APPLICATIONS OF GROUP VIII METALS TO ORGANIC SYNTHESIS

A Thesis Presented By

Andrew David White

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Whiffen Laboratory,
Department of Chemistry,
Imperial College,
London. SW7 2AY

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Abstract

This thesis is divided into three chapters on Iron, Ruthenium, and Osmium. A review on the applications of organo-iron compounds in stoichiometric organic synthesis is presented together with a review of ruthenium oxidative mechanisms and recent oxidative applications of ruthenium complexes.

The osmium oxo imido complex $OsO_3(NOct^t)$ and its adduct complexes with diazabicyclo[2.2.2]octane, quinuclidine and 1,3,5,7-tetra-azatricyclo[3.3.1.1.^{3,7}] decane were prepared. An X-ray structure was obtained for $[OsO_3(NOct^t)]_2$.dabo. The reactions of these complexes with alkenes was investigated . The intermediate osmium oxo imido esters were isolated and characterised. A Raman and infra-red study was performed on the ^{15}N labelled $OsO_3(^{15}NOct^t)$. The tetraoxoosmate(VII) compound $(PhP_4)[OsO_4]$ was used as a stoichiometric homogeneous oxidant in dichloromethane. The compound oxidises benzylic and allylic alcohols to the aldehyde or ketone selectively.

A mild and versatile catalytic system has been developed for the high yield oxidation of alcohols to aldehydes and ketones using the new tetra-*n*-propyl and tetra-*n*-butylammonium perruthenates $(R_4N)[RuO_4]$ with N-methylmorpholine as co-oxidant. The procedure compares favourably with those published in the literature. The system tolerates a wide range of labile functional groups, and α-chiral centres are not racemised during oxidation. The reactions proceed rapidly at room temperature in dichloromethane, using 0.5 mol% of catalyst. The addition of 4Å sieves improved the procedure.

The synthesis of a major fragment of the ionophore antibiotic CP-61,405 is described in 13 steps from [2S]methyl-3-hydroxy-2-methylpropionate. The key methodology involved construction of a ferrilactone unit from a methylene epoxide. Subsequent controlled high pressure carbonylation to yield a β,γ-unsaturated δ-lactone and directed hydrogenation ensure the correct stereochemistry. Further modification affords the fragment [2RS,5R,6S](*t*-butyldiphenylsilyl oxy-2'S-propan-2-yl)5-

methyl-2-phenylsulphonyltetrahydro-2H-pyran. Similar methodology was applied to synthetic efforts towards *erythro*-6-acetoxyhexadeconolide, the major component of the mosquito (*culex pipiens fatigans*) ovi-position attractant pheromone, and a useful δ-lactone for the anti-parasitic avermectin natural products. The η^4-trimethylenemethane irontricarbonyl molecule was prepared in excellent yield from 3-chloro-2-chloromethyl prop-1-ene and diiron nonacarbonyl under ultrasonic conditions.

Contents

Acknowledgements

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Finally I would like to thank my parents for their loyal support and my wife Jenny whose trust, understanding and love was incalculable.

To Jennifer

and my Parents

Abbreviations

Ac	acetyl
bpy	2,2'-bipyridyl
CAN	ceric ammonium nitrate
COSY	correlation spectroscopy
m-CPBA	*meta*-chloroperbenzoic acid
Cp	cyclopentadienyl
dabo	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL-H	diisobutyl aluminium hydride
DMAP	4-(dimethylamino)pyridine
DMSO	dimethylsulphoxide
ESCA	electron scatterring for chemical analysis
Fp	cyclopentadienylirondicarbonyl
HMDS	hexamethyldisilazane
IR	infra-red
KHMDS	potassium hexamethyldisilazane
LDA	lithium diisopropyl amide
Ms	methanesulphonyl (mesyl)
nmr	nuclear magnetic resonance
nOe	nuclear Overhauser effect
qncd	quinuclidine
SEM	2-(trimethylsilyl)ethoxymethyl
tatd	1,3,5,7-tetra-azatricyclo[3.3.1.1^{3,7}]decane
TBAP	tetra-n-butylammonium tetraoxoruthenate(VII)
THF	tetrahydrofuran
TPAP	tetra-n-propylammonium tetraoxoruthenate(VII)
trpy	2,2',2"-terpyridine

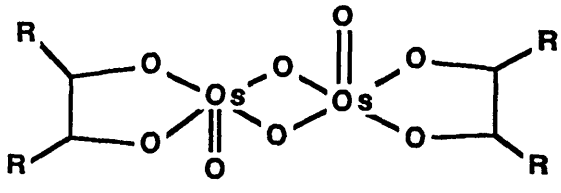
Chapter 1. Osmium

1.1 Introduction

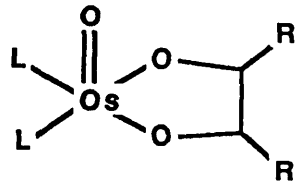
The work presented in section 1.1 considers the known reactions of the tetrahedral oxoimido system $Os^{VIII}O_3(NR)$ with alkenes and the chemistry of the di, tri, and tetra substituted imido species is mentioned. Since it seems likely that the processes involved are analogous to those involved in the OsO_4 - alkene reaction, this account is prefaced by an introduction to the OsO_4 reaction with alkenes.

1.1a Chemistry of Osmium Tetroxide

The most important reaction with OsO_4 is the stereospecific *cis* hydroxylation of alkenes. This has been used extensively in organic synthetic chemistry.[1] The reaction probably occurs *via* formation of osmium (VI) ester complexes of structure (1) or (2) (where L = tertiary amine).

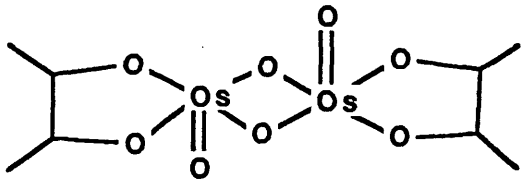


(1)



(2)

These osmium (VI) esters have been conclusively proven by X-Ray crystal structures of (3), the tetramethylethylene complex[2] and (4), where L = quinuclidine.[3] In solution the dimeric complex (4) dissociates to the monomeric trigonal dipyramidal complex (5).



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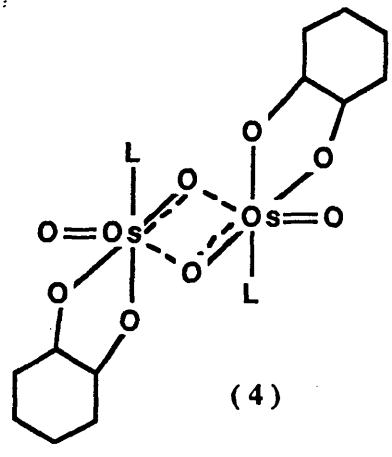

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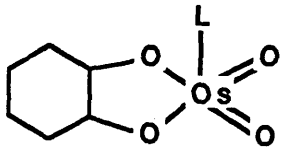
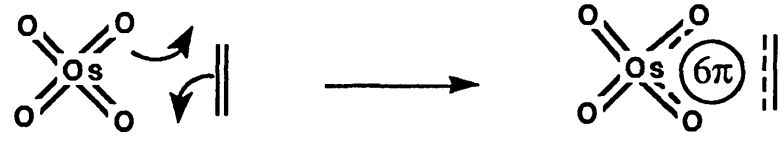
(5) 

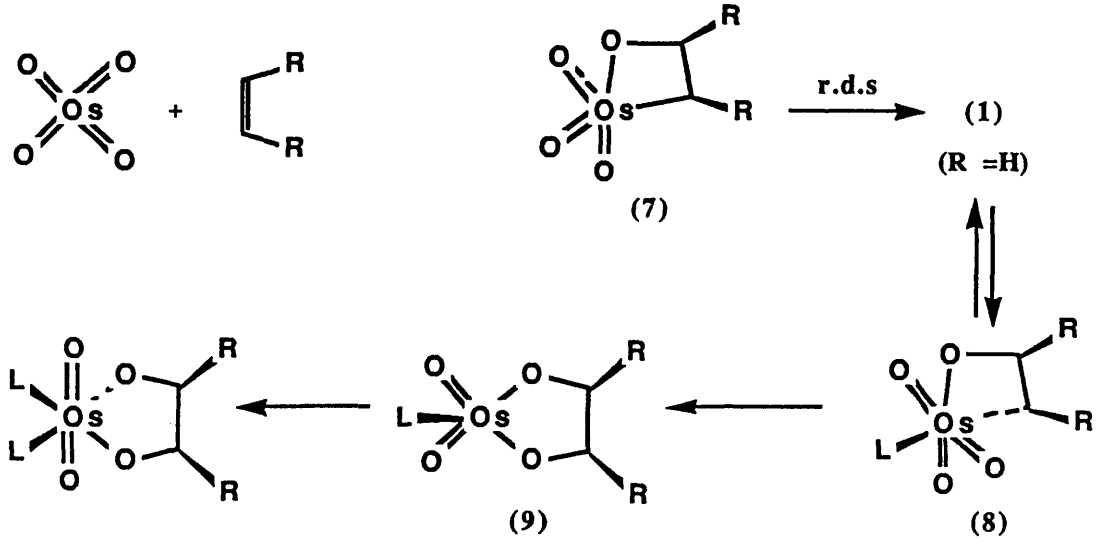
These intermediates all comply with Criegee's original [4 + 2] cycloaddition mechanism. It was assumed that the reaction proceeds *via* a concerted 6π electron cyclisation. The symmetric 5-membered ring transition state (6) in scheme 1, explains the stereoselective *cis* addition.



(6)

Scheme 1

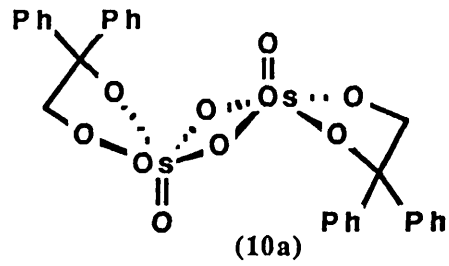
However this mechanism involves direct nucleophilic attack of carbon on oxygen and an alternative mechanism has been proposed. Sharpless[5,10] has invoked the formation of an asymmetric oxametallacyclobutane (7), since this involves a strained angle at the metal centre, the intermediate (7) then rearranges and dimerises to yield (1) (scheme 2).



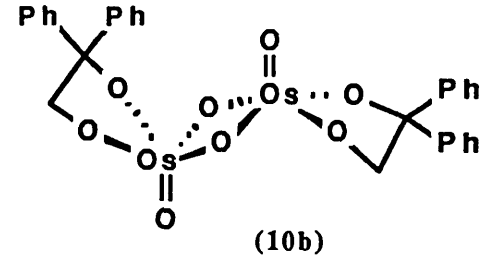
Scheme 2

This mechanism is consistent with kinetic data which suggests a two step process for the formation of the osmium(VI) ester[6] and with the observation that nucleophiles attack OsO_4 at the metal centre exclusively and not on oxygen.[7,11] Also the dramatic increase in reaction rate on addition of tertiary amines L can be explained. Coordination of pyridine for example to (7) produces an octahedral complex (8) and triggers reductive insertion of the Os-C bond into an oxo group yielding (9).

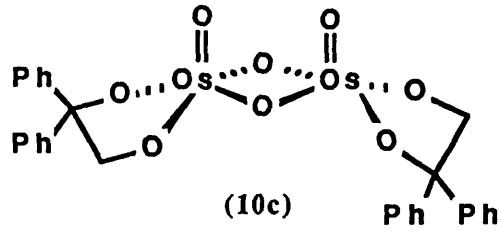
Spectroscopic evidence was put forward for the presence of the oxametallacyclobutane intermediates in the reaction between OsO_4 and 1,1-diphenylethylene.[8] However the nmr spectra were reassigned by Casey.[9] Isomers of the dimeric osmium(VI) (10a-d) complexes provide a better fit for the data.



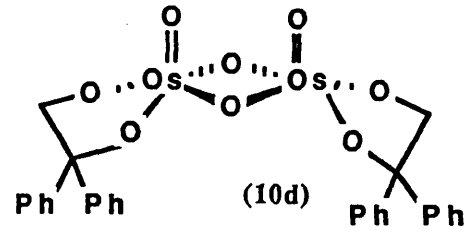
(10a)



(10b)

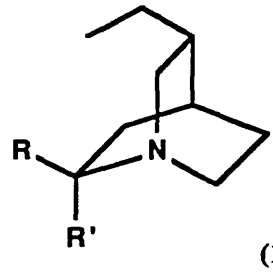


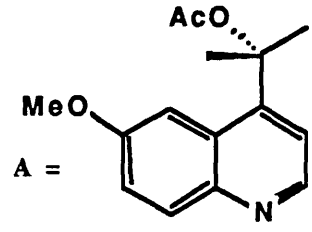
(10c)



(10d)

Sharpless has utilized the stereoselectivity of the reaction with alkenes to induce chirality in the vicinal diol, with optical yields of up to 83%. A stoichiometric equivalent of a chiral pyridine ligand (11a) (11b), which is coordinated to osmium through a quinuclidine nitrogen is stirred with OsO_4 and the alkene in toluene.[10]





(11a, R = H, R' = A)

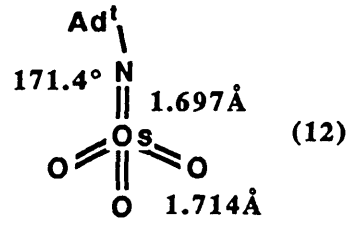
(11b, R = A, R' = H)

Several tertiary amide complexes of OsO_4 have been isolated. Thus OsO_4 reacts with a ligand L to yield $L.2OsO_4$ (L = 1,3,5,7-tetra-azatricyclo[3.3.1.$1^{3,7}$]decane, 1,4-diazabicyclo[2.2.2]octane, pyrazine and 5-methylpyridine) and $L.OsO_4$ (L = quinuclidine, isoquinoline, phthalazine, and pyridazine). The $L.OsO_4$ adducts react with alkenes R to give the adduct esters $L.[OsO_2(O_2R)]$ (4) and (5) (for R = cyclohexene), which can be hydrolysed to the *cis* diols.[11]

1.1b Known Oxo-Imido Complexes of Osmium and their Chemistry

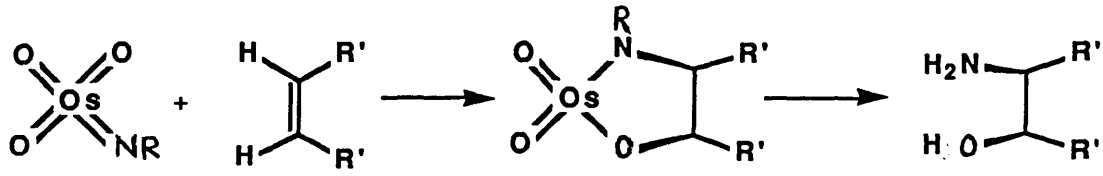
(i) Monoimido Species - Trioxo(N-*tert*-alkylimido)osmium(VIII)

The first osmium imido complex to be prepared was $OsO_3(NBu^t)$ made by reaction of OsO_4 with *tert*-butylamine in pentane.[12] Ligroin[12] and water[13] have also been used as solvents. The other species made by similar methods are the *tert*-amyl,[14] 1-adamantyl,[14] and *tert*-octyl[12] complexes. The X-Ray crystal structure of the 1-adamantyl (12) complex shows the osmium to be tetrahedrally coordinated.[15]



(12)

Sharpless and co-workers have shown that alkenes react with $OsO_3(NR)$ in carbon tetrachloride at 25°C to yield unidentified intermediate "osmium esters" which can then be converted to 1,2-hydroxyamines on treatment with $LiAlH_4$.[13](scheme 3)



Scheme 3

The reaction can be rendered catalytic by using co-oxidants such as chloroamine-T[16] and N-chloro-N-argento carbamates.[17] The reactions always proceed to yield the products resulting from C-N bond formation at the least substituted end of the alkene. It is remarkable that these reagents exhibit a preference for delivery of nitrogen to the alkene carbons rather than oxygen. The steric bulk of the *tert*-alkyl group should render this mode of reaction less favourable. Literature precedent will be presented in section 1.2c.

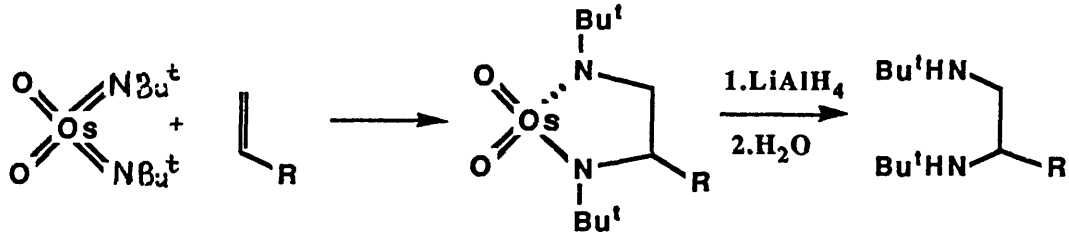
Trioxo(*tert*-butylimido)osmium(VIII) $OsO_3(NBu^t)$ forms weak 1:1 complexes in the solid state with amines such as quinuclidine, 3-quinuclidine, and 3-quinuclidinyl

acetate; and 1:2 complexes (1L : 2Os) with 1,3,5,7-tetra-azatricyclo[3.3.1.1^{3,7}]decane and 1,4-diazabicyclo[2.2.2]octane.[18]

(ii) Bis imido species- Dioxo bis(N-*tert*-alkylimido)osmium(VIII) $OsO_2(NR)_2$

The reaction of OsO_4 or trioxo(*tert*-butylimido)osmium(VIII) with the required amount of N-*tert*-butyltriphenylphosphinimine yields $OsO_2(NBu^t)_2$. The 1-adamantyl imido complex $OsO_2(N\text{-}Ad)_2$ and the mixed species $OsO_2(N\text{-}Ad)(NAm^t)$ were similarly prepared using N-1-adamantyltriphenyl phosphimine.[13] The X-ray crystal structure of $OsO_2(NBu^t)_2$ shows the expected tetrahedral structure. However one of the imido groups is linear (Os-N-C angle = 178.9(9)°).[15] Linearity has been interpreted to indicate triple bond character in the metal-nitrogen bond.[19] Bending appears to occur when insufficient metal d orbitals are available for π-bonding with two nitrogen p orbitals.[19] Also a bent M-N-R geometry can be expected when a linear, 4 electron donor NR ligand would cause the electron count (EAN rule) of the complex to exceed 18 electrons. The infra-red and nmr data of the complex however suggest that both the imido groups are equivalent in solution.

The reaction of $OsO_2(NBu^t)_2$ with alkenes followed by reductive work-up yields stereospecific diamines (scheme 4). The intermediate osmium(VI) ester complexes (13) were isolated with the alkenes dimethyl and diethyl fumarate.[13] Again the preference for Os-N rather than Os-O bond formation is predominant.

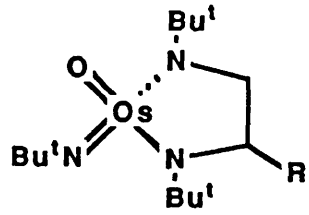


Scheme 4

(iii) Tris Imido Species - Oxotris(N-*tert*-alkylimido)osmium(VIII) $OsO(NR)_3$

The reaction of OsO_4, $OsO_3(NBu^t)$, and $OsO_2(NBu^t)_2$ with N-*tert*-butyl-*tri*-

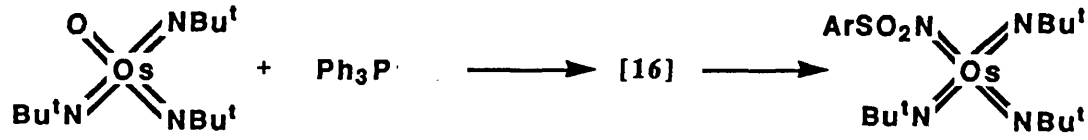
n-butylphosphinimine (14) yields $OsO(NBu^t)_3$. (The less nucleophilic triphenyl phosphinimine only yields the bis complex.) The mixed complex $OsO(NAd)_2(NBu^t)$ can be prepared from $OsO_2(NAd)_2$ and (14). On reaction with alkenes, $OsO(NBu^t)_3$ yields the vicinal after work-up. The intermediate ester (15) has been isolated,[13] derived from the alkene dimethylfumarate.



(15)

(iv) Tetrakis Imido Species- $Os(NR)_4$

Tetra-imido complexes of the type $(ArSO_2N)Os(NBu^t)_3$, Ar = 2,4,6-trimethylphenyl, 2,4,6-tri-*iso*-propylphenyl, and *p*-toluyl, have been isolated.[20] The synthesis involves reduction of $OsO_3(NBu^t)_3$ with triphenylphosphine to yield an unisolated intermediate (16) which reacts with $ArSO_2NNaCl$ to yield the tetraimido complex.(scheme 5) It is essential to "bulk up" the aromatic group, otherwise hydrolysis occurs to yield $OsO(NBu^t)_3$.[20]



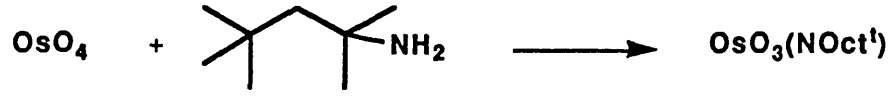
Scheme 5

1.2 The Chemistry of Trioxo(*tert*-octylimido)osmium(VIII)

1.2a Introduction

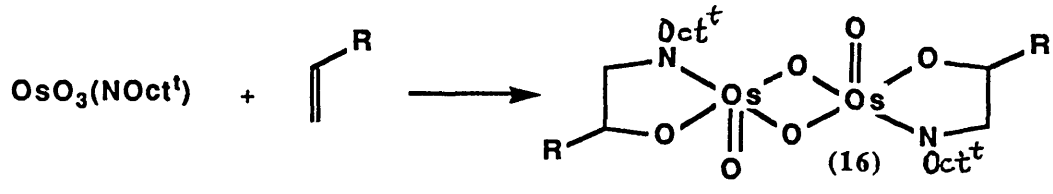
The work presented in chapters 1.2 - 1.5 describes the new reactions of trioxo (*tert*-octylimido)osmium(VIII) and its bridgehead amine adducts with alkenes. The nitrogen ^{15}N labelled compound trioxo(^{15}N-*tert*-butylimido)osmium(VIII) [$OsO_3(^{15}NBu^t)$] has been prepared and the vibrational spectra compared with the ^{14}N naturally abundant compound. The selective stoichiometric oxidation of activated alcohols to aldehydes and ketones by the reagent tetraphenylphosphonium tetraoxo osmate(VII) is presented, together with a brief introduction to the known Os(VII) chemistry.

1.2b Preparation of Trioxo(*tert*-octylimido)osmium(VIII)



There is only one early report of this compound.[12] It has now been prepared by reaction of OsO_4 and *tert*-octylamine in water at 0-5°C. The bright yellow solid has been characterised by nmr, Raman, and infra-red spectroscopy. The Raman and infra-red spectra shown in Table 1 have been measured for the solid and solution. (The Raman spectra in CCl_4 and the infra-red spectra in toluene) . The Os-O stretch appears around 920cm^{-1} and the Os-N stretch around 1205cm^{-1}. These are in agreement with the infra-red data for $OsO_3(NBu^t)$.[13]

1.2c Reactions of trioxo(N-*tert*-octylimido)osmium(VIII) with alkenes



The alkene in ether is added to a solution of $OsO_3(NOct^t)$ in the same solvent at room temperature in a sealed flask. The green or brown product is filtered off after 12 - 24 hours. Alkanolaminato oxo-osmium(VI) complexes (16) have been prepared with dimethylfumarate $(CHCO_2Me)_2$, methylmethacrylate $CH_2C(Me)CO_2Me$ and methyl

acrylate $CH_2C(Me)CO_2H$. The resulting ester complexes have strong infra-red bands near 940cm^{-1} assigned as the Os-O stretch. The spectra are similar in profile to those tetraoxo-osmium(VI) esters[2] and the alkanol *tert* -butyl-aminato osmium (VI) ester complexes[21] previously prepared. The structure of the latter has been confirmed by an X-ray structure on the *tert* -butylimido isobutylene complex.[22] (fig.1)

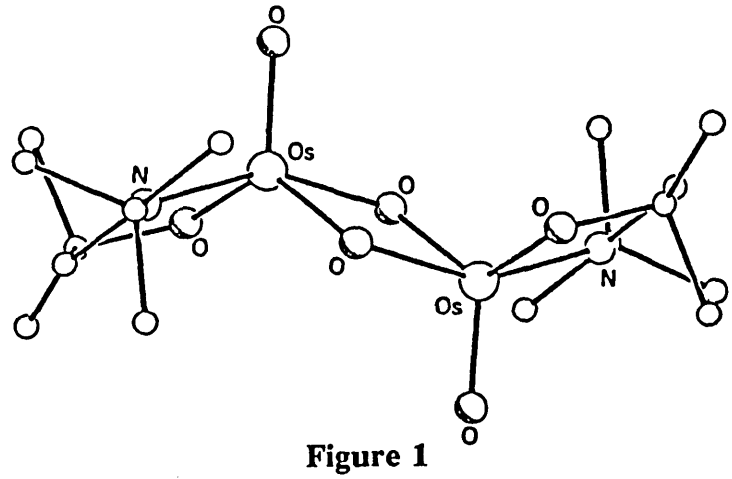
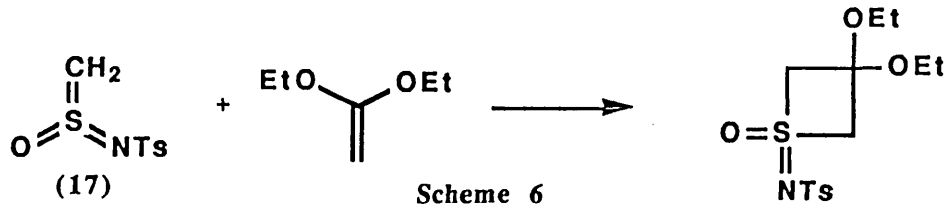


Figure 1

The ester has an *anti* configuration with square based pyramidal osmium (VI) atoms linked by a planar Os_2O_2 bridge (mean Os-O bridge distance 1.92Å); the axial Os-O distance is 1.67Å and the Os-N distance 1.91Å.

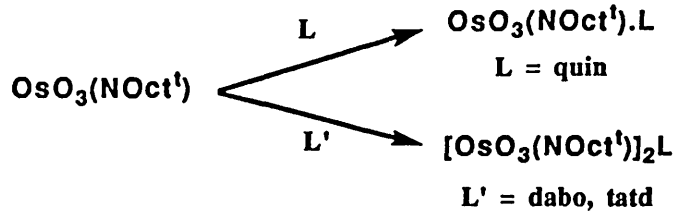
A remarkable feature of this reaction with alkenes is that the trioxyalkylimido reagents exhibit a strong preference for delivery of nitrogen to one of the carbon double bond atoms. This is surprising because of the steric bulk of the tertiary group on the nitrogen. However literature precedent for this behaviour is illustrated with the work of Johnson.[23] The preference of nitrogen over oxygen in the reactions of related sulphur species with alkenes is apparent. The most striking example is in the reaction of iminosulfene (17) with the enol ether to yield the [2 + 2] adduct resulting from addition across the carbon-sulphur bond.(scheme 6) In this example the alkene has a choice of three first row atoms (C,N,O) to select from and it opts for carbon, farthest to the left in the periodic table. This rule of selection (C>N>O) appears to hold for all known [2 + 2] additions of sulphur species with alkenes. This effect clearly extends to other elements apart from sulphur in our case.



(17)

Scheme 6

1.3a Preparation of $[OsO_3(NOct^t)]_nL$ Complexes (L = Bridgehead Amine)



Trioxo(N-*tert*-octylimido)osmium(VIII) reacts with bridgehead amines to form bright orange adduct complexes [21] in ether at room temperature; when allowed to stir for 1.5-2 hours. A 1 : 1 complex is formed for L = quinuclidine (qncd). The $OsO_3(NOct^t)$.qncd complex is more soluble than others prepared by this method and is precipitated by addition of 40/60 petroleum ether.

The 1 : 2 adduct complexes are obtained for L = 1,4-diazabicyclo[2.2.2]octane (dabo) and L = 1,3,5,7-tetra-azatricyclo[3.3.1.$1^{3,7}$]decane (tatd).

The structure of the $[OsO_3(NOct^t)]_2$dabo complex has been confirmed by X-ray.[24] (fig. 2) The crystals were obtained as orange needles by slow crystallisation from a solution of $OsO_3(NOct^t)$ (0.14 g, 0.4mmol) and dabo (0.03 g, 0.2mmol in ether (5 ml). They are monoclinic with a = 6.541(1), b = 28.652(4), c = 15.981(2)Å, β = 92.82(1), U = 2991.4Å (at 19°C), space group $P2_1/c$, and Z = 4. Intensity data was collected on a Nicolet R3m/Eclipse S140 diffractometer system, using graphite-monochromated Cu Kα radiation. A total of 3742 independent reflections were measured (to θ = 55°) of which 1096 where judged to be "unobserved." The structure was solved by a combination of Patterson and Fourier methods, and least squares refinement has reached R = 0.058. The central portion of the molecule is subjected to conformational disorder. Program system SHELXTL[25] was used throughout calculations.

Figure 2 shows that the molecule is binuclear, with the amine bridging two $OsO_3(NOct^t)$ units. The osmium atoms have distorted trigonal bipyramidal coordination

in which the equatorial positions are occupied by oxo ligands with a mean Os-O bond length of 1.71(1)Å, which is similar to that found in OsO_4 itself.[26] The axial positions are taken by the *tert*-octyl imido group, (with a mean Os-N (imido) bond length of 1.73(1)Å, comparable with such distances found in other osmium imido complexes[15]), and the bridging cage amine. The Os-N (cage) distances are very long with a mean of 2.45(1)Å, even longer than the 2.37Å distances observed in OsO_4.qncd and 2.42Å in $[OsO_4]_2$.tatd.[3] This difference probably arises from the greater *trans* influence of the imido as compared with the oxo ligand.

The vibrational spectra are fully consistent with this structure. Three Os-O stretches are observed in the infra-red spectrum of the solid at 883, 873, and 845cm^{-1}, with Raman bands at 887, 875, and 850cm^{-1}; the Os-N imide stretch is around 1170cm^{-1} in the infra-red and Raman. In toluene or carbon tetrachloride solutions however, two Os-N bands appear at 1210 and 1170 cm^{-1}, and in the $\upsilon_{(Os-O)}$ regions there are infra-red bands at 924, 914, 880 and 873cm^{-1} (at 929, 912, 889 and 878cm^{-1} in the Raman). The 1210cm^{-1} band and the $\upsilon_{(Os-O)}$ stretches above 900 cm^{-1} appear in solutions of $OsO_3(NOct^t)$ also. It is clear that dissociation is occurring, presumably to free $OsO_3(NOct^t)$ and $OsO_3(NOct^t)$.dabo in solution. This conclusion is supported by molecular weight studies on the complex in benzene solution (found 488, calculated 841), clearly indicating dissociation. It is interesting to note that the analogous adduct with osmium tetroxide $[OsO_4]_2$.dabo retains its binuclear structure in benzene.[11]

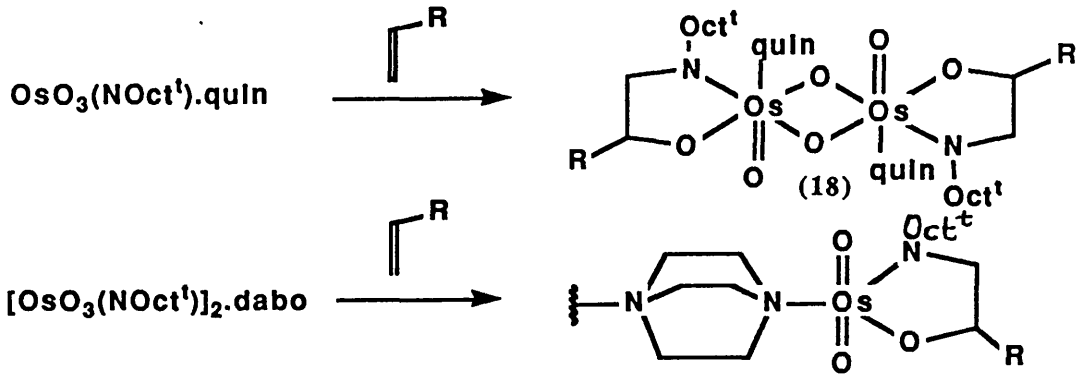
Table 1

Complex	$\upsilon_{(Os-O)}$ cm^{-1}	$\upsilon_{(Os-N)}$ cm^{-1}
$OsO_3(NOct^t)$	927 916	1207
	922 914 906	1206
	(924 914)	(1203)
	(924p 918dp)	(1210)
$[OsO_3(NOct^t)]_2$.dabo	883 873 845	1167
	887 850	1174
	(924 914 880 873)	(1210 1170)
	(929 912 889 878)	(1170)

(Figures in parentheses are in solution, infra-red in toluene and Raman in CCl_4,Raman data are underlined.)

The $4f_{7/2}$ and $4f_{5/2}$ binding energies in the ESCA spectrum are at 53.0 and 57.7eV respectively. These are consistent with osmium being in the octavalent state (for $K[Os^{VIII}O_3N]$ the corresponding values are 53.3 and 56.1eV.

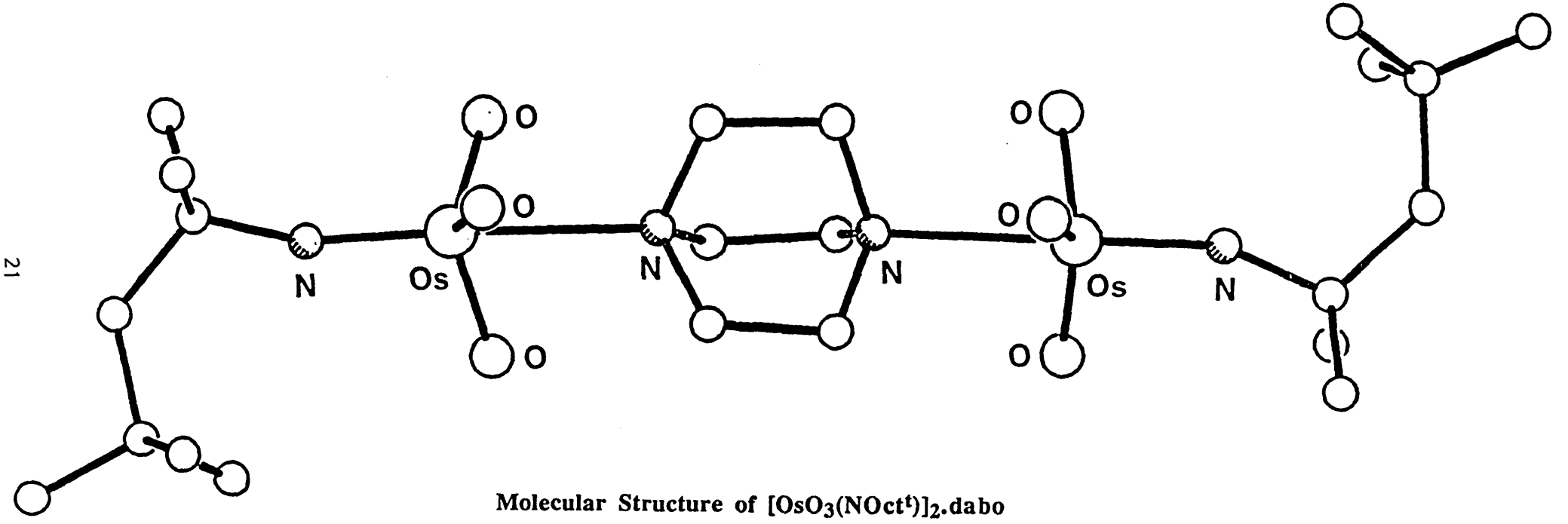
1.3b Reactions of Bridgehead Adducts with Alkenes



The reaction of $[OsO_3(NOct^t)]_2$dabo with alkenes at room temperature in ether for 20-24 hours yield the novel green ester complexes (18) of stoichiometry $[OsO_2(ORNOct^t)]_2$dabo. Complexes are prepared for alkenes: methylmethacrylate $CH_2C(Me)CO_2Me$, dimethylfumarate $(CHCO_2Me)_2$, methylacrylate$CH_2C(Me)CO_2H$, acrylonitrile $CH_2CH(CN)$ and diethyl fumarate $(CHCO_2Et)_2$. The quinuclidine adduct complexes (19) are prepared *in situ* by stirring $OsO_3(NOct^t)$, quinuclidine and the alkene in ether at room temperature for 12-24 hours. The green complexes are isolated for alkenes: dimethylfumarate $(CHCO_2Me)_2$, methylmethacrylate $CH_2C(Me)CO_2Me$ and diethylfumarate $(CHCO_2Et)_2$.

The vibrational spectra are consistent with those obtained for the $[OsO_2]_n.L$ (n = 1,2) ester complexes previously prepared[27] with the Os-O stretch being between 835 and 895cm^{-1}. A series of analogous ester complexes with a *t*-butyl and 1-adamantylimido ligand are known, prepared by N.T. McManus.[24] These show similar vibrational spectra.

Crystals suitable for X-ray could not be isolated despite many attempts. The quinuclidine adduct esters are thought to have a structure similar to that obtained for the



Molecular Structure of $[OsO_3(NOct^t)]_2$.dabo

Figure 2

ester complex of OsO_4.qncd and cyclohexene[3] with an asymmetric Os_2O_2 bridge system shown in figure 3. This complex dissociates in solution to the monomer but we were unable to obtain accurate molecular weight data on our complexes in solution because of their inherent insolubility in benzene.

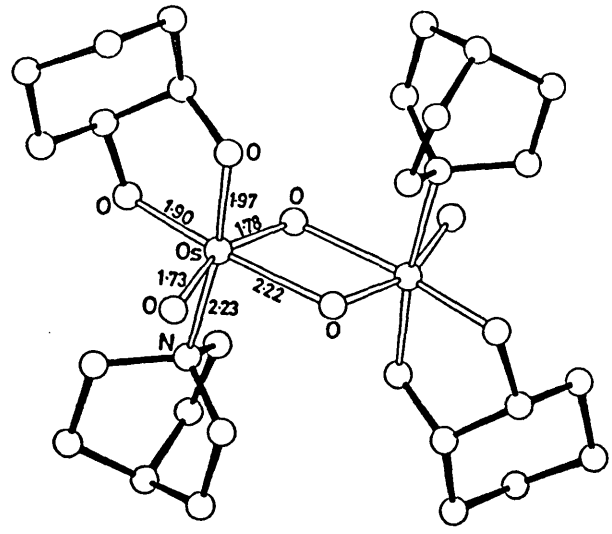


Figure 3

The structure of the dabo adduct ester complexes is not proven but micro-analysis results show a stoichiometry of $[OsO_2(ORNOct^t)]_2$dabo. It is therefore not unreasonable to expect structures of the type (19).

1.4 ^{15}N Substitution Studies on Trioxo(*tert*-butylimido)Osmium(VIII) $OsO_3(NBu^t)$

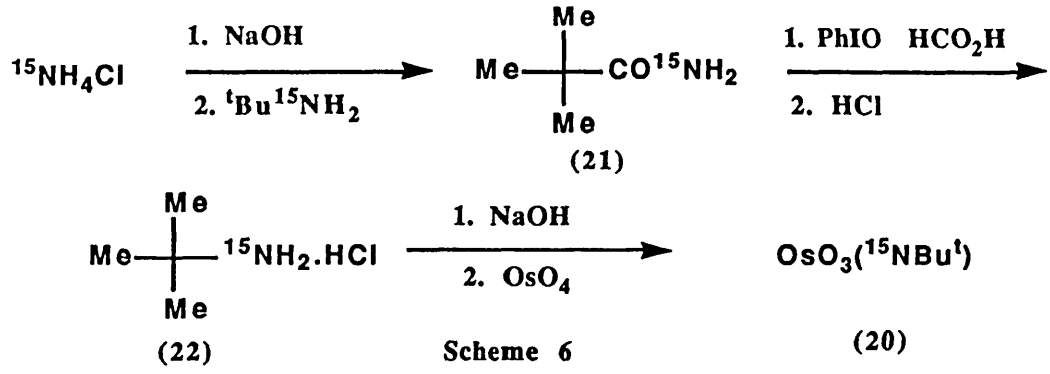
1.4a Introduction

Although there are several infra-red studies of imido complexes including our own on $OsO_3(NBu^t)$,[21] and that of Sharpless and co-workers[13] on the same material, there is only one brief report on the Raman spectra.[28] A Raman and infra-red study of the compounds $OsO_3(NBu^t)$ and $OsO_3(^{15}NBu^t)$ has been undertaken.

1.4b Preparation of $OsO_3(^{15}NBu^t)$ (20)

The new compound $OsO_3(^{15}NBu^t)$ was made using ^{15}N labelled ammonium chloride as the source of labelled nitrogen (scheme 6). On treatment with sodium hydroxide in water, ^{15}N labelled ammonia[29] is generated *in situ* and on reaction with pivaloyl chloride in chloroform/water the amide (21) is formed in 72% yield. Then using a modified Hofmann degradation procedure with iodosylbenzene and formic acid[30] with an acidic work-up, the hydrochloride salt (22) of ^{15}N-*tert*-butylamine was

prepared in 79% yield. On treatment with base and osmium tetroxide the $OsO_3(^{15}NBu^t)$ (20) complex was formed in excellent overall yield; this is essential due to the cost of $^{15}NH_4Cl$ and OsO_4. The $OsO_3(NBu^t)$ naturally occurring analogue was prepared from *tert*-butylamine and OsO_4.[21]



Scheme 6

1.4c Raman and Infra-Red Study

The results are summarized in Table 3. The bands due to the Os-O stretch $\upsilon_{(Os-O)}$ are clearly divisible at 903 and 924cm^{-1} in the solid state at 917 and 932cm^{-1} in carbon tetrachloride, in the infra-red. The Raman bands are at 901 and 918cm^{-1} in the solid state, and 918 and 930cm^{-1} in solution (CCl_4). As expected the bands are exactly the same in the ^{14}N and ^{15}N compounds.

The Os-N symmetric stretch $\upsilon_{(Os-N)}$ is shifted to lower a wave number on going to the heavier isotope. The solution infra-red and Raman in CCl_4 show shifts of 17 and 4cm^{-1} respectively in good agreement with previously published data.[28] The solid state spectra pose rather a dilemma, the shifts of 35 and 34cm^{-1} for infra-red and Raman respectively seem rather too high and the spectra show "extra" bands which may be due to ligand stretches or bends only.

The Os-N asymmetric stretch which is almost certainly a weak band, could not be identified. The band is probably obscured by the strong Os-O stretches which on comparison with other systems[28] are in the same region. The Os-N bend $\delta_{(Os-O)}$ was identified at 478cm^{-1} (^{14}N) moving to 471cm^{-1} (^{15}N) in the infra-red solid spectrum, and from 477 to 470cm^{-1} in the Raman. This assignment was supported by consulting the spectra of the *tert*-butylamine hydrochloride salts. The nearest band that shifted

Table 3

Infra-Red (cm^{-1}) of Osmium Imido Complexes

Compound		$\upsilon_{Os=O}$	$\upsilon_{Os=N}$	$\delta_{Os=N}$	other bands
OsO_3NBu^t	KBr/CsI*	903 924	1214	478*	1157 367* 341* 317* 256*
	DCM	912 926	1208		1243 1160
	CCl_4	917 932	1216		
$^tBuNH_2.HCl$	KBr/CsI*				1217 994 935 880 450* 347*
$OsO_3{}^{15}NBu^t$	KBr/CsI*	903 924	1179	471*	1214 365* 341* 317* 256*
	DCM	912 926	1196		1213
	CCl_4 [37]	917 932	1201		1134
$^tBu^{15}NH_2.HCl$	KBr/CsI*				1217 994 935 880 448* 346*

Raman (cm^{-1}) of Osmium Imido Complexes

OsO_3NBu^t	KBr	901 918	1209	477	1159
	CCl_4	917 929	1215		1155
$OsO_3{}^{15}NBu^t$	KBr	901 918	1177	470	1149 1214
	CCl_4 [37]	918 930	1211		1152

was from 1510 (^{14}N) to 1502cm^{-1} (^{15}N). This is probably the N-H^{+} bend.[31]

1.5 Attempted Preparation of $OsO_2(NOct^t)_2$

The reaction of $OsO_3(NOct^t)$ with N-*tert*-octyltriphenylphosphinimine (prepared as for $Ph_3P{=}NBu^t$ [13]) in refluxing dichloromethane for 24 hours gave less than a 1% yield of an orange solid, presumably the di-imide, after column chromatography. The method that of Sharpless[13] was used successfully for the preparation of the *tert*-butyl analogue.

The reaction of OsO_4 with *tert*-octyltrimethylsilylamine (prepared *in situ* by addition of *n*-butyl lithium followed by trimethylsilylchloride to *tert*-octylamine) in hexane resulted only in $OsO_3(NOct^t)$, the mono-imido complex. The method, that of Nugent,[15] has been used for the preparation of various bis-imido complexes.

1.6 Preparation and Stoichiometric Oxidation of Alcohols with Tetraphenylphosphonium Tetraoxoosmate(VII) $(Ph_4P)[OsO_4]$

1.6a Introduction

The known analogue tetraphenylarsonium tetraoxoosmate(VII) is prepared by reaction of OsO_4 and $PhAr_4I$ in dichloromethane.[32] Dehnicke and co-workers found the reaction to be a reversible one-electron process (OsO_4/OsO_4^{-}) by cyclic voltammetry.

The black alkali metal analogues have since been prepared by Levison and co-workers[33] for $M.OsO_4$ (M = Na, K, Rb and Cs), by stirring OsO_4 with MI under a nitrogen atmosphere in acetone for 3 hours at 0°C. In water or dilute acid immediate disproportionation to OsO_4 and $Os^{VI}O_2.nH_2O$ occurs whilst in 1M alkali the products are $K_2[Os^{VI}O_2(OH)_4]$ and OsO_4. Ethanolic potassium hydroxide produces essentially quantitative conversion to *trans*-$K_2[OsO_2(OH)_4]$.

1.6b Tetraphenylphosphonium Tetraoxoosmate(VII) $(Ph_4P)[OsO_4]$

This compound was prepared independently by the method of Dehnicke[32] before it was reported by Levison.[33] Osmium tetroxide is stirred with

tetraphenylphosphonium iodide in dichloromethane. The resulting green product is taken up in methyl iodide to remove the triiodide impurity $Ph_4P^+I_3^-$. The complex has Os-O stretch bands at 872 and 855cm^{-1} in the infra-red and at 908 and 837cm^{-1} in the Raman.

1.6c Oxidation of Alcohols with Tetraphenylphosphonium Tetraoxoosmate(VII) $(Ph_4P)[OsO_4]$

The alcohol is stirred with 0.67 equivalents of $(Ph_4P)[OsO_4]$ in dichloromethane at room temperature. The aldehyde products were isolated by concentration of the mixture and subsequent flash chromatography on silica gel. The products were characterized by nmr and were all literature compounds. The results are illustrated in Table 2.

It is apparent that only benzylic and allylic alcohols are oxidized. The benzylic alcohols react faster than the allylic alcohols, reaction times varying from 30 minutes to 12 hours. No oxidation was observed for primary alkyl or secondary alcohols. The oxidation of cinnamyl alcohol proceeds without oxidation of the double bond.

Table 2

Reactant	Product	Yield(%)	Time(hr)
α-tetralol	α-tetralone	60	3
3,4-dimethoxybenzyalcohol	aldehyde	87	2
piperonyl alcohol	piperonal	84	2
geraniol	geranial	25	4
cinnamyl alcohol	cinnamaldehyde	79	1
octan-2-ol	-	N.R.	
lanost-8-en-3-ol	-	N.R.	
citronellol	-	N.R.	

The reactivity of $[OsO_4]^-$ contrasts vividly with OsO_4. It seems the tetraoxoosmate(VII) is a much more mild oxidant than OsO_4. The $[OsO_4]^-$ oxidant behaves in the same way as barium ruthenate, *trans*-$[Ba^{VI}(OH)_2O_3]$[35] and barium

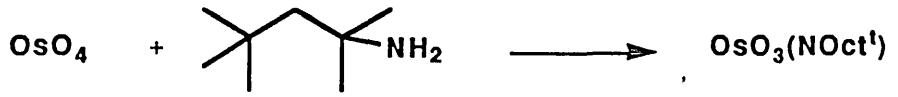
manganate,[36] in that it functions as a very selective, mild reagent for the dehydrogenation of activated alcohols.

The tetraoxoosmate(VII) ion functions as a three electron oxidant forming presumably $Os^{IV}O_2nH_2O$ in the reaction. This has been shown by stoichiometric oxidation of piperonyl alcohol. Ratios of 2/3 equivalents of $[OsO_4]^-$ or greater yield complete reaction by thin layer chromatography. Exactly half an equivalent of $[OsO_4]^-$ gives an isolated yield of 67% of the alcohol (75% is the maximum yield for a three electron oxidant) with obviously incomplete reaction by t.l.c.

All attempts to render this system catalytic using N-methylmorpholine-N-oxide, *tert*- and oxygen or air as co-catalyst failed.

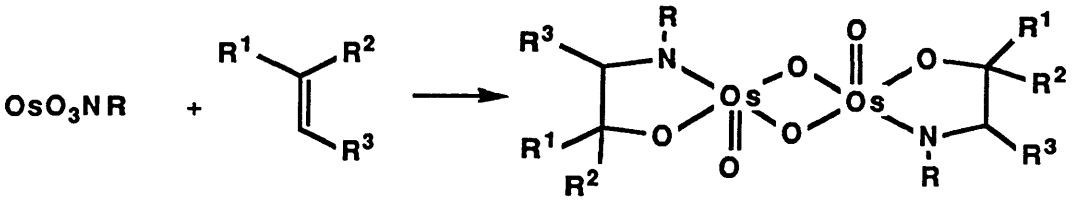
1.7 Osmium Experimental

Trioxo(*tert*-octylimido)osmium(VIII)



tert-Octylamine (0.44 g, 3.4 mmol) was added to a stirred solution of osmium tetroxide (0.86 g, 3.4 mmol) in water (8 ml) at 5°C. The mixture was stirred for 30 min, filtered and washed with iced water (3 x 10 ml) to yield the imido compound (1.34 g, 87%) as a yellow solid, (Found : C, 26.4; H, 4.60; N, 3.80. $C_8H_{17}NO_3Os$ requires C, 26.3; H, 4.65; N, 3.83%), I.R. $\upsilon_{max.}$ (KBr disc) 1 224 (υ_{Os-N}), 928 (υ_{Os-O}), and 812cm^{-1} (υ_{Os-O}), Raman $\upsilon_{max.}$ 1 193 (υ_{Os-N}), and 812cm^{-1} (υ_{Os-O}), $\delta(CDCl_3$, 90 MHz) 2.07 (2H, s, CH_2), 1.74 (6H, s, $C(Me)_2$), and 1.10 (9H, s, $C(Me)_3$)

Alkanolaminato Oxo-osmium(VI) $[OsO_2(OR'NR)]_2$ (16)

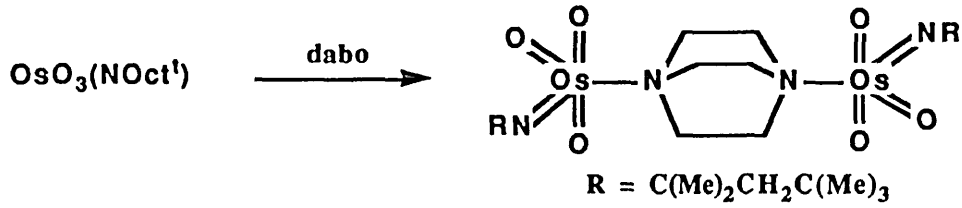


R = $C(Me)_2CH_2C(Me)_3$

(16a) R^1 = Me, R^2 = CO_2Me, R^3 = H
(16b) R^1 = Me, R^2 = CO_2H, R^3 = H
(16c) R^1 = H, R^2 = CO_2Me, R^3 = CO_2Me

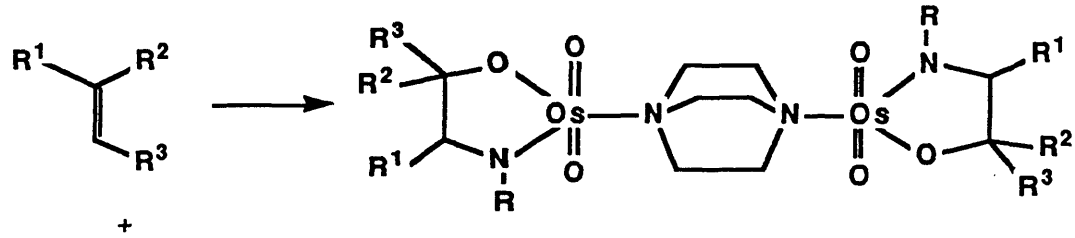
The alkene (0.14 mmol) in ether (2 ml) was added to a solution of $OsO_3(NOct^t)$ (0.05 g, 0.14 mmol) in ether (2 ml). The solution was stirred at room temperature for two hr and filtered to give the osmium (VI) ester (16c) (0.01 g, 5%) as a green solid, (Found : C, 32.8; H, 4.91; N, 2.78. $C_{28}H_{48}N_2O_{14}Os_2$ requires C, 33.0; H, 4.91; N, 2.75%), $\upsilon_{max.}$ (KBr disc) 812cm^{-1} (υ_{Os-O}).Ester (16b) as a black solid (0.14 g, 73%), (Found : C, 30.8; H, 4.99; N, 3.16. $C_{24}H_{46}N_2O_{10}Os_2$ requires C, 31.9; H, 5.10; N, 3.10%), $\upsilon_{max.}$ (KBr disc) 770cm^{-1} (υ_{Os-O}). Ester (16a) as a brown solid (0.12 g, 63%) (from petrol), (Found : C, 34.0; H, 5.77; N, 3.00. $C_{26}H_{50}N_2O_{10}Os_2$ requires C, 33.5; H, 5.37; N, 3.00%), $\upsilon_{max.}$ (KBr disc) 820cm^{-1} (υ_{Os-O}).

Bis[Trioxo(*tert*-octylimido)osmium(VIII)]diazabicyclo[2.2.2]octane adduct



Trioxo(*tert*-octylimido)osmium(VIII) (0.101 g, 0.28 mmol) was added to a stirred solution of dabo (0.015 g, 0.138 mmol) in THF (3 ml). The mixture was stirred at room temperature for 3 hr, then concentrated *in vacuo* to *ca.* 0.25 ml and petrol (10 ml) added. The mixture was stirred at -5°C overnight and filtered to give the adduct (0.054 g, 53%) as orange needles, m.p. 122°C, (Found : C, 31.5; H, 5.47; N, 6.60. $C_{24}H_{46}N_4O_6Os_2$ requires C, 31.3; H, 5.46; N, 6.65%), $\upsilon_{max.}$ (KBr disc) 1 210 (υ_{Os-N}), 875 (υ_{Os-O}), and 850cm^{-1} (υ_{Os-O}), δ($CDCl_3$, 60 MHz) 3.1 (16H, m, CH_2 in octyl and dabo), 1.4 (12H, m, $C(Me)_2$), and 0.8 (18H, m, $C(Me)_3$), (spectrum complex because of dissociation in solution), cryoscopic molecular weight in benzene = 460 g.

Bis[Alkanolaminato Oxo-osmium(VI)] diazabicyclo[2.2.2] octane Adducts(19)

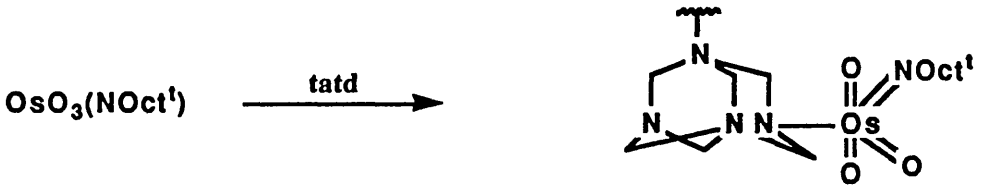


(19a) $R^1 = CO_2Me$, $R^2 = Me$, $R^3 = H$
(19b) $R^1 = CN$, $R^2 = R^3 = H$
(19c) $R^1 = CO_2Me$, $R_2 = H$, $R^3 = CO_2Me$
(19d) $R^1 = Me$, $R^2 = CO_2H$, $R^3 = H$
(19e) $R^1 = CO_2Et$, $R^2 = H$, $R^3 = CO_2Et$

The alkene (0.22 mmol) in ether (2 ml) was added to a stirred solution of dabo adduct (0.10 g, 0.12 mmol) in ether (2 ml). The mixture was stirred overnight, concentrated *in vacuo* and petrol (10 ml) added. The mixture was filtered and washed with petrol to give the ester (19a) (0.08 g, 62%) as a green solid, (Found : C, 36.9; H, 5.95; N, 5.22. $C_{32}H_{62}N_4O_{10}Os_2$ requires C, 36.8; H, 5.95; N, 5.37%), $\upsilon_{max.}$ (KBr disc) 850 (υ_{Os-O}), and 860cm^{-1} (υ_{Os-O}) . Ester (19b) as a green solid (0.07 g, 55%),

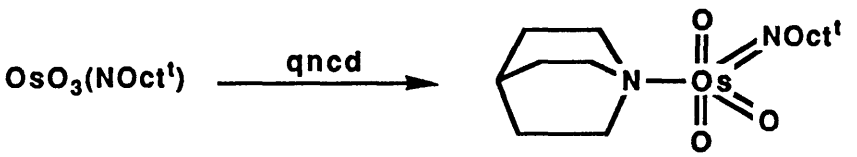
(Found : C, 35.0; H, 5.33; N, 8.53. $C_{28}H_{52}N_6O_6Os_2$ requires C, 35.4; H, 5.48; N, 8.86%), $\upsilon_{max.}$ (KBr disc) 887 (υ_{Os-O}) and 860cm^{-1} (υ_{Os-O}). Ester (19c) as a dark green solid (0.037 g, 27%) (Found : C, 36.0; H, 5.54; N, 4.84. $C_{34}H_{62}N_4O_{14}Os_2$ requires C, 36.1; H, 5.48; N, 4.95%), $\upsilon_{max.}$ (KBr disc) 883 (υ_{Os-O}), and 858cm^{-1} (υ_{Os-O}) . Ester (19d) as a dark green solid (0.10 g, 80%), (Found : C, 34.9; H, 5.67; N, 5.39. $C_{30}H_{58}N_4O_{10}Os_2$ requires C, 35.5; H, 5.72; N, 5.52%), $\upsilon_{max.}$ (KBr disc) 885 (υ_{Os-O}) and 860cm^{-1} (υ_{Os-O}). Ester (19e) as a green solid (0.048 g, 31%) (Found : C, 37.8; H, 5.77; N, 4.95.$C_{38}H_{70}N_4O_{14}Os_2$ requires C, 38.4; H, 5.90; N, 4.72%), $\upsilon_{max.}$ (KBr disc) 884 (υ_{Os-O}) and 859cm^{-1} (υ_{Os-O}).

