A THESIS

entitled

1,4-DIENES: COMPLEXATIONS TO, AND REARRANGEMENTS PROMOTED BY METALS

by

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To my parents

and

Kathy

CONTENTS

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DECLARATION

The work presented herein has been carried out in the laboratories of the Department of Chemistry and Molecular Sciences at the University of Warwick, under the supervision of Dr. B. T. Golding and is thought to be original except where due and proper acknowledgement has been made.

SUMMARY

The co-ordination chemistry of monoenes and conjugated dienes to Rh(I) is well documented, but little is known about the co-ordination of "skipped" dienes (1,4-dienes). Hence, the model compounds, (E,E)-, (E,Z)-, (Z,Z)-hepta-2,5-diene, the corresponding dien-4-ols and dienol-acetates were prepared and their complexations to E_2Rh(I)pd* and E_2Rh(I)hfpd* were studied. (E,E)- and (E,Z)-hepta-2,5-diene reacted with both complexes to give bidentate complexes whereas the (Z,Z)-isomer gave only an unstable bis(monodentate) complex. Interestingly, with E_2Rh(I)hfpd, (E,E)-hepta-2,5-dien-4-ol gave a bidentate complex whereas the corresponding (E,Z)- and (Z,Z)-isomers gave only crystalline complexes which were characterised (by ^{1}H n.m.r., i.r., m.s., and combustion analysis) as bis(monodentate) complexes. It is believed that these complexes are stabilised by an intramolecular hydrogen bond interaction, and this is supported by i.r. spectral studies and the observations that other allylic alcohols (e.g. prop-2-en-1-ol and but-3-en-2-ol) also form crystalline complexes when reacted with E_2Rh(I)hfpd. With the dienol acetates only (E,E)-4-acetoxyhepta-2,5-diene formed a stable complex and it was later deduced that all of the isomeric dienol acetates were catalytically transformed from 3-acetoxy-1,4-dienes to 1-acetoxy-2,4-dienes. The regio- and stereospecificity of these rearrangements was not thought to be of great use for selective modification.

The results of the above complexations were used as a guide for the study of the complexations of fatty acid substrates to E_2Rh(I)pd and E_2Rh(I)hfpd. Hence, (E)- and (Z)-9-octadecene, (Z,Z)-octadeca-6,9-diene, and (Z,Z,Z)-octadeca-3,6,9-diene were prepared and reacted with E_2Rh(I)pd and E_2Rh(I)hfpd. Two equivalents of both

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*Page (x) for abbreviations

(E)- and (Z)-9-octadecene displaced ethylene from the complexes to give bis(monoene) complexes whereas the (Z,Z)- and (Z,Z,Z)-isomers gave unstable bis(monodentate) complexes. Similar reactions were observed for the corresponding methyl esters, but methyl (E,E)-octadec-9,12-dienoate was observed to give a bidentate complex. Similarly, the triglycerides, 1,2-dioleyl-3-palmitoylglycerol and 1,3-dielaideyl-3-palmitoylglycerol gave bidentate complexes.

Although the Rh(I) promoted rearrangements of the isomeric 4-acetoxyhepta-2,5-dienes were of little use for selective modification, *cis*-bis(benzonitrile/acetonitrile)palladium(II)chloride, [Pd(II)a/b] and tetrakis(triphenylphosphine)palladium(0), $\{[P(Ph)_3]_4Pd(0)\}$ were observed to facilitate the catalytic transformation of "skipped" dienol acetates, within minutes at RT, in a highly regio- and stereospecific manner. Thus, the Pd(II)-catalysed isomerisation of (E,E)-4-acetoxyhepta-2,5-diene gave (E,E)-2-acetoxyhepta-3,5-diene while (Z,Z)-4-acetoxyhepta-2,5-diene gave (E,Z)-2-acetoxyhepta-3,5-diene. Most interestingly (E,Z)-4-acetoxyhepta-2,5-diene was transformed to (E,Z)-2-acetoxyhepta-3,5-diene indicating a highly regio- and stereospecific reaction at the (E)-double bond. The Pd(0)-catalysed isomerisation of (E,E)-, (E,Z)- and (Z,Z)-4-acetoxyhepta-2,5-dienes gave only (E,E)-2-acetoxyhepta-3,5-diene. The belief that different mechanisms are operating for the Pd(0) and Pd(II)-catalysed isomerisations was further supported by the observations that (E)- and (Z)-3-acetoxyhexa-1,4-diene were catalytically transformed by Pd(0) to give only (E,E)-1-acetoxyhexa-2,4-diene whereas Pd(II)-catalysed isomerisation of the (E)-isomer gave only (E)-2-acetoxyhexa-3,5-diene while the (Z)-isomer gave ∿ 60% (E)-2-acetoxyhexa-3,5-diene plus ∿ 30% (E,E)-1-acetoxyhexa-2,4-diene. All of the above results were further supported by the results of the isomerisations of some C_{10} dienol acetates.

ABBREVIATIONS

1.	$E_2Rh(I)pd$	2,4-pentanedionatobis(ethylene)rhodium(I)
2.	$E_2Rh(I)hfpd$	1,1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis-(ethylene)rhodium(I)
3.	Pd(II)a	bis(acetonitrile)palladium(II)dichloride
4.	Pd(II)b	bis(benzonitrile)palladium(II)dichloride
5.		Fatty acids and related structures may be abbreviated as follows: e.g. (Z,Z)-octadeca-9,12-dienoic acid (Z,Z)-9,12-18:(2) where 9,12 denotes the positions of the double bonds, 18 denotes the number of carbon atoms in the chain and (2) denotes the total number of double bonds
6.	n.m.r.	nuclear magnetic resonance
7.	δ	chemical shift
8.	p.p.m.	parts per million
9.	TMS	tetramethylsilane
10.	J	coupling constant
11.	Hz	hertz (cycles per second)
12.	I.r.	infra-red
13.	cm	centimetres
14.	U/V	ultraviolet/visible
15.	nm	nanometres
16.	λ	wavelength
17.	ϵ	molecular extinction coefficient
18.	g.l.c.	gas-liquid chromatography
19.	R	relative retardation
20.	R_f	retardation factor

21.	t.l.c.	thin layer chromatography
22.	m	milli
23.	mm	millimetres of mercury
24.	b.p.	boiling point
25.	^{o}C	degrees Centigrade
26.	m.p.	melting point
27.	MW	molecular weight
28.	conc.	concentrated
29.	μ	micro
30.	t	tertiary
31.	MS	mass spectrum
32.	M^{+}	molecular ion
33.	aq.	aqueous
34.	DMF	dimethylformamide
35.	DMSO	dimethylsulphoxide
36.	THF	tetrahydrofuran
37.	RT	room temperature
38.	s	second
39.	hr	hour
40.	$d.^{6}$	hexadeuterio-
41.	AcOH	acetic acid
42.	AcO-	acetate
43.	ED	ethylenediamine
44.	EI	electron impact
45.	FD	field desorption
46.	FI	field ionisation

FATTY ACID NOMENCLATURE

1.	Oleic acid	(Z)-octadec-9-enoic acid
2.	Elaidic acid	(E)-octadec-9-enoic acid
3.	Linoleic acid	(Z,Z)-octadeca-9,12-dienoic acid
4.	Linolenic acid	(Z,Z,Z)-octadeca-9,12,15-trienoic acid
5.	Linoelaidic acid	(E,E)-octadeca-9,12-dienoic acid
6.	Arachidonic acid	(Z,Z,Z,Z)-eicosa-5,8,11,14-tetraenoic acid

PUBLICATION

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Pd(II)-catalysed isomerisations of

3-acetoxy-1,4-dienes to 1-acetoxy-2,4-dienes:

Stereochemical and preparative aspects.

CHAPTER 1

1. INTRODUCTION

The most important compounds containing the "skipped" 1,4-pattern of unsaturation are naturally occurring fatty acids and related compounds. The biological and economic importance of these acids is emphasised by the fact that certain fatty acids cannot be biosynthesised by mammals, but are essential dietary components. The most important essential fatty acid (EFA) is linoleic acid [(Z,Z)-9,12-octadecadienoic acid]. Argentation separation[1] is one of the most common methods of separation of unsaturated compounds, but Ag(I)-containing separatory systems have certain disadvantages in that they are sensitive to light and heat, and in some cases can cause isomerisation of the substrate. Hence, there is a need to develop new methods which are capable of separating unsaturated substrates, both on an analytical and industrial scale, and which do not have the same disadvantages as methods based on argentation separation.

Similarly, because of the recently elucidated biological importance of fatty acids[2], new methods for their selective modification are continually under investigation. This type of modification also has economic importance because abundant naturally occurring fatty acids could be selectively modified to generate more economically viable fats and oils.

1.1 Argentation Separation of Fatty Acids and the nature of the Metal-Olefin Bond

It has been known for many years that there are inter-

actions between silver(I) ions and unsaturated compounds (olefins)[1]. This phenomena was first studied quantitatively by Winstein and Lucas *et al.*[3] as early as 1934. They determined the equilibrium constants for the reaction of silver(I) ions with a number of acyclic and alicyclic olefins by measuring the partitioning of the olefin between an aqueous silver nitrate solution and carbon tetrachloride. However, the first real appreciation of the possibilities of argentation as the basis for separation of unsaturated lipophilic compounds was made by Nichols in 1952[3c]. In the first study of silver complexes of lipid compounds, the equilibrium constants for the interaction of methyl oleate and methyl elaideate with Ag^+ were determined by distribution between isooctane and aqueous methanol-$AgNO_3$ mixtures. On the basis of the results, Nichols predicted that counter-current distribution or paper chromatography could be adapted to incorporate $AgNO_3$ and thus facilitate the separation of methyl oleate from methyl elaideate, and also other olefinic compounds in general.

In the time between this statement and the development of an efficient process for chromatographic separation, some isomeric cyclooctenes were separated as crystalline, silver-adducts[4]. Hydrogenation of cyclooctatetraene (Raney nickel catalyst) gave primarily *cis*-cyclooctene, which was purified by reaction with aq. $AgNO_3$ to give the Ag^+-adduct as large colourless crystals (m.p. 51°C). Alternatively, reduction with zinc dust in aq. sodium hydroxide gave principally 1,3,6-cyclooctatriene. Reaction of this crude product with $AgNO_3$/aq.ethanol gave a crystalline solid containing predominantly the Ag^+-1,3,6-cyclooctatriene adduct together with a small amount of the corresponding 1,3,5-adduct.

The first chromatographic application of silver-olefin complexation did not follow Nichols' predicted development. The

usefulness of g.l.c. for the separation of olefins was illustrated[5] by the selectivity of a silver nitrate-triethyleneglycol stationary phase for the separation of simple olefins (pentenes, hexenes, octenes), and was quickly developed as a simpler alternative to the classical methods of separation, such as distribution and fractional crystallisation of adducts[6]. However, argentation g.l.c. has little relevance to the separation of lipids because of the high temperatures required to obtain practical retention times for the lipids. At temperatures above 65°C, the $AgNO_3$-stationary phases are rapidly decomposed and all resolving power is lost. Thus, it was not until nine years after Nichols' original prediction, that methyl oleate and methyl elaideate were separated from each other using counter-current distribution between 0.2 M $AgNO_3$ in 90% methanol and hexane[7]. This method has not been extensively used for the separation of lipids, presumably because of the time required to construct an efficient separatory apparatus. Thus, the potential of argentation separation was not fully realised until the development of t.l.c.[8] and column argentation chromatography[9]. Both procedures facilitated the separation of methyl oleate from methyl elaideate, and of these esters from saturated and polyunsaturated esters.

De Vries[9] also demonstrated the separation of unsaturated triglycerides according to the total number of double-bonds present. By the use of double impregnation of silica gel with $AgNO_3$ and boric acid, Morris[8] achieved the simultaneous separation of *threo*- and *erythro*-, saturated and unsaturated dihydroxy esters.

It was quickly realised that the separations of lipids and fatty acids using argentation chromatography were more subtle than the initial gross separations indicated. Thus, argentation chromatography affords the following classes of separation:

(1) separation according to the total degree of unsaturation in the lipids;

(2) separation according to the geometry (E or Z) of the double bonds;

(3) separation according to the position of a double bond in a lipid chain.

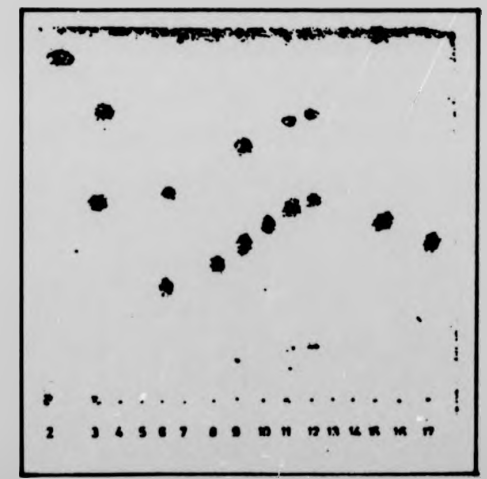
The most common application of argentation chromatography is in the separation of a lipid mixture into fractions containing different numbers of double bonds. Separations of fatty acid methyl esters can be carried out on a relatively large scale by column chromatography on silver-impregnated silica gel[10] or on silver-impregnated florosil[11], to overcome slow elution rates. The use of ion-exchange resins has also been reported and offers the advantage that polar solvents can be used for elution without leaching of the Ag^+ from the column[12].

In our hands, argentation-fast column chromatography has proven particularly useful for the separation of positional and geometric isomers of linolenic acid and also for the separation of the important components of turmeric[13]. The argentation-chromatographic separation of some C_{18} methyl esters, according to the degree of unsaturation is illustrated in Fig. 1.1.A.

Besides effecting separations according to the degree of unsaturation, one of the most useful attributes of argentation chromatography is its ability to separate compounds with non-conjugated unsaturation according to the geometry of the double bonds. In this, the method has an advantage over mercuric adduct formation, which does not differentiate between *cis*- and *trans*-double bonds. As already mentioned, the (Z)- and (E)-isomers of methyl 9-octadecenoate (oleate and elaideate respectively) were separated by an argentation process (*cf.* Fig. 1.1.A) and since then,

Thin-layer chromatogram of fatty acid methyl esters and simple lipids on Silica Gel G impregnated with silver nitrate (5% w/w). Developing solvent was diethyl ether–light petroleum 5:95 and spots were located by spraying with 50% H_2SO_4 and charring. Samples: *A*, methyl stearate; *B*, methyl elaidate; *C*, methyl oleate; *D*, mixture of stearate, oleate, and linoleate; *E*, methyl esters from faecalith lipids; *F*, mixture of cholesteryl stearate, cholesteryl oleate, and cholesteryl linoleate; *G*, sperm oil, i.e., a wax-ester mixture.

Fig. 1.1.A taken from ref. 17



Thin-layer chromatogram of isomeric methyl octadecenoates on silver nitrate–Silica Gel G (30–70). The position of the double bond is indicated by the sample number, the samples being the 2-, 3-, 6-, 9-, 11- and 12-*trans*-octadecenoates, the 3-, 6-, 8-, 9-, 10-, 11-, 12- and 15-*cis*-octadecenoates and the vinyl compound, 17-octadecenoate. The plate was developed, at −15°, three times with toluene (to one half, three-quarters and the full height of the plate respectively) and spots were located by spraying with chlorosulphonic acid–acetic acid (1:2) and charring.

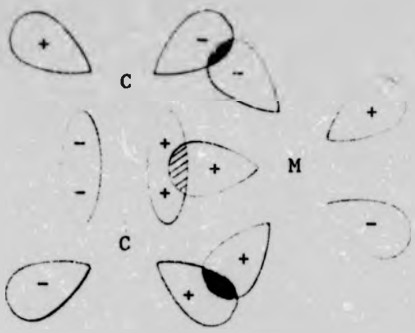
Fig. 1.1.B taken from Ref. 17

argentation chromatography has proven particularly useful in studies on the mechanism, and intermediates of hydrogenation[14].

Argentation chromatography also has the ability to separate positional isomers of unsaturated fatty acids. Thus, 9,11-, 9,12-, and 9,15-octadecadienoates were readily separated from butter fats and identified as isomers of linoleic acid[15]. Similar separations of (Z)-7-, 9-, and 11-octadecenoates have also been reported[16]. Work accomplished by Morris and co-workers[17] has shown that for a series of isomeric methyl octadecenoates (Δ^2 - Δ^{17}) there is a decreasing mobility on argentation t.l.c. from Δ^2 - Δ^5, then progressively increasing mobility to Δ^{12} followed by decreasing mobility to Δ^{17} (Fig. 1.1.B).

The Ag^+-olefin interaction at the Δ^2 double bond adjacent to the carboxylic ester terminus will be severely weakened by the electron-withdrawing effect of this group and possibly by some steric repulsion. The maxima shown for Δ^{11}/Δ^{12} must be due to a conformational effect wherein double bonds present at the centre of the chain are buried in saturated lipophilic pockets and are relatively inaccessible to the Ag^+ ions.

The Ag^+-olefin bond is usually described in molecular orbital terms using the theory which Dewar[18] proposed and which Chatt and Duncanson[19] subsequently extended to include platinium(II)-olefin complexes. The bonding according to the Dewar-Chatt-Duncanson model essentially involves a σ-bond, from a filled π-orbital of the olefin to an empty hybrid orbital on the metal, complemented by a π-back bond from a filled hybrid orbital on the metal to the empty π^* (antibonding) orbital of the olefin. More recently this theory has been modified slightly and an old idea has been revived wherein there may also be contributions from a metallocyclopropane structure (Fig. 1.1.C)[20].



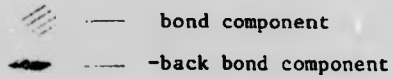


Fig. 1.1.C

The final overall structure of the metal olefin species will depend on the relative degrees of π-back-bonding and σ-bonding. The examples shown above are the extreme modes of bonding and in most metal-olefin complexes the bonding will lie somewhere between these two.

From the above description it can be seen that a net movement of charge either away from, or towards the olefin will affect the spectroscopic properties of a metal-olefin complex. If the predominant factor in the bonding were the σ-component then this would result in an overall movement of charge density from the olefin to the metal and this would be reflected in the ^{1}H n.m.r. spectrum where the double-bond protons would be deshielded and moved downfield relative to those of unco-ordinated olefin. Conversely, if the π-back-bond were the predominant component then the double-bond protons of a co-ordinated olefin would experience a shielding effect and would be moved upfield relative to those of an unco-ordinated olefin in the ^{1}H n.m.r. spectrum. For Ag(I)-olefin complexes the first case is applicable because

complexation of propene to $AgBF_4$ is observed to result in a downfield shift for the protons of the co-ordinated double bond. This downfield shift is observed both with ^1H n.m.r.[21] and ^{13}C n.m.r.[22] spectroscopy. It would also be expected that any electron withdrawing substituents present on the olefin would reduce the stability of Ag(I)-olefin complex, by way of reducing the electron density at the olefin double bond which is available for bond formation. Thus, for complexes of the type $(olefin)_2AgBF_4$ the relative stabilities of a series of complexes have been ascertained as propene > ethylene > vinyl chloride[21a]. This would account for the very weak retention of methyl-2-octadecenoate by argentation t.l.c. (Fig. 1.1.B).

In general, the effect of substitution on the olefin is to reduce the stability of the metal-olefin complex although the Ag(I)-propene complex is exceptional in that a second substitution is required to obtain this effect [Ag(I)-2-methylpropene]. This effect can be explained in terms of both an enthalpy and an entropy effect. As an olefin approaches a metal any steric interaction would be increased by the presence of substituents and once co-ordinated the rotation of the olefin about the metal-olefin bond would be restricted.

The observation that argentation chromatography effects the separation of *cis*/*trans*-isomers indicates that Ag(I)-olefin complex formation is affected by olefin geometry. In general *cis*-olefins form more stable complexes than *trans*-olefins (Table 1.1.D) and it would seem that this is controlled by enthalpy rather than entropy factors[23]. *Cis*-olefins, as indicated by their higher heats of hydrogenation[24] are generally more "strained" than *trans*-olefins and this strain is reduced on complex formation.

In support of this "relief of strain" hypothesis it has been found that where the free *trans*-olefin is more "strained"

Metal	Olefin	Stability Constants[a]		ΔH		ΔS	
		Cis	*Trans*	*Cis*	*Trans*	*Cis*	*Trans*
Ag^{1}	$CH_3CH=CHCH_3$	$K_{Ag} = 4.9$	$K_{Ag} = 1.6$	- 3.4	- 2.6	- 8.2	- 7.7
	$CD_3CD=CDCD_3$	$K_{Ag} = 5.9$	$K_{Ag} = 1.8$	- 3.56	- 2.75	- 8.5	- 8.0
	$C_2H_5CH=CHCH_3$	$K_{Ag} = 5.6$	$K_{Ag} = 1.8$	- 3.6	- 2.9	- 8.5	- 8.7
	$C_2H_5OCH=CHCH_3$	$K'_{Ag} = 3.13$	$K'_{Ag} = 0.54$	- 3.9	- 3.2	-11.0	-12.1
	$C_2H_5OCH=CHC_2H_5$	$K'_{Ag} = 4.24$	$K'_{Ag} = 0.73$	- 4.5	- 3.3	-12.0	-12.0

[a] $K_{Ag} = [Ag^+][olefin]/[Ag\text{-}olefin]^+$ at 25°C. K'_{Ag} at 20°C (taken from Ref. 23)

Table 1.1.D

than the *cis*-olefin, as in β-chlorovinyl ethyl ether (ClCH=CHOEt)[25] and 1,2-dichloroethylene[26], the *trans*-olefin forms the more stable complex with silver. Also the actual bonds between *cis*-olefin and metal are stronger than between *trans*-olefin and metal. This could arise because the distortions required to reduce non-bonded interaction in *trans*-olefin-metal complexes reduce the effective orbital overlap and hence the bond strength.

The bonding in Rh(I)-olefin complexes differs from that in Ag(I)-olefin complexes in that the π-back bond component predominates over the σ-bond component. This is supported by ^{1}H n.m.r. spectroscopic evidence because the double bond protons of a co-ordinated olefin experience an upfield shift, relative to those of the unco-ordinated olefin, on complexation to Rh(I). A similar effect is observed using ^{13}C n.m.r. spectroscopy[22] and these effects would only occur if there was a significant shielding effect caused by a nett transfer of charge from the metal to the olefin *via* a π-back donation[27].

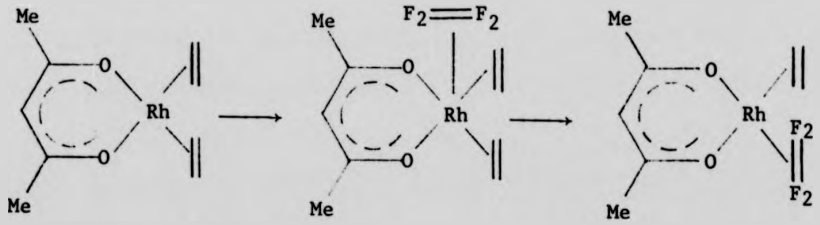
Rh(I) shows similar behaviour to Ag(I) in complexation to *cis*- and *trans*-olefins, i.e. Rh(I)-*cis*-olefin complexes are favoured, but the opposite behaviour in relation to the effect of electron-withdrawing substituents on the olefin (Table 1.1.E).

Olefin	$K \times 10^3$ (25°C)
(Z)-but-2-ene	4.1 ± 0.3
(E)-but-2-ene	2.0 ± 0.3
CH_2=CHCl	170 ± 19
CH_2=CHF	320 ± 22
(E) CHF=CHF	1240 ± 360
(Z) CHF=CHF	1590 ± 330

K_E - equilibrium constant

Table 1.1.E (taken from Ref. 28)

Although electron-withdrawing halogen substituents on the olefin reduce the electron density which is available for π-bond formation, this is more than compensated for by the fact that the energy level of the π* antibonding orbitals are lowered, thus facilitating charge transfer from filled metal orbitals to these π* orbitals. Interestingly, kinetic measurements have shown that although displacement of ethylene in E_2Rh(I)pd by tetrafluoroethylene is thermodynamically favoured, it occurs slower, by a factor of 10^6, than ethylene exchange[28].



(A)

Fig. 1.1.F

It is known that displacement of ethylene from E_2Rh(I)pd proceeds by nucleophilic attack of olefin, to give a 5-coordinate intermediate (A, Fig. 1.1.F). The above results suggest that although the π-back-bonding predominates in the Rh(I)-olefin bond, it is the σ-bond component which is of critical importance in the formation of the 5-co-ordinate intermediate (A).

The nature of the counter ligand also affects the strength of the Rh(I)-olefin bond. For a series of E_2Rh(I)pd complexes it has been shown that increasing the electron-withdrawing capacity of the substituents (1 and 5) on the pentanedionato-ring causes a

reduction in the upfield shift of the double bond protons in the ^{1}H n.m.r. spectrum, i.e. the order of upfield shift in the ^{1}H n.m.r. spectrum on co-ordination is pentan-2,4-dione > 1,1,1-trifluoropentan-2,4-dione > 1,1,1,5,5,5-hexafluoropentan-2,4-dione[27b]. These results are in agreement with an overall predominance of the π-back-bond component because the presence of electron withdrawing substituents on the counter ligand would reduce the electron density at Rh(I) which is available for back-donation to the π* orbitals of the olefin.

1.2 Selective Modification of Fatty Acids

The economic and biological importance of fatty acids has led to the development of methods for their selective modification. The economic importance of selective modification revolves around the need for efficient conversions of readily available, naturally occurring fatty acids into economically more viable products. The biological importance is based upon the need to develop efficient methods for the preparation of biologically active intermediates.

The chemical reactions used for these modifications may, or may not mimic biosynthetic routes. Some of the intermediates produced can be used for further metabolic studies. Interest in the area of selective modification has increased following the elucidation of the biochemical pathways relating fatty acids, leukotrienes and prostaglandins. Arachidonic acid [(Z,Z,Z,Z)-5,8,11,14-eicosatetraenoic acid] has a key role in the biosynthesis of these compounds, being selectively enzymatically oxidised, but until recently there had been no report of selective chemical oxidation of arachidonic acid and other related fatty acids. Direct epoxidation of arachidonic acid by peroxyacids, e.g. m-chloroperoxybenzoic acid, is essentially non-

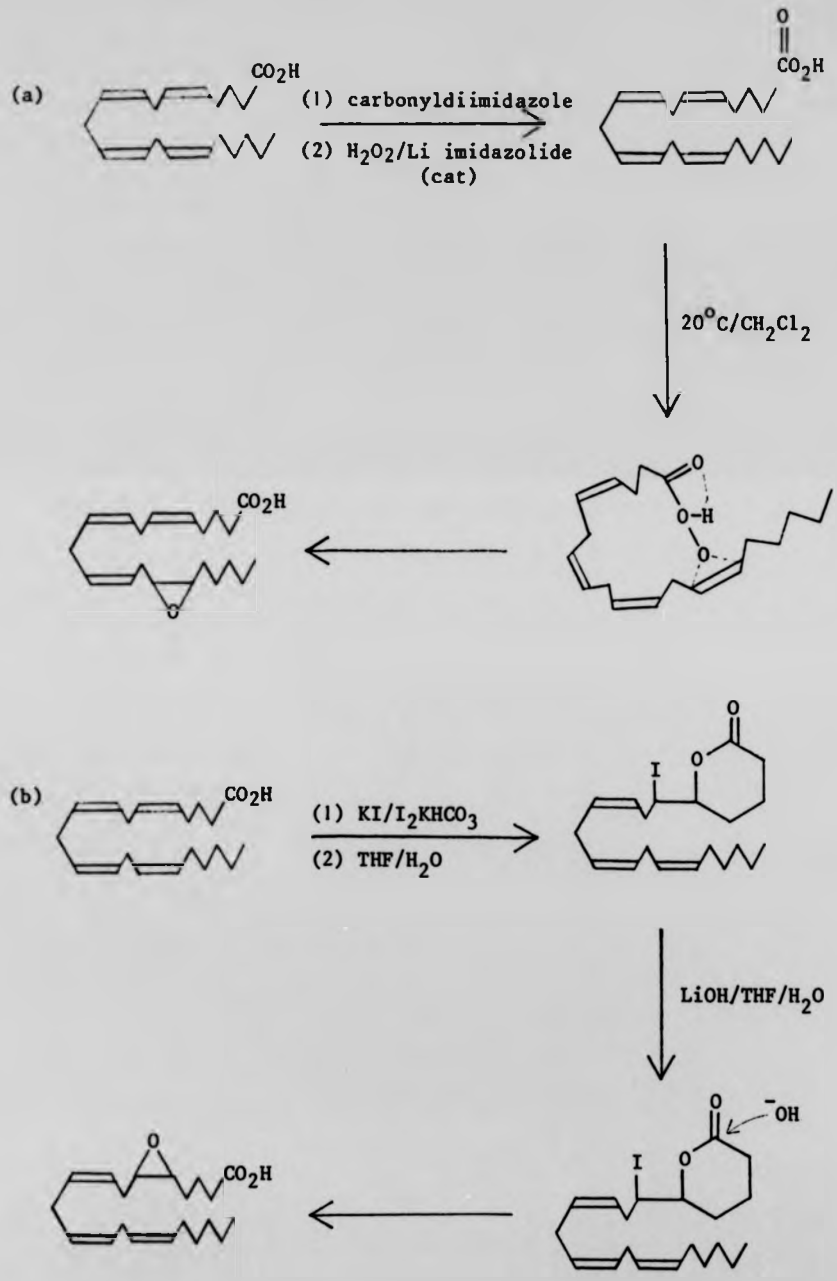

(a)
CO2H
(1) carbonyldiimidazole
(2) H2O2/Li imidazolide
(cat)
O
CO2H
20°C/CH2Cl2
O
O-H
O
CO2H
O
(b)
CO2H
(1) KI/I2KHCO3
(2) THF/H2O
O
O
I
LiOH/THF/H2O
O
-OH
O
I
O
O
CO2H

Fig. 1.2.G

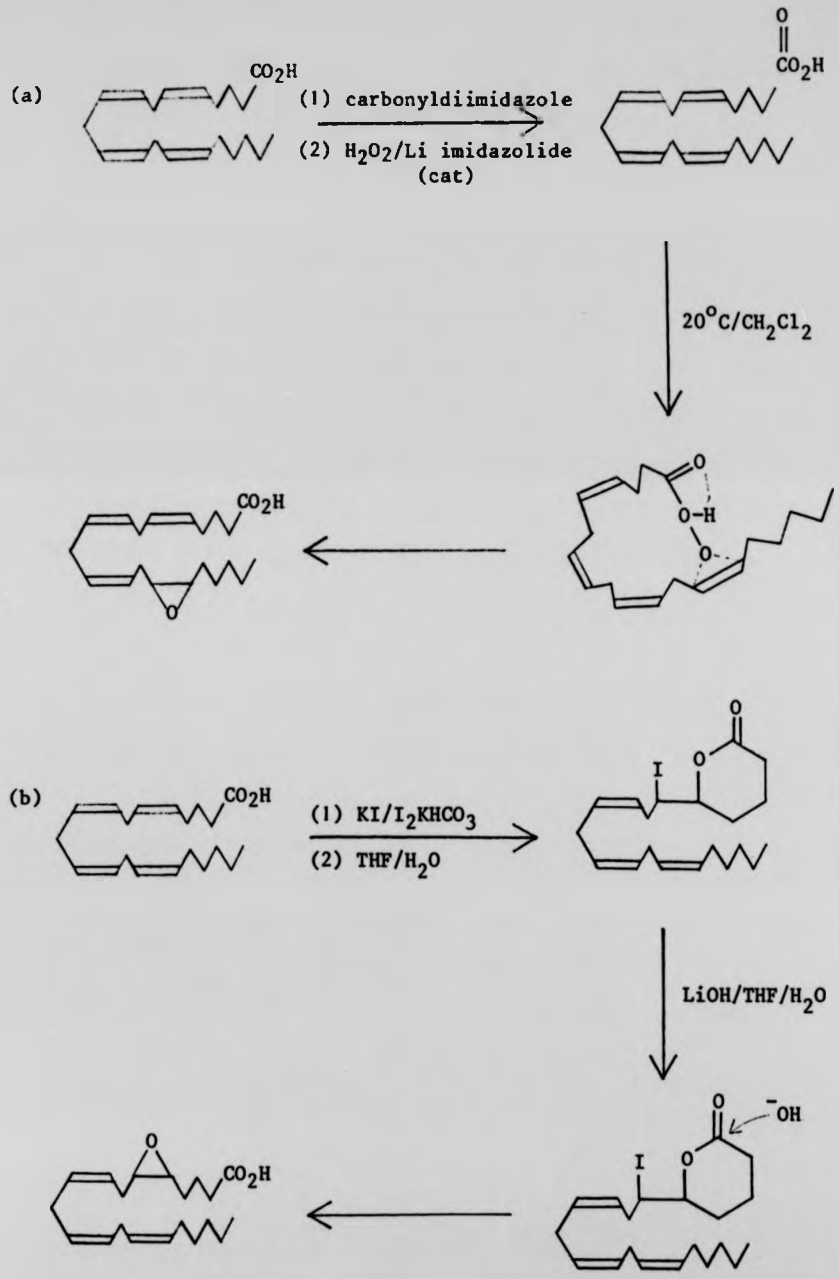

(a)
CO2H
(1) carbonyldiimidazole
(2) H2O2/Li imidazolide
(cat)
O
CO2H
20°C/CH2Cl2
O
O-H
O
CO2H
O
(b)
CO2H
(1) KI/I2KHCO3
(2) THF/H2O
O
O
I
LiOH/THF/H2O
O
-OH
O
I
O
O
CO2H

Fig. 1.2.G

selective and leads to a mixture of all possible positional epoxides[29]. However, Corey[30] has been able to obtain selective epoxidation of arachidonic acid at the double bonds closest to, and farthest from the carboxyl terminus (Fig. 1.2.G). In one case a highly selective, intramolecular epoxidation was achieved (Fig. 1.2.Ga).

Initially, peroxyarachidonic acid was generated by reaction of arachidonic acid with carbonyldiimidazole, followed by treatment with H_2O_2 and catalytic lithium imidazolide to give the peroxyacid. Presumably, the basic catalyst is required to generate the ^-OOH nucleophile which then displaces the imidazolide group. On standing, at 20°C in CH_2Cl_2 at high dilution, the peroxyacid was converted to > 98% *cis*-14,15-epoxyarachidonic acid. Similarly, *cis*-8,11,14-eicosatrienoic acid was converted to *cis*-14,15-epoxy-8,11-eicosadienoic acid. This remarkably selective internal epoxidation of the $\Delta^{14,15}$ double-bond of arachidonic acid clearly occurs *via* intramolecular oxygen transfer and indicates that the 15-membered cyclic intermediate shown in Fig. 1.2.Ga, is energetically favourable compared to alternative geometries involving proximate double-bonds and hence smaller ring sizes.

Using an alternative approach, Corey was also able to achieve selective epoxidation of the $\Delta^{5,6}$ double-bond. Treatment of pure arachidonic acid in THF - H_2O (2:1) with $KHCO_3$, KI and I_2 at 0°C generated the intermediate δ-lactone, which on treatment with 0.2 M LiOH in THF - H_2O (3:2) gave *cis*-5,6-epoxyarachidonic acid. Attempts to prepare 9,10-epoxyoctadecanoic acid (epoxyoleic acid) by the intermolecular epoxidation reaction were not successful, because with peroxyoleic acid internal epoxidation was very slow, and a competing intramolecular epoxidation gave 9,10-epoxyperoxyoleic acid.

More recently, using a similar approach, Corey[31] has

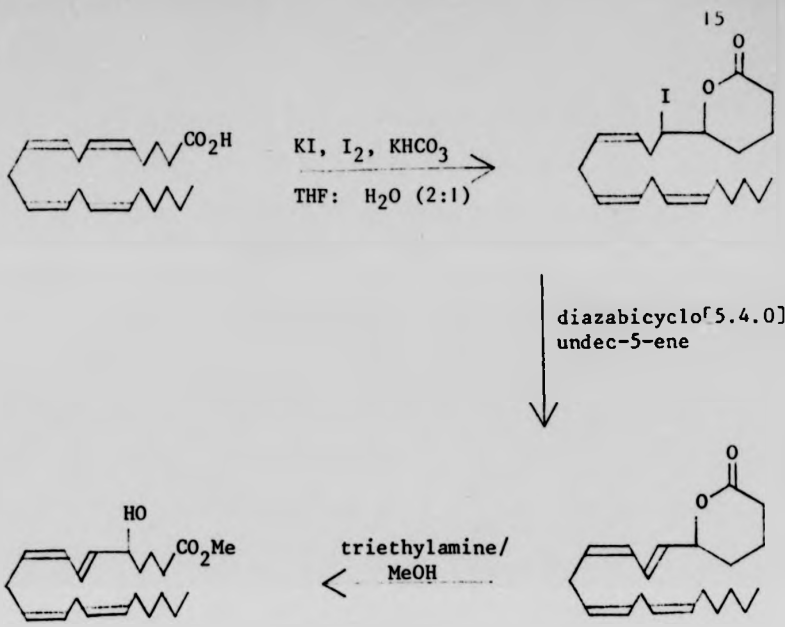
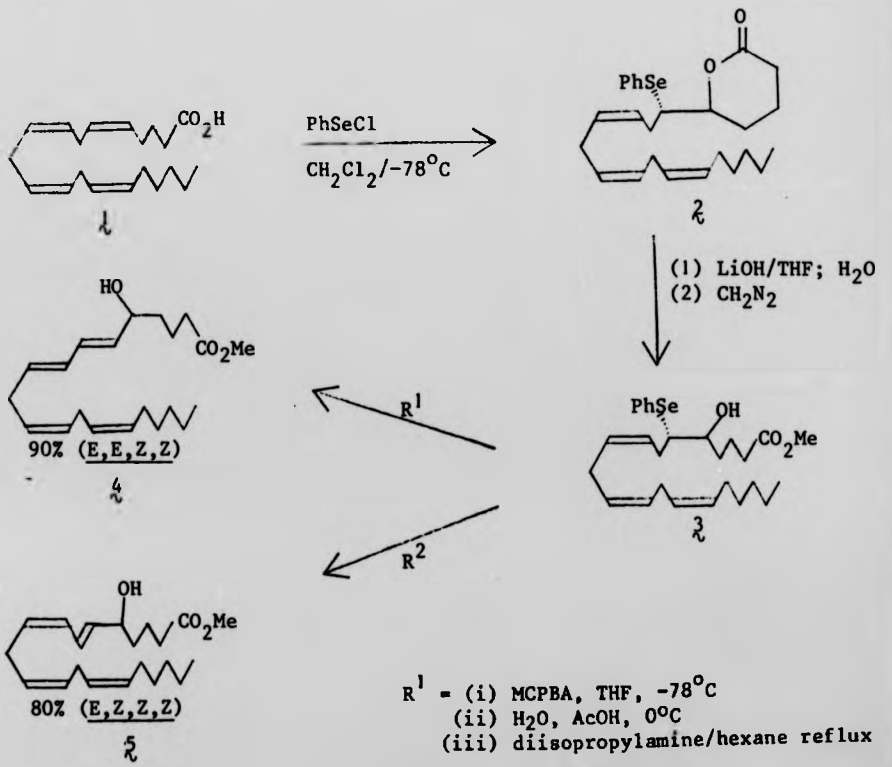


Fig. 1.2.K



R^1 = (i) MCPBA, THF, -78°C
(ii) H_2O, AcOH, 0°C
(iii) diisopropylamine/hexane reflux

R^2 = (i) H_2O_2, THF, H_2O, THF
(ii) CH_2N_2, Et_2O

Fig. 1.2.L

prepared *cis*-5-hydroperoxy-6,8,11,14-eicosatetraenoic acid (5HPETE), the first intermediate in the biosynthetic process (*cf.* Fig. 1.3.h) leading from arachidonic acid to leukotrienes and prostaglandins (Fig. 1.2.K).

The δ-iodolactone was generated from arachidonic acid as previously described, and was then dehydrohalogenated to give the corresponding tetraene-lactone. Base hydrolysis (triethylamine-methanol) gave methyl 5-hydroxy-6,8,11,14-eicosatetraenoate which was converted to the corresponding peroxide by initial reaction with methanesulphonyl chloride followed by treatment with H_2O_2. Saponification of the methyl ester was effected by using a large excess of LiOH and H_2O_2 to give the required acid (5-HPETE).

An alternative approach to the synthesis of this acid has been developed by Baldwin and his co-workers[32]. This method utilises the useful phenylselenolactonisation reaction described by Nicolaou[33] (Fig. 1.2.L).

Baldwin reacted arachidonic acid with phenylselenyl chloride at - 78°C to give a phenylselenyl lactone (2). This lactone was then hydrolysed and re-esterified with diazomethane to give the phenyl-selenyl alcohol (3). Variation of the conditions for the oxidative elimination of the selenoxide group gave either predominantly methyl 5-hydroxy-(E,E,Z,Z)-6,8,11,14-eicosatetraenoate or the corresponding (E,Z,Z,Z)-isomer. The notable feature of this oxidation is that the elimination process occurs selectively away from the hydroxyl function.

Gunstone and co-workers[34] have also succeeded in generating this important structural fragment ($-CH\overset{Z}{=}CH-CH\overset{E}{=}CH-CHOH-$) from methyl epoxyoleate (Fig. 1.2.N).

Treatment of methyl epoxyoleate with lithium diethylamide was found to give the desired product. However, treatment with BF_3:

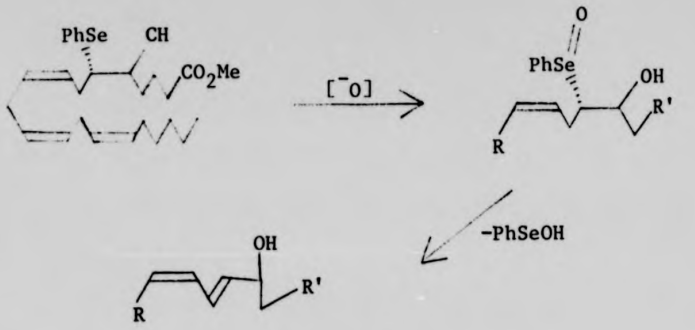


Fig. 1.2.M

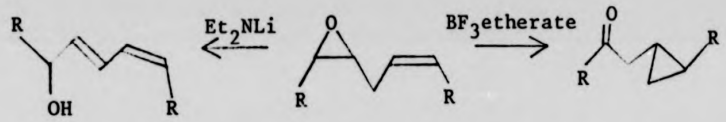


Fig. 1.2.N

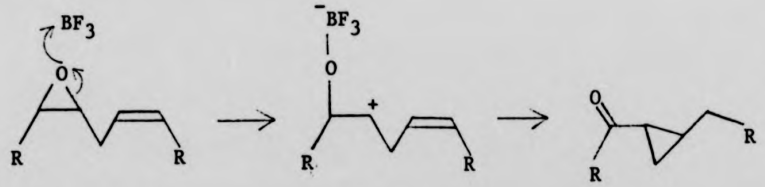
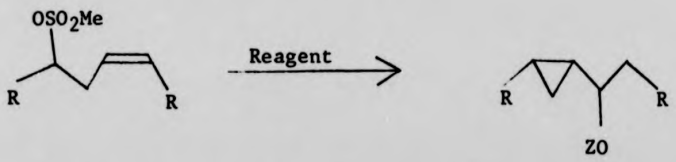


Fig. 1.2.P



Reagent = (i) NaOMe, MeOH; (Z = OMe, 56%)
(ii) NaOAc, AcOH; (Z = OAc, 36%)
(iii) H_2O, CH_3CN, $CaCO_3$; (Z = OH, 63%)

Fig. 1.2.Q

etherate gave an unexpected product, which was found to be a cyclopropyl ketone. The production of this compound can be rationalised in terms of the formation and subsequent quenching of a homoallylic carbonium ion (Fig. 1.2.P).

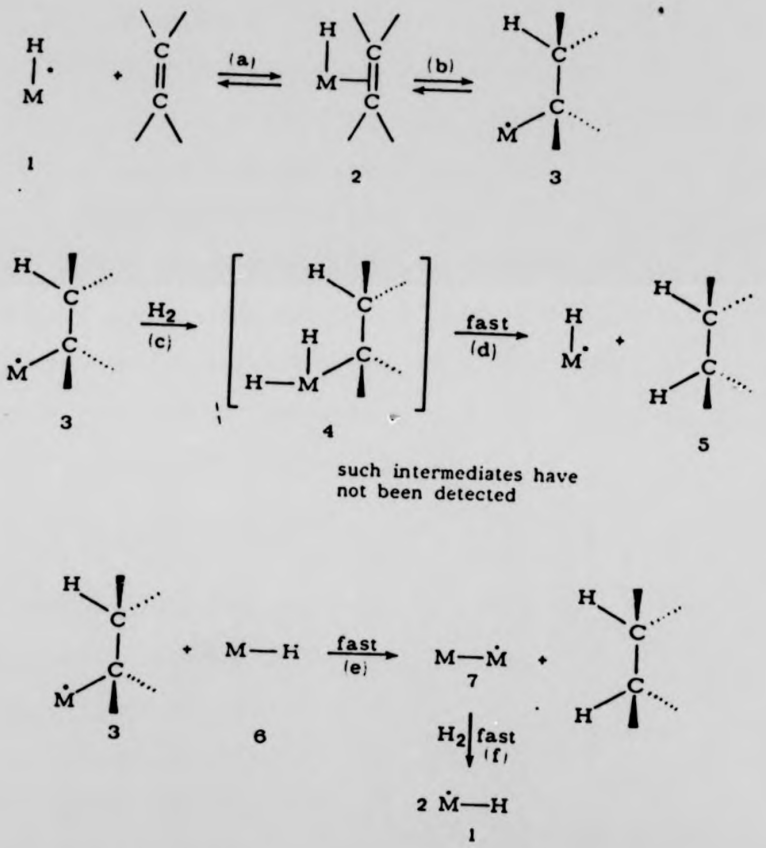
It was also found that the cyclopropane ring was more easily generated from the appropriate tosylate or mesylate (Fig. 1.2.Q)[35].

The most important industrial method for selective modification of fatty acids is catalytic hydrogenation. Selective conditions for heterogenous hydrogenation usually mean high temperature, low pressure and the use of a non-isomerising catalyst. This method is used extensively in the margarine and edible oil industry, but it is somewhat indiscriminate when compared to homogeneous hydrogenation, which offers a superior alternative for selective hydrogenation. There are two well established mechanisms for homogeneous hydrogenations.

Monohydride Catalysis[36]

A proposed generalised mechanism for monohydride-catalysed hydrogenation is shown in Fig. 1.2.R[37]. The major uncertainty in this mechanism concerns the hydrogenolysis of the metal-alkyl intermediate. This may involve simple oxidative-addition of hydrogen followed by reductive-elimination of the metal-alkyl intermediate to give a metal-metal species (binuclear reductive-elimination). The monohydride catalyst could then be regenerated by reaction of this species with hydrogen. With non-conjugated olefins the first step requires complexation of the olefin to a co-ordinatively unsaturated metal hydride, followed by hydride transfer to give a metal-alkyl species. The reversibility of these two steps accounts for the observed isomerisation and isotope exchange in non-conjugated olefins[38].

There are then two possibilities for further reaction of



The probable mechanism for "monohydride" hydrogenation catalysts. An asterisk indicates a site of unsaturation which is required for the indicated reaction to take place. Extraneous ligands may inhibit these steps.

Fig. 1.2.R from ref. 37

the metal-alkyl species:

(i) Oxidative-addition of hydrogen to give an alkyl-metal dihydride species which undergoes a reductive elimination to give alkane, plus regenerated monohydride catalyst.

(ii) Reaction with a second molecule of monohydride catalyst to give alkane plus a dimeric metal species, which reacts with hydrogen to regenerate the monohydride-metal catalyst.

To date the alkyl-metal dihydride intermediates proposed for route (i) have not been observed, but James and co-workers[39] have obtained evidence to support the alternative route. During hydrogenation studies with Ru(III) complexes [RuX_3L_2 (X = Br, Cl; L = PPh_3, $AsPh_3$] the process shown below was observed.

$$H\text{-}Ru^{III} + X\text{-}Ru^{III} \rightarrow 2Ru^{II} + H^+ + X^-$$

This result constituted the first observation of a reaction which is analogous to the latter stages of the proposed mechanism for monohydride-catalysed, homogeneous hydrogenation.

Halpern[40] has also obtained evidence which indicates that certain homogeneous hydrogenations, involving monohydride metal carbonyl catalysts, proceed *via* a free radical mechanism. The hydrogenation of α-methylstyrene by hydridopentacarbonylmanganese was monitored by ^1H n.m.r. spectroscopy at - 78°C, and a chemically induced dynamic nuclear polarisation effect (CIDNP) was observed, providing direct evidence for a free radical pathway. On the basis of kinetic results Halpern proposed the following mechanism (Fig. 1.2.S).

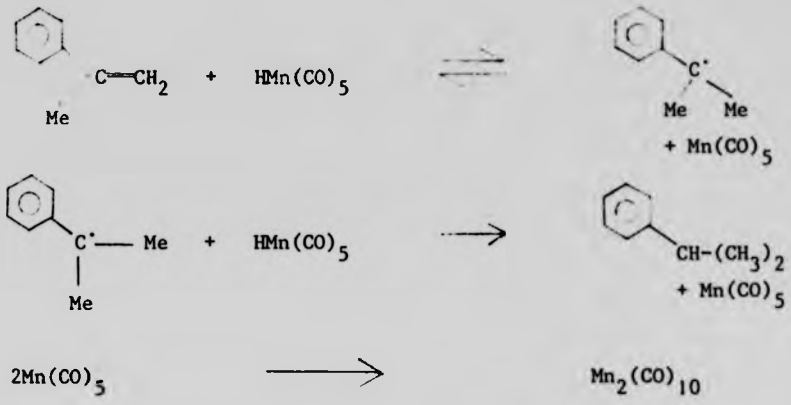


Fig. 1.2.S

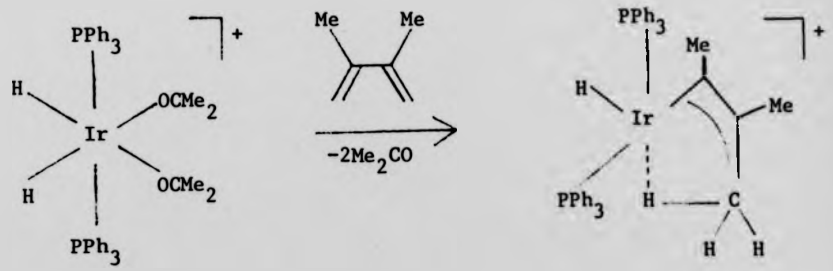


Fig. 1.2.U

Fig. 1.2.V

Dihydride Catalysts

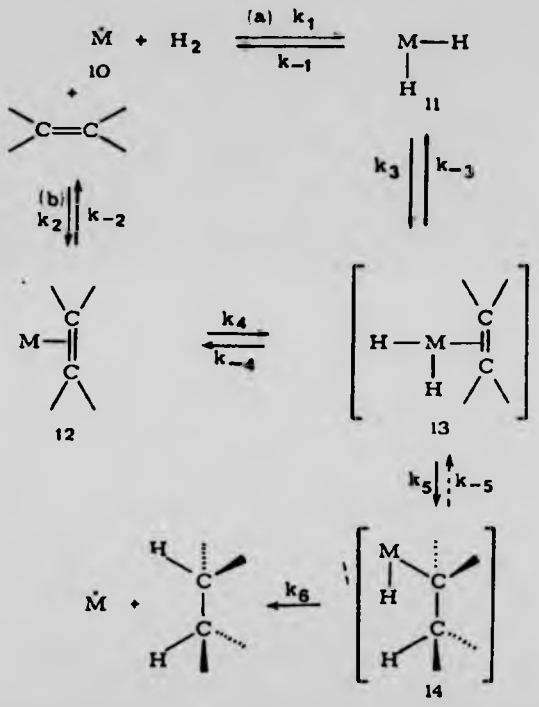
A proposed generalised mechanism for this class of hydrogenation is shown in Fig. 1.2.T. It can be seen that the reaction can proceed by either of two pathways (a or b). In path (a) an oxidative-addition of hydrogen to an unsaturated metal complex generates a *cis*-dihydride. In a number of cases these complexes are isolable and fully characterised. Iridium *cis*-dihydride complexes have been prepared and shown to be active hydrogenation catalysts, and more interestingly these complexes have been shown to react with dienes to give iridium-allyl species which exhibit a C-H---Ir^{III} interaction[41] (Fig. 1.2.U).

In the generalised mechanism (Fig. 1.2.T) the *cis*-dihydride can then add olefin to give a monoene-metal dihydride species. This step must involve displacement of a previously co-ordinated ligand (possibly solvent, e.g. acetone in Fig. 1.2.U) by the incoming olefin. By an alternative path (b), the two previously described steps are reversed, i.e. the olefin is co-ordinated prior to oxidative-addition of hydrogen. The next step in both pathways is then migratory insertion which proceeds *via* a *cis*-addition of the M-H bond to the olefin.

That addition proceeds with *cis*-stereochemistry was first illustrated by the addition of deuterium to maleic acid to give *meso*-1,2-dideuterosuccinic acid (Fig. 1.2.V).

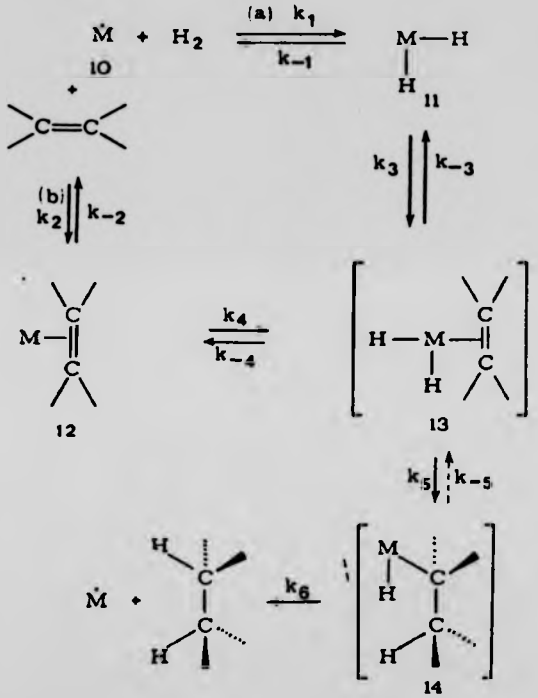
The failure to observe intermediate (14) in Fig. 1.2.T, the absence of olefin rearrangement and isotopic scrambling can be accounted for by the relative rates of the final steps, i.e. $k_6 >> k_5$. This mechanism is probably best established for Wilkinson's catalyst [chloro-*tris*-(triphenylphosphine)rhodium(I)][42].

In the field of fatty acid chemistry, arene-chromium carbonyl



Generalized mechanisms for "dihydride" hydrogenation catalysts. The accompanying ligands are not shown. In compound 10, at least one site of unsaturation must be present, although there are occasionally two sites. Complex 11 must be unsaturated for the subsequent olefin coordination step to occur. This unsaturation can result either from ligand dissociation or from addition of H_2 to a doubly unsaturated complex. Complex 14 would be unsaturated unless a ligand has been taken up from the solution, which is the usual case.

Fig. 1.2.T from ref. 37



Generalized mechanisms for "dihydride" hydrogenation catalysts. The accompanying ligands are not shown. In compound 10, at least one site of unsaturation must be present, although there are occasionally two sites. Complex 11 must be unsaturated for the subsequent olefin coordination step to occur. This unsaturation can result either from ligand dissociation or from addition of H_2 to a doubly unsaturated complex. Complex 14 would be unsaturated unless a ligand has been taken up from the solution, which is the usual case.

Fig. 1.2.T from ref. 37

complexes have stimulated the most interest because they uniquely catalyse the hydrogenation of polyunsaturated fatty acids and esters to *cis*-monounsaturated products. The mechanism of action of these complexes has been elucidated by the use of deuterium labelling[43].

It was observed that reduction of methyl sorbate [methyl (E,E)-hexa-2,5-dienoate] by deuterium in the presence of methyl benzoate-$Cr(CO)_3$ gave methyl 2,4-dideuterio-3-hexenoate as the major product (95%). Non-deuterated and monodeuterated products were either absent or negligible. In a partially reduced sample, the methyl sorbate remaining was found to contain no deuterium, whereas the methyl-3-hexenoate was found to possess two deuterium atoms per molecule. Free methyl benzoate was also detected in the reaction mixture during the course of the reaction and in the final product. These results were interpreted in terms of a mechanism (Fig. 1.2.W) involving initial dissociation of methyl benzoate from the methyl benzoate-$Cr(CO)_3$ complex, as the rate-determining step. The almost exclusive formation of a dideuterated product was interpreted as an indication that a dideuteride (dihydride) chromium intermediate is formed as the second step in the hydrogenation. This would be followed by addition of a deuterium to either the 2- or 5-position of olefin, to give an allyl-chromium deuteride intermediate which then proceeds *via* a migratory insertion to give the dideuterated product (Fig. 1.2.W).

