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SYNTHESIS OF CYCLOPENTANOID DERIVATIVES *VIA* A METAL-ASSISTED (3+2) CYCLOADDITION REACTION

A Thesis Submitted for the Degree of
Doctor of Philosophy

by

Christopher Martin Exon

Department of Chemistry

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To my parents

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to my supervisor, Professor Ray Baker, for his encouragement and guidance throughout the duration of this work. Thanks are also due to Doctor Ralph Turner, my supervisor at ICI Ltd., Pharmaceutical Division, Alderley Edge.

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UNIVERSITY OF SOUTHAMPTON

ABSTRACT

FACULTY OF SCIENCE

CHEMISTRY

Doctor of Philosophy

SYNTHESIS OF CYCLOPENTANOID DERIVATIVES *VIA* A METAL ASSISTED (3+2) CYCLOADDITION REACTION

by Christopher Martin Exon

The reactions of (η'-allyl)Fp complexes with electron-deficient olefins and acetylenes, and the replacement of the iron complex of the cyclopentyl-Fp complexes thus formed with an organic functionality have been investigated. Cyclic adducts were the exclusive products from the reaction of the simple (η'-allyl)Fp complex (20a) and the (η'-3-methoxyallyl)Fp complex (28) with olefinic species, whereas linear adducts (arising from a H-transfer process), as well as cyclic products, were isolated from the reaction of the (η'-2-methoxyallyl)Fp complex (66) with unsaturated moieties. The reactivity of the 2-methoxyallyl complex was observed to be substantially greater than that of either (20a) or (28).

Ammonium ceric nitrate oxidation of alcoholic solutions of cyclopentyl-Fp and 2-methoxycyclopentyl-Fp complexes led to the replacement of the Fp group with a carboxylic ester functionality. Similar treatment of 1-methoxycyclopentyl-Fp complexes gave a mixture of ketalic and olefinic derivatives. Reaction of cyclopentyl-Fp complexes with gaseous hydrochloric acid afforded products resulting from a ring-opening process, as well as cyclic adducts arising from the replacement of the Fp complex with a proton. Analogous treatment of 2-methoxycyclopentyl-Fp complexes resulted in the elimination of FpOMe to give cyclopentene derivatives. A mixture of brominated and olefinic derivatives were isolated from the reaction of cyclopentyl-Fp complexes with N-bromopyridinium bromide.

A preliminary study of the possible uses of the metal assisted (3+2) cycloaddition reaction in the synthesis of a variety of cyclopentanoid natural products was also performed.

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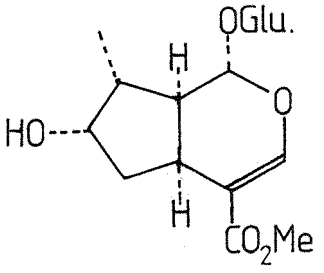
CHAPTER ONE

Introduction

Introduction

A number of classes of naturally occurring compounds are characterised by a substituted cyclopentane unit. These include the iridoid glycosides[1], prostaglandins[2] and cyclopentanoid insect terpenoids[3], of which loganin (1), PGE_1 (2) and iridodial (3) are examples respectively.



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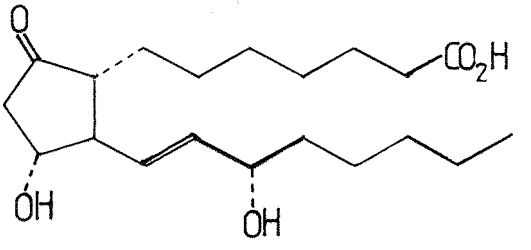

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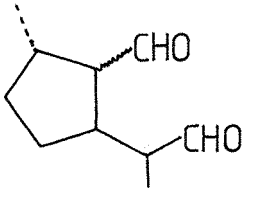

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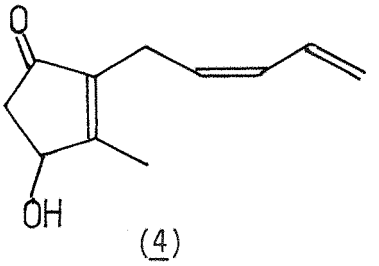

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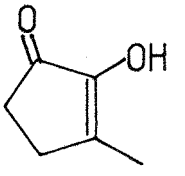

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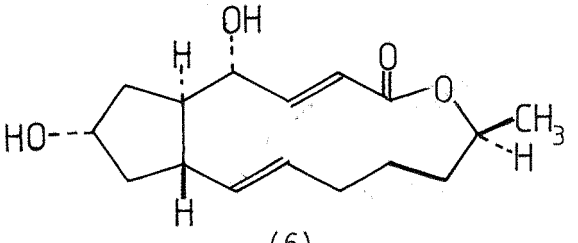

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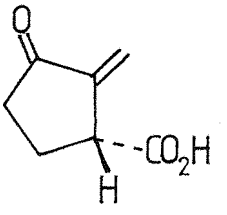


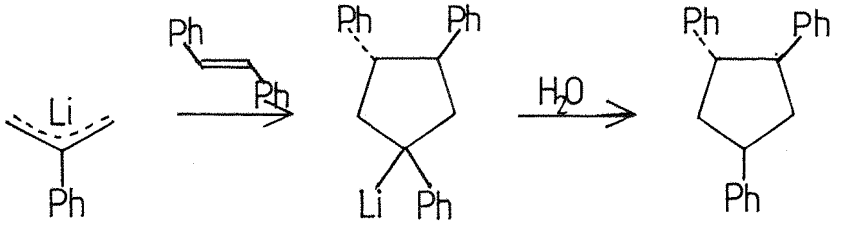
(7)

Further illustrations of biologically active cyclopentanoid natural products are provided by pyrethrolone (4), corylone (5), brefeldin A (6) and sarkomycin (7).

The total synthesis of compounds of this type presents considerable difficulties due to the complexity of their structures. Numerous conceptually different routes have been devised however to both natural and modified

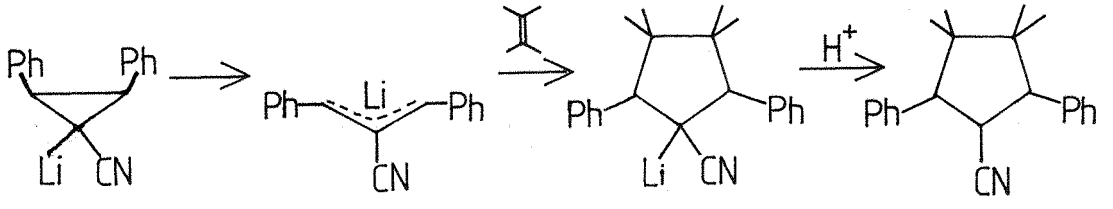
prostaglandins[2], and to a lesser extent to many other cyclopentanoid natural products. These are in general based on simple cyclopentane derivatives, although in a number of syntheses the ring is formed in the latter stages by an intramolecular cyclisation reaction. It was thought that an alternative and perhaps more convenient method for the construction of the complex five-membered ring system could be *via* a (3+2) cycloaddition reaction.

The cycloaddition of an allyl anion to activated olefins has been reported by several workers[4-7]. Kauffmann[4] found that 2-phenylallyllithium (8) formed by treating α-methylstyrene with lithium diisopropylamide, could be reacted with *trans*-stilbene to give the cyclopentane derivative (9) in 41% yield (Scheme 1). Further work by Martens[6] demonstrated that allyl anions with a nitrile group attached to the central carbon atom readily undergo analogous cycloadditions with styrene, 1,1-diphenylethylene, and acetonaphthylene, as well as *trans*-stilbene (Scheme 2). The electron withdrawing group effecting charge stabilisation of the initial cycloadduct. Similarly, treatment of

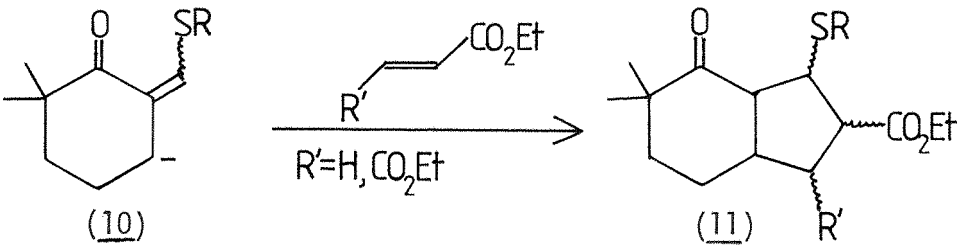


(8) (9)

Scheme 1



Scheme 2

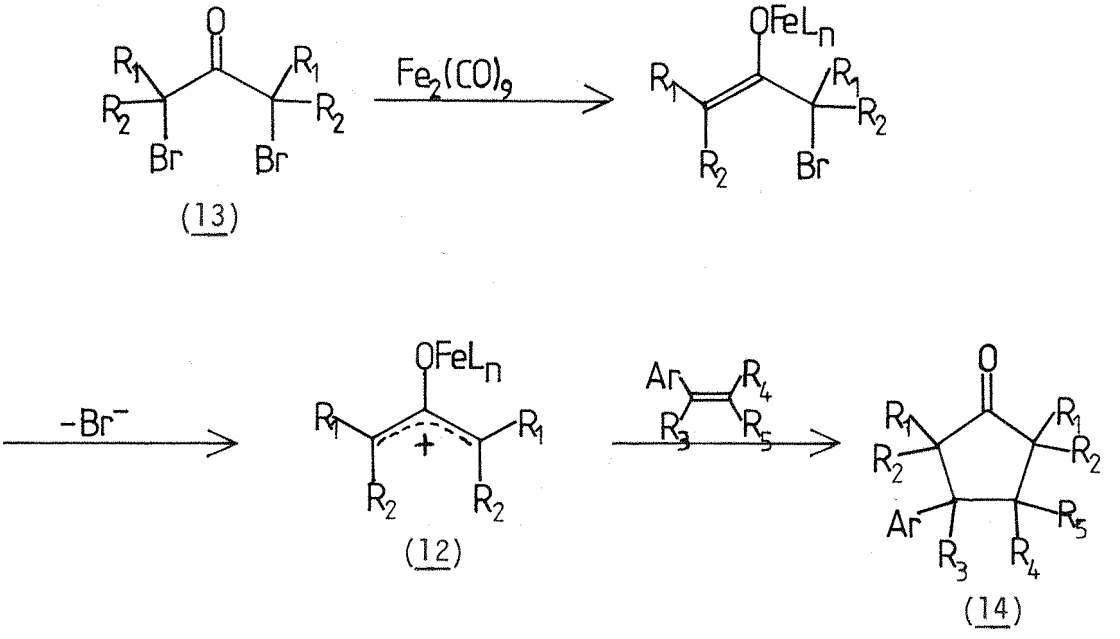


(10) (11)

Scheme 3

2-thiomethylenecyclohexanone with lithium diisopropylamide generated a thioallyl anion (10), which reacted with ethyl acrylate and diethylfumarate to afford hydrindanones of structure (11) (Scheme 3)[7].

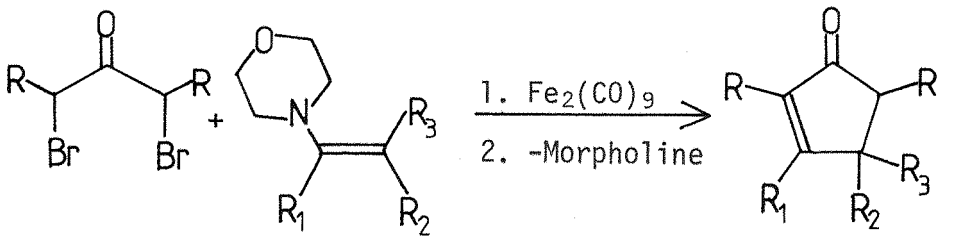
In recent years a variety of (3+2) cycloaddition reactions have appeared in the literature, involving transition metal organometallic complexes. Noyori *et al* discovered that the cationic 2-oxyallyl species (12), generated by the reaction of α, α'-dibromoketones (13) with diiron nonacarbonyl[8,9], could be trapped with aromatic olefins to give the corresponding 3-arylcyclopentanones (14), in fair to good yields (Scheme 4)[10,11]. This reaction has been applied to the synthesis



(13) (12) (14)

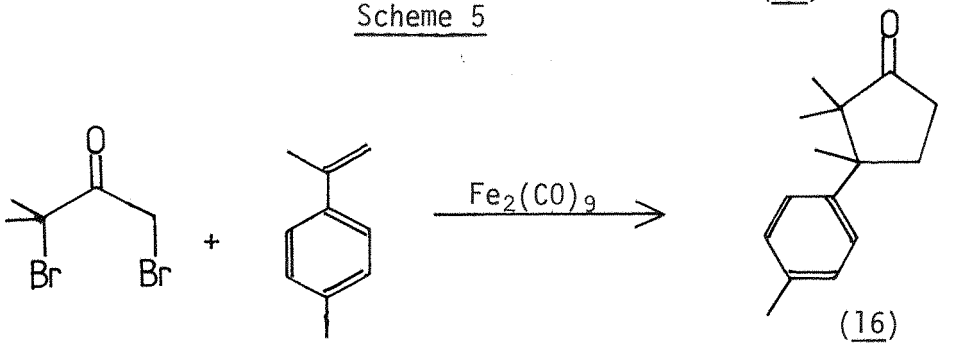
Ln = Br, CO, solvent, etc; R_1 - R_5 = alkyl, aryl or H

Scheme 4



(15)

Scheme 5

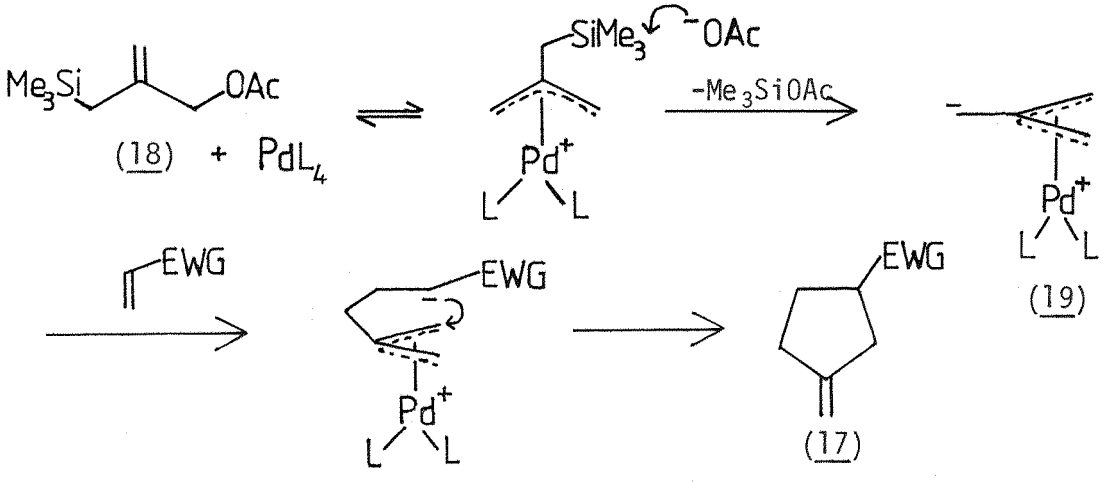


(16)

Scheme 6

of cyclopentenones (15, Scheme 5)[12,13], and a cuprene type terpene, α-cuparenone (16, Scheme 6)[14].

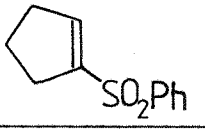
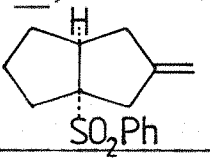
The preparation of methylenecyclopentane derivatives (17) has recently been accomplished by Trost and Chan[15], using a palladium (0) catalyst. They found that in the presence of tetrakis(triphenylphosphine) palladium, 2-acetoxymethyl-3-allyltrimethylsilane (18) could be reacted with olefins bearing an electron-withdrawing group (EWG = $-CO_2R$, -CN, -COR, $-SO_2$), resulting in the formation of the cycloadduct (17). This annulation reaction is thought to proceed via a zwitterionic intermediate (19), which adds to the olefin in a stepwise manner (Scheme 7)[16]. Table 1 illustrates some of the products and yields obtained.



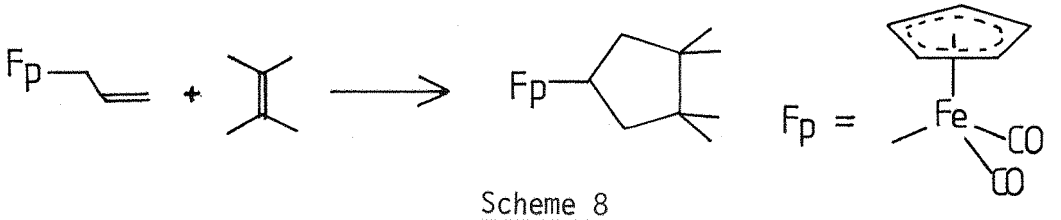
Scheme 7

TABLE 1

Methylenecyclopentane Annulations[15]

Olefin	Product	Yield (%)
Methyl acrylate	15, EWG = $-CO_2Me$	68
Acrylonitrile	15, EWG = -CN	35
Methyl vinyl ketone	15, EWG = -COMe	30
		58

The metal assisted (3+2) cycloaddition reaction of dicarbonyl (η^5-cyclopentadienyl) (η'-allyl)iron complexes [hereafter denoted as (η'-allyl)Fp complexes] with unsaturated units (Scheme 8) has been extensively investigated by Rosenblum[17-21] and by Wojcicki[22-25]. This process could provide a viable route to precursors in the synthesis of



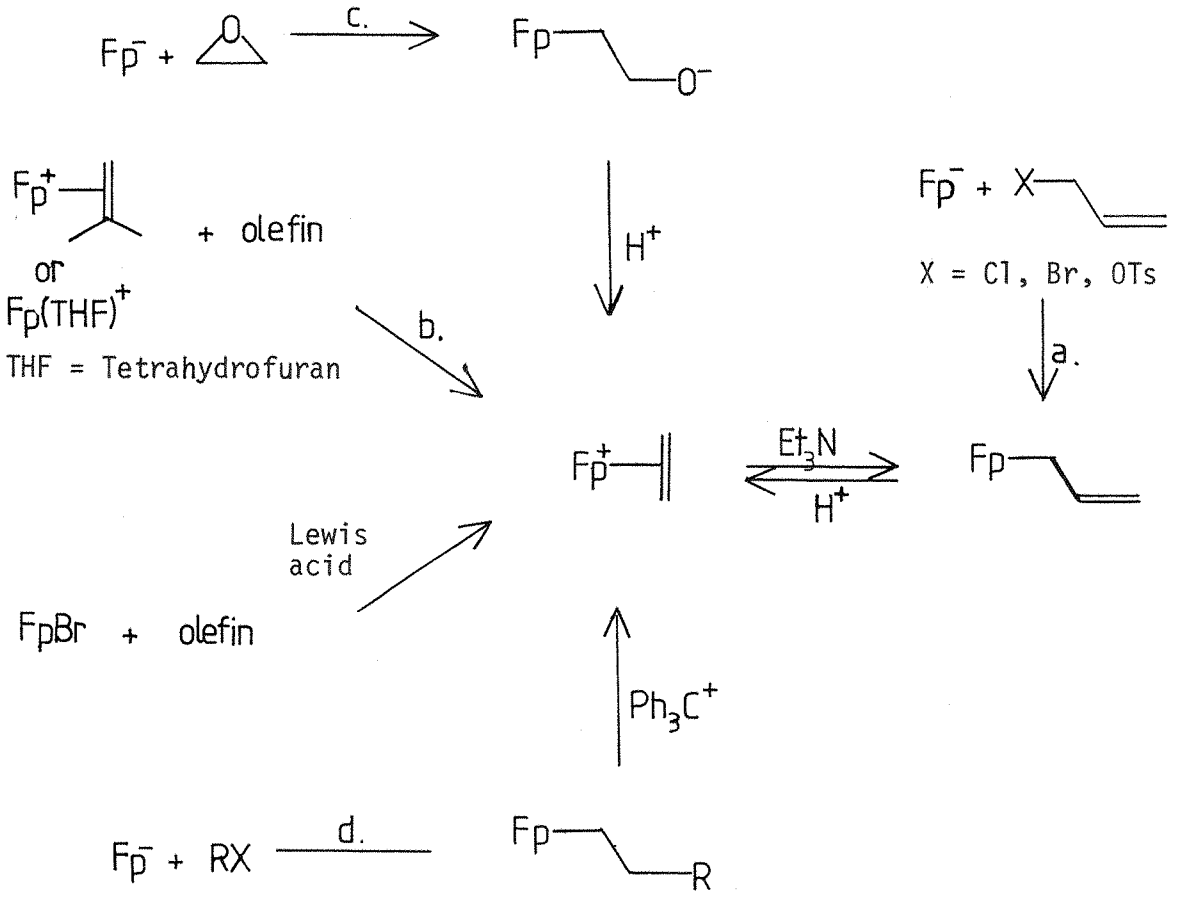
Scheme 8

a variety of cyclopentanoid natural products. Therefore, as a background to the present study, a brief review of the preparation, reactions and demetalation of dicarbonyl(η^5-cyclopentadienyl)iron (i.e. Fp) complexes is presented.

General methods for the preparation of (η'-allyl)Fp complexes

Two general methods have been reported for the preparation of (η'-allyl)Fp complexes; that of direct metalation of allyl halides or tosylates[21,24,26-28] with the dicarbonyl(η^5-cyclopentadienyl)ferrate

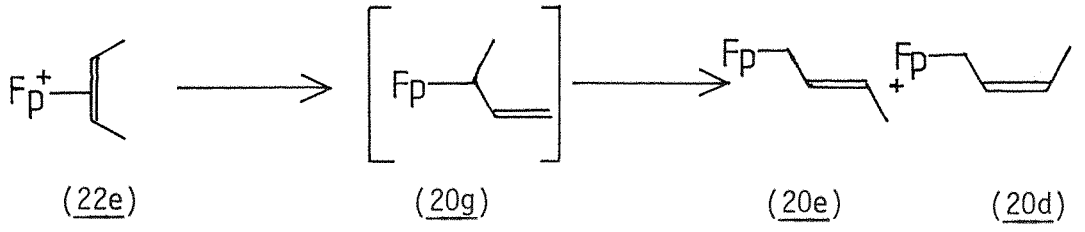
anion (Fp^-)[29], or by the deprotonation of dicarbonyl (η^5-cyclopentadienyl)(η^2-olefin)iron cations [$Fp(\eta^2\text{-olefin})^+$][18,20,21]. These olefin complexes are in turn available from a number of sources. The first reported preparations included the reaction of FpBr with simple olefins in the presence of a Lewis acid, usually aluminium trichloride[30], protonation of (η'-allyl)Fp complexes[26], and hydride abstraction from alkyl-Fp complexes[31]. More recently, these cations have been prepared by the reaction of the Fp anion with an epoxide followed by treatment with acid[32], and through an exchange reaction with the readily dissociable Fp(isobutylene)[21,23] and Fp(tetrahydrofuran)[34] cations. Scheme 9 provides a summary of these transformations, which are treated in more detail below.



Scheme 9

(a) Metalation

The metalation of simple allyl chlorides with the complexed Fp anion was first reported in 1963 by Green and Nagy[26], and has since been widely used for the preparation of a large number of primary and secondary (η'-allyl)Fp complexes (20 and 21)[21,24,27,28]. The starting materials, products and yields of some of the metalation reactions investigated are summarised in Table 2. It has been discovered[21,27] that, in general, allyl chlorides give higher yields than the corresponding bromides or tosylates. In addition, reactions which could lead to either primary or secondary (η'-allyl)Fp complexes were found to yield only the former[27]. This result may be due to preferential metalation at a primary carbon atom. However, it has been observed[21] that (20d) and (20e) are formed from the deprotonation of the Fp(cis-2-butene) cation (22e) with triethylamine (Scheme 10). As the initial product in this reaction



Scheme 10

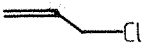
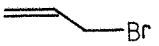
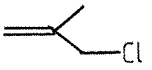
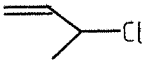
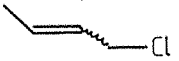
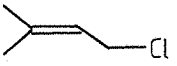
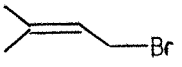
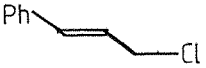
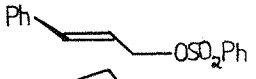
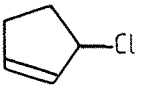
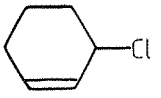
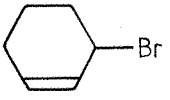
must be the isomeric (1-methallyl)Fp complex (20g), then metalation at a secondary carbon atom followed by allylic rearrangement cannot be excluded as an alternative mechanism.

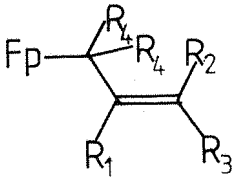
(b) Synthesis of Fp(olefin) cations

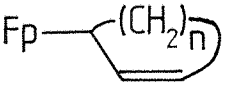
A variety of methods are now available for the synthesis of Fp(η^2-olefin) cations (22 and 23). The most common method is an exchange reaction (reaction b, Scheme 9) with the Fp(isobutylene) complex (22b)[21,23] or Fp(tetrahydrofuran) [Fp(THF)] complex[34], achieved by heating a chlorocarbon solution of the cation in the presence of an excess of displacing olefin. This reaction is limited however to the formation of cations more stable than (22b) or the Fp(THF) complex, and stability generally decreases with olefin substitution. The yields obtained for a number of simple olefins are summarised in Table 3.

TABLE 2

(η'-allyl)Fp complexes prepared by metalation

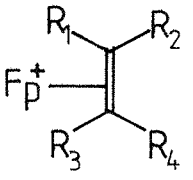
Allyl species	Product	Yield (%)	Ref.
	20a	91	21,26
	20a	25	21
	20b	88	21,24
	20d+e (1:2)	94	21
	20d+e (3:4)	84	21
	20c	88	28
	20c	52	21
	20f	72	28
	20f	22	21
	21a	60	21
	21b	91	21
	21b	6	21

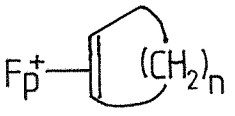




	R_1	R_2	R_3	R_4
20a	H	H	H	H
b	Me	H	H	H
c	H	Me	Me	H
d	H	Me	H	H
e	H	H	Me	H
f	H	H	Ph	H
g	H	H	H	Me,H

	n
21a	2
b	3





	R_1	R_2	R_3	R_4
22 a	H	H	H	H
b	Me	Me	H	H
c	H	H	H	Me
d	H	H	H	Et
e	H	Me	H	Me
f	Me	H	H	Me
g	H	H	H	Ph
h	Ph	H	H	Ph
i	H	Ph	H	Ph
j	H	H	H	$CH{=}CH_2$
k	H	H	H	CHO
l	Me	H	H	CO_2Et
m	H	H	H	CH_2OMe

	n
23 a	2
b	3
c	4
d	5

TABLE 3

Yields of $[Fp(\eta^2\text{-olefin})]BF_4$ from the exchange reaction

Olefin	Yields from 22b (%)	Yields from the Fp(THF) cation (%)	Yields from the BF_3 reaction (%)
Ethylene	44	92	-
Cyclopentene	100	-	-
Cyclohexene	2	17	92
Cycloheptene	100	75	99
Cyclooctene	51	-	-
1,4-cyclohexadiene	10[a]	80[a]	98[a]
1,5-Cyclooctadiene	80[a]	78[a]	86[a]
Norbornadiene	54[a]	89[a]	-

[a]Yield of 1:1 adduct

The importance of steric factors in the exchange reaction is demonstrated by the low yields obtained with cyclohexene. It has been postulated that this result is due to serious steric interactions between the organometallic radical and an axial homoallylic proton in the ring, thus preventing the incoming olefin from displacing the isobutylene or THF ligands. To overcome this problem Reger and Coleman[34] bubbled boron trifluoride through a methylene chloride solution containing the Fp(THF) complex and the olefin in order to complex out the THF as a BF_3-THF adduct. Under these conditions the yield of the cyclohexene complex was improved to 92%.

In such circumstances where the exchange process cannot be employed, the epoxide reaction sequence (reaction c, Scheme 9)[32] provides an alternative and facile method for the synthesis of the required complex cation. Treatment of the epoxides at room temperature with the Fp anion, one of the most powerful organometallic nucleophiles known[35], results in their rapid conversion to the corresponding alkoxide. These, on reaction *in situ* with two equivalents of fluoroboric or hexafluorophosphoric acid, are converted instantaneously, and in high overall yield, to their respective Fp(η^2-olefin) complexes. Table 4 provides a summary of some cations prepared from the corresponding epoxides.

TABLE 4

Conversion of epoxides to Fp(η^2-olefin) cations

Epoxide	Fp(η^2-olefin) cation	Yield (%)[32]
Ethylene oxide	22a	90
Propylene oxide	22c	91
1-Butene oxide	22d	91
cis-2-Butene oxide	22e	64
trans-2-Butene oxide	22f	50
Styrene oxide	22g	62
trans-Stilbene oxide	22h	83
cis-Stilbene oxide	22i	82
Cyclopentene oxide	23a	47
Cyclohexene oxide	23b	60
Cycloheptene oxide	23c	31
Butadiene oxide	22j	91
Acrolein oxide	22k	90
trans-Ethyl crotonate oxide	22l	96
3-Methoxypropene oxide	22m	78[a]

[a]Ref 20

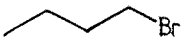
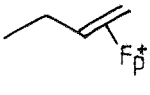
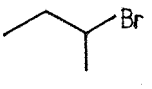
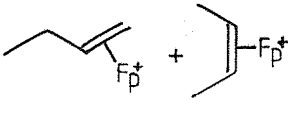
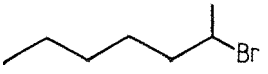
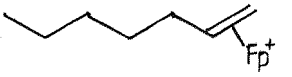
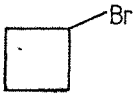
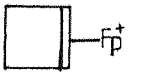
The transformation of epoxides to olefin complexes was found to be a highly stereoselective process, as *cis*- and *trans*-2-butene, *cis*- and *trans*-stilbene and *trans*-ethyl crotonate were all converted to the corresponding olefin complexes with greater than 98% retention of configuration[32]. This stereochemical result was readily accounted for[32] by a mechanism involving initial S_N2 opening of the epoxide, followed by a *trans* migration of the organometallic group concerted with loss of water from the oxonium ion formed on protonation of the alcohol. The same group of workers[32] discovered that the relative rates of reaction of the Fp anion with terminal and internal epoxides reflects the large steric demand of the reagent. Thus, while the reaction with terminal epoxides is essentially complete within several minutes, several hours are required for complete consumpton of internal epoxides.

Compounds containing functional groups susceptible to nucleophilic attack can also be reacted in this manner, as demonstrated by the conversion of the epoxides of crotonate and acrolein in high yield to the olefin complexes (22k) and (22l)

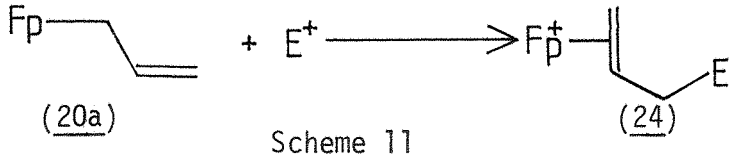
Fp(η^2-olefin) complexes may alternatively be prepared by a two step process involving initial addition of the Fp anion to an alkyl halide, followed by β-hydride abstraction with tritiltetrafluoroborate (reaction d, Scheme 9)[21,36,37]. Some examples of the products obtained from this reaction are presented in Table 5.

TABLE 5

Preparation of Fp(η^2-olefin) cations from alkyl halides

Alkylhalide	Yield of alkyl-Fp complex (%)	Fp(η^2-olefin) BF_4	Yield	Ref
	96		50	36
	30		82	36
	40		82	37
	50		81	21

A small number of C-3 substituted olefin complexes have been synthesised by reaction of the simple (η^3-allyl)Fp complex (20a) with cationic electrophiles (Scheme 11)[20]. Table 6 summarises the range of complexes obtained in this manner.

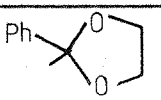


(20a) (24)

Scheme 11

TABLE 6

C-3 substituted Fp(η^2-olefin) cations[20]

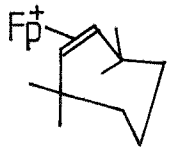
Complex	E	Yield %	Complex	E	Yield %
24a	$-SO_2Me$	80	24e		95
24b	-Me	85	24f	$-CH(OMe)_3$	a
24c	-COMe	a	24g	-Br	87
24d	$-CH(OMe)_2$	78			

[a]Yield not given

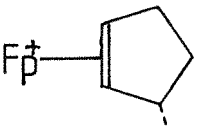
(c) Deprotonation of Fp(η^2-olefin) cations

Deprotonation of the readily available Fp(η^2-olefin) species (22) and (23) with tertiary amines occurs rapidly below room temperature[18,20,21] and constitutes a second general route to (η^3-allyl)Fp complexes. The reaction appears to be highly stereospecific, proceeding by loss of an allylic proton *trans* to the metal-olefin bond. Thus, while the cyclopentene, cyclohexene and cyclooctene complexes (23a,b,d) are smoothly deprotonated, the cycloheptene complex (23c) is inert. An

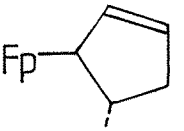
examination of models[18] indicated that, in contrast to the situation in the other cycloalkene complexes, no *trans*-allylic protons are available in the preferred conformation (25) of complex(23c).



(25)



(26) a X=CN, b X=SO_3H, c X=Me

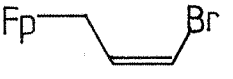


(27)

A further example of the stereospecificy of the deprotonation process is the conversion of the cyclopentene complexes (26a-c) to the (η'-allyl)Fp complexes (27a-c), respectively[18]. This result is especially striking for (26a,b), in which the cyano and sulphonic acid groups would otherwise be expected to control the course of the reaction.

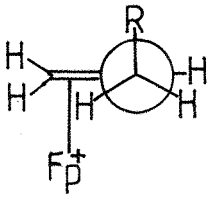
The deprotonation of monosubstituted Fp(η^2-olefin) cations generally leads to predmoninant, or exclusive, formation of (*trans*-η'-allyl)Fp complexes[20]. This suggested that thermodynamic factors of product stability were determinant in the reaction. However, this did not account for the exclusive formation of the (*cis*-η'-allyl)Fp complexes (28) and (29) in the deprotonation of (22m) and (24g). Rosenblum also showed[20] that the

(28)

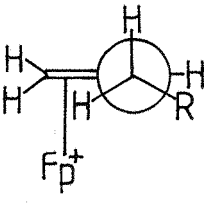


(29)

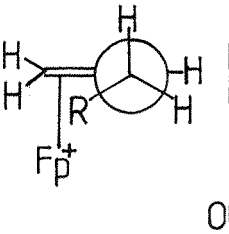
cis-methoxyl complex is not formed by isomerisation of an initially generated *trans*-isomer. It would therefore appear that this reaction is best explained in terms of a kinetic deprotonation process, in which conformational effects play a dominant role[20]. Hence, although conformation (30a) for monosubstituted olefin complexes may be favoured on steric grounds, for deprotonation to occur the reaction must proceed preferentially *via* (30b) and (30c). Of these, the less sterically hindered conformer (30b) would yield (*trans*-η'-allyl)Fp complexes on deprotonation.



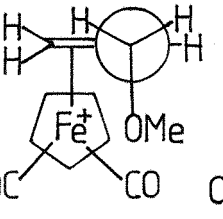
(30a)



(30b)



(30c)



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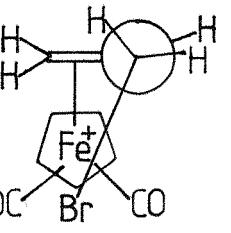
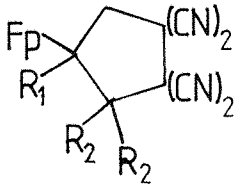


(32)

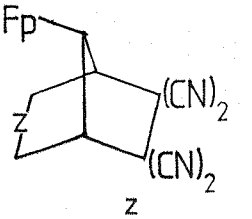
With respect to cations (22m) and(24g), models have indicated[20] that the methoxyl oxygen atom in (22m) may readily approach within bonding distance of one of the carbonyls (31), whereas the larger carbon-bromine bond in (24g) allows the halogen atom to interact with both ligands (32). These cations, on deprotonation, must give rise to (*cis*-η'-allyl)Fp complexes.

Metal assisted (3+2) cycloaddition reactions

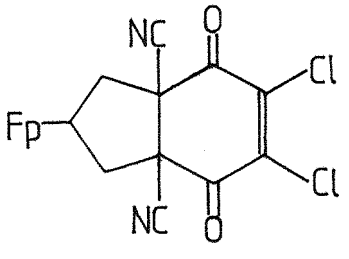
In 1971 it was observed[17] that the simple (η'-allyl)Fp complex (20a) entered into a rapid (3+2) cycloaddition reaction with tetracyanoethylene (TCNE) at room temperature. This reaction has since been applied to the synthesis of a large number of cyclic and bicyclic TCNE adducts (33)and (34) in high yields.[20,21,24]



		R_1	R_2	Refs
33	a	H	H	17, 21
	b	Me	H	17, 21
	c	H	Me	21, 24
	d	H	H, Me	21, 25
	e	H	H, Ph	21,
	f	H	H, OMe	20
	g	H	H, Br	20
	h	H	H, COMe	20
	i	H	H, $CH(OMe)_2$	20
	j	H	H, $CHPh(OCH_2)_2$	20
	k	H	H, CO_2Me	20



		z
34[21]	a	CH_2
	b	$(CH_2)_2$
	c	$(CH_2)_3$
	d	$(CH_2)_4$
	e	(CH=CH)



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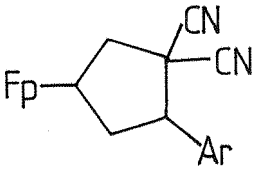

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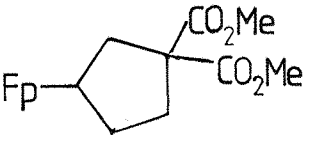

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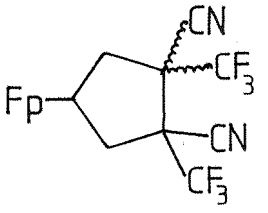
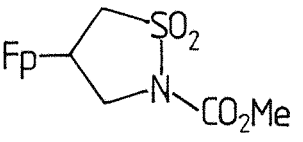


(38)



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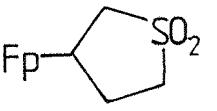

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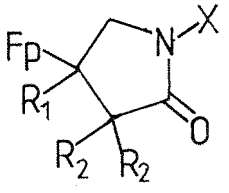
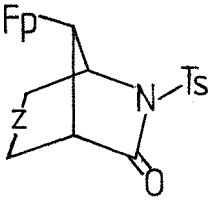


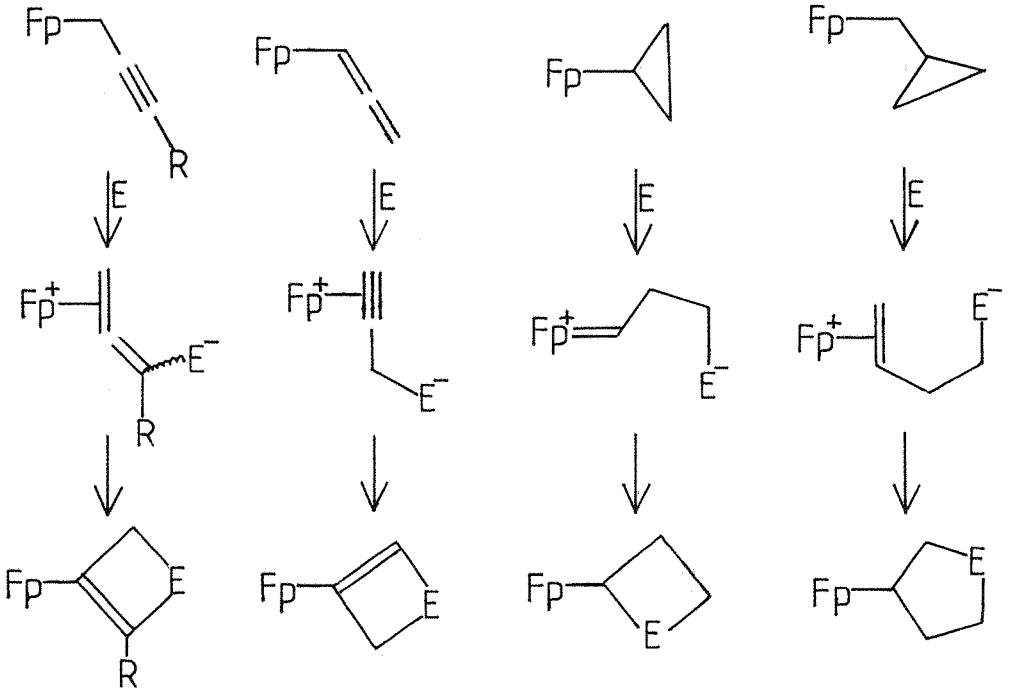
	R_1	R_2	X	Refs.
41 a	H	H	SO_2Cl	18, 21
b	H	Me	SO_2Cl	22, 23
c	H	H, Ph	SO_2Cl	22, 23
d	H	M	Ts	18, 21
e	Me	H	Ts	18, 21
f	H	Me	Ts	21
g	H	H, Ph	Ts	21
h	H	H, OMe	Ts	20
i	H	H	Ms	18
j	H	H	$2,5\text{-}Cl_2C_6H_3$	18, 21
k	H	Me	$COCl_3$	21



		z
42[18,21]	a	$(CH_2)_2$
	b	$(CH_2)_3$
	c	(CH=CH)

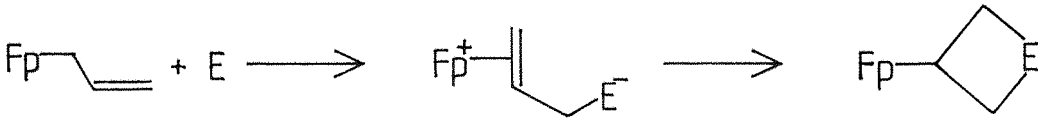
A variety of other electrophilic unsaturated moieties have been shown to undergo an identical (3+2) cycloaddition reaction with complex (20a). These moieties include dichlorodicyano-p-quinone[17], 2,2-dicyano-o-chlorostyrene, dimethylmethylenemalonate[21], 1,2-dicyano-1,2-bis(trifluoromethyl)ethylene[25], N-sulphonyl urethane[21], and sulphene[21], which on reaction with complex (20a) yield the adducts (35-40) respectively. Similarly, many isocyanates have been reacted with both acyclic and cyclic (η^1-allyl)Fp complexes to give condensation products, examples of whose structures are given by compounds (41) and (42)[18,20-23]. No products were obtained however with either p-quinone[17], tetrachloro-p-quinone[19], ethyl isocyanate[18] or phenyl isocyanate[18], in similar reactions.

A number of closely related metal assisted cycloaddition reactions in which the metal is acting as an electron donor centre, have also been observed with (η'-propargyl)iron[18,23-25,38-45], (η'-allenyl)iron[38], (cyclopropyl)iron[46] and (cyclopropylmethyl)iron[17] complexes (Scheme 12).



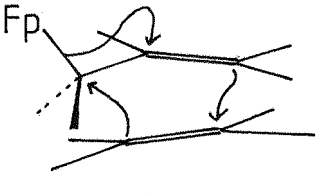
Scheme 12

Two different mechanisms have been formulated[17] to account for these (3+2) cycloaddition reactions; that of a two step process involving initial formation of a dipolar ion (43) and its subsequent collapse through an internal cyclisation reaction (Schemes 12 and 13), and a concerted ($\pi_{2a} + \pi_{2s} + \sigma_a$) process (Scheme 14). Of these, the



(43)

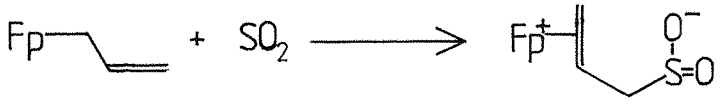
Scheme 13



Scheme 14

mechanism involving a substantial ionic intermediate is believed[17,24] to be the more likely from the following observations and comparisons.

(1) A dipolar metal-olefin complex (44) has been detected and characterised in the reaction of (20a) with SO_2[47] (which like TCNE, is a good electrophile).



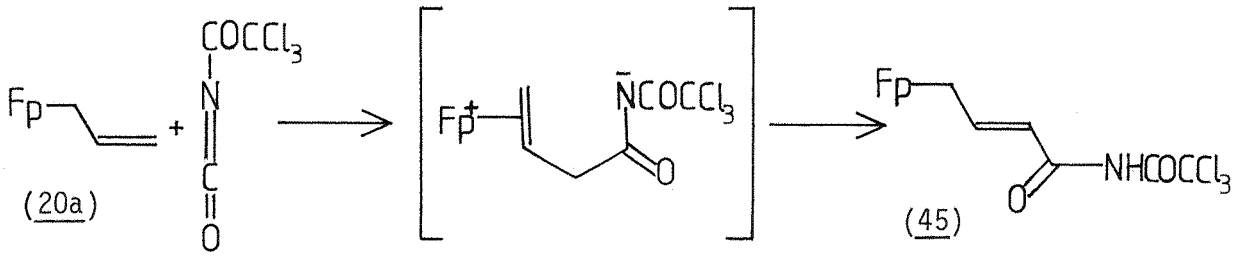
(20a) (44)

(2) The reactions of olefins with TCNE proceed via an ionic mechanism[48].

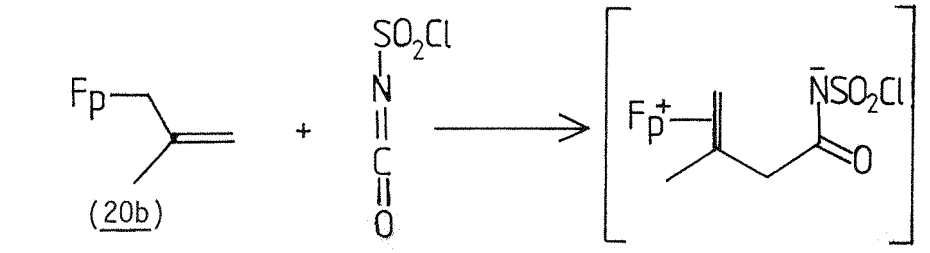
(3) The Fp complex has the capacity to stabilise the positive charge in both the dipolar intermediate and in the transition state leading to it, as demonstrated by the comparative stability of Fp(η^2-olefin) cations (22) and (23)[18,20,21,32,33].

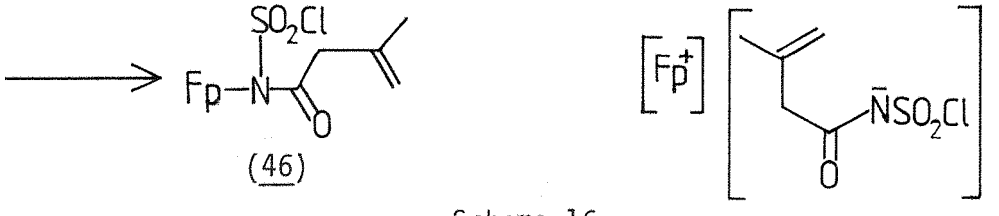
(4) The reaction between $FpCH_2C{\equiv}CCH_3$ and TCNE requires less than 60 sec. in acetonitrile, about 60 sec. in THF or benzene, and approximately 30 min. in pentane[24], this dependence of rate on the polarity of solvent being consistent with an ionic mechanism.

Further evidence of a dipolar intermediate is provided by a number of processes which have been observed to compete with closure of the zwitterion. These include proton transfer[21], insertion[23], and intramolecular zwitterion decomposition[18]. The former two processes lead to linear products, and are exemplified by the reaction of complex (20a) with trichloroacetyl isocyanate to give exclusively the *trans* product (45) (Scheme 15)[21], and by the reaction of (20b) with chlorosulphonyl isocyanate, which affords complex (46) as the sole product (Scheme 16)[23].



Scheme 15





Scheme 16

It is interesting to note that insertion does not occur between complex (20b) and toluenesulphonyl isocyanate[18]. Instead a normal cyclisation product is isolated. This was thought to be due to increased anion stabilisation and hence a higher dipolar ion equilibrium concentration for the reaction leading to insertion, which would provide a competitive pathway for irreversible transformation of the dipolar ion, either by direct competition or by a mechanism involving prior dissociation to an ion pair (47)[21].

Intramolecular zwitterion decomposition is illustrated by the reaction of chlorosulphonyl isocyanate and methyl N-sulphonylmethane with the cyclic (η^3-allyl)Fp complex (21a), which exclusively yield the cations (26a) and (26b) through loss of the chlorosulphonate anion or methyl cyanate from the presumed intermediate dipolarion[18]. In these examples, the zwitterion is highly stabilised and displacement by the anionic terminus at the metal is not stereochemically possible, hence irreversible decomposition of the anion is preferred over cyclisation[21].

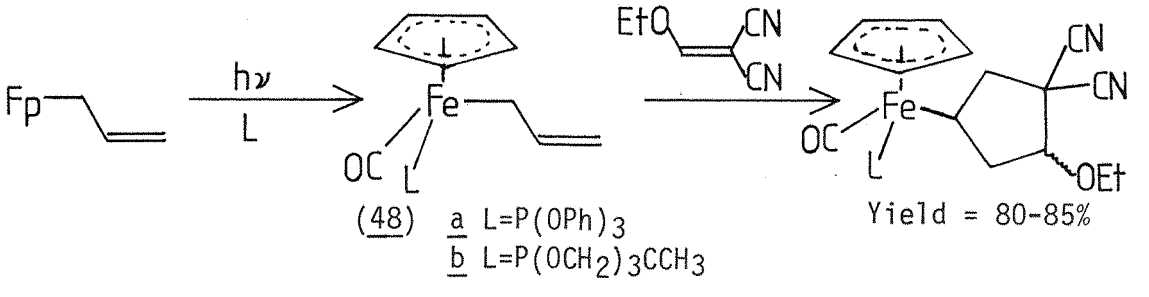
The observation that p-quinone and tetrachloro-p-quinone fail to react with simple (η'-allyl)Fp complexes is probably due to their inability to stabilise the substantial negative charge of the dipolar ion. This is indicated by a comparison of their electron affinities[49] with those of the more reactive olefins (Table 7).

