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Isomerisation of ω-hydroxyalkenes under hydroxycarbonylation conditions in palladium catalysed aqueous phase systems

Adriana Ionescu, Markus Ruppel, Ola F. Wendt *

Organic Chemistry, Department of Chemistry, Lund University, P.O. Box 124, S-221 00 Lund, Sweden

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Abstract

The ω-hydroxyolefins 3-buten-1-ol, 3-buten-1-methyl-1-ol and 4-penten-1-ol were subjected to hydroxycarbonylation conditions in water in the presence of $PdCl_2(PhCN)_2$ and 4–8 equiv. of water soluble tris(3-sodiumsulfonatophenyl)phosphine (TPPTS), or *N*-bis(*N*′,*N*′-diethyl-2-aminoethyl)-4-aminomethylphenyl-diphenylphosphine (N3P). Under conditions of high conversion, the olefins primarily undergo isomerisation through a chain walking mechanism with selectivities for aldehyde ranging from 65% to 98%, with the lower values for longer chain alcohols. The lactones formed as the minor product are almost exclusively branched, indicating that in the first step 2,1-insertion is strongly favoured over 1,2-insertion. In the N3P system also linear lactone is produced at lower conversion. Running the reaction in D_2O produces multiple deuterium incorporation in all positions of the carbon chain. A mechanism is discussed.

Keywords: Palladium; Biphasic reactions; Hydroxycarbonylation; Isomerisation; Homogeneous catalysis

1. Introduction

Hydroxycarbonylation of olefins to carboxylic acids (Scheme 1) in aqueous biphasic systems was simultaneously discovered by three research groups [1]. Since then, there has been an extensive study of this reaction, mostly using the water-soluble phosphine tris(3-sodiumsulfonatophenyl)phosphine (TPPTS) as ligand and styrene and styrene derivatives as model substrates [2]. As expected for substrates with moderate to low water solubility [2a], the rate determining step is mass transfer between aqueous and organic layers. One way to avoid this problem and to allow for mechanistic investigations is to use water-soluble olefins, such as 3-buten-1-ol (**1**). However, substrates like **1** have been shown to undergo isomerisation reactions. Stille reported that while simple olefins undergo methoxycarbonylation in the presence of $PdCl_2$, $CuCl_2$ and sodium butyrate to provide succinates, functionalised olefins like 3-butenol gave mixtures of products, due to isomerisation of the double bond [3]. On the other hand, later synthetic and mechanistic studies of palladium catalysed alkoxycarbonylation reactions of 3-butenols and acetylenic alcohols to give lactones, report no signs of isomerisation [4]. Isomerisation of higher olefins (1-hexene, 1-octene, 1-decene, and 4-pentenoic acid) under hydroxycarbonylation conditions has also been reported [1a,5].

Here, we report on the Pd catalysed reactions of ω-hydroxyolefins under hydroxycarbonylation conditions, using two water soluble phosphine ligands: *N*-bis(*N*′, *N*′-diethyl-2-aminoethyl)-4-aminomethylphenyl-diphenylphosphine (N3P) and the bulkier, but electron poorer TPPTS (Chart 1). The main products of these reactions

* Corresponding author. Tel.: +46 46 2228153.
E-mail address: ola.wendt@organic.lu.se (O.F. Wendt).

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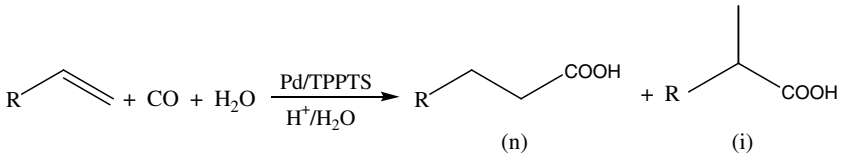


Scheme 1. The hydroxycarbonylation reaction.

