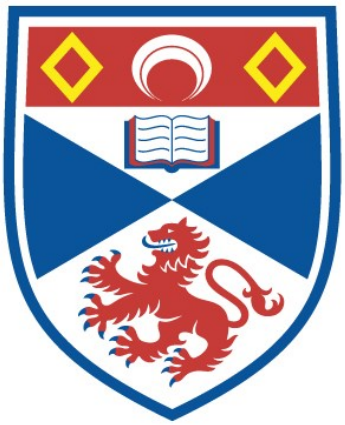
RHODIUM CATALYSED HYDROCARBONYLATION REACTIONS

Michael Charles Simpson

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



1995

RHODIUM CATALYSED HYDROCARBONYLATION REACTIONS

a thesis presented by

Michael Charles Simpson

to the

UNIVERSITY OF ST. ANDREWS

in application for

THE DEGREE OF DOCTOR OF PHILOSOPHY

ST. ANDREWS October 1994

DECLARATION

I, Michael Charles Simpson, hereby certify that this thesis has been composed by myself, that it is a record of my own work, and it has not been accepted in partial or complete fulfilment of any other degree or professional qualification.

Signed... :.....Date.....4/10/94.....

I was admitted to the Faculty of the University of St. Andrews under Ordinance General No.12 on .1st October 1990..and as a candidate for the degree of Ph.D. on.1st October 1991.....

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I hereby certify that the candidate has fulfilled the conditions of resolution and regulations appropriate to the degree of Ph.D.

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"It was the best of times, it was the worst of times,
it was an age of wisdom, it was an age of foolishness,
it was the epoch of belief, it was the epoch of incredulity,
it was the season of Light, it was the season of Darkness,
we had everything before us, we had nothing before us."

Charles Dickens - 'A Tale of Two Cities'.

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I must thank my family for sticking with me for most of my education while I 'avoided the real world' as they put it. I sincerely hope my Mother and Fathers 'new' lives apart are happy ones.

Lastly, a big hug and thank you to my girl-friend Heather Ann Thompson for her loving understanding during the last year, not the easiest one I have gone through.

Abbreviations Used in this Thesis

atm/s.	atmosphere/s
^{n}Bu	n-butyl
Et	ethyl
^{n}Pr	n-propyl
^{n}Oc	n-octyl
cy	cyclohexyl
acac	acetylacetonate
hr/s.	hour/s
Cp	cyclopentadiene
COD	cyclooctadiene
OAc	ethanoate
NBD	norbornadiene
Diphos	1,2-bis(diphenylphosphino)ethane
DIOP	2,3-O-isopropyllidene-2,3-dihydroxy-1,4-bisdiphenylphosphino)butane
Pe	pentyl
Ph	phenyl
hυ	irradiation
Cp*	pentamethylcyclopentadiene
i.r.	infra-red
nmr	nuclear magnetic resonance
glc	gas liquid chromatography
GCMS	gas chromatography - mass spectroscopy
b.p.	boiling point
r.t.	room temperature
^{i}Pr	isopropyl

Abstract

The one step hydrohydroxymethylation which can be used to transform C_n alkenes into $C_{(n+1)}$ alcohols has been explored for functionalised alkenes. The catalyst system used for this study was generated *in situ* from $[Rh_2(OAc)_4]$, PEt_3, CO/H_2 and ethanol.

The main alkene investigated was 2-propen-1-ol, because of the potential to produce 1,4-butanediol by a novel route, which it indeed does in reasonable yield. Of interest the branched chain product was not the expected 2-methyl-1,3-propanediol, but 2-methylpropan-1-ol. 1,4-butanediol and 2-methylpropan-1-ol make up the majority of the final products, no aldehydic intermediates from the possible hydroformylation reaction were detected.

A mechanism is proposed for the formation of 2-methylpropan-1-ol, the key steps of which are; protonation of a metal acyl species (on the acyl oxygen) to form a metal hydroxycarbene intermediate, dehydration of the hydroxycarbene species (conjugation being the driving force for this step), oxidative addition of hydrogen to the metal centre, a single hydrogen atom transfer to the carbene carbon, a σ-π allylic rearrangement of the substrate based ligand, followed by reductive elimination of a vinyl alcohol. This rapidly rearranges to 2-methylpropanal, which is hydrogenated by this system to give 2-methylpropan-1-ol.

The mechanism was studied using 'black box' studies, recently developed deuterium labelling techniques (in one experiment 18 different isotopomers were formed, this technique could quantify them all) and some model studies.

The effect on product distribution was examined by systematic variation of the reaction conditions and ligands.

The reaction was expanded to other substrates such as propenyl halide, propenyl ethers, propenyl cyanide and ketones. Propenyl ethers gave similar reaction products to 2-propen-1-ol, whilst propenyl halides gave esters and ethers.

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Chapter 1 - Rhodium trialkylphosphine complexes in homogeneous catalysis

1.1 Introduction

A enormous amount of chemistry has been performed on homogeneous rhodium triarylphosphine systems. But comparatively little has been done on analogous trialkylphosphine systems. This is due to the ease of handling triarylphosphines in comparison to trialkylphosphines. For example PPh_3 is an air stable solid, whereas PMe_3 is flammable, smelly, pyrophoric and easily oxidised. Modern handling techniques are now making the manipulation of these compounds commonplace, so their chemistry is becoming more accessible.

Trialkylphosphines have some interesting properties, such as steric bulk. Short chain alkyl groups on the phosphine can exert considerably less steric demands than any triarylphosphine. Another property of trialkylphosphines is their basicity, so they can modify the electronic properties of a metal centre, such as rhodium, that they are formally bonded to.

These properties make trialkylphosphine ligands of considerable interest in their application to homogeneous rhodium catalytic systems.

For the purposes of the review, trialkylphosphine is defined as a monodentate phosphine, containing three purely alkyl groups (including cycloalkyl groups). Occasional mentions of diphosphines, triarylphosphines and phosphites are included for comparison purposes.

The review is split into six sub-sections; hydroformylation, hydrogenation, hydrogen transfer, other addition reactions, photochemistry and other reactions.

1.2 Hydroformylation

Formally, hydroformylation is the addition of a hydrogen atom and a formyl group to a carbon-carbon double bond. Cobalt compounds have been known as homogeneous hydroformylation catalysts since the 1930's, but rhodium compounds have only been exploited since the late 1950's.

Normally two aldehydes are formed. Addition of the formyl group to the terminal carbon atom gives a straight chain product, whereas addition of the formyl group to the internal carbon atom gives a branched chain

product. It is useful to quote the selectivity of these products, when hydroformylating terminal alkenes, as a ratio in the form of straight: branched chain products or n:i ratio as it commonly termed. Straight chain products tend to be more commercially valuable, so a high n:i ratio is often desired.

Much is known about the use of triarylphosphines in this area, but less is known about trialkylphosphines used in conjunction with rhodium compounds.

1.2.1 Straight Chain Alkenes

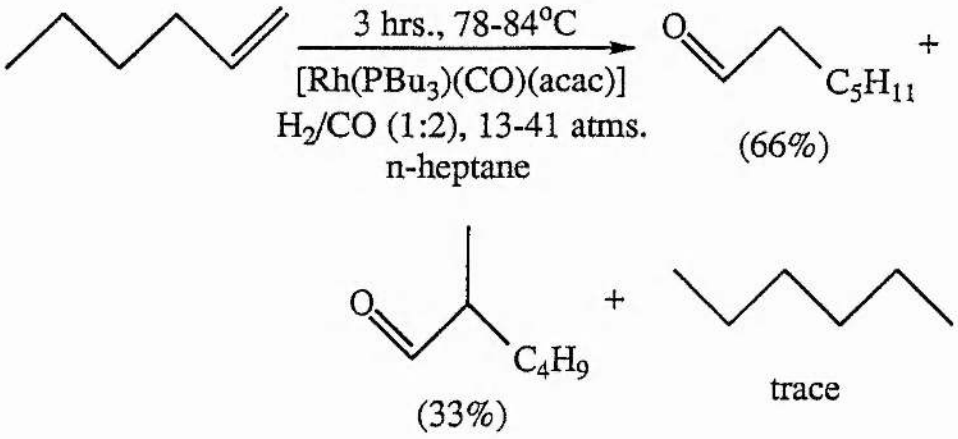
Early research into hydroformylation reactions catalysed by rhodium complexes tended to centre on straight chain alkenes of chain length C_{5-6}, presumably because of the ease of handling, as they are liquids at room temperature.

One of the first mentions of trialkylphosphines in a rhodium catalysed homogeneous system was as early as 1963, in a patent by Slaugh (Shell International)[1]. She took tributylphosphine, rhodium chloride, sodium acetate and ethanol and hydroformylated 1-pentene to ethyl hexanoate and various branched chain isomers. This was achieved at 92 atms. CO/H_2 (1:1) at 195°C for 3.5 hours. Presumably the ester is formed from a Reppe attack of ethanol onto the metal acyl species.

In a subsequent addition to the patent, more data was published[2]. After just 2.5 hours, 80% conversion had been achieved. The product distribution being C_6 aldehydes (93%), C_6 alcohols (5.4%). The normal to branched chain ratio being 2.5:1. On analysing the reaction after 12 hours, the product distribution had changed to C_6 aldehydes (59.9%), C_6 alcohols (24.9%), showing the hydroformylation reaction to be quicker than the subsequent hydrogenation reaction.

Lawrenson and Foster (B.P.) centred their research on 1-hexene[3]. The catalyst of choice for them was $[Rh(CO)(PR_3)_2(A)]$ (where R tended to be ^nBu, but could also be Et, ^nPr, ^nOc or cy. A tended to be a simple carboxylate anion, e.g. O_2CCH_3 or acac).

This catalyst tended to hydroformylate (with a poorly competing hydrogenation reaction) thus;



The conversion was 86%. Using Rh: substrate ratios of 1:100-5,000 favoured the formation of alcohols, whilst ratios of 1: 50,000-5,000,000 favoured aldehyde formation.

Johnson and Lawrenson went on to show that by using alcohols as solvent the reaction rate was enhanced at lower temperatures and also favours alcohol formation. Alcoholic solvents of > C_4 were used because acetals were formed when shorter chain alcohols were used. The catalysts employed were the same as above[4].

While these reactions commonly showed n:i ratios of 2:1, the hydroformyation of propene using [RhCp(CO)(P^nBu_3)] gave only a 1:1 mixture of butanol and 2-methylpropan-1-ol[5]. A slight improvement in this ratio (> 1:1) was made using [Rh(acac)(CO)(P^nBu_3)][6]. It is desirable to produce n-butanal, which has two major commercial outlets, as n-butanol and 2-ethylhexanol. By 1976 n:i ratios of 8-16:1 were being produced on an industrial scale[7], but only using rhodium/ PPh_3 systems.

Work published in 1968 showed some data on the various product distributions of various hydroformylated octenes. When using cobalt/ trialkylphosphine sytems, starting with a single terminal or internal mono-octene, a mixture of all 4 possible isomers of C_9 aldehydes (nonanal, 2-methyloctanal, 2-ethylheptanal and 2-propylhexanal) was formed. But using rhodium/ trialkylphosphine systems, only two isomers (nonanal and 2-methyloctanal) were formed for oct-1-ene (the n:i rátio was 1.5:1). In the same paper it was shown that 2-butene hydroformylates to give 2-methylbutanal in the presence of excess phosphine, but isomerises rapidly without the excess phosphine present. The authors

suggest that a phosphine ligand must be lost from the catalyst to allow isomerisation to occur. Therefore excess phosphine hinders this process[8].

Also in 1968 Pruett and Smith hydroformylated 1-octene over Rh/C 5% (simply as a source of rhodium), in the presence of P^nBu_3 and attained a n:i ratio of 2.5:1[9,10].

B.P. were not the only company attempting to hydroformylate propene. In 1975 Exxon patented the use of $[(P^nBu_3)_3Rh]_2$; the n:i ratio being described as "high" (probably ~2:1)[11]. In 1977 Tanaka (Mitsui Petrochemicals) patented a 1,5-cyclooctadiene/imidazole/rhodium trimer modified with phosphines or amines. Triethylphosphine was one of the preferred phosphines. The n:i ratio reported for propene hydroformylation was 2.5:1 and 90% conversion was attained after 2.5 hours at 64-6°C. Other simple substrates (e.g. 1-hexene) were also hydroformylated by Tanaka's system[12].

The first hydride catalyst precursor was patented in 1980 by Hughes (Celanese Corporation), this utilised $[Rh(CO)(H)(P^iOc_3)_3]$ along with some analogous triarylphosphine compounds. With 1-hexene as substrate, the best results were reported when a large excess of free phosphine was present in the system[13].

Franks and Hartley studied long chain alkyl phosphines and their effect on yield and isomerisation for a given system. The rhodium compound used was $[RhCl(CO)L_2]$ (L=P^nBu_3, P^nOc_3 or $P^n(C_{16}H_{33})_3$) and the trends found were the longer the chain length, the lower the yield but proportionately more isomerisation occurred[14].

A study was carried out on 1,3-butadiene using Rh_2O_3 modified with various phosphines [PMe_3, PEt_3, P^nOc_3, P^iPr_3, P^tBu_3 and $P(c\text{-}C_3H_5)_3$], the reaction conditions were fairly severe (200 atms.; CO/H_2,1:1, 130°C), but selectivities were reasonable (in the monoaldehyde n/i > 10. In the dialdehyde ratio n,n:n,i tended to be in the order of 1:2-5), the yields are between 43-77%. It was found that P^iPr_3 gave a slightly faster rate and better selectivity than PPh_3[15].

In most of the above examples trialkylphosphines come out second best to triarylphosphine ligands (e.g. PPh_3), although they were comparable in a few.

Recently a report[16] by Cole-Hamilton and MacDougall (1990) and a patent[17] co-authored with Green (B.P., 1991) suggested that $C_{(n+1)}$ alcohols, exclusively, could be made directly from alkenes using H_2 and CO over a rhodium/ tri-n-alkylphosphine catalyst in ethanol as solvent/

reagent. The same reaction in THF produces aldehydes after short reaction times but longer reaction times again lead to alcohols as products. Using branched trialkylphosphines in ethanol, causes the production of acetals. The catalysts could be preformed such as $RhH(PEt_3)_3$ or *in situ* generated, e.g. $Rh_2(OAc)_4$ with free PEt_3. The n:i ratio obtained for these systems were ~2:1.

Alternatively Okano has shown that gaseous H_2 and CO can be replaced by paraformaldehyde in hydroformylation reactions, trialkylphosphine complexes such as $[RhH_2(O_2COH)(P^iPr_3)_2]$ were especially active for 1-hexene hydroformylation.

$+(CH_2O)_n$

$[RhH_2(O_2COH)(P^iPr_3)_2]$

120°C, 20 hrs., THF

$C_6H_{13}CHO + C_6H_{13}CH_2OH$

(67%) (4%)

$+C_6H_{13}CO_2CH_3 + C_6H_{14}$

(13%) (3%)

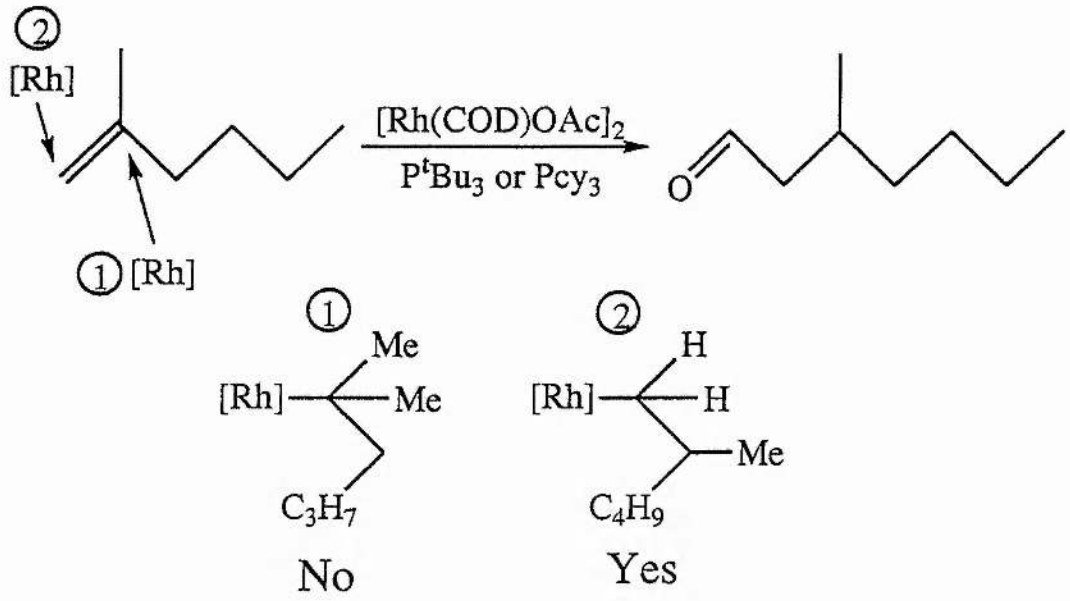
The overall conversion in the above reaction was 100%. However, when using PPh_3 derived catalysts the yield was virtually 0%. A rise in temperature in the above reaction to 150°C caused an increase in formation of alcohols and esters, at the expense of aldehydes. When using $C_6H_{13}CHO$ as substrate, instead of hex-1-ene, then alcohols and esters were again formed. This suggests that at least one pathway to making alcohols and esters involves the disproportionation of the aldehyde initially formed[18]. In a subsequent paper Okano added complexes such as $[RhH(N_2)L_2]$ ($L=P^tBu_3$, P^iPr_3), $[Rh_2H_2(\mu\text{-}N_2)(Pcy_3)_4]$, $[RhHL_3]$ ($L=P^iPr_3$, PEt_3), as active catalysts in hydroformylation using paraformaldehyde [19].

Okano's compounds were the first examples of trialkylphosphines proving superior to triarylphosphines in rhodium based hydroformylation reactions.

1.2.2 Hindered and Internal Alkenes

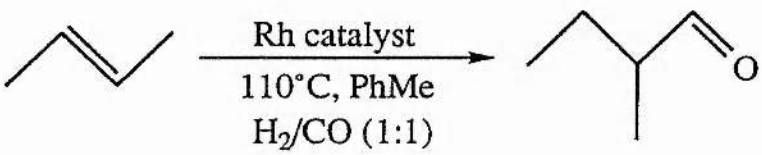
Using the catalyst precursor $[Rh(COD)OAc]_2$ modified with P^tBu_3 or Pcy_3, Roobeek and van Leeuwen (Shell, 1983) showed that it was possible to hydroformylate cyclohexene. These reactions were carried out at low pressures (10-20 atms.) and reasonable temperatures (70-

90°C). Due to the symmetry of the substrate only one product, cyclohexanal was formed. When using either of the two aforementioned phosphines the rates were similar to that obtained with PPh_3, but sluggish compared to those with bulky triarylphosphites. The selectivity is also near to 100% in 2-methylhex-1-ene, the straight chain isomer being preferred, due to steric factors not allowing the formation of the branched isomer. This is shown schematically below[20].

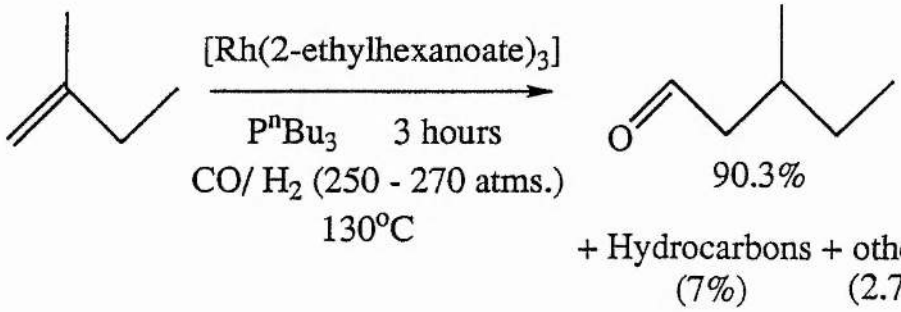


Young (Exxon, 1987) patented the hydroformylation of α-substituted α-alkenes. For example using $[Rh(acac)(CO)_2]$ and highly hindered tricycloalkylphosphines (ring size 3-14 C atoms), aldehydes and alcohols could be made in ~21% yield. This was compared to 0.3% when using PPh_3[21].

At about the same time Tau (Calenese Corp.) patented the hydroformylation of 2-butene. Rhodium/hydride/carbonyl/phosphine compounds were used. The phosphines containing the same three C_{3-10} (cyclo)alkyl groups and it was stipulated that the cone angle should be 159-171° . 88% conversion and 98% selectivity were achieved, 2-methylbutanal being produced in 32:1 ratio over other products[22].



Bernhagen, Weber and Springer (Rührchemie, 1982) produced a 4 step procedure to convert 2-methylbutene to 2-hydroxy-2,3-dimethylpentan-1-ol[23], a useful synthon in the pharmaceutical industry for the production of carbamates, which find applications as tranquillizers and blood pressure lowering agents. The first step of the procedure involves the hydroformylation of methylbutene, which is outlined below. The conversion quoted was 100%.

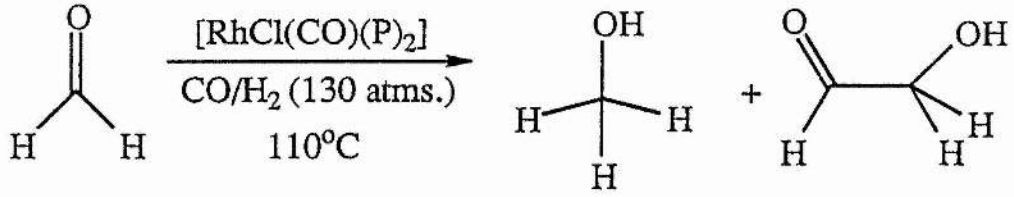


Aquila, Himmele, Fliege and Siegel (BASF, 1976) patented a process that hydroformylated 2-methylbut-1-en-4-ol using an in situ catalyst prepared from a rhodium complex and various phosphines, including P^nBu_3 and Pcy_3. Yields of 2-hydroxy-4-methyltetrahydropyran were 85-90%. The product was then reduced using a suitable hydrogenation catalyst to give 3-methylpentane-1,5-diol, which has been used in the production of polyurethanes[24].

1.2.3 1,2-Ethanediol (ethylene glycol)

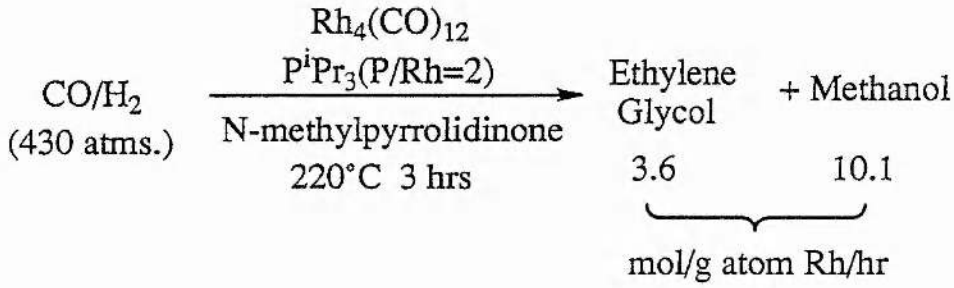
There has been considerable interest in discovering new routes to 1,2-ethanediol, especially by the homogeneous hydroformylation/ hydrogenation of carbon monoxide. 1,2-ethanediol is useful as a starting material for polyester fibres and organic solvents, or as a non-volatile antifreezing agent. As will be seen in the following references, methanol is a major by-product.

The first reported synthesis of 1,2-ethanediol using rhodium/ phosphine systems was in 1979. 2-hydroxyethanal was the final product which could be easily be hydrogenated into 1,2-ethanediol[25].



P=Pcy_3	2.5%	9%
P=P^nBu_3	4.8%	3.7%
P=PPh_3 (best)	2.3%	39.8%

In 1985 a patent was published by Wada *et al* focussing on the production of 1,2-ethanediol and methanol from CO and H_2 over Rh/ trialkylphosphine systems using a N-containing base[26]. For example,



In the above reaction the yields varied considerably, the best quoted production rates for 1,2-ethanediol were > 30 mol/ g Rh/ hour .

It was found that bulky trialkylphosphines were the most useful ligands in 1,2-ethanediol formation. Complexes containing arylphosphines, alkyl or aryl phosphites and small cone angled alkyl phosphines all decomposed to form inactive clusters, $[Rh_9P(CO)_{21}]^{2-}$ being one of the major species identified. From high pressure i.r. studies, it was proposed that $[HRh(CO)_3(phosphine)]$ was the main catalytically active species[27]. Subsequently yields were increased slightly using carboxylate ligands e.g. compounds such as $[Rh(PhCOO)(CO)(PR_3)_2]$ (R=^{i}Pr or cy) were found to be quite effective[28].

A strange effect was discovered whilst varying the pressure of the system. When the pressure was doubled from 500 to 1000 atms. the activity for P^iPr_3 and Pcy_3 systems doubled. For the system containing P^nBu_3, the enhancement was ca. twenty fold. This was investigated using high pressure i.r. and it was found that in the P^nBu_3 system rhodium carbonyl clusters, $[Rh_9P(CO)_{21}]^{2-}$ and $[Rh_6(CO)_{15}]^{2-}$, were the

predominant species at 500 atms. But at 1000 atms. two species thought to be $[HRh(CO)_4]$ and $[HRh(CO)_3(P^nBu_3)]$, were the main species present[29].

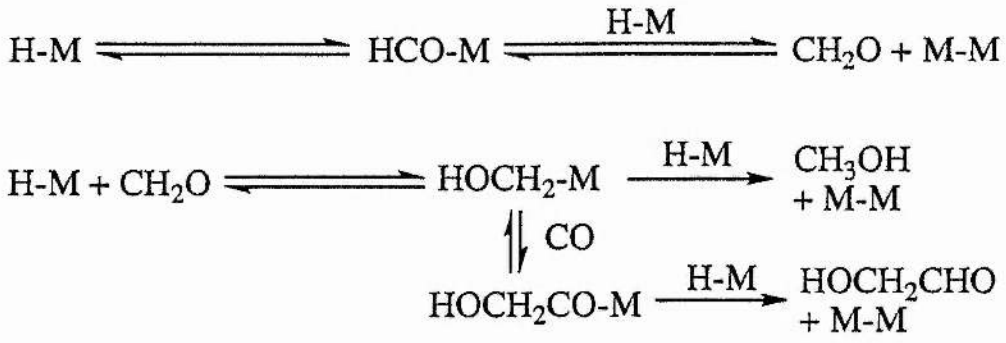
On cooling down their catalytic mixtures (originating from $[Rh(CO)_2(acac)]$ and P, P= P^iPr_3 or $P[c\text{-}C_5H_9]_3$), Wada *et al* (1987) found a strong i.r. absorption at 1959-1960 cm^{-1}. The rhodium complexes formed were isolated and found to be $[Rh(CO)_3P]_2$. These complexes could be used as the starting catalyst and the activity was unchanged. An equilibrium was thought to exist at ambient temperatures in the catalytic system. The arrowed species was suspected to be the active catalyst[30].

$$[Rh(CO)_3PR_3]_2 + H_2 \rightleftharpoons [HRh(CO)_xPR_3] + (3\text{-}x)CO$$

Earlier work on optimising the Rh/ phosphine ratio for the best yield of 1,2-ethanediol found that the ratio Rh/ phosphine = 1 was the best for bulky phosphines[31]. This seems to be in agreement with the active species containing only one PR_3 group.

Four patents brought out by H. Watanabe (1987) showed the range of supporting ligands/ co-catalyst that could be used. For instance N-oxides, phosphine oxides, 1,4-diazabutadiene derivatives, silicon compounds. Even cationic rhodium complexes can be used[32]. Y. Watanabe showed that other ligands could be successfully employed. One of his rhodium compounds contained a phenol or subtituted phenol group incorporated in the active catalyst[33]. His research group also showed that high boiling solvents with amines could give high conversions and selectivity to 1,2-ethanediol. So $[Rh(CO)(p\text{-}MeOC_6H_4O)\{P(Bu)(CMe_3)_2\}_2]$ (20 mmol) in tetraglyme (30 cm^3) and N-octylpyrrolidine (20 cm^3) at 215°C for 10 minutes would give 1,2-ethanediol (56.9 mmol) and methanol (9.5 mmol) from H_2/CO. The low boiling products could be distilled off, and the system would run again without any loss in activity[34].

A mechanistic study, published by Ishino et al (Sumitumo Chemicals, 1992), concluded that the following mechanism was in operation;



H-M= $HRh(CO)_3L$ or $HRh(CO)_4$

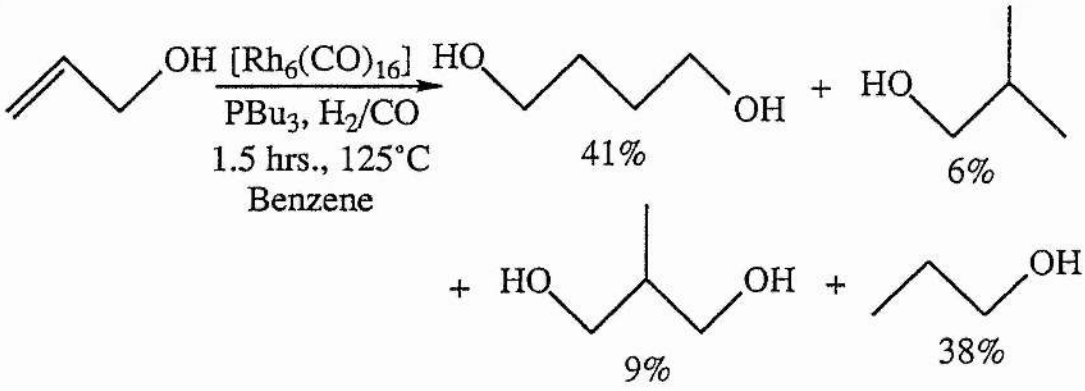
Formaldehyde formation is the rate determining step in the above scheme. The reductive eliminations all resulted in binuclear metal products, from which the momonuclear species could be regenerated as shown below;

$$[Rh_2(CO)_6L_2] \xrightleftharpoons{H_2} [2HRh(CO)_3L]$$

Based on these studies it can be seen that bulky trialkylphosphine ligands effectively stabilise the rhodium hydride mononuclear species. Phosphine ligands also facilitate CO insertion into the M-H bond[35].

1.2.4 Hydroformylation of 2-propen-1-ol: a route to 1,4-butanediol

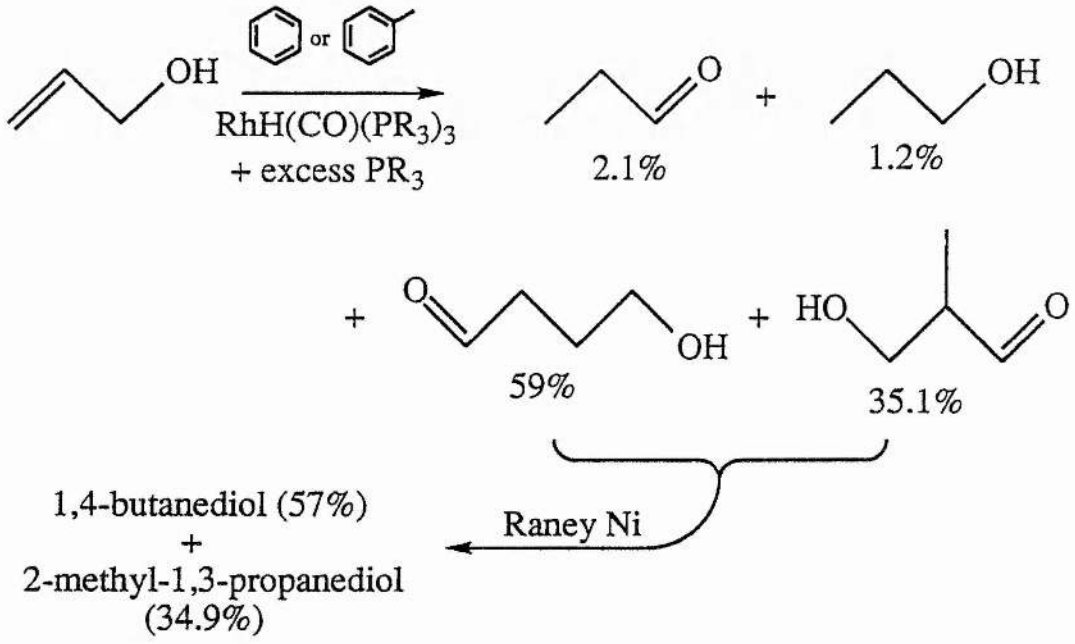
1,4-Butanediol is another important industrial chemical and many studies have been carried out based on hydroformylating 2-propen-1-ol. Smith (General Electric Co.) patented the use of rhodium carbonyl complexes with a wide variety of phosphines[36]. The phosphines that gave the best results were trialkylphosphines. The product distribution was as follows;



At the same time Fell and Barl brought out a paper on (un)substituted 2-propen-1-ol hydroformylation. 2-propen-1-ol was hydroformylated (followed by hydrogenation) to 1,4-butanediol and 2-methyl-1,3-propanediol , using a similar catalyst to that used by Smith (using trialkyl or triarylphosphines). Substituted allyl alcohols (e.g. $HOCH_2CH=CMe_2$) were only hydroformylated in low yield, but without any isomerisation[37].

Alternatively Kummer (BASF, 1975) showed that cyclic acetals of $CH_2=CHCHO$ (with 1,3-diols), could be hydroformylated using Rh or Co complexes with trialkylphosphines to give mixtures, which after hydrogenation over Raney Ni, contained 1,4-butanediol[38].

Shimizu (Kuraray, 1976) showed that the hydroxyaldehydes could be formed in high yield using $[RhH(CO)(PR_3)_3]$ (R=Bu, cy). The yields were[39];



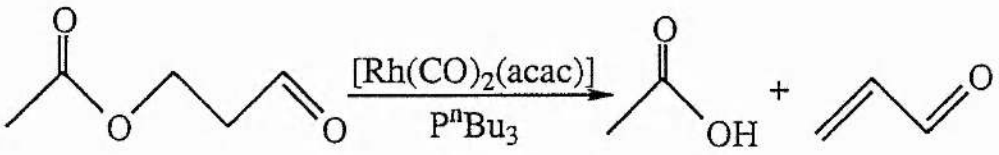
Pittman and Honnich (1981) produced a detailed report on hydroformylating 2-propen-1-ol utilising $[RhH(CO)(phosphine)_3]$ or resin based systems. The majority of phosphines were triarylphosphines or diphosphines, but a lone mention of P^nBu_3 is quite surprising, the yield of straight chain aldehyde is 39.7% (c.f. 74.6% the best quoted), but the branched chain aldehyde was only 1.4%, giving a n:i ratio of 28:1! But 'higher boiling products' (probably alcohols or esters) accounted for

46.4% of the yield, while propanal made up another 12.4%. So even though the n:i ratio is amazingly high, the overall production of 4-hydroxybutanal is below average for this type of system[40].

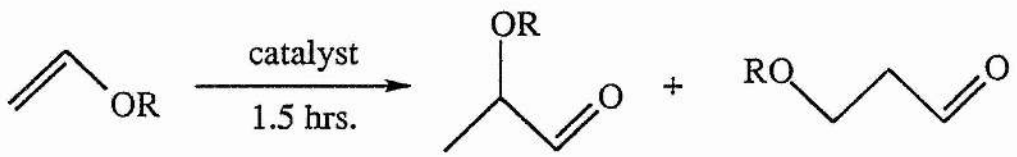
Drent (Shell,1984) patented a process which produced 1,4-butanediol in up to 69% yield. The process involved a soluble rhodium salt [e.g. $Rh(acac)(CO)_2$], a straight chain trialkylphosphine (PR_3 where R = e.g. Me, Et, ^{n}Bu, ^{n}Oc) and a carbonitrile solvent of the general formula $R'CH_2CH_2CH_2CN$ (R'=H or hydrocarbyl group)[41].

1.2.5 Hydroformylation of Vinyl Groups

Vinyl esters were first looked at by Abatjoglou and Bryant (1981). They showed that triarylphosphines and substituted triarylphosphines coupled with rhodium compounds catalysed the hydroformylation of vinyl esters[42]. Surprisingly branched chain products predominate, mainly due to slow decomposition of the straight chain product. Trialkylphosphine systems were found to be especially active at degrading the straight chain product, as shown below;



Lin and Brader (1985) investigated vinyl ethers as possible substrates for hydroformylation using rhodium/phosphine systems[43]. Hydroformylation had previously been achieved using cobalt catalysts at high pressures and high temperatures. The catalytic process used rhodium carbonyls and a phosphine, P^nBu_3 being one of the ones mentioned. The Lin and Brader system is illustrated in the following equation;

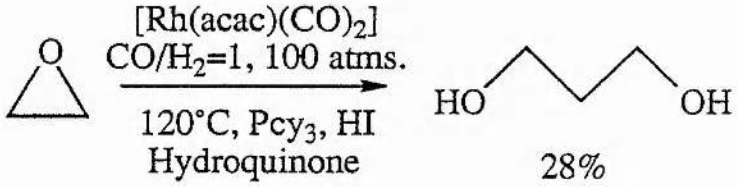


R=^{n}Bu, Ph, Et, Me,^{s}Bu, C_2H_3

Conversions are in the range 70-100% and n:i ratio are ~1:1. The propanals produced can be oxidised, then pyrolysed to give acrylic acids.

Ono, Miyama and Kasuga (Mitsui Toatsu Chemicals, 1986) examined the hydroformylation of vinyl chloride, producing 2-chloropropanal, which is a useful intermediate in many industrial processes. So using $Rh_6(CO)_{16}$ and P^nBu_3 or Pcy_3, vinyl chloride can be converted to 2-chloropropanal in 12-14% yield and 81.5-83.1% selectivity (the best phosphine employed was triphenylphosphine, giving 29.5% yield and 88.4% selectivity)[44].

Epoxides, which are similar to vinyl compounds, have been explored by Murphy, Aguilo and Smith (Hoechst Celanese Corp.), they took ethene oxide and turned it into 1,3-propanediol in 28% yield using the conditions below[45].

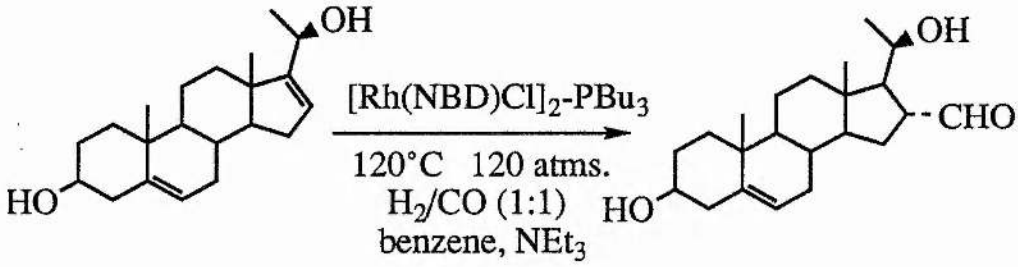


1.2.6 Miscellaneous Hydroformylations

As discussed in the first part of this section, hydroformylation has been often used for low molecular weight monoenes. These are easily separable from the catalyst by distillation. Sato, Kawaragi and Takai investigated various trialkylphosphine rhodium systems for tackling high boiling point products, which cannot be separated as normal due to catalytic decomposition at high temperatures. Other methods such as 'heterogenising' the catalyst by anchoring it or removing the catalyst (e.g. by adsorption onto activated carbon) also have their problems.

The high boiling point substrates that were hydroformylated consisted of unsaturated fatty acids (16 to 18 carbon atoms). A soluble rhodium compound (e.g. $[Rh(acac)(CO)_2]$) which reacted with phosphines to formed the catalyst *in situ*. The phosphines used were unusual in the fact that each phosphines alkyl groups totalled 27 or more carbon atoms (e.g. P^nOc_3, $P^n(C_{12}H_{25})_3$ etc.). The hydroformylation conversion was high (> 95%), of which > 95% were aldehydes. In comparison the conversion dropped to 60% when PEt_3 was used, and 5% using PPh_3 [46].

Another example of the more specialized uses of the trialkylphosphine/ rhodium systems, is the hydroformylation of a steroid skeleton[47].



The yield was 88% with a selectivity of > 99%.

1.2.7 Concluding remarks on hydroformylation systems

Hydroformylation of simple terminal alkenes using rhodium/ trialkylphosphine systems is inferior to the equivalent rhodium/ triarylphosphine systems, unless the trialkylphosphine systems are activating other molecules to produce reagents to allow the hydroformylation, then superior results can be obtained.

In general hydroformylation is best carried out using triarylphosphine systems, although some specialist syntheses seem possible utilising trialkylphosphine/ rhodium systems.

1.3 Hydrogenation

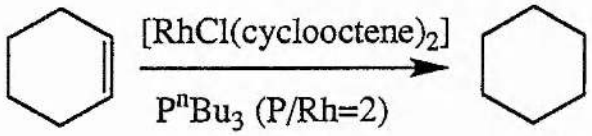
1.3.1 Hydrogenation of Alkenes

Hydrogenation using rhodium compounds is a well known process for alkenes, especially involving such compounds as $[RhCl(PPh_3)_3]$ - Wilkinsons catalyst. By stark contrast very few compounds utilising trialkylphosphines have been mentioned in the literature.

Early mentions of trialkylphosphine/ rhodium catalysts came from Wilkinson, Osborn, van der Ent and Montelatici (1968) using $RhClP_3$ (P= PPh_3, PPh_2Et, $PPhEt_2$ or PEt_3) for hydrogenating cyclohexene. PPh_3 was 40 times more active than PEt_3[48]. And in the same year Horner, Büthe, and Siegel published work on the hydrogenation of 1-hexene. An *in situ* catalyst was used, the precursor being $[Rh(COD)Cl]_2$ or $[Rh(C_2H_4)_2Cl]_2$.

$P(p\text{-}MeOC_6H_4)_3$ (the most active added phosphine) was 20 times more active than P^nBu_3[49].

Another early example of a trialkylphosphine/ rhodium hydrogenation system appeared in a patent by Coffey (I.C.I., 1968). Various rhodium complexes (e.g. $[RhCl(cyclooctene)_2]_2$ or $[RhCl(butadiene)_2]$) were modified using phosphine ligands, PPh_3 being one of the best. P^nBu_3 was an order of magnitude slower than the best reported in the patent (tri-p-methoxyphenylphosphine)[50].



r.t., THF, 50 mins 60% yield
(c.f. Best 86%)

In 1969, Strohmeier and Rehder-Stirnweiss published comparative work on different phosphines (PPh_3, $P(OPh)_3$, Pcy_3) using $[RhCl(CO)(phosphine)_2]$ on the hydrogenation of 1-heptene[51].

Using PPh_3, the reaction was complete after 3 hours, producing 80% heptane and 20% cis/ trans 2-heptene (the yield of heptane creeps up slowly after this due to the very slow hydrogenation of 2-heptene). Using Pcy_3, the reaction was > 80% complete after 5 hours, the product distribution being heptane ~75% and 2-heptene ~25%. Using $P(OPh)_3$ the reaction was 10% complete after 5 hours, the product ratios being similar to those obtained with the other phosphines.

Van der Plank, van der Ent, Onderelinden and van Oosten experimented with cationic rhodium complexes, such as $[RhL_2H_2]^+$ (L = P^iBu_3, PMe_3) that were prepared *in situ*, to partially hydrogenate long chain dienes with a view to applying this methodology to fats and oils.

PMe_3 containing systems hydrogenate trans double bond preferentially and P^iBu_3 cis double bonds. No explanation was given. PMe_3 also isomerised the position of the remaining double bond to a greater extent than P^iBu_3. Using PMe_3, 60-70% of the dienes converted to monoenes, the remainder were either fully hydrogenated or isomerisation products of the initial dienes[52].

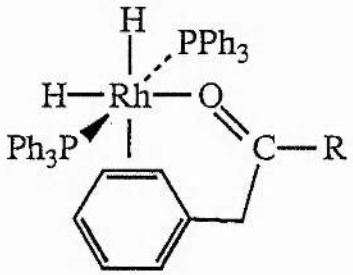
1.3.2 Aldehyde and Ketone Hydrogenation

In contrast to alkene hydrogenation, trialkylphosphine/ rhodium systems tend to be more effective (compared to the triarylphosphine/ rhodium systems) in the hydrogenation of carbonyl groups. Aldehydes can therefore be hydrogenated to alcohols.

Schrock and Osborn (1970) were the first to find that rhodium complexes containing or modified by basic phosphines could hydrogenate carbonyl groups. PMe_3 was the only purely trialkylphosphine investigated, producing high yields of alcohols[53].

Fujitsu *et al* found that high yields of alcohols could be formed from a range of aldehydes using $[Rh(NBD)(PEt_3)_2]^+ ClO_4^-$ dissolved in alcohols[54]. Between 79% and 97% conversion could be obtained from aromatic aldehydes (e.g. benzaldehyde) and ~40% in aliphatic aldehydes.

Replacing PEt_3 with PMe_3 gave conversion approximately half the above. Replacing PEt_3 with PPh_3 gave negligible conversion, except when the aldehydic substrate used was phenylacetaldehyde. (Conversion was 45.7% c.f. 47.8% for PMe_3 and 79.8% for PEt_3). This was thought to be due to an intermediate in the reaction thus;



Normally the site occupied by the phenyl group is taken by a solvent molecule. Diphos used in conjunction with $[Rh(NBD)(PEt_3)_2]^+ ClO_4^-$ gave no conversion.

Ketones could also be hydrogenated using the Fujitsu system[55]. The conversions quoted (without much distinction between aromatic methyl ketones or aliphatic methyl ketones) were in the range 47.6-100%.

The rate of reaction of aldehyde was nearly an order of magnitude higher than for ketones. One notable exception was methoxymethyl methyl ketone, which was similar in hydrogenation rate to the aldehydes. The reason attributed to this was the electron withdrawing effects of the methoxy group in the ketone.

Hydrogenation of unsaturated ketones showed that alkeneic groups tended to be hydrogenated in preference to carbonyl groups. For instance when methyl vinyl ketone was hydrogenated the alkeneic groups were completely hydrogenated within half-an-hour. The carbonyl group was only 60% hydrogenated after 20 hours, leaving 40% methyl ethyl ketone.

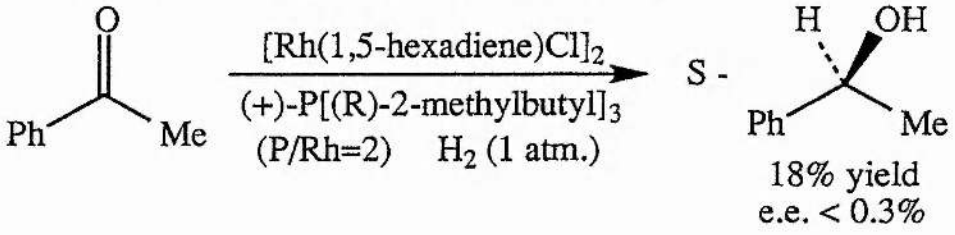
MacDougall and Cole-Hamilton using $[RhH(PEt_3)_4]$ found that aldehydes could be cleanly hydrogenated to give alcohols in alcoholic solvents. Conditions used to effect transformations such as heptanal to heptanol in high yield were 120°C under 40 atms. CO/H_2 (1:1)[16, 56].

Alper and Grushin used $[Rh(H)(Pcy_3)_2Cl_2]$ to hydrogenate α,β unsaturated aldehydes and ketones (the alkene being preferentially hydrogenated)[57]. Yields were high (generally 90-96%, 100% conversion) but co-catalysts such as water (aldehydes) or $NaOH_{aq}$ (ketones) were necessary, thus biphasic systems were formed. Mild conditions of room temerature and 1 atm. pressure were all that was required. Another attractive feature of this system is that $[Rh(H)(Pcy_3)_2Cl_2]$ is easy to handle and air stable. Once activated it converts to $[Rh(H)_2(Pcy_3)_2Cl]$ (isostructual and isoelectronic with $[Rh(H)_2Cl(PPh_3)_2]$, which is the active hydrogenation species in the Wilkinson's catalyst system).

Watanabe and Wada (Mitsubishi Chemicals, 1987) showed that formaldehyde could be hydrogenated over $[Rh(CO)_2(acac)]$ modified with P^nBu_3 (using reaction conditions of 150°C, 145 atms. of H_2 and reaction time of one hour), giving 73.9% MeOH at 100% conversion[58].

1.3.3 Asymmetric Hydrogenation

Trialkylphosphines have been used in conjunction with rhodium systems for asymmetric synthesis. Most are present simply as ligands stabilising the rhodium centre, but there are reports of attempts to use chiral alkyl groups on the phosphine, but with little success[59], thus;



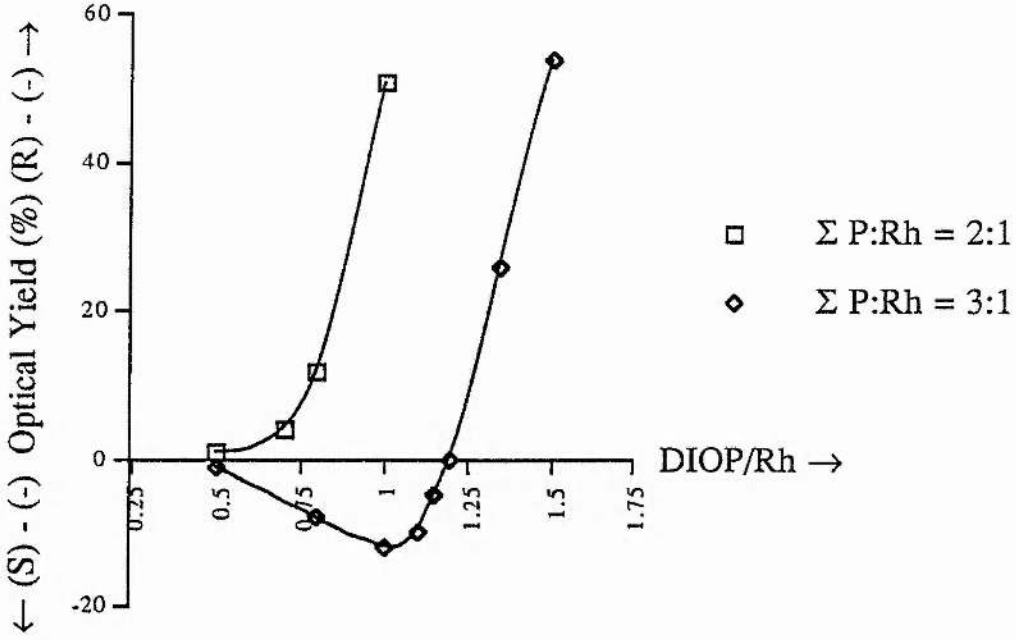
Brunner and Leyerer (1987), used $[Rh(COD)ClPR_3]$ (R=(S)-(+)-$MeCH_2CHMeCH_2$-) to hydrogenate (Z)-α-N-acetamidocinnamic acid in 15% e.e.[60]

In 1978 Marko *et al* hydrogenated (Z)-α-N-acetamidocinnamic acid methyl ester using $[Rh(COD)(OOCR^*)]_2$ (OOCR* being the anion of a chiral carboxylic acid) and phosphines in benzene/ methanol (1:1)[61]. Complete conversion took from a few minutes up to 24 hours. Interestingly the phosphine has an influence on e.e, the best phosphine for optical yield tested was PMe_3, this gave an e.e. of 13%, followed by P^nOc_3 (9.5%). Aryl, arylalkyl and di-phosphines gave < 1% e.e.

A report[62] on a similar rhodium compound using the chiral carboxylic acid (+)-N-acetylphenylalanine, gave similarly disappointing optical yields of between 5-10% with various substrates.

In a brief review entitled "Phosphine complexes of rhodium as homogeneous catalysts", which was centred on enantiomeric synthesis[63], Markó mentioned a curious feature about a $[Rh(NBD)Cl_2]$ and (+)-DIOP system. When hydrogenating acetophenone, the optical yield of the R-(+) alcohol was 51%. But on addition of free trialkylphosphine (Rh:DIOP:PR_3, 1:1:1), product became predominately S-(-) alcohol (ee = 12%) [R = ^{n}Bu or ^{n}Pe)].

