A STUDY OF SOME
TRICARBONYL(\(\eta^4\)-CYCLOHEXA-1,3-DIENE)IRON COMPLEXES
FOR USE IN ORGANIC SYNTHESIS

A thesis submitted to the Australian National University in partial fulfilment of the requirements for the degree of Doctor of Philosophy

by

B.M. RATNAYAKE BANDARA

Research School of Chemistry
Australian National University
January 1981
Dedicated to my parents

Science is merely an extension of common sense

Albert Einstein
DECLARATION

All the work reported in this thesis is the candidate's own, except where due reference is made in the text.

B.M. Ratnayake Bandara
I thank all those who have been helpful in the production of this thesis.

I am grateful to Professor A.J. Birch for inspiration, encouragement and supervision in the course of this work, and for helpful comments on the manuscript, Dr W.D. Raverty for guidance as a friend and a colleague, Dr T-C. Khor for assistance in some experiments as indicated in chapter 6 (Experimental), Professor L.N. Mander, Drs M. Bennet, G.R. Stephenson, and Mr A.I. Day for valuable discussions, Drs A. Dunand and G.B. Robertson for determination of the X-ray crystal structures of tricarbonyl(η⁴-1,6α-dimethoxycarbonylcyclohexa-l,3-diene)iron and tricarbonyl(η⁴-1,6α-dimethoxycarbonylcyclohexa-l,3-diene)iron, Dr A.S. Narula for provision of some useful references concerning gabaculine, and Mrs J. Jeffress for typing the thesis.

The award of a scholarship by the Australian National University is greatly appreciated. Grateful acknowledgement is made for the facilities provided throughout my study, and for the financial assistance to attend RACI conferences in Hobart (1979) and Melbourne (1980) by the Research School of Chemistry.
ABSTRACT

This thesis describes a study of physical and chemical properties of tricarbonyliron complexes of some substituted cyclohexadienes for their use in organic synthesis. The work is mostly on ester complexes.

In chapter 2 are discussed the methods for successful determination of the stereochemistry of a substituent attached to the cyclohexadiene ligand of a tricarbonyliron complex. The vicinal coupling constants of the hydrogens attached to the sp^3 carbons are characteristic of the stereochemistry of a substituent. This leads to typical splitting patterns for methylene protons when they are flanked by two vicinal protons. Both stereoisomers are, however, required for use of chemical shifts (^1H NMR, aromatic solvent induced shifts, lanthanide induced shifts or ^13C NMR) and mass spectroscopy for such stereochemical problems.

In chapter 3, the discussion is centred on the stereoelectronic effects in the complexation of cyclohexadienes with pentacarbonyliron. The reactive iron species [Fe(CO)]_4 or Fe(CO)]_3 may coordinate initially to an ester or an anhydride substituent. This initial chelation which leads to sterically more crowded products is, however, a competitive process between the ester or the anhydride group and the diene bonds. The classical steric hindrance of the ester group to result in less crowded stereoisomer becomes more prominent in the examples where the electron density of the olefinic bonds is increased with methoxy groups.

In chapter 4, the lateral activation by Fe(CO)]_3 group in the control of classical reactivity of substituents is illustrated with the alkaline hydrolysis of several complex esters. The l-CO_2 Me group is less reactive due to electron release from the metal to the diene, which is transmitted to the ester group probably in a mesomeric fashion. The ester groups on the same side as the metal (i.e. B) are less easily cleaved by base than
the \( \alpha\text{-C}_2\text{O}_2\text{Me} \). Half-esters are available from dicarboxylic complexes using this steric control or the electronic modulation by the \( \text{Fe(CO)}_3 \).

In chapter 5, alternative methods for the formation of cationic complexes from esters are investigated. A new method for the generation of cations was developed which involved acid-catalysed decarbonylation of \( \alpha\text{-C}_2\text{O}_2\text{H} \) groups resulting in cations. However, when confronted with a choice between decarbonylation and demethoxylation, the latter predominates. \( \text{l-Alkyl substituted cations can be obtained by dehydroxylation of alcohols obtained from the metal-alkyl reactions of ester complexes.} \)

In chapter 6, the scope of dienyl cations as synthetic equivalents is expanded with successful addition of lithiumalkyls and reversible and hindered nucleophiles such as menthol. The former has been achieved by use of methylene chloride as the solvent at low temperatures \((-78^\circ\text{C})\), the latter by use of Hünig base as a 'nucleophilic catalyst'. The optical resolution of cations is possible by use of optically active alcohols.

In chapter 7, an alternative route to the optically pure complexes of known absolute configuration is illustrated by classical resolution of tricarbonyl(\(\eta^4\)-1-carboxycyclohexa-1,3-diene)iron. The potential use of the resulting enantiomers in a novel asymmetric synthesis of natural gabaculine and a determination of its absolute configuration is indicated with regio- and stereo-selective C-N bond-formation reactions with \( \text{l-C}_2\text{O}_2\text{Me} \) salts to result in a number of gabaculine analogues.
A WORD ABOUT NOMENCLATURE AND STRUCTURE-REPRESENTATION

The IUPAC (International Union of Pure and Applied Chemistry) nomenclature is used in this thesis with the following additions.

When numbering complexes, the highest priority is always given to the metal-coordinated diene ($\eta^4$) or dienyl ($\eta^5$) system. For convenience, the hapto number $1,2,3,4,5-$ is abbreviated as $\eta^5-$ and $1,2,3,4-\eta-$ as $\eta^4-$.

The prefixes $\alpha-$ and $\beta-$ denote the steric relationship of an atom or a group to the metal; $\beta-$ indicates the same side as the metal and $\alpha-$ the opposite side (see footnote in page 4).

Thick and broken lines represent the relative stereochemistry (see footnote in page 3). In the case of an absolute configuration, the sign of the optical rotation accompanies the structure.
ABBREVIATIONS

$[\alpha]_\lambda^T$ - specific rotation at temperature $T^\circ C$ and at wavelength $\lambda$ (deg cm$^2$ g$^{-1}$)

Ar - aryl

ASIS - aromatic solvent induced shift(s)

aq. - aqueous

b.p. - boiling point

Bu - butyl

CD - circular dichroism

dil. - dilute

DMF - dimethylformamide

DMSO - dimethylsulfoxide

$\epsilon$ - molar extinction coefficient (cm$^2$ mol$^{-1}$)

Et - ethyl

$\text{Eu(fod-d_9)}_3$ - tris(1,1,1,2,2,3,3-heptafluoro-7,7-di[2H$_3$]methyl-8,8,8-[$^2$H$_3$]octane-4,6-dionate)europium(III)

h - hour(s)

i - iso, e.g. as in i-Pr

IR - infra red

LIS - lanthanide induced shift(s)

LSR - lanthanide shift reagent(s)

M - molecular ion, when mass spectral fragments are reported

- molar concentration (mol l$^{-1}$), when solutions are specified

max - maximum

Me - methyl

min - minute(s)
m.p. - melting point
MS - mass spectroscopy
n - normal, e.g. as in n-Bu
NMR - nuclear magnetic resonance
n - hapto
ORD - optical rotatory dispersion
Ph - phenyl
Pr - propyl
t - tertiary, e.g. as in t-Bu
TFA - trifluoroacetic acid
tlc - thin layer chromatography
TMS - tetramethylsilane
UV - ultra violet
v/v - volume per volume
Chapter 1

Scheme 1.1 Some chemical transformations of tricarbonyl($n^4$-2-methoxycyclohexadienylium)iron hexafluorophosphate to illustrate its synthetic equivalence to aryl and cyclohexa-2-enone fragments

Scheme 1.2 Some substituted tricarbonyl(cyclohexadienyl)iron cations as synthetic equivalents

Scheme 1.3 Some chemical routes to the formation of tricarbonyl-(cyclohexadienyl)iron cations from neutral complexes

Chapter 2

Table 2.1 Chemical shifts of allylic methoxycarbonyl and methine protons

Table 2.2 Some examples to illustrate the consistency of coupling constants in a given steric series

Table 2.3 Dihedral angles from X-ray structures

Table 2.4 Aromatic solvent induced shifts (ASIS)

Table 2.5 $^{13}$C NMR chemical shifts

Table 2.6 Major mass spectral fragments of some dicarbonyliron complexes

Table 2.7 Some mass spectral fragments of isomeric tricarbonyl-($n^4$-dimethoxycarbonylcyclohexa-1,3-diene)iron complexes

Figure 2.1 Methylene splitting pattern characteristic of an adjacent $\alpha$-substituent

Figure 2.2 $\text{CH}_2(\alpha)$-splitting patterns; computer-simulated and observed

Figure 2.3 Methylene splitting pattern characteristic of an adjacent $\beta$-substituent

Figure 2.4 $\text{CH}_2(\beta)$-splitting patterns; computer-simulated and observed

Figure 2.5 Shifts of $\text{CO}_2\text{Me}$ resonances on sequential addition of $\text{Eu(fod-d)}_9$$_3$

Chapter 3

Table 3.1 Product distribution in the reaction of methyl cyclohexa-2,5-dienecarboxylate with $\text{Fe(CO)}_5$ under different conditions
Complexation of blocked dienes

Theoretically possible steric approaches of Fe(CO)$_n$ to the nuclear bonds of dimethyl cyclohexa-2,5-diene-1,3-dicarboxylate and the resulting allyl intermediates leading to all six possible isomeric complexes

Alkaline hydrolysis of esters with excess 20% aqueous NaOH/MeOH

Some crystal data of tricarbonyl(n$_4$-1,6$\beta$-dimethoxycarbonylcyclohexa-1,3-diene)iron

Some crystal data of tricarbonyl(n$_4$-1,6$\alpha$-dimethoxycarbonylcyclohexa-1,3-diene)iron

Some examples for bond shortening due to mesomeric involvement of the diene

Involvement of carbanions in the conversion of $\beta$-CO$_2$Me complexes to $\alpha$-CO$_2$H and 1-CO$_2$Me complexes under alkaline hydrolysis conditions

Possible routes to the formation of unsubstituted and 1-CHO cations from 1-carboxyl complexes

Products from the reactions of tricarbonyl(n$_4$-5$\alpha$,5$\beta$-dimethoxycarbonylcyclohexa-1,3-diene)iron with MeLi and MeMgBr

A possible mechanism for the formation of tricarbonyl(n$_4$-5$\beta$-methoxycarbonylcyclohexa-1,3-diene)iron from tricarbonyl(n$_4$-5$\alpha$,5$\beta$-dimethoxycarbonylcyclohexa-1,3-diene)iron

Some examples to illustrate the availability of procationic complexes from aromatic substrates

Products from the reaction of tricarbonyl(cyclohexadienyl)iron cations with lithiumalkyls in methylene chloride
### CONTENTS

#### Chapter 1

**Introduction**

1.1 The tricarbonyliron group as a modulator for electronic requirements  
1.2 Stereo- and regio-selective C-C and C-X bond formation with tricarbonylcyclohexadienyliron salts  
1.2.1 Cationic complexes as synthetic equivalents  
1.3 Availability of cationic complexes  
1.3.1 Hydride abstraction  
1.3.2 Acid-catalysed demethoxylation  
1.4 Acid-catalysed isomerisation  
1.5 Introduction of Fe(CO)$_3$ to the organic ligand  
1.5.1 Complexation of cyclohexadienes  
1.5.2 Stereo- and enantio-selectivity of complexation  
1.6 Fe(CO)$_3$ as a cis-diene protecting group, and stereo- and regio-control factor for classical reactivity  
1.7 Removal of Fe(CO)$_3$ from the organic ligand  
1.8 Present project  

#### Chapter 2

Stereochemistry of tricarbonylcyclohexa-1,3-dieniron complexes  

2.1 Introduction  
2.2 $^1$H NMR chemical shifts  
2.3 Splitting patterns  
2.3.1 α-Stereochemistry  
2.3.2 β-Stereochemistry  
2.4 Lanthanide induced shifts (LIS); stereochemistry and basicity  
2.5 Aromatic solvent induced shifts (ASIS)  
2.6 $^{13}$C NMR  
2.7 Tricarbonylcyclohexadienyliron cations  
2.8 Mass spectrometry  
2.9 Remarks in conclusion
Chapter 3
Stereoselectivity of complexation of cyclohexadiene esters with pentacarbonyliron

3.1 Introduction
3.2 Is isomerisation of ester complexes possible during their formation?
3.3 Effect of complexation conditions
3.4 Effect of more polar and sterically bulky substituents
3.5 Effect on stereochemistry of increased electron availability in the olefinic bonds (methoxy substituents)
3.6 Effect of an electron withdrawing substituent at the olefinic site (methoxycarbonyl group)
3.7 Effect of methyl substituents
   3.7.1 Complexation of blocked cyclohexa-1,4-dienes
3.8 Steric effects in cyclohexa-1,3-dienes
3.9 Conclusion

Chapter 4
Tricarbonyliron as a lateral control group in the alkaline hydrolysis of some cyclohexa-1,3-diene esters

4.1 Introduction
4.2 Monocarboxylic esters; regioselectivity
4.3 Dicarboxylic esters
4.4 Blocked ester complexes; stereoselectivity
4.5 Outlook

Chapter 5
Tricarbonylcyclohexadienyliron salts from decarbonylation and dehydroxylation; procationic complexes

5.1 Introduction
5.2 Acid-catalysed decarbonylation
5.3 Dehydroxylation
   5.3.1 Alcohols from ester complexes
   5.3.2 Cations from alcohols
   5.3.3 l-Substituted cations from unsubstituted cations
5.4 Summary: aromatic substrates + procationic complexes + organic cations
Chapter 6

The formation of C-C and C-X (X = O, S, Se) bonds by reaction of tricarbonylcyclohexadienyliron salts with lithiumalkyls and labile RXH (R = alkyl and aryl)

6.1 Introduction 73
6.2 Alkylation with lithiumalkyls 74
6.3 Reactions with RXH 75
6.4 Outlook 79

Chapter 7

Enantiomeric tricarbonyliron complexes of known absolute configuration via optical resolution of tricarbonyl(n^1-carboxycyclohexa-1,3-diene)iron; approaches to the asymmetric synthesis of natural gabaculine

7.1 Introduction 80
7.2 Optical resolution of tricarbonyl(n^1-carboxycyclohexa-1,3-diene)iron and the absolute configuration of the products 84
7.3 Approaches to the synthesis of natural gabaculine 87
7.4 Outlook 87

Experimental

General 89
Chapter 2 91
Chapter 3 94
Chapter 4 109
Chapter 5 124
Chapter 6 138
Chapter 7 144

References 153
CHAPTER 1

INTRODUCTION

A major factor in organic synthesis is the proper activation and protection of simpler structural units for construction of complex molecules. The enormous number of organotransition-metal compounds, synthesised since the discovery of ferrocene in 1951, provides an almost limitless variety of electronic and steric potentialities from which activating and protecting groups may be selected.

Metal complexes may be used in organic synthesis either as catalysts or stoichiometric reagents. When used in stoichiometric amounts, careful consideration need be given to cost of starting materials, convenience in preparation and handling of intermediate complexes, ready application of the known chemical reactions on the coordinated organic ligand, and facile removal of the metallic group under mild conditions. A group of compounds which appear to satisfy these criteria, are the tricarbonyliron complexes of dienes.

There are three mechanistic features of the tricarbonyliron group in diene complexes, that are useful to rationalize the chemistry of these compounds and to understand the activating and protecting effect of Fe(CO)₃. They are the electronic modulator action of Fe(CO)₃ (e.g. stabilisation of otherwise unstable dienes and dienyl cations), its lateral steric situation with respect to the organic ligand (e.g. stereo-selectivity, chirality), and its involvement in allyl intermediacy (e.g. rearrangements with some electron-deficient reagents leading to specific products). Examples are discussed below, particularly in relation to some chemistry of tricarbonylcyclohexa-1,3-dieneiron complexes.
1.1 The tricarbonyliron group as a modulator for electronic requirements

The introduction of a Fe(CO)₃ may increase the resonance energies of the dienyl system. Consequently, reactive dienyl species which may be useful as structural units in synthesis, can be trapped as stable tricarbonyliron complexes. Examples include Fe(CO)₃ complexes of cyclobutadiene (1), quinodimethane (2), the enone tautomer of phenol (3) and the cyclohexadienyl cation (4).

Stability of 1 as well as its ability to undergo aromatic substitution reactions may be considered to result from withdrawal of electrons by Fe(CO)₃ from an otherwise antiaromatic cyclobutadiene. The isolation of 2 and 3 may be rationalized by similar electronic considerations. The remarkable stability of 4 compared to that of protonated benzene may be accounted for by delocalisation of the positive charge on to the metal. Alternatively viewed, the metal now releases electrons from its d-orbitals to the electron-deficient organic ligand.

This electronic modulator action by Fe(CO)₃, i.e. electron release or withdrawal as required by the organic ligand, is also manifested in a variety of physical and chemical properties of a number of diene complexes, e.g. IR spectra, X-ray structure parameters, dipole moment measurements, oxidation potential measurements, Hammet plots, chemical shifts, pKₐ values, change in properties upon displacement of a CO by cyclopentadienyl ligand, and acetylation at the phenyl ring.
attached to a terminal position of a diene complex under mild conditions.\textsuperscript{24c}

The modulator action of Fe(CO)\textsubscript{3} is understandable in terms of molecular orbital theories\textsuperscript{26} for diene complexes.\textsuperscript{27} The electron transfer to the metal may occur from the bonding \(\pi\)-orbitals of the diene to the empty hybrid orbitals of the metal; this is also referred to as 'forward coordination'. Flow of electron density to the organic ligand, also known as back-donation, is possible from the filled d-orbitals of the metal to the low-lying anti-bonding \(\pi\)-orbitals of the dienyl system.\textsuperscript{28}

The complex 1 has been used as an equivalent of cyclobutadiene in the synthesis of Dewar benzenes,\textsuperscript{29} cubanes\textsuperscript{30} and several other polycyclic systems.\textsuperscript{18} 2-Indanones have been obtained from 2.\textsuperscript{31} The enone 3 is a mild arylating agent for aromatic amines.\textsuperscript{32} A variety of nucleophiles has been added to 4 resulting in the formation of C-C and C-X (\(X = H, \text{halogen, N, P, O, S}\)) bonds;\textsuperscript{2,9} the selectivity of such processes are discussed below.

1.2 Stereo- and regio-selective C-C and C-X bond formation with tricarbonylcyclohexadienyliron salts

\begin{center}
\begin{tikzpicture}
% Diagram code here
\end{tikzpicture}
\end{center}

(see footnote\textsuperscript{1})

\footnote{The structures represent (\(\pm\))-compounds, unless stated otherwise.}
The nucleophiles usually add to one terminus of the cyclohexadienyl segment, although addition of iodide\(^{33}\) to the metal has been noted. Addition to the organic ligand takes place, with few exceptions,\(^{34}\) stereospecifically \(\alpha\) to the iron group, as evidenced by X-ray studies\(^{35}\) and spectral and chemical information.\(^{14,32,36}\) \(\beta\)-Adducts have been observed with reversible nucleophiles like alcohols in the presence of acid,\(^{34a}\) or when the addition may occur via initial coordination\(^{37}\) of the nucleophile to the metal group, for example metal hydride donors.\(^{34b}\) In the case of reversible nucleophiles like alcohol, initial coordination to a metal carbonyl may still afford the \(\alpha\)-adducts\(^{38}\) possibly through a dissociative rearrangement of a carboalkoxy intermediate.\(^{39}\)

Another attractive feature of this reaction as well as steric control is the frequent regioselectivity in the case of unsymmetrical cations. The adducts from 1-CO\(_2\)Me (5) and 2-OMe (6) cations, for example, usually correspond to reaction at the 5-position.\(^{9a,40}\)

*Nomenclature in this series is confusing; "endo" to Fe(CO)\(_3\) is "exo" to the carbon ring, and it seems better to the organic chemist to use a more neutral system of designation. Natural product nomenclature is adapted here to designate groups on the same side as Fe(CO)\(_3\) by \(\beta\)- and on the opposite side by \(\alpha\)-.
The 2-methyl cation in this series, however, which is a much more weakly directing group, clearly shows some dependence of regioselectivity on the nature of the nucleophile. Reagents like aromatic amines, 1,2-bis(trimethylsiloxy)-1-cycloalkenes and allyl silanes react exclusively at the 5-position of the cation, while hydride (from sodium borohydride), cyanide and hydroxide add to both 1- and 5-positions in approximately equal proportion.

In order to understand the regiochemistry of the additions, attempts have been made by Davies, Green and Mingos to derive correlations with charge distributions and molecular orbital considerations. Such approaches in conjunction with steric factors may be useful for predictive purposes. The kinetic studies of these reactions by Kane-Maguire et al. may prove helpful to rationalize the role of nucleophiles and the reaction conditions on regioselectivity.

A kinetic study in this laboratory of the reaction of a series of substituted dienyl salts with acetylacetone has provided a quantitative estimate of the dependence of reactivity on cation substitution. 2-Methoxy substituted cations were found to react more slowly than the unsubstituted salts while 1-methoxycarbonyl substituted salts react faster. Multisubstitution appears to display additive effects.

1.2.1 Cationic complexes as synthetic equivalents

The above selective bond-forming reactions, with or without further modification in the organic ligand, and accompanied by the removal of metal, would lead to the designation of these cyclohexadienyl salts as synthetic equivalents. This is initially discussed for cyclohexa-1,3-dienyl, aryl and cyclohex-2-enone fragments.

As an illustration, the reactions of the 2-0Me cation with sodium cyanide and trialkynylborate salts are shown in Scheme 1.1. The 2-0Me
Scheme 1.1. Some chemical transformations of tricarbonyl(n°-2-methoxy-cyclohexadienylium)iron hexafluorophosphate (6) to illustrate its synthetic equivalence to aryl and cyclohexa-2-enone fragments.
Scheme 1.2. Some substituted tricarbonyl(cyclohexadienyl)iron cations as synthetic equivalents.
cation may be considered as the equivalent of cyclohexa-1,3-dienyl (7),
aryl (8) and cyclohexa-2-enone (9) fragments. Other substituted cations
may be viewed similarly as depicted in Scheme 1.2.

One example of the designated steric significance of the positive
charge is that an enantiomeric cation will lead to production of the
diene or the enone as one optical isomer, of known absolute configuration
if that of the cation is known.

A racemic cation and a chiral nucleophile, on the other hand, will
produce a diastereomeric mixture which upon successful separation will
yield optical antipodes of the complexed portion. In the case of reversible
nucleophiles, chiral cations may be obtained from the separated mixture.
However, this strategy for production of chiral cations has not been
realized hitherto because of the lack of efficient mild methods to add
hindered but labile and reversible nucleophiles to these cations. A
potentially useful method is discussed in chapter 6.

The successful application of these cations as synthetic equivalents
in organic synthesis depends on the range of nucleophiles available for
efficient formation of C-C bonds. More 'fundamental' reagents like
Grignard reagents, lithiumalkyls\textsuperscript{14} and lithium enolates\textsuperscript{49} have resulted in
decomposition or reductive dimerisation of the salt, consequently leading
to poor or no yield of the expected adducts. The decomposition may be a
result of irreversible addition to the metal group. Radical intermediacy
may be a plausible explanation for dimeric products which have also been
observed in the reaction of Zn or Zn/Cu couple with both cyclic\textsuperscript{9a} and
acyclic\textsuperscript{52} dienyl salts.

Success has been achieved by use of milder alkylating reagents, e.g.
dialkylcadmium and dialkylcuprate,\textsuperscript{53} or 'masked' reagents, e.g. enamines,\textsuperscript{54}
allyl silanes\textsuperscript{43} and silyl derivatives of enol ethers.\textsuperscript{42,55} A successful
re-examination of lithiumalkyls in these reactions is presented in chapter 6.
Scheme 1.3. Some chemical routes to the formation of tricarbonyl(cyclohexadienyl)iron cations from neutral complexes.
In favourable cases, these cations may be used in the synthesis of natural products. A potential application of \(1\text{-CO}_2\text{Me}\) cation may be, for example, a new synthesis of natural gabacluline (chapter 7).

\[
\text{CO}_2\text{H} \\
\text{NH}_2
\]

### 1.3 Availability of cationic complexes

The interaction of some diene complexes with appropriate electrophiles which are compatible with the \(\text{Fe(CO)}_3\) group may lead to the formation of cations. The interaction usually involves a detachment of an allylic atom (e.g. \(\text{H}^\Theta\) by \(\text{Ph}_3\text{C}^\Theta\)) or a group (e.g. \(\text{OMe}^\Theta\) by \(\text{H}^\Theta\)). In some cases, a positive centre generated initially at a carbon external to the ring may shift on to an allylic position in the ring (Scheme 1.3).

Possible elaboration of these principles (Scheme 1.3) to define new and alternative routes to prepare cations is illustrated in chapter 5 with the examples of acid-catalysed decarbonylation of carboxy complexes, and dehydroxylation of alcohols derived from the carboxyl complexes.

#### 1.3.1 Hydride abstraction

Hydride abstraction from neutral complexes, resulting in cation formation, is usually effected by brief treatment with \(\text{Ph}_3\text{C}^\Theta\text{PF}_6\) or \(\text{Ph}_3\text{C}^\Theta\text{BF}_4\) in acetonitrile or methylene chloride. The salts are commonly isolated by precipitation on addition of ether. When prolonged reaction conditions are applied, it is desirable to treat the trityl reagent with a solid base (e.g. \(\text{CaCO}_3\) or \(\text{MgCO}_3\)) to prevent complications due to possible acid-catalysed rearrangements.
In the tricarbonylcyclohexene-1,3-diene transition state, it is usually an α-hydrogen which is abstracted, presumably because the steric bulk of the reagent (Ph₃C⁺) and the Fe(CO)₅ precludes 6-attack. The abstraction of β-hydrogen, however, has been noted in a few cases where sterically rigid Fe(CO)₅ complexes with alkenes. 2,4-Diene and 3-cholesta-1,3-diene are examples of alkenes which undergo rapid opening in the course of the reaction. This is possibly due to scrambling of the metal from one face to the other in the course of the reaction, which case the terminal olefin.

Another stereoelectronic feature of the abstraction reaction is that the presence of an α-substituent (e.g., alkyl) on the adjacent carbon prevents hydride removal. The reaction can, therefore, be rationalized in terms of the abstractor's involvement of their steric environment.

In unsymmetrical complexes, the reactivity and regioselectivity of the abstraction is dependent on the nature and the position of the substituents. The products are often diastereomeric complexes where a single hydride is abstracted irreversibly. The behavior of the substituted complexes may be rationalized by assuming that the transition state of the reaction is closer to the carbene products, as the reaction is more syn-selective. In this case, the carbene is an excellent nucleophile and the rate is affected by the absolute configuration of the carbene. The syn preference is best for donor groups such as Me₂CO and dienyl.

A model which is useful for estimation of the distribution of positive charges in unsymmetrical carbene complexes is the formal charge on the carbene. The possible order of stability is: formal charge 1, 2 > 3, 4 > 2, 4 > 1.

Alternative methods for formation of carbene complexes are desirable because hydride abstraction by Ph₃C⁺ becomes more rapid under the conditions of the reaction.
In the tricarbonylcyclohexa-1,3-dieneiron series, it is usually an α-hydrogen which is abstracted, presumably because the steric bulk of the reagent (Ph₃C⁺) and the Fe(CO)₃ precludes β-attack. The abstraction of β-hydrogen has, however, been noted in a few cases where sterically rigid Fe(CO)₃ complexes of cholesta-2,4-diene and 5α-cholesta-1,3-diene were treated under prolonged vigorous conditions. This is possibly due to scrambling of the metal from one face to the other in the course of the reaction, in which case the α-rule still hold.

Another stereochemical feature of the abstraction reaction is that the presence of an α-substituent (e.g. alkyl) on the adjacent methylene carbon prevents hydride removal. The reaction can, therefore, be employed as an alternative method for separation of α- and β- substituted isomers and establishment of their stereochemistry.

In unsymmetrical complexes, the regioselectivity of hydride abstraction is dependent on the nature and the position of substituents. The products from 1-substituted complexes where 5α-H is abstracted predominantly may reflect the steric influence of the substituent. The behaviour of 2-substituted complexes may be rationalized by assuming that the transition state of the reaction is closer to the cationic products, on the basis that the reaction is under kinetic control. The electron-withdrawing CO₂Me prefers attachment to less positively charged position, while the converse is true for donor groups such as OMe.

A model which is useful for estimation of the distribution of positive charge on the individual carbons is based on ¹³C NMR studies of the cations. A possible order of magnitude of formal charge on the dienyl segment is: 1,5-C < 3-C < 2,4-C.

Alternative methods for formation of cations are desirable because hydride abstraction by Ph₃C⁺ imposes what are often undesirable steric
requirements in the precursor, i.e. absence of \(\alpha\)-substituents, and it frequently also lacks regioselectivity.

1.3.2 Acid-catalysed demethoxylation

Demethoxylation is normally performed by dropwise addition of the methoxy complex to ice-cold concentrated sulfuric acid\(^{50}\) containing a little formic acid.\(^{34b}\) Decomposition is apparently reduced in the presence of a small concentration of carbon monoxide provided by the formic acid. For isolation purposes, the cation is then converted into the hardly-soluble PF\(_6\) salt by an anion exchange reaction with aqueous NH\(_4\)PF\(_6\).

Products from demethoxylation\(^{9a,50}\) show that the carbon to which the methoxy group was formerly attached, always finishes up at one terminus of the resulting dienyl cation. Thus, in favourable cases, it is possible to prepare specifically substituted single cations even from mixtures of neutral isomeric complexes.

The product, the 3-Me cation \(\text{13}\) in the example quoted, cannot be obtained pure by hydride abstraction\(^{14}\) from the corresponding neutral complex.

The protonation of basic groups (e.g. morpholino) present on the diene carbons appears to inhibit demethoxylation. A complication is noted also in the 1,4-dimethoxy complex \(\text{14}\) where the expected 2-OMe cation \(\text{6}\) is formed only in poor yield, the enone \(\text{3}\) being the major product.\(^{65}\)
It has been shown\textsuperscript{9a,50} by use of deutero-acid that the mechanism for demethoxylation appears to be analogous to that for acid-catalysed isomerisation of neutral complexes\textsuperscript{66} (section 1.4), where the protonation of the iron occurs initially. The probably reversible series of isomerisations essentially leads to irreversible loss of OMe as shown.

Parenthetically quoting, acylium ions from Friedel-Crafts reagents, presumably being intermediate between H\textsuperscript{+} and Ph\textsubscript{3}C\textsuperscript{+} in size, can either
abstract a hydride or undergo electrophilic substitution reaction through iron-mediation as in the case of acid-catalysed isomerisation. The nature of products of this reaction considerably depends on the reaction conditions.

1.4 Acid-catalysed isomerisation

Tricarbonylcyclohexa-1,3-dieneiron complexes in the presence of protic acids, isomerise to give products with an overall shift of the coordinated double bonds around the cyclohexane ring. In cases examined so far, methoxycarbonyl substituents appear to finish at the 1-position, but alkyl substituents at the 2-position. This dependence on the nature of the substituent of the occupation of specific positions in the equilibrated product is understandable by virtue of the fact that an electron withdrawing substituent, capable of mesomeric interaction with the diene system, should encourage more back-donation to greater stability of the complex, when it is in linear conjugation with the diene system.

Isomerisations of unsubstituted and alkyl substituted complexes with deuterio acids give products corresponding to deuterium incorporation at both the \( \beta \)-positions (e.g. \( { }^{17} \overset{D}{H} \) and \( { }^{17} \overset{D}{H} \)). This implies initial deuteration (or protonation) at the iron, consistent with a large deuterium isotope effect. It is postulated that subsequent transfer of
the deuterium on the β-face to one terminus of the diene segment results in an allyl intermediate (e.g. 15) by analogy with intermediates which have been isolated\textsuperscript{73} in the acyclic series, during similar reactions resulting in syn-anti isomerisations. Such an allyl intermediate may lose a proton via Fe(CO)\textsubscript{3} to yield a new neutral complex.

Both 1-CO\textsubscript{2}Me (11) and 2-CO\textsubscript{2}Me (12) complexes give only the mono-deuterated product 18.\textsuperscript{51} To explain this requires the postulation of a selective transfer of the proton to one terminus only of the diene. Proton transfer seems to occur in such a way that the methoxycarbonyl occupies one end of the resulting allyl intermediate\textsuperscript{51,74} (cf. 15).

These acid-catalysed isomerisation of alkyl or methoxycarbonyl substituted complexes can provide new and specifically substituted isomers. In conjunction with the removal of iron, with or without further elaboration, the reaction would lead to potential availability of a wide range of specifically substituted cyclohexa-1,3-dienes.

1.5 Introduction of Fe(CO)\textsubscript{3} to the organic ligand

The precursors for the above cations are tricarbonylcyclohexa-1,3-dieneiron complexes which can be prepared by thermal or photochemical reaction\textsuperscript{24c} of an appropriate organic ligand with an iron carbonyl reagent.
capable of releasing an Fe(CO)₃ moiety. The organic precursors can be cyclohexa-1,3-dienes,⁷⁵ their isomers, particularly 1,4-dienes,⁷⁶ or 1,3-diene equivalents such as cyclohexenes with a detachable substituent at an allylic position.⁷⁷ The available Fe(CO)₃ equivalents include Fe(CO)₅, Fe₂(CO)₉, Fe₃(CO)₁₂ and Fe(CO)₃ complexes of α,β-unsaturated ketones.⁹,⁷⁸ The most commonly used method involves boiling the appropriate diene with Fe(CO)₅ with reflux in a high boiling, inert or weakly coordinating solvent, usually di-n-butyl ether.⁹, 36, 78b The other three reagents only need milder conditions. Fe(CO)₃ complexes of α,β-unsaturated ketones, however, effectively transfer the Fe(CO)₃ moiety to 1,3-dienes only.⁷⁹ Fe(CO)₅ may be used as a milder reagent in the presence of an oxidative reagent like Me₃N⁸⁰ which presumably assists the breakdown with loss of carbonyl to give the intermediate coordinatively unsaturated iron species such as Fe(CO)₄.

Complexation may occur via reactive Fe(CO)₄⁸¹ or Fe(CO)₃⁸² which are generated by thermal, photolytic or oxidative cleavage of the iron carbonyl reagent. Which species is involved primarily, has not been established with certainty.

1.5.1 Complexation of cyclohexadienes

A number of reports provides methods for preparation of cyclohexa-1,3-dienes.⁸³ A convenient and direct method for the preparation of cyclohexa-1,4-dienes is the Birch reduction of benzenoid compounds⁸⁴ although other methods like Diels-Alder condensation of acyclic precursors are also available.⁸⁵

Benzenoid compounds from which 1,4-dienes have been derived for complexation include benzene,⁸⁶ methylenbenzene, dimethylbenzenes,⁵⁰ trimethylbenzene,⁸⁶b, 87 methoxybenzene,¹⁴, 36, 50 dimethoxybenzenes,¹⁴, 65 methoxymethylbenzenes,¹⁴, 36, 50 benzoic acid, 2-methylenbenzoic acid,⁵¹ methoxybenzoic acids,⁷⁰ naphthalenes,¹⁴ and anthracenes.¹⁴, 88
In most cases, cyclohexa-1,4 dienes yield mixtures of isomeric tricarbonylcyclohexa-1,3-dieneiron complexes. Mechanistic studies of the isomerisation show that no free conjugated diene is involved in the process. The study by Alper et al. using cyclohexa-1,4-diene with both methylene groups deuterated gave a deuterium distribution in the product, which led these authors to suggest an allyl intermediate in the reaction.

Further support for the involvement of an allyl intermediate comes from the complexation of 4-vinylcyclohexene and (+)-limonene, the related iron carbonyl-promoted rearrangements of mono-olefines, and the thermal rearrangement of deuterium labelled tricarbonyl(1-phenylcyclohexa-1,3-diene)iron.

1.5.2 Stereo- and enantio-selectivity of complexation

Examples in the literature give some indication of the steric course of the complexation. (-)-Phellandrene, for example, gives the α-isopropyl isomer as the major product. It is possible that complexation leads to the preferential formation of the thermodynamically more stable isomer. Alternatively, the product distribution may be determined kinetically by the steric hindrance exerted by the isopropyl group towards the approach of reactive iron carbonyl species, Fe(CO)ₙ (n = 3 or 4).
In cases where such a substituent group may form a weak association with the metal moiety during complexation, the metal may be directed towards the more hindered face of the diene. Whitesides et al.\(^9\) have observed the thermodynamically less stable \(\beta\)-isomer 20 as one of the products in the reaction of enneacarbonyliron with a mixture of cis- and trans-dimethyl cyclohexa-2,5-dienecarboxylate. A similar observation has been made\(^7,9\) in the complexation of methyl cyclopropane-2,3-dicarboxylate where the \(^1\)H NMR of the mixture of isomeric complexes indicates tricarbonyl(5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene)iron as the major product. An elaborate study of this reaction (chapter 3) is useful, in view of the resulting availability of a method for the preparation of otherwise less available \(\beta\)-isomers. The latter compounds being available, it may also be possible to find correlations between stereochemistry and spectral properties (chapter 2), although it has been noted\(^5,7\) previously that Fe(CO)\(_3\) operates a deshielding effect on the \(\beta\)-substituents in the \(^1\)H NMR.
In all cases so far examined, metal carbonyl promoted isomerisation of unconjugated dienes is a highly stereoselective process. Consequently, isomerisations involving chiral dienes will result in efficient production of optically active complexes. (+)-Limonene and (+)-carvone are two such examples. The Fe(CO)$_3$ complexes of (+)-pulegone and (-)-3β-acetyloxypregna-5,16-diene-20-one have been reacted with prochiral 1-methoxycyclohexa-1,3-dienes. So far optical yields (<40%) of these reactions appear too low to justify use of these complexes in asymmetric synthesis. The low enantiomeric excess may be accounted for either by thermal liberation of free Fe(CO)$_3$ species, or lack of specificity in the initial complexation of the enone. Another possibility is that the transfer process may not be totally specific. The enantiomeric excess may be increased by effecting the induction under appropriate low temperature or other conditions.
1.6 Fe(CO)$_3$ as a cis-diene protecting group, and stereo- and regio-control factor for classical reactivity

Complexed dienes, π-electrons being involved in coordination to iron, do not show the usual diene reactions like Diels-Alder cycloadditions or catalytic hydrogenations. The Fe(CO)$_3$ group has been used in this respect to protect the cis-diene system of some terpenes and steroids.

The work of Barton et al. and Birch et al. in the synthesis of epiergosterol, illustrates how the reactivity of a carbonyl function on the organic ligand can be influenced by the Fe(CO)$_3$ group. The bulk of the Fe(CO)$_3$ hinders approach of the hydride reagent to the face of the ligand to which the metal is attached, resulting in stereospecific reduction of the ketone and formation of the alcohol.
An example of regio-control by the Fe(CO)$_3$ on the reactivity of a substituent may be found in hydrolysis of CO$_2$Me complexes.\textsuperscript{51} The 1-CO$_2$Me complex 11 is inert to alkaline hydrolysis while the 2-CO$_2$Me isomer 12 readily cleaves to give the corresponding acid. Under acidic conditions, however, the 1-CO$_2$Me complex 11 can be hydrolysed to yield the 1-CO$_2$H complex. Further investigation of the reaction is desirable in order to understand the role of Fe(CO)$_3$, and to more fully define its scope as a selective reaction in synthesis and for structural studies. Chapter 4 describes present attempts along these lines including steric effects by Fe(CO)$_3$ on the reaction.

### 1.7 Removal of Fe(CO)$_3$ from the organic ligand

In order to gain the maximum benefit from Fe(CO)$_3$ complexes in organic synthesis, a method for efficient disengagement of the organic ligand from the metal must be available. Ligand displacement and oxidation are two possible approaches. Stronger coordinating ligands like triphenylphosphine have been noted to displace either CO or the diene.\textsuperscript{98} However, application of this method is not general because the Fe-diene
bond is rather strong due to synergic bonding interactions and, therefore, it may be difficult to cleave during displacement reactions.

Oxidation at the Fe(CO)₃ group is the more common method. The possible oxidants include ammonium ceric nitrate,⁹⁹ Collins reagent,¹⁰⁰ manganese dioxide,¹⁴ ferric chloride,⁹⁷,⁹⁹b,¹⁰¹ cupric chloride,¹⁰² silver nitrate,¹² lead tetraacetate,³⁰ and trimethylamine-N-oxide.¹⁰³ Caution needs to be exercised in the choice of oxidant and also the reaction conditions because, unlike the case of acyclic diene complexes, the liberated cyclohexadienes are often prone to further oxidation to highly stable aromatic species.

