ASYMMETRIC SYNTHESIS VIA IRON ACYL COMPLEXES

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Doctor of Philosophy

by

J.C. Walker, B.A.

Keble College

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Asymmetric Synthesis via Iron Acyl Complexes

J.C. Walker

Keble College, Oxford

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Abstract

This thesis describes the applications to asymmetric synthesis of the highly diastereoselective carbon-carbon bond forming reactions of α,β-unsaturated acyl ligands bound to the chiral iron auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$.

Chapter 1 briefly reviews the use of chiral auxiliaries in asymmetric synthesis.

Chapter 2 discusses the conformation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ with reference to its X-ray crystal structure. A method for determining the absolute configuration of (+)- and (-)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ is described as well as methods for determining their optical purities.

Chapter 3 describes methods for the preparation of α,β-unsaturated acyl complexes. The Peterson reaction between the enolate derived from $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ and aldehydes gives complexes of the type $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHR]$ as mixtures of E and Z isomers. Sodium hydride-induced elimination of methanol from either diastereoisomer of the corresponding β-methoxy acyl complex gives the E isomer stereoselectively. Complexes of the type $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COC(R){=}CH_2]$ are similarly prepared from the corresponding β-menthoxy acyl complexes. The conformations of E- and Z-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHR]$ are discussed with reference to the X-ray crystal structures of the β-methyl substituted complexes.

Chapter 4 describes the formation of lithium dienolates from $Z\text{-}[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHCH_2R]$. Exclusive γ-deprotonation is rationalised in terms of initial coordination of the alkyllithium to the acyl oxygen. Reaction with electrophiles occurs at the α-position with high diastereoselectivity (>100:1) and gives only an E geometry about the β,γ-double bond.

Chapter 5 describes the highly diastereoselective tandem Michael addition-alkylation reactions of $E\text{-}[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHR]$ to give α- and/or β-substituted acyl complexes. The alkyl groups of the alkyllithium and the electrophile are introduced to the same face of the original carbon-carbon double bond, the Michael addition being rationalised in terms of initial coordination of the alkyllithium to the acyl oxygen. The same Michael adducts are formed when either diastereoisomer of the corresponding β-methoxy and β-menthoxy acyl complexes is treated with two equivalents of the alkyllithium followed by an electrophile. Oxidative decomplexation gives α- and/or β-substituted carboxylic acids or amides. $Z\text{-}[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHCH{=}CHCH_3]$ displays Michael addition reactivity towards n-butyllithium whereas $Z\text{-}[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHCH{=}CH_2]$ displays 1,6-conjugate addition reactivity.

Chapter 6 describes the highly diastereoselective Michael addition of lithium benzylamide to and subsequent alkylation of enantiomerically pure E α,β-unsaturated acyl complexes. Oxidative decomplexation gives the corresponding β-lactams with high optical purities (>100:1).

Chapter 7 describes the highly diastereoselective (>100:1) synthesis of quaternary carbon centres *via* Michael addition of n-butyllithium to α-substituted-α,β-unsaturated acyl complexes followed by reaction with a carbon electrophile.

Chapter 8 describes the completely enantioselective synthesis of (2S)-(-)-bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid from the asymmetric Diels-Alder reaction between (S)-(+)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ and cyclopentadiene.

To my father

Acknowledgements

Firstly, I should like to thank my supervisor, Dr. S.G. Davies, for the support and encouragement he has given me during my time in the D.P.

I would also like to thank all the members of the group I have had the pleasure of working with over the past two years, for their help, advice and friendship. I am particularly grateful to those who took time to proof read this thesis.

Thanks must also go to Drs. K.H. Sutton and R.H. Jones for obtaining the X-ray crystal structure data that appear in this thesis, and to all the technical staff at the Dyson Perrins Laboratory, especially Mrs. McGuinness and Dr. R.T. Aplin.

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Abbreviations

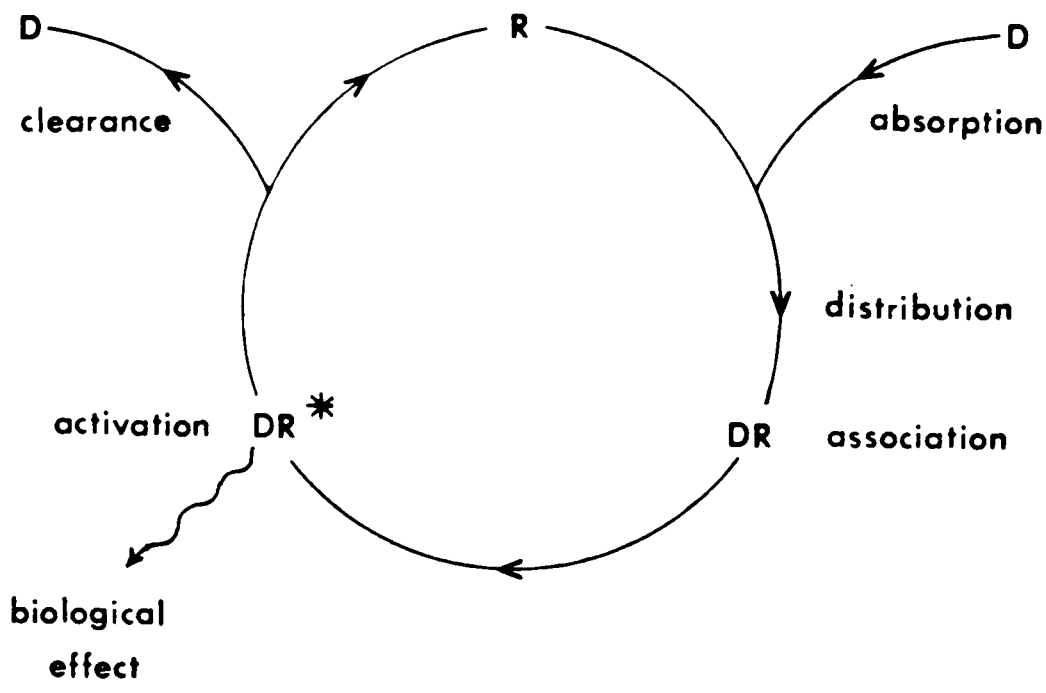
R	organic radical
E^+	electrophile
Nu^-	nucleophile
X_C	chiral auxiliary group
Me	CH_3
Et	CH_2CH_3
i-Pr	$CH(CH_3)_2$
n-Bu	$CH_2CH_2CH_2CH_3$
t-Bu	$C(CH_3)_3$
Cy	cyclohexyl
Mn	(R)-menthyl
Bn	benzyl
Tr	trityl
Ph	phenyl
Ar	aryl
Ac	acetyl
TfO	triflate
Ft	phthalimido
X	Cl, Br or I
THF	tetrahydrofuran
HMPA	hexamethylphosphoramide
TMEDA	N,N,N',N'-tetramethylethylenediamine
Py	pyridine
LDA	lithium diisopropylamide
LICA	lithium isopropylcyclohexylamide
SAMP	(S)-(-)-1-amino-2-(methoxymethyl)-pyrrolidine

RAMP	(R)-(+)-1-amino-2-(methoxymethyl)-pyrrolidine
DMBB	5-(1,3-dimethylbutyl)-5-ethylbarbituric acid
e.e.	enantiomeric excess
d.e.	diastereoisomeric excess
$\nu_{max.}$	infrared absorption peak
br	broad
m	medium
w	weak
s	strong
vs	very strong
n.m.r.	nuclear magnetic resonance
s	singlet
d	doublet
t	triplet
q	quartet
m	multiplet
$\{^1H\}$	proton decoupled
m/z	mass to charge ratio
A	Angstrom

CHAPTER 1

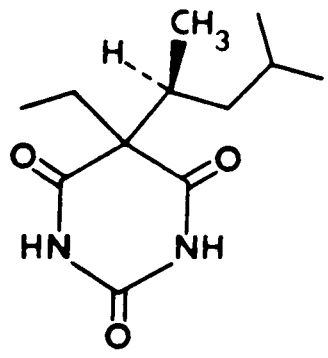
INTRODUCTION

It is becoming increasingly apparent that the effects of chiral molecules on biological systems depend on their absolute configurations. The interaction in an activated complex(DR^*) between a receptor(R) and a single enantiomer of a drug(D) may bring about desirable biological effects, whereas the diastereoisomeric interaction between the receptor and the other enantiomer of the drug may cause undesirable activity (scheme 1).

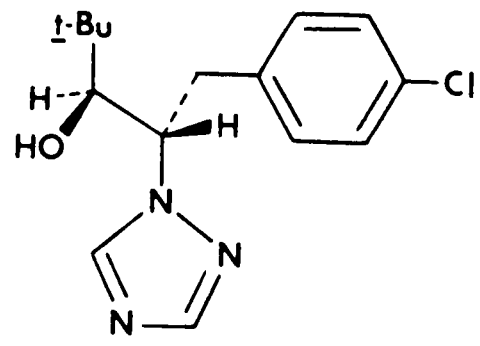


Scheme 1: General mechanism of drug action.

For example, the S enantiomer 1 of the barbiturate DMBB is a sedative whilst the R enantiomer is a convulsant.[1] Similarly, Paclobutrazol shows low fungicidal activity with high growth regulatory activity in the SS configuration 2 but the inverse activity in the RR configuration.[2]



(S)-1



(SS)-2

Furthermore, the *in vivo* effects of absorption, distribution and clearance may also be enantioselective. It is therefore important for chiral molecules to be available in optically pure form if their medicinal applications or uses as fungicides, plant growth regulators, insecticides etc. are to be investigated.

I. Synthesis of enantiomerically pure organic compounds

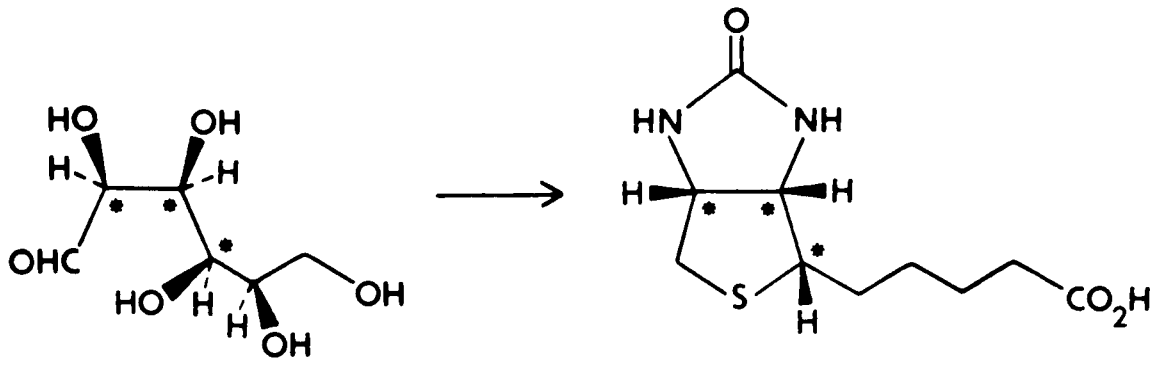
Although the last decade has seen a tremendous explosion in the number of methods directed towards the synthesis of enantiomerically pure organic compounds, three general approaches have emerged.

1. Resolution

Classical resolution is the least general of the methods available, often requiring a considerable amount of trial and error before the best system for the separation of diastereoisomers is developed. It also imposes certain functionality restraints on the substrate molecule. In particular, the presence of an acidic or basic group is desirable. To avoid waste of materials resolution must also be carried out at the earliest possible stage during a synthesis as for example, in Corey's synthesis of $PGF_{2\alpha}$.[3]

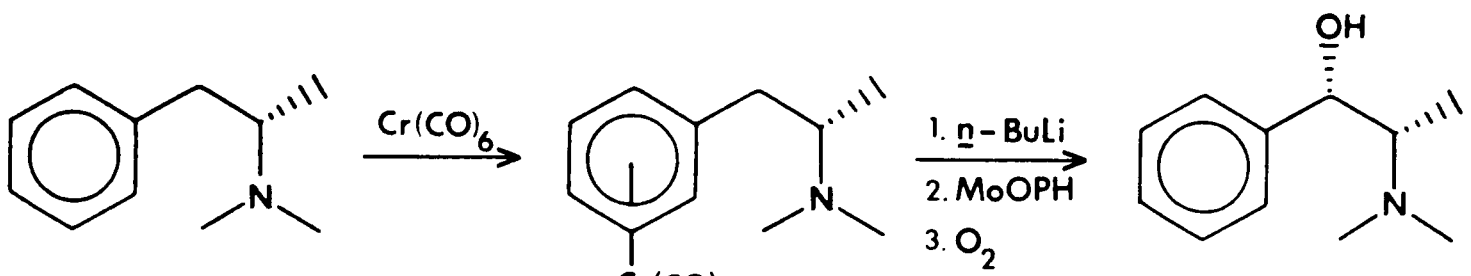
2. Chiral building blocks from the chiral pool

Modification of readily available optically pure compounds such as carbohydrates,[4] α-amino acids, hydroxy acids and terpenes has been successfully employed in the synthesis of a range of natural products in optically pure form.[5] The starting material may contain either (i) more chiral centres than in the target molecule as in for example, the synthesis of biotin from D-mannose,[6]



D-mannose Biotin

or (ii) a single chiral centre which is used to stereoselectively generate the required number of chiral centres in the target molecule as in for example, the synthesis of (+)-N-methylpseudoephedrine from (+)-N,N-dimethylamphetamine using arene chromium tricarbonyl complexes.[7]



This approach is not general however, due to the limited number of optically pure starting materials available. In addition, most syntheses necessarily have to incorporate protection and deprotection steps.

3. Asymmetric synthesis[8]

Potentially the most general route to single enantiomers, this approach involves the association of an optically pure chiral auxiliary with a substrate molecule and the conversion of a prochiral group stereoselectively to a chiral group. The transformation is usually carried out by selective addition to one face of an unsaturated enantiotopic functional group such as a carbonyl group, an enolate anion

or the carbon-carbon double bond of an olefin or α,β-unsaturated carbonyl system. In a successful application of asymmetric synthesis, the desired enantiomer must be prepared in high optical and chemical yield with the chiral product being readily separable from the chiral auxiliary without racemisation. Furthermore, the optically pure chiral auxiliary should be recoverable quantitatively. The chiral auxiliary group, often derived from a readily available optically pure natural product, may form part of a chiral catalyst as in enzyme reactions,[9] the asymmetric epoxidation of allylic alcohols[10] and the asymmetric hydrogenation of olefins.[11] More commonly in stoichiometric reactions, the chiral auxiliary group forms part of the original substrate molecule. In particular, chiral auxiliaries bound to enolates have found widespread use in the asymmetric synthesis of chiral carbonyl compounds.[8]

II. Asymmetric synthesis using chiral enolates

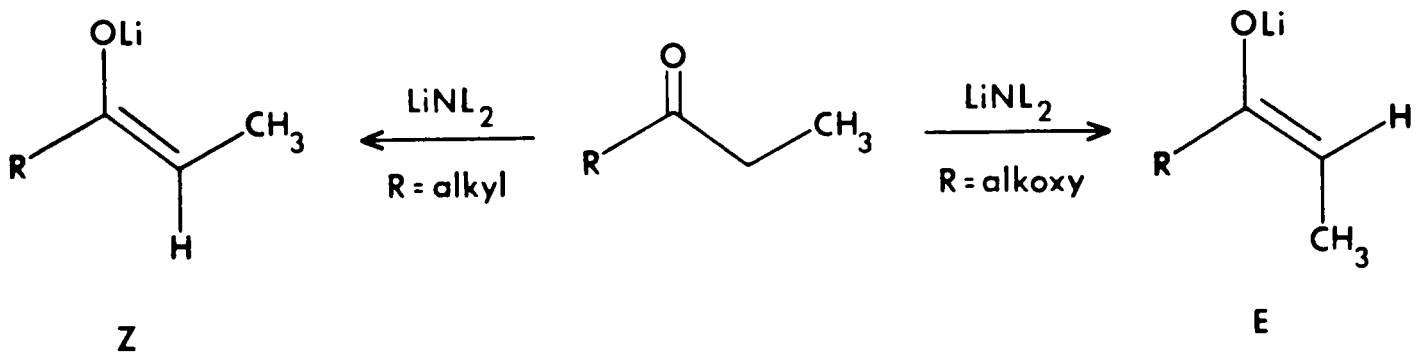
In order for a chiral enolate to be elaborated with a high degree of diastereoselectivity, two stereochemical requirements must be satisfied. Firstly, the chiral carbonyl precursor must undergo highly selective deprotonation to generate a geometrically pure enolate. Secondly, the chiral auxiliary group should block one of the faces of the enolate so that all reactions take place from the least hindered face.

1. Enolate geometry

Generally for ketones in which R is bulky, deprotonation with sterically hindered lithium bases under kinetic conditions gives Z enolates.[12]† Esters in which R is alkoxy favour E enolate formation.[13]

† Z refers to when the substituents of highest priority according to the Cahn-Ingold-Prelog system, are on the same side of the double bond. E refers to when they are on opposite sides.

Ireland has rationalised these results in terms of chair-like cyclic transition states.[14]

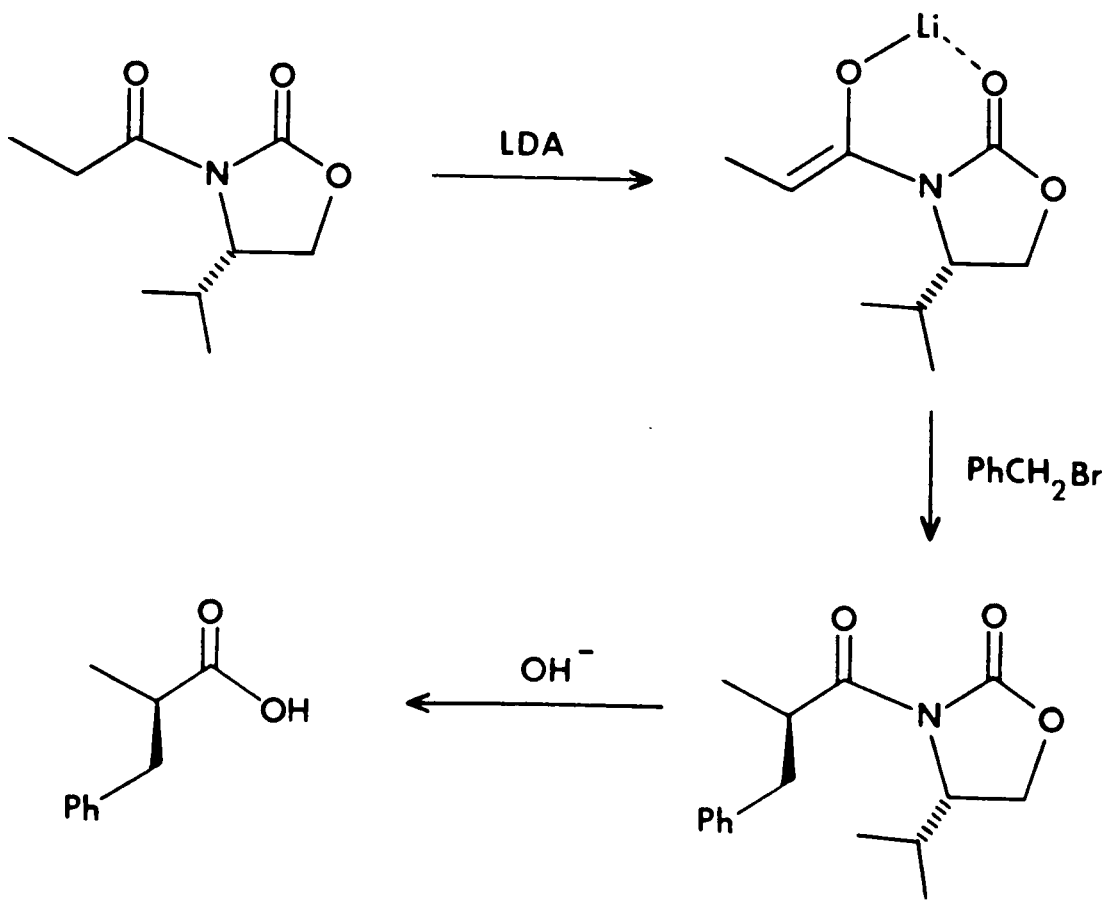


Z E

Both n.m.r. studies on the corresponding trimethylsilyl enol ethers[15] and Claisen rearrangements via either the silyl enol ether[16] or the enolate itself,[14] have been used to determine the geometry of enolates.

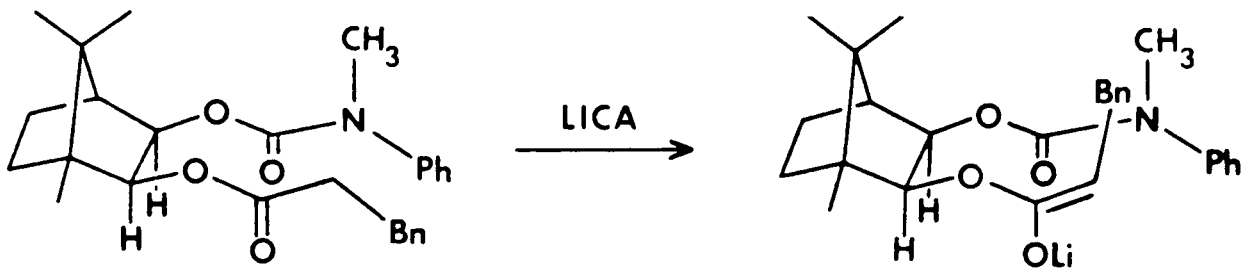
2. Alkylation of chiral enolates[17]

Evans has described the asymmetric synthesis of α-substituted propionic acids using chiral imide enolates derived from (S)-valine. The high diastereoselectivites (> 99:1) are believed to originate from the rigidity imparted on the Z enolate by the formation of a temporary chelate ring. Subsequent alkylation from the face of the enolate away from the isopropyl group gives the observed absolute stereochemistry in the product.[18]

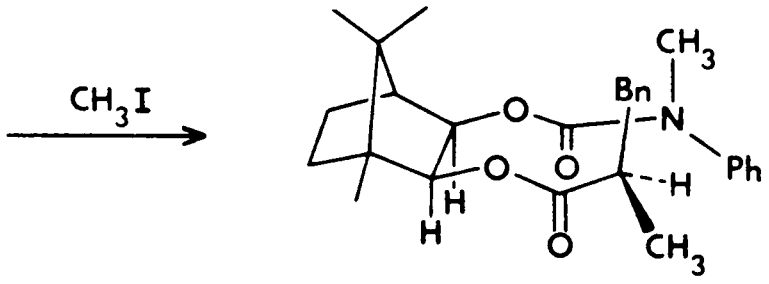


Chelation control has also been utilised in the alkylation of chiral metalloenamines derived from optically pure α-amino acids[19] and azaenolates derived from chiral oxazolines.[20]

When non-bonding interactions restrict rotation about the bond between the enolate and the chiral auxiliary, good diastereoselectivities are achieved.[21] Thus, the Z enolate 4 derived from ester 3 is alkylated with a diastereoselectivity of 95:5.[22]

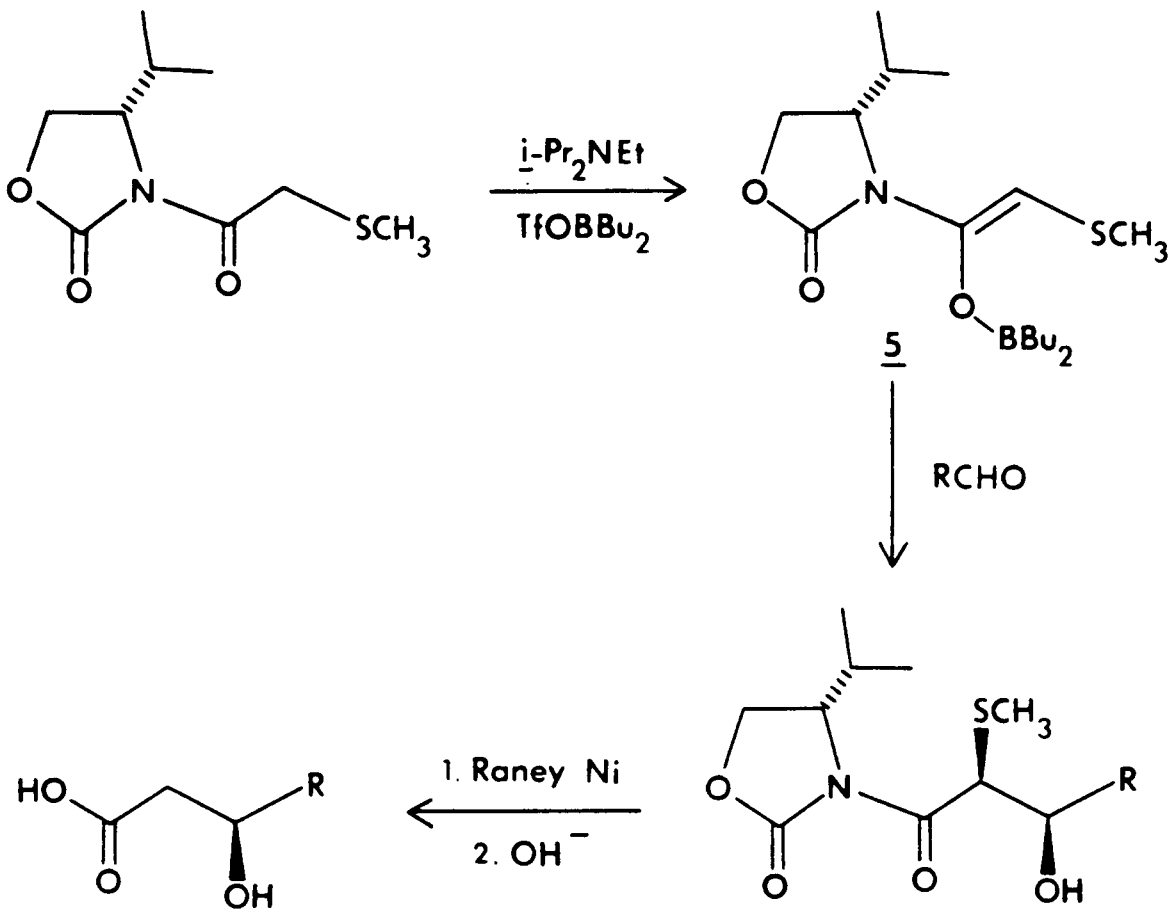


3 4



3. Aldol reactions of chiral enolates

Many examples of diastereoselective aldol reactions between chiral enolates and aldehydes now exist and this area has been extensively reviewed.[23] In one particular case, β-hydroxy acids with optical purities of up to 99:1 were formed after the aldol reaction of boron enolate 5 and deprotection.[24]

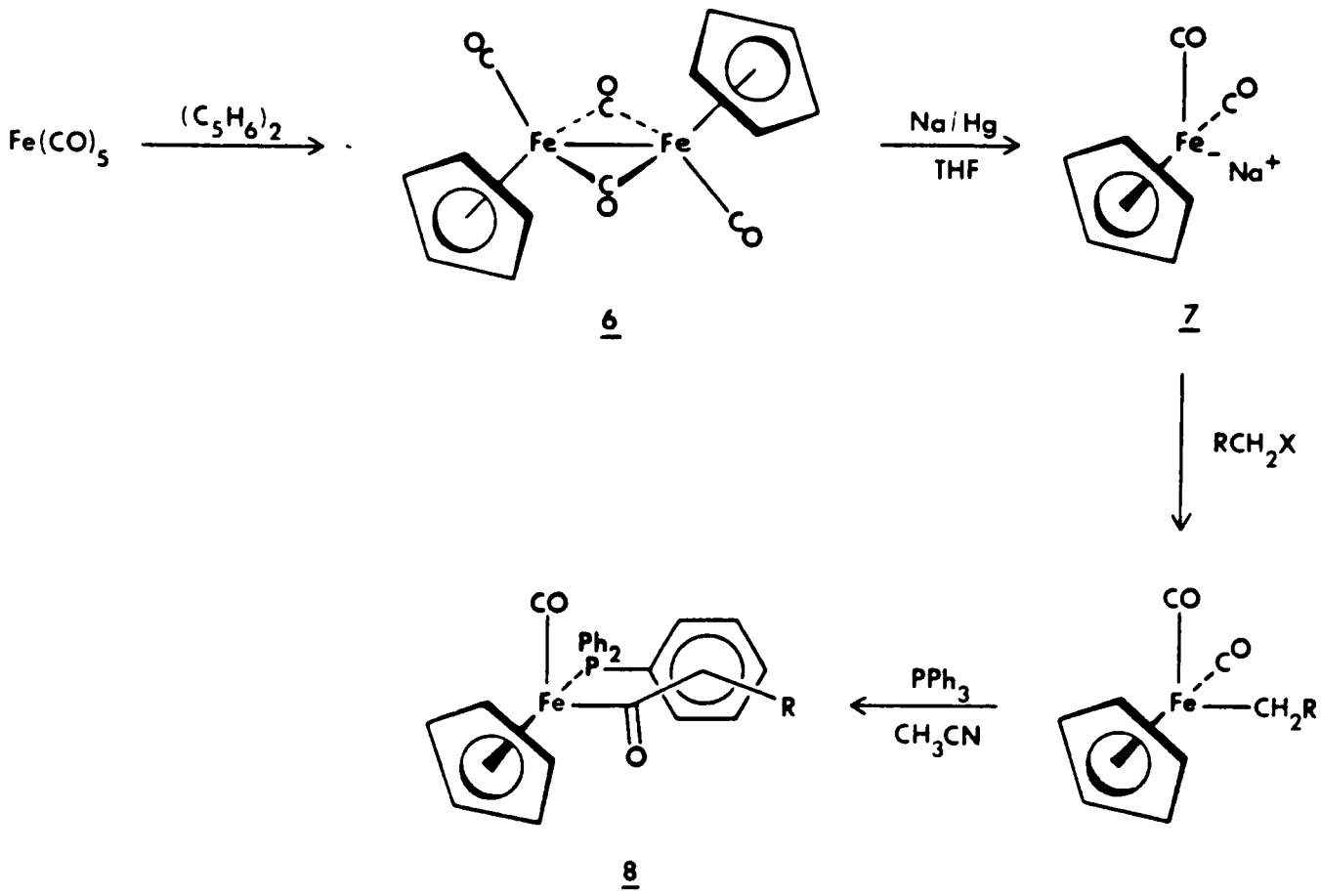


Organotransition metal complexes are finding an increasing number of applications in organic synthesis.[25] Although iron acyl complexes of the type $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2R]$ were prepared as long ago as 1966,[26] the chiral enolates derived from these complexes have only recently been prepared and used in asymmetric synthesis.

III. Asymmetric synthesis using chiral iron acyl complexes

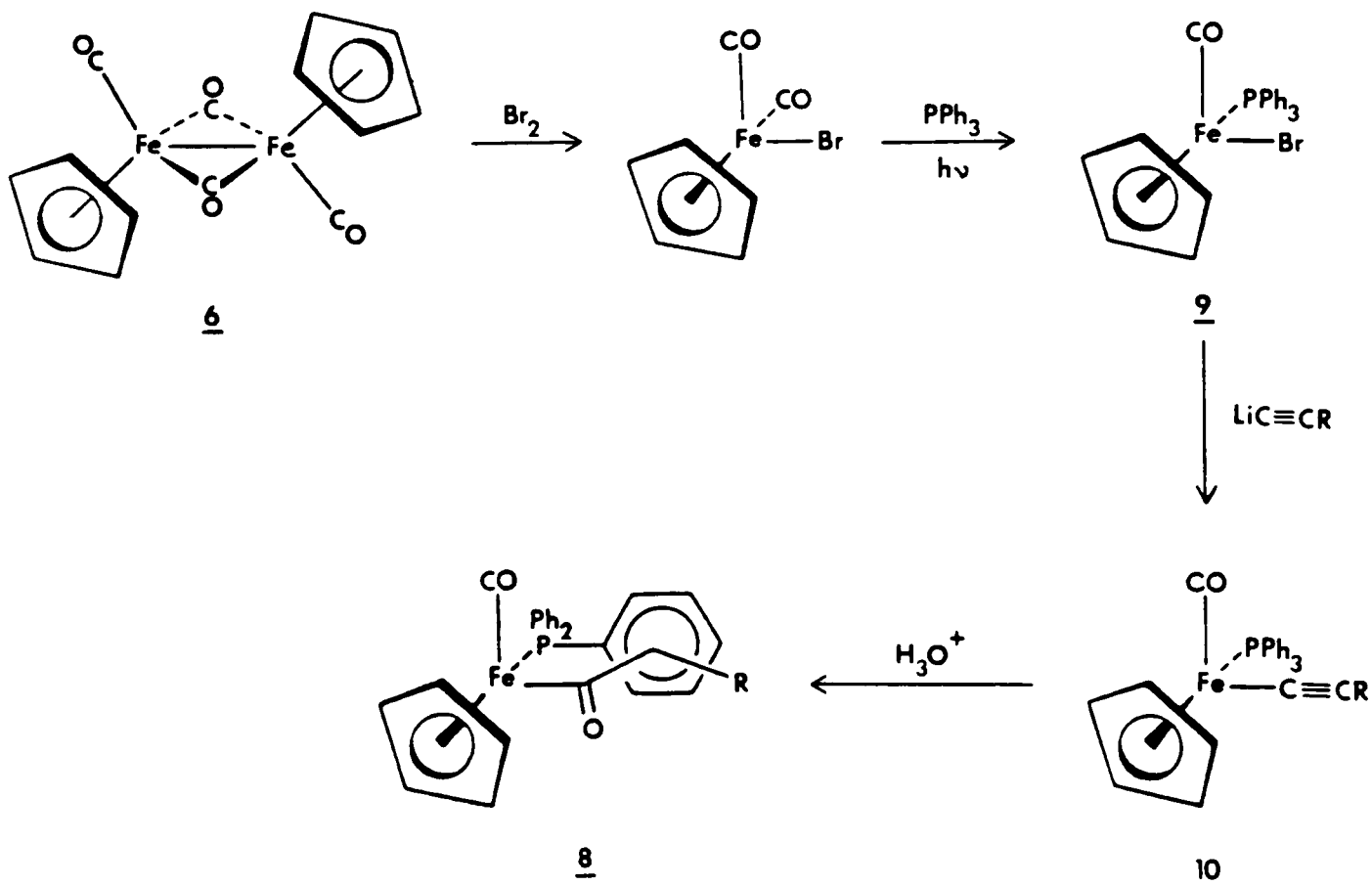
1. Synthesis of iron acyl complexes

Iron acyl complexes are prepared in high yield starting from iron pentacarbonyl. Heating iron pentacarbonyl together with dicyclopentadiene gives the iron dimer 6[27] which is cleaved over sodium amalgam to give the nucleophilic iron species 7. Alkylation[28] and further heating in the presence of triphenylphosphine gives the corresponding acyl complexes 8.[29]



6 7 8

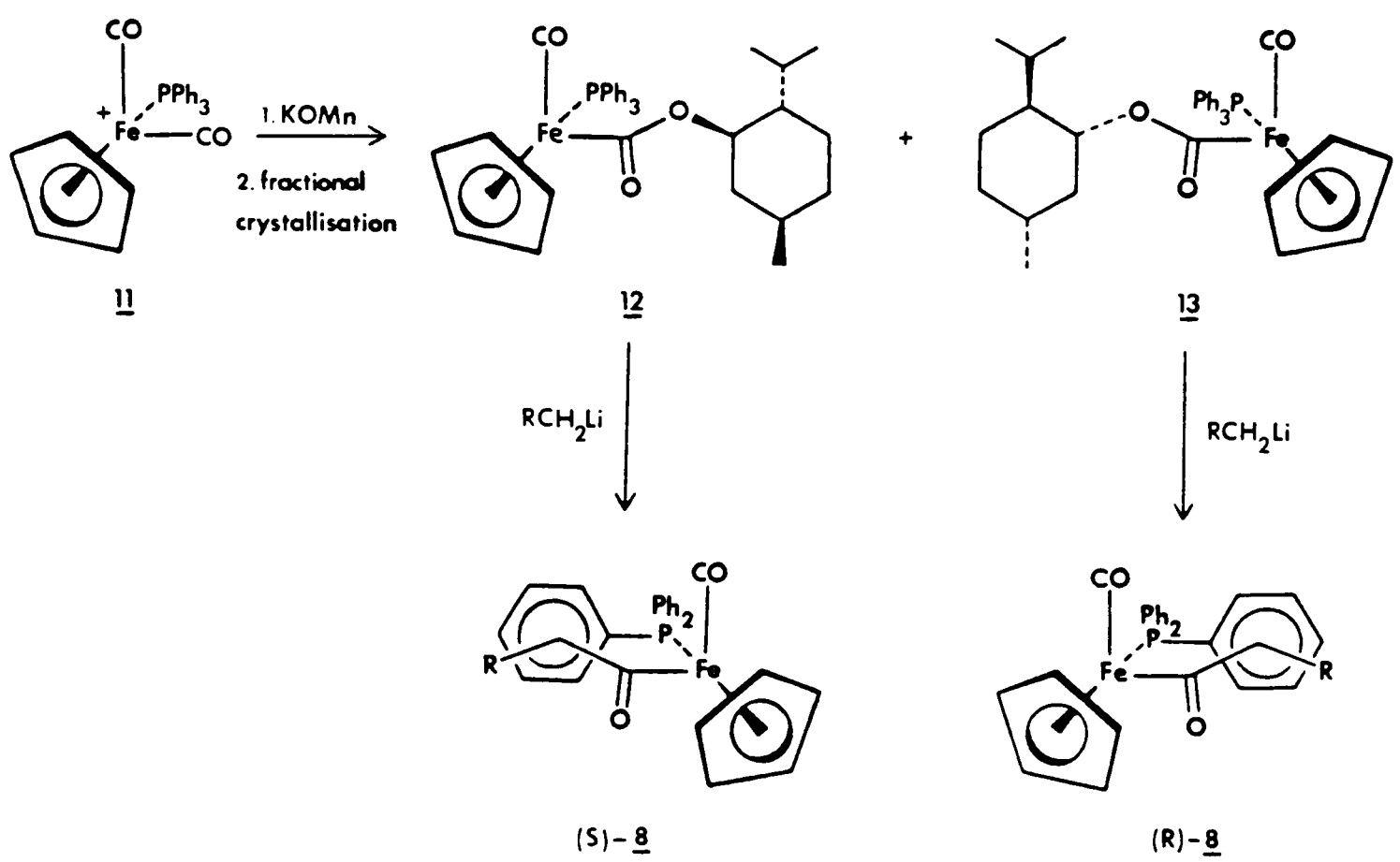
Alternatively, iron acyl complexes can be prepared from the iron bromide 9 which is also available from the iron dimer 6.[30,31] Lithium acetylides react with 9 to give acetylide complexes 10. These upon mild acid hydrolysis give the corresponding acyl complexes 8.[31]



6 9 10 8

2. Resolution of iron acyl complexes

Since the iron atom in acyl complexes of the type $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2R]$ 8 is coordinated to four different ligands, such complexes are chiral.† Although the syntheses described in section 1 above give acyl complexes in racemic form, optically active iron acyl complexes may also be prepared.[33,34] The resolved diastereoisomeric mentholate esters 12 and 13, formed from cation 11 and potassium mentholate, are converted to optically active acyl complexes (S)- and (R)-8 by reaction with alkyllithium reagents.

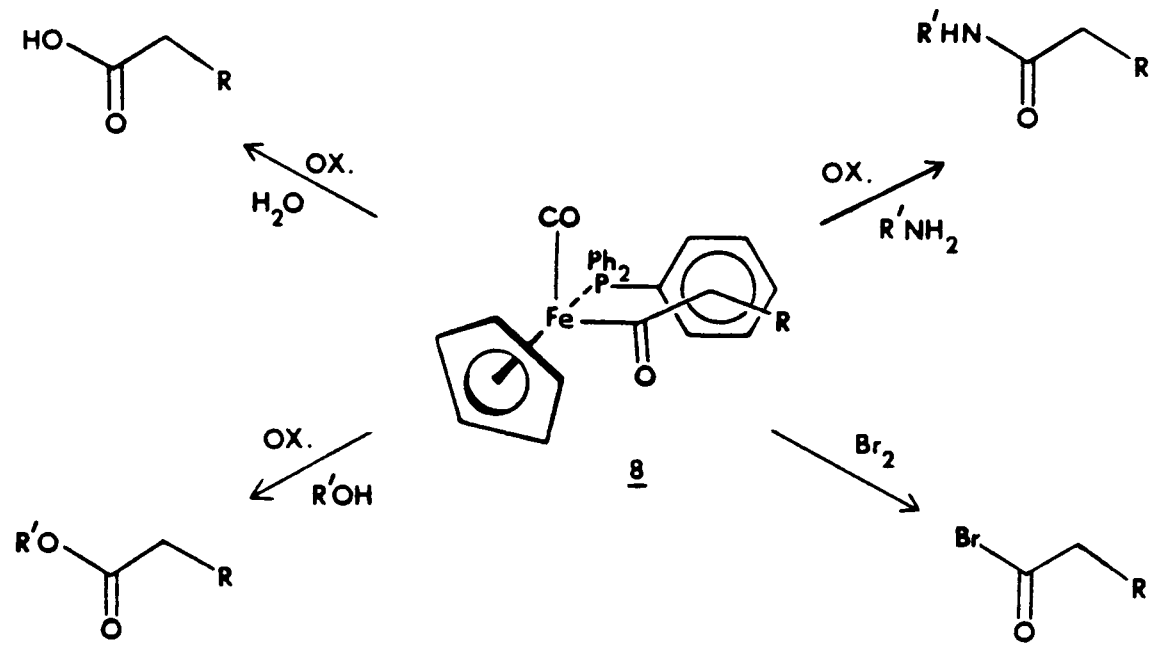


The resolved acyl complexes are configurationally stable even at elevated temperatures.[33]

† Ligand priority order $(\eta^5\text{-}C_5H_5) > PPh_3 > CO > COCH_2R$.[32] Unless otherwise stated, all iron complexes that appear in this thesis are racemic. For the purposes of clarity only complexes with the R configuration at iron are shown.

3. Decomplexation of iron acyl complexes

In order for iron acyl complexes to find use as reagents for organic synthesis, the iron moiety must be readily removable. It is known that iron acyl complexes are decomplexed with one electron oxidants such as bromine, cerium(IV) salts, N-bromosuccinimide etc. to give carboxylic acids, esters and amides in the presence of water, alcohols and amines respectively.[35] When bromine is used as the oxidant the organometallic product is the iron bromide 9, thus providing a method whereby the chiral $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ moiety can be recycled.[36]

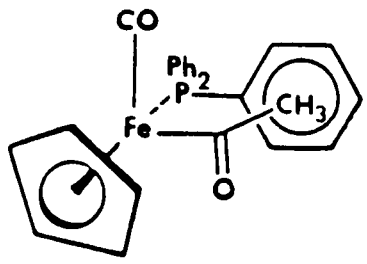


Oxidative decomplexation has been found to proceed with retention of stereochemistry at the α-centre.[37]

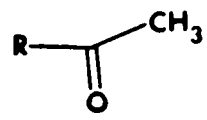
4. Diastereoselective elaboration of iron acyl ligands

a. Alkylations

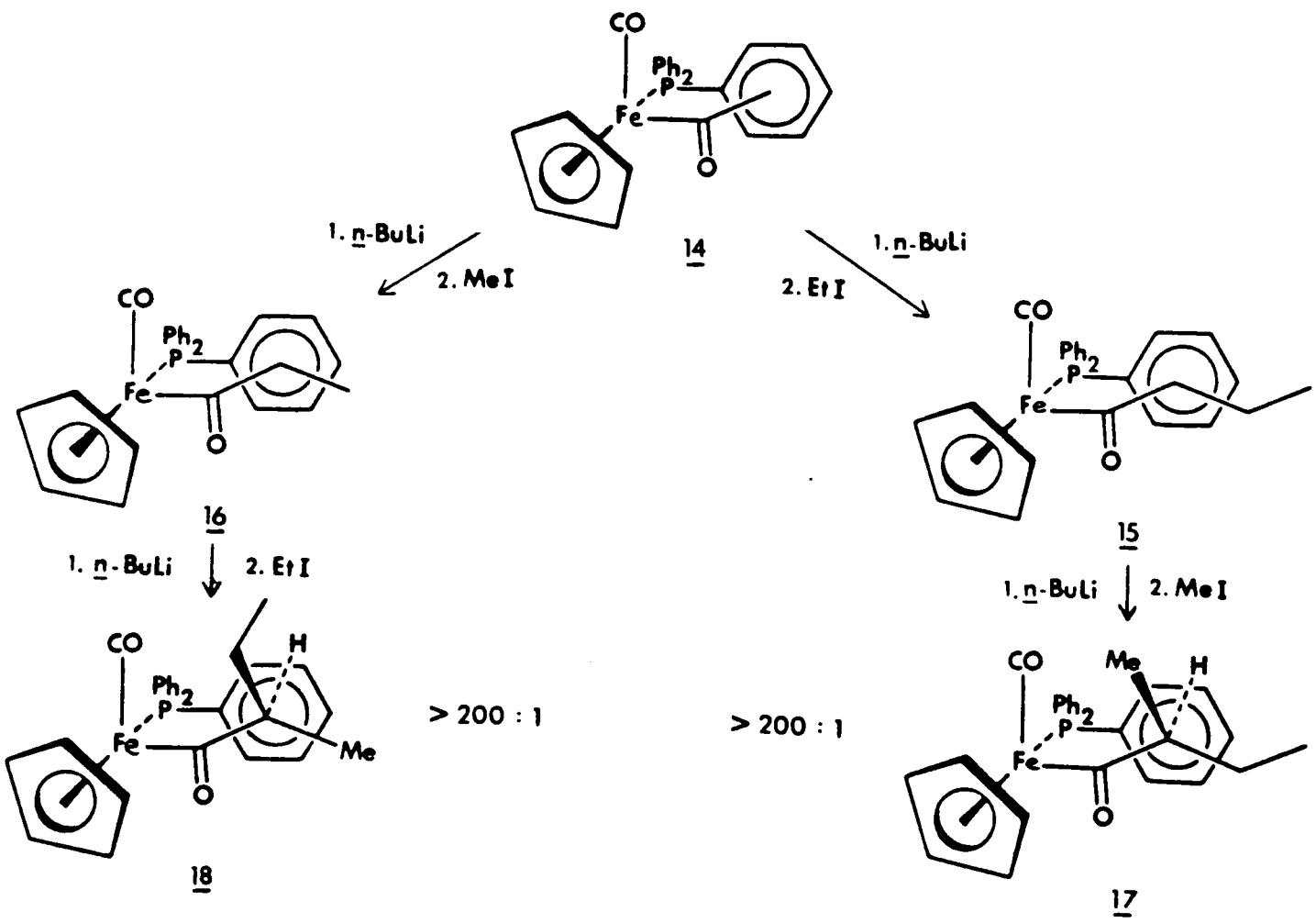
The acyl ligand in the methyl acyl complex 14 is superficially equivalent to a methyl ketone. However, due to the electron releasing effect of the iron moiety, the α-protons in complex 14 are much less acidic than those in a methyl ketone. Consequently, only very strong bases such as n-butyllithium and LDA deprotonate complex 14.[38]



14



The enolate generated from complex 14 in THF at -78°C is found to undergo clean monoalkylation at the α-carbon with a variety of alkyl halides.[38,39] Thus, quenching with ethyl iodide and methyl iodide gave the propyl and ethyl acyl complexes 15 and 16 respectively in high yield (> 80%). Complex 15 was also deprotonated with n-butyllithium. Methylation gave diastereoisomer 17 of the s-butyl acyl complex with a diastereoselectivity of greater than 200:1 as deduced by ^{1}H n.m.r. spectroscopy.[40,41] † The relative stereochemistry between the iron and α-centres was shown to be RS,SR by X-ray crystallography.[40] Similarly, (RR,SS)-18 was prepared with high diastereoselectivity (> 200:1) by deprotonation and ethylation of complex 16.[41]



† The ^{13}C satellites in the ^{1}H n.m.r. spectrum provided an internal standard for the assessment of diastereoisomeric purity.

The ^{1}H n.m.r. spectrum of (RS,SR)-17 contains a doublet at δ1.01 due to the α-methyl group. The corresponding signal in the ^{1}H n.m.r. spectrum of (RR,SS)-18 appears at δ0.17 and reflects the location of the α-methyl group in this diastereoisomer directly over the centre of one of the phenyl rings of the triphenylphosphine ligand.† This difference in chemical shift values is found to be common to all those acyl complexes possessing an α-methyl group and therefore enables ^{1}H n.m.r. spectroscopy to be used to deduce the relative configuration between the iron and α-centres.[43]

The X-ray crystal structure of complex 17[40] (Figure 1) reveals that in the solid state, the acyl oxygen and the carbon monoxide ligand adopt an anti relationship. Furthermore, the iron atom and the atoms of the carbon monoxide and acyl ligands all lie in a plane approximately parallel to the plane of one of the phenyl groups of the triphenylphosphine ligand. These planes define the upper and lower faces respectively of an imaginary box which effectively represents an 'excluded volume' into which no external reagents can penetrate (figure 1). If it is assumed that these conformational preferences are retained in solution, then the stereochemical features of complex 17 may be used to rationalise the high levels of asymmetric induction observed in the alkylation reactions described above.

† This has been verified by a X-ray crystal structure analysis of the related complex (RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_2NEt_2)COCH(CH_3)Et].[42]

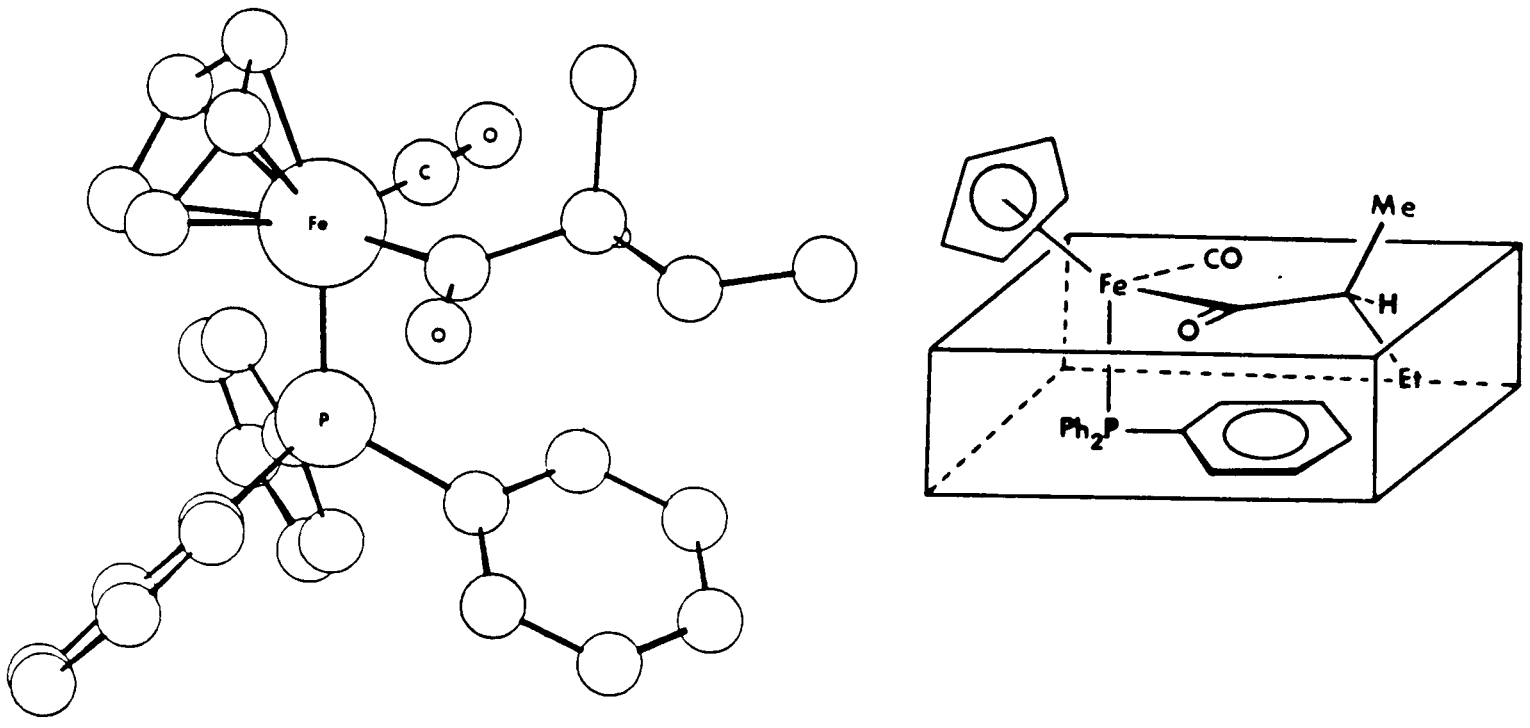
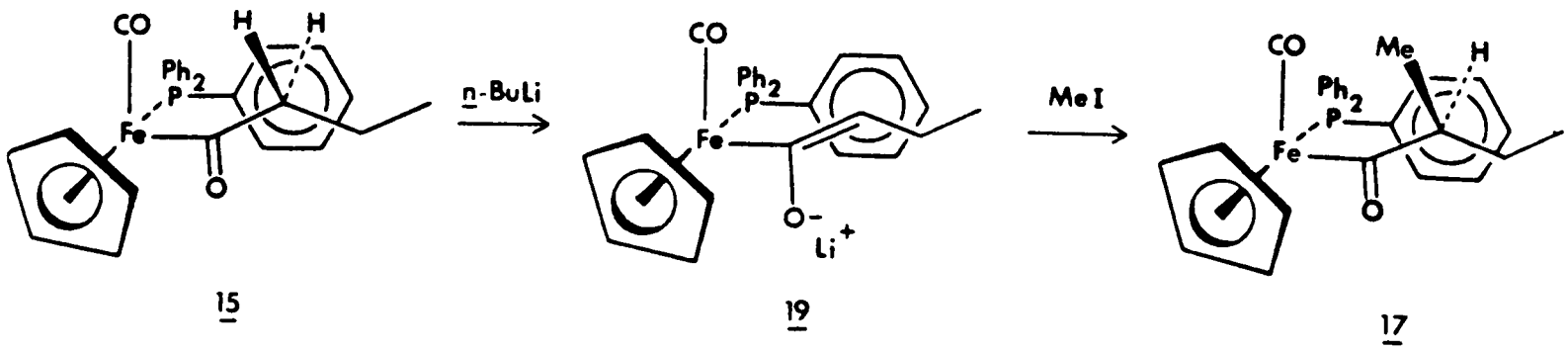


Figure 1: X-ray crystal structure and schematic diagram of complex 17.

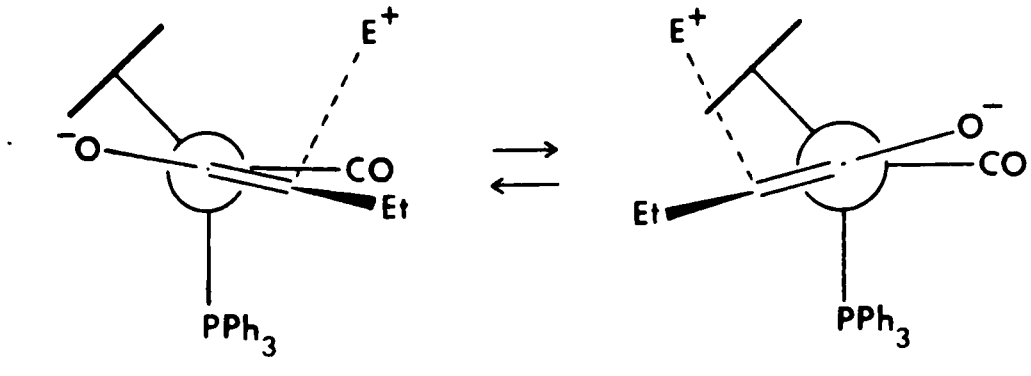
Both molecular models and calculations[41] predict that the preferred conformation of the acyl ligand in for example, the propyl acyl complex 15 is the one in which the ethyl group is syn to the acyl oxygen i.e. anti to the large iron moiety, such that one of the α-protons occupies the most sterically demanding site between the carbon monoxide and triphenylphosphine ligands.† Removal of the other proton by n-butyllithium approaching from the face of the acyl ligand away from the triphenylphosphine ligand generates the E enolate 19.



15 19 17

† See also the X-ray crystal structure of complex 17.

Methylation of E enolate 19 in the anti (CO to acyl) conformation again from the unshielded face gives (RS,SR)-17 as observed. Methylation of the alternative syn enolate is strongly disfavoured on steric grounds as it would require the incoming electrophile to pass close to if not through the space occupied by the cyclopentadienyl ligand (figure 2). In accordance with this model, increasing the size of the electrophile enhances the diastereoselectivity of the alkylations.[41]



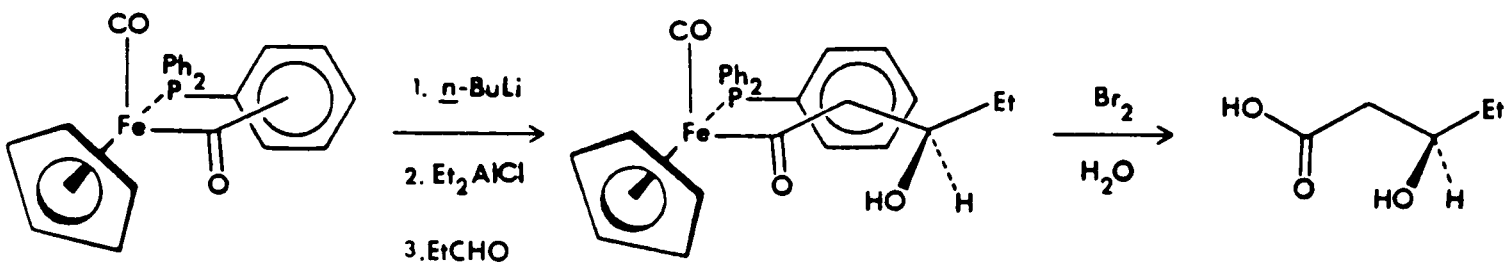
anti-19 ⇌ syn-19

Figure 2: Alkylation of syn and anti enolates of complex 19.

Therefore, in terms of specific enolate generation and large energy differences between transition states leading to diastereoisomeric products, acyl ligands bound to the chiral auxiliary [(η^5-C_5H_5)Fe(CO)-(PPh_3)] fulfil the requirements of an enolate system that can be usefully employed in asymmetric synthesis.

b. Aldol reactions

The aldol reaction between the lithium enolate derived from complex 14 and aldehydes shows little diastereoselectivity.[43] β-Hydroxy acyl complexes e.g. (RR,SS)-20 are however, obtained with greater than 100:1 diastereoselectivity from the reaction between the corresponding aluminium enolate and aldehydes.[36,44]



14 20

> 100 : 1

Changing the enolate counterion to tin reverses the diastereoselectivity.[45]

These highly diastereoselective carbon-carbon bond-forming reactions of acyl ligands bound to the chiral iron auxiliary, when combined with known decomplexation procedures, make iron acyl complexes attractive reagents for the asymmetric synthesis of chiral organic molecules.

IV. Objectives

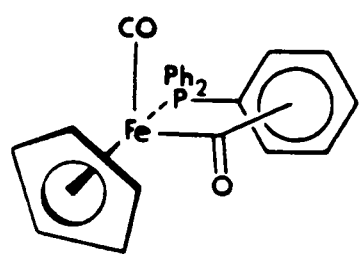
α,β-Unsaturated acyl ligands bound to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ have not been reported in the chemical literature to date. Our aims were to devise methods for the preparation of such complexes and then by controlling both the conformation adopted by the ligand i.e. cisoid vs. transoid and which of the diastereotopic faces of the ligand is attacked by reagents, to develop highly diastereoselective Michael addition and Diels-Alder reactions of such complexes. Removal of the chiral auxiliary would enable useful chiral building blocks to be synthesised as essentially single enantiomers.

CHAPTER 2

STUDIES ON THE METHYL ACYL COMPLEX $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$

I. Introduction

The wide variety of elaborated iron acyl complexes available from the enolate derived from the parent methyl acyl complex 14[39] made the large scale preparation of this complex desirable.



14

Although the reactions of the enolate derived from complex 14 are believed to proceed via the conformation in which the acyl-derived oxygen and the carbon monoxide ligand have an anti relationship[40], no detailed conformational analysis of complex 14 has been reported. Furthermore, if the highly diastereoselective carbon-carbon bond forming reactions of acyl ligands attached to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$[36,40] are to be exploited in asymmetric synthesis, the enantiomerically pure methyl acyl complex 14 of known absolute configuration is required, together with convenient methods of assessing its optical purity. Even though methods for preparing optically active samples of complex 14 have been known for some time,[33,34] the absolute configuration of the resolved complexes has not been unambiguously assigned in the literature nor has any means of assessing its optical purity been described. Previous methods for determining the absolute configuration of complex 14 have relied on the tentative correlations between the circular dichroism (CD) spectrum of optically active 14 and the CD spectra of related complexes of known absolute configuration. For example, the absolute configurations of the iron acyl complexes$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COR]$ (R=CH_3, Et) were assigned on

the basis of a comparison of their CD spectra with that of the carbene complex (RS)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)C(CH_3)NHCH(CH_3)Ph]BF_4[46] whose absolute configuration is known.[47]

In the conversion of the resolved mentholate esters [(η^5-C_5H_5)Fe(CO)-(PPh_3)($CO_2C_{10}H_{19}$)][48] of known absolute configuration[49] to optically pure 14, Brunner stated that inversion of configuration at the iron centre was occurring on the basis of the mirror-image relationship between the CD spectra of the starting and product complexes.[33] The absolute configurations of related chiral iron acyl complexes have also been assigned using similar correlations.[50,51]

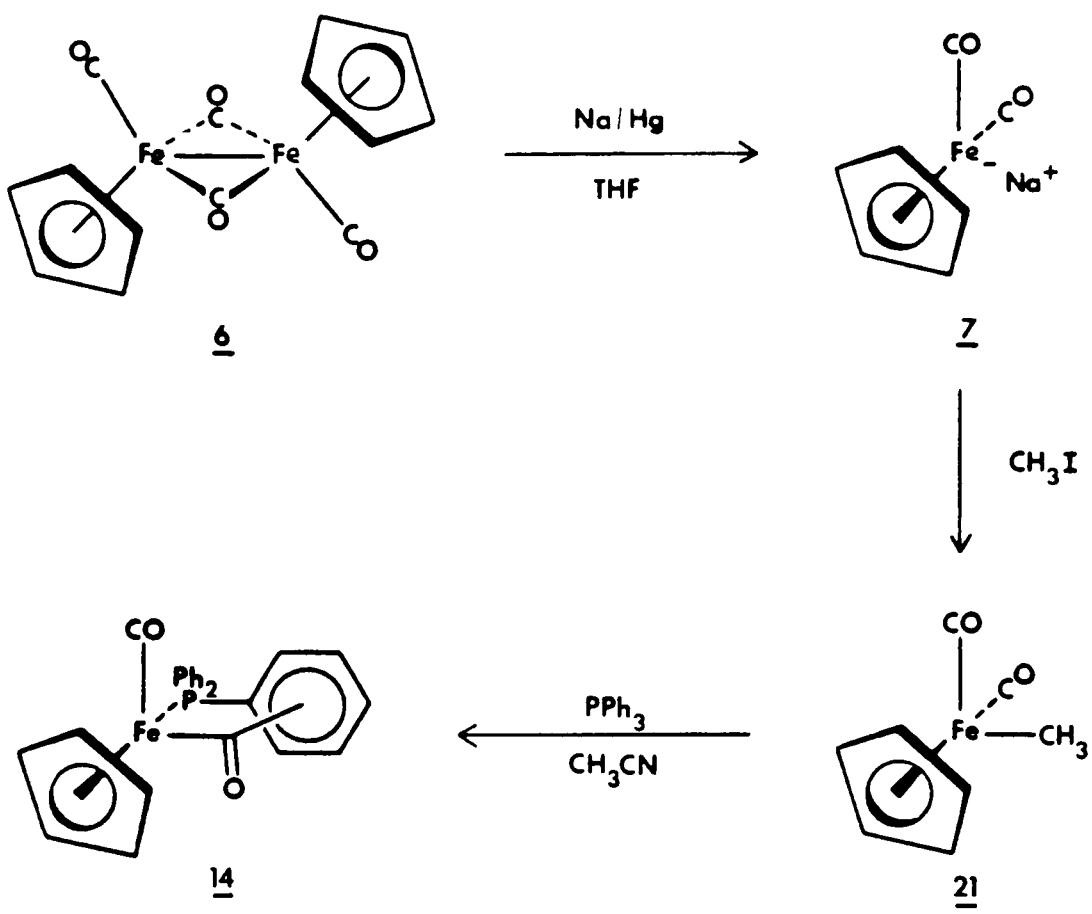
The fallibility of the CD correlation was demonstrated in one case[50] where the CD spectrum of a chiral iron complex bore no simple morphological correspondence to that of any other iron acyl complex of that type, and in another case[52] where it actually led to an incorrect assignment of absolute stereochemistry. From the data available, it appears that only when two groups X in complexes of the type [(η^5-C_5H_5)Fe(CO)(L)X] are very similar and the corresponding CD curves are superimposable can one draw tentative conclusions about absolute configurations.[53]

In one report,[53] the configuration of (+)-14 was related chemically to the known absolute configuration of (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)-$CH_2OC_{10}H_{19}$] by conversion of both of these complexes to the iron ethyl complex (+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)CH_2CH_3]. The enantioselectivities of these transformations were not however stated.

II. Large scale preparation of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$]

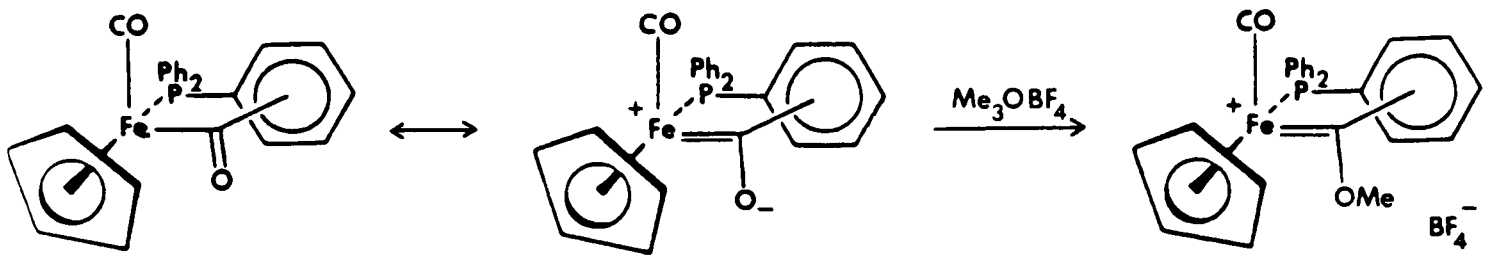
With modifications to the literature procedure,[29] 100 g of the iron dimer 6, itself prepared on a 300 g scale from iron pentacarbonyl and

dicyclopentadiene,[27] was cleaved in THF over 2% sodium amalgam to give the nucleophilic iron species 7. The iron methyl complex 21, obtained from the reaction between anion 7 and methyl iodide, was heated with triphenylphosphine in acetonitrile under reflux. Crystallisation gave 185 g (72%) of the pure methyl acyl complex 14 as bright orange needles.



6 7 14 21

Complex 14 exhibits some interesting spectroscopic properties common to all other iron acyl complexes of this type. The infrared spectrum of complex 14 contains a very strong absorption at 1915 cm^{-1} due to the metal-bound carbon monoxide ligand and in addition an intense absorption at 1600 cm^{-1} due to the acyl group. This latter value is approximately 120 cm^{-1} lower than that due to aliphatic ketones and implies that the zwitterionic resonance form 22 makes a significant contribution to the ground state of complex 14. This polarity is reflected chemically in the O-methylation reaction of complex 14 with trimethyloxonium tetrafluoroborate to give the cationic carbene complex 23.[54]



14 22 23

The cyclopentadienyl protons in complex 14 appear as a doublet in the 300 MHz ^{1}H n.m.r. spectrum due to coupling (J_{PH} 1.2 Hz) to the phosphorous of the triphenylphosphine ligand, whilst the proton decoupled ^{31}P n.m.r. spectrum exhibits a single peak at δ72.8.

III. X-ray crystal structure and conformational analysis of (R,S)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$

Although several X-ray crystal structures of related iron acyl complexes have appeared in the literature,[36,40,53,55,56] no such solid state structure determination has been performed on the important parent methyl acyl complex 14. A single rhombic crystal of complex 14, obtained from diethyl ether, was therefore submitted for an X-ray crystal structure analysis. Figure 3 shows the X-ray crystal structure of complex 14. Full X-ray data is given in appendix 1 and selected bond lengths, bond angles and torsional angles are listed in Table 1.

The iron centre is pseudooctahedral with three of the six coordination sites occupied by the cyclopentadienyl ligand. The bond angles between the carbon monoxide, triphenylphosphine and acyl ligands are all approximately 90° and between any of these ligands and the centroid of the cyclopentadienyl ligand approximately 120°. One of the phenyl groups of the triphenylphosphine ligand is also positioned approximately parallel to a plane containing the carbon monoxide ligand, the iron atom and the oxygen

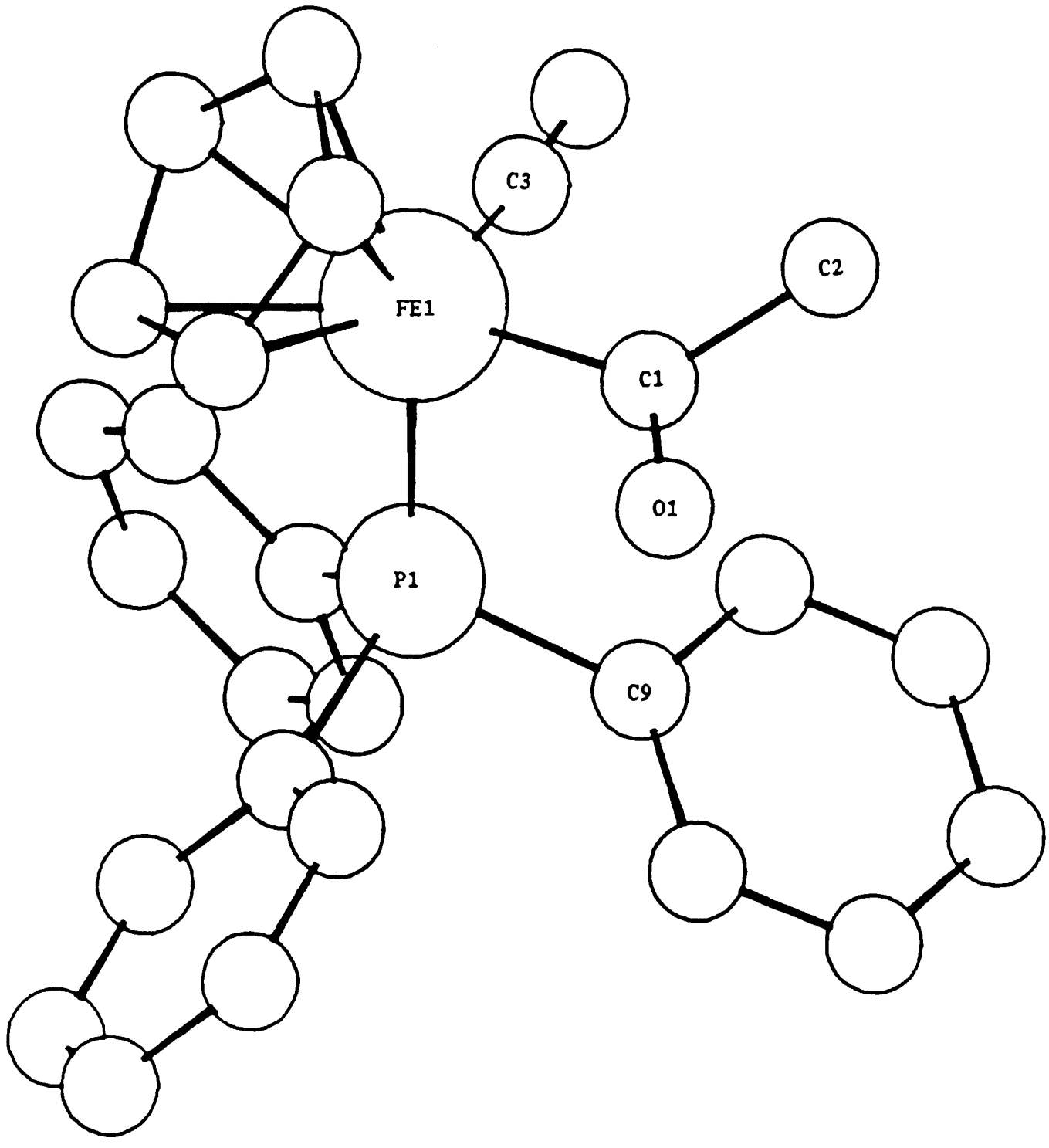


Figure 3: X-ray crystal structure of (R,S)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14.

Bond lengths (A)		Bond angles (°)	
Fe(1) - P(1)	2.1941(7)	C(3) - Fe(1) - C(1)	94.2(1)
Fe(1) - C(1)	1.944(3)	C(3) - Fe(1) - P(1)	92.8(1)
Fe(1) - C(3)	1.750(3)	C(1) - Fe(1) - P(1)	89.85(9)
C(1) - O(1)	1.195(4)	Fe(1) - C(1) - O(1)	124.3(2)
C(1) - C(2)	1.535(5)	C(2) - C(1) - O(1)	115.3(3)
		C(2) - C(1) - Fe(1)	120.3(3)

Torsional angles (°)	
C(3) - Fe(1) - C(1) - O(1)	-161
C(1) - Fe(1) - P(1) - C(9)	-29

Table 1: Selected X-ray data with e.s.d.'s in parentheses for (R,S)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14.

and two carbon atoms of the acyl ligand. In addition, the acyl oxygen is orientated anti with respect to the carbon monoxide ligand.

Extended Huckel calculations have been performed on the model complex [(η^5-C_5H_5)Fe(CO)($PPhH_2$)$COCH_3$] with the single phenyl ring of the phosphine restricted to lie below the acyl ligand.[57] They show that the steric interactions between the acyl ligand and the phenyl group are responsible for the acyl ligand lying in the plane containing the iron atom, carbon monoxide ligand and the acyl-carbon atom. This model fails to show however, any strong energy preference for the anti carbon monoxide to acyl oxygen conformation over the alternative syn arrangement. Furthermore, ab initio SCF MO calculations made on [(η^5-C_5H_5)Fe(CO)(PH_3)$COCH_3$] predicted that the syn conformation had the more favourable electrostatic

arrangement. The X-ray crystal structure of complex 14 however, revealed that because of the twist of the triphenylphosphine propellor, one C-H bond of a second proximate phenyl group was orientated towards the acyl oxygen (figure 4).

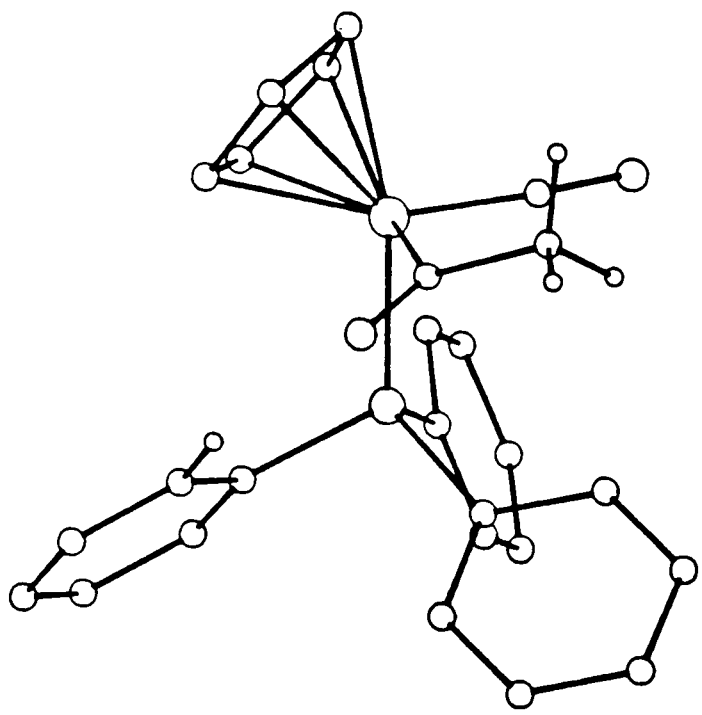


Figure 4: X-ray crystal structure of 14 showing proximity of the second phenyl group to the acyl oxygen.

Further calculations confirmed that the steric interactions between this second phenyl group and the methyl group in the syn conformation destabilised this arrangement relative to the anti conformation.

IV. Determination of the optical purity of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$

As no asymmetric induction can accompany the carbonyl insertion reaction of the iron methyl complex 21 with triphenylphosphine, the methyl acyl complex 14 was formed as a racemic mixture. The use of the chiral shift reagent $Eu(tfc)_3$,tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato] europium (III), allowed the two enantiomers of complex 14 to be discriminated. Addition of aliquots of a solution of $Eu(tfc)_3$ in deuterochloroform to a solution of complex 14 also in deuterochloroform

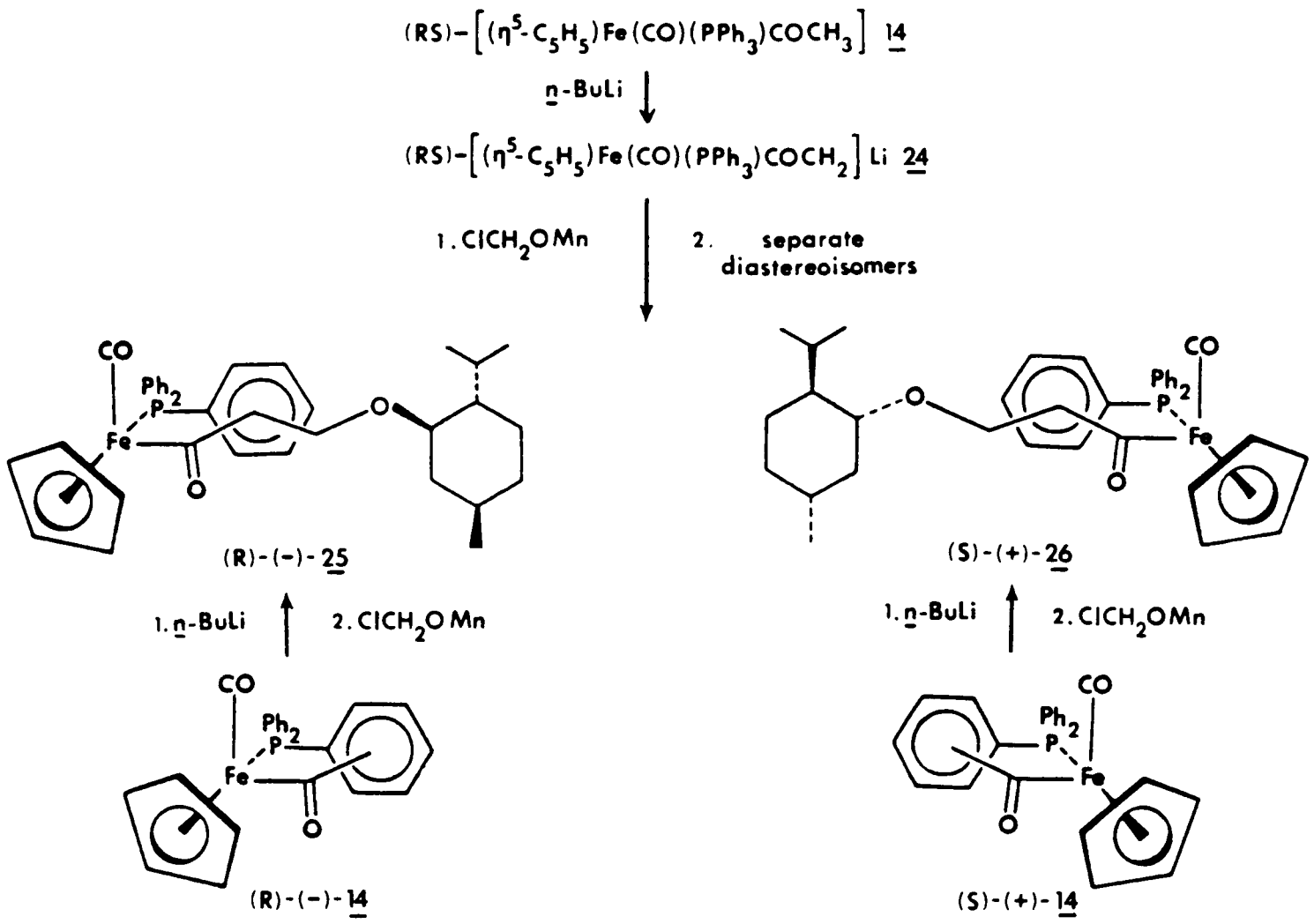
resulted in clean separation of the methyl singlets in the 300 MHz ^1H n.m.r. spectrum due to the two enantiomers. Other chiral shift reagents have been used in combination with iron acyl complexes.[50,52]

The use of $Eu(tfc)_3$ thus provides a reliable method for determining the optical purity of the resolved methyl acyl complex 14. Indeed, samples of (+)- and (-)- 14[58] [$[\alpha]_{546}$ ± 288° (c 0.04, C_6H_6)[34]] prepared by a modification of Brunner's procedure[33] were each shown to consist of a single enantiomer by ^1H n.m.r. spectroscopy using the above method. These results substantiate for the first time that the rotations of ± 288° refer to the optically pure methyl acyl complexes.

V. Determination of the absolute configuration of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$[59]

Treatment of the racemic methyl acyl complex 14 in THF at -78°C with n-butyllithium gave a dark red solution of the lithium enolate 24. Addition of chloromethyl (R)-menthyl ether,† prepared by chloromethylation of (l)-menthol,[60] generated a 1:1 mixture of the diastereoisomers 25 and 26 (92%) which were partially separable by chromatography on alumina and totally separable by flash chromatography on silica. Complexes 25, $[\alpha]_D^{20}$ -150° (c 0.4, C_6H_6), and 26 $[\alpha]_D^{20}$ + 65° (c 0.4, C_6H_6), were distinguished by the difference in the chemical shifts of the doublets due to the methyl groups of the menthyl moiety and the complex multiplets due to the protons α and β to the acyl group in the 300 MHz ^1H n.m.r. spectrum.

† (l)-Menthol is (1R,2S,5R)-(-)-2-isopropyl-5-methylcyclohexan-1-ol. Menthyl is the radical formed by the loss of the 1-hydroxy group. In (R)-menthyl the R refers to the configuration at the 1-position.



An X-ray crystal structure analysis of diastereoisomer 25 obtained as single crystals from diethyl ether, together with the known absolute configuration of (l)-menthol,[61] established the absolute configuration at the iron centre as R [32] as shown in figure 5. Full X-ray data is given in appendix 2 and selected bond lengths, bond angles and torsional angles are listed in Table 2.

Bond lengths (A)		Bond angles (°)	
Fe(1) - P(1)	2.191(8)	C(14) - Fe(1) - C(1)	92.0(1)
Fe(1) - C(1)	1.98(3)	C(14) - Fe(1) - P(1)	93.2(1)
Fe(1) - C(14)	1.73(3)	C(1) - Fe(1) - P(1)	91.9(8)

Torsional angle (°)	
C(14) - Fe(1) - C(1) - O(1)	-134

Table 2: Selected X-ray data with e.s.d.'s in parentheses for (R)-(-)-{(η5-C5H5)Fe(CO)(PPh3)COCH2CH2O[(R)-menthyl]} 25.

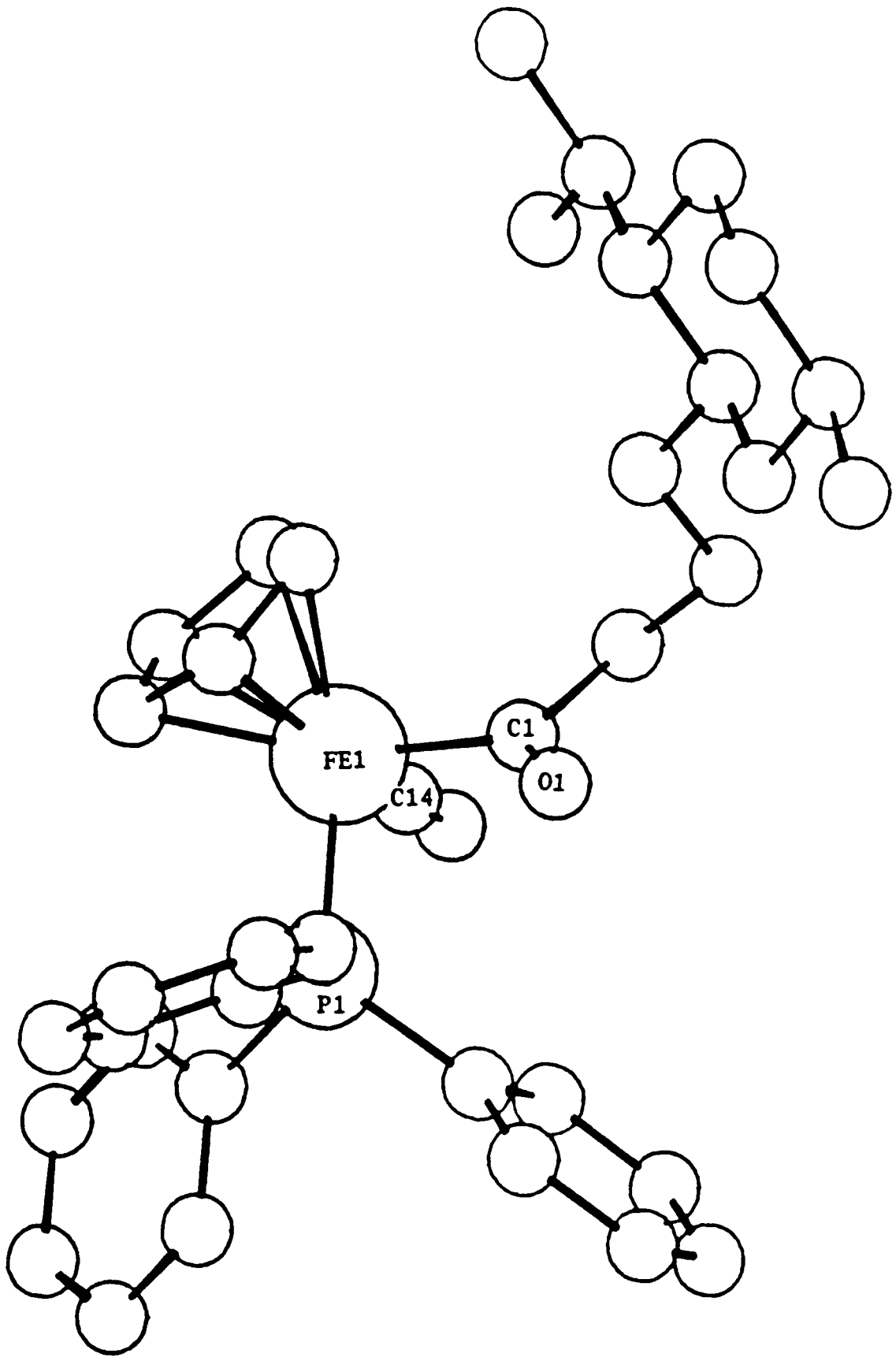


Figure 5: X-ray crystal structure of (R)-(-)-{(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_2CH_2O$[(R)-menthyl]} 25.

