acetic acid, CH_3COOH. The pK_a of acetic acid is 4.76, which is very similar to the pK_a of 4.8 measured for the carboxylate ligand of the chromium complex **(69)**. This is the main evidence for supposing that the equilibrium observed represents protonation of a carboxylate anion. However, further support is provided by the observation that hydroxide addition to tricarbonyl iron groups can occur to form a carboxylate derivative as discussed in Section 3.3 and shown in Schemes 3.7 and 3.8.

3.3 Measurements of Rates and Equilibria for the Reaction of Tricarbonyl (η^5-Cycloheptadienyl) Iron Tetrafluoroborate.

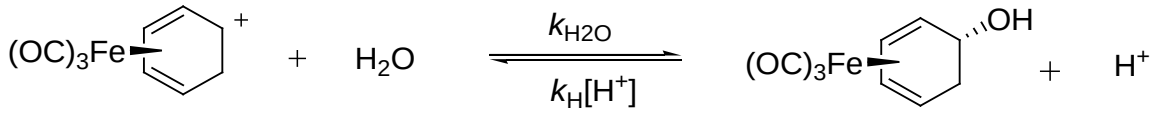
The tricarbonyl (η^5-cycloheptadienyl) iron cation **(62)** was studied to provide a comparison to a complex previously studied within this group, tricarbonyl (η^5-cyclohexadienyl) iron **(45)**.[60] The coordinated cycloheptadiene hydrate **(70)** can be generated from a solution of the corresponding cation salt **(62)** by the addition of mild base as shown in Scheme 3.5. This is analogous to the reaction of the coordinated cyclohexadienyl complex as reported by Birch *et al.*[22] where the *exo* isomer is favoured as shown in Scheme 3.6.



(62) **(70)**

pK_R = 4.2

Scheme 3.5

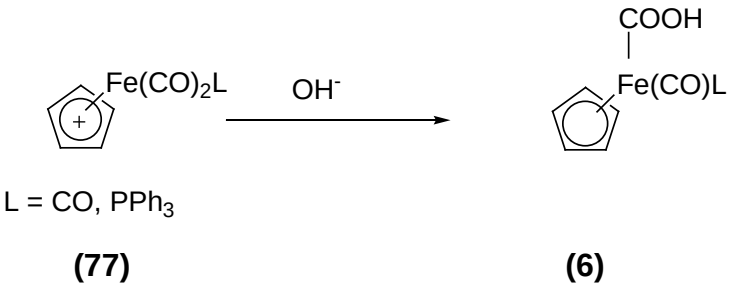


(45) **(46)**

pK_R = 4.6

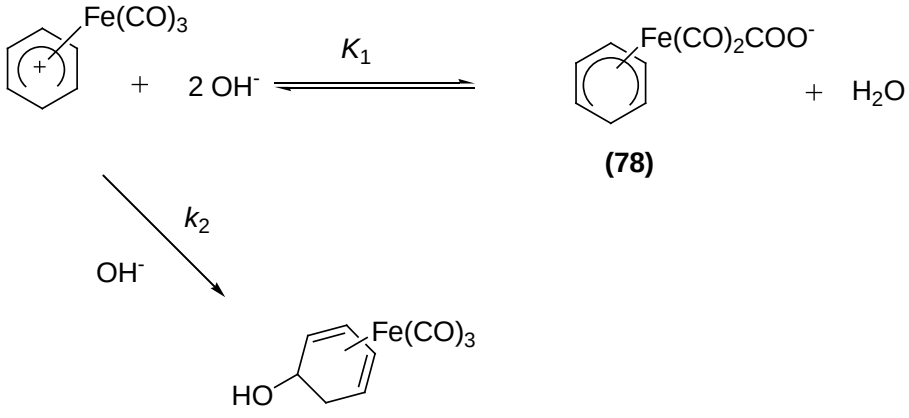
Scheme 3.6

Hydroxide attack at the carbonyl rather than the ring system of tricarbonyl iron-complexed cyclic dienyl cations has been reported previously.[78,79] In the case of cyclopentadienyl complexes, metallocarboxylic acids **(76)** were isolated by reacting carbonyl η^5-cyclopentadienyl iron complexes **(77)** with sodium hydroxide as shown in Scheme 3.7.[79]



Scheme 3.7

The mechanism of the addition of an hydroxide nucleophile to tricarbonyl η^5-cyclohexadienyl iron was examined by Atton and Kane-Maguire in 1983.[78] A conclusion was made that the carboxylate acid **(78)** species was formed in rapid equilibrium, as shown in Scheme 3.8, followed by irreversible hydroxide addition to the ring. The hydroxide catalysed rate constant, k_2, was determined to be 1 x 10^5 M^{-1} s^{-1} at 0 ºC. It was then estimated that increasing the temperature to 25 ºC increased the rate by a factor of 2.5. These observations were made at high hydroxide concentrations only.



Scheme 3.8

The rates and equilibria for the reaction of tricarbonyl (η^5-cyclohexadienyl) iron **(45)** were also previously investigated in this group, as summarized in Scheme 3.6 (page 91) and Table 3.1.[60] Measurements were carried out in aqueous buffered solutions at 25 °C and it was found that reactions in solutions below pH 8 in phosphate, cacodylate, acetate and methoxyacetate buffers were consistent with the interconversion shown in Scheme 3.6. It was found in solutions above pH 8 in borate, carbonate and amine buffers that the reaction is no longer reversible and it was proposed that this could be due to nucleophilic reactions of the buffers with the cation.[80]

The pK_R values for the tricarbonyl cyclohepta -dienyl **(62)** and -trienyl **(63)** iron cations were previously reported by Pettit *et al.* in a communication, and were measured at 30 ºC in water. However a full paper was never published and some of the values appear to be in error.[81,82]

In this work, the rate of hydrolysis of tricarbonyl (η^5-cycloheptadienyl) iron **(62)** was measured by quenching a solution of the cation tetrafluoroborate salt in dilute aqueous acid into aqueous cacodylate buffers to give a final pH range from 5.3 – 6.8. The reverse ionisation reaction was measured by quenching substrate that had been allowed to hydrolyse in aqueous solution (by leaving it in water for 30 minutes) into aqueous acetate and chloroacetate buffers, as well as aqueous perchloric acid, over a pH range from 2.0 to 5.6. The monitoring wavelength was 220 nm. Measurements at different buffer concentrations showed no buffer catalysis in the cacodylate buffers, and what was likely to be buffer breakdown in some of the less concentrated acetate and chloroacetate buffers, this is due to the capacity of the buffer reaching the limits at which it can be used.

A pH-rate profile for these reactions was prepared by plotting logs of the first order rate constants measured in perchloric acid and buffer solutions against pH as shown in Figure 3.3. The rate constants for the ionisation of the hydrolysed species **(70)** and hydrolysis of tricarbonyl (η^5-cycloheptadienyl) iron **(62)** shown in Scheme

3.5 were used to construct this pH profile and it is based on the rate constants recorded in Tables 2.15 to 2.18 (Section 2.2.6). The structure of the pH profile reflects the change from forward to reverse reaction on changing the acidity of the reaction medium. In the pH range 0 – 4.2, the measured rate constants correspond to the ionisation of the coordinated cycloheptadiene hydrate **(70)** to the coordinated cation. At pH 4.2, there is an inflection point in the pH profile and the measured rate constants represent the sum of the forward and reverse rate constants for this reaction. Above pH 4.2, the dominant rate constant is that for the hydrolysis reaction of tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)**.

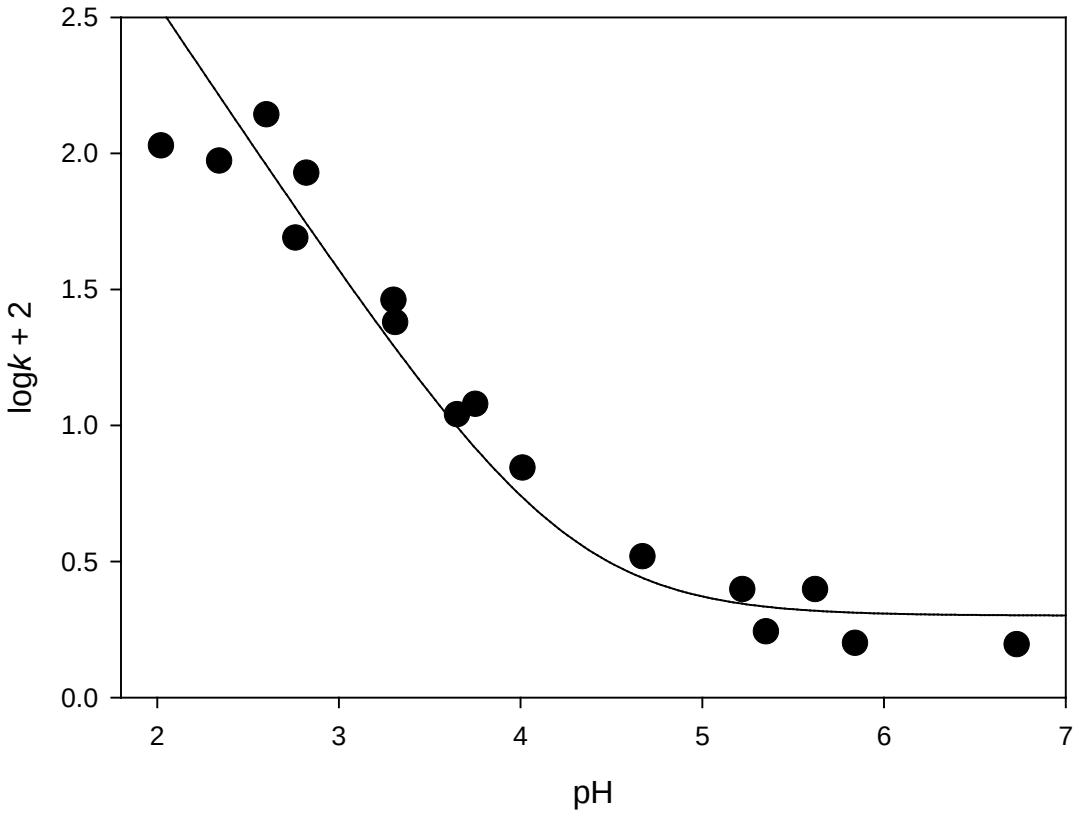


Figure 3.3 pH-rate profile (log k_{obs} *versus* pH) for the hydrolysis of tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)** to the corresponding coordinated alcohol **(70)**.

The kinetic expression for this reaction is given in Equation 3.3 and the line drawn through the points is the best fit achieved to this which uses values of k_{H2O} = 2.00 x 10^{-2} s^{-1} and k_H = 3.53 x 10^2 s^{-1}. The values of k_{H2O} and k_H can be combined to give an equilibrium constant for the process, $K_R = k_{H2O} / k_H$ = 2.00 x 10^{-2} s^{-1}/ 353 M^{-1} s^{-1} = 5.72 x 10^{-5} M^{-1}, and this corresponds to pK_R = 4.24 ± 0.25.

$$k_{obs} = k_H[H^+] + k_{H2O} \qquad (3.3)$$

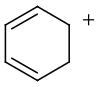
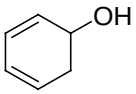
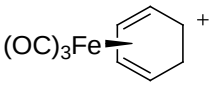
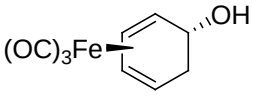
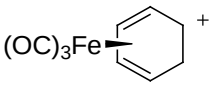
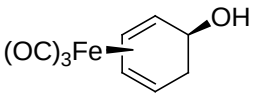
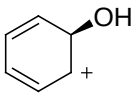
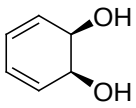
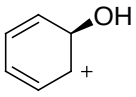
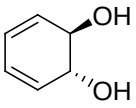
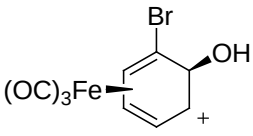
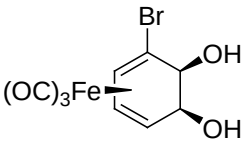
$$k_{obs} = 3.53 \times 10^2 \pm (0.55 \times 10^2)\ M^{-1}s^{-1}\ [H^+] + 2.00 \times 10^{-2} \pm (0.39 \times 10^{-2})s^{-1} \qquad (3.4)$$

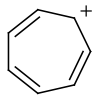
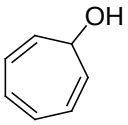
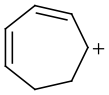
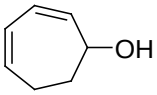
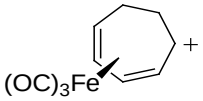
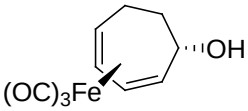
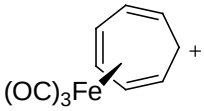
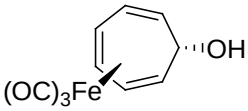
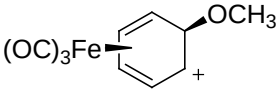
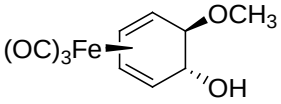
This result is in good agreement with the estimate of pK_R of 4.4 determined based on ionisation rates measured in perchloric acid and rates for hydrolysis of the cation measured in acetate and cacodylate buffers above pH 5 (see Section 2.2.6.3 in the results).

3.4 Comparisons of Kinetic and Equilibrium Data.

There have been extensive studies performed on the reactivity of complexed and non-complexed cyclic dienes and trienes. These can provide a reference data set to which the tricarbonyl (η^4-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)**, and tricarbonyl (η^5-cycloheptadienyl) iron **(62)** can be compared. These comparisons allow the effects of coordination to tricarbonyl iron and tricarbonyl chromium to be explored. Table 3.1 lists the acid-catalysed rate constant, k_H, for the formation of carbocations from their corresponding alcohols which are shown in the Table. It also shows the pH-independent rate constants for hydrolysis of these carbocations, k_{H2O}, and equilibrium constants, pK_R, for hydrolysis of the cations (where $K_R = k_{H2O}/k_H$).

Table 3.1 Rate constants and pK_R values for coordinated and uncoordinated dienes and trienes.

Cation	Corresponding Alcohol	k_H (M^{-1} s^{-1})	k_{H2O} (s^{-1})	pK_R
 **(44)**	 **(2)**	180 [a]	3.6×10^{4} [a]	-2.3 [a,d]
 **(45)**	 **(46)**	7.2×10^{3} [b]	0.18 [b]	4.6 [b]
 **(45)**	 **(48)**	2.0×10^{-3} [c]	4.0×10^{-8} [c]	4.5 [c]
 **(87)**	 **(3)**	0.11 [e]	-	-
 **(87)**	 **(4)**	5.0×10^{-6} [k]	-	-
 **(66)**	 **(49)**	8.0×10^{-8}	-	-

Cation	Corresponding Alcohol	k_H (M^{-1} s^{-1})	k_{H2O} (s^{-1})	pK_R
 **(42)**	 **(79)**	-	-	4.7[f]
 **(84)**	 **(80)**	-	-	-11.6[g]
 **(62)**	 **(70)**	353	0.02	4.2[i]
 **(63)**	 **(81)**	-	-	-5[h]
 **(86)**	 **(83)**	129.4[j]	0.205	2.8

[a] D. Lawlor *et al.*[83], [b]M. Galvin[60,80] , [c]S. Pelet[61], [d]A. McCormack *et al.*[59], [e]A.C. O'Donoghue[84] [f]Pettit *et al.*[81], [g]D. Lawlor[85], [h]Mayr *et al.* (calculated value)[70], [i] based on pH profile (see Figure 3.3), [j]C. O'Meara[75], [k]A. McCormack[86]

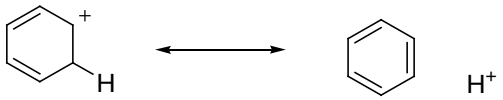
3.4.1 Equilibrium Constants.

The equilibrium constant, pK_R, for the tricarbonyl cycloheptadienyl iron cation **(62)** determined in this work was found to be 4.2. This value is obtained from the pH-rate profile constructed (see Figure 3.3). A comparison can be made to previously determined pK_R values for related compounds. The pK_R for the uncoordinated tropylium ion **(42)** is 4.7[82] and, on comparison with the tricarbonyl iron coordinated cycloheptadienyl cation **(62)**, the difference in the pK_R values, ΔpK_R = 0.5, shows that these species have similar stabilities. The tropylium cation **(42)** is subject to aromatic stabilisation whereas complexation to iron tricarbonyl stabilises the cycloheptadienyl cation **(62)**. However, the pK_R of the tricarbonyl iron complex of the cycloheptatrienyl cation **(63)** has been estimated to be -5[77] showing that it is much less stable than the cycloheptadienyl complex **(62)** (ΔpK_R = 9.2) and that the effect of the additional double bond in the seven-membered ring is to reduce the stability of the cation complex significantly. A comparison can also be made between the coordinated and uncoordinated cycloheptatrienyl cations **(63)** and **(42)** (ΔpK_R = 9.7) The relative instability of the tropylium cation when it is coordinated to iron tricarbonyl must be due to the loss of aromatic stabilisation the cation undergoes as a result of the η^5 coordination that is required by the tricarbonyl iron.

A comparison can also be made between a coordinated and uncoordinated cycloheptadienyl cation. A pK_R of -11.6 has been determined for the 1,3-cycloheptadienyl cation **(84)**, a isomer of the 1,3-cycloheptadienyl cation that is complexed to iron tricarbonyl in **(62)**. It can be seen that coordination to iron tricarbonyl is highly stabilizing giving ΔpK_R = 15.8.

There is also a stabilizing effect resulting from coordination of the cyclohexadienyl cation to iron tricarbonyl however the effect is not as marked as for the cycloheptadienyl species. The pK_R values for the coordinated cyclohexadienyl cation **(45)** and the uncoordinated cyclohexadienyl (or benzenonium) cation **(44)** are 4.6[60,80] and -2.3[59,83] respectively, giving Δp K_R = 6.9. This observation is

consistent with the uncomplexed cation **(44)** undergoing stabilisation by "aromatic" hyperconjugation in this case.[87] This occurs as a result of C-H hyperconjugation that is enhanced by a contribution from a no-bond resonance form of the cyclohexadienyl cation that is aromatic as shown in Scheme 3.9 below.



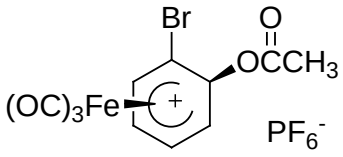
(44)

Scheme 3.9

When the coordinated cyclohexadienyl cation **(45)** is compared with the coordinated cycloheptadienyl cation **(62),** a relatively minor difference of $\Delta p\ K_R$ = 0.4 is observed.

Previous work within the group involved the study of rates and equilibria for the reactions of tricarbonyl (6-methoxycyclohexa-2,5-dien-1-yl) iron **(86)**.[75] An equilibrium constant of 2.8 was measured for this cation and, on comparison with the coordinated cyclohexadienyl cation **(45)**, the difference in stability ($\Delta p\ K_R$ = 1.8) indicates that the β-methoxy group has a destabilising effect on the cation complex. This is caused by the unfavourable effect that the electronegative oxygen has on the stability of the carbocation.

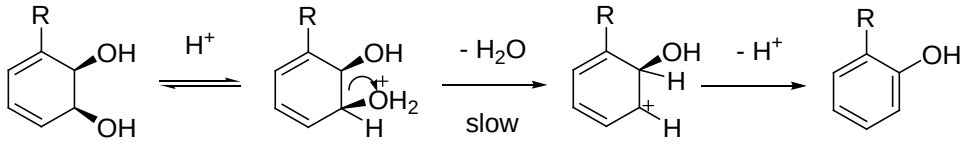
A pK_R value of 0.2 to 0.5 was estimated for tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)**. This cation is less stable than the coordinated cyclohexadienyl cation **(45)** (ΔpK_R = 4.1 to 4.4) as both the electronegative oxygen and bromo substituents destabilise the positive charge. On comparison to tricarbonyl (6-methoxycyclohexa-2,5-dien-1-yl) iron **(86)**, it can be seen that the presence of the bromo substituent destabilises the cation complex further ($\Delta p\ K_R$ = 2.3 to 2.6).



(51)

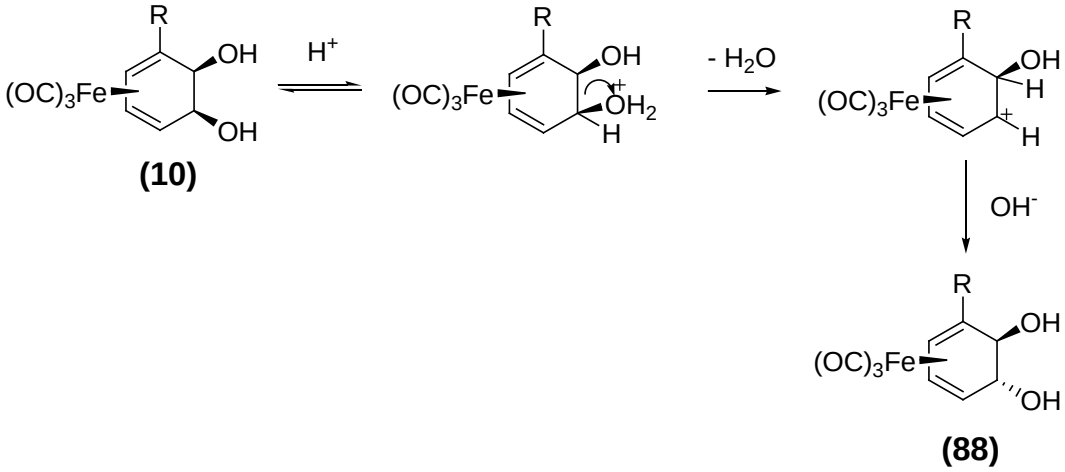
3.4.2 Comparisons of Acid Catalysed Rate Constants.

When comparing rate constants between coordinated and uncoordinated substrates, it is helpful to recognise differences in the mechanisms between their reactions. The protonation of benzene hydrate **(2)** results in the formation of the corresponding cation intermediate which deprotonates rapidly to form benzene.[88] Acid-catalysed ionisation of the *cis*-dihydrodiol **(3)** gives the corresponding cation intermediate and subsequent deprotonation gives phenol.[89] The mechanism for the dehydration reaction involves the generation of a carbocation intermediate **(87)** in the rate-determining step. This can be followed by direct formation of the aromatic product by deprotonation as shown in Scheme 3.10. Alternatively, the carbocation can undergo a hydride shift (NIH shift)[90] followed by deprotonation to form a cyclohexadienone, which tautomerises to the phenolic product. It is proposed that the deprotonation will be a fast step because the cation intermediate thus forms a phenol product that is stabilised by aromatisation.[86] In contrast, when the arene dihydrodiol is coordinated to a tricarbonyl iron moiety the corresponding tricarbonyl iron cyclohexadienyl cation that forms undergoes nucleophilic attack instead of deprotonation as shown in Scheme 3.11.[14] Despite this difference, rate constants for carbocation formation can be measured and compared for both coordinated and uncoordinated substrates.