When aromatic products are required, Pd/C may be used in benzene or toluene under reflux conditions.¹⁴ In this case it is possible that the diene is aromatised prior to the cleavage of the metal. A tricarbonyliron group coordinated to benzene is unstable, as many attempts to prepare benzene-Fe(CO)₃ have been unsuccessful.²⁸ Examples of iron coordinated to benzene can be found in sandwich complexes of the type ²₃¹⁰⁴ (also see section 2.8).

With certain combinations of oxidants and complexes, the oxidation may take place at the organic ligand rather than at the Fe(CO)₃ group. Oxidative cyclisation resulting in furanoid systems has been observed by
use of manganese dioxide, thallium trifluoroacetate or ferric chloride on silica gel on certain alcohols, the hydroxy group of which is two carbons away from an allylic carbon. The hydroxy group may be available in the form of a keto-enol equilibrium.

An unusual and possibly synthetically useful reaction is the oxidation of the compounds of the type 24 with I2/pyridine to afford 3-methylcarbazoles

The reaction conditions, the products and their yields being variable, the oxidant of choice for a given system is usually found after a large amount of trial and error. Commercially available trimethylamine-N-oxide dihydrate in N,N-dimethylacetamide has proved to be useful in several cases where the dienes are not sensitive to base-catalysed isomerisation.
According to mechanistic studies, initial attack of Me₃NO at the electron-deficient C atom of Fe-CO results in elimination of a CO₂ molecule, leading to the formation of an aminedicarbonyliron intermediate. The analogous stepwise cleavage of CO from this intermediate would lead to the observed diene.

\[
diene-\text{Fe}(\text{CO})_3 + \text{Me}_3\text{NO} \rightarrow diene-\text{Fe}(\text{CO})_2.\text{NMe}_n + \text{CO}_2
\]

\[
diene-\text{Fe}(\text{CO})_2.\text{NMe}_n \rightarrow \text{diene}
\]

1.8 Present project

Despite the expected high stability of tricarbonyldieneiron complexes with electron-withdrawing substituents, rather little chemistry has been explored in the cyclohexadiene series with substituents like CO₂Me₅₁,₇₀ and Cl₅₈. The diene precursors for the former are easily available from reduction of aromatic compounds. This thesis is centred on a study of spectroscopic and chemical properties of carboxyl complexes for their use in organic synthesis.

The points that highlight the present project in the previous discussion are noted here. The complexation of diene esters may provide β-substituted complexes otherwise less available from other methods, which are also required to establish an efficient model for assignment of α- and β-stereochemistry (chapter 2). The complexation process itself is of particular interest, in view of a study on stereo-electronic effects in the introduction of the Fe(CO)₃ group to the organic ligand (chapter 3).

Alkaline hydrolysis of esters may be useful as an example for demonstration of regio- and stereo-control effects of the Fe(CO)₃ group on classical reactivity, and also as a tool for selective reactions in synthesis (chapter 4). It has already been shown with esters in the tricarbonylcyclobutadieneiron series that a variety of classical organic reactions
may be applied at the ester group in these complexes. Conversions into acids and alcohols are rather important, in view of alternative methods for formation of cyclohexadienyl cations, e.g. decarboxylation and dehydroxylation (chapter 5). Carboxy groups may provide a useful handle for optical resolution of these complexes realizing their use in asymmetric synthesis, e.g. natural gabaculine (chapter 7).

Investigation with some cationic complexes of methods for effective formation of C-C bonds with reactive nucleophiles, e.g. lithiumalkyls, and C-X (X = O, S, Se) bonds with labile and reversible nucleophiles, e.g. phenols and hindered alcohols, is presented in chapter 6.
CHAPTER 2

STEREOCHEMISTRY OF TRICARBONYLCYCLOHEXA-1,3-DIENEIRON COMPLEXES

2.1 Introduction

A knowledge of the configuration is of fundamental importance in discussing the stability and reactivity of a compound. Empirical rules which seem to hold in suggesting stereochemistry of the title compounds are: cationic complexes react under kinetic control entirely or mainly from the α-face (section 1.2); hydride abstraction by Ph₃C⁺ usually occurs at the α-face and is prevented by the presence of an α-substituent (section 1.3.1); some electrophilic substitutions, e.g. Frêdel-Crafts acetylation, mainly occur on the β-face (section 1.3.2); rearrangements catalysed by acid occur on the β-face (section 1.4). Deductions from these rules lead to a coherent set of conclusions in accord with experimental results.

However, a direct means for determination of the configuration, other than X-ray analysis, would provide useful confirmations in routine applications. The possible applicability of NMR and mass spectra (MS) in this connection has been examined. The conclusions which emerge are that if a pair of stereoisomers is available these spectral methods indicate with a fair degree of certainty which has the α- and which the β-substituent. With the possible exception of examination of splitting patterns of CH₂ adjacent to the substituted position, discussed below, no clear absolute determination seems possible at present with one isomer only. In the case of dienyl cations, stereochemistry may be assigned by consideration of the splitting of 6-H.
RESULTS AND DISCUSSION

The epimeric diesters 25 and 26 are available (chapter 3), and their structures have been confirmed by X-ray analysis.\textsuperscript{111} NMR techniques for steric determinations involve chemical shifts and coupling constants, particularly in relation to the use of different solvents and lanthanide shift reagents (LSR).\textsuperscript{112}

\(^1\text{H} \) NMR shifts on the dienyl segment of both neutral and cationic complexes have been extensively used to assign regiochemistry.\textsuperscript{14,36,70} An analysis of long range H,H coupling in relation to the planarity of the diene segment is found in the literature.\textsuperscript{113} The examination here for stereochemistry is concentrated on the protons attached to tetrahedral carbons and to the substituent itself.
The chemical shift of the $\beta$-CO$_2$Me in the diester 25 ($\delta$ 3.66) is slightly higher than that of the $\alpha$-CO$_2$Me in 26 ($\delta$ 3.60) in agreement with the generally observed deshielding effect of Fe(CO)$_3$ on $\beta$-substituents. 53c, 70, 114

The isomeric monoesters 27 and 28, reported earlier as a mixture, 51, 70 have now been separated (section 3.2). Only one isomer of the pair was observed to undergo hydride abstraction and on this basis it was assigned the structure 27. This assignment is in accord with the chemical shift of the $\beta$-CO$_2$Me ($\delta$ 3.65) which is higher than the $\alpha$-CO$_2$Me ($\delta$ 3.56). Table 2.1 gives the chemical shifts of a range of CO$_2$Me (25 - 36) which, on the assumption that $\beta$-CO$_2$Me resonates at lower field than the $\alpha$-CO$_2$Me, form a self consistent set of data supported by consideration of the CH$_2$ splitting pattern data below. It is also consistent with other information including in some cases relative rates of hydrolysis (chapter 4). A generally observed feature is that $\beta$-CO$_2$Me appear at $\delta \geq 3.63$ and $\alpha$-CO$_2$Me
<table>
<thead>
<tr>
<th>δ₂-CO₂Me (compound)</th>
<th>δα-CO₂Me (compound)</th>
<th>Δδ₂-CO₂Me α-CO₂Me</th>
<th>δβ-H (compound)</th>
<th>δα-H (compound)</th>
<th>Δδβ-H α-H</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.66</td>
<td>3.60</td>
<td>0.06</td>
<td>3.50</td>
<td>2.40</td>
<td>1.10</td>
</tr>
<tr>
<td>(25)</td>
<td>(26)</td>
<td></td>
<td>(26)</td>
<td>(25)</td>
<td></td>
</tr>
<tr>
<td>3.65</td>
<td>3.56</td>
<td>0.09</td>
<td>2.90</td>
<td>2.48</td>
<td>0.42</td>
</tr>
<tr>
<td>(27)</td>
<td>(28)</td>
<td></td>
<td>(28)</td>
<td>(27)</td>
<td></td>
</tr>
<tr>
<td>3.63</td>
<td>3.60</td>
<td>0.03</td>
<td>3.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(29)³⁰</td>
<td>(30)³⁰</td>
<td></td>
<td>(30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.63</td>
<td>3.55</td>
<td>0.08</td>
<td>3.26</td>
<td>2.92</td>
<td>0.34</td>
</tr>
<tr>
<td>(31)</td>
<td>(32)</td>
<td></td>
<td>(32)</td>
<td>(31)</td>
<td></td>
</tr>
<tr>
<td>3.76</td>
<td>3.63</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(33)⁴⁹</td>
<td>(34)⁴⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.70</td>
<td>3.62</td>
<td>0.08</td>
<td>3.40</td>
<td>2.97</td>
<td>0.43</td>
</tr>
<tr>
<td>(35)</td>
<td>(35)</td>
<td></td>
<td>(35)</td>
<td>(35)</td>
<td></td>
</tr>
<tr>
<td>3.73</td>
<td>3.63</td>
<td>0.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(36)</td>
<td>(36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Δδ₂-CO₂Me α-CO₂Me = δ₂-CO₂Me - δα-CO₂Me; Δδβ-H α-H = δβ-H - δα-H
at $\delta \leq 3.63$ so that on this basis alone a reasonably certain assignment of stereochemistry requires both isomers.

The proton attached to the same carbon as the allylic substituent also shows (Table 2.1) significant effects of $\alpha$- or $\beta$-configuration, the $\beta$-H resonating at lower field than the corresponding $\alpha$-H by 0.34 - 1.10 ppm. Based on these and previous conclusions, it can be suggested that $\delta_{\beta-CO_2Me} > \delta_{\alpha-CO_2Me}$ and $\delta_{\beta-H} > \delta_{\alpha-H}$, enabling members of available pairs to be distinguished.

2.3 Splitting patterns

The methylene protons adjacent to the carbon to which an $\alpha$- or $\beta$-substituent is attached, display splitting patterns characteristic of the stereochemistry. In some cases, the patterns are discernible only in the presence of a lanthanide shift reagent (LSR). In the following discussion, the methylene splitting pattern characteristic of an adjacent $\alpha$-substituent is referred to as "CH$_2(\alpha)$-splitting". Analogously, "CH$_2(\beta)$-splitting" implies the pattern for a $\beta$-substituent.

2.3.1 $\alpha$-Stereochemistry

R = N$_3$ (37), OMe (32), OPh (40), SPh (41), CN (43), CMe$_2$CHO (45), CO$_2$H (46)

At $\delta \leq 3.63$ so that on this basis alone a reasonably certain assignment of stereochemistry requires both isomers.

The proton attached to the same carbon as the allylic substituent also shows (Table 2.1) significant effects of $\alpha$- or $\beta$-configuration, the $\beta$-H resonating at lower field than the corresponding $\alpha$-H by 0.34 - 1.10 ppm. Based on these and previous conclusions, it can be suggested that $\delta_{\beta-CO_2Me} > \delta_{\alpha-CO_2Me}$ and $\delta_{\beta-H} > \delta_{\alpha-H}$, enabling members of available pairs to be distinguished.

2.3 Splitting patterns

The methylene protons adjacent to the carbon to which an $\alpha$- or $\beta$-substituent is attached, display splitting patterns characteristic of the stereochemistry. In some cases, the patterns are discernible only in the presence of a lanthanide shift reagent (LSR). In the following discussion, the methylene splitting pattern characteristic of an adjacent $\alpha$-substituent is referred to as "CH$_2(\alpha)$-splitting". Analogously, "CH$_2(\beta)$-splitting" implies the pattern for a $\beta$-substituent.

2.3.1 $\alpha$-Stereochemistry

R = N$_3$ (37), OMe (32), OPh (40), SPh (41), CN (43), CMe$_2$CHO (45), CO$_2$H (46)
A range of α-substituted complexes, some examples of which are given above, showed CH₂ splitting patterns similar to that of the α-CO₂Me diester 26 (Fig 2.1). The compounds 37 - 45, 49 - 52 and 54 - 61 were available from the addition of appropriate nucleophiles to the corresponding salts. The assignment of the α-stereochemistry to the compounds which were prepared by the sequence complexation and acid-catalysed isomerisation (47, section 4.2) or base-catalysed hydrolysis (46 and 48, sections 4.2 and 4.3.1), was based on the observation that they were unaffected by Ph₃C⁺.

The coupling constants and the chemical shifts responsible for the pattern were deduced from the spectra which had reasonably large Δν/J...
Figure 2.1. Methylene splitting pattern characteristic of an adjacent α-substituent.
TABLE 2.2

Some examples to illustrate the consistency of coupling constants (Hz) in a given steric series

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Compound</th>
<th>$J_{\alpha, \beta}$</th>
<th>$J_{6, \beta}$</th>
<th>$J_{6, \alpha}$</th>
<th>$J_{4, \beta}$</th>
<th>$J_{4, \alpha}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>15.5</td>
<td>12.0</td>
<td>3.7</td>
<td>3.5</td>
<td>2.8</td>
</tr>
<tr>
<td>40</td>
<td>15.5</td>
<td>11.0</td>
<td>4.0</td>
<td>3.5</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>(15.1)$^{58}$</td>
<td>(9.1)$^{58}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>15.5</td>
<td>10.0</td>
<td>4.0</td>
<td>4.0</td>
<td>3.0</td>
</tr>
<tr>
<td>47</td>
<td>16.0</td>
<td>10.0</td>
<td>4.0</td>
<td>3.5-4.0</td>
<td>3.0</td>
</tr>
<tr>
<td>49</td>
<td>15.0</td>
<td>10.0-11.0</td>
<td>3.5-4.0</td>
<td>3.5</td>
<td>2.5-3.0</td>
</tr>
<tr>
<td>54</td>
<td>15.0</td>
<td>10.0</td>
<td>4.0</td>
<td>3.5</td>
<td>3.0</td>
</tr>
</tbody>
</table>
By application of double-resonance techniques, the spin-monocoupling also showed that the long-range couplings would be insignificant in this respect, the important contributors being chemical and vicinal couplings. The coupling constants were, surprisingly, of the same order of magnitude. Non-representative examples are given in Table 2.2.

\[
\begin{array}{cccc}
\text{Computer - simulation} & \Delta \delta_0, \text{p.p.m.} & \text{Observed} & \text{e.g.} \\
0.87 & & & 49 \\
0.35 & & & 43, 52 \\
0.16 & & & 46 \\
-0.15 & & & 62 \\
-0.28 & & & 62, 62 \\
-0.36 & & & 62 \\
\end{array}
\]

**Figure 2.2.** CH$_2$(α)-splitting patterns; computer-simulated and observed.
values, by application of double-resonance techniques. The spin-decoupling also showed that the long-range couplings would be insignificant in this respect, the important contributors being geminal and vicinal couplings. The coupling constants were, surprisingly, of the same order of magnitude. Some representative examples are given in Table 2.2.

A computer-simulation (NMRSIM program)\(^1\)\(^{42}\) of the CH\(_2\)(\(\alpha\))-splitting was performed, based on \(J\) and \(\delta\) values indicated for the \(\alpha\)-CO\(_2\)Me diester 26 in Fig 2.1. \(\Delta\delta^\beta_\alpha\) (\(= \delta_\beta\)-H of CH\(_2\) - \(\delta_\alpha\)-H of CH\(_2\)) was varied. Results are depicted in Fig 2.2. Several compounds corresponded to the patterns where \(\Delta\delta^\beta_\alpha\) = 0.35 to 1.00 ppm, e.g. 37-45, 47-61 and 63.

\[\text{L} = \text{CO(62), PPh}_3(63)\]

An example for a more complicated pattern, possibly due to a small \(\Delta\delta^\beta_\alpha\), is provided by the \(\alpha\)-COMe complex 62 whose stereochemistry has been unambiguously determined by Lewis \textit{et al.}\(^{35a}\). The replacement of one carbonyl by a Ph\(_3\)P (63)\(^{68a}\) results in the typical CH\(_2\)(\(\alpha\))-splitting pattern (Fig 2.1), with the possible indication that \(\Delta\delta^\beta_\alpha\) may be increased appreciably by appropriate ligand displacements.

In the presence of Eu(fod-d\(_5\))\(_3\), \(4 \times 10^{-1}\) mol \(g^{-1}\), the compound 62 showed CH\(_2\)(\(\alpha\))-splitting but with effective reversal of the order of chemical shifts (\(\delta\)) for \(\text{H}_\beta\) and \(\text{H}_\alpha\) of the methylene protons. The computer simulation corresponded to \(\Delta\delta^\beta_\alpha\) = - 0.36 ppm. The LSR upon complexation with the \(\alpha\)-acetyl group, produces a greater downfield shift at the adjacent \(\alpha\)-H than at the corresponding \(\beta\)-H.
Magnetically the CH$_2$ protons can be made significantly non-equivalent in the presence of a paramagnetic shift reagent or by appropriate ligand displacement, and the simplified pattern can lead to the deduction of coupling constants. The use of LIS seems superior to ligand displacement because the latter process cannot be effected directly and reversibly.

2.3.2 β-Stereochemistry

In the presence of Eu(fod-d$_9$)$_3$, 1.5 x 10$^{-1}$ mol g$^{-1}$, the β-CO$_2$Me ester gave the pattern shown in Fig 2.3, from which, $\Delta \nu / J$ being significantly large, the appropriate $\delta$ and $J$ were extracted in the usual way for computer simulation studies.

The simulation of the CH$_2$(β)-splitting by variation of $\Delta \delta_{\alpha}^\beta$ gave patterns resembling those resulted from sequential addition of LSR to the β-CO$_2$Me diester 25 (Fig 2.4).

\[
\begin{align*}
R^2 &= H; R = CO_2Me(27), CO_2H (64), \\
&= CO_2CH_2CO(O)Br (65), Me (66)^44 \\
R^2 &= OMe; R = Me (67)^36
\end{align*}
\]

Simulation of the CH$_2$(β)-splitting of the compounds 27, 64 and 65 required $\Delta \delta_{\alpha}^\beta = 0.35$ ppm. Both β-Me complexes 66 and 67 gave patterns corresponding to $\Delta \delta_{\alpha}^\beta = -0.60$ and -0.80 ppm, respectively. The structures
Figure 2.4. CH$_2$(β)-splitting patterns; computer-simulated and observed.
Figure 2.3. Methylene splitting pattern characteristic of an adjacent $\beta$-substituent.
Dihedral angles from X-ray structures

<table>
<thead>
<tr>
<th>Dihedral angle (°)</th>
<th>25</th>
<th>26</th>
<th>33</th>
<th>68*</th>
</tr>
</thead>
<tbody>
<tr>
<td>6(β) - C(6) - C(5) - H_β</td>
<td>15(1)</td>
<td>0(3)</td>
<td>3(2)</td>
<td>3(3)</td>
</tr>
<tr>
<td>6(β) - C(6) - C(5) - H_α</td>
<td>106(2)</td>
<td>118(3)</td>
<td>120(2)</td>
<td>107(5)</td>
</tr>
<tr>
<td>6(α) - C(6) - C(5) - H_β</td>
<td>133(1)</td>
<td>123(2)</td>
<td>114(2)</td>
<td>112(3)</td>
</tr>
<tr>
<td>6(α) - C(6) - C(5) - H_α</td>
<td>12(2)</td>
<td>5(2)</td>
<td>32(2)</td>
<td>7(5)</td>
</tr>
<tr>
<td>R(4) - C(4) - C(5) - H_β</td>
<td>57(2)</td>
<td>54(3)</td>
<td>50(2)</td>
<td>30(6)</td>
</tr>
<tr>
<td>R(4) - C(4) - C(5) - H_α</td>
<td>64(2)</td>
<td>69(3)</td>
<td>69(2)</td>
<td>81(6)</td>
</tr>
<tr>
<td>θ</td>
<td>43.4</td>
<td>42.1</td>
<td>42.5</td>
<td>42.3</td>
</tr>
</tbody>
</table>

θ = the angle between the normals to the planes through C(1), C(2), C(3), C(4) and C(4), C(5), C(6), C(1)

* For compound 68, the deviations have been calculated from the assumed errors in the location of H atoms from electron density difference maps.
of 65, 66 and 67 have been confirmed by either conversion to known compounds (e.g. $65 \rightarrow 27$, section 3.4) or by hydride abstraction (e.g. 67).

It is very likely that $\beta$-H of the CH$_2$ of 66 and 67 resonates at a higher field than its epimeric $\alpha$-H.

Consistency in coupling constants for a given steric series, in spite of the diversity of substituents, suggests that the dihedral angles possibly featuring Karplus relations, $^{117}$ may be approximately uniform for these complexes. A justification comes from the torsional angles extracted from the X-ray structures $^{111}$ of 25, 26, 35 and 68 (Table 2.3).

2.4 Lanthanide induced shifts (LIS); stereochemistry and basicity

Shift reagents have been used in classical organic chemistry $^{112}$ and in one instance to differentiate isomeric tricarbonyldieneiron complexes in a mixture. $^{34a}$

Fig 2.5 shows the shifts (CO$_2$Me resonances) on sequential addition of Eu(fod-d$_9$)$_3$ to CDCl$_3$ solutions of the diesters 25, 26 and 35. With increasing concentration the $\alpha$-CO$_2$Me of 35 increased in $\delta$ to a greater extent than the $\beta$-CO$_2$Me of the same molecule. This was anticipated; Fe(CO)$_3$ should hinder the complexing of the $\beta$-CO$_2$Me.

Another conclusion from shift studies on 25 and 26 is an indication of the high basicity of the 1-CO$_2$Me compared to the 6-CO$_2$Me, already
Figure 2.5. Shifts of CO$_2$Me resonances on sequential addition of Eu(fod-d$_9$)$_3$.
TABLE 2.4

Aromatic solvent induced shifts (ASIS)

\[ \Delta_\delta^{\text{CDCl}_3} = \delta^{\text{CDCl}_3} - \delta^{\text{C}_6\text{D}_6}, \text{ ppm} \]

<table>
<thead>
<tr>
<th>Compound</th>
<th>ASIS ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{Fe} )</td>
<td>+0.08</td>
</tr>
<tr>
<td>( \text{OC}_3 )Fe</td>
<td>+0.64</td>
</tr>
<tr>
<td>( \text{OC}_3 )Fe</td>
<td>+0.76</td>
</tr>
<tr>
<td>( \text{OC}_3 )Fe</td>
<td>+0.78</td>
</tr>
</tbody>
</table>

The complexes 25, 26 and 27 have been examined (Table 2.4) in terms of the relationship of benzene with the diene forming the NOR and 1,3-diene-1,3-diene. In the parent tricarbonyl-cyclohexa-1,3,5-triene, 1,3-diene from the Fe(III) produces a very strong shift compared with the uncomplexed diene. With an Fe(III) complex, no similar effect is observed with a reduction of ASIS for H -0.18 ppm and -0.04 for the diene and 1,3-diene, respectively. 25 does not at present seem possible to derive concrete correlations to assign stereochemistry on the basis of ASIS alone.
inferred from very slow alkaline hydrolysis of the $1-\text{CO}_2\text{Me}$ (chapter 4). The slope of the plot of LIS vs. concentration of the reagent is a measure of binding.\textsuperscript{118} Both $25$ and $26$ showed a significantly larger slope for the $1-\text{CO}_2\text{Me}$ than the $6-\text{CO}_2\text{Me}$. The much greater selectivity that manifests between the $1$- and $6\beta-\text{CO}_2\text{Me}$ of $25$ compared with the $\alpha$- and $\beta-\text{CO}_2\text{Me}$ of $35$, must be a composite of steric and basicity effects. Complexing occurs to $\text{C}=\text{O}$ rather than $\text{OMe}$,\textsuperscript{118c} so the greater polarisation of the carbonyl of $1-\text{CO}_2\text{Me}$ is probably effected by electron-donation from the diene-Fe(\text{CO})$_3$ system.

The $6\alpha$-H of $25$, the $6\beta$-H of $26$ and the $\alpha$- and $\beta$-H of $35$ all show significant shifts, probably because of interactions through bonds rather than space.\textsuperscript{119}

2.5 Aromatic solvent induced shifts (ASIS)

The ASIS are useful in assignments of configurations involving polar groups.\textsuperscript{112} The complexes $25$, $26$ and $35$ have been examined (Table 2.4) in terms of $\delta_{\text{CDCl}_3} - \delta_{\text{C}_6\text{D}_6} = \Delta\delta_{\text{CDCl}_3}^{\text{C}_6\text{D}_6}$.

The ASIS are believed to arise from dipole interactions of benzene with the positive centres of the solute, and values vary considerably with the structure.\textsuperscript{112,120} In these compounds either or both Fe(\text{CO})$_3$ and $\text{CO}_2\text{Me}$ could be involved. In the parent tricarbonylcyclohexa-1,3-dieneiron, the Fe(\text{CO})$_3$ produces a very large $\Delta\delta_{\text{CDCl}_3}^{\text{C}_6\text{D}_6}$ compared with the uncomplexed diene. With an $1-\text{CO}_2\text{Me}$, an effect in the opposite direction is observed with a reduction of $\Delta\delta_{\text{CDCl}_3}^{\text{C}_6\text{D}_6}$ for the $2$-H in $25$ and $26$. A $6-\text{CO}_2\text{Me}$ in addition results in a negative $\Delta\delta_{\text{CDCl}_3}^{\text{C}_6\text{D}_6}$ for $6\beta$-H (- 0.10 ppm) and a positive $\Delta\delta_{\text{CDCl}_3}^{\text{C}_6\text{D}_6}$ for $6\alpha$-H (+ 0.15 ppm). However, the complex $35$ shows $\Delta\delta_{\text{CDCl}_3}^{\text{C}_6\text{D}_6}$ - 0.08 and - 0.04 for the $\beta$-H and $\alpha$-H, respectively. It does not at present seem possible to derive concrete correlations to assign stereochemistry on the basis of ASIS alone.
### TABLE 2.5

<table>
<thead>
<tr>
<th></th>
<th>26[1,6α-(CO₂Me)₃]</th>
<th>25[1,6β-(CO₂Me)₃]</th>
<th>Δδ₂⁵ = δ₂⁶ - δ₂⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe(CO)₃</td>
<td>209.077 (s)</td>
<td>208.422 (s)</td>
<td>+ 0.655</td>
</tr>
<tr>
<td>CO₂⁻</td>
<td>172.321 (s)</td>
<td>172.716 (s)</td>
<td>- 0.395</td>
</tr>
<tr>
<td>CO₂⁻</td>
<td>169.989 (s)</td>
<td>170.378 (s)</td>
<td>- 0.389</td>
</tr>
<tr>
<td>C-2</td>
<td>88.305 (d)</td>
<td>87.007 (d)</td>
<td>+ 1.298</td>
</tr>
<tr>
<td>¹JCH = 177.7 Hz</td>
<td>¹JCH = 179.7 Hz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-3</td>
<td>85.059 (dd)</td>
<td>84.539 (d)</td>
<td>+ 0.520</td>
</tr>
<tr>
<td>¹JCH = 171.9 Hz</td>
<td>¹JCH = 170.0 Hz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>²JCH = 7.8 Hz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-1</td>
<td>62.982 (s)</td>
<td>65.839 (s)</td>
<td>- 2.857</td>
</tr>
<tr>
<td>C-4</td>
<td>58.827 (d)</td>
<td>61.034 (d)</td>
<td>- 2.207</td>
</tr>
<tr>
<td>¹JCH = 162.1 Hz</td>
<td>¹JCH = 160.0 Hz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 x OMe</td>
<td>51.165 (q)</td>
<td>50.905 (q)</td>
<td>+ 0.260</td>
</tr>
<tr>
<td>¹JCH = 146.5 Hz</td>
<td>¹JCH = 146.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-6</td>
<td>40.646 (d)</td>
<td>37.789 (d)</td>
<td>+ 2.857</td>
</tr>
<tr>
<td>¹JCH = 136.7 Hz</td>
<td>¹JCH = 136.7 Hz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-5</td>
<td>30.127 (t)</td>
<td>32.724 (t)</td>
<td>- 2.597</td>
</tr>
<tr>
<td>¹JCH = 130.9 Hz</td>
<td>¹JCH = 128.9 Hz</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Crowding of carbons in organic molecules, shown by resonance of $^{13}\text{C}$ at higher fields than similar non-crowded carbons, has been deduced from spectra and used for steric assignments in organic molecules.\textsuperscript{112} Examination of 25 and 26 using double resonance techniques permit assignments shown in Table 2.5. The more compressed isomer 25 shows small upfield shifts ($<1$ ppm) for Fe(CO)$_3$, both OMe and C-3. Rather higher upfield shifts can be seen for C-2 and C-6. The remaining C of 25 show downfield shifts (2-3 ppm) compared with corresponding atoms in 26. While attempts could be made to explain these shifts, based on exact X-ray structures, it is again obvious that the practical organic chemist, faced with a steric assignment would not be greatly helped.

2.7 Tricarbonylcyclohexadienyliron cations

\begin{equation}
\begin{array}{c}
\text{(CO)$_3$Fe} \quad \text{CO$_2$Me} \\
\text{69} \\
\end{array}
\end{equation}

\begin{equation}
\begin{array}{c}
\text{(CO)$_3$Fe} \quad \text{CO$_2$Me} \\
\text{70} \\
\end{array}
\end{equation}

The $^1\text{H}$ NMR spectra of the epimeric cations 69 and 70 were examined. The $\beta$-CO$_2$Me cation 69 which was obtained from hydride abstraction from the ester 27, displayed a CO$_2$Me resonance at $\delta$ 3.84 and a singlet at $\delta$ 3.04 assignable to 6-H. The corresponding protons of the $\alpha$-CO$_2$Me cation 70 appeared at $\delta$ 3.51 and 3.83 (triplet). The latter was prepared by acid catalysed demethoxylation of 30.
From this somewhat limited data it would appear that the generalisation $\delta_{\beta} \text{CO}_2\text{Me} > \delta_{\alpha} \text{CO}_2\text{Me}$, $\delta_{\beta} \text{H} > \delta_{\alpha} \text{H}$ is also valid for the cations in this series. Deuterium labelling studies have also indicated that $\beta$-H of methylene protons resonates at lower field.\textsuperscript{72}

The X-ray structure\textsuperscript{121} of tricarbonyl($\eta^5$-2-methoxycyclohexadienyl)iron tetrafluorborate reveals that the $6_\beta$-H is approximately parallel to the dienyl system while the $6_\alpha$-H is almost normal to it. Inspection of the coupling constants of $6$-H above would indicate similar structural feature for $6_\alpha$-H of 70 and $6_\beta$-H of 69.

In favourable cases, the splitting of $6$-H can provide further correlation concerning the stereochemistry, a singlet being characteristic of a $\beta$-substituent and a triplet an $\alpha$-substituent. By way of example, the $\alpha$-tBu cation 71\textsuperscript{116} formed from demethoxylation of 52 shows its $6_\beta$-H as a triplet at $\delta$ 2.5.

Mass spectroscopy

Mass spectral fragmentation of organic stereoisomers can sometimes be logically related to configurations.\textsuperscript{122}

Electron impact on diene-Fe(CO)\textsubscript{3} complexes is assumed to lead to an electron-deficient system in such a manner that the Fe maintains the deficiency at as low a level as possible, leading to stepwise loss of CO.\textsuperscript{123} If other coordinating groups are attached to Fe, which are more
strongly electron-donating than CO, loss of the diene group from Fe (radical ion LFe, Table 2.6) and a corresponding decrease in intensity of radical ion FeC₆H₆ is observed. Attachment of an aromatic ligand to Fe as in 72 also results in preferential loss of the diene portion.

The efficient attachment of electron-deficient iron to the aromatic ring in the mass spectrometer seems to result in aromatisation of the complexed diene after loss of CO from the diene-Fe(CO)₃ complex. Loss of H or other substituents from sp³ carbons is required for such aromatisation, and is stereospecific at least in the cyclohexadiene case itself, involving loss of both β-hydrogens. This may well occur via intermediate transfer of H to Fe, supported by the observation of Fe(C₅H₅)H as a fragment in the analogous cyclopentadienyl complexes, and C₆(Me)₆FeH in the arene complex 72. Migration of a substituent from the ligand to metal has also been observed (RFe in Table 2.6), the presence of FeOMe in the spectrum of diester complexes (Table 2.7) and C₆Me₆FeOMe in the spectrum of 72.

This iron-mediated loss of substituents from the organic ligand is of particular interest, in view of stereochemical implications. An analysis of the mass-spectral fragments of five isomeric diester complexes
Major mass spectral fragments of

\[
\text{L(CO)}_2\text{Fe} \quad (\equiv \text{M})
\]

<table>
<thead>
<tr>
<th>Radical ion</th>
<th>( M )</th>
<th>( M-\text{CO} )</th>
<th>( M-2\text{CO}-2\text{H} )</th>
<th>( \text{FeC}_6\text{H}_6 )</th>
<th>( =M-2\text{CO}-2\text{H}-\text{L} )</th>
<th>( \text{LFe} )</th>
<th>( \text{RFe} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( m/z )</td>
<td>220 (07)</td>
<td>192 (33)</td>
<td>162 (09)</td>
<td>134 (100)</td>
<td>134 (100)</td>
<td>84 (10)</td>
<td>87 (02)</td>
</tr>
<tr>
<td>Relative abundance</td>
<td>316 (10)</td>
<td>288 (29)</td>
<td>258 (100)</td>
<td>134 (18)</td>
<td>134 (18)</td>
<td>180 (39)</td>
<td>133 (03)</td>
</tr>
<tr>
<td>( \text{P(OMe)}_3 )</td>
<td>394 (05)</td>
<td>366 (10)</td>
<td>336 (100)</td>
<td>134 (100)</td>
<td>134 (100)</td>
<td>258 (04)</td>
<td>133 (03)</td>
</tr>
<tr>
<td>( \text{PBu}_3 )</td>
<td>454 (06)</td>
<td>426 (11)</td>
<td>396 (26)</td>
<td>134 (100)</td>
<td>134 (100)</td>
<td>318 (81)</td>
<td>133 (03)</td>
</tr>
<tr>
<td>( \text{PPh}_3 )</td>
<td>498 (04)</td>
<td>470 (10)</td>
<td>440 (02)</td>
<td>134 (100)</td>
<td>134 (100)</td>
<td>362 (100)</td>
<td>133 (14)</td>
</tr>
<tr>
<td>( \text{AsPh}_3 )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( ^{+}m/z \ 256 \) corresponds to \( \text{LFe}-2\text{H} \)}
Some mass spectral fragments of isomeric tricarbonyl(\(n^4\)-dimethoxycarbonyl-cyclohexa-1,3-diene)iron complexes

<table>
<thead>
<tr>
<th>Radical ion</th>
<th>(m/\nu)</th>
<th>1,6(\beta)-(25)</th>
<th>1,6(\alpha)-(26)</th>
<th>5(\beta),6(\beta)-(31)</th>
<th>5(\alpha),6(\alpha)-(32)</th>
<th>5(\alpha),6(\beta)-(35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>336</td>
<td>0.04</td>
<td>7.5</td>
<td>0.35</td>
<td>11.0</td>
<td>0.1</td>
</tr>
<tr>
<td>M-OMe</td>
<td>305</td>
<td>8.5</td>
<td>0.6</td>
<td>7.5</td>
<td>1.2</td>
<td>0.2</td>
</tr>
<tr>
<td>M-CO</td>
<td>308</td>
<td>7.5</td>
<td>5.0</td>
<td>3.3</td>
<td>9.0</td>
<td>23.0</td>
</tr>
<tr>
<td>M-2CO</td>
<td>280</td>
<td>43.0</td>
<td>36.0</td>
<td>55.0</td>
<td>65.0</td>
<td>47.5</td>
</tr>
<tr>
<td>M-3CO</td>
<td>252</td>
<td>37.5</td>
<td>39.5</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>M-Fe(CO)(_3)-2H</td>
<td>194</td>
<td>32.5</td>
<td>31.0</td>
<td>3.5</td>
<td>18.0</td>
<td>7.0</td>
</tr>
<tr>
<td>FeC(_6)H(_6)</td>
<td>134</td>
<td>100.0</td>
<td>100.0</td>
<td>70.0</td>
<td>81.0</td>
<td>77.0</td>
</tr>
<tr>
<td>Fe0Me</td>
<td>87</td>
<td>12.0</td>
<td>9.0</td>
<td>33.0</td>
<td>13.0</td>
<td>16.0</td>
</tr>
</tbody>
</table>
25, 26, 31, 32 and 36 is given in Table 2.7. The results do indicate that loss of OMe from the molecular ion is more prominent with \( \beta \)-CO\(_2\)Me, than for \( \alpha \)-CO\(_2\)Me. Again, however, the significance of a given result is likely to be assessable only if a pair of isomers is available.

2.9 Remarks in conclusion

The most useful spectroscopic parameter for distinguishing \( \alpha \)- and \( \beta \)-stereochemistry appears to be the vicinal coupling constants of the hydrogens attached to sp\(^3\)-carbons. The hydrogens on the same side as the metal (i.e. \( \beta \)) have a vicinal coupling constant of \( \sigma \alpha \) 10-12 Hz while the corresponding value for \( \alpha \)-hydrogens is \( \sigma \alpha \) 8 Hz. The consistency of coupling constants in a given steric series leads to the observation of CH\(_2\) splitting patterns (Fig 2.1 and 2.3) characteristic of stereochemistry of the examples where the CH\(_2\) is flanked by two vicinal protons. In some cases the simplification of the spectrum, preferably by use of a paramagnetic shift reagent, is necessary for estimation of coupling constants and/or observation of the pattern.

For confirmation of the configuration in terms of other spectroscopic parameters such as chemical shifts, lanthanide induced shifts (LIS), aromatic solvent induced shifts (ASIS) and mass spectral fragmentations, may require both stereoisomers.

Usually \( \delta \beta \)-substituent > \( \delta \alpha \)-substituent. The esters discussed above, for example, show \( \delta \beta \)-CO\(_2\)Me > 3.63 > \( \delta \alpha \)-CO\(_2\)Me. However, one has to be cautious with the generalisation that \( \delta \beta \)-H > \( \delta \alpha \)-H, as exceptions to this have been noted with \( \beta \)-Me complexes 66 and 67. Larger LIS are observed for \( \beta \)-CO\(_2\)Me than \( \alpha \)-CO\(_2\)Me due to steric reasons. Preferential loss of a \( \beta \)-substituent (e.g. OMe) through iron-mediation is possible in the mass-probe.
3.1 Introduction

Substituted tricarbonyldieneiron complexes need to be readily available in a pure form if they are to be employed as synthetic intermediates. The reaction of substituted cyclohexa-1,4-dienes with pentacarbonyliron usually results in a mixture of isomeric complexes, the major isomer being the less crowded α-isomer when there is a choice with alkyl or similar substituents (section 1.5.2). The more crowded β-CO₂Me 27 has, however, been noted⁷⁰,⁹³ as the major product from the complexation of the 1,4-diene 73, implying an energetically favourable interaction between the ester function and the incoming metal portion during the process of complex formation. A similar observation has been made by Whitesides and coworkers.⁹² Further examination of this stereoelectronic interaction has been hitherto prevented due to the inability to separate the isomeric components of the products.

In view of the important synthetic significance of such a stereoselective process, further studies were carried out in order to verify the initial observation and to establish what degree of stereoselectivity can be achieved in different structures and under different conditions. This study shows that the distribution of products depends to a great extent on the initial coordination-site at the organic ligand. Single isomers can be obtained with appropriate substitution.
RESULTS AND DISCUSSION

3.2 Is isomerisation of ester complexes possible during their formation?

The reaction of the diene \( \text{73} \) with pentacarbonyliron has been reported \(^{70} \) to give a mixture of isomeric complexes \( \text{27} \) (5β-CO\(_2\)Me), \( \text{28} \) (5α-CO\(_2\)Me) and \( \text{12} \) (2-CO\(_2\)Me). Initial complexation of the reactive iron species with the ester group has been suggested in order to explain the preferential formation of the more sterically crowded isomer \( \text{27} \). One possible mode of formation of the other products \( \text{28} \) and \( \text{12} \) is through isomerisation during the reaction of an initially formed 5β-CO\(_2\)Me complex \( \text{27} \). To test this possibility, the pure isomer \( \text{27} \) was needed in order to subject it to the complexation conditions.

The 5β-CO\(_2\)Me complex \( \text{27} \) could not be fully separated directly from its isomers by conventional methods including chromatography on AgNO\(_3\)-impregnated silica. Separation was, however, accomplished by fractional crystallisation of the mixture of carboxy complexes obtained by alkaline hydrolysis. Methylation (Me\(_2\)SO\(_4\)) of the individual acids afforded the pure \( \text{27} \) (5β-CO\(_2\)Me) and \( \text{28} \) (5α-CO\(_2\)Me). The steric structures were confirmed
by both chemical (hydride abstraction) and physical means (\(^1\)H NMR, chapter 2). The 2-CO\(_2\)Me complex \(12\) was readily obtained from the complexation of the available corresponding 1,3-diene.\(^{51}\)

The pure complexes \(27, 28\) and \(12\) were subjected to the complexation conditions used in reactions with the diene \(73\). In all cases, the starting complex was recovered indicating that the original mixture is kinetically determined presumably through coordination of \(\text{Fe(CO)}\(_n\) (n = 3\(^{82}\) or 4\(^{81}\)) with the diene \(73\) and subsequent isomerisations via allylic intermediates.