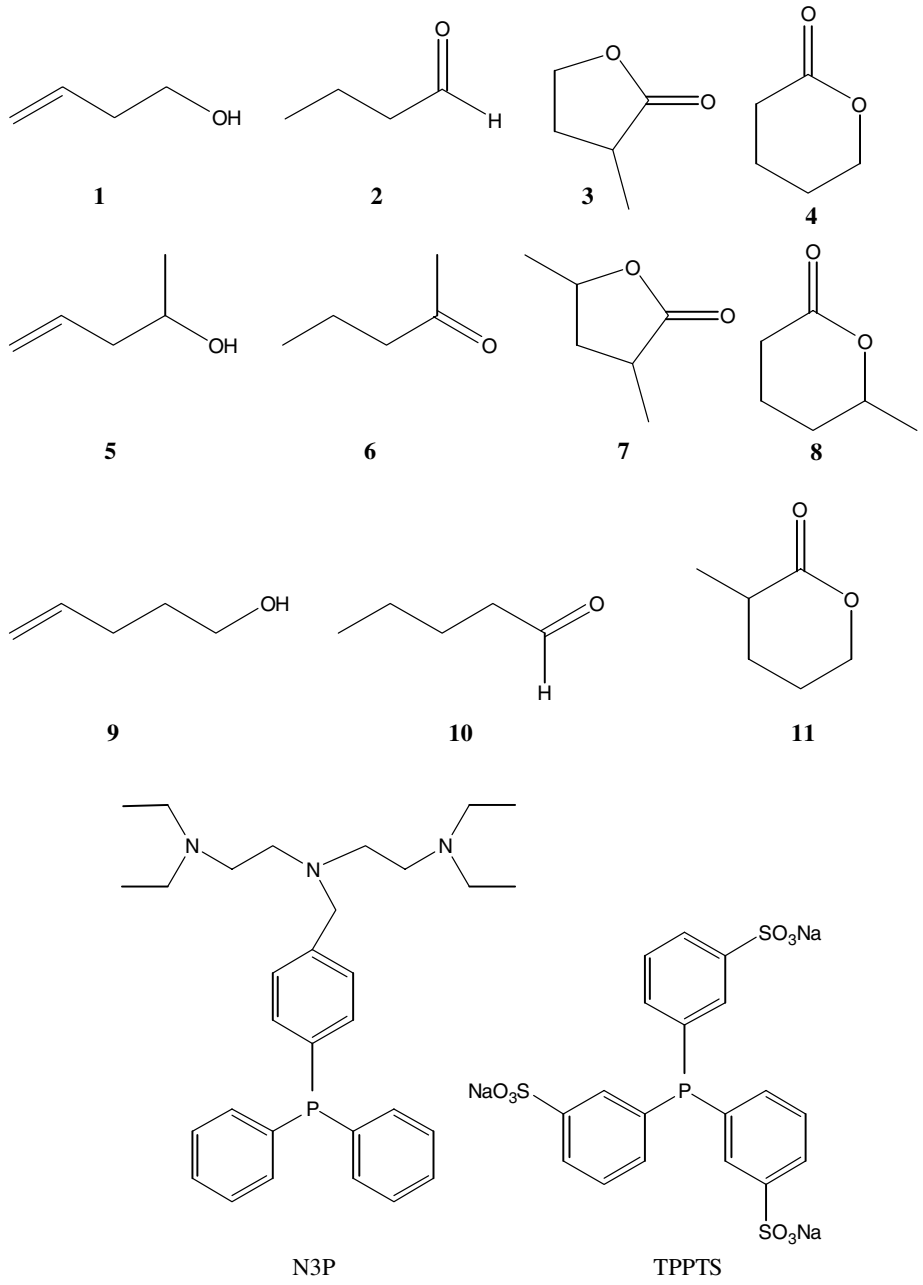


Chart 1.

were not the lactones from the intramolecular alkoxycarbonylation, but the corresponding aldehyde, as a result of an isomerisation reaction. To gain a deeper insight into the mechanism of isomerisation versus hydroxycarbonylation we also report on HP NMR spectroscopy studies of reaction intermediates and a deuterium labelling study.

2. Experimental

2.1. General procedures

All reactions and manipulations were conducted using standard Schlenk techniques. All starting materials were

purchased and used without further purification. All solvents were deoxygenated with a nitrogen or argon purge prior to use. ^{1}H and ^{31}P NMR spectra were recorded at 300 and 121 MHz, respectively, on a VARIAN Unity 300 MHz spectrometer. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, using a BRUKER ARX 500 MHz spectrometer. The high pressure NMR experiments were performed using a sapphire tube assembly [6]. ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR chemical shift are reported in ppm downfield from tetramethylsilane. ^{1}H NMR chemical shifts were referenced to the residual hydrogen signal of the deuterated solvents. In the $^{13}C\{^{1}H\}$ NMR measurements, the signal of CD_2Cl_2 (55.8 ppm) was used as reference. ^{31}P NMR chemical shifts are reported in ppm downfield from an external 85% solution of orthophosphoric acid. Fast atom bombardment (FAB) mass spectroscopic data were obtained on a JOEL SX-102 spectrometer applying 3-nitrobenzyl alcohol as matrix and CsI as calibrant. The hydroxycarbonylations were performed in a 50 ml AUTOCLAVE ENGINEERS HASTALOY™ autoclave equipped with a sampling valve and temperature and stirring speed controllers. Gas chromatographic analyses were carried out on a VARIAN 3300 instrument equipped with a 25 m CP-SIL 19 fused silica capillary column.

2.2. Aqueous phase hydroxycarbonylations

In a typical experiment, $[PdCl_2(PhCN)_2]$ (0.021 mmol) and the specified amount of ligand (P/Pd ratio = 4 or 8) were placed in a flask in the glove box. The flask was charged with 12 ml of water, previously acidified with *p*-toluenesulfonic acid (acid/olefin ratio: 0.7), and the mixture was vigorously stirred until the Pd precursor was completely dissolved. The resulting aqueous solution was placed in the autoclave previously loaded with the substrate (substrate/Pd ratio = 50). The flask, which had contained the catalytic solution, was rinsed with 3 ml of water and the resulting solution was transferred into the autoclave. After five pressurising–depressurising cycles with CO to remove traces of nitrogen and air, the aqueous solution was heated to the selected temperature and then pressurised with CO under vigorous stirring. After the reaction, the autoclave was cooled to room temperature, slowly depressurised, and the reaction mixture was transferred into a Schlenk tube under nitrogen. The hydroxycarbonylation mixture was extracted with ether (6.5 ml) for 10 min. A sample of 3 ml of the ether layer was separated, dried over $MgSO_4$ and analysed by GC and GC–MS.

2.3. Synthesis of butyraldehyde 2,4-dinitrophenylhydrazone (*12a*)

Following the general procedure in 2.2. ($T = 65$ °C, $P_{CO} = 15$ bar) and using 3-buten-1-ol (1.043 mmol, 0.0892 ml) as substrate gave a yellow aqueous product solution, which was extracted with 5 ml and 3 ml of diethyl ether. The combined organic phases were transferred into a freshly prepared solution of 200 mg 2,4-dinitrophenylhydrazine, 2 ml conc. H_2SO_4 (96%), 3 ml H_2O and 8 ml methanol. The resulting orange solution was cooled to 5 °C over night, and this provided thin, shiny, orange needles. They were filtered and then recrystallised from a hot solution of 4 ml methanol and 1 ml H_2O by cooling the solution to −18 °C. Yield: 0.052 g (20%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.02 (t, $^{3}J_{HH}$ 7.41 Hz, 3H, CH_3), 1.66 (t, $^{3}J_{HH}$ 7.41 Hz, 2H, CH_2), 2.41 (dt, $^{3}J_{HH}$ 7.41 Hz, $^{3}J_{HH}$ 5.47 Hz, 2H, CH_2), 7.53 (t, $^{3}J_{HH}$ 5.47 Hz, 1H, C(O)H), 7.92 (d, $^{3}J_{HH}$ 9.59 Hz, 1H, $H6_{arom.}$), 8.29 (dd, $^{3}J_{HH}$ 9.59 Hz, $^{4}J_{HH}$ 2.62 Hz, 1H, $H5_{arom.}$), 9.11 (d, $^{4}J_{HH}$ 2.62 Hz, 1H, $H3_{arom.}$), 11.01 (b, 1H, NH).