(3) **(87)**

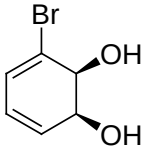
Scheme 3.10



(10) **(88)**

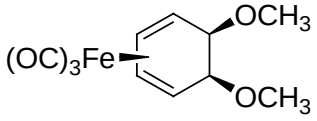
Scheme 3.11

The rate constant for the ionisation of tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** was determined to be 8.0 x 10^{-8} M^{-1} s^{-1}. This can be compared to the corresponding uncoordinated *cis*-bromodiol **(72)** for which a rate constant of 16 M^{-1} s^{-1} was reported by Boyd *et al*.[89] Thus, coordination to tricarbonyl iron results in stabilisation of the bromo-substituted *cis* arene diol to acid-catalysed ionisation by a factor of 2.0 x 10^8 M^{-1} s^{-1}. A similar trend was already discussed in the previous section in relation to the stabilisation that coordination to iron tricarbonyl confers on cyclohexadienyl and cycloheptadienyl.



(72)

It was not possible to measure k_H for the tricarbonyl iron complex of the unsubstituted *cis* benzene dihydrodiol as the complex has not been prepared in a pure form to date and is known to decompose during attempted purification by flash chromatography.[63] An alternative investigated previously in this group was the corresponding coordinated dimethoxy complex **(85)**.[75] It can be seen that this tricarbonyl *cis*-5,6-dimethoxycyclohexa-1,3-diene iron complex **(85)** showed a similar lack of reactivity in acid to the *cis*-bromo diol complex **(49)** and an ionisation rate constant of 8.0 x 10^{-6} M^{-1} s^{-1} was measured[75] which is 10^4 times slower than that for the uncomplexed *cis* benzene dihydrodiol **(3)**. Assuming that the change from methoxy to hydroxyl groups has only a small effect, the iron tricarbonyl moiety again shows a large rate-retarding effect on the acid-catalysed reaction. The dimethoxy complex is 100 times more susceptible to acid-catalysed ionisation than tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** and this is attributed to the additional destabilising effect of the bromo substituent on the carbocation complex that will form.



(85)

The effect of coordination to iron tricarbonyl on the rate of ionisation in acid of *trans*-benzene dihydrodiol **(4)** can be estimated by comparing the rate constant of 5.0 x 10^{-6} M^{-1} s^{-1} measured for **(4)** with that for tricarbonyl (*trans*-6-methoxy-cyclohexa-2,4-diene-1-ol) iron **(83)** of 129.4 M^{-1} s^{-1}. In this case, the uncoordinated species is much more stable and reacts 2 x 10^7 times more slowly than the tricarbonyl iron complex of its methoxy analogue. This observation contrasts with the effect that coordination to iron tricarbonyl iron had on the *cis* dihydrodiols as, in this case, ionisation rates were decreased significantly by complexation.

On examining the *exo* and *endo* tricarbonyl cyclohexadienol iron complexes **(46)** and **(48)**, it can be seen that there is a significant difference between the rates of ionisation of the *exo* and *endo* cyclohexadienol complexes (8.3 x 10^3 M^{-1} s^{-1} and 2 x 10^{-3} M^{-1} s^{-1} respectively) and the *exo* complex is over 10^6 fold more reactive than the *endo* isomer. Studies by Johnson *et al*.[91] on the methoxy derivatives of **(46)** and **(48)** showed by equilibrium in a methanol solution, that there is only a small difference in the thermodynamic stability of the isomers. It is assumed that a similar situation would apply to **(46)** and **(48)** and their difference in reactivity has been proposed by Galvin *et al.* to arise due to a larger kinetic barrier to reaction for the *endo* isomer **(48)**.[80] A stereoelectronic effect similar to that resulting in inversion of stereochemistry being preferred over retention in S_N2 substitution is thought to be responsible.[80]

The rate constant for formation of the tricarbonyl cycloheptadienyl iron cation **(62)** from the corresponding hydrate **(70)** was found to be 353 M^{-1} s^{-1}. This cycloheptadiene hydrate complex **(70)** is an *exo* isomer and thus shows a similar reactivity to that of the *exo* isomer of the corresponding six-membered ring complex **(46)** being slightly less reactive (24-fold difference). A comparison can also be made to *trans*-tricarbonyl 6-methoxycyclohexa-2,4-diene-1-ol iron **(83)** which also has an *exo* hydroxyl group and a comparable ionisation rate of 129.4 M^{-1} s^{-1} was found.

3.4.3 Comparisons of Rate Constants for Hydrolysis.

The rate constant, k_{H2O}, for conversion of the cyclohexadienyl cation to the hydrate **(2)** listed in Table 3.1 has been estimated from data for pK_R and k_H for the formation of this ion by Lawlor *et al*.[83] The rate constant is 2.3 × 10^4 s^{-1}, which is 10^5 times faster than for hydrolysis of the coordinated methoxycyclohexadienyl **(86)** and cyclohexadienyl **(45)** tricarbonyl iron cations and 10^6 times faster than hydrolysis of the cycloheptadienyl complex **(62)**. Surprisingly, this is much greater than the corresponding difference in rate constants, k_H, for acid-catalysed

formation of coordinated and uncoordinated cyclohexadienyl cations from the hydrolysis products **(46)** and **(2)** which is only a factor of 40. The coordination of the tricarbonyliron thus seems to affect the rate of hydrolysis more than the rate of ionisation.

On comparison of the reactivities of the cycloheptadienyl complex **(62)** and the cyclohexadienyl complex **(45)**, it is found that the seven-membered ring complex **(62)** undergoes hydrolysis 10 times more slowly than the six-membered ring analogue **(45)** and a decrease in rate on a similar scale (20-fold) occurs when it undergoes acid-catalysed ionisation.

The tricarbonyl cyclohexadienyl iron **(45)** and tricarbonyl methoxycyclohexadienyl iron **(86)** cations react at almost the same rate to form the corresponding hydrate complexes (k_{H2O} = 0.18 s^{-1} and 0.205 s^{-1} respectively). This relatively small difference confirms that the *endo* methoxy group must not a have a large impact on the reactivity of the coordinated cations.

3.4.4 Comparisons of Stereochemistry

In Section 3.4.2, the significant difference in acid-catalysed ionisation rates between the *exo* and *endo* tricarbonyl cyclohexadienol iron complexes **(46)** and **(48)** was discussed. The *exo* isomer is over 10^6 times more reactive and this effect is thought to arise from a difference in kinetic barriers. A similar trend is also observed when rate constants for acid-catalysed reactions of tricarbonyl *cis*-5,6-dimethoxycyclohexa-1,3-diene iron **(85)** (k_H = 8.0 x 10^{-6} $M^{-1}s^{-1}$) and tricarbonyl (*trans*-5-hydroxy-6-methoxycyclohexa-1,3-diene) iron **(83)** (k_H = 129.4 $M^{-1}s^{-1}$) are compared. The *endo* (or *cis*) complex **(85)** has two methoxy substituents and the *exo* (or *trans*) complex **(83)** has a methoxy and a hydroxyl substituent but, as already suggested, this is not likely to have a large effect on their relative

reactivities. Thus ionisation of the *endo* isomer is 2 x 10^7 times slower than for the *exo* isomer.

A comparable difference in kinetic barrier exists for the uncoordinated *cis* and *trans* benzenedihydrodiols **(3)** and **(4)**. In this case, again there is only a very small difference in stabilities of the diol reactants[92] yet the ratio of rates of the acid catalysed rate constants k_{cis} / k_{trans} is 2.2 x 10^4. However, in striking contrast to the metal-coordinated substrates, it is the *cis*-diol rather than the *trans*-diol which is the more reactive. Therefore the explanation for the effect of stereochemistry or reactivity must be quite different in the two cases. For the uncoordinated diols, the difference is believed to be due to more favourable hyperconjugation with the carbocation centre by an axial β-C-H than by the β-C-OH bond in the transition state for reaction of the *cis*-diol. It is clear that this cannot play any part in the reactions of the iron tricarbonyl-coordinated dimethoxy and hydroxyl-methoxy cyclohexadiene. In these cases, it seems most likely that the reverse attack of water on the coordinated carbocation occurs on the opposite side of the cation from the tricarbonyl iron coordination in a bimolecular nucleophilic substitution S_N2-like displacement. As there is little or no difference in equilibrium constants for *endo* and *exo* reactions, this difference must represent a difference in energies of the transition state which applies also to the reverse process of acid-catalysed formation of the coordinated cations. As explained in Section 3.6, this has implications for the synthetic conversion of *cis*-benzenedihydrodiols to their *trans*-isomers.

3.5 Summary of the Synthesis of Organic and Organometallic Substrates.

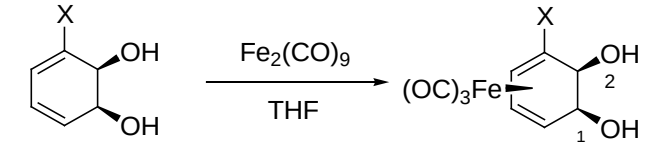
In this work, a range of organic and organometallic compounds were synthesised, purified and characterised. One branch of the synthesis involved using bromo- and trifluoromethyl- substituted *cis* benzene dihydrodiols as substrates in the development of the four-step synthetic route to convert them to their corresponding *trans* isomers. In the other, a number of seven-membered ring complexes were synthesised with the intention of using them to examine the effect on reactivity of an extra carbon in the ring system. The cycloheptadiene and cycloheptatriene complexes prepared were coordinated to either iron tricarbonyl, iron dicarbonyl triphenylphosphine or, in one instance, to chromium tricarbonyl.

3.5.1 *trans*-Arene Dihydrodiols.

The synthetic pathway to produce arene *trans*-dihydrodiols from their readily available *cis*-analogues proposed by Boyd and Sharma[12] and discussed in Section 1.1.1 (page 5) involves the synthesis of intermediates that are tricarbonyl iron complexes. Complexation to tricarbonyl blocks the top face of the complex during the formation of the *trans* isomer and thus has a stereodirecting effect[93] and there is an added benefit that tricarbonyl iron complexation stabilises the intermediates in the synthetic pathway. The *cis*-benzenedihydrodiol substrates used were obtained from the Questor Centre in Queen's University Belfast where they are produced in bulk by fermentation in a bioreactor.

3.5.1.1 Tricarbonyliron Complexes of Arene Dihydrodiols.

Tricarbonyl (η^4-*cis*-3-Bromocyclohexa-3,5-diene-1,2-diol) iron **(49)** and tricarbonyl (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(50)** were prepared using a direct complexation technique following a similar procedure to that developed by Suemune *et al.*[63] as shown in Scheme 3.12.



X = Br, CF_3

(9)

(49) = Br

(50) = CF_3

Scheme 3.12

The reactions with diironnonacarbonyl in THF were carried out using anhydrous conditions under nitrogen or argon, and the crude products were purified using flash chromatography. The products were characterised using IR and NMR spectroscopy. A COSY NMR spectrum was used to facilitate the ^{1}H NMR characterisation and a summary of the ^{1}H NMR spectral data is shown in Table 3.2.

Table 3.2 Summary of ^{1}H NMR data for tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol iron **(49)** and tricarbonyl (η^4-*cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol iron **(50)**.

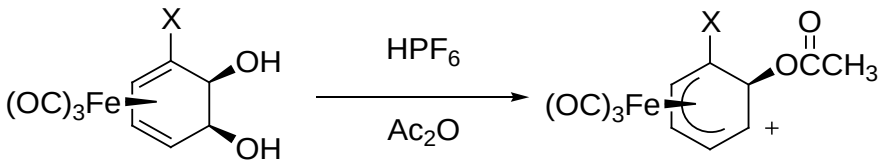
Compound	**δ_H (ppm)**						
(49)	2.95 (1H, d, OH_2)	3.10 (1H, m, H_6)	3.12 (1H, s, OH_1)	3.87 (1H, m, H_1)	3.94 (1H, dd, H_2)	5.15 (1H, ddd, H_5)	5.67 (1H, dd, H_4)
(50)[64]	2.69 (1H, s, OH)	2.87 (1H, s, OH)	3.27 (1H, m, H_6)	3.93 (2H, m, H_1, H_2)	5.25 (1H, dd, H_5)	5.65 (1H, dd, H_4)	

As a large excess of diironnonacarbonyl was used in these reactions (3 equivalents), significant amounts of iron pentacarbonyl form as a side product and this compound must be isolated from the crude product and decomposed by treatment with bromine water or bleach[17]. In addition, pyrophoric iron can form which is hazardous on workup and has to be treated with acid. A protocol prepared for carrying out this reaction safely was followed (Appendix A). Due to the amounts of the side products formed, the scale of the reaction was limited to a maximum of 5 g of diironnonacarbonyl.

3.5.1.2 Tricarbonyl Cyclohexadienyl Iron Monoester Complexes.

The next step was to form the cation species of complexes **(51)** and **(52)** using a similar procedure to that described by Pearson *et al.*[64] as shown in Scheme 3.13. The reaction was carried out by first reacting the *cis*-diol complexes with acetic anhydride in dichloromethane to give their diacetate derivatives. The corresponding cations were then formed on addition of hexafluorophosphoric acid.

These species were found to be unstable and were used directly without further purification in the next step.



(49) = Br **(51)** = Br

(50) = CF_3 **(52)** = CF_3

Scheme 3.13

^{1}H NMR data for cations **(51)** and **(52)** shows the formation of the products from the disappearance of signals at 2.95 and 3.12 ppm for compound **(51)** and 2.69 and 2.87 for compound **(52)** which represent the loss of hydroxyl groups and the appearance of a new signal at 2.25 ppm with an integration of three protons representing the acetate group as shown in Table 3.3.

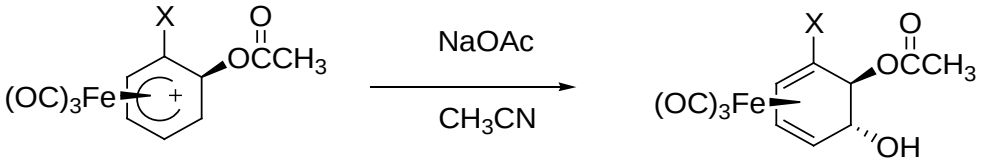
The decomposition of the cation complexes was monitored by ^{1}H NMR spectroscopy over time. It was found that for the bromo-substituted cation complex **(51)**, approximately 50% decomposition had occurred after 24 hours, and new signals in the aromatic region were observed in the spectrum. After 4 days, virtually all of this cation complex was found to have decomposed to give bromobenzene. The trifluoromethyl complex **(52)** was found to decompose more quickly to give ~ 85 % trifluoromethylbenzene in under 24 hours.

Table 3.3 Summary of ^{1}H NMR data for cation complexes, tricarbonyl (η^5-1-acetoxy-2-bromocyclohexadienyl) iron **(51)** and tricarbonyl (η^5-1-acetoxy-2-trifluoromethylcyclohexadienyl) iron **(52)**.

Compound	δ_H (ppm)					
(51)	2.25 (3H, s, CH_3)	4.33 (1H, d, H_6)	5.32 (1H, br s, H_1)	5.88 (1H, m, H_5)	6.53 (1H, d, H_3)	7.01 (1H, apt t, H_4)
(52)	2.25 (3H, s, CH_3)	4.53 (1H, d, H_6)	5.27 (1H, s, H_1)	6.01 (1H, m, H_5)	6.60 (1H, d, H_3)	7.21 (1H, t, H_4)

3.5.1.3 Formation of *trans*-Complexes.

The crude cation salt was dissolved in acetonitrile at 0 °C. A 100% crude yield for the previous reaction was assumed when calculating the equivalents of reagents for this step. An aqueous solution of sodium hydrogen carbonate was originally used as the source of nucleophile in this reaction.[75] However it was later found that the milder base sodium acetate could be used instead as shown in Scheme 3.14.



(51) = Br
(52) = CF_3

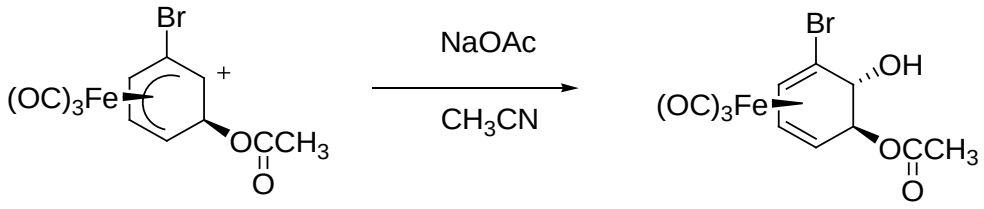
(53) = Br
(54) = CF_3

Scheme 3.14

The formation of the products can be observed in the ^{1}H NMR spectra from the presence of new signals at 4.52 and 4.45 ppm for complexes **(53)** and **(54)** respectively which represent the *trans*-hydroxyl groups as shown in Table 3.4.

Characterisation by ^{1}H NMR spectroscopy has shown that there is a side product of up to 25% present in the bromo-substituted complex **(53)** and approximately 3% in the trifluoromethyl-substituted complex **(54)**. The impurity was previously observed in the group when the trifluoromethyl complex was synthesised but was not identified.[75] It was proposed that this side product was either the *cis* product or the other regioisomer of the *trans* complex. Figure 3.4 shows an example of the ^{1}H NMR spectrum of the bromo *trans* complex **(53)** with the impurity present.

The regioisomer in which the acetate and hydroxyl group positions are exchanged would only arise if the corresponding cation regioisomer formed as a side product in the previous step as shown in Scheme 3.15. It has been reported by Stephenson *et al.* that the cation regioisomer can form as a side product during the cation formation step and that the ratio varied depending on the substituent at the 3-position.[14] They determined the ratio of the regioisomers using NMR spectra recorded at an operating frequency of 400 MHz. However, no characterisation data or details on the type of NMR spectroscopy involved were provided. The levels of the regioisomer reported were < 1 % for the trifluoromethyl-substituted complex and 22% for the chloro-substituted complex and the cation complex with a bromo substituent was not examined. The ^{1}H NMR spectra of the cation complexes **(51)** and **(52)** synthesised in this work did not show any evidence of the presence of regioisomers. Nonetheless, it is possible that the reason that these signals were not observed was because the carbocation regioisomers were interconverting rapidly on the NMR timescale resulting in a single NMR spectrum for the two species. Low temperature NMR studies are recommended to establish if this is the case although the instability of the cation complex would required that the compound be made immediately prior to the experiment.



(89) **(90)**

Scheme 3.15

The other possibility is that the impurity is the *cis* isomer of the *trans* complexes **(53)** and **(54)** and arises due to *syn* addition of the hydroxide nucleophile to the cation. However, the kinetic data presented in Table 3.1 show that it is much more difficult to convert a *cis*-dihydrodiol complex to the corresponding carbocation than to ionise its *trans* isomer and there is a difference in rates of 10^7. Using the principle of microscopic reversibility,[73] this reactivity difference will also apply to the reverse (hydroxide addition) reaction. For this reason, it is thought unlikely that the side product is the *cis* isomer of the complex; however, conclusive identification of the side product has not yet been achieved. A hydrolysis reaction was carried out on the acetate groups in *trans* complexes **(53)** and **(54)** to compare the resulting spectra directly with the original *cis* complexes **(49)** and **(50)** as described in Section 3.6.3. Due to poor resolution in the spectrum and interfering solvent and main product signals, it was not possible to confirm that the side products were not the *cis* complexes.

Table 3.4 Summary of ^{1}H NMR spectral data for tricarbonyl (η^4-*trans*-2-acetoxy-3-bromocyclohexa-4,5-diene-1-ol) iron **(53)** and tricarbonyl (η^4-*trans*-2-acetoxy-3-trifluoromethylcyclohexa-4,5-diene-1-ol) iron **(54)**.

Compound	**δ_H (ppm)**						
(53)	2.19 (3H, s, CH_3)	2.92 (1H, m, $H_{6)}$	2.97 (1H, d, H_2)	3.95 (1H, dd, H_1)	4.52 (1H, s, OH)	5.38 (1H, ddd, H_5)	5.82 (1H, dd, H_4)
(54)	2.15 (3H, s, CH_3)	3.15 (2H, m, H_2, H_6)	3.95 (1H, apt d, H_1)	4.45 (1H, s, OH)	5.49 (1H, apt t, H_5)	5.84 (1H, m, H_4)	

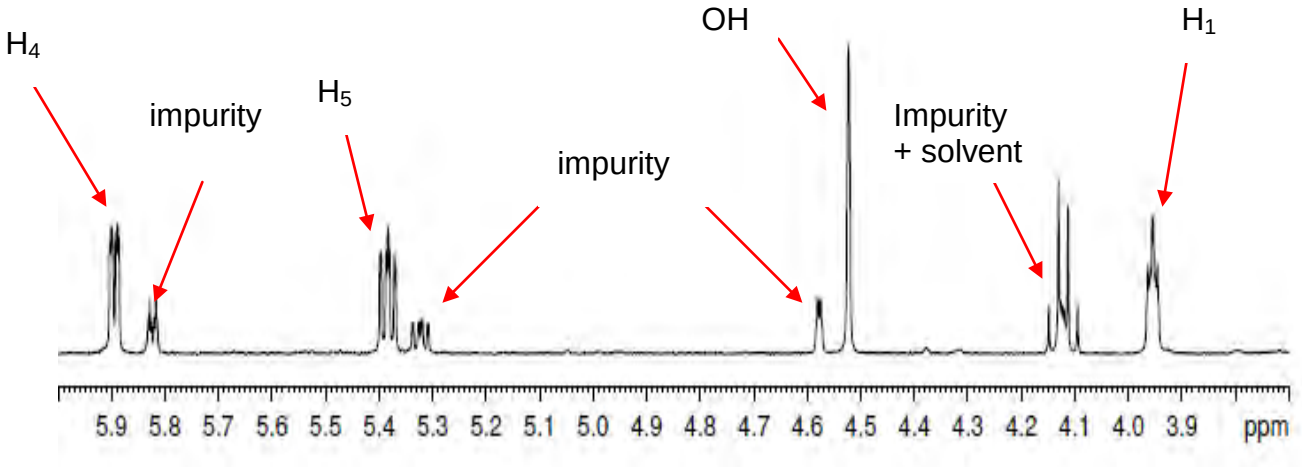


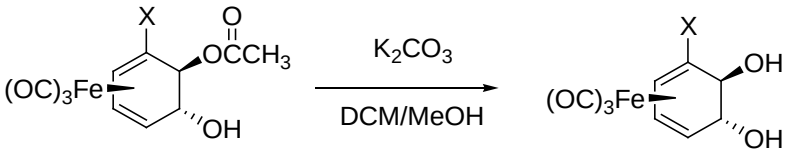
Figure 3.4 Segment of ^{1}H NMR spectrum of tricarbonyl (η^4-*trans*-2-acetoxy-3-bromocyclohexa-4,5-diene-1-ol) iron **(53)** showing impurity signals.[i]

[i] The full ^{1}H-NMR spectrum can be found in Appendix C.