That the catalyst will only reduce conjugated dienes, or dienes capable of conjugation was confirmed by the observations that monoenes (e.g. 1- and 2-hexene) and 1,5-hexadiene were not reduced. Apparently the catalyst cannot promote conjugation of a 1,5-diene, but 1,4-dienes are slowly hydrogenated indicating that a slow conjugative step precedes hydrogenation. The catalyst is

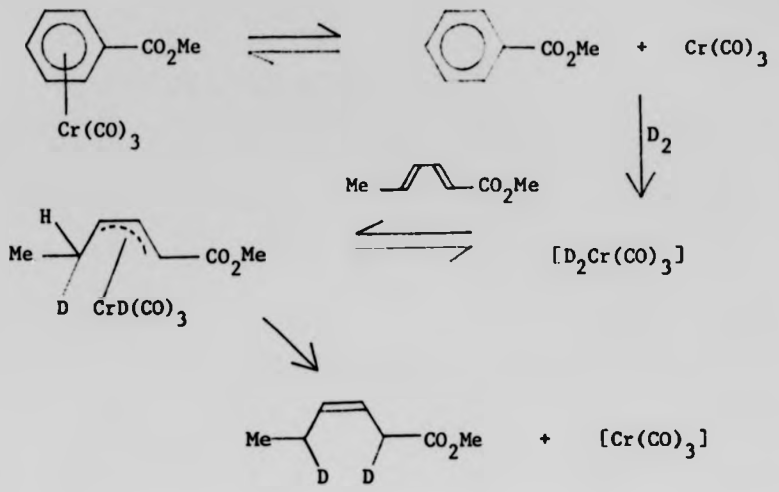


Fig. 1.2.W

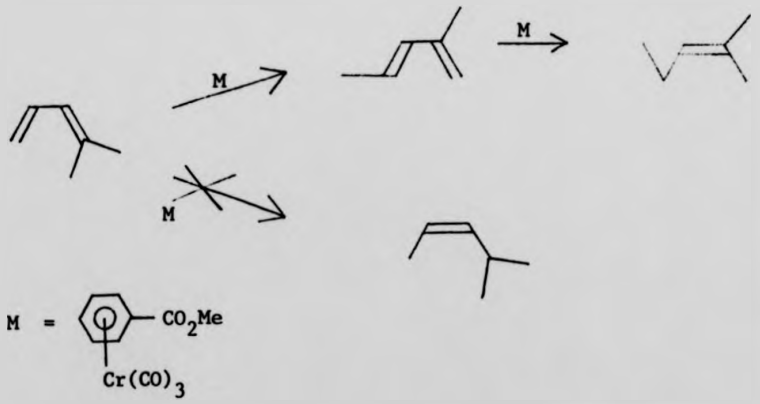
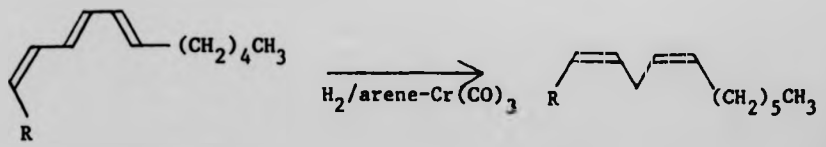


Fig. 1.2.X



α-eleostearic acid

linoleic acid
(> 80%)

R = $-(CH_2)_6CO_2H$

Fig. 1.2.Z

Catalytic Hydrogenation of Octadecadienoic Fatty Esters
with Chromium Tricarbonyl Catalysts under 30 Atm. of Hydrogen Pressure

Substrates 9 mmol	$Cr(CO)_3$ Complexes 1 mmol	Temp °C	Time hr	Glpc Analysis % Monoene	Diene	Infrared *trans*[b] %
Methyl linoleate (*cis*-9,*cis*-12-dienoate)	Methyl benzoate	175	3	94.8	5.2	12.4
	Benzene	165	8	79.0	21.0	6.1
Alkali-conjugated linoleate (*cis*-9,*trans*-11-, and *trans*-10,*cis*-12-dienoate)	Methyl benzoate	175	1.5	97.0	3.0	10.1
	Benzene	165	4	98.8	1.2	8.8
	Cycloheptatriene	125	1	98.0	2.0	14.5
Methyl *cis*-9,*trans*-11-octadecadienoate	Methyl benzoate	175	1.5	97.0	2.1	14.8
	Benzene	165	4	100	0	7.9
	Cycloheptatriene	125	3.5	95	5	8.9
Methyl *trans*-9,*trans*-11-octadecadienoate	Methyl benzoate	175	1	97.8	2.2	7.4
	Benzene	165	2	100	0	9.1
	Cycloheptatriene	125	1	95.4	3.4	7.7
Methyl *cis*-9,*cis*-15-octadecadienoate	Methyl benzoate	175	7	1.6	98.4[c]	34.5

[a] Solvent, cyclohexane (50 ml)

[b] Expressed as methyl elaidate (*trans*-9-octadecenoate)

[c] Diene peak was partially resolved into three isomeric components

Table 1.2.Y (taken from Ref. 43)

also capable of effecting positional isomerisation in conjugated dienes. This was illustrated by the hydrogenation of 4-methyl-1,3-pentadiene which gave 2-methyl-2-pentene as the only product, rather than 4-methyl-2-pentene. This product can be accounted for by the initial isomerisation of 4-methyl-1,3-pentadiene to 2-methyl-1,3-pentadiene *via* a 1,5-hydrogen shift, followed by hydrogenation to the monoene.

Various arene-$Cr(CO)_3$ catalysts have been employed successfully for the hydrogenation of fatty acids and esters. The results from some of these hydrogenations are shown in Table 1.2.Y, and it can be seen that the arene-$Cr(CO)_3$ catalysts are highly selective for the reduction of (Z,Z)-, (E,Z)- and (E,E)-dienes, to give (Z)-monoenes. However, the intervention of isomerisation (*via* 1,5-hydrogen shifts) gives rise to a considerable number of positional isomers in all cases except with (E,E)-conjugated dienes, where the hydrogenation is > 95% regio- and stereoselective.

Two further observations have increased the utility of this catalyst system:

(i) In the above series it was noted that the hydrogenation of 1,3-dienes was much faster than the hydrogenation of 1,4-dienes, because of the necessary conjugative step.

(ii) Conjugated (E,E)-dienes were observed to react much faster than either (E,Z)- or (Z,Z)-dienes.

These observations have proved particularly useful for the hydrogenation of α-eleostearic acid [(Z,E,E)-9,11,13-octadecatrienoic acid] using arene-$Cr(CO)_3$ catalysts (Fig. 1.2.Z)[44]. Hydrogenation of α-eleostearic acid in the presence of an arene-$Cr(CO)_3$ complex was observed to give linoleic acid (> 80%) confirming that (E,E)-conjugated dienes react preferentially to give (E,Z)-conjugated dienes and both

of these in turn react faster than "skipped" 1,4-dienes. This type of reduction has proved economically important for the hydrogenation of soybean oil. This oil is an important edible oil, with a high linoleate content, (*cf.* Section 1.3 for biological importance), but also containing sufficient amounts of (E,E)-conjugated compounds to impair the flavour. Arene-$Cr(CO)_3$-catalysed hydrogenation removes these systems and hence eliminates the off-flavours, while in some cases increasing the linoleate content of the oil.

1.3 Biological Significance of Fatty Acids

Recognition that some unsaturated fatty acids could not be synthesised by mammals, but were essential dietary components[45], led to the designation of essential and non-essential fatty acids (EFA and NEFA).

The principal symptoms of EFA deficiency in mammals have been identified as cessation of growth, dermal deterioration, excessive loss of body fluid and impaired kidney function. Subsequent to these early findings it was established that linoleic acid [(Z,Z)-9,12-octadecadienoic acid: 9,12-18(2)] is the essential fatty acid with major biological activity[46].

The metabolic fate of any ingested exogenous fatty acid is determined by the relative rates of a number of competing reactions:

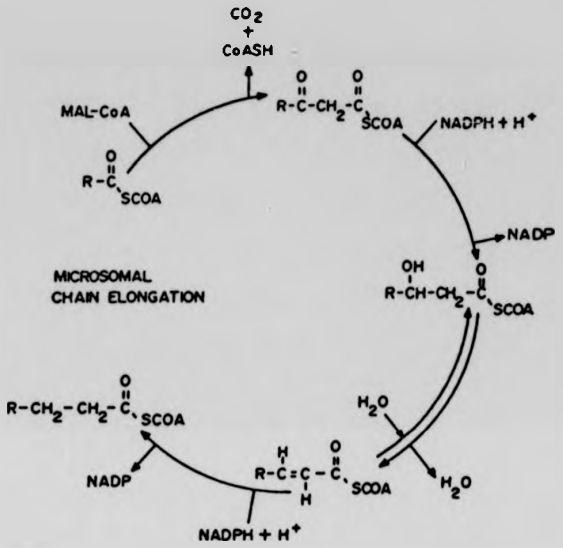
(1) chain elongation,

(2) chain shortening (retroconversion)

(3) desaturation

(4) conversion to a variety of lipids

(5) complete breakdown (β-oxidation)



Reaction pathway for the microsomal chain elongation of fatty acids.

Fig. 1.3.a (taken from Ref. 53)

The biochemical pathway for fatty acid chain elongation in mammals is illustrated in Fig. 1.3.a. In early studies on the factors controlling this process Chaikoff *et al.*[47] observed [^{14}C]acetate incorporation into long chain fatty acids when rat liver microsomes were added to a system containing supernatant, ATP, HCO_3^-, NADPH and Mg^{2+}. Substitution of acetyl-CoA by malonyl-CoA in these systems resulted in even greater incorporation. Although these studies suggested that microsomes contained a malonyl-CoA-dependent chain elongation system it was not until work by Nugteren[48] that the importance of this alternative pathway was generally recognised. He demonstrated that the conversion of myristate (C_{14}) to palmitate (C_{16}) proceeded

according to Fig. 1.3.a and it was observed that reactions 2, 3 and 4 (reduction, dehydration and reduction, respectively) all proceeded more rapidly than did overall chain elongation, establishing that the initial condensation is the rate limiting step. This observation was further supported by Sprecher[49] who has shown that when palmitate (C_{16}) is chain elongated to stearate (C_{18}) the rate of condensation equals the overall rate of reaction. It was also observed that ATP and CoASH must be present to facilitate the chain elongation process, but the presence of the appropriate fatty acyl-CoA derivative obviated the need for these co-factors, indicating that the fatty acyl-CoA derivatives were the actual substrates for chain elongation.

In addition to serving as substrates for chain elongation some unsaturated fatty acids undergo partial cleavage reactions and the resulting products are re-esterified into tissue lipids. This process is frequently referred to as partial degradation, or retroconversion. Those fatty acids which are substrates for this conversion are listed in Table 1.3.b and from the products it can be seen that this process may involve either the loss of a single two-carbon fragment or the loss of a double-bond and either a two- or four-carbon fragment.

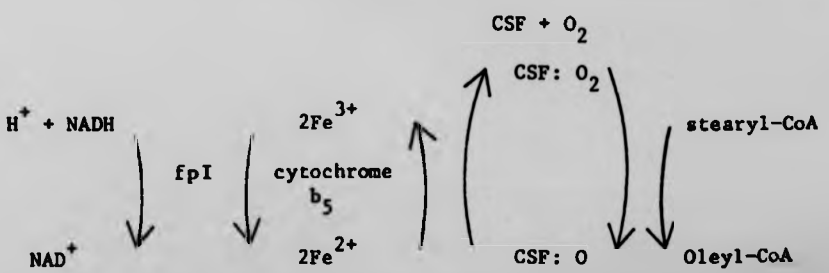
Substrate	Products
11-20:(1)	9-18:(1)
10,13-20:(2)	8,11-18:(2)
11,14-20:(2)	9,12-18:(2)
7,10,13-22:(3)	5,8,11-20:(3)
10,13,16-22:(3)	8,11,14-20:(3)
6,9,12,15-21:(4)	4,7,10,13-19:(4)
4,7,10,13-22:(4)	5,8,11-20:(3) and 7,10,13-22:(3)
6,9,12,15-22:(4)	4,7,10,13-20:(4)
7,10,13,16-22:(4)	5,8,11,14-20:(4)
4,7,10,13,16-22:(5)	7,10,13,16-22:(4) and 5,8,11,14-20:(4)

Table 1.3.b

N.B. In the above nomenclature the initial numbers are the positions of the (Z)-double-bonds, followed by the number of carbon atoms in the chain and the number of double bonds in brackets. Certain other fatty acids will be abbreviated in this manner later on in this Thesis.

It is evident from the fatty acids listed above that a wide variety are capable of undergoing chain shortening, but the substrate must have at least twenty carbon atoms. Linoleic acid (C_{18}) is not a substrate for retroconversion even though the potential product [7,10-16:(2)] is readily chain-elongated to yield linoleate[50]. Kunau[51] has also ascertained that if a fatty acid is to lose both a double-bond and two or more carbon atoms then the first double-bond of the substrate must be in the 4-position.

The first demonstration of the nature of the desaturation reaction was provided by Bloomfield and Bloch[52]. In mammalian systems the necessary co-factors are molecular oxygen and NADH. The substrate is fatty acyl-CoA and an electron transport system is necessary, consisting of cytochrome b_5 reductase, coupling cytochrome b_5 to the terminal, cyanide-sensitive oxidase. This system has strictly only been demonstrated for the desaturase converting stearyl-CoA [18:(0)] to oleyl-CoA [9-18:(1)], but since all other desaturases involve O_2 and NADH and are membrane-bound it is assumed that they have essentially the same electron transport system (Fig. 1.3.c)[53].



Flavoprotein 1 - NADH - cytochrome b_5 reductase
CSF - cyanide sensitive factor

Fig. 1.3.c

The metabolic processes which affect fatty acids are best illustrated by considering the reactions involved in the linoleate sequence (Fig. 1.3.d)[54].

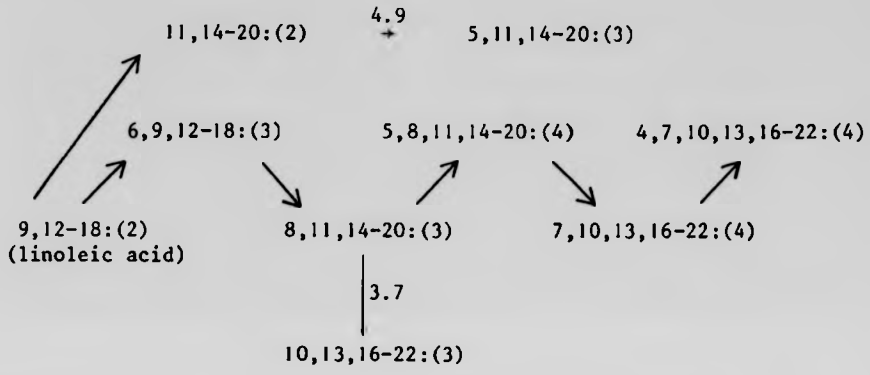


Fig. 1.3.d

When linoleate is supplied *via* the diet it is either incorporated into tissue lipids or desaturated to linolenic acid [6,9,12-18:(3)]. This explains why exclusion of linolenic acid from the diet does not produce adverse effects in mammals, i.e. it is a non-essential fatty acid. Once formed, this acid is chain-elongated to give 8,11,14-20:(3), which itself can be further extended, to give 10,13,16-20:(3), desaturated to arachidonic acid [5,8,11,14-20:(4)] or incorporated into lipids.

Compositional analysis[55] showed that < 3% of rat liver lipids are 8,11,14-20:(3), whereas arachidonate is one of the major polyunsaturated fatty acids found in most liver lipids. Thus, the principal biosynthetic rôle of 8,11,14-20:(3) must be to serve as a precursor for arachidonate. Once arachidonic acid is produced it may be chain-elongated to 7,10,13,16-22:(4), followed by desaturation to 4,7,10,13,16-22:(5). However, experiments have shown[56] that if

the latter acids are fed to rats they are not incorporated into the system, but are preferentially converted to arachidonic acid by retroconversion. The arachidonic acid so produced is then incorporated into lipids.

The biosynthetic pathway followed by oleic acid [(Z)-9-octadecenoic acid: 9-18:(1)], also consists of a series of desaturation and chain elongation reactions, and it is interesting to note that there is no direct cross-over between unsaturated metabolites from one sequence to the other (Fig. 1.3.e)[57].

Linoleate Sequence [18:(2)]

18:(2) → 18:(3) → 20:(3) → 20:(4) → 22:(4)

Oleate Sequence [18:(1)]

18:(0) → 18:(1) → 18:(2) → 20:(2) → 20:(3)

Linolenate Sequence [18:(3)]

18:(3) → 18:(4) → 20:(4) → 20:(5) → 22:(5) → 22:(6)

Fig. 1.3.e

Tissue lipids from rats raised on a balanced diet do not contain any polyunsaturated fatty acids derived from oleate. Conversely, when rats are maintained on a diet devoid of linoleic acid the principal fatty acid is 5,8,11-20:(3) derived from the oleate sequence. Competitive feeding studies and enzymatic experiments[58] suggest that a common enzyme may desaturate oleate, linoleate and linolenate. When linoleate is included in the diet there is competition with oleate for the same desaturase, and in this way the linoleate is preferentially metabolised.

The biological importance of fatty acids (especially linoleic acid) is further emphasised by the discovery that certain polyunsaturated

Selectivity in the Formation of Prostaglandin from Polyunsaturated Fatty Acids

Chain Length	Double Bond Position* (n-9)	(n-8)	(n-7)	(n-6)	(n-5)	(n-4)	(n-3)
18	-	-	(5,8,11)--	(6,9,12) 8%[a] (3,6,9,12)16%[a]	(7,10,13)--	(8,11,14)0%[b] (5,8,11,14)2%[c]	(9,12,15)0%[d]
19	-	-	(6,9,12)--	(7,10,13)88%[a] (4,7,10,13)60%[a] 20%[c]	(8,11,14) 2%[b] (5,8,11,14)43%[b]	(9,12,15)--	(10,13,16)--
20	(5,8,11)0%[a]	(6,9,12)0%[a]	(7,10,13)26%[a]	(8,11,14)100%[a,b] (5,8,11,14)104%[a] 107%[b] (2t,8,11,14) 18%[c]	(9,12,15) 3%[a]	(10,13,16)--	(11,14,17)0%[d] (5,8,11,14,17)8%[a] 0%[d]
21	-	-	(8,11,14)33%[b] (5,8,11,14)57%[b] (2t,8,11,14) 2%[c]	(9,12,15) 53%[a] (6,8,12,15) 37%[a]	(10,13,16)--	(11,14,17)--	(12,15,18)--
22	-	(8,11,14)0%[b] (5,8,11,14)2%[c]	(9,12,15)--	(10,13,16) 8%[a] (7,10,13,16)35%[e] 25%	(11,14,17)--	(12,15,18)--	(13,16,19)-- (4,7,10,13,16,19)0%[d]

*All double bonds are *cis* unless otherwise indicated. The symbol, --, indicates that data are not available for that isomer.

[a] Extent of PGE formation, as a percent of PGE_1 formed from 20:3(n-6), was measured by OD_{280} after alkali treatment.

[b] When significant PGE was formed, the identify was verified by g.l.c. and mass spectrometry (27).

[c] Rates of PGE formation, as a percent of the rate of PGE_1 formed from 20:3(n-6), were determined by quantitative conversion to PGB *versus* time. Product identity was verified by g.l.c. and mass spectrometry (11,28).

[d] Same as b, (29).

[e] The rate of O_2 uptake during the cyclooxygenase reaction as a percent of the rate of the reaction with 20:3(n-6) (30).

Rate of O_2 uptake as a percent of 20:4(n-6) reaction (31).

Table 1.3.f (taken from ref.54)

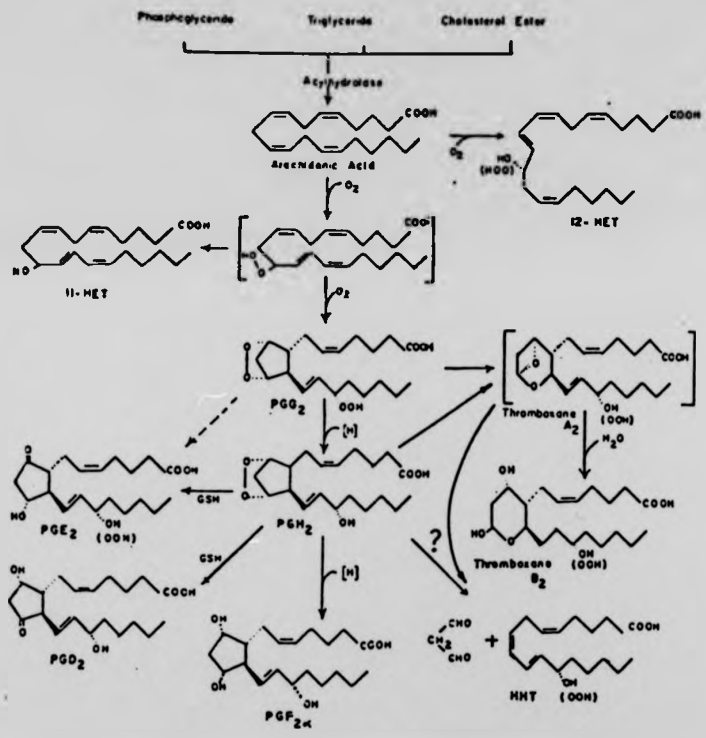
fatty acids are precursors to a series of highly important biologically active compounds (e.g. prostaglandins and leukotrienes). Prostaglandins are generated by the oxidation of polyunsaturated acids, such as arachidonic acid [5,8,11,14-20:(4): itself biosynthesised from linoleic acid], and they are produced whenever cells are injured, irrespective of whether the damage is mechanical, chemical, immunological or bacteriological. The appearance of prostaglandins seems to be the most sensitive index of cell damage and once formed they are almost certainly causative agents in the symptoms of inflammation.

The enzyme system which catalyses the oxidation of polyunsaturated fatty acids to endoperoxides, and their subsequent transformation to prostaglandins and other products, is a multi-enzyme complex known as the fatty acid cyclooxygenase system. Substrates for the cyclooxygenase are essential fatty acids and it has been demonstrated[59] that the structural requirements for conversion of fatty acids into prostaglandins are:

(i) The presence of at least 3 double-bonds at positions 8,11,14.

(ii) A free carboxylic acid function (methyl esters do not act as substrates).

The likely substrates for prostaglandin biosynthesis are listed in Table 1.3.f and it can be seen that arachidonic acid [5,8,11,14-20:(4)] and the trienoic acid [8,11,14-20:(4)] possess the optimum chain length (C_{20}) and double-bond position (the sixth carbon atom counted from the methyl terminus) for formation of prostaglandins. These compounds are not stored within the cell and so biosynthesis must precede release. The biosynthetic pathways for prostaglandins and the related thromboxanes are illustrated in Fig. 1.3.g.



Pathways for the biosynthesis of prostaglandins and thromboxanes.

Fig. 1.3.g taken from ref. 54

The first step must be enzyme-catalysed hydrolysis of a triglyceride to give arachidonic acid, because it is the free fatty acid which is active. This is followed by stereospecific removal of a C-13 proton and the conversion of the substrate into a C-11 hydroperoxide[60]. The next stage is a concerted reaction: the addition of oxygen at C-15 is followed by an isomerisation of the C-12 double-bond, ring closure between C-8 and C-12 and attack by an oxygen radical at C-9, thus forming the cyclic endoperoxide PGG_2[61]. This is followed by reduction of the 15-hydroperoxide group to the corresponding hydroxy group, thus forming the endoperoxide PGH_2. Both endoperoxides are unstable, spontaneously decomposing in aqueous solution to mixtures of prostaglandins, but they can be isolated in organic solvents and are stable at temperatures $< -20^{\circ}C$. Either of the intermediate endoperoxides (PGG_2 and PGH_2) can then be converted into the corresponding prostaglandin by an enzyme-catalysed process mediated by endoperoxide isomerases.

More recently it has been demonstrated that fatty acids are the precursors to a family of compounds known as leukotrienes. The physiological effects of these compounds were first described by Kellaway and Trethewie and they are now believed to play an important role in hypersensitivity and non-immunological inflammatory processes[62]. The compounds themselves were first identified by Borgeat and Samuelsson[63] and given the general name leukotrienes because of their origin from leukocytes, and the possession of a characteristic conjugated triene fragment. They may also be referred to as "slow reacting substances" (SRS) because of their slow contracting effect on smooth muscle. The discovery of leukotrienes, as well as the elucidation of their mechanism of formation, resulted from a comprehensive study of the metabolism of arachidonic acid [5,8,11,14-20: (4)] in leukocytes[63] (Fig. 1.3.h).

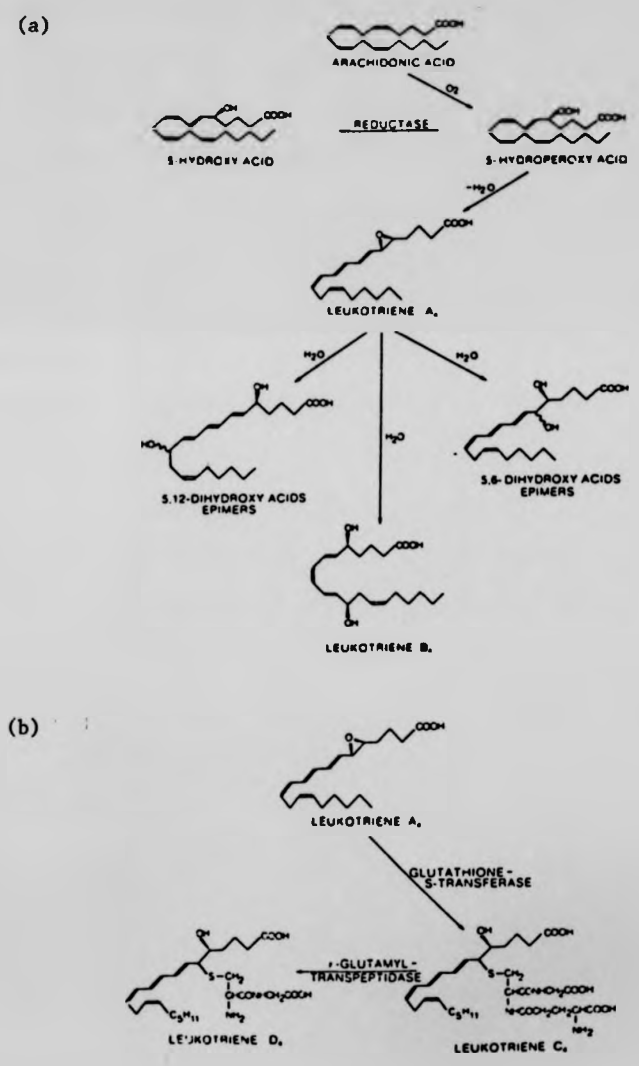


Fig. 1.3.h taken from ref. 63

In a first report Samuelsson[64] described the biosynthesis of (5S)-hydroxy-6,8,11,14-eicosatetraenoic acid, and (8S)-hydroxy-9,11,14-eicosatrienoic acid, from arachidonic acid and 8,11,14-eicosatrienoic acid, respectively. Later the presence of a further metabolite was reported by the same group: (5S, 12R)-dihydroxy-6,8,10,14-eicosatetraenoic acid (Leukotriene B_4) (Fig. 1.3.ha).[70] It was believed that a reactive intermediate existed, which linked the C_{20}-hydroxyacids and the C_{20}-dihydroxyacids, and the results of further trapping experiments using simple nucleophiles (H_2O, MeOH, etc.), led to the isolation and characterisation of 5,6-oxido-7,9,11,14-eicosatetraenoic acid (Leukotriene A_4) as that intermediate[65]. The structure was proved conclusively by Corey's total stereospecific synthesis of leukotriene A_4 and its conversion into leukotriene B_4[66]. Two further leukotrienes have also been identified in this sequence, (5S)-hydroxy-(6R)-S-glutathionyl-(E,E)-7,9-(Z,Z)-11,14-eicosatetraenoic acid (Leukotriene C_4)[67] and 5-hydroxy-6-5-cysteinylglycinyl-(E,E)-7,9-11,14-eicosatetraenoic acid (leukotriene D_4)[68] (Fig. 1.3.hb).

1.4 Materials and Methods

Unless otherwise stated, all solvents and chemicals used were of analytical grade. Anhydrous solvents were prepared as follows.

Benzene

AR benzene was washed successively with conc. H_2SO_4, water, dilute NaOH and water. Heating to reflux over and distillation from P_2O_5 under N_2, gave anhydrous benzene b.p. 80°C.

[$^2H_6$]benzene was obtained commercially in 99.5% purity and was stored over 4A molecular sieves.

Diethyl ether

AR diethyl ether was heated to reflux over, and fractionally distilled from $LiAlH_4$ under a stream of nitrogen, b.p. 35°C.

Ethanol

Clean, dry magnesium turnings (5 g) and iodine (0.5 g) were placed in a 2 l round-bottomed flask together with 100 cm^3 AR ethanol. The mixture was warmed until the iodine colour was discharged and a further 900 cm^3 of AR ethanol was then added. The mixture was heated to reflux, distilled (b.p. 78°C) and stored over 3A molecular sieves.

Methanol

An analogous procedure to that described for ethanol was used: b.p. 65°C.

Pentane

S.L.R. pentane was shaken with conc. H_2SO_4, until the acid layer was colourless, and was then washed with aqueous $NaHCO_3$. Heating to reflux over and distillation from P_2O_5 gave purified pentane (b.p. 36°C).

Pyridine

AR pyridine was heated to reflux with KOH pellets for 1 hour. Fractional distillation gave anhydrous pyridine (b.p. 115-116°C), stored over KOH.

Quinoline

Quinoline was prepared by the method of Skraup.[69]

Tetrahydrofuran

An analogous procedure to that described for diethyl ether was used: b.p. 65°C.

Toluene-4-sulphonyl Chloride

S.L.R. toluene-4-sulphonyl chloride (20 g) was recrystallised by

dissolving in $CHCl_3$ (65 cm^3) and petroleum ether (b.p. 40-60°C, 400 cm^3) followed by treatment with animal charcoal. Filtration, followed by evaporation of solvent under reduced pressure gave pure white crystals (m.p. 69°C).

Triglycerides

Any triglycerides used in this Thesis were provided by Unilever Ltd. and their purity was determined by g.l.c.

Rhodium Trichloride

Rhodium trichloride-trihydrate was obtained on loan from Johnson-Matthey Ltd.

1.5 Instruments

1.5.1 N.M.R. Spectra

^1H n.m.r. spectra were recorded by the author using a Perkin Elmer (Model R34) 220 MHz ^1H n.m.r. spectrometer, equipped with variable temperature and double resonance accessories. Solvents utilised were CCl_4, $CDCl_3$, d^6-acetone, d^4-methanol and D_2O, as indicated in the Experimental Sections.

Peaks are designated by their chemical shift (δ) in parts per million, relative to TMS except where indicated, followed in brackets by their relative integral value (e.g. 1 H, 2 H), their systematic number (e.g. H-1), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and the spin-spin coupling constant (J), in Hertz, where appropriate.

^{13}C n.m.r. spectra were recorded by Paul Benson on a Bruker (Model WH90) 22.63 MHz ^{13}C n.m.r. spectrometer equipped with variable temperature accessory. Peaks are designated as above and refer to

dissolving in $CHCl_3$ (65 cm^3) and petroleum ether (b.p. 40-60°C, 400 cm^3) followed by treatment with animal charcoal. Filtration, followed by evaporation of solvent under reduced pressure gave pure white crystals (m.p. 69°C).

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^{13}C n.m.r. spectra were recorded by Paul Benson on a Bruker (Model WH90) 22.63 MHz ^{13}C n.m.r. spectrometer equipped with variable temperature accessory. Peaks are designated as above and refer to

samples in $CDCl_3$, referenced against TMS. All spectra were run with decoupling from ^1H nuclei.

1.5.2 I.R. Spectra

Infra-red (i.r.) spectra were recorded on a Perkin Elmer (Model 257) grating infra-red spectrophotometer. Spectra were run using NaCl plates and calibrated using the 1603.4 cm^{-1} peak of polystyrene. Samples were either thin films, mulls (Nujol) or solutions (CCl_4). Peaks are designated by their wavenumber (cm^{-1}) as strong (s), medium (m) or weak (w) and as broad (br) or sharp (sh) where appropriate.

1.5.3 Ultraviolet/(U.V.) Spectra

U.v. spectra were recorded using a Cecil (Model CE505) double beam spectrophotometer with spectroscopic grade hexane as solvent, and holmium filter as reference.

1.5.4 Gas Liquid Chromatography (G.L.C.)

G.l.c. analyses were carried out using a Pye Unicam (Model 204) or Perkin Elmer (Model F11) flame ionisation gas chromatograph with N_2 as carrier gas.

1.5.5 Mass Spectra

Mass spectra were recorded on a Carlo Erba-Kratos instrument (MS80), except where stated otherwise. Peaks are quoted

as m/z, followed by their percentage intensity of the base peak (100%). The molecular ion is designated M^+.

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CHAPTER 2

STEREOSPECIFIC SYNTHESES OF HEXA-1,4- AND HEPTA-2,5-DIENES, DIENOLS AND DIENOL ACETATES

2.1 INTRODUCTION

The first efficient stereospecific synthesis of the isomeric hepta-2,5-dienes are presented, and possible alternative methods for their preparation are discussed. The syntheses of the title dienols and their derived acetates are also described with an examination of the stereochemical aspects of their preparation.

Ashe and co-workers[1] prepared hepta-2,5-diyne by the Cr(II) reduction of 4-bromohepta-2,5-diyne in THF at room temperature after it was observed that the bromide reacted exceedingly slowly with magnesium[2]. Reaction of hepta-2,5-diyne with dibutyltin dihydride gave a 1,4-dihydro-1,1-dibutyltin dihydride which was cleaved with acetic acid to give (E,E)-hepta-2,5-diene. Cleavage with deuterated acetic acid gave [^{2}H] labelled dienes (Fig. 2.1A).

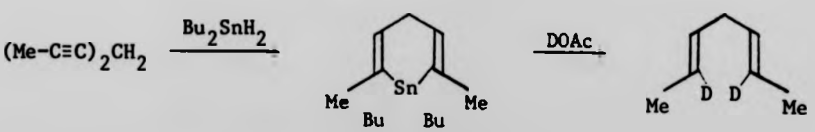


Fig. 2.1.A

The only other description of the isomeric hepta-2,5-dienes in the literature is as products which are formed during either dehydration of alcohols or polymerisation of alkenes. Descotes and co-workers[3] noted the production of (E,E)- and (E,Z)-hepta-2,5-dienes (45%) with (E)-hepta-1,5-diene (35%) during the alumina-catalysed dehydration of (E)-hepta-2-en-5-ol, while Takami[4] has developed a

catalyst derived from di-μ-chlorodi-π-allylpalladium, $AlCl_3$ and a tertiary phosphine, which is able to co-dimerise propylene and butadiene to a mixture containing predominantly (E)-methylhexadiene, with (E,E)- and (E,Z)-hepta-2,5-dienes.

Hence it can be seen that the syntheses described herein (Fig. 2.1.B) constitute the first efficient method of preparing all of the stereochemically pure hepta-2,5-dienes. Important features to note are:

(i) the use of Cu(I)-catalysis in the coupling of acetylenic Grignard reagents to give skipped diynes and enynes[5];

(ii) the stereospecific heterogenous catalytic reduction of acetylenes to predominantly (Z)-alkenes using Lindlar catalyst[6];

(iii) the stereospecific reduction of acetylenes (containing a propargylic group, either OH, CO_2H or CO_2R) with $LiAlH_4$ to give predominantly (E)-alkenes[7];

(iv) the reduction of terminal allylic halides by $LiAlH_4$ with retention of configuration at the double bond[8].

Grignard and Lapayre[9] first attempted to couple acetylenic Grignards, but on coupling phenylacetylene-magnesium bromide with diidomethane they achieved only an 8% yield of what was later found to be diphenylacetylene.

It was first noted as early as 1935[10] that copper salts affected the coupling of Grignard reagents, but it was not until Daneby[11] and co-workers added Cu(I)Cl to a mixture of allyl bromide and n-hexynylmagnesium bromide that the first efficient coupling was

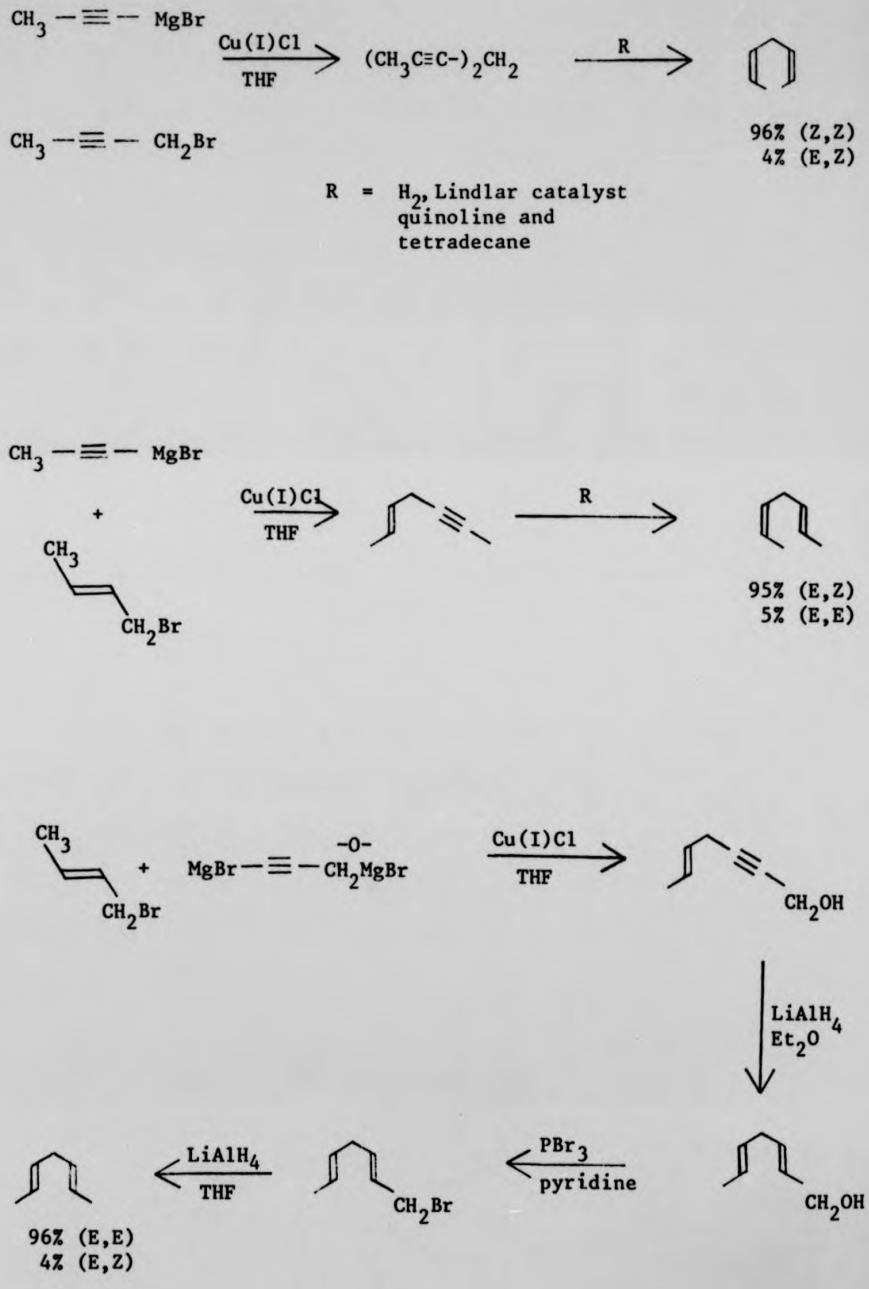

CH3 — ≡ — MgBr
Cu(I)Cl
THF
(CH3C≡C-)2CH2
R
96% (Z,Z)
4% (E,Z)
CH3 — ≡ — CH2Br
R = H2, Lindlar catalyst quinoline and tetradecane
CH3 — ≡ — MgBr
+
CH3
CH2Br
Cu(I)Cl
THF
R
95% (E,Z)
5% (E,E)
CH3
CH2Br
+
MgBr — ≡ — -O- CH2MgBr
Cu(I)Cl
THF
CH2OH
LiAlH4
Et2O
96% (E,E)
4% (E,Z)
LiAlH4
THF
CH2Br
PBr3
pyridine
CH2OH

Fig. 2.1.B

reported. This established that copper(I) salts, particularly the bromide, chloride and cyanide, acted as very efficient promotors for these couplings. Since then many acetylenic Grignards have been coupled with propargylic substrates to give diynes. This method is particularly prevalent in the synthesis of "skipped" methylene fatty acids[5,12], although an alternative method involves the use of Wittig reagents, as illustrated in the synthesis of (Z)-octadec-9-en-12-ynoic acid (Fig. 2.1.C)[13].

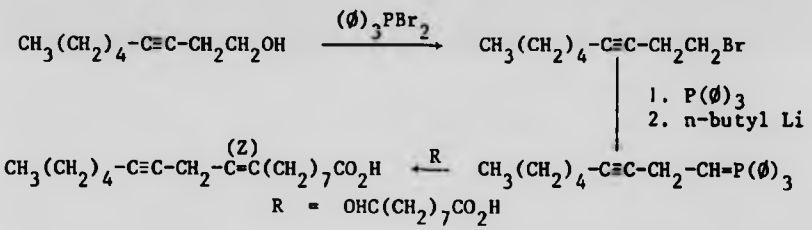


Fig. 2.1.C

The Wittig coupling was found to proceed with complete stereospecificity to give only the (Z)-double bond[14]. At one time it was believed that the stereochemical course of the Wittig reaction could not be controlled[15], but since then it has been shown[16] that careful manipulation of reaction conditions can lead almost completely to either *cis*- or *trans*-product.

The optimum conditions for coupling of acetylenic Grignard reagents have been ascertained[17] as: THF as solvent, Cu(I)Cl as promoter, short reaction times and neutral conditions for work-up. Sondheimer[18] utilised these conditions for the preparation of a series of "skipped diynes", to be used as precursors for macrocycles. Until this work the parent diyne, penta-1,4-diyne, had not been prepared, but using the above conditions the product was isolated and it was shown that re-arrangement to penta-1,3-diyne occurred

on treatment with base.

Previous attempts to prepare penta-1,4-diyne had used basic conditions (sodium acetylide/liquid ammonia), and hence the only isolated product was penta-1,3-diyne. However, "skipped" diynes can be generated under certain basic conditions[19]. Terminal alkynes can be coupled with propargyl halides in the presence of Cu(I)Cl and an amine (Fig. 2.1.D).

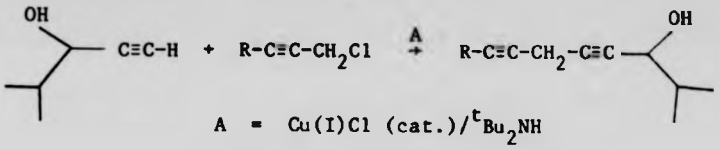


Fig. 2.1.D

It has been suggested that the amine has a dual role in the reaction in that it co-ordinates to Cu(I), and also removes the acid which is generated.

$$R\text{-}\equiv\text{-}H \;+\; Cu(I) \;\rightleftharpoons\; R\text{-}\equiv\text{-}Cu \;+\; H^{+}$$

In this system the propargyl halide must be disubstituted to obtain a "skipped" diyne. If R = H, then allene formation predominates.

More recently "skipped" dienes have been generated by the Pd(II) catalysed coupling of mono-alkenes[20], a reaction which appears to be regiospecific, but not stereospecific. A potentially more important reaction is the coupling of vinyl-lithium reagents with allylic halides (Fig. 2.1.E)[21].

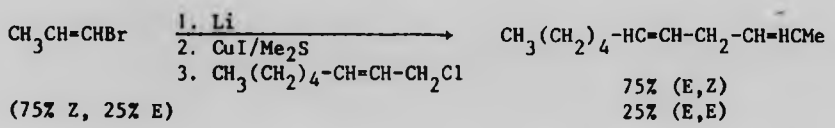


Fig. 2.1.E

This reaction is particularly useful in fatty acid synthesis because, like the Wittig reaction, it can lead to the production of (E,E) and (E,Z) "skipped" dienes, whereas catalytic hydrogenation of "skipped" diynes gives (Z,Z)-dienes. The preferred method of hydrogenation in the latter case involves the use of Lindlar catalyst ($Pd/CaCO_3$)[6a] in the presence of a poison (lead acetate and quinoline). The optimum conditions for obtaining a maximum percentage of (Z,Z)-diene with a minimum of over-reduced products and (E)-double bonds were determined by Pabon and co-workers[6b].

At room temperature in petroleum ether (40-60) or ethyl acetate, and in the presence of quinoline (1-2 $cm^3\ g^{-1}$ catalyst) and Lindlar catalyst, methyl nonadeca-10,13-diynoate was hydrogenated to 98.5% methyl-(Z,Z)-nonadeca-10,13-dienoate with only 1% *cis*-monoene and less than 0.5% conjugated diene. In the absence of quinoline large amounts of overhydrogenated products and products containing *trans*-double bonds were formed. Kinetic studies are consistent with the mechanism shown in Fig. 2.1.F.

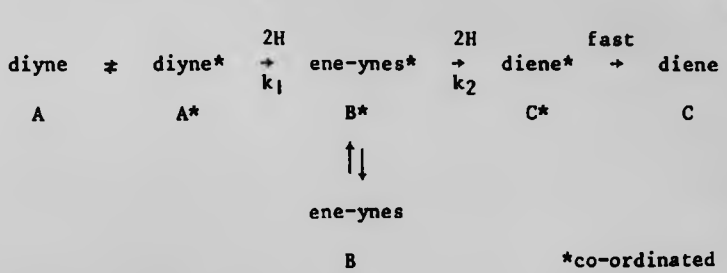


Fig. 2.1.F

Although this catalyst system is still well used, alternative methods for the reduction of acetylenes to *cis*-alkenes are available. Crandall and Ashby[22] have developed a system from MgH_2CuI, or Cu^tBuO, which is capable of the reduction of acetylenes to *cis*-alkenes with complete stereospecificity and no over-reduction. The reduction is believed to proceed *via* a "CuH" species (Fig. 2.1.G). However, there is evidence to suggest that the "CuH" reduction is initiated by an electron transfer process[7]. The fact that the (Z)-isomer is produced suggests delivery on one side of the face of the alkyne by the copper species.

Brown and co-workers[23] have reduced alkynes to *cis*-alkenes by hydroboration. Reaction of 2-pentyne or 3-hexyne with $NaBH_4:BF_3$ gives on work-up (Z)-2-pentene and (Z)-3-hexene, 99% (Z). The mechanism involves a *cis* addition of a boron hydrogen bond to the acetylene *via* a four centre transition state, followed by protonolysis with retention of configuration (Fig. 2.1.J). Metal-acid reduction with zinc or magnesium is also known to yield *cis*-alkenes[24].

In contrast to the above reductions, $LiAlH_4$ is known to reduce alkynes to *trans*-alkenes in a highly stereospecific process, and can give upwards of 98% (E)-specificity[7]. The reduction is facilitated by the presence of an α-OH, -OR, or $-CO_2R$ group, and is solvent dependent. $LiAlH_4$ can also reduce isolated alkynes under more forcing conditions[25]. In THF the product is predominantly (E)-alkene while in toluene the product is mostly (Z)-alkene. Alkali-metal/NH_3[7] reductions are also known to result in formation of predominantly (E)-alkenes from alkynes. Care must be taken in choice of the reaction conditions because overreduction, especially using lithium, is easy to achieve. The mechanism for this reaction is as shown (Fig. 2.1.K).

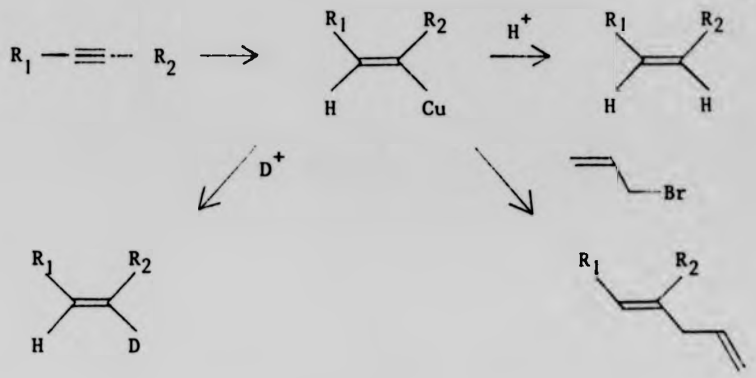


Fig. 2.1.G

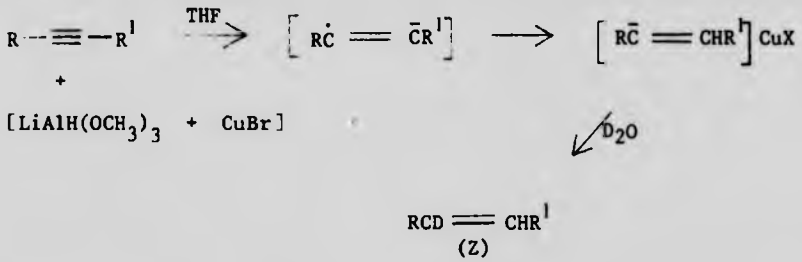


Fig. 2.1.H

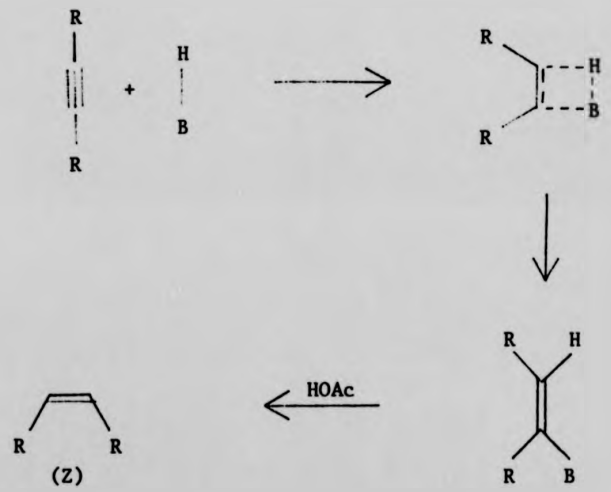
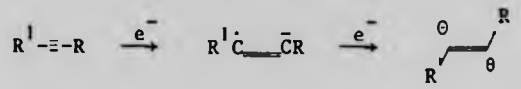


Fig. 2.1.J

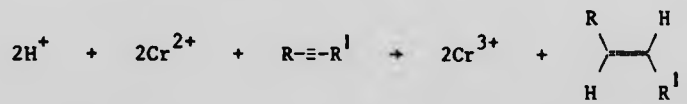


(A) (B) (C)

Fig. 2.1.K

Addition of one electron produces the radical-anion (B) which on addition of a second electron is converted to the dianion (C) which adopts the more stable *trans* configuration[26]. New reagents and solvents are continually increasing the flexibility of this type of reaction, e.g. non-conjugated acetylenes can be reduced with Na/THF-HMPA and ^{t}butanol at -33°C to give > 95% (E)-alkene[27].

Chromium(II) reduction of acetylenes is also a stereospecific process, leading to (E)-alkenes[28]. The overall stoichiometry of the reaction is given by:

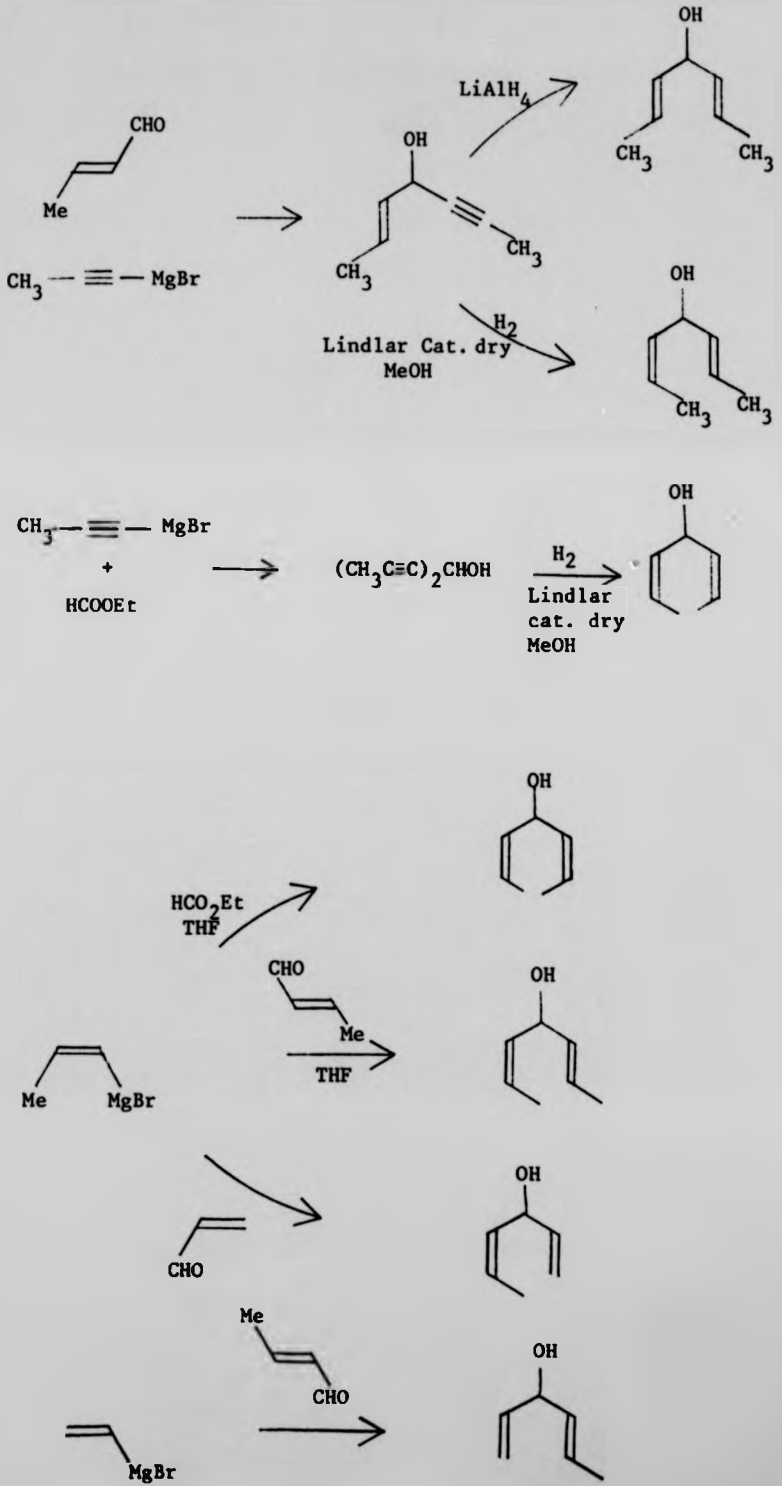


The mechanism of the reaction is thought to proceed *via* initial formation of an acetylene-chromous complex followed by attack of Cr^{2+} on this complex (Fig. 2.1.L)[29].

(E,E)-, (E,Z)- and (Z,Z)-hepta-2,5-dien-4-ols were synthesised as shown (Fig. 2.1.M). (E)-hept-2-en-5-yn-4-ol was prepared by coupling (E)-but-2-en-1-al with propynylmagnesium bromide. Reduction with $LiAlH_4$ gave (E,E)-hepta-2,5-dien-4-ol, whereas hydrogenation (H_2/MeOH/Lindlar catalyst) gave (E,Z)-hepta-2,5-dien-4-ol. Hepta-2,5-diyn-4-ol[2] was similarly reduced to give (Z,Z)-hepta-2,5-dien-4-ol.