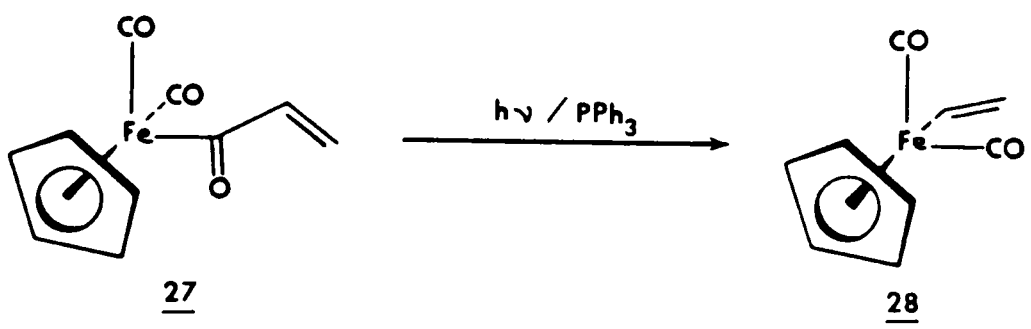
Alkylation of (-)- 14 with chloromethyl (R)-menthyl ether gave 25, $[\alpha]_D^{20}$ -150° (c 0.4, C_6H_6), as the exclusive product whereas (+)- 14[58] under the same conditions gave only 26, $[\alpha]_D^{20}$ + 65° (c 0.4, C_6H_6). Since the configuration at iron remains unchanged in these reactions of the attached acyl ligand, the absolute configuration of (-)- 14 can be unambiguously assigned as R and that of (+)- 14 as S. Furthermore, complexes 25 and 26 prepared from (-)- 14 and (+)- 14 respectively were diastereoisomerically pure by 500 MHz ^{1}H n.m.r. spectroscopy, thus providing an independent criterion for the enantiomeric purity of (-)- and (+)- 14. The advantage of this method over the chiral shift reagent experiment is that the diastereoisomeric purity of complexes 25 and 26 can be assessed to a higher degree of accuracy (less than 0.5%) than the diastereoisomeric complexes formed between the enantiomers of 14 and the paramagnetic europium (III) reagent (1%).[62]

CHAPTER 3

PREPARATION OF α,β-UNSATURATED IRON ACYL COMPLEXES

I. Introduction

There are only a few reports of α,β-unsaturated metal acyl complexes in the chemical literature. Previous syntheses of such complexes have involved (a) the reaction between the nucleophilic iron species $[(\eta^5\text{-}C_5H_5)\text{-}Fe(CO)_2]Na$ 7 and α,β-unsaturated acid chlorides,[63] (b) the oxidatively catalysed carbon monoxide insertion reactions of $\{(\eta^5\text{-}C_5H_5)Fe(CO)[P(OPh)_3](\eta^1\text{-alkenyl})\}$ complexes,[64] (c) the attack by phosphoranes on a carbon monoxide ligand of $[(\eta^5\text{-}C_5H_5)Fe(CO)_3]PF_6$[65] and (d) the treatment of the rhenium methyl ester $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(CO_2CH_3)]$ with vinylmagnesium bromide.[66] However, none of these methods are suitable for the efficient preparation of complexes in which an α,β-unsaturated acyl ligand is bound to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$. For instance, our attempt to prepare $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ by the reaction of either $[(\eta^5\text{-}C_5H_5)Fe(CO)_2PPh_3]PF_6$ or its methyl ester $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)CO_2CH_3]$ with vinylmagnesium bromide gave, in each case, a complex mixture of products.[67,68] Encouragingly, the reaction between the phosphorane $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCHP(CH_3)_3]$ and benzaldehyde gave stereoselectively E-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CHPh]$.[68] However, the low yield of this reaction (25%) precluded its use as a practical synthetic method. Finally, all efforts to replace one of the carbon monoxide ligands in the acryloyl complex 27 with a triphenylphosphine ligand resulted in decarbonylation to give the corresponding vinyl complex 28.[67,68]

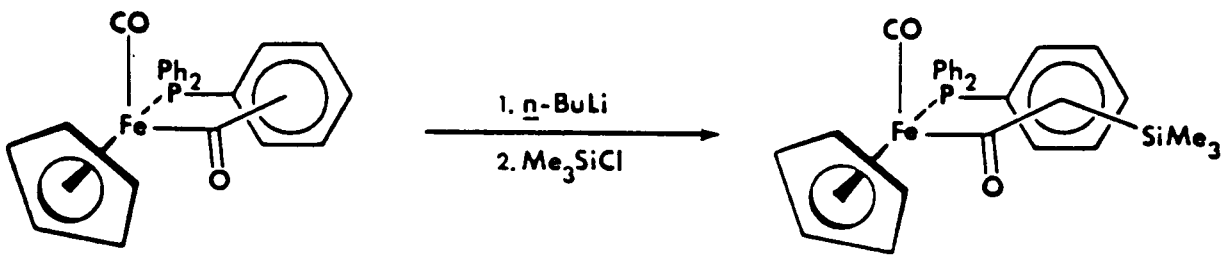


27 28

Although no reactions of metal bound α,β-unsaturated acyl ligands have been described previously, we envisaged that α,β-unsaturated acyl ligands bound to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ might hold considerable promise as chiral enoate synthons. It was desirable therefore, to develop convenient large scale stereoselective syntheses of these complexes.

II. The Peterson reaction between the enolate derived from $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ and aldehydes [68,69]

Deprotonation of the methyl acyl complex 14 with n-butyllithium in THF at -78°C followed by trapping of the resultant enolate with trimethylsilyl chloride generated the α-trimethylsilyl acyl complex $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ 29 in 98% yield.[39] Complex 29, which could be prepared in large quantities by this reaction, was purified by chromatography on deactivated alumina. Interestingly, chromatography on active alumina gave back the starting complex 14.



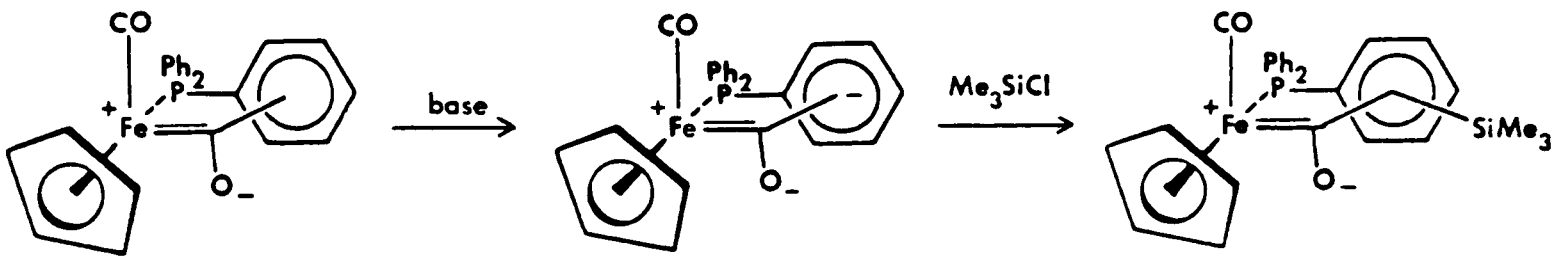
14 29

The isolation of complex 29 is in marked contrast to organic enolate anions which are almost invariably silylated on oxygen, with the following two exceptions:-

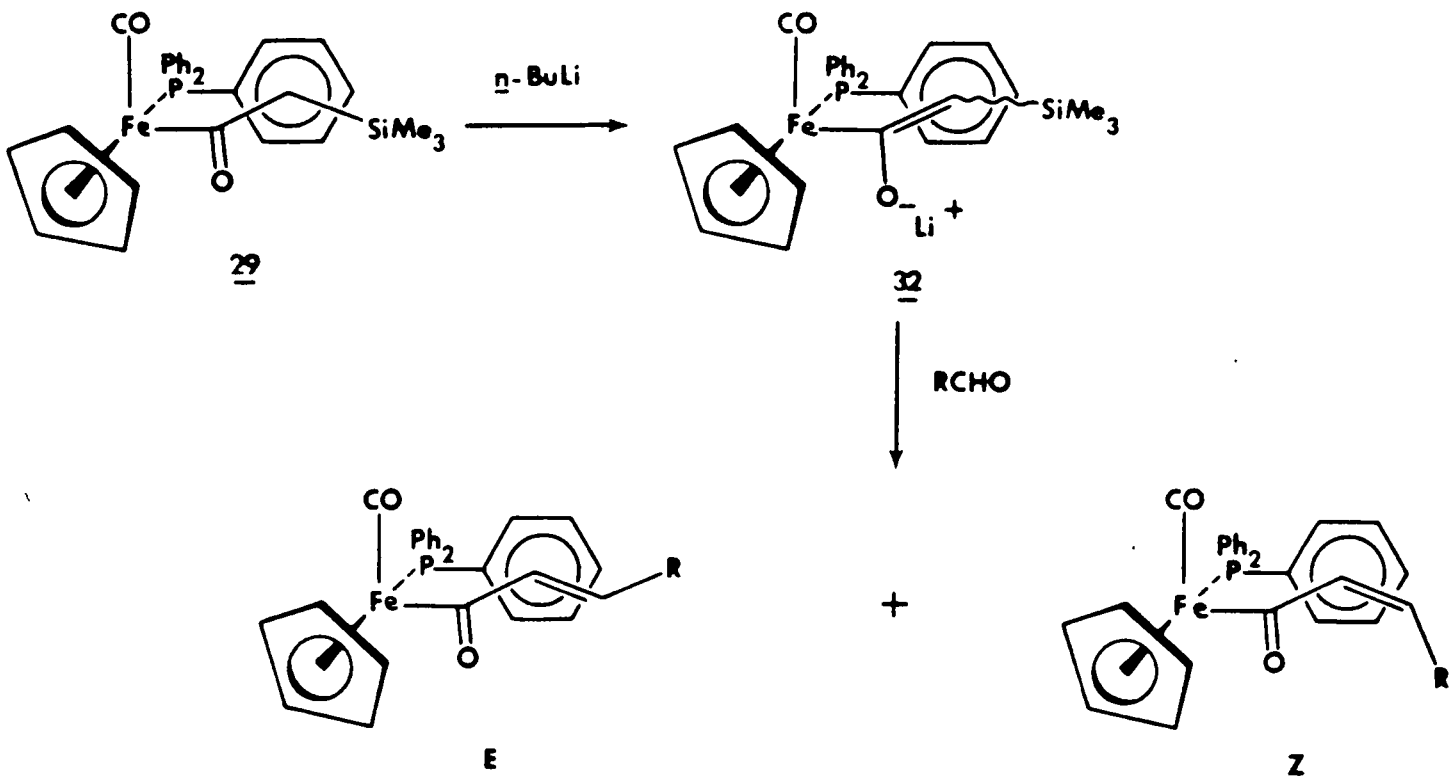
(a) the lithium enolates of alkyl acetates. For example, lithio methyl acetate and trimethylsilyl chloride at -78°C produce a mixture of O-silylated (65%) and C-silylated (35%) products, while lithio t-butyl acetate gives, almost exclusively (98%), the C-silylated ester. [70] These results reflect the degree of steric crowding around the ester oxygen.

(b) the dianions of acetoacetic esters. For example, methyl acetoacetate undergoes exclusive silylation at the terminal carbon.[71] ie. the centre with the largest orbital coefficient in the highest occupied molecular orbital.[72]

In light of the significant contribution made by the zwitterionic resonance form 22 of complex 14 (see chapter 2), an analogy may be drawn between this species and the monoanion of methyl acetoacetate 30. Similarly, the anion 24 is superficially analogous to the dianion of methyl acetoacetate 31. On this basis, anion 24 would be expected to undergo C-silylation as is observed.



The α-trimethylsilyl complex 29 was successfully employed in the Peterson olefination reaction.[73] Thus, addition of n-butyllithium to complex 29 followed by quenching of the lithium enolate 32 with acetaldehyde gave upon work-up, the α,β-unsaturated acyl complex $[(\eta^5\text{-}C_5H_5)\text{-}Fe(CO)(PPh_3)COCH{=}CHCH_3]$ in 88% yield as a 2:1 mixture of the E and Z isomers 33 and 34. The Peterson reaction was found to be a completely general method for the preparation of β-substituted-α,β-unsaturated acyl complexes. Quenching enolate 32 with propionaldehyde, acrolein or crotonaldehyde gave the corresponding complexes as a mixture of E and Z isomers in good yield.[68]



Complexes E,Z	R	Yield(%)	E:Z	J_E(Hz)	J_Z(Hz)
33,34	CH_3	88	2:1	15.0	11.2
35,36	Et	77	2:1	15.1	11.2
37,38	$CH=CH_2$	68	3:2	14.4	11.1
39,40	$CH=CHCH_3$	82	2:1	14.5	11.4

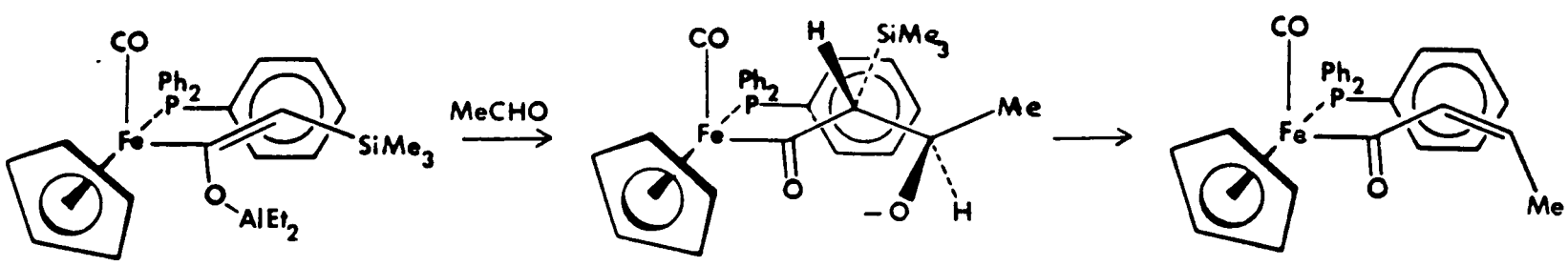
Table 3: Yields, selectivities and olefinic coupling constants for the α,β-unsaturated acyl complexes $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)\text{-}COCH=CHR]$.

In each case, the E and Z isomers were readily separable by chromatography on active alumina, the less polar Z isomers being eluted first. The double bond geometries in the pure complexes were determined on the

basis of the observed ^1H n.m.r. coupling constants between the olefinic protons, and for complexes 33 and 34, by X-ray crystallography (see below). Table 3 summarises the overall yields before separation in these olefination reactions together with the E:Z isomer ratio and olefinic coupling constants.

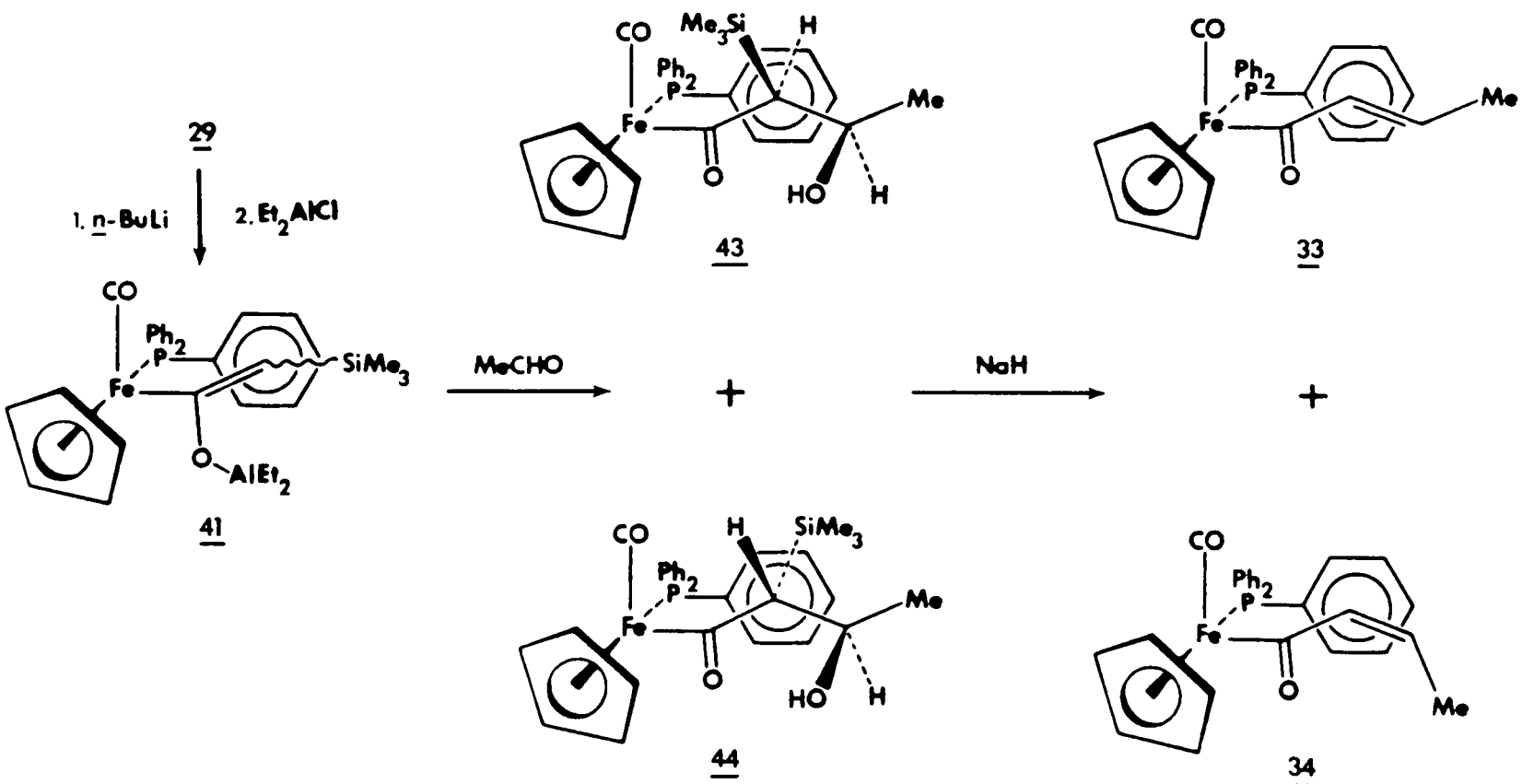
The addition of the lithium enolate derived from the ethyl acyl complex 16 to aldehydes has been shown to be essentially non-stereoselective[39,43] and therefore it is not surprising that the Peterson reaction shows little stereoselectivity. Presumably addition of the lithium enolate 32 to aldehydes generates a mixture of all four diastereoisomers of the intermediate α-trimethylsilyl-β-alkoxides, each of which spontaneously undergoes stereospecific syn elimination under the reaction conditions.

The addition of the E aluminium enolates derived from the complex $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_3]$ 16 to aldehydes is very stereoselective giving good stereochemical control over both the new α- and β-centres in the formation of the RRR,SSS diastereoisomer.[74] The addition of the E aluminium enolate 41, derived from the α-trimethyl silyl complex 29, to acetaldehyde is therefore anticipated to give predominantly diastereoisomer 42 of the β-alkoxide intermediate. Syn elimination would then generate the Z α,β-unsaturated acyl complex 34, which is the minor product from the Peterson reaction of the lithium enolate of complex 29.



41 42 34

Deprotonation of complex 29 with n-butyllithium followed by transmetallation with diethylaluminium chloride generated the aluminium enolate 41. Treatment with acetaldehyde gave, after methanolic work-up, a 1:1 mixture of two of the four possible diastereoisomeric α-trimethylsilyl-β-hydroxy acyl complexes 43 and 44 (two nine proton singlets at δ0.28 and 0.25 in the ^{1}H n.m.r. spectrum), together with small amounts of the starting complex 29 and the α,β-unsaturated acyl complex 33. The aluminium is presumably protecting, by coordination, the initial alkoxide against the syn elimination reaction. The tentative assignment of structures 43 and 44 to these diastereoisomers is consistent with the aluminium enolate 41 giving good stereochemical control at the β-centre, as before, but with the initial α-trimethylsilyl enolate 32 and 41 being formed as mixtures of E and Z isomers. This latter assumption is in agreement with the observed lack of stereoselectivity in the alkylation reactions of enolate 32.[42] Treatment of the mixture of 43 and 44 with sodium hydride in THF to effect syn elimination via the corresponding alkoxides, gave a 1:1 mixture of the E and Z isomers 33 and 34, also consistent with the proposed structures for 43 and 44. Attempts to effect acid-promoted (H^+ or BF_3) anti elimination led to extensive decomposition.



In order to demonstrate that optically pure α,β-unsaturated iron acyl complexes could be prepared using a Peterson olefination, the optically pure methyl acyl complex (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 [58] was transformed to (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2Si(CH_3)_3$] 29, $[\alpha]_D^{23}$ + 188.8° (c 0.13, C_6H_6), as described above. The lithium enolate derived from (S)-(+)-29 underwent a Peterson reaction with acetaldehyde to give a mixture of complexes 33 and 34. Separation and crystallisation gave optically pure (S)-(+)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH=CHCH_3$] 33, $[\alpha]_D^{23}$ + 175.3° (c 0.15, C_6H_6), and (S)-(+)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH=CHCH_3$] 34, $[\alpha]_D^{23}$ + 274.8° (c 0.12, C_6H_6).

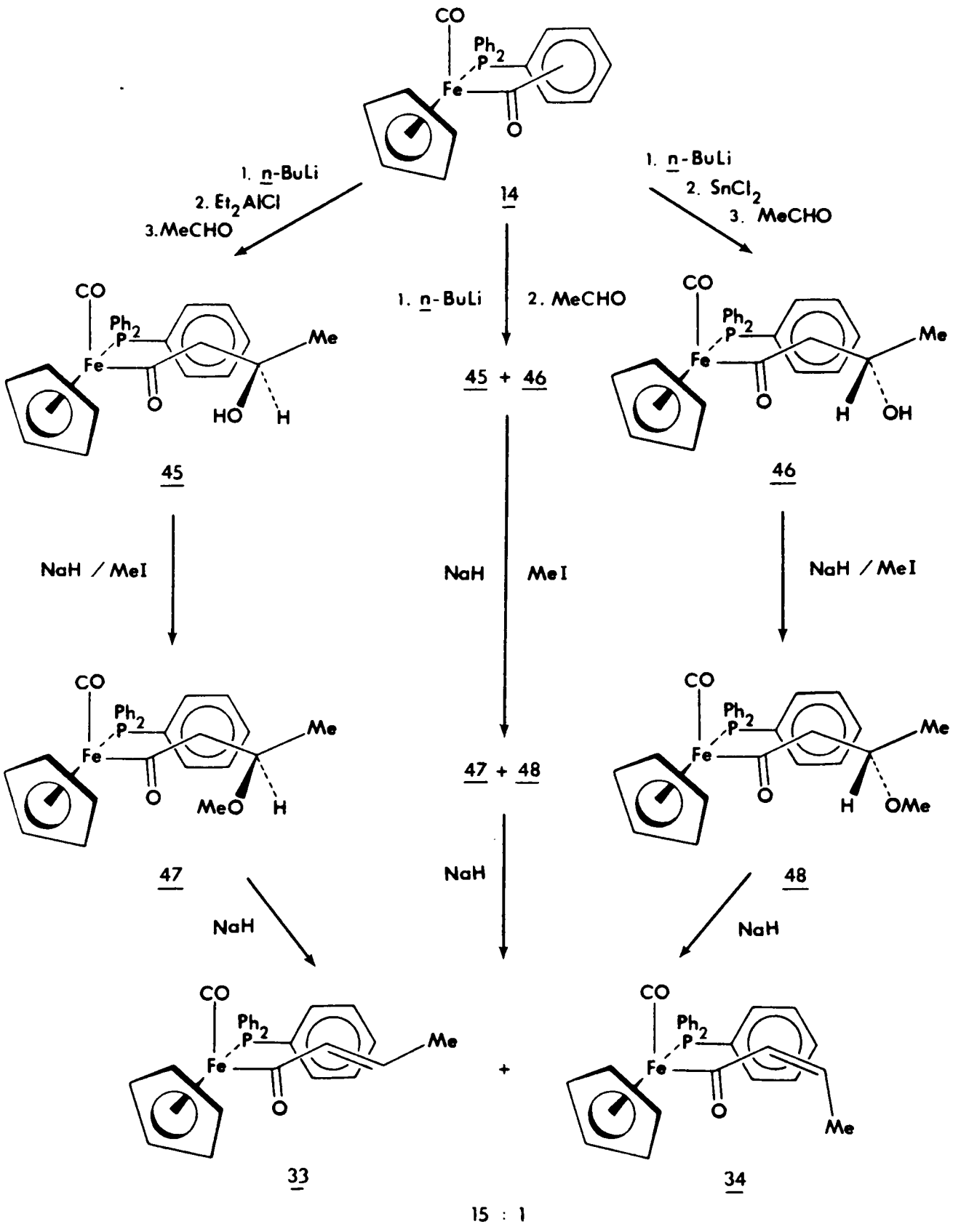
The Peterson reaction between [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCHSi(CH_3)_3$]Li 32 and ketones would provide a useful entry into β-disubstitued-α,β-unsaturated acyl complexes. Unfortunately, treatment of enolate 32 with acetone led to quantitative recovery of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2Si(CH_3)_3$] 29. The carbonyl group in ketones is less reactive towards nucleophiles than that in aldehydes due to both electronic and steric factors. Consequently enolisation of the ketone, with anion 32 acting as a base, occurs preferentially.

The reaction between the dianions of β-hydroxy acyl complexes, either as single diastereoisomers or as a mixture, and trimethylsilyl chloride has been used in the stereoselective synthesis of E α,β-unsaturated acyl complexes.[68] However, this extension of the Peterson reaction results in poor yields (<50%) of the product complexes.

III. The stereoselective synthesis of E β-substituted-α,β-unsaturated acyl complexes from β-methoxy acyl complexes[68]

An alternative strategy for the synthesis of α,β-unsaturated iron acyl ligands would involve a base-induced 1,2-elimination of a proton from the α-position together with a leaving group from the β-position of an

acyl ligand. The availability of β-hydroxy acyl complexes [(η^5-C_5H_5)-Fe(CO)(PPh_3)$COCH_2CH(OH)R$] as single diastereoisomers[36,44,45] from the parent methyl acyl complex, made these complexes attractive starting materials for such an approach. O-Methylation to replace the acidic proton of the hydroxyl group and subsequent base-induced elimination of methanol from the β-methoxy complexes [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)R$] would generate the desired α,β-unsaturated acyl complexes. Since the elimination could produce either the E or Z isomers, the stereochemistry

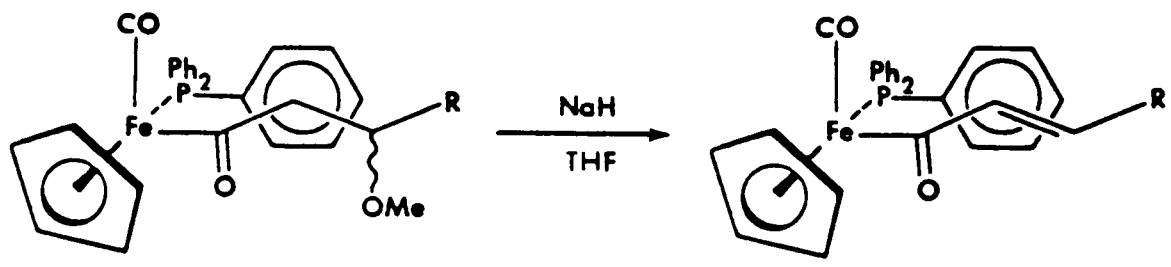


Scheme 2: Sodium hydride-induced elimination of methanol from β-methyl-β-methoxy acyl complexes.

of the elimination was initially studied by synthesising both diastereoisomers of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH(OH)CH_3]$. Diastereoisomers (RR,SS)-45 and (RS,SR)-46, formed in each case as a 7:1 diastereoisomeric mixture from the aluminium[36,44] and tin[45] enolates respectively, were individually O-methylated with sodium hydride and methyl iodide in THF (20°C) to give the β-methoxy complexes 47 and 48 again as 7:1 diastereoisomeric mixtures (scheme 2). Analysis of the products after prolonged treatment (66 h) of 47 and 48 with sodium hydride in THF at ambient temperature, showed that in both cases a 15:1 mixture of the E and Z isomers, 33 and 34 had been formed in high yield (95%). These results were confirmed when a 1.2:1 mixture of diastereoisomers 45 and 46, prepared from the lithium enolate of complex 14, was subjected to the same sequence of reactions to give the same mixture of 33 and 34 (92%). The 15:1 ratio of 33 to 34 was proved to represent the true stereoselectivity of the elimination by a control experiment in which the pure Z isomer 34 was treated separately with sodium hydride. No isomerisation to the E isomer 33 was observed.

This O-methylation-elimination procedure provides a general route to E β-substituted-α,β-unsaturated acyl complexes. Table 4 summarises the yields and stereoselectivities of the elimination reaction for different β-substituents.†

† Liebeskind has recently described a non-stereoselective synthesis of α,β-unsaturated acyl complexes from β-hydroxy complexes *via* acetylation and subsequent *t*-butoxide promoted elimination. This method also suffers from operational problems due to isomerisation to the corresponding β,γ-isomers under the reaction conditions.[75]



β-Methoxy Complex	R	Yield (%)	E:Z
49	H	56[a]	---
47,48	CH_3	92	15:1
50	Et	95	E only
51	n-Bu	50[a]	E only
52	t-Bu	0[a]	---
53	$CH=CH_2$	91	13:1

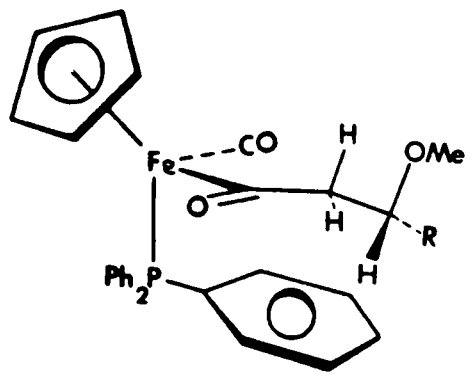
a. Good mass balance was observed with recovered starting complex.

Table 4: Yields and selectivities for the sodium hydride-induced elimination of methanol from β-methoxy complexes.

In spite of varying the reaction time and the amount of sodium hydride, the acryloyl complex (R=H) was always obtained as an inseparable mixture with the β-methoxy complex 49.[67] The reaction was completely stereoselective for ethyl and n-butyl β-substituents and only for β-methyl and β-vinyl substituents were small amounts of the Z isomers detectable. Although no elimination is observed from complex 52, the Peterson reaction described above provides a completely stereoselective route to E-[(η^5-C_5H_5)-Fe(CO)(PPh_3)COCH=CHt-Bu].[68]

The mechanism of the elimination reaction for either diastereoisomer of the β-methoxy complex must involve as a first step, deprotonation of

the acyl ligand to generate an E enolate. On both stereoelectronic and steric grounds, deprotonation occurs from 54 and 55 in conformations such that one α C-H bond is perpendicular to the plane of the acyl group and the other α hydrogen occupies the most sterically hindered position between the carbon monoxide and the triphenylphosphine ligands (Scheme 3). The stereoelectronic requirement for subsequent expulsion of methoxide is that the C-O (carbon to methoxy) bond is perpendicular to the plane of the enolate system. This can occur through either 56 or 57 from diastereoisomer 54 or, through 58 or 59 from diastereoisomer 55. Elimination



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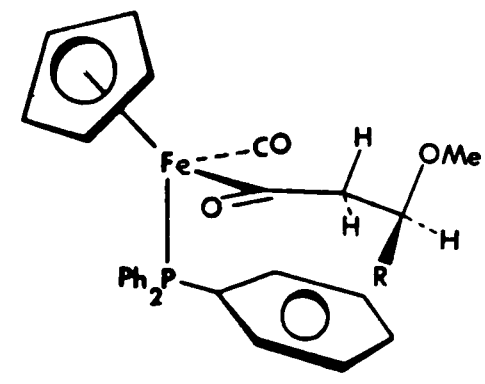

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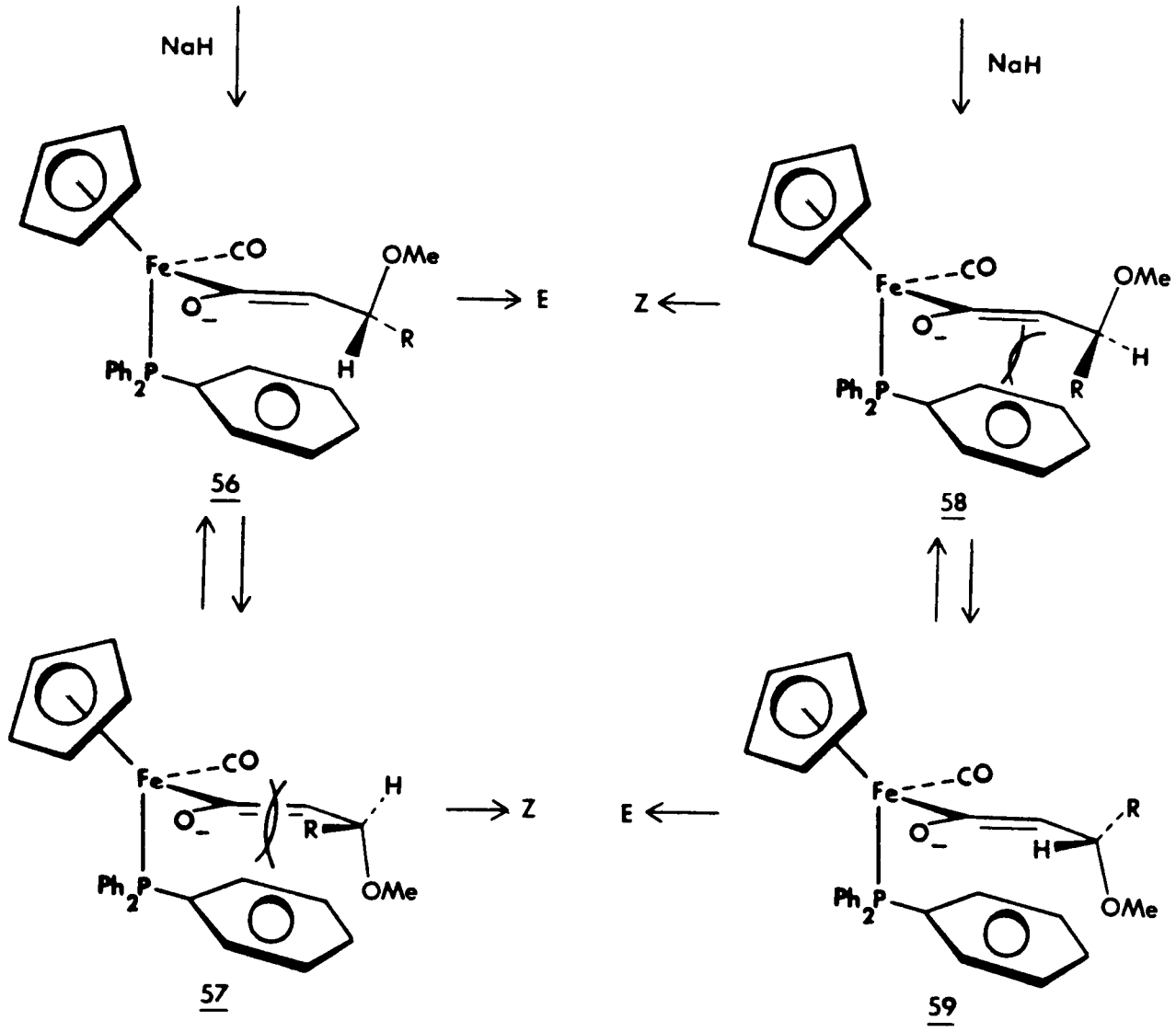


Scheme 3: Proposed mechanism for stereoselective formation of E α,β-unsaturated acyl complexes.

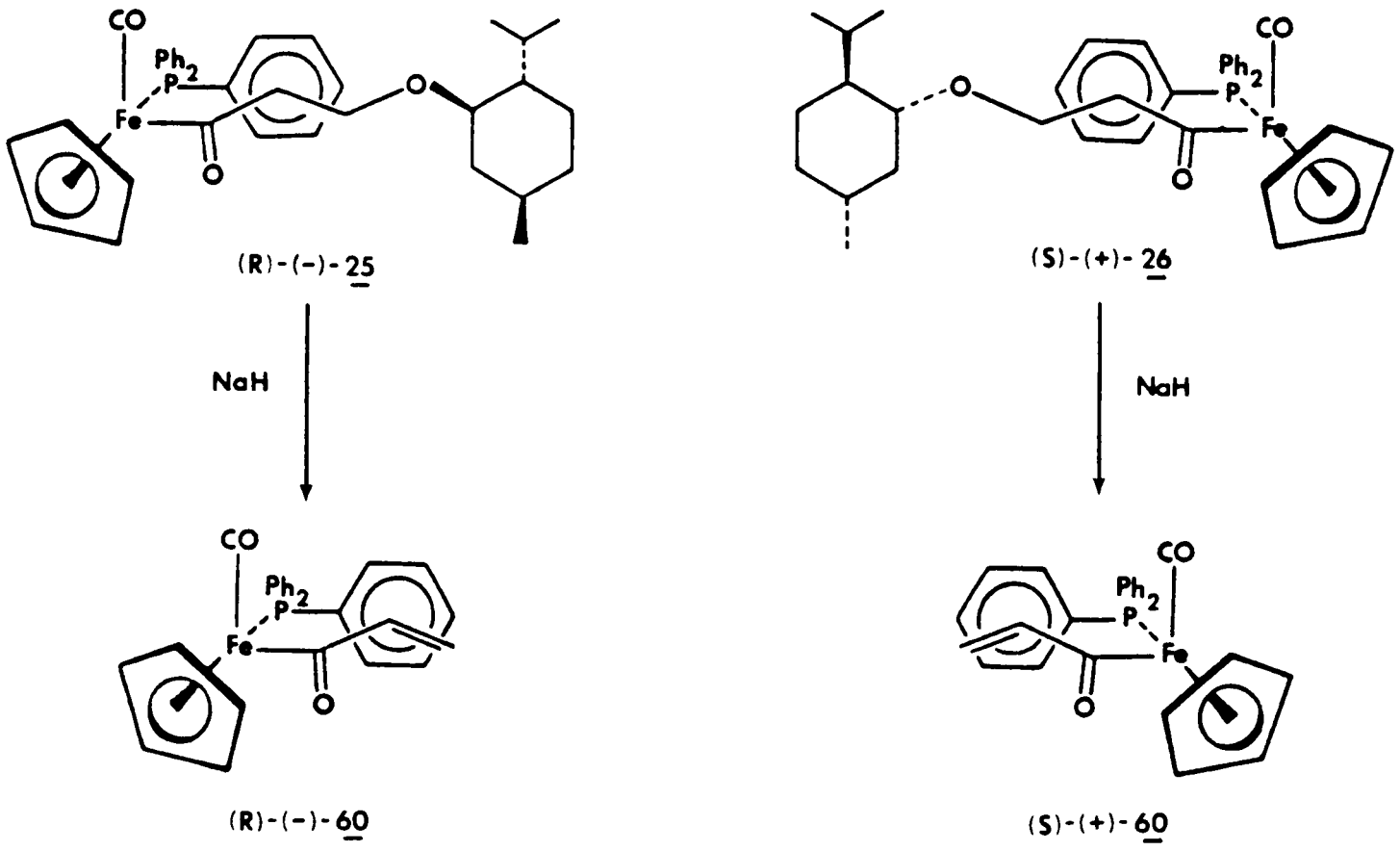
through 56 and 59, to give in both cases the E α,β-unsaturated acyl complex, is predicted to be the most favourable since these conformations avoid steric interactions between the acyl oxygen and R groups. However, for small groups like methyl or vinyl, some elimination through 57 and 58 to give the Z isomers can occur. Molecular models show that the pathway for departure of methoxide down towards the triphenylphosphine ligand is relatively unhindered. When R is t-butyl, either the initial deprotonation is sterically hindered, or the gross steric requirement of the t-butyl group prevents the stereoelectronically favourable conformation for elimination being achieved.

IV. Preparation of the optically pure acryloyl complexes (R)-(-)- and (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] and α-substituted-α,β-unsaturated acyl complexes

In view of the success achieved with the base-promoted elimination of methanol from β-methoxy iron acyl complexes, it was anticipated that β-menthoxy acyl complexes would undergo a similar elimination reaction to generate the corresponding α,β-unsaturated acyl complexes. Thus, a 1:1 diastereoisomeric mixture of the β-menthoxy acyl complexes 25 and 26 (chapter 2) was treated with sodium hydride in THF at 20°C to give in 81% yield the racemic parent acryloyl complex [(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60. This proved to be the most practical method of preparing complex 60 because any traces of unreacted starting material were easily separated from the product by chromatography on alumina. Complex 60 and its alternative precursor, the β-methoxy complex 49, were found to be inseparable by this or any other method. Attempts to make complex 60 by a Peterson reaction suffered from severe problems due to the base-promoted polymerisation of formaldehyde, resulting in only very low yields of the desired complex.[67]

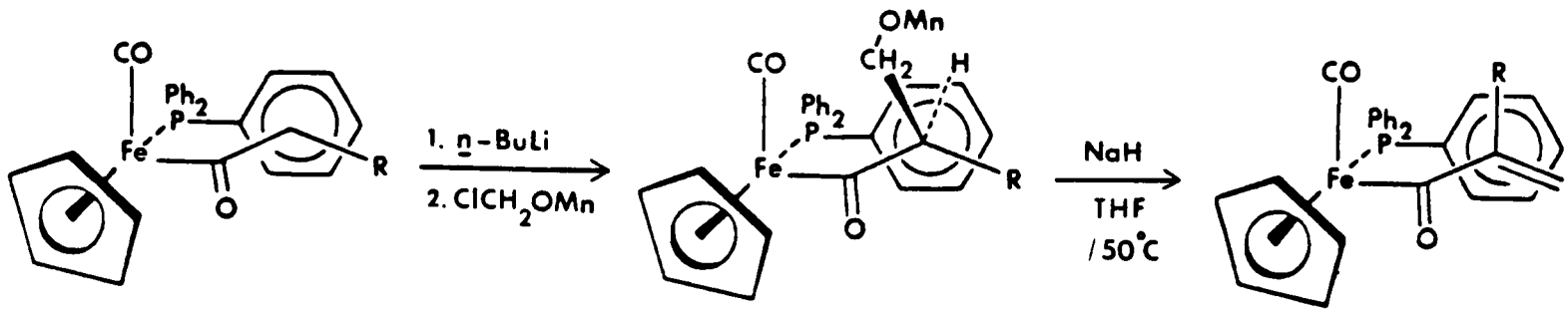
The separated diastereoisomers 25 and 26 of the β-menthoxy complex individually underwent elimination of (l)-menthol yielding the optically

pure parent acryloyl complexes (R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60, $[\alpha]_D^{22}$ -202.0° (c 0.11, C_6H_6), and (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60, $[\alpha]_D^{20}$ +202.°0 (c 0.11, C_6H_6) respectively.



This procedure was extended to the synthesis of α-methyl and α-ethyl substituted α,β-unsaturated iron acyl complexes. The racemic ethyl and propyl acyl complexes 16 and 15 were successively treated with n-butyl-lithium and chloromethyl (R)-menthyl ether in THF. In each case a 1:1 mixture of two out of the four possible diastereoisomers were formed. The ^{1}H n.m.r. spectrum of the mixture of the product complexes 61 and 62 contained two methyl doublets at δ0.39 and 0.35 whilst that of the mixture of complexes 63 and 64 contained two methyl triplets at δ0.42 and 0.40. These chemical shift values confirmed that stereoselective alkylation of the E enolates derived from complexes 16 and 15 in the anti (CO to acyl) conformation had occurred from the face away from the triphenylphosphine ligand, to generate the RRR and SSR relative configurations in the product complexes.[40,42] Attempted resolution of these diastereoisomers either by

chromatography or by fractional crystallisation unfortunately proved unsuccessful.



	RRR	SSR
R = Me	61	62
R = Et	63	64

R = Me 16

R = Et 15

R = Me 65

R = Et 66

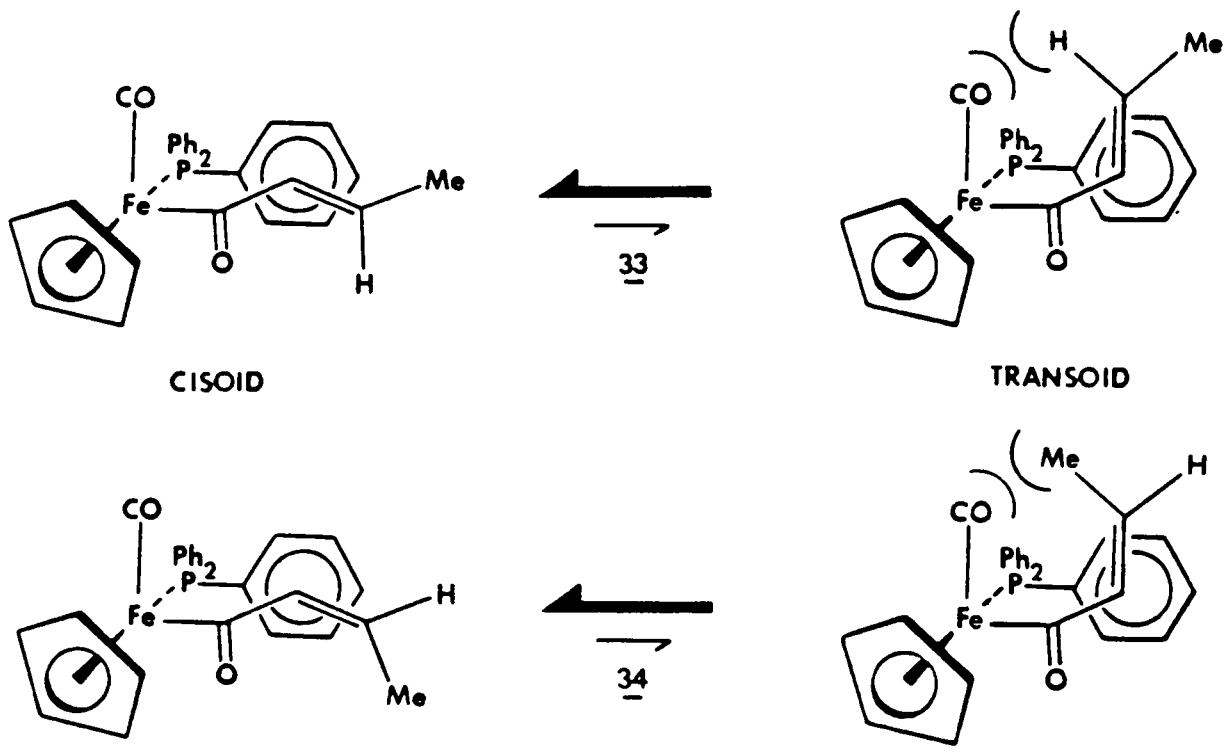
Complexes 61, 62 and 63, 64 were found to be resistant to the elimination of (l)-menthol under the reaction conditions previously employed. However, heating a THF solution of the complexes with sodium hydride at 50°C gave the racemic α-methyl- and α-ethyl-α,β-unsaturated acyl complexes 65 (39%) and 66 (46%) respectively. The moderate yields reflect the increased levels of decomposition under these new conditions.

In conclusion, the reactions described in this chapter provide convenient methods for the synthesis of E and Z β-substituted-α,β-unsaturated acyl complexes, the parent acryloyl complex and α-substituted-α,β-unsaturated acyl complexes, the former two in optically pure form.

V. X-ray crystal structures and conformational analyses of (R,S)-E- and (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$]

Assuming that, in common with all other iron acyl complexes of the type [(η^5-C_5H_5)Fe(CO)(PPh_3)COR], the acyl oxygen remains anti to the carbon monoxide ligand,[57] then molecular models and extended Huckel calculations[76] indicate a clear preference for both complexes 33 and 34 to adopt a cisoid conformation. Steric interactions between the carbon monoxide ligand and the β-hydrogen in complex 33, and the carbon monoxide ligand and the

β-methyl group in complex 34, would destabilise the corresponding transoid conformations.



These predictions were verified by X-ray crystal structure analyses of both complex 33 (figure 6) and complex 34 (figure 9), obtained as single crystals from dichloromethane-hexane. Full X-ray data for complex 33 is given in appendix 3 and selected bond lengths, bond angles and torsional angles listed in Table 5. The corresponding data for complex 34 is given in appendix 4 and Table 6 respectively.

In both cases, the geometry around the iron centre is close to octahedral and the acyl oxygen is anti to the carbon monoxide ligand. The conformation of the E α,β-unsaturated acyl ligand in complex 33 is cisoid with the torsional angle between the C=O and the C=C bonds being 39° (figure 7). The acyl ligand of the Z isomer 34 also adopts a cisoid conformation (figure 10), the corresponding torsional angle being 41°. Figures 8 and 11 show projections down the Fe-P axes of complexes 33 and 34 respectively . They illustrate that in both complexes, the triphenylphosphine ligand effectively shields one of the faces of the α,β-unsaturated acyl ligand.

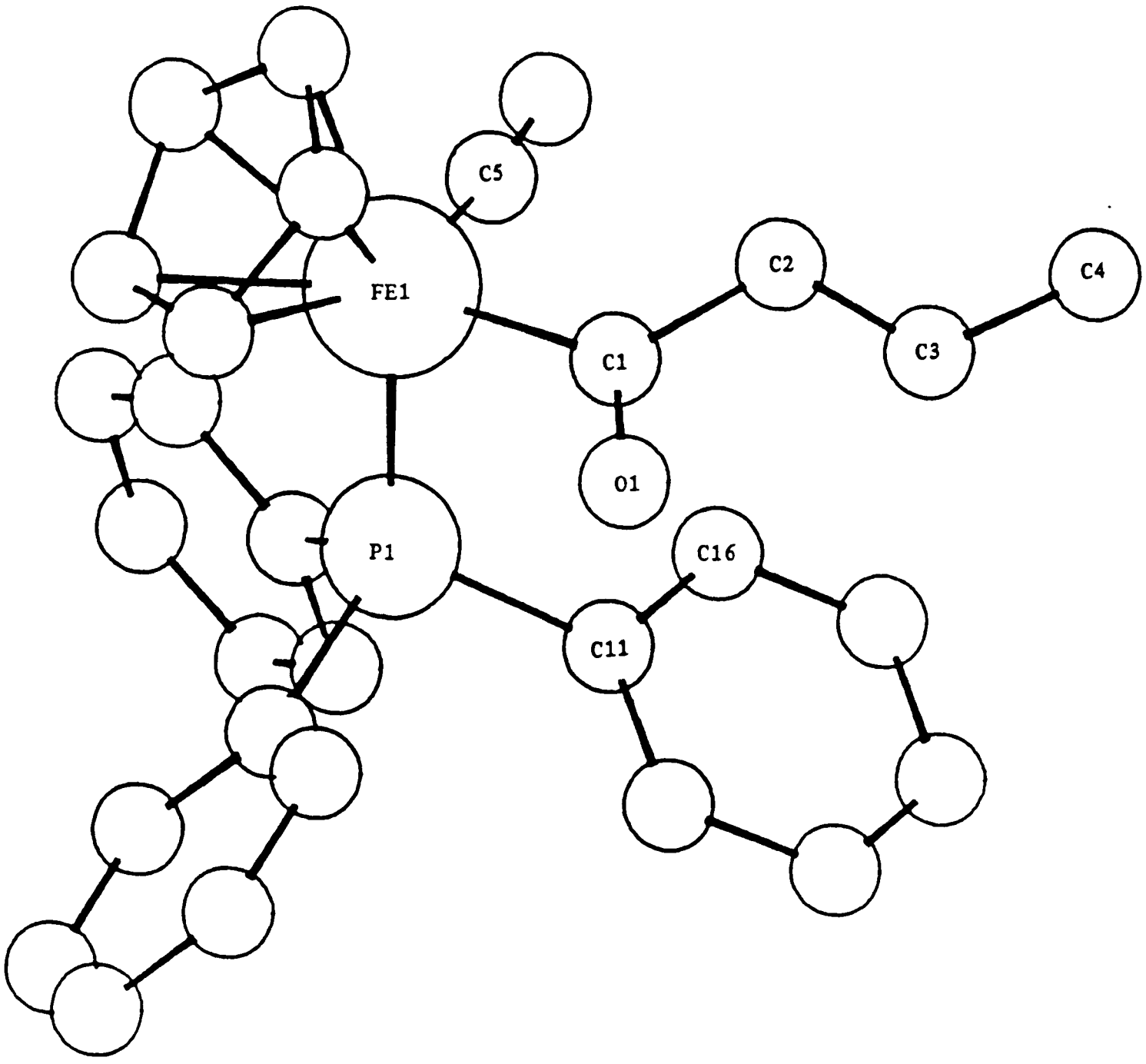


Figure 6: X-ray crystal structure of (R,S)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)-COCH=$CHCH_3$] 33.

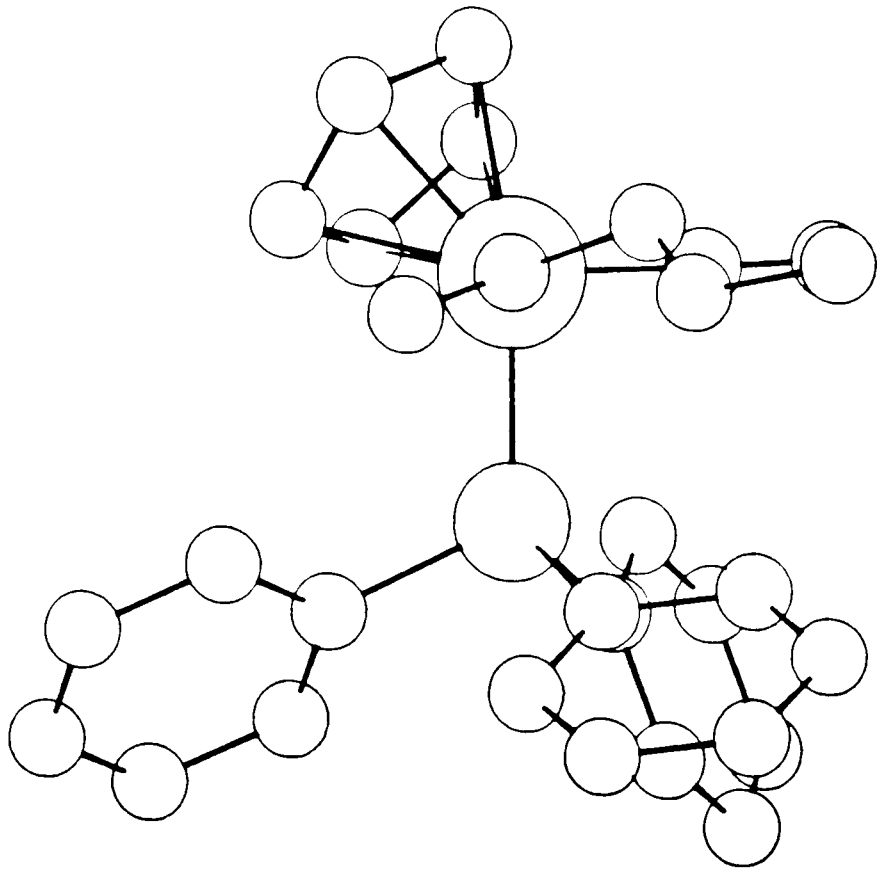


Figure 7: X-ray crystal structure of 33; C(1)-Fe(1) projection.

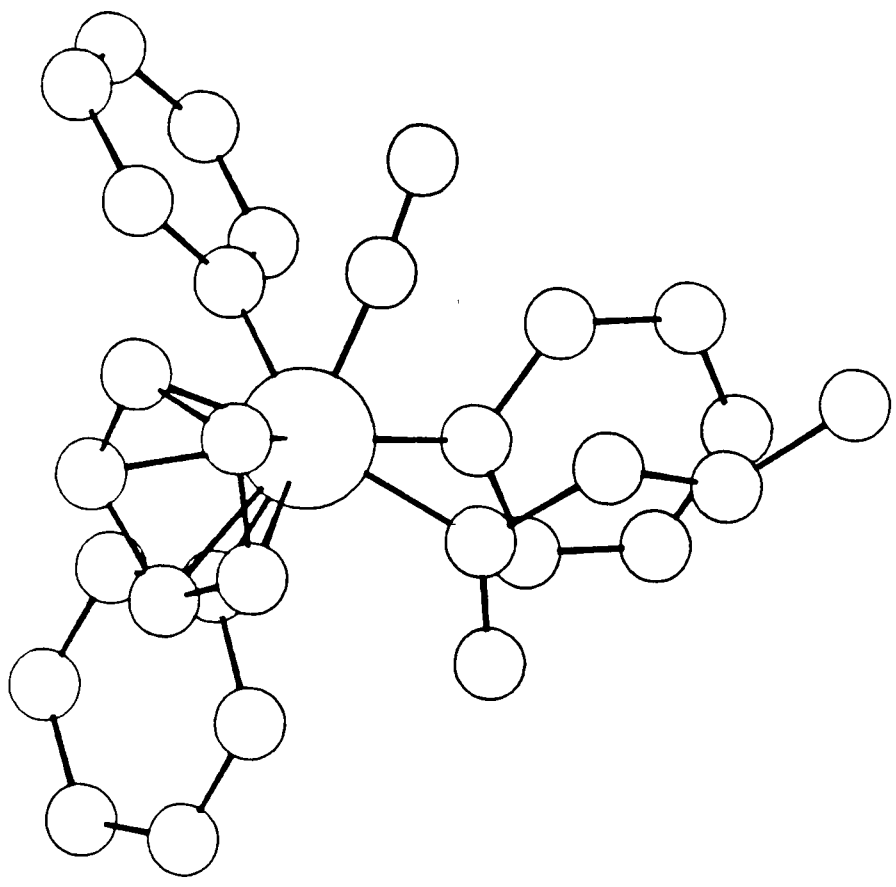


Figure 8: X-ray crystal structure of 33; Fe(1)-P(1) projection.

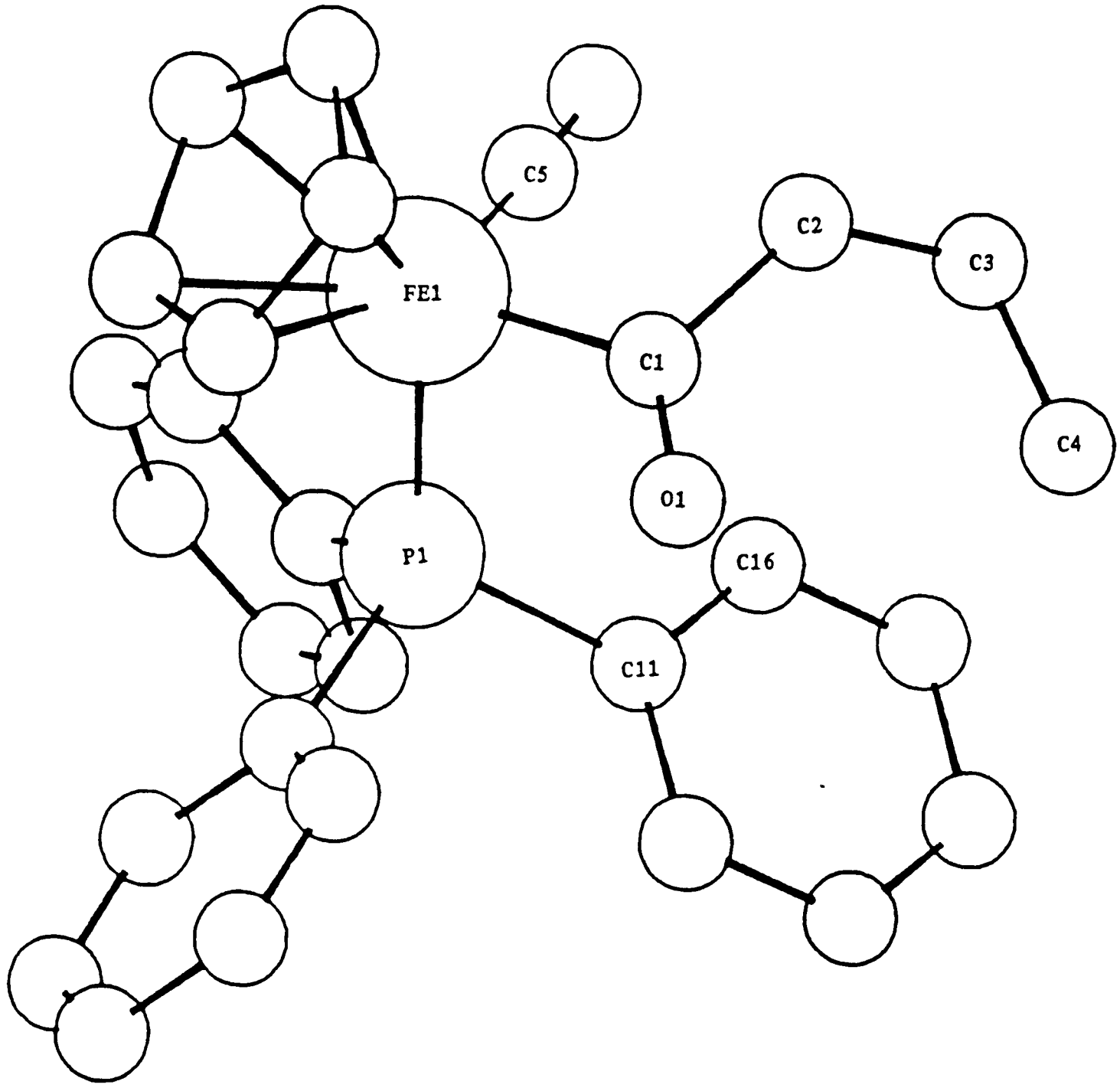


Figure 9: X-ray crystal structure of (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH{=}CHCH_3$] 34.

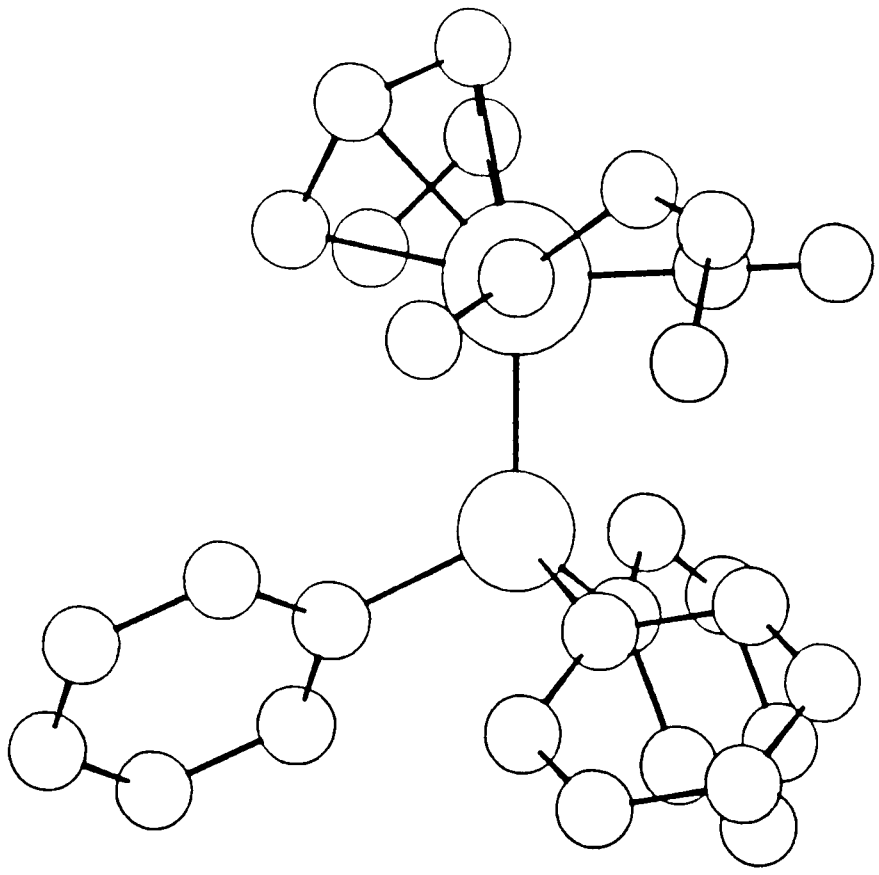


Figure 10: X-ray crystal structure of 34; C(1)-Fe(1) projection.

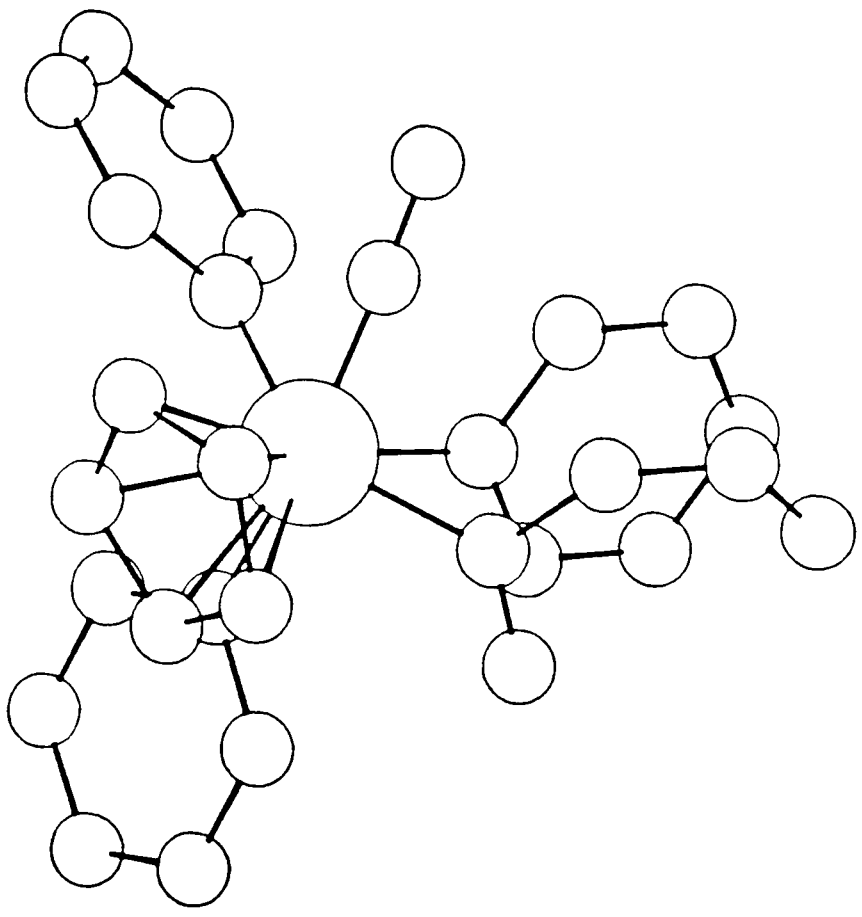


Figure 11: X-ray crystal structure of 34; Fe(1)-P(1) projection.

Bond lengths (A)		Bond angles (°)	
Fe(1)-P(1)	2.195(1)	C(1)-Fe(1)-C(5)	95.2(2)
Fe(1)-C(1)	1.958(3)	C(1)-Fe(1)-P(1)	89.2(1)
Fe(1)-C(5)	1.738(3)	P(1)-Fe(1)-C(5)	91.8(1)
C(1)-O(1)	1.223(4)	Fe(1)-C(1)-O(1)	122.9(3)
C(1)-C(2)	1.488(5)	Fe(1)-C(1)-C(2)	118.9(3)
C(2)-C(3)	1.316(6)	C(1)-C(2)-C(3)	121.7(4)
C(3)-C(4)	1.484(6)	C(2)-C(3)-C(4)	125.8(5)
		Fe(1)-P(1)-C(11)	116.1(1)

Torsional angles (°)	
C(5)-Fe(1)-C(1)-O(1)	-161
C(1)-Fe(1)-P(1)-C(11)	-30
C(1)-C(2)-C(3)-C(4)	171
C(5)-Fe(1)-C(1)-C(2)	18
C(3)-C(2)-C(1)-O(1)	39
Fe(1)-P(1)-C(11)-C(16)	-66

Table 5: Selected X-ray data with e.s.d.'s in parentheses for (R,S)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33.

Bond lengths (A)		Bond angles (°)	
Fe(1)-P(1)	2.196(2)	C(1)-Fe(1)-C(5)	93.0(3)
Fe(1)-C(1)	1.962(6)	C(1)-Fe(1)-P(1)	91.3(2)
Fe(1)-C(5)	1.753(9)	P(1)-Fe(1)-C(5)	92.4(2)
C(1)-O(1)	1.210(7)	Fe(1)-C(1)-O(1)	124.8(5)
C(1)-C(2)	1.497(9)	Fe(1)-C(1)-C(2)	115.8(5)
C(2)-C(3)	1.33(1)	C(1)-C(2)-C(3)	126.8(7)
C(3)-C(4)	1.47(1)	C(2)-C(3)-C(4)	127.9(8)
		Fe(1)-P(1)-C(11)	117.1(2)

Torsional angles (°)	
C(5)-Fe(1)-C(1)-O(1)	150
C(1)-Fe(1)-P(1)-C(11)	28
C(1)-C(2)-C(3)-C(4)	5
C(5)-Fe(1)-C(1)-C(2)	33
C(3)-C(2)-C(1)-O(1)	41
Fe(1)-P(1)-C(11)-C(16)	62

Table 6: Selected X-ray data with e.s.d.'s in parentheses for (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 34.

VI. Synthetic potential of α,β-unsaturated iron acyl complexes

The α,β-unsaturated acyl ligand in the general complex [(η^5-C_5H_5)Fe-(CO)(PPh_3)COCH=$CHCH_2R$] could in principle display three modes of reactivity towards nucleophiles:- (a) 1,2-addition, (b) 1,4- or Michael addition, or (c) γ-deprotonation to form dienolates. 1,2-Nucleophilic addition is disfavoured on electronic grounds due to the electron releasing effect of the iron moiety and on steric grounds due to the very large steric requirement of the iron auxiliary. In this last respect, the complexes resemble the unsaturated esters of o,o'-di-t-butyl-p-methoxyphenol in which the bulky ester group directs reaction away from the carbonyl group to the 4-position.[77] Michael addition and dienolate formation however, appear to be plausible modes of reactivity of such ligands. Our aim was to distinguish between these two modes utilising the stereochemical control of the chiral iron auxiliary in the highly diastereoselective generation of new chiral centres and ultimately, to extend the reactions to the asymmetric synthesis of useful chiral organic building blocks.

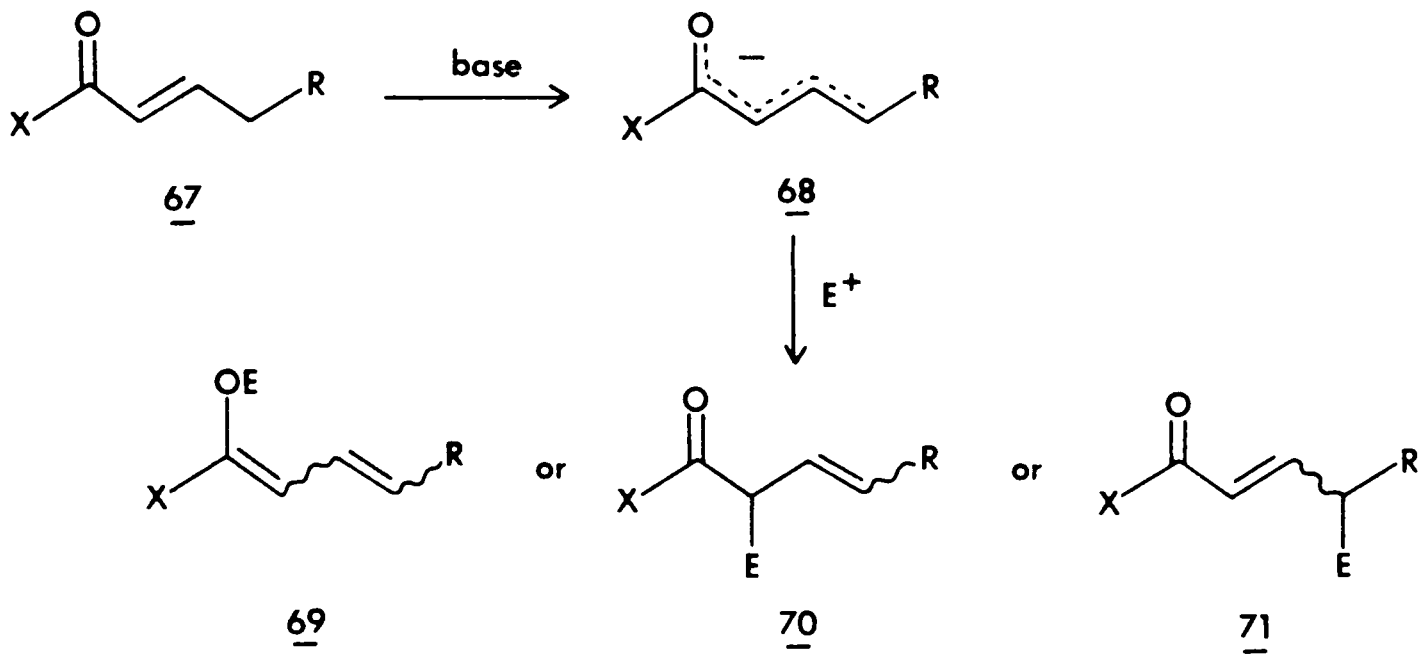
CHAPTER 4

STEREOSELECTIVE REACTIONS OF LITHIUM

DIENOLATES DERIVED FROM Z α,β-UNSATURATED IRON ACYL COMPLEXES

I. Introduction

α,β-Unsaturated carbonyl compounds 67 can undergo γ-deprotonation with strong non-nucleophilic bases to generate dienolates 68. Deprotonation is often performed in the presence of metal ion complexing agents, e.g. HMPA, to eliminate competitive 1,2- and 1,4-nucleophilic addition reactions. Quenching the dienolate with an electrophile can in principle lead to three products 69, 70 or 71 resulting from reaction at oxygen, the α-carbon and the γ-carbon centres respectively.

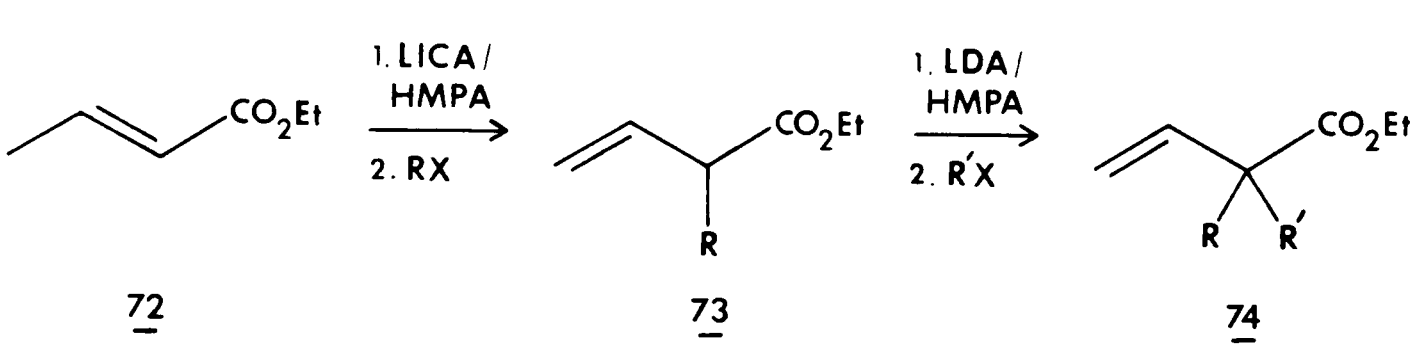


67 68 69 70 71

Reaction with electrophiles at oxygen is rarely observed. Although more of the total charge is localised on the oxygen atom due to a larger atomic orbital coefficient in the bonding molecular orbitals, the atomic orbital coefficients on the α- and γ-carbon atoms in the highest occupied molecular orbital are larger. Thus, for electrophiles having little charge and relatively low-lying lowest unoccupied molecular orbitals, reaction takes place preferentially on carbon.[72] The dienolate ion can therefore be regarded essentially as an ambident nucleophile reacting through the α- or the γ-carbon atom. Under kinetic conditions, reaction with electrophiles is generally found to occur at the α-carbon of dienolates to give the thermodynamically less stable β,γ-unsatuarated product. Simple molecular

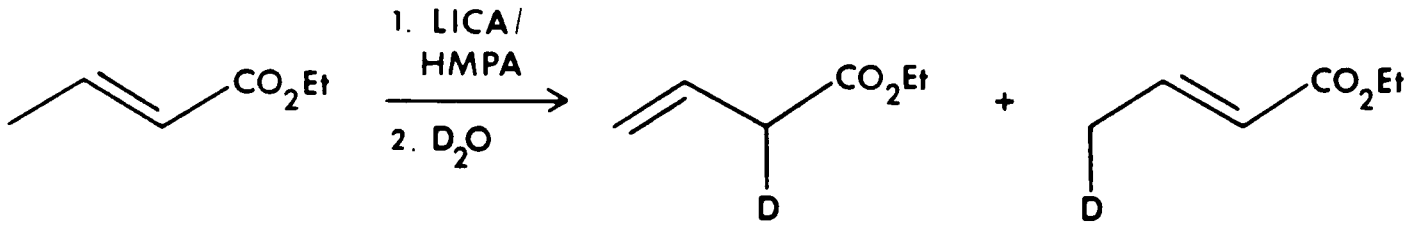
orbital calculations predict the α-carbon to be the carbon centre with the highest density of negative charge.[72] If the reaction with the electrophile is reversible or is carried out under thermodynamic conditions, substitution at the γ-carbon centre occurs preferentially to give the thermodynamically more stable α,β-unsaturated carbonyl compound. In practice however, it is found that the α:γ regioselectivity depends on a number of factors including the nature of the substrate, the electrophile, the metal counterion, solvent and temperature.

The pioneering studies of Rathke[78] revealed that the lithium dienolate derived from ethyl crotonate 72 underwent exclusive alkylation (e.g. CH_3I, $PhCH_2Br$) and reaction with acetone at the α-carbon to give the deconjugated β,γ-unsaturated carbonyl compound 73. The reaction was carried out in the presence of HMPA to eliminate competitive 1,4-conjugate addition.



72 73 74

These results were confirmed by Schlessinger who, with an LDA/HMPA modification, used a second dienolate formation-α-alkylation reaction to generate a quaternary carbon centre in adduct 74.[79] Quenching the lithium dienolate from ethyl crotonate with deuterium oxide led to deuterium incorporation only at the α-carbon in the β,γ-unsaturated isomer and only at the γ-carbon in recovered starting material. This demonstrated that the true α:γ regioselectivity of the protonation was 87:13 and that no isomerisation of the β,γ- to the α,β-unsaturated isomer was occurring.[78]

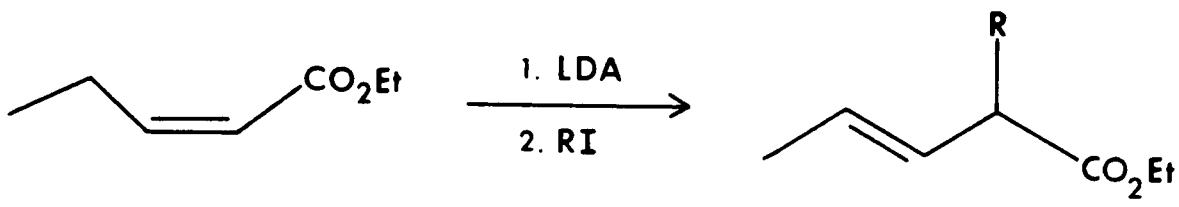


The reacton between the dianion from crotonic acid and benzaldehyde typically gave 4:1 mixtures of α:γ substituted products under a variety of conditions.[80] In contrast, the reaction of cyclohexanone and methyl iodide with the same dianion led mainly to γ-substitution (60:40),[81] illustrating the effect of the nature of the electrophile and the reaction conditions on the α versus γ regioselectivity.

Regioselective γ-alkylation could be achieved using copper dienolate anions from α,β-unsaturated acids [82] or lithium dienolates from γ-enamino-ketones,[83] and was also observed in the reversible aldol reaction of the lithium dienolates derived from 2-methyl- and 2,3-dimethylbut-2-enoates with aldehydes and ketones.[84] γ-Regioselectivity is also found to prevail if the α,β-unsaturated carbonyl function forms part of an aromatic system [85] or if the dienolate possesses a γ-sulphonyl group.[86]

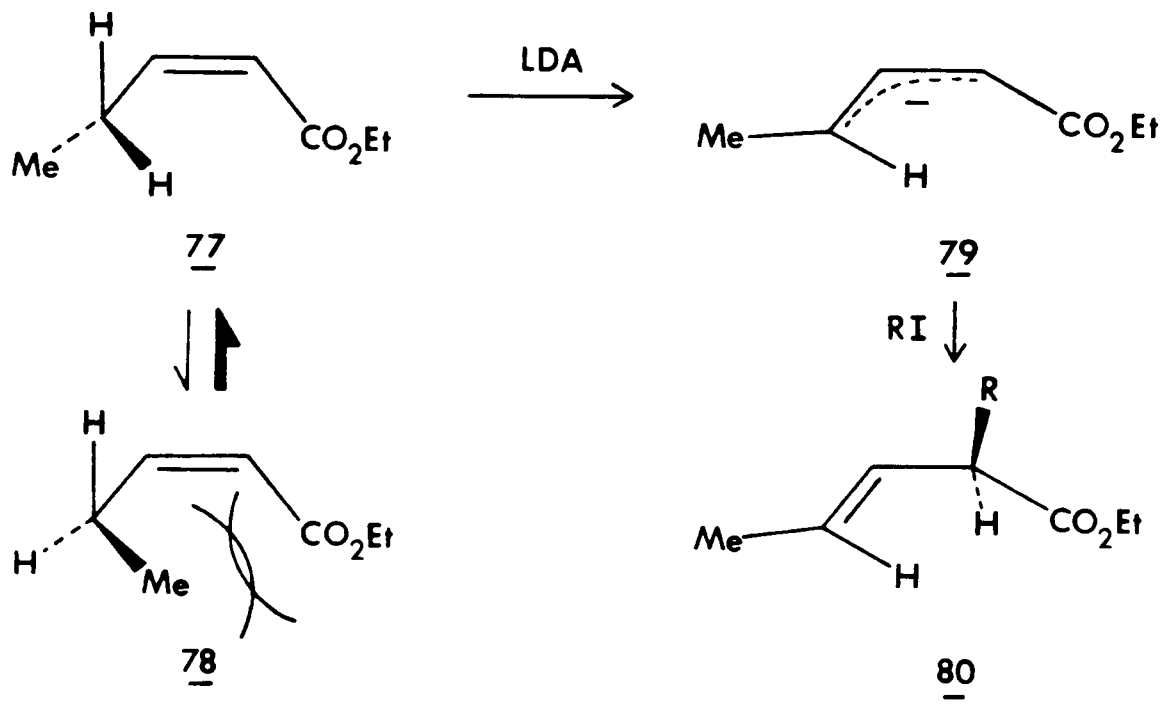
The competition between α- and γ—substitution in cyclic systems is found to be very sensitive to structural modifications. However, in general, when the dienolate contains a double bond exocyclic to the ring, γ-alkylation occurs preferentially.[87]

For α,β-unsaturated carbonyl compounds with a substituent at the γ-position, dienolate formation followed by reaction at the α-centre can give rise to two possible geometries about the new β,γ-double bond. Several studies have shown that Z α,β-unsaturated acids and esters give exclusively the E isomer of the deconjugated product.[88,89,90] For example, the reaction of ethyl-Z-pent-2-enoate 75 gave the E ester 76.[90]



75 76

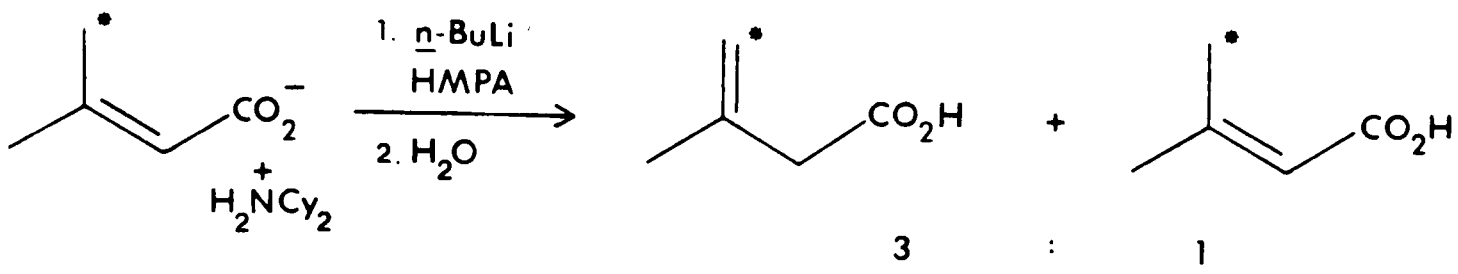
The stereoelectronic requirement for γ-deprotonation is that the C-H bond is orientated perpendicular to the plane of the α,β-unsaturated carbonyl system. The preferred conformation is presumably 77 in which the methyl group lies anti to the C-C double bond thus minimising interactions with the ester group which destabilise conformation 78. Deprotonation of 77 gives dienolate 79 which gives the E isomer 80 upon alkylation. Evidence, both theoretical and experimental, exists which indicates that the cisoid crotyl anion system 79 is more stable than the transoid arrangement.[91]



The corresponding E α,β-unsaturated carbonyl derivatives give predominantly, but not exclusively, the Z β,γ-isomers upon deprotonation and alkylation. This stereoselectivity was subsequently used in the synthesis of litsenolides A_2 and B_2.[90]

In an elegant series of deuteration experiments, Weiler has shown that the salt of 3-methyl-but-2-enoic acid and its methyl ester are kinetically deprotonated syn to the carbonyl function. Weiler suggested that directed

deprotonation of the proximate methyl group follows initial coordination of the lithium base to the carboxyl group.[92]



The dianion of 3-methyl-but-2-enoic acid has also been the subject of both ^{13}C n.m.r. and computational studies. They suggest a structure with a delocalised system in which the lithium ion lies above the plane of the dienolate. Location of the lithium in the molecular plane is accompanied by rotation of the γ-methylene group and loss of the fully delocalised system.[93]

Few examples of asymmetric synthesis using chiral dienolates have been reported to date. Oppolzer described the Michael addition reaction of a chiral ester dienolate to an α,β-unsaturated carbonyl compound in the synthesis of (-)-khusimone.[94]

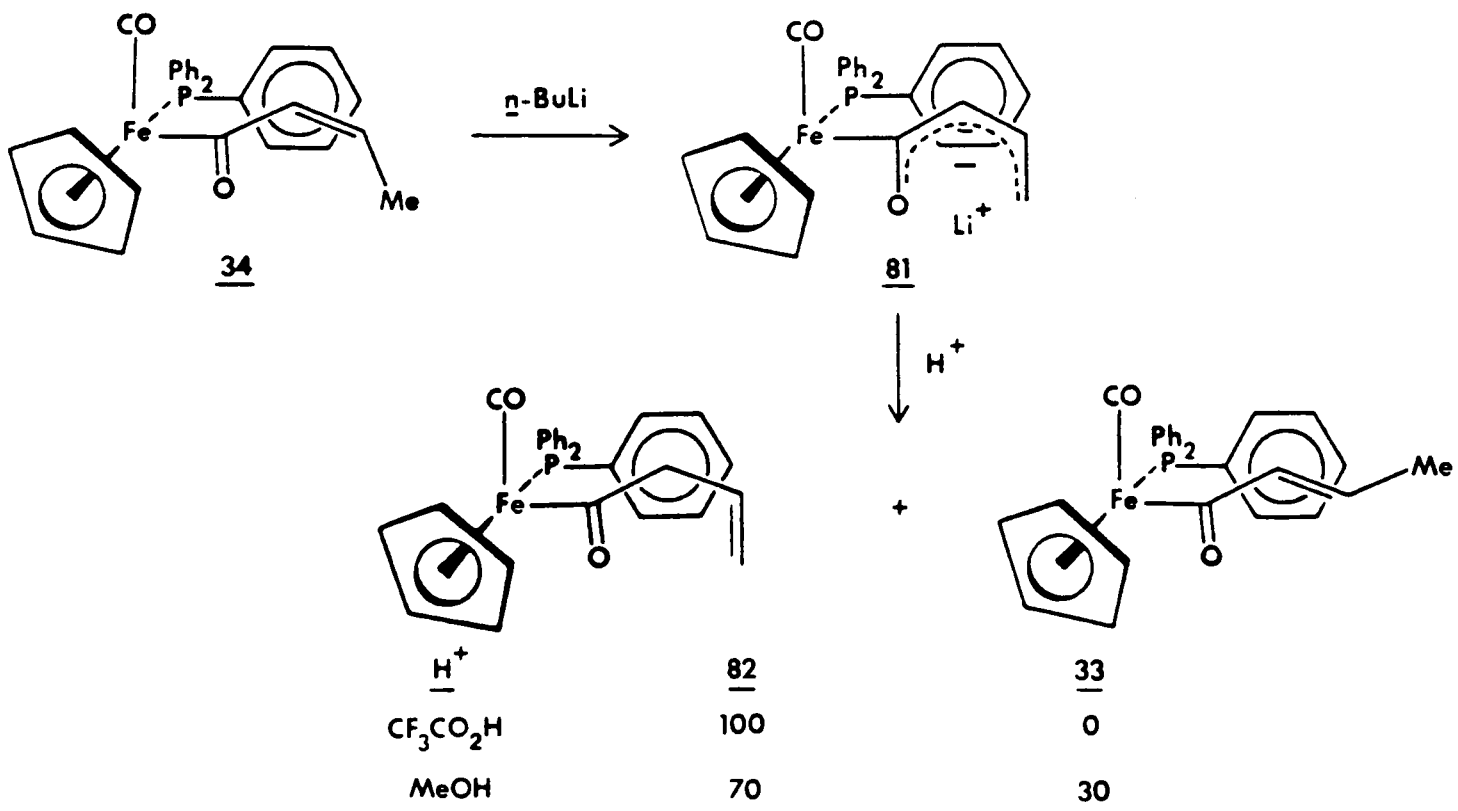
In the asymmetric Michael addition of alkyllithiums to chiral E oxazolines, Meyers reported the isolation of a minor biproduct derived from a dienolate formed by γ-deprotonation of the Z isomer of the chiral oxazoline.[95]

Chiral dienolates are in principle available from α,β-unsaturated acyl ligands bound to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$. On the basis of the previous studies described above, particularly the possibility of prior coordination of the lithium base to the acyl oxygen, it was anticipated that the Z isomers would be more likely to undergo γ-deprotonation than the corresponding E complexes. In any subsequent reaction with electrophiles, our aim was to achieve (a) high α- or γ-regioselectivity, (b) high diastereoselectivity in the creation of new

chiral centres and (c) stereoselective formation of either an E or Z geometry about the β,γ- or α,β -double bond.