It is recommended that future work to identify the side product should involve low temperature NMR studies on the cation complex **(51)** and that it might also be possible to isolate the side product from the *trans* complex **(53)** by semi-prep HPLC.

3.5.1.4 Hydrolysis of the Acetate Group on *trans*-Complexes.

This hydrolysis was carried out by dissolving complexes **(53)** and **(54)** in methanol/dichloromethane mixtures and stirring overnight in the presence of a catalytic amount of potassium carbonate as shown in Scheme 3.16.



(53) = Br **(55)** = Br

(54) = CF_3 **(56)** = CF_3

Scheme 3.16

A short filtration on a plug of silica gave the *trans* diol complexes, tricarbonyl (η^4-*trans*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(55)** and tricarbonyl (η^4-*trans*-3-trifluoro-methylcyclohexa-3,5-diene-1,2-diol) iron **(56)**. Upon examination of the ^{1}H NMR spectra, it was not possible to confirm whether the impurity (~10 %) arising was the corresponding *trans* regioisomer or the *cis* complexed diol **(49)** as reported in Section 2.3.2. Table 3.5 shows the ^{1}H NMR signals for the complexed *trans* diols **(55)** and **(56)** formed. The loss of signals at 2.19 and 2.15 ppm representing the acetate methyl groups in complexes **(53)** and **(54)** occurs, as does the appearance of new signals at 3.14 and 2.47 ppm representing the hydroxyl groups in complexes **(55)** and **(56)**. For the impurity present, the loss of the methyl signals and appearance of a second hydroxyl signal would be expected. However due to

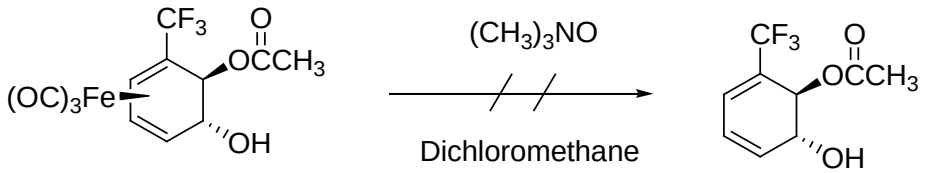
the small amount of sample available, not all of these signals could be distinguished.

Table 3.5 Summary of ^{1}H NMR data for tricarbonyl (η^4-*trans*-3-bromocyclohexa-3,5-diene-1,2-diol) iron **(55)** and tricarbonyl (η^4-*trans*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron **(56)**.

Compound	**δ_H (ppm)**						
(55)	3.14 (1H, d, OH)	3.46 (1H, apt s, H_6)	3.69 (1H, s, OH)	4.05 (1H, apt s, H_1)	4.48 (1H, apt s, H_2)	5.07 (1H, apt s, H_5)	5.61 (1H, apt s, H_4)
(56)	2.47 (1H, d, OH_2)	3.07 (1H, t, H_6)	3.49 (1H, s, OH_1)	3.81 (1H, d, H_1)	3.91 (1H, dd, H_2)	5.41 (1H, t, H_5)	5.73 (1H, d, H_4)

3.5.1.5 Decomplexation of the Tricarbonyliron Complexes.

Decomplexation was attempted on the trifluoromethyl-substituted complex **(54)** to give the corresponding *trans* analogues. This was performed using trimethylamine-*N*-oxide under anhydrous conditions as shown in Scheme 3.17. However it was found that the compound aromatised during the reaction. There are other decomplexing agents that could possibly be used including ferric chloride or ceric ammonium nitrate (CAN).[17]



(54)

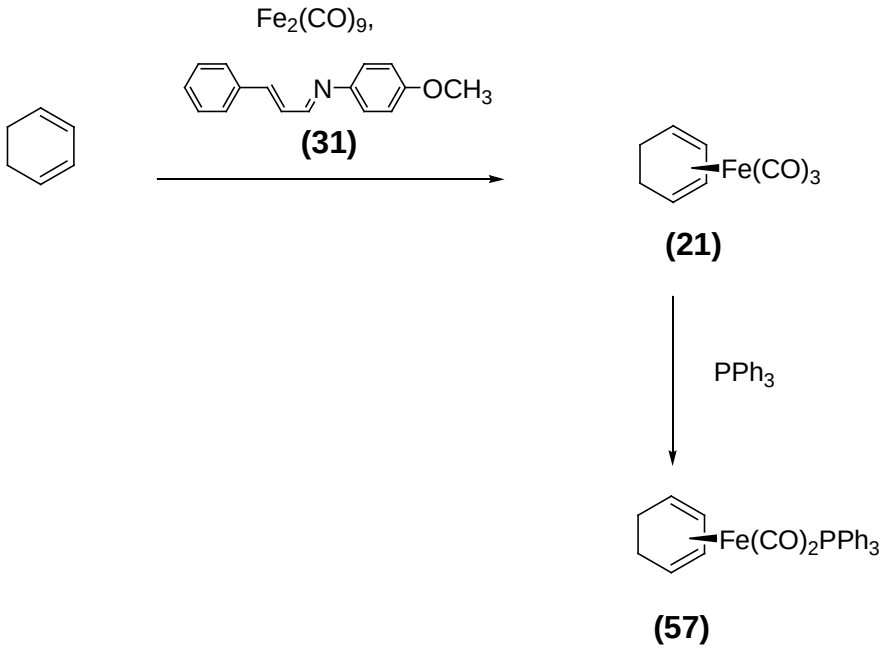
Scheme 3.17

3.5.2 Cyclohexadiene complexes.

Cyclohexadiene complexes, which had been previously studied in the group, were re-investigated. In order to complex the tricarbonyliron fragment to this substrate, an iron transfer catalyst was required.

3.5.2.1 Synthesis of Tricarbonyl (η^4-Cyclohexa-1,3-diene) Iron (21) and Dicarbonyl (η^4-Cyclohexa-1,3-diene) Triphenylphosphine Iron (57).

The iron transfer catalyst **(31)** was used to complex tricarbonyliron to cyclohexa-1,3-diene in a similar procedure to that described by Knölker *et al.* as shown in Scheme 3.18.[35]



Scheme 3.18

The diene was refluxed with the transfer reagent and diironnonacarbonyl under anhydrous conditions. The crude product was separated from the resulting iron pentacarbonyl side-product that formed, and then purified by flash chromatography to give tricarbonyl cyclohexa-1,3-diene iron **(21)**. This was then further reacted in a ligand exchange reaction by refluxing **(21)** with triphenylphosphine in cyclohexanol. Vacuum distillation at 2 mbar removed the cyclohexanol to give dicarbonyl cyclohexa-1,3-diene triphenylphosphine iron **(57)**. Table 3.6 shows the ^{1}H NMR data for compounds **(21)** and **(57)** where the effect of the triphenylphosphine fragment can be seen to move the chemical shift of the cyclohexadiene ligand protons upfield. This shift is due to an increase in electron density around the diene protons as the iron experiences greater electron density due to increased σ donor and reduced π acceptor ability of the triphenylphosphine ligand.[94]

Table 3.6 Summary of ^{1}H NMR data for complexes tricarbonyl (η^4-cyclohexa-1,3-diene) iron **(21)** and dicarbonyl (η^4-cyclohexa-1,3-diene) triphenylphosphine iron **(57)**.

Compound	δ_H (ppm)			
(21)	1.55 (4H, m, 2 x CH_2)	3.21 (2H, m, H_1, H_4)	5.29 (2H, dd, H_2, H_3)	
(57)	1.40 (4H, m, 2 x CH_2)	2.51 (2H, m, H_1, H_4)	4.84 (2H, dd, H_2, H_3)	7.36 (15H, m, PPh_3)

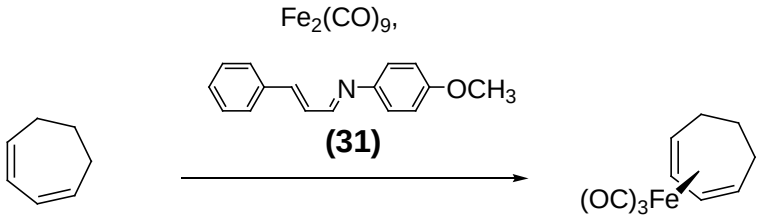
3.5.3 Iron Complexes of Seven-Membered Ring Systems.

Complexes of seven-membered ring systems were also investigated. In order to complex the tricarbonyliron fragment to these substrates, the iron transfer catalyst **(31)** was required in some cases.

3.5.3.1 Tricarbonyl Iron Complexes of Cycloheptadiene and Cycloheptatriene.

The iron transfer catalyst **(31)** was used to complex tricarbonyliron to cycloheptadiene and cycloheptatriene in a similar procedure to that described by Knölker *et al.* as shown in Scheme 3.19.[35] The diene or triene was refluxed with the transfer reagent **(31)** and diironnonacarbonyl under anhydrous conditions. The crude product was separated from the iron pentacarbonyl side-product that formed, and purified by flash chromatography to give tricarbonyl cycloheptadiene iron **(58)**

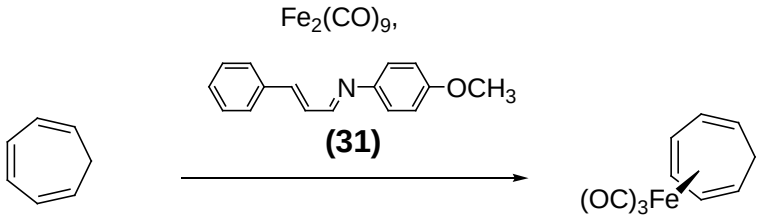
and tricarbonyl cycloheptatriene iron **(59)** in yields of 68% and 28% respectively. It was noted during the reaction with the cycloheptatriene that the complexed cycloheptadiene was also formed in small quantities as a side product, which was due to the reducing effect of the iron.[68] Due to their similar properties, the cyclohepta -diene **(58)** and -triene **(59)** complexes proved difficult to separate by chromatography.



(58)

Scheme 3.19

Cycloheptadiene is an expensive starting material (approximately €300 for 5 g) and therefore it was decided to attempt to reduce the tricarbonyl cycloheptatriene iron complex completely to the corresponding complexed diene. This was carried out using the relatively inexpensive cycloheptatriene (approximately €75 for 100 mL) which was reacted with iron pentacarbonyl and sodium borohydride in a toluene/iso-propanol mixture using a similar procedure to that described by Coqurel *et al.*[66] It was specified in the literature that the reaction needed to be kept under a positive pressure of carbon monoxide. This was achieved by fitting a balloon to the reaction apparatus which stored the CO evolved during the reaction. The sodium borohydride acted as a reducing agent to give the desired product **(58)** in a yield of 44%. While the reaction was successful, the yield was lower than when cycloheptadiene was used as a starting material.



(59)

Scheme 3.20

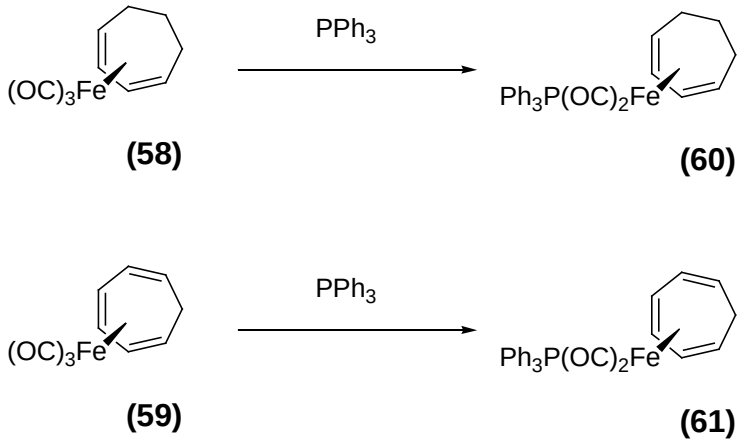
It was found that the complexed cycloheptatriene was less stable than the diene. The triene slowly decomposes at room temperature which is due to the presence of a free uncomplexed double bond.[68] The products were characterised using IR and NMR spectroscopy. Table 3.7 shows the ^{1}H NMR data for the compounds **(58)** and **(59)** where it can be seen that the *exo* and *endo* protons occur at different chemical shifts for both compounds. Apart from the additional methylene signals, the complexed cycloheptadiene has a similar spectrum to that of tricarbonyl cyclohexadiene iron **(21)**.

Table 3.7 Summary of ^{1}H NMR spectral data for complexes tricarbonyl (η^4-cycloheptadiene) iron **(58)** and tricarbonyl (η^4-cycloheptatriene iron) **(59)**.

Compound	**δ_H (ppm)**						
(58)[67]	1.15 (2H, m, H_{5exo}, H_{7exo})	1.42 (2H, m, H_{6exo}, H_{6endo})	1.92 (2H, m, H_{5endo}, H_{7endo})	2.95 (2H, m, H_1, H_4)	5.19 (2H, m, H_2, H_3)		
(59)[95]	1.65 (1H, m, H_{7exo})	2.00 (1H, m, H_{7endo})	2.63 (1H, m, H_4)	2.77 (1H, m, H_1)	4.56 (2H, m, H_2, H_3)	4.91 (1H, m, H_6)	5.55 (1H, m, H_5)

3.5.3.2 Ligand Exchange of Tricarbonyl Iron Complexes of Cycloheptadiene and Cycloheptatriene with Triphenylphosphine.

Following the successful complexation of tricarbonyl iron to cycloheptadiene and cycloheptatriene, a ligand exchange was performed on both using triphenyl-phosphine. This was done due to the effect of triphenylphosphine on the reactivity of the remaining carbonyl ligands towards nucleophiles. Substitution with a triphenylphosphine ligand decreases the likelihood of nucleophilic attack at a carbonyl ligand and thus increases the extent to which nucleophilic attack at the cycloheptadienyl or cycloheptatrienyl centre occurs. This is due to a change in the electronic environment in the complex which increases the electron density around the metal. The reaction was carried out using a similar procedure to that described by Pearson *et al.* as shown in Scheme 3.21.[67] The complexed diene or triene was refluxed with triphenylphosphine at 150 ºC to give the ligand exchange products dicarbonyl cyclohepta-1,3-diene triphenylphosphine iron **(60)** and dicarbonyl cyclohepta-1,3,5-triene triphenylphosphine iron **(61)** respectively.



Scheme 3.21

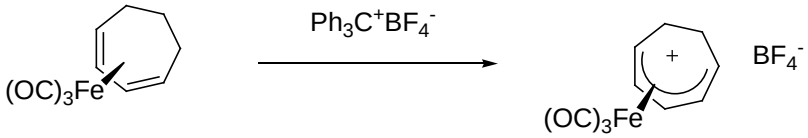
These reactions however, gave low yields with maximum yields of 8 % in the case of the diene species **(60)** and 16 % for the triene species **(61)** being obtained. Table 3.8 shows the ^{1}H NMR data for the compounds **(60)** and **(61)** showing an upfield shift for the cycloheptadiene complex similar to that of the corresponding cyclohexadiene complex **(57)**) when compared to the tricarbonyl complex **(58)**. This shift is due to an increase in electron density around the diene protons as the iron experiences greater electron density due to increased σ donor and reduced π acceptor ability of the triphenylphosphine ligand.[94]

Table 3.8 Summary of ^{1}H NMR data for complexes dicarbonyl (η^4-cycloheptadiene) triphenylphosphine iron **(60)** and dicarbonyl (η^4-cycloheptatriene) triphenylphosphine iron **(61)**.

Compound	**δ_H (ppm)**							
(60)[67]	1.10 (2H, m, 2 x H_6)	1.81 (4H, m, 2 x H_5, 2 x H_7)	2.43 (2H, br s, H_1,H_4)	4.63 (2H, m, H_2, H_3)	7.37 (15H, m, PPh_3)			
(61)[96]	2.00 (1H, m, H_{7exo})	2.27 (1H, m, H_{7endo})	2.48 (1H, br s, H_4)	2.65 (1H, br s, H_1)	4.62 (2H, m, H_2, H_3)	5.09 (1H, m, H_6)	5.79 (1H, m, H_5)	7.30 (15H, m, PPh_3)

3.5.3.3 Cycloheptadienyl Cation Complexes.

The cycloheptadiene complexes, tricarbonyl (η^4-cyclohepta-1,3-diene) iron **(58)** and dicarbonyl (η^4-cyclohepta-1,3-diene) triphenylphosphine iron **(60),** were converted to their cation analogues using procedures similar to those reported by Pearson[46] and Stephenson[69] as shown in Scheme 3.22 for the tricarbonyl iron complex. Complexes **(58)** and **(60)** were reacted with triphenylcarbenium tetrafluoroborate and underwent hydride reduction to give the cations in their salt forms, tricarbonyl (η^5-cyclohepta-1,3-dienyl) iron tetrafluoroborate **(62)** and dicarbonyl (η^5-cyclohepta-1,3-dienyl) triphenylphosphine iron tetrafluoroborate **(63)**.



(58) **(62)**

Scheme 3.22

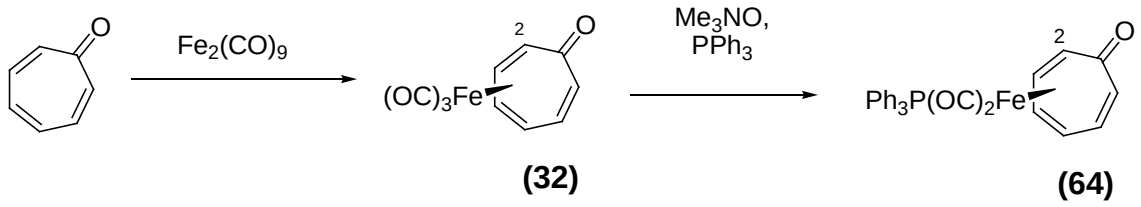
The reactivity of the cation **(62)** was then examined using UV-Vis spectroscopy and these results are discussed in Section 3.3. Table 3.9 shows the ^{1}H NMR spectral data for the compounds **(62)** and **(63)**. A triplet at around 7 ppm is indicative of the cation complexes.

Table 3.9 Summary of ^{1}H NMR data for tricarbonyl (η^5-cycloheptadienyl) iron tetrafluoroborate **(62)** and dicarbonyl (η^5-cycloheptadienyl) tri-phenylphosphine iron tetrafluoroborate **(63)**.

Compound	**δ_H (ppm)**					
(62)[46]	1.78 (2H,m, H_{6exo}, H_{7exo})	2.61 (2H, m, H_{6endo}, H_{7endo})	4.92 (2H, apt s, H_1, H_5)	5.97 (2H, m, H_2, H_4)	7.01 (1H, t, H_3)	
(63)[69]	1.76 (2H,m, H_{6exo}, H_{7exo})	2.12 (2H, m, H_{6endo}, H_{7endo})	4.18 (2H, m, H_1, H_5)	5.44 (2H, m, H_2, H_4)	6.83 (1H, t, H_3)	7.49 (15H, m, PPh_3)

3.5.3.4 Complexes of Cycloheptatrienone.

Cycloheptatrienone, commonly known as tropone, was complexed to tricarbonyl iron using diironnonacarbonyl by following a procedure similar to that described by Mayr *et al.*,[70] as shown in Scheme 3.23. It was found not to be necessary to use an tricarbonyl iron transfer reagent. To achieve a good yield for the reaction, it must be carried out in the absence of light. The resulting tricarbonyl cycloheptatrienone iron **(32)** was then reacted in a ligand exchange with triphenylphosphine to give dicarbonyl cycloheptatrienone triphenylphosphine iron **(64)** in a similar procedure to that described by Howell *et al.*[71]



(32) **(64)**

Scheme 3.23

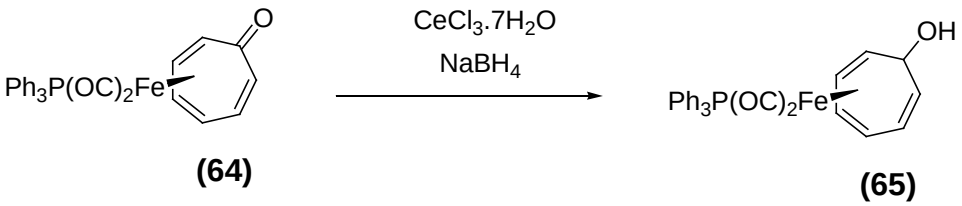
For the tropone complexes, all purification by flash chromatography was carried out using alumina rather than silica gel as recommended in the literature.[70] This is likely to be due to the compounds being sensitive to acid, as silica gel is inherently acidic in nature. Table 3.10 presents the ^{1}H NMR spectral data for complexes **(32)** and **(64)**. All protons are non-equivalent in both compounds, but H_3 and H_4 in the $Fe(CO)_3$ complex happen to have similar chemical shifts. The effect of the neighbouring carbonyl in both complexes and the triphenylphosphine ligand in **(64)** results in some upfield and downfield chemical shifts of protons when these spectra are compared to that of the cycloheptatriene complex **(59)**.

Table 3.10 Summary of ^{1}H NMR data for complexes tricarbonyl (η^4-cycloheptatrienone) iron **(32)** and dicarbonyl (η^4-cycloheptatrienone) triphenylphosphine iron **(64)**.

Compound	**δ_H (ppm)**						
(32)[70]	2.65 (1H, m, H_5)	3.09 (1H, m, H_2)	4.98 (1H, m, H_7)	6.32 (2H, m, H_3, H_4)	6.51 (1H, m, H_6)		
(64)[71]	2.13 (1H, m, H_5)	2.71 (1H, m, H_2)	4.91 (1H, m, H_3)	6.01 (1H, m, H_7)	6.50 (1H, m, H_4)	7.34 (1H, m, H_6)	7.43 (15H, m, Ph_3)

3.5.3.5 Preparation of Dicarbonyl Cycloheptatrienol Triphenylphosphine Iron.

The previously unreported compound dicarbonyl (η^4-cyclohepta-2,4,6-triene-1-ol) triphenylphosphine iron **(65)** was synthesised during this work. It was prepared using a procedure similar to that reported by Pearson, as shown in Scheme 3.24.[97] It was found that a large excess of reagents were required to achieve conversion to the product. Eleven equivalents of cerium chloride heptahydrate and 19 equivalents of sodium borohydride gave the complex **(65)** in a yield of 61 %.



(64) **(65)**

Scheme 3.24

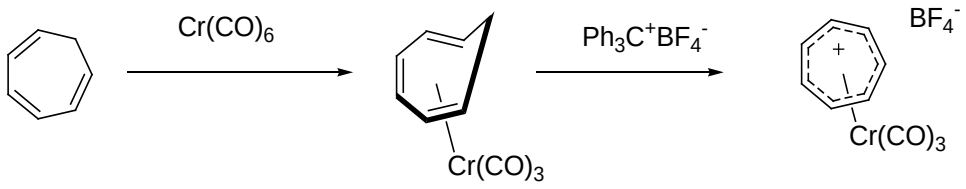
Purification was attempted by using both alumina and silica gel for flash chromatography; however in each case this resulted in decomposition of the complex. The complex was also found to slowly decompose in the presence of water, which proved problematic as a brine wash was required to remove the excess reagents. A large excess of sodium sulfate was used to absorb residual water remaining after this step. Table 3.11 shows the ^{1}H NMR data for dicarbonyl cyclohepta-2,34,6-triene-1-ol triphenylphosphine iron **(65)** with the OH signal occurring at 1.67 ppm and the proton on the adjacent carbon (H_1) appearing at 3.56 ppm, which are signals that do not occur in the starting material and therefore show the loss of the ketone functional group and presence of an alcohol.