(E)- and (Z)-hexa-1,4-dien-3-ols were prepared according to literature procedures[30]. (Z)-1-bromopropene was used both in the

Fig. 2.1.M


CHO
Me
CH3 — ≡ — MgBr
OH
CH3
CH3
LiAlH4
OH
CH3
CH3
H2
Lindlar Cat. dry
MeOH
OH
CH3
CH3
CH3 — ≡ — MgBr
+
HCOOEt
(CH3C≡C)2CHOH
H2
Lindlar
cat. dry
MeOH
OH
HCO2Et
THF
OH
CHO
Me
THF
Me
MgBr
OH
CHO
OH
Me
CHO
MgBr
OH

preparation of (Z)-hexa-1,4-dien-3-ol and the alternative preparations of (E,Z)- and (Z,Z)-hepta-2,5-dien-4-ols (Fig. 2.1.M). (Z)-1-bromopropene was itself prepared, by a modification of a published procedure[31], from α,β-dibromobutyric acid. It is known that in the absence of light bromine adds to double bonds in an *anti* (or *trans*) mode. Hence, formation of α,β-dibromobutyric acid, by bromination of crotonic acid in the absence of light, occurs *via* anti-addition to give the (2R*,3S*)-product. It has been postulated that when the salts of such dibromoacids fragment, they do so in a stereospecific manner to produce (Z)-vinyl halides (Fig. 2.1.N).

Norris[32] was able to produce (Z)-1-bromopropene by heating sodium α,β-dibromobutyrate in DMF at 70°C. The first fraction collected (38%) was found to be 99% (Z)-1-bromopropene (g.l.c. analysis), a subsequent fraction (38%) was found to contain 96% (Z)-, 4% (E)-1-bromopropene. This provides conclusive evidence that the decarboxylation is almost stereospecific. Norris noted that redistillation of the product gave increasing amounts of the (E)-isomer, whereas distillation with exclusion to light did not (*cf.* Fig. 2.3.2).

It has been shown[33] that (Z)-1-bromopropene can be converted to the (Z)-propenyllithium with 95% retention of configuration. However, n.m.r. studies on (Z)-propenylmagnesium bromide[34] show that the Grignard is generated with only 90% retention of configuration. Subsequent coupling of the (Z)-propenylmagnesium bromide with aldehyde proceeds with complete retention of configuration[34]. Other literature methods[35] for the preparation of 1-bromopropene have been described, but lead to mixtures of isomers. However, more recent work[36] shows that (E)- and (Z)-vinyl halides can be generated with 98% stereospecificity, Fig. 2.1.P. Thermolysis gives the *cis* product and protonolysis leads to the *trans* product. However, when R = Ø- the products are reversed; possibly because the bromination proceeds in a *syn* rather than *anti* mode,

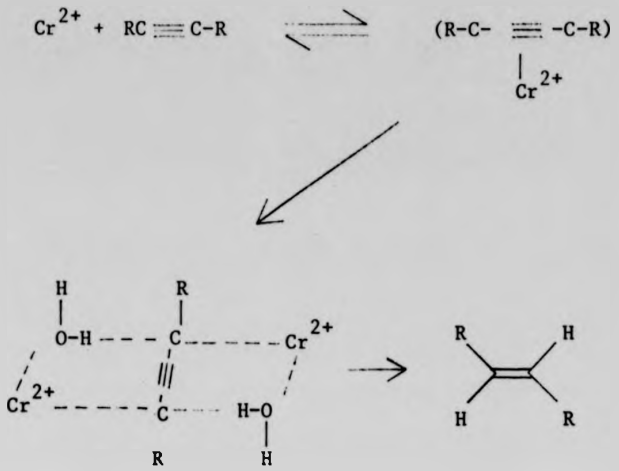
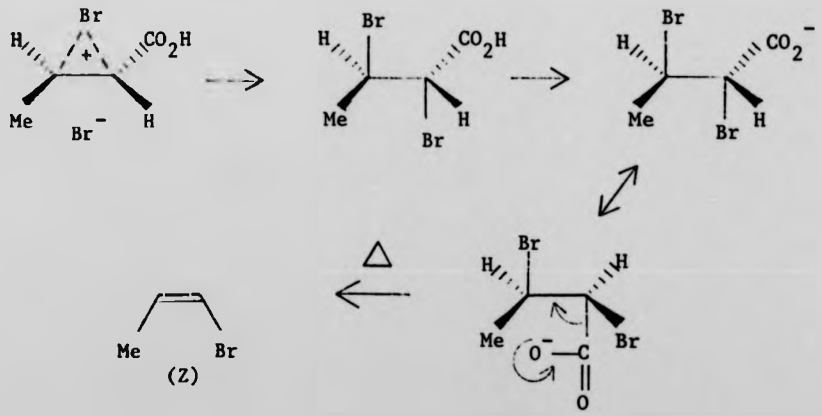


Fig. 2.1.L



R = $NaHCO_3$/cyclohexanone

Fig. 2.1.N

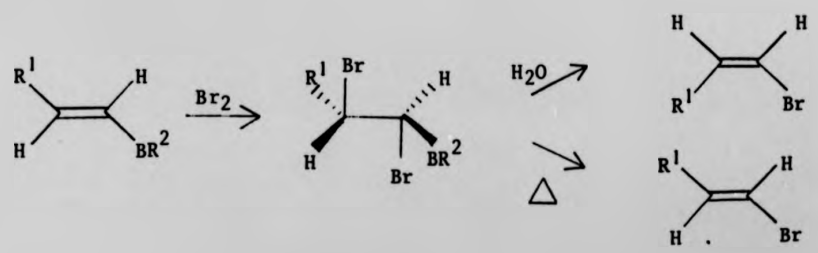


Fig. 2.1.P

or the elimination proceeds in a *syn*-manner[36].

2.2 SYNTHESIS OF HEXA-1,4- AND HEPTA-2,5-DIENES

2.2.1 Preparation of cyclohexa-1,4-diene

Benzene (3.9 g, 50 mmol), ethanol (15 cm^3) and dry liquid ammonia (60 cm^3, distilled from sodium) were stirred at -33°C, under a dry ice condenser, during the addition of sodium (2.8 g, 125 mmol). The ammonia was evaporated overnight and distilled water (40 cm^3) was cautiously added. The aqueous solution was extracted with pentane (3 x 50 cm^3), the extracts dried ($MgSO_4$), filtered and distilled to give cyclohexa-1,4-diene (2.58 g, 32 mmol), b.p. 85-87°C, in 64% yield.

^1H n.m.r. ($CDCl_3$): 2.66 (4 H, m), 5.69 (4 H, m) p.p.m.

2.2.2 Synthesis of (E,Z)-hepta-2,5-diene

Preparation of (E)-but-2-en-1-ol (crotyl alcohol)

A 50% ethereal solution of (E)-but-2-enal (37.0 g, 0.528 mol) was added dropwise to a stirred suspension of $LiAlH_4$ (10 g, 0.236 mol) in dry ether (100 cm^3). The solution was stirred at RT for 12 hours, followed by addition of water (10 cm^3), 15% NaOH (aq.) (10 cm^3). Drying ($MgSO_4$), filtration and fractional distillation gave (E)-but-2-enol (36.1 g, 0.51 mol) b.p. 120-122°C, in 96% yield.

^1H n.m.r. (CCl_4): 1.70 (3 H, d), 3.93 (2 H, br, d), 4.38 (O-H), 5.53 (2 H, m) p.p.m.

Preparation of (E)-brombut-2-ene (crotyl bromide)

A 50% solution of PBr_3 (36 g, 0.14 mol) in dry ether was added dropwise to a stirred solution of crotyl alcohol (28.8 g, 0.4 mol) and pyridine (10 g, 126 mmol), in dry ether at 0°C. The resulting solution was stirred at 4°C for 12 hours followed by addition of ice and 1 M H_2SO_4. The ethereal layer was separated, dried ($MgSO_4$) and fractionally distilled to give crotyl bromide (40.5 g, 0.3 mol), b.p. 99-101°C, in 75% yield.

^1H n.m.r. (CCl_4): 1.77 (3 H, d), 3.89 (2 H, d), 5.78 (2 H, m) p.p.m.

Preparation of (E)-hept-2-en-5-yne

Magnesium turnings (2.2 g, 90 mmol) were stirred in dry THF (20 cm^3) during the addition of a solution of ethyl bromide (10 g, 90 mmol) in dry THF (25 cm^3). Propyne was then bubbled for 1 hour, followed by addition of Cu(I)Cl (0.5 g) and a 50% solution of crotyl bromide (5.0 g, 37 mmol) in dry THF. After stirring for 12 hours at RT, 15% NH_4Cl (aq.) was added (sufficient to dissolve the ppt.) and the solution was extracted with ether (3 x 50 cm^3). The ethereal layer was dried ($MgSO_4$), filtered and distilled to give (E)-hept-2-en-5-yne (2.3 g, 24.5 mmol) b.p. 120-122°C, in 66% yield.

^1H n.m.r. (CCl_4): 1.68 (3 H, H-1, d), 1.78 (3 H, H-7, m), 2.75 (2 H, H-4, br, m), 5.34 (1 H, H-3, dt), 5.60 (1 H, H-2, dq) p.p.m.

Preparation of (E,Z)-hepta-2,5-diene

(E)-hept-2-en-5-yne (2.0, 32 mmol), quinoline (0.5 g) and Lindlar catalyst (0.5 g) were stirred under hydrogen, in hexadecane (12 cm^3). When uptake ceased the catalyst was removed by filtration through celite, and fractional distillation gave (E,Z)-hepta-2,5-diene (1.9 g, 20 mmol), b.p. 95-97°C, in 92% yield. G.l.c. analysis

($AgNO_3$/tetraethyleneglycol 50% w/w on chromosorb WHP 100/200) indicated 95% (E,Z), 5% (E,E). R = 0.81 relative to benzene (1).
^1H n.m.r. (CCl_4): 1.60 (3 H, H-1, d), 1.62 (3 H, H-7, d), 2.78 (2 H, H-4, dd), 5.33 (4 H, m) p.p.m.
I.r. (film): 3023 (s, sh), 2960 (s), 2925 (s), 2862 (m), 1655 (w), 1453 (m), 1400 (w, sh), 1378 (w), 960 (s), 680 (m) cm^{-1}.

2.2.3 Synthesis of (Z,Z)-hepta-2,5-diene

Preparation of but-2-yn-1-ol

Ethylmagnesiumbromide (0.23 mol) was generated by reaction of ethylbromide (25 g, 0.23 mol) with magnesium (5.6 g, 0.23 mol) in dry ether (25 cm^3). Propyne was then bubbled into the solution for 40 minutes, followed by formaldehyde gas (14 g, 0.46 mol), (prepared by heating paraformaldehyde at 200°C). After stirring for 12 hours at RT, 2 M H_2SO_4 (50 cm^3) was added, the ethereal layer was separated, washed with 2 M H_2SO_4 (30 cm^3) and 10% Na_2CO_3 (aq.) (2 x 25 cm^3), and finally dried ($MgSO_4$). Concentration and distillation gave but-2-yn-1-ol (5.1 g, 72.8 mmol), b.p. 38-40°C (14 mm), in 32% yield.
^1H n.m.r. (CCl_4): 1.83 (3 H, t), 3.00 (O-H), 4.22 (2 H, q) p.p.m.

Preparation of 1-bromobut-2-yne

But-2-yn-1-ol (5.0 g, 71.4 mmol) and dry pyridine (5 g) were dissolved in dry ether (50 cm^3) and stirred at 0°C during the dropwise addition of a 50% ethereal solution of PBr_3 (7.0 g, 25.8 mmol). The solution was stirred at 4°C for 12 hours, followed by addition of ice and 2 M H_2SO_4. The ethereal layer was separated, washed with 10% Na_2CO_3 (aq.), dried and distilled to give a yellow brown oil (7 g) which was re-distilled to give 1-bromobut-2-yne (6.1 g, 39.9 mmol),

b.p. 48-50°C (20 mm), in 56% yield.

^{1}H n.m.r. (CCl_4): 1.89 (3 H, t, J 2.3 Hz), 3.81 (2 H, q) p.p.m.

Preparation of hepta-2,5-diyne

Ethylmagnesium bromide (67.6 mmol) was generated from ethyl bromide (7.4 g, 67.6 mmol) and magnesium (1.65 g, 67.6 mmol) in dry THF (25 cm^3). Propyne was bubbled into the reaction mixture for 40 minutes, followed by addition of Cu(I)Cl (0.5 g) and a 50% solution of 1-brombut-2-yne (4.5 g, 33.8 mmol) in dry THF. After stirring for 12 hours at RT, ether (50 cm^3) was added followed by 15% NH_4Cl (aq.) (40 cm^3). The ethereal layer was separated, dried ($MgSO_4$), filtered and concentrated (rotary evaporator) to leave a brown oil. Distillation gave hepta-2,5-diyne (2.6 g, 28.3 mmol), b.p. 40-42°C (14 mm), in 85% yield.

^{1}H n.m.r. (CCl_4): 1.74 (2 x 3 H, t, J 2.3 Hz), 2.91 (2 H, sept), p.p.m.

Preparation of (Z,Z)-hepta-2,5-diene

Hepta-2,5-diyne (2.0 g, 21.7 mmol), quinoline (0.5 g) and Lindlar catalyst (0.5 g) were stirred in tetradecane (15 cm^3) under H_2. After 48 hours uptake ceased after only 50% reduction, hence more catalyst (0.5 g) was added and reaction continued to completion. Centrifugation, decantation and distillation gave an orange oil which was re-distilled to give (Z,Z)-hepta-2,5-diene (0.6 g, 6.25 mmol), b.p. 93-95°C, in 29% yield. G.l.c. analysis ($AgNO_3$/tetraethyleneglycol, 50% w/w on chromosorb WHP 100-120) indicated 96% (Z,Z), 4% (E,Z), R = 2 relative to benzene (1).

^{1}H n.m.r. (CCl_4): 1.63 (2 x 3 H, d, J 6.5 Hz), 2.74 (2 H, H-4, t), 5.32 (4 H, m) p.p.m.

I.r. (film): 3020 (s, sh), 2963 (s), 2920 (s), 2860 (m), 1658 (m), 1442 (m), 1400 (m), 1370 (m), 1010 (w), 680 (m) cm^{-1}.

2.2.4 Synthesis of (E,E)-hepta-2,5-diene

Preparation of (E)-hept-5-en-2-yn-1-ol

Ethylmagnesium bromide (0.18 mol) was generated from ethyl bromide (19.8 g, 0.18 mol) and magnesium (4.4 g, 0.18 mol) in dry THF (25 cm^3). A 50% solution of prop-2-yn-1-ol (5.1 g, 91 mmol) in dry THF was then added, followed by Cu(I)Cl (0.5 g), and (E)-1-bromobut-2-ene (12.27 g, 91 mmol) in dry THF (15 cm^3). After stirring for 12 hours at RT, 15% NH_4Cl (aq.) (50 cm^3) was added with ether (50 cm^3). The aqueous layer was separated, extracted with ether (3 x 20 cm^3) and the combined ethereal extracts were dried ($MgSO_4$). Filtration, concentration and distillation gave (E)-hept-5-en-2-yn-1-ol (6.3 g, 57 mmol) b.p. 48-52°C (0.5 mm), in 63% yield.

^1H n.m.r. (CCl_4): 1.70 (3 H, H-7, d), 2.90 (2 H, H-4, m), 3.80 (O-H, sh), 4.19 (2 H, H-1, t), 5.38 (1 H, H-5, dt), 5.63 (1 H, H-6, dq) p.p.m.

Preparation of (E,E)-hepta-2,5-dien-1-ol

A 50% ethereal solution of (E)-hept-5-en-2-yn-1-ol (5.3 g, 48 mmol) was slowly added to a stirred suspension of $LiAlH_4$ (1.87 g, 49 mmol) in dry ether (30 cm^3), under nitrogen. The solution was heated under reflux for 12 hours followed by addition of water (2 cm^3), 15% NaOH (2 cm^3) and water (10 cm^3). The white precipitate was removed by filtration, and concentration, followed by distillation of the filtrate gave (E,E)-hepta-2,5-dien-1-ol (5.0 g, 44.6 mmol), b.p. 93-95°C (14 mm), in 93% yield.

^1H n.m.r. (CCl_4): 1.68 (3 H, H-7, d), 2.69 (2 H, H-4, t), 3.40 (O-H), 3.98 (2 H, H-1, d), 5.40 (2 H, H-5 and H-6, m), 5.57 (2 H, H-2 and H-3, m) p.p.m.

Preparation of (E,E)-1-bromo-2,5-heptadiene

A 50% ethereal solution of PBr_3 (5.0 g, 18.5 mmol) was added dropwise to a stirred solution of (E,E)-hepta-2,5-dien-1-ol (6.0 g, 54 mmol) and pyridine (5 g), in dry ether (30 cm^3) at 0°C. The solution was stirred at 4°C for 12 hours, followed by addition of ice and 2 M H_2SO_4. The ethereal layer was separated, washed with 10% Na_2CO_3 (sq.) (25 cm^3), dried ($MgSO_4$), filtered, concentrated and distilled to give (E,E)-1-bromohepta-2,5-diene (6.3 g, 36 mmol), b.p. 88-91°C (12 mm) in 67% yield.

^1H n.m.r. (CCl_4): 1.63 (3 H, H-7, d), 2.72 (2 H, H-4, t), 3.85 (2 H, H-1, d), 5.36 (2 H, H-5 and H-6, m), 5.65 (2 H, H-2 and H-3, m) p.p.m.

Preparation of (E,E)-hepta-2,5-diene

A 50% solution of (E,E)-bromohepta-2,5-diene (6.0 g, 34.3 mmol) in dry THF was added dropwise to a stirred suspension of $LiAlH_4$ (1.3 g, 34.3 mmol) in dry THF (25 cm^3), under N_2. After 1 hour at 65°C, water (2 cm^3), 15% NaOH (2 cm^3) and water (10 cm^3) was added and the resulting precipitate was removed by filtration. The ethereal layer was dried ($MgSO_4$), filtered and fractionally distilled to give (E,E)-hepta-2,5-diene (2.5 g, 26 mmol) b.p. 95-97°C, in 76% yield. G.l.c. analysis ($AgNO_3$/tetraethyleneglycol, 50% w/w on chromosorb WHP 100-120) indicated 96% (E,E)-isomer, R = 0.52 relative to benzene (1), and 4% (E,Z)-isomer.

^1H n.m.r. (CCl_4): 1.63 (6 H, H-1, d, J 6.5 Hz), 2.60 (2 H, H-4, t), 5.35 (4 H, m) p.p.m.

I.r. (film): 3025 (m, sh), 2960 (s), 2918 (s), 2880 (m), 1452 (m), 1435 (m), 1378 (m, sh), 1070 (m), 960 (s) cm^{-1}.

2.3 SYNTHESIS OF HEXA-1,4- AND HEPTA-2,5-DIENOLS

2.3.1 (E,E)-hepta-2,5-dien-4-ol

Preparation of (E)-hepta-2-en-5-yn-4-ol

Ethylmagnesium bromide (0.2 mol) was generated in dry THF (20 cm^3) from ethyl bromide (22.4 g, 0.205 mol) and magnesium (5.0 g = 0.2 mol). Propyne was then bubbled into the resulting solution for 40 minutes, followed by addition of a 50% solution of (E)-but-2-enal (9.56 g, 0.136 mol) in dry THF. After stirring for 4 hours at RT, 15% NH_4Cl (aq.) (50 cm^3) was added. The aqueous phase was separated, washed with ether (3 x 20 cm^3), and the combined ethereal extracts were dried ($MgSO_4$), filtered, concentrated and distilled to give (E)-hept-2-en-5-yn-4-ol (13.7 g, 0.125 mol), b.p. 85-88°C (14 mm), in 91% yield.
^1H n.m.r. (CCl_4): 1.74 (3 H, H-1, d, J 6.6 Hz), 1.86 (3 H, H-7, d, J 2.2 Hz), 3.10 (O-H, br), 4.65 (1 H, H-4, d, br), 5.50 (1 H, H-3, dd, $H_{2,3}$ 16 Hz, $J_{3,4}$ 6 Hz), 5.77 (1 H, H-2, dq) p.p.m.

Preparation of (E,E)-hepta-2,5-dien-4-ol

$LiAlH_4$ (2.0 g, 52 mmol) was stirred in dry ether (25 cm^3), under nitrogen, during the dropwise addition of a 50% ethereal solution of (E)-hept-2-en-5-yn-4-ol (7.0 g, 64 mmol). The reaction was heated to reflux for 12 hours and then quenched with H_2O (10 cm^3), 15% NaOH (aq.) (10 cm^3) and more water (20 cm^3). Filtration, followed by drying ($MgSO_4$) and concentration (rotary evaporator), gave a pale yellow oil which was distilled to give (E,E)-hepta-2,5-dien-4-ol (6.5 g, 58 mmol), b.p. 72-74°C (14 mm), in 91% yield.
^1H n.m.r. (CCl_4): 1.70 (2 x 3 H, d, J 6 Hz), 3.45 (O-H, d), 4.36 (1 H, H-4, t), 5.47 (4 H, m, $J_{2,3}$ 16 Hz, $J_{3,4}$ 6 Hz) p.p.m.

I.r. (film): 3325 (s, br) [2.5% soln. in CCl_4 moves to 3615 (m, sh)], 3025 (m), 2960 (s), 2930 (s), 2915 (s), 1668 (m), 1453 (s), 1380 (m, sh), 1055 (m), 965 (s), 924 (m) cm^{-1}.

2.3.2 Synthesis of (E,Z)-hepta-2,5-dien-4-ol

Preparation of α,β-dibromobutyric acid

A 50% solution of bromine (56 g, 0.35 mol) in dichloromethane was added dropwise to a solution of (E)-but-2-enoic acid (30 g, 0.348 mol) in CH_2Cl_2, at 0°C, with exclusion to light. The solution was stirred at RT overnight and the solvent and excess bromine were removed under reduced pressure to leave a yellow crystalline solid. Recrystallisation gave α,β-dibromobutyric acid (55 g, 0.33 mol), m.p. 85-86°C, in 88% yield.

^1H n.m.r. (CCl_4): 1.93 (3 H, H-3, d), 4.35 (2 H, H-1 and H-2, m), 12.10 (O-H) p.p.m.

Preparation of (Z)-1-bromopropene

α,β-Dibromobutyric acid (60 g, 0.244 mol) was dissolved in cyclohexanone (50 cm^3) and stirred during the addition of sodium bicarbonate (102.6 g, 1.22 mol). The resulting suspension was heated at 100°C for 8 hours, and then fractionally distilled (fraction 40°C-90°C collected). Contaminating cyclohexanone was removed as the semicarbazide and distillation with exclusion to light gave (Z)-1-bromopropene (14.2 g, 0.117 mol), b.p. 58-60°C, in 48% yield.

^1H n.m.r. (CCl_4): 1.76 (3 H, H-3, d), 6.14 (2 H, H-1 and H-2, m) p.p.m.
I.r. (thin film): 3080 (m), 3010 (m), 2918 (m), 1640 (s), 1444 (m), 1370 (m), 1300 (s), 932 (s), 660 (s) cm^{-1}.

Preparation of (E,Z)-hepta-2,5-dien-4-ol

(i) (E)-hept-2-en-5-yn-4-ol (2.0 g, 18.2 mmol), quinoline (0.3 g), and Lindlar catalyst (0.3 g) were stirred in dry methanol (25 cm^3) under H_2. When uptake ceased the catalyst was removed by filtration through celite and the filtrate was concentrated and distilled to give (E,Z)-hepta-2,5-dien-4-ol (1.6 g, 14.3 mmol), b.p. 80-82°C (16 mm), in 79% yield.

^1H n.m.r. (CCl_4): 1.65 (3 H, H-1, d), 1.68 (3 H, H-7, d), 3.16 (O-H, br), 4.75 (1 H, H-4, t), 5.41 (4 H, m, $J_{2,3}$ 15 Hz, $J_{5,6}$ 10.5 Hz), p.p.m.

I.r. (film): 3320 (s, br), [2.5% in CCl_4 moves to 3620 (m, sh)], 3020 (s, sh), 2960 (s), 2918 (s), 2855 (s), 1658 (m), 1445 (m), 1375 (w), 1068 (w), 1015 (s), 960 (s), 918 (w), 680 (m) cm^{-1}.

(ii) Magnesium (0.9 g, 37 mmol), iodine (20 mg) and (Z)-1-bromopropene (6 drops) were heated in dry THF (15 cm^3) until reaction commenced. A 50% solution of (Z)-1-bromopropene (4.5 g, 37 mmol) in dry THF was then added dropwise, followed by Cu(I)Cl (0.2 g) and a 50% solution of (E)-but-2-enal (2.5 g, 37 mmol) in dry THF. After stirring for 5 hours at RT, 15% NH_4Cl (aq.) (25 cm^3) was added, the aqueous phase was separated and washed with ether (3 x 10 cm^3) and the combined ethereal extracts were dried ($MgSO_4$). Concentration and distillation gave (E,Z)-hepta-2,5-dien-4-ol (2.1 g, 18.75 mmol), b.p. 76-77°C (14 mm), in 50% yield.

^1H n.m.r. and i.r. were identical to the sample prepared by Lindlar reduction.

2.3.3 Synthesis of (Z,Z)-hepta-2,5-dien-4-ol

Preparation of hepta-2,5-diyn-4-ol

Propynylmagnesium bromide (0.21 mol) was generated as

described in the preparation of (E)-hept-2-en-5-yne. Cu(I)Cl (0.25 g) was added, followed by a 50% solution of ethyl formate (7.4 g, 0.1 mol) in dry THF. The reaction mixture was stirred for 12 hours and then quenched with 10% NH_4Cl (aq.) solution. The aqueous layer was separated, extracted with ether (2 x 25 cm^3), and the ethereal extracts combined, filtered and concentrated to give yellow crystals. These were re-crystallised from ether/pentane to give hepta-2,5-diyn-4-ol (6.25 g, 57.9 mmol), in 61% yield, as colourless needleshaped crystals, m.p. 103-104°C.

^1H n.m.r. (d^6 acetone: 1.80 (2 x 3 H, d, J 2.3 Hz), 4.73 (O-H, d, J 6 Hz), 5.00 (1 H, H-4, m) p.p.m.

Preparation of (Z,Z)-hepta-2,5-dien-4-ol

(i) Hepta-2,5-diyn-4-ol (1.1 g, 10.2 mmol), quinoline (0.3 g) and Lindlar catalyst (0.5 g) were stirred in dry methanol (20 cm^3) under H_2. When reaction was complete the catalyst was removed by filtration and the filtrate was concentrated and distilled to give (Z,Z)-hepta-2,5-dien-4-ol (0.8 g, 7.2 mmol), b.p. 85-87°C (16 mm), in 71% yield.

^1H n.m.r. (CCl_4): 1.70 (2 x 3 H, H-1, d), 2.73 (O-H, br), 5.13 (1 H, H-4, t), 5.39 (4 H, m, $J_{2,3}$ 10.5 Hz) p.p.m.

I.r. (film): 3320 (s, br) [2.5% CCl_4 solution 3610 (m, sh)], 3020 (s, sh), 2964 (s), 2915 (s), 2860 (m), 1660 (m), 1443 (m), 1364 (w), 1293 (w), 1023 (s), 952 (m), 923 (m), 680 (m) cm^{-1}.

(ii) Magnesium (1.65 g, 68 mmol), iodine (20 mg) and (Z)-1-bromopropene (5 drops) were heated in dry THF (15 cm^3). When reaction commenced a 50% solution of (Z)-1-bromopropene (8.2 g, 68 mmol) in dry THF was added dropwise. This was followed by addition of a 50% solution of ethyl formate (2.45 g, 33 mmol) in dry THF and stirring at RT for 4 hours. 15% NH_4Cl (aq.) (15 cm^3) was then added and

the ethereal layer was separated. The aqueous layer was extracted with ether (2 x 20 cm^3) and the combined ethereal extracts were dried ($MgSO_4$), filtered, concentrated and distilled to give (Z,Z)-hepta-2,5-dien-4-ol (1.84 g, 13.2 mmol) b.p. 84-86°C (14 mm) in 40% yield. ^1H n.m.r. and i.r. were identical to those of the sample prepared by Lindlar reduction.

2.3.4 Synthesis of (E)- and (Z)-hexa-1,4-dien-3-ol

Preparation of (Z)-hexa-1,4-dien-3-ol

(Z)-propenylmagnesium bromide (23.6 mmol), prepared by reacting magnesium (0.575 g, 23.6 mmol) with (Z)-1-bromopropene (2.86 g, 23.6 mmol) in dry THF (15 cm^3), was stirred at RT, during the addition of a 50% solution of prop-2-enal (1.33 g, 23.6 mmol) in dry THF. After 6 hours, 15% NH_4 NH_4Cl (aq.) (20 cm^3) was added, the aqueous phase was separated, extracted with ether (2 x 10 cm^3) and the combined ethereal extracts were dried ($MgSO_4$). Filtration, evaporation and distillation gave (Z)-hexa-1,4-dien-3-ol (0.92 g, 9.5 mmol), b.p. 56-60°C (14 mm), in 40% yield.
^1H n.m.r. ($CDCl_3$): 1.70 (3 H, H-6, d), 2.20 (O-H, br), 4.98 (1 H, H-3, dd), 5.10 (1 H, H-1, d, J 10 Hz), 5.30 (1 H, H-1, d, J 17 Hz), 5.43 (1 H, H-4, m), 5.60 (1 H, H-5, m), 5.90 (1 H, H-2, m) p.p.m.

Preparation of (E)-hexa-1,4-dien-3-ol

Magnesium (1.1 g, 47 mmol), vinyl bromide (5-6 drops), and iodine (20 mg) were warmed in dry THF (15 cm^3) until reaction was initiated. A 50% solution of vinyl bromide (5.0 g, 46.7 mmol) in dry THF was added dropwise and the solution was stirred for 6 hours at RT. 15% NH_4Cl (aq.) (15 cm^3) was then added, the aqueous layer

was separated, washed with ether (2 x 20 cm^3) and the combined ethereal extracts were dried ($MgSO_4$). Filtration, concentration and distillation gave (E)-hexa-1,4-dien-3-ol (3.5 g, 35.7 mmol) b.p. 45-48°C (14 mm) in 77% yield.

^1H n.m.r. (CCl_4): 1.71 (3 H, d), 2.20 (O-H, br), 4.45 (1 H, H-3, dd), 5.04 (1 H, H-1, d, J 10 Hz), 5.19 (1 H, H-1, d, H 17 Hz), 5.42 (1 H, H-4, dd), 5.60 (1 H, H-5, m), 5.80 (1 H, H-2, m) p.p.m.

2.3.5 Synthesis of C6 and C7 Acetoxydienes

(i) Preparation of (Z,Z)-4-acetoxyhepta-2,5-diene

(Z,Z)-hepta-2,5-dien-4-ol (0.2 g, 1.8 mmol) and acetic anhydride (0.367 g, 3.6 mmol) were dissolved in dry pyridine (10 cm^3) and stirred at RT for 6 hours. The solution was poured into water (20 cm^3), acidified with 5 M HCl (aq.) and extracted with ether (2 x 25 cm^3). The ethereal extracts were washed with 5 M HCl (aq.), 10% Na_2CO_3 (aq.), dried ($MgSO_4$), concentrated and distilled to give (Z,Z)-4-acetoxy-2,5-heptadiene (0.23 g, 1.49 mmol), b.p. 50-52°C (1 mm) in 85% yield.

^1H n.m.r. (CCl_4): 1.75 (2 x 3 H, H-1, d), 1.94 (3 H, s), 5.42 (2 x 2 H, m, $J_{2,3}$ 10.5 Hz), 6.22 (1 H, H-4, t) p.p.m.

I.r. (film): 3020 (m), 2965 (m), 2920 (m), 2863 (w), 1733 (s), 1660 (w), 1440 (m), 1367 (s), 1233 (s), 1010 (s), 940 (m), 920 (m), 895 (w), 720 (m) cm^{-1}.

(ii) (E,E)-4-acetoxyhepta-2,5-diene

Procedure: as in Part (i), 77% yield, b.p. 50-52 °C (1 mm).

^1H n.m.r. (CCl_4): 1.70 (2 x 3 H, H-1, d), 1.95 (3 H, s), 5.55 (4 H, m, $J_{2,3}$ 15 Hz and H-4, t) p.p.m.

I.r. (film): 3035 (m), 2965 (s), 2940 (s), 2920 (s), 2860 (s), 1733 (s), 1670 (m), 1450 (s), 1370 (s), 1233 (s), 1050 (m), 1012 (s), 963 (s), 945 (s), 895 (s) cm^{-1}.

(iii) (E,Z)-4-acetoxyhepta-2,5-diene

Procedure: as in Part (i), yield 70%, b.p. 45-47°C (0.5 mm).
^1H n.m.r. (CCl_4): 1.70 (3 H, H-1, d), 1.72 (3 H, H-7, d), 1.95 (3 H, s), 5.50 (4 H, m, $J_{2,3}$ 15 Hz, $J_{5,6}$ 10.5 Hz), 5.85 (1 H, H-4, t) p.p.m.
I.r. (thin film): 3025 (s), 2965 (s), 2920 (s), 2875 (m), 1733 (s), 1673 (m, sh), 1440 (s), 1368 (s), 1230 (s), 1010 (s), 944 (s), 895 (m), 740 (m) cm^{-1}.

(iv) (E)-3-acetoxyhexa-1,4-diene

Procedure: as in Part (i), yield 84%, b.p. 40-42°C (1 mm).
^1H n.m.r. (CCl_4): 1.85 (3 H, H-6, d, J 6.5 Hz), 1.98 (3 H, s), 5.14 (1 H, H-1, d, J 10.5 Hz), 5.23 (1 H, H-1, d, J 17 Hz), 5.40 (1 H, dd, $J_{4,5}$ 15 Hz), 5.58 (1 H, H-3, t), 5.75 (2 H, H-2 and H-5, m) p.p.m.
I.r. (film): 3090 (w), 3020 (w), 2930 (m), 1735 (s), 1438 (m), 1370 (s), 1230 (s), 1010 (s), 960 (s), 923 (s) cm^{-1}.

(v) (Z)-3-acetoxyhexa-1,4-diene

Procedure: as in Part (i), yield 97%, b.p. 38-40°C (1 mm).
^1H n.m.r. (CCl_4): 1.74 (3 H, H-6, d, J 6.5 Hz), 2.00 (3 H, s), 5.10 (1 H, H-1, d, J 10.5 Hz), 5.22 (1 H, H-1, d, J 17 Hz), 5.33 (1 H, H-4, dd, $J_{4,5}$ 10.5 Hz), 5.70 (2 H, H-2 and H-5, m), 5.94 (1 H, H-3, t) p.p.m.

2.4 SYNTHESIS OF π-ETHYLENE COMPLEXES OF Rh(I)

Preparation of di-μ-chlorotetrakis(ethylene)dirhodium(I)[37]

Rhodium trichloride-trihydrate (5.0 g, 19 mmol) was dissolved in distilled water (7.5 cm^3) and diluted with methanol (125 cm^3). The solution was then stirred under ethylene for 24 hours. The orange-brown precipitate was removed by filtration and the pH of the mother liquor was adjusted to ∿ 2.5 by addition of 20% NaOH. Continued stirring under ethylene gave more product and the combined precipitates were dried in vacuum (15 mm) to give di-μ-chlorotetrakis-(ethylene)dirhodium(I), (2.9 g, 7.5 mmol) in 78% yield.

^1H n.m.r. (CCl_4): 3.10 p.p.m.

I.r. (KBr disc): 3050 (w), 1620 (w), 1425 (m), 1213 (m), 990 (s) cm^{-1}.

2.4.1 Preparation of 2,4-pentanedionatobis(ethylene)rhodium(I)[37] [Rh(I)pd]

Di-μ-chlorotetrakis(ethylene)dirhodium(I) (3.7 g, 9.5 mmol), 2,4-pentanedione (2.0 g, 20 mmol) and diethylether (35 cm^3) were stirred under nitrogen at -20°C. A solution of potassium hydroxide (7.2 g, 129 mmol) in distilled water (25 cm^3) was then added over 15 min. The resulting solution was stirred at -10°C for 30 minutes and then diluted with ether. The ethereal layer was separated and the aqueous phase extracted with ether (3 x 20 cm^3). The combined ethereal extracts were dried ($MgSO_4$) filtered and concentrated whereupon crystallisation occurred. The solution was cooled (-78°C) and filtered to give orange crystals of 2,4-pentanedionatobis(ethylene)-rhodium(I) (3.2 g, 12.4 mmol), m.p. 144-145°C, in 65% yield.

^1H n.m.r. ($CDCl_3$: 1.97 (2 x 3 H, s), 2.92 (2 x 4 H, s, br), 5.33 (1 H, s) p.p.m.

^{1}H n.m.r. (d^{6} benzene): 1.72 (2 x 3 H, s), 2.92 (2 x 4 H, s, br), 5.05 (1 H, s) p.p.m.

^{13}C n.m.r. ($CDCl_3$): 2.887 (C-1), 58.91 (d, J Rh-C 13.5 Hz), 98.81 (C-2), 186.52 (C-3) p.p.m.

I.r. (nujol mull): 3060 (w, shoulder), 1573 (m, shoulder), 1550 (shoulder), 1518 (s), 1374 (s), 1270 (m), 1225 (w), 1020 (w), 990 (w) cm^{-1}.

MS (EI): m/z 258 (M^{+}, 19.9%), 230 (39, 6%), 202 (48.3%), 100 (97.1%), 85 (100%).

2.4.2 Preparation of 1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis(ethylene)rhodium(I) [E_2Rh(I)hfpd]

Ethyltrifluoroacetate (7.2 g, 50 mmol) was dissolved in dry ether and stirred with sodium methoxide (2.74 g, 50 mmol) under nitrogen. Trifluoroacetone (5.6 g, 50 mmol) was added dropwise and the solution was heated to reflux for 2 hours. Removal of solvent in vacuum gave a white powder which was re-crystallised from ether-pentane, to give sodium 1,1,1,5,5,5-hexafluoro-2,4-pentanedionate (10 g, 43 mmol) in 86% yield. This sodium salt (2.5 g, 10.7 mmol) was dissolved in dry ether (25 cm^3) and stirred with di-μ-chlorotetrakis(ethylene)dirhodium(I) (2.1 g, 5.4 mmol), under N_2, for 4 hours. Centrifugation, followed by decantation and evaporation gave a red-brown residue which was sublimed (40-60°C, 0.05 mm) to give 1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis(ethylene)-rhodium(I) (2.5 g, 6.7 mmol) m.p. 44-45, as red prisms, in 62.5% yield.

^{1}H n.m.r. (d^{6} benzene): 2.69 (2 x 4 H, br, s), 5.80 (1 H, s),

(CCl_4): 3.14 (2 x 4 H, br, s), 6.15 (1 H, s),

($CDCl_3$): 3.15 (2 x 4 H, br, s), 6.14 (1 H, s) p.p.m.

I.r. (CCl_4): 3133 (w), 3075 (m, sh), 3015 (m, sh), 1624 (s, sh), 1607 (s, sh), 1555 (m, sh), 1453 (s, sh), 1350 (m, sh), 1265 (s), 1205 (s), 1156 (s), 1100 (s, sh), 993 (m, sh) cm^{-1}.

MS (EI): m/z 366 (M^+ 37.0), 338 (53.6%), 309.5 (100%).

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CHAPTER 3

COMPLEXATIONS TO AND REARRANGEMENTS INDUCED BY RHODIUM(I)

3.1 INTRODUCTION AND DISCUSSION

In contrast to rhodium(I) complexes of simple olefins[1] and conjugated dienes[2] there are few reports of rhodium(I) complexes of "skipped" dienes. Indeed, at one time it was believed that bidentate complexes of substituted penta-1,4-dienes would be very difficult to obtain[3]. This is because of the considerable angle strain that would need to be accommodated to achieve sufficient overlap of orbitals between metal and olefin[4]. However, since then rhodium(I) complexes of penta-1,4-diene and cyclohexa-1,4-diene have been prepared[5] and the products of their thermally induced isomerisation identified[6]. The work herein describes the preparation of some novel rhodium(I) complexes of "skipped" dienes, dienols and their derived acetates.

The structures of these complexes have been assigned with the aid of ^{1}H n.m.r. spectroscopy, mass spectrometry, and literature precedents[7]. It is known that ethylene is displaced from 2,4-pentanedionatobis(ethylene)rhodium(I), [E_2Rh(I)pd] by other olefins, in a bimolecular reaction involving a five co-ordinate intermediate[8]. (E,E)-hepta-2,5-diene reacted with E_2Rh(I)pd and E_2Rh(I)hfpd, by such a mechanism to give bidentate complexes, which in the case of Rh(I)hfpd is crystalline (m.p. 55-57°C) and can be sublimed.

The complex is believed to have a structure similar to that shown in Fig. 3.1.A, although unlike the bis(ethylene) complex, molecular models indicate that the co-ordinated double bonds are not quite perpendicular to the plane of the pentanedionato ring[9].

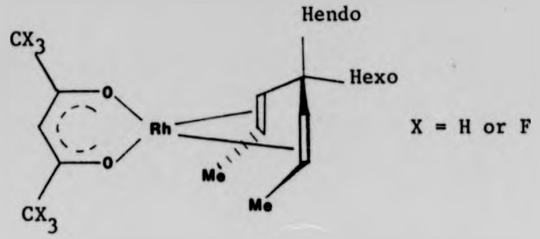


Fig. 3.1.A

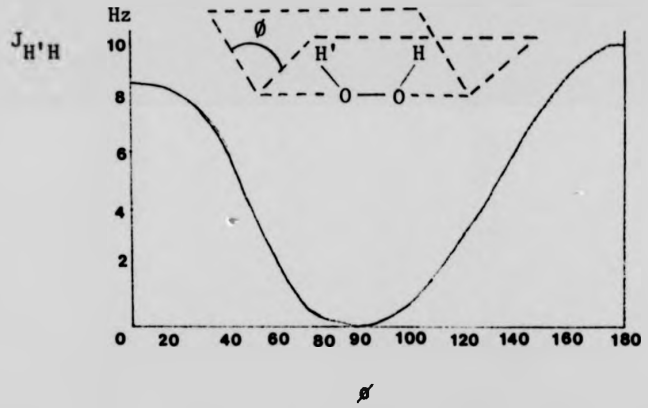
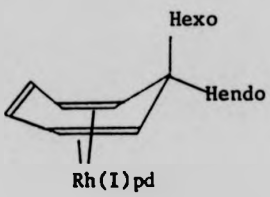


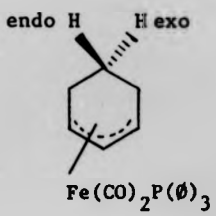
Fig. 3.1.B



^{1}H n.m.r. (d.^{6}benzene)

Hexo δ 2.74 J^{103}Rh-H 4 Hz

Hendo δ 3.56 J^{103}Rh-H 1 Hz



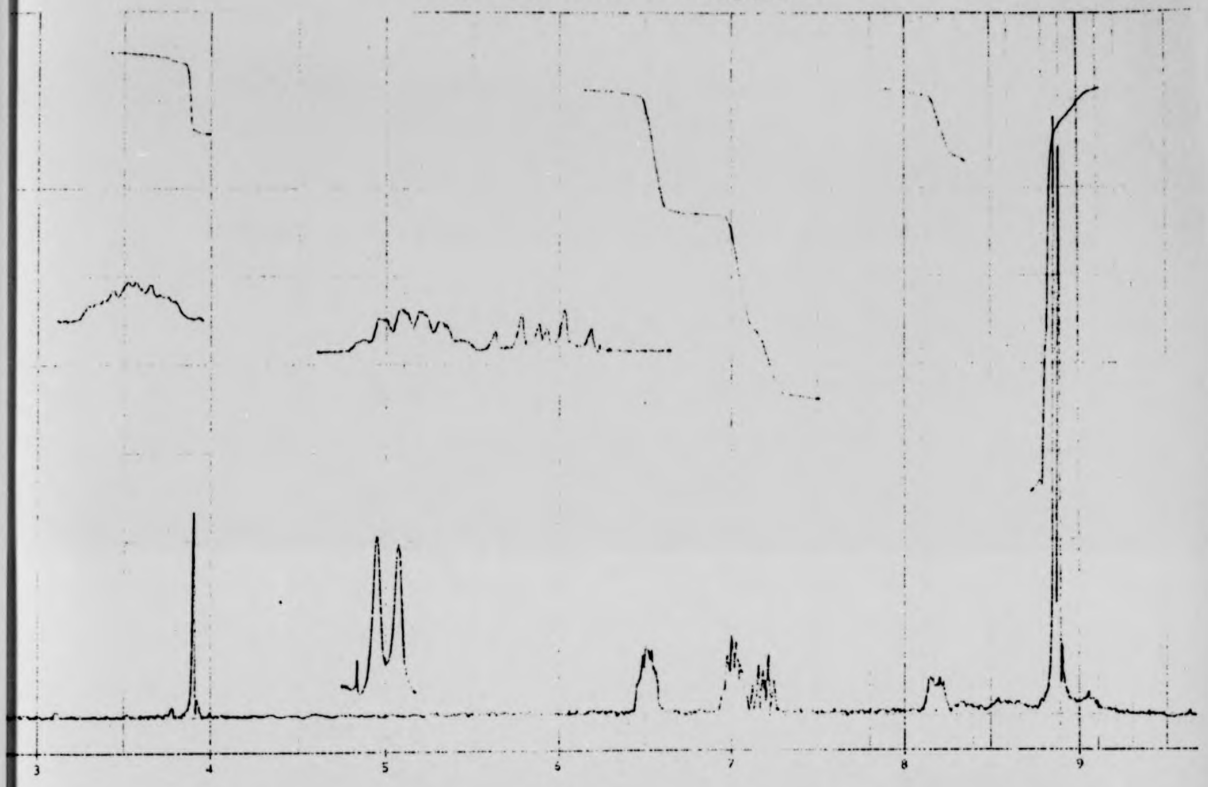
^{1}H n.m.r. (d.^{6}acetone)

Hexo δ 1.89

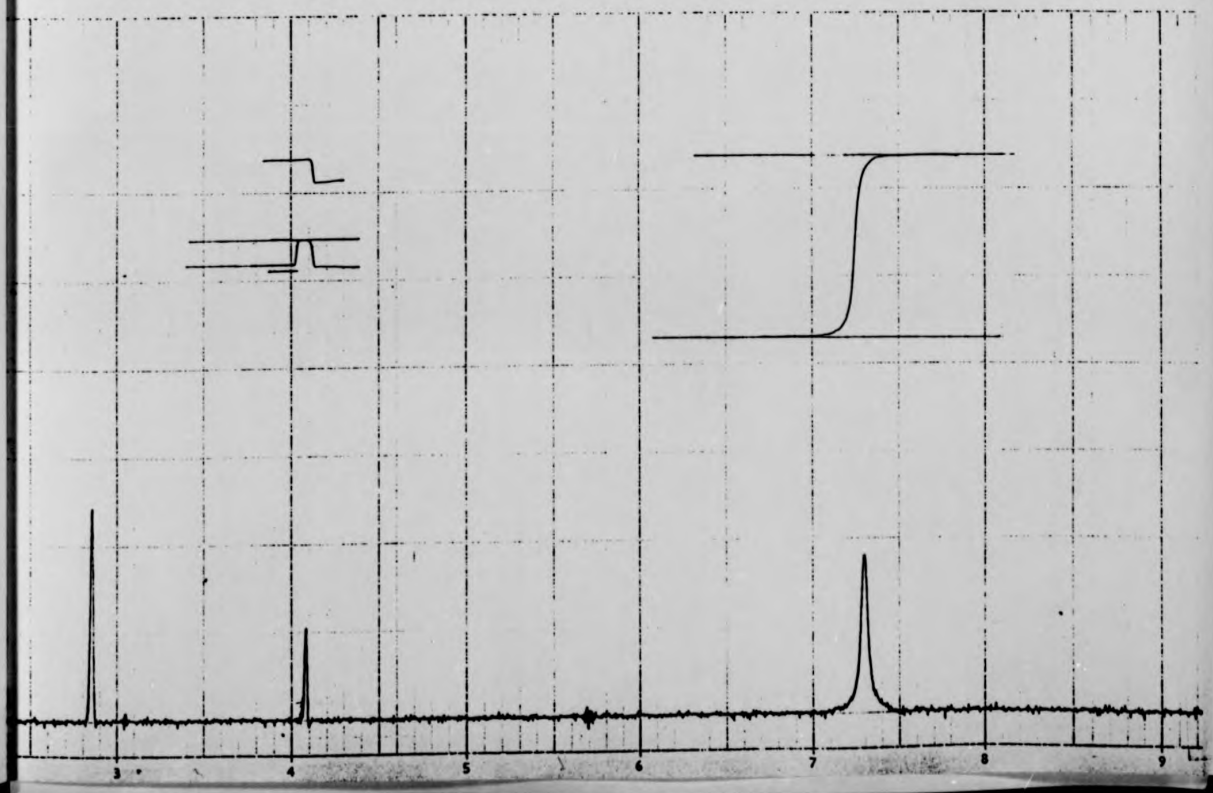
Hendo δ 2.75

Fig. 3.1.C

^{1}H n.m.r. spectrum of (E,E)-hepta-2,5-diene-Rh(I)hfpd
cf. Sec. 3.2.1 for assignments



^{1}H n.m.r. spectrum of Rh(I)hfpd *cf.* Sec. 2.4.2 for assignments



The proposed structure is supported by ^{1}H n.m.r. which indicates that on complexation the methyl groups experience a shielding effect and are moved upfield (δ 1.63 free, δ 1.02 co-ordinated). Selective irradiation of this resonance causes simplification of the signal at δ 2.89 (2 H-2). Co-ordination renders the protons at C-4 non-equivalent. They appear at δ 1.72 and δ 2.70 and have been assigned H-4 exo and H-4 endo respectively, with the aid of molecular models and literature precedents[7,10].

The dihedral angle (Ø) between H-4 exo and H-3 approaches 90^{o} and hence any coupling between these protons will be small. This is confirmed by ^{1}H n.m.r. spectroscopy because H-4 exo appears basically as a doublet (Jgem 12.8 Hz), with minor coupling to H-3 and ^{103}Rh. The dihedral angle (Ø) between H-4 endo and H-3 is about 20^{o} and this proton appears as a double triplet (Jgem 12.8 Hz, Jvic 7.2 Hz) with negligible coupling to ^{103}Rh. These observations are in complete agreement with literature examples (Fig. 3.1.C)[7].

Penta-1,4-diene was also reacted with both $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ to give crystalline complexes which were characterised by ^{1}H n.m.r., i.r. and mass spectrometry. They were found to be monomeric complexes and are thought to possess a similar structure to the (E,E)-hepta-2,5-diene complexes. The Rh(I)pd-pentadiene complex exhibited signals at δ 1.70 and δ2.83 (H-3 exo and H-3 endo respectively), and doublets at δ2.38 (H-1, *Jtrans* 12.4 Hz) and δ 2.38 (H-1, *Jtrans* 12.4 Hz) and δ 2.73 (H-1, *Jcis* 8 Hz). These couplings are significantly lower than those observed in uncoordinated terminal olefins and reflect the increase in bond length between C-1 and C-2 which occurs as a consequence of rhodium-olefin bond formation[11]. The ^{1}H n.m.r. spectrum of the Rh(I)hfpd-penta-1,4-diene complex shows a sharp resonance for the

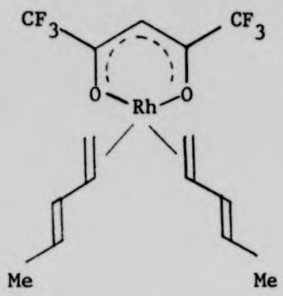
methine of the β-diketone, but only broad signals for the co-ordinated penta-1,4-diene. This could be explained in terms of a "flipping" of the double bonds between a co-ordinated and an uncoordinated state. To test this possibility (E)-penta-1,3-diene was reacted with $E_2Rh(I)hfpd$.

^1H n.m.r. spectroscopy indicated that after addition of one equivalent of diene a bidentate complex was formed, but the signals were not well resolved, as in the case of penta-1,4-diene. Addition of a second equivalent of diene clearly leads to the formation of a bis(monodentated) diene complex as shown in Fig. 3.1.D.

This does not arise in the reaction between penta-1,3-diene and $E_2Rh(I)pd$, where, even in the presence of excess diene a bidentate complex is formed[2]. For the hexafluoro-2,4-pentanedionato ligand the trifluoromethyl groups reduce the electron density on the metal which is available for back-donation and the rhodium-olefin bond strength will be reduced.

This is in agreement with the results from studies on several β-diketone-rhodium(I) complexes where it was noted that back donation increased in the order $(CF_3,CH_3) < (CH_3,CH_3) < [C-(Me)_3,C-(Me)_3]$[12].

These results are consistent with the idea that in the Rh(I)hfpd complexes of (E)-penta-1,3-diene and penta-1,4-diene the double bonds are undergoing an on-off exchange. For (E)-penta-1,3-diene the two double bonds show a marked difference in their ability to co-ordinate to rhodium(I) and hence, when an excess of diene is added a bis(monodentate) complex is formed in which the monosubstituted double bond is preferentially co-ordinated. This is in agreement with the work of Nelson who isolated the first bis(monodentate)-1,3-diene rhodium(I) complex[2] and confirmed its structure by x-ray crystallography (Fig. 3.1.E)[13].



^{1}H n.m.r. ($CDCl_3$): δ

1.30 (3 H, H-5, d)

2.10 (1 H, H-1 *trans*, d)

2.96 (1 H, H-2, m)

3.29 (1 H, H-1*cis*, d)

5.30 (1 H, H-3, m)

5.46 (1 H, H-4, m)

Fig. 3.1.D

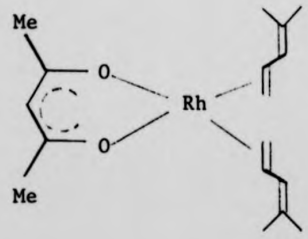


Fig. 3.1.E

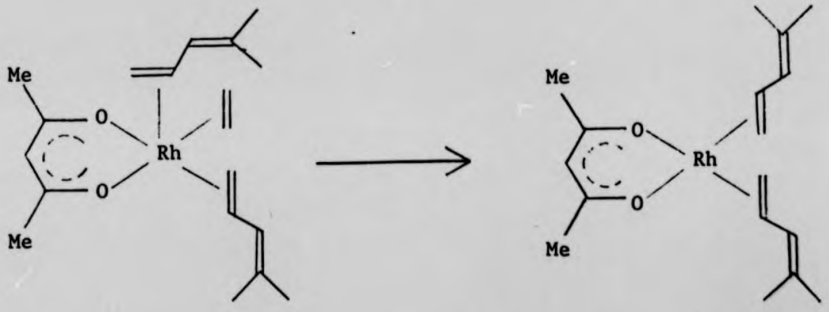


Fig. 3.1.F

2-Methylpenta-2,4-diene reacts with $E_2Rh(I)pd$ to give a bis(monodentate) complex, Fig. 3.1.E. However, (Z)-penta-1,3-diene was found to react with $E_2Rh(I)pd$ to give a bidentate complex indicating that steric interaction between *syn* substituents is not a factor in complex formation. Thus, bis(monodentate) complexation is favoured with 2-methylpenta-2,4-diene because of the different abilities of the two double bonds (one monosubstituted and one trisubstituted) to co-ordinate to Rh(I). This is consistent with the observation that rhodium(I) shows a preference in co-ordination to olefins of mono-substituted > (Z)-disubstituted > gem-disubstituted > trisubstituted > tetrasubstituted[1].

Initial attack of one molecule of 2-methylpenta-2,4-diene leads to a monoethylene complex. The trisubstituted double bond does not co-ordinate well to rhodium(I) and hence before the second molecule of ethylene is displaced the monosubstituted double bond of another molecule of 2-methylpenta-2,4-diene is able to co-ordinate (Fig. 3.1.F). More recently Grigg and co-workers[14] reported the isolation of a monodentate rhodium(I) complex of bis(methallyl) ether, but they were unable to prepare the bis(monodentate) complex.

Consideration of all these observations indicates that the possibility of forming a stable bis(monodentate) diene complex from a potential bidentate diene is enhanced by:

(i) The presence of two double bonds in the molecule which show markedly different abilities to co-ordinate to rhodium(I).

(ii) The presence of an electron withdrawing ligand chelated to the rhodium, e.g. hfpd in preference to pd.

Cyclohexa-1,4-diene was reacted with both $E_2Rh(I)pd$ and

E_2Rh(I)hfpd, to give crystalline complexes, characterised by ^{1}H n.m.r., i.r. and mass spectroscopy. Rhodium(I)cyclopentadienyl complexes of 3-methoxycarbonylcyclohexa-1,4-diene have been shown to possess the structure of Fig. 3.1.H[15].

The two saturated carbon atoms are bent away from the metal, out of the plane containing the four olefinic carbons giving the six-membered ring a boat conformation. This is in complete contrast to the uncomplexed olefins where it is believed that the cyclohexadiene ring is planar[16], and it is highly likely that as a result of the metal-olefin interaction the ring is forced into a boat conformation. This is not unexpected in view of the accepted theories of metal-olefin interaction[17], wherein there may be a contribution from metallocyclopropane structures leading to some sp^3 character at the olefinic carbon atoms.