TABLE 7

Electron affinities[49] of the olefins investigated by Rosenblum and Giering[17]

Olefin	Electron Affinity (eV)
TCNE	2.90
2,3-Dichloro-5,6-dicyano-p-quinone	3.00
Tetrachloro-p-quinone	2.50
p-Quinone	1.98

An increase in reactivity of the allyl system has recently been achieved by Rosenblum and Waterman[50] by replacing a carbon monoxide group of the simple Fp complex (20a) with $P(OPh)_3$ or $P(OCH_2)_3CCH_3$. They found that whereas no reaction occurred between ethoxymethylene-malononitrile and (20a), cyclic products were obtained with both the phosphite complexes (48a) and (48b) (Scheme 17) due to the increased electron density at the metal. To measure the relative reactivities



Scheme 17

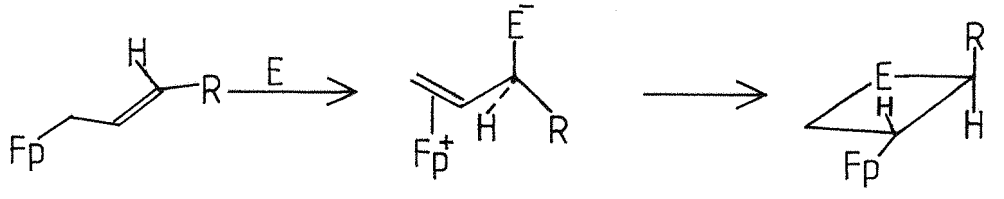
of these two complexes, competitive reactions were performed with limiting quantities of electrophilic olefins, 2,2-dicyano-styrene and ethoxymethylenemalononitrile. The results of these experiments are summarised in Table 8.

TABLE 8

Relative reactivities of (η'-allyl) complexes

Electrophile	Complex 20a	48a	48b
$PhCH=C(CN)_2$	1	180	
$PhCH=C(CN)_2$		1	5
$EtOCH=C(CN)_2$		1	10

The stereochemistry of metal assisted cycloaddition reactions has been shown[21] to correspond to a suprafacial addition of the electrophile to the allyl complex. Therefore, any geometric isomerism associated with a substituent at C-3 in the (η'-allyl)Fp complex is preserved in the product by the relationship between this substituent and the adjacent Fp group (Scheme 18)[21]. This has been demonstrated by

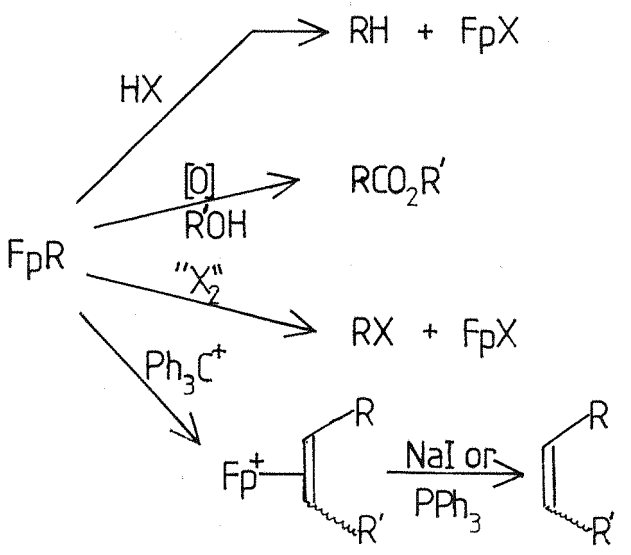


Scheme 18

the formation of TCNE adduct (33d) with a *cis:trans* ratio of 3:17 from an identical ratio of *cis*- and *trans*-butenyl complexes (20d and 20e).

Demetalation

The replacement of the organometallic group of alkyl-Fp complexes with an organic function has been carried out using a variety of procedures. These are outlined in Scheme 19.



Refs : 51-55

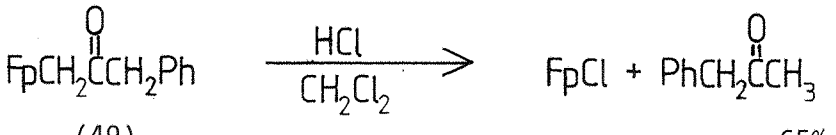
Refs : 56-60

Refs : 20,53,58, 61-64

Refs : 32,36,37 52,60

Scheme 19

Only a small number of proton cleavage reactions have been reported involving alkyl-Fp complexes. An example, is the cleavage of complex (49) by hydrogen chloride (Scheme 20)[54]. This type of reaction has been shown to proceed with a high degree of stereospecificity[55], as



(49)

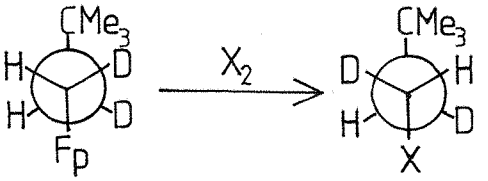
65%

Scheme 20

treatment of *cis*- or *trans*-4-methylcyclohexyl-Fp (59 and 60) with HCl-d or trifluoroacetic acid-d, gives the deuterated product with greater than 85% retention of configuration.

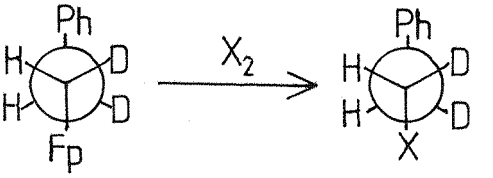
In comparison, halogenolysis of Fp-C bonds occurs with either inversion[58,61,63] or retention[53,62,64] depending on the alkyl-Fp complex investigated. For example, complex (50) was cleaved with inversion

(Scheme 21)[61,63] and (51) with retention (Scheme 22)[62,64]. To account for these results, a mechanism involving one and/or two oxidation steps (Scheme 23) has been postulated[53,64]. It is thought that in the case of



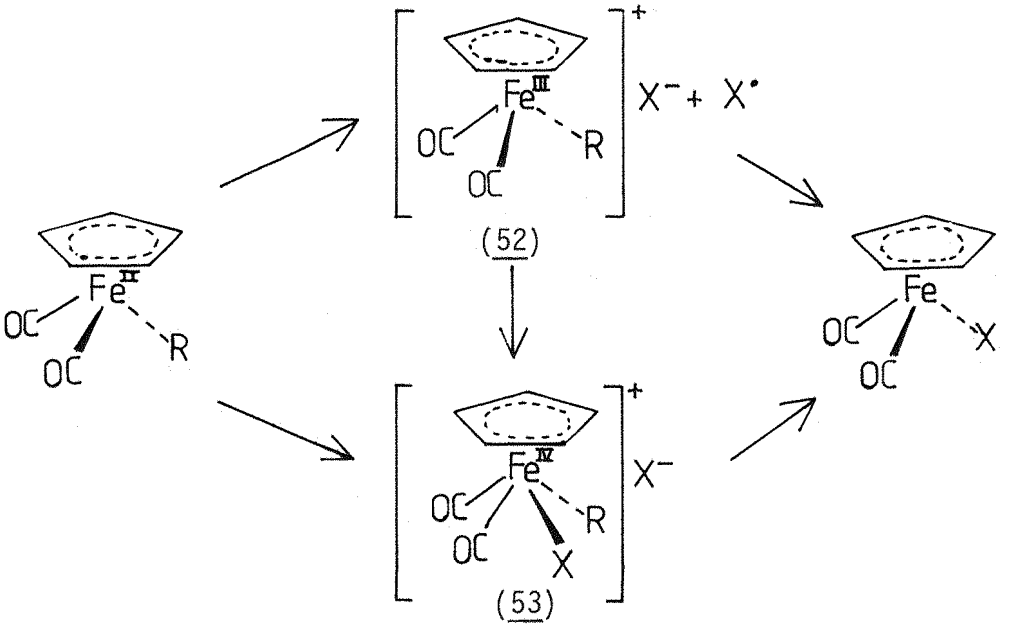
(50)

Scheme 21

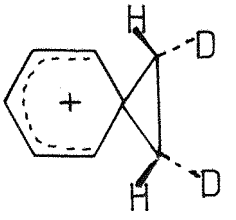


(51)

Scheme 22



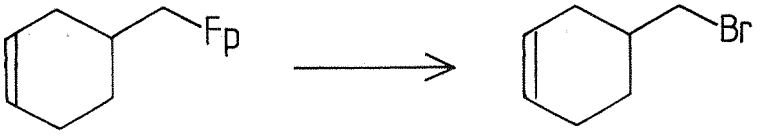
Scheme 23



(54)

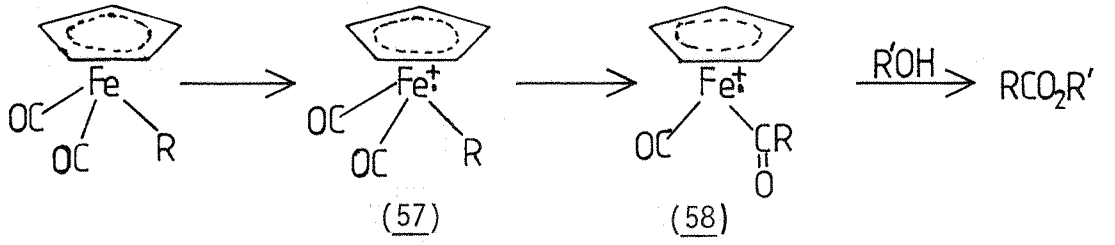
the phenylethyl iron derivative (51), the reaction probably proceeds through intermediate (53), which dissociates to yield FpBr and the phenonium ion (54). Backside nucleophilic attack will then lead to retention of configuration. No phenonium-like intermediate is possible however for the t-butyl analogue, and therefore inversion probably proceeds *via* intermediate (52) either by homolysis of the iron-carbon bond to give a radical which could react with X• with epimensation, or by direct attack on the α-carbon atom of the alkyl group by X• or X^- [64].

Cleavage of primary alkyl-Fp derivatives with N-bromopyridinium bromide or N-bromopyridinium perbromide was found to be a very rapid reaction and could be effected selectively at -78°C in the presence of a double bond[21]. This was illustrated by the conversion of (55) to (56)[21].



(55) (56)

The replacement of the Fp group with a carboxylic ester function has been readily achieved by the oxidation of alcoholic solutions of alkyl-Fp complexes with cupric chloride[57,59], ceric salts[56,60], oxygen[58] or bromine[58]. The reaction has been rationalised as a three step process (Scheme 24)[56,57] proceeding through the oxidised form of the iron complex (57), and that ligand transfer (R to carbonyl) within such a



(57) (58)

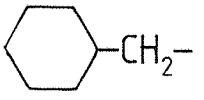
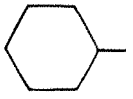
Scheme 24

species is greatly facilitated by the increased electron deficiency at the carbonyl carbon atom due to diminished back bonding from the metal. Subsequent nucleophilic displacement of the rearranged cation (58), which again is likely to be facilitated by the positive charge of the iron, results in the formation of the esterified product.

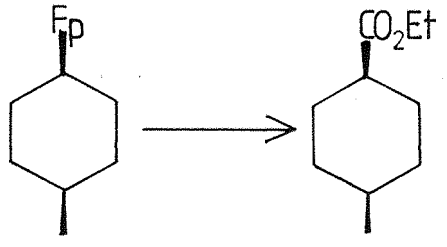
Nicholas and Rosenblum[57] have found that, in general, lower yields are obtained with secondary alkyl-Fp complexes and when secondary and tertiary alcohols are employed (Table 9).

TABLE 9

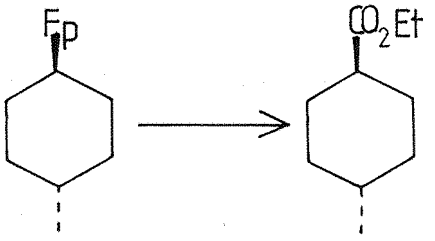
Yields of carboxylic esters from alkyl-Fp complexes

FpR	Alcohol (R'OH)	Yield of ester, RCO_2R' (%)
	EtOH	85
	i-PrOH	60
	t-BuOH	
	MeOH	64
	EtOH	48

The reaction appears to be highly stereospecific occurring with retention of configuration. Thus, oxidative carboxylation of *cis*- and *trans*-4-methylcyclohexyl-Fp (59 and 60) with cupric chloride in ethanol gives the corresponding *cis*- and *trans*-ethyl esters (61 and 62), respectively[57].

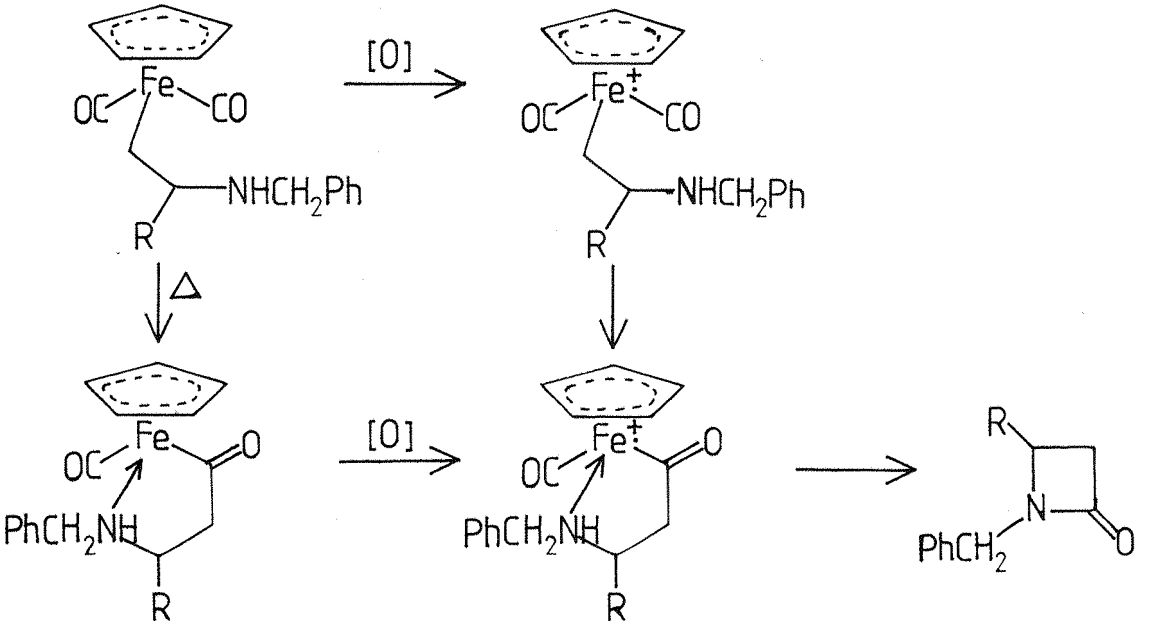


(59) (61)



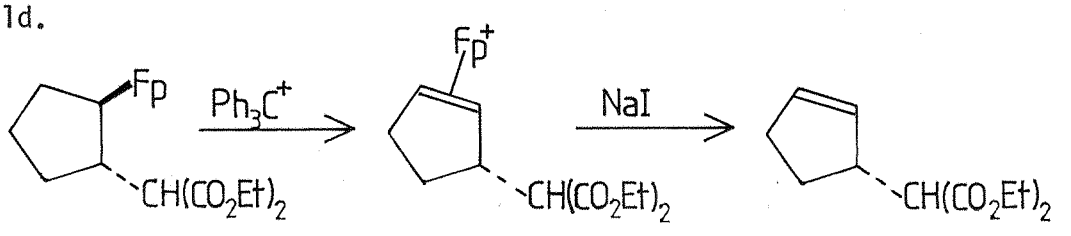
(60) (62)

This type of oxidative process has recently been used to synthesise a number of mono- and bicyclic β-lactams (Scheme 25)[65]. Moderate yields of the required product were obtained with the oxidising reagents lead dioxide and silver oxide.



Scheme 25

Conversion of alkyl-Fp complexes to Fp(η^2-olefin) cations, followed by treatment with sodium iodide to liberate the alkene, constitutes a fourth general method for replacing the Fp group with an organic function[32,36,37,60]. Baird *et al*[36,37] have utilised this process to convert cations of the type listed in Table 5 into their respective olefins in essentially quantitative yields. Similarly, treatment of cation (64) (generated from the cyclopentyl complex (63) by reaction with trityl tetrafluoroborate) with sodium iodide afforded the olefin (65) in 84% yield.



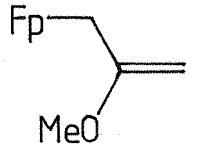
(63) (64) (65)

CHAPTER TWO

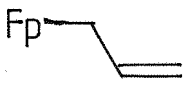
Reactions of Dicarbonyl (η^5-Cyclopentadienyl) (η'-allyl)iron Complexes with Olefins and Acetylenes

Introduction

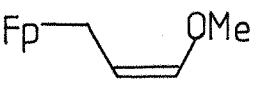
Reactions of dicarbonyl (η^5-cyclopentadienyl) (η'-allyl)iron complexes have so far been limited to those involving extremely electron-deficient olefins. It was considered that the use of an electron-rich (η'-allyl)Fp complex might extend the scope of these processes. Dicarbonyl (η^5-cyclopentadienyl) (η'-2-methoxyallyl)iron (66) was therefore prepared[66,67] and its reactions with a variety of activated olefins and acetylenes, together with those of the simple (η'-allyl)Fp complex (20a) and (η'-3-methoxyallyl)Fp complex (28), investigated.



(66)



(20a)



(28)

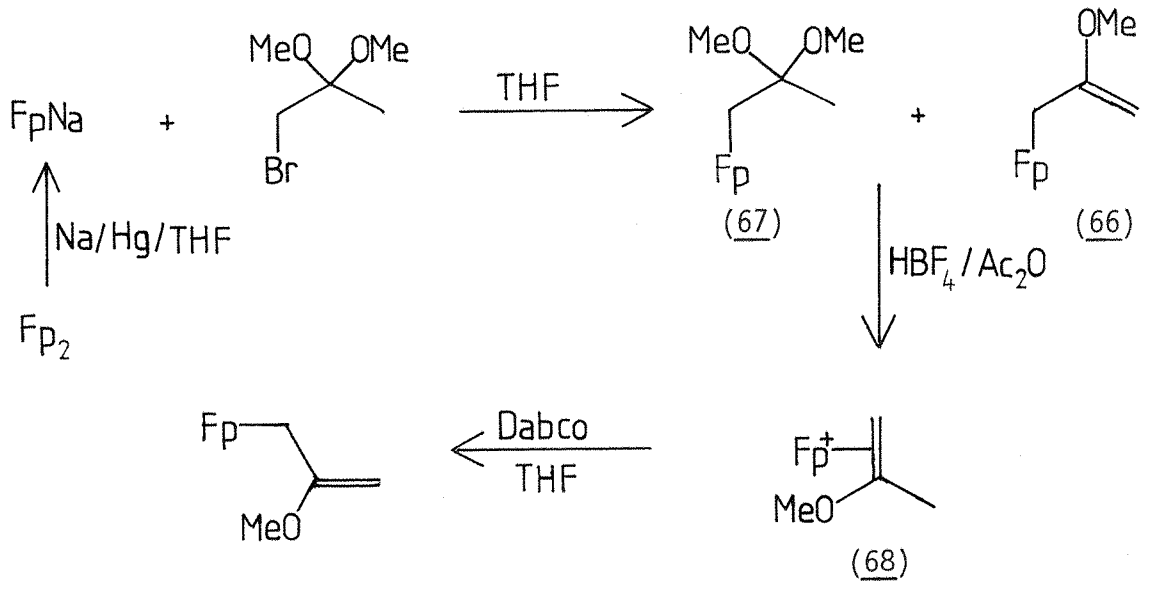
Results and Discussion

1. Synthesis of (η'-allyl)Fp complexes

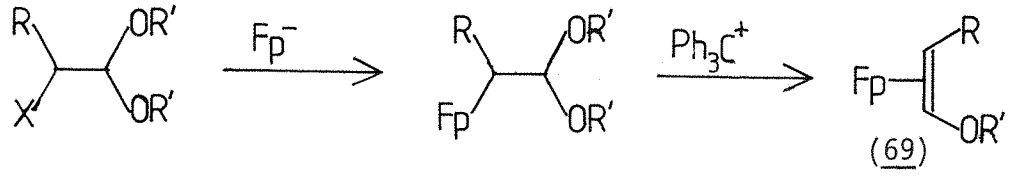
(a) Dicarbonyl (η^5-cyclopentadienyl) (η'-2-methoxyallyl)iron (66)[66,67]

The (η'-2-methoxyallyl)Fp complex (66) was prepared by the reaction sequence outlined in Scheme 26. Treatment of 1-bromo-2,2-dimethoxypropane with NaFp (generated from Fp_2 and 4% Na/Hg amalgam) in tetrahydrofuran (THF), gave the expected ketal (67) together with considerable quantities ($\sim$ 40%) of the methoxyallyl complex (66). This air sensitive mixture was converted into the air stable crystalline tetrafluoroborate salt (68) (isolated as the exclusive product in 75% overall yield) by treatment with fluoroboric acid in acetic anhydride. Similar cationic acetal species (69) have been prepared by Rosenblum *et al*[68] in an anal gous manner (Scheme 27).

Conversion of the cationic salt to the allyl complex by a deprotonation reaction was attempted using a variety of bases[69]. It was discovered, however, that in addition to the required product, several other Fp complexes could be formed in the reaction. These included the ketal (67), the hydrolysed product (70), olefins (71) and (72), and the ester complex (73). Table 10 provides a summary of the ratio of



Scheme 26



X = Cl,Br; R = H,Me; R' = Me,Et

Scheme 27

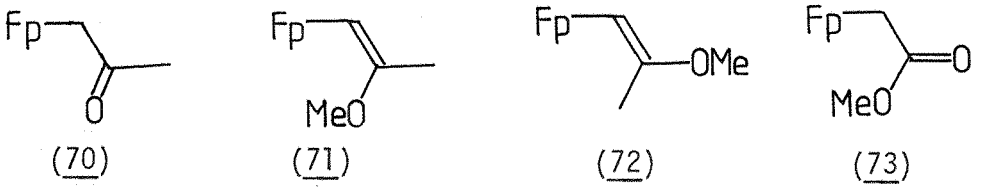


TABLE 10

Product ratios from the deprotonation of the Fp(η^2-olefin) cation (68)

Base[b]	Solvent[c]	Product ratio (±2%)[a] (66)	(67)	(70)	(71)	(72)	(73)
Dabco	CH_2Cl_2	46	4	17	15	7	10
Dabco	THF	74	∿1	7	7	6	7
NaH	THF	52	7	16	7	10	8
NaH	$MeOCH_2CH_2OMe$	67	11	21	-	-	-
Ph_3CLi	$MeOCH_2CH_2OMe$	69	14	12	-	-	5
$Et(^iPr)_2NOTs$	THF	32	8	4	19	25	12

(a) Estimated from the NMR spectrum of the crude reaction mixture

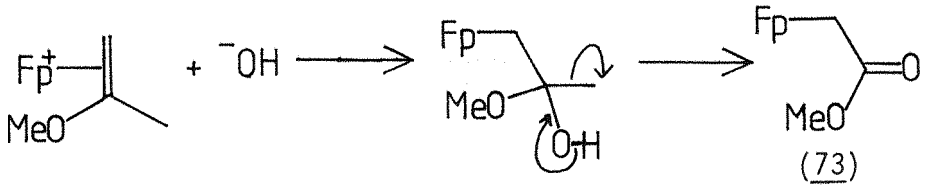
(b) Dabco = 1,4-diazobicyclo[2.2.2]octane

(c) THF = Tetrahydrofuran.

of products obtained with a number of bases. Triethylamine gave an adduct resulting from addition to the co-ordinated double bond. No products could be isolated using either n-butyllithium or lithium diisopropylamide.

From these results it was apparent that 1,4-diazobicyclo[2.2.2] octane (dabco) was the most convenient and successful reagent for this deprotonation, since it gave the allyl complex cleanly, in high yield (∿74%). The allyl complex was found to be extremely air and moisture sensitive, being readily hydrolysed to the ketone (70). Thus normal chromatographic procedures could not be used to purify (66) as such treatment led exclusively to the isolation of $FpCH_2COMe$[69]. However, as the cation (68) appears to be stable indefinitely when kept under an inert atmosphere, salt formation followed by deprotonation as required has proved to be a useful method of storage and regeneration of the 2-methoxyallyl complex.

An interesting by-product of the deprotonation reaction was the ester complex $FpCH_2CO_2Me$. This compound has also been prepared by the reaction of NaFp with methyl chloroacetate[68]. A mechanism can be postulated to account for its formation (Scheme 28), but it involves

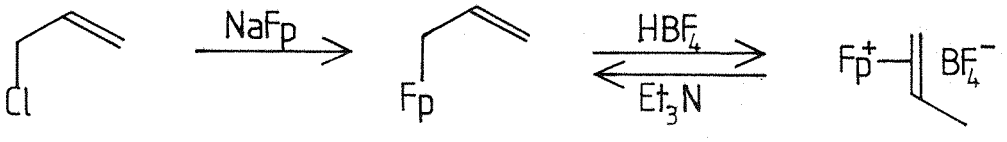


Scheme 28

preferential loss of a methyl anion over a methoxyl anion, which seems unlikely. Work by T.S. Abram[69] showed that the addition of water or acid did not cause an increase in the amount of ester formed. However, an increase was observed when hydroxide ion [e.g. $Ca(OH)_2$] was present in the reaction mixture. It was also observed that the addition of an excess of dabco resulted in none of the ester complex being formed. This suggests that a process competitive with deprotonation (such as Scheme 28) gives rise to (73).

(b) Dicarbonyl (η^5-cyclopentadienyl) (η'-allyl)iron (20a)

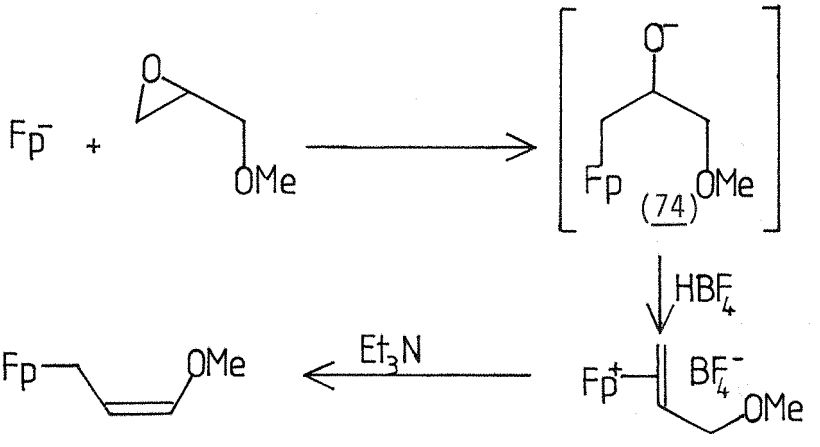
In a modification of the procedure described by Green and Nagy[26], allyl chloride was reacted with NaFp, and the product treated with fluoroboric acid to give the tetrafluoroborate salt in 86% overall yield. The allyl complex was regenerated quantitatively from the salt by treatment with triethylamine (Scheme 29).



Scheme 29

(c) Dicarbonyl (η^5-cyclopentadienyl) (η'-3-methoxyallyl)iron (28)

The *cis*-3-methoxyallyl complex (28) was prepared by the method of Rosenblum *et al*[20], by reacting the Fp anion with 1,2-epoxy-3-methoxypropane to give the intermediate alkoxide (74). This was converted *in situ*, to the tetrafluoroborate salt (72% overall yield) by the addition of fluoroboric acid. Reaction of this cation with triethylamine afforded the required allyl species in quantitative yield (Scheme 30).



Scheme 30

2. Reactions of (η'-allyl)Fp complexes with electron-deficient olefins and acetylenes

(a) General procedure

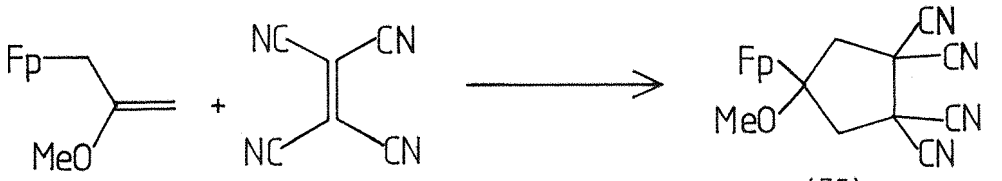
In a typical reaction the appropriate (η'-allyl)Fp complex was generated from the corresponding Fp(η^2-olefin)tetrafluoroborate salt by treatment with base, and then reacted in the crude form with an excess of the olefin or acetylene, all operations being performed in an inert atmosphere. Products were isolated by the removal of solvent under reduced pressure followed by column chromatography on neutral alumina (normally Act. III) or florisil.

(b) Reactions of dicarbonyl (η^5-cyclopentadienyl) (η'-2-methoxyallyl) iron (66)

(i) Tetracyanoethylene (TCNE)

Reaction of the (η'-2-methoxyallyl)Fp complex with TCNE in methylene chloride occurred rapidly at room temperature, to afford

a yellow-green crystalline adduct (75) in quantitative yield[66,67]. Although the product could not be purified by chromatographic methods, addition of THF, or diethylether, to the reaction mixture precipitated the adduct in sufficient purity for full spectral analysis.



(75)

Comparison of the ^1H nuclear magnetic resonance (NMR) spectra of the TCNE adduct and the 2-methoxyallyl complex indicated a characteristic shift (δ = 3.51 to δ = 3.23) for the methoxyl resonance on going from a vinylic position β to the Fp group to one which is quarternary and α to the iron complex.

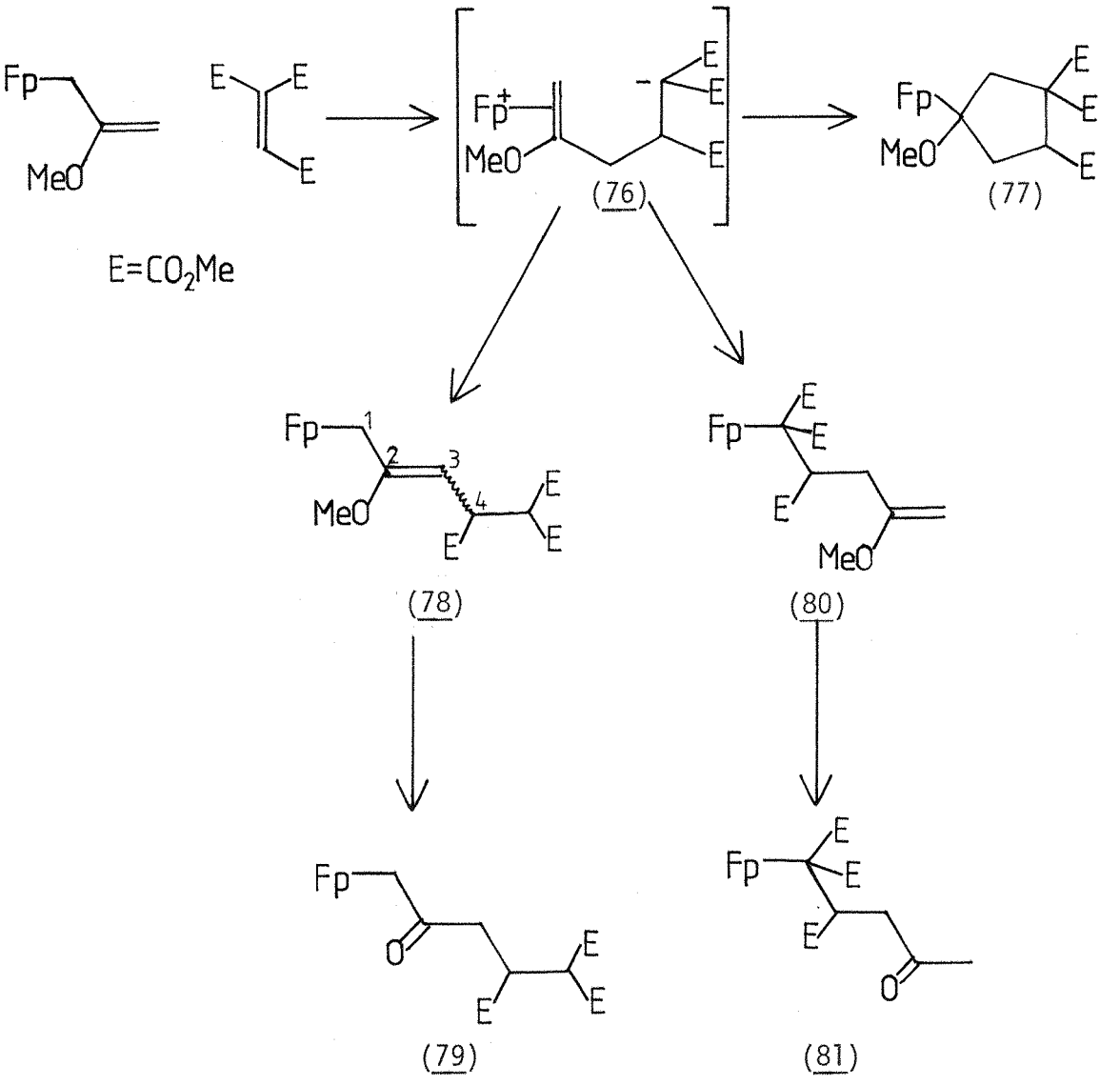
(ii) Trimethyl ethylenetricarboxylate [$MeO_2CCH = C(CO_2Me)_2$]

Trimethyl ethylenetricarboxylate was prepared according to the procedures of House[70] and Hamelin[71]. Reaction of one equivalent of this olefin with the allyl complex in dimethylformamide gave, after column chromatography on neutral alumina (Act. III), three 1:1 adducts in approximately a 6:1:3 ratio, together with the ketone $FpCH_2COMe$. In this reaction it is feasible that the collapse of the intermediate zwitterion (66) could follow several routes - (i) cyclisation, (ii) H-transfer, and (iii) insertion. The latter two processes would give rise to linear products which could in turn be hydrolysed on the column to afford ketones (79) and (81) (Scheme 31).

After examination of the spectral data, the three adducts were assigned the structures (78), (77) and (79) respectively, on the basis that:-

(i) The NMR frequencies of the $-CH_2-$, methoxyl, and cyclopentadiene (Cp) groups of adduct (78) compared favourably with those of the allyl complex (66). The IR spectrum contained an olefinic absorbtion and a C≡O stretch at similar wave number to the C≡O stretch in (78).

(ii) The NMR and IR spectra of the cyclic adduct (73) contained methoxyl, Cp and carbon monoxide frequencies similar to those of the TCNE adduct (75). The absence of olefinic and ketone resonances was also observed.



Scheme 31

(iii) Adduct (79) contains carbon monoxide, ketone, $FpCH_2$- and Cp functionalities identical to those of $FpCH_2COMe$.

In the NMR spectrum of the H-transfer product (78) the $-CH_2-$ group was observed as two doublets, centred at δ = 1.80 and 2.17 (J = 9.5 Hz). This is presumably due to the ester functionality at C-4 (relative to the iron complex) causing a distortion in the molecule which results in the two protons becoming non-equivalent.

The NMR spectrum of the crude reaction mixture showed no hydrolysed product (79), hence it appeared that hydrolysis was occurring on the alumina column. Exclusive formation of the ketone (79) was achieved in 38% isolated yield by treatment of an aqueous THF solution of the reaction mixture with p-toluenesulphonic acid.

TABLE 11

Reactions of complex (66) with trimethyl ethylenetricarboxylate[a]

Solvent[b]	Product Yields (%)[c] (77)	(78)	(79)	$FpCH_2COMe$
DMF[d]	5	31	18	29
DMF	18	24	7	-
DMF	6	15	26	-
DMF	16	30	3	-
CH_2Cl_2[d]	9	29	-	36
CH_2Cl_2	22	28	5	-
CH_2Cl_2	25	10	7	-
THF	0	64	0	-
THF	6	21	16	-
THF	-	-	38[e]	-
Benzene	8	50	3	-

(a) Reactions were generally performed with two equivalents of olefin, at room temperature, for 20 hrs.

(b) DMF = Dimethylformamide; THF = tetrahydrofuran

(c) Isolated yield

(d) Using 1.1 equivalents of olefin

(e) After treatment with aqueous acid.

A summary of the yields obtained employing a variety of reaction conditions is provided in Table 11. From the results obtained it appears that the solvent has an influence on the direction in which the reaction proceeds, since the H-transfer product was formed almost exclusively in THF and benzene, whereas DMF and methylene chloride gave a mixture of the two adducts. It is also apparent that the product ratio can vary

considerably under essentially the same reaction conditions. This is thought to be due to the presence of trace quantities of base in some of the reaction mixtures but not in others, as the addition of dabco to a reaction performed in methylene chloride caused a change in the ratio of H-transfer to cyclic products from approximately 1:1 to 11:1. It was also observed that the use of two equivalents of dabco in the deprotonation of cation (68) led to the isolation of substantial quantities (~ 0.15 equivalents) of the base with the allyl complex, after removal of the THF under reduced pressure followed by extraction with pentane. This result is surprising since dabco is virtually insoluble in pentane, although it may be complexing to the allyl complex or to any THF not removed during work up. It seems likely therefore that the anomalies in the product ratio are due to the use of excess dabco in a number of deprotonation reactions. Similarly, the presence of acid (e.g.:- dabco-HBF_4) in the reaction mixture would also be expected to promote the H-transfer process.

To investigate the effect of solvent on the rate of reaction, samples were removed after various reaction times and worked up by the removal of solvent under reduced pressure and filtration of a diethyl-ether solution of the residues through a neutral alumina (Act III) plug. The amount of $FpCH_2COMe$ present was then estimated from the NMR spectrum of the crude product. From the results obtained (Table 12) it was apparent that the more polar the solvent, as indicated by its dielectric constant (Table 12)[72], the more rapid the reaction.

TABLE 12

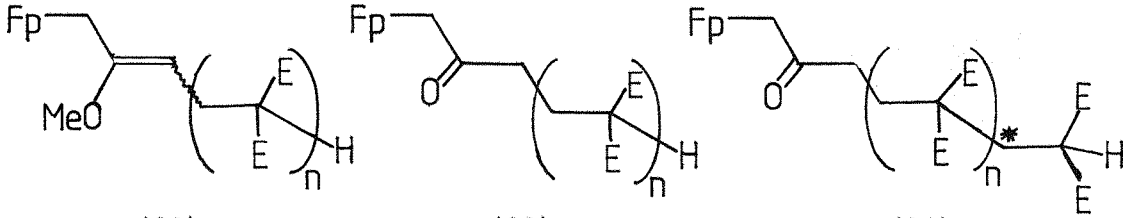
Effect of solvent on the reaction rate

Solvent	Dielectric Constant at 25°C	Reaction Time (hrs)	% of $FpCH_2COMe$ Present
DMF	36.71	0.5	<10
CH_2Cl_2	8.93	0.5	40
		3	20
		21	15
THF	7.58	1.25	25
		3.5	15
		20	10
Benzene	2.275	-	-

(iii) Diethyl methylenemalonate [$H_2C=C(CO_2Et)_2$]

Diethyl methylenemalonate, prepared by the method of Kunichika *et al*[73] is an extremely unstable olefin, which readily polymerises in the pure state[74]. Reactions involving this material were therefore performed using freshly distilled samples.

Column chromatography on neutral alumina (Act III) of the products obtained from the reaction of the allyl complex with two equivalents of the olefin, in DMF at room temperature, resulted in the separation of three major fractions. The NMR spectrum of the first band isolated contained two singlets at δ = 2.03 and 3.41 which correlated with the $FpCH_2$- and methoxyl resonances of the H-transfer adduct obtained with trimethyl ethylenetricarboxylate. This product was therefore assigned the structure (82a). It appears to be a mixture of polymeric H-transfer products since the intensity ratio of ester peaks to the rest of the spectrum is too high for it to be solely the 1:1 adduct. The second fraction consisted mainly of $FpCH_2COMe$ ($\sim$ 25% yield) and the third, polymeric hydrolysed H-transfer products (83a).



(82) (83) (84)

a E = CO_2Et
b E = CO_2Me

n = 1,2 etc.

To confirm that (83a) was the hydrolysed product, both (82a) and the crude reaction mixture were treated with p-toluenesulphonic acid in aqueous THF. This resulted in exclusive formation of the polymeric ketones (83a).

When the reaction was performed in benzene, and one equivalent of the olefin employed, only two fractions were isolated from the column. In analogy to the reaction performed in DMF, the first fraction contained the polymeric, unhydrolysed, H-transfer product. The second, however, consisted of an inseparable 1:3 mixture of $FpCH_2COMe$ and the 1:1 adduct

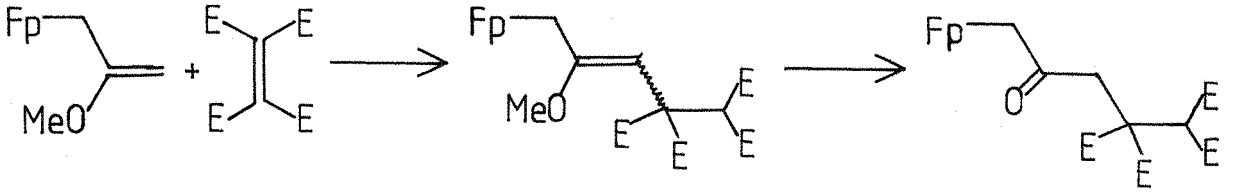
(83a , n=1), obtained in approximately 30% yield. The major difference between the NMR spectrum of this adduct (83a) and that of the polymeric ketone is the absence of a doublet at δ = 2.56 (J≈6Hz), assigned to the $-C\overset{*}{H}_2-$ group of adduct (84).

(iv) Dimethyl methylenemalonate [$H_2C=C(CO_2Me)_2$]

$FpCH_2COMe$ was the only product that could be isolated, by column chromatography, from the reaction of dimethyl methylene-malonate with the allyl complex in DMF, THF or diethyl ether although a brightly coloured band did remain at the top of the column. By performing the reaction in benzene, the polymeric H-transfer adduct (82b) was obtained, however, along with $FpCH_2COMe$. It was assumed that the coloured band that remained on the column was the hydrolysed H-transfer product (83b).

(v) Tetramethyl and tetraethyl ethylenetetracarboxylate [$(RO_2C)_2C=C(CO_2R)_2$]

Reaction of tetramethyl ethylenetetracarboxylate (prepared in a similar manner to that described for tetraethyl ethylene-tetracarboxylate[75]) with the 2-methoxyallyl complex, at room temperature, afforded exclusively the H-transfer product (85) as an amber oil. The



E = CO_2Me, CO_2Et (85) (86)

best yields were obtained from reactions performed in DMF, by using a vast excess of the olefin and by hydrolysis of the crude product to the ketone (86) with p-toluene-sulphonic acid in aqueous THF before column chromatography (Table 13).

TABLE 13

Reactions of the 2-methoxyallyl complex with tetramethyl and tetraethyl ethylenetetracarboxylate

	Molar Equivs of olefin	Solvent	Reaction time (hrs)	Product Yields (%)[a] (85)	(86)
$E=CO_2Me$	2	DMF	70	13	-
	3	DMF	70	8	6
	4	THF	93	-	14[b]
	4	DMF	70	-	39[b]
	5	DMF	93	7	16
	5	DMF	94	-	26[b]
$E=CO_2Et$	3	DMF	94	-	12
	4	DMF	48	-	16

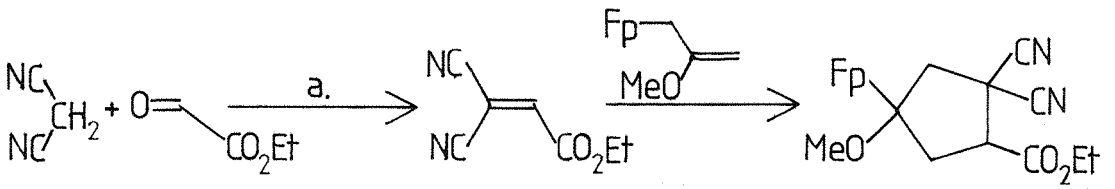
(a) Isolated yields after column chromatography on neutral alumina (Act III).

(b) Crude product was treated with aqueous THF plus p-toluene sulphonic acid before column chromatography.

Tetraethyl ethylenetetracarboxylate also gave the H-transfer adduct, but in slightly lower yields (Table 13). This product was completely hydrolysed to the ketone on neutral alumina.

(vi) Ethyl-3,3-dicyanoacrylate [$EtO_2CCH=C(CN)_2$]

Ethyl 3,3-dicyanoacrylate was prepared in 16% yield by a Knoevenagel reaction between malononitrile and ethyl glyoxylate (Scheme 32). This olefin afforded the cyclic adduct (87) as the sole product on reaction with the allyl complex in DMF at room temperature for three hours. The yellow solid adduct, isolated in yields of 45% and



(a) β-Alanine, H_2O, EtOH

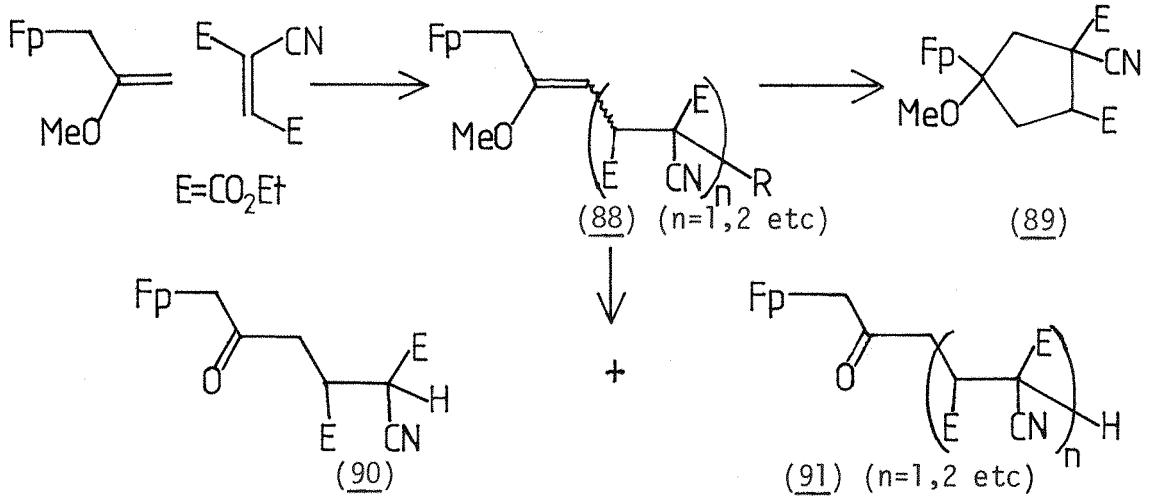
(87)

Scheme 32

32% after column chromatography on florisil and neutral alumina (Act III) respectively, was further purified by recrystallisation from hexane-diethyl ether. The low yield for this reaction is probably due to product decomposition during chromatography, as the NMR spectrum of the crude product indicated quantitative conversion to (87). By performing the reaction in methylene chloride for 20 hours the yield was increased to 58%.

(vii) Diethyl 1-cyanoethylene-1,2-dicarboxylate [$EtO_2CCH=C(CO_2Et)CN$]

Diethyl 1-cyanoethylene-1,2-dicarboxylate was prepared as the *trans*-isomer (with respect to the ester groups) according to the procedure described by Hall and Ykman[76] for the synthesis of dimethyl 1-cyanoethylene-1,2-dicarboxylate. Examination of the NMR spectrum of the crude product, obtained from a reaction performed in methylene chloride using one equivalent of the olefin, indicated that the reaction had produced a mixture of linear and cyclic products. The ratio of these products varied between reactions, although H-transfer appeared to be the predominant process. The spectrum also contained a large number of cyclopentadienyl peaks (> 5), probably due to the formation of polymeric species.



Considerable problems were encountered in the isolation and purification of the products from the above reaction. Column chromatography on neutral alumina (Act III) only afforded $FpCH_2COMe$, with the bulk of the products remaining at the top of the column, even after elution with ethyl acetate. Three fractions were isolated however by using neutral alumina (Act IV). The first consisted of a mixture of polymeric H-transfer adducts (88) (∿ 14% yield) and the cyclic adduct (89) (∿ 2% yield), the second $FpCH_2COMe$, and the third, the hydrolysed 1:1 H-transfer adduct (90) (Yield = 27%). Considerable quantities of material could not be recovered from the column.

In an attempt to obtain the desired ketone in high yield, the crude reaction mixture was treated with aqueous THF and p-toluenesulphonic acid. Purification on neutral alumina (Act IV) resulted in the isolation of the 1:1 adduct (90) in 19% yield, as well as a mixture of $FpCH_2COMe$ (∿ 13% yield) and (89) (∿ 6% yield). Attempts to further purify the ketone by column chromatography resulted in the product remaining at the top of the column. This suggests that hydrolysis of some of the H-transfer adduct (88) occurred during chromatography rather than beforehand (i.e. by the treatment with acidic aqueous THF) and that it was then probably removed from the column before it could fully complex with the alumina.

By using neutral alumina (Act V) or a short florisil column the polymeric hydrolysed adduct (91) was isolated in low yield.

Summarising the results obtained with diethyl 1-cyanoethylene-1,2-dicarboxylate it appears that:-

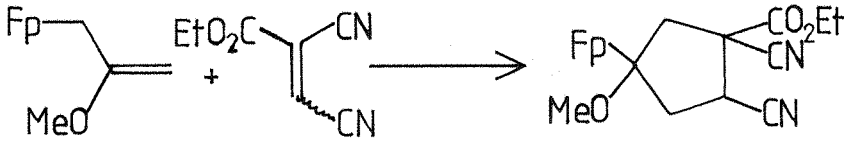
(i) the H-transfer process is favoured over cyclisation

(ii) polymeric species are formed

(iii) hydrolysis of these polymeric species occurs readily on neutral alumina and florisil to give products which can only be isolated in low yields.