Table 3.11 Summary of ^{1}H NMR data for dicarbonyl (η^4-cyclohepta-2,4,6-triene-1-ol) triphenylphosphine iron **(65)**.

Compound	δ_H (ppm)								
(65)	1.67 (1H, d, OH)	2.37 (1H, m, H_5)	3.02 (1H, m, H_2)	3.56 (1H, dd, H_1)	4.76 (1H, m, H_3)	4.93 (1H, m, H_4)	5.14 (1H, dt, H_7)	5.88 (1H, m, H_6)	7.46 (15H, m, Ph_3)

3.5.4 Chromium Complexes of Cycloheptatriene.

Cycloheptatriene was complexed with chromium tricarbonyl to provide a comparison to the tricarbonyl iron complex described in Section 3.5.3.3. The difference between these complexes arises due to the ability of chromium to coordinate to all 3 double bonds in the triene, while iron can only complex to 2 double bonds.[44] The tricarbonyl η^6-cycloheptatriene chromium complex **(40)** was then reacted further to form its corresponding cation, tricarbonyl η^7-cycloheptatrienyl chromium tetrafluoroborate **(41),** using similar conditions to those described by Munro and Pauson, as shown in Scheme 3.25.[98]



(40) **(41)**

Scheme 3.25

The coordination of cycloheptatriene to chromium tricarbonyl proved difficult as chromium hexacarbonyl sublimes and can precipitate during the reaction and block the condenser. A method of dealing with this was to use a large bore air condenser topped with a water condenser so the condensed solvent would wash the reagent back into the reaction.[49] However, in the early stages of the reaction, the reagent needed to be prodded back into the reaction flask using a wire before the condenser blocked completely. Another difficulty with this synthesis is the instability of the complex when in solution, as it is both light and air sensitive.[50] As a result no purification was undertaken and the product **(40)** was used directly in the next reaction to form the cation **(41)**. Once the cation is formed, the complex becomes aromatic and is therefore relatively stable.[50]

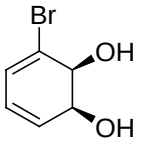
Table 3.12 shows the ^{1}H NMR data for tricarbonyl cycloheptatriene chromium **(40)** and tricarbonyl cycloheptatrienyl chromium tetrafluoroborate **(41)**. As the cation **(41)** is aromatic and therefore has seven chemically equivalent protons only one signal is observed.

Table 3.12 Summary of ^{1}H NMR data for complexes tricarbonyl (η^6-cycloheptatriene) chromium **(40)** and tricarbonyl (η^7-cycloheptatrienyl) chromium tetrafluoroborate **(41)**.

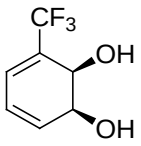
Compound	**δ_H (ppm)**				
(40)	1.75 (1H, m, H_{7endo})	2.96 (1H, m, H_{7exo})	3.39 (2H, m, H_1, H_6)	4.83 (2H, m, H_2, H_5)	6.04 (2H, m, H_3, H_4)
(41)	6.71 (7H, br s)				

3.6 Implications for *Cis* to *Trans* Conversion of Benzene Dihydrodiols.

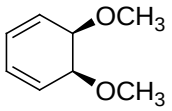
One of the main aims of this study was to investigate a metal coordination route for the conversion of *cis* arene dihydrodiol complexes to their *trans* isomers[12] and optimise the conditions. This synthetic pathway was attempted on two *cis* arene dihydrodiol substrates, 3-bromocyclohexa-3,5-diene-1,2-diol **(72)** and 3-trifluoromethyl-cyclohexa-3,5-diene-1,2-diol **(73)** as shown in Chart 3.2. Previous work in the group involved probing the application of the proposed route to the *cis*-dimethoxy analogue **(82)** also shown in Chart 3.2.[75] The reactivity of the intermediates in the pathway was also studied by measuring their rates of reaction which allowed implications for the synthetic route to be considered. This section summarises the relevant kinetic measurements undertaken as well as conclusions that can be drawn in relation to the conditions for each step of the *cis* to *trans* conversion route.



(72)



(73)



(82)

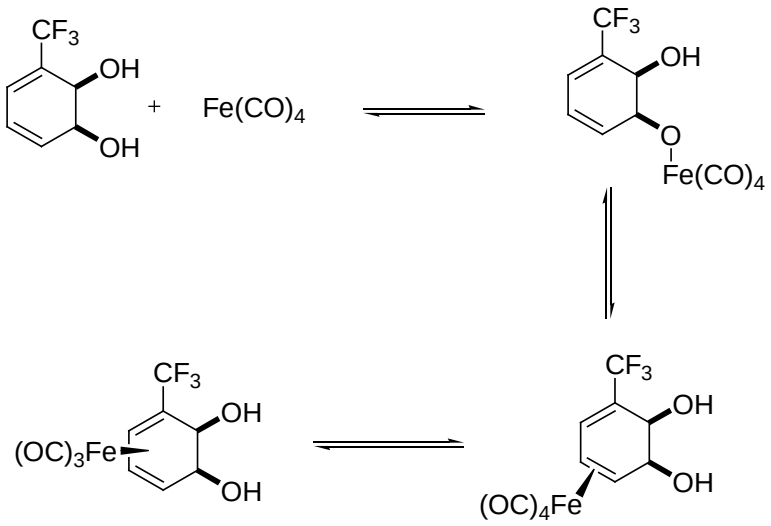
Chart 3.2

3.6.1 Coordination Step.

As discussed in Section 2.1.1, page 30, the *cis* arene dihydrodiols **(72)** and **(73)** were complexed with diironnonacarbonyl to form their corresponding tricarbonyl iron complexes. Based on equilibrium studies carried out by Johnson *et al.*[91] on the *exo* and *endo* isomers of methoxy cyclohexadienyl complexes, the conclusion is that there is little difference in stability between the *exo* and the *endo*

complexes.[75] It seems clear therefore that the *endo* complex does not experience any strong stabilisation for the interaction between the iron atom and the hydroxy groups as has been proposed in the literature.[91] It was also confirmed that the reaction of the *cis*-diols with diironnonacarbonyl yields an *endo* complex in preference to the *exo* complex.

A mechanism for the reaction of diironnonacarbonyl with a cyclic diene was proposed by Pearson.[64] The mechanism involved the hydroxyl substituents acting as a stereodirectors in the reaction as shown in Scheme 3.26. In this instance, a $Fe(CO)_4$ complex, which is generated by the cleavage of $Fe_2(CO)_9$, adds to a hydroxyl group initially, and is then transferred to the olefin group on the diene. Finally loss of CO yields the $Fe(CO)_3$-coordinated species.



Scheme 3.26

3.6.2 Cation Formation Step.

In the kinetic studies carried out on the ionisation of the bromo-substituted complex **(49)** (see Section 3.1), it was necessary to use a strong acid to initiate the ionisation reaction, which would suggest that formation of the cation would prove to

be a difficult step in the synthetic route to a *trans* product. Synthetic conditions reported in the literature require the use of hexafluorophosphoric acid (HPF_6) in acetic anhydride for the ionisation to occur.[14,64] The complexes were found to be difficult to protonate but once the cations were formed they were stable enough to allow nucleophilic addition to occur. However, the cations did decompose over time and an investigation showed that they underwent conversion to their uncoordinated aromatic analogues in a matter of days (see Section 3.1.2).

3.6.3 Nucleophilic Attack Step.

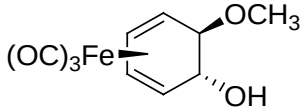
The next step in the pathway was nucleophilic attack of hydroxide ion on the complexed cation. Kinetic measurements were attempted, but the reaction was too fast to be monitored even when employing a rapid mixing apparatus. Measurements performed previously in the group on the tricarbonyl methoxycyclohexadienyl iron cation **(86)** show that the rate constant, k_{H2O}, for the reaction of the cation with a nucleophile was 0.205 M^{-1} s^{-1} which is much faster than for cation formation from the *cis*-dimethoxy complex **(85)** for which k_H was 8.0 x 10^{-6} M^{-1} s^{-1}. This implies that the cation is easily converted to the corresponding *trans* complex when quenched into aqueous solvent and that it should be an easy step to perform synthetically.

This step was originally carried out synthetically using sodium hydrogen carbonate as the base.[14] It was then shown that the milder base, sodium acetate, worked well also. Addition of a nucleophile to other sites in the complex, the metal or the carbonyl ligands for example, was not observed. However a side product was found to form to some extent for the reaction of the bromo-substituted complex (up to 25 %), and to minor degree (up to 3 %) for the trifluoromethyl-substituted complex.

This side product is suggested to arise as a result of some of the alternative regioisomer of the cation complex forming in the previous step. This regioisomer would then undergo nucleophilic attack to give a structural isomer of the expected product in which the acetate and hydroxyl substituent positions are exchanged. It would be recommended that the trifluoromethyl-substituted diol substrate be used preferentially as the side reaction occurs to a lesser extent. Substitution of the diol with a more electron-withdrawing group appears to reduce the amount of side product that forms.

3.6.4 Decomplexation Step.

The final step of the synthesis is the decomplexation of the coordinated *trans* complex. Decomplexation can be difficult to achieve and can be destructive to certain functional groups on the organic ligand. It has been reported in the literature that decomplexation is possible using trimethylamine-*N*-oxide, and due to the mild basic conditions involved, the reagent has been found to be successful for many organic ligands.[17,99] Decomplexation was attempted several times on the trifluoromethyl-substituted *trans* complex, but the desired product was not isolated and the uncomplexed diol was found to have aromatised. Previous work in this group has shown decomplexation of the related methoxy-substituted complex **(83)**.[75] Thus, it is expected that the appropriate conditions for this step can be developed.



(83)

3.7 Summary.

A proposed synthetic route to convert bromo- and trifluoromethyl- substituted arene *cis* dihydrodiols to their *trans* isomers was investigated. The coordinated cation intermediates formed from the acid-catalysed ionisation of the *cis* complexes required the use of strong acids in order to generate the cations. The acid-catalysed rate constant for the formation of the bromo-substituted carbocation complex was determined. However, a rate for the corresponding reaction of the trifluoromethyl-substituted complex was not measured (see Section 2.2.2, page 47). The reverse reaction for the hydrolysis of the bromo-substituted cation was found to be too fast to measure even when employing a rapid mixing apparatus but a pK_R of 0.5 was estimated. The final step of the synthetic pathway, decomplexation of the tricarbonyl iron fragment from the *trans* complexes, proved difficult and has not been achieved to date as the uncomplexed compounds readily aromatised under the reaction conditions.

The tricarbonyl iron coordinated cycloheptadienyl cation complex was synthesised and kinetic measurements were performed on it. The hydrolysis reaction of the complexed cycloheptadienyl cation to its corresponding alcohol was studied, as was the reverse ionisation reaction allowing a pH-rate profile to be constructed and a pK_R value of 4.2 was determined. The tricarbonyl cycloheptatrienyl chromium complex was also studied in this work. It is proposed that it forms a zwitterionic complex which has a carboxylate ligand in weak base. Equilibrium between this zwitterion and a protonated cationic form in which the carboxylate is converted to the carboxylic acid is postulated to occur in weakly acid solutions. A pK_a value for this protonation of 4.8 was determined.

Future work would include further studies on the reactivities of the seven-membered ring complexes including direct spectrophotometric measurement of the equilibrium constant, pK_R, for the tricarbonyl cycloheptadienyl iron cation, and optimisation of conditions to achieve the final decomplexation step for the *cis* to

trans arene dihydrodiol synthetic route as well as further studies to identify the side product observed in the NMR spectra of the *trans* complexes **(53)** and **(54).**

Chapter 4

Experimental

Chapter 4 Experimental

4.1 General Materials and Instrumentation.

Infrared spectra were recorded over the 4000-400 cm^{-1} operating range on a Perkin Elmer Spectum GX FT-IR spectometer. Potassium bromide discs were prepared in the case of solid samples. For solids with low melting points, a dispersion on calcium fluoride or sodium chloride plates was used. This was prepared by dissolving a sample in dichloromethane or chloroform, distributing a thin liquid film on the plate surface and allowing it to evaporate. Melting points were determined in capillary tubes using an Electothermal 9100 Series melting point apparatus. Sonication was carried out using a Branson 2510 sonic bath operating at 40 kHz (see pg 167). Microanalysis was carried out by the Microanalytical Unit, School of Chemistry and Chemical Biology, University College Dublin. Nuclear magnetic resonance (NMR) spectra were recorded in deuterated chloroform with tetramethylsilane (TMS) as an internal reference unless otherwise stated. The spectra were recorded on a Bruker Avance III 400 instrument operating at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, 376 MHz for ^{19}F NMR and 162 MHz for ^{31}P NMR spectroscopy. Thin layer chromatography was carried out using aluminium-backed or plastic-backed Merck Kieselgel F_{254} or plastic-backed alumium oxide F_{254} plates. Plates were visualized by UV light using a Camag 254 nm lamp and stained if necessary using a potassium permanganate dip [$KMnO_4$ (3 g), K_2CO_3 (20 g), 5% aqueous NaOH (5 mL) and water (300 mL)] or anisaldehyde dip [anisaldehyde (18 mL), acetic acid (3.75 mL), 95% ethanol (338 mL), sulfuric acid (12.5 mL)] with further heating. Flash chromatography was carried out as described by Leonard *et al.*,[100] using silica gel (Merck, Grade 9385, 230 – 300 Mesh, 60 Angstrom) or alumina (Brockman, Neutral, activity I).

All commercially available reagents were used as supplied. Anhydrous reagents were purchased in Sure-Seal™ bottles from Sigma-Aldrich and used as received. All glassware used for moisture sensitive reactions was washed, dried in an oven and cooled in a dessicator over potassium bromide. All moisture sensitive reactions were performed using anhydrous conditions under a nitrogen or argon atmosphere.

The arene *cis*-diols, *cis*-3-bromocyclohexa-3,5-diene-1,2-ol and *cis*-3-trifluoromethylcyclohexa-3,5-diene-1,2-diol were obtained from the Questor Centre in Queen's University Belfast from Professor Derek Boyd where they are produced in bulk by fermentation in a bioreactor.

4.2 Nomenclature.

Nomenclature systems used in the scientific literature for complexes similar to those described in this thesis can vary and often do not adhere to the IUPAC conventions. All complexes discussed in this thesis were named according to the IUPAC recommendations for organic and organometallic chemistry.[101]

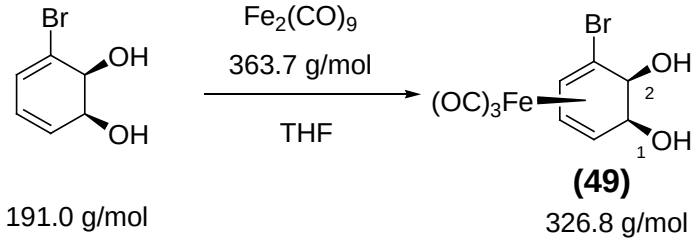
Appendix B provides a list of the complexes prepared in this work along with their structures and corresponding names.

4.3 Synthesis of Organic and Organometallic Substrates.

4.3.1 Synthesis of Tricarbonyl *trans*-(η^4-2-Acetoxy-3-bromocyclohexa-3,5-diene-1-ol) Iron (53).

4.3.1.1 Synthesis of Tricarbonyl (η^4-*cis*-3-Bromocyclohexa-3,5-diene-1,2-diol) Iron (49).

This reaction was carried out using similar conditions to those described by Suemune *et al.* [102]



A protocol for safe handling of diironnonacarbonyl is described in Appendix A. *cis*-3-Bromocyclohexa-3,5-diene-1,2-diol (0.22 g, 1.1 mmol) was dissolved in dry THF (15 mL). Diironnonacarbonyl (1.16 g, 3.18 mmol) was added and washed in with dry THF (10 mL) to form a dark red solution. The reaction mixture was refluxed under argon for 3 hours until TLC analysis showed that no starting material remained. The reaction mixture was run through a short flash column (diethyl ether eluent) and the solvent was removed under reduced pressure to yield a brown oil. This was then purified by flash chromatography on silica (1:1 cyclohexane:ethyl acetate, R_f = 0.35) yielding the product **(49)** as a yellow solid (0.24 g, 66%).

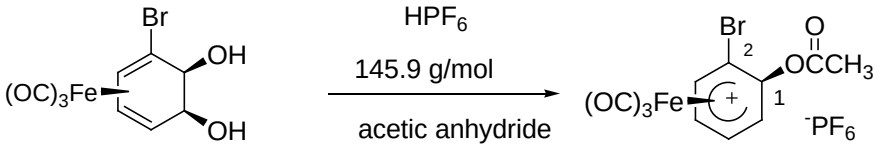
^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.95 (1H, d, *J* = 4.4 Hz,OH_2), 3.10 (1H, m,H_6), 3.12 (1H, d, *J* = 4.8 Hz, OH_1), 3.87 (1H, m, H_1), 3.94 (1H, dd, *J* = 4.4 Hz, J = 6.0 Hz, H_2), 5.15 (1H, ddd, $J_{5,4}$ = 4.4 Hz, *J* = 6.8 Hz, J = 0.8 Hz, H_5), 5.67 (1H, dd, *J* = 1.2 Hz, $J_{4,5}$ = 4.4 Hz, H_4).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 65.9, 68.2 (C1, C2), 73.3 (C6), 79.2 (C3), 81.0 (C5), 87.3 (C4).[i]

υ_{max} (thin film, DCM)/cm^{-1}: 3351 (O-H stretch), 2890 (*sp*^{3} C-H stretch), 2062, 1990 (C=O stretches), 1633 (C=C stretches), 1218, 1065 (C-O stretch), 974, 847, 739 (*sp*^{2} C-H bends).

4.3.1.2 Synthesis of Tricarbonyl (η^5-1-Acetoxy-2-bromocyclohexa-2,4-dienyl) Iron Hexafluorophosphate (51).

This reaction was carried out using similar conditions to those described by Pearson *et al.* [64]



(49)
326.8 g/mol

(51)
497.8 g/mol

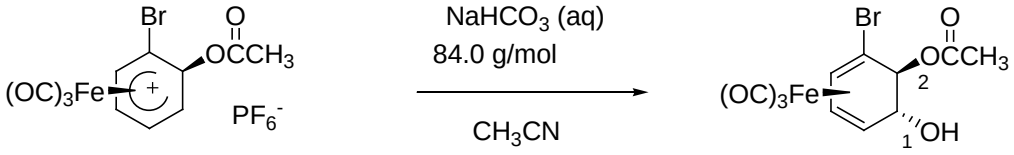
[i] The C=O signal was not intense enough to be seen in the ^{13}C NMR spectrum.

Tricarbonyl 3-bromocyclohexa-3,5-diene-1,2-diol iron **(49)** (0.13 g, 0.39 mmol) was dissolved in dichloromethane (1 mL) and stirred on a salt ice bath until a temperature of 0 ºC was reached. Acetic anhydride (1 mL) and hexafluoro-phosphoric acid (0.23 mL, 1.56 mmol) were added dropwise to give a dark yellow solution. The reaction mixture was stirred on ice for 3 hours until it was shown that no starting material remained by TLC analysis (1:1 cyclohexane:ethyl acetate, R_f = 0.50). The reaction mixture was then added dropwise to diethyl ether (10 mL) forming a yellow precipitate. The solvent was decanted and the residue washed three times with ether (5 mL). The crude product was isolated as a yellow **(51)** solid.[i]

^{1}H NMR (400 MHz, CD_3CN) δ: 2.25 (3H, s, CH_3), 4.33 (1H, d, $J_{6,5}$ = 7.6 Hz, H_6), 5.32 (1H, br s, H_1), 5.88 (1H, m, H_5), 6.53 (1H, d, J = 6.0 Hz, H_3), 7.01 (1H, apt t, J = 5.0 Hz, H_4).

4.3.1.3 Synthesis of Tricarbonyl (η^4-*trans*-2-Acetoxy-3-bromocyclohexa-4,5-diene-1-ol) Iron (53).

This reaction was carried out using similar conditions to those described by Pearson *et al.*[64]



(51)
497.8 g/mol

(53)
369.9 g/mol

[i] This cation is unstable and begins to decompose in under 24 hours, thus it is used directly without further purification.

Tricarbonyl 1-acetoxy-2-bromocyclohexa-2,4-dienyl iron hexafluorophosphate **(51)** (0.15 g, 0.28 mmol) was dissolved in acetonitrile (2 mL) and cooled on an ice bath to 0 °C. Sodium hydrogen carbonate[i] (0.10 g, 1.2 mmol) was dissolved in the minimum amount of distilled water (~ 2-3 mL) and was also cooled on an ice bath to 0 °C. The dienyl salt was then added dropwise to the base and the mixture was allowed gradually to return to room temperature. The reaction mixture was extracted with diethyl ether and dried over anhydrous magnesium sulfate. The solvent was evaporated from the filtrate under reduced pressure and the residue was purified by flash chromatography (1:1 cyclohexane:ethyl acetate, R_f product = 0.30) to give **(53)** as a yellow oil (84 mg, 81%).[ii]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.19 (3H, s, CH_3), 2.92 – 2.95 (1H, m, H_6), 2.97 (1H, d, $J_{2,1}$ = 2.8 Hz, H_2), 3.95 (1H, dd, $J_{1,2}$ = 2.8 Hz, $J_{1,6}$ = 1.2 Hz, H_1), 4.52 (1H, s, OH), 5.38 (1H, ddd, J = 6.0 Hz, J = 4.8 Hz, J = 0.8 Hz, H_5), 5.82 (1H, dd, J = 2.8 Hz, J = 0.8 Hz, H_4).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 49.3 (CH_3), 53.0 (C1), 57.3 (C6), 75.9 (C3), 81.2 (C2), 82.4 (C3), 87.1 (C4), 147.8 (ester CO), 197.2 [$Fe(CO)_3$].

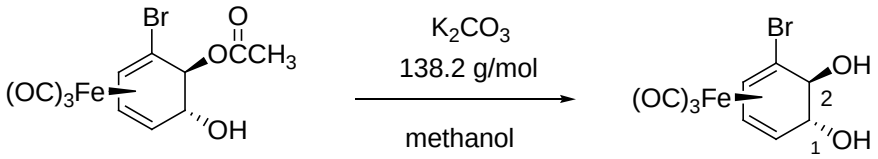
υ_{max} (dispersion, DCM)/cm^{-1}: 3422 (O-H stretch), 2929 (sp^3 C-H stretch), 2063, 1992 (iron C=O stretches), 1730 (ester C=O stretch), 1373 (C-O stretch), 1238 (C-O stretch), 1037 (C-Br stretch).

[i] Sodium acetate was also used in subsequent synthesis.