With the above information in mind, it would seem reasonable to suggest structure Fig. 3.1.J for cyclohexa-1,4-diene complexes of Rh(I)pd and Rh(I)hfpd. In the ^{1}H n.m.r. spectra of these complexes Hexo appears as a double doublet (Jgem 8 Hz, J ^{103}Rh 2.5 Hz). Selective irradiation of the double bond protons caused no change in the multiplicity of the peak showing the absence of any vicinal coupling ($\phi \sim 90^{\circ}$). The ^{103}Rh-Hexo coupling (2.5 Hz) is in agreement with other examples[2,3]. Hendo is a double multiplet, with a geminal coupling (8 Hz) and smaller couplings to vicinal protons and ^{103}Rh(I).

Cycloocta-1,5-diene was reacted with E_2Rh(I)pd and E_2Rh(I)hfpd to give bidentate, monomeric complexes which were fully characterised. Indeed, in this case 1,5-co-ordination seems to be extremely favourable because 1,3- and 1,4-cyclooctadiene-rhodium(I) complexes are known to isomerise to the 1,5-isomer, probably *via* a Rh(III) hydride intermediate[18].

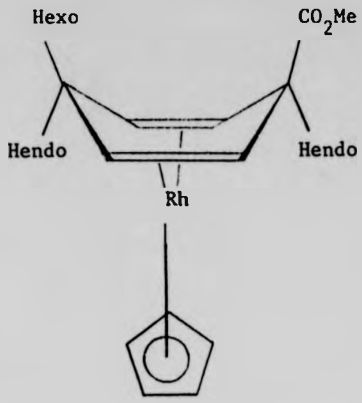


Fig. 3.1.H

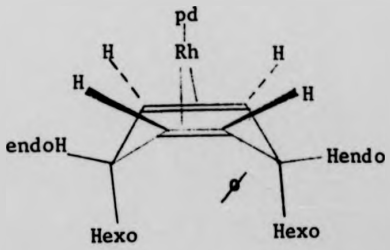


Fig. 3.1.J

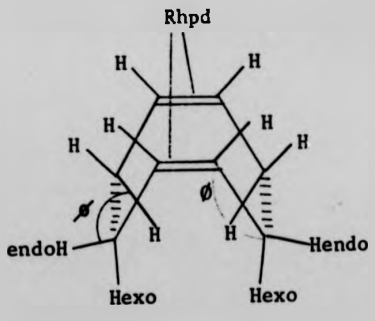
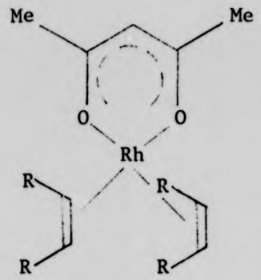


Fig. 3.1.K

The x-ray crystallographic structure of 2,4-pentanedionato (cyclo-octa-1,5-diene) rhodium(I) has been determined[19] and is known to have a structure similar to that shown in Fig. 3.1.K. However, the olefin is slightly twisted such that the complex lacks symmetry. In the ^{1}H n.m.r. spectrum H exo appears as a doublet, coupled only to H endo (Jgem 8 Hz). The dihedral angles (Ø) preclude any further coupling and there is no apparent coupling to ^{103}Rh.

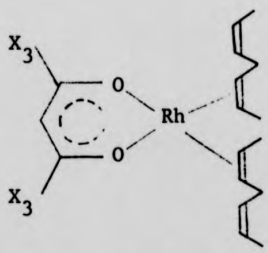
In considering whether (E,Z)- and (Z,Z)-hepta-2,5-diene will co-ordinate to Rh(I) to give stable bidentates other factors besides those already mentioned must be considered. In any (E,Z)-"skipped" diene complex there will be a steric interaction between a *cis* C-1 substituent and a *cis* C-6 substituent. In the case of (E,Z)-hepta-2,5-diene these would be a methyl group and a hydrogen atom. However, it would appear that these steric constraints can be accommodated. Herberhold and co-workers[20] reacted (Z)- and (E)-1,2-dimethoxyethylene with $E_2Rh(I)pd$ and were able to isolate complexes with either one or two ethylenes displaced. More surprisingly they found that the ^{1}H n.m.r. spectrum of the bis[(Z)-1,2-dimethoxyethylene]rhodium(I) complex is temperature dependent. At 90°C the methyl groups appear as a singlet and the olefinic protons as a doublet coupled to ^{103}Rh. On cooling to 50°C the methyl signals are resolved into two singlets and the olefinic protons into two doublets indicating the structure is as shown in Fig. 3.1.L. This rotational isomerism also occurs in bis(propene) complexes of Rh(I)pd[21].

Hence, (E,Z)-hepta-2,5-diene was reacted with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ to give oils which have been assigned as bidentate complexes by ^{1}H n.m.r. spectroscopy. In the Rh(I)hfpd complex



R = OMe

Fig. 3.1.L



X = H or F

Fig. 3.1.G

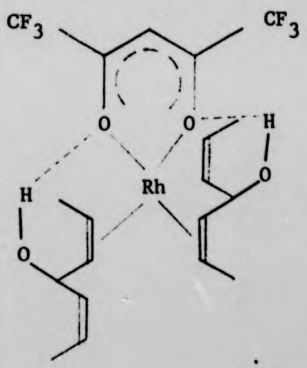
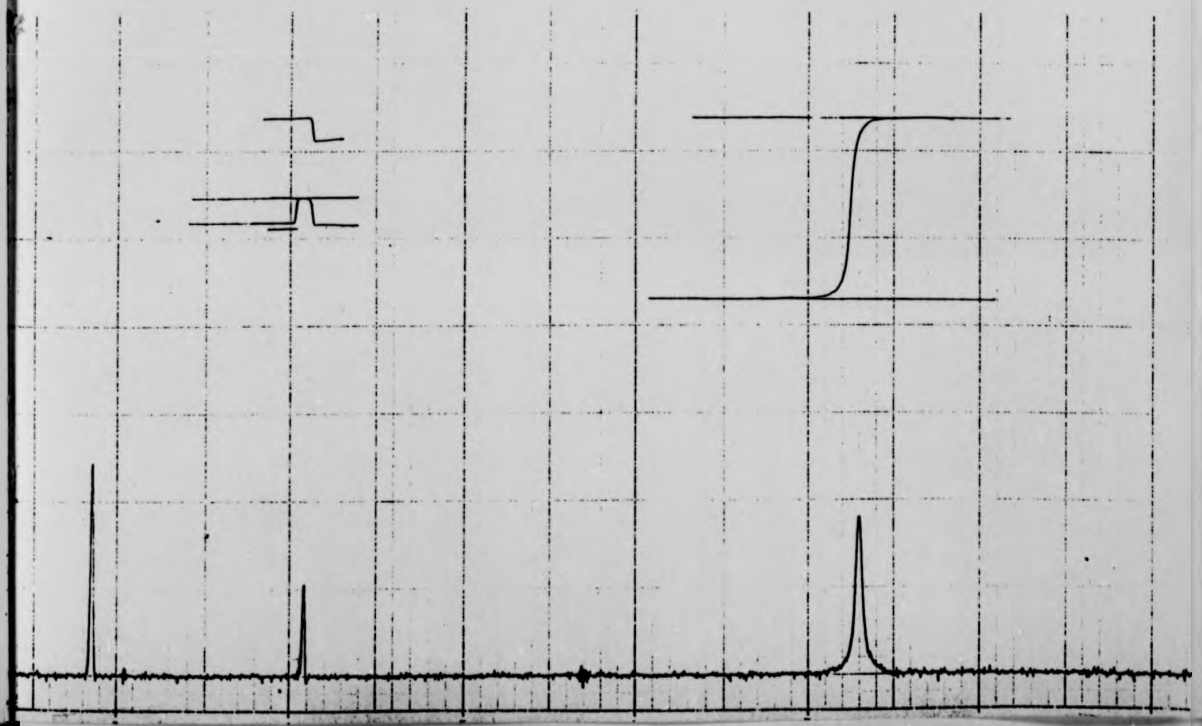


Fig. 3.1.M

^{1}H n.m.r. spectrum of bis[(Z,Z)-hepta-2,5-dien-4-ol]Rh(I)hfpd
cf. Sec. 3.3.3 for assignments

^{1}H n.m.r. spectrum of Rh(I)hfpd *cf.* Sec. 2.4.2 for assingments



the (E)-double bond seemed to be undergoing an on-off exchange, as indicated by the C-1 methyl resonance which appeared as a broad singlet at 20°C. However, at -20°C this signal was resolved into a doublet (J 6 Hz).

With (Z,Z)-hepta-2,5-diene the severe steric interaction between two *cis* methyl groups precludes formation of a bidentate complex. A similar situation arises with (Z,Z)-hexa-2,4-diene which does not co-ordinate to rhodium(I), but is catalytically transformed to (E,E)- and (E,Z)-hexa-2,4-diene[22]. However, (Z,Z)-hepta-2,5-diene displaced ethylene from both E_2Rh(I)pd and E_2Rh(I)hfpd and oils were isolated in both cases. The ^{1}H n.m.r. spectra of these complexes were poorly resolved, but there is evidence to suggest that the complexes are unstable bis(monodentate) complexes (Fig. 3.1.G), e.g. [Rh(I)pd complex δ: 1.75 (6 H, d), 1.87 (6 H, d) 5.50 (4 H, m) p.p.m.].

In contrast to the bis(monodentate) complexes of (E)-penta-1,3-diene and 2-methylpenta-2,4-diene, the (Z,Z)-hepta-2,5-diene complex is unstable because the double bonds in the diene are identical. They will show the same ability to co-ordinate to Rh(I) and this could lead to a facile exchange process in solution.

Although the (Z,Z)-hepta-2,5-diene-rhodium(I) complexes are unstable, (Z,Z)- and (E,Z)-hepta-2,5-dien-4-ols were found to react with E_2Rh(I)hfpd to give air stable, crystalline, bis(monodentate) complexes. These were fully characterised (^{1}H n.m.r., i.r., mass spectroscopy, and combustion analysis). Two equivalents of (Z,Z)-hepta-2,5-dien-4-ol react with one equivalent of E_2Rh(I)hfpd to give a yellow crystalline product, m.p. 118-120°C. The ^{1}H n.m.r. spectrum indicates co-ordinated olefin [δ 2.45 (H-2) and 2.88 (H-3)] and uncoordinated olefin [δ 5.52, (H-5 and H-6)], while infra-red spectra suggest that the hydroxyl group is intramolecularly hydrogen bonded (Fig. 3.1.M).

(Dilution of a solution in CCl_4 from 5% to 0.5% did not alter the position or shape of the absorbance at 3270 cm^{-1}.)

It is highly probable that the hydrogen bonding contributes considerably to the stability of this complex as indicated by the instability of the (Z,Z)-hepta-2,5-diene complex. Also the corresponding Rh(I)pd complex, where hydrogen bonding would be reduced, is an oil and the ^1H n.m.r. spectrum is not well resolved. Electron impact mass spectrometry of the complex (Fig. 3.1.M) failed to give a molecular ion; the highest peak, m/z 422, can be assigned to the complex minus one olefin ligand. However, using the technique of field desorption the molecular ion (M^+ 534) was observed along with peaks at m/z 532, 516 ($-H_2O$) and 500.

Similarly, (E,Z)-hepta-2,5-dien-4-ol reacts with Rh(I)hfpd to give a bis(monodentate) complex, as an air stable yellow crystalline solid, m.p. 88-89°C. In this complex there is the possibility of isomerism because theoretically either the *cis* or *trans* double bonds can co-ordinate to rhodium(I). Previous work indicates that the *cis* double bond would co-ordinate preferentially, but ^1H n.m.r. spectroscopy shows it is the *trans* double bond that is co-ordinated. As with the (Z,Z)-isomer, i.r. spectroscopy indicates that the hydroxyl group is intramolecularly bonded (0.5% CCl_4: 3260 cm^{-1}). Electron impact mass spectrometry fails to give a molecular ion, but field desorption (m/z: M^+ 534, 532, 516 ($-H_2O$), 500) indicates that the complex is monomeric.

(E,E)-hepta-2,5-dien-4-ol and (E)-hexa-1,4-dien-3-ol reacted with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ to give bidentate complexes, even in the presence of excess olefin, and ^1H n.m.r. and i.r. spectra indicate that the hydroxyl group is exo to the metal. Any stabilisation which may be afforded to bis(monodentate) complexes by intramolecular

hydrogen bonding is not sufficient to overcome the propensity of (E,E)-1,4- and 2,5-dienes to form bidentate complexes.

Allylic Alcohol	m.p.°C	Combustion Analysis		δ(O-H)
		C	H	
Prop-2-en-1-ol	93.94	31.01 (31.18)	3.08 (3.03)	[a]6.40
But-3-en-2-ol	117d	34.38 (34.48)	3.77 (3.79)	[a]6.80
(Z)-but-2-en-1,4-diol	113-114	32.12 (32.52)	3.53 (3.59)	[b]2.87 (3) 4.29 (1)
(Z,Z)-hepta-2,5-dien-4-ol	118-120	42.71 (42.73)	4.67 (4.63)	6.80
(E,Z)-hepta-2,5-dien-4-ol	88-89	42.71 (42.91)	4.67 (4.22)	[c]6.80

[a] d_6 benzene
[b] d_6 acetone
[c] $CDCl_3$/-15°C

Analysis: expected (found)

Table 3.1.N

Further reactions of E_2Rh(I)hfpd show that a number of primary or secondary allylic alcohols displace ethylene to give well defined crystalline complexes (Table 3.1.N).

Prop-2-en-1-ol and but-3-en-2-ol gave yellow-orange crystalline complexes whose i.r. spectra indicate that the hydroxyl groups are intramolecularly hydrogen bonded (0.5% CCl_4: 3320 cm^{-1}). The ^1H n.m.r. spectra show a reduction in the coupling constants upon co-ordination (J *cis* 7.8 Hz, J *trans* 13.3 Hz), and a considerable downfield shift for O-H would suggest that these groups are hydrogen bonded to the oxygens of the pentanedionato-ligand in the plane of the ring, and are thus experiencing an anisotropic deshielding effect.

In the ^1H n.m.r. spectra of the (Z,Z)- and (E,Z)-hepta-2,5-dien-4-ol complexes with Rh(I)hfpd the hydroxyl groups are not observed at room temperature. However, in $CDCl_3$ at -20^oC the resonance is observed at δ 6.80.

With (Z)-but-2-en-1,4-diol the ^1H n.m.r. spectrum is more complicated than would have been expected. The hydrogens of the co-ordinated double bonds are easily assigned (δ 3.22) as are the hydroxyl-protons (exchange with D_2O), but it would appear that the protons of the $-CH_2OH$ groups have become non-equivalent because they appear as two separate resonances (δ 3.68, dd, J 12.7 Hz and 5.1 Hz) and (δ 4.14, m). It is interesting to note that (E)-but-2-en-1,4-diol and 2-methyl-but-3-en-2-ol do not give well defined crystalline complexes upon reaction with $E_2Rh(I)hfpd$, but geraniol reacts to give a well defined bidentate complex (Fig. 3.1.Pa). It is believed that nerol, the geometrical isomer of geraniol would be forced to co-ordinate to give a bis(monodentate) complex.

Bidentate co-ordination would be precluded because of the severe steric interaction between two *cis*-substituents as shown in Fig. 3.1.Pb.

Prior to this work no organometallic complexes of unconjugated diene alcohols had been reported, but much work involving conjugated dienols had been published. (E,E)-hexa-2,4-dien-1-ol and (E,E)-hepta-3,5-dien-2-ol react with $[Rh(I)(\eta^2\text{-}C_8H_{14})_2Cl]_2$ to give monomeric complexes of stoichiometry $[Rh(I)(dienol)_2Cl]$[23] which are known to adopt the square pyramidal structure found for $[Fe(\eta^4\text{-butadiene})_2Cl]$[24]. All attempts to isolate a pure Rh(I) cyclopentadienide-dienol complex have failed, but on treating a crude sample of this complex with HBF_4 protonation occurs (Fig. 3.1.Q).[23]

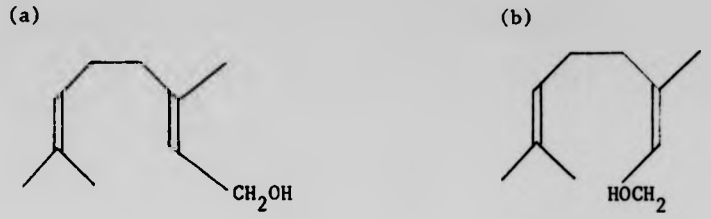


Fig. 3.1.P

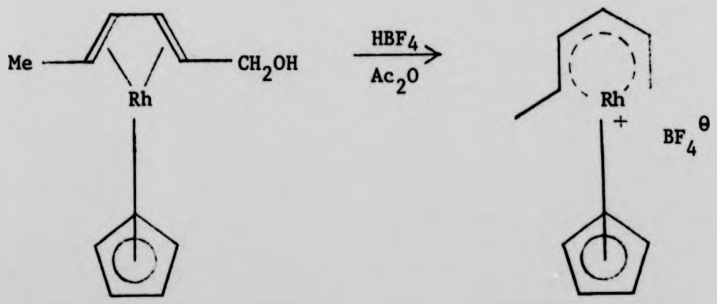


Fig. 3.1.Q

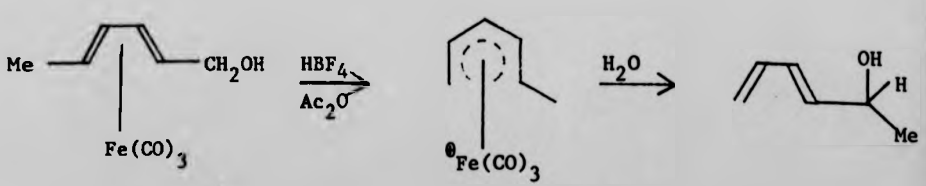


Fig. 3.1.R

This type of chemistry is particularly prevalent with iron tricarbonyl complexes of conjugated dienols[25], where it is known that formation and subsequent quenching of these complexes proceeds in a highly stereoselective manner[26] (Fig. 3.1.R).

In all known complexes of aldehydes, ketones, esters and carboxylic acids with Rh(I), little change is observed in the stretching frequency of the carbonyl group on complexation to the metal. This has been interpreted to mean that there is no interaction between metal and carbonyl group[23,27]. Reactions of (E,E)-4-acetoxyhepta-2,5-diene with E_2Rh(I)hfpd, and (E)-3-acetoxyhexa-1,4-diene with E_2Rh(I)pd and E_2Rh(I)hfpd give rise to bidentate complexes in which the acetate group is in the exo position. This is supported by ^{1}H n.m.r. and i.r. spectroscopy which indicate that Hendo is a clear triplet and the carbonyl stretching frequency (1732 cm^{-1}) is virtually unchanged from that in the free diene.

In addition to forming complexes with "skipped" dienes, dienols and their derived acetates, rhodium(I) was also observed to facilitate isomerisation of dienols and their acetates.
The dienol (E)-hexa-1,4-dien-3-ol was isomerised by E_2Rh(I)hfpd (5 mol % in [d^6.]benzene at 80°C) to (E)-hex-2-en-4-one. Similarly (E,E)- and (E,Z)-hepta-2,5-dien-4-ols were isomerised to mixtures containing 85% (E)-hept-2-en-4-one and 15% (E,E)-hepta-2,5-dien-4-one.

The major products are formed by a conjugation of the double bonds to give an enol intermediate which tautomerises to a ketone, while the minor product arises by a catalytic dehydrogenation reaction.

Well established mechanisms exist for the metal-assisted isomerisation of alkenes.

(i) Isomerisation *via* metal-alkyl intermediates[28,29,30,31]

This is essentially an intermolecular metal-hydride addition

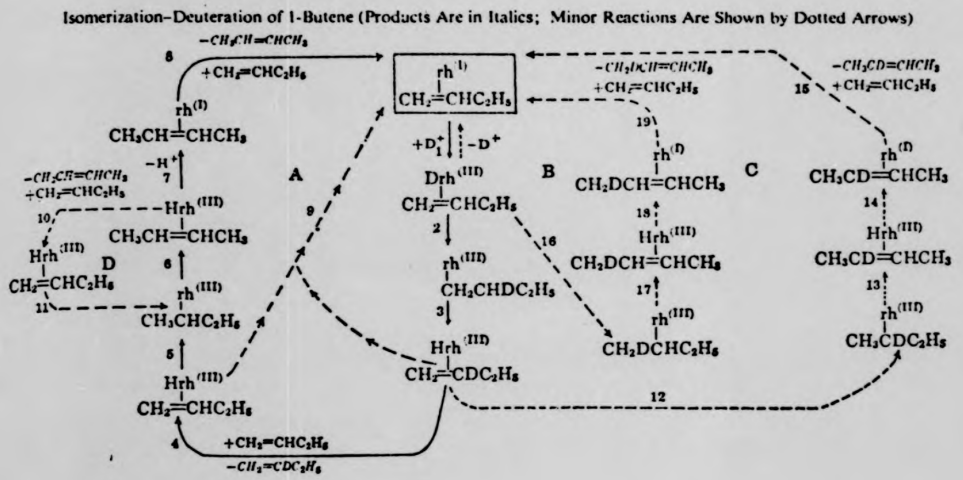


Fig. 3.1.U (taken from ref. 28)

elimination process in which the essential species in the sequence is a metal hydride-alkene complex. Initial co-ordination of the alkene generates the alkene-metal hydrido complex which rapidly undergoes a hydride-ligand migration reaction to form a metal-alkyl species (Fig. 3.1.S). The migration probably occurs *via* a four centre transition state and provided the alkene and hydride groups are mutually *cis*, is extremely rapid. Once formed, the metal-alkyl species can undergo a β-elimination reaction *via* either of two pathways, A or B (Fig. 3.1.T).

Path (A) is merely the reverse of the initial process and results in no net migration of the double bond, but it may well result in hydrogen exchange or incorporation of deuterium. Path (B), in which hydrogen abstraction occurs at a site other than that at which initial addition occurred, results in net migration. Provided the alkene co-ordinated to the metal can exchange with alkene present in the reaction medium then the above sequence constitutes a catalytic isomerisation cycle.

This mechanism is well established for the isomerisation of terminal olefins. Cramer[28], by addition of HCl to $E_2Rh(I)pd$ and di-μ-chlorotetrakis(ethylene)dirhodium(I) was able to generate Rh(III)-hydride species which are capable of isomerising linear terminal alkenes to disubstituted olefins. By following the course of the reactions in deuteromethanol it was established conclusively that the isomerisation proceeds *via* an intermolecular metal-hydride addition-elimination process. The results, which exclude both the carbene and π-(η^3-allyl) metal hydride pathways (which will be discussed later) have been summarised (Fig. 3.1.U).

More recent studies[29] have confirmed this mechanism by quantitative microwave analysis of (^{2}H)-propenes formed by deuterium exchange of propene with CH_3OD, catalysed by rhodium, nickel and

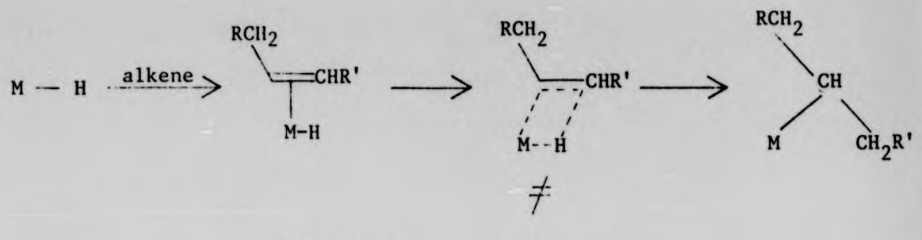


Fig. 3.1.S

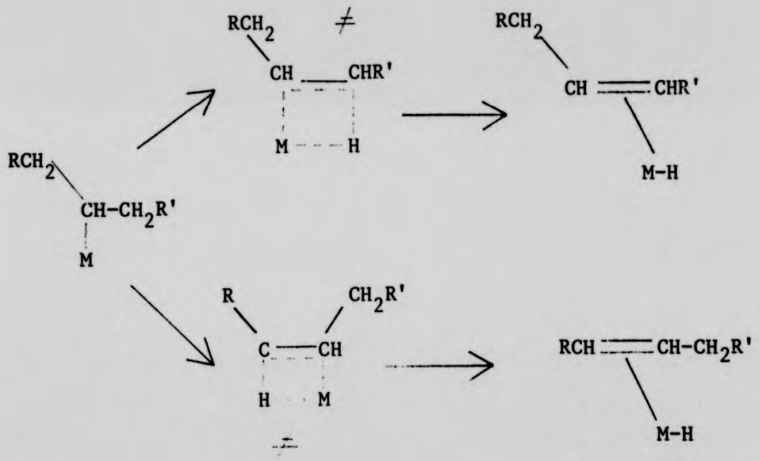


Fig. 3.1.T

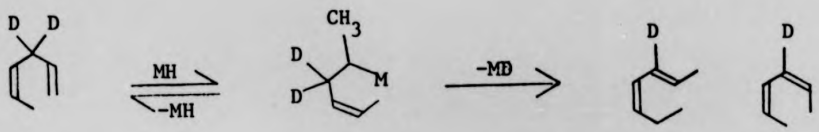


Fig. 3.1.V

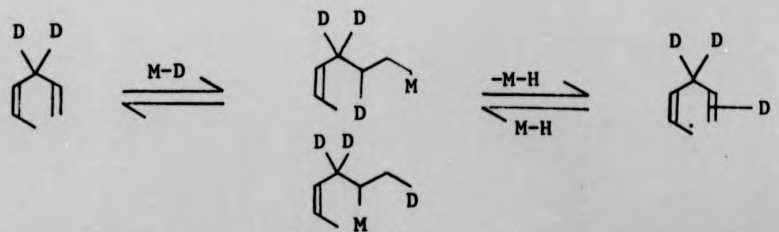


Fig. 3.1.W

platinum. "Skipped" dienes have also been shown to isomerise by this mechanism. Using 3,3-dideutero-(Z)-hexa-1,4-diene Miller and co-workers[31] were able to establish that the products, (E,Z)- and (Z,Z)-hexa-2,4-diene contained deuterium predominantly in the 3-position (Fig. 3.1.V).

They rationalised that deuterium migration elsewhere was brought about by the elimination of M-D, which can then of course catalyse further conjugation with deuterium incorporation (Fig. 3.1.W).

(ii) Isomerisation *via* metal-allyl intermediates[6,32,33,34]

An alternative pathway leading to alkene isomerisation is by the formation of a metal-allyl complex. In this sequence co-ordination is followed by hydrogen abstraction from an sp^3-hybridised carbon centre adjacent to the double bond, to give a hydrido-metal-allyl species (Fig. 3.1.X).

In such species the allyl effectively occupies two co-ordination sites in the complex. This mechanism is generally only viable with metals in which the (n+2) oxidation state is readily attainable, e.g.

[Rh(I) → Rh(III), Fe(0) → Fe(II) and Ni(0) → Ni(II)]

It can be clearly seen from the above scheme that the π-allyl mechanism leads to a 1,3-hydrogen shift, whereas the metal-alkyl mechanism leads to a 1,2-hydrogen shift. The two mechanisms can therefore be distinguished experimentally by deuterium labelling studies. The isomerisation of allyl alcohol to propionaldehyde by reaction with $Fe(CO)_5$ has been reported by Emerson and Pettit, and a possible mechanism involving the intermediacy of a π-allyl hydridoiron tricarbonyl complex was proposed[35]. However, it was not until deuterium labelling studies were undertaken that substantial evidence was obtained to support this mechanism. Rosenberg and co-workers monitored the rearrangement of [1,1-$^2H_2$]prop-2-en-1-ol

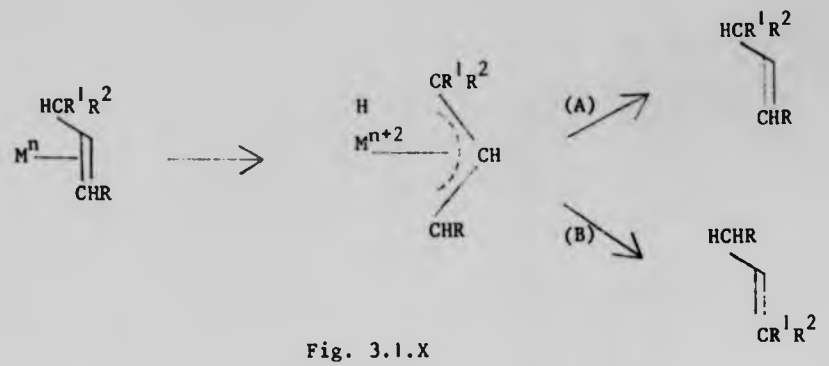


Fig. 3.1.X

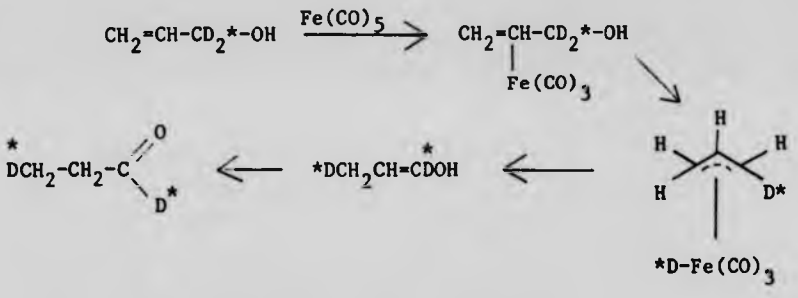


Fig. 3.1.Y

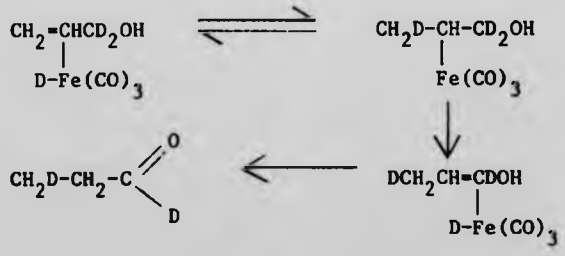


Fig. 3.1.Z

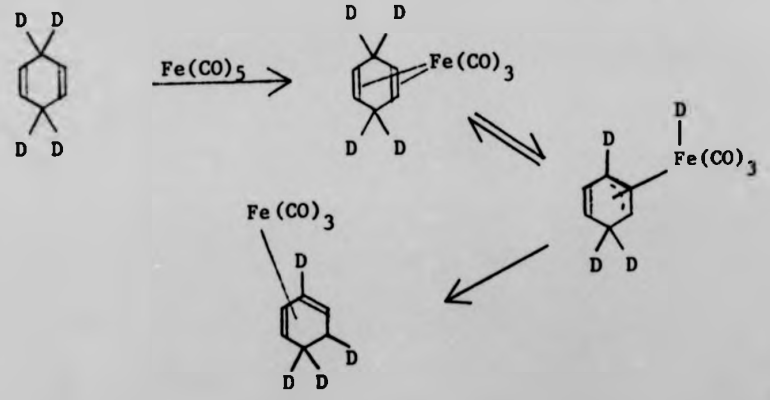


Fig. 3.1.a

(allyl alcohol) by $Fe(CO)_5$ and analysed the product, propionaldehyde (Fig. 3.1.Y).

Analysis showed that deuterium in the final product was present only in the methyl group and the aldehyde proton, thereby confirming the proposed mechanism. An alternative mechanism was proposed by Manuel[36], but can be discounted (Fig. 3.1.Z).

For this route to be operative, a completely stereoselective transfer of deuterium to the terminal carbon atom would be needed to avoid incorporation of deuterium into the methylene group of the propionaldehyde.

Using deuterated olefins, Alper and co-workers[34] were able to prove that the π-allyl mechanism is also involved in the isomerisation of "skipped" dienes. 3,3,6,6-Tetradeuteriocyclohexa-1,4-diene was found to isomerise to 3,5,6,6-tetradeuteriocyclohexa-1,3-diene in the presence of $Fe(CO)_5$ (Fig. 3.1.a).

This result is totally consistent with a π-allyl mechanism. More recently in a comprehensive study of 1,3- and 1,4-dienes, Nelson and co-workers have established that [Rh(I).cp.diene] complexes undergo thermally induced isomerisation in non-protic solvents. Measurements of kinetics and product distribution in the 1,4- and 1,3-isomerisations show they are consistent with a mechanism involving a (η^3-allyl) hydrido intermediate, while it would appear that in the *cis-trans*-isomerisations of the 1,3-dienes interconversion proceeds *via* an η^3-η^1-η^3-pathway. These points are illustrated in the mechanism proposed for isomerisation of 2-methylpenta-1,4-diene (Fig. 3.1.b).

Two important experimental observations were taken into account, (i) the equal initial rates of formation of *cis* and *trans* 2-methylpenta-1,3-diene and (ii) the slower rate of formation of the 4-methyl isomer. The first step of the mechanism is envisaged

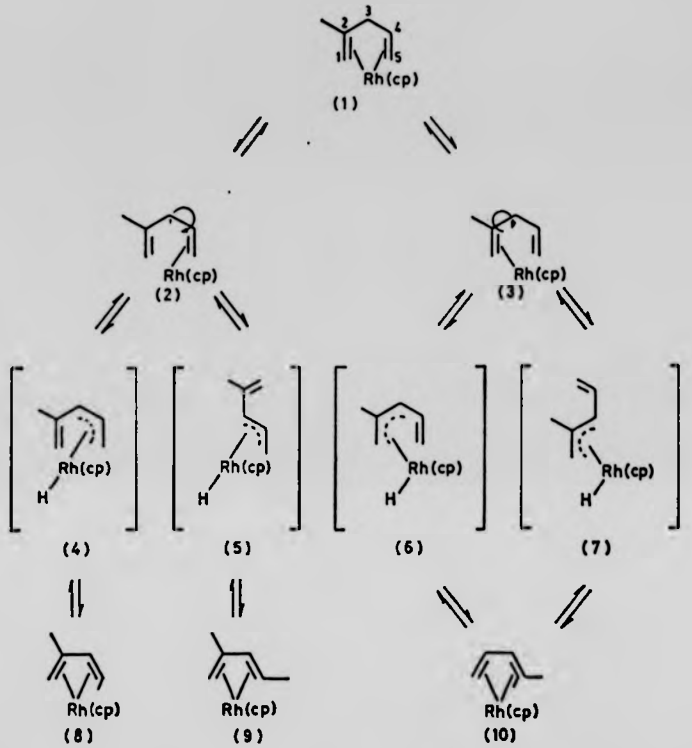


Fig. 3.1.b taken from Ref. 22

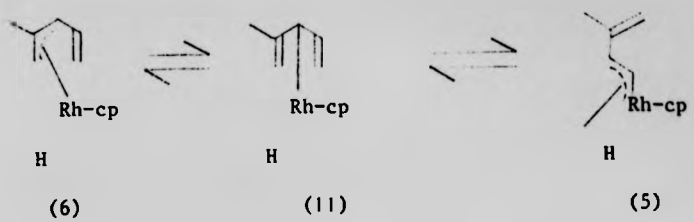


Fig. 3.1.c

as a de-co-ordination of one of the two double bonds co-ordinated to the rhodium(I). It can be seen that two possible complexes can arise, (2) and (3), but it is known that methyl substituents destabilise rhodium(I)-η^2-alkene bonds[1] so the dissociation of the disubstituted double bond will be the thermodynamically favoured process. Thus, the concentration of (2) will exceed that of (3). The free double bond is now able to rotate and on hydrogen transfer this gives rise to two (η^3-allyl) hydrido-rhodium(III) intermediates, (4) and (5). The rates of formation of these will be similar because only one rotation is required in (2) to interconvert one to the other. A reverse hydrogen transfer from the metal to C-5 gives rise to 4-methylpenta-1,3-diene. The isomerisation of (10) to the thermodynamically more favoured *trans*-2-methylpenta-1,3-diene is accommodated by the mechanism, but an alternative route to (9) involves a direct conversion of (6) to (5) *via* a σ-bonded η^1-allyl species (11). Dynamic π-σ-π-interconversions are well known for palladium (η^3-allyl) complexes[37].

The mechanism which constitutes an alternative to the (π-allyl) metal hydride sequence involves a sigmatropic 1,3-suprafacial hydrogen shift (Fig. 3.1.d).

It is proposed that the hydrogen migrates across the face of the olefinic ligand, opposite to that which the metal is bonded, and does not therefore, become directly involved with the metal orbitals. In an elegant experiment Rosenberg[38] prepared compounds (A) and (B) to investigate whether an $Fe(CO)_5$ catalysed isomerisation would proceed *via* this mechanism (Fig. 3.1.f).

As shown in Fig. 3.1.g, rearrangement of (A) into the ketone would be expected to occur only if a suprafacial 1,3-hydrogen shift is operative. Clearly the migrating hydrogen is not correctly positioned to allow formation of a (π-allyl) hydridoiron complex.

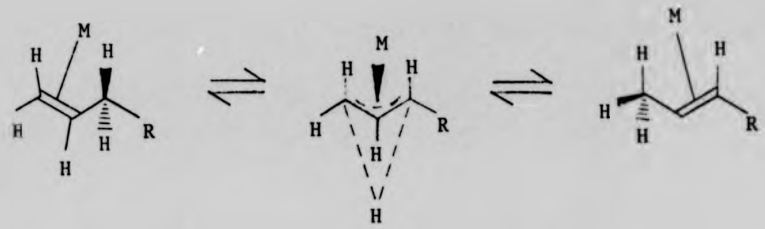


Fig. 3.1.d

(A) (B)

Fig. 3.1.f

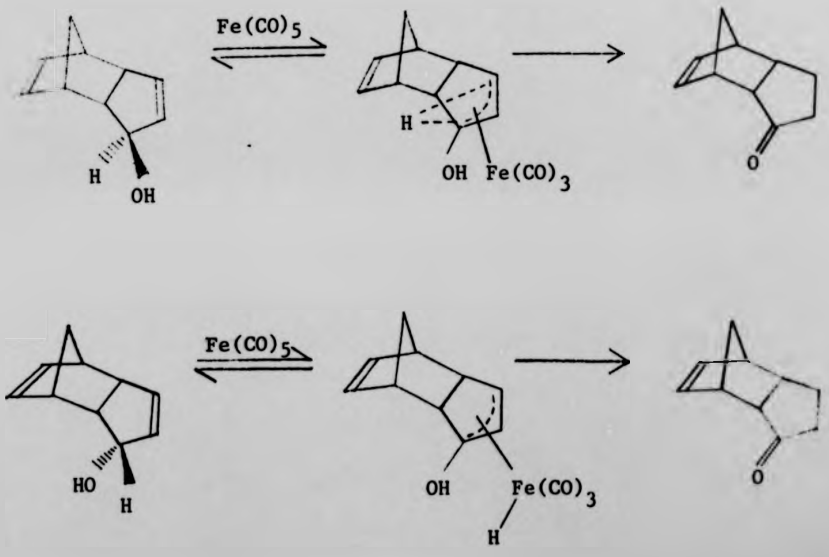


Fig. 3.1.g

Compound (B) was found to isomerise to the ketone (Fig. 3.1.g), but prolonged heating of (A) did not facilitate isomerisation. These results preclude a 1,3-suprafacial shift whilst endorsing the π-allyl mechanism.

A fourth possibility involves isomerisation *via* a carbene intermediate. This type of reaction is envisaged as occurring *via* a transition state which involves a suprafacial-1,2-hydrogen shift.

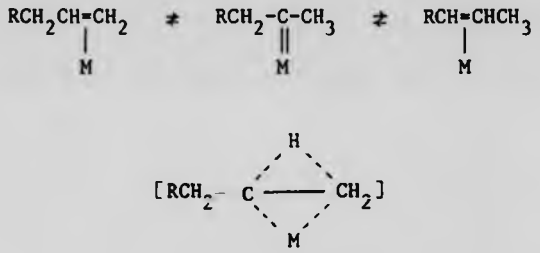


Fig. 3.1.h

There appears to be no direct evidence for such a process occurring in this type of isomerisation, but there is reasonable evidence to show that carbene ligands can rapidly convert to the corresponding olefin ligand (Fig. 3.1.j)[39].

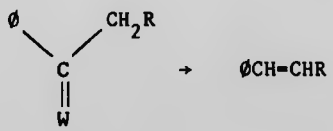
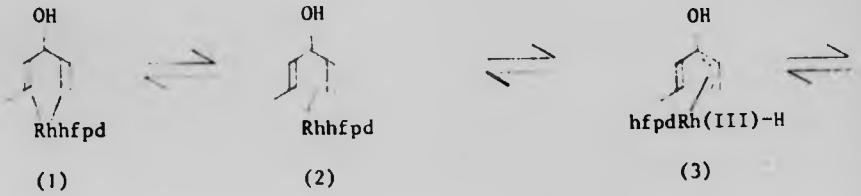
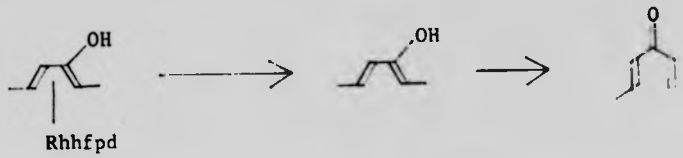


Fig. 3.1.j

Now considering all the evidence presented it would seem likely that the alkyl-metal isomerisation mechanism is not operative in the observed isomerisation of (E)-hexa-1,4-dien-3-ol. The reaction was carried out in an aprotic solvent with $E_2Rh(I)hfpd$ as catalyst [$E_2Rh(I)pd$ is known to be inactive in this mechanism in



(1) (2) (3)



(4) (5) (6)

Fig. 3.1.k

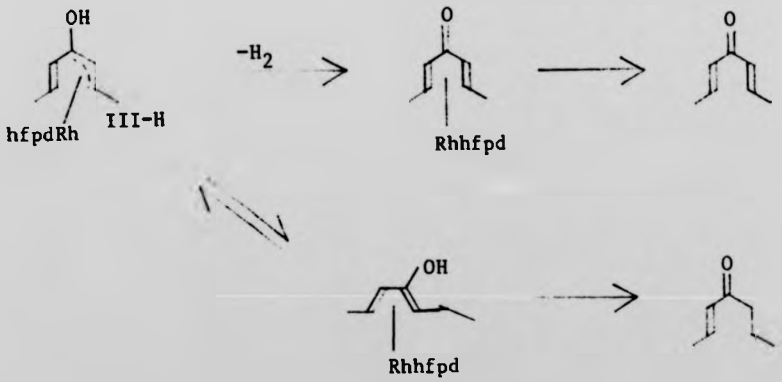


Fig. 3.1.1

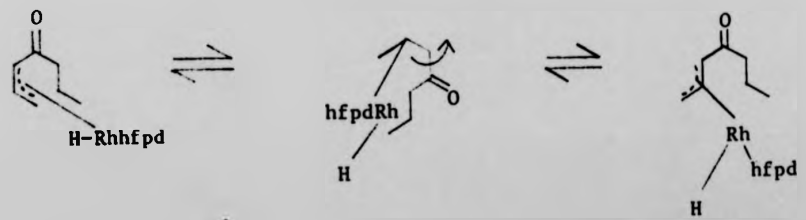


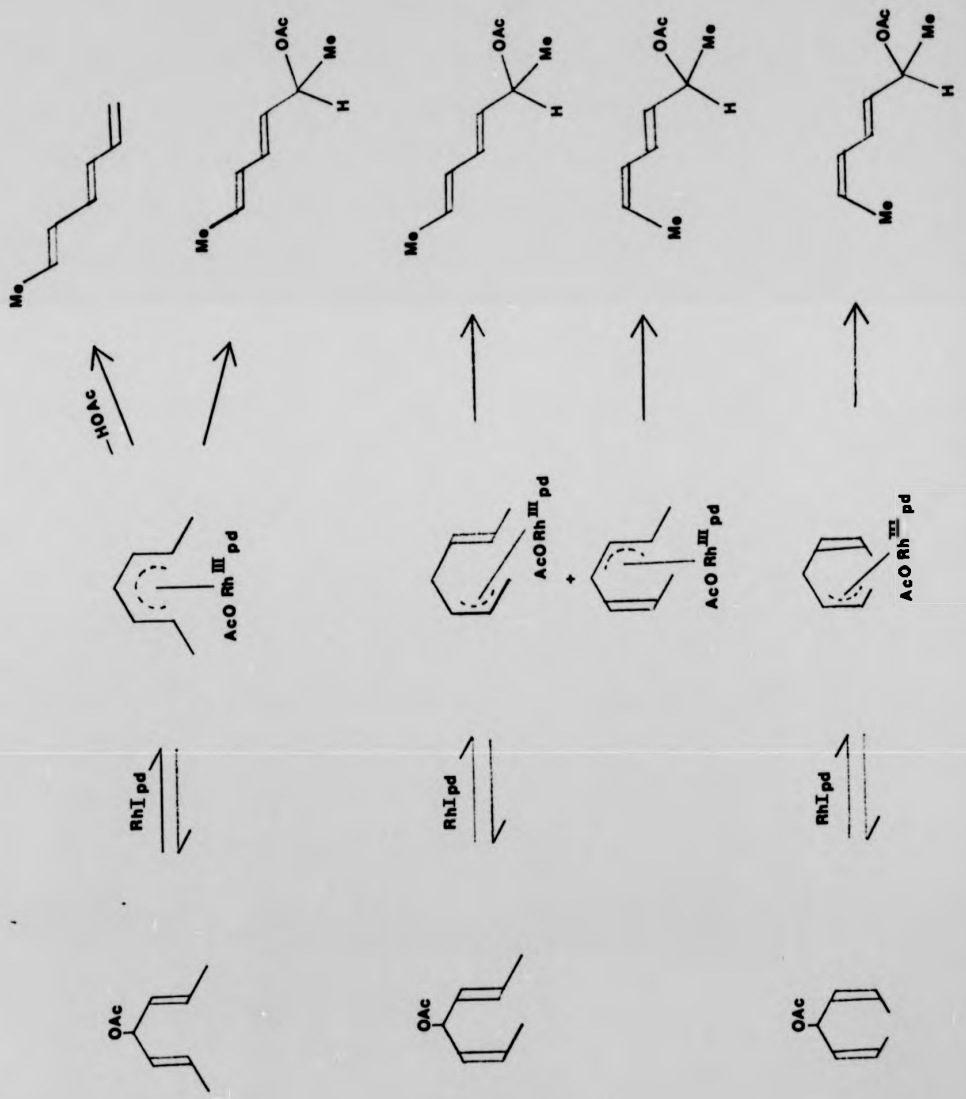
Fig. 3.1.m

the absence of co-catalyst, e.g. HCl]. Hence a π-allyl mechanism is proposed (Fig. 3.1.k).

^{1}H n.m.r. spectroscopy indicates that (E)-hexa-1,4-dien-3-ol co-ordinates to Rh(I)hfpd to give a bidentate complex (1). Dissociation of the thermodynamically less favoured double bond, followed by abstraction of hydrogen gives the (η^3-allyl) rhodium(III) hydride (3). Return of hydrogen and olefin exchange gives the enol (5) which tautomerises to (E)-hept-2-en-4-one. The same mechanism is applicable to the isomerisation of (E,E)-hepta-2,5-dien-4-ol with one adjustment in that the intermediate (η^3-allyl) species can either proceed by transfer of hydride to (E)-hept-2-en-4-one, or can eliminate hydrogen and give rise to (E,E)-hepta-2,5-dien-4-one (Fig. 3.1.l).

It is known that rhodium can abstract hydrogen from alcohols to give ketones[40], and therefore the dehydrogenation process does not seem unreasonable. With (E,Z)-hepta-2,5-dien-4-ol the initial major products are (E)- and (Z)-hept-2-en-4-one whereas the major final product is (E)-hept-2-en-4-one. Hence it would appear that a *syn-anti* conversion is involved in this isomerisation (Fig. 3.1.m). Hence it can be seen that the results of the rhodium-induced isomerisation of "skipped" dienols can be accommodated by a mechanism involving an η^3-allyl intermediate similar to the one proposed by Nelson.[22]

E_2Rh(I)pd was also observed to catalyse the isomerisation of 4-acetoxyhepta-2,5-dienes. (E,E)-4-acetoxyhepta-2,5-diene was converted to a mixture containing (E,E)-2-acetoxyhepta-3,5-diene and hepta-1,3,5-triene (1:1). The (E,Z)-isomer was converted to a mixture containing (E,E)- and (E,Z)-2-acetoxyhepta-3,5-diene (6:4), whereas the (Z,Z)-isomer was converted to (E,Z)-2-acetoxyhepta-3,5-diene. The mechanism probably proceeds by an oxidative addition of the acetate to rhodium(I) to give a rhodium(III) species. In the case of the


Me
OAc
Me
H
Me
OAc
Me
H
Me
OAc
Me
H
Me
OAc
Me
H
Me
-HOAc
AcO Rh III pd
AcO Rh III pd
+
AcO Rh III pd
AcO Rh III pd
RhI pd
RhI pd
RhI pd
OAc
OAc
OAc

3:1:n

(E,E) isomer this probably gives rise to an η^5-dienyl whereas with the (E,Z)- and (Z,Z)-isomers the intermediate is likely to be an η^3-allyl (Fig. 3.1.n).

This would account for the formation of the hepta-1,3,5-triene in the case of the (E,E)-isomer. It should be noted that isomerisation of either a *cis* or a *trans* double bond leads to the formation of a *trans* double bond, and that there is a slight preference to form *trans* η^3-allyls over *cis* η^3-allyls as judged by the (60:40) ratio for the isomerisation of (E,Z)-4-acetoxyhepta-2,5-diene. These isomerisations are mechanistically related to those of the dienols, but a more detailed discussion of acetate rearrangements will be presented in Chapter 5.

CONCLUSIONS

In complexations with hepta-2,5-dienes to give bidentate complexes E_2Rh(I)pd and Rh(I)hfpd show a preference of (E,E) > (E,Z) >> (Z,Z). The (Z,Z) isomer does not give bidentate complexes, but unstable bis(monodentate) complexes, whereas (E)-penta-1,3-diene and 2-methylpenta-2,4-diene give stable bis(monodentate) complexes. These observations indicate that bis(monodentate) diene complexation is favoured by:

(i) the presence of two double bonds in the diene (1,3 or 2,5) which show markedly different abilities to co-ordinate to Rh(I);

(ii) the presence of an electron withdrawing ligand on Rh(I), e.g. hfpd instead of pd.

(Z,Z)- and (E,Z)-hepta-2,5-dien-4-ol react with E_2Rh(I)hfpd to give crystalline complexes whose stability can be ascribed to intra-

molecular hydrogen bonding. This is supported by ^{1}H n.m.r. and i.r. spectroscopy, and also by the observation that other allylic alcohols (Table 3.1.N) form similar complexes.

The Rh(I) promoted rearrangements are consistent with the operation of π-allyl mechanism similar to the one proposed by Nelson *et al.*[22].

3.2 COMPLEXATIONS OF PENTA-1,4-; HEXA-1,4-; HEPTA-2,5-; AND OCTA-1,5-DIENES TO Rh(I)

3.2.1 (E,E)-hepta-2,5-diene

(a) (E,E)-hepta-2,5-diene (26.4 mg, 0.257 mmol), was dissolved in dry ether (1 cm^3) and added to E_2Rh(I)hfpd (100 mg, 0.274 mmol). When evolution ceased, the solvent was removed, (rotary evaporator), to give red-brown crystals which were sublimed (40-50°C, 0.1 mm) to give 1,1,1,5,5,5-hexafluoro-2,4-pentanedionato-[(E,E)-hepta-2,5-diene]-rhodium(I) (61 mg, 0.15 mmol), m.p. 55-57°C, in 55% yield.
^{1}H n.m.r. (d^6 benzene): 1.02 (2 x 3 H, H-1, d, J 6 Hz), 1.72 (1 H, H-4 exo, m), 2.70 (1 H, H-4 endo, dt, Jgem 12.8 Hz, Jvic 7.2 Hz), 2.89 (2 H, H-2, m), 3.38 (2 H, H-3, m), 6.00 (1 H, H-3 acac, s) p.p.m.

(b) (E,E)-hepta-2,5-diene (37.3 mg, 0.388 mmol) was reacted with E_2Rh(I)pd (100 mg, 0.388 mmol) as described in (a) to give an orange oil which did not crystalline from pentane at -78°C.
^{1}H n.m.r. (d^6 benzene): 1.34 (2 x 3 H, H-1, d), 1.75 (2 x 3 H, H-1 acac, s), 2.04 (1 H, H-4 exo, m), 3.00 (2 H, H-3, m, and H-4 endo, m), 3.59 (2 H, H-3, m), 5.11 (1 H, H-3 acac, s) p.p.m.

3.2.2 (E,Z)-hepta-2,5-diene

(a) (E,Z)-hepta-2,5-diene was reacted with E_2Rh(I)hfpd, as

described in procedure (1a), to give a red oil which could not be crystallised.

^{1}H n.m.r. ($CDCl_3$): 1.08 (3 H, H-1, brs at RT, d at -20°C), 1.58 (3 H, H-7, d), 2.50 (1 H, H-4 exo, m), 3.25 (2 H, H-6, m, and H-3, m), 4.30 (1 H, H-5, m), 6.05 (1 H, H-3 acac, s) p.p.m.

(b) (E,Z)-hepta-2,5-diene was reacted with E_2Rh(I)pd as described in procedure (1b) to give an orange oil.

^{1}H n.m.r. ($CDCl_3$): 1.10 (3 H, H-1,d), 1.53 (3 H, H-7, d), 2.40 (1 H, H-4 exo, m), 3.00 (1 H, H-6, m) 3.21 (1 H, H-4 endo, dt), 3.45 (1 H, H-2, m), 3.85 (1 H, H-3, m) 4.05 (1 H, H-5, m) 5.30 (1 H, H-3 acac, s) p.p.m.

3.2.3 (Z,Z)-hepta-2,5-diene

(Z,Z)-hepta-2,5-diene (2 molequivalents) was reacted with both E_2Rh(I)pd and E_2Rh(I)hfpd, as described in procedure (1a). The products were isolated as oil which did not give well resolved ^{1}H n.m.r. spectra. However, as with the C18 dienes and (Z,Z)-hepta-2,5-dien-4-ol rhodium complexes, a characteristic feature was the appearance of multiplets in the free alkene region [e.g. ^{1}H n.m.r. ($CDCl_3$): 5.40 and 5.65 p.p.m.].

3.2.4 Cyclohexa-1,4-diene

(a) Cyclohexa-1,4-diene (62 mg, 0.775 mmol) was dissolved in dry ether (1 cm^3) and added to E_2Rh(I)pd (200 mg, 0.775 mmol). Removal of solvent gave an orange solid which was recrystallised from ether-pentane at -78°C to give 2,4-pentanedionato (cyclohexa-1,4-diene) rhodium(I) (199 mg, 0.7 mmol), m.p. 120-121°C, in 91% yield.

^{1}H n.m.r. ($CDCl_3$): 1.90 (2 x 3 H acac, s), 3.09 (2 H, H-3 exo, dd, J 8 Hz and J Rh-H 2.5 Hz), 3.40 (4 H, m), 4.06 (2 H, H-3 endo, m), 5.33 (1 H, H-3 acac, s) p.p.m.

I.r. (10% CCl_4): 2840 (m, sh), 1570 (s), 1520 (s), 1395 (s, sh), 1270 (m, sh), 1200 (w), 1155 (w), 1015 (w) cm^{-1}.

M.s. (EI): m/z 282 (M^+, 30.5%), 182 (50.2%), 100 (19.4%), 78 (100%).

(b) Cyclohexa-1,4-diene (50 mg, 0.625 mmol) was reacted with E_2Rh(I)hfpd (242.5 mg, 0.625 mmol) as described in Part (a) to give red-brown crystals of 1,1,1,5,5,5-hexafluoro-2,4-pentanedionato (cyclohexa-1,4-diene) rhodium(I), (224 mg, 0.574 mmol), m.p. 91-92°C in 92% yield.

^{1}H n.m.r. ($CECl_3$): 3.25 (2 H, H-3 exo, dd, J 8 Hz and J Rh-H 2.5 Hz), 3.67 (4 H, m), 4.14 (2 H, H-3 endo, m), 6.12 (1 H, H-3 acac, s) p.p.m.

I.r. (10% CCl_4): 2990 (m, sh), 2845 (m, sh), 1605 (m), 1470 (s, sh), 1350 (m, sh), 1265 (s, sh), 1220 (s, sh), 1170 (s, sh), 1100 (s, sh), 965 (w) cm^{-1}.

M.s. (EI): m/z 390 (M^+, 39.9%), 182 (100%), 139 (77.1%), 103 (61.4%), 78 (75.2%), 69 (80.0%).