Bis[trioxo(*tert*-octylimido)osmium(VIII)].1,3,5,7-tetraazatricyclo[3.3.1.1^{3,7}] decane adduct



1,3,5,7-tetra-azatricyclo[3.3.1.1^{3,7}]decane (0.04 g, 0.286 mmol) in chloroform (2 ml) was added to a solution of imido adduct (0.105 g, 0.286 mmol) in chloroform (1 ml), the mixture was stirred for 12 hr concentrated *in vacuo* to 0.5 ml and petrol (20 ml) added, the precipitate was filtered to give the adduct complex (0.09 g, 72%) (Found : C, 30.8; H, 5.36; N, 11.9. $C_{22}H_{46}N_6O_6Os_2$ requires C, 30.8; H, 5.32; N, 9.65%), $\upsilon_{max.}$ (KBr disc) 1 212 (υ_{Os-N}), 888 (υ_{Os-O}) and 875cm^{-1} (υ_{Os-O}).

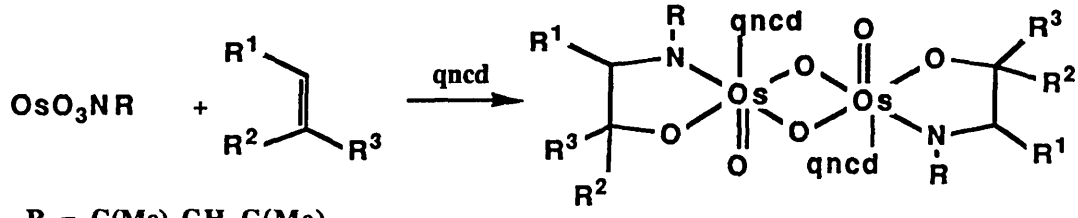
Trioxo(*tert*-octylimido)osmium(VIII)].quinuclidine



Quinuclidine (0.031 g, 0.028mmol) in ether (2 ml) was added to a solution of imido compound (0.102 g, 0.28 mmol) in ether (2 ml). The mixture was stirred for 1 hr at room temperature, concentrated *in vacuo*, dissolved in petrol (2 ml) and cooled

for 2 hr at 0°C. The mixture was then filtered and washed with cold petrol to give the adduct (0.011 g, 8%) as orange needles (Found : C, 37.7; H, 6.26; N, 5.84. $C_{15}H_{29}N_2O_3Os_2$ requires C, 37.8; H, 6.30; N, 5.88%), $\upsilon_{max.}$ (KBr disc) 1 210 (υ_{Os-N}), 885 (υ_{Os-O}) and 870cm^{-1} (υ_{Os-O}).

Alkanolaminato Oxo-osmium(VI).quinuclidine Adducts(18)

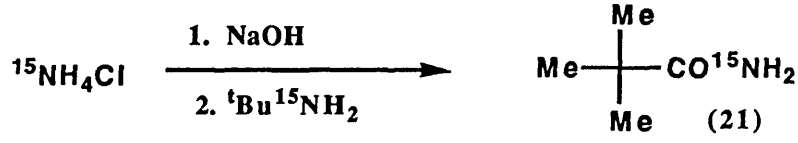


R = $C(Me)_2CH_2C(Me)_3$

(19a) $R^1 = R^3 = CO_2Me$, $R^2 = H$
(19b) $R^1 = H$, $R^2 = CO_2Me$, $R^3 = Me$
(19c) $R^1 = R^3 = CO_2Et$, $R^2 = H$

Quinuclidine (0.021 g, 0.189 mmol) was added to a solution of imido compound (0.069 g, 0.189 mmol) in ether (5 ml). The solution was stirred for 30 min and then the alkene (0.189 mmol) added. The mixture was stirred overnight and filtered to give the ester (18a) (0.04 g, 34%) as green cubes, (Found : C, 40.9; H, 6.19; N, 4.33. $C_{42}H_{76}N_4O_{14}Os_2$ requires C, 40.6; H, 6.13; N, 4.51%), $\upsilon_{max.}$ (KBr disc) 891 (υ_{Os-O}), and 852cm^{-1} (υ_{Os-O}) . Ester (18b) (0.035 g, 32%) as green plates, (Found : C, 41.8; H, 6.61; N, 4.82. $C_{40}H_{76}N_4O_{10}Os_2$ requires C, 47.7; H, 6.59; N, 4.86%), $\upsilon_{max.}$ (KBr disc) 880 (υ_{Os-O}) and 860cm^{-1} (υ_{Os-O}). Ester (18c) as green needles (0.044 g, 35%) (Found : C, 42.6; H, 6.52; N, 4.24. $C_{46}H_{84}N_4O_{14}Os_2$ requires C, 42.6; H, 6.48; N, 4.32%), $\upsilon_{max.}$ (KBr disc) 892 (υ_{Os-O}), and 853cm^{-1} (υ_{Os-O}) .

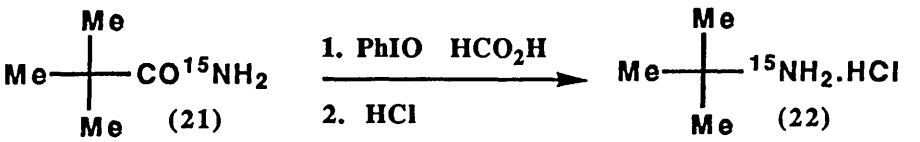
^{15}N-Pivaloylamide(21)



^{15}N-ammonium chloride (1.0 g, 18.3 mmol) was added to a solution of NaOH (27.3 ml of a 1.5*M* aqueous solution) at 0°C. A cooled solution of pivaloyl chloride (2.03 ml, 6.5 mmol) in chloroform (110 ml) was added, and the two phase mixture

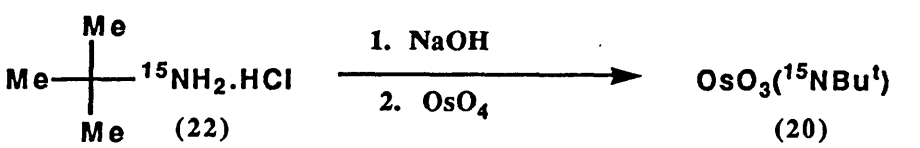
stirred vigorously for 2 hr at 0°C. The organic layer was separated, washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to give the amide (21) (1.2 g, 72%) as a white solid, (Found : C, 58.6; H, 10.6; N,13.8. $C_5H_{11}{}^{15}NO$ requires C, 58.8; H, 10.9; N, 14.7%), $\upsilon_{max.}$ (CCl_4) 1 679 (υ_{C-O}), δ($CDCl_3$, 90 MHz) 1.22 (9H, s, *t*-Bu), m/z 102 (M^+) and 87 (M^+ - Me).

^{15}N-*tert*-Butylamine.Hydrochloride Salt (22)



Freshly prepared iodosylbenzene[36] (2.75 g, 12.5 mmol) was added to a solution of amide (21) (1.10 g, 10.78 mmol) in acetonitrile (18 ml) and water (6 ml). The mixture was stirred vigorously while formic acid (1.63 ml, 43 mmol) was added dropwise, then stirred overnight at room temperature, HCl (45 ml of a 1*M* aqueous solution) was added and the mixture extracted with ether. The aqueous layer was concentrated *in vacuo* to yield a white solid which was purified by recrystallisation in ethanol/water to give the amine hydrochloride salt (22) (0.94 g, 79%) as white plates, (Found : C, 42.1; H, 11.1; N,13.1. $C_4H_{12}{}^{15}NCl$ requires C, 43.4; H, 10.9; N, 13.6%), $\upsilon_{max.}$ (KBr disc) 2 954, 2 890, 2 796, 2 705, 2 594, 2 494, 2 078, 1 610, 1 502, 1 401, 1 374, and 1 217cm^{-1} δ($CDCl_3$, 90 MHz) 1.48 (9H, d, *J* 2.5 Hz, *t*-Bu), m/z 74 (M^+-HCl).

Trioxo(*tert*-butyl^{15}N imido)osmium(VIII)(20)



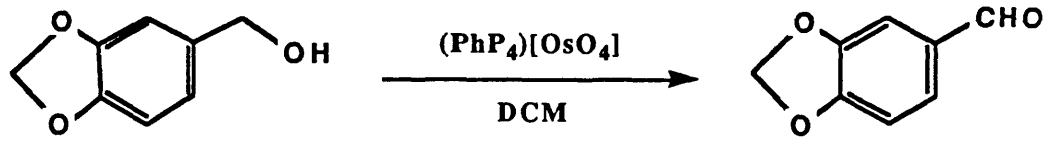
Sodium hydroxide (0.34 g, 8.5 mmol) in water (3 ml) was added to a cold solution of labelled amine (22) (0.94 g, 8.5 mmol) in water (2 ml). The mixture was then added dropwise to a stirred solution of OsO_4 (1.08 g, 4.25 mmol) in water (30 ml) at 0°C. The mixture was stirred for 2 hr at room temperature and filtered. The

residue was washed with cold water (3 x 10 ml) and dried *in vacuo* to give the ^{15}N imido compound. (20) (1.3 g, 99%) as a yellow solid, (Found : C, 15.5; H, 2.73; N, 4.52. $C_4H_9{}^{15}NO_3Os$ requires C, 15.5 H, 2.92; N, 4.83%), $\upsilon_{max.}$ (KBr/CsI discs), 1 179 (υ_{Os-N}), 924 (υ_{Os-O}), 903 (υ_{Os-O}), and 471cm^{-1} (δ_{Os-N}). $\delta(CDCl_3$, 90 MHz) 1.65 (9H, d, *J* 3 Hz, *t*-Bu), m/z 312 (M^+ Os^{192}), 310 (M^+ Os^{190}), 297 (M^+ - Me Os^{192}), and 295 (M^+ -Me Os^{190}).

Tetraphenylphosphonium Tetraoxoosmate(VII) $(Ph_4P)[OsO_4]$

A solution of osmium tetroxide (0.79 g, 3.09 mmol) in dichloromethane (5 ml) was added dropwise to a stirred solution of tetraphenylphosphonium iodide (1.37 g, 2.94 mmol) in dichloromethane (10 ml) at 0°C. After 15 min carbon tetrachloride (5 ml) was added and the mixture filtered to give a solid which was stirred with methyl iodide (20 ml) for 15 min, filtered and dried *in vacuo* to give a green solid (1.22 g, 70%) (Found : C, 47.9; H, 3.13. $C_{24}H_{20}O_4POs$ requires C, 48.6; H, 3.37%), $\upsilon_{max.}$ I.R. (KBr disc) 872 (υ_{Os-O}) and 855cm^{-1} (υ_{Os-O}), Raman $\upsilon_{max.}$ 908 (υ_{Os-O}) and 837cm^{-1} (υ_{Os-O}), m/z 339 (Ph_4P^+).

Typical Oxidation with $(Ph_4P)[OsO_4]$



Tetraphenylphosphonium tetraoxoosmate(VII) (73.2 mg, 12.3 mmol) was added to a solution of piperonyl alcohol (28.0 mg, 0.184 mmol) in dichloromethane (2 ml). The mixture was stirred at room temperature for 2 hr then concentrated *in vacuo* and purified by column chromatography on silica gel eluting with 25% ether in petrol to give the known piperonal (23.2 mg, 84%) as an oil, $\delta(CDCl_3$, 90 MHz) 9.70 (1H, s, CHO), 7.35(2H, m, Ph-H *ortho* to OCH_2O), 6.80(1H, d, *J* 8 Hz,Ph-H *meta* to OCH_2O), and 6.02(2H, s, CH_2).

Chapter 1 References

1. M.Schroder, *Chem. Rev.*,1980, **80**, 187.

2. R.J.Collin, J.Jones, and W.P.Griffith, *J. Chem. Soc., Dalton Trans.*, 1974, 1094; R.J.Collin, W.P. Griffith, F. Phillips, and A.C. Skapski, *Biochim. Biophys. Acta*, 1974, **354**, 152.

3. B.A.Cartwright, W.P.Griffith, M.Schroder, A.C.Skapski, *J. Chem. Soc.,Chem. Commun.*, 1978, 853.

4. R.Criegee, B.Marchand, and H.Wannowius, *Liebigs Ann. Chem.*, 1942, **550**, 99; R.Criegee, *ibid.*, 1936, **522**, 75; M.J.S.Dewar, *J. Am. Chem. Soc.*,1952, **74**, 3341; M.J.S.Dewar and H.C.Longuet-Higgins, *Proc. R. Soc. London Sect. A*, 1952, **214**, 482.

5. K.B.Sharpless, A.Y.Teranishi, and J.-E.Backvall, *J. Am. Chem. Soc.*, 1977, **99**, 3120; M.Zelikoff and H.A.Taylor, *ibid.*, 1950, **72**, 5039.

6. L.R.Subbaraman, J.Subbaraman, and E.J.Behrman, *Bioinorg. Chim.*, 1971, **1**, 35; L.R.Subbaraman, J.Subbaraman, and E.J.Behrman , *Inorg. Chem.*, 1972, **11**, 2621; R.L.Clarke and E.J.Behrman, *ibid.*, 1975, **14**, 1425.

7. M.L.Hair and P.L.Robinson, *J. Chem. Soc.*, 1958, 106; W.P. Griffith, A.C.Skapski, K.A.Woode, and M.J.Wright, *Inorg. Chim. Acta*, 1978, **31**, L413.

8. M.Schroder and E.C.Constable, *J. Chem. Soc., Chem. Commun.*, 1982, 734.

9. C.P.Casey, *J. Chem. Soc., Chem. Commun.*, 1983, 126.

10.S.G.Hentges and K.B.Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 4263.

11.M.J.Cleare, P.C.Hydes, W.P.Griffith, and M.J.Wright, *J. Chem. Soc., Dalton Trans.*, 1977, 941.

12. N.A.Milas and M.I.Iliopulos, *J. Am. Chem. Soc.*, 1959, **81**, 6089.

13. A.O.Chong, K.Oshima, and K.B.Sharpless, *J. Am. Chem. Soc.*,1977, **99**, 3420.

14. D.W.Patrick, L.K.Truesdale, S.A.Biller, and K.B.Sharpless, *J. Org. Chem.*,1978, **43**, 2628.

15. R.L.Harlow, R.J.McKinney, and W.A.Nugent, *J. Am. Chem. Soc.*,1979, **101**, 7265.

16. E.Herranz and K.B.Sharpless, *J. Org. Chem.*, 1978, **43**, 2544.

17. E.Herranz S.A.Biller, and K.B.Sharpless, *J. Am. Chem. Soc.*, 1978, **100**, 3596.

18. S.G.Hentges and K.B.Sharpless, unpublished results.

19. B.L.Haymore and W.A.Nugent, *Coord. Chem. Rev.*, 1980, **31**, 123.

20. S.G.Hentges and K.B.Sharpless, private communication.

21. W.P.Griffith, N.T.McManus, and A.D.White, *J. Chem. Soc., Dalton Trans.*, 1986, 1035.

22. W.P.Griffith, N.T.McManus, A.C. Skapski, and A.J.Neilson, *Inorg. Chim. Acta,* 1985, **103**, L5.

23. C.R.Johnson and E.U.Jonsson, *J. Am. Chem. Soc.*, 1970, **92**, 3815.

24. W.P.Griffith, N.T.McManus, A.C. Skapski, and A.D.White, *Inorg. Chim. Acta,* 1985, **105**, L11.

25. G.M.Sheldrick, "SHELXTL", an integrated system for solving refining and displaying crystal structures from diffraction data, revision 4, Nicolet Instrument Co. Ltd., 1983.

26. H.M.Seip and R.Stølevik, *Acta Chem. Scand.*, 1966, **20**, 385.

26a ESCA data measured by M.Morris.

27. W.P.Griffith, A.J.Neilson, and M.Schroder, *J. Chem. Soc., Dalton Trans.*, 1979, 1607.

28. W.P.Griffith, A.J.Neilson, and M.J.Taylor, *J. Chem. Soc., Dalton Trans.*, in press.

29. A.S.Radhakrishna, C.G.Rao, R.K.Varma, B.B.Singh, and, S.P.Bhatnager, *Synthesis,* 1983, 538.

30. E.W.Della, B.Kasum, and K.P.Kirkbride, *J. Am. Chem. Soc.*, 1987, **109**, 2746.

31. W.Kemp, "Qualitative Organic Analysis", McGraw-Hill, 1979.

32. E.Bilger, J.Pebler, R.Weber, and K.Dehnicke, *Z. Naturforsh,* 1984, **396**, 259.

33. W.Levason, M.Tajik, and M.Webster, *J. Chem. Soc., Dalton Trans.*, 1985, 1735.

34. Raman spectrum run by A.El-Hendawy.

35. G.Green, W.P.Griffith, D.M.Hollinshead, S.V.Ley, and M.Schroder, *J. Chem. Soc., Perkin Trans. I,* 1984, 681.

36. H.Fironszabadi and E.Ghaderi, *Tetrahedron Lett.,* 1978, **19**, 839.

37. Raman spectra run by A.C.Dengel.

Chapter 2. Ruthenium

2.1 Introduction

This chapter contains a review of the mechanistic work performed on ruthenium oxidative systems (Section 2.2a) and recent advances in the development of ruthenium oxidants (Section 2.2b). The work presented in section 2.4 describes the development of a new and versatile catalytic system for the oxidation of primary and secondary alcohols to aldehydes and ketones respectively.

2.2 Ruthenium Species as Oxidants

Introduction

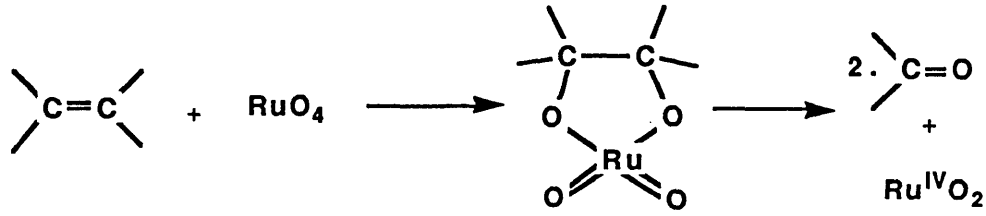
The use of ruthenium tetroxide has been reported in the literature for the past twenty years.[1] The organic chemist, however, is increasingly demanding more selective oxidizing agents and RuO_4, which cleaves double bonds and also attacks a variety of other functional groups,[1-3] is clearly unsuitable. The obvious extension has been the use of perruthenates $[RuO_4]^-$, ruthenates $[RuO_4]^{2-}$, $Ru^{III}Cl_3.nH_2O$, and $RuCl_2(PPh_3)_3$ species stoichiometrically or catalytically in the presence of a co-oxidant.

The use of practical catalytic systems and the development of selective catalysts by the "tuning" of reactivity with the appropriate ligands are the current aims in the field of ruthenium oxidative chemistry, which is reviewed briefly, in section 2.2b.

2.2a Mechanistic Studies in Ruthenium Oxidative Chemistry

Ruthenium Tetroxide Oxidation of Alkenes

There is very little known of the mechanism resulting in cleavage of double bonds (scheme1).



Scheme 1

The rate of reaction is directly dependent on the concentration of both alkene and oxidant, and is decreased by electron withdrawing groups on the alkene.[4] The

greater tendency of RuO_4 to cleave double bonds compared with OsO_4 is probably related to the greater relative instability of the Ru(VI) ester

Scheme 1 is consistent with the results of Wolfe[5] which indicated that adipaldehyde was an intermediate in the oxidation of cyclohexene to adipic acid. Also it is known that the reaction does not proceed *via* the corresponding diketone; when cyclohexadione is oxidized the major product is glutaric acid (56%) together with adipic acid (28%) and succinic acid(3%). Obviously the oxidation of cyclohexene, which gives only adipic acid, cannot be proceeding *via* the intermediate diketone.

A kinetic study has been carried out on a number of unsaturated carboxylic acids by sodium ruthenate in aqueous base at 85°C. (Sodium ruthenate does not react with alkenes at normal temperatures). The results suggest the reaction proceeds *via* a complex mechanism which involves Ru(IV) and Ru(VI) diesters as intermediates.[6]

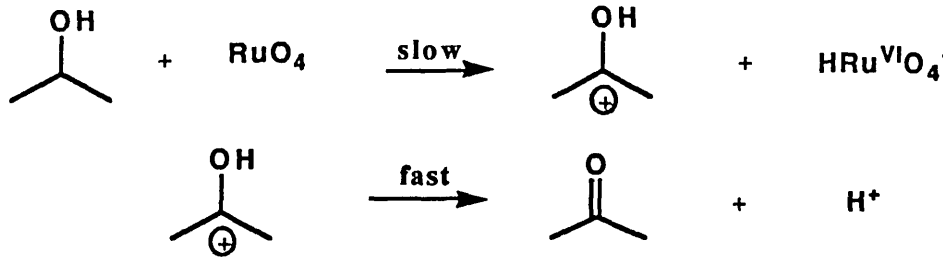
(i) Ruthenium Tetroxide Oxidation of Alcohols

The RuO_4 oxidation of 2-propanol has been extensively studied by Lee and Van den Engh[7] in aqueous perchloric acid solutions. Two different rate laws became apparent . In moderate to high acidity (1 - 6.5*M* $HClO_4$) the reaction was first order with respect to oxidant and alcohol and inversely dependent on $[H^+]$ concentration. At high acidity (6.5 - 10*M* $HClO_4$) the rate was independent of RuO_4 concentration and directly proportional to $[H^+]$ concentration.

The mechanism was formulated as a rate determining hydride transfer, (scheme 2) except at high concentrations where carbonium ion formation became rate limiting (scheme 3). Additional evidence was also cited. A primary deuterium isotope effect (k_H/k_D = 4.6) was observed. Electron donating substituents accelerated the rate of reaction. The activation parameters $\Delta H^{\dagger}$ and $\Delta S^{\dagger}$ were similar to other known hydride transfer rate limiting mechanisms.[8] Ethers and alcohols are oxidized by RuO_4 with equal ease which suggests that an ester mechanism as proposed for chromic acid oxidations,[9] does not apply. A single product (acetone) was obtained quantitatively (scheme 2) .The fact that reaction rate decreased with increasing acidity was explained on the assumption that $(CH_3CHOH_2CH_3)^+$, the conjugate acid of 2-propanol, would

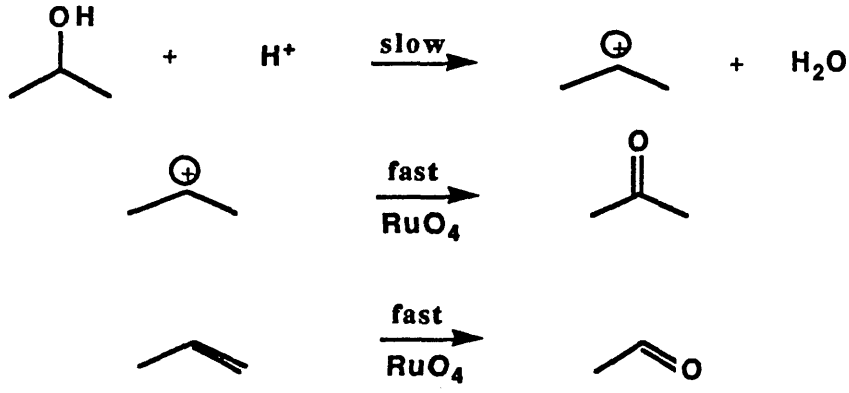
be resistant to a hydride transfer mechanism. Unlike the lower oxidation state species RuO_4 is not strongly solvated by water.[10] The transition state would have a higher demand for water, and consequently higher acidities would result in a reduction in rate as the water concentration lowered.

Moderate Acidity



Scheme 2

High Acidity

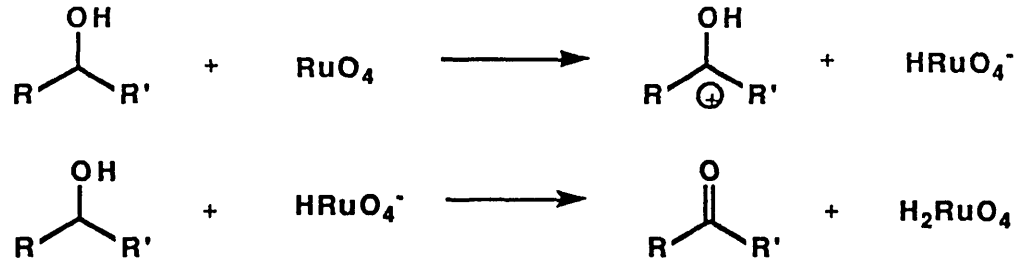


Scheme 3

There is strong evidence suggest that carbonium ion formation at high acidity was prelavent. The deuterium isotope effect was found to be unity ($k_H/k_D = 1.3 \pm 0.3$). The rate of reaction was 1st order in alcohol and independent of RuO_4, indicating that the rate determining step was prior to oxidation. Electron donating groups increased the rate of reaction. The rate was proportional to acidity and two products, acetone (77%) and acetaldehyde (22%) were obtained. The products suggest that the carbonium ion exists in equilibrium with propene, which would be oxidatively cleaved to yield acetaldehyde (scheme 3).

Lee[11] later established that RuO_4 oxidized cyclobutanol by a pair of successive 2 electron transfer steps. This was based on the work of Rocek who displayed that

cyclobutanol could be used to determine whether an oxidant acts as a one or a two electron donor. The observation that cyclobutanone was the only product in carbon tetrachloride suggested a pair of successive two electron transfers, consistent with Lee's[7] previous mechanism (scheme 4).



Scheme 4

The final product of the reaction is $Ru^{IV}O_2$. The intermediate ruthenium(VI) species must be further reduced by a reaction with a second mole of alcohol in another two electron transfer step. The reactivity of $H_2[RuO_4]$ in carbon tetrachloride is presumably much greater than that of $[RuO_4]^{2-}$ in aqueous solution, thus explaining why $H_2[RuO_4]$ could never be detected by spectroscopic or other means.

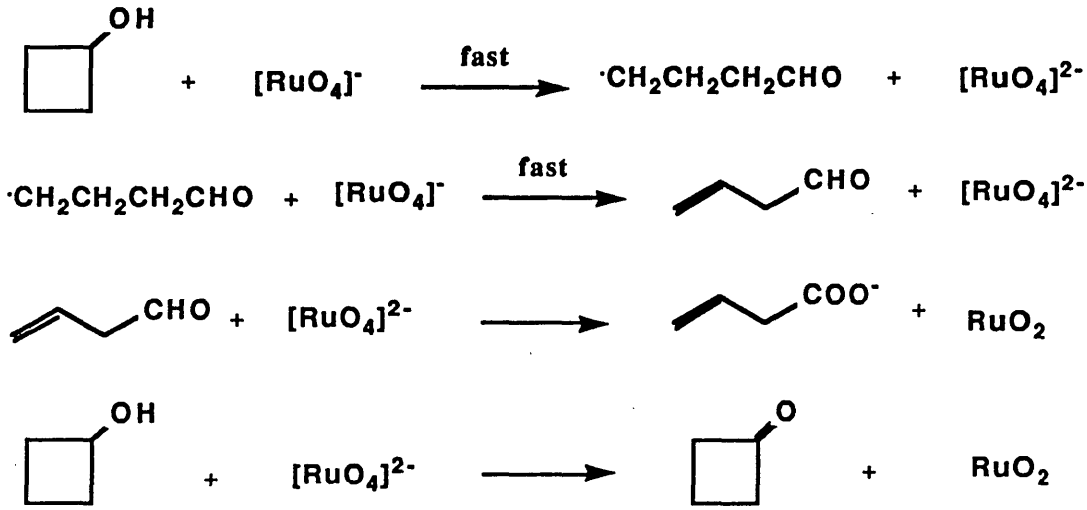
(ii) Ruthenate $[RuO_4]^{2-}$ and Perruthenate $[RuO_4]^-$ Oxidation of Alcohols

There has been some doubt as to the species involved in the sodium ruthenate oxidation of alcohols. In basic solutions below pH 12 the perruthenate ion $[RuO_4]^-$ is stable. Burke and Healy[13] originally postulated $[RuO_4]^-$ as the reactive species; this has since been disproved by Griffith[15] and Lee[14] independently.

The oxidation of 2-propanol was shown to be 1st order with respect to alcohol and ruthenate ion. Perruthenate could only arise *via* disproportionation of ruthenate, (impossible since the reaction is 1st order in ruthenate) or the presence of traces of impurity, eg. IO^{4-} or ClO^- causing reduction of the $[RuO_4]^-$ ion. However distilled RuO_4 used for making $[RuO_4]^{2-}$ reacted at the same rate. Addition of sodium periodate to a reaction did produce some perruthenate; when propan-2-ol was added the $[RuO_4]^-$ was reduced to $[RuO_4]^{2-}$ and the the reaction proceeded at the same rate as those which contained no $NaIO_4$.

Several workers have cited product evidence against the involvement of

perruthenate.[14,15] Under aqueous basic conditions perruthenate is known to cleave double bonds;[15,16] but ruthenate will not react with an alkene unless heated to 85°C with an activated alkene.[6] In fact ruthenate solutions have often been used to oxidize unsaturated alcohols,[17] without cleavage of the double bond. The products obtained from cyclobutanol oxidation are also definitive. With classic one-electron transfer agents such as Cr(IV), Ce(IV), Mn(II), and V(V), carbon-carbon cleavage occurs and non-cyclic products are obtained. With two electron oxidants such as Cr(VI) and Cr(V) cyclobutanone is the major product. When cyclobutanol was oxidized by $Na_2[RuO_4]$, cyclobutanone was obtained in quantitative yield. However, using $Na[RuO_4]$, as oxidant the maximum yield of cyclobutanone was 33%.[14,15] Furthermore the $[RuO_4]^-$ oxidation was observed to pass through two distinct steps, initially involving rapid reduction to $[RuO_4]^{2-}$, which then reacts more slowly to give RuO_2 (scheme 5). When the second stage was eliminated by quenching with sodium arsenate, before slow oxidation commenced, very little cyclobutanone was obtained.[14]

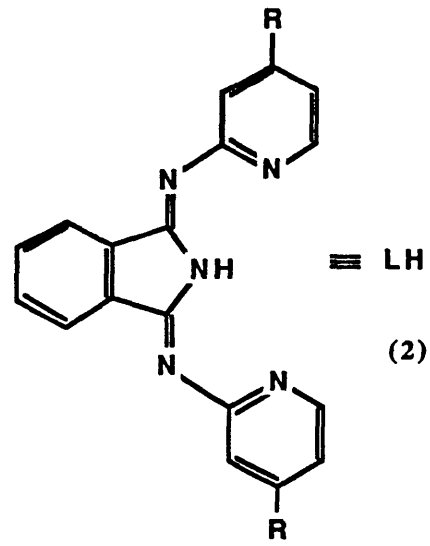


Scheme 5

Thus we can assume that in aqueous base, ruthenate is a two electron oxidant and perruthenate an initial one electron oxidant and an overall three electron oxidant; also perruthenate is not an active species in stoichiometric ruthenate oxidations. However all the above work applied to stoichiometric systems, and under catalytic conditions the presence of perruthenate cannot be totally discounted. The importance of perruthenate may well be a function of pH, with $[RuO_4]^-$ being stable between 7 and 12 and $[RuO_4]^{2-}$ being stable in more basic solutions above pH 12.

(iii) Ruthenium(III) Complexes as Catalysts in the Oxidation of Alcohols

The work of Gagne and Marks[18] stands alone between the pioneering work of Lee[7,6,11,14,16] and the most recent mechanistic work. The ruthenium complex (1,3-bis(4-methyl-2-pyrimidylimino)isoindoline) trichlororuthenium(III) (1) catalyses the aerobic oxidation of alcohols in basic solution at 70°C. Primary and secondary alcohols are oxidized to the aldehyde and ketone respectively. The complex (1) contains a ruthenium(III) cation bound to a neutral tridentate isoindolene ligand (2) and three chloride ions, forming a psuedo octahedral environment around the metal ion. It is not known whether the proton is associated with the pyrrole nitrogen or one of the imine nitrogens. A study of the reactivity of (1) was undertaken in order to probe the mechanism of oxidation.

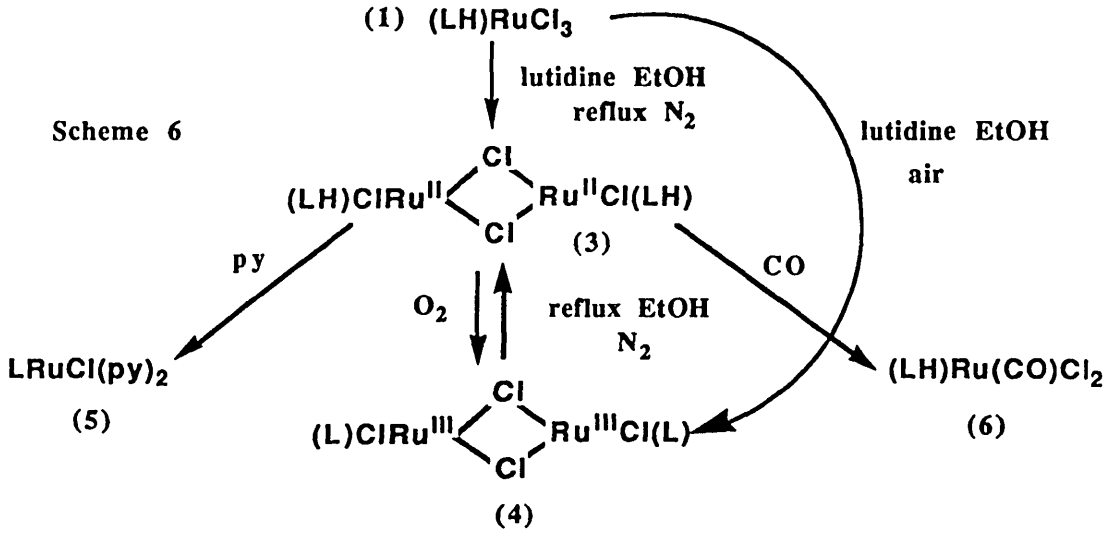


≡ LH

(2)

The complex reacts as shown in scheme 6 with ethanol in the presence of a base (lutidine) to yield the ruthenium(II) chloro-bridged dimer (3). The dimer complex (3) forms the neutral complex (5) on reaction with pyridine, which suggests that pyridine is a strong enough base to deprotonate the ligand. On exposure to carbon monoxide the monomeric Ru(II) complex (6) is formed. Oxygen uptake by (3) at room temperature gave a stoichiometry of 0.25 O_2/Ru, suggesting a simple one electron oxidation of each Ru atom to yield the dimer (4), which could also be prepared by stirring (1) in ethanol and base under oxygen at room temperature. The Ru(III) dimer (4) can be converted to the Ru(II) dimer (3) upon heating in ethanol for 20 hours in the absence of air. The insoluble Ru(II) dimer (3) does not form when the base used is sodium ethoxide.

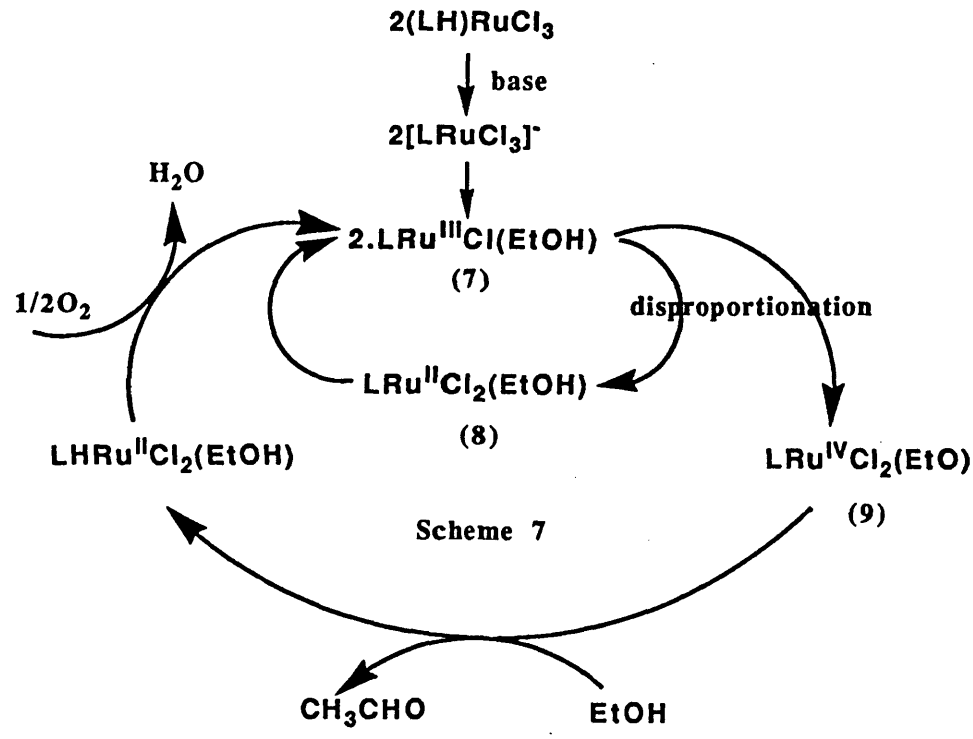
Scheme 6



The following observations were noted during oxidations: The catalytic reaction goes faster when a stronger base is used; stoichiometric oxidation occurs in an oxygen free atmosphere; and the use of a coordinating base hinders the catalytic oxidation. A possible pathway could be written for oxidation involving the dimeric complexes as intermediates. The oxidation of ethanol to acetaldehyde is a two electron process, being formally attributed to a one electron change per metal centre Ru(II/III) in the dimer complex. However this pathway seems unlikely as the dimer complexes are insoluble and no insoluble material was observed at any time upon oxidation. A more likely scheme was proposed, consistent with all the evidence (scheme 7).

The dissolution in basic ethanol leads to deprotonation of the ligand, and the resulting complexes were observed electrochemically. Cyclic voltammograms of solutions of $LHRuCl_3$ in acetonitrile suggested that chloride ion may be readily replaced by a solvent molecule. Furthermore the loss of chloride is suggested by the formation of dimers in ethanol. The complex (7) could be the precursor to the isolated complex (4). The first step in the proposed catalytic cycle is the disproportionation of (7) to (8) and (9). This would account for the fact that O_2 is not needed for stoichiometric oxidation. The disproportionation of Ru(III) complexes is well known.[19] The disproportionation, observed together with subsequent oxidation by the formed Ru(IV) species, is also favoured by basic solutions, in which the alcohol in the Ru(IV) species would be largely deprotonated. The disproportionation equilibrium would also be

favored by protonation of the Ru(II) species (8) . The Ru(IV) species (9) then functions as a two electron oxidant, oxidizing the coordinated alkoxide or alcohol to the aldehyde or ketone. It has been suggested that the reaction proceeds through a β-hydride transfer, forming a ruthenium hydride, and this has been observed for other systems.[20] Hydride transfer could occur, although no evidence of a hydride intermediate was observed. (Meyer[21] has shown hydride transfer to be the mechanism in the oxidation of alcohols by $[Ru^{IV}=O]^{2+}$ species.) The Ru(II) complex (8) formed by disproportionation and by oxidation, may be oxidized by O_2 to complete the catalytic cycle. The reaction of the isolated dimer (3) with oxygen supports this postulate.



Scheme 7

The Hydride Transfer Mechanism in the Oxidation of Alcohols by Ruthenium (IV)Complexes

The kinetics of oxidation of a series of alcohols by $[(bpy)_2(py)Ru^{IV}(O)]^{2+}$ (bpy = 2,2'-bipyridine) in acetonitrile and aqueous solution were studied by Meyer[21] and co-workers. The reactions are 1st order in both alcohol and $[Ru^{IV}=O]^{2+}$. Large C-H isotope effects are observed but solvent isotope effects are negligible. Spectral evidence in conjugation with isotope effect data, suggests that oxidation of alcohols occurs by a

two electron hydride transfer mechanism:

$$[Ru^{VI}=O]^{2+} + R_1R_2CHOH \longrightarrow Ru^{II}\text{-}OH_2^{+} + R_1R_2C=O$$

The possibility of a one electron transfer was discounted using stopped flow experiments. Also, oxidation of cyclobutanol by a similar complex $[(trpy)_2(py)Ru^{IV}(O)]^{2+}$ gives cyclobutanone as the major product,[22] a result indicative of a two electron oxidant. Meyer[21] attempts to fathom the intimate nature of the hydride transfer mechanism by assessing the vibrationally induced electronic coupling.

2.2b Recent Advances in Ruthenium Oxidative Chemistry

Introduction

There are several transcripts on the stoichiometric and catalytic oxidation reactions of ruthenium tetroxide,[1,23,24,25] sodium ruthenate,[14,15,23] and sodium perruthenate.[15,16] $RuCl_3$,RuO_2 and Ru metal have also been used in conjunction with various co-oxidants.[26]

The scope of reactivity of oxidative ruthenium complexes can be divided into two basic reactions: (i) hydride or hydrogen atom abstraction leading to oxidation of alcohols or (ii) oxo transfer leading to epoxidation, oxidative cleavage of double bonds, allylic oxygen insertion and ultimately hydroxylation of alkanes. The latter has been shown to proceed with high stereoselectivity using chromic acid.[27]

(i) Oxidation of Alcohols

Ruthenium tetroxide generated *in situ* from activated RuO_2[28] or from periodate[29] and hypochlorite[28] in a water/chloroform system is a general method for the oxidation of sugars. However the reactions do not work well for alcohols which have low solubilities in water. This problem has been circumvented by Kiely[30] by the use of 1 mole% of the phase transfer catalyst benzyltriethyl ammonium chloride.

Drago[31] and co-workers have developed a trinuclear ruthenium carboxylate catalyst , $Ru^{III}O(O_2CR)_6L_3^n$ (R = CH_3 or C_2H_5; L = H_2O or PPh_3; n = 0, +1). It is an efficient catalyst for the selective oxidation of primary alcohols and secondary alcohols

to the aldehydes and ketones respectively, catalysed aerobically under mild conditions. Catalysis by these complexes is thought to involve intramolecular disproportionation, precluding the need for basic conditions required by the proposed Ru(III) disproportionation system of Gagne and Marks.[18] The catalysis may well involve the reduced Ru(III)Ru(III)Ru(II) trimer as an intermediate.[32]

The study of ruthenium oxo complexes as active electrocatalysts is a matter of current interest.[33] Anson and co-workers[33] have shown that the Ru(IV) complexes *trans*-$[Ru^{IV}(TMC)O(NCO)]ClO_4$ and *trans*-$[Ru^{IV}(TMC)O(N_3)]ClO_4$ (tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetra-azacyclotetradecane) are active catalysts for the oxidation of benzyl alcohol to the aldehyde in acetonitrile (scheme 8). The catalysts gradually lose their activity; this is attributed to the spoiling decomposition reactions observed on oxidation to the Ru(V) state.

The presence of the oxo ligand appears to be necessary but insufficient to obtain an active catalyst alone. Indeed *trans*-$[Ru^{VI}(TMC)(O)_2]^{2+}$ [34] and *trans*-$[Ru^{V}(TMC)(O)_2]^{2+}$ [35] are both relatively unreactive towards benzyl alcohol. The reason probably lies simply in the weaker oxidizing power of the complexes.

$$Ru^{IV} - e^- \longrightarrow Ru^{V}$$

$$Ru^{V} + PhCH_2OH \xrightarrow{slow} Ru^{IV} + PhC{\cdot}HOH + H^+$$

$$Ru^{V} + PhC{\cdot}HOH \xrightarrow{fast} Ru^{IV} + PhCHO + H^+$$

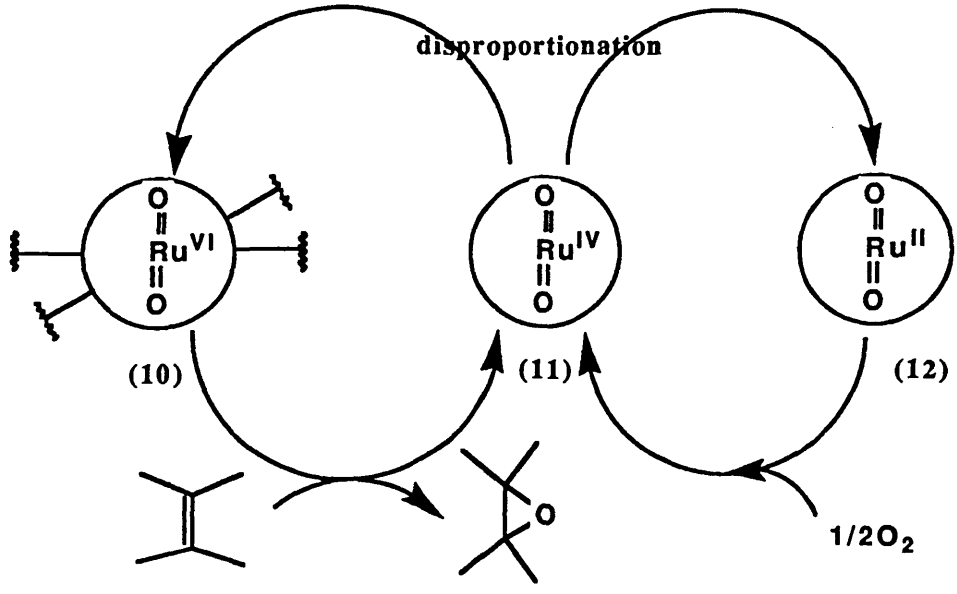
Scheme 8

The ligand *trans* to the oxo group in the Ru(V) mono oxo complexes seems to exert a strong effect on the reactivity. Ligands such as chlorine *trans* to the oxo group make the complex a stronger oxidant, than for example a *trans* oxo (dioxo) or nitrogen donor ligand. This could help to explain why the rates of catalysed oxidation do respond simply to to changes in the oxidizing strength, as possible $p\pi^*(Ru) - p\pi(O)$ interactions may change the ability of the oxo group to help stabilize the departing proton of the alcohol.

(ii) Epoxidation of Alkenes

The behaviour of oxidants can be modified by coordinating an electron rich ligand to the metal centre, thus increasing the basicity of the metal centre and moderating its oxidizing power. Balavoine and co-workers[36] exploited the $RuCl_3$/periodate[15] system by adding bipyridyl as a ligand before addition of the alcohol. Good yields of epoxide were isolated except in the case of terminal double bonds. The likely mechanism seems to be transfer of oxygen to a $Ru_2(bipy)_2$ type complex from iodate. The metal oxo intermediate[37] then transfers oxygen to the alkene. Sharpless[38] has proposed oxametallocycles as possible intermediates in this process.

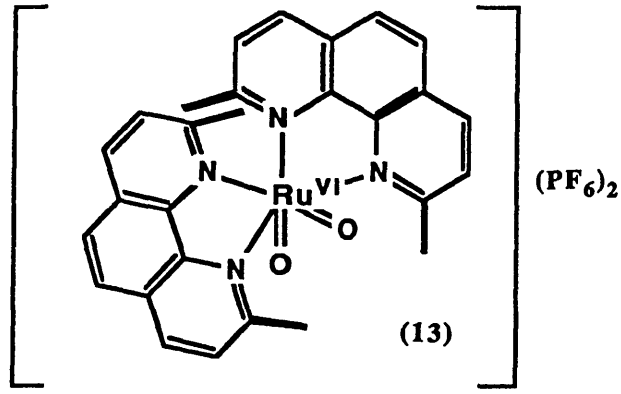
Groves and Quinn[39] have discovered that dioxo(tetramesitylporphorinato) ruthenium(VI) [$Ru^{VI}(TMP)(O)_2$] catalyses the aerobic epoxidations of alkenes at room temperature and pressure. Subsequent work showed that the *ortho* buttressing of the TMP ligand was essential for catalytic activity (scheme 9) and indeed the tetra-*p*-tolyl-porphyrin $Ru(TTP)(THF)_2$, which forms the μ-oxo dimer on oxygenation,[40] was found to be totally inactive. A possible catalytic cycle was proposed (scheme 9). The initially formed Ru^{IV}=O complex (11) disproportionates to the Ru(II) (12) and Ru(VI) dioxo compound (10). Thus complex (12) is the active species towards O_2 and complex (10) is the active epoxidative species.



Scheme 9

The Ru(VI) dioxo unit has been prepared by other workers and found to be an efficient oxygen transfer reagent. Kochi[41] reported compounds of the type *trans*-$(O_2)Ru(py)_2(OAc)_2$ and found that triphenylphosphine is oxidized to triphenyl phosphine oxide and that cyclohexene yields cyclohexanone (40%) and small amounts of cyclohexene oxide. The major product is thought to arise from prior allylic insertion of oxygen into cyclohexene.[42]

Drago[43] has found that the sterically crowded Ru(VI) complex (13) is an efficient catalyst for the oxidation of alkenes by dioxygen. Not suprisingly the complex is very similar in reactivity to the $[Ru^{VI}(TMP)(O)_2]$ complex of Groves and Quinn.[39]



(13)

Che and co-workers[44,45,46] have recently reported an array of ruthenium oxo complexes: The complex $[Ru^{III}(N_4O)(OH_2)][ClO_4]_2$ (N_4OH = Bis[2-(2-pyridyl)ethyl] [2-hydroxy-2-(2-pyridyl)ethyl]-amine)[44] induces the transfer of oxygen to alkenes from iodosylbenzene (PhIO) via the intermediate Ru^V=O species. The epoxide is the major product.

The complex $[Ru^{IV}(chbae)(PPh_3)(py)]$[45] ($chbaeH_4$ = 1,2-bis(3,5-dichloro-2-hydroxy benzamido)ethane) also catalyses the oxidation of alkenes in the presence of PhIO. With cyclohexene both the C-H and the C-C bonds were attacked, resulting in cyclohexene oxide (10%) and cyclohexenone (11%). The reactive species was thought to be the Ru^{VI}=O complex.

2.3 Studies with Tetra-Alkylammonium Perruthenates as Catalysts for the Oxidation of Alcohols

Introduction

The oxidation of the hydroxyl group is one of the most common and important transformations in organic synthesis. The development of new oxidative systems is essential with the expanding needs of the synthetic chemist. There are many factors that influence the choice of oxidizing agent, such as: ease of handling, disposal of excess or noxious side products, selectivity and cost. A versatile catalytic system is the obvious goal if a method is to compete with the commonly used Swern procedure[47] or chromium reagents.[48]

2.3a The Catalytic System

The use of tetra-*n*-butylammonium perruthenate as a stoichiometric oxidant has been reported.[49] A highly successful catalytic system has been developed using tetra-*n*-butyl (*n*-Bu4N)[RuO4] (TBAP) or tetra-*n*-propylammonium perruthenate (*n*-Pr4N)[RuO4] (TPAP) as the catalytic oxidant,[50] with N-methylmorpholine-N-oxide as co-oxidant. The choice of tetra-alkyl ammonium ion as cation (tetra-*n*-butyl or tetra-*n*-propyl ammonium) allowed the system to be used in an organic solvent, dichloromethane. The reagents are easy to use, applicable to a wide range of substrates and selectively oxidize primary alcohols to aldehydes and secondary alcohols to ketones.

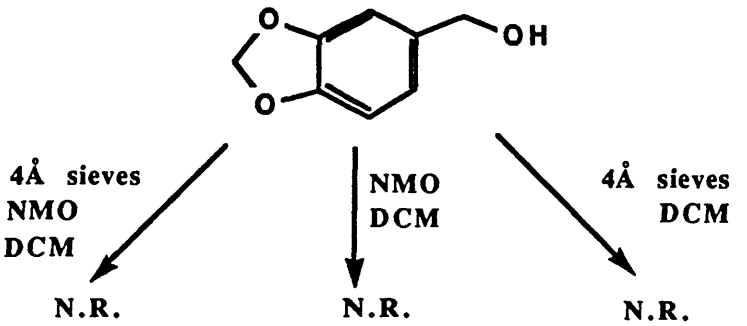
The oxidation experiments are listed in Table 1. Labile functional groups such as epoxides, tetrahydropyranyl ethers, silyl ethers, esters, double bonds and indoles remain intact. The oxidation of alcohols containing α-chiral centres gave products without any detectable racemisation. Entry 28 shows the oxidation of (-)[2S]methyl-3-*t*-butyldiphenylsilyloxy-2-methylpropanol; the rotation of the aldehyde product was $[\alpha]_D$ = -25.3° [c=2.81,$CHCl_3$], using the TPAP procedure. The Swern procedure on a large scale racemises the product, giving rotations of less than $[\alpha]_D$ = -3°. The oxidation of compounds containing double bonds (Entries 5,6,7) proceed in good yield without attack of the double bond. This is interesting as sodium perruthenate in

aqueous dilute base is known to cleave double bonds.[15,16] Obviously the organic soluble system is much more selective.

The oxidations generally proceed rapidly at room temperature (0.2 - 6 hours) in dichloromethane using less than 0.5 mole% of TPAP or TBAP. The addition of 4Å molecular sieves is beneficial since they remove the water formed in the reaction and the water of crystallization of the N-methyl-morpholine-N-oxide (NMO). Pre-dried NMO is of course preferable, it is best dried with $MgSO_4$ in a dichloromethane solution prior to use as the solid anhydrous NMO is extremely hygroscopic.

N-methyl-morpholine-N-oxide has been used successfully in other catalytic systems as a co-oxidant.[51,52] It can be prepared from N-methylmorpholine[52] or bought very cheaply as an aqueous solution which can be dried.

Control experiments were performed with piperonyl alcohol (scheme 10). The alcohol was stirred with combinations of the other reagents in the reaction apart from the catalyst. The negative results proving that $R_4N[RuO_4]$ is, or generates, the reactive species.



Scheme 10

The early experiments were done using TBAP prepared by a fusion route. Ruthenium trichloride is fused with potassium nitrate and potassium hydroxide to give the ruthenate species $[RuO_4]^{2-}$, which on dissolution in water, is then oxidized to perruthenate with chlorine. The precipitate of potassium perruthenate was dissolved in water and treated with tetra-*n*-butylammonium hydroxide. The green precipitate of TBAP is collected and washed with water immediately after preparation. The immediate work-up was essential as different batches of Aldrich tetra-*n*-butylammonium hydroxide did not generally behave similarly; this could possibly be due to trace alcohol impurities.

This problem was circumvented by the development of a "one-pot" procedure for the large scale preparation of tetra-*n*-propylammonium perruthenate (TPAP). Ruthenium trichloride was stirred with sodium periodate for 6 hours to generate RuO_4 *in situ* which was then bubbled into a cooled 1*M* solution of KOH, containing tetra-*n*-propylammonium hydroxide. The green TPAP product was filtered off and the process repeated until the RuO_4 was exhausted. The Aldrich *n*-$Pr_4N.OH$ seemed to be much more reliable than the corresponding *n*-butyl analogue, though this may of course be due to the fact that the immediate ruthenium precursor in the two preparative methods is different.

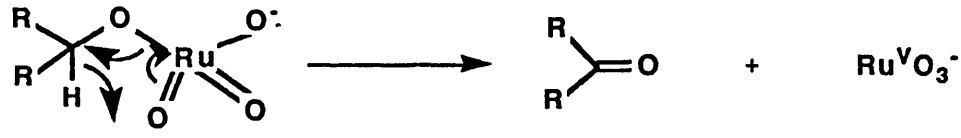
tert-Butylhydroperoxide (*t*-BuOOH), was also used successfully as a co-oxidant for the oxidation of piperonyl alcohol, but with some substrates the reaction proved too vigorous and even ignited in one case with 3-methylbutan-1-ol. Analysis of the reaction by g.l.c. with other "more controlled" simple substrates showed the reaction was not as selective and gave a variety of products.

2.3b The Reaction Mechanism

The perruthenate system has been shown by stoichiometric oxidations of piperonyl alcohol to be a three electron oxidant. However the oxidation of cyclobutanol proceeds to give one product, cyclobutanone in high yield (Entry 16). This is in direct contrast to Rocek's proposals[12]: an odd electron oxidant is supposed to yield a number of products *via* radical mechanisms and an even electron oxidant provides one product, cyclobutanone by two electron oxidation.

It is speculative to propose mechanisms for oxidative reactions of this nature without detailed mechanistic work. The chromium alcohol oxidation mechanism has been revised several times.[53] However it is tempting to suggest a two electron oxidation of alcohol by $[Ru^{VII}O_4]^-$ to generate an Ru(V) species which could then combine with an unreacted Ru(VII) species to yield two Ru(VI) species which could then oxidize another mole of alcohol *via* a two electron pathway. This thermodynamically unfavourable process would need to be faster than any process by which Ru(V) could generate radical intermediates by hydrogen atom abstraction.

The behaviour of perruthenate in the dichloromethane system contrasts vividly with the aqueous results obtained by several workers,[15,16] who report the cleavage of double bonds by $Na[RuO_4]$ and the observance of non-cyclic products in the oxidation of cyclobutanol. The reaction probably proceeds through an intermediate ruthenium ester of the type shown (scheme 11).



Scheme 11

The catalytic system could differ from the stoichiometric one. The reactions do not work as well on a larger scale, and this may well be due to slow decomposition of Ru(V) intermediates negligible on a small scale as the reaction has already gone to completion. Also as the concentration of co-oxidant falls together with the concentration of the remaining alcohol, and the concentration of the coordinatively unsaturated by-product N-methylmorpholine rises as reaction proceeds. Thus there is more chance of an intermediate undergoing another process other than reoxidation to Ru(VII) as the reaction progresses.

