Rhodium-catalyzed hydroformylation of vinylidenic olefins: the different behaviors of the isomeric alkyl–metal intermediates as the origin of the β-regioselectivity

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Abstract

The β-regioselective hydroformylation of the vinylidenic olefins 2-phenylpropene (**1a**), 2-methylpropene (**1b**) and 2,3,3-trimethylbutene (**1c**) was investigated via deuterioformylation experiments [100°C, 100 atm, $Rh_4(CO)_{12}$] carried out at partial substrate conversion. The crude reaction mixtures were directly submitted to ^2H NMR analyses. The results obtained allowed to conclude that whereas the primary rhodium–alkyl intermediate undergoes migratory insertion on CO, giving the corresponding linear aldehyde, the tertiary rhodium–alkyl intermediate, when it does form (i.e., in the case of **1a** and **1b** but not in the case of **1c**), undergoes β-hydride elimination exclusively, accounting for the almost complete β-regioselectivity. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

It is known that the rhodium-catalyzed hydroformylation of phenyl or alkyl substituted vinylidenic olefins **1** gives the corresponding normal aldehydes **2** with almost complete chemo- and β-regioselectivity [1–3] (Scheme 1).

Considering that vinylidenic olefins are useful precursors of pharmaceuticals [4,5], the ra-tionalization of the observed β-regioselectivity constitutes a wanted goal in terms of synthetic utility as well as mechanistic aspects.

According to the generally accepted mechanism of the rhodium-catalyzed hydroformylation, this remarkable β-regioselectivity can be rationalized on the basis of two different hypotheses (Scheme 2): (a) only the primary alkyl–rhodium intermediate **p**, precursor of the corresponding acyl and hence of the β-aldehyde, is formed (Scheme 2a); (b) both the primary **p** and the tertiary **t** alkyls are obtained (Scheme 2a and b) but only **p** is able to give the

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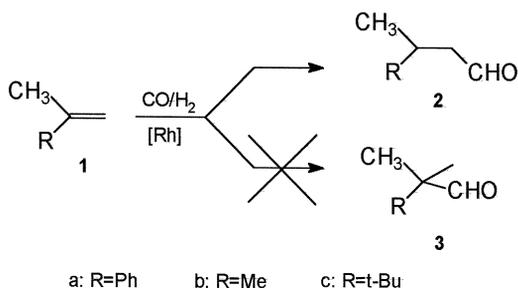
Scheme 1.

corresponding acyl and hence the normal aldehyde **2**, the alkyl **t** undergoing complete β-hydride elimination (Scheme 2b).

In the case of a completely aromatic vinylidenic olefin, i.e., 1,1-diphenylethene, a preliminary investigation [3], carried out by deuterioformylation experiments at 100°C and partial substrate conversion, showed that both the primary and the tertiary alkyls were formed but whereas the former was converted into the corresponding linear aldehyde, the latter gave β-hydride elimination exclusively.

The formation, under hydroformylation conditions, of a tertiary alkyl–metal complex is quite interesting because very few tertiary alkyl–metal compounds have been described until now; some of them contain a *tert*-butyl group linked to the metal [6–8], some other are believed to be formed by isomerization of the primary alkyl-isomer via reversible hydrogen 2–3 migration [9,10].

In this frame we decided to investigate the origin of the β-regioselectivity in the rhodium-catalyzed hydroformylation of different vinylidenic olefins, namely 2-phenylpropene (**1a**), 2-methylpropene (**1b**), 2,3,3-trimethylbutene (**1c**) (Scheme 1), in order to establish if the formation of a tertiary alkyl–metal intermediate is a general trend for these substrates or if it depends on the nature of the groups bound to the vinylidenic carbon atom. To this end rhodium-catalyzed hydro- and deuterioformylation experiments at partial and complete substrate conversion were carried out and the crude reaction mixture directly analyzed via ^{2}H NMR checking the presence of deuterium atom in the unconverted substrates. This approach has been successfully employed by us [11–15] and successively by some other authors [16–18] in order to obtain direct information on the nature and fate of the alkyl–metal intermediates involved in the vinyl substrates hydroformylation.