^{13}C NMR/DEPT (125 MHz, $CDCl_3$): δ 13.70 (CH_3), 19.74 (CH_2), 34.44 (CH_2), 116.51 ($C^{6}H_{arom.}$), 123.52 ($C^{5}H_{arom.}$), 129.96 ($C^{3}H_{arom.}$), 137.82 ($C^{1}_{arom.}$), 145.16 ($C^{2}_{arom.}$), 151.21 ($C^{4}_{arom.}$), 152.39 (C(O)H). EI-MS: m/z = 252 $[M]^{+}$.

2.4. Synthesis of butyraldehyde-d_3 2,4-dinitrophenylhydrazone (*12b*)

Using the same procedure as in Section 3.3, but applying pure D_2O as the solvent gave shiny, orange needles of **12b**. Yield: 0.044 g (17%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.99–1.09(m), 1.63–1.75(m), 2.35–2.44(m), 7.53 (d, $^{3}J_{HH}$ 3.9 Hz, 1H, C(O)H), 7.93 (d, $^{3}J_{HH}$ 9.89 Hz, 1H, $H6_{arom.}$), 8.30 (dd, $^{3}J_{HH}$ 9.89 Hz, $^{4}J_{HH}$ 2.34 Hz, 1H, $H5_{arom.}$), 9.12 (d, $^{4}J_{HH}$ 2.40 Hz, 1H, $H3_{arom.}$), 11.02 (b, 1H, NH).

^{13}C NMR/DEPT (125 MHz, $CDCl_3$): see Table 3 for the shifts of the alkyl chain, 116.38 ($C^{6}H_{arom.}$), 123.37 ($C^{5}H_{arom.}$), 129.83 ($C^{3}H_{arom.}$), 137.71 ($C^{1}_{arom.}$), 145.04 ($C^{2}_{arom.}$), 151.08($C^{4}_{arom.}$), 152.25 (C(O)H). EI-MS: m/z = 252–256 $[M]^{+}$.

2.5. NMR studies of reaction intermediates

A D_2O solution of $PdCl_2$(6 mM) and TPPTS (P/Pd = 6) was subjected to CO at 1.7 bar for 15 min. Trifluoroacetic acid was added to give a 60% (v/v) solution, which was stirred for 2 h. The yellow solution was subjected to three freeze–pump–thaw cycles to remove dissolved CO and, under argon, 1.5 equiv. of 3-butene-1-ol was added. An NMR sample was taken and subjected to 1.7 bar CO for 1.5 h and then 50 bar CO for 3 h. The solution was afterwards concentrated under vacuum and 1,4-dioxane was added, furnishing a yellow precipitate, which was analysed by NMR and IR. Half of the precipitate was hydrolysed at 80 °C for 1 h under argon and the other half was hydrolysed under 50 bar CO at 80 °C for 1 h. During the whole procedure, NMR samples were taken at regular intervals. The products of hydrolysis were identified by GC.

3. Results and discussion

3.1. The hydroxycarbonylation of ω-hydroxyalkenes

The aqueous phase hydroxycarbonylation of **1** was carried out in the presence of [$PdCl_2$ ($PhCN)_2$] and the phosphine ligand. The reactions were run under various temperatures and carbon monoxide pressures, in the presence of *p*-toluenesulfonic acid. Beside 3-buten-1-ol (**1**), two heavier hydroxy-substituted olefins, 3-buten-1-methyl-1-ol (**5**) and 4-penten-1-ol (**9**) were used as substrates (entries 11 and 12, Table 1). The products are known compounds and were identified by GC–MS. All results are summarised in Table 1 and all structures are given in Chart 1.

Under the present conditions, the stability of the catalyst system is dependent on the P/Pd ratio. The formation of metallic palladium was observed in experiments operating at a TPPTS/Pd molar ratio of 4 and this decomposition of the catalyst probably explains the relatively low conversion in entries 1–5 (see Table 1) compared to entries 6–12 in which a TPPTS/Pd molar ratio of 8 was applied. In these latter experiments, no formation of metallic palladium metal was observed and the conversion of the substrate was quantitative. N3P provided better stabilisation of the catalyst and at a ratio of 4, palladium black was observed only at high temperature (95 °C). At a ratio of 8, no palladium black was observed, but the conversion dropped dramatically to 11% at low temperature and low pressure (run 21). Only at 95 °C and a P/Pd ratio of 8 the conversion was quantitative. Thus, a high P/Pd ratio not only provides stabilisation but also decreases the conversion due to coordinative saturation.

Also the product distribution is affected by the P/Pd ratio and the CO pressure. At a TPPTS/Pd ratio of 8 the selectivity for the aldehyde was always higher than 90%. However, at a TPPTS/Pd ratio of 4 the **2**/**3** ratio was considerably lower, in the range of ca. 1–10:1. It cannot be excluded that there is a contribution to the catalysis from the Pd black formed in entries 1–5. A similar aldehyde/lactone ratio is observed in the N3P experiments where palladium black is formed. Optimal isomerisation requires a TPPTS/Pd = 8 (run 7) but a N3P/Pd = 4 (run 13). For N3P/Pd = 8, the aldehyde/lactones ratio is under 10 at 65 °C (runs 21, 22) but much higher at 95 °C (runs 19, 20), showing that the isomerisation is favoured at higher temperatures with this ligand whereas the opposite holds true for the case where TPPTS/Pd = 8 (vide infra).

Moreover, at a given P/Pd ratio, there was also a variation in the product distribution as the partial pressure of CO was varied, but this variation is not continuous; instead the aldehyde/lactone ratio goes through a minimum at an intermediate CO pressure of 50 bar.