Table 1

Alcohol	Product	TBAP % yield	TBAP t/h	TPAP %yield	TPAP t/h
1. *n*-butanol	*n*-butanone	94c	0.8	95c	1
2. *n*-octanol	*n*-octanal	92c	4		
3. 3-methylbutan-1-ol	3-methylbutan-1-al	64c	3		
4. citronellol	citronellal	75a	5		
5. undec-10-en-1-ol	undec-10-en-1-al	70a	3		
7. geraniol	geranial	79b	5		
8. E-cinnamyl alcohol	E-cinnamaldehyde	91a	3	75a	5
9. chrysanthemyl alcohol	chysanthemaldehyde	90a	5	76a	0.5
10. benzyl alcohol	benzaldehyde	80b	2	71a	0.5
11. *o*-chlorobenzyl alcohol	*o*-chlorobenzaldehyde	81b	4		
12. 4-methoxybenzyl alcohol	4-methoxybenzaldehyde			68a	12
13. piperonyl alcohol	piperonal	89b	3	70a	1
14. 2-hydroxybenzyl alcohol	2-hydroxybenzaldehyde	49b	3		
15. hexan-2-ol	hexan-2-one	99c	3		
16. cyclobutanol	cyclobutanone	95c	1.1		

Table 1

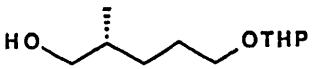
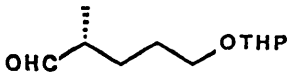
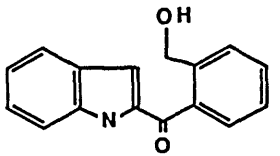
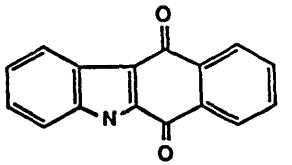
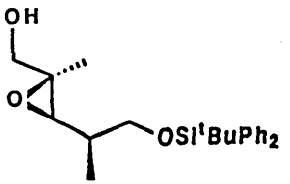
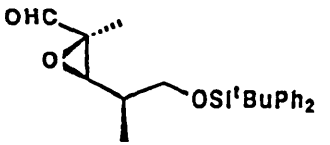
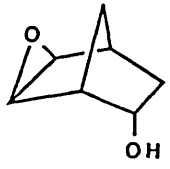
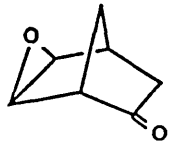
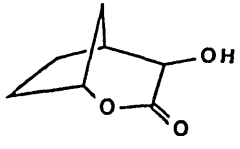
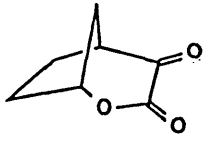
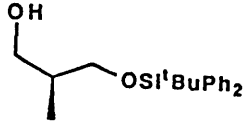
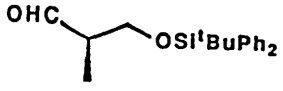
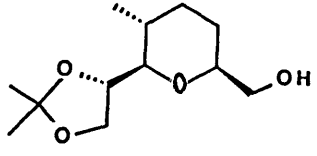
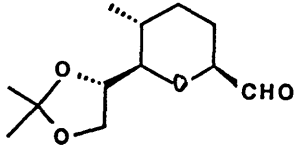
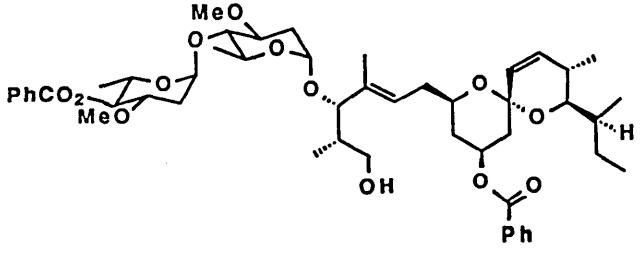
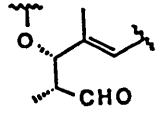
Alcohol	Product	% yield	t/h	%yield	t/h
17. cyclopentanol	cyclopentanone	99c	2.5		
18. cyclohexanol	cyclohexanone	99c	1		
19. (±)-menthol	(±)-menthone	85a	1		
20. *endo*-norborneol	bicyclo[2.2.1]heptan-2-one	73a	0.3		
21. 5α-androstan-17β-ol-3-one	5α-androstan-3,17-dione	96a	6	99a	1.5
22. lanost-8-en-3β-ol	lanost-8-en-3-one	86a	6	81a	1.5
23. 		71a	0.7		
24. 		85a	5		
25. 		64a	0.8	70a	1

Table 1

	Alcohol	Product	% yield	t/h	%yield	t/h
26.			73a	0.5		
27.			80a	1.5		
28.			50a	5	63a	6
29.			50a	1.5		
30.[54]					70a	0.5

a Isolated yield b 2,4 dinitrophenylhydrazone derivative c g.l.c. yield (uncorrected)

2.4 Experimental

Potassium Tetraoxoruthenate(VII)

Ruthenium trichloride $RuCl_3.nH_2O$ (4 g, of hydrate containing 41.6% Ru) was added portionwise to a fused mixture of KOH (6.0 g, 0.107 mol) and KNO_3 (2.0 g, 0.02 mol). The mixture was heated with a bunsen flame for 5 min then allowed to cool to room temperature and dissolved in water (30 ml). The solution was cooled to *ca* 5°C and chlorine gas bubbled in, until a fine black precipitate appeared. (Care must be taken not to over oxidize to RuO_4). The mixture was filtered to give potassium perruthanate, $K[RuO_4]$ (1.06 g, 63%) as a black micro-crystalline product.

Tetra-*n*-Butylammonium Tetraoxoruthenate(VII)

$$KRuO_4 \xrightarrow{n\text{-}Bu_4N.OH} (n\text{-}Bu_4N)[RuO_4]$$

Tetra-*n*-Butylammonium hydroxide (50 ml of a 40% aqueous solution) was added to a solution of potassium perruthenate in water (200 ml) at *ca* 5°C. The mixture was immediately filtered, the filtrate washed with cold water (3 x 10 ml) and dried *in vacuo* to give *n*-$Bu_4N[RuO_4]$ (3.61 g, 91%) as a green solid, (Found : C, 46.4; H, 8.79. $C_{16}H_{36}O_4Ru$ requires C, 47.2; H, 8.90%), $\upsilon_{max.}$ (KBr disc) 832cm^{-1} (asymmetric $Ru{=}O_2$ stretch).

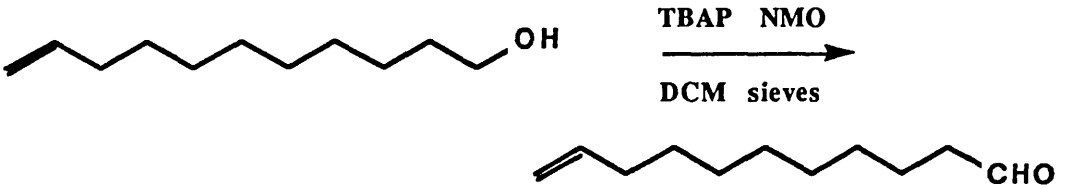
Tetra-*n*-Propylammonium Tetraoxoruthenate(VII)

$$RuCl_3.nH_2O \xrightarrow[\substack{2.\ 1M\ NaOH \\ n\text{-}Pr_4N.OH}]{1.\ NaIO_4} (Pr_4N)[RuO_4]$$

Ruthenium trichloride $RuCl_3.nH_2O$ (1.5 g, of hydrate containing 41.6% Ru) in water (20 ml) was stirred in a sealed flask overnight with a solution of sodium periodate (5.5 g, 26mmol) in water (50 ml). The ruthenium tetroxide formed *in situ* was bubbled with nitrogen pressure into a solution of tetra-*n*-propylammonium hydroxide (5 ml of a 1M aqueous solution) and sodium hydroxide (40 ml of 1*M*

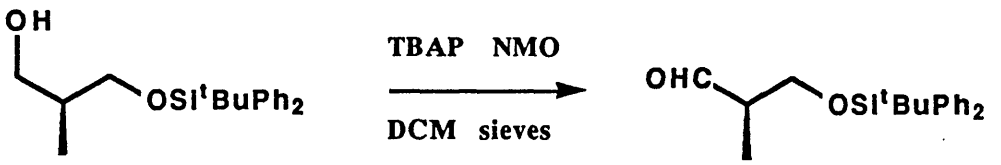
aqueous solution) and water (10 ml) at *ca* 0°C. The precipitate formed was filtered every 15-20 min, washed with cold water (2 x 2 ml) and dried *in vacuo*. The combined residues gave *n*-Pr4N[RuO4] (1.76 g, 87%) as a green solid, (Found : C, 40.7; H, 8.05. $C_{12}H_{28}O_4Ru$ requires C, 41.0; H, 8.03%), $\upsilon_{max.}$ IR (KBr disc) 830cm^{-1} (asymmetric Ru=O_2 stretch), $\upsilon_{max.}$ Raman (KBr disc) 844cm^{-1} (asymmetric Ru=O_2 stretch).

Typical Oxidation with Tetra-*n*-Butylammonium Perruthenate



TBAP (1.9 mg, 1.8 mmol) was added to a stirred solution of undec-10-en-1-ol (44.2 mg, 0.26 mmol) and N-methylmorpholine-N-oxide (53 mg, 1.5 equiv) in dichloromethane (3 ml) with 4Å molecular sieves (0.2 g). The mixture was stirred for 6 hr, diluted with dichloromethane and washed with $Na_2S_2O_3$, $CuSO_4$, water and brine, dried ($MgSO_4$), filtered, concentrated *in vacuo* and purified by column chromatography on silica gel eluting with 2% ether in petrol to give the known undec-10-en-1-al (30.2 mg, 70%) as an oil, δ($CDCl_3$, 90 MHz) 9.78(1H, t, *J* 1.5 Hz, CHO), 5.8(1H, m, 10-H olefinic), 4.98(2H, m, 11-H olefinics), 2.40 (2H, m, 2-H_2), 2.01(2H, m, 9-H_2), 1.6(2H, m, 3-H_2), and 1.35(12H, s, 6 x CH_2).

Typical Oxidation with Tetra-*n*-Propylammonium Perruthenate



For experimental see chapter 3.

The Work-Up

The wash with sulphite or any typical sulphur based aqueous regent, removes the perruthenate from the organic layer into the aqueous layer. The wash with saturated $CuSO_4$ removes the N-methylmorpholine formed in the reaction into the aqueous layer.

The first wash was not always successful, this resulted in formation of a course precipitate on washing with $CuSO_4$. The mixture was then filtered through a pad of celite and the work up continued. The products were either characterized directly as the aldehyde by nmr and infra-red, or the 2,4-dinitrophenylhyrazone derivative made by standard methods. The oxidations of simple or volatile substrates was followed by g.l.c. analysis and the results are uncorrected.

Chapter 2 References

1. D.G.Lee, and M.van den Engh, in "Oxidation in Organic Chemistry Part B", Ed. W.S.Trahanovsky, Chapter 4, Academic Press, New York, 1973.

2. D.G.Lee in "Oxidation, Techniques and Application in Organic Synthesis," Ed. R.L.Augustine, New York, 1979.

3. P.N.Rylander, *Engelhard Ind., Tech. Bull.*, 1969, 9, 135.

4. W.A.Dorset and D.G.Lee, unpublished results.

5. S.Wolfe, S.K.Hasan, and J.R.Campbell, *J. Chem. Soc., D,* 1970, 1420.

6. V.S.Chang, S.Helliwell, and D.G.Lee, *J. Org. Chem.*, 1976, 41, 3646.

7. D.G.Lee, and M.Van den Engh, *Can. J. Chem.*, 1972, 50, 2000.

8. E.J.Strojny, R.T.Iwamasa, and L.K.Frevel, *J. Am. Chem. Soc.*,1971, 93, 1171.

9. R.Brownell, A.Leo, Y.W.Chang, and F.H.Westheimer, *J. Am. Chem. Soc.*,1960, 82, 406.

10. R.E.Connick and D.A.Fine, *J. Am. Chem. Soc.*, 1960, 82, 4187.

11. J.Cleland, D.G.Lee, M.E.Olsen, and U.A.Spitzer, *Can. J. Chem.*, 1976, 54, 2124.

12. J.Rocek and A.E.Radkowsky, *J. Am. Chem. Soc.*, 1973, 95, 7123; J.Rocek and D.E.Aylward, *J. Am. Chem. Soc.*, 1975, 97, 5452; K.Meyer and J.Rocek, *J. Am. Chem. Soc.*,1972, 94, 1209; J.Rocek and A.E.Radkowsky, *J. Org. Chem.*,1973, 38, 89.

13. L.D.Burke and J.F.Healy, *J. Chem. Soc., Dalton Trans.*, 1982, 1091; L.D.Burke and J.F.Healy , *J. Electroanal. Chem.*, 1981, 124, 327.

14. L.N.Congson, D.G.Lee, M.E.Olsen, and U.A.Spitzer, *Can. J. Chem.*, 1984, 62, 1835.

15. G.Green, W.P.Griffith, D.M.Hollinshead, S.V.Ley,and M.Schroder, *J. Chem. Soc., Perkin Trans. I,* 1984, 681.

16. V.S.Chang, S.Helliwell, and D.G.Lee, *J. Org. Chem.*,1976, 41, 3644.

17. S.Chandrasekaran, E.J.Corey, R.L.Danheiser, B.Gopalan, J.-L.Gras, G.E.Keck, S.D.Larsen, and P.Siret, *J. Am. Chem. Soc.*, 1978, 100, 8034;

T.A.Foglia and Y. Nakano, *J. Am. Oil. Chem. Soc.*, 1982, 59, 163.

18. R.R.Gagne and D.N.Marks, *Inorg. Chem.*,1984, 23, 65.

19. D.P.Rudd and H.Taube, *Inorg. Chem.*,1971, 10, 1543; S.E.Diamond, F.Mares, and B.S.Jovrog, *J. Am. Chem. Soc.*, 1979, 101, 5067.

20. A.Dobson and S.D. Robinson, *Inorg. Chem.*,1977, 16, 137; S.E.Diamond and F.Mares, *Organomet. Chem.*, 1977, 142, C55; J.Chat, A.E.Field, and B.L.Shaw, *J. Chem. Soc.*, 1964, 3466.

21. T.J.Meyer and L.Roecker, *J. Am. Chem. Soc.*, 1987, 109, 746, and references therein.

22. T.J.Meyer and M.S.Thompson, *J. Am. Chem. Soc.*, 1982, 104, 4106.

23. "Gmelin Handbook, Pt Supp., " Vol A1, pg. 261, Springer-Verlag.

24. H. Mimoun in "Comprehensive Coordination Chemistry," Vol. 61.3, in press.

25. P.Muller, in "The Chemistry of the Functional Groups Ethers, Crown Ethers, and Hydroxyl Groups", Ed. S.Patai, Vol 1, 1980, 493.

26. M.Dubeck and K.A.Keblys, Ethyl Corp., 1968, U.S. 3 409 649.

27. K.B.Wiberg and G.Foster, *J. Am. Chem. Soc.*,1961, 83, 423.

28. C.P.Bryant and C.L.Stevens, *Methods Carbohydr. Chem.*, 1972, 6, 337.

29. D.C.Baker, D.Horton, and C.G.Tindall,Jr., *Methods Carbohydr. Chem.*, 1976, 7, 3.

30. D.E.Kiely and P.E.Morris, *J. Org. Chem.*, 1987, 52, 1149.

31. C.Bilgrien, S.Davies, and R.S.Drago, *J. Am. Chem. Soc.*,1987, 109, 3786.

32. A.Spencer and G.Wilkinson, *J. Chem. Soc., Dalton Trans.*, 1972, 1570.

33. F.C.Anson, C.M.Che, and K.Y.Wong, *Inorg. Chem.*,1987, 26, 737; and references therein.

34. C.M.Che, C.K.Poon, and K.Y.Wong, *Inorg. Chem.*, 1985, 24, 1797.

35. C.M.Che and K.Y.Wong, *J. Chem. Soc., Chem. Commun.*, 1986, 229.

36. G.Balavoine, C.Eskenazi, F.Meunier, and H.Riviere, *Tetrahedron Lett.*, 1984, 25, 3187.

37. T.J.Meyer and B.A.Moyer, *Inorg. Chem.*,1981, 20, 436.

38. J.-E.Backwall, K.B.Sharpless, and A.Y.Teranishi, *J. Am. Chem. Soc.*, 1977,

92, 3120; H.Mimoun, L.Sajus, and I.Serree de Roch,*Tetrahedron,* 1970, 26, 37.

39. J.T.Groves and R.Quinn, *J. Am. Chem. Soc.,* 1985, 107, 5790.

40. C.E.Barnes, P.J.Brothers, T.J.Collins, J.P.Collman, J.C.Gallucci, J.A.Ibers, and T.Ozawa, *J. Am. Chem. Soc.,* 1984, 106, 5151.

41. J.K.Kochi and T.C.Lau, *J. Chem. Soc., Chem. Commun.,* 1987, 798.

42. J.K.Kochi, P.M.Michaud, and K.Srinivasan, *J. Am. Chem. Soc.,* 1986, 108, 2309.

43. C.L.Bailey and R.S.Drago, *J. Chem. Soc., Chem. Commun.,* 1987, 179.

44. C.M.Che and V.W.W.Yam, *J. Am. Chem. Soc.,*1987, 109, 1262.

45.C.M.Che, W.K.Cheng, W.H.Leung, and T.C.W.Mak, *J. Chem. Soc., Chem. Commun.,* 1987, 418.

46. C.M.Che, W.H.Leung, and C.K.Poon, *J. Chem. Soc., Chem. Commun.,* 1987, 173.

47. A.J.Mancuso, and D.Swern, *Synthesis,* 1981, 165.

48. M.D'Duria, G.Piancatelli, and A.Scettri, *Synthesis,* 1982, 245; E.J.Corey and G.Schmidt, *Tetrahedron Lett.,* 1979, 20, 399; *ibid.,*1980, 21, 731.

49. A.C.Dengel, W.P.Griffith, and R.A.Hudson, *Transition Met. Chem.,* 1985, 10, 98.

50. W.P.Griffith, S.V.Ley, G.P.Whitcombe, and A.D.White, *J. Chem. Soc., Chem. Commun.,* 1987, 1625.

51. K.Akashi, K.Oshima, and K.B.Sharpless, *Tetrahedron Lett.,* 1976, 27, 2503.

52. V.VanRheenen, R.C.Kelly, and D.Y.Cha, *Tetrahedron Lett.,*1976, 27, 1973.

53. K.B.Wiberg in "Oxidation in Organic Chemistry Part A," Chapter 2, Ed. K.B.Wiberg, Academic Press, London, 1965; J.Rocek and A.E.Radkowsky, *J. Am. Chem. Soc.,* 1973, 95, 7123.

54. Experiment performed by S.Mukherjee.

Chapter 3. Iron

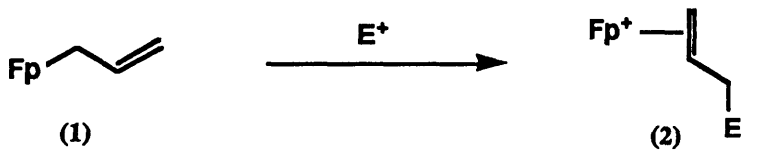
3.1 Recent Developments in the Use of Organoiron Compounds in Organic Synthesis

Introduction

The use of organometallics in organic synthesis has been expanding rapidly for the past 15 years. The use of organoiron complexes has been reviewed extensively and this work covers the highlights of the past three and a half years. The review deals with the different types of iron complexes separately.

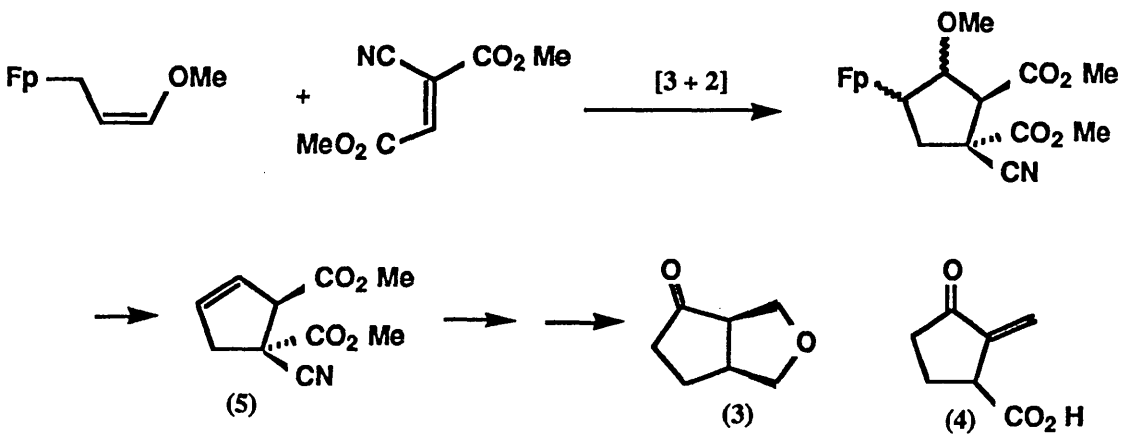
3.1a σ-Allyl-irondicarbonyl-η^5-cyclopentadienyl Complexes

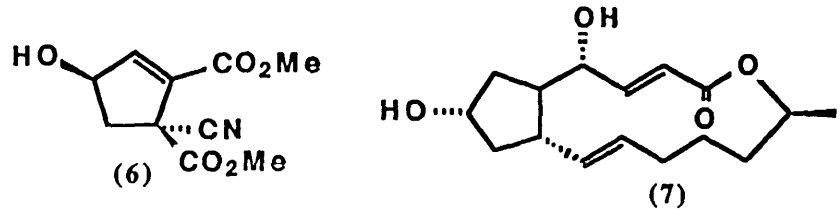
The metal allyl system (1) is a nucleophilic species interacting with electrophiles to form cationic η^2-Fp(alkene) complexes (2) (Fp = $Fe(CO)_2$-η^5-C_5H_5) which undergo subsequent cycloaddition reactions, or straightforward nucleophilic reactions. (scheme1)



Scheme 1

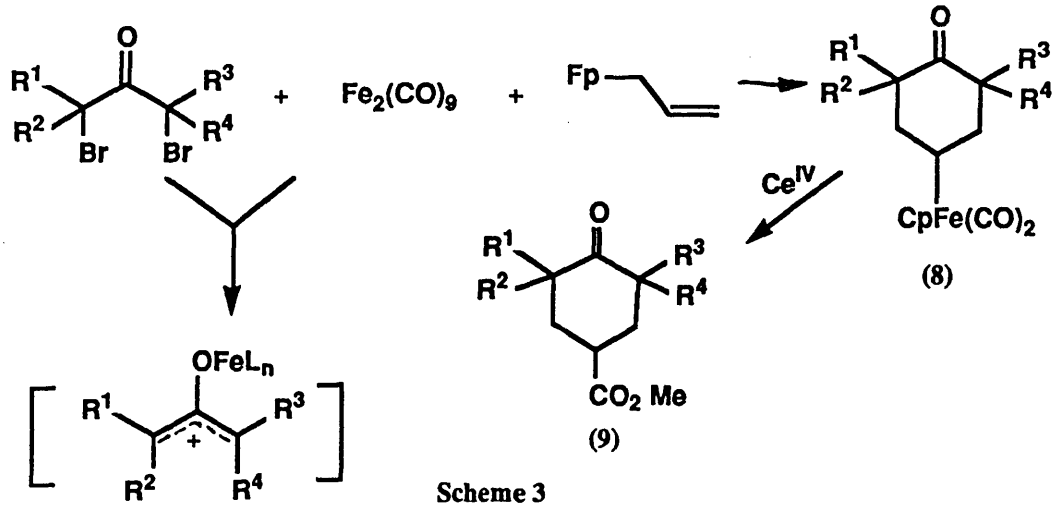
The [3+2] cycloaddition with electron deficient alkenes has been applied to a plethora of olefinic substrates[1a], but Baker[2] and co-workers have made an intermediate (3) which is a direct precursor to the anti tumor agent sarkomycin[3] (4) (scheme 2). Elaboration of the intermediate (5) to (6) by treatment with *t*-butylhydroperoxide yields a possible intermediate for the synthesis of Brefeldin A[4](7).





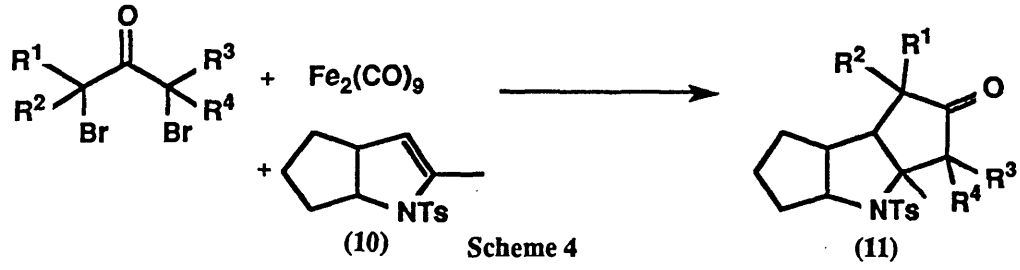
Scheme 2

The [3+2] cycloaddition reactions of the cationic oxy allyl unit have been extensively employed.[1b] However Hegedus[5] has used the η^1-allyl-Fp system in a novel [3+3] cycloaddition with the "ambiphilic" cationic oxy allyl complex obtained from $Fe_2(CO)_9$ and α,α-dihaloketones to give 6 membered rings (9) (scheme 3).



Scheme 3

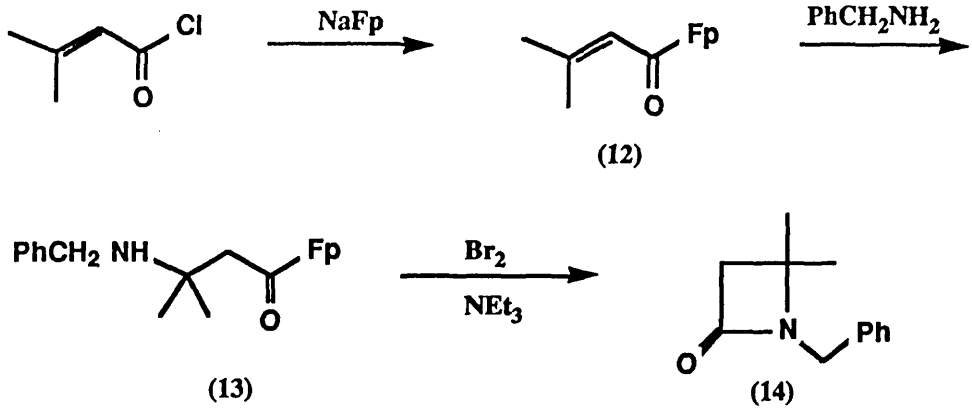
The reaction suffers from the same limitations as the [3+2] series in that only α-substituted ketone substrates work. The crude σ-alkyl iron species (8) are oxidized to the esters with concommitant carbon monoxide insertion. Fused cyclopentanones[5] (11) were made by [3+2] cycloaddition reaction with the N-tosyl enamine[6] (10) (scheme 4). Again only geminally alkylated products are possible *via* these reactions.



Scheme 4

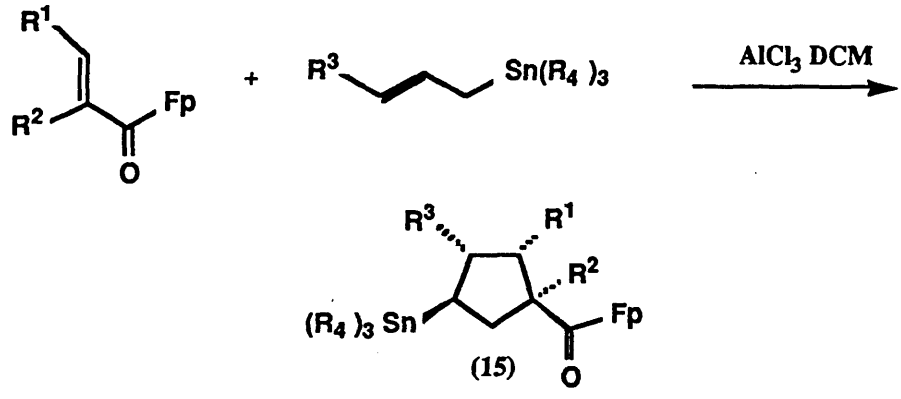
Michael type addition of amines to α,β-enoyl Fp substrates (12) has resulted in the synthesis of β-lactams[7] (14). The Fp compound made from the requisite acid

chloride is treated with an an amine generating the β-aminoalkanoyl complex (13) which on treatment with bromine in the presence of triethylamine generates the β-lactam (14) in good yield (scheme 5).



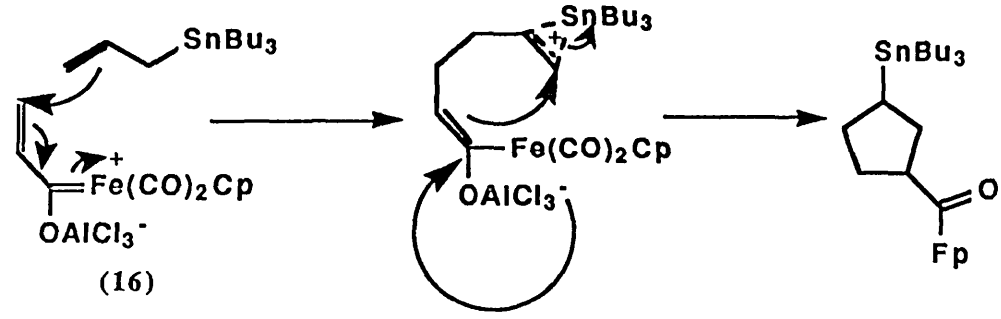
Scheme 5

Herdon[8] has also used α,β-unsaturated acyl iron complexes in a [3+2] cycloaddition reaction with allyl stannanes to synthesise substituted cyclopentanoid derivatives (15) (scheme 6). The allyl stannane reacts at -26°C in the presence of aluminium chloride to give the *cis* stereoisomers in moderate yields.



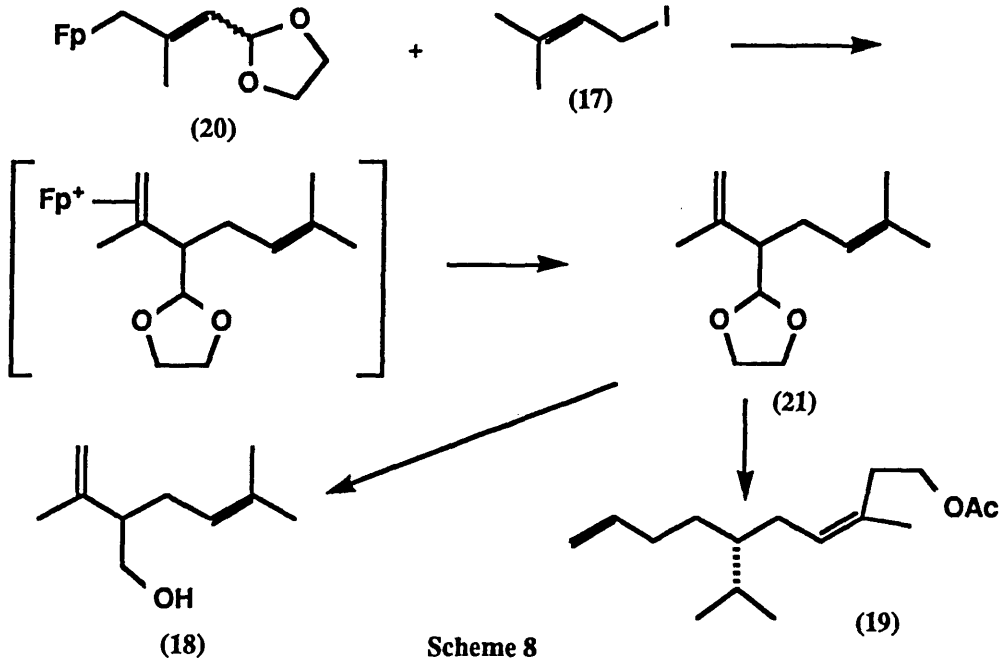
Scheme 6

The mechanism was thought to proceed *via* the carbene complex (16) formed by complexation with $AlCl_3$, followed by electrophilic attack from the allyl stannane giving intermediate tin carbocations stabilised by hyperconjugative interaction[9] with the alkyl tin moiety. Attack by the enolate then affords the product (scheme 7).



Scheme 7

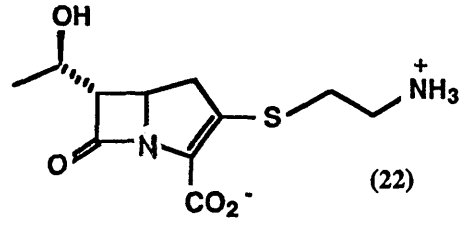
Electrophilic attack of allyl iodide (17) on η^1-allyl Fp complexes has been utilised by Rosenblum[10] in the synthesis of Lavandulol (18) and the red scale pheromone (19). Reaction with the Fp compound (20) results in acetal (21) in 30% yield which can be readily modified further to the two natural products (scheme 8).



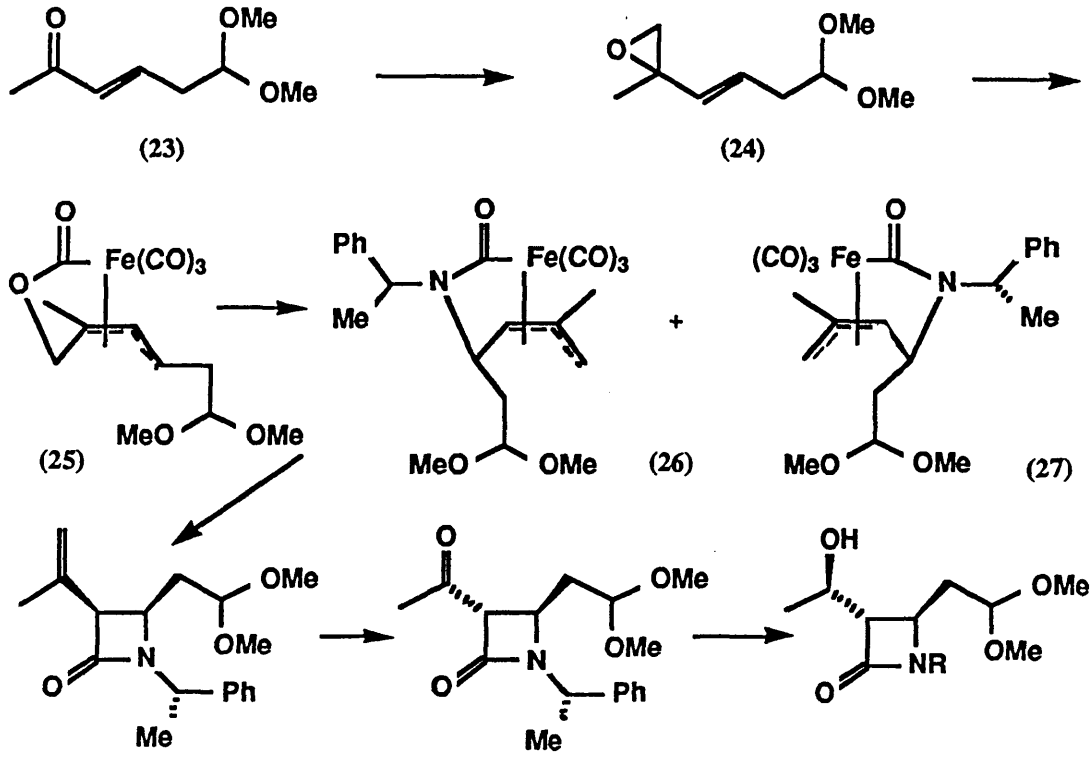
Scheme 8

3.1b η^3-Ferrilactone and Ferrilactam Complexes

π-Allyltricarbonyl lactone (ferrilactone) complexes are useful precursors for the preparation of simple lactones[11] and lactams.[12] The method was applied to the synthesis of (+) thienamycin[13] (22), a β-lactam antibiotic, in these laboratories.

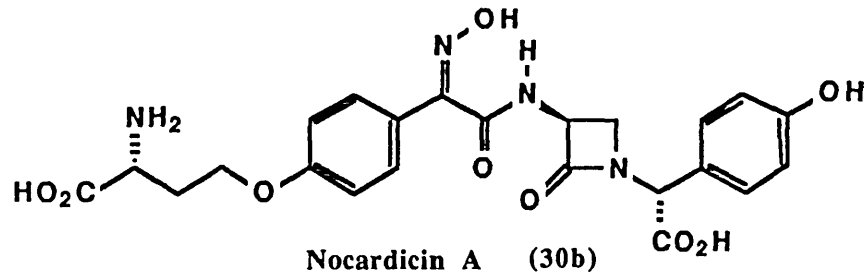


The enone (23) gave alkenyl epoxide (24) on treatment with dimethyl sulphonium methylide. Reaction with $Fe_2(CO)_9$ in THF gave the ferrilactone (25). Insertion of (-)-α-methylbenzyl amine into (25) gave the diastereomeric ferrilactams (26) and (27) *via* an S_N2' like reaction. These isomers were easily separable and characterised by further reaction. Oxidation of the ferrilactam (26) with ceric ammonium nitrate gave the β-lactam (28). Further modification by ozonolysis, stereoselective reduction and removal of the α-methylbenzyl group afforded (29), a known intermediate in the synthesis[14] of (22) in its chiral form (scheme 9).

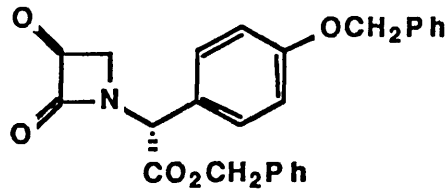


Scheme 9

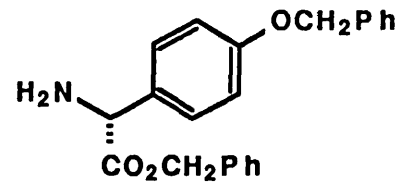
Similar methodology has been applied to the synthesis of (30a), a precursor for the synthesis of the nocardicin antibiotics[15](30b). The structure is built up *via* the ferrilactone derived from isoprene, which undergoes an S_N2' reaction with D-(-)-*p*-hydroxyphenylglycine (31) to give the ferrilactams which on subsequent modification afford the intermediate (29).



Nocardicin A (30b)



(30a)



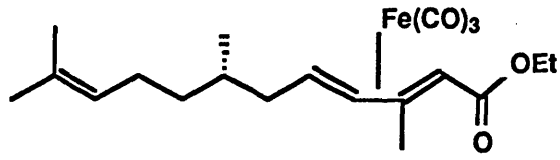
(31)

3.1c η^4-Diene Complexes

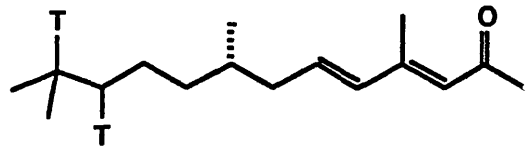
The coordination of the tricarbonyl iron group to 1,3 dienes is of interest to the organic chemist because it provides a tool for moderating the reactivity of the unsaturated system toward, for example, hydrogenation, electrophilic reactions and Diels-Alder reactions. Thus a reaction control or protection is invoked. It provides a source of steric bulk, controlling the stereochemical course of a reaction, or it can be used to stabilize the tricarbonyldienylium cation described in section 3.1d

(i) Protection of a 1,3-Diene with the $Fe(CO)_3$ Group

The iron carbonyl adduct is used in the synthesis of hydroprene,[16] (32) an insect growth regulator. It protects an (E,E) dienoate (33) while the terminal double bond is selectively tritium labelled affording (32).



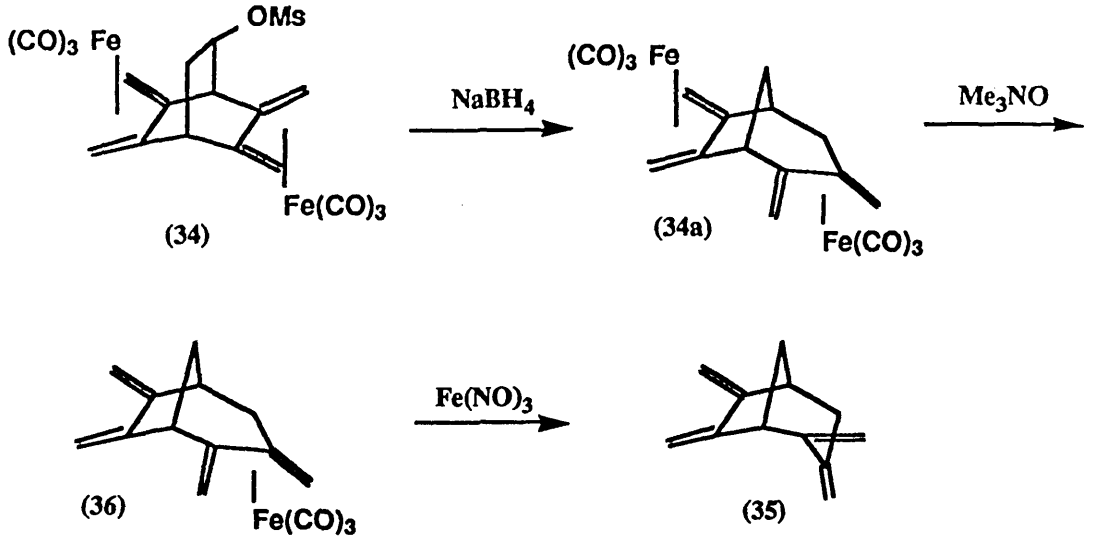
(33)



(32)

Gabioud and Vogel[17] use the group to protect the dienes of the molecule (34) in the synthesis of the novel compound (35).The mesylate prepared from the corresponding alcohol was reduced and rearranged into (34a) by sodium borohyride in $CF_3CH(OH)CF_3$ in 73% yield. The C-5,C-6 $Fe(CO)_3$ group was oxidized selectively

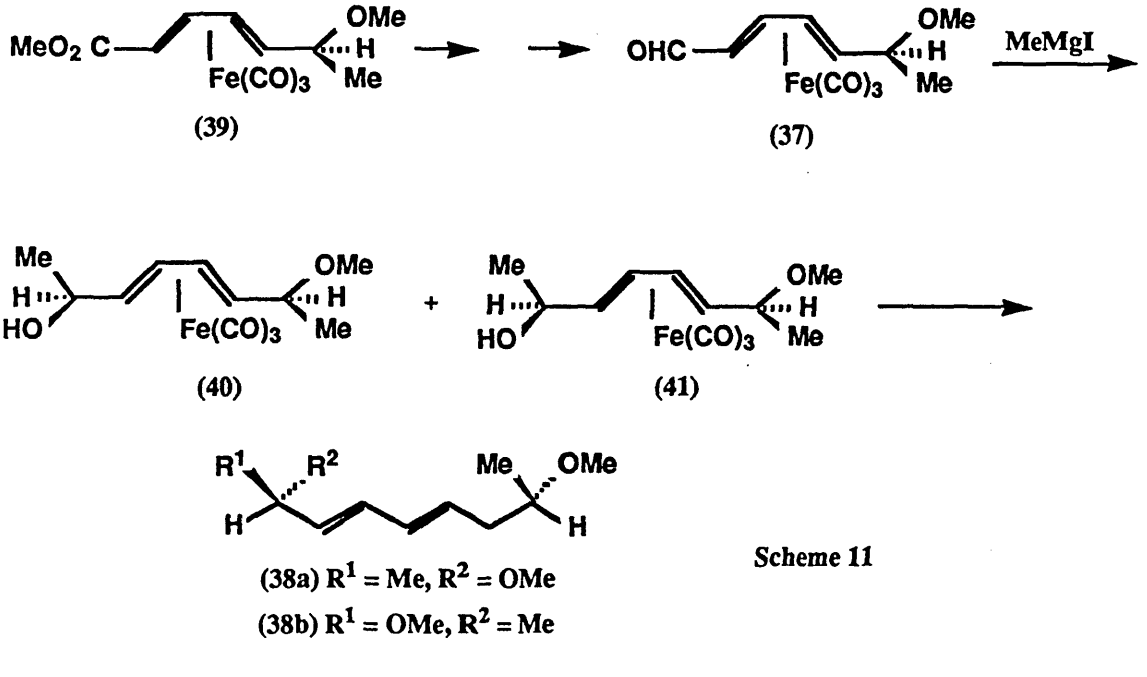
with trimethylamine oxide to give (36), but removal of the second $Fe(CO)_3$ group required the use of $Fe(NO_3)_3$ yielding the novel bicyclic structure of (35) (scheme 10).



Scheme 10

(ii) General Use in Synthesis

The functionalised butadienyl complexes (37) allow a stereoselective synthesis of dienes (38) which have known relative configuration.[18] Reduction and oxidation of (39) give the aldehyde (37) which on treatment with MeMgI gave the complexes (40) and (41) which are easily separable by chromatography. Protection and decomplexation of (40) and (41) afford the optically pure (38a) and (38b) (scheme 11).



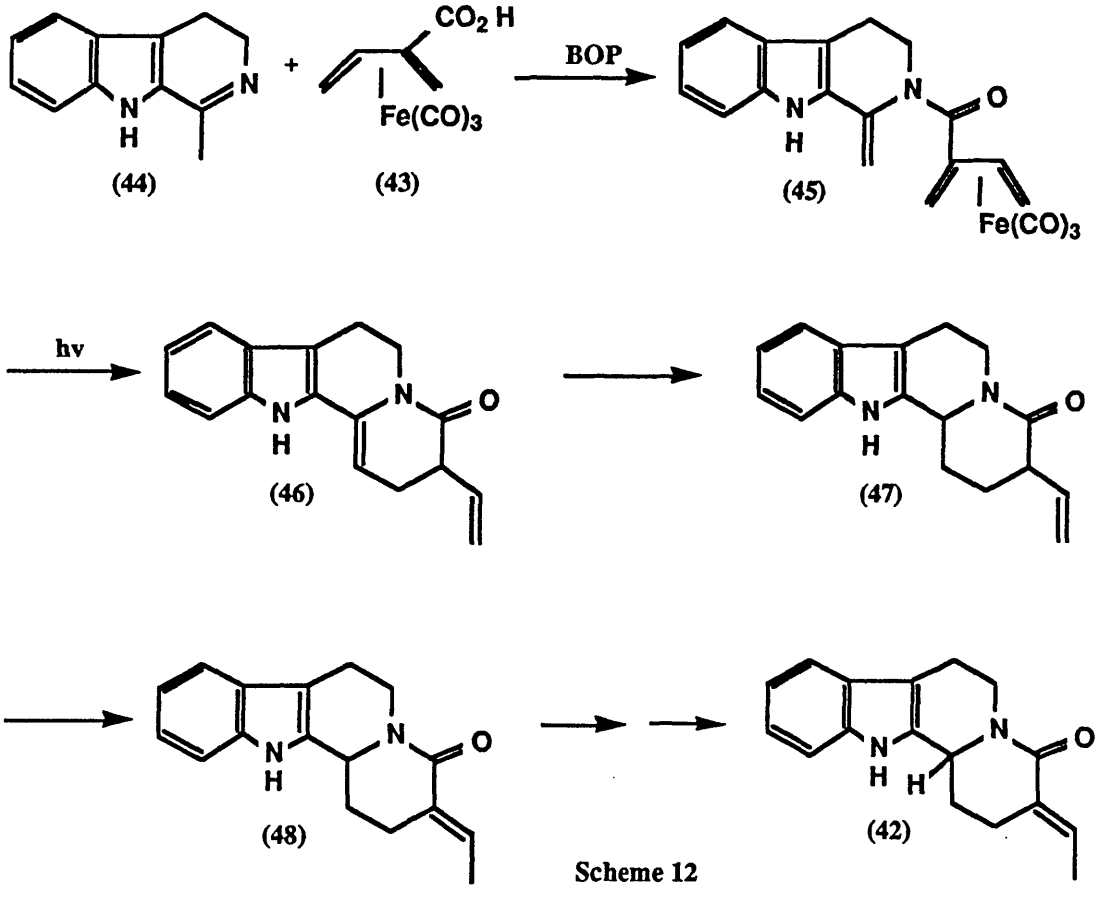
(38a) R^1 = Me, R^2 = OMe

(38b) R^1 = OMe, R^2 = Me

Scheme 11

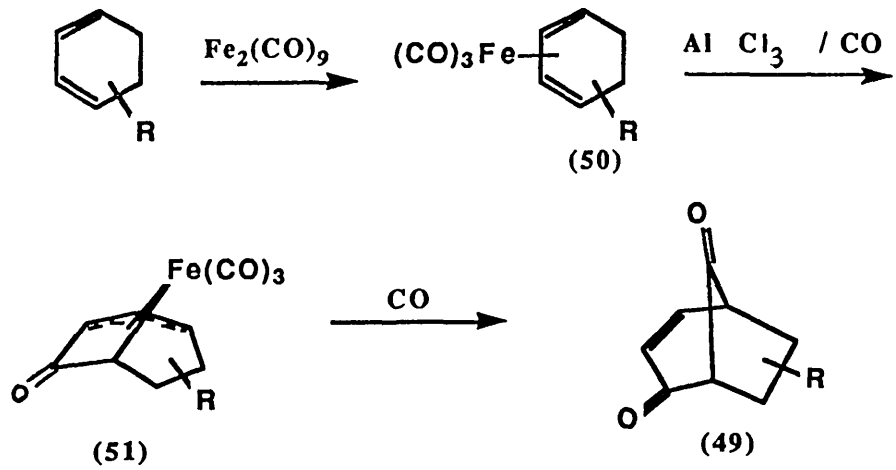
The diene-$Fe(CO)_3$ unit has a two fold use in the synthesis of the alkaloid (±)-

Deplancheine[19] (42). The $Fe(CO)_3$ unit stabilises the diene of (43), the precursor of which is susceptable to [4+2] cycloaddition under the reaction conditions. Treatment of (43) with imine (44) affords the enamide (45) using (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP)[20] as coupling agent. A tandem exited oxidation/cyclisation of the η^4 diene complex occurs on u.v. irradiation to give (46). After reduction of the internal double bond to (47), diiron nonacarbonyl was the reagent of choice for ensuring stereocontrolled double bond shift into conjugation to give the E isomer (48). Other reagents afforded mixtures of the E and Z isomers. Further modification afforded the natural product (42) (scheme 12).



Scheme 12

The $Fe(CO)_3$ diene unit is employed in a double carbonylation procedure on substituted cyclohexadienes,[21] giving the bicyclo[2.2.1]octane carbon skeleton (49) found in many terpenoid natural products.[22] The Lewis acid mediated ring enlargement of (50) produces the intermediate alkyl allyl complexes (51) with high regioselectivity; further carbonylation affords the product Bicyclo[3.2.1]octanes (49) (scheme 13).

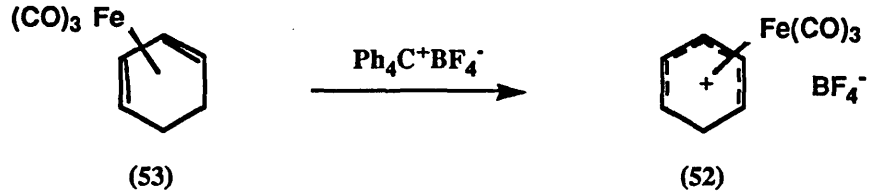


Scheme 13

The first step constitutes effectively a carbon monoxide insertion into one of the double bonds.[23] The second step involves migratory insertion of CO into the Fe-C1 bond which forms the acyl unit, followed by reductive elimination which links the acyl unit with C-5. The Lewis acid mediated insertion of CO into $Fe(CO)_3$ diene complexes is well known.[24]

3.1d Tricarbonyldienylium Complexes

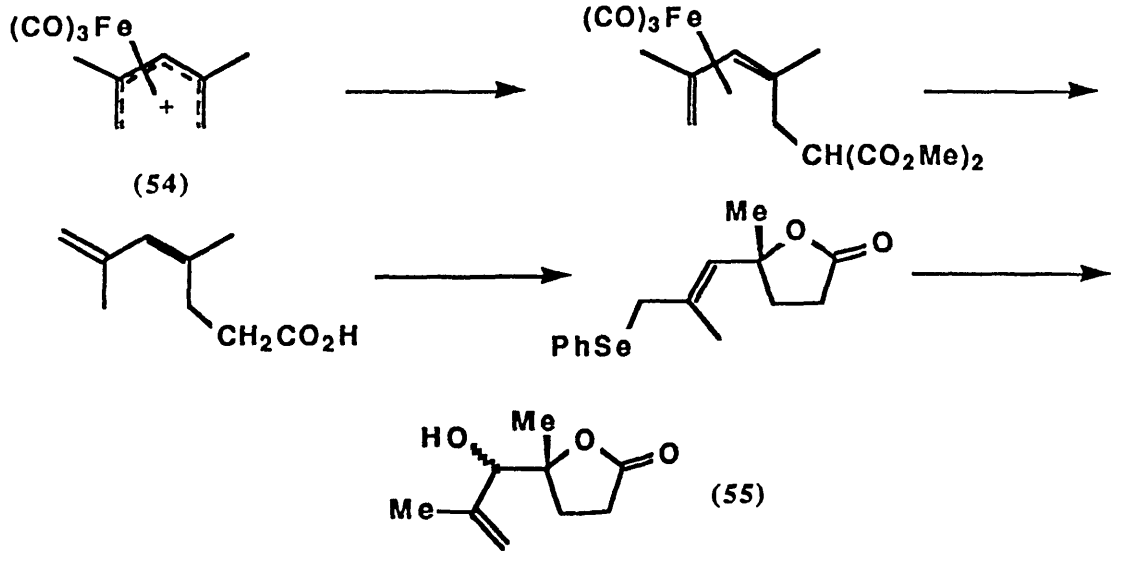
First reported in 1960,[25] the preparation of tricarbonylcyclohexadienylium iron tetrafluoroborate (52) (scheme 14) *via* a quantitative hydride abstraction from the diene complex (53), has resulted in many reports on this system.[1a]



Scheme 14

(i) Acyclic Dienylium Complexes

The modification of dienylium complex (54) results in lactone (55). Thus the moiety can be used to specifically functionalize 1,3 dienes[26] (scheme 15). This route is analogous to that for a sequence of cyclic dienylium complexes explained in the next section.

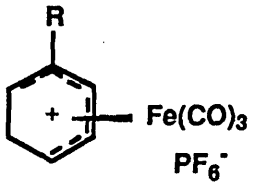


Scheme 15

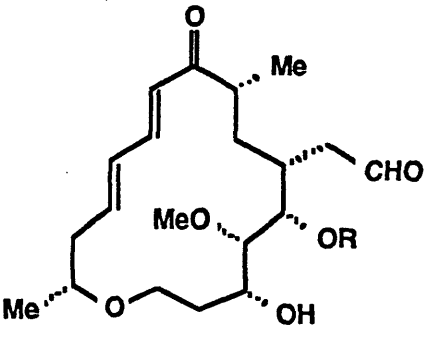
(ii) Cyclic Dienylium Complexes

The availability, *via* Birch reduction of, dihydroaromatic compounds and the well established use of these in synthesis obviously makes the derived tricarbonyl iron complexes extremely interesting intermediates. The parent complex (52) is very easily prepared, unlike the corresponding acyclic derivatives which are more difficult to handle.

The tricarbonyldienyl iron complexes (56) and (57)[26] are used as precursors to a range of dienyl acetic acid derivatives from which (58) an intermediate in the total synthesis of Carbomycin B (59), a 16-membered ring macrolide,[27] could be obtained.



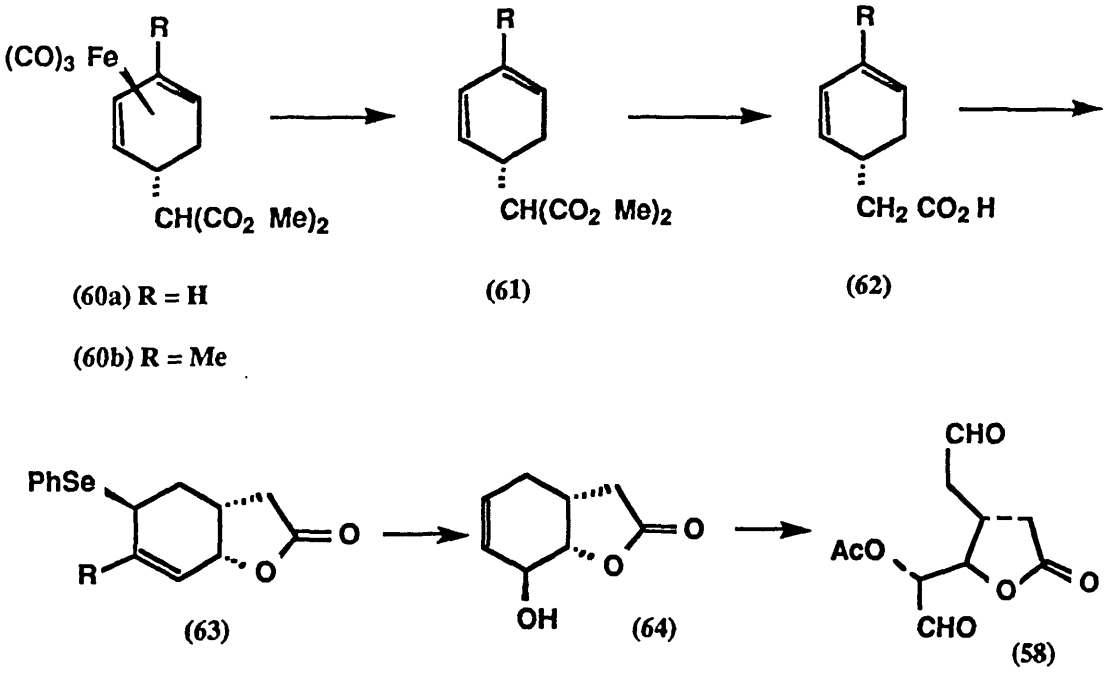
(56) R = H
(57) R = Me



(59)

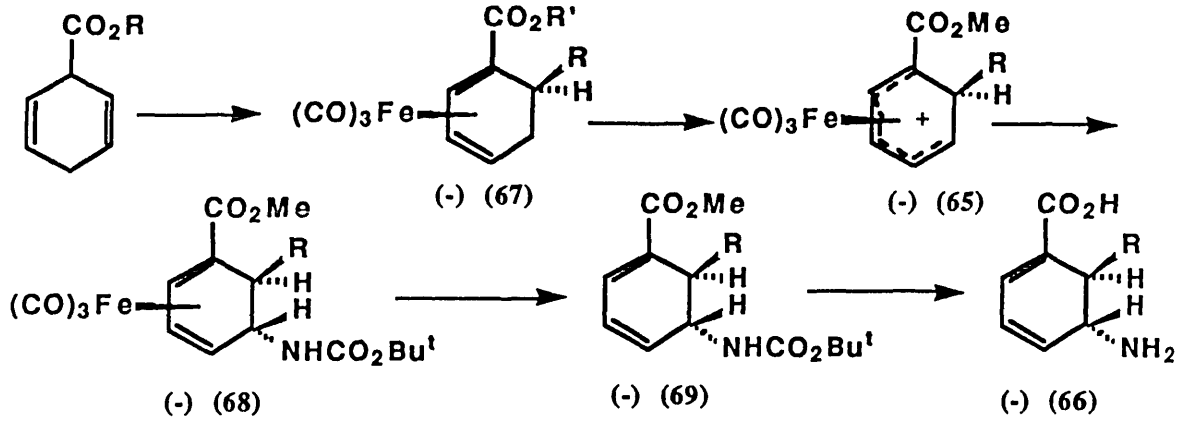
Treatment of (56) or (57) with $NaCH(CO_2Me)_2$ gives (60) quantitatively. The complexes are demetallated to (61) and converted to the carboxylic acid derivatives *via* standard procedures. The phenylselenolactonization of these dienes occurs in a regio and stereo controlled manner with conjugate attachment of the PhSe group *anti* to the

lactone moiety to give the lactones (63). Oxidation with concommitant selenoxide (2,3) sigmatropic rearrangement gives (64) which on further modification gives the carbomycin B precursor as the dialdehyde (58) (scheme 16).