For further discussion of this sequence a consideration of the conformation of the free 1,4-diene is useful. Rabideau and coworkers\(^{127}\) have used homoallylic coupling constants (\(^1\)H NMR) to determine the preferred conformation of cyclohexa-1,4-dienes. Their results suggest that cyclohexa-1,4-dienes assume a nearly planar conformation which is evident from homoallylic coupling constants between 7.5 and 8.3 Hz. Cyclohexa-1,4-dienes in this study also displayed coupling constants in this range, and are, therefore, considered to exist in a planar or a near-planar conformation in the following discussion.

The approach of the coordinatively unsaturated iron species \(\text{Fe(CO)}\(_n\) to the olefinic bonds of cyclohexa-1,4-diene could occur from either side of the plane of the molecule. A bulky group attached to one methylene carbon would be expected to interfere by steric hindrance, and complexation would then take place predominantly on the side opposite to the bulky allylic substituent, as has been observed with (-)-phellandrene.\(^{40}\) Since it does not in this case, another effect is operating. Initial interaction of the \(\text{Fe(CO)}\(_n\) with the \(\pi\)-electrons of the ester carbonyl, would favour approach of \(\text{Fe(CO)}\(_n\) to C=C from this direction. The mechanism of conjugation is probably through H-transfer via \(\text{Fe(CO)}\(_3\) and allyl complexes (section 1.5.1).\(^{76,89}\) This implies that H shift must occur on the same side as the Fe, i.e. only from the 4-position with \(\beta\)-approach, but there is a choice between 1- and 4- with the \(\alpha\)-approach (see Scheme 3.1). The
approximate equality of 28 and 12 (see Table 3.1) suggests that the selectivity between the two allylic hydrogens is low. The ratio of (27) to combined (28) and (12) represents the ratio of initial β- to α-attack.

3.3 Effect of complexation conditions

The complexation of the diene ester 73 with Fe(CO)₅ was examined under various conditions with a view to gaining further insight into the complexation process, and to see whether the reaction conditions could be controlled to produce one specific isomer. Results are shown in Table 3.1.

Reaction time does not appear to have any significant effect on the selected isomer ratio under thermal conditions, although prolonged heating caused extensive decomposition. Surprisingly similar ratios were obtained at both high temperatures (thermal conditions), and near room temperatures under photochemical conditions. This observation together with the result from the application of complexation conditions to the pure complexes 27, 28 and 12 which were isolated unchanged suggests that the complexation product is essentially kinetic controlled and the reaction largely irreversible even at high temperatures. Complexation studies with acyclic hexadienes have also indicated the kinetic-control character of the reaction.

The polar nature of the initial coordination of the Fe(CO)₅ group with the ester function is evident from the results of the complexation in the more polar methanol (see Table 3.1). Here the percentage of 5β-isomer is lower, indicating that the steric effect of the substituents is taking over from ester complexing. Although the isomer ratio is affected by solvent, conditions could not be found to produce either the pure α- or the pure β-CO₂Me complex.
### TABLE 3.1

Product distribution in the reaction of methyl cyclohexa-2,5-dienecarboxylate (73) with Fe(CO)$_5$ under different conditions

<table>
<thead>
<tr>
<th>Reaction conditions</th>
<th>Yield(%)$^b$</th>
<th>Isomer ratio$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27 : 28 : 12</td>
<td></td>
</tr>
<tr>
<td>n-Bu$_2$O, reflux, 18h</td>
<td>50$^c$</td>
<td>74 : 13 : 13</td>
</tr>
<tr>
<td>n-Bu$_2$O, reflux, 20h</td>
<td>56$^c$</td>
<td>70 : 15 : 15</td>
</tr>
<tr>
<td>n-Bu$_2$O, reflux, 36h</td>
<td>30</td>
<td>60 : 10 : 30</td>
</tr>
<tr>
<td>n-Bu$_2$O, reflux, 18h</td>
<td>56$^{c,d}$</td>
<td>80 : 10 : 10</td>
</tr>
<tr>
<td>Et$_2$O, hv, 4h</td>
<td>43</td>
<td>75 : 15 : 10</td>
</tr>
<tr>
<td>n-hexane, hv, 4h</td>
<td>27</td>
<td>70 : 15 : 15</td>
</tr>
<tr>
<td>MeOH, hv, 2h</td>
<td>07</td>
<td>50 : 25 : 25</td>
</tr>
<tr>
<td>n-BuOH, hv, 18h</td>
<td>02</td>
<td>50 : 25 : 25</td>
</tr>
</tbody>
</table>

$^a$ Isomer ratio was calculated from $^1$H NMR spectra.

$^b$ The yield after distillation at 80-82°C/0.01 mmHg.

$^c$ Recovered diene and Fe(CO)$_5$ from the first run were reacted again.

$^d$ Fe(CO)$_5$ in n-Bu$_2$O was added dropwise to the diene in n-Bu$_2$O with stirring while the reaction mixture was brought to reflux over a period of ca 4h.
3.4 Effect of more polar and sterically bulky substituents

Variations in the structure of the ester function were made to see if changes in polarity or hindrance could decisively affect the α:β ratio. p-Bromophenacetyl cyclohexa-2,5-dienecarboxylate \( 78 \) was investigated in the hope that the extra carbonyl group should assist β-selectivity. A method of Durst\(^{128}\) proved the most satisfactory for esterification of the diene acid. Other methods\(^{129}\) gave larger amounts of aromatic products which were difficult to remove. Reaction of the diene \( 78 \) with Fe(CO)\(_5\) under thermal conditions gave a complex mixture of products comprising \( p \)-bromocetophenone, \( p \)-bromophenacyl benzoate and a low yield of a yellow unstable oil which was consistent in spectroscopic properties with the 5β-isomer \( 65 \). The assigned stereochemistry was inferred from the splitting pattern of methylene protons characteristic of an adjacent β-substituent (section 2.3.2). This assignment was confirmed by treatment of the oil with zinc/acetic acid\(^{129}\) to give tricarbonyl(η\(^5\)-5β-carboxycyclohexa-1,3-diene)iron \( 64 \), which after methylation yielded the 5β-CO\(_2\)Me ester \( 27 \), identical (\(^1\)H NMR,IR) with the complex described above. Whether selective or not, the yield is too poor to make the process of any practical interest.
3.5 Effect on stereochemistry of increased electron availability in the olefinic bonds (methoxy substituents)

![Chemical Structure]

A dramatic reversal of stereoselectivity was observed on complexing the dimethoxy diene 79. Under standard thermal conditions the ester gave mainly 80, and only traces of other isomeric complexes which were not isolated. The structure 80 was determined by normal spectroscopic techniques, and the stereochemistry was assigned from the characteristic coupling constant of the two β-protons (11 Hz) and the chemical shifts of 5β-H (δ 2.90) and 5α-CO2Me (δ 3.58). Further confirmation of the stereochemistry was provided by resistance of the compound to hydride abstraction by trityl reagents.

More detailed investigation of the complexation70 of methyl 2-methoxycyclohexa-2,5-diene carboxylate 74 resulted in a mixture of three complexes: 29 (1-0Me, 6β-CO2Me), 30 (1-0Me, 6α-CO2Me) and 77 (1-0Me, 2-CO2Me) in a ratio of 5:6:9 (1H NMR). The complexes 30 and 77 must arise from the α-approach of Fe(CO)₅ to the diene. The β-approach now, gives only the minor isomer 29.
The dimethoxy diene 81 in which either face has a substituent, a CO₂Me or a Me group in a geminal relationship, gave both β-CO₂Me and α-CO₂Me complexes, 33 and 34, respectively, in equal proportions.⁴⁹ As discussed below, the diene without methoxy substituents, i.e. 85, formed only the β-CO₂Me isomer 90.

These results show that the coordinatively unsaturated Fe(CO)₅ approaches the diene by direct initial attachment mainly to the π-electrons of C=C rather than to the methoxycarbonyl group, when the electron density is increased by methoxy substituents. The effect is most marked with the dimethoxy ester 79.

It is particularly interesting that 79 and 81 retain the two OMe in the products, whereas the dimethoxydiene lacking CO₂Me gives mainly monomethoxy complexes.⁶⁵ The probable mechanism of loss involves initial double bond migration away from the OMe, a process which must be inhibited here by the influence of CO₂Me.

3.6 Effect of an electron withdrawing substituent at the olefinic site (methoxycarbonyl group)

To determine the effect of an additional electron withdrawing substituent, the substrate dimethyl cyclohexa-2,5-diene-1,2-dicarboxylate 75 was prepared from trans-cyclohexa-3,5-diene-1,2-dicarboxylic acid.¹³⁰ The diester 75 with Fe(CO)₅ under thermal conditions gave in good total yield (74-93%) a mixture of three complexes, identified (chapter 2) as 25 [1,6β-(CO₂Me)₂], 26 [1,6α-(CO₂Me)₂] and 35 [5α,6β-(CO₂Me)₂] in a ratio of 1:3:1. Comparison of the ¹H NMR of the mixture and the composite of the three pure isomers confirmed that no other isomers were present in the crude product in detectable amount. Change of solvent from di-n-butyl ether to xylene for complexation afforded only a poor yield (< 30%) of the same complexes with an isomer ratio 25:26:35 of 4:7:4.
Scheme 3.1. Theoretically possible steric approaches of Fe(CO)$_n$ to the nuclear bonds of dimethyl cyclohexa-2,5-diene-1,2-dicarboxylate and the resulting allyl intermediates leading to all six possible isomeric complexes.
In order to consider a mechanism for the formation of products, all theoretically possible steric approaches of Fe(CO)$_n$ to the nuclear bonds (82) and the resulting allyl intermediates leading to all six possible isomers are shown in the Scheme 3.1. The fact that the compounds 32 [5α,6α-(CO$_2$Me)$_2$] and 83 [1,2-(CO$_2$Me)$_2$] are not observed in the reaction products suggests that the approach $d$ is unfavourable indicating that 1-CO$_2$Me group transfers the Fe(CO)$_n$ to the adjacent double bond ($a$ approach). Absence of 84 [2,3-(CO$_2$Me)$_2$] indicates that requisite allyl intermediate is highly unfavoured, although the hydrogens (H' and H") would transfer in equal probability to the iron atom in the absence of a methoxycarbonyl group substituted at the 1-olefinic position as noted previously (section 3.2). The unfavourable nature of this allyl intermediate may be attributed to the steric compression resulting from two adjacent CO$_2$Me groups in a planar geometry. The formation of equal amounts of 25 and 35 as reaction products in both n-Bu$_2$O and xylene, suggests that 6-CO$_2$Me group transfers the Fe(CO)$_n$ group to the equidistant double bonds ($a$ and $b$ approach) in roughly equal proportions, the electron withdrawing methoxy-carbonyl group at the 1-position having seemingly little effect in this respect. The initial coordination of Fe(CO)$_n$ group with either 1-CO$_2$Me or 6-CO$_2$Me group in the diene 75 is of similar probability as the amount of complex 26 is approximately equal to the sum of 25 and 35, both in n-Bu$_2$O and xylene.

3.7 Effect of methyl substituents

Complexation of methyl 2-methylcyclohexa-2,5-dienecarboxylate 76 with Fe(CO)$_5$ has been found$^{51}$ to give a mixture of several isomeric complexes. Because of the formation of several isomers, it is difficult to extract any useful information regarding the stereochemical direction.
TABLE 3.2

Complexation of blocked dienes \([\text{Fe(CO)}_5/\text{nBu}_2\text{O}, \text{reflux}]\)

<table>
<thead>
<tr>
<th>Diene</th>
<th>Reaction time (h)</th>
<th>Yield (%)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>(R^1=\text{Me}), (R^2=\text{H})</td>
<td>18</td>
<td>44</td>
<td>90</td>
</tr>
<tr>
<td>(R^1=\text{CH}_2\text{Ph}), (R^2=\text{H})</td>
<td>40</td>
<td>98</td>
<td>91</td>
</tr>
<tr>
<td>(R^1=\text{CH}_2\text{Me}), (R^2=\text{H})</td>
<td>40</td>
<td>98</td>
<td>92</td>
</tr>
<tr>
<td>(R^1=R^2=\text{Me}), (R^3=\text{H})</td>
<td>40</td>
<td>88</td>
<td>93</td>
</tr>
<tr>
<td>(R^1=R^3=\text{Me}), (R^2=\text{H})</td>
<td>40</td>
<td>76</td>
<td>94</td>
</tr>
</tbody>
</table>
It was anticipated that replacing one of the methylene protons by a suitable blocking group would reduce this complexity by limiting the number of possible allyl intermediates. This led to the study of a series of blocked cyclohexa-1,4-dienes. 93

3.7.1 Complexation of blocked cyclohexa-1,4-dienes

Some blocked dienes (85-89, Table 3.2) were prepared for this study by reductive alkylation of benzoic or methylbenzoic acids with the appropriate alkylation agent (see experimental), followed by methylation of the carboxy group with Me₂SO₄. The results of the complexation with Fe(CO)₅ are given in the Table 3.2. The structures of the complexes 90-94 were deduced from their spectral properties. The α-stereochemistry of the methoxycarbonyl groups was further evident from their resistance to alkaline hydrolysis (chapter 4).

The fact that only α-CO₂Me complexes (90-94) were observed from the corresponding 1,4-dienes, suggests that the Fe(CO)₅ is transferred to double bonds only from the same side as the methoxycarbonyl group. This may be envisaged as a composite effect of initial stereochemical interaction of the Fe(CO)₅ group with the ester function and steric hindrance from the methyl or benzyl groups on the opposite side. Steric hindrance by an isopropyl group is also manifested in the complexation of (-)-phellandrene, where a 4:1 ratio of α-iPr (19):β-iPr complexes has been observed.

The absence of any α-CO₂Me complexes from 88 and 89, the dienes derived from 2- and 3- methylbenzoic acids, respectively, indicates that the inductive effect of Me at olefinic bonds is not sufficient to activate the double bond like OMe and permit competitive direction of the Fe(CO)₅ group from the side opposite to the CO₂Me group in the manner already discussed. Apparently, the effect of a methyl group is sufficient to induce selectivity between the two double bonds after the initial coordination of Fe(CO)₅ with the ester group.
3.8 Steric effects in cyclohexa-1,3-dienes

The dienes above all involve isomerisation of a 1,4- into a 1,3-diene. In order to determine the extent of steric direction during complexation, with a preformed cyclohexa-1,3-diene, and also the directive effect of an anhydride group, cis-cyclohexa-3,5-diene-1,2-anhydride \( \text{95}^{132} \) was reacted. The product obtained in low yield under photochemical conditions, was a mixture of the \( \beta \)- and \( \alpha \)-anhydride complexes (\( \text{96} \) and \( \text{97} \) respectively) in a ratio of 4:1. The reaction of the anhydride \( \text{95} \) with enneacarbonyliron in refluent butan-2-one afforded a similar mixture containing the \( \beta \)-complex \( \text{96} \) in a 1:2 ratio to the presumably more thermodynamically stable \( \alpha \)-complex \( \text{97} \).
Formation of the more crowded $\beta$-isomer $96$ as the major compound in the photochemical reaction with ether as solvent could result from stereochemical direction of the Fe(CO)$_n$ group to the nuclear bonds through an initial coordination with the polar anhydride function. Otherwise, the direct approach to the diene should have produced the less crowded $\alpha$-isomer $97$. An alternative explanation involving selective decomposition of $\alpha$-isomer $97$ during the course of the reaction seems to be eliminated by the result of the complexation with more severe conditions with Fe$_2$(CO)$_9$ in refluent butan-2-one, where the $\alpha$-isomer was observed as the major product. In this case it is possible that the selectivity by initial coordination is reduced because of competition by the butan-2-one which dissolves Fe$_2$(CO)$_9$ to a deeply coloured solution apparently with formation of a rather stable adduct.

![Diagram](image)

Complexation of $\text{cis}$-dimethyl cyclohexa-3,5-diene-1,2-dicarboxylate $98^{133}$ with Fe(CO)$_5$ in ether under photochemical conditions gave, in good yield, a mixture of $\beta$- and $\alpha$-isomers ($31$ and $32$ respectively) in 2:1 ratio. The observation of the sterically crowded, and thermodynamically very unstable $\beta$-isomer $31$ as the major product provides a clear-cut example for the initial stereochemical direction of the Fe(CO)$_n$ group by the ester function.
3.9 Conclusion

Complexation of cyclohexadiene esters with pentacarbonyliron under the usual experimental conditions is kinetically controlled. The distribution of isomeric products is determined by stereoelectronic factors, polarity of the medium and substituents on the diene being significant variables. Initial competition between methoxy-carbonyl group and nuclear bonds for coordinatively unsaturated iron species, Fe(CO)$_n$, can be pushed in one direction by proper choice of substituents rather than the reaction conditions. Methoxy substituents which increase the electron density at the olefinic bonds favour the initial coordination of Fe(CO)$_n$ to the diene resulting preferential formation of $\alpha$-CO$_2$Me isomer. The $\beta$-CO$_2$Me isomer can be formed as the sole product by imposing steric constraints towards $\alpha$-approach of Fe(CO)$_n$ as in blocked cyclohexadienes.
CHAPTER 4

TRICARBONYLIRON AS A LATERAL CONTROL GROUP IN THE ALKALINE HYDROLYSIS OF SOME CYCLOHEXA-1,3-DIENE ESTERS

4.1 Introduction

Selective reactivities of similar functional groups in the same molecule are frequently needed for synthetic purposes. This is often achieved by incorporating, reversibly, into the molecular skeleton, groups which act by steric and/or electronic effects. In selective hydrolyses of classical organic esters, for example, the presence of a t-butyl group in an ester function tends to slow its alkaline hydrolysis or activate it to acid hydrolysis. The ability to achieve reversible incorporations of such protecting groups may cause problems particularly with multifunctional molecules.

The concept of superimposed lateral control of reactivity\textsuperscript{34b} is illustrated here by the alkaline hydrolysis of some Fe(CO)\textsubscript{3} complexes of cyclohexa-1,3-diene esters. The steric occupation of one face of the diene could lead to stereoselective reactions (section 1.6), and the electron releasing or withdrawing character of the iron fragment as decided by the ligands (section 1.1), could alter the electron density at functional groups like CO\textsubscript{2}R directly attached to the diene, resulting in selective reactions with differently situated groups.

Alkaline hydrolysis of classical organic esters has been extensively investigated and, therefore, the perturbations at CO\textsubscript{2}R due to Fe(CO)\textsubscript{3} should be readily detectable and the selectivity effects of Fe(CO)\textsubscript{3} on classical reactivity at the organic ligand may be rationalized conveniently. Another reason for choice of CO\textsubscript{2}R for examination is that this, and CO\textsubscript{2}H, are reactive groups which can desirably be manipulated for further synthetic purposes. Selective hydrolysis of diesters is not readily possible with the uncomplexed parent compounds discussed here.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Ester</th>
<th>Reaction condition</th>
<th>Yield</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Ester 1" /></td>
<td>a</td>
<td>&gt;95%</td>
<td><img src="image" alt="Product 1" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Ester 2" /></td>
<td>a</td>
<td>94%</td>
<td><img src="image" alt="Product 2" /></td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Ester 3" /></td>
<td>a</td>
<td>85%</td>
<td><img src="image" alt="Product 3" /></td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Ester 4" /></td>
<td>a</td>
<td>75%</td>
<td><img src="image" alt="Product 4" /></td>
</tr>
</tbody>
</table>

*Alkaline hydrolysis of esters with excess 20% aqueous NaOH/MeOH

\(M = \text{Fe(CO)}_3\)
<table>
<thead>
<tr>
<th>Entry</th>
<th>Ester</th>
<th>Reaction condition</th>
<th>Yield</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td><img src="image" alt="Ester 99" /></td>
<td>a</td>
<td>&gt;95%</td>
<td><img src="image" alt="Product 99" /></td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="Ester 47" /></td>
<td>a</td>
<td>&gt;95%</td>
<td><img src="image" alt="Product 47" /></td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="Ester 101" /></td>
<td>a</td>
<td>&gt;90%</td>
<td><img src="image" alt="Product 101" /></td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="Ester 102" /></td>
<td>a</td>
<td>75%</td>
<td><img src="image" alt="Product 102" /></td>
</tr>
<tr>
<td>9</td>
<td><img src="image" alt="Ester 103" /></td>
<td>a</td>
<td>79%</td>
<td><img src="image" alt="Product 103" /></td>
</tr>
<tr>
<td>10</td>
<td><img src="image" alt="Ester 104" /></td>
<td>a</td>
<td>80%</td>
<td><img src="image" alt="Product 104" /></td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Entry</th>
<th>Ester</th>
<th>Reaction condition</th>
<th>Yield</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td><img src="image" alt="Ester 26" /></td>
<td>a</td>
<td>81%</td>
<td><img src="image" alt="Product 48" /></td>
</tr>
<tr>
<td>12</td>
<td><img src="image" alt="Ester 105" /></td>
<td>b</td>
<td>94%</td>
<td><img src="image" alt="Product 48" /></td>
</tr>
<tr>
<td>13</td>
<td><img src="image" alt="Ester 25" /></td>
<td>a</td>
<td>74%</td>
<td><img src="image" alt="Product 48" /></td>
</tr>
<tr>
<td>14</td>
<td><img src="image" alt="Ester 29 30 77" /></td>
<td>a</td>
<td>90%</td>
<td><img src="image" alt="Product 53 112" /></td>
</tr>
</tbody>
</table>

**Reaction condition**
- a: reflux in toluene
- b: reflux in dichloromethane

**Yield**
- 5: 6: 9

R = Me \((106)\), H \((107)\)
<table>
<thead>
<tr>
<th>Entry</th>
<th>Ester</th>
<th>Reaction condition</th>
<th>Yield</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td><img src="image1" alt="Ester" /></td>
<td>a</td>
<td>80%</td>
<td><img src="image2" alt="Product" /></td>
</tr>
<tr>
<td>16</td>
<td><img src="image3" alt="Ester" /></td>
<td>a</td>
<td>76%</td>
<td><img src="image4" alt="Product" /></td>
</tr>
<tr>
<td>17</td>
<td><img src="image5" alt="Ester" /></td>
<td>c</td>
<td>40%</td>
<td><img src="image6" alt="Product" /></td>
</tr>
<tr>
<td>18</td>
<td><img src="image7" alt="Ester" /> + <img src="image8" alt="Ester" /></td>
<td>c</td>
<td>40%</td>
<td><img src="image9" alt="Product" /> + <img src="image10" alt="Product" /></td>
</tr>
<tr>
<td>19</td>
<td><img src="image11" alt="Ester" /></td>
<td>c</td>
<td>95%</td>
<td><img src="image12" alt="Product" /></td>
</tr>
<tr>
<td>20</td>
<td><img src="image13" alt="Ester" /></td>
<td>c</td>
<td>70%</td>
<td><img src="image14" alt="Product" /></td>
</tr>
</tbody>
</table>

- a = 5-10°C, 2h;  
- b = 5-10°C, 1h;  
- c = 55-60°C, 6h.
RESULTS AND DISCUSSION

4.2 Monocarboxylic esters; regioselectivity

The esters 11, 12, 27 and 28 were subjected to an identical mild alkaline hydrolysis procedure. The results are shown in Table 4.1. Notably the complex 11 was recovered, a result consistent with previous ones, while esters 12 and 28 gave the corresponding carboxylic acids. The 5β-CO₂Me complex 27 gave rise not only to 5β-CO₂H, but to minor proportions of the stereoisomer with a 5α-CO₂H, corresponding to 28, and the unhydrolysed 1-CO₂Me isomer 11 which was recovered by extraction of the alkaline solution. The products were identified from their spectral properties, particularly ¹H NMR, in the usual way. The result with 5β-CO₂Me 27 is explicable on the same basis as that with the more extensively investigated 25 [1,6β-(CO₂Me)₂] below.

To examine possible effects of other substituents than CO₂Me, the preparation and reactions of some 1-CO₂Me complexes containing Me and OMe were examined.

The complexes 47 (6α-Me,1-CO₂Me) and 99 (2-Me,1-CO₂Me) were produced as a mixture from 2-methylbenzoic acid by the sequence: Birch reduction, methylation, complexation and isomerisation. Since the mixture could not be separated by standard physical methods, use was made of hydride abstraction, which is known to be inhibited by adjacent α-substituents. In consequence unreacted 47 was recovered and separated from tricarbonyl-(η⁵-1-methoxycarbonyl-2-methylcyclohexadienylium)iron hexafluorophosphate 100. The isomer 99 was obtained by reduction of the salt with sodium borohydride.
The complex 101 (3-Me, 1-CO₂Me) resulted from a similar sequence starting with 3-methylbenzoic acid, and the complexes 102 (2-OMe, 1-CO₂Me), 103 (3-OMe, 1-CO₂Me) and 104 (4-OMe, 1-CO₂Me) were prepared according to the literature. The 1-CO₂Me complexes containing Me or OMe at the 2-, 3-, 4- or 6α-positions (entries 5-10, Table 4.1), were recovered largely unchanged from alkaline hydrolysis under the conditions noted, so the ester group is still deactivated.

4.3 Dicarboxylic esters

For this study, the complexes 25 [1,6β-(CO₂Me)₂], 26 [1,6α-(CO₂Me)₂], 31 [5β,6β-(CO₂Me)₂] and 35 [5α,6β-(CO₂Me)₂] were available from benzene-1,2-dicarboxylic acid (chapter 3). The 1,4-dimethoxycarbonyl complex 105 was obtained from dimethyl cyclohexa-1,3-diene-1,4-dicarboxylate. Results of the hydrolysis are shown in Table 4.1.

In the case of the 1,6α-dimethoxycarbonyl complex 26 only the 6α-CO₂Me was cleaved which is consistent with the results with 1-CO₂Me of the monocarboxylic esters above. However, either one or both ester groups of 1,4-dimethoxycarbonyl complex 105 were hydrolysed to give the corresponding acids 106 and 107. The presence of an electron withdrawing
group at the 4-position, therefore, enhances the rate of basic hydrolysis. Nevertheless, the rate of hydrolysis is qualitatively much slower than that of the uncomplexed ester, as is also true for the mono-substituted 1-CO₂Me.

The observation that an electron withdrawing group at one terminus of the diene system facilitates the cleavage of 1-CO₂Me group of 105, suggests that a reduction of electron density at the ester carbonyl carbon for any effective chemical interaction of 1-CO₂Me with OH⁻. This is indicative of the addition of OH⁻ to ester carbonyl carbon as the rate limiting step, conforming with the widely observed B₂ac mechanism. 135

As expected, the 1-CO₂Me group of the half ester 48 was cleaved to give the corresponding diacid 108 in good yield under prolonged acidic conditions employed by Birch and Williamson 51 for the hydrolysis of 1-CO₂Me complex 11.

![Chemical Structures](image)

The observation of relatively very much slower alkaline hydrolysis for 1-CO₂Me complexes than for the corresponding uncomplexed dienes, indicates that the complexation must reduce the reactivity of ester carbonyl to OH⁻ by an electron-donation effect. This is also demonstrated by the higher pKₐ of complexed diene acids. 24c The electron donation is
TABLE 4.2

Some crystal data\textsuperscript{111} of tricarbonyl(\(\eta^4\)-1,6-B-dimethoxycarbonylcyclohexa-1,3-diene)iron \textsuperscript{25}

(The crystals are triclinic, space group \(\text{PT}\) with unit cell parameters \(a = 6.883(1)\,\text{Å}, b = 8.949(1)\,\text{Å}, c = 11.438(2)\,\text{Å},\) \(\alpha = 91.50(1)^\circ, \beta = 101.78(1)^\circ\) and \(\gamma = 96.48(1)^\circ.\) The unit cell contains two molecular units, \(Z = 2\))

<table>
<thead>
<tr>
<th>Bond distances (Å)</th>
<th>Angles (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(1)-C(2) 1.441(2)</td>
<td>C(7)-C(1) 1.484(2)</td>
</tr>
<tr>
<td>C(2)-C(3) 1.406(2)</td>
<td>C(6)-C(11) 1.521(2)</td>
</tr>
<tr>
<td>C(3)-C(4) 1.412(2)</td>
<td>Fe-C(1)    2.115(1)</td>
</tr>
<tr>
<td>C(4)-C(5) 1.506(2)</td>
<td>Fe-C(2)    2.034(1)</td>
</tr>
<tr>
<td>C(5)-C(6) 1.535(2)</td>
<td>Fe-C(3)    2.058(1)</td>
</tr>
<tr>
<td>C(6)-C(1) 1.530(2)</td>
<td>Fe-C(4)    2.112(1)</td>
</tr>
</tbody>
</table>

---

![Crystal structure diagram](image-url)
TABLE 4.3

Some crystal data\(^{111}\) of tricarbonyl(\(\eta^4\)-1,6\(\alpha\)-dimethoxycarbonylcyclohexa-
1,3-diene)iron 26

(The crystals are monoclinic, space group \(P\alpha\) with unit cell parameters
\(a = 7.469(2)\), \(b = 13.403(5)\), \(c = 6.978(2)\) Å and \(\beta = 93.85(2)^\circ\). The
unit cell contains two molecular units, \(Z = 2\) )

<table>
<thead>
<tr>
<th>Bond distances (Å)</th>
<th>Angles (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(1)-C(2) 1.433(2)</td>
<td>C(1)-Fe-C(2) 40.44(6)</td>
</tr>
<tr>
<td>C(2)-C(3) 1.410(3)</td>
<td>C(2)-Fe-C(3) 40.14(8)</td>
</tr>
<tr>
<td>C(3)-C(4) 1.414(3)</td>
<td>C(3)-Fe-C(4) 39.82(9)</td>
</tr>
<tr>
<td>C(4)-C(5) 1.505(3)</td>
<td>Fe-C(2) 2.049(2) C(4)-Fe-C(1) 76.64(7)</td>
</tr>
<tr>
<td>C(5)-C(6) 1.539(3)</td>
<td>Fe-C(3) 2.058(2) H1(C5)-C(5)-H2(C5) 109.9(32)</td>
</tr>
<tr>
<td>C(6)-C(1) 1.522(2)</td>
<td>Fe-C(4) 2.092(2)</td>
</tr>
</tbody>
</table>
TABLE 4.4

Some examples for bond shortening due to mesomeric involvement of the diene (bond lengths in Å).

![Chemical structures](image)

(REF 138)

(REF 139)

(REF 139)

(REF 140)

(REF 141)
presumably accomplished by back-bonding on demand from the d-orbitals of Fe and its transmission to carbonyl in mesomeric fashion. The enhanced basicity of the 1-CO₂Me in 25 and 26 has also been demonstrated by enhanced lanthanide induced shifts (LIS) in ¹H NMR (section 2.4). Mesomeric involvement of the carbonyl through C(1)-CO₂Me is shown by the X-ray bond lengths of 25 (Table 4.2) and 26 (Table 4.3). The bond C(1)-CO₂Me is significantly shorter than C(4) - C(5), C(5) - C(6), C(6) - C(1) and C(6) - CO₂Me. Similar bond shortening is observed in the acyclic complexes where mesomeric involvement of the diene is possible (Table 4.4).

The reduced reactivity of 1-CO₂Me group in these complexes cannot be a result of a steric factor due to the presence of Fe(CO)₃ moiety. The metal is approximately equidistant from each diene C atom (Tables 4.2 and 4.3). Consequently, the expected steric influence (if any) of Fe(CO)₃ should be approximately the same for the 1-CO₂Me and the 2-CO₂Me. As noted above, this is not the case; 2-CO₂Me is cleaved readily under mildly alkaline conditions. The enhanced LIS of 1-CO₂Me group (Fig 2.5) also indicates that Fe(CO)₃ does not inhibit the steric approach of a particular reagent towards a 1-CO₂Me. The possibility of direct coordination of 1-CO₂Me to the metal is very unlikely considering the distances between the metal and the carbonyl carbon (3.123 Å for 25, 3.061 Å for 26) or the carbonyl oxygen (4.070 Å for 25, 3.887 Å for 26) of 1-CO₂Me.

In the light of the present work, the conclusions of Nametkin et al. on the reduced reactivity (Pinner reaction, LiAlH₄ reduction), of 1-CN group of 109, are queried. These workers concluded that steric factors caused by the presence of the Fe(CO)₃ fragment are most responsible for the type of nitrile group reactivity in these π-complexes. They suggested the possibility that the 1-CN group may act as a monodentate ligand and produce a bond with the metal resulting in a lower polarity of the nitrile group. The latter postulation further contradicts
Alkaline hydrolysis of 1,6β-dimethoxycarbonyl complex 25 resulted in 6α-CO₂H 48 (entry 13, Table 4.1) with exclusive epimerisation at the 6-position. The reaction with NaOD/D₂O/MeOD gave, after quenching before completion, an acid, the ¹H NMR spectrum of which lacked the double-doublet at δ 3.46 corresponding to the 6β-H of 48. The absence of a 6β-H was further manifested in the 5-CH₂ splitting pattern. The mass spectrum of the product corresponded to 95% -d₁. The acid is therefore 110. The recovered 6β-CO₂Me complex also contained 35% of α-deuterium (MS, ¹H NMR). The results can be coordinated with the 5β-CO₂Me complex 27, the intermediate being a mesomeric anion (Scheme 4.1).

The 1-CO₂Me complex 11 is the thermodynamically most stable isomer. However, this is only partially produced by the isomerisation since hydrolysis of the 5β-CO₂Me ester to the salt of 5β-CO₂H or 5α-CO₂H will tend to inhibit the deprotonation required to produce 11 via the carbanion (Scheme 4.1). The formation of the deuterated ester 111 (6α-D) is presumably due to kinetic protonation of the carbanion from the less hindered α-face in competition with reaction at the β-face to give the less compressed and less hindered α-CO₂Me which then is rapidly hydrolysed.
Scheme 4.1. Involvement of carbanions in the conversion of $\beta$-CO$_2$Me complexes to $\alpha$-CO$_2$H and 1-CO$_2$Me complexes under alkaline hydrolysis conditions.
The 6α-H of 25 [1,6β-(CO₂Me)₂] was deprotonated completely while, in the case of 27 (5β-CO₂Me) it occurred only to a minor extent. This is possibly due to electronic or/and steric effects from the 1-CO₂Me group of 25. To test for either possibility, the 1-CO₂Me complex 11 was treated with NaOD/D₂O/MeOD, and the complexes 29 (1-OMe,6β-CO₂Me) and 31 [5β,6β-(CO₂Me)₂] were subjected to alkaline hydrolysis.

No deuterium was incorporated to the 1-CO₂Me complex 11 even after prolonged reaction. Without separation of the complex 29 (1-OMe,6β-CO₂Me) from its isomeric components, the mixture of 29, 30 (1-OMe,6α-CO₂Me) and 77 (1-OMe,2-CO₂Me) (5:6:9, section 3.5) was subjected to hydrolysis. The acidic product obtained in 90% yield composed only 53 (1-OMe,6α-CO₂H) and 112 (1-OMe,2-CO₂H) in 1:1 ratio. The pure isomers 30 and 77 gave the corresponding acids in good yield (87-93%). Clearly 6β-CO₂Me 29 had epimerised during the reaction. The 5β,6β-dimethoxycarbonyl complex 31 gave the acid 113, again indicating epimerisation of one of the β-CO₂Me group. The same acid resulted from 5α,6β-(CO₂Me)₂ complex 35.

The results show that the acidity of 6α-H of 25 [1,6β-(CO₂Me)₂] is not enhanced due to any electronic effect by 1-CO₂Me. The removal of the 6α-H from 25, 29 and 31 should be assisted by release of steric compression and by a favourable energy change on conjugation between carbonyl and the resulting anion.

Further support for the postulation of an enhancement of steric compression at 6β-CO₂Me due to the presence of a substituent at the 1-position comes from examination of the X-ray parameters of 25. The 6β-CO₂Me of 25 is closer to the 1-CO₂Me group than to the Fe(CO)₃ segment; the distances between the carbonyl carbon of 6β-CO₂Me and the atoms, Fe, the closest carbonyl carbon of Fe(CO)₃, the carbonyl carbon and oxygen of 1-CO₂Me are respectively 3.945, 3.594, 2.943 and 2.652 Å.
4.4 Blocked ester complexes; stereoselectivity

The use of ester complexes with an acidic proton replaced by a suitable substituent was examined since such substitution prevents any epimerisation, and enables an estimate to be made of the severity of conditions required to obtain the $\beta$-CO$_2$H complexes from the $\beta$-CO$_2$Me.

The blocked diene ester complexes 90, 91 and 93 are available (section 3.7.1). The CO$_2$Bu complex 114 was actually a by-product in one preparation of the complex 90 using n-butyl ether contaminated with trace amounts of mineral acid and n-butanol. The results of the application of alkaline hydrolysis conditions on these esters are shown in the Table 4.1 (entries 17 to 20).

In contrast to the uncomplexed (but unconjugated) diene starting materials, the CO$_2$Me of the complexes is much more resistant to alkaline hydrolysis. A larger alkoxy group (114), or a bulky $\alpha$-group (91) or Me at the 1-position (93) requires still more drastic conditions (see entries 18-20, Table 4.1). The Fe(CO)$_3$ seems to be exerting a classical hindrance effect to approach of OH$^-$ and/or solvation of the ionic transition intermediate. There may still be a possibility of a direct electron-release effect of Fe(CO)$_3$ in stabilising $\beta$-CO$_2$R. However, X-ray parameters$^{111}$ of 6$\beta$-CO$_2$Me complex 25 and tricarbonyl ($\eta^5$-1,3-dimethoxy-5$\beta$-methoxycarbonyl-5$\alpha$-methylcyclohexa-1,3-diene)iron 33 show that Fe(CO)$_3$ group is located sufficiently far away from the $\beta$-CO$_2$Me to preclude any overlap of filled d-orbitals of Fe with the LUMO of the ester carbonyl; the distances between Fe and the carbonyl carbon of $\beta$-CO$_2$Me group are 3.945 Å (25) and 3.689 Å (33). Hence Fe(CO)$_3$ cannot release electrons to the $\beta$-CO$_2$Me.
A reaction of possible synthetic importance is the clean hydrolysis of the diester 36 to a monocarboxylic acid 116. The expectation that the $\alpha$-CO$_2$Me has been hydrolysed, is supported by the disappearance of the higher (6) methoxycarbonyl signal ($^1$H NMR). Methoxycarbonyl on the $\beta$-face resonate at a lower field than the corresponding $\alpha$-protons (section 2.2). This reaction is a clear-cut example of the stereoselectivity of the hydrolysis of $\alpha$-CO$_2$Me and $\beta$-CO$_2$Me.

4.5 Outlook

On a qualitative basis, the ester complexes are hydrolysed more slowly than the uncomplexed diene esters. The ease of hydrolysis of a given complex depends on the position of substitution of the ester group and its steric environment. The regioselectivity is illustrated by the resistance of 1-CO$_2$Me complexes to hydrolyse in the absence of an electron withdrawing group at the 4-position. Where epimerisation is prevented as in blocked esters, $\beta$-CO$_2$R is less easily cleaved than $\alpha$-CO$_2$R. In suitably substituted esters, a single carboxy complex may be found from a mixture of $\alpha$- and $\beta$-isomers as a result of epimerisation of $\beta$-CO$_2$Me.
Alkaline hydrolysis provides a chemical means for purification, separation and structural assignment of ester complexes. The detachment of Fe(CO)_3 from half esters by reaction with odd-electron oxidants or Me_3NO.2H_2O, would lead to organic acids which are difficult to synthesize through classical routes.

The synthetic possibilities that the carboxy functionality provides in these complexes, include the formation of reactive intermediates such as acid chlorides, decarbonylation to form organic cations (section 5.2), and classical resolution of diene complexes to provide chiral intermediates for asymmetric synthesis (chapter 7).
CHAPTER 5
TRICARBONYLCYCLOHEXADIENYLIRON SALTS FROM DECARBONYLATION AND DEHYDROXYLATION; PROCATIONIC COMPLEXES

5.1 Introduction

The role of tricarbonylcyclohexadienyliron salts in organic synthesis is discussed elsewhere.\textsuperscript{34b} The chemist who is in need of a specifically substituted cation for either synthetic or mechanistic studies would find it useful to have a set of defined conditions whereby appropriate precursors could be determined readily.