[ii] A side product was also present, at a level of approximately 25% based on the ^{1}H NMR spectrum.

4.3.1.4 Tricarbonyl (η^4-*trans*-3-Bromocyclohexa-3,5-diene-1,2-diol) Iron (55).

This reaction was carried out using similar conditions to those described by Kartha *et al.*[103] The purpose of preparing this complex was to attempt to facilitate characterisation of the side product present in **(53)**.



(53)
369.9 g/mol

(55)
327.9 g/mol

Tricarbonyl *trans*-(2-bromo-3-trifluoromethylcyclohexa-4,5-diene-1-ol) iron **(53)** (60 mg, 0.16 mmol) was dissolved in methanol (8 mL). Finely crushed potassium carbonate (2 mg, 0.014 mmol) was added. The reaction mixture was stirred for 24 hours and then passed through a short silica column using methanol. The solvent was removed to yield the product **(55)** as a brown oil (51 mg, 97%, R_f = 0.50).[i]

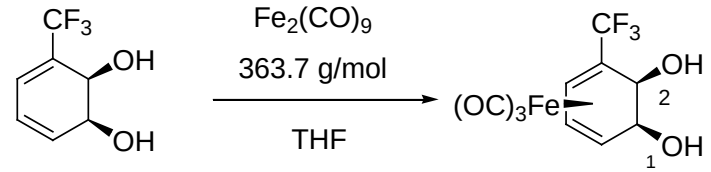
^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.14 (1H, d, OH), 3.46 (1H, apt s, H_6), 3.69 (1H, s, OH), 4.05 (1H, apt s, H_1), 4.48 (1H, apt s, H_2), 5.07 (1H, apt s, H_5,), 5.61 (1H, apt s, H_4).[ii]

[i] Signals for the side product were found in the ^{1}H NMR spectrum at a level of approximately 10%.
[ii] The resolution of the ^{1}H NMR spectrum may have been affected by the presence of paramagnetic iron salts.[6]

4.3.2 Synthesis of Tricarbonyl (η^4-*trans*-2-Acetoxy-3-trifluoromethylcyclohexa-3,5-diene-1-ol) Iron (54).

4.3.2.1 Synthesis of Tricarbonyl (η^4-*cis*-3-Trifluoromethylcyclohexa-3,5-diene-1,2-diol) Iron (50).

This reaction was carried out using similar conditions to those described by Suemune *et al.* [102]



(50)

180.1 g/mol 315.9 g/mol

A protocol for safe handling of diironnonacarbonyl is described in Appendix A. *cis*-3-Trifluoromethylcyclohexa-3,5-diene-1,2-diol (0.21 g, 1.1 mmol) was dissolved in anhydrous THF (15 mL). Diironnonacarbonyl (1.17 g, 3.22 mmol) was added and was rinsed in with THF (10 mL) forming a dark red/black solution. The reaction mixture was stirred at 50 ºC under argon for 3 hours until TLC analysis showed that no starting material remained. The reaction mixture was passed through a short flash column (diethyl ether eluent) and the solvent was removed under reduced pressure to yield a green oil. This was then purified by flash chromatography on silica (1:1 cyclohexane:ethyl acetate, R_f product = 0.38) yielding the product **(50)** as a yellow solid (0.19 g, 52%).

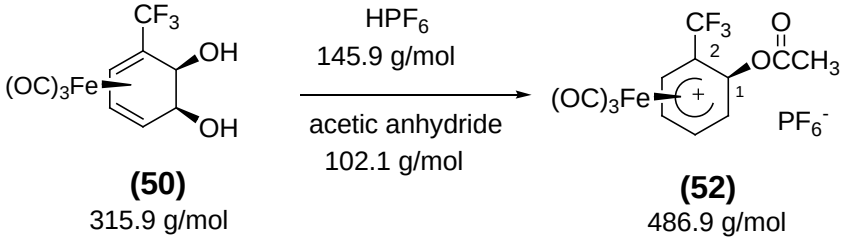
^{1}H NMR (400MHz, $CDCl_3$): δ: 2.69 (1H, s, OH), 2.87 (1H, s, OH), 3.27 (1H, m, H_6), 3.93 (2H, m, H_1, H_2), 5.25 (1H, dd, $J_{5,6}$= 6.4Hz, $J_{5,4}$ = 4.8Hz, H_5), 5.65 (1H, dd, $J_{4,5}$ = 4.8Hz, $J_{4,6}$ = 1.6 Hz, H_4).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 66.7, 67.0 (C1, C2), 67.6 (C6), 81.9 (C3), 84.1 (C5), 84.2 (C4).[i]

υ_{max} (dispersion, DCM)/cm^{-1}: 3324 (O-H stretch), 2902 (sp^3 C-H stretch), 2067, 1988 (C=O stretches), 1227 (C-F stretch).

4.3.2.2 Synthesis of Tricarbonyl (η^5-1-Acetoxy-2-trifluoromethyl-cyclohexadienyl) Iron Hexafluorophosphate (52).

This reaction was carried out using similar conditions to those described by Pearson *et al*.[64]



(50)
315.9 g/mol

(52)
486.9 g/mol

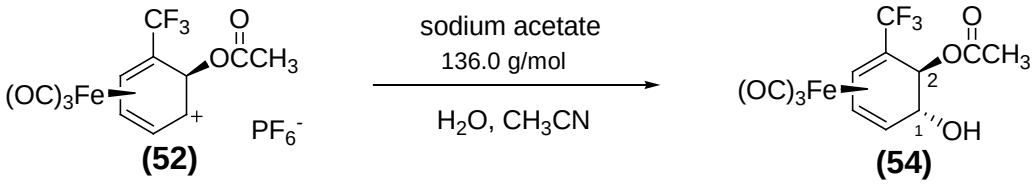
Tricarbonyl 3-trifluoromethylcyclohexa-3,5-diene-1,2-diol iron **(50)** (0.09 g, 0.3 mmol) was dissolved in dichloromethane (1 mL) and stirred on a salt ice bath until a temperature of 0 ºC was reached. Acetic anhydride (1 mL) and hexa-fluorophosphoric acid (0.16 mL, 1.12 mmol) were added dropwise forming a dark yellow solution. The reaction mixture was stirred on ice for 4 hours and it was then added dropwise to diethyl ether (10 mL) forming a yellow precipitate. The solvent was decanted and the residue washed three times with diethyl ether (5 mL). The crude was isolated as a yellow solid.[ii]

[i] The carbonyl signals could not be distinguished from the baseline of the ^{13}C – NMR spectrum.
[ii] This cation is unstable and thus is used directly without further purification.

^{1}H NMR (400 MHz, CD_3CN) δ: 2.25 (3H, s, CH_3), 4.53-4.55 (1H, d, $J_{6,5}$ = 7.6 Hz, H_6), 5.27 (1H, s, H_1), 6.01-6.05 (1H, m, H_5), 6.60-6.62 (1H, d, $J_{3,4}$ = 6.0 Hz, H_3), 7.21-7.24 (1H, t, $J_{4,3}$ = 5.6 Hz, H_4).

4.3.2.3 Synthesis of Tricarbonyl (η^4-2-*trans*-Acetoxy-3-trifluoromethylcyclohexa-3,5-diene-1-ol) Iron (54).

This reaction was carried out using similar conditions to those described by Pearson *et al.*[64]



(52) 490.0 g/mol

(54) 362.0 g/mol

Tricarbonyl (1-acetoxy-2-trifluoromethylcyclohexa-2,4-dienyl) iron hexafluorophosphate **(52)** (0.46 g, 0.94 mmol) was dissolved in acetonitrile (anhydrous, 5 mL) and cooled on an ice bath to 0°C. Sodium acetate (0.52 g, 3.84 mmol) was dissolved in the minimum amount of distilled water (4 mL) and was also cooled on an ice bath to 0 °C. The dienyl salt was then added dropwise to the acetate solution and the mixture was allowed gradually to return to room temperature. The reaction mixture was extracted with diethyl ether (3 x 20 mL) and dried over anhydrous magnesium sulfate. The solvent was evaporated from the filtrate under reduced pressure and the residue was purified by flash chromatography (1:1 cyclohexane:ethyl acetate, R_f = 0.39) to give a yellow oil (0.16 g, 47 %).[i]

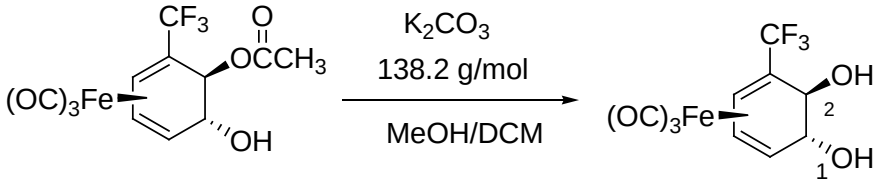
[i] Signals for the side product were found in the ^{1}H NMR spectrum at a level of approximately 3%.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.15 (3H, s, CH_3), 3.15 (2H, m, H_2 and H_6), 3.95 (1H, apt d, *J* = 4.0 Hz, H_1,), 4.45 (1H, s, OH), 5.49 (1H, apt t, *J* = 5.2 Hz, H_5), 5.84 (1H, m, H_4).

υ_{max} (dispersion, DCM)/cm^{-1}: 3055 (OH stretch), 2988 (sp^3 C-H stretch), 2071, 2009 (iron C=O stretches), 1741 (C=O ester stretch), 1422 (CF_3 stretch), 1276 (C-O stretch).

4.3.2.4 Synthesis of Tricarbonyl (η^4-*trans*-3-Trifluoromethylcyclohexa-3,5-diene-1,2-diol) Iron (56).

This reaction was carried out using similar conditions to those described by Kartha *et al.*[103] The purpose of preparing this complex was to attempt to facilitate characterisation of the side product present in **(54)**.



(54)
362.0 g/mol

(56)
315.9 g/mol

Tricarbonyl *trans*-(2-acetoxy-3-trifluoromethylcyclohexa-4,5-diene-1-ol) iron **(54)** (40 mg, 0.11 mmol) was dissolved in a mixture of methanol:dichloromethane (1:1, 8 mL). Finely crushed potassium carbonate (4 mg, 0.02 mmol) was added. The reaction mixture was stirred for 24 hours and then passed through a short silica column using methanol as eluent (R_f = 0.35). The solvent was removed under reduced pressure to give the product as a pale brown solid (30 mg, 86%).

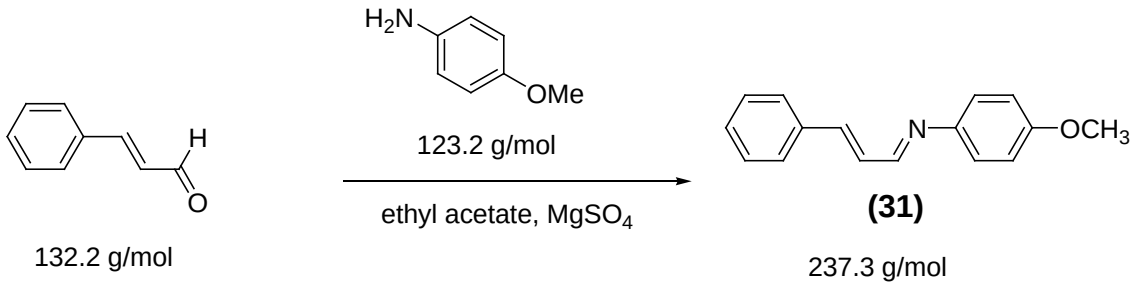
^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.47 (1H, d, *J* = 4Hz, OH_2), 3.07 (1H, t, *J* = 4.4 Hz, H_6), 3.49 (1H, s, OH_1), 3.81 (1H, d, *J*= 3.6 Hz, H_1), 3.91 (1H, dd, *J* = 4.0 Hz, J = 6.8 Hz, H_2), 5.41 (1H, t, *J* = 5.6 Hz, H_5), 5.73 (1H, d, *J* = 4.0 Hz, H_4).

υ_{max} (dispersion, $CHCl_3$)/cm^{-1}: 3055, 2988 (OH stretches). 2071, 2009 (C=O stretches), 1740 (C=C diene stretch), 1289 (C-CF_3 stretch), 703 (Fe-C bend).

4.3.3 Synthesis of Dicarbonyl (η^4-Cyclohexa-1,3-diene) Triphenylphosphine Iron (57).

4.3.3.1 Synthesis of 1-(4-Methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (31) (Tricarbonyliron Transfer Complex).

This reaction was carried out using similar conditions to those described by Knölker *et al.*[26]



Trans-cinnamaldehyde (11.04 g, 84 mmol) and *p*-anisidine (9.81 g, 79 mmol) were dissolved in ethyl acetate (150 mL). Magnesium sulfate (4 g) was added to give a brown solution with a white suspension. This was stirred under nitrogen for 48 hours to give a brown solution with green/yellow crystals and hydrated magnesium sulfate suspended. The solution was filtered and the residue washed with ethyl acetate (3 x 50 mL). The solvent was removed from the filtrate on the rotary evaporator slowly at a water bath temperature of 40 ºC until crystallisation began.

Pentane (100 mL) was added to the warm solution and, upon leaving in the freezer overnight, crystals formed. These were filtered under vacuum and washed with cold pentane (50 mL) to yield the product as dark green crystals (6.20 g).

Crystals were noticed to have appeared in the filtrate after the initial filtration. These were dissolved with ethyl acetate and the solvent removed slowly so that they crystallised as described above. Filtration under vacuum yielded the product as light green crystals (1.72 g), to give a total yield of 42 % [7.92 g, R_f = 0.14 (1:1 cyclohexane:ethylacetate), melting point 119 – 122 ºC].

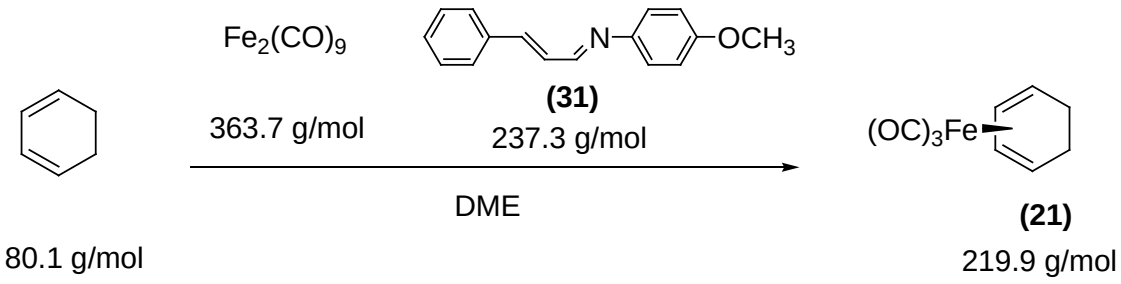
^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.83 (3H, s, OCH_3), 6.90 – 6.94 (2H, m, -CH=CH-), 7.07 – 7.54 (9H, m, aromatic H), 8.26 – 8.34 (1H, m, N=CH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.4 (O-CH_3), 114.4, 122.2 (2 x CH methoxyphenyl), 127.4, 128.8, 128.9 (phenyl CH's), 129.4 (-CH=CH-), 135.8 (C phenyl), 143.1 (-CH=CH-), 144.5, 158.4 (C-O methoxyphenyl), 159.8 (C=N).

υ_{max} (KBr)/cm^{-1}: 3020 (C-H stretch), 1626 (C=N stretch), 1605, 1505 (C=C stretches), 1247 (C-O stretch), 1031 (C-N stretch).

4.3.3.2 Synthesis of Tricarbonyl (η^4-Cyclohexa-1,3-diene) Iron (21).

This reaction was carried out using similar conditions to those described by Knölker *et al.*[26]



Cyclohexa-1,3-diene (3.04 g, 38.0 mmol), diironnonacarbonyl (5.01 g, 13.4 mmol) and 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (0.99 g, 4.2 mmol) were dissolved in dimethoxyethane (anhydrous, 20 mL) to form a red solution which was refluxed at 82 ºC for 24 hours under nitrogen. The reaction was monitored by TLC analysis. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica (9:1 pentane:ethyl acetate, R_f = 0.60) yielding the product as a yellow oil (4.05 g, 49%).

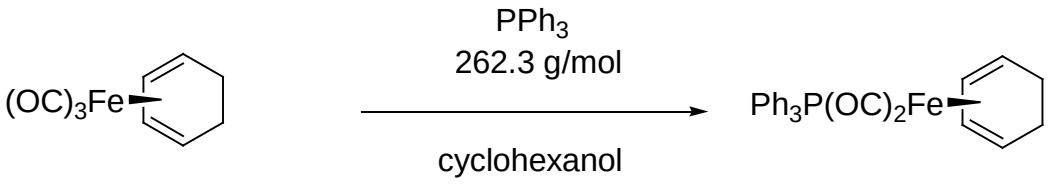
^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.55-1.79 (4H, m, 2 x CH_2), 3.21 (2H, m, H_1, H_4), 5.29 (2H, dd, *J* = 2.8 Hz, *J* = 5.2 Hz, H_2, H_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.8 (C5, C6), 61.4 (C1, C4), 84.4 (C2, C3), 211.2 [$Fe(CO)_3$].

υ_{max} (thin film, $CHCl_3$)/cm^{-1}: 3008 (sp^2 C-H stretch), 2946 (sp^3 C-H stretch), 2043 (br, C=O stretch), 1962 (C=O stretch).

4.3.3.3 Synthesis of Dicarbonyl (η^4-Cyclohexa-1,3-diene) Triphenyl-phosphine Iron (57).

This reaction was carried out using similar conditions to those described by Pearson *et al.*[104]



(21)

219.9 g/mol

(57)

454.1g/mol

Tricarbonyl cyclohexa-1,3-diene iron (1.02 g, 4.62 mmol) and triphenylphosphine (1.27 g, 4.83 mmol) were dissolved in cyclohexanol (30 mL) and refluxed at 170 ºC for 24 hours under nitrogen. The reaction mixture was allowed to cool and petroleum ether (b.p. 40 – 60 ºC, 100 mL) was then added and the mixture was stirred on an ice bath for 2 hours. The resulting precipitate [complexed $Fe(CO)_3(PPh_3)_2$] was removed by filtration. The petroleum ether was removed from the filtrate on the rotary evaporator and the cyclohexanol was removed by vacuum distillation at 2 mbar to give a yellow/brown residue. This was recrystallised from *n*-hexane to yield the product as yellow/orange crystals (0.35 g, 17 %, R_f = 0.50 (9:1 pet.ether:ethyl acetate), mp 118.2 – 118.9 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.40-1.74 (4H, m, 2 x CH_2), 2.51 (2H, m, H_1, H_4), 4.84 (2H, dd, *J* = 3.2 Hz, *J* = 7.6 Hz, H_2, H_3), 7.36-7.51 (15H, m, PPh_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.6 (C5, C6), 61.1 (C1, C4), 84.7 (C2, C3), 128.1-136.5 (PPh_3).[i]

[i] The carbonyl signals could not be distinguished from the baseline of the ^{13}C – NMR spectrum.

^{31}P NMR (161 MHz, $CDCl_3$) δ: 70.4 (PPh_3).

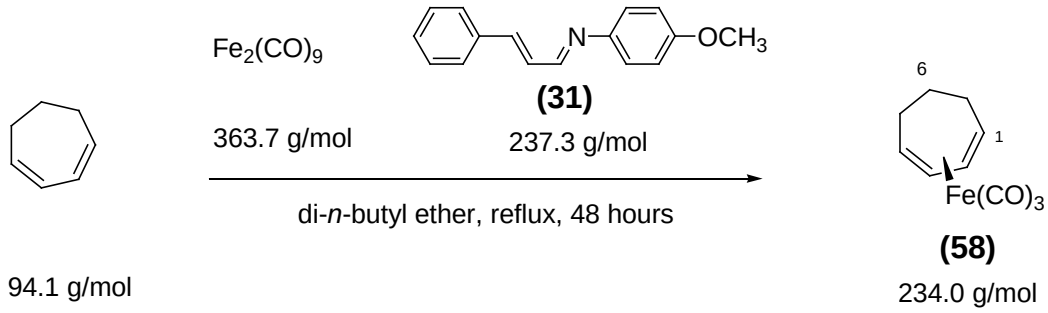
υ_{max} (thin film, $CHCl_3$)/cm^{-1}: 3018 (sp^2 C-H stretch), 2897 (sp^3 C-H stretch), 1897, 1963 (C=O stretches), 1434 (C=C aromatic stretch), 1090 (P-C stretch).

4.3.4 Synthesis of Dicarbonyl (η^4-Cyclohepta-1,3-diene) Triphenylphosphine Iron (60) and of Dicarbonyl (η^4-Cyclohepta-1,3,5-triene) Triphenylphosphine Iron (61).

4.3.4.1 Synthesis of Tricarbonyl (η^4-Cyclohepta-1,3-diene) Iron (58).

Method A:

This reaction was carried out using similar conditions to those described by Knölker *et al.*[35]

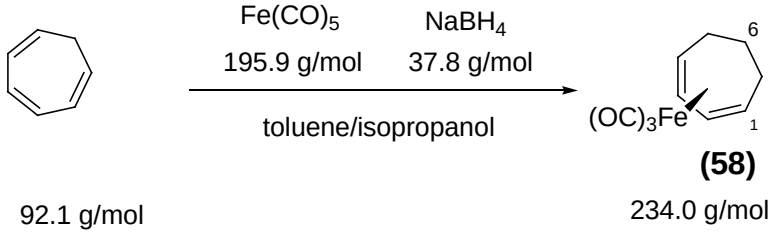


Cyclohepta-1,3-diene (1.48 g, 15.7 mmol), diironnonacarbonyl (2.71 g, 7.45 mmol) and 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (0.57 g, 2.4 mmol) were dissolved in anhydrous di-*n*-butyl ether (70 mL) to form a red solution which was refluxed at 100 ºC for 48 hours under nitrogen. The reaction was monitored by TLC analysis (9:1 *n*-hexane: ethyl acetate). The solvent was removed under

reduced pressure and the residue was purified by flash chromatography on silica using 100% *n*-hexane to yield the product (R_f = 0.60) as a yellow oil (2.50 g, 68 %).

Method B:

This reaction was carried out using similar conditions to those described by Coqurel *et al.*[66]



92.1 g/mol

(58)

234.0 g/mol

Cycloheptatriene (0.77 mL, 7.2 mmol) and iron pentacarbonyl (3.0 mL, 23 mmol) were stirred in a 1:1 mixture of anhydrous toluene and anhydrous isopropanol (10 mL). Sodium borohydride (0.04 g, 1.05 mmol) was added in one portion to give an orange solution. A balloon was applied to maintain a positive pressure of the CO evolved during the reaction, and the reaction was allowed to stir at room temperature for 10 minutes to give a red solution. This was then heated at 100 ºC for 4 days. The reaction was monitored by TLC analysis (4:1 pentane: ethyl acetate). The reaction mixture was purified by flash chrom-atography on silica using 100% pentane to yield the product (R_f =0.60) as a golden oil (0.73 g, 44 %).