Scheme 16

The dienylium complex (65) was used in a synthesis of Gabaculine[28] (66,R=H), a naturally occurring amino acid, which may be useful for the treatment of certain nervous disorders.[29] Complex (67, R=H,R'=H) was resolved *via* the phenyl ethyl ammonium salt, by crystallization and regeneration of the acid by treatment with dilute HCl. Methylation and hydride abstraction, which occurs only from the face opposite the metal and only at C-5 gives the resolved cation (65).[In principle the resolution step can be avoided by chiral transfer of $Fe(CO)_3$ from a suitable donor complex although this procedure has not been fully developed.[30]]

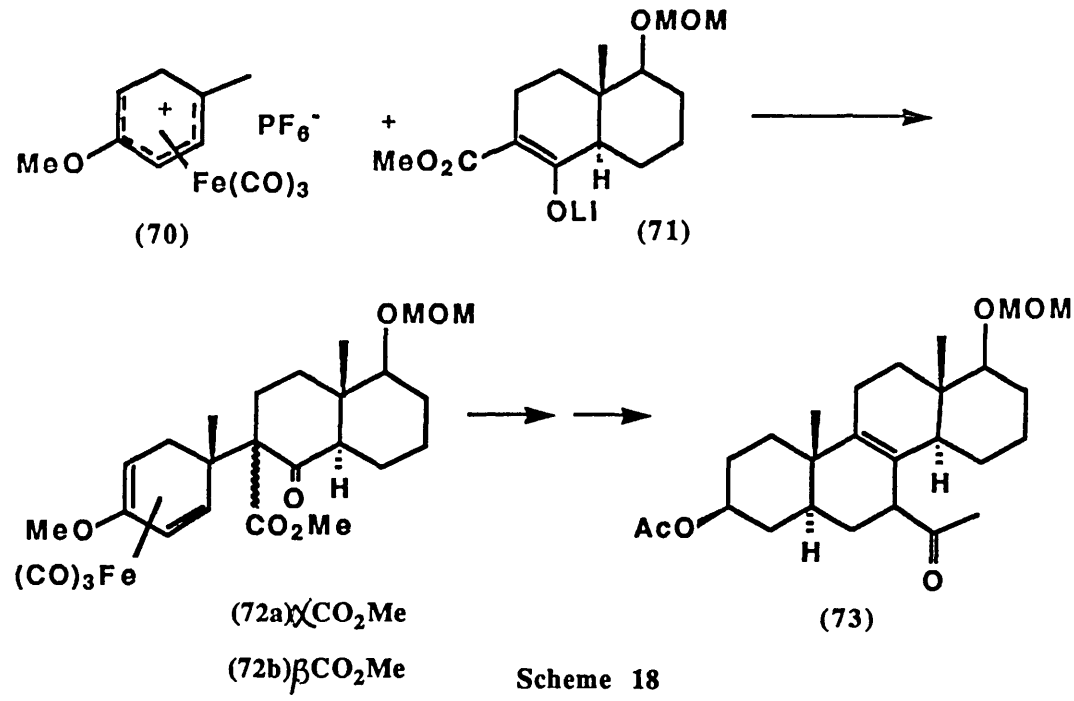


Scheme 17

Treatment of (65) with *t*-butyl carbamate and Hunig's base gives (68) *via* irreversible addition of the nucleophile. Decomplexation gives the known[31] gabaculine precursor (69) (scheme 17).The procedure represents one solution to a classical stereochemical problem of producing new asymmetry at full resolution and then removing the inducing asymmetry.

(iii) Approaches to Steroid Synthesis

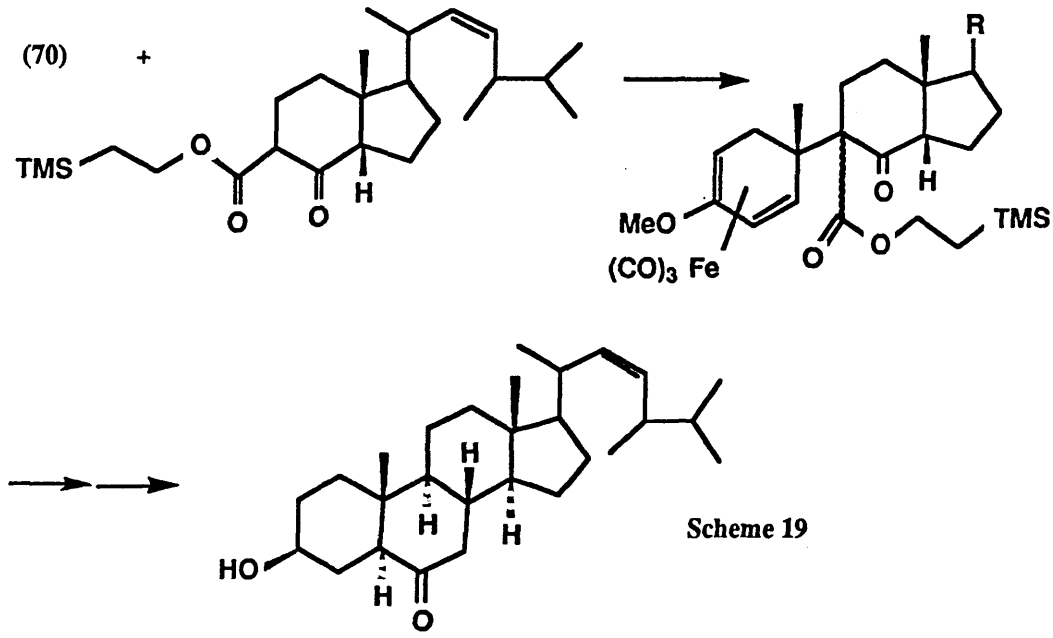
The reaction of tricarbonyl(4-methoxy-1-methylcyclohexadienyl)iron with various enolates gives rise to steroid precursors. Reaction of (70) with the keto ester nucleophile (71) gives the complexes (72) as the major products. Subsequent modification in eight steps affords the D-homosteroid[32] (73) (scheme 18)



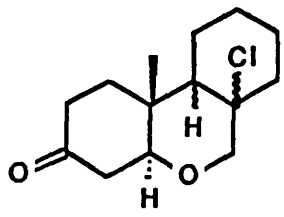
Scheme 18

The chiral steroid intermediate[33] (74) has been made in 6 steps using the dienyl cation (70) and the enolate of (75); further modification affords (74) (scheme 19).

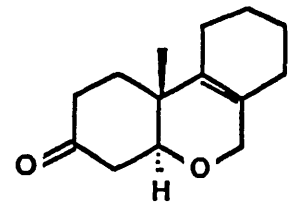
Mincione and co-workers[34] have also used the dienylium cation (70) in the synthesis of a series of model tricyclic oxa compounds (76-78) and lactones (79,80) *via* this methodology.



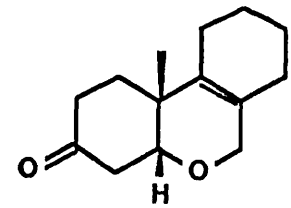
Scheme 19



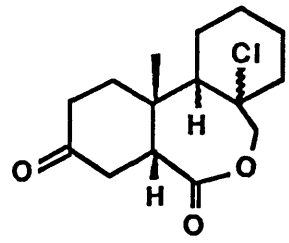
(76)



(77)



(78)



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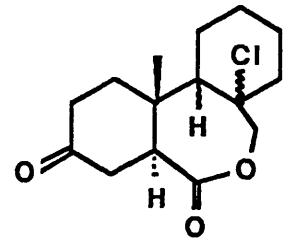
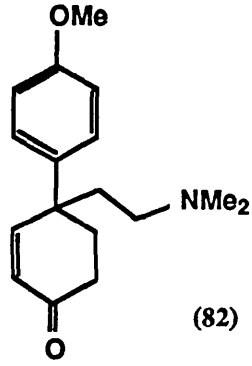


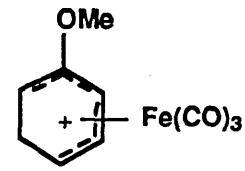
(80)

(iv) Approaches to Alkaloid Synthesis

The tricarbonyl(4-methoxycyclohexadienyl)iron cation (81) is used as a synthetic equivalent of the *p*-anisyl cation in a formal synthesis of (±)-*o*-methyljoubertiamine (82)[35], an alkaloid of pharmacological interest.[36]

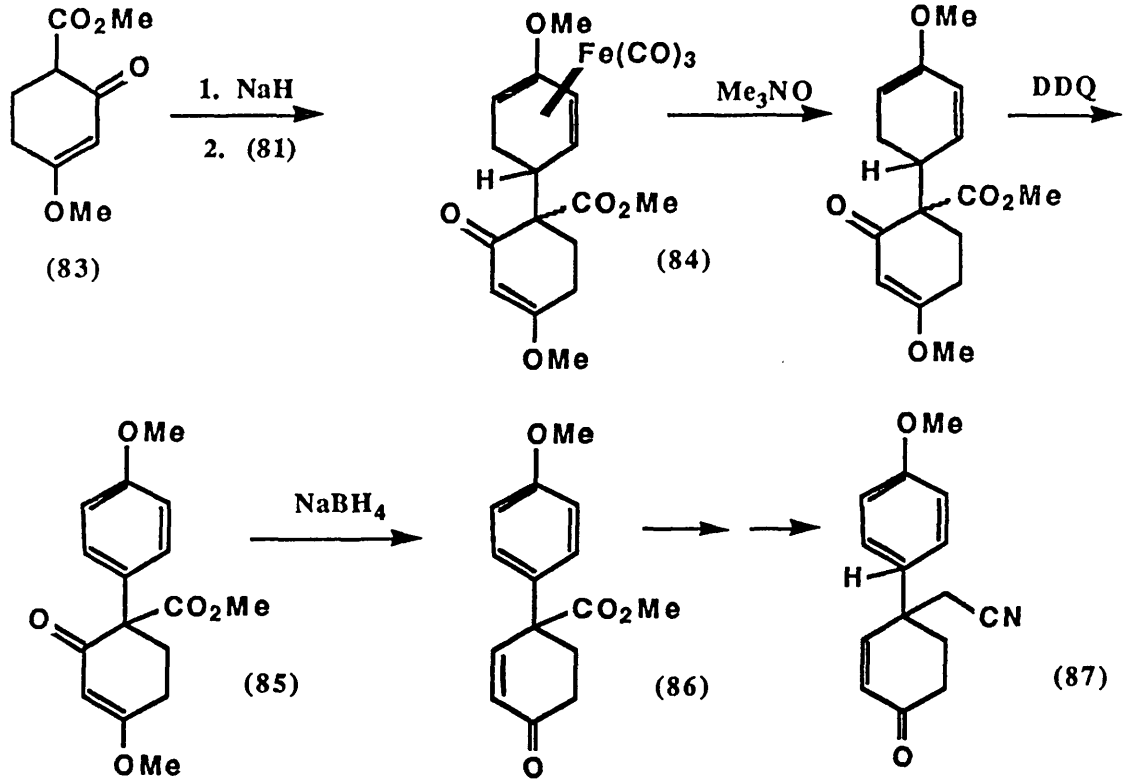


(82)



(81)

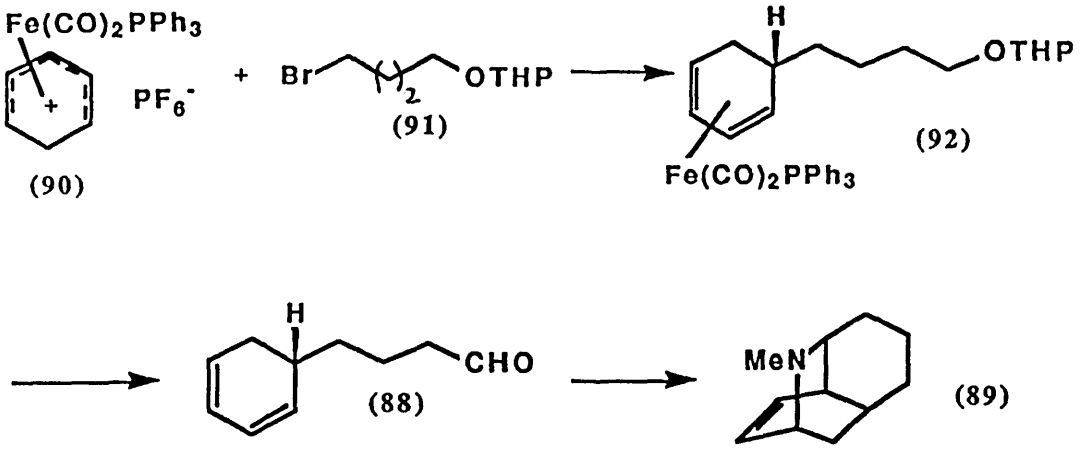
Reaction of the sodium enolate of (83) with the dienyl complex (81) gave (84) in 92% yield. Decomplexation of the sensitive (84) with trimethylammonium oxide,[37] then oxidation to the aromatic species (85) with DDQ followed by borohydride reduction afforded ester (86). Further homologation gave the known intermediate (87) in the Sanchez[38] synthesis of (82) (scheme 20).



Scheme 20

Grieco[39] has used the methodology of Pearson[40] to construct the cyclohexadiene system (88) required for the intramolecular Diels-Alder reaction of the immonium ion of (88) which leads to the alkaloid (±) Dihydrocannivonine[41] (89).

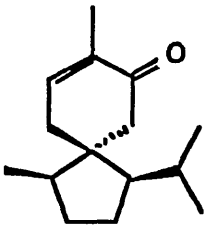
Treatment of the dienylium cation (90) with the Grignard reagent derived from (91) affords exclusively (92) in very high yield. Simultaneous demetallation and THP cleavage with $CuCl_2$ followed by Swern oxidation affords (88) (scheme 21).



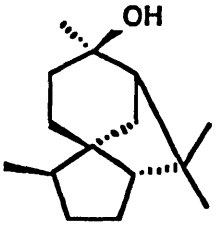
Scheme 21

(v) Synthesis of Spirocyclic Compounds

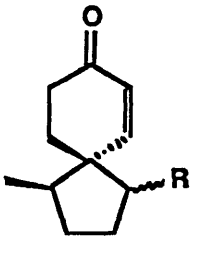
The intramolecular nucleophile addition to dienylium complexes with branched substituents is a synthetically useful process, particularly for molecules having crowded spiro centres. The chemistry developed is a possible approach to racemic acorenone (93) and Cedrol (94). The model compounds (95 a,b) were synthesed[42] to establish the methodology required for the synthesis of (97b), used in the Oppolzer route to acorenone or (97a) used in the Corey route to cedrol.



(93)



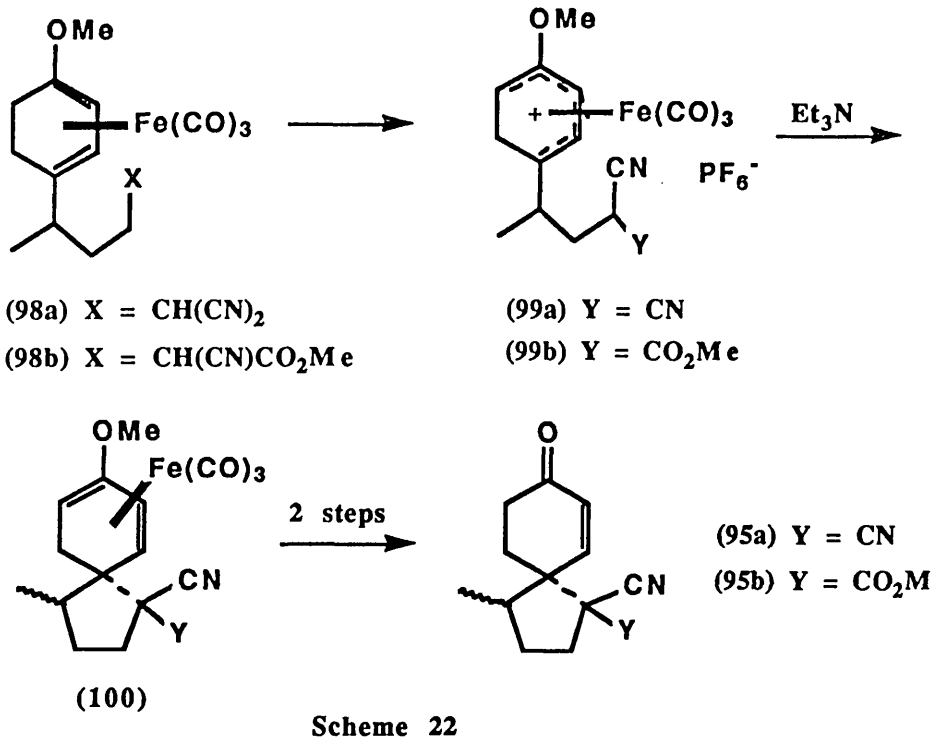
(94)



(97a) R = α -$^{i}C_3H_7$

(97b) R = β -$^{i}C_3H_7$

The diene complexes (98) were prepared in 5 steps from *p*-methoxy-acetophenone. Treatment of (98) with tritylhexafluorophosphate gave the intermediates (99) which with triethylamine yielded the diastereomeric (100) in 54% overall yield from (98). The intramolecular nucleophile addition occurs *trans* to the $Fe(CO)_3$ group. Mild decomplexation followed by acid hydrolysis afforded the spirocyclic enones (95) (scheme 22).



(98a) X = $CH(CN)_2$
(98b) X = $CH(CN)CO_2Me$

(99a) Y = CN
(99b) Y = CO_2Me

(95a) Y = CN
(95b) Y = CO_2Me

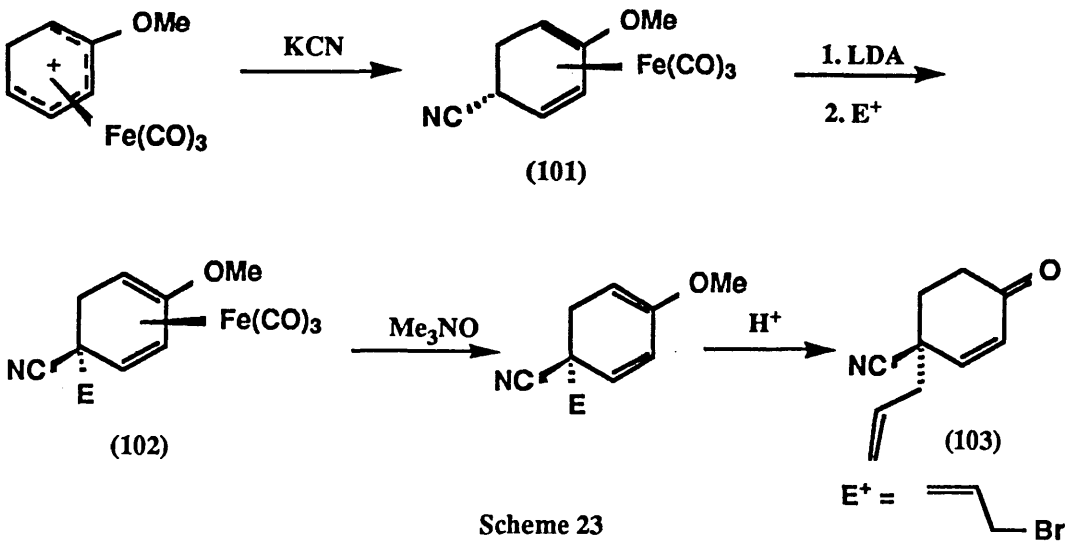
(100)

Scheme 22

3.1e Tricarbonyldienyliron Anionic Complexes

The stereospecific protonation of some cyclohexadienyl $Fe(CO)_3$ anions or alkylation of these species provides quaternary centres. Regiospecific electrophilic attack is achieved in the same position as initial nucleophilic attack in the precursor cationic complexes.

The anions[43] derived from (101), by treatment with lithium diisopropyl amide, on reaction with an electrophile give the products (102) resulting from *exo* attack (scheme 23).



(101)

(102)

(103)

E^+ =

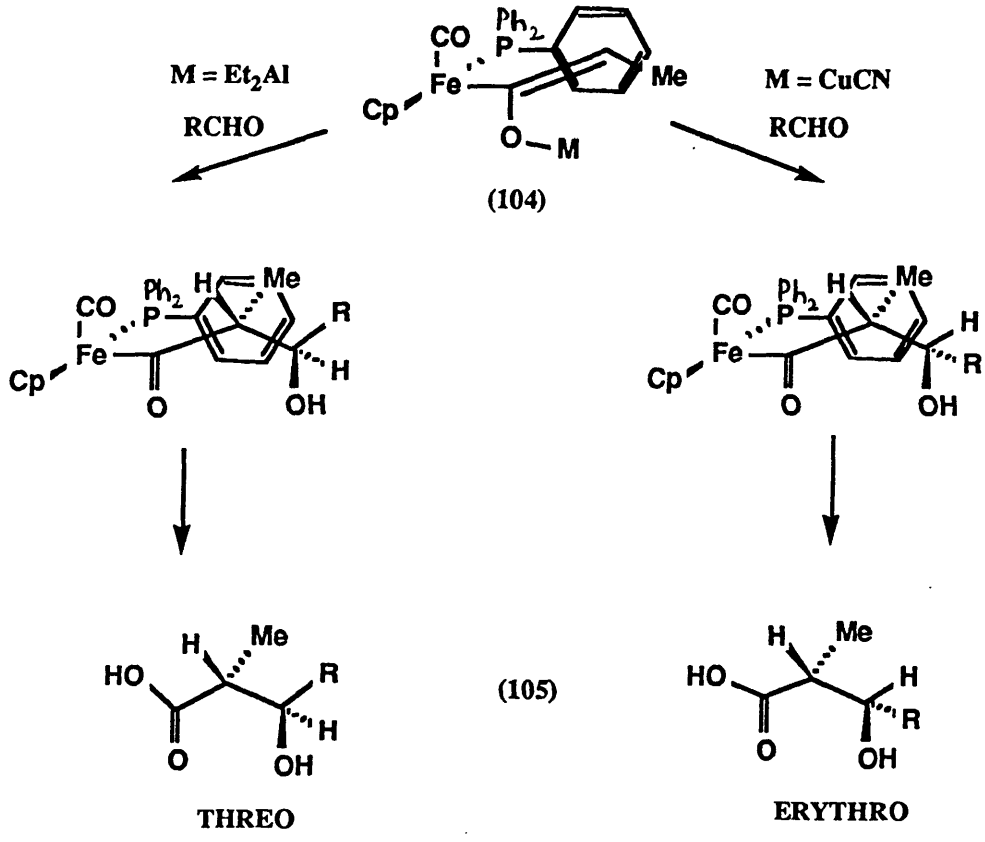
Scheme 23

Thus on disengagement of the iron ligand and treatment with acid resin the optically pure 4,4-disubstituted cyclohex-2-enones (103) are produced. The corresponding 3-OMe series also afford the 5,5 disubstituted enone products.

3.1f Chiral Iron Complexes

The use of a chiral iron complex to stereoselectively synthesise chiral building blocks has been pursued by Davies and co-workers[44] for many years. Recently the method has been extended to aluminium and copper enolates which have been used successfully in stereoselective aldol condensations.[45]

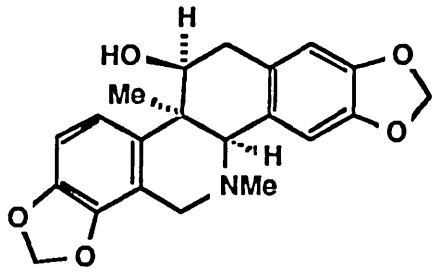
The aluminium and copper enolates (104) derived from (η^5-C_5H_5)Fe(CO)(PPh_3) $COCH_2Me$ provide chiral propionate enolate equivalents which on reaction with aldehydes provide stereoselective syntheses of *threo* and *erythro*-α-methyl-β-hydroxy acids[46] (105) respectively (scheme 24).



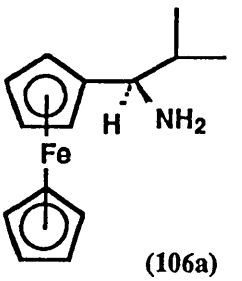
Scheme 24

The 1-Ferrocenyl-2-methylpropyl substituent[47] (106) has been used as a chiral auxiliary in the asymmetric syntheses of the benzophenanthridine alkaloids (+) and (-)

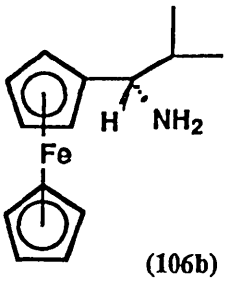
Corynoline[48] (107).



(107)

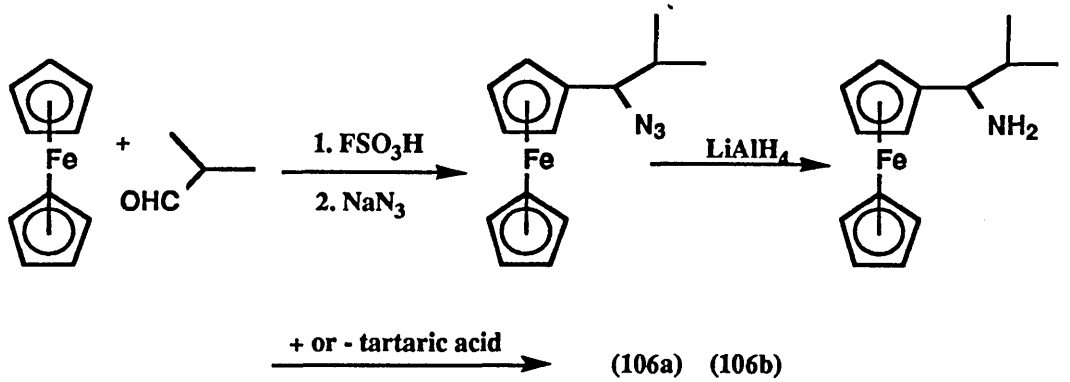


(106a)



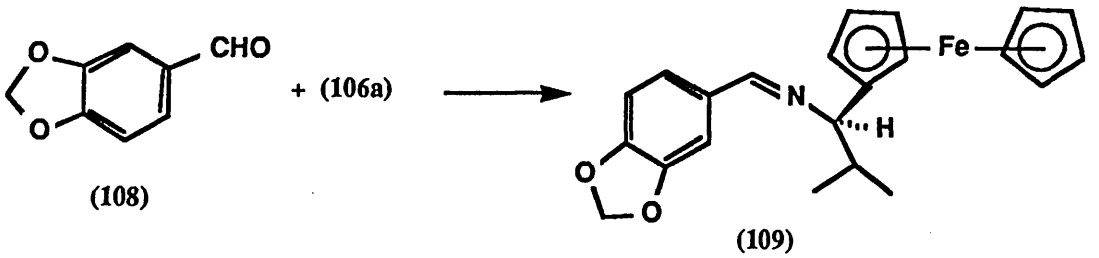
(106b)

The chiral amines were prepared *via* a resolution with (+) and (-) tartaric acids on the racemic material, made from ferrocene (scheme 25).



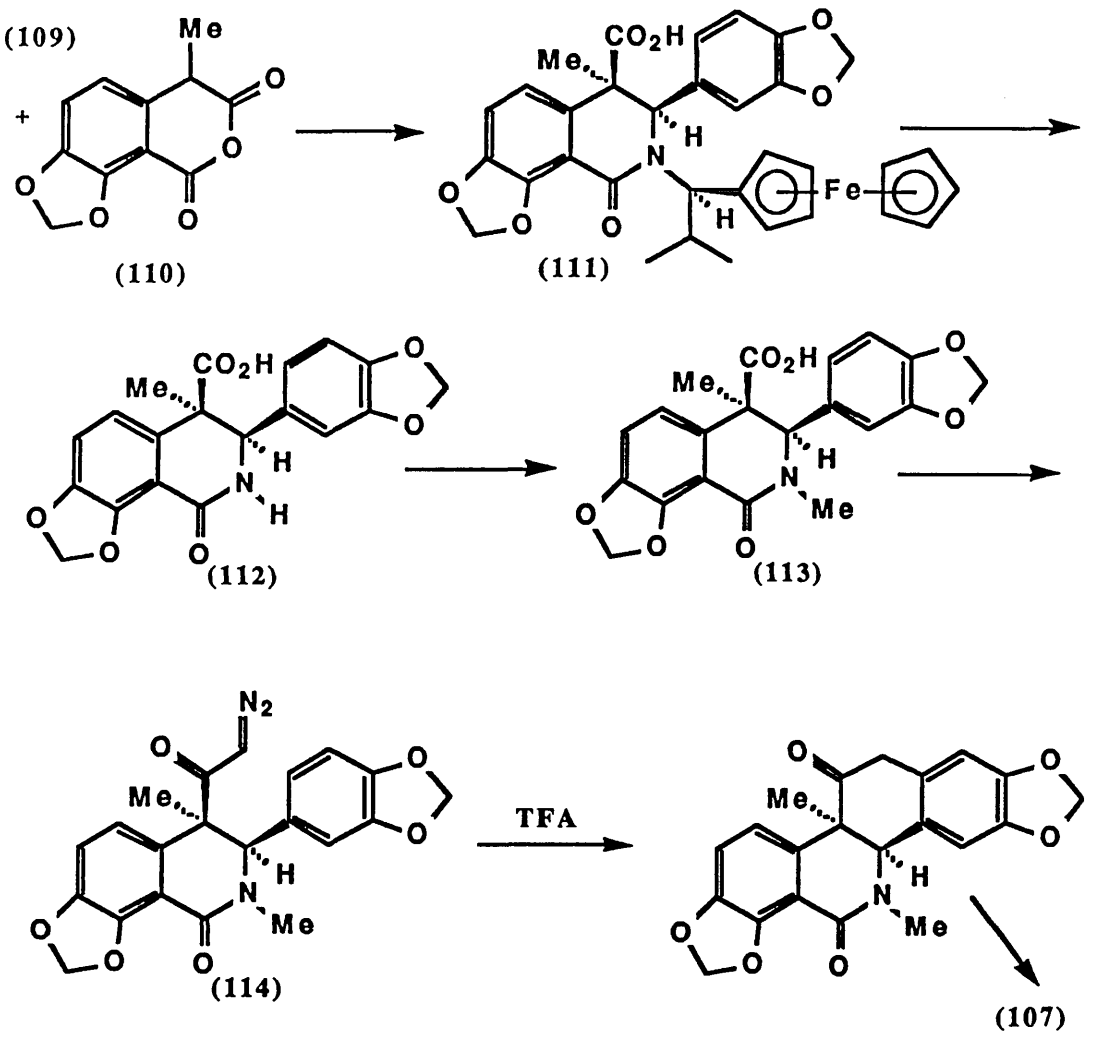
Scheme 25

Reaction of piperonal (108) with (106a) in refluxing benzene gave the chiral Schiff base (109). Treatment with (110)[49] afforded the intermediate (111) in an 81% yield. The chiral auxiliary was removed under acidic conditions to give (112). Further dimethylation and methyl ester hydrolysis gave the acid (113). The acid was converted to (+) corynoline in three steps *via* the diazoketone (114) and cyclisation in the presence of TFA (scheme 26).The synthesis was repeated to make (-) corynoline using the (S)-(+)-ferrocenyl amine.



(108)

(109)

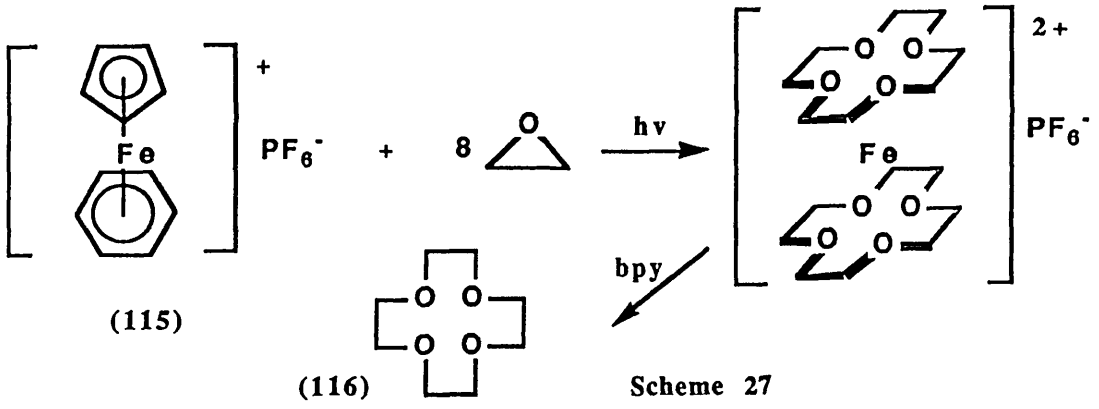


Scheme 26

1.3g Miscellaneous

Synthesis of Crown Ethers

The iron(II) complex (115) has been used in the synthesis of 12-crown-4 [50] (116). Irradiation of (115) with ethylene oxide gave the 12-crown-4 ether iron complex (117) which was decomplexed to the crown ether (116) with 2,2'-bipyridine (scheme 27).



(115)

(116)

Scheme 27

Chapter 3 Review References

1. A.J.Pearson in "Comprehensive Organometallic Chemistry" Ed. Wilkinson, Stone, and Abel, Vol. 8, pg. 39; R.Noyori and Y.Hayakawa, *Tetrahedron,* 1985, 41, 5879; A.J.Pearson, *Pure and Applied Chem.,* 1983, 55, 1767; D.M.Hollinshead, Ph.D. Thesis, Imperial College, London, 1984.

2. R.Baker, R.B.Keen, M.D.Morris, and R.W.Turner, *J. Chem. Soc., Chem. Commun.,* 1984, 987.

3. J.N.Marx and G.Minaskanian, *J. Org. Chem.,* 1982, 47, 3306.

4. R.Baker, V.B.Rao, and E.Erdik, *J. Organometallic Chem.,* 1983, 243, 451.

5. L.S.Hegedus and M.S.Holden, *J. Org. Chem.,* 1985, 50, 3920.

6. L.S.Hegedus, M.S.Holden, and J.M.Mckearin, *Org. Synth.,* 1984, 62, 48.

7. I.Ojima and H.B.Kwon, *Chem. Lett.,* 1985, 1327.

8. J.W.Herndon, *J. Am. Chem. Soc.,* 1987, 109, 3165.

9. H.J.Berwin, M.L.Hall, J.Jerkunica, and T.G.Traylor, *Pure and Applied Chem.,* 1972, 30, 606.

10. J.Celebuski and M.Rosenblum, *Tetrahedron,* 1985, 41, 5741.

11. G.D.Annis, S.V.Ley and C.R.Self, and R.Sivaramakrishnan, *J. Chem. Soc., Perkin Trans. I,* 1981, 270; R.Aumann, H.Ring, C.Kruger, and R.Goddard, *Chem. Ber.,* 1979, 112, 3644.

12. G.D.Annis, E.M.Hebblethwaite, S.T.Hodgson, D.M. Hollinshead, and S.V.Ley, *J. Chem. Soc., Perkin Trans. I,* 1983, 2851.

13. S.T.Hodgson, D.M. Hollinshead, and S.V.Ley, *J. Chem. Soc., Chem. Commun.,* 1984, 494.

14. T.Kametani, S.-P.Huang, T.Nagahara, S.Yokohama, and M.Ihara, *J. Chem. Soc., Perkin Trans. I,* 1981, 964.

15. S.T.Hodgson, D.M. Hollinshead, S.V.Ley, C.M.R.Low, and D.J.Williams, *J. Chem. Soc., Perkin Trans. I,* 1985, 2375.

16. M.F.Boehm and G.D.Prestwich, *J. Org. Chem.,* 1987, 52, 1349.

17. R.Gabiond and P.Vogel, *J. Org. Chem.,* 1986, 51, 2385.

18. R.Gree, J.Kessabi, P.Mosset, J.Martelli, and R.Carrie, *Tetrahedron Lett.,* 1984,

25, 3697.

19. G.Lesma, G.Palmisano, and S.Tollari, *J. Chem. Soc., Perkin Trans. I,* 1984, 1593.

20. B.Castro, G.Elvin, C.Selve, and R.Seyer, *Synthesis,* 1977, 413.

21. P.Eilbracht, R.Jelitte, and P.Trabold, *Chem. Ber.,* 1986, 119, 169.

22. A.A.Newman, "Chemistry of Terpines and Terpenoids", 1972.

23. P.Eilbracht, R.Jelitte, and, L.Walz, *Chem. Ber.,* 1984, 117, 3473.

24. W.R.Roth and J.D.Meier, Tetrahedron Lett., 1967, 2053;
B.F.G.Johnson, J.Lewis and D.J.Thompson, Tetrahedron Lett., 1974, 3789.

25. E.O.Fisher and R.D.Fisher, *Angew. Chem.,* 1960,72,919.

26. A.J.Pearson and T.Ray, *Tetrahedron,* 1985,41,5765.

27. K.Tatsuta, Y.Ameniya, S.Maniwa, and M.Kinoshita, *Tetrahedron Lett.,* 1980,21,2837.

28. B.M.R.Bandara, A.J.Birch, and L.F.Kelly, *J. Org. Chem.,* 1984,49,2496.

29. A.Barbeau, *Lancet II,* 1973,1499; E.Roberts, *Biochim. Pharmacol.,* 1974, 23,2637.

30. A.J.Birch, W.D.Raverty, and G.R.Stephenson, *Tetrahedron Lett.,* 1980,21, 197.

31. K.Kobayashi, S.Miyazawa, A.Terahara, H.Mishima, and H.Kurihara, *Tetrahedron Lett.,* 1976,537.

32. A.J.Pearson and T.Ray, *Tetrahedron Lett.,* 1985,26,2981.

33. E.Mincione, P.Bovicelli, S.Cerrini, and D.Lamba, *Heterocycles,* 1985,23, 1607.

34. E.Mincione, P.Bovicelli, M.Chandler, and A.R.D.Jacono, *Heterocycles,* 1985,23,75.

35. A.J.Pearson, I.C.Richards, and D.V.Gardner, *J. Org. Chem.,* 1984,49,3887.

36. J.M.Watt and M.G.Breyer-Brandwijk,"The Medicinal and Poisenous Plants of Southern and Eastern Africa", E. and S.Livingstone,Ltd.,London,1962,pg.11.

37. Y.Shvo and E.Hazum, *J. Chem. Soc., Chem. Commun.,* 1974,336.

38. I.H.Sanchez and F.R.Tallabs, *Chem. Lett.,* 1981,891.

39. P.A.Grieco and S.D.Larsen, *J. Org. Chem.,* 1986,51,3553.

40. A.J.Pearson and J.Yoon, *Tetrahedron Lett.*, 1985,26,2399.

41. D.A.Evans,A.M.Golob, N.S.Mandel, and G.S.Mandel, *J. Am. Chem. Soc.*, 1978,100,8170.

42. A.J.Pearson and T.R.Perrior, *J.Organometallic Chem.*, 1985,285,253.

43. A.J.Birch and L.F.Kelly, *J. Org. Chem.*, 1985,50,712.

44. G.J.Baird, J.A.Daudy, S.G.Davies, and K.Prout, *J. Chem. Soc., Chem. Commun.*, 1983, 1202.

45. D.A.Evans, J.V.Nelson, and T.R.Taber, *Top. Stereochem.*, 1982,13,1; T.Mukaiyama, *Organic Reactions*, 1982,28,203.

46. S.G.Davies, I.M.Dorder-Hedgecock, and P.Warner, *Tetrahedron Lett.*, 1985,26,2125.

47. M.Cushman and J.-K.Chen, *J. Org. Chem.*, 1987,52,1517.

48. N.Takai, *Chem. Pharm. Bull.*, 1963,11,1306.

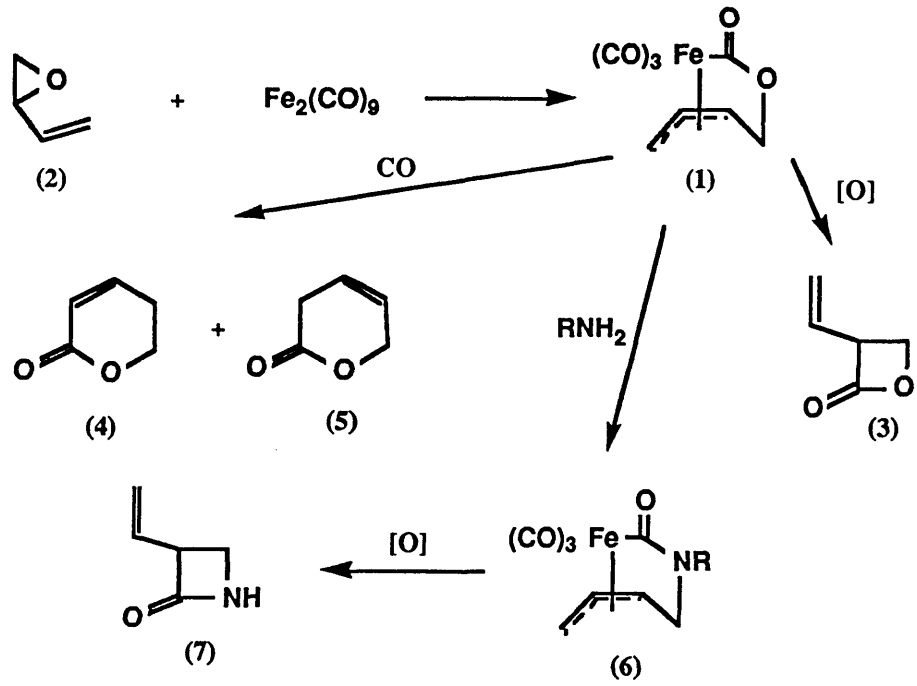
49. M.Cushman, A.Abbaspour, and Y.P.Gupta, *J. Am. Chem. Soc.*, 1983,105, 2873.

50. K. Meier and G.Rihs, *Angew. Chem.*,1985,97,879.

3.2a Synthetic Studies Utilizing the Ferrilactone Unit

Introduction

The ferrilactone unit (1), a useful synthetic intermediate for the preparation of lactones and lactams, is readily obtained by treatment of a vinyl epoxide (2) with coordinatively unsaturated iron carbonyl species. The most practical method is treatment of (2) with diiron nonacarbonyl in THF. The oxidation of these complexes with Ce^{IV} predominantly yields β-lactones[1] (3) while high pressure carbonylation affords the δ-lactones (4) or (5)[2] depending on experimental conditions.The ferrilactones may be converted to the corresponding ferrilactams (6) *via* an SN2' reaction with amines[3] in the presence of a Lewis acid. Subsequent oxidation of the complexes affords a β-lactam(7).(Scheme 1) The carbonylation procedure has also been used in work described in this thesis to prepare more challenging synthetic targets.

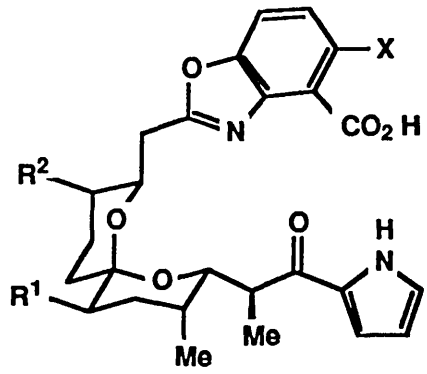


Scheme 1

Synthetic Studies Towards CP-61,405

Introduction

The poly-ionophore antibiotic CP-61,405 was first isolated from *streptomyces routienii* in 1985, and is a member of a small group of carboxylic ionophores.[4]



(9) A23187 $R^1 = R^2 = Me$, X = NHMe

Cezomycin $R^1 = R^2 = Me$, X = H

X-14885A $R^1 = H$, $R^2 = Me$, X = OH

(8) CP-61,405 $R^1 = R^2 = H$, X = OH

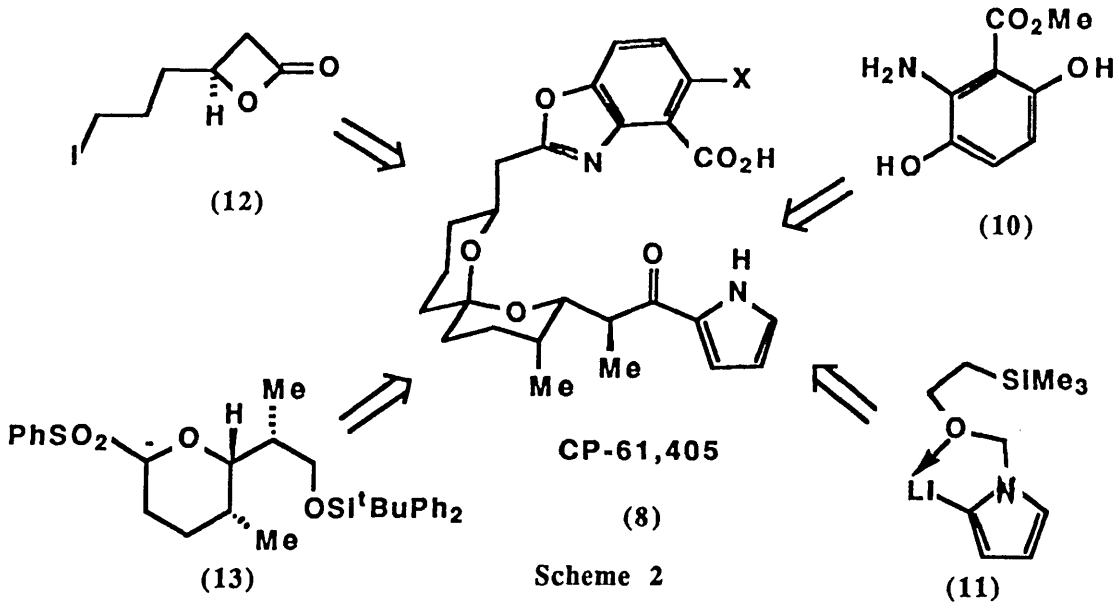
AC7230 $R^1 = R^2 = Me$, X = OH

These molecules specifically coordinate divalent cations[5] which results in their transport through cell membranes *in vivo*.[6] Calcimycin (A23187) (9), first isolated in 1972, has attracted the most attention[7] owing to its good biological profile. A23187 was isolated from a *Streptomyces chartreusensis* strain as its Ca^{2+}/Mg^{2+} salt; the X-ray structures of the free acid[8] and the 2:1 Ca^{2+} complex[9] have been determined. The structure reveals that the calcium is bound to four oxygen atoms, 2 nitrogens and one water molecule. Two intramolecular hydrogen bonds occur between the pyrrole NH and the carboxylate binding oxygen which aids binding of the two calcimycin molecules. Each molecule is bound to calcium, through one carboxylate oxygen, the pyrrole carbonyl oxygen, and the benzoxazole nitrogen atoms.

Calcimycin (9) has been used to study the effects of divalent cations within cellular physiological processes.[10]

The Synthetic Approach to CP-61,405

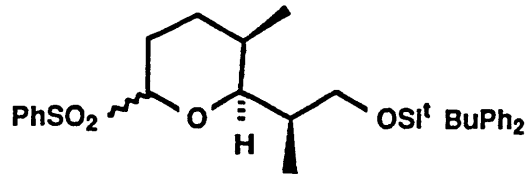
Then proposed synthesis involves the convergent coupling of four fragments, (scheme 2) two of which (10,11) have been prepared previously in these laboratories.[11]



Scheme 2

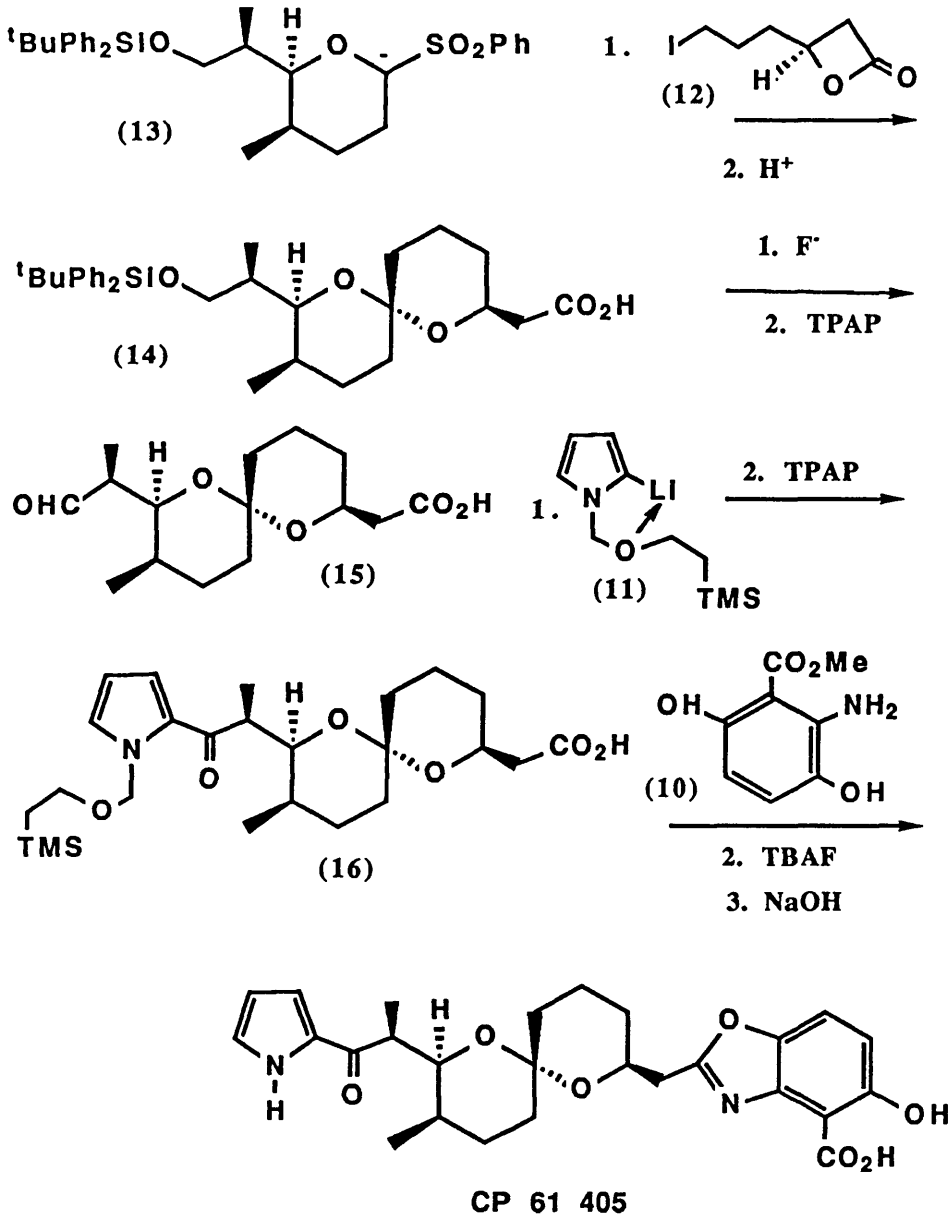
The proposed route envisages initial coupling of fragments (12) and (13) (scheme 2) to form the spiroacetal (14). Deprotection of (14) and oxidation with the TPAP reagent should then afford the aldehyde (15). This aldehyde on coupling with the SEM protected 2-lithio pyrrole[12] (11), and subsequent oxidation would produce the fragment (16).The final benzoxazole unit (10)[13] may be introduced by reaction of the acid with (10) and a strong dehydrating agent, by coupling of the amine and acid, and subsequent dehydration to give the N-SEM protected methyl ester which on removal of the protecting group with tetra-*n*-butylammonium fluoride and ester hydrolysis should give the natural product CP-61,405 (8) (scheme 3). The synthesis of fragment (13) is described in this thesis.

Synthesis of Fragment (13)



(13)

The key steps in the preparation of (13) are the construction of a β,γ unsaturated δ-lactone *via* iron carbonyl methodology[14] which on subsequent hydrogenation should afford the correct relative stereochemistry found in (13). The construction of the ferrilactone unit (28,29) from the vinyl epoxide (27) may be accomplised in a variety of ways. The most reasonable one is outlined in scheme 4.


tBuPh2SiO
SO2Ph
(13)
1.
(12)
2. H+
1. F-
2. TPAP
CO2H
(14)
OHC
(15)
2. TPAP
1.
(11)
TMS
CO2Me
OH
NH2
(10)
2. TBAF
3. NaOH
(16)
CP 61 405

Scheme 3

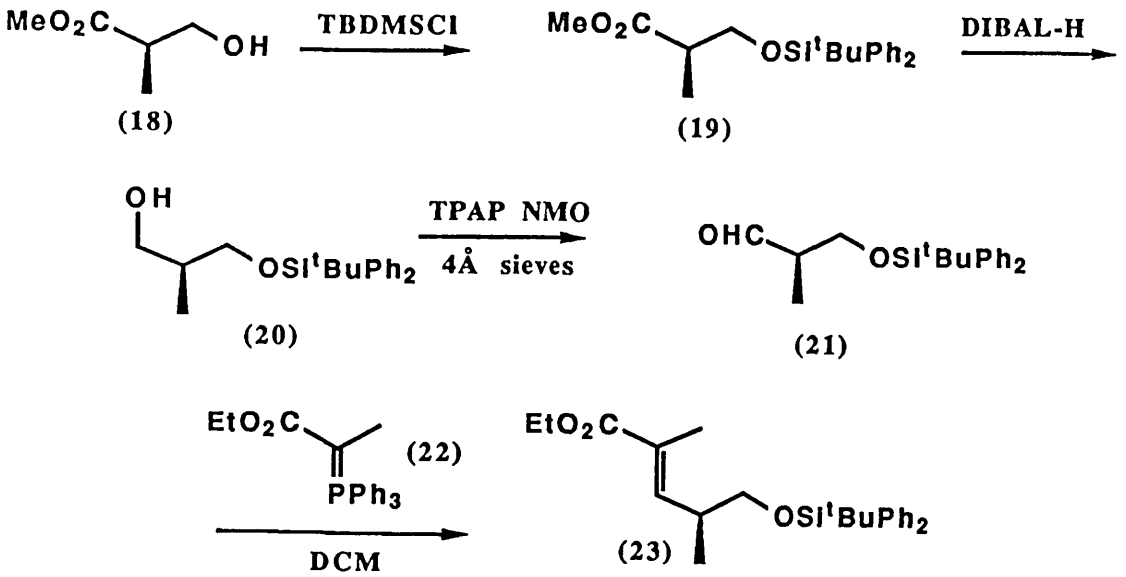
The position of the double bond in the final δ-lactone product (30) can be guarenteed by careful control of the reaction temperature.[2a]

Synthetic Route

The first step in the synthesis involves the preparation of the chiral aldehyde (21) from the commercially available ester (18). Compound (18) was protected with the *t*-butyldiphenyl- silyl group in quantitative yield and reduced to the alcohol (20) with diisobutyl aluminium hydride in 87% yield. The oxidation of (20) to aldehyde (21) proved a troublesome step. Swern oxidation afforded racemised aldehyde on a large scale and the use of PCC on a large scale was tedious because of the problems associated with diposal of the chromium residues. We found the method of choice turned out to be the use of the catalytic reagent tetra-*n*-propylammonium perruthenate (TPAP) developed earlier in work described in this thesis using N-methylmorpholine-N-oxide as co-oxidant, which gave the aldehyde (21) in an excellent 68% yield. The reaction is easy to perform and gives an optically pure product with no detectable racemisation.

The aldehyde (21) was reacted with the stabilised Wittig reagent 1-carboethoxyethylidene triphenylphosphorane (22) in dichloromethane at room temperature to give the alkene(23) in 77% yield (scheme 4).

Before proceeding with the synthesis it was necessary to firmly establish the geometry of the double bond in (23) since this was crucial to the success of the subsequent Sharpless asymmetric epoxidation reaction. A nOe nmr experiment was therefore carried out on the product (23) (fig 1). Saturation of the olefinic methyl resonance at δ 1.8 would be expected to give a positive nOe result at resonance for the olefinic position if the compound had the Z configuration or alternatively at the absorbance for the proton at C-4 if the compound had E-geometry.