For the generation of a title cation is required the direct or indirect creation of a positive charge on an allylic ring carbon of a neutral complex (section 1.3). This is possible with some neutral complexes by interaction with certain electrophiles (= electron acceptors, cationoid reagents) which are compatible to Fe(CO)\textsubscript{3} group, e.g. H\textsuperscript{+}, Ph\textsubscript{3}C\textsuperscript{+}. The compounds that lead to cationic complexes by an electrophilic interaction, are described here as "procationic complexes" (cf. the terms prochiral and prodrugs).

Hydride abstraction by Ph\textsubscript{3}C\textsuperscript{+} to form cations usually occurs from the α-face (section 1.3.1). This is prevented by the presence of an adjacent α-substituent. This reaction is sometimes not regioselective. For acid catalysed removal of labile groups such as OMe (section 1.3.2) to result in cations, procationic complexes should be formed from dienes having these specific substituents. Alternative routes to cations as well as procationic complexes are, therefore, very useful.

The present study concentrates on the formation of cations by elaboration of methoxycarbonyl groups. The carboxy complexes available from the hydrolysis of esters (chapter 4) are examined for the possibility of acid catalysed decarbonylation. Carbocations formed by loss of carboxy groups from classical organic compounds like pivalic acid in the presence of concentrated sulphuric acid have been noted.\textsuperscript{143} Analogously, stable tricarbonylcyclohexadienyliron cations can be generated.
From the present study, it also follows that the carboxyl complexes in the cyclohexadiene series are compatible in the use of metalalkyl reagents (e.g. MeLi and MeMgBr) and the reaction leads to the formation of tertiary alcohols in good yields. Interestingly, the reaction shows some stereoselectivity for \( \beta \)-methoxycarbonyl group of 36, and no regioselectivity for esters 11, 12 and 106, unlike alkaline hydrolysis (chapter 4). 1-Alkyl substituted cations can be formed from the alcohols derived from 1-CO\(_2\)Me complexes. The mechanism here involves the detachment of 5\( \beta \)-H rather than 5\( \alpha \)-H.

An alternative route to 1-alkyl substituted cations is described starting from unsubstituted salts through the sequence nitrile,\(^{14}\) ketone,\(^{35a}\) alcohol\(^{144}\) and cation.

RESULTS AND DISCUSSION

5.2 Acid-catalysed decarbonylation

The acids 46 and 48 gave the cations 4 and 117, respectively, in cold sulfuric acid.\(^{74}\) The carboxyl-substituted cations are, as already noted,\(^{51}\) more reactive than others towards nucleophiles, including water.
Their high reactivity is supported by the kinetic data now available for a series of substituted cations. The 2-CO\textsubscript{2}Me cation \textit{117}, for example, reacted almost instantaneously with water to give the alcohol \textit{49} and the ether \textit{118}, when attempts were made to precipitate a salt by the addition of aqueous NH\textsubscript{4}PF\textsubscript{6}. The hexafluorophosphate salt of \textit{117} can, however, be generated in an overall yield of 47% from a mixture of the alcohol and the ether by treatment with HPF\textsubscript{6}-etherate.

 Examination of the acid \textit{51} was of particular interest in view of the competition between the groups, namely OH and CO\textsubscript{2}Me that are cleaved.

The splitting of diene protons of the alcohol \textit{49} and the ether \textit{118} together with their resistance to mild alkaline hydrolysis (section 4.2) was confirmative of the 1-CO\textsubscript{2}Me group. The hydroxy function (IR, D\textsubscript{2}O exchange, MS) of the alcohol was shown to occupy the 6\textalpha-position from its CH\textsubscript{2} splitting pattern characteristic of an adjacent \alpha-substituent (section 2.3.1). Corresponding splitting, diagnostic of stereochemistry, was not discernible in the case of the ether possibly due to its diastereomeric nature. The ether \textit{118} is formed presumably via the addition of the alcohol \textit{49} to the salt \textit{117}. Normally, the addition of alcohols to the salts produces \alpha-alkoxy complexes (section 6.3). Based on this general observation the ether was assigned the stereochemistry as shown in the structure \textit{118}. This stereochemistry was further supported by the analogous
ether 119 for which CH$_2$(α)-splitting pattern was observed. The ether 119$^5$ was available from the reaction of the unsubstituted salt 4 with water.

There is evidence that a β-CO$_2$H is unaffected by concentrated sulfuric acid. A mixture of 46 (α-CO$_2$H) and 64 (β-CO$_2$H) gave a cationic product corresponding only to the content of the former, while most of the latter was recovered unchanged. The acid 115 was also unaffected.

Examination of the acid 53 was of particular interest, in view of the competition between two groups, namely OMe and CO$_2$H, to be cleaved. In fact, only OMe is lost and the product is the α-CO$_2$H cation 120. This process is presumably$^9\alpha,50$ as shown below. The $^1$H NMR of 120 isolated as

![Diagram](image-url)
Scheme 5.1. Possible routes to the formation of unsubstituted and 1-CHO cations from 1-carboxyl complexes.
its PF$_6^-$ salt by treatment with aqueous NH$_4$PF$_6$, showed five dienyl protons as well as the triplet at $\delta$ 3.83 (6-H) identical to those of the 6$_{\alpha}$-CO$_2$Me cation 70 (section 2.7). Infra red (KBr) absorptions at 3500-2500 cm$^{-1}$ confirmed the presence of CO$_2$H group.

The mechanism proposed by Hammett$^{145}$ for decarbonylation of classical carboxylic acids may rationalize the formation of the cations 4 and 117.

$$\text{RCOOH} + \text{H}_2\text{SO}_4 \rightarrow \text{RCOOH}_2 + \text{HSO}_4^\Theta$$

$$\text{RCOOH}_2 \rightarrow \text{RCO}_2\Theta + \text{H}_2\text{O}$$

$$\text{RCO}_2\Theta \rightarrow \text{R}_2\Theta + \text{CO}$$

The 1-carboxyl complexes did not react despite the expectation of possible production of a dienyl cation via allyl intermediates as shown in Scheme 5.1. The absence of the unsubstituted cation 4 indicates that protonation does not occur at the 1-carbon. This is in line with arguments which explain the introduction of only one D with deutero-acid in the acid catalysed isomerisations of carboxyl complexes (section 1.4). The intermediates which could have led to the formation of 1-CHO cation 121$^{58}$ are probably energetically unfavourable, although they are plausible by analogy with dehydroxylation reactions (section 5.3.2.).

The stereoselectivity of the decarbonylation is probably because the protonation of a $\beta$-CO$_2$H requires iron mediation. Subsequent transfer of a proton to the diene is kinetically more favourable, as evident from the result where demethoxylation occurs in preference to decarbonylation. This leads to a low probability that the $\beta$-CO$_2$H is protonated and hence such complexes are recovered unchanged.

5.3 Dehydroxylation

Dehydroxylation has an advantage over demethoxylation in that the hydroxy group does not have to be present in the organic precursor.
Alcohols have already been noted in the tricarbonylcyclohexadiene-iron series by modification of the carbonyl type functionality. Examples include diborane reduction of 122 (1-CO$_2$H) and 123 (2-CO$_2$H),$^{51}$ NaBH$_4$, and MeLi reactions of 124 (1-CHO) and 125 (1-COMe),$^{60}$ the action of MeMgI on 62 (5$\alpha$-COMe),$^{144}$ and Reformatsky reaction,$^{146}$ NaBH$_4$ treatment$^{14}$ and the action of lithiumalkyls$^{147}$ on the enone 3. Alcohols derived from 122, 124, 125 and 3 have been converted to cations.

$$R = CO_2H \ (122) \quad R = CO_2Me \ (12)$$
$$= CHO \ (124) \quad = CO_2H \ (123)$$
$$= COMe \ (125) \quad = COMe \ (129)$$

A study on dehydroxylation of alcohols, formed from carboxyl complexes, to result in cations seemed useful, considering the fact that a number of Me and OMe substituted ester complexes are readily available from benzoic acids (chapters 3 and 4). There is also the potential possibility of having them optically pure via resolution of the carboxy complexes (section 7.2).
5.3.1 Alcohols from ester complexes

The monesters 11, 12, and 102 were reacted with MeLi or MeMgBr at low temperatures to yield the corresponding isopropyl alcohols 126, 127, and 128 respectively. Unlike the enone 3 where lithiumalkyl reactions have been possible in CH$_2$Cl$_2$ while decomposition is observed in ethereal solvents, the esters reacted smoothly in both ether and CH$_2$Cl$_2$ producing high yields of alcohols (70-95%). However, the metalalkyl reagent had to be in excess (3 eq) for no obvious mechanistic reason, otherwise intermediate acetyl complexes (e.g. 125 and 129) accompanied the alcohols. The identification of the products was straightforward from their spectral properties. The literature method for the formation of the alcohol 126 involves several steps starting from acyclic organic substrates. 60
The deuterium-labelled alcohol 130 was required for verification of certain mechanistic points in the dehydroxylations discussed below. The synthesis involved two steps starting from 1-CO₂Me cation 5. Boro-deuteride (> 98% - d) reduction of the salt in acetonitrile provided the 1-CO₂Me complex 131 with D incorporation (> 95% - d₁,MS) at the 5α-position. The position of D, which was assigned unequivocally by ¹H NMR using double resonance techniques, was in agreement with the results of usual nucleophilic additions to the above salt (chapter 7) and the formation of the undeuterated salt from 131 by treatment with Ph₃C⁺PF₅⁻. As expected, the reaction of the ester 131 with MeLi gave the alcohol 130 (> 95% - d₁,MS) the structure of which was determined by ¹H NMR using double resonance techniques and D₂O exchange experiments.

Scheme 5.2. Products from the reactions of tricarbonyl(n⁴-5α,5β-dimethoxycarbonylcyclohexa-1,3-diene)iron 36 with MeLi and MeMgBr.
The diester 36 was of particular interest, in view of stereoselective reactions (cf. its alkaline hydrolysis, section 4.4). The reaction of 36 with MeLi gave in 75% yield at least six products which were separated by tlc (Scheme 5.2). The most mobile band constituted methyl benzoate and the 5β-CO₂Me ester 27 (section 2.2) which were identified by use of an authentic sample (¹H NMR). The ¹H NMR of 132 (5β-CO₂Me, 5α-CO₂Me) showed its inner and outer diene protons at usual chemical shifts (δ 5.38 and 3.26 respectively), and the methylene protons as an ABX at δ 2.34. The singlets at δ 3.62 (3H) and 2.07 (3H) accounted for α-CO₂Me and β-CO₂Me, respectively (IR 1730, 1710 cm⁻¹). The absence of a methyl singlet at δ ≈ 3.63 suggested the α-CO₂Me steric assignment for 132 (section 2.2, the diester 36 shows it β-CO₂Me at δ 3.73 and α-CO₂Me at 3.63). The assignment of stereochemistry for the isomeric alcohols 133 and 134 was again based on the chemical shifts of their CO₂Me. The methoxycarbonyl of 133 appeared at δ 3.63 while that of 134 at δ 3.80. The diastereotopic Me of the β-(1'-hydroxyisopropyl) complex 133 resonated at δ 1.19 (3H) and 1.06 (3H), while those of 134 appeared as a singlet at δ 1.06 (6H). Interestingly, the outer diene proton closer to the blocked carbon displayed an upfield shift as high as 0.2 ppm when going from β-(1'-hydroxyisopropyl) 133 to α-(1'-hydroxyisopropyl) 134. The least mobile component was identified as 5α-OH ester 135 from its spectral properties in comparison to those reported. 51

The reaction of the diester 36 with MeMgBr afforded the isomeric alcohols 133 and 134 (2:1) in significant amounts (65%). The presence of the complexes 27, 132 and 135 in trace amounts in the product was noted (tlc).

The 5β-CO₂Me complex 27 arises from the loss of α-CO₂Me from 36, which is more prominent with MeLi. This may occur through a retro-aldol type cleavage at one or two stages of the reaction, A or/and B (Scheme 5.3).
Scheme 5.3. A possible mechanism for the formation of tricarbonyl($\eta^6$-5µ-methoxycarbonylcyclohexa-1,3-diene)iron 27 from tricarbonyl-($\eta^6$-5α,5β-dimethoxycarbonylcyclohexa-1,3-diene)iron 36.
The exact instance cannot be established from the present data without speculation. 27 is formed from the resulting carbanion C which has already been noted in the alkaline hydrolysis of 27 (section 4.4). The formation of 5α-OH ester 135 is puzzling.

In contrast to the results of alkaline hydrolysis (section 4.4), both Meli and MeMgBr react preferentially from the β-face of 36, the latter being more selective. This implicates an initial coordination between the metalalkyl reagent and the Fe(CO)₃ group, E or F.

5.3.2 Cations from alcohols

In consistency with previous observations, the treatment of 1-(1'-hydroxyisopropyl) complex 126 with HBF₄ gave the 1-isopropyl cation 136 in good yield. When 126 was reacted with Ph₃C⁺PF₆⁻, the same cation 136 resulted indicating dehydroxylation rather than hydride abstraction.
The low temperature $^1$H NMR studies of 126 in 95% H$_2$SO$_4$ has enabled Jablonski and Sorensen$^{60}$ to observe an intermediate cation 137 leading to 136. This rearrangement in 99% H$_2$SO$_4$ is, however, accompanied by the formation of the cycloheptadienyl cation 138. Apparently, the medium dependence of this reaction is not well understood. Analogously, when 126 was reacted with trifluoroacetic acid (TFA), the isolated salt (as PF$_6^-$ salt, 48% yield) showed in its $^1$H NMR spectrum resonances (e.g. singlets at $\delta$ 1.51 and 1.20 of equal integration; for other resonances see Experimental) in addition to those of 136 (e.g. doublets at $\delta$ 1.08 and 0.96 corresponding to diastereotopic methyl groups). The ratio of the integration of the resonances at $\delta$ 1.51, 1.20, 1.08 and 0.96 was 1:1:2:2. Any possibility for the presence of the isomeric 2-isopropyl cation 139$^{147}$ was eliminated by comparison of $^1$H NMR spectra. In view of an indirect isolation of the unidentified cation, the mixture of salts was reacted with KCN. The product, obtained in 60% yield, corresponded to a 3:1 mixture of 140 and 141. Reaction of the 1-isopropyl cation 136 with KCN gave a similar mixture of 140 and 141 in 79% yield.
Whether the salt 138 was formed or not in the reaction of 126 with TFA, the nature of products that result from dehydroxylation of 1-\(1'\)-hydroxyalkyl) complexes appears to depend on the acid used.

Considering a mechanism for conversion of 137 into 136, two possible intermediates 142 and 143 are in compliance with the results from kinetic measurements and reactions in deutero acids. The intermediacy of 142 has been questioned by Lewis et al., in a report which appeared at the time of writing the present work. These authors favour the proposition of 143, based on their results from the protonation of the triene 144 at low temperatures.
Whichever is the intermediate, the formation of 136 from 126 (1-CMe₂OH) requires the detachment of one of the hydrogens at 5-position of 126. Jablonski and Sorensen assumed it to be the 5α-H on the basis of the work of Whitesides et al. who showed stereospecific deuterium exchange of β-hydrogens of tricarbonyl(n⁴-cyclohexa-1,3-diene)iron in the presence of deuterio-acids.

The reaction of the 5α-deuterioalcohol 130 with either HBF₄ or Ph₃C⁺PF₆⁻ gave the cation 145 which retained deuterium. The resonance at δ 4.18 corresponding to the 5-H of the undeuterated salt 136, was absent in the ¹H NMR of 145. The presence of 5-D of 145 was further evident from the multiplicity of the resonances at δ 5.85 (doublet, J = 5 Hz, 4-H) and 2.92 (doublet, J = 16 Hz, 6β-H).

The retention of deuterium in the dehydroxylation of 145 confirms that 5β-H is detached from 1-(l'-hydroxyalkyl) complexes in these reactions.
5.3.3 1-Substituted cations from unsubstituted cations

The 5α-(1′-hydroxyalkyl) complexes 146 and 147 were prepared in good yield from the reaction of the ketones 62 and 148, respectively, with MeMgBr or MeLi. The ketones 62 and 148 were obtained in good yield from the reaction of the nitrile 43 with MeMgBr and PhMgBr, respectively. The α-stereochemistry of the products was confirmed from their $^1$H NMR spectra which displayed CH$_2$ splitting patterns characteristic of an adjacent α-substituent.

As noted above, α-substituted cations can be formed from precursor α-haloalkyl complexes by nucleophilic displacement.

Some examples to illustrate the availability of the precursor α-haloalkyl complexes from α-haloalkyl ketones are given in Scheme 5.6.

\[
\begin{align*}
\text{R} &= \text{Me} \quad (146) \\
\text{R} &= \text{Ph} \quad (147)
\end{align*}
\]

\[
\begin{align*}
\text{R} &= \text{Me} \quad (136) \\
\text{R} &= \text{Ph} \quad (149)
\end{align*}
\]
The treatment of the 5α-(1'-hydroxyalkyl) complexes 146 and 147 with TFA, HBF₄ or Ph₃C⁺ provided the 1-alkyl substituted cations 136 and 149, respectively, in 55-73% yield.

Comparison of the results of TFA-treatment on 1-(1'-hydroxyisopropyl) complex 126 and 5α-(1'-hydroxyisopropyl) complex 146 indicates that the two compounds follow different mechanisms. In the latter case, the cation 136 is formed from the intermediate 150 presumably via a [1,2] hydride shift.

5.4 Summary: aromatic substrates → procationic complexes → organic cations

As noted above, dienyl cations can be formed from procationic complexes by detachment of certain atoms or groups, e.g. H, OMe, OH or CO₂H, using an appropriate electrophile, e.g. H⁺ or Ph₃C⁺. During the reaction a ring substituent (e.g. OMe) may be isomerised to an allylic position and cleaved. In some cases, the positive charge generated by cleavage of a substituent (e.g. 1'-OH) on a side chain attached at 1- or 5-position of the ring, may shift to an allylic position of the ring to form a stable cation.

Some examples to illustrate the availability of the procationic complexes from aromatic substrates, are given in Scheme 5.4.
Scheme 5.4. Some examples to illustrate the availability of procationic complexes from aromatic substrates.

a, Ph₃C⁺; b, H⁺; c, RLi; d, RMgBr; e, CN → COR c or d; f, a and then H₂O; g, OH⁻
CHAPTER 6

THE FORMATION OF C-C AND C-X (X = O, S, Se) BONDS BY REACTION OF TRI-CARBONYLCYCLOHEXADIENYLIRON SALTS WITH LITHIUMALKYLS AND LABILE RXH (R = ALKYL AND ARYL)

6.1 Introduction

The utilization of the title salts as synthetic equivalents, primarily involves their bond-formation reactions with nucleophiles (= electron donors, anionoid reagents). A number of reports on the addition of a variety of nucleophiles to these salts is available in the literature (section 1.2).

However, these salts have not been hitherto found compatible with the lithio-derivatives which are commonly used in classical organic chemistry to form C-C bonds with electrophiles. The problems included extensive decomposition and reductive dimerisation of the cationic salts (section 1.2.1), the latter observation being suggestive of an involvement of free radical intermediates. In the present investigation to overcome these problems, it was found that lithiumalkyls react with dienyl salts in methylene chloride at low temperatures (-78°C) to give the corresponding adducts in high yields.

Another problem hitherto has been the difficulty of adding nucleophiles to complexes where the products are reversible. A potential availability of optically active cationic complexes via the addition of reversible chiral nucleophiles, has not been realized due primarily to the lack of mild methods to effect addition of hindered and labile nucleophiles efficiently. Previous attempts with menthol, for example, has resulted in only poor yields of the expected adducts (ca 5%). The conclusions that emerge from the present study are that, in the presence of Hunig base (i.e. ethyl-diisopropylamine), the adducts from labile nucleophiles such as phenol and menthol are formed even at low temperatures (0°C), and can be isolated in high yields. The reaction appears to follow a displacement type of mechanism rather than straight addition.
RESULTS AND DISCUSSION

6.2 Alkylations with lithiumalkyls

Considering the possible involvement of free radicals in the reaction of cationic salts with alkyl lithium, a re-examination of this reaction seemed desirable, in the presence of a radical scavenger, e.g. 2,4,6-tris (1,1-dimethylethyl)phenol. The initial experiment with MeLi and the unsubstituted cation 4 in CH$_2$Cl$_2$ at -78°C in the presence of the radical scavenger (3-5% mol), gave in high yields the expected adduct 151.\textsuperscript{14,53c}

\[ R = \text{H (4)} \]
\[ = \text{OMe (6)} \]
\[ = \text{Me (152)} \]

The blank experiment without the radical scavenger afforded the same product 151 in high yield (Table 6.1). The use of ethereal solvents (Et$_2$O or THF) at -78°C provided low yields of the product 151 as noted\textsuperscript{14,53a} previously. Methylene chloride (solvent) being considered as the factor for success in the alkylation, the salts 4, 6 and 152 were reacted with R'Li (R' = Me, nBu, iPr and tBu) at -78°C. The results are shown in Table 6.1.
<table>
<thead>
<tr>
<th>Cation</th>
<th>MeLi</th>
<th>BuLi</th>
<th>iPrLi</th>
<th>tBuLi</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>87% (80%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>90% (90%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>77% (52%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>79% (69%)&lt;sup&gt;e,f&lt;/sup&gt;</td>
</tr>
<tr>
<td>152</td>
<td>96% (60%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>96% (81%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>94% (55%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>87% (71%)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(75:25)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>(70:30)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>(90:10)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>(80:20)&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>94% (50%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>84% (58%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>94% (10%)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>(100:0)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>(90:10)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>(90:10)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>(60:40)&lt;sup&gt;g,h&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- <sup>a</sup> Isolated yields, not optimised. Spectral data are identical with those previously reported.<sup>53</sup>
- <sup>b</sup> LiMe₂Cu; c R₂Cd; d R₂Zn; e Li(tBuCuSPh); the best yields selected from previous work.<sup>53</sup>
- <sup>f</sup> Contains a very small amount of an unidentified impurity.
- <sup>g</sup> The ratio of the isomers corresponding to the additions at 5- and 1-positions, respectively; as estimated from <sup>1</sup>H NMR spectra.
- <sup>h</sup> The ratio of the isomers isolated.
With the 2-Me cation \textit{152}, the addition occurred predominantly at the 5-position, in agreement with previous studies\textsuperscript{53} using other alkylation reagents. However, the anticipated completely regioselective character of 2-0Me cation \textit{6} was not observed with \textit{R'Li} (\textit{R' = nBu, iPr, tBu}) where both products corresponding to additions at 1- and 5-positions were formed. These are the first examples of nucleophilic addition at a 1-position of a 2-0Me cation. With tBuLi, the addition at the 1-position was as high as 40\%. This may be due to the high reactivities of lithiumalkyls in nucleophilic additions relative to organo-zinc, -cadmium or -cuprate reagents. The isomer ratio of the products corresponding to the additions at 5- and 1- positions in the alkylation of 2-0Me cation \textit{6} is consistent with this factor. The same trend was not found in the case of 2-Me cation \textit{152}. This is not comprehensible at present although the known\textsuperscript{34b} reactivity order 2-Me cation \textit{152} > 2-0Me cation \textit{6}, is reflected in the relative % addition of \textit{R'Li} (\textit{R' = Me, nBu}) at the 1-position of each salt.

Whether methylene chloride functions as a radical scavenger or modulates the reactivity of lithiumalkyls by solvation, the reason for the initial choice of CH\textsubscript{2}Cl\textsubscript{2} as the solvent was the partial solubility of the PF\textsubscript{6}\textsuperscript{+} salt in CH\textsubscript{2}Cl\textsubscript{2}. The disappearance of the salt could then be observed visually as the reaction proceeds.

This method has the distinct advantage in that the lithiumalkyls are usually the starting materials for other organometallic reagents like dialkylzinc, organocuprates\textsuperscript{53} and allylsilanes\textsuperscript{43} which have been used successfully for alkylation of the dienyl cations.

6.3 Reactions with RXH

\[
\text{Fe(CO)}_{3}.C_{6}H_{7}.PF_{6}\Theta + \text{ROH} \xrightarrow{+} \text{Fe(CO)}_{3}.C_{6}H_{7}.OR + \text{HPF}_{6}
\]

The alkoxy adducts, which are acid labile, may be isolated from the reaction mixture by removal of the resulting acid (e.g. HPF\textsubscript{6}), using an appropriate base.
The unsubstituted salt 4 reacted with phenol, phenylthiol, \textit{p}-nitrophenylthiol and phenylselenol in CH$_2$Cl$_2$ at room temperature in the presence of Hunig base to give 40, 58 41, 53c 153 and 42, respectively, in high yields (85-90%). The disappearance of the PF$_6$ salt upon the addition of Hunig base was usually within five minutes. While the reaction proceeded smoothly with Hunig base either at 0°C or room temperature, slightly reddish brown solutions were observed with triethylamine at room temperature indicating some decomposition. In the case of potassium carbonate, longer reaction times (> 24 h) were needed for complete disappearance of the yellow salt. The products were purified by passage through a short column of basic alumina or by recrystallization; when passed through silica phenoxy groups exchanged with hydroxy. The adducts from the above reactions were readily identified from their spectral properties. The stereochemistry was assigned unequivocally from methylene splitting patterns characteristic of an adjacent \textit{\alpha}-substituent (section 2.3.1).
Analogously, menthol and isopropanol were added to the 2-OMe salt 6 and 2-Me salt 152 in the presence of Hunig base at 0°C to give the adducts 154 and 54, respectively in high yields.

The addition of Hunig base or triethylamine by itself to a suspension of the salt 4 in CH$_2$Cl$_2$ resulted almost instantaneously in a homogeneous solution. The infra red spectrum of the solution showed bands (2050, 1980 cm$^{-1}$) for neutral Fe(CO)$_3$ group. The addition of petroleum to the cooled (-40°C) solution resulted in an unstable solid residue, the $^1$H NMR of which showed signals at $\delta$ 5.4, 3.4 and 2.9 corresponding to inner and outer protons indicating the absence of a positive charge on the diene segment. This solid residue gave the adduct 39 in 49% yield when stirred in CH$_2$Cl$_2$ with methanol. The use of pyridine as the base afforded almost quantitatively a stable pale yellow solid which showed spectral properties consistent with the structure 155. The salt 155 did not react with methanol. The addition of pyridine to a solution of the salt 4 and methanol in acetonitrile resulted in 155, and no 39 was isolated.

\[ R^1 = \text{OMe}, \ R^2 = \text{menthyl} \quad (154) \]
\[ R^1 = \text{H}, \ R^2 = \text{Me} \quad (39) \]
\[ R^1 = \text{Me}, \ R^2 = \text{iPr} \quad (54) \]
Considering a mechanism, the involvement of the tertiary amine \((NR_3^+)\) can be envisaged in three different ways.

(1)

i. \(RXH + \cdot NR_3^+ \rightarrow RX^+ + R_3^+NH\)

ii. \(Fe(CO)_3.C_6H_7PF_6^+ + RX^+ \rightarrow Fe(CO)_3.C_6H_7.XR + PF_6^\)

(2)

i. \(Fe(CO)_3.C_6H_7PF_6^+ + RXH \rightarrow Fe(CO)_3.C_6H_7.XR + HPF_6\)

ii. \(HPF_6 + \cdot NR_3^+ \rightarrow R_3^+NH PF_6^\)

(3)

i. \(Fe(CO)_3.C_6H_7PF_6^+ + \cdot NR_3^+ \rightarrow Fe(CO)_3.C_6H_7.NR_3^+PF_6^\) \((156)\)

ii. \(Fe(CO)_3.C_6H_7.NR_3^+PF_6^\) \((156)\) + \(RXH \rightarrow Fe(CO)_3.C_6H_7.XR + R_3^+NH PF_6^\)

The above experimental results do indicate the intermediacy of \(156\). A stable quaternary ammonium salt of the type \(156\) has been isolated previously\(^{105}\) with 2-0Me cation and 3-(pyrrolidin-1-yl)estra-3,5-diene-17-one. For ionization of \(RXH\) by a tertiary amine requires certain activation in \(RXH\); tertiary amines are not, for example, protonated by phenylthiol.\(^{152}\) The formation of \(156\) may require less activation energy. The conversion of the ammonium salt \(156\) to the adduct \(157\) depends possibly on their relative stabilities. In the case of pyridine, the pyridinium salt \(155\) was isolated. The significant stability of \(155\) may be accounted for by the delocalisation of positive charge on the pyridine ring. Had mechanism (2) been operative, the 5α-0Me adduct \(39\) should have formed from the mixture of 4, methanol and pyridine.

The mechanism is clearly (3). The tertiary amine functions as a 'nucleophilic catalyst'. The isolation of acid labile adducts \(157\) has been possible, the free acid (HPF\(_6\)) being trapped as the quaternary ammonium salt \(R_3^+NH PF_6^\). A displacement reaction analogous to \(156 \rightarrow 157\)
has been reported with neutral complexes under reflux conditions.\textsuperscript{34a}

\begin{center}
\begin{tikzpicture}
\begin{scope}[every node/.style={anchor=west}]
\node at (0,0) {MeO \( \text{(CO)}_3 \text{Fe} \)};
\node at (1,0) {OEt};
\end{scope}
\end{tikzpicture}
\hspace{1cm}
\begin{tikzpicture}
\begin{scope}[every node/.style={anchor=west}]
\node at (0,0) {HNEt}_2;
\node at (1,0) {reflux, THF \ 30 \ min};
\end{scope}
\end{tikzpicture}
\begin{tikzpicture}
\begin{scope}[every node/.style={anchor=west}]
\node at (0,0) {MeO \( \text{(CO)}_3 \text{Fe} \)};
\node at (1,0) {NEt}_2;
\end{scope}
\end{tikzpicture}
\end{center}

6.4 Outlook

The scope of the reaction conditions employed for alkylation of dienyl salts with lithiumalkyls\textsuperscript{153} is almost limitless as apparent from further work along these lines.\textsuperscript{147} The reaction may be extended to other types of cations and lithio-derivatives including acyl equivalents. Grignard reagents have also been reacted with cationic complexes successfully. The use of methylene chloride as the solvent at low temperatures has enabled the alkylation of tricarbonyliron complexes of cyclohexadienones with lithiumalkyls.

Now achieved has been the optical resolution\textsuperscript{147} of cationic complexes by efficient addition of optically active alcohols, using Hunig base as the 'nucleophilic catalyst'.

Some potential uses of chiral tricarbonyliron-cyclohexadienone complexes for organic synthesis are based on the production of a new, enantiopure, 

particularly important finding. The tricarbonyliron-cyclohexadienone system allows the preparation of cationic complexes by stereospecific nucleophilic attack by various optically active alcohols. The chiral complexes can be obtained with high ee \textsuperscript{147} and a broad range of enantiomeric synthesis of natural products, including \textsuperscript{147} and \textsuperscript{147}.


7.1 Introduction

Some potential uses of chiral tricarbonylcyclohexadienyliron salts for organic synthesis are based on the production of a new resolved chiral centre, by stereo-specific nucleophilic attack (e.g. chapter 6) followed by removal of the initial chirality on detachment of the Fe(CO)$_3$ (section 1.7). To make full use of this capability involves a knowledge of the absolute configurations of the chiral cations, and an ability to produce them in fully resolved form.

An approach to preparations of the chiral cations is the production of related neutral complexes, reactions for conversion of the latter into the cations being stereo-selective (section 1.3, chapter 5). Although chiral transfer of Fe(CO)$_3$ to cyclohexadienes has been accomplished and the absolute configurations of some of the substituted cations (2-OMe and 2-Me 156) which can be derived from the initial products are known, they are only partially resolved (section 1.5.2).

Tricarbonyl($n^4$-1-carboxycyclohexa-1,3-diene)iron 122 belongs to a particularly important series. The CO$_2$H group provides a basis for classical resolutions. Further 1-carboxyl$^{51}$ and 1-alkyl substituted cations can be derived from 122 (section 5.3.2), providing a model for a number of synthetic processes. The reaction of enantiomeric 1-carboxyl cations of known absolute configurations with appropriate nitrogenous nucleophiles may, for example, be the only practicable route to a direct asymmetric synthesis of natural gabaculine 10 and a determination of its
Gabaculine 10 was discovered in a culture filtrate of *Streptomyces toyocaenies* subspecies 1039 by Mishima and coworkers in 1976.\(^{57a}\) Gabaculine, isolated as an amorphous powder, \([\alpha]_D = -454^\circ (C = 1, H_2O)\), was assigned the structure 10 on the basis of physical and chemical data. This unusual naturally occurring amino acid is a topic of current biochemical interest because it is an inhibitor of \(\gamma\)-aminobutyric aminotransferase, an enzyme that is directly involved in the metabolism of GABA (\(\gamma\)-aminobutyric acid), an important inhibitory transmitter in the nervous system.\(^{154}\)

Total synthesis of (±)-gabaculine has been reported in the literature by three groups of workers.\(^{57}\) Mishima's procedure involved seven steps from methyl cyclohexa-1,4-diene-1-carboxylate with approximately 20% overall yield of gabaculine.\(^{57a}\) Sharpless synthesized gabaculine from cyclohexa-3-ene-1-carboxylic acid in 23% overall yield, the key reaction being a direct allylic amination of \(L\)-\(\text{b}-\text{butyl cyclohexa-3-ene-1-carboxylate}\) using \(\text{bis}(N\text{-p-toluenesulfonyl})\text{sulfodiimide}.\(^{57b}\) Trost obtained racemic gabaculine in 45% overall yield from cyclohexa-3-ene-1-carboxylic acid. The key step here was the amination of an allylic acetate at an allylic
position with 4,4'-dimethoxybenzhydrylamine and tetrakis(triphenylphosphine) palladium.\textsuperscript{57c}

The present study describes the availability of tricarbonyliron complexes of known absolute configuration via the classical resolution of 1-CO\textsubscript{2}H complex \textsuperscript{122}, using (-)-1-phenylethylamine. The model studies for asymmetric synthesis of natural gabaculine are discussed, using racemic 1-CO\textsubscript{2}Me cations and nitrogenous nucleophiles.

RESULTS AND DISCUSSION

7.2 Optical resolution of tricarbonyl(\eta\textsuperscript{4}-1-carboxycyclohexa-1,3-diene)iron and the absolute configuration of the products

The classical resolution\textsuperscript{110} of 1-CO\textsubscript{2}H complex \textsuperscript{122} was achieved through the salts of (-)-1-phenylethylamine.\textsuperscript{155} Recrystallized from CHCl\textsubscript{3}-acetone, the salt was separated into more and less soluble fractions which were recrystallized to constant rotation from acetone. The less soluble diastereomeric salt, after treatment with dilute HCl, gave (+)-tricarbonyl(\eta\textsuperscript{4}-1-carboxycyclohexa-1,3-diene)iron \textsuperscript{157}, m.p. 147-149°C, [\alpha]\textsubscript{D}\textsuperscript{25} + 136° (C = 3, acetone). The more soluble diastereomeric salt afforded the (-)-isomer, m.p. 147-149°C, [\alpha]\textsubscript{D}\textsuperscript{25} - 136°. The total yield of resolved acid was 34%. The ORD curves are not simple ones but show extrema at 414-422 nm, [\alpha]\textsubscript{\lambda}\textsuperscript{25} (+) or (-) 55°, and at 484-490 nm, [\alpha]\textsubscript{\lambda}\textsuperscript{25} (+) or (-) 214°; they do not cross the zero line and [\alpha]\textsubscript{D} is sufficient to indicate the configuration.

To find the absolute configuration, the (+) acid \textsuperscript{157} was reduced by BH\textsubscript{3}-Me\textsubscript{2}S with BF\textsubscript{3}-Et\textsubscript{2}O in refluxing THF, resulting in conversion of the 1-CO\textsubscript{2}H group into a 1-Me group to yield the (-)-1-methyl complex \textsuperscript{158}. The same complex has been produced\textsuperscript{44} by borohydride reduction from the (-)-tricarbonyl(\eta\textsuperscript{5}-2-methylcyclohexadienyl)iron hexafluorophosphate, [\alpha]\textsubscript{D}\textsuperscript{25} = - 2.5° (C = 9, MeCN) of the known absolute configuration \textsuperscript{158} shown.
Some (-)-tricarbonyl(n^1-2-methylcyclohexa-1,3-diene)iron 159 formed simultaneously has been separated by chromatography on silica impregnated with silver nitrate.

There is no obvious mechanism for, or expectation of, racemisation in these processes so that \([\alpha]_D^{25} = -18^\circ\ (C = 1, \text{CHCl}_3)\) is believed to be that of the optically pure isomer 158. This contrasts with \([\alpha]_D^{25} = -1.7^\circ\ (C = 3, \text{CHCl}_3)\) for 158 obtained via the transfer method\(^9\) and reduction of 156, which leads to an enantiomeric excess (e.e.) of only about 10%. The observed value of \([\alpha]_D^{25} = -1.5^\circ\ (C = 7, \text{CHCl}_3)\) for 159 produced in the same reduction process with presumably the same e.e. leads to about \([\alpha]_D^{25} = -15^\circ\) as the calculated value for pure 159.
7.3 Approaches to the synthesis of natural gabaculine

1-Methoxycarbonyl substituted salts 5, 100, 160, 161 and 162 are available from benzoic acids 51,70 (chapter 4). N,N-Dimethylamine and aniline reacted with the salt 160 (1-CO₂Me, 3-Me) regio- and stereospecifically at 5-position to give, in good yields, the α-adducts 163 and 164, respectively. The α-stereochemistry of the products was unequivocally assigned, J₅,₆₈ being 10-11 Hz (section 2.9).

The regio-specificity of the above addition indicates that gabaculine skeleton 10 may be achieved by reaction of 1-CO₂Me salt 5 with an appropriate nucleophile. The stereo-specificity of the addition implicates the possibilities of an asymmetric synthesis of natural gabaculine by use of an enantiomeric 1-CO₂Me cation.
The use of liquid ammonia as the nucleophile with the unsubstituted cation 4, resulted in the dimeric amine 165 in high yield. The reaction with NaNH₂ led to decomposition.

The formation of the dimeric product 165 is analogous to the reaction of acyclic cations with liquid ammonia. The mechanism is straight-forward. The initially formed 5α-NH₂ adduct is possibly more reactive and/or soluble (in MeCN) than NH₃ itself.

The ammonium salt 166 was obtained in good yield from the reaction of 100 (1-CO₂Me, 2-Me) with hexamethyldisilazane. The ammonium group was noted in the IR spectrum (3225, 3200, 3125, 1575 cm⁻¹) and the ¹H NMR spectrum (MeCN) where the hump at δ 4.5 disappeared in the presence of D₂O. The mass spectrum of the adduct, however, displayed a fragmentation pattern corresponding to the dimeric compound 167 [e.g. m/z 582 (M), 554 (M-CO) etc, 291 (M/2)]. Possibly this indicates an initial radical dimerisation process in the mass probe.
The 5α-NH₂ compound obtained by treatment of the ammonium salt 166 with an aqueous Na₂CO₃ solution was unstable and proved unsuitable for subsequent reactions to form desired gabaculine derivatives.

The alkaline hydrolysis of the diene salt 112 gave the phthalo derivative of gabaculine 112. Microscopic test indicated the presence of an acetylene derivative, but no derivatives were isolated. The isolated compounds were identified as succinic acid, succinic anhydride, succinyl chloride, and succinimide. The removal of metal from 168 was accomplished in 71% yield by prolonged (3 days) treatment with Me₃NO·H₂O in N,N-dimethylacetamide at 0-5°C. The diene 171 was obtained almost quantitatively from 168 under photolytic conditions (20 hours) in the presence of FeCl₃·6H₂O/methanol/benzene. However, in the subsequent attempts to reproduce the result,
the diene 171 was accompanied by significant amounts (15-25%) of aromatic material. In the absence of light, ferric chloride did not cleave the metal even after prolonged reaction conditions (4 days).

\[
\begin{align*}
\text{R} &= \text{Me} \quad (171) \\
\text{R} &= \text{H} \quad (172)
\end{align*}
\]

The alkaline hydrolysis of the diene ester 171 gave the phthaloyl derivative of gabaculine 172. Ninhydrin test indicated the presence of an amino acid, probably gabaculine (tlc),\(^{57b}\) when dephthaloylation was attempted, with hydrazine. The isolated product was, however, mainly benzoic acid indicating the requirement of a protecting group which can be removed under milder conditions.

Carbamates could be converted into NH₂ groups under very mild acidic conditions. Preliminary studies (not reported here) indicate success in the use of potassium ditertiarybutoxycarbamate. If the rotation of the phthaloyl derivative of gabaculine can be found, the result above will define its absolute configuration. So far, natural gabaculine has not been available to us.