(viii) Ethyl 2,3-dicyanoacrylate [$NCCH=C(CO_2Et)CN$]

Ethyl 2,3-dicyanoacrylate was prepared in a *cis:trans* ratio (with respect to the cyano groups) of 8:1 by the method of Noren and Hall[77]. Reaction of this olefin with the allyl complex in methylene chloride at room temperature, afforded the cyclic adduct (92) as a mixture of diastereoisomers, as indicated by the presence of a number of methoxyl resonances in the δ = 2.95-3.30 range of the NMR spectrum.

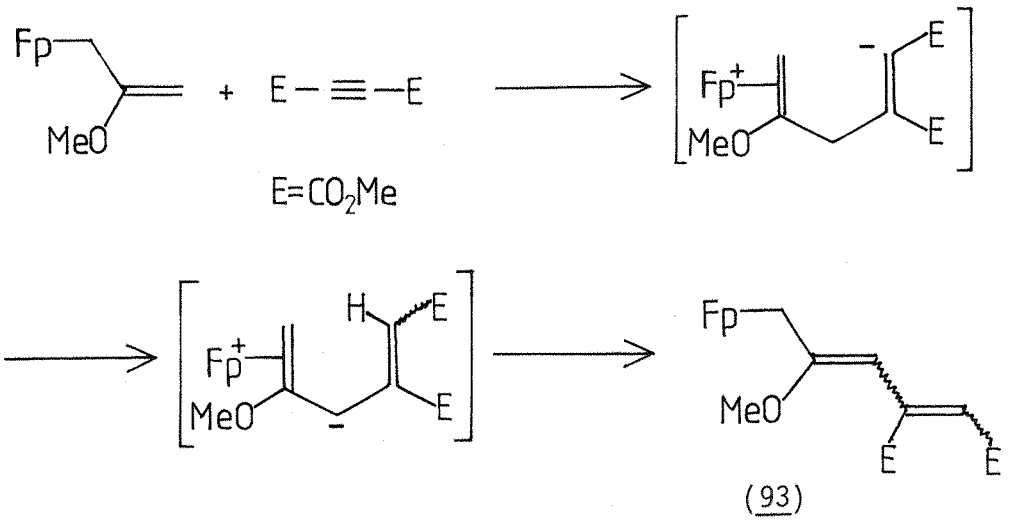


(92)

These adducts were purified on neutral alumina (Act IV or V) in yields of 64-71%, or on florisil in 52% yield. Chromatography on neutral alumina (Act III) proved unsuccessful.

(ix) Dimethyl acetylenedicarboxylate [$MeO_2CC{\equiv}CCO_2Me$]

Reaction of dimethylacetylenedicarboxylate (DMAD)[78] with the 2-methoxyallyl complex in THF or DMF at room temperature gave a single product, in variable yields (Table 14)[66,69], which was purified by column chromatography on neutral alumina (Act III), although separation from any $FpCH_2COMe$ present proved difficult. This adduct was assigned the structure of the H-transfer product (93) (Scheme 33) on the basis that the NMR spectrum indicated the presence of two dissimilar olefinic protons, together with vinylic methoxyl and $FpCH_2$ functionalities. It is interesting to note that, presumably due to conjugation, this product does not hydrolyse during chromatography.



Scheme 33

TABLE 14

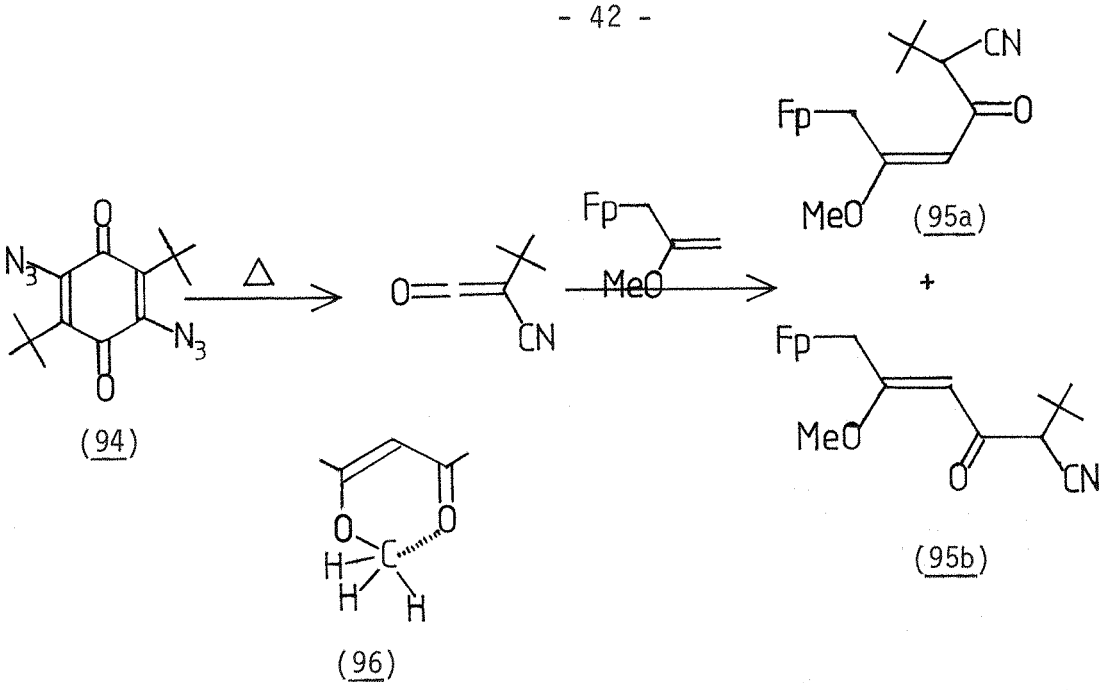
Reactions of DMAD with complex (66)

Molar Equivs of DMAD	Solvent	Reaction Time (hrs)	Product Yield (%)[a] $FpCH_2COMe$ (92)	
1	THF	24	17	25
1	DMF	20	10	41
2	DMF	3	Trace	63

(a) Isolated yields

(x) ^{t}Butylcyanoketene [$O{=}C{=}C(CN)C(CH_3)_3$]

^{t}Butylcyanoketene was generated according to the method of Weyler *et al*[79], by refluxing a benzene solution of the quinone (94) for 2 hours. Addition of this solution to the allyl complex at room temperature resulted in the exclusive formation of a linear product assigned the structure (95)[69]. The NMR spectrum of the crude product contained two t-butyl, two cyclopentadienyl and two vinylic methoxyl resonances in a 3:2 ratio, presumably corresponding to the isomers (95a) and (95b). Column chromatography on neutral alumina (Act III) however caused the isomerisation



(94) (96) (95a) (95b)

of the major product to the minor one, which was isolated in 63% yield. Since the *trans*-configuration is likely to be the more stable of the two, due to dipole-dipole interactions between the methoxyl and ketone groups (96), it was thought that the major product from the reaction is the *cis*-isomer (95a) which isomerises to the *trans*-isomer (95b) on the column.

As with the DMAD H-transfer product, no hydrolysis of the adducts occurred on neutral alumina.

(xi) Unreactive olefins and acetylenes

No products were isolated from the reaction of the 2-methoxyallyl complex with methyl acrylate, acrylonitrile, *cis*-dimethyl ethylene-1,2-dicarboxylate, *trans*-1,2-dicyanoethylene, methyl cinnamate, ethyl 3-nitroacrylate[80], β-nitrostyrene[81], tetraacetylethylene[82], maleic anhydride, p-quinone, methyl propiolate[83] and bis-trimethylsilylacetylene, employing the reaction conditions summarised in Table 15. All reactions were performed in DMF.

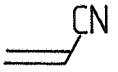
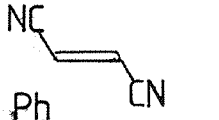
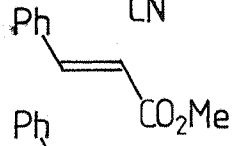
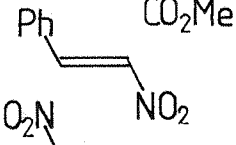
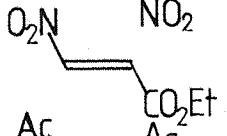
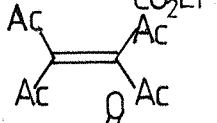
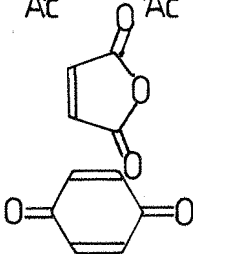
(c) Reactions of dicarbonyl(η^5-cyclopentadienyl) (η'-allyl)iron (20a)

(i) Olefins (97a-h)

Reaction of the simple (η'-allyl)Fp complex (20a) with olefins (97a-g) resulted in the exclusive formation of cyclic adducts (98). The yields of the reactions, together with the reaction conditions employed, are summarised in Table 16.

TABLE 15

Unreactive olefins and acetylenes

Olefin/Acetylenes		Molar Equivs of the Olefin/Acetyelenes	Reaction Time (hrs)
		3	97[b]
	a.	1	48[b], 24[c]
	a.	1	48[b], 24[c]
	a.	1.25	48[b], 24[c]
	a.	1	24[b], 68[c]
	a.	4	20[b], 24[c]
		1.25	24[b]
	a.	1	24[b], 24[c]
		1	24[b], 24[c]
		1	24[b], 36[c]
$HC{\equiv}CCO_2Me$	a.	4	24[b], 24[c]
$Me_3SiC{\equiv}CSiMe_3$	a.	1	24[b], 24[c]

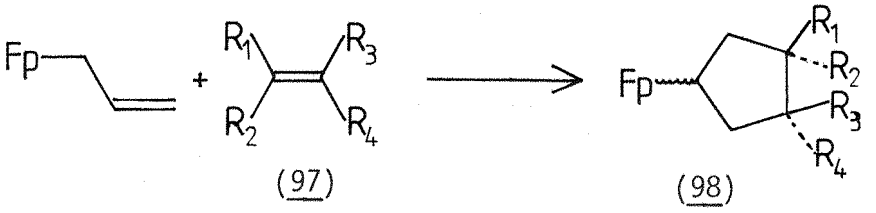
(a) These reactions were performed by T.S. Abram, and the results are produced with due acknowledgement.

(b) At room temperature

(c) At 40-45^{o}C

TABLE 16

Reactions of complex (20a) with the electron deficient olefins (97a-h)



(97) (98)

	R_1	R_2	R_3	R_4
a	CO_2Me	CO_2Me	H	H
b	CO_2Et	CO_2Et	H	H
c	CO_2Me	CO_2Me	H	CO_2Me
h	CO_2Me	CO_2Me	CO_2Me	CO_2Me
d	CN	CN	H	CO_2Et
e	CO_2Et	CN	H	CO_2Et
f	CO_2Et	CN	H	CN
g	CN	CO_2Et	H	CN

Olefin	Molar Equivs of olefin	Solvent	Reaction Time (hrs)	Recovered starting Material (%)	Yield of Product (98) (%)[a]
97a	2	CH_2Cl_2	20	-	64[b]
	1.25	Et_2O	20	-	66[b]
97b	2	THF	20	56	26(62)
	2	DMF	20	20	63(80)
	2	CH_2Cl_2	20	Trace	70
97c	2	DMF	20	58	21(51)
	2.5	DMF	70	50	24(59)
	3	DMF	70	-	42[c]
	3	DMF	70	-	80[d]
	3	DMF	90	-	50
	2	THF	70	62	0
	2	CH_2Cl_2	70	53	0
	2	Benzene	70	58	0

TABLE 16 (Continued)

Olefin	Molar Equivs of Olefin	Solvent	Reaction Time (hrs)	Recovered Starting Material (%)	Yield of Product (98) (%)[a]
97h	3	DMF	70	92	0
97d	1.1	CH_2Cl_2	1	-	67
97e	1.1	DMF	1	-	69
	1.1	CH_2Cl_2	1	-	81
97f,g	1.11	CH_2Cl_2	1	-	83[e]
	1.25	CH_2Cl_2	1	-	94[f]

(a) Isolated yields from column chromatography on neutral alumina (Act III). Yields based on unrecovered starting material are given in parenthesis.

(b) Ref. 21.

(c) Averaged over three reactions.

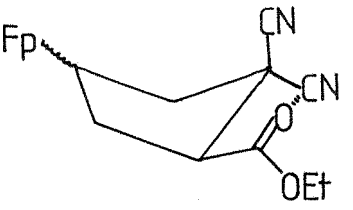
(d) Obtained on only one occasion.

(e) From florisil column.

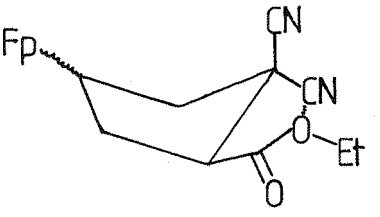
(f) From neutral alumina (Act V) column.

The cyclic adducts (98) were in general air stable and crystalline, existing as a mixture of diastereoisomers. This was indicated by the presence of two cyclopentadienyl resonances and several $-OCH_3$ singlets or $-OCH_2-$ quartets in the NMR spectra.

It was also observed that the spectrum for adduct (98d) contained more than two $-OCH_2-$ quartets. This suggests that each diastereoisomer of (98d) exists in two conformations. These two conformers may have resulted from dipole-dipole interactions between the carbon atom of a nitrile functionality and either the carbonyl, or the ether, oxygen atoms of the ester group (99a and 99b).

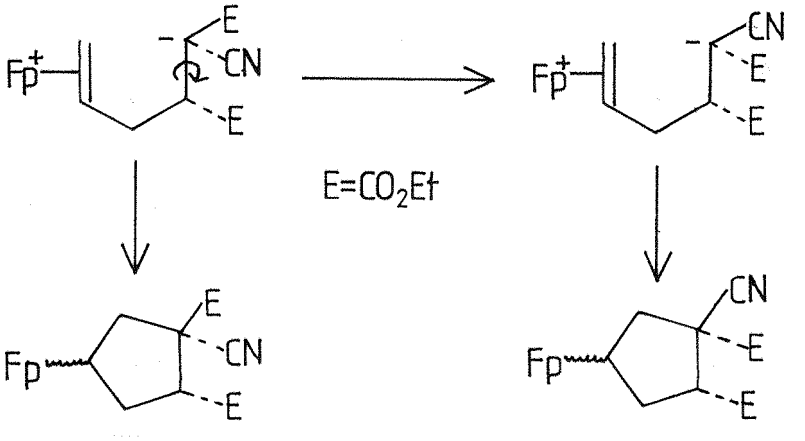


(99a)



(99b)

It is feasible that bond rotation about the indicated carbon-carbon bond of the dipolar intermediate in the reaction with diethyl 1-cyanoethylene-1,2-dicarboxylate (Scheme 34) may lead to the formation of the cyclic adduct (100) as well as (98e). Williams and Wojcicki[25] have shown however that the thermodynamically more stable *trans*-configuration of 1,2-dicyano-1,2-bis(trifluoromethyl)ethylene reacts



Scheme 34

(98e) (100)

(101) (102)

with complex (20b) to give almost exclusively the *trans*-cyclic adduct (101), whereas the *cis*-olefin isomerises during the reaction, by bond rotation, to afford a mixture of (101) and (102) in a ratio of 3:1. Therefore, it is probable that (98e) was the predominant product in the reaction of (97e) with (20a).

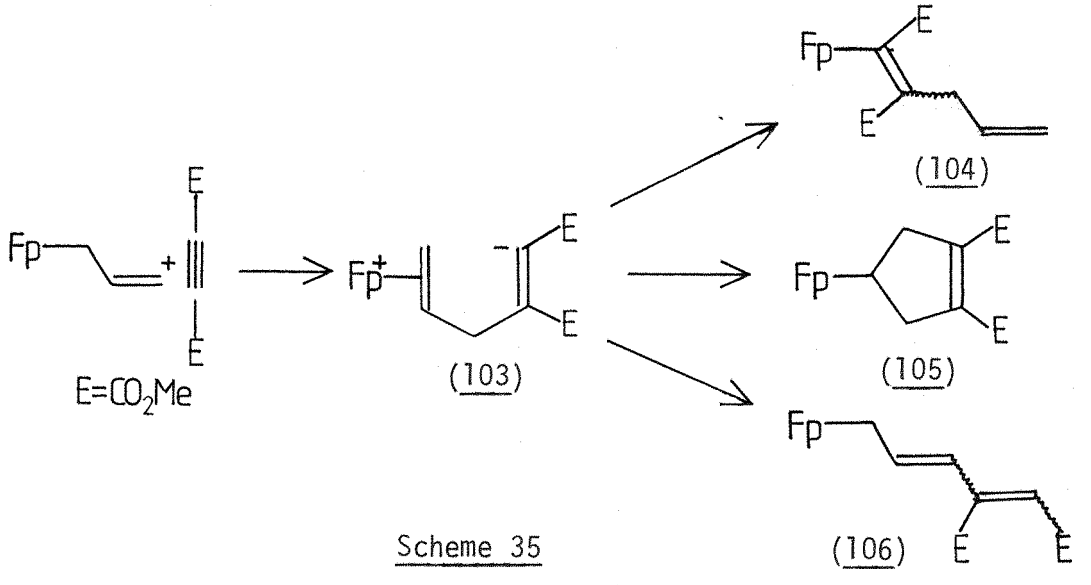
From the above results, it is apparent that the solvent is an important factor in these processes since trimethyl ethylenetricarboxylate only afforded the cyclic adduct when the reaction was performed in DMF. No products were isolated by using methylene chloride, THF or benzene. In addition (98b) was obtained in higher yields in DMF and methylene chloride than in THF. This may be due to polymerisation of the olefin in THF before reaction with the allyl complex.

Another interesting result is that no reaction was observed between (20a) and tetramethyl ethylenetetracarboxylate. This implies that the simple (η'-allyl)Fp complex (20a) is not as reactive as the 2-methyoxy-allyl complex (66).

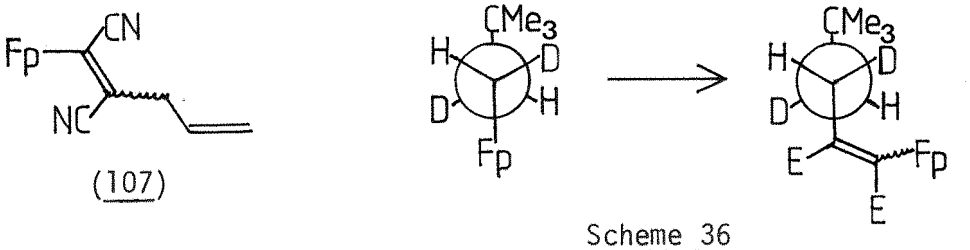
(ii) Acetylenes

Reaction of the (η'-allyl)Fp complex with two equivalents of DMAD in DMF, at room temperature, for 90 hours resulted in the formation of three 1:1 adducts in a ratio of 17:5:78[69]. These products were isolated in an overall yield of 54% after column chromatography on neutral alumina (Act III).

As previously observed, the collapse of the dipolar intermediate (103) could be expected to follow several routes as outlined in Scheme 35.



Scheme 35



Scheme 36

Williams and Wojcicki[84] discovered that insertion is the exclusive process in the reaction of (20a) with dicyanoacetylene, affording adduct (107) in 30% yield. The insertion of DMAD into alkyl-Fp complexes (Scheme 36) has also been reported by Whitesides *et al*[58].

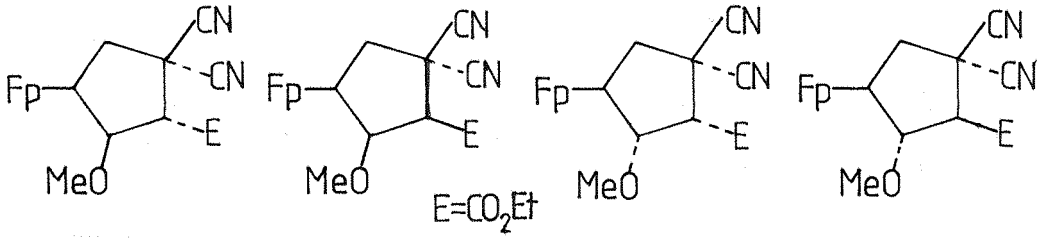
Examination of the NMR spectrum of the adduct which was obtained in 9% yield indicated that this was the insertion product (104), since the spectrum contained a doublet at δ = 3.09 corresponding to the $-CH_2-$ group, as well as three olefinic resonances. (A comparison of the spectral data for adducts 104 and 107 is given in the experimental section). The major and minor products showed the spectral characteristics of the cyclic and H-transfer adducts respectively, and therefore were assigned the structures (105)and(106).

Only starting material was isolated (in 83% yield) from the reaction of (20a) with four equivalents of methyl propiolate in DMF at room temperature for 80 hours.

(d) Reactions of dicarbonyl (η^5-cyclopentadienyl) (η'-3-methoxyallyl) iron (28) with olefins and acetylenes

The cyclic adducts (108-110) were the exclusive products from the reaction of olefins (98b-g) and DMAD with the (*cis*-η'-3-methoxyallyl)Fp complex (28). Table 17 summarises the reaction conditions employed and the yields obtained. Tetramethyl ethylenetetracarboxylate and methyl propiolate gave no observable reaction.

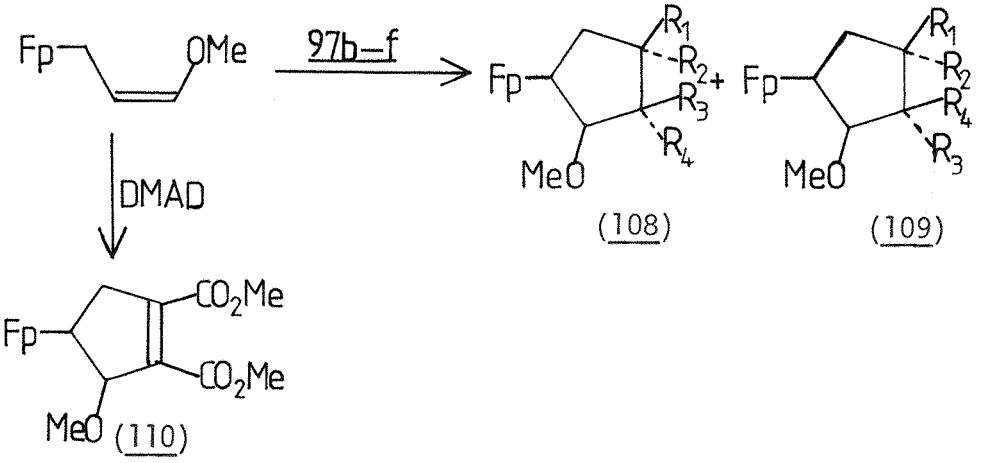
Two cyclic products, easily separated by column chromatography on florisil, were isolated in a 3:2 ratio from the reaction between ethyl 1,2-dicyanoacrylate (97d) and (28). It can be postulated that this process could lead to the formation of four diastereoisomers (108d, 109d, 111a, 111b). It is unlikely, however, that a mixture of *cis*-and *trans*-isomers (with respect to the Fp and methoxyl groups) are formed, as the



(108d) (109d) (111a) (111b)

TABLE 17

Reactions of complex (28) with electron deficient olefins and acetylenes



b	CO_2Et	CO_2Et	H	H
c	CO_2Me	CO_2Me	H	CO_2Me
d	CN	CN	H	CO_2Et
e	CO_2Et	CN	H	CO_2Et
f	CO_2Et	CN	H	CN
g	CN	CO_2Et	H	CN

Olefin	Molar Equivs of olefin	Solvent	Reaction Time (hrs)	Product Yield (%)
19b	3	DMF[d]	92	5[a]
	4	DMF[d]	90	25[b]
19c	3	DMF	66	4[a]
	4	DMF	90	16[b]
19d	1.1	CH_2Cl_2	3	85[c] (108:109 ≃ 3:2)
19e	1.1	CH_2Cl_2	3	89[c] (108:109 ≃ 2:3)
	1.1	DMF	6	80[c]

TABLE 17 (Continued)

Olefin	Molar Equivs of Olefin	Solvent	Reaction Time (hrs)	Product Yield (%)
19f,g		CH_2Cl_2	3	86[c] (108:109 ≃ 1:1)
Acetylene				
DMAD	e	DMF	e	77[a]
	10	DMF	45	66[a]
	10	DMF	70	68[a]
	10	CH_2Cl_2	92	51[a]

(a) Isolated by column chromatography on neutral alumina (Act III).

(b) Isolated by column chromatography on florisil and then neutral alumina (Act III).

(c) Isolated by column chromatography on florisil.

(d) Dilute solution.

(e) Four equivalents for 48 hours plus a further two equivalents for 24 hours.

NMR spectrum of the product obtained with DMAD (110) contained only single peaks for the cyclopentadienyl and methoxyl resonances. This suggests that the Fp and methoxyl functionalities are either *cis* or *trans*, but not a mixture of the two. Rosenblum *et al* have shown[21] that any geometric isomerism associated with a substituent at C-3 in the allyl complex is retained in the product (see Chapter One). Hence it can be assumed that the two products isolated from the reaction of (97d) with (28) have the *cis* arrangement of Fp and methoxyl groups, as in (108d) and (109d).

The structure (108d) was assigned to the major product as the C-2 proton resonated as a doublet of a doublet in the NMR spectrum (Table 18), which indicates a β,β,α configuration for the C-1 - C-3 protons. This proton, however, resonated as a triplet in the spectrum of the minor product, indicating that the C-1 - C-3 protons are β,β,β, as in (109d).

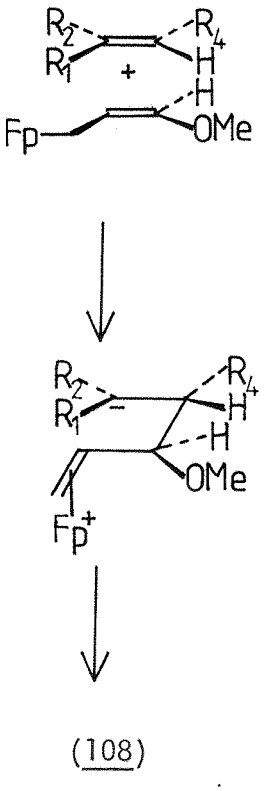
TABLE 18

C-2 and C-3 proton magnetic resonances of (108d) and (109d)

Isomer	Proton	Chemical Shift (δ value)	Multiplicity	Coupling Constant (Hz)
108d	C-2	3.95	dd	2.5 and 5.5
108d	C-3	3.45	d	2.5
109d	C-2	4.04	t	3.5
109d	C-3	3.34	d	3.5

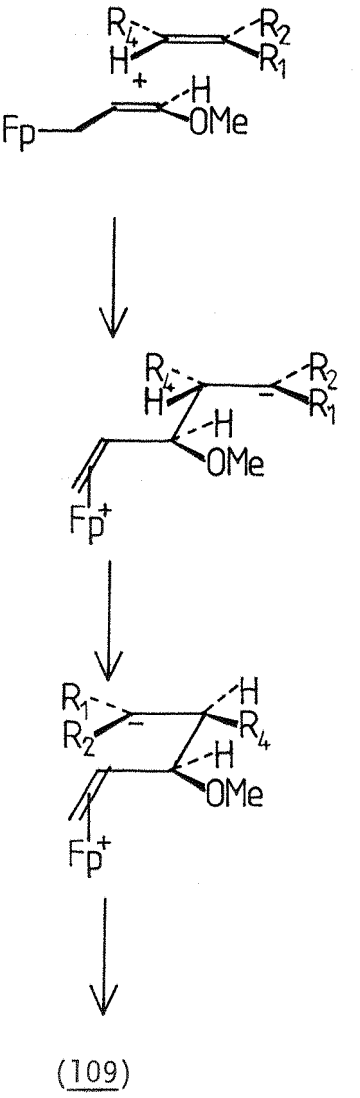
(a) d = doublet, dd = doublet of a doublet, t = triplet

Mixtures of cyclic products (108e, 109e and 108f,g, 109f,g) were also obtained with olefins (97e) and (97f,g). The ratio in which the adducts were isolated varied depending on the olefin employed (see Table 17). No isomerisation of (108) or (109) was observed during chromatography. It is likely that the allyl complex would approach the olefin such that the methoxyl and R_4 substituents are in the more sterically favoured *trans*-configuration in the dipolar intermediate. Two processes could be postulated which would initially give this configuration (Schemes 37 and 38). In the case of diethyl 1-cyanoethylene-1,2-dicarboxylate (97e) the considerable steric bulk of the ester functionalities would be expected to favour the latter of these two processes (Scheme 38), resulting in the formation of (109e) in higher yield. By replacing one of the ester groups with a cyano functionality the steric hindrance may be reduced to such an extent that either the former process (Scheme 37) predominates, as with ethyl 3,3-dicyanoacrylate (97d), or that the olefin can approach the allyl complex equally from any direction giving a 50:50 mixture as with ethyl 2,3-dicyanoacrylate (97f,g).



(108)

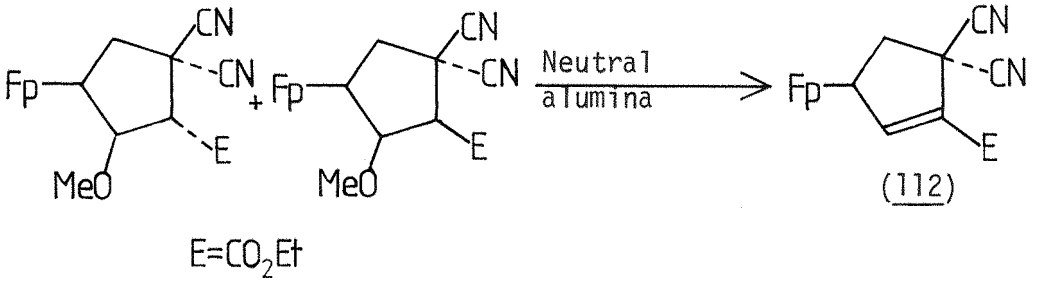
Scheme 37



(109)

Scheme 38

It was discovered that column chromatography on neutral alumina led to the elimination of methanol from the adducts (108d) and (109d) (Scheme 67). In general, (108d) was isolated in low yield (< 15%)



E=CO_2Et

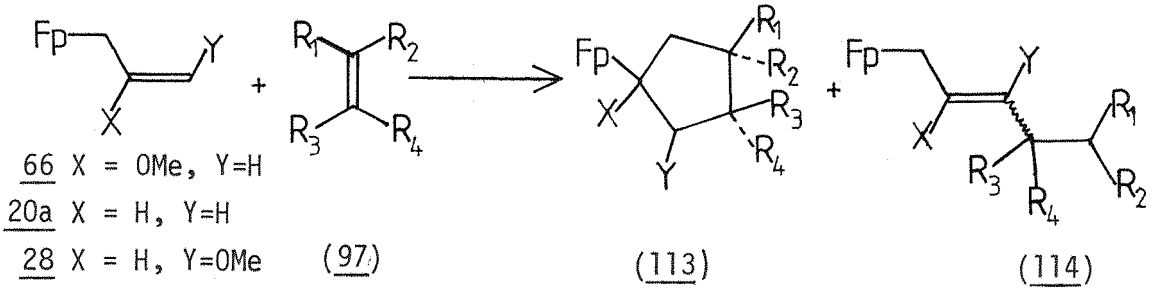
Scheme 67

from the column, whereas (109d) always gave the product of elimination. This provides further evidence that these adducts have the stereochemistry shown since a *trans*-E2 elimination reaction is the more favoured. No elimination of methanol was apparent from adducts (108, 109b,c,e,f).

The isolation of (108d)and (109d) was achieved in high yield by column chromatography on florisil. The NMR spectra of both isomers consisted of two quartets for the $-OCH_2-$ resonance. This, as with the cyclic adduct (98d), is probably due to the existence of two conformations of each isomer.

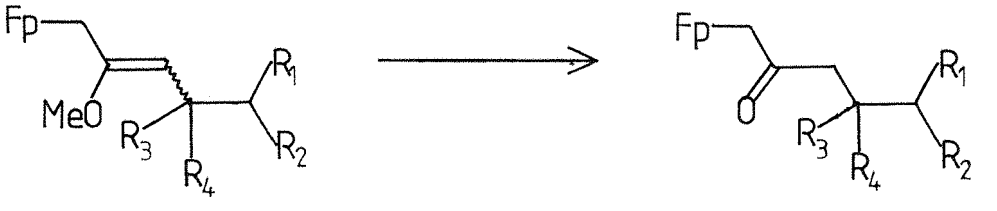
Further Discussion

A summary of the products (113, 114), yields and conditions employed in the reactions of the (η'-allyl)Fp complexes (66), (20a) and (28) with electron-deficient olefins and acetylenes is provided in Table 19.



66 X = OMe, Y=H
20a X = H, Y=H
28 X = H, Y=OMe (97) (113) (114)

The H-transfer products obtained with complex (66) were susceptible to hydrolysis, and indeed this occurred to a large extent during chromatography of the crude reaction mixture, thereby giving substantial quantities of the ketone (Scheme 39). Hydrolysis could also be



Scheme 39

TABLE 19

Reactions of complexes (66),(20a) and (28) with electron deficient olefins

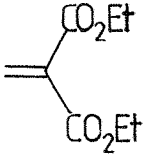
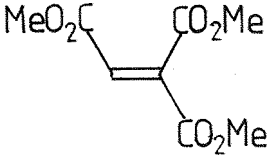
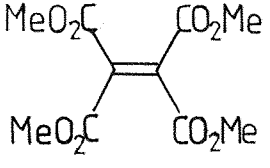
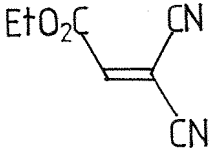
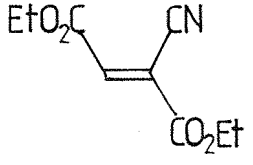
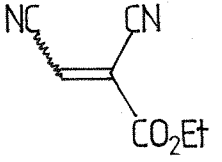
Olefin	Complex	Molar Equivs of olefin	Solvent	Reaction Time (hrs)	Product Yield (%)[a]	Product Ratio (%) Cyclic	H-Transfer
	66	1	DMF or Benzene	20	-	-	Polymer -
	20a	2	CH_2Cl_2	20	70	100	-
	20a	2	DMF	20	63	100	-
	28	4	DMF	90	25	100	-
	66	2	CH_2Cl_2	8	55	40	60
	66	2	DMF	2	50[b]	23	77
	66	2	THF	8	54[b]	6	94
	66	2	Benzene	20	61	13	87
	20a	3	DMF	90	50	100	-
	20a	2	CH_2Cl_2 THF, or Benzene	70	0	-	-
	28	4	DMF	90	16	100	-
	66	4	DMF	70	39[c]	-	100
	20a	3	DMF	70	0	-	-

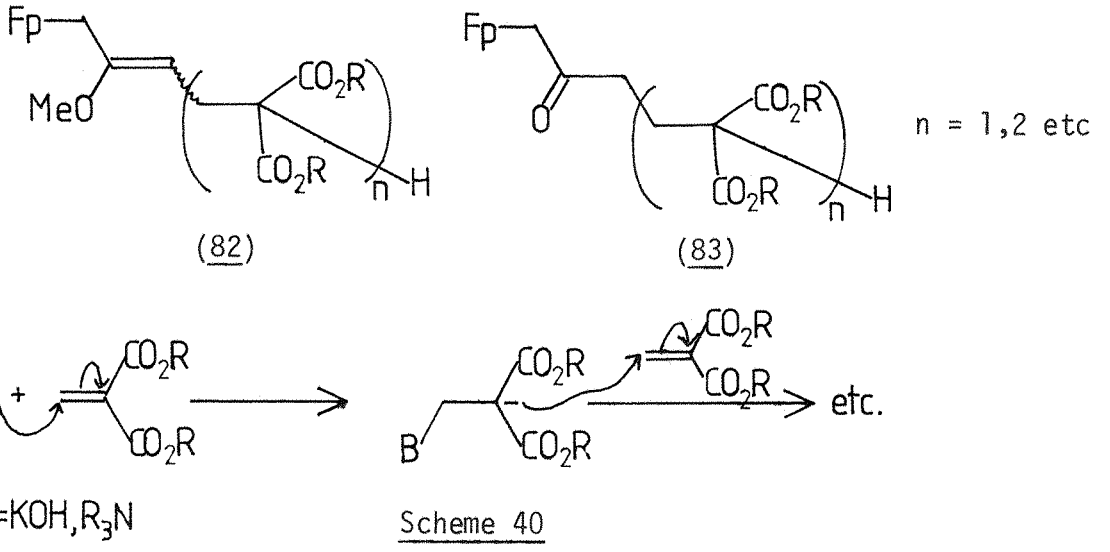
TABLE 19
(Continued)

Olefin	Complex	Molar Equivs of Olefin	Solvent	Reaction Time (hrs)	Product Yield (%)[a]	Product Ratio (%) Cyclic H-Transfer
	66	1.1	CH_2Cl_2	20	58	100 -
	20a	1.1	CH_2Cl_2	1	67	100 -
	28	1.1	CH_2Cl_2	3	85	100 -
	66	1.1	CH_2Cl_2	1	-	Polymer + Cyclic
	20a	1.1	CH_2Cl_2	1	81	100 -
	28	1.1	CH_2Cl_2	3	89	100 -
	66	1.1	CH_2Cl_2	1	71	100 -
	20a	1.1	CH_2Cl_2	1	83	100 -
	28	1.1	CH_2Cl_2	3	86	100 -

(a) Isolated yield

(b) Yields and product ratios averaged over several reactions

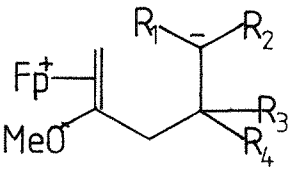
(c) Crude product treated with aqueous THF plus p-toluene-sulphonic acid before chromatography.



Scheme 40

induced by treatment with p-toluenesulphonic acid in aqueous tetrahydrofuran. The reaction of (66) with dimethyl or diethyl methylene-malonate gave the polymeric species (82) which could be hydrolysed to (83). Similar base catalysed polymerisation of these olefins (Scheme 40) have been reported by Hopff *et al*[85]. Polymeric adducts were also formed with diethyl 1-cyanoethylene-1,2-dicarboxylate.

From the results obtained, it is apparent that the (η'-2-methoxyallyl)Fp complex (66) is considerably more reactive than both the simple (η'-allyl)Fp complex (20a) and the (η'-3-methoxyallyl)Fp complex (28), since no reaction was observed between the latter two complexes and tetramethyl ethylenetetracarboxylate (97h). Complex (66) however failed to react with moderately activated olefins. Furthermore, whereas the C-2 methoxyl group tends to promote reaction, the opposite is observed with C-3 substitution, resulting in lower yields being obtained with (28) compared to complex (20a) when the less reactive olefins (97b and 97c) were employed. It is also clear that the C-2 methoxyl group leads to the formation of considerable quantities of linear products. This may be explained by the increased stability of the intermediate zwitterion (115) for which processes other than ring closure may then become important. Cyclisation is additionally disfavoured on steric grounds as metal-quarternary bonds are formed, and also because the considerable steric bulk of the ester functionalities

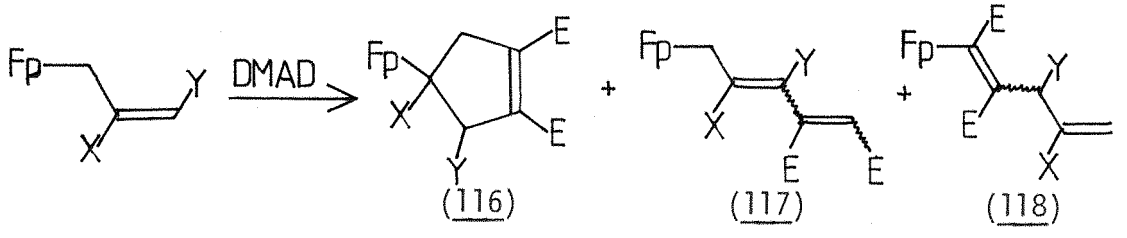


(115)

would hinder the closure of the anion to the cation. Thus, H-transfer becomes the predominant process with olefins containing more than one ester group. This steric hindrance is reduced however by the presence of a number of cyano functionalities, as in olefins (97d), (97f,g) and TCNE, such that cyclisation becomes the preferred process. It is interesting that for complex (28) the C-3 methoxyl substitution entirely eliminates H-transfer, so giving a greater specificity to the reactions of this compound. This is further highlighted by the reaction of DMAD with these complexes (Table 20).

TABLE 20

Reactions of DMAD with complexes (66), (20a) and (28)



(116) (117) (118)

66 x = OMe, Y = H
20a x = H, Y = H
28 x = H, Y = OMe

E = CO_2Me

(η'-allyl)Fp	Molar Equivs of DMAD	Solvent	Reaction Time (hrs)	Product Yield (%)	Product Ratio (%) 116	117	118
66	2	DMF	3	70	-	100	-
20a	2	DMF	91	57	78	5	17
28	6	DMF	67	77	100	-	-

The choice of solvent appears to be an important factor in a number of these reactions. For example, no products could be isolated from the reaction of the simple (η'-allyl)Fp complex (20a) with trimethyl ethylenetricarboxylate in methylene chloride or THF. However, a good yield of the cyclic adduct was obtained in DMF. This result is best explained in terms of the polarity of the solvent, since the reaction is more likely to proceed if the intermediate zwitterion is stabilised by a solvent of high polarity, such as DMF (as indicated by its dielectric constant, Table 12).

Summary

From the results obtained it can be concluded that the reactions of the simple (η'-allyl)Fp complex (20a) and the (η'-3-methoxyallyl)Fp complex (28) with olefinic species leads to the exclusive formation of cyclic adducts. These two complexes appear to be of comparable reactivity, although (20a) tended to give higher yields with the less reactive olefins. In comparison, large quantities of linear products were obtained in the reaction of the (η'-2-methoxyallyl)Fp complex (66) with a number of unsaturated moieties. Complex (66) was also observed to be considerably more reactive than the other complexes. This increase in reactivity was insufficient, however, to bring about reaction with moderately electron-deficient olefins such as methyl acrylate, acrylonitrile, maleic anhydride, etc.

CHAPTER THREE

Demetalation Reactions

Introduction

For the (3+2) cycloaddition reactions of (η'-allyl)Fp complexes with unsaturated units to be of synthetic use, a convenient method for the replacement of the organometallic group of alkyl-Fp complexes with an organic function is required. The removal of the Fp complex from the adducts prepared in this study was therefore investigated using a variety of procedures. These included:

(i) oxidative carboxylation (RFp → RCO_2R')[56-60]

(ii) acid cleavage (RFp → RH)[51-55]

(iii) bromination (RFp → RBr)[20, 53,58,61-64]

(iv) β-hydride abstraction, followed by liberation of the olefin ($R'CH_2CHRFp \rightarrow R'CH{=}CHR$)[32,36,37,52,60]

Results and Discussion

1. Oxidative Carboxylation

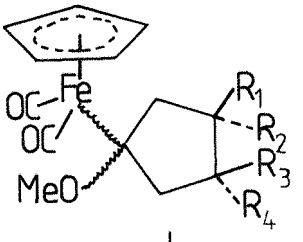
(a) General procedure

To a solution of the Fp adduct in either methanol or ethanol, previously saturated with carbon monoxide, was added four equivalents of ammonium ceric nitrate [$(NH_4)_2Ce(NO_3)_6$] in one portion at room temperature. Carbon monoxide was then bubbled through the solution while the reaction was continued for approximately sixteen hours (overnight). The products were isolated by removal of the solvent under reduced pressure and extraction of an aqueous solution of the residue with benzene. Adducts obtained in this manner were generally purified by column chromatography on florisil, although NMR analysis of the crude product proved useful. No attempt was made to optimise the yields of these reactions.

Use of diethyl ether or methylene chloride for the extraction of the crude reaction mixtures led to the isolation of organometallic complex by-products. These organometallic compounds caused the NMR spectra to be broadened, and were difficult to remove by chromatographic procedures. This problem was not encountered when using benzene as the extraction solvent.

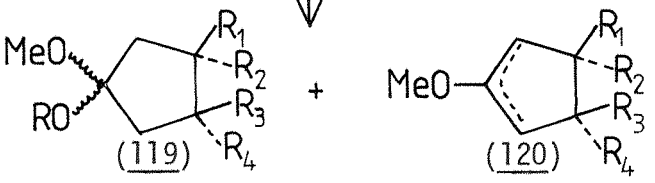
(b) 1-Methoxycyclopentyl-Fp complexes

Treatment of alcoholic solutions of the cyclic adducts (75) and (87) with the ceric salt resulted in the formation of the ketal (119) and olefin (120) in the yields and ratios given in Table 21[66,69]. No identifiable products were obtained, however, from the oxidation of (77)



	R_1	R_2	R_3	R_4
75	CN	CN	CN	CN
87	CN	CN	H	CO_2Et
77	CO_2Me	CO_2Me	H	CO_2Me
92	CO_2Et	CN	H	CN

Ce^{IV}/ROH/CO



	R_1	R_2	R_3	R_4
a	CN	CN	CN	CN
b	CN	CN	H	CO_2Et
c	H	CO_2Et	CN	CN

TABLE 21

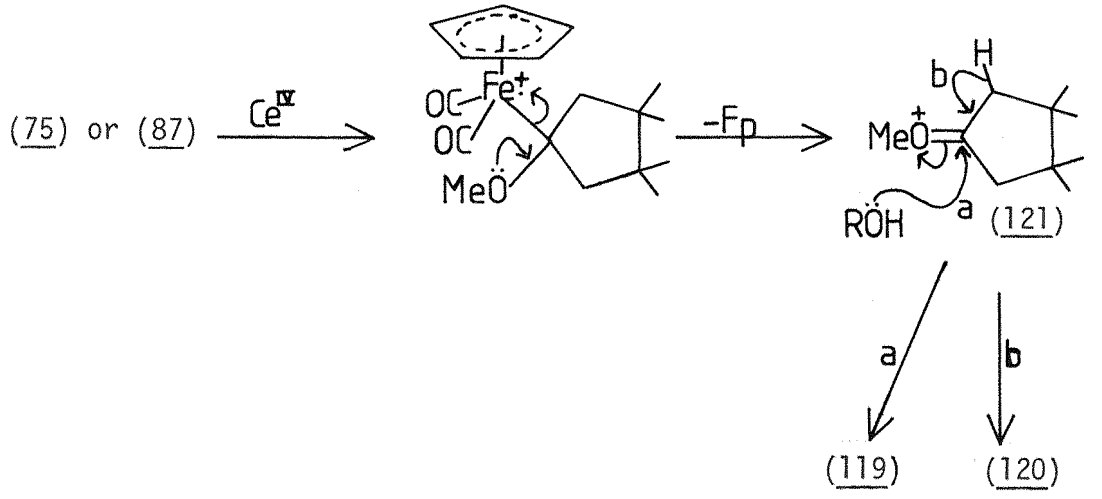
Cerium (IV) oxidation reactions of 1-methoxycyclopentyl-Fp complexes

Fp adduct	ROH	Product yield (%)	Product Ratio (%)[c] Ketal (119)	Olefin (120)
75	MeOH	Quantitative[a]	88	12
75	EtOH	Quantitative[a]	66	34
87	MeOH	92[b]	89	11

(a) The product could not be purified by column chromatography

(b) Isolated yield after column chromatography on florisil

(c) Estimated from the NMR spectrum of the mixture.

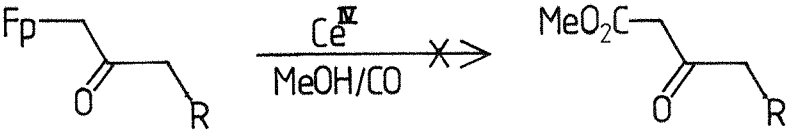


Scheme 41

and (92). The mechanism of this reaction probably involves the intermediate cation (121) which can either undergo attack by ROH or collapse through the loss of a proton (Scheme 41). The increase in yield of the olefin on using ethanol as the solvent was possibly due to steric factors, since an increase in the steric bulk of the incoming group would be expected to disfavour ketal formation.

(c) Linear alkyl-Fp complexes

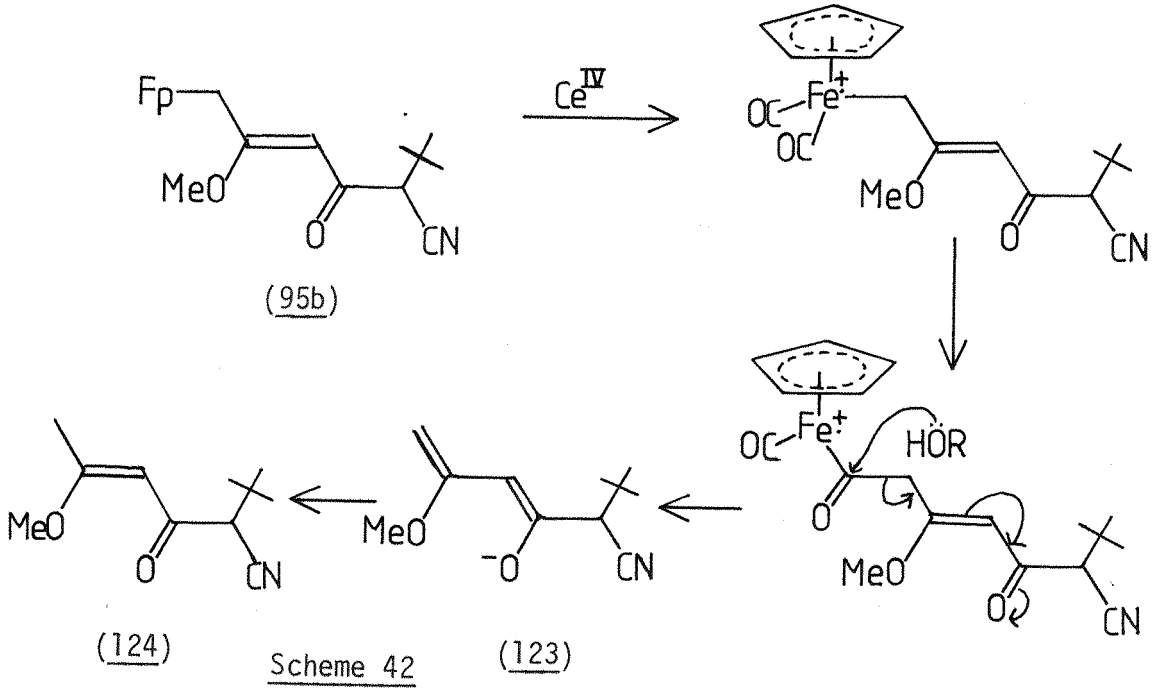
Surprisingly, oxidation of ketone (70) in methanol afforded none of the expected product, methylacetoacetate (122a). Instead what appears to be a mixture of polymeric species was isolated. A similar result was obtained on oxidation of adduct (79).