MeO2C
OH
TBDMSCl
OSi^tBuPh2
DIBAL-H
(18)
(19)
TPAP NMO
4Å sieves
OHC
(20)
(21)
EtO2C
(22)
PPh3
DCM
(23)
DIBAL-H
Ti(o^iPr)4 tBuOOH
D(-)DET
(24)
Swern
Ph3P=CH2
(25)
(26)
Fe2(CO)9
(CO)3Fe
(27)
(28)
exo
(29)
endo

Scheme 4

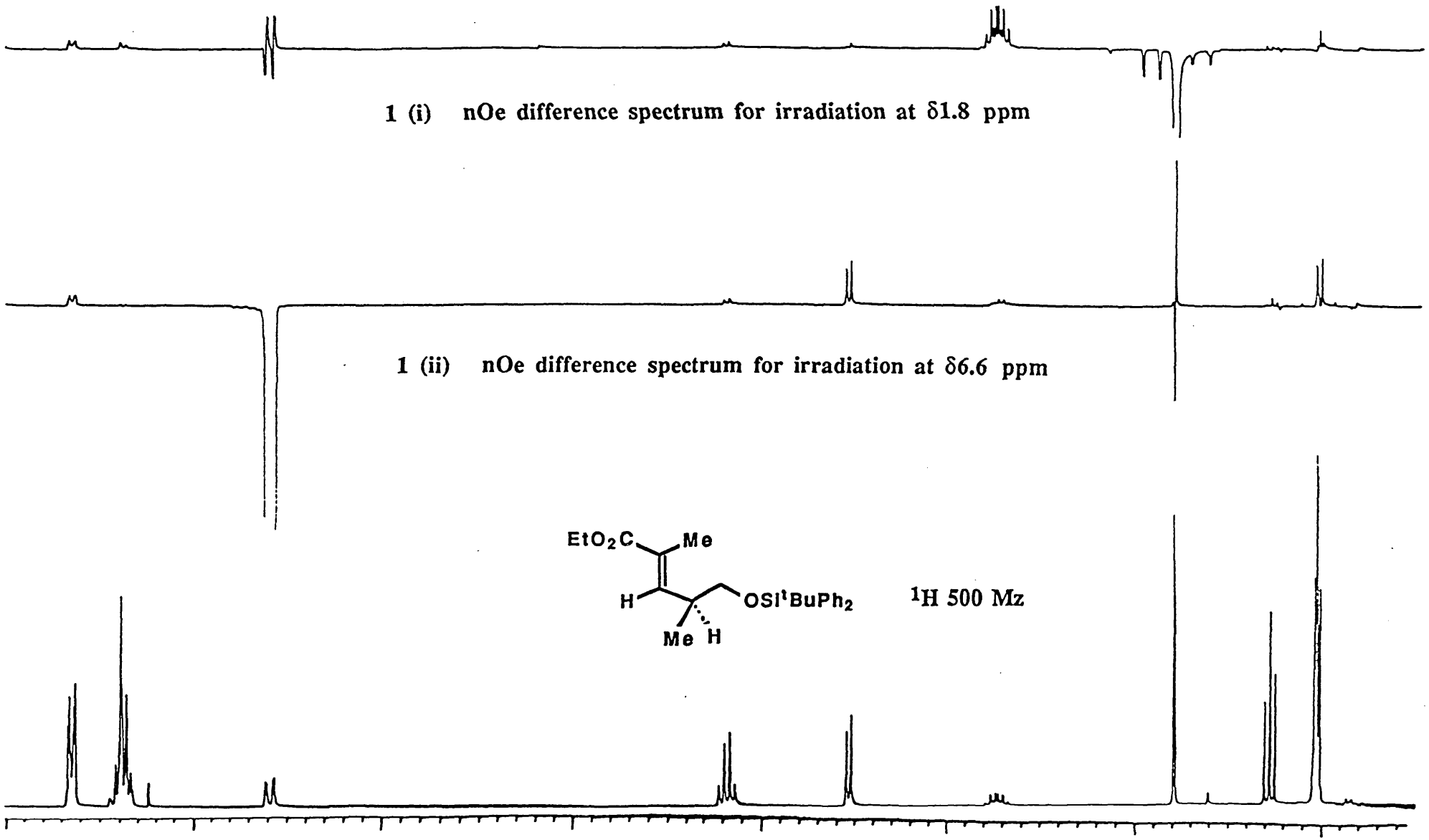
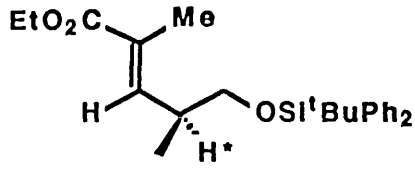
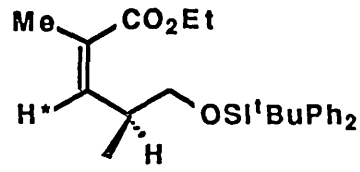

1 (i) nOe difference spectrum for irradiation at δ1.8 ppm
1 (ii) nOe difference spectrum for irradiation at δ6.6 ppm
EtO2C
Me
H
OSi tBuPh2
Me H
1H 500 Mz

Figure 1

Largest nOe's expected for irradiation of olefinic Me at H*



E

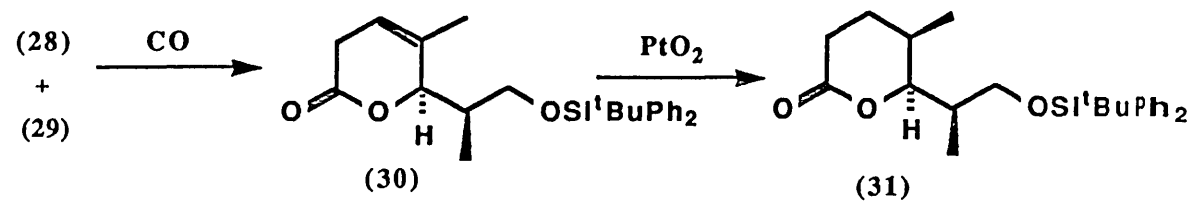


Z

From the difference spectrum in Fig 1 (i), the nOe at the C-4 proton position indicates that the alkene prepared was in fact the required E isomer, obtained in 77% yield. (The signal at δ 6.6 is only due to coupling and is not a nOe) No trace of the cis isomer was detected by t.l.c. analysis.

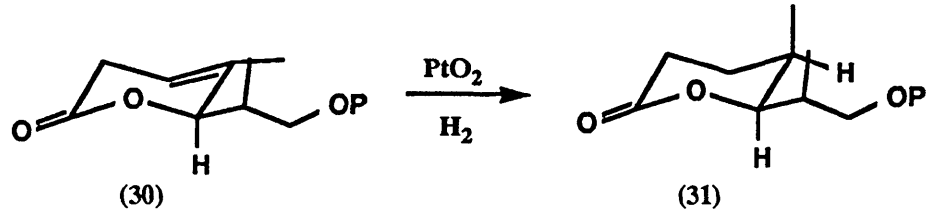
The E alkene was reduced to the alcohol (24) using 2.2 equivalents of diisobutylaluminium hydride at -78°C in 97% yield. The allylic alcohol was then subjected to Sharpless asymmetric epxodation, (scheme 5) using D-(-)-diethyl tartrate as the chiral auxiliary to ensure approach from the top face of the molecule to give (25) in 97% yield. The epoxy alcohol was oxidized by the Swern method (75%) or our TPAP[15] procedure (70%) to the epoxy aldehyde (26). Methylenation with the non-stabilized Wittig reagent methylidene triphenylphosphorane gave the required vinyl epoxide (27). The base used for the generation of the ylide in this reaction was important. The use of *n*-butyl lithium, for example, with the bromide only resulted in a low 50% yield of (27). The use of potassium hexamethyldisilazide[16] generated *in situ* from KH and hexamethyldisilazane at -30°C on the other hand gave greater than 90% yields of the product.

The vinyl epoxide (27) was converted into the *exo* and *endo* ferrilactones (28) and (29) respectively using the standard procedures. The reaction was achieved by $Fe_2(CO)_9$ in THF at room temperature, or under ultrasonic conditions in benzene using $Fe_2(CO)_9$ or by the original sequence of irradiating a solution in benzene containing $Fe(CO)_5$. The ferrilactones (28) and (29) require special handling conditions since solutions should be evaporated at low temperature (*ca* 0°C) and the neat compounds should not be evacuated owing to rapid decarboxylation. The lactones were best dried by final evaporation under a stream of dry argon.



Scheme 5

Treatment of the compounds (28) and (29) with carbon monoxide at a pressure of 250 atm, and 90°C pleasingly gave the β,γ-unsaturated δ-lactone (30) in 68% yield.(scheme 5) If the reaction temperature was raised to 150°C then mixtures containing the α,β-unsaturated compound were obtained. It is also essential that the bomb in which reactions are carried out using benzene as solvent, was pressurised before the heating process, otherwise only a small amount of the required product and the iron tricarbonyl diene complex were isolated.



The lactone (30) was hydrogenated as a crude mixture from the carbonylation reaction to afford an overall 52% yield over the two steps. Alternatively the pure lactone (30) may be hydrogenated. (in 92% yield from lactone). The hydrogenation was carried out catalytically over PtO_2 with the H_2 being delivered from the least hindered face of the molecule to give the required product (31), with the methyl group on C-5 becoming axially positioned (scheme 5). The structure of (31) has been elucidated using nmr methods (Spectrum and COSY fig. 2). Also the use of the Macromodel[17] computer programme for molecular modelling provided additional support for the proposed structure.

Macromodel predicts the most energetically favourable conformation, providing dihedral angles and coupling constants very similar to the experimental observations. The two possible compounds are shown. (fig. 3)

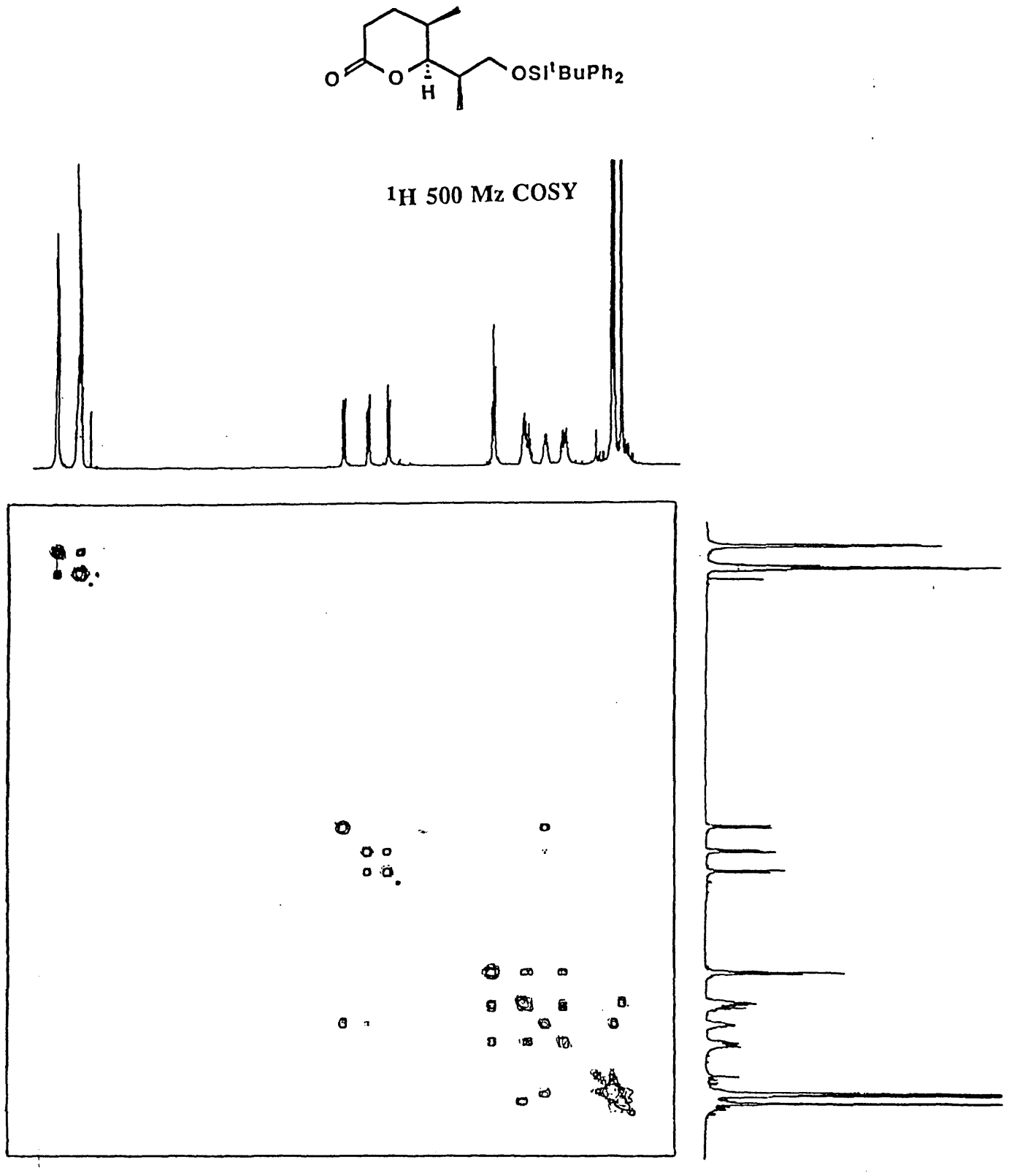


Figure 2a

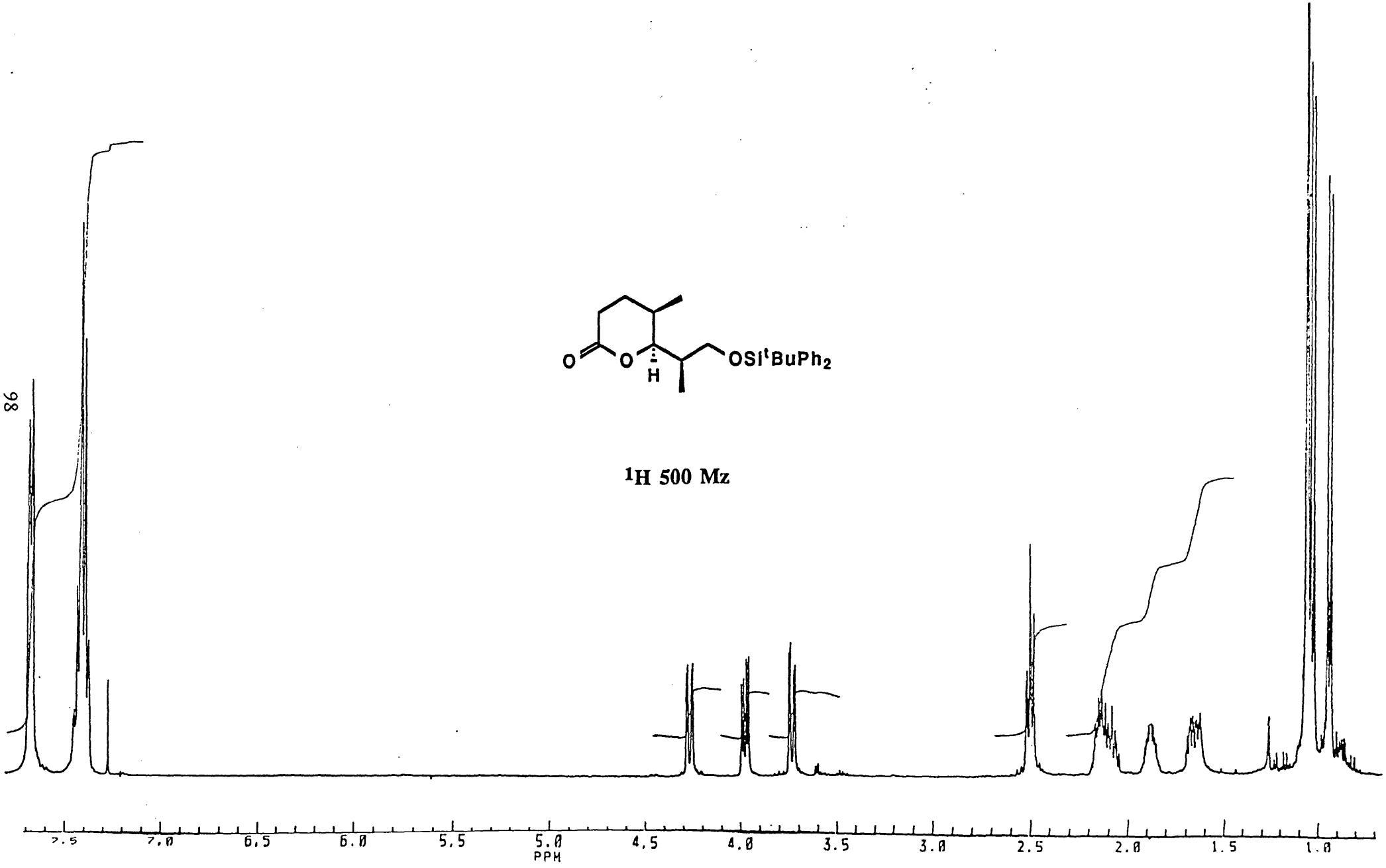

O
O
H
OSi^{t}BuPh$_2$
^{1}H 500 Mz
98
7.5
7.0
6.5
6.0
5.5
5.0
PPM
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

Figure 2b

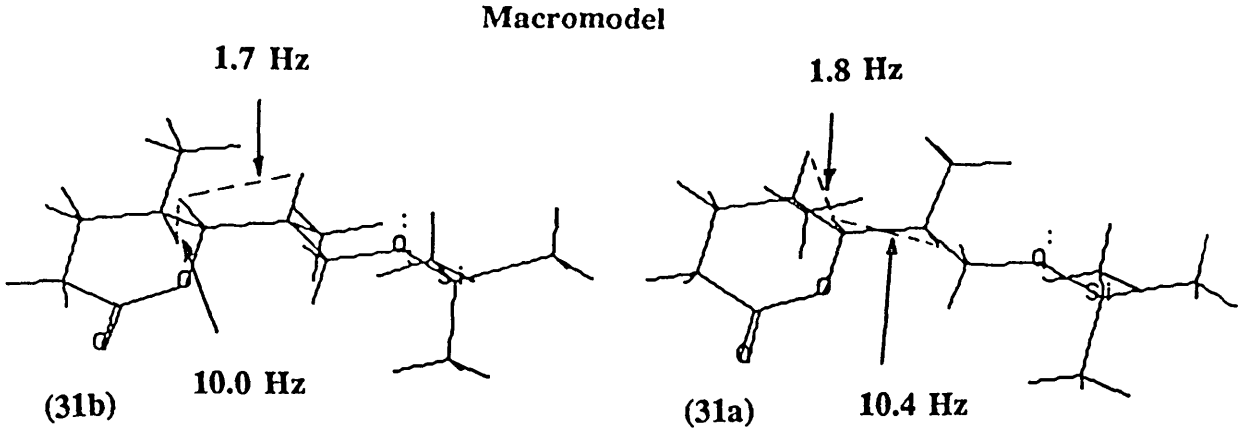
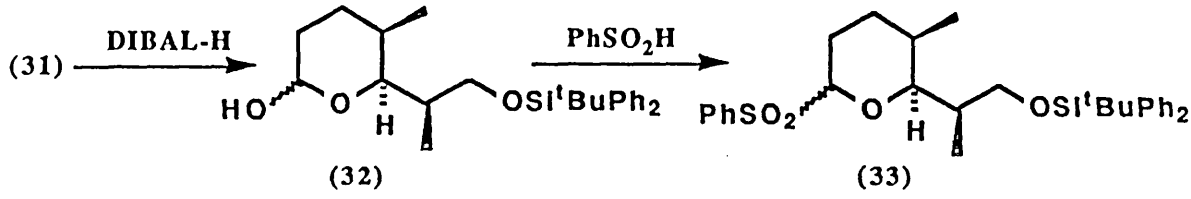


Figure 3

The required material (31a) has predicted vicinal coupling constants of *J* 1.8 Hz between the protons on C-5 and C-6 and *J* 10.4 Hz between the protons on C-6 and the sidechain.The unwanted stereoisomer (31b) has predicted coupling constants of *J* 10.0 Hz between the protons at C-5 and C-6 with the C-6 to sidechain proton coupling a small *J* 1.7 Hz.

The COSY nmr spectrum (fig 2) shows a double doublet at δ=4.28 ppm for the resonance assigned to the 5-H proton with *J* 2 Hz and 10.3 Hz. The 10.3 Hz coupling is undoubtedly due to the proton resonating at δ=1.88; this must be the sidechain proton since the other (1H value) signal (at δ=1.65 ppm) was also showing coupling to 4-H_2 and 3-H_2, (lactone ring protons) and must therefore be the 5-H ring proton resonance. Thus the coupling between the protons at C-6 and the sidechain is 10.3 Hz and the C-5 and C-6 vicinal coupling is 2 Hz, exactly as predicted by Macromodel structure (31a) and not in agreement with predictions for the other possible stereoisomer (31b).

The lactone (31) was converted to a 3:1 mixture of diasteriomeric lactols (32) in 74% yield by treatment with 1.1 equivalents of diisobutylaluminium hydride at -78°C. The final product sulphone (13) was obtained in 75% yield by treatment of these lactols (32) with freshly prepared benzene sulphonic acid (scheme 6).



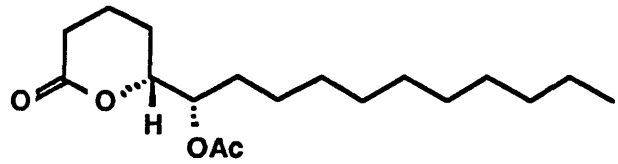
Scheme 6

The target portion (13) of the natural product CP-61,405 has therefore been synthesised in only 13 steps. All reactions in the sequence are amenable to scale-up.

3.2b Synthetic Studies Towards the Ovi-Position Attractant Pheromone of the Mosquito *Culex Pipiens Fatigans*

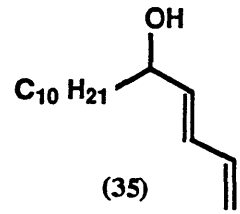
Introduction

Erythro-6-acetoxy-5-hexadeconolide (34) has been identified as the major component of the ovi-position attractant pheromone of the mosquito *culex pipiens fatigans.*[18]



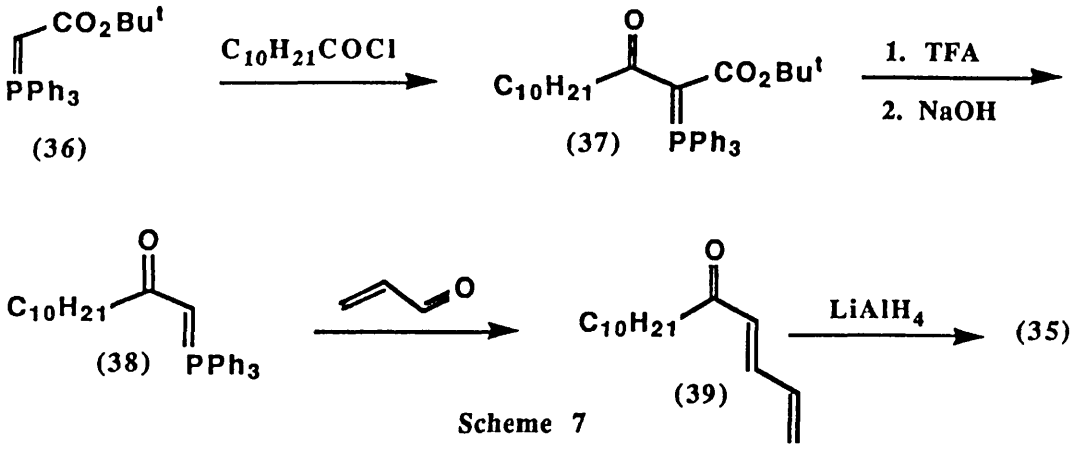
(34)

This insect species occurs worldwide, especially in tropical regions where it is believed to be involved in the transmission of the tropical diseases malaria and filariasis to man. Several literature syntheses have been published but most require esoteric reagents, are long or involve racemic structures.[19] A synthetic route to a chiral active enantiomer has been achieved in work described in this thesis *via* a 9 step process using an improved route to the key intermediate (35).



(35)

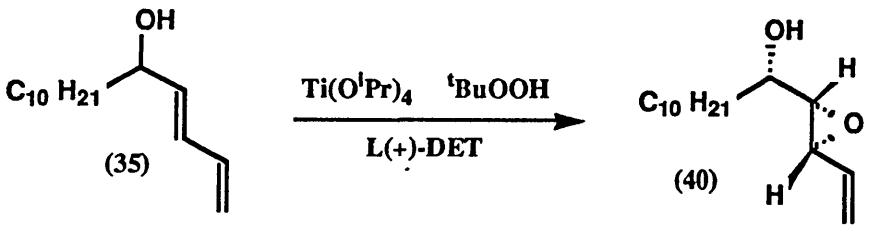
The initial synthesis was based on a Sharpless kinetic resolution[20] of (35) ultimately leading to the *erythro* product (34). The intermediate (35) was prepared in 4 steps (scheme 7).



Scheme 7

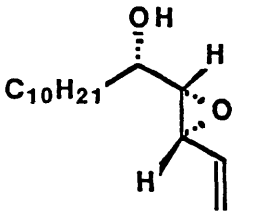
The known stabilised Wittig reagent[20] (36), on reaction with undecanoyl chloride, gives the ylide (37) in 91% yield.[21] Treatment of (37) with trifluoroacetic acid afforded the crude salt which on basic work-up produced the phosphorane (38) in 71% yield. Treatment of the phosphorane (38) with acrolein in dichloromethane gave the dienone (39) but in a disappointing 26% yield. This troublesome reaction was best achieved by heating a dilute mixture of (38) in dichloromethane for 15 min. The use of more than 10 equivalents of acrolein on a small scale, or of more than 0.5 ml on a larger scale, generally resulted in an insoluble acrolein polymer and a very low yield of the desired product. The key intermediate (35) was then prepared *via* lithium aluminium hydride reduction of dienone (39) in ether at room temperature in 81% yield.

The intermediate (35) undergoes a successful Sharpless kinetic resolution using L-(+)-diethyl tartrate to produce the required *erythro* epoxy alcohol (40) (scheme 8).



Scheme 8

The 400 MHz nmr of (40) shows 3 olefinic proton resonances (fig. 4). The terminal two olefinic absorbtions are easily distinguishable with *Jtrans*=21 Hz, *Jcis*=12.5 Hz and the geminal coupling constant ^2J=2 Hz.The COSY 400MHz nmr spectrum (fig 5) allows assignment of the epoxy and 5-H protons. The double doublet at δ 3.35 ppm is the signal for the epoxy proton at C-3 which is coupled to the olefinic



^1H 400 Mz

Figure 4

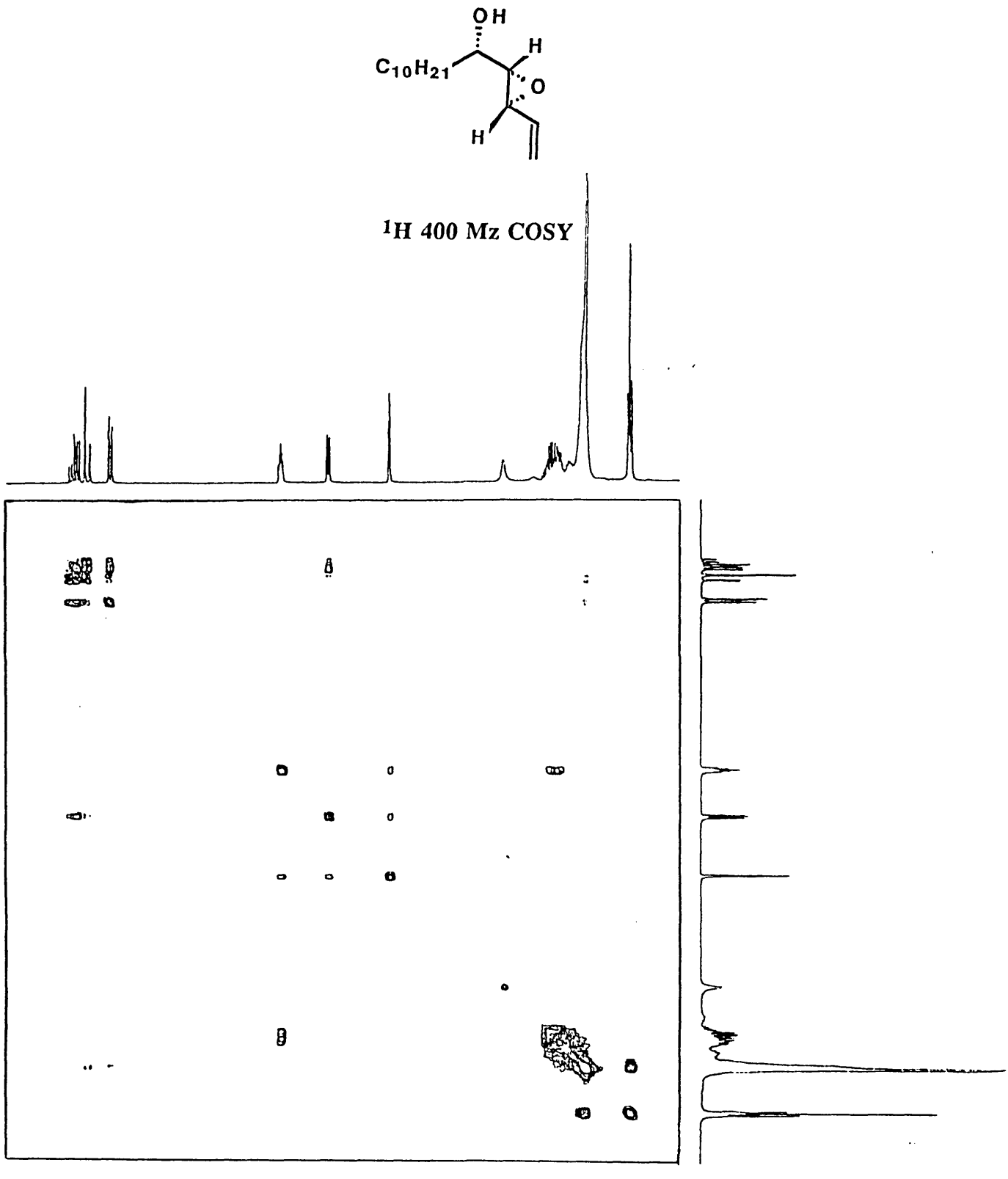
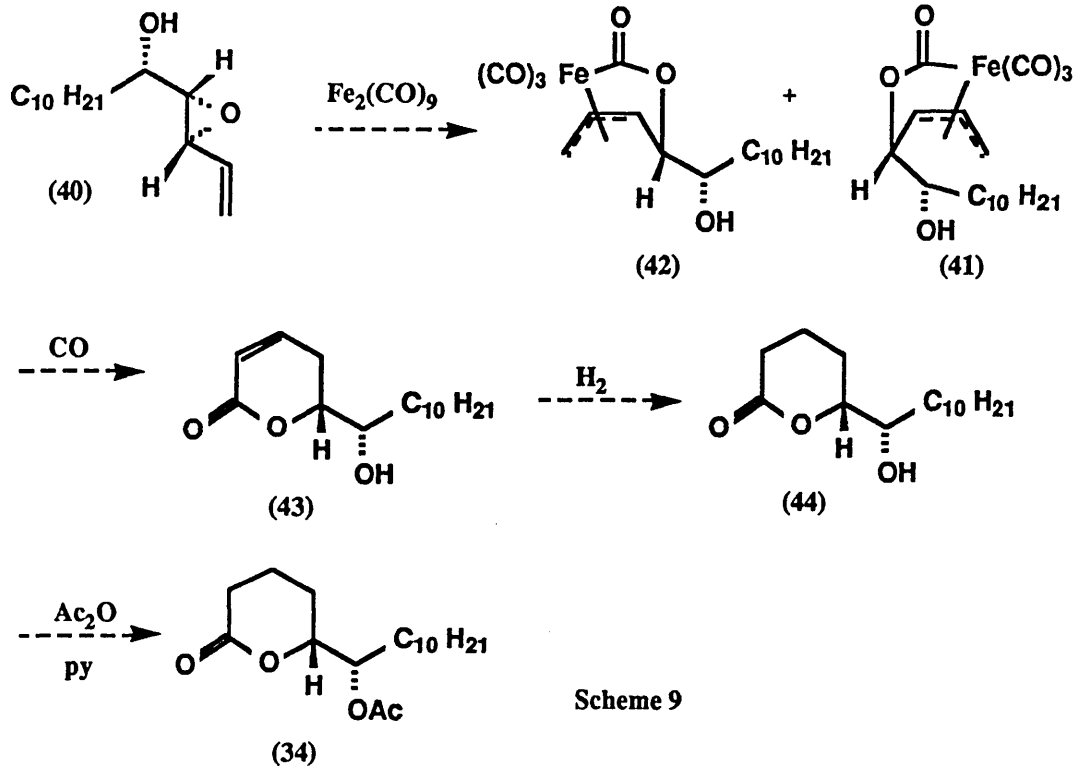


Figure 5

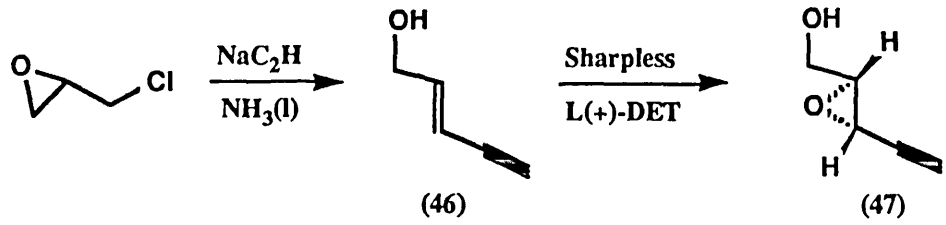
proton at C-2 with J= 9.5 Hz and the C-4 epoxy proton with J=3 Hz. The triplet at δ 2.93 ppm is the C-4 epoxy proton resonance arising from a similar coupling constant of J=3 Hz with the C-5 proton. The multiplet olefinic proton at C-2 resonates as a double double doublet with *Jtrans* 21, *Jcis* 12.5 and ^3J=9.5 Hz therefore giving rise to seven signals.

Subsequent elaboration by ferrilactonisation and high pressure carbonylation should afford the *erythro* product (scheme 9)



Scheme 9

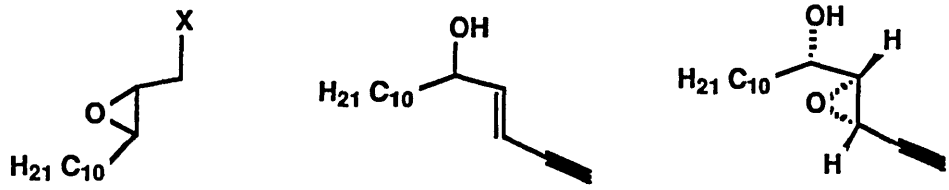
The fact that the route was not amenable to scale-up, resulted in an alternative route to the intermediate (45) being developed. The model compound (46) was made *via* treatment of epichlorohydrin with sodium acetylide in liquid ammonia (scheme 10) by the method of Heilbron.[23] The allylic alcohol (46) underwent successful Sharpless epoxidation to give the epoxide (47) in 70% yield. Therefore the target compound required is (48), from which Heilbron's methodology should ensure formation of the required unsaturated alcohol (45). (scheme 11)



(46) (47)

Scheme 10

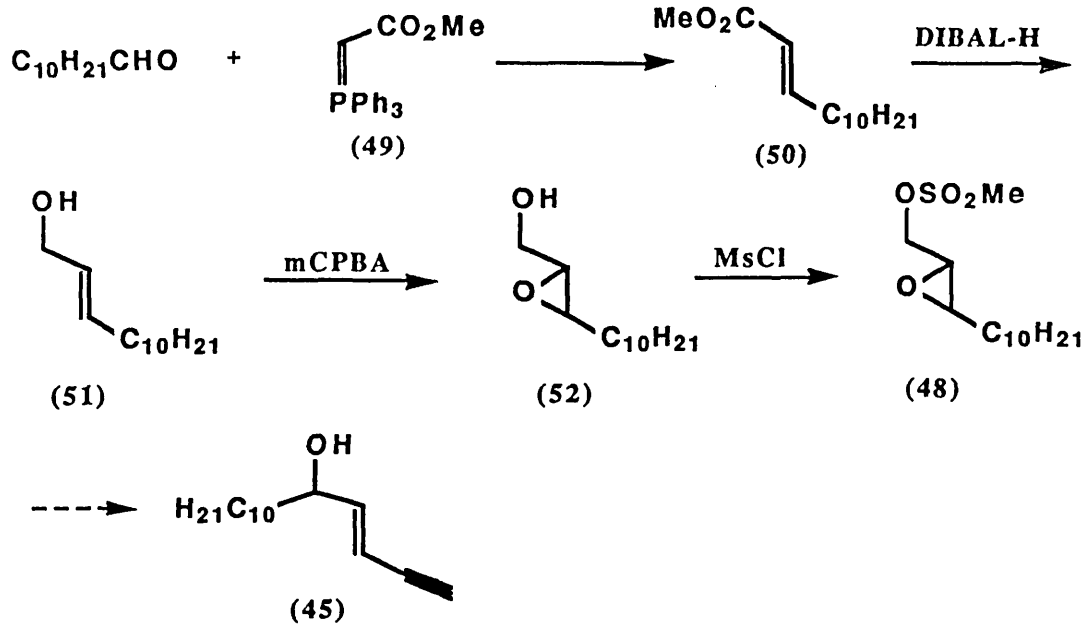
The Sharpless reaction is known to proceed successfully with an alkyne intermediate such as (45). The successful asymmetric epoxidation of an alken-yn-ol has been reported by Bernet and Vasella.[24]



(48) (45) (47)

Scheme 11

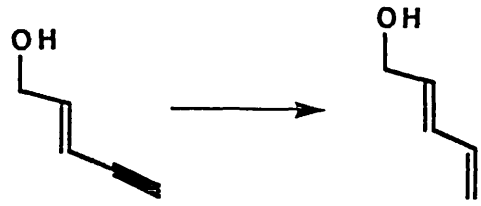
The intermediate (48) was prepared in 4 steps in excellent overall yield (scheme 12). Treatment of undecanoyl aldehyde with methoxycarbonylmethylidene triphenylphosphorane (49) in dichloromethane yields the unsaturated ester (50), with a 75% yield of the E-isomer, *Jtrans*=16 and *Jcis* =7 Hz. Reduction with diisobutylaluminium hydride to the alcohol (51) proceeds in 97% yield. The allylic alcohol was then converted to the epoxide (52) with *m*-chloroperbenzoic acid in 77% yield, in the usual manner. The epoxy alcohol was converted to the corresponding mesylate (48) (80%) or the tosylate (77%) using standard procedures.The reaction of (48) with sodium acetylide was known to proceed well with similar substrates[23] and should yield (45) (scheme 12).



Scheme 12

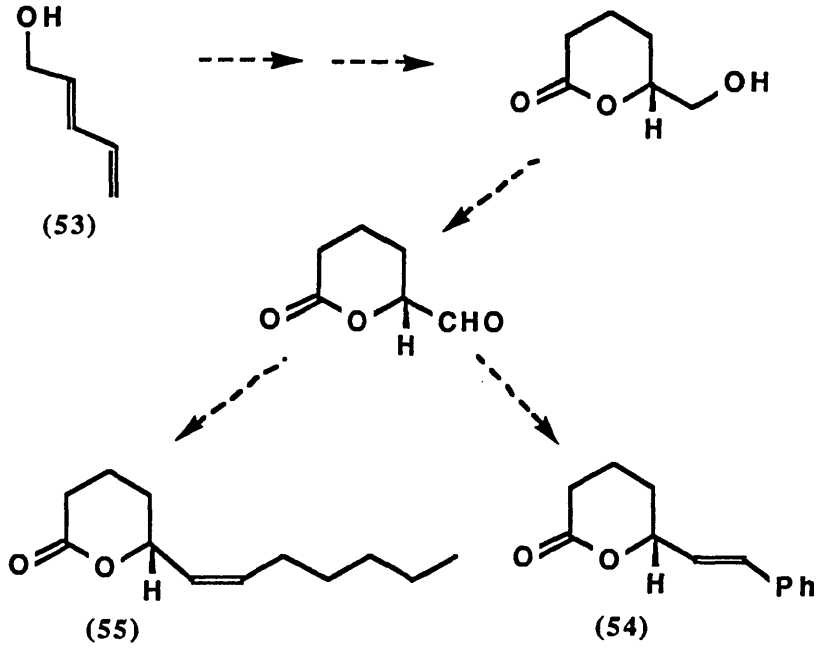
Epoxidation of (45) followed by cataytic hydrogenation to the vinyl epoxide should then yield the intermediate (40) as previously prepared. All steps are applicable to large scale operation.

Pent-2,4-dienol(53)



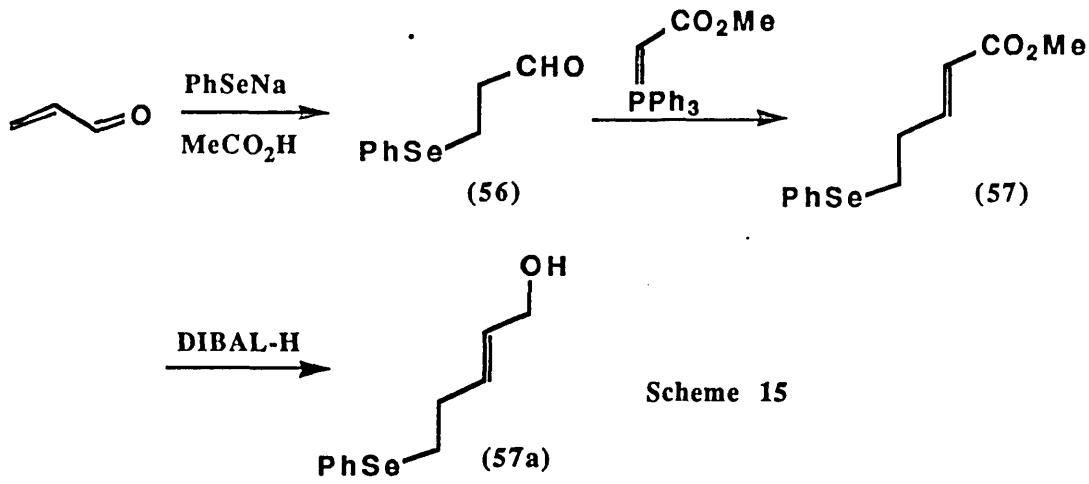
(46) **Scheme 13** (53)

The diene (53) can of course be made from selective catalytic hydrogenation of the alkyne (46) (scheme 13). Our interest in this system was two fold; namely to provide a model for the pheromone (34) synthesis and, to make use of the fact that these substrates (46) and (53) when carried through the ferrilactonisation route are also direct intermediates for the synthesis of other natural products such as Argentilactone[25] (54) and Goniothalamin[26] (55) (scheme 14). The Heilbron sodium acetylide reaction[23] is an ideal precursor to these natural products. However in our studies we developed a potentially successful route to these compounds which resulted in some interesting new methodology.



Scheme 14

The proposed sequence to these molecules invoved 1,4-addition of phenylselenol to acrolein (scheme 15).



Scheme 15

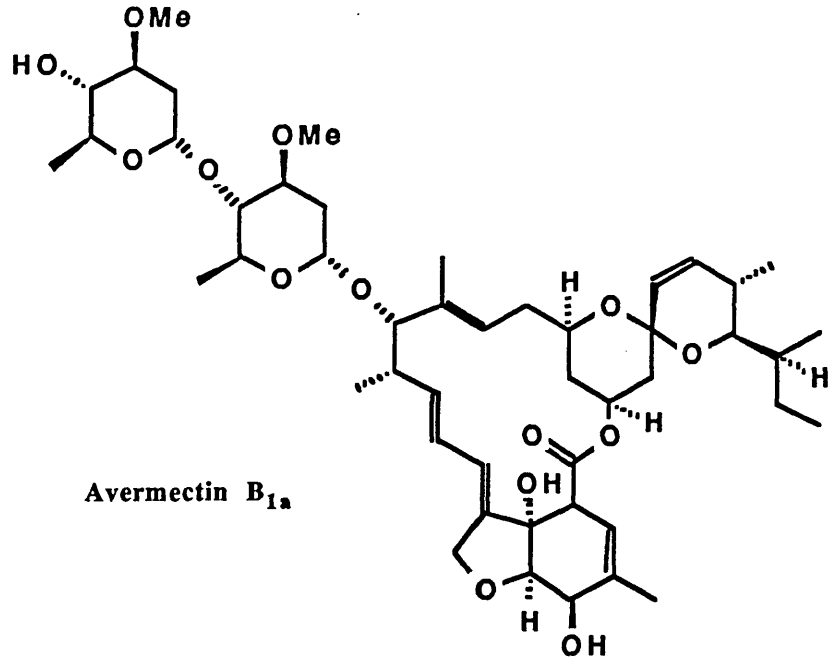
Sodium phenylselenide was generated under ultrasonic conditions from diphenyldiselenide and sodium metal,[27] then quenched with an equivalent of acetic acid and this mixture was then reacted with acrolein. Pleasingly after work-up a 56% yield of the aldehyde (56) was isolated.

The elaboration of the aldehyde (56) via a stabilised Wittig reaction led to the E-alkene (57) in 77% yield. Diisobutylalumium hydride reduction of (57) afforded the alcohol (57a) in 97% yield. Unfortunately elimination to give the diene by treatment with sodium bicarbonate solution and mCPBA at room temperature failed to give any product diene with both ester (57) or alcohol (57a). We believe that the product is formed; however, owing to its volatility it is difficult to isolate under the experimental conditions studied. The route was not investigated further owing to shortage of time; however, it could be anticipated that on a larger scale these reactions would be successful.This method could represent a new general route for the synthesis of terminal diene units from α,β-unsaturated carbonyl moieties.

Synthetic Studies Towards An Avermectin B1a Intermediate

Introduction

The avermectins and related molecules are currently enjoying intense synthetic interest as they are potent antiparasitic agents.[28]



Avermectin B_{1a}

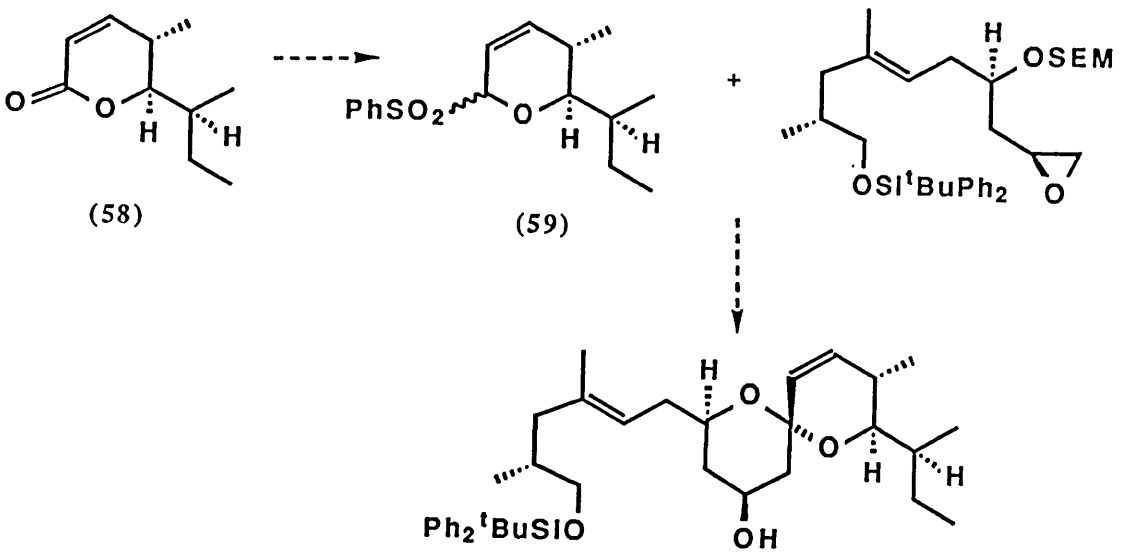
The C-11 to C-25 fragment of the related milbemycins has been synthesed by this group.[29] For this thesis an alternative synthesis of these fragments by a more convergent and practical approach was studied. The δ-lactone (58) is a precursor to the phenyl sulphone (59) which was required for spiroacetalisation to afford the spiroacetals (60) (scheme 16).

The δ-lactone (58) formed by carbonylation of the requisite ferrilatones was thought to have the most stable conformation with the 5-methyl group pseudo-equatorially disposed. The α,β-unsaturated δ-lactone should be formed by the high temperature carbonylation. Alternatively formation of the β,γ-unsaturated δ-lactone under milder lower temperature conditions followed by isomerisation of the double bond into conjugation should also yield the required product.

Attempted Synthesis

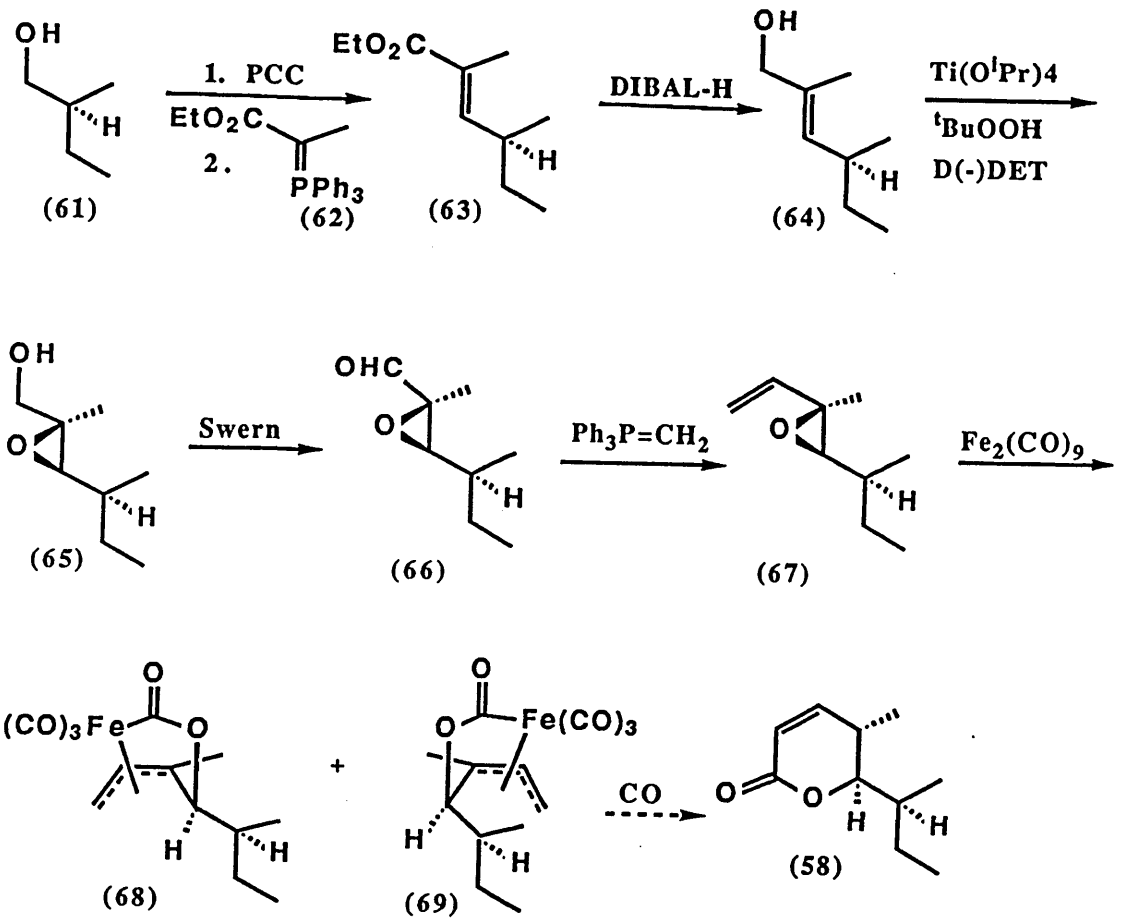
The starting material for this synthesis was commercially available 2S-methylbutanol (61). The first oxidation step proved difficult owing to extreme volatility of the aldehyde, practically it proved wise to perform the next coupling reaction on the aldehyde, *in situ*. Swern oxidation unfortunately caused racemisation of the racemisation of the aldehyde *in situ* as the subsequent Wittig reaction was rather slow (ca 12 h). Oxidation with pyridinium chlorochromate was used as this proceed better than the catalytic TPAP method. The reactions were monitered by g.l.c. to maximise the formation of the aldehyde. Treatment of the crude aldehyde in dichloromethane with 1-carboethoxyethylidenetriphenyl phosphorane (62) resulted in the E-unsaturated ester (62) in 48% overall yield. The olefinic signal of (63) appears as a doublet of quartets coupled to the trans methyl group with a coupling of ^4J 1.5 Hz; and the 4-H proton with a vicinal coupling of ^3J 10 Hz. The spectrum is very similar to that obtained previously for the CP-61,405 analogue earlier in this thesis. Diisobutylaluminium hydride reduction of (63) afforded the alcohol (64) in 65%. The Sharpless asymmetric epoxidation of (64) using D-(-)-diethyltartrate to ensure approach of the oxygen from the top face of the molecule gave the epoxide (65) in 61%. Swern oxidation of (65) gave the aldehyde (66) in 91% yield with the singlet aldehydic proton at δ=8.85 ppm. Reaction with the non-stabilised Wittig reagent methylidenetriphenylphosphorane generated in situ with potassium hexamethyldisilazide[16] as the base gave the vinyl epoxide (67) in 80% yield (scheme 16). The olefinic region of the nmr spectrum shows three separate double doublets with the *trans* coupling constant *Jtrans*=17 and the *cis* coupling constant *Jcis* =10 Hz. The geminal coupling constant between the two terminal olefinic resonances is ^2J =2 Hz.

The exo and endo ferrilactones (68) and (69) respectively, were isolated in 50% combined yield by treatment of the vinyl epoxide (67) with $Fe_2(CO)_9$ in THF. Unfortunately the only high pressure experiment carried out to date on (67) and (68) was incorrectly performed owing to a wrong heating and pressurisation sequence resulting in only a small amout of the η^4 diene complex. No further material was available at the time for completion of this synthesis, but the work is being continued in



(58) (59) (60)

Scheme 16



(61) (62) (63) (64) (65) (66) (67) (68) (69) (58)

Scheme 17

these laboratories.

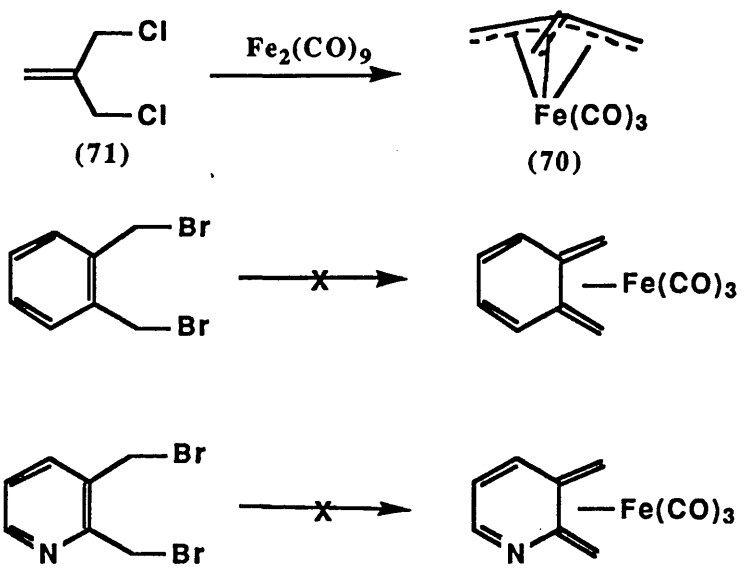
3.3 The Trimethylenemethaneirontricarbonyl System

Introduction

The trimethylenemethaneirontricarbonyl system TMM-$Fe(CO)_3$ (70) was first made by Emerson and co-workers[30] in 1966. The reaction of dihalo-unsaturated moieties with iron carbonyls has long been known.[32] The best recorded literature yield for the thermal reaction between 3-chloro-2-chloromethyl-1-propene (71) and disodium tetracarbonylferrate was a 32% of (70).[32] Little chemistry of related derivatives has been reported.[33]

Preparation and Attempted Functionalisation of TMM-$Fe(CO)_3$

The reaction of $Fe_2(CO)_9$ under our previously developed ultrasonic conditions in 30/40 petroleum ether resulted in a quantitative yield of TMM-$Fe(CO)_3$.[34] (scheme 18)



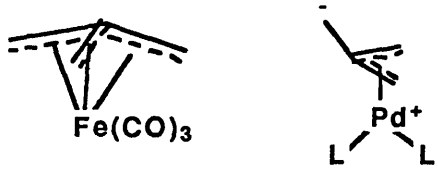
Scheme 18

This is a remarkably mild and effective process compared to the previous thermal routes.[32] Unfortunately extension of this to other dihalides such as ortho-dibromoxylene and 2,3-dibromomethylpyridine, failed to give the desired products although starting material was consumed in the reactions. (scheme 18)

The reaction of TMM-$Fe(CO)_3$ with nucleophiles such as phenyl lithium, Cyclohexanone (lithium enol), and pyrrole-N-grignard failed to give any isolable products under a range of temperatures and experimental conditions.

Electrophilic attack of electron deficient olefins on the TMM-$Fe(CO)_3$ moiety has been examined. Treatment with tetracyanoethylene or dimethylfumarate under ultrasonic conditions gave no cycloadduct. A 5% yield of cycloadduct has been reported with tetracyanoethylene in a thermal reaction.[32] Attempted formation of the trimethylenemethane fragment in situ by treatment with ceric ammonium nitrate or the milder iron ligand disengagement ligand Me_3NO [36] failed to give any recognisable products.

This apparent lack of reactivity has not been commented upon in the literature. However an inspection of the X-ray[36] and electron intensity data[37] of derivatives of (70) is enlightening. The X-ray studies show the peripheral carbons to be bent in towards the iron atom. The electron density is in the form of a parachute, with the peripheral carbons more strongly bonded to iron than the centre one. This in direct contrast to Trost's reactive trimethylenemethane system,[38] (scheme 19) in which all the peripheral carbons show nucleophilic character and react with electron deficient olefins via nucleophilic attack and subsequent ring closure.



Scheme 19

This unreactivity could be counteracted by replacement of carbon monoxide ligands with strongly electron donating phosphine ligands. A literature synthesis of TMM-$Fe(PR)_3$ does in fact exist[40] but full experimental details were not given and the yields were very low, consequently the work could not be repeated and the hypothesis tested out.

References

1. G.D.Annis, S.V.Ley, C.R.Self, and R.Sivaramakrishnan, *J. Chem. Soc., Perkin Trans. I,* 1981, 270.

2. R.Aumann, H.Ring, C.Kruger, and R.Goddard,*Chem. Ber.,* 1979, 112, 3644; G.D.Annis, S.V.Ley, and R.Sivaramakrishnan, *J. Organomet. Chem.*,1979, 182, C11.

3. S.T.Hodgson, D.M.Hollinshead, and S.V.Ley, *J. Chem. Soc., Chem. Commun.*,1984, 494.

4. CP-61,405 : U.S.P. 4 547 523/1985.

5. "Polyether Antibiotics, Naturally Occuring Acid Ionophores", Ed. J.W.Westley, Dekker, 1983, Vol 2.