With TPPTS only the 5-ring 3-methyltetrahydro-2-furanone (**3**) is formed, but with N3P both **3** and the 6-ring tetrahydro-2H-pyran-2-one (**4**) are formed. Their distribution

Table 1
Results of the aqueous phase hydrocarboxylation of hydroxyalkenes under various conditions

Run	Substrate (ligand)	P/Pd	*T* (°C)	P_{CO} (bar)	Conversion (%)	Selectivity (%)		Aldehyde/lactone ratio and (*n*/*i*)
						Aldehyde	Lactone	
1[a,c]	**1** (TPPTS)	4	65	0	8.2	100.0 (**2**)	–	–
2[c]	**1** (TPPTS)	4	65	15	63.5	89.3 (**2**)	10.7 (**3**)	8.3
3[c]	**1** (TPPTS)	4	65	50	48.1	82.2 (**2**)	17.8 (**3**)	4.6
4[c]	**1** (TPPTS)	4	65	75	68.0	90.7 (**2**)	9.3 (**3**)	9.7
5[c]	**1** (TPPTS)	4	75	15	62.1	41.5 (**2**)	58.5 (**3**)	0.7
6	**1** (TPPTS)	8	75	15	100.0	90.9 (**2**)	9.1 (**3**)	10
7	**1** (TPPTS)	8	65	15	100.0	98.2 (**2**)	1.8 (**3**)	54.6
8[b]	**1** (TPPTS)	8	65	15	100.0	92.5 (**2**)	7.5 (**3**)	12.3
9	**1** (TPPTS)	8	65	50	100.0	96.0 (**2**)	4.0 (**3**)	24.0
10	**1** (TPPTS)	8	65	75	100.0	97.3 (**2**)	2.7 (**3**)	36.0
11	**5** (TPPTS)	8	65	15	100.0	68.0 (**6**)	16.0 (**7**); 16.0 (**8**)	2.1; (1)
12	**9** (TPPTS)	8	65	15	100.0	65.0 (**10**)	35 (**11**)	1.9
13	**1** (N3P)	4	65	15	54.1	99.0 (**2**)	1.0 (**4**)	99.0
14[b]	**1** (N3P)	4	65	15	32.7	78.5 (**2**)	3.4 (**3**); 18.1 (**4**)	3.6; (5.4)
15	**1** (N3P)	4	65	50	83.5	82.0 (**2**)	14.0 (**3**); 4.0 (**4**)	4.6; (0.3)
16	**1** (N3P)	4	65	75	60.6	97.4 (**2**)	2.6 (**3**)	37.5
17[c]	**1** (N3P)	4	95	15	62.0	83.6 (**2**)	8.6 (**3**); 7.8 (**4**)	5.1; (0.9)
18[c]	**1** (N3P)	4	95	50	69.6	85.1 (**2**)	14.9 (**3**)	5.7
19	**1** (N3P)	8	95	50	100.0	96.0 (**2**)	4.0 (**3**)	24
20	**1** (N3P)	8	95	15	100.0	98.0 (**2**)	2.0 (**3**)	49
21	**1** (N3P)	8	65	15	11.1	67.4 (**2**)	28.3 (**3**); 4.3 (**4**)	2.1; (0.1)
22	**1** (N3P)	8	65	50	68.8	66.7 (**2**)	33.3 (**3**)	2

General reaction conditions. Precursor: $PdCl_2(PhCN)_2$ (1,4 mM); olefin/Pd ratio: 50; acid/olefin ratio: 0.7; acid: *p*-toluenesulfonic acid; solvent: H_2O; total volume: 15 ml; 3 h.

[a] This reaction was carried out under an argon atmosphere as a blank reaction.

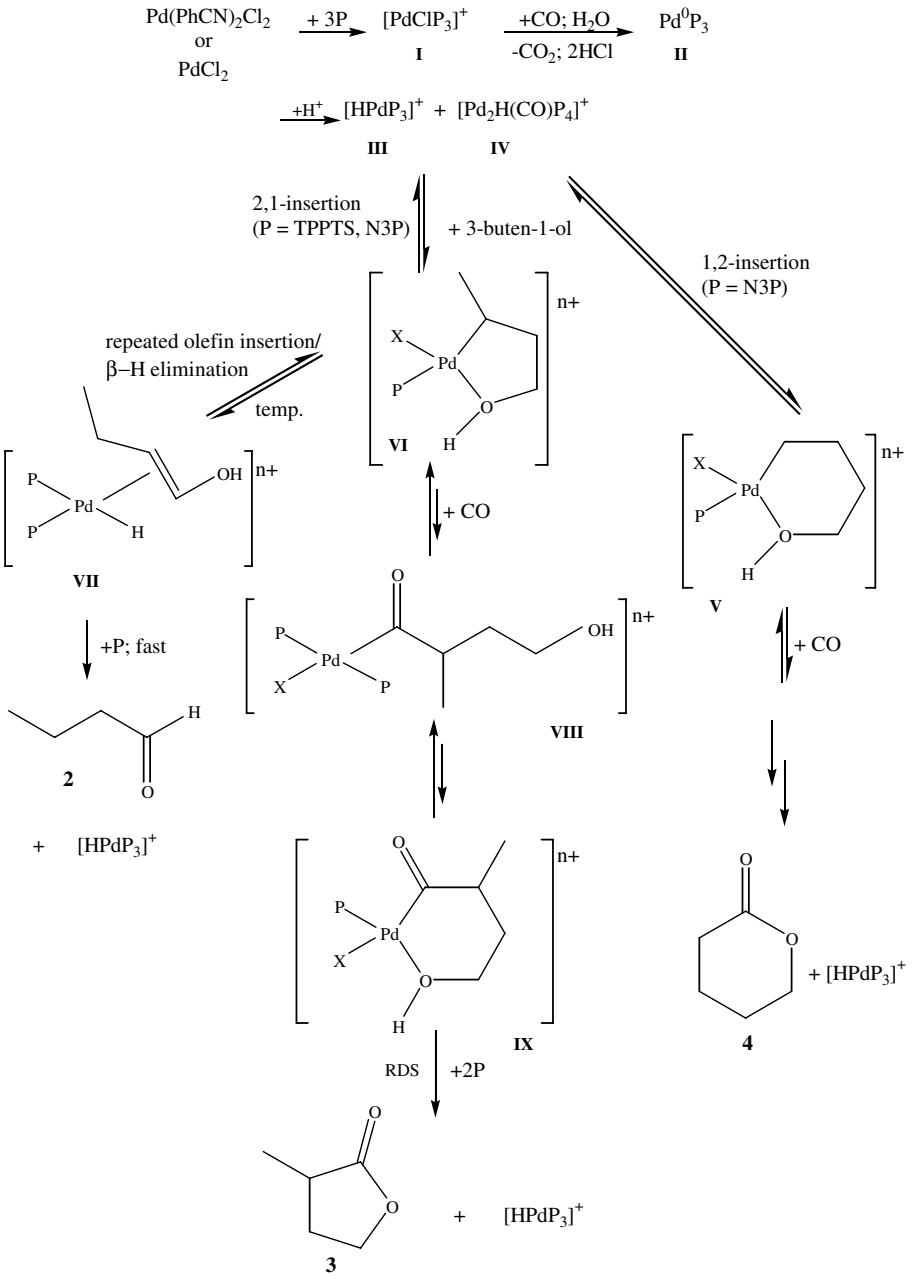
[b] D_2O as solvent; the given values are averages over 3 independent experiments under described conditions.