7.4 Outlook

A variety of carboxy complexes are available from the alkaline or acidic hydrolysis of esters (chapter 4). Classical resolution of these acids may provide a vast range of optically pure intermediates for application in asymmetric synthesis.
The utilization of Fe(CO)$_3$ as a lateral activating group in the synthesis of gabaculine has some distinct advantages over the previous approaches: the possibility of synthesizing both (-)-gabaculine, naturally occurring enantiomer, and (+)-gabaculine; the determination of their absolute configurations; the flexibility for the preparation of substituted gabaculines using substituted 1-methoxycarbonyl cations.

Other data are presented in the following order: chemical shifts (δ), integration (number of nuclei), multiplicity in terms of usual abbreviations (e.g., s for a singlet, d for a doublet, t for a triplet, q for a quartet, dd for a doublet of doublets and m for a multiplet), coupling constants (J) and assignment. NMR frequencies are given in Hz, values and within brackets are indicated assignments and, if relevant, the relative abundance in percentage of the base peak.
EXPERIMENTAL

GENERAL

Infrared (IR) spectra were recorded on a Perkin-Elmer 257 instrument, using polystyrene as a calibrant. $^1$H NMR spectra were measured for solutions in CDCl$_3$, unless stated otherwise, with TMS as the internal standard on JEOL Minimar 100 and Varian HA100 spectrometers. $^{13}$C NMR spectra were recorded on a JEOL FX60 instrument operating at 15.04 MHz. The mass spectra (MS) were recorded on an AEI MS902 double-focussing mass spectrometer, using heptacosafluorotributylamine as the reference for determination of high resolution data. Melting points (m.p.) were determined on a Reichert hot stage apparatus and are uncorrected. Optical rotations were measured on a Benedix NPL Automatic Polarimeter 143C. Optical rotatory dispersion (ORD) and circular dichroism (CD) curves were recorded on a JASCO Optical Rotatory Dispersion Recorder, model ORD/UV-5, with Sproul Scientific SS 20 CD Modification. Ultraviolet (UV) spectra were recorded on a Varian DMS90 UV Visible Spectrophotometer. Microanalyses were performed by the Australian National University Analytical Services Unit.

NMR data are presented in the following order: chemical shifts (δ), integration (number of nuclei), multiplicity in terms of usual abbreviations (e.g. s for a singlet, d for a doublet, t for a triplet, q for a quartet, dd for a doublet of doublets and m for a multiplet), coupling constants (Hz), and assignment. MS fragments are given as m/z values, and within brackets are indicated assignment and, if relevant, the relative abundance as a percentage of the base peak.
Column chromatography was carried out using Merck silica gel 60 (70-230 mesh ASTM), silica gel H (type 60), or basic alumina 90 (activity 4, 70-230 mesh ASTM) as the absorbent. Thin layer chromatography (tlc) was performed on plates (20 cm x 20 cm x 1 mm) and microslides (analytical) coated with Merck Kieselgel KGF,254. The tlc plates were visualised using ultraviolet light. Solvent mixtures are expressed as a ratio, volume to volume (v/v). Light petroleum refers to the fraction which boils between 60°C and 80°C.

All reactions were carried out under nitrogen. Commercially available solvents of analytical grade were used without further purification, unless stated otherwise.
CHAPTER 2

Availability of compounds

The methods of preparations and the characterisations of the compounds for which the references have not been indicated in the discussion (chapter 2), are presented in the Experimental for other chapters.

**Tricarbonyl(η⁵-6α-methoxycarbonylcyclohexadienylium)iron hexafluorophosphate**

A solution of tricarbonyl(η⁴-1-methoxy-6α-methoxycarbonylcyclohexa-1,3-diene)iron (500 mg, 1.62 mmol) in nitromethane (0.3 ml) was added dropwise with occasional stirring to ice-cooled conc. H₂SO₄ (1.5 ml) containing a few drops of formic acid. After 10-15 min, an ice-cooled aqueous solution (3-5 ml) of NH₄PF₆ (2-3 g) was added with vigorous stirring. The yellow precipitate was collected by filtration, washed several times with water then by ether. The air-dried salt was dissolved in a minimum amount of nitromethane and filtered into a mixture of ether and light petroleum (2:1, ca 25 ml). The precipitated salt (70), after vacuum drying, afforded 295 mg, 43%; ν<sub>max</sub>(KBr) 2130, 1980, 1740 cm⁻¹; δ(CD₃CN) 6.94 (1H, t, J₂,₃ = J₃,₄ = 7 Hz, 3-H), 5.98 (2H, t, J₁,₂ = J₄,₅ = 7 Hz, 2- and 4-H), 4.39 (2H, t, J = 7 Hz, 1- and 5-H), 3.83 (1H, t, J₁,₆β = J₅,₆β = 7 Hz, 6-H), 3.51 (3H, s, CO₂Me).

**η⁶-Hexamethylbenzene(η⁴-2-methoxycarbonylcyclohexa-1,3-diene)iron**

A suspension of dry (C₆Me₆)₂Fe(II)(PF₆)₂ (300 mg) and 1% Na/Hg (5 ml) in freshly distilled THF (20 ml) was stirred at room temperature for 1 h. The mercury was filtered off. Methyl cyclohexa-1,3-diene-2-carboxy-
late (1 g) in THF (3 ml) was added to it and the mixture stirred at 40 °C overnight. THF was removed in vacuo and the residue was taken in hexane.
Removal of solid matter by filtration and concentration of the hexane solution gave a reddish solid which was placed in a sublimation apparatus (40 °C/0.1 mmHg) for a period of 24 h to remove any hexamethylbenzene.
The unsublimed residue was crystallized (n-hexane, -78 °C) giving air-sensitive dark reddish-brown crystals (≈ 100 mg, ≈ 50%), \( \nu_{\text{max}} 2900, 2840, 1700, 1450 \text{ cm}^{-1} \); \( \delta(C_6D_6) \) 4.75 (1H, d, \( J = 6 \text{ Hz} \), 3-H), 3.44 (3H, s, CO\(_2\)Me), 2.27 (1H, m, diene 1-H), 2.05 (1H, m, 4-H), 1.8 (18H, s, C\(_6\)Me\(_6\)), 1.5-1.0 (4H, m, 5,6-H); \( m/z \) 356 (90%, M), 341 (10%, M-CO\(_2\)Me), 249 (39%, C\(_6\)Me\(_6\)FeOMe), 219 (62%, C\(_6\)Me\(_6\)FeH), 218 (59%, C\(_6\)Me\(_6\)Fe), 194 (11%, FeC\(_8\)H\(_{10}\)O\(_2\)), 162 (67%, C\(_6\)Me\(_6\)), 161 (47%, C\(_{12}\)H\(_{17}\)), 147 (100%, C\(_{11}\)H\(_{15}\)), 134 (27%, FeC\(_6\)H\(_6\)), 105 (29%, C\(_6\)H\(_5\)CO); (Found: C, 67.6; H, 7.9. \( C_{20}H_{28}O_2Fe \) requires C, 67.4; H, 7.9%).

Lanthanide shift reagent (LSR) studies on tricarbonyl(η⁴-1,6α-dimethoxy carbonylcyclohexa-1,3-diene)iron 25, tricarbonyl(η⁴-1,6α-dimethoxycarbonyl- cyclohexa-1,3-diene)iron 26 and tricarbonyl(η⁴-5α,6β-dimethoxycarbonyl- cyclohexa-1,3-diene)iron 35

A 2.2 M solution of tris(1,1,2,2,3,3-heptafluoro-7,7-di[H\(_3\)]methyl-8,8,8-[\(^2\)H\(_3\)]octane-4,6-dionate)europium(III) in deuterchloroform was added sequentially in 5 µl portions to the compound (35 mg, 0.13 mmol) in deuterchloroform (0.4 ml) at ambient temperature. The \(^1\)H NMR of the solution was recorded after each addition, using a Varian HA 100 spectrometer at 100 MHz with TMS as lock.
Computer-simulation studies

The NMRSIM program was used with the assistance of Mr M.J. Whittaker. The chemical shifts and the coupling constants depicted in the Fig 2.1 and 2.3 were fed into a DEC PDP11/45 computer. Simulation of the observed patterns (Fig 2.4 and 2.5, respectively) was achieved by variation of the difference in chemical shifts of β-H and α-H of methylene protons.

Aromatic solvent induced shift (ASIS) studies

The ¹H NMR of each compound (Table 2.6) was recorded both in deuterochloroform and hexadeuterobenzene on a JOEL Minimar 100 spectrometer.
CHAPTER 3

General procedure for complexation of dienes with pentacarbonyliron

Complexation was performed under 'thermal' or 'photochemical' conditions. The thermal reaction, unless specified otherwise, involved boiling the diene with excess filtered pentacarbonyliron ($\alpha > 2.0-3.0$ equivalents) in di-n-butyl ether (freshly filtered through basic alumina; $\alpha > 10$ ml for 1 g of diene) under reflux for 18-20 h. After cooling to ambient temperature, the reaction mixture was filtered through Celite and solvent removed, together with excess Fe(CO)$_5$, under aspirator pressure ($\alpha > 12$ mmHg, 60-70°C, in a Büchi rotary evaporator). The residue was passed through a short column of silica gel H(type 60), using a mixture of ether and light petroleum (1:1) as the eluant. Unreacted diene (if any) was removed by recrystallization or distillation under reduced pressure; in the case of some blocked ester complexes, unreacted diene was removed by alkaline hydrolysis where the complex remained unchanged (chapter 4).

The photochemical method involved the irradiation under reflux, of the mixture of the diene, pentacarbonyliron and the solvent with ultraviolet light from Clemco 16 x 12 W UV lamps (280 nm). The work-up was similar to that described above.

General procedure for preparation of cyclohexa-1,4-diene esters from benzoic acids

The method involved Birch reduction ($\text{Li/} \text{NH}_3$) of the aromatic acid and subsequent methylation of either the lithium salt of the reduced acid ($\text{Me}_2\text{SO}_4/\text{MeOH}$), or the isolated free acid ($\text{Me}_2\text{SO}_4/\text{K}_2\text{CO}_3/$acetone). Birch reduction of benzoic acids was carried out in a conical flask (a 3 l flask for 0.5 mol scale) using liquid ammonia ($\alpha > 0.5$ l for 0.5 mol of acid).
transferred directly from an inverted cylinder. The aromatic acid was added portion-wise with magnetic stirring. Lithium wire cut into small pieces (2-5 cm lengths) was added to the flask as rapidly as the foaming allowed, until a permanent blue colour was maintained for 30 min. About 2.5 equivalent of lithium was usually required for the reduction. Towards the end of the reaction the walls of the conical flask were washed with ether to retain any unreacted material to the flask. Solid NH$_4$Cl was cautiously added to destroy the blue colour. The ammonia was allowed to evaporate overnight and the remaining residue either methylated without further purification or the acid was isolated and methylated subsequently.

To isolate the reduced compound, the residue obtained above was dissolved in a minimum amount of water and ice-cold dil. HCl (20%) added until the mixture was acidic (litmus). The product was taken up in ether (4 x 200 ml for 0.5 mol scale). Combined ether extracts were washed with brine and water, dried (MgSO$_4$) and concentrated at aspirator pressure. The methyl ester was obtained by boiling the crude acid with Me$_2$SO$_4$ and excess anhydrous K$_2$CO$_3$ in acetone under reflux in the usual way.

To obtain the methyl ester without isolation of the intermediate acid, excess Me$_2$SO$_4$ (ca. 3 ml for 1 g of acid) was added cautiously to an ice-cold suspension in methanol (ca. 15 ml for 1 g of acid) of the above residue from Birch reduction. The reaction mixture was stirred at ambient temperature for 24 h, diluted with ice-cold water, and extracted with light petroleum. The petroleum extract was worked up in the usual way.
Separation of the mixture of tricarbonyl(n\(^4\)-5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene)iron 27, tricarbonyl(n\(^4\)-5\(\alpha\)-methoxycarbonylcyclohexa-1,3-diene)-iron 29 and tricarbonyl(n\(^4\)-2-methoxycarbonylcyclohexa-1,3-diene)iron 12

Complexation of methyl cyclohexa-2,5-dienecarboxylate 73 \(^{51}\) obtained as above under thermal conditions afforded a mixture of 27, 29 and 12 in a ratio of 70:15:15 (\(^1\)H NMR) in 56\% yield (Table 3.1). The isomer ratio was calculated from the integration of the resonances at \(\delta\) 6.08 (d, 3-H of 12), 5.4-5.3 (m, 2- and 3-H of 27 and 29), 3.65 (s, CO\(_2\)Me of 27 overlapped with the signal for 1-H of 12) and 3.56 (s, CO\(_2\)Me of 29) (see below for full spectral information of the pure isomers).

The mixture of the ester complexes (6.35 g, 0.023 mol) was stirred magnetically with an aqueous solution of sodium hydroxide (20\%, 200 ml) in methanol (300 ml) at 5-10°C for 2 h. The crude mixture (6.0 g, 90\%) of carboxy complexes (see Experimental, chapter 4, for work-up procedure), was fractionally recrystallized (from CHCl\(_3\) and n-hexane) with slow cooling giving an initial crop of pale yellow crystals (1.75 g, 28\%) of tricarbonyl(n\(^4\)-5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene)iron 64. An analytical sample was obtained by further recrystallization from CHCl\(_3\)-hexane, m.p. 116-119°C (decomp.); \(\nu\)\(_{\text{max}}\) (CHCl\(_3\)) 3200-2480 (br, CO\(_2\)H), 2040, 1955, 1700 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 9.3 (br s, CO\(_2\)H), 5.30 (2H, m, 2- and 3-H), 3.30 (2H, m, 1- and 4-H), 2.57 (1H, m, \(J_{5,6\alpha} = 8\) Hz, \(J_{5,6\beta} = 4-6\) Hz, 5-H), 2.24 (2H, m, \(J_{6\beta,6\alpha} = 15\) Hz, \(J_{6\beta,4} = 4\) Hz, 6\(\beta\)-H), 1.89 (1H, m, \(J_{6\alpha,4} = 3\) Hz, 6\(\alpha\)-H); m/z 264 (M), 236 (M-CO), 208 (M-2CO), 180 (M-3CO); (Found: C, 45.3; H, 3.6\%). C\(_{10}\)H\(_8\)O\(_5\)Fe requires C, 45.5; H, 3.1\%). \(\text{CH}_2(\beta)\)-splitting pattern (section 2.3).

The mother liquor was concentrated and cooled (4°C) giving a second crop (1.78 g, 28\%) of yellow crystals. \(^1\)H NMR indicated the presence of both 5\(\alpha\)- and 5\(\beta\)-carboxy complexes, 46 and 64 respectively, in a ratio of
Efficient fractional sublimation of the solid gave two crystalline solids identified as tricarbonyl(\(\eta^4\)-5\(\alpha\)-carboxycyclohexa-1,3-diene)iron 46 (m.p. 91-93°C, 90-100°C/0.05 mmHg) and 5\(\beta\)-carboxy complex (110°C/0.05 mmHg), the former being more volatile. The 5\(\alpha\)-carboxy complex 46 displayed the following spectral characteristics:

\[ \nu_{\max} (\text{CHCl}_3) 3200-2480 \text{ cm}^{-1}; \delta (\text{CDCl}_3) \]

\[ 9.8 \text{ (br s, CO}_2 \text{H), 5.4 (2H, m, 2- and 3-H), 3.12 (2H, m, 1- and 4-H), 2.92 (1H, m, 5-H), 2.09 (1H, m, 6\(\beta\)-H), 1.87 (1H, m, 6\(\alpha\)-H); m/z 264 (M), 236 (M-CO), 208 (M-2CO), 180 (M-3CO); (Found: C, 45.5; H, 3.3%). \]

A third crop of crystals (1.36 g, 21%) from the recrystallization consisted of 5\(\beta\)-, 2- and 5\(\alpha\)-carboxy complexes in a ratio of 7:4:2 as indicated from \(^1\)H NMR. The isomer ratio was calculated from the resonances at \(\delta\)

\[ 6.16 \text{ (d, 3-H of 2-carboxy complex), 5.4-5.3 (m, 2- and 3-H of 5\(\beta\)- and 5\(\alpha\)-carboxy complexes), 3.76 (d, 1-H of 2-carboxy complex), 2.92 (m, 5-H of 5\(\alpha\)-carboxy complex) and 2.57 (m, 5-H of 5\(\beta\)-carboxy complex). The spectral characteristics of 2-carboxy complex and the corresponding methoxycarbonyl ester have been reported elsewhere.}^{51}

Methylation (Me\(_2\)SO/K\(_2\)CO\(_3\)/acetone) of 5\(\alpha\)-carboxy complex 46 (1.1 g, 4.2 mmol) gave tricarbonyl(\(\eta^4\)-5\(\alpha\)-methoxycarboxycarbonylcyclohexa-1,3-diene)iron 29 as a yellow oil (b.p. 96-98°C/0.7 mmHg, 1.16 g, 99%); \(\nu_{\max}\) (film)

\[ 2050, 1970, 1735 \text{ cm}^{-1}; \delta (\text{CDCl}_3) 5.4 (2H, m, 2- and 3-H), 3.56 (3H, s, CO\(_2\)Me), 3.1 (2H, m, 1- and 4-H), 2.9 (1H, m, 5-H), 2.09 (1H, m, 6\(\beta\)-H), 1.87 (1H, m, 6\(\alpha\)-H). \]

\[ CH_2(\alpha)\)-splitting pattern. The complex 29 was unaffected by Ph\(_3\)C\(\Phi\)PF\(_6\).\]

Tricarbonyl(\(\eta^4\)-5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene)iron 27 was similarly obtained in 75% yield by methylation of 5\(\beta\)-carboxy complex 64.
$\nu_{\text{max}}$ (film) 2050, 1960, 1730 cm$^{-1}$; $\delta$(CDCl$_3$) 5.28 (2H, m, 2- and 3-H), 3.65 (3H, s, CO$_2$Me), 3.28 (2H, m, 1- and 4-H), 2.48 (1H, m, $J_{5,6\alpha} = 8$ Hz, $J_{5,6\beta} = 4-6$ Hz, 5-H), 2.24 (1H, m, $J_{6\beta,6\alpha} = 15$ Hz, 6-R-H), 1.89 (1H, m, $J_{6\alpha,4} = 4$ Hz, 6-x-H); $m/\alpha$: 278 (M), 250 (M-CO), 222 (M-2CO), 194 (M-3CO).

CH$_2$(2)-splitting pattern. Treatment of the ester 27 (100 mg, 0.36 mmol) with Ph$_3$CBr (140 mg, 0.36 mmol) in acetonitrile (2 ml) at ambient temperature for 30 min afforded, upon precipitation from Et$_2$O and light petroleum (2:1), a yellow crystalline solid (93 mg, 61%). The salt was identified as tricarbonyl($n^5$-6B-methoxycarbonylcyclohexadienylium)iron hexafluorophosphate, $\nu_{\text{max}}$(KBr) 2120, 1970, 1740 cm$^{-1}$; $\delta$(CD$_3$CN) 7.17 (1H, t, J = 7 Hz, 3-H), 5.91 (2H, t, J = 7 Hz, 2- and 4-H), 4.26 (2H, d, J = 7 Hz, 1- and 5-H), 3.84 (3H, s, CO$_2$Me), 3.04 (1H, s, 6-H).

Application of complexation conditions to tricarbonyl($n^4$-5B-methoxycarbonylcyclohexa-1,3-diene)iron 27, tricarbonyl($n^4$-5x-methoxycarbonylcyclohexa-1,3-diene)iron 29 and tricarbonyl($n^4$-2-methoxycarbonylcyclohexa-1,3-diene)iron 12.

Each compound (100 mg) dissolved in di-n-butyl ether (5 ml) was heated with pentacarbonyliron (0.1 ml) for 20 h under reflux. The crude products (90% from 27, 70% from 29 and 75% from 12) displayed $^1$H NMR resonances identical to the starting ester complex. A small amount of aromatic material was noted ($^1$H NMR) in each case.

Reaction of methyl cyclohexa-2,5-dienecarboxylate 73 with pentacarbonyliron under different conditions.

The reaction conditions and yields are given in Table 3.1. The thermal conditions were applied for large amounts of the diene precursor.
(5-10 g) while photochemical conditions with smaller amounts (2 g, 500 ml of solvent).

**Reaction of p-bromophenacyl cyclohexa-2,5-dienecarboxylate 78 with pentacarbonyliron**

A mixture of potassium cyclohexa-2,5-dienecarboxylate (7.0 g, 43.2 mmol), p-bromophenacyl bromide (6.0 g, 21.6 mmol) and 18-crown-6 ether (1.32 g, 5 mmol, 0.05 M) in acetonitrile was stirred magnetically under reflux for 1 h. The mixture was cooled, filtered and concentrated. Removal of 18-crown-6 by filtration through a column of silica in benzene gave after recrystallization from EtOH/H₂O the diene precursor 78 as white crystals (5.0 g, 70%), m.p. 73-75°C; ν_max (nujol) 1725 (strong, phenacyle CO), 1705 (strong, ester CO), 1640 (weak), 1585 (weak); δ(CDCｌ₃) 7.69 (4H, AB q, aromatic H), 5.87 (4H, br s, diene H), 5.27 (2H, s, CO₂CH₂CO), 3.93 (1H, t, J₁,₄ = 8 Hz, 1-H), 2.63 (2H, d, 4-H).

Complexation of the diene ester 78 with Fe(CO)₅ under thermal conditions afforded a dark brown sticky residue which was distilled (150°C/0.001 mmHg) giving the unstable complex tricarbonyl(η⁴-p-bromophenacylcyclohexa-1,3-diene)iron 65 in very low yield (ca 5%) contaminated (¹H NMR) with small amounts of p-bromophenacyl benzoate (comparison with authentic sample) and p-bromocetophenone (authentic sample). The instability and small amounts of material available prevented separation of these impurities, and acceptable combustion analysis could not be obtained; however, the structure of the major component was confirmed by conversion (see below) into known compounds. The spectral characteristics of 65 are: ν_max(CHCl₃) 2045, 1970, 1735, 1700 cm⁻¹; δ(CDCｌ₃) 7.3 (m, aromatic H), 5.24 (m, 2- and 3-H, and CO₂CH₂CO), 3.2 (m, 1- and 4-H), 2.62 (m, 5-H), 2.23 (m, 6-H), 1.88 (m, 6α-H); m/z 406 and 404 (M-2CO).
378 and 376 (M-3CO), 320 and 318 (M-3CO-Fe-2H). CH$_2$(6)-splitting pattern. Removal of the p-bromophenacyl group with Zn/CH$_3$CO$_2$H at room temperature for 1 h gave 58-carboxy complex 64 ($^1$H NMR), methylation ($Me_2SO_4$) of which afforded 58-methoxycarbonyl complex 27 ($^1$H NMR, IR, tlc) identical with authentic sample.

Reaction of methyl 3,5-dimethoxycyclohexa-2,5-dienecarboxylate 79 with pentacarbonyliron

The diene precursor 79 was prepared in 71% yield from 3,5-dimethoxybenzoic acid by the general procedure described above; $\nu_{max}$ (film) 1730, 1695, 1660, 1595 cm$^{-1}$; $\delta$(CDCl$_3$) 4.78 (2H, d, $J_{1,2} = J_{1,6} = 3.5$ Hz, 2- and 6-H), 3.93 (1H, dt, $J_{1,4} = 7.5$ Hz, 6-H), 3.70 (3H, s, CO$_2$Me), 3.60 (6H, s, 2x0Me), 2.78 (2H, d, 4-H).

Complexation of the crude ester 79 (500 mg, 2.53 mmol) under thermal conditions for 40 h afforded a viscous brownish oil. Passage through a column of silica gel H (type 60), using light petroleum and Et$_2$O (10%) as the eluant gave a homogeneous (tlc) viscous yellow oil (550 mg, 64%) which was identified as tricarbonyl(n$_4$-1,3-dimethoxy-5a-methoxycarbonylcyclohexa-1,3-diene)iron 80, $\nu_{max}$ (film) 2035, 1965, 1725 cm$^{-1}$; $\delta$(CDCl$_3$) 5.39 (1H, d, $J_{2,4} = 2$ Hz, 2-H), 3.58 (6H, s, 3-OMe and CO$_2$Me), 3.36 (3H, s, 1-OMe), 3.17 (1H, dd, $J_{4,5} = 4$ Hz, 4-H), 2.90 (1H, m, 5-H), 2.42 (1H, dd, $J_{6\beta,6\alpha} = 14$ Hz, $J_{6\beta,5} = 11$ Hz, 6$\beta$-H), 1.87 (1H, dd, $J_{6\alpha,5} = 5$ Hz, 6$\alpha$-H); m/z 338 (M), 310 (M-CO), 282 (M-2CO), 254 (M-3CO). The ester 80 did not react with Ph$_3$C=PF$_6$.

Reaction of methyl 2-methoxycyclohexa-2,5-dienecarboxylate 74 with pentacarbonyliron

Lithium/ammonia reduction of methyl 2-methoxybenzoate (10 g, 60 mmol) in the presence of water 158 (1.62 g, 90 mmol) gave the diene precursor
74\textsuperscript{70} (9.8 g, 97%). The complexation of the crude ester (9.8 g, 58 mmol) under thermal conditions afforded, after subsequent passage through a column of silica gel as above, a viscous yellow oil (10 g, 55%) comprising a mixture of three isomeric complexes (tlc, \textsuperscript{1}H NMR, \textsuperscript{70} MS): tricarbonyl(\eta^4-1-methoxy-6β-methoxycarbonylcyclohexa-1,3-diene)iron \textsuperscript{29}, tricarbonyl(\eta^4-1-methoxy-6α-methoxycarbonylcyclohexa-1,3-diene)iron \textsuperscript{30} and tricarbonyl(\eta^4-1-methoxy-2-methoxycarbonylcyclohexa-1,3-diene)iron \textsuperscript{77}.

The isomer ratio of 29:30:77 was calculated to be 5:6:9 from the integration of the resonances at \(\delta(\text{CDCl}_3)\) 5.41 (2-H of \textsuperscript{29}), 5.28 (2-H of \textsuperscript{30}), 5.10 (3-H of \textsuperscript{30}), 4.87 (3-H of \textsuperscript{29}) and 4.56 (3-H of \textsuperscript{77}).

Reaction of dimethyl cyclohexa-2,5-diene-1,2-dicarboxylate \textsuperscript{75} with pentacarbonyliron

\textit{Trans}-cyclohexa-3,5-diene-1,2-dicarboxylic acid, prepared by reduction\textsuperscript{130,159} of benzene-1,2-dicarboxylic acid with Na/Hg in CH\textsubscript{3}CO\textsubscript{2}H/CH\textsubscript{3}CO\textsubscript{2}Na, was isomerised\textsuperscript{130} in water to obtain cyclohexa-2,5-diene-1,2-dicarboxylic acid which upon methylation with BF\textsubscript{3}-MeOH gave the diene precursor \textsuperscript{75} as a colourless oil, b.p. 90-91°C/0.4 mm Hg, in 76% yield; \(\nu_{\text{max}}\) (film) 1740 (strong), 1715 (strong), 1680, 1650 \text{cm}^{-1}; 
\(\delta(\text{CDCl}_3)\) 7.12 (1H, t with fine splitting, \(J_{3,4} = 3.5\) Hz, \(J_{1,3} = 1\) Hz, \(J_{3,5} = 6.5\) Hz, 3-H), 5.82 (2H, m, 5- and 6-H), 4.08 (1H, t with fine splitting, \(J_{1,4} = 7.5\) Hz, \(J_{1,6} = 1\) Hz, 1-H), 3.71 (3H, s, 2-CO\textsubscript{2}Me), 3.66 (3H, s, 1-CO\textsubscript{2}Me), 2.90 (2H, dd with fine splitting, 4-H); \(\delta(\text{C}^{13}\text{C},\text{CCl}_4)\) 171.16 (s, CO\textsubscript{2}Me), 165.70 (s, CO\textsubscript{2}Me), 137.52 (d, \(1J_{\text{CH}} = 162.1\) Hz, 3-C), 125.06 (d of multiplets, \(1J_{\text{CH}} = 161.1\) Hz, \(2J_{\text{CH}} = 5.9, 7.8\) Hz, 6-C), 122.72 (d of multiplets, \(1J_{\text{CH}} = 164.1\) Hz, \(2J_{\text{CH}} = 5.9, 7.8\) Hz, 5-C), 51.8 (q, \(1J_{\text{CH}} = 146.5\) Hz, OMe), 51.42 (q, \(1J_{\text{CH}} = 146.5\) Hz, OMe), 42.20 (d, \(1J_{\text{CH}} = 131.8\) Hz, 1-C), 27.14 (t, \(1J_{\text{CH}} = 129.9\) Hz, 4-C).
Complexation of the diene ester 75 (1.23 g, 6.28 mmol) with Fe(CO)$_5$ (5 ml) under thermal conditions gave a mixture of three (tlc) isomeric complexes (1.56 g, 74%). The yield varied from 74% to 93% at different runs. The components of the mixture were separated by tlc (benzene: acetonitrile 20:1, α 100 mg on each plate).

The most mobile (tlc) compound was identified as tricarbonyl(n$^4$-5α,6β-dimethoxycarboxylcyclohexa-1,3-diene)iron 35. Pale yellow needles, m.p. 62-63°C (from light petroleum); $\nu_{\text{max}}$ (CHCl$_3$) 2055, 1989, 1727 cm$^{-1}$; δ(CDC$_3$) 5.38 (2H, m, 2- and 3-H), 3.70 (3H, s, 6β-CO$_2$Me), 3.62 (3H, s, 5α-CO$_2$Me), 3.40 (1H, dd, J$_{5,6}$ = 4.5 Hz, J$_{5,4}$ = 3.6 Hz, 5-H), 3.32 (1H, dt, J$_{1,2}$ = 6.5 Hz, J$_{1,6}$ = 2.0 Hz, J$_{1,3}$ = 1.7 Hz, 1-H), 3.17 (1H, ddd, J$_{4,3}$ = 6.5 Hz, J$_{4,4}$ = 1.7 Hz, 4-H), 2.97 (1H, dd, 6-H); m/z 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 47.1; H, 3.7%).

C$_{13}$H$_{12}$O$_7$Fe requires C, 46.5; H, 3.6%). The determination of the coupling constants and the assignment of resonances in the $^1$H NMR were made by application of double resonance techniques in the presence of Eu(fod-d$_9$)$_3$, 1.1 x 10$^{-1}$ mol $^{-1}$.

The second band (tlc) corresponded to tricarbonyl(n$^4$-1,6α-dimethoxycarboxylcyclohexa-1,3-diene)iron 26. Yellow crystals, m.p. 55-56°C (from light petroleum); $\nu_{\text{max}}$ (CHCl$_3$) 2058, 1990, 1722, 1702 cm$^{-1}$; δ(CDC$_3$) 6.23 (1H, dt, J$_{2,3}$ = 4.5 Hz, J$_{2,4}$ = J$_{2,6}$ = 1.0 Hz, 2-H), 5.43 (1H, ddd, J$_{3,4}$ = 7.5 Hz, J$_{3,5\alpha}$ = 0.9 Hz, 3-H), 3.66 (3H, s, 1-CO$_2$Me), 3.57 (3H, s, 6α-CO$_2$Me), 3.43 (1H, ddd, J$_{6,5\alpha}$ = 12.0 Hz, J$_{6,5\beta}$ = 3.7 Hz, 6β-H), 3.21 (1H, m, J$_{4,5\alpha}$ = 2.8 Hz, J$_{4,5\beta}$ = 3.5 Hz, 4-H), 2.38 (1H, m, J$_{5\beta,5\alpha}$ = 15.5 Hz, 5 -H), 1.81 (1H, m, 5α-H); m/z: 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 46.4; H, 3.6%).

The third tlc band gave tricarbonyl(n$^4$-1,6β-dimethoxycarboxylcyclohexa-1,3-diene)iron 25. Yellow crystals, m.p. 92-93°C (from light petroleum); $\nu_{\text{max}}$ (CHCl$_3$) 2060, 1988, 1722, 1697 cm$^{-1}$; (CDC$_3$) 5.91 (1H, dt, J$_{2,3}$ =
4.5 Hz, \( J_{2,4} = 1 \text{ Hz}, 2-\text{H} \), 5.31 (1H, dd, \( J_{3,4} = 6.5 \text{ Hz}, 3-\text{H} \)), 3.68 (3H, s, 1-CO\(_2\)Me), 3.63 (3H, s, 6\( \beta \)-CO\(_2\)Me), 3.41 (1H, m, \( J_{4,5} = 3 \text{ Hz}, 4-\text{H} \)), 2.35 (1H, dd, \( J_{6,5\alpha} = 8 \text{ Hz}, J_{6,5\beta} = 6 \text{ Hz}, 6-\text{H} \)), 2.26-1.5 (2H, m, 5-\text{H} ); m/z: 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 46.8; H, 3.9%).

The structures of \( 25 \) and \( 26 \) were confirmed by X-ray analysis. 111

The isomer ratio of the above compounds prior to TLC was estimated from \( ^1\text{H NMR} \) to be 25:26:35:1:3:1. The integration of the resonances at 6.23 (2-\text{H} of \( 26 \)), 5.91 (2-\text{H} of \( 25 \)) and 5.38 (2- and 3-\text{H} of \( 35 \)) was considered for this calculation.

The mixture of three isomeric complexes (TLC), produced in < 30% yield upon boiling the diene and \( \text{Fe(CO)}_5 \) in xylene under reflux for 18 h, was found to be \( 25, 26 \) and \( 35 \) in a ratio of 4:7:4 (\(^1\text{H NMR} \)).

**Reaction of blocked cyclohexa-1,4-diene esters with pentacarbonyliron**

Tricarbonyl(n\( ^4 \)-5\( \beta \)-methoxycarbonyl-5\( \alpha \)-methylcyclohexa-1,3-diene)iron 90 93

Reductive methylation \(^{131} \) of benzoic acid, followed by methylation (Me\(_2\)SO\(_4\)) of the resulting acid yielded methyl 1-methylcyclohexa-2,5-dienecarboxylate \( 85 \), \( \delta(\text{CDCl}_3) \) 5.8 (4H, s, diene H), 3.67 (3H, s, CO\(_2\)Me), 2.64 (2H, s, 4-H), 1.31 (3H, s, Me).

The complexation of the ester \( 85 \) (2 g, 13 mmol) under thermal conditions gave a viscous yellow oil (1.65 g). The \(^1\text{H NMR} \) of the product indicated the presence of unreacted diene (30%) and the complex ester \( 90 \) (35%). Starting material was only partially removed by passage through a column of silica H (type 60), using benzene and acetonitrile (5% v:v). Separation was achieved by selective hydrolysis of the unreacted starting material. The mixture was dissolved in methanol, and stirred with an aqueous solution of NaOH (excess) at 5-10°C for 2 h. The complex ester which was extracted from the mixture with light petroleum, was found to be
completely free of the starting diene. The overall yield of the complex 90 was 44\% (based on the diene reacted in the complexation process).

Yellow crystals, m.p. 53-54°C (from light petroleum); $\nu_{\text{max}}$ (CHCl$_3$) 2045, 1975, 1715 cm$^{-1}$; $\delta$(CDCl$_3$) 5.30 (2H, m, 2- and 3-H), 3.66 (3H, s, CO$_2$Me), 3.37 (1H, dd, $J_{3,4} = 6$ Hz, $J_{2,4} = 2$ Hz, 4-H), 3.06 (1H, m, 1-H), 2.58 (1H, dd, $J_{6\beta,6\alpha} = 16$ Hz, $J_{6\beta,6\beta,1} = 3.5$ Hz, 6\beta-H), 1.52 (1H, dd, $J_{6\alpha,1} = 2.7$ Hz, 6\alpha-H), 1.20 (3H, s, Me); $m/\mu$. 292 (M), 264 (M-CO), 236 (M-2CO), 208 (M-3CO); (Found: C, 50.0; H, 4.2\%. C$_{12}$H$_7$O$_3$Fe requires C, 49.4; H, 4.1\%).

Tricarbonyl($\eta^4$-5\alpha-benzyl-5\beta-methoxycarbonylcyclohexa-1,3-diene)iron 91

Reductive alkylation$^{131}$ of benzoic acid with benzyl bromide$^{160}$ gave 1-benzyl-cyclohexa-2,5-dienecarboxylic acid (92\% yield), methylation (Me$_2$SO$_4$) of which afforded methyl 1-benzylcyclohexa-2,5-dienecarboxylate 86 in 98\% yield as an oil, $\nu_{\text{max}}$ (film) 1725 (strong), 1635 (weak), 1600 (weak); $\delta$(CDCl$_3$) 7.15 (5H, s, aromatic H), 5.80 (4H, s, diene H), 3.61 (3H, s, CO$_2$Me), 2.98 (2H, s, CH$_2$-Ph), 2.43 (2H, narrow m, 4-H).

Complexation of the crude ester 86 (1.5 g, 6.9 mmol) under thermal conditions for 40 h gave a yellow solid (2.51 g, 98\%) identified as 91.

Yellow crystals, m.p. 61-62°C (from light petroleum); $\nu_{\text{max}}$ (CHCl$_3$) 2050, 1970, 1730 cm$^{-1}$; $\delta$(CDCl$_3$) 7.10 (5H, s, aromatic H), 5.27 (2H, m, 2- and 3-H), 3.63 (3H, s, CO$_2$Me), 3.30 (1H, dd, $J_{3,4} = 6$ Hz, $J_{2,4} = 2$ Hz, 4-H), 3.03 (1H, m, 1-H), 2.77 (2H, s, CH$_2$-Ph), 2.53 (1H, dd, $J_{6\beta,6\alpha} = 16$ Hz, $J_{6\beta,6\beta,1} = 4$ Hz, 6\beta-H), 1.77 (1H, dd, $J_{6\alpha,1} = 2.7$ Hz, 6\alpha-H); $m/\mu$. 368 (M), 340 (M-CO), 312 (M-2CO), 284 (M-3CO); (Found: C, 58.6; H, 4.4\%. C$_{18}$H$_{16}$O$_3$Fe requires C, 58.7; H, 4.4\%).
Tricarbonyl[\(n^4\)-5\(\alpha\)-(3',5'-dimethoxy)benzyl-5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene]iron 92

Methyl 1-(3',5'-dimethoxy)benzylcyclohexa-2,5-dienecarboxylate 87

(1.5 g, 5.2 mmol), prepared from the sequence: reductive alkylation (3,5-dimethoxybenzylbromide \(161\)) of benzoic acid and methylation (Me\(_2\)SO\(_4\)), was reacted with Fe(CO)\(_5\) (3.0 ml) under thermal conditions for 40 h to give 92 as a yellow solid (2.19 g, 98%). Yellow crystals, m.p. 84-85°C (from light petroleum); \(\nu\) max (CHCl\(_3\)) 2040, 1985, 1715, 1600, 1595 cm\(^{-1}\);

\(\delta\) (CDCl\(_3\)) 6.30 (1H, t, \(J_{2',4'} = 2\) Hz, 4'-H); 6.15 (2H, d, 2'- and 6'-H), 5.31 (2H, m, 2- and 3-H), 3.70 (6H, s, 2 x OMe), 3.63 (3H, s, CO\(_2\)Me), 3.28 (1H, dd, \(J_{3,4} = 6\) Hz, \(J_{2,4} = 2\) Hz, 4-H), 3.05 (1H, m, 1-H), 2.69 (2H, AB q, CH - Ar), 2.49 (1H, dd, \(J_{6\beta,6\alpha} = 16.2\) Hz, \(J_{6\beta,1} = 3.7\) Hz, 6\(\beta\)-H), 1.78 (1H, dd, \(J_{6\alpha,1} = 3\) Hz, 6\(\alpha\)-H); m/z 428 (M), 400 (M-CO), 372 (M-2CO), 344 (M-3CO); (Found: C, 55.9; H, 4.7%. C\(_{12}\)H\(_{20}\)O\(_7\)Fe requires C, 56.1; H, 4.7%).

Tricarbonyl(\(n^4\)-1,6\(\alpha\)-dimethyl-6\(\beta\)-methoxycarbonylcyclohexa-1,3-diene)iron 93

Methyl 1,2-dimethylcyclohexa-2,5-dienecarboxylate 88 was prepared in 81% yield from reductive methylation of 2-methylbenzoic acid followed by methylation of the resulting dihydro acid, \(\nu\) max (film) 1725 cm\(^{-1}\);

\(\delta\) (CDCl\(_3\)) 5.9-5.4 (3H, m, 3-, 5- and 6-H), 3.67 (3H, s, CO\(_2\)Me), 2.71 (2H, m, 4-H), 1.68 (3H, m, coupled to diene- and 4-H, 2-Me), 1.37 (3H, s, 1-Me).