2. Results and discussion

2.1. Hydroformylation experiments

The hydroformylation of the olefins **1a–c** was carried out in benzene at 100°C, constant total gas pressure of 100 atm ($CO/H_2 = 1/1$) and employing $Rh_4(CO)_{12}$ as the catalyst precursor. The substrate conversion and the composition of the reaction mixtures (Table 1) were
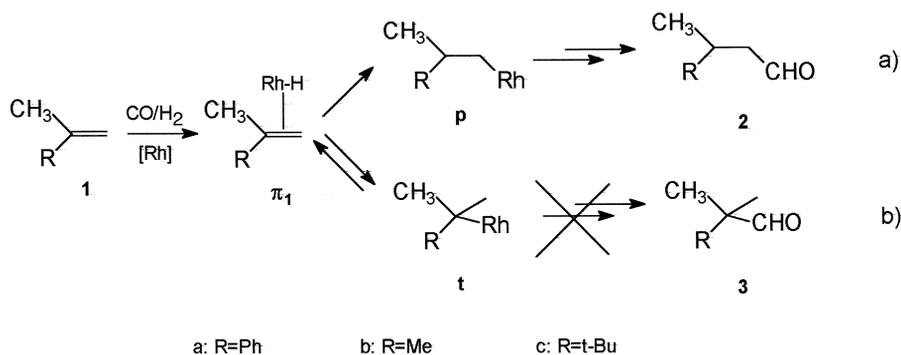
Scheme 2.

Table 1
Hydroformylation of the vinylidenic olefins $RC(CH_3)=CH_2$ **1a–c** at complete substrate conversion[a] with $Rh_4(CO)_{12}$ as catalytic precursor

Substrate	R	Rh/sub	Reaction time (h)	Hydroformylation yield (%)	2/3[c]
1a	Ph	1/100	3	92[b]	>99/1
1b	Me	1/1000	1	100	~100/0
1c	t-Bu	1/1000	1.5	100	~100/0

[a] Determined via GLC by using the following internal standards: o-xylene (in the case of **1a**) and toluene (in the case of **1b** and **1c**), ±1% accuracy; reaction conditions: 2.78 mmol of vinylidenic olefin, 5 ml of benzene; autoclave volume 25 ml; 100 atm total pressure, CO/H_2 (1:1).
[b] A 8% of hydrogenation product was also detected.
[c] **2**: $RCH(CH_3)CH_2CHO$; **3**: $RC(CH_3)_2CHO$.

evaluated by GC analysis, using appropriate internal standards. All the experiments were carried out both at partial and complete conversion of the substrate. The reaction time for a complete conversion was higher for the olefin **1a**, containing a phenyl group, with respect to that observed in the case of the completely aliphatic olefins **1b–c**. The chemoselectivity into aldehydes was very high in all the cases (> 92%). The regioselectivity was greater than 99% in favor of the linear aldehyde for **1b** and **1c** while traces of branched aldehyde were observed only in the case of **1a** (Table 1).

2.2. Deuterioformylation experiments

The deuterioformylation runs were carried out under the same experimental conditions adopted for the hydroformylation, except that a CO/D_2 (1:1) gas mixture was used. Deuterioformylation and hydroformylation experiments, carried out under identical conditions of temperature and pressure, give the same chemo- and regioselectivity. All the deuterioformylation experiments were interrupted at partial substrate conversion (≤ 30%) (Tables 2 and 3) and the crude reaction mixtures were directly examined by ^2H NMR analysis. ^2H NMR spectra of the crude deuterioformylation mixture arising from **1a**, **1b** and **1c** are shown in Fig. 1.
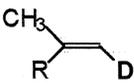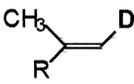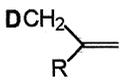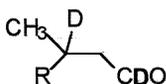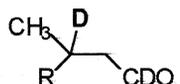
The chemical shifts of the deuterium atoms present on the unconverted olefins and on the aldehydes as well as the relative intensities of the olefinic species are reported in Table 2. The number of moles of deuterated olefin for one mole of deuterated aldehyde formed are reported in Table 3.