To examine this further the ΣP:Rh was held steady at either 2:1 or 3:1 and the ratio of DIOP:PR_3 varied. The graphs obtained are shown below;



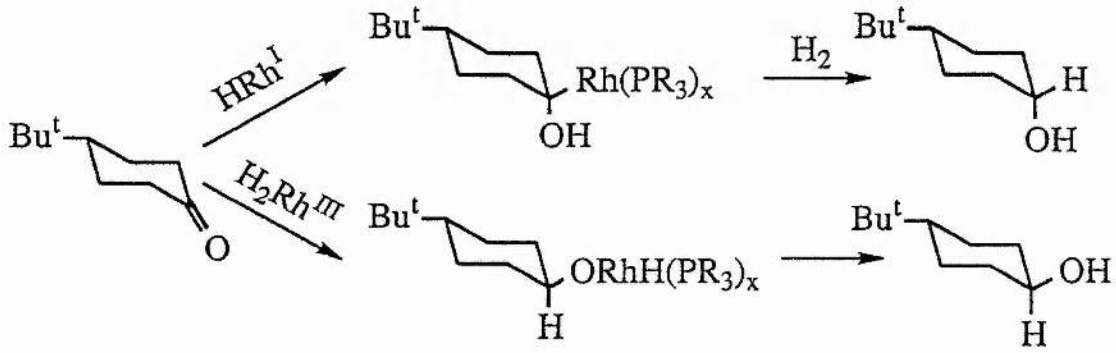
Graph showing the influence of P^nBu_3 on the enantioselectivity due to *in situ* catalysts formed from $[Rh(NBD)Cl]_2$ and (+)-DIOP on the asymmetric hydrogenation of acetophenone

The trace for a 2:1 P:Rh ratio is simple to explain, with no free phosphine available, two catalytic species are present. One giving an optical yield (DIOP), the other not (PR_3). The 3:1 trace is more complex, possibly indicating a third mixed phosphine species with one PR_3 and a monodentate DIOP. The free end of the DIOP causes a reverse in stereochemistry compared with the bidentate system.

Further work by Markó, Tórós, Heil and Kollar[64] looked at the stereochemistry of hydrogenation of cyclic ketones (especially 4-^{t}butylcyclohexanone). They found that, for $[Rh(NBD)Cl_2] + PR_3$ (R=Bu or Ph), predominantly trans alcohol was formed (slowly in the case of PPh_3). On addition of base (NEt_3), the system using PPh_3 started giving cis alcohol, while the selectivity in the P^nBu_3 system remained unchanged. Preformed $[HRh(PR_3)_4]$ gave cis alcohols using either phosphine. It was conjectured that the equilibrium below was set up in the system.

$$[H_2Rh^{III}(PR_3)_xCl] + B \rightleftharpoons [HRh^{I}(PR_3)_x] + BH^+ + Cl^-$$

The reason for the change in selectivity appears to be the way that Rh^I and Rh^{III} coordinate to a C=O bond. Rh^{III} attacks the O part because it is a 'hard' donor, so forming a Rh-O bond. Rh^I initially bonds through the double bond and after a H-transfer, a Rh-C bond is formed. So for 4-t-butylcyclohexanone, the pathways below come into operation, explaining the different stereochemistries of the product.

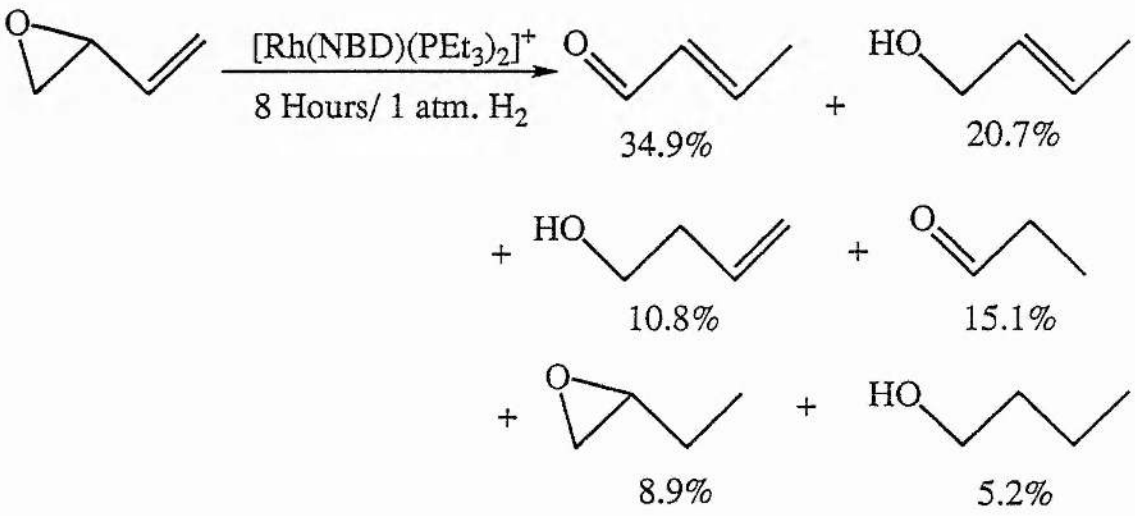


1.3.4 Miscellaneous Hydrogenations

Fujitsu showed that epoxides could be hydrogenated using a cationic $[Rh(NBD)(phosphine)_2]^+[ClO_4]^-$ catalyst (phosphine= PEt_3, PMe_3, PPh_3 or Diphos). The two most successful epoxides being styrene oxide and 3,4-epoxybut-1-ene, both giving anti products[65, 66].

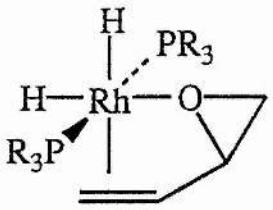
Styrene oxide, with PEt_3 gave 90% conversion to $PhCH_2CH_2OH$ (66%), $PhCH_2CHO$ (trace) and oligomers (22%). PMe_3 achieved only 40% conversion (alcohols: oligomers being ~1:1). PPh_3 and Diphos giving 100% conversion, but in both cases > 50% of the yield was oligomers. The conditions for the above hydrogenations were; H_2 (1 atm.) at 30°C for 6 hours in aqueous diglyme.

3,4-epoxybut-1-ene was 100% converted in the yields shown below, in 8 hours (oligomers making up the rest of the products);

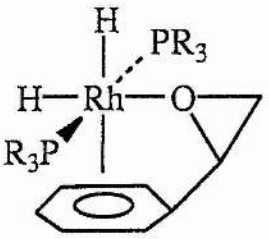


By comparison 1,2-epoxybutane only gave 0.65% conversion in 100 hours.

Similar to Fujitsu's proposed intermediate in the hydrogenation of acetophenone (mentioned earlier), Fujitsu attributed the reactivities of 3,4-epoxybut-1-ene and styrene oxide to the intermediates below. The unsaturated part of the molecule again takes the place of a solvent molecule.



3,4-epoxybut-1-ene



styrene oxide

Okano, Yoshida and Otsuka found that [RhH(P^iPr_3)$_3$] and [Rh_2H_2(μ-H_2)(Pcy_3)$_4$] were active catalysts at ambient temperature (unlike any previous homogeneous system, for any metal) for hydrogenating nitriles[67]. [RhH(P^iPr_3)$_3$] was especially active, giving 100% conversions with $Me(CH_2)_4CN$ and ^iPrCN (20°C under H_2 [1 atm.], for 20 hours). Substrates with nitrile groups directly attached to aromatic groups made the transformation sluggish (45% conversion using [RhH(P^iPr_3)$_3$]), but substrates with nitrile groups not directly attached (e.g. benzyl) were more active. The drawback of the catalytic system is the activity to alkeneic groups that may also be present in the molecule, because these could be partially hydrogenated as well.

At elevated temperatures (110°C under a steady stream of nitrogen) both catalysts served as dehydrogenation catalysts, to turn amines into nitriles. e.g. benzylamine was converted to benzonitrile (27%) in 24 hours.

1.3.5 Concluding remarks on hydrogenation

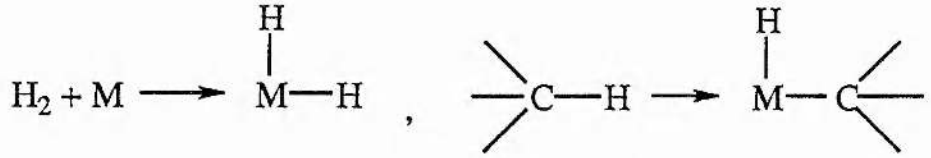
Hydrogenation of simple alkenes using rhodium/ trialkylphosphine systems are not particularly efficient. Better catalytic systems exist to perform these sort of hydrogenations.

This is not the case for carbonyl groups where rhodium/ trialkylphosphine systems prove to be the best catalysts for this application in general.

Trialkylphosphines play a supporting role while other ligands induce the chirality in some asymmetric hydrogenation systems. Attempts to do asymmetric hydrogenation using chiral alkyl groups on the phosphine led only to poor e.e.

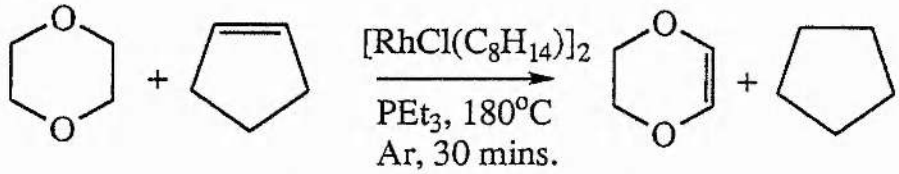
1.4 Hydrogen Transfer

Hydrogen transfer simply involves the transfer of two hydrogen atoms from a donor molecule to an acceptor molecule. A similarity in the oxidative addition steps of hydrogen transfer and hydrogenation can be recognised. Instead of an H-H bond breaking an H-C (or H-O) bond is broken, as shown;



Much work has been done on hydrogen transfer, but the first mention in the literature of a rhodium/ trialkylphosphine system is by Gregorio, Pregalia and Ugo (1968) who showed that $[HRh(CO)(L)_3]$(L = PEt_3, P^tBu_3, PEt_2Ph, $PMePh_2$) was capable of effecting hydrogen transfer from alcohols (benzyl alcohol being the only one specifically mentioned) to terminal alkenes (normally 1-octene) in the presence of potassium benzoate. Turnovers of 35 in 4 hours were recorded[68].

Trialkylphosphine systems were not mentioned again until 1975 by Masters, Kiffen and Visser[69]. They studied many metals (cobalt, tantalum and iron to name but a few), with many ligands (mostly phosphines), the best they found was an *in situ* system generated from bis(cyclooctene)chlororhodium(I) dimer, with a 4 molar equivalent (per rhodium) of PEt_3, P^nPr_3 or P^nBu_3. This caused > 83% conversion (93% in the case of P^nPr_3) using 1,4-dioxane as the donor with cyclopentene being the acceptor.



A popular sacrificial donor employed is isopropanol. Spogliarich, Tencich, Kasper and Graziani (1982) used it to hydrogenate various ketones (e.g. 4-^{t}butylcyclohexanone) and alkenes (e.g. 3-methylcyclohexene)[70]. Again *in situ* systems were used, the soluble rhodium precursor being either $[Rh(cyclooctene)_2Cl]_2$ or [Rh(1,5-cyclooctadiene)Cl]$_2$. An iridium system was tried as well, but found not to be as effective.

Transfer hydrogenation of 4-t-butylcyclohexanone with [Rh(1,5-cyclooctadiene)Cl]$_2$ allied with various phosphines and a cocatalyst of KOH (in the ratio KOH: Rh, 10:1), was carried out at 83°C. When PPh_3 was used a conversion of 97% (77% cis isomer) was achieved in 5 minutes, Pcy_3 produced 98% (55% cis) in 120 minutes. P^tBu_3 gave 86% (49% cis) after 180 minutes.

As is to be expected, a large excess of phosphine inhibits the reaction. The presence of alkenes also inhibit the reaction, since they are slower than ketones to hydrogenate and compete well for the active sites on the rhodium centres.

Alkene hydrogenation, as just mentioned, can be accomplished in the same catalytic system. Rates (as already stated) are low, e.g. only 9% of cyclohexene had reacted to form cyclohexane, in 180 minutes.

Using non-symmetric alkenes it was shown that isomerisation was also occurring. 3-methylcyclohexene gave methylcyclohexane (30%) and 1-methylcyclohexene (60%) in 420 minutes. To investigate whether isomerisation was a pre-requisite in the hydrogenation 1-methylcyclohexene was examined as the initial substrate, only 5.5% had hydrogenated in 180 minutes.

Also in 1982 Tani, Suwa, Tanigawa, Yoshida , Okano and Otsuka showed that the complexes [{$RhH(Pcy_3)_2$}$_2$(μ-N_2)] and [$RhH(P^iPr_3)_3$] were active catalysts for hydrogenation of ketones using either H_2 or ^{i}PrOH as the hydrogen source. Yields were 88-93% for H_2 and 35-99% for ^{i}PrOH for various substrates e.g. PhCOPh, MeCOCOMe[71].

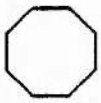
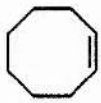
Felföldi, Kapocsi and Bartok also studied the transfer hydrogenation of alkylcyclohexanones. They showed that when the alkyl group was in the 2 position, this had the major directing effect forcing the cis isomer to predominate. When the alkyl group was in the more distant 4 position the phosphine basicity was the greater factor influencing which isomer was dominant. PPh_3 favoured cis, P^tBu_3 marginally favoured trans[72].

Schumann, Blum et al (1984) found that compounds of the formula [$Rh_2(CO)_2(P^tBu_3)_2Cl(SR)$] (R= alkyl or (un)substituted phenyl group) could transfer hydrogenate α,β-unsaturated ketones using formic acid, producing CO_2 as the sacrificial donor product[73].

$$C_6H_5CH{=}CHC(O)C_6H_5 + HCO_2H \xrightarrow[\substack{22\ hrs.\\ Toluene\\ 97°C}]{cat.} C_6H_5CH_2CH_2C(O)C_6H_5 + CO_2$$

Marcec (1986), used a $[Rh_2(OAc)_4]$ based *in situ* system to carry out hydrogen transfer from 2-propanol to cyclohexanone. Rhodium acetate itself was inactive but with nitrogen based ligands conversions up to 88% (using 2,2'-dipyridine) in 1 hour were obtained. Tributylphosphine gave 40% conversion in the same time, whilst the yield using triphenylphosphine was only 28%[74].

Maguire and Goldman (1991) showed that $[RhCl(CO)(PMe_3)_2]$ could be thermally activated (as oppose to uv light activated, see later in this review under photochemical reactions) to give $[RhCl(PMe_3)_2]$, a highly active transfer hydrogenation species for alkanes thus;

Norbornene +  $\xrightarrow[\substack{H_2\ (70\ atms.)\\ 25\ hours,\ 60°C}]{[RhCl(CO)(PMe_3)_2]}$ Norbornane + 

The above managed 560 catalytic turnovers in 25 hours. At 100°C 950 catalytic turnovers were achieved in less than 15 minutes.

Without H_2 pressure no activity was recorded. It is conjectured that the two equilibria below were in operation after initial formation of $[RhCl(PMe_3)_2]$;

(a) $[RhCl(PMe_3)_2] + \text{alkane} \rightleftharpoons [RhCl(PMe)_2(H)_2] + \text{alkene}$

(b) $[RhCl(PMe_3)_2(H)_2] + CO \rightleftharpoons [RhCl(CO)(PMe_3)_2] + H_2$

It can clearly be seen that large pressures of H_2 will keep equilibrium (b) far to the left, so $[RhCl(PMe_3)_2(H)_2]$ can go on to hydrogenate the acceptor alkene[75].

In a subsequent paper it was reported that $[Rh(PMe_3)_2ClL]$ (L= P^iPr_3, Pcy_3, PMe_3) or $[Rh(PMe_3)_2Cl]_2$ are also good, if not better precursors for the thermal hydrogen transfer reaction[76].

M. Tanaka *et al* (1991) showed that $[Rh(PMe_3)_2Cl]_2$ would react with ethene to give $[RhCl(CH_2{=}CH_2)(PMe_3)_2]$. This in a solution of

cyclooctane at 170°C under ethene (11 atms.), gave 3 turnovers to cyclooctene (ethane being the other product) in 15 hours. At higher pressures ethylcyclooctane and cyclooctene were produced. The system worked well up to 230°C and 70 atms. pressure realising 32 turnovers (beyond that significant metallic deposition occured)[77].

MacDougall and Cole-Hamilton have recently shown that ethanol can be used as a hydrogen source in an attractive hydrocarbonylation process under CO pressure to convert alkenes into alcohols[16, 56].

1.4.1 Concluding remarks on hydrogen transfer

Hydrogen transfer is an attractive reaction because it cuts out the need to handle gaseous hydrogen. Although only a few processes produce reasonable turnovers, the work of Cole-Hamilton and MacDougall has shown that the field of hydrogen transfer has potential to become a useful synthetic methodology.

1.5 Miscellaneous Addition Reactions

1.5.1 Hydrosilylation

Wilkinson, Osborn and de Charentenay (1968) tested $[RhCl(PPh_3)_3]$ as a hydrosilylation catalyst on 1-hexene. They also tested other rhodium compounds for comparison purposes, one being $[RhCl(CO)(PEt_3)_2]$.

The latter turned out to be the worst of four tested, managing to hydrosilylate only 2% of the 1-hexene in 55 hours. $[RhCl(PPh_3)_3]$, $[RhCl(CO)(PPh_3)_2]$ and $[(CO)_2RhCl]_2$ were all better[78].

Haszeldine, Parish and Taylor (1974) used $[RhClL_3]$ (L=phosphine) complexes to hydrosilylate hex-1-ene. L was varied using many aryl or alkaryl phosphines to vary the electronic properties of the metal centre. The only trialkylphosphine used was Pcy_3. Again this gave the worst hydrosilylation results of the many tested. $[RhCl(Pcy_3)_3]$ had only caused ~10% of $HSiEt_3$ to react after 1 hour, all other catalysts tried had converted over 80% of the silane in 40 minutes[79].

In stark contrast Rejohn and Hetflejs (1975) published work on the hydrosilylation of hex-1-ene using Et_3SiH, $(EtO)_3SiH$ or Cl_3SiH over an

in situ catalyst generated from $[RhCl(COD)]_2$ and various phosphines. Pcy_3 was found to be the most active phosphine of those tried[80].

Howe, Lung and Nile examined rhodium (II) compounds and found them highly active as hydrosilylation catalysts[81]. The most effective being $[RhCl_2(Pcy_3)_2]$ which could hydrosilylate 1-octene using $HSiEt_3$ in 100% conversion to produce $C_8H_{17}SiEt_3$ with 100% selectivity within 8 hours at 100°C. It could also hydrosilylate dienes (in greater than 70% conversion to monoene silanes), cyclic and non-cyclic ketones (> 78%) and even alkynes, as represented below.

$$n\text{-}C_4H_9C{\equiv}CH + HSiMe_2Ph \longrightarrow \text{cis and trans } n\text{-}C_4H_9CH{=}CHSiMe_2Ph$$

63% yield (cis/trans ~1)

1-hexyne was investigated in more detail and sampled at periods during its 8 hour reaction. The cis: trans ratio was always close to 1:1.

Since most catalysts give a product that is predominantly trans, due to cis addition of the hydrogen atom and silyl group (mixtures of cis and trans products from rhodium catalyst have a precedent in the literature[82, 83]), the authors propose two possible explanations. Either addition is not stereospecific or slow stereospecific addition takes place followed by rapid isomerisation. Other rhodium catalysts, however, show only slow cis/trans isomerisation[82, 83].

There is a brief mention in a patent by Takatsuna *et al* to $[RhCl_3(PEt_3)_3]$ being a useful catalyst for the conversion of allyl amines to γ-aminopropylsilanes. Yields are reported to be 80-90% and selectivity of γ to β being ~450:1 within 2 hours[84].

In 1990 another patent (Inaba and Kimae, Chisso Corp.) dealing with the hydrosilylation of allyl amine appeared[85]. This one focused on trialkylphosphines and showed that they gave better γ to β ratios than triarylphosphines (PEt_3 gave 55:1, PPh_3 gave 24:1). So;

$$+ (EtO)_3SiH \xrightarrow[PEt_3,\ 120°C]{[RhCl(COD)]_2} H_2N(CH_2)_3Si(OEt)_3 + H_2NCH_2CHMeSi(OEt)_3$$

(74%) (1%)

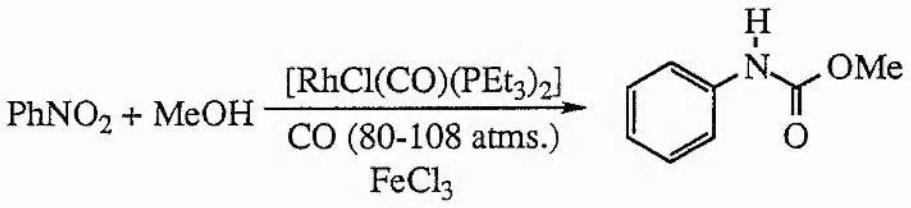
The conversion was 75% in the above reaction.

Bartok, Kapocsi and Felföldi published a paper on the hydrosilylation of cyclic ketones using $[RhCl(PPh_3)_3]$, but a brief section of this paper dwelt upon the effects of changing the phosphine ligand. PBu_3 was as active as other ligands, giving 95-100% conversion in 30 minutes at 25°C. PBu_3 being the smallest cone angled phosphine tried gave the highest yield, after hydrolysis, of cis-4-t-butylcyclohexanone (the only substrate studied for the ligand variance)[86].

1.5.2a Carbonylation

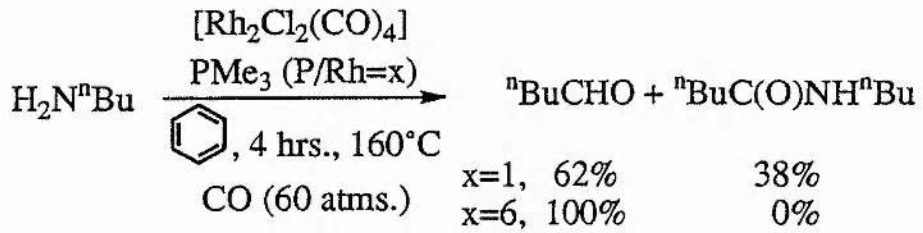
Carbonylation is simply the process of CO insertion into a chemical bond (e.g. C-Cl, C-H or N-H can be carbonylated to produce C-(CO)-Cl, C-(CO)-H or N-(CO)-H respectively).

ICI (1966) published a patent on the production of urethanes from nitrocompounds, CO, and alcohols/phenol using various homogeneous metal catalysts, the most effective tested was $[RhCl(CO)(PEt_3)_2]$[87].



100% conversion

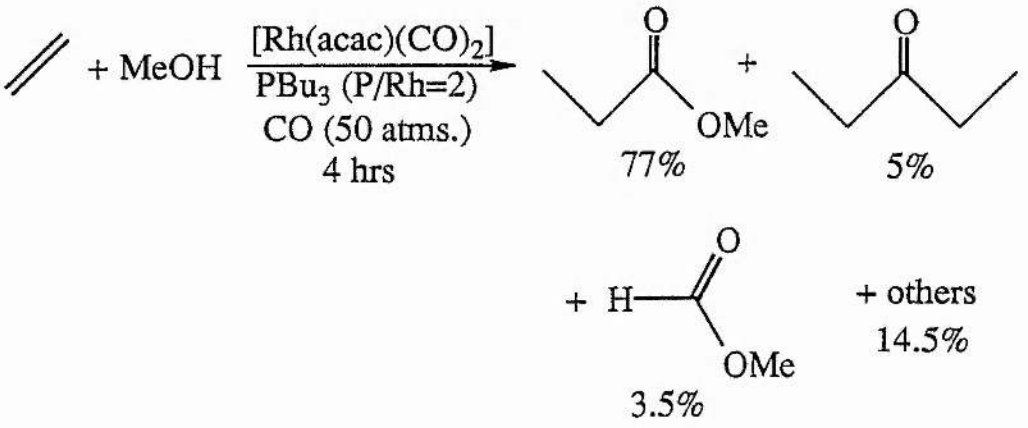
Durand and Lassau (1969) showed that primary amines could be turned into amides and substituted ureas by using $[Rh_2Cl_2(CO)_4]$ with various phosphine ligands[88], e.g.



Another attractive carbonylation is the reaction of alkenes with CO in the presence of alcohols to produce carboxylic acids and/ or esters. A

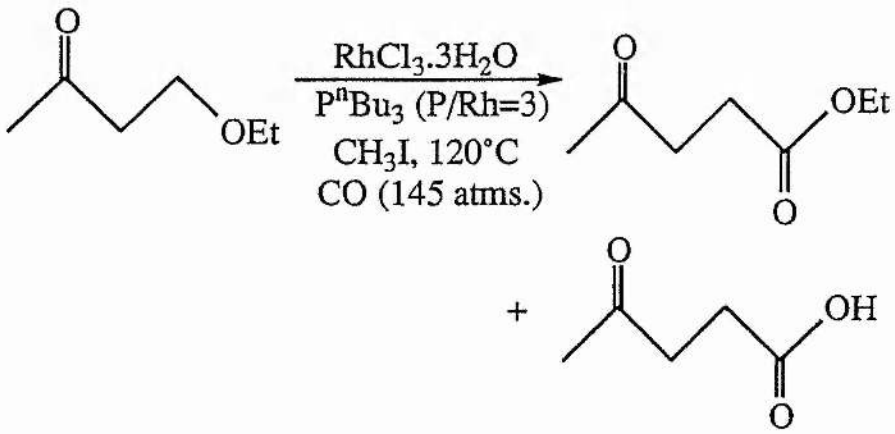
patent published by Monsanto (1974) upgraded existing cobalt technology by using rhodium based chemistry.

A soluble rhodium compound (the only stipulation made is that it must be halide free), a phosphine, an alcohol and an alkene were put under CO pressure. A typical reaction is shown below[89];



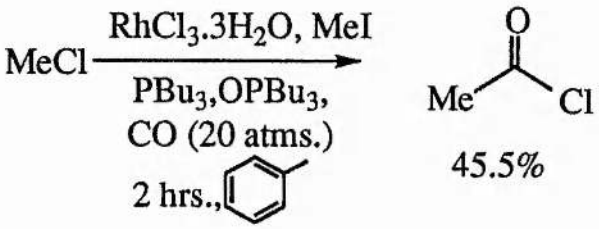
The conversion in the above reaction is 58%.

Matsui (Maruzen Oil Co., 1976) published results on his attempts to produce levulinic acid ($CH_3COCH_2CH_2CO_2H$) from methyl vinyl ketone. Attempts to hydroformylate and hydrocarboxylate methyl vinyl ketone failed. However a substrate easily derived from methyl vinyl ketone (3-buten-2-one) [by addition of ethanol], was used and sucessfully carbonylated. Rhodium/iodide systems used for this reaction were substantially improved (especially yields of free levulinic acid) on the addition of PPh_3 or P^nBu_3[90].



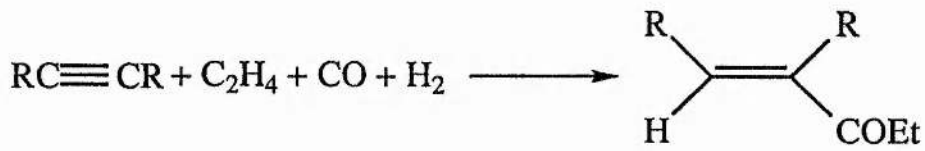
The conversion in the above reaction was 100%, without added P^nBu_3 the above two products constituted 24.4% of the final mixture. With added P^nBu_3 the yield became 34.5%.

Kurijama (Mitsubishi Gas Chemical Co.) produced a patent dealing with the production of acetyl chloride from methyl chloride and CO[91]. The example quoted is;

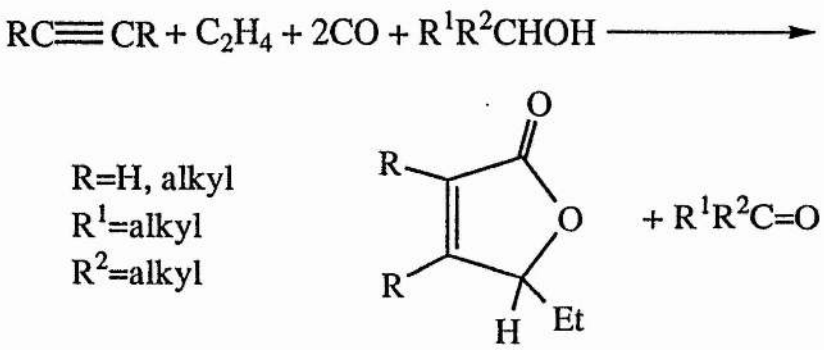


An East German patent describes a process for the production of 2-methylbutanoic acid and derivatives from 2-methylpropene or 2-methylpropan-1-ol with CO using $[RhX_2(PR_3)_2]$(X= monovalent anion, R= alkyl, cycloalkyl, aryl). Few details are disclosed except $[RhCl_2(Pcy_3)_2]$was used in benzene with CO and isobutene to give 2-methylbutanoic acid[92].

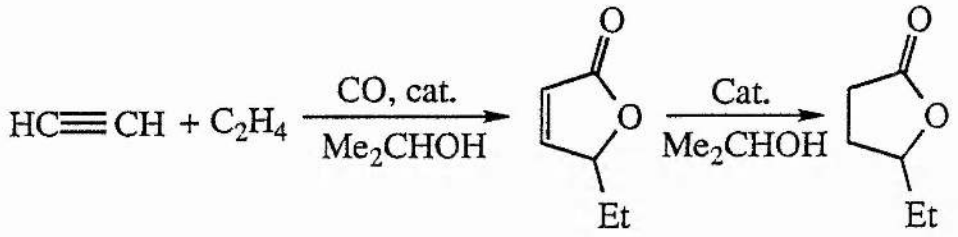
Hong, Mise and Yamazaki (1991) showed that by varying the H-source, alkynes and ethene could be coupled and carbonylated over a rhodium/ trialkylphosphine catalyst to give a variety of products[93]. Using H_2 as the hydrogen source the following reaction occured;



If an alcohol was employed as the hydrogen source, then the reaction changed to give the following product;

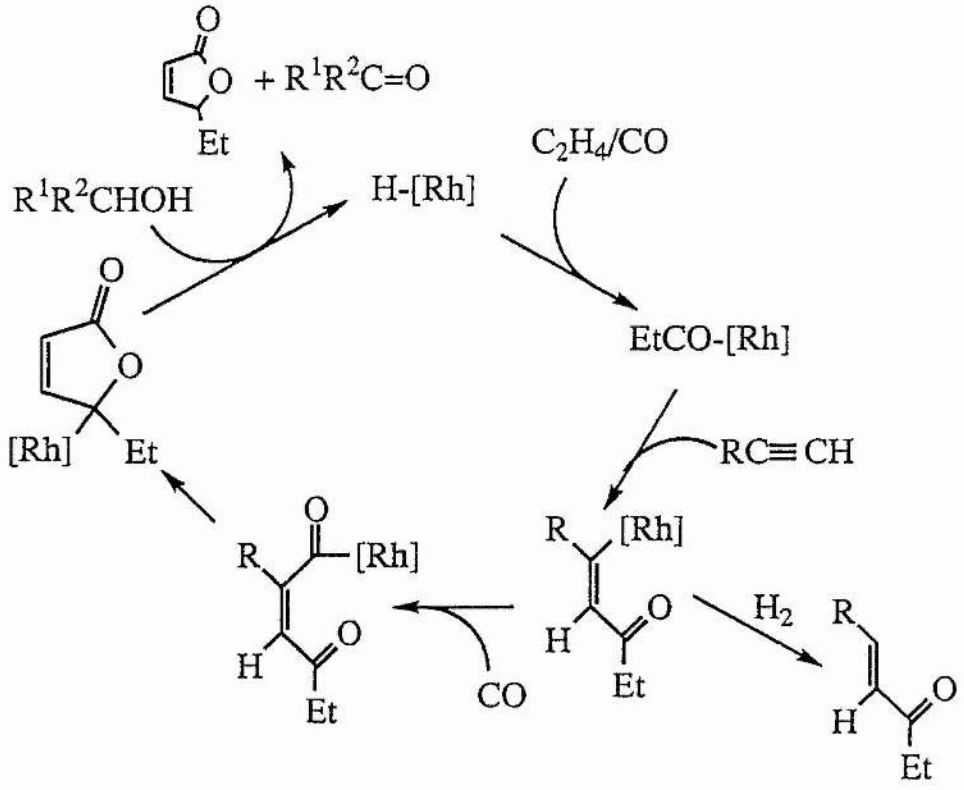


The furanone produced could also be further reduced to give a γ-caprolactone. For example;

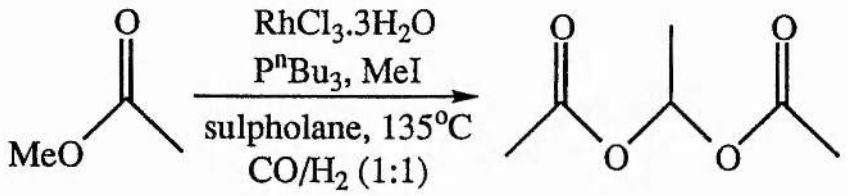


A systematic study was carried out which looked at the effects of different phosphines on the system. The system comprised $Rh_4(CO)_{12}$ and phosphine in a secondary alcohol. More basic phosphines (than PPh_3) reduced the activity of the catalyst (PEt_3 gave 18 turnovers/ Rh atom/ hour, PPh_3 gave 108 turnovers/ Rh atom/ hour) and also suppressed the secondary hydrogenation step (PEt_3 giving a ratio of furanone: lactone of 8:1, PPh_3 giving a ratio of 1:107).

With a few exploratory experiments, it was deduced that the mechanism was as shown below;



Ethylidene diacetate (1,1-diacetoxyethane) could be prepared in high yield from dimethyl ether and/ or methyl acetate[94]. Ethylidene diacetate can be used as a solvent or a starting material for the production of vinyl acetate or acetic anhydride.



The above reaction occured in 90% conversion with 80% selectivity to the above product. No mechanism was proposed for the reaction.

Weston, Gash and Cole-Hamilton (1994) have reported the double carbonylation of a geminal dihalide in the presence of $[Rh_2OAc_4]$, PEt_3 (optional) and EtOH. They showed that CH_2I_2 can be turned into $CH_2(CO_2Et)_2$ in moderate conversions (8-50%) giving low yields of the diethylmalonate. The diether, EtI and $EtCO_2Et$ are other reported products from this reaction[95].

1.5.2b Decarbonylation

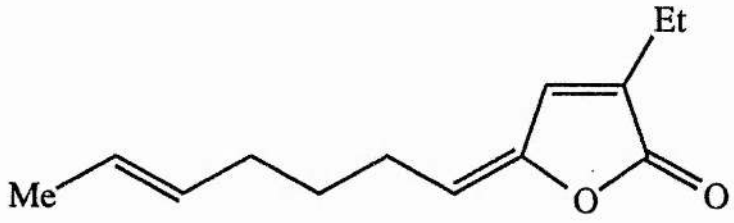
The first decarbonylation reaction to be reported using rhodium/ trialkylphosphine systems was by Tsuji and Ohno (Toyo Royon Co., 1968). The catalyst they examined was $[RhX(CO)P_2]$ (X= halide, P= phosphine). 2-chlorocarbonylnapthalene was decarbonylated to give 2-chloronapthalene in ~70% yield (conditions employed were 180-200°C for 2 hours)[96].

Goldman, Goldman and Abu-Hasanayn (1992) found that $[Rh_2(PMe_3)_4Cl_2]$ decarbonylated aldehydes in stoichiometric quantities to give alkanes and $[Rh(PMe_3)_2(CO)Cl]$[97]. Due to the ease at which similar dicarbonyl complexes lose one CO ligand under mild conditions[98], Goldman *et al* also explored $[Rh_2(PMe_3)_2(CO)_2Cl_2]$ and after a decarbonylation reaction using this complex, they isolated $[Rh(PMe_3)(CO)_2Cl]$. This could be converted back to the dimer on purging the catalytic solution with argon, so completing the cycle. Rates were not high (3.6 turnovers/ hour at 100°C, aldehyde = HCO-n-$C_{11}H_{23}$)

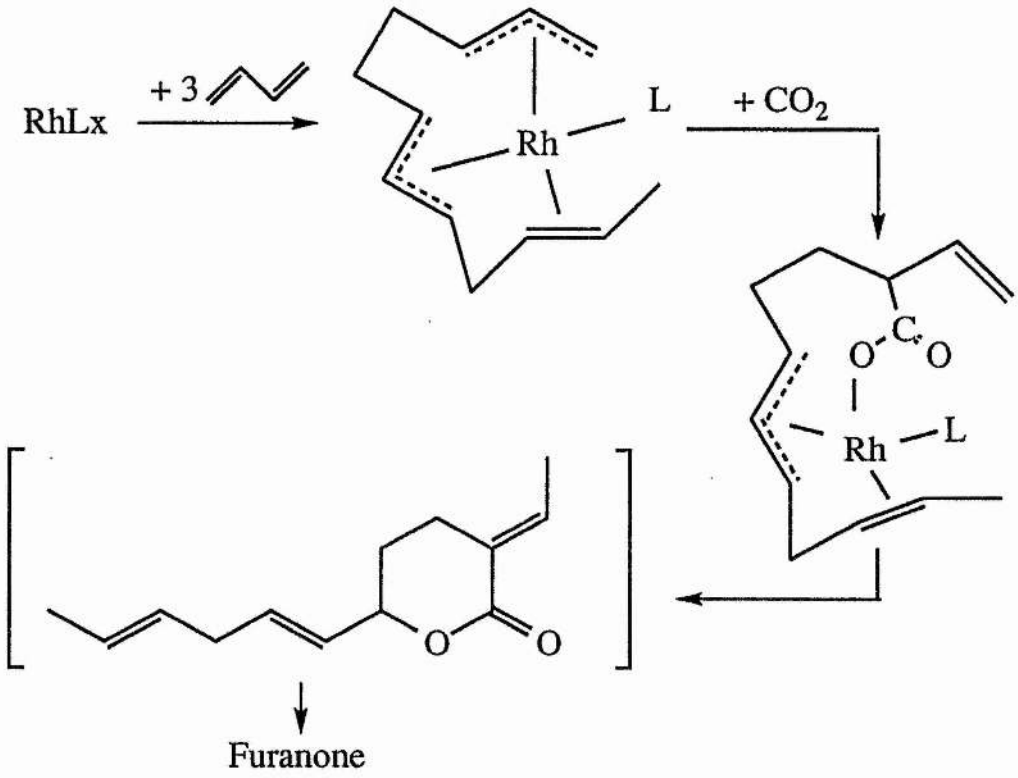
but the system was reported to be just as active after 72 hours, with no sign of catalyst decomposition.

1.5.3 Reactions involving CO_2

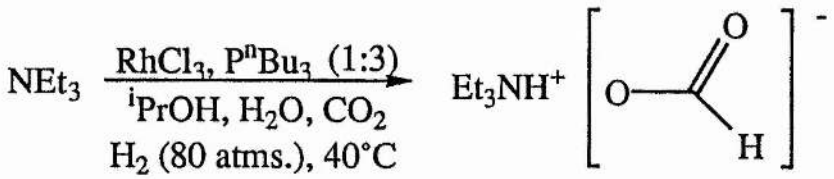
CO_2 was found to react with butadiene in the presence of a rhodium/ phosphine system to produce;



$[Rh(CH_2{=}CH_2)_2(acac)]$-$PEt_3$ proved to be the best catalyst for the transformation[99]. The mechanism is not known, but may be as follows;



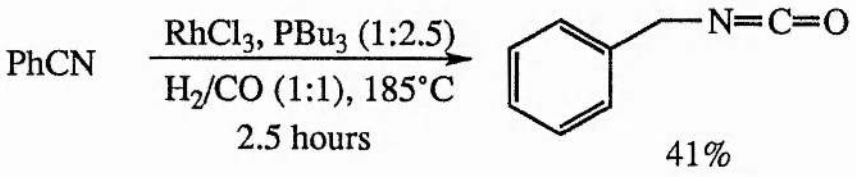
Kent (BP Chemicals, 1985) published a patent for the reaction of amines, or similar, with CO_2 and H_2 to form formate salts[100], for example;



The conversion in the above example was > 70%.

1.5.4 Nitriles to Isocyanates.

Ono and Mizoguchi (Asaki Chemicals, 1974) discovered that heating nitriles, CO and H_2 in the presence of rhodium compounds and phosphines, they could generate isocyanates, useful chemicals in organic synthesis[101]. For example;

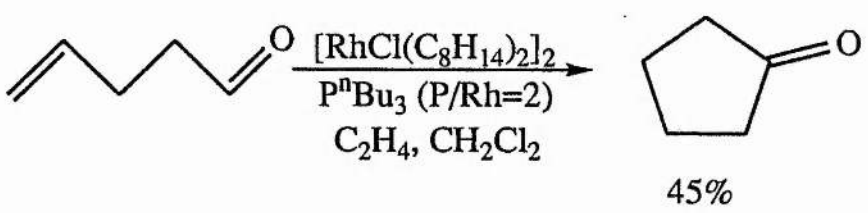


> 90% conversion

1,4-dicyanobenzene could also be converted to the expected diisocyanate in similar yield.

1.5.5 Intramolecular Hydroacylation of unsaturated Aldehydes.

Larock, Oertle and Potter reported the synthesis of 5-membered ring cyclic ketones from 4,5-unsaturated aldehydes[102].Thus;



Tri-p-tolyl, tri-p-anisyl and tris(p-dimethylaminophenyl)phosphine were the best ligands giving > 90% yield. PEt_3 and Pcy_3 gave yields of between 30 and 70%.

The reaction was tolerant of other functional groups in the reactant aldehyde, but only 5 membered rings could be synthesised.

1.5.6 Aldehydes + Activated Organic compounds

Milstein (duPont, 1986) showed that C-H bonds activated by a nitro group could be added across the C-O bond of aldehydes with a reaction similar to catalysed aldol condensation[103].

$$MeNO_2 + MeCHO \xrightarrow[23^\circ C,\ 0.5\ hours]{[Rh(PMe_3)_3Cl]} \underset{> 90\%}{MeCH(OH)CH_2NO_2}$$

1.5.7 Kharasch Reaction

An interesting communication by Cable, Adams, Bailey, Crosby and White (1991), suggested that the Kharasch reaction (addition of a perhaloalkane to an alkene) for some rhodium based systems was going via a different mechanism from the generally accepted radical route. It was proposed that the reaction for rhodium (I) compounds may proceed via oxidative addition of the perhalocarbon to rhodium, followed by stepwise transfer to the coordinated alkene.

$CBrCl_3$ was added to $[RhCl(CO)(PMe_3)_2]$ and $[RhBr(CCl_3)Cl(CO)(PMe_3)_2]$ was isolated. Both were active catalysts for the addition of $CBrCl_3$ to styrene[104].

1.5.8 Concluding remarks on miscellaneous addition reactions

Rhodium trialkylphosphine systems can be used to effect many addition reactions over mainly carbon-carbon double bonds. The two most important being hydrosilylation and carbonylation. Both of these classes of addition reactions can be accomplished in high yield.

1.6 Photochemical Reactions

Faltynek (1980) first reported the use of rhodium/ trialkylphosphine systems in photocatalysis. He observed that under near UV irradiation hydrosilylation occured between $[(CH_3)_2SiH]_2O$ and $[H_2C{=}CHSi(CH_3)_2]O$, when exposed to air[105].

The reaction used a Rh(I)/ PBu_3 based process, rhodium being introduced as $RhCl_3.3H_2O$ or $Rh_2(CO)_4Cl_2$. The reaction is aided by the presence of air or an oxidising agent, this was thought to stimulate the reaction below;

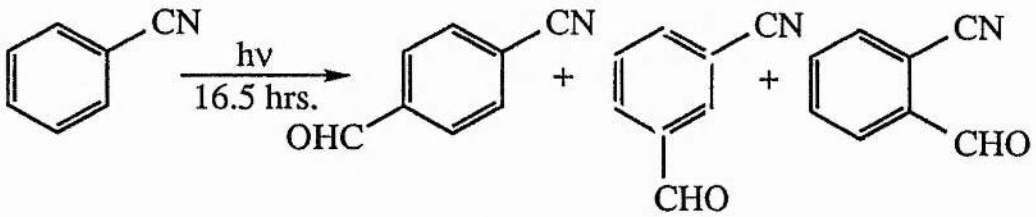
$$PR_3 + {}^1/_2O_2 \xrightarrow{h\nu} P(O)R_3$$

So it was thought that once a phosphine had disociated from the complex, then it would be removed by the preceding reaction, so leaving an uncoordinated site open for catalysis to proceed.

1.6.1 Photocatalytic C-H activation

The field was dormant for several years before Tanaka (1987) found that benzene could be converted into benzaldehyde (and products formed from benzaldehyde) under mild conditions (37°C, CO (1 atm.), hν), using $[RhCl(CO)(PMe_3)_2]$[106]. 47.8 turnovers had been achieved after 94 hours of reaction. If PPh_3 or $P(OMe)_3$ were used, the catalyst was virtually inactive (<1 turnover in 16 hours). It was concluded that the higher the electron density on the metal centre, the easier for the metal centre to achieve catalysis. Oxidative addition reactions are favoured by electon rich centres.

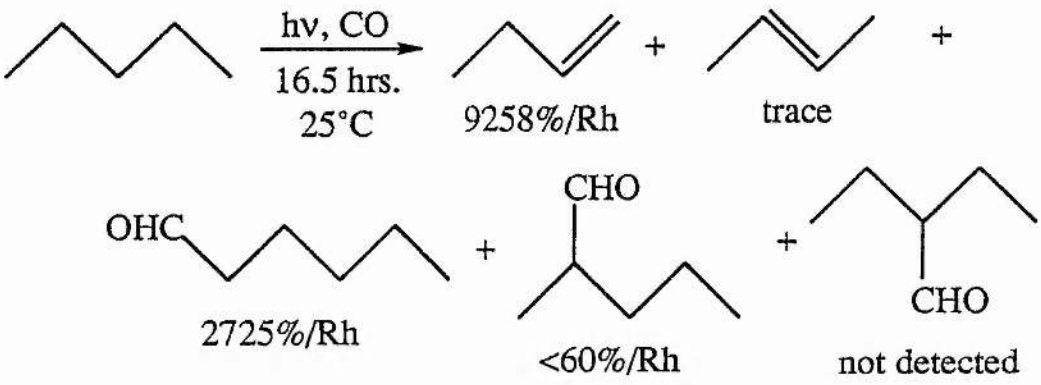
Aromatic nitriles could have CO inserted into C-H bonds;



14% 85% 1%

The above reaction achieved an overall conversion of 82%[107].

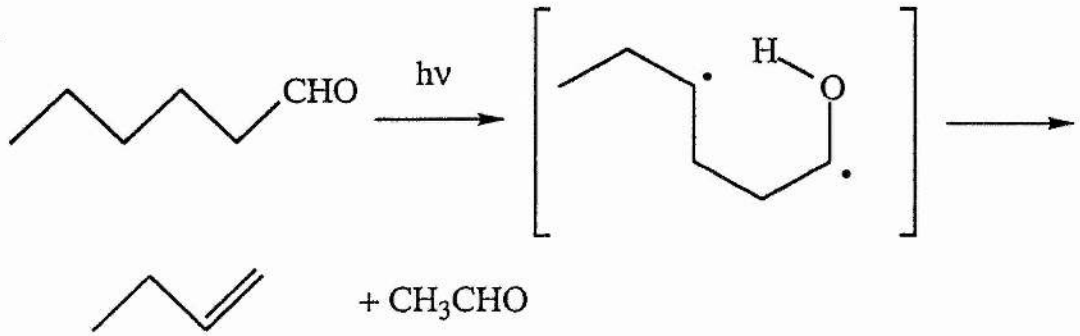
Tanaka *et al* went on to report dozens of reactions using his $[RhCl(CO)(PMe_3)_2]$ catalyst. Most of these (up to 1990) have been reviewed[108]. The most important is the catalytic carbonylation of straight chain alkanes to linear aldehydes;



+ ethanal	+ ethanol	+ n-$C_6H_{13}OH$
2180%/Rh	1510%/Rh	920%/Rh

Not only is this a rare example of C-H activation in an unreactive alkane, but more importantly it was the first example where such a transformation could be rendered catalytically. It also gives the commercially desirable straight chain aldehyde[109]. The main bulk of the products are terminal, again implying that the terminal CH_3 contains the activated part of the molecule. It was concluded that this may be due to the thermodynamic stability of the primary alkyl hydrido rhodium complex formed. This idea has been proposed before for the activation of n-alkanes by [Cp*Rh(PMe_3)][110]. Negligible isomerisation products are produced. Turnovers are reasonable (e.g. 110 in 16.5 hours) considering that CO is probably hindering the formation of the initial catalytic species, ie. loss of coordinated CO.

It is proposed that the $C_{(n-1)}$ alkenes are formed by a Norrish type II reaction. The normal stimulus for this is UV light of 290 nm wavelength. Pyrex glass absorbs all light below 300 nm. It was assumed that there was a slight overlap of the Norrish activation band after the cut-off to cause the reaction. The mechanism for this reaction is shown below.



Similar products are obtained from the reaction with decane under CO, using the standard conditions for all these reactions shown so far: $[RhCl(CO)(PMe_3)_2]$, constant hν, room temperature and a reaction time of 16.5 hours (unless otherwise stated).

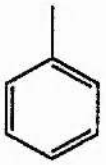
Decane ⟶ 1-nonene (2860%/Rh) + 2-nonene (23%/Rh) +

decanal (1-, 2-, 3-, 4-, 5-) (1590%/Rh (92: 3: 2: 1: 2)) +

ethanal (798%/Rh) + ethanol (671%/Rh) + 1-decanol (284%/Rh)

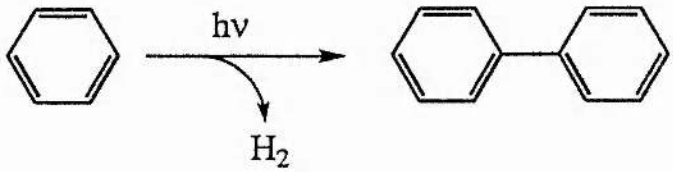
Isocyanides could be coupled in place of CO so that Schiff bases could be prepared from alkanes or aromatics. Thus pentane and benzene could be converted to $MeN{=}CHC_5H_{11}$ and $MeCHC_6H_5$ respectively using MeNC[111, 112].

When disilanes are used in conjunction with toluene silylation occured on both the ring and methyl carbon atoms[113];



$+ Me_3SiSiMe_3 \xrightarrow{h\nu} MeC_6H_4(2\text{-},3\text{-},4\text{-})SiMe_3 + PhCH_2SiMe_3$

In the absence of CO, C-C coupling e.g. of aromatics or dehydrogenation occurs. Thus benzene gives diphenyl and H_2.



In the abstract it is reported that evidence for intermediate radical formation is obtained in the above reaction[114]. The catalyst could also be used to dimerise substrates; alkanes could be dimerised to dienes[115], esters could be dimerised as follows[116];

$$EtCO_2Me \xrightarrow{h\nu} EtCO_2(CH_2)_3CO_2Me + MeO_2C(CH_2)_4CO_2Me$$

Alkanes could be photocatalytically dehydrogenated to alkenes with H_2 evolution, although the reaction for e.g. hexane was non-specific giving a mixture of alkenes;

$$\text{Hexane} \xrightarrow[55^{\circ}C]{h\nu} \text{1-hexene + 2-hexene + 3-hexene + } H_2$$

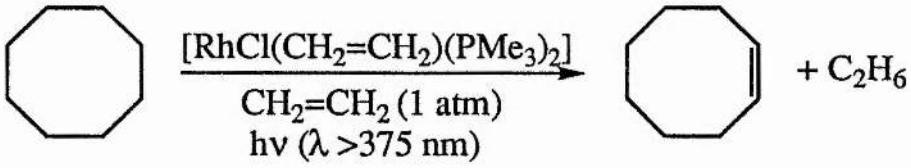
				turnovers
without PMe_3	7	77	5	5.4
with PMe_3 3hrs.	70	24	6	4.0
(P:Rh = 5:1) 22hrs.	51	40	9	18.7
with PMe_3 3hrs.	86	12	3	0.6
(P:Rh =10:1)22hrs.	67	26	7	7.2

As can be seen from the figures above, with more free PMe_3 available, a decrease in the amount of internal alkene formed was reported. If the reaction was allowed to proceed, an increase in the percentage of internal alkene was observed. This suggests that terminal alkenes initially form, but that the catalytic system is also an active isomerisation catalyst[117].

Higher rates of dehydrogenation using cyclohexane were observed (up to 200 catalytic turnovers h^{-1} at 96°C)[118].

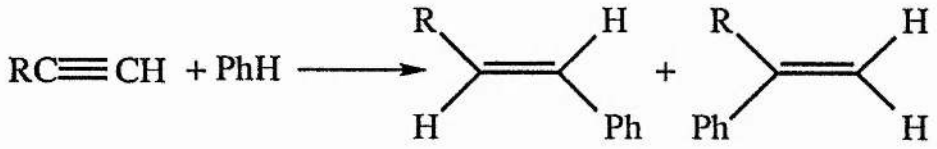
Jones and Hessel (1990), like Tanaka, showed that isocyanides could be inserted into the C-H bond of a benzene molecule under irradiation[119, 120]. $[RhCl(P^iPr_3)_2(CNR)]$ (R= neopentyl) was the best of the catalysts tried (PMe_3 and PEt_3 analogues were the only other monodentate phosphines ligands tested), but only low turnovers (0-7.7) were quoted. Surprisingly these, unlike Tanaka's catalyst $[Rh(P^nBu_3)_2(CO)(Cl)]$[111], did not promote the insertion of isocyanides into alkanes.