Complexation of the diene 88 (4.0 g, 26.3 mmol) with Fe(CO)\(_5\) under thermal conditions for 40 h gave a viscous oil (6.74 g, 88%) homogeneous in tlc. The compound was identified as 93, \(\nu\) max (film) 2045, 1980, 1730 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 5.2 (2H, m, 2- and 3-H), 3.70 (3H, s, CO\(_2\)Me), 3.07 (1H, m, 4-H), 2.57 (1H, dd, \(J_{5\alpha,5\beta} = 16\) Hz, \(J_{4,5\beta} = 3-4\) Hz, 5\(\beta\)-H), 1.72 (1H, dd,
$J_{4,5\alpha} = 3$ Hz, $5\alpha$-H), 1.47 (3H, s, 1-Me), 1.20 (3H, s, 6$\alpha$-Me); $m/z$ 306 (M), 278 (M-CO), 250 (M-2CO), 222 (M-3CO).

Tricarbonyl($\eta^3$-2,6$\alpha$-dimethyl-6$\beta$-methoxycarbonylcyclohexa-1,3-diene)iron 94

Methyl 1,3-dimethylcyclohexa-2,5-dienecarboxylate 89 was prepared in 86% yield from 3-methylbenzoic acid as above. $\nu_{\text{max}}$ (film) 1735 cm$^{-1}$; $\delta$(CDCl$_3$) 5.78 (2H, br s, 5- and 6-H), 5.5 (1H, narrow m, 2-H), 3.67 (3H, s, CO$_2$Me), 2.57 (2H, br s, 4-H), 1.74 (3H, br s, 3-Me), 1.33 (3H, s, 1-Me).

Complexation of the diene 87 (4.0 g, 26.3 mmol) with Fe(CO)$_5$ under thermal conditions for 40 h afforded a viscous yellow oil (5.80 g, 76%) homogeneous by tlc. The product was identified as 94, $\nu_{\text{max}}$ (film) 2050, 1980, 1735 cm$^{-1}$; $\delta$(CDCl$_3$) 5.28 (1H, d, $J = 6$ Hz, 3-H), 3.73 (3H, s, CO$_2$Me), 3.38 (1H, d, $J = 1.5$ Hz, 1-H), 2.92 (1H, m, 4-H), 2.57 (1H, dd, $J_{5\alpha,5\beta} = 16$ Hz, $J_{5\beta,4} = 4$ Hz, 5$\beta$-H), 2.15 (3H, s, 2-Me), 1.5 (1H, dd, $J_{5\alpha,4} = 3$ Hz, 5 -H), 1.20 (3H, s, 6$\alpha$-Me); $m/z$ 306 (M), 278 (M-CO), 250 (M-2CO), 222 (M-3CO).

Complexation of cis-cyclohexa-3,5-diene-1,2-anhydride 95

The diene precursor 95 was prepared by the reaction of trans-cyclohexa-3,5-diene-1,2-dicarboxylic acid with acetic anhydride. M.p. 108-110°C (lit. 108-109.5°C), $\nu_{\text{max}}$ (nujol) 1860, 1785 cm$^{-1}$; $\delta$(C$_6$D$_6$) 5.35 (4H, narrow m, diene H), 2.82 (2H, s, methine H).

Cis-anhydride 95 (1.0 g, 6.7 mmol) was reacted with Fe$_2$(CO)$_9$ (3.64 g, 10 mmol) in butan-2-one (20 ml) under reflux for 4.5 h. The crude residue obtained after normal work-up was sublimed at 96-100°C/0.001 mmHg to obtain yellow crystals (170 mg, 10%). The product was identified as a
2:1 mixture of tricarbonyl(η⁴-5β,6β-anhydridocyclohexa-1,3-diene)iron 96 and tricarbonyl(η⁴-5α,6α-anhydridocyclohexa-1,3-diene)iron 97, from the following spectral properties. ν_max (nujol) 2065, 2000, 1860, 1787 cm⁻¹; δ(CDCl₃) 5.56 (dd, 2- and 3-H of 97), 5.33 (dd, 2- and 3-H of 96), 3.48 (narrow m, 5- and 6-H of 97), 3.24 (m, 1- and 4-H of 94 and 97), 2.98 (m, 5- and 6-H of 96 and 97); m/z 290 (M), 262 (M-CO), 234 (M-2CO), 206 (M-3CO). The isomer ratio was deduced from the integration of resonances at δ 5.56 and 5.33.

Physical separation of the deeper yellow crystals in the mixture and subsequent recrystallization from CHCl₃ and light petroleum gave yellow crystals, which had physical properties consistent with the 5α,6α-anhydridocyclohexa-1,3-diene structure 97, m.p. 162-163°C; ν_max (CHCl₃) 2060, 1995, 1858, 1778 cm⁻¹; δ(CDCl₃, HA100 instrument) 5.62 (2H, dd, 2- and 3-H), 3.51 (2H, t, J_5,4 = J_6,1 = 4.5 Hz, 5- and 6-H), 3.23 (2H, m, 1- and 4-H); (M calculated for C₁₁H₆O₆Fe 290.9514, found 290.9520).

Complexation of the cis-anhydride 95 (500 mg, 3.3 mmol) with Fe(CO)₅ (1.7 ml) in diethylether (500 ml) under photochemical conditions for 4-5 h gave a brownish sticky residue which after sublimation at 96-100°C/0.001 mmHg afforded pale yellow crystals (30 mg, < 5%). The product was identified (¹H NMR, IR, MS) as a mixture of 5β,6β-anhydrido 96 and 5α,6α-anhydrido 97 complexes in a ratio of 4:1.

Reaction of cis-dimethyl cyclohexa-3,5-diene-1,2-dicarboxylate 98 with pentacarbonyliron

Esterification of cis-cyclohexa-3,5-diene-1,2-anhydride (3.0 g, 22.4 mmol) with BF₃-Et₂O-MeOH gave the diene precursor 98 as a colourless oil (2.9 g, 75%). ν_max(CHCl₃) 1748 (strong), 1610 (weak), 1590 (weak) cm⁻¹; δ(CDCl₃) 5.94 (4H, m, diene H), 3.6 (8H, s, 2 x CO₂Me and methine H).
The *cis*-diester 98 (1.0 g, 5.1 mmol) and Fe(CO)$_5$ (2.0 ml) in Et$_2$O (1 l) were reacted under photochemical conditions for 4.5 h. The crude product (1.85 g) obtained after normal work-up was sublimed at reduced pressure to yield a yellow solid (1.43 g, 83%). The product composed of two compounds (t1c), was separated by fractional recrystallization from light petroleum.

The first crop afforded major component as moderately unstable buff crystals, m.p. 106-107°C, and had properties consistent with tricarbonyl(η$_4$-5β,6β-dimethoxycarbonylcyclohexa-1,3-diene)iron 31, $\nu_{\text{max}}$(CHCl$_3$) 2055, 1985, 1730 cm$^{-1}$; $\delta$(CDCl$_3$) 5.26 (2H, m, 2- and 3-H), 3.63 (6H, s, 2xCO$_2$Me), 3.22 (2H, m, 1- and 4-H), 2.92 (2H, s, 5- and 6-H); m/z 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 46.4; H, 3.8%. C$_{13}$H$_{12}$O$_7$Fe requires C, 46.5; H, 3.6%).

Second crop gave stable yellow prisms, m.p. 97-98°C, which had properties consistent with tricarbonyl(η$_4$-5α,6α-dimethoxycarbonylcyclohexa-1,3-diene)iron 32, $\nu_{\text{max}}$(CHCl$_3$) 2050, 1980, 1730 cm$^{-1}$; $\delta$(CDCl$_3$) 5.50 (2H, m, 2- and 3-H), 3.55 (6H, s, 2xCO$_2$Me), 3.26 (2H, narrow m, 5- and 6-H), 3.10 (2H, m, 1- and 4-H); m/z 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 46.8; H, 3.7%).

The isomer ratio of 31 and 32 prior to separation was calculated to be 2:1 from the integration of resonances at $\delta$ 5.50, 5.26, 3.63, 3.55, 3.10 and 2.92.
CHAPTER 4

General procedure for the preparation of cyclohexa-1,3-diene methyl esters

To a suspension in methanol ($\approx 25$ ml for $1 \times 10^{-2}$ mol of the aromatic precursor) of the residue obtained after evaporation of liquid ammonia in the Birch reduction step of substituted or unsubstituted benzoic acid (see Experimental, chapter 3), was added excess $\text{Me}_2\text{SO}_4$ ($\approx 7$ ml for $1 \times 10^{-2}$ mol of the acid) and KOH (1-2 g for $1 \times 10^{-2}$ mol of the acid). The reaction mixture was heated under reflux for 5 h. The cooled mixture was diluted with water ($\approx 75$ ml for $1 \times 10^{-2}$ mol of acid), and extracted with light petroleum. The combined petroleum extracts were washed with a solution of aqueous ammonia (to destroy excess $\text{Me}_2\text{SO}_4$) and water, and concentrated at the aspirator pressure to give the desired ester.

Preparation of the ester complexes for hydrolysis studies

Tricarbonyl($\eta^4$-1-methoxycarbonylcyclohexa-1,3-diene)iron 11,
tricarbonyl($\eta^4$-2-methoxycarbonylcyclohexa-1,3-diene)iron 12, 51
tricarbonyl($\eta^4$-1-methoxy-2-methoxycarbonylcyclohexa-1,3-diene)iron 102,
tricarbonyl($\eta^4$-3-methoxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 103
and tricarbonyl($\eta^4$-4-methoxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 104 70 were prepared according to literature.

Tricarbonyl($\eta^4$-1-methoxycarbonyl-3-methylcyclohexa-1,3-diene)iron 101

The complexation of methyl 4-methylcyclohexa-1,3-diene-2-carboxylate (2.75 g, 18 mmol) with pentacarbonyl under thermal conditions (see Experimental, chapter 3) for 40 h gave, after normal work-up, a viscous yellow oil, 3.65 g, 70%, which displayed spectroscopic properties consistent
with tricarbonyl(\(\eta^4\)-3-methoxycarbonyl-1-methylcyclohexa-1,3-diene)iron; 
\(\nu_{\text{max}}\) (film) 2040, 1975, 1720 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 6.1 (1H, s, 2-H), 3.82 (3H, s, CO\(_2\)Me), 3.7 (1H, m, 4-H), 2.1-2.2 (m, methylene H), 1.66 (3H, s, Me).

The crude ester (2.0 g) was boiled in methanol (150 ml) containing H\(_2\)SO\(_4\) (15 ml) under reflux for 24 h. Ice-cold brine was added to the cooled reaction mixture, and the isomerised complex was extracted into light petroleum. The petroleum extract was washed with water, dried (MgSO\(_4\)) and concentrated under reduced pressure. The resulting viscous yellow oil (2.0 g, 100%) was identified as 101. Yellow crystals, m.p. 74-75°C (from light petroleum); \(\nu_{\text{max}}\) (CHCl\(_3\)) 2055, 1980, 1700 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 5.89 (1H, s, 2-H), 3.65 (3H, s, CO\(_2\)Me), 3.36 (1H, m, 4-H), 2.08 (3H, s, Me), 2.05-1.28 (4H, m, methylene H); (M calculated for \(\text{C}_{12}\text{H}_{12}\text{O}_5\text{Fe}\) 292.0034, found 292.0035).

Tricarbonyl(\(\eta^4\)-1-methoxycarbonyl-6a-methylcyclohexa-1,3-diene)iron 47

The application to 2-methylbenzoic acid of the reaction sequence metal/ammonia reduction-isomerisation-methylation, complexation and acid-catalysed isomerisation as above afforded in comparable yields a viscous yellow oil which was subsequently identified as a 1:1 mixture of 47 and tricarbonyl(\(\eta^4\)-1-methoxycarbonyl-2-methylcyclohexa-1,3-diene)iron 99. This mixture could not be separated by conventional physical means. To the crude mixture of complexes (10.0 g, 34 mmol) was filtered in a solution of triphenylcarbenium hexafluorophosphate (13.3 g, 34 mmol) in acetonitrile (40 ml) containing a small amount (tip of a spatula) of MgCO\(_3\). After stirring the dark brown solution at ambient temperature for 30 min, a 2:1 mixture of diethyl ether and light petroleum was added to the reaction mixture to precipitate the resultant cationic complex which was collected by filtration and dried under suction. The filtrate was reserved for
isolation of the 6α-methyl complex. Recrystallisation of the yellow precipitate from MeCN/Et₂O/light petroleum gave a yellow crystalline solid (4.8 g, 11 mmol, 32%) identified as tricarbonyl(n⁵-1-methoxycarbonyl-2-methylcyclohexadienylium)iron hexafluorophosphate 100, decom. > 176°C; ν_max(KBr) 2135, 2090, 2070, 1710 cm⁻¹; δ(CD₃CN) 7.17 (1H, d, J₃,₄ = 5 Hz, 3-H), 5.84 (1H, dd, J₄,₅ = 8 Hz, 4-H), 4.7 (1H, dd, J₅,₆ = 7 Hz, 5-H), 3.87 (3H, s, CO₂Me), 3.3 (1H, dd, J₆α,₆β = 15-16 Hz, 6β-H), 2.5 (3H, s, Me), 2.07 (1H, d, 6α-H); (Found: C, 33.3; H, 2.9%. C₁₂H₁₁O₅PF₆Fe requires C, 33.1; H, 2.5%).

The filtrate obtained above was concentrated and cooled to ca - 30°C. The resulting triphenylmethane crystals were filtered off. Distillation of the filtrate in vacuo gave 47 as a yellow oil, 4.0 g, 14 mmol, 40%; b.p. 85-90°C/0.1 mmHg (kugelrohr); ν_max (film) 2050, 1985, 1690 cm⁻¹; δ(CDC₁₃) 6.06 (1H, d, J₂,₃ = 4 Hz, 2-H), 5.42 (1H, dd, J₄,₅ = 6 Hz, 3-H), 3.68 (3H, s, CO₂Me), 3.18 (1H, m, J₄,₅ = 3.5-4.0 Hz, J₄,₆α = 3.0 Hz, 4-H), 2.70 (1H, m, 6α-H), 2.29 (1H, m, J₅α,₅β = 16 Hz, J₅β,₆β = 10 Hz, 5β-H), 1.44 (1H, m, 5α-H), 0.88 (3H, d, J₆α₆β,Me = 6 Hz, Me); (M calculated for C₁₂H₁₂O₅Fe 292.0034, found 292.0036. ^CH₂(α)-splitting pattern (section 2.3).

Tricarbonyl(n¹-1-methoxycarbonyl-2-methylcyclohexa-1,3-diene)iron 99

Tricarbonyl(n⁵-1-methoxycarbonyl-2-methylcyclohexadienylium)iron hexafluorophosphate 100 (200 mg, 0.46 mmol) was added to a suspension of NaBH₄ (25 mg, 6.0 x 10⁻¹ mmol) in MeCN (8 ml) at 0°C and stirred magnetically for 1 h. After addition of brine, the neutral complex was taken in light petroleum. The petroleum extract was washed with water, dried (MgSO₄) and concentrated at aspirator pressure to result in a viscous yellow oil.
(123 mg, 92%). The compound displayed physical properties consistent with the structure of 99. An analytical sample was obtained by passage through a short column of basic alumina (activity 4) using light petroleum and ether (10%), b.p. 85-90°C/0.1 mmHg (kugelrohr); $\nu_{\text{max}}$ (CHCl$_3$) 2055, 1990, 1690 cm$^{-1}$; $\delta$(CDCl$_3$) 5.17 (1H, d, $J_{3,4} = 6-7$ Hz, 3-H), 3.70 (3H, s, CO$_2$Me), 3.19 (1H, m, 4-H), 2.47 (3H, s, Me), 2.11-1.29 (4H, m, methylene H); (M calculated for C$_{12}$H$_{12}$O$_7$Fe 292.0034, found 292.0038).

Tricarbonyl($\pi^4$-1,4-dimethoxycarbonylcyclohexa-1,3-diene)iron 105

Dimethyl cyclohexa-1,3-diene-1,4-dicarboxylate was prepared from cyclohexane-1,4-dicarboxylic acid according to literature methods,$^{134}$ m.p. 84-85°C (lit.$^{134}$ m.p. 85-85.5°C); $\delta$(CDCl$_3$) 7.09 (2H, s, diene H), 3.78 (6H, s, 2 x CO$_2$Me), 2.53 (4H, s, methylene H). The diene ester (1.0 g, 4.9 mmol) and Fe(CO)$_5$ (1 ml) in nBu$_2$O (15 ml) was heated under reflux with occasional addition of 1 ml portions (x 3) of Fe(CO)$_5$ over a period of 30 h. The reaction mixture was cooled to room temperature before each addition, and the mixture was brought to reflux gradually. Normal work-up afforded 105 as a yellow crystalline solid, 1.67 g, 96%; m.p. 60-61°C (from light petroleum); $\nu_{\text{max}}$ (CHCl$_3$) 2040, 1995, 1697 cm$^{-1}$; $\delta$(CDCl$_3$) 6.13 (2H, s, 2- and 3-H), 3.72 (6H, s, 2 x CO$_2$Me), 2.5-2.3 (2H, m, 5β- and 6β-H), 1.97-1.3 (2H, m, 5α- and 6α-H); $m/z$ 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 46.5; H, 3.6%. C$_{13}$H$_{12}$O$_7$Fe requires C, 46.5; H, 3.6%).

Tricarbonyl($\pi^4$-5α,5β-dimethoxycarbonylcyclohexa-1,3-diene)iron 36

Dimethyl cyclohexa-2,5-diene-1,1-dicarboxylate, prepared in 70% yield by addition of methyl chloroformate to the lithium enolate of methyl cyclohexa-2,5-dienecarboxylate using the method of Cregge et al.$^{162}$ was
obtained as a colourless liquid b.p. 76-77°C/0.15 mmHg; δ(CDC$_3$) 5.8 (4H, s, diene H), 3.67 (3H, s, CO$_2$Me), 2.64 (2H, s, methylene H), 1.31 (3H, s, Me). Complexation of this diene (6.0 g, 31 mmol) with Fe(CO)$_5$ (8 ml) under thermal conditions (see Experimental, chapter 3) gave a viscous yellow liquid (5.2 g), the $^1$H NMR of which indicated the presence of the required complex 36 contaminated with the starting diene (5%). The complex was purified by recrystallization from light petroleum at -18°C giving 36 as yellow crystals (4.3 g, 42%), m.p. 56.5-57.5°C; $\nu_{max}$(CHCl$_3$) 2045, 1980, 1740-1720 cm$^{-1}$; δ(CDC$_3$) 5.38 (2H, m, 2- and 3-H), 3.73 (3H, s, 5α-CO$_2$Me), 3.63 (3H, s, 5β-CO$_2$Me), 3.31 (1H, d, $J_{3,4} = 6$ Hz, 4-H), 3.18 (1H, m, 1-H), 2.53-2.13 (2H, m, 6-H); m/z 336 (M), 308 (M-CO), 280 (M-2CO), 252 (M-3CO); (Found: C, 46.5; H, 3.3%. C$_{13}$H$_{12}$O$_7$Fe requires C, 46.5; H, 3.6%).

General procedure for alkaline hydrolysis

An ice-cooled 20% aq NaOH solution (10 ml) was added in small aliquots to an ice-sooled solution of the ester (0.02 mol) in methanol (20 ml). The mixture was stirred magnetically at 5-10°C for further 2 h, diluted with water (75 ml) and washed with petroleum ether (30/40) (4 x 25 ml). The combined petroleum extracts were washed several times with water, dried (MgSO$_4$), concentrated in vacuo, and kept aside for the identification of the neutral component. The aqueous solution was acidified with ice-cooled HCl (20%), and extracted with ether (4 x 25 ml). The combined ether extract was washed with water, dried (MgSO$_4$), and concentrated in vacuo to obtain the acidic product.
Entries 1-4, Table 4.1; alkaline hydrolysis of the complex esters derived from benzoic acid

Reaction conditions and the yields are given in Table 4.1.

Tricarbonyl($\eta^4$-2-carboxycyclohexa-1,3-diene)iron resulted from 2-CO$_2$Me complex 12, displayed spectral properties identical to those reported.$^{51}$

Tricarbonyl($\eta^4$-5α-carboxycyclohexa-1,3-diene)iron 46 obtained from 5α-CO$_2$Me complex 28, displayed spectral properties identical to those noted previously (see Experimental, chapter 3).

Hydrolysis of tricarbonyl($\eta^4$-5β-methoxycarbonylcyclohexa-1,3-diene)-iron 27 (500 mg, 1.8 mmol) afforded a neutral component (25 mg, 5%) and an acidic product (356 mg, 75%). The spectral properties of the neutral component were consistent with a 1:1 mixture of the starting material (27) and tricarbonyl($\eta^4$-1-methoxycarbonylcyclohexa-1,3-diene)iron 11. The $^1$H NMR of the acidic product was a composite of the spectra of tricarbonyl($\eta^4$-5β-carboxycyclohexa-1,3-diene)iron 64 and the 5α-isomer 46 (see Experimental, chapter 3). The integration of the resonances at δ 2.57 (5-H of 64) and δ 2.92 (5-H of 46) indicated that that 64 was the major product and 46 the minor product (< 10%). Fractional recrystallization of the mixture of acids from CHCl$_3$ and light petroleum gave pure 64 ($^1$H NMR, 116-119°C decomp.) as the first crop.

Entries 5-10, Table 4.1; application of alkaline hydrolysis conditions on methyl and methoxy substituted 1-CO$_2$Me complexes

Tricarbonyl($\eta^4$-1-methoxycarbonyl-2-methylcyclohexa-1,3-diene)iron 99, tricarbonyl($\eta^4$-1-methoxycarbonyl-6α-methylcyclohexa-1,3-diene)iron 47, tricarbonyl($\eta^4$-1-methoxycarbonyl-3-methylcyclohexa-1,3-diene)iron 101,
tricarbonyl($\eta^4$-2-methoxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 102, 
tricarbonyl($\eta^4$-3-methoxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 103 
and tricarbonyl($\eta^4$-4-methoxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 104 
were considered for this study. In each case, no acidic product was 
obtained. The neutral product contained the unreacted starting material 
($^1$H NMR, IR). The yields are given in Table 4.1.

Entries 11-13, Table 4.1; alkaline hydrolysis of diester complexes 

Tricarbonyl($\eta^4$-1,4-dimethoxycarbonylcyclohexa-1,3-diene)iron 105 
(500 mg, 1.5 mmol) gave, under usual hydrolysis conditions, a mixture of 
monocarboxy and dicarboxy complexes. The complex with the higher solubility 
in CHCl$_3$ was identified as tricarbonyl($\eta^4$-1-carboxy-4-methoxycarbonyl- 
cyclohexa-1,3-diene)iron 106 (297 mg, 62%). Yellow crystals, m.p. 170-172$^\circ$C 
(from CHCl$_3$ and light petroleum); $\nu_{\text{max}}$(CHCl$_3$) 3200-2700 (br, CO$_2$H), 2065, 
2000, 1700 cm$^{-1}$; $\delta$(CDCl$_3$) 9.1 (1H, br s, CO$_2$H), 6.1 (2H, s, 2- and 3-H), 
3.71 (3H, s, CO$_2$Me), 2.29 (2H, m, 5$\beta$- and 6$\beta$-H), 1.51 (2H, m, 5$\alpha$- and 
6$\alpha$-H); m/z 322 (M), 294 (M-CO), 266 (M-2CO), 238 (M-3CO); (Found: C, 44.8, 
H, 3.2%. C$_{12}$H$_{10}$O$_7$Fe requires C, 44.8; H, 3.1%).

The complex less soluble in CHCl$_3$ was identified as tricarbonyl($\eta^4$- 
1,4-dicarboxycyclohexa-1,3-diene)iron 107 (147 mg, 32%). The same 
compound was obtained by alkaline hydrolysis (NaOH/MeOH, RT, 2-3 h) of the 
monocarboxy complex 105. Pale yellow crystals, decomp. $>$ 230$^\circ$C (from 
acetone); $\nu_{\text{max}}$(KBr) 3350-2350 (br, CO$_2$H), 2075, 2015, 1990, 1710 cm$^{-1}$; 
$\delta$(d$_6$-DMSO) 11.0 (hump, CO$_2$H), 6.1 (2H, s, 2- and 3-H), 2.15 (2H, m, 
5$\beta$- and 6$\beta$-H), 1.49 (2H, m, 5$\alpha$-H and 6$\alpha$-H); (M calculated for C$_{11}$H$_8$O$_7$Fe 
307.9619, found 307.9614).

The alkaline hydrolysis of tricarbonyl($\eta^4$-1,6$\alpha$-dimethoxycarbonyl- 
cyclohexa-1,3-diene)iron 26 (1.500 g, 4.44 mmol) gave tricarbonyl($\eta^4$-6$\alpha$-
carboxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 48 (1.152 g, 81\%).

Yellow crystals, decom. > 150°C (from CHCl₃ and light petroleum); νmax (CHCl₃) 3500-2300 (br, CO₂H), 2035, 1987, 1700 cm⁻¹; δ(CDCCl₃) 10.21 (1H, s, CO₂H), 6.21 (1H, d, J₂,₃ = 4.5 Hz, 2-H), 5.43 (1H, dd, J₃,₄ = 7.5 Hz, J₃,₅ = 0.9 Hz, 3-H), 3.67 (3H, s, CO₂Me), 3.46 (1H, dd, J₆,₇₅ = 12 Hz, J₆,₅α = 3.7 Hz, 6-H), 3.23 (1H, m, J₁,₂₄ = 1 Hz, J₄,₅α = 2.8 Hz, J₄,₅β = 3.5 Hz, 4-H), 2.40 (1H, m, J₅α,₅β = 15.5 Hz, 5β-H), 1.91 (1H, m, 5α-H); m/z 322 (M), 294 (M-CO), 266 (M-2CO), 238 (M-3CO); (Found C, 44.6; H, 3.3 \% . C₁₂H₁₀O₇Fe requires C, 44.8; C, 3.1 \%). δ CH₂(a)-splitting pattern (section 2.3).

Under similar conditions tricarbonyl(η⁴-1,6β-dimethoxycarbonyl-
cyclohexa-1,3-diene)iron 25 (100 mg) gave a carboxy complex (71 mg, 74 \%) which displayed spectroscopic properties identical to those of 48. A little amount of unreacted diester 25 was noted (tlc, IR) in the neutral fraction.

Entry 14, Table 4.1; alkaline hydrolysis of 5:6:9 mixture of tricarbonyl-
(η⁴-1-methoxy-6β-methoxycarbonylcyclohexa-1,3-diene)iron 29, tricarbonyl-
(η⁴-1-methoxy-6α-methoxycarbonylcyclohexa-1,3-diene)iron 30 and
tricarbonyl(η⁴-1-methoxy-2-methoxycarbonylcyclohexa-1,3-diene)iron 77.

The 5:6:9 mixture (see Experimental, chapter 3) of 29 (1-OMe,
6β-CO₂Me), 30 (1-OMe, 6α-CO₂Me) and 77 (1-OMe, 2-CO₂Me), (10 g, 36 mmol)
was subjected to alkaline hydrolysis conditions as described above. The
tlc of neutral component (410 mg, 4 \%) indicated the presence of at least
2 complexes (IR). The ¹H NMR was a composite of tricarbonyl(η⁴-2-methoxy-
1-methoxycarbonylcyclohexa-1,3-diene)iron 10270 and tricarbonyl(η⁴-1-
methoxycarbonylcyclohexa-1,3-diene)iron 1151 in a ratio of 2:1. The
¹H NMR of the acidic product (8.5 g, 90 \%) was a composite (1:1) of
tricarbonyl\(\eta^6\)-6α-carboxy-1-methoxycyclohexa-1,3-diene)iron \(53\) and tricarbonyl\(\eta^6\)-2-carboxy-1-methoxycyclohexa-1,3-diene)iron \(112\), which were separated and identified as given below. The isomer ratio (1:1) was estimated from the integration of the resonances at \(\delta 5.88\) (3-H of \(112\)), 5.5 (2-H of \(53\)), 5.16 (3-H of \(53\)), 3.64 (0Me of \(112\)) and 3.48 (0Me of \(53\)). Fractional recrystallization from CHCl\(_3\) and light petroleum afforded \(53\) as less soluble yellow crystals, 3.08 g, 38%, m.p. 150-152°C (decomp.); \(\nu_{\text{max}}\)(CHCl\(_3\)) 3300-2500 (br, CO\(_2\)H), 2045, 1975, 1705 cm\(^{-1}\); δ(CDC\(_3\)) 9.1 (hump, CO\(_2\)H), 5.5 (1H, d, \(J_{2,3} = 4.5\) Hz, 2-H), 5.16 (1H, dd, \(J_{3,4} = 6\) Hz, 3-H), 3.48 (3H, s, 0Me), 3.39 (1H, dd, \(J_{5a,6} = 10\) Hz, \(J_{5a,6} = 4\) Hz, 4-H), 2.99-1.80 (2H, m, 5-H); (M calculated for C\(_{10}\)H\(_{10}\)O\(_5\)Fe 265.9877, found 265.9876). CH\(_2\)(α)-splitting pattern corresponding to \(\Delta\delta^B < 0.35\) ppm (Section 2.3).

The second crop (2.1 g, 25%) from recrystallization contained both \(53\) and \(112\) in a ratio of 1:1 (\(^1\)H NMR).

The third crop (1.1 g, 12%) displayed spectral properties consistent with the structure of tricarbonyl(\(\eta^6\)-2-carboxy-1-methoxycyclohexa-1,3-diene)iron \(112\), decomp. > 180°C, \(\nu_{\text{max}}\)(CHCl\(_3\)) 3300-2500 (br, CO\(_2\)H), 2050, 1980, 1710 cm\(^{-1}\); δ(CDC\(_3\)) 9.0 (hump, CO\(_2\)H), 5.94 (1H, d, \(J_{3,4} = 6.5\) Hz, 3-H), 3.66 (3H, s, 0Me), 3.32 (1H, m, 4-H), 2.2-1.8 (4H, m, 5- and 6-H); (M calculated for C\(_{10}\)H\(_{10}\)O\(_5\)Fe 265.9877, found 265.9873).

Methylation (Me\(_3\)SO\(_4\)) of the acids \(53\) (1-OMe, 6α-CO\(_2\)H) and \(112\) (1-OMe, 2-CO\(_2\)H) gave in good yield (85-90%), tricarbonyl(\(\eta^6\)-1-methoxy-6α-methoxycarboxylcyclohexa-1,3-diene)iron \(30\) and tricarbonyl(\(\eta^6\)-1-methoxy-2-methoxycarboxylcyclohexa-1,3-diene)iron \(77\), respectively.

Alkaline hydrolysis of \(30\) afforded in 87% yield, \(53\) only (\(^1\)H NMR). Similarly, \(77\) gave in 93% yield \(112\) only (\(^1\)H NMR).
Entries 15 and 16, Table 4.1; tricarbonyl($\eta^4$-5α,6β-dicarboxycyclohexa-1,3-diene)iron 113

The alkaline hydrolysis of tricarbonyl($\eta^4$-5β,6β-dimethoxycarbonyl-cyclohexa-1,3-diene)iron 31 (200 mg, 0.6 mmol) gave tricarbonyl($\eta^4$-5α,6β-dicarboxycyclohexa-1,3-diene)iron 113 (148 mg, 80%). Pale yellow crystals, decomp. > 165°C (from acetone and CHCl₃); νmax (nujol) 3300-2600 (br, CO₂H), 2050, 1965, 1700; δ(d₆-acetone) 9-8 (hump, CO₂H), 5.55 (2H, m, 2- and 3-H), 3.30 (3H, m, 1-, 4- and 6-H), 2.90 (1H, narrow m, 5-H); m/z 280 (M-CO), 252 (M-2CO), 224 (M-3CO); (Found: C, 42.8; H, 2.6%. C₁₁H₈O₇Fe requires C, 42.9; H, 2.6%).

Under similar conditions tricarbonyl($\eta^4$-5α,6β-dimethoxycarbonyl-cyclohexa-1,3-diene)iron 35 gave, in 76% yield, the same dicarboxy complex 113 (IR, ¹H NMR).

Entries 17-20, Table 4.1; application of alkaline hydrolysis conditions on blocked diene ester complexes

Under usual hydrolysis conditions (5-10°C, 2 h), tricarbonyl($\eta^4$-5β-methoxycarbonyl-5α-methylcyclohexa-1,3-diene)iron 90, the 3:1 mixture of 90 and tricarbonyl($\eta^4$-5β-butoxycarbonyl-5α-methylcyclohexa-1,3-diene)-iron 114, tricarbonyl($\eta^4$-5α-benzyl-5β-methoxycarbonylcyclohexa-1,3-diene)-iron 91 and tricarbonyl($\eta^4$-1,6α-dimethyl-6β-methoxycarbonylcyclohexa-1,3-diene)iron 93 were recovered unchanged (¹H NMR). The latter two compounds 91 and 93 did not react even at 55-60°C (6 h).

Alkaline hydrolysis of tricarbonyl($\eta^4$-5β-methoxycarbonyl-5α-methyl-cyclohexa-1,3-diene)iron 90 (250 mg, 0.86 mmol) at 55-60°C (6 h) gave tricarbonyl($\eta^4$-5β-carboxy-5α-methylcyclohexa-1,3-diene)iron 115 (95 mg, 40%). Significant amount of brownish residue was observed due to
decomposition in the course of the reaction. Yellow crystals, m.p. 135-136.5°C (from CHCl₃ and light petroleum); ν_max(CHCl₃) 3300-2400 (br, CO₂H), 2050, 1985, 1700 cm⁻¹; δ(CDCl₃) 11.27 (1H, br s, CO₂H), 5.32 (2H, m, 2- and 3-H), 3.36 (1H, dd, J₃,₄ = 6 Hz, J₂,₄ = 2.5 Hz, 4-H), 3.08 (1H, m, 1-H), 2.61 (1H, dd, J₆α,₆β = 16 Hz, J₁,₆β = 4 Hz, 6β-H), 1.54 (1H, dd, J₁,₆α = 3 Hz, 6α-H), 1.26 (3H, s, Me); m/z 250 (M-CO), 222 (M-2CO), 194 (M-3CO); (Found: C, 47.6; H, 3.7%. C₁₁H₁₀O₅Fe requires C, 47.5; H, 3.6%).

The 3:1 mixture of 5β-methoxycarbonyl complex 90 and 5β-n-butoxy-carbonyl complex 114 was obtained as a minor component in one preparation of 90 (see Experimental, chapter 3) using n-Bu₂O contaminated with n-butanol and trace amount of mineral acid. When this mixture (450 mg) was subjected to alkaline hydrolysis (55-60°C, 6h), the neutral product (52 mg, 0.16 mmol) displayed spectral properties consistent with the structure of tricarbonyl(n⁴-5β-butoxycarbonyl-5α-methylcyclohexa-1,3-diene)iron 114, ν_max(CHCl₃) 2055, 1975, 1730 cm⁻¹; (CDCl₃) 5.31 (2H, m, 2- and 3-H), 4.09 (2H, t, J₁,₂ = 6 Hz, -OCH₂-), 3.40 (1H, dd, J₂,₄ = 2 Hz, J₃,₄ = 6 Hz, 4-H), 3.08 (1H, m, 1-H), 2.60 (1H, dd, J₁,₆β = 3.5 Hz, J₆α,₆β = 16 Hz, 6β-H), 1.70-1.36 (5H, m, 6α-, 2 x 2'- and 2 x 3'-H), 1.20 (3H, s, Me), 0.94 (3H, t, J₃,₄ = 6.5 Hz, 3 x 4'-H); m/z 334 (M), 306 (M-CO), 278 (M-2CO), 250 (M-3CO). The acidic product (130 mg, 0.47 mmol) was identified as 115 (IR, ¹H NMR).

Tricarbonyl(n⁴-5α-carboxy-5β-methoxycarbonylcyclohexa-1,3-diene)iron 116

Tricarbonyl(n⁴-5α,5β-dimethoxycarbonylcyclohexa-1,3-diene)iron 36 (300 mg, 0.89 mmol) afforded, after alkaline hydrolysis, a yellow solid residue (241 mg, 84%) which was identified as 116. Unstable yellow crystals, m.p. 98-99°C (from CHCl₃ and light petroleum); ν_max(CHCl₃)
3400-2400 (br, CO$_2$H), 2045, 1980, 1720 cm$^{-1}$; $\delta$(CDCl$_3$) 11.2 (1H, s, CO$_2$H), 5.38 (2H, m, 2- and 3-H), 3.78 (3H, s, CO$_2$Me), 3.32 (1H, dd, $J_{3,4} = 6$ Hz, $J_{2,4} = 2$ Hz, 4-H), 3.20 (1H, m, 1-H), 2.56-2.20 (2H, m, 6-H); m/z 322 (M), 294 (M-CO), 266 (M-2CO), 238 (M-3CO); (Found: C, 44.7; H, 3.2\%.

C$_{12}$H$_{10}$FeO$_7$ requires C, 44.8; H, 3.1\%).

Alkaline hydrolysis of uncomplexed diene esters

Cyclohexa-1,3-dienecarboxylic acid

A mixture of tricarbonyl($\eta^4$-1-methoxycarbonylcyclohexa-1,3-diene)iron 11 (700 mg, 2.5 mmol) and trimethylamine-N-oxide dihydrate (2.0 g, 18 mmol) in N,N-dimethylacetamide (15 ml) was stirred at ambient temperature for 10 h. The reaction mixture was filtered through Celite, which was washed through with water and light petroleum. The petroleum extract of the diene ester was washed with water, dried (MgSO$_4$), and concentrated giving 200 mg (58\% yield) of crude methyl cyclohexa-1,3-dienecarboxylate contaminated with trace amount of aromatic material, $\delta$ (CDCl$_3$) 6.96 (1H, d, J = 5 Hz, 2-H), 6.06 (2H, m, 3- and 4-H), 3.73 (3H, s, CO$_2$Me), 2.3 (4H, m, methylene H). Alkaline hydrolysis (5-10°C, 2 h) afforded cyclohexa-1,3-dienecarboxylic acid 140 mg, 78\%; $\nu_{\text{max}}$(CHCl$_3$) 3500-2500 (br, CO$_2$H), 1685, 1590 cm$^{-1}$; $\delta$(CDCl$_3$) 12.1 (s, CO$_2$H), 7.1 (1H, d, J = 5 Hz, 2-H), 6.11 (2H, m, 3- and 4-H), 2.37 (4H, m, methylene H).

Cyclohexa-1,3-diene-1,4-dicarboxylic acid

Dimethyl cyclohexa-1,3-diene-1,4-dicarboxylate (150 mg, 0.77 mmol), prepared above, was subjected to alkaline hydrolysis conditions (5-10°C/2 h) to give cyclohexa-1,3-diene-1,4-dicarboxylic acid as the only product (119 mg, 92\%), m.p. 348-351°C (lit.$^{134}$ 349-351°C); $\delta$(d$_6$-DMSO) 12.0 (2H, hump, CO$_2$H), 7.0 (2H, s, diene H), 2.46 (4H, s, methylene H).
1-Benzylcyclohexa-2,5-diene-1-carboxylic acid

Methyl 1-benzylcyclohexa-2,5-diene-1-carboxylate 86 (200 mg, 0.88 mmol) was subjected to alkaline hydrolysis (RT, 2 h) to result 1-benzylcyclohexa-2,5-diene-1-carboxylic acid (176 mg, 94%); $\nu_{\text{max}}$ (CHCl$_3$) 3500-2400 cm$^{-1}$ (br, CO$_2$H), 1700 (strong), 1635 (weak), 1600 (weak); $\delta$(CDCl$_3$) 11.89 (1H, s, CO$_2$H), 7.19 (5H, s, C$_6$H$_5$), 5.83 (4H, s, diene H), 3.02 (2H, s, CH$_2$Ph), 2.42 (2H, m, methylene H).

1-Methylcyclohexa-2,5-diene-1-carboxylic acid

Methyl 1-methylcyclohexa-2,5-diene-1-carboxylate 85 gave under similar conditions (RT, 2 h) the corresponding acid (IR, $^1$H NMR) in 87% yield.