6. B.C.Pressman, *Ann. Rev. Biochem.,* 1976, 45, 501.

7. P.W.Reed and H.A.Lardy, *J. Biol. Chem.*,1972, 247, 6970.

8. M.O.Chaney, P.V.Demarco, N.D.Jones, and J.L.Occolowitz, *J. Am. Chem. Soc.,* 1974, 96, 1932.

9. G.D.Smith and W.L.Duax, *J. Am. Chem. Soc.*,1976, 98, 1578.

10. C.Tissier, J.Juillard, M.Dupin, and G.Jeminet, *J. Chim. Phys.,* 1979, 76, 611; D.R.Pfeiffer, R.W.Taylor, and H.A.Lardy, *Ann. N. Y. Acad. Sci.,* 1978, 307, 402.

11. H.M.Organ Ph.D. Thesis, Imperial College, 1987.

12. M.P.Edwards, A.M.Doherty, S.V.Ley, and H.M.Organ, *Tetrahedron,*1986, 42, 3723.

13. M.Prudhomme and G.Jeminet, *Experientia,* 1983, 39, 256; M.Prudhomme, G.Dauphin, J.Guyot, and G.Jeminet, *J. Antibiotics,* 1984, 37, 627; M.Prudhomme, G.Dauphin, and G.Jeminet, ibid., 1986, 39, 934; J.M.Aizpurna and C.Palomo, *Bull. Soc. Chim. Fr.*, 1984, II-142.

14. A.M.Horton, D.M.Hollinshead, and S.V.Ley, *Tetrahedron*, 1984, 40, 1737.

15. W.P.Griffith, S.V.Ley, G.P.Whitcombe, and A.D.White, J. Chem. Soc., Chem. Commun., 1987, 1625.

16. R.K.Boeckman,Jr., J.O.Gardner, K.A.Parker, and G.Stork, *J. Am. Chem. Soc.,* 1976, 98, 1578.

17. C. Altana, C.A.G.Haasnoot, and F.A.A.M. De Leeuw, *Tetrahedron,* 1980, 36, 2783.

18. B.R.Laurence and J.A.Pickett, *J. Chem. Soc., Chem. Commun.,* 1982, 59 and references therein.

19. C.Fuganti, P.Grasselli, and S.Servi, *J. Chem. Soc., Chem. Commun.,* 1982, 1285; K.Mori and T.Otsuka, *Tetrahedron,* 1983, 39, 3267; Y.Masaki, K.Nagata, and K.Kaji, *Chem. Lett.,* 1983, 1835; T.Sato, M.Watanabe, M.Honda, and T.Fugisawa, *Chem. Lett.,* 1984, 1175; Lin Guo-qiang, Xu Hai-jian, Wu Bi-chi, Guo Guong-zhong, and Zhou Wei-shan, *Tetrahedron Lett.,* 1985, 26, 1233; N.C.Barua and R.R.Schmidt, *Tetrahedron,* 1986, 42, 4471.

20. A.Pfenninger, *Synthesis,* 1986, 89.

21. D.L.Burman and M.P.Cooke,Jr., *J. Org. Chem.,* 1982, 47, 4955.

22. D.M.Hollinshead, personal communication.

23. L.J.Haynes, I.Heilbron, E.R.H.Jones, and F.Sondheimer, *J. Chem, Soc.,* 1947, 1583.

24. B.Bernet and A.Vasella, *Tetrahedron Lett.,* 1983, 24, 5491.

25. J.D.Bonafide, H.A.Priesthap, and E.A.Ruveda, *Phytochemistry,* 1976, 1579.

26. J.R.Hlubucek and A.V.Robertson, *Aust. J. Chem.,* 1967, 20, 2199.

27. S.V.Ley, C.M.R.Low, and I.A.O'Neil, *Tetrahedron,* 1986, 42, 5363.

28. M.H.Fisher and Mrozik in "Macrolide Antibiotics" Ch. 14, 533. Academic Press 1984.

29. D.Culshaw, P.Grice, S.V.Ley, and G.A.Strange, *Tetrahedron Lett.,* 1985, 26, 5837.

30. G.F.Emerson, K.Ehrlich, W.P.Giering, and P.C.Lauterbur, *J. Am. Chem. Soc.,* 1966, 88, 3172.

31. A.J.Pearson in "Comprehensive Organometallic Chemistry" Ed. Wilkinson, Stone, Abel, Vol. 8, 939.

32. R.Pettit and J.S.Ward, *J. Chem. Soc., Chem. Commun.,* 1970, 1419.

33. T.Nishimura, R.Noyori, and H.Takaya, *J. Chem. Soc., Chem. Commun.,* 1969, 89.

34. S.V.Ley, C.M.R.Low, and A.D.White, *J. Organometallic Chem.*, 1986, 302, C13.

35. Y.Shvo and E.J.Hazum, *J. Chem. Soc., Chem. Commun.*, 1974, 336.

36. M.R.Churchill and K.Gold, *Inorg. Chem.*, 1969, 8, 401; A.N.Nesmeyanov, I.S.Astakhova, G.P.Zol'nikova, I.I.Kritskaya, and Yu.T.Struchkov, *J. Chem. Soc., Chem. Commun.*, 1970, 85.

37. J.-M.Savariault and J.F.Labarre, *Inorg. Chim. Acta*, 1976, 19, L53.

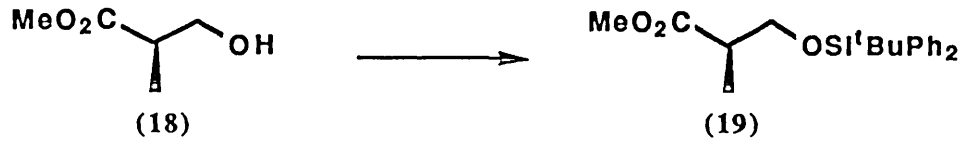
38. B.M.Trost and D.M.T.Chan, *J. Am. Chem. Soc.*, 1979, 101, 6429.

39. J.-M.Grosselin, H.Le Bozec, C.Moinet, L.Toupet, and P.H.Dixneuf, *J. Am. Chem. Soc.*, 1985, 107, 2809.

40. J.A.Nieuwland, T.H.Vaughn, and R.R.Vogt, *J. Am. Chem. Soc.*, 1934, 56, 2120.

IR spectra were recorded as neat thin films on a Perkin-Elmer 983G infrared spectrometer. ^1H NMR spectra were obtained in $CDCl_3$ solution, at 90 MHz on a Jeol FX 90Q, at 250 MHz on a Bruker WH-250, at 400 MHz on a Bruker WH-400 and at 500 MHz on a Bruker AM-500, chemical shifts are recorded in ppm (δ) relative to $CHCl_3$ (δ = 7.26ppm). Mass spectra and high resolution mass spectral data were performed on a VG micromass 7070B instrument. Microanalyses were performed in the Imperial College Chemistry Department microanalytical laboratory. Melting points were determined on a Kofler hot plate apparatus and are uncorrected. Thin layer chromatographic analysis was carried out on precoated, glass backed plates (Merck Kieselgel 60 F) and column chromatography was conducted on silica gel under low pressure using Merck Kieselgel 60 (230-400 mesh ASTM). Solvents were distilled from the appropriate drying agents under argon and used immediately. Light petroleum (b.p. 40-60°C) used for chromatographic purposes was redistilled before use. Moisture sensitive reactions were performed in oven-dried glassware (>150°C, 24h) under a positive pressure of argon. Evaporation of solvents were carried out at aspirator pressure on a Buchi rotory evaporator.

[2S]Methyl-3-*t*-Butyldiphenylsilylmethylpropionate(19).-



(18) (19)

4-N,N-Dimethylaminopyridine (0.7 g, 5.8 mmol) and triethyl amine (24.1 ml, 0.17 mmol) were added to a solution of (18)(17 g, 0.14 mmol) in dry dichloromethane (300 ml) under argon at 0°C. *t*-Butyldiphenylsilyl chloride (41.2 ml, 0.16 mol) was added *via* a syringe pump and the solution stirred for 2 h, then stored below 0°C overnight. The mixture was poured into water and extracted with dichloromethane. The extract was washed with saturated ammonium chloride, water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 5% ether in petrol, to give the silyl protected ester (19) (51.3 g, 100%) as an oil, (Found : C, 70.6; H, 8.00. $C_{21}H_{28}O_3Si$ requires C, 70.7; H, 7.92%), $\upsilon_{max.}$ (neat thin film) 2 933, 2 858, 1 741, 1 428, 1 200, and 1 113 cm^{-1}, $\delta(CDCl_3$, 250 MHz) 7.7-7.4 (10H, m, Ph), 3.77 (2H, m, CH_2OSi), 3.68 (3H,s, OMe), 2.72 (1H, q, *J* 7 Hz, CH), 1.16 (3H, d, *J* 7 Hz, Me), and 1.02(9H, s, *t*-Bu), m/z 341 (M^+ - Me), 325 (M^+ - OMe), and 299 (M^+ - *t*-Bu), $[\alpha]_D = -17.1°$, [c = 2.20, $CHCl_3$]

[2S]3-*t*-Butyldiphenylsilyloxy-2-methylpropanol(20).-

(19) (20)

Di-isobutyl aluminium hydride (64.6 ml of a 1.5*M* solution in toluene) was added dropwise *via* a syringe pump to a stirred solution of ester (19) (15.7 g, 44 mmol) in dry toluene (250 ml) under argon at -78°C. The solution was stirred for 1.5 h, quenched with water (1.74 ml, 98 mmol) and allowed to warm to room temperature; upon gelling (*ca* 0.5-1 h), the slurry was poured onto solid Na_2SO_4 overlayed with ethyl acetate. The mixture was stirred vigorously until, upon standing, the solution cleared. The ethyl acetate was decanted through a pad of celite and the process repeated twice. The combined filtrates

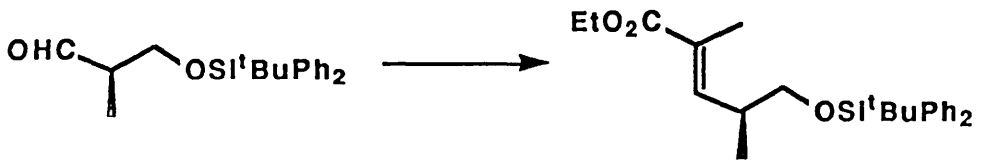
were evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 20% ether in petrol, to give the alcohol (20) (29.8 g, 87%) as an oil, (Found : C, 73.3; H, 8.73. $C_{20}H_{28}O_2Si$ requires C, 73.1; H, 8.59%), $\upsilon_{max.}$ (neat thin film)3 366, 2 958, 2 858, 1 471, 1 427, and 1 112 1 20 cm^{-1}, $\delta(CDCl_3$, 250 MHz) 7.7-7.4 (10H, m, Ph), 3.66 (4H, m, 2 x CH_2O), 2.57 (1H, br, OH), 2.00 (1H, m, CH), 1.07(9H, s, *t*-Bu), and 0.83 (3H, d, *J* 7 Hz, Me), m/z 271 (M^+ - *t*-Bu), $[\alpha]_D$ = -5.7°, [c = 2.41, $CHCl_3$].

[2S]3-*t*-Butyldiphenylsilyloxy-2-methylpropanal(21).-

(20) (21)

Anhydrous N-methylmorpholine-N-oxide (5.3 g, 45 mmol) and tetra-*n*-propylammonium perruthenate (0.1 g, 0.3 mmol) were added to stirred solution of alcohol (20) (12.3 g, 37 mmol) in dry dichloromethane (250 ml) over 4Å molecular sieves (3 g). The mixture was stirred for 4 h, washed with $CuSO_4$ solution, filtered through a celite pad, washed with water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10% ether in petrol, to give the aldehyde (21) (4.1 g, 63%, based on recovered starting material) as an oil, (Found : C, 73.6; H, 8.13. $C_{20}H_{26}O_2Si$ requires C, 73.6; H, 8.03%), $\upsilon_{max.}$ (neat thin film) 2 993, 2 714, 1 735, 1 471, 1 428, and 1 112 cm^{-1}, $\delta(CDCl_3$, 250 MHz) 9.78 (1H, d *J* 1.5 Hz, CHO), 7.7-7.4 (10H, m, Ph), 3.88 (2H, m, CH_2OSi), 2.58 (1H, m, CH), 1.10 (3H, d, *J* 7 Hz, Me), and 1.05 (9H, s, *t*-Bu), m/z 269 (M^+ - *t*-Bu), $[\alpha]_D$ = -25.3°, [c = 2.81, $CHCl_3$].

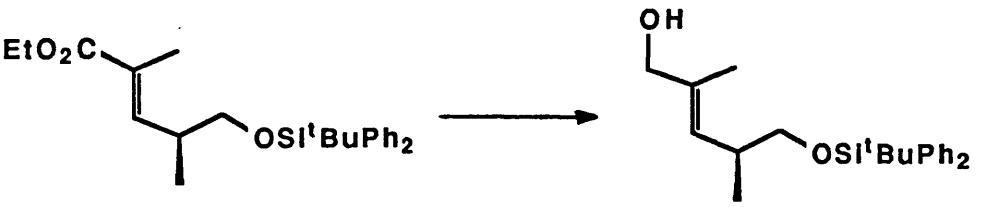
[4S]E-Ethyl-5-*t*-Butyldiphenylsilyloxy-2,4-dimethyl pent-2- enote(23).-



(21) (23)

1-Carboethoxyethylidene triphenylphosphorane (5.44 g, 15.9 mmol) in dichloromethane (200 ml) was added to a stirred solution of aldehyde (21) (4.0 g, 12.3 mmol) in dichloromethane (50 ml) at room temperature. The mixture was stirred overnight, evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 5% ether in petrol, to give the alkene (23) (3.9 g, 77%) as an oil, (Found : C, 73.1; H, 8.55. $C_{25}H_{34}O_3Si$ requires C, 73.3; H, 8.35%), $\upsilon_{max.}$ (neat thin film) 2 959, 2 932, 2 858, 1 709, 1 649, 1 509, 1 427, 1 235, and 1 112 cm^{-1}, $\delta(CDCl_3, 250\ MHz)$ 7.7-7.4 (10H, m, Ph), 6.60 (1H, d, *J* 10 Hz, olefinic CH), 4.18 (2H, q, *J* 7 Hz, ethyl CH_2), 3.55 (2H, d, *J* 7 Hz, CH_2OSi), 2.75 (1H, m, CH), 1.82 (3H, d, *J* 1.5 Hz, olefinic Me), 1.30 (3H, t, *J* 7 Hz, ethyl Me), and 1.06 (12H, s, *t*-Bu and Me), m/z 353 (M^+ - *t*-Bu), $[\alpha]_D$ = -2.2°, [c = 1.56, $CHCl_3$].

[4S]E-5-*t*-Butyldiphenylsilyloxy-2,4-dimethylpent-2-enol(24).-

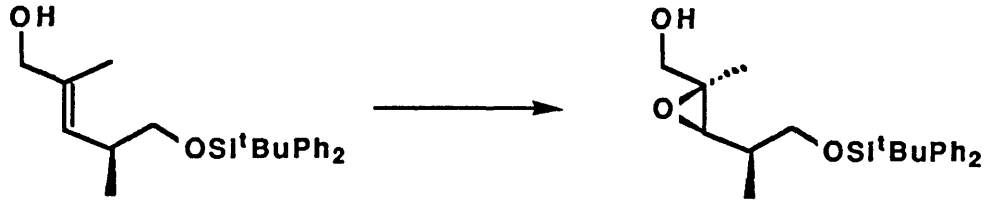


(23) (24)

Di-isobutyl aluminium hydride (10.9 ml of a 1.5*M* solution in toluene) was added dropwise to a stirred solution of ester (23) (3.5 g, 8.5 mmol) in dry toluene (50 ml) under argon at -78°C. The solution was stirred for 30 min, quenched with water (5.5 ml, 98 mmol) and allowed to warm to room temperature; upon gelling the slurry was stirred with solid $NaHCO_3$ and an excess of ethyl acetate. The ethyl acetate solution upon clearing was decanted through a celite pad and the process repeated twice. The combined filtrates were evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with

20% ether in petrol, to give the alcohol (24) (2.7 g, 90%) as an oil, (Found : C, 74.7; H, 8.86. $C_{23}H_{32}O_2Si$ requires C, 75.0; H, 8.75%), $\upsilon_{max.}$ (neat thin film) 3 337, 2 958, 2 858, 1 589, 1 427, and 1 113 cm^{-1}, $\delta(CDCl_3$, 250 MHz) 7.6-7.4 (10H, m, Ph), 5.13 (1H, dq, *J* 9.5 Hz and 1.5 Hz, olefinic CH), 3.93 (2H, s, CH_2OSi), 2.61 (1H, m, CH), 1.58 (3H, d, *J* 1.5 Hz, olefinic Me), 1.02 (9H, s, *t*-Bu), and 0.98 (3H, d, *J* 7 Hz, Me), m/z 311 (M^+ - *t*-Bu) and 293 (M^+ - *t*-Bu - H_2O) $[\alpha]_D = +18.9°$, [c = 1.33, $CHCl_3$].

[2R,3R,4S]5-*t*-Butyldiphenylsilyloxy-2,3-epoxy-2,4-dimethyl pentanol(25).-

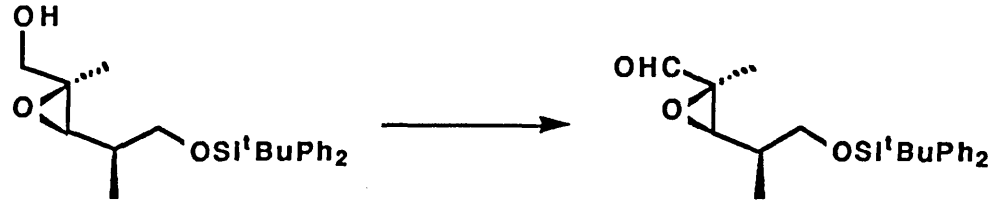


(24) (25)

To dry dichlomethane (40 ml) under argon at -20°C was added titanium tetraisopropoxide (1.76 ml, 5.9 mmol); D-(-)-diethyltartrate (1.01 ml, 5.91 mmol); (the mixture was stirred for 5 min before next addition) alcohol (24) (2.09 g, 5.9 mmol) in dichloromethane (5 ml); and *t*-butylhydroperoxide (3.94 ml of a 3*M* solution in toluene). The mixture was stirred overnight at -20°C, then 10% aqueous tartaric acid (15 ml) was added and the mixture stirred for 30 min at -20°C, and for 1 h at room temperature or until the aqueous phase cleared.The organic layer was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to afford the crude product contaminated with *t*-butylhydroperoxide. The oil was diluted with ether (30 ml), cooled to 5°C and stirred with NaOH (12 ml of a 1*M* aqueous solution) for 30 min at 5°C. The organic phase was washed with brine, dried (Na_2SO_4), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10 to 30% ether in petrol, to give the epoxide (25) (2.22 g, 97%) as an oil, (Found : C, 71.7; H, 8.43. $C_{23}H_{32}O_3Si$ requires C, 71.8; H, 8.39%), $\upsilon_{max.}$ (neat thin film) 3 450, 2 932, 2 859,1 589,1 470,1 427, 1 389, and 1 112 cm^{-1}, $\delta(CDCl_3$, 250 MHz) 7.6-7.4 (10H, m, Ph), 3.65 (4H, m, 2 x CH_2O), 2.94 (1H, d, *J* 9.5 Hz, epoxy

CH), 1.60 (1H, m, CH), 1.25 (3H, s, epoxy Me), 1.03 (9H, s, *t*-Bu), and 1.00 (3H, d, *J* 6.5 Hz, Me), m/z 309 (M^+ - *t*-Bu - H_2O), $[\alpha]_D$ = +17.3°, [c = 0.78, $CHCl_3$].

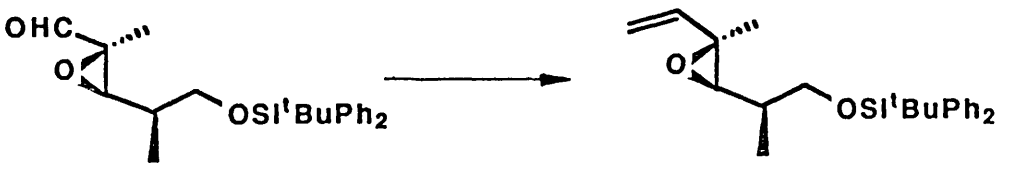
[2S,3R,4S]5-*t*-Butyldiphenylsilyloxy-2,3-epoxy-2,4-dimethyl pentanal(26).-



(25) (26)

Dimethyl sulphoxide (0.063 ml, 0.45 mmol) was added dropwise to a solution of oxalyl chloride (0.039 ml, 0.45 mmol) in dry dichloromethane (10 ml) at -60°C. The mixture was stirred for 5 min then the alcohol (25) (0.151 g, 0.41 mmol) in dichloromethane (2 ml) added. The solution was stirred for a further 20 min at -60°C, then quenched with triethylamine (0.28 ml, 2.03 mmol) and allowed to warm to room temperature. The mixture was poured into water and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10% ether in petrol, to give the aldehyde (26) (0.112 g, 75%) as an oil, (Found : C, 72.0; H, 8.11. $C_{23}H_{30}O_3Si$ requires C, 72.2; H, 7.90%), $\upsilon_{max.}$ (neat thin film) 2 961, 2 933, 2 858, 1 727, 1 471,1 428, and 1 112 cm^{-1}, δ($CDCl_3$, 400 MHz) 8.86 (1H, s, CHO), 7.7-7.4 (10H, m, Ph), 3.83 (2H, dq, *J* 9 and 5 Hz, CH_2OSi), 3.11 (1H, d, *J* 10 Hz, epoxy CH), 1.65 (1H, m, CH), 1.40 (3H, s, epoxy Me), 1.11 (9H, s, *t*-Bu), and 1.06 (3H, d, *J* 8 Hz, Me), m/z 325 (M^+ - *t*-Bu), $[\alpha]_D$ = -59.3°, [c = 1.21, $CHCl_3$].

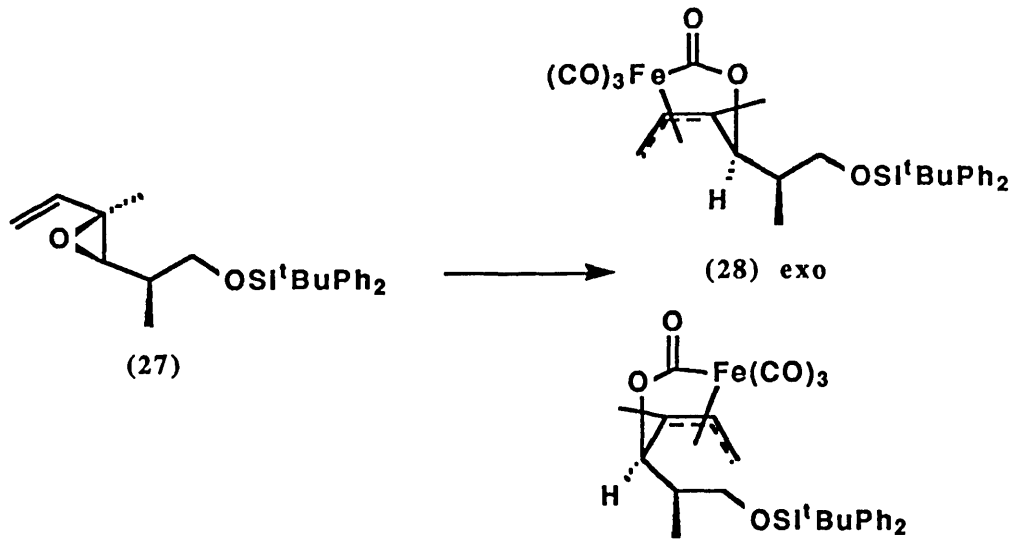
[3R,4R,5S]6-*t*-Butyldiphenylsilyloxy-3,4-epoxy-3,5-dimethyl-hexene(27).-



(26) (27)

Hexamethyldisilazane (1.33 ml, 6.3 mmol) was added to a suspension of KH [0.72 g of 35% by weight paraffin oil dispersion, washed with THF (3 x 10 ml)] in THF (10 ml) and stirred for 30 min under argon. The solution of potassium hexamethyldisilazide was allowed to settle, then added dropwise to methyltriphenyl phosphonium bromide (2.25 g, 6.3 mmol) in toluene (20 ml) at -20°C. The mixture the mixture was allowed to warm to room temperature and then cooled back to -20°C to allow complete formation of the yellow ylide. The aldehyde (26) (0.68 g, 1.84 mmol) in THF (5 ml) was added dropwise, the mixture was warmed to room temperature, poured into brine and extracted with ether. The extract was dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 1% ether in petrol, to give the alkene(27) (0.66 g, 97%) as an oil, $\upsilon_{max.}$ (neat thin film) 2 960, 2 932, 2 858, 1 639, 1 589, 1 471,1 427, and 1 112 cm^{-1}, $\delta(CDCl_3$, 400 MHz) 7.7-7.4 (10H, m, Ph), 5.69 (1H, dd, *J* 17 and 10 Hz, 2-H), 5.33 (1H, d, *J* 17 Hz, *trans* 1-H), 5.19 (1H, d, *J* 10 Hz, *cis* 1-H), 3.78 (2H, dq, *J* 10 and 6 Hz, CH_2OSi), 2.75 (1H, d, *J* 9 Hz, epoxy CH), 1.64 (1H, m, CH), 1.42 (3H, s, epoxy Me), 1.10 (9H, s, *t*-Bu), and 1.07 (3H, d, *J* 8 Hz, Me) (Found M^+ - *t*-Bu, 323.147 3. $C_{20}H_{23}O_2Si$ requires M^+ - *t*-Bu, 323.146 7), m/z 323 (M^+ - *t*-Bu), $[\alpha]_D$ = -3.0°, [c = 1.84, $CHCl_3$].

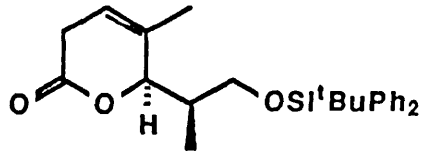
exo and *endo*-[4R,5S]π-Allyl-1,2,3-η^3-(4-formyloxyhex-2-en-3-ylato-3,5-dimethyl-6-*t*-butyldiphenylsilyloxy)tricarbonyliron(28,29).-



Di-ironnonacarbonyl (0.67 g, 1.84 mmol) was added to a solution of alkene (27) (0.66 g, 1.78 mmol) in dry THF (25 ml) under argon. The mixture was stirred for 4 h then evaporated *in vacuo*, (without immersion in water bath, on a cardice rotary evaporator) and purified by column chromatography on silica gel, eluting with petrol and 40% ether in petrol, to give the ferrilactones (28) and (29) (0.74 g, 75%) as a light yellow oil, $\upsilon_{max.}$ (neat thin film) 2 960, 2 858, 2 077, 2 009, 1 676,1 471,1 428, 1 112, and 1 007 cm^{-1}, δ($CDCl_3$, 250 MHz, major isomer) 7.8-7.2 (10H, m, Ph), 3.90 (3H, m, 2-H and 6-H_2), 3.43 (1H, d, *J* 4 Hz, 4-H), 2.50 (1H, dd, ^3J 8 and ^2J 2 Hz, *cis*1-H), 2.33 (1H, dd, ^3J 13 and ^2J 2 Hz, *trans*1-H), 1.82 (1H, m, 5-H), 1.25 (3H, s, 3-Me), 1.18 (9H, s, *t*-Bu), and 1.13 (3H, d, *J* 8 Hz, Me) (Found M^+ - 4CO, 436.153 1. $C_{24}H_{32}OSiFe$ requires M^+ - 4CO, 436.152 1), m/z 504 (M^+ $Fe(CO)_3$ diene complex), 464 (M^+ - Fe(CO)), 436 (M^+ - $Fe(CO)_2$), 420 (M^+ $Fe(CO)_3$ diene complex - Fe(CO)), 407 (M^+ - Fe(CO) - *t*-Bu), 379 (M^+ - $Fe(CO)_2$ - *t*-Bu), 351 (M^+ - $Fe(CO)_3$ - *t*-Bu), and 379 (M^+ - $Fe(CO)_4$ - *t*-Bu).

[2'S,6S](*t*-Butyldiphenylsilyloxy-2'S-propan-2-yl)5-methyl-3,6-dihydro-pyran-2H-2-one(30).-

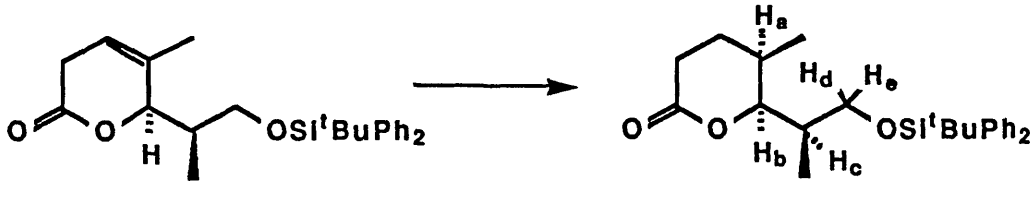
(28) + (29) ⟶



(30)

The ferrilactones (28) and (29) (0.3 g, 0.56 mmol) in dry benzene (5 ml) were heated at 90°C for three days under a pressure of 240 atm of carbon monoxide in a high pressure bomb. The mixture was then filtered through a cotten wool plug, evaporated *in vacuo* and purified by column chromatography on Fluorosil, eluting with 10% ether in petrol, to give the β,γ-unsaturated δ-lactone (30) (0.156 g, 68%) as an oil, $\upsilon_{max.}$ (neat thin film) 2 929, 2 856, 1 742, 1 589, 1 461, 1 427, 1 388, 1 211, and 1 111 cm^{-1}, δ($CDCl_3$, 400 MHz) 7.7-7.4 (10H, m, Ph), 5.46 (1H, br, olefinic 4-H), 4.82 (1H, br, 6-H), 3.59 (2H, m, dihydropyran 3-H_2), 2.92 (2H, m, 1'-CH_2OSi), 2.18 (1H, m, sidechain 2'-H), 1.70 (3H, dd, *J* 1.5 and 1 Hz, 5-Me), 1.10 (3H, d, *J* 6.5 Hz, sidechain 2'-Me), and 1.05 (9H, s, *t*-Bu), (Found M^+ - *t*-Bu, 351.141 2. $C_{21}H_{23}O_3Si$ requires M^+ - *t*-Bu, 351.141 6), m/z 351 (M^+ - *t*-Bu), $[\alpha]_D$ = -13.4°, [c = 3.02, $CHCl_3$].

[5R,6S](*t*-Butyldiphenylsilyloxy-propan-2S'-yl)5-methyl-tetra-hydro-pyran-2H-2-one(31).-

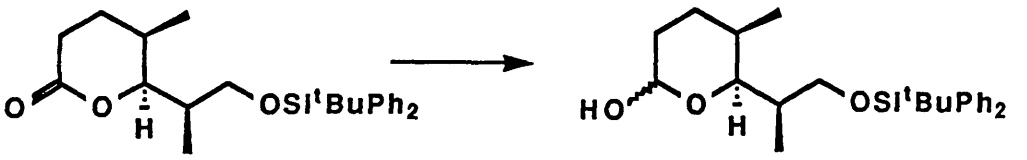


(30) (31)

The unsaturated δ-lactone (30) (0.14 g, 0.34 mmol) was stirred vigorously in methanol (5 ml) with a trace of PtO_2 under an atmosphere of H_2 for 5 h. The mixture was then diluted with ether, filtered through celite, evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10% ether in petrol, to give the δ-lactone (31) (98 mg, 71%) as an oil, $\upsilon_{max.}$ (neat thin film) 2 931, 2 857, 1 741, 1 461, 1 427, 1 389,

and1 112 cm^{-1}, δ($CDCl_3$, 400 MHz) 7.7-7.4 (10H, m, Ph), 4.26 (1H, dd, J_{ba} 2 and J_{bc} 10.5 Hz, 6-H_B), 3.97 (1H, dd, J_{de} 10 and J_{dc} 4 Hz, 1'-H_D *anti* to H_C), 3.73 (1H, dd, J_{ed} 10 and J_{ec} 2.5 Hz, 1'-H_E *syn* to H_C), 2.50 (2H, td, *J* 7.5 and 2.5 Hz, 3-H_2), 2.12 (2H, m, 4-H_2), 1.88 (1H, m, sidechain 2'-H_C), 1.65 (1H, m, 5-H_A), 1.07 (9H, s, *t*-Bu), 1.04 (3H, d, *J* 7 Hz, sidechain 2'-Me), and 0.95 (3H, d, *J* 7 Hz, 5-Me), (Found $\underline{M}^+$ - *t*-Bu, 353.156 9. $C_{21}H_{25}O_3Si$ requires $\underline{M}^+$ - *t*-Bu, 353.157 3), m/z 353 ($\underline{M}^+$ - *t*-Bu), $[\alpha]_D$ = +44.2°, [c = 2.94, $CHCl_3$].

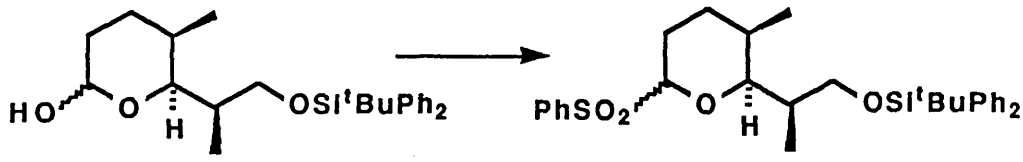
[2RS,5R,6S](*t*-Butyldiphenylsilyloxy-2'S-propan-2-yl)5-methyl-tetrahydro-pyran-2H-2-ols(32).-



(31) (32)

Di-isobutyl aluminium hydride (0.11 ml of a 1.5*M* solution in toluene) was added to a solution of δ-lactone (32) (55 mg, 0.134 mmol) in dry toluene (10 ml) under argon at -78°C. The solution was stirred for 30 min, quenched with water (0.25 ml) and allowed to warm to room temperature and stirred for a futher hour. The solution was then poured into water and extracted with ethyl acetate. The extract was washed with water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 15% ether in petrol, to give a 3:1 mixture of diastereomeric lactols (32) (41 mg, 74%) as an oil, $\upsilon_{max.}$ (neat thin film) 3 418, 2 930, 2 857, 1 589, 1 459, 1 427, 1 388, and 1 112 cm^{-1}, δ($CDCl_3$, 250 MHz) 7.8-7.3 (10H, m, Ph), 5.18 (1H, br, OH), 4.3 (1H, m, 2-H), 3.93 (1H, m, 6-H), 3.70 (1H, dd, *J* 2.5 and 9.5 Hz, $C\underline{H}_AH_BOSi$), 3.42 (1H, dd, *J* 2 and 9.5 Hz, $CH_A\underline{H}_BOSi$), 2.4-1.3 (6H, m, 3-H_2, 4-H_2, 5-H, and sidechain 2'-H), 1.08 (9H, s, *t*-Bu), 1.01 (3H, d, *J* 7 Hz, sidechain 2'-Me), and 0.94 (3H, d, *J* 7 Hz, 5-Me), (Found $\underline{M}^+$ - *t*-Bu, 355.172 7. $C_{21}H_{27}O_3Si$ requires $\underline{M}^+$ - *t*-Bu, 355.173 0), m/z 394 ($\underline{M}^+$ - *t*-Bu - H_2O) and 355 ($\underline{M}^+$ - *t*-Bu) $[\alpha]_D$ = +5.0°, [c = 3.77, $CHCl_3$].

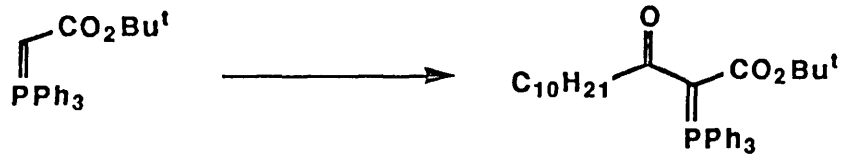
[2RS,5R,6S](*t*-Butyldiphenylsilyloxy-2'S-propan-2-yl)5-methyl-2-phenylsuphonyltetrahydro-2H-pyran(33).-



(32) (33)

Freshly prepared phenylsulphinic acid (13.8 mg, 0.079 mmol) and a trace of camphorsuphonic acid were added to a solution of lactols (32) (40 mg, 0.097 mmol) in dichloromethane (15 ml) at room temperature. The mixture was stirred overnight, diluted with dichloromethane, washed with saturated $NaHCO_3$, evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 25% ether in petrol, to give a mixture of diastereomeric sulphones (33) (39 mg, 75%) as an oil, $\upsilon_{max.}$ (neat thin film) 2 931, 2 857, 1 427, 1 303, 1 150 and 1 110 cm^{-1}, $\delta(CDCl_3, 250\ MHz)$ 7.7-6.9 (15H, m, Ph), 4.67 (1H, d, *J* 8 Hz, 6-H), 3.97 (1H, dd, *J* 2.5 and 10 Hz, CH_AH_BOSi), 3.43 (1H, dd, *J* 3.5 and 10 Hz, CH_AH_BOSi), 3.43 (1H, t, *J* 9.5 Hz, 2-H), 2.45-2.2 (2H, m, 3-H_2) 2.1-1.5 (4H, m, 4-H_2, 5-H, and sidechain 2'-H), 0.94 (3H, d, *J* 7 Hz, 5-Me), *t*-Bu), 1.01 (3H, d, *J* 7 Hz, sidechain 2'-Me), 0.96 (9H, s, *t*-Bu), 0.92 (3H, d,*J* 6.5 Hz, Me), and 0.92 (3H, d,*J* 7 Hz, Me) (Found M^+ - *t*-Bu, 479.170 4. $C_{27}H_{31}O_4SSi$ requires M^+ - *t*-Bu, 479.171 2), m/z 479 (M^+ - *t*-Bu), $[\alpha]_D$ = +44.4°, [c = 0.124, $CHCl_3$].

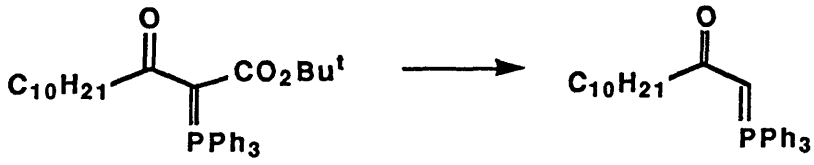
t-Butyl-3-oxo-2-(triphenylphosphoranylidene)tridecanoate (37),-



(36) (37)

Undecanoyl chloride (4.75 g, 46.4 mmol) was added dropwise to a vigorously stirred solution of t-butoxycarbonylmethylidinetriphenylphosphorane (36) (17.5 g, 46.4 mmol) in dry benzene (180 ml) at 8-10°C for 5 min, then at room temperature for 30 min. Ether (120 ml) was added to precipitate the remaining hydrochloride salt formed, and the mixture was filtered. The filtrate was evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with ether, to give the ylide (37) (11.5 g, 91%) as an oil, (Found : C, 77.1 H, 8.45. $C_{35}H_{45}O_3P$ requires C, 77.2; H, 8.33%), $\upsilon_{max.}$ (neat thin film) 2 927, 2 854, 1 654, 1 549, 1 437, 1 363, 1 303, 1 174, 1 108, and 1 082cm^{-1}, δ($CDCl_3$, 90 MHz) 7.8-7.4 (15H, m, Ph), 2.85 (2H, t, *J* 7 Hz, 4-CH_2), 1.65 (2H, br, 5-CH_2), 1.26(14H, s, 7 x CH_2 chain), 1.08 (9H, s, CH_2OMs), and 0.88 (3H, t, 6.5 Hz, Me), m/z 487 (M^+ - *t*-Bu), and 471 (M^+ - *t*-BuO).

Triphenylphosphoranylidenedodecan-2-one(38),-

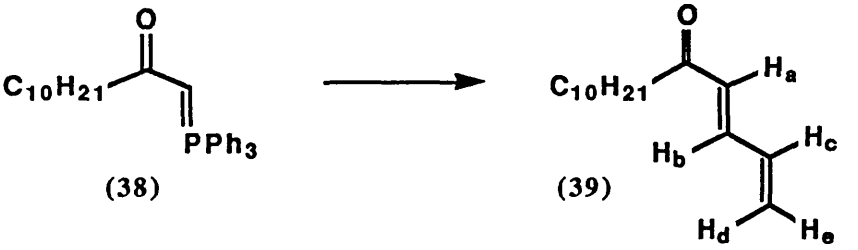


(37) (38)

The ylide (37) (11.5 g, 21.1 mmol) was heated in trifluoroacetic acid (35 ml) for 1 h, the solvent was removed *in vacuo* and the remaining TFA was removed by azeotropic distillation with benzene (3 x 50 ml). The crude salt was taken up in ethanol (75 ml) and water (30 ml) and 1*M* NaOH added until the solution remained alkaline. The mixture was then poured into water and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with ether, to give the ylide (38) (6.7 g, 71%) as

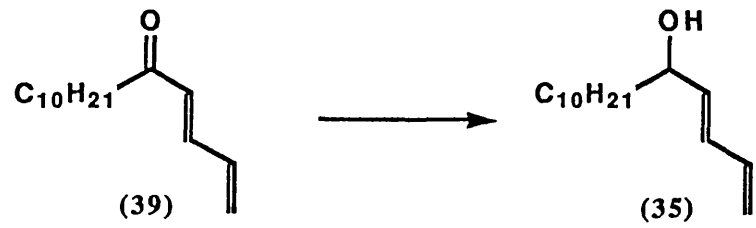
white plates, m.p. 69-71°C (Found : C, 80.8 H, 8.49. $C_{35}H_{45}O_3P$ requires C, 81.0; H, 8.39%), $\upsilon_{max.}$ (CCl_4) 2 926, 2 854, 2 207, 1 573, 1 397, and 1 107cm^{-1}, δ($CDCl_3$, 90 MHz) 7.3-7.8 (15H, m, Ph), 3.3 -3.8 (1H, br, phosphoranylidene C-H), 2.30 (2H, t, 3-H_2), 1.67 (2H, br, 4-H_2) 1.27(14H, s, 7 x CH_2 chain), 0.88 (3H, t, *J* 6.5 Hz), , m/z 444 (M^+), 429 (M^+ - Me), 415 (M^+ - C_2H_5), 401 (M^+ - C_3H_7), 387 (M^+ - C_4H_9), and 373 (M^+ - C_5H_{11}).

E-5-Oxo-Pentadeca-1,3-diene(39),-



Freshly distilled acrolein (0.4 ml, 6.0 mmol) was added dropwise to boiling solution of ylide (38) (0.306 g, 0.69 mmol) in dry dichloromethane (2.5 ml) under argon, and the solution stirred for 15 min. Ether (150 ml) was added and the mixture filtered through celite, evaporated *in vacuo* and purified by column chromatography on Fluorosil, eluting with ether, to give the diene (39) (40 mg, 26%) as an oil, $\upsilon_{max.}$ (thin neat film) 2 929, 2 854, 1 689, 1 621, 1 592, 1 466,1 255 and 1 108cm^{-1}, δ($CDCl_3$, 250 MHz) 7.13 (1H, dd, J_{ba} 15.5 and J_{bc} 11 Hz, 3-H_B), 6.47 (1H, dt, J_{cd} 17 and J_{cb} =J_{ce},10Hz, 2-Hc), 6.18 (1H, d, J_{ab} 15.5Hz, 4-H_A), 5.66 (1H, d, J_{dc} 17 Hz, 1-H_D), 5.53 (1H, d, J_{ec} 10 Hz, 1-H_E), 2.57 (2H, t, *J* 6.5 Hz, 6-H_2), 1.62 (2H, m, 7-H_2), and 0.88 (3H, t, *J* 6 Hz, 15-Me), (Found M^+, 222.198 4. $C_{15}H_{26}O$ requires M^+, 222.198 4), m/z 222 (M^+), 207 (M^+ - Me), 193 (M^+ - C_2H_5), 179 (M^+ - C_3H_7), and 193 (M^+ - C_4H_9).

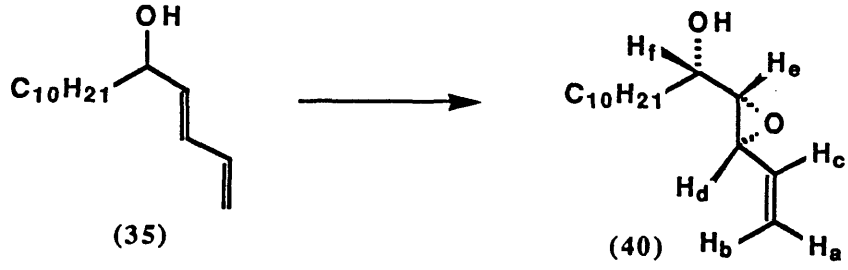
E-Pentadeca-1,3-dien-5-ol(35),-



(39) (35)

Lithium aluminium hydride (20 mg, 0.57 mmol) was added to a solution of ketone (39) (103 mg, 0.46 mmol) in dry ether (10 ml). The mixture was stirred for 2 h, then quenched with water dropwise, diluted with excess ether and filtered through celite. The filtrate was washed with brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10% ether in petrol, to give the alcohol (38) (84 mg, 81%) as an oil, (Found : C, 80.1; H, 12.5. $C_{15}H_{28}O$ requires C, 80.3; H, 12.6%), $\upsilon_{max.}$ (thin neat film) 3 346, 2 925, 2 854, 1 605, 1 466, and 1 003 cm^{-1}, $\delta(CDCl_3, 90\ MHz)$ 6.6-5.0 (5H, m, olefinics), 4.15 (1H, m, 5-H), 1.50 (2H, m, 6-H_2), 1.26 (16H, s, 8 x CH_2 chain), 0.88 (3H, t, *J* 5.5 Hz, 15-Me), m/z 224 (M^+) and 206 ($M^+ - H_2O$).

[3R,4S,5S]-3,4-Epoxypentadeca-1-en-5-ol(40),-

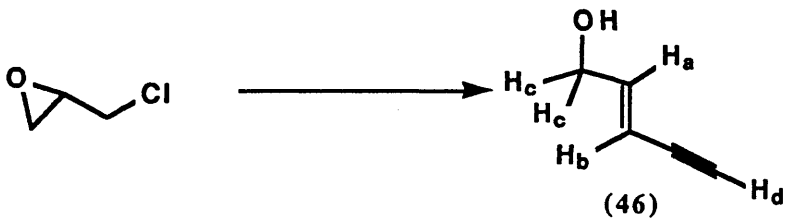


(35) (40)

To dry dichlomethane (2 ml) under argon at -20°C was added titanium tetraisopropoxide (0.072 ml, 0.24 mmol); L-(+)-diethyltartrate (0.041 ml, 0.24 mmol); (the mixture was stirred for 5 min before next addition) alcohol (35) (108 mg, 0.48 mmol) in dichloromethane (2 ml); and *t*-butylhydroperoxide (0.16 ml of a 3*M* solution in toluene). The mixture was stirred for 1.5 h then 10% aqueous tartaric acid (1.5 ml) was added and the mixture stirred for 30 min at -20°C, and for 2 h at room

temperature. The organic layer was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to afford the crude product contaminated with *t*-butylhydroperoxide. The oil was diluted with ether (10 ml), cooled to 5°C and stirred with NaOH (2 ml of a 1*M* aqueous solution) for 30 min at 5°C. The organic phase was washed with brine, dried (Na_2SO_4), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10% ether in petrol, to give the epoxide (40) (39 mg, 68% based on theoretical 50% yield) as needles, m.p. 46°C, (Found : C, 75.0; H, 12.0. $C_{15}H_{28}O_2$ requires C, 75.0; H, 11.7%), $\upsilon_{max.}$ ($CHCl_3$) 3 576, 3 482, 2 929, 2 854, 1 639, 1 464, 1 379, 1 077, and 984 cm^{-1}, δ($CDCl_3$, 400 MHz) 5.61 (1H, heptad, J_{cb} 21, J_{ca} 12.5, and J_{cd} 9.5 Hz, olefinic 2-Hc), 5.50 (1H, dd, J_{bc} 21 and J_{ba}2 Hz, olefinic 1-H_B), 5.30 (1H, dd, J_{ac} 12.5, and J_{ab} 2 Hz, olefinic 1-H_A), 3.85 (1H, m, 5-H_F), 3.45 (1H, dd, J_{dc} 9.55.50 (1H, dd, J_{bc} 21 and J_{ba}2 Hz, olefinic 1-H_B), 1.65 (16H, s, 8 x CH_2 in chain), and 0.88 (3H, t, *J* 8.5 Hz, 15-Me), m/z 240 (M^+), 222 (M^+ - H_2O), and 211 (M^+ - C_2H_5), $[\alpha]_D$ = +0.2°, [c = 1.36, $CHCl_3$].

E-Pent-2-en-4-yn-1-ol(46),-

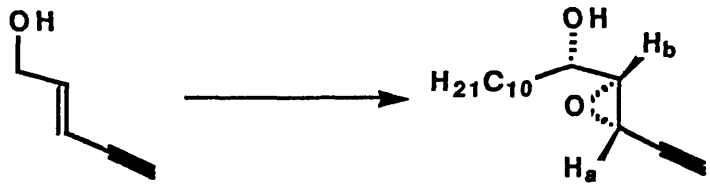


(46)

Sodium metal (35.4 g, 1.54 mmol) was added slowly to a solution of liquid ammonia (1.5 L) with a trace of iron trichloride, on persistance of a grey colour the mixture was stirred vigorously under a continuous atmosphere of acetylene, (the acetylene was passed sequentially through a mercury safety valve; a -78°C trap to remove acetone; dried in a conc. H_2SO_4 trap; and passed through a blank into the reaction) for 2 h with a soda-lime drying tube. Epichlorohydrin (60 ml, 0.77 mol) was added dropwise over 45 min and the reaction cooled to -78°C and stirred under nitrogen overnight. The mixture was quenched with solid NH_4Cl (80 g) and the ammonia allowed to boil off. Ether (1 L) was added and the mixture filtered. The residue was

dissolved in water and extracted with ether. The combined ethereal solutions were washed with 1*M* H_2SO_4, water and brine, dried ($MgSO_4$), evaporated *in vacuo* and and purified by distillation to give the alcohol (46) (24.1 g, 38%) as a liquid, b.p. 91°C (740mm,Hg), $\upsilon_{max.}$ (neat thin film) 3 293, 2 866, 2 866, 1 639, 2 103, 1 630, 1 369, 1 092, 996, 956, cm^{-1}, δ($CDCl_3$, 90 MHz), 6.33 (1H, dt, J_{ba}16 and J_{ac}5 Hz, olefinic 2-H_A), 5.69 (1H, dq, J_{ba}16 and $J_{bc} = J_{bd}$ 2 Hz,olefinic H_B), 4.18 (2H, dd,J_{ca}5 and J_{cb}2 Hz, CH_2O), 2.89 (1H, d, J_{db}5 Hz alkyne H_D), and 2.80 (1H, br, OH).

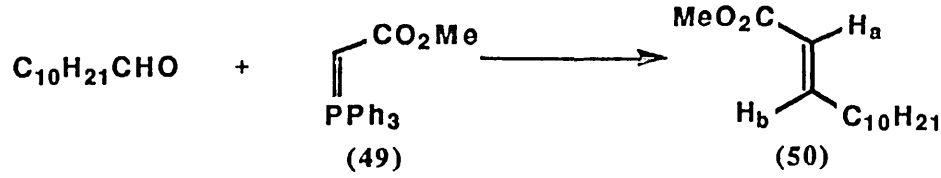
[2R,3S]2,3-Epoxy-pent-4-yn-1-ol(47),-



(46) (47)

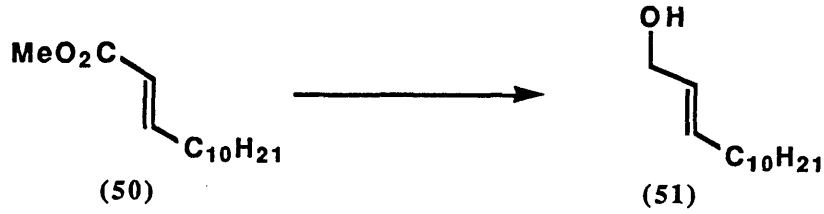
To dry dichloromethane (75 ml) under argon at -20°C was added titanium tetraisopropoxide (3.63 ml, 12.2 mmol); L-(+)-diethyltartrate (2.09 ml, 12.2 mmol); (the mixture was stirred for 5 min before next addition) alcohol (46) (1.0 g, 12.2 mmol); and *t*-butylhydroperoxide (8.13 ml of a 3*M* solution in toluene). The mixture was stirred overnight at -20°C then 15% aqueous tartaric acid (30 ml) was added and the mixture stirred for 30 min at -20°C, and for 1 h at room temperature. The organic layer was washed with water, brine, dried (Na_2SO_4), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 50% ether in petrol, to give the epoxide (47) (0.65 g, 54%), as a liquid,3 402, 3 287 $\upsilon_{max.}$ (neat thin film) 3 402, 3287, 2 930, 2 871, 2 126, 1 630, 1 432, 1 312, 1 234, 1 097, 1 074, and 881 cm^{-1}, δ($CDCl_3$, 90 MHz), 3.96 (1H, dd, ^2J 13 and ^3J 2 Hz, CH_CH_DOH), 3.66 (1H, dd, ^2J 13 and ^3J 3.5 Hz, CH_CH_DOH), 3.45 (1H, t, $J_{ab} = {}^4J$ 2 Hz, H_A), 3.33 (1H, m, H_B), 2.38 (1H, d, ^4J 2 Hz, alkyne), $[\alpha]_D = +11.6°$ [c = 1.07, $CHCl_3$].

E-Methyl-tridec-2-enoate(50),-



Undecanoyl aldehyde (4.1 g, 24.1 mmol) was added to a stirred solution of methyl(triphenylphosphoranylidene)acetate (10.21 g, 30.6 mmol) in dry dichloromethane (100 ml) at room temperature for 24 h, the mixture was then evaporated *in vacuo* and purified by column chromatography, pre-loading on silica gel with dichloromethane and eluting with 2% ether in petrol, to give the ester (57) (3.82 g, 70%) as an oil, $\upsilon_{max.}$ (neat thin film) 2 926, 2 854, 1 726, 1 657, 1 434,1 270, 1 197, and 1 175 cm^{-1}, $\delta(CDCl_3, 90\ MHz)$, 6.95 (1H, dt, J_{ba} 16 and 7 Hz, 3-H_B), 5.77 (1H, dt, J_{ab} 16 and 1.5 Hz, 2-H_A), 3.68 (3H, s, ester Me), 2.17 (2H, m, 4-H_2), 1.24 (16H, s, 8 x CH_2 in chain), and 0.85 (3H, t, J 5 Hz, 13-Me), (Found M^+, 226.193 7. $C_{14}H_{26}O_2$ requires M^+, 226.193 3), m/z 226 (M^+), 211 (M^+ - Me), and 195 (M^+ - OMe).

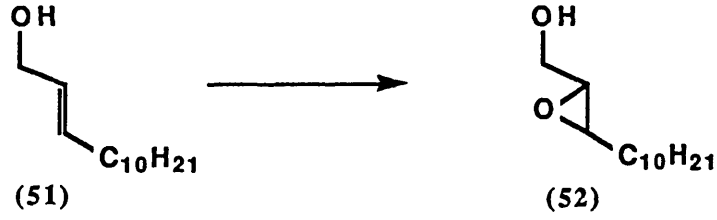
E-Tridec-2-enol(51),-



Di-isobutyl aluminium hydride (24 ml of a 1.5*M* solution in toluene) was added dropwise to a solution of ester (50) (0.186 g, 0.69 mmol) in dry toluene (20 ml) under argon at -78°C. The solution was stirred for 30 min, quenched with water (12 ml) and allowed to warm to room temperature; upon gelling the slurry was stirred with solid Na_2CO_3 and an excess of ethyl acetate. The ethyl acetate solution, upon clearing, was decanted through a celite pad and the process repeated twice. The combined filtrates werre evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 25% ether in petrol, to give the alcohol (51) (3.15 g, 97%) as an oil,

(Found : C, 78.8; H, 13.4. $C_{13}H_{26}O$ requires C, 78.7; H, 13.2%), $\upsilon_{max.}$ (neat thin film) 3 318, 2 924, 2 853, 1 670, 1 466, 1 376, 1 091, 1 005, and 969 cm^{-1}, δ($CDCl_3$, 90 MHz) 5.65 (2H, m, olefinics), 4.08 (2H, d, *J* 4.5 Hz, CH_2O), 2.01 (2H, m, 4-H_2), and 1.27 (16H, s, 8 x CH_2 in chain), and 0.88 (3H, t, *J* 5.5 Hz 13-Me), m/z 198 (M^+), 152 (M^+ - H_2O), and 152 (M^+ - H_2O - C_2H_4).

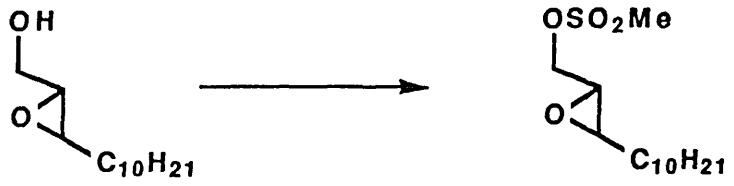
2,3-Epoxy-tridecanol(52),-



(51) (52)

m-Chloroperbenzoic acid (1.55 g of 80-90% *m*CPBA) was added to a solution of alcohol (51) (1.02 g, 5.14 mmol) in dry dichloromethane (100 ml), the mixture was stirred overnight then washed with sodium bisulphite, sodium bicarbonate and water, the organic extract was then filtered through celite. The filtrate was washed with brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 50% ether in petrol, to give the epoxide (52) (0.85 g, 77%) as needles, m.p. 56°C, (Found : C, 72.4; H, 12.3. $C_{13}H_{26}O_2$ requires C, 72.8; H, 12.1%), $\upsilon_{max.}$(CCl_4) 3 599, 3 472, 2 925, 2 856, 1 605, 1 464, 1 378, 1 200, 1 013, and 9878cm^{-1}, δ($CDCl_3$, 90 MHz) 3.70 (2H, m, epoxy 2-H and 3-H), 1.49 (2H, m, 4-H_2), **1.27** (16H, s, 8 x CH_2 in chain), and 0.87 (3H, t, 13-Me), m/z 199 (M^+ - Me), 183 (M^+ - OMe), and 171 (M^+ -C_3H_7).