The ^2H NMR resonances were assigned by comparison with the analogous signals present in the ^1H NMR spectra (solvent C_6D_6) of the corresponding hydroformylation mixtures.

In the ^2H NMR spectrum relative to the deuterioformylation of **1a** (Fig. 1a), in addition

Table 2
^2H NMR chemical shifts (δ, ppm)[a] of deuterated species arising from deuterioformylation of **1a–c** at partial substrate conversion

Subst.	R	Z-1-d$_1$-**1**	E-1-d$_1$-**1**	3-d$_1$-**1**	1,3-d$_2$-**2**	1,3-d$_2$-**2**
1a	Ph	4.86 (19[b])	5.1 (21[b])	1.79 (60[b])	9.10	2.81
1b	Me	4.68 -[b]	4.68 -[b]	1.56 (73[b])	9.36	1.81
1c	t-Bu	-	-	-	9.80	1.98

[a] Referred to C_6D_6 as external standard; 46 MHz, C_6H_6, 25°C.
[b] Relative intensities; in the case of **1b** the value for $(CH_3)_2C=CHD$ species was 27%.

Table 3
Deuterioformylation of the vinylidenic olefins $RC(CH_3)=CH_2$ **1a–c** at partial substrate conversion[a] with $Rh_4(CO)_{12}$ as catalytic precursor

Substrate	R	Rh/sub	Conversion (%)	$\Sigma(d_1\text{-}1)/(1,3\text{-}d_2\text{-}2)$[b]
1a	Ph	1/100	30	2.0
1b	Me	1/1000	27	0.21
1c	t-Bu	1/1000	29	0

[a] Determined via GLC by using the following internal standards: o-xylene (in the case of **1a**) and toluene (in the case of **1b** and **1c**), ±1% accuracy. Reaction conditions: 2.78 mmol of vinylidenic olefin, 5 ml of benzene; autoclave volume 25 ml; 100 atm total pressure, CO/D_2 (1:1). For the chemo- and regioselectivity see the values in Table 1.
[b] $\Sigma(d_1\text{-}1) = RC(CH_3)=CHD + RC(CH_2D)=CH_2$; $1,3\text{-}d_2\text{-}2 = RCD(CH_3)CH_2CDO$; molar ratio based on the formyl group as 100% D.

to the signals of the dideuterated aldehyde **2a** ($1,3\text{-}d_2\text{-}2a$ species) at 9.10 ppm and 2.81 ppm, three resonances at 5.22 ppm, 4.86 ppm and 1.79 ppm are also present, due to different deuterium atoms in the unconverted substrate.

The signals at 5.22 ppm and 4.86 ppm were respectively assigned to the E and Z geometric isomers arising from the olefin deuterated at the terminal position of the double bond ($1\text{-}d_1\text{-}$**1a**). The resonance at lowest frequency is due to a deuterium atom of the methyl group bound to the vinylidene moiety ($3\text{-}d_1\text{-}$**1a** species).

The ^{2}H NMR spectrum of the sample obtained from the deuterioformylation of **1b** (Fig. 1b) shows, in addition to the resonances of the aldehyde **2b** at 9.36 and 1.81 ppm ($1,3\text{-}d_2\text{-}$**2b** species), two low intensity signals at 4.68 and 1.56 ppm, due to the deuterated unconverted olefin (the former arising from the deuterium atom on the vinylidenic moiety in the species $1\text{-}d_1\text{-}$**1b**, the latter from the deuterium atom on the methyl group, in the species $3\text{-}d_1\text{-}$**1b**).