[c] Formation of metallic palladium.

varies from pure **4** at low P/Pd ratio, temperature and pressure (run 13) to pure **3** at very high pressure (run 16), or when at least two of the above three reaction conditions are increased (runs 18, 19, 20, 22). The isomerisation is the main reaction also for substrates **5** and **9**. However, the extent of isomerisation is lower than for **1**, for which 98% aldehyde was formed under identical conditions (run 7). Instead, 32–35% of the reacting alkenes end up as the lactones **7** and **8** in the case of substrate **5** (run 11), or the lactone **11** in the case of substrate **9** (run 12). The relative rate of isomerisation is normally lower for higher olefins and the methyl group in olefin **5** can account for a degree of steric hindrance, hampering the formation of **6**.

3.2. Mechanistic considerations

The proposed mechanism for the hydroxycarbonylation of 3-buten-1-ol is shown in Scheme 2. As outlined by Sheldon, the complex $[PdCl(TPPTS)_3]^+$ of type **I** is obtained by dissolving $PdCl_2$ or the bis-benzonitrile complex in an aqueous TPPTS solution. We confirmed the structure of **I** by ^{31}P NMR analysis, showing a triplet at 33.9 ppm and a doublet at 30.7 ppm [7a]. This solution was subjected to 1.7 bar CO providing the zerovalent complex $Pd(TPPTS)_3$ **II**, which exhibited a broad ^{31}P NMR resonance at 22.9 ppm [7]. When the solution was acidified, three new, rather broad signals appeared under 1.7 bar CO, at



Scheme 2. The proposed mechanism of hydroxycarbonylation of 3-buten-1-ol (P = TPPTS or N3P; X = Cl^- ($n = 0$); X = CO, D_2O ($n = 1$)).

27.5 ppm, 21.6 ppm and 20.5 ppm. Two of them, at 27.5 ppm and 20.5 ppm correspond to the unresolved doublet and triplet of the Pd-hydride complex $[PdH(TPPTS)_3]^+$ **III** as reported by Sheldon [8]. We also observed this monomeric hydride in ^1H NMR spectroscopy, showing a double triplet at −7.9 ppm with $^2J_{Ptrans-H} = 175$ Hz and $^2J_{Pcis-H} = 15$ Hz. The third signal in the ^{31}P NMR spectrum at 21.6 ppm, can be attributed to the dimeric hydride-bridged complex $[Pd_2(\mu\text{-}H)(\mu\text{-}CO)(TPPTS)_4]^+$ **IV**. This complex was not observed earlier under 1 bar CO [8], but by increasing the carbon monoxide pressure it was easily formed. The dimeric hydride gives a pentet at −7.4 ppm in the ^1H NMR spectrum with $^2J_{P-H} = 40$ Hz, due to coupling to four equivalent phosphorous atoms. We obtained further confirmation by a high pressure ^{13}C NMR spectrum at 50 bar ^{13}CO, where the dimer gives a double pentet at 213.6 ppm with $^2J_{C-P} = 30$ Hz and $^2J_{C-H} = 10$ Hz. The fast ligand exchange, which accounts for the equivalence of all four phosphorous atoms, could not be frozen even at low temperatures, as observed earlier for corresponding diphosphine complexes [9].

Using N3P, we have earlier isolated two reaction intermediates of the type **V** and **VIII** [5b], the alkyl complex being the most stable one, due to its chelated form. Attempts to obtain similar complexes in the TPPTS system were therefore undertaken. Thus, the solution containing the hydride-complexes of type **III** and **IV** (with TPPTS) was carefully degassed and after the addition of the olefin under argon, a new signal at 19.9 ppm appeared at the expense of the hydride signals. This signal can be assigned to an alkyl complex since it is formed in the absence of carbon monoxide. The peak remained unchanged also when the solution was left under 50 bar CO for several hours. The same peak was obtained when the addition of the olefin was made under CO atmosphere. For characterisation, the solution was concentrated and diluted with 1,4-dioxane to obtain a precipitate which was first analyzed by ^{31}P NMR spectroscopy in D_2O. This proved to be a mixture of TPPTS oxide, complex **II** and the alkyl complex at 19.9 ppm. IR analysis of the precipitate revealed, beside the stretching frequencies of complex **II** [10], several bands of stretching vibration of saturated CH groups between 2968 and 2858 cm^{-1}, the band of deformational vibration of saturated CH groups (1465 cm^{-1}) and an intense band in the region of low frequencies, which can be assigned to the stretching vibration of a Pd–O bond (537 cm^{-1}) [11]. A ^{13}C NMR spectrum showed no evidence for the presence of any Pd-acyl species. It seems that the α-insertion and formation of a Pd-acyl complex is hampered also at high carbon monoxide pressures, indicating that the equilibrium for CO migratory insertion lies to the left. The IR spectrum and the high stability of the alkyl complex even under CO pressure are indications of a cyclic alkyl complex. This could either be the result of a 1,2- or 2,1-insertion, complexes **V** or **VI**. Based on the exclusive formation of lactone **3** and the deuterium labelling experiments (vide infra), we propose that only 2,1-insertion takes place with TPPTS as a ligand and that the signal at 19.9 ppm is assigned to a complex of type **VI**.