(70) R=H (120a)

(79) R=CH(CO_2Me)CH(CO_2Me)$_2$ (122b)

Treatment of a methanolic solution of the linear compound (95b) with the ceric salt did result however in the formation of a single product (124) in 95% isolated yield after column chromatography[69]. This replacement of the Fp functionality with a proton may have proceeded



(95b)

(124) Scheme 42 (123)

via the intermediate enol anion (123), by the mechanism given in Scheme 42.

(d) Cyclopentyl-Fp complexes

The carboxylated derivatives (125b-g, i) and (126) were the exclusive products isolated (in the yields summarised in Table 22) from the cerium (IV) oxidation of Fp adducts (98b-g, i) and (105). The NMR spectra of the crude products indicated that these reactions had proceeded to give a mixture of isomeric compounds.

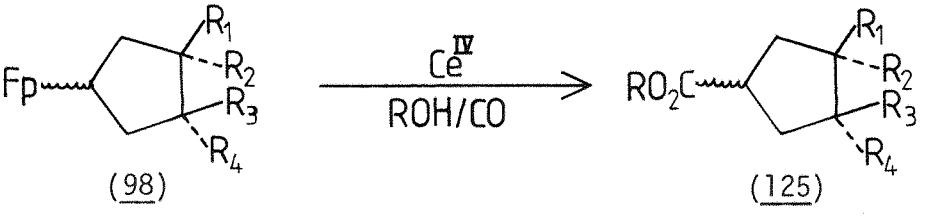
(e) 2-Methoxycyclopentyl-Fp complexes

Treatment of alcoholic solutions of the 2-methoxycylopentyl-Fp complexes (108d-g, i) (109d-g, i) and (110) with ammonium ceric nitrate also resulted in the replacement of the Fp group with an ester functionality. The isolated yields of the carboxylated derivatives obtained (127, 128 and 129) are summarised in Table 23.

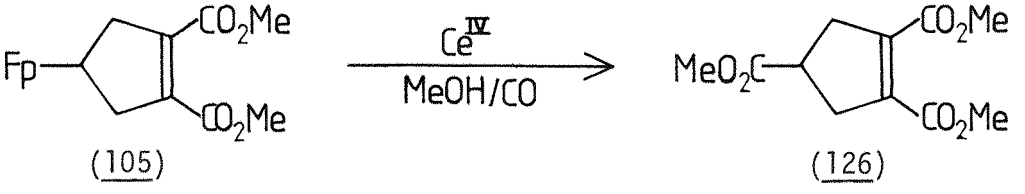
Nicholas and Rosenblum[57] have shown that the oxidative carboxylation of alkyl-Fp complexes occurs with retention of configuration. Thus, as the NMR spectra of the crude products contained only one methoxyl resonance, it was assumed that the oxidation of the 2-methoxycycloalkyl complexes had also proceeded with retention. Derivatives (128d-g) isomerised

TABLE 22

Oxidative carboxylation of cyclopentyl-Fp complexes



b	CO_2Et	CO_2Et	H	H
c	CO_2Me	CO_2Me	CO_2Me	CO_2Me
d	CN	CN	H	CO_2Et
e	CO_2Et	CN	H	CO_2Et
f	CO_2Et	CN	H	CN
g	CN	CO_2Et	H	CN
i	CN	CN	CN	CN



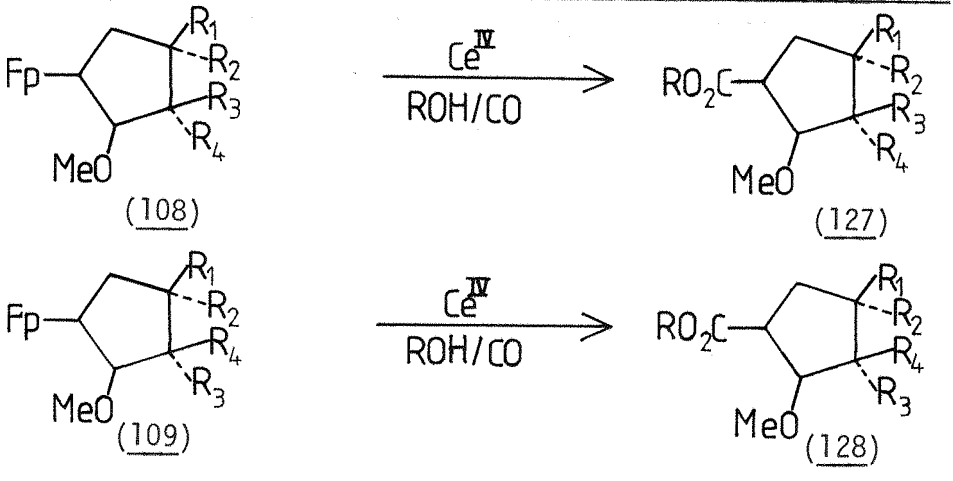
Fp adduct	ROH	Product	Product Yield (%)[a]
98b	EtOH	125b	62
c	MeOH	c	63
d	EtOH	d	77[b]
e	EtOH	e	60
f,g	EtOH	f,g	63
i	MeOH	i	70[b]
105	MeOH	126	87[b]

(a) Isolated yield

(b) Initial investigation of this reaction was carried out by T.S. Abram[69].

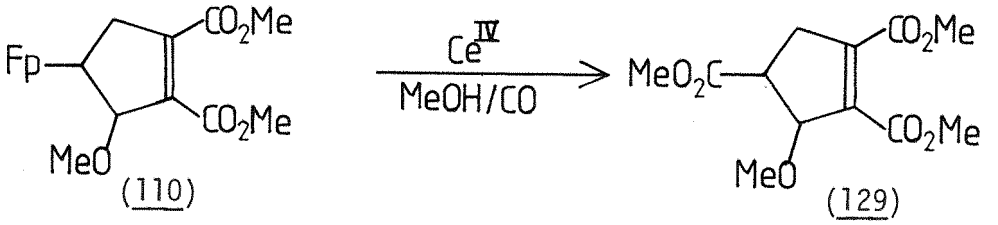
TABLE 23

Oxidative carboxylation of 2-methoxycyclopentyl-Fp complexes



(108) (127) (109) (128)

	R_1	R_2	R_3	R_4
d	CN	CN	H	CO_2Et
e	CO_2Et	CN	H	CO_2Et
f	CO_2Et	CN	H	CN
g	CN	CO_2Et	H	CN
i	CN	CN	CN	CN



(110) (129)

Fp adduct	ROH	Product	Product Yield (%)[a]
108d	EtOH	127d	71
e	EtOH	e	58
f,g	EtOH	f,g	75
i	MeOH	i	93[c]
109d	EtOH	128d	77
e	EtOH	e	41[b]
f,g	EtOH	f,g	53[b]
110	MeOH	129	25

(a) Isolated yield
(b) Isolated as a mixture of isomers after column chromatography
(c) This product could not be purified by column chromatography

however during chromatography to afford a mixture of isomers. This was demonstrated by the presence of a number of methoxyl resonances in the NMR spectra of the chromatographically isolated products. This isomerisation (of 128d-g) provides further evidence that adducts (128d-g) have the structures shown, since a derivative with an all *cis*-arrangement of substituents would be expected to rearrange to one with a more stable configuration on the column.

The low isolated yield of the DMAD adduct (129) is thought to be due to decomposition during chromatography, as the NMR spectrum of the crude product indicated quantitative conversion to (129).

(f) Summary

The cerium (IV) oxidation of cyclopentyl- and 2-methoxycyclopentyl-Fp complexes resulted in the expected replacement of the Fp group with an ester functionality. Similar treatment of 1-methoxycyclopentyl-Fp complexes however afforded a mixture of ketal and olefin derivatives.

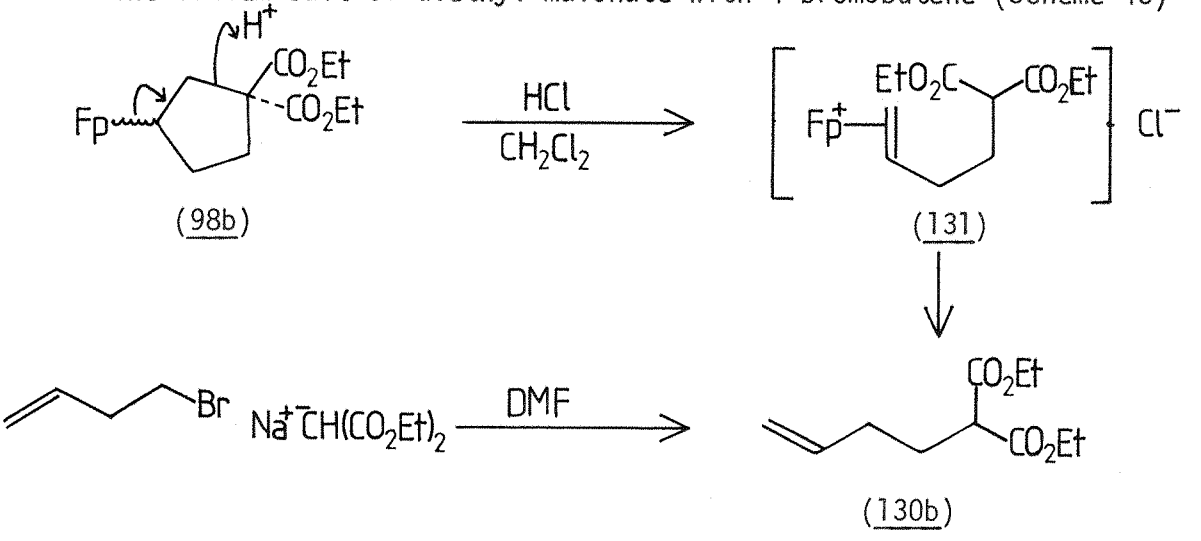
2. Acid Cleavage

(a) General procedure

Hydrogen chloride gas was passed through a solution of the Fp adducts in methylene chloride for one hour. The reaction mixture was then set aside overnight in a well-stoppered flask. Completion of reaction was indicated by IR, since the carbon monoxide stretching frequencies of the product, FpCl, (ν_{max} = 2050 and 2005 cm^{-1}) differs considerably from that of the starting materials (ν_{max} ≈ 2000 and 1950 cm^{-1}). On a number of occasions further treatment with hydrogen chloride was required to bring about complete reaction. After removal of the solvent under reduced pressure, the residue was dissolved in carbon tetrachloride and exposed to sunlight for several hours to decompose the FpCl present[54], during which time a green solid precipitated. This solid was then filtered off and the filtrate concentrated to yield the crude product, which was purified by flash chromatography[86] on silica gel.

(b) Cyclopentyl-Fp complexes

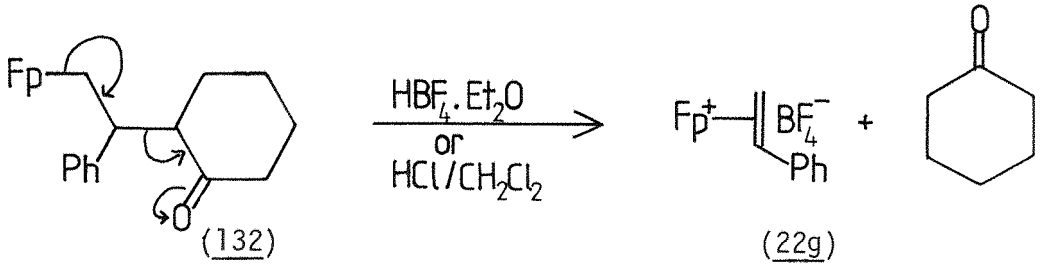
A single product was isolated, in 67% yield, from the reaction of the Fp adduct (98b) with HCl. The spectral data for this product was identical to that of diethyl 3-butenylmalonate (130b) prepared by the reaction of the sodium salt of diethyl malonate with 4-bromobutene (Scheme 43)[87].



(98b) (131) (130b)

Scheme 43

The IR spectrum of the crude reaction mixture indicated that the reaction had proceeded *via* the cationic intermediate (131), since the spectrum contained carbon monoxide frequencies (ν_{max} = 2075 and 2040 cm^{-1}) characteristic of an Fp(η^2-olefin) complex. A similar process has also been observed by Rosenblum *et al*[60], who found that treatment of an ether solution of complex (132) with $HBF_4.Et_2O$ led to the immediate and



(132) (22g)

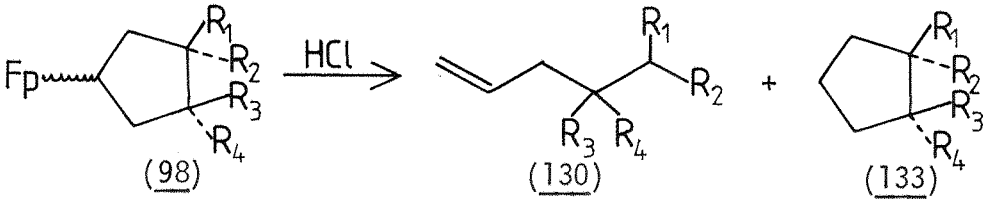
Scheme 44

quantitative precipitation of Fp(styrene)BF_4 (22g), and to the formation of cyclohexanone (Scheme 44). The same reaction was effected with HCl in methylene chloride, although somewhat less rapidly[60].

Although analogous linear products (130c and 130e) were obtained from the reaction of adducts (98c) and (98e) with HCl, Fe-C bond cleavage to afford cyclic derivatives (133c and 133e) was also observed. The product yields and ratios are summarised in Table 24. The formation of these cyclic products may be due to the presence of the electron-withdrawing

TABLE 24

Acid cleavage of cyclopentyl-Fp complexes



(98) (130) (133)

	R_1	R_2	R_3	R_4
b	CO_2Et	CO_2Et	H	H
c	CO_2Me	CO_2Me	H	CO_2Me
e	CO_2Et	CN	H	CO_2Et

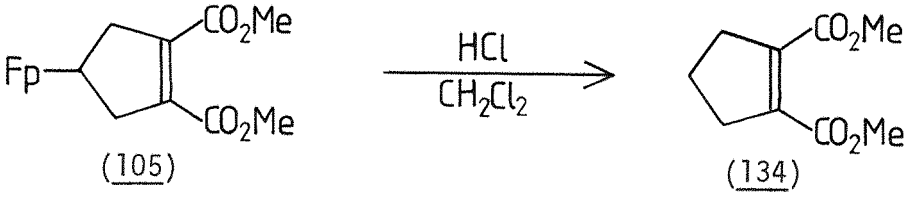
Fp adduct	Product Yield (%)[a]	Product Ratio (%)[b] 130	133
98b	67	100	-
c	70	50	50
e	61	33	67
105	75	100	-

(a) Isolated yield

(b) Estimated from the NMR spectrum of the mixture

group R_4, causing a reduction in the electron density at the C-4 carbon atom (to which R_1 and R_2 are attached) such that the ring-opening process becomes less favoured.

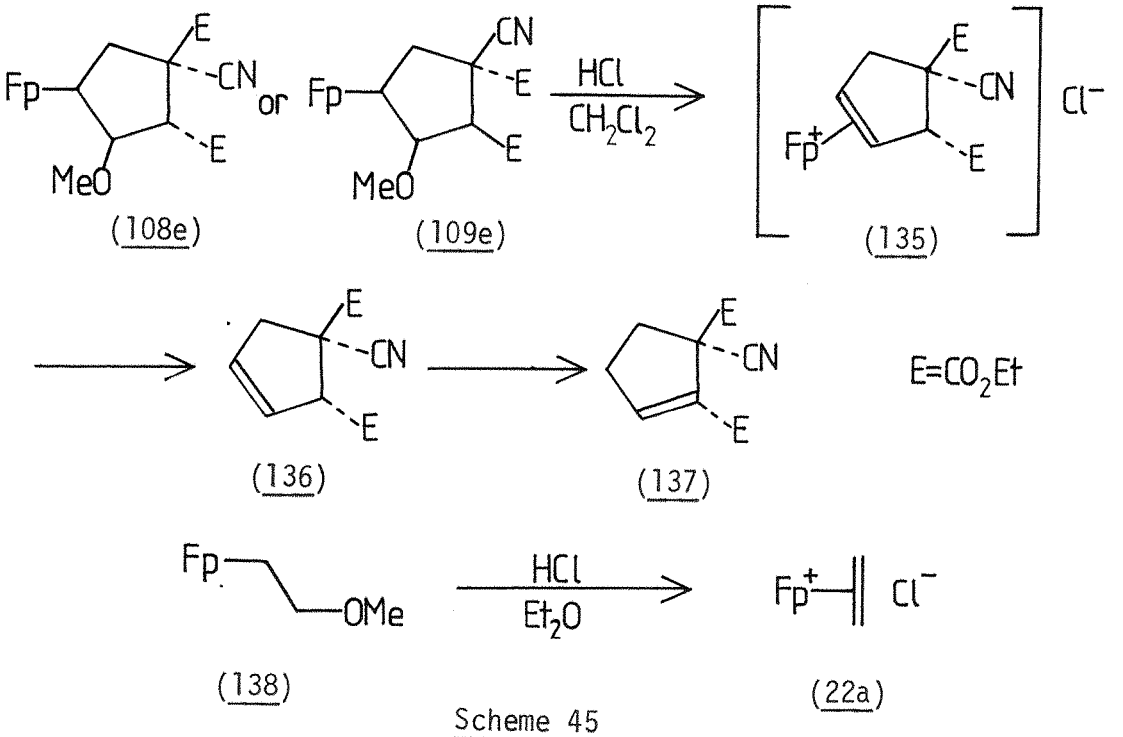
The cyclic derivative (134) was the exclusive product from the reaction of the DMAD adduct (105) with HCl (Table 24). The spectral data for this compound was identical to that reported for dimethyl cyclopentene-1,2-dicarboxylate[88].



(105) (134)

(c) 2-Methoxycyclopentyl-Fp complexes

Treatment of a methylene chloride solution of adducts (108e) and (109e) with hydrogen chloride resulted in the exclusive formation of olefin (136), which was isolated in yields of 75-81%. The IR spectrum of the crude reaction mixture indicated that the reaction had proceeded *via*



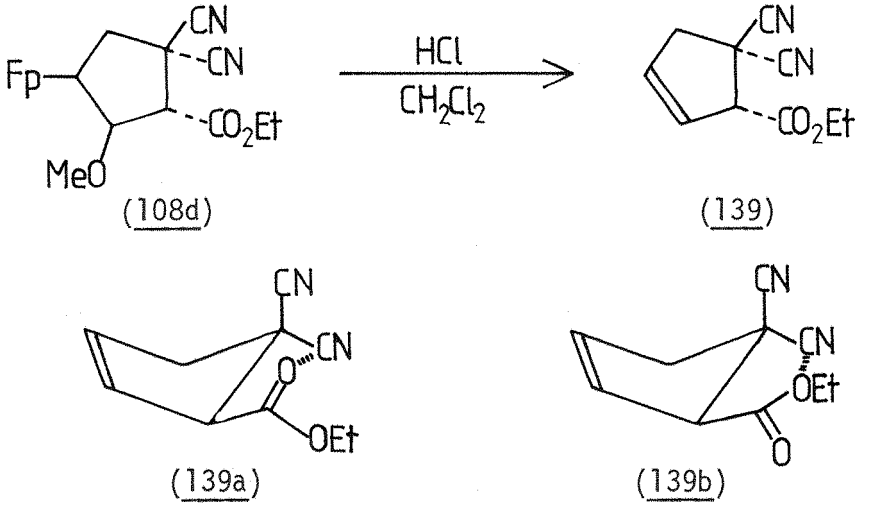
(108e) (109e) (135) (136) (137) (138) (22a)

Scheme 45

an Fp(η^2-olefin) cation (probably 135). Busetto *et al* have converted the 2-methoxyethyl-Fp complex (138) to the Fp(η^2-ethylene) cation (22a) in a similar manner (Scheme 45)[89].

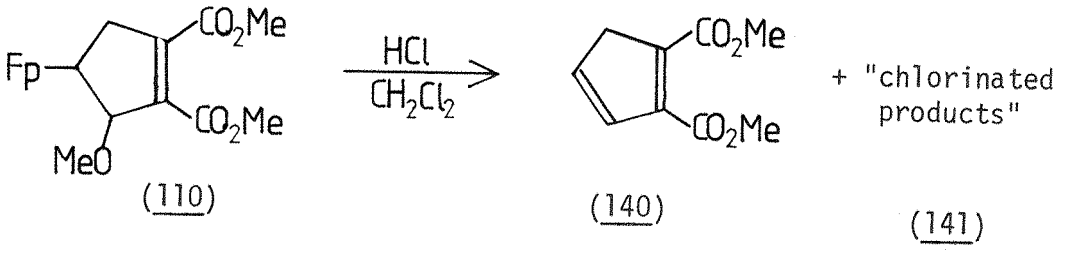
The NMR specrum of (136) was very unusual, in that the olefinic protons resonated as a broad singlet (δ=5.90) instead of the expected complex multiplet. Treatment of an ethanolic solution of this olefin with sodium ethoxide isomerised the double bond to give the α,β-unsaturated ester (137), in which the olefinic proton resonated as a triplet (δ= 7.15, J≈2Hz) as expected.

Fp adduct (108d) also gave the eliminated product (139) in 56% yield on reaction with HCl. The $-OCH_2-$ protons of this olefin were found to resonate as two quartets of equal intensity, which suggests that (139) exists in two conformations (as with the Fp adducts 78d, 108d and 109d - see Chapter Two). The occurrence of two discrete conformations may arise from dipole-dipole interactions between the carbon atom of one of the nitrile functionalities and either the carbonyl, or ether, oxygen atoms of the ester group (139a and 139b).



(108d) (139) (139a) (139b)

Reaction of the DMAD adduct (110) with HCl occurred rapidly at room temperature to afford a mixture of products which could not be separated by flash chromatography. Examination of the NMR and mass spectra of the mixture (the mass spectrum is given in Table 25) indicated the presence of the olefin (140) and a chlorinated derivative (141) (or derivatives) of this olefin (i.e. 140 + HCl).



(110) (140) (141)

TABLE 25

Mass spectrum of the mixture of (140) and (141)

m/e	Intensity (%)	Ion assignment
187	10	141 - OMe
183	43	141 - Cl
182	10	140
154	40	141 - CO_2Me
158	30	141 - H, CO_2Me
151	100	140 - OMe
124	54	140 - CO_2CH_2

(d) Summary

Linear products resulting from a ring-opening process, together with those arising from the replacement of the Fp group with a hydrogen atom, were isolated (in varying ratios) from the reaction of cyclopentyl-Fp complexes with HCl. Similar treatment of 2-methoxy-cyclopentyl-Fp complexes resulted in the elimination of FpOMe to give cyclopentene derivatives as the sole products.

3. Bromination

(a) General procedure

To a solution of the Fp adduct in methylene chloride at approximately -70°C was added 1-3 equivalents of N-bromopyridinium bromide in one portion. The reaction mixture was then allowed to come to room temperature, with an additional 1-2 equivalents of the brominating

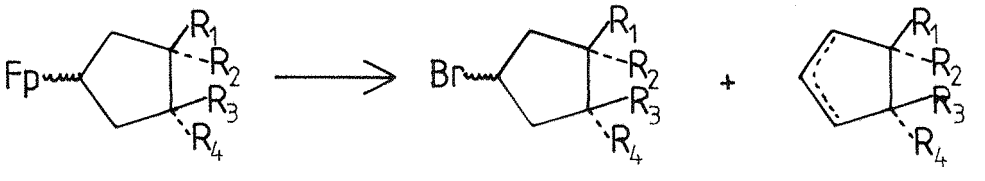
reagent being added when the temperature had reached -20°C. The extent of reaction was again monitored by IR spectroscopy. On reaching room temperature the solution was either filtered through a short column of neutral alumina (Act III) (or florisil) or washed with saturated aqueous sodium thiosulphate solution to remove the excess N-bromopyridinium bromide present. After removal of the solvent under reduced pressure the residue was, in general, dissolved in a 50:50 mixture of diethyl ether/petroleum ether (40-60) and exposed to sunlight for several hours to decompose any FpBr present. The solution was then filtered, the filtrate concentrated and the crude product purified by column chromatography on neutral alumina (Act III).

(b) Cyclopentyl-Fp complexes

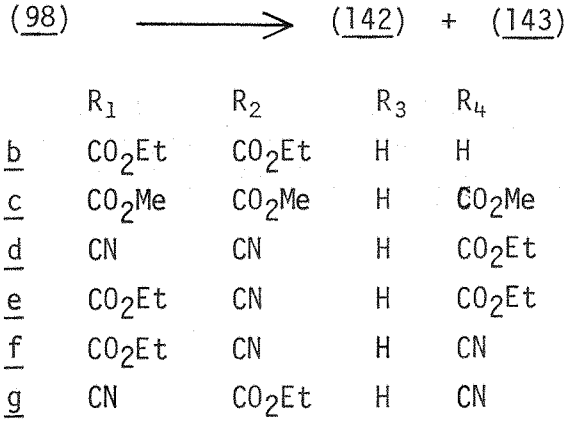
Treatment of a methylene chloride solution of Fp adducts (98b,c,e) with N-bromopyridinium bromide afforded, after work up, a mixture of brominated and olefinic products (Scheme 46). No analogous compounds could be isolated however from the bromination of complexes (98d) and (98f,g), although the IR spectra of the reaction mixtures indicated complete reaction. The reaction conditions employed and the yields and ratios of the products obtained are summarised in Table 26. No attempt was made to optimise the yields of (142) and (143), or to effect reaction with complexes (98d) and (98f,g), by using a different brominating reagent or by varying the reaction conditions.

TABLE 26

Bromination of cyclopentyl-Fp complexes



(98) (142) (143)



Scheme 46

Fp Adduct	Molar equivalents of N-bromo pyridinium bromide added at:- -70°C	-20°C	Procedure for the removal of excess bromide	Product yield (%)[d]	Product ratio (%)[a] 142	143
98b	2	-	a	85	65	35
b	1	1	b	76	65	35
c	1	1	a	29	75	25
c	1	1	b	43	75	25
d	3	2	a	0	-	-
e	1.5	1.5	b		60	40
f,g	2	2	c	0	-	-

(a) Washed with saturated aqueous sodium thiosulphate solution

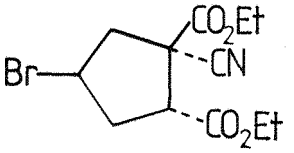
(b) Filtered through a short neutral alumina column (Act III) or (c) a short florisil column.

(d) Isolated yield

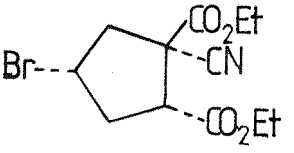
(e) Estimated from the NMR spectrum of the mixture

It has been postulated[33,64] that brominolysis of iron-carbon bonds involves initial formation of an iron radical cation by an oxidative process. This intermediate could then undergo direct attack either by Br· or Br^- (see Chapter One). Steric factors may disfavour this process however with the cyclopentyl-Fp complexes such that the elimination of FpH also occurs.

The brominated product (142e) was isolated as a mixture of two isomers (144a and 144b), which were partially separated by flash chromatography on silica gel. It is probable that the bromination reaction



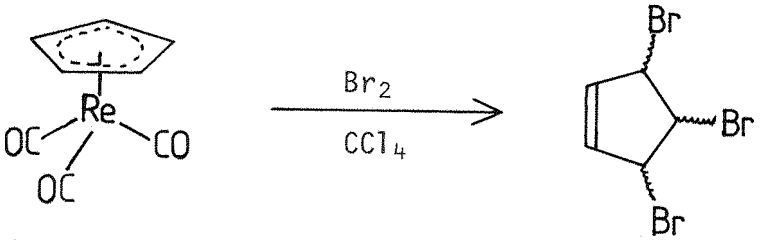
(144a)



(144b)

has occurred with inversion of configuration[61,63,64]. Hence, it can be concluded that the Fp adduct (98e) must also exist as a mixture of isomers.

3,4,5-Tribromocyclopentene (145) was the only product isolated, in approximately 20% yield, from the reaction of (98d) and (98f,g) with N-bromopyridinium bromide. This unusual compound was thought to have arisen from the bromination of the cyclopentadienyl group of the Fp complex, as treatment of a carbon tetrachloride solution of tricarbonyl (η^5-cyclopentadienyl) rhenium (146) with bromine at room temperature afforded 3,4,5-tribromocyclopentene in 21% yield (Scheme 47)[90]. Compound (145) was formed to a lesser extent from the bromination of adducts (98b,c,e).



(146) (145)

Scheme 47

The low isolated yields obtained in a number of reactions, together with the failure to isolate any of the desired product (142) from the bromination of adducts (98d) and (98f,g), may be due to the decomposition of the brominated adduct (142) on irradiation with sunlight, since the crude reaction products (142, 143, FpBr, etc) were obtained in high yield (70-100%). In addition, FpBr was separated from (142b) and (143b) by column chromatography on neutral alumina (Act III). The isolation procedure involving decomposition of the iron complex with light followed by filtration was not required in this case, which could account for the high isolated yield of these two derivatives, (142b) and (143b). Separation of FpBr from adducts (142c,e) and (143c,e) could not be effected by chromatographic means however, as the retention times for these adducts were too similar to that of the iron complex on neutral alumina, silica gel and florisil.

4. β-Hydride Abstraction Followed by Olefin Liberation

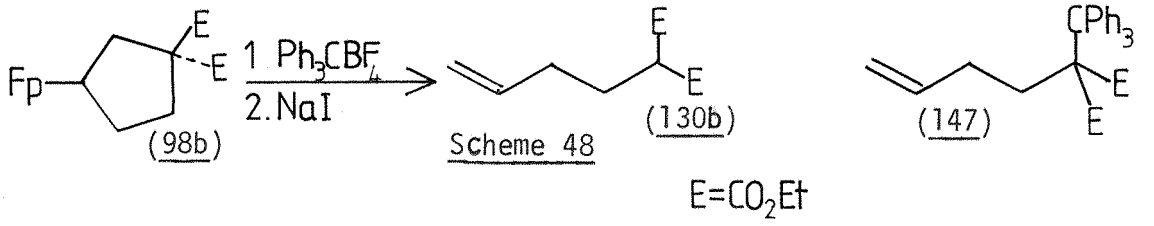
(a) General procedure

A solution of the Fp adduct in methylene chloride was treated with one equivalent of trityl tetrafluoroborate at 45°C and the progress of the reaction monitored by IR spectroscopy. Complete reaction was normally indicated after approximately three hours. The reaction mixture was then cooled to 0°C and diethyl ether added to precipitate the Fp(η^2-olefin) tetrafluoroborate salt. This was collected, dissolved in acetone (without further purification) and treated with two equivalents of sodium iodide for one hour at room temperature. The solvent was then removed *in vacuo* and the crude product purified by flash chromatography[86] on silica gel. The FpI formed in the reaction was removed by exposure of a carbon tetrachloride solution of the mixture to sunlight for several hours, followed by filtration to remove the decomposed adduct.

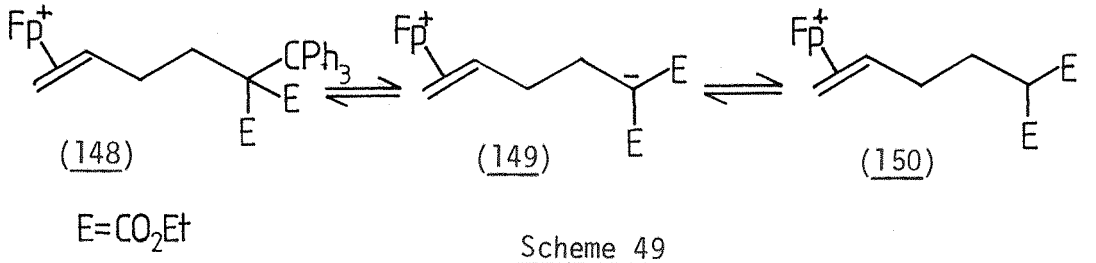
(b) Cyclopentyl-Fp complexes

Reaction of the cyclopentyl-Fp complex (98b) with trityl tetrafluoroborate and then sodium iodide resulted in the formation of the linear product (130b) in 51% yield (Scheme 48). A number of analogous reactions have recently been reported by Rosenblum *et al*[60]. For example,

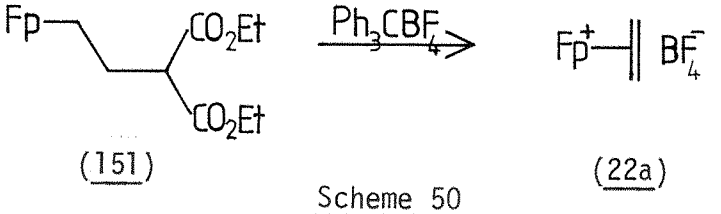
the malonate adduct (151) was converted to the ethylene cation (22a) on treatment with trityl tetrafluoroborate in methylene chloride at 45°C (Scheme 50)[60]. The formation of the linear compound (130b) is surprising in that a ring-opening process would be expected to yield the trityl derivative (147). One possible explanation for this result is that the considerable steric bulk of the trityl group may have destabilised the cation (148) such that dissociation to the zwitterion (149) occurred



Scheme 48



Scheme 49

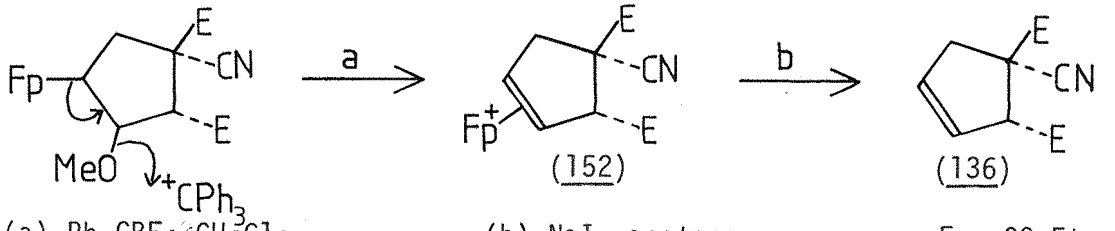


Scheme 50

under the reaction conditions employed. Addition of a proton to this dipolar ion would then lead to the requied Fp(η^2-olefin)cationic intermediate (150, Scheme 49). Alternatively, HBF_4 may have been generated in the reaction mixture, and this may have reacted with (98b) in an identical manner to that earlier described for the HCl reaction.

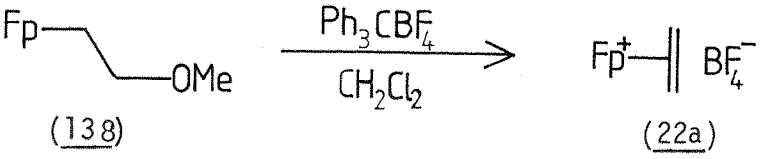
(c) 2-Methoxycycloalkyl-Fp complexes

The olefinic derivative (136) was the exclusive product (isolated in 62% yield) from the treatment of the Fp adduct (108e) with the trityl cation, followed by reaction of the intermediate Fp(η^2-olefin) tetrafluoroborate salt (152) with sodium iodide (Scheme 51). This



Scheme 51

elimination of FpOMe has also been observed by Rosenblum *et al* in the reaction of the 2-methoxyethyl-Fp complex (138) with trityl tetrafluoroborate in methylene chloride at 0°C (Scheme 52)[91].



(138) (22a)

Scheme 52

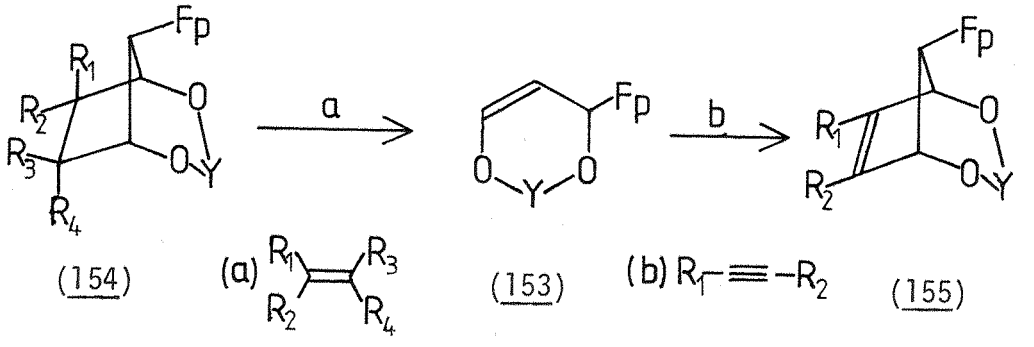
CHAPTER FOUR

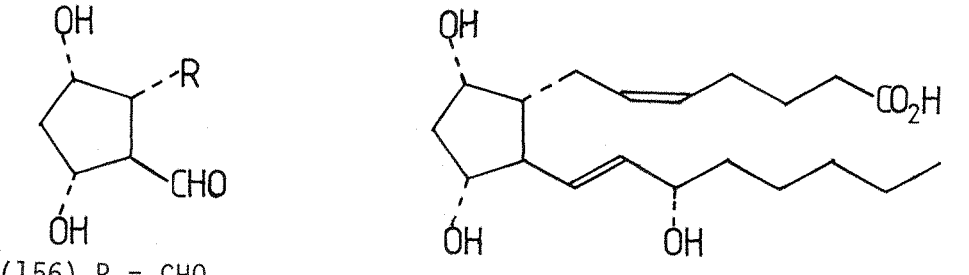
Synthesis of Cyclopentanoid Natural Products *via* a Metal Assisted (3+2) Cycloaddition Reaction; A Preliminary Study

1. PGFα Type Prostaglandins

Introduction

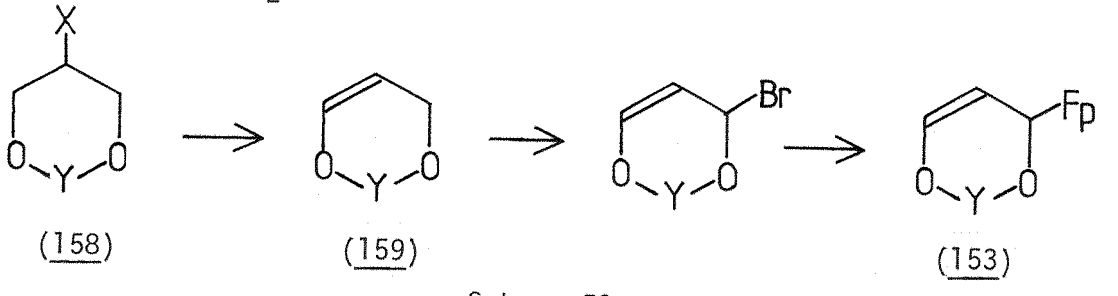
We reasoned that the reaction of an appropriate (η'-allyl)Fp complex (153, Y = protecting group) with a suitable electron-deficient olefin, or acetylene, could lead to bicyclic derivatives (154, 155) which could then





(156) R = CHO
(157) R = CH_2CHO

(1)



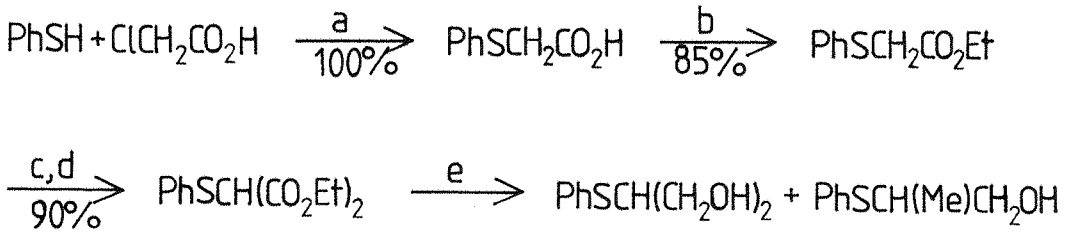
(158) (159) (153)

Scheme 53

be converted to intermediates (156, 157) of value in the synthesis of PGF_{α} type prostaglandins, such as $PGF_{2\alpha}$ (1). The preparation of the Fp complex (153) by the route outlined in Scheme 53 was therefore investigated.

Results and Discussion

A route to the protected propene-1,3-diol (159) was devised involving the reduction of diethyl (phenylthio)malonate (160) followed by protection of the diol thus formed. A dehydrosulphenylation reaction[92] should then give rise to the required olefin. Although the diester (160) was prepared in high overall yield by the procedure described by Huntress and Olsen (Scheme 54)[93], reduction of this adduct with lithium aluminium



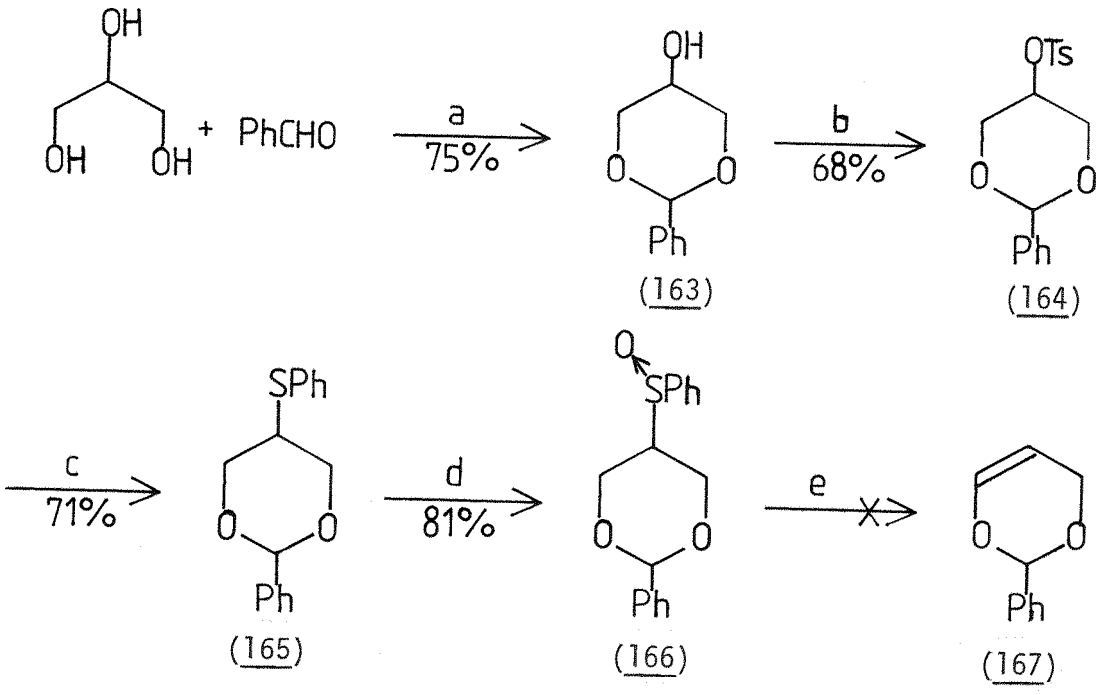
(160) (161) (162)

(a) aq NaOH
(b) cH_2SO_4, EtOH
(c) $(CO_2Et)_2$
(d) Δ
(e) $LiAlH_4$, THF

Scheme 54

hydride afforded 2-phenylthiopropane-1,3-diol (161) in only 20% yield. Starting material, thiophenol and 2-phenylthiopropane-1-ol (162) were also isolated from the reaction mixture. The formation of the latter compound (162) was surprising since the removal of a hydroxyl group by lithium aluminium hydride normally requires the presence of a Lewis acid[94]. Several workers[95,96] have encountered similar difficulties in the reduction of analogous compounds. A different approach to the protected 2-phenylthiopropane-1,3-diol (158, X = SPh) was therefore adopted.

In a modification of the method of Foster *et al*[97], a mixture of *cis*- and *trans*-5-hydroxy-2-phenyl-1,3-dioxane (163) was prepared (in approximately an 8:1 ratio of *cis:trans*) by an acid catalysed reaction between glycerol and benzaldehyde. The *cis*-isomer was thought[96] to have predominated in the product mixture as, in the preferred conformation (163a) of this isomer, the phenyl group occupies the more favoured equatorial position, with the hydroxyl group consequently axial (where hydrogen-



(a) cH_2SO_4

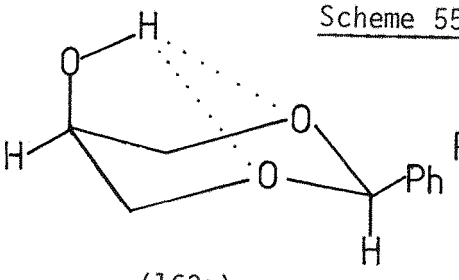
(b) TsCl, pyridine

(c) NaSPh, DMF

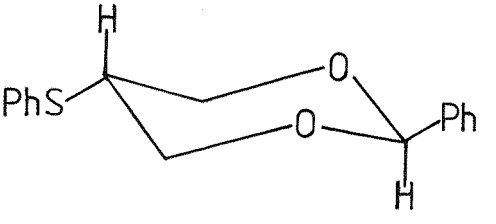
(d) MCPBA, CCl_4

(e) Δ

Scheme 55



(163a)



(165a)

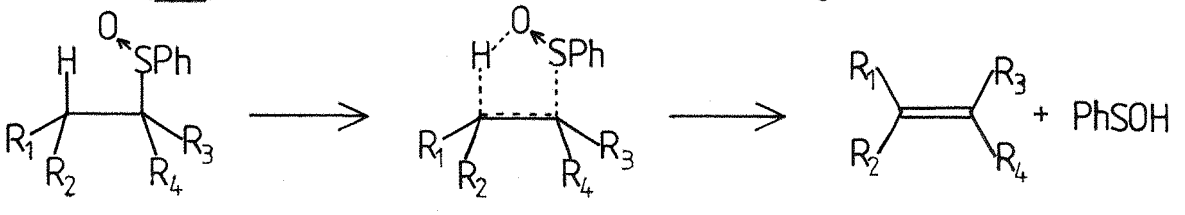
bonding with the ring-oxygen atoms can occur). Conversion of the alcohol (163) into the *cis*-p-toluenesulphonate (164)[98], and reaction of the latter with sodium phenylsulphide in dimethylformamide (DMF) afforded the phenylthio-derivative (165)[95], which was assumed to have the *trans*-configuration (165a) (the result of an S_N2 displacement process). This product (165) an oxidation with m-chloroperbenzoic acid (MCPBA) gave the phenylsulphoxide (166) in high overall yield (Scheme 55). The elimination of benzene sulphenic acid (PhSOH) from the sulphoxide (166) was then attempted using a variety of reaction conditions. These conditions, together with the results obtained, are summarised in Table 27.

TABLE 27

Attempted dehydrosulphenylation of the phenylsulphoxide (166)

Temp (^{o}C)	Solvent	Reaction time (hrs)	Recovered starting material (%)	Products Isolated
80	Refluxing benzene	24	100	-
110-111	Refluxing toluene	120	50	None
137-142	Refluxing xylene	17	0	None
140-150	DMF	24	0	None

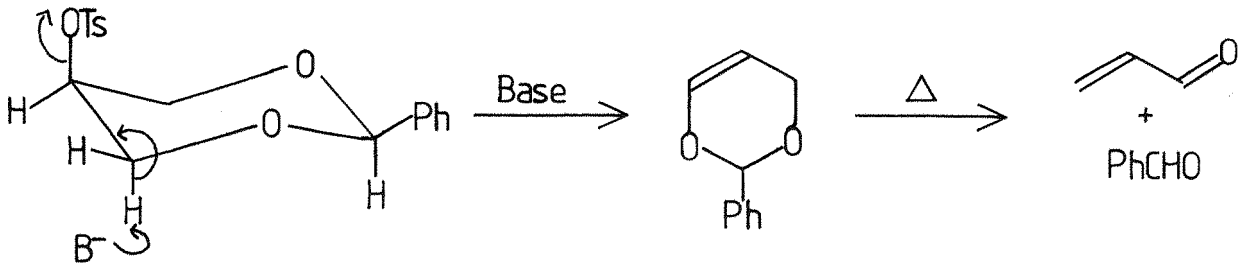
It has been shown[92] that dehydrosulphenylation proceeds *via* a syn elimination mechanism (Scheme 56). In the case of the cyclic phenylsulphoxide (166), considerable deformation of the ring would have to occur



Scheme 56

before the required syn conformation could be achieved. Hence, from the results obtained (Table 27) it appears that 80^{o}C (refluxing benzene) was too low a temperature to bring about this deformation and elimination. On using higher temperatures loss of starting material (166) was observed, although no products could be isolated after the removal of the solvent under reduced pressure. This suggested that decomposition of either the sulphoxide (166) or the olefinic product (167) had occurred, possibly to derivatives of similar boiling point to the solvents employed in the reaction.

2-Phenyl-1,3-dioxin (167) was prepared in yields of 14%, 48% and 89% respectively, by the reaction of 2-phenyl-5-(p-toluenesulphonyloxy)-1,3-dioxane (164) with either solid potassium hydroxide[99], n-butyllithium in tetrahydrofuran, or potassium t-butoxide in dimethylsulphoxide. On



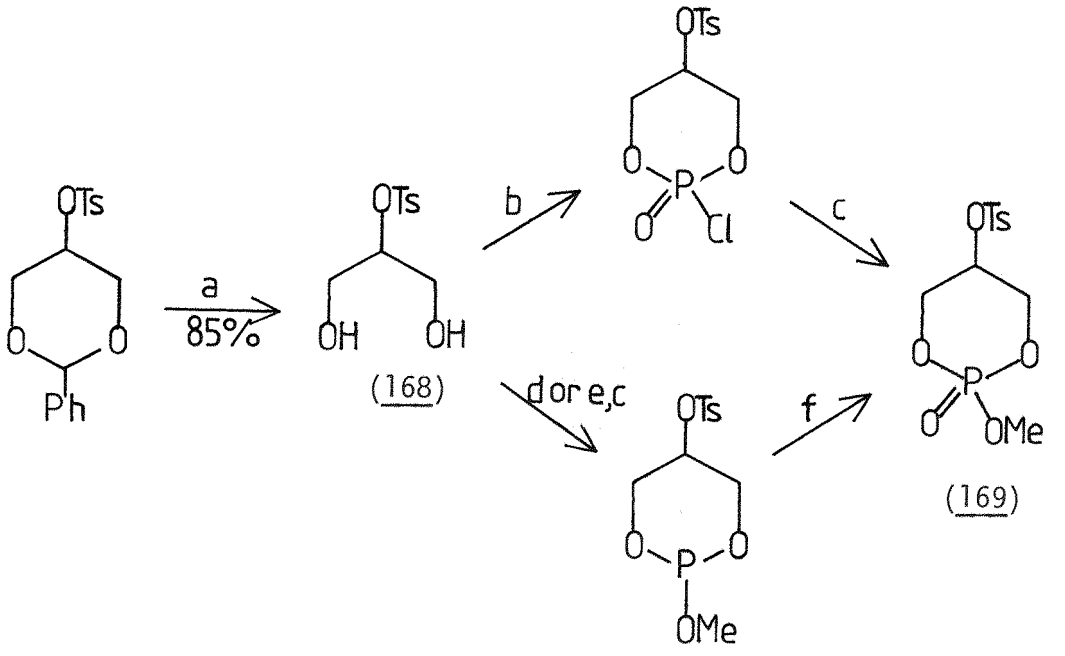
(164) (167)

Scheme 57

heating a carbon tetrachloride solution of this olefin under reflux, a *retro*-Diels Alder reaction occurred to afford acrolein and benzaldehyde (Scheme 57). The complete lack of desired products from the above mentioned attempted dehydrosulphenylation reaction (166→167) may therefore be accounted for by the elimination of PhSOH, followed by rearrangement of the olefin (167). As both acrolein and benzaldehyde are relatively low boiling liquids they would be removed along with the solvents.