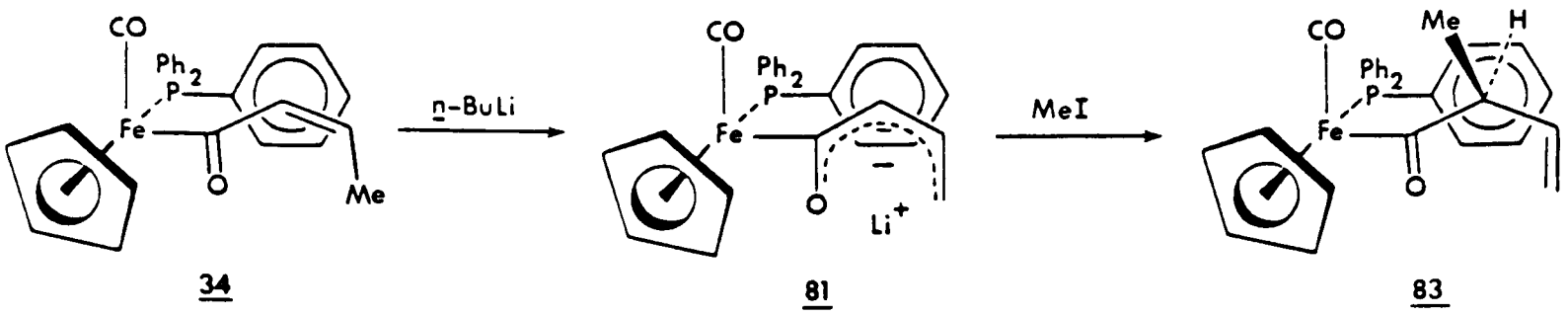
II. Stereoselective α-alkylation of the lithium dienolate derived from Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$][96]

Addition of n-butyllithium to the Z-crotonyl complex 34 in THF at -78°C generated a dark red-coloured solution characteristic of the formation of an enolate. The reaction was quenched at -78°C with trifluoroacetic acid to give after chromatography, a single product whose ^{1}H n.m.r. spectrum contained two doublets (δ4.89 and 4.78) and a multiplet (δ5.61) each due to a single olefinic proton. In addition, the two olefinic carbons in the off-resonance ^{13}C n.m.r. spectrum appeared as a doublet and a triplet. On the basis of these and other spectroscopic data, the product was identified as the β,γ-unsaturated acyl complex 82. It was presumed that complex 34 had undergone exclusive γ-deprotonation to form lithium dienolate 81 which was then regioselectively protonated at the α-position. Addition of methanol, instead of trifluoroacetic acid, to 81 gave a mixture (70:30) of complex 82 and the E-crotonyl complex 33. In the latter case, complex 33 presumably arose from alkoxide-promoted isomerisation of complex 82 as has previously been observed.[75]



H^+	82	33
CF_3CO_2H	100	0
MeOH	70	30

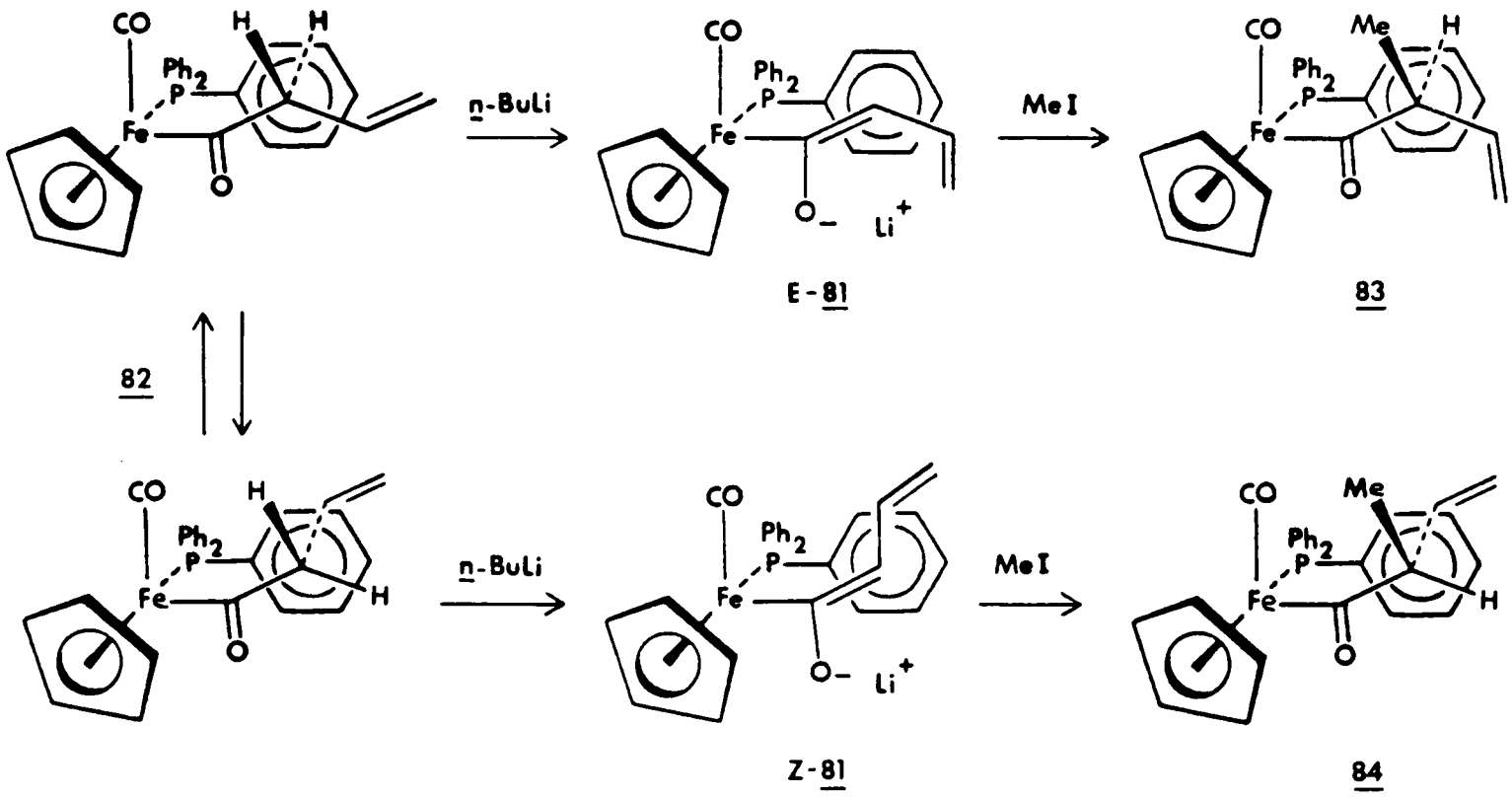
Addition of methyl iodide to dienolate 81, generated as before, gave the α-methyl-β,γ-unsaturated complex 83 identified by signals due to three olefinic protons and an α-methyl group in the ^{1}H n.m.r. spectrum.



34 81 83

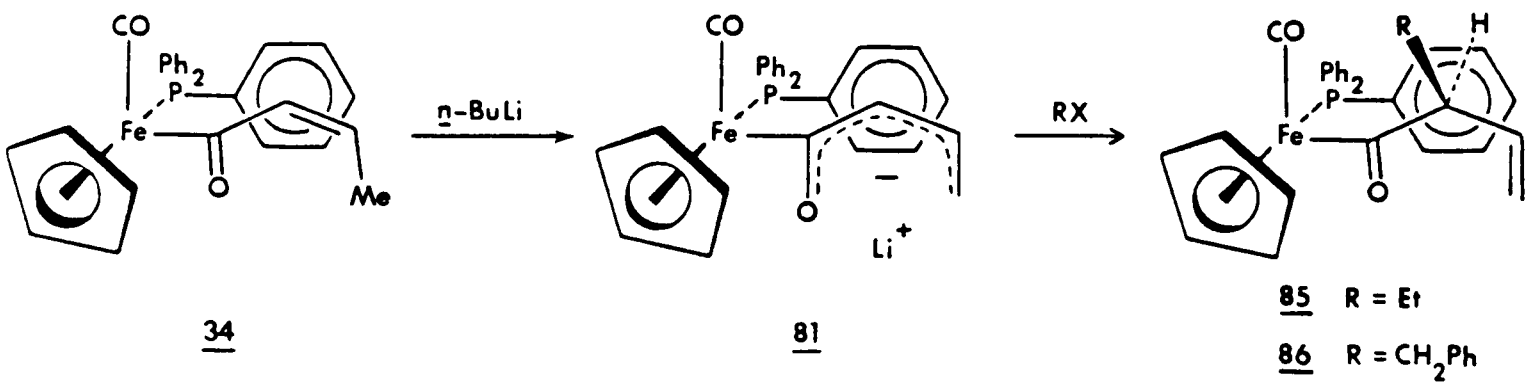
In the ^{1}H n.m.r. spectrum of complex 83 the intensity of the methyl doublet due to the minor diastereoisomer was less than that of the ^{13}C satellites of the methyl doublet due to the major diastereoisomer. The diastereoselectivity of the methylation could therefore be stated as being greater than 100:1. The relative configuration between the iron and α-centres in the major diastereoisomer was established as RS,SR from the chemical shift (δ1.10) of the major α-methyl doublet.[43]

Dienolate formation and methylation of complex 82 also generated complex 83 but with a reduced diastereoselectivity of 30:1. Deprotonation of the more stable conformation of complex 82 in which one C-H bond is perpendicular to the plane of the acyl group and the other hydrogen is in the most sterically demanding position between the carbon monoxide and triphenylphosphine ligand, leads to the formation of E-81. Subsequent α-methylation away from the triphenylphosphine ligand gives the major RS,SR diastereoisomer 83. However, free rotation about the α,β-single bond provides a route whereby deprotonation of the alternative conformation can occur to give Z-81 and the RR,SS diastereoisomer 84 upon diastereofacial α-methylation.

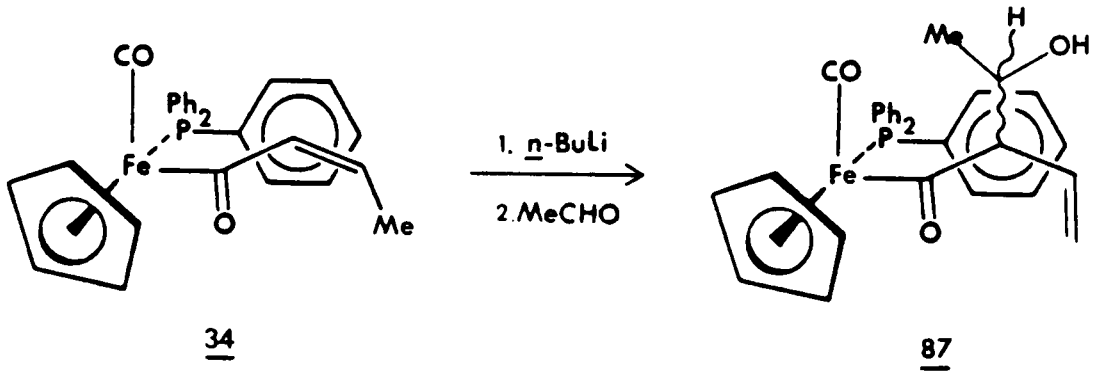


In contrast, the original α,β-double bond in complex 34 necessarily leads to the formation of E-81 upon γ-deprotonation and hence to the increased diastereoselectivity observed in the formation of 83.

Alkylation of dienolate 81 with ethyl iodide and benzyl bromide also occurred exclusively at the α-position to give the diastereoisomerically pure complexes 85 and 86 respectively. The enhanced diastereoselectivity with increased size of the electrophile is consistent with the trend predicted theoretically and observed experimentally.[41] The relative configurations in the product complexes were assigned as RS,SR by analogy with the relative stereochemistry in the major diastereoisomer from the methylation reaction.



The reaction between the dienolate derived from complex 34 and acetaldehyde was completely α-regioselective but, as in the reaction between the lithium enolate of the ethyl acyl complex 16 and aldehydes,[43] only moderately diastereoselective. Complex 87 obtained in 93% yield, was formed as a 32:9:2:1 mixture of diastereoisomers.



34 87

The X-ray crystal structure analysis of the Z-crotonyl complex 34 (chapter 3) shows that the α,β-unsaturated acyl ligand adopts an anti (CO to acyl) and a cisoid conformation in the solid state. It is presumed that the steric interactions between the β-methyl group and the carbon monoxide ligand destabilise the alternative transoid conformation (chapter 3). The exclusive formation of dienolate 81 from complex 34 may be rationalised in terms of initial coordination of n-butyllithium to the electron-rich acyl oxygen (figure 12). Directed deprotonation[92] of the proximate methyl group in complex 34 would generate dienolate 81 in the cisoid conformation. Although the cisoid conformation of 81 is predicted to be the most stable,[91] it may be in equilibrium with the corresponding transoid conformation. Both conformations however, are expected to undergo α-alkylation stereoselectively from the face away from the phenyl group of the triphenylphosphine ligand to give the observed RS,SR relative configuration in the product complex.

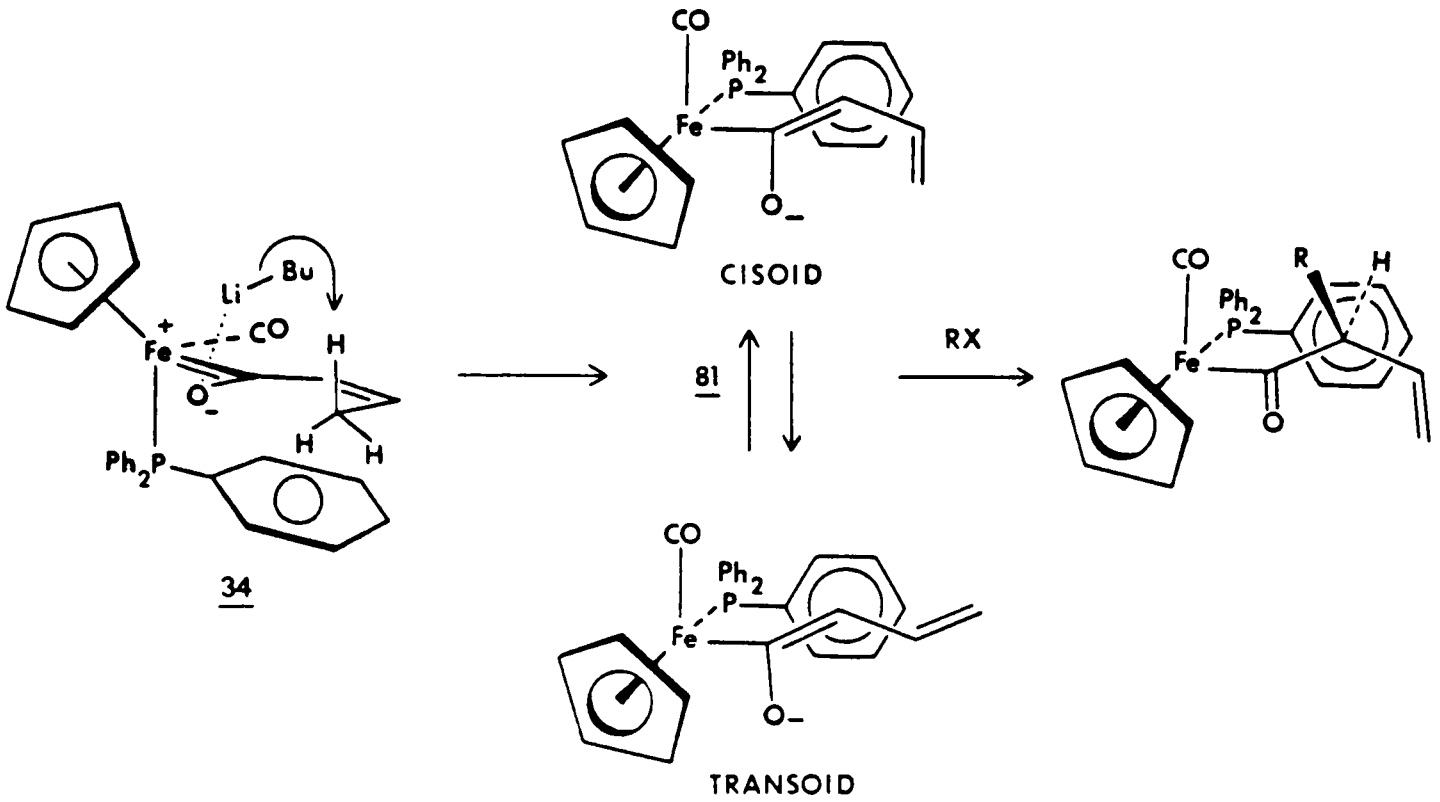
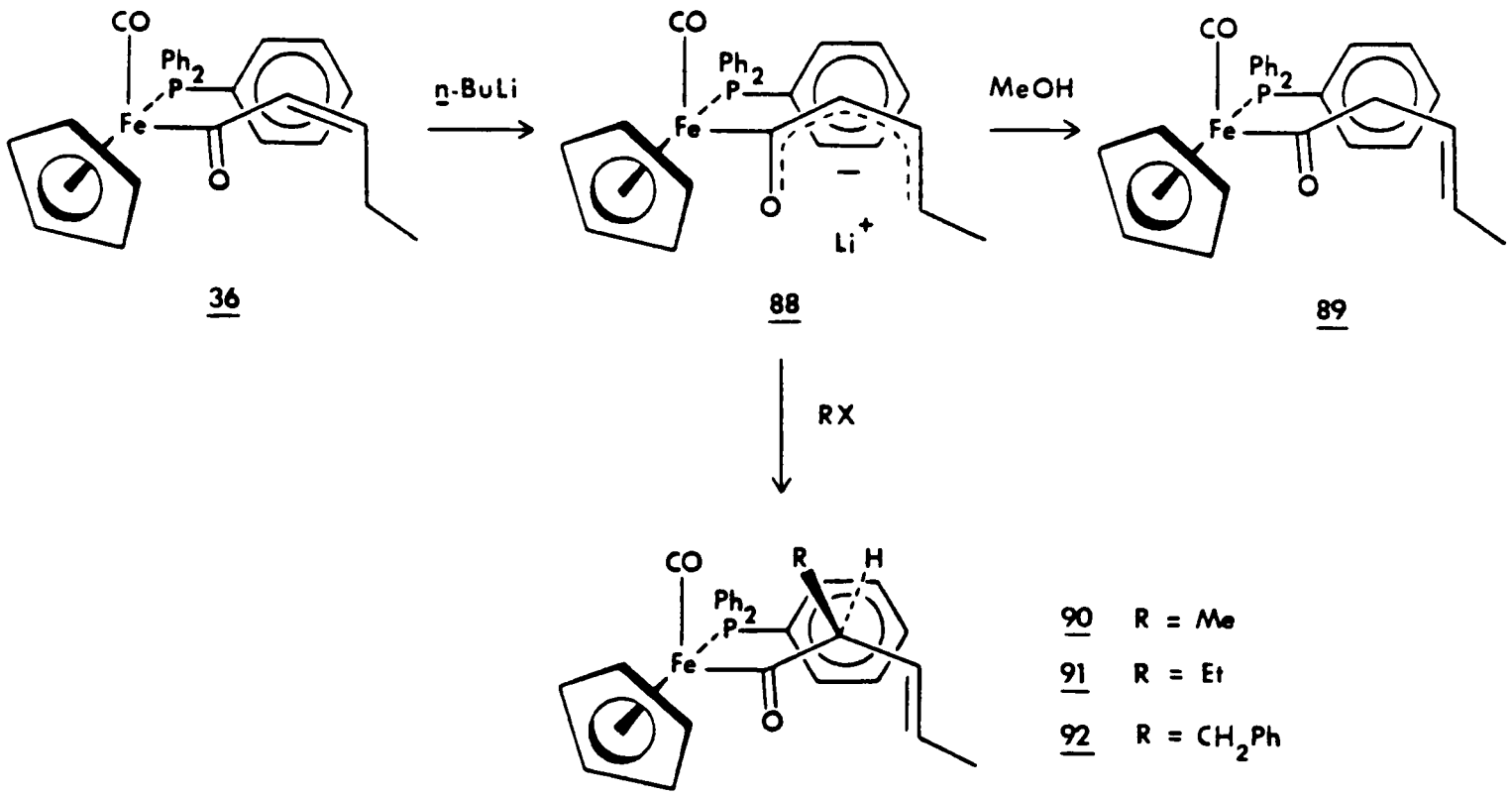


Figure 12: Directed γ-deprotonation of Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)-COCH=$CHCH_3$] 34.

III. Stereoselective α-alkylation of the lithium dienolate derived from Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHEt][97]

Treatment of Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHEt] 36 with n-butyllithium in THF at -78°C generated a dark red solution of an enolate. Quenching with methanol gave a single product identified by ^{1}H n.m.r. spectroscopy as the β,γ-unsaturated complex 89. The ^{1}H n.m.r. spectrum contained a three proton doublet at δ1.59 due to the allylic methyl group and two complex multiplets at δ3.55 and 3.22 due to the two diastereotopic α-protons. The E β,γ-double bond geometry was established from the ^{1}H n.m.r. coupling constant (J = 15.5 Hz) between the vinyl protons obtained from a computer simulation of the methyl group-decoupled 500 MHz ^{1}H n.m.r. spectrum. The formation of complex 89 is consistent with exclusive γ-deprotonation of complex 36 to form dienolate 88 followed by regioselective α-protonation.



Addition of methyl iodide to the dienolate 88 derived from complex 36, gave the (RS,SR)-α-methyl-E-β,γ-unsaturated complex 90 with a diastereoselectivity of greater than 100:1 and only an E geometry about the β,γ-double bond. The methyl doublet due to the major RS,SR diastereoisomer 90 appeared at δ1.02 in the 300 MHz ^{1}H n.m.r. spectrum, whilst the double bond geometry followed from the trans coupling constant (J = 16 Hz) between the olefinic protons.

Alkylation of dienolate 88 with the larger electrophiles ethyl iodide and benzyl bromide gave complexes 91 and 92 as single diastereoisomers by ^{1}H and ^{13}C n.m.r. spectroscopy. By analogy with the formation of complex 90, the relative configurations in 91 and 92 were assigned as RS,SR.

On the basis of the X-ray crystal structure of the Z-crotonyl complex 34, the acyl ligand in Z-[$(\eta^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHEt$] 36 is predicted to adopt a cisoid conformation in order to avoid steric interactions between the β-ethyl group and the carbon monoxide ligand. In addition, the preferred conformation of the β-ethyl substituent would be that in which the methyl group is anti to the α,β-unsaturated double bond thus minimising

steric interactions with the acyl oxygen (figure 13). Initial coordination of n-butyllithium to the acyl oxygen may again be invoked to rationalise the exclusive formation of dienolate 88 from complex 36. Directed deprotonation[92] of the proximate methylene group would generate dienolate 88 in the cisoid conformation and with the γ-methyl group in the exo rather than the sterically disfavoured endo position.[90] Although an equilibrium may exist between the cisoid conformation and the corresponding transoid arrangement, both would be expected to undergo α-alkylation from the face away from the triphenylphosphine ligand. This would give both the observed RS,SR relative configuration and E geometry about the β,γ-double bond in the product complexes.

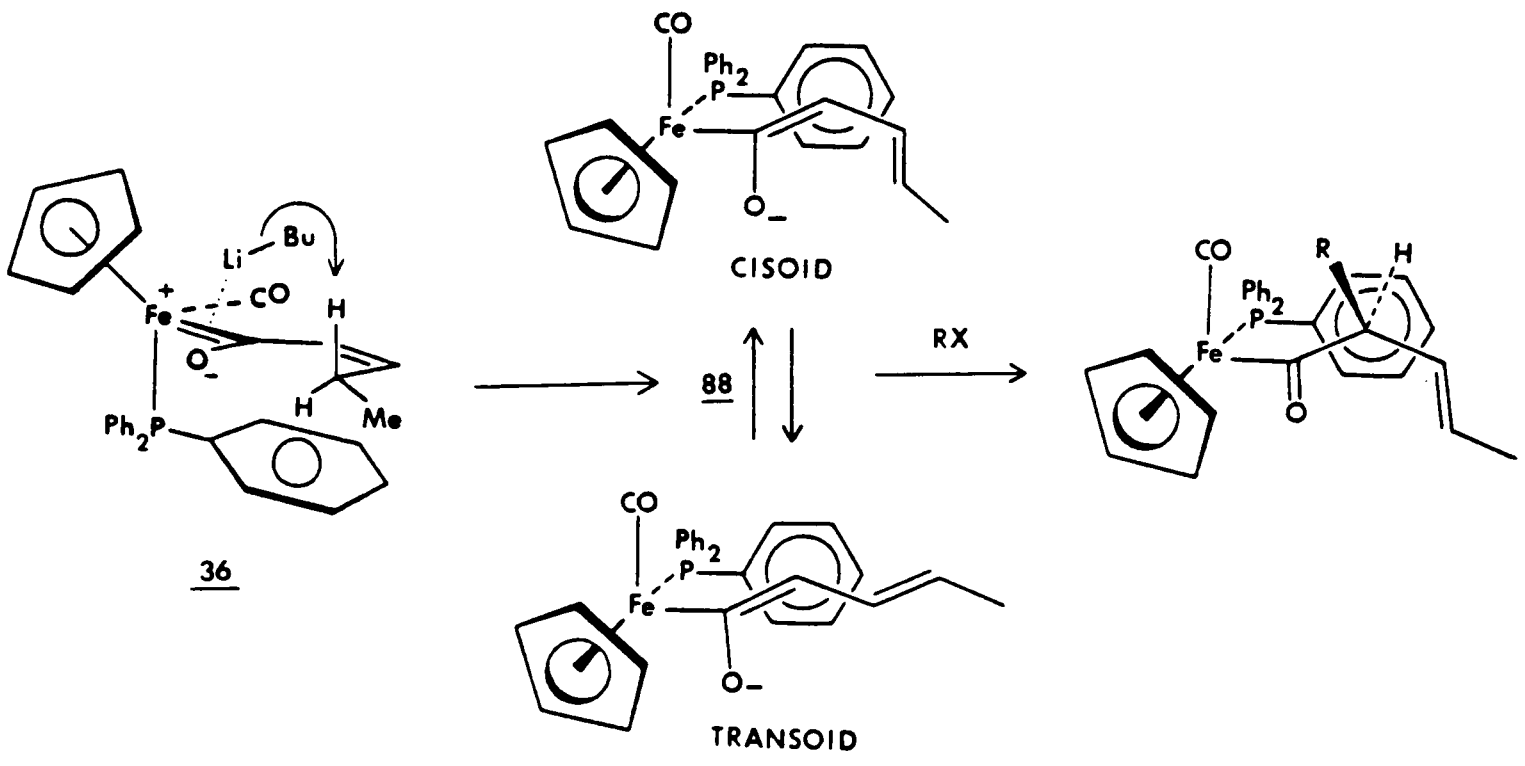


Figure 13: Directed γ-deprotonation of Z-[η^5-(C_5H_5)Fe(CO)(PPh_3)-COCH=CHEt] 36.

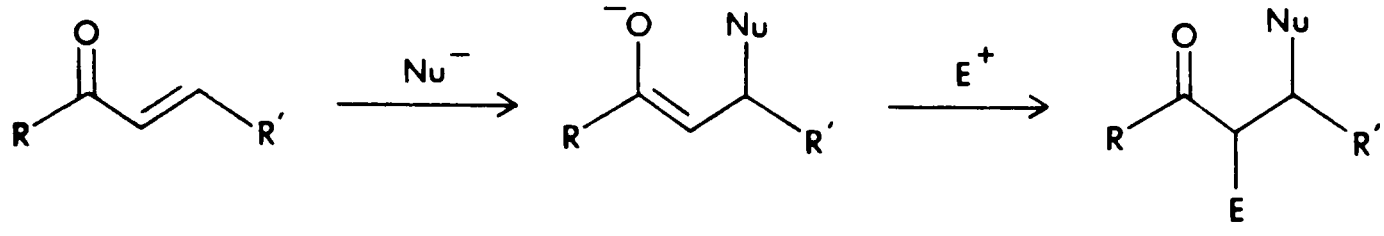
In contrast to dienolates that have previously appeared in the literature, the chiral lithium dienolates derived from Z α,β-unsaturated iron acyl complexes show exceptional degrees of regioselectivity and diastereoselectivity in their reactions with electrophiles. Without exception they undergo α-alkylation with very high diastereoselectivities and give only an E geometry about the β,γ-double bond.

CHAPTER 5

STEREOCONTROLLED ASYMMETRIC TANDEM MICHAEL ADDITIONS AND ALKYLATIONS OF E α,β-UNSATURATED IRON ACYL COMPLEXES

I. Introduction

The 1,4-conjugate or Michael addition reaction of carbon nucleophiles to α,β-unsaturated carbonyl compounds is one of the most widely used carbon-carbon bond forming reactions in organic chemistry. The enolate generated by the Michael addition may be quenched with a carbon electrophile allowing the formation of a second carbon-carbon bond in the same reaction.

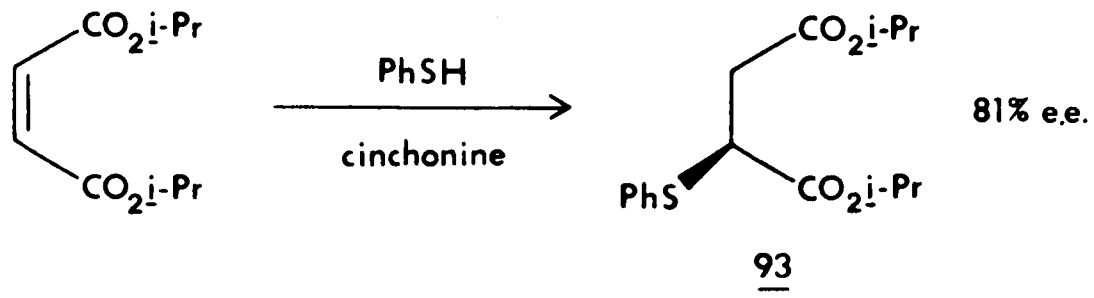


Stereochemically, these reactions generate two new chiral centres α and β to the carbonyl group. With the continuing emphasis on the synthesis of optically pure molecules of definite absolute configuration, it is desirable for these two new chiral centres to be introduced with both a high degree of diastereoselectivity and enantioselectivity. In recent years, an increasing number of successful examples of asymmetric synthesis through the Michael addition reaction have appeared.[98] In principle, the chiral auxiliary group can form part of any of three components involved in the Michael reaction; the base, if the addition is base-catalysed, the attacking nucleophile or the α,β-unsaturated carbonyl compound. All three types of approach have been used.

1. Chiral basic catalysts

The Michael additions of β-keto esters to α,β-unsaturated carbonyl derivatives in the presence of chiral amine[99] and cobalt[100] catalysts gave the corresponding adducts with moderate to low e.e.'s.

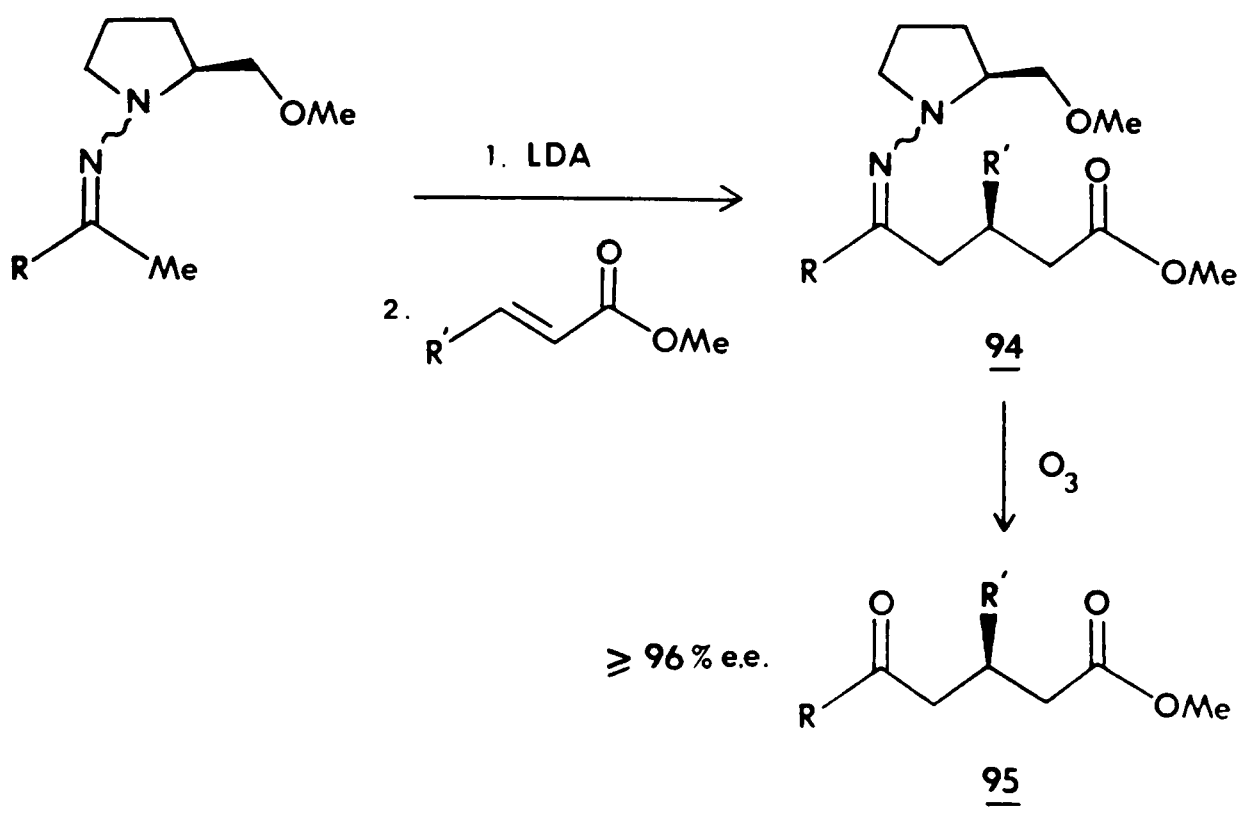
An e.e. of 81% was shown by the product 93 from the cinchonine-catalysed addition of thiophenol to diisopropyl maleate.[101] However, the generally low levels of asymmetric induction have not made this approach synthetically useful.



93

2. Chiral nucleophiles

One of the most successful reactions under this category has been developed by Enders and coworkers and involves the Michael addition of chiral α-lithio SAMP/RAMP hydrazones to α,β-unsaturated esters. Ozonolysis of the adducts 94 gave β-substituted-δ-ketoesters 95 with greater than 96% e.e.[102] This methodology has since been used in the asymmetric synthesis of pheromones of the small forest and red wood ants.[103]



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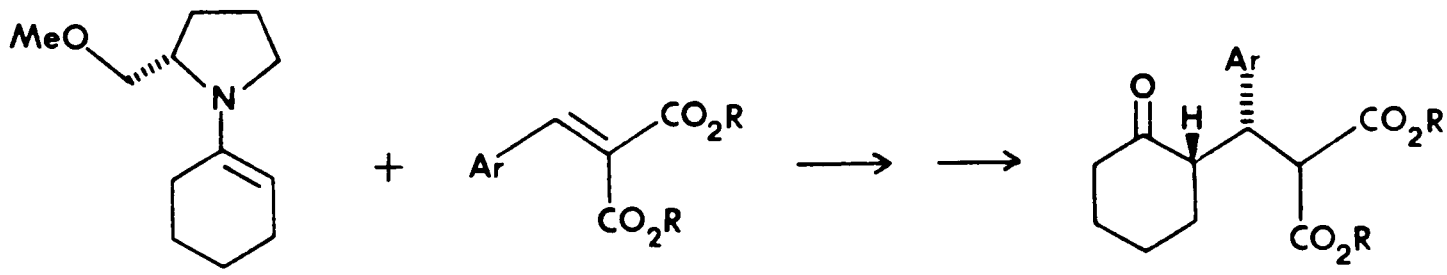
95

Chiral ester [104] and amide [105] enolates derived from (-)-8-phenylmenthol and (S)-prolinol respectively, displayed moderate threo diastereoselectivity and enantioselectivity in their 1,4-additions to E-crotonate esters. The asymmetric Michael addition of a chiral ester dienolate was used as part of the synthesis of (-)-khusimone by Oppolzer.[94]

The propensity for organocuprates to undergo efficient Michael addition to a wide variety of α,β-unsaturated carbonyl substrates has stimulated interest in chirally modified reagents of the form $R(Z^*)CuLi$ and $R(Z^*)CuMgBr$ (e.g. Z^* = (S)-prolinol, (S)-N-methylprolinol).[106] Generally low e.e.'s (<26%) have so far been achieved. However, the Michael reaction of a phosphine-stabilised vinyl copper reagent to 2-methylcyclopenten-2-one gave a chiral steroid fragment with 71% e.e.[107]

Chiral copper azaenolates and cyclic enones have given adducts with up to 75% e.e.[108]

Although the reaction of chiral enamines with prochiral α,β-unsaturated carbonyl compounds generally gave poor optical yields of products,[109] Seebach has described the highly diastereoselective and enantioselective Michael addition of (2S)-1-(1-cyclohex-1-yl)-2-(methoxymethyl)pyrrolidine 96 to Knoevenagel condensation products 97 of aromatic aldehydes.[110]



96 97

d.e. > 88%

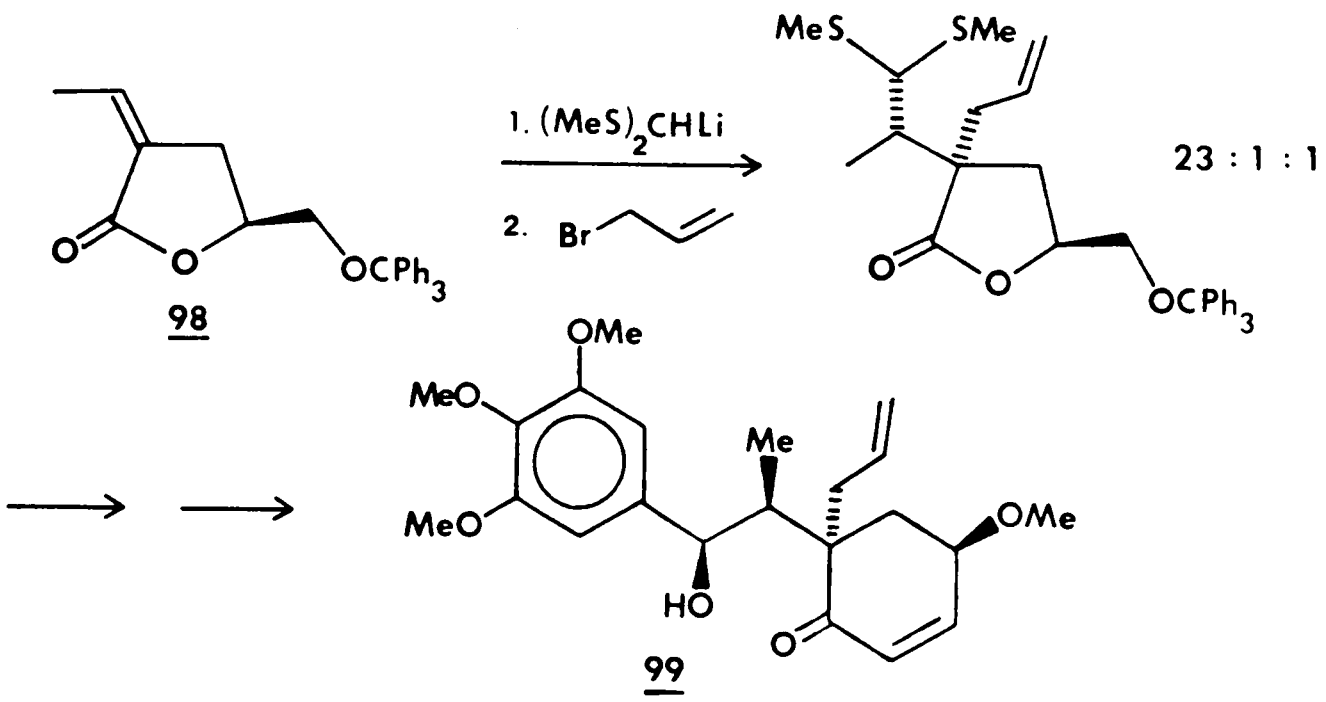
e.e. > 80%

Moderate to low e.e's have been reported in the use of the anions derived from β-hydroxy esters,[111] butanolides,[112] sulphoxides [113] and oxazepines [114] as chiral nucleophiles in Michael addition reactions.

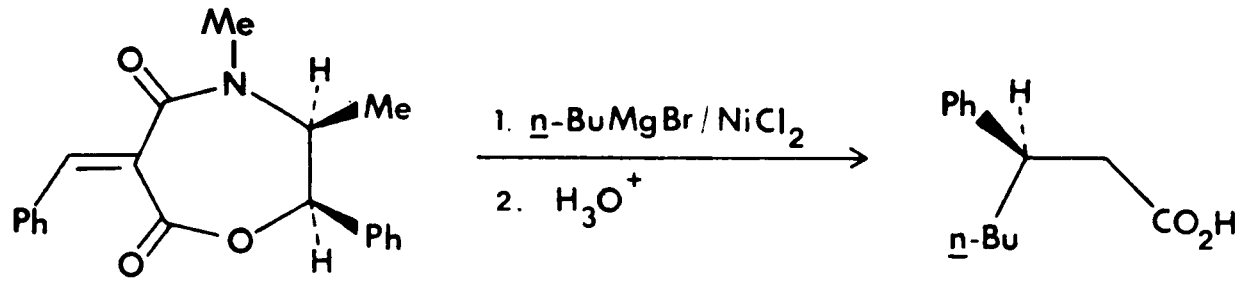
The generally low levels of asymmetric induction obtained using this approach illustrate the difficulty in developing a system that differentiates to any high degree between the two possible diastereotopic pathways of attack on the prochiral faces of the α,β-unsaturated carbonyl system. The approach which has been far more successful and consequently received much more attention, introduces a chiral auxiliary group into the α,β-unsaturated carbonyl compound. In practice, it is found easier to fix the conformation of this system using chelation and steric effects in such a manner as to direct the nucleophile selectively to the least hindered of the diastereotopic faces.

3. Chiral α,β-unsaturated carbonyl derivatives

When part or all of the α,β-unsaturated carbonyl moiety is contained in a ring, good stereocontrol can be achieved in the formation of the β-centre and, in some cases, the α-centre. A recent total synthesis of (-)-megaphone 99, described by Koga, used a one-pot tandem asymmetric Michael addition-alkylation reaction of a chiral α-alkylidene-γ-butyrolactone 98 to generate the desired relative and absolute stereochemistry. The two new carbon-carbon bonds were formed away from the bulky trityl group.[115]

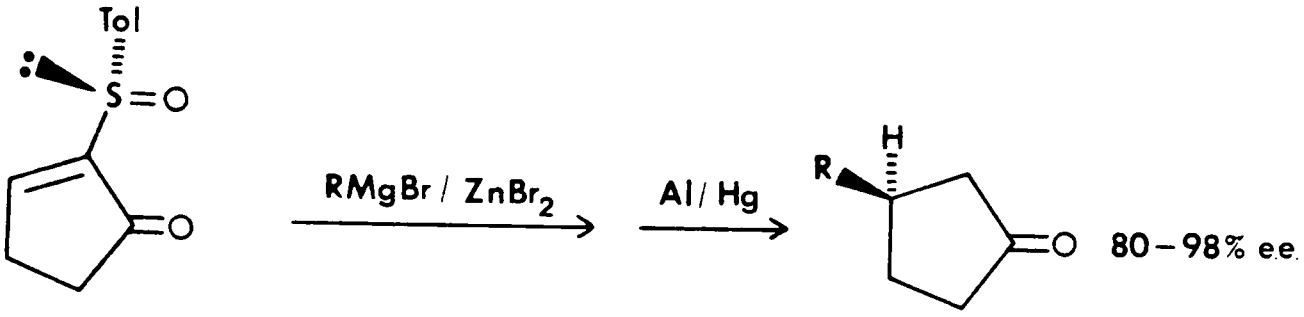


Chiral oxazepines 100 derived from (l)-ephedrine undergo Michael addition by Grignard reagents from the least hindered face of the double bond. Hydrolysis of the adducts gave β-alkanoic acids with 58-99% e.e. Each antipode was formed in high optical purity from the respective E and Z isomers of the oxazepine.[116]



100

Posner [117] has widely reported the Michael addition reaction of Grignard reagents to optically pure 2-(arylsulphinyl)-2-cycloalken-2-ones in the presence of zinc bromide. Reduction gave R-3-substituted cycloalkanones in high optical purity.[118]



The reaction is believed to occur via a rigid chelate in which the zinc ion is bound to the oxygens of the carbonyl and sulphinyl groups. Nucleophilic attack to one face of the double bond away from the bulky tolyl group gives the absolute stereochemistry observed in the product (figure 14).

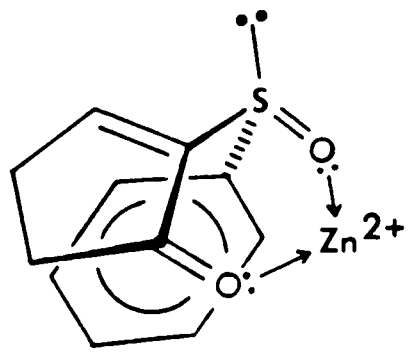
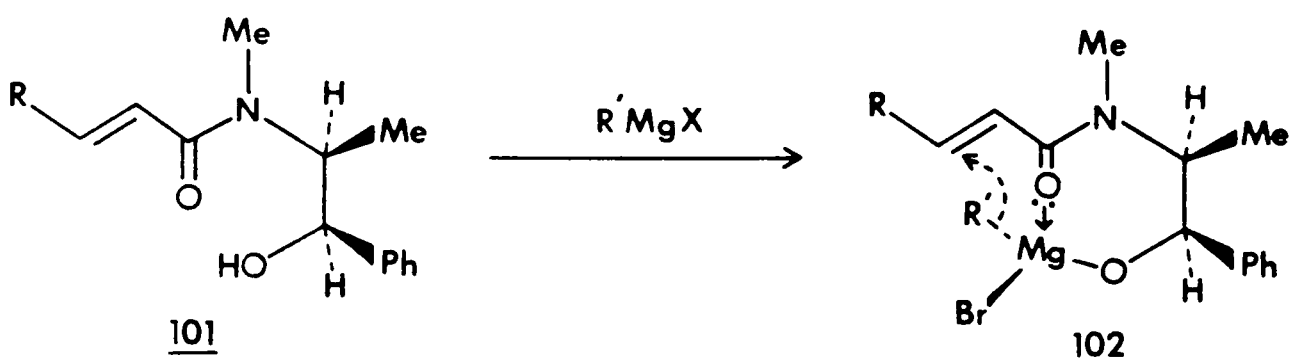


Figure 14: Chelation control in the Michael reaction of 2-cyclopenten-2-one sulphoxide.

In the absence of added metal ions, reaction occurs via the conformation in which the dipoles of the carbonyl and sulphinyl groups are in opposite directions to give the product with the S configuration with up to 98% e.e.[119]

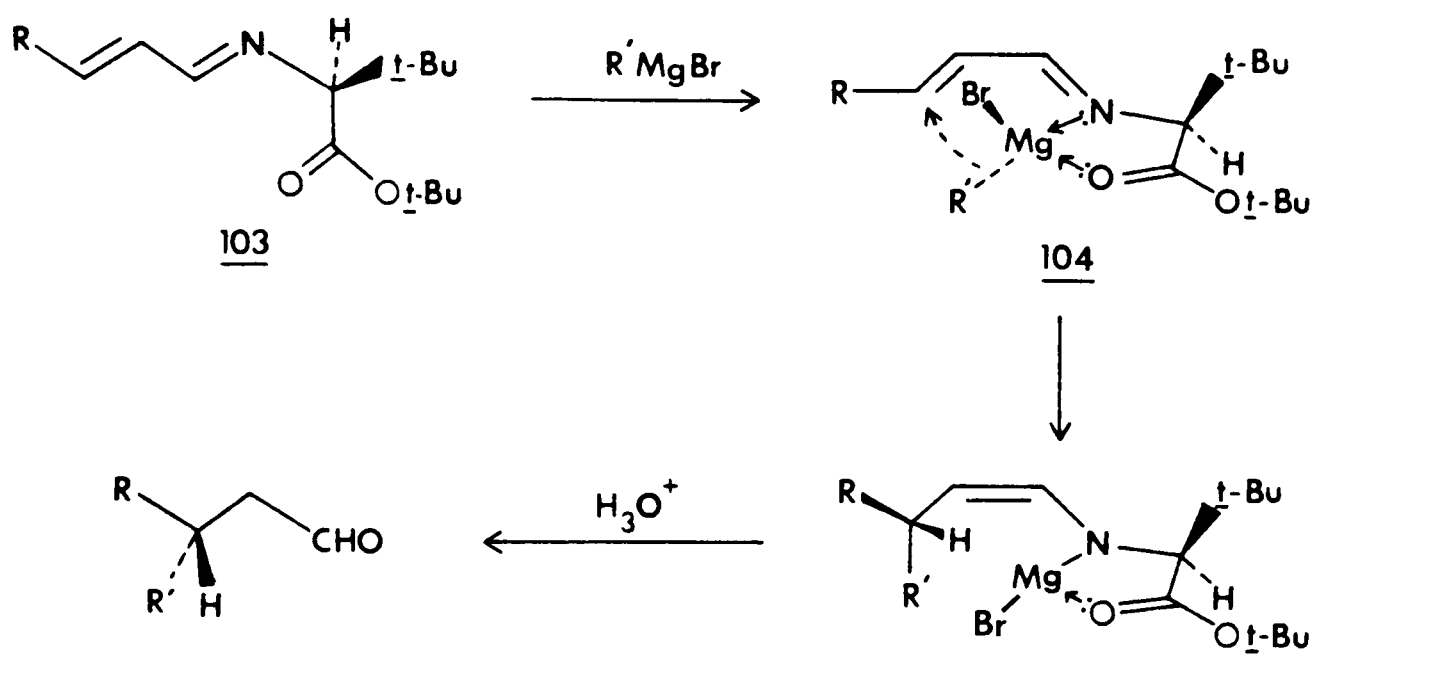
The formation of a temporary chelate complex is a commonly adopted strategy for achieving stereochemical control in Michael additions to acyclic systems. Thus, β-substituted alkanoic acids with up to 99% e.e. were obtained from the conjugate addition of Grignard reagents to α,β-unsaturated amides 101 derived from (1)-ephedrine. Nucleophilic attack away from the methyl and phenyl groups in a chelate complex of the type 102 gives the absolute stereochemistry observed in the acids.[120]



Similar chiral acids were obtained in moderate to excellent e.e.'s from amides utilising either (S)-proline [121] or (S)-γ-trityloxymethyl-γ-butyrolactams [122] as the chiral auxiliary group.

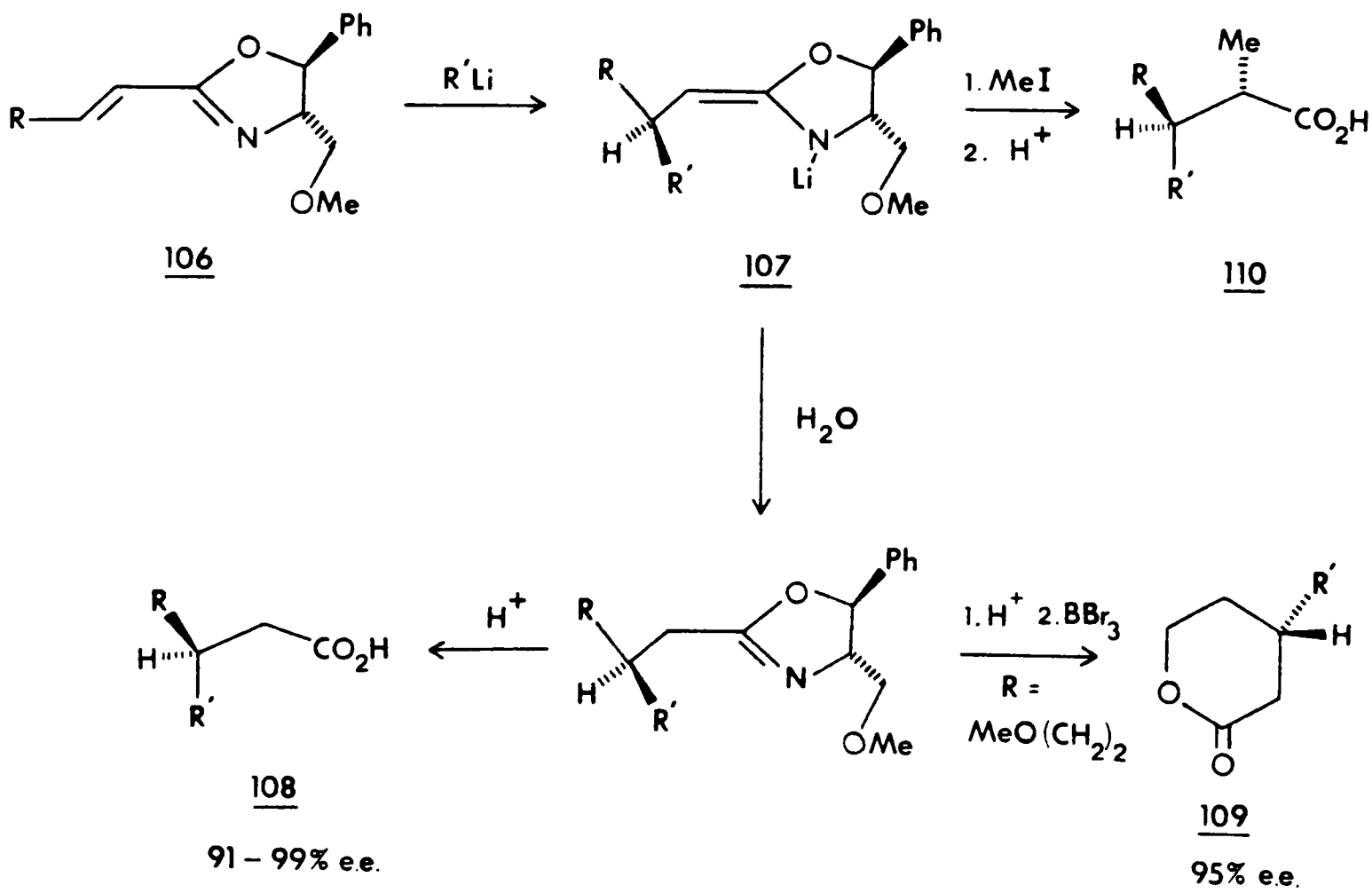
In many instances, chiral α,β-unsaturated carbonyl equivalents have found use in the asymmetric synthesis of β-substituted carbonyl compounds. In particular, the method developed by Koga for the Michael addition of Grignard reagents to α,β-unsaturated aldimines 103 of t-leucine-t-butyl ester gave, in some cases, β-substituted aldehydes with high e.e's.[123] Again, a chelate model 104 is invoked to rationalise the diastereo-

selectivity and absolute configuration of the products. In the asymmetric synthesis of the antileukemic sesquiterpene (+)-ivalin, trapping out the intermediate enamine 105 with methyl iodide led to a mixture of epimers at the α-centre.[124] The method was also applied to the diastereoselective and enantioselective synthesis of 2-substituted and 1,2-disubstituted cycloalkanecarboxaldehydes.[125]



103 104 105

Meyers has utilised the highly diastereoselective addition of alkyllithiums to chiral oxazolines 106 to synthesise chiral β-substituted



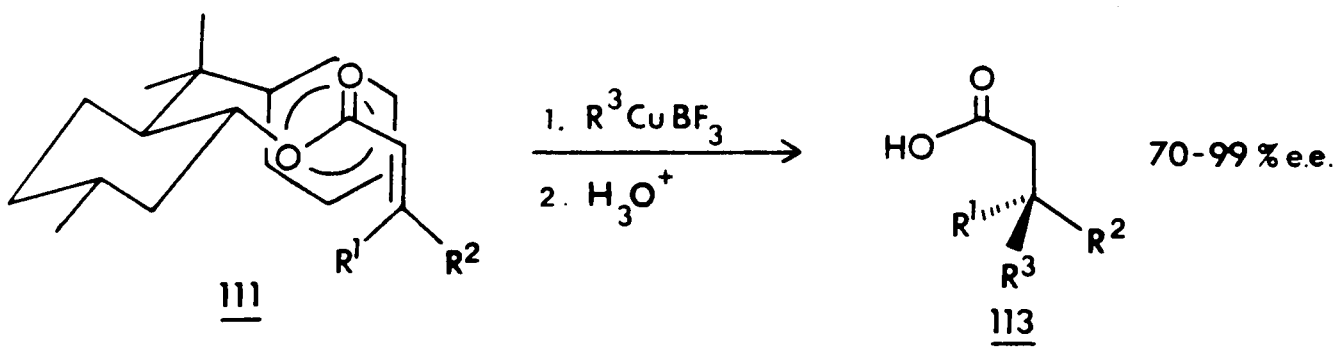
106 107 110 108 109

alkanoic acids 108 and δ-lactones 109.[95,126] Alkylation of the initially formed azaenolate 107 with methyl iodide, in the presence of TMEDA, proceeded with high diastereoselectivity. Hydrolysis afforded the corresponding chiral 1,2,2-trisubstituted acids 110.[127]

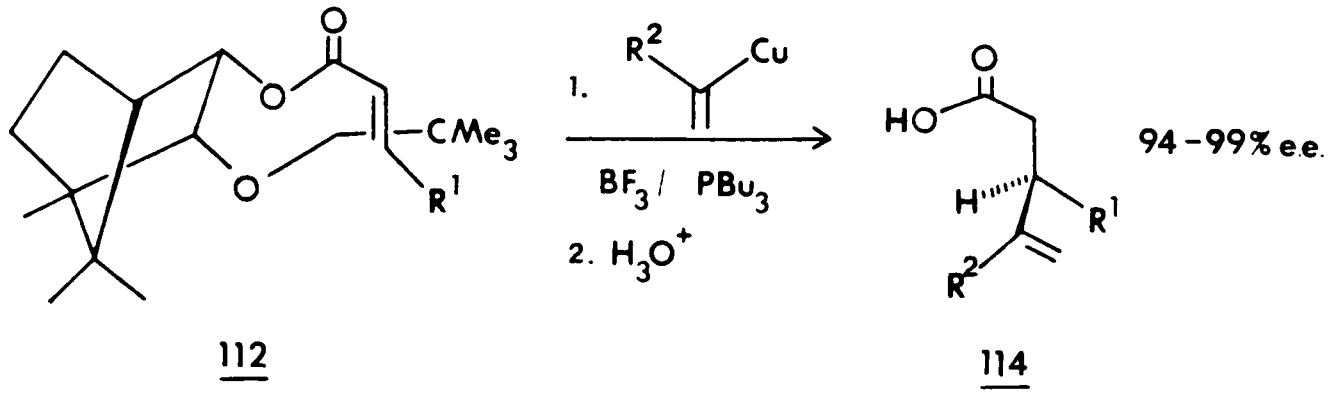
Similarly, asymmetric conjugate addition of alkyllithiums to chiral naphthyloxazolines followed by stereoselective trans alkylation gave 1,1,2-trisubstituted-1,2-dihydronaphthalenes with high e.e.[128]

β-Substituted carbonyl compounds have also been prepared with moderate e.e's by the Michael addition reaction of chiral oxazolidines derived from (l)-ephedrine,[129] chiral α,β-unsaturated acetals[130] and chiral aminals.[131]

In a different approach, Oppolzer has used the steric effects of conformationally biased menthol- and camphor-derived α,β-unsaturated carbonyl compounds to direct nucleophiles to one of the diastereotopic faces of the carbon-carbon double bond.[132] For example, the reaction between alkyl cuprates and the chiral derivatives 111 [133] and 112 [134] gave, after hydrolysis, β-alkanoic acids 113 and 114 respectively, with typically high e.e's. The latter reaction was used in the asymmetric synthesis of the California Red Scale Pheromone. In both cases, nucleophilic attack is considered to take place from the least sterically hindered face of the double bond in the conformations shown.



111 113



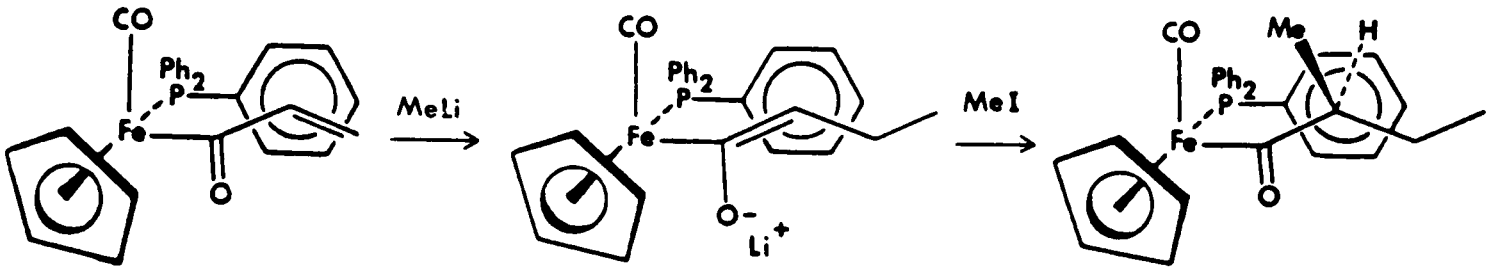
112 114

Helmchen has reported the use of similar substrates.[135]

4. Summary

The asymmetric Michael addition of carbon nucleophiles to E α,β-unsaturated carbonyl compounds containing a chiral auxiliary group provides a general route to chiral carbonyl compounds. The major limitation with present methods is that, generally, stereochemical control is only exerted over the formation of the β-centre. Few attempts have been made to control the stereochemistry at the α-centre. Furthermore, the usual hydrolytic removal of the chiral auxiliary group is incompatible with the retention of stereochemistry at the α-centre. The enantioselectivities in the Michael additions described above, although excellent in some cases, are found to be strongly dependent both on the nature of the substrate and the nucleophile. It was of considerable interest therefore to investigate whether the analogous E α,β-unsaturated acyl ligands bound to the chiral auxiliary [$(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)$] would undergo a similar Michael addition type of reactivity with alkyllithium reagents, in contrast to the dienolate formation displayed by the Z isomers. According to our model, in which we propose initial coordination of the alkyllithium to the acyl oxygen of the α,β-unsaturated acyl ligand in the cisoid conformation, the γ-protons are held at a greater distance from the alkyllithium in the E isomer than in the corresponding Z isomer. 1,4-Conjugate addition to the more proximate β-centre in the E isomer might therefore be expected to compete with γ-deprotonation.

Our preliminary studies had shown that successive addition of methyllithium and methyl iodide to the acryloyl complex 60 in THF at -78°C gave the RS,SR diastereoisomer of the s-butyl acyl complex 17 with a diastereoselectivity of greater than 30:1.[67]



60 19 17

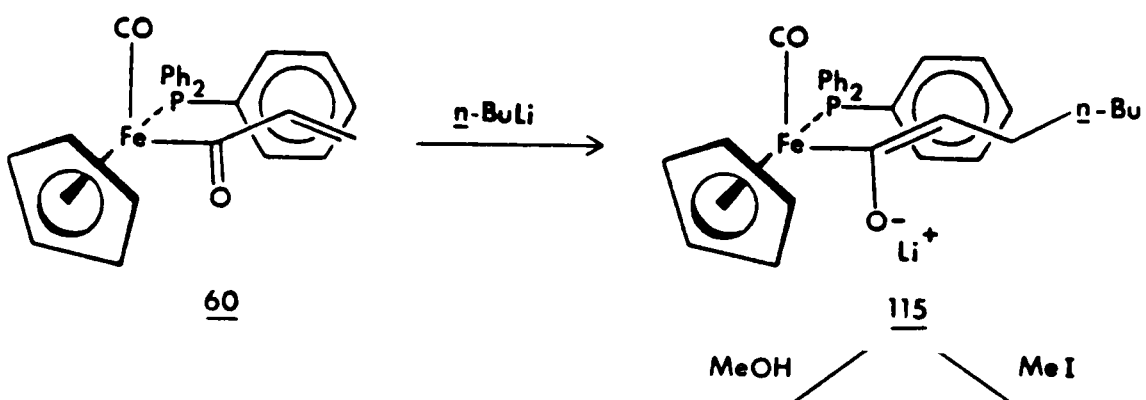
Complex 17 was believed to have arisen from stereoselective methylation of E enolate 19 [40] in the anti (CO to acyl) conformation from the face away from the triphenylphosphine ligand. It was proposed that E enolate 19 itself was generated by Michael addition of methyllithium to the α,β-unsaturated acyl complex 60 adopting the cisoid and anti (CO to acyl) conformation. The reaction was also accompanied by the formation of a mixture of dimeric acyl complexes which were not further characterised, but were presumed to have arisen from Michael addition of enolate 19 to a second molecule of complex 60.

With this example as a lead, our aim was to develop the Michael addition-alkylation reactions of the acryloyl complex 60 and to extend them to E α,β-unsaturated iron acyl complexes. It was hoped that the iron centre would exert both high diastereoselective and enantioselective control over the formation of new chiral centres at the α- and/or β-positions. Mild oxidation would then give chiral α- and/or β-substituted carboxylic acid derivatives.

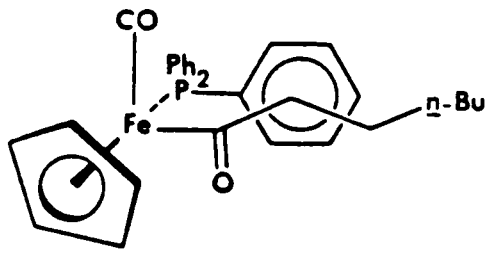
II. Michael addition of alkyllithiums to and subsequent diastereoselective alkylations of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ 60

In order to investigate further the Michael addition reactivity of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ 60, a THF solution of the complex was added dropwise to n-butyllithium in THF at -78°C to generate a dark red

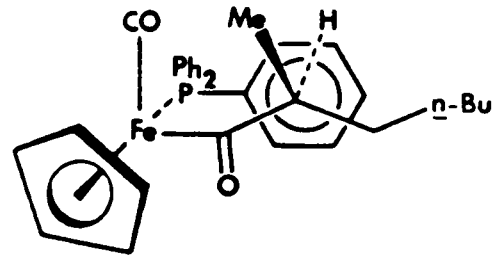
solution characteristic of the formation of an enolate. An inverse addition procedure was adopted in an attempt to minimise the formation of any dimeric species by always maintaining an excess of n-butyllithium during the addition. Quenching with methanol and work-up gave the hexyl acyl complex 116 in only 35% yield together with dimeric acyl complexes which were not further characterised. Thus, complex 60 was still competitively reacting with enolate 115, generated by Michael addition of n-butyllithium to complex 60. Any remaining enolate 115 gave complex 116 upon protonation.



60 115



116



117

By adding a more dilute THF solution of complex 60 over a longer period of time and then quenching with methyl iodide, the α-methyl hexyl-acyl complex 117 (62%) was formed to the exclusion of any other acyl complexes and with a diastereoselectivity of 75:1. The RS,SR relative configuration between the iron and α-centres was deduced from the chemical shift (δ1.00) of the α-methyl doublet in the ^{1}H n.m.r. spectrum.[43] The formation of the RS,SR diastereoisomer 117 is consistent with methylation of E enolate 115 in the anti (CO to acyl) conformation from the face away from the triphenylphosphine ligand. Enolate 115 must be generated by

Michael addition of n-butyllithium to complex 60 in the cisoid and anti (CO to acyl) conformation.

Experimental evidence therefore suggests that complex 60 only undergoes Michael addition in the cisoid conformation and not the alternative transoid conformation. This may be rationalised in terms of initial coordination of the alkyllithium to the acyl oxygen of 60. Examination of molecular models shows that the β-centre is much less distant from the coordinated alkyllithium when the acyl ligand adopts a cisoid conformation than when it adopts the alternative transoid arrangement (figure 15). The nucleophile is therefore delivered preferentially to the cisoid conformation and away from the triphenylphosphine ligand to generate an E enolate.

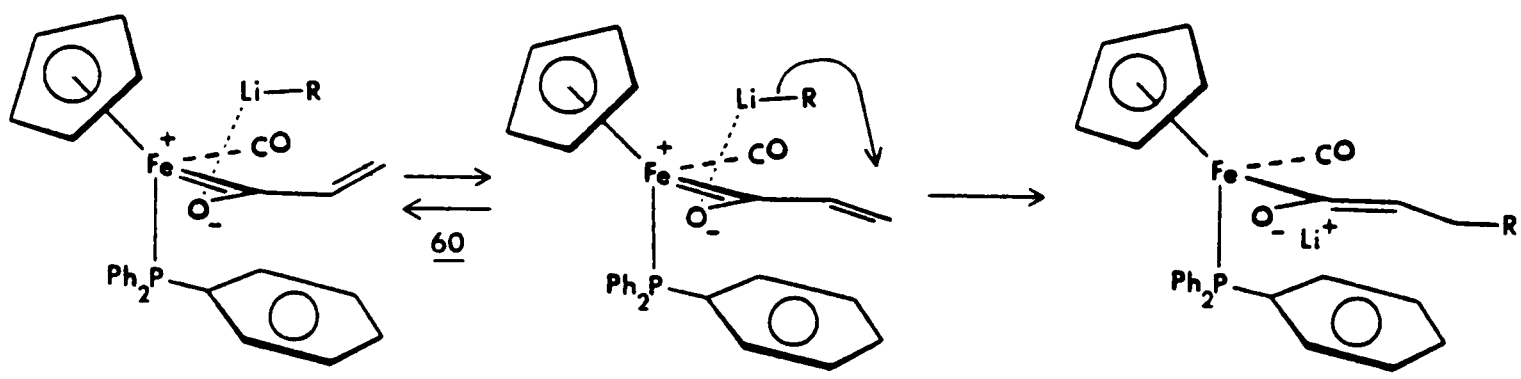


Figure 15: Delivery of an alkyllithium to complex 60 in the cisoid conformation.

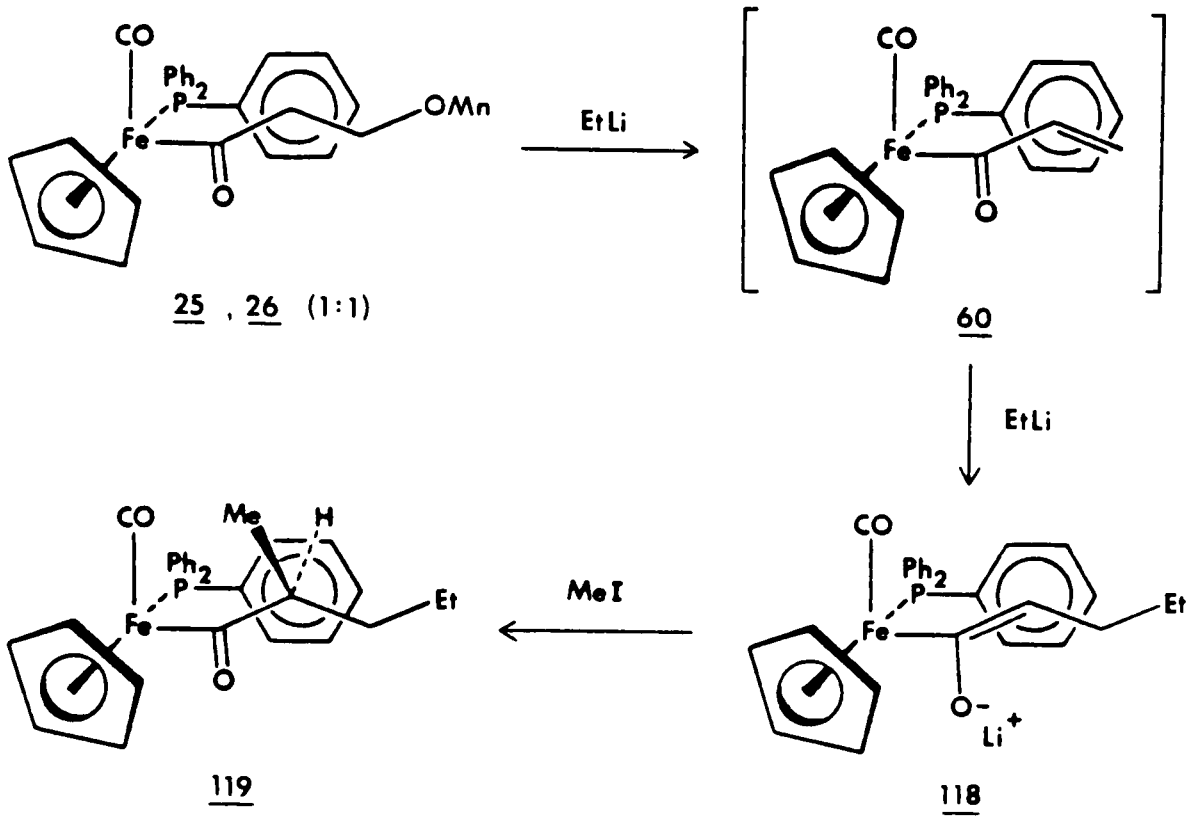
Preventing this initial coordination by addition of a lithium complexing agent, for example TMEDA, may result in Michael addition of n-butyllithium occurring to both cisoid and transoid conformations to generate E and Z enolates respectively. Subsequent methylation of the anti (CO to acyl) conformation of the enolate from the least hindered face would lead to reduced diastereoselectivity in the formation of the RS,SR diastereoisomer 117. However, when complex 60 was added to a THF solution of n-butyllithium containing two equivalents of TMEDA and the reaction quenched with methyl iodide, the RS,SR diastereoisomer 117 was formed with

an equally high diastereoselectivity. This suggests that either complex 60 exists exclusively in the cisoid conformation, or that nucleophilic attack by n-butyllithium at the β-carbon in the transoid conformation is disfavoured. Molecular models reveal that this latter pathway is subject to steric interactions between the incoming nucleophile and the cyclopentadienyl ligand.

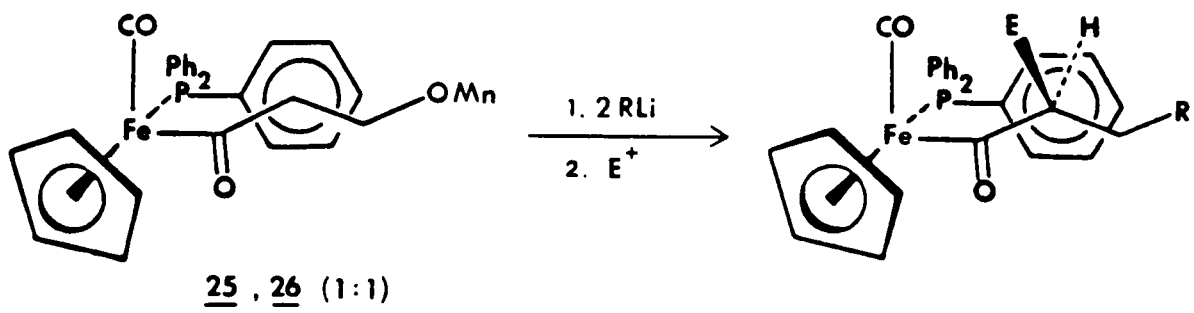
It has already been shown that the non-nucleophilic base, sodium hydride, promotes the elimination of (1)-menthol from both diastereoisomers, 25 and 26, of the β-menthoxy complex {$(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)$-$COCH_2CH_2O$[(R)-menthyl]} to give the acryloyl complex 60. On this basis, it was anticipated that treatment of complexes 25 and 26 with two equivalents of an alkyllithium followed by an electrophile would lead directly to the Michael addition products. Elimination of (1)-menthol from complexes 25 and 26 induced by the first equivalent of the alkyllithium reagent would generate complex 60 in situ. Subsequent Michael addition to 60 of the second equivalent followed by alkylation would then give the desired Michael adducts.

Addition of two equivalents of ethyllithium to a 1:1 mixture of the diastereoisomers 25 and 26 in THF at -78°C generated an enolate as indicated by the formation of an intense red-coloured solution. Addition of methyl iodide and work-up gave complex 119 (55%), identified by comparison with an authentic sample,[136] together with uncharacterised dimeric species. Complex 119 was formed with a diastereoselectivity of greater than 100:1 as determined by ^1H n.m.r. spectroscopy. The major α-methyl doublet at δ1.00 established the relative configuration between the iron and α-centres as RS,SR [43]. Presumably, complex 119 is derived from methylation from the least hindered face of E enolate 118, itself generated by Michael addition of ethyllithium to complex 60 in the

cisoid and anti (CO to acyl) conformation. Complex 60 must be generated in situ from ethyllithium-induced elimination of (1)-menthol from complexes 25 and 26.



The 1:1 mixture of complexes 25 and 26 were also treated with two equivalents of n-butyllithium, t-butyllithium and phenyllithium and, in each case, the enolate generated was separately quenched with methanol and methyl iodide. In the reaction with n-butyllithium, an inverse addition procedure was employed to avoid formation of any dimeric complexes. No such precautions were necessary for t-butyllithium or phenyllithium as only monomeric complexes were formed after successive addition of the lithium reagent and the electrophile. This suggests that in these cases, the enolate generated by Michael addition to the intermediate acryloyl complex 60 is too sterically conjested to react with a second molecule of complex 60. The yields and diastereoselectivities of these reactions are given in Table 7.



Complex	R	E^+	Yield (%)	RS,SR : RR,SS [a] diastereoselectivity
116	n-Bu	H	69	--
120	t-Bu	H	78	--
121	Ph	H	60	--
119	Et	CH_3	55	>100:1
117	n-Bu	CH_3	73	>100:1
122	t-Bu	CH_3	49	30:1
123	Ph	CH_3	65	>100:1

a. Determined by 300 MHz ^1H n.m.r. spectrscopy.

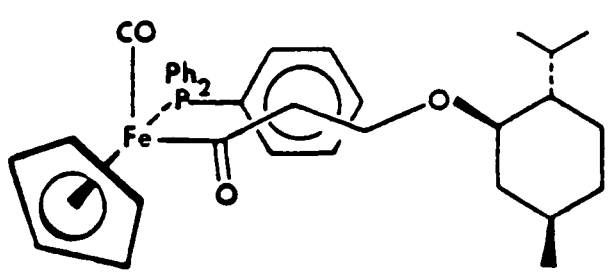
Table 7: Yields and diastereoselectivities for the formation of Michael adducts from complexes 25 and 26.

The diastereoselectivities of the above reactions are found generally to be higher than those for deprotonation of the appropriate acyl ligand followed by methylation (typically 30:1 [137]). This reflects the greater propensity for the E enolate to be formed by Michael addition of the alkyllithium to the α,β-unsaturated acyl ligand in the cisoid conformation than by simple deprotonation of the acyl ligand.

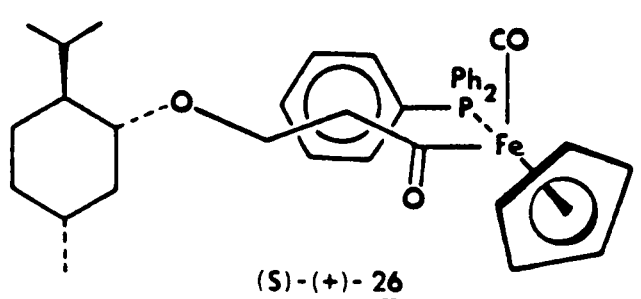
The 1:1 mixture of β-menthoxy complexes can be resolved into the diastereoisomerically pure complexes (R)-25 and (S)-26 by flash chromatography on silica (chapter 2). It was envisaged that elimination of (l)-menthol by an alkyllithium reagent would generate the optically pure acryloyl complexes (R)-60 and (S)-60 respectively, in situ. Michael addition and diastereoselective alkylation would then give the corres-

ponding RS and SR α-substituted acyl complexes. Complexes (R)-25 and (S)-26 were therefore individually treated with two equivalents of ethyllithium followed by methyl iodide. Work-up and crystallisation gave (RS)-119, $[\alpha]_D^{20}$ -237.0° (c 0.07, C_6H_6) and (SR)-119, $[\alpha]_D^{25}$ +238.0° (c 0.10, C_6H_6) respectively, each with a diastereoselectivity of greater than 100:1.

Since the starting complexes, of known absolute configuration, were diastereoisomerically pure by 300 MHz ^1H n.m.r. spectroscopy and the asymmetric carbon-carbon bond formation proceeded with greater than 100:1 diastereoselectivity, the optical purity of (RS)-119 and (SR)-119 must be in excess of 100:1. They must also have the absolute configurations as stated.

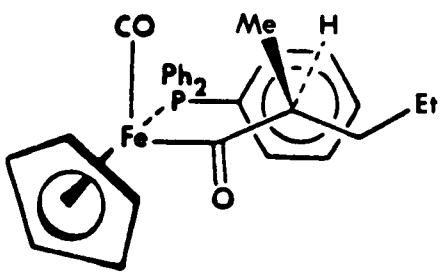


(R)-(-)-25



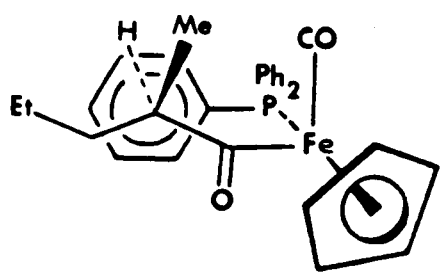
(S)-(+)-26

1. 2 EtLi | 2. MeI



(RS)-119

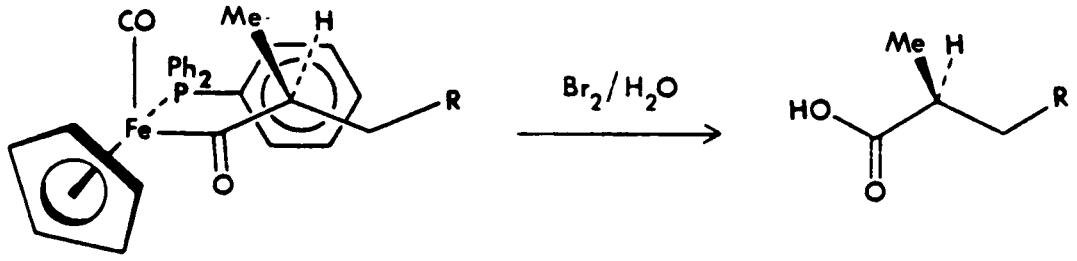
1. 2 EtLi | 2. MeI



(SR)-119

From these reactions, it can be concluded that the β-menthoxy complexes $\{(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_2O[(R)\text{-menthyl}]\}$, either as a 1:1 mixture or as resolved diastereoisomers, are synthetically equivalent to the racemic or optically pure acryloyl complexes respectively. They undergo reaction with a range of alkyllithium reagents, even t-butyllithium, to provide convenient one-pot syntheses of α-substituted acyl complexes with very high diastereoselectivity.