3.2.5 Penta-1,4-diene

(a) Penta-1,4-diene was reacted with E_2Rh(I)hfpd as described in procedure (1a) to give an orange crystalline product, 1,1,1,5,5,5-hexafluoro-2,4-pentanedionato (penta-1,4-diene)rhodium(I) (49 mg, 0.13 mmol) m.p. 125-126°C, in 96% yield.

^{1}H n.m.r. ($CDCl_3$): 2.15 (1 H, H-3 exo, m), 2.80 (4 H, H-1, m), 3.40 (1 H, H-endo, m), 4.40 (2 H, H-2, m), 6.12 (1 H, H-3 acac, s) p.p.m. All signals were broad, even at -50°C.

I.r. (10% CCl_4): 3090 (w), 3030 (w), 2990 (w), 2935 (w), 2870 (w),

1600 (s), 1460 (s, sh), 1354 (m, sh) 1260 (s), 1215 (s), 1165 (s), 1100 (s, sh), 965 (m, sh), 680 (m, sh) cm^{-1}.

M.s. (EI): m/z 378 (M^+, 65.7%), 168 (100%), 103 (96.9%), 67 (57.3%).

(a) E_2Rh(I)pd was reacted with penta-1,4-diene as described in procedure (1a) to give orange-yellow crystals of 2,4-pentanedionato (penta-1,4-diene)rhodium(I).

^{1}H n.m.r. (d^6 benzene): 1.70 (1 H, H-3 exo, m), 1.75 (2 x 3 H acac, s), 2.38 (2 H, H-1, d, J *trans* 12.4 Hz), 2.73 (2 H, H-1, d, J *cis* 8 Hz), 2.83 (1 H, H-3 endo, dt, Jgem 12.4 Hz, Jvic 6.5 Hz), 3.96 (2 H, H-2, m), 5.12 (1 H, H-3 acac, s) p.p.m.

3.2.6 Cycloocta-1,5-diene

(a) Cycloocta-1,5-diene (18.75 mg, 0.174 mmol) was reacted with E_2Rh(I)pd (44.8 mg, 0.174 mmol) as described in procedure (1a). The product was recrystallised from ether-pentane to give yellow crystals of 2,4-pentanedionato (cycloocta-1,5-diene)rhodium(I) (51.8 mg, 0.167 mmol), m.p. 136-137°C, in 97% yield.

^{1}H n.m.r. ($CDCl_3$): 1.82 (4 H exo, d, J 8 Hz), 1.95 (2 x 3 H acac, s), 2.47 (4 H endo, m), 4.09 (4 H, m), 5.33) (1 H, H-3 acac, s) p.p.m.

I.r. (1% CCl_4: 3000 (m, sh), 2940 (s), 2875 (s), 2825 (s, sh), 1568 (s), 1510 (s), 1430 (m), 1395 (s), 1263 (s, sh), 1198 (m, sh), 1170 (w, sh), 1145 (w, sh), 1020 (m, sh), 960 (m, sh), 925 (m, sh), 875 (w, sh) cm^{-1}.

M.s. (EI): m/z 310 (M^+ 100%), 208 (45.1%), 207 (13.5%), 103 (11.0%), 83 (32.2%).

(b) Cycloocta-1,5-diene was reacted with E_2Rh(I)hfpd as described in Part (a) to give orange-yellow crystals of 1,1,1,5,5,5-hexafluoro-2,4-pentanedionato(cycloocta-1,5-diene),

m.p. 95-97°C, in 92% yield.

^{1}H n.m.r. (d^6 benzene): 1.38 (4 H, H exo, d, J 7.9 Hz), 2.00 (4 H, H endo, m), 4.12 (4 H, m), 6.02 (1 H, H-3 acac, s) p.p.m.

I.r. (CCl_4): 3010 (w), 2945 (m), 2886 (m), 2840 (m, sh), 1622 (s), 1606 (s), 1555 (m), 1458 (s), 1347 (m), 1255 (s), 1210 (s), 1156 (s), 1100 (s), 970 (m), 680 (m) cm^{-1}.

M.s. (EI): m/z 418 (M^+ 57.8%), 211 (100%), 157 (34.6%), 103 (43.4%), 69 (34.6%).

3.3 COMPLEXATIONS OF SOME ALLYLIC ALCOHOLS AND ACETOXYDIENES TO Rh(I)

3.3.1 (E)-hexa-1,4-dien-3-ol

(a) (E)-hexa-1,4-dien-3-ol (25 mg, 0.255 mmol) was dissolved in dry ether and added to E_2Rh(I)pd (65.6 mg, 0.255 mmol). Removal of solvent gave an orange oil which could not be crystallised, 2,4-pentanedionato [(E)-hexa-1,4-dien-3-ol]rhodium(I).

^{1}H n.m.r. ($CDCl_3$): 1.28 (3 H, H-6, d, J 6.2 Hz), 1.68 (O-H), 1.92 (2 x 3 H acac, s), 2.46 (1 H, H-1, d, J *trans* 12.3 Hz), 2.62 (1 H, H-1, d, J *cis* 7.9 Hz), 3.35 (1 H, H-5, m), 3.96 (1 H, H-4, m), 4.13 (1 H, H-2, m), 5.10 (1 H, H-3 endo, t, J 6.5 Hz), 5.31 (1 H, H-3 acac, s) p.p.m.

(b) The above procedure was repeated using E_2Rh(I)hfpd (37.5 mg, 0.1 mmol) and (E)-hexa-1,4-dien-3-ol (10 mg, 0.1 mmol), to give a red oil which could not be crystallised.

^{1}H n.m.r. ($CDCl_3$): 1.31 (3 H, H-6, d), 1.78 (1 H, O-H), 2.85 (2 H, H-1, m), 3.70 (1 H, H-5, m), 4.26 (1 H, H-4, m), 4.42 (1 H, H-2, m), 5.15 (1 H, H-3, m), 6.12 (1 H, H-3, m), 6.12 (1 H, H-3 acac, s) p.p.m. All signals except (H-3 acac) were broad, even at -30°C.

3.3.2 (E,E)-hepta-2,5-dien-4-ol

(a) (E,E)-hepta-2,5-dien-4-ol (13.1 mg, 0.12 mmol) was reacted with $E_2Rh(I)hfpd$ (44 mg, 0.12 mmol) as described in procedure (1a) to give a red oil.

^1H n.m.r. ($CDCl_3$): 1.25 (2 x 3 H, H-1, d, J 6.2 Hz), 1.85 (1 H, O-H), 3.50 (2 H, H-2, m), 4.15 (2 H, H-3, m), 5.20 (1 H, H-4 endo, t, J 6.5 Hz), 6.10 (1 H, H-3 acac, s) p.p.m.

Addition of a further equivalent of dienol produced no change in spectrum.

I.r. (2.5% CCl_4): 3610 (w, sh), 3050 (w), 2950 (w), 2910 (m), 1620 (s), 1605 (s), 1555 (m), 1462 (s), 1378 (m), 1348 (m), 1255 (s), 1206 (s), 1150 (s), 1100 (m), 1070 (m), 1036 (m), 968 (w) cm^{-1}.

(b) (E,E)-hepta-2,5-dien-4-ol (13.1 mg, 0.117 mmol) was reacted with $E_2Rh(I)pd$ (30 mg, 0.17 mmol), as described above to give an orange oil.

^1H n.m.r. ($CDCl_3$): 1.25 (2 x 3 H, H-1, d, J 6.2 Hz), 1.85 (1 H, O-H), 1.87 (2 x 3 H acac, s), 3.15 (2 H, H-2, m), 3.87 (2 H, H-3, m), 5.13 (1 H, H-4 endo, t, J 6.5 Hz), 5.30 (1 H, H-3 acac, s) p.p.m.

3.3.3 (Z,Z)-hepta-2,5-dien-4-ol

(a) (Z,Z)-hepta-2,5-dien-4-ol (57.3 mg, 0.512 mmol) was dissolved in dry ether (1 cm^3) and added to $E_2Rh(I)hfpd$ (93.5 mg, 0.255 mmol). The solvent was removed (rotary evaporator) to leave an orange precipitate which recrystallised from ether: pentane to give orange-yellow crystals of 1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis-[(Z,Z)-hepta-2,5-dien-4-ol]-rhodium(I), (124 mg, 0.232 mmol), m.p. 118-120°C, in 91% yield. Combustion analysis; expected (found):

C 42.71% (42.73%), H 4.67% (4.63%).

^{1}H n.m.r. (d^6 benzene): 1.44 (2 x 3 H, H-1, d, J 6.5 Hz), 1.62 (2 x 2 H, H-7, d, J 6.5 Hz), 2.45 (2 H, H-2, m), 2.88 (2 H, H-3, m), 5.15 (2 H, H-4, t), 5.52 (4 H, 2H-5 and 2H-6, m), 6.06 (1 H, H-2 acac, s) p.p.m.

I.r. (0.5% and 2.5%, CCl_4): 3270 (m, br), 3020 (m, sh), 2935 (w), 1658 (s), 1460 (s), 1348 (m), 1248 (s), 1210 (s), 1150 (s), 1100 (w), 1010 (w), 950 (w), 680 (w) cm^{-1}.

M.s. (FI): m/z 534 (M^+), 532, 516, 500.

(b) Reaction of (Z,Z)-hepta-2,5-dien-4-ol with E_2Rh(I)pd, as described above, gave an orange oil which could not be crystallised. ^{1}H n.m.r. indicated formation of a complex analogous to the Rh(I)hfpd complex, but spectra were ill-defined with broad and indistinct resonances.

3.3.4 (E,Z)-hepta-2,5-dien-4-ol

(a) (E,Z)-hepta-2,5-dien-4-ol (31 mg, 0.277 mmol), was dissolved in dry ether (1 cm^3) and added to E_2Rh(I)hfpd (50 mg, 0.137 mmol). Removal of solvent gave orange crystals which were crystallised from ether:pentane to give 1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis-(E,Z)-hepta-2,5-dien-4-ol-rhodium(I) (63 mg, 0.188 mmol), m.p. 88-89°C, in 86% yield. Combustion analysis: expected (found): C 42.71 (42.91%) H 4.67 (4.22%).

^{1}H n.m.r. (d^6 benzene): 1.51 (4 x 3 H, m), 3.03 (2 H, H-2, m), 3.89 (2 H, H-3, m), 4.73 (2 H, H-4, m) 5.48 (4 H, 2H-5 and 2H-6, m), 6.02 (1 H, H-3 acac, s) p.p.m.

I.r. (0.5%, CCl_4): 3260 (br), 3010 (w), 2970 (m), 2910 (m), 1643 (s), 1605 (s), 1454 (s), 1335 (m), 1196 (m), 1155 (s) cm^{-1}.

M.s. (EI): m/z 422 (10.0%), 212 (12.6%, 196 (9.7%), 97 (84.5%) 69 (100%).

M.s. (FI): m/z 534 (M^+) 532, 516, 500.

3.3.5 Prop-2-en-1-ol (allyl alcohol)

Allyl alcohol (16 mg, 0.275 mmol) was dissolved in dry ether (1 cm^3) and added to E_2Rh(I)hfpd (50 mg, 0.137 mmol). Removal of solvent gave yellow crystals which were recrystallised from ether:pentane to give 1,1,1,5,5,5-hexafluoro-2,4-pentanedionato-bis(prop-2-en-1-ol)rhodium(I) (51 mg, 0.12 mmol), m.p. 93-94°C in 87% yield. Combustion analysis: expected (found): C 31.01 (31.18%), H 3.08 (3.03%).

^{1}H n.m.r. (d^6 benzene): 1.96 (2 H, H-3, d, J *cis* 7.8 Hz), 2.87 (2 H, H-2, m), 3.18 (2 H, H-3, d, J *trans* 13.3 Hz), 3.48 (4 H, H-1, m), 6.07 (1 H, H-3 acac, s), 6.40 (1 H, O-H) p.p.m.

I.r. (0.5%, CCl_4: 3320 (m, br), 3010 (w), 2920 (w), 1622 (m, sh), 1445 (m, sh), 1258 (s, sh), 1220 (s, sh), 1160 (s), 1100 (m, sh), 1018 (m, sh), 995 (w, sh), 685 (w, sh) cm^{-1}.

M.s. (EI): m/z 368 (12.0%), 208 (7.2%), 139 (100%), 69 (98.5%).

M.s. (FI): m/z 426 (M^+).

3.3.6 But-3-en-2-ol

But-3-en-2-ol (20 mg, 0.277 mmol) was reacted with E_2Rh(I)hfpd (50 mg, 0.136 mmol), as described for allyl alcohol. The yellow crystals were recrystallised from ether:pentane to give 1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis(but-3-en-2-ol)rhodium(I) (51 mg, 0.112 mmol), m.p. 117°C, d, in 82% yield.

Combustion analysis: expected (found): C 34.38 (34.48%), H 3.77 (3.79%).

^{1}H n.m.r. (d^6 benzene): 1.18 (2 x 3 H, H-1, d, J 6.6 Hz), 1.90 (2 H, H-4, J *cis* 7.8 Hz), 2.80 (2 H, H-3, m), 3.18 (2 H, H-4, d, J *trans* 13.3 Hz), 3.86 (2 H, H-2, m), 6.20 (1 H, H-3 acac, s), 6.80 (2 H, O-H) p.p.m.

I.r. (0.5%, CCl_4): 3320 (m, br), 3005 (w), 2930 (s), 1630 (m), 1450 (m, sh), 1225 (s), 1165 (s), 1000 (m), 996 (w) cm^{-1}.

M.s. (EI): m/z 382 (3.0%), 208 (8.0%), 139 (100%), 69 (62.2%).

3.3.7 (Z)-but-2-en-1,4-diol

(Z)-but-2-en-1,4-diol (24 mg, 0.273 mmol) was dissolved in ether: acetone (3:1) and added to E_2Rh(I)hfpd (50 mg, 0.137 mmol). An orange precipitate was formed, removed by filtration, and washed with ether to give yellow crystals of 1,1,1,5,5,5-hexafluoro-2,4-pentanedionatobis[(Z)-but-2-en-1,4-diol]rhodium(I) (56 mg, 0.115 mmol), m.p. 113-114°C, in 84% yield.

Combustion analysis: expected (found): C 32.12 (32.52%), H 3.53 (3.59%).

^{1}H n.m.r. (d^6 acetone): 2.87 (3 H, O-H), 322 (4 H, 2H-2 and 2H-3, m), 3.68 (4 H, H-1, dd, Jgem 12.7 Hz, $J_{1,2}$ 5.1 Hz), 4.14 (4 H, H-1', m), 4.29 (1 H, O-H), 6.20 (1 H, H-3 acac, s) p.p.m.

I.r. (0.5% CCl_4: 3360 (m, br), 1630 (m), 1270 (s), 1215 (s), 1160 (s), 765 (s) cm^{-1}.

M.s. (EI): m/z 398 (7.2%), 381 (14.0%), 209 (17.2%), 139 (75.0%), 69 (100%).

N.B. (E)-but-2-en-1,4-diol did not give a crystalline product, and the ^{1}H n.m.r. spectrum was complex.

3.3.8 (E,E)-4-acetoxyhepta-2,5-diene

(E,E)-4-acetoxyhepta-2,5-diene (21 mg, 0.137 mmol) was dissolved in dry ether (1 cm^3) and added to $E_2Rh(I)hfpd$ (50 mg, 0.137 mmol). Removal of solvent gave a red oil.

^1H n.m.r. ($CDCl_3$): 1.24 (2 x 3 H, H-1, d, J 6.5 Hz), 1.93 (3 H, s), 3.44 (2 H, H-2, m), 4.11 (2 H, H-3, m), 5.90 (1 H, H-4, t, J 6.5 Hz), 6.12 (1 H, H-3 acac, s) p.p.m.

I.r. (2% CCl_4): 3020 (w), 2970 (w), 2020 (w), 2855 (w), 1742 (m) - (C=O, unchanged from free diene), 1625 (m), 1550 (m), 1420 (m), 1268 (s), 1222 (s), 1155 (s), 1095 (w), 1028 (m), 963 (w) cm^{-1}.

3.3.9 (E)-3-acetoxyhexa-1,4-diene

(a) (E)-3-acetoxyhexa-1,4-diene (10 mg, 71.4 mmol) was reacted with $E_2Rh(I)hfpd$ (26.1 mg, 71.4 mmol) as described above to give a red oil.

^1H n.m.r. ($CDCl_3$): 1.26 (3 H, H-6, d, J 6.5 Hz), 1.94 (3 H, s), 1.69 (1 H, H-1, d, J *trans* 12.5 Hz), 1.85 (1 H, H-1, d, J *cis* 8.0 Hz), 3.59 (1 H, H-5, m), 4.19 (1 H, H-4, m), 4.35 (1 H, H-2, m) 5.90 (1 H, H-3, t), 6.14 (1 H, H-3 acac, s) p.p.m.

(b) (E)-3-acetoxyhexa-1,4-diene was reacted with $E_2Rh(I)pd$ as described above to give an orange oil.

^1H n.m.r. ($CDCl_3$): 1.28 (3 H, H-6, d, J 6.6 Hz), 1.93 (3 x 3 H acac, s), 2.40 (1 H, H-1, d, J *trans* 12.5 Hz), 2.65 (1 H, H-1, d, J *cis* 8.0 Hz), 3.30 (1 H, H-5, m), 3.92 (1 H, H-4, m), 4.09 (1 H, H-2, m), 5.32 (1 H, H-3 acac, s), 5.86 (1 H, H-3, t) p.p.m.

3.3.10

Reactions between (E,E)-4-acetoxyhepta-2,5-diene and $E_2Rh(I)pd$ lead only to isomerisation. This also occurs in the reactions of (E,Z)- and (Z,Z)-4-acetoxyhepta-2,5-dienes with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$.

3.4 Rh(I) INDUCED REARRANGEMENTS OF 3-ACETOXY-1,4- AND 4-ACETOXY-2,5-DIENES AND DIENOLS

3.4.1 (E,E)-4-acetoxyhepta-2,5-diene

(E,E)-4-acetoxyhepta-2,5-diene (0.5 mg, 3.25 mmol) was dissolved in dry benzene (5 cm^3) and maintained at 80°C in the presence of 5 mol per cent $E_2Rh(I)pd$ (41 mg, 0.15 mmol). After 4 hours, the ^1H n.m.r. spectrum indicated complete reaction. Fractional distillation gave (i) 55% (E,E)-1,3,5-heptatriene (143 mg, 1.5 mmol) and (ii) 45% (E,E)-2-acetoxyhepta-3,5-diene (200 mg, 1.3 mmol).

(i) ^1H n.m.r. (d^6 benzene): 1.53 (3 H, H-7, d, J 6.5 Hz), 4.96 (1 H, H-1, d, J *cis* 10 Hz), 5.10 (1 H, H-1, d, J *trans* 17 Hz), 5.48 (1 H, H-6, m), 6.10 (3 H, m), 6.30 (1 H, m) p.p.m.

(ii) ^1H n.m.r. ($CDCl_3$): 1.31 (3 H, H-1, d, J 6 Hz), 1.75 (3 H, H-7, d, J 6.5 Hz), 2.00 (3 H, s), 5.35 (1 H, H-2, m, $J_{2,3}$ 6 Hz), 5.50 (1 H, H-3, dd, $J_{3,4}$ 15.5 Hz, $J_{2,3}$ 6 Hz), 5.73 (1 H, H-6, dq, $J_{5,6}$ 15.5 Hz, $J_{6,7}$ 6.5 Hz), 6.00 (1H, H-5, dd, J 10.5 Hz and 15.5 Hz), 6.19 (1 H, H-4, dd, J 15.5 Hz and $J_{4,5}$ 10.5 Hz) p.p.m.

I.r. (film): 3020 (m, sh), 2965 (s), 2910 (m), 2855 (m), 1730 (s), 1652 (m), 1443 (m), 1365 (s), 1230 (s), 1142 (m), 1042 (s), 990 (s), 945 (s), 830 (w) cm^{-1}.

U.v.: $\lambda_{max}^{n\text{-hexane}}$ 227 nm

ϵ 27900

M.s. (EI): m/z 154 (M^+, 5.5%), 112 (13.7%), 95 (83.5%), 79 (49.1%), 42 (100%).

3.4.2 (E,Z,)-4-acetoxyhepta-2,5-diene

(E,Z)-4-acetoxyhepta-2,5-diene was thermolysed with 5 mol % $E_2Rh(I)pd$ in d^6 benzene as described above. After 24 hours ^1H n.m.r. indicated complete reaction to give (E,Z) and (E,E)-2-acetoxyhepta-2,5-diene (60:40) as judged by ^1H n.m.r. spectroscopy.

^1H n.m.r. ($CDCl_3$): for (E,E)-isomer *cf.* Section 3.4.1.

(E,Z): 1.31 (3 H, H-1, d, J 6 Hz), 1.78 (3 H, H-7, d), 2.00 (3 H, s), 5.32 (1 H, H-2, m), 5.70 (1 H, H-3, dd, $J_{3,4}$ 1.5 Hz, $J_{2,3}$ 6 Hz), 5.70 (1 H, H-6, dq, $J_{5,6}$ 11 Hz, $J_{6,7}$ 7.5 Hz), 6.08 (1 H, H-5, dd, $J_{4,5}$ 10.5 Hz and $J_{5,6}$ 11 Hz), 6.62 (1 H, H-4, dd, J 15.5 Hz and 10.5 Hz) p.p.m.

3.4.3 (Z,Z)-4-acetoxyhepta-2,5-diene

Treatment with 5 mol % $E_2Rh(I)pd$ and thermolysis in benzene for 50 hours gave (E,Z)-2-acetoxyhepta-3,5-diene, b.p. 85-87°C (2 mm).

^1H n.m.r. ($CDCl_3$): *cf.* Section 3.4.2.

I.r. (film): 3020 (m, shoulder), 2070 (s), 2935 (s), 1735 (s), 1438 (m), 1365 (s), 1228 (s), 1160 (m, sh), 1123 (m, sh), 1025 (s, sh), 993 (s, sh), 940 (s, sh), 845 (w, sh), 720 (m) cm^{-1}.

M.s. (EI): m/z 154 (M^+, 16.3%), 112 (24.0%), 95 (39.2%), 79 (100%), 43 (84.5%).

3.4.4 (E)-hexa-1,4-dien-3-ol

(E)-hexa-1,4-dien-3-ol (0.3 g, 3.1 mmol) was dissolved in dry benzene (5 cm^3) and thermolysed with 5 mol % $E_2Rh(I)hfpd$ (56 mg, 0.15 mmol) at 80°C. After 60 hours, ^1H n.m.r. indicated reaction was complete, leading to one product. Distillation gave (E)-hex-2-en-4-one (0.27 g, 27.5 mmol) in 90% yield (identical with a sample prepared from ethyl-magnesium bromide and croton-aldehyde).

^1H n.m.r. (d^6 benzene): 0.92 (3 H, t), 1.28 (3 H, H-1, d, J 6.6 Hz), 2.05 (2 H, q), 5.89 (1 H, H-3, d, J 15.5 Hz), 6.47 (1 H, H-2, dq, J 15.5 Hz and 6.6 Hz) p.p.m.

I.r. (film): 3020 (w), 2965 (m, sh), 2935 (m), 1672 (s), 1621 (m), 1448 (m), 1372 (m, sh), 1354 (m), 1330 (m), 1205 (m, sh), 1121 (w), 970 (m, sh), 810 (m, sh) cm^{-1}.

M.s. (EI): m/z 98 (M^+, 4.7%), 69 (100%).

3.4.5 (E,E)-hepta-2,5-dien-4-ol

(E,E)-hepta-2,5-dien-4-ol (60 mg, 0.536 mmol) was thermolysed with 5 mol % $E_2Rh(I)hfpd$ (7 mg, 26.8 mmol) in d^6 benzene at 80°C. After 12 hours distillation gave a mixture containing (i) 85% (E)-hept-2-en-4-one (identical with a sample prepared from the coupling of crotonaldehyde and n-propylmagnesiumbromide), and (ii) 15% (E,E)-hepta-2,5-dien-4-one (identical with a sample prepared by MnO_2 oxidation of (E,E)-hepta-2,5-dien-4-ol).

(i) ^1H n.m.r. (d^6 benzene): 0.82 (3 H, H-7, t), 1.39 (3 H, H-1, d, J 6.5 Hz), 5.91 (1 H, H-3, dd, $J_{2,3}$ 15.2 Hz and $J_{1,3}$ 1.3 Hz), 6.46 (1 H, H-2, m) p.p.m.

(ii) ^{1}H n.m.r. (d^6 benzene): 1.43 (2 x 3 H, H-1, d), 6.16 (2 H, H-3, dd, J 15.2 Hz and 1.3 Hz), 6.74 (2 H, H-2, m) p.p.m.

3.4.6 (E,Z)-hepta-2,5-dien-4-ol

Treatment with 5 mol % E_2Rh(I)hfpd, as in Section 3.4.5, gave, after 12 hours at 80°C, a mixture containing ~ 85% (E)- and (Z)-hept-2-en-4-one. Further reaction (36 hours) gave 85% (E)-hept-2-en-one and 15% (E,E)-hepta-2,5-dien-4-one.

3.4.7 (Z,Z)-hepta-2,5-dien-4-ol

Treatment with 5 mol % E_2Rh(I)hfpd as described in Section 3.3.5 gave only 20% reaction after 3 days at 80°C, the major product being (Z)-hept-2-en-4-one.

3.4.8 (E,E)-, (E,Z)- and (Z,Z)-hept-2,5-dienes

Treatment with 5 mol % E_2Rh(I)pd and E_2Rh(I)hfpd, at 80°C in d^6 benzene for 72 hours did not facilitate isomerisation. Thermolysis of 1,1,1,5,5,5-hexafluoro-2,4-pentanedionato [(E,E)-hepta-2,5 diene]rhodium(I), in d^6 benzene, at 80°C gave a similar result.

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CHAPTER 4

SYNTHESIS OF C_{18} ALKENES AND THEIR COMPLEXATIONS TO Rh(I)

4.1 The preparations of (E)- and (Z)-octadec-9-enes, (Z,Z)-octadeca-6,9-diene and (Z,Z,Z)-octadeca-3,6,9-triene are described, and the complexations of these compounds, and the corresponding methyl esters, to Rh(I) are discussed in the light of previous results (Chapter 3).

(E)- and (Z)-octadec-9-ene, (Z,Z)-octadeca-6,9-diene and (Z,Z,Z)-octadeca-3,6,9-triene were prepared as shown in Fig. 4.1.A. Thus, (E)- and (Z)-octadec-9-enoic (elaidic and oleic acid) were converted to methyl oleate and methyl elaideate respectively, by acid catalysed esterification in methanol.

This reaction is known to proceed smoothly to produce pure product without any geometrical isomerisation[1]. (Z,Z)-octadeca-9,12-dienoic acid (linoleic acid) and (Z,Z,Z)-octadeca-9,12,15-trienoic acid are more sensitive to acidic conditions[2] and were therefore converted to the corresponding methyl esters by reaction with diazomethane at $-70^{\circ}C$ in ether. This method is known to cause little, if any, isomerisation under the conditions[3]. An alternative method for this conversion involves the use of BF_3: methanol reagent[4]. The extent to which this reagent has been used, however, has been limited because of significant amounts of by-product formation during esterification. Lough[5] has reported the formation of methoxy-substituted fatty acids during the esterification of unsaturated fatty acids with BF_3: MeOH.

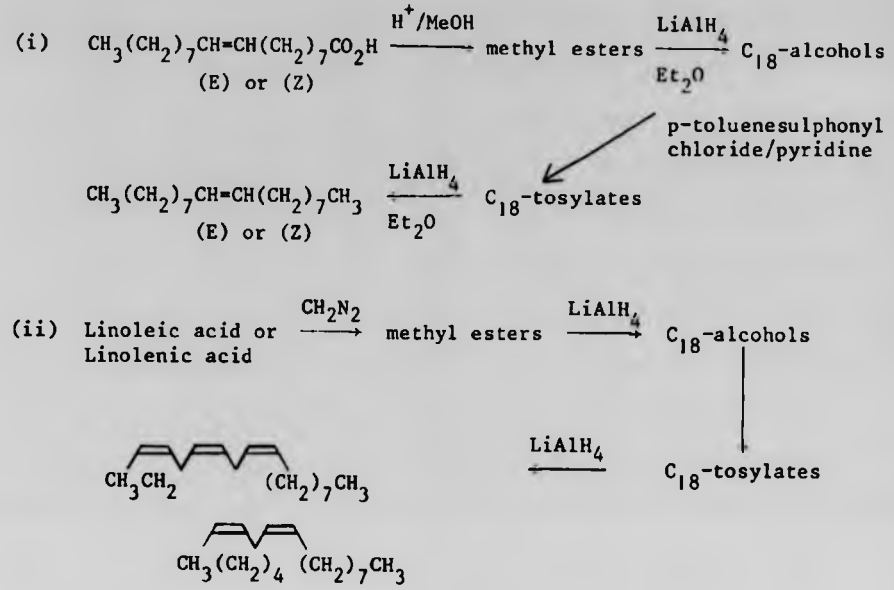


Fig. 4.1.A

This observation is supported by the report of methoxy-ester formation during the methanolysis of oleic acid by BF_3:MeOH[6]. A thorough investigation[7] into methyl ester formation using this reagent has ascertained that impure samples of BF_3:MeOH are capable of producing artefacts under harsh conditions, but under normal conditions high yields of pure ester are obtained.

Reduction of all four methyl esters with $LiAlH_4$ in diethyl ether gave oleyl, elaideyl, linoleyl and linolenyl alcohols in > 90% yield. This reaction has been used extensively for reduction of unsaturated fatty acids and their esters and is reported to proceed without isomerisation or double bond reduction[8].

Conversion of the alcohols to tosylates by reaction with p-toluenesulphonylchloride in pyridine, followed by reduction with lithium aluminium hydride gave (E)- and (Z)-octadec-9-ene, (Z,Z)-octadeca-6,9-diene and (Z,Z,Z)-octadeca-3,6,9-triene[9]. In an alternative

procedure, Mangold and co-workers converted oleyl, elaideyl and linoleyl alcohols to the corresponding mesylates by reaction with sulphonyl chloride/triethylamine reagent. Their justification for this approach was that difficulties had previously been encountered in the purification of tosylates[10], while in another case 20% chloride substitution was observed during the tosylation of oleyl alcohol[11]. Using the procedure described in the experimental section these problems were never encountered and the tosylates were conveniently purified by fast column chromatography[12]. More recently (E)- and (Z)-octadec-9-enes have been reported[13] as products during the metathesis of methyl oleate. This process is now known to proceed *via* a chain process involving metal carbene intermediates. The overall reaction for the production of the octadec-9-enes can be written as follows (Fig. 4.1.B).

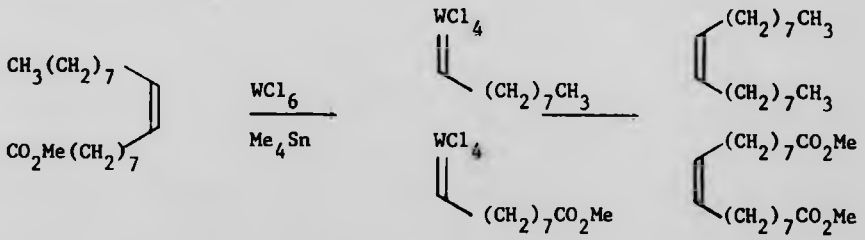


Fig. 4.1.B

In a study of this process Nakamura *et al.*[14] observed that for the metathesis of methyl oleate the co-catalyst activity decreased in the following order:

$$Et_3B, \quad Bu_3B, \quad Et_2BCl, \quad Et_3SiH, \quad TiH_4.$$

If stereochemically pure octadecenes are required, then care must be taken to avoid conditions which could conceivably cause isomerisation. It is known that under the right conditions, acid and base are capable of causing the isomerisation of double bonds. Ast[15] observed conjugative isomerisation during the saponification

of triglycerides with KOH/MeOH, while (Z,Z)-octadeca-6,9-diene and linoleyl alcohol have been shown to isomerise to conjugated isomers when heated with KOH/diethyleneglycol (Table 4.1.C).

Table 4.1.C (Taken from Ref. 16)

		Temperature of Reaction			
(Original)	(%)	120°	150°	180°	234°
Acetate					
18:1(9)	0.9	0.9	0.9	0.7	0.8
18:2(9,12)	99.1	98.0	86.7	5.0	4.5
18:2conj. *cis,trans*	-	1.1	11.0	85.0	54.2
18:2conj. *cis,cis*	-	-	1.4	3.9	13.8
18:2conj. *trans,trans*	-	-	-	4.9	26.6
Hydrocarbon					
18:1(9)	0.8	0.8	0.8	0.9	0.7
18:2(9,12)	99.2	99.2	96.4	46.9	5.1
18:2conj. *cis,trans*	-	-	1.6	45.7	39.2
18:2conj. *cis,cis*	-	-	0.5	3.0	13.8
18:2conj. *trans,trans*	-	-	0.7	3.5	41.2

Under mildly alkaline conditions linoleic acid can be isomerised to a mixture containing (Z,E)-octadeca-9,11-dienoic acid and (E,Z)-octadeca-10,12-dienoic acid, while linolenic acid gives a more complex mixture[16]. This is not the case with oleic acid where even at 280°C with NaOH/glycerol only very limited double-bond migration is observed. Use of fused NaOH however, gives considerable double-bond migration. In these isomerisations the static double bond normally retains its geometrical configuration, but the migrating double bond

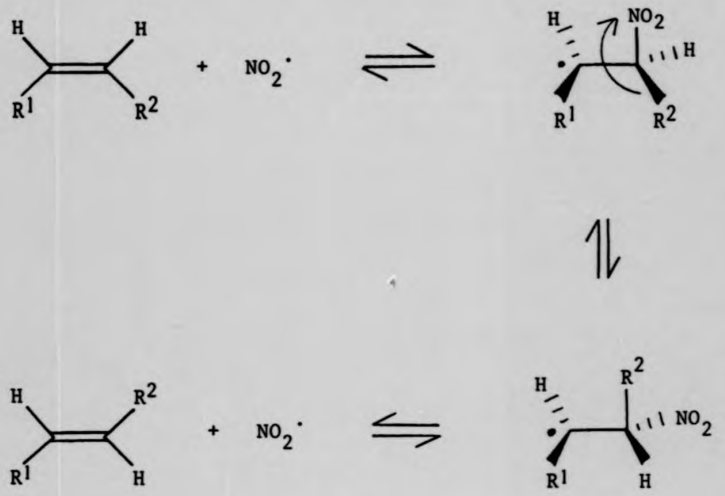


Fig. 4.1.D

if originally *cis* becomes predominantly *trans*, but if originally *trans* appears to form both *cis* and *trans* double bonds in equal proportions[17].

Acid- and base-catalysed isomerisations usually lead to geometrical and positional isomerisation, but with certain catalysts it is possible to obtain selective geometrical isomerisation. A particularly useful catalyst for this isomerisation is nitrous acid, generated from $NaNO_2$ and HNO_3. With oleic acid *cis-trans* equilibration is achieved in > 15 mins. at 90°C with 0.8% (w/w) HNO_2 [18].

Nitrous acid is known to decompose to N_2O_3, NO_2 and NO, and of these it was reported that NO_2 was the most active promoter of isomerisation with as little as 0.2% by-product being formed. It is known that the reaction is initiated by radical addition to the double bond to give a nitroalkyl radical, followed by rotation and loss of nitro radical to form the isomeric olefin (Fig. 4.1.D)[19].

Another type of catalyst useful for geometrical isomerisation which does not simultaneously form positional isomers is the thiyl radical, generated from either mercaptans or sulphides. Kircher[20] was the first to apply this method of isomerisation to unsaturated fatty acids and observed that *cis-trans* equilibration was reached within 8 hours at RT. Addition of the mercaptan to the double-bond was found to be a considerably slower process than isomerisation. Arenesulphinic acids have also been observed to catalyse *cis-trans* isomerisation, equilibration being achieved in < 15 mins. with 0.1 mol % catalyst, to give about 80% *trans* isomer[21]. This reaction is also believed to be radical-initiated (Fig. 4.1.E).

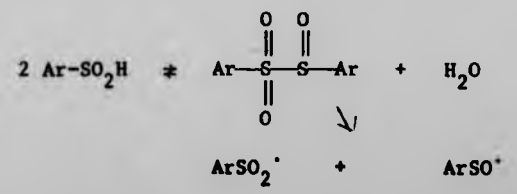


Fig. 4.1.E

The *trans* isomer produced by these reactions usually predominates and for unsaturated fatty acids can be separated by fractional crystallisation. Other catalysts (I_2, Se_2, K^tBuO) facilitate both geometrical and positional isomerisation[22].

One of the main methods for the separation of geometrical and positional isomers of unsaturated fats and lipids is argentation chromatography. This method relies on the Ag^+-olefin interaction as a basis for separation, and although the technique can be very effective, it does have limitations in that it is expensive, sensitive to light and heat, and pro-oxidant. For these reasons it was decided to explore the possibility of using Rh(I) complexes to separate unsaturated fats and lipids. E_2Rh(I)pd and E_2Rh(I)hfpd were thought to be particularly useful complexes for this purpose because:

(1) they are readily available and fairly stable to air and light;

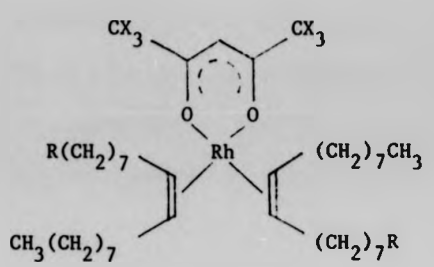
(2) the ethylene is readily displaced by other olefins;

(3) E_2Rh(I)pd and E_2Rh(I)hfpd should not promote geometrical or positional isomerisation of the double bonds present in unsaturated fatty acyl groups, under neutral conditions in aprotic solvents;

(4) they possess a counter ligand which can be modified to enable attachment to polymeric supports[23]; this would facilitate easy handling and rapid recovery.

To explore the potential applications of Rh(I) complexes for the separation of unsaturated fats and lipids, the model octadecenes and their methyl esters, together with some triglycerides were reacted with E_2Rh(I)pd and E_2Rh(I)hfpd and the products were characterised by spectroscopic techniques.

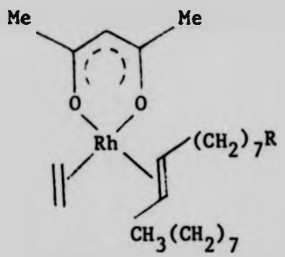
Reaction of two equivalents of either (Z)-octadec-9-ene or



X = H or F

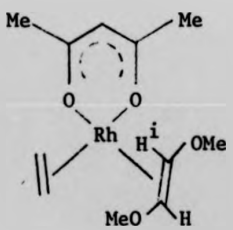
R = CH_3 or $-CH_2Me$

Fig. 4.1.F



R = $-CH_3$ or $-CO_2Me$

Fig. 4.1.K

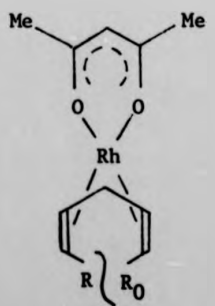


^1H n.m.r. d.^{8}toluene

H^i δ 4.36 p.p.m.

H^a δ 6.35 p.p.m.

Fig. 4.1.J



R = $CH_3(CH_2)_4$

R_0 = $CH_3(CH_2)_7$

Fig. 4.1.L

methyl (Z)-octadec-9-enoate with $E_2Rh(I)pd$ or $E_2Rh(I)hfpd$ caused vigorous evolution of ethylene and on removal of solvent gave oils which could not be crystallised. The ^1H n.m.r. spectra of these complexes indicate the formation of 2:1 complexes as shown in Figure 4.1.F.

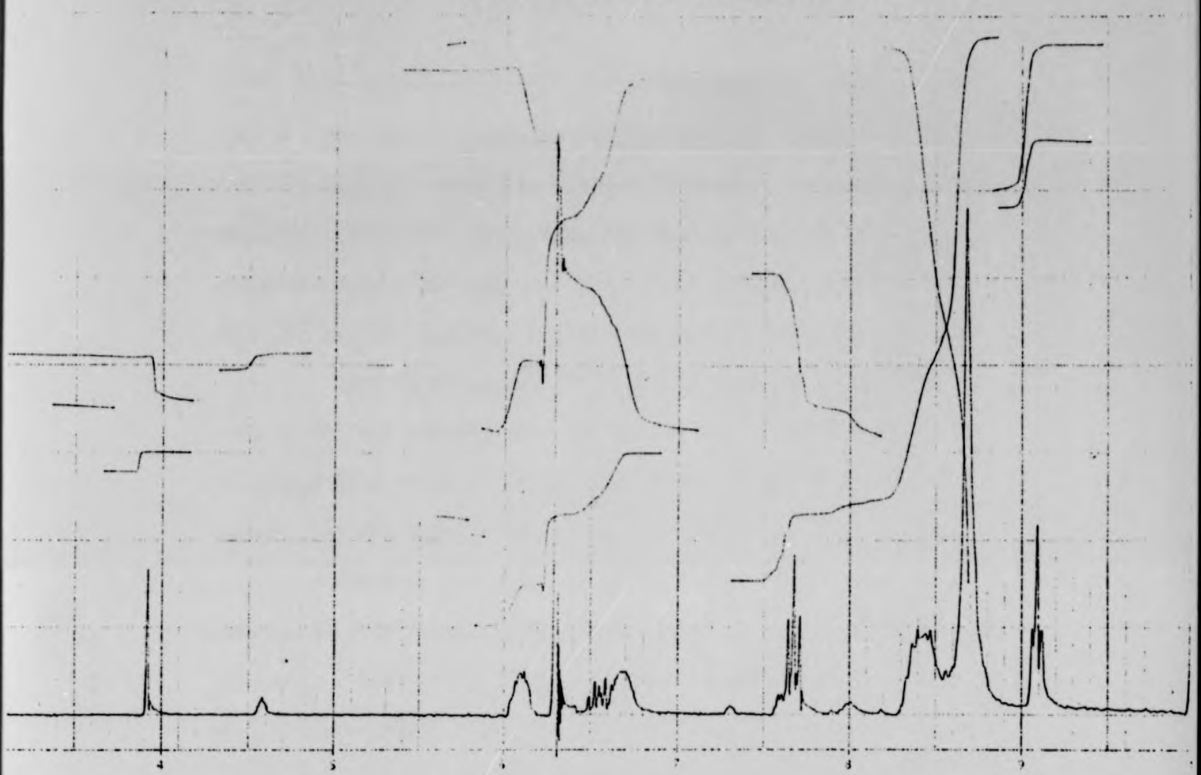
Table 4.1.G

Compound	Rh(I)pd		Rh(I)hfpd
	δ^aH-9,H-10	Me acac	δ^aH-9,H-10
(Z)-octadec-9-ene	2.55	1.72	2.72
Methyl (Z)-octadec-9-enoate	2.55	1.72	2.68
(E)-octadec-9-ene	-	1.69/1.78	2.37 endo 4.13[b] exo
Methyl (E)-octadec-9-enoate	-	1.70/1.79	2.35 endo 4.09 exo

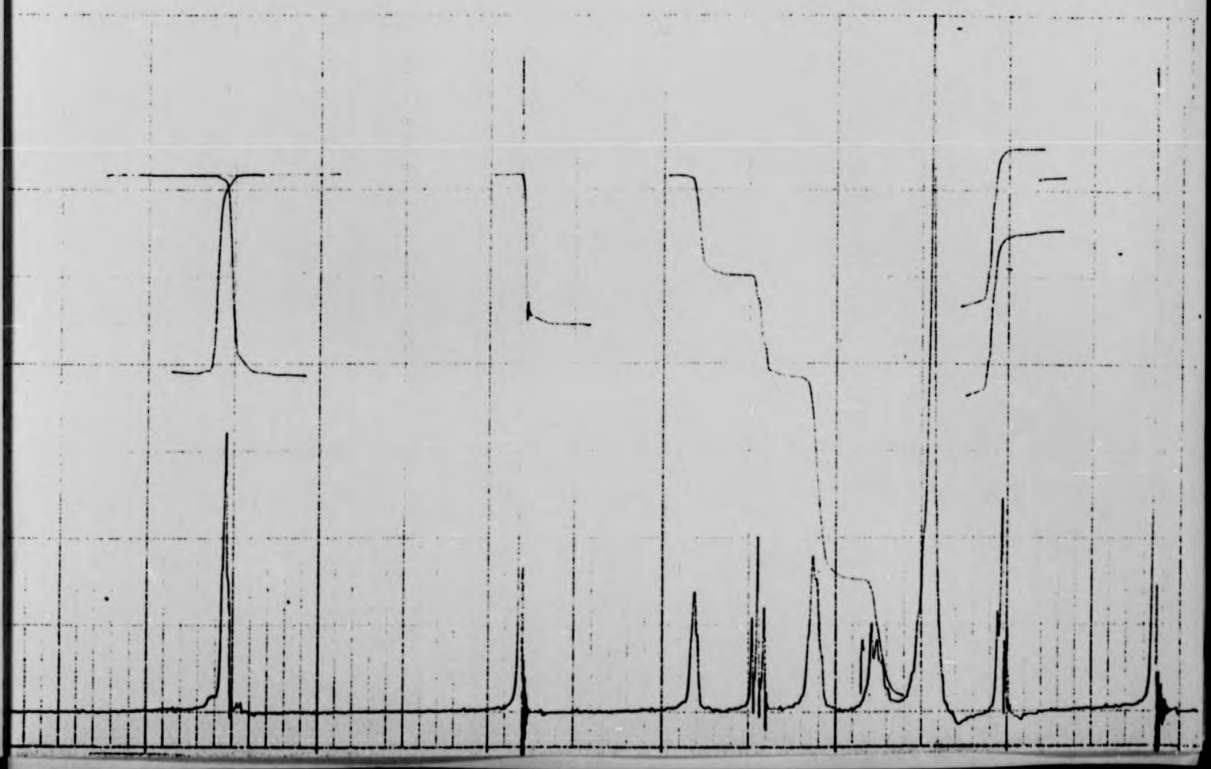
[a] d^6benzene
[b] $CDCl_3$

This structure (Fig. 4.1.F) is supported by ^{13}C n.m.r. spectroscopy, which for the Rh(I)pd-(Z)-octadec-9-ene complex shows C-9 as a doublet (J Rh-C 13.3 Hz) at 78.5 p.p.m. (Figures 4.1.H). This compares with a value of (J Rh-C 14 Hz) for the 2,4-pentanedionatobis-(ethylene)rhodium(I) complex[24]. (E)-octadec-9-ene and methyl (E)-octadec-9-enoate, when reacted with $E_2Rh(I)hfpd$ in the manner described above, gave complexes whose ^1H n.m.r. spectra are consistent with a structure similar to that shown in Figure 4.1.F. However, reaction of (E)-octadec-9-ene and methyl (E)-octadec-9-enoate with $E_2Rh(I)pd$ led predominantly to displacement of only one ethylene ligand to give a monoethylene complex shown in Figure 4.1.J.

^{1}H n.m.r. spectrum of methyl linoelaideate-Rh(I)hfpd
cf. Sec. 4.4.4 for assignments



^{1}H n.m.r. spectrum of methyl linoelaideate



Addition of an excess of (E)-olefin increased the amount of bis-complex, but the monoethylene complex was only removed by repeated redissolving and removal of solvent *in vacuo*. Complexes of this type have been reported[25] during the reaction of methoxy-substituted ethylenes with $E_2Rh(I)pd$, and as with (E)-octadec-9-ene the exo and endo (H^i and H^a) olefinic protons are easily distinguished (Fig. 4.1.K).

With (Z,Z)-octadeca-6,9-diene, (Z,Z,Z)-octadeca-3,6,9-triene, and the corresponding methyl esters, the formation of bidentate complexes with Rh(I) is precluded because of the steric interaction between two *cis* substituents (Fig. 4.1.L)[26].

However, two equivalents of these olefins displace ethylene completely from $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ to give bis(monodentate) complexes. The ^1H n.m.r. and ^{13}C n.m.r. spectra of the products are particularly complex (Fig. 4.1.M) and can be interpreted in either of two ways. Firstly, any one of the double bonds of the diene or triene can co-ordinate to Rh(I) giving rise to positional isomers and if rotation is restricted, rotational isomers[27]; secondly, it may be possible for the unco-ordinated double bond to co-ordinate to Rh(I) in an intramolecular displacement reaction. It is highly likely that a series of positional isomers are formed, as is indicated by the complexity of the co-ordinated olefin region of the ^{13}C n.m.r. spectra, but it is not clear whether intramolecular displacements can occur in these complexes (Fig. 4.1.N).

In contrast to the (Z,Z)-diene, methyl (E,E)-octadeca-9,12-dienoate reacted with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ to give bidentate complexes. The ^1H n.m.r. spectra of these complexes (Fig. 4.1.P) are consistent with the structure shown in Fig. 4.1.Q.

It can be seen that the reactions of the isomeric fatty acid derivatives with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ are analogous to those described for the simple "skipped" dienes, (E,E)-, (Z,Z)- and

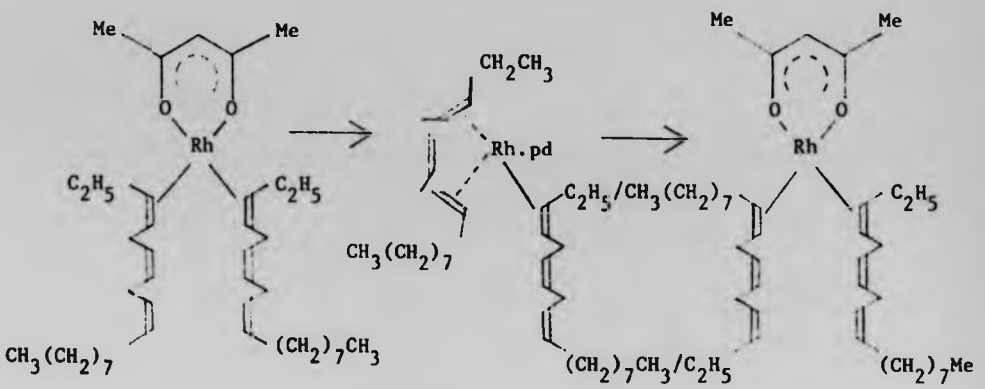
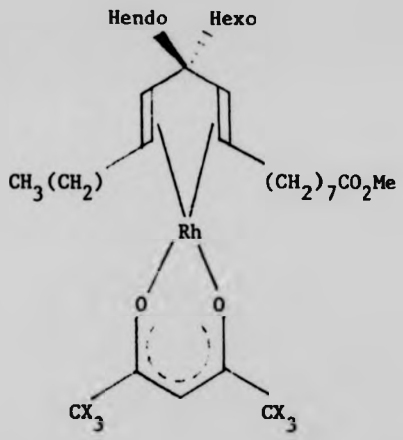


Fig. 4.1.N



X = F

a 2.39 Hexo

a 3.44 Hendo

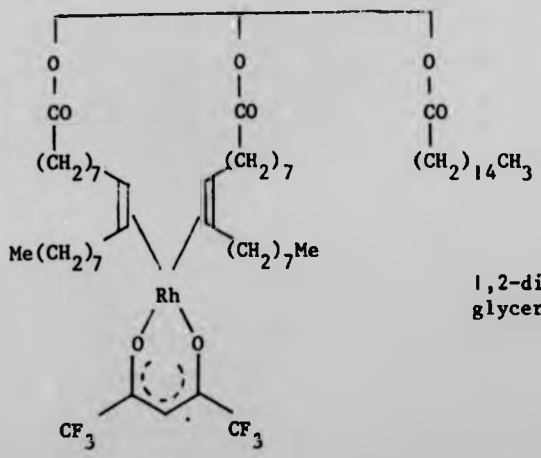
X = H

a 2.21 Hexo

a 3.32 Hendo

a-d.^{6}benzene

Fig. 4.1.Q



1,2-dioleyl-3-palmitoyl-glycerol + E_2Rh(I)hfpd

Fig. 4.1.R

(E,Z)-hepta-2,5-dienes (Chapter 3). The conclusions to be drawn from these complexation studies are:

(1) (E,E)-"skipped" dienes react with $E_2RH(I)pd$ and $E_2Rh(I)hfpd$ to give *only* bidentate complexes.

(2) (Z)-(C_{18})-monoenes react with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ to give bis(monoene) complexes, whereas (E)-(C_{18})-monoenes can react to give either monoethylene:monoalkene complexes or bis(monoene) complexes.

(3) (Z,Z)-(C_{18})-dienes and (Z,Z,Z)-C_{18} trienes are unable to form bidentate complexes, but give complex mixtures of bis(monodentate) diene and triene products.

Interestingly, it has been found that the triglycerides 1,2-dioleyl-3-palmitoylglycerol,1,3-dielaideyl-2-palmitoylglycerol, and 1,2-dielaideyl-3-palmitoylglycerol react with $E_2Rh(I)hfpd$ (1:1) to give bidentate complexes (Fig. 4.1.R).

The scope of these complexations to rhodium(I) is yet to be tested in full because competition studies would be needed to ascertain if rhodium(I) exhibited preferential co-ordination to a particular C_{18} alkene. However, considering the results presented, it may be possible to exploit the differences in the modes of co-ordination of (Z)-, (E)-, (E,E)-, (Z,Z)- and (Z,Z,Z)-C_{18} alkenes to Rh(I)pd complexes to obtain separation of complex mixtures. A chromatographic process can be envisaged with the $E_2Rh(I)pd$ complexes bound to a solid polymer support. This would be the most appropriate method in terms of efficiency of separation, regeneration of the support and overall cost.

In recent years attempts have been made to combine the advantages of homogenous and heterogenous catalysis mostly by using systems which comprise a transition metal complex bound to an organic support, substituted with functional groups which can act as a ligand.

Such supported catalysts have been used successfully for hydrogenation[28], hydroformylation[28,29], and hydrosilylation[30]. However, inorganic supports possess greater thermal and hydrolytic stability, which would be advantageous for chromatographic separation. A particularly useful support would be silica gel.

To form a chemical bond between a ligand and the surface of silica, a molecule containing the ligating group or a group that may be readily converted to a liganding group, is reacted with the surface silanols. In principle, this may be accomplished in several ways (Fig. 4.1.S).

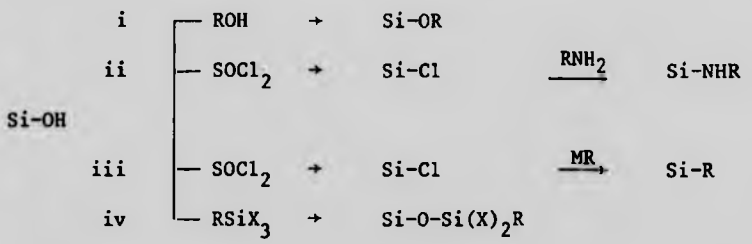


Fig. 4.1.S

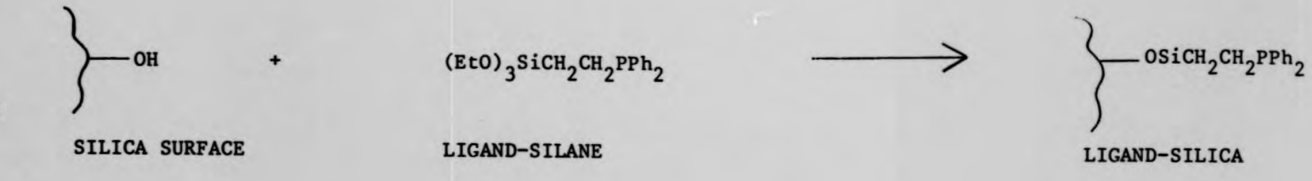
In practice, method (iv) is preferred for bonding ligating groups to silica because:

(i) it produces an Si-O unit at the surface which is more hydrolytically and thermally stable than either an Si-O-C or an Si-N-C unit;

(ii) a wide range of organofunctional compounds of the type $RSiX_3$ are available;

(iii) it is a one-step reaction which proceeds under mild conditions.