$[RhCl(CO)(PMe_3)_2]$ has an absorption at 360 nm. In the search for visible light assisted reactions (as opposed to UV for $[RhCl(CO)(PMe_3)_2]$), Tanaka *et al* found that $[RhCl(CH_2{=}CH_2)(PMe_3)_2]$ absorbs at 416nm and can be active for many of the previously mentioned reactions.



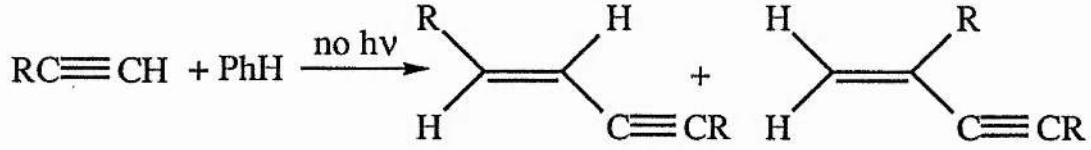
At 70°C 160 catalytic turnovers h^{-1} were observed. At 30°C it fell to 77 h^{-1}. Ethene is the sacrificial hydrogen acceptor in this reaction[121].

With the [RhCl(CO)(PMe_3)$_2$] system, Goldman and Boese found that alkynes could be inserted into the carbon-hydrogen bond of a benzene molecule[122], thus



R=			
	^{n}Pr	68%	14%
	^{t}Bu	48%	10%
	Ph	0%	90%
	$MeOC_6H_4$	0%	95%

When the above reaction is carried out in the absence of light and thermally activated at 25-50°C, then the product distribution changes to;



R=			
	^{n}Pr	37%	63%
	^{t}Bu	100%	0%
	Ph	0%	100%
	$MeOC_6H_4$	0%	100%

As can be seen the benzene plays no part in the reaction and a normal acetylene dimerisation occurs.

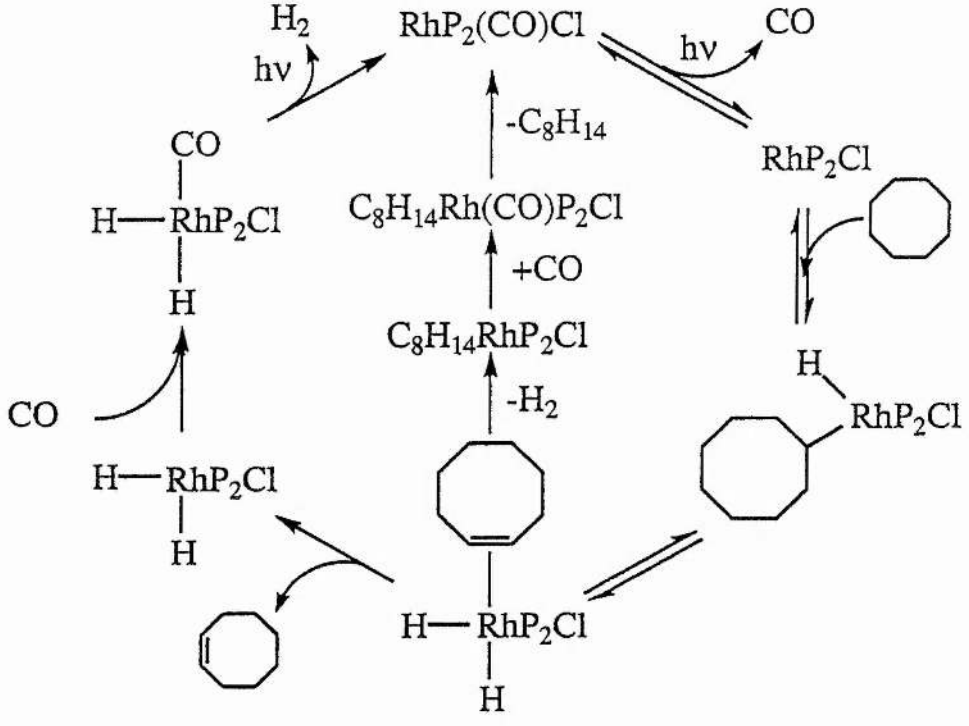
Saito and Nomura have published similar chemistry to Tanaka. They used the same catalyst [RhCl(CO)(PMe_3)$_2$] as Tanaka, but were more interested in the production of dihydrogen from alkanes. In fact Saito and Nomura (1987) were the first group to show that [RhCl(CO)(PR_3)$_2$] [R=

Me, Et, Ph] were suitable catalysts for hydrogen evolution from alkanes. The report went on to state that the rate is similar on substituting a secondary alcohol for the alkane[123].

In studies on heptane, they found that large amounts of internal alkenes were formed. They showed from subsequent experiments that there were secondary products arising from isomerisation of the initially formed terminal alkenes. High temperatures and low catalyst concentration suppressed the isomerisation, suggesting that alkene coordination to the metal centre was a necessary prerequisite[124, 125, 126].

Goldman *et al* were also attracted to this field, again for alkane activation. They showed considerable interest in the mechanistic side of the same system, due to the suggestion that one of the active intermediates is a 16 electron alkyl complex.

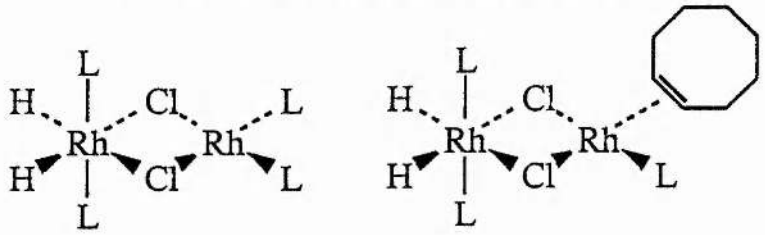
Whereas Tanaka proposes that just the initial catalytic species $[RhCl(PMe_3)_2]$ is photogenerated. Goldman *et al* proposed a mechanism[127, 128] that involved two photochemical steps, CO loss and photoextrusion of hydrogen gas . Goldman's proposed mechanism runs as follows ;



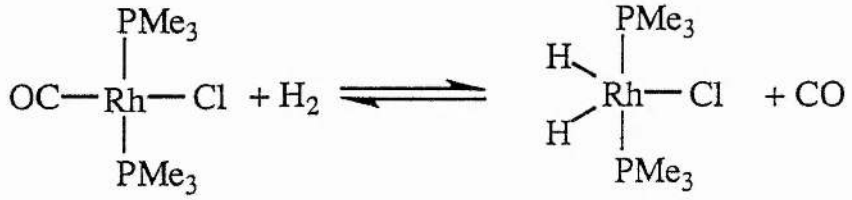
The transfer hydrogenation mechanism was also probed with D_2 to see if hydrogen gas was first being released then reincorporated into the

catalyst for the subsequent hydrogenation of the acceptor, but no significant hydrogen scrambling was reported.

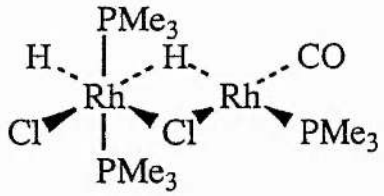
Further work has been carried out on the mechanism by Goldman and Shih. They explored the stoichiometric addition of alkane to the catalyst [Rh(P^iPr_3)$_2$Cl]. On probing the resulting solution using nmr, they found [RhL_2ClH_2], [RhL_2Cl_2H] (L= P^iPr_3) and four dimers, two of which are shown below; the other two were not fully characterised[129].



Goldman in conjunction with Eisenberg and Duckett probed this further using para-hydrogen induced polarisation and nmr[130]. This technique is especially sensitive to metal hydrides, giving up to 200 times improvement in signal-to-noise ratio over non-enriched hydrogen. They investigated the equilibrium;

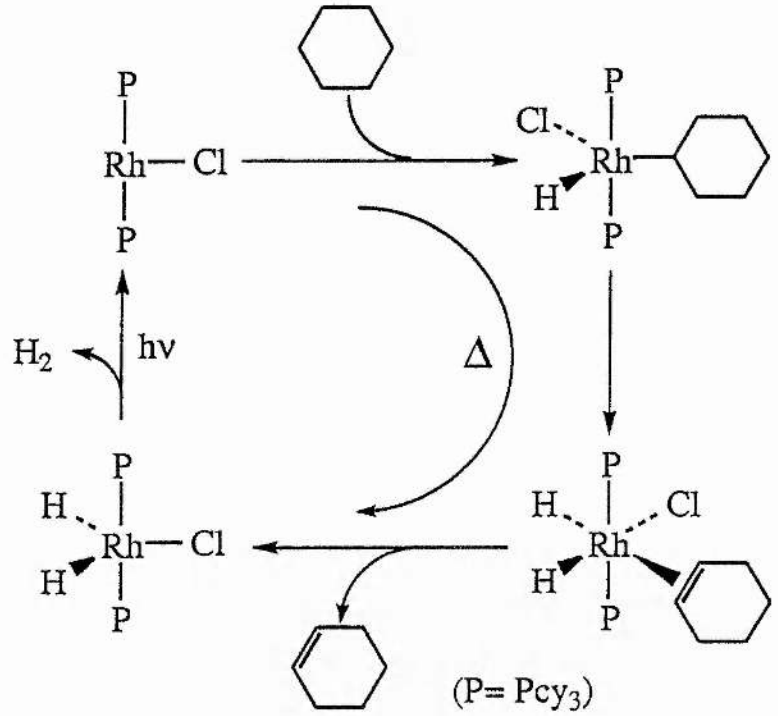


And on the basis of the study they found that other species were also formed these included [Rh(H)$_2$(PMe_3)$_3$Cl)] and



This is an important observation, because [RhClCO(PMe_3)] (3 coordinate, 14e$^-$, Rh^I) and [$RhH_2Cl(PMe_3)_2$] (5 coordinate, 16e$^-$, Rh^{III}), are very reactive and both are incipiently stabilised by the formation of the dimer. It poses the question as to how often reaction catalytic intermediates may be stabilised in this way.

Later Saito, this time with Murayama and Itagaki (1994) showed that cyclohexane gave cyclohexene and H_2 under irradiation using $[RhCl(Pcy_3)_2]$. They entered the mechanistic debate by proving that no H_2 evolution occured without irradiation, and the only step that required irradiation was the loss of H_2. The mechanism they propose is shown below[131].



1.6.2 Concluding remarks on photochemical reactions

Carbon-hydrogen bond activation may be possibly the most important reaction that rhodium/ trialkylphosphine complexes catalyse. In just seven years a large number of transformations have been carried out using the normally chemically inert alkanes, displaying remarkable selectivity.

This suggests that the photochemical C-H activation of alkanes may have the potential to be converted into commercial processes, indeed several patents have already appeared in the chemical literature dealing with this system. The big drawback is the low turnover of most systems examined, although respectable rates of 200 turnovers h^{-1} have been observed in favourable cases.

1.7 Miscellaneous Reactions

1.7.1a Water Gas Shift Reaction (WGSR) and related Chemistry

The reaction revolves around the equilibrium shown below;

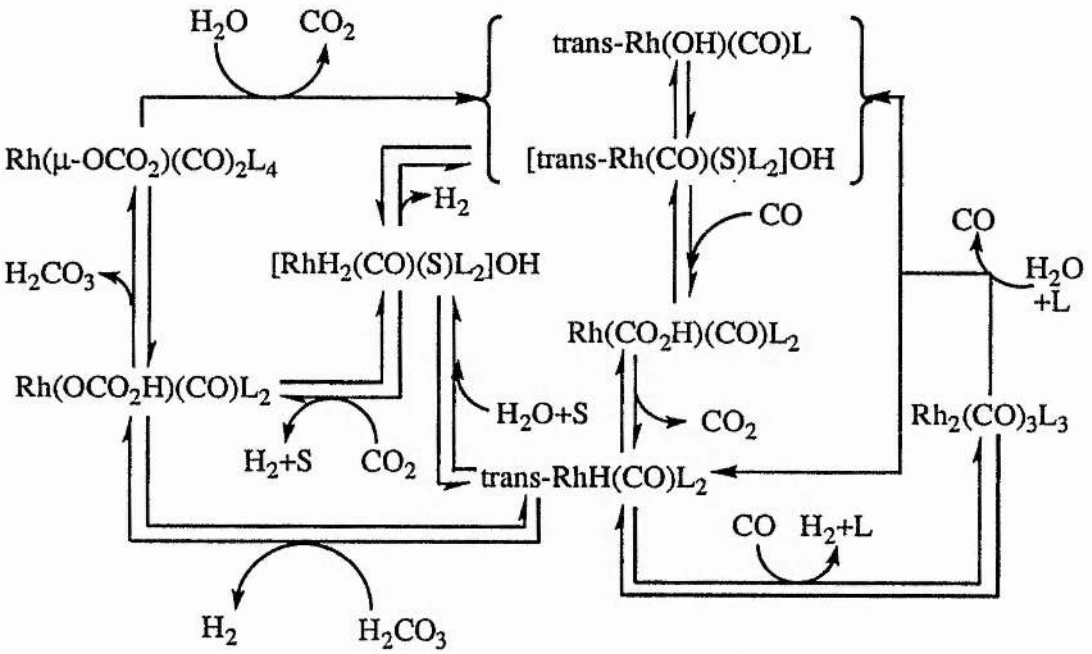
$$CO + H_2O \rightleftharpoons CO_2 + H_2$$

It is an attractive reaction due to its potential for the production of hydrogen from coal. The thermodynamics of the above equilibrium are such that the lower the temperature, the further to the right the equilibrium lies. Without a catalyst present the reaction is extremly slow.

The late seventies/ early eighties saw considerable work on various homogeneous metal systems to catalyse the above[132]. The advantage over heterogeneous systems that do the same is the ability to work at much lower temperatures. Working with liquid water changes the thermodynamics so that the equilibrium lies much more to the right. ∴ temperatures of < 100°C are preferred. Heterogeneous systems work with gaseous reagents.

Yoshida and Otsuka *et al* produced the first big breakthrough by finding that $[RhHL_3]$ (L=PEt_3, P^iPr_3), $[Rh_2H_2(\mu\text{-}H_2)(Pcy_3)_4]$, trans-$[RhH(N_2)\{PPh(^tBu)_2\}_2]$ and $[RhH(P^tBu_3)_2]$ all served as catalytic precursors for the WGSR under relatively mild conditions (100°C > T > 50°C).

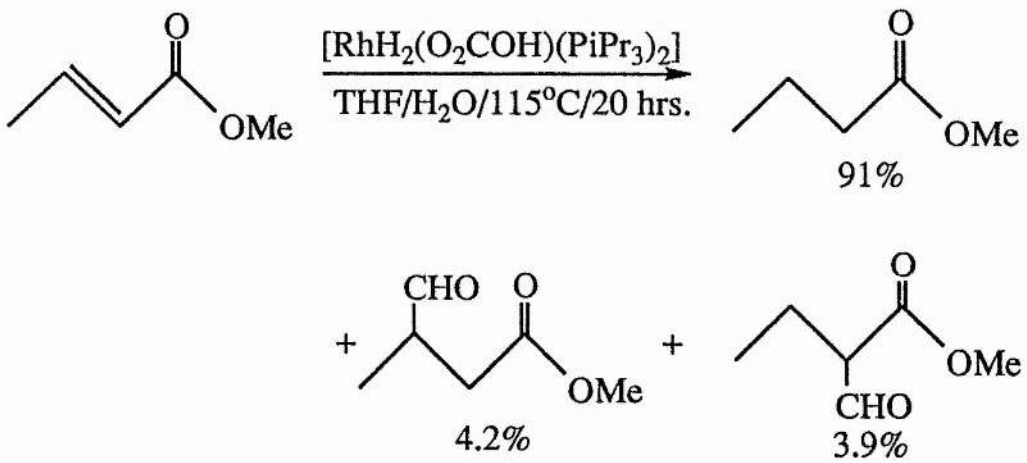
Using model studies and by isolating various intermediates using different ligands and solvents, they were able to propose a mechanism[132], thus;



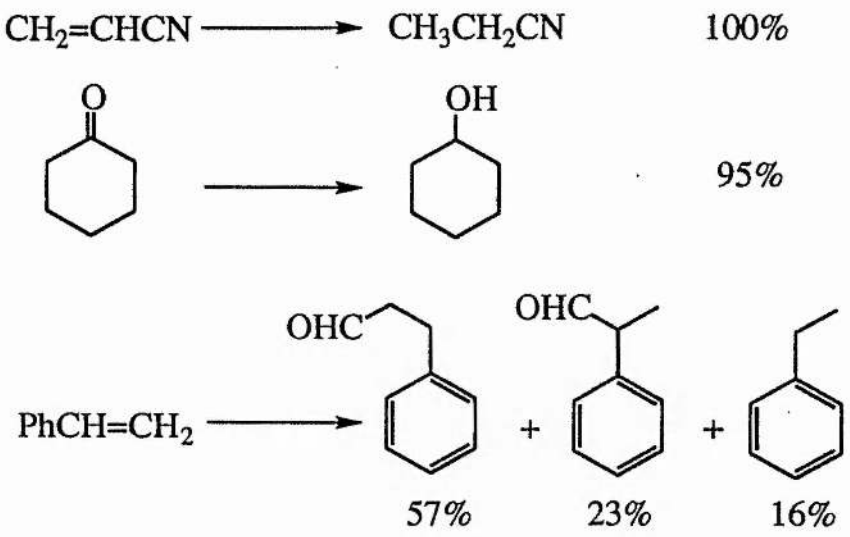
L=P^{i}Pr$_3$, S=solvent

Okano and Kiji showed that WGSR chemistry could be used in such a way that water could be a H_2 source for a variety of reactions. So alkenes could be hydrogenated and/or hydroformylated. Aldehydes and ketones could also be hydrogenated.

In a typical reaction;

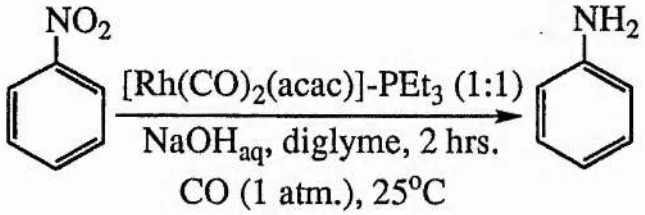


They also demonstrated the following transformations, under similar conditions[133];



Nomura, Ishano and Hazama (Sumitomo Chemicals, 1991) produced an elegant reaction using a $[Rh(CO)_2(acac)]$ -phosphine system to catalyse CO/H_2O to reduce aromatic nitro compounds to amines.

The system was especially active when the phosphine was PEt_2Ph or PEt_3.



The catalytic turnover in the above system was 241. On rising the temperature to 50°C, the turnover became 861 in the same time frame. Substituted nitro compounds could also be reduced, e.g. p-chloronitrobenzene could be reduced to p-chloroaniline in > 99% selectivity[134, 135].

1.7.1b Dihydrogen Generation

Otsuka, Yoshida and Okano (1980) published work on the possibility of catalysing hydrogen production from water using tralkylphosphine rhodium compounds[136]. They showed that water added to $[RhHL_3]$ (L= P^iPr_3) in pyridine gave a cationic dihydride complex $[RhH_2(py)_2L_2]^+$ with OH^- as a counter anion. Addition of ^{t}BuNC or CO liberated H_2 from this complex when in THF, leaving

$[Rh(CO)(py)L_2]^+OH^-$ (in the case of using CO). Further addition of CO causes the loss of CO_2. The resulting complex can again take on water, so WGSR chemistry is observed.

Cole-Hamilton and Jones (1981) also showed that H_2 production from $[RhHL_3]$ (L= P^iPr_3) was a possibility, this time from acidic aqueous solution. H_2 production was rapid on irradiation[137].

Cole-Hamilton *et al* in a review on the role of noble metal hydrides in H_2 production added that the irradiation of the above occured in the visible region. In the review it was also stated that $[RhH(PEt_3)_3]$ generates H_2 on heating the complex in dilute acids (such as sulphuric or phosphoric)[138].

Delgado-Leita, Luke, Jones and Cole-Hamilton (1982) showed that $[RhH(P^iPr_3)_3]$ and $[RhH(CO)(P^iPr_3)_2]$ are capable of producing H_2, CO and RH from primary alcohols under irradiation. If secondary alcohols are used, ketones are formed along with H_2. If the last reaction is done in the absence of light, but in the presence of 1-hexene, then hydrogen transfer occurs producing ketone and hexane[139].

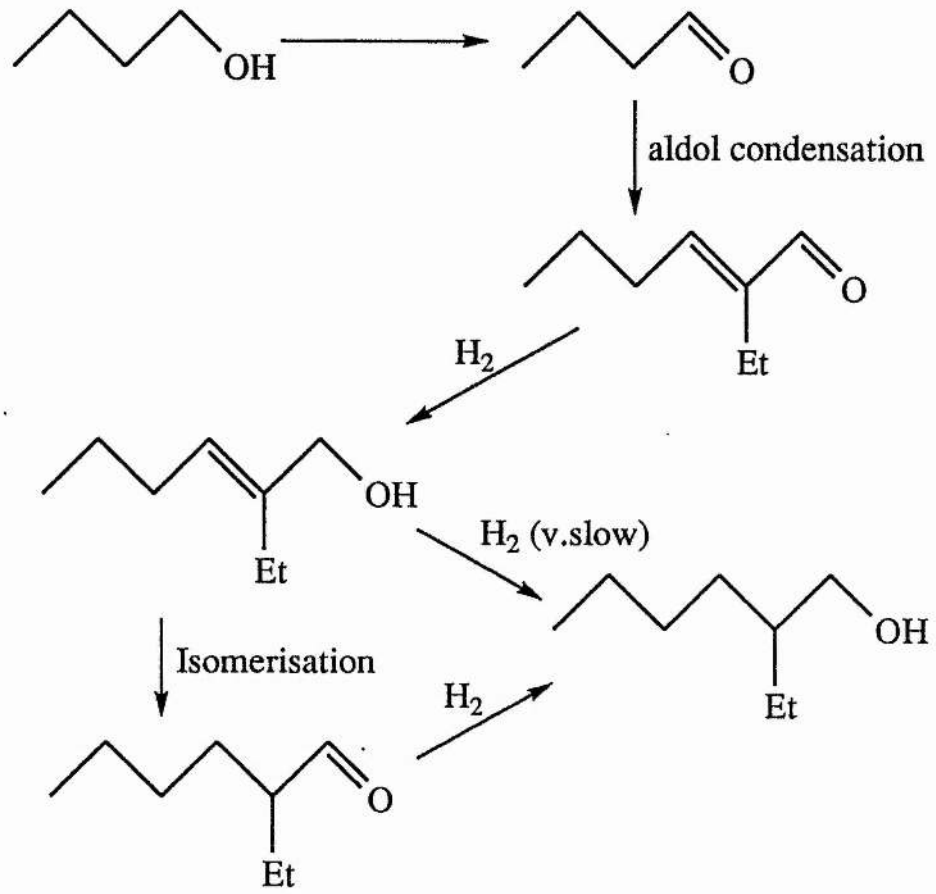
In 1987 Morton, Cole-Hamilton, Schofield and Pryce reported that rapid hydrogen production could be achieved, thermally, from 2,3-butanediol. 2,3-butanediol is easily obtainable from fermentation reactions. $[RhH(P^iPr_3)_3]$ could produce hydrogen at rates of 66 turnovers an hour, but $[RhCl(PPh_3)_3]$ and $[Rh(bipy)_2]Cl$ were both about twice as active[140]. In a full paper published on the above, platinum and ruthenium catalysts were compared with rhodium ones. $[Rh(bipy)_2]Cl$ and $[RuH_2(N_2)(PPh_3)_3]$ turned out to be the two most successful[141].

1.7.2 Dimerisation and Condensation Reactions

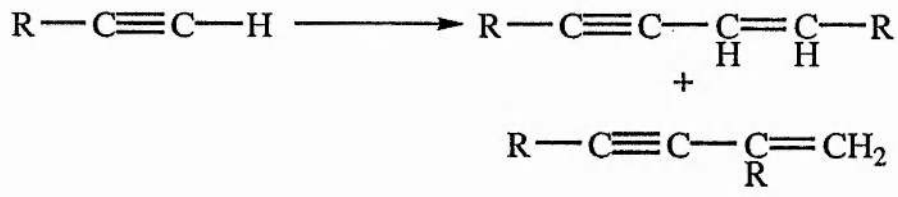
Pregalia and Gregorio published a patent (with Conti, 1968) and a paper (with Ugo, 1972) on the condensation of alcohols by rhodium/ trialkylphosphine systems[142, 143]. The reason why this was attempted was to try to model the same reaction that occurs under heterogeneous conditions.

This reaction is of particular importance since it allows the formation of e.g. the commercially important plasticiser, 2-ethylhexanol in one step from butanol, whilst the usual procedure involves the aldol condensation of butanal followed by hydrogenation. Either butanal or butanol are available from hydroformylation reactions.

The transformation was performed over $[Rh(CO)_2Cl]_2$/ $8PEt_3$ or $RhCl_3.3H_2O$/ $4P^nBu_3$. The yields were generally 85-90%. The proposed route is as follows;



Yoshikawa, Kiji and Furukawa (1977) published a paper on alkyne dimerisation[144]. The effects on linear/branched dimer formation were explored (as shown below).



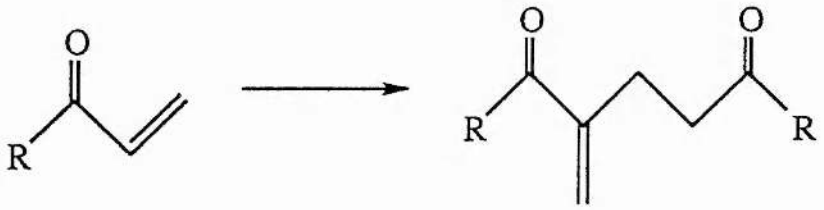
Rhodium compounds (e.g. $[RhCl(PPh_3)_3]$) had been previously shown to be active catalysts for reaction[145, 146]. Eighteen different phosphines were studied (using $[Rh_2Cl_2(C_8H_{14})_4]$ as catalyst precursor). There included P^nBu_3 and Pcy_3. P^nBu_3 yielded 30.8% (selectivity was ~3:1 branched to straight chain dimer) at 92°C (15 hours) and 45.7% at

110°C (10 hours), these results were amongst the best quoted. Pcy_3 managed less than 5% under both sets of conditions mentioned for P^nBu_3.

The conclusions drawn from the study were that electron donating ligands promoted the formation of linear product (P^nBu_3 one of two that were very good) unless they were very bulky (> 160°) then they favoured formation of branched product, due to steric hindrance.

Vinogradov *et al* looked at various dimerisation reactions catalysed by $[RhCl(PMe_3)_3]$[147],one of these being alkyne dimerisation. They showed that various terminal alkynes could be dimerised in 77-85% conversion (95-98% of the product being dimer), the selectivity (linear/branched) was 1.4-2.4. Aromatic and branched alkyl alkynes were not activated in this system. The work also included nmr experiments used to elucidate a mechanism for the reaction.

The same group published work on the dimerisation of methyl vinyl ketone using $[RhCl(PMe_3)_3]$[148, 149].



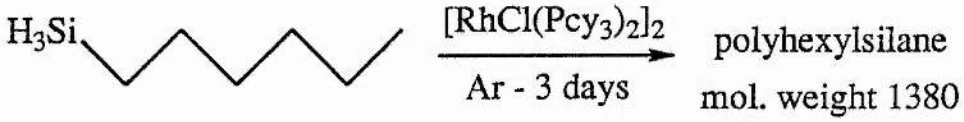
Again they use nmr to probe the mechanism, but the mechanism for this is more tentative and is still under investigation.

1.7.3 Oligomerisation and Polymerisation Reactions

Takesada, Yamasaki and Hagihara (1968) reported that $[Rh(COD)(PEt_3)Cl]$ catalysed the polymerisation of methylacetylene and phenylacetylene to linear polymers at room temperature. The complex was not as effective as $[Rh(COD)(PPh_3)Cl]$ and $[Rh(COD)(PPh_3)Ph]$[150].

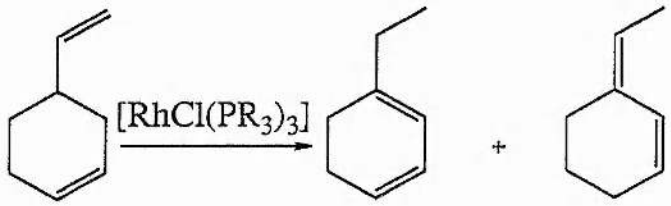
A brief mention of cyclooligomerisation of alkynes using [Rh(1,5-hexadiene)Cl]$_2$ and PMe_3 was made in a publication by Springer, Klinger and Wendt (1991). The only data disclosed in the abstract was that phenylacetylene could be dimerised to give products that had a linear: branched ratio of 5:4[151].

Berris, Diefebach and Steven (Ethyl corp.) patented the synthesis of polysilanes for use in solar cells by the polymerisation of 1-silylhexane[152]. So;



1.7.4 Isomerisation Reactions

Isomerisation is quite often observed in rhodium/ trialkylphosphine systems whilst accomplishing other reactions. Surprisingly there are only a few examples where trialkylphosphine/ rhodium system are used for isomerisation alone. In the catalysed isomerisation of vinylcyclohex-3-ene[153], a mixture of two products was obtained, ethyl-1,3-cyclohexadiene and ethylidenecyclohexene. Two catalyst were examined for this transformation, $[RhCl(PR_3)_3]$, (R= Ph, $^iPr_3$). P^iPr_3 was the more active and selective.



No selectivity or conversion data given.

Blum, Schumann *et al* (1984) using $[Rh_2(CO)_2(P^tBu_3)_2Cl(SR)]$ (R= alkyl or (un)substituted phenyl group) as the catalyst, found that they could isomerise1-octen-3-ol, 4-allylanisole and trans-stilbene oxide into 3-octanone, cis/ trans-4-(1-propenyl)anisole and deoxybenzoin respectively, often in 100% conversion[73].

1.7.5 Alcoholysis of Silanes

Corriu and Moreau used rhodium based catalysts to react secondary alcohols with silanes[154]. The aim of this work was to make trifunctional silanes with different substituents to induce chirality. The first step of this

method was to use a rhodium catalyst to obtain monosubstitution on the silane.

$$\underset{1 \;:\; 1}{RSiH_3 + {}^{i}PrOH} \xrightarrow[C_6H_6]{[RhCl(Pcy_3)_2]} \underset{36\%}{RSi(O^{i}Pr)H_2} + \underset{64\%}{RSi(O^{i}Pr)_2H} + H_2$$

R= α-napthyl

The same result were obtained using acetone instead of isopropanol. The catalyst featured above was as good as any tested. Most of the reactions were carried out using Wilkinson's catalyst.

A chiral silane was produced, but it failed to give any significant chirality in the products obtained from hydrosilation reactions attempted with it.

1.7.6 Hydrogenolysis of Haloarenes

Grushin and Alper (1990) published work using $[RhL_2(H)Cl_2]$ (L= Pcy_3, $P^{i}Pr_3$) under biphasic (or phase transfer) conditions for the dehalogenation of aromatic chlorides[155]. Initially the catalyst loses HCl to form $[RhL_2CL]$, the active species. The general conditions are shown below for a typical transformation;

$$RCl + H_2 \xrightarrow[40\%\ NaOH,\ PhCH_2N(C_2H_5)_3{}^{+}Cl^{-}]{[Rh(H)(Pcy_3)_2Cl_2],\ toluene} RH + HCl$$

R is an aromatic ring, with or without other functional groups. Chlorobenzene produces benzene in 100% yield and 97% conversion in 24 hours at 25°C. Substituted aromatics need to be reacted at elevated temperatures to attain similar conversions.

1.7.7 Ketone Production

Eaborn, Pidcock and Dent (1970) found a novel reaction using $[RhCl(CO)(PEt_3)_2]$ to form aldehydes and ketones from benzoylchlorides in the presence of triethylsilane[156]. Yields of 27% ketone and 4%

aldehyde were produced. It was suggested that these products arise from reductive elimination of various catalytic intermediates.

1.7.8 H-D Exchange Reactions

As part of their work on dihydrogen production Otsuka, Yoshida, Okano and Saito (1980) reported that $[RhH(P^iPr_3)_2]$ and $[Rh_2H_2(\mu\text{-}N_2)(Pcy_3)_4]$ were both capable of exchanging D for H on a benzene ring using D_2O as the hydrogen source[157]. The systems were active enough to incorporate D into the methyl group of toluene, as well as the aromatic positions.

In 1990 Grushin, Vymenits and Vol'pin also published some work on H-D exchange between gaseous H_2 and aromatic compounds such as d_6-benzene or d_8-toluene. The reaction was catalysed by $[L_2Rh(H)Cl_2]$ (L = P^iPr_3 or Pcy_3) with KOH as co-catalyst. No data on the extent of exchange was mentioned in the abstract[158].

1.7.9 Synthesis of Trisubstituted Alkenes

The title reaction was found accidentally during attempts to synthesise rhodium carbene complexes by Wolf, Brandt, Fries and Werner[159]. Overall the reaction concerns the coupling of a diazo compound with an alkene (ethene or monosubstituted) to generate the above mentioned trisubstituted alkenes. Four catalysts were found to be active for this reaction, trans-$[MCl(=CRR')(P^iPr_3)_2]$ (M = Ir, Rh), $[RhCl(P^iPr_3)_2]$ and trans-$[RhCl(=CH_2)(P^iPr_3)_2]$. An example of the reaction is shown in the scheme below;

$$N{=}N{=}CRR' + C_2H_3R'' \xrightarrow{[RhCl(P^iPr_3)_2]} RR'C{=}CHCH_2R''$$

Turnover numbers can be as high as 515. For example 9-diazofluorene can be coupled with ethene, propene or styrene. Another example is diphenyldiazomethane coupling with ethene to give 1,1-diphenylpropene.

1.8 Concluding Remarks

Rhodium/ trialkylphosphine complexes prove to be very versatile in most fields associated with homogeneous catalysis.

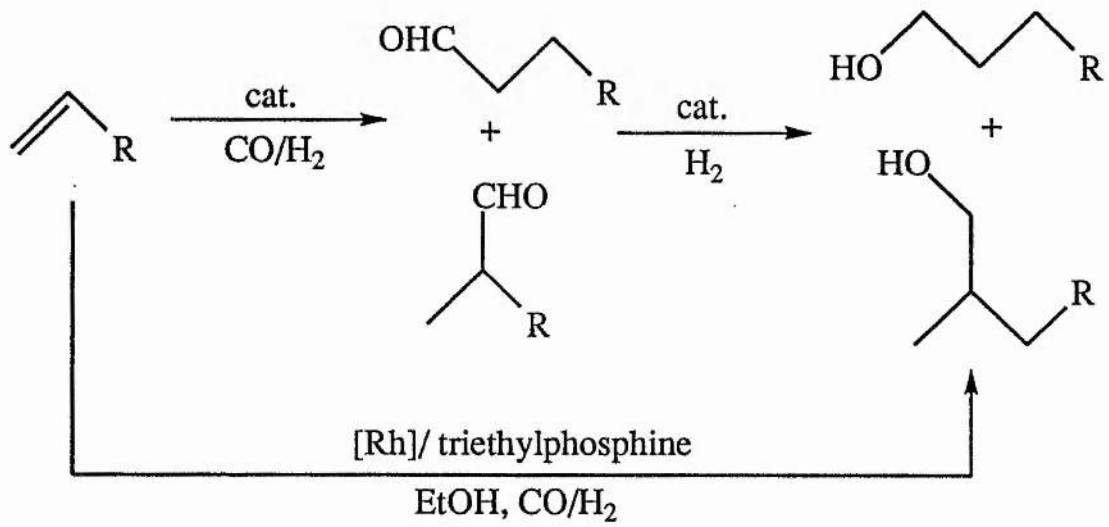
Generally the equivalent rhodium triarylphosphine systems will carry out the same reaction in similar or better yields. But trialkyphosphine ligands in rhodium based systems prove to be much more active than other systems in such transformations as carbonyl hydrogenation, hydrogen transfer, WGSR, one step alkene to alcohol conversions and C-H bond activation, the latter being of immense interest to many chemists.

These systems are aided by the basicity of the phosphine ligands, allowing the rhodium catalytic centre to be richer in electon density than if other phosphines (or equivalent ligands e.g. phosphites) are used. This extra electron density allows certain catalytic steps to proceed easier, such as oxidative addition, protonation etc.

Chapter 2 - Reactions Involving 2-propen-1-ol as Substrate

2.1 Introduction

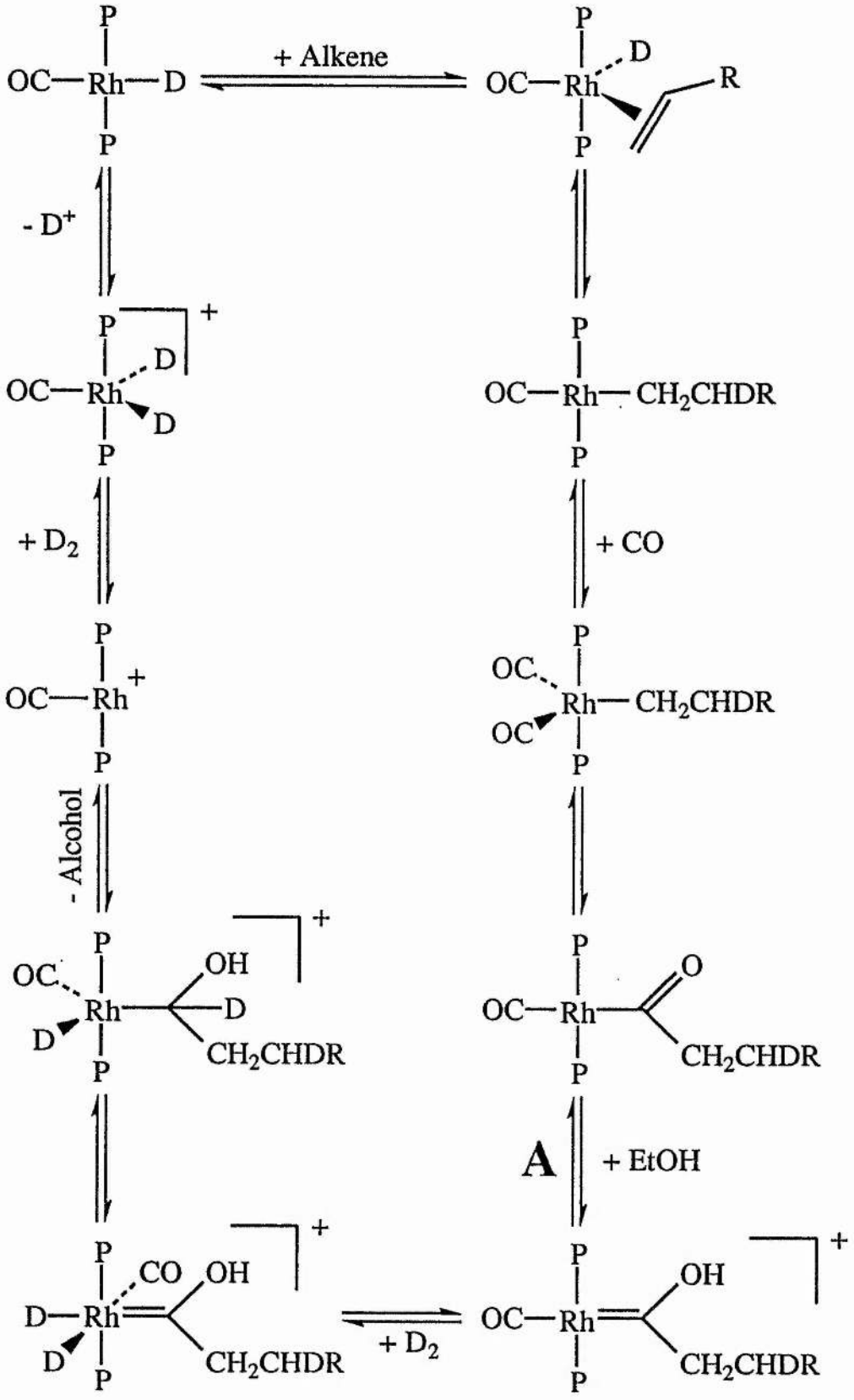
Recent work by MacDougall and Cole-Hamilton showed that using rhodium catalysts containing trialkylphosphines, in alcoholic solvents (MeOH, EtOH, ^{i}PrOH, ^{t}BuOH), hex-1-ene could be hydrocarbonylated directly to heptan-1-ol and 2-methylhexan-1-ol[16]. Labelling studies showed that the relevant aldehydes are not intermediates in this reaction and a mechanism was proposed which led directly to $C_{(n+1)}$ straight and branched chain alcohols in just one step, as opposed to the conventional two step process which proceeds via hydroformylation to aldehydic products, followed by a subsequent hydrogenation reaction. Scheme 2.1 summarises these two routes.



Scheme 2.1 - Conventional (upper) route and MacDougall/ Cole-Hamilton (lower) route for the transformation of terminal alkenes to $C_{(n+1)}$ alcohols.

The mechanism for the hydrohydroxymethylation reaction (the MacDougall/ Cole-Hamilton route) is shown in scheme 2.2.

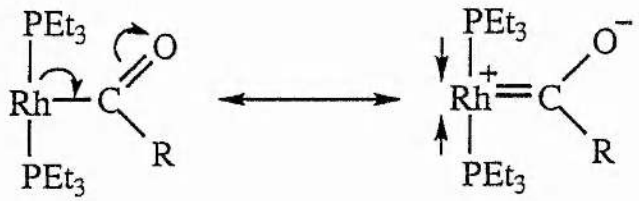
The mechanism has its basis on a standard hydroformylation mechanism until step A is encountered. Step A shows the protonation of the acyl oxygen, forming a hydroxycarbene species, which can then



Scheme 2.2 - Proposed Hydrohydroxymethylation mechanism

undergo oxidative addition of hydrogen. Two hydrogen atom migrations leads to reductive elimination of the alcohol. For this mechanism to operate it is essential to have a mild proton source present, normally the solvent. Without this the conventional route would be followed leading to the formation of aldehydes. This indeed is observed when ethanol is replaced with a non-protic solvent in the MacDougall/Cole-Hamilton system, although hydrogenation of the formed aldehydes to give some alcohol does occur, at least in tetrahydrofuran[56].

The protonation of the acyl group is very sensitive to what phosphine is used. Only PMe_3, PEt_3 and P^nBu_3 seem to promote this effect. This fact is attributed to the greater electron donating effect of trialkylphosphines compared to e.g. PPh_3. Because the phosphine is donating electron density to the molecule, this leads to a build up of negative charge on the acyl oxygen atom. This would aid protonation of the acyl oxygen. A diagrammatic representation is shown in scheme 2.3.



Scheme 2.3 - Possible electronic stabilisation in the catalyst

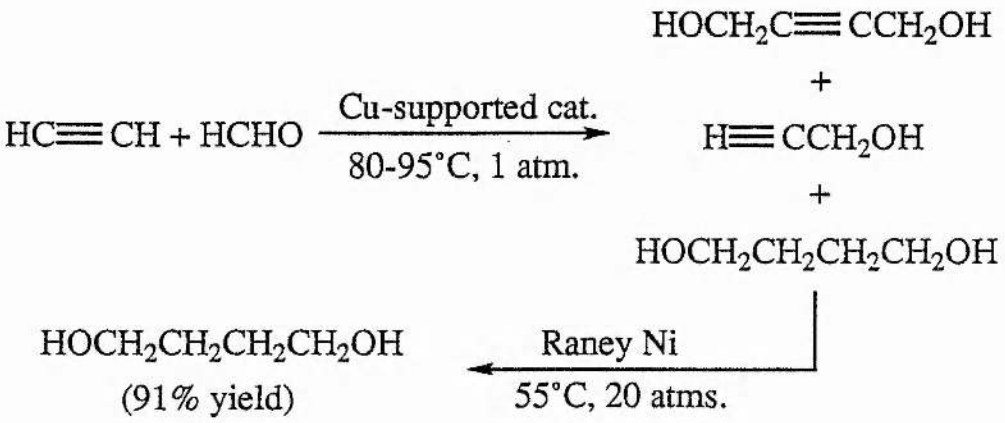
It was of considerable interest to extend this reaction to functionalised alkenes. One of the most attractive of these being 2-propen-1-ol which could produce 1,4-butanediol. Since the aldehydes derived from hydroformylation of 2-propen-1-ol are not the desired product and may be unstable with respect to possible dehydration, cyclisation or condensation reactions, a catalytic process which converted 2-propen-1-ol to 1,4-butanediol in one step would be highly desirable.

1,4-butanediol has many applications ranging from being a precursor for polymers such as polyurethanes and polyesters (due to its bifunctionality), to the synthesis of tetrahydrofuran and butyrolactone. Tetrahydrofuran is a common solvent used in many chemical processes, whereas butyrolactone is used in polymer production or as a speciality polymer solvent.

2.1.1 Methods of 1,4-butanediol production

In this section, modern methods for 1,4-butanediol synthesis, on an industrial scale are reviewed together with advances in laboratory based synthesis. A recent article (1991) by Brownstein[160] shows the current technologies that are employed by industry (in the U.S.) for the production of 1,4-butanediol and tetrahydrofuran.

The oldest technology and still the one that supplies the majority of the world demand is based on the Reppe reaction. It was developed in the late 1940's. The outline of the process is shown in scheme 2.4[161].

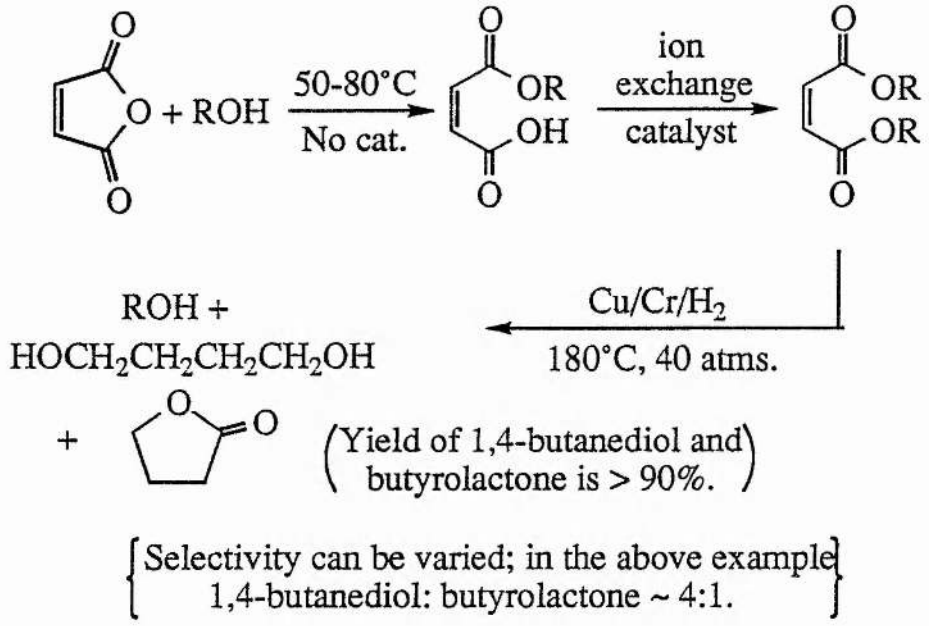


Scheme 2.4 - Outline of Reppe chemistry to produce 1,4-butanediol

The obvious disadvantage of this process is the need to handle acetylene, this coupled with the high cost of acetylene in some places around the world (e.g. Japan), has prompted considerable research into alternative methods.

One of the up and coming technologies which has been commercialised in Japan is maleic anhydride hydrogenation, normally via conversion of the anhydride into a diester. This is summarised in scheme 2.5.

One of the big disadvantages of this process is the (relatively) high cost of the starting material. In the chemical literature maleic or succinic acids/ anhydrides have received much attention and homogeneous systems (Ru modified with phosphines)[162] as well as heterogeneous systems (e.g. Re, Cu and Zn containing catalyst)[163, 164] are now known for this transformation. These hydrogenations are all quoted as proceeding in high yield (> 90%).



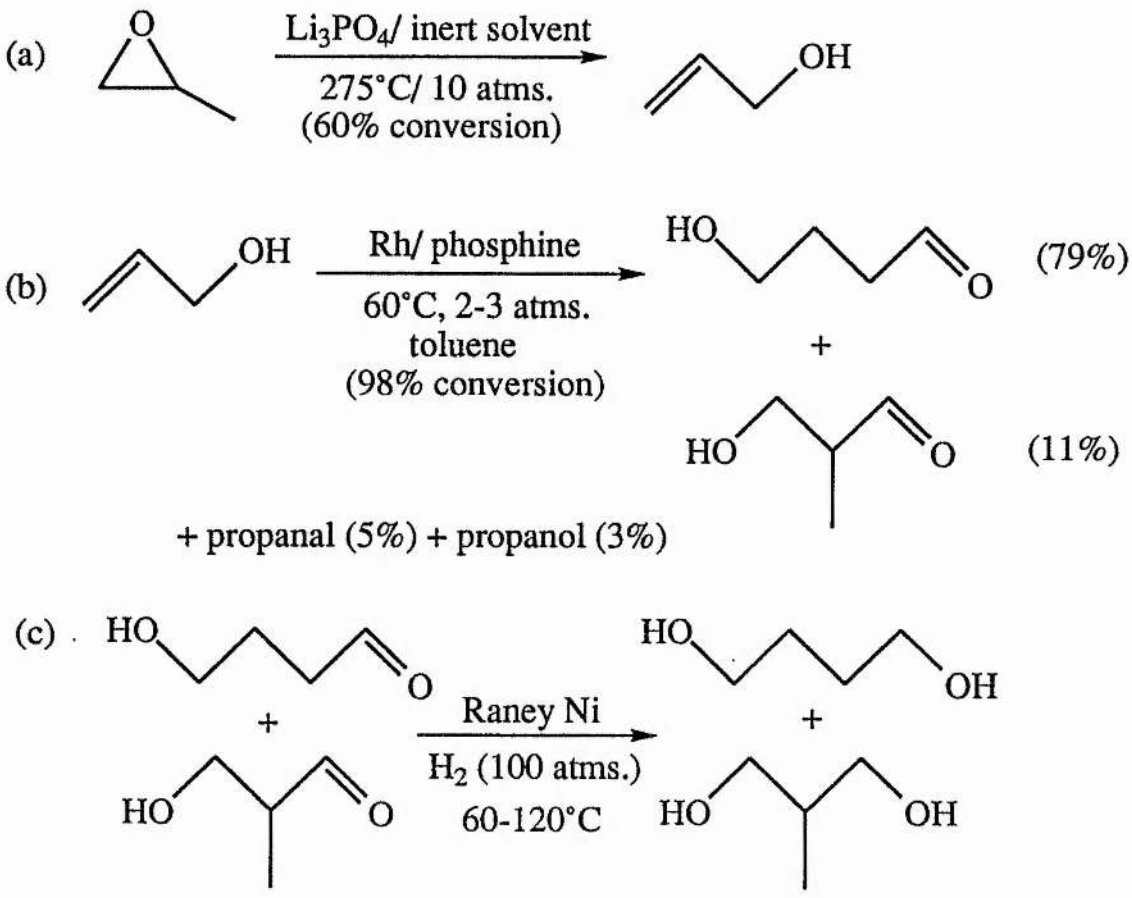
Scheme 2.5 - Outline of maleic anhydride hydrogenation.

In the U.S. a plant has recently been built which produces 1,4-butanediol from propene oxide. This technology is licensed from Kuraray[165, 166], and is known as the Kuraray process. This technology is currently the best available involving 2-propen-1-ol[167]. The process is illustrated in scheme 2.6.

The Kuraray process does suffer from some problems, namely to do with side reactions and separation.

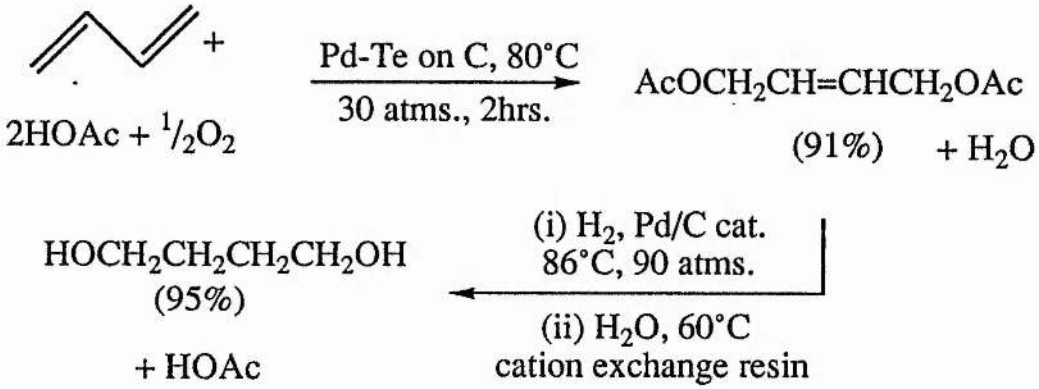
The separation problem comes at the very end when the diols have to be steam distilled under reduced pressure, not the most convenient separation to carry out on a large scale.