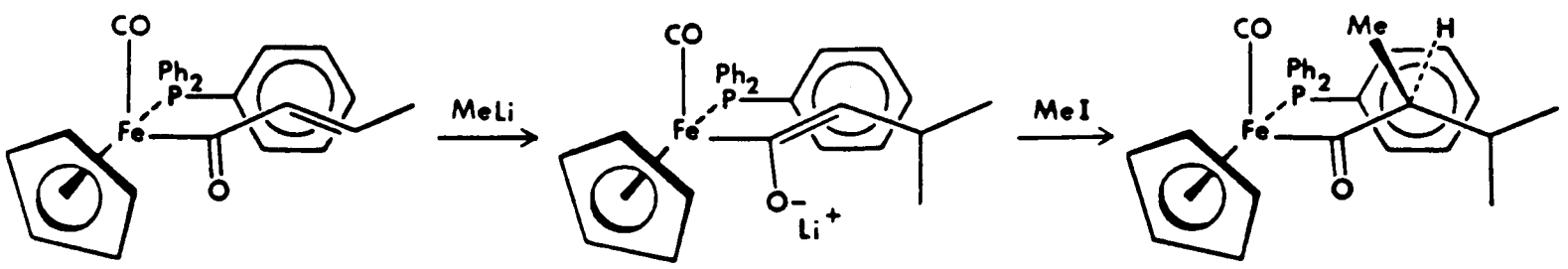
In order to demonstrate that the above Michael adducts can be converted to the corresponding carboxylic acid derivatives, bromine was added to wet THF solutions of the racemic α-methyl butyl complex 119 and the racemic α-methyl hexyl acyl complex 117. Work-up gave 2-methylpentanoic acid and 2-methylheptanoic acid in unoptimised yields of 39% and 36% respectively.



119 R = Et
117 R = n-Bu

III. Diastereoselective tandem Michael addition-alkylation reactions of E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$][69,138]

In an initial experiment, methyllithium was added to the E crotonyl complex 33 in THF at -78°C to give an enolate as indicated by the formation of a dark red solution. Quenching with methyl iodide gave a single product identified as complex 125 (60%) by the presence of three methyl doublets at δ0.91, 0.53 and 0.33 in the ^{1}H n.m.r. spectrum. Good stereochemical control was observed in the formation of the α-centre (>100:1). The RS,SR relative configuration was assigned to complex 125 on the basis of the α-methyl doublet (confirmed by decoupling experiments) at δ0.91 in the ^{1}H n.m.r. spectrum.[43]



33 124 125

The formation of complex 125 is consistent with methylation of E enolate 124 in the anti (CO to acyl) conformation occurring from the face away from the triphenylphosphine ligand. Enolate 124 is derived from Michael addition of methyllithium to the E crotonyl ligand in the cisoid and anti (CO to acyl) conformation. This reaction may again be rationalised in terms of initial coordination of methyllithium to the electron-rich acyl oxygen in complex 33, followed by delivery to the ligand in the cisoid and anti (CO to acyl) conformation (figure 16).

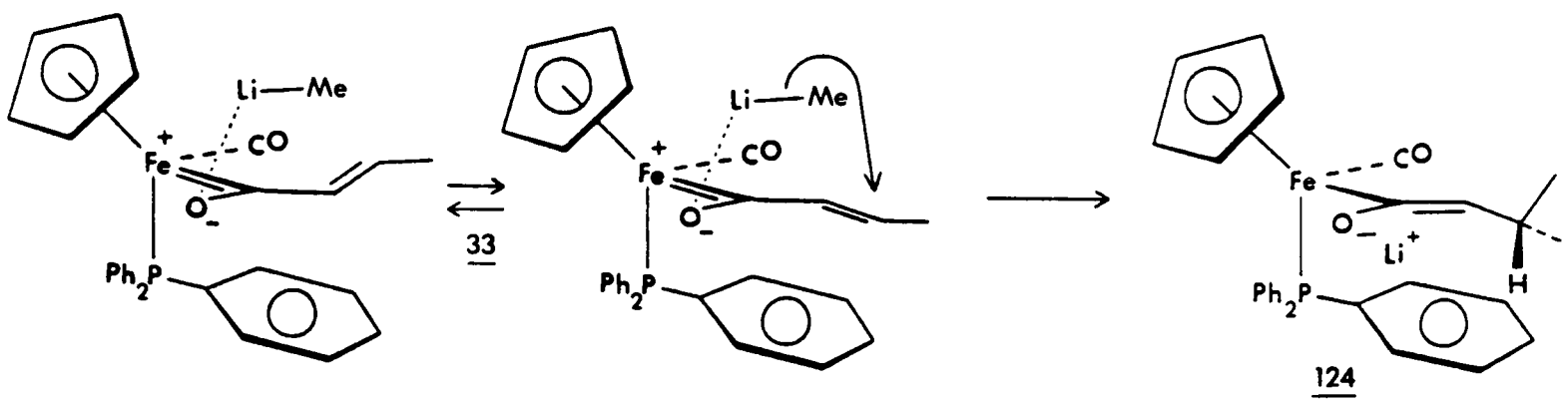


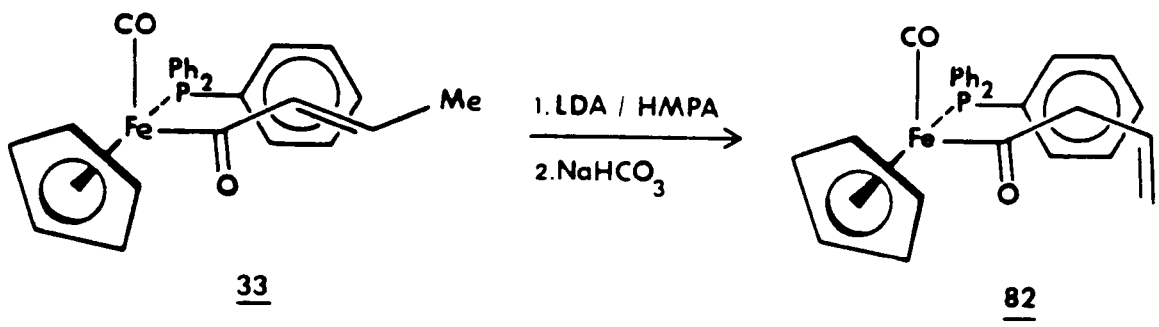
Figure 16: Delivery of methyllithium to complex 33 in the cisoid conformation.

Michael addition could conceivably occur through the corresponding transoid conformation. However, examination of molecular models shows that the β-centre in the transoid conformation is much more distant from the coordinated methyllithium than the same centre in the cisoid arrangement (figure 16). The complex derived from the Z enolate therefore consitutes less than 1% of the yield of (RS,SR)-125.

Similarly, the acidic γ-protons in both conformations of the E crotonyl ligand are more distant from the coordinated methyllithium than the β-centre in the cisoid conformation. Consequently, no products derived from the corresponding lithium dienolate are observed.

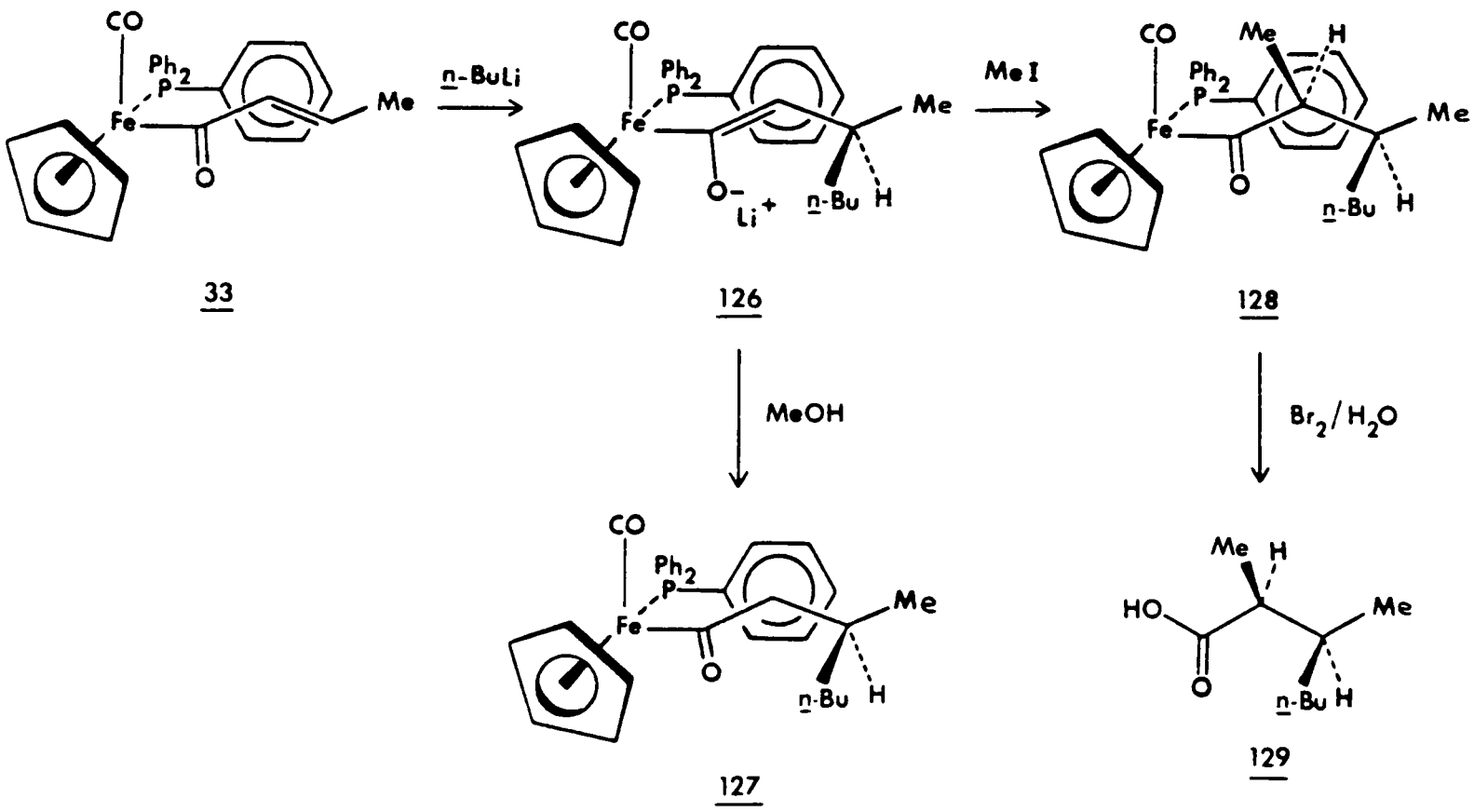
Further evidence for this coordination model was provided by Liebeskind in a recent communication. Treatment of the E crotonyl

complex 33 with LDA in the presence of HMPA followed by aqueous sodium bicarbonate gave the β,γ-unsaturated complex 82. The product was that derived from regioselective α-protonation of the lithium dienolate formed by exclusive γ-deprotonation of complex 33. The presence of HMPA prevents coordination of methyllithium to the acyl oxygen and leads to deprotonation of the acidic γ-protons by the alkyllithium in a standard deprotonation of the E isomer.[139]



33 82

Complex 33 also underwent Michael addition with n-butyllithium in THF at -78°C. Quenching the enolate with methanol and work-up gave the β-methyl hexyl acyl complex 127 (82%) with a diastereoselectivity of in excess of 100:1, as deduced by ^{1}H and ^{13}C n.m.r. spectroscopy.



33 126 128

127 129

Evidently formation of a new chiral centre at the β-position proceeds with a high degree of stereoselectivity. If it is assumed that 1,4-addition is occurring to the E crotonyl ligand in the cisoid and anti (CO to acyl) conformation away from the triphenylphosphine ligand as above, then the relative configuration between the iron and β-centres in complex 127 may be assigned as RS,SR.

Methylation of enolate 126, generated in an identical manner, led to the isolation of the α,β-dimethyl hexyl acyl complex 128 (93%) in which two new chiral centres had been generated at the α- and β-positions. Out of the four possible diastereoisomers of complex 39, ^{1}H, ^{13}C and ^{31}P n.m.r. spectroscopy revealed that one had been formed to essentially the exclusion of the other three, the diastereoselectivity being greater than 100:1:1:1.† The relative configuration between the iron and the α-centre was established as RS,SR from the chemical shift of the α-methyl doublet at δ0.98 in the ^{1}H n.m.r. spectrum.[43] That between the α- and β-centres was deduced as SS,RR by oxidative decomplexation of complex 128, with bromine in aqueous THF, to the known erythro carboxylic acid 129.[140] The isolation of the diastereoisomerically pure erythro isomer confirmed that removal of the chiral iron auxiliary was not accompanied by epimerisation at either the α- or β-centre. The relative configurations in complex 128 were therefore established as RSS,SRR. The formation of complex 128 is consistent with Michael addition of n-butyllithium occurring to the E crotonyl ligand in the cisoid and anti (CO to acyl) conformation from the least hindered face. Methylation of the resulting E enolate 126, in the anti (CO to acyl) conformation, again occurs away from the triphenylphosphine ligand to give the observed product.

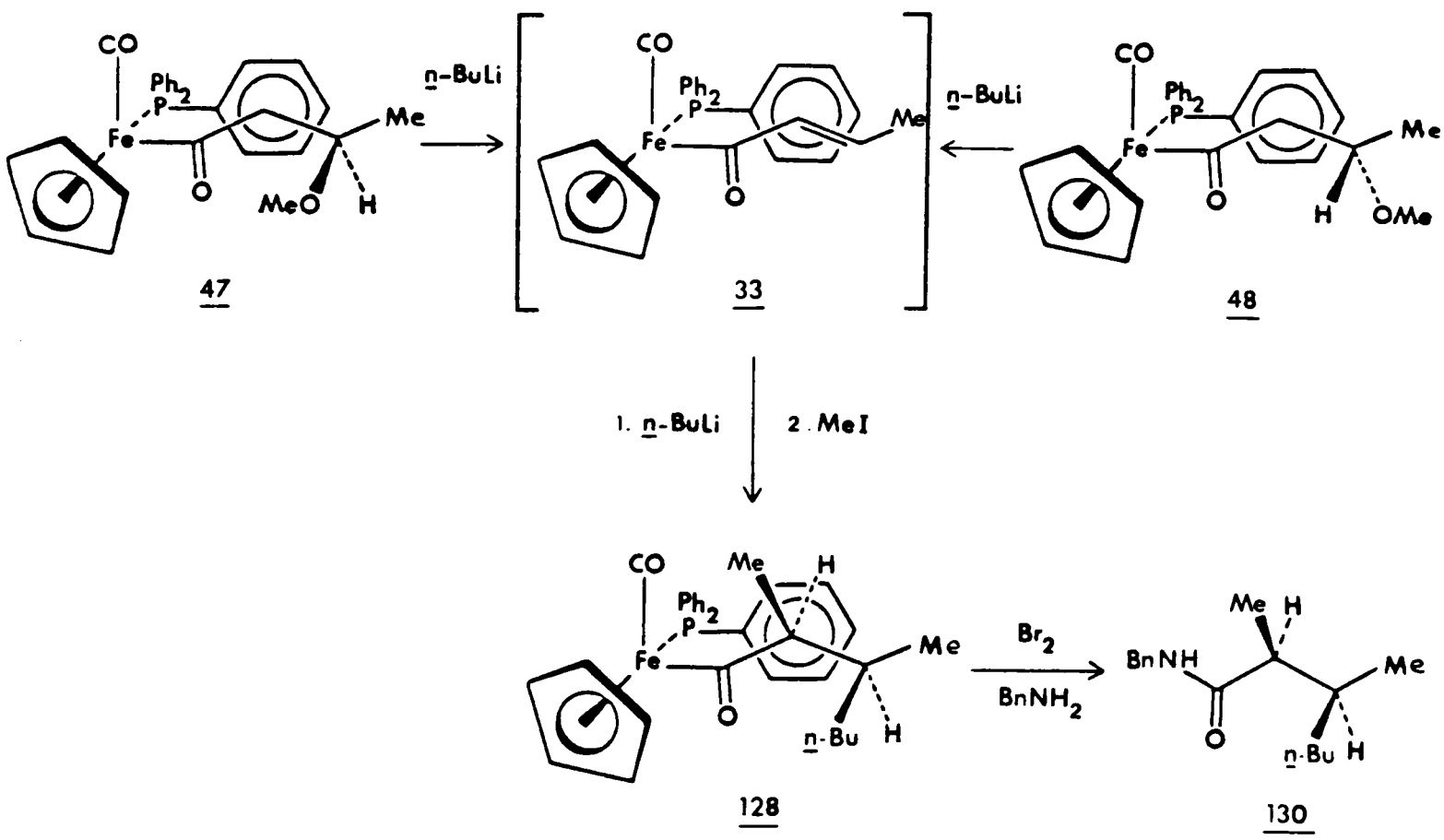
† The 300 MHz ^{1}H n.m.r. spectrum was of sufficient quality that the ^{13}C satellites due to the major diastereoisomer were clearly visible, thus providing an internal standard for the diastereoisomeric purity.

Since the reaction of complex 33 with n-butyllithium and then methanol to give complex 127 proceeded via the same enolate 126, the relative configuration in 127 can now be unambiguously assigned as RS,SR.

The E-crotonyl complex 33 was found not to form Michael adducts with sodium methoxide nor the lithium derivatives of acetaldehyde, ethyl propionate or pent-1-yne. Presumably in these cases, Michael addition is reversible and the enolate that would be generated is thermodynamically unstable with respect to complex 33 and the anion.

In view of the elimination-Michael addition reactivity shown by both diastereoisomers 25 and 26 of the β-menthoxy acyl complex when treated with two equivalents of an alkyllithium reagent, it was anticipated that similar reactivity would be shown by both diastereoisomers 47 and 48 of the β-methyl-β-methoxy acyl complex.

Addition of two equivalents of n-butyllithium to either diastereoisomer 47 or 48 of the β-methyl-β-methoxy acyl complex (each used as a 7:1 diastereoisomeric mixture) in THF at -78°C generated an enolate.

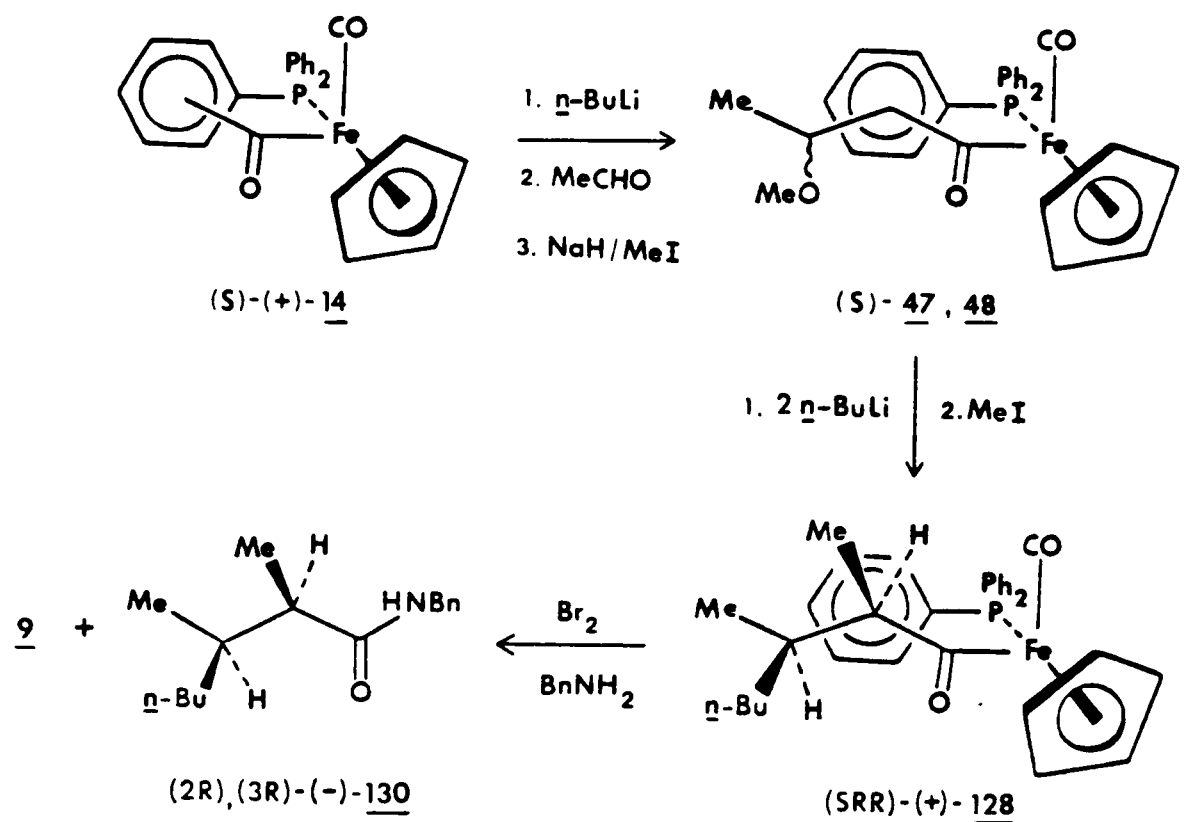


Quenching with methyl iodide gave, in both cases, the(RSS,SRR)-α,β-dimethyl hexyl acyl complex 128 as a single diastereoisomer (diastereoselectivity >100:1:1:1). The product from each reaction was identical to that obtained from Michael addition of n-butyllithium to the E crotonyl complex 33 followed by methylation of the enolate generated. Presumably, the first equivalent of n-butyllithium promotes, in both cases, elimination of methanol via an E1CB mechanism similar to that described in chapter 3, generating complex 33 in situ. Subsequent diastereoselective Michael addition of the second equivalent of n-butyllithium followed by methylation gives(RSS,SRR)-128.

The yield of the carboxylic acid derivative from the oxidative decomplexation of complex 128 was greatly improved by isolation of the corresponding amide. Thus, addition of bromine to complex 128 in dichloromethane at -40°C followed by benzylamine gave the diastereoisomerically pure erythro-N-benzyl-2,3-dimethylheptanamide 130 in 74% yield. Again, decomplexation had occurred with complete retention of stereochemistry at both the α- and β-centres.

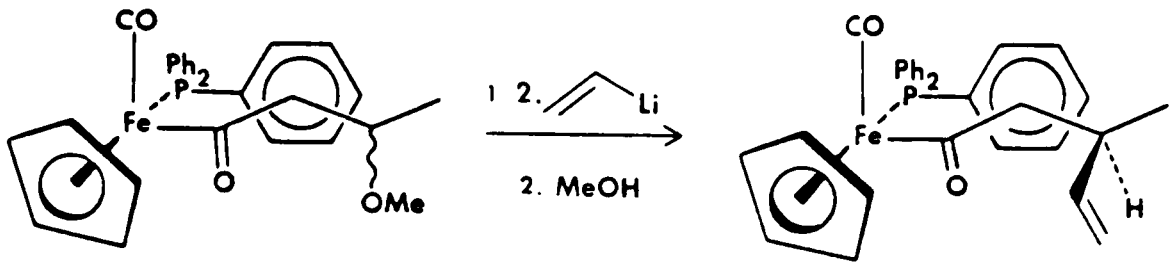
Application of the above elimination-Michael addition and decomplexation reactions to resolved acyl complexes would enable erythro-N-benzyl-2,3-dimethylheptanamide 130 to be prepared in optically active form.

The optically pure (S)-(+)-methyl acyl complex 14 [58] was successively treated with n-butyllithium and acetaldehyde. The essentially 1:1 mixture of β-hydroxy complexes was O-methylated and the resulting β-methoxy complexes (S)-47 and (S)-48 treated with two equivalents of n-butyllithium followed by methyl iodide. Work-up gave (SRR)-(+)-128, $[\alpha]_D^{24}$ +228.0° (c 0.29, C_6H_6), with a diastereoselectivity of greater than 100:1:1:1. The ^1H n.m.r. spectrum of (SRR)-128 was identical to that of (RSS,SRR)-128 prepared above. Decomplexation of (SRR)-128 with bromine in the presence of benzylamine occurred to give (2R),(3R)-(-)-N-benzyl-2,3-dimethylheptanamide 130, $[\alpha]_D^{24}$ -5.3° (c 1.23, C_6H_6), in 81% yield.



Decomplexation had again occurred without epimerisation at either the α- or β-centre. Since (SRR)-128 was derived from optically pure (S)-(+)-14 and was formed with a diastereoselectivity of greater than 100:1:1:1, it follows that (2R),(3R)-130 must have an optical purity of greater than 100:1 and the absolute configuration as stated. Additionally, the iron bromide 9 was isolated from the reaction mixture. It was found to have a very small optical rotation and, although complex 9 is not known in optically pure form, it appears that decomplexation with bromine causes racemisation at the iron centre. A similar result was obtained in the decomplexation of related iron acyl complexes with iodine.[34]

Addition of two equivalents of vinyllithium to a 1:1 mixture of the racemic complexes 47 and 48 promoted similar elimination-Michael addition behaviour. Protonation with methanol gave the β-vinyl complex 131 with a 50:1 diastereoselectivity, the relative stereochemistry being assigned as RR,SS by analogy with the formation of (RSS,SRR)-128.

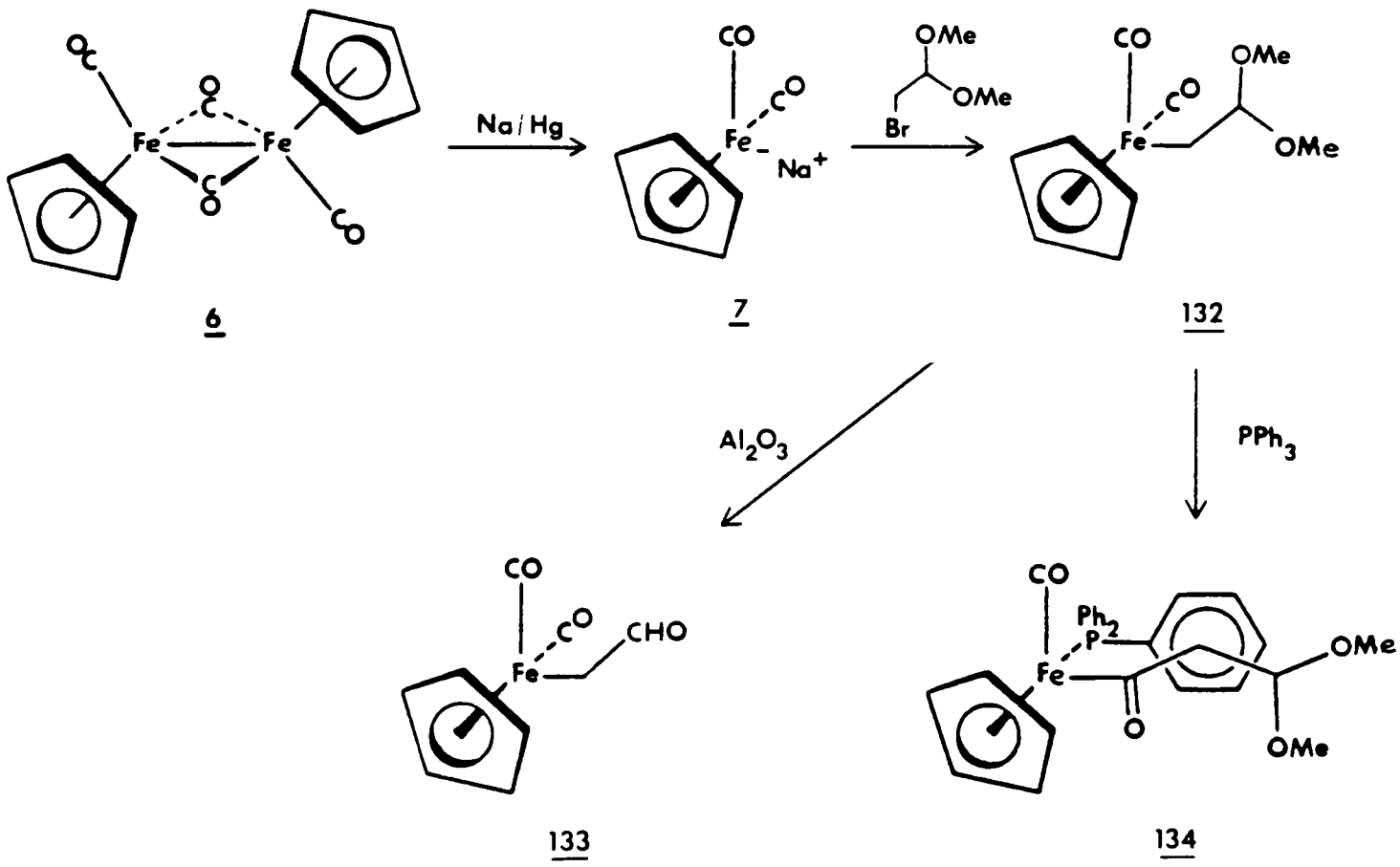


47 , 48 131

These reactions highlight the exceptional stereochemical control exerted by the chiral iron centre. In a single reaction, a complex containing a mixture of stereochemistries at the β-centre is converted into essentially a single diastereoisomer of a complex possessing two new chiral centres α and β to the acyl group.

The sequential elimination-Michael addition reaction of the diastereoisomers 47 and 48 of the β-methyl-β-methoxy acyl complex could in principle be extended to the readily available β-dimethoxy acyl complex 134.

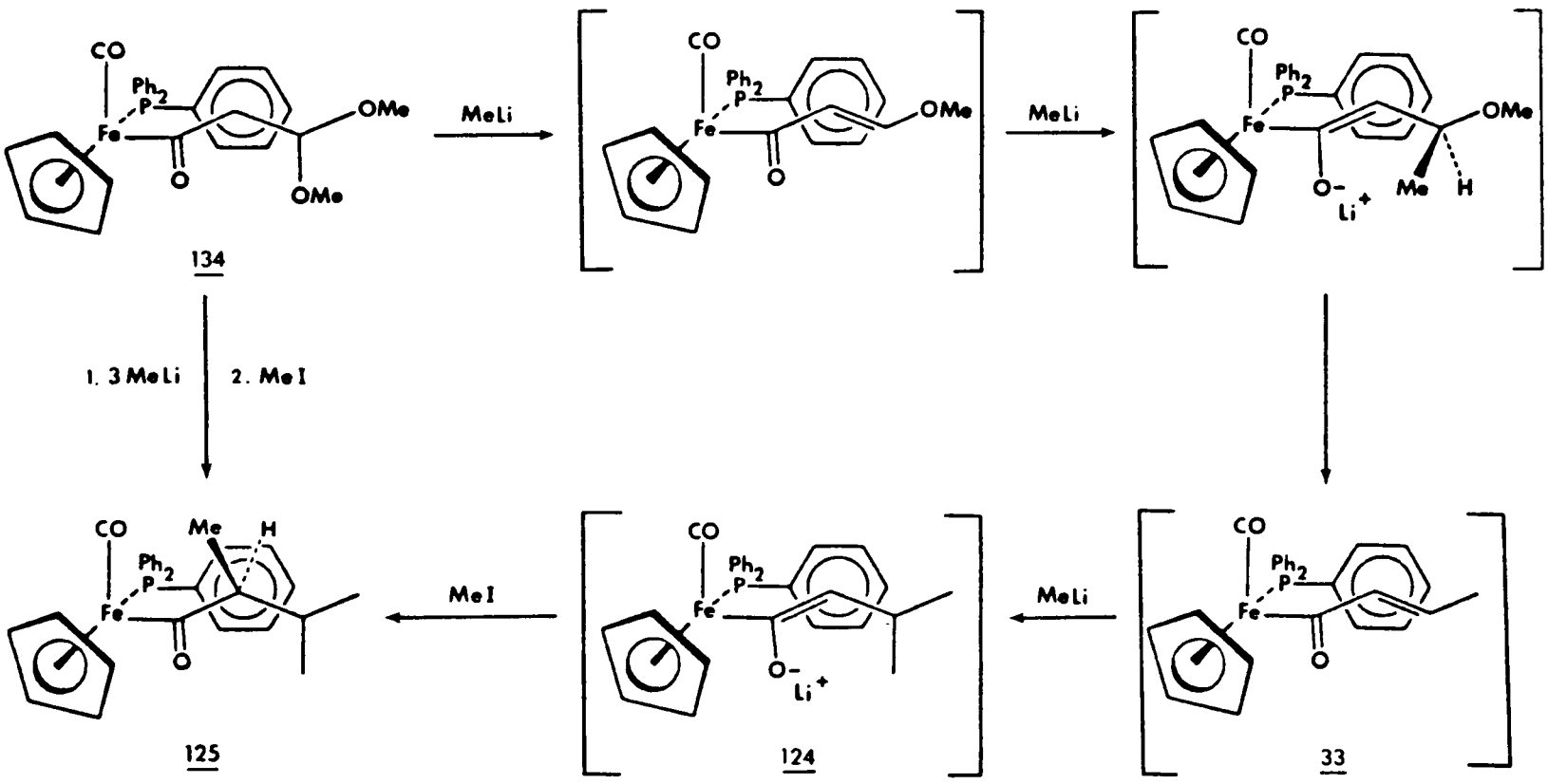
Complex 134 was prepared according to the literature procedure.[39] Thus, the iron dimer 6 was cleaved over sodium amalgam in THF and the resulting nucleophilic iron species 7 treated with bromoacetaldehyde dimethyl acetal to give the iron alkyl complex 132.[141]



6 7 132 133 134

Complex 132 was isolated by extraction with light petroleum (30:40°C) and crystallisation. Attempts to purify complex 132 by chromatography on alumina caused hydrolysis to the aldehyde complex 133.[141] Heating complex 132 under reflux in acetonitrile gave the desired carbonyl-inserted product 134 in 32% overall yield.

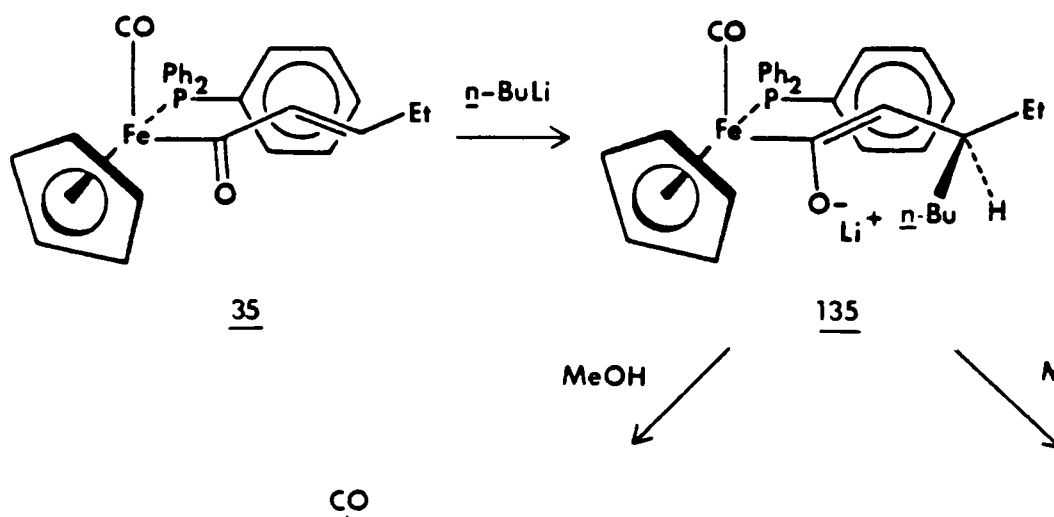
Treatment of the β-dimethoxy acyl complex 132 with three equivalents of methyllithium followed by methyl iodide yielded the previously characterised complex 125 as a single diastereoisomer (diastereoselectivity >100:1). The formation of complex 125 is consistent with two sequential base-induced elimination-Michael addition reactions occurring *via* the E crotonyl complex 33 to give E enolate 124. Diastereoselective methylation of 124 in the *anti* (CO to acyl) conformation away from the triphenylphosphine ligand gives the observed relative stereochemistry in the product (scheme 4).



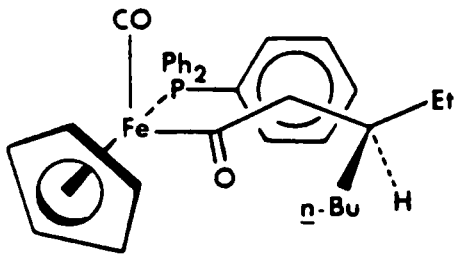
Scheme 4: Sequential methyllithium-induced elimination-Michael addition reactions of complex 132.

IV. Diastereoselective tandem Michael addition-alkylation reactions of E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHR] (R=Et,n-Bu)

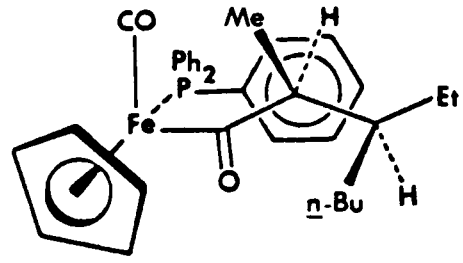
In an extension of the diastereoselective tandem Michael addition-alkylation reactions of E α,β-unsaturated acyl complexes, the E β-ethyl substituted-α,β-unsaturated acyl complex 35 was treated with n-butyllithium and the enolate generated quenched with methanol. Complex 136 was isolated in 79% yield as a 40:1 mixture of diastereoisomers, the major diastereoisomer being assigned the RS,SR relative configuration on the basis of previous results.



35 135



136



137

Enolate 135, generated in an identical manner, was also quenched with methyl iodide. Both ^1H and ^{13}C n.m.r. spectroscopy indicated that the two new chiral centres in complex 137 had been formed with a high degree of diastereoselectivity (>100:1:1:1). The relative configuration in complex 137 was unambiguously determined as RSS,SRR by an X-ray crystal structure analysis (figure 17). Full X-ray data is given in appendix 5 and selected bond lengths, bond angles and torsional angles are listed in Table 8.

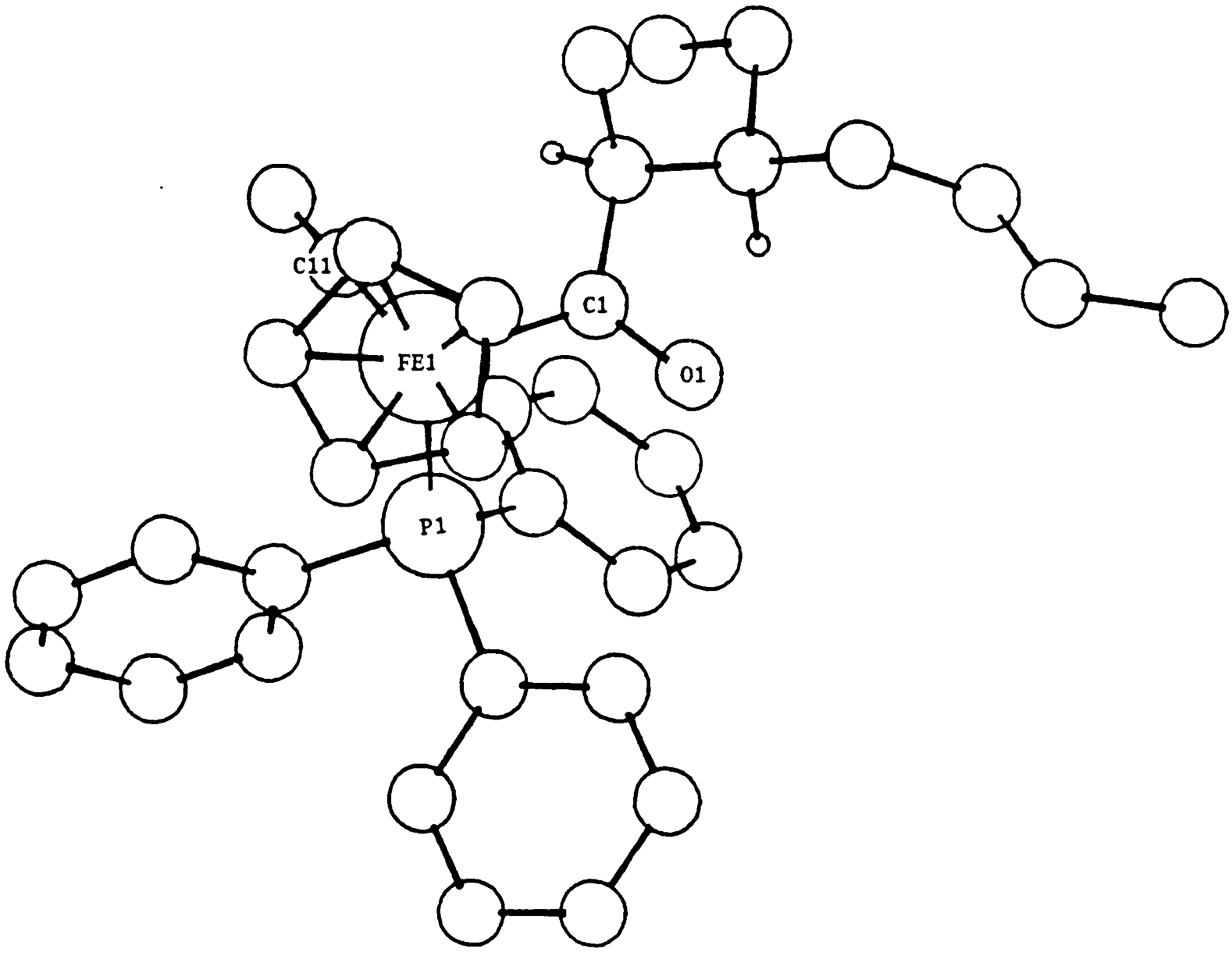


Figure 17: X-ray crystal structure of (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH(CH_3)CH(Et)$n-Bu] 137.

Bond lengths (A)		Bond angles (°)	
Fe(1)-P(1)	2.197(3)	C(1)-Fe(1)-P(1)	89.7(3)
Fe(1)-C(1)	1.96(1)	C(11)-Fe(1)-P(1)	92.4(4)
Fe(1)-C(11)	1.74(1)	C(11)-Fe(1)-C(1)	94.5(5)

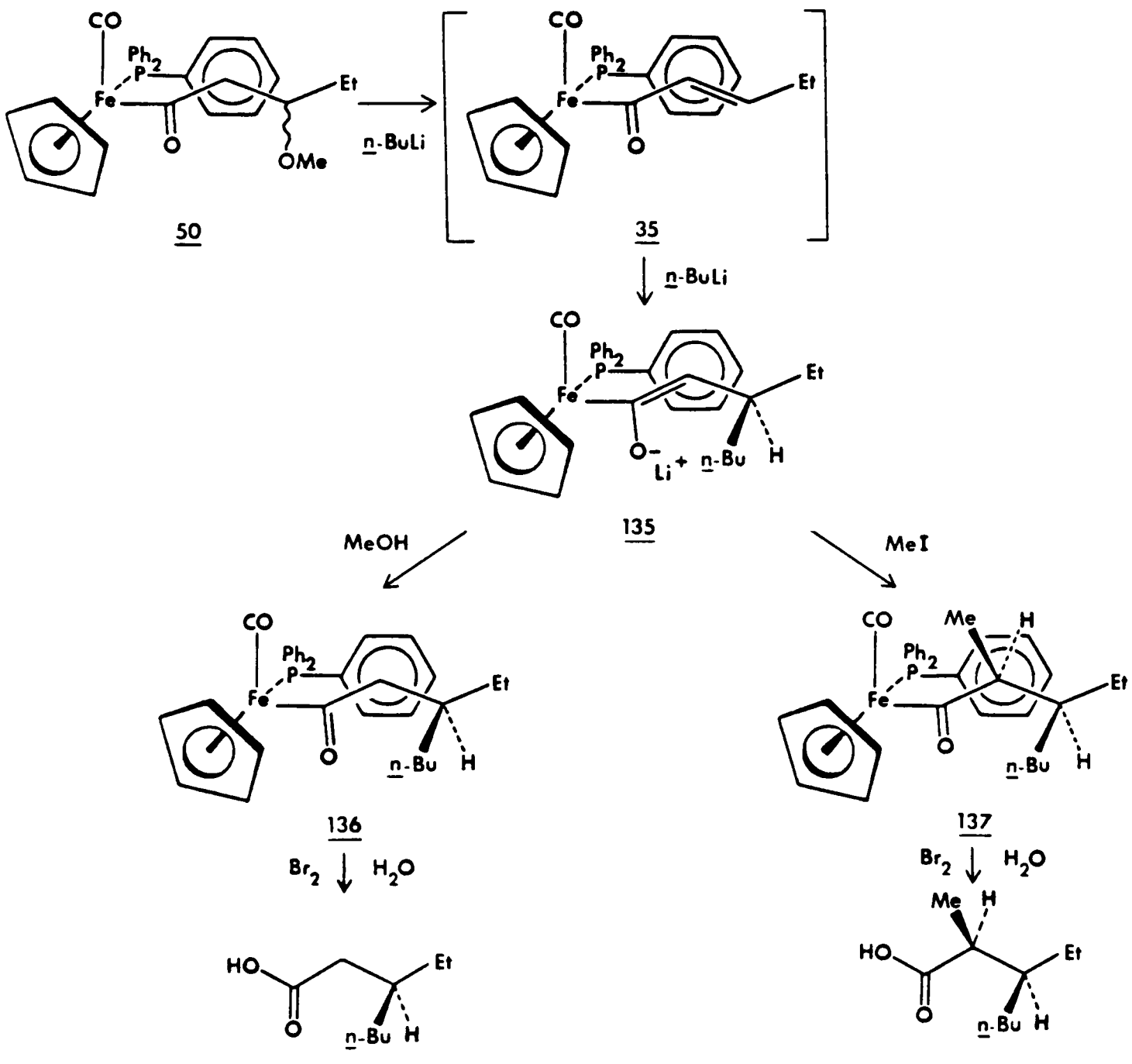
Torsional angle (°)	
C(11)-Fe(1)-C(1)-O(1)	-156

Table 8: Selected X-ray data with e.s.d.'s in parentheses for (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(Et)n-Bu] 137.

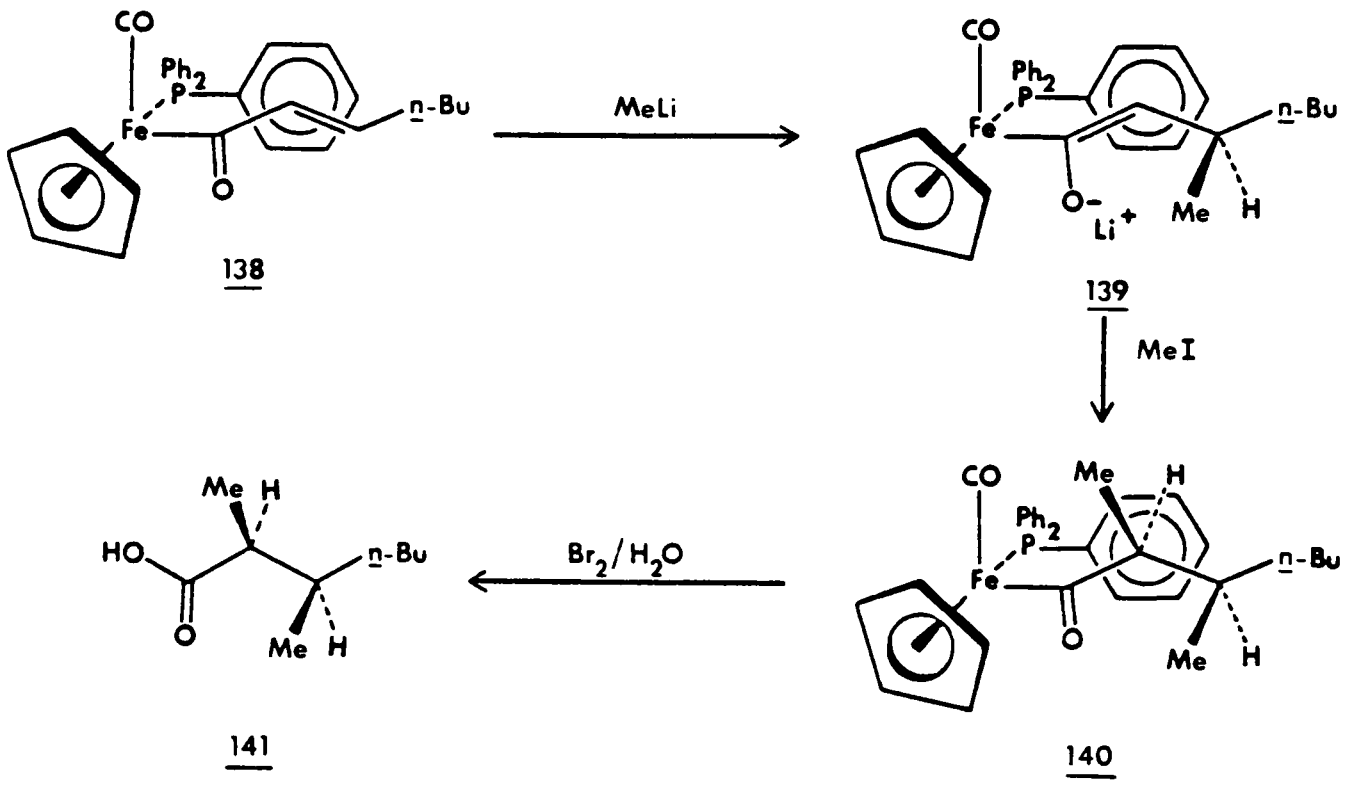
In addition to the pseudooctahedral geometry about the iron centre and the anti relationship between the carbon monoxide ligand and the acyl oxygen, figure 17 shows that the n-butyl and methyl groups have been introduced to the same face of the original α,β-carbon-carbon double bond. This corresponds to the face that was originally away from the triphenylphosphine ligand with the α,β-unsaturated acyl ligand adopting a cisoid and anti (CO to acyl) conformation; the conformation shown by X-ray crystallography to be adopted by complex 33 in the solid state (chapter 3). Further evidence is therefore provided for n-butyllithium, presumably initially coordinated to the acyl oxygen, undergoing Michael addition to the α,β-unsaturated acyl ligand of 35 in the cisoid and anti conformation away from the triphenylphosphine ligand. Subsequent methylation of the E enolate 135 generated in the anti conformation, again from the least hindered face, gives the observed relative configuration in the product complex 137.

The E β-ethyl-α,β-unsaturated acyl complex 35 was also generated in situ by the addition of two equivalents of n-butyllithium to a 1:1 mixture

of the diastereoisomers of complex 50. The enolate 135 formed by Michael addition of n-butyllithium to complex 35 was, in separate experiments, protonated with methanol and methylated with methyl iodide to give complexes 136 and 137 respectively with excellent diastereoselectivities. Complexes 136 and 137 were identified by comparison with the authentic samples made previously. Oxidative decomplexation of complex 136 with bromine in the presence of water gave 3-ethylheptanoic acid in 80% yield. Removal of the chiral iron auxiliary from complex 137 proceeded without epimerisation at either the α-or β-centres to give a single diastereoisomer of 3-ethyl-2-methylheptanoic acid as determined by ^{1}H and ^{13}C n.m.r. spectroscopy.



The diastereoselective preparation of the RSS,SRR diastereoisomer 128 of the α,β-dimethyl hexyl acyl complex by the Michael addition of n-butyllithium to the E crotonyl complex 33 followed by methylation with methyl iodide, has already been demonstrated. The RSR,SRS diastereoisomer was made with equally high diastereoselectivity (>100:1:1:1) by the Michael addition of methyllithium to the E β-n-butyl-α,β-unsaturated acyl complex 138 followed by methylation of the enolate 139. The α-methyl doublet at δ0.87 in the ^{1}H n.m.r. spectrum again enabled the relative stereochemistry between the iron and α-centres in the product complex 140 to be assigned as RS,SR.[43] In this case oxidative decomplexation with bromine in aqueous THF gave the known threo carboxylic acid 141.[140]

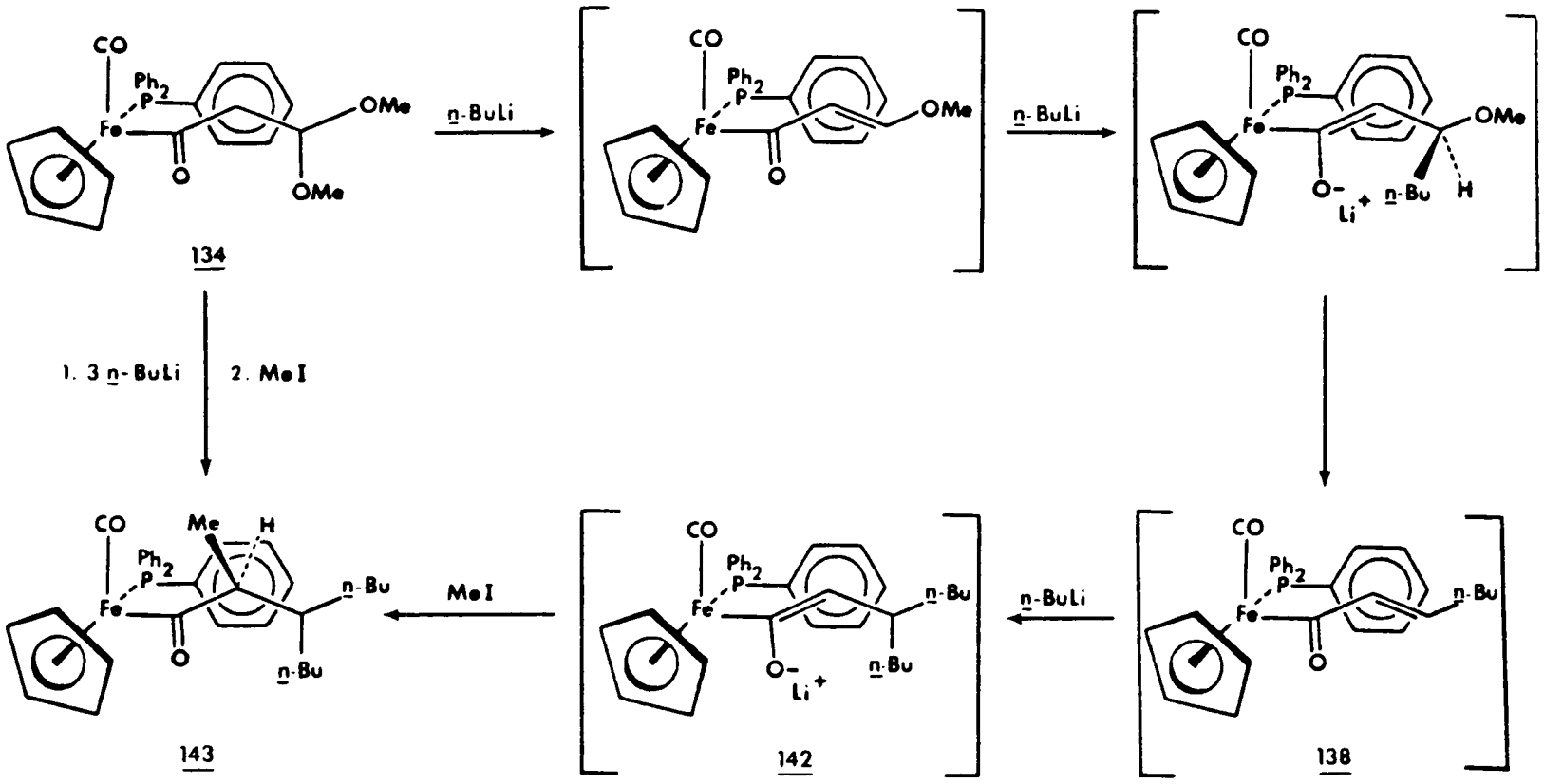


138 139 140 141

The isolation of the diastereoisomerically pure threo acid 141 from complex 140 and also the pure erythro acid 129 from complex 128 demonstrates two points. Firstly, that removal of the chiral iron auxiliary is not accompanied by epimerisation at the α- or β-centres and secondly, that the stereochemistry of the carboxylic acid derivative obtained upon decomplexation is not controlled by thermodynamic factors but by the stereochemical outcome of the tandem Michael addition-alkylation reaction.

This example illustrates how simple interchange of the β-alkyl substituent with the alkyl group of the lithium reagent leads to inversion of stereochemistry at the β-centre in the Michael adducts.

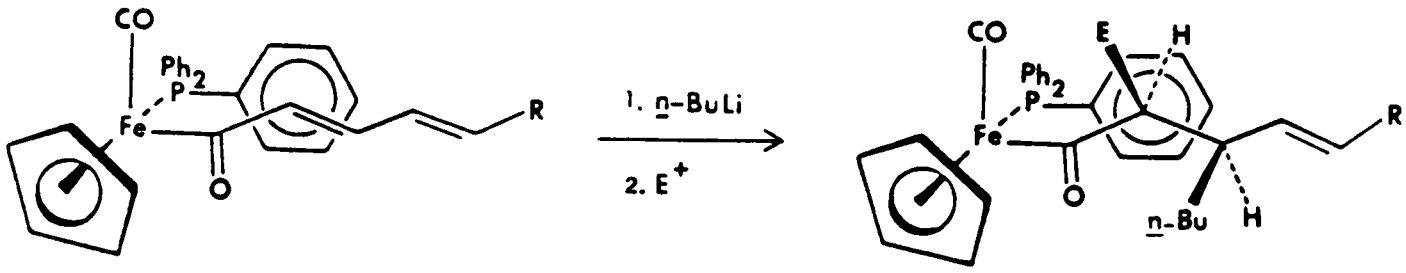
Michael addition of n-butyllithium to the E β-n-butyl-α,β-unsaturated acyl complex 138 is presumably one of the steps in the formation of the (RS,SR)-α-methyl-β-di-n-butyl substituted acyl complex 143 from the β-dimethoxy acyl complex 134. Treatment of 134 with three equivalents of n-butyllithium followed by methyl iodide gave complex 143 in 66% yield. Two sequential methoxide elimination-Michael addition reactions generate E enolate 142 which is diastereoselectively methylated as before to give complex 143 (α-methyl doublet at δ0.92 in the ^{1}H n.m.r. spectrum [43]), (scheme 5).



Scheme 5: Sequential n-butyllithium-induced elimination-Michael addition reactions of complex 134.

V. Diastereoselective tandem Michael addition-alkylation reactions of E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CHR] (R=H,CH_3)

The E isomers of [(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CHR] (R=H) 37 and (R=CH_3) 39 were individually treated with n-butyllithium and the enolates quenched with either methanol or methyl iodide to give the corresponding β- and α,β-substituted products. The yields and diastereoselectivities are given in Table 9.



Adduct	R	E	Yield (%)	Diastereoselectivity
144	H	H	82	>100:1[a]
145	CH_3	H	77	>100:1[a]
146	H	CH_3	83	>100:1:1:1[a]
147	CH_3	CH_3	87	4:1:0:0[b]

a. Only single diastereoisomers were observable by ^1H and ^{13}C n.m.r. spectroscopy.

b. Two of the four possible diastereoisomers were observable by ^1H and ^{13}C n.m.r. spectroscopy.

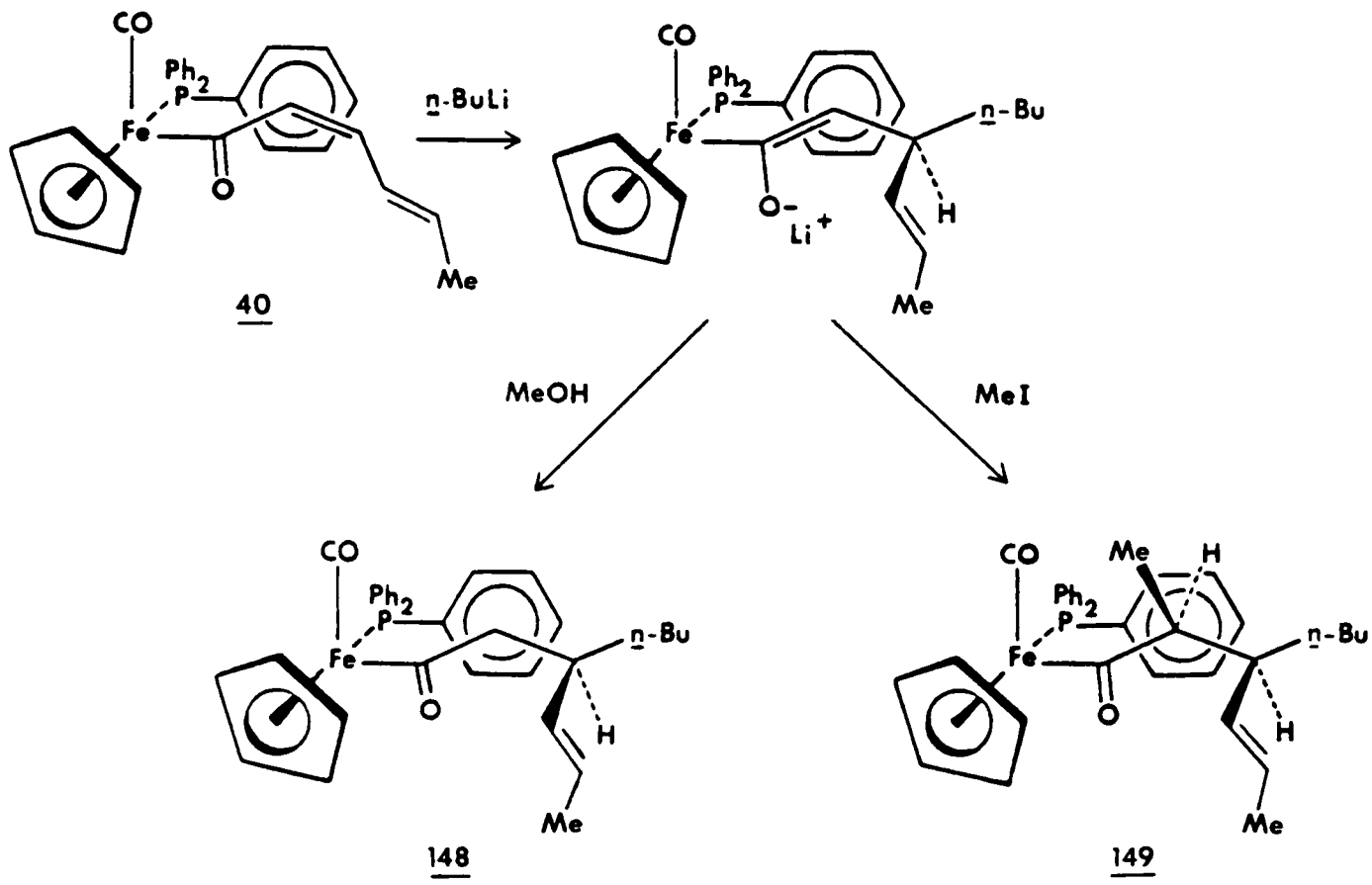
Table 9: Yields and diastereoselectivities of the adducts from Michael addition-alkylation of E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CHR] (R=H,CH_3).

The relative configurations in the complexes were assigned as RS,SR (E=H) and RSR,SRS (E=CH_3) by analogy with the stereochemistry of the Michael addition-alkylation reactions of E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHR] (R=CH_3,Et,n-Bu). The relative stereochemistry between the iron and α-centres in complexes 146 and 147 was confirmed as RS,SR by the

appearance of α-methyl doublets at δ1.02 and 1.00 in their respective ^{1}H n.m.r. spectra.[43] The generation of both α- and β-centres proceeded with a high degree of stereoselectivity with the exception of those in complex 147. The new chiral β-centre is formed stereoselectively as shown in the case where the enolate is simply protonated. However, in agreement with results from the related E β-phenyl- and E β-2-furyl-α,β-unsaturated acyl complexes,[142] the stereochemistry that the newly formed β-centre induces at the α-centre is believed to oppose that induced by the iron centre with a consequent reduction in the overall diastereoselectivity in the tandem reaction. This is in contrast to the usual double stereodifferentiation [143] observed in the tandem Michael addition-alkylation reaction.

VI. Diastereoselective reactions of Z-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)-COCH=CHCH=CHR] (R=H,CH$_3$)

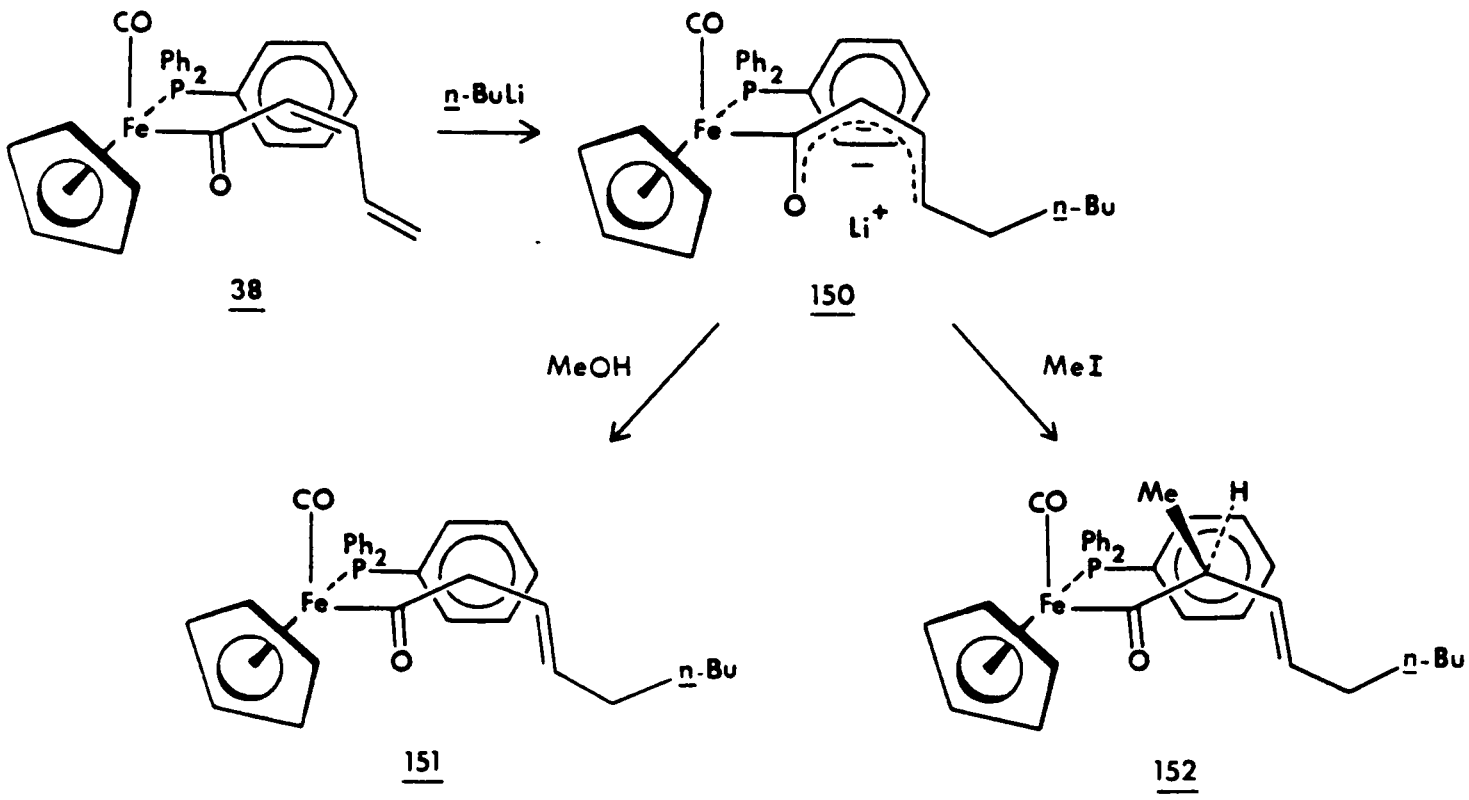
The absence of acidic γ-protons in the Z isomers of [(η^5-C_5H_5)Fe(CO)-(PPh$_3$)COCH=CHCH=CHR] (R=H,CH$_3$) precluded dienolate formation by γ-deprotonation. It was predicted therefore that these complexes too would display Michael addition reactivity towards n-butyllithium. Addition of n-butyllithium to Z-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH=CHCH=CHCH$_3$] 40 generated an enolate which in separate experiments was quenched with methanol and methyl iodide. In each case, the products derived from 1,4-conjugate addition, RS,SR-148 and RSS,SRR-149, were isolated as single diastereoisomers as shown by ^{1}H n.m.r. spectroscopy. The diastereoselective (>100:1:1:1) formation of RSS,SRR-149 is in contrast to the moderate stereochemical control observed in the formation of the α-centre in RSR,SRS-147. In the former case, the newly formed β-centre is believed to act in conjunction with the iron centre in inducing the same stereochemistry at the α position (double stereodifferentiation).



40 148 149

Treatment of the β-vinyl-α,β-unsaturated acyl complex 38 with n-butyllithium in THF at -78°C generated an enolate which was quenched with methanol. The presence of olefinic signals in the ^{1}H n.m.r. spectrum due to only two protons and the appearance of both olefinic carbons as doublets in the off-resonance ^{13}C n.m.r. spectrum indicated that the β,γ-unsaturated acyl complex 151 had been formed. The formation of complex 151 is consistent with n-butyllithium undergoing 1,6-conjugate addition to complex 38 to generate dienolate 150 which is then regioselectively protonated at the α-centre (chapter 4). The olefinic signals in the ^{1}H n.m.r. spectrum were too complex for the geometry about the resulting β,γ-double bond to be determined.

Similarly, quenching dienolate 150 with methyl iodide gave complex 152 with a diastereoselectivity of greater than 100:1. The major diastereoisomer had the RS,SR relative configuration as deduced from the chemical shift of the α-methyl doublet at δ1.02 in the ^{1}H n.m.r. spectrum,[43] and also an E geometry about the β,γ-double bond (J_{trans} = 15.5 Hz).



An X-ray crystal structure analysis of complex 38 (figure 18) shows that the torsional angle between the two carbon-carbon double bonds is -176°, sufficiently small to indicate extensive conjugation between the terminal double bond and the α,β-unsaturated acyl system. Full X-ray data for complex 38 is given in appendix 6 and selected bond lengths, bond angles and torsional angles are listed in Table 10.

Bond lengths (A)		Bond angles (°)	
Fe(1)-P(1)	2.201(2)	C(1)-Fe(1)-P(1)	92.1(2)
Fe(1)-C(1)	1.943(8)	C(6)-Fe(1)-P(1)	91.1(2)
Fe(1)-C(6)	1.731(8)	C(6)-Fe(1)-C(1)	93.5(3)
C(1)-O(1)	1.209(9)	Torsional angles (°)	
C(1)-C(2)	1.49(1)	C(6)-Fe(1)-C(1)-O(1)	-145
C(2)-C(3)	1.34(1)	O(1)-C(1)-C(2)-C(3)	+40
C(3)-C(4)	1.43(1)	C(1)-C(2)-C(3)-C(4)	-5
C(4)-C(5)	1.30(1)	C(2)-C(3)-C(4)-C(5)	-176.

Table 10: Selected X-ray data with e.s.d.'s in parentheses for (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CH_2] 38.

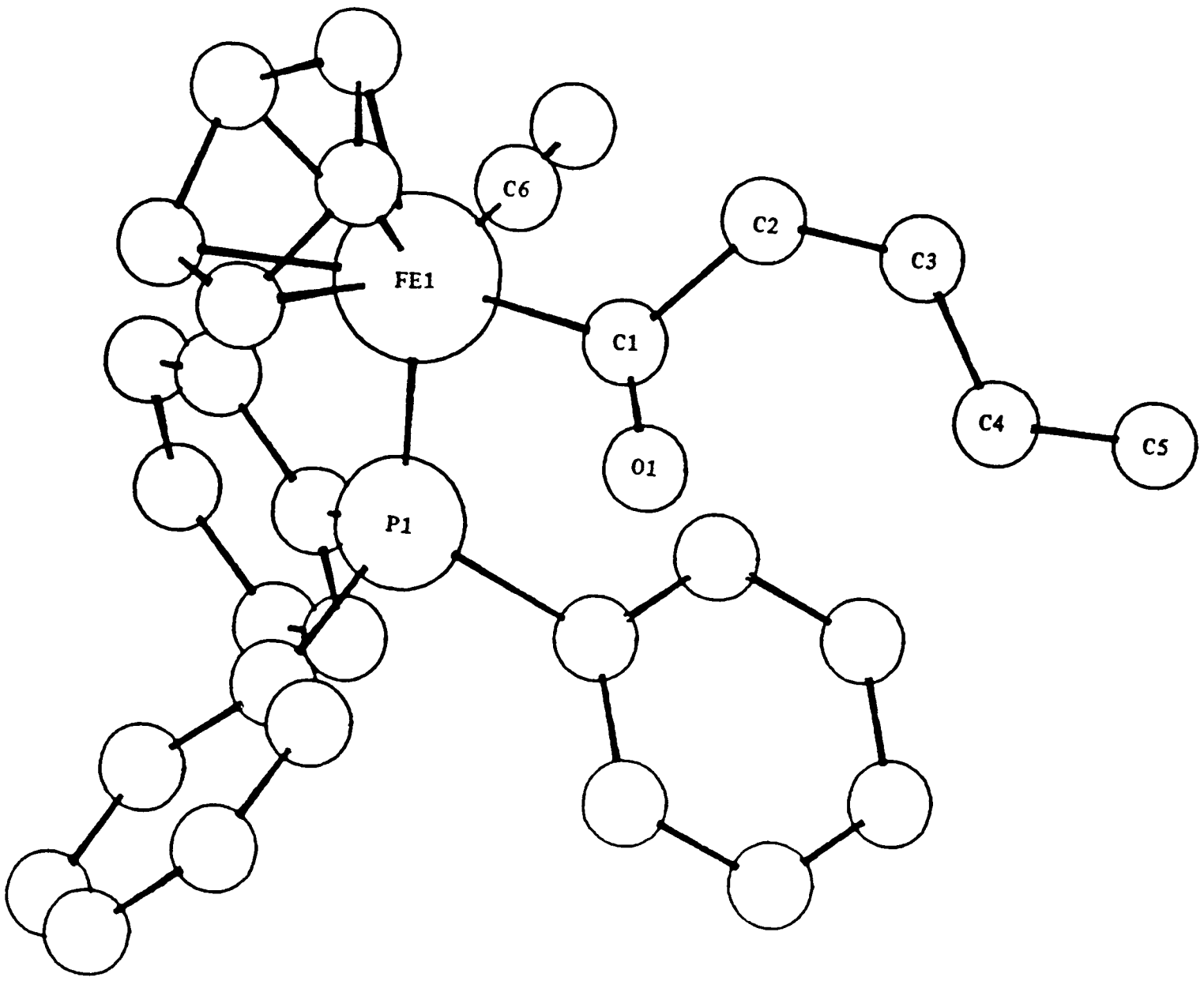
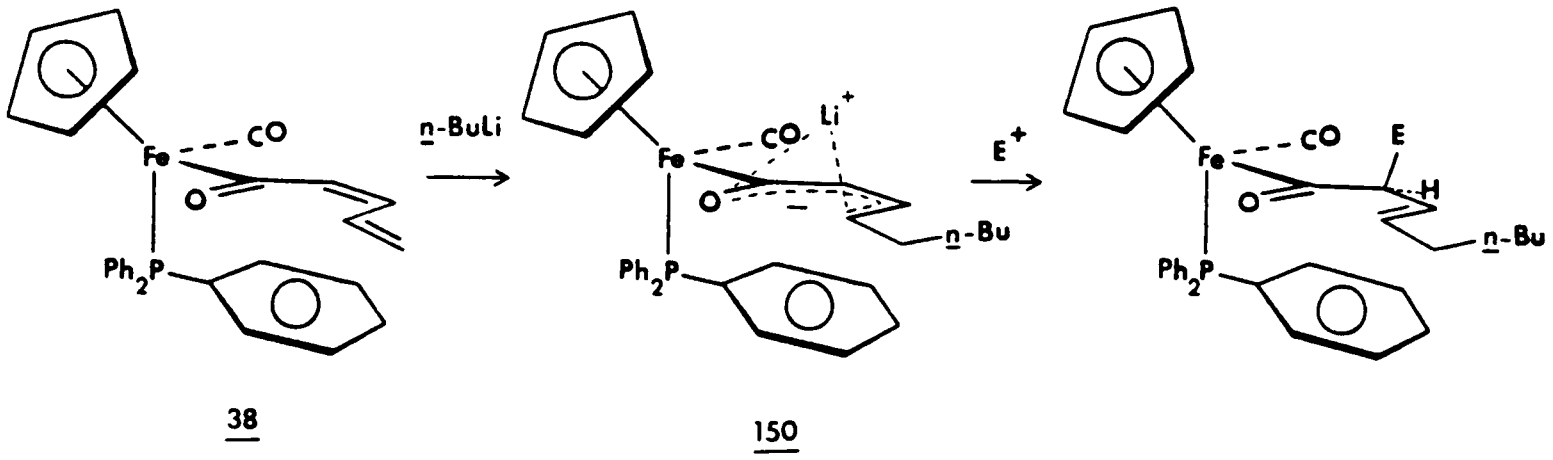


Figure 18: X-ray crystal structure of (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH{=}CHCH{=}CH_2$] 38.

The E β,γ-double bond in the product complexes 151 and 152 indicates that regioselective α-protonation and methylation of dienolate 150 occurs with the n-pentyl group in the exo rather than the sterically disfavoured endo position. This in turn could only arise if 1,6-conjugate addition was occurring to complex 38 in the cisoid-transoid conformation (scheme 6); the conformation adopted by complex 38 in the solid state. If the reaction between complex 38 and n-butyllithium is subject to product development control, then formation of the more stable dienolate 150, via 1,6-conjugate addition to the least substituted carbon centre, is favoured over formation of the enolate derived from 1,4-conjugate addition. Under these circumstances, the reaction presumably proceeds through a transition state resembling dienolate 150 in which a lithium ion chelates to the acyl oxygen and the γ-carbon.



38 150

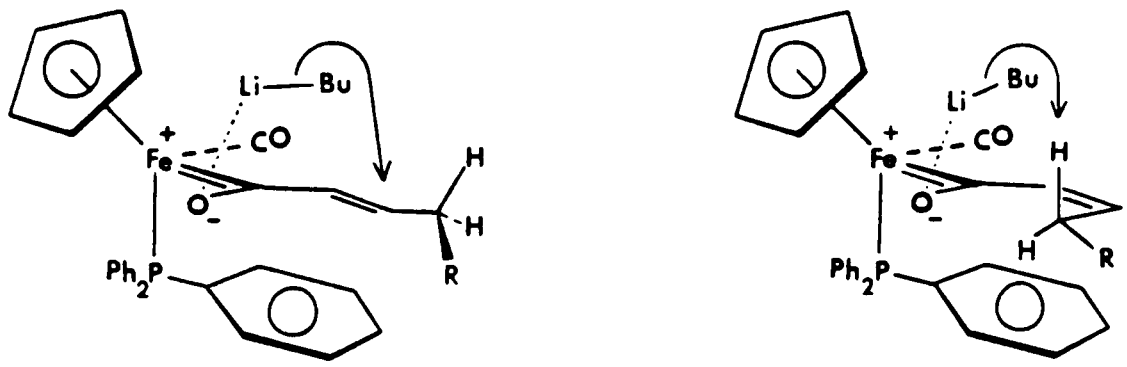
Scheme 6: 1,6-Conjugate addition to complex 38.

VII. Summary

The tandem Michael addition-alkylation reactions of E α,β-unsaturated iron acyl complexes, used directly or generated in situ from β-methoxy or β-menthoxy complexes, proceed with high diastereoselectivity to give essentially single diastereoisomers of α- and/or β-substituted acyl complexes. The two new groups are added to the same face of the original carbon-carbon double bond. Oxidative decomplexation proceeds without

epimerisation to give the corresponding α- and/or β-substituted carboxylic acid derivatives, with high optical purities if resolved acyl complexes are used.

The stereoselective Michael addition reaction of E α,β-unsaturated acyl complexes may be rationalised in terms of initial coordination of the alkyllithium reagent to the acyl oxygen. Nucleophilic attack at the β-centre of the ligand in the cisoid conformation away from the triphenyl-phosphine ligand then generates an E enolate. Similar coordination in the corresponding Z isomers is followed by base abstraction of the proximate γ-proton to form lithium dienolates (scheme 7).



Scheme 7: Michael addition versus dienolate formation.

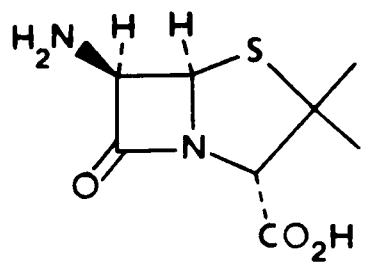
CHAPTER 6

ASYMMETRIC SYNTHESIS OF β-LACTAMS

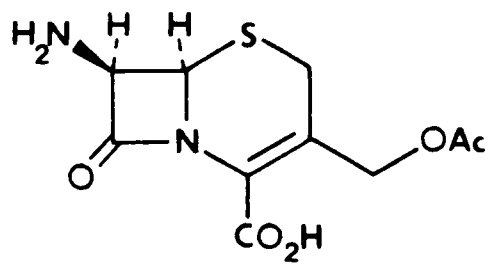
I. Introduction

In the fifty years since β-lactam antibiotics such as the penicillins and cephalosporins were first used in the treatment of infectious diseases caused by bacteria, a large number of methods for the synthesis of β-lactams have been developed.[144,145] It is known that antibacterial activity is shown by only one of the enantiomers of a chiral β-lactam.[144] The aim has therefore been to develop methods that lead selectively to the desired optically pure β-lactam without the need for a wasteful resolution step during the synthetic sequence.

The enantioselective conversion of various tripeptides to novel β-lactams using enzymes has been achieved but generally not on a synthetically useful scale.[146] A large number of optically pure semi-synthetic β-lactams have been synthesised from the readily available penicillin and cephalosporin parent compounds namely, 6-aminopenicillanic acid (6-APA) and 7-aminocephalosporin acid (7-ACA).[144]



6-APA



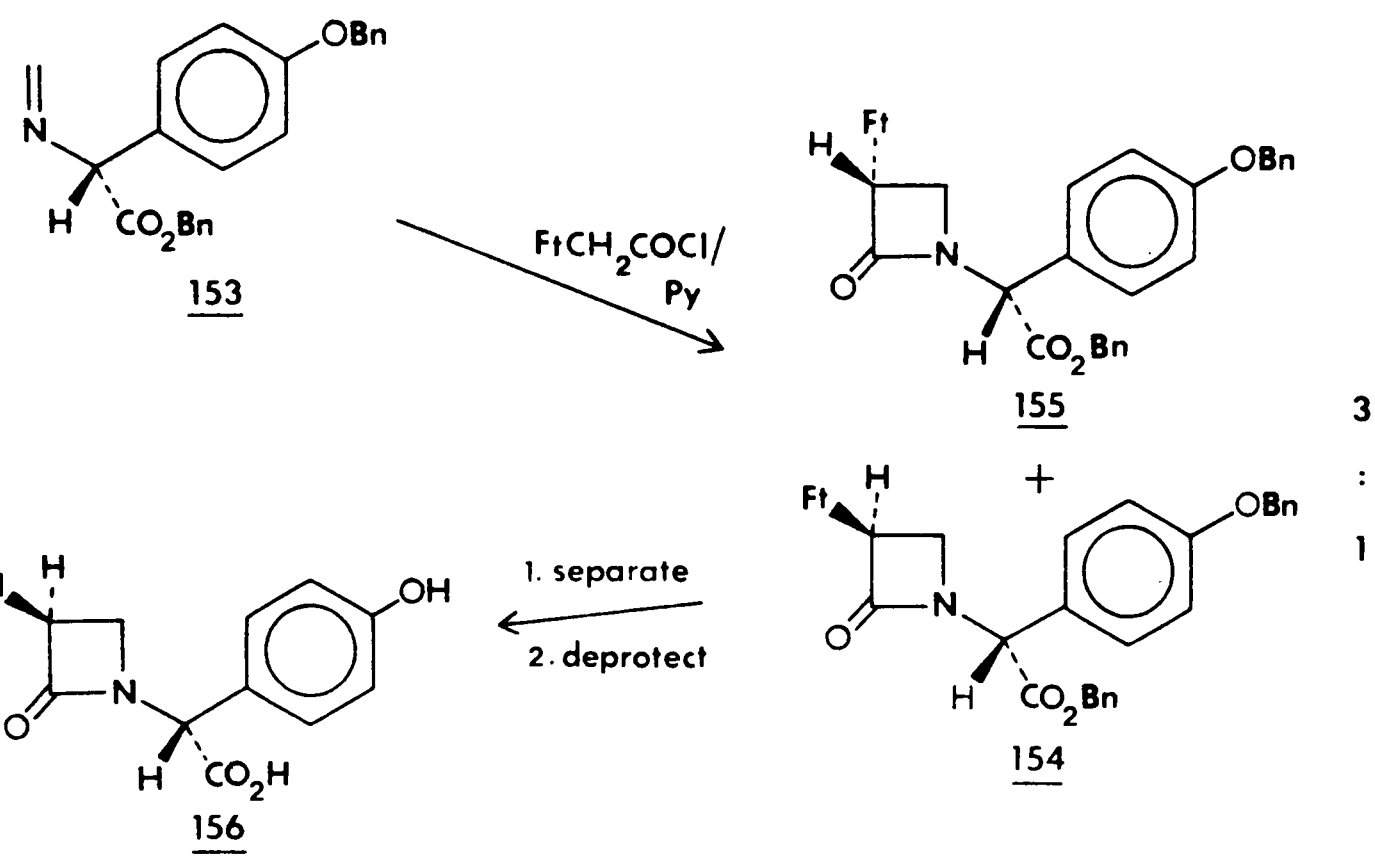
7-ACA

Similarly, enantiomerically pure α-amino acids have been used in the synthesis of chiral β-lactams.[5] These two approaches are not general however, due to the restrictive number of suitable starting materials.

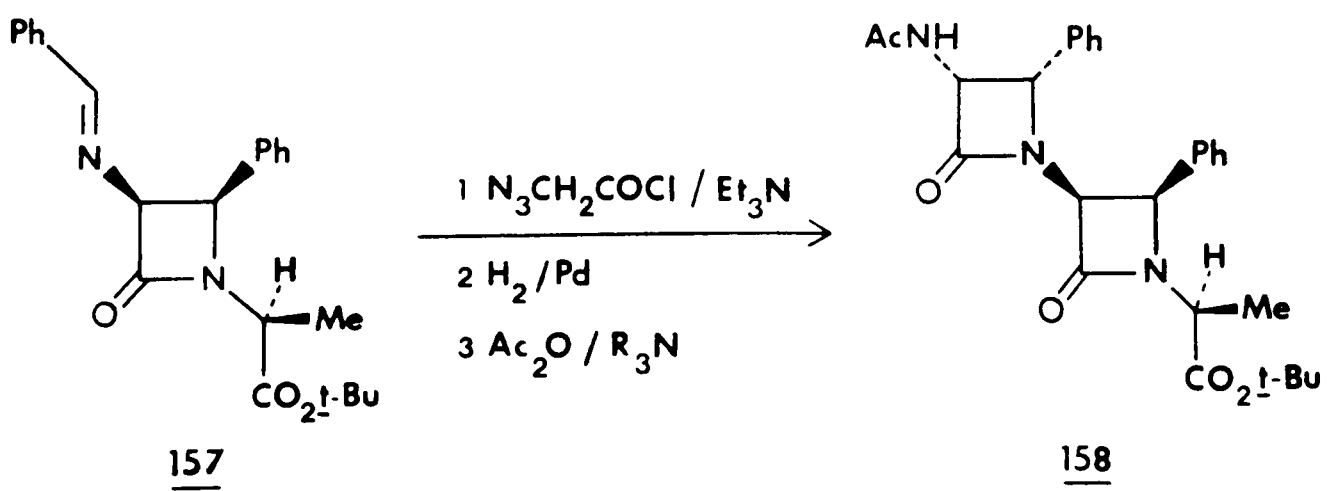
Although asymmetric synthesis would in principle allow the incorporation of much more structural variation into the β-lactam nucleus with a view to enhancing biological activity, very few reports on the application of such an approach to the synthesis of chiral β-lactams have

appeared. Those that have, almost invariably have been concerned with the asymmetric synthesis of monocyclic β-lactams by the cycloaddition of an imine and an enolisable carboxylic acid derivative. Although the imine component generally carries the chiral auxiliary group, there are examples in which the auxiliary resides in the other component.