Howell and co-workers[31] prepared rhodium supported complexes as described in Figs. 4.1.T and 4.1.U. The first method (Fig. 4.1.T) involves reaction of a ligand silane with the silica gel surface,



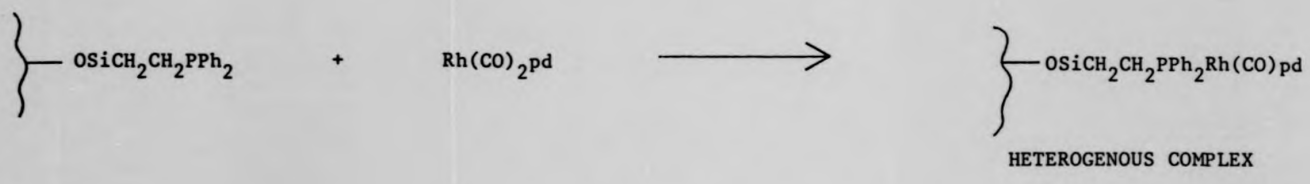
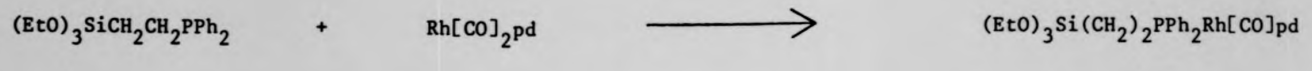


Fig. 4.1.T



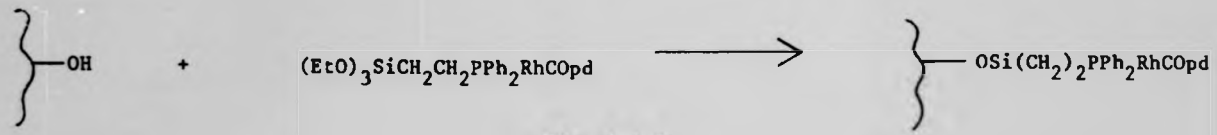


Fig. 4.1.U

followed by reaction of the ligand silica with the metal complex precursor. The second method involves reaction of the ligand-silane with the metal complex precursor prior to attachment to the silica surface. This second method is not available when organic polymers (e.g. polystyrene) are used as supports and it is only available with inorganic supports because the linking reaction proceeds at a point in the ligand molecule removed from the donoratoms, under relatively mild conditions. The chief advantage of preparing the complex in this way is that it eliminates a large degree of uncertainty about the nature of the surface species.

Table 4.1.V

Ligand Silica	Complex Precursor
SIL-$(CH_2)_2PPh_2$	$(CO)_2$Rhpd
SIL-$(CH_2)_2PPh_2$	a
SIL-$(CH_2)_2CN$	a
SIL-$(CH_2)_3NH_2$	a
SIL-$(CH_2)_3NEt_2$	a
SIL-$(CH_2)_4C_5H_4N$	a
SIL-p$C_6H_4CH_2N(CH_2Ph)_2$	a
SIL-$(CH_2)_3SH$	a

a = $[RhCl(CO)_2]_2$

The ligand-silicas described in Table 4.1.V were reacted with the rhodium(I)carbonyl complexes to give silica-supported Rh(I)carbonyl complexes. Howell observed that the reaction of Rh(I)$(CO)_2$pd with tertiary phosphine ligand-silica proceeded to give displacement of one carbonyl group, whereas reaction with $[Rh(I)(CO_2)_2Cl]_2$ resulted in cleavage of the halide bridge and retention of both carbonyl groups. Similar results were observed with the nitrogen donor ligand-

silicas and the sulphur donor ligand-silica, and are consistent with the displacement reactions of the free ligands[32,33]. Some work related to this was reported by Čapkā and Hetflejs[34] who investigated the applicability of several inorganic materials as supports for transition metal complexes.

The supported transition metal complexes were prepared as follows:

$$Y\text{-}Z + MXn \rightarrow Y\text{-}Z\text{---}MXn\text{-}m$$

Y = alumina, silica, molecular sieves, glass

Z = $-PPh_2$, $Si\text{-}(CH_2)_2PPh_2$,

$Si(CH_3)\text{-}(CH_2)_3\text{-}CN$, $Si(CH_2)_3\text{-}N(CH_3)_2$,

$Si(CH_2)_2\text{-}C_5H_4N$

MZ_n = $PdCl_2$, $RhCl_3$, and H_2PtCl_6

Three different methods were employed to introduce the functional groups [-CN, N-(Me)$_2$, $-C_5H_4N$, and P(Ø)$_3$], each utilising the reactivity of the surface hydroxyl groups of the inorganic support.

(i) The support (4A sieves) was reacted with PBr_3 to give oxyphosphorus bromide which was subsequently converted to the phenyl derivative by reaction with phenylmagnesium bromide. This procedure however, was observed to give a substantial decrease in surface area.

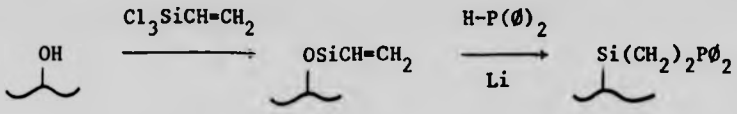
(ii) Inorganic oxide supports (alumina, silica, glass) were treated with alkoxy or chlorosilanes containing suitable organofunctional groups. The Si-OR or Si-Cl groups of these compounds readily react with surface hydroxyl groups.

$$\rangle\!\!-OH + XSi(CH_2)_nY \rightarrow \rangle\!\!-O\text{-}Si(CH_2)_nY$$

X = C_2H_5O, -Cl

Čapkă estimated that the bond strength of the surface silanol bond was about 23.6 kcal mol^{-1}. These bonds are susceptible to hydrolysis, but Čapkă argues that even if this occurs hydrogen bonding between the surface and the hydrolysed ligand will be sufficient to hold the ligand in place.

(iii) The inorganic support was first reacted with a chlorosilane containing an alkene function. The product was then treated with lithium/diphenylphosphine as shown below.



The transition metal complex can then be generated by treatment of the supported ligand with the appropriate metal precursor.

More recently, Tundo and Venturello[35] have successfully attached phase transfer catalysts to silica. The activity of the silica was increased prior to functionalisation by refluxing with 35% HCl. This procedure is known to cleave strained siloxane species which are present on the surface of the silica (Fig. 4.1.W)[36].

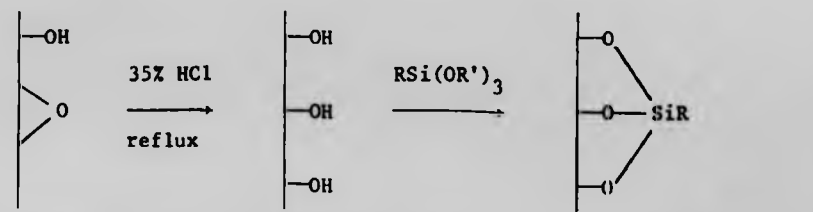
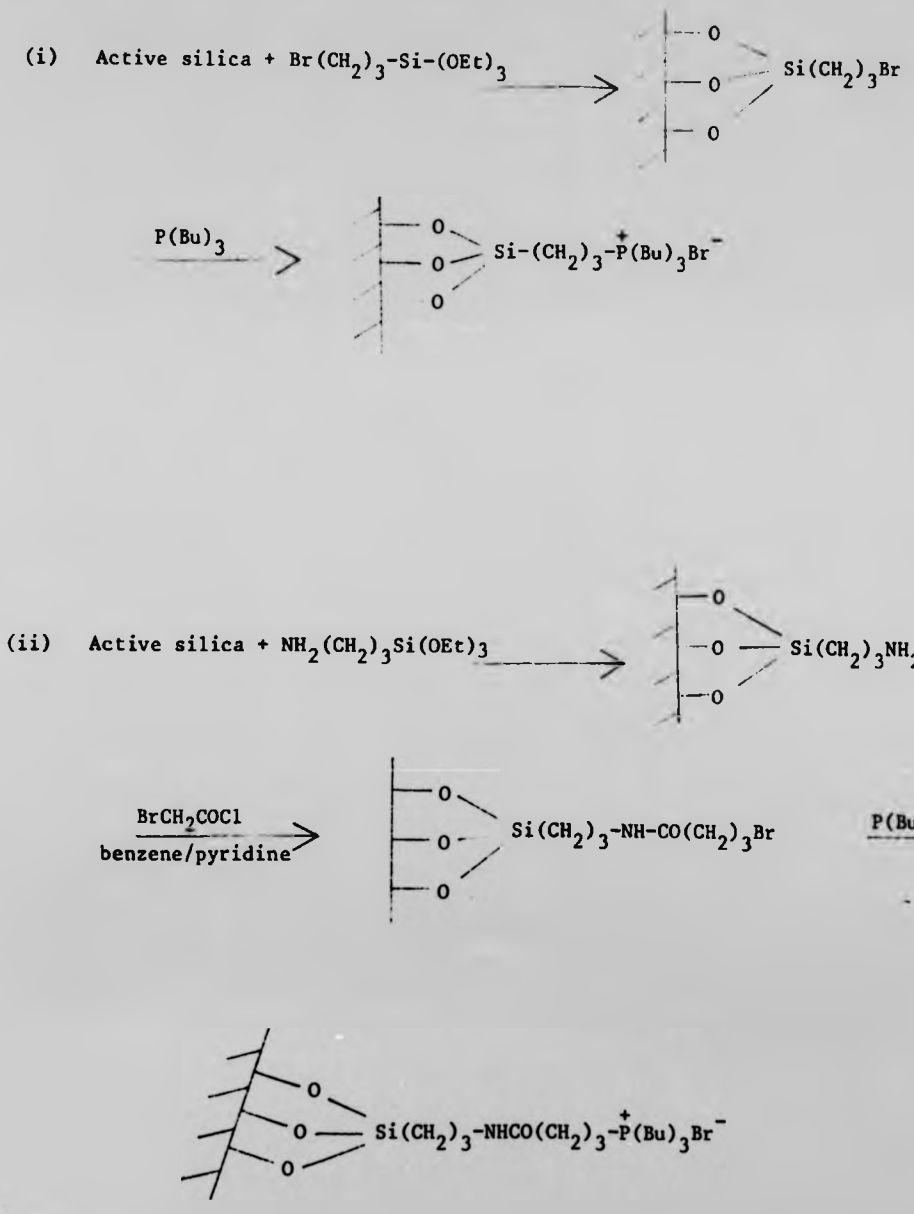


Fig. 4.1.W

Fig. 4.1.X


(i) Active silica + $Br(CH_2)_3$-Si-$(OEt)_3$
$Si(CH_2)_3Br$
$P(Bu)_3$
$Si-(CH_2)_3-\overset{+}{P}(Bu)_3Br^-$
(ii) Active silica + $NH_2(CH_2)_3Si(OEt)_3$
$Si(CH_2)_3NH_2$
$BrCH_2COCl$
benzene/pyridine
$Si(CH_2)_3$-NH-CO$(CH_2)_3Br$
$P(Bu)_3$
$Si(CH_2)_3$-NHCO$(CH_2)_3-\overset{+}{P}(Bu)_3Br^-$

Having activated the silica it was functionalised by reaction with triethoxysilyl derivatives containing the required functional groups, e.g. Fig. 4.1.X. This method is analogous to the one developed by King[37] and Leyden[36] who prepared amine ligands attached to silica and used them to co-ordinate to metal species, e.g. Cu(II), Fe(II), Hg(II) and Mn(II).

In our work the procedure used to attach 2,4-pentanedione to silica gel is summarised in Fig. 4.1.Y. Allyl bromide was reacted with the sodium salt of 2,4-pentanedione to give 3-allyl-2,4-pentanedione. This is analogous to the procedure of Hauser[38] who alkylated 2,4-pentanedione with methallyl chloride and purified the product by fractional distillation. This method has the disadvantage of producing both C-alkylated and O-alkylated products. In general O-alkylation is favoured when the equilibrium concentration of enol is relatively high, as with β-diketones. One of the main methods[39] for achieving C-alkylation employs thallium (I) enolates which appear to give exclusively C-alkylation products on treatment with alkyl halides. However, thallium does have the disadvantages of reducing the nucleophilicity of the enolate as judged by the required reaction conditions, and of being relatively toxic. To overcome these problems Clarke *et al.*[40] have used tetraalkylammonium fluorides to obtain very hgih yields of C-alkylated products with 2,4-pentanedione. In the presence of the fluoride anion the β-diketone behaves as a hydrogen bond electron acceptor and thereby forms a tightly bonded complex anion with fluoride. Presumably, the oxygen atoms are not only shielded by the large cation, but also by the enol hydroxy-fluoride hydrogen bond. Fluoride undoubtedly prefers the enol hydroxy group to the α-CH group for hydrogen bonding and it is known that β-diketones with at least one α-hydrogen are totally enolised in the presence of fluoride[41].

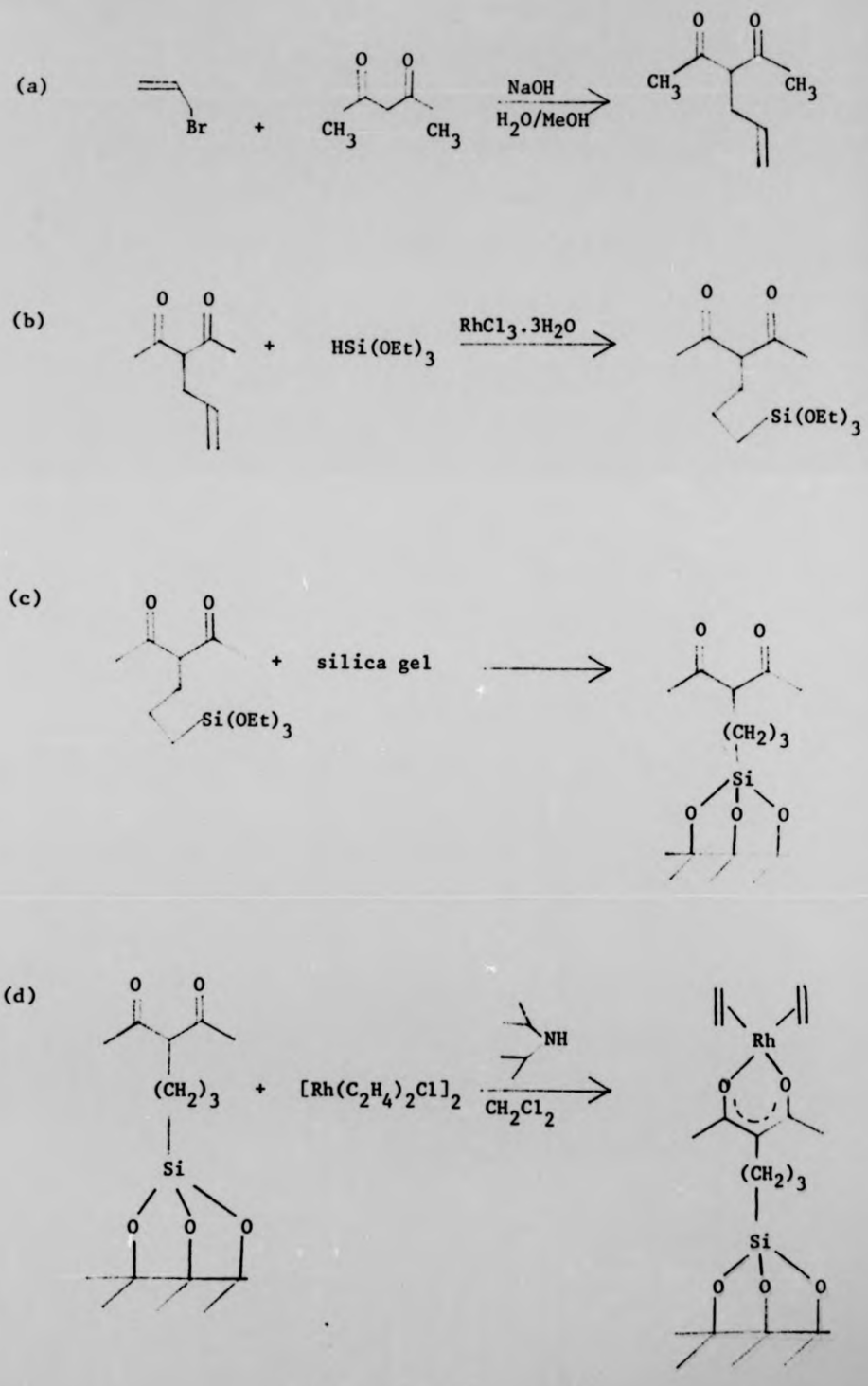

(a)
Br
+
CH3
CH3
NaOH
H2O/MeOH
(b)
+
HSi(OEt)3
RhCl3.3H2O
Si(OEt)3
(c)
+
silica gel
Si(OEt)3
(CH2)3
Si
(d)
(CH2)3
+
[Rh(C2H4)2Cl]2
NH
CH2Cl2
Rh

Fig. 4.1.Y

The enchanced reactivity of these species arises by transfer of electron density from the fluoride *via* the hydrogen bond, the overall result being to shield the oxygen atom thus inhibiting O-alkylation, while increasing the nucleophilicity. Using this method > 98% C-alkylations of 2,4-pentanedione have been reported using primary alkyl halides, and with isopropyl iodide > 90% C-alkylation was observed.

Although tetraalkylammonium fluorides are very efficient promotors of this process they do have the disadvantages of being expensive and extremely hygroscopic. Recently a system has been developed which maintains the selectivity of C-alkylation while considerably reducing the cost and increasing the tolerance to moisture. KF deposited on celite[42] has been reported to possess all of these characteristics and has been used in the C-alkylation of 2,4-pentanedione.

Functionalisation of 3-allyl-2,4-pentanedione was achieved by $RhCl_3.3H_2O$ catalysed hydrosilylation (Fig. 4.1.Yb). Stirring the neat olefin with 0.5 mol % $RhCl_3$ for five days at RT, with $HSi(OEt)_3$, followed by distillation, gave 1-(2,4-pentanedione)-3-triethoxysilylpropane in quantitative yield. Hydrosilylation reactions can also lead to olefin rearrangement, exchange reactions at silicon and may have long induction periods. These factors add to the belief that the mechanism of this reaction is complex, but a speculative mechanism has been proposed which takes into account some important experimental observations (Fig. 4.1.Z)[43].

Reversible *cis* Si-H oxidative-addition is followed by reversible hydride migratory insertion and then irreversible reductive-elimination of the silane occurs. The reversibility of the first two steps accounts for the observation of isotopic exchange involving the

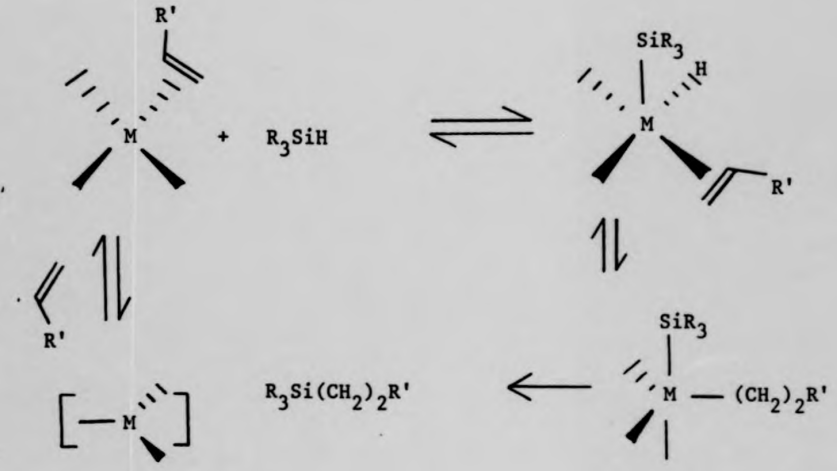


Fig. 4.1.Z

Si-H bond[44]. Using an excess of $DSiCl_3$ for the hydrosilylation of 2-methylpropene Ryan[44] observed that the recovered silane contained both $HSiCl_3$ (2258 cm^{-1}) and $DSiCl_3$ (1645 cm^{-1}), the products being identified by i.r. spectroscopy. However, it is still unclear whether the olefin substrate is co-ordinated prior to, or subsequent to, oxidative-addition of the Si-H bond. Other rhodium complexes catalyse hydrosilylation, but the reactions do not proceed as efficiently as with $RhCl_3$. $[Rh(C_2H_4)_2Cl]_2$ effects the hydrosilylation of 1-hexene, but only yields 50% 1-triethoxysilylhexane[45], while $RhCl(PPh_3)_3$ gives 20% (E)-/(Z)-hex-2-ene and (E)-hex-3-ene as by-products[46]. Howell[31] effected the hydrosilylation of 3-allyl-2,4-pentanedione and triethoxysilane with Pt-on-charcoal catalyst and obtained a 60% yield.

In our system the triethoxysilyl-2,4-pentanedione ligand was attached to the silica gel surface by heating to reflux a mixture of the ligand and silica gel in xylene for 24 hours. The amount of β-diketone attached to the surface was ascertained by reaction with copper acetate followed by removal of the copper(II) ions and titrimetric analysis. This procedure gave a value of 2.34% Cu(II) or 0.38 mmol of β-diketone per gram of silica gel. It was then envisaged that the silica-bound β-diketone would react with $[Rh(C_2H_4)_2Cl]_2$ in the presence of base to give a bis(ethylene)rhodium(I) complex (Fig. 4.1.Yd). A homogenous brown product was obtained after 2 hours stirring at RT, but unfortunately ethylene was not displaced from this complex by reaction with either 1-hexene or cyclooctadiene.

There are three possible explanations to account for this observation.

(1) Ethylene is displaced from the complex by Hünig's base (diisopropylethylamine) during production of the Rh-modified silica gel.

(2) Ethylene is displaced from the complex by the surface silanol groups of silica gel.

(3) Ethylene is retained by the complex and cannot be displaced because of steric inaccessibility.

The more likely of these is (3) because ethylene evolution was not observed on stirring either Hünig's base or silica gel with $[Rh(C_2H_4)_2Cl]_2$ in CH_2Cl_2. It is believed, therefore, that this problem can be overcome by using silica gel with a larger particle size.

4.2 SYNTHESIS OF C_{18} ALKENES

4.2.1 Synthesis of (Z)-Octadec-9-ene

Preparation of methyl (Z)-9-octadecenoate (Methyl oleate)

(Z)-9-octadecenoic acid, (10 g, 35 mmol) was dissolved in anhydrous methanol (10 cm^3), with conc. H_2SO_4*, and the resulting solution was heated to reflux for 6 hours. The flask was cooled and $NaHCO_3$ (0.5 g) was added. The solution was filtered, dried ($MgSO_4$) and the methanol removed under reduced pressure to leave a pale yellow oil. Distillation gave methyl oleate (7.7 g, 26 mmol) b.p. (0.4 mm) 141-142°C, in 75% yield, pure by t.l.c. (SiO_2:3 petroleum ether (40-60), 1 diethyl ether, R_f 0.76).

^1H n.m.r. (CCl_4): 0.90 (3 H, H-18, t), 1.29 (22 H, m), 1.95 (4 H, 2H-8 and 2H-11, m), 2.12 (2 H, H-2, t), 3.10 (3 H, s), 5.30 (2 H, H-9 and H-10, m) p.p.m.

Preparation of (Z)-9-octadecen-1-ol (oleyl alcohol)

Lithium aluminium hydride (1.0 g, 26 mmol) was stirred in dry diethyl

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*Catalytic amount

ether, under nitrogen. An ethereal solution of methyl oleate (7.4 g, 25 mmol) was then added dropwise over 15 mins. The resulting solution was then heated to reflux for 2 hours. Water (1 cm^3) was then slowly added, followed by 15% NaOH (aq.) (1 cm^3) and a further volume of water (10 cm^3). The white granular ppt. was filtered and the ethereal solution dried ($MgSO_4$) and filtered. Removal of ether under reduced pressure gave oleyl alcohol (6.1 g, 23 mmol), b.p. (0.01 mm) 90-92°C, in 92% yield, pure by t.l.c. (SiO_2:3 petroleum ether (40-60); 1 diethyl ether R_f 0.38).

^1H n.m.r. (CCl_4): 0.90 (3 H, t), 1.29 (22 H, m), 1.95 (4 H, 2 H-8 and 2 H-11, m), 3.50 (2 H, H-2, t), 5.30 (2 H, H-9 and H-10, m) p.p.m.

I.r. (film): 3310 (br), 3020 (m, sh), 2900 (s), 1650 (w), 1460 (m), 1380 (m), 1050 (m) cm^{-1}.

Preparation of (Z)-9-octadecenyl-p-toluene sulphonate (oleyl tosylate)

Oleyl alcohol (5.0 g, 19 mmol) was dissolved in dry pyridine (10 cm^3) and cooled to 0°C. Recrystallised p-toluene sulphonyl chloride (3.9 g, 20 mmol) was dissolved in dry pyridine (10 cm^3), and added to the pre-cooled, stirred solution, over 15 minutes. The reaction was stirred at 0°C until precipitation of pyridinium hydrochloride ceased (60 mins.). The precipitate was then dissolved in cold water, the solution poured on to 5 M HCl (aq.) and extracted with CH_2Cl_2. The aqueous layer was further extracted with CH_2Cl_2 and the combined extracts were washed with 10% Na_2CO_3 solution. The CH_2Cl_2 solution was dried (Na_2CO_3) and evaporated under reduced pressure to leave the tosylate as a pale yellow oil. Fast column chromatographic purification gave oleyl tosylate (5.8 g, 13.7 mmol) in 76% yield, pure by t.l.c. (SiO_2:3 pentane; 1 diethyl ether R_f 0.60).

^1H n.m.r. (CCl_4): 0.89 (3 H, t), 1.28 (22 H, m), 1.97 (2 x 2 H, m), 3.43 (3 H, s), 3.97 (2 H, t), 5.30 (2 H, m), 7.58 (4 H, dd) p.p.m.

I.r. (film): 3050 (m, sh), 2960 (s), 2925 (s), 1650 (w), 1600 (m, sh), 1365 (s), 1175 (s), 1100 (m, sh) cm^{-1}.

Preparation of (Z)-9-octadecene

Oleyl tosylate (10 g, 23 mmol) in dry ether (50 cm^3) was added dropwise to a stirred suspension of lithium aluminium hydride (1.0 g, 26 mmol) in dry ether, under N_2, during 20 minutes. The resulting solution was heated to reflux for 60 hours. Work-up, as described for oleyl alcohol, gave a white granular precipitate which was removed by filtration. The ethereal solution was dried ($MgSO_4$), filtered and evaporated to leave a colourless oil which was distilled to give (Z)-9-octadecene (4.0 g, 15.9 mmol) b.p. 90-92°C (0.1 mm), in 69% yield, pure by t.l.c. (SiO_2: 3 pentane; 1 ether R_f 0.83).

^1H n.m.r. (CCl_4): 0.88 (6 H, H-1, t), 1.29 (12 x 2 H, m), 2.02 (4 H, dt), 5.35 (2 H, H-9, t) p.p.m.

^{13}C n.m.r. ($CDCl_3$, TMS): 14.18 (G-1), 22.87 (C-2), 27.40 (C-8), 29.56 (C-6/C-7), 29.77 (C-5), 29.99 (C-4), 32.15 (C-3), 129.96 (C-9) p.p.m.

I.r. (film): 3020 (m, sh), 2930 (s), 2860 (m, sh), 1475 (m), 1370 (m, sh) cm^{-1}.

4.2.2 Synthesis of (Z,Z)-octadeca-6,9-diene

Preparation of methyl (Z,Z)-octadeca-9,12-dienoate (methyl linoleate)

(Z,Z)-octadeca-9,12-dienoic acid (linoleic acid) (8.0 g, 0.0285 mol) was dissolved dry diethyl ether (40 cm^3) and cooled to 0°C. Diazomethane (170 cm^3 of a 0.213 M ethereal solution, 36.2 mmol) was then cautiously added. Excess diazomethane and ether were removed in a stream of nitrogen to give methyl linoleate (7.5 g, 25.5 mmol) b.p. 111-113°C (0.01 mm), pure by t.l.c.

(SiO_2: 4 petroleum ether (40-60); 1 diethyl ether, R_f 0.70).
^1H n.m.r. (CCl_4): 0.90 (3 H, t), 1.33 (16 H, m, br), 2.05 (4 H, m), 2.20 (2 H, t), 2.72 (2 H, t), 3.60 (3 H, s), 5.39 (2 x 2 H, m) p.p.m.

Preparation of (Z,Z)-octadeca-9,12-dien-1-ol (linoleyl alcohol)

Methyl linoleate (7.5 g, 25.5 mmol) was reduced by $LiAlH_4$ (1.0 g, 26 mmol) using the procedure as described for methyl oleate. Work-up gave linoleyl alcohol (5.9 g, 22 mmol) as a colourless oil in 87% yield, pure by t.l.c. (SiO_2: 1 pentane; 1 ether, R_f 0.47).
^1H n.m.r. (CCl_4): 0.90 (3 H, t), 1.31 (16 H, m), 2.04 (4 H, m), 2.73 (2 H, t), 3.48 (2 H, t), 5.28 (4 H, m) p.p.m.
I.r. (film): 3320 (m, br), 3050 (m, sh), 2920 (s), 2850 (s), 1650 (w), 1464 (m), 1056 (m, br) cm^{-1}.

Preparation of (Z,Z)-octadeca-9,12-dienyl-p-toluene sulphonate (linoleyl tosylate)

Linoleyl alcohol (5.61 g, 21 mmol) was converted to the corresponding tosylate by reaction with p-toluene sulphonyl chloride (6.3 g, 33 mmol) in pyridine, according to the procedure described for oleyl tosylate. Work-up gave linoleyl tosylate (7.6 g, 18 mmol) as a yellow oil, pure by t.l.c. (SiO_2: 1 pentane; 1 ether, R_f 0.58).
^1H n.m.r. (CCl_4): 0.89 (3 H, t), 1.26 (16 H, m), 2.00 (4 H, m), 2.42 (3 H, s), 2.70 (2 H, t), 3.95 (2 H, t), 5.30 (2 x 2 H, m), 7.55 (4 H, dd) p.p.m.
I.r. (film): 3060 (w), 3025 (m, sh), 2910 (s), 2875 (s), 1650 (w), 1600 (m, sh), 1460 (m), 1360 (s), 1180 (s), 1100 (m) cm^{-1}.

Preparation of (Z,Z)-octadeca-6,9-diene

Lithium aluminium hydride (0.67 g, 17.6 mmol) was stirred in dry diethyl ether (60 cm^3), under N_2, during the dropwise addition of a 50% ethereal

solution of linoleyl tosylate (7.3 g, 17.3 mmol). The resulting solution was heated to reflux for 60 hours. Work-up, as described for (Z)-octadec-9-ene gave (Z,Z)octadeca-6,9-diene (3.51 g, 14 mmol) b.p. 85-87°C, (0.1 mm), in 81% yield, pure by t.l.c. (SiO_2: 3 pentane; 1 ether, R_f 0.89).

^1H n.m.r. (CCl_4): 0.89 (6 H, m), 1.27 (18 H, m), 2.07 (4 H, m), 2.71 (2 H, t), 5.35 (4 H, m) p.p.m.

^{13}C n.m.r. ($CDCl_3$): 14.17 (C-1, C-18), 22.94 (C-2, C-17), 25.87 (C-8), 27.43 (C-5, C-11), 29.64 (C-13), 29.83 (C-14), 29.96 (C-4, C-15), 31.85 (C-16), 32.24 (C-3), 128.17 (C-7, C-9), 130.19 (C-6, C-10) p.p.m.

I.r. (film): 3010 (m, sh), 2960 (s), 2925 (s), 2850 (s), 1648 (w), 1455 (m), 1368 (w, sh) cm^{-1}.

M.s. (EI): m/z 250 (M^+, 39.8%), 138 (19.0%), 124 (28.6%), 110 (50.4%), 96 (74.5%), 81 (90.1%), 67 (100%).

4.2.3 Synthesis of (Z,Z,Z)-octadeca-3,6,9-triene

Preparation of methyl (Z,Z,Z)-octadeca-9,12,15-trienoate (methyl linolenate)

Linolenic acid (4.9 g, 0.0176 mol) was dissolved in dry ether and cooled to -70°C. Diazomethane in ether (90 cm^3, 0.026 mol of a 0.288 M solution) was then added slowly at -70°C. Excess diazomethane and ether were removed in a stream of nitrogen to leave methyl linolenate (4.45 g, 0.0152 mol), b.p. 82-84 (0.05 mm), in 87% yield, pure by t.l.c. (SiO_2: 4 petroleum ether: 1 ether, R_f 0.66).

^1H n.m.r. (CCl_4): 0.96 (3 H, t), 1.30 (4 x 2 H, m), 1.57 (2 H, m), 2.03 (2 x 2 H, m), 2.20 (2 H, t), 2.74 (2 x 2 H, m), 3.59 (3 H, s), 5.26 (3 x 2 H, m) p.p.m.

Preparation of (Z,Z,Z)-octadeca-9,12,15-trien-1-ol (linolenyl alcohol)

Methyl linolenate (4.3 g, 14.7 mmol) was reduced with $LiAlH_4$ (0.84 g, 22 mmol) in dry ether, under N_2, as described for methyl linoleate. Work-up using water and 15% NaOH (aq.) gave a white precipitate which was removed by filtration. Concentration and distillation of the filtrate gave linolenyl alcohol (3.6 g, 13.6 mmol) in 92% yield, pure by t.l.c. (SiO_2: diethyl ether R_f 0.68).

I.r. (film): 3320 (br), 3020 (m, sh), 2930 (s), 2860 (s), 1640 (w), 1030 (m) cm^{-1}.

Preparation of (Z,Z,Z)-octadeca-9,12,15-trienyl-p-toluene sulphonate (linolenyl tosylate)

Linolenyl alcohol (3.6 g, 13.6 mmol) was dissolved in dry pyridine and stirred at 0°C during the dropwise addition of a 50% solution of p-toluenesulphonylchloride (4.0 g, 21 mmol) in dry pyridine. After 110 minutes at 0°C the reaction mixture was worked-up, as described for linoleyl tosylate, to give linolenyl tosylate (5.5 g, 13.2 mmol) in 97% yield, pure by t.l.c. (SiO_2: 2 pentane; 1 diethyl ether, R_f 0.63).

^1H n.m.r. (CCl_4): 0.94 (3 H, t), 1.24 (12 H, m), 1.95 (4 H, H-8 and H-17, m), 2.40 (3 H, s), 2.73 (4 H, 2 H-11 and 2 H-14, m), 3.90 (2 H, t), 5.25 (6 H, m), 7.51 (4 H, dd) p.p.m.

I.r. (film): 3050 (w), 3010 (m, sh), 2920 (s), 2850 (m, sh), 1650 (w), 1600 (m, sh), 1360 (s), 940 (s) cm^{-1}.

Preparation of (Z,Z,Z)-octadeca-3,6,9-triene

Linolenyl tosylate (5.4 g, 13.0 mmol) was reduced with $LiAlH_4$ (0.67 g, 17.6 mmol) in dry ether (200 cm^3), as described for linoleyl tosylate. Work-up using H_2O and 15% NaOH (aq.), filtration, concentration and distillation of the filtrate gave (Z,Z,Z)-octadeca-3,6,9-triene

(2.1 g, 8.5 mmol), b.p. 80-82 (0.05 mm), in 61% yield, pure by t.l.c. (SiO_2: 2 pentane; 1 diethyl ether, R_f 0.8).

^1H n.m.r. (CCl_4): 0.85 (3 H, H-18, t), 0.95 (3 H, H-1, t), 1.24 (12 H, m), 2.04 (4 H, m), 2.80 (4 H, m), 5.35 (6 H, m) p.p.m.

^{13}C n.m.r. ($CDCl_3$): 14.17 (C-1, C-18), 20.67 (C-2), 22.81 (C-17), 25.74 (C-5, C-8), 27.10 (C-11), 27.36 (C-12), 29.44 (C-13), 29.70 (C-14), 30.48 (C-15), 32.04 (C-16), 127.26 (C-9), 127.78 (C-4), 128.37 (C-6, C-7), 130.44 (C-10), 131.94 (C-3) p.p.m.

I.r. (film): 3020 (m, sh), 2955 (s), 2930 (s), 2860 (s), 1648 (m) cm^{-1}.

M.s. (EI): m/z 248 (M^+, 6.5%), 192 (20.5%), 108 (75%), 79 (100%).

4.2.4 Synthesis of (E)-octadec-9-ene

Preparation of methyl (E)-9-octadecenoate (methyl elaideate)

Elaidic acid (10 g, 35 mmol) was added to anhydrous methanol (20 cm^3) and conc. H_2SO_4 (0.2 g). The resulting solution was heated to reflux for 6 hours. Work-up in a manner previously described for methyl oleate gave methyl elaideate (9.1 g, 31 mmol), b.p. 92-94°C (0.001 mm), in 88% yield, pure by t.l.c. (SiO_2: 4 petroleum ether (40-60), 1 diethyl ether R_f 0.55).

^1H n.m.r. (CCl_4): 0.89 (3 H, t), 1.28 (22 H, m), 1.94 (4 H, m), 2.15 (2 H, t), 3.60 (3 H, s), 5.33 (2 H, m) p.p.m.

Preparation of (E)-9-octadecen-1-ol (elaideyl alcohol)

Methyl elaideate (9.0 g, 30 mmol) was reduced by $LiAlH_4$ (1.1 g, 30 mmol) in dry ether, under N_2, as previously described for oleyl alcohol. Work-up gave elaideyl alcohol (8.0 g, 29 mmol) m.p. 35-37°C, as colourless crystals (recrystallised from diethyl ether, pentane), in 98% yield, pure by t.l.c. (SiO_2: 2 petroleum ether (40-60);

1 diethyl ether, R_f 0.34).

^1H n.m.r. (CCl_4): 0.89 (3 H, t), 1.30 (22 H, m), 1.95 (4 H, m), 3.54 (2 H, t), 5.35 (2 H, m) p.p.m.

I.r. (film): 3300 (m, br), 2950 (s), 2875 (s), 1460 (m), 1375 (m), 1050 (w), 965 (w) cm^{-1}.

Preparation of (E)-9-octadecenyl-p-toluenesulphonate (elaideyl tosylate)

Elaideyl alcohol (7.8 g, 29 mmol) was dissolved in dry pyridine (20 cm^3) and cooled to 0°C. Recrystallised p-toluenesulphonylchloride (8.5 g, 44.5 mmol) dissolved in dry pyridine was added dropwise at 0°C and stirring maintained at 0°C until precipitation ceased (100 minutes). Work-up, in a manner previously described for oleyl tosylate, gave elaideyl tosylate (11.1 g, 26.3 mmol) as a partially crystalline oil in 91% yield, pure by t.l.c. (SiO_2: 3 petroleum ether; 1 diethyl ether, R_f 0.88).

^1H n.m.r. (CCl_4): 0.89 (3 H, t), 1.25 (22 H, m), 1.94 (4 H, m), 2.43 (3 H, s), 3.94 (2 H, t), 5.32 (2 H, m), 7.53 (2 x 2 H, dd) p.p.m.

I.r. (film): 3065 (w, shoulder), 3010 (w, shoulder), 2910 (s), 2850 (s), 1600 (m, sh), 1460 (m), 1360 (s), 1180 (s), 1100 (w), 950 (m, br), 810 (w) cm^{-1}.

Preparation of (E)-octadeca-9-ene

Elaideyl tosylate (10 g, 23.7 mmol) was dissolved in dry diethyl ether (50 cm^3) and added dropwise to a stirred solution of $LiAlH_4$ (1.0 g, 26 mmol) in dry diethyl ether (200 cm^3). The solution was heated to reflux for 48 hours under N_2. Work-up as previously described for (Z)-octadec-9-ene gave (E)-octadec-9-ene (5.56 g, 22 mmol), b.p. 92-93°C (0.01 mm), in 93% yield, pure by t.l.c. (SiO_2: 4 pentane; 1 diethyl ether, R_f 0.9).

^{1}H n.m.r. (CCl_4): 0.90 (2 x 3 H, t), 1.26 (24 H, m), 1.96 (4 H, m) 5.33 (2 H, m) p.p.m.

^{13}C n.m.r. ($CDCl_3$): 14.10 (C-1), 22.75 (C-2), 29.31 (C-7), 29.44 (C-5, C-6), 29.77 (C-4), 32.04 (C-3), 32.69 (C-8), 130.38 (C-9) p.p.m.

I.r. (film): 3020 (m, shoulder), 2955 (s), 2925 (s), 2850 (s), 1460 (m, sh), 1370 (w, sh), 980 (m, sh) cm^{-1}.

4.3 COMPLEXATIONS OF C_{18} ALKENES TO Rh(I)

4.3.1 Thermal Stability of (E)- and (Z)-9-octadecenes in the Presence of Catalytic E_2Rh(I)pd

(a) Samples of (E)- and (Z)-9-octadecene (15 mg, 59 µmol) were monitored by ^{1}H n.m.r. and t.l.c. [SiO_2-10% $AgNO_3$: 9 pentane, 1 CH_2Cl_2, R_f 0.50 (E), 0.28 (Z)], before and during incubation at 80°C in d.^{6}benzene. No isomerisation was observed after 24 hours. The procedure was repeated in the presence of E_2Rh(I)pd (10 mol %) and after 24 hours at 80°C ^{1}H n.m.r. and t.l.c. indicated no isomerisation.

Thermal stability of (Z,Z)-octadeca-6,9-diene in the Presence of Catalytic E_2Rh(I)pd

(b) (Z,Z)-octadeca-6,9-diene (15 mg, 60 µmol) in d.^{6}benzene was monitored by ^{1}H n.m.r. and t.l.c. (SiO_2-10% $AgNO_3$: 20 toluene; 5 acetone R_f 0.66), before and during incubation at 80°C. The diene was found to be free of other isomers (positional and geometric) before and after heating. The procedure was repeated in the presence of 2,4-pentanedionatobis(ethylene)rhodium(I) and no isomerisation was observed.

Thermal stability of (Z,Z,Z)-octadeca-3,6,9-triene in the presence of catalytic E_2Rh(I)pd

(c) Analysis of (Z,Z,Z)-octadeca-3,6,9-triene by t.l.c. (SiO_2-10% $AgNO_3$: 20 toluene; 5 acetone, R_f 0.29 [95%, 0.42 (5%), indicated the presence of ∿ 5% other isomer(s) (probably a *trans* impurity)]. Incubation of a sample of (Z,Z,Z)-octadeca-3,6,9-triene at 80°C for 24 hours produced no change in the isomer ratio as monitored by t.l.c. and ^{1}H n.m.r. Treatment with 2,4-pentanedionatobis(ethylene)-rhodium(I) (10 mol %) at 80°C for 24 hours, in d.^{6}benzene, did not facilitate further isomerisation as judged by t.l.c. (as described) and ^{1}H n.m.r.

4.3.2 Reaction of (Z)-octadec-9-ene with E_2Rh(I)pd and E_2Rh(I)hfpd

(a) (Z)-octadec-9-ene (0.196 g, 0.775 mmol) was dissolved in dry ether (0.5 cm^3) and added to E_2Rh(I)pd (0.1 g, 0.388 mmol). The solvent was removed in vacuum and the residue redissolved in ether. Further evaporation gave an orange oil which could not be crystallised from ether:pentane at -78°C.

^{1}H n.m.r. ($CDCl_3$): 0.88 (4 x 3 H, t), 1.29 (24 x 2 H, m), 1.79 (2 x 3 H, s), 2.03 (8 H, H-8, dt), 2.37 (4 H, H-9, m), 5.15 (1 H, s) p.p.m.

^{1}H n.m.r. (d.^{6}benzene): 0.92 (4 x 3 H, t), 1.26 (20 x 2 H, m), 1.59 (4 x 2 H, m), 1.72 (2 x 3 H, s), 1.84 (4 H, H-8, m), 2.38 (4 H, H-8, m), 2.55 (4 H, H-9, m), 5.03 (1 H, s) p.p.m.

^{13}C n.m.r. ($CDCl_3$): 14.17 (C-1) 22.88 (C-2 and C-1 acac), 27.36 (C-8), 29.31, 29.51, 29.90, (C-4), 32.11 (C-3), 78.38/78.97 (C-9, d, J_{Rh-C} 13.3 Hz) p.p.m.

I.r. (film): 3000 (w, shoulder), 2910 (s), 2850 (s), 1575 (m), 1520 (m), 1380 (m) cm^{-1}.

(a) (Z)-octadec-9-ene (50 mg, 0.198 mmol) was dissolved in dry diethyl ether and added to $E_2Rh(I)hfpd$ (36 mg, 99 μmol). Procedure (a) was then followed to give a dark red oil which did not crystallise from ether: pentane at -78°C.
^1H n.m.r. ($CDCl_3$): 0.88 (4 x 3 H, t), 1.28 (24 x 2 H, m), 1.63 (4 H, H-8, m), 1.82 (4 H, H-8, m), 2.72 (4 H, H-9, m), 5.95 (1 H acac, s) p.p.m.

4.3.3 Reaction of (E)-octadec-9-ene with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$

(a) (E)-octadec-9-ene (0.186 g, 0.777 mmol) was dissolved in dry diethyl ether and added to 2,4-pentanedionatobis(ethylene)rhodium(I) (0.1 g, 0.388 mmol). The procedure was then as for the (Z)-isomer.
^1H n.m.r. indicated formation of a mixture consisting of a 1:1 complex, unreacted *trans* olefin and Rh(I) complex. Further redissolving and pumping gave a small increase in the amount of 1:1 complex as indicated by ^1H n.m.r. signals of the bidentate ligand and co-ordinated olefins.
^1H n.m.r. (d.^{6}benzene): 1.69 (3 H acac, s), 1.78 (3 H acac, s), 2.4 (1 H, H-9 endo, m), 4.23 (1 H, H-9 exo, m) p.p.m.
^{13}C n.m.r. ($CDCl_3$): 79.09/79.68 (d, J_{Rh-C} 13.25 Hz).

(b) (E)-octadec-9-ene (50 mg, 0.198 mmol) was dissolved in dry ether and added to $E_2Rh(I)hfpd$ (142 mg, 0.396 mmol). Removal of solvent and redissolving, three times, gave a dark red oil whose ^1H n.m.r. indicated a 2:1 complex.
^1H n.m.r. ($CDCl_3$): 0.88 (4 x 3 H, t), 1.25 (24 x 2 H, m), 1.70

(2 x 2 H, m), 2.12 (2 x 2 H, m), 2.37 (2 H, H-9 endo, m), 4.13 (2 H, H-9 exo, m), 6.01 (1 H, s) p.p.m.

4.3.4 Reaction of (Z,Z)-octadeca-6,9-diene with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$

(Z,Z)-octadeca-6,9-diene (0.1 g, 0.399 mmol) was dissolved in dry diethyl ether and added to 2,4-pentanedionatobis(ethylene)rhodium(I) (51.5 mg, 0.199 mmol). The solvent was removed under vacuum to give an orange oil whose ^1H and ^{13}C n.m.r. spectra indicated a 2:1 complex containing both co-ordinated and unco-ordinated olefin.

^1H n.m.r. (d.^{6}benzene): 5.64, 6.10 p.p.m. (unco-ordinated double bonds).

^{13}C n.m.r. ($CDCl_3$): 76.24, 77.02, 78.51 (co-ordinated olefin), 128.43, 129.54 (free olefin) p.p.m.

The above procedure was repeated using $E_2Rh(I)hfpd$ and the ^1H n.m.r. indicated a similar situation, i.e. formation of a 2:1 complex.

^1H n.m.r. ($CDCl_3$): 2.37 (m, co-ordinated olefin), 5.45 and 5.67 (m, free olefin) p.p.m.

4.3.5 Reaction of (Z,Z,Z)-octadeca-3,6,9-triene with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$

(Z,Z,Z)-octadeca-3,6,9-triene was reacted with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ as described for (Z,Z)-octadeca-6,9-diene. In both cases oils were isolated which gave complicated ^1H and ^{13}C n.m.r. spectra, but which showed features consistent with a 2:1 complex containing both co-ordinated and unco-ordinated olefin.

^1H n.m.r. (d.^{6}benzene): 5.57 and 6.05 p.p.m.

^{13}C n.m.r. ($CDCl_3$): 77.02, 78.45, 79.23, 79.81 (co-ordinated olefin); 127.65, 128.24, 129.73, 130.32 (unco-ordinated olefin) p.p.m.

4.4 COMPLEXATIONS OF METHYL C_{18} ALKENOATES AND SOME TRIGLYCERIDES TO Rh(I)

4.4.1 Preparation of pure samples of C_{18} methyl esters

Methyl (E)- and (Z)-9-octadecenoates were analysed by t.l.c. [SiO_2; 10% $AgNO_3$: 4 pentane, 1 ether, R_f 0.60 (E), 0.42 (Z)] and found to be pure. Methyl (Z,Z)-octadeca-9,12-dienoate was similarly found to consist of only one spot on t.l.c. (SiO_2, 10% $AgNO_3$: 3 pentane, 1 ether, R_f 0.62). However, methyl (Z,Z,Z)-octadeca-9,12,15-trienoate was found to contain *ca.* 5% impurity by t.l.c. [SiO_2, 10% $AgNO_3$: 4 pentane: 1 ether, R_f 0.25 (*ca.* 95%), R_f 0.38 (*ca.* 5%)], probably a *trans* impurity. The ester was purified by fast column chromatography. The silica gel was prepared by addition of Kieselgel 60 (230-400) (175 g) to a solution of silver nitrate (26.25 g) in ethanol: water (437.5: 26.25). The suspension was stirred for 15 minutes in the dark and the ethanol was then removed under reduced pressure. Finally, the silica gel was activated by heating in a vacuum oven. A sample of methyl (E,E)-octadeca-9,12-dienoate (methyl linoelaideate) (99% pure) was obtained from Sigma.

4.4.2 Reaction of methyl (Z)-octadec-9-enoate with E_2Rh(I)pd and E_2Rh(I)hfpd

(a) Methyl oleate (23 mg, 77.6 μmol) was dissolved in dry ether (1 cm^3) and added to E_2Rh(I)pd (10 mg, 38.8 μmol). The solvent was removed (rotary evaporator) and the residue dissolved in d.^{6}benzene. ^{1}H n.m.r. (d.^{6}benzene): 0.91 (2 x 3 H, t), 1.30 (2 H, m), 1.59 (4 H, m), 1.72 (2 x 3 H, s), 1.85 (4 H, 2H-8 and 2H-11, m), 2.13 (4 H, H-2, t), 2.35 (4 H, 2H-8 and 2H-11, m), 2.55 (4 H, 2H-9, and 2H-10, m), 3.36

(2 x 3 H, s), 5.06 (1 H, s) p.p.m.

(b) Methyl (Z)-octadec-9-enoate was reacted with $E_2Rh(I)hfpd$ as described above. The resulting red oil gave R_f 0.42 (SiO_2: 4 pentane; 1 ether).

^1H n.m.r. (d.^{6}benzene): 0.92 (2 x 3 H, t), 1.30 (40 H, m), 1.59 (4 H, m), 1.75 (4 H, m), 1.99 (4 H, m), 2.14 (4 H, H-2, t), 2.68 (4 H, 2 H-9 and 2 H-10, m), 3.36 (2 x 3 H, s), 5.99 (1 H, s) p.p.m.

4.4.3 Reaction of methyl (E)-octadeca-9-enoate with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$

(a) The procedure was repeated as for methyl oleate (Section 4.4.2) and the resulting orange oil was dissolved in d.^{6}benzene. The ^1H n.m.r. spectrum indicated, as with (E)-9-octadecene, the formation of mainly 1:1 complex.

^1H n.m.r. (d.^{6}benzene): 1.70 (3 H acac, s), 1.79 (3 H acac, s), 5.04 (1 H, s) n.b. also peaks at 1.40, 1.83, 4.07 and 4.23 p.p.m.

(b) The procedure was repeated as in (Section 4.4.2b) and the residue was analysed by t.l.c. [SiO_2: 4 pentane; 1 ether, R_f 0.58 (complex), 0.70 (methyl elaideate)] and ^1H n.m.r. and found to contain mostly 2:1 complex with some unreacted starting materials.

^1H n.m.r. ($CDCl_3$): 0.89 (6 H, t), 1.35 (40H, m), 1.96 (4 H, m), 2.29 (4 H, t), 3.09 (2 H, endo, m), 3.65 (6 H, s), 4.09 (2 H, exo, m), 6.04 (1 H, s) p.p.m.

4.4.4 Reaction of methyl (E,E)- and (Z,Z)-octadeca-9,12-dienoates with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$

(1a) $E_2Rh(I)hfpd$ (25 mg, 69 μmol) was dissolved in dry ether (1 cm^3) and added to methyl linoelaideate (20 mg, 69 μmol). The

solvent was removed in vacuum and the residual oil dissolved in $CDCl_3$. ^1H n.m.r. ($CDCl_3$): 0.89 (3 H, t), 1.30 (14 H, m), 1.58 (6 H, m), 2.30 (2 H, t), 2.39 (1 H, H-11 exo, m), 3.30 (2 H, H-9 and H-13, m) 3.44 (1 H, H-11 endo, dt, Jgem 13 Hz, Jvic 6.7 Hz), 3.68 (3 H, s), 3.89 (2 H, H-10 and H-12, m), 6.06 (1 H, s) p.p.m.

(1b) $E_2Rh(I)pd$ was reacted with methyl linoelaideate as above. ^1H n.m.r. ($CDCl_3$): 0.89 (3 H, t), 1.30 (14 H, m), 1.60 (6 H, m), 1.84 (2 x 3 H, s), 2.21 (1 H, H-11 exo, m), 2.30 (2 H, t), 2.98 (2 H, H-9 and H-13, m), 3.32 (1 H, H-11 endo, dt, Jgem 13 Hz, Jvic 6.7 Hz), 3.60 (2 H, H-10, H-12, m), 3.65 (3 H, s), 5.24 (1 H, s) p.p.m.

(2) Reaction of methyl (Z,Z)-octadeca-9,12-dienoate with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$ in the ratio 2:1 gave ^1H n.m.r. spectra similar to that for (Z,Z)-octadeca-6,9-diene with peaks characteristic of co-ordinated and unco-ordinated olefin, e.g. ^1H n.m.r. ($CDCl_3$): 2.70 (4 H, m), 5.45 (2 H, m), 5.65 (2 H, m) p.p.m.

Methyl (Z,Z,Z)-octadeca-9,12,15-trienoate gave complex spectra on reaction with $E_2Rh(I)pd$ and $E_2Rh(I)hfpd$. No assignments were made.

4.4.5 Reaction of $E_2Rh(I)hfpd$ with some triglycerides

(a) 1,2-Dioleoyl-3-palmitoylglycerol (0.1 g, 116 μmol) (97%) was dissolved in dry ether (0.5 cm^3) and added to $E_2Rh(I)hfpd$ (42.6 mg, 116 μmol). The solvent was evaporated and the residue dissolved in d.^{6}benzene.

^1H n.m.r.: 0.91 (3 x 3 H, t), 1.30 (70 H, m), 1.55 (14 H, m), 2.14 (6 H, m), 2.69 (4 H, 2H-9 and 2H-10), 4.10 (2 H, m), 4.31 (2 H, m), 5.34 (1 H, m), 6.00 (1 H, s) p.p.m.

(b) Using the same procedure two equivalents of 1,3-dipalmitoyl-2-oleoylglycerol and 1,2-dipalmitoyl-3-oleoylglycerol were each reacted

with one equivalent of $E_2Rh(I)hfpd$ to give 2:1 complexes have chemical shifts virtually identical to those described above, e.g. co-ordinated double bond protons ^1H n.m.r. (d.^{6}benzene): 2.70 (4 H, 2H-9, 2H-10, m) p.p.m.

(c) Under the same conditions as in Part (a) 1,2-dielaideyl-3-palmitoylglycerol and 1,3-dielaideyl-2-palmitoylglycerol gave ~ 80% reaction after one removal of solvent. Repeated pumpings gave virtually complete displacement of ethylene to yield 1:1 complexes whose ^1H n.m.r. spectra differed from (a) only in the chemical shifts of the olefinic protons of the co-ordinated double bonds, e.g. ^1H n.m.r. (d.^{6}benzene): 4.03 (2 H endo, m), 4.23 (2 H exo, m) p.p.m.

Reaction of methyl hexadecanoate (methyl palmitate) with $E_2Rh(I)pd$

Methyl palmitate (15 mg, 55.5 μmol) was dissolved in dry ether and added to $E_2Rh(I)pd$ (14.3 mg, 55.5 μmol). The solvent was evaporated and the residue dissolved in $CDCl_3$. ^1H n.m.r. indicated no reaction.

4.5 PREPARATION OF A MODIFIED SILICA GEL

Preparation of 1-[3-(2,4-pentanedione)]-3-triethoxysilylpropene

Triethoxysilane (8.57 g, 52.2 mmol), 3-allyl-2,4-pentanedione (7.32 g, 52.2 mmol) and $RhCl_3.3H_2O$ (50 mg, 0.25 mmol) were stirred at RT for 5 days. Filtration followed by distillation gave the product (14.6 g, 48.0 mmol) b.p. 30-50°C (0.01 mm), in 92% yield.

^1H n.m.r. (CCl_4): 0.92 (2 H, m), 1.12 (9 H, t and 2 H, m), 2.00 (6 H, s and 2 H, m), 3.75 (6 H, q), 5.26 and 11.70 (1 H, methine and enol) p.p.m.