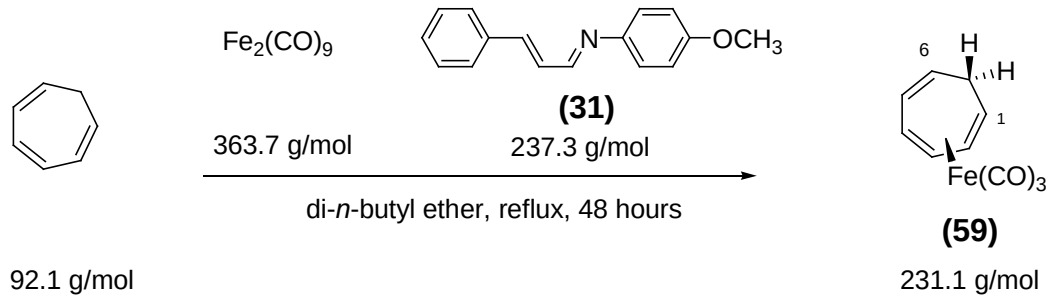
^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.15 – 1.32 (2H, m, H_{5exo}, H_{7exo}), 1.42-1.91 (2H, m, H_{6endo}, H_{6exo}), 1.92-1.97 (2H, m, H_{5endo}, H_{7endo}), 2.95-2.99 (2H, m, H_1, H_4), 5.19-5.21 (2H, m, H_2, H_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.9 (C6), 28.1 (C5, C7), 59.6 (C1, C4), 87.9 (C2, C3), 211.9 [$Fe(CO)_3$].

υ_{max} (thin film, neat)/cm^{-1}: 2929 (C-H stretch), 2041, 1964 (C=O stretches), 1441 (C=C stretch).

4.3.4.2 Synthesis of Tricarbonyl (η^4-Cyclohepta-1,3,5-triene) Iron (59).

This reaction was carried out using similar conditions to those described by Knölker *et al.*[35]



Cyclohepta-1,3,5-triene (4.0 mL, 40 mmol), diironnonacarbonyl (4.14 g, 11.4 mmol) and 1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (0.96 g, 4.0 mmol) were dissolved in anhydrous di-*n*-butylether (80 mL) to form a dark brown/black solution which was refluxed at 150 ºC for 48 hours under nitrogen. The reaction was monitored by TLC analysis (100 % *n*-hexane). The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica using 100 % *n*-hexane as the eluent to yield the product (R_f = 0.60) as an orange oil (2.57g, 28 %).[i]

[i] This reaction also produces the corresponding tricarbonyl cycloheptadiene iron complex as a side product.

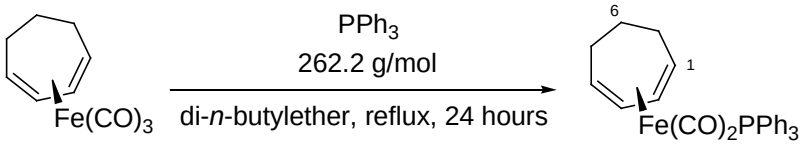
^{1}H NMR (400 MHz, C_6D_6) δ: 1.65-1.99 (1H, m, H_{7exo}), 2.00-2.08 (1H, m, H_{7endo}), 2.63-2.65 (1H, m, H_4), 2.77-2.80 (1H, m, H_1), 4.56-4.59 (2H, m, H_2, H_3), 4.91- 4.96 (1H, m, H_6), 5.55 - 5.61 (1H, m, H_5).

^{13}C NMR (100 MHz, C_6D_6) δ: 27.9 (C7), 56.0, 59.4, 60.3, 87.7, 87.9, 93.1 (C1-C6), 211.5 ($Fe(CO)_3$).

υ_{max} (thin film, neat)/cm^{-1} : 3029 (sp^2 C-H stretch), 2045, 1966 (C=O stretches).

4.3.4.3 Synthesis of Dicarbonyl (η^4-Cyclohepta-1,3-diene) Triphenyl-phosphine Iron (60).

This reaction was carried out using similar conditions to those described by Pearson *et al.*[67]



(58) 234.0 g/mol

(60) 468.3 g/mol

Cyclohepta-1,3-diene tricarbonyliron (0.22 g, 0.94 mmol) was dissolved in anhydrous di-*n*-butyl ether (20 mL) and heated to 150 ºC under nitrogen forming a brown solution. Triphenylphosphine (0.25 g, 0.94 mmol) was dissolved in anhydrous di-*n*-butyl ether (10 mL) and added dropwise to the reaction mixture. The reaction was heated at 140 ºC overnight until TLC analysis (1:1 di-ethyl ether: *n*-hexane, R_f = 0.45) showed that all starting material had reacted. The reaction mixture was then cooled and filtered through Celite™ and the filter pad was rinsed

with di-*n*-butyl ether. The solvent was then removed under reduced pressure and the resulting yellow oil was recrystallised from ether-hexane to give the product as a yellow solid (0.036 g, 8 %).[i]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.10-1.36 (2H, m, H_{6exo}, H_{6endo}), 1.81-1.94 (4H, m, H_{5exo}, H_{5endo}, H_{7exo}, H_{7endo}), 2.43 (2H, br s, H_1, H_4), 4.63-4.64 (2H, m, H_2, H_3), 7.37-7.70 (15H, m, PPh_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.5 (C6), 28.4 (C5, C7), 57.2 (C1, C4), 87.9 (C2, C3), 128.1 – 135.9 (phenyl).[ii]

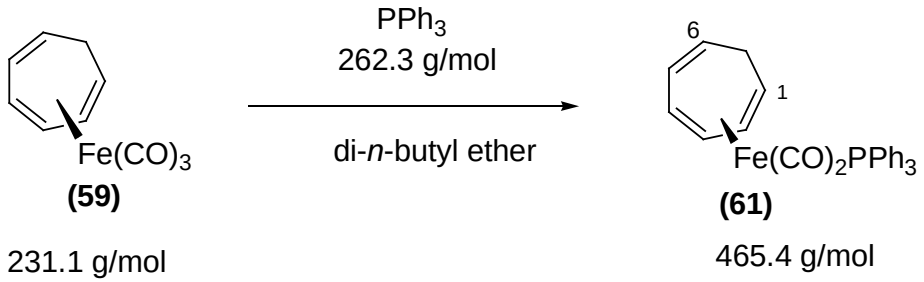
^{31}P NMR (161 MHz, $CDCl_3$) δ: 68.5 (PPh_3).

υ_{max} (thin film, $CHCl_3$)/cm^{-1}: 3054 (sp^2 C-H stretch), 1883, 1938 (C=O stretches), 1437 (C=C stretch), 1189 (P-C stretch), 495 (Fe-C bend).

[i] Some PPh_3 was recovered during the recrystallisation as white needles and was removed from the product using a tweezers.
[ii] The carbonyl signals could not be distinguished from the baseline of the ^{13}C – NMR spectrum.

4.3.4.4 Synthesis of Dicarbonyl (η^4-Cyclohepta-1,3-triene) Triphenylphosphine Iron (61).

This reaction was carried out using similar conditions to those described by Pearson *et al.*[67]



Tricarbonyl cycloheptatriene iron (0.51g, 2.2 mmol) was dissolved in di-*n*-butyl ether (anhydrous, 20 mL) and heated to 150 ºC under nitrogen forming a brown solution. Triphenylphosphine (0.25 g, 0.94 mmol) was dissolved in anhydrous di-*n*-butyl ether (10 mL) and added dropwise to the reaction mixture. The reaction was heated at 140 ºC overnight until TLC analysis (1:1 diethyl ether:*n*-hexane, R_f = 0.33) showed that all starting material had reacted. The reaction mixture was then cooled and filtered through Celite™ and the filter pad was rinsed with di-*n*-butyl ether. The solvent was removed under reduced pressure and the resulting yellow oil was recrystallised from ether-hexane to give the product as an orange/yellow solid (0.66 g, 16 %, mp 121.1 – 123.0 ºC).[i]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.00-2.06 (1H, m, H_{7exo}), 2.27-2.40 1H, (m, H_{7endo}), 2.48 (1H, br s, H_4), 2.65 (1H, br s, H_1), 4.62-4.74 (2H, m, H_2,H_3), 5.09- 5.12 (1H, m, H_6), 5.79 - 5.84 (1H, m, H_5), 7.30 – 7.79 (15H, m, Ph_3).

[i] Purification of this compound was carried out by an undergraduate project student, Ann-Katrin Holik.

^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.9 (C7), 53.6 (C4), 58.6 (C1), 88.4 (C2, C3), 93.9 (C6), 124.2 (C5), 128.2-135.9 (Ph_3).[i]

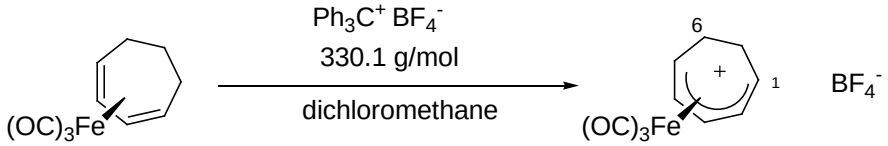
^{31}P NMR (161 MHz, $CDCl_3$) δ: 69.1 (PPh_3).

υ_{max} (thin film, $CHCl_3$)/cm^{-1}: 3056 (*sp*^{2} C-H stretch), 1914, 1973 (C=O stretches), 1646 (C=C stretch), 1092 (P-C stretch), 564 (Fe-C bend).

4.3.5 Synthesis of η^5-Cycloheptadienyl Complexes.

4.3.5.1 Synthesis of Tricarbonyl (η^5-Cyclohepta-1,3-dienyl) Iron Tetrafluoroborate (62).

This reaction was carried out using similar conditions to those described by Pearson *et al.*[46]



(58) 234.0 g/mol

(62) 319.8 g/mol

Tricarbonyl cycloheptadiene iron (0.26 g, 1.0 mmol) was dissolved in anhydrous dichloromethane (2 mL) under argon. To this a solution of triphenylcarbenium tetrafluoroborate (0.43 g, 1.28 mmol) in anhydrous dichloromethane (4 mL) was added dropwise. The yellow solution turned dark brown initially, then orange and a precipitate then formed. Further equivalents of triphenylcarbenium tetrafluoroborate

[i] The carbonyl signals could not be distinguished from the baseline of the ^{13}C – NMR spectrum.

(0.53 g, 1.61 mmol) were added in portions and the reaction mixture was stirred overnight. The reaction was monitored by TLC (9:1 *n*-hexane: ethyl acetate, R_f = 0.37). The reaction had not gone to completion, but the precipitate was filtered and washed with cold dichloromethane to isolate the product as a pale yellow solid (0.27 g, 85 %, mp – darkens at 240 ºC, does not melt below 300 ºC).

^{1}H NMR (400 MHz, CD_3CN) δ: 1.78 (2H, m, H_{6exo}, H_{7exo}), 2.61 (2H, m, H_{6endo}, H_{7endo}), 4.92 (2H, apt s, H_1, H_5), 5.97 (2H, m, H_2, H_4), 7.01 (1H, t, J = 6.4 Hz, H_3).

^{13}C NMR (100 MHz, CD_3CN) δ: 32.2 (C6, C7), 94.5 (C1, C5), 100.5 (C3), 103.7 C2, C4).[i]

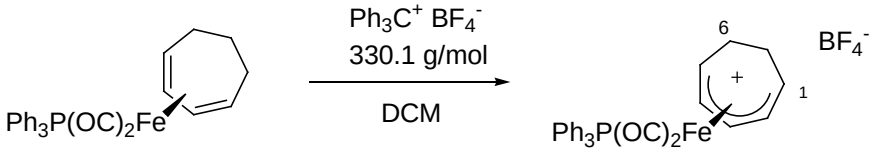
^{19}F NMR (376 MHz, CD_3CN) δ: -151.2 (BF_4^-).

υ_{max} (KBr)/cm^{-1} : 3020 (C-H stretch), 2107, 2061 (C=O stretches), 1633 (C=C stretch).

[i] The carbonyl peaks could not be distinguished from the baseline of the ^{13}C -NMR spectrum.

4.3.5.2 Synthesis of Dicarbonyl (η^5-Cyclohepta-1,3-dienyl) Triphenylphosphine Iron Tetrafluoroborate (63).

This reaction was carried out using similar conditions to those described by Stephenson *et al.*[69]



(60)

468.3 g/mol

(63)

554.1 g/mol

Dicarbonyl cycloheptadiene triphenylphosphine iron (0.15 g, 0.32 mmol) was dissolved in anhydrous dichloromethane (10 mL) under argon. To this a solution of triphenylcarbenium tetrafluoroborate (0.15 g, 0.45 mmol) in anhydrous dichloromethane (5 mL) was added dropwise. The resulting green solution was stirred at room temperature for 1 hour. Diethyl ether (40 mL) was added and the solution was stirred on an ice bath to form a precipitate. The precipitate was filtered and washed with cold diethyl ether to give the product as a bright yellow solid (0.17 g, 96 %, R_f = 0.50, mp 192.0 – 193.3 ºC).

^{1}H NMR (400 MHz, CD_3CN) δ: 1.76 (2H, m, H_{6exo},H_{7exo}), 2.12 (2H, m, H_{6endo},H_{7endo}), 4.18 (2H, m, H_1,H_5), 5.44 (2H, m, H_2,H_4), 6.83 (1H, t, J = 5.2 Hz, H_3).

^{31}P NMR (161 MHz, CD_3CN) δ: 59.1 (PPh_3).

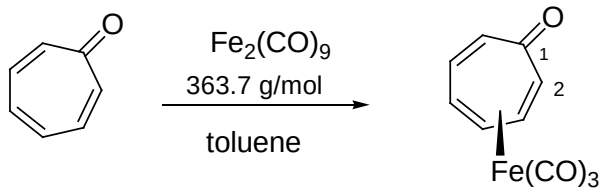
^{19}F NMR (376 MHz, CD_3CN) δ: -151.8 (BF_4^-).

υ_{max} (thin film, $CHCl_3$)/cm^{-1}: 3066 (sp^2 C-H stretch), 2042, 1998 (C≡O stretches), 1056 (P-Ph stretch), 721 (B-F stretch), 496 (Fe-C bend).

4.3.6 Synthesis of Dicarbonyl (η^4-Cyclohepta-2,4,6-triene-1-ol) Triphenylphosphine Iron (65).

4.3.6.1 Synthesis of Tricarbonyl (η^4-Cycloheptatrienone) Iron (32).

This reaction was carried out using similar conditions to those described by Mayr *et al.*[70]



(32)

106.1 g/mol

245.9 g/mol

Tropone (0.58 mL, 6.0 mmol) was added to anhydrous toluene (10 mL) giving a very dark red solution. Diironnonacarbonyl (5.00 g, 13.7 mmol) was added and washed in with anhydrous toluene (15 mL) forming a black solution. The reaction was heated to 55 ºC in the absence of light under nitrogen for 90 mins. After cooling, the reaction mixture was chromatographed directly on neutral alumina (activity I) (50: 50 dichloromethane: diethyl ether), yielding the product (R_f = 0.60) as a red oil which upon leaving overnight in the freezer gave a red/orange solid (1.31 g, 89 %, melting point 64.4 – 64.9 ºC).

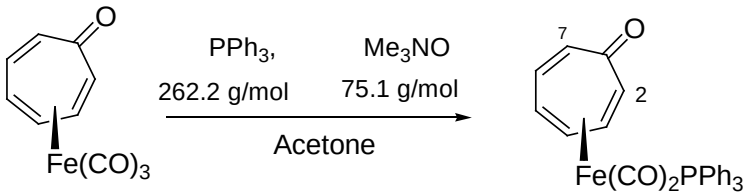
^{1}H NMR (400 MHz, $CDCl_3$) δ*:* 2.65 (1H, m, H_5), 3.09 (1H, m, H_2), 4.98 (1H, m, H_7), 6.32 (2H, m, H_3, H_4), 6.51 (1H, m, H_6).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.4 (C5), 61.2 (C2), 91.5, 96.1 (C3, C4), 122.5 (C7), 148.2 (C6), 198.8 (C≡O).

υ_{max} (thin film, CH_2Cl_2)/cm^{-1}: 2061, 2005 (C=O stretches), 1633 (C=O stretch ketone), 1606 (C=C stretch).

4.3.6.2 Synthesis of Dicarbonyl (η^4-Cycloheptatrienone) Triphenylphosphine Iron (64).

This reaction was carried out using similar conditions to those described by Howell *et al.*[71]



(32) 245.9 g/mol

(64) 480.2 g/mol

Tricarbonyl tropone iron (1.00 g, 4.06 mmol) and triphenylphosphine (1.62 g, 6.18 mmol) were dissolved in acetone (40 mL) forming an orange solution. Trimethylamine-*N*-oxide (0.53 g, 7.06 mmol) was added to give a deep red solution which was refluxed under nitrogen with vigorous stirring. The reaction was monitored by TLC analysis for six hours with periodic addition of trimethylamine-*N*-

oxide (1.12 g, 14.9 mmol). Following literature results the reaction did not reach completion at this stage but the work up was begun. The reaction mixture was cooled and filtered on a pad of Celite™ and rinsed with diethyl ether. The solvent was removed under reduced pressure and the residue was dissolved in 1:1 ethyl acetate:petroleum ether (40 – 60 ºC). After filtration and removal of the solvent the residue was purified by flash chromatography on neutral alumina (activity I) (1:1 ethyl acetate: petroleum ether) to yield the product (R_f = 0.40) as a red solid (0.97 g, 50 %, melting point 173 – 174 ºC).

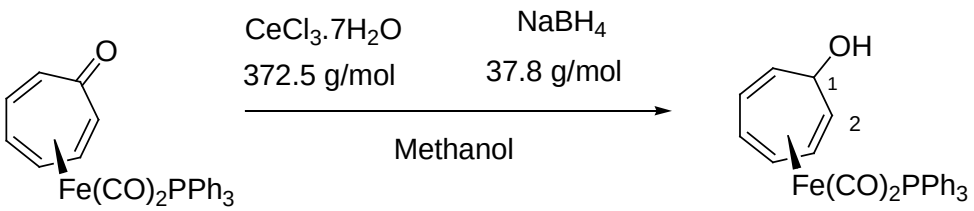
^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.13 (1H, m, H_5), 2.71 (1H, m, H_2), 4.91 (1H, m, H_3), 6.01 (1H, m, H_7), 6.50 (1H, m, H_4), 7.34 (1H, m, H_6), 7.43 (15H, br s, Ph_3).

^{31}P NMR (161 MHz, $CDCl_3$) δ: 63.2 (PPh_3).

υ_{max} (thin film, CH_2Cl_2)/cm^{-1}: 1992, 1936 (C=O stretches), 1627 (C=O stretch, ketone), 1598 (C=C stretch).

4.3.6.3 Synthesis of Dicarbonyl (η^4-Cyclohepta-2,4,6-triene-1-ol) Triphenylphosphine Iron (65).

This reaction was carried out using similar conditions to those described *by* Pearson *et al.*[97]



(64)

480.2 g/mol

(65)

482.2 g/mol

Dicarbonyl (cycloheptatrienone) triphenylphosphine iron (0.19 g, 0.42 mmol) was dissolved in methanol (10 mL) to give a red solution. Cerium chloride heptahydrate (1.70 g, 4.56 mmol) was added and the reaction mixture stirred for 10 minutes. The reaction was then cooled to 0 ºC on an ice bath and sodium borohydride (0.74 g, 19.60 mmol) was added in small portions with a further addition of methanol (10 mL). A gas was observed evolving at this point. The reaction was monitored by TLC analysis on alumina plates (1:1 cyclohexane: ethyl acetate, R_f = 0.68). A colour change was observed from red to orange initially and then to yellow when the reaction was completed. The reaction mixture was poured into 30 mL of saturated brine, and extracted with diethyl ether (3 x 20 mL). The organic layers were combined, washed with brine and dried over anhydrous sodium sulfate. The solvent was then removed under reduced pressure with no heat on the water bath to give the product as a dark orange solid (0.12 g, 61%, melting point 105.0 – 106.0 ºC).[i]

[i] This product was found to decompose when it was attempted to purify it by both silica and alumina column chromatography.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.67 (1H, d, *J* = 10 Hz, OH), 2.37 (1H, m, H_5), 3.02 (1H, m, H_2), 3.56 (1H, dd, *J* = 2.4 Hz, $J_{1,OH}$ = 10 Hz, H_1), 4.76 (1H, m, H_3), 4.93 (1H, m, H_4), 5.14 (1H, dt, $J_{7,OH}$ = 10.8 Hz, $J_{7,1}$ = 2.4 Hz, H_7), 5.88 (1H, m, H_6) 7.46 (15H, m, phenyl).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.0 (C5), 64.7 (C1), 65.9 (C2), 83.6 (C3), 94.9 (C4), 126.3 (C7), 131.9 (C6), 128.2 – 135.0 (Ph).[i]

^{31}P NMR (161 MHz, $CDCl_3$) δ: 67.5 (PPh_3).

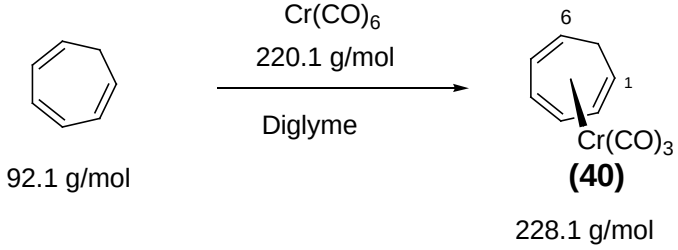
υ_{max} (thin film, $CHCl_3$)/cm^{-1}: 3019 (OH stretch), 1978, 1920 (C=O stretches), 1520 (C=C-Fe stretches), 1435 (P-Ph stretch), 1215 (C-OH stretch).

Elemental Analysis: Required: C 67.24, H 4.81, Fe 11.58, P 6.42.
Found: C 66.46, H 5.60, Fe 8.58, P 6.65.[ii]

4.3.7 Synthesis of Tricarbonyl (η^7-Cycloheptdienyl) Chromium Tetrafluoroborate (41).

4.3.7.1 Synthesis of Tricarbonyl (η^6- Cycloheptatriene) Chromium (40).

This reaction was carried out using a similar procedure to that reported by Munro and Pauson.[51]



92.1 g/mol

(40)

228.1 g/mol

[i] The CO signals could not be distinguished from the baseline of the ^{13}C NMR spectrum, however the experiment had been run for 10,000 scans to pick up the signals on the cycloheptatrienone ring.
[ii] The differences in the elemental analysis are due to the presence of solvent in the sample and decomposition of the product.