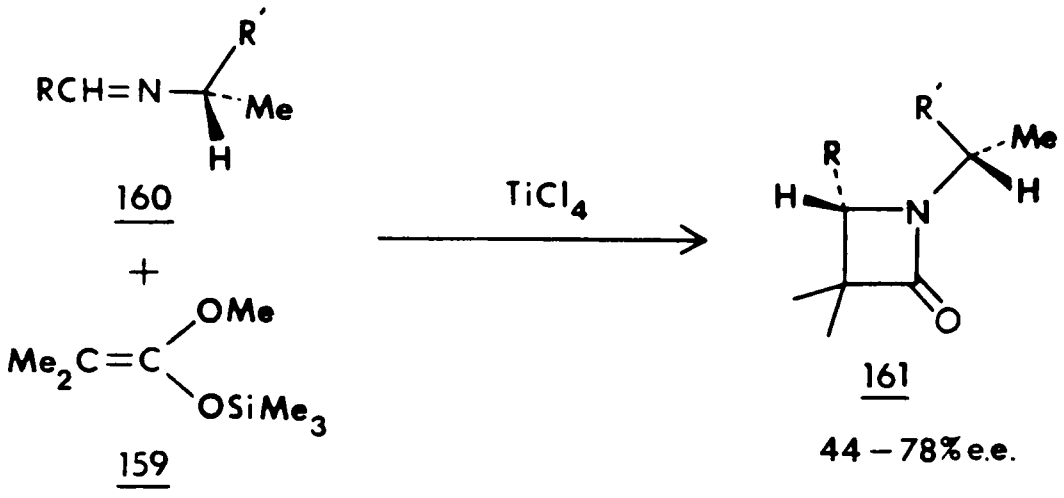
Addition of phthalimidoacetyl chloride and pyridine to the chiral formamidine 153 led to a 3:1 mixture of β-lactams 154 and 155. Subsequent separation and deprotection furnished optically pure 3-aminonocardicinic acid 156 indistinguishable from the β-lactam obtained by degradation of nocardicin A.[147]



Extremely high stereoselectivity was observed in the asymmetric cycloaddition between azidoketene and β-lactam 157 to give the optically pure bis-β-lactam 158, the precursor of a stereochemically pure tri-peptide.[148]

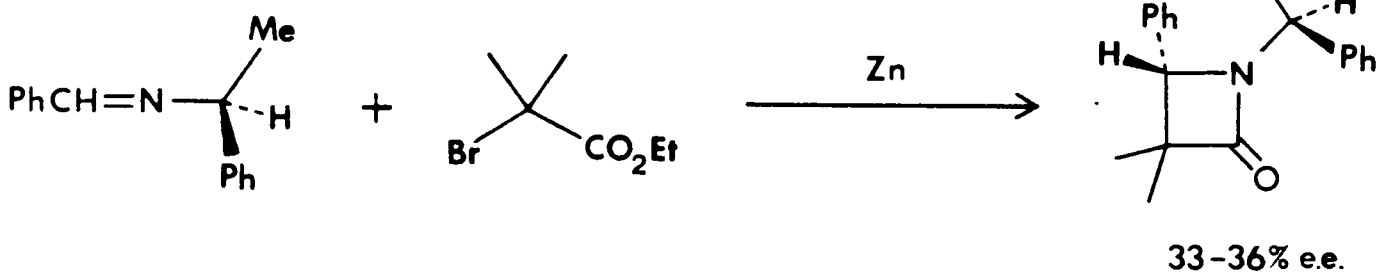


Ojima has shown that the reaction between dimethylketene silyl acetal 159 and (S)-alkylidene(1-arylethyl)amines 160 in the presence of titanium tetrachloride gave (S)-β-lactams 161 with 44-78% e.e.[149]

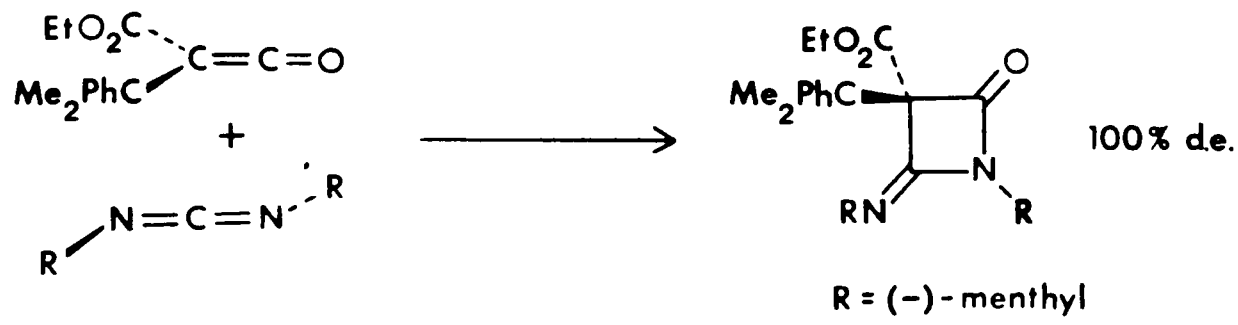


Extension of this titanium tetrachloride-mediated reaction to imines derived from chiral α-amino esters gave the corresponding β-lactams with increased diastereoisomeric purities of up to 99%.[150]

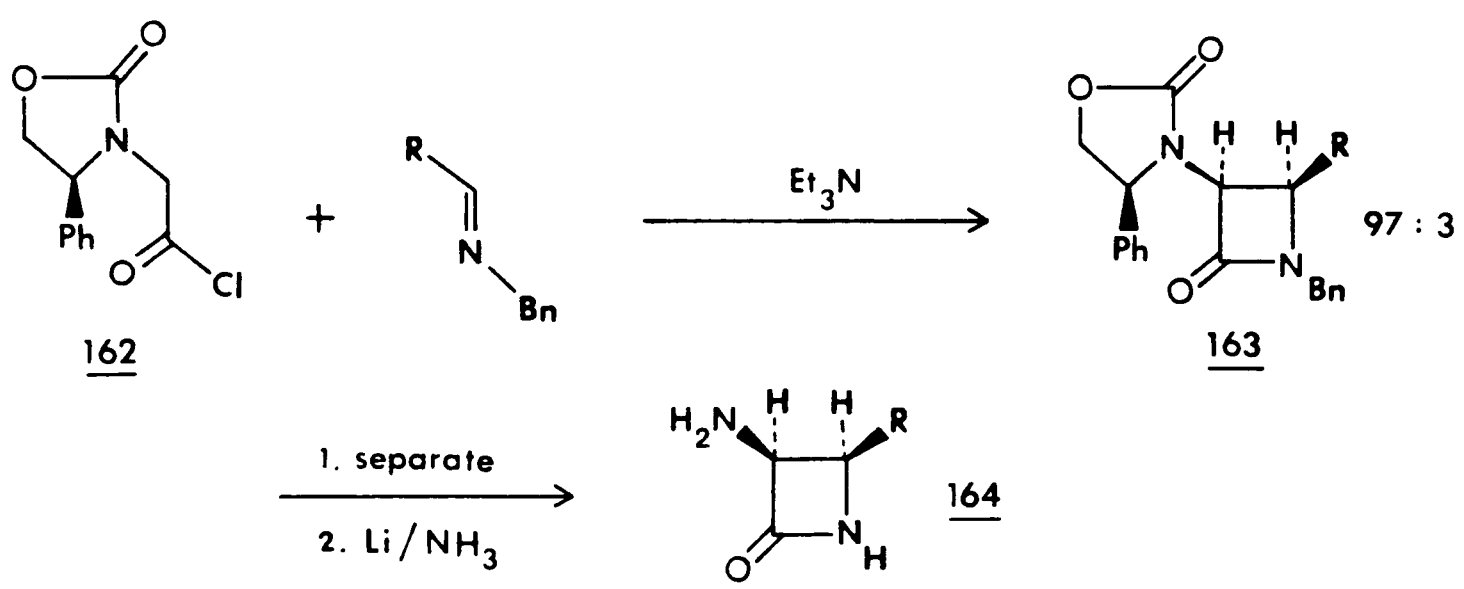
The reaction between chiral aldimines formed from benzaldehyde and (R)-(+)- or (S)-(-)-α-methylbenzylamine and the Reformatsky reagent prepared from ethyl α-bromoisobutyrate provided β-lactams with 33-36% e.e.[151]



In a reaction which involved prochiral ketenes directly, cyclo-addition with chiral carbodiimides proceeded regiospecifically via ionic intermediates to give 3-iminoazetidin-2-ones with moderate to very high diastereoselectivities.[152]

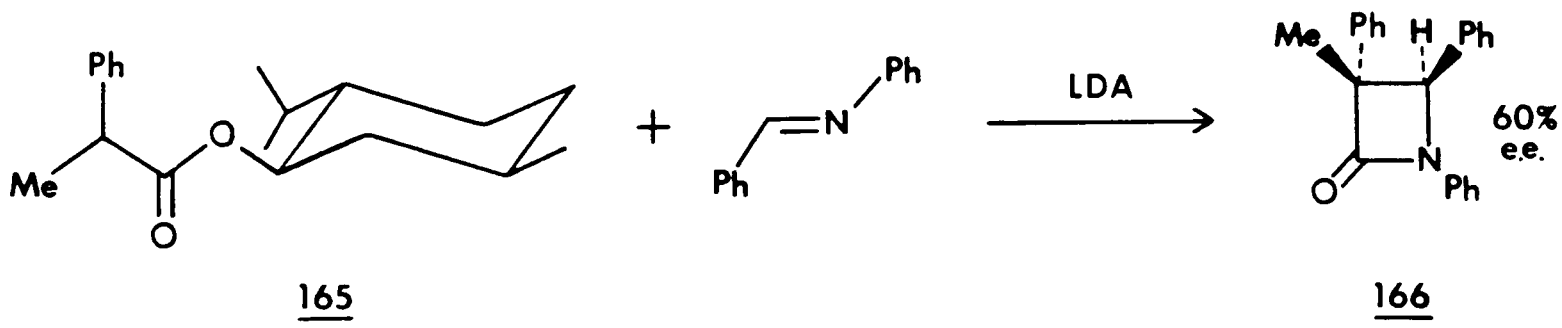


Of the cycloaddition reactions that form a β-lactam in which the chiral auxiliary group constitutes part of the enolisable carboxylic acid derivative, Evans has recently reported that the reaction of (4S)-phenyl-oxazolidylacetyl 162 with N-benzylimines in the presence of triethylamine formed the cycloadducts 163 with diastereoselectivities of up to 97:3. Subsequent separation and dissolving metal reduction afforded optically pure β-lactams 164 in good overall yields.[153] This asymmetric cyclo-addition formed the basis of the first enantioselective synthesis of the carbacephalosporin nucleus.[154]



162 163 164

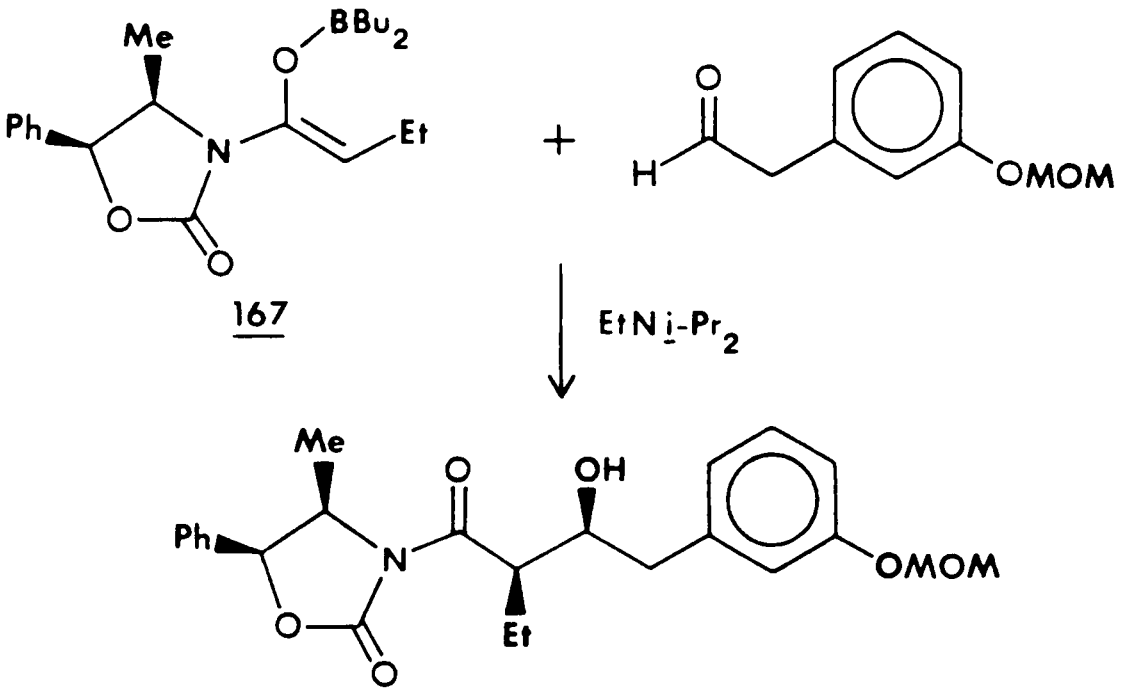
Condensation of the anion of (-)-menthyl ester 165 with N-benzyl-ideneaniline gave only the trans-β-lactam 166 in 85% yield with 60% e.e.[155]



165 166

Cationic dimethyl vinylidene complexes containing the chiral iron auxiliary [(η^5-C_5H_5)Fe(CO)(PPh_3)] and imines formed [2+2] cycloadducts with low diastereoselectivity (8:5). Oxidation gave β-lactams in poor yields.[156]

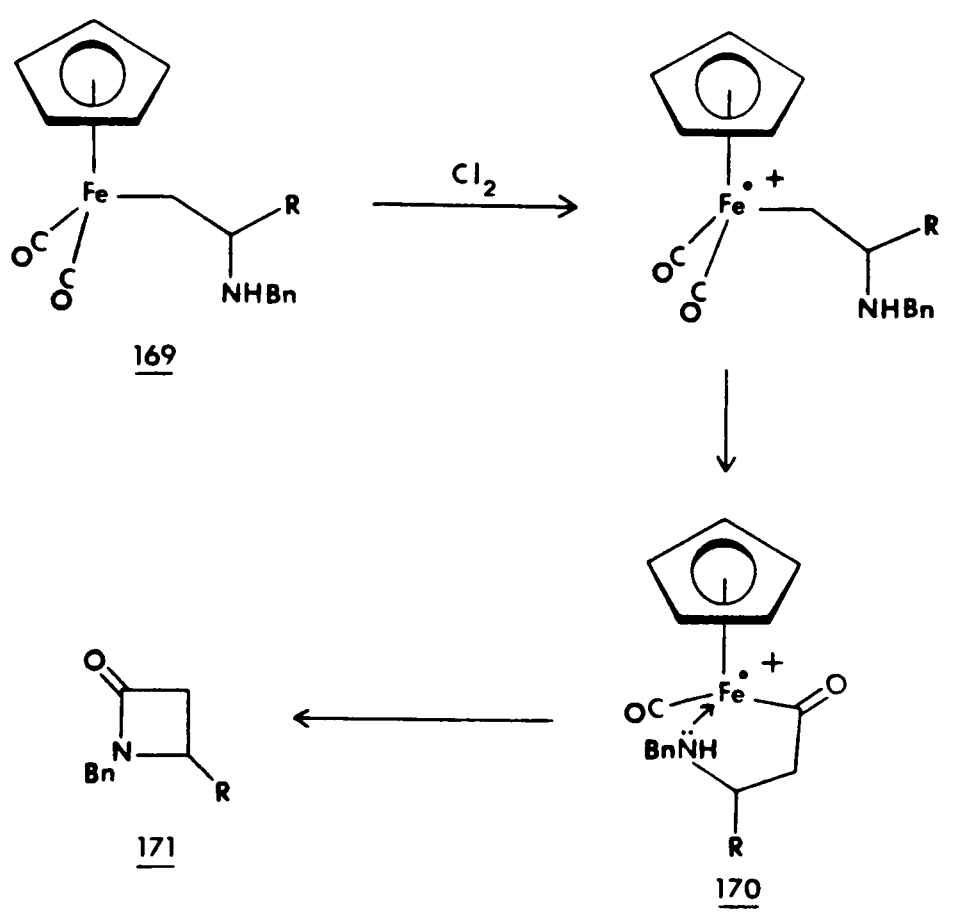
Finally, in a quite different approach to the asymmetric synthesis of the chiral β-lactam nucleus, Evans utilised the asymmetric aldol reaction of the chiral boron enolate 167 with phenylacetaldehyde to generate the desired absolute stereochemistry in the β-lactam precursor 168. Subsequent steps gave the enantiomerically pure carbapenem PS-5 in 13% overall yield.[157]



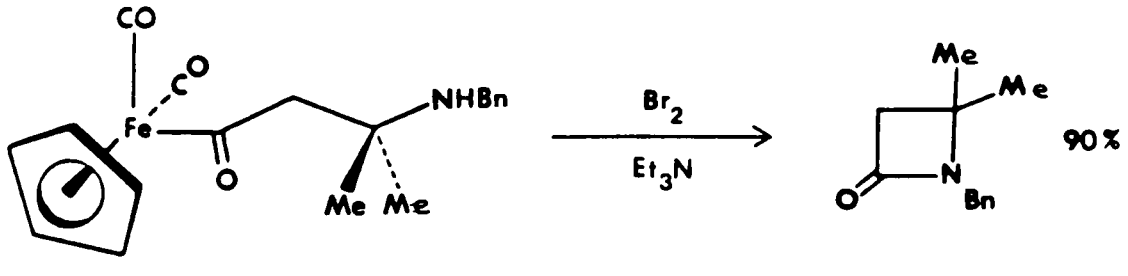
In summary, the range of methods available to date for the asymmetric synthesis of β-lactams is very limited. The cycloaddition reaction generally proceeds with only moderate diastereoselectivity, necessitating in some cases separation of intermediate diastereoisomers if the optically pure β-lactam is to be obtained. Removal of the chiral auxiliary can also prove to be a problem. All these features highlight the need for a general, flexible asymmetric procedure that will enable β-lactams to be generated with high optical purities.

II. β-Lactams from β-amino iron acyl complexes

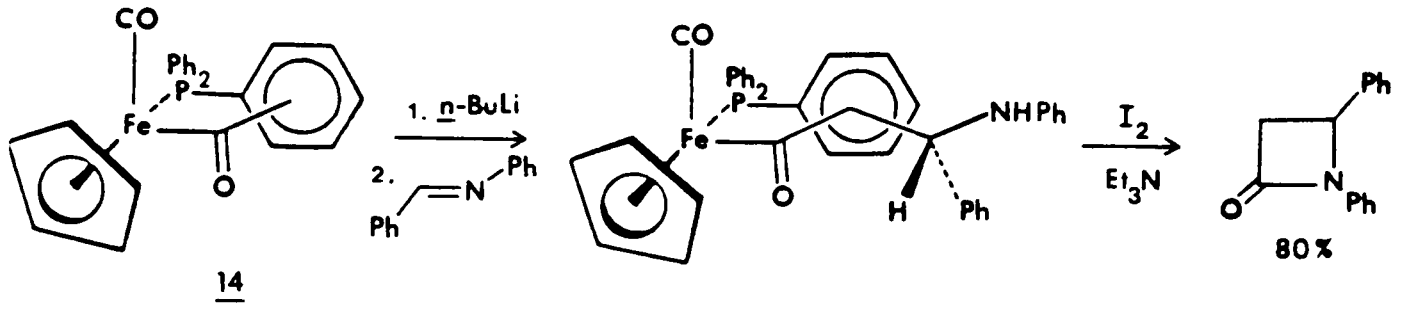
β-Amino iron acyl complexes have been shown to be organometallic precursors of β-lactams. Rosenblum first reported that oxidative de-complexation of the β-amino iron alkyl complex 169 with chlorine proceeded through the intermediate acyl complex 170 to give β-lactam 171 in 47% yield.[158] A similar intermediate was also proposed in the synthesis of bicyclic β-lactams.[159] Further evidence for this mechanism has subsequently appeared.[160]



The direct conversion of iron dicarbonyl β-amino acyl complexes to β-lactams in good yield using bromine has recently been described by Ojima.[161]



Work by Davies[162] and Liebeskind[163] has already demonstrated that β-amino acyl ligands bound to the chiral auxiliary [(η^5-C_5H_5)Fe(CO)-(PPh_3)] derived from the diastereoselective reaction between the methyl acyl complex 14 and imines, can be smoothly converted to the corresponding β-lactam in high yield.



14

In principle, similar β-amino iron acyl complexes could alternatively be synthesised by Michael addition of the anion derived from a primary amine to α,β-unsaturated acyl ligands bound to the chiral auxiliary [(η^5-C_5H_5)Fe(CO)(PPh_3)], followed by quenching of the resulting enolate with an electrophile. Any diastereoselectivity in this tandem addition-alkylation reaction similar to that described in chapter 5 would provide, after decomplexation, a method for the asymmetric synthesis of β-lactams.

III. Asymmetric synthesis of (3R),(4S)-(-)-3,4-dimethyl-N-benzyl-azetidin-2-one[138,164]

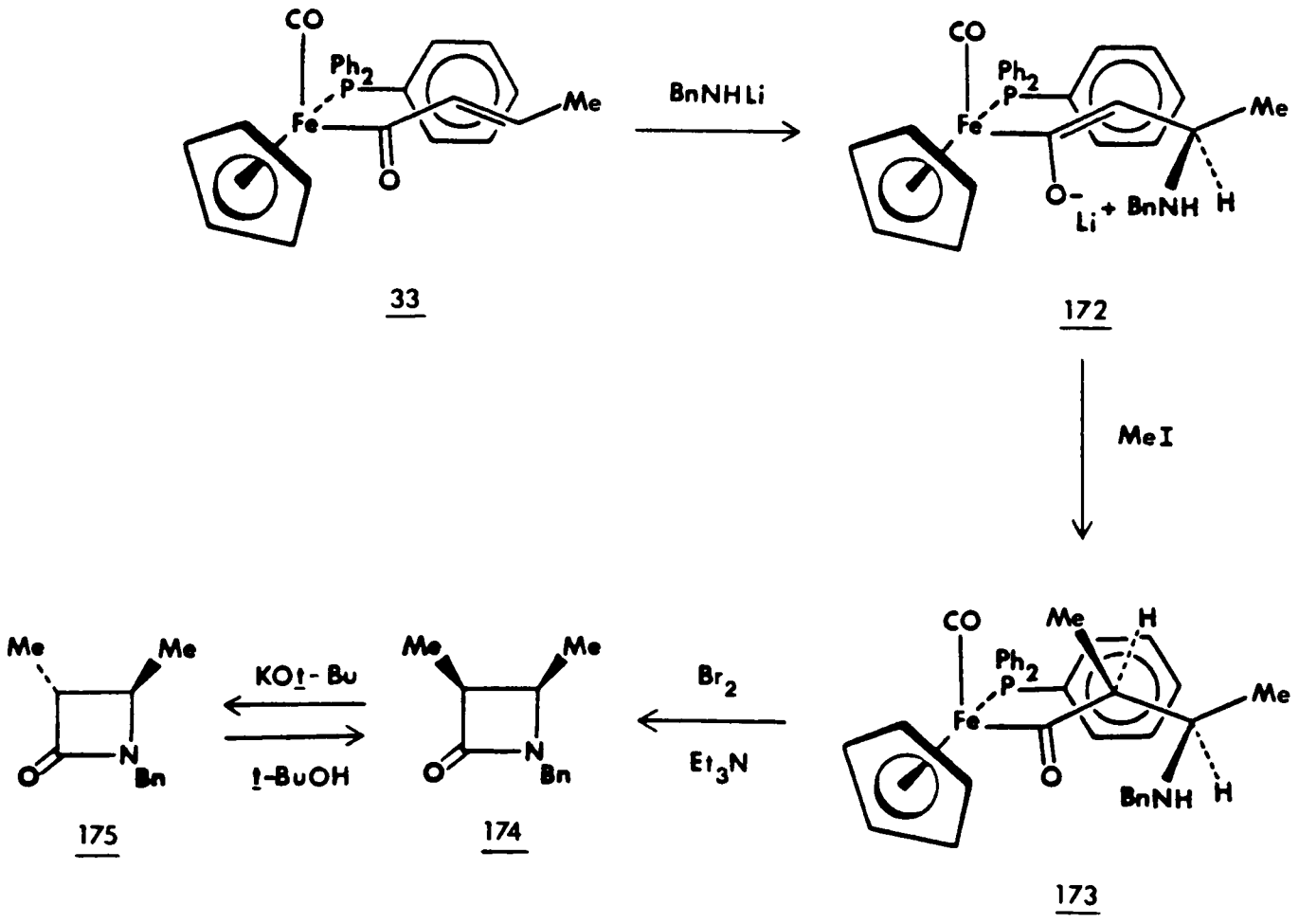
In view of the diastereoselective Michael addition reactivity shown by the E-crotonyl complex 33 towards alkyllithium reagents, it was of interest to determine if similar reactivity was displayed towards lithium benzylamide. Benzylamine was chosen as the primary amine due to the ease with which the benzyl group could be removed to liberate the free amine during any synthetic application. Trapping the enolate resulting from

Michael addition of lithium benzylamide to complex 33 with methyl iodide would generate two new chiral centres in the β-amino acyl complex and ultimately in the β-lactam after decomplexation. In order to investigate the diastereoselectivity of this tandem Michael addition - methylation reaction, lithium benzylamide, prepared from benzylamine and n-butyl-lithium, was added to the racemic E-crotonyl complex 33 in THF at -78°C. The generation of a dark red solution suggested that an enolate had been formed. Quenching the reaction with methyl iodide followed by work-up and chromatography gave a very polar complex as the sole product. In addition to the intense absorptions at 1910 and 1580 cm^{-1} due to the carbon monoxide ligand and the acyl group respectively, the infrared spectrum of the product included an absorption at 3330 cm^{-1} attributable to the N-H stretching mode. The ^1H n.m.r. spectrum contained a complex aromatic signal due to twenty protons, an AB system at δ3.67, 3.32 due to two diastereotopic benzyl protons and also two methyl doublets at δ1.12 and 0.54. All of the spectroscopic data was consistent with formation of the α,β-dimethyl-β-amino acyl complex 173 (91%) as a single diastereoisomer (diastereoselectivity > 100:1:1:1†). The doublet at δ1.12 in the ^1H n.m.r. spectrum due to the α-methyl group, as confirmed by decoupling experiments, enabled the relative stereochemistry between the iron and α-centres to be assigned as RS,SR.[43] The relative configuration between the α- and β-centres was confirmed as SR,RS by oxidative decomplexation of complex 173 using bromine in dichloromethane at -78°C to the known β-lactam, cis-3,4-dimethyl-N-benzylazetidin-2-one 174.[158]

† ^{13}C n.m.r. satellites in the ^1H n.m.r. spectrum of complex 173 were used to assess the diastereoisomeric purity.

Since no trace of the trans isomer 175 could be detected, removal of the chiral iron auxiliary must have proceeded without epimerisation at either the α- or β-centre.[74] The relative configuration in complex 173 was therefore established as RSR,SRS. By analogy with the reactivity described in chapter 5, its formation is consistent with Michael addition of lithium benzylamide occurring to complex 33 in the cisoid and anti (CO to acyl) conformation away from the triphenylphosphine ligand to generate enolate 172, which is then selectively methylated from the least hindered face in the same anti (CO to acyl) conformation.

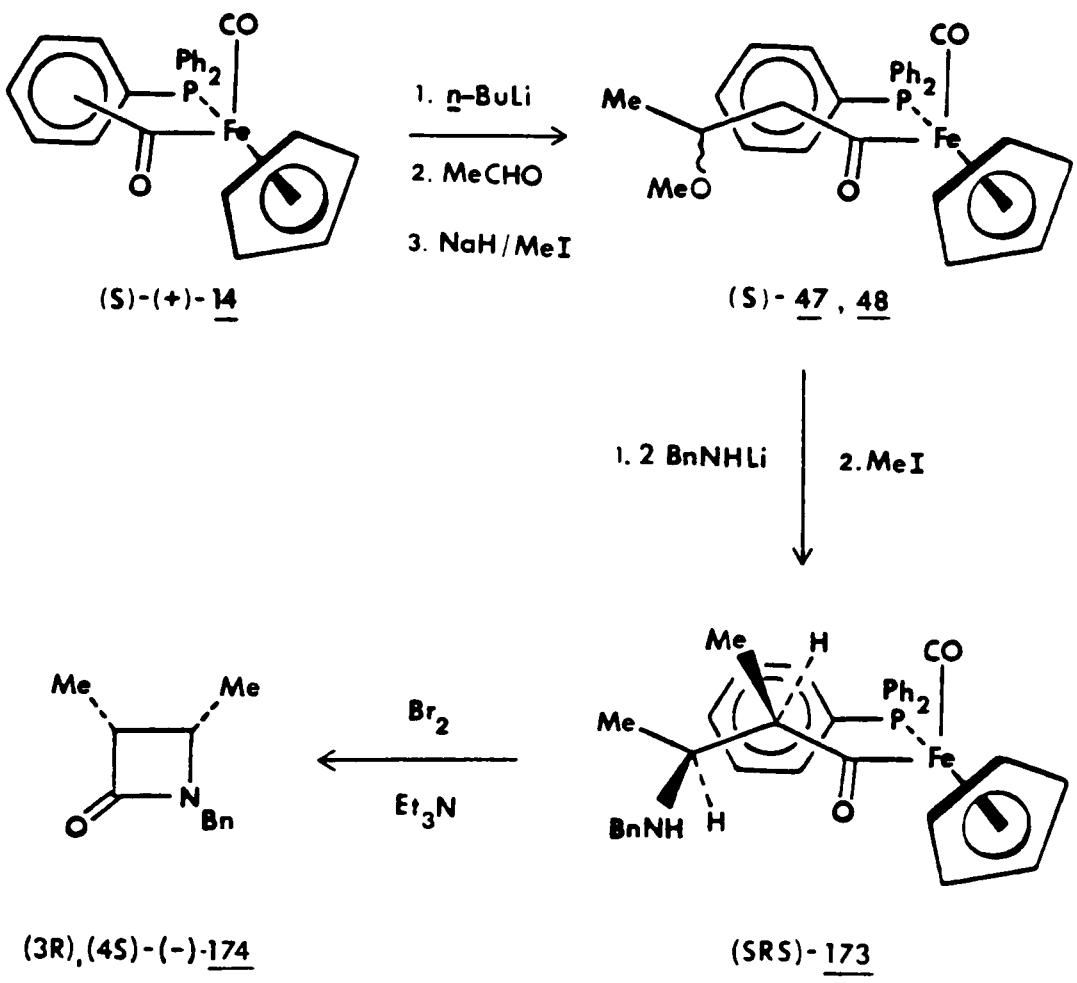
Epimerisation of 174 by treatment with potassium t-butoxide in t-butanol gave a 1:2 mixture of 174 and its trans epimer 175,[158] thus demonstrating that the stereochemical outcome of the decomplexation reaction is not determined by the formation of the thermodynamically most stable β-lactam but by the stereochemistry of the tandem Michael addition-alkylation reaction.



33 172 173 174 175

Having demonstrated the highly diastereoselective tandem Michael addition-methylation of complex 33, extension of this reactivity to resolved iron acyl complexes would allow β-lactam 174 to be produced in high optical purity.

The optically pure (S)-(+)-methyl acyl complex 14, whose absolute configuration has been unambiguously assigned (chapter 2), was treated successively with n-butyllithium and acetaldehyde to give an essentially 1:1 mixture of the corresponding β-hydroxy complexes. Clean O-methylation with sodium hydride-methyl iodide gave the (S)-β-methoxy complexes 47 and 48 which were treated with two equivalents of lithium benzylamide and then methyl iodide. The (S)-α,β-dimethyl-β-amino acyl complex 173 was obtained directly, presumably via the intermediacy of (S)-33 (chapter 5). Without purification, (SRS)-173 was decomplexed with bromine to (3R),(4S)-(-)-3,4-dimethyl-N-benzylazetidin-2-one 174, $[\alpha]_D^{24}$ -29.2° (c 0.69, $CHCl_3$), in 42% yield. The absence of any of the trans isomer 175 again indicated that

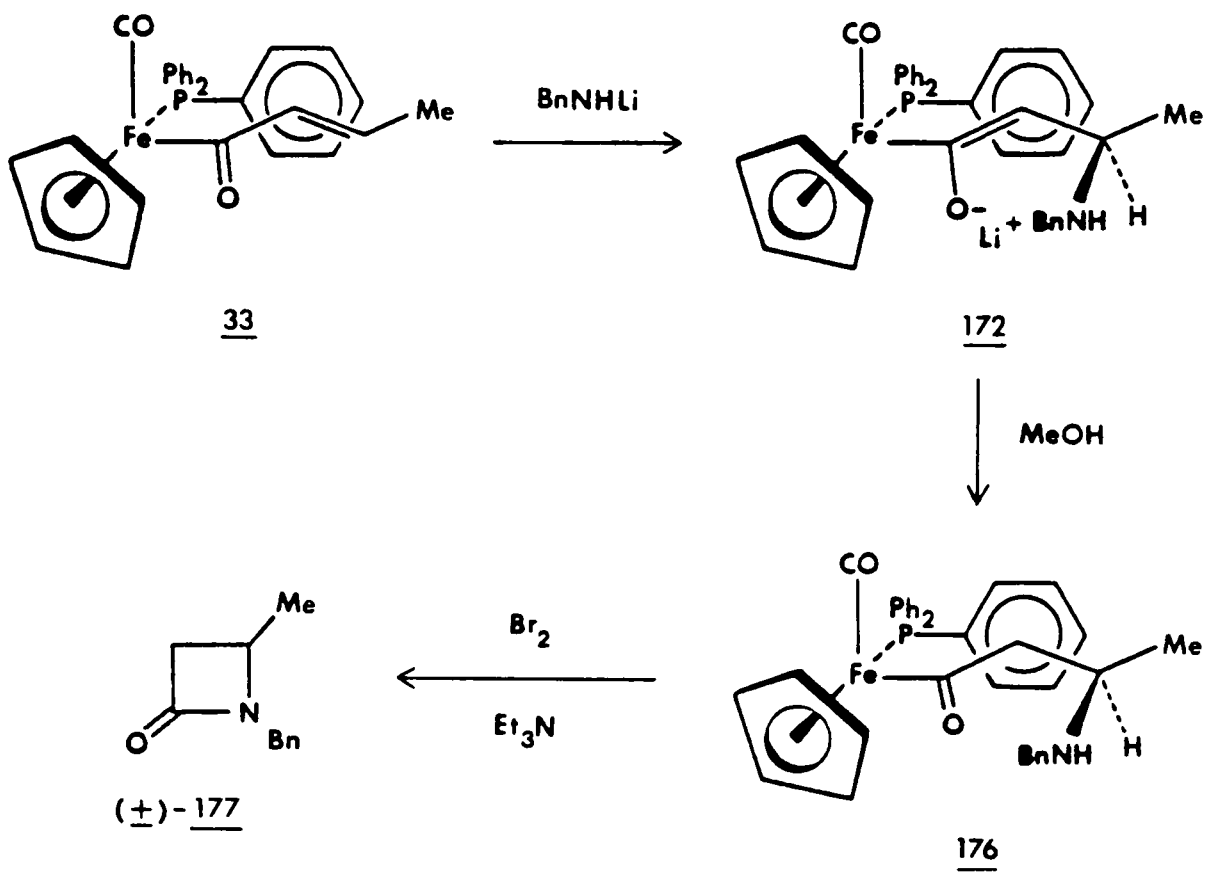


decomplexation had occurred without epimerisation at either the α- or β-centre. This when combined with the fact that the starting (S)-(+)-methyl acyl complex 14 was optically pure and that the derived complex (SRS)-173 was formed with greater than 100:1:1:1 diastereoselectivity, necessitates that (3R),(4S)-(-)-174, not previously known in optically active form, has an optical purity of greater than 100:1 and the absolute configuration as stated.†

IV. Asymmetric synthesis of (4S)-(-)-4-methyl-N-benzylazetidin-2-one[138,164]

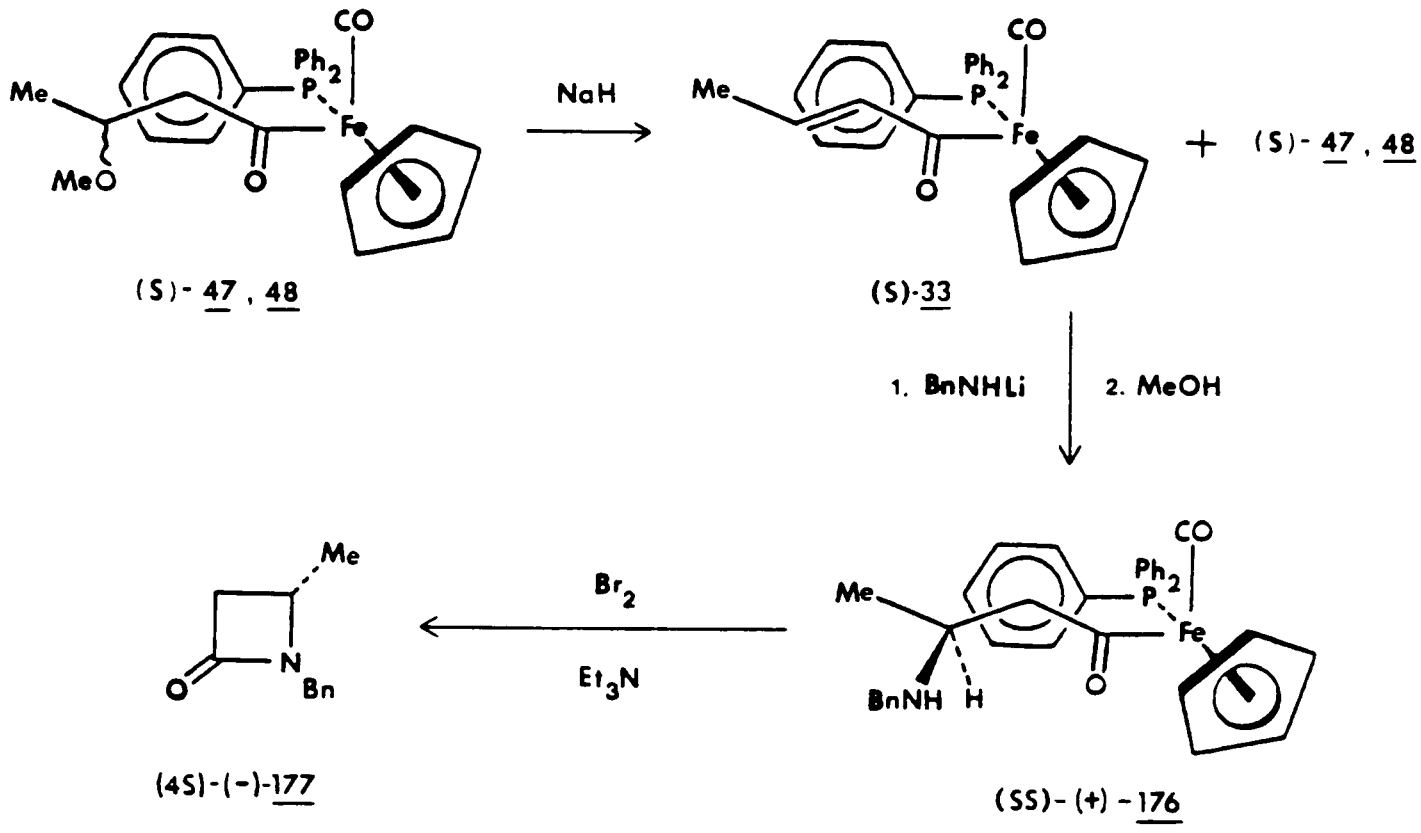
Addition of lithium benzylamide to complex 33 followed by protonation of the resulting enolate with methanol gave a single diastereoisomer of the β-methyl-β-amino acyl complex 176 (92%) as deduced by ^{1}H (single β-methyl doublet at δ0.68) and ^{13}C n.m.r. spectroscopy. The relative stereochemistry in complex 176 was assigned as RR,SS by analogy with the stereochemical outcome of the Michael addition of lithium benzylamide to complex 33 followed by methylation as described in the previous section. Complex 176 must have the same relative configuration at the β-centre as that in complex 173 since both reactions proceed *via* the same enolate 172, arising from Michael addition of lithium benzylamide to complex 33 in the *cisoid* and *anti* (CO to acyl) conformation. Protonation of enolate 172 gives the observed product 176. The known racemic β-lactam, 4-methyl-N-benzylazetidin-2-one 177 [158,161,165] was obtained in 55% yield upon oxidative decomplexation of complex 176 with bromine in dichloromethane at -78°C.

† The diastereoselective but racemic synthesis of the β-amino iron acyl complex 173 by Michael addition of lithium benzylamide to complex 33 followed by methylation has subsequently been verified by Liebeskind.[139]



These reactions were subsequently extended to the asymmetric synthesis of β-lactam 177. The (S)-β-methoxy complexes 47 and 48, derived from the optically pure (S)-(+)-methyl acyl complex 14 as described above, were subjected to sodium hydride-induced elimination of methanol in THF (see chapter 3). Complex (S)-33 was isolated together with recovered starting material (S)- 47 and 48 which as an inseparable mixture (2:1 respectively), was treated with excess lithium benzylamide followed by methanol.

A single observable diastereoisomer of the (S),(2S)-(+)-β-methyl-β-amino acyl complex 176, $[\alpha]_D^{21}$ + 143.0° (c 0.44, C_6H_6), was obtained as the sole product (81%). Presumably, the remaining (S)-β-methoxy complexes 47 and 48 underwent base-induced elimination of methanol to generate (S)-33 *in situ*, prior to diastereoselective Michael addition of lithium benzylamide. Oxidative decomplexation of (S),(2S)-176 gave (4S)-(-)-4-methyl-*N*-benzylazetidin-2-one 177, $[\alpha]_D^{24}$ -38.5° (c 2.1, CH_3OH) [lit.[166] $[\alpha]_D^{21}$ -34.5° (c 3.0, CH_3OH)], in 65% yield. Since no epimerisation is expected during the decomplexation step, (4S)-(-)-177 must have an optical purity of greater than 100:1 and the 4S absolute configuration.



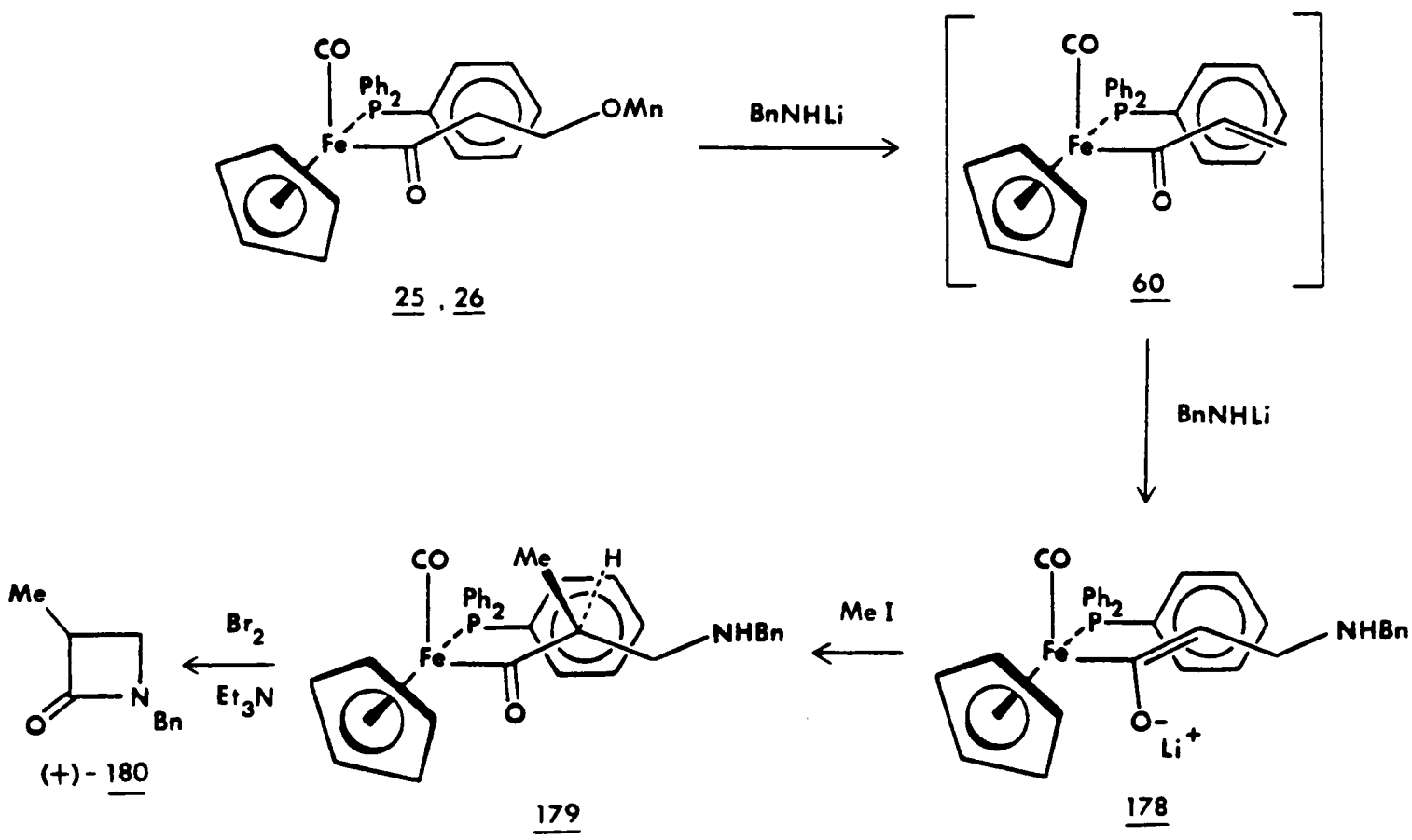
V. Asymmetric synthesis of (3S)-(-)-3-methyl-N-benzylazetidin-2-one[164]

As described in chapter 5, treatment of the β-menthoxy acyl complexes 25 and 26 with two equivalents of an alkyllithium resulted in initial alkyllithium-induced elimination of methanol to give as an intermediate, the acryloyl complex 60. Subsequent Michael addition of the second equivalent of the alkyllithium generated an E enolate which was methylated to give the RS,SR diastereoisomer 117 of the α-methyl hexyl acyl complex with very high diastereoselectivity. Similar reactivity may be envisaged between complexes 25 and 26 and lithium benzylamide to give the corresponding α-methyl-β-amino acyl complex.

Addition of two equivalents of lithium benzylamide to complexes 25 and 26 (1:1) in THF at -78°C generated a dark red solution characteristic of the formation of an enolate. Quenching the reaction with methyl iodide

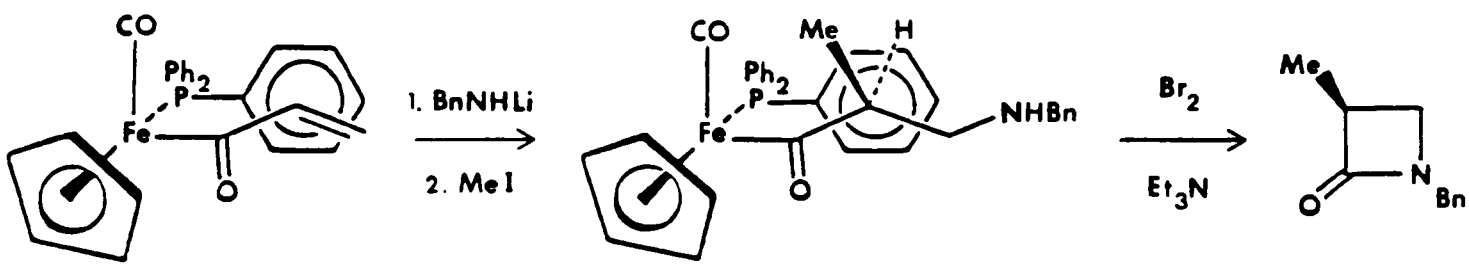
followed by work-up and chromatography gave recovered starting material 25 and 26 (20%; 1:1) together with a polar product identified by ^{1}H n.m.r. spectroscopy as the α-methyl-β-amino acyl complex 179 (40%; diastereoselectivity >100:1). The ^{1}H n.m.r. spectrum contained a methyl doublet at δ1.15 which allowed the relative stereochemistry between the iron and α-centres in complex 179 to be assigned as RS,SR.[43] Complex 179 presumably arose from methylation of E enolate 178 in the anti (CO to acyl) conformation from the least hindered face. E enolate 178 was assumed to have been generated by Michael addition of lithium benzylamide to acryloyl complex 60 in the cisoid conformation, which in turn was formed in situ by lithium benzylamide-induced elimination of (1)-menthol from complexes 25 and 26.

Oxidative decomplexation of complex 179 with bromine in dichloromethane at -78°C gave the known racemic β-lactam, 3-methyl-N-benzylazetidin-2-one 180 in 49% yield.[165,167]



In order to demonstrate that the above reactivity could be used in the asymmetric synthesis of β-lactam 180 and also to confirm the intermediacy of complex 60 in the reaction, the optically pure acryloyl complex (R)-60 was treated with lithium benzylamide in THF at -78°C. Addition of methyl iodide gave (RS)-179 with greater than 100:1 diastereoselectivity which,without purification,was decomplexed to (3S)-(-)-3-methyl-N-benzyl-azetidin-2-one 180 (75%), $[\alpha]_D^{21}$ -32.0° (c 0.33, $CHCl_3$), not previously known in optically active form.

The decomplexation of β-amino iron acyl ligands is known to proceed without loss of stereochemical integrity at the α-centre (see section III). This when combined with the fact that (R)-60 was originally derived from the diastereoisomerically pure β-menthoxy complex 25 and that (RS)-179 was formed with a diastereoselectivity of greater than 100:1, necessitates that (3S)-(-)-180 has an optical purity of greater than 100:1 and the 3S absolute configuration.



(R)-(-)-60 (RS)-179 (3S)-(-)-180

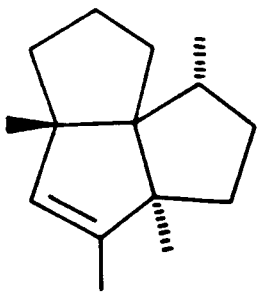
In conclusion, the reactions described in this section show that Michael addition of lithium benzylamide to optically pure α,β-unsaturated iron acyl complexes followed by alkylation of the enolate generated proceeds with very high diastereoselectivity. Subsequent oxidative decomplexation provides a general route for the asymmetric synthesis of α- and/or β-substituted-N-benzyl-β-lactams with high optical purities.

CHAPTER 7

STEREOSELECTIVE SYNTHESIS OF QUATERNARY CARBON CENTRES

I. Introduction

Although chiral quaternary carbon centres are a common structural feature of many natural products, for example isocomene 181,[168] the spirosesquiterpene acorone 182 [169] and the alkaloid joubertiamine 183,[170] synthetic reactions which allow the enantioselective generation of such centres are among the most restricted in organic synthesis.[171]



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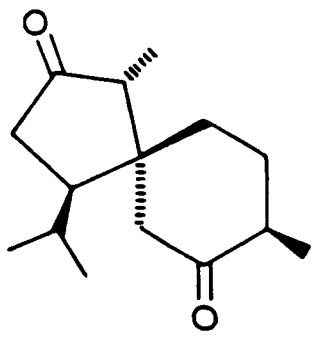

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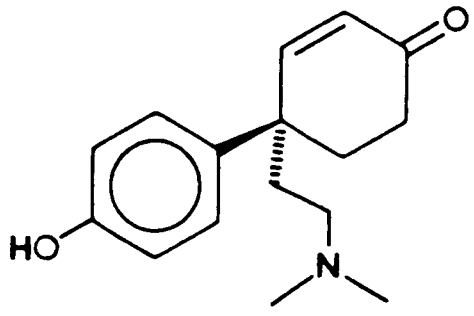


183

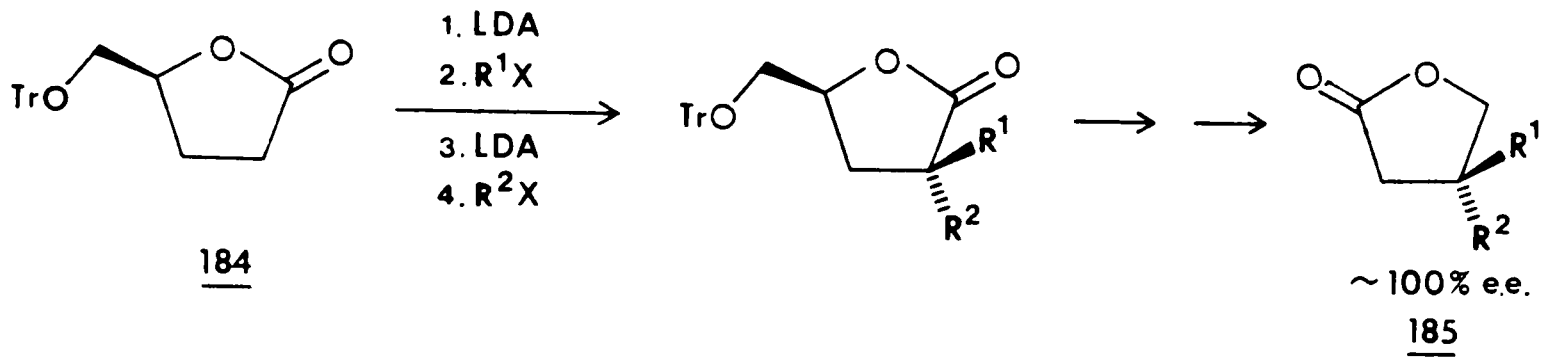
Those that are available however, fall into one of three categories.

1. Reaction of trisubstituted nucleophilic carbon centres with electrophiles

In this the most common approach to the asymmetric synthesis of quaternary carbon centres, a trisubstituted nucleophilic carbon centre is initially generated as an enolate or enolate equivalent that forms part of a permanent or temporary ring system. The least hindered face of the enolate, rendered diastereotopic by the presence of a chiral auxiliary group or a chiral catalyst, is then attacked by a carbon electrophile to give the chiral quaternary centre.

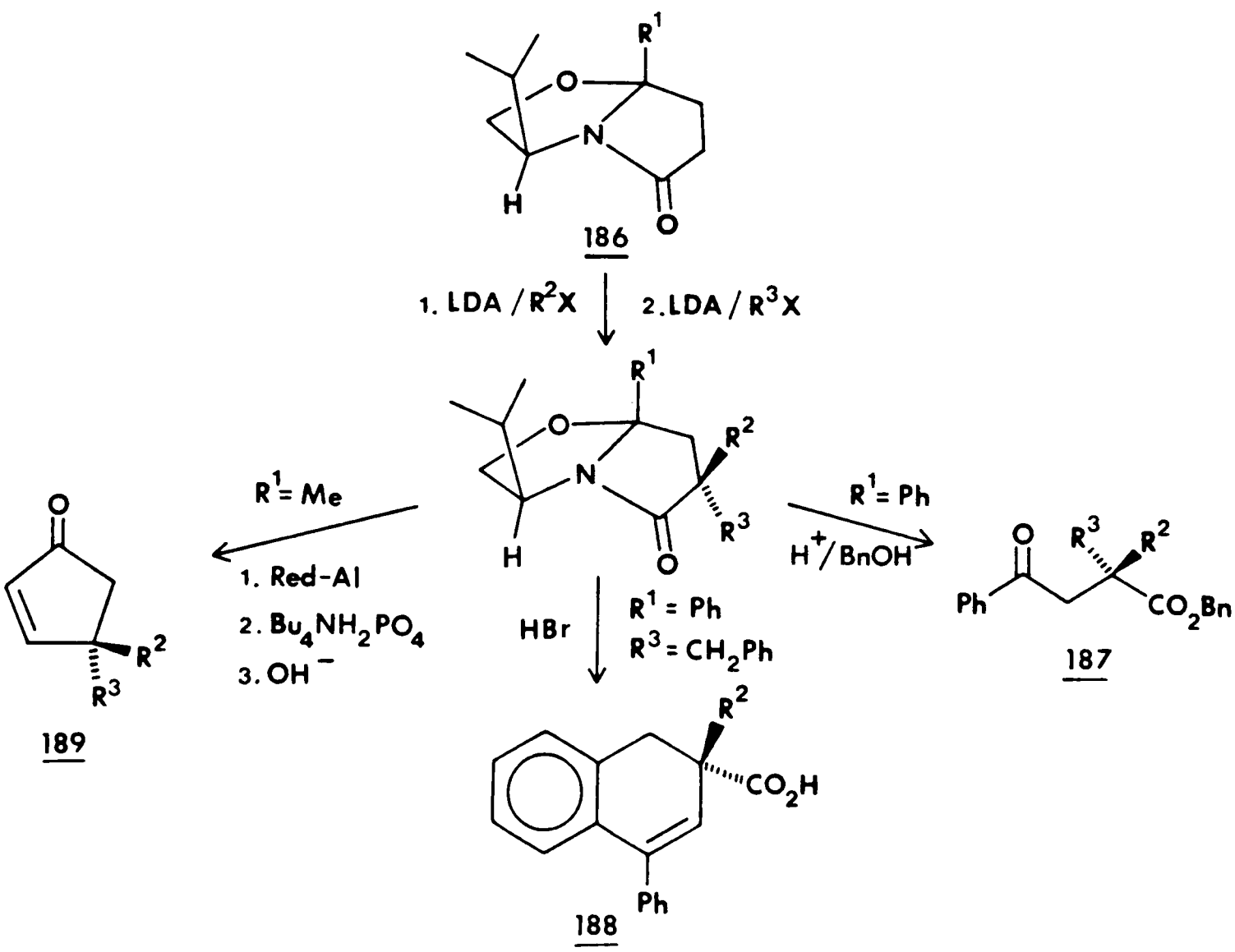
Koga has described one of the most successful applications of this approach in the asymmetric synthesis of β,β-disubstituted γ-butyrolactones. Stereoselective sequential dialkylation of the enolate derived from (S)-γ-trityloxymethyl-γ-butyrolactone 184 away from the bulky trityl group,

followed by a lactone-carbonyl transposition, gave the optically pure lactones 185 containing a quaternary carbon centre.[172] These reactions have subsequently been used in the asymmetric synthesis of eburnamine indole alkaloids[173] and the gibbane framework.[174]



184 185

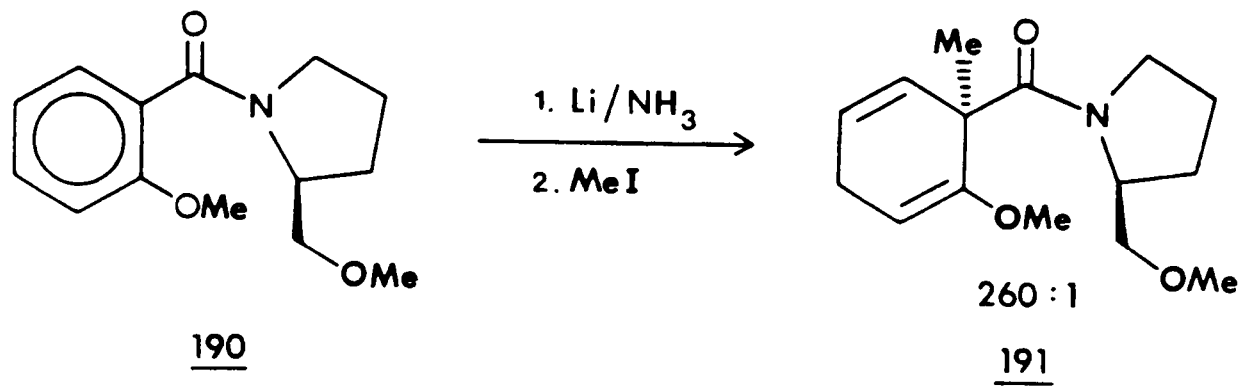
Using a similar dialkylation sequence with up to 40:1 diastereoselectivity, Meyers has reported the asymmetric synthesis of 2,2-dialkyl-4-keto carboxylic acids 187,[175] 3,3-dialkyl-3,4-dihydronaphthalenes 188 [175] and 4,4-dialkyl-2-cyclopentenones 189 [176] based on the bicyclic lactam 186 prepared from (l)-valinol and the corresponding 3-keto carboxylic acid.



189 187 188

An extension of this reactivity to the asymmetric synthesis of 4,4-disubstituted cyclohexenones,[177] (+)-mesembrine[178] and (-)-α-cuparenone[179] has subsequently appeared.

The asymmetric Birch reductive methylation of 190 containing (L)-prolinol as the chiral auxiliary group gave the corresponding 3,3-disubstituted cyclohexa-1,4-diene 191 with a diastereoselectivity of 260:1.[180]

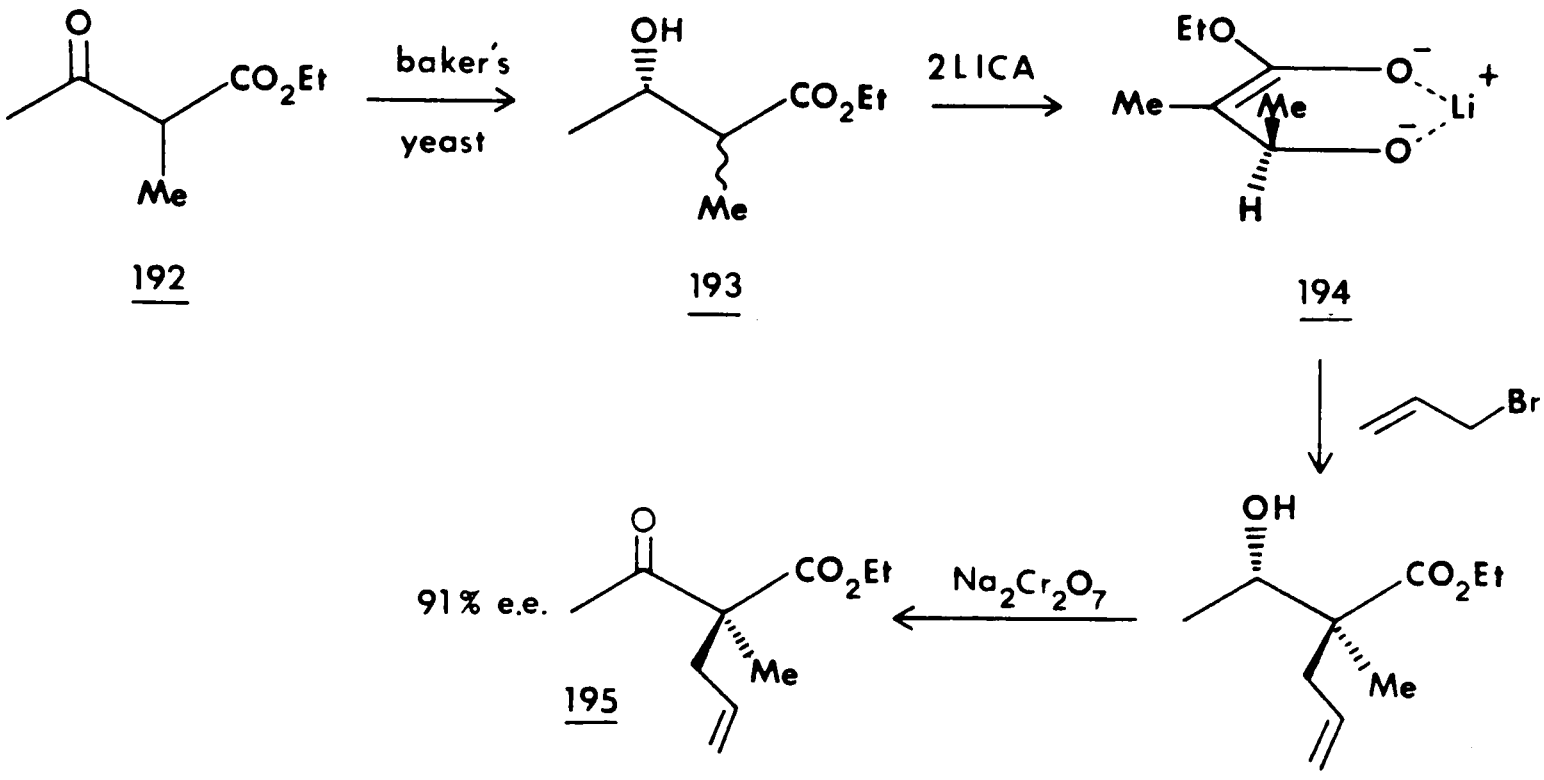


190 191

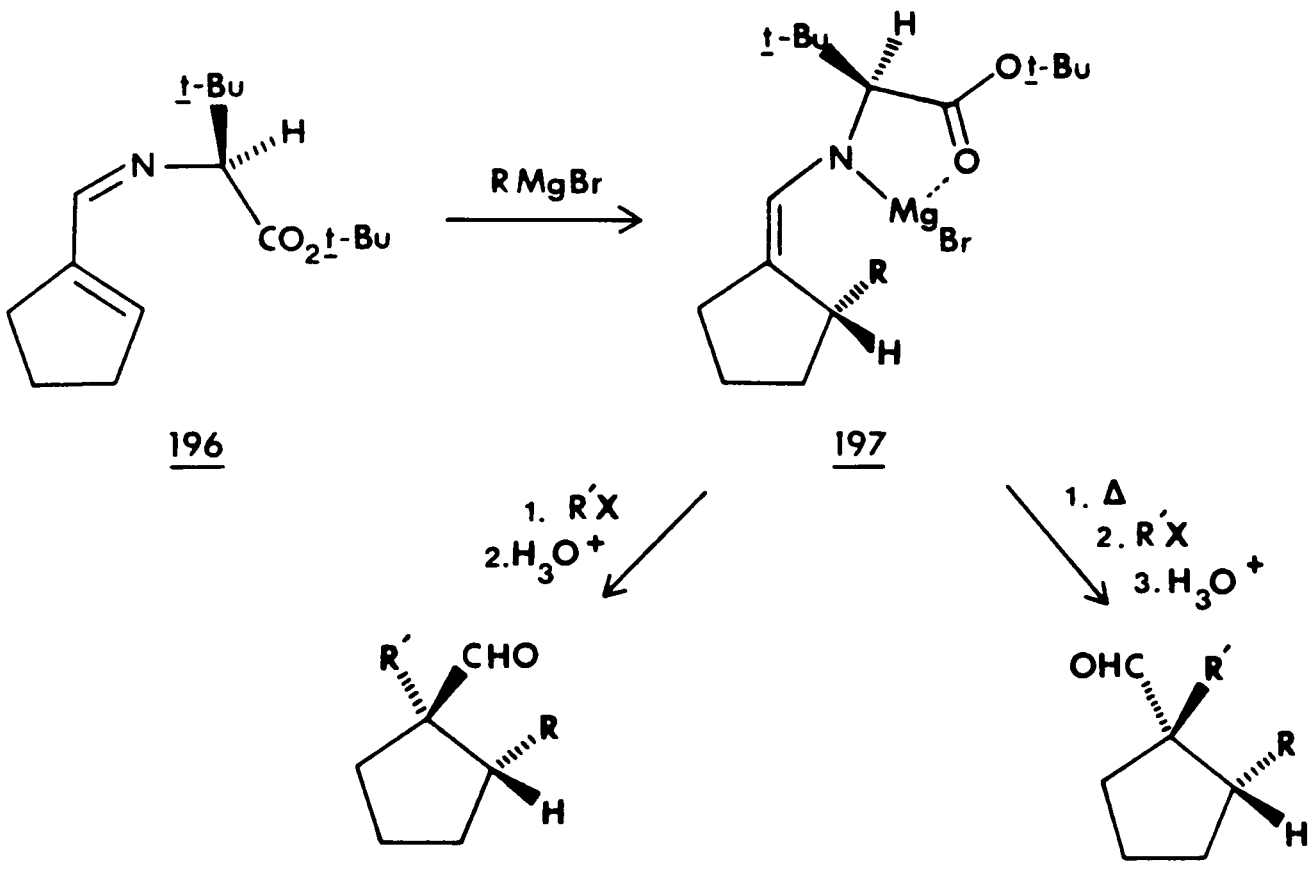
Enantioselective deprotonation of symmetrically substituted ketones using chiral amide bases under kinetically controlled conditions gave chiral α,α-disubstituted cyclohexanones with 25% e.e.[181]

Many of the examples of the diastereoselective formation of quaternary carbon centres in acyclic systems are believed to involve the formation of a temporary chelate complex. Thus, the chiral alcohol 193 obtained from the enantioselective Baker's yeast reduction of the 2-methyl-3-keto ester 192, was converted to 195 containing a chiral quaternary carbon centre with 91% e.e. via alkylation from the least hindered face of the chelated dianion 194.[182] Similar methodology was used in the enantioselective synthesis of 4,4-and 6,6-disubstituted cyclohex-2-en-1-ones.[183]

Koga has used chiral chelated lithioenamines in the asymmetric synthesis of α,α-dialkyl-β-keto esters[184] and α,α-dialkyl cyclic ketones[185] with moderate to high e.e.



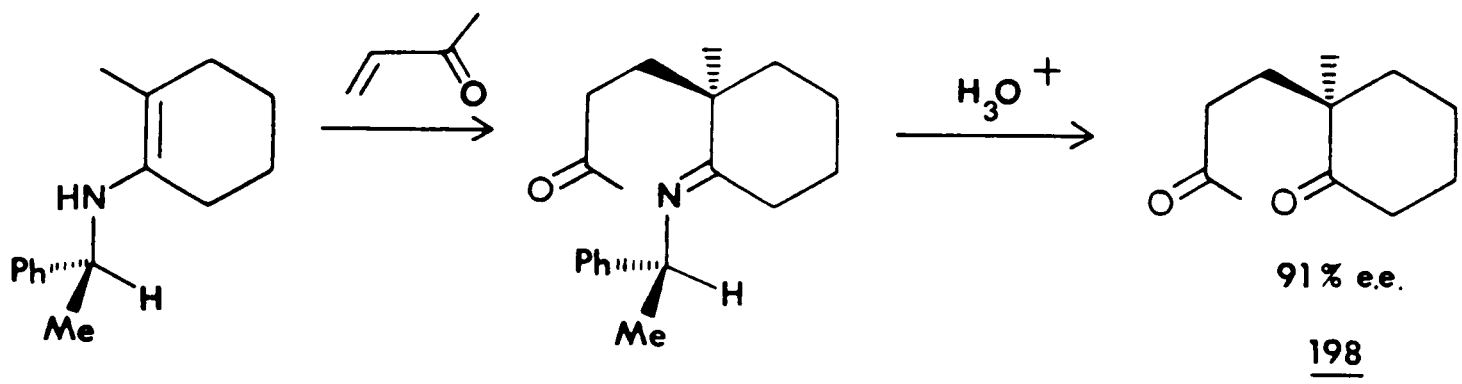
Quaternary carbon centres have been formed with high e.e. by alkylation of the nucleophilic carbon centre generated by Michael addition to a chiral α,β-unsaturated carbonyl system or its synthetic equivalent.



Koga has reported that 1,4-addition of Grignard reagents to chiral α,β-unsaturated aldimines 196 followed by alkylation of the resulting magnesioenamines 197 and hydrolysis, gave trans- or cis-1,2-disubstituted cycloalkanecarboxaldehydes with a quaternary carbon at the 1-position in 82-93% e.e.[186] The tandem Michael addition to and methylation of a similar substrate constituted one of the steps in the asymmetric synthesis of the antileukemic sesquiterpene (+)-ivalin.[187]

Conjugate addition to chiral 1-naphthyloxazolines[188] and a chiral exo-α-alkylidene-γ-butyrolactone[189] occurred with modest diastereoselectivity to furnish after subsequent steps 1,2-dihydronaphthalene aldehydes and (-)-megaphone respectively, both containing chiral quaternary carbon centres.

The enantioselective synthesis of quaternary carbon centres through Michael-type alkylation of chiral enamines to prochiral α,β-unsaturated carbonyl compounds was first reported by Yamada in the asymmetric synthesis of (R)-(+)-4-methyl-4-phenyl-2-cyclohexenone (54% e.e.)[190] and more recently by Pfau in the synthesis of diketone 198.[191]



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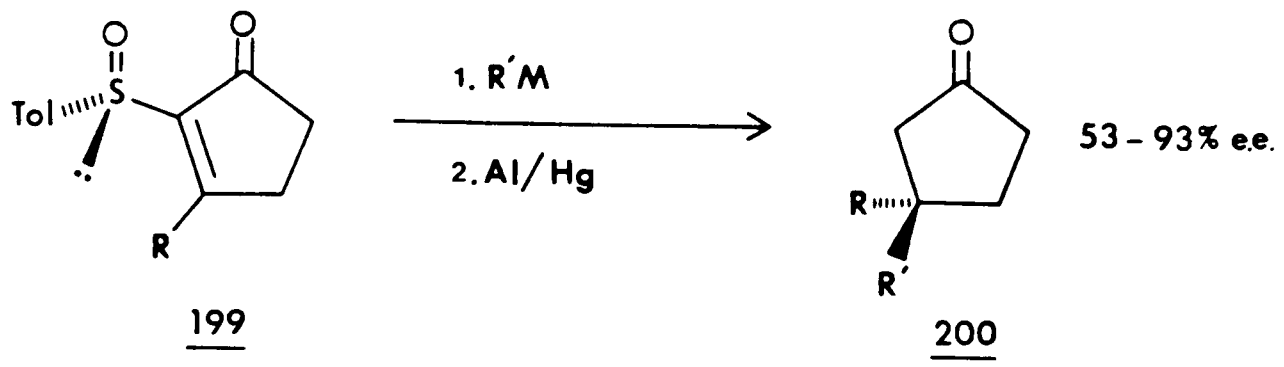
Although chiral catalysts, for example alkaloids,[192] chiral crown ethers[193] and chiral palladium allyl complexes,[194] have also been employed in alkylation and Michael reactions to form quaternary carbon centres adjacent to a carbonyl group, the optical yields have generally been low.

2. Reaction of trisubstituted electrophilic carbon centres with nucleophiles

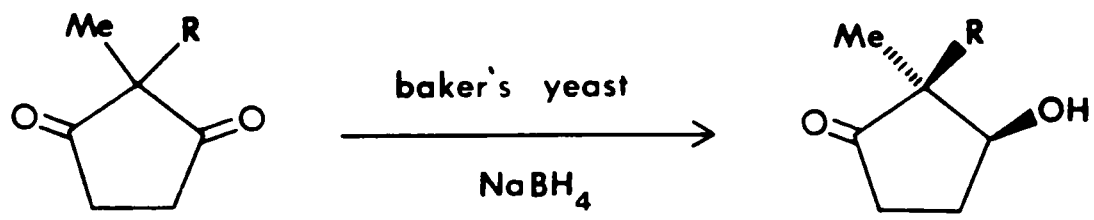
In a reversal of the above reactivity, Posner has described the enantioselective synthesis of 3,3-disubstituted cyclopentanones 200, including (+)-α-cuparenone, by Michael addition of organometallic reagents to optically pure 3,3-disubstituted-2-(arylsulphinyl)cycloalkenones 199.[195]



199 200

3. Prochiral substrates containing quaternary carbon centres

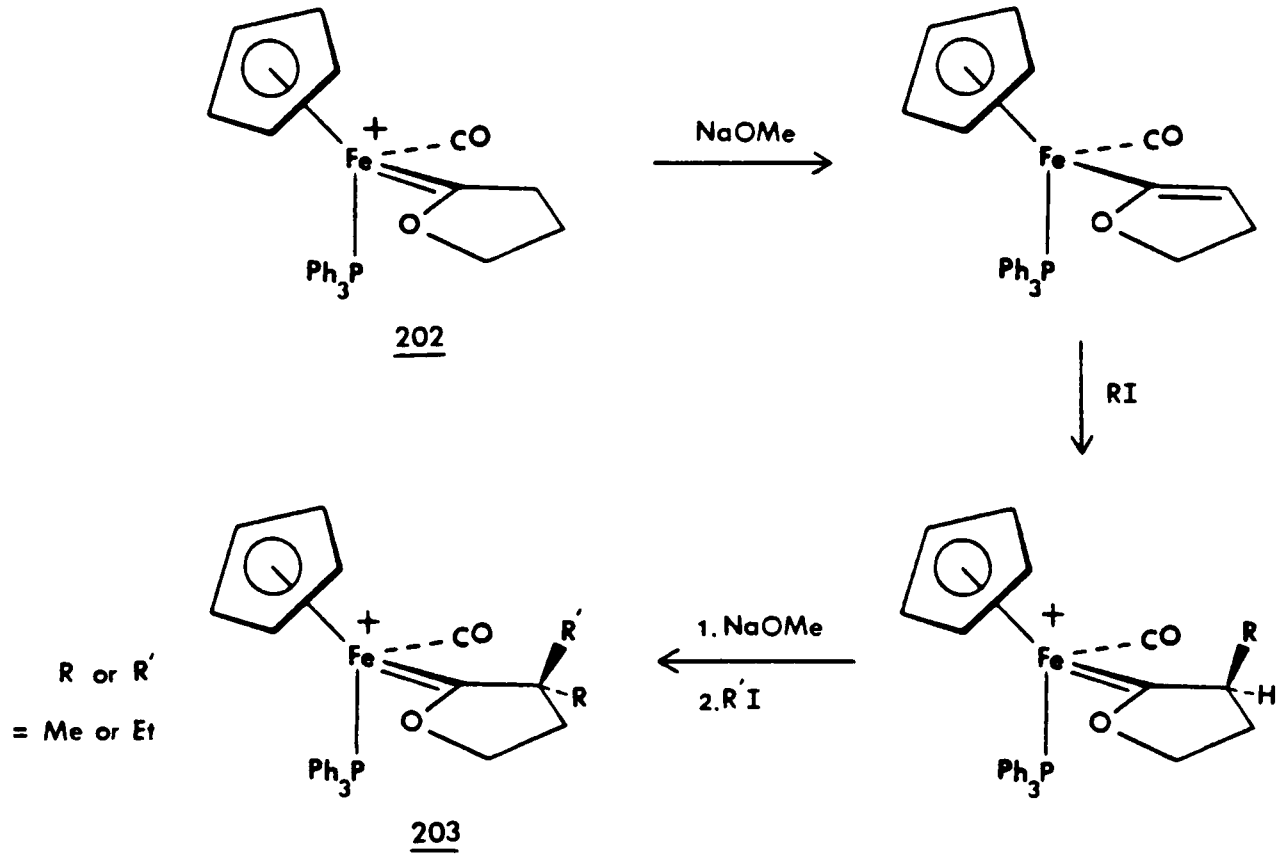
Examples exist of enzymatic processes whereby prochiral precursors bearing quaternary carbon centres are converted chemically into optically active derivatives. Conversion of prochiral dialkyl malonates into their chiral monoesters by porcine liver esterase[196] in a few cases occurred with good enantioselectivity, as did the reduction of prochiral 2,2-disubstituted-1,3-cyclopentanediones 201 with Baker's yeast and sodium borohydride.[197]



201 > 98 % ee

4. Summary

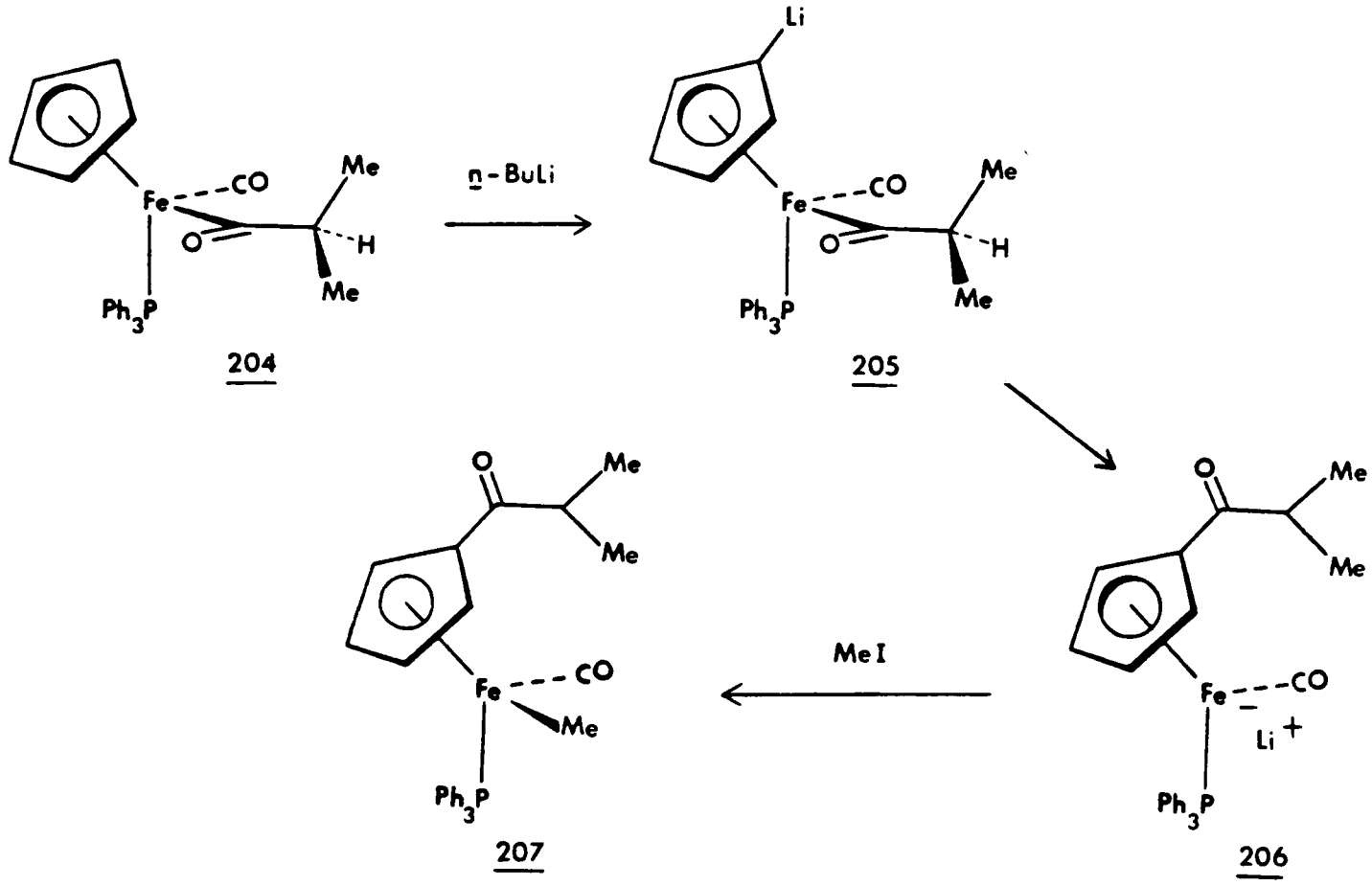
The methods that exist to date for the asymmetric synthesis of quaternary carbon centres are far from general being essentially restricted to cyclic systems and suffering from varying optical yields. Our aim was to utilise the stereochemical control of the chiral iron auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ in the development of a general method for the stereoselective construction of quaternary carbon centres. The use of this auxiliary in a stereoselective synthesis of quaternary carbon centres has already been described by Davies and Curtis.[198] Repeated deprotonation and alkylation of the cyclic carbene complex 202 gave, via alkoxylvinyl intermediates, complexes 203 with greater than 98% diastereoselectivity with decomplexation leading to 2,2-dialkyl-γ-butyrolactones.



202 203

Our previous studies[199] have shown that acyl complexes with tertiary centres α to the acyl group cannot be usefully elaborated by deprotonation and alkylation. The preferred conformation of the isopropyl complex 204 is that in which the α-hydrogen lies in the most sterically demanding position

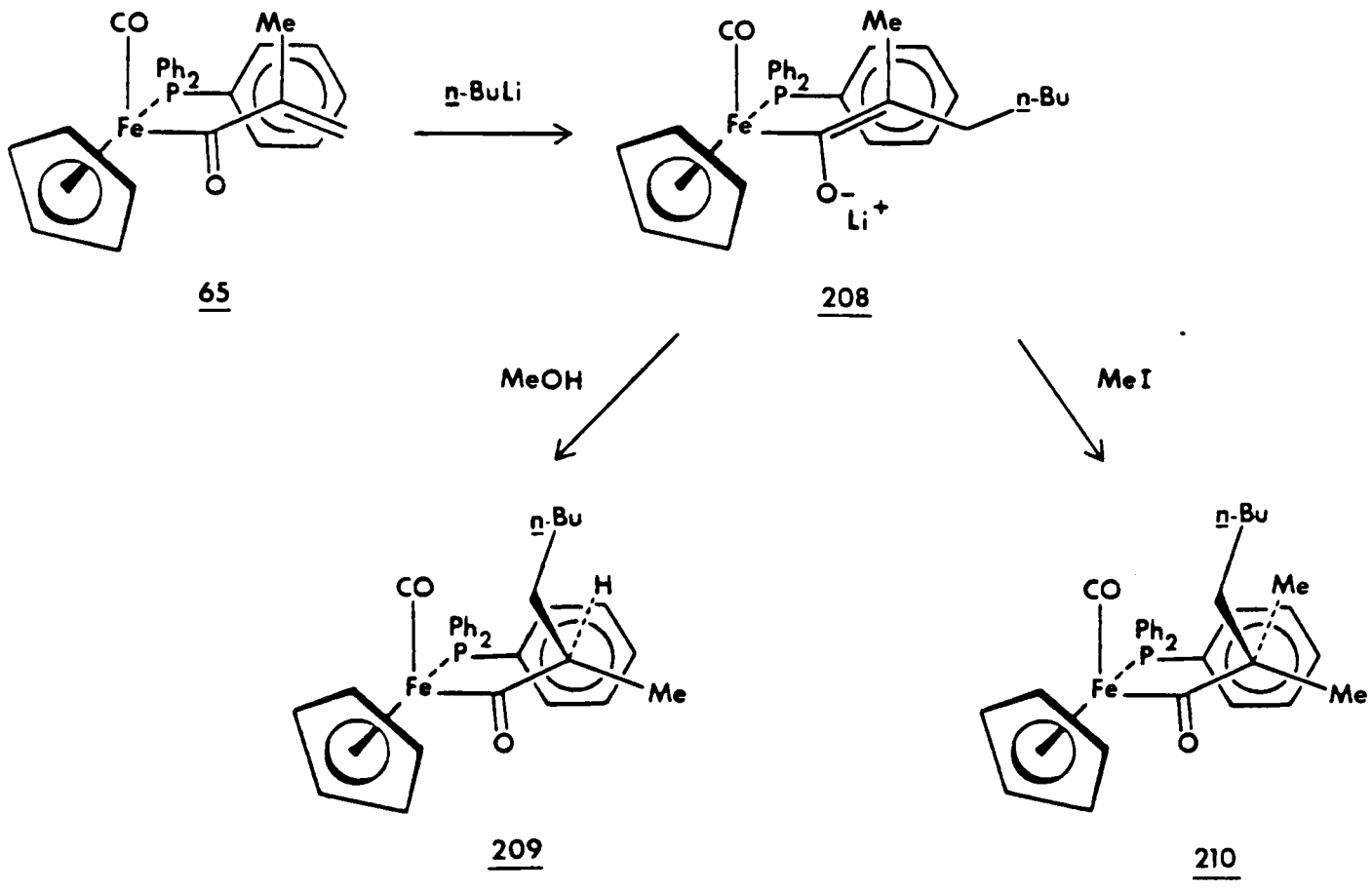
between the carbon monoxide and triphenylphosphine ligands. Deprotonation at this site is disfavoured sterically because the base would have to enter the 'excluded volume' between the plane of the acyl group and the phenyl group of the triphenylphosphine ligand. The preferred site for deprotonation is instead the cyclopentadienyl ligand. Thus, treatment of complex 204 with n-butyllithium generated complex 205 which was found to undergo a rearrangement reaction in which the acyl ligand migrated from the iron atom to the cyclopentadienyl ligand. Methylation of the nucleophilic iron species 206 gave the iron methyl complex 207 [199]. Base-promoted migration of acyl ligands from the metal atom to the cyclopentadienyl ligand is also shown by the analogous monosubstituted ruthenium[199] and rhenium acyl complexes.[200]



We envisaged that a possible alternative method of generating a disubstituted enolate attached to the chiral iron auxiliary would be via a Michael addition of an alkyllithium to an α-substituted-α,β-unsaturated acyl ligand. Alkylation would then give the desired complex containing a quaternary carbon centre α to the acyl group.