The side reactions can occur with the intermediate aldehydes. Such side reactions as aldol condensations, dehydrations and acetal formation can all decrease the yield of the desired 1,4-butanediol.



Scheme 2.6 - Outline of the Kuraray process.

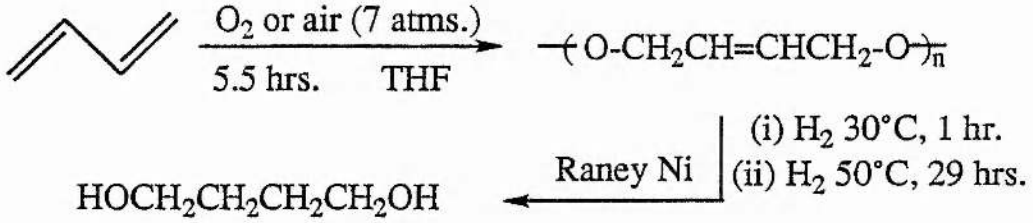
Much research has been done on other processes for the production of 1,4-butanediol. One of the more attractive for the large scale production of 1,4-butanediol is the acetoxylation of butadiene[168]. See scheme 2.7 for a brief outline.



Scheme 2.7 - Butadiene acetoxylation to give 1,4-butanediol

This process gives excellent selectivity to the branched chain product, but the catalyst lifetime tends to be short.

Butadiene is also used in another process for 1,4-butanediol production. It is oxidised up to a peroxybutene polymer, which is then hydrogenated over Raney nickel to give 1,4-butanediol (30%) along with 1,2-butanediol and 1,2-butenediol. Scheme 2.8 gives an outline.



Scheme 2.8 - Butadiene oxidation to give 1,4-butanediol

The major drawback, which has deterred most research in this area is the highly explosive nature of the peroxy-polymer. The nickel catalyst also suffers from a very short lifetime.

An interesting (but not yet commercially viable) route is the biological production of 1,4-butanediol from sugars using various enzymes (e.g. Rhizopus arrhizus). It is suggested that intermediates in these breakdowns are C_4 carboxylic acids[169].

Butyrolactone (which along with tetrahydrofuran are the two major products produced from 1,4-butanediol), can be hydrogenated back to 1,4-butanediol. This process can be carried out with a variety of catalysts, normally heterogeneous in nature, in high conversion (90%) and selectivity (95%)[170, 171]. Another material which can be hydrogenated to give 1,4-butanediol is 1,4-butynediol. This is one of the reactions that occurs in the Reppe process (scheme 2.4). Again this can occur in high yield (98%) over a range of catalysts[172].

Hydroformylation of 2,3-dihydrofuran to give 4-hydroxybutanal and 2-hydroxytetrahydrofuran catalysed by $[HRu(CO)(Cl)(PPh_3)_3]$ has been patented. The product mixture can then be hydrogenated over Raney nickel to produce 1,4-butanediol (> 80% yield)[173].

As mentioned earlier 2-propen-1-ol hydroformylation is an important step of a commercial route to 1,4-butanediol (the Kuraray process). Section 1.2 of this thesis deals with some rhodium/ phosphine systems which can also effect this transformation. Recently a review[165]

on "Advances in the hydroformylation of olefins containing functional groups", mentions most papers of interest up to 1987. One paper from that review which deserves a more detailed mention is by Pittman Jnr. and Honnick[174]. They worked with rhodium/ PPh_3 systems, some supported on resins and some with other added phosphine ligands. Conversions of up to 100% were reported and selectivities to aldehydes were also near 100%. The n:i ratio was between 1.5-4.7:1 in all cases.

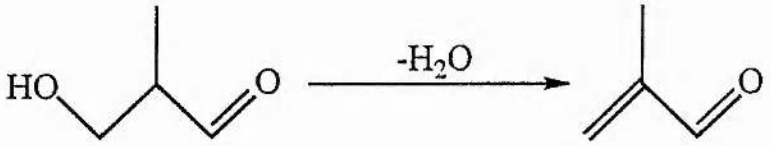
Kaneda, Imanaka and Teranishi reported that amine modified $Rh_6(CO)_{16}$ clusters were capable of catalysing water gas shift reactions. They utilised these to effect hydroformylation of 2-propen-1-ol using CO/H_2O and could produce 1,4-butanediol directly in 72% yield, with no trace of C_4 aldehydes nor of the expected branched chain product 2-methyl-1,3-propanediol. The other products of this reaction are propan-1-ol (17%), propanal (1%) and butyrolactone (8%). When a bidentate amine is used 1,4-butanediol is the major product. If a monodentate amine is used butyrolactone is the major product[175]. Butyrolactone is produced via an intramolecular cyclisation of a metal acyl species. It is suggested that an extra coordination site is needed for this to happen, so the bidentate ligand suppresses this by not freeing an extra site as easily as the monodentate amine.

Other metals have been explored, a recent example is the Ru-EDTA system developed by Taqui Khan. Again it utilises CO/H_2 from WGSR chemistry to hydroformylate 2-propen-1-ol. Products from this reaction are 4-hydroxybutanal (35%), butyrolactone (25%), 2,3-dihydrofuran (25%), 1,4-butanediol (1%) and a trace of formaldehyde[176].

Some advances on the Kuraray technology have been reported in the literature. Deshpande *et al* claim that if the reaction is carried out in long chain alcohols, higher selectivity to the straight chain product is observed and the overall reaction rate was higher. The best alcohol quoted was 1-octanol, which gave 99.2% conversion in 46 minutes (~1000 turnovers) with the n:i ratio being 15.2:1. 'Other products' make up 4% of the final reaction mixture[177].

The same group also published work on this catalytic system but this time under biphasic conditions[178]. They demonstrated that the catalyst could be recycled with higher efficiency than the normal homogeneous system and with a lower loss of activity in subsequent reactor runs. In their article it is suggested that interaction of aldehyde intermediates with the rhodium complex deactivates the catalyst, but this is minimised in a

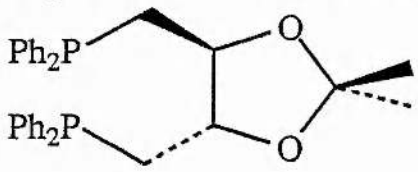
biphasic system, hence the higher activity. This is not a new suggestion. Kuraray Corp. have also released some results showing that α,β-unsaturated aldehydes inhibit the hydroformylation reaction[179]. But diphosphines dramatically reduce this effect. The α,β-unsaturated aldehyde is produced from the unstable 3-hydroxy-2-methylpropanal dehydrating to 2-methylpropanal. This is displayed in scheme 2.9.



Scheme 2.9 - The dehydration of 3-hydroxy-2-methylpropanal.

Bryant and Abatjoglou have also studied the Kuraray process. They suggest that phosphonium compounds and $OPPh_3$ deactivate the catalyst, along with the 2-methyl-2-propanal, but the phosphonium species are washed away when the water extraction, an integral part of the process, is carried out[180].

Maki, Fujita and Murumo (Showa Denko K. K.) have made use of some bidentate phosphines to modify $[HRh(CO)(PPh_3)_3]$. Using trans-4,5-bis[(diphenylphosphino)methyl]-2,2-dimethyl-1,3-dioxolane (scheme 2.10), 96% conversions of 2-propen-1-ol gave 2-hydroxytetrahydrofuran (86%) and 3-hydroxy-2-methylpropanal. These could then be hydrogenated over a suitable catalyst to give the two diols[181].



Scheme 2.10 - trans-bis[(diphenyl-phosphino)methyl]-2,2-dimethyl-1,3-dioxolane

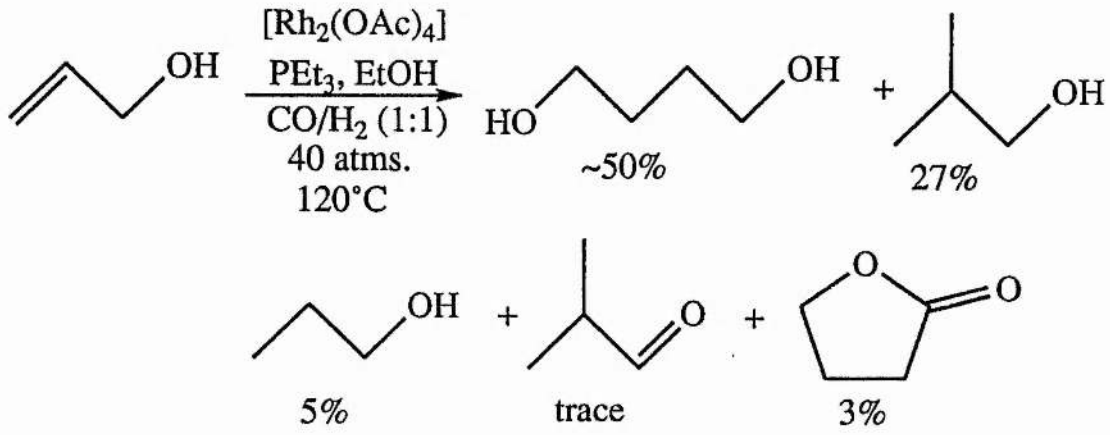
2.2 Results and discussion

2.2.1 Catalytic hydrocarbonylation of 2-propen-1-ol

Catalytic reactions using 2-propen-1-ol with CO and H_2 have been carried out using $[Rh_2(OAc)_4.2MeOH]$, dissolved in ethanol, in the presence of PEt_3 as catalytic precursor. Standard conditions of 120°C, CO/H_2 (1:1, 40 atms.) and 4 hour reaction time have been investigated

with a substrate to rhodium ratio of ~200:1. The catalytic system is similar to one employed by J.K. MacDougall[56].

On introducing 2 propen-1-ol into the system, the major products detected were 1,4-butanediol and the unexpected 2-methylpropan-1-ol. Minor products detected were butyrolactone and 2-methylpropanal.

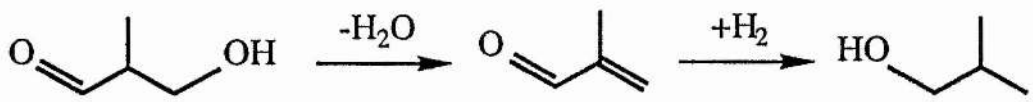


Scheme 2.11 - Reaction products of 2-propen-1-ol

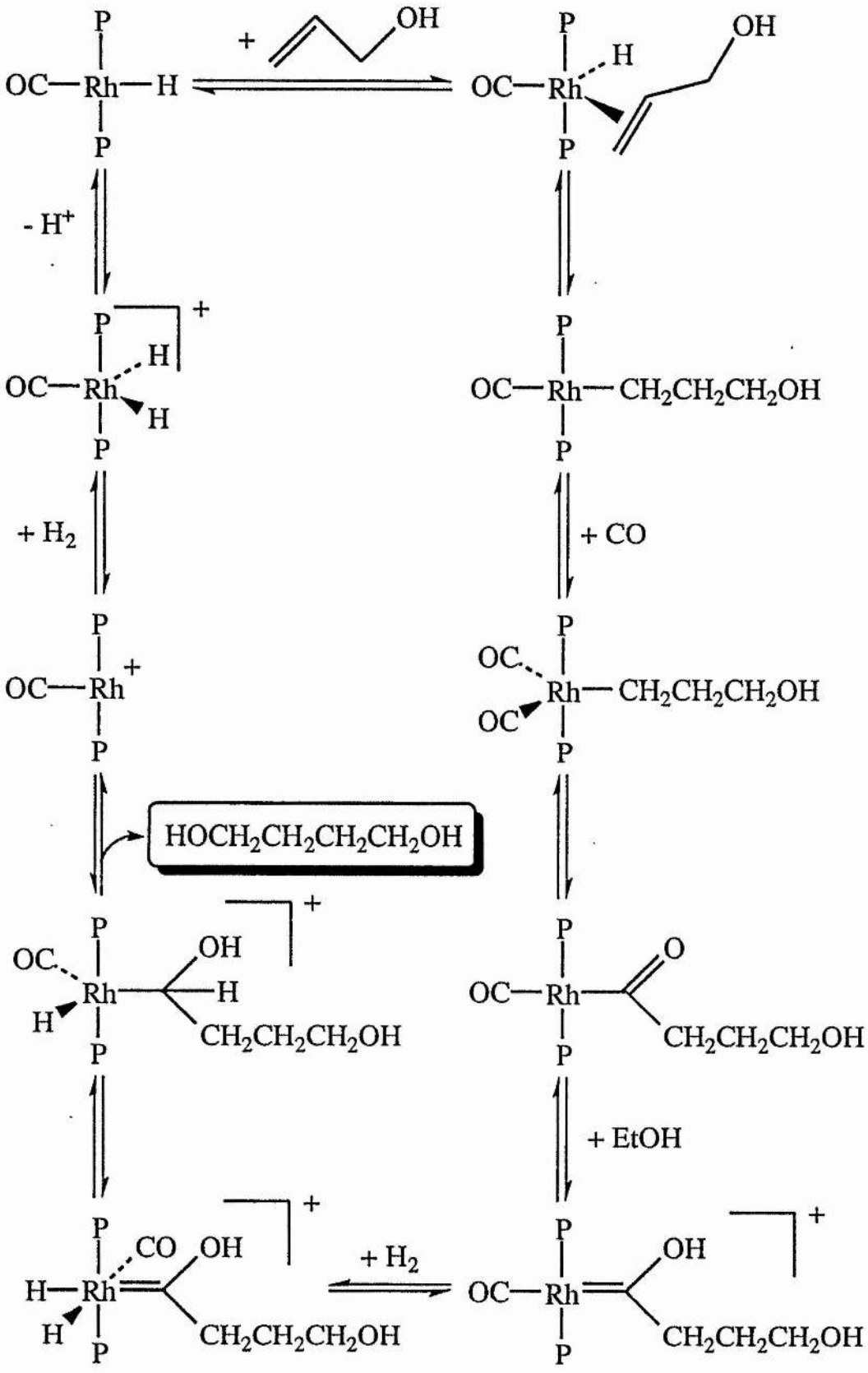
The production of 1,4-butanediol can be attributed to a mechanism essentially the same as the one proposed by MacDougall and Cole-Hamilton. This is displayed in scheme 2.12 (n.b. P = PEt_3).

The notable points of this reaction are; the lack of 2-methyl-1,3-propanediol branched product and the unexpected production of 2-methylpropan-1-ol. Smith also observed the production of 2-methylpropan-1-ol in a similar catalytic system[36].

It is known that 3-hydroxy-2-methylpropanal, (as other γ-hydroxyaldehydes e.g. in aldol condensation reactions), quite easily dehydrates to form 2-methyl-2-propenal[174]. This could then hydrogenate to 2-methylpropan-1-ol, as shown in scheme 2.13.



Scheme 2.13 - possible route to 2-methylpropan-1-ol via 2-methyl-2-propenal



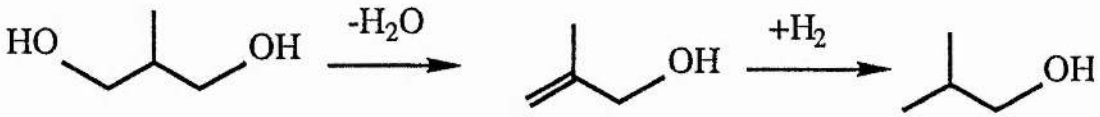
Scheme 2.12 - Mechanism depicting the formation of 1,4-butanediol

In order to test whether the proposed sequence of the reaction was occurring, the intermediate in scheme 2.13, 2-methyl-2-propenal, was examined as the initial substrate under the normal reaction conditions, in place of the 2-propen-1-ol.

The 2-methyl-2-propenal did react but not by straightforward hydrogenation as expected, < 5% hydrogenated. The other products from this reaction (which have not been identified), were not detected in the hydrocarbonylation of 2-propen-1-ol, by glc or GCMS.

This seems to rule out the production of significant amounts of branched aldehyde, in the 2-propen-1-ol reaction. The pathway shown in Scheme 2.13 is probably not the source of 2-methylpropan-1-ol.

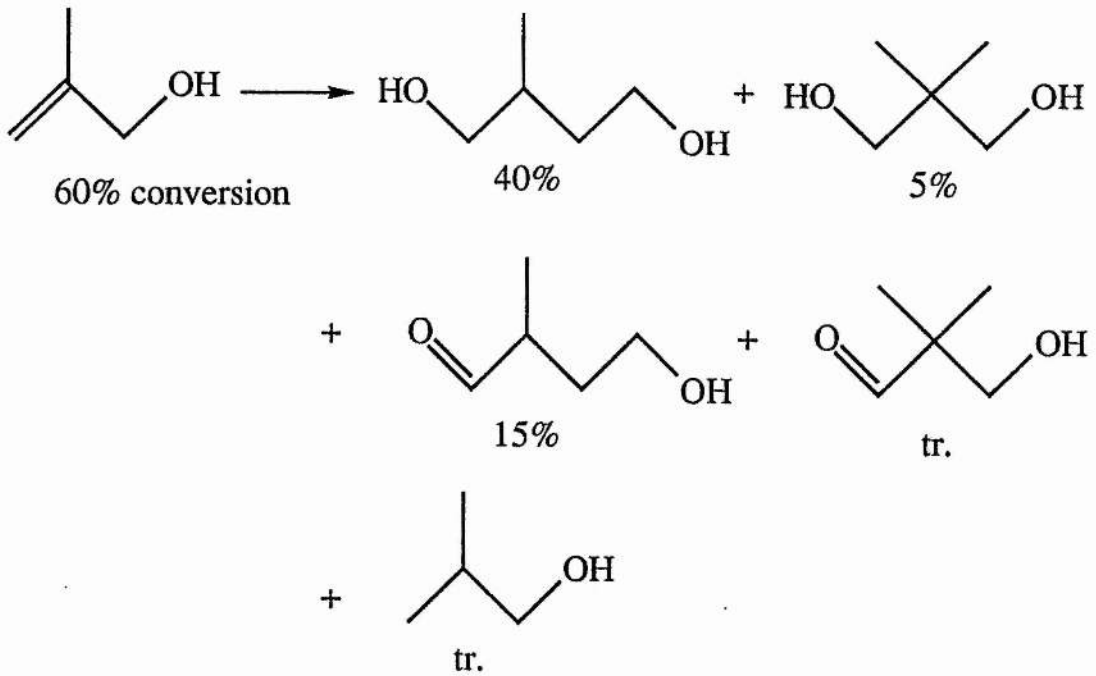
The branched diol (2-methyl-1,3-propanediol) could form directly without going through the aldehyde stage, as seems to be the case for the 1,4-butanediol. So perhaps the 2-methyl-1,3-propanediol, if it is produced, is dehydrating to 2-methyl-2-propen-1-ol. This could then hydrogenate to 2-methylpropan-1-ol. This is summarised in scheme 2.14. It should be noted, however, that the driving force for dehydration of the diol is less than that for the γ-hydroxyaldehyde. In the latter case a double bond conjugated with the aldehyde group greatly increases the stability of the product.



Scheme 2.14 - Production of 2-methylpropan-1-ol via 2-methyl-2-propen-1-ol

As before, the intermediate in the above scheme, 2-methyl-2-propen-1-ol, was investigated in place of the 2-propen-1-ol, using the standard conditions for the reaction.

Again only a very small amount of the substrate did hydrogenate (< 5%). The majority of the substrate went on to react to form standard hydroformylation products; i.e. aldehydes and alcohols. These are shown in scheme 2.15.



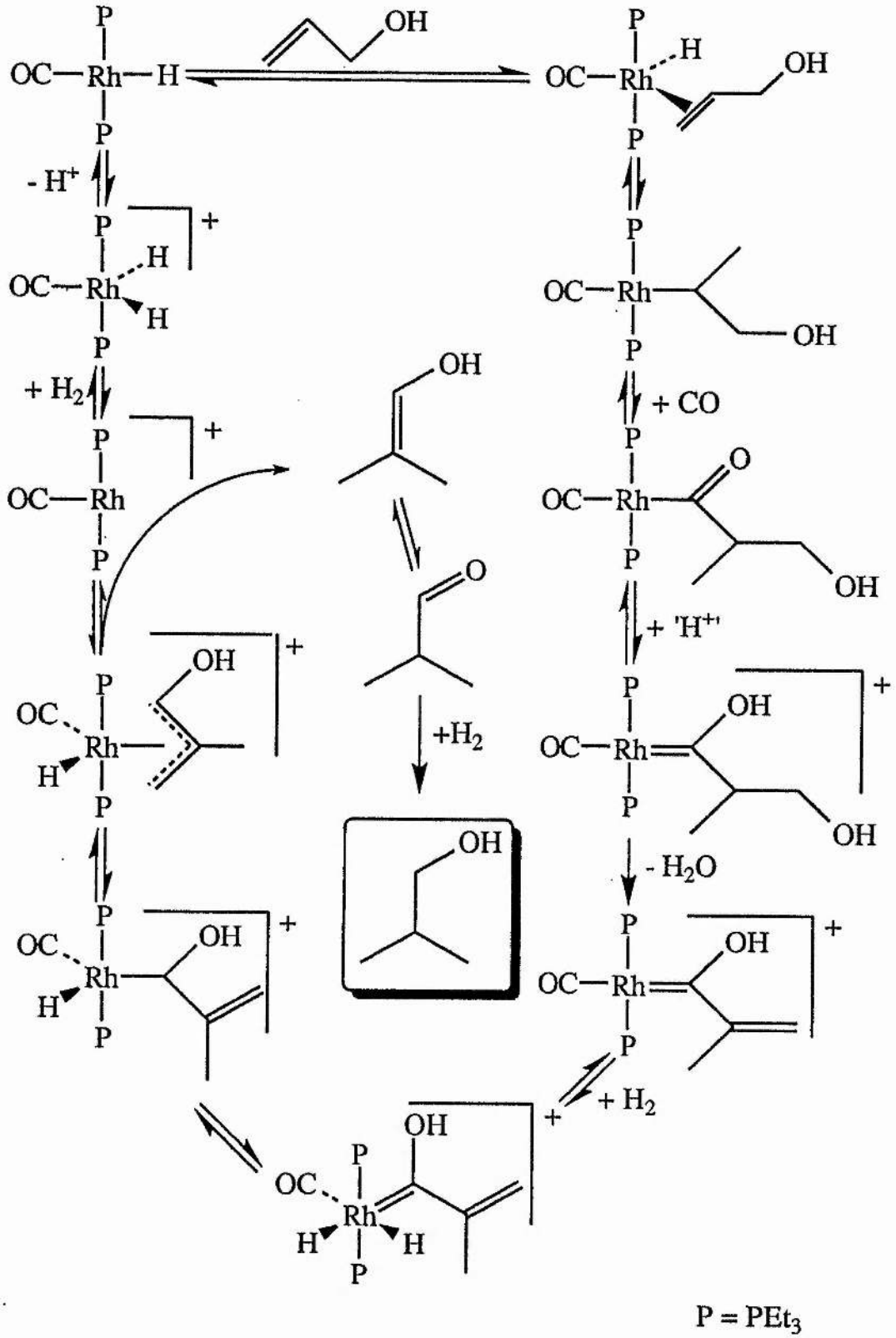
Scheme 2.15 - Products obtained from using 2-methyl-2-propen-1-ol as initial substrate

Since the majority of the 2-methyl-2-propen-1-ol is not hydrogenating, we can rule out the production of 2-methylpropan-1-ol from 2-methyl-1,3-propanediol as proposed in scheme 2.14.

2-methyl-1,3-propanediol was subsequently investigated as a substrate. No reaction occurred, which also rules it out as an intermediate in the products of 2-methylpropan-1-ol.

2-methylpropan-1-ol must be formed from a reaction involving Markownikoff insertion into the Rh-C bond and there must be a dehydration followed by a hydrogenation on the reaction pathway. Since the dehydration does not occur from any of the possible forming products, it seems likely that it must occur from a metal bound intermediate.

As was mentioned in the introduction, it has been shown that under certain conditions with Rh-PEt_3 complexes as catalysts, the solvent can protonate, or at least hydrogen bond to the acyl intermediate formed from CO insertion into the metal alkyl bond, to form a hydroxycarbene intermediate. If this mechanism is used as a basis for the reaction scheme then we can propose the mechanism shown in scheme 2.16 for the



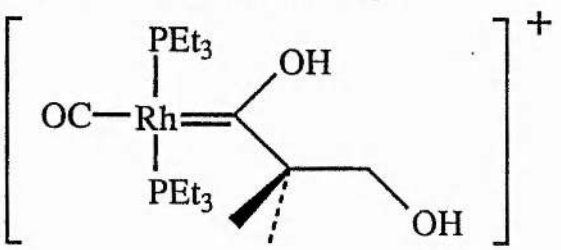
Scheme 2.16 - Postulated mechanism for the production of 2-methylpropan-1-ol

production of the 2-methylpropan-1-ol. (n.b. It should be noted that the counter anion is not displayed for clarity, the anion being ethoxide; EtO^-.)

The important step in the mechanism is the dehydration at the hydroxycarbene stage. It can be seen that conjugation could be the driving force for this to happen.

2.2.2 Evidence in support of the mechanism

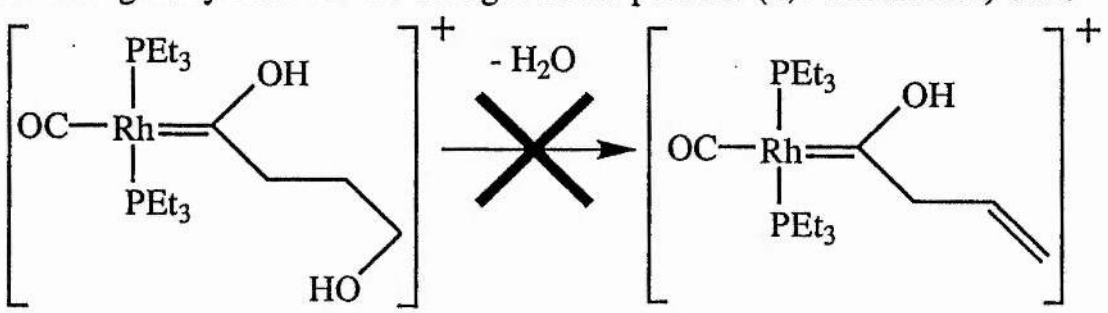
We already have one very important piece of evidence for this mechanism from the attempted hydrocarbonylation of 2-methyl-2-propen-1-ol. From the hydroxycarbene intermediate in this reaction (scheme 2.17) similar to that postulated from 2-methylpropan-1-ol, it is clear that the same type of dehydration cannot occur. This is because there is no hydrogen β to the hydroxyl group.



Scheme 2.17 - Catalytic intermediate in the reaction involving 2-methyl-2-propen-1-ol

Hence no comparable product to 2-methylpropan-1-ol should be observed and, indeed, none is.

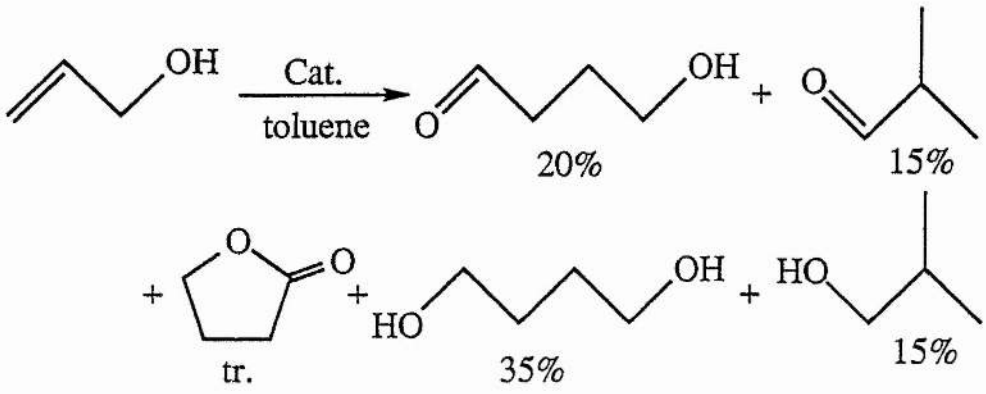
Another piece of evidence already obtained to back up this mechanism, is the fact only the branched chain product is formed by a reaction involving dehydration. The straight chain product (1,4-butanediol) does



Scheme 2.18 - Preclusion of dehydration in the straight chain hydroxycarbene analogue

have a β-hydrogen to abstract, but the resulting dehydration is not driven by the formation of a conjugated system. See scheme 2.18.

More information was gained from experimental runs where the solvent was changed from ethanol to toluene. This would reduce but not eliminate the protonation step to form the hydroxycarbene from the acyl, because the 2-propen-1-ol molecules could act as the proton source. The reaction products are shown in scheme 2.19.



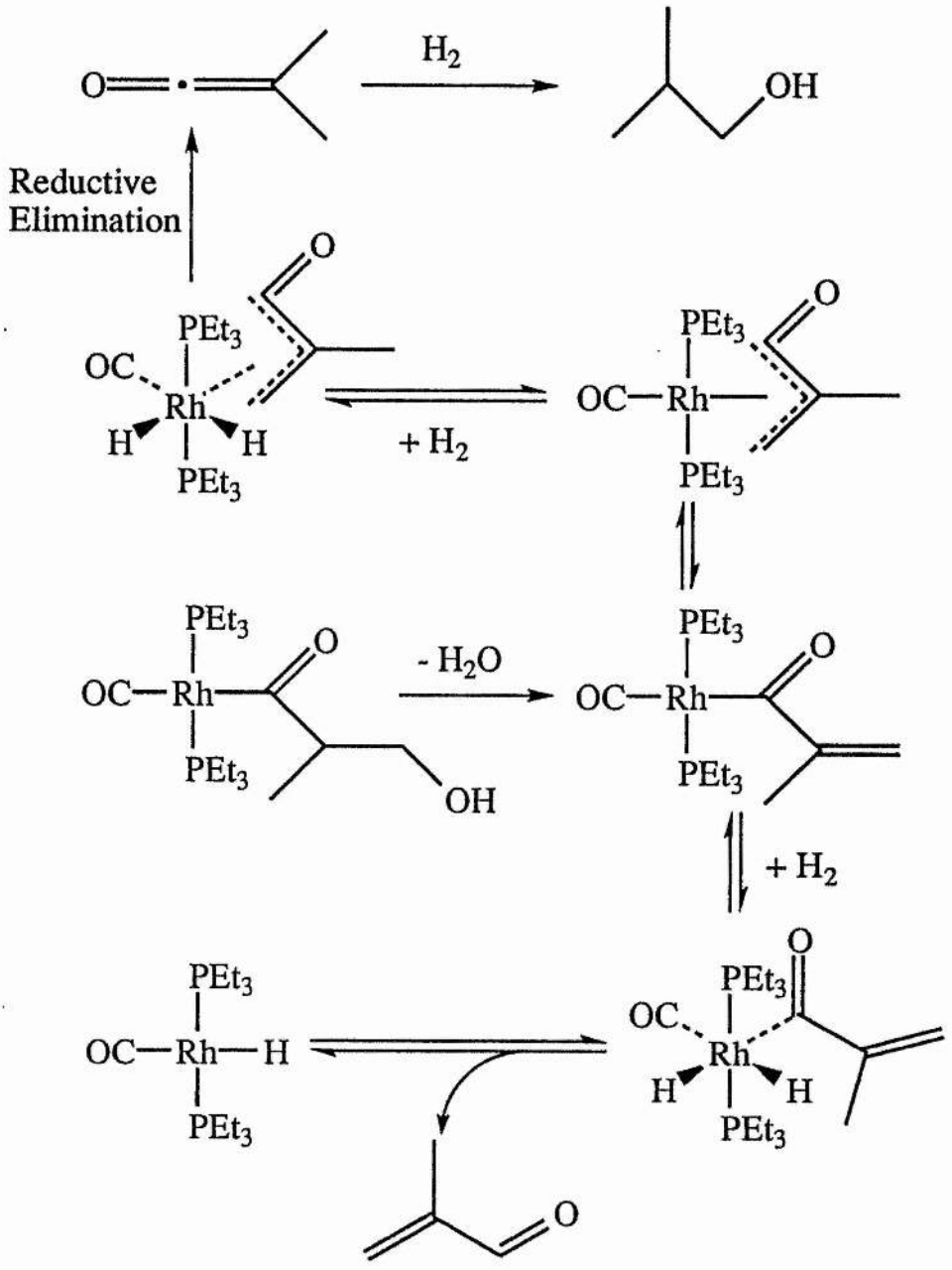
Scheme 2.19 - Reaction products when the solvent is changed from ethanol to toluene

Points to note from this are the production of the straight chain diol and the straight chain aldehyde, but more importantly the production of 2-methylpropanal and 2-methylpropan-1-ol. It can be conjectured that with fewer proton sources present, the normal hydroformylation mechanism becomes competitive with the hydrohydroxymethylation reaction.

No branched hydroxyaldehyde was identified in this reaction. This implies that the dehydration process is rapid upon protonation to form a hydroxycarbene and the oxidative addition of hydrogen is not competitive with this process.

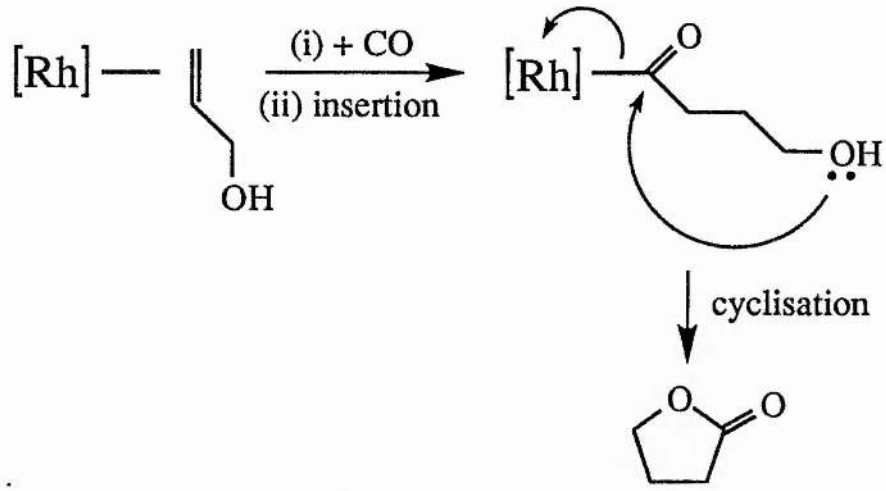
We can also be sure that the dehydration does not occur from the acyl intermediate, even though this too would give a conjugated system, since oxidative addition of H_2 followed by reductive elimination would lead to 2-methyl-2-propenal which is not observed as a product. This route is summarised in Scheme 2.20.

Another possible product from the acyl intermediate dehydrating could be a ketene. This does not seem likely and no products supporting its formation are detected. This is also summarised in scheme 2.20.



Scheme 2.20 - Product pathways from the acyl intermediate if no hydroxycarbene species is formed

The other identified product is butyrolactone; this is in small yield and can be explained by the intramolecular attack of the terminal OH^- on the acyl C atom. (See scheme 2.21). This is also seen as a low yield product in the reaction involving 2-propen-1-ol.



Scheme 2.21 - Simplified cyclisation of straight chain hydroxy species to form butyrolactone.

The final piece of black box evidence is that when 2-methylpropanal was examined as the initial substrate (to see if hydrogenation occurred to give 2-methylpropan-1-ol) the reaction proceeded cleanly to produce only 2-methylpropan-1-ol in near quantitative yield.

2.3 Varying Reaction Conditions

Using the standard reaction conditions of $[Rh_2(OAc)_4.2MeOH]$ (2.3 x 10^{-5} moles), EtOH (4 cm^3), 2-propen-1-ol (1 cm^3, 0.014 moles), PEt_3 (5 x 10^{-4} moles) and CO/H_2 (1:1, 40 atms.) for 4 hours in a pre-heated oven set at 120°C, the product distribution was as follows;

	MPA	PRO	MPO	BTR	BDO
%	tr.	5	27	3	50

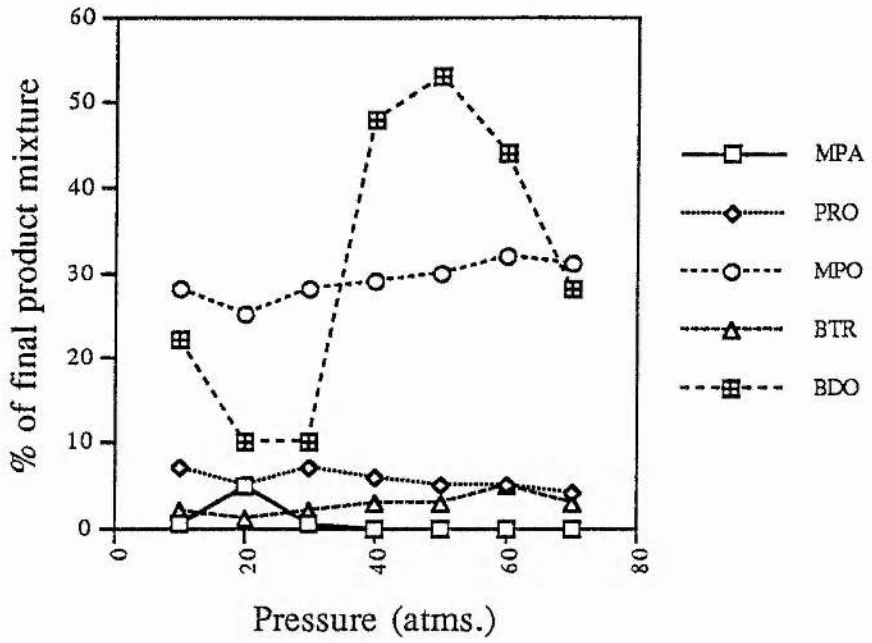
MPA = 2-methylpropanal, PRO = propan-1-ol, MPO = 2-methylpropan-1-ol, BTR = butyrolactone, BDO = 1,4-butanediol

The 1,4-butanediol data tended to be quite variable, for instance in was not uncommon to obtain two-fold or greater variation in the same sample on consecutive glc runs. Further details are given in the experimental section of these difficulties.

2.3.1 Effect of changing the total pressure of the system

No significant change (allowing for errors and ignoring the 1,4-butanediol data) can be seen (Graph 2.3.1) as the total pressure is changed from 10-70 atms. When the pressure drops below 10 atms. unidentified products start to appear.

Graph 2.3.1 - Graph of product yield vs. total pressure



MPA = 2-methylpropanal; PRO = propan-1-ol; MPO = 2-methylpropan-1-ol; BTR = butyrolactone; BDO = 1,4-butanediol. Conditions employed are; $[Rh_2(OAc)_4.2MeOH]$, 2.3 x 10^{-5} moles; EtOH, 4cm^3; 2-propen-1-ol, 0.14 moles; PEt_3, 5 x 10^{-4} moles; CO/H_2, (1:1); reaction time 4 hours at 120°C.

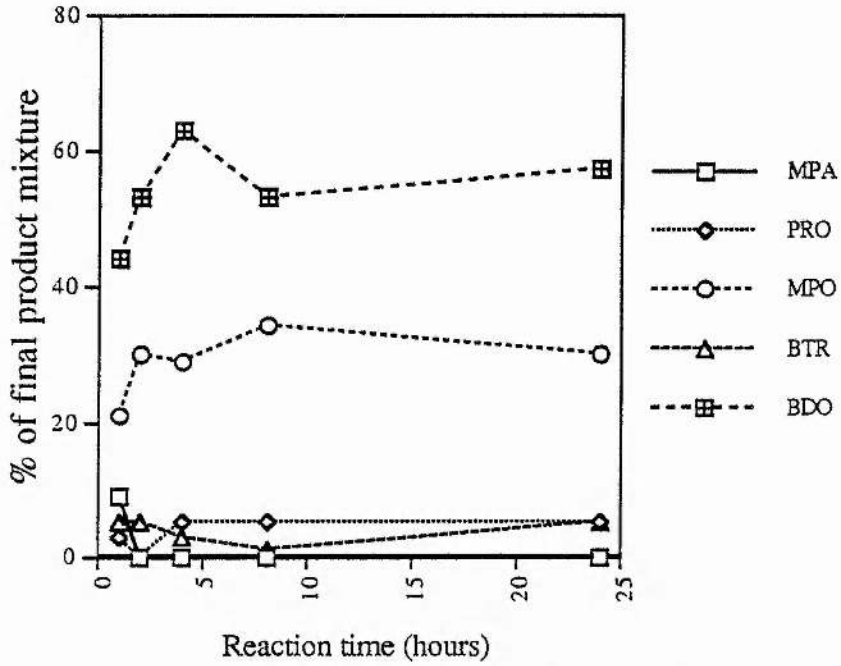
2.3.2 Effect of varying the reaction time

Due to the inefficiency of heating the autoclaves used for the reactions in a pre-heated oven (experiments carried out by Narayanan[182] showed that it took over two hours for the inside of the autoclave to reach 120°C), heating sleeves were used to heat the autoclaves (an internal temperature of 120°C was reached in under 30 minutes). To see if the quicker heating procedure affected the product distribution, a run at 120°C was carried out. No noticeable difference was observed (except that 1,4-butanediol production seemingly increased by 10%).

Graph 2.3.2 shows the product distribution with change in reaction time. The data suggest that the initial reaction of the 2-propen-1-ol was

complete within 1 hour since no free 2-propen-1-ol was observed. The yield of 2-methylpropan-1-ol had not yet reached a maximum due to the fact that not all the 2-methylpropanal had been hydrogenated. Beyond two hours only a trace of 2-methylpropanal could ever be detected. This is very strong evidence that 2-methylpropanal is an intermediate on the pathway to 2-methylpropan-1-ol.

Graph 2.3.2 - Graph of product yield vs. reaction time (carried out in heating sleeves)



MPA = 2-methylpropanal; PRO = propan-1-ol; MPO = 2-methylpropan-1-ol; BTR = butyrolactone; BDO = 1,4-butanediol. Conditions employed are; $[Rh_2(OAc)_4.2MeOH]$, 2.3 x 10^{-5} moles; EtOH, 4cm^3; 2-propen-1-ol, 0.14 moles; PEt_3, 5 x 10^{-4} moles; CO/H_2, 40 atms. (1:1); reaction temperature, 120°C.

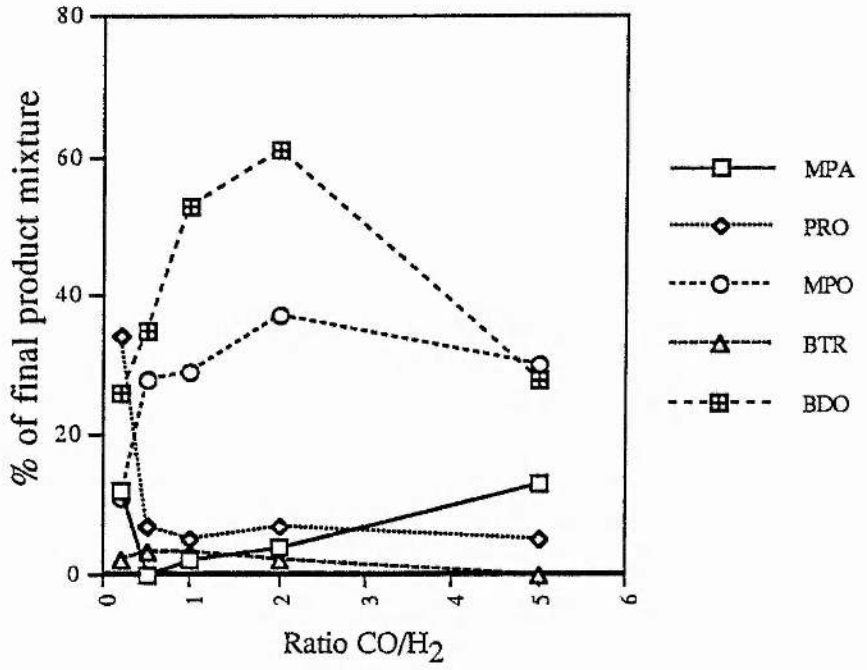
On the basis of this observation we can assign a lower ceiling on the turnover rate of this system of > 200 hour^{-1}.

2.3.3 Effect of varying CO/H_2 ratio

Graph 2.3.3 shows the data gained for a series of experiments where the CO/H_2 ratio was varied.

When the ratio of the gas composition (CO/H_2) is between 0.5 and 2 then the product distribution does not alter to any significant extent for all products except 1,4-butanediol. Owing to no other significant product formation or the observation of any of the initial substrate in the final product mixture, it is assumed that 1,4-butanediol data is misleading.

Graph 2.3.3 - Graph of product yield vs. CO/H_2 ratio



MPA = 2-methylpropanal; PRO = propan-1-ol; MPO = 2-methylpropan-1-ol; BTR = butyrolactone; BDO = 1,4-butanediol. Conditions employed are; $[Rh_2(OAc)_4.2MeOH]$, 2.3 x 10^{-5} moles; EtOH, 4cm^3; 2-propen-1-ol, 0.14 moles; PEt_3, 5 x 10^{-4} moles; CO/H_2, 40 atms.; reaction time 4 hours at 120°C.

When the more extreme ends of the graph are reached, the reaction products distributions significantly change. Also new reaction products are detected.

At $CO/H_2 = 5$, the concentration of 2-methylpropanal becomes quite significant. This possibly signifies a slow down in the hydrogenation reaction of 2-methylpropanal, which seems likely since there is a comparatively low partial pressure of hydrogen. Another possibility is the fact that CO may be reacting with the catalyst to form less reactive dicarbonyl species.

The other products formed from this reaction have not been identified. From glc data they appear not to be in any significant concentration in the resultant product mixture.

At $CO/H_2 = 0.2$, the amount of propan-1-ol in the reaction mixture becomes very significant. A high partial pressure of hydrogen favours isomerisation to propanal which is then hydrogenated. The overall reaction rate also seems to drop, due to the fact 2-propen-1-ol is detected in the final reaction mixture (~20%).

There are significant amounts of other products in the reaction. Most are long retention time products which have not been analysed. One of the products has been tentatively assigned as 2-methylpentan-1-ol, which

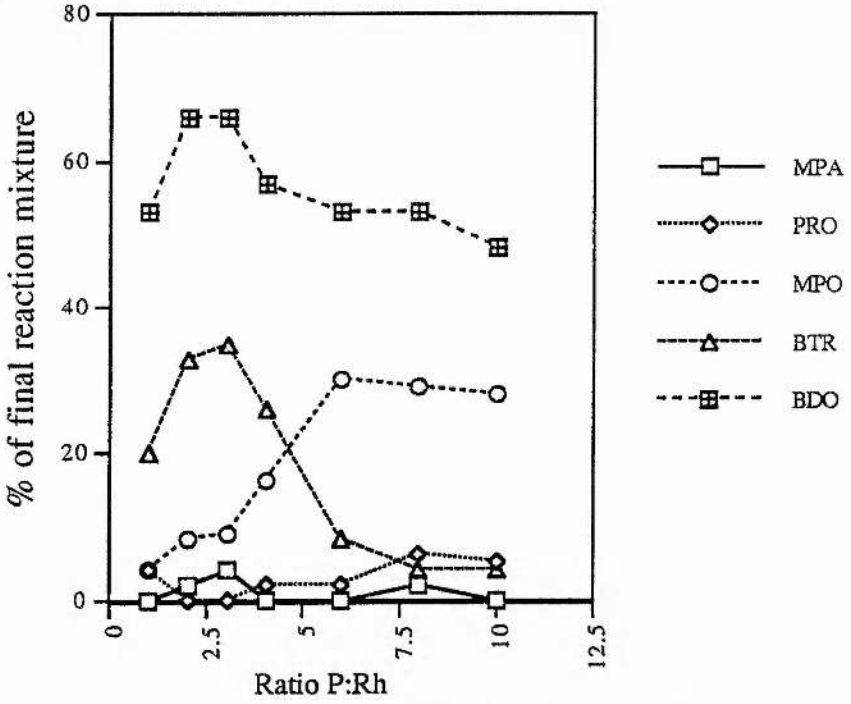
is a Guerbet type product from propanal (i.e. the hydrogenation product of the aldol condensation). Another product in a trace amount is 4-hydroxybutanal. This suggests that the hydroformylation reaction becomes a little competitive at high partial pressures of hydrogen.

When either the CO or H_2 is left out of the autoclave, no reaction is observed. This is presumably because the initial catalytic species cannot be formed in either case. MacDougall and Cole-Hamilton showed that with preformed catalysts gaseous CO only could be used and the solvent alcohol acted as hydrogen source[16].

2.3.4 Effect of varying PEt_3 concentration

Graph 2.3.4 shows the effect on product distribution of varying the amount of PEt_3 added. It appears that 1,4-butanediol production is maximised at a P:Rh ratio of 2 but the reaction is somewhat inhibited at higher PEt_3 concentrations.

Graph 2.3.4 - Graph of product yield vs. PEt_3 concentration



MPA = 2-methylpropanal; PRO = propan-1-ol; MPO = 2-methylpropan-1-ol; BTR = butyrolactone; BDO = 1,4-butanediol. Conditions employed are; $[Rh_2(OAc)_4.2MeOH]$, 2.3 x 10^{-5} moles; EtOH, 4cm^3; 2-propen-1-ol, 0.14 moles; CO/H_2, 40 atms. (1:1); reaction time 4 hours at 120°C.

The formation of 2-methylpropan-1-ol increases up to a P:Rh ratio of 6:1, whilst the amount of butyrolactone which is a favoured product at low phosphine concentrations decreases as the P:Rh ratio is increased.

Since butyrolactone formation occurs by intramolecular nucleophilic attack of the terminal OH group onto the acyl C atom, this reaction will be favoured if there is a low electron density on this acyl C atom. A low electron density on this acyl C atom will also disfavour protonation of the acyl intermediate, thus disfavouring the formation of 2-methylpropan-1-ol. The data of graph 2.3.4 can then be rationalised if the catalytic species present at high concentrations of PEt_3 is $[RhH(CO)(PEt_3)_2]$ whilst at low $[PEt_3]$ it is $[RhH(CO)_2(PEt_3)]$. The latter, having the good π acceptor CO replacing the good σ donor (PEt_3), will have much less electron density on the metal and hence will favour the formation of butyrolactone and disfavour the formation of 2-methylpropanal.

The remarkable observation however is that at low $[PEt_3]$, almost all of the product is derived from the straight chain alkyl (anti-Markownikoff insertion). In general the 1,4-butanediol: 2-methylpropan-1-ol ratio is in the order of 2:1. However, 1,4-butanediol is the more valuable product so that higher ratios would be desirable.

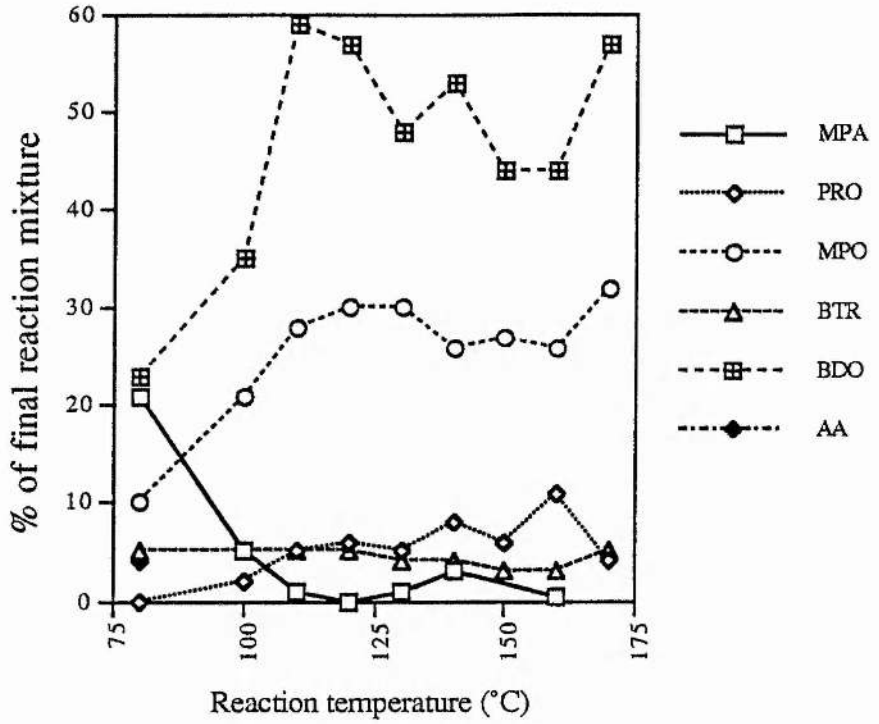
The dehydration step seems to be less favoured because the protonation of the branched chain acyl species is not occurring to the same extent as higher $[PEt_3]$. But if the branched alkyl has a sufficient lifetime then β-hydrogen extraction may occur and isomerisation to the sterically favoured straight chain product may occur.