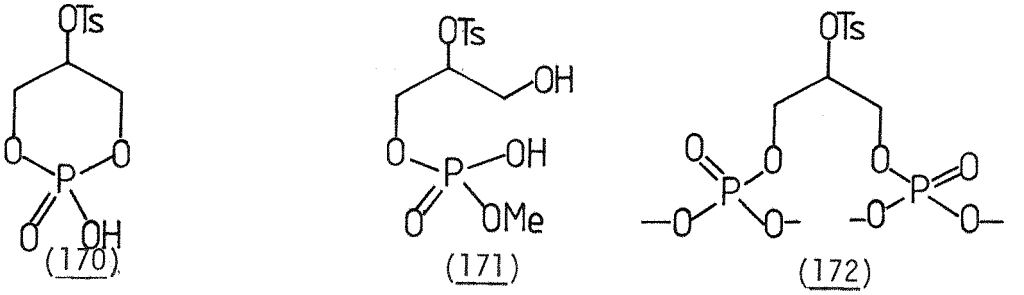
The next step in the reaction sequence is the allylic bromination of 2-phenyl-1,3-dioxin employing N-bromosuccinimide. This reaction could not be carried out using the standard reaction conditions[100], since the olefin (167) rapidly decomposed at the reaction temperatures normally employed (e.g. refluxing carbon tetrachloride). Irradiation of the reaction mixture with visible light, and performing the reaction in the presence of a radical initiator, at lower temperatures resulted in none of the desired allylic bromide being formed. This was indicated by NMR analysis. Similar problems have been encountered by Shelton and Ciadella in the attempted allylic bromination of dihydropyran[101].

It was considered that the stability of the protected propene-1,3-diol (159) could be increased by using a phosphorus protecting group, since phosphorus-oxygen bonds are considerably stronger than carbon-oxygen bonds. Treatment of the p-toluenesulphonate (164) with acidic aqueous methanol led to the formation of 2-(p-toluenesulphonyloxy)-propane-1,3-diol (168) in 85% yield. Low yields (<6%) of the desired cyclic phosphate (169) were obtained however on reaction of this diol with either (1) phosphorus oxychloride followed by treatment with methanol,



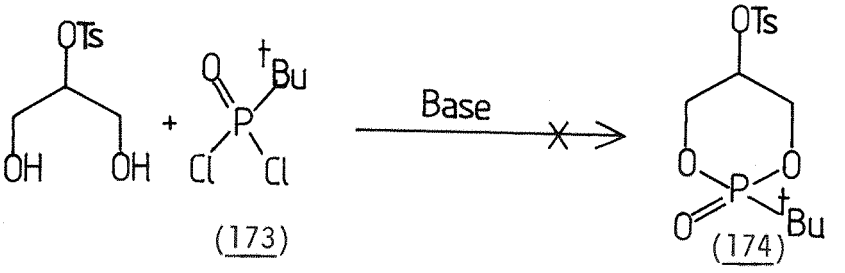
(a) 1N H_2SO_4, MeOH
(b) $POCl_3$, CH_2Cl_2
(c) MeOH
(d) $P(OMe)_3$, Toluene
(e) PCl_3, CH_2Cl_2
(f) N_2O_4, CH_2Cl_2

Scheme 58



(2) trimethylphosphite followed by oxidation of the product with dinitrogen tetroxide, or (3) phosphorus trichloride followed by treatment of the product with methanol and dinitrogen tetroxide (Scheme 58). The low yields of these reactions may be due to hydrolysis of the required product (169), giving cyclic or linear dialkylphosphate esters (170 or 171), during column chromatography on neutral alumina (Act III). Alternatively, polymeric species (172) may have been formed in the reaction.

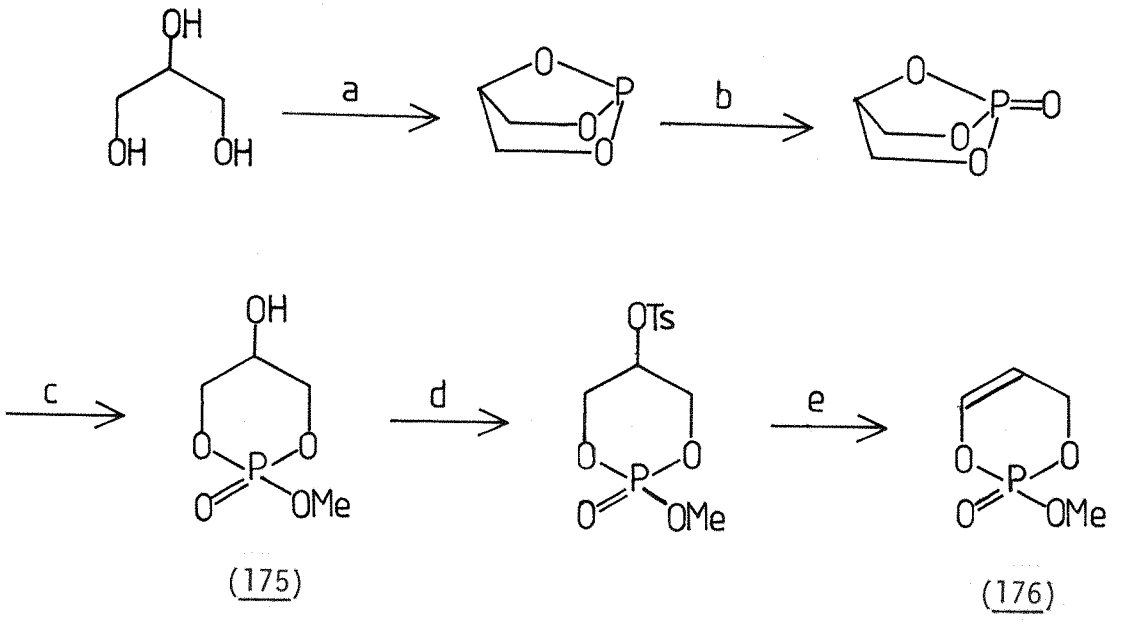
A base catalysed condensation reaction of the 1,3-diol (168) with t-butylphosphonyldichloride (173)[102] also failed to give the desired cyclic derivative (174) (Scheme 59).



(173) (174)

Base = R_3N, pyridine, $NaHCO_3$, K_2CO_3, NaH or n-BuLi

Scheme 59



(175) (176)

(a) $P(OMe)_3$, NaOMe
(b) N_2O_4
(c) MeOH
(d) TsCl
(e) Base

Scheme 60

Although this was not attempted, it may be possible to prepare the phosphorus protected propene-1,3-diol *via* the known phosphate ester (175)[103,104] (see Scheme 60). Allylic bromination followed by metalation could then lead to the desired (η'-allyl)Fp complex (153).

2. Brefeldin A

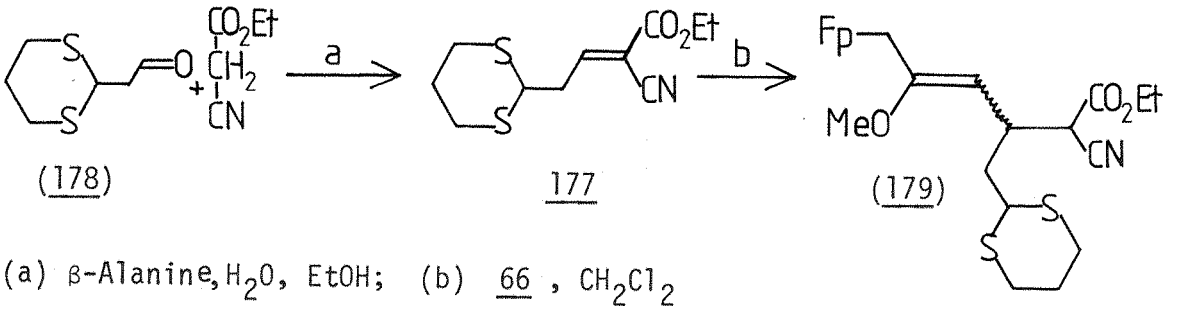
Reaction of ethyl 2-cyano-4,4-trimethylenedithiocrotonate (177) with (η'-allyl)Fp complexes

It was considered that a (3+2) cycloaddition reaction between the (η'-2-methoxyallyl)Fp complex (66) or the simple (η'-allyl)Fp complex (20a) and olefins such as ethyl 2-cyano-4,4-trimethylenedithiocrotonate (177) could lead to synthetic precursors of a number of cyclopentanoid natural products. Two proposed syntheses of brefeldin A (2) involving a (3+2) cycloaddition reaction are presented in Scheme 62.

Ethyl 2-cyano-4,4-trimethylenedithiocrotonate (177) was prepared by a Knoevenagel condensation reaction between 3,3-trimethylenedithiopropanal (178)[105] and ethyl cyanoacetate, catalysed by β-alanine (Scheme 61). The product was only partially purified by flash chromatography on silica gel[85] as separation from the ethyl cyanoacetate present proved difficult. Distillation *in vacuo* resulted in considerable decomposition of the olefin.

Reaction of olefin (177) with the 2-methoxyallyl complex (66), in methylene chloride at room temperature for 2 hours, afforded the linear adduct (179) (*cf* the desired cyclic adduct 180) in 54% isolated yield (Scheme 61). Surprisingly, no hydrolysis of this product occurred during chromatography on neutral alumina (Act III). A cyclic product (181) was obtained however from the reaction between the olefin (177) and the simple (η'-allyl)Fp complex (20a), performed in dimethylformamide at room temperature for 20 hours. This cyclic adduct (181) was isolated in 41% yield after column chromatography on neutral alumina (Act. III). Attempts to cleave the iron-carbon bond of adduct (181) with N-bromopyridinium bromide failed however to give the brominated product (182).

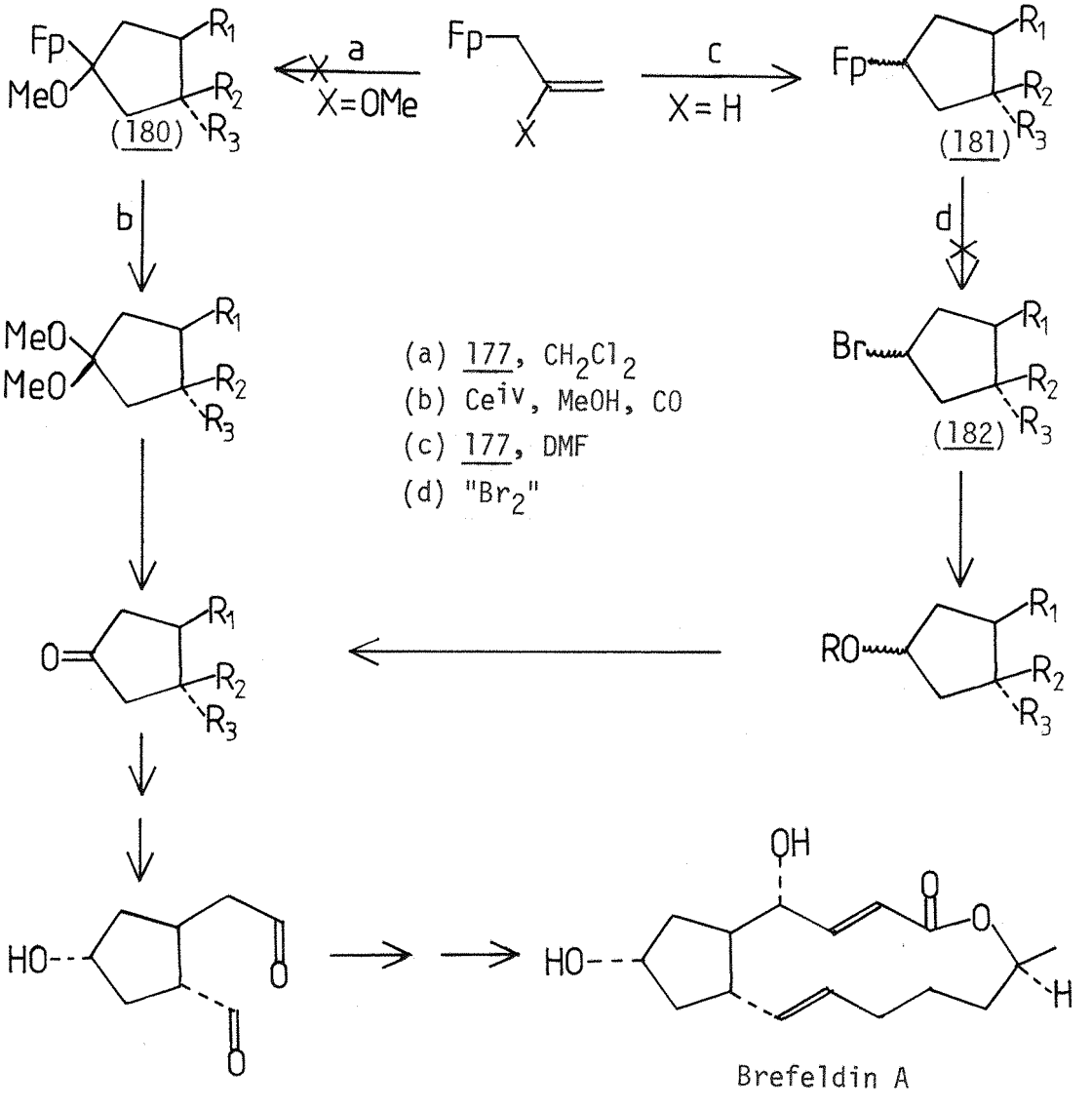
No reaction was observed between ethyl 1-cyano-4,4-trimethylenedithiocrotonate (177) and the (η'-3-methoxyallyl)Fp complex (28) over 24 hours, at room temperature, when the reaction was performed in dimethyl formamide, although the NMR spectrum of the crude product indicated complete loss of the olefin. This may have been due to the decomposition of olefin (177) before reaction with the Fp complex (28) could occur.



(178) 177 (179)

(a) β-Alanine, H_2O, EtOH; (b) 66 , CH_2Cl_2

Scheme 61



(180) (181) (182)

(a) 177, CH_2Cl_2
(b) Ce^{IV}, MeOH, CO
(c) 177, DMF
(d) "Br_2"

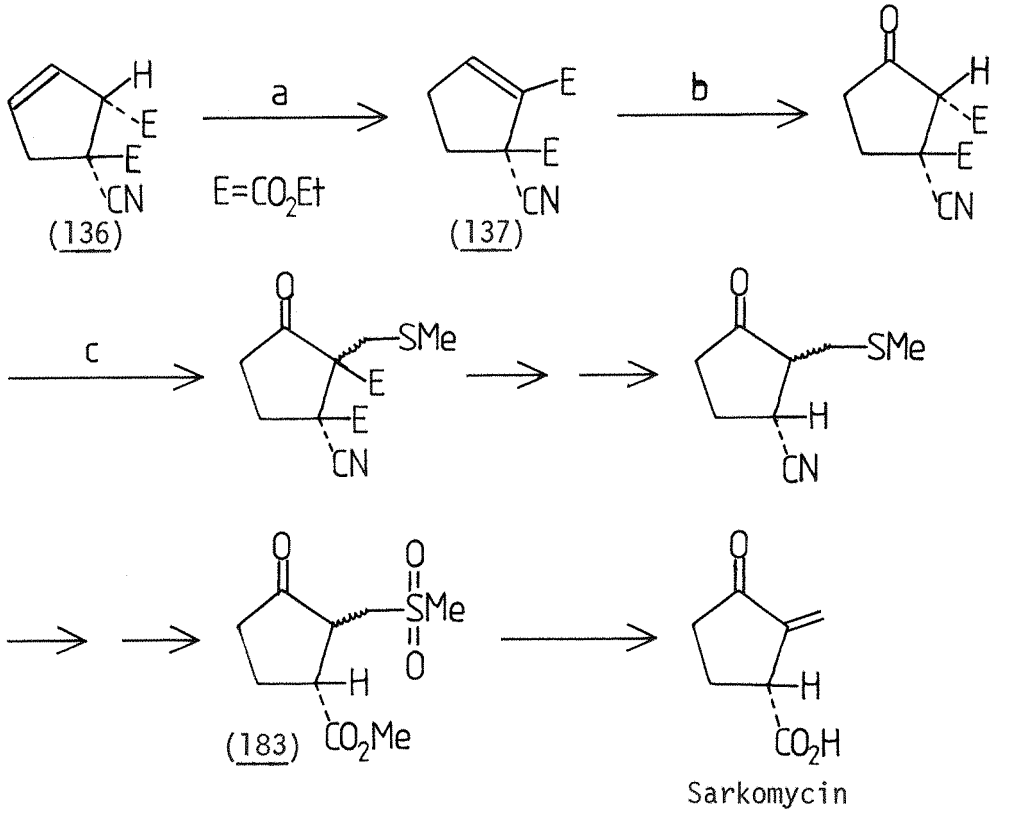
Brefeldin A

R_1=CH_2 ; R_2=CN ; R_3=CO_2Et

Scheme 62

3. Sarkomycin

Boeckman *et al*[106] have synthesised the antitumour agent sarkomycin (7) *via* the sulphone (183). It was considered that it could be possible to prepare this adduct (183) from diethyl 1-cyano-3-cyclopentene-1,3-dicarboxylate (136) by the route outlined in Scheme 63.



(a) NaOEt,EtOH

(b) [O]

(c) KOt-Bu, $MeSCH_2I$

Scheme 63

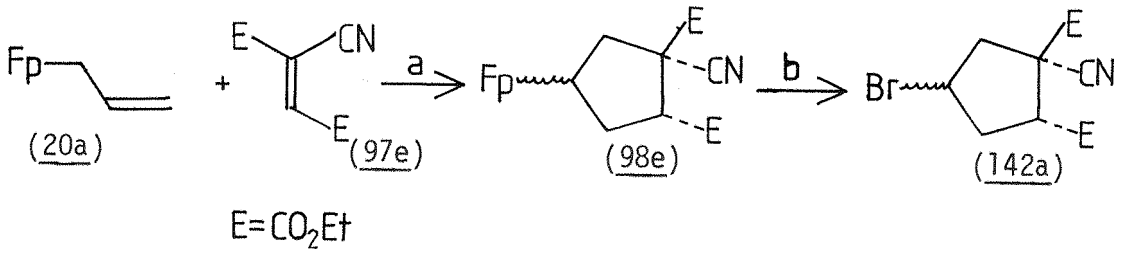
Isomerisation of the cyclopentene derivative (136) to the α,β-unsaturated ester (137) was achieved in 78% yield by the treatment of an ethanolic solution of this olefin with sodium ethoxide, at room temperature, for 30 seconds. Lower yields were obtained when longer reaction times were employed, whereas only 25% isomerisation occurred on heating a pyridine solution of (136) for 24 hours at approximately 100°C. No reaction was observed on treatment of (136) with sodium acetate in diethyl ether.

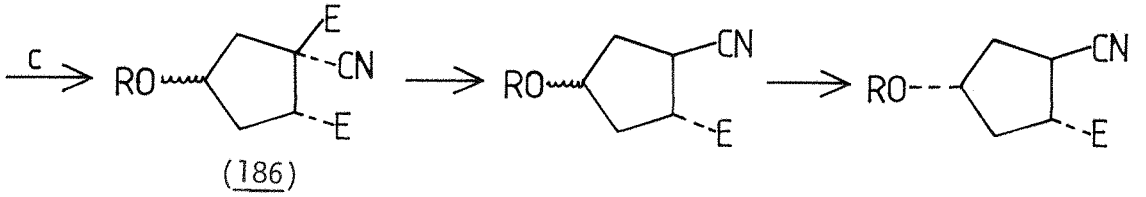
Although unchanged starting material was the only material isolated from the attempted dimethylsulphoxide oxidation of the α,β-unsaturated ester (137), several alternative methods have been reported[107] which could bring about this conversion. It should, therefore, be possible to synthesise sarkomycin by the proposed route (Scheme 63).

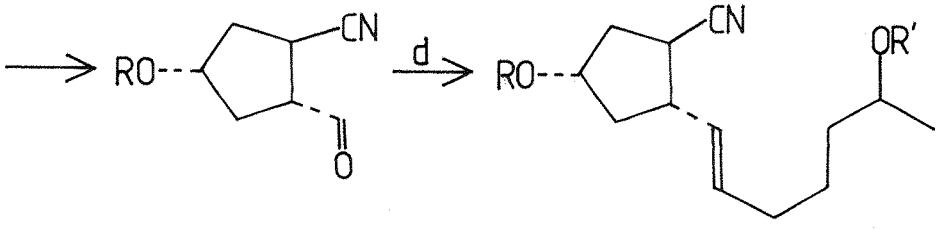
4. Future Work

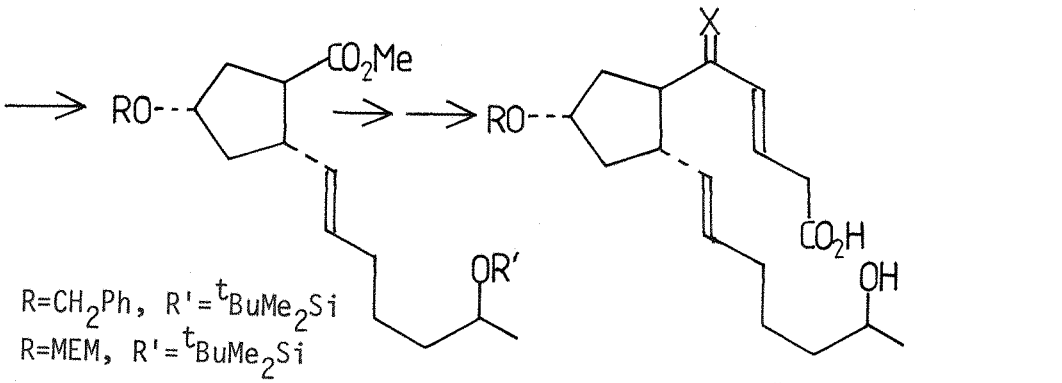
Corey[108] and Bartlett[109] have reported the total synthesis of racemic brefeldin A (2) *via* the intermediates (184b,c) and (185). It was postulated that reaction of diethyl 4-bromo-1-cyanocyclopentane-1,2-dicarboxylate (142e) with the sodium salt of benzyl alcohol might lead to the benzyl ether (186, R=CH_2Ph), a possible precursor of these intermediates. The proposed reaction sequence for the conversion of (186) to (184) is outlined in Scheme 64. For this synthesis to be viable however, the yield of the bromination reaction (98e → 142e) would have to be improved. In addition, problems could be encountered in the formation of the benzyl ether as elimination of HBr or reaction with the ester functionalities is also possible.

Allylic oxidation of the cyclopentene derivative (136), followed by decarboethoxylation of the α,β-unsaturated ketone (187) thus formed, could lead to the formation of a useful intermediate (188) for the synthesis of PGA type prostaglandins (189). Alternatively, a similar intermediate (190) could be prepared from the products isolated from the oxidative carboxylation of Fp adducts (108e) and (109e) (see Chapter Three). Schemes 65 and 66 provide a summary of these synthetic possibilities.





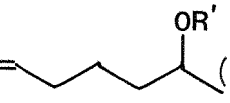




184a R=CH_2Ph, R'=$^tBuMe_2Si$
b R=MEM, R'=$^tBuMe_2Si$
c R=MEM, R'=H

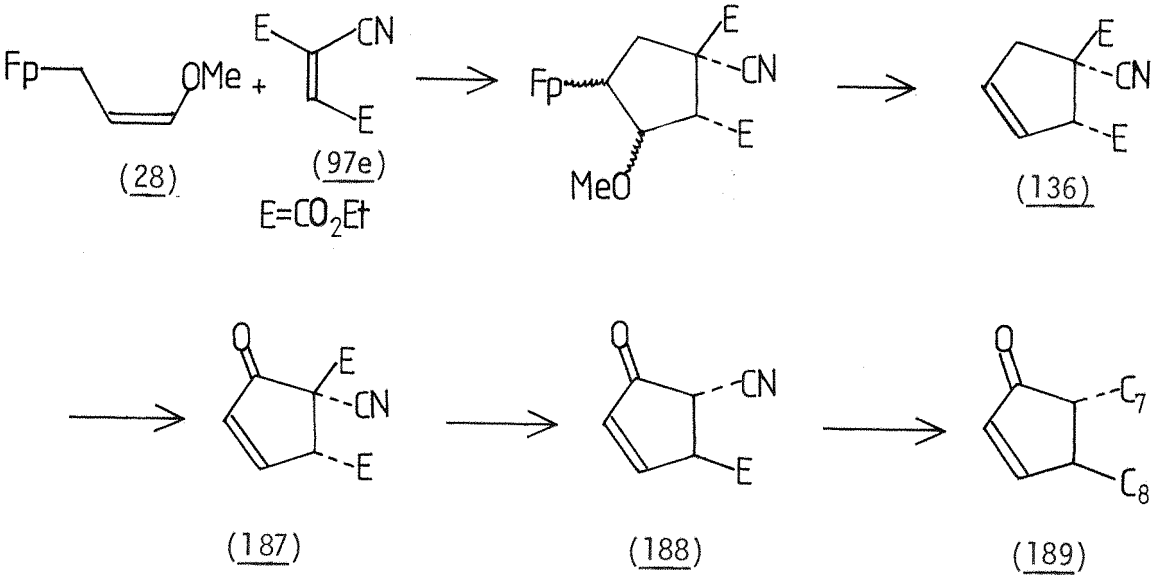
185a X = H, OMEM
b X = O

⟶ Brefeldin A

(a) CH_2Cl_2, 81%
(b) N-bromopyridinium bromide, CH_2Cl_2
(c) $PhCH_2ONa$
(d) Ph_3P= 

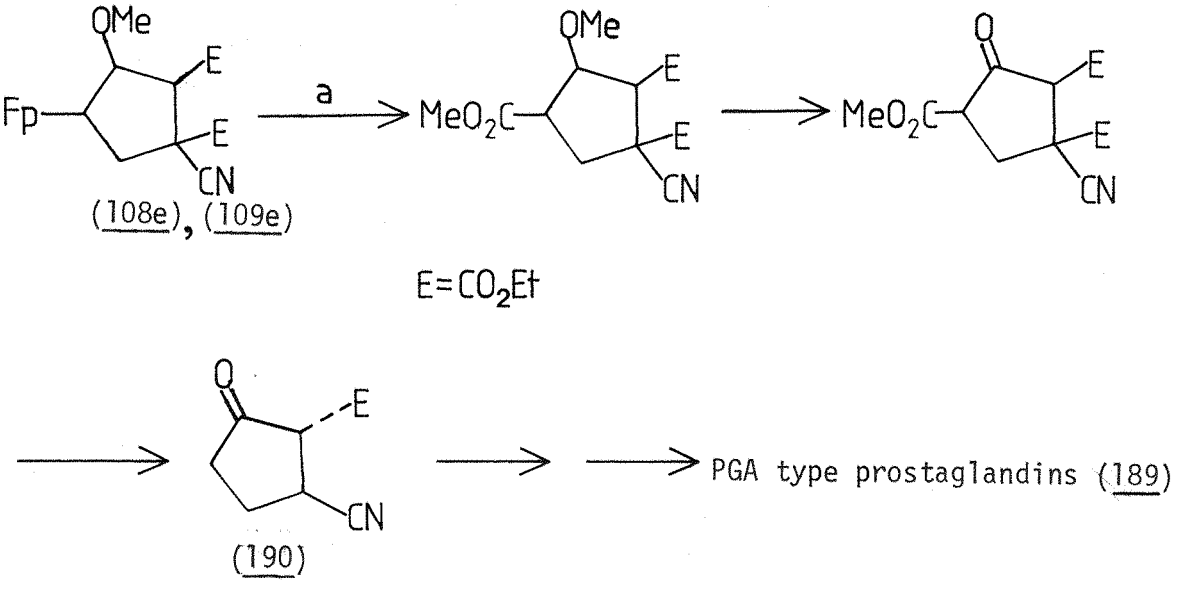
(R'=$^tBuMe_2Si$)

Scheme 64



(a) CH_2Cl_2, 89%
(b) HCl, CH_2Cl_2, 75%
(c) [O]
(d) $-CO_2Et$

Scheme 65



(a) Ce^{iv}, MeOH, CO

Scheme 66

CHAPTER FIVE

Experimental

General Details

NMR spectra were obtained at 60 MHz on a Perkin -Elmer R12, and at 100 MHz on an XL100 Fourier Transform instrument in deuterochlorform, unless otherwise stated, with tetramethylsilane (TMS) as the internal reference. In all cases the resonances are quoted as δ values (TMS = 0); coupling constants (J) are given in Hz. Infra-red (IR) spectra were recorded on a Perkin-Elmer 157G spectrometer, generally as solutions in methylene chloride, chloroform, or carbon tetrachloride. The absorption bands are given in cm^{-1} relative to a polystyrene standard (1603 cm^{-1}). The following abbreviations are used to define the signals in the NMR and IR spectra.

NMR - s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, b = broad.

IR - s = strong, m = medium, w = weak.

Mass spectra (MS) were run on either an AEI MS 12 spectrometer employing a VG Digispec Data Acquisition machine, or a Kratos MS 30 in conjugation with a Data General Nova 3 computer utilising the DS 50 S Data System. An ionising potential of 70 eV was used unless otherwise stated. The major ion fragments (m/e), together with those of structural importance, are quoted as percentages of the base peak (100%). Elemental analyses were recorded by Butterworth Laboratories Ltd., University College, London, and ICI Pharmaceutical Division, Alderley Edge. Melting points were determined in sealed capillaries and are uncorrected.

Column chromatography was performed with 100-200 mesh silica gel (W. R. Grace Ltd), neutral alumina (Woelm, Act. III-V), or 100-200 mesh florisil (Floridin). A ratio of approximately 30:1 column packing: material to be chromatographed (w/w) was used. Flash column chromatography[85] was performed with 230-400 mesh silica gel (Merk, Type 60). Analytical thin-layer chromatography (TLC) was carried out using microscope slides with approximately 0.2 mm thickness of silica gel $HF_{254+366}$ (Merk, Type 60), or pre-coated silica gel plates (Merk, Type 25 UV_{254}). Visualisation was effected by a combination of UV fluorescence, iodine vapour, or spraying with aqueous potassium permanganate solution.

All operations involving organometallic complexes were performed in a nitrogen or argon atmosphere. Solvents were dried by standard procedures, degassed, and stored under nitrogen or argon and over molecular sieves. Ether refers to diethyl ether and petrol to petroleum ether (40-60^{o}C). Other reagents were used as supplied or prepared as described below.

Reagent Preparation

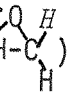
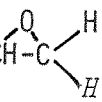
(a) 1-Bromo-2,2-dimethoxypropane

1-Bromo-2,2-dimethoxypropane was prepared from bromoacetone by the method of Jacobson *et al*[110]. Yield : 77%, bp_{14} 52-53°C (lit.[110] bp_{80} 83-86).

NMR 1.44(3H,s,Me), 3.23(6H,s,OMe), 3.37(2H,s,CH_2).

(b) 1,2-Epoxy-3-methoxypropane

1,2-Epoxy-3-chloropropane was converted to 1-methoxy-2-hydroxy-3-chloropropane, and then to 1,2-epoxy-3-methoxypropane according to the procedure of Flores-Gallardo and Pollard[111]. Overall yield : 50%, bp 110-116°C (lit.[111] bp 53.5-53.7°C).

NMR 2.50(1H,q,J=5 and 6Hz,-CH- ), 2.55(1H,q,J=5 and 7Hz,-CH- ), 2.82-3.10(2H,m,CH_2OMe), 3.32(3H,s,OMe), 3.46, 3.60(2H,2xt,J=11Hz and J=10.5Hz,-CH_2OCH_3).

(c) N-Bromopyridinium bromide

N-Bromopyridinium bromide was isolated in 94% yield from the reaction of pyridine with bromine, performed in carbon tetrachloride[112]. Mp 56-58°C.

(d) Trityl tetrafluoroborate

Trityl tetrafluoroborate was synthesised in 88% yield from triphenyl methanol[113] according to the procedure described by Dauben *et al*[114].

Olefin Preparation

(a) Dimethyl and diethyl methylenemalonate (97a,b)

Diethyl methylenemalonate (97b) was prepared by the method of Kunichika *et al*[73], *via* a Knoevenagel reaction between diethyl malonate and paraformaldehyde in acetic acid, catalysed by anhydrous cupric acetate. The crude product was stored in benzene to prevent polymerisation and distilled prior to use. Yield : 51%, bp_{14} 90-92°C (bp_{14} crude product : 80-105°C, lit[115] bp_{760} 210°C).

NMR 1.32(6H,t,J=7Hz,$CO_2CH_2CH_3$), 4.28(4H,q,J=7Hz,$CO_2CH_2CH_3$), 6.44(2H, s,$C=CH_2$).

Dimethyl methylenemalonate (97a)[116] was prepared in a similar manner to that described for the diethyl derivative[73]. Yield : 28%, $bp_{0.2}$ 48-50°C (bp of crude product 80-100°C).

NMR 3.84(6H,s,CO_2Me), 6.60(2H,s,$C=CH_2$).

(b) Trimethyl ethylenetricarboxylate (97c)

Method A : Reaction of the sodium salt of diethyl malonate with ethyl bromoacetate, followed by bromination-dehydrobromination of the product thus formed, afforded trimethyl ethylenetricarboxylate (97c) in 36% overall yield[70].

Method B : 97c was also prepared *via* a Knoevenagel reaction between methyl glyoxylate[117] and dimethyl malonate, performed in refluxing acetic anhydride as described by Joucla and Hamelin[71]. Bp_{20} 147-153°C.

NMR 3.83, 3.89 and 3.92(each 3H,each s,CO_2Me), 6.96(1H,s,C=CH).

(c) Tetramethyl and tetraethyl ethylenetetracarboxylate

Tetraethyl ethylenetetracarboxylate was prepared from diethyl bromomalonate by the method of Corson and Benson[75]. Yield : 52%, mp(from ethanol) 47-51°C (lit[75] mp 52.5-53.5°C).

NMR 1.32(12H,t,J=7Hz,$CO_2CH_2CH_3$), 4.26(8H,q,J=7Hz,$CO_2CH_2CH_3$).

Tetramethyl ethylenetetracarboxylate (97h) was obtained in an analogous manner to that reported[75] for the tetraethyl derivative. Yield : 34%, mp (from methanol) 119-120°C (lit[118] mp 119-120°C).

NMR 3.87(12H,s,CO_2CH_3).

(d) Ethyl 3,3-dicyanoacrylate (97d)

To a mixture of freshly distilled malononitrile (27.75 g, 0.42 mol) and ethyl glyoxylate[117] (51.0 g, 0.50 mol) at 0°C, was added a solution of β-alanine (600 mg, 6.7 mmol) in water (60 ml) over 15 minutes. Ethanol (∿90 ml) was then added until the mixture became homogeneous. After stirring at room temperature for approximately 20 hours the resulting solution was poured into water (600 ml) and extracted with ether (4 x 200 ml). The combined extracts were washed with water (200 ml), dried over anhydrous sodium sulphate, and the solvent removed *in vacuo*. The residue was flash distilled at 200°C, 0.5-1.0 Torr, and the major fraction collected (26 g), bp 80-120°C. Redistillation afforded ethyl 3,3-dicyanoacrylate as a colourless oil, which solidifed on cooling. Yield : 16%, $bp_{0.5}$ 90-91°C, mp [from diethyl ether-petroleum ether (40-60°)] 38-39°C.

NMR 1.39(3H,t,J=7Hz,$CO_2CH_2C\mathit{H}_3$), 4.41(2H,q,J=7Hz,$CO_2C\mathit{H}_2CH_3$), 7.16(1H, s,C=CH).

IR ($CHCl_3$); 2235(2,C≡N), 1732(s,C=O), 1616(m,C=C).

MS 150(1.1,*M*), 122(11), 105(100,*M*-OEt), 78(14), 77(22,*M*-CO_2Et), 66(12), 45(15), 32(22).

Elemental Analysis Calculated for $C_7H_6N_2O_2$: C, 56.00; H, 4.03; N, 18.66
Found : C, 55.33; H, 4.14; N, 18.55

(e) Diethyl 1-cyanoethylene-1,2-dicarboxylate (97e)

Diethyl 1-cyanoethylene-1,2-dicarboxylate (97e) was prepared by the procedure described by Hall and Ykman[76] for dimethyl 1-cyanoethylene-1,2-dicarboxylate.

To a solution of ethyl cyanoacetate (101.7 g, 0.9 mol) in absolute ethanol (500 ml) at approximately 10°C was added sodium (20.7 g, 0.9 mol) over 2.5 hours followed by ethyl bromoacetate (50.1 g, 0.3 mol) dissolved in absolute ethanol (75 ml). The reaction mixture was stirred for 22 hours at room temperature, then poured into a mixture of concentrated hydrochloric acid (113 ml) and ice (750 g). Water was added (400 ml) and the mixture divided into three fractions (∿ 600 ml each). Each fraction

was extracted with methylene chloride (3 x 200 ml), the organic layer backwashed with water (100 ml), dried overnight over anhydrous sodium sulphate, the solvent removed *in vacuo* and the residue distilled *in vacuo* to yield crude diethyl cyanosuccinate (55.75 g). Redistillation afforded slightly impure diethyl cyanosuccinate in 68% yield (40.8 g, $bp_{0.3}$ 102-104°C).

To a solution of diethyl cyanosuccinate (27.2 g, 68.4 mmol) and benzyl peroxide (0.13 g) in carbon tetrachloride (100 ml) was added a solution of bromine (4.1 mls, 13.5 g, 74 mmol) in carbon tetrachloride (15 mls) portionwise under irradiation with visible light. Irradiation was maintained for 3 hours after completion of addition. Removal of the solvent *in vacuo* gave the crude brominated product as a red oil.

The crude bromide was dissolved in ether (100 ml) and triethylamine (9 ml, 6.53 g, 64.5 mmol) was added dropwise with cooling. The reaction mixture was kept for 30 minutes at 5°C and 45 minutes at room temperature, then filtered and solvent removed *in vacuo*. The crude product was fractionally distilled twice under reduced pressure to give diethyl 1-cyanoethylene-1,2-dicarboxylate in 62% yield (16.8 g, $bp_{0.1}$ 84-88°C) from the ethane.

NMR 1.38(6H,t,J=7Hz,$CO_2CH_2CH_3$), 4.41(4H,bq,J=7Hz,$CO_2CH_2CH_3$), 7.49 (1H,s,C=CH)

IR (CH_2Cl_2); 2240(w,C≡N), 1730(s,C=O), 1640(w,C=C)

(f) Ethyl 2,3-dicyanoacrylate (97f,g)

Ethyl 2,3-dicyanopropionate was prepared *via* the reaction between glycolonitrile[119] and ethylcyanoacetate according to the procedure of Dickinson *et al*[120], and then converted to ethyl 2,3-dicyanoacrylate (97f,g) by the method of Noren and Hall[77]. The olefin was isolated in a *cis:trans* ratio (with respect to the cyano groups) of 8:1. Yield (from glycolonitrile) : 19%, $bp_{0.2}$ 91-93°C (lit[77] $bp_{0.1}$ 78-80°C).

NMR 1.30(3H,t,J=7Hz,$CO_2CH_2CH_3$), 4.45(2H,q,J=7Hz,$CO_2CH_2CH_3$), 6.76 (0.11H,s,H-C(CN)=C(H)-CO_2Et), 7.17(0.89H,s,H-C(CN)=C(CN)-CO_2Et).

(g) Tetraacetylethylene

Tetraacetylethylene was prepared by the method of Adembri *et al*[82] in 22% yield from acetylacetonate. Mp (from benzene) 144-146°C (lit[82] mp 139-140°C).

NMR 2.33(12H,s,Me)

Ir ($CHCl_3$); 1704, 1692(s,C=O)

(h) Ethyl 3-nitroacrylate

Ethyl 3-nitroacrylate was prepared from ethyl acrylate, *via* ethyl 2-iodo-nitropropionate, by the method of McMurray and Musser[80]. Yield : 70%, mp (from pentane) *ca* 20°C (lit[80] mp 26-26.5°C).

NMR 1.35(3H,t,J=7Hz,$CO_2CH_2CH_3$), 4.33(2H,q,J=7Hz,$CO_2CH_2CH_3$), 7.08 and 7.72(2H,ABq,J=14Hz,CH=CH).

(i) β-Nitrostyrene

β-Nitrostyrene was synthesised according to the procedure of Worrall[81] in 80% yield, mp (from ethanol) 56-58°C (lit[81] 57-58°C)

NMR 7.52-8.17(7H,m)

(j) Dimethyl acetylenedicarboxylate (DMAD)

DMAD was prepared from the mono-potassium salt of acetylenedicarboxylic acid as described by Huntress *et al*[78]. Yield : 70%, $bp_{0.9}$ 55°C (lit[78] bp_{19} 95-98°C).

NMR 3.84(6H,s,OMe)

(k) Methyl propiolate

Propargyl alcohol was converted to propiolic acid by the procedure of Wolfe[121], and then esterified by the method of Grove[83]. Yield : 70%, bp_{760} 102°C (lit[83] bp_{760} 100°C).

NMR 2.95(1H,s,C≡CH), 3.76(3H,s,OMe)

(l) t-Butylcyanoketene

2,5-Di-t-butyl-p-quinone was converted to 2,5-diazido-3,6-di-t-butyl-p-quinone (94) in 72% overall yield by the reaction sequence (consisting of 5 steps) reported by Weyler *et al*[79]. The ketene was then generated quantitatively by heating a benzene solution of the diazide to reflux for 2 hours.

NMR 9.23(9H,s,^{t}Bu)

(m) Ethyl 1-cyano-4,4-trimethylenedithiocrotonate (177)

A solution of dithiane (48 g, 0.4 mol) in anhydrous THF (*ca* 600 ml) was cooled to -60°C under Argon and n-butyllithium (200 ml,1.5M solution in hexane) added over 30 minutes. After stirring at -30 - -40°C for 3 hours bromoacetaldehyde diethyl acetal (48 ml 0.32 mol) was added and the reaction mixture allowed to warm to room temperature overnight. Water (400 ml) was then added and the mixture was extracted with ethyl acetate (2x400 ml). The combined extracts were washed with water (100 ml), dried over anhydrous sodium sulphate and the solvent removed *in vacuo*. Distillation of the residue afforded unchanged starting materials (*ca*. 8 g, $bp_{0.1}$ < 110°C) and 1,1-diethoxy-3,3-trimethylenedithiopropane[122] in 65% yield (45.7 g, $bp_{0.1}$ 110°C).

NMR 1.21(6H,t,J=7Hz,OCH_2CH_3), 1.80-2.30(4H,m,$SCH_2CH_2CH_2S$ and $CHCH_2CH$)
2.75 - 3.00(4H,m,$SCH_2CH_2CH_2S$), 3.60 and 3.64(each 2H,each q,
J=7Hz,OCH_2CH_3), 4.13[1H,t,J=7Hz,CH_2CHS), 4.80(1H,t,J=6Hz,CH_2CHOEt)

A solution of 1,1-diethoxy-3,3-trimethylenedithiopropane (10 g, 42 mmol), 20% aqueous perchloric acid solution (6 ml) and water (44 ml) in dioxane (90 ml) was heated for 2 hours at 40-50°C. The reaction mixture was then extracted with ether (1 x 100 ml plus 4 x 50 ml), and the combined organic layers were washed with saturated aqueous sodium chloride solution (6 x 50 ml) and dried over anhydrous sodium sulphate. The solvent was removed *in vacuo* to give 3,3-trimethylenedithiopropanal[105] (6.67 g, 97% crude yield) of sufficient purity to be used in the next step without further purification.

NMR 1.70-2.40(2H,m,$SCH_2CH_2CH_2S$), 2.70-3.16(6H,m,$SCH_2CH_2CH_2S$ and CH_2CHO) 4.50(1H,t,J=7Hz,CH_2CHS), 9.75(1H,t,J≈1.75Hz,CHO).

A solution of 3,3-trimethylenedithiopropanal (6.6 g, 41 mmol) ethyl cyanoacetate (3.88 g, 34 mmol), acetic acid (0.7 ml, 0.73 g) and β-alanine (20 mg, 0.22 mmol) in benzene (40 ml) was heated to reflux for 20 hours. The water produced in the reaction was removed azeotropically using a Dean and Stark apparatus. After removal of the solvent *in vacuo* the residue was partitioned between ether (150 ml) and water (50 ml), and the aqueous layer discarded. The organic layer was then washed with saturated aqueous sodium chloride solution (50 ml) dried (anhydrous sodium sulphate) filtered through celite and the solvent removed *in vacuo*. Flash chromatography of the above crude product (7.2 g), eluting with ether-petrol (3:2), afforded an inseparable mixture of ethyl 1-cyano-4,4-trimethylenedithiocrotonate (179) and ethyl cyanoacetate (as a yellow oil, 6.47 g, *ca* 78% yield), in a ratio of approximately 9:1. Distillation resulted in considerable decomposition of the olefinic product, although it could be isolated in low yield (45% crude, $bp_{0.2-0.3}$ 160.170°C).

NMR 1.36(3H,t,J=7Hz,$CO_2CH_2CH_3$), 1.71-2.31(2H,m,$SCH_2CH_2CH_2S$), 2.80-3.14(6H,m,$SCH_2CH_2CH_2S$ and $CHCH_2CH=C$), 4.20(1H,t,J=8Hz,CH_2CHS), 4.34(2H,q,J=7Hz,$CO_2CH_2CH_3$), 7.67(1H,t,J=7.5Hz,C=CH).

IR ($CHCl_3$); 2235(w,C≡N), 1735(s,C=O), 1665(m,C=C)

MS 257(5,*M*), 122(5), 121(9), 120(7), 119(100,*M*-HC=C(CN)CO_2Et), 106(8), 75(4), 73(6).

Preparation of (η'-Allyl)Fp Complexes

1. Dicarbonyl (η^5-cyclopentadienyl)ferrate anion (Fp-)[29,67]

A 4% sodium amalgam was prepared by the careful addition of sodium (3 g, 0.13 mol), in small portions, to mercury (650 g, 3.25 mol) which was rapidly stirred throughout. Considerable quantities of heat were evolved during the addition. The amalgam was allowed to return to room temperature over approximately 1 hour and a solution of bis (cyclopentadienyliron dicarbonyl)[122] (i.e. Fp_2; 10.62 g, 30 mmol) in tetrahydrofuran (THF; 100 ml) was added in one portion and the reaction mixture efficiently stirred for 20 hours. The amber THF solution of FpNa was then separated from the amalgam and transferred *via* syringe.

2. Dicarbonyl (η^5-cyclopentadienyl)(η'-2-methoxyallyl)iron (66)[66,67,69]

(a) Reaction of FpNa with 1-bromo-2,2-dimethoxypropane[66,67]

A THF solution of FpNa (60 mmol in 100 ml of THF, see above) was cooled to 0^oC and a solution 1-bromo-2,2-dimethoxypropane (11g, 60 mmol) dissolved in THF (10 ml) was added dropwise over 30 minutes. The yellow-brown solution was stirred at 0^oC for a further 30 minutes and at room temperature for 3 hours. The solvent was then removed *in vacuo*, the residue extracted with pentane (*ca* 200 ml), and the pentane extract filtered through a sinter under a constant head of nitrogen. Removal of the solvent *in vacuo* afforded an air sensitive amber oil (13.8 g) containing a mixture (*ca* 2:1) of the 2,2-dimethoxypropane-Fp complex (67) and the (η'-2-methoxyallyl)Fp complex (66).

(b) Conversion of (66) and (67) to the Fp (η^2-olefin) tetrafluoroborate salt (68)[66,67]

The above mixture was taken up in ether (40 ml) and added dropwise over 15 minutes to a 40% aqueous solution of fluoroboric acid (10 ml, 60 mmol, technical solution) in acetic anhydride (100 ml) at 0^oC. The reaction mixture was stirred at 0^oC for 30 minutes and ether (*ca* 300 ml) was then added slowly over 1 hour. A heavy orange precipitate rapidly separated after addition of only a small portion (50 ml) of

ether. The precipitate was filtered and washed with ether (*ca* 200 ml). The remaining solvent was removed from the salt *in vacuo* affording (68) (15.02 g, 75% yield from Fp_2) as an orange crystalline solid, mp 90-91°C. The salt could be stored indefinately under vacuum and was handled in air without incurring any noticeable loss.

(c) Regeneration of the (η'-2-methoxyallyl)Fp complex (66) from salt (68)[66,67,69]

To a suspension of salt (68) (1.5 g, 4.5 mmol) in THF (20 ml) at 0°C was added 1,4-diazabicyclo[2.2.2]octane (Dabco) (0.5 g, 4.5 mmol, freshly recrystallised from ether) in one portion. The reaction mixture was stirred at 0°C for 30 minutes and at room temperature for 1 hour. The solvent was then removed *in vacuo*, the residue extracted with pentane (*ca* 40 ml) and filtered through a sinter under a constant head of nitrogen. Removal of solvent *in vacuo* afforded a mixture (1.06 g, *ca* 95% yield) of the allyl complex (66), the ketone $FpCH_2COCH_3$ (70)[126], olefins (71) and (72), and the ester complex $FpCH_2CO_2Me$ (73). The ratio of these products (estimated as 11:1:1:1:1 of 66:70:71:72:73 from the NMR spectrum of the mixture) varied slightly between deprotonation reactions. The yields of the adducts obtained from the reactions between this allyl complex (66) and unsaturated moieties were therefore calculated assuming exclusive formation of the (η'-2-methoxyallyl)Fp complex from the salt (68).