Cycloheptatriene (2.42 g, 26.2 mmol) and chromium hexacarbonyl (2.05 g, 9.32 mmol) were dissolved in anhydrous diglyme (20 mL). An air condenser with a water condenser on top was used when heating the reaction and the reaction was carried out in the absence of light and under nitrogen. The reaction mixture was heated to 160 ºC to give a red solution. During the initial heating stage, some $Cr(CO)_6$ condensed out and began to block the air condenser. This was cleared and once the reaction was refluxing the condensed solvent washed the metal complex back into the reaction flask. After 11 hours the reaction had turned brown/black and was removed from the heat. The solvent removed by rotary evaporation to give a brown oil that was dissolved in hot petroleum ether (b.p. 60 – 80 ºC), cooled and filtered to give a brown solid (0.98 g) and a red filtrate. An NMR spectrum was attempted on the brown solid. It was found to be insoluble in chloroform, acetone and only slightly soluble in DMSO, only solvent peaks appear in the NMR spectrum. The solvent was removed from the filtrate and the resulting oil was recrystallised from petroleum ether (b.p. 60 – 80 ºC). The product, when in solution, was found to be unstable in presence of light, air and also upon storage at -18 ºC, and the crude was used directly in the next reaction to prevent further decomposition during recrystallisation (see page 166). However a small portion was recrystallised to determine the NMR spectra.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.75 (1H, m, H_{7endo}), 2.96 (1H, m, H_{7exo}), 3.39 (2H, m, H_1, H_6), 4.83 (2H, m, H_2, H_5), 6.04 (2H, m, H_3, H_4).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.6 (C7), 56.6 (C1, C6), 98.1 (C2, C5) 100.9 (C3, C4), 203.7 (C=O).

υ_{max} (thin film, CH_2Cl_2)/cm^{-1}: 2917 (C-H stretch), 1974, 1906, 1882 (C=O stretches), 1456 (CH_2 bend), 528 (C-Cr bend).

4.3.7.2 Synthesis of Tricarbonyl (η^7-Cycloheptatrienyl) Chromium (41) Tetrafluoroborate.

This reaction was carried out using a similar procedure to that reported by Munro and Pauson.[51]

(40) 228.1 g/mol

(41) 313.9 g/mol

Triphenylcarbenium tetrafluoroborate (0.67 g, 2.0 mmol) in anhydrous dichloromethane (15 mL) was added dropwise to a solution of tricarbonyl cycloheptatriene chromium(0) in anhydrous dichloromethane (10 mL). The red solution turned dark green and a precipitate formed. This was filtered and washed with acetone to give the product as a deep orange solid (0.070 g, 10 %, melting point > 300 ºC).

^{1}H NMR (400 MHz, DMSO) δ: 6.71 (7H, br s).

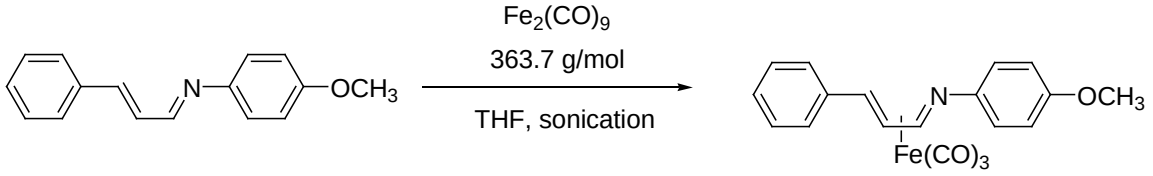
^{19}F NMR (376 MHz, DMSO) δ: -148 (BF_4).

υ_{max} (KBr)/cm^{-1}: 3022 (C-H stretch), 2008 (C=O stretch), 1633 (C=C stretch), 610 (HC=CH stretch), 499 (C-Cr bend).

4.3.8 Additional Synthesis.

4.3.8.1 Synthesis of Tricarbonyl [1-(4-Methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene] Iron (28).

This reaction was carried out using similar conditions to those described by Knölker *et al.*[26]



(31)
237.3 g/mol

(28)
373.1 g/mol

1-(4-Methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene (0.52 g, 2.2 mmol) was dissolved in anhydrous tetrahydrofuran (5 mL). Diironnonacarbonyl (0.99 g, 2.7 mmol) in anhydrous THF (10 mL) was then added to form a yellow suspension. The reaction mixture was sonicated under nitrogen at 40 kHz at a water bath temperature between 30 – 40 ºC for 16 hours to form a deep red solution. The reaction was monitored by TLC (4:1 pentane:diethyl ether). The residue was purified by flash chromatography on silica using 9:1 pentane:diethyl ether eluent to yield the product (R_f = 0.40) as a red solid (0.41 g, 50%, mp 126.1 – 126.6 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.37 (1H, d, $J_{4,3}$ = 9.2 Hz, H_4), 3.75 (3H, s, OCH_3), 5.67 – 5.70 (1H, dd, $J_{3,2}$ = 2.8 Hz, $J_{3,4}$ = 10.4 Hz, H_3), 6.74 (2H, d, J = 8.8 Hz, methoxy phenyl), 6.93 (2H, d, J = 8.8 Hz, methoxy phenyl), 7.00 (1H, d, $J_{2,3}$ = 2.0 Hz, H_2), 7.21 – 7.45 (5H, m, phenyl).

υ_{max} (KBr)/cm^{-1} : 3057 (sp^2 CH stretch), 2048, 1987, 1965 (C=O stretches), 1629 (C=N stretch), 1505 (C=C stretch), 1248 (C-O stretches), 1038 (C-N stretch).

4.4 Reagents Used for Kinetic and Equilibrium Measurements.

4.4.1 Solvents.

Methanol and acetonitrile were HPLC grade and were obtained from Sigma-Aldrich Ireland Limited. Water was HPLC grade (Romil Super Purity Solvent) obtained from Lennox Laboratory Supplies Limited.

4.4.2 Acids, Bases and Buffers.

Perchloric acid solutions were prepared from BDH Analar grade concentrated acid (70%) and standardised with sodium hydroxide solution (Fixanal®) using phenolphthalein as indicator.

Sodium hydroxide solutions were prepared from pellets (Sigma-Aldrich, ≥ 98 %) and standardized with hydrochloric acid solution (Fixanal®) using phenolphthalein as indicator.

Buffer solutions were prepared by partial neutralisation of the base with hydrochloric or perchloric acid or by partial neutralisation of the acid with sodium hydroxide. Commercial reagents were used without further purification. All pK_a values for buffers were obtained from Perrin and Dempsey.[105]

Acetate buffers were prepared from sodium acetate trihydrate (Riedel de Haën, 99.5%) and perchloric acid.

Cacodylate buffers were prepared from sodium cacodylate trihydrate (Sigma Life Sciences, 98%) and perchloric acid.

Chloroacetate buffers were prepared from chloroacetic acid (Sigma Aldrich, 99%) and sodium hydroxide.

4.4.3 Instrumentation for Kinetic and Equilibrium Measurements.

4.4.3.1 UV Spectrophotometry.

A Varian Cary 50 scan spectrophotometer was used which covered the range from 190 – 800 nm with a Xenon lamp as the light source. This spectrophotometer was a dual beam instrument and was equipped with an eighteen cell changer compartment. The instrument could be operated in either single or spectral wavelength monitoring modes. 1 cm wide quartz cuvettes fitted with Teflon caps were used and the temperature in the cell compartment was maintained at 25.0 ± 0.1 ºC by water circulated from a thermostated water bath (Julabo, ED5).

4.4.3.2 UV Spectrophotometry Using a Fast Mixing Apparatus.

To monitor reactions for which the lifetime is measured in seconds, a fast mixing apparatus must be used. For this study, an RX 2000 rapid kinetics stopped-flow mixing device accessory (Applied Photophysics) was used.[106] This allows the monitoring of reactions which are up to a thousand times faster than those which can be measured when manual mixing is performed.

A thermostatted water bath was connected to the RX 2000 accessory to maintain the temperature of the sample solution at 25.0 ± 0.1°C. The rapid mixing device contains two Hamilton syringes, which along with an inlet tube from the water bath, are connected to a specialised cuvette *via* an umbilical tube. The cell is constructed with the standard dimensions of 10 x 10 mm so as

to be readily connected to standard instrumentation with a cuvette compartment of this size. The cell is a microcell made of silica and fitted with four windows with path lengths of either 2 mm or 10 mm. During this study, a pathlength of 10 mm was used.

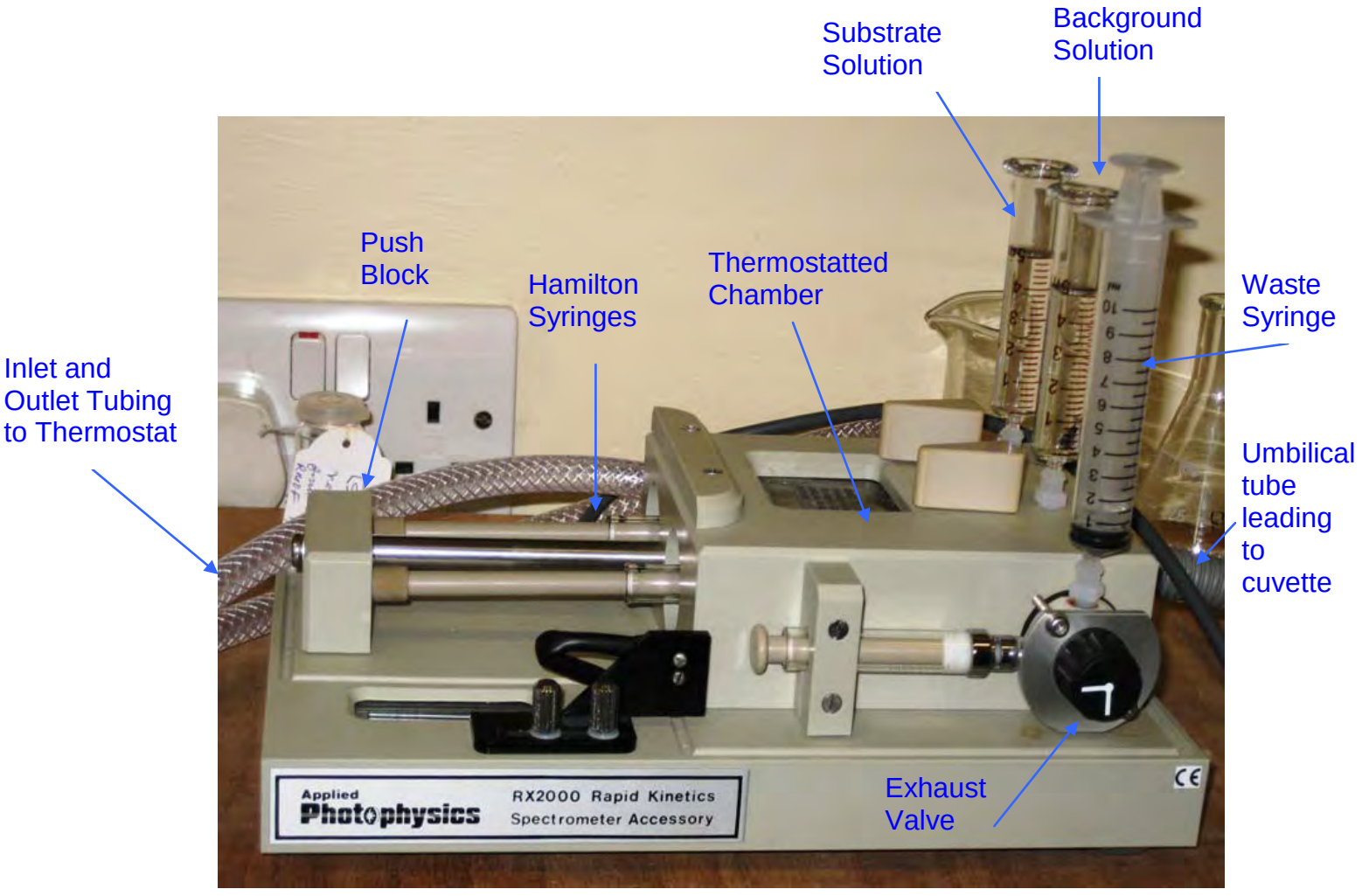


Chart 4.1 Picture of the RX 2000 Rapid Kinetics Stopped-Flow Mixing Accessory (Applied Photophysics).

4.5 Kinetic and Equilibrium Measurements.

All measurements were made at 25 ºC in aqueous solution unless otherwise stated.

4.5.1 Equilibrium Measurements.

The equilibrium constant, pK_R, obtained for the ionisation of tricarbonyl cycloheptadienenol iron **(70)** and the hydrolysis of tricarbonyl cycloheptadienyl iron **(62)** were determined from kinetic measurements for these reactions performed in aqueous solution (Section 2.2.6 pg 59).

The pK_a value obtained for the interconversion between the tricarbonyl cycloheptatriene chromium zwitterion, and its protonated form, was determined spectrophotometrically by the method of Albert and Serjeant.[107] Spectra were recorded for the fully ionised species and fully unionised species and also for the partially ionised species as described in Section 2.2.5 on page 55. The equilibrium constant for this ionisation was calculated according to the method described in Section 4.5.2 which follows.

4.5.2 Calculation of Spectrophotometrically Determined Equilibrium Constants.

Using an equilibrium method, determination of the equilibrium constant, pK_a, for formation of the tricarbonyl chromium protonated zwitterion **(69)** examined in this study involved manipulating the data to provide a plot of absorbance versus pH using Sigmaplot software.[108] The best fit line through the data points was required in order for the pK_a value to be obtained at the point of inflection. The equations governing the best fit lines were derived as follows.

The equilibrium constant, K_a, for the reaction expressed in Scheme 4.1 is given in Equation 4.1 where $[A^-]$ is the concentration of the coordinated tricarbonyl chromium zwitterion complex **(68)** and [AH] is the concentration of the coordinated protonated zwitterion **(69)**.

$$[AH] \rightleftharpoons [A^-] + [H^+]$$

Scheme 4.1

$$K_a = [A^-]\,[H^+]/\,[AH] \qquad (4.1)$$

Chart 4.2 shows the hypothetical absorbances that would be observed when the coordinated protonated zwitterion cation (A_{AH}) and coordinated zwitterion (A_{A^-}) are in their fully formed states respectively. The absorbance, A, refers to any absorbance measured when an incomplete reaction has been observed from either the cation **(69)** to the zwitterion complex **(68)** or from the zwitterion complex **(68)** to the cation **(69)**.

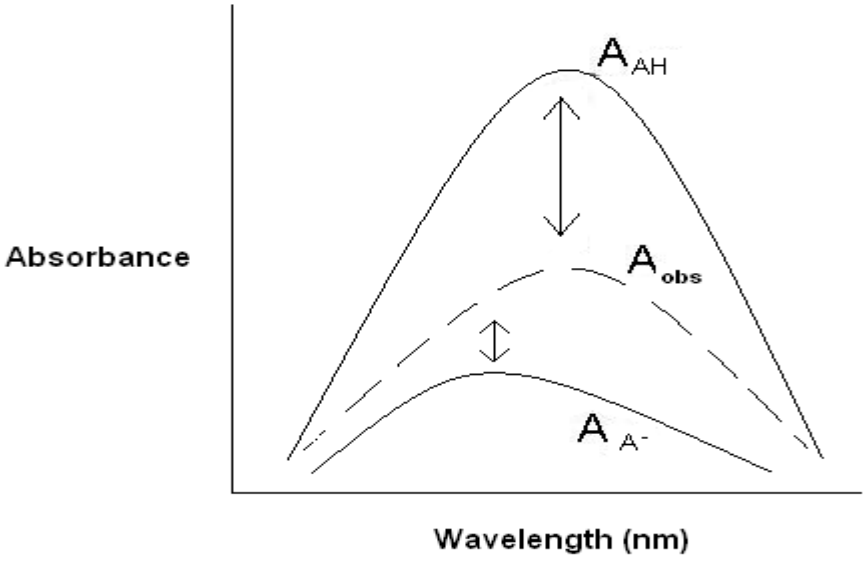


Chart 4.2 **A diagram of absorbance versus wavelength showing the hypothetical spectra of A_{AH}, A_{A^-}, and A.[60]**

Assuming the total concentration of [AH] and [A^-] remains constant, the ratio of the observed absorbances is related to the concentrations as shown in Equation 4.2.

$$(A_{AH} - A) / (A - A_{A^-}) = [A^-] / [AH] \qquad (4.2)$$

Substituting for [A^-] / [AH] in Equation 4.1 using Equation 4.2 provides Equation 4.3 which, when rearranged to express the equation in terms of A, affords Equation 4.4.

$$K_a = [H^+] \{(A_{AH} - A) / (A - A_{A^-})\} \qquad (4.3)$$

$$A = \{K_a A_{A^-} + A_{AH}[H^+]\} / \{K_a + [H^+]\} \qquad (4.4)$$

The absorbance, A, can be calculated for each pH value if [H^+], A_{A^-}, K_a and A_{AH} are known. These constraints are iterated to provide a best fit of calculated to observed values of A, showing the calculated values as a continuous plot of A versus pH. Equation 4.4, the equation that governs the absorbance versus pH plots is shown in Section 3.2 on page 90, as Equation 3.1.

4.5.3 Kinetic Measurements.

Kinetic measurements were made by accurately pipetting 2.0 cm^3 of aqueous acid or buffer solution into a 1 cm wide quartz spectrophotometric cell that was allowed to reach a constant temperature of 25 °C in the cell compartment of the spectrometer over 10 minutes. The reaction was initiated by injecting substrate solution into the reaction solution using a Hamilton microlitre syringe. The concentration of the substrate solution was usually 10^{-3} - 10^{-5} M in spectroscopic grade methanol or acetonitrile, which gave a final concentration of 10^{-5} – 10^{-6} M in the UV cell.

4.5.4 Calculations for Kinetic Measurements.

First Order Kinetics

First order rate constants, k_{obs}, determined by UV spectrophotometry were calculated in two ways:

1. By inputting absorbance versus time measurements into Sigmaplot v 8.0 software and then using the regression wizard to fit the first order plot to a regression equation. For a first order increase in absorbance with time, the data were fitted to an exponential rise to maximum as in Equation 4.5:

$$y = y_0 + a(1-e^{-bx}) \qquad (4.5)$$

   Where x = time, y = absorbance and b = k_{obs}. For a first order decrease in absorbance, the data were fitted to an exponential decay equation as in Equation 4.6:

$$y = y_0 + ae^{-bx} \qquad (4.6)$$

   Where x = time, y = absorbance and b = k_{obs}.

2. By using the UV-Vis spectrophotometer software, Cary Win UV Scanning Kinetics program v 3.0 or Cary Win UV Kinetics program v 3.0, and selecting the “analyse data” function to fit the first order plot to a regression equation. Results obtained with this software were compared to those obtained using Sigmaplot v 8.0 and they agreed. Approximately three half-lives were followed in each first order run.

Second order rate constants were obtained as $k_2 = k_{obs} / [H^+]$ or more often from a plot of k_{obs} versus $[H^+]$.

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Appendix A

Protocol for Use and Disposal of Diironnonacarbonyl

Appendix A – Protocol for Use of Diironnonacarbonyl

Handling and Storage.

- Diironnonacarbonyl must be stored under inert gas in the freezer at all times. Incorrect storage results in decomposition to produce finely divided particles of pyrophoric iron.
- Before use, the diironnonacarbonyl should be left in the fume hood for around 15 minutes before opening the container, to allow the contents to come to room temperature.
- All handling of diironnonacarbonyl must be carried out in the fume hood. It must be weighed out on a balance under a blanket of argon in the fume hood. (An inverted funnel attached to an argon line is used.)
- All glassware that will come in contact with the diironnonacarbonyl should be pre-dried in an oven and cooled in a dessicator.
- Spillages must be immediately cleaned up using acetone and 1 M aqueous HCl and all utensils that were in contact with diironnonacarbonyl must be rinsed with acetone. If pyrophoric iron develops and the material starts to produce smoke, 1M aqueous HCl should be used to quench the reacting iron.[i]
- Once opened, diironnonacarbonyl must be sealed under argon or nitrogen before returning to the freezer.
- All postgraduates handling diironnonacarbonyl must receive training from their supervisor the first time they do so.

[i] Keep 1M HCl on hand at all times when diironnonacarbonyl is in use.

Protocol for removal and treatment on pyrophoric iron, iron pentacarbonyl and triirondodecacarbonyl side products formed during reaction.[i]

- A short silica gel gravity column is performed to remove any pyrophoric iron from the reaction mixture. The silica should then be quenched using dilute HCl and water. This is left overnight and the dilute acid solution that elutes from the column can then be disposed of down the sink in the fume hood.
- Any iron pentacarbonyl formed during the reaction, isolated as a yellow liquid in the rotary evaporator trap during the work up, should be treated with the utmost care. The iron pentacarbonyl is quenched using household bleach or bromine water [prepared by shaking bromine (3g) with water (100 cm^3) until a homogenous solution is obtained]. Treatment must be carried out in the fumehood. When gas evolution stops, the solution is diluted with water and disposed of down the sink in the fumehood.
- The triirondodecacarbonyl that can form is a green solid, which is separated from the product on the second silica (flash) column. This is treated with a dilute basic solution (e.g. sodium hydroxide solution) to adjust the pH to 10-11 and is then treated with bleach. This is done slowly in order to control the temperature. The resulting solution is left to stand overnight. The solution is then adjusted to pH 7 by slow addition of dilute HCl and is then disposed of down the sink of the fume hood.
- All postgrads performing this protocol must receive training from their supervisor the first time they do so.

[i] S.E. Gibson, *Transition Metals in Organic Synthesis, A Practical Approach*, 1st ed., Oxford University Press, London, **1997**, Chapter 3.

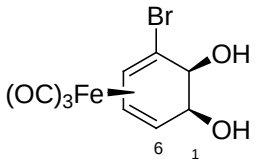
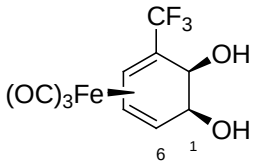
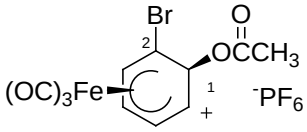
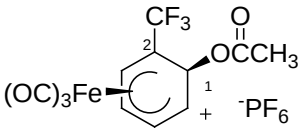
Protocol for the disposal of decomposed diironnonacarbonyl.

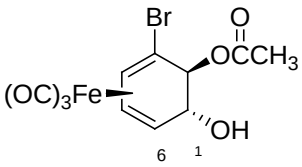
- Diironnonacarbonyl should opened with caution with 1 M HCl and a fire extinguisher on hand should any fumes or sparks be apparent.
- Into a 5 L flask, the solid is then added slowly in portions to a 1 M solution of base (e.g KOH, NaOH) of pH 10 – 11 under magnetic stirring.
- The empty containers are rinsed into the basic solution using acetone.
- Household bleach is then added slowly to the base solution, the volume depending on amount of solid being disposed, while monitoring the temperature and pH. The pH is adjusted to 10 as necessary using HCl. A gas is evolved during this process.
- The solution is stirred overnight. Thereafter, 200 mL of water is added to the flask, and the pH is then adjusted to 7 using small additions of HCl.
- This is then left to stir for 24 – 48 hours to leave a solid residue, which is then filtered and disposed of in solid waste. The filtrate is flushed down the fumehood sink with plenty of water.
- All postgrads performing this protocol must receive training from their supervisor the first time they do so

Appendix B

Structures of Complexes Prepared and Names

Compounds are named by the IUPAC system. Where more than one name is given, additional names are the commonly used names found in the literature.