II. Diastereoselective tandem Michael addition-alkylation reactions of α-substituted-α,β-unsaturated acyl complexes [201]

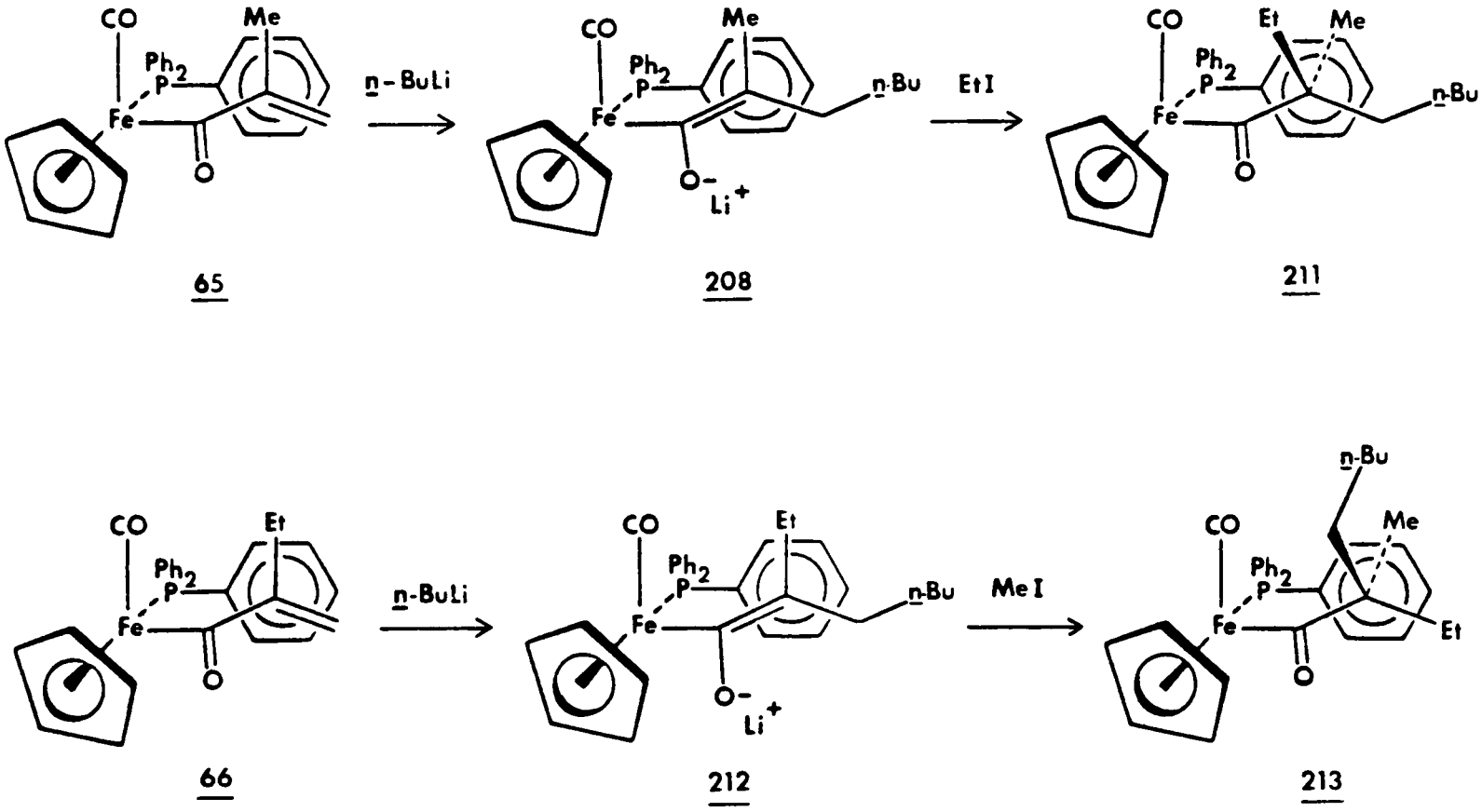
In order to investigate the reactivity of α-substituted α,β-unsaturated acyl complexes towards alkyllithium reagents, complex 65, prepared as described in chapter 3, was in an initial experiment treated with n-butyllithium in THF at -78°C to generate a dark red solution characteristic of the formation of an enolate. The reaction mixture was cooled to -100°C and then quenched with methanol to give upon work-up the α-methyl hexyl acyl complex 209 in 89% yield and with a diastereoselectivity of greater than 100:1. The relative configuration between the iron centre and the new chiral centre at the α-position was assigned as RR,SS on the basis of the α-methyl doublet at δ0.18 in the ^{1}H n.m.r. spectrum.[43] Complex 209 is the alternative diastereoisomer to the RS,SR complex 117 prepared by methylation of the enolate generated by Michael addition of n-butyllithium to the acryloyl complex 60 (see chapter 5). Comparison of the ^{1}H n.m.r. spectrum of this latter complex (α-methyl doublet at δ1.01[43]) with that of (RR,SS)-209 confirmed the diastereoisomeric purity of complex 209. The diastereoselective formation of complex 209 is consistent with protonation of E enolate 208 occurring from the face away from the triphenylphosphine ligand, the enolate adopting an anti (CO to acyl) conformation. Initial coordination of n-butyllithium to the acyl oxygen of 65 followed by delivery to the β-centre which is least distant from the alkyllithium when the acyl ligand adopts a cisoid conformation would in turn generate E enolate 208. Molecular models reveal that in the cisoid conformation of complex 65, the acyl ligand is likely to be twisted out of line with the carbon monoxide ligand and the iron atom such that the methyl group is in the space between the carbon monoxide and cyclopentadienyl ligands, thus minimising interactions with the carbon monoxide ligand.



Quenching enolate 208 with a carbon electrophile would allow the introduction of a quaternary carbon centre α to the acyl group. Complex 65 was thus treated with n-butyllithium and then methyl iodide. A single product was isolated which was shown to be an acyl complex by the intense absorption at 1600 cm^{-1} in the infrared spectrum. The appearance of two methyl singlets at δ0.97 and 0.66 in the ^{1}H n.m.r. spectrum and a low intensity signal at δ61.3 in the ^{13}C n.m.r. spectrum which showed no evidence of C-H coupling in the corresponding off-resonance spectrum, confirmed that methylation of enolate 208 had not occurred on oxygen but at the α-carbon atom to generate a quaternary carbon centre in the product complex 210.

Having demonstrated that the disubstituted enolate 208 attached to the chiral iron auxiliary could be generated by Michael addition of n-butyllithium to the α-substituted-α,β-unsaturated acyl complex 65 and subsequently quenched with methyl iodide, it was of considerable interest to investigate the stereoselectivity of the formation of chiral quaternary

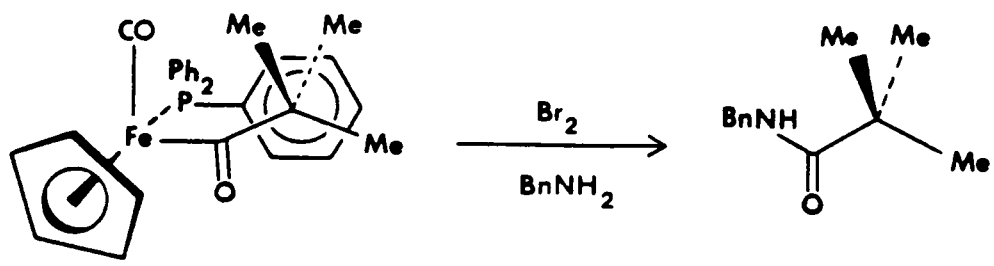
carbon centres. The enolate 208 generated by Michael addition of n-butyllithium to complex 65 was therefore quenched with ethyl iodide. Work-up gave the acyl complex 211 in 82% yield containing a chiral quaternary carbon centre. The cyclopentadienyl protons and the protons due to the three methyl groups in complex 211 appeared as single signals in the ^1H n.m.r. spectrum suggesting the predominant formation of a single diastereoisomer. In order to confirm the diastereoisomeric purity of complex 211 and to illustrate the generality of the stereoselective quaternary carbon centre forming reaction, the alternative diastereoisomer 213 was prepared in 80% yield by n-butyllithium addition to the α-ethyl-substituted-α,β-unsaturated acyl complex 66 followed by quenching of the enolate 212 with methyl iodide.



Complexes 211 and 213 were each found to be diastereoisomerically pure by ^1H and ^{13}C n.m.r. spectroscopy (i.e. diastereoselectivity > 100:1). By analogy with the protonation reaction of E enolate 208 in the anti (CO to acyl) conformation from the least hindered face to form (RR,SS)-209, it was assumed that reaction of the same enolate with ethyl

iodide,again from the face away from the triphenylphosphine ligand, would generate the RS,SR diastereoisomer 211 of the complex containing a chiral quaternary α-carbon centre. The relative configuration in complex 213 was therefore assigned as RR,SS presumably resulting from methylation of E enolate 212 in the anti (CO to acyl) conformation again from the least hindered face. Enolate 212 was envisaged as having been formed by Michael addition of n-butyllithium to complex 66 in the cisoid conformation.

The conversion of an α-trisubstituted acyl complex to the corresponding amide was demonstrated by the oxidative decomplexation of the α-t-butyl complex 214 [202] with bromine in the presence of benzylamine. Work-up and chromatography gave the pure amide 215 in 57% yield identified by absorptions at 3480 (N-H) and 1660 (C=O) cm^{-1} in the infrared spectrum and a nine proton singlet at δ1.24 in the ^1H n.m.r. spectrum.



214 215

In conclusion, the tandem Michael addition-alkylation reactions of α-substituted-α,β-unsaturated acyl ligands bound to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ described in this section provide a highly stereoselective method for the synthesis of chiral quaternary carbon centres.

CHAPTER 8

ASYMMETRIC DIELS-ALDER REACTIONS

I. Introduction

The simultaneous regioselective and stereoselective construction of two new sigma bonds in the Diels-Alder reaction has made this one of the most powerful synthetic methods available to the organic chemist.[203] In recent years, significant advances have been made in the development of asymmetric versions. The stereodifferentiating intermolecular [204] reaction between a dienophile and a diene, usually in the presence of a Lewis acid, has been used to generate up to four chiral centres with predictable relative and absolute configuration.[205,206,207,208] There are examples in which the chiral auxiliary group resides separately in the diene [209,210] and Lewis acid [211] components. However, in the majority of cases it is the dienophile which carries the chiral auxiliary.

Although fumarates,[212] α,β-unsaturated ketones,[210,213] crotonates [214,215] and α,β-enoates with a chiral β-substituent [216,217] have been used as chiral dienophiles in asymmetric Diels-Alder reactions, work has essentially been concentrated on the Lewis acid-mediated cycloaddition of 1,3-dienes to chiral acrylates.

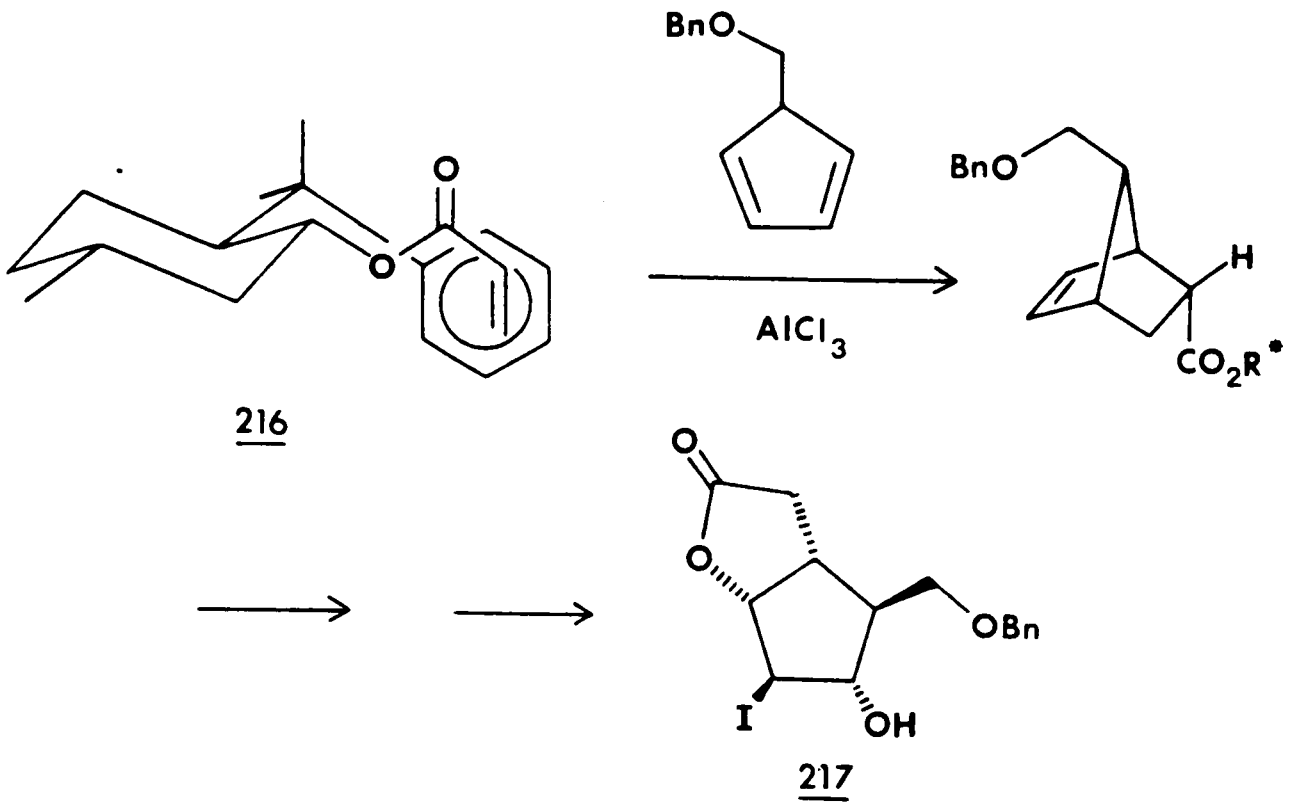
Chiral acrylate equivalents

a. Acrylates derived from chiral alcohols

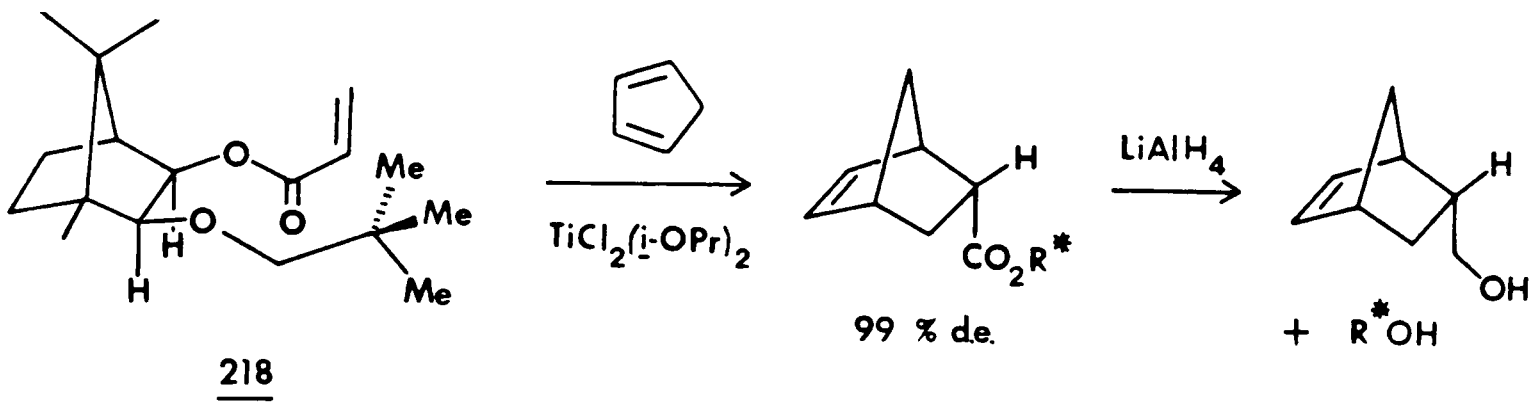
The highly diastereoselective aluminium trichloride-mediated *endo* addition of a cyclopentadiene to acrylate 216 derived from (-)-8-phenylmenthol was first reported by Corey in the asymmetric synthesis of the key prostaglandin intermediate 217.[218]

Oppolzer attributed the π-face selectivity to the involvement of the conformation in which the *anti* arrangement of the carbonyl group and the olefinic bond caused the phenyl ring to shield the C_α *re* face† and permit more facile addition of the diene to the *si* face.

† Enantiotopic and diastereotopic faces can be named by an extension of the Cahn-Ingold-Prelog system.[219]



Similar conformational preferences in acrylates derived from a wide variety of chiral menthyl and norbornyl alcohols,[220] cis-3-hydroxyisobornyl ethers [221] and 3-alkylborneols and isoborneols [222] were shown by Oppolzer to result in good to excellent diastereoselection in the formation of cycloadducts. In one particular case, the titanium dichloride diisopropoxide-induced cycloaddition of cyclopentadiene to the neopentyl ether 218 gave the corresponding adduct with 96% endo selectivity and over 99% diastereofacial differentiation.[221]



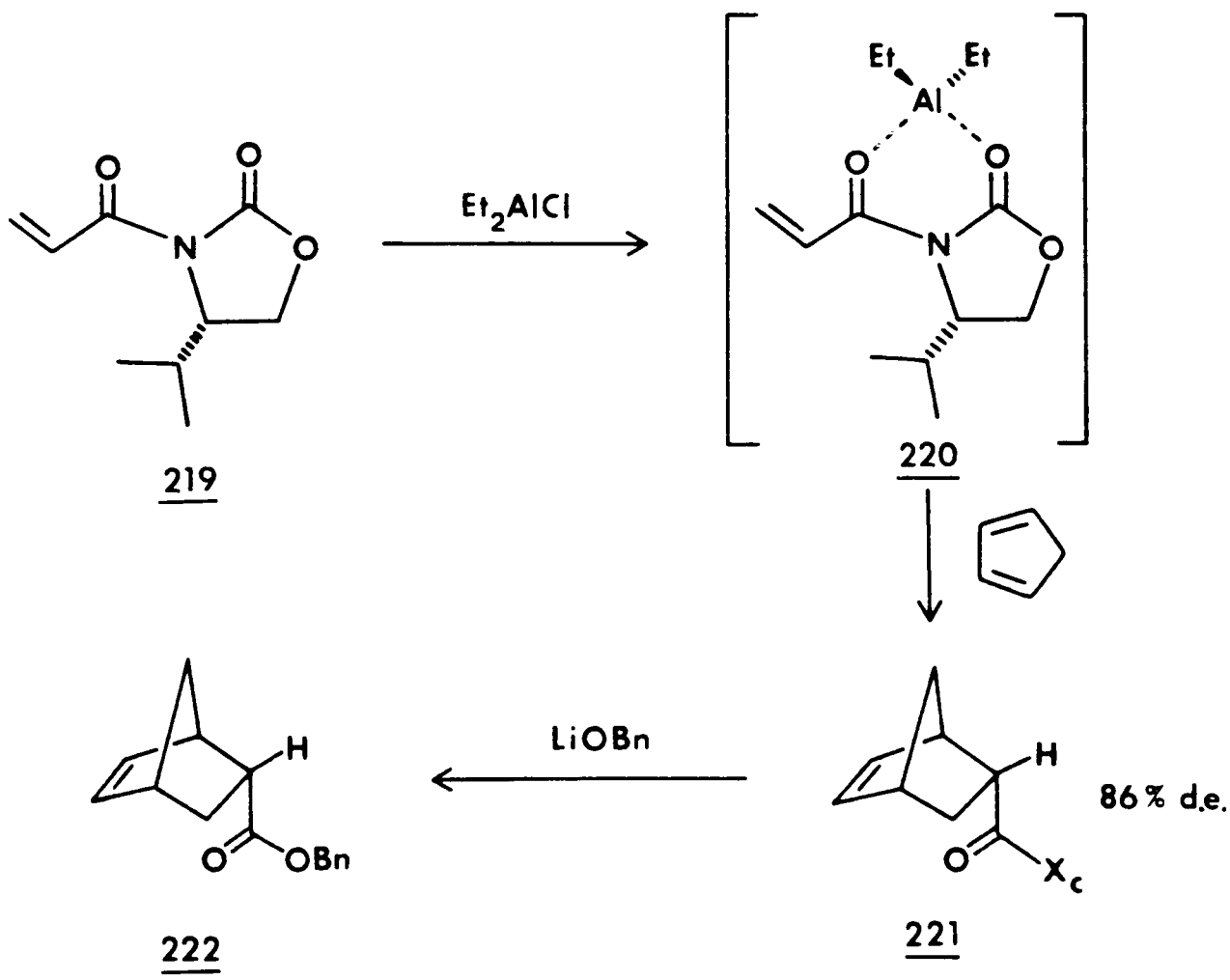
An intermediate in the synthesis of (R)-(-)-sarkomycin was prepared from the cycloadduct obtained from the reaction of 218 with 1,3-butadiene.[223]

In other successful applications of chiral acrylates as dienophiles in asymmetric Diels-Alder reactions, camphor-10-sulphonic acid derivatives,[224] (S)-(+)-3,3-dimethyl butan-2-ol,[225] (S)-ethyl lactate [226,227] and D-pantolactone [228] were used as chiral auxiliaries.

The relative orientation of the acrylate and the diene in the transition state, as well as the role played by the Lewis acid in enhancing regioselectivity, diastereoselectivity and enantioselectivity, have been the subjects of recent mechanistic proposals.[206,208]

b. N-acryloyl compounds

The diethylaluminium chloride-induced addition of cyclopentadiene to chiral N-acryloyloxazolidone 219, derived from (S)-valinol, gave norbornene 221 with 99% endo selection and 86% diastereofacial differentiation. The stereochemical course of the addition was rationalised in terms of endo addition occurring to the least hindered face of the chelate complex 220. Treatment of 221 with lithium benzyloxide furnished the benzyl ester 222. Equally selective inverse π-face topicity was displayed by the (1S,2R)-norephedrine-derived dienophile.[214]



219 220 221 222

Cycloaddition of cyclopentadiene to a chiral N-acryloylsultam in the presence of diethylaluminium chloride or titanium tetrachloride proceeded with 96-99% endo and 93-98% π-face selectivity.[215]

In view of these extensive studies, it was of considerable interest to determine whether the chiral acryloyl complex [(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH{=}CH_2$] 60 could also function as a chiral dienophile equivalent in asymmetric Diels-Alder reactions.

II. Asymmetric Diels-Alder reaction between [(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH{=}CH_2$] 60 and cyclopentadiene [229]

In an initial experiment, the racemic acryloyl complex [(η^5-C_5H_5)Fe-(CO)(PPh_3)$COCH{=}CH_2$] 60 was treated with freshly prepared cyclopentadiene in dichloromethane at room temperature. Even after prolonged treatment and heating, no evidence of cycloaddition was observed. Presumably the electron releasing effect of the iron moiety reduces the electronic disparity between the two components sufficiently for the Diels-Alder reaction to be thermodynamically unfavourable.

It was anticipated that the electron density in the C-C double bond of complex 60 could be reduced by coordination of a Lewis acid to the acyl oxygen. One equivalent of zinc (II) chloride [230] was therefore added to complex 60 in dichloromethane, prior to treatment with cyclopentadiene. After several hours at room temperature, the dichloromethane solution, originally orange in colour, became yellow. In view of the characteristic yellow colour shown by iron carbene complexes,[54] this suggested that coordination of the zinc ion to the acyl oxygen had occurred. Work-up and chromatography gave a single acyl band which was much less polar than the starting acyl complex 60. The ^1H n.m.r. spectrum of this product contained two doublet of doublets at δ6.07 and 5.71, each due to one

vinylic proton, a doublet at δ4.44 due to five cyclopentadienyl protons and two broad one-proton singlets at δ3.45 and 2.62 characteristic of bridgehead protons. These signals together with other spectroscopic data were consistent with the formation of a Diels-Alder adduct between complex 60 and cyclopentadiene (54%). Smaller cyclopentadienyl-proton doublets at δ4.48 and 4.35 in the ^{1}H n.m.r. spectrum were attributed to two out of the remaining three possible diastereoisomers of the cycloadduct. The diastereoselectivity of the reaction was deduced from the ^{1}H n.m.r. spectrum as being 10:1:1.

In order to determine whether the major diastereoisomer was that derived from endo or exo addition of cyclopentadiene to complex 60, this inseparable 10:1:1 mixture of diastereoisomers was oxidatively decomplexed with ammonium ceric nitrate in aqueous THF to give the corresponding bicyclo[2.2.1]hept-5-ene-2-carboxylic acid. Comparison of the ^{1}H n.m.r. spectrum of the crude acid with those of authentic samples revealed that the acid had been formed as a 5:1 mixture of endo to exo isomers. This ratio implies that the major diastereoisomer from the Diels-Alder reaction originated from kinetic endo addition of cyclopentadiene to the α,β-unsaturated acyl ligand in complex 60.† Presumably, the transition state leading to the endo adduct is stabilised by a secondary interaction between the highest occupied molecular orbital and the lowest unoccupied molecular orbital of the acryloyl and diene components.[72] It follows therefore that the two minor diastereoisomers were derived from exo addition of the diene. The correlation between the stereochemistry in the organometallic precursor and that in the decomplexed acid again illustrates that oxidative removal of the chiral iron auxiliary proceeds without loss of stereochemistry at the α-centre.[74]

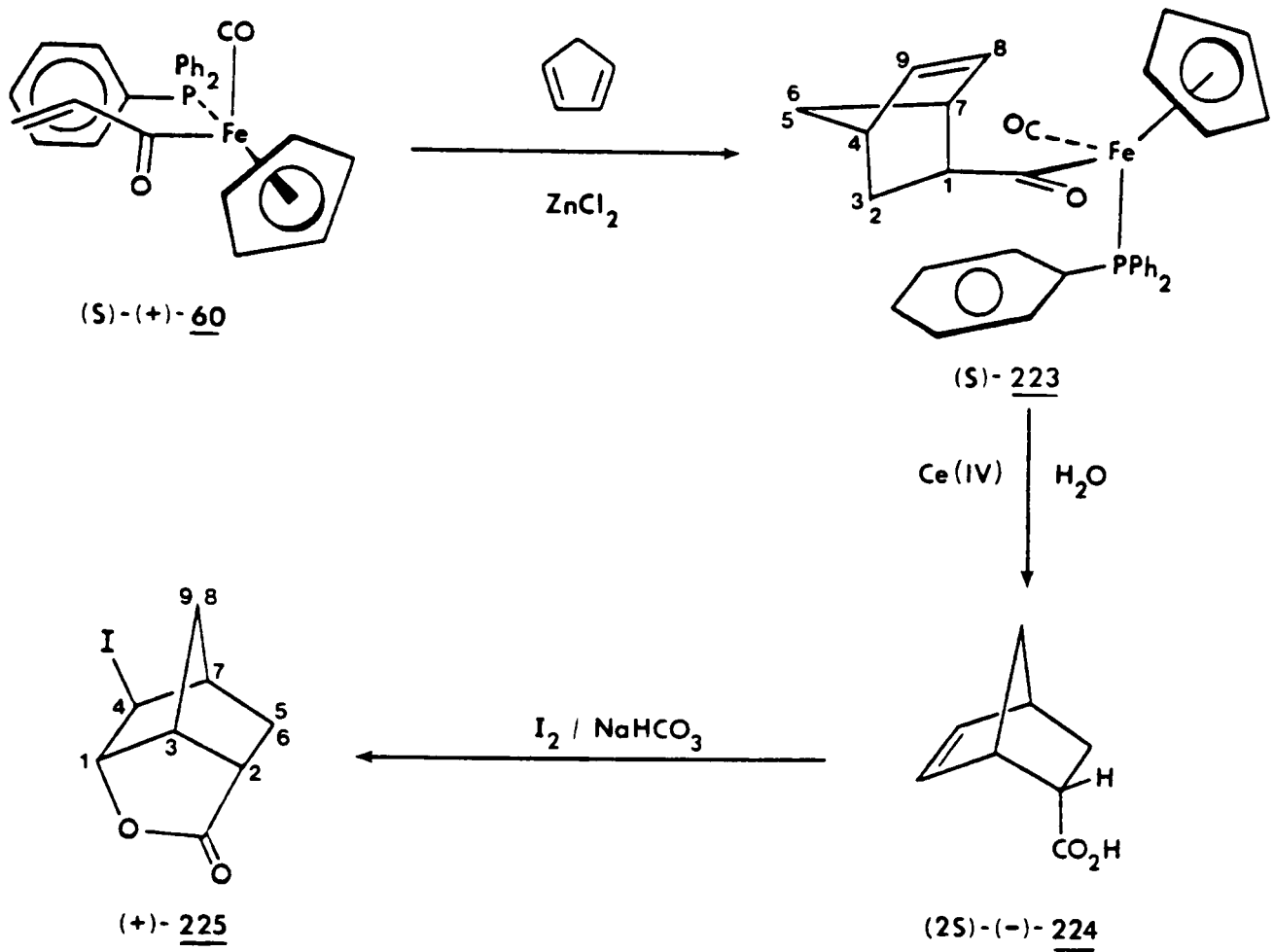
† The endo selective ethylaluminium dichloride-mediated Diels-Alder reaction between 1,3-dienes and $[(\eta^5\text{-}C_5H_5)Fe(CO)_2COCH{=}CHR]$ (R=H, CH_3) has recently been reported.[231]

In an attempt to improve the kinetically controlled endo selectivity, the reaction was repeated at -40°C. Although no cyclisation occurred at this temperature with zinc (II) chloride as the Lewis acid, the use of one equivalent of the more electrophilic boron trifluoride gave the same three diastereoisomers of the cycloadduct with an improved diastereoselectivity of 21:1:1, albeit in much reduced yield (26%).

At this stage however, it was not possible to deduce whether endo addition was occurring selectively to the C_α re or to the C_α si face of the α,β-unsaturated acyl ligand. In order to distinguish between these two possibilities and to extend the above reactions to the asymmetric synthesis of bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid, the optically pure acryloyl complex (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 was used as the chiral acrylate dienophile equivalent. The cycloaddition reaction between (S)-(+)-60 and cyclopentadiene in the presence of one equivalent of zinc (II) chloride proceeded smoothly (88%) in dichloromethane at room temperature to give the same three Diels-Alder adducts with a slightly modified diastereoselectivity of 21:3:1. The major isomer, (S)-223, was again derived from endo addition of the diene. The inseparable mixture of diastereoisomers was subjected to ammonium ceric nitrate oxidation in aqueous THF, yielding predominantly (2S)-(-)-bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid 224 whose absolute configuration is known.[232]

The formation of the acid (2S)-(-)-224 is consistent with endo addition of cyclopentadiene to the α,β-unsaturated acyl ligand of (S)-(+)-60 in the cisoid and anti (CO to acyl) conformation from the face of the C-C double bond away from the triphenylphosphine ligand (ie. the C_α re face). Despite coordination of the zinc ion to the acyl oxygen, the cisoid conformation of (S)-(+)-60 is still presumably favoured over the

alternative transoid conformation, which suffers from severe steric destabilisation due to the interactions between one of the β-hydrogens and the carbon monoxide ligand.



(S)-(+)-60

(S)-223

(+)-225

(2S)-(-)-224

The endo addition to (S)-(+)-60 was confirmed as being completely enantioselective by conversion of the crude acid (2S)-(-)-224 into the corresponding iodolactone (+)-225 (65%). Without purification 225 was shown to have an enantiomeric excess of greater than 95% {$[\alpha]_{436}^{20}$ + 226° (c 2.0, C_6H_6)}. This crude value could only have arisen if the major diastereoisomer in the 21:3:1 mixture was derived entirely from endo addition and the minor diastereoisomers from exo addition. Purification by a single crystallisation gave optically pure (+)-225, $[\alpha]_{436}^{20}$ + 238.4° (c 0.55, C_6H_6).[226]

Since iodolactone (+)-225 can be converted back to the acid, (2S)-(-)-224,[233] the asymmetric Diels-Alder reaction of (S)-(+)-[(η^5-C_5H_5)Fe(CO)-(PPh_3)COCH=CH_2] 60 provides a method whereby (2S)-(-)-bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid 224 can be prepared in optically pure form.

EXPERIMENTAL

General Experimental Techniques

All experiments and purifications were carried out under an atmosphere of nitrogen (except when otherwise stated), all reaction solvents were deoxygenated (except when otherwise stated) and standard vacuum line and Schlenk tube techniques were used throughout.[234] Solvents were removed under reduced pressure.

Solvents. THF was distilled from sodium benzophenone ketyl under nitrogen. Dichloromethane was distilled from calcium hydride under nitrogen. Petroleum ether refers to that fraction of light petroleum boiling between 40°C and 60°C and hexane refers to that fraction boiling between 67°C and 70°C. Other solvents were used as supplied.

Reagents. n-Butyllithium was used as a 1.6M solution in hexane. Sodium hydride, supplied as a 50% dispersion in oil, was washed with petroleum ether and dried under vacuum before use. Aldehydes were dried over calcium chloride. All other reagents were used as supplied.

Chromatography was performed on grade I alumina or grade I alumina deactivated with 10% by weight of water (grade V), under an atmosphere of nitrogen. In the cases where diastereoselectivities were to be determined, all coloured bands were collected. Flash chromatography was performed on silica gel (15 μm) according to the procedure of Still et al.[235]

Infrared spectra were obtained as Nujol mulls (unless otherwise stated) on a Perkin-Elmer 297 instrument, calibrated against polystyrene (3027 and 1601 cm^{-1}).

N.m.r. spectra. ^{1}H n.m.r. spectra were recorded on a Bruker WH 300 (300.13 MHz) spectrometer in $CDCl_3$ solutions unless otherwise stated. ^{13}C n.m.r. spectra were recorded on a Bruker AM 250 (62.90 MHz) spectrometer in $CDCl_3$ solutions unless otherwise stated. Both ^{1}H and ^{13}C n.m.r. spectra were referenced to tetramethylsilane using internal solvent peaks. ^{31}P n.m.r. spectra were recorded on a Bruker AM 250 (101.26 MHz) spectrometer in $CDCl_3$ solutions and were referenced to external 85% orthophosphoric acid. All chemical shifts are quoted as δ values.

Mass spectra were obtained by Dr. R.T. Aplin on a V.G. Micromass ZAB 1F instrument, using field desorption techniques.

Elemental microanalyses were carried out by Mrs. V. Lamburn (Oxford) and the University of Manchester Microanalysis Service.

Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]_2$ 6 [27]

Dicyclopentadiene (1.4 l, 11.4 mol) was placed in a 3 l three-necked round-bottomed flask fitted with a thermometer, an overhead mechanical stirrer and a reflux condenser. The flask was attached to a vacuum line *via* the reflux condenser and the dicyclopentadiene was thoroughly saturated with nitrogen. Iron pentacarbonyl (320 ml, 2.4 mol) was filtered through a plug of glass wool and added to the flask. The reaction mixture was briefly degassed and then heated under reflux (140°C; 26 h). On slow cooling (20°C), a mass of dark purple crystals separated out from the reaction mixture. These were collected on a large buchner funnel in air, washed with petroleum ether (4 x 250 ml) and dried under vacuum in a hot water bath (*ca*. 70°C) to give $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]_2$ 6 (325 g, 76%), $\nu_{max.}$ 1955 vs and 1935 vs (terminal C≡O), 1755 vs cm^{-1} (bridging C≡O) [lit.,[236] (KI disc) 1965, 1950, 1782 and 1770 cm^{-1}]; ^1H n.m.r. δ4.79 (s, C_5H_5).

Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ 14 [26,29]

Mercury (1040 g) was placed in a 2 l three-necked round-bottomed flask fitted with a nitrogen inlet, an overhead mechanical stirrer and a suba-seal. Sodium metal (18 g, 0.79 mol) was added in portions (*ca*. 1 g) over 0.5 h with stirring and whilst maintaining a nitrogen atmosphere. The stirrer was lifted from the surface of the amalgam and the amalgam left to cool. $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]_2$ 6 (100.5 g, 0.28 mol) was added to the flask followed by THF (750 ml). The apparatus was degassed and stirred under nitrogen (24 h; 20°C). The orange solution of $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]Na$ 7 was decanted *via* a canula into a 2 l three-necked round-bottomed flask fitted with a nitrogen inlet, an overhead mechanical stirrer and a suba-seal. After the solution was transferred, the suba seal was replaced by a pressure equalised dropping funnel containing methyl iodide (49 ml, 0.79 mol, dried over $CaCl_2$) in THF (25 ml). The methyl iodide solution was added to the

stirred solution in the flask over 1 h at 0°C to give an olive green suspension which was stirred for a further 19 h (20°C) under nitrogen. The stirrer and dropping funnel were replaced by glass stoppers and the solvents removed under reduced pressure (vacuum line through a pre-trap, keeping the solution at 20°C or below). The resulting red-brown cake was triturated with light petroleum ether (30-40°C, 500 ml then 2 x 100 ml) to give a deep red-orange solution of $[(\eta^5\text{-}C_5H_5)Fe(CO)_2CH_3]$ 21. The solution of 21 was filtered through Celite (8 cm depth) under nitrogen using a frit (8 cm dia., medium porosity) fitted to a 1 l three-necked round-bottomed flask equipped with a nitrogen inlet and suba-seal. The Celite was washed through with light petroleum ether (30-40°C, 100 ml) and the combined filtrates reduced in volume to ca. 100 ml under reduced pressure at 20°C. Degassed acetonitrile (500 ml) was added and the remaining light petroleum ether (30-40°C) removed under reduced pressure.

The acetonitrile solution of 21 was poured onto triphenylphosphine (148 g, 0.56 mol) contained in a 2 l three-necked round-bottomed flask fitted with a reflux condenser, a nitrogen inlet, a suba-seal and a large magnetic stirrer. The mixture was shielded from the light and heated under reflux (66 h). The solvent was removed under reduced pressure to give a solid orange residue which was dissolved in dichloromethane (800 ml) and filtered through alumina (grade I, 10 cm depth) using a frit as above. The filtrate was reduced in volume to ca. 600 ml at which point crystals had just begun to appear. Addition of degassed hexane (150 ml) and cooling (5°C) gave a large quantity of orange needles. These were filtered off and the crystals washed with degassed hexane (2 x 50 ml) and dried under vacuum in a hot water bath (ca. 50°C) to give $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ 14 (185.5 g, 72%), $\nu_{max.}$ 1915 vs (C≡O), 1600 s cm^{-1} (C=O) [lit.,[26] ($CHCl_3$) 1920 vs, 1598 s cm^{-1}]; ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 2.32 (3H, s, CH_3) [lit.,[26] δ7.59 (s), 4.62 (s), 2.52 (s)]; $^{31}P\{^1H\}$ n.m.r. δ72.8.

Determination of the optical purity of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 using Eu(tfc)$_3$

Addition of 8 µl of a solution of tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium (III) (12 mg in 200 µl $CDCl_3$) to a solution of (±)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 (9 mg in 700 µl $CDCl_3$) resulted in clean separation of the methyl singlets due to the two enantiomers in the 300 MHz ^{1}H n.m.r. spectrum, (S)-(+)-14 δ2.66, (R)-(-)-14 δ2.58.

Preparation of chloromethyl (R)-menthyl ether [60]

(l)-Menthol (61.5 g, 0.39 mol) was powdered and mixed thoroughly with paraformaldehyde (12.7 g, 0.40 mol). Dry hydrogen chloride gas was passed through the mixture of solids at 0°C for 8 h to give a colourless liquid consisting of two layers which were separated. The lower aqueous layer was extracted with diethyl ether (2 x 30 ml) and the extracts combined with the upper organic layer. The diethyl ether solution was dried (Na_2SO_4), filtered and evaporated. Distillation of the residue gave chloromethyl (R)-menthyl ether as a colourless liquid (29.9 g, 37%) (lit.,[60] 84%), b.p. 60°C (0.01 mmHg) [lit.,[60] 60°C (0.08 mmHg)]; ^{1}H n.m.r. δ5.59, 5.55 (2H, AB system, J_{AB} 5.2 Hz, $ClCH_2O$), 3.52 (1H, dt, $J_{1,2}$ 10.7 Hz, 4.4 Hz, OCH), 2.13 (2H, m, cyclohexyl H), 1.67 (2H, m, cyclohexyl H), 1.41 (1H, m, cyclohexyl H), 1.24 (1H, m, cyclohexyl H), 1.09 - 0.76 (3H, m, cyclohexyl H), 0.93 (3H, d, $J_{1,2}$ 6.6 Hz, CH_3), 0.90 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3), 0.80 (3H, d, $J_{1,2}$ 6.9 Hz, CH_3) [lit.,[60] δ5.53 (2H, s), 3.50 (1H, m), 2.0 - 0.4 (18H, m)].

Preparation of a 1:1 mixture of the diastereoisomers 25 and 26 of {(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2O$[(R)-menthyl]}

n-Butyllithium (10.0 ml, 16.0 mmol) was added to an orange solution of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 (6.48 g, 14.3 mmol) in THF (80 ml) at -78°C to give a dark red solution. After stirring (-78°C; 1 h), chloromethyl (R)-menthyl ether (4.0 ml, 17 mmol) was added and the mixture stirred for a further 3 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 30 ml) and filtered through alumina (grade V). The filtrate was concentrated and chromatographed on alumina (grade I). A single orange band was eluted with diethyl ether - dichloromethane (3:1). Removal of solvent gave orange microcrystals of {(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2O$-[(R)-menthyl]} as a 1:1 mixture of diastereoisomers 25 and 26 (7.76 g, 87%) (spectroscopic data are given below).

Resolution of the diastereoisomers 25 and 26 of {(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH_2CH_2O$[(R)-menthyl]}

The 1:1 mixture of complexes 25 and 26 (205 mg) was dissolved in diethyl ether (1 ml) and flash chromatographed on silica (6 cm depth, 7 cm dia.) using petroleum ether(60-80°C) - diethyl ether (22:3) as eluant.

Removal of solvent from the first orange fraction gave (S)-(+)-26 as fine orange crystals (100 mg) (Found: C, 71.7; H, 7.0; P, 5.0. $C_{37}H_{43}FeO_3P$ requires C, 71.4; H, 7.0; P,5.0%); $[\alpha]_D^{25}$ +65° (c 0.4, C_6H_6); $\nu_{max.}$ 1910 vs (C≡O), 1610 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.23 (3H, m, $COCH_2CH_2O$), 2.88 (1H, dt, $J_{1,2}$ 10.2 Hz, 4.2 Hz, CH_2OCH), 2.80 (1H, m, $COCH_2CH_2O$), 2.13 (1H, dseptets, $J_{1,2}$ 7.0 Hz, 2.5 Hz, $CH(CH_3)_2$), 1.95 (1H, m, cyclohexyl H), 1.66 - 0.67 (7H, m, cyclohexyl H), 0.89 (3H, d, $J_{1,2}$ 9.7 Hz, CH_3), 0.86 (3H, d, $J_{1,2}$ 10.6 Hz, CH_3), 0.74 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3); ^{13}C {^1H}

n.m.r. δ 136.5 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.6 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 10.0 Hz, Ph C_{meta}), 85.3 (s, C_5H_5), 79.2 (s), 65.8 (s, $CO\underline{C}H_2$), 64.5 (s), 48.2 (s), 40.6 (s), 34.7 (s), 31.6 (s), 25.5 (s), 23.4 (s), 22.4 (s), 21.0 (s), 16.3 (s); ^{31}P $\{^1H\}$ n.m.r. δ72.5; m/z 622 (M^+).

Removal of solvent from the second orange fraction and crystallisation from diethyl ether (ca. 1 ml) gave (R)-(-)-25 as red blocks (100 mg). (Found: C, 71.4; H, 7.0; P, 5.0. $C_{37}H_{43}FeO_3P$ requires C, 71.4; H, 7.0; P, 5.0%); $[\alpha]_D^{20}$ -150° (c 0.4, C_6H_6); $\nu_{max.}$ 1910 vs (C≡O), 1625 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.42 (5H, d, J_{PH} 1.0 Hz, C_5H_5) 3.56 (1H, m, $COCH_2CH_2OCH$), 3.21 (1H, m, $COCH_2CH_2OCH$), 2.82 (3H, m, $COCH_2CH_2OCH$), 2.10 (1H, dseptets, $J_{1,2}$ 7.1 Hz, 2.6 Hz, $C\underline{H}(CH_3)_2$), 1.98 (1H, m, cyclohexyl H), 1.62 - 0.67 (7H, m, cyclohexyl H), 0.89 (3H, d, $J_{1,2}$ 6.6 Hz, CH_3), 0.86 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3), 0.73 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ136.5 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.3 (s, C_5H_5), 79.0 (s), 65.9 (s,$CO\underline{C}H_2$), 64.6 (s), 48.2 (s), 40.6 (s), 34.7 (s), 31.6 (s), 25.6 (s), 23.5 (s), 22.4 (s), 21.0 (s), 16.4 (s); ^{31}P $\{^1H\}$ n.m.r. δ72.5; m/z 622 (M^+).

Alkylation of (R)-(-)- and (S)-(+)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ 14 with chloromethyl (R)-menthyl ether.

n-Butyllithium (0.16 ml, 0.26 mmol) was added to (R)-(-)-14 [58] (100 mg, 0.22 mmol) in THF (20 ml) at -78°C to give a dark red solution. After stirring (-78°C; 1 h), chloromethyl (R)-menthyl ether (0.1 ml, 0.42 mmol) was added and the mixture stirred for a further 3 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 10 ml) and filtered through

alumina (grade V). The filtrate was concentrated and chromatographed on alumina (grade I). A single orange band was eluted with diethyl ether - dichloromethane (3:1). Removal of solvent gave (R)-(-)-25 (90 mg, 66%); $[\alpha]_D^{20}$ -150° (c 0.4, C_6H_6), identical in all respects to (R)-(-)-25 prepared above.

Using the same procedure, (S)-(+)-14 [58] (100 mg, 0.22 mmol) was treated successively with n-butyllithium (0.16 ml, 0.26 mmol) and chloromethyl (R)-menthyl ether (0.1 ml, 0.42 mmol) to give (S)-(+)-26 (91 mg, 66%); $[\alpha]_D^{20}$ +65° (c 0.4, C_6H_6), identical in all respects to (S)-(+)-26 prepared above.

Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ 29 [39]

n-Butyllithium (25.1 ml, 40.2 mmol) was added to $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ 14 (11.8 g, 25.9 mmol) in THF (400 ml) at -78°C to give a dark red solution. After stirring (-78°C; 3.5 h), trimethylsilyl chloride (8.0 ml, 63.1 mmol, freshly distilled from CaH_2) was added in one portion and the mixture stirred for a further 1 h (-78°C). Warming to room temperature over 2 h and removal of solvent gave an orange solid which was extracted with dichloromethane (3 x 20 ml) and filtered through alumina (grade V). Removal of solvent gave $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ 29 as fine orange crystals (13.4 g, 98%) (lit.,[39] 84%); ^{1}H n.m.r. δ 7.5 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 2.76, 1.73 (2H, AB system, J_{AB} 11.5 Hz, CH_2), 0.02 (9H, s, CH_3) [lit.,[39] δ7.6 - 7.3 (m), 4.43 (d), 2.76, 1.73 (AB system), 0.01 (s)].

The Peterson reaction between $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ 29 and aldehydes

In a typical procedure, n-butyllithium (1.9 ml, 3.04 mmol) was added to $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Si(CH_3)_3]$ 29 (1.5 g, 2.85 mmol) in THF (60 ml)

at -78°C to give a dark red solution. After stirring (-78°C; 1 h), the aldehyde (2 equivalents, dried over $CaCl_2$) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 15 ml) and filtered through alumina (grade V).

The overall yields and selectivities of the reactions with acetaldehyde, propionaldehyde, acrolein and crotonaldehyde are summarised in Table 3 (p. 30). The E and Z isomers were separated by chromatography on alumina (grade I)† and crystallised from dichloromethane-hexane (orange needles).

E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33. Elution with dichloromethane gave complex 33 (58%) (Found: C, 70.4; H, 5.3; P, 6.5. $C_{28}H_{25}FeO_2P$ requires C, 70.0; H, 5.25; P, 6.45%); $\nu_{max.}$ 1920 vs (C≡O), 1575 s and 1565 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.50 (1H, d, J_{trans} 15.0 Hz, COCH), 5.50 (1H, dq, J_{trans} 15.0 Hz, $J_{1,2}$ 6.8 Hz, C<u>H</u>CH_3), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 1.57 (3H, dd, $J_{1,2}$ 6.8 Hz, $J_{1,3}$ 1.6 Hz, CH_3); ^{13}C {^1H} n.m.r. δ270.5 (d, J_{PC} 23.7 Hz, C=O), 220.8 (d, J_{PC} 31.9 Hz, C≡O), 146.3 (d, J_{PC} 4.2 Hz, CO<u>C</u>H), 136.5 (d, J_{PC} 43.0 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.7 Hz, Ph C_{ortho}), 129.6 (d, J_{PC} 1.8 Hz, Ph C_{para}), 128.0 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 124.3 (s, <u>C</u>HCH_3), 85.4 (s, C_5H_5), 16.8 (s, CH_3); ^{31}P {^1H} n.m.r. δ73.2; <u>m/z</u> 480 (M^+), 452 (M^+-28).

Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 34. Elution with diethyl ether - dichloromethane gave complex 34 (30%) (Found: C, 69.8; H, 5.2; P, 6.5. $C_{28}H_{25}FeO_2P$ requires C, 70.0; H, 5.25; P, 6.45%); $\nu_{max.}$ 1915 vs (C≡O), 1615 s and 1580 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.57 (1H, dq, J_{cis} 11.2 Hz, $J_{1,3}$ 1.7 Hz, COCH), 4.73 (1H, dq, J_{cis}

† In each case, the Z isomer was eluted first.

11.2 Hz, $J_{1,2}$ 7.0 Hz, C<u>H</u>CH_3), 4.43 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 1.33 (3H, dd, $J_{1,2}$ 7.0 Hz, $J_{1,3}$ 1.7 Hz, CH_3); ^{13}C {^1H} n.m.r. δ273.1 (d, J_{PC} 22.6 Hz, C=O), 220.5 (d, J_{PC} 31.6 Hz, C≡O), 144.6 (d, J_{PC} 5.2 Hz, CO<u>C</u>H), 136.6 (d, J_{PC} 42.9 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.9 Hz, Ph C_{ortho}), 129.6 (d, J_{PC} 1.7 Hz, Ph C_{para}), 128.0 (d, J_{PC} 9.9 Hz, Ph C_{meta}), 118.9 (s, <u>C</u>HCH_3), 85.4 (s, C_5H_5), 14.8 (s, CH_3); ^{13}P {^1H} n.m.r. δ73.1; <u>m/z</u> 480 (M^+), 452 (M^+-28).

E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_2CH_3$] <u>35</u>. Elution with dichloromethane - ethyl acetate (4:1) gave complex <u>35</u> (50%) (Found: C, 70.7; H, 5.6; P, 6.3. $C_{29}H_{27}FeO_2P$ requires C, 70.5; H, 5.5; P, 6.3%); $\nu_{max.}$ 1910 vs (C≡O), 1575 s and 1555 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.44 (1H, dt, J_{trans} 15.1 Hz, $J_{1,3}$ 1.4 Hz, COCH), 5.49 (1H, dt, J_{trans} 15.1 Hz, $J_{1,2}$ 6.5 Hz, C<u>H</u>CH_2), 4.43 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 1.97 - 1.87 (2H, m, CH_2), 0.94 (3H, t, $J_{1,2}$ 7.5 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.7 (d, J_{PC} 31.6 Hz, C≡O), 143.8 (d, J_{PC} 3.6 Hz, CO<u>C</u>H), 136.4 (d, J_{PC} 43.0 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 130.4 (s, <u>C</u>HCH_2), 129.6 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.4 (s, C_5H_5), 24.2 (s, CH_2), 12.9 (s, CH_3); ^{31}P {^1H} n.m.r. δ73.1; <u>m/z</u> 494 (M^+).

Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_2CH_3$] <u>36</u>. Elution with diethyl ether - dichloromethane (1:1) gave complex <u>36</u> (27%) (Found: C, 70.6; H, 5.7; P, 6.2. $C_{29}H_{27}FeO_2P$ requires C, 70.5; H, 5.5; P, 6.3%); $\nu_{max.}$ 1900 vs (C≡O), 1615 s and 1580 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 6.49 (1H, dt, J_{cis} 11.2 Hz, $J_{1,3}$ 1.5 Hz, COCH), 4.59 (1H, dt, J_{cis} 11.2 Hz, $J_{1,2}$ 7.0 Hz, C<u>H</u>CH_2), 4.41 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 1.92 - 1.59 (2H, m, CH_2), 0.78 (3H, t, $J_{1,2}$ 7.0 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.5 (d, J_{PC} 31.5 Hz, C≡O), 143.0 (d, J_{PC} 4.4 Hz, CO<u>C</u>H), 136.6 (d, J_{PC} 43.2 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.3 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.2 Hz, Ph C_{meta}), 126.6 (s, <u>C</u>HCH_2), 85.4 (s, C_5H_5), 22.0 (s, CH_2), 14.3 (s, CH_3); ^{31}P {^1H} n.m.r. δ73.1; <u>m/z</u> 494 (M^+).

E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CH_2] 37. Elution with dichloromethane - ethyl acetate (1:1) gave complex 37 (40%) (Found: C, 70.8; H, 5.4; P, 6.4. $C_{29}H_{25}FeO_2P$ requires C, 70.75; H, 5.1; P, 6.3%); $\nu_{max.}$ 1915 vs (C≡O), 1590 s and 1565 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.51 (1H, d, J_{trans} 14.4 Hz, COCH), 6.23 - 6.11 (1H, m, C<u>H</u>CH_2), 5.78 (1H, dd, J_{trans} 15.0 Hz, $J_{1,2}$ 10.8 Hz, CHC<u>H</u>CH), 5.40 - 5.30 (2H, m, CH_2), 4.45 (5H, d, J_{PH} 1.5 Hz, C_5H_5); ^{13}C {^1H} n.m.r. δ220.5 (d, J_{PC} 33.3 Hz, C≡O), 143.8 (br s, CO<u>C</u>H), 136.3 (s, CH), 136.2 (d, J_{PC} 43.0 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 125.0 (s, CH), 122.9 (s, CH_2), 85.5 (s, C_5H_5); ^{31}P {^1H} n.m.r. δ72.8; <u>m/z</u> 492 (M^+).

Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CH_2] 38. Elution with dichloromethane gave complex 38 (28%) (Found: C, 70.7; H, 5.1; P, 6.3. $C_{29}H_{25}FeO_2P$ requires C, 70.75; H, 5.1; P, 6.3%); $\nu_{max.}$ 1915 vs (C≡O), 1595 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.43 (1H, d, J_{cis} 11.1 Hz, COCH), 6.27 - 6.14 (1H, m, C<u>H</u>CH_2), 5.21 - 4.94 (3H, m, C<u>H</u>CHC<u>H</u>$_2$), 4.43 (5H, d, J_{PH} 1.4 Hz, C_5H_5); ^{13}C {^1H} n.m.r. δ220.3 (d, J_{PC} 31.4 Hz, C≡O), 142.1 (d, J_{PC} 5.3 Hz, CO<u>C</u>H), 136.3 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 134.7 (s, CH), 133.3 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 121.2 (s, CH_2), 120.5 (s, CH), 85.4 (s, C_5H_5); ^{31}P {^1H} n.m.r. δ72.8; <u>m/z</u> 492 (M^+).

E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=$CHCH_3$] 39. Elution with dichloromethane - ethyl acetate (2:3) gave complex 39 (57%) (Found: C, 71.5; H, 5.5; P, 6.2. $C_{30}H_{27}FeO_2P$ requires C, 71.2; H, 5.4; P, 6.1%); $\nu_{max.}$ 1915 vs (C≡O), 1580 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.47 (1H, d, J_{trans} 14.5 Hz, COCH), 5.91 (3H, m, C<u>H</u>=C<u>H</u>=C<u>H</u>CH_3), 4.44 (5H, d, J_{PH} 1.2 Hz, C_5H_5) 1.78 (3H, d, $J_{1,2}$ 4.9 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.6 (d, J_{PC} 31.5 Hz, C≡O), 141.8 (s, CO<u>C</u>H) 136.3 (d, J_{PC} 42.9 Hz, Ph C_{ipso}), 136.3 (s, CH), 133.3 (d, J_{PC} 9.8 Hz, Ph C_{ortho}), 130.7 (s, CH), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 10.0 Hz, Ph C_{meta}), 125.7 (s, CH), 85.4 (s, C_5H_5), 18.6 (s, CH_3); ^{31}P {^1H} n.m.r. δ73.3; <u>m/z</u> 506 (M^+), 478 (M^+-28).

Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=$CHCH_3$] 40. Elution with diethyl ether - dichloromethane (1:1) gave complex 40 (25%) (Found: C, 71.3; H, 5.5. $C_{30}H_{27}FeO_2P$ requires C, 71.2; H, 5.4%); $\nu_{max.}$ 1915 vs and 1905 vs (C≡O), 1595 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.38 (1H, d, J_{cis} 11.4 Hz, COCH), 5.97 (1H, ddq, J_{trans} 15.1 Hz, $J_{1,2}$ 10.6 Hz, $J_{1,3}$ 1.1 Hz, CH=CHCH$_3$), 5.70 (1H, dq, J_{trans} 15.1 Hz, $J_{1,2}$ 6.8 Hz, CHCH$_3$), 5.09 (1H, t, $J_{1,2}$ 11.0 Hz, COCH=CH), 4.43 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 1.62 (3H, dd, $J_{1,2}$ 6.8 Hz, $J_{1,3}$ 1.2 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.3 (d, J_{PC} 31.4 Hz, C≡O), 140.0 (d, J_{PC} 4.3 Hz, COCH), 136.5 (d, J_{PC} 42.7 Hz, Ph C_{ipso}), 134.8 (s, CH), 133.3 (d, J_{PC} 10.4 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 121.1 (s, CH), 85.4 (s, C_5H_5), 18.2 (s, CH_3); ^{31}P {^1H} n.m.r. δ73.2; m/z 506 (M^+), 478 (M^+ - 28).

Reaction of the aluminium enolate 41 with acetaldehyde and subsequent base-induced elimination to E- and Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33 and 34

n-Butyllithium (0.8 ml, 1.28 mmol) was added to [(η^5-C_5H_5)Fe(CO)-(PPh_3)($COCH_2Si(CH_3)_3$)] 29 (505 mg, 0.96 mmol) in THF (20 ml) at -78°C and the resulting dark red solution stirred (-78°C; 1h). Diethylaluminium chloride (1.0 ml, 1.8 M soln. in toluene, 1.8 mmol) was added to the reaction mixture which was warmed to -40°C and stirred for a further 1 h. The mixture was cooled to -100°C and a solution of acetaldehyde (0.2 ml, 3.6 mmol) in THF (3 ml) was added dropwise. After stirring (-100°C; 1.5h), methanol (1 ml) was added and the solution warmed to room temperature. Removal of solvent gave an orange gelatinous mixture which was dissolved in dichloromethane (20 ml). The dichloromethane solution was washed with saturated aqueous $NaHCO_3$ (20 ml). The layers were separated and the aqueous layer washed with further portions of dichloromethane (2 x 20 ml). The combined dichloromethane layers were concentrated and

chromatographed on alumina (grade V). Elution with diethyl ether - dichloromethane (1:1) gave a single orange band which, upon removal of solvent, was shown by ^{1}H n.m.r. spectroscopy to consist primarily of a 1:1 mixture of complexes 43 and 44 (468 mg, 86%); ^{1}H n.m.r. δ7.5 - 7.3 (30H, m, Ph), 4.43 (10H, s, C_5H_5), 0.50 (3H, d, $J_{1,2}$ 8.0 Hz, CH_3), 0.34 (3H, d, $J_{1,2}$ 8.0 Hz, CH_3), 0.28 (9H, s, $Si(CH_3)_3$), 0.25 (9H, s, $Si(CH_3)_3$). The product also contained small amounts of the starting complex 29 and the α,β-unsaturated acyl complex 33.

The product was combined with sodium hydride (200 mg, 8.33 mmol) and THF (20 ml). Stirring (20°C; 20 h), removal of solvent, extraction with dichloromethane (2 x 15 ml) and filtration through alumina (grade V) gave an orange solution. The solvent was removed to give an orange solid identified by ^{1}H n.m.r. spectroscopy as a 1:1 mixture of the E and Z complexes 33 and 34 (360 mg, 92%).

Preparation of (S)-(+)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33 and (S)-(+)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 34

Following an identical procedure to that used in the preparation of (R,S)-29 (p.139), (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 [58] (700 mg, 1.54 mmol) was treated successively with n-butyllithium (1.3 ml, 2.08 mmol) and trimethylsilyl chloride (0.3 ml, 2.37 mmol). The crude product was chromatographed on alumina (grade V) using diethyl ether as the eluant. Crystallisation from hexane gave (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2Si(CH_3)_3$] 29 as orange needles (520 mg, 64%); $[\alpha]_D^{23}$ +188.8° (c 0.13, C_6H_6). The ^{1}H n.m.r. spectrum of (S)-(+)-29 was identical to that of (R,S)-29.

The lithium enolate 32, derived from (S)-(+)-29 (367 mg, 0.70 mmol) and n-butyllithium (0.6 ml, 0.96 mmol), was treated with acetaldehyde (0.2 ml, 3.6 mmol) as in the Peterson reaction described above (p.139).

Work-up, chromatography and crystallisation gave (S)-(+)-E-[(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH{=}CHCH_3$] 33 (202 mg, 60%); $[\alpha]_D^{23}$ +175.3° (c 0.15, C_6H_6) and (S)-(+)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH{=}CHCH_3$] 34 (94 mg, 28%); $[\alpha]_D^{23}$ +274.8° (c 0.12, C_6H_6). The ^{1}H n.m.r. spectra of (S)-(+)-33 and (S)-(+)-34 were identical to those of (R,S)-33 and (R,S)-34 respectively.

Preparation of β-hydroxy acyl complexes

The β-hydroxy acyl complexes (RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH$-$(OH)CH_3$] 45 and (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OH)CH_3$] 46 were prepared according to the literature procedures from the aluminium [36,44] and tin [45] enolates of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 respectively. Both (RR,SS)-45 and (RS,SR)-46 were prepared as 7:1 diastereoisomeric mixtures.

The β-hydroxy acyl complexes [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OH)R$] (R=CH_3, Et, n-Bu, t-Bu and $CH{=}CH_2$) were prepared from the lithium enolate derived from [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 and the respective aldehyde according to the literature procedure.[36] The diastereoisomeric ratios in the product complexes were typically 1.2:1. The preparation of [(η^5-C_5H_5)-Fe(CO)(PPh_3)$COCH_2CH(OH)CH{=}CH_2$] is illustrative:- n-butyllithium (4.5 ml, 7.20 mmol) was added to a solution of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14 (3.01 g, 6.63 mmol) in THF (50 ml) at -78°C. After stirring (-78°C; 1 h), acrolein (0.6 ml, 9.0 mmol) was added at -78°C and the reaction mixture stirred for a further 3.5 h (-78°C). Addition of methanol (1 ml), removal of solvent and addition of dichloromethane (30 ml) gave an orange solution which was filtered through alumina (grade V) and chromatographed on alumina (grade I). The first orange fraction was eluted with ethyl acetate to give, upon removal of solvent, an orange solid identified by ^{1}H n.m.r. spectroscopy as the starting complex 14. Removal of solvent from the second orange fraction, eluted with dichloromethane - ethyl acetate - methanol (2:7:1) gave [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OH)CH{=}CH_2$] as a 1.5:1

mixture of the RS,SR and RR,SS diastereoisomers (2.60 g, 77%). The RS,SR diastereoisomer was identified by comparison of its spectroscopic data with those of an authentic sample prepared from the aluminium enolate derived from complex 14.[36]

RS,SR diastereoisomer (obtained as orange rods from dichloromethane -hexane) (Found: C, 68.2; H, 5.3; P, 5.9. $C_{29}H_{27}FeO_3P$ requires C, 68.25; H, 5.3; P, 6.1%); $\nu_{max.}$ 3510 m (OH), 1925 vs (C≡O), 1575 s and 1565 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 -7.3 (15H, m, Ph), 5.58 - 5.47 (1H, m, C<u>H</u>=CH_2), 5.07 - 4.92 (2H, m, CH=C<u>H</u>$_2$), 4.45 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.68 (1H, m, C<u>H</u>OH), 3.59 (1H, d, $J_{1,2}$ 2.6 Hz, CHO<u>H</u>), 2.87 (2H, d, $J_{1,2}$ 6.0 Hz, $COCH_2$); ^{13}C {^1H} n.m.r. δ220.1 (d, J_{PC} 30.9 Hz, C≡O), 139.5 (s, <u>C</u>H=CH_2), 136.1 (d, J_{PC} 43.5 Hz, Ph C_{ipso}), 133.2 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.9 (s, Ph C_{para}), 128.1 (d, J_{PC} 9.8 Hz, Ph C_{meta}), 113.2 (s, CH=<u>C</u>H$_2$), 85.5 (s, C_5H_5), 71.2 (d, J_{PC} 4.2 Hz, CO<u>C</u>H$_2$), 69.8 (s, CHOH); ^{31}P {^1H} n.m.r. δ71.4; <u>m/z</u> 510 (M^+).

RR,SS diastereoisomer; ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.62 -5.48 (1H, m, C<u>H</u>=CH_2), 5.14 - 4.92 (2H, m, CH=C<u>H</u>$_2$), 4.44 (5H, d, J_{PH} 1.4 Hz, C_5H_5), 4.22 (1H, m, C<u>H</u>OH), 3.24, 2.66 (2H, ABX system, J_{AB} 17.2 Hz, $COCH_2$), 2.95 (1H, d, $J_{1,2}$ 2.8 Hz, CHO<u>H</u>); ^{13}C {^1H} n.m.r. δ220.1 (d, J_{PC} 30.9 Hz, C≡O), 139.6 (s, <u>C</u>H=CH_2), 136.1 (d, J_{PC} 43.5 Hz, Ph C_{ipso}), 133.2 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.9 (s, Ph C_{para}), 128.1 (d, J_{PC} 9.8 Hz, Ph C_{meta}), 113.7 (s, CH=<u>C</u>H$_2$), 85.2 (s, C_5H_5), 71.2 (d, J_{PC} 4.2 Hz, CO<u>C</u>H$_2$), 69.7 (s, CHOH); ^{31}P {^1H} n.m.r. δ72.1.

<u>General procedure for the O-methylation of β-hydroxy acyl complexes. Preparation of complexes 47, 48 and 50 - 53.</u>

The diastereoisomeric mixture of the β-hydroxy acyl complex (typically 2.5 g) was combined with sodium hydride (3 equivalents). THF (50 ml) was added and the reaction mixture stirred for 0.5 h at 20°C. After addition of

methyl iodide (3 equivalents), the solution was stirred for a further 20 h (20°C). Removal of solvent, extraction with dichloromethane (3 x 10 ml) and filtration through alumina (grade V) gave an orange solution which was concentrated and chromatographed on alumina.

The β-methoxy complexes were collected as single fractions, analysed by ^{1}H n.m.r. spectroscopy and obtained as orange needles from dichloromethane - hexane.

(RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH_3$] 47 Elution with diethyl ether (alumina, grade V) gave complex 47 (95%, diastereoisomeric purity 7:1) (Found: C, 67.8; H, 5.8; P, 5.9. $C_{29}H_{29}FeO_3P$ requires C, 68.0; H, 5.7; P, 6.05%); $\nu_{max.}$ 1905 vs and 1895 vs (C≡O), 1610 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.48 (1H, m, CH), 3.37, 2.52 (2H, ABX system, J_{AB} 16.6 Hz, CH_2), 3.22 (3H, s, OCH_3), 0.69 (3H, d, $J_{1,2}$ 6.0 Hz, CH_3); ^{13}C {^{1}H} n.m.r. δ220.3 (d, J_{PC} 30.3 Hz, C≡O), 136.5 (d, J_{PC} 43.2 Hz, Ph C_{ipso}), 133.2 (d, J_{PC} 10.1 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.3 (s, C_5H_5), 72.9 (s, CH), 72.2 (d, J_{PC} 5.4 Hz, CH_2), 55.8 (s, OCH_3), 18.8 (s, CH_3); ^{31}P {^{1}H} n.m.r. δ72.5; m/z 512 (M^+).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH_3$] 48. Elution with diethyl ether (alumina, grade V) gave complex 48 (95%, diastereoisomeric purity 7:1) (Found: C, 67.8; H, 5.9; P, 6.0. $C_{29}H_{29}FeO_3P$ requires C, 68.0; H, 5.7; P, 6.05%); $\nu_{max.}$ 1910 vs (C≡O), 1610 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.40 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.30 (1H, m, CH), 3.06 (3H, s, OCH_3), 2.91 (2H, m, CH_2), 1.00 (3H, d, $J_{1,2}$ 6.1 Hz, CH_3); ^{13}C {^{1}H} n.m.r. δ220.2 (d, J_{PC} 29.6 Hz, C≡O), 136.4 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 73.1 (s, CH), 71.5 (d, J_{PC} 5.3 Hz, CH_2), 55.5 (s, OCH_3), 19.9 (s, CH_3); ^{13}P {^{1}H} n.m.r. δ72.4; m/z 512 (M^+).

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH_2CH_3$] 50. Elution with diethyl ether (alumina, grade V) gave complex 50 as a 1.2:1 mixture of RR,SS and RS,SR diastereoisomers (80%) (Found: C, 68.3; H, 6.2; P, 5.8. $C_{30}H_{31}FeO_3P$ requires C, 68.45; H, 5.9; P, 5.8%); $\nu_{max.}$ 1910 vs (C≡O), 1605 s cm^{-1} (C=O); m/z 526 (M^+). RR,SS diastereoisomer; ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.36 - 3.20 (1H, m, CH), 3.25 (3H, s, OCH_3), 3.05 - 2.46 (2H, m, $COCH_2$), 1.44 -1.03 (2H, m, $C\underline{H}_2CH_3$), 0.69 (3H, t, $J_{1,2}$ 7.3 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.3 (d, J_{PC} 22.6 Hz, C≡O), 136.5 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.7 Hz, Ph C_{meta}), 85.3 (s, C_5H_5), 77.8 (s, CH), 69.7 (d, J_{PC} 5.2 Hz, $CO\underline{C}H_2$), 56.6 (s, OCH_3), 25.9 (s, $\underline{C}H_2CH_3$), 9.3 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.6. RS,SR diastereoisomer; ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.42 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.36 - 3.20 (1H, m, CH), 3.05 - 2.46 (2H, m, $COCH_2$), 3.02 (3H, s, OCH_3), 1.44 - 1.03 (2H, m, $C\underline{H}_2CH_3$), 0.82 (3H, t, $J_{1,2}$ 7.3 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.3 (d, J_{PC} 39.3 Hz, C≡O), 136.4 (d, J_{PC} 43.2 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.6 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.7 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 77.9 (s, CH), 69.1 (d, J_{PC} 5.4 Hz, $CO\underline{C}H_2$), 56.1 (s, OCH_3), 27.1 (s, $\underline{C}H_2CH_3$), 9.6 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.3.

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)$n-Bu] 51. Elution with dichloromethane - ethyl acetate (1:1) (alumina, grade I) gave complex 51 as a 1:1 mixture of RR,SS and RS,SR diastereoisomers (60%) (Found: C, 68.9; H, 6.5; P, 5.65. $C_{32}H_{35}FeO_3P$ requires C, 69.3; H, 6.4; P, 5.6%); $\nu_{max.}$ 1905 vs (C≡O), 1610 s and 1575 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (30H, m, Ph both isomers), 4.42 (5H, s, C_5H_5), 4.40 (5H, s, C_5H_5), 3.39 - 2.44 (6H, m, $COCH_2CH$ both isomers), 3.24 (3H, s, OCH_3), 2.99 (3H, s, OCH_3), 1.32 - 0.83 (12H, m, $CH_2CH_2CH_2$ both isomers), 0.86 (3H, t, $J_{1,2}$ 7.0 Hz, CH_3), 0.84 (3H, t, $J_{1,2}$ 7.3 Hz, CH_3); m/z 554 (M^+).

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)$t-Bu] 52. Elution with dichloromethane - ethyl acetate (1:1) (alumina, grade I) gave complex 52 as a 1.2:1 mixture of RS,SR and RR,SS diastereoisomers (76%) (Found: C, 69.4; H, 6.5; P, 5.65. $C_{32}H_{35}FeO_3P$ requires C, 69.3; H, 6.4; P, 5.6%); $\nu_{max.}$ 1905 vs (C≡O), 1610 s and 1590 s cm^{-1} (C=O); m/z 554 (M^+). RS,SR diastereoisomer; ^{1}H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.41 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.39 - 2.44 (3H, m, CH_2CH), 2.74 (3H, s, OCH_3), 0.78 (9H, s, $C(CH_3)_3$). RR,SS diastereoisomer δ7.5 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.39 - 2.44 (3H, m, CH_2CH), 3.36 (3H, s, OCH_3), 0.67 (9H, s, $C(CH_3)_3$).

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH=CH_2$] 53. Elution with dichloromethane - ethyl acetate (1:1) (alumina, grade I) gave complex 53 as a 1:1 mixture of RS,SR and RR,SS diastereoisomers (99%) (Found: C, 68.5; H, 5.4; P, 5.8. $C_{30}H_{29}FeO_3P$ requires C, 68.7; H, 5.6; P, 5.9%); $\nu_{max.}$ 1910 vs (C≡O), 1605 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.5 - 7.3 (30H, m, Ph both isomers), 5.70 - 4.97 (6H, m, $CH=CH_2$ both isomers), 4.44 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 4.40 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.76 (2H, m, $CH(OCH_3)$ both isomers), 3.43, 2.43 (2H, ABX system, J_{AB} 16.6 Hz, $COCH_2$), 3.20 (3H, s, OCH_3), 3.08 (3H, s, OCH_3), 3.04, 2.84 (2H, ABX system, J_{AB} 16.0 Hz, $COCH_2$); m/z 524 (M^+).

Preparation of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2OCH_3$] 49

n-Butyllithium (3.5 ml, 5.40 mmol) was added to [(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_3$] 14 (1.23 g, 2.70 mmol) in THF (40 ml) at -78°C to give a dark red solution. After stirring (-78°C; 1 h), chloromethyl methyl ether (0.6 ml, 7.90 mmol) was added and the mixture stirred for a further 2.5 h (-78°C). Methanol (2 ml) was added and the solution was warmed to room temperature. Removal of solvent, extraction with dichloromethane (2 x 10 ml) and filtration through alumina (grade V) gave an orange solution which was chromatographed on alumina (grade V). A single orange band was eluted with dichloromethane. Concentration and addition of hexane gave

$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_2OCH_3]$ 49 as orange rhombic crystals (0.87 g, 65%); ^{1}H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.44 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 3.37 (1H, m, CH_2O), 3.22 (1H, m, CH_2O), 3.20 (3H, s, OCH_3), 3.00 (1H, m, $COCH_2$), 2.76 (1H, m, $COCH_2$). Complex 49 was identified by comparison of its ^{1}H n.m.r. data with those of an authentic sample.[67]

General procedure for the sodium hydride - induced elimination of methoxide from β-methoxy acyl complexes

The β-methoxy acyl complex (typically 200 mg) and sodium hydride (10 equivalents) were combined as solids. THF (15 ml) was added and the reaction mixture stirred (20°C; 66 h). The solvent was removed and the dark orange residue extracted with dichloromethane (3 x 10 ml) and filtered through alumina (grade V).

The α,β-unsaturated acyl complexes were purified by chromatography on alumina (grade I), as described above for the Peterson reaction, and analysed by ^{1}H n.m.r. spectroscopy. The spectroscopic data for $[(\eta^5\text{-}C_5H_5)$-$Fe(CO)(PPh_3)COCH{=}CH_2]$ 60 are given below (p.151). The yields and selectivities for the sodium hydride - induced elimination of methanol from the β-methoxy acyl complexes 47 - 53 are summarised in Table 4 (p.36).

Preparation of (R,S)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ 60

The 1:1 mixture of diastereoisomers 25 and 26 of $\{(\eta^5\text{-}C_5H_5)Fe(CO)$-$(PPh_3)COCH_2CH_2O[(R)\text{-menthyl}]\}$ (1.08 g, 1.74 mmol) and sodium hydride (329 mg, 13.7 mmol) were combined as solids. THF (40 ml) was added and the reaction mixture stirred (20°C; 41 h). The solvent was removed and the dark orange residue was extracted with dichloromethane (3 x 15 ml) and filtered through alumina (grade V). The filtrate was concentrated and chromatographed on alumina (grade I). A yellow band was eluted with diethyl ether - dichloromethane (1:1). Removal of solvent gave a 1:1 mixture of the starting

complexes 25 and 26 as an orange solid (100 mg, 10%). A yellow band was eluted with dichloromethane - ethyl acetate (1:1). Removal of solvent and crystallisation from dichloromethane - hexane gave (R,S)-[(η^5-C_5H_5)Fe(CO)-(PPh_3)COCH=CH_2] 60 as orange rods (660 mg, 81%) (Found: C, 69.2; H, 5.0; P, 6.6. $C_{27}H_{23}FeO_2P$ requires C, 69.55; H, 5.0; P, 6.6%); $\nu_{max.}$ 1910 vs (C≡O), 1600 s and 1555 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 6.60 (1H, dd, J_{trans} 17.0 Hz, J_{cis} 10.2 Hz, COCH), 4.93 (1H, dd, J_{trans} 17.0 Hz, J_{gem} 1.7 Hz, CH_2), 4.53 (1H, dd, J_{cis} 10.2 Hz, J_{gem} 1.7 Hz, CH_2), 4.45 (5H, d, J_{PH} 0.7 Hz, C_5H_5); ^{13}C {^1H} n.m.r. δ220.5 (d, J_{PC} 31.4 Hz, C≡O), 149.9 (s, CH), 136.3 (d, J_{PC} 42.8 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 10.6 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 10.3 Hz, Ph C_{meta}), 111.0 (s, CH_2), 85.4 (s, C_5H_5); ^{31}P {^1H} n.m.r. δ72.9; m/z 466 (M^+).

Preparation of (R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 and (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60

Using an identical procedure to that described above for the preparation of (R,S)-60, (R)-(-)-25 (600 mg, 0.96 mmol) and sodium hydride (305 mg, 12.7 mmol) gave (R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 (370 mg, 83%); $[\alpha]_D^{22}$ -202.0° (c 0.11, C_6H_6). Similarly, (S)-(+)-26 (1.07 g, 1.72 mmol) and sodium hydride (490 mg, 20.4 mmol) gave (S)-(+)-[(η^5-C_5H_5)-Fe(CO)(PPh_3)COCH=CH_2] 60 (700 mg, 87%); $[\alpha]_D^{20}$ +202.0° (c 0.11, C_6H_6).

Preparation of (RR,SS)-{(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2O[(R)-menthyl]} 61 and 62

n-Butyllithium (1.0 ml, 1.5 mmol) was added to [(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_2CH_3$] 16 (620 mg, 1.32 mmol) in THF (15 ml) at -78°C to give a dark purple solution. After stirring (-78°C; 1 h), chloromethyl (R)-menthyl ether (0.4 ml, 2.0 mmol) was added and the mixture stirred for a further 4 h (-78°C). The solution was warmed to room temperature over 2 h

to give a dark orange solution. The solvent was removed and the residue extracted with dichloromethane (2 x 20 ml). Filtration through alumina (grade V) and chromatography on alumina (grade I) gave a single orange band eluted with diethyl ether - dichloromethane (5:1). Removal of solvent gave a 1:1 mixture of (RRR)-61 and (SSR)-62 as orange microcrystals (640 mg, 76%); $\nu_{max.}$ 1915 vs (C≡O), 1615 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (30H, m, Ph both isomers), 4.47 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 4.46 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.88 - 2.81 (8H, m, COC<u>H</u>(CH_3)C<u>H_2</u>OC<u>H</u> both isomers), 2.29 - 0.75 (36H, m, menthyl H both isomers), 0.39 (3H, d, $J_{1,2}$ 6.7 Hz, COCHC<u>H_3</u>), 0.35 (3H, d, $J_{1,2}$ 6.8 Hz, COCHC<u>H_3</u>); <u>m/z</u> 636 (M^+).

<u>Preparation of (RR,SS)-{(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(Et)CH_2O[(R)-menthyl]} 63 and 64</u>

<u>n</u>-Butyllithium (1.8 ml, 2.88 mmol) was added to [(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_2CH_2CH_3$] <u>15</u> (1.15 g, 2.39 mmol) in THF (20 ml) at -78°C to give a dark purple solution. After stirring (-78°C; 1.5 h), chloromethyl (R)-menthyl ether (0.8 ml, 4.0 mmol) was added and the mixture stirred for a further 2.5 h (-78°C). The solution was warmed to room temperature over 2 h and the solvent was removed. The residue was extracted with dichloromethane (2 x 20 ml), filtered through alumina (grade V) and chromatographed on alumina (grade I). A single orange band was eluted with diethyl ether which, upon removal of solvent, gave a 1:1 mixture of (RRR)-63 and (SSR)-64 as orange microcrystals (870 mg; 56%); $\nu_{max.}$ 1915 vs (C≡O), 1615 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (30H, m, Ph both isomers), 4.49 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 4.46 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 4.00 - 2.73 (8H, m, COC<u>H</u>(Et)C<u>H_2</u>OC<u>H</u> both isomers), 2.27 - 0.73 (40H, m, COCH(C<u>H_2</u>CH_3) and menthyl H both isomers), 0.42 (3H, t, $J_{1,2}$ 7.4 Hz, CH_2C<u>H_3</u>), 0.40 (3H, t, $J_{1,2}$ 7.4 Hz, CH_2C<u>H_3</u>); <u>m/z</u> 650 (M^+).

Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COC(CH_3)=CH_2]$ 65

The 1:1 mixture of (RRR)-61 and (SSR)-62 (420 mg, 0.66 mmol) and sodium hydride (230 mg, 9.5 mmol) were combined as solids. THF (20 ml) was added and the reaction mixture heated at 50°C with stirring for 15 h. Removal of solvent, extraction with dichloromethane (2 x 10 ml) and filtration through alumina (grade V) gave an orange solution. Concentration and chromatography on alumina (grade I) gave a single orange fraction eluted with diethyl ether - dichloromethane (2:1). Removal of solvent and crystallisation from dichloromethane - hexane gave $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)\text{-}COC(CH_3)=CH_2]$ 65 as orange rhombic crystals (125 mg, 39%) (Found: C, 69.9; H, 5.3; P, 6.0. $C_{28}H_{25}FeO_2P$ requires C, 70.0; H, 5.25; P, 6.45%); $\nu_{max.}$ 1915 vs (C≡O), 1560 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.48 (1H, br s, C=CH_2), 5.42 (1H, br s, C=CH_2), 4.47 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 1.31 (3H, s, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ221.5 (d, J_{PC} 32.8 Hz, C≡O), 158.2 (d, J_{PC} 3.7 Hz, CO<u>C</u>CH_3), 136.7 (d, J_{PC} 42.8 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 10.1 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.9 Hz, Ph C_{meta}), 120.6 (s, CH_2), 85.2 (s, C_5H_5), 18.8 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ72.1; m/z 480 (M^+), 452 (M^+-28).

Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COC(Et)=CH_2]$ 66

Following an identical procedure to that used in the preparation of complex 65, treatment of the 1:1 mixture of (RRR)-63 and (SSR)-64 (200 mg, 0.31 mmol) with sodium hydride (185 mg, 7.7 mmol) gave $[(\eta^5\text{-}C_5H_5)Fe(CO)\text{-}(PPh_3)COC(Et)=CH_2]$ 66 as fine orange needles (70 mg, 46%) (Found: C, 70.3; H, 5.5; P, 6.6. $C_{29}H_{27}FeO_2P$ requires C, 70.5; H, 5.5; P, 6.3%); $\nu_{max.}$ 1920 vs (C≡O), 1560 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.57 (1H, d, J_{gem} 0.8 Hz, C=CH_2), 5.39 (1H, d, J_{gem} 1.4 Hz, C=CH_2), 4.46 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 1.84 (1H, m, CH_2), 1.38 (1H, m, CH_2), 0.78 (3H, t, $J_{1,2}$ 7.4 Hz, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ221.6 (d, J_{PC} 33.6 Hz, C≡O),

164.2 (s, CO<u>C</u>=CH_2), 136.7 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 10.1 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 119.3 (s, C=<u>C</u>H_2), 85.3 (s, C_5H_5), 24.3 (s, CH_2), 12.5 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ72.0; <u>m/z</u> 494 (M^+), 466 (M^+-28).