Column chromatography of (66) on neutral alumina (Act III) with ether-petrol (1:1-1:3) afforded the hydrolysed adduct ($FpCH_2COCH_3$) in quantitative yield.

(d) Preparation of $FpCH_2CO_2Me$ (73)

$FpCH_2CO_2Me$ was prepared in a similar manner to that described by Rosenblum *et al*[68].

A solution of FpNa, prepared from the dimer Fp_2 (1.77 g, 5 mmol), in THF (20 ml) was added slowly to methyl bromoacetate (1.53 g, 10 mmol) dissolved in THF (10 ml) at 0°C. The reaction mixture was stirred at 0°C for 30 minutes then allowed to warm to room temperature during 1 hour. The solvent was removed *in vacuo*, the residue extracted with hexane, and the extracts concentrated and chromatographed on neutral alumina (Act III).

$FpCH_2CO_2Me$ was eluted with petrol-ether (9:1) in 4% yield (95 mg; lit yield[68] = 10%) as an amber oil.

(e) Investigation of the formation of $FpCH_2CO_2Me$ from the deprotonation of the Fp(η^2-olefin) complex (68)

Treatment of (68) with:

(i) Dabco plus p-toluenesulphonic acid[69]

The Fp(η^2-olefin) complex (68) (300 mg, 0.9 mmol) was added to a solution of p-toluenesulphonic acid (170 mg, 0.9 mmol) and dabco (200 mg, 1.8 mmol) in THF (20 ml) at 0^oC. The NMR spectrum of the crude product, obtained employing the normal reaction and work-up procedures, indicated no increase in the amount of $FpCH_2CO_2Me$ formed (*ca* 5%).

(ii) Dabco plus water

To a solution of the salt (300 mg, 0.9 mmol) in THF (15 ml) at 0^oC was added water (8 mg, 0.5 mmol) followed by dabco (100 mg, 0.9 mmol). As with the reacton above no increase in the amount of ester complex formed was observed in the NMR spectrum of the crude product.

(iii) Dabco plus calcium hydroxide

Calcium hydroxide (*ca* 120 mg, 1.6 mmol) and dabco (180 mg, 1.6 mmol) were added to a solution of the salt (68) (540 mg, 1.6 mmol) in THF (10 ml) at 0^oC. After performing the normal reaction and work-up procedures the crude product was chromatographed on neutral alumina (Act III), eluting with ether-petrol (1:9), to give $FpCH_2CO_2Me$ in 30% yield (120 mg).

(iv) Two equivalents of dabco

Two equivalents of dabco (1.0 g, 9.0 mmol) were added, in one portion, to a solution of the salt (68) (1.5 g, 4.5 mmol) in THF (20 ml) at 0^oC. After stirring at 0^oC for 30 minutes and at room temperature for 1 hour, the solvent was removed *in vacuo* and the residue extracted with pentane (*ca* 40 ml). The extract was filtered, and the solvent removed *in vacuo* to give a mixture (1.07 g) of the allyl complex (66), $FpCH_2COCH_3$, and dabco in a ratio of 10:1:2. NMR analysis indicated that none of the ester complex (73) was present.

3. Dicarbonyl (η^5-cyclopentadienyl) (η'-allyl)iron (20a)[24,26]

(a) Preparation of the Fp(η^2-propene) tetrafluoroborate salt (22c) *via* the (η'-allyl)Fp complex (20a)

To a solution of FpNa (60 mmol) in THF (100 ml) at 0°C was added freshly distilled allyl chloride (10 g, 10.6 ml, 13 mmol) dissolved in THF (10 ml). After stirring at 0°C for 45 minutes, the reaction mixture was allowed to warm to room temperature over 1 hour and then concentrated *in vacuo*. The residue was extracted with pentane (*ca* 400 ml), filtered through a sinter under a constant head of nitrogen, and the solvent was removed *in vacuo* to give the (η'-allyl)Fp complex (20a) in 96% (12.5 g) crude yield.

This crude product was dissolved in ether (30 ml) and added dropwise to a 40% aqueous solution of fluoroboric acid (12 ml, 72 mmol, technical solution) in acetic anhydride (50 ml) at 0°C. The reaction mixture was stirred at this temperature for 30 minutes and ether was added to precipitate the Fp(η^2-propene)tetrafluoroborate salt (22C) as a bright yellow solid. This precipitate was collected, washed well with ether (*ca* 200 ml) and dried *in vacuo* to afford the salt in 86% (15.75 g) overall yield from Fp.

(b) Regeneration of the (η'-allyl)Fp complex (20a) from the salt (22c)

A solution of the Fp salt (22c) (2 g, 65 mmol) in methylene chloride (20 ml) was cooled to 0°C and triethylamine (2 ml, 1.45 g, 14 mmol) added in one portion. After stirring at 0°C for 30 mins and at room temperature for 30 minutes, the solvent was removed *in vacuo* and the residue extracted with pentane (*ca* 40 ml). The pentane extract was filtered under nitrogen and concentrated to give the (η'-allyl)Fp complex (20a) in quantitative yield (*ca* 1.4 g) as an amber oil. Although reactions were generally performed using the crude product, the allyl complex (20a) could be purified by column chromatography on neutral alumina (Act III) (the complex being isolated on elution with petrol).

4. Dicarbonyl (η^5-cyclopentadienyl)(η'-3-methoxyallyl)iron (28)[20]

(a) Preparation of the Fp(η^2-olefin) tetrafluoroborate salt (22m)[20]

1,2-Epoxy-3-methoxypropane (5.28 g, 60 mmol) was added to a solution of FpNa (*cf* 60 mmol) in THF (100 ml) and the reaction mixture stirred at 0°C for 45 minutes. A 40% aqueous solution of fluoroboric acid (20 ml, 120 mmol, technical solution) in acetic anhydride (30 ml) was then added. After stirring at 0°C for a further 15 minutes, ether (*ca* 250 ml) was added to precipitate the crude product, which was collected and dried *in vacuo*. This precipitate was then dissolved in boiling methylene chloride, filtered (to remove $NaBF_4$) and the solution concentrated (to *ca* 50 ml). Addition of ether (*ca* 150 ml) to this solution, followed by filtration, afforded the desired tetrafluoroborate salt (22m) in 72% overall yield from Fp_2.

(b) Generation of the (η'-3-methoxyallyl)Fp complex (28) from the salt (22m)

A suspension of the salt (22m) (1.38 g, 4.1 mmol) in methylene chloride (10 ml) was cooled to 0°C, and triethylamine (0.6 ml, 0.43 g, 4.3 mmol) was added in one portion. After stirring at 0°C for 30 minutes and at room temperature for 30 minutes, the solvent was removed under reduced pressure, and the residue extracted with pentane (*ca* 40 ml). The extract was filtered, then concentrated to give the crude product (28), as an orange-brown solid, in essentially quantitative yield. This allyl complex could be purified by column chromatography on neutral alumina (Act III) [eluting with petrol-ether (9:1)], although the crude product was generally used in the (3+2) cycloaddition reactions investigated.

Reactions of (η'-Allyl)Fp Complexes with Electron-Deficient Olefins and Acetylenes

1. General procedure

To a solution of the allyl complex (*ca* 2 mmol) in either dimethylformamide (DMF), tetrahydrofuran (THF), methylene chloride or benzene (5-15 ml) was added the unsaturated moiety (1-10 equivalents) dissolved in the same solvent (1-5 ml). The reaction mixture was then stirred at room temperature for the reaction times indicated. After removal of the solvent under reduced pressure (DMF and THF at 0.1 Torr, and methylene chloride and benzene at 14 Torr), the crude product was chromatographed on either neutral alumina (*ca* 30 g, Act. III-V) or florisil (*ca* 30 g) employing a 20 mm x 30 cm column. The residue was, in general, applied to the column as a solution in benzene (2-5 ml), the solvent being removed on elution with petrol. The products were then eluted with ether-petrol. In a number of cases the products were further purified by recrystallisation from hexane-ether.

2. Reactions of dicarbonyl (η^5-cyclopentadienyl) (η'-2-methoxyallyl)iron (66)

(a) Tetracyanoethylene[66,67]

A solution of TCNE (384 mg, 3.0 mmol, freshly sublimed) in THF (2.5 ml) was added dropwise, over 5 minutes, to the 2-methoxyallyl complex (66) (652 mg, 2.6 mmol) dissolved in methylene chloride (20 ml) at room temperature. The green-black solution became noticeably warm and a black precipitate formed after 5 minutes. After stirring the solution for 2 hours, hexane (*ca* 40 ml) was added slowly to complete the precipitation of the TCNE adduct (75), which was collected and washed with hexane (*ca* 100 ml). This adduct was isolated as a yellow-green crystalline solid, mp 158-159^{o}C(dec.), in 73% yield (711 mg; 96% yield assuming the allyl complex to be 75% pure).

(b) Trimethyl ethylenetricarboxylate (97c)

(i) Standard reaction

The reaction of the allyl complex (66) (490 mg, 2.0 mmol) with trimethyl ethylenetricarboxylate (97c) (800 mg, 4.0 mmol)

performed in methylene chloride (20 ml) for 20 hours was carried out employing the general reaction procedure. Column chromatography of the crude product on neutral alumina (Act III) resulted in the isolation of the following complexes.

1. $FpCH_2CO_2Me$ (30 mg, 6%) plus the H-transfer adduct (78) (245 mg, 28%) on elution with ether petrol (2:3).

2. $FpCH_2COMe$ (37 mg, 8%) plus the cyclic derivative (72) (200 mg, 22%) on elution with ether-petrol (3:2).

3. The hydrolysed H-transfer adduct (79) (44 mg, 5%) on elution with ether.

All three addition products were isolated as unstable amber oils, although crystallisation of the hydrolysed H-transfer adduct (79) (to give a yellow, air-stable, crystalline solid; mp 66-67°C) was induced by cooling a solution of this complex in hexane-ether to -20°C overnight.

Table 11 (Page 33, Chapter Two) summarises the product yields and ratios obtained when the reaction of the allyl complex (66) with trimethyl ethylenetricarboxylate was performed in DMF, THF and benzene, as well as methylene chloride.

(ii) Treatment of an aqueous THF solution of the crude product with p-toluenesulphonic acid

Water (*ca* 0.5 ml) followed by p-toluenesulphonic acid (*ca* 20 mg) were added to a solution of the allyl complex (538 mg, 2.2 mmol) and the olefin (79c) (870 mg, 4.3 mmol) in THF (30 ml) which had previously been stirred at room temperature for 20 hours. The mixture was then stirred for a further six hours at room temperature. After removal of the solvent, *in vacuo*, the residue was chromatographed as described above, to give the hydrolysed H-transfer adduct (79) in 38% yield (363 mg).

(iii) Reaction performed in the presence of 1,4-diazobicyclo[2.2.2] octane

To a solution of the allyl complex (190 mg, 0.77 mmol) in methylene chloride (5 ml) was added dabco (90 mg, 0.87 mmol), followed by a solution of trimethyl ethylenetricarboxylate (313 mg, 1.55 mmol)

in methylene chloride (5 ml). The reaction mixture was stirred at room temperature for 2.5 hours. The solvent was then removed *in vacuo* and the residue chromatographed on neutral alumina (Act III). Elution with ether-petrol afforded the H-transfer adduct (78), the cyclic derivative (77), and the hydrolysed H-transfer adduct (79) in yields of 21% (74 mg), 5% (18 mg) and 37% (128 mg) respectively (i.e. in a ratio of 11:1 of linear : cyclic adducts, *cf* to the normal 1:1 ratio).

(c) Diethyl methylenemalonate (97b)

(i) Reaction performed in dimethylformamide

The standard procedure was employed for the reaction of the 2-methoxyallyl complex (550 mg, 2.2 mmol) with diethyl methylenemalonate (97b) (760 mg, 4.4 mmol), performed in DMF (10 ml). Column chromatography of the crude product on neutral alumina (Act III) with the solvents detailed below resulted in the isolation of the polymeric H-transfer adducts (82a) (166 mg), $FpCH_2COMe$ (142 mg, 27%) and the hydrolysed polymeric H-transfer adducts (83a) (188 mg). These three complexes were isolated on elution of the column with ether-petrol (1:1), ether-petrol (3:2) and ether respectively.

(ii) Reaction performed in benzene

Column chromatography of the residue obtained by performing the above reaction in benzene (50 ml) on neutral alumina (Act III) eluting with ether-petrol also afforded the polymeric H-transfer adducts (82a) (219 mg), plus an inseparable mixture of $FpCH_2COMe$ (50 mg, 10%) and the hydrolysed 1:1 H-transfer adduct (265), (83a, n=1) (265 mg, 29%).

(iii) Treatment of an aqueous THF solution of the crude product with p-toluenesulphonic acid

The crude product, obtained from the reaction of (66) (280 mg, 1.5 mmol) with diethyl methylenemalonate (316 mg, 1.8 mmol) carried out in benzene (40 ml), was dissolved in THF (5 ml) and then treated with water (0.5 ml) and p-toluenesulphonic acid (20 mg) as described in section 2 (b,ii) of this Chapter. Column chromatography on neutral alumina (Act III) with ether petrol (3:2) then gave a mixture of the polymeric ketones (83a) and $FpCH_2COMe$ in approximately a 5:2 ratio (11 mg).

These hydrolysed adducts (83a) were also isolated as the exclusive products from analagous treatment of the polymeric H-transfer adducts (82a).

(d) Dimethyl methylenemalonate (97a)

Dimethyl methylenemalonate (97a) (265 mg, 1.8 mmol) dissolved in benzene (10 ml), was added to a solution of the allyl complex (380 mg, 1.5 mmol) in benzene (30 ml), and the mixture stirred at room temperature for 20 hours. The solvent was then removed *in vacuo* and the residue chromatographed on neutral alumina (Act III). Elution of the column with ether-petrol (3:2) resulted in the isolation of an inseperable mixture of $FpCH_2COMe$ (*ca* 69 mg, 19%) and the polymeric H-transfer product (82b) (154 mg).

(e) Tetramethyl ethylenetetracarboxylate (97h)

A solution of the allyl complex (410 mg, 1.7 mmol) and tetramethyl ethylenetetracarboxylate (1.7 g, 6.5 mmol) in DMF (10 ml) was stirred for 70 hours at room temperature. After removal of the solvent *in vacuo*, the residue was dissolved in THF (5 ml) and treated with water (0.5 ml) plus p-toluenesulphonic acid (20 mg) for 6 hours. The reaction mixture was then concentrated and the crude product chromato--raphed on neutral alumina (Act III) to give the hydrolysed linear complex (86, $E=CO_2Me$) in 39% yield (320 mg) as an amber oil.

(f) Tetraethyl ethylenetetracarboxylate

The reaction between (66) (540 mg, 2.2 mmol) and tetraethyl ethylenetetracarboxylate (2.75 g, 8.7 mmol), performed in DMF (10 ml) for 48 hours employing the standard reaction procedure, afforded a mixture of $FpCH_2COMe$ (160 mg, 31% yield) and the hydrolysed H-transfer adduct (86, $E=CO_2Et$) (187 mg, 16% yield). This mixture was eluted from a neutral alumina (Act III) column with ether-petrol (3:1).

(g) Ethyl 3,3-dicyanoacrylate (97d)

To a solution of the allyl complex (300 mg, 1.2 mmol) in methylene chloride (15 ml) was added ethyl 3,3-dicyanoacrylate (240 mg, 1.6 mmol) dissolved in the same solvent (5 ml). The mixture was stirred for 20 hours and the solvent then removed *in vacuo*. Chromatography of the residue thus obtained gave the cyclic derivative (87) in 58% yield

(275 mg), as a yellow crystalline solid [mp 96-98°C (from hexane-ether], on elution with ether-petrol (1:1).

When the reaction was performed in DMF for three hours, this adduct was isolated in yields of 45% and 32% after column chromatography on florisil and neutral alumina (Act III) respectively, on elution with ether-petrol (1:1).

(h) Diethyl 1-cyanoethylene-1,2-dicarboxylate (97e)

(i) Standard reaction

Diethyl 1-cyanoethylene-1,2-dicarboxylate (97e) (476 mg, 2.4 mmol) was reacted with the allyl complex (600 mg, 2.4 mmol) in methylene chloride (20 ml) for 2.5 hours using the general reaction procedure. The crude product was then chromatographed on neutral alumina (Act IV) to give the following complexes.

1. A mixture of polymeric H-transfer adducts (88) (*ca* 110 mg) and the cyclic adduct (89) (*ca* 26 mg, 2%) on elution with ether-petrol (2:3).

2. $FpCH_2COMe$ (*ca* 120 mg, 21%) on elution with ether-petrol (2:3).

3. The hydrolysed 1:1 H-transfer adduct (90) (280 mg, 27%) on elution with ether-petrol (3:1).

All three products were isolated as amber oils.

Chromatography of the crude product on either neutral alumina (Act V) or florisil afforded the hydrolysed polymeric adducts (91), in low yield (< 25%), on elution with ether-petrol (3:1).

(ii) Treatment of an aqueous THF solution of the crude product with p-toluenesulphonic acid

The product mixture, obtained from the reaction of the allyl complex (330 mg, 1.3 mmol) with (97e) (262 mg, 1.3 mmol) in methylene chloride (30 ml), was dissolved in THF (10 ml) and treated with water (1 ml) and p-toluenesulphonic acid (*ca* 20 mg) for 30 mins. After removal of the solvent *in vacuo* the residue was chromatographed on neutral alumina (Act IV) and a mixture of $FpCH_2COMe$ (*ca* 42 mg, 13% yield) and the

cyclic adduct (89) (*ca* 34 mg, 6% yield), plus the hydrolysed product (90) (114 mg, 19% yield), eluted with ether–petrol.

(i) Ethyl 2,3-dicyanoacrylate (97f,g)

The general reaction procedure was employed for the reaction of ethyl 2,3-dicyanoacrylate (97f,g) (273 mg, 1.8 mmol) with (66) (450 mg, 1.8 mmol) in methylene chloride (15 ml) for 1 hour. The crude product was chromatographed on neutral alumina (Act IV) and the cyclic adduct (92), eluted with ether-petrol (3:1) in 64% yield (460 mg), isolated as a yellow crystalline solid, mp (from hexane-ether) 148-149°C.

Column chromatography on neutral alumina (Act V) and florisil, with ether, resulted in the isolation of (92) in yields of 71% and 52% respectively.

(j) Dimethyl acetylenedicarboxylate (DMAD)[66,69]

DMAD (0.5 ml, 568 mg, 4.0 mmol) was added in one portion to a solution of the allyl complex (500 mg, 2.0 mmol) in DMF (5 ml), and the reaction mixture stirred at room temperature for 3 hours. The solvent was then removed *in vacuo*, and the residue chromatographed on neutral alumina (Act III). Elution with ether-petrol (2:3) afforded the linear adduct (93), as an amber oil, in 63% yield (492 mg).

Alternative reaction conditions were also employed for this reaction and these are summarised, together with the yields of (93) obtained, in Table 14 (Page 41, Chapter Two).

(k) t-Butylcyanoketene[69]

A solution of 2,5-diazido-3,6-di-t-butyl-p-quinone (94) (400 mg, 1.3 mmol) in benzene (10 ml) was refluxed for 2 hours to convert the diazide into t-butylcyanoketene (*ca* 2.5 mmol)[78]. This solution was then cooled to room temperature and added in one portion to the allyl complex (66) (450 mg, 1.8 mmol) dissolved in benzene (10 ml). After stirring at room temperature for 2 hours, the solvent was removed *in vacuo* and the residue chromatographed on neutral alumina (Act III). Elution with ether-petrol (1:3) afforded the H-transfer adduct (95b) as a yellow crystalline solid, mp 104-105°C, in 63% yield (425 mg).

(l) Unreactive olefins and acetylenes

The 2-methoxyallyl complex (66) was reacted in turn with methyl acrylate, acrylonitrile[69], *cis*-dimethyl ethylene-1,2-dicarboxylate[69] *trans*-1,2-dicyanoethylene[69], methyl cinnamate[69], ethyl 3-nitroacrylate, β-nitrostyrene[69], tetraacetylethylene[69], maleic anhydride, p-quinone, methyl propiolate and bis-trimethylsilylacetylene[69] employing the standard reaction procedure and the reaction conditions given in Table 15(p 43 Chapter Two).

(m) Ethyl 1-cyano-4,4-trimethylenedithiocrotonate (177)

To a solution of (66) (544 mg, 2.2 mmol) in methylene chloride (15 ml) was added ethyl 1-cyano-4,4-trimethylenedithiocrotonate (177) (*ca* 90% pure, 760 mg, *ca* 2.8 mmol) also dissolved in methylene chloride (5 ml). The reaction mixture was then stirred at room temperature for 2 hours. After removal of the solvent *in vacuo*, the residue was chromatographed on neutral alumina (Act III) to give the H-transfer adduct (179) in 54% yield (595 mg). This product was isolated from the column as an amber oil on elution with ether -petrol (1:2 - 1:1).

3. Reactions of dicarbonyl (η^5-cyclopentadienyl) (η'-allyl)iron (20a)

The general reaction and chromatographic procedures were employed (unless otherwise stated) for the reactions of the simple (η'-allyl)Fp complex (20a) with electron-deficient olefins and acetylenes. Unreacted starting material (i.e. 20a) was eluted from the neutral alumina and florisil columns with ether-petrol (1:19).

(a) Dimethyl methylenemalonate (97a)

20a : 330 mg, 1.5 mmol
Solvent : CH_2Cl_2 (15 ml)
Column Chromatography : neutral alumina (Act III)
Product : 98a[21]
Yield : 350 mg, 64%

97a : 390 mg, 2.7 mmol
Reaction Time : 20 hours
Eluent : ether-petrol (1:3-1:1)

(b) Diethyl methylenemalonate (97b)

i) 20a : 400 mg, 1.8 mmol — 97b : 680 mg, 3.9 mmol
Solvent : CH_2Cl_2 (15 ml) — Reaction Time : 20 hours
Column Chromatography : Neutral alumina (Act. III)
Product : 98b — Eluent : ether-petrol (1:1)
Description : yellow solid, mp (from hexane-ether) 69.0-70.5°C
Yield : 500 mg, 70%

ii) 20a : 260 mg, 1.2 mmol — 97b : 410 mg, 2.4 mmol
Solvent : DMF (10 ml) — Reaction Time : 26 hours
Isolated yield of 98b : 295 mg, 64% (80% based on unrecovered 20a)

iii) 20a : 247 mg, 1.11 mmol — 97b : 400 mg, 2.3 mmol
Solvent : THF (20 ml) — Reaction Time : 20 hours
Isolated yield of 98b : 117 mg, 26% (62% based on unrecovered (20a)

(c) Trimethyl ethylenetricarboxylate (97c)

i) 20a : 478 mg, 2.2 mmol — 97c : 1.33 g, 6.6 mmol
Solvent : DMF (10 ml) — Reaction Time : 70 hours
Column Chromatography : Neutral alumina (Act. III)
Product : 98c — Eluent : Ether-petrol (1:1)
Description : Yellow solid, mp (from hexane-ether) 103.5-105.5
Yield : 738 mg, 80%

ii) 20a : 1.5 mmol — 97c : 3.0 mmol
Solvent : CH_2Cl_2(20 ml), THF(20 ml) or Benzene (20 ml)
Reaction Time : 70 hours
Yield of 98c : 0%
Yield of recovered 20a : 53-62%.

iii) Additional reaction conditions investigated, together with the yields of (98c) obtained, are summarised in Table 16 (Chapter Two).

(d) Ethyl 3,3-dicyanoacrylate (97d)

20a : 655 mg, 3.0 mmol — 97d : 500 mg, 3.3 mmol
Solvent : CH_2Cl_2 (20 ml) — Reaction Time : 1 hour
Column Chromatography : neutral alumina (Act. III)
Product : 98d — Eluent : Ether-petrol (1:1)
Description : yellow solid, mp(from hexane-ether) 86-88°C
Yield : 735 mg, 67%

(e) Diethyl 1-cyanoethylene-1,2-dicarboxylate (97e)

i) 20a : 340 mg, 1.6 mmol — 97e : 340 mg, 1.7 mmol
Solvent : DMF (7 ml) — Reaction Time : 1 hour
Column Chromatography : neutral alumina (Act III)
Product : 98e — Eluent : ether-petrol (1:1–3:1)
Description : Amber oil
Yield : 444 mg, 69%

ii) 20a : 640 mg, 2.9 mmol — 97e : 640 mg, 3.2 mmol
Solvent : CH_2Cl_2 (30 ml) — Reaction Time : 1 hour
Isolated Yield of 98e : 990 mg, 81%

(f) Ethyl 2,3-dicyanoacrylate (97f,g)

i) 20a : 335 mg, 1.5 mmol — 97f,g : 254, 1.7 mmol
Solvent : CH_2Cl_2 (15 ml) — Reaction Time : 1 hour
Column Chromatography : florisil
Product : 98f,g — Eluent : ether-petrol (3:1)
Description : yellow solid, mp (from ether) 115-120°C
Yield : 467 mg, 83%

ii) As in i)
Column Chromatography : neutral alumina (Act V)
Product : 98f,g — Eluent : ether
Yield ; 700 mg crude, 94%

(g) Tetramethyl ethylenetetracarboxylate (97h)

20a : 269 mg, 1.2 mol

97h : 960 mg, 3.7 mmol

Solvent : DMF (10 ml)

Reaction time : 70 hours

Column Chromatography : neutral alumina (Act III)

Product Yield : 0%

Yield of recovered 20a : 247 mg, 92%

(h) Dimethyl acetylenedicarboxylate (DMAD)[69]

20a : 470 mg, 2.2 mmol

DMAD : 640 mg, 4.5 mmol

Solvent :DMF (5 ml)

Reaction Time : 20 hours

Column Chromatography : neutral alumina (Act III)

Product : 104 plus 106

Eluent : ether-petrol (1:4)

Description : amber oils

Yield of 104 plus 106 : 93 mg, 12% (104:106 *ca* 9:2)

Product : 105

Eluent : ether-petrol (1:3-1:2)

Description : yellow solid, mp 94-96^{o}C

Yield:326 mg, 42%

(i) Methyl propiolate

20a : 400 mg, 1.8 mmol

Methyl propiolate : 0.65 ml, 7.2 mmol

Solvent : DMF (5 ml)

Reaction Time : 80 hours

Column Chromatography : neutral alumina (Act III)

Product Yield : 0%

Yield of recovered 20a : 330 mg, 83%

(j) Tetracyanoethylene (TCNE)[21]

To a solution of the simple (η^3-allyl)Fp complex (20a) (1.175 g, 5.4 mmol) in methylene chloride (15 ml) at room temperature was added TCNE (770 mg, 6.0 mmol) dissolved in THF (5 ml) After stirring at this temperature for one hour, hexane (*ca* 50 ml) was added slowly to the reaction mixture to precipitate the TCNE adduct (95i) as a green solid. This precipitate was collected and dried *in vacuo* to afford (98i) in 95% yield (1.781 g).

(k) Ethyl 1-cyano-4,4-trimethylenedithiocrotonate (177)

20a : 390 mg, 1.8 mmol — 177 : 600 mg (*ca* 90% pure), *ca* 2 mmol

Solvent : DMF (10 ml) — Reaction Time : 20 hours

Column Chromatography : neutral alumina (Act III)

Product : 181 — Eluent : ether-petrol (2:1)

Description : amber solid, mp (from hexane-ether) 122-124°C (dec)

Yield : 348 mg, 41% (*ca* 60% based on unrecovered 20a)

4. Reactions of dicarbonyl (η^5-cyclopentadienyl) (η'-3-methoxyallyl)iron (28)

The general reaction and chromatographic procedures were employed (unless otherwise stated) for the reactions of the (η'-3-methoxyallyl)Fp complex (28) with electron-deficient olefins and acetylenes. Unreacted (28) was recovered from the neutral alumina and florisil columns on elution with ether-petrol (1:4).

(a) Diethyl methylenemalonate (97b)

i) 28 : 450 mg, 1.8 mmol — 97b : 1.05 g, 6.1 mmol

Solvent : DMF (7 ml) — Reaction Time : 92 hours

Column Chromatography : neutral alumina (Act III)

Product : 108b — Eluent : ether-petrol (1:3)

Description : amber oil

Yield : 40 mg, 5% (8% based on unrecovered 28)

ii) 28 : 520 mg, 2.1 mmol — 97b : 1.38 g, 8.0 mmol

Solvent : DMF (15 ml) — Reaction Time : 90 hours

Column chromatography : florisil followed by neutral alumina (Act III)

Product : 108b — Eluent : ether-petrol (1:3)

Description : amber solid (after recrystallisation from hexane-ether) mp 63-65°C

Yield : 224 mg, 25% (44% based on unrecovered 28)

(b) Trimethyl ethylenetricarboxylate (97c)

i) 28 : 560 mg, 2.3 mmol — 97c : 1.37 g, 6.8 mmol
Solvent : DMF (8 ml) — Reaction Time : 66 hours
Column chromatography : neutral alumina (Act III)
Product : 108c, 109c — Eluent : ether-petrol (1:1-3:1)
Description : amber oil
Yield : 45 mg crude, 4% (14% based on unrecovered 28)

ii) 28 : 520 mg, 2.1 mmol — 97c : 1.69 g, 8.4 mmol
Solvent : DMF (15 ml) — Reaction Time : 90 hours
Column Chromatography : florisil followed by neutral alumina (Act III)
Product : 108c, 109c — Eluent : ether-petrol (3:1)
Description : yellow solid, mp 124-125°C
Yield : 147 mg, 16% (24%based on unrecovered 28)

(c) Ethyl 3,3-dicyanoacrylate (97d)

i) Standard reaction

28 : 410 mg, 1.7 mmol — 97d : 303 mg, 2.0 mmol
Solvent : CH_2Cl_2 (20 ml) — Reaction Time : 3 hours
Column Chromatography : florisil
Product 108d — Eluent : ether-petrol (1:1)
Description : amber solid, mp (from hexane-ether) 88-89°C
Yield : 320 mg, 49%

Product : 109d — Eluent : ether-petrol (3:1)
Description : yellow solid, mp (from hexane-ether) 149-140°C
Yield : 240 mg, 36%

ii) Elimination of methanol from (108d) and (109d)

Reaction of the 3-methoxyallyl complex (28) (645 mg, 2.6 mmol) with ethyl 3,3-dicyanoacrylate (97d) (412 mg, 2.7 mmol) was carried out in methylene chloride (20 ml) employing the standard reaction procedure.

Column chromatography of the crude product, obtained after removal of the solvent *in vacuo*, on neutral alumina (Act III) afforded the cyclic adduct (108d) in 13% yield (153 mg), plus the olefinic derivative (112) in 32% yield (287 mg). These two products were eluted from the column with ether-petrol (1:1) and ether respectively.

(d) Diethyl 2,3-dicyanoacrylate (97e)

i) 28 : 625 mg, 2.5 mmol — 97e : 546 mg, 2.8 mmol
Solvent : CH_2Cl_2 (20 ml) — Reaction Time : 3 hours
Column Chromatography : florisil
Product : 108e — Eluent : ether-petrol (2:3)
Description : yellow solid, mp (from hexane-ether) 98.5-99.5
Yield : 366 mg, 33%

Product : 109e — Eluent : ether-petrol (3:2)
Description : amber solid, mp(from hexane-ether) 102-103°C
Yield : 631 mg, 56%

ii) 28 : 465 mg, 1.9 mmol — 97e : 400 mg, 2.0 mmol
Solvent : DMF (7 ml) — Reaction Time : 6 hours
Yield of 108e : 224 mg, 27%
Yield of 109e : 444 mg, 53%

(e) Ethyl 2,3-dicyanoacrylate (97f,g)

i) Standard work up procedure

28 : 585 mg, 2.4 mmol — 97f,g : 390 mg, 2.6 mmol
Solvent : CH_2Cl_2 (20 ml) — Reaction Time : 3 hours
Column Chromatography : florisil
Product : 108f,g — Eluent : ether-petrol (1:1-3:1)
Description : yellow solid, mp (from hexane-ether) 135-136°C
Yield : 412 mg, 44%

Product : 109f,g — Eluent : CH_2Cl_2 then Acetone
Description : yellow solid, mp (from hexane-ether) 162-163°C
Yield : 395 mg, 42%

ii) Alternative work up procedure

To a solution of the 3-methoxyallyl complex (28) (625 mg, 2.5 mmol) in methylene chloride (15 ml) was added ethyl 2,3-dicyanoacrylate (97f,g) (416 mg, 2.8 mmol) also dissolved in methylene chloride (5 ml). The reaction mixture was stirred at room temperature for 3 hours, and the solvent removed *in vacuo*. The residue was then extracted with ether (*ca* 50 ml) and the brown solid (Crude 109f,g) (485 mg, 48%) collected. Concentration of the filtrate, followed by column chromatography of the residue on florisil eluting with ether-petrol (1:1) afforded the cyclic adduct (108f,g) in 32% yield (317 mg).

(f) Tetramethyl ethylenetetracarboxylate (97h)

28 : 426 mg, 1.7 mmol
Solvent : DMF (10 ml)
Column Chromatography : neutral alumina (Act III)
Product Yield : 0%

97h : 2.2 g, 8.5 mmol
Reaction Time : 67 hours

(g) Dimethyl acetylenedicarboxylate (DMAD)

DMAD (0.8 ml, *ca* 6 mmol) was added in one portion to a solution of the allyl complex (20a) (367 mg, 1.5 mmol) in DMF (10 ml). After 48 hours at room temperature an additional two equivalents of DMAD (0.4 ml, *ca* 3 mmol) was added, and the reaction allowed to continue for 20 hours. The solvent was then removed under reduced pressure and the residue chromatographed on neutral alumina (Act III). The cyclic derivative (110) was eluted with ether petrol (1:1) in 77% yield (446 mg), and recrystallised from hexane-ether to give a yellow solid, mp 94-96^{o}C. Additional reaction conditions investigated, together with the yields of (110) obtained, are summarised in Table 17 (Chapter Two).

(h) Methyl propiolate

28 : 475 mg, 1.9 mmol

Methyl propiolate : 1.0 ml, *ca* 11 mmol

Solvent : DMF (6 ml)

Reaction Time : 92 hours

Column Chromatography : neutral alumina (Act III)

Product Yield : 0%

Yield of recovered 28 : 330 mg, 69%

(i) Tetracyanoethylene (TCNE)

A solution of TCNE (220 mg, 1.7 mmol) in THF (4 ml) was added to the allyl complex (28) (390 mg, 1.6 mmol) dissolved in methylene chloride (10 ml), and the reaction mixture was stirred at room temperature for 30 minutes. Hexane (*ca* 50 ml) was then added to precipitate the product, which was collected and dried *in vacuo* to give the TCNE adduct (108i) in 74% yield (440 mg) as a green-brown solid.

(j) Ethyl 1-cyano-4,4-trimethylenedithiocrotonate (177)

28 : 500 mg, 2.0 mmol

177 : 1.04 g (*ca* 90% pure) *ca* 3.6 mmol

Solvent : DMF (10 ml)

Reaction Time : 20 hours

Column Chromatography : florisil

Product Yield : 0%

Yield of recovered 28 : 343 mg, 69%

Demetalation Reactions

Oxidative Carboxylation

1. General procedure

To a solution of the Fp adduct (*ca* 0.5 mmol) in either anhydrous methanol or ethanol (40 ml), previously purged with carbon monoxide for 2 hours, was added four equivalents of ammonium ceric nitrate [$(NH_4)_2$ Ce $(NO_3)_6$] in one portion, at room temperature. Carbon monoxide was then bubbled through the solution overnight. After removal of the solvent *in vacuo*, water (50 ml) was added to the solid residue and the aqueous solution extracted with benzene (4 x 25 ml). The combined organic extracts were dried over anhydrous sodium sulphate, the solution filtered and concentrated, and the crude product chromatographed on florisil eluting with ether-petrol.

2. 1-Methoxycyclopentyl-Fp complexes

(a) 3,3,4,4-Tetracyano-1-methoxycyclopentyl-Fp (75)[66,69]

i) 75 : 750 mg, 2 mmol Ce^{iv} salt : 5.5 g, 10 mmol
Solvent : MeOH (40 ml)
Product : 119a (R=Me) plus 120a (light-yellow solid)
Yield of crude product : 506 mg, quantitative (119a:120a, 88:12)

These two products (119a and 120a) were too polar to be purified by column chromatography, although recrystallisation from chloroform afforded the ketal adduct (119a,R=Me), in low yield (<10%), as a white solid, mp 143-144°C.

ii) 75 : 750 mg, 2 mmol Ce^{iv} salt : 5.0 g, 9 mmol
Solvent : EtOH (30 ml)
Product : 119a (R=Et) plus 120a
Yield of crude product : 600 mg, quantitative (119a:120a, 66:34)
Recrystallisation from chloroform followed by sublimation (80-120°C, 0.04 Torr) afforded the ketal (119a, R=Et) in 4% yield (20 mg) as a white solid, mp 149-151°C.

(b) 4,4-Dicyano-3-ethoxycarbonyl-1-methoxycyclopentyl-Fp (87)[69]

87 : 250 mg, 0.63 mmol — Ce^{iv} salt : 1.4 g, 2.5 mmol
Solvent : MeOH (30 ml)
Product : 119b (R=Me) plus 120b — Column eluent : ether-petrol (2:3 - 3:2)
Yield : 143 mg, 92% (119b : 120b, 9:1)

(c) 3,3,4-Trimethoxycarbonyl-1-methoxycyclopentyl-Fp (77)

77 : 200 mg, 0.4 mmol — Ce^{iv} salt : 1.1 g, 2.0 mmol
Solvent : MeOH (10 ml)
Product : unknown — R_f : 0.5; ether-petrol (1:1)
Yield : 31 mg

NMR 1.60-3.50(11 units,bm), 3.14, 3.20(8 units,2xs), 3.73, 3.79 (34 units,2xbs)

IR ($CHCl_3$); 1735-1740 (s,C=O)

MS 273(18), 240(55), 213(81), 209(75), 197(64), 186(71), 181(55), 153(71), 59(100)

(d) 3,4-Dicyano-3-ethoxycarbonyl-1-methoxycyclopentyl-Fp (92)

92 : 175 mg, 0.4 mmol — Ce^{iv} salt : 964 mg, 1.7 mmol
Solvent : MeOH (50 ml)
Product : unknown — Column Eluent : ether:petrol (3:1)
Yield : 34 mg

NMR 1.43(3H,t,J=7Hz), 2.15-2.70(2H,m), 2.80-3.05(2H,m), 3.25-4.00 (4H,m), 4.50(2H,q,J=7Hz)

3. Linear alkyl-Fp complexes

(a) $FpCH_2COMe$ (70)

70 : 400 mg, 1.7 mmol
Solvent : MeOH (60 ml)
Product : unknown
Yield : 65 mg

Ce^{iv} salt : 2.81 g, 5.1 mmol

Column Eluent : ether

NMR 2.18(3 units,bs), 2.18-2.65(4 units,m), 3.10-3.60(4 units,bm), 3.74(4 units,s), 3.74-4.00(3 units,m).

IR (CH_2Cl_2); 1745-1750(s,C=O)

cf Methyl acetoacetate

NMR 2.20(3H,s,Me), 3.50(2H,s,CH_2), 3.78(3H,s,OMe)

(b) 4,5,5-Trimethoxycarbonyl-2-oxopentyl-Fp (79)

79 : 387 mg, 0.9 mmol
Solvent : MeOH (40 ml)
Product : unknown
Yield : 130 mg

Ce^{iv} salt : 1.95 g, 3.6 mmol

Column Eluent : ethylacetate-petrol (1:1-3:1)

NMR 2.90-3.55(10 units,bm), 3.71(5 units,s), 3.76(15 units,bs)

(c) 5-t-Butyl-5-cyano-2-methoxy-4-oxo-2-pentenyl-Fp (95b)[69]

95b : 152 mg, 0.41 mmol
Solvent : MeOH (30 ml)
Product : 124
Yield : 76 mg, 95%

Ce^{iv} salt : 1.0 g, 1.8 mmol

R_f : 0.52; ether-petrol (1:3)

4. Cyclopentyl-Fp complexes (98b-g,i) and (105)

(a) 3,3-Diethoxycarbonylcyclopentyl-Fp (98b)

98b : 175 mg, 0.45 mmol
Solvent : EtOH (60 ml)
Product : 125b
Yield : 80 mg, 62%

Ce^{iv} salt : 1.01 g, 1.8 mmol

R_f : 0.65; ether-petrol (1:3)

(b) 3,3,4-Trimethoxycarbonylcyclopentyl-Fp (98c)

98c : 260 mg, 0.62 mmol
Solvent : MeOH (60 ml)
Product : 125c
Yield : 118 mg, 63%

Ce^{iv} salt : 1.36 g, 2.5 mmol

R_f : 0.17; ether-petrol (1:3)

(c) 4,4-Dicyano-3-ethoxycarbonylcyclopentyl-Fp (98d)

98d : 386 mg, 1.05 mmol
Solvent : EtOH (30 ml)
Product : 125d
Yield : 212 mg, 77%

Ce^{iv} salt : 2.5 g, 4.5 mmol

R_f : 0.72; ether-petrol (1:1)

(d) 3-Cyano-3,4-diethoxycarbonylcyclopentyl-Fp (98e)

98e : 525 mg, 1.3 mmol
Solvent : EtOH (40 ml)
Product : 125e
Yield : 235 mg, 60%

Ce^{iv} salt : 2.77 g, 5.1 mmol

R_f : 0.32; ether-petrol (1:3)

(e) 3,4-Dicyano-3-ethoxycarbonylcyclopentyl-Fp (98f,g)

98f,g : 160 mg, 0.4 mmol
Solvent : EtOH (50 ml)
Product : 125f,g
Yield : 72 mg, 63%

Ce^{iv} salt : 950 mg, 1.7 mmol

R_f : 0.47; ether-petrol (1:1)

(f) 3,3,4,4-Tetracyanocyclopentyl-Fp (98i)

98i : 175 mg, 0.5 mmol
Solvent : MeOH (50 ml)
Product : 125i
Crude yield : 130 mg, 70%

Ce^{iv} salt : 1.1 g, 2.0 mmol

Although (125i) could not be purified by column chromatography, sublimation (100-105°C, 0.05 Torr) gave the pure adduct, as a white solid (mp 85-86°), in very low yield (*ca* 3 mg, 3%).

(g) 3,4-Dimethoxycarbonyl-3-cyclopentenyl-Fp (105)

105 : 230 mg, 0.63 mmol — Ce^{iv} salt : 1.4 g, 2.5 mmol
Solvent : MeOH (30 ml)
Product : 126 — R_f : 0.56; ether-petrol (1:1)
Yield : 135 mg, 87%

5. 2-Methoxycyclopentyl Fp complexes (108d-g,i) (109d-g,i) and (110)

(a) 4,4-Dicyano-3-ethoxycarbonyl-2-methoxycyclopentyl-Fp

i) Isomer (108d)

108d : 170 mg, 0.43 mmol — Ce^{iv} salt : 936 mg, 1.7 mmol
Solvent : EtOH (50 ml)
Product : 127d — R_f : 0.84; ether-petrol (1:1)
Yield : 89 mg, 71%

ii) Isomer (109d)

109d : 160 mg, 0.4 mmol — Ce^{iv} salt : 880 mg, 1.6 mmol
Solvent : EtOH (60 ml)
Product : 128d — R_f : 0.33; ether-petrol (1:1)
Yield : 91 mg, 77%

(b) 4-Cyano-3,4-diethoxycarbonyl-2-methoxycyclopentyl-Fp

i) Isomer (108e)

108e : 190 mg, 0.43 mmol — Ce^{iv} salt : 936 mg, 1.7 mmol
Solvent : EtOH (50 ml)
Product : 127e — R_f : 0.81; ether-petrol (1:1)
Yield 84 mg, 58%

ii) Isomer (109e)

109e : 160 mg, 0.36 mmol — Ce^{iv} salt : 788 mg, 1.4 mmol

Solvent : EtOH (50 ml)

Product : 128e (plus isomer) — R_f : 0.56; ether-petrol (1:1) [R_F of isomer : 0.75; ether-petrol (1:1)]

Yield : 50 mg, 41%

(c) 3,4-Dicyano-4-ethoxycarbonyl-2-methoxycyclopentyl-Fp

i) Isomer (108f,g)

108f,g : 130 mg, 0.33 mmol — Ce^{iv} salt : 716 mg, 1.3 mmol

Solvent : EtOH (30 ml)

Product : 127f,g — R_f (127f): 0.49; ether-petrol (1:1); R_f (127g) : 0.62; ether-petrol (1:1)

Yield : 72 mg, 75%

ii) Isomer (109f,g)

109f,g : 210 mg, 0.53 mmol — Ce^{iv} salt : 1.16 g, 2.1 mmol

Solvent : EtOH (50 ml)

Product : 128f,g (plus isomers) — R_f of mixture : 0.21 and 0.60; ether-petrol (1:1)

Yield : 82 mg, 53%

(d) 3,3,4,4-Tetracyano-2-methoxycyclopentyl-Fp (108i)

108i : 200 mg, 0.53 mmol — Ce^{iv} salt : 1.12g, 2.0 mmol

Solvent : MeOH(40 ml)

Product : 127i

Crude Yield : 128 mg, 93% (this product could not be purified by column chromatography on florisil).

(e) 3,4-Dimethoxycarbonyl-2-methoxy-3-cyclopentenyl-Fp (110)

110 : 200 mg, 0.51 mmol — Ce^{iv} salt : 1.12 g, 2.0 mmol
Solvent : MeOH (60 ml)
Product : 129 — R_f : 0.42; ether-petrol (1:1)
Crude Yield : 142 mg, quantitative
Yield of purified product : 35 mg, 25%

Acid Cleavage

1. General Procedure

Hydrogen chloride gas was bubbled through a solution of the Fp adducts (*ca* 0.4 mmol) in methylene chloride (*ca* 40 ml) at 0°C for 1 hour, and the reaction mixture was then set aside, in a well-stoppered flask, for the reaction times indicated. After removal of the solvent *in vacuo*, the residue was dissolved in carbon tetrachloride (*ca* 50 ml) and exposed to sunlight for three hours to decompose the FpCl present, during which time a green solid precipitated. This solid was then filtered off, the filtrate concentrated and the crude product purified by flash chromatography[86] (10g of silica gel; 20 mm column).

2. Cyclopentyl-Fp complexes (98b,c,e) and (105)

(a) 3,3-Diethoxycarbonylcyclopentyl-Fp (98b)

98b : 130 mg, 0.33 mmol — Reaction Time : 20 hours
Column Eluent : ether-petrol (1:1)
Product : 130b — R_f : 0.20; ether-petrol (1:9)
Yield : 48 mg, 67%

This product was identical, by NMR, IR MS and TLC, to an authentic sample of diethyl 3-butenylmalonate (130b) prepared by the reaction of 4-bromobutene with the sodium salt of diethyl malonate[87].

(b) 3,3,4-Trimethoxycarbonylcyclopentyl-Fp (98c)

98c : 95 mg, 0.23 mmol — Reaction Time : 40 hours

Column Eluent : ether-petrol (1:2)

Product : 130c plus 133c — R_f : 0.33 and 0.40; ether-petrol (2:3)

Yield : 40 mg, 70% (130c:133c, 1:1)

(c) 3-Cyano-3,4-diethoxycarbonylcyclopentyl-Fp (98e)

98e : 200 mg, 0.48 mmol — Reaction Time : 40 hours

Column Eluent : ether petrol (1:4)

Product : 130e plus 133e — R_f : 0.17 and 0.19; ether-petrol (1:4)

Yield : 70 mg, 61% (130e:133e, 1:2)

(d) 3,4-Dimethoxycarbonyl-3-cyclopentenyl-Fp (105)

105 : 98 mg, 0.27 mmol — Reaction Time : 40 hours

Column Eluent : ether-petrol (1:4)

Product : 134 — R_f : 0.18; ether-petrol (1:4)

Yield : 38 mg, 76%

3. 2-Methoxycyclopentyl-Fp complexes (108d), (108e), (109e) and (110)

(a) 4,4-Dicyano-3-ethoxycarbonyl-2-methoxycyclopentyl-Fp (108d)

108d : 240 mg, 0.60 mmol — Reaction Time : 24 hours

Column Eluent : ether petrol (1:1)

Product : 139 — R_f : 0.27; ether-petrol (1:1)

Yield : 64 mg, 56%

(b) 4-Cyano-3,4-diethoxycarbonyl-2-methoxycyclopentyl-Fp

i) Isomer (108e)

108e : 120 mg, 0.27 mmol — Reaction Time : 20 hours

Column Eluent : ether-petrol (1:4)

Product : 136 — R_f : 0.34; ether-petrol (1:2)

Yield : 52 mg, 81%

ii) Isomer (109e)

109e : 120 mg, 0.27 mmol — Reaction Time : 20 hours
Product : 136
Yield : 48 mg, 75%

(c) 3,4-Dimethoxycarbonyl-2-methoxy-3-cyclopentenyl-Fp (110)

110 : 165 mg, 0.43 mmol — Reaction Time : 30 minutes
Column Eluent : ether-petrol (1:2)
Product : 140 plus 141 — R_f : 0.19 and 0.23; ether-petrol (1:2)
Yield : 43 mg (140:141, *ca* 11:9)

Bromination of cyclopentyl-Fp complexes (98b-g)

(a) 3,3-Diethoxycarbonylcyclopentyl-Fp (98b)

(i) N-Bromopyridinium bromide (67 mg, 0.28 mmol) was added in one portion to a solution fo the Fp adduct (98b) (110 mg, 0.28 mmol) in methylene chloride (10 ml) at approximately -70°C. After 60 minutes IR spectral analysis indicated incomplete reaction. Additional brominating reagent (67 mg, 0.28 mmol) was therefore added, and the reaction mixture allowed to come to room temperature over 3 hours. The solution was then filtered, the solvent removed *in vacuo* and the residue chromatographed on neutral alumina (Act III) eluting with ether petrol (1:3). This afforded a mixture of the brominated and olefinic derivatives (142b) and (143b) in approximately 76% yield (57 mg; 142b:143b, *ca* 65:35). R_f : 0.16 and 0.20 ether-petrol (1:19).