The ^{2}H NMR spectrum of the reaction mixture obtained from deuterioformylation of **1c** (Fig. 1c) only shows two signals at 9.80 and 1.98 ppm relative to the normal aldehyde **2c** ($1,3\text{-}d_2\text{-}$**2c**).
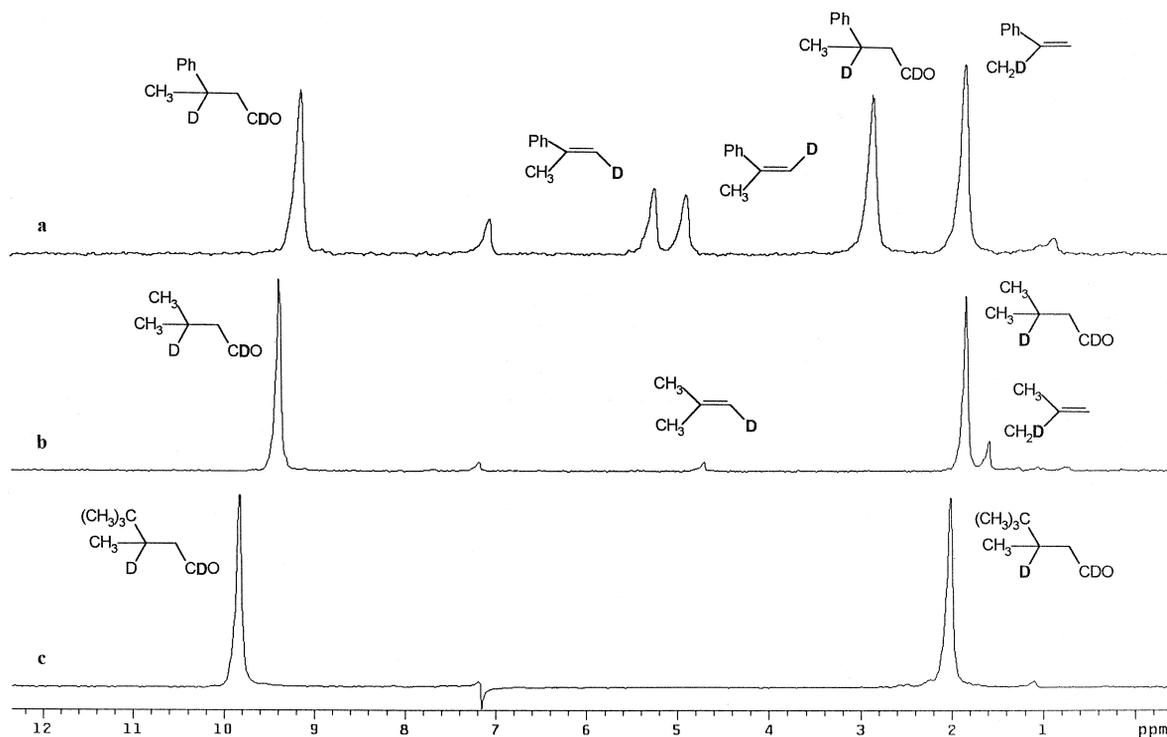

Fig. 1. ^{2}H NMR spectra (46 MHz, 25°C, C_6D_6 as external standard) of the crude reaction mixtures in benzene, obtained by deuterioformylation of 2-phenylpropene (a), 2-methylpropene (b) and 2,3,3-trimethylbutene (c), at partial substrate conversion.

The formation of deuterated olefins under deuterioformylation conditions can be reasonably explained taking into account the reversible formation of the tertiary alkyl–metal intermediate as well as the isotopic effect that favours Rh–H elimination with respect to the Rh–D one.

As reported in Scheme 3 in the case of **1a**, the tertiary alkyl–metal intermediate **t** gives, via β-hydride elimination, three complexes π_2, π_3 and π_4 in which the deuterated E and Z olefins 1-d_1-**1a** and 3-d_1-**1a** undergo a fast exchange with unlabelled **1a**, the prevalent species at low conversion.

The analogous Scheme 4 accounts for the formation of the two isomeric deuterated olefins 1-d_1-**1b** and 3-d_1-**1b** in the case of **1b** hydroformylation.

The Scheme 5 explains the exclusive formation of the linear aldehyde 1,3-d_2-**2c** in the deuterioformylation of **1c**.