It is generally accepted that monodentate phosphines give more branched acids ($n/i < 1$) [12] and this is also the case for the TPPTS system [1]. The formation of the branched lactones **3**, **7** and **11** through 2,1-insertion may reflect this general preference, which is then the result of the selectivity of the first insertion step. At low to moderate CO pressures the chelate binding obviously precludes the *cis* coordination of CO, which is a prerequisite for CO insertion into the Pd-C bond. We cannot fully exclude that complex **V** is also formed (in fast equilibrium with **VI**, since we see only one ^{31}P NMR signal), but it seems unreasonable that it should be less reactive than **VI** and if it forms we would expect to see also the six-membered lactone product. No hydroxycarbonylation products were formed by hydrolysis (80 °C, no CO present) of the precipitate containing complex **VI**, only butanal. Upon heating under hydroxycarbonylation conditions (80 °C, 50 bar CO), complex **VI** gives merely butanal and traces of lactone **3**. As in the catalysis experiments, the 6-ring δ-valerolactone (**4**) formed by hydroxycarbonylation of the linear isomer **V** is not observed, again corroborating that the alkyl complex be formulated as **VI**. Similarly, substrate **9** exclusively gives the six-membered lactone **11**, originating from an initial 2,1-insertion. The situation is different for substrate **5**, where the methyl group α to the hydroxyl obviously destabilises the 2,1-insertion product to give equal amounts of lactones **7** and **8**.

For N3P the situation is different. Here the 1,2-insertion is a viable alternative giving both 5- and 6-ring lactones **3** and **4**. The latter is favoured only at low P/Pd ratio, low temperature and low pressure (runs 13, 14 in Table 1). It can be noted that conditions giving high conversion also give exclusive formation of **3**. Contrary to expectations based on steric requirements it therefore seems that the 1,2-insertion is favoured by coordinative unsaturation and the use of a less bulky phosphine. It has been observed earlier in the context of hydroformylation that the use of bulky phosphines give more branched product, and this was explained by bulkier phosphines giving a lower phosphine coordination number [13].

The last step in the lactone formation is a nucleophilic attack by the hydroxyl group at the carbonyl carbon atom. Obviously only at high CO pressures can this process compete with chain walking to give butanal; the formation of lactone increases as the partial pressure of CO increases as seen when comparing runs 2 and 3, 7 and 9 or 13 and 15. Surprisingly, lactone formation does not continue to increase as the CO pressure is further increased (runs 4, 10, 16). A high CO concentration should promote the acylation reaction and inhibit the chain-walking reaction, by coordinating to the open coordination site. However, in order to obtain the lactone, the acyl complex has to be quenched by an intramolecular nucleophilic attack of the hydroxyl group at the carbonyl carbon atom, which presumably is an irreversible, rate determining step. There

are two different possible mechanisms for this intramolecular attack – it can occur with or without coordination of the hydroxyl group to the metal centre (from intermediate **VIII**). The observation that the formation of the lactone increases as the CO-pressure increases from 15 to 50 bar but then decreases as the CO pressure is increased even further to 75 bar can possibly be explained by an initial coordination of the alkoxy group under formation of the cyclic derivative **IX** [14]. The hydroxyl group which is a relatively weak ligand can probably not effectively compete with CO as the concentration of CO in the reaction solution exceeds a certain level. Lactone formation as a function of the partial pressure of CO therefore goes through a maximum at an intermediate CO pressure.

At higher temperature, however, the situation changes in the TPPTS system and the esterification process, which is rather slow at low temperature, becomes relatively fast at 75 °C (runs 5 and 6) and the yield of lactone formed thus becomes larger than that obtained at 65 °C. At a first glance, one should expect the contrary, an increase of aldehyde/lactone ratio, due to a faster β-H elimination at higher temperature, like in the N3P system. However, both rate determining steps are first-order intra-molecular processes and in view of this it is not surprising that a change of ancillary ligand can shift the selectivity.

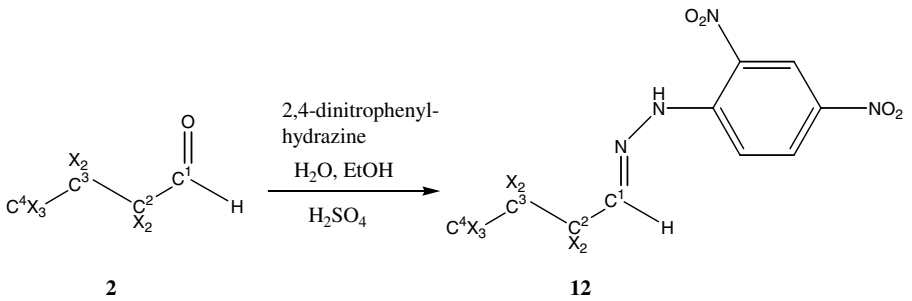
3.3. Deuterium labelling experiments

In order to gain further information about the mechanism behind the catalytic transformation of 3-buten-1-ol to butanal some deuterium labelling experiments, using D_2O as the solvent, were carried out. The conditions chosen were the same as those previously shown to give a high yield of butanal (entries 7 and 13, Table 1). In general, compared to the experiments carried out in H_2O, the corresponding reactions in D_2O exhibited lower butanal/lactone ratios (entries 7, 8 and 13, 14 in Table 1). This difference reflects the kinetic isotope effect and implies that more C–H bond breaking is involved in the reaction to give butanal [15].

A mass spectroscopic analysis of the deuterium labelled products indicated the presence of one to five deuterium atoms in the deuterated butanal but the position of these D-atoms in the carbon chain could not be established by the MS analysis. Instead, the aldehyde was converted to its corresponding 2,4-dinitrophenylhydrazone (**12b**), which was characterised by MS and NMR (^1H, ^{13}C, DEPT) analysis. Comparison between the data obtained for **12b** and data for the unlabeled hydrazone (**12a**) showed the presence of several deuterium atoms, distributed on different carbons of the carbon chain (Scheme 3).