Preparation of SIL-O-Si$(CH_2)_3$-CH$(COCH_3)_2$

Purified t.l.c. grade silica (1.0 g) was suspended in xylene (12 cm^3) with water (0.2 cm^3) and stirred at RT for 15 minutes. 1-[3-(2,4-pentanedione)]-3-triethoxysilylpropane (1 cm^3) was then added and the solution was stirred for 24 hours. The silica gel was then removed by filtration, washed repeatedly with AR toluene and dried under *vacuo* (35^oC/0.001 mm).

Estimation of β-diketone content of ligand-silica

Copper(II)acetate (4.00 g, 20 mmol) was dissolved in DMF (20 cm^3). SIL-O-Si-$(CH_2)_3$-CH_2-$(COCH_3)_2$ (0.500 g) was then added and the resulting solution was stirred for 24 hours. The silica was then filtered and washed with DMF (7 cm^3), H_2O (5 cm^3), dioxane (3 cm^3), acetone (3 cm^3) CH_2Cl_2 (5 cm^3), and dried under *vacuo*. The resulting silica gel was then stirred with conc. HCl (2 cm^3) for 2 hours and then washed [DMF (9 cm^3) plus conc. HCl (1 cm^3)] to give a bright yellow solution. This solution (2.00 cm^3) was taken and 2M NH_3 was added until the yellow solution became blue. The pH was adjusted to ~ 4.5, 10% KI solution (10 cm^3) was added, and the solution was titrated with a standardised sodium thiosulphate solution (0.0102M) using a starch indicator. This procedure was repeated (3x) to give an overall Cu(II) content of 0.1907 mmol) which is equivalent to 0.38 mmol g^{-1} silica gel.

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CHAPTER 5

Pd(0) AND Pd(II) CATALYSED RE-ARRANGEMENTS OF C_6, C_7 AND C_{10} ACETOXYDIENES

5.1 INTRODUCTION AND DISCUSSION

The stimulus to explore the organic chemistry of palladium stems from the development of the Wacker process, an efficient industrial method for the conversion of ethylene to acetaldehyde using soluble palladium catalysts[1] (Fig. 5.1.A). This process was believed to proceed by initial formation of a π-Pd-olefin complex which is then attacked by water followed by re-arrangement to give a σ-Pd-alkyl species. This in turn reorganised to give acetaldehyde and Pd(0), which is oxidised by Cu(II) salts to regenerate the active catalyst. The first proposed mechanism shown in Fig. 5.1.A, shows *cis*-attack by hydroxide, but this is now known to be incorrect. The recently elucidated mechanism involves *trans*-attack by water on the coordinated ethylene to give a σ-bonded Pd-alkyl (Fig. 5.1.B). The deduction of the stereochemistry[39] of this step was aided by the results of Åkermark[2] who noted the stereospecific conversion of *trans*-1,2-dideuterioethylene to *threo*-1,2-dideuteriochloroethanol, which was converted to the corresponding epoxide and characterised spectroscopically.

In the above mechanism the intermediate is a σ-bonded Pd-alkyl species, but it is also well established[3] that if substituted olefins are reacted with palladium salts then the initially formed π-Pd-olefin complex is readily transformed to a π-η^3-allylpalladium complex. Complexes of this type have been invoked as intermediates in many palladium-catalysed rearrangements and the existence of such intermediates is strongly supported by the isolation and characterisation of stoichiometric complexes, e.g. Smith and co-workers have prepared π-η^3-allylpalladium chloride dimer and determined the structure by x-ray crystallography (Fig. 5.1.E). As illustrated in Fig. 5.1.E, the allyl group is

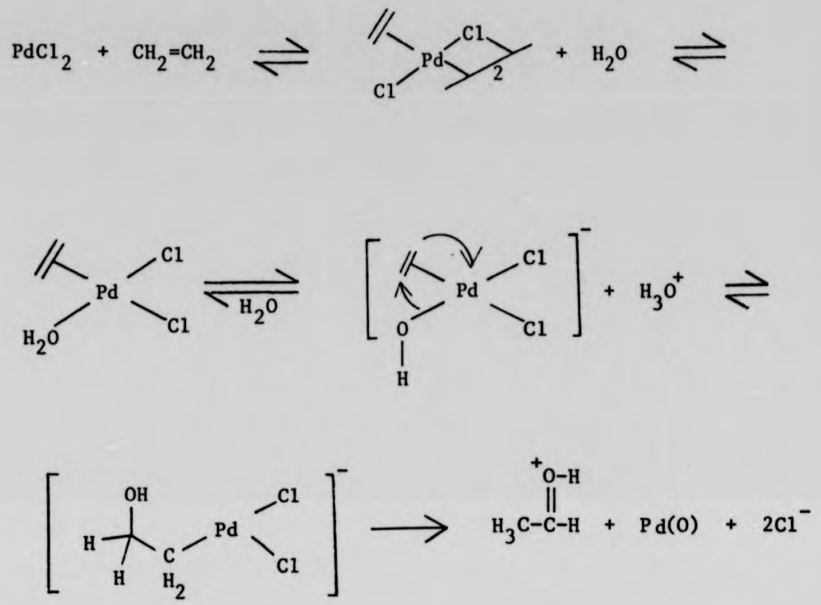
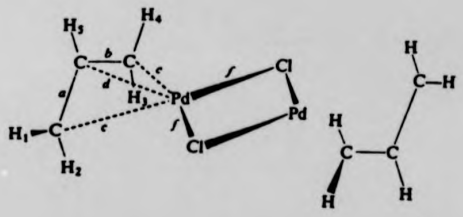


Fig. 5.1.A

Fig. 5.1.B



a. 1.357Å

b. 1.395Å

c. 2.132Å

d. 2.108Å

e. 2.121Å

Fig. 5.1.E

π-bonded to the metal and effectively occupies two co-ordination sites, the remaining two being occupied by bridging chlorines. The carbon-carbon bond lengths are approximately equal and the central carbon atom is close to sp^2 hybridised (angle CCC 119.8 ± 0.9°).

All three carbon atoms are about equidistant from the metal and the allyl group is not perpendicular to the Pd_2Cl_2-plane, but at an angle of 111.5° ± 0.9°. The *anti*-hydrogens (H-2 and H-3) are significantly closer to the metal (2.1 Å) than the *syn*-hydrogens (H-1 and H-4), (2.96 Å); thus, they experience a shielding effect. This is supported by ^1H n.m.r. spectroscopic studies because the *anti*-hydrogens resonate at higher field. Monoallylpalladium complexes are frequently air-stable crystalline compounds which can readily be obtained from simple starting materials. The main methods employed for their preparation are as follows:

(1) From mono-olefins

Hüttel *et al.*[5] investigated the reactions of alkyl substituted propenes with palladium chloride in 50% aqueous acetic acid and noted the production of varying quantities of π-allyl complexes (Fig. 5.1.F). Their mechanism of formation probably involves initial abstraction of a proton from an allylic position, followed by insertion of the metal into a *syn* allylic C-H bond and loss of HCl (Fig. 5.1.G). However, direct proton abstraction cannot be ruled out because Ketley and Braatz[6] have recently observed that several weak inorganic bases (Na_2CO_3, $NaHCO_3$, Na_2HPO_4) will promote the conversion of alkene-palladium chloride π-complexes into π-allyl complexes at RT.

(2) Dienes

(i) 1,3-Dienes

The first π-allylpalladium complex $(C_4H_6PdCl)_2$ was isolated from the reaction of butadiene and $(PhCN)_2PdCl_2$ in benzene[10]. It

27%

32% or 43%

90%

Fig. 5.1.F

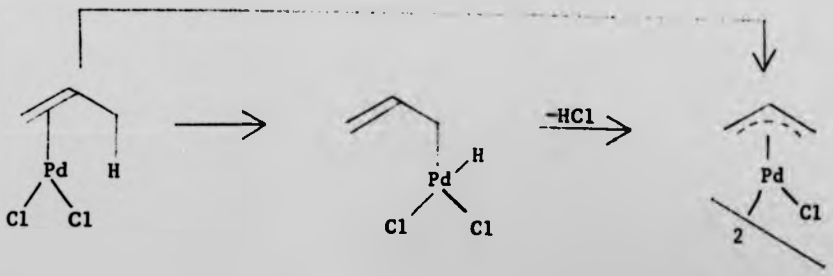


Fig. 5.1.G

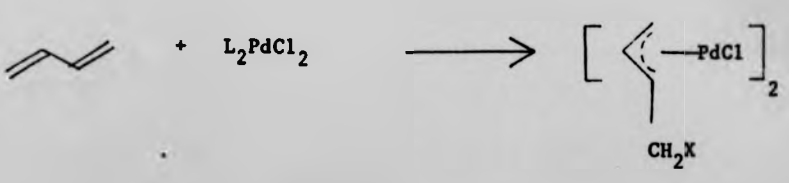


Fig. 5.1.H

was originally formulated as a butadiene complex, but was later shown to be chloro-(2-chloromethylallyl)palladium dimer (Fig. 5.1.H). If the solvent is changed to methanol then the substituent becomes -OMe.

The mechanism by which these products arise show some interesting features. Donati and Conti[8] observed that at low temperature (-40°C and -20°C respectively), butadiene and 1,3-cyclo-octadiene gave π-olefin complexes from which the diene could be recovered unchanged by addition of 1,5-cyclooctadiene. The 1,3-cyclo-octadiene complex was stable up to 110°C, but the butadiene complex was transformed into the π-η^3-allyl complex at temperatures above -20°C (Fig. 5.1.J).

These results are consistent with a mechanism involving initial co-ordination of one double bond, followed by addition of Pd-X to that bond to generate the π-allylpalladium complex (Fig. 5.1.K).

(ii) 1,2-Dienes (Allenes)

Allene itself is known to give rise to two different complexes on reaction with palladium chloride (Fig. 5.1.L). Complex (a) is the major product in non-polar solvents (e.g. benzene), whereas complex (b) can be isolated from reactions in methanol, benzonitrile or dichloromethane[9]. Alkyl-substituted allenes only give complexes whose structures are analagous to structure (a). Schultz *et al.*[9] have investigated the mechanism of this reaction and concluded that the first step involves co-ordination to allene followed by insertion of C=C into the Pd-Cl bond. This generates two possible intermediates, (a') and (b') which give rise to the different products, (a) and (b) (Fig. 5.1.M).

(iii) Allylic halides, alcohols and related compounds

Hüttel and Kratzer[35] first reported the synthesis of π-allylic complexes from allyl chloride and palladium chloride in 50% aqueous acetic acid, while Smidt and Hafner[35] were able to generate the same

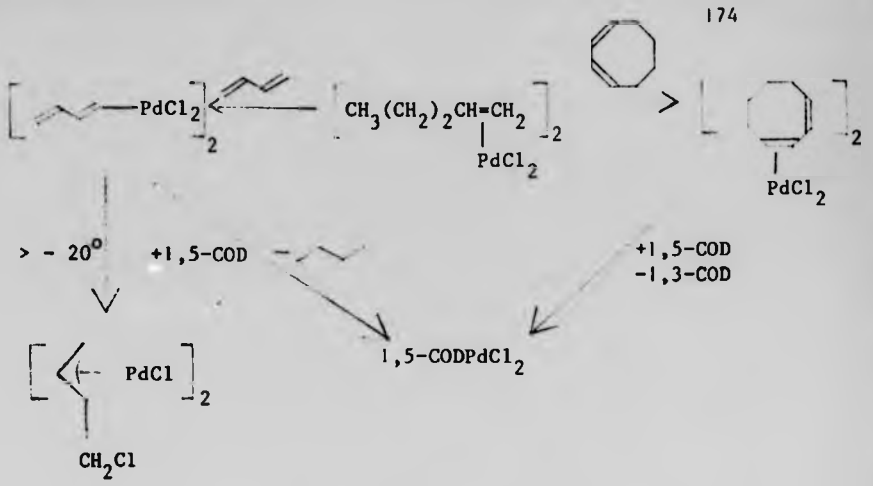


Fig. 5.1.J

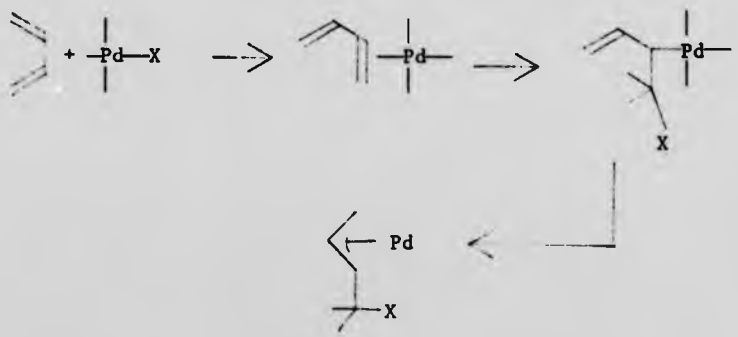


Fig. 5.1.K

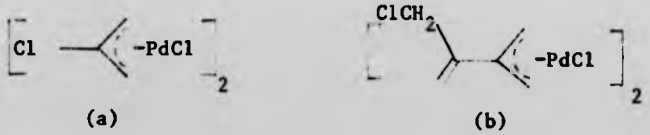


Fig. 5.1.L

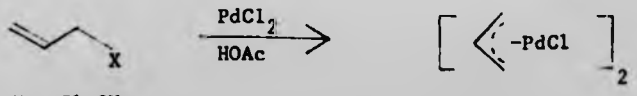


Fig. 5.1.N

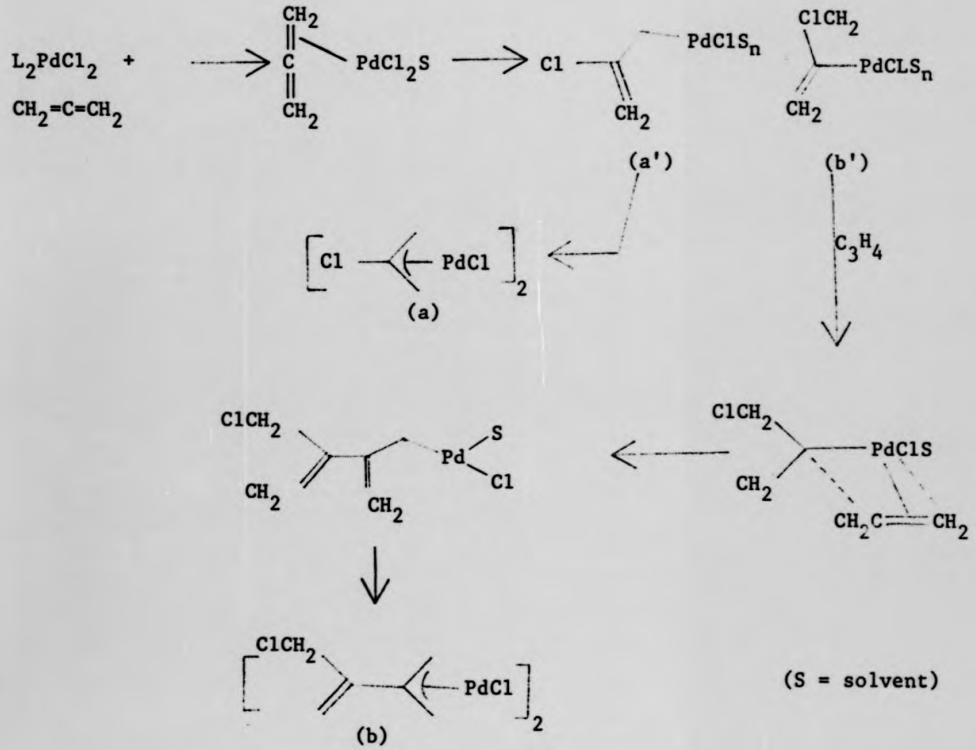

L2PdCl2 +
CH2=C=CH2
CH2
C
PdCl2S
CH2
Cl
PdClSn
CH2
ClCH2
PdCLSn
CH2
(a')
(b')
Cl
PdCl
2
(a)
C3H4
ClCH2
CH2
Pd
S
Cl
CH2
ClCH2
PdClS
CH2
CH2C
CH2
ClCH2
PdCl
2
(b)
(S = solvent)

Fig. 5.1.M

complex by using allyl alcohol (Fig. 5.1.N). More recently it has been observed that $[P(Ph)_3]_4Pd(0)$ will oxidatively add to allylic chlorides and allylic acetates to give π-allylpalladium species.

These methods for preparing π-allylpalladium complexes require stoichiometric quantities, but recently it has been recognised that palladium complexes are extremely efficient at promoting allylic rearrangements under catalytic conditions, presumably *via* π-allylpalladium intermediates. Over the past decade a vast amount of work has been accomplished which exploits the ability of palladium complexes to catalyse selectively the reactions of allylic substrates. This has proved particularly advantageous in the field of synthetic organic chemistry and has been comprehensively reviewed[13,38]. The main advantages of using palladium complexes are:

(i) they are readily prepared and easy to handle because they are frequently crystalline and air-stable;

(ii) they effect the required transformations in catalytic quantities under very mild conditions, often within minutes at RT;

(iii) by careful choice of catalyst and conditions it is possible to obtain *only* or *predominantly* the desired product.

The rhodium(I) promoted rearrangements of "skipped" acetoxydienes described in Chapter 3 were not sufficiently selective to be of use in organic synthesis. However, for the reasons stated above, it was believed that stereoselective control could be obtained in the palladium-catalysed rearrangements of these dienes. If this is the case then these rearrangements could provide valuable synthetic routes to biosynthetically important fatty acids and other related compounds.

Fig. 5.1.P

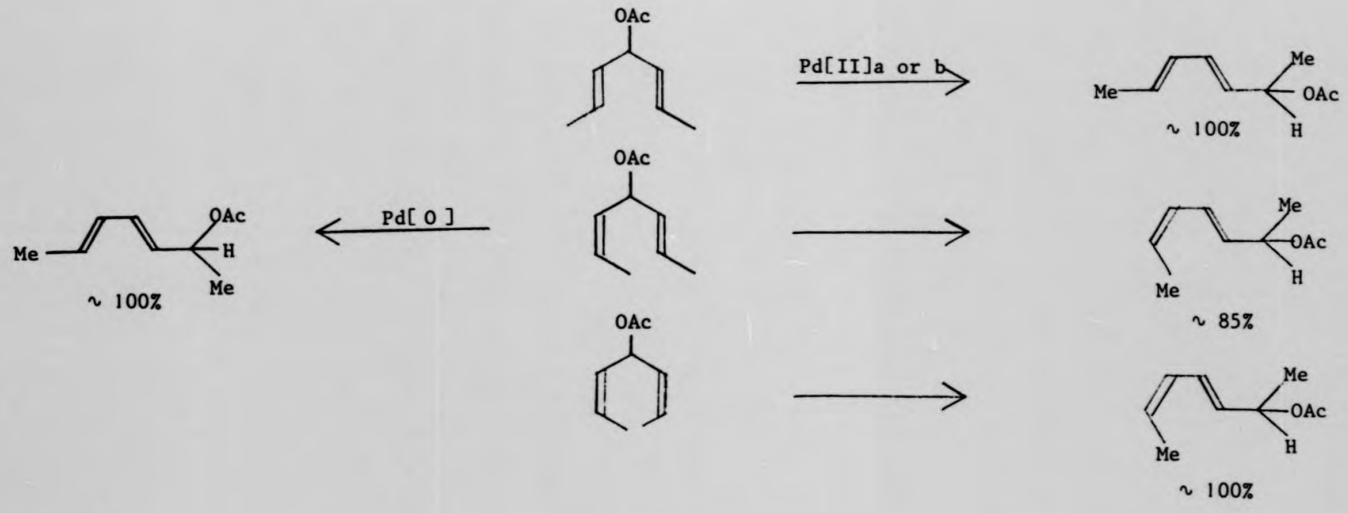
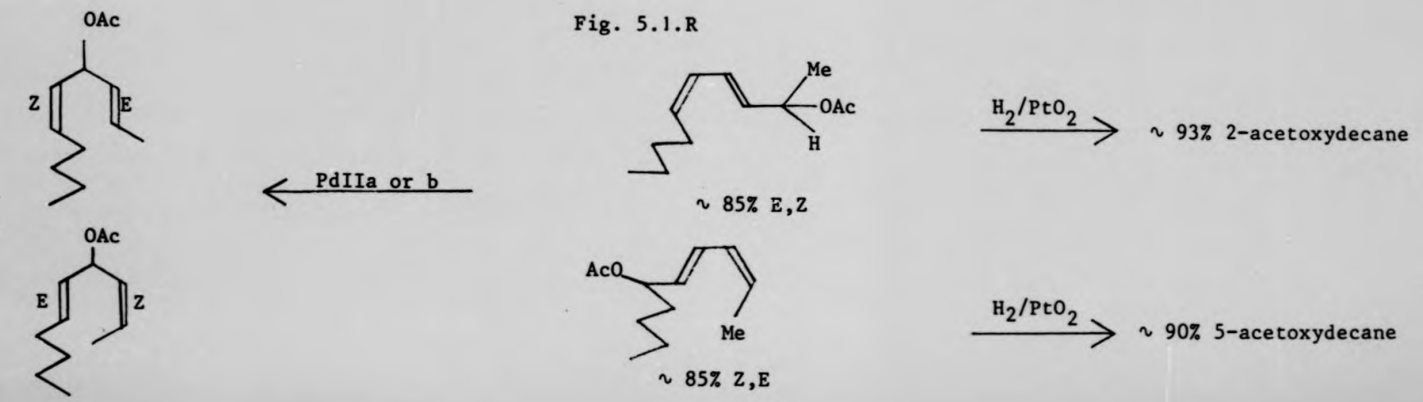


Fig. 5.1.R



Catalytic amounts of $(PhCN)_2PdCl_2$* and $(MeCN)_2PdCl_2$* were observed to convert (E,E)-4-acetoxyhepta-2,5-diene to (E,E)-2-acetoxyhepta-3,5-diene within minutes at RT. Similarly, (Z,Z)-4-acetoxyhepta-2,5-diene was converted to (E,Z)-2-acetoxyhepta-3,5-diene, but the reaction required 30 minutes to proceed to completion. This indicates a preference for reaction with *trans*-double bonds and this was most effectively demonstrated by the conversion of (E,Z)-4-acetoxyhepta-2,5-diene to (E,Z)-2-acetoxyhepta-3,5-diene (Fig. 5.1.P). The Pd(II)-catalysed rearrangements of these "skipped" acetoxydienes are occurring preferentially at *trans*-double bonds and hence in the case of (E,Z)-"skipped" dienes this gives control over the direction of allylic rearrangement. It should also be noted that irrespective of the starting configuration of migrating double bond, a *trans*-double bond is always generated[14].

To further illustrate these points the substrates (Z,E)- and (E,Z)-4-acetoxydeca-2,5-diene were treated with catalytic amounts of Pd(II)-complexes (Fig. 5.1.R). (E,Z)-4-acetoxydeca-2,5-diene was converted to *ca.* 85% (E,Z)-2-acetoxydeca-3,5-diene, and catalytic hydrogenation of the product followed by g.l.c. analysis indicated ∿95% 5-acetoxydecane. Similarly, (Z,E)-4-acetoxydeca-2,5-diene gave *ca.* 85% (Z,E)-6-acetoxydeca-2,4-diene and catalytic hydrogenation followed by g.l.c. analysis indicated 90% 5-acetoxydecane and 10% 2-acetoxydecane. The apparent discrepancy between the percentages of the (E,Z)- and (Z,E)-products, and the percentages of the corresponding hydrogenation products can be explained by considering the methods of preparation of the substrates. Both substrates were prepared by coupling the appropriate α,β-unsaturated aldehyde with a vinyl-Grignard reagent derived either from (Z)-1-bromopropene or (Z)-1-bromohexene.

It is known that the methods used to prepare these bromides

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*Later referred to as Pd(II)b and Pd(II)a respectively.

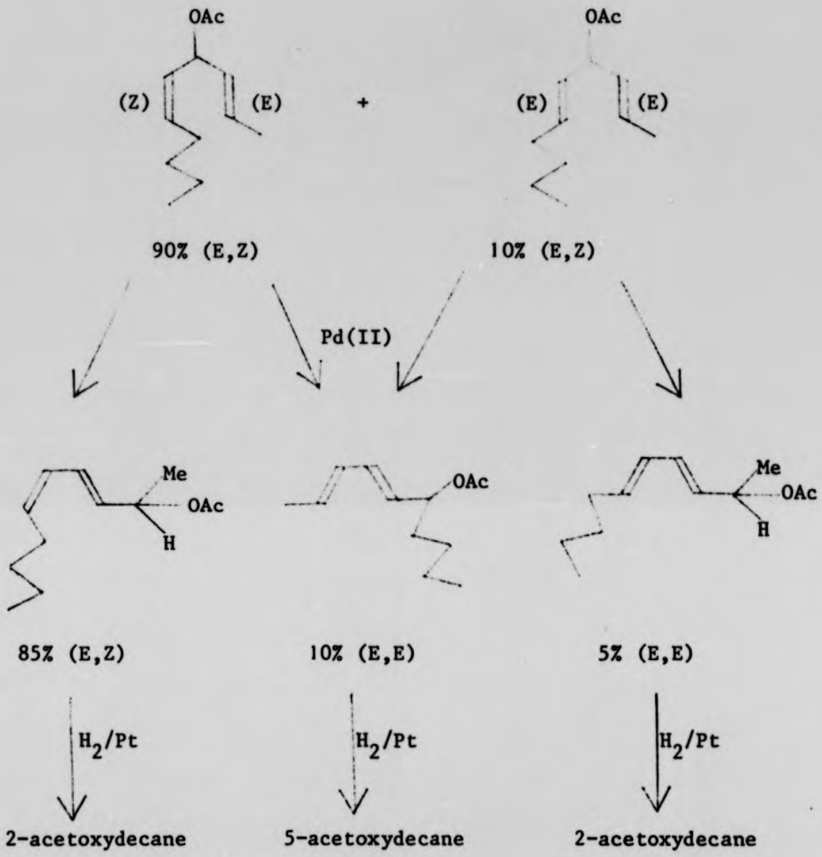


Fig. 5.1.S

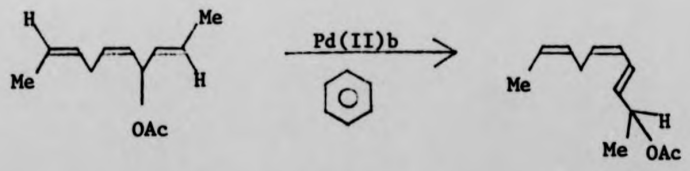


Fig. 5.1.U

give products with purity > 99%[15] and it has been shown that the coupling of these Grignard reagents with aldehydes proceeds with complete retention of configuration[16]. However, formation of the Grignard reagent from (Z)-alkenyl bromides has been shown[17] to give a mixture containing 90-95% (Z)- and 5-10% (E)-isomer, hence the (E,Z)- and (Z,E)-acetoxydecadienes may contain up to 10% (E,E)-impurity. Reconsideration of the isomerisation of (E,Z)-4-acetoxydeca-2,5-diene is shown in Fig. 5.1.S. This reaction scheme is totally consistent with the experimental observations for both the isomerisation of the (2E,5Z)-acetoxydecadiene and the (2Z,5E)-acetoxydecadiene, i.e. production of ∿ 85% (E,Z)-isomerised product, and an approximate 90:10 ratio of 2- and 5-acetoxydecanes upon hydrogenation.

From the results presented it can be seen that the Pd(II)-catalysed rearrangements are approximately 95% selective for the *trans*-double bond in an (E,Z)-"skipped" diene. This was confirmed by the isomerisation of (E,Z,Z)-4-acetoxydeca-2,5,8-triene. This compound was prepared by the coupling of hexa-1,4-diynylmagnesium bromide with (E)-but-2-enal, followed by catalytic hydrogenation (Lindlar catalyst) and acetylation. It is known that under the conditions employed for the reduction only a very small percentage of (E,E,Z)-product is generated[18]. Treatment of (E,Z,Z)-4-acetoxydeca-2,5,8-triene with a catalytic amount of Pd(II)b (5 mol%) caused a smooth conversion to (E,Z,Z)-2-acetoxydeca-3,5,8-triene (Fig. 5.1.U). ^{1}H n.m.r. spectroscopy indicated *ca.* 95% (E,Z,Z)-isomer with *ca.* 5% (E,E,Z)-isomer, as predicted by Fig. 5.1.S.

It has previously been reported[19] that Pd(II) salts catalyse the exchange of allylic esters and the exchange and isomerisation of allylic acetates[20], e.g. (E)-1-acetoxybut-2-ene to 2-acetoxybut-3-ene. One mechanism proposed for this reaction involves

an acetoxypalladation-deacetoxypalladation sequence (Fig. 5.1.V).

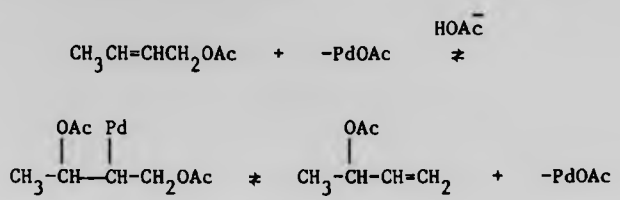


Fig. 5.1.V

This mechanism implies that exchange of the acetate group should occur when and *only* when there is isomerisation. Henry[21] obtained evidence to support this mechanism during studies on the Pd(II)-catalysed isomerisation of crotyl propionate in acetic acid/LiOAc. It was observed that (E)-but-2-enylpropionate (crotyl propionate) was converted to 2-acetoxybut-3-ene, i.e. isomerisation *with* exchange. Surprisingly, a second process was observed which involved isomerisation *without* exchange. This reaction was unexpected and had no clear analogy to other Pd(II)-catalysed reactions, although formally it has similarity to the Pd(II)-catalysed isomerisation of olefins[22] which are thought to proceed *via* a 1,3-hydride shift (Fig. 5.1.W).

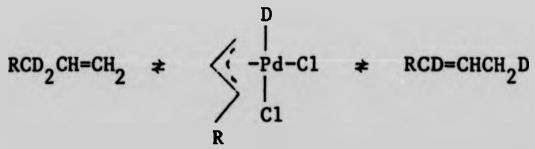


Fig. 5.1.W

The mechanism of this reaction was probed further by the use of [^{18}O]labelled crotyl propionate where the oxygen label was located only at the ester oxygen. If the reaction proceeds *via* a π-allylpalladium(II)acetate formed by breaking the -C-^{18}O*- ester bond then two of the possibilities for the [^{18}O]distribution are either complete retention of the label in the ester oxygen or

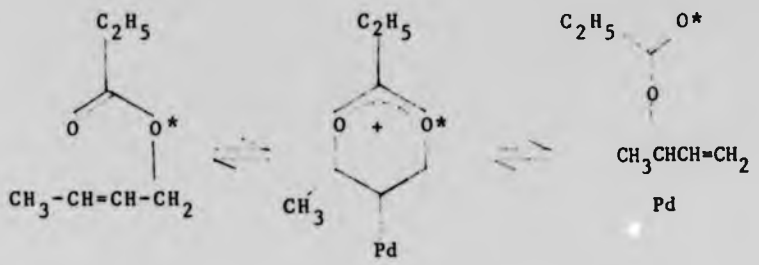


Fig. 5.1.X

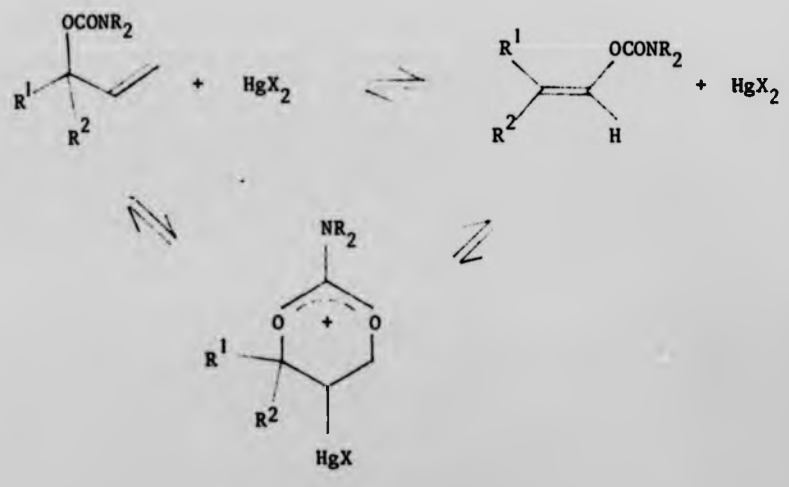


Fig. 5.1.Y

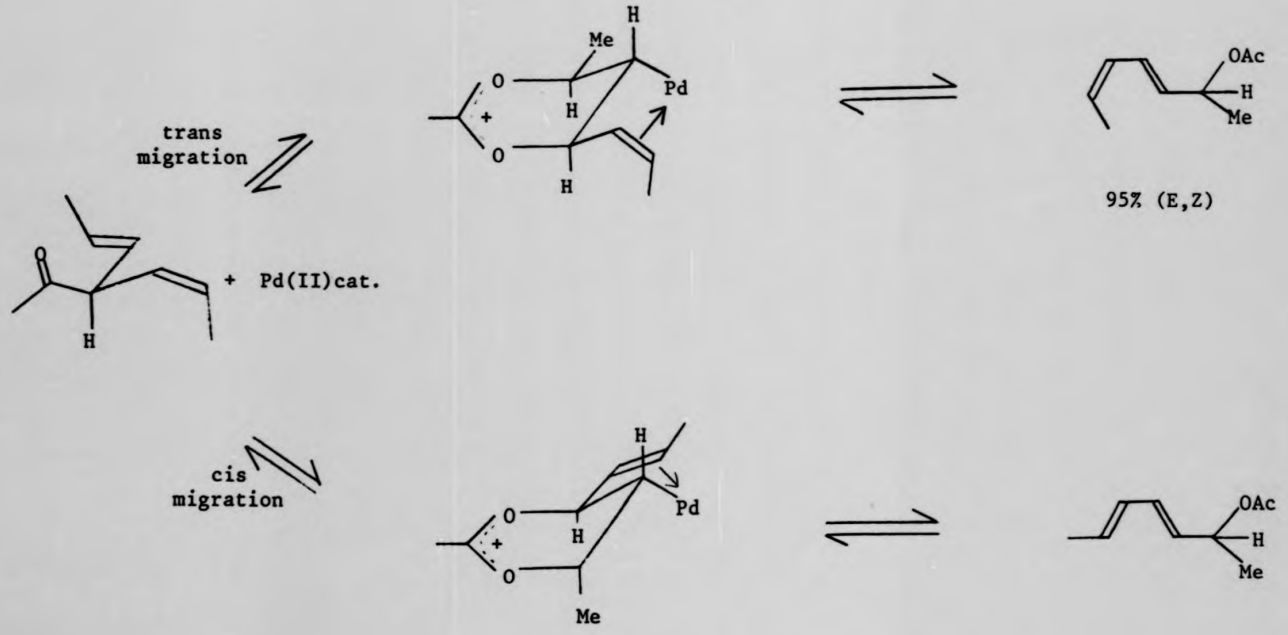

trans
migration
+ Pd(II)cat.
H
Me
O
Pd
H
O
H
OAc
H
Me
95% (E,Z)
cis
migration
H
Pd
O
H
O
Me
OAc
H
Me

Fig. 5.1.a

complete scrambling with the label equally divided between ester and carbonyl oxygen. Henry observed neither of these, but instead it was noted that the [^{18}O]label was completely transferred to the carbonyl oxygen.

It is proposed that the first step in the mechanism is formation of a π-complex followed by an intramolecular attack involving neighbouring carboxylate participation to give an acetoxonium ion intermediate (Fig. 5.1.X). Henry's proposed mechanism is consistent with the experimental observation that the [^{18}O]label is completely transferred from ester oxygen to carbonyl oxygen and is further supported by the observation that replacing the propionate group by a trifluoro-acetate function results in a 500-fold rate decrease.

The presence of an electron-withdrawing group (e.g. $-CF_3$) at the carbonium ion centre of the proposed intermediate will destabilise this intermediate thereby reducing the rate of reaction. An analogous acetoxonium ion has been invoked by Overman[23] to rationalise the observed equilibration of allylic carbamates by catalytic amounts of mercury salts. The acetoxonium ion is also well established[22,24] as an intermediate in solvolysis reactions (Fig. 5.1.Z).

Henry suggests that this intermediate is likely to occur in other Pd(II)-catalysed rearrangements in which neighbouring group participation is possible. The isomerisations of the 4-acetoxyhepta-2,5-dienes and 4-acetoxydeca-2,5-dienes almost certainly proceed *via* a 1,3-acetoxonium ion intermediate and this could explain the selectivity in the isomerisation of (E,Z)-substrates (Fig. 5.1.a). The reaction must be proceeding under kinetic control *via* the lower energy pathway which involves formation of an acetoxonium ion by reaction at the (E)-double bond as opposed to the (Z)-double bond, even though this generates the thermodynamically less stable, conjugated

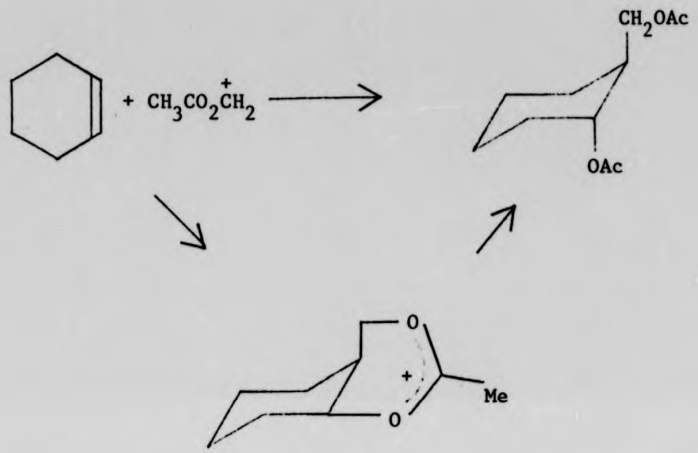


Fig. 5.1.Z

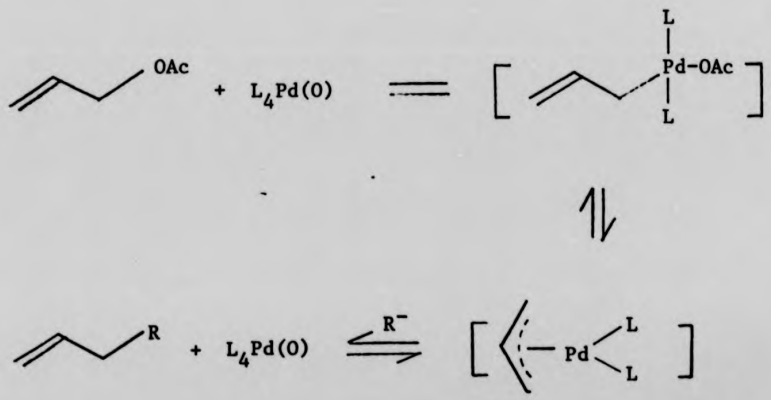
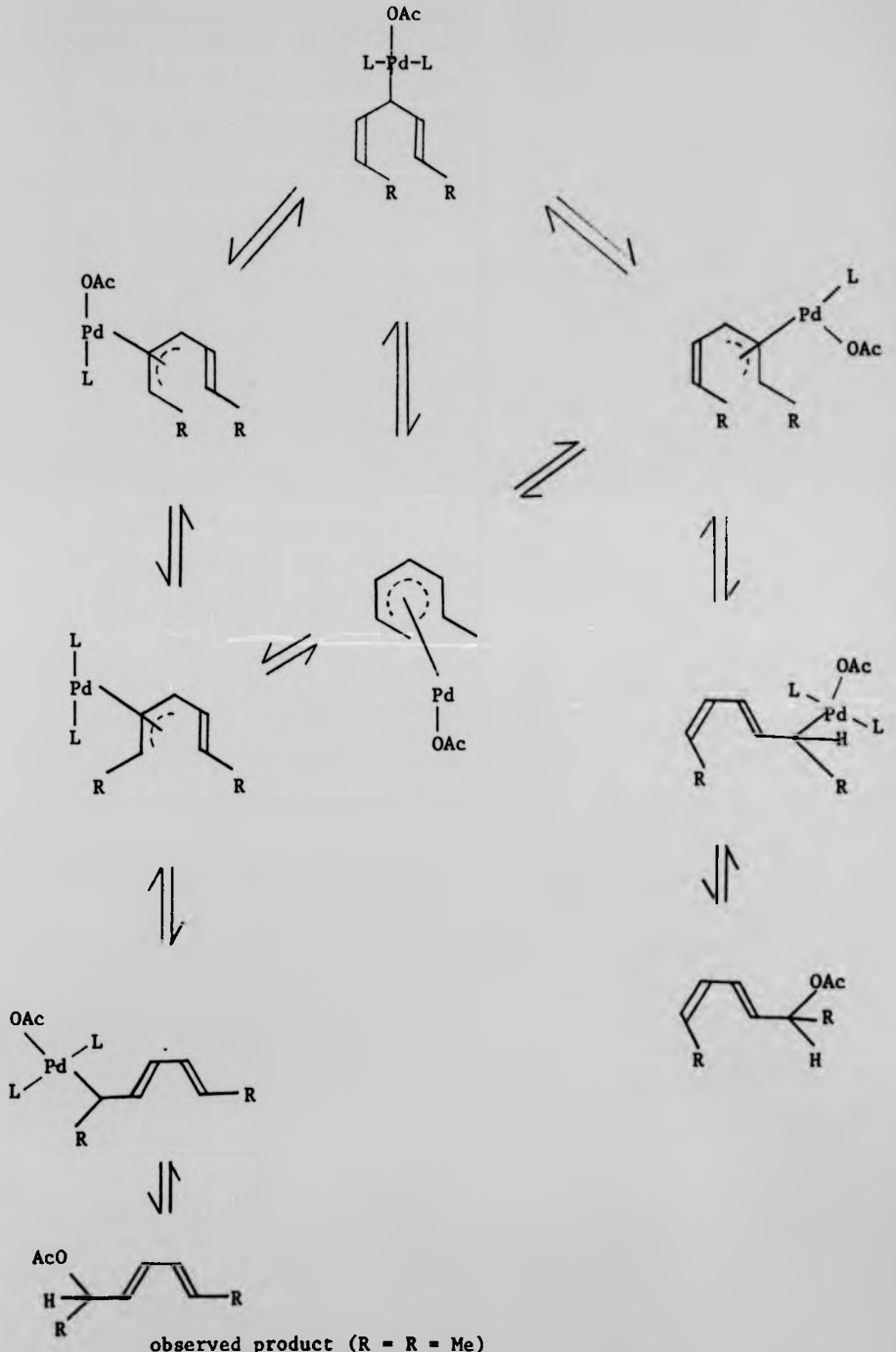


Fig. 5.1.b



observed product (R = R = Me)

Fig. 5.1.c

diene product [(E,Z) as opposed to (E,E)]. This is supported by the observation that if the reaction mixture is left for much longer periods of time before work-up, i.e. in excess of 2 hours, then slowly increasing amounts of (E,E)-product are observed. In an attempt to investigate this process further, (E,E)-6-acetoxydeca-2,4-diene was prepared and treated with a catalytic amount of Pd(II)b. No reaction was observed at RT, but on warming to 80°C the acetate was quickly converted into (E,E,E)-deca-2,4,6-triene.

In contrast to the palladium(II)-catalysed rearrangements of 4-acetoxyhepta-2,5-dienes, the $[P(Ph)_3]_4Pd(0)$ rearrangements proceed within seconds at RT to give (E,E)-2-acetoxyhepta-3,5-diene as the only product, irrespective of the configuration of the starting olefin [(E,E), (E,Z) or (Z,Z)] (Fig. 5.1.P). These isomerisations are probably not proceeding *via* a 1,3-acetoxonium ion intermediate, but it is known that Pd(0) complexes will oxidatively add to allylic acetates to generate π-η^3-allylpalladium species (Fig. 5.1.b)[10a].

In the absence of another incoming nucleophile (R), the acetate returns to the allyl species and in the case of substituted allylic acetates generates the isomerised product. If the reaction sequence shown in Fig. 5.1.c is operative, then having $R \neq R$ should generate a mixture of positional isomers, and this was observed for the $[P(Ph)_3]_4Pd(0)$-catalysed isomerisation of (E,Z)-4-acetoxydeca-2,5-diene, which gave (E,E)-2-acetoxydeca-3,5-diene and (E,E)-6-acetoxydeca-2,4-diene (Fig. 5.1.d).

That different mechanisms are operative for the Pd(0) and Pd(II) isomerisations was further illustrated by the isomerisations of (E)- and (Z)-3-acetoxyhexa-1,4-dienes (Fig. 5.1.e).

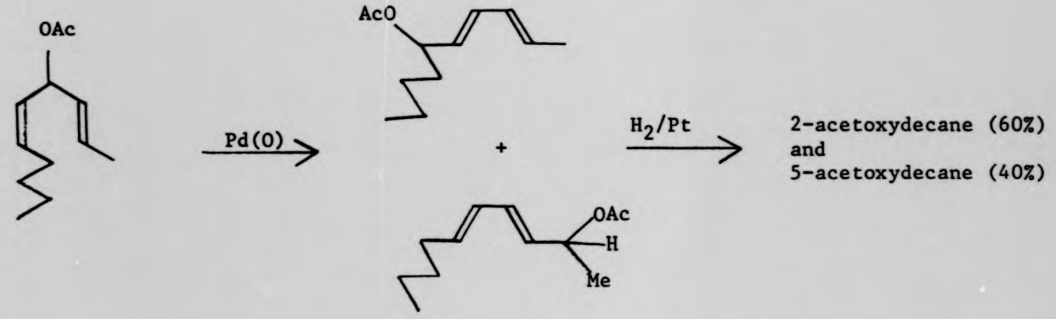


Fig. 5.1.d

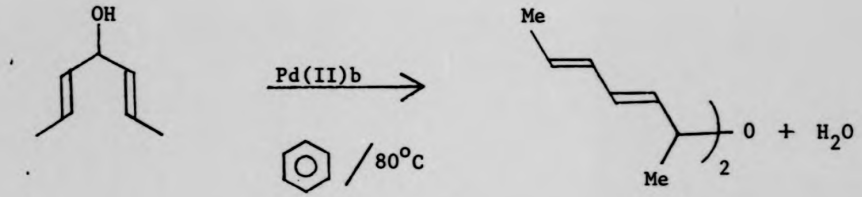


Fig. 5.1.f

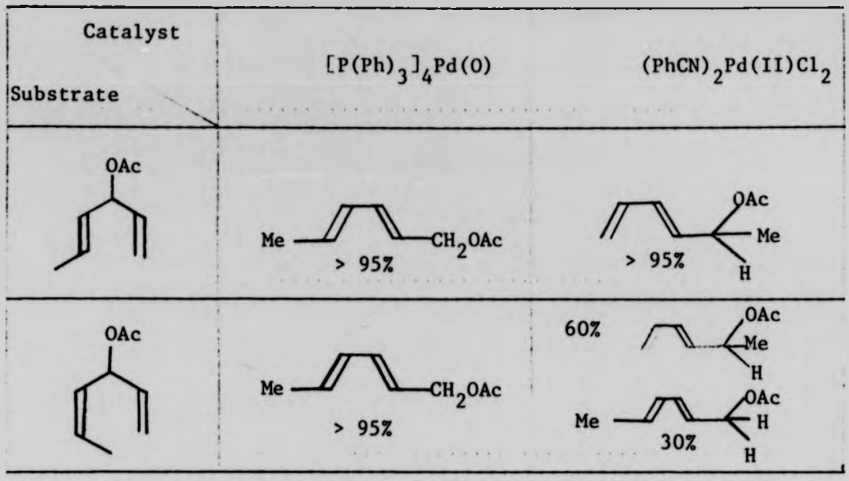


Fig. 5.1.e

These results indicate that Pd(0)-promoted isomerisations give preferential reaction at the terminal olefin and generate the thermodynamically stable product as expected. However, it can be seen that the Pd(II)-catalysed isomerisations show a preference for reactivity of *trans*-disubstituted > *cis*-disubstituted > monosubstituted and this reactivity must be reflected in the stabilities of the different acetoxonium ion intermediates.

Studies of isomerisations of some "skipped" dienols by Pd(II) and Pd(0) complexes proved less rewarding. However, treatment of (E,E) or (E,Z)-hepta-2,5-dien-4-ol with 5 mol % Pd(II)b in benzene at 80°C gave a quantitative yield of the unsaturated ether shown in Fig. 5.1.f. It is known that reaction of Pd(II) complexes with allyl alcohols generates π-allylpalladium species. Nucleophilic attack by excess alcohol can then generate the observed products. ^{1}H n.m.r. spectroscopy inicated that the product possessed the all *trans*-geometry irrespective of the configuration of the starting olefin, (E,E) or (E,Z).

From a consideration of the results presented for the palladium induced isomerisation of allylic acetates several conclusions can be drawn.

(1) The Pd(II)-catalysed isomerisations of 3-acetoxy-1,4-dienes proceed *via* an acetoxonium ion intermediate, whereas the Pd(O)-catalysed isomerisations proceed *via* a classical π-allylpalladium species. This difference can be exploited for synthetic purposes because it leads to stereochemically different products.

(2) The Pd(II)-catalysed isomerisations of 3-acetoxy-1,4-dienes occur preferentially at (E)-disubstituted double bonds. This circumstance is favourable for synthetic applications because:

(i) (E,Z)-3-acetoxy-1,4-dienes are easy to prepare from α,β-unsaturated aldehydes, and they are converted stereospecifically to (2E,4Z)-1-acetoxy-2,4-dienes by Pd(II) a/b complexes;

(ii) the preferred direction of allylic rearrangement can be predicted:

$$RCH\overset{(E)}{=\!=}CHCHOAcCH\overset{(Z)}{=\!=}CHR_2 \rightarrow RCHOAcCH\overset{(E)}{=\!=}CH-CH\overset{(Z)}{=\!=}CHR_2$$

(3) The structural fragment ($-CH\overset{(E)}{=\!=}CH-CH\overset{(Z)}{=\!=}CHR_2$) occurs in several natural substrances[25] or their products of degradation[26]. As demonstrated, it can be efficiently generated by Pd(II)-catalysed isomerisation of (E,Z)-3-acetoxy-1,4-dienes, and it is also known that transfer of chirality occurs during Pd(II)-catalysed rearrangements of allylic acetates.

The work concerning Pd(II)-catalysed rearrangements described previously, directed us towards an attempted synthesis of (Z,Z,E)-12-hydroxyheptadeca-5,8,10-trienoic acid. This acid is a known degradation

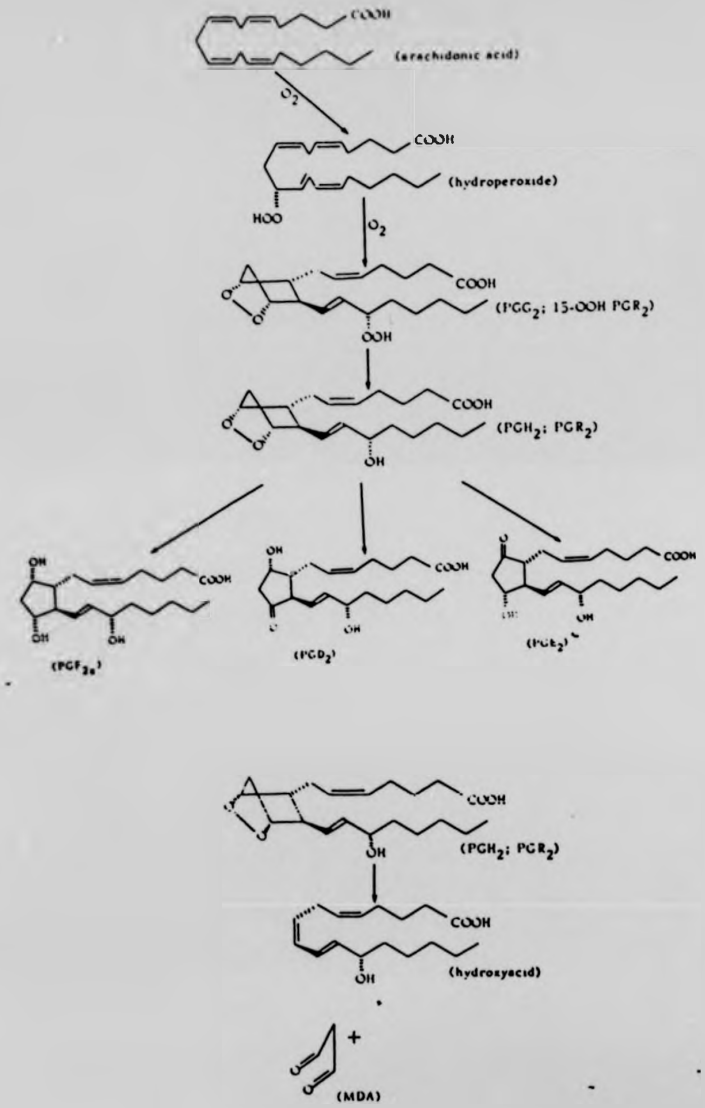


Fig. 5.1.g

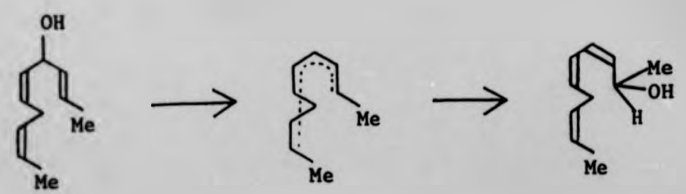


Fig. 5.1.1

product of biosynthetically derived endoperoxides, precursors to prostaglandins[27]. The projected biosynthetic pathway inter-relating arachidonic acid [(Z,Z,Z,Z)-eicosa-5,8,11,14-tetraenoic acid], hydroperoxides, endoperoxides and prostaglandins is illustrated in Fig. 5.1.g.

The hydroperoxides shown in Fig. 5.1.g, and other related molecules have also been implicated in the biosynthesis of "slow reacting substances" (SRS), important agonists in asthma and hypersensitivity[28].

Our approach to the synthesis of (Z,Z,E)-12-hydroxyheptadeca-5,8,10-trienoic acid was based upon two observations:

(i) the Pd(II)-catalysed stereospecific conversion of (E,Z,Z)-4-acetoxydeca-2,5,8-triene to (E,Z,Z)-2-acetoxydeca-3,5,8-triene;

(ii) the attempted purification of (E,Z,Z)-4-hydroxydeca-2,5,8-triene by fast column silica gel chromatography[29] gave (E,Z,Z)-2-hydroxydeca-3,5,8-triene (*ca.* 90% E,Z,Z).

The Pd(II) isomerisations were discussed earlier, but the second observation was somewhat surprising. It had previously been reported[33] that acid-catalysed isomerisation of (Z)-3-hydroxyhexa-1,4-diene gave (Z)-2-hydroxyhexa-3,5-diene, but this was found to be incorrect. Both (E)- and (Z)-3-hydroxyhexa-1,4-dienes are isomerised to (E)-2-hydroxyhexa-3,5-diene. To explore the silica-catalysed isomerisations further, (E,E)-, (E,Z)- and (Z,Z)-4-hydroxyhepta-2,5-dienes were stirred with silica gel in CH_2Cl_2.