From the relative intensities of deuterium resonances of aldehyde and olefin (Table 3) it can be concluded that only 0.2 mole of olefin

and hence of **t** alkyl per mole of aldehydes are formed in the case of **1b** whereas 2 moles of olefins and hence of **t** alkyl per mole of aldehyde are obtained for **1a**.

The results obtained for **1a** are in agreement with those reported for the deuterioformylation of 1,1-diphenylethene [3] and they confirm the tendency of a phenyl group to favor the formation of the tertiary alkyl metal intermediate with respect to the primary one. It is of interest to compare these results with those previously reported for the deuterioformylation of styrene under the same experimental conditions [100°C, $Rh_4(CO)_{12}$]. For this last substrate, the formation of the primary alkyl is not reversible as it is completely transformed into the linear aldehyde [11]. The secondary rhodium–alkyl intermediate partially undergoes β-hydride elimination and partially generates the branched aldehyde. In the case of 2-phenylpropene and 1,1-diphenylethene, the tertiary alkyl does form but it gives β-hydride elimination only.

As far as aliphatic vinylidenic olefins are concerned, the formation of the **t** alkyl takes
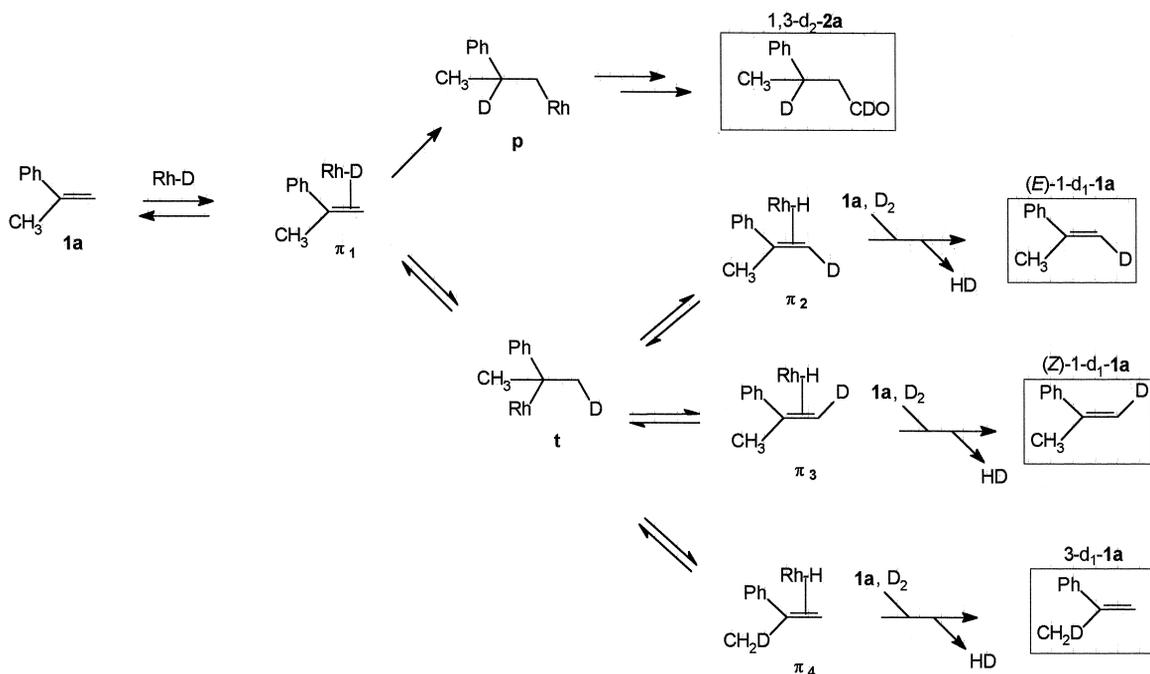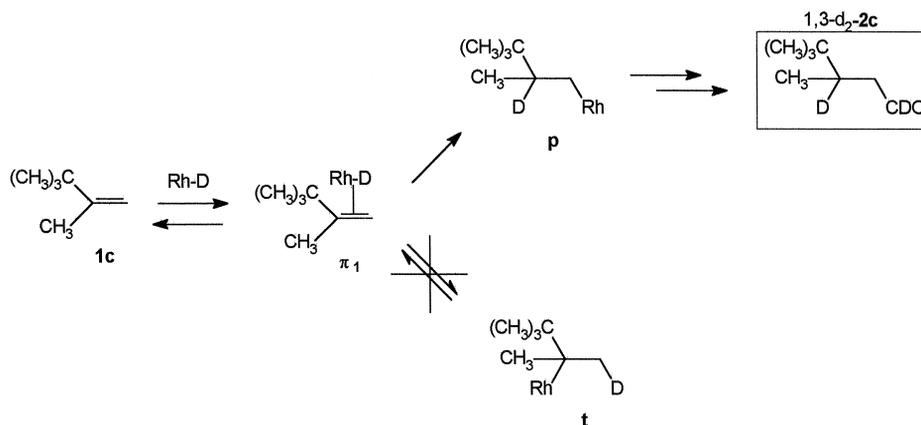