<u>Preparation of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH=CH_2$] 82</u>

<u>n</u>-Butyllithium (0.15 ml, 0.24 mmol) was added to Z-[(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH=CHCH_3$] <u>34</u> (52 mg, 0.11 mmol) in THF (10 ml) at -78°C to give a deep red solution. After stirring (-78°C; 1 h), trifluoroacetic acid (excess) in THF (2 ml; -78°C) was added dropwise and the reaction mixture stirred for a further 15 min (-78°C). The resulting light red solution was poured onto saturated aqueous $NaHCO_3$ solution (15 ml). Dichloromethane (10 ml) was added and the organic layer separated and chromatographed on alumina (grade I). Elution with dichloromethane - ethyl acetate (2:1), removal of solvent and crystallisation from dichloromethane - hexane gave [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH=CH_2$] <u>82</u> as orange rhombic crystals (47 mg, 90%) (Found: C, 70.1; H, 5.4; P, 6.5. $C_{28}H_{25}FeO_2P$ requires C, 70.0; H, 5.25; P, 6.45%); $\nu_{max.}$ 1905 vs (C≡O), 1610 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.61 (1H, m, C<u>H</u>=CH_2), 4.89 (1H, d, J_{cis} 10.1 Hz, CH=C<u>H</u>$_2$), 4.78 (1H, d, J_{trans} 17.1 Hz, CH=C<u>H</u>$_2$), 4.45 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.61, 3.25 (2H, ABX system, J_{AB} 15.5 Hz, $COCH_2$); ^{13}C $\{^1H\}$ n.m.r. δ220.5 (d, J_{PC} 31.0 Hz, C≡O), 136.4 (d, J_{PC} 42.7 Hz, Ph C_{ipso}), 134.2 (s, <u>C</u>H=CH_2), 133.3 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 115.5 (s, CH=<u>C</u>H_2), 85.2 (s, C_5H_5), 70.3 (d, J_{PC} 5.4 Hz, CO<u>C</u>H_2); ^{31}P $\{^1H\}$ n.m.r. δ72.3: <u>m/z</u> 480 (M^+), 439 (M^+-41).

Addition of methanol to the deep red solution generated from complex 34 (234 mg, 0.49 mmol) and n-butyllithium (0.7 ml, 1.16 mmol) in THF (20 ml) at -78°C, gave an orange solution. Warming to room temperature over 2 h and removal of solvent gave an orange residue which was extracted with dichloromethane (2 x 15 ml) and filtered through alumina (grade V). The filtrate was chromatographed on alumina (grade I). Elution with dichloromethane and removal of solvent gave complex 82 as orange microcrystals (164 mg, 70%). Elution with dichloromethane - ethyl acetate (1:1) and removal of solvent gave E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33 as fine orange crystals (70 mg, 30%). The products were identified by comparison of their ^{1}H n.m.r. spectra with those of authentic samples.

General procedure for the reaction between dienolate 81 and electrophiles to give complexes 83, 85, 86 and 87

n-Butyllithium (0.7 ml, 1.12 mmol) was added to Z-[(η^5-C_5H_5)Fe(CO)-(PPh_3)COCH=$CHCH_3$] 34 (500mg, 1.04 mmol) in THF (30 ml) at -78°C to give a deep red solution. After stirring (-78°C; 2 h), the electrophile (2 equivalents) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 10 ml) and filtered through alumina (grade V).

The product complexes were purified by chromatography on alumina (grade I), analysed by ^{1}H n.m.r. spectroscopy to determine diastereoselectivities and obtained as orange needles from dichloromethane - hexane.

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH=CH_2] 83. Elution with diethyl ether - dichloromethane (3:1) gave complex 83 (94%, diasteroisomeric purity >100:1) (Found: C, 70.3; H, 5.4; P, 6.3. $C_{29}H_{27}FeO_2P$ requires C, 70.5; H, 5.5; P, 6.3%); $\nu_{max.}$ 1915 vs (C≡O), 1592 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.21 (1H, ddd, J_{trans} 17.8 Hz, J_{cis} 10.5 Hz, $J_{1,2}$ 7.7 Hz, C<u>H</u>=CH_2), 4.71 (2H, m, CH=C<u>H</u>$_2$), 4.46 (5H, d, J_{PH} 1.1 Hz,

C_5H_5), 3.64 (1H, quintet, $J_{1,2}$ 7.3 Hz, COCH), 1.10 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3 major diastereoisomer), 0.39 (3H, d, $J_{1,2}$ 6.3 Hz, CH_3 minor diastereoisomer); ^{13}C $\{^1H\}$ n.m.r. δ220.7 (d, J_{PC} 31.6 Hz, C≡O), 140.2 (s, $\underline{C}H=CH_2$), 136.5 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 10.0 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 113.0 (s, $CH=\underline{C}H_2$), 85.1 (s, C_5H_5), 71.6 (d, J_{PC} 5.4 Hz, $CO\underline{C}H$), 17.1 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ71.8; m/z 494 (M^+).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(Et)CH=CH_2] 85. Elution with diethyl ether - dichloromethane (1:1) gave complex 85 (95%, diastereoisomeric purity >100:1) (Found: C, 70.6; H, 5.9. $C_{30}H_{29}FeO_2P$ requires C, 70.9; H, 5.75%); $\nu_{max.}$ 1910 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.19 (1H, ddd, J_{trans} 17.2 Hz, J_{cis} 10.2 Hz, $J_{1,2}$ 3.6 Hz, $C\underline{H}=CH_2$), 4.72 (2H, ddd, J_{trans} 17.2 Hz, J_{cis} 10.2 Hz, J_{gem} 2.2 Hz, $CH=C\underline{H}_2$), 4.44 (5H, d, J_{PH} 0.9 Hz, C_5H_5), 3.43 (1H, dt, $J_{1,2}$ 9.8 Hz, 3.6 Hz, COCH), 1.85 - 1.20 (2H, m, $C\underline{H}_2CH_3$), 0.79 (3H, t, $J_{1,2}$ 7.4 Hz, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ220.6 (d, J_{PC} 30.3 Hz, C≡O), 138.3 (s, $\underline{C}H=CH_2$), 136.5 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 9.6 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 10.0 Hz, Ph C_{meta}), 115.2 (s, $CH=\underline{C}H_2$), 85.1 (s, C_5H_5), 80.6 (d, J_{PC} 4.1 Hz, $CO\underline{C}H$), 24.2 (s, $\underline{C}H_2CH_3$), 11.8 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ72.1; m/z 508 (M^+).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_2Ph)CH=CH_2] 86. Elution with diethyl ether - dichloromethane (1:1) gave complex 86 (90%, diastereoisomeric purity >100:1) (Found: C, 73.6; H, 5.7. $C_{35}H_{31}FeO_2P$ requires C, 73.7; H, 5.5%); $\nu_{max.}$ 1910 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.2 (20H, m, Ph), 5.10 (1H, ddd, J_{trans} 15.7 Hz, J_{cis} 10.1 Hz, $J_{1,2}$ 3.7 Hz, $C\underline{H}=CH_2$), 4.66 (2H, ddd, J_{trans} 15.7 Hz, J_{cis} 10.1 Hz, J_{gem} 2.0 Hz, $CH=C\underline{H}_2$), 4.27 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.98 (1H, m, COCH), 3.12, 2.35 (2H, ABX system, J_{AB} 13.3 Hz, CH_2Ph); ^{13}C $\{^1H\}$ n.m.r. δ220.6 (d, J_{PC} 31.2 Hz, C≡O), 140.8 (s, CH_2Ph C_{ipso}), 137.1 (s, CH_2Ph C_{meta}), 136.6 (d, J_{PC}

43.6 Hz, Ph C_{ipso}), 133.6 (d, J_{PC} 10.4 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 129.4 (s, CH_2Ph C_{ortho}), 128.0 (d, J_{PC} 8.8 Hz, Ph C_{meta}), 125.6 (s, CH_2Ph C_{para}), 116.4 (s, CH=$\underline{C}H_2$), 85.1 (s, C_5H_5), 80.9 (d, J_{PC} 4.5 Hz, CO$\underline{C}$H), 38.4 (s, $\underline{C}H_2Ph$); ^{31}P $\{^1H\}$ n.m.r. δ72.1; m/z 570 (M^+).

$\{(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH[CH(OH)CH_3]CH=CH_2\}$ 87. Elution with diethyl ether - dichloromethane (4:1, alumina, grade V) gave complex 87 (93%, 32:9:2:1 diastereoisomeric mixture) (Found: C, 68.7; H, 5.6; P, 5.7. $C_{30}H_{29}FeO_3P$ requires C, 68.7; H, 5.6; P, 5.9%); $\nu_{max.}$ 3490 m (O-H), 1910 vs (C≡O), 1575, 1565, 1555 s cm^{-1} (C=O); ^1H n.m.r. δ 7.5 - 7.3 (15H, m, Ph), 5.40 - 4.91 (3H, m, $CH=CH_2$), 4.47 (5H, d, J_{PH} 1.4 Hz, C_5H_5 major diastereoisomer), 4.44, 4.42, 4.39 (5H, d, J_{PH} 1.4 Hz, C_5H_5 minor diastereoisomers), 4.06 (1H, dq, $J_{1,2}$ 6.3 Hz, 0.9 Hz, C$\underline{H}CH_3$), 3.83 (1H, dd, $J_{1,2}$ 9.6 Hz, 1.8 Hz, COCH), 3.64 (1H, s, OH), 1.00, 0.73, 0.66 (3H, d, $J_{1,2}$ 6.0 Hz, CH_3 minor diastereoisomers), 0.95 (3H, d, $J_{1,2}$ 6.3 Hz, CH_3 major diastereoisomer); m/z 524 (M^+).

Preparation of (RS,SR)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH=CH_2]$ 83 from $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH=CH_2]$ 82

n-Butyllithium (0.15 ml, 0.24 mmol) was added to complex 82 (65 mg, 0.14 mmol) in THF (10 ml) at -78°C to give a deep red solution. After stirring (-78°C; 1 h), methyl iodide (0.2 ml, 3.2 mmol) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature, removal of solvent and extraction with dichloromethane (2 x 10 ml) gave an orange oil which was filtered through alumina (grade V) and chromatographed on alumina (grade I). Elution with dichloromethane gave complex 83 (55 mg, 81%) as a 30:1 mixture of diastereoisomers.

General procedure for the reaction between dienolate 88 and electrophiles to give complexes 89, 90, 91 and 92

n-Butyllithium (0.8 ml, 1.28 mmol) was added to Z-[(η^5-C_5H_5)Fe(CO)-(PPh_3)COCH=CHEt] 36 (500 mg, 1.01 mmol) in THF (30 ml) at -78°C to give a deep red solution. After stirring (-78°C; 2 h), the electrophile (2 equivalents) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 10 ml) and filtered through alumina (grade V).

The product complexes were purified by chromatography on alumina (grade I), analysed by ^{1}H n.m.r. spectroscopy to determine diastereoselectivities and obtained as orange needles from dichloromethane - hexane.

E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH$=$CHCH_3$] 89. Elution with dichloromethane gave complex 89 (60%) (Found: C, 70.4; H, 5.4; P, 6.3. $C_{29}H_{27}FeO_2P$ requires C, 70.5; H, 5.5; P, 6.3%); $\nu_{max.}$ 1908 vs (C≡O), 1592 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.22 (1H, m, J_{trans} 15.5 Hz, $J_{1,3}$ 0.5 Hz, 0 Hz, C<u>H</u>CH_3), 5.25 (1H, m, J_{trans} 15.5 Hz, $J_{1,2}$ 7.1 Hz, 5.8 Hz, CH_2C<u>H</u>), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.54 (1H, m, J_{gem} 15.4 Hz, $J_{1,2}$ 5.8 Hz, $J_{1,3}$ 0.5 Hz, $COCH_2$), 3.21 (1H, m, J_{gem} 15.4 Hz, $J_{1,2}$ 7.1 Hz, $J_{1,3}$ 0 Hz, $COCH_2$), 1.59 (3H, d, $J_{1,2}$ 4.5 Hz, CH_3); ^{13}C {^{1}H} n.m.r. δ220.5 (d, J_{PC} 31.4 Hz, C≡O), 136.5 (d, J_{PC} 43.0 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 10.4 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}) 128.0 (d, J_{PC} 9.7 Hz, Ph C_{meta}), 126.8 (s, -CH=), 126.2 (s, -CH=), 85.1 (s, C_5H_5), 69.3 (d, J_{PC} 5.3 Hz, $COC\underline{H}_2$), 17.9 (s, CH_3); ^{31}P {^{1}H} n.m.r. δ72.8; m/z 494 (M^+), 466 (M^+-28), 439 (M^+-55).

(RS,SR)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH$=$CHCH_3$] 90. Elution with diethyl ether gave complex 90 (86%, diastereoisomeric purity >100:1) (Found: C, 70.7; H, 5.7; P, 6.0. $C_{30}H_{24}FeO_2P$ requires C, 70.9; H, 5.75; P, 6.1%); $\nu_{max.}$ 1902 vs (C≡O), 1592 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.20 (1H, dq, J_{trans} 16.0 Hz, $J_{1,2}$ 6.3 Hz, CH=C<u>H</u>CH_3),

4.83 (1H, ddq, J_{trans} 15.2 Hz, $J_{1,2}$ 8.3 Hz, $J_{1,3}$ 1.5 Hz, CHC<u>H</u>=CH), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.68 (1H, quintet, $J_{1,2}$ 7.5 Hz, COCH), 1.52 (3H, dd, $J_{1,2}$ 6.4 Hz, $J_{1,3}$ 1.6 Hz, CH=CHC<u>H</u>$_3$), 1.02 (3H, d, $J_{1,2}$ 6.9 Hz, COCHC<u>H</u>$_3$ major diastereoisomer), 0.38 (3H, d, $J_{1,2}$ 6.8 Hz, COCHC<u>H</u>$_3$ minor diastereoisomer); ^{13}C {^1H} n.m.r. δ220.7 (d, J_{PC} 31.5 Hz, C≡O), 136.7 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 132.7 (s, -CH=), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 124.2 (s, -CH=), 84.9 (s, C_5H_5), 71.5 (d, J_{PC} 5.0 Hz, CO<u>C</u>H), 18.0 (s, CH_3), 18.0 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.6; <u>m/z</u> 508 (M^+).

(RS,SR)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(Et)CH=CHCH$_3$] <u>91</u>. Elution with diethyl ether - dichloromethane (1:1) gave complex <u>91</u> (87%, diastereoisomeric purity >100:1) (Found: C, 71.05; H, 6.1. $C_{31}H_{31}FeO_2P$ requires C, 71.3; H, 6.0%); $\nu_{max.}$ 1900 vs (C≡O), 1595 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.17 (1H, dq, J_{trans} 15.3 Hz, $J_{1,2}$ 6.4 Hz, C<u>H</u>CH$_3$), 4.75 (1H, ddd, J_{trans} 15.3 Hz, $J_{1,2}$ 9.5 Hz, $J_{1,3}$ 1.6 Hz, C<u>H</u>=CHCH$_3$), 4.42 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.44 (1H, dt, $J_{1,2}$ 9.8 Hz, 3.7 Hz, COCH), 1.55 (3H, dd, $J_{1,2}$ 6.4 Hz, $J_{1,3}$ 1.6 Hz, CHC<u>H</u>$_3$), 1.72 - 1.64 (1H, m, C<u>H</u>$_2$CH$_3$), 1.27 - 1.15 (1H, m, C<u>H</u>$_2$CH$_3$), 0.76 (3H, t, $J_{1,2}$ 7.4 Hz, CH$_2$C<u>H</u>$_3$); ^{13}C {^1H} n.m.r. δ220.7 (d, J_{PC} 31.4 Hz, C≡O), 136.8 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 9.4 Hz, Ph C_{ortho}) 130.7 (s, <u>C</u>H=CHCH$_3$), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 126.3 (s, CH=<u>C</u>HCH$_3$), 85.0 (s, C_5H_5), 80.3 (d, J_{PC} 5.3 Hz, CO<u>C</u>H), 24.7 (s, CH_2), 18.1 (s, CH_3), 11.8 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.8;. <u>m/z</u> 522 (M^+).

(RS,SR)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_2Ph)CH=CHCH$_3$] <u>92</u>. Elution with dichloromethane gave complex <u>92</u> (90%, diastereoisomeric purity >100:1) (Found: C, 73.7; H, 5.65. $C_{36}H_{33}FeO_2P$ requires C, 74.0; H, 5.7%); $\nu_{max.}$ 1910 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.1 (20H, m, Ph), 5.15 (1H, dq, J_{trans} 15.1 Hz, $J_{1,2}$ 6.4 Hz, CH=C<u>H</u>CH$_3$), 4.67 (1H, ddq, J_{trans} 15.1 Hz, $J_{1,2}$ 9.1 Hz, $J_{1,3}$ 1.6 Hz, CH=C<u>H</u>CH$_3$), 4.21 (5H,

d, J_{PH} 1.2 Hz, C_5H_5), 3.96 (1H, m, COCH), 2.33, 2.99 (2H, ABX system, J_{AB} 13.3 Hz, C$\underline{H_2}$Ph), 1.47 (3H, dd, $J_{1,2}$ 6.4 Hz, $J_{1,3}$ 1.5 Hz, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ220.6 (d, J_{PC} 31.3 Hz, C≡O), 141.2 (s, CH_2Ph C_{ipso}), 136.8 (d, J_{PC} 41.9 Hz, Ph C_{ipso}), 133.6 (d, J_{PC} 9.7 Hz, Ph C_{ortho}), 129. 6 (s, CH_2Ph C_{meta}), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.6 Hz, Ph C_{meta}), 127.4 (s, CH_2Ph C_{ortho}), 125.5 (s, CH_2Ph C_{para}), 85.0 (s, C_5H_5), 80.5 (d, J_{PC} 2.5 Hz, CO$\underline{C}$H), 38.9 (s, $\underline{C}H_2Ph$), 18.3 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ73.0; m/z 584 (M^+).

Preparation of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2$n-Bu] 116

[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 (84 mg, 0.18 mmol) in THF (10 ml) was added dropwise over 10 min to n-butyllithium (0.2 ml, 0.3 mmol) in THF (5 ml) at -78°C to give a dark red solution. After stirring (-78°C; 1.5 h), methanol (1 ml) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 10 ml) and filtered through alumina (grade V). The filtrate was concentrated and chromatographed on alumina (grade I). A yellow band was eluted with diethyl ether. Removal of solvent gave [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2$n-Bu] 116 as fine orange crystals (33 mg, 35%) (spectroscopic data are given below (p.162)). Elution with dichloromethane and removal of solvent gave orange microcrystals, shown by ^1H n.m.r. spectroscopy to consist of a complex mixture of dimeric acyl compounds (63 mg, 35%). These products were not characterised further.

Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH_2$n-Bu] 117

[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 (84 mg, 0.18 mmol) in THF (15 ml) was added dropwise over 15 min to n-butyllithium (0.2 ml, 0.3 mmol) in THF (5 ml) at -78°C to give a dark red solution. After stirring (-78°C; 1.5 h),

methyl iodide (0.2 ml, 3.2 mmol) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 10 ml) and filtered through alumina (grade V). The filtrate was concentrated and chromatographed on alumina (grade I). A single yellow band was eluted with diethyl ether. Removal of solvent gave (RS,SR)-[(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH(CH_3)CH_2$n-Bu] 117 as fine orange crystals (60 mg, 62%, diastereoisomeric purity 75:1) (spectroscopic data are given below (p.163)).

Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH_2$n-Bu] 117 in the presence of TMEDA

TMEDA (0.15 ml, 1.0 mmol, dried over molecular sieves) was added to n-butyllithium (0.3 ml, 0.48 mmol) in THF (5 ml) at -78°C to give a pale yellow solution. After stirring (-78°C; 1 h), [(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH{=}CH_2$] 60 (80 mg, 0.17 mmol) in THF (10 ml) was added dropwise over 10 min. The resulting dark red solution was stirred (-78°C; 1h) and quenched with methyl iodide (0.2 ml, 3.2 mmol). Warming to room temperature, removal of solvent and extraction with dichloromethane (2 x 10 ml) gave an orange solution. Filtration through alumina (grade V) and removal of solvent gave (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH_2$n-Bu] 117 (75 mg, 82%) with a diastereoisomeric purity of greater than 75:1 (spectroscopic data are given below (p.163)).

General procedure for the reaction of diastereoisomers 25 and 26 with two equivalents of an alkyllithium and an electrophile. Preparation of complexes 116, 117 and 119 - 123

The alkyllithium (2 equivalents) was added to the 1:1 mixture of diastereoisomers 25 and 26 of {(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2O$[(R)-menthyl]} (typically 500 mg) in THF (20 ml) at -78°C to give a dark red

solution.† After stirring (-78°C; 2 h), the electrophile (2 equivalents) was added and the mixture stirred for a further 2 h. Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 10 ml) and filtered through alumina (grade V).

The product complexes were purified by chromatography on alumina and, where appropriate, analysed by ^{1}H n.m.r. spectroscopy to determine diastereoselectivities.

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2$n-Bu] 116. Elution with diethyl ether and crystallisation from hexane (-30°C) gave complex 116 as orange blocks (69%) (Found: C, 71.0; H, 6.4; P, 5.9. $C_{31}H_{33}FeO_2P$ requires C, 71.0; H, 6.3; P, 5.9%); $\nu_{max.}$ 1900 vs (C≡O), 1620 s and 1605 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.42 (5H, d, J_{PH} 0.9 Hz, C_5H_5), 2.91 - 2.50 (2H, m, $COCH_2$), 1.27 - 0.94 (8H, m, $(CH_2)_4$), 0.84 (3H, t, $J_{1,2}$ 7.1 Hz, CH_3); ^{13}C {^{1}H} n.m.r. δ220.6 (d, J_{PC} 31.5 Hz, C≡O), 136.6 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 10.4 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 66.4 (d, J_{PC} 5.0 Hz, $CO\underline{C}H_2$), 31.7 (s, CH_2), 28.8 (s, CH_2), 25.1 (s, CH_2), 22.5 (s, CH_2), 14.0 (s, CH_3); ^{31}P {^{1}H} n.m.r. δ72.6; m/z 524 (M^+), 496 (M^+-28).

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2$t-Bu] 120. Elution with diethyl ether and crystallisation from diethyl ether - hexane (-30°C) gave complex 120 as fine yellow crystals (78%) (Found: C, 71.2; H, 6.1; P, 5.9. $C_{31}H_{33}FeO_2P$ requires C, 71.0; H, 6.3; P, 5.9%); $\nu_{max.}$ 1900 vs (C≡O), 1610 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 2.78 (1H, m, $COCH_2$), 2.53 (1H, m, $COCH_2$), 1.22 (1H, m, CH_2C), 0.83 (1H, m, CH_2C), 0.74 (9H, s, CH_3); ^{13}C {^{1}H} n.m.r. δ220.6 (d, J_{PC} 31.4 Hz, C≡O), 136.6 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.4 Hz,

† In the case of n-butyllithium, an inverse addition procedure was adopted.

Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.1 (s, C_5H_5), 62.1 (s, CO$\underline{C}H_2$), 38.4 (s, $\underline{C}H_2C$), 29.6 (s, $\underline{C}(CH_3)_3$), 29.2 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.5; m/z 524 (M^+), 496 (M^+-28).

[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2Ph$] 121. Elution with diethyl ether - dichloromethane (2:1) and removal of solvent gave complex 121 as orange microcrystals (60%); ^1H n.m.r. δ7.6 - 6.9 (20H, m, Ph), 4.40 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 3.15 (1H, m, COCH), 2.84 (1H, m, $C\underline{H}_2Ph$), 2.59 (1H, m, $C\underline{H}_2Ph$), 2.16 (1H, m, COCH) [lit.,[39] δ7.8 - 6.9 (m), 4.4 (s), 3.6 -2.2 (m)].

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH_2Et$] 119. Elution with dichloromethane - ethyl acetate (1:1) and crystallisation from dichloromethane - hexane (-30°C) gave complex 119 as orange needles (55%, diastereoisomeric purity >100:1); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 4.44 (5H, d, J_{PH} 1.4 Hz, C_5H_5), 2.74 (1H, m, COCH), 1.00 (3H, d, $J_{1,2}$ 7.2 Hz, $CHC\underline{H}_3$), 0.96 - 0.42 (4H, m, CH_2CH_2), 0.65 (3H, t, $J_{1,2}$ 6.3 Hz, $CH_2C\underline{H}_3$); m/z 510 (M^+). The ^1H n.m.r. data were identical to those of an authentic sample.[136]

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH_2$n-Bu] 117. Elution with diethyl ether and crystallisation from hexane gave complex 117 as orange rhombic crystals (73%, diastereoisomeric purity >100:1) (Found: C, 71.1; H, 6.5; P, 5.9. $C_{32}H_{35}FeO_2P$ requires C, 71.4; H, 6.55; P, 5.75%); $\nu_{max.}$ 1905 vs (C≡O), 1605 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.45 (5H, s, C_5H_5), 2.78 - 2.67 (1H, m, COCH), 1.28 - 0.48 (8H, m, $(CH_2)_4$), 1.00 (3H, d, $J_{1,2}$ 7.1 Hz, $CHC\underline{H}_3$ major diastereoisomer), 0.83 (3H, t, $J_{1,2}$ 7.2 Hz, $CH_2C\underline{H}_3$), 0.17 (3H, d, $J_{1,2}$ 7.1 Hz, $CHC\underline{H}_3$ minor diastereoisomer); ^{13}C {^1H} n.m.r. δ221.0 (d, J_{PC} 31.2 Hz, C≡O), 136.7 (d, J_{PC} 42.4 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.2 Hz, Ph C_{meta}), 85.3 (s, C_5H_5), 67.6 (d, J_{PC} 5.1 Hz, CO$\underline{C}H$), 32.1 (s, CH_2), 26.8 (s, CH_2), 22.6 (s, CH_2), 16.2 (s, CH_3), 14.1 (s, CH_3); ^{31}P {^1H} n.m.r. δ71.2; m/z 538 (M^+).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2t-Bu] 122. Elution with diethyl ether and crystallisation from diethyl ether - hexane gave complex 122 as orange rhombic crystals (49%, diastereoisomeric purity 30:1) (Found: C, 71.45; H, 6.7. $C_{32}H_{35}FeO_2P$ requires C, 71.4; H, 6.55%); $\nu_{max.}$ 1905 vs (C≡O), 1600 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.45 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.09 (1H, m, COCH), 1.03 (3H, d, $J_{1,2}$ 6.9 Hz, CHC<u>H</u>$_3$ major diastereoisomer), 0.96 - 0.48 (2H, m, CH_2), 0.75 (9H, s, $C(CH_3)_3$), 0.30 (3H, d, $J_{1,2}$ 6.5 Hz, CHC<u>H</u>$_3$ minor diastereoisomer); ^{13}C {^{1}H} n.m.r. δ221.0 (d, J_{PC} 31.5 Hz, C≡O), 137.0 (d, J_{PC} 42.4 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.7 Hz, Ph C_{meta}), 84.9 (s, C_5H_5), 65.1 (d, J_{PC} 4.9 Hz, CO<u>C</u>H), 43.5 (s, CH_2), 30.5 (s, C(<u>C</u>H$_3$)$_3$), 30.4 (s, <u>C</u>(CH_3)$_3$), 18.3 (s, CH<u>C</u>H$_3$); ^{31}P {^{1}H} n.m.r. δ71.7; <u>m/z</u> 538 (M^+), 510 (M^+-28).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2Ph] 123. Elution with diethyl ether - dichloromethane (11:1) and crystallisation from dichloromethane - hexane gave complex 123 as orange blocks (65%, diastereoisomeric purity >100:1) (Found: C, 72.9; H, 5.6; P, 5.7. $C_{34}H_{31}FeO_2P$ requires C, 73.1; H, 5.6; P, 5.55%); $\nu_{max.}$ 1900 vs (C≡O), 1605 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.1 (20H, m, Ph), 4.48 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.00 (1H, m, COCH), 1.92 - 1.80 (2H, m, CH_2), 0.87 (3H, d, $J_{1,2}$ 7.1 Hz, CH_3); <u>m/z</u> 558 (M^+).

<u>Preparation of (RS)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2Et] 119 and (SR)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2Et] 119</u>

Following the general procedure described above (p.161), treatment of (R)-(-)-25 (400 mg, 0.64 mmol) with ethyllithium (3.0 ml, 0.8 M soln. in diethyl ether, 2.4 mmol) and methyl iodide (0.5 ml, 8.03 mmol) gave (RS)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2Et] 119 (300 mg, 92%); $[\alpha]_D^{20}$ -237.0° (c 0.07, C_6H_6). Similarly, treatment of (S)-(+)-26

(1.65 g, 2.66 mmol) with ethyllithium (13 ml, 0.8 M soln. in diethyl ether, 10.4 mmol) and methyl iodide (1 ml, 16.1 mmol) gave (SR)-(+)-[(η^5-C_5H_5)Fe-(CO)(PPh_3)COCH(CH_3)CH_2Et] 119 (1.21 g, 90 %); $[\alpha]_D^{25}$ +238.0° (c 0.10, C_6H_6).

The ^{1}H n.m.r. spectra of the products showed that both (RS)-(-)-119 and (SR)-(+)-119 had diastereoisomeric purities of greater than 100:1.

General procedure for the oxidative decomplexation of iron acyl complexes to the corresponding carboxylic acids

Bromine (2 equivalents) in THF (2 ml) was added dropwise to a stirred solution of the complex (typically 600 mg) in THF - water (25:1) at 0°C to give a dark brown solution. After stirring (0°C; 3 h), saturated aqueous $Na_2S_2O_3$ (1 ml) was added. Removal of THF, addition of water (15 ml) and acidification (pH 1) gave a dark green solution which was extracted with diethyl ether (3 x 20 ml). The green organic layer was concentrated (20 ml) and washed successively with saturated aqueous $NaHCO_3$ (20 ml) and water (2 x 20 ml). The combined aqueous layers were acidified (pH 1) and extracted with diethyl ether (3 x 15 ml). The extracts were washed with water (20 ml) and dried (Na_2SO_4). Filtration and removal of solvent gave the crude acid which was chromatographed on silica.

Preparation of 2-methylpentanoic and 2-methylheptanoic acids

The general decomplexation procedure described above was followed.

2-Methylpentanoic acid.[237] Elution with diethyl ether and removal of solvent gave 2-methylpentanoic acid as a colourless oil (39%); ^{1}H n.m.r. δ2.47 (1H, m, C<u>H</u>CO_2H), 1.66 (1H, m, CHC<u>H_2</u>), 1.37 (3H, m, C<u>H_2</u>C<u>H_2</u>), 1.18 (3H, d, $J_{1,2}$ 6.9 Hz, CHC<u>H_3</u>), 0.92 (3H, t, $J_{1,2}$ 7.0 Hz, CH_2C<u>H_3</u>).

2-Methylheptanoic acid.[238] Elution with diethyl ether and removal of solvent gave 2-methylheptanoic acid as a colourless oil (36%); ν_{max}.

($CHCl_3$) 3520 br (O-H), 1710 vs cm^{-1} (C=O); ^1H n.m.r. δ2.46 (1H, m, C<u>H</u>CO_2H), 1.74 - 0.81 (8H, m, $(CH_2)_4$), 1.18 (3H, d, $J_{1,2}$ 6.9 Hz, CHC<u>H</u>$_3$), 0.89 (3H, t, $J_{1,2}$ 6.8 Hz, CH_2C<u>H</u>$_3$) [lit.,[238] δ1.16 (d, $J_{1,2}$ 7 Hz, CHC<u>H</u>$_3$)]; ^{13}C {^1H} n.m.r. δ182.9 (CO_2H), 39.3 (CH), 33.5 (CH_2), 31.7 (CH_2), 26.8 (CH_2), 22.5 (CH_2), 16.8 (CH_3), 14.0 (CH_3); <u>m/z</u> (CI/NH_3) 162 (M^+ + 18).

<u>General procedure for the Michael addition of alkyllithiums to E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33 followed by reaction with electrophiles to give complexes 125, 127 and 128</u>

The alkyllithium (1.2 equivalents) was added to complex <u>33</u> (typically 500 mg) in THF (25 ml) at -78°C to give a dark red solution. After stirring (-78°C; 2 h for the addition of <u>n</u>-butyllithium and -40°C; 2 h for methyllithium), the electrophile (2 equivalents) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 10 ml) and filtered through alumina (grade V).

The product complexes were purified by chromatography on alumina (grade I), analysed by ^1H n.m.r. spectroscopy in order to determine diastereoselectivities and obtained as orange needles from hexane (-30°C).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(CH_3)$_2$] <u>125</u>. Elution with diethyl ether gave complex <u>125</u> (60%, diastereoisomeric purity >100:1) (Found: C, 70.7; H, 6.2; P, 6.2. $C_{30}H_{31}FeO_2P$ requires C, 70.6; H, 6.1; P, 6.1%); $\nu_{max.}$ 1900 vs (C≡O), 1612 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 2.80 (1H, dq, $J_{1,2}$ 7.2 Hz, 2.8 Hz, COCH), 1.41 (1H, dseptets, $J_{1,2}$ 6.8 Hz, 2.8 Hz, C<u>H</u>(CH_3)$_2$), 0.91 (3H, d, $J_{1,2}$ 7.3 Hz, COCHC<u>H</u>$_3$), 0.53 (3H, d, $J_{1,2}$ 6.9 Hz, CH_3), 0.33 (3H, d, $J_{1,2}$ 6.8 Hz, CH_3); ^{13}C {^1H} n.m.r. δ221.2 (d, J_{PC} 31.5 Hz, C≡O), 136.9 (d, J_{PC} 42.1 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 72.4 (s, CO<u>C</u>H), 26.4 (s, <u>C</u>H(CH_3)$_2$), 21.6 (s, CH_3), 17.1 (s, CH_3), 10.8 (s, CH_3); ^{31}P {^1H} n.m.r. δ71.7; <u>m/z</u> 510 (M^+).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(CH_3)$n-Bu] 127. Elution with diethyl ether gave complex 127 (82%, diastereoisomeric purity >100:1) (Found: C, 71.55; H, 6.9; P, 5.8. $C_{32}H_{35}FeO_2P$ requires C, 71.4; H, 6.55; P, 5.75%); $\nu_{max.}$ 1905 vs (C≡O), 1620 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.40 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 2.91, 2.34 (2H, ABX system, J_{AB} 16.6 Hz, $COCH_2$), 1.70 - 0.89 (7H, m, $CH(CH_2)_3$), 0.86 (3H, t, $J_{1,2}$ 7.0 Hz, $CH_2\underline{CH_3}$), 0.41 (3H, d, $J_{1,2}$ 6.6 Hz, $CH\underline{CH_3}$); ^{13}C {^1H} n.m.r. δ220.8 (d, J_{PC} 31.4 Hz, C≡O), 136.7 (d, J_{PC} 42.9 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.3 (s, C_5H_5), 74.1 (d, J_{PC} 4.8 Hz, $CO\underline{CH_2}$), 36.8 (s, CH_2), 29.3 (s, CH), 29.3 (s, CH_2), 23.0 (s, CH_2), 19.7 (s, CH_3), 14.1 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.4; m/z 538 (M^+).

(RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(CH_3)$n-Bu] 128. Elution with petroleum ether - diethyl ether (1:1) gave complex 128 (93%, diastereoisomeric purity >100:1:1:1) (Found: C, 72.0; H, 6.8; P, 5.5. $C_{33}H_{37}FeO_2P$ requires C, 71.7; H, 6.75; P, 5.6%); $\nu_{max.}$ 1908 vs (C≡O), 1598 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.42 (5H, d, J_{PH} 1.4 Hz, C_5H_5), 2.77 (1H, dq, $J_{1,2}$ 7.3 Hz, 3.0 Hz, COCH), 1.26 - 0.61 (7H, m, $CH(CH_2)_3$), 0.97 (3H, d, $J_{1,2}$ 7.4 Hz, $COCH\underline{CH_3}$ major diastereoisomer), 0.82 (3H, t, $J_{1,2}$ 6.9 Hz, $CH_2\underline{CH_3}$), 0.47 (3H, d, $J_{1,2}$ 6.8 Hz, $CH\underline{CH_3}$), 0.23 (3H, d, $J_{1,2}$ 6.9 Hz, $COCH\underline{CH_3}$ minor diastereoisomer); ^{13}C {^1H} n.m.r. δ221.2 (d, J_{PC} 31.4 Hz, C≡O), 136.9 (d, J_{PC} 42.3 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 72.7 (d, J_{PC} 4.4 Hz, $CO\underline{CH}$), 32.4 (s, CH), 31.3 (s, CH_2), 30.0 (s, CH_2), 23.1 (s, CH_2), 18.2 (s, CH_3), 14.3 (s, CH_3), 11.8 (s, CH_3); ^{31}P {^1H} n.m.r. δ71.8; m/z 552 (M^+).

Preparation of erythro-2,3-dimethylheptanoic acid 129

The general decomplexation procedure described above (p.165) was followed.

Elution with diethyl ether and removal of solvent gave erythro-2,3-dimethylheptanoic acid 129 as a colourless oil (27%, diastereoisomeric purity >100:1); $\nu_{max.}$ ($CHCl_3$) 3500 br (O-H), 1700 vs cm^{-1} (C=O); ^1H n.m.r. δ2.35 (1H, quintet, $J_{1,2}$ 6.7 Hz, C<u>H</u>CO_2H), 1.75 (1H, m, C<u>H</u>$(CH_3)CH_2$), 1.47 - 0.82 (6H, m, $(CH_2)_3$), 1.11 (3H, d, $J_{1,2}$ 7.1 Hz, CH(C<u>H</u>$_3$)CO_2H), 0.92 (3H, d, $J_{1,2}$ 6.8 Hz, CH(C<u>H</u>$_3$)CH_2), 0.87 (3H, t, $J_{1,2}$ 6.9 Hz, CH_2C<u>H</u>$_3$); ^{13}C {^1H} n.m.r. δ181.6 (CO_2H), 44.5 (<u>C</u>HCO_2H), 35.8 (CH), 32.9 (CH_2), 29.2 (CH_2), 22.8 (CH_2), 17.1 (CH_3), 14.0 (CH_3), 13.6 (CH_3); <u>m/z</u> (CI/NH_3) 176 (M^+ + 18). The ^1H n.m.r. spectrum of 129 was identical to that of an authentic sample.[140]

<u>Preparation of (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(CH_3)n-Bu] 128 from (RR,SS)- and (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH_3$], 47 and 48</u>

n-Butyllithium (0.5 ml, 0.80 mmol) was added to (RR,SS)-[(η^5-C_5H_5)-Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH_3$] 47 (150 mg, 0.29 mmol, 7:1 diastereoisomeric mixture) in THF (20 ml) at -78°C to give a dark red solution. After stirring (-78°C; 2.5 h), methyl iodide (0.5 ml, 8.03 mmol) was added and the mixture stirred for a further 3 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 20 ml) and filtered through alumina (grade V). Removal of solvent gave (RSS,SRR)-128 as an orange powder (144 mg, 89%, diastereoisomeric purity >100:1:1:1). The ^1H n.m.r. spectrum was identical to that of (RSS,SRR)-128 prepared previously (p.167).

Similarly, treatment of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)$-CH_3] 48 (190 mg, 0.37 mmol, 7:1 diastereoisomeric mixture) with n-butyllithium (0.6 ml, 0.96 mmol) and methyl iodide (0.5 ml, 8.03 mmol) gave (RSS,SRR)-128 (158 mg, 77%, diastereoisomeric purity >100:1:1:1).

Preparation of erythro-N-benzyl-2,3-dimethylheptanamide 130

Bromine (0.04 ml, 0.78 mmol) in dichloromethane (2 ml) was added dropwise to a solution of (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH-(CH_3)n-Bu] 128 (220 mg, 0.40 mmol) in dichloromethane (15 ml) at -40°C to give a dark brown solution. After stirring (-40°C; 1 h), benzylamine (0.13 ml, 1.2 mmol) was added and the mixture warmed to room temperature. The solution was concentrated and chromatographed on silica. Elution with petroleum ether - diethyl ether (2:1) and removal of solvent gave [(η^5-C_5H_5)-Fe(CO)(PPh_3)Br] 9 as a green solid, identified by comparison of its infrared spectrum [$\nu_{max.}$ 1960 vs cm^{-1} (C≡O)] with that of an authentic sample. Elution with petroleum ether - diethyl ether (1:2) and removal of solvent gave erythro-N-benzyl-2,3-dimethylheptanamide 130 as white crystals (73 mg, 74%, diastereoisomeric purity >100:1) (Found: C, 77.5; H, 10.4; N, 5.6. $C_{16}H_{25}NO$ requires C, 77.7; H, 10.2; N, 5.7%); $\nu_{max.}$ ($CHCl_3$) 3450 m (N-H), 1660 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.4 - 7.3 (5H, m, Ph), 5.72 (1H, br, NH), 4.45 (2H, m, CH_2Ph), 2.02 (1H, quintet $J_{1,2}$ 7.1 Hz, COCH), 1.70 - 1.00 (7H, m, $CH(CH_2)_3$), 1.14 (3H, d, $J_{1,2}$ 7.0 Hz, $CHCH_3$), 0.91 (3H, d, $J_{1,2}$ 6.7 Hz, $CHCH_3$), 0.89 (3H, t, $J_{1,2}$ 7.0. Hz, CH_2CH_3); ^{13}C {^{1}H} n.m.r. (C_6D_6) δ175.1 (C≡O), 139.9 (Ph C_{ipso}), 46.9 (COCH), 43.3 ($PhCH_2$), 36.4 ($CHCH_2$), 33.3 (CH_2), 29.4 (CH_2), 23.3 (CH_2), 17.7 (CH_3), 15.2 (CH_3), 14.3 (CH_3); m/z (ACE/NH_3) 247 (M^+), 91 (M^+-156).

Preparation of (SS)- and (SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)CH_3$] 47 and 48 from (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14

n-Butyllithium (2.1 ml, 3.1 mmol) was added to (S)-(+)-14 [58] (1.0 g, 2.2 mmol) in THF (30 ml) at -78°C and the resulting dark red mixture stirred (-78°C; 1 h). A solution of acetaldehyde (0.4 ml, 7.2 mmol) in THF (2 ml) was added dropwise. After further stirring (-78°C; 2 h), methanol (0.5 ml) was added and the solution warmed to room temperature. Removal of solvents, extraction with dichloromethane (3 x 20 ml) and

filtration through alumina (grade V) gave an orange solution which was concentrated and chromatographed on alumina (grade I). Elution with dichloromethane - ethyl acetate (1:1) and removal of solvent gave the starting complex (S)-(+)-14. Elution with dichloromethane - methanol (10:1) and removal of solvent gave (SS)- and (SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH_2CH(OH)CH_3$] as a 1.4:1 diastereoisomeric mixture (1.04 g, 95%).[36] Sodium hydride (200 mg, 8.3 mmol) and THF (30 ml) were added to this mixture which was stirred (20°C; 0.5 h). Addition of methyl iodide (1.1 ml, 16.9 mmol), further stirring (20°C; 40 h) and removal of solvents gave an orange oil which was extracted with dichloromethane (3 x 30 ml) and filtered through alumina (grade V). Concentration and chromatography on alumina (grade I) gave a single yellow band eluted with dichloromethane - ethyl acetate (4:1) identified by ^{1}H n.m.r. spectroscopy as a 1.4:1 mixture of (SS)-47 and (SR)-48 (860 mg, 80%).

Preparation of (SRR)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(CH_3)n-Bu] 128

(SRR)-(+)-128 was prepared from (SS)- and (SR)-[(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_2CH(OCH_3)CH_3$], 47 and 48 using an identical procedure to that described above (p.168) for the preparation of (RSS,SRR)-128 from (RR,SS)-47 and (RS,SR)-48. Thus, the 1.4:1 mixture of (SS)-47 and (SR)-48 (356 mg, 0.70 mmol), upon treatment with n-butyllithium (1.0 ml, 1.6 mmol) and methyl iodide (0.4 ml, 6.4 mmol), gave (SRR)-(+)-[η^5-C_5H_5)Fe(CO)-(PPh_3)COCH(CH_3)CH(CH_3)n-Bu] 128 (317 mg, 81%, diastereoisomeric purity >100:1:1:1); $[\alpha]_D^{24}$ +228.0° (c 0.29, C_6H_6).

Preparation of (2R),(3R)-(-)-N-benzyl-2,3-dimethylheptanamide 130

Using an identical procedure to that described above (p.169) for the preparation of (±)-130, (SRR)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH-(CH_3)n-Bu] 128 (317 mg, 0.57 mmol) was decomplexed with bromine (0.04 ml, 0.78 mmol) in the presence of benzylamine (0.13 ml, 1.2 mmol). The crude

reaction mixture was chromatographed on silica. Elution with petroleum ether - diethyl ether (2:1) and crystallisation (petroleum ether - diethyl ether) gave $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)Br]$ 9; $[\alpha]_D^{20}$ -48.8° (c 0.04, C_6H_6). Elution with petroleum ether - diethyl ether (1:2) and removal of solvent gave (2R),(3R)-(-)-N-benzyl-2,3-dimethylheptanamide 130 (114 mg, 81%, diastereoisomeric purity >100:1); $[\alpha]_D^{24}$ -5.3° (c 1.23, C_6H_6).

Preparation of $(RR,SS)\text{-}[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH(CH_3)CH{=}CH_2]$ 131

t-Butyllithium (0.6 ml, 2.36 M soln. in pentane, 1.45 mmol) was added to vinyl bromide (0.05 ml, 0.74 mmol) in THF (3 ml) at -78°C. Stirring (-78°C; 1 h) gave a pale yellow solution of vinyllithium.[239] This was added to a 1:1 mixture of (RR,SS)-47 and (RS,SR)-48 (142 mg, 0.27 mmol) in THF (10 ml) at -78°C to give a dark red solution. After stirring (-78°C; 3.5 h), methanol (0.4 ml) was added and the solution warmed to room temperature. Removal of solvent, extraction with dichloromethane (2 x 15 ml) and filtration through alumina (grade V) gave an orange solution which was chromatographed on alumina (grade I). Elution with diethyl ether - dichloromethane (2:1) and removal of solvent gave $(RR,SS)\text{-}[(\eta^5\text{-}C_5H_5)\text{-}Fe(CO)(PPh_3)COCH_2CH(CH_3)CH{=}CH_2]$ 131 as orange microcrystals (59 mg, 43%, diastereoisomeric purity 50:1); $\nu_{max.}$ 2015 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.76 - 5.64 (1H, m, $CH{=}CH_2$), 4.90 -4.80 (2H, m, $CH{=}CH_2$), 4.40 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.01, 2.48 (2H, ABX system, J_{AB} 16.5 Hz, $COCH_2$), 2.38 (1H, m, $CHCH_3$), 0.53 (3H, d, $J_{1,2}$ 6.6 Hz, CH_3); $^{13}C\ \{^1H\}$ n.m.r. δ144.8 (s, $CH{=}CH_2$), 136.6 (d, J_{PC} 42.8 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 111.3 (s, $CH{=}CH_2$), 85.3 (s, C_5H_5), 72.7 (s, $COCH_2$), 33.5 (s, $CHCH_3$), 19.2 (s, CH_3); $^{31}P\ \{^1H\}$ n.m.r. δ72.3; m/z 508 (M^+).

Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH(OCH_3)_2]$ 134 [39]

$[(\eta^5\text{-}C_5H_5)Fe(CO)_2]_2$ 6 (4 g, 11.3 mmol) in THF (80 ml) was stirred over 2% sodium amalgam (50 g) at 20°C for 16 h to give a dark orange solution of $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]$ Na 7. The solution was decanted and cooled to -78°C. Bromoacetaldehyde dimethyl acetal (5.3 ml, 45.2 mmol) was added and the solution stirred at -78°C (1 h) and then at 0°C (4 h). The solvent was removed and the dark red residue extracted with petroleum ether (30-40°C, 4 x 25 ml). The solution was concentrated (ca. 50 ml), filtered through sand † and cooled (-30°C) to give $[(\eta^5\text{-}C_5H_5)Fe(CO)_2CH_2CH(OCH_3)_2]$ 132 as orange blocks (3.39 g, 56%); $\nu_{max.}$ 2015 vs and 1950 vs cm^{-1} (C≡O) [lit.,[141] (KBr) 1998 and 1944 cm^{-1}]; ^1H n.m.r. (C_6D_6) δ4.55 (1H, t, $J_{1,2}$ 5.5 Hz, $CH_2\underline{CH}$), 4.13 (5H, s, C_5H_5), 3.34 (6H, s, CH_3), 1.66 (2H, d, $J_{1,2}$ 5.5 Hz, $\underline{CH_2}CH$) [lit.,[141] (CS_2) δ4.7 (s), 4.24 (t), 3.15 (s), 1.40 (d)].

Complex 132 (3.39 g, 12.7 mmol) and triphenylphosphine (5.0 g, 19.1 mmol) were dissolved in acetonitrile (40 ml) and the solution heated under reflux, in the absence of light, for 5 d. The solvent was removed and the dark red oil extracted with dichloromethane (3 x 20 ml) and filtered through alumina (grade V). The filtrate was concentrated and chromatographed on alumina (grade I). Elution with diethyl ether - ethyl acetate (1:1) and concentration of the eluate gave $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH(OCH_3)_2]$ 134 as orange needles (3.9 g, 58%); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.49 (1H, dd, $J_{1,2}$ 6.6 Hz, 4.0 Hz, $C\underline{H}(OCH_3)_2$), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.33, 2.66 (2H, ABX system, J_{AB} 15.8 Hz, $COCH_2$), 3.29 (3H, s, OCH_3), 3.13 (3H, s, OCH_3) [lit.,[39] δ7.7 - 6.9 (m), 4.91 (dd), 4.30 (d), 3.75 (dd),

† Filtration through alumina (grade V) gave $[(\eta^5\text{-}C_5H_5)Fe(CO)_2CH_2CHO]$ 133; $\nu_{max.}$ 2000 vs and 1950 vs (C≡O), 1630 s cm^{-1} (C=O) [lit.,[141] 2030, 1983 and 1655 cm^{-1}]; ^1H n.m.r. (C_6D_6) δ9.53 (1H, t, $J_{1,2}$ 5.0 Hz, CHO), 4.01 (5H, s, C_5H_5), 1.62 (2H, d, $J_{1,2}$ 5.0 Hz, CH_2) [lit.,[141] (CS_2) δ9.3 (t), 4.8 (s), 1.6 (d)].

3.25 (s), 3.12 - 3.06 (m)]; ^{13}C {^1H} n.m.r. δ220.2 (d, J_{PC} 31.0 Hz, C≡O), 136.4 (d, J_{PC} 43.2 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 10.2 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.9 Hz, Ph C_{meta}), 101.4 (s, $\underline{C}H(OCH_3)_2$), 85.3 (s, C_5H_5), 67.6 (d, J_{PC} 4.0 Hz, $CO\underline{C}H_2$), 54.1 (s, OCH_3), 52.5 (s, OCH_3); ^{31}P {^1H} n.m.r. δ72.5.

Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(CH_3)_2$] 125 from [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)_2$] 134

Methyllithium (1.3 ml, 2.02 mmol) was added to complex 134 (255 mg, 0.48 mmol) in THF (20 ml) at -78°C. The mixture was warmed to -40°C and stirred (2 h) to give a dark red solution. After cooling (-78°C), methyl iodide (0.4 ml, 6.42 mmol) was added and the solution stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 20 ml) and filtered through alumina (grade V). Chromatography on alumina (grade I) gave, upon elution with diethyl ether and removal of solvent,(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(CH_3)_2$] 125 as orange microcrystals (124 mg, 50%, diastereoisomeric purity >100:1). The ^1H n.m.r. spectrum of the product was identical to (RS,SR)-125 prepared from complex 33 as described above (p.166).

Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(Et)n$-Bu] 136 and (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(Et)n$-Bu] 137 from E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHEt] 35

In a typical procedure, n-butyllithium (1.2 equivalents) was added to E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHEt] 35 (500 mg, 1.01 mmol) in THF (25 ml) at -78°C to give a dark red solution. After stirring (-78°C; 2 h), methanol (excess) or methyl iodide (2 equivalents) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature

and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 10 ml) and filtered through alumina (grade V). The product complexes were purified by chromatography on alumina (grade I), analysed by ^{1}H n.m.r. spectroscopy in order to determine diastereoselectivities and obtained as orange needles from hexane (-30°C).

(RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(Et)$n-Bu] 136. Elution with diethyl ether gave complex 136 (79%, diastereoisomeric purity 40:1) (Found: C, 71.9; H, 7.0; P, 5.8. $C_{33}H_{37}FeO_2P$ requires C, 71.7; H, 6.75; P, 5.6%); $\nu_{max.}$ 1905 vs (C≡O), 1610 s and 1582 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.40 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 2.92, 2.42 (2H, ABX system, J_{AB} 16.7 Hz, $COCH_2$), 1.56 - 0.83 (9H, m, $C\underline{H}_2C\underline{H}$-$(C\underline{H}_2)_3$), 0.87 (3H, t, $J_{1,2}$ 7.0 Hz, $(CH_2)_3C\underline{H}_3$), 0.61 (3H, t, $J_{1,2}$ 7.3 Hz, $CH_2C\underline{H}_3$); ^{13}C {^{1}H} n.m.r. δ220.6 (d, J_{PC} 31.4 Hz, C≡O), 136.6 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 10.5 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 71.1 (d, J_{PC} 5.4 Hz, $CO\underline{C}H_2$), 35.2 (s, CH), 33.1 (s, CH_2), 28.8 (s, CH_2), 25.7 (s, CH_2), 23.2 (s, CH_2), 14.1 (s, CH_3), 10.9, (s, CH_3); ^{31}P {^{1}H} n.m.r. δ72.5; m/z 552 (M^+), 524 (M^+-28).

(RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(Et)$n-Bu] 137. Elution with diethyl ether gave complex 137 (63%, diastereoisomeric purity >100:1:1:1) (Found: C, 72.1; H, 7.2; P, 5.5. $C_{34}H_{39}FeO_2P$ requires C, 72.1; H, 6.9; P, 5.5%); $\nu_{max.}$ 1910 vs (C≡O), 1605 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.42 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.08 (1H, dq, $J_{1,2}$ 7.2 Hz, 2.7 Hz, COCH), 1.27 - 0.68 (15H, m, $CH_3CH_2CH(CH_2)_3$-CH_3), 0.91 (3H, d, $J_{1,2}$ 7.3 Hz, $COCH(C\underline{H}_3)$); ^{13}C {^{1}H} n.m.r. δ221.3 (d, J_{PC} 31.5 Hz, C≡O), 137.1 (d, J_{PC} 42.1 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.2 Hz, Ph C_{meta}), 85.0 (s, C_5H_5), 69.0 (d, J_{PC} 4.6 Hz, $CO\underline{C}H$), 38.1 (s, CH), 29.9 (s, CH_2), 29.3 (s, CH_2), 24.5 (s, CH_2), 23.3 (s, CH_2), 14.3 (s, CH_3), 12.4 (s, CH_3), 11.9 (s, CH_3); ^{31}P {^{1}H} n.m.r. δ72.6; m/z 566 (M^+).

Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH$(Et)n-Bu] 136 and (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH$(Et)n-Bu] 137 from [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)$Et] 50

An identical method was followed to that described for the preparation of (RS,SR)-136 and (RSS,SRR)-137 from complex 35 (p.173). Treatment of [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OCH_3)$Et] 50 (145 mg, 0.28 mmol) with n-butyllithium (0.4 ml, 0.64 mmol) and methanol (0.2 ml) gave (RS,SR)-136 (120 mg, 79%, diastereoisomeric purity >40:1). Similarly, treatment of complex 50 (1.94 g, 3.69 mmol) with n-butyllithium (6 ml, 9.6 mmol) and methyl iodide (1 ml, 16.1 mmol) gave (RSS,SRR)-137 (1.63 g, 78%, diastereoisomeric purity >100:1:1:1).

Preparation of 3-ethylheptanoic and 3-ethyl-2-methylheptanoic acids

The general decomplexation procedure described above (p.165) was followed.

3-Ethylheptanoic acid.[95] Elution with diethyl ether gave 3-ethylheptanoic acid as a colourless oil (77%); $\nu_{max.}$ ($CHCl_3$) 3500 br (O-H), 1700 vs cm^{-1} (C=O); ^1H n.m.r. δ2.28 (2H, d, $J_{1,2}$ 6.9 Hz, $C\underline{H}_2CO_2H$), 1.81 (1H, m, CH), 1.43 - 1.25 (8H, m, $(C\underline{H}_2)_3CH_3$ and $C\underline{H}_2CH_3$), 0.90 (3H, t, $J_{1,2}$ 7.0 Hz, CH_3), 0.89 (3H, t, $J_{1,2}$ 7.4 Hz, CH_3); ^{13}C {^1H} n.m.r. δ180.3 (CO_2H), 38.6 ($\underline{C}H_2CO_2H$), 36.2 (CH), 33.0 (CH_2), 28.7 (CH_2), 26.2 (CH_2), 22.9 (CH_2), 14.0 (CH_3), 10.7 (CH_3); m/z (CI/NH_3) 176 (M^+ + 18).

3-Ethyl-2-methylheptanoic acid. Elution with diethyl ether gave 3-ethyl-2-methylheptanoic acid as a colourless oil (28%, diastereoisomeric purity >100:1); $\nu_{max.}$ ($CHCl_3$) 3500 br (O-H), 1700 vs cm^{-1} (C=O); ^1H n.m.r. δ2.56 (1H, m, $C\underline{H}CO_2H$), 1.67 (1H, m, $C\underline{H}(CH_2)_2$), 1.46 - 1.22 (8H, m, $(C\underline{H}_2)_3CH_3$ and $C\underline{H}_2CH_3$), 1.09 (3H, d, $J_{1,2}$ 7.0 Hz, $CHC\underline{H}_3$), 0.90 (3H, t, $J_{1,2}$ 7.4 Hz, CH_3), 0.89 (3H, t, $J_{1,2}$ 6.7 Hz, CH_3); ^{13}C {^1H} n.m.r. δ183.2 (CO_2H), 41.9 ($\underline{C}HCO_2H$), 41.4 ($\underline{C}H(CH_2)_2$), 29.5 (CH_2), 29.1 (CH_2), 24.0 (CH_2), 23.0 (CH_2), 14.0 (CH_3), 12.2 (CH_3), 11.5 (CH_3); m/z (CI/NH_3) 190 (M^+ + 18).

Preparation of (RSR,SRS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(CH_3)n-Bu] 140

Methyllithium (3.0 ml, 1.55M soln. in diethyl ether, 4.7 mmol) was added to E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHn-Bu] 138 [240] (1.25 g, 2.40 mmol) in THF (30 ml) at -78°C to give a dark purple solution. The reaction mixture was stirred at -78°C for 1 h and then at -40°C for 0.5 h. After cooling to -78°C, methyl iodide (0.5 ml, 8.0 mmol) was added and the solution stirred (-78°C; 3 h). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 15 ml) and filtered through alumina (grade V). Chromatography on alumina (grade I), with diethyl ether as the eluant, gave a single orange fraction. Concentration (ca. 5 ml) and cooling (-30°C) gave (RSR,SRS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(CH_3)n-Bu] 140 as orange needles (880 mg, 70%, diastereoisomeric purity >100:1:1:1) (Found: C, 71.45; H, 6.5; P, 5.6. $C_{33}H_{37}FeO_2P$ requires C, 71.7; H, 6.75; P, 5.6%); $\nu_{max.}$ 1898 vs (C≡O), 1610 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 2.94 (1H, dq, $J_{1,2}$ 7.2 Hz, 2.2 Hz, COCH), 1.38 - 0.91 (7H, m, $CH(CH_2)_3$), 0.87 (3H, t, $J_{1,2}$ 7.0 Hz, CH_2CH_3), 0.87 (3H, d, $J_{1,2}$ 7.2 Hz, $COCHCH_3$), 0.23 (3H, d, $J_{1,2}$ 6.8 Hz, $CHCH_3$); ^{13}C {^1H} n.m.r. δ221.2 (d, J_{PC} 32.4 Hz, C≡O), 136.9 (d, J_{PC} 41.6 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 10.0 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.4 Hz, Ph C_{meta}), 85.0 (s, C_5H_5), 71.7 (d, J_{PC} 4.7 Hz, COCH), 35.8 (s, CH_2), 30.7 (s, CH), 29.8 (s, CH_2), 23.0 (s, CH_2), 14.2 (s, CH_3), 14.2 (s, CH_3), 10.8 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.0; m/z 552 (M^+).

Preparation of threo-2,3-dimethylheptanoic acid 141

The general decomplexation procedure described above (p.165) was followed.

Elution with diethyl ether and removal of solvent gave threo-2,3-dimethylheptanoic acid 141 as a colourless oil (29%, diastereoisomeric purity >100:1); $\nu_{max.}$ ($CHCl_3$) 3520 br (O-H), 1700 vs cm^{-1} (C=O); ^1H

n.m.r. δ2.43 (1H, m, C<u>H</u>CO_2H), 1.89 (1H, m, C<u>H</u>CH_2), 1.35 - 1.17 (6H, m, $(CH_2)_3$), 1.09 (3H, d, $J_{1,2}$ 7.0 Hz, $CH(C\underline{H}_3)CO_2H$), 0.90 (3H, d, $J_{1,2}$ 6.8 Hz, $CH(C\underline{H}_3)CH_2$), 0.90 (3H, t, $J_{1,2}$ 6.6 Hz, $CH_2C\underline{H}_3$); ^{13}C {^1H} n.m.r. δ182.8 (CO_2H), 43.9 (<u>C</u>HCO_2H), 35.1 (CH), 34.4 (CH_2), 29.4 (CH_2), 22.7 (CH_2), 15.6 (CH_3), 14.0 (CH_3), 11.7 (CH_3); <u>m/z</u> (CI/NH_3) 176 (M^+ + 18). The ^1H n.m.r. spectrum of <u>141</u> was identical to that of an authentic sample.[140]

<u>Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(n-Bu)$_2$] 143</u>

<u>n</u>-Butyllithium (2.5 ml, 3.75 mmol) was added to [(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_2CH(OCH_3)_2$] <u>134</u> (483 mg, 0.92 mmol) in THF (20 ml) at -78°C to give a dark red solution. After stirring (-78°C; 2 h), methyl iodide (0.4 ml, 6.42 mmol) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 20 ml) and filtered through alumina (grade V). Chromatography on alumina (grade I), with diethyl ether as eluant, gave a single orange fraction. Concentration (<u>ca</u>. 10 ml) and cooling (-30°C) gave (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)-$COCH(CH_3)CH(\underline{n}\text{-}Bu)_2$] <u>143</u> as an orange powder (360 mg, 66%, diastereoisomeric purity >100:1) (Found: C, 72.5; H, 7.2; P, 5.2. $C_{36}H_{43}FeO_2P$ requires C, 72.4; H, 7.1; P, 5.3%); $\nu_{max.}$ 1895 vs (C≡O), 1610 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 -7.3 (15H, m, Ph), 4.41 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.01 (1H, dq, $J_{1,2}$ 7.2 Hz, 2.6 Hz, C<u>H</u>CH_3), 1.36 - 0.62 (13H, m, $(CH_2)_3CH$-$(CH_2)_3$), 0.92 (3H, d, $J_{1,2}$ 7.2 Hz, $CHC\underline{H}_3$), 0.89 (3H, t, $J_{1,2}$ 7.1 Hz, $CH_2C\underline{H}_3$), 0.82 (3H, t, $J_{1,2}$ 6.7 Hz, $CH_2C\underline{H}_3$); ^{13}C {^1H} n.m.r. δ221.4 (d, J_{PC} 33.0 Hz, C≡O), 137.1 (d, J_{PC} 41.4 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.2 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 85.1 (s, C_5H_5), 69.5 (d, J_{PC} 3.8 Hz, CO<u>C</u>H), 36.6 (s, CH), 31.9 (s, CH_2), 30.2 (s, CH_2), 29.9 (s, CH_2), 29.6 (s, CH_2), 23.3 (s, CH_2), 23.3 (s, CH_2), 14.2 (s, CH_3), 14.2 (s, CH_3), 11.9 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.7; <u>m/z</u> 594 (M^+), 566 (M^+-28).

General procedure for the reaction of E- and Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)-COCH=CHCH=CHR] (R=H, CH_3) with n-butyllithium and electrophiles. Preparation of complexes 144 - 149, 151 and 152

n-Butyllithium (1.2 equivalents) was added to the complex (typically 200 mg) in THF (20 ml) at -78°C to give a dark red solution. After stirring (-78°C; 2 h), methanol (excess) or methyl iodide (2 equivalents) was added and the mixture stirred for a further 2 h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (3 x 15 ml) and filtered through alumina (grade V). The orange filtrate was concentrated and chromatographed on alumina (grade I).

The product complexes were eluted with diethyl ether, analysed by ^1H n.m.r. spectroscopy in order to determine diastereoselectivities and obtained as orange needles or as orange blocks from hexane (-30°C).

(RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH$(n-Bu)$CH=CH_2$] 144. (82% from complex 37, diastereoisomeric purity >100:1) (Found: C, 72.3; H, 6.7; P, 5.6. $C_{33}H_{35}FeO_2P$ requires C, 72.0; H, 6.4; P, 5.6%); $\nu_{max.}$ 1905 vs (C≡O), 1598 s and 1580 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.36 (1H, ddd, J_{trans} 18.7 Hz, J_{cis} 10.6 Hz, $J_{1,2}$ 8.2 Hz, CH-CH=), 4.76 (2H, m, $CH=CH_2$), 4.41 (5H, d, J_{PH} 0.8 Hz, C_5H_5), 2.98, 2.43 (2H, ABX system, J_{AB} 16.1 Hz, $COCH_2$), 2.31 (1H, m, CH-CH=), 1.28 - 1.08 (6H, m, $(CH_2)_3$), 0.86 (3H, t, $J_{1,2}$ 6.8 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.5 (d, J_{PC} 31.3 Hz, C≡O), 143.2 (s, $CH=CH_2$), 136.5 (d, J_{PC} 42.7 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 10.4 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.6 Hz, Ph C_{meta}), 112.8 (s, $CH=CH_2$), 85.4 (s, C_5H_5), 71.2 (d, J_{PC} 5.3 Hz, $COCH_2$), 39.6 (s, CH), 34.2 (s, CH_2), 29.4 (s, CH_2), 22.9 (s, CH_2), 14.1 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.2; m/z 550 (M^+).

(RR,SS)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH$(n-Bu)CH=$CHCH_3$] 145. (77% from complex 39, diastereoisomeric purity >100:1) (Found: C, 72.4; H, 6.7; P, 5.6. $C_{34}H_{37}FeO_2P$ requires C, 72.3; H, 6.6; P, 5.5%); $\nu_{max.}$ 1900 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.16 (1H, dq, J_{trans} 15.1 Hz, $J_{1,2}$ 6.4 Hz, CH=CHCH$_3$), 4.97 (1H, ddq, J_{trans} 15.1 Hz, $J_{1,2}$ 8.1 Hz, $J_{1,3}$ 1.4 Hz, CH=CHCH$_3$), 4.40 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 2.92, 2.37 (2H, ABX system, J_{AB} 16.0 Hz, $COCH_2$), 2.26 (1H, m, CHCH=CH), 1.57 (3H, dd, $J_{1,2}$ 6.3 Hz, $J_{1,3}$ 1.2 Hz, CH=CHCH$_3$), 1.30 - 1.00 (6H, m, $(CH_2)_3$), 0.86 (3H, t, $J_{1,2}$ 7.0 Hz, CH_2CH_3); m/z 564 (M^+), 536 (M^+-28).

(RSR,SRS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)$CH(n-Bu)$CH=CH_2$] 146. (83% from complex 37, diastereoisomeric purity >100:1:1:1) (Found: C, 72.4; H, 6.8; P, 5.5. $C_{34}H_{37}FeO_2P$ requires C, 72.3; H, 6.6; P, 5.5%); $\nu_{max.}$ 1895 vs (C≡O), 1610 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.37 (1H, ddd, J_{trans} 19.0 Hz, J_{cis} 10.3 Hz, $J_{1,2}$ 8.7 Hz, CH-CH=CH_2), 4.81 (2H, m, CH=CH_2), 4.42 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 2.87 (1H, dq, $J_{1,2}$ 7.4 Hz, 2.5 Hz, COCH), 1.80 (1H, m, CH-CH=CH_2), 1.37 - 0.80 (6H, m, $(CH_2)_3$), 1.02 (3H, d, $J_{1,2}$ 7.4 Hz, $CHCH_3$), 0.80 (3H, t, $J_{1,2}$ 7.0 Hz, CH_3); ^{13}C {^1H} n.m.r. δ221.1 (d, J_{PC} 31.4 Hz, C≡O), 142.3 (s, CH=CH_2), 136.9 (d, J_{PC} 42.3 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 10.0 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.9 Hz, Ph C_{meta}), 113.6 (s, CH=CH_2), 85.2 (s, C_5H_5), 70.4 (d, J_{PC} 5.3 Hz, COCH), 43.6 (s, CH), 30.2 (s, CH_2), 28.2 (s, CH_2), 22.9 (s, CH_2), 14.2 (s, CH_3), 12.4 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.0; m/z 564 (M^+), 536 (M^+-28).

(RSR,SRS)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)$CH(n-Bu)$CHCHCH_3$] 147. (87% from complex 39, diastereoisomeric purity 4:1:0:0) (Found: C, 73.0; H, 6.7; P, 5.3. $C_{35}H_{39}FeO_2P$ requires C, 72.7; H, 6.8; P, 5.35%); $\nu_{max.}$ 1910 vs (C≡O), 1605 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.23

(1H, dq, J_{trans} 14.7 Hz, $J_{1,2}$ 6.4 Hz, CH=C<u>H</u>CH$_3$), 5.04 (1H, dd, J_{trans} 14.7 Hz, $J_{1,2}$ 8.2 Hz, C<u>H</u>=CHCH$_3$), 4.43 (5H, d, J_{PH} 1.0 Hz, C_5H_5 minor diastereoisomer), 4.42 (5H, d, J_{PH} 1.2 Hz, C_5H_5 major diastereoisomer), 2.92 (1H, m, COCH), 1.77 (1H, m, C<u>H</u>CH=CH), 1.62 (3H, dd, $J_{1,2}$ 6.3 Hz, $J_{1,3}$ 1.3 Hz, CH=CHC<u>H</u>$_3$), 1.35 - 0.96 (6H, m, $(CH_2)_3$), 1.00 (3H, d, $J_{1,2}$ 7.3 Hz, COCHC<u>H</u>$_3$ major diastereoisomer), 0.81 (3H, t, $J_{1,2}$ 7.0 Hz, CH$_2$C<u>H</u>$_3$), 0.00 (3H, d, $J_{1,2}$ 6.4 Hz, COCHC<u>H</u>$_3$ minor diastereoisomer); <u>m/z</u> 578 (M^+).

(RS,SR)-E-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH$_2$CH(<u>n</u>-Bu)CH=CHCH$_3$] <u>148</u>. (89% from complex <u>40</u>, diastereoisomeric purity >100:1) (Found: C, 72.65; H, 6.6. $C_{34}H_{37}FeO_2P$ requires C, 72.3; H, 6.6%); $\nu_{max.}$ 1900 vs (C≡O), 1620 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.5 - 7.3 (15H, m, Ph), 5.31 (1H, dq, J_{trans} 15.3 Hz, $J_{1,2}$ 5.9 Hz, CH=C<u>H</u>CH$_3$), 5.14 (1H, ddq, J_{trans} 15.3 Hz, $J_{1,2}$ 8.1 Hz, $J_{1,3}$ 1.4 Hz, C<u>H</u>=CHCH$_3$), 4.39 (5H, d, J_{PH} 0.9 Hz, C_5H_5), 3.05, 2.44 (2H, ABX system, J_{AB} 16.8 Hz, COCH$_2$), 2.18 (1H, m, COCH$_2$C<u>H</u>), 1.63 (3H, dd, $J_{1,2}$ 6.2 Hz, $J_{1,3}$ 1.3 Hz, CHC<u>H</u>$_3$), 1.29 - 0.73 (6H, m, $(CH_2)_3$), 0.82 (3H, t, $J_{1,2}$ 7.0 Hz, CH$_2$C<u>H</u>$_3$); ^{13}C {^{1}H} n.m.r. δ220.7 (d, J_{PC} 31.5 Hz, C≡O), 136.6 (d, J_{PC} 44.5 Hz, Ph C_{ipso}), 136.3 (s, CH), 133.4 (d, J_{PC} 9.7 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 123.3 (s, CH), 85.4 (s, C_5H_5), 72.1 (s, CO<u>C</u>H$_2$), 38.6 (s, COCH$_2$<u>C</u>H), 34.3 (s, CH$_2$), 29.6 (s, CH$_2$), 22.8 (s, CH$_2$), 18.0 (s, CH$_3$), 14.1 (s, CH$_3$); ^{31}P {^{1}H} n.m.r. δ72.5; <u>m/z</u> 564 (M^+), 536 (M^+-28).

(RSS,SRR)-E-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH$_3$)CH(<u>n</u>-Bu)CH=CHCH$_3$] <u>149</u>. (77% from complex <u>40</u>, diastereoisomeric purity >100:1:1:1) (Found: C, 72.8; H, 7.0; P, 5.3. $C_{35}H_{39}FeO_2P$ requires C, 72.7; H, 6.8; P, 5.35%); $\nu_{max.}$ 1900 vs (C≡O), 1610 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.03 (1H, dq, J_{trans} 15.1 Hz, $J_{1,2}$ 5.0 Hz, CH=C<u>H</u>CH$_3$), 4.81 (1H, dd, J_{trans} 15.1 Hz, $J_{1,2}$ 8.6 Hz, C<u>H</u>=CHCH$_3$), 4.42 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 2.77 (1H, quintet, $J_{1,2}$ 6.1 Hz, COCH), 1.77 (1H, m, C<u>H</u>CH=CH), 1.56 (3H, dd, $J_{1,2}$ 6.2 Hz, $J_{1,3}$ 1.3 Hz, CH=CHC<u>H</u>), 1.22 - 0.53 (6H, m, $(CH_2)_3$), 1.00

(3H, d, $J_{1,2}$ 7.3 Hz, COCHC<u>H</u>$_3$), 0.82 (3H, t, $J_{1,2}$ 7.0 Hz, $CH_2C\underline{H}_3$); ^{13}C $\{^1H\}$ n.m.r. δ221.3 (d, J_{PC} 31.7 Hz, C≡O), 136.9 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.6 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 123.9 (s, CH), 85.5 (s, C_5H_5), 70.6 (d, J_{PC} 5.0 Hz, CO<u>C</u>H), 42.6 (s, CH), 32.0 (s, CH_2), 30.0 (s, CH_2), 22.7 (s, CH_2), 18.0 (s, CH_3), 14.4 (s, CH_3), 14.2 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ71.4; <u>m/z</u> 578 (M^+).

E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH$=$CHCH_2$<u>n</u>-Bu] <u>151</u>. (89% from complex <u>38</u>) (Found: C, 72.35; H, 6.4; P, 5.7. $C_{33}H_{35}FeO_2P$ requires C, 72.0; H, 6.4; P, 5.6%); $\nu_{max.}$ 1910 vs (C≡O), 1620 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.27 (2H, m, CH=CH), 4.44 (5H, d, J_{PH} 1.0 Hz, C_5H_5), 3.57 (1H, m, $COCH_2$), 3.20 (1H, m, $COCH_2$), 1.94 (2H, m, CH=CH$C\underline{H}_2$), 1.28 (6H, m, $(CH_2)_3$), 0.89 (3H, t, $J_{1,2}$ 6.8 Hz, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ220.5 (d, J_{PC} 31.5 Hz, C≡O), 136.5 (d, J_{PC} 42.7 Hz, Ph C_{ipso}), 133.3 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 132.0 (s, <u>C</u>H=CH), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.1 (s, C_5H_5), 69.3 (d, J_{PC} 5.7 Hz, CO$C\underline{H}_2$), 32.6 (s, CH_2), 31.4 (s, CH_2), 29.2 (s, CH_2), 22.5 (s, CH_2), 14.1 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ72.7; <u>m/z</u> 550 (M^+), 522 (M^+-28).

(RS,SR)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH$=$CHCH_2$<u>n</u>-Bu] <u>152</u>. (76% from complex <u>38</u>, diastereoisomeric purity >100:1) (Found: C, 72.3; H, 6.6; P, 5.4. $C_{34}H_{37}FeO_2P$ requires C, 72.3; H, 6.6; P, 5.5%); $\nu_{max.}$ 1908 vs (C≡O), 1605 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 5.19 (1H, dt, J_{trans} 15.5 Hz, $J_{1,2}$ 6.6 Hz, CH=C<u>H</u>CH_2), 4.83 (1H, dd, J_{trans} 15.5 Hz, $J_{1,2}$ 8.2 Hz, C<u>H</u>=$CHCH_2$), 4.44 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 3.66 (1H, quintet, $J_{1,2}$ 7.5 Hz, COCH), 1.85 (2H, m, CH=CH$C\underline{H}_2$), 1.31 - 1.20 (6H, m, $(CH_2)_3$), 1.02 (3H, d, $J_{1,2}$ 7.0 Hz, $CHC\underline{H}_3$ major diastereoisomer), 0.88 (3H, t, $J_{1,2}$ 6.8 Hz, $CH_2C\underline{H}_3$), 0.37 (3H, d, $J_{1,2}$ 7.0 Hz, $CHC\underline{H}_3$ minor diastereoisomer); ^{13}C $\{^1H\}$ n.m.r. δ220.7 (d, J_{PC} 31.5 Hz, C≡O), 136.7 (d, J_{PC} 42.5 Hz, Ph C_{ipso}), 133.5 (d, J_{PC} 10.3 Hz, Ph C_{ortho}), 131.4 (s,-CH=), 129.8 (s,-CH=), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.6 Hz, Ph C_{meta}), 85.0

(s, C_5H_5), 71.5 (d, J_{PC} 4.8 Hz, CO<u>C</u>H), 32.7 (s, CH_2), 31.5 (s, CH_2), 29.1 (s, CH_2), 22.5 (s, CH_2), 18.2 (s, CH_3), 14.1 (s, CH_3); $^{31}P\{^1H\}$ n.m.r. δ72.8; <u>m/z</u> 564 (M^+), 536 (M^+-28).

<u>General procedure for the preparation of β-amino acyl complexes</u>

<u>n</u>-Butyllithium (1.2 equivalents) was added to benzylamine (1.3 equivalents) in THF (20 ml) at -20°C to give an intense purple solution. The solution was stirred (-20°C; 1 h), cooled to -78°C and added dropwise to the α,β-unsaturated acyl complex (typically 250 mg) in THF (30 ml) at -78°C to give a deep red solution. After stirring (-78°C; 2 h), the electrophile (4 equivalents) was added and the mixture stirred for a further 1 h (-78°C). Warming to room temperature and removal of solvent gave an orange solid which was dissolved in dichloromethane (20 ml) and filtered through Celite.

The product complexes were purified by chromatography on alumina (grade I), analysed by ^1H n.m.r. spectroscopy in order to determine diastereoselectivities and obtained as orange needles from dichloromethane - hexane.

<u>General procedure for the oxidative decomplexation of β-amino acyl complexes to β-lactams</u>

Bromine (2 equivalents) in dichloromethane (2 ml) was added dropwise to a solution of the β-amino acyl complex (typically 500 mg) in dichloromethane (15 ml) at -78°C to give a dark brown solution. After stirring (-78°C; 1 h), triethylamine (excess) was added and the mixture warmed to room temperature. Removal of solvent (below 20°C) gave a tacky green solid. Short path distillation of this residue (100°C, 0.1 mmHg) afforded the crude β-lactam which was further purified by chromatography on silica gel.

Preparation of (RSR,SRS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(CH_3)NHCH$_2$Ph] 173

Complex 173 was prepared from complex 33 using the general procedure described above (p.182). Elution with dichloromethane - ethyl acetate - methanol (10:9:1) gave complex 173 (91%, diastereoisomeric purity >100:1:1:1) (Found: C, 71.9; H, 6.0; N, 2.4; P, 5.1. $C_{36}H_{36}FeNO_2P$ requires C, 71.9; H, 6.0; N, 2.3; P, 5.15%); $\nu_{max.}$ 3330 w (N-H), 1910 vs (C≡O), 1580 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.5 - 7.2 (20H, m, Ph), 4.44 (5H, d, J_{PH} 1.2 Hz, C_5H_5), 3.67, 3.32 (2H, AB system, J_{AB} 13.9 Hz, C$\underline{H}_2$Ph), 2.68 (1H, m, COCH), 1.72 (1H, m, C$\underline{H}$(CH_3)N), 1.12 (3H, d, $J_{1,2}$ 7.5 Hz, CH(C$\underline{H}_3$)N), 0.54 (3H, d, $J_{1,2}$ 6.4 Hz, COCH(C$\underline{H}_3$)); ^{13}C {^{1}H} n.m.r. δ220.7 (d, J_{PC} 31.5 Hz, C≡O), 141.3 (s, CH_2Ph C_{ipso}), 136.4 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.2 (d, J_{PC} 9.5 Hz, Ph C_{ortho}), 129.5 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.1 Hz, Ph C_{meta}), 126.1 (s, CH_2Ph C_{para}), 85.5 (s, C_5H_5), 71.5 (d, J_{PC} 5.2 Hz, CO$\underline{C}$H), 51.2 (s, $\underline{C}$H(CH_3)N), 51.1 (s, $\underline{C}H_2$Ph), 17.5 (s, CH(C$\underline{H}_3$)N), 10.0 (s, COCH(C$\underline{H}_3$)); ^{31}P {^{1}H} n.m.r. δ70.7; m/z 601 (M^+).

Preparation of (±)-cis-3,4-dimethyl-N-benzylazetidin-2-one 174

β-Lactam 174 was prepared from (RSR,SRS)-173 using the general procedure described above (p.182). Elution with acetone - diethyl ether (1:9) gave β-lactam 174 as a colourless oil (69%, diastereoisomeric purity >100:1); $\nu_{max.}$ (neat) 1740 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.4 - 7.2 (5H, m, Ph), 4.59, 4.04 (2H, AB system, J_{AB} 15.2 Hz, C$\underline{H}_2$Ph), 3.63 (1H, dq, $J_{1,2}$ 6.4 Hz, 5.4 Hz, C$\underline{H}$(CH_3)N), 3.22 (1H, dq, $J_{1,2}$ 7.6 Hz, 5.4 Hz, CO$\underline{C}$H(CH_3)), 1.16 (3H, d, $J_{1,2}$ 7.6 Hz, COCH(C$\underline{H}_3$)), 1.07 (3H, d, $J_{1,2}$ 6.4 Hz, CH(C$\underline{H}_3$)N) [lit.,[158] δ7.23 (5H, m, Ph), 4.52, 4.00 (2H, d, $J_{1,2}$ 15.5 Hz, C$\underline{H}_2$Ph), 3.51 (1H, m, $J_{1,2}$ 6.3 Hz, 6.0 Hz, C$\underline{H}$(CH_3)N), 3.13 (1H, m, $J_{1,2}$ 7.5 Hz, 6.0 Hz, COCH), 1.11 (3H, d, $J_{1,2}$ 7.5 Hz, CH_3), 1.01 (3H, d, $J_{1,2}$ 6.3 Hz, CH_3)]; ^{13}C {^{1}H} n.m.r. δ171.2 (C=O), 136.2 (Ph C_{ipso}), 128.7 (Ph C_{ortho}/C_{meta}), 128.2 (Ph C_{meta}/C_{ortho}), 127.6 (Ph C_{para}), 50.5 (CO$\underline{C}$H), 47.0 ($\underline{C}$H(CH_3)N), 43.9 ($\underline{C}H_2$Ph), 13.5 (COCH(C$\underline{H}_3$)), 8.8 (CH(C$\underline{H}_3$)N); m/z 189 (M^+).

Epimerisation of (±)-cis-3,4-dimethyl-N-benzylazetidin-2-one 174

The cis-β-lactam 174 (80 mg, 0.42 mmol) and potassium t-butoxide (10 mg, 0.09 mmol) in t-butanol (4 ml) were heated (50°C; 15 h). The reaction mixture was poured into water (5 ml) and extracted with diethyl ether (3 x 4 ml). The ether extracts were dried (Na_2SO_4) and filtered. The solvent was removed to give a colourless oil (75 mg, 95%) identified by ^1H n.m.r. spectroscopy as a 1:2 mixture of the cis-β-lactam 174 and its trans-epimer 175. (±)-Trans-3,4-dimethyl-N-benzylazetidin-2-one 175; ^1H n.m.r. δ7.4 - 7.2 (5H, m, Ph), 4.61, 4.07 (2H, AB system, J_{AB} 15.2 Hz, $C\underline{H}_2Ph$), 3.15 (1H, dq, $J_{1,2}$ 6.1 Hz, 2.0 Hz, $C\underline{H}CH_3$), 2.73 (1H, dq, $J_{1,2}$ 7.4 Hz, 1.5 Hz, $C\underline{H}CH_3$), 1.27 (3H, d, $J_{1,2}$ 7.4 Hz, CH_3), 1.20 (3H, d, $J_{1,2}$ 6.1 Hz, CH_3) [lit.,[158] δ7.28 (5H, s, Ph), 4.62, 4.05 (2H, AB system, J_{AB} 15 Hz, CH_2Ph), 3.16 (1H, dq, $J_{1,2}$ 6 Hz, 2 Hz, NCH), 2.74 (1H, dq, $J_{1,2}$ 6 Hz, 2 Hz, CHCO), 1.25 (3H, d, $J_{1,2}$ 6 Hz, CH_3), 1.17 (3H, d, $J_{1,2}$ 6 Hz, CH_3)].

Preparation of (3R),(4S)-(-)-3,4-dimethyl-N-benzylazetidin-2-one 174

The 1.4:1 mixture of (SS)-47 and (SR)-48 (prepared above (p.169)) (501 mg, 0.98 mmol) was treated successively with lithium benzylamide [generated from benzylamine (0.35 ml, 3.2 mmol) and n-butyllithium (1.4 ml, 2.24 mmol)] and methyl iodide (0.4 ml, 6.4 mmol) according to the general procedure for the preparation of β-amino acyl complexes (p.182). An identical work-up gave (SRS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(CH_3)$-$NHCH_2Ph$] 173 (153 mg, 26%, diastereoisomeric purity >100:1:1:1) which was oxidatively decomplexed, following the general procedure described above (p.182), to (3R), (4S)-(-)-3,4-dimethyl-N-benzylazetidin-2-one 174 (20 mg, 42%); $[\alpha]_D^{24}$ -29.2° (c 0.69, $CHCl_3$).

Preparation of (RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(CH_3)NHCH_2Ph$] 176

Complex 176 was prepared from complex 33 using the general procedure described above (p.182). Elution with dichloromethane - ethyl acetate - methanol (10:9:1) gave complex 176 (92%, diastereoisomeric purity >100:1) (Found: C, 71.6; H, 5.8; N, 2.4; P, 5.0. $C_{35}H_{34}FeNO_2P$ requires C, 71.55; H, 5.8; N, 2.4; P, 5.3%); $\nu_{max.}$ 3300 w,br (N-H), 1910 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.2 (20H, m, Ph), 4.40 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 3.69, 3.56 (2H, AB system, J_{AB} 12.9 Hz, $C\underline{H}_2Ph$), 3.08, 2.68 (2H, ABX system, J_{AB} 18.3 Hz, $COCH_2$), 2.64 (1H, m, $C\underline{H}CH_3$), 0.68 (3H, d, $J_{1,2}$ 6.1 Hz, CH_3); ^{13}C {^1H} n.m.r. δ220.5 (d, J_{PC} 31.4 Hz, C≡O), 141.1 (s, CH_2Ph C_{ipso}), 136.5 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.4 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.2 (s, CH_2Ph C_{ortho}), 128.1 (d, J_{PC} 8.5 Hz, Ph C_{meta}), 126.6 (s, CH_2Ph C_{para}), 85.4 (s, C_5H_5), 73.2 (d, J_{PC} 5.4 Hz, $CO\underline{C}H_2$), 51.3 (s, $\underline{C}H_2Ph$), 49.7 (s, $\underline{C}HCH_3$), 20.0 (s, CH_3); ^{31}P {^1H} n.m.r. δ72.2; m/z 587.