(ii) To a solution of the Fp adduct (98b) (80 mg, 0.21 mmol) in methylene chloride (10 ml) at -70°C was added N-bromopyridinium bromide (49 mg, 0.21 mmol). The reaction mixture was then allowed to warm to -20°C over 3 hours and a further equivalent of the brominating reagent (49 mg, 0.21 mmol) was added. On reaching room temperature the methylene chloride solution was washed with saturated aqueous sodium thiosulphate solution

(10 ml), the aqueous layer backwashed with methylene chloride (2 x 10 ml) and the organic extracts were combined and washed with saturated aqueous sodium chloride solution (20 ml). The organic extract was then dried over anhydrous magnesium sulphate, the solvent removed *in vacuo*, and the residue chromatographed on neutral alumina (Act III). Elution with ether-petrol (1:3) afforded the mixture of (142b) and (143b) in approximately 95% yield (46 mg, 142b:143b, *ca* 65:35).

(b) 3,3,4-Trimethoxycarbonylcyclopentyl-Fp (98c)

(i) The Fp adduct (98c) (134 mg, 0.32 mmol) in methylene chloride (10 ml) was cooled to -70°C and treated with N-bromopyridinium bromide (75 mg, 0.32 mmol). The reaction mixture was then allowed to come to room temperature over 4 hours, N-bromopyridinium bromide (76 mg, 0.32 mmol) being added when the temperature reached -20°C. After filtration of the solution through neutral alumina (Act III; 2cmx6cm column), eluting with methylene chloride the solvent was removed *in vacuo*, the residue dissolved in ether-petrol (50 ml; 1:1) and exposed to sunlight for 6 hours to decompose the FpBr present. This solution was then concentrated and the crude product chromatographed on neutral alumina (Act III). Elution with ether-petrol (1:1) afforded a 75:25 mixture of the brominated and olefinic products (142c) and (143c) in approximately 43% yield (42 mg). R_f : 0.31; ether-petrol (1:2).

(ii) 98c : 180 mg, 0.43 mmol

N-Bromopyridinium Bromide : 102 mg, 0.43 mmol at -60°C plus 102 mg at -20°C

Reaction Procedure : Identical to that described for the bromination of (98b) in (a,ii) except that the crude product was dissolved in ether-petrol (50 ml; 1:1) and exposed to sunlight for 7 hours before column chromatography on neutral alumina (Act III)

Product : 142c plus 143c

Yield : 39 mg, *ca* 29% (142c:143c, *ca* 3:1)

(c) 4,4-Dicyano-3-ethoxycarbonylcyclopentyl-Fp (98d)

98d : 160 mg, 0.43 mmol

N-Bromopyridinium Bromide : 314 mg, 1.32 mmol at -70°C and 210 mg, 0.89 mmol at -15°C

Reaction Procedure : identical to that described for the bromination of (98c) in (b,ii)

Product : None

(d) 3-cyano-3,4-diethoxycarbonylcyclopentyl-Fp (98e)

98e : 245 mg

N-Bromopyridinium Bromide : 212 mg, 0.89 mmol, at -70°C plus 212 mg at -15°C

Reaction Procedure : Identical to that given for the bromination of (98c) in (b,i).

Product : 142e plus 143e

R_f : 0.37, 0.44 and 0.55, ether-petrol (1:3)

Column Eluent : ether petrol (1:3)

Yield : 55 mg, *ca* 32% (142e:143e, *ca* 3:2)

Flash chromatography (6g silica gel; 10 mm column) eluting with ether-petrol (3:7) resulted in the isolation of the following three fractions.

1. 7 mg of either (144a) or (144b); R_f : 0.44; ether-petrol (1:3)
2. 28 mg of a mixture of (143e), (144a) and (144b)
3. 13 mg of the other isomer of (144) plus some of the olefinic adduct (143e)

(e) 3,4-Dicyano-3-ethoxycarbonylcyclopentyl-Fp (98f,g)

To a solution of the Fp adduct (98f,g) (184 mg, 0.5 mmol) in methylene chloride (10 ml) at -70°C was added N-bromopyridinium bromide (239 mg, 1.0 mmol) in one portion. The reaction mixture was then allowed to come to -15°C, and a further two equivalents of brominating reagent (239 mg, 1.0 mmol) was added. After stirring at room temperature for 20 hours an IR spectrum indicated complete reaction. The solution was filtered through florisil (2cmx5cm column) while eluting with methylene chloride and the solvent removed *in vacuo*. The residue was then dissolved in ether (50 ml) and exposed to sunlight for three hours to decompose any FpBr present. After filtration and removal of the solvent under reduced pressure, the crude product was purified by flash chromatography (6g silica gel; 10 mm column) eluting with ether-petrol (3:2)

to give 3,4,5-tribromocyclopentene (145) (26 mg, 17%), plus a mixture of unidentifiable derivatives (19 mg).

3,4,5-Tribromocyclopentene[90]:

NMR 4.94(1H,bs,CHBrC*H*BrCHBr), 5.15(2H,bs,C*H*BrCHBrC*H*Br), 6.13(2H, bs,CH=CH)

IR 1600 (m,C=C)

MS 306(0.4), 304(0.4), 227(49), 225(100), 223(54), 146(39), 145(16), 144(39), 143(15), 65(82), 39(32)

(f) 3-Cyano-3-ethoxycarbonyl-4-(2,2-trimethylenedithioethyl)cyclopentyl-Fp (181)

181 : 170 mg, 0.36 mmol

N-Bromopyridinium Bromide : 128 mg, 0.54 mmol at -70°C plus 128 mg at -20°C

Reaction procedure : Identical to either the procedure described for the bromination of (98b) in (a,i), or that described for (98) in (b,ii).

Product : None

β-Hydride abstraction followed by olefin liberation

1. 3,3-Diethoxycarbonylcyclopentyl-Fp (98b)

(i) β-Hydride Abstraction

A solution of trityl tetrafluoroborate (140 mg, 0.42 mmol) in methylene chloride (2 ml) was added dropwise to a solution of the Fp adduct (98b) (166 mg, 0.43 mmol) in the same solvent (3 ml) at 45°C. After stirring at this temperature for 2 hours an IR spectrum indicated complete reaction. The reaction mixture was then cooled to 0°C and the

intermediate Fp(η^2-olefin) salt precipitated by the addition of ether (*ca* 30 ml). The solvent was decanted off and the residue washed with ether (*ca* 20 ml) and dried *in vacuo* to give the salt in 66% crude yield (134 mg).

IR (CH_2Cl_2); 2075, 2035(s,C≡O)

(ii) Olefin liberation

To a solution of the salt (134 mg, *ca* 0.28 mmol) in acetone (2 ml) was added, sodium iodide (85 mg, 0.57 mmol), in one portion, and the reaction mixture stirred at room temperature for 1 hour. After removal of the solvent under reduced pressure, the residue was extracted with methylene chloride (*ca* 10 ml) and the extracts were filtered (to remove excess sodium iodide) and concentrated. Th crude product was then dissolved in carbon tetrachloride (20 ml), the solution exposed to sunlight for 3 hours (to decompose the FpI present), filtered and the solvent removed *in vacuo*. Flash chromatography[86] (10 g silica gel, 20 mm column), eluting with ether-petrol (1:4) afforded diethyl 3-buteynyl-malonate (130b) in 51% yield (46 mg) from (98b).

2. 4-Cyano-3,4-diethoxycarbonyl-2-methoxycyclopentyl-Fp; Isomer (108e)

(i) β-Hydride Abstraction

108e : 119 mg, 0.27 mmol
Trityl Tetrafluoroborate : 90 mg, 0.27 mmol
Reaction Procedure : Identical to that described for (98b) above
Crude Yield of intermediate salt (152) : 112 mg, *ca* 76%
IR (CH_2Cl_2); 2075, 2030(s,C≡O).

(ii) Olefin libertion

152 : 112 mg, *ca* 0.20 mmol
Sodium Iodide : 63 mg, 0.42 mmol
Reaction Procedure : Identical to that described for (98b) above
Column Eluent : ether-petrol (1:4)
Product : 136
Yield : 39 mg, 62% (from 108e)

Synthesis of Cyclopentanoid Natural Products *via* a Metal-Assisted (3+2) Cycloaddition Reaction; A Preliminary Study

1. PGFα type prostaglandins

Reduction of diethyl (phenylthio)malonate (160)

A solution of diethyl (phenylthio)malonate (160)[92] (2.68 g, 10 mmol) in anhydrous ether (10 ml) was added dropwise to a suspension of lithium aluminium hydride (0.76 g, 20 mmol) in dry ether (10 ml) at 0°C. Stirring was maintained at this temperature for 30 hours. The excess reagent was then destroyed by cautious addition of water (*ca* 1 ml), the reaction mixture acidified with 6N hydrochloric acid solution, and the ether layer collected and mixed with further ethereal extracts of the aqueous phase (3 x 20 ml). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate solution (3 x 10 ml), dried over anhydrous sodium sulphate, and concentrated. Distillation of the residue afforded a lower boiling fraction containing thiophenol (odour) and a fraction ($bp_{0.1}$ 140-160°) containing a mixture of compounds. Preparative thin-layer chromatography [0.5 mm silica gel, ether-petrol (1:1)] of this mixture resulted in the isolation of 2-phenylthiopropane-1,3-diol (161) and 2-phenylpropane-1-ol (162) in yields of 20% (0.77 g) and 8% (0.13 g) respectively.

2-Phenylthiopropane-1,3-diol (161); Rf = 0.06 [ether-petrol(1:1)]

NMR 2.95(2H,s,OH), 3.40(1H,qt,J=6Hz,OCH_2CHCH_2O), 3.82(4H,d,J=6Hz, OCH_2CHCH_2O), 7.40(5H,m,Ph)

MS, 184(46,*M*), 136(27), 123(27), 110(100), 109(69), 77(20), 45(31), 44(69).

2-Phenylthiopropane-1-ol; R_f = 0.29 [ether-petrol (1:1)]

NMR 1.30(3H,d,J=6.5Hz,$CHCH_3$), 2.23(1H,bs,OH), 3.00-3.85(3H,m, $CHCH_2OH$), 7.34(5H,m,phenyl).

MS 168(46,*M*), 137(100), 123(26), 110(75), 109(51), 65(24), 51(24), 45(27).

5-Hydroxy-2-phenyl-1,3-dioxane (163)

In a modification of the procedure described by Foster *et al*[97], a continuous stream of air was drawn through a mixture of redistilled benzaldehyde (20 g, 0.19 mole), glycerol (22 g, 0.24 mmol) and concentrated sulphuric acid solution (1 drop) at approximately 95°C. Benzene (50 ml) was then added and the water produced in the reaction (*ca* 4 ml) removed azeotropically overnight, using a Dean and Stark apparatus. After removal of the benzene *in vacuo*, the residue was seeded and stored at 0°C for 3 hours. The crystalline product was collected, dissolved in benzene (*ca* 100 ml), washed with dilute aqueous ammonia solution (2 x 50 ml) and recovered by the removal of the solvent *in vacuo*. Recrystallisation from benzene-petroleum ether (60-80°C) afforded a mixture of *cis* and *trans*-5-hydroxy-2-phenyl-1,3-dioxane (163) in 72% yield (24.4 g), mp 52-56°C; R_f = 0.22-0.27 [ether petrol (2:1)]

NMR 3.58(2H,m,CH_2CHOH), 4.08(4H,d,J=1.5Hz,OCH_2CHCH_2O), 5.43($\frac{1}{8}$H, s,CHPh of *trans*-isomer), 5.55($\frac{7}{8}$H,s,CHPh of *cis*-isomer), 7.41(5H,m,Ph)

MS 180(50,*M*), 178(64), 107(100), 105(72), 91(28), 79(52), 77(64) 51(30)

2-Phenyl-5-phenylsulphoxide-1,3-dioxane (166)

5-Hydroxy-2-phenyl-1,3-dioxane (163) was tosylated by the method of Matheson and Angyal[68], and converted to the phenylthio-derivative (165) (in 48% yield from the alcohol) by the method of Baig and Owen[96].

A solution of 2-phenyl-5-phenylthio-1,3-dioxane (165) (0.4 g, 1.5 mmol) in anhydrous carbon tetrachloride (30 ml) was cooled to 0°C and m-chloroperbenzoic acid (0.30 g, 1.5 mmol based on 85% purity) in carbon tetrachloride (10 ml) was added with vigorous stirring. After 20 hours at room temperature TLC analysis indicated complete loss of starting material [R_f (165) = 0.77; ether-petrol (1:5)]. The reaction mixture was then poured into a separating funnel containing ether (10 ml) and 10% aqueous sodium sulphite solution (10 ml). The organic layer was separated, backwashed with saturated aqueous sodium hydrogen carbonate solution

(2 x 10 ml), dried over anhydrous sodium sulphate, and concentrated to give the phenylsulphoxide (166) as a white solid in 80% yield (0.34 g), mp (from ethanol) 121-122°C; R_f = 0.27 [ether-petrol (2:1)].

NMR (d^6-DMSO); 3.84-4.20(5H,m,OCH_2CHCH_2O), 5.58(1H,s,CHPh), 7.40 (5H,m,Ph)

MS 288(0.8,*M*), 271(26), 164(11), 163(100), 107(18), 106(16), 105(18), 91(19), 57(19)

Attempted elimination of benzene sulphenic acid from 2-phenyl-5-phenylsulphoxide-1,3-dioxane (166)

(i) The crude phenylsulphoxide (166) (288 mg, 1.0 mmol) was dissolved in either benzene, toluene or xylene (20 ml), and the resulting solution heated to reflux in the presence of calcium carbonate (200 mg, 2.0 mmol). After the time periods given in Table 27 (Chapter Four) the solvents were removed *in vacuo* to afford starting material in the reactions performed in benzene and toluene (280 mg and 150 mg respectively), and a trace of diphenyl disulphide (PhS-SPh) when xylene was employed as the solvent.

(ii) A solution of the sulphoxide (166) (288 mg, 1.0 mmol) in DMF (20 ml) was heated to 140-150°C for 24 hours in the presence of calcium carbonate (200 mg, 2.0 mmol). After cooling to room temperature, water (30 ml) was added and the aqueous phase extracted with ether (3 x 20 ml). The combined extracts were then dried over anhydrous sodium sulphate and concentrated to give a solid (27 mg), of which diphenyl disulphide [NMR 7.30(10H,m)] was the major component.

2-Phenyl-1,3-dioxin (167)

(i) A mixture of powdered potassium hydroxide (10 g, 180 mmol) and the p-toluenesulphonate (164) (10 g, 30 mmol) was placed under vacuum (0.1 Torr) and heated to 125°C according to the procedure of Fischer *et al*[99]. A colourless liquid distilled, which was redistilled ($bp_{0.08}$ *ca* 70°C) to give 2-phenyl-1,3-dioxin (107) in 14% yield (0.7 g).

(ii) n-Butyllithium (5.0 mmol) in hexane (3.5 mls) was added dropwise to a solution of the p-toluenesulphonate (164) (1.67 g, 5.0 mmol) in anhydrous THF (20 ml) cooled to -70°C under nitrogen. After completion of addition the reaction mixture was allowed to come to room temperature. Water (10 ml) was then added, the organic layer separated, dried over anhydrous sodium sulphate and concentrated. NMR analysis of the crude product (0.84 g, quantitative yield) indicated that the reaction had proceeded to give a 60:40 mixture of 2-phenyl-1,3-dioxin (167) [R_f = 0.62; ether-petrol (1:1)] and 1-phenyl-1-pentanol [R_f = 0.61; ether-petrol (1:1)].

1-Phenyl-1-pentanol:

NMR[123] 0.70-2.00(9H,m,^{n}Bu), 2.05(1H,s,OH), 4.65(1H,t,J=7Hz, CH_2CHPh), 7.34(5H,s,Ph).

(iii) A solution of the p-toluenesulphonate (164) (10 g, 30 mmol) in dimethyl sulphoxide (60 ml) was added, with stirring, to a solution of potassium t-butoxide (6.7 g, 60 mmol) in dimethyl sulphoxide (30 ml). An ice bath was used to maintain a reaction temperature of 20-25°C. After stirring at this temperature for 30 minutes, pentane (10 ml) was added, the reaction mixture was stirred for an additional minute, and then poured into ice-water (100-150 ml). The hydrocarbon layer was separated and the aqueous phase extracted with pentane (3 x 10 ml). The combined extracts were washed with saturated aqueous sodium chloride solution (3 x 15 ml), dried over anhydrous sodium sulphate, and the solvent removed *in vacuo*. Distillation of the residue afforded 2-phenyl-1,3-dioxin (167), $bp_{0.08}$ 69-71°C (lit[99] $bp_{0.1}$ 72-75°C), in 89% yield (4.43 g).

2-Phenyl-1,3-dioxin:

NMR (CCl_4); 4.43(2H,bs,$CHCH_2O$), 4.97(1H,m,$CH=CHCH_2$), 5.82(1H,s, $CHPh$), 6.67(1H,bd,J=6Hz,$OCH=CHCH_2$), 7.50(5H,m,Ph)

MS 162(0,*M*), 106(87), 105(86), 78(20), 77(100), 56(34), 55(24), 51(49), 50(25)

Thermal rearrangement of 2-phenyl-1,3-dioxin (167)

A solution of 2-phenyl-1,3-dioxin (*ca* 100 mg) in carbon tetrachloride (10 ml) was heated to reflux in an atmosphere of nitrogen for 4.5 hours. NMR analysis of the solution after this time period indicated the presence of unreacted starting material, acrolein and benzaldehyde in a ratio of approximately 2:3:3.

Attempted bromination of 2-phenyl-1,3-dioxin with N-bromosuccinimide (NBS)

General Procedure

A solution of the olefin (167) plus 1–1.5 equivalents of NBS in carbon tetrachloride (3-10 ml) was stirred in the presence of a radical initiator (either benzoyl peroxide or ultra-violet light) at 15-80°C for the reaction times indicated. After cooling to 0°C, the reaction mixture was filtered, and the filtrate washed with water (2 x *ca* 5 ml), dried over anhydrous sodium sulphate and concentrated. The residue was then analysed by NMR spectroscopy. In general, either unreacted starting material, benzaldehyde or unidentifiable compounds [NMR (CCl_4); 2.50(6H,bs), 3.90 (5H,bm), 6.20(1H,s,), 7.30(12H,m)] were isolated from the reactions investigated.

Reaction conditions employed

(i) 167 : 100 mg, 0.62 mmol — NBS : 122 mg, 0.69 mmol

CCl_4 : 5 ml — Radical Initiator : benzoyl peroxide (0.26 mg)

Temp : 80°C — Reaction Time : 4 hours

Isolate Adducts : benzaldehyde and unreacted starting material (*ca* 1:1), plus a trace of the unidentifiable products.

Yield : 70 mg

(ii) 167 : 270 mg, 1.67 mmol — NBS : 330 mg, 1.85 mmol

CCl_4 : 3 ml — Radical Initiator : benzoyl peroxide

Temp : 25°C — Reaction Time : 24 hours

Isolated Adducts : unreacted starting material plus a trace of benzaldehyde and the unidentifiable products.

Yield : 180 mg

(iii) 167 : 1.72 g, 11 mmol — NBS : 2.058 g, 12 mmol

CCl_4 : 10 ml — Radical Initiator : ultra violet light

Temp : 80°C — Reaction Time : 4.5 hours

Isolated Adducts : predominantly benzaldehyde

Yield : 0.91 g

(iv) 167 : 1.0 g, 6.2 mmol — NBS : 1.1 g, 6.2 mmol

CCl_4 : 5 ml — Radical Initiator : ultra violet light

Temp : 15°C — Reaction Time : 20 hours

Isolated Adducts : unreacted starting material, plus a trace of benzaldehyde and the unidentifiable products.

Yield : 0.86 g

(v) 167 : 1.0 g, 6.2 mmol — NBS : 1.6 g, 9.0 mmol

CCl_4 : 5 ml — Radical Initiator : ultra violet light

Temp : 15°C — Reaction Time : 20 hours

Isolated Adducts : predominantly benzaldehyde

Yield : 0.46 g.

2-(p-Toluenesulphonyloxy)propane-1,3-diol (168)

To a solution of 2-phenyl-5-(p-toluenesulphonyloxy)-1,3-dioxane (164) (8.6 g, 26 mmol) in methanol (122 ml) at 55°C was added 1N sulphuric acid solution (105 ml) preheated to the same temperature. The reaction mixture was stirred at 55-60°C for 20 hours, then cooled and neutralised with dilute aqueous ammonia solution. After removal of methanol and benzaldehyde under reduced pressure, the residual solution was extracted with ether (5 x 30 ml), the combined extracts dried over anhydrous sodium sulphate, and concentrated to give a thick oil which solidifed on cooling. Recrystallisation from ethyl acetate-petrol afforded 2-(p-toluenesulphonyloxy)propane-1,3-diol in 78% yield (4.95 g), mp 49-50°C (lit[124] mp 53-54°C); R_f = 0.52 (ethyl acetate).

NMR (d^6-DMSO); 2.46(3H,s,ArMe), 3.57(4H,d,J=5Hz,OCH_2CHCH_2O), 4.29(1H,qt,J=5Hz,OCH_2CHCH_2O), 4.69(2H,s,OH), 7.45 and 7.75 (each 2H, each d,J=8Hz, ArH)

MS 246(0,*M*), 198(18), 156(10), 155(80), 92(18), 91(100), 65(21), 43(11), 39(8)

CMR δ(ppm) (d^6-DMSO); 21.1($ArCH_3$), 59.5(OCH_2), 84.1($CHOSO_2$), 127.7 and 129.9(ArCH), 133.9 and 144.6(ArC).

2-(p-Toluenesulphonyloxy)propane-1,3-phosphate (169)

(i) To vigourously stirring anhydrous methylene chloride (40 ml) maintained at 0°C and under nitrogen was added a solution of 2-(p-toluenesulphonyloxy)propane-1,3-diol (168) (2.68 g, 11 mmol) and pyridine (1.8 ml, 1.76 g, 22 mmol) in methylene chloride (20 ml) simultaneously with a solution of phosphorus oxychloride (1.67 g, 11 mmol) also in methylene chloride (20 ml). After completion of addition (*ca* 1 hour) the reaction mixture was stirred at room temperature for 2 hours and a solution of methanol (0.5 ml, 0.44 g, 12 mmol) and pyridine (0.9 ml, 11 mmol) in methylene chloride (20 ml) was added dropwise. The resulting solution was stirred at room temperature for a further 1.5 hours, the solvent was then removed *in vacuo* and the residue chromatographed twice on neutral alumina (Act III). Elution with ethyl acetate afforded the cyclic phosphate ester (169) in 3.5% yield (123 mg); R_f = 0.26 (ethyl acetate).

(ii) 2-(p-Toluenesulphonyloxy)propane-1,3-diol (168) (2.07 g, 8.4 mmol) in anhydrous toluene (40 ml) was heated to 90-95°C and freshly distilled trimethyl phosphite (1.05 g, 8.5 mmol) was added rapidly to the stirred solution. The solution was heated to 100°C for 2 hours, during which time the methanol produced in the reaction was removed by distillation at atmospheric pressure. The solvent and excess trimethyl phosphite were then removed under reduced pressure and the residue chromatographed on neutral alumina (Act III) to give the crude phosphite as a colourless oil [962 mg; R_f = 0.67 (ethyl acetate)], on elution with ethyl acetate.

This crude product (962 mg) was dissolved in dry methylene chloride (40 ml) and cooled to -50°C under nitrogen. Dinitrogen tetroxide (purified and dried by the method of Cox and Westheimer[125]) was then distilled into the solution until a faint green colour appeared. The reaction mixture was allowed to come to room temperature over four hours, and the solvent and excess dinitrogen tetroxide removed under reduced pressure. Column chromatography of the residue on neutral alumina (Act III) eluting with ethyl acetate afforded the phosphate ester (169) in 5.5% yield (150 mg).

(iii) A solution of freshly distilled phosphorus trichloride (2.36 g, 17 mmol) in methylene chloride (45 ml) and a solution of 2-p-toluenesulphonyloxypropane-1,3-diol (4.2 g, 17 mmol) and triethylamine (4.8 ml, 3.48 g, 35 mmol) in the same solvent (45 ml) were added simultaneously to vigorously stirred anhydrous methylene chloride (90 ml) at 0°C and under nitrogen. After completion of addition (*ca* 1 hour), the reaction mixture was stirred at room temperature for 3 hours. The solvent was then removed *in vacuo*, and the residue extracted with anhydrous ether (100 ml). The extract was filtered, the filtrate cooled to 0°C and a solution of methanol (0.7 ml, 0.62 g, 17 mmol) and triethylamine (2.4 ml, 1.74 g, 17 mmol) in ether (20 ml) was introduced. The reaction mixture was allowed to come to room temperature over 2 hours, filtered, and the filtrate concentrated to give the desired phosphite as a colourless oil (2.49 g). This crude product was purified and oxidised with nitrogen tetroxide as described in (ii) above, to give the cyclic phosphate ester (109) in 5% yield (253 mg).

2- p-Toluenesulphonyloxypropane -1,3-phosphate (169):

NMR 2.47(3H,s,ArMe), 3.82(3H,d,J=11Hz,POMe), 4.00-4.80(5H,m, OCH_2CHCH_2O), 7.43 and 7.89 (each 2H, each d,J=9Hz,ArH)

MS 324(5), 323(12), 322(100,*M*), 259(8), 258(89), 202(9), 151(5), 134(4)

Attempted condensation of 2-(p-toluenesulphonyloxy)propane-1,3-diol (168) with t-Butylphosphonyl dichloride (173)

A solution of 2-(p-toluenesulphonyloxy)propane-1,3-diol (*ca* 4 mmol), t-butylphosphonyl dichloride[102] (*ca* 4 mmol) and two equivalents of base in either methylene chloride or chloroform (*ca* 20 ml) was heated to reflux, under nitrogen, for the reaction times given in Table 28. TLC and NMR analysis of the crude product, obtained after removal of the

TABLE 28

Reaction conditions employed for the attempted condensation of (168) with (173)

Base	Solvent	Reaction Temp. (^{o}C)	Reaction Time (hrs)
Et_3N	CH_2Cl_2	40	30
Pyridine	CH_2Cl_2	40	30
$NaHCO_3$	CH_2Cl_2	40	120
$NaHCO_3$[a]	CH_2Cl_2	61	120
K_2CO_3	CH_2Cl_2	40	60

a) plus a catalytic amount of copper powder.

solvent *in vacuo* indicated that no reaction had occurred.

Both sodium hydride in THF at 0^{o}C, and n-butyllithium in THF at -70^{o}C reacted with the 1,3-diol (168) to give unidentifiable products on work up. (NB these products contained no p-toluenesulphonate functionality, as shown by NMR analysis).

2. Sarkomycin

Isomerisation of diethyl 1-cyano-3-cyclopentene-1,2-dicarboxylate (136) to diethyl 1-cyano-2-cyclopentene-1,2-dicarboxylate (137)

(a) Sodium ethoxide in ethanol

To a solution of diethyl-1-cyano-3-cyclopentene-1,2-dicarboxylate (136) (155 mg, 0.65 mmol) in anhydrous ethanol (1 ml) was added sodium ethoxide (prepared from 15 mg, 0.65 mmol, of sodium) dissolved

in ethanol (1 ml). After stirring at room temperature for 30 seconds, the reaction mxiture was neutralised with 0.1 N hydrochloric acid solution and then partitioned between methylene chloride (10 ml) and saturated aqueous sodium chloride solution (10 ml). The organic layer was separated, the aqueous phase further extracted with methylene chloride (4 x 10 ml) and the combined extracts dried over anhydrous magnesium sulphate and concentrated. Flash chromatography[85] (10 g silica gel, 20 mm column) eluting with ether-petrol (1:1) afforded diethyl 1-cyano-2-cyclopentene-1,2-dicarboxylate (137) in 78% yield (121 mg); R_f = 0.19 [ether-petrol (1:2)], *cf* R_f (136) = 0.34 [ether-petrol (1:2)].

The yield of the isomerised product (137) decreased to 38% yield on stirring the reaction mixture for 5 minutes.

(b) Pyridine

A solution of the cyclopentene derivative (136) (110 mg, 0.46 mmol) in anhydrous pyridine (1 ml) was heated to 100°C for 24 hours. After cooling to room temperature, the reaction solution was poured into a mixture of water (10 ml) and methylene chloride (10 ml) and the organic layer separated. The aqueous phase was then further extracted with methylene chloride (3 x 10 ml), backwashed with 1N hydrochloric acid solution (3 x 10 ml), dried over anhydrous magnesium sulphate and concentrated. Column chromatography of the residue on florisil afforded a 50:50 mixture of unreacted starting material (136) and the isomerised product (137) in a combined yield of 47% on elution with ether-petrol (2:1-3:1).

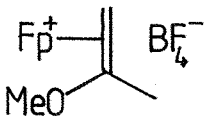
(c) Sodium acetate in ether

Fused sodium acetate (60 mg, 0.73 mmol) was added to a solution of the olefin (136) (33 mg, 0.14 mmol) in anhydrous ether (2 ml), and the reaction mixture was heated to reflux for 4 hours. TLC analysis at this time indicated that no reaction had occurred.

Attempted oxidation of diethyl 1-cyano-2-cyclopentene-1,2-dicarboxylate (137) with dimethyl sulphoxide

A stirred solution of the cyclopentene derivative (137) (34 mg, 0.14 mmol) in dimethyl sulphoxide (1 ml) was heated at 160-170°C for 5 hours, and allowed to cool to room temperature overnight. The solution was then poured into a mixture of water (5 ml) and ether (5 ml) the organic layer was separated and the aqueous layer extracted with ether (2 x 5 ml). The combined extracts were washed with water (2 x 5 ml) and saturated aqueous sodium chloride solution (5 ml), dried over anhydrous sodium sulphate and concentrated to give unreacted starting material in 82% recovered yield (28 mg).

68[66,67]

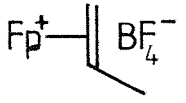


NMR — (d^6-Acetone); 2.47(3H,s,Me), 2.93(2H,s,C=CH_2), 3.92(3H,s,OMe), 5.67(5H,s,Cp).

IR — (Acetone); 2046, 2004(s,C≡O), 1520(m, C=C)

Elemental Analysis — Calculated for $C_{11}H_{13}BF_4FeO_3$: C, 39.34; H, 3.87
Found : C 38.90, H 3.60.

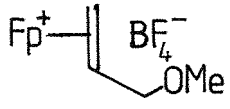
22c[21]



NMR — (d^6-Acetone). 1.90(3H,d,J=6Hz,CHCH_3), 4.06(1H, d,J=9Hz, *cis* CH=CH_2), 5.00-5.75(1H,m,CH=CH_2), 5.94(5H,s,Cp), .64(1H,d,J=15Hz, *trans* CH=CH_2).

IR — (Acetone); 2070, 2035(s,C≡O).

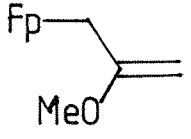
22m[20]



NMR[20] — (CD_3NO_2); 3.35(3H,s,OMe), 3.56(1H,d,J=15Hz, *trans* CH=CH_2), 3.98(2H,d,J=4Hz, CHCH_2OMe), 4.04(1H,d, J=8Hz, *cis* CH=CH_2), 5.30(1H,m,CH=CH_2), 5.68(5H,s,Cp).

IR[20] — (KBr), 2050, 2000(s,C≡O).

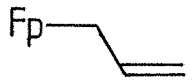
66[66,67]



NMR — 2.00(2H,bs,FpCH_2), 3.51(3H,s,OMe), 3.72 and 3.85 (each 1H, each bd, J=2Hz, C=CH_2), 4.73(5H,s,Cp).

IR — (CCl_4); 2005, 1958(s,C≡O), 1656, 1625(m,C=C).

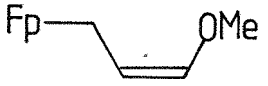
20a[21,26]



NMR 2.10(2H,d,J=8Hz, $FpCH_2CH$), 4.40-5.07(2H,m, $CH=CH_2$), 4.67(5H,s,Cp), 5.70-6.34(1H,m,$CH_2CH=CH_2$)

IR (neat film); 1990, 1940(s,C≡O), 1602(m,C=C)

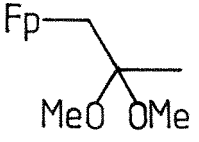
28[20]



NMR 2.16(2H,d,J=8Hz,$FpCH_2CH$), 3.45(3H,s,OMe), *ca.* 4.6 (1H,m,$CH_2CH=CHOMe$), 4.67(5H,s,Cp), 5.64(1H,d, J=6Hz,$CH=CHOMe$)

IR ($CHCl_3$); 1998, 1945(s,C≡O), 1635(m,C=C).

67[66,67]



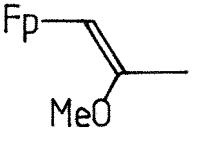
NMR 1.30(3H,s,Me), 1.65(2H,s,CH_2), 3.15(6H,s,OMe), 4.80(5H,s,Cp)

70[126]

NMR 1.77(2H,s,CH_2), 2.07(3H,s,Me), 4.83(5H,s,Cp)

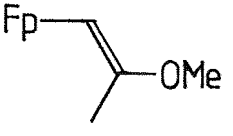
IR (CCl_4), 2030, 1960(s,C≡O), 1656(s,C=O).

71[69]



NMR 2.16(3H,s,Me), 3.60(3H,s,OMe), 4.78(5H,s,Cp), 5,28(1H,m,CH=C)

72[69]



NMR 1.82(3H,s,Me), 3.64(3H,s,OMe), 4.78(5H,s,Cp), 5.48(1H,m,CH=C).

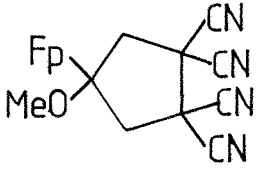
73[68] $FpCH_2CO_2Me$

NMR 1.54(2H,s,CH_2), 3.61(3H,s,CO_2Me), 4.87(5H,s,Cp).

IR ($CHCl_3$); 2018, 1970(s,C≡O), 1675(s,C=O), 1096 (m,C-O-C)

MS (15eV); 250(0.2,M), 222(28,*M*-CO), 194(100,*M*-2CO), 186(43), 152(29), 130(14), 66(18), 65(15), 42(31)

75[66,67]



NMR (d^6-Acetone); 2.84 and 3.81(each 2H, each d, J= 13Hz, CH_2), 3.25(3H,s,OMe), 5.29(5H,s,Cp)

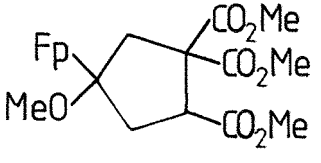
NMR ($CDCl_3$); 2.59 and 3.49, 3.23 and 5.00

IR (Acetone); 2008, 1956(s,C≡O)

MS 376(0,*M*), 186(26), 173(57), 147(24), 122(30), 121 (100, FeCp), 66(32), 56(42), 42(37)

Elemental Analysis Calculated for $C_{17}H_{12}FeN_4O_3$: C, 54.28; H, 3.22; N, 14.90. Found : C, 54.09; H, 3.23; N, 14.83

77

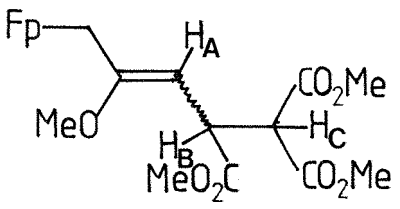


NMR 1.90-3.00(4H,bm,CH_2 and CH_2CH), 3.04(3H,s,OMe), 3.68(6H,s,CO_2Me), 3.79(3H,s,CO_2Me), *ca.* 3.80(1H, m,CH_2CH), 4.90(5H,s,Cp)

IR ($CHCl_3$); 2000, 1950(s,C≡O), 1735(s,C=O ester)

MS (25eV); 450(0,*M*), 362(100), 302(56), 213(88), 181 (66), 153(92), 121(74), 69(54), 59(66)

78

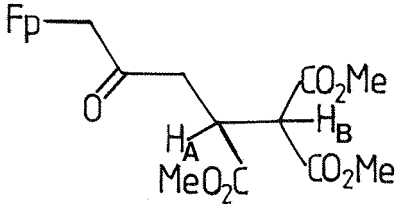


NMR 1.80 and 2.17(each 1H, each d, J=9.5Hz, $FpCH_2$), 3.43(3H,s,OMe), 3.68, 3.70 and 3.73(each 3H, each s, CO_2Me), 3.74-4.10(3H,m,H_A-H_C), 4.80(5H,s,Cp)

IR ($CHCl_3$); 2000, 1955(s,C≡O), 1735(s,C=O ester, 1625 (m,C=C)

MS 450(0,*M*), 394(49,*M*-2CO), 252(100), 152(59), 122(33), 121(62), 111(24), 59(27), 56(25).

79



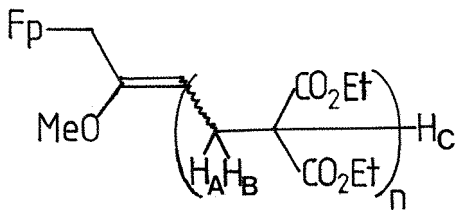
NMR 1.73(2H,t,J=1.25Hz, $FpCH_2$), 2.91(2H,t,J=5Hz,$COCH_2$) 3.50(1H,m,H_A), 3.72(3H,s,CO_2Me), 3.76(6H,s,CO_2Me) 3.90(1H,d,J=7.5Hz, H_B), 4.88(5H,s,Cp)

IR ($CHCl_3$); 2010, 1970(s,C≡O), 1740(s,C=O ester), 1650 (m,C=O ketone)

MS (25eV); 436(0,*M*), 349(40), 348(99), 177(19), 169 (26), 122(26), 121(100), 95(29), 56(26).

Elemental Analysis Calculated for $C_{18}H_{20}FeO_9$: C, 49.56; H, 4.62.
Found : C, 49.34, H, 4.65

82a

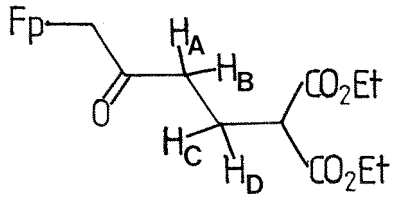


n=1,2, etc

NMR 1.26(13H,t,$CO_2CH_2CH_3$), 2.03(2H,s,$FpCH_2$), 2.58 (3.5H,bt,J=10Hz, H_A and H_B), 3.41(3H,s,OMe); 3.43-4.80(2H,m,C=CH and H_C), 4.21(9H,q,$CO_2CH_2CH_3$), 4.80, 4.88 and 4.95(3.5, 1.0 and 0.5H, each s, Cp).

IR ($CHCl_3$); 2000, 1950(s,C≡O), 1730(s,C=O ester), 1660(w,C=C)

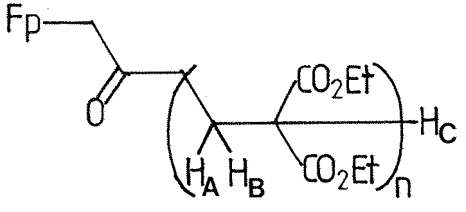
83a (n=1)



NMR 1.36(6H,t,$CO_2CH_2CH_3$), 1.74(2H,s,$FpCH_2$), 2.00-2.50(4H,m,H_A-H_D), 3.47(1H,t,J=6Hz, $CHCO_2Et$), 4.24(4H,q,$CO_2CH_2CH_3$), 4.90(5H,s,Cp).

IR ($CHCl_3$); 2010, 1965(s,C≡O), 1725(s,C=O ester), 1635(m,C=O ketone)

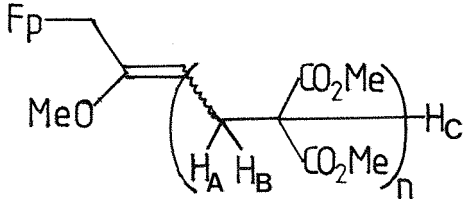
83a



n=1,2, etc

NMR 1.25(12H,t,$CO_2CH_2CH_3$), 1.74(2H,s,$FpCH_2$), 1.97-2.50 (5H,m,$COCH_2CH_2CE_2$, H_A and H_B), 2.56(1.67H,d, J=6Hz, CH_2CHCO_2Et), 3.53(1H,bt,J=6Hz,H_C), 4.21(8H, bq,$CO_2CH_2CH_3$), 4.88 and 4.96(0.7 and 4.3H, each s, Cp).

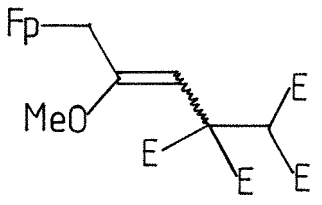
82b



n=1,2 etc

NMR 2.05(2H,s,$FpCH_2$), 2.57(4H,bt,J=6Hz, H_A and H_B), 3.41(3H,s,OMe), 3.74 (14H,bs,CO_2Me, C=CH and H_C), 4.82(5H,s,Cp).

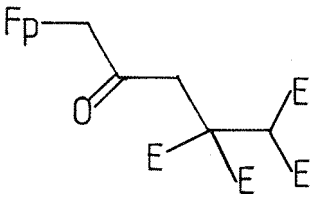
85 (E=CO_2Me)



NMR 1.99(2H,s,$FpCH_2$), 3.42(3H,s,OMe), 3.77(12H,s, CO_2Me), *ca.* 3.77(1H,s,C=C*H*), 4.45(1H,s,*CH*CO_2Me), 4.83(5H,s,Cp).

IR ($CHCl_3$); 2000, 1955(s,C≡O), 1740(s,C=O ester).

86 (E=CO_2Me)

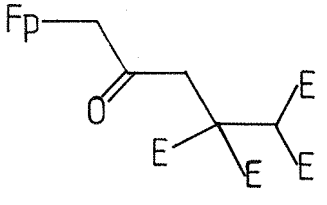


NMR 1.78(2H,s,$FpCH_2$), 3.49(2H,s,$COCH_2$), 3.78 and 3.80 (each 6H, each s, CO_2Me), 4.35(1H,s,*CH*CO_2Me), 4.89(5H,s,Cp).

IR ($CHCl_3$); 2010, 1965(s,C≡O), 1740(s,C=O ester), 1645(m,C=O ketone)

MS (25eV); 494(0,*M*), 407(23), 406(52), 194(27), 153(26), 121(100), 69(40), 59(29), 56(29).

86 (E=CO_2Et)

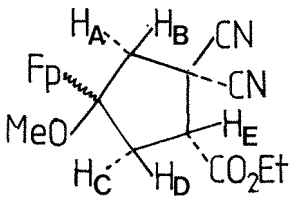


NMR 1.28(12H,t,$CO_2CH_2CH_3$), 1.78(2H,s,$FpCH_2$), 3.40 (2H,s,$COCH_2$), 4.28(8H,q,$CO_2CH_2CH_3$), *ca.* 4.33 (1H,s,$CHCO_2Et$), 4.90(5H,s,Cp)

IR ($CHCl_3$); 2005, 1965(S,C≡O), 1730(s,C=O ester), 1645(m,C=O ketone).

MS (25eV); 550(0,*M*), 186(47), 121(100), 95(14), 89 (13), 65(15), 56(29), 45(26), 43(21).

87



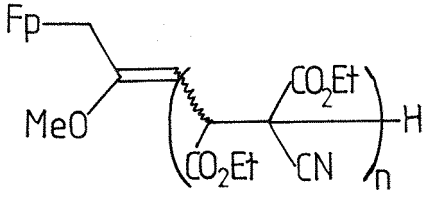
NMR 1.35(3H,t,$CO_2CH_2CH_3$), 2.13(1H,dd,J=14 and 12Hz, H_C), 2.63(1H,d,J=14Hz,H_A), 2.81(H,ddd,J=14, 6.5 and 3Hz, H_D), 3.16(3H,s,OMe), 3.26(1H,dd,J=14 and 3Hz, H_B), 3.65(1H,dd,J=12 and 6.5Hz H_E), 4.30 and 4.31 (2H, each q, 1:1 ratio, $CO_2CH_2CH_3$), 4.92(5H,s,Cp)

IR ($CHCl_3$); 2242(w,C≡N), 2000, 1960(s,C=O), 1735 (s,C=O ester)

MS 398(0.9,*M*), 276(27), 221(47), 194(50), 166(48), 147(23), 122(36), 121(100), 56(27).

Elemental Analysis Calculated for $C_{18}H_{18}FeN_2O_5$: C, 54.29; H, 4.56; N, 7.04. Found : C, 53.64; H, 4.59; N, 7.09.

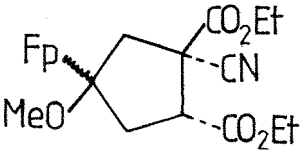
88



n = 1,2 etc.

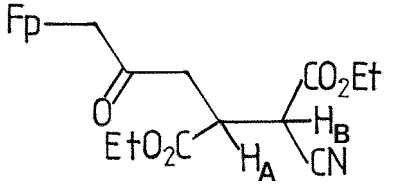
NMR 1.28 and 1.33(12H,m,$CO_2CH_2CH_3$), 3.54(3H,s,OMe), 4.22(8H,m,$CO_2CH_2CH_3$), 4.82(5H,s,Cp).

89



NMR 1.26(6H,bt,$CO_2CH_2CH_3$), 3.20(2H,s,OMe), 4.14 and 4.19(each 2H, each q,$CO_2CH_2CH_3$), 4.89(5H,s,Cp).

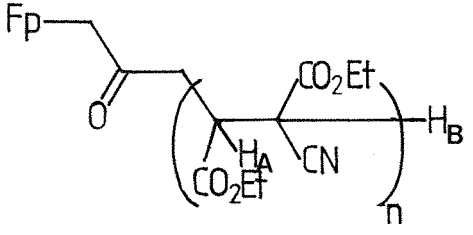
90



NMR 1.27 and 1.32(each 3H, each t,$CO_2CH_2CH_3$), 1.78 (2H,s,$FpCH_2$), 2.90-3.20(2H,bm,$COCH_2CH$), 3.55(1H, m,H_A), 4.22(5H,m,$CH_2CH_2CH_3$ and H_B), 4.90(5H,s,Cp).

IR ($CHCl_3$); 2020, 1965(s,C≡O), 1740(s,C=O ester), 1645(m,C=O ketone).

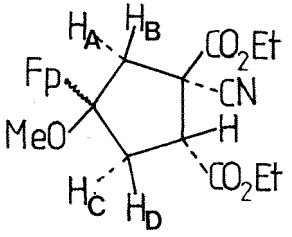
91



NMR 1.27 and 1.33(10H, each t,$CO_2CH_2CH_3$), 1.78(2H,s, $FpCH_2$), 2.98-3.20(2H,bdd,J≈4 and 9Hz,$COCH_2$), 3.40-3.75(2H,m,H_A), 4.23(5H,m,$CO_2CH_2CH_3$ and H_B), 4.90(5H,s,Cp).

n = 1,2 etc.

92



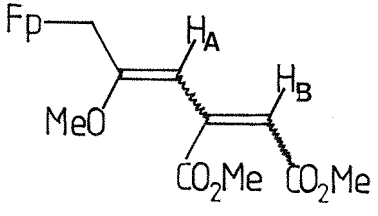
NMR 1.36(3H,t,$CO_2CH_2CH_3$), 2.35(1H,t,J=12Hz,H_C), 2.64(1H,d,J=14Hz,H_A), 2.78-3.04(1H,m,H_D), 3.06(1H,bd,J=14Hz,H_B), 3.18(3H,s,OMe), 3.66 (1H,dd,J=12 and 6Hz,H_E), 4.36(2H,q,$CO_2CH_2CH_3$), 3.91(5H,s,Cp).

[N.B. NMR of (crude product) 3.02, 3.18 and 3.28 (each s, ratio *ca* 3:4:1, OMe]

IR ($CHCl_3$); 2240(w,C≡N), 2000, 1960(s,C≡O), 1747 (s,C=O ester)

MS (25eV), 398(0,*M*), 186(17), 147(38), 122(34), 121 (100), 95(19), 56(37), 42(19), 41(18).

93[66]

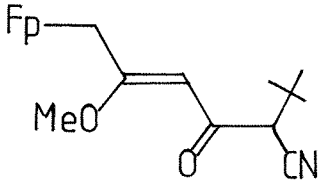


NMR 2.69(2H,s,CH_2), 3.62(6H,s,CO_2Me and OMe), 3.70 (3H,s,CO_2Me), 4.89(5H,s,Cp), 5.48(1H,d,J=2.5Hz, H_A), 6.29(1H,d,J=2.5Hz,H_B).

IR (CH_2Cl_2); 2005, 1960(s,C≡O), 1718(s,C=O ester), 1688(m,C=O), 1625(w,C=C).

MS (25eV); 390(0,*M*), 334(15,*M*-2CO), 177(18), 149(20), 122(20), 121(100), 96(19), 95(23), 56(32).

95b[69]



NMR 1.16(9H,s,^{t}Bu), 2.55(2H,s,CH_2), 3.18(1H,s,COCH), 3.70(3H,s,OMe), 4.90(5H,s,Cp), 5.46(1H,s,C=CH).

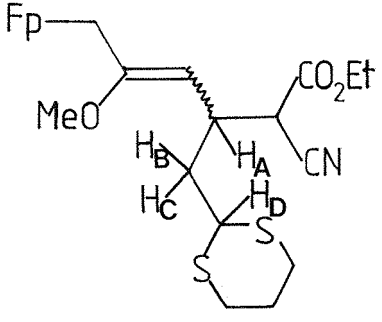
[NMR (95a) 3.58(3H,s,OMe)]

IR ($CHCl_3$); 2230(w,C≡N), 2008, 1966(s,C≡O), 1646 (w,C=O ketone), 1520(S)

MS (25eV); 371(0,*M*), 315(21,*M*-2CO), 186(58), 139 (36), 121(54), 99(100), 59(43), 57(46), 56(46), 41(44)

Elemental Analysis Calculated for $C_{18}H_{21}FeNO_4$: C, 58.24; H, 5.70, N, 3,77. Found : C, 58.29; H, 5.92; N, 3.74.