Deuterium-labelling studies

Treatment of tricarbonyl(n$_4$-1,6-dimethoxycarbonylcyclohexa-1,3-diene)iron 25 and tricarbonyl(n$_4$-1-methoxycarbonylcyclohexa-1,3-diene)iron 11 with NaOD/D$_2$O/MeOD

Sodium (115 mg, 5 mmol) was added to ice-cold MeOD (5 ml). To this solution was added D$_2$O (2 ml) dropwise at 0°C. The diester complex 25 (45 mg, 0.13 mmol) dissolved in MeOD (1 ml) was added to the alkaline solution, and the reaction mixture was stirred magnetically at 5-10°C for 1 h. The reaction mixture was worked up as described above. The neutral component (14 mg, 31%) displayed IR and tlc identical to those of the diester 25. $\delta$(CDCl$_3$) 5.91 (1H, dt, $J_{2,3} = 4.5$ Hz, $J_{2,4} = 1$ Hz, 2-H), 5.31 (1H, dd, $J_{3,4} = 6.5$ Hz, 3-H), 3.68 (3H, s, 1-CO$_2$Me), 3.63 (3H, s, 6H-CO$_2$Me), 3.41 (1H, m, 4-H), 2.35 ($\alpha$ 0.5H, 6-H), 2.26-1.5 (2H, m, 5α- and 5β-H). Mass spectroscopic analysis indicated mono-deuterium incorporation.
of 35%. These spectral properties were consistent with a composite of 25 and tricarbonyl(\(\eta^4\)-1,6\(\beta\)-dimethoxycarbonyl-6\(\alpha\)-[\(^2\)H\(_1\)]cyclohexa-1,3-diene)iron 111.

The acidic component (23 mg, 55%) was identified as tricarbonyl(\(\eta^4\)-6\(\alpha\)-carboxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 110.

\[ \nu_{\text{max}}(\text{CHCl}_3) \text{ 3500-2300 (br, CO}_2\text{H), 2035, 1987, 1700 cm}^{-1}; \delta(\text{CDCl}_3) 9.1 \text{ (hump, CO}_2\text{H), 6.21 (1H, d, J}_{2,3} = 4.5 \text{ Hz, 2-H), 5.43 (1H, dd, J}_{3,4} = 7.5 \text{ Hz, 3-H), 3.67 (3H, s, CO}_2\text{Me), 3.23 (1H, m, 4-H), 2.40 (1H, dd, J}_{5\alpha,5\beta} = 15.5 \text{ Hz, J}_{4,5\beta} = 3.7 \text{ Hz, 5\(\beta\)-H), 1.91 (1H, dd, J}_{4,5\alpha} = 2.8 \text{ Hz, 5\(\alpha\)-H). Mass spectroscopic analysis indicated 95% monodeuterium incorporation.} \]

Under similar conditions with NaOD/D\(_2\)O/MeOD, tricarbonyl(\(\eta^4\)-1-methoxycarbonylcyclohexa-1,3-diene)iron 11 was isolated unaffected (IR, \(^1\)H NMR, MS). No deuterium incorporation was observed even after prolonged conditions (RT, 6 h).

Acidic hydrolysis of tricarbonyl(\(\eta^4\)-6\(\alpha\)-carboxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 48

A suspension of the monocarboxy ester 48 (450 mg, 1.4 mmol) in 20% H\(_2\)SO\(_4\) (50 ml) was boiled under reflux for 24 h. The reaction mixture was cooled and diluted with water (ca 50 ml). The solid material in the mixture was extracted into ether (ca 25 ml x 4). The combined ether extract was washed several times with water, dried and concentrated to result in a pale yellow solid (398 mg, 92%) which had spectral properties consistent with the structure of tricarbonyl(\(\eta^4\)-1,6\(\alpha\)-dicarboxycyclohexa-1,3-diene)iron 108. Pale yellow crystals, decomp. > 216°C (from acetone and CHCl\(_3\)); \[ \nu_{\text{max}}(\text{KBr}) \text{ 2060, 1990, 1705 cm}^{-1}; \delta(d_6\text{-acetone}) 6.28 (1H, d, J}_{2,3} = 4.5 \text{ Hz, 2-H), 5.68 (1H, dd, J}_{3,4} = 6.0 \text{ Hz, 3-H), 3.40 (2H, m, 4- and 6-H), 2.43} \]
(1H, m, 5β-H), 1.90 (1H, m, 5α-H); m/z 308 (M), 280 (M-CO), 252 (M-2CO), 224 (M-3CO); (Found: C, 43.0; H, 2.9%. C₁₁H₉O₇Fe requires C, 42.9; H, 2.6%). CH₂(α)-splitting pattern (Section 2.3).

The carboxyl compound 48 (1.0 g, 3.1 eq/t) was magnetically stirred with conc. H₂SO₄ (15 ml) at 0-5°C for 10 min., whereas water (2 ml) was added dropwise. The mixture was stirred for 1 h. diluted with water (50 ml) and extracted with ether (3 x 25 ml). Combined ether extracts were washed with brine and water, dried (MgSO₄) and concentrated to a yellow sticky residue (400 mg). In a solution of the residue in dry 

CH₂Cl₂ (3 ml) was added H₂P₂O₅-etherate (2 ml), and the mixture was stirred magnetically for 35 min. The yellow crystalline precipitate obtained upon addition of dry ether, was washed several times with dry ether and dried in vacuum to give tricarboxyl[11'-methoxy-carboxy-6,6'-dihydronaphthalenyl]-

iron hexafluorophosphate [117 (6.6 eq, AF₃, 9 8.6 Hz, 3H), 8.70; 8.70; 1700 cm⁻¹; δ(C₅,CH) 7.7 (1H, d, J = 5-6 Hz, 3H), 6.03 (1H, d, J = 5-6 Hz, 4-H), 4.93 (1H, d, J = 6 Hz, 1-H). 6.2 (1H, d, J = 6 Hz, 3-H). 3.73 (2H, t, CO-CH), 2.22 (2H, m, 60-H), 1.7 (1H, e, 3-60-H). 1.6 Hz, 60-H).

To isolate the 2-C₆H₅-C₂H₄-C₂H₄ an aqueous solution of HClO₄ was added to the reaction mixture which was obtained after the treatment of 48 (400 mg) with conc. H₂SO₄ (15 ml). However, a yellow sticky residue (200 mg) was formed. This was soluble in ether and indicated the presence of at least two compounds (117). The mixture was separated by passage through a column of silica H (Kureha), using a mixture of n-hexane and EtOAc (100). The compound obtained from the first eluted displayed spectral properties consistent with heptacarboxyl[11'-methoxy-carboxy-6,6'-dihydronaphthalenyl]-

iron hexafluorophosphate [117 (6.6 eq, AF₃, 9 8.6 Hz, 3H), 8.70; 8.70; 1700 cm⁻¹; δ(C₅,CH) 7.7 (1H, d, J = 5-6 Hz, 3H), 6.03 (1H, d, J = 5-6 Hz, 4-H), 4.93 (1H, d, J = 6 Hz, 1-H). 6.2 (1H, d, J = 6 Hz, 3-H). 3.73 (2H, t, CO-CH), 2.22 (2H, m, 60-H), 1.7 (1H, e, 3-60-H). 1.6 Hz, 60-H).
CHAPTER 5

Treatment of carboxy complexes with conc. H$_2$SO$_4$

Tricarbonyl($\eta^4$-6$\alpha$-carboxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 48 and conc. H$_2$SO$_4$

The carboxy complex 48 (1.0 g, 3.1 mmol) was magnetically stirred with conc. H$_2$SO$_4$ (5 ml) at 0-5°C for 10 min., whereafter water (2 ml) was added dropwise. The mixture was stirred for 1 h, diluted with water (50 ml), and extracted with ether (3 x 25 ml). Combined ether extracts were washed with brine and water, dried (MgSO$_4$) and concentrated to a yellow sticky residue (690 mg). To a solution of the residue in dry CH$_2$Cl$_2$ (3 ml) was added HPF$_6$-etherate (2 ml), and the mixture was stirred magnetically for 15 min. The yellow crystalline precipitate obtained upon addition of dry ether, was washed several times with dry ether and dried *in vacuo* to give tricarbonyl($\eta^5$-2-methoxycarbonylcyclohexadienyl)iron hexafluorophosphate 117 (6.6 mg, 47%). $\nu_{\text{max}}$(KBr) 2120, 2090, 2070, 1720 cm$^{-1}$; $\delta$(CD$_3$CN) 7.7 (1H, d, $J_{3,4}$ = 5-6 Hz, 3-H), 5.83 (1H, t, $J_{4,5}$ = 5-6 Hz, 4-H), 4.63 (1H, d, $J_{1,6\beta}$ = 6 Hz, 1-H), 4.3 (1H, t, $J_{5,6\beta}$ = 6 Hz, 5-H), 3.73 (3H, s, CO$_2$Me), 3.3-2.8 (1H, m, 6\(\alpha\)-H), 1.7 (1H, d, $J_{6\beta,6\alpha}$ = 16 Hz, 6\(\alpha\)-H).

To isolate the 2-CO$_2$Me cation as its PF$_6$ salt, an aqueous solution of NH$_4$PF$_6$ was added to the reaction mixture which was obtained after the treatment of 48 (400 mg) with conc. H$_2$SO$_4$ (2 ml). However, a yellow sticky residue (240 mg) was formed. This was soluble in ether and indicated the presence of at least two compounds (tlc). The mixture was separated by passage through a column of silica H (type 60), using a mixture of n-hexane and Et$_2$O (30%). The compound obtained from the first eluant displayed spectral properties consistent with hexacarbonyl($\eta^4$,$\eta^1$-1,1'-dimethoxy-carbonyl-6$\alpha$,6'$\alpha$-oxybiscyclohexa-1,3-diene)diiron 118, $\nu_{\text{max}}$(CHCl$_3$) 2060,
1980, 1700 cm⁻¹; δ(DCl₃) 6.13 (2H, dd, *J*₂,₃ = J₂',₃' = 4.5 Hz, 2- and 2'-H), 5.49 (2H, dd, J₃,₄ = 6 Hz, 3- and 3'-H), 4.30 (2H, dd, *J*₆',₅', = 10-11 Hz, 6- and 6'-H), 3.71 (3H, s, CO₂Me), 3.65 (3H, s, CO₂Me'), 3.02 (2H, m, 4- and 4'-H), 2.26 (2H, m, 5β- and 5β'-H), 1.64 (2H, m, 5α- and 5α'-H), *the double doublets at δ 6.13 and 4.30 arise from the overlap of the signals due to diastereometrically non-equivalent protons; m/z 278, 276, 266, 264, 250, 248, 238, 236, 208.

The less mobile compound was identified as tricarbonyl(n⁴-6α-hydroxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 49, ν_max(CHCl₃) 3000 (OH), 2050, 1990, 1697 cm⁻¹; δ(DCl₃) 6.18 (1H, d, J₃,₄ = 4.5 Hz, 2-H), 5.67 (1H, dd, J₂,₃ = 6 Hz, 3-H), 4.77 (1H, dd, J₆,₅α = 10-11 Hz, J₆,₅β = 3.5-4.0 Hz, 6-H), 3.72 (3H, s, CO₂Me), 3.28 (1H, br s, D₂O exchange, OH), 3.04 (1H, m, 4-H), 2.48 (1H, m, J₄,₅β = 4 Hz, J₅α,₅β = 15 Hz, 5β-H), 1.62 (1H, m, 5α-H); m/z 294 (M), 266 (M-CO), 238 (M-2CO), 210 (M-3CO), 192 (M-3CO-H₂O).

Tricarbonyl(n⁴-5α-carboxycyclohexa-1,3-diene)iron 46 and conc. H₂SO₄.

The carboxy complex 46 (150 mg, 0.6 mmol) was reacted with conc. H₂SO₄ as above. After anion exchange with aqueous NH₄PF₆, afforded tricarbonyl(n⁵-cyclohexadienyl)iron hexafluorophosphate 4 (118 mg, 56%) which was identified by use of an authentic sample ¹⁴(¹H NMR).

A 3:1 mixture of tricarbonyl(n⁴-5β-carboxycyclohexa-1,3-diene)iron 64 and tricarbonyl(n⁴-5α-carboxycyclohexa-1,3-diene)iron 46 with conc. H₂SO₄.

The 3:1 mixture of 64 and 46 (220 mg, 0.8 mmol) was treated with cold conc. H₂SO₄ as described above. The brownish sticky residue was washed several times with Et₂O (α 100 ml). The ether washings were combined and washed with brine and water, dried (MgSO₄) and concentrated to give a
yellow solid (61 mg, 28%). The compound was identified as the 5β-carboxy complex 64 (IR, $^1$H NMR).

Tricarbonyl($^n$-5β-carboxy-5α-methylcyclohexa-1,3-diene)iron 115 and conc. H$_2$SO$_4$

The carboxy complex 115 (100 mg, 0.4 mmol) was treated with cold conc. H$_2$SO$_4$ acid for 30 min. The work-up as above afforded the unreacted acid (65 mg, 65%).

Tricarbonyl($^5$-6α-carboxycyclohexadienyl)iron hexafluorophosphate 120

Tricarbonyl($^n$-6α-carboxy-1-methoxycyclohexa-1,3-diene)iron 53 (150 mg, 0.5 mmol) was reacted with conc. H$_2$SO$_4$ (1 ml) at 0-5°C for 10 min. Anion exchange with aqueous NH$_4$PF$_6$ as above afforded the crystalline 6α-carboxy salt 120 (131 mg, 63%); $\nu$$_{max}$(KBr) 3500-2500 (br, CO$_2$H), 2120, 2070, 1720 cm$^{-1}$; $\delta$(CD$_3$CN) 6.94 (1H, t, J = 6 Hz, 3-H), 5.95 (2H, t, J = 7 Hz, 2- and 4-H), 4.39 (2H, t, J = 7 Hz, 1- and 5-H). 3.83 (1H, t, J = 7 Hz, 6-H).

Formation of alcohols from ester complexes

General procedure for reaction of ester complexes with MeLi and MeMgBr

Metalalkyl reagent (MeLi or MeMgBr, 3 equivalents or as specified below) was added dropwise by syringe techniques to a magnetically stirred solution of the ester complex in dry CH$_2$Cl$_2$ or Et$_2$O ($\alpha\alpha$ 10 ml for 1 mmol of the complex) at -78°C. The reaction mixture was stirred for further 2 h, and quenched with dil. HCl (10%). The product was extracted in the same solvent (CH$_2$Cl$_2$ or Et$_2$O; 2 x volume used in the reaction).
organic layer was washed with water, dried (MgSO₄) and concentrated under reduced pressure. The resulting residue was purified by passage through a short column of basic alumina (activity 4), using a 1:1 mixture of Et₂O and light petroleum.

Tricarbonyl[η⁴-1-(1'-hydroxyisopropyl)cyclohexa-1,3-diene]iron 126 and tricarbonyl[η⁴-1-acetylcylohexa-1,3-diene]iron 125

Tricarbonyl[η⁴-1-methoxycarbonylcyclohexa-1,3-diene]iron 11 (1.0 g, 3.6 mmol) was reacted with MeLi (1.4 M in ether, 7.7 ml) in CH₂Cl₂ (35 ml) at -78°C to give a homogeneous (tlc) yellow residue (1.0 g, 100%). Recrystallization from light petroleum afforded yellow crystals of 126 (710 mg, 91%), m.p. 60-61°C (lit. 60 63-63.5°C); \( \nu_{\text{max}} (\text{CHCl}_3) \) 3620 (OH), 2040, 1970 cm⁻¹; \( \delta (\text{CDCl}_3) \) 5.69 (1H, d, \( J_{2,3} = 4.5 \text{ Hz}, 2-\text{H} \)), 5.16 (1H, dd, \( J_{3,4} = 6 \text{ Hz}, 3-\text{H} \)), 3.04 (1H, m, 4-\( \text{H} \)), 1.82-1.45 (4H, m, 5- and 6-\( \text{H} \)), 1.47 (3H, s, Me), 1.37 (3H, s, Me), 1.30 (1H, s, D₂O exchange, OH); \( m/z \) 278 (M), 250 (M-CO), 232 (M-CO-H₂O), 222 (M-2CO), 196 (M-3CO).

The use of less amount of MeLi (2 equivalents) with the 1-CO₂Me complex 11 (500 mg) in Et₂O at -35°C for 2 h resulted in a mixture of two compounds (tlc). The less mobile fraction from a column of silica H (type 60), using petroleum and Et₂O (10%) gave the hydroxy complex 126 (315 mg, 63%). The first eluant gave a yellow oil (128 mg, 27%), the spectroscopic properties of which were consistent with the structure of tricarbonyl[η⁴-1-acetylcylohexa-1,3-diene]iron 125, \( \nu_{\text{max}} \) (film) 2050, 1985, 1675 cm⁻¹; \( \delta (\text{CDCl}_3) \) 6.09 (1H, d, \( J_{2,3} = 4.5 \text{ Hz}, 2-\text{H} \)), 5.44 (1H, dd, \( J_{3,4} = 6 \text{ Hz}, 3-\text{H} \)), 3.45 (1H, m, 4-\( \text{H} \)), 2.35-1.4 (m, methylene \( \text{H} \)), 2.25 (3H, s, Me); \( m/z \) 262 (M), 234 (M-CO), 206 (M-2CO), 178 (M-3CO), 176 (M-3CO-2H).
Tricarbonyl[\(\eta^4\)-2-(1'-hydroxyisopropyl)cyclohexa-1,3-diene]iron 127 and tricarbonyl[\(\eta^4\)-2-acetylcylohexa-1,3-diene]iron 129

Tricarbonyl(\(\eta^4\)-2-methoxycarbonylcyclohexa-1,3-diene)iron 12 (500 mg, 1.8 mmol) was reacted with MeMgBr (1.5 M in ether, 3.6 ml) in ether (20 ml) at -78°C for 2 h to give 127 as a yellow solid (450 mg, 90%). M.p. 53-55°C (from light petroleum); \(\nu_{\text{max}}\) (CHCl\(_3\)) 3620 (OH), 2040, 1970 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 5.33 (1H, dd, \(J_{3,4} = 6\) Hz, \(J_{1,3} = 2\) Hz, 3-H), 3.47 (1H, m, 4-H), 3.17 (1H, m, 1-H), 1.8-1.2 (m, methylene H), 1.57 (s, Me), 1.53 (s, Me); m/z 278 (M), 250 (M-CO), 222 (M-2CO), 194 (M-3CO), 176 (M-3CO-C\(_2\)H\(_2\)), 174 (M-3CO-C\(_2\)H\(_2\)-2H); (Found: C, 51.4; H, 5.2%. \(\text{C}_{12}\text{H}_{14}\text{O}_4\text{Fe}\) requires C, 51.8; H, 5.0%).

The use of less amount of MeMgBr (2 equivalents) resulted in a mixture of two complexes, the less mobile (tlc) being the 2-(1'-hydroxyisopropyl) complex 127. The other compound, isolated as a yellow oil, was identified as tricarbonyl(\(\eta^4\)-2-acetylcylohexa-1,3-diene)iron 129, \(\nu_{\text{max}}\) (CHCl\(_3\)) 2050, 1980, 1680 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 6.00 (1H, dd, \(J_{3,4} = 6\) Hz, \(J_{1,3} = 2\) Hz, 3-H), 3.73 (1H, m, 1-H), 3.50 (1H, m, 4-H), 2.40 (3H, s, Me), 1.8-1.0 (4H, m, 5- and 6-H); m/z 262 (M), 234 (M-CO), 206 (M-2CO), 178 (M-3CO), 176 (M-3CO-2H).

Tricarbonyl[\(\eta^4\)-1-(1'-hydroxyisopropyl)-2-methoxycylohexa-1,3-diene]iron 128

Tricarbonyl(\(\eta^4\)-2-methoxy-1-methoxycarbonylcyclohexa-1,3-diene)iron 102 (1.0 g, 3.25 mmol) was reacted with MeLi (1.4 M in ether, 6.9 ml) in CH\(_2\)Cl\(_2\) (30 ml) at -78°C for 2 h to give a viscous yellow oil (1.0 g, 100%). Recrystallization from light petroleum afforded yellow crystals (691 mg, 69%), m.p. 85-87°C; \(\nu_{\text{max}}\) (CHCl\(_3\)) 3555 (OH), 2040, 1970 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 4.93 (1H, d, \(J_{3,4} = 7\) Hz, 3-H), 3.72 (3H, s, OMe), 3.46 (1H, ...
br s, $D_2O$ exchange, OH), 2.60 (1H, dt, $J_{4,5} = 3$ Hz, 4-H), 1.86-1.54 (m, methylene H), 1.44 (6H, s, 2 x Me); (M calculated for $C_{13}H_{16}O_5Fe$ 308.0347, found 308.0348; found: C, 51.4; H, 5.3%. Requires C, 50.7; H, 5.2%).

Tricarbonyl[$η^4$-1-(1'-hydroxyisopropyl)-5α-[2$^2H_1$]cyclohexa-1,3-diene]iron

Tricarbonyl($η^5$-1-methoxycarbonylcyclohexadienyl)iron hexafluorophosphate 5 (1.0 g, 2.37 mol) was added to a suspension of NaBD$_4$ (126 mg, 3.0 mmol, D > 95%, Merck) in MeCN (30 ml) at 0°C. The mixture was stirred magnetically for 1 h, diluted with water ($ca$ 200 ml), and extracted with light petroleum. The petroleum extract was washed with brine and water, dried (MgSO$_4$) and concentrated to obtain a viscous yellow oil (574 mg, 87%). The compound was identified as tricarbonyl($η^4$-1-methoxycarbonyl-5α-[2$^2H_1$]-cyclohexa-1,3-diene)iron 131, $ν_{\text{max}}$ (film) 2060, 1990, $\nu_{\text{max}}$ (CDC$_3$) 51.97 cm$^{-1}$; $\delta$(CDCl$_3$) 6.05 (1H, d, $J_{2,3} = 4$ Hz, 2-H), 5.35 (1H, dd, $J_{3,4} = 6.5$-7.0 Hz, 3-H), 3.68 (3H, s, CO$_2$Me), 3.34 (1H, ddd, $J = 3.5$ Hz, 4-H), 2.19 (1H, dd, $J_{6a,6b} = 14.5$ Hz, $J_{5,6b} = 12.0$ Hz, 6α-H), 1.88 (1H, dm, 5-H), 1.4 (1H, dm, 6α-H); $m/z$ 279 (M), 251 (M-CO), 223 (M-2CO), 197 (M-3CO); $^1$H NMR was calculated (MS) to be $> 95$%.

The 5α-deuterio ester 130 (500 mg, 1.8 mmol) was reacted with MeLi (1.4 M in ether, 3.85 ml) in CH$_2$Cl$_2$ (20 ml) at -78°C for 2 h to obtain a yellow semi-solid (498 mg, 99%). Recrystallization from light petroleum afforded yellow crystals (418 mg, 82%), m.p. 62-63.5°C. The compound was identified as tricarbonyl[$η^4$-1-(1'-hydroxyisopropyl)-5α-[2$^2H_1$]cyclohexa-1,3-diene]iron 130, $ν_{\text{max}}$ (CHCl$_3$) 3550 (OH), 2040, 1970 cm$^{-1}$; $\delta$(CDCl$_3$) 5.69 (1H, d, $J_{2,3} = 4.5$-5.0 Hz, 2-H), 5.16 (1H, dd, $J_{3,4} = 6.0$ Hz, 3-H), 3.04 (1H, ddd, $J_{4,5} = 2.5$ Hz, $J = 1$ Hz, 4-H), 1.82-1.45 (3H, m, 5- and 6-H), 1.47 (3H, s, Me), 1.37 (3H, s, Me), 1.30 (1H, s, $D_2O$ exchange, OH);
m/z 279 (M), 251 (M-CO), 233 (M-CO-H₂O), 223 (M-2CO), 197 (M-3CO); %D was calculated to be > 95%.

Reaction of tricarbonyl(\(\pi^4\)-5\(\alpha\),5\(\beta\)-dimethoxycarbonylcyclohexa-1,3-diene)-iron 36 with MeLi and MeMgBr

The diester complex 36 (1.0 g, 2.98 mmol) was reacted with MeLi (1.4 M in ether, 6.4 ml) in CH₂Cl₂ (30 ml) at -78°C for 2 h to give a viscous yellow oil (842 mg) comprising of at least five compounds (tlc, Rf = 0.70, 0.52, 0.43, 0.29, 0.08). The mixture was separated by tlc (αα 200 mg on each plate), using a 1:1 mixture of Et₂O and light petroleum.

The spectral properties (¹H NMR, MS) of the fraction (172 mg) corresponding to Rf = 0.70, were consistent with a mixture of tricarbonyl(\(\pi^4\)-5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene)iron 27 (20% yield, calculated from ¹H NMR) and methylbenzoate (2% yield).

The band at Rf = 0.52 gave a yellow solid (332 mg, 35%) which displayed the spectral properties consistent with tricarbonyl(\(\pi^4\)-5\(\beta\)-acetyl-5\(\alpha\)-methoxycarbonylcyclohexa-1,3-diene)iron 132, m.p. 90-92°C (first transition), 115-117°C (complete melting); \(\nu_{max}(CHCl₃)\) 2040, 1975, 1730, 1710 cm⁻¹; δ(CDCl₃) 5.38 (2H, m, 2- and 3-H), 3.62 (3H, s, CO₂Me), 3.26 (2H, m, 1- and 4-H), 2.34 (2H, m, 6-H), 2.07 (3H, s, COMe); (Found: C, 48.8; H, 3.8%. \(\text{C}_{13}\text{H}_{12}\text{O}_6\text{Fe}\) requires C, 48.8; H, 3.8%).

The third band (Rf = 0.43) gave a yellow solid (43 mg, 4%) which was identified as tricarbonyl[\(\pi^4\)-5\(\beta\)-(1'-hydroxyisopropyl)-5\(\alpha\)-methoxycarbonylcyclohexa-1,3-diene]iron 133, m.p. 69-71°C (from light petroleum), \(\nu_{max}(CHCl₃)\) 3560-3420 (br, OH), 2050, 1980, 1715, 1690 cm⁻¹; δ(CDCl₃) 5.29 (2H, m, 2- and 3-H), 3.63 (3H, s, CO₂Me), 3.36 (1H, m, 1-H), 3.20 (1H, dd, J₃,₄ = 7 Hz, J₂,₄ = 1.5 Hz, 4-H), 3.53 (1H, dd, J₆α,₆β = 16 Hz,
The fourth band (Rf = 0.29) afforded a yellow oil (74 mg, 7%) which was identified as tricarbonyl[\(\eta^4\)-5\(\alpha\)-(1'-hydroxyisopropyl)-5\(\beta\)-methoxycarbonylcyclohexa-1,3-diene]iron [134], \(\nu_{\text{max}}(\text{CHCl}_3) 3550-3400 \) (br, \(\text{OH}\)), 2050, 1980, 1720 cm\(^{-1}\); \(\delta(\text{CDCl}_3) 5.40 \) (2H, m, 2- and 3-H), 3.80 (3H, s, CO\(_2\)Me), 3.28 (1H, dd, \(J_{3,4} = 7 \) Hz, \(J_{2,4} = 1.5 \) Hz, 4-H), 3.16 (1H, m, 1-H), 2.88 (1H, hump, \(\text{OH}\)), 2.54 (1H, dd, \(J_{6\alpha,6\beta} = 16 \) Hz, \(J_{6\beta,1} = 4 \) Hz, 6\(\beta\)-H), 1.93 (1H, dd, \(J_{6\alpha,1} = 2 \) Hz, 6\(\alpha\)-H), 1.06 (6H, s, 2 x Me); \(m/z\) 308 (M-CO), 280 (M-2CO), 252 (M-3CO).

The least mobile band (Rf = 0.08) gave a yellow oil (65 mg, 7%) and was identified as tricarbonyl[\(\eta^4\)-5\(\alpha\)-hydroxy-1-methoxycarbonylcyclohexa-1,3-diene]iron [135], \(\nu_{\text{max}}(\text{CHCl}_3) 3350 \) (OH), 2060, 1980, 1710 cm\(^{-1}\); \(\delta(\text{CDCl}_3) 6.25 \) (1H, d, \(J_{2,3} = 4 \) Hz, 2-H), 5.48 (1H, dd, \(J_{3,4} = 6 \) Hz, 3-H), 4.26 (1H, dt, \(J_{5,6} = 10 \) Hz, \(J_{4,5} = 3 \) Hz, 5-H), 3.68 (3H, s, CO\(_2\)Me), 3.22 (1H, dd, 4-H), 2.0 (1H, br s, D\(_2\)O exchange, \(\text{OH}\)), 2.84 (1H, dd, \(J_{6\alpha,6\beta} = 16 \) Hz, 6\(\beta\)-H), 1.36 (1H, dd, \(J_{6\alpha,5} = 3 \) Hz, 6\(\alpha\)-H); \(m/z\) 294 (M), 266 (M-CO), 238 (M-2CO), 210 (M-3CO), 192 (M-3CO-H\(_2\)O).

With MeMgBr (1.0 M in ether, 4.5 ml), the diester 36 (500 mg) gave under reaction conditions as above, a viscous yellow oil (497 mg) which indicated the presence of the components discussed above (Rf = 0.70, 0.52, 0.43, 0.29 and 0.08). The products corresponding to Rf = 0.70, 0.52 and 0.08 were of very low concentration (tlc) and, therefore, were not isolated. The third band (Rf = 0.43) gave the 5\(\beta\)-(1'-hydroxyisopropyl) complex 133 (215 mg, 43%). Similarly the band at Rf = 0.29 gave the 5\(\alpha\)-(1'-hydroxyisopropyl) complex 134 (110 mg, 22%).
Formation of cations by dehydroxylation of alcohols

Reaction of tricarbonyl[η^4-1-(1'-hydroxyisopropyl)cyclohexa-1,3-diene]iron 126 with HBF_4 and Ph_3C_PF_6

The 1-(1'-hydroxymethyl) complex 126 (150 mg, 0.54 mmol) in propionic anhydride (0.2 ml) was treated with HBF_4-etherate (0.5 ml) at 0°C. The mixture was stirred magnetically for 30 min. A 2:1 mixture of Et_2O and light petroleum was added, and the yellow precipitate was washed several times with the same solvent mixture. The yellow solid was dissolved in a minimum amount of water, to which was added an aqueous solution of NH_4PF_6. The resulting precipitate was filtered, air-dried, dissolved in nitromethane, and re-precipitated by the addition of Et_2O and light petroleum (2:1). The solvent was removed by filtration and the yellow solid was dried in vacuo to give tricarbonyl(n^5-1-isopropylcyclohexadienylium)iron hexafluorophosphate 136 (181 mg, 80%), ν_max (KBr) 2120, 2080 cm^-1; δ(CD_3CN) 6.98 (1H, t, J = 5-6 Hz, 3-H), 5.85 (1H, t, J = 5-6 Hz, 4-H), 5.48 (1H, d, J = 6 Hz, 2-H), 4.18 (1H, t of multiplets, J_4,5 = J_5,6B = 6 Hz, J = 1 Hz, 5-H), 2.92 (1H, dd, J_6α,6B = 16 Hz, 6B-H), 2.4-2.1 (2H, m, 6B-H and CHMe_2), 1.08, 0.96 (3H, 3H, d, d, J = 7 Hz, CHMe_2).

To a solution of the hydroxy complex 126 (278 mg, 1.00 mmol) in MeCN (1 ml) was filtered a suspension of Ph_3C_PF_6 (400 mg, 1.03 mmol) and MgCO_3 (ca 25 mg) in MeCN (2 ml). The mixture was stirred at ambient temperature for 30 min. A 2:1 mixture of Et_2O and light petroleum was added to precipitate the yellow cationic complex. The dissolution of the yellow solid in nitromethane and re-precipitation with Et_2O and light petroleum gave, after drying in vacuo, a yellow solid (240 mg, 57%). The salt displayed spectral properties (IR, ^1H NMR) identical to those of the 1-isopropyl cation 136.
Reaction of tricarbonyl($\eta^4$-1-(1'-hydroxyisopropyl)cyclohexa-1,3-diene)iron 126 with trifluoroacetic acid. Tricarbonyl($\eta^4$-5α-cyano-5β-isopropylcyclohexa-1,3-diene)iron 140 and tricarbonyl($\eta^4$-5α-cyano-1-isopropylcyclohexa-1,3-diene)iron 141

The hydroxy complex 126 (230 mg) was treated with trifluoroacetic acid (1.5 ml) at 0°C for 30 min. The resulting cationic product was isolated as the PF$_6^-$ salt by the same procedure as that for 126 with HBF$_4$. Yield 169 mg, 48%. $\nu_{\text{max}}$(KBr) 2120, 2080 cm$^{-1}$; $\delta$(CD$_3$CN) 6.98 (12 mm, t, J = 5-6 Hz, 3-H of 136 and ?), 5.85 (17 mm, m, 4-H of 136 and ?), 5.48 (8.5 mm, d, J = 6 Hz, 2-H of 136), 4.18 (15-17 mm, m, 5-H of 136 and ?), 3.62 (5 mm, s, ?), 3.16, 2.92 (16 mm, dd, dd, J = 6 Hz, J = 16 Hz, ? and 6β-H of 136), 2.4-2.1 (28 mm, m, 6α-H and CHMe$_2$ of 136 and ?), 1.51 (12-13 mm, s, ?), 1.20 (12-13 mm, s, ?), 1.08, 0.96 (26 mm, 26 mm, d, d, J = 7 Hz, CHMe$_2$ of 136).

To a solution of the above mixture of cationic complexes (169 mg) in MeCN (2 ml) was added an aqueous solution of KCN (200 mg) in 0.5 ml water. The reaction mixture was stirred for 30 min, diluted with water ($\approx$ 50 ml), and the neutral complex was extracted with light petroleum. Petroleum extract was washed with brine and water, dried (MgSO$_4$) and concentrated to give a viscous yellow oil (114 mg, 60%). Separation on tlc (light petroleum : ether :: 4:1) afforded two compounds (Rf = 0.37, 0.09). The more mobile complex was identified as tricarbonyl($\eta^4$-5α-cyano-5β-isopropylcyclohexa-1,3-diene)iron 140, $\nu_{\text{max}}$(CHCl$_3$) 2220, 2060, 1980 cm$^{-1}$; $\delta$(CDCl$_3$) 5.34 (2H, m, 2- and 3-H), 2.94 (2H, m, 1- and 4-H), 2.25 (1H, dd, J = 15, 12 Hz, 6β-H), 1.85, 1.74 (2H, heptet, J = 6.5-7.0 Hz, dd, J = 15, 3.5 Hz, CHMe$_2$ and 6α-H), 1.12 (6H, d, J = 6.5-7.0 Hz, CHMe$_2$); (M calculated for C$_{13}$H$_{13}$O$_3$NFe 287.0245, found 287.0241). The compound
corresponding to Rf = 0.09 was identified as tricarbonyl(η⁴-5α-cyano-1-isopropylcyclohexa-1,3-diene)iron 141, m.p. 135-136.5°C (from light petroleum); \( \nu_{\text{max}}(\text{CHCl}_3) \) 2220, 2055, 1980 cm⁻¹; \( \delta(\text{CDCl}_3) \) 5.86 (1H, d, \( J_{2,3} = 4.5 \text{ Hz}, 2-\text{H} \)), 5.22 (1H, dd, \( J_{3,4} = 6 \text{ Hz}, 3-\text{H} \)), 2.98, 2.90 (2H, one half of the dt buried under the m at \( \delta \) 2.90, 5-H and 4-H), 2.24 (1H, dd, \( J_{5\beta,6\beta} = 11-12 \text{ Hz}, J_{6\alpha,6\beta} = 15 \text{ Hz}, 6\beta-\text{H} \)), 1.74 (1H, dd, \( J_{5\beta,6\alpha} = 3.5 \text{ Hz}, 6\alpha-\text{H} \)), 1.43, 1.39 (7H, s, s, CHMe₂); (M found 287.0243). The isomer ratio of 140 and 141 was calculated to be 3:1 from the \(^1\text{H} \) NMR of the mixture prior to separation.

The reaction of the 1-isopropyl cation 136 with KCN afforded a similar mixture of 140 and 141 in 79% yield.

Tricarbonyl(η⁶-1-isopropyl-5-[²H₁]cyclohexadienyl)iron hexafluorophosphate 145

Tricarbonyl[η⁴-1-(1'-hydroxyisopropyl-5α-[^²H₁]cyclohexa-1,3-diene]iron 130 (150 mg) in propionic anhydride (0.2 ml) was treated with HBF₄-etherate (0.5 ml) at 0°C. The mixture was worked up as above to obtain 145 (151 mg, 64%), \( \nu_{\text{max}}(\text{KBr}) \) 2120, 2080 cm⁻¹; \( \delta(\text{CD₃CN}) \) 6.98 (1H, t, \( J = 5-6 \text{ Hz}, 3-\text{H} \)), 5.85 (1H, d, \( J_{3,4} = 5 \text{ Hz}, 4-\text{H} \)), 5.48 (1H, d, \( J_{2,3} = 6 \text{ Hz}, 2-\text{H} \)), 2.92 (1H, d, \( J_{6\alpha,6\beta} = 16 \text{ Hz}, 6\beta-\text{H} \)), 2.4-2.1 (2H, m, 6α-H and CHMe₂), 1.08, 0.96 (3H, 3H, d, d, \( J = 7 \text{ Hz}, \text{CHMe₂} \)).

The reaction of 130 (150 mg) with Ph₃C±PF₆ (200 mg) in MeCN (1 ml) afforded 145 (115 mg, 49%).
Conversion of tricarbonyl(\(\eta^5\)-cyclohexadienylium)iron hexafluorophosphate 4 to tricarbonyl(\(\eta^5\)-1-(1'-phenylethyl)cyclohexadienylium)iron hexafluorophosphate 149 and tricarbonyl(\(\eta^5\)-1-isopropylcyclohexadienylium)iron hexafluorophosphate 136

To a stirred solution of the unsubstituted salt 4 (4.0 g, 11 mmol) in CH\(_3\)CN (30 ml), an aqueous solution of KCN (1 g in ca 3 ml of H\(_2\)O) was added. After 30 min. of further stirring, the mixture was diluted with water (ca 300 ml). Petroleum extract of the neutral product was washed with brine and water, dried (MgSO\(_4\)) and concentrated to give tricarbonyl-(\(\eta^4\)-5a-cyanocyclohexa-1,3-diene)iron 14 as pale yellow crystals (2.4 g, 93%), m.p. 87-89°C (lit 14 88-89°C).

To a stirred solution of the cyano complex 43 (1.0 g, 4.2 mmol) in dry ether (50 ml) was added PhMgBr (1.16 M in ether, 18.2 ml) dropwise at room temperature. The reaction mixture was stirred for a further 30 min., quenched with 10% HCl (10 ml), and diluted with water (ca 200 ml). The product was extracted into light petroleum. Combined petroleum extracts were washed with brine and water, dried (MgSO\(_4\)) and concentrated. Slightly reddish yellow viscous residue was eluted through a short column of basic alumina (activity 4), using light petroleum and ether (10%, v:v). The concentration of the eluant gave a homogeneous yellow oil (1.14 g, 83%) which was identified as tricarbonyl(\(\eta^4\)-5a-benzoylcyclohexa-1,3-diene)iron 148, \(\nu_{\text{max}}\) (CHCl\(_3\)) 2050, 1975, 1945, 1690, 1600, 1580 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 7.9 (2H, M, aromatic H), 7.48 (3H, m, aromatic H), 6.42 (2H, m, 2- and 3-H), 3.93 (1H, dt, \(J = 10.4\) Hz, 5-H), 3.26 (1H, m, 4-H), 3.08 (1H, m, 1-H), 2.3-1.8 (2H, m, 6-H); (M calculated for C\(_{16}\)H\(_{12}\)FeO\(_4\) 324.0085, found 324.0087); \(\frac{1}{2}\) CH\(_2\)(\(\alpha\))-splitting pattern (Section 2.3.1).
The 5a-COPh complex 148 (350 mg, 1.1 mmol) was reacted with MeMgBr (1.5 M in ether, 2.0 ml) in ether (15 ml) at -78°C for 2 h. After usual work-up and passage through basic alumina (activity 4), using a 1:1 mixture of light petroleum and ether, a viscous yellow oil was obtained, 323 mg, 91%. The compound was identified as tricarbonyl[n^4-5a-(1'-hydroxy-1'-phenylethyl)cyclohexa-1,3-diene]iron 147. ν<sub>max</sub>(CHCl<sub>3</sub>) 3560-3400 (br, OH), 2020, 1960, 1595 cm<sup>-1</sup>; δ(CDC<sub>3</sub>) 7.22 (5H, m, aromatic H), 5.26 (2H, m, 2- and 3-H), 2.63 (3H, m, 1-, 4- and 5-H), 1.96-1.3 (m, D<sub>2</sub>O exchange at δ1.76, 6-H and OH), 1.46, 1.38 (3H, s, s, Me); m/z 340 (M), 312 (M-CO), 284 (M-2CO), 256 (M-3CO); (M-CO calculated for C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>Fe 312.0449, found 312.0455). 1<sup>1</sup>H NMR <sup>(a)</sup>-splitting pattern was discernible after D<sub>2</sub>O exchange. The ratio of the peak heights at δ 1.46 and 1.38 was 3:8.