The dehydration step of the branched chain mechanism is crucial in the determination of the final product. It is most likely that this step is irreversible, so once it has been breached the 2-methylpropanal will be the resultant product. Further evidence to strengthen the claim that the dehydration step is irreversible is that addition of water does not effect the product distribution.

2.3.5 Effect of varying the reaction temperature

The data displayed on graph 2.3.5 suggests that when the reaction temperature is above 110°C the product distribution does not alter a great deal. Below 110°C a drop in yield of the products is observed. Other products (unidentified) also start appearing. At 80°C, 2-methylpropanal is the favoured branched product but at high temperature this is hydrogenated to 2-methylpropan-1-ol. Once again this is further evidence that the production of 2-methylpropan-1-ol is via 2-methylpropanal.

Graph 2.3.5 -Graph of product yield vs. reaction temperature



MPA = 2-methylpropanal; PRO = propan-1-ol; MPO = 2-methylpropan-1-ol; BTR = butyrolactone; BDO = 1,4-butanediol. Conditions employed are; $[Rh_2(OAc)_4.2MeOH]$, 2.3 x 10^{-5} moles; EtOH, 4cm^3; 2-propen-1-ol, 0.14 moles; PEt_3, 5 x 10^{-4} moles; CO/H_2, 40 atms. (1:1); reaction time 4 hours.

2.3.6 Effect of varying phosphine ligand

As was evident from chapter 1, phosphines are most versatile ligands because of the comparative ease of changing the electronic density and/or the steric crowding at a catalytic metal centre. By using alternative phosphine ligands, so called 'tuning' of the catalyst can be carried out.

Using hex-1-ene as substrate under conditions similar to those explored in this work, it has been shown that the nature of the phosphine can alter the nature of the products formed (see table 2.1)[56]. Whereas trialkylphosphines produce alcoholic products if the alkyl is primary, P^iPr_3 gives largely aldehydes. Triarylphosphines give mixtures of acetals and aldehydes whilst mixed alkylarylphosphines gives mixtures of alcohols and aldehydes.

Using standard conditions similar to those in footnote [a] in table 2.1 (except with a shorter reaction time of 4 hours), a range of ligands was examined using 2-propen-1-ol as the substrate. The first investigated was PPh_3.

Table 2.1 Hydroformylation using various ligands

Catalyst[a] {[$Rh_2(OAc)_4$]}	Acetals % yield	n:i	C_7 aldehydes % yield	n:i	C_7 alcohols % yield	n:i
No ligand	48	2.0	40	0.4	10	0.2
+ P^iPr_3	tr.		79	1.1	19	0.2
+ $PEtPh_2$	tr.		66	1.1	28	6.2
+ DMPE[b]	tr.		10	0.9	17	0.5
+ PEt_2Ph	tr.		3	0.0	89	2.6
+ PMe_3	-		tr.		99	2.5
+ PEt_3[c]	-		tr.		103	2.4
+ P^nBu_3	-		-		106	2.4
+ PPh_3[d]	Yes		Yes			

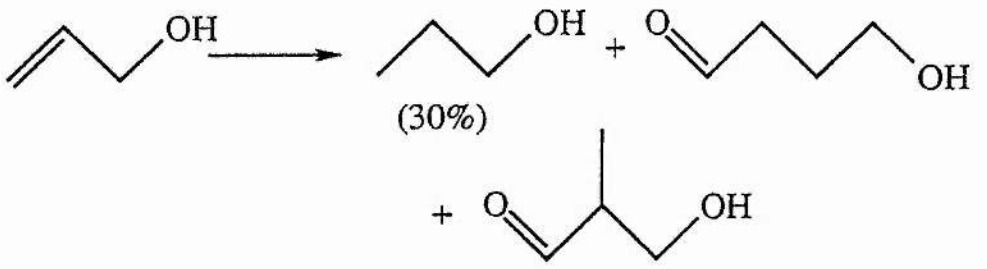
[a] Conditions [$Rh_2(OAc)_4$], 0.004 moldm^{-3}; hex-1-ene, 1 cm^3; ethanol, 4 cm^3; pressure CO/H_2 (1:1), 37-52 atms.; temperature, 120-125°C; time 16 hrs.

[b] DMPE, bis dimethylphosphinoethane.

[c] 80°C.

[d] [$RhHCO(PPh_3)_3$] instead of [$Rh_2(OAc)_4$].

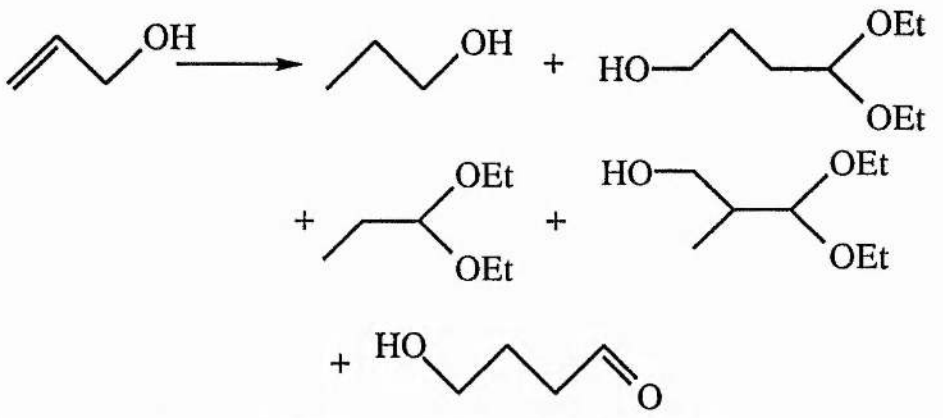
It was of no surprise that on replacing PEt_3 with PPh_3, 2-propen-1-ol produces the classical hydroformylation products, aldehydes (4-hydroxybutanal and 3-hydroxy-2-methylpropanal). These were the same products as the Kuraray system, which was not unexpected since the catalytic system is very similar except that the solvent is ethanol rather than toluene. At the end of 4 hours there was still some of the initial substrate remaining (~ 5%). The products are depicted in scheme 2.24.



Scheme 2.24 - Main products obtained from the standard system using PPh_3 instead of PEt_3

The branched and straight chain aldehydes constituted the majority of the final reaction mixture, no formal analysis of the n:i ratio was attempted, but glc data suggests that the n:i ratio is ~2.5-4:1. The hydrogenation products of the aldehydes (1,4-butanediol and 2-methyl-1,3-propanediol) were also detected in trace amounts.

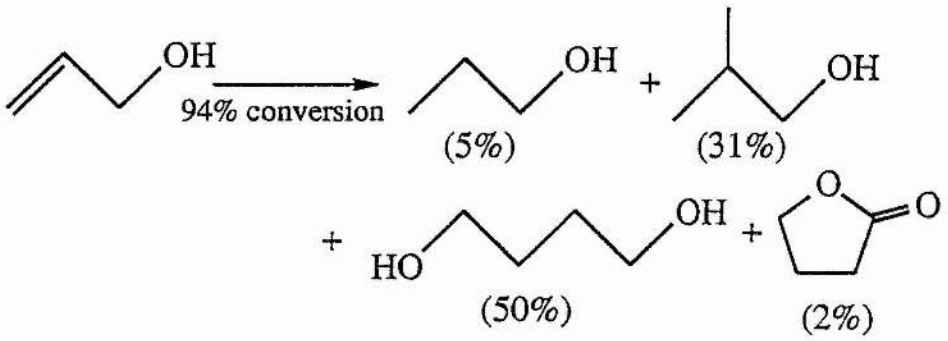
Bulky trialkylphosphines, P^nOc_3 and Pcy_3 were also examined. The reaction products using either of these were mainly acetals, conversion was > 98%. The main products of these reactions are shown in scheme 2.25.



Scheme 2.25 - Main products obtained from using bulky trialkylphosphines instead of PEt_3 in the standard system

The largest product (> 50%) was the acetal of propanal, 1,1-diethoxypropane. Propanal can be formed from the isomerisation of 2-propen-1-ol, a reaction which is known to be catalysed by rhodium phosphine systems[183]. The two other acetals are not unexpected being the acetals of the standard hydroformylation products, but the n:i ratio for these is ~1:5. With P^nOc_3 a small amount of 4-hydroxybutanal is formed, along with a trace of butyrolactone and 1,4-butanediol. When Pcy_3 was used, none of these three products was detected, suggesting perhaps that the formation of the acetals is metal catalysed rather than acid catalysed.

The small trialkylphosphine PMe_3 was used instead of PEt_3 in the reaction. The products from this were the same as for PEt_3, largely 2-methylpropan-1-ol and 1,4-butanediol. The yields and the products are shown in scheme 2.26.



Scheme 2.26 - Products and yields when using PMe_3 in place of PEt_3 in the standard system

The final phosphine to be investigated was P^iPr_3. This gave hydroformylation products on the whole, but also gave alcohols (1,4-butanediol and 2-methylpropan-1-ol) in small yield (totalling ~10%). No experiments were conducted to see if these came from hydrogenation of the aldehydes or if they were products of the hydroxycarbene route. The main product from using this ligand was propan-1-ol (40%). Only a trace of 2-propen-1-ol could be detected. The aldehydes had a large n:i ratio of ~10:1. But it must be stressed that the overall yield of these was probably only ~30-40%.

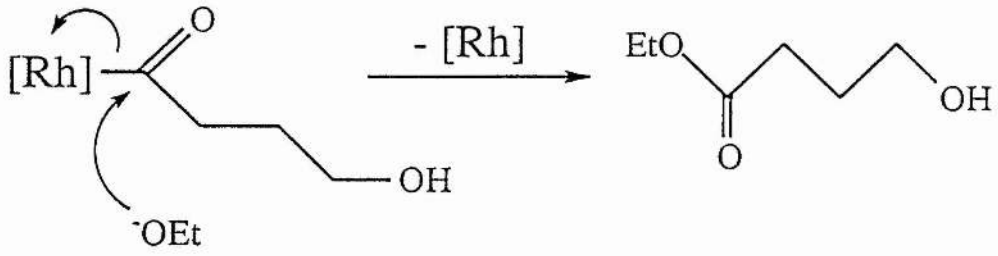
Table 2.2 - Effect of phosphine on the products using 2-propen-1-ol as the substrate[a]

Phosphine	Products (%)				
	Propan-1-ol	Acetals	Aldehydes		Alcohols
			(%)	n/i	
PPh_3	30	-	50-60	2.5-4	-
P^iPr_3	40	-	30-40	10	< 10
PEt_3	5	-	-		> 75
PMe_3	5	-	-		> 80
P^nOc_3	Yes	Yes	tr.	-	tr.
Pcy_3	Yes	Yes	-		-

[a] Conditions $[Rh_2(OAc)_4]$, 2.3 x 10^{-5} moles; 2-propen-1-ol, 1 cm^3; ethanol, 4 cm^3; pressure CO/H_2 (1:1), 40 atms.; temperature, 120°C; time 4 hrs; heating method pre-heated oven.

Overall it must be concluded from this study that changing the phosphine ligand, dramatically changes the reaction products (see table 2.2). The direct formation of 1,4-butanediol only occurs with PMe_3 and PEt_3. P^iPr_3 perhaps gives some direct alcohol formation, but the majority of the products are the expected products from a normal hydroformylation reaction, the same is true from using PPh_3. P^nOc_3 and Pcy_3 give mostly the acetals and it seems that acetals are being formed from a metal catalysed reaction between the aldehydes and ethanol. P^iPr_3, PPh_3, P^nOc_3 and Pcy_3 are possibly all too sterically demanding to allow the approach of the ethanol molecule near the acyl group of the catalytic intermediate, ∴ protonation of the oxygen atom cannot occur. PPh_3 is also probably not basic enough to give the rhodium centre the extra electron density required for the formation of the carbene species.

All phosphines investigated except PMe_3 and PEt_3 gave small amounts of products (< 10%) which have long glc retention times. These were tentatively assigned as esters. These could be formed by Reppe reactions. See scheme 2.27. But equally they could be aldol condensation products or acetals with 2-propen-1-ol or with themselves. These possibilities have not been investigated.



Scheme 2.27 - Possible route to esters via Reppe chemistry

Other solvents apart from ethanol were investigated; it is of interest to see that the system works in such solvents as 2-methylpropan-1-ol and propan-1-ol, both products of the reaction mixture (product yields not quantified).

2.4 Conclusions

A new process for producing 1,4-butanediol has been found. The separation of the resulting products has been made easier than the existing processes, due to a > 120°C difference in boiling points between the major products, 2-methylpropan-1-ol (b.p. 108°C) and 1,4-butanediol (b.p. 230°C).

The formation of 2-methylpropan-1-ol is of considerable interest and a mechanism for its formation has been proposed, with evidence to back it up. Further evidence for this mechanism will be presented in chapters 3 and 4.

Because the product alcohols are formed without any evidence for formation of aldehydes, this process does not suffer from the disadvantages of other processes such as catalytic deactivation, side reactions (such as aldol condensations, dehydrations and acetal formation) or two separate steps (i.e. hydroformylation followed by hydrogenation) which may require two separate catalytic systems.

Like other systems there is a small problem with hydrogenation of the initial substrate, but since this seems to account for only ~ 5% of the final product mixture, it is not a major problem.

During the systematic variation of reaction parameters discussed in this chapter, it has become clear that it is possible to produce much higher n:i ratios under some conditions. Thus, by carrying out the reaction in toluene (where protonation of the acyl species occurs to a lesser extent) or by using low PEt_3:Rh ratios which lead to $[RhH(CO)_2PEt_3]$ as the active species and hence to an acyl O atom that is less readily protonated, it seems that the dehydration step is less favoured. This may mean that the branched alkyl has sufficient lifetime to β-H abstract and hence to isomerise back to the sterically preferred straight chain species.

Chapter 3 - Deuterium labelling studies

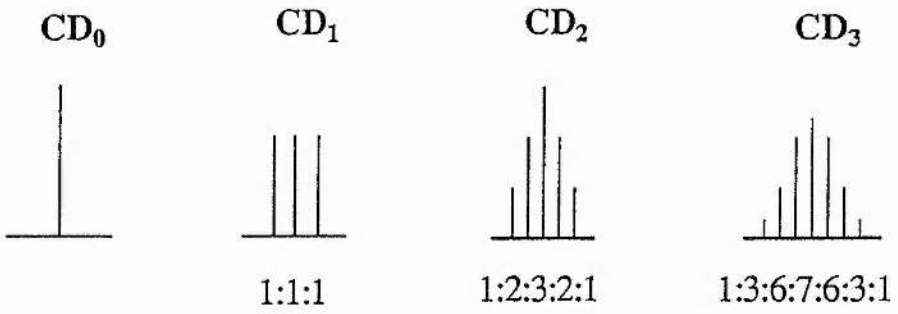
3.1 Introduction

Various isotopes have been used as aids in the elucidation of mechanisms in inorganic chemistry. Commonly used isotopes for labelling are ^{2}H, ^{13}C, ^{14}C and ^{18}O. ^{14}C products are analysed using a scintillation counter detector connected to a glc[184]. The other isotopic products are analysed by mass spectrometry and/or nmr. Mass spectrometry and ^{14}C give information about which products have labels incorporated, whereas nmr gives more information about where the isotopes have ended up in the product.

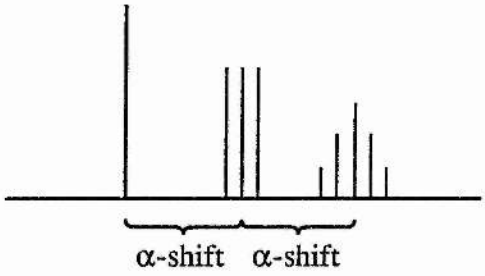
Modern nmr techniques have been used in the studies of biological mechanisms to good effect to study the incorporation of deuterium atoms into the various compounds produced. These techniques have not been extensively exploited by mechanistic chemists to date for studying reactions catalysed by soluble metal complexes.

3.2 Theory

A deuterium atom has spin I = 1, so in a proton-decoupled ^{13}C nmr spectrum we would expect to see the following splittings for the various possible deuterium incorporations at any given carbon resonance;



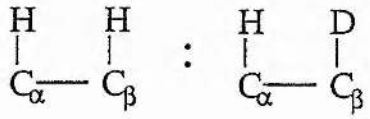
For each D atom attached to a carbon atom an α-shift is obtained. To illustrate, a methylene group, which on a particular carbon has a mixture of isotopic substitutions, CD_2, CHD and CH_2, would be expected to produce the following resonances;



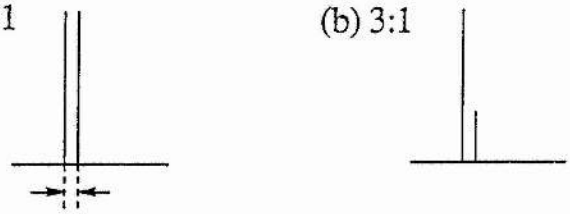
These α-shifts tend to be of the order of 0.4 ppm. The α-shift can be similar to the C-D coupling constant (at least at 75.5 MHz observation), causing an overlap of signals. So the observed signal will probably not be as clear cut as shown above.

This is not the only effect seen at 75.5 MHz. β-shifts can also be seen on adjacent carbons, a few illustrative examples are shown thus;

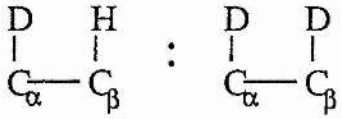
(i) For an isotopic mixture with the ratios shown, the spectra would be expected to be as illustrated;



^{13}C of C_α, (a) 1:1 (b) 3:1

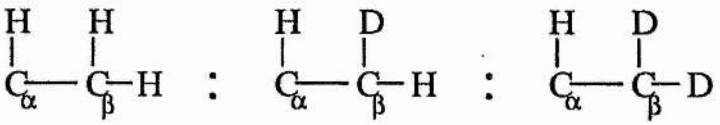


(ii) An isotopic mixture;

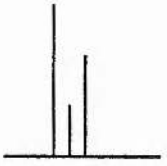


^{13}C of C_α, (a) 1:1 (b) 2:3

(iii) An isotopic mixture;



^{13}C of C_α in the ratio 3:1:2,



β-shifts tend to be in the order of 0.1 ppm.

Although signal splitting due to deuterium incorporation can give a qualitative guide to which carbon atoms have been deuteriated, they cannot easily be used to provide quantitative information about the extent of deuterium incorporation because the Overhauser enhancements on the signals due to CH_2, CHD and CD_2 are different, so do not allow direct comparison.

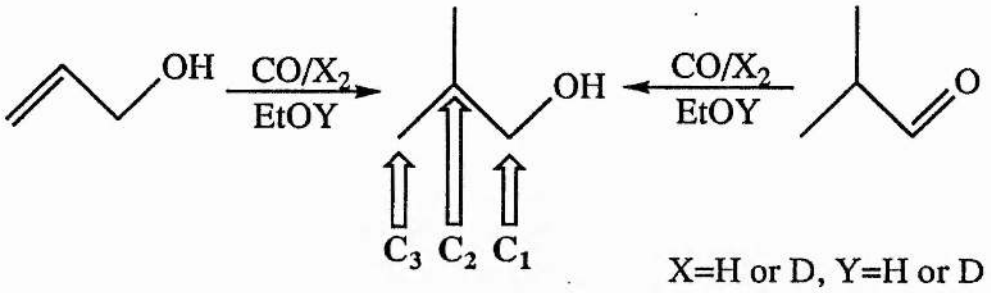
The Overhauser problem can be overcome by using different pulse sequences or relaxation agents, but a simpler approach to quantitative analysis is to use the β-shifted resonances. These resonances show no coupling to deuterium. Since β-couplings are generally very small, the Overhauser enhancement of the carbon atoms β to the H or D atom are very similar. The relative areas of these signal can therefore be used to obtain quantitative information about the amount of deuterium at any position in the molecule.

3.3 Analysis of 2-methylpropan-1-ol at 75.5 MHz

As described in Chapter 2, 2-propen-1-ol can be hydrocarbonylated to give 1,4-butanediol and 2-methylpropan-1-ol (as the major products). 2-methylpropan-1-ol can also be made by the hydrogenation of 2-methylpropanal. These reactions were carried out as in Chapter 2, but using isotopically labelled reagents under identical conditions. So EtOD was used instead of EtOH and/or D_2 instead of H_2.

Therefore 6 different sets of isotopic mixtures of 2-methylpropan-1-ol were made and analysed using nmr (all samples are run in $CDCl_3$). All

the data for this chapter is gathered together in three tables (tables 3.8, 3.9, 3.10) at the end of this chapter.



An attempt to calculate error values has been made. It has to be stated that the errors have only been calculated on measurement of peak heights or integral, i.e. there may be baseline errors. No attempt has been made to deconvolute data which would give a less ambiguous value for partially overlapping peaks. (A more detailed explanation is given in the discussion, section 3.5.). Most nmr samples contain large amounts of ethanol, these peaks in the spectra have been marked with an asterisk (*).

3.3.1 2-methylpropan-1-ol made from 2-methylpropanal, EtOD and CO/D_2 (1:1)

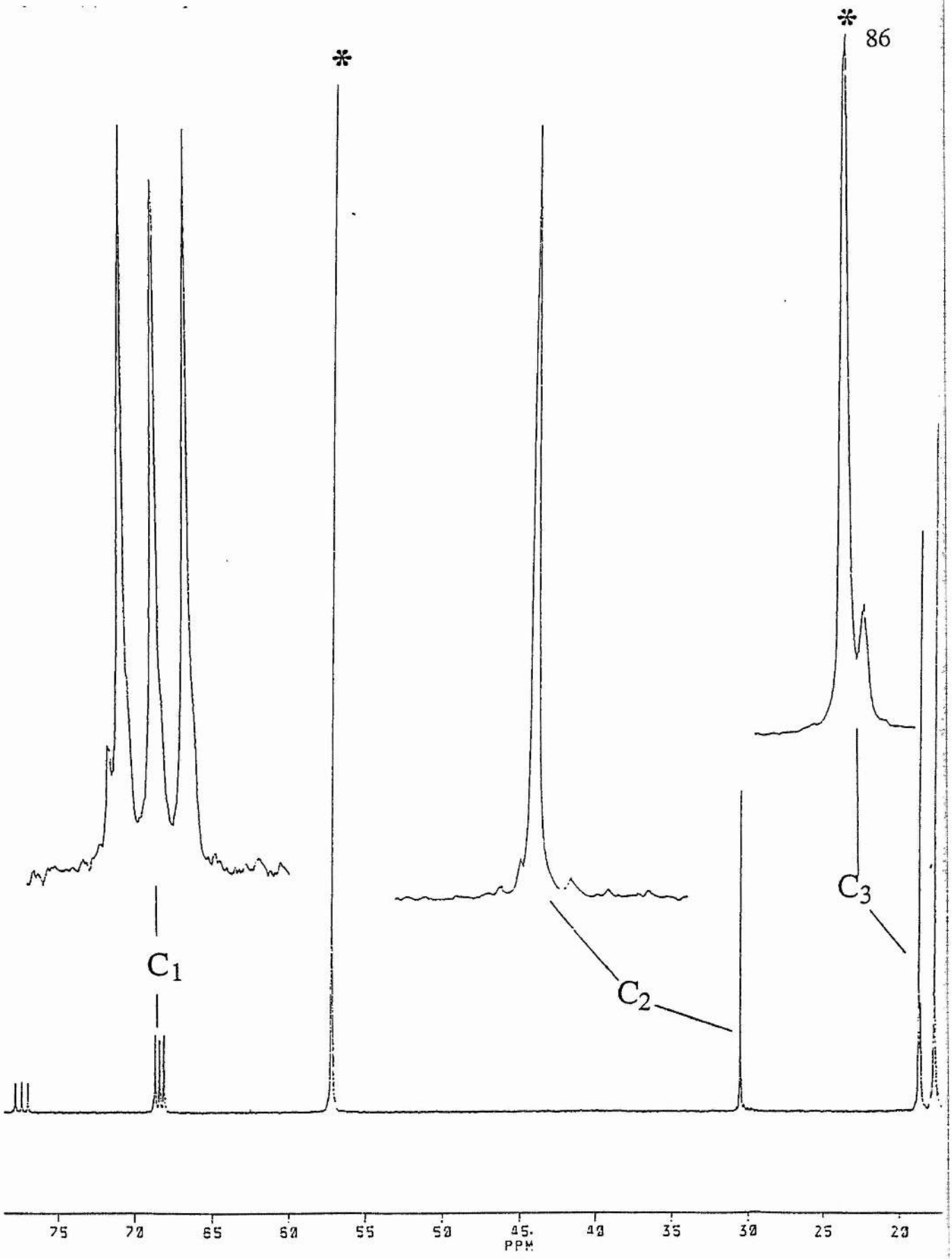
The $^{13}C\{^1H\}$ spectra of the 2-methylpropan-1-ol produced from 2-methylpropanal and D_2/CO in EtOD (1:1) is shown in Spectrum 3.1.

The C_3 signal is made up of two singlets in the ratio 84.1:15.9. There is no evidence for α-shifted 1:1:1 triplets so there is no D on C_3. The singlets are 0.115 ppm apart, indicating that they are β-shifted. This gives direct information on the deuterium incorporation on C_2, since this is the only hydrogen/deuterium atom β to C_3. We can therefore state that the H:D ratio on C_2 is 84.1:15.9.

The C_1 signals, consist of a triplet and a singlet. The only information about the D incorporation on C_1 that can be extracted from this data is the fact that C_1 is predominantly CHD with a very small component containing CH_2.

To obtain quantitative information about C_1, the resonance associated with C_2 must be analysed.

This shows a doublet of singlets and a doublet of triplets (the triplets being difficult to observe), the high field signal in each set being the stronger. The singlets are in the ratio 4.9:95.1.



Spectrum 3.1 - 2-methylpropan-1-ol synthesised from 2-methylpropanal, EtOD and D_2/CO (1:1)

If we assume that there are negligible secondary isotope effects then we can assign the composition of the isotopic mixture thus;

$(CH_3)_2CHCHDOH/D$	80%
$(CH_3)_2CDCHDOH/D$	15%
$(CH_3)_2CHCH_2OH/D$	4.1%
$(CH_3)_2CDCH_2OH/D$	0.8%

This seems a rather trivial example, since this can be worked out from the ^1H spectrum (see discussion section 3.5) using the same assumptions. But it is included to show the method for the more complex mixtures that follow.

3.3.2 2-methylpropan-1-ol made from 2-methylpropanal, EtOH and CO/D_2 (1:1)

The $^{13}C\{^1H\}$ spectra of the 2-methylpropan-1-ol produced from 2-methylpropanal and CO/D_2 in EtOH is shown in spectrum 3.2.

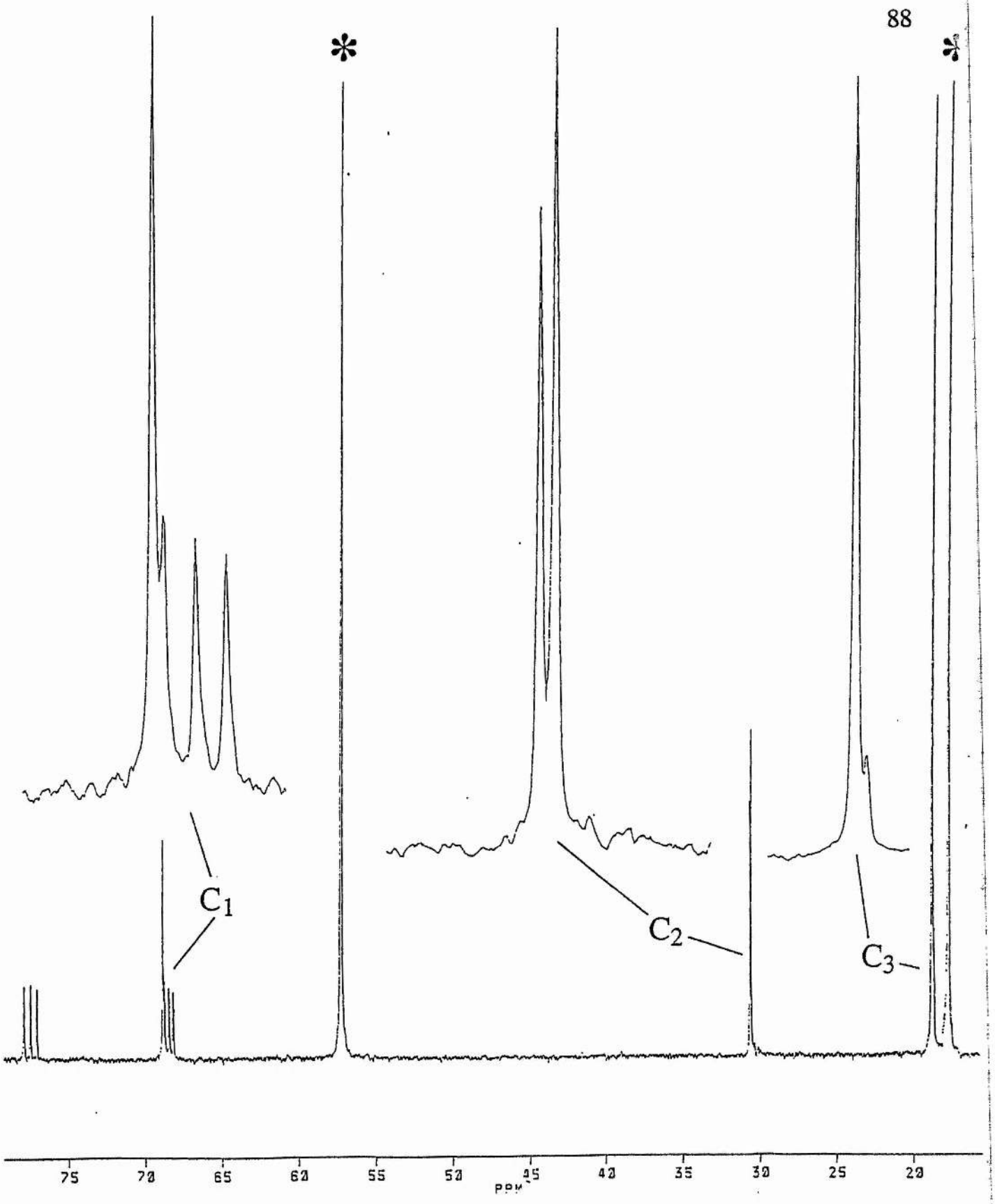
The C_3 signals are two singlets 0.119 ppm apart (one β-shift). These are in the ratio 88.2:11.8. Thus the H:D ratio (for C_2) is the same since there are no other C atoms β to C_3.

For the C_2 resonance, two singlets are observed that are in the ratio 43.9:56.1, since there is no perceivable deuterium incorporation into the methyl groups, this can be taken as the ratio of CH_2:CHD in C_1 (the C_2 signal does contain two 1:1:1 triplets arising from the 11.8% of the molecules that contain C_2D, but these are difficult to distinguish from the baseline).

This produces the following isotopomer compositions;

$(CH_3)_2CHCHDOH/D$	50%
$(CH_3)_2CDCHDOH/D$	6.6%
$(CH_3)_2CHCH_2OH/D$	39%
$(CH_3)_2CDCH_2OH/D$	5.2%

The C_1 signal is a singlet ($C_1H_2C_2H$) and two triplets (C_1HDC_2H and C_1HDCD). The second triplet is only noticeable as a hump to the high field side of each signal of the first triplet. One can conceive the presence of a second singlet, but this is not resolved.



Spectrum 3.2 - 2-methylpropan-1-ol synthesised from 2-methylpropanal, EtOH and D_2/CO (1:1)

3.3.3 2-methylpropan-1-ol made from 2-methylpropanal, EtOD and CO/H_2 (1:1)

The analysis is made as for the above two examples (data can be found in tables 3.9 and 3.10) to give us;

$(CH_3)_2CHCHDOH/D$	16%
$(CH_3)_2CDCHDOH/D$	1.4%
$(CH_3)_2CHCH_2OH/D$	76%
$(CH_3)_2CDCH_2OH/D$	6.5%

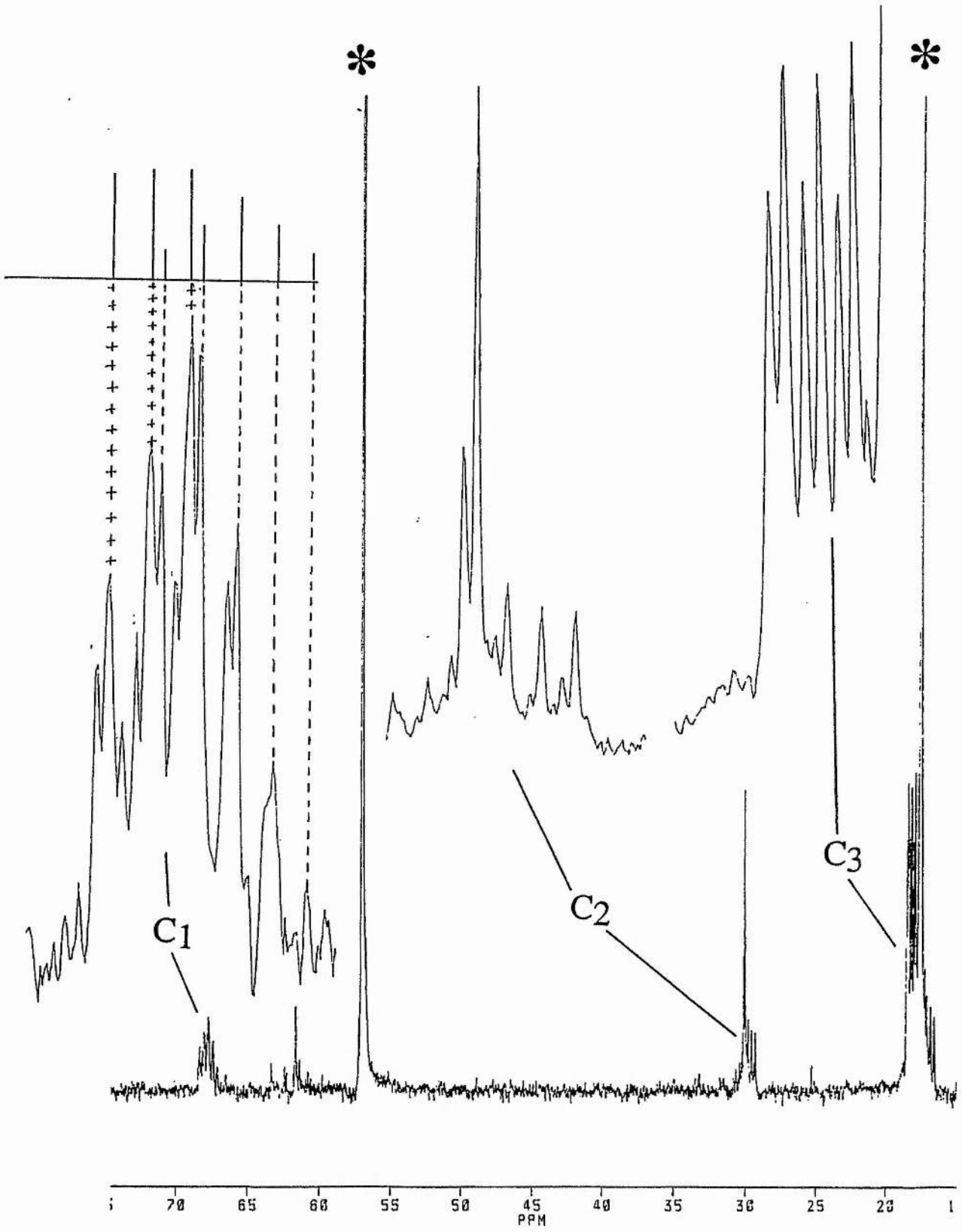
3.3.4 2-methylpropan-1-ol made from 2-propen-1-ol, EtOD and CO/D_2 (1:1)

The $^{13}C\{^1H\}$ spectrum of 2-methylpropan-1-ol obtained using 2-propen-1-ol, EtOD and D_2/CO (1:1) is shown in spectrum 3.3.

The resonance from C_3 appears as two triplets. Each line in the triplet is the same height, suggesting that all the C_3 signal is due to CH_2D. In other cases, where CH_3 is also present, the lowest field line of each triplet is increased in intensity. From the relative ratios of the two triplets, which arise because of β-shifting of the resonances due to C_3 being attached to C_2 with either H or D, we can directly determine the H/D ratio on C_2 as 44.0:56.0.

The C_1 resonance consists of two triplets and two quintets arising from CHD and CD_2 attached to C_2 with H or D. Once again the H:D ratio on C_2 can be calculated as 44.0:56.0, although with the overlap of peaks an element of uncertainty appears in the calculations based on the C_1 resonance. There is no evidence for CH_2 being present in the C_1 resonance. Analysis of the C_2 resonance then allows us to determine the CHD/CD_2 ratio on C_1. The C_2 resonance appears as two singlets (from CH) and two triplets (from CD). The singlets arise from C_2 experiencing 3 or 4 β-shifts, i.e. from $(CH_2D)_2CHCHDOH/D$ and $(CH_2D)_2CHCD_2OH/D$. The CHD/CD_2 ratio on C_1 can then be assessed as 31.0:69.0.

With only 4 isotopomers present, it is straightforward to estimate the amounts of each isotopomer present in the mixture if it is assumed that secondary isotope effects are negligible. The calculation has been performed and the results are as following.



Spectrum 3.3 - 2-methylpropan-1-ol synthesised from 2-propen-1-ol, EtOD and D_2/CO (1:1), with C_1 highlighted

$(CH_2D)_2CDCD_2OH/D$	39%
$(CH_2D)_2CHCD_2OH/D$	30%
$(CH_2D)_2CDCHDOH/D$	17%
$(CH_2D)_2CHCHDOH/D$	14%

3.3.5 2-methylpropan-1-ol made from 2-propen-1-ol, EtOH and CO/D_2 (1:1)

The $^{13}C\{^1H\}$ inverse gated spectrum obtained for the 2-methylpropan-1-ol produced using 2-propen-1-ol and EtOH in D_2/CO (1:1) is shown in spectrum 3.4.

The resonance from C_2 shows five singlets, each separated by *ca.* 0.08 ppm (β-shift). The failure to observe any triplets suggests that this C atom is mostly C-H. The resonance from C_3 shows a doublet of 1:1:1 triplets, separated by one β-shift of 0.08 ppm, with the left hand peak of each triplet being of greater intensity than the others. The triplets arise from CH_2D attached to CH or CD on C_2. The increased intensity of the left hand resonance of each triplet arises from CH_3 attached to CH or CD on C_2.

The signal from C_1 arises from a singlet, a 1:1:1 triplet and a 1:2:3:2:1 quintet being superimposed (the complexity of this signal means that it is not possible to see the β-shifted resonances from C_1 attached to C_2D). Since $J_{C\text{-}D}$ in this case is slightly less than the α-shift on the 75.5 MHz instrument used, this resonance is extremely complex but still interpretable.

This means the 18 products A'-J' and A"-J" (see table 3.1) are all present in the reaction mixture.

In order to carry out the analysis of the relative amounts of these 18 products, we first make the assumption that secondary isotope effects are so small that the H/D ratio on C_2 is the same for all otherwise equivalent pairs of molecules, so for the rest of the analysis, we define A=A'+A", B=B'+B" and so on. The major signal from C_2 appears as five singlets of relative intensity 1.2:5.9:24.2:44.9:23.7. These arise from C atoms experiencing 0, 1, 2, 3 or 4 β-shifts respectively. Isotopomer A lies furthest down field. Simultaneous equations can now be set up.

Spectrum 3.4 - 2-methylpropan-1-ol synthesised from 2-propen-1ol, EtOH and D_2/CO (1:1), with C_1 highlighted

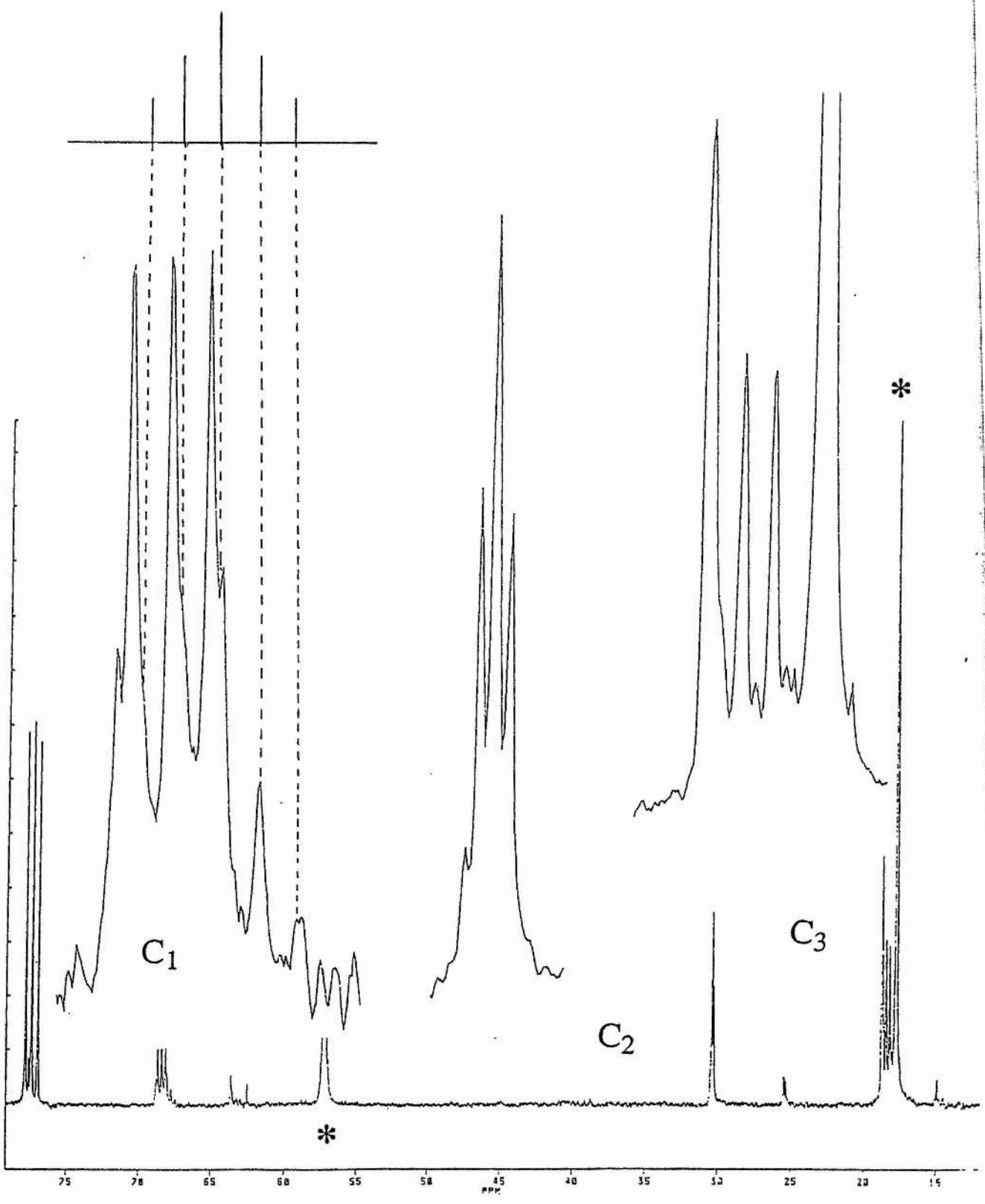


Table 3.1 - Labels given to isotopomers of 2-methylpropan-1-ol obtained upon hydrocarbonylation of 2-propen-1-ol using EtOH and D_2

Isotopomer	Label	No. of β-deuteriums to C_2
$(CH_3)_2CHCH_2OH/D$	A'	0
$(CH_3)_2CDCH_2OH/D$	A"	0
$(CH_3)_2CHCHDOH/D$	B'	1
$(CH_3)_2CDCHDOH/D$	B"	1
$(CH_3)_2CHCD_2OH/D$	C'	2
$(CH_3)_2CDCD_2OH/D$	C"	2
$(CH_3)(CH_2D)CHCH_2OH/D$	D'	1
$(CH_3)(CH_2D)CDCH_2OH/D$	D"	1
$(CH_3)(CH_2D)CHCHDOH/D$	E'	2
$(CH_3)(CH_2D)CDCHDOH/D$	E"	2
$(CH_3)(CH_2D)CHCD_2OH/D$	F'	3
$(CH_3)(CH_2D)CDCD_2OH/D$	F"	3
$(CH_2D)_2CHCH_2OH/D$	G'	2
$(CH_2D)_2CDCH_2OH/D$	G"	2
$(CH_2D)_2CHCHDOH/D$	H'	3
$(CH_2D)_2CDCHDOH/D$	H"	3
$(CH_2D)_2CHCD_2OH/D$	J'	4
$(CH_2D)_2CDCD_2OH/D$	J"	4

If a-j are the relative amounts of A-J, we know from the intensities of the five signals from C_2 that;

$$a=0.012$$
$$b+d=0.059$$
$$c+e+g=0.242$$
$$f+h=0.449$$
$$j=0.237$$

There are various ways in which other suitable equations can be constructed, the easiest one is to assume that the labelling pattern on C_1 does not affect the relative amounts of label on C_3, that is whether C_1 is CH_2, CHD or CD_2, the ratio of $(CH_2D)_2$ to $(CH_2D)(CH_3)$ on C_3 will be the same. Similarly, the ratio of $(CH_2D)(CH_3)$ to $(CH_3)_2$ on C_3 will be the

same regardless of the labelling on C_1. This gives rise to the following equations;

f/j=e/h=d/g
and c/f=b/e=a/d

Then an estimate of the value of f/j is obtained from an analysis of the C_3 resonance in the inverse gated decoupled spectrum of the sample (i.e. a spectrum in which nOes have been removed. This data is subject to error if the delay in the pulse sequence is of insufficient length to allow full relaxation). This tells us that the signal from C_3 is made up of 14% CH_3 and 86% CH_2D. Since the CH_3 can come from compounds with $(CH_3)_2$ or $(CH_3)(CH_2D)$ on C_3, we arbitrarily select a value of 10% for the amount arising from $(CH_3)(CH_2D)$. We can then solve for all the unknowns and obtain the percentage values for all 18 products. These are collected together in table 3.8 (see section 3.6). The value of 10% can be varied and it turns out that the amounts of the various products are rather insensitive to what value is selected, provided it is in the range 5-15%.

However the number of assumptions made in this analysis means that it is desirable to have another method available for the analysis of complex mixtures of this kind. Fortunately, better quality information is available from $^{13}C\{^1H,^2H\}$ nmr spectra. See section 3.4.

3.3.6 2-methylpropan-1-ol made from 2-propen-1-ol, EtOD and CO/H_2 (1:1)

A similar analysis to the one carried out in section 3.3.4 using data collected in table 3.5 can be performed to quantify the 4 possible isotopomers with the following results:

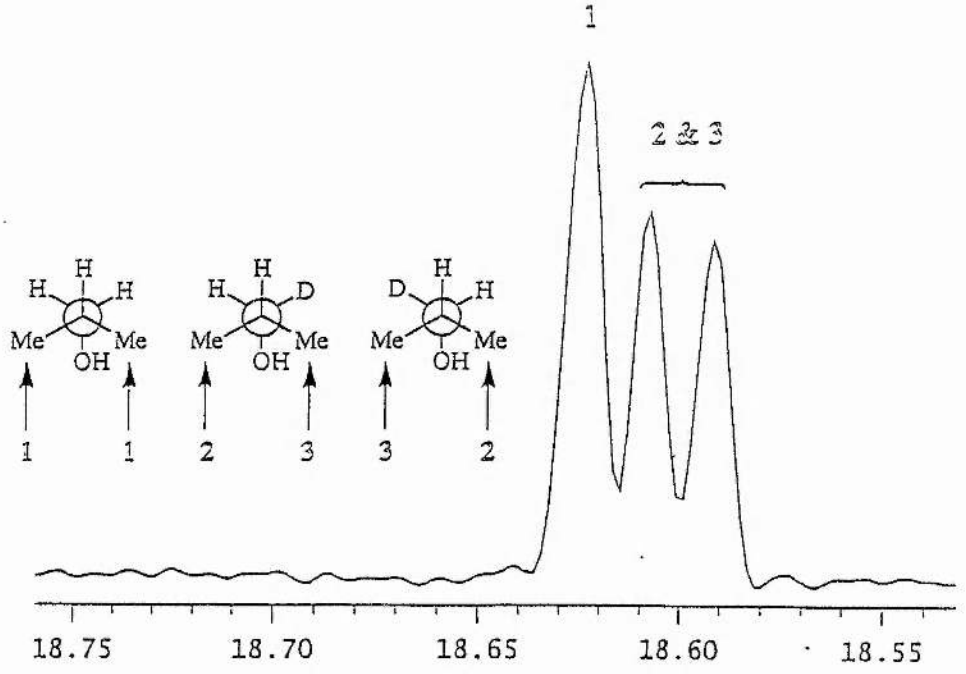
$(CH_3)_2CHCH_2OH/D$	49%
$(CH_3)_2CDCH_2OH/D$	29%
$(CH_3)_2CHCHDOH/D$	14%
$(CH_3)_2CDCHDOH/D$	8.2%

3.4 Analysis of 2-methylpropan-1-ol at 151 MHz

Because of the problems associated with analysis using $^{13}C\{^{1}H\}$ nmr spectra of the complex mixture of isotopomers produced from 2-propen-1-ol and D_2 in EtOH, an alternative method was employed. The method was first used by Brown and co-workers[185, 186]. This method involves the measurement of ^{13}C resonances whilst decoupling both ^{1}H and ^{2}H. Measuring the spectra at higher field (151 MHz), it is then possible not only to see $\alpha + \beta$ shifts, but also γ-shifts. In favourable cases, β-shifts from different types of β-D can be resolved, as can γ-shifts from different types of γ-D. γ-shifts tend to be ~0.01-0.02 ppm

3.4.1 2-methylpropan-1-ol made from 2-methylpropanal, EtOH and CO/D_2 (1:1)

The analysis was carried out as before at 75.5 MHz (see section 3.3.3). The resolution of the signals allowed us to see not just α- and β-shifts, but γ-shifts also. The clarity of the signals allowed us to resolve inequivalent methyl groups. This is illustrated using spectrum 3.5.



Spectrum 3.5 - Resolution of resonances arising from inequivalent methyl groups

3.4.2 2-methylpropan-1-ol made from 2-propen-1-ol, EtOD and D_2 analysed at 151 MHz.

The better resolution of the spectrum obtained at 151 MHz indicates that the mixture is more complex than was suggested by the $^{13}C\{^1H\}$ spectrum measured at 75.5 MHz. Spectrum 3.6 shows the resonances of 2-methylpropan-1-ol. The spectra are not only proton decoupled but in some cases deuterium decoupled also, so triplets and quintets collapse to singlets. This is well illustrated by the C_1 signal. Without deuterium decoupling, the signal is made up of a doublet of triplets and a doublet of quintets, the decoupling allows us to glean useful information from this resonance. For instance we can see instantly that the signal corresponds to only CHD and CD_2, with no trace of CH_2, as previously reported from analysis of the C_2 resonance in the 75.5 MHz $^{13}C\{^1H\}$ spectrum.

The C_2 resonance is better resolved than in the 75.5 MHz spectrum and reveals features that were not appreciated in the lower field spectrum. Deuterium decoupling causes a pair of singlets and a pair of triplets to collapse into two pairs of singlets. On closer inspection, each pair of singlets is actually four almost separate signals. The set to higher field are better resolved. There are also small resonances at δ 29.32 and δ 29.81 which are unassigned but may arise from C_2 atoms with a trace of CD_2H at C_3. There is a possibility that resonances from this kind of C_3 atom are to be found at δ 17.79 and δ 17.67.