Scheme 3.
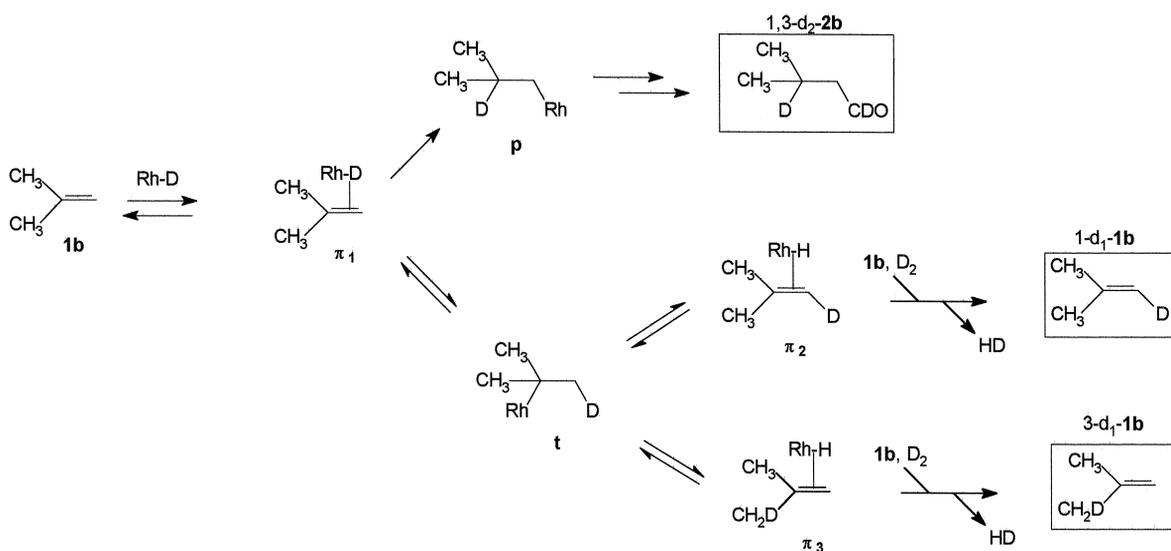
Scheme 4.

place in the case of 2-methylpropene but not for 2,3,3-trimethylbutene, bearing the bulky *tert*-butyl group on the vinylidenic moiety. Therefore in the case of **1c** the steric hindrance of the bulky alkyl groups bound to the double bond depresses the formation of the branched alkyl metal intermediates. It should be noted that, in the case of 1-hexene deuterioformylation [13] carried out under the same experimental conditions [$Rh_4(CO)_{12}$, 100°C], both the primary and secondary alkyl–metal intermediates are formed in a similar amount and undergo migratory in-

sertion on CO, the β-hydride elimination mainly occurring for the latter isomer.