The analogous treatment of 5a-COPh complex 148 (320 mg) with MeLi (1.4 M, 1.5 ml) in CH<sub>2</sub>Cl<sub>2</sub> (10 ml) at -78°C for 2 h afforded the same alcohol 147 (300 mg, 88%). The ratio of the peak heights of the 1<sup>1</sup>H NMR resonances at δ 1.46 and 1.38 was 1:4.

The alcohol 147 (100 mg, 0.3 mmol) in propionic anhydride (0.3-0.5 ml) was reacted with HBF<sub>4</sub>-etherate (0.5 ml). Anion exchange with aqueous NH<sub>4</sub>PF<sub>6</sub> gave tricarbonyl[n^5-1-(1'-phenylethyl)cyclohexadienylum]iron hexafluorophosphate 149 (103 mg, 73%). ν<sub>max</sub>(KBr) 2115, 2065, 1600 cm<sup>-1</sup>; δ(CD<sub>3</sub>CN) 7.3 (5H, m, aromatic H), 6.92 (1H, t, J = 6 Hz, 3-H), 5.82 (1H, t, J = 6 Hz, 4-H), 5.31 (1H, d, J = 5.6 Hz, 2-H), 4.20 (1H, t, J = 6 Hz, 5-H), 3.53 (1H, q, J = 7 Hz, CHMePh), 3.03 (1H, dd, J = 16.6 Hz, 6 -H), 2.28 (1H, d, J = 16 Hz, 6 -H), 1.41, 1.24 (3H, d, d, J = 7 Hz, Me). The ratio of the integration of the resonances at δ 1.41 and 1.24 was 23:5.

The reaction of the alcohol 147 with TFA (and then, NH<sub>4</sub>PF<sub>6</sub>) or Ph<sub>3</sub>C<sup>®</sup>PF<sub>6</sub> gave the same salt 149 in 62% and 55% yield, respectively. The 1<sup>1</sup>H NMR spectrum of 147 in TFA indicated the quantitative conversion of the alcohol 147 to the dienyl cation 149.
Analogously, the reaction of the cyano complex 43 with MeMgBr (5 equivalents) gave tricarbonyl($\eta^4$-5α-acetylcyclohexa-1,3-diene)iron 62$^{35a}$ in 78% yield. The reaction of the acetyl complex 62 with MeMgBr (1.5-2.0 equivalents) afforded tricarbonyl($\eta^4$-5α-(1'-hydroxyisopropyl)-cyclohexa-1,3-diene)iron 146$^{144}$ in 84% yield. ν$_{max}$(CHCl$_3$) 3350 (OH), 2050, 1980 cm$^{-1}$; δ(CDC$_3$) 5.38 (2H, m, 2- and 3-H), 3.11 (2H, m, 1- and 4-H), 2.0 (1H, s, D$_2$O exchange, OH), 1.87 (1H, m, J = 10 Hz, 5-H), 1.7-1.6 (2H, m, 6-H), 1.1 (6H, s, 2 x Me); m/z 278 (M), 250 (M-CO), 222 (M-2CO), 196 (M-3CO), 178 (M-3CO-D$_2$O).

The reaction of the 5α-(1'-hydroxyisopropyl) complex 146 with either HBF$_4$-etherate (procedure as above) or Ph$_3$C=PF$_6^-$ afforded the same cation ($^1$H NMR), tricarbonyl($\eta^5$-1-isopropylcyclohexa-1,3-dienyl)iron hexafluorophosphate 136 (yield 45-60%).
CHAPTER 6

General procedure for alkylation of tricarbonylcyclohexadienyliron salts with lithiumalkyls

Lithiumalkyl[1-1.2 equivalents; in pentane or hexane except for Meli (in ether)] was added dropwise to a stirred suspension of the cationic salt (1 equivalent) in dry CHCl₂ (10 ml for 1 mmol of the salt) at -78°C. When the yellow suspension turned to a clear or turbid solution (usually within 5-45 min.), a solution of 10% aqueous HCl (ca 2 ml) was added to destroy any excess lithiumalkyl. Light petroleum (2 x volume of CHCl₂) was added and the organic layer washed with water, dried (MgSO₄) and concentrated. The crude product was purified by eluting through a short column of basic alumina (grade 4) with light petroleum. The yields of the isolated products are given in Table 6.1.

Spectral data of the adducts from lithiumalkyls (MeLi, nBuLi, iPrLi and tBuLi and tricarbonyl(η⁵-cyclohexadienyl)iron hexafluorophosphate 4, tricarbonyl(η⁵-2-methylcyclohexadienyl)iron hexafluorophosphate 152 and tricarbonyl(η⁵-2-methoxycyclohexadienyl)iron hexafluorophosphate 6 were identical to those previously reported with other alkylating reagents (Li₂Cu, R₂Cd, R₂Zn, and LiRCuSPh). These experiments were performed with the assistance of Dr T.C. Khor.

Tricarbonyl(η⁴-l-methoxy-6α-tertiarybutylcyclohexa-1,3-diene)iron and tricarbonyl(η⁴-2-methoxy-5α-tertiarybutylcyclohexa-1,3-diene)iron

The reaction of the 2-0Me salt 6 (2.0 g, 5.1 mmol) with tBuLi (4 ml of 1.52 M soln. in pentane/hexane, 20% excess) for 1 h under the conditions described above gave a yellow oil (1.25 g, 80%). The 1H NMR
was consistent with the presence of a 40:60 mixture of isomers corresponding to the adducts at the 1- and 5-positions of the salt, respectively; isomer ratio was calculated from the OMe resonances at δ 3.42 (the product corresponding to addition at 1-position) and δ 3.64 (addition at 5-position). The mixture was separated by medium pressure liquid chromatography (MPLC) on a Merck Lobar silica gel column, using petroleum (40/60) and methylene chloride (10%) at a rate of 10 ml min⁻¹. The recovery was > 90%.

The compound (0.46 g) corresponding to the more mobile band was identified as tricarbonyl(n°-l-methoxy-6α-tertiarybutylcyclohexa-1,3-diene)-1 iron; νmax(CHCl₃) 2040, 1970 cm⁻¹; δ(CDCl₃) 5.57 (1H, dt, J2,3 = 4.2 Hz, J2,4 = J2,6B = 1.2 Hz, 2-H), 4.99 (1H, dd, J3,4 = 6.0 Hz, 3-H), 3.42 (3H, s, OMe), 2.73 (1H, m, 4-H), 2.43 (1H, ddd, J2,5B = 10.5 Hz, J5B,6B = 3.0 Hz, 6B-H), 2.04 (1H, m, J5α,5B = 14.5 Hz, J4,5B = 3.5 Hz, 5α-H), 1.68 (1H, m, J5α,4 = 3.0 Hz, 5α-H), 0.87 (9H, s, CMe); (M-CO calculated for C₁₇H₁₈FeO₂ 278.0605, found 278.0613). CH₂(α)-splitting pattern (Section 2.3.1).

The compound (0.69 g) corresponding to the second band was identified as tricarbonyl(n°-2-methoxy-5α-tertiarybutylcyclohexa-1,3-diene)iron; νmax(CHCl₃) 2040, 1970 cm⁻¹; δ(CDCl₃) 5.19 (1H, dd, J3,4 = 6.4 Hz, J1,3 = 2.2 Hz, 3-H), 3.64 (3H, s, OMe), 3.35-3.24 (1H, m, 1-H), 2.66 (1H, dm, 4-H), 2.0-1.4 (3H, s, 5- and 6-H), 0.80 (9H, s, CMe₃); (M-CO, found 278.0571).

General procedure for addition of ArXH (X=O,S,Se) to tricarbonyl(n°-cyclohexadienylium)iron hexafluorophosphate 4 in the presence of Hüning base

To a stirred suspension of the salt 4 (500 mg, 1.37 mmol) and ArXH (X=O,S,Se, 2-3 mmol) in dry CH₂Cl₂ (25 ml) was added ethyl(diisopropylamine
(= Hünig base, 200 mg) at 0°C. When a clear yellow solution was observed (αα 10-15 min.), the solvent was removed under reduced pressure. The neutral product was taken into light petroleum. The residue, obtained after concentration of the petroleum extract, was purified either by passage through a short column of basic alumina (activity 4) (using light petroleum), or by recrystallization from light petroleum at -18°C.

Tricarbonyl(n⁴-5α-phenoxy)cyclohexa-1,3-diene)iron 40

By reacting the unsubstituted salt 4 with phenol, the adduct 40 was obtained in 85% yield, after passage through a short column of alumina. The compound showed physical properties similar to those reported. The ¹H NMR showed at δ 2.10 (6β-H) and 1.69 (6α-H), the methylene splitting pattern characteristic of an adjacent α-substituent (Section 2.3.1).

Tricarbonyl(n⁴-5α-phenylthiocyclohexa-1,3-diene)iron 41

The reaction of the salt 4 with thiophenol afforded the adduct 41, m.p. 68-69°C (lit. 53°C 67-69°C), in 92% yield.

Tricarbonyl[n⁴-5α-(p-nitrophenylthio)cyclohexa-1,3-diene]iron 153

The reaction of the salt 4 with p-nitrothiophenol afforded the adduct 153, m.p. 106-108°C (decomp.), in 93% yield. v max (CHCl₃) 2050, 1980, 1580, 1340 cm⁻¹; (CDCl₃) 8.12 (2H, d, J = 9 Hz, aromatic H), 7.28 (2H, d, J = 9 Hz, aromatic H), 5.06 (2H, m, 2- and 3-H), 3.88 (1H, dt, J = 10 Hz, J = 3.5 Hz, 5-H), 3.24 (2H, m, 1- and 4-H), 2.52 (1H, m, J = 4 Hz, 6β-H), 1.72 (1H, m, J = 16 Hz, 6α-H); m/z 373 (M), 345
(M-CO), 317 (M-2CO), 308, 389 (M-3CO); (Found: C, 48.3; H, 3.0; N, 3.8; S, 8.8%). C\textsubscript{15}\textsubscript{11}\textsubscript{5}H\textsubscript{NS}0Fe requires C, 48.3; H, 3.0; N, 3.8; S, 8.6%.

CH\textsubscript{2}\textsubscript{(α)}-splitting pattern.

Tricarbonyl(\textit{n}^\textit{4}-5α-phenylselenocyclohexa-1,3-diene)iron 42

The reaction of the salt 4 with phenylselenol gave the adduct 42, m.p. 53-54°C, in 94% yield. \(\nu_{\text{max}}(\text{CHCl}_3)\) 2040, 1970, 1575 cm\(^{-1}\); \(\delta(\text{CDCl}_3)\) 7.51 (2H, m, aromatic H), 7.27 (3H, m, aromatic H), 5.28 (2H, m, 2- and 3-H), 3.69 (1H, dt, \(J_5,6β = 10\) Hz, \(J_{5,6α} = 3.5\) Hz, 5-H), 3.37 (1H, m, 4-H), 3.11 (1H, m, 1-H), 2.33 (1H, m, \(J_{6α,6β} = 15.5\) Hz, \(J_{6α,6β} = 4\) Hz, 6β-H), 1.78 (1H, m, 6α-H); \(m/z\) 594, 592 (M\(^+\)), 538, 536 (M\(^+\)-2CO), 510, 508 (M\(^+\)-3CO), 482, 480 (M\(^+\)-4CO), 454, 452 (M\(^+\)-5CO), 426, 424 (M\(^+\)-6CO), 349, 347 (M\(^+\)-6CO-Ph), M\(^+\) = [Fe(CO)\textsubscript{3}C\textsubscript{3}H\textsubscript{Se}]\(_2\); (Found: C, 48.1; H, 3.0; Se, 21.3%). C\textsubscript{15}\textsubscript{12}\textsubscript{3}H\textsubscript{Se0}Fe requires C, 48.0; H, 3.2; Se, 21.1%. CH\textsubscript{2}(α)-splitting pattern.

Tricarbonyl(\textit{n}^\textit{4}-2-methyl-5α-(2-propoxy)cyclohexa-1,3-diene)iron 54

Tricarbonyl(\textit{n}^\textit{5}-2-methylcyclohexadienyl)iron hexafluorophosphate 152 (500 mg, 1.32 mmol) was reacted with isopropanol (0.5 ml) as above, to result in 54 as a yellow oil (297 mg, 77%) after passage through basic alumina, \(\nu_{\text{max}}\) (film) 2035, 1965 cm\(^{-1}\); \(\delta(\text{CDCl}_3)\) 5.33 (1H, d, \(J_{3,4} = 6\) Hz, 3-H), 3.92 (1H, dt, \(J_5,6β = 10\) Hz, \(J_{5,6α} = 4\) Hz, 4-H), 3.53 (1H, heptet, \(J = 6\) Hz, CHMe\(_2\)), 2.88 (2H, m, 1- and 4-H), 2.28-2.12 (4H, m, overlapped with the singlet at \(\delta 2.12, 6β\text{-H}, 2\text{-Me}\), 1.50 (1H, m, \(J_{6α,6β} = 15\) Hz, 6α-H), 1.10, 1.04 (6H, s, s, diastereotopic CHMe\(_2\)); (M calculated for C\textsubscript{13}\textsubscript{16}\textsubscript{4}H\textsubscript{Fe0} 292.0398, found 292.0343). CH\textsubscript{2}(α)-splitting pattern.
Tricarbonyl[\(\eta^5\)-5α-menthoxycyclohexa-1,3-diene]iron 154

The reaction of 2-OMe salt 6 (2.0 g, 5.1 mmol) with (-)-menthol (2.4 g, 15.3 mmol) in CH\(_2\)Cl\(_2\) at 0°C in the presence of Hünig base (656 mg, 5.1 mmol) for 2 h afforded, after work-up as above, a yellow viscous liquid (1.74 g, 88%). The product was identified as 154; \(v_{\text{max}}\) (CHCl\(_3\)) 2040, 1975 cm\(^{-1}\), \(\delta\) (CD\(_6\)) 4.72 (m, 3-H), 3.81 (m, 5α-H), 3.00 (s, OMe of one diastereomer), 2.97 (s, OMe of the other diastereomer), 2.95 (m, 1-H), 2.77 (m, 1′-H of the menthoxyl group of one diastereomer), 2.56 (m, 4-H), 2.38 (m, 1′-H of the menthoxyl group of the other diastereomer), 2.3-1.8 (m, 6-H), 1.7-1.0 (m, remaining H of the menthoxyl group); m/z 404(M), 376(M-CO), 348(M-2CO), 346(M-2CO-2H), 316(M-3CO-2H).

The spectral assignment (\(^1\)H NMR) was confirmed by comparison of the \(^1\)H NMR spectra of the pure diastereomers separated by chromatographic means. The separation was performed by Dr T.C. Khor with a recovery of >90%. The optical antipodes of 2-OMe cation 6, which were obtained by dealkoxylation of the pure diastereomers, displayed [\(\alpha\)]\(_D\)\(^{25}\) -119° (MeCN, C=2) and +112° (MeCN, C=2).

Reaction of tricarbonyl(\(\eta^5\)-cyclohexadienyl)iron hexafluorophosphate 4 with (a) Hünig base (b) triethylamine (c) pyridine

(a) To a magnetically stirred suspension of the salt 4 (500 mg, 1.37 mmol) in dry CH\(_2\)Cl\(_2\) (25 ml) was added Hünig base (200 mg) at 0°C. A homogeneous yellow solution was observed almost instantaneously, \(v_{\text{max}}\) (CH\(_2\)Cl\(_2\)) 2050, 1980 cm\(^{-1}\). The solution was cooled to -40°C, and light petroleum added to precipitate an unstable slightly brownish yellow solid. The solvent was removed from the mixture and the solid was washed several times with light petroleum cooled to -40°C. The \(^1\)H NMR spectrum of the
solid was run in CD$_2$Cl$_2$ as rapidly as possible at ambient temperature. However, line broadening, probably due to paramagnetic material was observed. $\delta$ 5.4 (br m, 2- and 3-H), 3.4, 2.9 (br m, br m, l-, 4- and 5-H and N-CH), 1.8-0.7 (br m, 6-H and Me).

To the stirred solution of the residue in CH$_2$Cl$_2$ (20 ml) was added methanol (0.5 ml), and the reaction mixture brought to 0°C gradually. After work-up as above, a yellow oil (168 mg, 49%) was obtained. The product was identified as tricarbonyl(n$^4$-5α-methoxycyclohexa-1,3-diene)-iron 39 from the spectral properties. 14

(b) Analogously, a suspension of the salt 4 in CH$_2$Cl$_2$ turned to a clear yellow solution upon the addition of triethylamine at -10°C, v$_{\text{max}}$ 2050, 1980 cm$^{-1}$. Unlike in the case of Hüning base, the yellow solution turned brown on warming to ca 5°C.

(c) To a magnetically stirred solution of the salt 4 (500 mg) in MeCN (5 ml) was added pyridine (200 mg) at 0°C. After 5 min. of further stirring, ether was added to precipitate a stable off-white solid. The precipitate was collected by filtration, washed with ether, and air-dried, 620 mg, 99%. Pale yellow crystals, decomp. > 215°C (from acetone and CH$_2$Cl$_2$), were identified as tricarbonyl(n$^4$-5α-pyridiniumcyclohexa-1,3-diene)iron hexafluorophosphate 155. v$_{\text{max}}$(KBr) 2065, 1980, 1500 cm$^{-1}$; $\delta$(CD$_3$CN) 8.62 (2H, d, J = 6 Hz, 2$^1$- and 6$^1$-H of the pyridinium ring), 8.38 (1H, t, J = 7-8 Hz, 4$^1$-H of the pyridinium ring), 7.9 (2H, t, J = 6-7 Hz, 3$^1$- and 5$^1$-H of the pyridinium ring), 5.82 (2H, m, 2- and 3-H), 5.24 (1H, dt, J = 11 Hz, J$^{5\beta,6\beta} = 5$ Hz, J$^{5\beta,6\alpha} = 5$ Hz, J$^{5\beta,4\beta} = 3.5$-4.0 Hz, 5$\beta$-H), 3.28-3.12 (2H, m, 1- and 4-H), 2.84 (1H, m, J$^{6\beta,6\alpha} = 16$ Hz, 6$\beta$-H), 1.8 (1H, m, 6α-H); (Found: C, 38.0; H, 3.1; P, 7.2; F, 24.9; N, 2.9%. C$_{14}$H$_{12}$PFNOFe requires C, 38.0; H, 2.7; P, 7.0; F, 25.7; N, 3.2%). CH$_2$($^\alpha$)-splitting pattern (Section 2.3.1).
CHAPTER 7

Optical resolution of (±)-tricarbonyl(η⁴-l-carboxycyclohexa-1,3-diene)iron 122

(+)-tricarbonyl(η⁴-l-carboxycyclohexa-1,3-diene)iron 157 and (-)-tricarbonyl-
(η⁴-l-carboxycyclohexa-1,3-diene)iron 157

(±)-Acid 122 was prepared from tricarbonyl(η⁴-2-methoxycarbonyl-
cyclohexa-1,3-diene)iron 12 by a modification of the method described by
Birch and Williamson. The ester 12 (22 g, 7.9 x 10⁻² mol) and concen-
trated H₂SO₄ (40 ml) in methanol (200 ml) was heated under reflux for 24 h.
Some methanol (ca 100 ml) was removed from the cooled reaction mixture
under reduced pressure. Water (200 ml) was added to it, and the mixture
heated under reflux for 30 h. The cooled mixture was extracted into ether.
The combined ether extracts were washed with brine and water, dried
(MgSO₄) and concentrated to result in the (+)-acid 122 as a yellow
solid (19.8 g, 95%).

To a magnetically stirred solution of the (±)-acid 122 (19 g,
7.2 x 10⁻² mol) in chloroform and acetone (3 to 1 by v/v, 400 ml), was
added (-)-1-phenylethylamine (9.5 ml, 7.5 x 10⁻² mol, EGA-chemie, optical
purity > 99%) dropwise. After the addition was complete, a slightly
yellowish white precipitate formed, and the mixture was stirred for further
10 min. The precipitate was collected by filtration; the filtrate was
kept aside for isolation of the other diastereomer. The precipitate was
washed with chloroform and dried under suction to obtain 17.2 g of the
salt, [α]D²⁵ + 6° (acetone, C=1). This was recrystallized several times
until the optical rotation was constant, [α]D²⁵ +68° (acetone, C=1).
This diastereomer (7.4 g) was dissolved in acetone and aqueous HCl added
to it. The removal of acetone at the rotary evaporator resulted in a yellow crystalline precipitate which was collected by filtration and washed with water. Recrystallization from chloroform and light petroleum afforded (+)-tricarbonyl(\(n^1\)-1-carboxycyclohexa-1,3-diene)iron 157 as yellow crystalline solid (4.46 g, 23-24%), m.p. 147-149°C, \([\alpha]_D^25 + 136^\circ\) (acetone, C=3); \([\alpha]_{414}^25 + 55^\circ\) (minimum), \([\alpha]_{484}^25 + 214^\circ\) (maximum).

The filtrate kept aside above gave, after concentration and cooling at 0°C overnight, a second crop (6.2 g), \([\alpha]_D^25 - 95^\circ\) (acetone, C=1).

Recrystallization of this salt to constant rotation as above afforded the second diastereomer (3.24 g), \([\alpha]_{422}^25 - 126^\circ\) (acetone, C=1). Acid hydrolysis of this salt as above gave (-)-tricarbonyl(\(n^1\)-1-carboxycyclohexa-1,3-diene)iron as a yellow crystalline solid (1.94 g, 10-11%), \([\alpha]_{490}^25 - 136^\circ\) (acetone, C=3); \([\alpha]_{422}^25 - 55^\circ\) (maximum), \([\alpha]_{484}^25 - 214^\circ\) (minimum).

(-)-tricarbonyl(\(n^4\)-1-methylcyclohexa-1,3-diene)iron 158

To a magnetically stirred solution of (+)-1-carboxy acid 157 (200 mg, 0.76 mmol) in freshly distilled THF (10 ml) was added 2 ml of a 10 M solution of borane in dimethylsulfide (0.2 ml). Boron trifluoride-etherate (5 ml) was added dropwise and the mixture heated under reflux (ca 50°C) for 4 h. The cooled greenish solution was poured over a mixture of ice and NaCl. The product was extracted into light petroleum. Combined petroleum extracts were washed with brine and water, dried (MgSO\(_4\)) and concentrated to give a yellow oil, 150 mg, 84%. The product was identified as the (-)-1-methyl complex 158, b.p. 50°C/0.5 mmHg (kugelrohr); \([\alpha]_D^25 = - 18^\circ\) (C=1, CHCl\(_3\)); \(\nu_{\text{max}}\) (CHCl\(_3\)) 2030, 1965 cm\(^{-1}\); \(\delta\) (CDCl\(_3\)) 5.16 (2H, m, 2- and 3-H), 3.12 (1H, m, 4-H), 1.92-1.63 (7H, singlet at \(\delta 1.63\) overlapped on a multiplet, 5- and 6-H and Me); \(m/\alpha\) 234 (M), 206 (M-CO),
178 (M-2CO), 150 (M-3CO); (Found: C, 51.2; H, 4.3%. C\textsubscript{10}H\textsubscript{10}O\textsubscript{3}Fe requires C, 51.3; H, 4.3%).

**Approaches to the synthesis of natural gabaculine**

Tricarbonyl($n^5$-1-methoxycarbonylcyclohexadienylium)iron hexafluorophosphate 5\textsuperscript{-5} and tricarbonyl($n^5$-1-methoxycarbonyl-2-methylcyclohexadienylium)iron hexafluorophosphate 100 (chapter 4) were prepared from the corresponding 1-methoxycarbonyl esters, using Ph$_3$C\textsuperscript{6}PF$_6$.

Tricarbonyl($n^5$-1-methoxycarbonyl-3-methylcyclohexadienylium)iron hexafluorophosphate 160

The reaction of tricarbonyl($n^4$-1-methoxycarbonyl-3-methylcyclohexa-1,3-diene)iron 101 (10 g, 3.4 x 10\textsuperscript{-1} mol, chapter 4) with Ph$_3$C\textsuperscript{6}PF$_6$ (13.4 g, 3.5 x 10\textsuperscript{-1} mol) in the usual way (experimental, chapter 4) afforded the 1-CO Me, 3-Me salt 160 (11 g, 74%). M.p. 165-166°C (from acetonitrile, ether and light petroleum); $\nu_{\text{max}}$(KBr) 2130, 2090, 1710 cm\textsuperscript{-1}; $\delta$(CD\textsubscript{3}CN) 6.65 (1H, s, 2-H), 5.96 (1H, d, $J_{4,5}$ = 7.5 Hz, 4-H), 4.70 (1H, t, $J_{5,6\beta}$ = 7 Hz, 5-H), 3.84 (3H, s, CO$_2$Me), 3.26 (1H, dd, $J_{6\alpha,6\beta}$ = 15 Hz, 6\textalpha-H), 2.82 (3H, s, Me), 1.86 (1H, d, 6\textalpha-H); (Found: C, 33.4; H, 2.6%.

C\textsubscript{12}H\textsubscript{11}OPF\textsubscript{6}Fe requires C, 33.1; H, 2.5%.

(a) With N,N-dimethylamine and aniline

Tricarbonyl[$n^4$-5\textalpha-((N,N-dimethylamine)-1-methoxycarbonyl-3-methylcyclohexa-1,3-diene]iron 163

To a stirred and cooled (-40°C) solution of tricarbonyl($n^5$-1-methoxycarbonyl-3-methylcyclohexadienylium)iron hexafluorophosphate 160
To a stirred solution of tricarbonyl(η⁵-1-methoxycarbonyl-3-methyl-cyclohexadienylium)iron hexafluorophosphate 160 (150 mg, 0.34 mmol) in dry CH₂Cl₂ (10 ml), was added aniline (200 mg). The mixture was stirred for 30 min, and the solvent was removed under reduced pressure. Unreacted aniline was separated by tlc, using benzene and acetonitrile (5% v:v).

The compound isolated from the most mobile yellow band, was identified as 164 (83 mg, 63%), νmax(CHCl₃) 3325, 2050, 1985, 1705, 1600 cm⁻¹; δ(CDCl₃) 7.17 (2H, m, aromatic H), 6.70 (3H, m, aromatic H), 6.17 (1H, br s, 2-H), 4.13 (1H, ddd, J = 10, 4 Hz, 5-H), 3.70 (3H, s, CO₂Me), 3.39 (1H, dd, J = 4, 2 Hz, 4-H), 3.20-2.93 (2H, m, 6α-H and NH), 1.27 (1H, dd, J = 15, 4 Hz, 6α-H); m/z 383 (M), 355 (M-CO), 327 (M-2CO), 299 (M-3CO).
(b) With liquid ammonia

Hexacarbonyl(\(n^h, n'^h-5a, 5a\)-aminobiscyclohexa-1,3-diene)diiron \(165\)

A solution of tricarbonyl(\(n^5\)-cyclohexadienylium)iron hexafluorophosphate \(4\) (1.0 g, 3.0 mmol) in MeCN (10 ml) was added to magnetically stirred liquid ammonia (ca 50 ml). Ammonia was evaporated overnight. Acetonitrile was removed under reduced pressure. An aqueous solution of Na\(_2\)CO\(_3\) was added to it. The neutral product was extracted into ether. Combined ether extracts were washed with water, dried (MgSO\(_4\)), and concentrated to result a sticky yellow residue (600 mg, 88%). The product was identified as the amine \(165\); \(\nu_{\text{max}}\) (film) 3320 (NH), 2045, 1980, 1430 cm\(^{-1}\); \(\delta\)(CDCl\(_3\)) 5.43, 5.26 (4H, dd, dd, \(J=5.0-5.5\) Hz, 2-, 2'-, 3- and 3'-H), 3.25-2.84 (7H, m, 1-, 1'-, 4-, 4'-, 5- and 5'-H and NH), 2.18 (2H, m, \(J=15, 10, 4\) Hz, 6\(\theta\)- and 6\(\theta\)'-H), 1.24 (2H, m, \(J=15, 3\) Hz, 6\(a\)- and 6\(a\)'-H); \(m/z\) 453 (M), 425 (M-CO), 395 (M-2CO-2H), 367 (M-3CO-2H), 339 (M-4CO-2H), 311 (M-5CO-2H), 283 (M-6CO-2H). \(+\) CH\(_2\)(\(\alpha\))-splitting pattern (Section 2.3.1).

(c) With hexamethyldisilazane

Tricarbonyl(\(n^h-5a\)-ammonium-1-methoxycarbonyl-2-methylcyclohexa-1,3-diene)-iron hexafluorophosphate \(166\)

Hexamethyldisilazane (0.5 ml) was added to a magnetically stirred solution of tricarbonyl(\(n^b-1\)-methoxycarbonyl-2-methylcyclohexadienylium)-iron hexafluorophosphate \(100\) (100 mg, 0.23 mmol). The mixture was stirred for 1 h, and the solvents removed under reduced pressure. The residue was washed with ether to obtain \(166\) as a yellow solid (75 mg, 72%). \(\nu_{\text{max}}\) (nujol) 3225, 3200, 3125, 2075, 2030, 2000, 1980, 1705, 1575 cm\(^{-1}\); \(\delta\)(CD CN) 5.48 (1H, d, \(J_{3,4}^\alpha=6\) Hz, 3-H), 4.5 (2H, hump, D O exchange, NH\(_2\)), 3.68 (4H, singlet overlapped on a multiplet, CO Me and 5-H), 2.96 (1H, m, 4-H).
2.70 (1H, dd, $J_{6\alpha,6\beta} = 16$ Hz, $J_{6\beta,5} = 11$ Hz, 6β-H), 2.47 (3H, s, Me),
1.44 (1H, dd, $J_{6\alpha,5} = 4$ Hz, 6-H); m/z 582, 554, 550, 526, 498, 470,

(d) With potassium phthalimide

Tricarbonyl[$\eta^1$-methoxycarbonyl-5α-(N-phthalimido)cyclohexa-1,3-diene]iron 168

To a magnetically stirred suspension of potassium phthalimide (1.5 g, 8.1 mmol) in acetonitrile (20 ml) was added a solution of tricarbonyl[$\eta^5$-l-methoxycarbonylcyclohexadienylium]iron hexafluorophosphate 5 (3.0 g, 7.1 mmol) in acetonitrile (20 ml). The mixture was stirred for 30 min. and the solvents removed under reduced pressure. The neutral product was taken into a 1:1 mixture of light petroleum and ether. The combined ether extracts were concentrated to obtain a yellow solid. Recrystallization of the solid from light petroleum and chloroform afforded yellow crystals (2.9 g, 97%) of tricarbonyl[$\eta^1$-methoxycarbonyl-5α-(N-phthalimido)cyclohexa-1,3-diene]iron 168, m.p. 166-167.5°C, $\nu_{\text{max}}$(CHCl$_3$) 2040, 1980, 1760, 1730, 1700 cm$^{-1}$; $\delta$(CDCl$_3$) 7.9 (4H, m, aromatic H), 6.37 (1H, d, $J_{2,3} = 5$ Hz, 2-H), 5.66 (1H, dd, $J_{3,4} = 6$ Hz, 3-H), 4.96 (1H, ddd, $J_{5,6\beta} = 12$ Hz, $J_{5,6\alpha} = J_{5,4} = 4$ Hz, 5-H), 3.76 (3H, s, CO$_2$Me), 2.97 (1H, m, 4-H), 2.81 (1H, dd, $J_{6\alpha,6\beta} = 15$ Hz, 6β-H), 1.88 (1H, dd, 6α-H); (M calculated for C$_{19}$H$_{13}$NO$_7$Fe 423.0041, found 423.0034).

Tricarbonyl[$\eta^1$-methoxycarbonyl-2-methyl-5α-(N-phthalimido)cyclohexa-1,3-diene]iron 169

The reaction of tricarbonyl[$\eta^5$-methoxycarbonyl-2-methylcyclohexadienylium]iron hexafluorophosphate 100 (206 mg, 4.7 x 10$^{-1}$ mmol) with potassium phthalimide (100 mg, 5.4 x 10$^{-1}$ mmol) according to the same
procedure as above gave the adduct 169. Recrystallization from light petroleum and chloroform afforded yellow crystals (195 mg, 96%), m.p. 152-153°C; $\nu_{\text{max}}(\text{CHCl}_3)$ 2040, 1980, 1760, 1730, 1700 cm$^{-1}$; $\delta(\text{CDCl}_3)$ 7.8 (4H, m, aromatic H), 5.48 (1H, d, $J_{3,4} = 6$ Hz, 3-H), 4.49 (1H, ddd, $J_{5,6\beta} = 11$ Hz, $J_{5,6\alpha} = J_{5,4} = 4$ Hz, 5-H), 3.74 (3H, s, CO$_2$Me), 2.8 (2H, m, 4- and 6$\beta$-H), 2.66 (3H, s, Me), 1.92 (1H, dd, $J_{6\beta,6\alpha} = 15.5$ Hz, 6$\alpha$-H); m/z 437 (M), 409 (M-CO), 405 (M-OMe), 381 (M-2CO), 353 (M-3CO); (Found: C, 55.1; H, 3.6; N, 3.2%. C$_{20}$H$_7$O$_6$NFe requires C, 55.0; H, 3.5; N, 3.2%).

Tricarbonyl[η$^4$-1-methoxycarbonyl-3-methyl-5$\alpha$-(N-phthalimido)cyclohexa-1,3-diene]iron 170

Tricarbonyl[η$^5$-1-methoxycarbonyl-3-methylcyclohexadienylium]iron hexafluorophosphate 160 (1.0 g, 2.3 mmol) was reacted with potassium phthalimide (550 mg, 3.0 mmol) as above to obtain the adduct 170 (980 mg, 98%), m.p. 135-137°C (from light petroleum and chloroform); $\nu_{\text{max}}(\text{CHCl}_3)$ 2045, 1985, 1770, 1735, 1700 cm$^{-1}$; $\delta(\text{CDCl}_3)$ 7.75 (4H, m, aromatic H), 6.21 (1H, br s, 2-H), 4.93 (1H, ddd, $J_{5,6\beta} = 11.5$ Hz, $J_{5,6\alpha} = 4.0-4.5$ Hz, $J_{5,4} = 3$ Hz, 5-H), 3.71 (3H, s, CO$_2$Me), 2.92, 2.75 (2H, dd, dd, $J_{2,4} = 1.7$ Hz, $J_{6\beta,6\alpha} = 15$ Hz, 4- and 6$\beta$-H), 2.20 (3H, s, Me), 1.70 (1H, dd, 6$\alpha$-H); m/z 437 (M), 409 (M-CO), 406 (M-OMe), 381 (M-2CO), 353 (M-3CO); (Found: C, 55.3; H, 3.6; N, 3.1%. C$_{20}$H$_7$O$_6$NFe requires C, 55.0; H, 3.5; N, 3.2%).

(e) Removal of Fe(CO)$_3$

Methyl 5-(N-phthalimido)cyclohexa-1,3-diene-1-carboxylate 171

Trimethylamine-N-oxide dihydrate (4.0 g, 36 mmol) was added at 0°C to a solution of tricarbonyl[η$^4$-1-methoxycarbonyl-5$\alpha$-(N-phthalimido)cyclohexa-
1.3-diene]iron 168 (1.77 g, 4.2 mmol) in N,N-dimethylacetamide (25 ml). The mixture was stirred magnetically for 3 days at 0-5°C, and filtered through celite. Ice-cooled water ($\alpha\alpha$ 200 ml) was added to it and the organic product was extracted into a 1:1 mixture of ether and light petroleum. The combined ether extracts were washed several times with water, dried (MgSO$_4$) and concentrated to result in a white crystalline residue (840 mg, 71%). The compound was identified as methyl 5-(N-phthalimido)cyclohexa-1,3-diene-1-carboxylate 171, m.p. 146-147°C (from light petroleum and chloroform); $\lambda_{max}$ (EtOH) 289 (c 10850), 240 (shoulder, c 12500), 231 (shoulder, c 20280), 219 (c 37500) nm; $\nu_{max}$ (CHCl$_3$) 1775, 1710, 1640, 1610, 1580 cm$^{-1}$; $\delta$(CDCl$_3$) 7.76 (4H, m, aromatic H), 7.08 (1H, ddd, $J_{2,3} = 5.5$ Hz, $J_{2,6} = J_{2,4} = 1.0$ Hz, 2-H), 6.22 (1H, ddd, $J_{3,4} = 9$-10 Hz, $J_{3,5} = 2.4$ Hz, 3-H), 6.0 (1H, dd, $J_{4,5} = 3$ Hz, 4-H), 5.22 (1H, ddd, $J_{5,6} = 11$-12, 13-14 Hz, 5-H), 3.74 (3H, s, CO Me), 3.05-2.7 (2H, m, 6-H); m/z 283 (M), 281 (M-2H), 250, 224, 136; (Found: C, 67.6; H, 4.7; N, 5.0%. C$_{16}$H$_{13}$NO requires C, 67.8; H, 4.6; N, 4.9%).

Metal group was cleaved also under photochemical conditions. The phthalimido adduct 168 (200 mg) and excess ferric chloride hexahydrate (500 mg) in methanol (5 ml) and benzene (5 ml) was stirred magnetically for 20 h in the presence of visible light from a 250 W lamp. The reaction mixture was filtered through celite and diluted with water ($\alpha\alpha$ 100 ml). The organic product was taken into benzene. The combined benzene extracts were washed with water, dried (MgSO$_4$) and concentrated to give the diene 171 as a white solid (130 mg, 96%).

However, at different runs under photochemical conditions, the diene 171 accompanied aromatic products (15-25%, $^1$H NMR).

A mixture of the phthalimido adduct 168 and ferric chloride hexahydrate in methanol and benzene (in the proportions as above) was stirred
magnetically for 4 days in a flask wrapped with aluminium foil. The work-up as above afforded the starting material 168 (IR, \(^1\)H NMR) in 90% recovery. The same result was observed by replacement of methanol with ethanol.

(f) Alkaline hydrolysis of the diene ester 171

A solution of methyl 5-(N-phthalimido)cyclohexa-1,3-diene-1-carboxylate 171 (175 mg, 6.2 x 10\(^{-1}\) mmol) in methanol (5 ml) and potassium hydroxide (500 mg) in water (5 ml) were stirred magnetically for 2 h. Upon acidification with 10% HCl was formed a white amorphous powder insoluble in water or ether. The solid was collected by filtration and dried \textit{in vacuo}, 163 mg, 98%. The product was identified as 5-(N-phthalimido)-cyclohexa-1,3-diene-1-carboxylic acid 172, m.p. 210-215°C; \(\delta\) (d\(_6\)-DMSO) 7.7 (4H, m, aromatic H), 7.12 (1H, m, 2-H), 6.14 (2H, m, 3- and 4-H), 5.1 (ca 1H, m, 5-H) 2.8 (ca 2H, m, 6-H); \(m/z\) 269 (M), 267 (M-2H), 250, 224, 122 (C\(_6\)H\(_5\)CO\(_2\)H).

(g) Attempts on dephthaloylation of the diene acid 172

To a stirred suspension of 5-(N-phthalimido)cyclohexa-1,3-diene-1-carboxylic acid 172 (169 mg) in ethanol was added hydrazine hydrate (2.0 ml) at 0°C. The mixture was stirred magnetically at 0-5°C for 3 days at which stage, ninhydrin test indicated the formation of an amino acid, possibly gabaculine (tlc analysis\(^{57b}\) using 7.5 EtOH, 2.5 H\(_2\)O, trace NH\(_4\)OH). The mixture was filtered through celite and concentrated under reduced pressure. The \(^1\)H NMR spectrum of the residue (43 mg, 56%) corresponded to benzoic acid.
REFERENCES

   (b) R.B. King, in ref 3, p.525.


(b) J.A. Gladysz, Aldrichimica Acta, 12, 13 (1979).


44 G.R. Stephenson, personal communication (1980).
49 L.F. Kelly, personal communication (1980).
68 (a) W. D. Raverty, personal communication (1979).
     (e) J. d'Angelo, Tetrahedron, 32, 2979 (1976).
     (b) E.M. Kaiser, Synthesis, 391 (1972).
     (e) J. d'Angelo, Tetrahedron, 32, 2979 (1976).
     (b) E.M. Kaiser, Synthesis, 391 (1972).
(d) A.A. Petrov and K.B. Rall, J. Gen. Chem. (USSR), 26, 1779 (1956).


R.B. King, in ref 3, p.397.


111 A. Dunand and G.B. Robertson, unpublished results.
116 T.C. Khor, personal communication.


    (c) J.D. Connelly and R. McCrindle, *Chem. and Ind. (Lond).* , 379 (1965).


123  J. Müller, in ref. 3, p.113, and references therein.


135 p.349, 354 and 386 in ref. 17.
142 J.S. Evans, NMRSIM Program, Dept. Chem., Lawrence Uni., Appleton, Wisconsin, USA.
149 (a) P.170 in ref. 17.