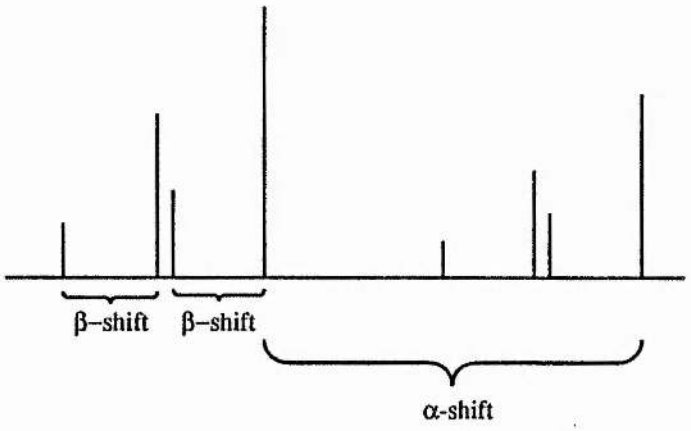
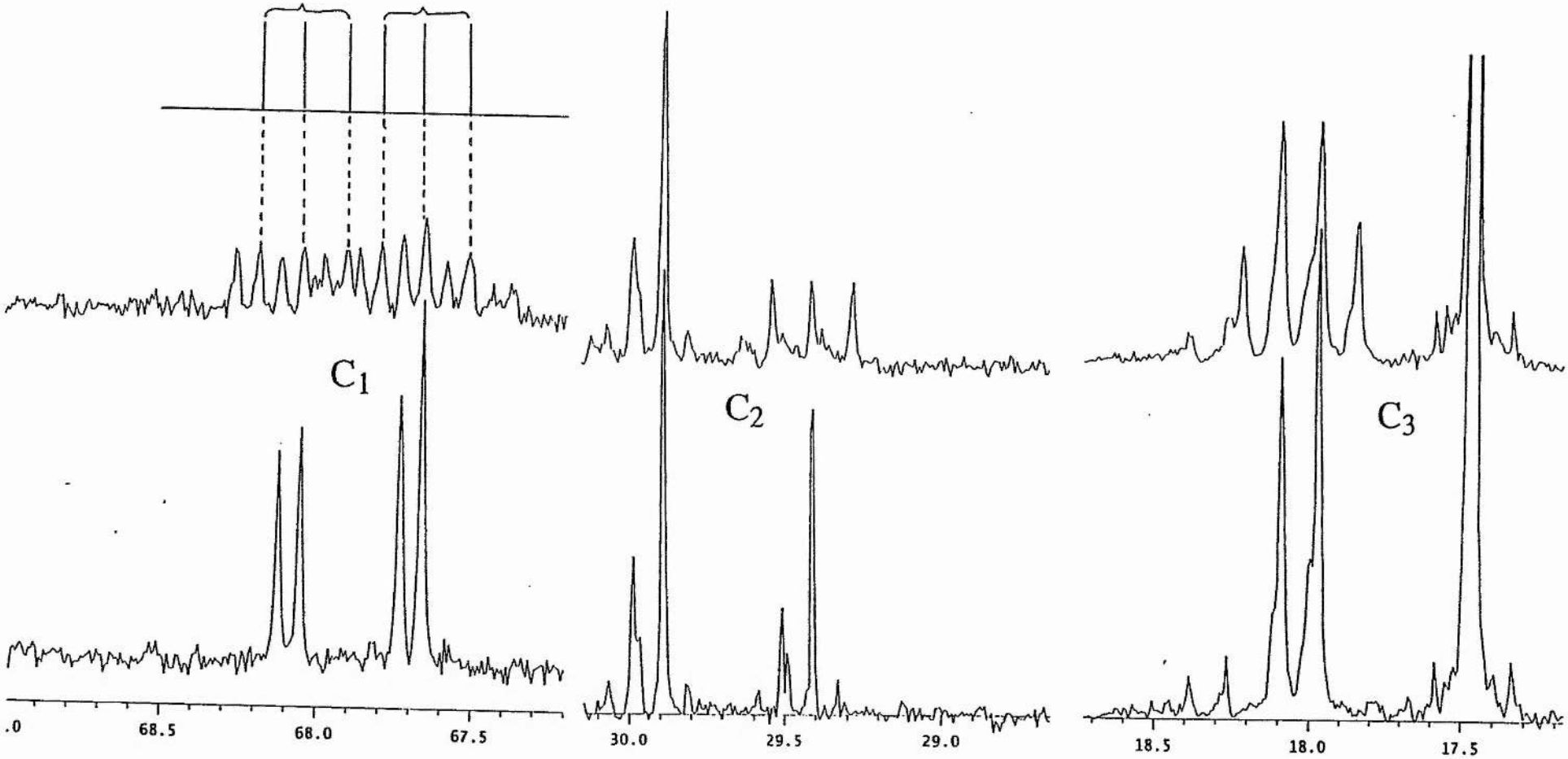


Figure 3.1 - Stylised C_2 (methine) region of Spectrum 3.6

Figure 3.1 represents the eight signals from C_2 seen in Spectrum 3.6. The four signals on the left (lower field) are due to C-H in the C_2



Spectrum 3.6 - 2-methylpropan-1-ol synthesised from 2-propen-1-ol, EtOD and D_2/CO. Upper resonances are $^{13}C\{^1H\}$ the lower resonances are $^{13}C\{^1H,^2H\}$

position. Therefore, the four on the right (higher field) are due to C-D in the C_2 position. Each set of four signals contains one signal with x β-shifts, two with (x+1) β-shifts and the remaining one with (x+2) β-shifts. These are shown in figure 3.2.

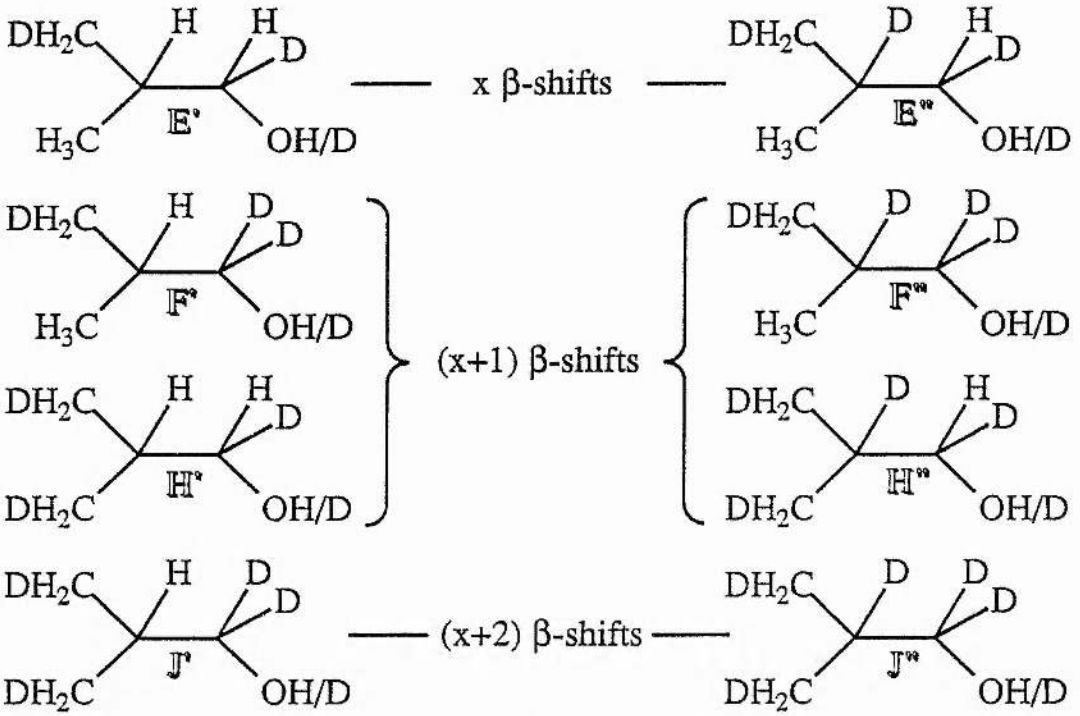


Figure 3.2 Legend showing Labels given to Product Isotopomers

If we assign the largest signal in each set to $(CH_2D)_2CH/DCD_2OH$, on the basis of the C_3 data, which shows us that most of the methyl groups are CH_2D and only a few are CH_3 and the C_1 data which shows that CD_2 predominates given that the Overhauser effect increases the relative intensity of the C_1H_2D resonances, it follows that the next largest signal is from $(CH_2D)_2CH/DCHDOH$ and the other two signals arise from $(CH_2D)(CH_3)CH/DCD_2OH$ and $(CH_2D)(CH_3)CH/DCHDOH$.

From the integrations/ heights of the peaks we can now derive two sets of ratios e':f':h':j' and e":f":h":j" (4.5: 20.3: 11.3: 63.8, 6.6: 20.8 :12.3: 60.4 respectively).

Using the C_1 data, we can gain the rest of the information we need to solve the quantitative analysis, without assuming anything about secondary isotope effects.

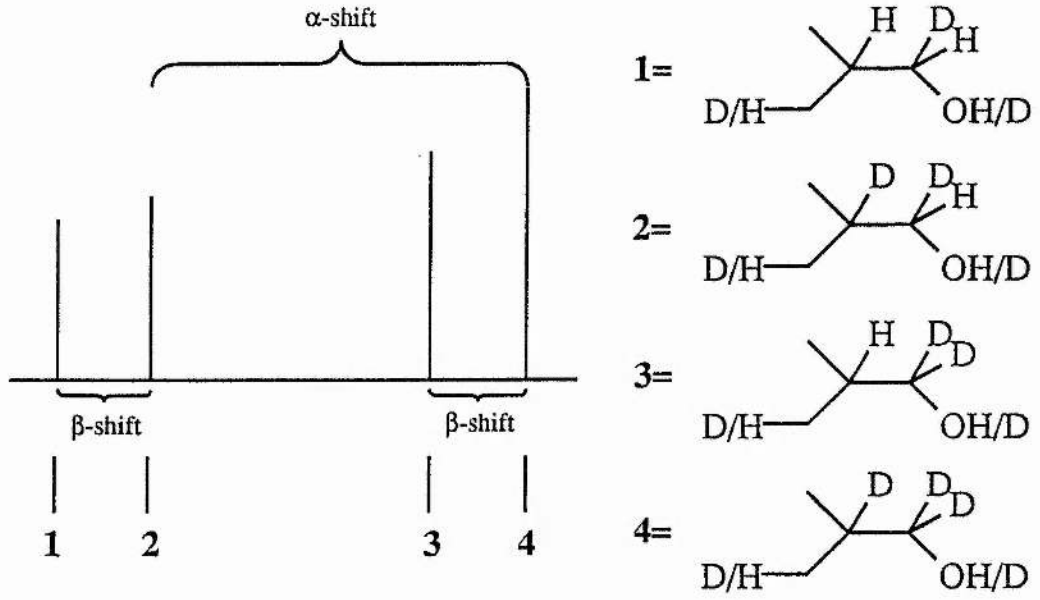


Figure 3.3 Stylised C_1 (methylene) region of Spectrum 3.6.

The ratios **1**:**2** and **3**:**4** can be measured (47.7:52.3, 42.0:58.0 respectively).

We can now combine the data thus;

e'+ h' (i.e. **1**) : e"+h" (i.e. **2**) ≡ 47.7: 52.3
f'+j' (i.e. **3**) : f"+j" (i.e. **4**) ≡ 42.0: 58.0

Since we know e':h', e":h", f':j' and f":j", the quantity of each isotopomer present can be calculated thus;

$(CH_3)(CH_2D)CHCHDOH/D$	E'	2.1%
$(CH_3)(CH_2D)CHCD_2OH/D$	F'	4.7%
$(CH_2D)_2CHCHDOH/D$	H'	9.7%
$(CH_2D)_2CHCD_2OH/D$	J'	27%
$(CH_3)(CH_2D)CDCHDOH/D$	E"	3.4%
$(CH_3)(CH_2D)CDCD_2OH/D$	F"	7.1%
$(CH_2D)_2CDCHDOH/D$	H"	11%
$(CH_2D)_2CDCD_2OH/D$	J"	35%

The 75.5 MHz data suggested only 4 isotopomers, 151 MHz data suggested that 8 isotopomers are in fact present. All 8 showed resolvable methine resonances (C_2). If the isotopomers are quantified substituting

CH_3 with CH_2D as if no CH_3 existed, then the 75.5 MHz data compares favourably with the 151 MHz (within ~4%). (See Table 3.9)

A note of caution comes from the 151 MHz data. Even though the signals caused by CH_3 are small in Spectrum 3.6, ~17.4 % of the isotopomers in the mixture contain a single CH_3 group. The signal looks small, but even though it contains some nOe, ~82.6% of the isotopomers have two CH_2D methyl groups and ~17.4% contain one. The fact that such a significant amount of CH_3 groups goes undetected in the 75.5 MHz spectrum gives some indication of the limitations of that type of analysis.

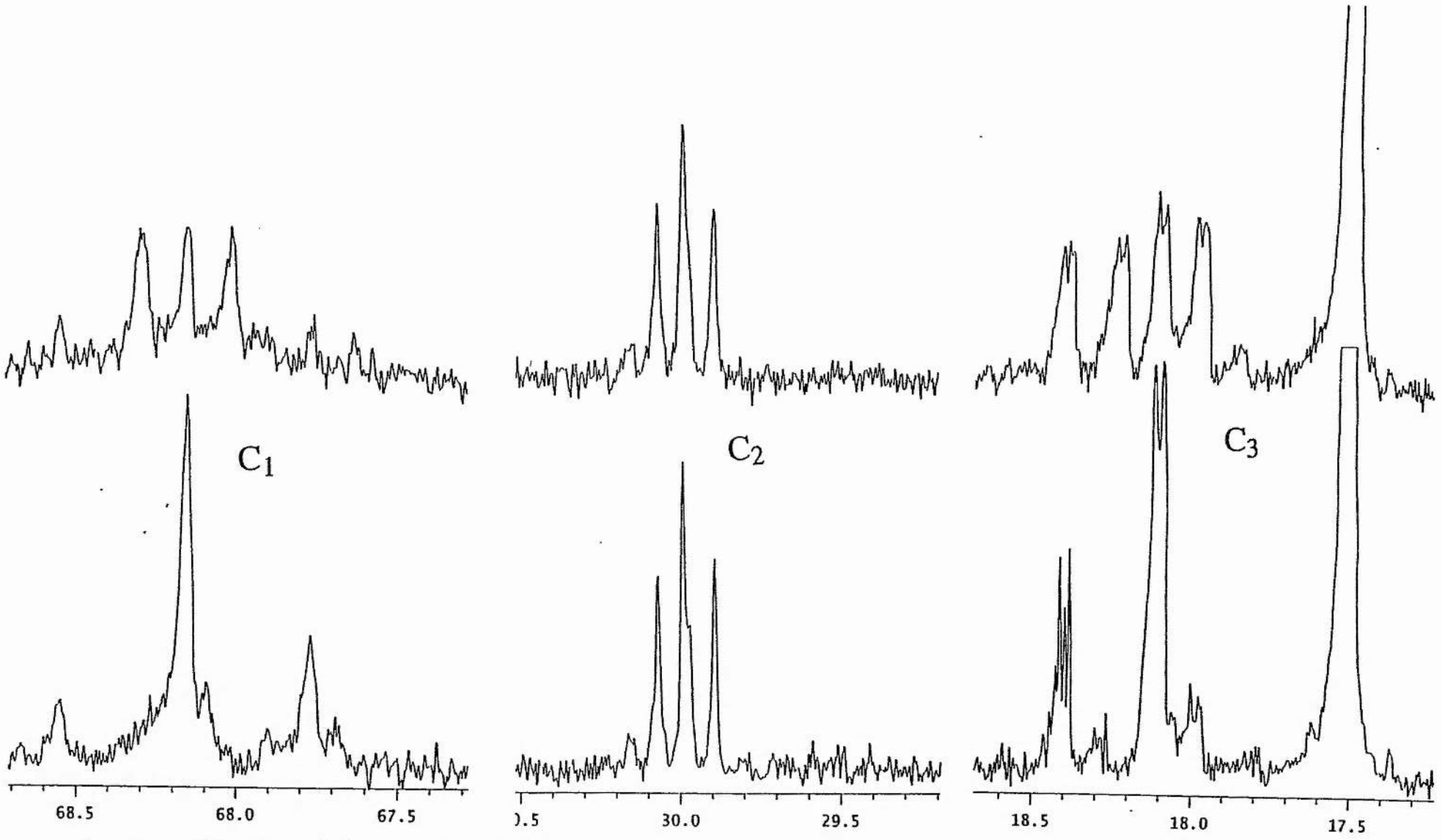
One more interesting conclusion can be drawn from the comparison with the data taken at lower field strength. The assumption about secondary isotope effects is not strictly accurate, but not a bad approximation. (The H/D ratios from C_1 measured from the spectrum are 47.7: 52.3 and 42.0: 58.0. If the assumption about secondary isotope effects was strictly accurate then these two ratios should be the same).

3.4.3 Analysis of 2-methylpropan-1-ol produced from 2-propen-1-ol, CO/D_2 (1:1) and EtOH at 151 MHz

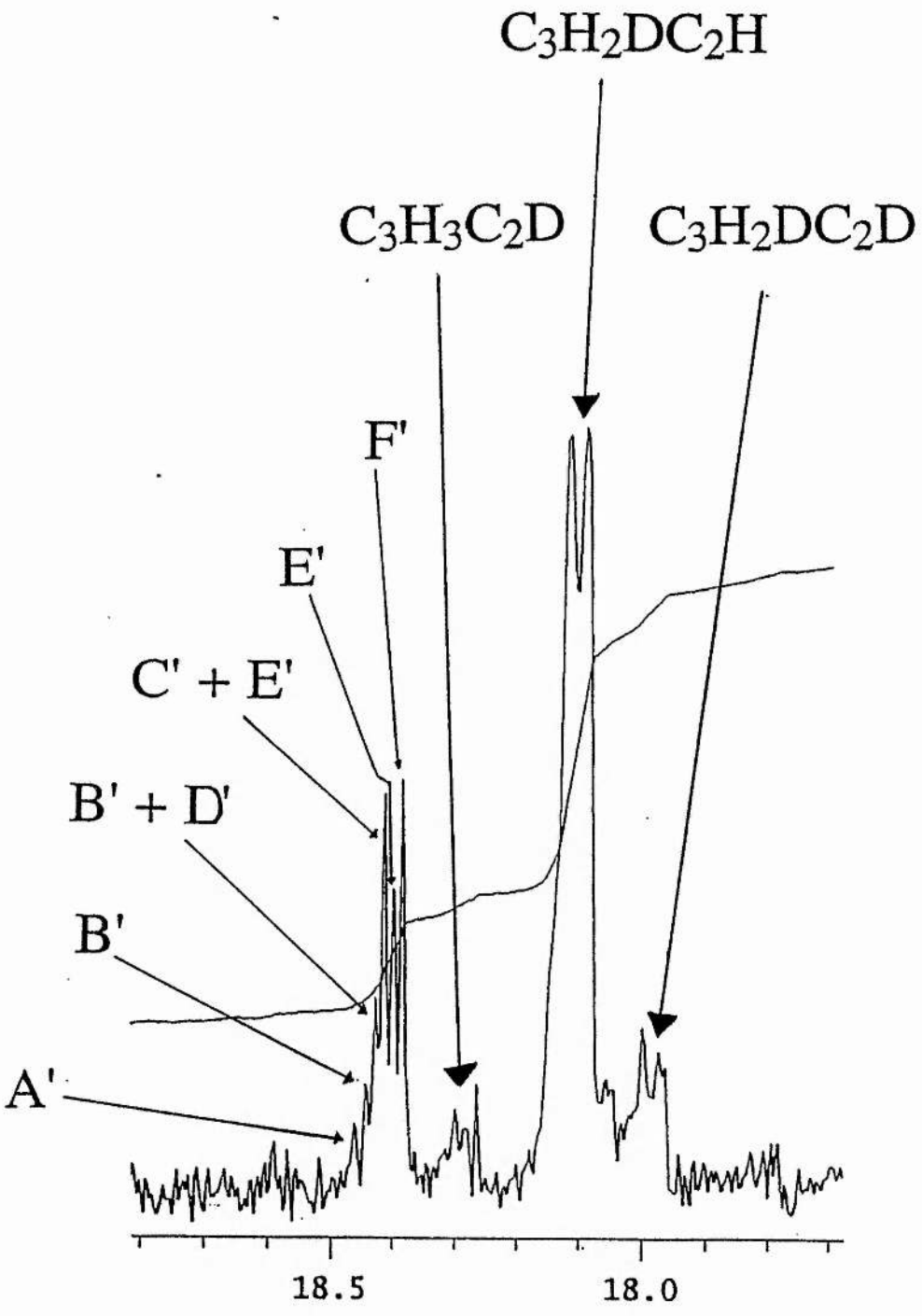
The $^{13}C\{^1H,^2H\}$ spectrum obtained for the 2-methylpropan-1-ol produced from 2-propen-1-ol and D_2/CO in EtOH (1:1) is shown in spectrum 3.7. The resonance from C_2H, which is similar to that obtained in the $^{13}C\{^1H\}$ spectrum measured at 75.5 MHz, is split into five signals corresponding to C atoms experiencing 0, 1, 2, 3 or 4 β-shifts with decreasing δ values. Their relative intensities are 16:74:253:434:222 respectively. It is worth noting that the signals corresponding to 2 and 3 β-shifts show further splitting, but are not fully resolved.

$$a' = 0.016$$
$$b'+d' = 0.074$$
$$c'+e'+g' = 0.253$$
$$f'+h' = 0.434$$
$$j' = 0.222$$

The resonance from CH_3 on C_3 shows very much better resolution in the $^{13}C\{^1H,^2H\}$ spectrum (spectrum 3.7) appearing as 6 singlets (in the $^{13}C\{^1H\}$ spectrum at 75.5 MHz only a single peak is observed - see



Spectrum 3.7 - 2-methylpropan-1-ol synthesised from 2-propen-1ol, EtOH and D_2/CO. Upper resonances are $^{13}C\{^1H\}$ the lower resonances are $^{13}C\{^1H,^2H\}$



Spectrum 3.8 - Assignments of C_3 signal of d_x-2-methylpropan-1-ol synthesised from EtOH and CO/D_2.

spectrum 3.4). The assignment of these resonances is helped by the earlier observation of inequivalent methyl groups in diastereomers (section 3.4.1). This then allows the full assignment of the 6 singlets obtained from the CH_3 groups on C_3 of the complex mixture as follows in increasing order of chemical shift; [F'], [E'], [C' + E'], [B' + D'], [B'], [A']. These assignments are shown in spectrum 3.8. Assuming that the two diastereoisomers of E' are present in equal amounts, which is likely since the chiral centre on C_1 is believed to be formed by hydrogenation of the carbonyl group in 2-methylpropanal and there is unlikely to be a diastereoselectivity generated by the difference between CH_3 and CH_2D on C_2; remembering that A', B' and C' each contain two CH_3 groups (i.e. doubles the signal); and setting b' + d' to 0.074 as required by the C_2 resonance, it is then possible to calculate the relative proportions of the different isotopomers as follows:

$$f' = 0.160$$
$$e' = 0.234$$
$$d' = 0.031$$
$$b' = 0.043$$
$$c' = 0.019$$
$$a' = 0.016$$

The final values g',h',j' can be calculated from the equations constructed from the signals for C_2.

$$g' = 0.253 - c' - e' = 0$$
$$h' = 0.434 - f' = 0.274$$
$$j' = 0.222$$

Finally, with the assumption that the H/D ratio on C_2 is the same for all isotopomers (0.82:0.18, obtained from integration of the unshifted and β-shifted resonances of C_3 or C_1) which seems to be valid since the shapes of β-shifted and non-β-shifted resonances on C_3 and C_1 are the same, it is possible to calculate the proportion of each of the 18 isotopomers in the complex mixture:

$(CH_3)_2CHCH_2OH/D$	A'	=	1.3%
$(CH_3)_2CHCHDOH/D$	B'	=	3.5%

$(CH_3)_2CHCD_2OH/D$	C'	=	1.5%
$(CH_3)(CH_2D)CHCH_2OH/D$	D'	=	2.5%
$(CH_3)(CH_2D)CHCHDOH/D$	E'	=	19.1%
$(CH_3)(CH_2D)CHCD_2OH/D$	F'	=	13.1%
$(CH_2D)_2CHCH_2OH/D$	G'	=	0.0%
$(CH_2D)_2CHCHDOH/D$	H'	=	22.5%
$(CH_2D)_2CHCD_2OH/D$	J'	=	18.2%
$(CH_3)_2CDCH_2OH/D$	A"	=	0.3%
$(CH_3)_2CDCHDOH/D$	B"	=	0.8%
$(CH_3)_2CDCD_2OH/D$	C"	=	0.4%
$(CH_3)(CH_2D)CDCH_2OH/D$	D"	=	0.6%
$(CH_3)(CH_2D)CDCHDOH/D$	E"	=	4.3%
$(CH_3)(CH_2D)CDCD_2OH/D$	F"	=	2.9%
$(CH_2D)_2CDCH_2OH/D$	G"	=	0.0%
$(CH_2D)_2CDCHDOH/D$	H"	=	4.9%
$(CH_2D)_2CDCD_2OH/D$	J"	=	4.0%

3.5 Discussion of Results

Many conclusions can be drawn from the data collected above. The first and most obvious is that the higher the field of the nmr machine, the easier the data collected becomes to interpret. Another aid to easier interpretation is to take complimentary spectra (looking at ^{13}C nuclei) one set with just protons decoupled and one set that have proton and deuterium nuclei decoupled.

Most of the data that has been collected, especially at 75.5 MHz, have errors associated with (a) physical measurement of peak integrals from the spectra, (b) signal overlap. As previously mentioned, errors of type (a) have been assigned error values (included in tables 3.8, 3.9 and 3.10). The values are not normally worse than 1% of the total, unless the signal to noise ratio is low.

Errors of type (b) have not been formally analysed, but in the more ambiguous cases the spectra have been enlarged and cut up trying to take account of signal overlap, then the areas have been calculated on weights of individual parts of the spectra. Errors of the type (b) tend to inflate small values and underestimate larger values of the integrals examined.

One thing that is very clear from the study is the proliferation of data that comes available upon increasing the field of the nmr machine.

Signals are resolved better and hidden information in 75.5 MHz spectra becomes available on 151 MHz spectra.

A factor that becomes apparent from the data is the number of isotopomers produced in some of the reactions, more than is expected from a cursory glance at the mechanism discussed in chapter 2 and shown in scheme 2.16. If we first look at the data generated from the hydrogenation of 2-methylpropanal, we can find some general trends which we can be useful in interpreting the 2-propen-1-ol reaction. These data collected can be compared to ^1H data also collected. The ^1H data are absolute in these cases because the molecule contains a moiety (the methyl groups) that undergoes no detectable chemical exchange with the solvent or the gas phase during the reaction.

Table 3.2 Comparison of ^{13}C and ^1H data for hydrogenation of 2-methylpropanal (^{13}C data @ 75.5 MHz, ^1H data @ 300 MHz)

	% D incorporation					
Origin	D_2/ EtOD		D_2/ EtOH		H_2/ EtOD	
of data	C_1*	C_2	C_1*	C_2	C_1*	C_2
^1H	98%	10%	60%	7%	23%	5%
^{13}C	95%	15%	56%	12%	18%	8%

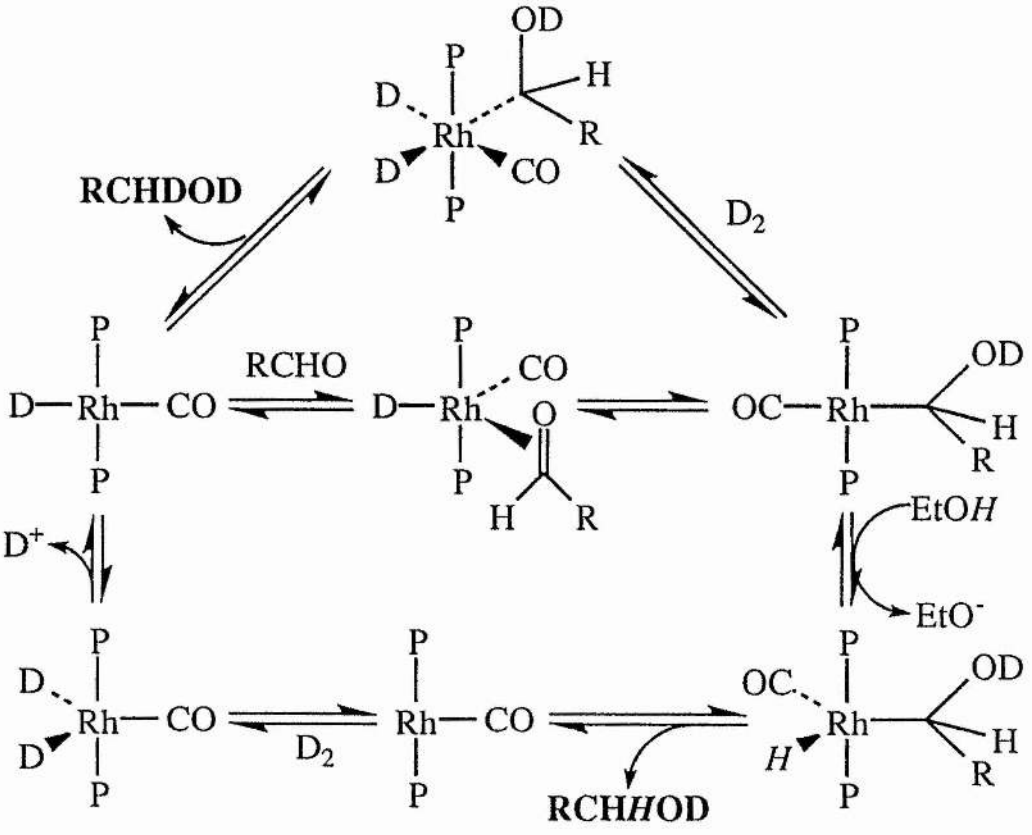
* Defined as percentage of C_1HD, other products have C_1H_2.

As predicted the errors for the ^{13}C data (shown in table 3.2) are an under estimation of the higher values and over estimation of the lower values.

It seems that for C_1 most of the label is coming from the gas phase, but there is a significant contribution from the acidic hydrogen atom of the solvent. Similar results have been observed in the hydrogenation of heptanal using a similar system[56]. It was also suggested that the hydrogenation was occurring by two distinct mechanisms, these mechanisms are shown in scheme 3.1.

For the hydrogenation of 2-methylpropanal in $EtOD/D_2$, the labelling pattern on C_1 should be entirely CHD. A small amount of extra

H is incorporated and this probably arises from keto-enol tautomerism of the substrate giving rise to exchange of some of the OD protons for OH. This then can be incorporated onto C_1 by the lower mechanism of scheme 3.1 and kinetic isotope effects will enhance the amount of H that appears. Nevertheless, the amount of this type of exchange is small (only 2%) so it is ignored in the subsequent analysis. The observation of D on C_2 confirms that the proposed keto-enol tautomerism does occur.



Scheme 3.1 - Two possible mechanism for the hydrogenation of 2-methylpropanal.

The proportion of 2-methylpropan-1-ol made by each pathway of scheme 3.1 can be calculated as follows;

For D_2/EtOH, 40% is H and 60% is D (H/D = 0.67) $\therefore$ on C_1 60% comes from the gas phase and 40% comes from the solvent.

For H_2/EtOD, 77% is H and 23% is D (H/D = 3.35) $\therefore$ on C_1 77% comes from the gas phase and 23% comes from the solvent.

Now we can say that the overall isotope effect (the ratio of the above two figures) is;

$$k_H/k_D = {}^{3.35}/_{0.67} = 5.0$$

If we make the assumption that both isotope effects are the same then each individual isotope effect is simply the square root of the overall isotope effect ($\sqrt{5}$~2.24). But the gas phase reaction is sped up and the solution reaction is slowed down. So for the reaction involving H_2/EtOH or D_2/EtOD the reaction ratios for each route are calculated and produce the value of 1.5 (H/D multiplied or divided by 2.24, 3.35/2.24 or 0.67 x 2.24). So we can say that approximately 60% of the aldehyde hydrogenation goes by the gas phase route and approximately 40% goes via the cationic route in the reaction where H_2 and EtOH are employed.

The ^{13}C data obtained from using 2-propen-1-ol can also be checked against the ^{1}H data in a self consistent way. But one of the protic integrals has to be assigned a value on the basis of the ^{13}C data, then the other signal intensities can be compared. For this analysis we have arbitrarily selected C_3 to be set from the ^{13}C data.

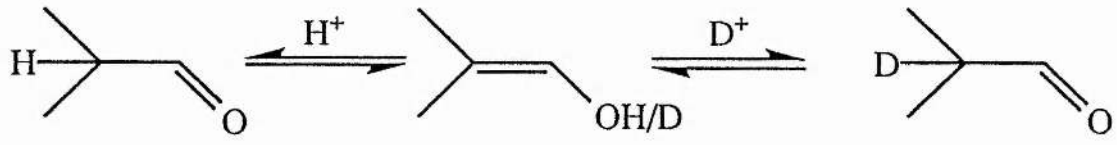


Diagram 3.1 - Possible mechanism for isotopic incorporation into C_2 by keto - enol isomerisation

Again as can be seen in table 3.3, the data is a good fit for 151 MHz, within a reasonable error. For the 75.5 MHz data the fit is poor, again showing advantages of using the higher field. We can therefore be relatively confident that this style of analysis yields usable data. It can now be used to validate the mechanism proposed in chapter 2. The mechanism is repeated in scheme 3.2, but showing isotopic substitution. The legend for the isotopic labelling is; D originates from the gas phase, *H* reflects the isotopic composition of the solution.

Table 3.3 Comparison of ^{13}C and ^{1}H data for hydrocarbonylation of 2-propen-1-ol (^{13}C data @ 151 MHz and 75.5 MHz, ^{1}H data @ 300 MHz)

% D incorporation

Origin	D_2/ EtOD			D_2/ EtOH			H_2/ EtOD		
of data	C_1	C_2	C_3	C_1	C_2	C_3	C_1	C_2	C_3
^{1}H	170%	54%	184%	138%	22%	143%	38%	48%	0%
$^{13}C^{a}$	174%	57%	184%	136%	18%	143%	-	-	-
$^{13}C^{b}$	169%	56%	200%	107%	5%	184%	22%	37%	0%

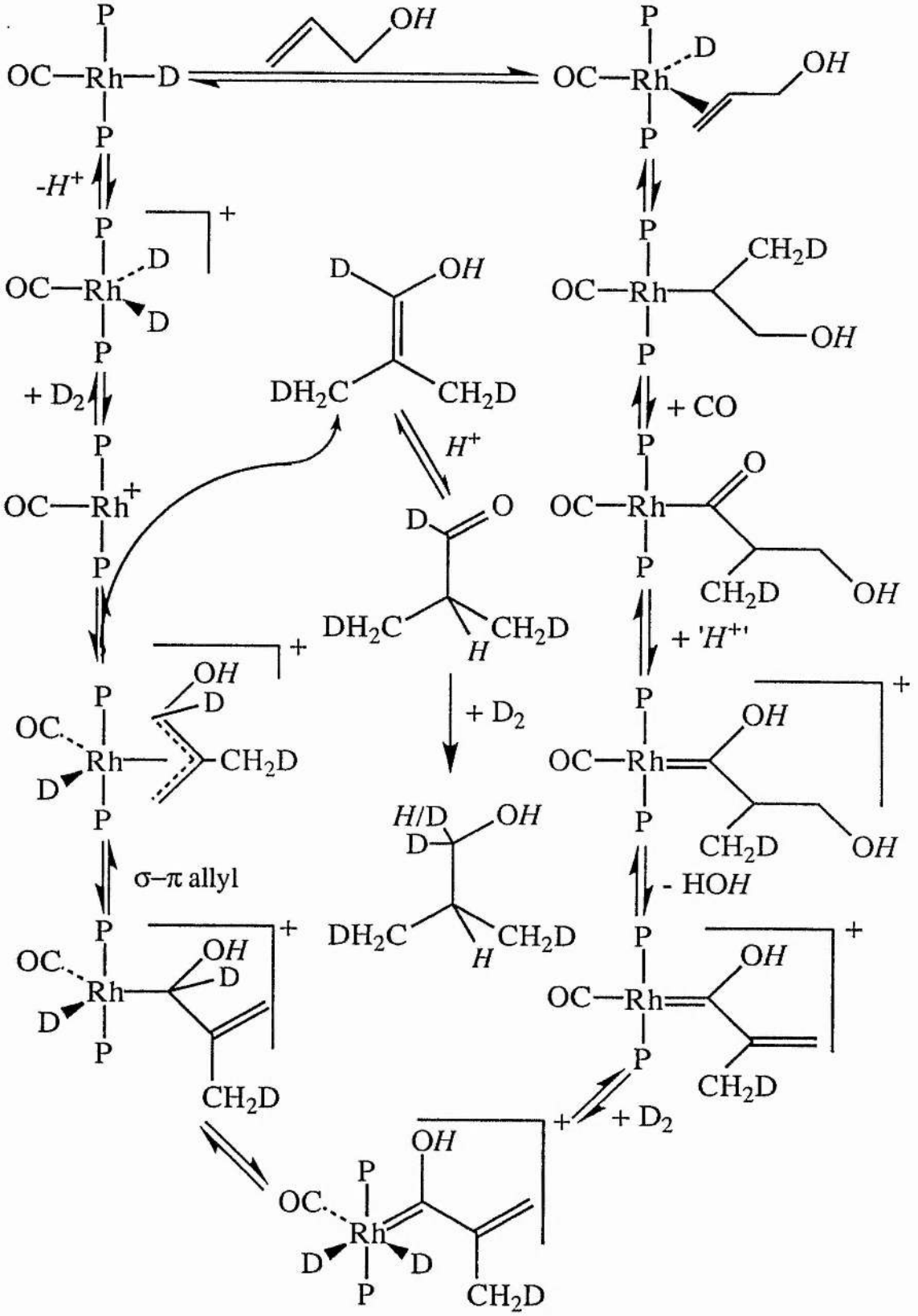
a - 151 MHz data, **b** - uncorrelated 75.5 MHz data.

There are a few problems when considering the isotopic composition of the solvent and the effect is complex to model because of the various protic sources, which are;

(1) The solvent-OH/D, (2) the initial substrate-OH, (3) 1 mol of H/D^{+} (released from the gas phase from catalyst regeneration) per mol of substrate consumed, (4) 1 mol H^{+} (from the substrate due to the dehydration) per mol of 2-methylpropan-1-ol formed, (5) ~1.4 moles of H/D^{+} (from the gas phase through the hydrogenation of 2-methylpropanal) per mol of 2-methylpropan-1-ol formed. The last number reflects the two ways of aldehyde hydrogenation shown in scheme 3.1. Thus, the isotopic composition of the solvent is always changing as the reaction runs.

3.5.1 Isotopic labelling pattern for C_3

If the mechanism is followed round, all the C_3 labelling should be CH_2X, where X comes from the gas phase. Generally this is true, but there is a noticeable solvent effect. See table 3.4.



Scheme 3.2 - 2-methylpropan-1-ol production mechanism incorporating isotopic origins.

Table 3.4 Isotopic composition of C_3 made from various isotopic sources

	$(CH_3)_2$ (%)	$(CH_3)(CH_2D)$ (%)	$(CH_2D)_2$ (%)
$EtOD/H_2$[a]	100	-	-
$EtOH/D_2$	8	42	50
$EtOD/D_2$	0	17	83

a-taken at 75.5 MHz, the rest at 151 MHz

For D_2, EtOD > 90% of the methyl groups contain D, leaving ~ 8-9% that contain H. The H must be coming from the solvent, conceivably the exchange with a hydrogen atom from one of the cationic intermediates. See scheme 3.3.

Scheme 3.3 - Possible exchange of 'solvent'-O*H* with cationic rhodium catalytic intermediates.

Using D_2/EtOH the solvent effect is far more pronounced with ~29% of the methyl groups having H incorporation, as expected because the OH concentration is much higher than for the $EtOD/D_2$ reaction.

The data taken for H_2/EtOD suggests there is no incorporation of D from the solvent, but we already know that the 75.5 MHz data may not be fully resolved, although isotope effects will also slow down any D incorporation from the solvent.

3.5.2 Isotopic labelling pattern for C_2

The labelling on C_2 depends strongly upon the solvent composition. The C_2 hydrogen atom is introduced during the tautomerisation of the enol to the aldehyde (see diagram 3.2), but a small contribution comes from the gas phase, as we saw from the hydrogenation of 2-

methylpropanal (e.g. 7% using D_2/EtOH). The results are brought together for 2-propen-1-ol and 2-methylpropanal (for comparison) in table 3.5.

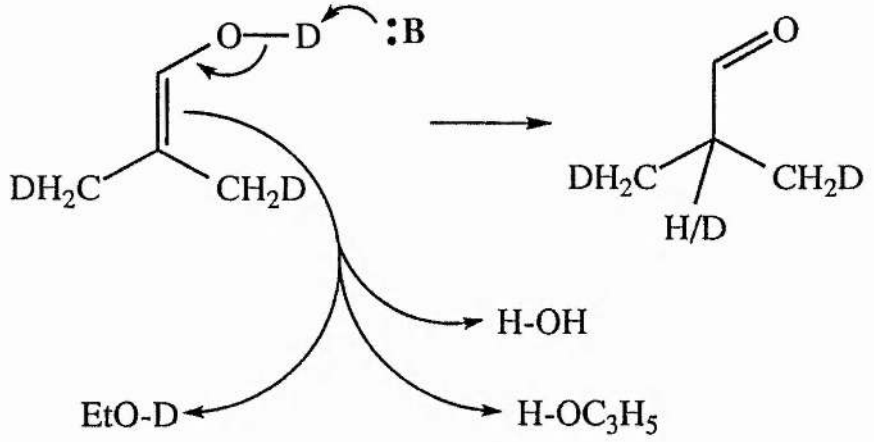


Diagram 3.2 Illustration of some of the various hydrogen ion sources to aid the tautomerisation of 2-methyl-1-propen-1-ol

Table 3.5 Isotopic composition of C_2 made from various isotopic sources

	2-propen-1-ol		2-methylpropanal	
	CH(%)	CD(%)	CH(%)	CD(%)
EtOD/H_2	63	37	95	5
EtOH/D_2	82	18	93	7
EtOD/D_2	43	57	90	10

The kinetic effect for the solvent can be calculated for the addition of a solvent hydrogen ion during the keto-enol tautomerisation. If 2-methylpropan-1-ol is assumed to account for 28% of the final product mixture, then the final solvent composition can be calculated.

If we can calculate the final solvent composition and the initial isotopic solvent composition, we can combine this data with the known C_2 isotopic composition (table 3.5) to arrive at kinetic isotope effect values (data displayed in table 3.6). The kinetic isotope effect is measured as k_H/k_D, i.e. a measure of how much more likely a H atom will bond in a certain position than a D atom.

From table 3.6 it can be seen that provided the kinetic isotope effect is between 3.4 and 4 then the labelling fits with the mechanism, for the

D_2/EtOD experiment. This figure is comparable with literature values for similar equilibrium (isotope effects for the ketonisation of vinyl alcohol to ethanol have been measured as 4.7 for the acid catalysed reaction or 3.4 for the faster base catalysed reaction[187], whilst that for the ketonisation of 2-propen-1-ol catalysed by a rhodium complex has an upper limit of 4[188].

Table 3.6 - Solvent composition and hence kinetic isotope effect required to give correct isotopic labelling[a]

		Solvent Composition		k_H/k_D	
	C_2[H/D]	Start	Final	Start	Final
EtOD/H_2	1.70 (1.1)	0.22	0.56	7.7 (5.0)	3.0 (2.0)
EtOH/D_2	4.55 (3.5)	100/0	4.44	-	1.02 (0.8)
EtOD/D_2	0.75 (0.85)	0.22	0.21	3.4 (3.9)	3.6 (4.0)

[a] Figures in brackets correspond to calculations based on ^1H data, the non bracketed data is calculated from ^{13}C data.

3.5.3 Isotopic labelling pattern for C_1

For C_1 of 2-methylpropan-1-ol obtained from the hydrocarbonylation of 2-propen-1-ol, one of the two H/D atoms should be derived exclusively from the gas phase, whilst the other is incorporated during the hydrogenation of 2-methylpropanal. As discussed above, this can come from the gas phase or the solvent. All the data for this section is collected together in table 3.7.

The easiest experiment to model is that using EtOH in D_2 since the solution OH composition is 100% H at the beginning of the reaction and 70% H at the end. Whilst in the hydrogenation of 2-methylpropanal it varies from 100-82% (although it should be noted that the overall concentration of OH protons is 1.2 x higher in the hydrocarbonylation reaction because of the presence of OH in the substrate). Broadly then, for the hydrocarbonylation of 2-propen-1-ol, C_1 should always bear 1 D atom (from the gas phase), in practice 95% of the molecules do and it should be ~56% CD_2 and 44% CHD. In practice it is 40% CD_2 and 55% CHD, the difference presumably arises largely from the higher overall OH concentration.

For EtOD/D_2, one D atom should come from the gas phase whilst the hydrogenation step should give ~60% D from the gas phase and ~40% from the solution OH/D, since this is 82% D and 18% H throughout the reaction, the final composition should be 93% CD_2 and 7% CHD if no isotope effect operates. Since we have suggested that an isotope effect of 2.2 operates on the pathway involving incorporation from the solution phase ~67% D and 33% H should be incorporated via this mechanism, giving an expected corporation of 87% CHD and 13% CD_2. The observed values of 76% CHD and 24% CD_2 are not identical to these values, but are sufficiently close for us to feel that they are not in contention of the proposed mechanism, particularly as the pathway that incorporates 5% of H onto the product obtained from 2-methylpropanal and D_2/CO in EtOD has not been considered in this analysis, but will be responsible for > 5% H incorporation because there is substantially more OH in the solution from 2-propen-1-ol.

For the reaction of 2-propen-1-ol with H_2/CO in EtOD, C_1 of the product should always bear 1 H atom (from the gas phase) as is observed, but large changes in the composition of the solvent during the reaction mean that it is not easy to calculate the expected CH_2:CHD ratio, but the similarity to that observed for the 2-methylpropanal reaction again suggests that the incorporation of this other H/D atom is via hydrogenation of 2-methylpropanal.

Table 3.7 Isotopic composition of C_1(%H) made from various isotopic sources for 2-propen-1-ol and 2-methylpropanal

	2-propen-1-ol			2-methylpropanal*	
	CH_2	CHD	CD_2	CH_2	CHD
EtOD/H_2	78	22	-	82(77)	18(23)
EtOH/D_2	5	55	40	44(40)	56(60)
EtOD/D_2	-	26	74	5(2)	95(98)

* numbers in brackets correspond to more accurate ^{1}H data

3.6 Conclusions

In this chapter it has been shown that ^{13}C nmr provides a powerful tool for determining the exact quantitative distribution of deuterium

labels in mixtures of multiple partially deuteriated products from catalytic reactions. For mixtures in the present work containing up to four different isotopomers, the intensities of β-shifted resonances in $^{13}C\{^{1}H\}$ nmr spectra measured at medium field give enough information for a full analysis. For more complex mixtures this method does not give sufficient data for the analysis without making assumptions which may contain significant errors. Using high field $^{13}C\{^{1}H,^{2}H\}$ nmr allows these problems to be overcome and a full detailed analysis can be performed.

Once the analysis has been performed, the distribution of the isotopic labels can give usable information about the mechanism for the formation of the products that have been analysed.

Isotopomer	Label	D_2/EtOD		D_2/EtOH		H_2/EtOD	
		75.5 MHz†	151 MHz†	75.5 MHz*	151 MHz¶	75.5 MHz†	151 MHz#
$(CH_3)_2CHCH_2OH/D$	A'			1	1.3	49.0(15)	
$(CH_3)_2CDCH_2OH/D$	A"			0	0.3	28.8(15)	
$(CH_3)_2CHCHDOH/D$	B'			4	3.5	14.0(15)	
$(CH_3)_2CDCHDOH/D$	B"			0	0.8	8.2(15)	
$(CH_3)_2CHCD_2OH/D$	C'			2	1.5		
$(CH_3)_2CDCD_2OH/D$	C"			0	0.4		
$(CH_3)(CH_2D)CHCH_2OH/D$	D'			2	2.5		
$(CH_3)(CH_2D)CDCH_2OH/D$	D"			0	0.6		
$(CH_3)(CH_2D)CHCHDOH/D$	E'		2.1(3)	4	19.1		
$(CH_3)(CH_2D)CDCHDOH/D$	E"		3.4(6)	0	4.3		
$(CH_3)(CH_2D)CHCD_2OH/D$	F'		4.7(3)	2	13.1		
$(CH_3)(CH_2D)CDCD_2OH/D$	F"		7.1(4)	0	2.9		
$(CH_2D)_2CHCH_2OH/D$	G'			16	0		
$(CH_2D)_2CDCH_2OH/D$	G"			1	0		
$(CH_2D)_2CHCHDOH/D$	H'	13.6(6)	9.7(3)	40	22.5		
$(CH_2D)_2CDCHDOH/D$	H"	17.3(6)	10.9(7)	3	4.9		
$(CH_2D)_2CHCD_2OH/D$	J'	30.4(6)	26.8(5)	23	18.2		
$(CH_2D)_2CDCD_2OH/D$	J"	38.6(6)	35.1(7)	1	4.0		

* All values quoted as 0% in this column signify < 0.5%. No errors have been calculated.
† The bracketed numbers are errors of type (a).
# No data was taken at 151 MHz for H_2/EtOD.
¶ No errors calculated.

Table 3.8 - Composition of mixtures obtained from 2-propen-1-ol using different isotopic starting materials, calculated from data taken at 75.5 and 151 MHz. (Spectra ran in $CDCl_3$)

Isotopomer	Label	D_2/EtOD		D_2/EtOH		H_2/EtOD	
		75.5 MHz†	151 MHz#	75.5 MHz†	151 MHz†	75.5 MHz†	151 MHz#
$(CH_3)_2CHCH_2OH/D$	A'	4.2(9)		38.8(5)	38.1(4)	76.0(11)	
$(CH_3)_2CDCH_2OH/D$	A"	0.8(9)		5.2(5)	4.1(4)	6.5(11)	
$(CH_3)_2CHCHDOH/D$	B'	80.0(9)		49.5(5)	49.8(4)	16.2(11)	
$(CH_3)_2CDCHDOH/D$	B"	15.1(9)		6.6(5)	8.0(4)	1.4(11)	
$(CH_3)_2CHCD_2OH/D$	C'						
$(CH_3)_2CDCD_2OH/D$	C"						
$(CH_3)(CH_2D)CHCH_2OH/D$	D'						
$(CH_3)(CH_2D)CDCH_2OH/D$	D"						
$(CH_3)(CH_2D)CHCHDOH/D$	E'						
$(CH_3)(CH_2D)CDCHDOH/D$	E"						
$(CH_3)(CH_2D)CHCD_2OH/D$	F'						
$(CH_3)(CH_2D)CDCD_2OH/D$	F"						
$(CH_2D)_2CHCH_2OH/D$	G'						
$(CH_2D)_2CDCH_2OH/D$	G"						
$(CH_2D)_2CHCHDOH/D$	H'						
$(CH_2D)_2CDCHDOH/D$	H"						
$(CH_2D)_2CHCD_2OH/D$	J'						
$(CH_2D)_2CDCD_2OH/D$	J"						

† The bracketed numbers are errors of type (a).
# No data was taken at 151 MHz for H_2/EtOD or D_2/EtOD.
¶ No errors calculated.

Table 3.9 - Composition of mixtures obtained from 2-methylpropanal using different isotopic starting materials, calculated from data taken at 75.5 and 151 MHz. (Spectra ran in $CDCl_3$)

Sample	C_1		C_2		C_3		C_1H	C_2H	C_3H
	δ(relative intensity)	J_{C-D}	δ(relative intensity)	J_{C-D}	δ(relative intensity)	J_{C-D}	δ(relative intensity)	δ(relative intensity)	δ(relative intensity)
Authentic	69.51s		30.96s		19.14s		3.33 (2)	1.77sp (1)	0.90d (6)
Exchanged with D_2O	68.75s		30.58s		18.73s				
2-methylpropanal									
+ D_2/ CO/ EtOH	68.78s		30.61s (0.439(4))		18.77s (0.882(4))		3.33d	1.75sp	0.88d
	68.39t	21.6	30.51s (0.561(4))		18.65s (0.118(4))		(1.40)	(0.93)	(6)
+ H_2/ CO/ EtOD	69.09s		30.77s (0.824(15))		18.96s (0.922(4))		3.34d	1.75sp	0.88d
	68.71t	21.4	30.67s (0.176(15))		18.85s (0.078(5))		(1.77)	(0.95)	(6)
+ D_2/ CO/ EtOD	68.75s		30.58s (0.049(6))		18.73s (0.841(6))		3.30d	1.77sx	0.85d
	68.36t	21.4	30.49s (0.951(5))		18.62s (0.159(6))		(1.02)	(0.90)	(6)
			30.25t	18.4					
2-propen-1-ol									
+ D_2/ CO/ EtOH	68.86s		30.66s (0.016)		18.75s		3.31d	1.74sx	0.88t
	68.47t	21.4	30.55s (0.074)		18.64s		(0.54)	(0.68)	(4)
	68.09qu	21.8	30.47s (0.232)		18.22t (0.82)	19.2			
			30.39s (0.434)		18.37t (0.18)	19.2			
			30.30s (0.222)						
+ H_2/ CO/ EtOD	69.0s		20.67s		18.84s (0.63)		3.32bd	1.76sp	0.88d
	68.9s		29.93t	18.8	18.72s (0.37)		(1.62)	(0.52)	(6)
+ D_2/ CO/ EtOD	68.30t (0.44)	21.8	30.27s (0.310(5))		18.33t (0.440(3))	19.3	3.31b	1.71bsp	0.88d
	68.22t (0.56)	21.8	30.18s (0.690(5))		18.22t (0.560(3))	19.3	(0.29)	(0.44)	(4)
	67.94qu	21.5	29.79t	19.6					
	67.86qu	21.5	29.70t	19.6					

Table 3.10- ^{13}C and ^{1}H nmr data taken at 75.5 MHz (C) and 300 MHz (H) of 2-methylpropan-1-ol made from various reactions recorded in $CDCl_3$ at 298K

Chapter 4 - Model Studies and High Pressure nmr Studies

4.1 High Pressure Studies

Attempts to observe the rhodium complexes that were formed prior to entry into the catalytic cycle, were made using high pressure nmr apparatus. It is already known from previous studies by MacDougall and Cole-Hamilton[56] what species are present at atmospheric pressure using a pre-formed catalyst ([$RhH(PEt_3)_3$]). It was anticipated that these studies would show that the catalytic precursor [$Rh_2(OAc)_4.2MeOH$] would generate similar species under actual reaction conditions.