Preparation of (±)-4-methyl-N-benzylazetidin-2-one 177

β-Lactam 177 was prepared from (RR,SS)-176 using the general procedure described above (p.182). Elution with acetone - diethyl ether (1:9) gave β-lactam 177 as a colourless oil (68%); $\nu_{max.}$ (neat) 1750 s cm^{-1} (C=O) [lit.,[158] 1750 cm^{-1}]; ^1H n.m.r. δ7.3 - 7.2 (5H, m, Ph), 4.60, 4.11 (2H, AB system, J_{AB} 15.2 Hz, $C\underline{H}_2Ph$), 3.58 (1H, m, $C\underline{H}CH_3$), 3.07, 2.54 (2H, ABX system, J_{AB} 14.4 Hz, $COCH_2$), 1.22 (3H, d, $J_{1,2}$ 6.1 Hz, CH_3) [lit.,[158] δ7.3 (5H, s, Ph), 4.65, 4.06 (2H, d, $J_{1,2}$ 15 Hz, $C\underline{H}_2Ph$), 3.56 (1H, m, $C\underline{H}CH_3$), 3.05 (1H, dd, $J_{1,2}$ 4.9 Hz, 14.5 Hz, $COCH_2$), 2.48 (1H, dd, $J_{1,2}$ 2.5 Hz, 14.5 Hz, $COCH_2$), 1.17 (3H, d, $J_{1,2}$ 6 Hz, CH_3)]; ^{13}C {^1H} n.m.r. δ166.8 (C=O), 136.1 (Ph C_{ipso}), 128.7 (Ph C_{meta}/C_{ortho}), 128.2 (Ph C_{ortho}/C_{meta}), 127.6 (Ph C_{para}), 47.0 ($\underline{C}HCH_3$), 44.4 (CH_2), 44.2 (CH_2), 18.5 (CH_3); m/z 175 (M^+).

Preparation of (4S)-(-)-4-methyl-N-benzylazetidin-2-one 177

Sodium hydride (150 mg, 6.3 mmol) and the 1.4:1 mixture of (SS)-47 and (SR)-48 (prepared above (p.169)) (855 mg, 1.67 mmol) were combined as solids. THF (25 ml) was added and the reaction mixture stirred (20°C; 48 h). Removal of solvent, extraction with dichloromethane (3 x 10 ml) and filtration through alumina (grade V) gave an orange solution which was chromatographed on alumina (grade I). A single yellow band was eluted with dichloromethane - ethyl acetate (1:1) which, upon removal of solvent, gave an orange powder (700 mg) identified by ^{1}H n.m.r. spectroscopy as a 2:1 mixture of (S)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33 and the starting complexes 47/48. This mixture was treated successively with lithium benzylamide [generated from benzylamine (0.3 ml, 2.75 mmol) and n-butyl-lithium (1.5 ml, 2.4 mmol)] and methanol (0.8 ml) according to the general procedure for the preparation of β-amino acyl complexes (p.182). An identical work-up gave (SS)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(CH_3)NHCH_2Ph$] 176 (690 mg, 81%, diastereoisomeric purity > 100:1); $[\alpha]_D^{21}$ +143.0° (c 0.44, C_6H_6). Oxidative decomplexation, following the general procedure described above (p.182), gave (4S)-(-)-4-methyl-N-benzylazetidin-2-one 177 (106 mg, 65%); $[\alpha]_D^{24}$ -38.5° (c 2.1, CH_3OH) {lit.,[166] $[\alpha]_D^{21}$ -34.5° (c 3.0, CH_3OH)}.

Preparation of (RS,SR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH_2NHCH_2Ph$ 179

The 1:1 mixture of complexes 25 and 26 (363 mg, 0.58 mmol) was treated successively with lithium benzylamide [generated from benzylamine (0.2 ml, 1.8 mmol) and n-butyllithium (0.9 ml, 1.44 mmol)] and methyl iodide (0.2 ml, 3.2 mmol) according to the general procedure for the preparation of β-amino acyl complexes (p.182). Elution with dichloro-methane gave recovered starting material 25/26 (100 mg, 20%). Elution with dichloro-methane - ethyl acetate - methanol (2:7:1) gave complex 179

(137 mg, 40%, diastereoisomeric purity > 100:1) (Found: C, 71.8; H, 5.8; N, 2.3; P, 5.3. $C_{35}H_{34}FeNO_2P$ requires C, 71.6; H, 5.8; N, 2.4; P, 5.3%); $\nu_{max.}$ ($CHCl_3$) 1915 vs (C≡O), 1585 s cm^{-1} (C=O); ^1H n.m.r. δ7.5 - 7.2 (20H, m, Ph), 4.45 (5H, d, J_{PH} 0.8 Hz, C_5H_5), 3.47 (2H, s, $C\underline{H}_2Ph$), 2.91 (1H, m, $C\underline{H}CH_3$), 1.94 (2H, m, CH_2N), 1.15 (3H, d, $J_{1,2}$ 7.3 Hz, CH_3 major diastereoisomer), 0.68 (1H, br, NH), 0.31 (3H, d, $J_{1,2}$ 6.7 Hz, CH_3 minor diastereoisomer); ^{13}C {^1H} n.m.r. δ220.8 (d, J_{PC} 31.5 Hz, C≡O), 136.5 (d, J_{PC} 42.9 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.8 Hz, Ph C_{ortho}), 129.7 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.1 Hz, Ph C_{meta}), 85.4 (s, C_5H_5), 67.0 (d, J_{PC} 5.0 Hz, CO$\underline{C}$H), 54.2 (s, CH_2), 51.6 (s, CH_2), 15.7 (s, CH_3); ^{31}P {^1H} n.m.r. δ71.0; m/z 587 (M^+).

Preparation of (+)-3-methyl-N-benzylazetidin-2-one 180

β-Lactam 180 was prepared from (RS,SR)-179 using the general procedure described above (p.182). Elution with acetone - diethyl ether (1:9) gave β-lactam 180 as a colourless oil (49%); $\nu_{max.}$ ($CHCl_3$) 1740 vs cm^{-1} (C=O); ^1H n.m.r. δ7.4 -7.2 (5H, m, Ph), 4.40, 4.35 (2H, AB system, J_{AB} 15.1 Hz, $C\underline{H}_2Ph$), 3.29, 2.79 (2H, ABX system, J_{AB} 5.2 Hz, CH_2N), 3.22 (1H, m, $C\underline{H}CH_3$), 1.32 (3H, d, $J_{1,2}$ 7.4 Hz, CH_3) [lit.,[167] δ7.27 (5H, s, Ph), 4.40 (2H, s, $C\underline{H}_2Ph$), 3.20, 2.68 (2H, ABX system, J_{AB} 5.5 Hz, CH_2N), 3.00 (1H, m, $C\underline{H}CH_3$), 1.27 (3H, d, $J_{1,2}$ 7.3 Hz, CH_3)]; ^{13}C {^1H} n.m.r. δ171.1 (C=O), 135.8 (Ph C_{ipso}), 128.7 (Ph C_{ortho}/C_{meta}), 128.0 (Ph C_{meta}/C_{ortho}), 127.6 (Ph C_{para}), 46.6 (CH_2N), 44.5 ($\underline{C}HCH_3$), 13.6 (CH_3); m/z 175 (M^+).

Preparation of (3S)-(-)-3-methyl-N-benzylazetidin-2-one 180

(R)-(-)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 (370 mg, 0.79 mmol) was treated successively with lithium benzylamide [generated from benzylamine (0.15 ml, 1.37 mmol) and n-butyllithium (0.65 ml, 1.04 mmol)] and methyl

iodide (0.2 ml, 3.2 mmol) according to the general procedure for the preparation of β-amino acyl complexes (p.182). An identical work-up gave (RS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2NHCH_2Ph] 179 (61 mg, 13%, diastereoisomeric purity > 100:1) which was oxidatively decomplexed, following the general procedure described above (p.182), to (3S)-(-)-3-methyl-N-benzylazetidin-2-one 180 (14 mg, 75%); $[\alpha]_D^{21}$ -32.0° (c 0.33, $CHCl_3$).

General procedure for the Michael addition of n-butyllithium to [(η^5-C_5H_5)Fe(CO)(PPh_3)COC(CH_3)=CH_2] 65 and subsequent reaction with electrophiles. Preparation of complexes 209, 210 and 211

n-Butyllithium (1.5 equivalents) was added to [(η^5-C_5H_5)Fe(CO)(PPh_3)COC(CH_3)=CH_2] 65 (typically 200 mg, 0.42 mmol) in THF (15 ml) at -78°C to give a dark red solution. After stirring (-78°C; 2h), the electrophile (2 equivalents) was added† and the mixture stirred for a further 2h (-78°C). Warming to room temperature and removal of solvent gave an orange oil which was extracted with dichloromethane (2 x 15 ml) and filtered through alumina (grade V).

The product complexes were purified by chromatography on alumina (grade I), analysed by ^{1}H n.m.r. spectroscopy in order to determine diastereoselectivities and obtained as orange needles from hexane (-30°C).

(RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH_2n-Bu] 209. Elution with diethyl ether - dichloromethane (4:1) gave complex 209 (89%, diastereoisomeric purity > 100:1) (Found: C, 71.3; H, 6.5; P, 5.6. $C_{32}H_{35}FeO_2P$ requires C, 71.4; H, 6.55; P, 5.75%); $\nu_{max.}$ 1910 vs (C≡O), 1590 s cm^{-1} (C=O); ^{1}H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.43 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 2.81 (1H, ddq, $J_{1,2}$ 9.2 Hz, 3.8 Hz, 6.5 Hz, COCH), 1.81 (1H, m, CH(CH_3)CH_2),

† When methanol was used to quench the reaction, the solution was cooled to -100°C prior to addition.

1.34 - 1.00 (7H, m, $(CH_2)_4$), 0.90 (3H, t, $J_{1,2}$ 6.8 Hz, $CH_2\underline{CH_3}$), 0.18 (3H, d, $J_{1,2}$ 6.5 Hz, $CH\underline{CH_3}$); ^{13}C $\{^1H\}$ n.m.r. δ221.0 (d, J_{PC} 31.4 Hz, C≡O), 136.7 (d, J_{PC} 42.6 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 10.0 Hz, Ph C_{ortho}), 129.6 (s, Ph C_{para}), 128.0 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.4 (s, C_5H_5), 66.9 (d, J_{PC} 3.7 Hz, CO$\underline{C}$H), 32.3 (s, CH_2), 32.2 (s, CH_2), 26.7 (s, CH_2), 22.7 (s, CH_2), 14.7 (s, CH_3), 14.1 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ71.1; m/z 538 (M^+), 510 (M+ - 28).

[$(\eta^5$-$C_5H_5)Fe(CO)(PPh_3)COC(CH_3)_2CH_2$n-Bu] 210. Elution with diethyl ether gave complex 210 (75%) (Found: C, 71.6; H, 6.9; P, 5.8. $C_{33}H_{37}FeO_2P$ requires C, 71.7; H, 6.75; P, 5.6%); $\nu_{max.}$ 1895 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.40 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 1.27 - 0.86 (8H, m, $(CH_2)_4$), 0.97 (3H, s, CH_3), 0.86 (3H, t, $J_{1,2}$ 7.2 Hz, $CH_2\underline{CH_3}$), 0.66 (3H, s, CH_3); ^{13}C $\{^1H\}$ n.m.r. δ222.5 (d, J_{PC} 35.1 Hz, C≡O), 137.0 (d, J_{PC} 41.2 Hz, Ph C_{ipso}), 133.9 (d, J_{PC} 9.3 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.8 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 84.9 (s, C_5H_5), 61.3 (s, CO$\underline{C}(CH_3)_2$), 39.3 (s, CH_2), 32.9 (s, CH_2), 25.2 (s, CH_3), 25.2 (s, CH_3), 24.0 (s, CH_2), 22.7 (s, CH_2), 14.1 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ70.0; m/z 552 (M^+).

(RS,SR)-[$(\eta^5$-$C_5H_5)Fe(CO)(PPh_3)COC(CH_3)(Et)CH_2$n-Bu] 211. Elution with petroleum ether - diethyl ether (1:3) gave complex 211 (82%, diastereoisomeric purity > 100:1) (Found: C, 72.2; H, 7.1; P, 5.7. $C_{34}H_{39}FeO_2P$ requires C, 72.1; H, 6.9; P, 5.5%); $\nu_{max.}$ 1905 vs (C≡O), 1590 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.35 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 1.55 - 0.75 (9H, m, $(C\underline{H_2})_4$ and $CC\underline{H_2}CH_3$), 0.92 (3H, s, CCH_3), 0.83 (3H, t, $J_{1,2}$ 7.2 Hz, $CH_2\underline{CH_3}$), 0.71 (3H, t, $J_{1,2}$ 7.3 Hz, $CH_2\underline{CH_3}$), 0.37 (1H, m, $CC\underline{H_2}CH_3$); ^{13}C $\{^1H\}$ n.m.r. δ222.5 (d, J_{PC} 35.1 Hz, C≡O), 137.1 (d, J_{PC} 41.6 Hz, Ph C_{ipso}), 133.9 (d, J_{PC} 9.3 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.8 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 64.4 (s, CO$\underline{C}CH_3$), 36.1

(s, CH_2), 32.9 (s, CH_2), 29.2 (s, CH_2), 23.2 (s, CH_2), 22.6 (s, CH_2), 22.3 (s, CH_3), 14.1 (s, CH_3), 9.4 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ69.5; m/z 566 (M^+).

Preparation of (RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COC(CH_3)(Et)CH_2n-Bu] 213

[(η^5-C_5H_5)Fe(CO)(PPh_3)COC(Et)=CH_2] 66 (100 mg, 0.18 mmol) was treated successively with n-butyllithium (0.2 ml, 0.32 mmol) and methyl iodide (0.2 ml, 3.2 mmol) following an identical procedure to that described above (p.188) for the preparation of complexes 209, 210 and 211 from complex 65. The product was chromatographed on alumina (grade I), eluted with diethyl ether and analysed by ^1H n.m.r. spectroscopy. Crystallisation from hexane gave (RR,SS)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COC(CH_3)(Et)CH_2n-Bu] 213 as red plates (90 mg, 80%, diastereoisomeric purity > 100:1) (Found: C, 72.0; H, 7.0; P, 5.6. $C_{34}H_{39}FeO_2P$ requires C, 72.1; H, 6.9; P, 5.5%); $\nu_{max.}$ 1895 vs (C≡O), 1600 s cm^{-1} (C=O); ^1H n.m.r. δ7.6 - 7.3 (15H, m, Ph), 4.36 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 1.56 - 1.65 (10H, m, $(CH_2)_4$ and CCH_2CH_3), 0.90 (3H, t, $J_{1,2}$ 6.8 Hz, $(CH_2)_4CH_3$), 0.88 (3H, s, CCH_3), 0.29 (3H, t, $J_{1,2}$ 7.4 Hz, CCH_2CH_3); ^{13}C $\{^1H\}$ n.m.r. δ222.6 (d, J_{PC} 33.3 Hz, C≡O), 137.1 (d, J_{PC} 41.1 Hz, Ph C_{ipso}), 133.9 (d, J_{PC} 9.3 Hz, Ph C_{ortho}), 129.4 (s, Ph C_{para}), 127.8 (d, J_{PC} 9.3 Hz, Ph C_{meta}), 85.2 (s, C_5H_5), 64.1 (s, $COCCH_3$), 36.2 (s, CH_2), 33.0 (s, CH_2), 28.6 (s, CH_2), 24.2 (s, CH_2), 23.6 (s, CH_3), 22.8 (s, CH_2), 14.2 (s, CH_3), 8.2 (s, CH_3); ^{31}P $\{^1H\}$ n.m.r. δ69.5; m/z 566 (M^+).

Preparation of N-benzyl-2,2-dimethylpropanamide 215

Bromine (0.05 ml, 0.97 mmol) in dichloromethane (1 ml) was added dropwise to a solution of [(η^5-C_5H_5)Fe(CO)(PPh_3)COC(CH_3)$_3$] 214 [202] (229 mg, 0.46 mmol) in dichloromethane (10 ml) at -40°C to give a dark brown solution. After stirring (-40°C; 1h), benzylamine (0.2 ml, 1.8 mmol) was

added and the mixture warmed to room temperature. A saturated aqueous solution of $Na_2S_2O_3$ (10 ml) was added to give two layers. The green dichloromethane layer was separated, concentrated and chromatographed on silica. Elution with petroleum ether - diethyl ether (3:1) and removal of solvent gave $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)Br]$ 9 as a green solid, identified by comparison of its infrared sepctrum [$\nu_{max.}$ 1960 vs cm^{-1} (C≡O)] with that of an authentic sample. Elution with petroleum ether - diethyl ether (1:1) and removal of solvent gave N-benzyl-2,2-dimethylpropanamide 215 as fine white crystals (50 mg, 57%) (Found: C, 75.2; H, 9.0; N, 7.05. $C_{12}H_{17}NO$ requires C, 75.35; H, 9.0; N, 7.3%); $\nu_{max.}$ ($CHCl_3$) 3480 s (N-H), 1660 vs cm^{-1} (C=O); ^1H n.m.r. δ7.38 - 7.21 (5H, m, Ph), 5.91 (1H, br, NH), 4.45 (2H, d, $J_{1,2}$ 5.6 Hz, $C\underline{H}_2Ph$), 1.24 (9H, s, CH_3); ^{13}C {^1H} n.m.r. δ178.2 (C=O), 138.7 (Ph C_{ipso}), 128.7 (Ph), 127.6 (Ph), 127.4 (Ph), 43.6 ($Ph\underline{C}H_2$), 38.7 ($CO\underline{C}$), 27.6 (CH_3); m/z (ACE/NH_3) 191 (M^+), 91 (M^+ - 100), 57 (M^+ -134).

Preparation of the Diels-Alder adduct 223 between $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ 60 and cyclopentadiene

Freshly cracked dicyclopentadiene (1 ml) was added to a mixture of zinc (II) chloride (187 mg, 1.37 mmol) and $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH{=}CH_2]$ 60 (685 mg, 1.47 mmol) in dichloromethane (25 ml) at room temperature. The reaction mixture was stirred (20°C; 16h) to give a clear yellow solution which was filtered through alumina (grade V) and chromatographed on alumina (grade I). Elution with diethyl ether - dichloromethane (1:1) and removal of solvent gave the Diels-Alder adduct 223 as a yellow solid. The product was analysed by ^1H n.m.r. spectroscopy (diastereoisomeric purity 10:1:1) and crystallised from hexane (-30°C) to give complex 223 as yellow blocks (420 mg, 54%) (Found: C, 72.2; H, 5.7; P, 5.75. $C_{32}H_{29}FeO_2P$ requires C, 72.2; H, 5.5; P, 5.8%); $\nu_{max.}$ 1905 vs (C≡O), 1600 s cm^{-1}

(C=O); ^{1}H n.m.r. major diastereoisomer δ7.5 - 7.3 (15H, m, Ph), 6.07 (1H, dd, $J_{8,9}$ 5.6 Hz, $J_{4,9}$ 3.1 Hz, H_9), 5.71 (1H, dd, $J_{8,9}$ 5.6 Hz, $J_{7,8}$ 2.7 Hz, H_8), 4.44 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 3.45 (1H, br s, H_7), 3.33 (1H, m, H_1), 2.62 (1H, br s, H_4), 1.26 (1H, m, H_5 or H_6), 1.13 (1H, m, H_5 or H_6), 0.78 (1H, ddd, J 11.5 Hz, 4.3 Hz, 2.6 Hz, H_2 or H_3), 0.59 (1H, ddd, J 11.9 Hz, 8.3 Hz, 3.8 Hz, H_2 or H_3), minor diastereoisomers δ4.48 (5H, d, J_{PH} 1.3 Hz, C_5H_5) and 4.35 (5H, d, J_{PH} 1.0 Hz, C_5H_5); ^{13}C {^{1}H} n.m.r. major diastereoisomer δ221.0 (d, J_{PC} 31.6 Hz, C≡O), 136.9 (s,-CH=), 136.3 (d, J_{PC} 42.7 Hz, Ph C_{ipso}), 133.4 (d, J_{PC} 9.6 Hz, Ph C_{ortho}), 131.2 (s, -CH=), 129.6 (s, Ph C_{para}), 127.9 (d, J_{PC} 9.5 Hz, Ph C_{meta}), 85.5 (s, C_5H_5), 71.7 (d, J_{PC} 6.0 Hz, CO<u>C</u>H), 49.3 (s), 46.1 (s), 43.2 (s), 27.5 (s), minor diastereoisomer δ85.3 (s, C_5H_5), 48.5 (s), 45.1 (s), 41.7 (s), 30.9 (s); <u>m/z</u> 532 (M^+).

<u>Preparation of bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid 224</u>

Ammonium ceric nitrate (652 mg, 1.2 mmol) was added to complex <u>223</u> in THF - water (19:1, 20 ml) at -78°C to give a dark green solution. The reaction mixture was stirred (-78°C; 0.5h), warmed to room temperature and filtered. Removal of THF, addition of water (20 ml) and extraction with diethyl ether (3 x 10 ml) gave a dark brown solution which was concentrated and chromatographed on silica. Elution with petroleum ether and removal of solvent gave triphenylphosphine as a white solid, identified by comparison of its ^{1}H n.m.r. spectrum with that of an authentic sample. Elution with petroleum ether - diethyl ethyl (1:1) and removal of solvent gave bicyclo[2.2.1]hept-5-ene-2-carboxylic acid as a colourless oil (34 mg, 25%). The acid was formed as a 5:1 mixture of the <u>endo</u> - <u>224</u> and <u>exo</u> isomers as determined by comparison of the ^{1}H n.m.r. spectrum of the acid with those of authentic samples; ^{1}H n.m.r. <u>endo</u>

isomer 224 δ6.22 (1H, dd, J_{cis} 5.6 Hz, $J_{1,2}$ 3.0 Hz, -CH=), 6.00 (1H, dd, J_{cis} 5.6 Hz, $J_{1,2}$ 2.8 Hz, -CH=), 3.24 (1H, br s, CH=CHCH), 3.00 (1H, dt, $J_{1,2}$ 9.4 Hz, 4.0 Hz, CHCO$_2$H), 2.93 (1H, br s, CH=CHCH), 1.93 (1H, ddd, $J_{1,2}$ 11.7 Hz, 9.3 Hz, 3.7 Hz, CH_2), 1.48 - 1.28 (3H, m, CH_2), exo isomer δ6.14 (2H, m, CH=CH), 3.11 (1H, br s, CH=CHCH), 2.26 (1H, m, CH_2).

Boron trifluoride-mediated Diels-Alder reaction

Boron trifluoride - diethyl ether complex (0.03 ml, 0.24 mmol) was added to [(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 (103 mg, 0.22 mmol) in dichloromethane (20 ml) at -40°C to give a yellow solution. Freshly cracked dicyclopentadiene (1 ml) was added to the mixture, which was stirred for a further 3h (-40°C). After the addition of methanol (0.5 ml), the solution was warmed to room temperature. Removal of solvent and extraction with dichloromethane (3 x 10 ml) gave a yellow solution which was filtered through alumina (grade V) and chromatographed on alumina (grade I). Elution with diethyl ether - dichloromethane (1:1) and removal of solvent gave complex 223 as fine yellow crystals (31 mg, 26%, diastereoisomeric purity 21:1:1).

Preparation of (+)-iodolactone 225

Following an identical procedure to that described above (p.191) for the preparation of complex 223, (S)-(+)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CH_2] 60 (700 mg, 1.5 mmol) was treated with cyclopentadiene (1.5 ml) in the presence of zinc (II) chloride (200 mg, 1.47 mmol) to give (S)-223 (700 mg, 88%, diastereoisomeric purity 21:3:1). This mixture was oxidatively decomplexed with ammonium ceric nitrate (866 mg, 1.58 mmol) as described above (p.192) to give crude (2S)-(-)-bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid 224 (59 mg, 33%); $[\alpha]_D^{21}$ -81° (c 3.0, EtOH) [lit.,[228] $[\alpha]_D^{20}$ -147° (c 3.0, EtOH)], contaminated with the corresponding exo acid.

Saturated aqueous $NaHCO_3$ (4 ml) and iodine (322 mg, 1.27 mmol) in THF (2 ml) were added successively to the crude mixture of acids (57 mg, 0.41 mmol) in diethyl ether (1 ml) at 0°C.[241] The purple reaction mixture was stirred (0°C; 5.5h) and quenched with saturated $Na_2S_2O_3$ (2 ml). Water (15 ml) was added and the solution extracted with diethyl ether (3 x 10 ml). The organic layer was washed with brine (2 x 10 ml) and water (10 ml), and dried (Na_2SO_4). Filtration and removal of solvent gave iodolactone 225 as a white solid (80 mg, 67%); $[\alpha]_{436}$ +226° (c 2.0, C_6H_6). Crystallisation from diethyl ether - hexane gave iodolactone 225; $[\alpha]_{436}$ +238.4° (c 0.55, C_6H_6) [lit.,[226] $[\alpha]_{436}$ +239° (c 2.0, C_6H_6)]; $\nu_{max.}$ ($CHCl_3$) 1780 vs cm^{-1} (C=O); ^1H n.m.r. δ5.14 (1H, d, J 5.1 Hz, H_1), 3.90 (1H, d, J 2.6 Hz, H_4), 3.21 (1H, dt, J 4.9 Hz, 1.2 Hz, H_3), 2.74 (1H, br s, H_7), 2.58 (1H, dd, J 11.1 Hz, 4.7 Hz, H_2), 2.41 (1H, dd, J 11.5 Hz, 1.7 Hz, H_5 or H_6), 2.09 (1H, ddd, J 13.6 Hz, 11.2 Hz, 4.0 Hz, H_8 or H_9), 1.86 (2H, m, H_5 or H_6 and H_8 or H_9); ^{13}C {^1H} n.m.r. δ179.1 (CO_2), 88.9 (CHO), 46.7 (CH), 46.5 (CH), 37.3 (CH_2), 37.3 (CH), 34.5 (CH_2), 29.7 (CH); m/z (CI/NH_3) 282 (M^+ + 18).

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APPENDICES

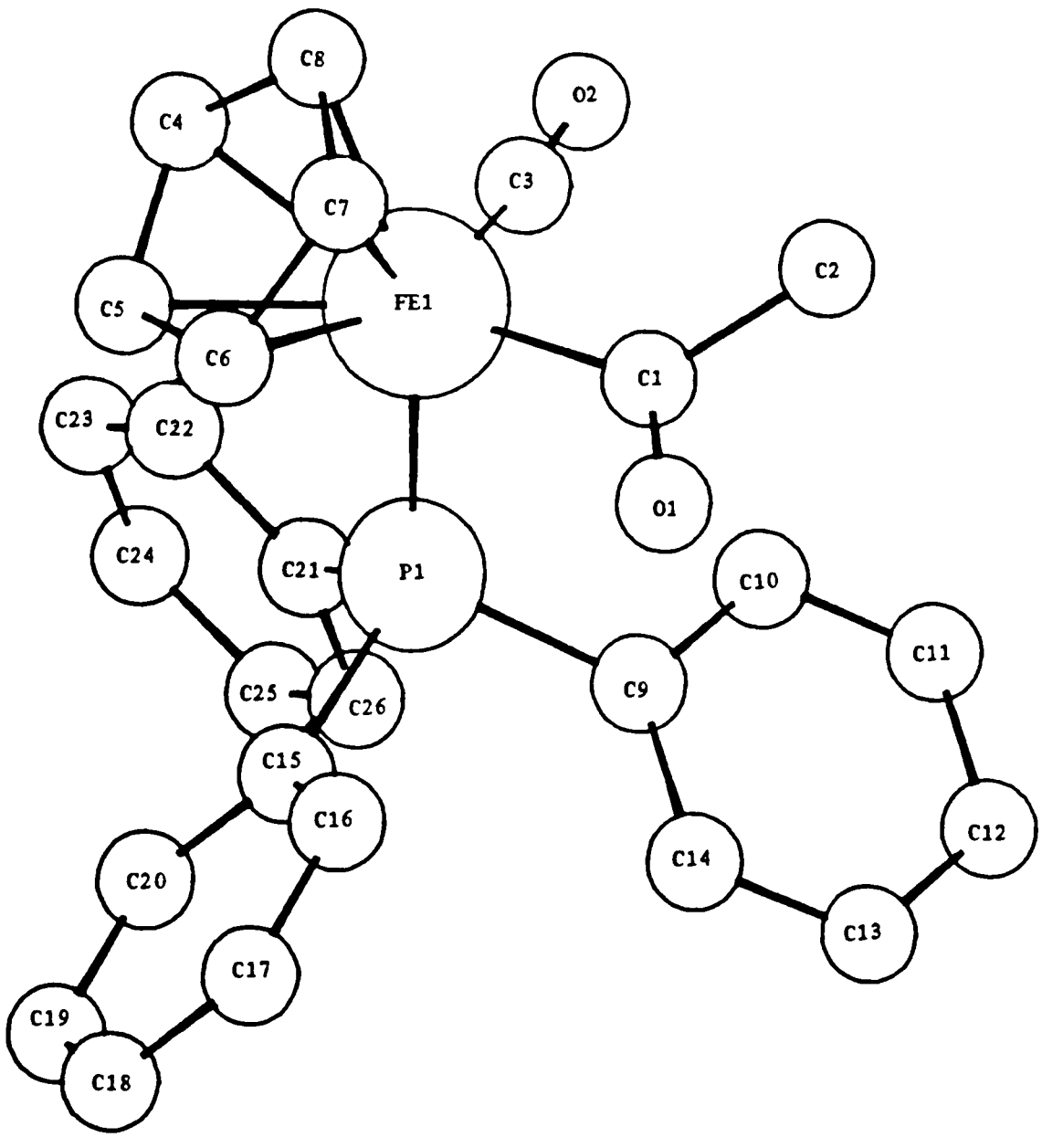
General

Crystal data for the X-ray crystal structure analyses contained in this thesis, which were measured using Enraf-Nonius CAD-4 diffractometers, are presented below. Graphite monochromated Molybdenum or Copper X-radiation (as specified below) and the $\omega/2\theta$ scan technique were used to measure reflection intensities out to a Bragg angle θ, also given below. The space group was, in each case, determined unambiguously as a result of the structure analysis but initially indicated by systematic absences of appropriate reflections. The cell parameters were determined, in each case, by least squares refinement; the setting angles of 25 accurately centred reflections being used. The data were corrected for Lorentz, polarisation and absorption effects and equivalent reflections were merged. Reflections with $I>3\sigma(I)$ were considered to be observed and were used in the structure analyses. The structures were solved by Patterson or direct methods and refined by least squares techniques. Final full-matrix least squares refinement included, in each case, parameters for atomic positions, temperature factors, an overall scale factor and an extinction parameter. All hydrogen atoms were included in calculated positions, being allowed to "ride" on their respective carbon atoms. Final difference Fourier syntheses showed no significant residual electron density and detailed analyses failed to reveal any systematic errors in the structure solutions. All calculations were performed with the CRYSTALS package on the Chemical Crystallography Laboratory VAX 11/750 computer.

Appendix 1

Crystal data for (R,S)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14

$C_{26}H_{23}FeO_2P$, M=454.28, monoclinic, a=7.880(4), b=18.838(2), c=15.120(2)A, β=94.93(3)°, U=2236.1A^3, Z=4, D_{calc}=1.35 Mgm^{-3}, μ(Mo-Kα)=7.84 cm^{-1}, θ_{max}=27.5°, crystal dimensions 0.98 x 0.25 x 0.27 mm, 3435 reflections I>3σ(I), relative transmission factors 1.00 - 1.11, space group $P2_1/n$, R=0.035, R_w=0.047.



Final Atomic Coordinates and Equivalent Isotropic Temperature Factors

with Estimated Standard Deviations in Parentheses

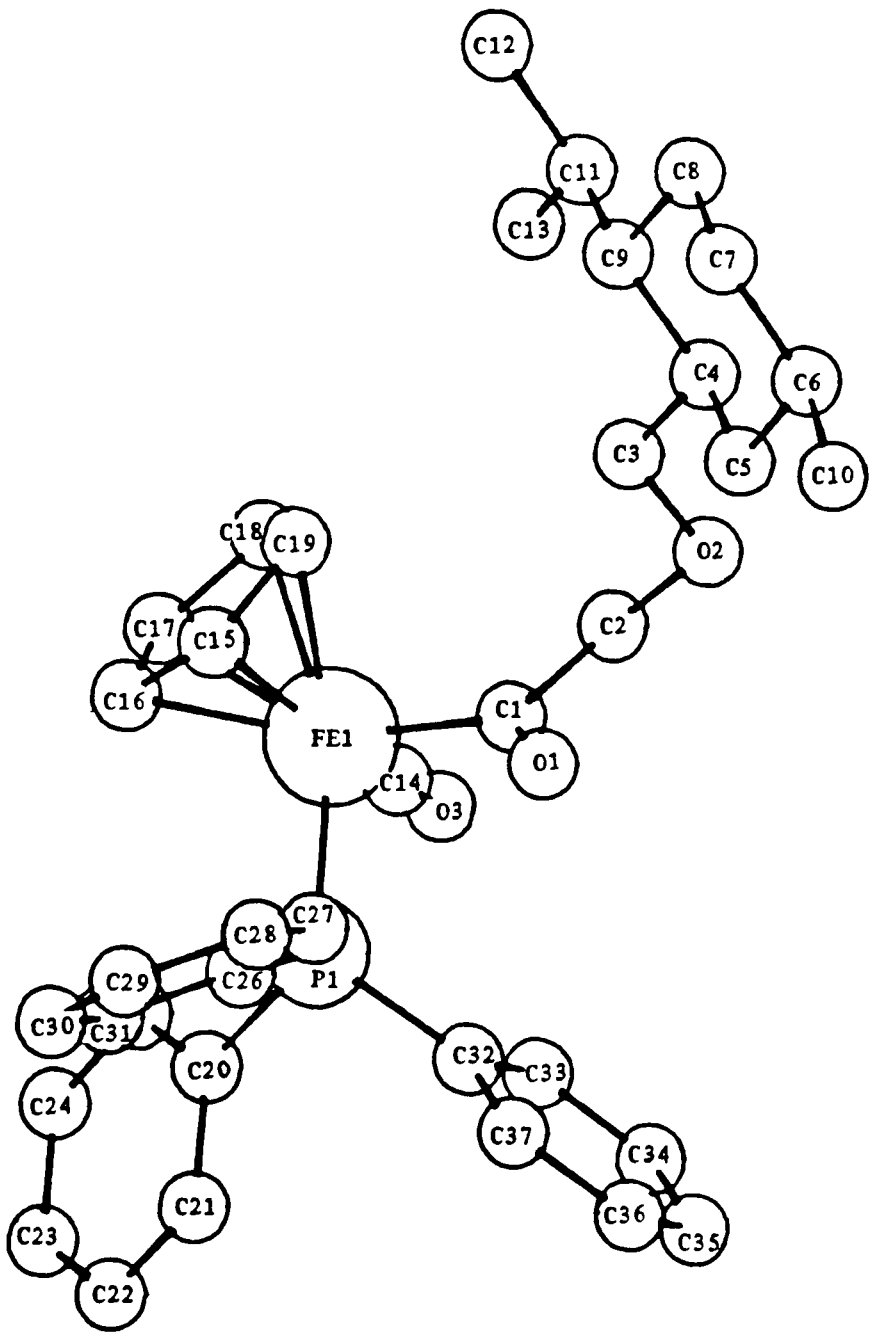
(R,S)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_3$] 14.

Atom	x/a	y/b	z/c	U(iso)
FE(1)	0.11766(4)	0.13868(2)	0.15846(2)	0.0331
P(1)	0.26809(7)	0.13264(3)	0.28726(4)	0.0284
O(1)	0.0309(4)	-0.0004(1)	0.2015(2)	0.0686
O(2)	0.4147(3)	0.1533(2)	0.0609(2)	0.0684
C(1)	0.1081(4)	0.0356(2)	0.1537(2)	0.0449
C(2)	0.1961(7)	-0.0049(3)	0.0822(4)	0.0780
C(3)	0.2994(4)	0.1444(2)	0.0999(2)	0.0464
C(4)	0.0160(4)	0.2365(2)	0.1082(2)	0.0486
C(5)	-0.0313(4)	0.2263(2)	0.1946(2)	0.0475
C(6)	-0.1287(4)	0.1630(2)	0.1961(2)	0.0467
C(7)	-0.1426(3)	0.1350(2)	0.1093(2)	0.0453
C(8)	-0.0519(4)	0.1788(2)	0.0550(2)	0.0475
C(9)	0.4020(3)	0.0534(1)	0.3072(2)	0.0335
C(10)	0.5286(4)	0.0410(2)	0.2501(2)	0.0433
C(11)	0.6337(4)	-0.0179(2)	0.2611(2)	0.0515
C(12)	0.6136(5)	-0.0653(2)	0.3282(3)	0.0556
C(13)	0.4899(5)	-0.0534(2)	0.3856(3)	0.0595
C(14)	0.3848(4)	0.0057(2)	0.3752(2)	0.0510
C(15)	0.1453(3)	0.1346(1)	0.3851(2)	0.0326
C(16)	0.0137(3)	0.0850(1)	0.3899(2)	0.0397
C(17)	-0.0788(4)	0.0828(2)	0.4639(2)	0.0453
C(18)	-0.0432(4)	0.1304(2)	0.5326(2)	0.0495
C(19)	0.0843(4)	0.1804(2)	0.5280(2)	0.0479
C(20)	0.1783(3)	0.1823(2)	0.4540(2)	0.0405
C(21)	0.4259(3)	0.2034(1)	0.3096(2)	0.0326
C(22)	0.4030(4)	0.2692(2)	0.2689(2)	0.0464
C(23)	0.5194(5)	0.3238(2)	0.2870(2)	0.0505
C(24)	0.6617(4)	0.3129(2)	0.3448(2)	0.0465
C(25)	0.6880(4)	0.2480(2)	0.3850(2)	0.0447
C(26)	0.5710(3)	0.1936(1)	0.3684(2)	0.0386
H(1)	0.2558(7)	0.0296(3)	0.0453(4)	0.19(3)
H(2)	0.2808(7)	-0.0390(3)	0.1112(4)	0.38(8)
H(3)	0.1085(7)	-0.0315(3)	0.0436(4)	0.43(9)
H(4)	0.0847(4)	0.2768(2)	0.0873(2)	0.056(9
H(5)	-0.0016(4)	0.2584(2)	0.2463(2)	0.07(1)
H(6)	-0.1784(4)	0.1421(2)	0.2489(2)	0.06(1)
H(7)	-0.2060(3)	0.0910(2)	0.0897(2)	0.052(9
H(8)	-0.0372(4)	0.1712(2)	-0.0094(2)	0.050(9
H(9)	0.5433(4)	0.0751(2)	0.2006(2)	0.038(8
H(10)	0.7242(4)	-0.0260(2)	0.2197(2)	0.09(1)
H(11)	0.6881(5)	-0.1082(2)	0.3351(3)	0.08(1)
H(12)	0.4774(5)	-0.0871(2)	0.4357(3)	0.09(1)
H(13)	0.2949(4)	0.0136(2)	0.4169(2)	0.09(1)
H(14)	-0.0128(3)	0.0510(1)	0.3398(2)	0.036(7)
H(15)	-0.1717(4)	0.0471(2)	0.4675(2)	0.07(1)
H(16)	-0.1101(4)	0.1283(2)	0.5858(2)	0.07(1)
H(17)	0.1090(4)	0.2149(2)	0.5778(2)	0.06(1)
H(18)	0.2699(3)	0.2186(2)	0.4499(2)	0.050(9)
H(19)	0.3011(4)	0.2770(2)	0.2258(2)	0.06(1)
H(20)	0.5008(5)	0.3711(2)	0.2576(2)	0.08(1)
H(21)	0.7455(4)	0.3521(2)	0.3580(2)	0.08(1)
H(22)	0.7920(4)	0.2402(2)	0.4266(2)	0.08(1)
H(23)	0.5907(3)	0.1467(1)	0.3984(2)	0.031(7)

Appendix 2

Crystal data for (R)-{(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2O$[(R)-menthyl]} 25

$C_{37}H_{43}FeO_3P$, M=622.56, orthorhombic, a=16.077(4), b=13.680(5), c=15.221(5)A, U=3348A^3, Z=4, D_{calc}=1.24 Mgm^{-3}, μ(Mo-Kα)=5.46 cm^{-1}, θ_{max}=27°, crystal dimensions 0.9 x 0.3 x 0.2 mm, 2807 reflections I>3σ(I), relative transmission factors 1.00 - 1.09, space group $P2_12_12_1$, R=0.042, R_w=0.057.



Final Atomic Coordinates and Equivalent Isotropic Temperature Factors with Estimated Standard Deviations in Parentheses

(R)-{(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2O$[(R)-menthyl]} 25.

Atom	x/a	y/b	z/c	U(iso)
FE(1)	0.0462(2)	0.1191(3)	0.0425(2)	0.0380
P(1)	0.1629(4)	0.1968(5)	0.0682(5)	0.0372
C(1)	0.097(2)	-0.008(2)	0.073(2)	0.0465
C(2)	0.041(2)	-0.082(2)	0.121(2)	0.0568
C(3)	0.061(3)	-0.187(2)	0.097(2)	0.0546
C(4)	0.053(2)	-0.296(2)	-0.028(2)	0.0496
C(5)	0.146(2)	-0.310(2)	-0.042(2)	0.0583
C(6)	0.167(3)	-0.405(3)	-0.088(3)	0.0741
C(7)	0.119(3)	-0.415(4)	-0.172(3)	0.0858
C(8)	0.027(3)	-0.403(4)	-0.156(3)	0.0846
C(9)	0.005(2)	-0.304(3)	-0.111(2)	0.0651
C(10)	0.262(3)	-0.411(4)	-0.103(4)	0.0969
C(11)	-0.086(3)	-0.288(5)	-0.097(4)	0.1059
C(12)	-0.134(8)	-0.30(1)	-0.183(6)	0.14(2)
C(13)	-0.125(9)	-0.206(9)	-0.044(8)	0.14(2)
C(112)	-0.144(5)	-0.229(6)	-0.155(6)	0.14(2)
C(113)	-0.138(5)	-0.359(6)	-0.042(6)	0.14(2)
C(14)	0.010(2)	0.135(2)	0.148(2)	0.0450
C(15)	0.052(2)	0.112(3)	-0.096(2)	0.0561
C(16)	0.020(2)	0.204(3)	-0.070(2)	0.0571
C(17)	-0.054(2)	0.189(3)	-0.022(2)	0.0574
C(18)	-0.068(2)	0.087(3)	-0.019(2)	0.0594
C(19)	-0.004(2)	0.040(3)	-0.065(2)	0.0565
C(20)	0.153(2)	0.326(2)	0.102(2)	0.0411
C(21)	0.223(2)	0.380(2)	0.122(2)	0.0500
C(22)	0.217(2)	0.477(2)	0.147(2)	0.0576
C(23)	0.139(2)	0.519(2)	0.153(2)	0.0591
C(24)	0.068(2)	0.467(2)	0.134(2)	0.0582
C(25)	0.075(2)	0.369(2)	0.108(2)	0.0497
C(26)	0.229(2)	0.206(2)	-0.029(2)	0.0427
C(27)	0.268(2)	0.122(3)	-0.062(2)	0.0578
C(28)	0.315(2)	0.126(3)	-0.138(3)	0.0659
C(29)	0.322(3)	0.213(3)	-0.184(3)	0.0679
C(30)	0.283(2)	0.295(3)	-0.153(2)	0.0649
C(31)	0.237(2)	0.293(2)	-0.076(2)	0.0516
C(32)	0.230(2)	0.153(2)	0.157(2)	0.0444
C(33)	0.197(2)	0.148(3)	0.240(2)	0.0683
C(34)	0.246(3)	0.121(4)	0.312(3)	0.0814
C(35)	0.328(3)	0.098(3)	0.300(3)	0.0742
C(36)	0.360(3)	0.102(4)	0.220(4)	0.0830
C(37)	0.314(2)	0.131(3)	0.146(3)	0.0716
O(1)	0.165(1)	-0.033(2)	0.053(2)	0.0630
O(2)	0.038(1)	-0.199(1)	0.007(1)	0.0521
O(3)	-0.016(2)	0.147(2)	0.219(1)	0.0631

Final Atomic Coordinates and Equivalent Isotropic Temperature Factors with Estimated Standard Deviations in Parentheses

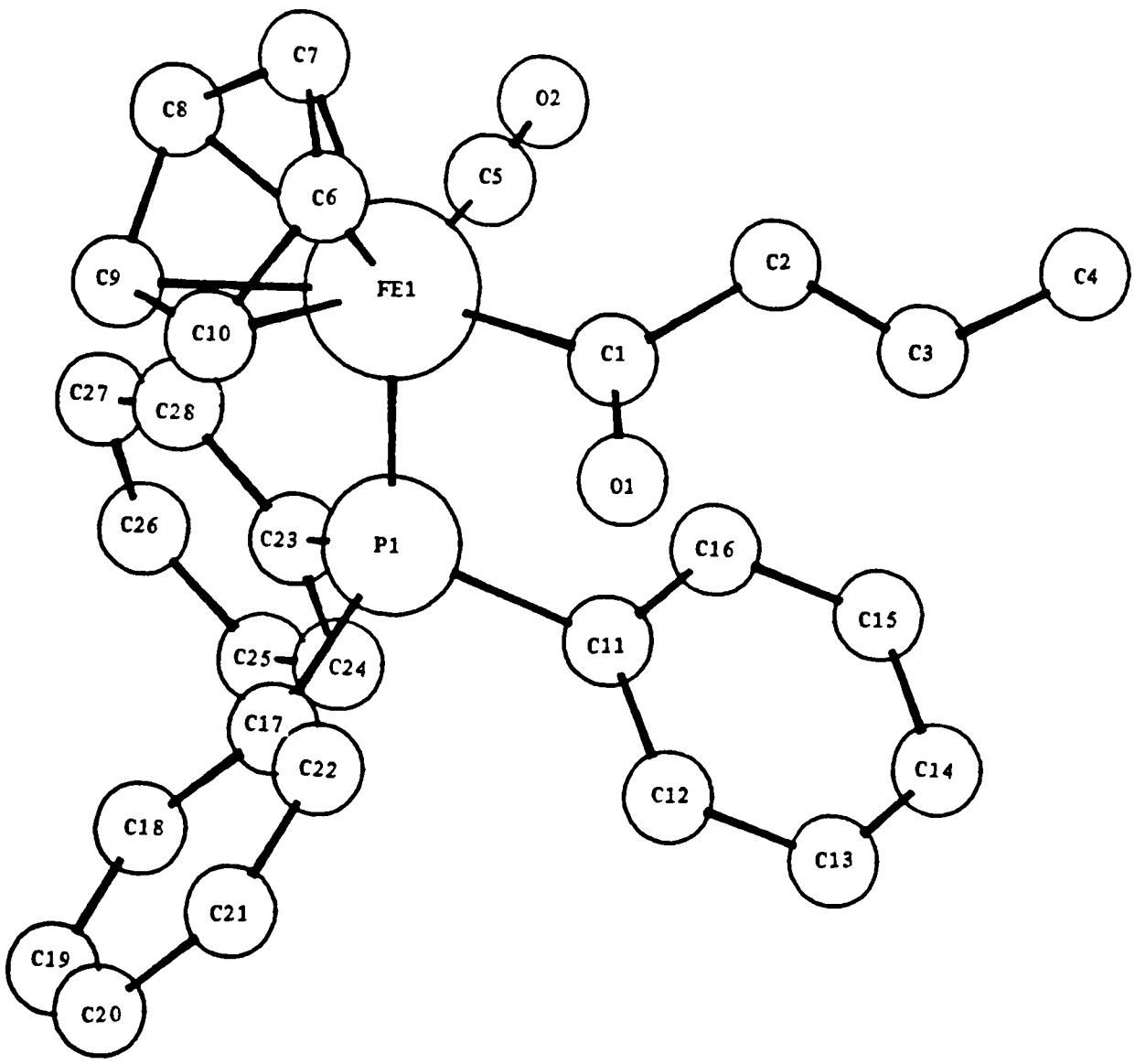
(R)-{(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH_2O$[(R)-menthyl]} 25.

Atom	x/a	y/b	z/c	U(iso)
H(1)	0.047(2)	-0.074(2)	0.190(2)	0.0600
H(2)	-0.020(2)	-0.068(2)	0.110(2)	0.0600
H(3)	0.075(3)	-0.235(2)	0.146(2)	0.0600
H(4)	0.026(3)	-0.221(2)	0.054(2)	0.0600
H(5)	0.014(2)	-0.353(2)	-0.023(2)	0.0600
H(6)	0.175(2)	-0.307(2)	0.016(2)	0.0600
H(7)	0.166(2)	-0.254(2)	-0.080(2)	0.0600
H(8)	0.151(3)	-0.466(3)	-0.053(3)	0.0600
H(9)	0.127(3)	-0.484(4)	-0.206(3)	0.0600
H(10)	0.136(3)	-0.366(4)	-0.220(3)	0.0600
H(11)	0.009(3)	-0.460(4)	-0.118(3)	0.0600
H(12)	-0.004(3)	-0.412(4)	-0.215(3)	0.0600
H(13)	0.021(2)	-0.249(3)	-0.158(2)	0.0600
H(14)	0.280(3)	-0.475(4)	-0.140(4)	0.0600
H(15)	0.296(3)	-0.406(4)	-0.054(4)	0.0600
H(16)	0.280(3)	-0.356(4)	-0.150(4)	0.0600
H(17)	-0.106(3)	-0.355(5)	-0.080(4)	0.0500
H(117)	-0.064(3)	-0.310(5)	-0.155(4)	0.0500
H(18)	-0.196(8)	-0.29(1)	-0.167(6)	0.0500
H(118)	-0.201(5)	-0.238(6)	-0.133(6)	0.0500
H(19)	-0.128(8)	-0.35(1)	-0.227(6)	0.0500
H(119)	-0.138(5)	-0.209(6)	-0.212(6)	0.0500
H(20)	-0.114(8)	-0.23(1)	-0.203(6)	0.0500
H(120)	-0.122(5)	-0.167(6)	-0.113(6)	0.0500
H(21)	-0.182(9)	-0.197(9)	-0.033(8)	0.0500
H(121)	-0.197(5)	-0.340(6)	-0.041(6)	0.0500
H(22)	-0.095(9)	-0.228(9)	0.014(8)	0.0500
H(122)	-0.131(5)	-0.428(6)	-0.061(6)	0.0500
H(23)	-0.096(9)	-0.142(9)	-0.060(8)	0.0500
H(123)	-0.114(5)	-0.352(6)	0.020(6)	0.0500
H(24)	0.105(2)	0.104(3)	-0.132(2)	0.0600
H(25)	0.044(2)	0.272(3)	-0.088(2)	0.0600
H(26)	-0.091(2)	0.244(3)	0.003(2)	0.0600
H(27)	-0.117(2)	0.051(3)	0.013(2)	0.0600
H(28)	0.003(2)	-0.035(3)	-0.080(2)	0.0600
H(29)	0.280(2)	0.347(2)	0.119(2)	0.0600
H(30)	0.269(2)	0.520(2)	0.160(2)	0.0600
H(31)	0.134(2)	0.590(2)	0.173(2)	0.0600
H(32)	0.010(2)	0.501(2)	0.145(2)	0.0600
H(33)	0.022(2)	0.328(2)	0.098(2)	0.0600
H(34)	0.265(2)	0.059(3)	-0.027(2)	0.0600
H(35)	0.339(2)	0.064(3)	-0.168(3)	0.0600
H(36)	0.357(3)	0.218(3)	-0.243(3)	0.0600
H(37)	0.287(2)	0.359(3)	-0.190(2)	0.0600
H(38)	0.212(2)	0.356(2)	-0.055(2)	0.0600
H(39)	0.137(2)	0.170(3)	0.251(2)	0.0600
H(40)	0.220(3)	0.115(4)	0.372(3)	0.0600
H(41)	0.365(3)	0.073(3)	0.349(3)	0.0600
H(42)	0.423(3)	0.090(4)	0.213(4)	0.0600
H(43)	0.342(2)	0.134(3)	0.088(3)	0.0600

Appendix 3

Crystal data for (R,S)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33

$C_{28}H_{25}FeO_2P$, M=480.3, monoclinic, a=15.480(5), b=18.904(5), c=8.055(2)A, β=95.63(2)°, U=2345.8A^3, Z=4, D_{calc}=1.36 Mgm^{-3}, μ(Mo-Kα)= 7.30 cm^{-1}, θ_{max}=25°, crystal dimensions 0.78 x 0.20 x 0.18 mm, 2842 reflections I>3σ(I), relative transmission factors 1.00 - 1.22, space group $P2_1/n$, R=0.038, R_w=0.046.



Final Atomic Coordinates and Equivalent Isotropic Temperature Factors with Estimated Standard Deviations in Parentheses

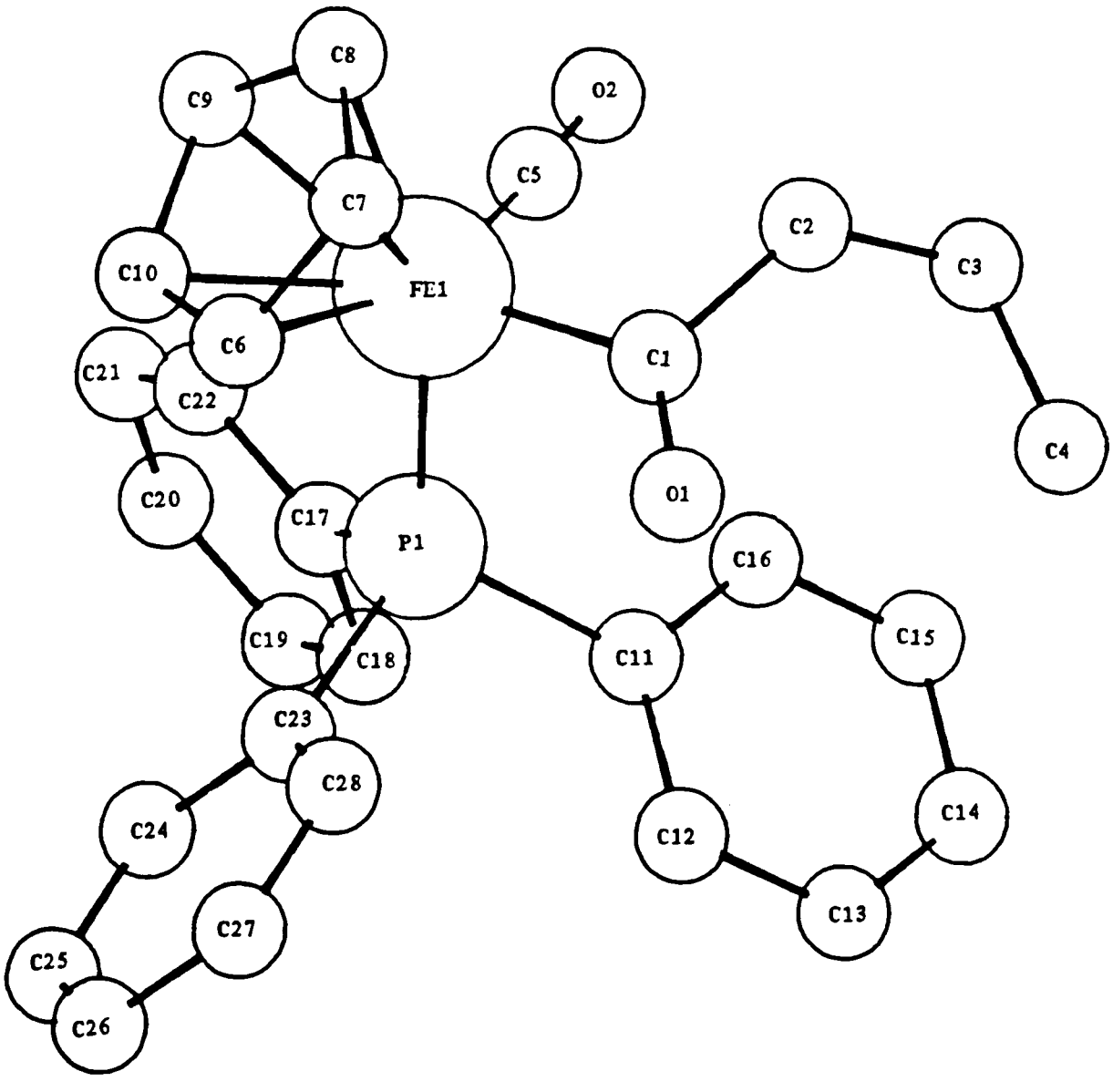
(R,S)-E-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 33.

Atom	x/a	y/b	z/c	U(iso)
FE(1)	0.17634(3)	0.14239(2)	0.11773(4)	0.0337
P(1)	0.30198(4)	0.13633(3)	0.26907(8)	0.0295
C(1)	0.1725(2)	0.0389(2)	0.1115(4)	0.0419
C(2)	0.1085(3)	0.0014(2)	0.2063(4)	0.0545
C(3)	0.1287(3)	-0.0574(2)	0.2889(5)	0.0638
C(4)	0.0741(4)	-0.0935(3)	0.4046(6)	0.0858
C(5)	0.1209(2)	0.1502(2)	0.2943(4)	0.0435
C(6)	0.1301(2)	0.1357(2)	-0.1376(4)	0.0519
C(7)	0.0743(2)	0.1787(2)	-0.0533(4)	0.0556
C(8)	0.1228(3)	0.2372(2)	0.0125(4)	0.0539
C(9)	0.2078(3)	0.2299(2)	-0.0304(4)	0.0542
C(10)	0.2123(2)	0.1665(2)	-0.1230(4)	0.0520
C(11)	0.3195(2)	0.0579(1)	0.4034(3)	0.0335
C(12)	0.3802(2)	0.0062(2)	0.3794(5)	0.0526
C(13)	0.3889(3)	-0.0519(2)	0.4857(6)	0.0627
C(14)	0.3383(3)	-0.0589(2)	0.6139(5)	0.0579
C(15)	0.2779(3)	-0.0081(2)	0.6399(4)	0.0502
C(16)	0.2676(2)	0.0499(2)	0.5335(4)	0.0425
C(17)	0.3980(2)	0.1379(1)	0.1515(3)	0.0345
C(18)	0.4650(2)	0.1862(2)	0.1844(4)	0.0431
C(19)	0.5360(2)	0.1850(2)	0.0908(4)	0.0517
C(20)	0.5405(2)	0.1362(2)	-0.0349(4)	0.0517
C(21)	0.4736(2)	0.0887(2)	-0.0704(4)	0.0497
C(22)	0.4018(2)	0.0892(2)	0.0215(4)	0.0432
C(23)	0.3231(2)	0.2073(1)	0.4239(3)	0.0348
C(24)	0.3824(2)	0.1985(2)	0.5638(4)	0.0433
C(25)	0.3981(2)	0.2526(2)	0.6779(4)	0.0508
C(26)	0.3556(3)	0.3158(2)	0.6554(5)	0.0548
C(27)	0.2957(3)	0.3252(2)	0.5184(5)	0.0565
C(28)	0.2792(2)	0.2707(2)	0.4040(4)	0.0470
O(1)	0.2214(2)	0.0034(1)	0.0348(3)	0.0567
O(2)	0.0833(2)	0.1601(2)	0.4080(3)	0.0636
H(1)	0.0469(3)	0.0301(2)	0.2234(4)	0.045(2)
H(2)	0.1994(3)	-0.0732(2)	0.2775(5)	0.045(2)
H(3)	0.0607(4)	-0.1344(3)	0.3726(6)	0.045(2)
H(4)	0.0032(4)	-0.0704(3)	0.3734(6)	0.045(2)
H(5)	0.0972(4)	-0.0894(3)	0.5172(6)	0.045(2)
H(6)	0.1167(2)	0.0892(2)	-0.1893(4)	0.045(2)
H(7)	0.0118(2)	0.1687(2)	-0.0455(4)	0.045(2)
H(8)	0.0970(3)	0.2779(2)	0.0630(4)	0.045(2)
H(9)	0.2595(3)	0.2602(2)	-0.0038(4)	0.045(2)
H(10)	0.2592(2)	0.1491(2)	-0.1523(4)	0.045(2)
H(11)	0.4209(2)	0.0151(2)	0.3053(5)	0.045(2)
H(12)	0.4330(3)	-0.0853(2)	0.4592(6)	0.045(2)
H(13)	0.3348(3)	-0.1046(2)	0.6817(5)	0.045(2)
H(14)	0.2332(3)	-0.0164(2)	0.7222(4)	0.045(2)
H(15)	0.2259(2)	0.0851(2)	0.5424(4)	0.045(2)
H(16)	0.4602(2)	0.2229(2)	0.2672(4)	0.045(2)
H(17)	0.5820(2)	0.2185(2)	0.1159(4)	0.045(2)
H(18)	0.5943(2)	0.1315(2)	-0.0834(4)	0.045(2)
H(19)	0.4741(2)	0.0526(2)	-0.1490(4)	0.045(2)
H(20)	0.3523(2)	0.0571(2)	-0.0018(4)	0.045(2)
H(21)	0.4147(2)	0.1570(2)	0.5780(4)	0.045(2)
H(22)	0.4406(2)	0.2503(2)	0.7657(4)	0.045(2)
H(23)	0.3762(2)	0.3583(2)	0.7183(4)	0.045(2)
H(24)	0.2705(3)	0.3680(2)	0.4950(5)	0.045(2)
H(25)	0.2395(2)	0.2785(2)	0.3145(4)	0.045(2)

Appendix 4

Crystal data for (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 34

$C_{28}H_{25}FeO_2P$, M=480.3, monoclinic, a=7.935(2), b=18.972(5), c=15.218(6)A, β=92.64(2)°, U=2288.5A^3, Z=4, D_{calc}=1.39 Mgm^{-3}, μ(Mo-Kα)=7.7 cm^{-1}, θ_{max}=25°, crystal dimensions 0.53 x 0.16 x 0.14 mm, 1398 reflections I>3σ(I), relative transmission factors 1.00 - 1.09, space group $P2_1/n$, R=0.033, R_w=0.042.



Final Atomic Coordinates and Equivalent Isotropic Temperature Factors with Estimated Standard Deviations in Parentheses

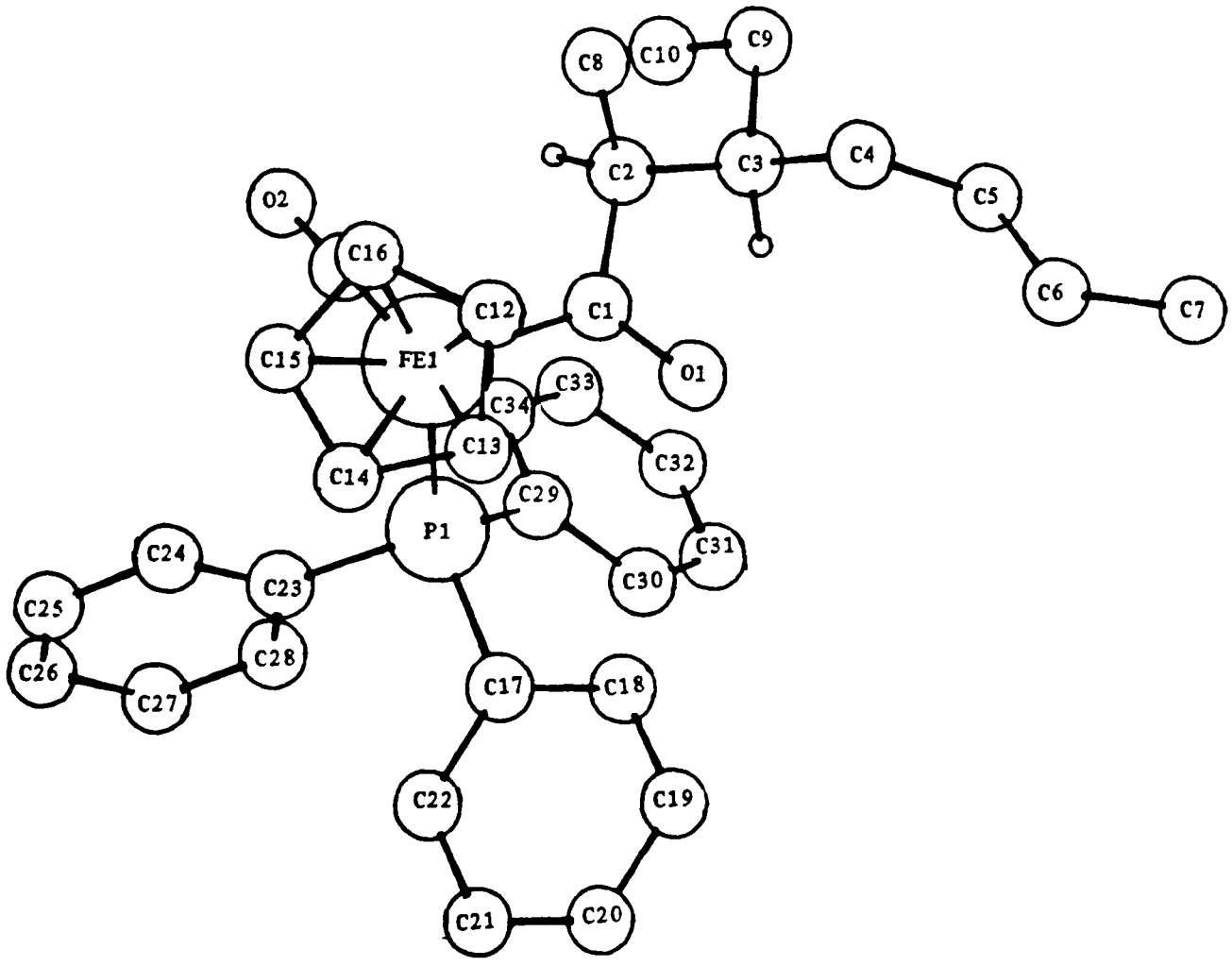
(R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=$CHCH_3$] 34.

Atom	x/a	y/b	z/c	U(iso)
FE(1)	-0.1478(1)	-0.14643(4)	-0.16649(5)	0.0332
P(1)	-0.2904(2)	-0.13557(7)	-0.29288(9)	0.0295
C(1)	-0.1411(9)	-0.0438(3)	-0.1510(4)	0.0358
C(2)	-0.208(1)	-0.0166(4)	-0.0671(4)	0.0601
C(3)	-0.300(1)	0.0411(5)	-0.0574(6)	0.0652
C(4)	-0.347(1)	0.0946(4)	-0.1239(7)	0.0809
C(5)	-0.332(1)	-0.1553(3)	-0.1084(4)	0.0321
C(6)	0.0959(9)	-0.1685(4)	-0.2096(4)	0.0284
C(7)	0.1110(9)	-0.1403(4)	-0.1232(5)	0.0306
C(8)	0.023(1)	-0.1855(4)	-0.0684(5)	0.0465
C(9)	-0.0408(9)	-0.2425(4)	-0.1192(5)	0.0466
C(10)	0.0053(9)	-0.2322(4)	-0.2060(5)	0.0448
C(11)	-0.4241(9)	-0.0569(3)	-0.3080(4)	0.0234
C(12)	-0.405(1)	-0.0078(3)	-0.3749(4)	0.0421
C(13)	-0.513(1)	0.0486(3)	-0.3838(5)	0.0534
C(14)	-0.642(1)	0.0573(3)	-0.3277(5)	0.0473
C(15)	-0.665(1)	0.0085(3)	-0.2611(4)	0.0440
C(16)	-0.555(1)	-0.0480(3)	-0.2513(4)	0.0335
C(17)	-0.4467(9)	-0.2052(3)	-0.3165(4)	0.0234
C(18)	-0.586(1)	-0.1949(3)	-0.3745(4)	0.0325
C(19)	-0.7014(9)	-0.2480(4)	-0.3912(4)	0.0376
C(20)	-0.678(1)	-0.3137(4)	-0.3523(5)	0.0434
C(21)	-0.540(1)	-0.3249(3)	-0.2951(5)	0.0473
C(22)	-0.426(1)	-0.2714(3)	-0.2772(4)	0.0423
C(23)	-0.1630(9)	-0.1348(3)	-0.3908(3)	0.0237
C(24)	-0.1926(9)	-0.1813(3)	-0.4611(4)	0.0388
C(25)	-0.093(1)	-0.1773(4)	-0.5341(4)	0.0458
C(26)	0.035(1)	-0.1281(4)	-0.5370(4)	0.0442
C(27)	0.0656(9)	-0.0823(3)	-0.4669(4)	0.0387
C(28)	-0.0325(9)	-0.0855(3)	-0.3940(4)	0.0317
O(1)	-0.0836(6)	-0.0027(2)	-0.2026(3)	0.0536
O(2)	-0.4506(7)	-0.1636(3)	-0.0701(3)	0.0547
H(1)	-0.179(1)	-0.0438(4)	-0.0122(4)	0.0500
H(2)	-0.348(1)	0.0490(5)	0.0015(6)	0.0500
H(3)	-0.420(1)	0.1321(4)	-0.0998(7)	0.0500
H(4)	-0.408(1)	0.0710(4)	-0.1748(7)	0.0500
H(5)	-0.241(1)	0.1163(4)	-0.1440(7)	0.0500
H(6)	0.1430(9)	-0.1468(4)	-0.2630(4)	0.0500
H(7)	0.1723(9)	-0.0963(4)	-0.1050(5)	0.0500
H(8)	0.007(1)	-0.1786(4)	-0.0041(5)	0.0500
H(9)	-0.1057(9)	-0.2836(4)	-0.0973(5)	0.0500
H(10)	-0.0230(9)	-0.2643(4)	-0.2567(5)	0.0500
H(11)	-0.311(1)	-0.0136(3)	-0.4157(4)	0.0500
H(12)	-0.498(1)	0.0840(3)	-0.4314(5)	0.0500
H(13)	-0.722(1)	0.0980(3)	-0.3350(5)	0.0500
H(14)	-0.759(1)	0.0148(3)	-0.2199(4)	0.0500
H(15)	-0.570(1)	-0.0828(3)	-0.2031(4)	0.0500
H(16)	-0.601(1)	-0.1481(3)	-0.4039(4)	0.0500
H(17)	-0.8022(9)	-0.2399(4)	-0.4318(4)	0.0500
H(18)	-0.760(1)	-0.3528(4)	-0.3650(5)	0.0500
H(19)	-0.524(1)	-0.3723(3)	-0.2672(5)	0.0500
H(20)	-0.328(1)	-0.2795(3)	-0.2349(4)	0.0500
H(21)	-0.2838(9)	-0.2175(3)	-0.4583(4)	0.0500
H(22)	-0.114(1)	-0.2101(4)	-0.5849(4)	0.0500
H(23)	0.105(1)	-0.1252(4)	-0.5898(4)	0.0500
H(24)	0.1596(9)	-0.0474(3)	-0.4695(4)	0.0500
H(25)	-0.0105(9)	-0.0525(3)	-0.3435(4)	0.0500

Appendix 5

Crystal data for (RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(Et)n-Bu] 137

$C_{34}H_{39}FeO_2P$, M=566.50, monoclinic, a=16.225(4), b=7.973(2), c=24.275(5)A, β=105.36(2)°, U=3028A^3, Z=4, D_{calc}=1.24 Mgm^{-3}, μ(Cu-Kα)=47.13cm^{-1}, θ_{max}=55°, crystal dimensions 0.58 x 0.26 x 0.02 mm, 1453 reflections I>3σ(I), absorption correction by empirical methods, space group $P2_1/c$, R=0.055, R_w=0.072.



Final Atomic Coordinates and Equivalent Isotropic Temperature Factors with Estimated Standard Deviations in Parentheses

(RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(Et)n-Bu] 137.

Atom	x/a	y/b	z/c	U(iso)
FE(1)	0.8706(1)	0.0842(2)	0.35606(8)	0.0560
P(1)	0.7685(2)	0.2150(4)	0.3829(1)	0.0486
O(1)	0.7311(5)	0.005(1)	0.2652(3)	0.0683
O(2)	0.9594(6)	0.394(1)	0.3455(4)	0.0847
C(1)	0.7991(7)	0.083(1)	0.2772(5)	0.0572
C(2)	0.8263(7)	0.171(2)	0.2276(5)	0.0571
C(3)	0.7530(8)	0.192(2)	0.1750(4)	0.0719
C(4)	0.7268(9)	0.023(2)	0.1445(6)	0.1065
C(5)	0.635(1)	0.034(3)	0.1057(9)	0.2305
C(6)	0.587(1)	-0.123(3)	0.116(1)	0.2934
C(7)	0.504(2)	-0.134(3)	0.069(1)	0.2718
C(8)	0.9035(8)	0.083(2)	0.2176(6)	0.0953
C(9)	0.776(1)	0.314(2)	0.1314(5)	0.1206
C(10)	0.790(1)	0.495(2)	0.1548(8)	0.1255
C(11)	0.9218(8)	0.271(2)	0.3486(5)	0.0587
C(12)	0.904(1)	-0.163(2)	0.3401(7)	0.0819
C(13)	0.855(1)	-0.165(2)	0.3787(7)	0.0726
C(14)	0.899(1)	-0.076(2)	0.4277(6)	0.0736
C(15)	0.9760(9)	-0.021(2)	0.4193(7)	0.0775
C(16)	0.9789(9)	-0.070(2)	0.3642(8)	0.0829
C(17)	0.6945(6)	0.081(2)	0.4087(5)	0.0499
C(18)	0.6493(7)	-0.046(2)	0.3730(5)	0.0611
C(19)	0.5931(8)	-0.149(2)	0.3900(6)	0.0697
C(20)	0.5826(9)	-0.127(2)	0.4445(7)	0.0823
C(21)	0.6275(9)	-0.008(2)	0.4810(6)	0.0757
C(22)	0.6836(7)	0.097(2)	0.4630(5)	0.0639
C(23)	0.8053(8)	0.364(1)	0.4426(4)	0.0477
C(24)	0.8835(8)	0.342(2)	0.4800(6)	0.0656
C(25)	0.9091(8)	0.447(2)	0.5273(6)	0.0789
C(26)	0.860(1)	0.577(2)	0.5347(6)	0.0746
C(27)	0.7799(9)	0.607(2)	0.4962(6)	0.0802
C(28)	0.7545(8)	0.497(2)	0.4513(5)	0.0618
C(29)	0.6975(7)	0.347(1)	0.3272(5)	0.0501
C(30)	0.6115(7)	0.318(2)	0.3087(6)	0.0726
C(31)	0.5627(9)	0.421(2)	0.2673(7)	0.1022
C(32)	0.597(1)	0.558(2)	0.2480(6)	0.0861
C(33)	0.6806(9)	0.587(2)	0.2670(5)	0.0665
C(34)	0.7305(8)	0.480(2)	0.3065(5)	0.0619

Final Atomic Coordinates and Equivalent Isotropic Temperature Factors

with Estimated Standard Deviations in Parentheses

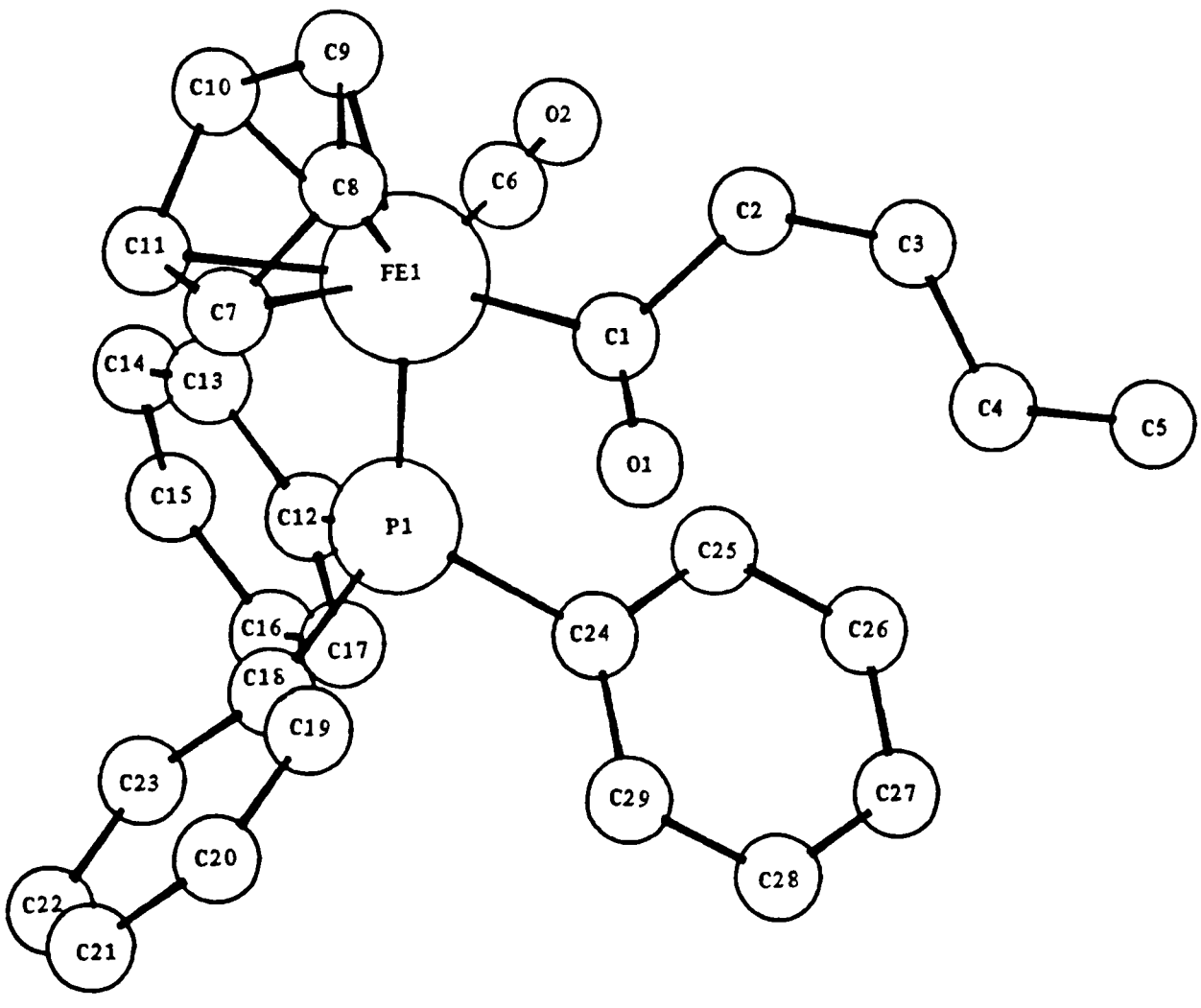
(RSS,SRR)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(Et)n-Bu] 137.

Atom	x/a	y/b	z/c	U(iso)
H(1)	0.8479(7)	0.287(2)	0.2394(5)	0.0700
H(2)	0.7032(8)	0.237(2)	0.1874(4)	0.0700
H(3)	0.7605(9)	0.001(2)	0.1163(6)	0.0900
H(4)	0.7366(9)	-0.070(2)	0.1733(6)	0.0900
H(5)	0.627(1)	0.102(3)	0.0701(9)	0.0900
H(6)	0.604(1)	0.089(3)	0.1314(9)	0.0900
H(7)	0.613(1)	-0.174(3)	0.087(1)	0.0900
H(8)	0.599(1)	-0.195(3)	0.151(1)	0.0900
H(9)	0.480(2)	-0.248(3)	0.059(1)	0.0900
H(10)	0.491(2)	-0.062(3)	0.034(1)	0.0900
H(11)	0.477(2)	-0.083(3)	0.098(1)	0.0900
H(12)	0.9503(8)	0.075(2)	0.2539(6)	0.0900
H(13)	0.9251(8)	0.143(2)	0.1881(6)	0.0900
H(14)	0.8844(8)	-0.032(2)	0.2037(6)	0.0900
H(15)	0.831(1)	0.275(2)	0.1249(5)	0.0900
H(16)	0.730(1)	0.313(2)	0.0943(5)	0.0900
H(17)	0.807(1)	0.570(2)	0.1267(8)	0.0900
H(18)	0.836(1)	0.497(2)	0.1918(8)	0.0900
H(19)	0.735(1)	0.535(2)	0.1613(8)	0.0900
H(20)	0.889(1)	-0.219(2)	0.3018(7)	0.0700
H(21)	0.797(1)	-0.218(2)	0.3725(7)	0.0700
H(22)	0.879(1)	-0.058(2)	0.4629(6)	0.0700
H(23)	1.0209(9)	0.044(2)	0.4473(7)	0.0700
H(24)	1.0264(9)	-0.044(2)	0.3463(8)	0.0700
H(25)	0.6589(7)	-0.059(2)	0.3342(5)	0.0700
H(26)	0.5618(8)	-0.238(2)	0.3637(6)	0.0700
H(27)	0.5400(9)	-0.197(2)	0.4571(7)	0.0700
H(28)	0.6205(9)	0.002(2)	0.5206(6)	0.0700
H(29)	0.7167(7)	0.183(2)	0.4897(5)	0.0700
H(30)	0.9217(8)	0.251(2)	0.4727(6)	0.0700
H(31)	0.9655(8)	0.428(2)	0.5555(6)	0.0700
H(32)	0.881(1)	0.650(2)	0.5690(6)	0.0700
H(33)	0.7443(9)	0.705(2)	0.5014(6)	0.0700
H(34)	0.6971(8)	0.512(2)	0.4237(5)	0.0700
H(35)	0.5857(7)	0.223(2)	0.3253(6)	0.0700
H(36)	0.5000(9)	0.398(2)	0.2525(7)	0.0700
H(37)	0.561(1)	0.632(2)	0.2182(6)	0.0700
H(38)	0.7067(9)	0.687(2)	0.2531(5)	0.0700
H(39)	0.7934(8)	0.501(2)	0.3206(5)	0.0700

Appendix 6

Crystal data for (R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CH_2] 38

$C_{29}H_{25}FeO_2P$, M=492.34, monoclinic, a=7.895(2), b=19.216(6), c=15.727(5)A, β=94.63(2)°, U=2378A^3, Z=4, D_{calc}=1.38 Mgm^{-3}, μ(Cu-Kα)=59.3 cm^{-1}, θ_{max}=60°, crystal dimensions 0.75 x 0.45 x 0.15 mm, 2105 reflections I>3σ(I), relative transmission factors 1.00 - 3.06, space group $P2_1/n$, R=0.067, R_W=0.083.



Final Atomic Coordinates and Equivalent Isotropic Temperature Factors

with Estimated Standard Deviations in Parentheses

(R,S)-Z-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH=CHCH=CH_2] 38.

Atom	x/a	y/b	z/c	U(iso)
FE(1)	0.1108(1)	-0.15559(5)	0.17766(7)	0.0371
P(1)	0.2621(2)	-0.13996(8)	0.3000(1)	0.0332
O(1)	0.0607(7)	-0.0117(3)	0.2000(4)	0.0613
O(2)	0.4139(8)	-0.1841(3)	0.0932(4)	0.0667
C(1)	0.108(1)	-0.0565(4)	0.1532(5)	0.0456
C(2)	0.167(1)	-0.0371(5)	0.0691(6)	0.0631
C(3)	0.264(1)	0.0178(5)	0.0515(6)	0.0612
C(4)	0.320(1)	0.0729(5)	0.1084(6)	0.0616
C(5)	0.406(1)	0.1261(6)	0.0834(7)	0.0834
C(6)	0.293(1)	-0.1699(4)	0.1260(5)	0.0444
C(7)	-0.135(1)	-0.1741(5)	0.2178(6)	0.0552
C(8)	-0.148(1)	-0.1494(4)	0.1338(5)	0.0508
C(9)	-0.067(1)	-0.1937(5)	0.0822(6)	0.0562
C(10)	-0.002(1)	-0.2494(5)	0.1327(7)	0.0635
C(11)	-0.043(1)	-0.2376(5)	0.2171(7)	0.0564
C(12)	0.4182(9)	-0.2086(3)	0.3271(4)	0.0375
C(13)	0.400(1)	-0.2736(4)	0.2898(6)	0.0521
C(14)	0.514(1)	-0.3272(4)	0.3097(7)	0.0622
C(15)	0.654(1)	-0.3154(5)	0.3675(6)	0.0585
C(16)	0.676(1)	-0.2506(4)	0.4046(5)	0.0502
C(17)	0.5600(9)	-0.1972(4)	0.3849(5)	0.0472
C(18)	0.1418(8)	-0.1343(3)	0.3940(4)	0.0343
C(19)	0.0100(9)	-0.0853(4)	0.3933(5)	0.0425
C(20)	-0.086(1)	-0.0786(4)	0.4644(5)	0.0528
C(21)	-0.048(1)	-0.1197(5)	0.5345(5)	0.0551
C(22)	0.079(1)	-0.1685(4)	0.5364(5)	0.0540
C(23)	0.1742(9)	-0.1760(4)	0.4650(4)	0.0404
C(24)	0.3985(9)	-0.0623(3)	0.3103(4)	0.0387
C(25)	0.5200(9)	-0.0536(4)	0.2525(5)	0.0445
C(26)	0.632(1)	0.0027(4)	0.2595(6)	0.0542
C(27)	0.621(1)	0.0510(4)	0.3229(6)	0.0560
C(28)	0.498(1)	0.0426(4)	0.3800(7)	0.0653
C(29)	0.389(1)	-0.0132(4)	0.3742(5)	0.0531
H(1)	0.122(1)	-0.0695(5)	0.0142(6)	0.0900
H(2)	0.308(1)	0.0203(5)	-0.0129(6)	0.0900
H(3)	0.285(1)	0.0694(5)	0.1746(6)	0.0900
H(4)	0.442(1)	0.1661(6)	0.1314(7)	0.0900
H(5)	0.443(1)	0.1316(6)	0.0179(7)	0.0900
H(6)	-0.186(1)	-0.1495(5)	0.2735(6)	0.0900
H(7)	-0.215(1)	-0.1015(4)	0.1123(5)	0.0900
H(8)	-0.053(1)	-0.1868(5)	0.0136(6)	0.0900
H(9)	0.067(1)	-0.2947(5)	0.1103(7)	0.0900
H(10)	-0.008(1)	-0.2711(5)	0.2725(7)	0.0900
H(11)	0.295(1)	-0.2816(4)	0.2408(6)	0.0900
H(12)	0.494(1)	-0.3789(4)	0.2805(7)	0.0900
H(13)	0.746(1)	-0.3572(5)	0.3844(6)	0.0900
H(14)	0.787(1)	-0.2417(4)	0.4501(5)	0.0900
H(15)	0.5793(9)	-0.1459(4)	0.4151(5)	0.0900
H(16)	-0.0185(9)	-0.0530(4)	0.3363(5)	0.0900
H(17)	-0.189(1)	-0.0400(4)	0.4643(5)	0.0900
H(18)	-0.120(1)	-0.1129(5)	0.5909(5)	0.0900
H(19)	0.106(1)	-0.2019(4)	0.5926(5)	0.0900
H(20)	0.2760(9)	-0.2151(4)	0.4652(4)	0.0900
H(21)	0.5302(9)	-0.0917(4)	0.2009(5)	0.0900
H(22)	0.727(1)	0.0099(4)	0.2128(6)	0.0900
H(23)	0.709(1)	0.0956(4)	0.3272(6)	0.0900
H(24)	0.489(1)	0.0803(4)	0.4321(7)	0.0900
H(25)	0.293(1)	-0.0202(4)	0.4203(5)	0.0900