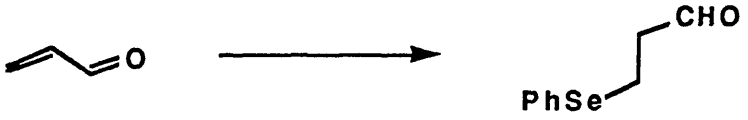
2,3-Epoxytridecanyl methane sulphonate(48),-



(52) (48)

Triethylamine (1.6 ml, 11.5 mmol) and methylsulphonyl chloride (0.302 ml, 3.9 mmol) were added to a solution of epoxide (52) (0.82 g, 3.82 mmol) in dichloromethane (100 ml) at 0°C under argon. The mixture was stirred for 5 min, poured into water and extracted with ether, the extract was washed with water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 30% ether in petrol, to give the mesylate (48) (0.89 g, 80%) as plates, m.p. 55°C, (Found : C, 57.4; H, 9.69. $C_{14}H_{28}O_4S$ requires C, 57.5; H, 9.65%), $\upsilon_{max.}$ (CCl_4) 2 927, 2 855, 1 464, 1 369, 1 180, 1 378, and 958cm^{-1}, δ($CDCl_3$, 90 MHz) 4.48 (1H, dd, *J* 11.5 and 3 Hz, CH_AH_BOS), 4.21 (1H, dd, *J* 11.5 and 6 Hz, CH_AH_BOS), 3.08 (3H, s, SO_2Me), 3.0-2.8 (2H, m, epoxy 2-H and 3-H), 2.55 (2H, m, 4-H_2), 1.28 (16H, s, 8 x CH_2 in chain), and 0.88 (3H, t, 5.5 Hz, 13-Me) m/z 183 (M^+ - CH_2OMs).

3-Phenylselenenylpropanal(56),-

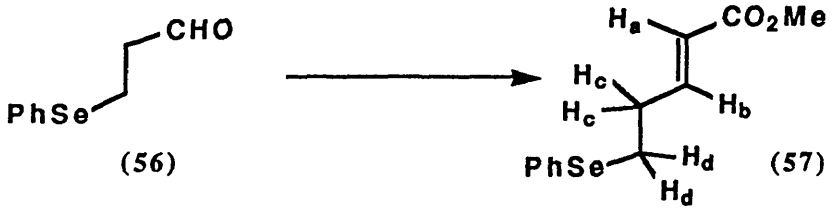


(56)

Diphenyldiselenide (1.4 g, 4.5 mmol), sodium (0.43 g of a 50% dispersion in paraffin) and a trace of benzophenone were subjected to ultrasound in a sealed 25 ml round bottemed flask for 2 h or until the mixture goes pale yellow. Acetic acid (2 ml) was added and the mixture stirred for 10 min, then freshly distilled acrolein (0.5 ml) was added dropwise with vigourous stirring. The mixture was stirred for a further 10 min and poured into water, extracted with ether, washed twice with saturated $NaHCO_3$, brine, dried (Na_2SO_4), evaporated *in vacuo* and purified by column chromatography

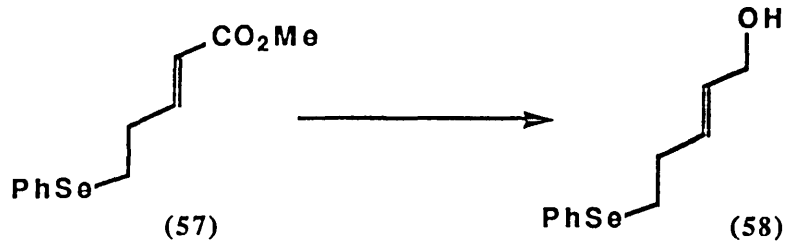
on silica gel, eluting with 20% ether in petrol, to give the aldehyde (56) (1.07 g, 56%) as a yellow oil oil, $\upsilon_{max.}$ (neat thin film) 2 826, 2 724, 1 719, 1 577, 1 477,1 436, and 1 022 cm^{-1}, δ($CDCl_3$, 90 MHz) 9.78 (1H, t, *J* 11 Hz, CHO), 7.4-7.2 (5H, m, Ph), and 3.00 (4H, m, 2 x CH_2), (Found M^+, 213.989 5. $C_9H_{10}OSe$ requires M^+, 213.989 7), m/z 214 (M^+ ^{80}Se), and (M^+ ^{78}Se).

Methyl-5-phenylselenenylpent-2-enoate(57),-



the aldehyde (56) (0.604 g, 2.84 mmol) and methyl(triphenylphos phoranylidene) acetate (1.04 g, 2.84 mmol) were stirred at room temperature in dichloromethane for 6 h. The mixture was evaporated *in vacuo* and purified by column chromatography on silica gel, loading in toluene and eluting with 3% ether in petrol, to give the ester (57) (0.586 g, 77%) as a pale yellow oil, (Found : C, 53.7; H, 5.49. requires $C_{12}H_{14}O_2Se$ C, 53.5; H, 5.24%), $\upsilon_{max.}$ (neat thin film) 2 947, 1 721, 1 654, 1 435,1 280, and 1 204 cm^{-1}, δ($CDCl_3$, 500 MHz) 7.5-7.3 (5H, m, Ph), 6.94 (1H, dt, J_{ba} 16 and J_{bc} 7 Hz, 3-H_B), 5.86 (1H, dt, J_{ab} 16 and J_{ad} 1.5 Hz, 2-H_A), 2.98 (2H, t, *J* 7 Hz, CH_2Se), and 2.60 (2H, dq, J_{cd} 7 and J_{ca} 1.5 Hz, 4-H_2), m/z 270 (M^+ ^{80}Se), 268(M^+ ^{78}Se), and (M^+ ^{80}Se - OMe).

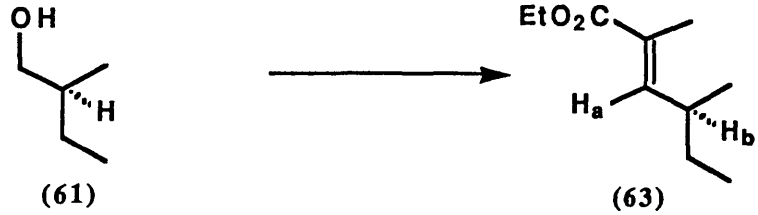
5-phenylselenenylpent-2-enol(57a),-



(57) (58)

Di-isobutyl aluminium hydride (1.07 ml of a 1.5*M* solution in toluene) was added dropwise to a solution of ester (57) (0.186 g, 0.69 mmol) in dry toluene (20 ml) under argon at -78°C. The solution was stirred for 30 min, quenched with water (0.027ml, 1.52 mmol) and allowed to warm to room temperature. The mixture was poured into water and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 30% ether in petrol, to give the alcohol (57a) (0.15 g, 91%) as an oil, (Found : C, 55.8; H, 6.07. requires $C_{11}H_{14}OSe$ C, 54.8; H, 5.85%), $\upsilon_{max.}$ (neat thin film) 3 360, 2 933, 2 872 1 582, 1 484, 1 439, and 970 cm^{-1}, $\delta(CDCl_3$, 250 MHz) 7.5-7.3 (5H, m, Ph), 5.69 (2H, m, olefinics), 4.08 (2H, d, *J* 2.5 Hz, CH_2O), 2.95 (2H, t, *J* 6.5 Hz, CH_2Se), and 2.47 (2H, m, 4-CH_2), and 1.35 (1H, br, OH), m/z 242 (M^+ ^{80}Se), and 240(M^+ ^{78}Se).

[4S]E-Ethyl-2,4-dimethylhex-2-enoate(62).-

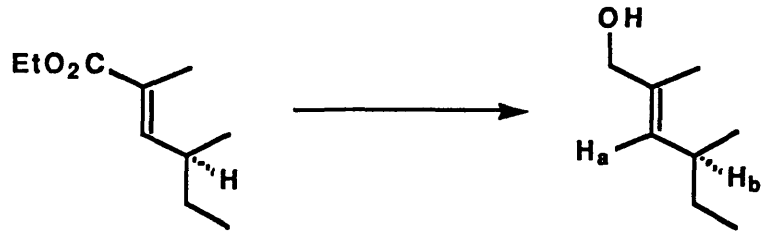


(61) (63)

Pyridinium chlorochromate (20 g, 92.8 mmol) was added portionwise to 2S-methylbutanol (4.03 g, 45.7 mmol) in dichloromethane (250 ml) at 0°C. The mixture was stired overnight at room temperature then 1-carboethoxyethylidene triphenylphosphorane (61) (15.6 g, 46.7 mmol) in dichoromethane (1 L) was added and the solution stirred for 24 h. The solvent was removed by distillation and the crude

product purified by column chromatography on silica gel, eluting with 2% ether in petrol, to give the ester (62) (3.44 g, 48%) as a liquid $\upsilon_{max.}$ (neat thin film) 2 962, 2 929, 1 709, 1 458, 1 273, 1 237, 1 154, and 1 098 cm^{-1}, $\delta(CDCl_3$ 400 MHz) 6.53 (1H, dq, J_{ab} 10, and ^4J 1.5 Hz, olefinic H_A), 4.19 (2H, q, J 7 Hz, ethyl ester CH_2) 2.41 (1H, m, 4-H_B), 1.84 (3H, d, J 1.5 Hz, olefinic Me), 1.40 (2H, m, 5-H_2), 1.30 (3H, t, J 7 Hz, ethyl ester Me), 1.00 (3H, d, 6.5 Hz, 4-Me), and 0.86 (3H, t, J 7.5 Hz, 6-Me), (Found M^+, 170.131 0. $C_{10}H_{18}O_2$ requires M^+, 170.130 7), m/z 170 (M^+), 155 (M^+ - Me), and (M^+ - C_2H_5). $[\alpha]_D$ = +12.1°, [c = 2.09, $CHCl_3$].

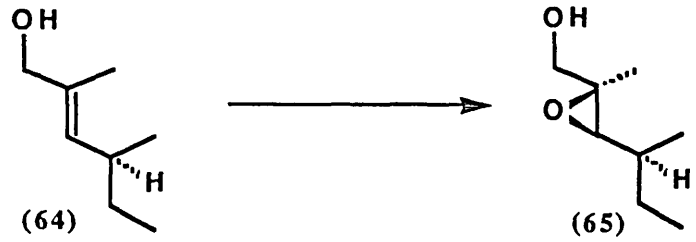
[4S]E-2,4-dimethylhex-2-enol(63),-



(63) (64)

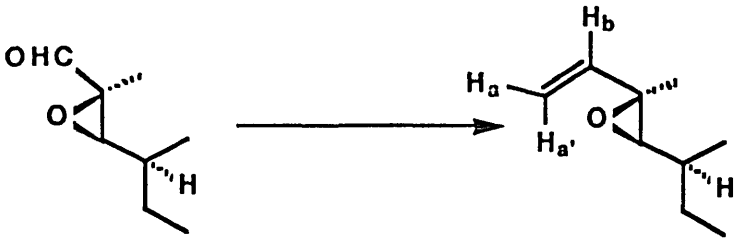
Di-isobutyl aluminium hydride (31.0 ml of a 1.5*M* solution in toluene) was added dropwise *via* a syringe pump to a stirred solution of ester (62) (3.32 g, 19.5 mmol) in dry toluene (250 ml) under argon at -78°C. The solution was stirred for 30 min, quenched with water (16 ml) and allowed to warm to room temperature; upon gelling the slurry was stirred with solid NaHCO3 and an excess of ethyl acetate. The ethyl acetate solution upon clearing was decanted through a celite pad and the process repeated twice. The combined filtrates were evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 15% ether in petrol, to give the alcohol (63) (1.63 g, 65%) as a liquid $\upsilon_{max.}$ (neat thin film) 3 432, 2 962, 2 873, 1 459, 1 382, 1 074, and 1 037 cm^{-1}, $\delta(CDCl_3$ 250 MHz) 5.18 (1H, dq, J_{ab} 10, and ^4J 1.5 Hz, olefinic H_A), 4.00 (2H, s, CH_2) 2.28 (1H, m, 4-H_B), 1.68 (3H, d, J 1.5 Hz, olefinic Me), 1.50 (1H, br, OH), 1.27 (2H, m, 5-H_2), 0.93 (3H, d, 6.5 Hz, 4-Me), and 0.84 (3H, t, J 7.5 Hz, 6-Me), (Found M^+, 128120 1. $C_8H_{16}O$ requires M^+, 128.120 1), m/z 128 (M^+), $[\alpha]_D$ = +11.1°, [c = 0.62, $CHCl_3$].

[2R,3R,4S]2,3-Epoxy-2,4-dimethylhexanol(64),-



To dry dichloromethane (30 ml) under argon at -20°C was added titanium tetraisopropoxide (1.56 ml, 5.24 mmol); D-(-)-diethyltartrate (0.041 ml, 0.24 mmol); (the mixture was stirred for 5 min before next addition) alcohol (63) (0.671 g, 5.24 mmol) in dichloromethane (5 ml); and *t*-butylhydroperoxide (3.49 ml of a 3*M* solution in toluene). The mixture was stirred overnight at -20°C then 10% aqueous tartaric acid (15 ml) was added and the mixture stirred for 30 min at -20°C, and for 1 h at room temperature. The organic layer was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to afford the crude product contaminated with *t*-butylhydroperoxide. The oil was diluted with ether (30 ml), cooled to 5°C and stirred with NaOH (12 ml of a 1*M* aqueous solution) for 30 min at 5°C. The organic phase was washed with brine, dried (Na_2SO_4), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10 to 30% ether in petrol, to give the epoxide (64) (0.459 g, 61%) as a liquid, $\upsilon_{max.}$ (neat thin film) 3 432, 2 962, 2 873, 1 459, 1 382, 1 074, and 1 037 cm^{-1}, $\delta(CDCl_3$ 250 MHz) 3.66 (2H, d, *J* 12.5, CH_2O), 2.70 (1H, d,J_{ab}10 Hz, epoxy 3-H), 1.94 (1H, br, OH), 1.33 (3H, m, 4-H and 5-H_2), 1.27 (3H, s, epoxy Me), 1.04 (3H, d, 6.5 Hz, 4-Me), and 0.88 (3H, t, *J* 6.5 Hz, 6-Me), (Found M^+ - H_2O, 126.104 5. $C_8H_{14}O$ requires M^+ - H_2O, 126.104 5), m/z 145 (M^+H) and 97 (M^+ - C_4H_9), $[\alpha]_D$ = +11.8°, [c = 0.21, $CHCl_3$].

[2S,3R,4S]2,3-Epoxy-2,4-dimethylhexanal(65).-



(66) (67)

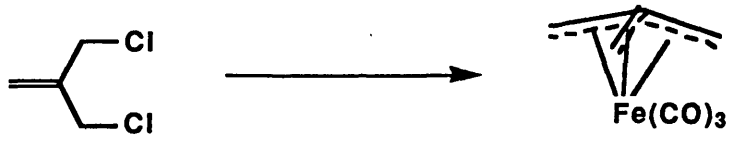
Dimethyl sulphoxide (0.482 ml, 6.8 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.297 ml, 3.4 mmol) in dry dichloromethane (10 ml) at -60°C. The mixture was stirred for 5 min then the alcohol (64) (0.445 g, 3.09 mmol) in dichloromethane (2 ml) added. The solution was stirred for a further 20 min at -60°C, then quenched with triethylamine (2.15 ml, 15.4 mmol) and allowed to warm to room temperature. The mixture was poured into water and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 10% ether in petrol, to give the aldehyde (65) (0.756 g, 92%) as a liquid, $\upsilon_{max.}$ (neat thin film) 2 965, 2 875, 1 725, 1 461, 1 389, 1 080, 1 010, and 878 cm^{-1}, δ($CDCl_3$ 250 MHz) 8.85 (1H, s, CHO), 2.81 (1H, d,*J* 8.5 Hz, epoxy 3-H), 1.40 (3H, s, epoxy Me), 1.5-1.2 (4H, m, 4-H and 5-H_2), 1.13 (3H, d, *J* 6 Hz, 4-Me and 0.87 (3H, t, *J* 6.5 Hz, 6-Me), (Found M^+ - Me, 127.076 3. $C_8H_{12}O$ requires M^+ - Me, 127.076 0), m/z 142 (M^+), 113 (M^+ - CHO), and 85 (M^+ - C_4H_9), $[\alpha]_D$ = +11.8°, [c = 0.21, $CHCl_3$].

[3R,4R,5S]3,4-Epoxy-3,5-dimethylheptene(66),-

Hexamethyldisilazane (2.45 ml, 11.6 mmol) was added to a suspension of KH [1.4 g of 35% by weight paraffin oil dispersion, washed with THF (3 x 10 ml)] in THF (10 ml) and stirred for 30 min under argon. The solution of potassium hexamethyldisilazide was allowed to settle, then added dropwise to methyltriphenylphosphonium bromide (4.14 g, 11.6 mmol) in toluene (10 ml) at -20°C. The mixture the mixture was allowed to warm to room temperature and then cooled back to -20°C to allow complete formation of the yellow ylide. The aldehyde

(26) (0.304 g, 2.14 mmol) in THF (5 ml) was added dropwise, the mixture was warmed to room temperature, poured into brine and extracted with ether. The extract was dried ($MgSO_4$), evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with 30% ether in petrol, to give the alkene(66) (0.212 g, 70%) as a liquid, $\upsilon_{max.}$ (neat thin film) 2 957, 2 925, 2 855, 1 639, 1 461, 1 379, 1 070, 986, 916, and 885 cm^{-1}, $\delta(CDCl_3$, 90 MHz), 5.76 (1H, dd, $J_{ba'}$17 and J_{ba}10 Hz, olefinic 2-H_B), 5.34 (1H, dd, $J_{a'b}$17 and $J_{aa'}$ 2 Hz, olefinic 1-$H_{A'}$), 5.19 (1H, dd, J_{ab}10 and $J_{aa'}$ 2 Hz, olefinic 1-H_A), 2.52 (1H, d, *J* 8 Hz, epoxy 5-H), 1.40 (3H, s, epoxy 3-Me), 1.3-1.25 (3H, m, 5-H and 6-H_2), 1.15 (3H, d, *J* 5 Hz, 5-Me), and (3H, t, *J* 7.5 Hz, 7-Me).

η^4-Trimethylenemethaneirontricarbonyl(70),-



(71) (70)

3-chloro-2-chloromethylpropene (0.60 ml, 5.2 mmol) was sonolysed with diiron nonacarbonyl (1.9 g, 5.2 mmol) in dry 30/40 petroleum ether for 1 h in a sealed flask under argon. The resulting mixture was carefully concentrated at *ca* 0°C and the residue purified by Kugelrohr distillation at room temperature (0.1 mm Hg) to give the TMM-$Fe(CO)_3$ complex (70) (0.91 g, 90%) as a yellow liquid, $\upsilon_{max.}$ (neat thin film) 3 066, 2 999, 2 065, 1 997, 1 476, 1 455, 917, and 803 cm^{-1}, $\delta(CDCl_3$ 90 MHz) 2.01 (6H, s, methylene protons)

Publications

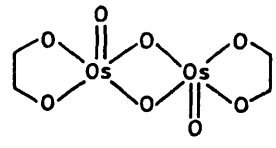
Studies on Transition-metal Oxo and Nitrido Complexes. Part 8.[1] Reactions of Osmium Oxo-imido Complexes with Alkenes†

William P. Griffith,* Neil T. McManus, and Andrew D. White
Inorganic Chemistry Research Laboratories, Imperial College, London SW7 2AY

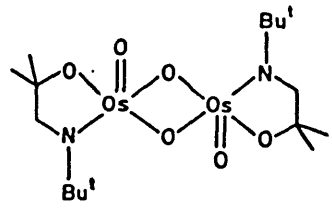
Reaction of $[OsO_3(NR)]$ [R = Bu^t, t-pentyl, adamant-1-yl (Ad), or 1,1,3,3-tetramethylbutyl (C_8H_{17})] and of $[OsO_2(NBu^t)_2]$ with alkenes R′ yields alkanolaminato and diaminato complexes of stoicheiometries $[\{OsO_2(OR'NR)\}_2]$ and $[OsO_2(NBu^tR'NBu^t)]$ respectively. The adducts $[OsO_3(NR)L]$ (R = Bu^t, t-pentyl, or C_8H_{17}; L = quinuclidine) and $[\{OsO_3(NR)\}_2L']$ {R = Bu^t or C_8H_{17}, L′ = 1,4-diazabicyclo[2.2.2]octane (dabo) or 1,3,5,7-tetra-azatricyclo[3.3.1.1^{3,7}]decane; R = t-pentyl, L′ = dabo} react with alkenes R′ to give $[OsO_2(OR'NR)L]$ and $[\{OsO_2(OR'NR)\}_2L']$. The structures of these complexes are discussed.

It has long been known[2] that osmium tetraoxide (OsO_4) reacts with alkenes R′ to give oxo-osmium 'monoesters,' now known to be oxo-bridged diolato dimers $[Os_2O_4(OR'O)_2]$ (I);[3] on hydrolysis these give *cis* diols.[2,4] Osmium(VIII) oxo(alkylimido) complexes $[OsO_3(NR)]$[5] will also react with alkenes to give unidentified species assumed to be monomeric alkanolaminato complexes.[6] On hydrolysis these give 2-aminoalcohols (HO)R′(NHR):[6,7] such reactions can be rendered catalytic with secondary oxidants such as chloramine-T[8] or *N*-argentio-*N*-chlorocarbamates.[9] Reaction of $[OsO_2(NR)_2]$ or of $[OsO(NR)_3]$ with alkenes R′ gives 1,2-diamines, (NHR)R′(NHR).[10]

In this work we investigate the nature of the osmium-containing complexes formed from $[OsO_3(NR)]$ and alkenes, the formation of adducts of $[OsO_3(NR)]$ with bridgehead amines and the reactions of these adducts with alkenes. We have briefly reported the *X*-ray crystal structure of the complex formed from $[OsO_3(NBu^t)]$ and isobutylene,[11] $[\{OsO_2(OCMe_2CH_2NBu^t)\}_2]$, and of the adduct $[\{OsO_3(NC_8H_{17})\}_2(dabo)]$ (C_8H_{17} = 1,1,3,3-tetramethylbutyl, dabo = 1,4-diazabicyclo[2.2.2]octane).[12]



(I)



(II)

Results and Discussion

A. Alkanolaminato Oxo-osmium(VI) *Complexes.* $[\{OsO_2(OR'NR)\}_2]$.—The known oxo-imido osmium(VIII) complexes are $[OsO_3(NR)]$ [R = Bu^t,[5,6,7,10] t-pentyl (C_5H_{11}),[7,10] adamant-1-yl‡ (Ad),[6,7] or C_8H_{17}[5]], $[OsO_2(NR^1)(NR^2)]$ ($R^1 = R^2$ = Bu^t or Ad; $R^1 = C_5H_{11}$, R^2 = Ad),[10] and $[OsO(NR^1)_2(NR^2)]$ ($R^1 = R^2$ = Bu^t; R^1 = Bu^t, R^2 = Ad).[10]

In this part of the work, concerned with the nature of the inorganic products of the reaction of $[OsO_3(NR)]$ with alkenes, we have mainly used the NBu^t and NC_8H_{17} complexes. The alkenes used were ethylene, propylene, isobutylene (CMe_2CH_2), acrylonitrile (CH_2CHCN), fumaronitrile [$(CHCN)_2$], methyl methacrylate ($CH_2CMeCOOMe$), methyl acrylate ($CH_2CHCOOMe$), and both dimethyl and diethyl fumarates, $(CHCOOR)_2$. A representative list of products with analytical and spectroscopic data is given in the Table.

Our preliminary *X*-ray study on $[\{OsO_2(OCMe_2CH_2NBu^t)\}_2]$ (3)[11] shows this to have structure (II), very similar to that found[3,13] for the diolato 'monoester' $[Os_2O_4(OC_2Me_4O)_2]$ formed from OsO_4 and tetramethylethylene, see structure of (I). Like (I) the monoester has an *anti* configuration with square-based pyramidal osmium(VI) atoms linked by a planar Os_2O_2 bridge (mean Os–O bridge distance 1.92 Å); the axial Os=O distance is 1.67 Å and the Os–N distance 1.91 Å.[11] Molecular weight data obtained cryoscopically in benzene for this complex and for complex (6) show that both are dimers in solution, as is also the case for the diolato complexes $[Os_2O_4(OR'O)_2]$.[3] Mass spectral (electron impact) data however gave parent ion and breakdown patterns for mononuclear species $[OsO_2(OR'NR)]$ so presumably the Os_2O_2 bridge is cleaved under such conditions.

Spectroscopic data.—In the Table we list i.r. and Raman data for the solids and some solutions in the 950—650 cm^{-1} regions where we know from previous studies[3] that Os=O and Os_2O_2(bridge) stretches occur. Bands in these regions are found for all these complexes irrespective of the nature of R′, so we assign the 950 cm^{-1} bands to ν(Os=O) and those near 650 cm^{-1} to an asymmetric ring stretch ν(Os_2O_2). In solution the bands are little shifted in the Raman or i.r. spectra. The ESCA (electron spectroscopy for chemical analysis) data give binding energies typical of osmium(VI) complexes (see section *D* below).

In the Experimental section we list ^{1}H n.m.r. data for complexes (2), (3), (5), (6), and (8) with suggested assignments. We assign shifts for protons adjacent to nitrogen (CH_n–N, *n* = 1 or 2) in the alkanolaminato ring at lower frequencies than for those adjacent to oxygen (CH_n–O) on the basis of normal shielding arguments for organic molecules.

It is noticeable from the ^{1}H n.m.r. spectra of complexes formed from asymmetric alkenes [*viz.* complexes (3), (5), (6), and (8) formed from isobutylene, methyl acrylate, and methyl

† *Non-S.I. unit employed:* eV ≈ 1.60 × 10^{-19} J.
‡ Adamantane = tricyclo[3.3.1.1^{3,7}]decane.

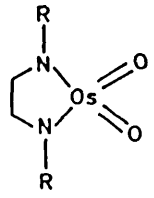
Table. Analytical and spectroscopic data

Complex	Analyses[a] C	H	N	Vibrational spectra[b] (cm^{-1}) ν(OsO)	ν(Os_2O_2) or ν(OsN)	ESCA Binding energies (eV)
(*a*) Imido and alkanolaminato						
(1) $[OsO_3(NC_{18}H_{17})]$	26.4 (26.3)	4.6 (4.7)	3.8 (3.8)	927*s*, 916vs *922vs*, *914s*, *906s* (924m, 914s) (*924p*, *918dp*)	1 207s *1 206w* (1 203) (*1 210w*)	
(2) $[\{OsO_2(OC_2H_4NBu^t)\}_2]$	20.9 (21.4)	3.6 (3.9)	3.9 (4.2)	960s	650m	
(3) $[\{OsO_2(OCMe_2CH_2NBu^t)\}_2]$[c]	26.5 (26.3)	4.7 (4.7)	3.7 (3.8)	960s	660m	
(4) $[\{OsO_2(OCHMeCH_2NBu^t)\}_2]$	24.5 (23.9)	4.3 (4.3)	3.6 (4.0)	939s *934s*	680m	
(5) $[\{OsO_2[OCH(COOMe)CH_2NBu^t]\}_2]$	24.5 (24.4)	3.8 (3.8)	3.3 (3.6)	955s	667m	52.1, 54.8
(6) $[\{OsO_2[OCMe(COOMe)CH_2NBu^t]\}_2]$[c]	26.6 (26.4)	4.2 (4.1)	3.3 (3.4)	958s	671m	52.3, 55.0
(7) $[\{OsO_2(OC_6H_{10}NBu^t)\}_2]$	29.5 (30.6)	4.9 (4.9)	3.4 (3.6)	977s *971s*	679m	52.1, 54.9
(8) $[\{OsO_2(OCMe_2CH_2NC_5H_{11})\}_2]$	29.0 (28.5)	5.0 (5.0)	3.7 (3.7)	*925s*		
(*b*) Diaminato						
(9) $[OsO_2\{NBu^t(CHCN)_2NBu^t\}]$	31.6 (32.6)	4.2 (4.6)	11.7 (12.7)	930w, 905s, 896vs (930w, 916vs) *901s*		52.0, 54.7
(*c*) Adducts and their esters						
(10) $[OsO_3(NC_8H_{17})(qncd)]$	37.7 (37.8)	6.3 (6.3)	5.8 (5.9)	885s, 870s	1 210vs	
(11) $[\{OsO_3(NC_8H_{17})\}_2(tatd)]$	31.4 (30.3)	5.2 (5.3)	9.6 (9.7)	880s, 875s	1 212vs	
(12) $[\{OsO_3(NC_8H_{17})\}_2(dabo)]$[c]	31.5 (31.3)	5.5 (5.5)	6.6 (6.7)	883m, 875vs, 845s *887s*, *878m*, *850w* (924s, 914s, 880m, 873s) (*929s*, *912m*, *889s*, *878w*)	1 167s *1 174m* (1 210, 1 170) (*1 204w*, *1 170w*)	53.0, 55.7
(13) $[OsO_2\{O(CHCOOMe)_2NBu^t\}(qncd)]$	35.6 (36.4)	5.3 (5.4)	4.8 (5.0)	900s, 864s *896s*, *862m* (*891p*, *859w*)		51.8, 54.5
(14) $[\{OsO_2[O(CHCOOMe)_2NBu^t]\}_2(dabo)]$	31.9 (30.9)	4.5 (4.6)	5.5 (5.5)	900s, 863s *897s*, *861m*		
(15) $[\{OsO_2[O(CHCOOMe)_2NBu^t]\}(tatd)]$	33.4 (32.4)	4.9 (4.9)	12.9 (11.8)	894s, 850m (*895vs*, *861m*)		
(16) $[OsO_2(OC_6H_{10}NBu^t)(qncd)]$	39.6 (40.6)	6.4 (6.4)	5.1 (5.6)	890vs, 850m *894vs*, *856w* *897p*, *860w*		51.8, 54.5
(17) $[OsO_2\{O(CHCOOMe)_2NAd\}(qncd)]$	42.8 (43.9)	5.6 (5.6)	4.2 (4.4)	889s, 865m (859s) *888s*, *961m* (*894p*, *859w*)		

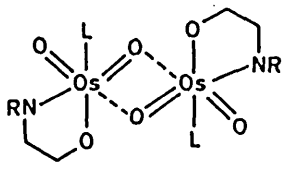
[a] Calculated analyses in parentheses. [b] Data on solids (solutions in parentheses: toluene for i.r. and CCl_4 for Raman); Raman data in italic (p = polarised, dp = depolarised). [c] Molecular weights in benzene (calculated values in parentheses): complex (3), 770 (734); (6), 860 (814); (12), 488 (841).

methacrylate] that these have added to the osmium so that their CH_2 groups are exclusively attached to the NR group, irrespective of whether the alkenes bear electron-withdrawing (COOMe) or electron-donating (Me) groups. This selectivity must be a direct consequence of the steric constraints imposed by the bulky alkyl groups (R) at the nitrogen atom.

B. Diaminato Oxo-osmium(VI) *Complexes*, $[OsO_2(NRR'NR)]$.—Sharpless and co-workers[10] have shown that such species are formed by reaction of $[OsO_2(NBu^t)_2]$ with dimethyl- and diethyl-fumarate, the complex formed with the latter being monomeric in benzene; structure (III) was proposed for these species. We have confirmed that these two complexes



(III)



(IV)

are monomeric and have made the new species $[OsO_2\{N\text{-}Bu^t(CHCN)_2NBu^t\}]$ (9) from fumaronitrile and $[OsO_2(N\text{-}Bu^t)_2]$. The Raman and i.r. spectra of (9) are similar in the solid state and, in the case of the i.r. spectrum, of the solution in toluene; this suggests that there is no change in structure from solid to solution. The presence of ν(OsO) bands near 900 cm^{-1} is characteristic of *cis*-dioxo complexes[14] and supports structure (III). The monomeric nature of these complexes has interesting implications for the mechanism of the OsO_4–alkene reaction: it has been suggested that the existence of a monomeric diolato intermediate $OsO_2(OR'O)$, analogous to (III), is unlikely because of the strain on the diolato ring for such a tetrahedral structure.[15]

C. Adducts of $[OsO_3(NR)]$ *with Bridgehead Amines.*—We have shown in earlier work that OsO_4 will form adducts of the type $[OsO_4L]$ (*e.g.* with L = quinuclidine, qncd) and $[(OsO_4)_2L']$ {*e.g.* with L′ = 1,3,5,7-tetra-azatricyclo-[3.3.1.1^{3,7}]decane (tatd) and with 1,4-diazabicyclo[2.2.2]octane (dabo)}[16] and reported the *X*-ray crystal structures of $[OsO_4(qncd)]$ and of $[(OsO_4)_2(tatd)]$.[17] It has recently been shown that $[OsO_3(NBu^t)]$ will form adducts $[OsO_3(NBu^t)L]$ with quinuclidine and with substituted quinuclidines,[18] and $[\{OsO_3(NBu^t)\}_2L']$ (L′ = tatd or dabo).

We have also prepared the new adducts $[OsO_3(NC_8H_{17})(qncd)]$ (10), $[\{OsO_3(NC_8H_{17})\}_2(tatd)]$ (11), and $[\{OsO_3(NC_8H_{17})\}_2(dabo)]$ (12), as well as the known corresponding species with $[OsO_3(NBu^t)]$, and reported the *X*-ray crystal structure of (12).[12] This has a symmetrical structure with the amine bridging two $OsO_3(NC_8H_{17})$ units. As in $[OsO_4(qncd)]$ and in $[(OsO_4)_2(tatd)]$[17] there is trigonal-bipyramidal co-ordination about the osmium with the oxo ligands in the equatorial positions (mean Os=O distance 1.71 Å, similar to the 1.706 Å found in the OsO_4 adducts).[17] The axial positions are occupied by the NC_8H_{17} nitrogen atoms {Os–N 1.73 Å, comparable with the 1.697 Å found for Os–N in $[OsO_3(NAd)]$[19]} and a long bond to the amine (Os–N 2.42 Å). This is slightly longer than the 2.37 Å observed in $[OsO_4(qncd)]$ and $[(OsO_4)_2(tatd)]$, perhaps reflecting a greater *trans*-weakening influence of the imido ligand as compared with the oxo ligand.

Vibrational spectra of these complexes in the solid state are similar in the ν(OsO) stretching region to those of the OsO_4 adducts, as expected in view of the structural similarities and the local C_{3v} symmetry about the osmium atoms. The Raman and i.r. spectra of solutions of the diazabicyclo[2.2.2]octane complex (12), however, also have bands characteristic of free $[OsO_3(NC_8H_{17})]$ in the ν(OsN) and ν(OsO) regions, so it appears that dissociation to $[OsO_3(NC_8H_{17})]$ and $[OsO_3(NC_8H_{17})(dabo)]$ occurs. The low molecular weight of the complex in benzene also indicates dissociation: the osmium tetraoxide analogue $[(OsO_4)_2(dabo)]$ shows no such dissociation, however.[16]

Attempts to prepare similar adducts of $[OsO_2(NBu^t)_2]$ were unsuccessful; it is unlikely that $[OsO_2(NR)_2L]$ or $[\{OsO_2(NR)_2\}_2L]$ species would exist for steric reasons, since at least one bulky NR ligand would necessarily have to lie in an equatorial position of the trigonal bipyramid *cis* to the amine. Attempts to make $[OsO_3(NR)(py)]$ (py = pyridine) were also unsuccessful, the main product being $[Os_2O_6(py)_4]$.

D. Reactions of $[\{OsO_3(NR)\}_nL]$ *with Alkenes.*—We have shown that $[OsO_4L]$ (L = quinuclidine, isoquinoline, or phthalazine) react with alkenes R′ to give green esters $[\{OsO_2(ORO')L\}_2]$[20] and have reported the *X*-ray crystal structure of the ester derived from cyclohexene, $[\{OsO_2(o\text{-}OC_6H_{10}O)(qncd)\}_2]$.[20,21] The 2:1 adducts $[(OsO_4)_2L']$ (L′ = tatd or dabo) similarly reacted with alkenes R′ to give $[OsO_3(OR'O)(tatd)]$ in the case of tatd and $[\{OsO_2(OR'O)\}_2(dabo)]$ in the case of 1,4-diazabicyclo[2.2.2]octane.[16] We seek here to elucidate the nature of the species formed by reaction of $[OsO_3(NR)L]$ and $[\{OsO_3(NR)\}_2L]$ with alkenes.

We find, not unexpectedly, that these reactions give products apparently analogous to those found for the OsO_4 adducts, though we have not yet succeeded in obtaining suitable crystals for *X*-ray study. The quinuclidine adducts $[OsO_3(NR)(qncd)]$ (R = Bu^t, C_5H_{11}, C_8H_{17}, or Ad) yield dark green complexes of stoicheiometry $[OsO_2(OR'NR)(qncd)]$. Their colour and the fact that their i.r. and Raman spectra show two bands in the ν(OsO) region near 880 cm^{-1} just as do the corresponding oxo species $[OsO_2(OR'O)(qncd)]$ suggests similar structures for both.

Our *X*-ray study on the cyclohexanediolato complex $[OsO_2(o\text{-}OC_6H_{10}O)(qncd)]$ showed this to be dimeric with an asymmetric Os_2O_2 bridge,[21] and we tentatively suggest an analogous structure, (IV), for the present species. They are too insoluble for reliable molecular weight studies to be obtained, but the similarity of the i.r. and Raman spectra of the solid complexes (13), (16), and (17) with those of their solutions suggests little change in structure from solid to solution. In the case of the tatd adducts $[\{OsO_3(NR)\}_2(tatd)]$ (R = Bu^t or C_8H_{17}) reactions with alkenes R′ gave green products of stoicheiometry $[\{OsO_2(OR'NR)\}(tatd)]$ as was the case with the corresponding reactions with $[(OsO_4)_2(tatd)]$.[16] Thus, reaction of $[\{OsO_3(NBu^t)\}_2(tatd)]$ with dimethyl fumarate gives a 48% yield of $[OsO_2\{O(CHCOOMe)_2NBu^t\}(tatd)]$, increased to 90% by addition of excess tatd suggesting that dissociation of the initial adduct to a 1:1 complex initially occurs. With dabo, on the other hand, the bridging role of the ligand in the adduct is apparently retained in the products with alkenes; thus, $[\{OsO_3(NBu^t)\}_2(dabo)]$ reacts with dimethyl fumarate to give $[\{OsO_2[O(CHCOOMe)_2NBu^t]\}_2(dabo)]$ (14) and a similar situation is observed for reactions of $[(OsO_4)_2(dabo)]$ with alkenes.[16]

In the Experimental section we list full ^1H n.m.r. data for three of the complexes (13)—(15); as with the alkanolaminato esters it appears that the methylene groups are adjacent to the bulky imido groups.

ESCA Data.—In the Table we report $4f_{\frac{7}{2}}$ and $4f_{\frac{5}{2}}$ binding energies for a number of the complexes described in the paper; it is known that such binding energies are indicative of the oxidation state of the osmium atom.[22,23] Although the $[OsO_3(NR)]$ species were too volatile for such studies the bis(imido) complex $[OsO_2(NBu^t)_2]$ gave high binding energies

as expected for osmium(VIII), as was the case for the adducts $[\{OsO_3(NC_8H_{17})\}_2L']$ (L' = tatd or dabo). All the other complexes listed in the Table are formally of osmium(VI) and indeed show lower binding energies, typically $4f_{\frac{7}{2}}$ and $4f_{\frac{5}{2}}$ of 52.0 and 55.0 eV respectively. We have found values of 52.3 and 55.0 eV for *trans*-$K_2[Os^{VI}O_2(OH)_4]$ and of 53.0 and 55.8 eV for the osmium(VII) complex $[PPh_4][OsO_4]$, analogous to $[AsPh_4][OsO_4]$ recently reported.[24]

Experimental

The complexes $[OsO_3(NR)]$ (R = Bu^t,[10] C_5H_{11},[10] Ad,[6] or C_8H_{17}[5]) and $[OsO_2(NBu^t)_2]$[10] were made as in the literature and gave satisfactory elemental analyses; data for $[OsO_3(NC_8H_{17})]$ only are listed in the Table since spectroscopic data for it are not available in the literature.

For the alkanolaminato species $[\{OsO_2(OR'NR)\}_2]$ the preparation of the isobutylene complex $[\{OsO_2(OCMe_2CH_2NBu^t)\}_2]$ is typical for one involving a gaseous alkene, while that for the methyl methacrylate complex $[\{OsO_2[OCMe(COOMe)CH_2NBu^t]\}_2]$ is typical for one involving a liquid alkene.

$[\{OsO_2(OCMe_2CH_2NBu^t)\}_2]$ (3).—A solution of $[OsO_3(NBu^t)]$ (0.15 g, 0.48 mmol) in diethyl ether (3 cm^3) was stirred under an atmosphere of isobutylene for 4 h. The resulting red-brown solid was filtered off and dried *in vacuo*. A further crop of solid was obtained by reducing the volume of solvent.

$[\{OsO_2[OCMe(COOMe)CH_2NBu^t]\}_2]$ (6).—To $[OsO_3(NBu^t)]$ (0.14 g, 0.4 mmol) in diethyl ether was added methyl methacrylate (0.06 g, 0.4 mmol) and the mixture stirred at room temperature for 15 h. The deep red product was filtered off and air-dried.

The known diaminato complexes $[OsO_2\{NBu^t(CHCOOR)_2NBu^t\}]$ (R = Me or Et) were made as in the literature;[10] we found however that the use of diethyl ether as solvent eliminates the need for t.l.c. separation. The complex $[OsO_2\{NBu^t(CHCN)_2NBu^t\}]$ (9) was made from $[OsO_2(NBu^t)_2]$ (0.16 g, 0.44 mmol) in diethyl ether (3 cm^3) with fumaronitrile (0.03 g, 0.38 mmol); it is deep red.

For the adducts $[OsO_3(NR)(qncd)]$ and $[\{OsO_3(NR)\}_2L']$ (L' = tatd or dabo) the preparation of the adducts with R = C_8H_{17} are typical.

$[\{OsO_3(NC_8H_{17})\}_2(dabo)]$ (12).— To $[OsO_3(NC_8H_{17})]$ (0.1 g, 0.3 mmol) in diethyl ether (3 cm^3) was added 1,4-diazabicyclo[2.2.2]octane (0.015 g, 0.14 mmol). The bright orange solid was filtered off and air-dried.

The adduct with quinuclidine is more soluble and for this addition of light petroleum (b.p. 40–60 °C; 4 cm^3) is necessary.

The alkanolaminato ester adducts $[OsO_2(OR'NR)(qncd)]$ and $[\{OsO_2(OR'NR)\}_2L']$ (L' = tatd or dabo) were made by methods of which the following is typical.

$[OsO_2(OC_6H_{10}NBu^t)(qncd)]$ (16).—To a solution of $[OsO_3(NBu^t)(qncd)]$, generated *in situ* by stirring a mixture of $[OsO_3(NBu^t)]$ (0.15 g, 0.5 mmol) and quinuclidine (0.06 g, 0.5 mmol) in diethyl ether (5 cm^3) for 20 min was added a slight excess of cyclohexene (0.05 g, 0.7 mmol). The mixture was stirred at room temperature for 12 h, cooled to −20 °C and the dark green solid filtered off.

Hydrogen-1 N.M.R. Spectra.—We report here a detailed list of the ^{1}H spectra, measured in C^2HCl_3, of five alkanolaminato and three alkanolaminato ester adducts. Chemical shifts (δ/p.p.m. relative to $SiMe_4$, with integrals and assignments in parentheses) are listed.

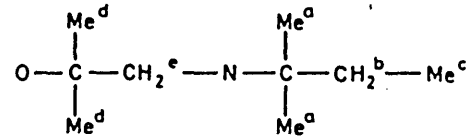
$[\{OsO_2(OC_2H_4NBu^t)\}_2]$ (2). 1.56 (s, 9 H, NBu^t), 4.20 (s, 1 H, CH′–N), 4.26 (s, 1 H, CH″–N), 4.52 (br s, 2 H, CH_2–O).

$[\{OsO_2(OCMe_2CH_2NBu^t)\}_2]$ (3). 1.44 (s, 6 H, Me_2C–O), 1.52 (s, 9 H, NBu^t), 4.02 (br s, 2 H, CH_2–N).

$[\{OsO_2[OCH(COOMe)CH_2NBu^t]\}_2]$ (5). 1.51 (s, 9 H, NBu^t), 3.67 (s, 3 H, $COOCH_3$), 4.45 (br s, 2 H, CH_2–N), 5.09 (br s, 1 H, CH–O).

$[\{OsO_2[OCMe(COOMe)CH_2NBu^t]\}_2]$ (6). 1.51 (s, 9 H, NBu^t), 1.84 (s, 3 H, CH_3–C–O), 3.68 (s, 3 H, $COOCH_3$), 4.21 (br s, 2 H, CH_2–N).

$[\{OsO_2(OCMe_2CH_2NC_5H_{11})\}_2]$ (8). 0.81 (t, J = 7 Hz, 3 H, CH_3^c), 1.48 (s, 6 H, N–CMe_2^a), 1.52 (s, 6 H, Me_2^d–C–O), 1.91 (q, J = 7 Hz, 2 H, $-CH_2^b$), 4.05 (br s, 2 H, CH_2^e–N). The atom numbering is shown below.



$[OsO_2\{O(CHCOOMe)_2NBu^t\}(qncd)]$ (13). 1.14 (s, 9 H, NBu^t), 1.65 (br s, 6 H, CH_2^b) 1.93 (br m, 1 H, CH^c), 3.08 (br m, 6 H, CH_2^a), 3.67 (s, 6 H, $COOCH_3$), 4.02 (s, 1 H, HC–N), 4.43 (s, 1 H, HC–O). The atom numbering for qncd is $N(CH_2^a)_3(CH_2^b)_3CH^c$.

$[\{OsO_2[O(CHCOOMe)_2NBu^t]\}_2(dabo)]$ (14). 1.17 (s, 9 H, NBu^t), 3.16 (s, 6 H, CH_2^a), 3.68 (s, 3 H, $COOCH_3$), 3.70 (s, 3 H, $COOCH_3$), 4.05 (s, 1 H, HC–N), 4.49 (s, 1 H, HC–O); CH_2^a are the protons of $N_2C_6H_{12}$.

$[OsO_2\{O(CHCOOMe)_2NBu^t\}(tatd)]$ (15). 1.21 (s, 9 H, NBu^t), 3.71 (s, 3 H, $COOCH_3$), 3.72 (s, 3 H, $COOCH_3$), 4.11 (s, 1 H, HC–N), 4.52 (s, 1 H, HC–O), 4.71 (br s, 12 H, CH_2^a); CH_2^a are the protons of $N_4C_6H_{12}$.

Infrared spectra were measured on a Perkin-Elmer 683 instrument as liquid paraffin mulls between caesium iodide plates, and Raman spectra as spinning discs in a KBr base using a Spex Ramalog 5 instrument with a krypton-ion laser with 6 147 Å or 5 682 Å excitation for red and yellow samples and 5 308 Å for green samples. ^{1}H N.m.r spectra were measured on a JEOL FX 90Q spectrometer. ESCA spectra were measured on a V.G. Escalab Mark II instrument at 10^{-9} Torr (*ca.* 1.33×10^{-7} Pa) with data collected at a pass energy of 20 eV and ultimate resolution of 0.7 eV. Samples were run as pressed discs on indium foil, correction being made for sample charging. Microanalyses were performed by Mr. K. Jones of the Microanalytical Department.

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References

1 Part 7, M. J. Wright and W. P. Griffith, *Transition Met. Chem.*, 1982, 7, 53.
2 R. Criegee, *Annalen*, 1936, **522**, 75; R. Criegee, B. Marchand, and H. Wannowius, *Annalen*, 1942, **550**, 99.
3 R. J. Collin, J. Jones, and W. P. Griffith, *J. Chem. Soc., Dalton Trans.*, 1974, 1094.
4 M. Schröder, *Chem. Rev.*, 1980, **80**, 187.
5 N. A. Milas and M. I. Iliopulos, *J. Am. Chem. Soc.*, 1959, **81**, 6089.
6 D. W. Patrick, L. K. Truesdale, S. A. Biller, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1975, **97**, 2305.

7 D. W. Patrick, L. K. Truesdale, S. A. Biller, and K. B. Sharpless, *J. Org. Chem.*, 1978, **43**, 2628.
8 E. Herranz and K. B. Sharpless. *J. Org. Chem.*, 1976, **41**, 177; 1978, **43**, 2544.
9 E. Herranz, S. A. Biller, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1978, **100**, 3596.
10 A. O. Chong, K. Oshima, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1977, **99**, 3420.
11 W. P. Griffith, N. T. McManus, A. C. Skapski, and A. J. Nielson, *Inorg. Chim. Acta*, 1985, **103**, L5.
12 W. P. Griffith, N. T. McManus, A. C. Skapski, and A. D. White, *Inorg. Chim. Acta*, 1985, **105**, 11.
13 R. J. Collin, W. P. Griffith, F. L. Phillips, and A. C. Skapski, *Biochim. Biophys. Acta*, 1974, **354**, 152; F. L. Phillips and A. C. Skapski, *J. Chem. Soc., Dalton Trans.*, 1975, 2586.
14 W. P. Griffith, *J. Chem. Soc. A*, 1969, 211.
15 K. B. Sharpless, A. Y. Tetranishi, and J-E. Backvall, *J. Am. Chem. Soc.*, 1977, **99**, 3120.
16 M. J. Cleare, P. C. Hydes, W. P. Griffith, and M. J. Wright, *J. Chem. Soc., Dalton Trans.*, 1977, 941.
17 W. P. Griffith, A. C. Skapski, K. A. Woode, and M. J. Wright, *Inorg. Chim. Acta*, 1978, **31**, L413.
18 S. G. Hentges and K. B. Sharpless, *J. Org. Chem.*, 1980, **45**, 2257.
19 W. A. Nugent, R. L. Harlow, and R. J. McKinney, *J. Am. Chem. Soc.*, 1979, **101**, 7265.
20 M. Schröder, A. J. Nielson, and W. P. Griffith, *J. Chem. Soc., Dalton Trans.*, 1979, 1607.
21 B. A. Cartwright, W. P. Griffith, M. Schröder, and A. C. Skapski, *J. Chem. Soc., Chem. Commun.*, 1978, 853.
22 D. J. Salmon and R. A. Walton, *Inorg. Chem.*, 1978, **17**, 2379.
23 J. P. Hall and W. P. Griffith, *J. Chem. Soc., Dalton Trans.*, 1980, 2410.
24 E. Bilger, J. Pebler, R. Weber, and K. Dehnicke, *Z. Naturforsch., Teil B*, 1984, **39**, 259.

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Partial Coordination in an Adduct of an Osmium Imido Complex: X-ray Molecular Structure of $[OsO_3(NOct^t)]_2 \cdot N_2C_6H_{12}$

WILLIAM P. GRIFFITH, NEIL T. McMANUS, ANDRZEJ C. SKAPSKI and ANDREW D. WHITE

Chemical Crystallography and Inorganic Chemistry Research Laboratories, Imperial College, London SW7 2AY, U.K.

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We have shown in earlier work [1, 2] that osmium tetroxide OsO_4 will form adducts with bridgehead amines in which there is a very long Os–N(amine) bond; we have called this 'partial coordination' [1]. We now show that the tetrahedral oxo-imido complex $OsO_3(NOct^t)$, formed by reaction of OsO_4 with tert-octylamine [3], forms a 2:1 adduct with 1,4-diazabicyclo[2,2,2]octane ($N_2C_6H_{12}$) to give the new complex $[OsO_3(NOct^t)]_2 \cdot N_2C_6H_{12}$, in which there is an even longer Os–N(amine) bond.

The complex was made as orange needles by slow crystallisation from a solution of $OsO_3(NOct^t)$ (0.14 g, 0.4 mmol) and 1,4-diazabicyclo[2,2,2]octane (0.03 g, 0.2 mmol) in diethylether (5 cm^3).

The crystals are monoclinic with $a = 6.541(1)$, $b = 28.652(4)$, $c = 15.981(2)$ Å, $\beta = 92.82(1)$, $U = 2991.4$ $Å^3$ (at 19 °C), space group $P2_1/c$ and $Z = 4$. Intensity data were collected on a Nicolet R3m/Eclipse S140 diffractometer system, using graphite-monochromated Cu Kα radiation. A total of 3742 independent reflections were measured (to $\theta = 55°$), of which 1096 were judged to be 'unobserved'. The structure was solved by a combination of direct, Patterson, and Fourier methods, and least-squares refinement has now reached $R = 0.058$. The central portion of the molecule is subject to conformational disorder. Program system SHELXTL [4] was used throughout the calculations.

Figure 1 shows that the molecule is binuclear, with the amine bridging two $OsO_3(NOct^t)$ units. The osmium atoms have distorted trigonal bipyramidal coordination in which the equatorial positions are occupied by oxo ligands with a mean Os–O bond length of 1.71(1) Å, which is similar to that found in OsO_4 itself [5]. The axial positions are taken by the tert-octylimido ligand, with a mean Os–N(imido) bond length of 1.73(1) Å, comparable with such distances found in other osmium oxo-imido complexes [6], and by the bridging cage amine. Here the Os–N(amine) distances are very long with a mean of 2.45(1) Å, longer than the 2.37 Å distances observed in $OsO_4 \cdot NC_7H_{13}$ and 2.42 Å in $[OsO_4]_2 \cdot N_4C_6H_{12}$ [1]. This difference could well arise from the greater *trans* influence of the imido as compared with the oxo ligand.

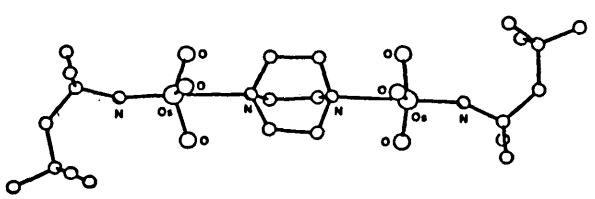

Fig. 1. Molecular structure of $[OsO_3(NOct^t)]_2 \cdot N_2C_6H_{12}$.

The vibrational spectra are fully consistent with this structure. Three $\nu_{Os=O}$ stretches are observed in the infrared spectrum of the solid at 883, 873 and 845 cm^{-1}, with Raman bands at 887, 875 and 850 cm^{-1}; the $\nu_{Os=N}$(imide) stretch is at 1170 cm^{-1} in the infrared and Raman. In toluene or carbon tetrachloride solutions, however, two $\nu_{Os=N}$ bands appear at 1210 and 1170 cm^{-1}, and in the $\nu_{Os=O}$ regions there are infrared bands at 924, 914, 880 and 873 cm^{-1} (at 929, 912, 889 and 878 cm^{-1} in the Raman). The 1210 cm^{-1} band and the $\nu_{Os=O}$ stretches above 900 cm^{-1} appear in solutions of OsO_3NOct^t also, and it is clear that dissociation has occurred, presumably to $OsO_3NOct^t \cdot N_2C_6H_{12}$ and to free OsO_3NOct^t. Such a conclusion is supported by molecular weight studies on the complex in benzene solution (found 488, calculated 841), clearly indicating dissociation. It is interesting that the analogous adduct with osmium tetroxide, $[OsO_4]_2 \cdot N_2C_6H_{12}$ retains its binuclear structure in benzene [2].

The $4f_{7/2}$ and $4f_{5/2}$ binding energies in the ESCA spectrum are at 53.0 and 55.7 eV respectively, consistent with the osmium being in the octavalent state (thus we find that for $K[OsO_3N]$ the corresponding binding energies are at 53.3 and 56.1 eV).

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References

1 W. P. Griffith, A. C. Skapski, K. A. Woode and M. J. Wright, *Inorg. Chim. Acta, 31*, L413 (1978).
2 M. J. Cleare, P. C. Hydes, W. P. Griffith and M. J. Wright, *J. Chem. Soc., Dalton Trans.*, 941 (1977).
3 N. A. Milas and M. I. Iliopulos, *J. Am. Chem. Soc., 81*, 6089 (1959).
4 G. M. Sheldrick, 'SHELXTL', an integrated system for solving, refining and displaying crystal structures from diffraction data, revision 4, Nicolet Instrument Ltd., Warwick, January 1983.
5 H. M. Seip and R. Stolevik, *Acta Chem. Scand., 20*, 385 (1966).
6 W. A. Nugent, R. L. Harlow and R. J. McKinney, *J. Am. Chem. Soc., 101*, 7265 (1979).

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RUTHENIUM AND OSMIUM COMPLEXES AS ORGANIC OXIDANTS*

W P GRIFFITH *and* A D WHITE

Department of Chemistry, Imperial College, London SW7 2AY UK

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The use of oxo complexes such as $[RuO_4]^{2-}$, *trans*-Ba $[RuO_3(OH)_2]$, *trans*-RuO_2 bipy Cl_2, $[RuO_3Cl_3]^-$ and $[RuO_4]^-$ as oxidants for alcohols is described. Primary alcohols are converted to aldehydes or carboxylic acids and secondary alcohols to ketones, usually without competing double-bond cleavage Structural aspects of the coordination chemistry involved in the oxidation of alkenes by OsO_4 and its amine adducts are briefly reviewed, and new data presented on analogous aspects of the reaction of $OsO_3(NOct^t)$ and its amine adducts with alkenes.

Key Words : Oxo Complexes of Ruthenium and Osmium; Oxidation of Alcohols and Alkenes

INTRODUCTION

IT has long been known that certain transition metal oxo species in high oxidation states will oxidise alcohols[1] (*e.g.* CrO_3, $[Cr_2O_7]^{2-}$, $[MnO_4]^-$ MnO_2, RuO_4], but a common problem is that competing double-bond cleavage may also occur with unsaturated alcohols. Since our discovery in 1979 of the catalytic system[2] ($[RuO_4]^{2-}$/$S_2O_8^{2-}$/aqueous OH^-), which cleanly oxidises a wide variety of primary alcohols to carboxylic acids and secondary alcohols to ketones without in most cases double bond cleavage, we have sought to develop other systems which might show selectivity in oxidation properties and to avoid aqueous media. Ruthenium in its higher oxidation states (VI, VII) has been the metal of choice.

Here we briefly review our earlier work on these systems and present new data : our interest in this field has not as yet been mechanistic, but this aspect has been studied by others.[3] We have also had a long-standing interest[4] in the structural chemistry behind the well-known[1,5] *cis*-hydroxylation of alkenes by OsO_4; our work in this area is briefly reviewed here and new data presented on the structural coordination chemistry involved in the hydroxyamination reactions[6] of osmium(VIII) imido complexes with alkenes.