A scaled down version of the catalytic system consisting of [$Rh_2(OAc)_4.2MeOH$], PEt_3 and 2-propen-1-ol in CD_3CD_2OD was introduced into a sapphire nmr tube and the apparatus was pressurised to 50 atms. with CO/H_2 (1:1). The system was then examined by ^{31}P nmr. All ^{31}P data for this section are shown in table 4.1.

Table 4.1 Nmr shifts assigned to species observed in the high pressure ^{31}P nmr compared to previous data taken by MacDougall

Species	High pressure nmr data[b]		Previously observed data[a]	
	δ (ppm)	J_{Rh-P}	δ (ppm)	J_{Rh-P}
$[RhH_2(PEt_3)_4]^+OEt^-$	19.9	110 Hz	19.5	101 Hz
	~5.0	-	4.3	89 Hz (J_{P-P} = 21 Hz)
$[Rh_2(CO)_2(PEt_3)_6]$	17.5	96 Hz	17.5[b]	96 Hz[b]

a Taken at -40°C, b Taken at 25°C

The ^{31}P nmr showed that two rhodium complexes were present along with some PEt_3, $OPEt_3$ and two unidentified phosphonium species. One of the species had two weak broad signals, one of the signals was centred on

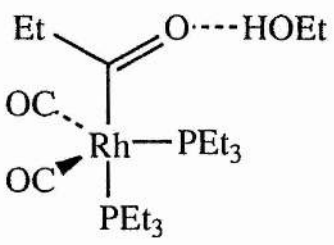
δ = 19.9 ppm, J_{Rh-P} = 110 Hz the other at δ = 4.3 ppm. This was assigned as $[RhH_2(PEt_3)_4]^+EtO^-$.

This species had previously been found as a transient in a reaction involving the mixing of $[RhH(PEt_3)_3]$ with d_6-EtOD, performed by MacDougall. The transient species is relatively short lived and the only species remaining after 12 hours was assigned as $[RhH(CO)(PEt_3)_3]$. If the same reaction was carried out in the presence of excess PEt_3, then $[RhH_2(PEt_3)_4]^+EtO^-$ was the major species observed immediately after mixing.

The other rhodium species found in the high pressure study had a sharp doublet centred at δ = 17.5 ppm, J_{Rh-P} = 96 Hz. This was also present in some of the studies carried out by MacDougall. MacDougall could not positively identify this complex referred to as complex A, but evidence obtained suggests that it was $[Rh_2(CO)_2(PEt_3)_6]$. This evidence was that on hydrogenation of complex A (achieved by bubbling H_2 through a solution containing complex A), $[RhH(CO)(PEt_3)_3]$ was obtained as the major species. Also the i.r. data for the CO stretching region suggested that only terminal carbonyls were present.

MacDougall found that she could generate this species along with others by either adding ethanol to $[RhH(PEt_3)_3]$ + CO in C_7D_8 or by bubbling CO through a solution of $[RhH(PEt_3)_3]$ in C_2D_5OD. In either case the unknown became the sole species on addition of an excess of PEt_3.

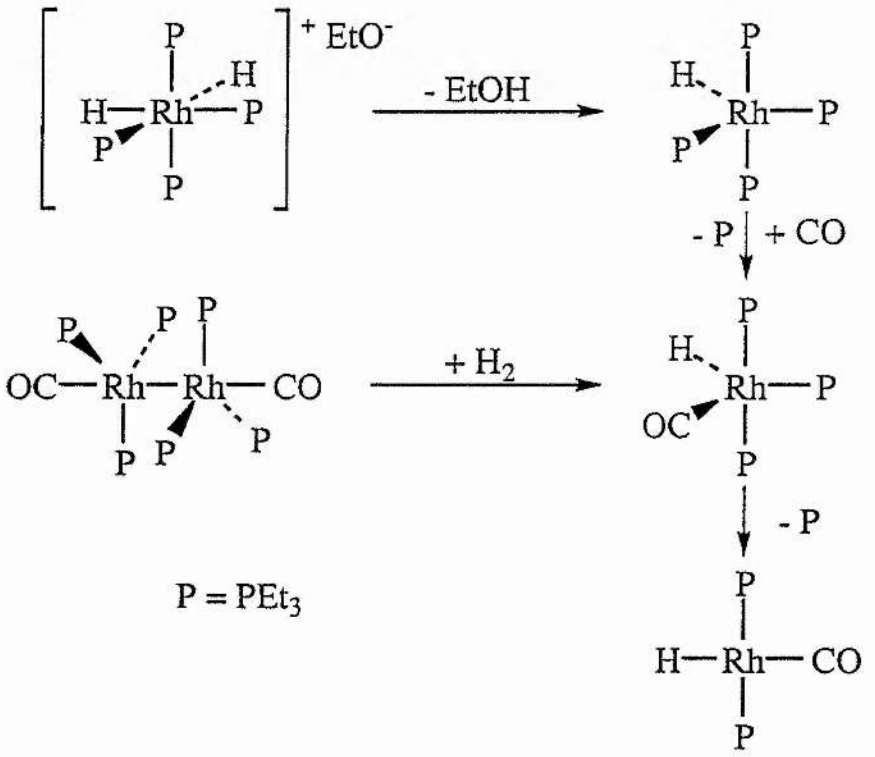
MacDougall found that $[Rh_2(CO)_2(PEt_3)_6]$ was the only rhodium species present upon completion of a hydrocarbonylation run (using hex-1-ene instead of 2-propen-1-ol) and that it was one of the two species present when high pressure studies were performed on a catalytic hydrocarbonylation reaction with ethene as the substrate and $[RhH(PEt_3)_3]$ as the catalyst precursor. The other species was identified as the species shown below.



If it assumed that complex A, which is found in both the high pressure study and the atmospheric studies carried out by MacDougall and Cole-Hamilton is $[Rh_2(CO)_2(PEt_3)_6]$, then it is easy to see how the two rhodium complexes observed in the ^{31}P high pressure nmr could be converted into the catalytic species $[RhH(CO)(PEt_3)_2]$ (scheme 4.1).

$[Rh_2(CO)_2(PEt_3)_6]$ could hydrogenate to form $[RhH(CO)(PEt_3)_3]$ which could lose a phosphine to generate the catalytic species mentioned above.

$[RhH_2(PEt_3)_4]^+EtO^-$ could be converted into the same species by loss of ethanol to give $[RhH(PEt_3)_4]$ which is known to easily eliminate PEt_3 to give $[RhH(PEt_3)_3]$[189], and as shown by MacDougall and Cole-Hamilton reacts with CO to form $[RhH(CO)(PEt_3)_3]$, this would lose a phosphine ligand as before to generate the catalytically active species, $[RhHCO(PEt_3)_2]$. It is also known from the work of MacDougall that all these species interchange with one another on the nmr timescale at 100°C.



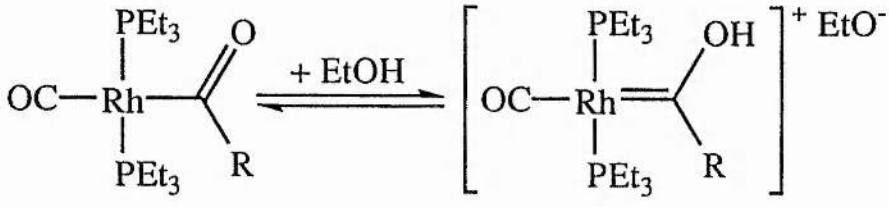
Scheme 4.1 - Possible routes to $[RhH(CO)(PEt_3)_2]$ from the rhodium complexes identified in the high pressure studies.

In conclusion, these high pressure studies have shown that the same rhodium species are found in systems starting from either $[RhH(PEt_3)_3]$ or from $[Rh_2(OAc)_4.2MeOH]$ + PEt_3 in ethanol under CO/H_2.

4.2 Model Studies

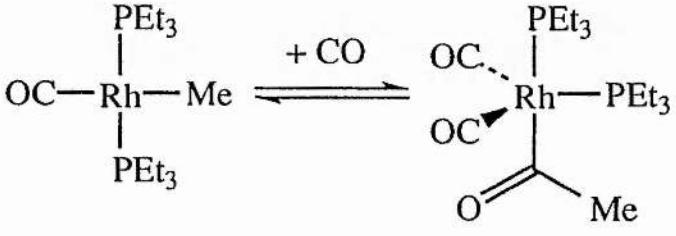
Three separate model experiments were carried out on molecules that resembled some of the catalytic intermediates from the proposed MacDougall/ Cole-Hamilton mechanism (scheme 2.2, chapter 2).

The step that was modelled was the addition of a proton to the acyl oxygen, step A of the mechanism (scheme 4.2).



Scheme 4.2 - Proposed acyl/ hydroxycarbene equilibrium operating in the catalytic mechanism

The common starting compound for these studies was $[Rh(CO)(CH_3)(PEt_3)_2]$ (prepared from $[RhCl(CO)(PEt_3)_2]$ and MeLi), which can be readily carbonylated in solution at room temperature and pressure to give an acyl species. This is illustrated in scheme 4.3.



Scheme 4.3 - Carbonylation of carbonylmethylbis(triethylphosphine)-rhodium(I)

The experiments carried out on the model acyl species were;

(i) Addition of aliquots of alcohol to the acyl species, whilst monitoring the acyl carbon atom via ^{13}C spectroscopy nmr.

(ii) Isolation of the acyl species, followed by protonation with ethanol. These species were examined by i.r. spectroscopy.

(iii) Generation of the acyl species *in situ*, in the presence of CD_3OD. Then decarbonylation of the model complex formed. These species were monitored by ^{13}C nmr spectroscopy.

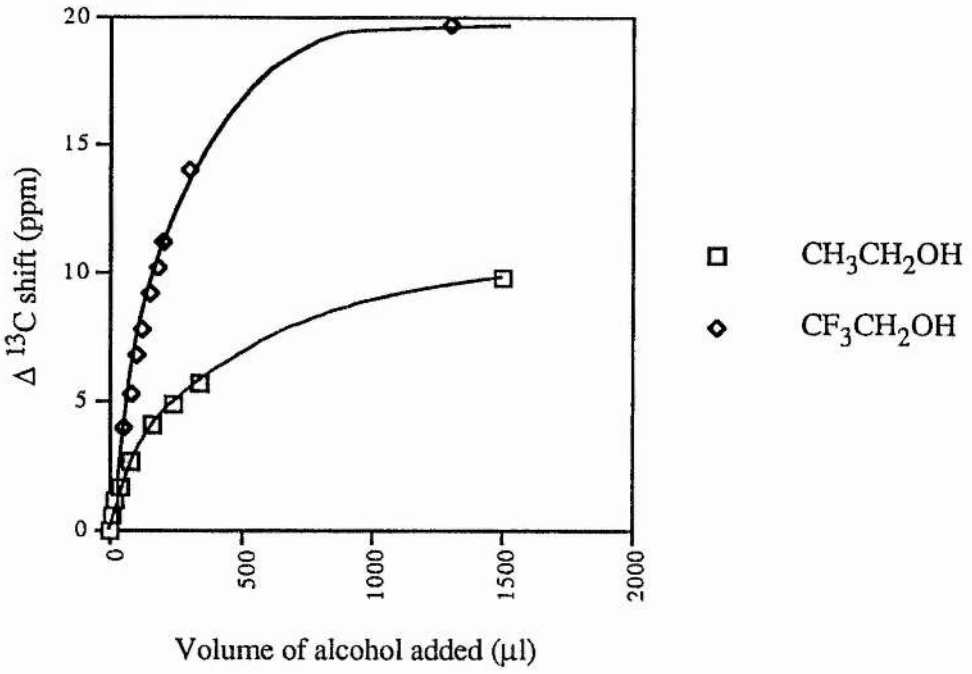
4.2.1 Alcohol addition studies

A previous study by MacDougall and Cole-Hamilton showed that the acyl resonance in the ^{13}C nmr spectrum could be moved downfield from $\delta = 238$ ppm to $\delta = 247$ ppm on a single addition of ethanol. An attempt to extend this study was carried out as follows;

A sample of $[Rh(CO)(CH_3)(PEt_3)_2]$ was dissolved in d_8-thf and the acyl species $[Rh(COCH_3)(CO)_2(PEt_3)_2]$ was generated *in situ* by simply bubbling CO through the solution. The ^{13}C nmr of this species was recorded, then aliquots of ethanol were added to this solution and the chemical shift of the acyl carbon was examined after every addition of ethanol. This procedure was repeated for 2,2,2-trifluoroethanol, the maximum chemical shift for the acyl C atom in this case being 257 ppm.. The results for these two experiments are shown in graph 4.1.

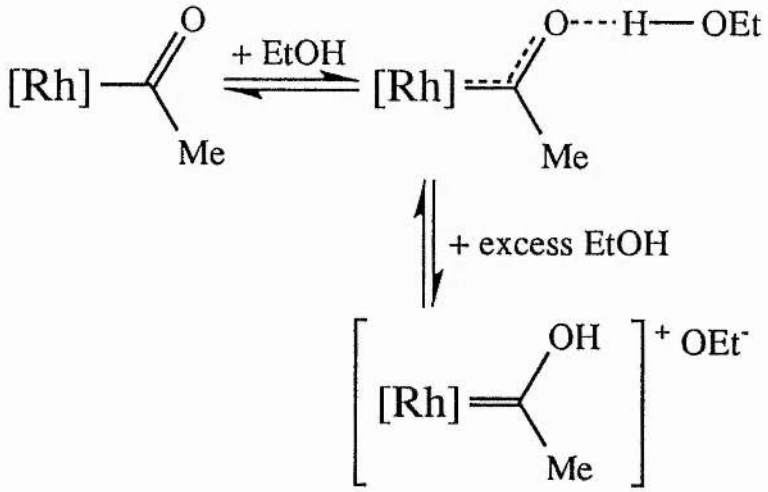
It was anticipated that the ^{13}C peak corresponding to the acyl carbon would move further downfield into the region that is normally associated with metal carbenes (290-355 ppm)[190, 191, 192].

The reaction hoped for is shown in scheme 4.4.



Graph 4.1 - Graph[a] illustrating the change in shift on the acyl peak upon addition of various alcohols

[a] The data point corresponding to 1500 μl of CH_3CH_2OH was generated in a separate experiment by dissolving $[Rh(CO)(CH_3)(PEt_3)_2]$ in CD_3CD_2OD, then CO was bubbled through the resulting solution.



Scheme 4.4 - Anticipated pathway from acyl to hydroxycarbene

As can be seen from graph 4.1 a true hydroxycarbene species has not been generated. The species formed seems to be best described as an acyl group with a hydrogen bonded interaction to an ethanol proton. This interaction is though the acyl oxygen atom. The rhodium species could be diagrammatically described as the intermediate postulated in scheme 4.4.

The final shift for the CF_3CH_2OH experiment was greater than for the one recorded when ethanol was used. This was as expected since trifluoroethanol has a lower pK_a value. Since the proton is more dissociated on the trifluoroethanol molecule it will form a stronger hydrogen bond to the acyl oxygen atom than will that of ethanol.

Protonation was attempted using stronger acids such as trifluoroacetic acid, but the anion just replaced some of the ligands on the rhodium. So acids with non-coordinating anions were tried, such as p-toluenesulphonic acid and triflic acid. These seemed too harsh for the molecule as no interpretable results were obtained for either of these acids.

The possible reason for the failure to produce a carbene resonance in these experiments could be attributed to the model compound. This species has two CO ligands compared to only one on the species proposed in the mechanism. CO being a good π-acceptor, removes some of the electron density from the metal centre, so the key feature of the catalyst, the electron rich metal centre, is diminished in the model compound. This means that the metal has less electron density, so the acyl oxygen is not as nucleophilic, therefore it follows that it stands less chance of being protonated.

In conclusion for this set of experiments, it has been shown that the acyl oxygen is open to attack from electrophiles. The protonating agent that is used has to be quite mild otherwise the nature of the catalyst is changed. Full protonation of the acyl oxygen is not observed, but a hydrogen bonded rhodium complex/ethanol molecule is formed.

4.2.2 I.r. studies

To support these nmr studies, infra-red spectroscopic studies were also carried out[193] The strategy for this study was to synthesise and isolate the acyl species, record the i.r. spectrum of the resulting compound, add ethanol to the model acyl complex, isolate any compound formed, then record another i.r. spectrum.

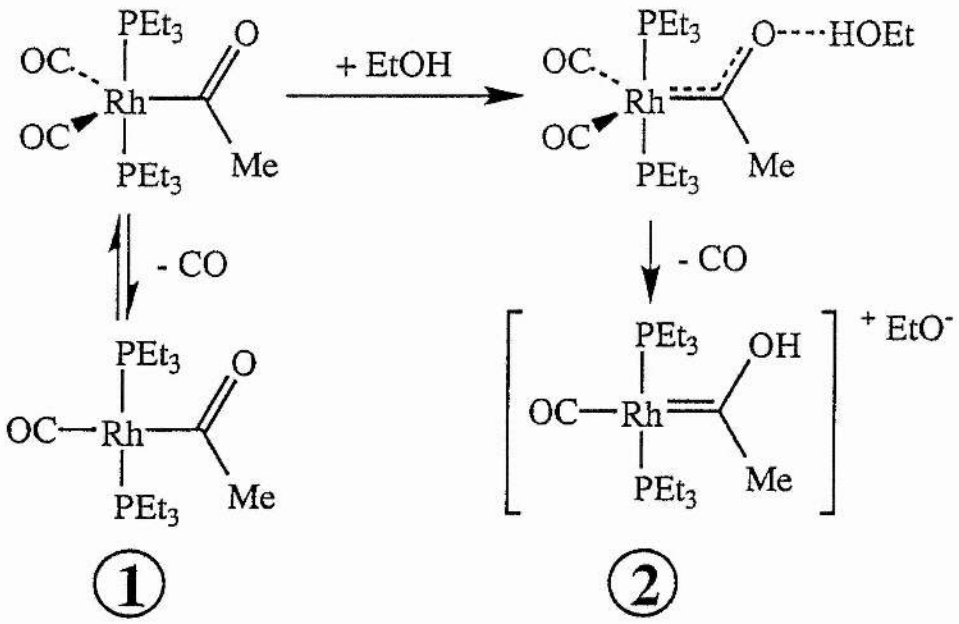
To isolate the acyl species, CO was bubbled through a solution of $[RhMeCO(PEt_3)_2]$ in Et_2O. Bubbling was continued to exaporate the solvent. When this was near dryness, the sample was put under cold vacuum (- 50°C) to remove the last traces of solvent.

I.r. studies showed the presence of the 5 coordinate acyl species but also another species, **1**, which may be $[Rh(COMe)(CO)(PEt_3)_2]$, the exact analogue of the proposed catalytic intermediate (for i.r. data, see table 4.2).

The acyl intermediate was then dissolved in ethanol and CO was again bubbled through the solution to evaporate the solvent. This was dried under cold vacuum to give a yellow oil.

A weak broad peak was observed for the isolated species centred at 1560 cm^{-1}. This signifies that the species isolated has a longer C-O bond than the species observed in solution by MacDougall[56]. This may not be a C-O single bond, but it suggests that the mono carbonyl species has been isolated as opposed to the dicarbonyl species.

The possible reaction steps described above are pictorially presented in scheme 4.5. Species 1 is the proposed isolated acyl and species 2 is the proposed isolated hydroxycarbene. I.r. data are brought together in table 4.2.



Scheme 4.5 - Proposed sequence of reactions with the acyl intermediate investigated using i.r.

Table 4.2 I.r. data for isolated species **1** and **2**, compared to data from a previous study by MacDougall

Species	Observed[a]	Previously observed[b]
	2006.5 cm^{-1}	2002 cm^{-1}
dicarbonyl	1977.5 cm^{-1}	1977 cm^{-1}
	1635 cm^{-1}	1627 cm^{-1}
+ **1**	1952 cm^{-1}	
2	1956 cm^{-1}	-
	1560 cm^{-1}	[c]1603 cm^{-1}

[a] Taken as nujol mulls; [b] Taken in d_8-thf; [c] possibly incorrectly assigned.

In conclusion, this study suggests that it may be possible to synthesise an analogue of the four coordinate hydroxycarbene species proposed as the key intermediate in the direct formation of alcohols from alkenes in hydrohydroxymethylation reactions catalysed by rhodium/ trialkylphosphine complexes. The i.r. evidence certainly shows there is an interaction between the acyl oxygen and the ethanol proton since the υ(C=O) is reduced in frequency.

4.2.3 Attempted nmr studies on the 4 coordinate hydroxycarbene complex

The observation in the i.r. study that the model acyl species may have had one of its CO ligands removed prompted another set of nmr experiments combining the ideas from the alcohol addition study and the i.r. study.

The strategy was to generate the model acyl species $[Rh(COCH_3)(CO)_2(PEt_3)_2]$ dissolved in a fully deuterated alcohol, then attempt to remove the labile CO ligand by bubbling argon through the solution. This could then be examined by ^{13}C nmr. All nmr data gained from this study are brought together in table 4.3. Solubility problems meant that the spectra of the final solution had to be accumulated at -20°C, a temperature at which the 5 coordinate complex is known to be undergoing

Berry pseudorotation on a timescale comparable with that of the nmr experiment[56].

Table 4.3 Nmr data gained from nmr study of the model complexes

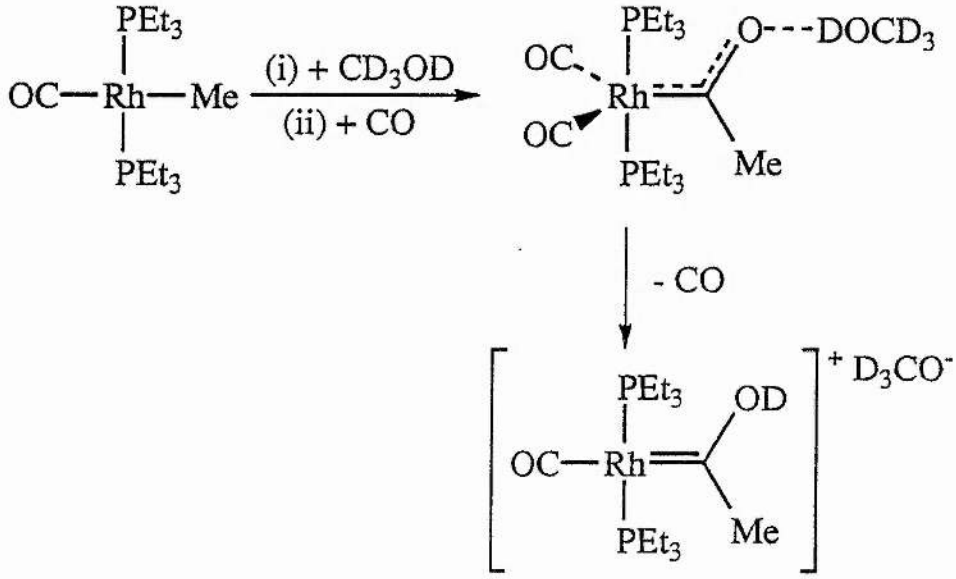
Species	Nmr data		
	δ (ppm)	Pattern	Coupling
$[Rh(\mathbf{CO}Me)(CO)_2(PEt_3)_2]$[a] in CD_3OD	252.9	ddd	J_{Rh-C} 84 Hz J_{P-C} 22 Hz J_{P-C} 17 Hz
$[Rh(COMe)(\mathbf{CO})_2(PEt_3)_2]$[a] in CD_3OD	200.8	dt	J_{Rh-C} 73 Hz J_{P-C} 20.5 Hz
$[Rh(CO\mathbf{Me})(CO)_2(PEt_3)_2]$[a] in CD_3OD	53.7	dd	J_{Rh-C} 28 Hz J_{P-C} 5 Hz
$[Rh(\mathbf{C}(OH)Me)(CO)(PEt_3)_2]$[b] in CD_3OD	301.2[c]	dt?	J_{Rh-C} 48 Hz
$[Rh(C(OH)Me)(\mathbf{CO})(PEt_3)_2]$[b] in CD_3OD	200.2	s[e]	
$[Rh(C(OH)\mathbf{Me})(CO)(PEt_3)_2]$[b] in CD_3OD	45.5	s[e]	

[a] Taken at -60°C; [b] taken at -20°C; [c] Not well resolved; [e] Coupling to phosphine lost.

$[Rh(CO)(CH_3)(PEt_3)_2]$ was dissolved in CD_3OD, then CO was bubbled through the solution to generate the acyl species. The ^{13}C nmr contained a resonance which was similar to the resonance at δ = 255 ppm observed in section 4.2.1 for the acyl species dissolved in CD_3CD_2OD (δ ~ 250 ppm). This was assigned to a species that contained an acyl functionality that was hydrogen bonded to CD_3OD.

After bubbling argon through this solution, the rhodium complex was re-examined using ^{13}C nmr. The spectrum contained a resonance centred at δ = 301.2 ppm which was assigned as the carbene carbon of the decarbonylated species $[Rh(=C(OH)CH_3)(CO)(PEt_3)_2]$. The resonance is within the generally recognised region indicative of ^{13}C carbene resonances (290-355 ppm)[190, 191, 192]. The relative intensities of the resonance at δ = 301.2 ppm and from the carbonyl C atom were ~1:1 indicating that 1 CO ligand had indeed been lost.

The reactions described in this section are summarised in scheme 4.6.



Scheme 4.6 - Reaction steps carried out to produce a hydroxycarbene species.

4.3 Conclusions

These studies have provided much more evidence to support the MacDougall/Cole-Hamilton hydrohydroxylmethylation mechanism.

The high pressure nmr studies have shown that the catalyst generated from $[Rh_2(OAc)_4.2MeOH]$ and PEt_3 contain similar species to those obtained from $[RhH(PEt_3)_3]$ and that the active catalytic species is probably $[RhH(CO)(PEt_3)_2]$.

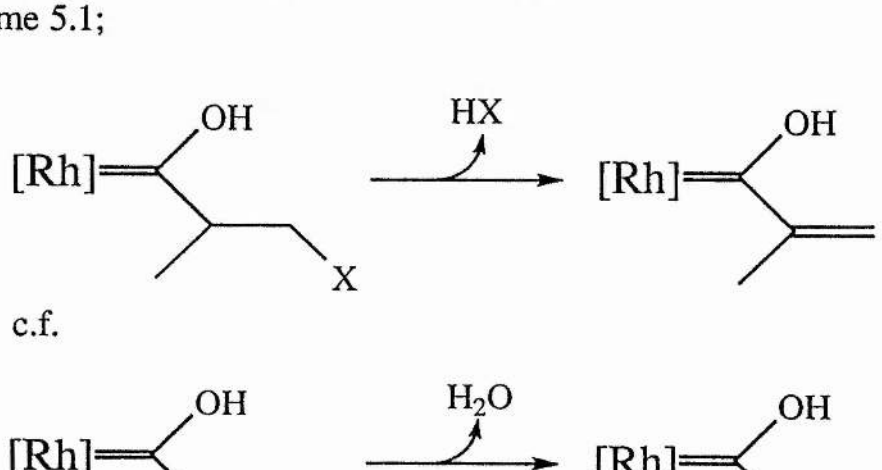
The three sets of model studies show that there is a definite interaction between the proton of the alcoholic solvent and the oxygen of the rhodium acyl species and that the four coordinate acyl postulated as an intermediate in the catalytic cycle will be fully protonated on the acyl oxygen atom to give a hydroxycarbene, if it is generated in an alcoholic solution.

Chapter 5 - Other Substrates

A variety of other substrates were investigated utilising the same catalytic system that was used for 2-propen-1-ol. Other substrates with the same propenyl functional group were investigated, such as propenyl halides, propenyl ethers and propenyl cyanide. The substrates examined were expected to react in a similar fashion to the MacDougall/ Cole-Hamilton reaction or to 2-propen-1-ol.

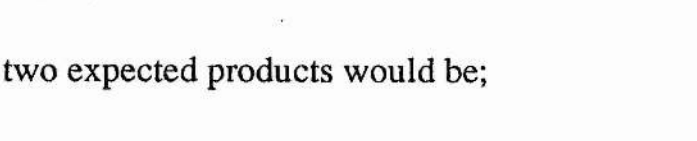
5.1 Propenyl halides

It was anticipated that propenyl halides would produce products analogous to those obtained for 2-propen-1-ol, i.e. the branched chain product formed would be 2-methylpropan-1-ol, due to the elimination of hydrogen halide as opposed to water. This is demonstrated below in scheme 5.1;

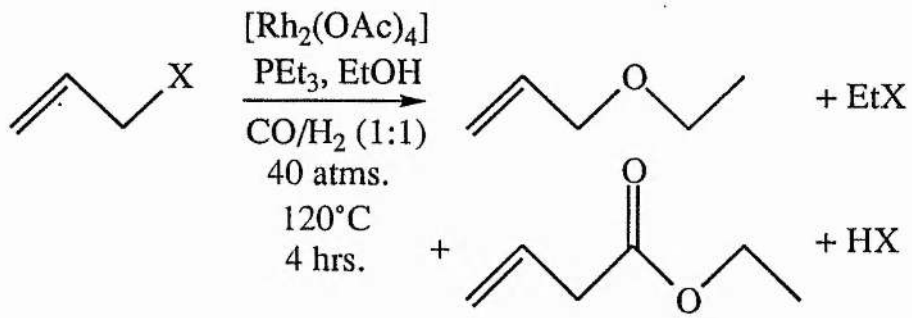


Scheme 5.1 - Expected similarity between 2-propen-1-ol and propenyl halide systems.

So the two expected products would be;



When the reaction was carried out using $[Rh_2(OAc)_4]$, PEt_3, EtOH, CO/H_2 (1:1), 120°C and 4 hours reaction time, the products were as follows;



Scheme 5.2 - Actual products observed from propenyl halides

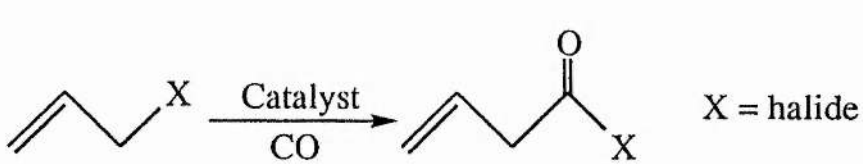
These seem to be the product of a standard carbonylation reaction. The quantification data for these reactions is shown in table 5.1, which is to be found in section 5.1.2.

The products seemed a little curious since the catalytic system was very active for the 2-propen-1-ol hydrohydroxymethylation reaction.

The production of esters and ethers will be looked at separately. Section 5.1.1 to 5.1.2 will examine the ester formation and 5.1.3 to 5.1.4 will look at ether formation.

5.1.1 Brief overview of carbonylation of propenyl halides and related compounds

The carbonylation of allylic and benzyl halides has been reasonably well documented in the literature. The general equation for the reaction is shown in scheme 5.3;



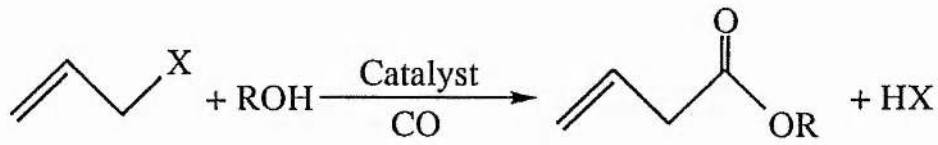
Scheme 5.3 - General carbonylation reaction of a propenyl halide.

In 1967 it was reported that $[Ni(CO)_4]$ catalysed the reaction above. The yields quoted were low due to the interaction of the halide ion with

the catalyst, thus deactivating it. Some evidence for a π-allyl nickel complex was obtained[194].

In 1969 the yield of the acid chloride (85% conversion, 95% selectivity) was dramatically improved using a $PdCl_2$ catalyst. It was found that if the catalyst contained a π-allyl ligand, the reaction was significantly quicker. Platinum and nickel complexes were also examined, but failed to give significant yields. The reaction was expanded to other allylic substrates e.g. 3-bromo-1-propene, 1-chloro-2-butene and 2-propen-1-ol. All carbonylated in yields between 3.5% (1,4-dichloro-2-butene) and 92% (3-acetoxy-1-propene)[195].

The disadvantage of the above two reactions is the high CO pressure (> 70 atms.) needed to drive them. A slightly different methodology was attempted which made the conditions far less drastic; thus carbonylation in the presence of alcohols was explored for the possibility of producing esters. The general equation for this is highlighted in scheme 5.4;



Scheme 5.4 - General equation for the production of esters from propenyl halides.

In 1977 a patent appeared on the carbonylation of benzyl and propenyl halides over rhodium complexes (e.g. $RhCl_3.3H_2O$, $[RhCl(PPh_3)_3]$) with a co-catalyst of HI or NaI, and $NaOCH_3$ in methanol. Benzyl chlorides could be transformed in high yield to give methyl 2-phenylethanoate (93%) and benzyl methyl ether. Also for propenyl chlorides high yields were reported of methyl 3-butenoate (73%) but side products of methyl 2-butenoate (18%) and methyl propenyl ether (5%) were also detected[196].

In 1979 the reaction of 3-chloro-1-propene with CO under phase transfer conditions was reported using $[Ni(CO)_4]$ based systems. So using a benzene/ $NaOH_{aq}$ system and an ammonium salt as phase transfer agent (e.g. tetrabutylammonium iodide), 3-chloro-1-propene could be converted into salts of 2- and 3-butenoic acid (2:3) in 85% total yield in ~400 minutes. This system could accomplish the transformations under 1 atm. of pressure and between 25-45°C[197].

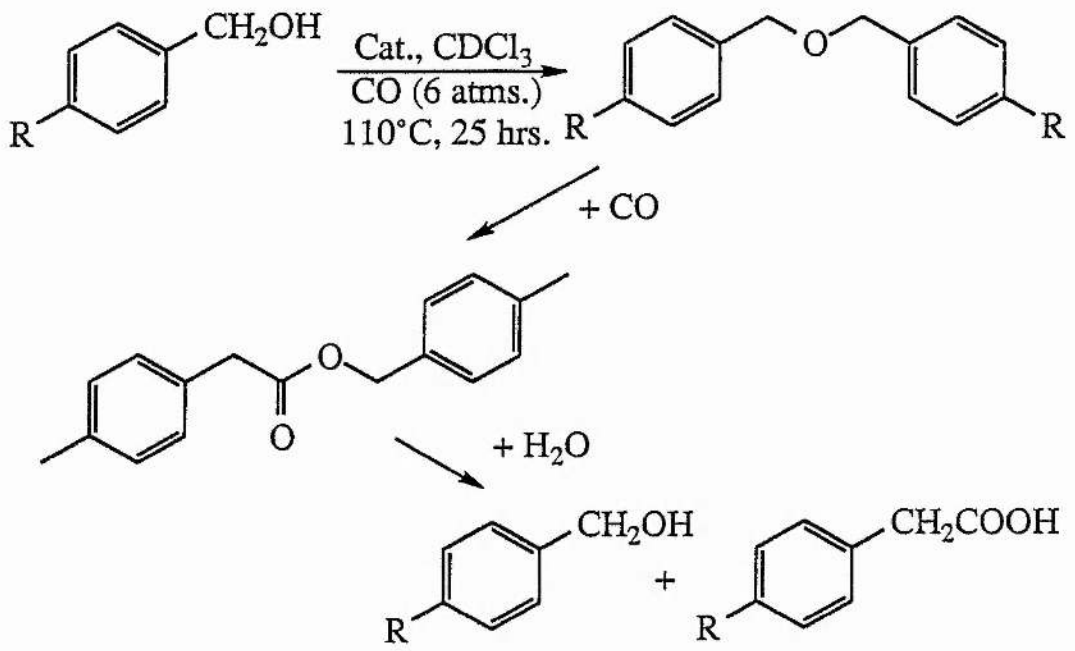
In 1988 it was reported that 3-chloro-1-propene could be carbonylated to give a high yield of esters in the presence of alcohols, in a two phase system. The use of water soluble catalysts makes this possible. The catalyst can be $[PdCl_2L_2]$ {L = $Ph_2P(m\text{-}C_6H_4SO_3Na)$, PPh_3} or $Na_2[PdCl_4]$. Conditions of 30°C, CO (1 atm.), benzene and $NaOH_{aq}$ were used to give yields of the esters between 70 and 90%, while the ratio of β,γ:α,β is between 76:24 to 96:4. Whilst the catalyst with the sulphonated phenyl group and the Na_2PdCl_4 were both water soluble, the catalyst with PPh_3 ligands was not. The activity of this catalyst is not significantly different to the others, the authors suggest that the reaction takes place at the interface of the two phases[198].

In 1991 a Russian paper reported that 3-chloro-1-propene was carbonylated to methyl esters in fair yield (23-56%) over $[Co_2(CO)_8]$ in 10 hours, the reaction was carried out in the presence of methanol and a base (e.g. K_2CO_3). In the same paper it was shown that the same system could yield diesters starting from α,α'-dichloro-p-xylene. For both substrates the yield of the esters versus the ether can be greatly affected by the nature of the base used. For instance, if K_2CO_3 was used in the presence of the latter substrate, no ether was formed and the yield of esters was 72%, but if Na_2CO_3 was used then the ether accounted for 69% of the yield and esters for 9%. MeI can also be used as a co-catalyst, it again causes large changes in the distribution of the products (e.g. with K_2CO_3 get 70% ether and no esters)[199].

A group of Chinese workers enhanced this methodology further by using palladium catalysts anchored to polymers such as poly(N-vinyl-2-pyrrolidone). They report that the activity and efficiency are higher than other systems so far reported. The ratio of isomers (β,γ:α,β) are around 4-5.1: 1. This system can accomplish turnovers of > 900 $hour^{-1}$ [200].

In 1992 a paper appeared on the carbonylation of benzyl alcohol to give benzyl carboxylic acid. The proposed mechanism is outlined in scheme 5.5.

The catalyst can be $[M(ClO_4)(CO)(PPh_3)_2]$, $[M(CO)(PPh_3)_3]ClO_4$ (M = Rh, Ir) or $[RhX(CO)(PPh_3)_2]$ (X = Cl, Br, OH). Both the intermediate ether and ester have been isolated and identified. Of interest to this study the same catalysts converts benzylbromide into phenylacetic acid in the presence of water[201].



Scheme 5.5 - Transformation of benzyl alcohol into benzylcarboxylic acid via carbonylation.

5.1.2 Results and discussion for ester production

As mentioned in the introduction the products from the reaction of 3-chloroprop-1-ene with CO/H_2 in EtOH, catalysed by $[Rh_2(OAc)_4.2MeOH]/PEt_3$ were not as we expected, but there is plenty of literature precedent for the reaction that actually occured.

The reaction appeared to be a carbonylation reaction alone, so this would suggest that it would still work without the presence of hydrogen gas. As expected when CO only was used instead of synthesis gas the reaction worked as before giving the same products.

Since we know from chapter 2 that the reaction system for 2-propen-1-ol is inactive without the presence of hydrogen, it can be concluded that some of the chloride ions are probably being utilised as ligands.

Table 5.1 - Products obtained from the reaction of various substrates in the catalytic system[a]

Substrate	Conversion (%)	Products (%) RCO_2Et	ROEt	EtX
CH_2=$CHCH_2Cl$	64	33	7	[b]
CH_2=$CHCH_2Br$	91	55	27	[b]
CH_2=$CHCH_2I$[e]	88	16	57	91
CH_2=$CHCH_2Cl$[c]	sig.	0	sig.	[b]
CH_2=$CHCH_2Cl$[d]	53	19	11	[b]
$C_6H_5CH_2Cl$	43	2	41	[b]
C_3H_7Cl	0	-	-	-
C_2H_5I	11	0	16	-
^tBuBr[f]	15	0	13	[b]

[a] $[Rh_2(OAc)_4.2MeOH]$ (2×10^{-5} mol), PEt_3 (4×10^{-4} mol), RX (1 cm^3), CO (40 atms.), 120°C, 4 hours. Propene is also detected as a reaction product. Due to its high volatility it was not quantified, propene is assumed to account for the mass imbalance seen on the table;

[b] Not quantified. Difficult to seperate EtCl, EtBr and EtOH on glc column used.

[c] No $[Rh_2(OAc)_4.2MeOH]$ or PEt_3; sig. = significant quantity (not quantified).

[d] $[RhCl(CO)(PEt_3)_2]$ as catalyst with no added phosphine.

[e] Trace of ethyl propanoate observed.

[f] Trace of 2-methylpropene observed.

The results in the table suggest that the overall reactivity of the propenyl halides is in the order RI > RBr > RCl (R = CH_2CHCH_2-), but that the selectivity towards the ester products is determined by the etherification reaction. The percentage of carbonylated product versus ether product is highest for chloride and lowest for iodide. In subsequent work by Payne[202] using heating bands as opposed to a pre-heated oven as the heating source, he showed that conversions could be improved to 100%. As discussed in chapter 2 this is due to the inefficiency of the oven as a heat source, so temperatures of 120°C take almost two hours longer to attain. No quantification of the higher conversion reaction products has been carried out.

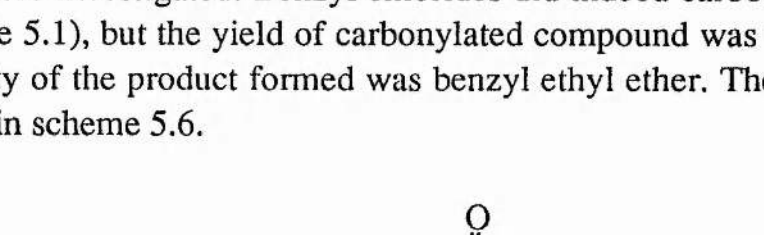
The ester produced is of interest. It is predominately ethyl 3-butenoate, with only the slightest trace of ethyl 2-butenoate. This seems

to suggest that this reaction gives similar selectivities (between β,γ:α,β esters) to the most selective of the ones reviewed. This transformation is also accomplished in the absence of base, unlike most of the review reactions which use a stoichiometric amount of base to remove the HX produced. In the system being investigated most of the X^- (only investigated for X = I) seems to end up as EtX, i.e. reaction with the alcohol. Free X^- must be present because it deactivates the autoclave for reaction runs involving 2-propen-1-ol for the following ~3-4 reaction runs. Also degradation is noticed inside lower grade stainless steel autoclaves after propenyl halide reactions have been conducted.

To test if the carbonylation was a general reaction that could be applied to other halide compounds, chloropropane was examined. As is seen in table 5.1 no carbonylation reaction occured (ether formation was not investigated).

Iodoethane also produced no carbonylated product, but some diethyl ether was detected and quantified (see table 5.1).

It was reasoned that the allyl group was possibly supplying some stabilisation effect to the overall system. To examine this benzyl chlorides were investigated. Benzyl chlorides did indeed carbonylate (as seen in table 5.1), but the yield of carbonylated compound was very low. The majority of the product formed was benzyl ethyl ether. The reaction is depicted in scheme 5.6.



Scheme 5.6 - Reaction of benzyl chloride under standard carbonylation conditions

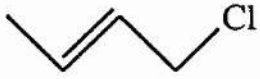
To complete this series of experiments, chlorobenzene was investigated in the catalytic system for any activity. No reaction of any type was observed.

Payne[202] and Weston[203] have conducted some further studies on this system, a number of pertinent discoveries have been made. The first is

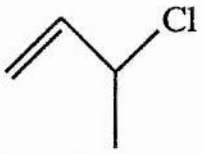
that the initial catalyst formed in this system is $[Rh(OAc)(CO)(PEt_3)_2]$. This can be isolated and characterised. All experiments conducted by Payne use this as the initial rhodium compound, in place of $[Rh_2(OAc)_4]$.

In stoichiometric studies Payne has shown that 3-chloroprop-1-ene can oxidatively add to the catalyst to give $[RhCl(OAc)(CH_2CH{=}CH_2)CO(PEt_3)_2]$[202] but that on standing this gives $CH_2{=}CHCH_2OAc$ and $[RhCl(CO)(PEt_3)_2]$ which can also add 3-chloroprop-1-ene.

The range of substrates studied was also increased, including 1-chlorobut-2-ene and 3-chlorobut-1-ene. See below



1-chlorobut-2-ene



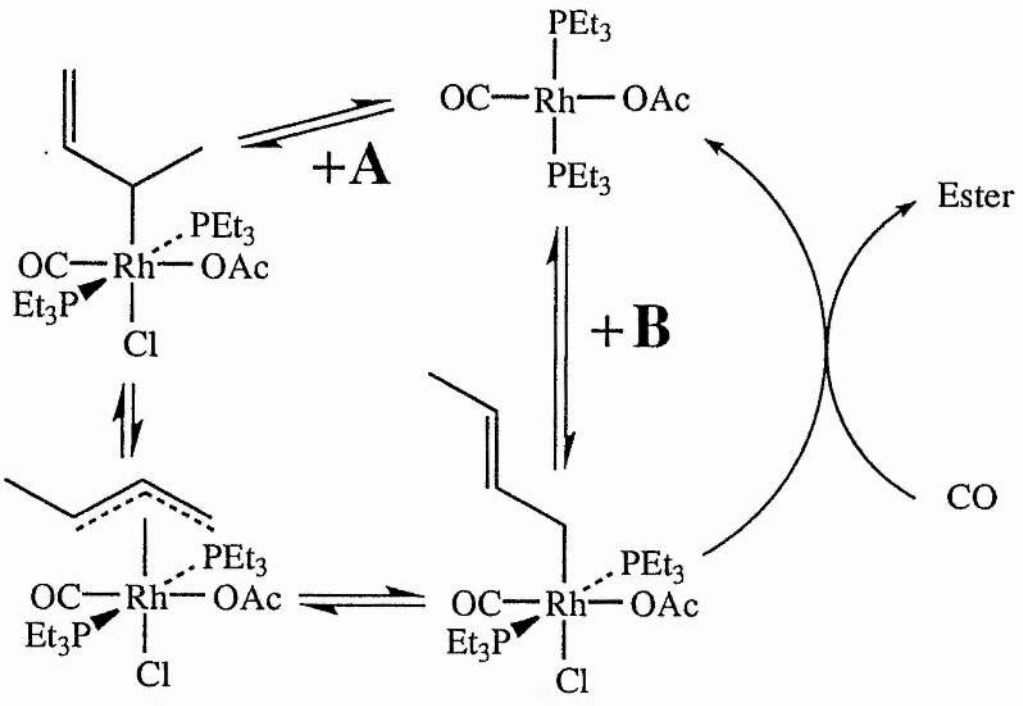
3-chlorobut-1-ene

Both these substrates surprisingly gave the same products;

Table 5.2 - Products and yields from two isomeric substrates

Substrate	Conversion	Product (%)
1-chlorobut-2-ene **A**	100%	E-ethyl pent-3-enoate (47%) Z-ethyl pent-3-enoate (8%) ethyl 1-methyl-2-propenyl ether (17%) C_8 dimers (10%)
1-bromobut-2-ene	100%	E-ethyl pent-3-enoate (31%) Z-ethyl pent-3-enoate (5%) ethyl 1-methyl-2-propenyl ether (22%) C_8 dimers (19%)
3-chlorobut-1-ene **B**	100%	E-ethyl pent-3-enoate (61%) Z-ethyl pent-3-enoate (9%) ethyl 1-methyl-2-propenyl ether (16%) C_8 dimers (14%)

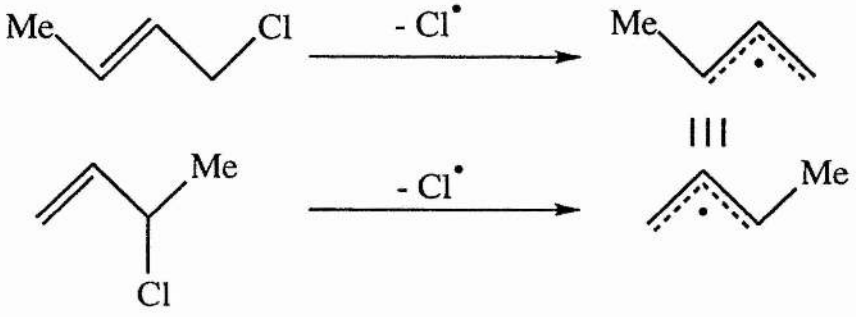
This seems to be a little odd but can be rationalised in terms of one of two mechanisms;

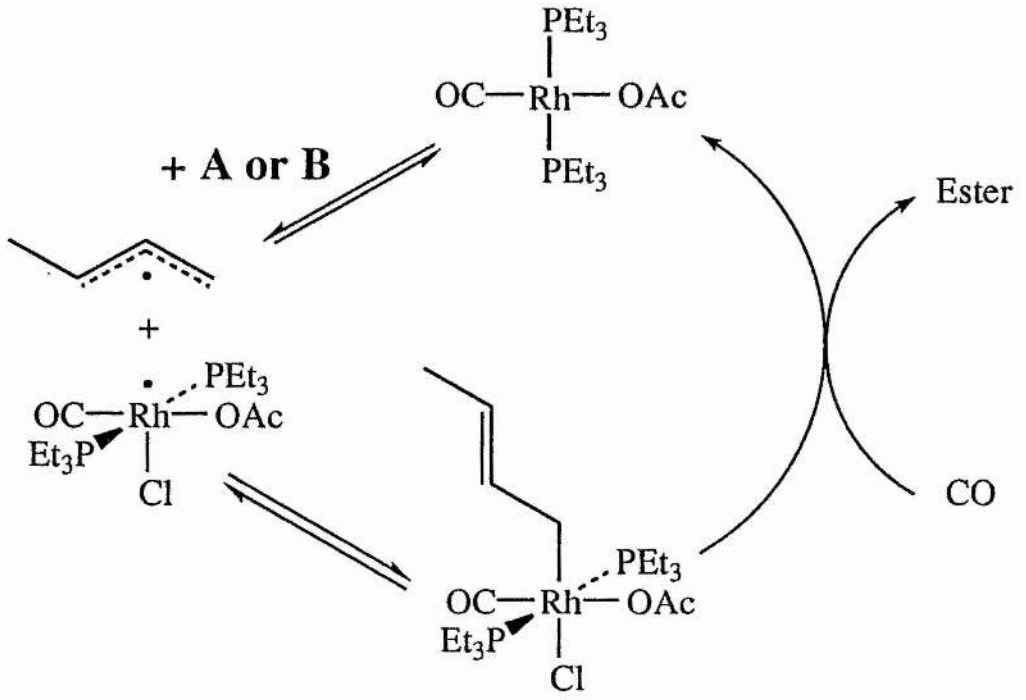


Scheme 5.7 - Non radical mechanism for the formation of the straight chain ester from either starting isomer.

This mechanism shows that a rearrangement via an η^3 intermediate is taking place to reduce the steric crowding at the metal centre; this must occur faster than the carbonylation reaction.

An alternative mechanism could be via radical intermediates; this is outlined in scheme 5.8. Both precursors **A** and **B** give the same allyl radical which is proposed to attack the rhodium centre to give only the straight chain product;





Scheme 5.8 - Radical based mechanism for the formation of straight chain ester from either isomer of chlorobutene discussed.

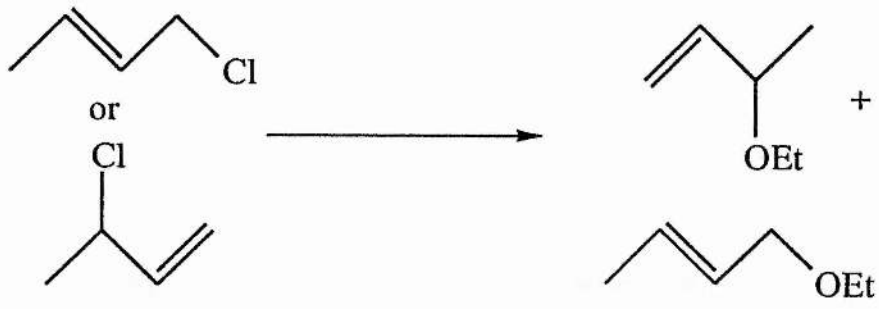
For these observations it is not clear which mechanism is actually operating. The evidence so far gained is the lack of η^3-allyl intermediates detected in the nmr. Werner *et al* has managed to isolate η^3-allyl intermediates and η^3-benzyl intermediates in rhodium systems[204], although they are extremely reactive.