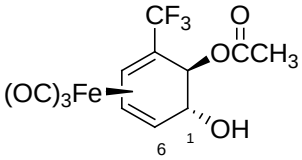
Structure	Name
 **(49)**	tricarbonyl (η^4-*cis*-3-bromocyclohexa-3,5-diene-1,2-diol) iron (0) tricarbonyl (η^4-1-*cis*-bromocyclohexa-3,5-diene-1,2-diol) iron (0)
 **(50)**	tricarbonyl (η^4-3-*cis*-trifluoromethylcyclohexa-3,5-diene-1,2-diol) iron (0) tricarbonyl (η^4-1-*cis*-triflouromethylcyclohexa-1,3-diene-5,6-diol) iron (0)
 **(51)**	tricarbonyl (η^5-1-acetoxy-2-bromocyclohexa-2,4-dienyl) iron (0) hexafluorophosphate tricarbonyl (η^5-6-acetoxy-1-bromocyclohexa-dienyl) iron (0) hexafluorophosphate
 **(52)**	tricarbonyl (η^5-1-acetoxy-2-trifluoromethyl-cyclohexadienyl) iron (0) hexafluorophosphate tricarbonyl (η^5-6-acetoxy-1-trifluoromethyl-cyclohexadienyl) iron (0) hexafluorophosphate



(53)

tricarbonyl (η^4-*trans*-2-acetoxy-3-bromocyclohexa-4,5-diene-1-ol) iron (0)

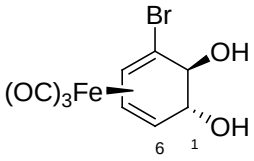
tricarbonyl (η^4-*trans*-6-acetoxy-5-hydroxy-1-bromocyclohexadiene) iron (0)



(54)

tricarbonyl *(*η^4 -*trans*-2-acetoxy-3-trifluoromethylcyclohexa-4,5-diene-1-ol) iron (0)

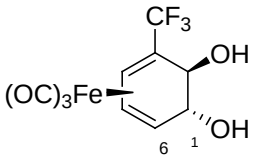
tricarbonyl (η^4-*trans*-6-acetoxy-5-hydroxy-1-trifluoromethylcyclohexadiene) iron (0)



(55)

tricarbonyl *trans*-(η^4-3-bromocyclohexa-3,5-diene-1,2-diol) iron (0)

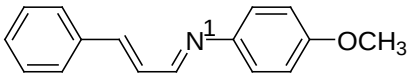
tricarbonyl *trans*-(η^4-6-bromocyclohexa-3,5-diene-1,2-diol) iron (0)



(56)

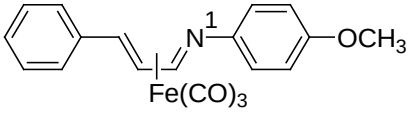
tricarbonyl *trans*- (η^4-3-trifluoromethylcyclo-hexa-3,5-diene-1,2-diol) iron (0)

tricarbonyl *trans*-(η^4-6-trifluorimethylcyclo-hexa-3,5-diene-1,2-diol) iron (0)



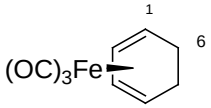
(31)

1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene



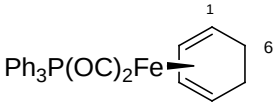
(28)

tricarbonyl [1-(4-methoxyphenyl)-4-phenyl-1-azabuta-1,3-diene] iron (0)



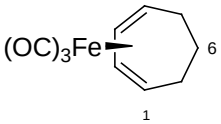
(21)

tricarbonyl (η^4-cyclohexa-1,3-diene) iron (0)



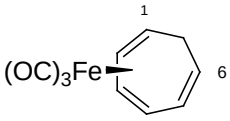
(57)

dicarbonyl (η^4-cyclohexa-1,3-diene) triphenylphosphine iron (0)



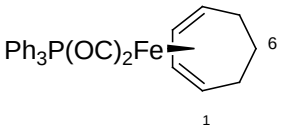
(58)

tricarbonyl (η^4-cyclohepta-1,3-diene) iron (0)



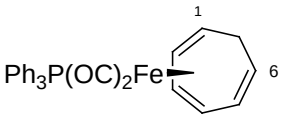
(59)

tricarbonyl (η^4-cyclohepta-1,3,5-triene) iron (0)



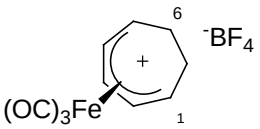
(60)

dicarbonyl (η^4-cyclohepta-1,3-diene) triphenylphosphine iron (0)



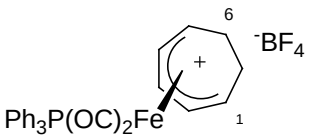
(61)

dicarbonyl (η^4-cyclohepta-1,3-triene) triphenylphosphine iron (0)



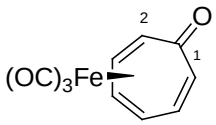
(62)

tricarbonyl (η^5-cyclohepta-1,3-dienyl) iron (0) tetrafluoroborate



(63)

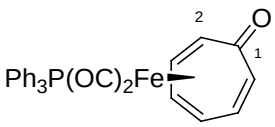
dicarbonyl (η^5- cyclohepta-1,3-dienyl) triphenylphosphine iron (0) tetrafluoroborate



(32)

tricarbonyl (n^4 -cyclohepta-2,4,6-trienone) iron (0)

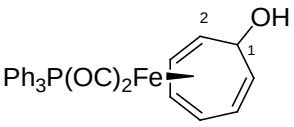
tricarbonyl tropone iron (0)



(64)

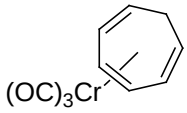
dicarbonyl (n^4-cyclohepta-2,4,6-trienone) triphenylphosphine iron (0)

dicarbonyl tropone triphenylphosphine iron (0)



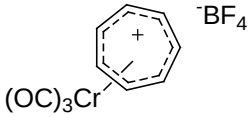
(65)

dicarbonyl (n^4 -cyclohepta-2,4,6-triene-1-ol) triphenylphosphine iron (0)



(40)

tricarbonyl (n^6-cyclohepta-1,3,5-triene) chromium (0)



(41)

tricarbonyl (n^7-cycloheptatrienyl) chromium (0) tetrafluoroborate

Appendix C

Full ^{1}H NMR Spectra Showing Decomposition Stages of (51) & Full ^{1}H NMR Spectrum of (53).

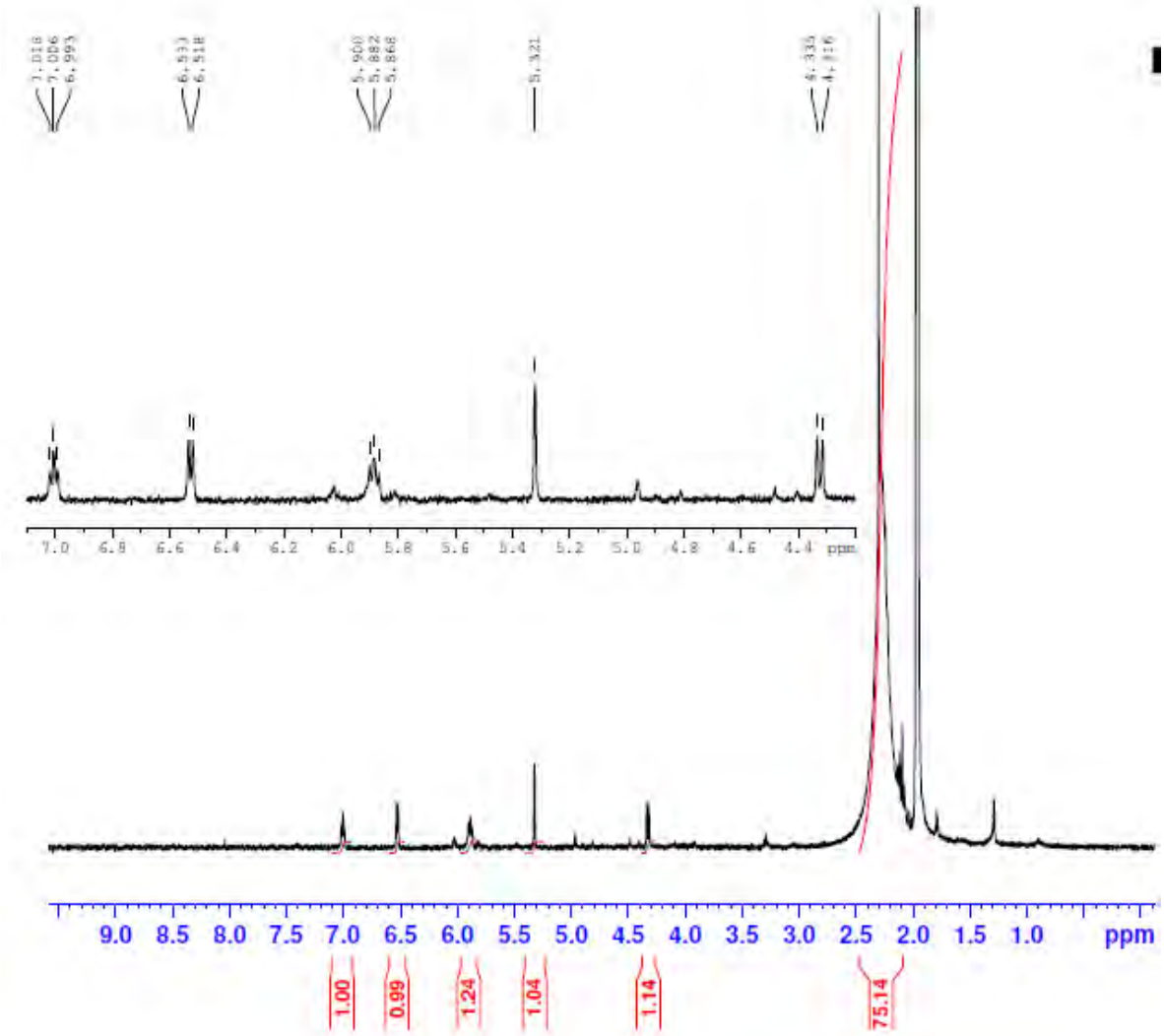


Figure A1 ^{1}H-NMR spectrum of freshly prepared tricarbonyl (η^{5}-1-acetoxy-2-bromocyclohexadienyl) iron **(51)** in deuterated acetonitrile.

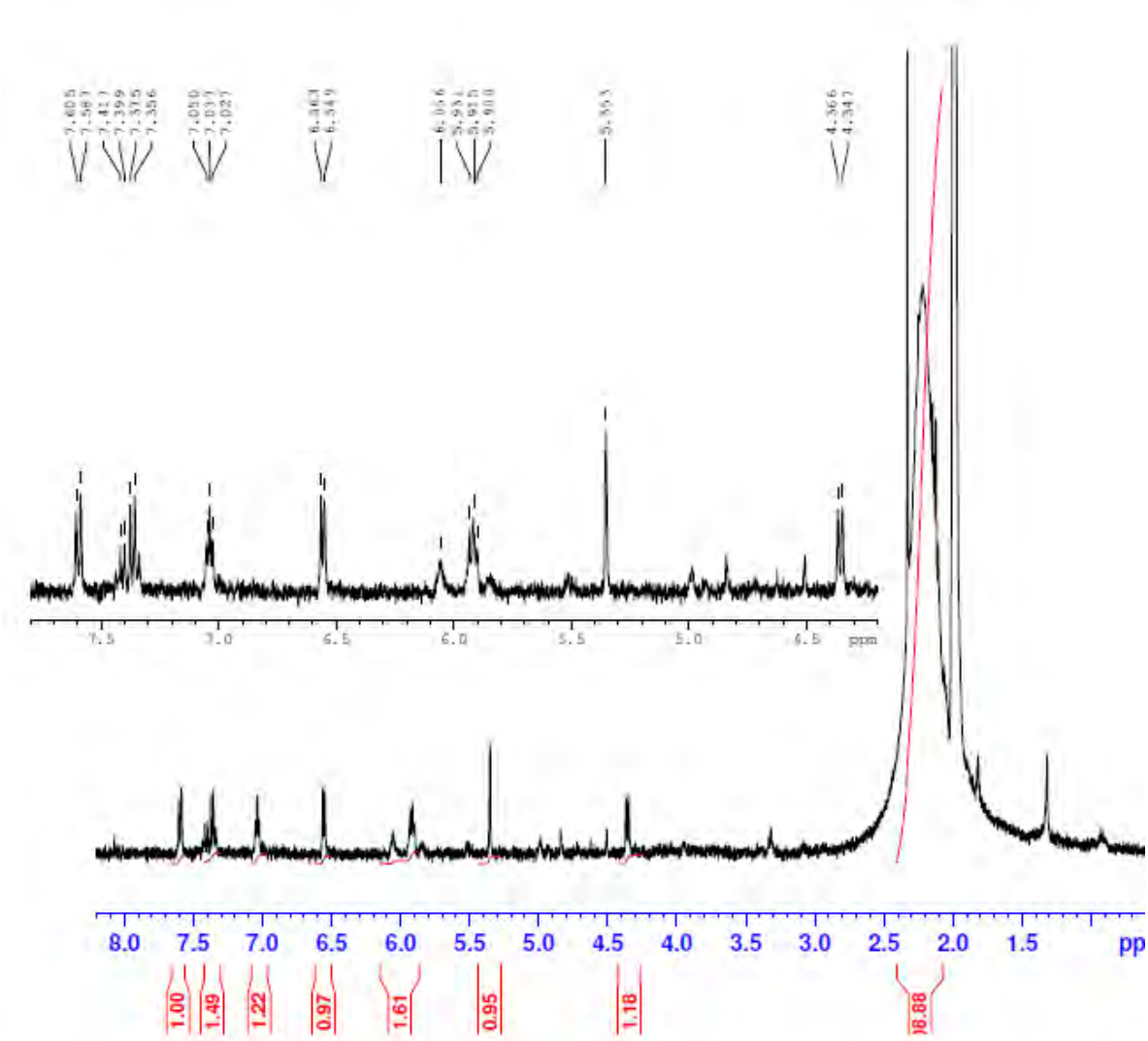


Figure A2 ^{1}H-NMR spectrum of tricarbonyl (η^{5}-1-acetoxy-2-bromocyclo-hexadienyl) iron **(51)** in deuterated acetonitrile after one day, showing the appearance of aromatic signals.

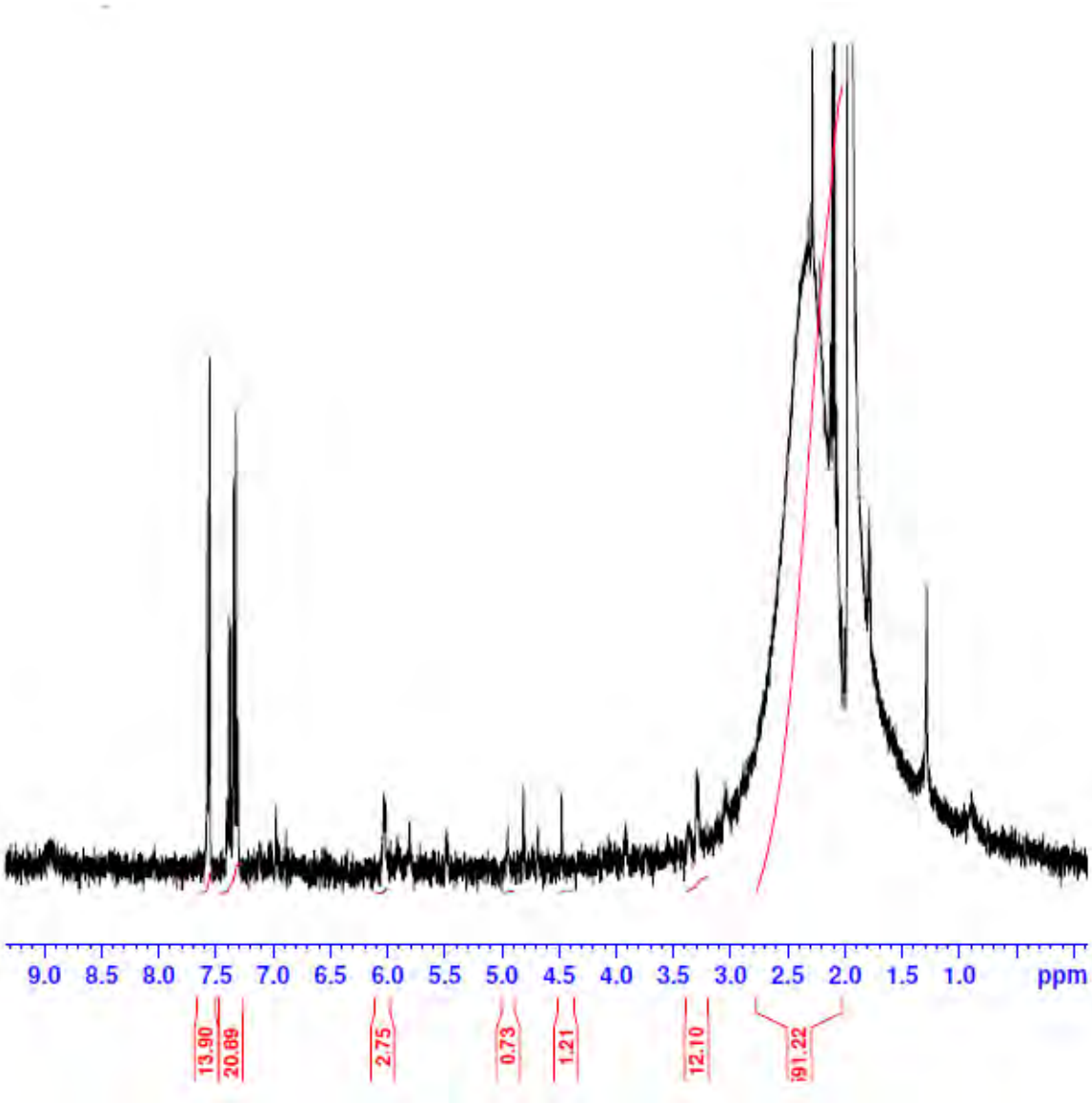


Figure A3 ^{1}H-NMR spectrum of tricarbonyl (η^{5}-1-acetoxy-2-bromocyclo-hexadienyl) iron **(51)** in deuterated acetonitrile after seven days, showing approximately 85% decomposition to bromobenzene.

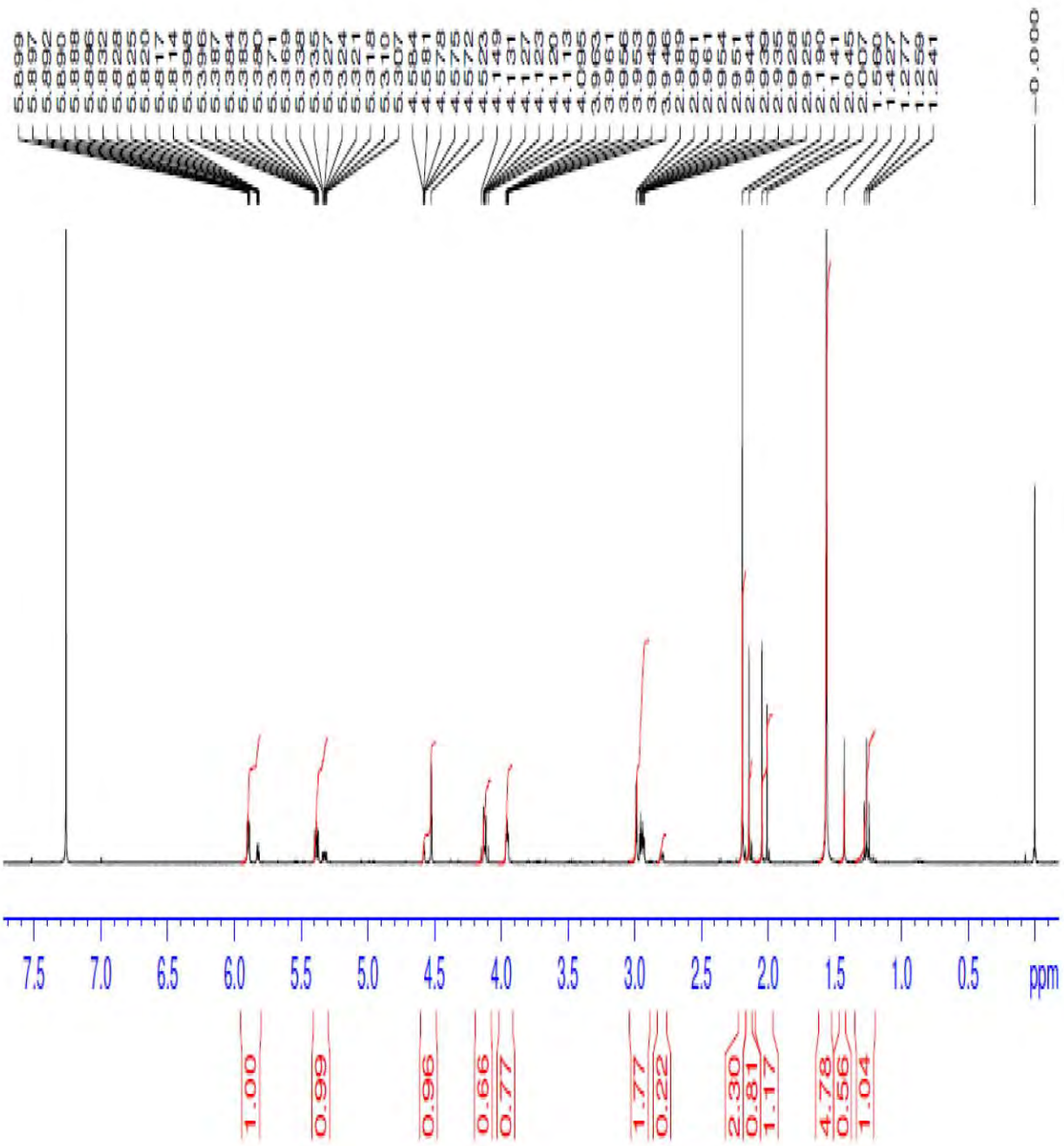


Figure A4 ^{1}H-NMR spectrum of tricarbonyl (η^4-*trans*-2-acetoxy-2-bromocyclo-hexa-4,5-diene) iron **(53)** in deuterated chloroform at 400 MHz.

Appendix D

Dissemination

Appendix D - Dissemination

Poster Presentations

"An Investigation of a Metal Complexing Route to Arene *trans*-Dihydrodiols.", C O'Connor, C. McDonnell and R. More O'Ferrall, Symposium for Physical Organic Chemistry, University of Strathclyde, Glasgow, Scotland, April 2009.

"An Investigation of a Metal Complexing Route to Arene *trans*-Dihydrodiols.", C O'Connor, C. McDonnell and R. More O'Ferrall, Chemical Synthesis and Chemical Biology Colloquium, University College Dublin, Dublin, Ireland, December 2008.