From the above results we can conclude that the selective formation of the linear aldehyde (β-regioselectivity) observed in the deuterio-formylation of both aromatic and aliphatic vinylidenic olefins does not exclude the forma-tion of a tertiary rhodium–alkyl intermediate **t**: in the case of 1,1-diphenylethene and 2-phenyl-propene this species is preferentially formed with respect to the primary one **p**. In the case of full aliphatic vinylidenic olefins the primary

Scheme 5.

alkyl intermediate **p** is mainly formed; the presence of the tertiary one in the pathway of the reaction is also detected, but its extent is low. However, in spite of the formation of a tertiary alkyl–metal intermediate, no quaternary aldehyde is found in the reaction products, because the migratory insertion of a tertiary alkyl on the CO coordinated to the rhodium atom is probably prevented from steric reasons; [1] consequently this intermediate exclusively undergoes β-hydride elimination. In conclusion the results obtained in the hydroformylation of the vinylidenic olefins **1a–c** clearly point out that the main differences between a primary and a tertiary alkyl–rhodium intermediate are concerned with the different behaviors of these species during the migratory insertion step rather than in their formation step.

Finally, it should be noted that the ^{2}H NMR analysis of the crude deuterioformylation reaction products is a direct and simple method to investigate the different behaviors of a primary, secondary and tertiary alkyl–metal intermediate under rhodium-catalyzed hydroformylation conditions. In particular, in the case of vinylidenic olefins, it must be stressed that the classical approach based on the sole analysis of regioisomeric ratios of the produced aldehydes would have led to the erroneous conclusion that no tertiary metal–alkyl intermediate was formed in the hydroformylation of 2-phenylpropene and 2-methylpropene, as no branched aldehyde is obtained.

3. Experimental

Benzene was dried over molecular sieves and distilled under nitrogen. The starting olefins were commercially available. $Rh_4(CO)_{12}$ was prepared as reported in the literature [21,22]. GC analyses of the reaction mixtures were performed on a Perkin-Elmer 8500 chromatograph equipped with a 12 m × 0.22 mm BP1 capillary column, using helium as carrier gas. ^{2}H NMR spectra of the crude products in benzene were carried out on a Varian VXR 300 spectrometer operating at 46 MHz for ^{2}H. Chemical shifts were referred to C_6D_6 as external standard.

3.1. Hydroformylation or deuterioformylation of vinylidenic olefins: general procedure

A solution of the vinylidenic olefin (2.78 mmol) and $Rh_4(CO)_{12}$ in benzene (5 ml) was introduced by suction into an evacuated 25-ml stainless steel autoclave. Carbon monoxide was introduced, the autoclave was then rocked and heated to 100°C, and hydrogen or deuterium was rapidly introduced up to 100 atm total pressure $(CO/H_2(D_2) = 1:1)$ at 100°C. When the gas absorption reached the value corresponding to the fixed conversion, the reaction mixture was siphoned out. The degree of conversion was measured by GLC, using *o*-xylene (with **1a**) and toluene (with **1b** and **1c**) as internal standard.

4. Summary

The origin of the β-regioselectivity in the hydroformylation of the vinylidenic olefins 2-phenylpropene (**1a**), 2-methylpropene (**1b**) and 2,3,3-trimethylbutene (**1c**) [100°C, 100 atm, $Rh_4(CO)_{12}$] was investigated via deuterioformylation experiments carried out at partial substrate conversion. ^{2}H NMR analysis of the crude reaction mixtures pointed out that the tertiary rhodium–alkyl intermediate is formed in the case of **1a** and **1b** but not in the case of **1c** because of the steric hindrance of the bulky *tert*-butyl group. The tertiary alkyl rhodium intermediate arising from **1a** and **1b** does not give migratory insertion on CO but exclusively undergoes β-hydride elimination. On the contrary

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[1] Indeed in the rhodium-catalyzed hydroformylation of some 1,1-disubstituted olefins containing a functional group in a suitable position with respect to the double bond [19,20] selective or exclusive formylation at the more substituted carbon atom was observed.

the linear rhodium–alkyl intermediates in all the cases undergo migratory insertion on CO, giving the corresponding acyl rhodium species and hence the primary aldehydes.

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