As seen in table 5.1 ^{t}BuBr was investigated since it too could produce a stabilised radical intermediate, but no carbonylated product was detected.

5.1.3 Brief overview of ether production from propenyl halides

As was seen in section 5.1.1, ethers are often produced alongside esters in carbonylation reactions.

There are a few literature examples of ethers exclusively being produced under relatively mild conditions from propenyl halides. The first of these is by Taylor *et al* (1972)[205] where he showed that allylic substrates could be converted to ethers using Rh^I or Cu catalysts. A very interesting observation was that 3-chlorobut-1-ene and 1-chlorobut-2-ene would form the same products; this is illustrated in scheme 5.9;



Scheme 5.9 - The production of two isomers of an ether from either of the two isomers of chlorobutene shown.

An ionic mechanism was proposed to explain these two isomers.

Another paper by Luft *et al* (1974) found the same phenomena using heterogeneous copper based catalysts (ratio of branched: straight chain ethers is ~1:1)[206].

These observations are not in agreement with the work by Payne who found predominantly the branched chain isomer. These results will be discussed later in section 5.1.4.

Propenyl ether formation has been of increasing importance in the past few years, because propenyl ethers have been found to be excellent temporary protecting entities for hydroxyl groups. This is of particular interest at the moment in carbohydrate chemistry[207]. These protected sugars can be synthesised by palladium catalysed reactions in high yield. The allyl ether is not synthesised from the propenyl halide, but from a propenyl carbonate. CO_2 is lost during the reaction, and the ether linkage is thus formed. The big advantage is strong bases do not have to be used, unlike in the more traditional Williamson ether synthesis.

Unfortunately this is not a general method for allyl ether production since in certain cases the CO_2 is not lost[208].

5.1.4 Production of ethers

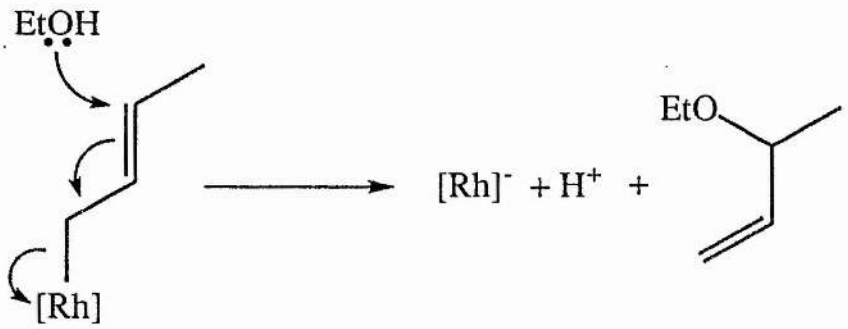
It was found that ethers could be produced from propenyl chloride and ethanol just by heating the mixture up with CO/H_2 (40 atms.) without a catalyst (see table 5.1).

To examine how mild the conditions needed to be to produce ethers propenyl bromide was reacted with ethanol under reflux. It was found

that using a catalytic amount of phosphine, partial conversion was attained (~30%). Long reaction times were needed for higher conversions (3 days).

The observation that ethers could be produced from just propenyl chloride and ethanol in an autoclave seems to suggest that ethers are being formed by an SN_1 or SN_2 mechanism.

The earlier observation by Payne that branched chain ethers were the predominant product seems to suggest that some metal catalysed etherification is taking place, scheme 5.10 shows a speculative mechanism for branched chain etherification.



Scheme 5.10 - Diagramatic representation of the formation of the branched chain ether.

5.1.5 Conclusions

It has been shown that it is possible to effect the carbonylation of propenyl halides to predominately the 3-butenoate ester. Ethers are produced as by-products from the reaction. In both cases the unsaturated moiety is untouched, i.e. no hydrogenation or hydrocarbonylation (in the presence of hydrogen) is observed.

Ether formation is dependent on the bond strength of the carbon halide bond. More ether is produced when this bond is weaker.

The yield of ester seems to be indirectly determined by the bond strength of the propenyl halide. When the bond strength is higher the etherification reaction is less competitive, therefore more of the final product mixture is ester. This conclusion is backed up by evidence obtained in table 5.2 by Payne, that the bromide equivalent of the 1-chlorobut-2-ene produces less ester (38%) than the original chloro compound (55%).

The reaction can be extended to benzyl halides also, but the production of carbonylated products is considerably lower.

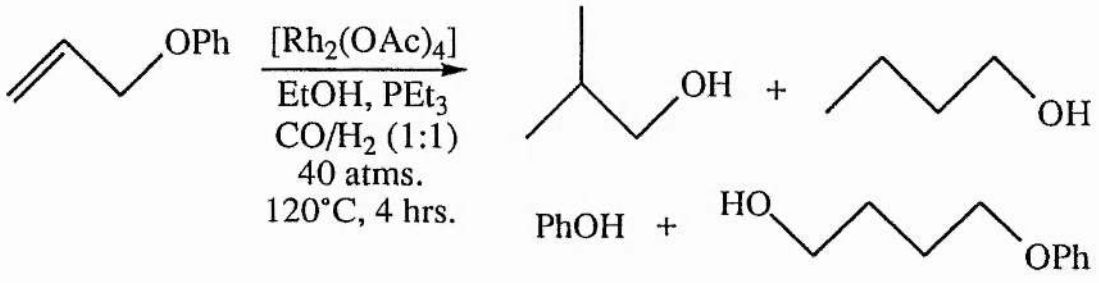
Most previously reported reactions of this kind need stoichiometric amounts of base to remove the HX produced from the carbonylation reaction. Our system seems to produce mainly EtX from reaction with solvent EtOH and no other added base is required.

5.2 Propenyl ethers

The observation that water loss can occur during the hydrohyroxymethylation of 2-propen-1-ol, at least on the pathway to the branched chain product (see chapter 2) prompted us to investigate the use of propenyl ethers as substrate since it was anticipated that the equivalent loss of alcohol might be favoured.

It is of interest to note that these propenyl ethers are produced in the carbonylation of propenyl halides, but do not react further. However, the active catalytic species in this system is different from that present in the hydrohydroxymethylation reactions.

Phenyl propenyl ether was introduced to the standard system and the following (unquantified reaction) products were observed (scheme 5.11).

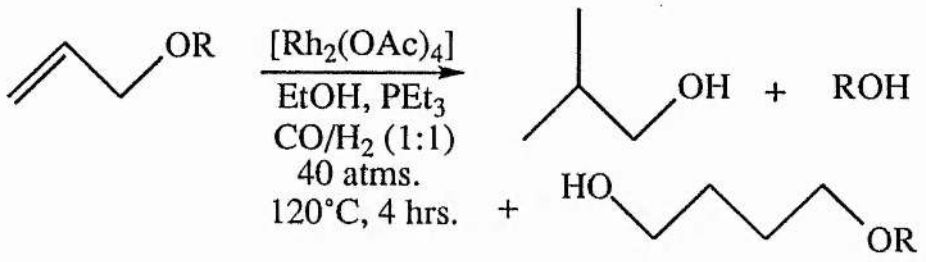


Scheme 5.11 - Reaction products obtained from phenyl propenyl ether.

The origin of the butan-1-ol was not investigated.

The other products are analogous to the 2-propen-1-ol reaction. The 2-methylpropan-1-ol and the phenol from the branched chain mechanism (elimination of PhOH compared to H_2O in the 2-propen-1-ol case) and 4-phenoxybutan-1-ol from the straight chain mechanism.

This was found to be a general reacton for the alkyl propenyl ethers also tested. Scheme 5.12 (R = ^{n}Pr, Et or -CH_2CHCH_2).



Scheme 5.12 - General reaction scheme for alkyl propenyl ethers

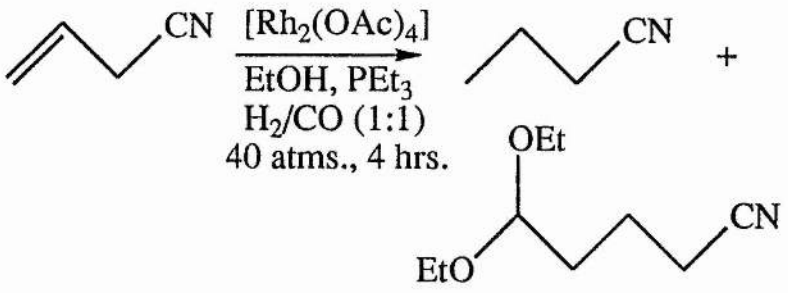
The one difference between the alkyl propenyl ethers and the aryl propenyl ethers is the production of butan-1-ol from the aryl ether.

Dipropenyl ether was also investigated for this system. The elimination product of this substrate if the branched chain mechanism was operating, would be 2-propen-1-ol. This could then react further to form the products expected of 2-propen-1-ol (i.e. 2-methylpropan-1-ol and 1,4-butanediol. This was the reaction observed.

Propenyl ethers reacted to form products comparable to 2-propen-1-ol as expected. This reaction seems to be general for alkyl propenyl ethers. The one aryl propenyl ether investigated suggested that a competitive reaction is operative.

5.3 Propenyl cyanide

Propenyl cyanide was expected to react in a similar fashion to 2-propen-1-ol. The major reaction product (> 50%) was the hydrogenation species seen in scheme 5.13. The reaction was in 100% conversion. The other product in reasonable yield (~20%) was the acetal also depicted in scheme 5.13.



Scheme 5.13 - Reaction products of propenyl cyanide.

Five more small peaks were also identified in trace amounts in the glc trace of the reaction mixture produced from propenyl cyanide using the conditions shown in scheme 5.13. These have been tentatively identified as the straight and branched chain aldehydes and alcohols, and also the branched chain acetal similar to the one in scheme 5.13.

The reaction seems to be mainly a straight hydrogenation versus hydroformylation system. The pathway for the formation of the diols is not clear in this reaction.

5.4 Methyl vinyl ketone

Knowing that aldehydes can be hydrogenated under the normal catalytic reaction conditions, it is of interest to investigate whether ketones could also be hydrogenated. The unsaturated ketone, methyl vinyl ketone was therefore investigated. Two products were observed, neither expected. Scheme 5.14 illustrates this reaction.

Scheme 5.14 - Reaction products from methyl vinyl ketone.

One product is just a straight hydrogenation product, the other appears to be an ethanol addition product, although this has been tentatively assigned by GCMS data alone. Further studies, including the use of D_2 would be of considerable interest for this reaction.

5.5 - Conclusions

This *in situ* generated catalytic system seems to manage a wide variety of catalytic transformations. This chapter shows some of the reactions that are possible - hydrogenation, hydroformylation, hydrohyroxymethylation, carbonylation and addition reactions.

Triethylphosphine rhodium complexes are versatile catalysts for a range of carbonylation and hydrogenation reactions of substituted alkenes. Different functional groups on the alkene can direct the reaction towards different types of product, sometimes with very different active metal complexes.

Chapter 6 - Experimental Techniques and Preparation of Starting Materials

6.1 Product analysis

6.1.1 Gas chromatography - mass spectroscopy, GCMS.

Qualitative analysis of products from catalytic runs was carried out by GCMS on an INCOS 50 GCMS system with a Hewlett Packard 5890 gas chromatograph.

Some glc were run with a HP17 (crossed linked 50% Ph-Me silicone) capillary column. The glc temperature program for this column was set to run at 50°C for 5 minutes, then ramped to 200°C at 10°C min^{-1}. Others were run on a BP1 (dimethylsiloxane) capillary column. The glc temperature program was set to run at 30°C for 5 minutes, then ramped at 34°C min^{-1} to 200°C then held at 200°C for 5 minutes.

Helium at 9 psi was used as carrier gas and the injector temperature was 200°C.

All catalytic samples analysed were run undiluted, as reaction mixtures, on removal from the autoclave.

6.1.2 Gas liquid chromatography, glc

Products of catalytic runs were analysed quantitatively by glc on a Philips PU 4500 chromatograph using nitrogen as the carrier gas, with the injector temperature set at 150°C and a flame ionisation detector at 200°C. The glc machine was equipped with a fused silica capillary column with a CP-Sil-19CB stationary phase. Reaction solutions (1 cm^3) with toluene (50 μl) as internal reference were prepared, then a sample (0.1 μl) was injected into the glc.

Standard solutions with known quantities of the materials to be quantified were prepared in ethanol (total volume 1 cm^3). To these solutions toluene (50 μl) was added. The materials quantified were 1,4-butanediol, 2-methylpropan-1-ol, 2-methylpropanal, γ-butyrolactone, propan-1-ol, 3-chloroprop-1-ene, 3-bromoprop-1-ene, 3-iodoprop-1-ene, ethyl propenyl ether, ethyl 3-butenoate, iodoethane, diethyl ether, benzyl chloride, ethyl 2-phenylethyl ether and 2-propen-1-ol.

A standard temperature program for the glc of 40°C for 5 minutes, ramped at 16°C min^{-1} for 10 minutes then held at 200°C for 5 minutes, was used for standards and reaction product analysis runs. To minimise errors each sample was quantified three times and the results averaged.

6.1.3 Problems associated with analysis of 1,4-butanediol.

Problems with the analysis of 1,4-butanediol were discovered. The area under the glc peak corresponding to 1,4-butanediol was not always reproducible from consecutive runs of the same sample. All other materials analysed gave acceptable reproducibility (within 10%).

The results quoted in chapter 2 for 1,4-butanediol were the result of running the standard solutions several times at each concentration, on several separate dates. The most consistent results were averaged and used as the basis for the quantitative analysis. Actual reaction mixtures were run three times, if all three results gave reasonable reproducibility they were averaged, if not the same sample was re-injected twice more, the two most inconsistent results rejected and the three remaining results averaged and used.

6.1.4 Nuclear magnetic resonance spectroscopy, nmr

All nmr run at St. Andrews were recorded on a Bruker AM 300 spectrometer (^{1}H, 300.1 MHz; ^{31}P, 121.5 MHz; ^{13}C, 75.5 MHz) in 5 mm glass tubes.

All nmr at Edinburgh were run by J. A. Parkinson on a 151 MHz (^{13}C) Varian VXr 600S spectrometer.

The catalytic deuterated reaction mixtures were fractionally distilled. The d_x 2-methylpropan-1-ol recovered from these separations were analysed in the presence of $CDCl_3$ (as an internal lock).

Rhodium compounds were dissolved in either perdeuterotoluene (C_7D_8), perdeuterotetrahydrofuran (C_4D_8O), perdeuteroethanol (C_2D_5OD) or perdeuteromethanol (CD_3OD), all deuterated solvents were used as supplied, but where possible they were degassed prior to use.

High pressure nmr were attempted on three different high pressure nmr apparatus, one borrowed from Dr. B. Mann from Sheffield, the other two designed and built in the department.

6.1.5 Infra-red spectroscopy, i.r.

All i.r. spectra were measured on a Perkin-Elmer 1710 fourier transform infrared spectrometer in the range 4000-450 cm^{-1}. Spectra were recorded either as nujol mulls or in a KBr solution cell.

6.2 Equipment and reagents

6.2.1 Vacuum lines

The vacuum work carried out for this thesis was carried out on a standard Schlenk line (with greaseless PTFE taps and ball and socket compression joints), using standard catheter tubing techniques. An inert atmosphere was provided by use of argon, which had been dried by passage through a column packed with chromium (II) absorbed on silica.

6.2.2 Solvents

Alcoholic solvents were dried by distillation, over magnesium, under an atmosphere of nitrogen or argon. Ether, petrol (b.p. 40-60°C) and thf were distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Toluene was dried by distillation over sodium under an atmosphere of nitrogen. CH_2Cl_2 was dried over phosphorous pentoxide, then distilled over CaH_2 under an atmosphere of nitrogen.

6.2.3 Substrates and standards

All materials used were distilled by the most convenient method from 'Purification of Laboratory Chemicals'[209], except for 2-methylpropan-1-ol which was distilled over CaO and 3-iodoprop-ene which was distilled in foil rapped apparatus. Iodoethane, methyl lithium (in ether), rhodium trichloride trihydrate, triethylphosphine, triisopropylphosphine,tricyclohexylphosphine,

triphenylphosphine, trimethylphosphine, and ethyl propenyl ether were used as supplied.

6.3 Catalytic experiments

6.3.1 Preparation of catalytic solutions

Catalytic solutions of $[Rh_2(OAc)_4.2MeOH]$ (some earlier work was carried out using $[Rh_2(OAc)_4]$) were made up so that the concentration was 1×10^{-2} mol dm^{-3}. This stock solution was stored under argon, after degassing.

6.3.2 Autoclave reactions

Hydrocarbonylation reactions were carried out in stainless steel autoclaves, which contained glass liners to aid product collection. A problem found with these glass liners was that the volatile solvents and products could condense between the liner and the side of the autoclave. This could effect the product concentrations when analysed after the experiment had been completed, if care was not taken to collect all the product. The pressure was carefully released upon completion of a reaction, after a suitable cooling period had passed (> 30 mins.), to ensure a minimum of volatiles were lost.

A typical autoclave run was as follows:-

The autoclave was charged up to > 20 atms. with the gaseous reagents. The autoclave was then vented, and was flushed in this manner a total of three times. A gentle stream of gas was then passed through the autoclave to allow injection through the open port, without letting any air in. A pressure of ~2-3 atms. was found to be quite adequate for this purpose. The liquid reagents were added, normally in the order catalyst (2.3×10^{-5} moles) + solvent (4 cm^3) first, followed by the functional alkene (1 cm^3), followed by the phosphine (5×10^{-4} moles). The injection port was closed, then the autoclave was charged up to the desired pressure and placed into a pre-heated oven. After the required time the autoclave was removed from the oven and allowed to cool in water. The autoclaves were carefully vented and the products collected and analysed by GCMS and glc.

For reactions carried out using D_2 in place of H_2, the general method was used with the following modifications, the autoclave was purged with with CO only; on addition of all the reactants the autoclave was charged with D_2 only up to 20 atms., then the total pressure was increased to 40 atms. using CO only.

When EtOD or other solvents were used, the catalyst was weighed directly into a glass sleeve, then sealed into the autoclave prior to flushing. When Pcy_3 or PPh_3 were used in place of PEt_3, the phosphine was weighed directly into the glass sleeve, then sealed into the autoclave prior to flushing.

Heating sleeves were used for heating the autoclaves in the studies on effects of temperature and time, on the product distribution.

6.4 Preparation of rhodium species

$[Rh_2(OAc)_4]$[210], $[Rh_2(OAc)_4.2MeOH]$[210]. $[RhCl(C_8H_{14})_2]_2$[211] and $[Rh(Cl)(CO)(PEt_3)_2]$[212] were all prepared by published literature methods.

All the following preparations were carried out under argon. All reagents used were distilled as above (sections 6.2.2 and 6.2.3), then degassed prior to use.

6.4.1 Preparation of carbonylmethylbis(triethylphosphine)rhodium(I)

$[Rh(CO)(CH_3)(PEt_3)_2]$ was prepared by reacting $[Rh(Cl)(CO)(PEt_3)_2]$ (0.7934 g, 1.97 mmol) with CH_3Li, (1.5 cm^3, 1.4 molar in ether) at -20°C, under an atmosphere of argon. The solution was allowed to warm up to room temperature. The yellow solution was filtered from the precipitated LiCl. The LiCl was washed with ether (2 cm^3) and filtered. To the combined filtrates petrol (2 cm^3) was added. The resulting solution was cooled to -110°C, then allowed to crystallise for 10 minutes. The yellow solid was collected by filtration and dried under vacuum for 30 minutes. Yield 0.6 g (76%).

6.4.2 Preparation of acetyldicarbonylbis(triethylphosphine)

Three similar preparation method for $[Rh(COCH_3)(CO)_2(PEt_3)_2]$ *in situ* were carried out depending on which experiment was being attempted.

(i) For alcohol addition studies;

$[Rh(CH_3)(CO)(PEt_3)_2]$ (0.1634 g) in C_4D_8O was transferred into a degassed nmr tube. CO was carefully bubbled through the solution until a deep yellow to pale yellow colour change had occurred (1 minute). A ^{13}C spectrum was recorded of the $[Rh(COCH_3)(CO)_2(PEt_3)_2]$ in solution at -60°C. To this solution known aliquots of an alcohol (C_2H_5OH or CF_3CH_2OH) were added and the ^{13}C nmr (at -60°C) was recorded after each addition.

(ii) For nmr modelling studies;

The yellow $[Rh(CO)(CH_3)(PEt_3)_2]$ was dissolved in CD_3OD (2.5 cm^3) and CO was passed through the solution for 1 minute. An aliquot of this (~1 cm^3) was transferred to a degassed nmr tube. ^{13}C and ^1H nmr spectra were recorded of this solution. Argon was bubbled through the solution in the nmr tube, again ^{13}C and ^1H nmr were recorded.

(iii) For i.r. studies;

$[Rh(COCH_3)(CO)_2(PEt_3)_2]$ was prepared by bubbling CO through a solution of $[Rh(CO)(CH_3)(PEt_3)_2]$ dissolved in ether. This was evaporated to near dryness by passing CO through the solution for 2 hours. The pale yellow residue remaining was evaporated further under vacuum at low temperature (< -50°C) for a further 30 minutes an i.r. was taken of this sample. Ethanol (~1 cm^3) was added, then the solution was evaporated to near dryness by bubbling CO through the solution then evaporated further under vacuum. The tube was then filled with CO. An i.r. was taken of this sample in a nujol mull. The same mull was re-examined after 4 hours.

The rest of the sample was dissolved in ethanol and allowed to crystallise at -78°C for 11 hours. White crystals were recovered by filtration from the solution and investigated by i.r. The crystals turned into a yellow oil, which quickly solidified (~2 seconds) into a yellow solid. This was examined as a nujol mull by i.r.

6.4.3 Attempted high pressure nmr studies

A solution containing [$Rh_2(OAc)_4.2MeOH$] (0.0090 g), 2-propen-1-ol (45 µl), PEt3 (40 µl) and d_6-EtOD were transferred to a sapphire nmr tube under argon. The tube was pressurised to 50 atms.(CO/H_2, 1:1). ^{31}P nmr spectra were then recorded.

6.5 Organic preparations

Ethyl 3-butenoate was prepared by a standard literature method[213].

6.5.1 Attempted ethyl propenyl ether synthesis

Bromoprop-1-ene (17 cm^3), ethanol (50 cm^3) and PEt_3 (1.2 cm^3) were refluxed with argon or CO bubbling through the reaction mixture overnight. The reaction was allowed to cool, then the mixture was analysed using GCMS.

In some experiments a cardice trap was used to liquefy any exhaust that was not caught by the condenser. Any material trapped in this way was analysed by GCMS.

6.5.2 Synthesis of HOC_4H_8OPh as a glc standard

To DMSO (20 cm^3) powdered KOH (2.24 g) was added. This was stirred for 5 minutes without completely dissolving. Phenol (0.94 g), quickly followed by 4-chlorobutanol (1 cm^3) was then added.

Stirring was continued for 45 minutes after which time the mixture was poured into water (75 cm^3), then extracted with CH_2Cl_2 (3 x 50 cm^3). The combined organic extracts were washed with water (5 x 20 cm^3), filtered through cotton wool and finally evaporated to ~1 cm^3.

The resulting solution was analysed by GCMS and glc.

Chapter 7 - Conclusions

The self-assembly catalyst system $[Rh_2(OAc)_4.2MeOH]$/ PEt_3/ EtOH/ CO/ H_2 was shown to be an active catalyst for hydrohydroxymethylation of 2-propen-1-ol. The anticipated straight chain product 1,4-butanediol was produced alongside the unexpected branched product 2-methylpropan-1-ol. These two products accounted for 75-90% of the final reaction mixture with the straight: branched chain ratio being ~2:1, the reaction reached 100% conversion within an hour.

It was found that even after short reaction times, no intermediate C_4 hydroxyaldehydes were detected for the normal hydroformylation reaction.

It was not clear how the 2-methylpropan-1-ol was being produced, two simple routes from 2-methyl-1,3-propanediol or 3-hydroxy-2-methylpropan-1-ol were ruled out, so a modified hydrohydroxymethylation mechanism was proposed.

The key steps of the mechanism are; protonation of a metal acyl species (on the acyl oxygen) to form a metal hydroxycarbene intermediate, dehydration of the hydroxycarbene species (conjugation being the driving force for this step), oxidative addition of hydrogen to the metal centre, a single hydrogen atom transfer to the carbene carbon, a σ-π allylic rearrangement of the substrate based ligand, followed by reductive elimination of a vinyl alcohol. This rapidly rearranges to 2-methylpropanal, which is hydrogenated by this system to give 2-methylpropan-1-ol.

The mechanism was examined in several ways;

(i) black box studies; these reactions were carried out by changing the reagents used in the reaction and drawing conclusions about the mechanism from the products formed.

(ii) deuterium labelling; by using a recently developed ^{13}C analytical technique, it was possible to distinguish between different isotopomers of d_x-2-methylpropan-1-ol. Using high field $^{13}C\{^1H,^2H\}$ nmr, it was possible to quantify up to 18 different isotopomers produced from a single reaction run.

(iii) model species; studies on some of the proposed mechanistic intermediates were carried out, and a metal hydroxycarbene species was identified. Other model studies showed that mild proton sources (alcohols) could interact with the acyl oxygen of a rhodium acyl complex to form hydrogen bonded compounds, presumably intermediates that occur during the transformation from metal acyl to hydroxycarbene species.

The effect of varying the reaction conditions and ligands was also investigated, such effects as phosphine concentration, reaction time, total pressure, synthesis gas composition and temperature were examined.

Other substrates briefly studied were propenyl halides, propenyl ethers, propenyl cyanides and ketones. It was of interest to note that although propenyl ethers react in a similar way to 2-propen-1-ol, propenyl halides gave carbonylation and etherification products via a different catalytic system derived from the same precursors.

7.1 Further studies

Although the work on 2-propen-1-ol is nearly complete, although D_2 studies on 1,4-butanediol would complete the investigation, much more work could be done on functionalised alkenes using the rhodium/ trialkylphosphine catalyst system.

The alkenes propenyl halides, propenyl ethers, propenyl cyanides, aldehydes and ketones all warrant further investigation, especially aryl propenyl ethers, due to the unknown pathway of formation for butan-1-ol from phenyl propenyl ether.

Initial indications that similar alkenes such as propenyl ethanoate, other allylic alcohols and 2,3-dihydrofuran could be of interest to investigate.

Other reaction types could also be explored with the catalyst hydrosilylation, hydroboration (no references were found to a rhodium/ trialkylphosphine accomplishing hydroboration) and alkylhalide activation.

References

1. L. H. Slaugh, Bel. Patent, 1963, 021662.

2. L. H. Slaugh and R. D. Mullineaux, U.S. Patent, 1966, 3239566.

3. For example see M. J. Lawrenson and G. Foster, Ger. Patent, 1969, 1812504, CA 71; 101313a.

4. P. Johnson and M. J. Lawrenson, U.S. Patent, 1972, 3660493.

5. M. J. Lawrenson, Brit. Patent, 1971, 1254222.

6. M. J. Lawrenson, Brit. Patent, 1972, 1284615.

7. R. Fowler, H. Connor and R.A. Baehl, *CHEMTECH*, 1976, 773.

8. B. Bell, W. Rupilius and F. Asinger, *Tetrahedron Lett.*, 1968, 29, 3261.

9. R. L. Pruett and J. A. Smith, *J. Org. Chem.*, 1969, 34, 327.

10. R. L. Pruett and J. A. Smith, U.S. Patent, 1975, 3917661.

11. G. B . McVicker, Ger. Patent, 2424526, CA 84; 89616k

12. M. Tanaka, K. Saeki and N. Kihara, Jpn. Kokai, 77 83,311, CA 87; 200792t.

13. R. O. Hughes, U.S. Patent 4201728, CA 93; 149769s.

14. S. Franks and F. R. Hartley, *J. Mol. Catal.*, 1981, 12, 121.

15. B .Bell and H. Bahrmann, *J. Mol. Catal.*, 1977, 2, 211.

16. J. K. MacDougall and D. J. Cole-Hamilton, *J. Chem. Soc., Chem. Commun.* 1990, 165.

17 J. K. MacDougall, D. J. Cole-Hamilton and M. J. Green, Eur. Patent, 420,510.

18 T. Okano, T. Kobayashi, H. Konishi and J. Kiji, *Tetrahedron Lett.*, 1982, 4967.

19. T. Okanoand and T. Yoshida, *Yuki Gosei Kagaku Kyokaihi* , 1983, 41, 359-64.

20. P. W. N. M. van Leeuwen and C. F. Roobeek, *J. Organomet. Chem.*, 1983, 258, 343.

21. D. A. Young, U.S. Patent, 1987, 4642388, CA 106; 175780p.

22. K. D. Tau, U.S. Patent, 1986, 4605781, CA 105; 193347m.

23. W. Bernhagen, H. Bahrmann and H. Springer, U.S. Patent, 1982, 4317945.

24. W. Aquila, W. Himmele, W. Fliege and H. Siegel, U.S. Patent, 1976, 3966827.

25. A. Spencer, Eur. Patent, 1979, 2908.

26. S. Nahamura, T. Deguchi, M. Tamura, Y. Hara, K. Murayama, H. Tanaka, M. Ishino, K. Wada and E. Watanabe, Brit. Patent, 1985, 2155010.

27. M. Tanaka, M. Ishino, T. Delguchi, S. Nakamura, *J. Organomet. Chem.*, 1986, 312, C75.

28. Y. Ohgomori, S. Yoshida and Y. Watanabe, *J. Chem. Soc., Chem. Commun.*, 1987, 829.

29. K. Murata, A. Matsuda, T. Masuda, E. Watanabe and K. Wada, *Bull. Chem. Soc. Jpn.*, 1987, 60, 1957.

30. Y. Tomotake, T. Matsuzaki, K. Murayama, E. Watanabe, K. Wada and T. Onoda, *J. Organomet. Chem.*, 1987, 320, 239.

31. H. Tanaka, Y. Hara, E. Watanabe, K. Wada and T. Onoda, *J. Organomet. Chem.*, 1986, 312, C71.

32. H. Watanabe, H. Wada and V. Hara, Jpn. Kokai, 61 263,938-41, CA 106; 195879f-1958826b.

33. S. Yoshida, M. Nakajima, H. Kinishita, Y. Okage and Y. Watanabe, Jpn. Kokai, 62 234,036, CA 109; 37508s.

34. S. Yoshida, H. Kinoshita and Y. Watanabe, Jpn. Kokai, 63 190,838, CA 111; 80331g.

35. M. Ishino, M. Tamura, T. Deguchi and S. Nakamura, *J. Catal.*, 1992, 133, 325.

36. W. E. Smith, Ger. Patent, 2758473, CA 89; 163050t.

37. B. Fell and M. Barl, *Chem. Ztg.*, 1977, 101, 343, CA 87; 167499c.

38. R. Kummer, Ger. Patent, 2401553, CA 83; 178295b.

39. T. Shimizu, Ger. Patent 2538364, CA 85; 45962m.

40. C. U. Pittman and W. D. Honnick, *Chem. Ind.* 1981, 5, 353.

41. E. Drent, Eur. Patent, 1985, 151, 822.

42. A. Abatjoglou and D .R. Bryant, *Prepr. Am. Chem. Soc. Div. Pet. Chem.*, 1981, 26, 27.

43. J. J. Lin and W. H. Brader Jnr., U.S. Patent, 1985, 4533756.

44. H. Ono, K. Miyama and T. Kasuga, Eur. Patent, 1986, 183199.

45. M. A. Murphy, A. Aguilo and B. L. Smith, Eur. Patent, 1988, 257967, CA 109, 75707p.

46. K. Sato, Y. Kawaragi and M. Takai, Eur. Patent, 1991, 407687.

47. S. Tórós, I. Gémes-Pésci, B. Heil, S. Maho and Z. Tuba, *J. Chem. Soc., Chem. Commun.*, 1992, 858.

48. S. Montelatici, A. van der Ent, J. A. Osborn and G. Wilkinson, *J. Chem.. Soc., (A)*, 1958, 1054.

49. L. Homer, H. Büthe and H. Siegel, *Tetrahedron Lett.*, 1968, 37, 4023.

50. R. S. Coffey, Brit. Patent, 1121643, CA 69, 60537q.

51. W.Strohmeier and W.Rehder-Stirnweiss, *J. Organomet. Chem.*, 1969, 19, 417.

52. P. van der Plank, A. van der Ent, A. L. Onderdelinden and J. van Oosten, *J. Am. Oil Chem. Soc.*, 1980, 57, 343.

53. R. R. Schrock and J. A. Osborn, *J. Chem. Soc., Chem. Commun.*, 1970, 567.

54. H. Fujitsu, E. Matsumura, K. Takesjita and I. Mochida, J. Org. Chem., 1981, 46, 5353.

55. H. Fujitsu, E. Matsumura, K. Takeshita and I. Mochida, *J. Chem. Soc. (Perkin Trans. 1)*, 1981, 2651.

56. J. K. MacDougall and D. J. Cole-Hamilton, *J. Chem. Soc., Chem. Commun.*, 1990, 165.

57. V. V. Grushin and H. Alper, *Organometallics*, 1991, 10, 831.

58. H. Wada and H. Watanabe, Jpn. Kokai, 1987, 62 145,033.

59. B. Heil, S. Tórós, S. Vastag and L. Markó, *J. Organomet. Chem.*, 1975, 94, C47.

60. H. Brunner and H. Leyerer, *Bull. Soc. Chim. Belg.*, 1987, 96, 353, CA 108; 167657e.

61. Z. Nagy-Magos, S. Vastag, B. Heil and L. Markó, *J. Organomet. Chem.* 1979, 171, 97.

62. Z. Zikanova, V. Vaisarova and J. Hetflejs, *Collect. Czech. Chem. Commun.*, 1986, 51, 1287.

63. L. Markó, *Pure Appl. Chem.*, 1979, 51, 2211.

64. S. Tórós, L. Kollar, B. Heil, and L. Markó, *J. Organomet. Chem.* 1983, 255, 377.

65. H. Fujitsu, E. Matsumura, S. Shurahama, K. Takeshita and I. Mochida, *J. Chem. Soc. (Perkin Trans 1.)*, 1982, 855.

66. H. Fujitsu, E. Matsumura, S. Shirahama, K. Takeshita and I. Mochida, *J. Org. Chem.*, 1981, 46, 2287.

67. T. Yoshida, T. Okana and S. Otsuka, *J. Chem. Soc., Chem. Commun.*, 1979, 870.

68. G. Gregorio, G. Pregaglia and R. Ugo, *Inorg. Chim. Acta*, 1969, 3, 89.

69. C. Masters, A. A. Kiffen and J. P. Visser, *J. Am. Chem. Soc.*, 1976, 98, 1357.

70. R. Spogliarich, A. Tencich and M. Graziani, *J. Organomet. Chem.*, 982, 240, 453.

71. K. Tani, K. Suwa, E. Tanigawa, T. Yoshida, T. Okano and S. Otsuka, *Chem. Lett.*, 1982, 261.

72. F. Felfoldi, I. Kapocsi and M. Bartok, *J. Organomet. Chem.*, 1984, 277,443.

73. H. Schumann, C. Gielusek, S. Jurgis, E. Hahn, J. Pickardt, J. Blum, Y. Sasson and A. Zoran, *Chem. Ber.*, 1984, 117, 2825.

74. R. Marcec, *React. Kinet. Catal. Lett.*, 1986, 31, 337.

75. J. A. Maguire and A. S. Goldman, *J. Am. Chem. Soc.* 1991, 113, 6706.

76. J. A. Maguire, A. Petrillo and A. S. Goldman, *J. Am.Chem. Soc.*, 1992, 114, 9492.

77. T. Sakakura, F. Abe and M. Tanaka, *Chem. Lett.*, 1991, 359.

78. F. deChanentenay, J. A. Osborn and G. Wilkinson, *J. Chem. Soc. (A)*, 1968, 787.

79. R. N. Haszeldine, R. V. Parish and R. J. Taylor, *J. Chem. Soc. (Dalton Trans.)*, 1974, 2311.

80. J. Rejohn and J. Hetflejs, *Collect. Czech. Chem. Commun.*, 1975, 40, 3680.

81. J. P. Howe, K. Lung and T. Nile, *J. Organomet. Chem.*, 1981, 208, 401.

82. I. Ojima, M. Kumagai and Y. Nagai, *J. Organomet. Chem.*, 1974, 66, C14.

83. K. A. Brady and T. A. Nile, *J. Organomet. Chem.*, 1981, 206, 299.

84. K. Takatsuna, M. Tachikawa, A. Shinohara, K. Shiozawa and Y. Okumura, Eur. Patent, 1989, 321174.

85. S. Inaba and Y. Kimae, Jpn. Kokai, 02 59,591, CA 112; 158630w.

86. K. Felföldi, I. Kapocsi and M. Bartók, *J. Organomet. Chem.*, 1989, 362, 411.

87. C. M. R. Davidson, Neth. Patent, 1966, 6603612, CA 66; 28511d.

88. D. Durand and C. Lassau, *Tetrahedron Lett.*, 1969, 28, 2329.

89. Monsanto., U.S. Patent, 1373568.

90. Y. Matsui, *Tetrahedron Lett.*, 1976, 14, 1107.

91. I. Kuriyama, Jpn. Kokai, 78 63,307; CA 89; 129066t.

92. Akademie der Wissenschaften, Ger. (East) Patent, DD 216,003.

93. P. Hong, T. Mise and H. Yamazaki, *J. Organomet. Chem.*, 1991, 412, 291.

94. E. Drent, Eur. Patent, 1982, 48046.

95. W. S. Weston, R. C. Gash and D. J. Cole-Hamilton, *J. Chem. Soc., Chem. Commun.*, 1994, 745.

96. J. Tsuji and K. Ohno, Jpn. Kokai, 68 08,442, CA 70; 11368.

97. F. Abu-Hasanayn, M. E. Goldman and A. S. Goldman, *J. Am. Chem. Soc.*, 1992, 114, 2520.

98. J. Gallay, D. DeMontauzon and R. Poilblanc, *J. Organomet. Chem.*, 1972, 38, 179.

99. A. Behr, K. O. Kuszak and R. He, *Int. Congr. Catal. Proc. 8th*, 1984, V565, CA 106; 101530r.

100. A. G. Kent, Eur. Patent, 1985, 151510, CA 104; 109029h.

101. S. Ono and Y. Mizoguchi, Jpn. Kokai, 74 31,639, CA 81; 25340w.

102. R. C. Larock, K. Oertle and G. F. Potter, *J. Am. Chem. Soc.*, 1980, 102, 190.

103. D. Milslein, U.S. Patent, 4581178.

104. C. J. Cable, H. Adams, N. A. Bailey, J. Crosby and C. White, *J. Chem. Soc., Chem. Commun.*, 1991, 165.

105. R. A. Faltynek, *Inorg. Chem.*, 1981, 20, 1357.

106. T. Sakakura and M. Tanaka, *Chem. Lett.*, 1987, 2, 249.

107. T. Sakakura and M. Tanaka, *Chem. Lett.*, 1987, 6,1113.

108. T. Sakakura and M. Tanaka, *Pure Appl. Chem.*, 1990, 62, 1147.

109. T. Sakakura, T. Hayashi and M. Tanaka, *Chem. Lett.*, 1987, 5, 859.

110. T. Sakakura, T. Sodeyama, K. Sasaki, K. Wada and M. Tanaka, *J. Am. Chem. Soc.*, 1990, 112, 7221.

111. M. Tanaka, T. Sakakura, Y. Tokunaga and T. Sodeyama, *Chem Lett.*, 1987, 12, 2373.

112. M. Tanaka, T. Sakakura and Y. Tokunaga, Jpn. Kokai, 01 96,162, CA 111; 133635t.

113. T. Sakakura, Y. Tokunaga, T. Sodeyama and M. Tanaka. *Chem. Lett.*, 1987, 12, 2375.

114. T. Sakakura, Y. Tokunaga, T. Sodeyama and M. Tanaka, *Chem. Lett.*, 987, 11, 2211.

115. T. Sakakura, Y. Tokunaga, T. Sodeyama and M. Tanaka, *Chem. Lett.*, 1988, 5, 885.

116. T. Sakakura, T. Sodeyama and M. Tanaka, *Chem. Lett.*, 1988, 4, 683.

117. T. Sakakura, T. Sodeyama and M. Tanaka, *Chem. Ind.*, 1988, 530.

118. T. Sakakura, T. Sodeyama and M. Tanaka, *New J. Chem.*, 1989, 13, 737.

119. W. D. Jones and E. T. Hessel, *New J. Chem.*, 1990, 14, 481.

120. W. D. Jones and E. T. Hessel, *Organometallics*, 1990, 9, 718.

121. T. Sakakura, F. Abe and M. Tanaka, *Chem. Lett.*, 1991, 297.

122. W. T. Boese and A. S. Goldman, *Organometallics*, 1991, 10, 782.

123. K. Nomura and Y. Saito, *J. Chem. Soc., Chem. Commun.*, 1988, 161.

124. Y. Saito and K. Nomura, Jpn. Kokai, 01 90,137, CA 111; 114729k.

125. Y. Saito and K. Nomura, *J. Mol. Catal.*, 1989, 54, 57.

126. K. Nomura, H. Kumagai and Y. Saito, *Shokubai*, 1988, 30, 204, CA 109; 56987p.

127. J. A. Maguire, W. T. Boese and A. S. Goldman, *J. Am. Chem. Soc.*, 1989, 111, 7088.

128. J. A. Maguire, W. T. Boese, M. E. Goldman and A. S. Goldman, *Coord. Chem. Rev.*, 1990, 97, 179.

129. K. Shih and A. S. Goldman, *Organometallics*, 1993, 12, 3390.

130. S. B. Duckett, R. Eisenberg and A. S. Goldman, *J. Chem. Soc., Chem. Commun.*, 1993,1185.

131. H. Itagaki, H. Murayama and Y. Saito, *Bull. Chem. Soc. Jpn.*, 1994, 67, 1254.

132. T. Yoshida, T. Okana, Y. Ueda and S. Otsuka, *J. Am. Chem. Soc.*, 1981, 103, 3411.

133. T. Okano, T. Kobayashi, H. Konishi and J. Kiji, *Bull. Chem. Soc. Jpn.*, 1981, 54, 3799.

134. K. Nomura, M. Ishino and M. Hazama, *J. Mol. Catal.*, 1991, 66, L19.

135. K. Nomura, M. Ishino and M. Hazama, *J. Mol. Catal.*, 1993, 78, 273.

136. T. Yoshida, T. Okano and S. Otsuka, *J. Am. Chem. Soc.*, 1980, 102, 5967.

137. R. F. Jones and D. J. Cole-Hamilton, *J. Chem. Soc., Chem. Commun.*, 1981, 58.

138. D. J. Cole-Hamilton, 'Photogeneration Hydrogen', eds. A. Harriman and M. A. West, Academic Press, New York, 1982, p. 105.

139. E. Delgado-Lieta, M. A. Luke, R. F. Jones and D. J. Cole-Hamilton, *Polyhedron*, 1982, 1, 839.

140. D. Morton, D. J. Cole-Hamilton, J. A. Schofield and R. J. Pryce, *Polyhedron*, 1987, 6, 2187.

141. D. Morton, D. J. Cole-Hamilton, I. D. Utuk, M. Paneque-Sosa and M. Lopez-Poveda, *J. Chem. Soc. (Dalton Trans.)*, 1984, 489.

142. G. Gregonrio, G. F. Pregaglia and R. Ugo, *J. Organomet. Chem.*, 1972, 37, 385.

143. G. Pregalia, G. Gregorio and F. Bonti, Fr. Patent, 1968, 1531261, CA 71; 70089a.

144. S. Yoshkawa, J. Kiji and J. Furukawa, *Makromol. Chem.*, 1977, 178, 1077.

145. H. Singer and G. Wilkinson, *J. Chem. Soc. (A)*, 1968, 849.

146. R. J. Kern, *J. Chem. Soc., Chem. Commun.*, 1968, 706.

147. I. P. Kovalev, K. V. Yeudakov, Y. A. Strelenko, M. G. Vinogradov and G. I. Nikishin, *J. Organomet. Chem.*, 1990, 386, 139.

148. M. G. Vinogradov, I. P. Kovalev and G. I. Nikishin, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 1987, 5, 1172, CA 108; 130979k.

149. I. P. Kovalev, Y. N. Kolmogorov, Y. A. Strelenko, A. V. Ignatenko, M. G. Vinogradov and G. I. Nikishin, *J. Organomet. Chem.*, 1990, 385, 173.

150. M. Takesada, H. Yamazaki and N. Hagihara, *Nippon Kagaku Zasshi*, 1968, 89, 1126, CA 70; 47912.

151. J. Wendt, U. Klinger and H. Singer, *Inorg. Chim. Acta*, 1991, 183, 133.

152. B. C. Berris, U.S. Patent, 1991, 5003100, CA 115; 115263y.

153. K. Madeja, W. Jabs, U. Hahn and W. Kalies, *Z. Chem.*, 1977, 17, 235, CA 87; 117386t.

154. R. J. P. Corriu and J. J. E. Moreau, *J. Organomet. Chem.*, 1977, 127,7.

155. V. V. Grushin and H. Alper, *Organometallics*, 1991, 10, 1620.

156. S. P. Dent, C. Eaborn and A. Pidcock, *J. Chem. Soc., Chem. Commun.*, 1970, 1703.

157. T. Yoshida, T. Okano, K. Saito and S. Otsuka, *Inorg. Chim. Acta*, 1980, 44, L135.

158. V. V. Grushin, A. B. Vymenits and M. E. Vol'pin, *Metalloorg. Khim.*, 1990, 3, 702, CA 113; 58574h.

159. J. Wolf, L. Brandt, A. Fries and H. Werner, *Angew. Chem. Int. Ed. Eng.*, 1990, 29, 510.

160. A. M. Brownstrein, *CHEMTECH*, 1991, 8, 506.

161. T. F. Rutledge, 'Acetylenic Compounds', Reinhold Book Corp., New York, 1968, p. 207.

162. e.g. H. Wada and Y. Hara, Jpn. Kokai 02 200,648, CA 113; 211818n.

163. e.g. S. Suzuki, H. Inagaki and H. Ueno, Jpn. Kokai, 02 233630, CA 114; 143117b.

164. e.g. S. Suzuki, H. Inagaki and H. Ueno, Eur. Patent, 1988, 373946.

165. C. Botteghi, R. Ganzerla, M. Lenarda and G. Moretti, *J. Mol. Chem.*, 1987, 40, 129.

166. M. Tamura and S. Kumano, *Chem. Econ. Eng. Rev.*, 1980, 12, 32.

167. N. Yoshimura, Y. Tokitoh, M. Matsumoto and M. Tamura, *Nippon Kagaku Kaishi,* 1993, 2, 119, CA 118; 126927f.

168. Mitsubishi Kasel Corp., *CHEMTECH*, 1988, 18, 759.

169. T. K. Ng, R. Hesser, B. Stieglitz, B. S. Grittiths and L. B. Ling, *Biotechnol. Bioeng. Symp.*, 1986, 17, 355, CA 107; 5677p.

170. W. De Thomas and P. D. Taylor, U.S. Patent 1989, 47, 97382.

171. P. S. Williams, Eur, Patent 1989, 341907, CA 112; 197622q.

172. W. Lambrecht, R. Thaetner, K. Ohl, P. Birke, R. Merk, M. Keck, R. Schoedel, H. J .Bisinger and M. Kraft, Ger. (East) DD 274,982, CA 113; 114642t.

173. S. N. Falling and G. W. Phillips, PCT Int. Appl. WO 92 20,667, CA 118;147188f.

174. C. U. Pittman and W. D. Honnick, *J. Org. Chem.*, 1980, 45, 2132.

175. K. Kameda, T. Imanaka and S. Teranishi, *Chem. Lett.* 1983, 1465.

176. M. M. Taqui-Khan, S. B. Halligudi and S. H. R. Abdi, *J. Mol. Catal.*, 1988, 48, 7.

177. R. Deshpande, S. S. Divekar, R. V. Gholop and R. V. Chaudhari, *Ind. Eng. Chem. Res.*, 1991, 30, 1389.

178. R. M. Deshpande, S. S. Divekar, B. M. Bhanage and R. V. Chaudhari, *J. Mol. Catal.*, 1992 ,75 , L19.

179. M. Tamura and N. Yoshimura, *Stud. Surf. Sci. Catal.*, 1989, 44, 307, CA 111; 9206q.

180. A. G. Abatjoglou and D. R. Bryant, *Arab. J. Sci. Eng.*, 1985, 10, 427.

181. K. Maki, T. Kujuta and K. Marumo, Jpn. Kokai, 04 169,579, CA 118; 6622f.

182. P. Narayanan, PhD Thesis, University of St. Andrews, 1991.

183. A. M. Trzeciak and J. J. Ziolkowski, *Rhodium Express*, 1993, 0, 7.

184. D. G. Parker, R. Pearce and D. W. Prest, *J. Chem. Soc., Chem. Commun.*, 1982, 1193.

185. J. M. Brown, A. E. Jerome, G. D. Hughes and P. K. Monaghan, *Aust. J. Chem.*, 1992, 45, 143.

186. W. Leitner, J. M. Brown and H. Brunner, *J. Am. Chem. Soc.*, 1993, 115, 152.

187. B. Capon and C. Zucco , *J. Am. Chem. Soc.*, 1982, 104, 7567.

188. S. H. Bergens and B. Bosnich, *J. Am. Chem. Soc.*, 1991, 113, 958.

189. T. Yohida, D. L. Thorn, T. Okano, S. Otsuka and J. A. Ibers, *J. Am. Chem. Soc.*, 1980, 102, 6451.

190. S. Anderson, A. F. Hill, A. M. Z. Slawin and D. J. William, *J. Chem. Soc., Chem. Commun.*, 1993, 266.

191. L. Jordi, J. M. Moreto, S. Ricart, J. M. Vinas, E. Molins and C. Miravitiles, *J. Organomet. Chem.*, 1993, 444, C28.

192. J. R. Tinder, R. R. Kohl, R. S. Bly and M. M. Hossain, *J. Organomet. Chem.*, 1993, 445,143.

193 Personal communication between D. J. Cole-Hamilton and M. Winter.

194. G. P. Chiusoli and L. Cassar, *Angew Chem.*, 1967, 79, 177.

195. D. Madema, R. van Helden and C. F. Kohll, *Inorg. Chim. Acta*, 1969, 3,255.

196. M. El-Chahawi, U. Prange and H. Richtzenhain, Ger. Patent, 1977, 2606655.

197. M. Foà and L. Cassar, *Gazz. Chim. Ital.*, 1979, 109, 619.

198. J. Kiji, T. Okano, W. Nishiumi and H. Konishi, *Chem. Lett.*, 1988, 957

199. K. Terekhora *et al*, *Zhurival Organicheskoi Khimii*, 1991, 27, 2368.

200. H. R. Gao, Y. Xu, S. J. Liao and D. R. Yu, *Chin. Chem. Lett.*, 1992, 3, 351.

201. C. S. Chin, H. J. Jung and S. Hong, *Bull. Korean Chem. Soc.*, 1992, 13, 391.

202. M. Payne, First Year Report, University of St. Andrews, 1994.

203. W. Weston, First Year Report, University of St. Andrews, 1993.

204. H. Werner, M. Schäfer, O. Nürnberg and J. Wolf, *Chem. Ber.*, 1994, 127, 27.

205. B. Taylor, *Amer. Chem. Soc. Div. Pet. Chem. Prep.*, 1972, 17, B141.

206. R. Fellous, J.-P.Rabine, L. Lizzani-Cuvelier and R. Luft, *Bull. Soc. Chim. Fr.*, 1974, 5, 923.

207. R. Lakhmiri, P. Lhoste and D. Sinou, *Tetrahedron Lett.*, 1989, 30, 4669.

208. A. P. Davis, B. J. Dorgan and E. R. Mageean, *J. Chem. Soc., Chem. Commun.*, 1993, 492.

209. D. D. Perrin and W. L. F. Armarego, 'Purification of Laboratory Chemicals', 3rd ed., Pergamon Press, London, 1988.

210. 'Inorganic Synthesis', Volume XIII, Ed. F. A. Cotton, McGraw-Hill, New York, 1972, p. 90.

211. 'Inorganic Synthesis', Volume XV, Ed. G. W. Parshall, McGraw-Hill, New York, 1974. p. 59.

212. J. Chatt and B. L. Shaw, J. Chem. Soc.(A), 1966, 1437.

213. 'Vogels textbook of practical organic chemistry, 4th ed., Longman, London, 1984, p. 512.