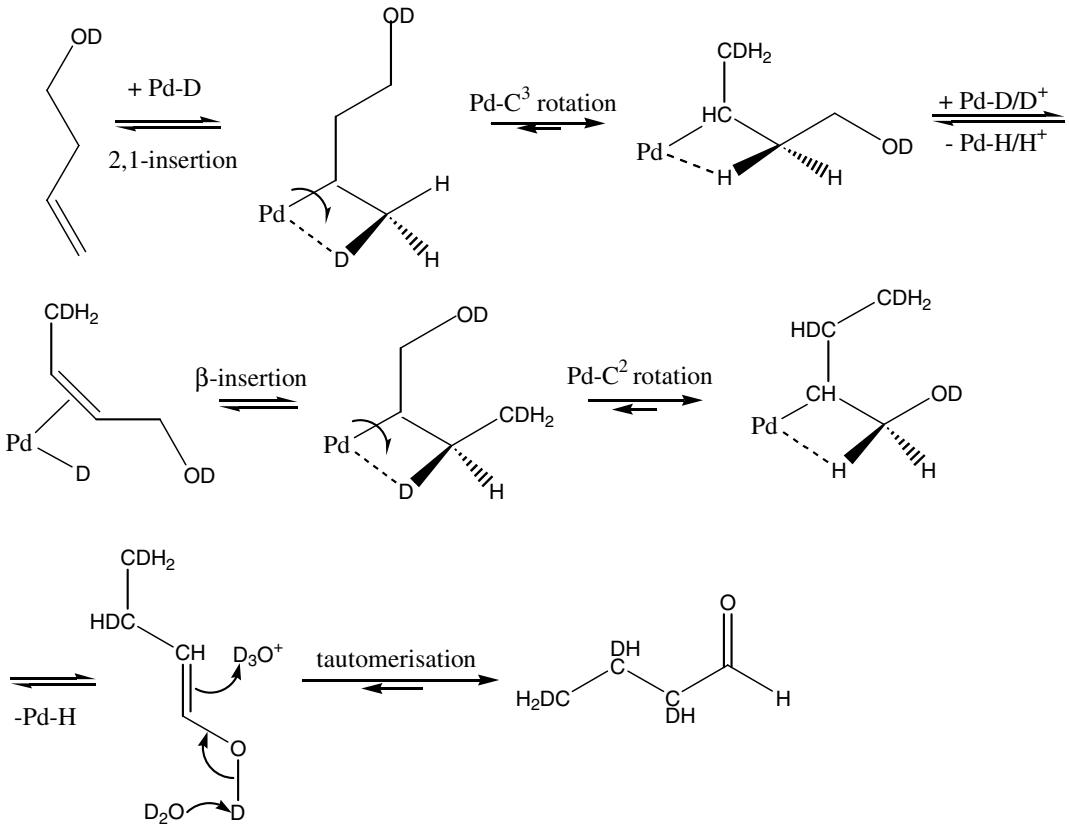
The deuterium isotope effect and the labelling experiments show that butanal is formed via alternating olefin insertion and β-hydrogen elimination reactions. Deuterium is incorporated upon olefin insertion into a Pd–D bond and if bond rotation takes place prior to β-hydrogen elimination, the olefin is left with an incorporated D-atom (Scheme 4). If there is a D^+/H^+ exchange on the palladium hydride, repeated olefin insertion/β-hydrogen elimination can result in the incorporation of multiple D-atoms per molecule [16]; this is also what we observe. The presence of a palladium hydride species explains why we see such a high degree of isomerisation. Earlier studies, where there is no or little isomerisation, have postulated non-hydridic pathways [17]. Palladium hydride species are known to be effective catalysts for olefin isomerisation [18] and late metal catalysts often exhibit facile metal migration along the chain (the so-called "chain walking mechanism") [19].

Quantitative EI-MS spectrum of the deuterium labelled hydrazones (compared with the MS of the unlabelled one) shows up to four deuterium atoms per molecule of hydrazone in the TPPTS system and up to five deuterium atoms in the N3P system. The ^2H NMR and ^1H NMR spectra show the deuterium content in different positions (Table 2). The results were obtained from quantitative ^2H NMR spectra by integration of the signals of the groups with deuterium incorporation and comparison with ^1H NMR spectra. ^{13}C NMR DEPT (135°) spectra show complex patterns due to various amounts of deuterium in positions C^2, C^3 and C^4. However, six predominant species with zero to two deuterons can be distinguished in the TPPTS system (see Table 3 and Fig. 1). At least seven species with zero to three deuterons are identifiable in the N3P system (see Table 3 and Fig. 2). Groups with two protons come up as anti-phase singlets ($–CH_2–$) or triplets ($CH_2D–$). Groups with three and one proton come up as in-phase singlets ($CH_3–$) and triplets (–CHD–), respective. Any CD_2 groups



2 12

Scheme 3. The formation of butyr-hydrazone (X = H or D).



Scheme 4. The deuterium incorporation into 3-buten-1-ol via the chain walking mechanism and enol tautomerisation (some hydrogens are left out for the sake of simplicity).

Table 2
Deuterium content in the labeled hydrazone **12b**

Ligand	Deuterium content via MS analysis (%)							Deuterium incorporation at each carbon via ^{2}H and ^{1}H NMR			
	0D	1D	2D	3D	4D	5D	NDM[b]	C^4	C^3	C^2	NDM[b]
TPPTS	7.62	39.19 (0.79)[a]	36.39 (0.1)[a]	14.93	1.87	0	1.64	0.68	0.36	0.50	1.54
N3P	0.48	5.00 (0.05)[a]	23.73 (0.01)[a]	61.26	8.43	1.1	2.75	0.60	0.42	1.60	2.62

[a] The numbers in brackets show the natural occurrence (%) of the respective deuterated species.
[b] Average number of deuterium atoms per molecule.

Table 3
Carbon shifts (ppm) in ^{13}C NMR DEPT for different species of the deuterated hydrazone **12b** (only the aldehyde chain)

Aldehyde chain	C^4		C^3		C^2	
	TPPTS	N3P	TPPTS	N3P	TPPTS	N3P
CH_3–CH_2–CH_2–CH=	13.57	13.72	19.59	19.53	34.31	34.34
CH_3–CH_2–CHD–CH=	13.54	13.61	19.44	19.38	33.94	33.95
CH_3–CHD–CH_2–CH=	13.46	13.46	19.24	19.19	34.22	34.24
CH_3–CHD–CHD–CH=	13.43	13.43	19.16	19.11	33.86	33.89
CH_2D–CH_2–CH_2–CH=	13.28	13.31	19.51	19.46	34.28	34.31
CH_2D–CH_2–CHD–CH=	13.25		19.36		33.92	
CH_2D–CH_2–CD_2–CH=		13.28		18.95		33.59
CH_2D–CHD–CD_2–CH=		13.25		18.68		33.53
$^1J_{CD}$ (Hz)	19.2		19.6		19.6	

disappear. It is hard to identify CD_2 signals in the ^{13}C spectrum, because they are in a lower quantity and appear as septets, therefore could being lost in the noise.