Periodic monitoring by ^1H n.m.r. spectroscopy showed that the (E,E)-isomer was converted completely to (E,E)-2-hydroxyhepta-2,5-dienes in < 5 hours while the (E,Z)-isomer was converted to a 50:50 mixture of (E,E)- and (E,Z)-2-hydroxyhepta-3,5-dienes in *ca.*

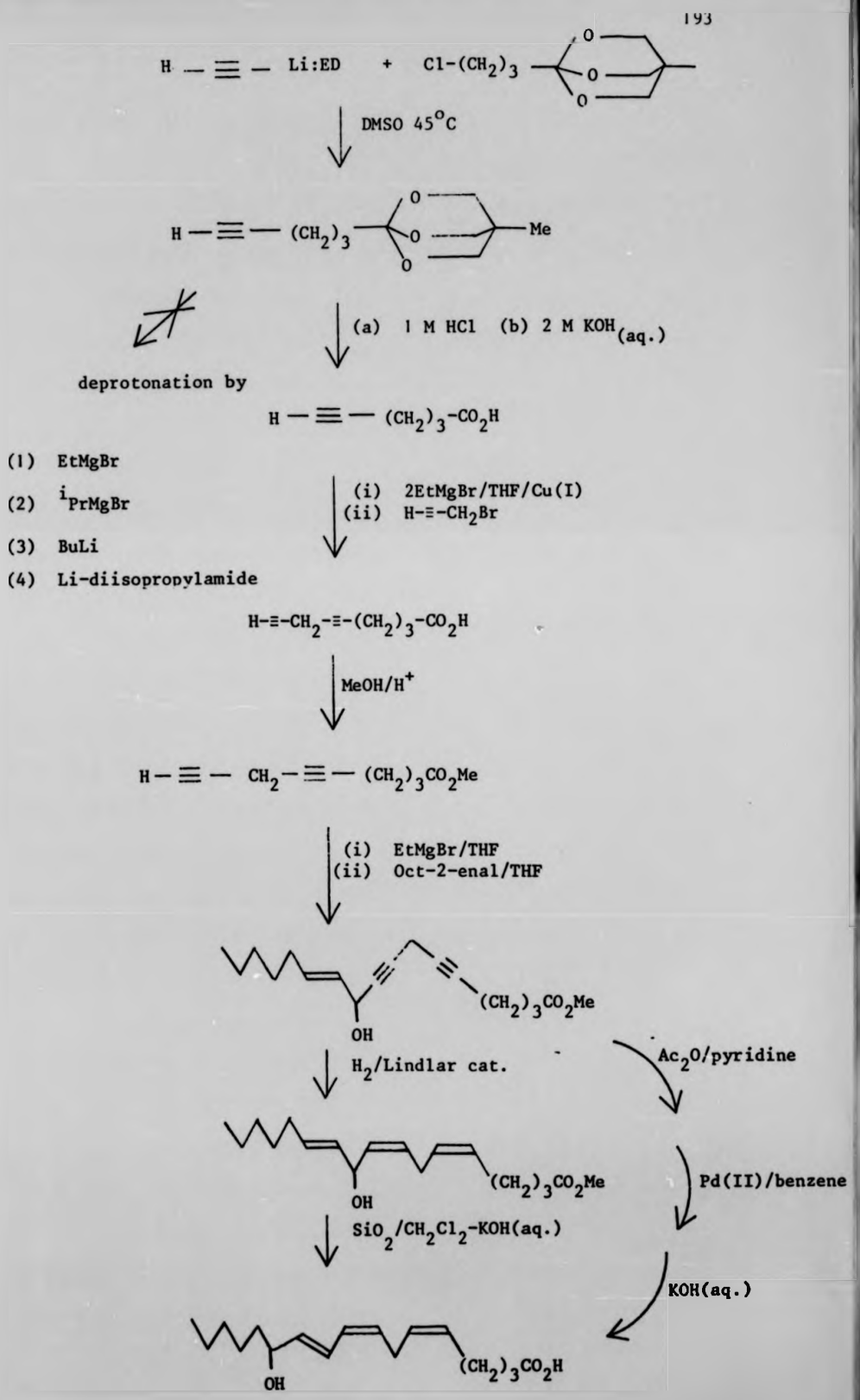

H — ≡ — Li:ED + Cl-(CH2)3
DMSO 45°C
H — ≡ — (CH2)3
Me
(a) 1 M HCl (b) 2 M KOH(aq.)
deprotonation by
H — ≡ — (CH2)3-CO2H
(1) EtMgBr
(2) iPrMgBr
(3) BuLi
(4) Li-diisopropylamide
(i) 2EtMgBr/THF/Cu(I)
(ii) H-≡-CH2Br
H-≡-CH2-≡-(CH2)3-CO2H
MeOH/H+
H — ≡ — CH2 — ≡ — (CH2)3CO2Me
(i) EtMgBr/THF
(ii) Oct-2-enal/THF
(CH2)3CO2Me
OH
H2/Lindlar cat.
Ac2O/pyridine
Pd(II)/benzene
SiO2/CH2Cl2-KOH(aq.)
KOH(aq.)

Fig. 5.1.j

12 hours. The (Z,Z)-isomer was only very slowly isomerised (48 hours) under these conditions. These results can be interpreted in either of two ways:

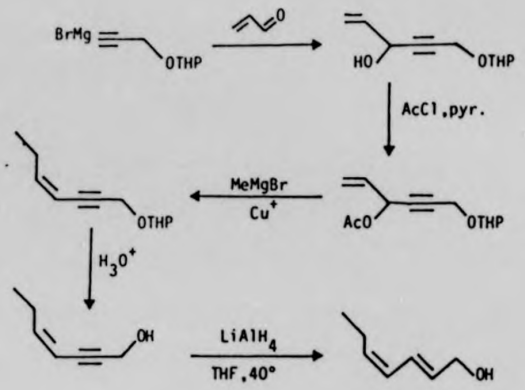
(1) the isomerisations are only stereo- and regio-specific under the exact conditions of fast column chromatography;

(2) the configuration of the intermediate carbonium ion formed during the silica-catalysed isomerisation of (E,Z,Z)-deca-2,5,8-trien-4-ol is maintained by a homoallylic interaction (Fig. 5.1.h).

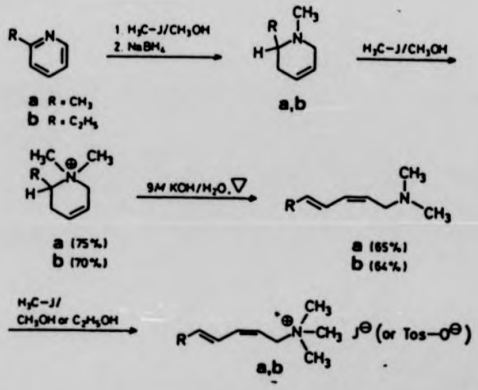
Whatever the reason for this retention of configuration at the (Z)-double bond it can be seen that this conversion is of great synthetic value.

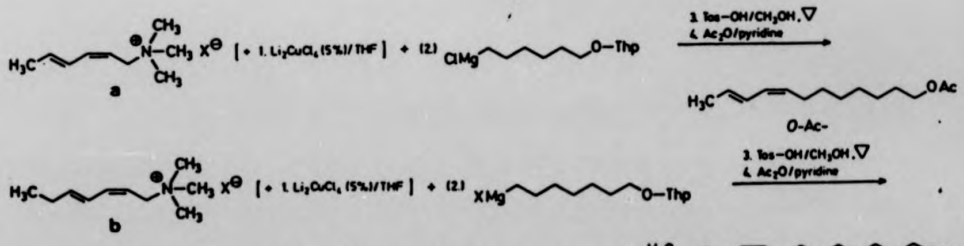
The route devised for the synthesis of (Z,Z,E)-12-hydroxyhepta-5,8,10-trienoic acid is illustrated in Fig. 5.1.j. 1-Chloropropyl-4-methyl-2,6,7-trioxabicyclo[2.2.0]octane (Cl-TOB) previously prepared by D. A. Howes[30] was coupled directly with a lithium acetylide-ethylene diamine complex[31]. Howes found that the Cl-TOB was unreactive towards magnesium while we observed that the acetylenic proton could not be effectively removed by Grignard reagent or lithium diisopropylamide. The protecting group was therefore removed at this stage to give hex-5-ynoic acid as a crystalline solid.

It was envisaged that this acid could then be coupled with propargyl bromide, as described by Osbond *et al.*[32], and the resulting diynoic acid methylated and further coupled with (E)-oct-2-enal to give methyl (E)-10-hydroxyheptadec-11-en-5,8-diynoate. Catalytic hydrogenation would give methyl (Z,Z,E)-10-hydroxyheptadeca-5,8,11-trienoate which could be isomerised by fast column silica gel chromatography and hydrolysed to give (Z,Z,E)-12-hydroxyhepta-5,8,10-trienoic acid. Alternatively, methyl (Z,Z,E)-10-hydroxyheptadeca-5,8,11-



Taken from Ref. 34(a)





Taken from Ref. 34(b)

Fig. 5.1.k

trienoate could be converted to the corresponding acetate and treatment with a catalytic amount of Pd(II)a or b, followed by hydrolysis would give the required acid. Any contaminating (Z,E,E)-isomer could be removed as the Diels-Alder adduct by reaction with maleic anhydride. Recently developed methods for the generation of (E,Z)-conjugated dienes are illustrated in Fig. 5.1.k[34], and it can be seen that the Pd(II)-catalysed isomerisations of substituted 3-acetoxy-1,4-dienes and the silica gel promoted isomerisation of substituted 4-hydroxy-2,5,8-trienes are comparable to, if not superior than these methods.

5.2 SYNTHESIS OF (4)-ACETOXYDECA-2,5-DIENES, (4)-ACETOXY-2,5,8-TRIENES AND PALLADIUM COMPLEXES

5.2.1 Synthesis of Complexes of Pd(0) and Pd(II)

(i) Preparation of dichlorobis(benzonitrile)palladium(II). Pd(II)b[36]

Palladium(II)chloride (2.5 g, 14 mmol) was suspended in distilled benzonitrile (50 cm^3) and heated to 140°C for 30 minutes. The solution was quickly filtered and poured into petroleum ether (40-60) (300 cm^3). The yellow precipitate was collected by filtration, washed with petroleum ether (40-60) and dried to give dichlorobis(benzonitrile)palladium(II) (5.27 g, 13.7 mmol) in 98% yield.

I.r. (nujol mull): 3060 (w), 3030 (w), 2280 (m), 1595 (m), 1454 (m), 1360 (m) cm^{-1}.

(ii) Preparation of dichlorobis(acetonitrile)palladium(II).Pd(II)a[36]

The procedure was repeated as described above using acetonitrile as solvent. Yellow orange crystals of dichlorobis(acetonitrile)palladium(II) were collected by filtration in 94% yield.

(iii) Preparation of tetrakis(triphenylphosphine)palladium(0)[37] $[P(Ph)_3]_4Pd(0)$

Palladium(II)dichloride (0.87 g, 4.9 mmol), triphenylphosphine (6.5 g, 25 mmol) and DMSO (60 cm^3) were heated to 150°C, under nitrogen. On complete dissolution, the solution was stirred for 10 minutes at 150°C followed by addition of hydrazine-hydrate (1.0 g, 20 mmol) during 2 minutes. The solution was then cooled and the yellow crystals were collected by filtration under nitrogen, washed with degassed ethanol (25 cm^3) and ether (25 cm^3), and dried under vacuum to give $Pd[P(Ph)_3]_4$ (5.1 g, 4.4 mmol), m.p. 116°C.d, in 90% yield.

5.2.2 Synthesis of (E,Z)-4-acetoxydeca-2,5-diene

Preparation of (E,E)-hepta-3,5-dien-2-ol

Methyl iodide (4.54 g, 32 mmol) in dry ether (10 cm^3) was slowly added to a stirred suspension of magnesium turnings (0.78 g, 32 mmol) in dry ether (10 cm^3). When reaction was complete (E,E)-hexa-2,4-dienal (2.5 g, 26 mmol) in dry ether (5 cm^3) was added, and the reaction mixture was stirred for 6 hours. 15% NH_4Cl (aq.) (25 cm^3) was then added. The aqueous phase was separated, washed with ether (2 x 25 cm^3) and the combined ethereal extracts dried ($MgSO_4$). Filtration, evaporation and distillation gave (E,E)-hepta-3,5-dien-2-ol (2.0 g, 18 mmol) b.p. 70-72°C (14 mm), in 69% yield.

^1H n.m.r. ($CDCl_3$): 1.27 (3 H, H-1, d, J 6 Hz), 1.76 (3 H, H-7, d, J 6.5 Hz), 2.18 (O-H), 4.30 (1 H, H-2, dq), 5.65 (2 H, H-3 and H-6, m), 6.10 (2 H, H-4 and H-5, m) p.p.m.

Preparation of (E,E)-2-acetoxyhepta-3,5-diene

Acetic anhydride (1.0 g, 9.8 mmol), (E,E)-hepta-3,5-dien-2-ol (0.8 g, 7.1 mmol) and dry pyridine (5 cm^3) were stirred at RT for 9 hours. The solution was then poured on to water (20 cm^3), acidified with 5 M HCl, extracted with ether (2 x 25 cm^3) and the combined ethereal extracts washed with 15% $NaHCO_3$ (aq.). The solution was then dried ($MgSO_4$), filtered, concentrated and distilled to give (E,E)-2-acetoxyhepta-3,5-diene (0.85 g, 5.5 mmol), b.p. 85-87°C (2 mm), in 78% yield.

^1H n.m.r. ($CDCl_3$): 1.31 (3 H, H-1, d, J 6 Hz), 1.75 (3 H, H-7, d, J 6.5 Hz), 2.01 (3 H, s), 5.35 (1 H, H-2, m), 5.50 (1 H, H-3, dd, $J_{3,4}$ 15.5 Hz, $J_{2,3}$ 6 Hz), 5.73 (1 H, H-6, dq, $J_{5,6}$ 15.5 Hz, $J_{6,7}$ 6.5 Hz), 6.00 (1 H, H-5, dd, $J_{4,5}$ 10.5 Hz, $J_{5,6}$ 15.5 Hz), 6.19 (1 H, H-4, dd) p.p.m.

Preparation of (E)-hept-2-enoic acid

Malonic acid (40 g, 384 mmol) was dissolved in dry pyridine (100 cm^3) and cooled to 0°C, prior to the addition of pentanal (33.0 g, 384 mmol). The reaction mixture was allowed to stand at RT for 60 hours and then heated to 90°C for 8 hours. Diethyl ether (200 cm^3) was then added and the solution was washed with 25% HCl (aq.) 2 x 100 cm^3). Evaporation of solvent gave a pale yellow oil which was distilled to give (E)-hept-2-enoic acid (35.1 g, 0.274 mol) b.p. 105-107°C (3 mm), in 71% yield.

^1H n.m.r. (CCl_4): 0.97 (3 H, H-7, t), 1.48 (4 H, H-5 and 2H-6, m), 2.27 (2 H, H-4, dt), 5.82 (1 H, H-2, d, $J_{2,3}$ 15.5 Hz), 7.50 (1 H, H-3, dt, $J_{2,3}$ 15.5 Hz, $J_{3,4}$ 6.5 Hz), 12.49 (CO_2H) p.p.m.

Preparation of α,β-dibromoheptanoic acid

(E)-hept-2-enoic acid (33.0 g, 0.26 mol) was dissolved in CH_2Cl_2 (100 cm^3) and cooled to 0°C during the addition of bromine (42 g, 0.26 mol).

The resulting solution was stirred at RT for 24 hours with exclusion to light, and the solvent was then removed under vacuum to leave a yellow oil which was crystallised from ether-pentane at -20°C to give α,β-dibromoheptanoic acid (72.6 g, 0.25 mol) in 97% yield, m.p. 70-72°C lit. 71.5°C.

^{1}H n.m.r. ($CDCl_3$): 0.96 (3 H, t), 1.45 (2 x 2 H, m), 1.83 (1 H, H-4, m), 2.25 (1 H, H-4, m), 4.40 (2 H, H-2 and H-3, m), 11.75 ($CO_2\underline{H}$) p.p.m.

Preparation of (Z)-1-bromohexene

α,β-dibromoheptanoic acid (48 g, 0.166 mol) was dissolved in acetone (200 cm^3) and stirred during the addition of $NaHCO_3$ (c) (57.5 g, 0.684 mol). The solution was then heated to reflux for 6 hours, filtered and evaporated to leave a brown oil. Distillation gave (Z)-1-bromohexene (10.5 g, 64.3 mmol) b.p. 40-42°C (14 mm), in 39% yield.

^{1}H n.m.r. (CCl_4): 0.93 (3 H, H-6, t), 1.39 (4 H, 2H-4 and 2H-5, m) 2.20 (2 H, H-3, dt), 6.07 (2 H, H-1 and H-2, m) p.p.m.

Preparation of (E,Z)-deca-2,5-dien-4-ol

Magnesium (0.6 g, 24.5 mmol), iodine (20 mg) and (Z)-1-bromohexene (6 drops) were heated in dry THF (10 cm^3) until reaction commenced. A 50% solution of (Z)-1-bromohexene (4.0 g, 24.5 mmol) in dry THF was then added slowly over 20 minutes followed by a 50% solution of (E)-but-2-enal (1.7 g, 24.5 mmol) in dry THF. The reaction mixture was stirred at RT for 8 hours followed by addition of 15% NH_4Cl (aq.) (20 cm^3). The aqueous layer was separated, washed with ether (2 x 20 cm^3) and the combined ethereal extracts were dried ($MgSO_4$). Filtration, concentration and distillation gave (E,Z)-deca-2,5-dien-4-ol (3.1 g, 20.1 mmol), b.p. 130-132°C (2 mm) in 82% yield.

^{1}H n.m.r. (CCl_4): 0.91 (3 H, H-10, t), 1.34 (4 H, m), 1.70 (3 H, H-1, d, J 7.5 Hz), 2.05 (2 H, H-7, m), 3.02 (O-H), 4.74 (1 H, H-4, t, $J_{3,4}$ 7.5 Hz), 5.45 (4 H, m, $J_{2,3}$ 15 Hz, $J_{5,6}$ 10.5 Hz) p.p.m.

Preparation of (E,Z)-4-acetoxydeca-2,5-diene

(E,Z)-deca-2,5-dien-4-ol (0.78 g, 5.1 mmol), acetic anhydride (0.56 g, 5.5 mmol) and dry pyridine (10 cm^3) were stirred at RT for 8 hours. The whole was then poured into water (25 cm^3), acidified with 5 M HCl (aq.), and extracted with ether (2 x 25 cm^3). The combined ethereal extracts were dried ($MgSO_4$), filtered, evaporated and distilled to give (E,Z)-4-acetoxydeca-2,5-diene (0.81 g, 4.2 mmol) b.p. 85-87°C (0.01 mm), in 81% yield.

^{1}H n.m.r. (CCl_4): 0.91 (3 H, H-10, t), 1.36 (4 H, m), 1.71 (3 H, H-1, d, J 6.5 Hz), 1.98 (3 H, s), 2.13 (2 H, H-7 m), 5.30-5.66 (4 H, m, $J_{2,3}$ 15 Hz, $J_{5,6}$ 10.5 Hz), 5.87 (1 H, H-4, t) p.p.m.

I.r. (film): 3025 (m), 2965 (s), 2930 (s), 2860 (m), 1740 (s), 1450 (m), 1365 (m, sh), 1240 (s), 1010 (m, sh), 935 (m, sh) cm^{-1}.

M.s. (EI): m/z 196 (M^+, 1.0%), 136 (13.4%), 107 (20.0%), 79 (59.1%) 43 (100%).

5.2.3 Synthesis of (Z,E)-4-acetoxydeca-2,5-diene

Preparation of methyl (E)-hept-2-enoate

(E)-hept-2-enoic acid (25 g, 0.195 mol) was dissolved in dry methanol and heated to reflux, in the presence of conc. H_2SO_4 (0.2 g) for 8 hours. Neutralisation ($NaHCO_3$), filtration, evaporation and distillation gave methyl (E)-hept-2-enoate (25.5 g, 0.18 mol) b.p. 60-62°C (14 mm) in 92% yield.

^{1}H n.m.r. (CCl_4): 0.92 (3 H, H-7, t), 1.41 (4 H, 2H-5 and 2H-6, m)

2.20 (2 H, H-4, m), 3.64 (3 H, s), 5.72 (H, H-2, d, J 15.5 Hz), 6.86 (1 H, H-3, dt, J 15.5 Hz and 6.5 Hz) p.p.m.

Preparation of (E)-hept-2-en-1-ol

(E)-methyl hept-2-enoate (20 g, 0.14 mol) was dissolved in dry ether (20 cm^3) and added dropwise to a stirred suspension of $LiAlH_4$ (1.5 g, 39 mmol) in dry ether (100 cm^3) at RT. After stirring for 4 hours the reaction mixture was quenched [H_2O (1 cm^3), 15% NaOH (1 cm^3) and water (10 cm^3)] and the precipitate removed by filtration. Concentration and distillation gave (E)-hept-2-enol (10 g, 88 mmol) in 63% yield, containing 10% 1-heptanol.

^1H n.m.r. (CCl_4): 0.95 (3 H, H-7, t), 1.36 (4 H, 2H-5 and 2H-6), 2.03 (2 H, H-4, m), 3.95 (2 H, H-1, d, J 7.5 Hz), 5.56 (2 H, H-2 and H-3, m) p.p.m.

Preparation of (E)-hept-2-en-1-al

(E)-hept-2-en-1-ol (10 g, 88 mmol) was dissolved in dry CH_2Cl_2(200 cm^3) and stirred at RT with pyridinium dichromate (47.0 g, 132 mmol) for 12 hours. The solution was then poured into pentane (200 cm^3) and silica gel was added until the supernatant was yellow. Filtration, concentration and distillation gave (E)-hept-2-enal (3.56 g, 31.7 mmol), b.p. 62-65°C (14 mm), in 36% yield.

^1H n.m.r. (CCl_4): 0.91 (3 H, H-7, t), 1.40 (2 H, H-6, m), 1.50 (2 H, H-5, m), 2.31 (2 H, H-4, m), 6.02 (1 H, H-2, dd, J 15.5 Hz and 9 Hz), 6.74 (1 H, H-3, dt), 9.45 (1 H, H-1, d) p.p.m.

Preparation of (Z,E)-deca-2,5-diene-4-ol

(Z)-1-bromopropene (6 drops), magnesium (0.22 g, 9.1 mmol) and iodine (20 mg) were heated in dry THF (10 cm^3) until reaction was induced.

(Z)-1-bromopropene (1.1 g, 9.1 -mol) in dry THF (5 cm^3) was then added dropwise over 15 minutes, followed by (E)-hept-2-enal (10 g, 8.9 mmol) in THF (5 cm^3). The reaction was stirred for 8 hours at RT. Work-up with 15% NH_4Cl (aq.) and final distillation gave (Z,E)-deca-2,5-dien-4-ol (0.69 g, 4.47 mmol) b.p. 135-137°C (2 mm), in 50% yield.

^1H n.m.r. (CCl_4): 0.90 (3 H, H-10, t), 1.35 (4 H, m), 1.68 (3 H, H-1, d, J 6.5 Hz), 2.02 (2 H, H-7, m), 2.70 (O-H), 4.75 (1 H, H-4, dd), 4.43 (4 H, m, $H_{2,3}$ 10.5 Hz, $J_{5,6}$ 15 Hz) p.p.m.

Preparation of (Z,E)-4-acetoxydeca-2,5-diene

(Z,E)-4-acetoxydeca-2,5-diene was prepared according to the procedure for the (E,Z)-isomer and was isolated in 86% yield, b.p. 85-87°C (0.01 mm).

^1H n.m.r. (CCl_4): 0.90 (3 H, H-10, t), 1.36 (4 H, m), 1.74 (3 H, H-1, d, J 6.5 Hz), 1.98 (3 H, s), 2.05 (2 H, H-7, m), 5.35 (2 H, m), 5.58 (2 H, m), 5.88 (1 H, H-4, t) p.p.m.

I.r. (film): 3025 (m), 2965 (s), 2945 (s), 2860 (m), 1740 (s), 1370 (m), 1250 (s), 960 cm^{-1}.

Preparation of decan-5-ol

Hexanal (1.0 g, 10 mmol) was dissolved in dry ether (15 cm^3) and butyl-lithium (10 mmol, 10 cm^3 1.0 M solution) was added dropwise under nitrogen at 0°C. 15% NH_4Cl (aq.) was added, and the ethereal layer was separated, dried ($MgSO_4$) concentrated and distilled to give decan-5-ol (1.5 g, 9.5 mmol) b.p. 98-100°C (14 mm) in 95% yield.

^1H n.m.r. (CCl_4): 0.90 (2 x 3 H, t), 1.35 (7 x 2 H, m), 2.56 (O-H), 3.47 (1 H, m, -CHOH) p.p.m.

Preparation of (2)- and (5)-acetoxydecanes

Decan-2-ol and decan-5-ol (1.0 g, 3.8 mmol) were reacted with acetic anhydride (0.39 g, 3.8 mmol) in dry pyridine. Work-up was as described for (E,Z)- and (Z,E)-4-acetoxydeca-2,5-dienes.

(i) 2-acetoxydecane, b.p. 102-104°C (0.05 mm)

^{1}H n.m.r. (CCl_4): 0.88 (3 H, t), 1.18 (3 H, d, J 6 Hz), 1.29 (14 H, m), 0.92 (3 H, s), 4.80 (1 H, H-2, m) p.p.m.

(ii) 5-acetoxydecane, b.p. 96-98 (0.05 mm)

^{1}H n.m.r. (CCl_4): 0.90 (2 x 3 H, t), 1.29 (10 H, m), 1.48 (4 H, m), 0.95 (3 H, s), 4.75 (1 H, H-5, m, J 6.1 Hz) p.p.m.

5.2.4 Synthesis of (E,Z,Z)-4-acetoxydeca-2,5,8-triene

Preparation of hexa-1,4-diyne

Magnesium (8.7 g, 358 mmol) and ethyl bromide (6 drops) were heated in dry THF (25 cm^3) until reaction was induced. Ethyl bromide (38.4 g, 352 mmol) in dry THF (40 cm^3) was then added dropwise over 30 minutes, followed by bubbling of a steady stream of propyne into the reaction mixture for 1 hour. Cu(I)Cl (1.0 g) was then added followed by a 50% solution of 3-bromopropyne (21 g, 176.5 mmol) in dry THF. The resulting solution was stirred at RT for 12 hours, followed by addition of 15% NH_4Cl (aq.) (100 cm^3). The whole was extracted with ether (2 x 100 cm^3) and the combined ethereal extracts were dried ($MgSO_4$), filtered and fractionally distilled to give hexa-1,4-diyne (5.3 g, 68 mmol) b.p. 79-81°C in 38% yield.

^{1}H n.m.r. (CCl_4): 1.78 (3 H, H-6, t), 1.95 (1 H, H-1, t, J 2.5 Hz), 3.05 (2 H, H-3, m) p.p.m.

I.r. (film): 3315 (m), 2245 and 2115 (w) cm^{-1}.

Preparation of (E)-dec-2-en-5,8-diyn-4-ol

Ethylmagnesium bromide (15.4 mmol) was generated in dry THF (25 cm^3) from magnesium (0.374 g, 15.4 mmol) and ethyl bromide (1.67 g, 15.4 mmol). A 50% solution of hexa-1,4-diyne (1.2 g, 15.4 mmol) in dry THF was then added slowly over 10 minutes, followed by a 50% solution of (E)-but-2-enal (1.0 g, 15.3 mmol) in dry THF. The reaction mixture was stirred for 8 hours followed by addition of 15% NH_4Cl (aq.) (20 cm^3). The ethereal layer was separated, combined with the ether (2 x 20 cm^3) washings of the aqueous phase, and dried ($MgSO_4$). Filtration, concentration and distillation gave (E)-dec-2-en-5,8-diyn-4-ol (1.34 g, 9.1 mmol) b.p. 96-98°C (0.05 mm) in 59% yield.

^1H n.m.r. (CCl_4): 1.73 (3 H, H-1, d, J 6.6 Hz), 1.76 (3 H, H-10, t, J 2.3 Hz), 3.12 (2 H, H-7, m), 3.78 (O-H), 4.71 (1 H, H-4, m, br), 4.54 (1 H, H-3, dd, $J_{2,3}$ 15.5 Hz), 5.77 (1 H, H-2, m) p.p.m.

Preparation of (E,Z,Z)-deca-2,5,8-trien-4-ol

(E)-dec-2-en-5,8-diyn-4-ol (1.3 g, 8.8 mmol) was dissolved in dry methanol (20 cm^3) with quinoline (0.5 g) and the solution was stirred under hydrogen with Lindlar catalyst (0.5 g). After ∿ 60% uptake more catalyst (0.5 g) was added and the reaction proceeded to completion. The catalyst was removed by filtration through celite and concentration (rotary evaporator) followed by distillation gave (E,Z,Z)-deca-2,5,8-trien-4-ol (0.98 g, 6.5 mmol), b.p. 103-105°C (0.1 mm), in 73% yield.

^1H n.m.r. (CCl_4): 1.59 (3 H, H-1, d, J 6.5 Hz), 1.65 (3 H, H-10, d, J 6.5 Hz), 2.79 (2 H, H-7, t), 4.04 (O-H), 1 H, H-4, t), 5.39 (4 H, m), 5.55 (2 H, H-3 and H-5, m) p.p.m.

Preparation of (E,Z,Z)-4-acetoxydeca-2,5,8-triene

(E,Z,Z)-deca-2,5,8-trien-4-ol (0.4 g, 2.63 mmol), acetic anhydride

(0.4 g, 3.9 mmol) and dry pyridine (5 cm^3) were stirred at RT for 12 hours. Work-up as described for (E,Z)- and (Z,E)-4-acetoxydeca-2,5-dienes gave a yellow oil which was distilled to give (E,Z,Z)-4-acetoxydeca-2,5,8-triene (0.37 g, 1.91 mmol), b.p. 73-75°C (0.05 mm) in 72% yield.

^1H n.m.r. (CCl_4): 1.64 (3 H, H-1, d, J 6.5 Hz), 1.70 (3 H, H-10, d, J 6.5 Hz), 1.96 (3 H, s), 2.86 (2 H, H-7, t), 5.38 (5 H, m, $J_{2,3}$ 15 Hz, $J_{5,6}$ 10.5 Hz, $J_{8,9}$ 10.5 Hz), 5.65 (1 H, m), 5.91 (1 H, H-4, t) p.p.m.

I.r. (film): 3030 (m), 2995 (m), 2935 (m), 1743 (s), 1450 (m), 1370 (s), 1240 (s), 1018 (m), 965 (m), 925 (w), 900 (w) cm^{-1}.

M.s. (EI): m/z 193 (4.0%), 134 (23.5%), 119 (27.6%), 91 (68.2%), 79 (66.1%), 43 (100 %).

5.2.5 Synthesis of (E,E)-6-acetoxydeca-2,4-diene

Preparation of (E,E)-hexa-2,4-dienoic acid chloride

(E,E)-hexa-2,4-dienoic acid (25 g, 0.22 mol) was dissolved in dry diethyl ether (100 cm^3). and heated to reflux with thionyl chloride (30 g, 0.25 mol) for 6 hours. The solvent and excess reagent were evaporated and the residue was distilled to give (E,E)-hexa-2,4-dienoic acid chloride (25.9 g, 0.198 mol) b.p. 78-80°C (14 mm) in 89% yield.

^1H n.m.r. (CCl_4): 1.92 (3 H, H-6, d), 6.00 (1 H, H-2, d, J 15 Hz), 6.25 (1 H, H-4, dd, $J_{3,4}$ 10.5 Hz, $J_{4,5}$ 15 Hz), 6.41 (1 H, H-5, m), 7.43 (1 H, H-3, dd, J 10.5 Hz and 15 Hz) p.p.m.

Preparation of (E,E)-hexa-2,4-dienal

Lithium aluminium hydride (1.45 g, 38.3 mmol) was stirred in dry ether (50 cm^3), at 0°C, during the addition of t-butanol (8.5 g, 115 mmol). The lithium tri-^{t}butoxylaluminium hydride in ether was then added dropwise to a solution of (E,E)-hexa-2,4-dienoic acid chloride

(5.0 g, 38.3 mmol) in dry ether (20 cm^3) at -78°C. After stirring for 1 hour the solution was warmed to RT, water (2 cm^3), 15% NaOH (aq.) (2 cm^3) and more water (5 cm^3) was added, and the resulting precipitate was removed by filtration. Concentration and distillation gave (E,E)-hexa-2,4-dienal (2.2 g, 22.9 mmol), b.p. 70-72°C (14 mm) in 60% yield.

^{1}H n.m.r. (CCl_4): 1.94 (3 H, H-6, d), 6.01 (1 H, H-2, dd, J 7 Hz and $J_{2,3}$ 15 Hz), 6.31 (2 H, H-4 and H-5, m), 7.04 (1 H, H-3, dd, $J_{3,4}$ 10.5 Hz, $J_{2,3}$ 15 Hz), 9.45 (1 H, H-1, d, J 7 Hz) p.p.m.

Preparation of (E,E)-deca-2,4-dien-6-ol

Magnesium (0.25 g, 10.4 mmol), iodine (20 g) and 1-bromobutane (6 drops) were warmed in dry ether (10 cm^3) until reaction was induced. 1-Bromobutane (1.4 g, 10.4 mmol) in dry ether (5 cm^3) was then added dropwise over 15 minutes, followed by a 50% solution of (E,E)-hexa-2,4-dienal (10 g, 10.4 mmol) in dry ether. After stirring for 4 hours at RT, 15% NH_4Cl (sq.) 10 cm^3 was added. The ethereal layer was separated, dried ($MgSO_4$), concentrated and distilled to give (E,E)-deca-2,4-dien-6-ol (1.47 g, 9.6 mmol), b.p. 105-107°C, in 92% yield.

^{1}H n.m.r. (CCl_4): 0.90 (3 H, H-10, t), 1.30 (4 H, m), 1.54 (2 H, H-7, m), 1.75 (3 H, H-1, d), 3.55 (O-H), 4.11 (1 H, H-6, m), 5.54 (H-5, dd, $J_{4,5}$ 15 Hz), 5.70 (1 H, H-2, m), 6.03 (1 H, H-3, dd, $J_{2,3}$ 15 Hz), 6.19 (1 H, H-4, dd) p.p.m.

Preparation of (E,E)-6-acetoxydeca-2,4-diene

(E,E)-deca-2,4-dien-6-ol (1.0 g, 6.5 mmol), acetic anhydride (0.7 g, 6.9 mmol) and dry pyridine (5 cm^3) were stirred at RT for 8 hours. Work-up, as described for (E,Z)-4-acetoxy-2,5-decadiene

yield a yellow oil which was distilled to give (E,E)-6-acetoxy-deca-2,4-diene (1.13 g, 5.84 mmol), b.p. 76-78°C (0.05 mm), in 90% yield.

^{1}H n.m.r. (CCl_4): 0.90 (3 H, t), 1.32 (4 H, m), 1.61 (2 H, m), 1.76 (3 H, H-1, d), 2.05 (3 H, s), 5.26 (1 H, H-6, m), 5.47 (1 H, H-5, dd), 5.75 (1 H, H-2, m), 6.03 (1 H, H-3, dd, $J_{2,3}$ 15 Hz) p.p.m.

5.3 Pd(0) AND Pd(II)-CATALYSED REARRANGEMENTS OF ACETOXYDIENES AND DIENOLS

5.3.1 4-Acetoxyhepta-2,5-dienes with Pd(0) and Pd(II)

(i) (E,E)-, (E,Z)- and (Z,Z)-4-acetoxyhepta-2,5-dienes (30 mg, 0.195 mmol) were dissolved in d.^{6}benzene with Pd(0) $[P(Ph)_3]_4$ (15.5 mg, 9.75 μmol, 5 mol %). ^{1}H n.m.r. spectroscopy indicated immediate and complete conversion within seconds to (E,E)-2-acetoxyhepta-3,5-diene.

Preparative procedure

(E,Z)-4-acetoxyhepta-2,5-diene (0.3 g, 1.95 mmol) was dissolved in dry benzene (2 cm^3) with 5 mol % $[P(Ph)_3]_4Pd(0)$ (155 mg, 97.5 μmol). The solvent was removed in vacuum and the residue distilled to give (E,E)-2-acetoxyhepta-3,5-diene (275 mg, 1.79 mmol), b.p. 85-87°C (2 mm), in 92% yield.

^{1}H n.m.r. (CCl_4): 1.28 (3 H, H-1, d, J 6 Hz), 1.75 (3 H, H-7, d, J 6.5 Hz), 1.97 (3 H, s), 5.28 (1 H, H-2, m, $J_{1,2}$ 6 Hz, $J_{2,3}$ 6 Hz), 5.34 (1 H, H-3, dd, $J_{3,4}$ 15.5 Hz), 5.70 (1 H, H-6, m), 5.93 (1 H, H-5, dd, $J_{4,5}$ 10.5 Hz, $J_{5,6}$ 15.5 Hz), 6.10 (1 H, H-4, dd) p.p.m.

I.r. (thin film): 3015 (m), 2970 (s), 2917 (m), 2855 (w), 1735 (s), 1660 (m), 1444 (m), 1370 (s), 1240 (s), 1141 (m), 1040 (s), 986 (s), 944 (m) cm^{-1}.

U/V: $\lambda_{max}^{n\text{-hexane}}$ 227 nm

ϵ 27800

M.s. (EI): m/z 154 (M^+ 5.5%), 112 (14.1%), 95 (85.0%), 79 (48.5%), 43 (100%).

(ii) (E,E)-, (E,Z)- and (Z,Z)-4-acetoxyhepta-2,5-dienes (30 mg, 0.195 mmol) was dissolved in d.^{6}benzene (0.5 cm^3) with Pd(II)b (3.7 mg, 9.74 µmol, 5 mol %) and monitored by ^{1}H n.m.r. After 10 minutes (E,E)-4-acetoxyhepta-2,5-diene was converted completely to (E,E)-2-acetoxyhepta-3,5-diene (spectroscopically identical with product from the Rh(I) isomerisation). (Z,Z)-4-acetoxyhepta-2,5-diene was converted to (E,Z)-2-acetoxyhepta-3,5-diene after 1.5 hours. (E,Z)-4-acetoxyhepta-2,5-diene however was converted to a mixture containing 80% (E,Z)-2-acetoxyhepta-3,5-diene after 20 minutes.

Preparative procedure

(E,Z)-4-acetoxyhepta-2,5-diene (0.5 g, 3.25 mmol) and Pd(II) a (42 mg, 0.16 mmol) were stirred in dry THF (10 cm^3) for 5 minutes. Solvent was removed in vacuum and the residue distilled to give 85% (E,Z)-2-acetoxy-3,5-heptadiene (0.46 g, 3.0 mmol), b.p. (2 mm) 84-86°C, in 92% yield. A pure sample of the (E,Z)-isomer was obtained by stirring the 85% mixture with an excess of maleic anhydride in dry ether for 1 week, the (E,E)-isomer being removed as the cyclo-addition product.

^{1}H n.m.r. (CCl_4): 1.30 (3 H, H-1, d, J 6 Hz), 1.76 (3 H, H-7, d, J 6.5 Hz), 1.98 (3 H, s), 5.33 (1 H, H-2, m), 5.49 (1 H, H-3, dd, $J_{3,4}$ 15.5 Hz), 5.58 (1 H, H-6, m), 5.90 (1 H, H-5, dd, $J_{5,6}$ 11 Hz, $J_{4,5}$ 10.5 Hz), 6.45 (1 H, H-4, dd, J 15.5 Hz and 10.5 Hz) p.p.m.

I.r. (film): 3015 (m), 2970 (s), 2915 (m), 1730 (s), 1438 (m),

1365 (s), 1225 (s), 1123 (m), 1030 (s), 975 (m), 940 (m), 845 (w), 710 (m, sh) cm^{-1}.

U/V $\lambda_{max}^{n\text{-hexane}}$ 228 nm

ϵ 23300

M.s. (EI): m/z 154 (M^+ 16.3%), 112 (24.0%), 95 (39.2%), 79 (100%), 43 (83.5%).

5.3.2 3-Acetoxyhexa-1,4-dienes with Pd(O) and Pd(II) Complexes

(i) (E)-3-acetoxyhexa-1,4-diene

(0.4 g, 2.86 mmol) and $[P(Ph)_3]_4Pd(0)$ (165 mg, 0.14 mmol), 5 mol %) was dissolved in dry benzene (5 cm^3) and stirred for 15 minutes. Evaporation of solvent and distillation gave (E,E)-1-acetoxyhexa-2,4-diene (372 mg, 2.66 mmol), b.p. 81-83°C (17 mm), in 93% yield, containing 10% (E)-2-acetoxyhexa-3,5-diene.

^1H n.m.r. (CCl_4): 1.78 (3 H, H-6, d, J 6.6 Hz), 2.00 (3 H, s), 4.49 (2 H, H-1, d, J 6.6 Hz), 5.54 (1 H, H-2, dd, J 6.6 Hz and $J_{2,3}$ 15 Hz), 5.70 (1 H, H-5, m), 5.99 (1 H, H-4, dd, $J_{3,4}$ 10.5 Hz, $J_{4,5}$ 15 Hz), 6.18 (1 H, H-3, dd, J 10.5 Hz and J 15 Hz) p.p.m.

I.r. (film): 3050 (s), 2952 (s), 2900 (m), 1740 (s), 1663 (m), 1450 (s), 1390 (s), 1238 (s), 1025 (s), 996 (s), 920 (m) cm^{-1}.

U/V $\lambda_{max}^{n\text{-hexane}}$ 227 nm

ϵ 31000

M.s. (EI): m/z 140 (M^+ 14.4%), 98 (9.0%), 79 (37%), 43 (60%), 28 (100%).

(ii) (Z)-3-acetoxyhexa-1,4-diene

(40 mg, 0.286 mmol) and 5 mol % $[P(Ph)_3]_4Pd(0)$ were dissolved in

d.^{6}benzene. The ^{1}H n.m.r. spectrum indicated immediate conversion into a mixture containing 80% (E,E)-1-acetoxyhexa-2,4-diene and 20% (E)-2-acetoxyhexa-3,5-diene.

(iii) (E)-3-acetoxyhexa-1,4-diene

(0.4 g, 2.86 mmol) and Pd(II)a (37 mg, 0.143 mmol) were dissolved in dry THF (5 cm^3) and stirred for 10 minutes. Removal of solvent under vacuum and distillation gave exclusively (E)-2-acetoxyhexa-3,5-diene (360 mg, 2.6 mmol), b.p. 36-38°C (4 mm) in 90% yield.

^{1}H n.m.r. (CCl_4): 1.30 (3 H, H-1, d, J 6.5 Hz), 1.98 (3 H, s), 5.08 (1 H, H-6, d, J *cis* 10.5 Hz), 5.20 (1 H, H-6, J *trans* 17 Hz), 5.30 (1 H, H-2, m), 5.61 (1 H, H-3, dd, $J_{2,3}$ 6.5 Hz, $J_{3,4}$ 15 Hz), 6.21 (2 H, H-4, dd and H-5, m) p.p.m.

I.r. (film): 3190 (w, sh), 2995 (s), 2948 (m), 1735 (s), 1605 (m, sh), 1443 (m), 1365 (s), 1230 (s), 1137 (s, sh), 1030 (s), 995 (s), 943 (s), 900 (s), 845 (m) cm^{-1}.

U/V $\lambda_{max}^{n\text{-hexane}}$ 221 nm

ε 26000

M.s. (EI): m/z 140 (M^+ 12.5%), 98 (15.4%), 79 (54.8%), 43 (100%).

(iv) (Z)-3-acetoxyhexa-1,4-diene

(25 mg, 0.178 mmol) was dissolved in d.^{6}benzene with 5 mol % Pd(II)b (5 mg, 13 μmol) and the reaction monitored by ^{1}H n.m.r. spectroscopy. After 48 hours at RT the starting material was totally converted into a mixture containing (E)-2-acetoxyhexa-3,5-diene (∿ 60%), (E,E)-1-acetoxyhexa-2,4-diene (30%) and (E,Z)-1-acetoxyhexa-2,4-diene (10%). The (E,Z)-isomer was identified by the resonance of H-3 at δ 6.50.

5.3.3 4-Acetoxydeca-2,5-dienes

(i) (E,Z)-4-acetoxydeca-2,5-diene

(0.5 g, 2.55 mmol) and 5 mol % Pd(II)a (33 mg, 0.13 mmol) were dissolved in dry THF (5 cm^3). After 10 minutes stirring at RT the solution was poured into pentane, filtered, evaporated and distilled to give ∿ 85% (E,Z)-2-acetoxydeca-3,5-diene (0.46 g, 2.35 mmol), b.p. 102-104°C (0.01 mm) plus ∿ 20% other isomers, in 92% yield.

^{1}H n.m.r. (CCl_4): 0.92 (3 H, H-10, t), 1.30 (3 H, H-1, d, J 6 Hz), 1.36 (4 H, m), 1.97 (3 H, s), 2.19 (2 H, H-7, m) 5.33 (1 H, H-2, m), 5.40 (1 H, H-6, m), 5.53 (1 H, H-3, dd, $J_{3,4}$ 15 Hz, $J_{2,3}$ 6.5 Hz), 5.86 (1 H, H-5, dd, $J_{4,5}$ 10.5 Hz, $J_{5,6}$ 11 Hz), 6.43 (1 H, H-4, dd, J 10.5 Hz and 15 Hz) p.p.m.

I.r. (film): 3020 (w), 2965 (s), 2930 (s), 2865 (m), 1735 (s), 1650 (w), 1448 (m), 1368 (s, sh), 1235 (s), 1123 (m), 1025 (s), 980 (m, sh), 945 (m, sh) cm^{-1}.

U/V $\lambda_{max}^{n\text{-hexane}}$ 228.5 nm

ε 25000

M.s. (EI): m/z 196 (M^+ 37.7%), 153 (28.3%), 136 (32.4%), 107 (34.7%), 93 (80.0%), 79 (98.6%), 43 (100%).

Hydrogenation (H_2/PtO_2/THF) and subsequent g.l.c. analysis (20% DEGS chromosorb WHP 100-120, 160°C) indicated 2-acetoxydecane (95%) and 5-acetoxydecane (5%) as the only products. These compounds co-chromatographed with authentic samples.

(ii) (E,Z)-4-acetoxydeca-2,5-diene

(100 mg, 0.51 mmol) and $[P(Ph)_3]_4Pd(0)$ (30 mg, 25.5 μmol, 5 mol %) were dissolved in d.^{6}benzene. ^{1}H n.m.r. spectroscopy indicated complete reaction in minutes to a mixture of (E,E)-2-acetoxydeca-3,5-diene

(80%) and (E,E)-5-acetoxydeca-2,4-diene (20%), the ratio being estimated from the methyl resonances at δ 1.28 and δ 1.73 respectively. Hydrogenation (H_2/PtO_2/THF) and subsequent g.l.c. analysis confirmed the ratio of 2-acetoxy: 5-acetoxy as 60:40 (20% DEGS chromosorb WHP 100-120, 160°C).

(iii) (Z,E)-4-acetoxydeca-2,5-diene

(0.5 g, 2.55 mmol) and Pd(II)a (33 mg, 127 μmol, 5 mol%) were dissolved in dry THF (5 cm^3). After stirring for 10 minutes, pentane was added and the solution was filtered, evaporated and distilled to give (Z,E)-6-acetoxydeca-2,4-diene (0.455 g, 2.32 mmol), b.p. 115-118°C (0.01 mm), plus 15% (E,E)-isomers, in 91% yield. Hydrogenation (H_2/PtO_2/THF) and subsequent analysis by g.l.c. indicated a ratio of 80:20 for 5-acetoxydecane: 2-acetoxydecane.

^1H n.m.r. (CCl_4): 0.91 (3 H, H-10, t), 1.30 (4 H, m), 1.59 (2 H, H-7, m), 1.67 (3 H, H-1, d, J 6.6 Hz), 1.97 (3 H, s), 5.20 (1 H, H-6, m), 5.46 (2 H, H-2 and H-5, m), 5.89 (1 H, H-3, dd, $J_{3,4}$ 10.5 Hz, $J_{2,3}$ 11 Hz), 6.45 (1 H, H-4, dd, $J_{4,5}$ 15 Hz) p.p.m.

I.r. (film): 3030 (w), 2970 (s), 2945 (s), 2865 (m), 1740 (s), 1454 (w), 1370 (m), 1240 (s), 1014 (m), 980 (w), 940 (w) cm^{-1}.

U/V $\lambda_{max}^{n\text{-hexane}}$ 230.5 nm

ε 20800

(iv) (E,E)-6-acetoxydeca-2,4-diene

(E,E)-6-acetoxydeca-2,4-diene (100 mg, 0.51 mmol) and Pd(II)b (9.6 mg, 26 μmol) were dissolved in d.^{6}benzene and monitored by ^1H n.m.r. No reaction was observed at RT, but on heating to 80°C a smooth transformation was observed. The solution was poured into pentane (1 cm^3), filtered and distilled to give

(E,E,E)-deca-2,4,6-triene (89 mg, 0.45 mmol), b.p. 80-82°C (14 mm) in 89% yield.

^{1}H n.m.r. (d.^{6}benzene): 0.89 (3 H, H-10, t), 1.35 (2 H, H-9, m), 1.66 (2 H, H-1, d, J 6.6 Hz), 2.03 (2 H, H-8, q), 5.60 (2 H, H-2 and H-7, m), 6.16 (4 H, m) p.p.m.

I.r. (film): 3015 (m), 2960 (s), 2930 (s), 2875 (m), 1639 (w), 1449 (m), 1375 (m), 1237 (s), 994 (s) cm^{-1}.

5.3.4 (E,Z,Z)-4-acetoxydeca-2,5,8-triene

(i) (E,Z,Z)-4-acetoxydeca-2,5,8-triene (0.3 g, 1.55 mmol) and Pd(II)a (20 mg, 7.7 μmol, 5 mol %) were dissolved in dry THF (5 cm^3). After 10 minutes pentane (2 cm^3) was added, the solution was filtered and distilled to give (E,Z,Z)-2-acetoxydeca-3,5,8-triene (279 mg, 1.44 mmol), b.p. 96-98°C (0.05 mm), in 93% yield, with apparently only 5% other isomers.

^{1}H n.m.r. (CCl_4): 1.32 (3 H, H-1, d, J 6.6 Hz), 1.66 (3 H, H-10, d, J 6.6 Hz), 5.45 (3 H, H-2, H-8 and H-9, m), 5.59 (1 H, H-5, dd, $J_{4,5}$ 10.5 Hz, $J_{5,6}$ 11 Hz), 6.47 (1 H, H-4, dd, $J_{3,4}$ 15 Hz) p.p.m.

I.r. (film): 3050 (s, sh), 3000 (s, sh), 2948 (s, sh), 1743 (s), 1450 (m), 1375 (s, sh), 1240 (s), 1138 (m), 1040 (s, sh), 982 (m), 948 (s) cm^{-1}.

U/V $\lambda_{max}^{n\text{-hexane}}$ 235 nm

ϵ 19400

M.s. (EI): m/z 194 (M^+, 3.2%), 7.9 (52.5%), 43 (100%).

Sample pyrollised.

(ii) (E,Z,Z)-4-acetoxydeca-2,5,8-triene (30 mg, 0.155 mmol), was treated with 5 mol % $[P(Ph)_3]_4Pd(0)$ (9 mg, 7.7 μmol) in

d.^{6}benzene. ^{1}H n.m.r. indicated immediate conversion to a mixture containing > 80% (E,E,Z)-2-acetoxydeca-3,5,8-triene, as judged by ^{1}H n.m.r.

^{1}H n.m.r. (d.^{6}benzene): 1.32 (3 H, H-1,d, J 6.8 Hz), 1.165 (3 H, H-10, d, J 6.8 Hz), 5.90 (1 H, H-5, dd, $J_{4,5}$ 10.5 Hz, $J_{5,6}$ 15.5 Hz), 6.20 (1 H, H-4, dd, $J_{3,4}$ 15 Hz) p.p.m.

5.3.5 (E,E)-, (E,Z)- and (Z,Z)-hepta-2,5-dien-4-ols

(i) (E,Z)- and (Z,Z)-hepta-2,5-dien-4-ols did not react with 5 mol % $[P(Ph)_3]_4Pd(0)$ when heated at 80°C for 24 hours. However, the (E,E)-isomer reacted within 10 hours, at 80°C to give hepta-1,3,5-triene.

^{1}H n.m.r. (d.^{6}benzene): 1.57 (3 H, H-7, d), 4.98 (1 H, H-1 *cis*, d, J 10.5 Hz), 5.12 (1 H, H-1 *trans*, d, J 15 Hz), 5.53 (1 H, m), 6.10 (3 H, m), 6.32 (1 H, m) p.p.m.

(ii) (E,E)-hepta-3,5-dien-2-ol

(30 mg, 0.267 mmol) was dissolved in d.^{6}benzene and heated to 80°C with Pd(II)b (5 mol %, 5 mg, 13.3 μmol). After 10 minutes ^{1}H n.m.r. spectroscopy indicated complete reaction. Distillation gave di-(E,E)-1-methyl-hexa-2,4-dienyl ether (26.2 mg, 0.127 mmol), b.p. 70-75°C (0.003 mm) in 95% yield.

^{1}H n.m.r.: 1.25 (2 x 3 H, H-1, dd), 1.57 (2 x 3 H, H-7, m), 4.00 (2 H, H-2, m), 5.50 (4 H, 2H-3 and 2H-6, m), 6.03 (4 H, 2H-4 and 2H-5, m) p.p.m.

I.r. (CCl_4): 3020 (m), 2980 (m), 2924 (m), 1625 (w), 1444 (m), 1365 (m), 1130 (m), 1064 (m), 980 (s) 735 (s) cm^{-1}.

M.s. (EI): m/z 206 (M^+ 12.2%).

5.4 ATTEMPTED PREPARATION OF (Z,Z,E)-12-HYDROXYHEPTADECA-5,8,10-TRIENOIC ACID

5.4.1 Preparation of 1-(pent-4-ynyl)-4-methyl-2,6,7-trioxabicyclo-[2.2.0]octane

Lithium acetylide:ethylene diamine complex (4.0 g, 43.5 mmol) was stirred in dry DMSO (12 cm^3) at 48°C during the dropwise addition of a 50% solution of 1-chloropropyl-4-methyl-2,6,7-trioxabicyclo[2.2.0]-octane (9.0 g, 43.5 mmol). The reaction mixture was stirred for 3 hours at 48°C and then quenched with H_2O. The whole was extracted with pentane (3 x 100 cm^3), the extracts dried ($MgSO_4$), filtered and evaporated to leave a yellow oil. Distillation gave 1-(pent-4-ynyl)-4-methyl-2,6,7-trioxabicyclo[2.2.0]octane (3.1 g, 15.8 mmol) as a colourless oil which crystallised on standing, in 36% yield, b.p. (0.001 mm) 105-111°C, m.p. 44-46°C.

^1H n.m.r. (CCl_4): 0.78 (3 H, H-4, s), 1.64 (4 H, m), 1.75 (1 H, H-1, t, J 2.2 Hz), 2.12 (2 H, m), 3.78 (6 H, s) p.p.m.

I.r. (film): 3255 (s), 2105 (w) cm^{-1}.

M.s. (EI): m/z 196.5 (M^+ 3.4 %), 95 (100%).

5.4.2 Preparation of hex-5-ynoic acid

1-(pent-4-ynyl)-4-methyl-2,6,7-trioxabicyclo[2.2.0]octane (2.0 g, 10 mmol) was dissolved in dichloromethane (10 cm^3) and stirred with 1 M HCl (aq.) (15 cm^3) for 30 minutes. The aqueous phase was separated, washed with CH_2Cl_2 and the combined organic phases stirred with 2 M KOH (aq.) (20 cm^3) for 2 hours. The aqueous phase was then acidified with 1 M HCl, extracted with CH_2Cl_2 (2 x 20 cm^3) and dried ($MgSO_4$). Filtration, concentration and distillation gave

hex-5-ynoic acid (0.9 g, 8 mmol), b.p. (9 mm) 104-106°C, in 80% yield.
^{1}H n.m.r. (CCl_4): 1.86 (2 H, H-3, m), 2.28 (2 H, H-4, m), 2.49 (2 H, H-2, t), 4.07 (1 H, H-6, t), 11.27 (1 H, O-H, s) p.p.m.
I.r. (film): 3285 (m), 2115 (w), 1705 (s) cm^{-1}.

5.4.3 Preparation of (E,Z,Z)-2-hydroxydeca-3,5,8-triene

The silica gel column was prepared as described in ref. 29. (E,Z,Z)-4-hydroxydeca-2,5,8-triene was applied to the column, eluted with distilled CH_2Cl_2, and the fractions identified by microscope slide t.l.c. Evaporation of solvent gave a quantitative yield of (E,Z,Z)-2-hydroxydeca-3,5,8-triene.
^{1}H n.m.r. (CCl_4): 1.20 (3 H, H-1, d), 1.68 (3 H, H-10, d), 2.93 (2 H, H-7, t), 3.70 (1 H, H-2, m), 5.45 (4 H, m), 5.96 (1 H, H-5, t, J 10.5 Hz), 6.40 (1 H, H-4, dd, $J_{4,5}$ 10.5 Hz, $J_{3,4}$ 15.0 Hz) p.p.m.

5.4.4 Isomerisation of (E)- and (Z)-3-hydroxyhexa-1,4-diene

(E)- and (Z)-3-hydroxyhexa-1,4-diene (50 mg, 0.5 mmol) were dissolved in 60% aqueous acetone/HCl (0.05 M eq.) for 30 minutes. Evaporation of the acetone, extraction with ether (25 cm^3) neutralisation, drying ($MgSO_4$) filtration and distillation gave 85% (E)-2-hydroxyhexa-3,5-diene with 15% (E,E)-hexa-2,4-dienol.
^{1}H n.m.r. (CCl_4): 1.21 (3 H, H-1, d), 3.36 (1 H, O-H), 4.22 (1 H, H-2, m), 5.02 (1 H, H-6, d, J 12.5 Hz), 5.13 (1 H, H-6, d, J 17 Hz), 5.66 (1 H, H-3, dd), 6.10 (1 H, H-4, dd), 6.25 (1 H, H-4, m) p.p.m.

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