EXPERIMENTAL

Ruthenium Complexes

Solutions of $[RuO_4]^{2-}$ were made as previously described[2,7] as were *trans*-Ba $[RuO_3(OH)_2]$[7] *trans*-RuO_2 bipy Cl_2(I),[7,8] (Ph_4P) $[RuO_2Cl_3]$ (II)[7] and $(n\text{-}Bu_4N)$ $[RuO_4]$[9]

*Presented at the INSA Golden Jubilee Symposium on *Recent Trends in Inorganic Chemistry* held in Calcutta in December 1985.

(III) [For (I) found C, 33.6; H, 2.4; Cl, 19.6; N, 7.9 per cent; RuO_2 bipy Cl_2 requires C, 33.3; H, 2.2; Cl, 19.7; N, 7.8 per cent. For (II) found C, 49.9; H, 3.5; Cl, 18.4 per cent (Ph_4P) $[RuO_2Cl_3]$ requires C, 49.8; H, 3.5; Cl, 18.4 per cent. For (III) found C, 46.4; H, 8.8; N, 3.4 per cent; (n-Bu_4N) $[RuO_4]$ requires C, 47.0; H, 8.9; N, 3.4 per cent].

Organic Oxidation—We have already described in the literature procedures for organic oxidations by $[RuO_4]^{2-}/[S_2O_8]^{2-}$ *trans*-$Ba[RuO_3(OH)_2]$, *trans* RuO_2 bipy Cl_2, $[RuO_2Cl_3]^-$ and n-$Bu_4N)$ $[RuO_4]$.[9] Similar methods to those used for $[RuO_4]^{2-}/S_2O_8^{2-}$ were used for the ruthenium(VI) periodato complex. Unless otherwise noted carboxylic acids were isolated as such and characterised by melting point and ^1H NMR, and aldehydes and ketones were isolated as 2,4-dinitrophenylhydrazone derivatives which were characterised in the normal way.

Osmium Complexes

Osmium tetraoxide was supplied by Johnson, Matthey Ltd. The imido complex OsO_3 (NOct^t) was made by a modification of the procedure of Milas and Iliopulos[10] (*see below*). The alkanolaminato species $[OsO_2(ORNOct^t)]_2$ were made from the alkene R (R = methylmethacrylate, CH_2 = CMe(COOMe); methylacrylate, CH_2 = CHCOOMe and dimethyl fumarate, MeCOOCH = CHCOOMe). The adducts $[OsO_3(NOct^t)]$. NC_7H_{13} (quinuclidine, NC_7H_{13}), and $[OsO_3(NOct^t)]_2.L$ (L = 1,4-diazabicyclo [2,2,2] octane, $N_2C_6H_{12}$; hexamethylenetetramine, $N_4C_6H_{12}$ were made from $OsO_3(NOct^t)$ and the amine. The "adduct esters" $OsO_2(ORNOct^t)$. NC_7H_{13}(R = CH_2 = CMeCOOMe; MeOOCCH = CHCOOMe; EtOOCCH = CHCOOEt) and $[OsO_2(ORNOct^t)]$. $N_2C_6H_{12}$ (R = acrylonitrile CH_2 = CH(CN); CH_2=CMeCOOMe; methacrylic acid CH_2=CMeCOOH; MeCOOCH=CHCOOMe) were made from the adducts and R. Microanalyses are given in Table I; we give here typical preparative methods for one compound of each class.

$OsO_3(NOct^t)$—To OsO_4(0.92g., 3.6mmol) in water at 0 °C was added *tert*-octylamine (0.47g., 3.6mmol) and the mixture stirred at room temperature for two hours. The product in yellow colour (1.20g., 9 per cent) was filtered off and dried *in vacuo*.

$[OsO_2(O(CHCOOMe)_2\ NOct^t)]_2$—To $OsO_3(NOct^t)$ (0.15g., 0.42mmol) in diethylether (4cm^3) was added dimethylfumarate (0.06g., 0.42mmol) and the solution stirred for 15 hours at room temperature. The product in green colour (0.02g., 10 per cent) was filtered off and dried *in vacuo*.

$[OsO_3(NOct^t)]_2\ N_2C_6H_{12}$—To $OsO_3(NOct^t)$ (1.2g., 3.3mmol) in diethylether (3cm^3) was added a solution of 1,4-diazabicyclo[2,2,2] octane (0.18g., 1.6mmol) in diethylether (2cm^3) and the solution stirred for two hours at room temperature. The product in orange colour (1.24g., 90 per cent) was filtered off and dried *in vacuo*.

$[OsO_2(O(CHCOOMe)_2\ NOct^t)]_2.N_2C_6H_{12}$—To $OsO_3(NOct^t)$ 0.11g., 0.13mmol) in diethylether 5cm^3) was added dimethylfumarate (0.02g., 0.13mmol) in diethylether

TABLE I

Microanalytical and infrared data

	C	H	N	ν(OsO)	ν(Os$_2$O$_4$) or ν(OsN)
$OsO_3(NOct^t)$	26.4 (26.3)	4.6 (4.6)	3.8 (3.8)	927s, 916vs	1207vs
$[OsO_3(OCHMeCOOMeCH_2NOct^t)]_2$	34.0 (33.5)	5.8 (5.4)	3.0 (3.0)	945s	650m
$[OsO_3(O(CHCOOMe)_2\ NOct^t)]_2$	32.8 (33.0)	4.9 (4.9)	2.8 (2.8)	930s	645m
$[OsO_3NOct^t].NC_7H_{13}$	37.7 (37.8)	6.3 (6.3)	5.8 (5.9)	885s, 870s	1220s
$[OsO_3NOct^t].N_2C_6H_{12}$	31.5 (31.3)	5.5 (5.5)	6.6 (6.7)	875s, 850s	1170m
$[OsO_3NOct^t].N_4C_4H_{12}$	31.4 (30.3)	5.2 (5.3)	9.6 (9.7)	888s, 875	1212s
$[OsO_3(O(CHCOOMe)_2\ NOct^t].NC_7H_{13}$	40.9 (40.6)	6.2 (6.1)	4.3 (4.5)	891s, 852	—
$[OsO_3O(CHCOOEt)_2\ NOct^t].NC_7H_{13}$	42.6 (42.6)	6.5 (6.5)	4.2 (4.3)	892s, 853	—
$[OsO_3OCHCNCH_2NOct^t]_2.N_2C_6H_{12}$	35.0 (35.4)	5.3 (5.5)	8.5 (8.9)	887s, 860	—

Frequencies in cm^{-1}

(2cm^3) and the solution stirred at room temperature for eight hours. The green product (0.04g., 25 per cent) was filtered off and dried *in vacuo*.

For microanalytical and infrared data see Table I. Microanalyses were performed by the Microanalytical Department at Imperial College; infrared spectra were measured on Perkin-Elmer 683 and 983G instruments. ^{1}H NMR spectra (for characterisation of organic products) were carried out on a Varian EM360. Raman spectra were measured on a Spex Ramalog 5 instrument with krypton-ion excitation at 6471 and 5308Å.

OXIDATION OF ALCOHOLS

(i) *Ruthenium(VI) Complexes*

The Ruthenate Ion, $[RuO_4]^{2-}$—This is known from Raman data (Table II) to be tetrahedral in aqueous alkali.[11,12] Lee showed in 1972 that $[RuO_4]^{2-}$ in *M* aqueous NaOH will oxidise benzyl and cinnamyl alcohols to the acids and *cyclo*hexanol to *cyclo*hexanone.[13] The clean oxidation of *cyclo*butanol to *cyclo*butanone suggested that two-electron processes were involved, and a hydride abstraction mechanism

TABLE II

Raman and infrared data on ruthenium and osmium oxo complexes

(a) *trans*-MO_3X_2		$Ba[RuO_3(OH)_2]$	OsO_3F_2[24]	XeO_3F_2[25]
$\nu_1(A_1'; \nu(MO_3)^s)$		795	947	807
$\nu_2(A_1'; \nu(MX_2)^s)$		383	619	567
$\nu_3(A_2''; \nu(MX_2))$		(515)	(646)	(632)
$\nu_4(A_2''; \delta(MX_2))$		(335)	(258)	(375)
$\nu_5(E'; \nu(MO_3)^{as})$		817(815)	929(928)	892(896)
$\nu_6(E'; \delta(MO_3)^{as})$		330(320)	317(316)	316(321)
$\nu_7(E'; \delta(MX_2)^{as})$			206	
$\nu_8(E'; \delta(OMX)^{as})$		324	348	361
(b) $[RuO_4]^{n-}\ \nu_1(A_1)$		$\nu_1(E)$	$\nu_1(F_2)$	$\nu_4(F_2)$
$[RuO_4]^{2-}$[11,12]	808	336(330)	837,790(812)	323(330)
H_2O	810p	330 dp	836 dp	330 dp
$[RuO_4]^{-}$[11,12]	830	339	840(846)	317(316)
CH_2Cl_2[9]	847p			
RuO_4[11]	881	324	922,906	336,330
H_2O	883p	318 dp	921 dp	332 dp
(c) *cis dioxo complexes*		$\nu^s(MO_2)$	$\nu^{as}(MO_2)$	
$(Ph_4P)\ [RuO_2Cl_4]$		891(892)	878(878)	
	CCl_4	887 p	(896)	
$[OsO_2(O_2C_8H_{10})\ NC_7H_{13}]_2$[29]		898	(903)	
	$CHCl_3$	923 p (919)	881 dp (879)	
(d) *Imido complexes*		$A_1(\nu(OsN))$	$A_1(\nu^s(OsO_2)^s)$	$E(\nu(OsO_2)^{as})$
$OsO_3(NOct^t)$		1206(1207)	922(927)	914,906(916)
		1210 p (1203)	924 p (974)	918 dp(914)
$[OsO_3(NOct^t)]_2.N_2C_6H_{12}$		1174(1167)	887(883)	878,850,(875, 845)
	CCl_4	1204 p, 1170 p	929 p, 880 p	912 dp, 878 dp
	Toluene	(1210, 1170)	(924,880)	(914,873)

Frequencies in cm^{-1}. Data on solids unless otherwise stated. Infrared frequencies in parentheses.

involving the final formation of ruthenim(IV) was proposed.[3] Subsequently, Corey *et al.* used $[RuO_4]^{2-}$ stoichiometrically for conversion of a hydroxyacid to a diacid as part of the stereospecific total synthesis of gibberellic acid.[14] We then developed a procedure whereby $[RuO_4]^{2-}$ in alkali was catalytically regenerated by persulphate as co-oxidant: typically aqueous *M* KOH containing 2×10^{-4} *M* ruthenium (as $RuCl_3.nH_2O$) and $M^I_2S_2O_8$ (0.06*M*, M^I = Na or K).[2] Such a solution will, often in half an hour or less, convert primary alcohols to carboxylic acids and secondary alcohols to ketones, a process which alkaline persulphate itself will not accomplish.[2,7] High catalytic turnovers are obtainable: thus, 53g. of 4-nitrobenzaldehyde is converted to 60g of the acid by 1.4×10^{-3} *M* ruthenate.[2] The mechanism is presumably

that proposed by Lee *et al.*[3] for stoichiometric $[RuO_4]^{2-}$ followed by regeneration of $[RuO_4]^{2-}$ by $S_2O_8^{2-}$. A suggestion that $[RuO_4]^-$ and not $[RuO_4]^{2-}$ is involved in these reactions[15] has been disproved[7]; thus, $[RuO_4]^-$ cleaves cinnamyl alcohol in aqueous solution but the $[RuO_4]^{2-}$ reagent does not.[7]

The catalytic reagent does suffer from some disadvantages, however. The use of aqueous media is often not suitable for water insoluble organic substrates (phase transfer agents are of limited help here,[7] though use of a 50 per cent *tert*-butanol-water solution does improve results[16]); the presence of base is an adverse factor for some organic substrates. Our original belief[2] that unsaturated alcohols are not cleaved by $[RuO_4]^{2-}$ needs modification: it is known that $[RuO_4]^{2-}$ attacks double bond at *ca* 85 °C,[17] and we find that allylic and homoallylic alcohols do not give clean oxidations, e.g. allyl alcohol, geraniol[7] (though suprisingly *o*-allylsalicylaldehyde is oxidised in high yield to the acid[16]). Presumably complexation of the alkyl moiety to ruthenium is involved, tending to deactivation of the alkoxy intermediate. However, isolated double bonds are unaffected, e.g. cinnamyl alcohol, borneol,[7]

TABLE III

A selection of oxidations effected by ruthenium oxo complexes

Oxidant	$[RuO_4]^{2-}/S_2O_8^{2+}$	*a* Ru periodate *b trans*-$Ba[RuO_2(OH)_2]$ *c trans*-$RuO_3bipyCl_2$	$Ph_4P[RuO_3Cl_3]$	*n*-$Bu_4N[RuO_4]$
Alcohol				
Benzhydrol	*K*(97,0.5)	*K*(95,48)[b]	*K*(68,0.1)	
Benzyl	*A*(98,1.5)	*A*(87,3)[a], K(99,48)[b]; K(68,12)[c]	*K*(68,0.1)	*K*(91,2)
Borneol	*K*(75,24)			
2-Chlorobenzyl	*A*(97,0.5)	*K*(99,48)[b]	*K*(99,0.5)	
5-Cholestan-3β-ol		*K*(93,1.5)[c]	*K*(100,15)	
Chrysanthemyl	*A*(66,7)		*K*(86,0.5)	*K*(16,3)
Cinnamyl	*A*(99,3)	*K*(98,14)[c]	*K*(76,1)	*K*(88,1)
*Cyclo*butanol	*K*(70,2)		*K*(96,0.5)	
*Cyclo*pentanol	*K*(87,2)		*K*(66,0.5)	*K*(77,2)
Geraniol	A(<10,20)	*K*(95,48)[b]	*K*(96,0.5)	*K*(34,3)
Menthol	*K*(63,240)	*A*(72,160)[a]; *K*(54,78)[c]	*K*(66,5)	*K*(38,3)
4-Methoxy-benzyl	*A*(98,5)	*A*(51,4)[a]	*K*(98,1)	*K*(91,3)
4-Nitrobenzyl	*A*(97,1)	*K*(85,48)[b]	*K*(98,1)	*K*(83,0.5)
Nonanol	*A*(94,12)		*K*(70,0.5)	
Octadecanol		*K*(87,3)[c]	*K*(90,0.5)	*K*(91,3)
Piperonyl		*A*(79,3)[a]		*K*(80,2)
Stearyl	*A*(78,6)	*K*(24,72)[b]	*K*(87,1)	
α-Tetralol	*K*(84,2)	*K*(33,48)[b]	*K*(99,0.5)	

A = acid, *K* = aldehyde or ketone. Yield (%) followed by reaction time (hours) in parentheses. Most data from refs (7 and 9) but some new material included.

cyclo-hex-3-ene-methanol,[2] although apparently ricinoleic acid undergoes a certain amount of cleavage with $[RuO_4]^{2-}$ when the latter is used stoichiometrically.[18] In Table III is a selection of oxidations by $[RuO_4]^{2-}/S_2O_8^{2-}$; for further data see ref. (7).

Ruthenium Periodato Complex—The complex formulated as $Na_6[Ru(OH)_2(IO_6)_2].18H_2O$ is[19], we find,[20] an effective oxidant of primary alcohols to carboxylic acids and of secondary alcohols to ketones (Table III) and its action can be rendered catalytic by addition of periodic acid as secondary oxidant. It does however cleave the double bond of cinnamyl alcohol and has to be used in weak base, so it offers no apparent advantage over $[RuO_4]^{2-}$. The active species involved is more likely to be a "ruthenyl" complex, possibly *trans*-$[RuO_2(HIO_6)_2]^{2-}$, although it has been claimed that ruthenium(VII) periodato complexes exist in alkaline solutions.[21] Clearly though the active species is not RuO_4 (which is produced from RuO_2 and IO_4^- in neutral solution[22]); it functions effectively as a six-electron oxidant which suggests that both ruthenium and coordinated periodate are acting as oxidants (periodate in weak alkali dose not oxidise alcohols under these conditions).

The better of the two reagents so far described is $[RuO_4]^{2-}$: it is efficient to use, easy to make and inexpensive. Both reagents are self-indicating in that the reappearance of a red colour indicates the end of the reaction. The $[RuO_4]^{2-}$ ion only rarely affects double bonds. The necessity of using it in aqueous base, however, reduces its attractions for some organic chemistry so we have sought new reagents which do not need base and will operate in non-aqueous media.

Barium Ruthenate, Trans-Ba $[RuO_3(OH)_2]$—This brick-red material, insoluble in all solvents, is made from barium ion and $[RuO_4]^{2-}$, and X-ray studies show it to have a trigonal bipyramidal structure(I) with the oxo ligand equatorial.[23] The Raman and infrared spectra of the solid (Table II) are easily interpreted on the basis of this D_{3h} structure: we give assignments and compare them with those for matrix-isolated OsO_3F_2[24] and for XeO_3F_2[25], both of which are thought to have similar D_{3h} structures.

Barium ruthenate functions as a weak two-electron heterogeneous reagent, oxidising only activated primary alcohols to aldehydes and secondary alcohols to ketones (Table III).[7] Long reaction times are necessary, due presumably to the heterogeneous nature of the reagent. Despite the presence of coordinated hydroxyl ligands no further oxidation of aldehydes to carboxylic acids occurs.

Trans-$RuO_2bipy\ Cl_2$—We made this complex in 1973 by reaction of *trans*-$[RuO_2Cl_4]^{2-}$ with 2,2′ bipyridyl.[8] It is readily soluble in dichloromethane and oxidises primary alcohols to aldehydes and secondary alcohols to ketones in good yield[7]; there are preliminary indications that it can function as a catalytic reagent using *tert*-butylhydroperoxide as a co-oxidant.[16] It is however difficult to make in a pure state and so we have made only a preliminary survey of its oxidation properties (Table III).

Trans-$(Ph_4P)_2[RuO_2Cl_4]$—This red material, made from $[RuO_4]^{2-}$, HCl and excess cation, appears to function in similar fashion to the more easily prepared $[RuO_2Cl_3]^-$, it dissociates to the latter in solution.[20]

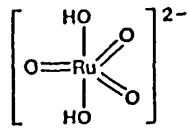
(Ph$_4$P) [*RuO$_2$Cl$_3$*]—This is made from $[RuO_4]^{2-}$ HCl and equimolar quantities of (Ph_4P) Cl; (Ph_4As) Cl may also be used. It is readily soluble in dichloromethane to give an emerald-green solution. Attempts to obtain simple crystals for X-ray study have so far failed, but the Raman and infrared spectra in the $\nu(Ru=O)$ (stretching) region of 800–1000cm^{-1} (Table II) suggests that *trans* O=Ru=O units, as found in *trans*-$[RuO_2(NH_3)_4]Cl_2$ are not present in the complex;[7,26] nor do the spectra resemble that of the $\mu\mu'$-dioxo "osmyl" complex $Os_2O_6py_4$.[27] The absence of strong infrared bands below 300cm^{-1} suggests that $\mu\mu'$-chloro bridges are absent. There are however similarities between the vibrational spectra of $[RuO_2Cl_3]^-$ and of $[Os_2O(O_2C_6H_{10}).NC_7H_{13}]_2$ in the $\nu(M=O)$ region for both solid and solution; the latter is known from X-ray studies to have an asymmetric $\mu\mu'$ dioxo structure (see below and XII)[28] and to be monomeric in solution, probably trigonal bipyramidal with equatorial oxo ligands.[29] We tentatively propose structures(II) and (III) for $[RuO_2Cl_3]^-$ in the solution and solid states respectively.

Solutions of $[RuO_2Cl_3]^-$ in dichloromethane effect clean and efficient oxidations of primary alcohols to aldehydes and of secondary alcohols to ketones (presumably the absence of water precludes formation of aldehyde hydrates and thereby inhibits further oxidation to carboxylic acids). The efficient oxidation of *cyclo*butanol to *cyclo*butanone suggest that it is a two-electron oxidant.[7] The oxidations in high yield of cinnamyl and chrysanthemyl alcohols and of the allylic geraniol suggest that competing double-bond cleavage does not occur (whereas $[RuO_4]^{2-}/S_2O_8^{2-}$ does not cleanly oxidise geraniol, and oxidises chrysanthemyl alcohol in relatively low yield[7]). There is also some selectivity : thus, drimanediol(IVa) is oxidised by one equivalent of $[RuO_2Cl_3]^-$ to the natural product *iso*-drimeniol(IVb) in 35 per cent yield, preferential oxidation of the least reactive alcohol site and no lactol oxidation having occurred; the natural insect anti-feedant polygodiol(IVc) is also formed.[7,30] However, oxidation of 5α-cholestan-3β,6β-diol(Va) gave the dione(Vb) without selective oxidation of axial *versus* equatorial alcohol groups.[7]

Thus $[RuO_2Cl_3]^-$ is a useful oxidant which does not seem to affect double bonds, and displays some oxidative selectivity. We have not however been able to render its action catalytic as yet. Clearly there is some future in studying ruthenium(VI) complexes of the form *trans*-$[RuO_2X_4]^{n-}$ or $[RuO_2X_3]^{n-}$ and varying *P* so as to change the redox properties and hence perhaps the oxidative selectivity of the systems.

(ii) Ruthenium(VII) and Osmium(VII) Complexes

The ruthenate ion $[RuO_4]^-$ is known from X-ray studies on $K[RuO_4]$ to be tetrahedral;[31] Raman and infrared data (Table II) suggest that this structure is retained in solution.[11,12] In aqueous solution it cleaves double bonds of unsaturated carboxylates, and a mechanism for this involving ruthenium(VI) esters has been proposed.[32] In aqueous solution it also cleaves oleates, ricinoleate and *erythro-dihydroxystearate*;[18] we found that such solution oxidised primary alcohols to carboxylic acids and secondary alcohols to ketones (with accompanying double-bond attack on crotyl and cinnamyl alcohols); *cyclo*butanol is not cleanly oxidised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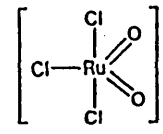
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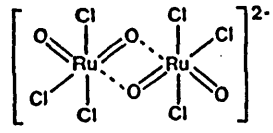
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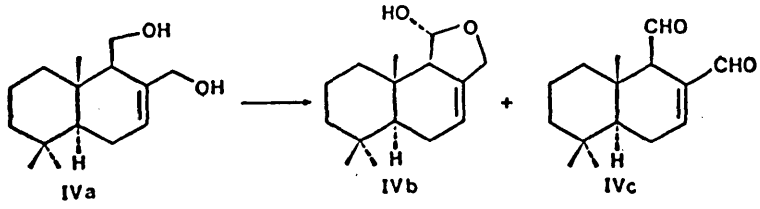
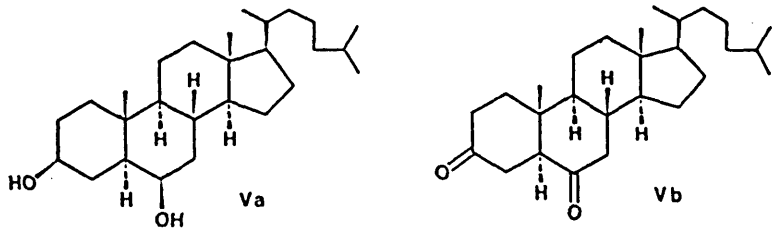
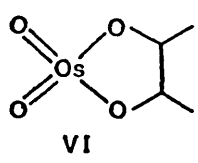
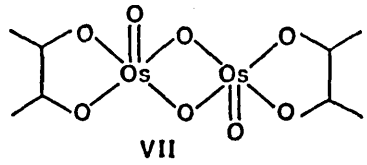

IVa IVb IVc

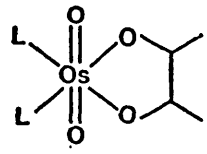

Va Vb

suggesting intermediacy of one- or three-electron processes.[7] The potassium salt is a rather ineffectual oxidant in 18-crown-6 and dichloromethane solution.[7]

Recently, we have developed the use of (n-Bu_4N)$[RuO^4]$, made from $[RuO_4]^-$ and the cation. This is readily soluble in dichloromethane to give a deep green solution, and Raman and infrared spectra (Table II) show $[RuO_4]^-$ to be present in such solutions. Primary alcohols are cleanly oxidised to aldehydes and secondary alcohols to ketones without, in the case of cinnamyl alcohol, double bond cleavage.[9]


VI


VII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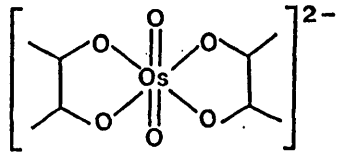
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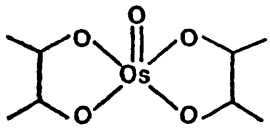
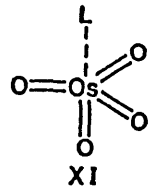

X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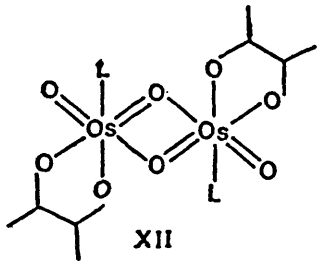
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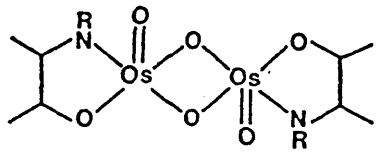
XIII

It seems to resemble the $[RuO_4]^-/S_2O_8^{2-}$ system[7] in giving low yields for oxidation of chrysanthemyl alcohol and geraniol, but is otherwise similar in action to $[RuO_2Cl_3]^-$; it appears to be a more efficient oxidant then ferrate, $[FeO_4]^{2-}$ [33,34], which is also potentially a three electron oxidant.

Oxidation of Alkenes

As already indicated our interest here has been in structural aspects of the coordination chemistry behind alkene oxidation by OsO_4 and OsO_3 (NR); we briefly summarise our work in this area on OsO_4 first.

Osmium Tetroxide, OsO_4

Reaction of OsO_4 with alkenes, dienes, trienes and alkynes has been comprehensively reviewed.[35] The early observation[36] that OsO_4 reacted with double bonds and development of a catalytic system [OsO_4–ClO_3^-] by K.A. Hofmann[37] for *cis*-hydroxylation of alkenes were rationalised in Criegee's classic paper.[5,38] He showed that reaction of OsO_4 with alkenes *R* gave "monoesters" $OsO_2(O_2R)$(VI), later shown by us to be dimers(VII) (from X-ray studies on $Os_2O_4(O_2C_2Me_4)_2$,[39] and molecular weight and infrared studies on other "monoesters"[40]). With amines *L* (e.g. pyridine, *iso*-quinoline) Criegee showed that the OsO_4-alkene reaction was accelerated[5] and that $OsO_2(O_2R)\,L_2$ (VIII) intermediates were formed;[5,19] X-ray studies on a number of such complexes have confirmed this.[41] Reaction of *trans*-$[OsO_2(OMe)_4]^{2-}$ with glycols *cis*-$R(OH)_2$ gives *trans*-$[OsO_2(O_2R)_2]^{2-}$;[5] our Raman and infrared data on $K_2[OsO_2(O_2C_2H_4)_2]$ suggest[4] that his proposed structure(IX) is correct. Acidification of *trans*-$[OsO_2(O_2R)_2]^{2-}$ gives $OsO(O_2R)_2$, the so-called "diesters"[5,38]; his proposed square-based pyramidal structure(X) is correct as show by our X-ray studies on $OsO(O_2C_2H_4)_2$,[42] a later X-ray on $OsO(O_2C_2Me_4)_2$,[43] and by chemical and spectroscopic data on other diesters.[40] With dienes and alkynes in the presence of amines *L* species analogous to(VIII) can be obtained; we have reported Raman and infrared data on such complexes[44] and given the X-ray crystal structure of the complex derived from *cyclo*-octa-1,5-dienes, $Os_2O_4(O_4C_6H_{12})py_4.4H_2O$.[45] Reaction of OsO_4 with suitable amines gives 1:1 adducts $OsO_4.L$ (*L*=pyridine,[4,5] quinuidine *iso*quinoline, quinuclidine NC_7H_{13}[46]) and $[OsO_4]_2.L'$ (*L'*= hexamethylenetetramine $N_4C_6H_{12}$, 1,4-diazabicyclo [2,2,2] octane, $N_2C_6H_{12}$[46]; the X-ray crystal structures of $OsO_4.NC_7H_{13}$(XI) and of $[OsO_4]_2.N_4C_6H_{12}$ showed the coordination about osmium to be trigonal bipyramidal, mean Os = 1.712Å with surprisingly little distortion of the OsO_4 moiety from tetrahedral; the Os-N (axial)distances are long, 2.37Å and 2.42Å in the two complexes respectively).[47] These adducts, which show little or no vapour pressure of OsO_4 and so may be used as "portable" forms of the tetroxide, react with alkenes,[46] dienes, trienes and alkynes[29] in much the same way as OsO_4 itself. Of interest from our previous discussion on $[RuO_2Cl_3]^-$ and later work on imido complexes is the complex $[OsO_2(O_2C_6H_8)_2\,(NC_7H_{13})]_2$, made from $OsO_4.NC_7H_{13}$ and *cyclo*hexene; its crystal structure(XII) shows it to have a coplanar but asymmetric Os_2O_2 bridge (Os=O 1.73, Os-O 2.22Å) and one terminal Os=O group (1.78Å) with 153° between the two Os=O bonds.[28] Implications of some of this work for the chemistry of biological tissue staining and fixation by OsO_4 have been considered.[48]

OsO_3(NOct^t)

This was the first oxo-imido complex to be isolated together with OsO_3 (NBu^t);[10] subsequently OsO_3(NAm^t) and OsO_3 (N-adamantyl) were prepared.[49]

Sharpless *et al.* have shown that $OsO_3(NR)$ with alkenes R' to give unidentified osmium comlexes which, on hydrolysis yield 1,2-hydroxyamines $HOR'(NHR)$;[6] such reactions can be rendered catalytic by the use of such secondary oxidants as chloramine-T.[50] We present here for the first data on the nature of the osmium intermediates formed by reaction of $OsO_3(NOct^t)$ with alkenes R; of the formation of adducts of $OsO_3(NOct^t)$ with amines; of the crystal structure of one of them; and of the reaction of the adducts with alkenes.

Reaction of OsO_3 ($NOct^t$) with alkenes R

The yellow imido complex reacts with R = methylmethacrylate, methylacrylate or dimethylfumarate to give green diamagnetic materials of empirical formula $OsO_3(NOct^t).R$. They have infrared (and Raman) bands near 950cm^{-1} close to those found for $\nu(Os=O)$ in monoesters $Os_2O_4(O_2R)_4$.[40] We have also shown by a single crystal X-ray study that the complex $OsO_3(NBu^t).CH_2CMe_2$ formed from $OsO_3(NBu^t)$ and *iso*-butylene is in fact $[OsO_2(OCMe_2\ CH_2NBu^t)]_2$ (XIII, R = Bu^t),[51] the analogue of the "monoester" $Os_2O_4(O_2R)_2$ obtained from alkenes and OsO_4(VII).[42,43] The bond parameters are close to those for $Os_2O_4(O_2C_2Me_4)_2$;[42] in $[OsO_2\ (OCMe_2CH_2NBu^t)]_2$ the terminal Os=O distance is 1.67Å, occupying the axial position of a square-based pyramid, the basal plane of which is defined by the alkanolaminato ring (Os-O 1.92, Os-N 1.91Å and the bridging oxo ligands (mean Os-O 1.92Å) of a coplanar Os_2O_2 bridge.[51] The complex is dimeric in benzene. The similarity of infrared spectra of this complex with those obtained from OsO_3 ($NOct^t$) and alkenes R suggest that the latter should be formulated similarly as $[OsO_2\ (ORNOct^t)]_2$.

Reaction of OsO_3 ($NOct^t$) with Bridgehead Amines

Hentges and Sharples showed that, just OsO_4 gave adducts with bulky amines,[46] so too did OsO_4 (NBu^t) with quinuclidine, substituted quinuclidines and hexamethylenetetramine; again as with OsO_4[4,5,38] the reaction with alkenes was thereby accelerated.[52]

We find that OsO_3 ($NOct^t$) reacts with quinuclidine to give OsO_3 ($NOct^t$) $.NC_7H_{13}$ and with hexamethylenetetramine 1,4-diazabicyclo and [2,2,2] octane (L') to give $[OsO_3(NOct^t)]_2\ N_2C_6H_{12}$, the X-ray crystal structure[53] of which is shown in Fig. 1. The structure is the analogue of $[OsO_4]_2\ .\ N_4C_6H_{12}$,[47] the coordination about the osmium being trigonal bipyramidal as in(XI) with the imido and

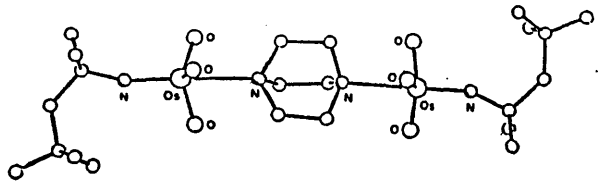

FIG 1 X-ray crystal structure of $[OsO_3(NOCt^b)]_2\ N_2C_6H_{12}$.

amine ligands taking up the axial positions as expected on steric grounds. The mean Os-O distance of 1.71Å is close to that in OsO_4 and those in OsO_4 adducts referred to above.[47] The Os-N amine distance of 2.45Å is even longer than those observed in the OsO_4 adducts. The Os-N (imide) distance of 1.73(I)Å is comparable with those found in other osmium imido complexes.[54] Molecular weight data show that the complex dissociates in benzene, presumably to OsO_3 ($NOct^t$).$N_2C_6H_{12}$ and free $OsO_3(NOct^t)$, (unlike $[OsO_4]_2$. $N_4C_6H_{12}$ which does not dissociate.[46]) The Raman and infrared spectra of OsO_3 ($NOct^t$) and of the adduct in the solid state and in solution show this clearly (Table II); as might be expected the ν (Os = O) bonds are assignable on the basis of local C_{3v} symmetry for the osmium.

Reaction of Adducts of OsO_3 ($NOct^t$) with Alkenes

Reaction of OsO_3 ($NOct^t$).NC_7H_{13} with *R*(*R* = methylmethacrylate dimethyl and dimethyl and diethylfumarates) gives green diamagnetic products of empirical formula $OsO_3(NOct^t).NC_7H_{12}.R$, while $[OsO_3(NOct^t)]_2.N_2C_6H_{12}$ and *R* (*R* = acrylo-nitrile, methylmethacrylate, methacrylic acid, methylacrylate) yields $[OsO_3$ ($NOct^t$)]$_2$. $N_2C_6H_{13}$. R_2. Though the products are microcrystalline we have not yet found a crystal suitable for a X-ray structure determination, and the solubility is too low for reliable molecular weight data. Howevere, replacement of the ν(OsN) and ν(Os = O) bands of $OsO_3(NOct^t)$ in the Raman and infrared by bands near 890 and 860cm^{-1} is reminiscent of the species $[OsO_2(O_2R).Ll_2$ (e.g. see data in Table II for $[OsO_2$ ($O_2C_6H_{10}$. $NC_7H_{13}]_2$) known from X-ray work[28] to have structure(VII). We tentatively propose an analogous structure(XIII), i.e. $[OsO_2$ ($ORNOct^t$) . $NC_7H_{13}]_2$ with an asymmetric Os_2O_2 bridge; in the case of the complex with 1,4-diazabicyclo [2,2,2] octane a polymeric structure $[OsO_2$ ($ORNOct^t)_2$ $N_2C_6O_{12}]_{2n}$ seems likely.

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REFERENCES

1. L A Fieser and M Fieser *Reagents for Organic Synthesis* Wiley London vol 1 *et seq.*
2. M Schroder and W P Griffith *J chem Soc chem Commun* (1979) 58
3. D G Lee V A Spitzer J E Cleland and M E Olson *Canad J Chem* 54 (1976) 2124
4. W P Griffith and R Rossetti *J chem Soc (Dalton Trans)* (1972) 1449
5. R Criegee and H Wannowius *Ann* 550 (1942) 89
6. D W Patrick L K Truesdale S A Biller and K B Sharpless *J org Chem* 43 (1978) 2628
7. G Green D Hollinshead W P Griffith and S V Ley *J chem Soc Perkin Trans* 1 (1981) 691
8. W P Griffith and D Pawson *J chem Soc Dalton Trans* (1973) 1315
9. A C Dengel and W P Griffith *Trans Met Chem (Weinheim)* 10 (1984) 98

10. N A Milas and N I Illopulos *J Am chem Soc* 81 (1959) 6089
11. W P Griffith *J chem Soc (A)* (1969) 1663
12. F Gonzales-Vilchez and W P Griffith *J chem Soc Dalton Trans* (1972) 1416
13. D G Lee D T Hall and J H McCleland *Canad J Chem* 50 (1972) 3741
14. E J Corey R L Danheiser S Chandrasekhar G E Kech B Gopalan S D Larsen P Siret and J-L Gras *J Am chem Soc* 100 (1978) 8034
15. C D Burke and J F Healy *J chem Soc Dalton Trans* (1982) 1091
16. D Hollinshead *private commun*
17. D G Lee S Helliwell and V S Chong *J org Chem* 41 (1976) 3646
18. Y Nakano and T A Foglia *J Am Oil Chem Soc* 59 (1982) 163
19. E E Mercer and S M Meyer *J inorg nucl Chem* 34 (1972) 777
20. S Anderson S Coote and W P Griffith *unpublished observations*
21. G I Rozovskii Z A Poshkute A Y Prokopchik and P K Norkus *Russ J inorg Chem* 18 (1973) 1432
22. J C Sheehan and R W Tulis *J org Chem* 39 (1974) 2264
23. G Nowogrocki F Abrahams J Trehouz and D Thomas *Acta Cryst* 332 (1976) 2413
24. I R Beattie H E Blayden R A Crocombe P C Jones and R S Ogden *J Raman Spectr* 4 (1976) 313
25. H R Claassen and J L Huston *J chem Phys* 55 (1971) 1505
26. W P Griffith *J chem Soc (A)* (1969) 211
27. A M H Galas M B Hursthouse E J Behrman W R Midden G Green and W P Griffith *Trans Met Chem* 6 (1981) 194
28. B A Cartwright W P Griffith M Schroder and A C Skapski *J chem Soc chem Commun* (1973) 853
29. M Schroder A J Nielson and W P Griffith *J chem Soc Dalton Trans* (1979) 1607
30. D M Hollinshead S C Howell S V Ley M Mahon R M Ratcliffe and P A Worthington *J chem Soc Perkin Trans I* (1983) 1579
31. M O Silverman and H A Levy *J Am chem Soc* 76 (1954) 3317
32. D G Lee S V Chang and S Helliwell *J org chem* 41 (1976) 3646
33. R J Audiette J W Quail and P J Smith *Tetrahedran Lett* 279 (1971); *idem J chem Soc chem Commun* 38 (1972)
34. Y Tsuda and S Nakajima *Chem Lett (Tokyo)* (1978) 397
35. M Schroder *Chem Revs* 80 (1980) 187
36. F C Phillips *Z anorg Chem* 6 (1984) 229
37. K A Hofmann O Ehrhar and O Schneider *Ber* 46 (1913) 1657
38. R Criegee *Ann* 522 (1936) 75
39. W P Griffith R J Collin F L Phillips and A C Skapski *Biochim Biophys Acta* 320 (1973) 745
40. R J Collin J Jones and W P Griffith *J chem Soc Dalton Trans* (1974) 1094
41. T J Kistenmacher L J Marzilli and M Rossi *Bioinorg Chem* 6 (1976) 347 and refs therein
42. W P Griffith R J Collin F L Phillips and A C Skapski *Biochim Biophys Acta* 354 (1974) 152
43. L O Atovmyan and Y A Sokolova *J struct chem USSR* 20 (1979) 642
44. M Schroder and W P Griffith *J chem Soc Dalton Trans* (1978) 1599
45. B A Cartwright M Schroder A C Skapski and W P Griffith *Inorg Chim Acta* 53 (1981) 129
46. M J Cleare P C Hydes W P Griffith and M J Wright *J chem Soc Dalton Trans* (1977) 941
47. W P Griffith A C Skapski K A Woode and M J Wright *Inorg Chim Acta* 31 (1978) L 413
48. W P Griffith and A J Nielson *J chem Soc Dalton Trans* (1979) 1048; W P Griffith and R J Collin *J Histochem Cytochem* 22 (1974) 992

49. A O Chong K Oshima and K B Sharpless *J Am chem Soc* 99 (1977) 3420
50. E Herranz and K B Sharpless *J org Chem* 41 (1976) 177; *idem* 43 (1978) 2544
51. W P Griffith A J Neilson N T McManus and A C Skapski *Inorg Chim Acta* 103 (1985) L 5; W P Griffith N McManus and A D White *J chem Soc Dalton Trans In press*
52. S G Hentges and K B Sharpless *J org Chem* 45 (1980) 2257
53. W P Griffith N T McManus A C Skapski and A D White *Inorg Chim Acta In press*
54. W A Nugent R C Harlow and R J McKinney *J Am chem Soc* 101 (1979) 7265

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Preliminary communication

APPLICATION OF ULTRASOUND TO THE PREPARATION OF TRICARBONYLIRON DIENE COMPLEXES

STEVEN V. LEY*, CAROLINE M.R. LOW and ANDREW D. WHITE
Department of Chemistry, Imperial College, London SW7 2AY (Great Britain)
(Received November 25th, 1985)

Summary

The reaction of nonacarbonyldiiron with 1,3-conjugated dienes is promoted by ultrasound and has been shown to give high yields of the corresponding η^4-(diene)tricarbonyliron complexes. In addition, 3-chloro-2-chloromethylprop-1-ene reacts with nonacarbonyldiiron in the presence of ultrasound to give a quantitative yield of the trimethylenemethanetricarbonyliron complex.

Recent investigations into the properties of η^4-(diene)tricarbonyliron complexes have begun to demonstrate their potential for use as synthetic intermediates [1]. Their interesting chemistry and the number of methods available for ready removal of the tricarbonyliron moiety [2, 3] has led to their exploitation as both protecting and stabilising groups for conjugated dienes. However, the major stumbling block to their general acceptance lies in the problems encountered in their preparation.

The sensitivity of both products and starting materials to aerial oxidation dictates that reactions must be carried out under inert atmospheres. Many examples of the reaction of dienes with carbonyliron species under the influence of heat or ultraviolet radiation have been published [2, 4]. The most commonly employed procedure involves heating the diene with pentacarbonyliron in a high boiling inert solvent, such as di-n-butyl ether, for long periods of time. Sensitivity of the product to peroxides present in these solvents often requires that the solvent be filtered through basic alumina immediately prior to use. However, despite all these precautions, yields of the diene complexes are seldom better than low to moderate [5] which therefore constitutes a major barrier to their general acceptance as synthetic intermediates. This is especially true where the demands of modern organic synthesis impose extremely high competitive standards. Similarly, the chemistry of trimethylenemethanetricar-

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bonyliron complexes remains unexplored despite the elegant use that Trost et al. [6] have made of the analogous palladium complexes.

Here we report a convenient high yielding method for the synthesis of both trimethylenemethanetricarbonyliron and a variety of η^4-(diene)tricarbonyliron complexes as a result of the exposure of a mixture of the substrate and nona-

SCHEME 1

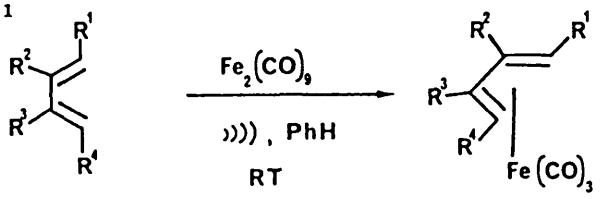

TABLE 1

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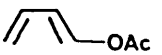
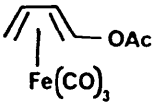
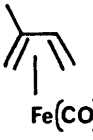
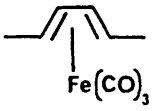
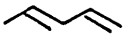
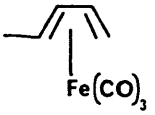
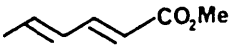
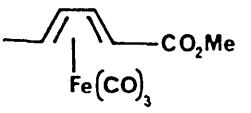
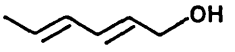
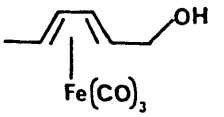
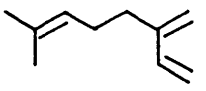
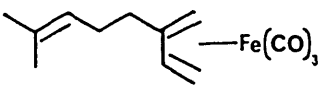
		100 %
		70 %
		50 %
		62 %
		100 %
		51%
		95%

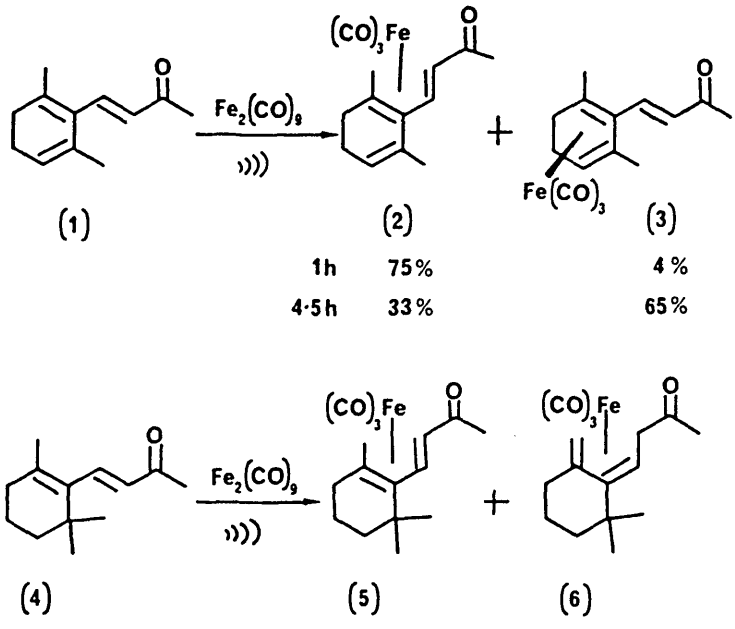
carbonyldiiron to ultrasound (Scheme 1)*. This method has also previously found application in the preparation of ferrilactone complexes from vinyl epoxides [7].

Preparation of η^4-(diene)tricarbonlyliron complexes

Nonacarbonyldiiron (1.1 eq) was added to a solution of the relevant diene (see Table 1) in benzene and the mixture sonolysed for 1 h, or until all the solid carbonyl had disappeared. Concentration of the reaction mixture and column chromatography of the residue on silica (40/60° petroleum ether/diethyl ether gradient) separated the required complex from any inorganic species. Yields in these reactions were essentially quantitative and limited solely by the volatility of the product.

The method was applied to a variety of dienes and the yields were consistently higher than previous literature preparations despite the fact that no attempt was made at optimisation.

The reaction with pseudionone (1) is of interest in that after 1 h it was possible to isolate a 75% yield of the kinetic product 2 which, on further exposure to ultrasound, isomerised to give a 1/2 ratio of the kinetic 2 and thermodynamic products 3, Scheme 2. Storing the 3,5-diene complex 2 overnight at −20°C resulted in almost complete conversion to the 5,9-diene complex 3. Hence, variation of the reaction time allows access to good yields of both isomers selectively. This was not possible by other conventional methods. The reaction of β-ionone (4) with $Fe_2(CO)_9$ gave a 4/1 mixture of the *endo* to



SCHEME 2

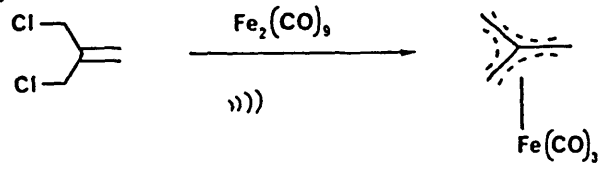
* In our previous paper ref. 7a we incorrectly reported that dienes failed to react with $Fe_2(CO)_9$ under ultrasonic conditions.
All sonolysis reactions were carried out in a Semat 80W 50KHz ultrasonic bath.

exo diene complexes 5 and 6 (Scheme 3) in contrast to Cais and Maoz [8] who obtained a 3/1 ratio in favour of the *exo* isomer 6 via the thermal reaction of β-ionone with $Fe(CO)_5$. However, it should also be noted that the combined overall yield of this reaction was only 21%.

Preparation of trimethylenemethanetricarbonyliron

Equimolar amounts of nonacarbonyldiiron and 3-chloro-2-chloromethyl-prop-1-ene (7) were sonolysed together in 30/40° petroleum ether for 1 h. Careful concentration of the solution and Kugelrohr distillation of the residue gave a remarkable 90% yield of the desired product 8 (Scheme 3). The previous best recorded yield was a meagre 30% described by Emerson et al. [9].

SCHEME 3



(7) (8)

In conclusion, having demonstrated the ease with which high yields of these complexes can now be obtained, we hope that this will promote increased use of such species as synthetic intermediates.

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References

1 For examples see: (a) D.H.R. Barton, A.A.L. Gunatilaka, T. Nakanishi, H. Patin, D.A. Widdowson and B.R. Worth, J. Chem. Soc., Perkin Trans. I, (1976) 821; (b) M. Franck-Neumann, F. Brion and D. Martina, Tetrahedron Lett., (1978) 5033; (c) A.J. Pearson and D.C. Rees, ibid., (1980) 3937.
2 For a general review see: (a) S.G. Davies, Organotransition Metal Chemistry: Applications to Organic Synthesis, 1982, Pergamon Press; (b) A.J. Pearson, Metallo-organic chemistry, 1985, John Wiley and Sons, Chapter 8.
3 J.M. Kern, D. Martina and M.P. Heitz, Tetrahedron Lett., 26 (1985) 737.
4 R. Pettit and G.F. Emerson, Adv. Organomet. Chem., 1 (1964) 1.
5 A.J. Deeming, in G. Wilkinson, F.G.A. Stone and E.W. Abel (Eds.) Comprehensive organometallic chemistry, Pergamon Press, Vol. 4, 1982, p. 377.
6 B.M. Trost and D.M.T. Chan, J. Am. Chem. Soc., 101 (1979) 6429 and 6432; 102 (1980) 6359.
7 (a) A.M. Horton, D.M. Hollinshead and S.V. Ley, Tetrahedron 40 (1984) 1737; (b) A.M. Horton and S.V. Ley, J. Organomet. Chem., 285 (1985) C17.
8 M. Cais, and N. Maoz, J. Organomet. Chem., 5 (1966) 370.
9 G.F. Emerson, K. Ehrlich, W.P. Giering and P.C. Lautebar, J. Am. Chem. Soc., 88 (1966) 3172.

Preparation and Use of Tetra-n-butylammonium Per-ruthenate (TBAP reagent) and Tetra-n-propylammonium Per-ruthenate (TPAP reagent)† as New Catalytic Oxidants for Alcohols

William P. Griffith, Steven V. Ley, Gwynne P. Whitcombe, and Andrew D. White

Department of Chemistry, Imperial College, London SW7 2AY, U.K.

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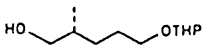
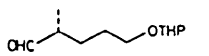
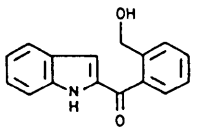
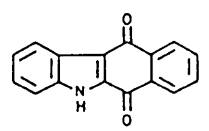
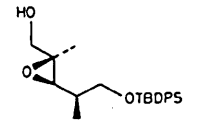
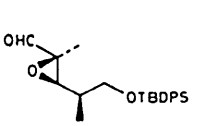
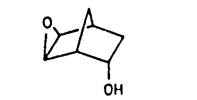
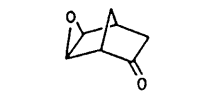
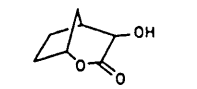
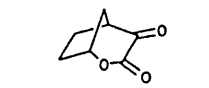
One of the most common transformations in organic synthesis is the oxidation of the hydroxy group and although certain procedures remain popular there is a constant need to develop new systems. Swern oxidants[1] are excellent but there are problems with obnoxious side products and difficulties of large-scale operation. Likewise the chromium oxidants[2,3] can cause problems during work-up of the products and disposal of the toxic residues. Catalytic alternatives to these well tried methods are therefore attractive, but must demonstrate clear advantages over these systems, be reliable and easy to use, and be applicable to a wide range of substrates.

Our previously reported ruthenium based oxidation catalyst, $[RuO_4]^{2-}/(S_2O_8)^{2-}$, functioned only in strong aqueous base and was therefore unsuitable for a number of oxidations.[4]

We report here the new catalytic oxidants tetra-n-butylammonium per-ruthenate (TBAP) and tetra-n-propyl ammonium per-ruthenate (TPAP) using *N*-methyl morpholine *N*-oxide (NMO) as co-oxidant. We have earlier reported the use of TBAP as a stoicheiometric oxidant.[5] These reagents function in organic solvents, are easy to prepare, and are selective. TBAP was obtained by dissolution of $K[RuO_4]$[6] (2.0 g, 9.8 mmol) in water (200 cm^3) at 5—10 °C followed by immediate addition of tetra-n-butylammonium hydroxide (50 cm^3 of a 40% aqueous solution). The resulting green precipitate of TBAP (3.61 g, 91%) must be filtered rapidly, washed with cold water (3 × 10 cm^3), and dried *in vacuo*. TPAP was more conveniently prepared. Hydrated ruthenium trichloride (1.5 g, 6.2 mmol) and sodium periodate (5.5 g, 0.026 mol) were stirred overnight in water (50 cm^3). The RuO_4 formed was transferred in an oxygen atmosphere into a solution of tetra-n-propylammonium hydroxide (5 cm^3 of 1 M aqueous solution), 10 cm^3 of water and 1 M sodium hydroxide

† Systematic names tetra-n-butylammonium tetra-oxoruthenate(VII) and tetra-n-propylammonium tetra-oxoruthenate(VII).

Table 1. Oxidation of alcohols using TBAP and TPAP.

Alcohol	Product	TBAP % Yield	TBAP t/h	TPAP % Yield	TPAP t/h
n-Butanol	n-Butanal	94[c]	0.8	95[c]	1
Undec-10-en-1-ol	Undec-10-en-1-al	70[a]	3		
Citronellol	Citronellal	75[a]	5		
E-Cinnamyl alcohol	*E*-Cinnamaldehyde	91[a]	3	75[a]	5
Chrysanthemyl alcohol	Chrysanthemaldehyde	90[a]	5	76[a]	0.5
Benzyl alcohol	Benzaldehyde	80[b]	2	71[a]	0.5
o-Chlorobenzyl alcohol	*o*-Chlorobenzaldehyde	81[b]	4		
4-Methoxybenzyl alcohol	4-Methoxybenzaldehyde			68[a]	12
3,4-Dimethoxybenzyl alcohol	3,4-Dimethoxybenzaldehyde	98[b]	1.5		
Piperonyl alcohol	Piperonaldehyde	89[b]	3	70[a]	1
Cyclobutanol	Cyclobutanone	95[c]	1.1		
(±)-Menthol	(±)-Menthone	85[a]	1.0		
endo-Norborneol	Bicyclo[2.2.1]heptan-2-one	73[a]	0.3		
5α-Androstan-17β-ol-3-one	5α-Androstan-3,17-dione	96[a]	6	99[a]	1.5
Lanost-8-en-3β-ol	Lanost-8-en-3-one	86[a]	6	81[a]	1.5
		71[a]	0.7		
		85[a]	5		
				70[a]	1
		73[a]	0.5		
		80[a]	1.5		

[a] Isolated yield. [b] 2,4-Dinitrophenylhydrazone derivative. [c] G.l.c. yield.

(40 cm³) at 0—5 °C. The green product (1.53 g, 87%) was removed by filtration every 20 min, washed with ice-cold water (2 × 2 cm³), and dried *in vacuo*.

In the oxidation experiments (Table 1) primary alcohols give aldehydes and secondary alcohols afford ketones, while labile functional groups such as epoxides, tetrahydropyranyl ethers, silyl ethers, esters, double bonds, indoles *etc.* remain intact. Importantly, oxidation of alcohols containing adjacent chiral centres gives products without any detectable racemisation. Typically the oxidations proceed rapidly (0.2—6 h) at room temperature in dichloromethane using less than 0.5 mole % of catalyst. We also find that addition of 4 Å molecular sieves to be beneficial since they remove both the water formed during reaction, and the water of crystallisation of the NMO.

Although we have not tested the ultimate limits of turnover and scale of reaction, these oxidations can be performed on a reasonable scale without any noticeable problems. Thus 4-methoxybenzyl alcohol (26.6 g, 0.19 mol) and piperonyl alcohol (10 g, 0.066 mol) are catalytically oxidised by TPAP to the corresponding aldehyde in 12 h, with 70 and 68% yields respectively, corresponding to catalytic turnovers of 215 and 210. During the oxidations on a >5 g scale it was useful to pre-dry the NMO by first treating the dichloromethane solution with anhydrous $MgSO_4$.

In a typical oxidation experiment the alcohol (0.5 mmol) was dissolved in CH_2Cl_2 (5 cm³) containing both the 4 Å sieves and NMO (0.1 g, 0.75 mmol). After stirring the mixture for 10 min, TBAP (or TPAP, 0.025 mmol) was added and the reaction followed by t.l.c. until complete. The initial green mixture darkened as the reaction proceeded. When complete, the mixture was diluted with CH_2Cl_2 (50 cm³) and then washed with sodium sulphite solution (10 cm³), brine (10 cm³) and finally saturated copper(II) sulphate solution (10 cm³). The organic layer was dried ($MgSO_4$), filtered, and worked up in the usual way to give the product.

Although in most of the experiments we have reported the use of TBAP, the convenience of preparation of TPAP makes this the superior reagent which we would recommend for future applications.

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References

1 A. J. Mancuso and D. Swern, *Synthesis*, 1981, 165.
2 M. D'Auria, G. Piancatelli, and A. Scettri, *Synthesis*, 1982, 245.
3 E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, 1979, **20**, 399; 1980, **21**, 731.
4 W. P. Griffith and M. Schröder, *J. Chem. Soc., Chem. Commun.*, 1979, 58; G. Green, W. P. Griffith, D. M. Hollinshead, S. V. Ley, and M. Schröder, *J. Chem. Soc., Perkin Trans. 1*, 1984, 681.
5 A. C. Dengel, W. P. Griffith, and R. A. Hudson, *Transition Metal Chem.*, 1985, **10**, 98.
6 M. D. Silverman and H. A. Levy, *J. Am. Chem. Soc.*, 1954, **76**, 3317.