The higher deuterium incorporation at C^4 compared to C^3 in both ligands systems corroborates the earlier conclusion that 2,1- insertion is favoured over 1,2-insertion. It can

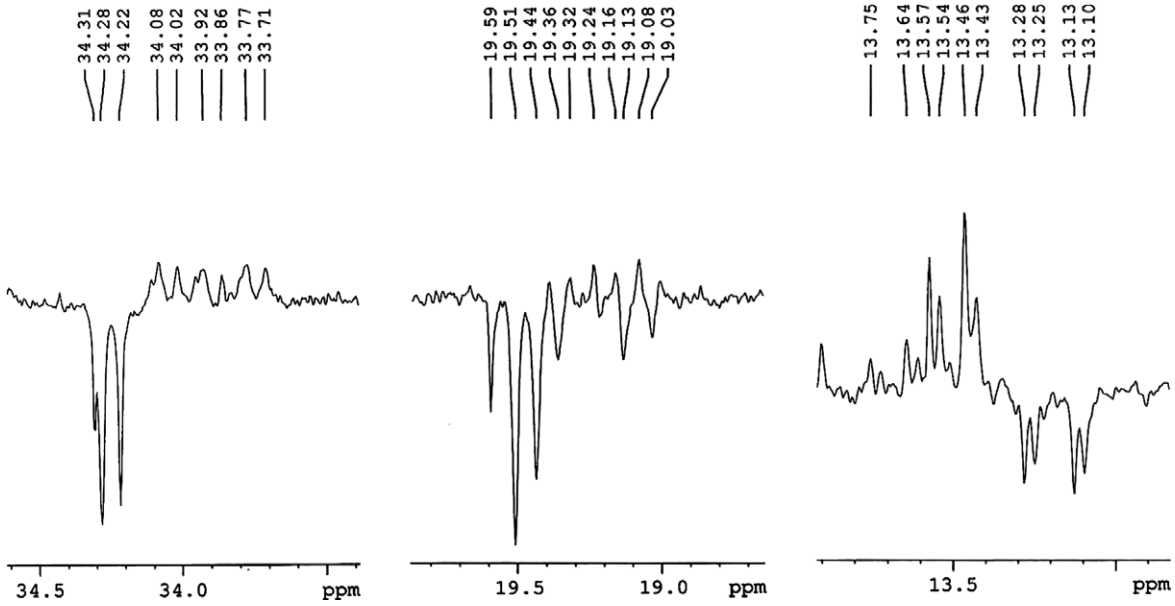


Fig. 1. ^{13}C NMR DEPT (135°) spectrum of the deuterium labelled hydrazone (TPPTS as ligand).

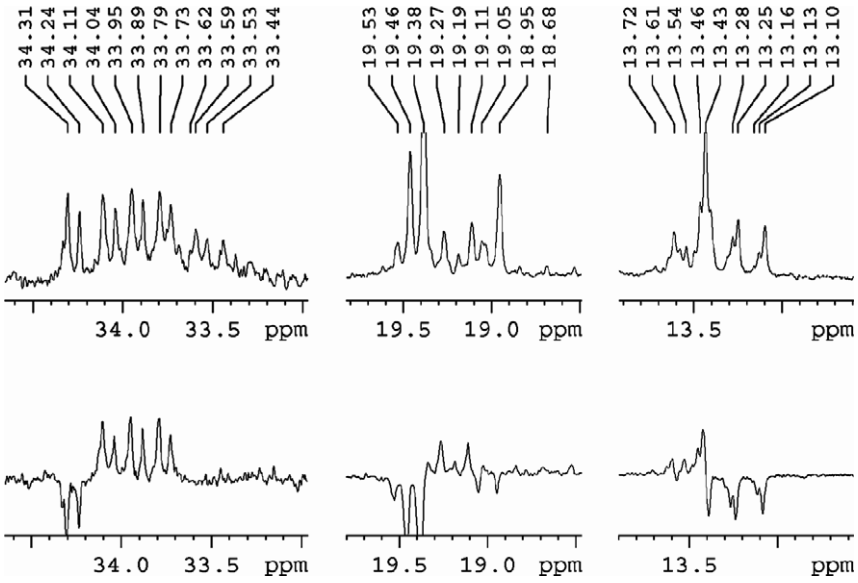


Fig. 2. ^{13}C NMR DEPT (135°) spectrum of the deuterium labelled hydrazone (N3P as ligand).

be noted that for the N3P system there is a less pronounced preference for deuterium incorporation in the 4-position and here we also see formation of the linear 6-ring lactone. Chain walking occurs along the carbon chain and in those cases where Pd–C rotation and H^+/D^+ exchange take place, deuterium can be incorporated in all positions. It is clear that bond rotation is often slower than elimination/insertion resulting in an average of 1.5 (TPPTS) or 2.6 (N3P) deuterium atoms/molecule. This is in line with measured reaction barriers [20]. The very high deuterium incorporation on C^2 in the N3P system is an indication that a different mechanism is operating. We suggest that in the N3P case with higher substitution rates, the enol tautomer is easily displaced from the metal centre and the tautomerisation is not metal catalysed. A classical acid catalysed tautomerisation reaction as indicated in Scheme 4 would lead to a high D-incorporation in the 2-position. In the TPPTS system the tautomerisation probably then takes place through metal catalysis, as proposed earlier for the Wacker chemistry [21].

4. Conclusions

In conclusion, ω-hydroxyolefins primarily undergo isomerisation through chain walking under hydroxycarbonylation conditions. For the bulky TPPTS system the lactones formed are almost exclusively branched, indicating that in the first step 2,1-insertion is strongly favoured over 1,2-insertion. In the N3P system this preference is less pronounced. The rate determining step in lactone formation is

probably an intramolecular attack by a chelated alkoxy function on the carbonyl. Multiple deuterium incorporation in D_2O points to Pd–H/Pd–D exchange being on the same time scale as chain walking.

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