179

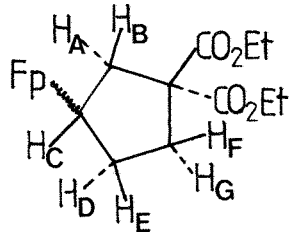


NMR 1.32 and 1.36(3H,eacht,$CO_2CH_2CH_3$), 180-2.50(7H,m, $FpCH_2$,H_A-H_C and $SCH_2CH_2CH_2S$), 2.86(4H,bm,$SCH_2CH_2CH_2S$), 3.51(3H,s,OMe), 3.70(1H,bt,J=4Hz,C=C*H*), 3.98-4.50(4H,m,$CO_2CH_2CH_3$, H_D and *CH*CN), 4.83(5H, s,Cp)

IR ($CHCl_3$); 2210(w,C≡N), 2010, 1955(s,C≡O), 1740(s, C=O ester), 1640(m,C=C).

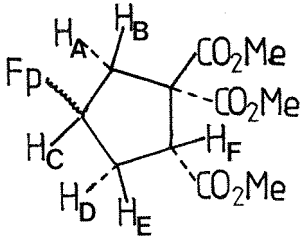
MS (25eV); 505(0,*M*), 186(54), 121(47), 119(100), 95(11), 69(17), 56(20), 45(15), 41(15).

98b



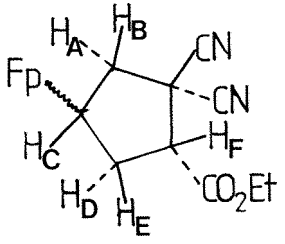
NMR	1.24(6H,t,$CO_2CH_2CH_3$), 1.73-2.78(7H,m,H_A-H_G) 4.18(4H,q,$CO_2CH_2CH_2$), 4.80(5H,s,Cp)
IR	($CHCl_3$); 2000, 1945(s,C≡O), 1720(s,C=O ester)
MS	(25eV); 390(0,*M*), 334(44,*M*-2CO), 293(48), 122 (36), 121(100), 95(43), 67(70), 66(37), 65(29)
Elemental Analysis	Calculated for $C_{18}H_{22}FeO_6$: C, 55.40; H, 5.68. Found : C, 55.13; H, 5.85

98c



NMR	1.60-3.06(5H,m,H_A-H_E), 3.67, 3.70, 3.75 and 3.97(9H,each s,CO_2Me) *ca* 3.70(1H,m,H_F), 4.83(5H, s,Cp)
IR	($CHCl_3$); 2000, 1950(s,C≡O), 1730(s,C=O ester)
MS	(25eV); 420(0,*M*), 364(53,*M*-2CO), 270(100), 212 (35), 151(39), 121(80), 93(39), 65(40), 59(44)
Elemental Analysis	Calculated for $C_{18}H_{20}FeO_8$: C, 51.45; H, 4.80 Found : C, 51.31; H, 4.59

98d



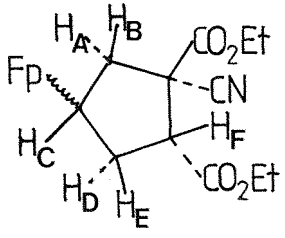
NMR 1.32, 1.33 and 1.35(3H,each t,$CO_2CH_2CH_3$), 1.76 - 2.95(5H,m,H_A-H_E), 3.32(0.3H,dd,J≃11 and 7Hz, H_F), 3.41(0.7H,dd,J=12 and 6Hz,H_F), 4.24, 4.25 and 4.28(4H,each q,$CO_2CH_2CH_3$), 4.88(5H,s,Cp)

IR ($CHCl_3$); 2248(w,C≡N), 2008, 1955(s,C≡O), 1737 (s,C=O ester)

MS (25eV); 368(0,*M*), 312(81,*M*-2CO), 285(52), 270 (48), 246(82), 219(100), 149(34), 147(40), 121(68)

Elemental Analysis Calculated for $C_{17}H_{16}FeN_2O_4$: C, 55.46; H, 4.38; N, 7.61. Found : C, 55.16; H, 4.40; N, 7.58

98e

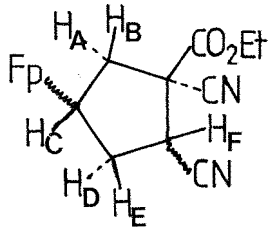


NMR 1.29 and 1.36 (each 3H,each t,$CO_2CH_2CH_3$), 1.78 -3.06(5H,m,H_A-H_E), 3.18-3.56(0.5H,m,H_F), 3.86(0.5H, dd,J=11 and 7.5Hz,H_F), 4.23 and 4.30(each 2H,each q, $CO_2CH_2CH_3$), 4.83 and 4.86(5H,each s, 1:1 ratio,Cp).

IR (CH_2Cl_2); 2245(w,C=N), 2010, 1952(s,C≡O), 1740(s, C=O ester)

MS (25eV); 415(0,*M*), 359(19,*M*-2CO), 293(57), 221(23), 149(24), 148(20), 121(100), 93(27), 92(21), 69(20).

98f,g



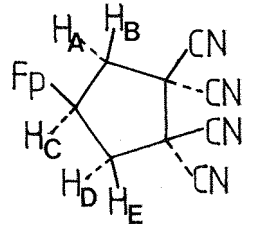
NMR — 1.36(3H,t,$CO_2CH_2CH_3$), 1.75-3.00(5H,m,H_A-H_E), 3.43(0.25H,bdd,J≈9.5 and 6Hz,H_F), 3.61(0.75H, dd,J=10 and 5.5Hz,H_F), 4.33(2H,q,$CO_2CH_2CH_3$), 4.83 and 4.89(5H,each s,5:1 ratio,Cp)

IR — ($CHCl_3$); 2240(w,C≡N), 2000, 1955(s,C≡O), 1740 (s,C=O ester)

MS — (25eV); 368(0,*M*), 312(10,*M*-2CO), 246(23), 121 (00), 93(43), 92(31), 91(25), 66(38), 65(42), 56(30)

Elemental Analysis — Calculated for $C_{17}H_{16}FeN_2O_4$: C, 55.46; H, 4.36; N, 7.61. Found : H, 4.56; C, 55.31; N, 7.45

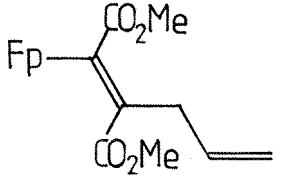
98i[21]



NMR — (d^6-Acetone); 2.35-3.37(5H,m,H_A-H_E), 5.00(5H,s, Cp)

IR[21] — (KBr); 2000, 1940(s,C≡O)

104[69]

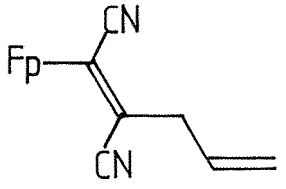


NMR — 3.09(2H,dd,J=6 and 1.5Hz,CH_2CH), 3.76(6H,s,CO_2Me) 4.77-5.18(2H,m,$CH=CH_2$), 4.97(5H,s,Cp), 5.46-6.15 (1H,m,$CH_2CH=CH_2$)

IR — (CCl_4); 2022, 1980(s,C≡O), 1700(s,C=O ester), 1633(m,C=C)

MS — (25eV); 360(0,*M*), 304(100,*M*-2CO), 180(26), 152(56) 122(50), 121(55), 69(33), 65(27), 56(26)

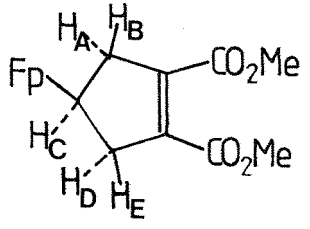
107[84]



NMR[84] 3.35(2H,d,J=6.5Hz,C*H*$_2$CH), 5.04(5H,s,Cp), 5.17-5.43(2H,m,CH=C*H*$_2$), 5.43-6.03(1H,m,CH$_2$C*H*=CH$_2$)

IR[84] (CH_2Cl_2); 2042, 1996(s,C≡O)

105[69]



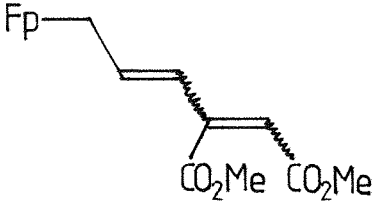
NMR 2.40-3.12(5H,m,H$_A$-H$_E$), 3.77(6H,s,CO$_2$Me), 4.81(5H,s,Cp)

IR ($CHCl_3$); 1999, 1945(s,C≡O), 1720(s,C=O ester), 1642(m,C=C)

MS 360(1.3,*M*), 304(100,*M*-2CO), 244(33), 210(70), 180(72), 152(71), 122(64), 121(60), 56(32)

Elemental Analysis Calculated for $C_{16}H_{16}FeO_6$: C, 53.36; H, 4.48. Found : C, 52.76; H, 4.52

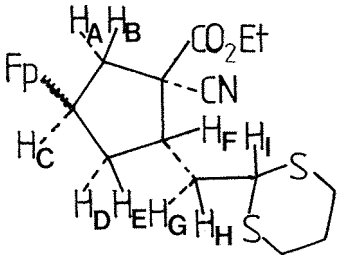
106[69]



NMR 2.14(2H,b d,J≃5Hz,C*H*$_2$CH), 3.74(6H,s,CO$_2$Me), 4.55.-5.15(2H,m,CH$_2$C*H*=C*H*), 4.95(5H,s,Cp), 6.87(1H,bs,C=C*H*CO$_2$Me)

IR (CCl_4); 2008, 1944(s,C≡O)

181



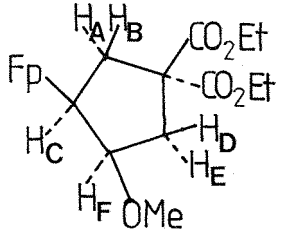
NMR 1.33(3H,t,$CO_2CH_2CH_3$), 1.70-3.00(8H,m,H_A-H_H) *ca* 2.00(2H,m,$SCH_2CH_2CH_2S$), 2.83(4H,m,$SCH_2CH_2CH_2S$), 3.99(1H,dd,J=8 and 7Hz,H_I), 4.26 (2H,q,$CO_2CH_2CH_3$), 4.83(5H,s,Cp)

IR (CH_2Cl_2); 2240(w,C≡N), 2000, 1947(s,C≡O), 1735(s,C=O ester)

MS (25eV); 475(0,*M*), 419(25,*M*-2CO), 353(78), 307(23), 279(46), 254(25), 121(73), 119(100), 41(22)

Elemental Analysis Calculated for $C_{21}H_{25}FeNO_4S_2$: C, 53.04; H, 5.30; N, 2.95. Found : C, 53.08; H, 5.41; N, 2.86

108b

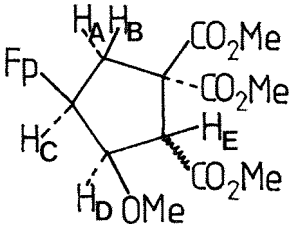


NMR 1.23(6H,t,$CO_2CH_2CH_3$), 1.95-2.90(5H,m,H_A-H_E), 3.20(3H,s,OMe), 3.57(1H,m,H_F), 4.20(4H,q, $CO_2CH_2CH_3$), 4.80(5H,s,Cp)

IR ($CHCl_3$); 2010, 1952(s,C≡O), 1722(s,C=O ester)

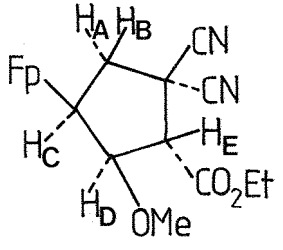
MS (25eV); 420(0,*M*), 364(24,*M*-2CO), 300(15), 299(100,*M*-2CO, Cp), 269(31), 122(17), 121(37), 93(13), 71(12)

108c



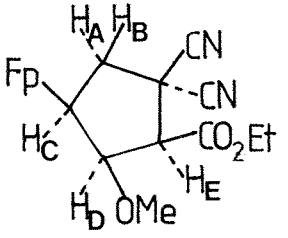
NMR	2.20-2.90(3H,m,H_A-H_C), 3.34(3H,s,OMe), 3.65, 3.69 and 3.72(each 3H, each s,CO_2Me), 3.96(2H,m,H_D and H_E), 4.78(5H,s,Cp)
IR	($CHCl_3$); 2005, 1955(s,C≡O), 1735(s,C=O ester)
MS	(25eV); 450(0,*M*), 394(11,*M*-2CO), 330(15), 329 (100,*M*-2CO,Cp), 299(22), 151(29), 121(32), 71(24) 65(15), 59(20)
Elemental Analysis	Calculated for $C_{19}H_{22}FeO_9$: C, 50.69; H, 4.93; Found : C, 50.66; H, 5.19

108d



NMR	1.37(3H,t,$CO_2CH_2CH_3$), 2.30-3.02(3H,m,H_A-H_C), 3.29 (3H,s,OMe), 3.45(1H,d,J=2.5Hz,H_E), 3.95(1H,dd,J=5.5 and 2.5Hz,H_D), 4.32 and 4.35(2H,each q, ratio of 1:1,$CO_2CH_2CH_3$), 4.83(5H,s,Cp)
IR	(CH_2Cl_2); 2240(w,C≡N), 2005, 1960(s,C≡O), 1735 (s,C=O ester)
MS	(25eV); 398(0,*M*), 342(27,*M*-2CO), 246(22), 219(18) 152(100), 149(19), 122(90), 121(73), 91(27)
Elemental Analysis	Calculated for $C_{18}H_{18}FeN_2O_5$: C, 54.29; H, 4.56; N, 7.04. Found : C, 54.3; H, 4.6; N, 7.3

109d



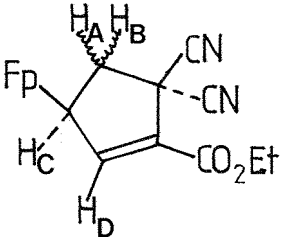
NMR 1.36(3H,t,$CO_2CH_2CH_3$), 2.38-2.92(3H,m,H_A-H_C), 3.34(1H,d,J=3.5Hz,H_E), 3.43(3H,s,OMe), 4.04 (1H,t,J=3.5Hz), 4.31 and 4.35(2H, each q, 1:1 ratio,$CO_2CH_2CH_3$), 4.85(5H,s,Cp)

IR (CH_2Cl_2); 2242(w,C≡N), 2010, 1960(s,C≡O), 1737 (s,C=O ester)

MS (25eV); 398(0,*M*), 342(30,*M*-2CO), 246(22), 219 (24), 152(100), 149(21), 122(94), 121(96), 91(68)

Elemental Analysis Calculated for $C_{18}H_{18}FeN_2O_5$: C, 54.29; H, 4.56; N, 7.04. Found : C, 53.66; H, 4.51; N, 7.30

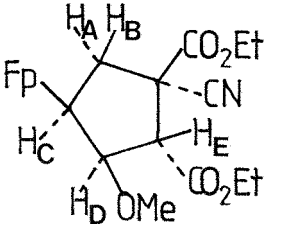
112



NMR 1.37(3H,t,$CO_2CH_2CH_3$), 2.64(1H,bdd,J=15 and 3Hz,H_A) 3.12-3.40(1H,m,H_B), 3.56(1H,m,H_C), 4.34(2H,bq, $CO_2CH_2CH_3$), 4.90(5H,s,Cp), 7.39(1H,bd,J=2.5Hz,H_D)

IR (CH_2Cl_2); 2242(w,C≡N), 2010, 1970(s,C≡O), 1700 (s,C=O ester), 1595(m,C=C)

108e



NMR 1.30 and 1.35(each 3H,eacht,$CO_2CH_2CH_3$), 2.10-2.50 (2H,m,H_A and H_B), 3.01(1H,ddd,J=12,6 and 6Hz,H_C), 3.18(3H,s,OMe), 3.71(1H,d,J=2.5Hz,H_E), 3.98(1H,dd, J=6 and 2.5Hz,H_D), 4.08-4.42(4H,m,$CO_2CH_2CH_3$), 4.82 (5H,s,Cp)

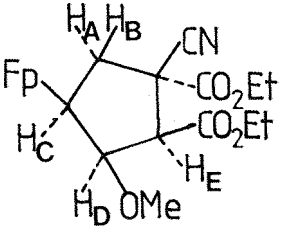
108e Continued

IR (CH_2Cl); 2010, 1960(s,C≡O), 1740(s,C=O ester)

MS (25eV); 445(0,*M*), 389(24,*M*-2CO), 324(100,*M*-2CO, Cp), 294(28), 122(29), 121(44), 93(24), 92(20), 40(30)

Elemental Analysis Calculated for $C_{20}H_{22}FeNO_7$: C, 53.94; H, 5.21; N, 3.15. Found : C, 53.94; H, 5.30; N, 3.00

109e



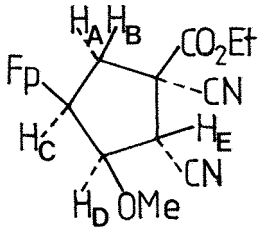
NMR 1.30 and 1.34(each 3H,each t,$CO_2CH_2CH_3$), 2.36-2.84(3H,m,H_A-H_C), 3.47(3H,s,OMe), 3.60(1H,d,J=3.5Hz,H_E), 4.02(1H,bt,J≈3.5Hz,H_D), 4.23 and 4.30 (each 2H,each q,$CO_2CH_2CH_3$), 4.82(5H,s,Cp)

IR (CH_2Cl_2); 2010, 1960(s,C≡O), 1740(s,C=O ester)

MS (25eV); 445(0,*M*), 389(21,*M*-2CO), 325(13), 324 (100,*M*-2CO,Cp), 294(21), 293(15), 121(22), 93(13) 92(14)

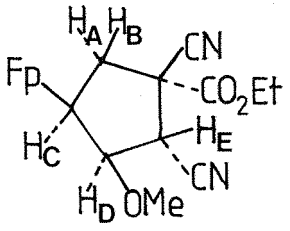
Elemental Analysis Calculated for $C_{20}H_{22}FeNO_7$: C, 53.94; H, 5.21; N, 3.15; Found : C, 53.8; H, 5.2; N, 2.9

108f



and

108g



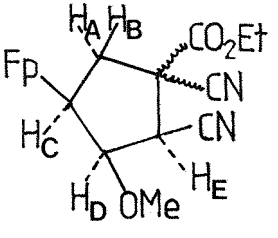
NMR — 1.35(3H,t,$CO_2CH_2CH_3$), 2.12-3.09(3H,m,H_A-H_C), 3.34 and 3.37(3H, each s, 4:1 ratio, OMe of 108f and 108g respectively), 3.75(1H,d,J=1.5 Hz,H_E), 3.90(1H,dd,J=5.5 and 1.5Hz,H_D), 4.31 (2H,q,$CO_2CH_2CH_3$), 4.84(5H,s,Cp)

IR — ($CHCl_3$); 2242(w,C≡N), 2010, 1970(s,C≡O), 1750 (s,C=O ester)

MS — (25eV); 398(0.1,*M*), 342(10,*M*-2CO), 246(36), 152(40), 149(38), 122(95), 121(100), 117(31), 91(29), 56(36)

Elemental Analysis — Calculated for $C_{18}H_{18}FeN_2O_5$: C, 54.29; H, 4.56; N, 7.04. Found : C, 54.09; H, 4.74; N, 6.89

109f,g



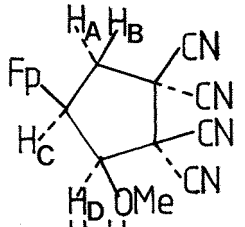
NMR — (d^6-Acetone); 1.33(3H,t,$CO_2CH_2CH_3$), 2.18-2.82 (3H,m,H_A-H_C), 3.65(3H,s,OMe), 3.74(1H,d,J=3Hz,H_E), 4.07(1H,bt,J=3Hz,H_D), 4.32(2H,q,$CO_2CH_2CH_3$), 5.06 (5H,s,Cp)

IR — ($CHCl_3$); 2242(2,C≡N), 2010, 1967(s,C≡O), 1740(s, C=O ester)

MS — (25eV); 398(0,*M*), 342(18,*M*-2CO), 271(32), 247(30), 246(57), 186(40), 152(47), 122(61), 121(100), 117(51)

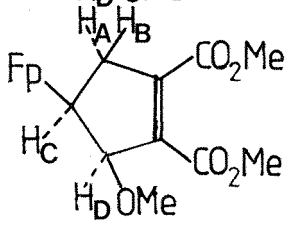
Elemental Analysis — Calculated for $C_{18}H_{18}FeN_2O_5$: C, 54.29; H, 4.56; N, 7.04; Found : C, 54.09; H, 4.68; N, 7.00

108i[20]



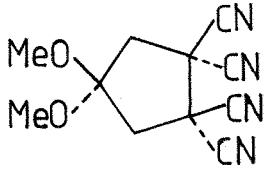
NMR	2.83(3H,m,H_A-H_C), 3.71(3H,s,OMe), 4.32(H,bd, J=3Hz,H_D), 4.92(5H,s,Cp)
IR[20]	(Neat film); 2243(w,C≡N), 2020, 1969(s,C≡O)

110



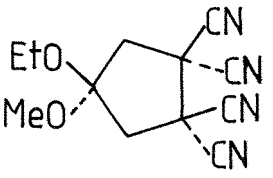
NMR	2.58-3.10(3H,m,H_A-H_C), 3.38(3H,s,OMe), 3.79 and 3.81(each 3H,each s,CO_2Me), 4.26(1H,bdd, J≃4 and 1.5Hz, H_D), 4.85(5H,s,Cp)
IR	($CHCl_3$); 2000, 1955(s,C≡O), 1715(s,C=O ester), 1632(m,C=C)
MS	(25eV); 390(0,*M*), 237(55), 122(43), 121(54), 119(100), 95(35), 92(29), 77(25), 63(25), 59(31)
Elemental Analysis	Calculated for $C_{17}H_{18}FeO_7$: C, 52.33; H, 4.65. Found : C, 52.38; H, 4.72.

119a (R=Me)[66]



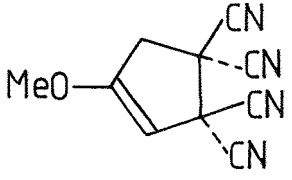
NMR	3.94(4H,s,CH_2), 4.35(6H,s,OMe)
IR	(CH_2Cl_2); 2258(w,C≡N)
MS	230(0,*M*), 200(11), 199(97,*M*-OMe), 152(24), 93 (10), 59(14), 44(35), 43(16), 40(100)
Elemental Analysis	Calculated for $C_{11}H_{10}N_4O_2$: C, 57.39; H, 4.38; N, 24.34. Found : C, 57.26; H, 4.41; N, 24.41

119a (R=Et)[66]



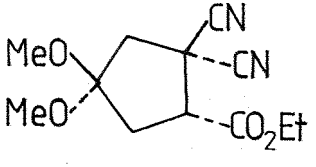
NMR	1.28(3H,t,OCH_2CH_3), 2.96(4H,s,CH_2), 3.34(3H,s, OMe), 3.52(2H,q,OCH_2CH_3)
IR	(CH_2Cl_2) : 2196(w,C≡N)
MS	(15eV); 244(0,*M*), 214(13), 213(100,*M*-OMe), 199 (89,*M*-OEt), 198(15), 185(16), 166(75), 138(91), 107(40)
Elemental Analysis	Calculated for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found : C, 58.66; H, 4.79; N, 22.80

120a[66]



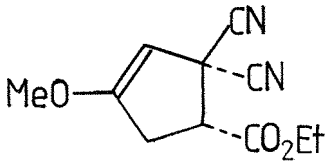
NMR	3.43(2H,d,J=2Hz,CH_2), 3.84(3H,s,OMe), 487(1H,bs C=CH)
IR	(CH_2Cl_2); 2196(w,C≡N), 1638(w,C=C)

119b[69]

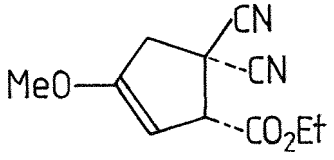


NMR	1.36(3H,t,$CO_2CH_2CH_3$), 2.16-2.87(4H,m,CH_2 and CH_2CH), 3.24 and 3.26(each 3H, each s,OMe), 3.51 (1H,dd,J=11 and 8.5Hz,$CHCO_2Et$), 4.32 and 4.34(2H, each q,1:1 ratio, $CO_2CH_2CH_3$)
IR	($CHCl_3$); 2250(w,C≡N), 1738(s,C=O ester)
MS	252(0,*M*), 221(25,*M*-OMe), 194(30), 180(16), 166(33), 152(100), 147(20), 145(18), 59(17)

120b[69]

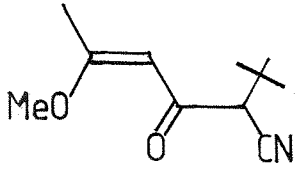


and/or



NMR (d^6-Acetone); 1.36(3H,t,$CO_2CH_2CH_3$), 3.06-3.44 (2H,m,CH_2), 3.65-3.90(1H,m,$CHCO_2Et$), 3.85(3H,s, OMe), 4.35(2H,bq,$CO_2CH_2CH_3$), 5.42(1H,bs,C=CH)

124[69]

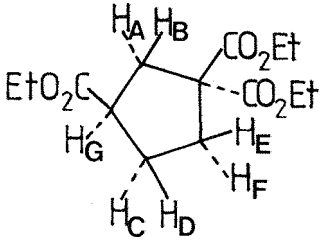


NMR 1.17(9H,s,^{t}Bu), 2.33(3H,s,Me), 3.21(1H,s,CHCN), 3.75(3H,s,OMe), 5.72(1H,s,C=CH)

IR ($CHCl_3$); 2230(w,C≡N), 1678(s,C=O ketone)

MS 195(0,*M*), 139(8), 127(2), 100(6), 99(100,*M*-^{t}BuCHCN), 89(4), 75(2), 59(3), 57(2)

125b

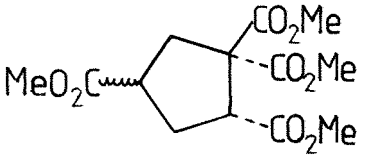


NMR 1.26(9H,t,$CO_2CH_2CH_3$), 1.84-2.72(6H,m,H_A-H_F), 2.94(1H,bqt,J=8Hz,H_G), 4.15(2H,q,$CO_2CH_2CH_3$), 4.21(4H,q,$CO_2CH_2CH_3$)

IR ($CHCl_3$); 1725(s,C=O ester)

MS 286(1.9,*M*), 241(48,*M*-OEt), 173(46), 167(77), 166(62), 140(57), 139(100), 111(46), 67(90)

125c

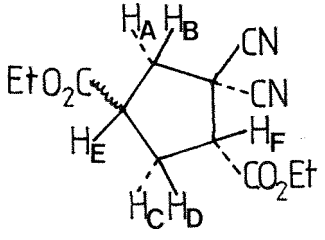


NMR 2.35(1H,t,J=7.5Hz), 2.45(1H,dd,J=14 and 6.5Hz), 2.72-3.50(3H,m), 3.58-3.90(1H,m), 3.70, 3.73 and 3.79(12H,each s,CO_2Me)

IR (CH_2Cl_2); 1737(s,C=0 ester)

MS (25eV); 302(0,*M*), 271(65,*M*-OMe), 270(22), 243 (45,*M*-CO_2Me), 210(36), 183(64), 151(100), 145(50)

125d

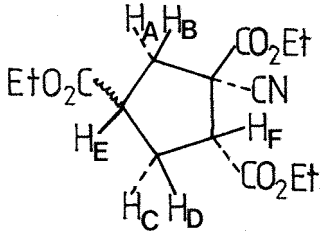


NMR 1.30 and 1.36(each 3H,each t,$CO_2CH_2CH_3$), 2.40-3.05(4H,m,H_A-H_D), 3.20(1H,bqt,J≃7Hz,H_E), 3.52(1H,dd, J=10 and 9Hz,H_E), 4.22(2H,q,$CO_2CH_2CH_3$), 4.33 and 4.34(2H,each q,ratio 1:1,$CO_2CH_2CH_3$)

IR ($CHCl_3$); 1730(s,C=0 ester)

MS 264(7,*M*), 219(63,*M*-OEt), 218(50), 191(62,*M*-CO_2Et), 164(62), 163(58), 123(39), 92(100), 55(42)

125e

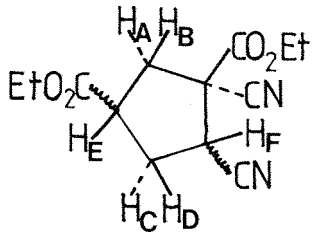


NMR 1.30 and 1.37(9H,eachs,1:1 ratio,$CO_2CH_2CH_3$), 2.38 -2.96(4H,m,H_A-H_D), 3.20(1H,dqt,J=8 and 2Hz,H_E), 3.35-3.77(1H,m,H_F), 4.27(6H,m,$CO_2CH_2CH_3$)

IR ($CHCl_3$); 1737(s,C=0 ester)

MS 311(11,*M*), 266(100,*M*-OEt), 238(40,*M*-CO_2Et), 210 (22), 194(21), 193(23), 165(27), 164(26), 92(56)

125f,g

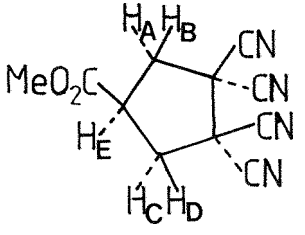


NMR 1.30 and 1.38(each 3H,each t,$CO_2CH_2CH_3$), 2.28 -2.92(4H,m,H_A-H_D), 3.16-3.44(1H,m,H_E), 3.58(1H, dd,J=10 and 8Hz,H_F), 4.19 and 4.38(each 2H,each q,$CO_2CH_2CH_3$)

IR (CH_2Cl_2); 1745(s,C=0 ester)

MS 264(13,*M*), 129(81,*M*-OEt), 192(38), 191(67), 151(43), 118(39), 92(100), 91(46), 55(41)

125i



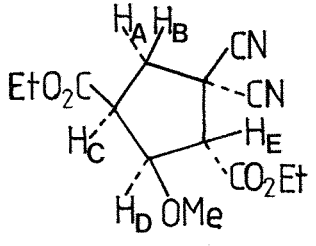
NMR (d^6-Acetone); 3.38(4H,bd,J=8Hz,H_A-H_D), 3.81(3H, s,CO_2Me), 3.88(1H,qt,J=8Hz,H_E)

IR (CH_2Cl_2); 2250(w,C≡N), 1746(s,C=0 ester)

MS 228(0,*M*), 197(21,*M*-OMe), 169(11,*M*-CO_2Me), 143 (100), 142(37), 68(19), 64(19), 59(98), 41(16), 39(17)

[N.B. Spectral data for adduct (126) is given on p 176]

127d

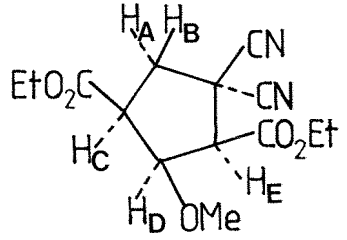


NMR 1.29 and 1.37(each 3H,each t,$CO_2CH_2CH_3$), 2.62-3.15(2H,m,H_A and H_B), 3.30-3.56(1H,m,H_C), 3.43 (3H,s,OMe), 3.55(1H,d,J=4.5Hz,H_E), 4.06-4.32(5H, m,$CO_2CH_2CH_3$ and H_D)

IR ($CHCl_3$); 1738(s,C=0 ester)

MS 294(1.0,*M*), 249(20,*M*-OEt), 217(28), 194(36), 170(51), 122(33), 101(100), 73(53), 71(30), 55(43)

128d

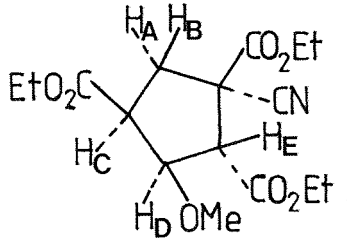


NMR 1.31 and 1.38(each 3H, each t,$CO_2CH_2CH_3$), 3.74 (1H,dd,J=17.5 and 13.5Hz,H_A), 3.20-3.71(3H,m, H_B, H_C and H_E), 3.48(3H,s,OMe), 4.16 and 4.18 (each 2H, each q,$CO_2CH_2CH_3$), 4.58(1H,t,J=4Hz, H_D)

IR ($CHCl_3$); 1738(s,C=O ester)

MS 294(4,*M*), 249(39,*M*-OEt), 186(45), 140(100), 105 (40), 101(74), 91(42), 73(54), 55(52)

127e

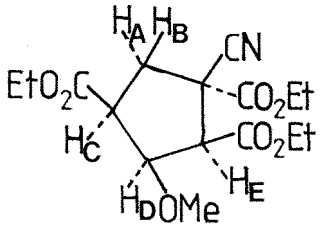


NMR 1.23-1.40(9H,m,$CO_2CH_2CH_3$), 2.50(1H,dd,J=6 and 3.5Hz,H_A), 2.82(1H,t,J=6Hz,H_B), 3.35-3.51(1H,m, H_C), 3.39(3H,s,OMe), 3.71(1H,d,J=2.5Hz,H_E), 4.05 -4.40(6H,m,$CO_2CH_2CH_3$), 4.47(1H,dd,J=3.5 and 2.5Hz, H_D)

IR ($CHCl_3$); 1740(s,C=O ester)

MS (25eV); 341(0,*M*), 396(31,*M*-OMe), 241(47), 195(100), 170(63), 167(67), 140(43), 105(99), 91(84), 57(46)

128e



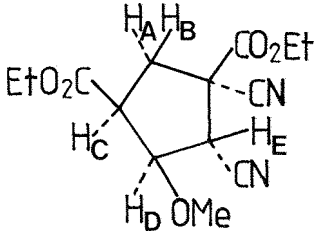
NMR 1.24-1.40(9H,m,$CO_2CH_2CH_3$), 2.21-2.6(2H,m,H_A and H_B), 3.00-3.25(1H,m,H_C), 3.50(3H,s,OMe), 3.64(1H,d,J=1.7Hz,H_E), 4.06-4.42(6H,m,$CO_2CH_2CH_3$), 4.50(1H,m,H_D).

[NMR (isomers) 3.40 and 3.44(each 3H,each s,OMe), 3.72(1H,d, J=3Hz,H_E)]

IR ($CHCl_3$); 1737(s,C=O ester)

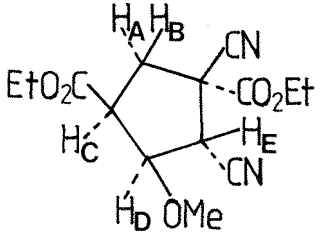
MS (25eV), 341(6,*M*), 296(42,*M*-OEt), 195(100), 167 (96), 149(98), 140(94), 103(98), 71(77), 57(66), 43(70)

127f



and

127g

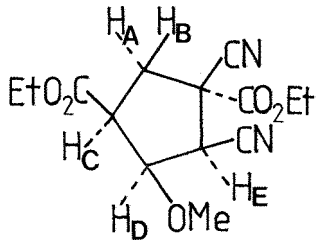


NMR 1.27 and 1.37(each 3H,each t,$CO_2CH_2CH_3$), 2.71 and 2.80(each 1H,each dd,J=30.5 and 14Hz, H_A and H_B), 3.12-3.65(1H,m,H_C), 3.48 and 3.50 (3H,each s, *ca* 4:1, OME of 127f and 127g respectively), 3.78(1H,d,J=6Hz,H_E), 4.06-4.52(5H, m,$CO_2CH_2CH_3$ and H_C)

IR (CH_2Cl_2); 1745(s,C=O ester)

MS 294(0,*M*), 249(26,*M*-OEt), 221(19,*M*-CO_2Et), 144(100), 117(20), 155(23), 98(33), 71(33), 55(20)

128f



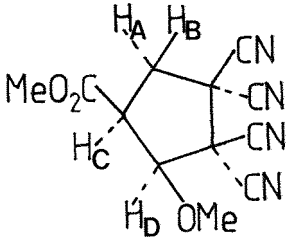
NMR 1.30 and 1.38(each 3H,each t,$CO_2CH_2CH_3$), 2.48 -2.98(2H,m,H_A and H_B), 3.01-3.17(1H,m,H_C), 3.54 (1H,d,J=12Hz,H_C), 3.64(3H,s,OMe), 4.08-4.50(5H, m,$CO_2CH_2CH_3$ and H_D)

[NMR (isomers) 3.48(3H,s,OMe), 3.79(1H,d,J=6Hz,H_C)]

IR (CH_2Cl_2); 1742(s,C=O ester)

MS 294(0.*M*), 249(22,*M*-OEt), 221(18,*M*-CO_2Et), 175(16), 144(100), 115(24), 113(19), 98(30), 71(28).

127i

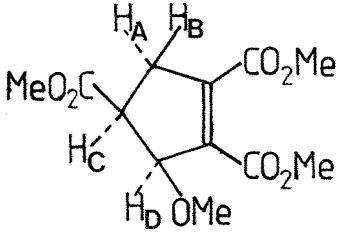


NMR 2.96(1H,dd,J=14 and 9.5Hz,H_B), 3.36-3.90(2H,m, H_A and H_C), 3.75(3H,s,OMe), 3.86(3H,s,CO_2Me), 4.79(1H,d,J=5.5Hz,H_D)

IR ($CHCl_3$); 2250(2,C≡N), 1750(s,C=O ester)

MS 258(15,*M*), 227(18*M*-OMe), 115(16), 75(99), 71(100), 59(70), 55(19), 41(18)

129

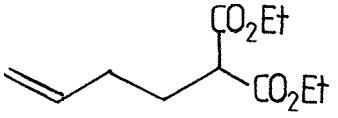


NMR 2.72(1H,dd,J=20 and 9.5Hz,H_B), 3.17-3.58(2H,m, H_A and H_C), 3.45(3H,s,OMe), 3.77, 3.82 and 3.84 (each 3H,each s,CO_2Me), 4.83(1H,dd,J=7 and 2.5Hz)

IR ($CHCl_3$); 1725(s,C=O ester), 1650(w,C=C)

MS 272(4,*M*), 240(52,*M*-HOMe), 210(95), 165(52), 153 (75), 75(74), 59(70), 209(71).

130b

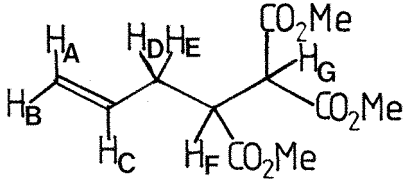


NMR 1.27(6H,t,$CO_2CH_2CH_3$), 2.05(4H,m,CH_2CH_2CH), 3.35(1H,t,J=7Hz,CH_2CHCO_2Et), 4.20(4H,q,$CO_2CH_2CH_3$), 4.93-5.15(2H,m,$CH=CH_2$), 4.77-4.99 (1H,m,$CH_2CH=CH_2$)

IR (CH_2Cl_2); 1730(s,C=O ester)

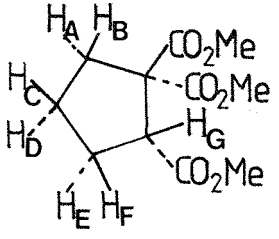
MS 214(0,*M*), 160(92), 133(30), 123(20), 120(55), 119(27), 95(27), 67(100), 57(32)

130c



and

133c



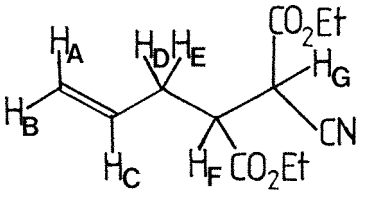
NMR 1.57-2.70(8H,m,H_D and H_E of 130c and H_A-H_F of 133c), 3.10-3.90(3H,m,H_F and H_G of 130c and H_G of 133c), 3.67, 3.71, 3.73, 3.77(18H,each s, CO_2Me of 130c and 133c), 4.94-5.16(2H,m, H_A and H_B of 130c), 5.50-5.93(1H,m,H_C of 133c)

IR (CH_2Cl_2); 1740(s,C=O)

MS 244(0,*M*), 213(13,*M*-OMe), 89(45), 87(25), 73(26), 59(40), 57(32), 45(100), 44(31), 43(69)

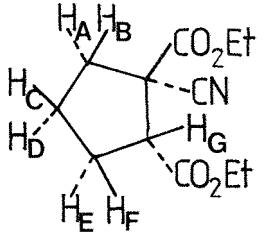
(130c : 133c; 1:1)

130e



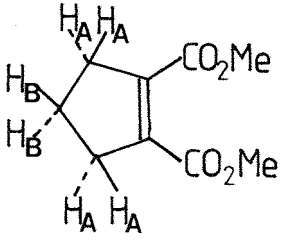
and

133e



(130e : 133e; 1:2)

134[88]



NMR 1.30 and 1.36(18 units,each t, $CO_2CH_2CH_3$), 1.80 -2.74(14 units,m,H_D and H_E of 130e and H_A-H_F of 133e), 3.07-4.00(4 units,m,H_F and H_G of 130e and H_G of 133e), 4.06-4.44(12 units,m,$CO_2CH_2CH_3$), 5.07 -5.36(2 units,m,H_A and H_B of 130e), 5.50-5.90(1 unit,m,H_C of 130e)

IR (CH_2Cl_2); 2250(w,C≡N), 1740(s,C=O ester)

MS (25eV); 239(4,*M*), 194(30,*M*-OEt), 166(28,*M*-CO_2Et) 127(39), 122(37), 99(33), 94(100), 93(26), 67(27)

NMR 1.98(2H,bqt,J=7.5Hz,H_B), 2.73(4H,t,J=7.5Hz,H_A), 3.80(6H,s,CO_2Me)

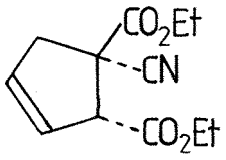
IR (CH_2Cl_2); 1733, 1715(s,C=O ester), 1645(m,C=C)

MS 184(10,*M*), 153(100,*M*-OMe), 152(75), 93(47), 67(52), 66(55), 57(51), 55(48), 41(58)

NMR[88] (CCl_4); 2.00(2H,qt,J=7Hz,H_B), 2.60(4H,t,J=6Hz,H_A), 3.64 and 3.65(each 3H,each s,CO_2Me)

IR[88] (neat film); 1730(s,C=O, ester), 1640(m,C=C)

136

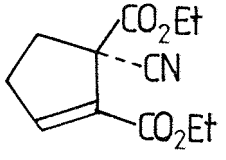


NMR 1.31 and 1.37(each 3H,each t,$CO_2CH_2CH_3$), 3.10 (2H,dd,J=3.5 and 1.5Hz,CH_2), 4.10-4.40(5H,m, $CO_2CH_2CH_3$ and $CHCO_2Et$), 6.90(2H,bs,CH=CH)

IR (CH_2Cl_2); 1740(s,C=0 ester)

MS (25eV); 237(5,*M*), 191(38,*M*-HOEt), 163(24), 138 (32), 118(23), 93(23), 92(100), 91(65), 65(22)

137

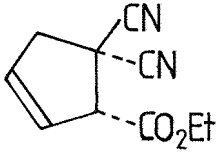


NMR 1.32 and 1.35(each 3H,each t,$CO_2CH_2CH_3$), 2.44-2.40(4H,m,CH_2CH_2), 4.29 and 4.31(each 2H,each q, $CO_2CH_2CH_3$), 7.15(1H,bt,J=2Hz,CH=C)

IR (CH_2Cl_2); 1720-1745(s,C=0 ester)

MS (25eV); 237(0,*M*), 192(10,*M*-OEt), 165(28), 164(17), 137(56), 120(13), 119(100), 92(33), 91(24), 65(15)

139

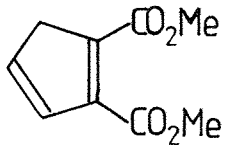


NMR 1.31 and 1.36(3H,each t,3:4 ratio, $CO_2CH_2CH_3$), 3.10 and 3.30(2H,m,3:4 ratio,CH_2), 3.91(1H,s,$CHCO_2Et$) 4.12-4.33(2H,m,$CO_2CH_2CH_3$), 6.87 and 6.97(2H,bs,3:4 ratio,CH=CH)

IR (CH_2Cl_2); 1742(s,C=0 ester)

MS 190(0,*M*), 124(27),117(22), 106(14), 92(24), 91(100), 71(14), 65(13), 56(13)

140



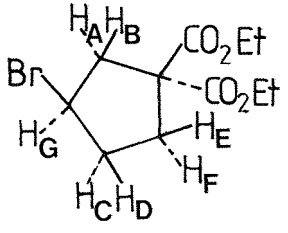
NMR 2.96-3.10(2H,m,CH_2), 3.78(6H,s,CO_2Me), 4.71 (1H,q,J=7Hz, $CH_2CH{=}CH$), 6.90(1H,bd, $CH_2CH{=}CH$)

[NMR (141) 3.66-4.13(*ca* 5H,m), 3.78(6H,s)]

IR (CH_2Cl_2); 1720-1745(s,C=O ester)

MS(140 141) 183(43), 159(40), 151(100), 139(41), 124(54), 79(43), 65(44), 59(79) [See also Page 70 Chapter Three]

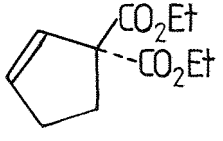
142b



NMR(142b) 1.26 and 1.27(each 3H,t,$CO_2CH_2CH_3$), 2.03-3.08 (6H,m,H_A-H_F), 4.09-4.35(4H,m,$CO_2CH_2CH_3$), 4.38 (1H,qt,J=5.5Hz,CHBr)

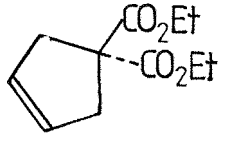
and

143b



NMR(143b) 1.26 and 1.27(each 3H,t,$CO_2CH_2CH_3$), 2.03-3.08 (4H,m,CH_2), 4.09-4.35(4H,m,$CO_2CH_2CH_3$), 5.60-6.06(2H,m,$CH{=}CH$)

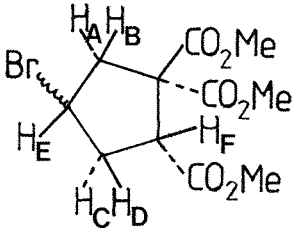
and/or



IR(142b 143b) (CH_2Cl_2); 1727(s,C=O ester)

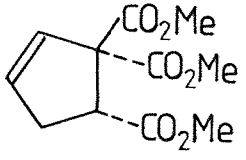
MS(142b, 143b) 249, 247(11, 142b-OEt), 213(30,142b-Br), 173(53), 139(68,143b-CO_2Et), 111(39), 89(45), 67(83), 45(100), 44(33), 43(50)

143c

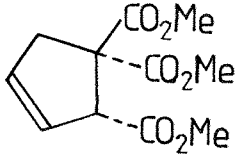


and

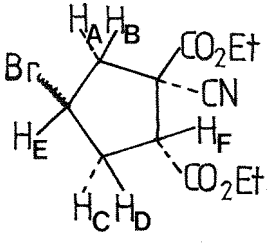
143c



and/or



142e



NMR(142c) 2.16-3.33(4H,m,H_A-H_D), *ca* 3.58(1H,m,H_F) 3.72, 3.75, 3.79 and 3.82(9H,each s,CO_2Me), 4.08 and 4.17(1H,each t,J=8.5Hz,1:1 ratio, H_E)

NMR(143c) 2.16-3.33(2H,m,CH_2), *ca* 3.58(1H,m,$CHCO_2Me$), 3.72, 3.75, 3.79 and 3.82(9H,each s,CO_2Me), 4.31-4.69(2H,m,CH=CH)

IR(142c, 143c) (CH_2Cl_2); 1740(s,C=O ester)

MS(142c, 143c) 293, 291(21 and 20, 142c - OMe), 292, 290(14 and 13, 142c - HOMe), 211(77, 143c - OMe), 171 (25), 151(100), 93(24), 69(60), 65(31), 59(59)

NMR(Isomer I) 1.30 and 1.39(each 3H,each t,$CO_2CH_2CH_3$), 2.40-3.24(4H,m,H_A-H_D), 3.99(1H,dd,J=10 and 8Hz,H_F), 4.14-4.68(5H,m,$CO_2CH_2CH_3$ and H_E)

NMR(Isomer II) 1.30 and 1.37(each 3H,each t,$CO_2CH_2CH_3$), 2.44-3.07(4H,H_A-H_D), 3.49(1H,dd,J=12 and 7Hz,H_F), 4.10-4.50(5H,m,$CO_2CH_2CH_3$ and H_E)

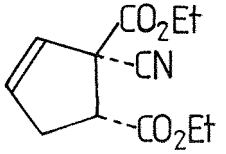
IR (CH_2Cl_2); 1745(s,C=O ester)

142e Continued

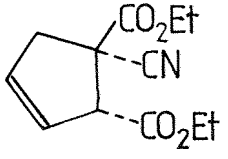
MS(Isomer I) (25eV); 319,317(3,*M*), 274, 272(12 and 14,*M*-OEt), 238(14,*M*-Br), 198(28), 174(35), 172(37), 164(23), 93(25), 92(100), 91(27), 65(43)

MS(Isomer II) 319, 317(0,*M*), 274, 272(8 and 10, *M*-OEt), 174(19), 172(19), 164(21), 120(15), 93(16), 92(68), 91(18), 65(17).

143e



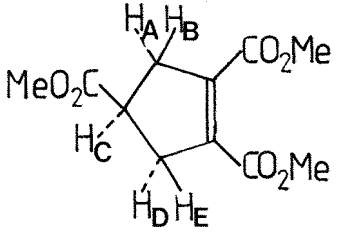
and/or



NMR 1.30 and 1.37(each 3H,each t,$CO_2CH_2CH_3$), 2.44-3.07(2H,CH_2) *ca* 3.68(1H,m,$CHCO_2Et$) 4.10-4.50(4H, m,$CO_2CH_2CH_3$), 5.66-6.30(2H,m,CH=CH)

IR (CH_2Cl_2); 1645(s,C=O ester), 1625, 1600(m,C=C)

126



NMR 2.96(3.44(5H,m,H_A-H_E), 3.74(3H,s,CO_2Me), 3.80 (6H,s,CO_2Me).

IR ($CHCl_3$); 1725(s,C=O ester), 1650(w,C=C).

MS 242(1.4,*M*), 211(12,*M*-OMe), 210(44,*M*-HOMe), 183 (8,*M*-CO_2Me), 152(10), 151(100), 95(8), 79(9), 59(16).

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