Rhodium-Catalyzed Hydroformylation of Isoprene: Unusual Accelerating Effects of Phosphorus Ligands and Gas Pressure

Humberto J. V. Barros, Cristiane C. Guimarães, Eduardo N. dos Santos, and Elena V. Gusevskaya*

Departamento de Química, Universidade Federal de Minas Gerais, 31270-901 Belo Horizonte, MG, Brazil

Received October 27, 2006

Rhodium-catalyzed hydroformylation of isoprene has been studied in the presence of various mono- and diphosphines. Using a large excess of the ligand, the reaction can be performed under mild conditions (80−100 °C, 40−80 atm) and results in three unsaturated aldehydes formed in a 95% combined selectivity. The study of the effects of the reaction variables revealed remarkable trends, opposite those usually observed with simple alkenes. The increase in the concentration of the phosphorus ligand and/or ligand basicity strongly accelerates the reaction. Moreover, the reaction shows unusual kinetics, being first order in both hydrogen and CO pressure under "common" hydroformylation conditions. The obtained data confirm that an $\eta^3-\eta^1$ rearrangement, which converts an η^3-allylrhodium intermediate resistant to CO insertion into the much more reactive η^1 complex, is the most critical step of this reaction.

Introduction

The hydroformylation of conjugated dienes could result in various interesting products;[1] however, these reactions have attracted much less attention than the hydroformylation of monoenes (alkenes). Conjugated dienes are very resistant to hydroformylation: e.g., in the presence of rhodium/monophosphine catalysts, butadiene reacts at least 3 orders of magnitude slower than 1-heptene.[2] Furthermore, a study on the hydroformylation of conjugated dienes and alkenes in a competitive situation shows that trace quantities of dienes compete against the excess of alkene for rhodium, forming very stable η^3-allyl complexes.[3] Thus, diene impurities can even poison rhodium catalysts, decelerating the hydroformylation of alkenes.[4,5]

Several works reporting the hydroformylation of conjugated dienes, mostly butadiene, isoprene, and 1,3-pentadiene, have been published. The reactions usually resulted in complex mixtures of saturated and unsaturated mono- and dialdehydes and required severe conditions (120−175 °C, 200−300 atm) with either cobalt/monophosphine[1] or rhodium/monophosphine[6,7] catalysts. Rhodium/diphosphine systems operate under milder conditions and give better selectivities and activities, but a substitution of diphosphines by triphenylphosphine virtually deactivates the catalysts.[2,8−11]

It is known that η^3-allyl complexes are very reluctant to the insertion of CO.[4] It has been suggested that for the hydroformylation of conjugated dienes to occur η^3-allyl complexes have to be converted into η^1-allyl complexes, where the CO insertion can take place more easily.[2,10,12] Thus, it is reasonable to expect that the ligand basicity and ligand to rhodium ratio, variables left almost unexplored in these reactions, should be very important for the catalyst activity, as the $\eta^3-\eta^1$ rearrangment can be favored by the excess of coordinating ligands.

We have recently communicated a remarkable effect of triphenylphosphine in the hydroformylation of conjugated dienes.[13] The increase in the P/Rh ratio to a point significantly accelerated the reactions of isoprene and myrcene, but not of limonene, a nonconjugated diene. This finding allowed development of efficient processes with rhodium catalysts promoted by triphenylphosphine, the most accessible, low cost, and stable phosphorus ligand employed in hydroformylation. Herein we report the results of a systematic study on the rhodium-catalyzed hydroformylation of isoprene in the presence of various mono- and diphosphines. The effects of the ligand nature, its concentration, and other reaction variables on the rate and selectivity of the hydroformylation as well as the structure of the products have been investigated.

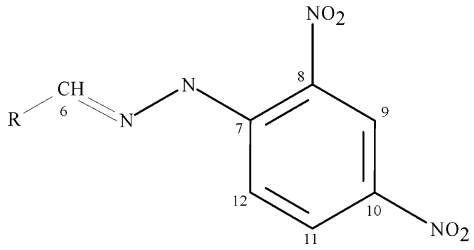
Isoprene has been chosen as a model conjugated diene, since we are particularly interested in the hydroformylation of natural monoterpenes[14−16] including myrcene,[12] which also contains a 2-substituted butadiene moiety in its structure. Isoprene is even less reactive in hydroformylation than butadiene.[2] This substrate was tested in most of the works on the hydroformylation of conjugated dienes; however, in rhodium systems, only diphos-

* To whom correspondence should be addressed. E-mail: elena@ufmg.br.

(1) Adkins, H.; Williams, J. L. R. *J. Org. Chem.* **1952**, *17*, 980.
(2) van Leeuwen, P. W. N. M.; Roobeek, C. F. *J. Mol. Catal.* **1985**, *31*, 345.
(3) Liu, G.; Garland, M. *J. Organomet. Chem.* **2000**, *608*, 76.
(4) *Rhodium Catalyzed Hydroformylation*; van Leeuwen, P. W. N. M., Claver, C., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2000.
(5) Walczuk, E. B.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4665.
(6) Fell, B.; Rupilius, W. *Tetrahedron Lett.* **1969**, *32*, 2721.
(7) Bahrmann, H.; Fell, B. *J. Mol. Catal.* **1980**, *8*, 329.
(8) Botteghi, C.; Branca, M.; Saba, A. *J. Organomet. Chem.* **1980**, *184*, C17.
(9) Bertozzi, S.; Campigli, N.; Vitulli, G.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **1995**, *487*, 41.
(10) Horiuchi, T.; Ohta, T.; Shirakawa, E.; Nozaki, K.; Takaya, H. *Tetrahedron* **1997**, *53*, 7795.
(11) Ohgmori, Y.; Suzuki, N.; Sumitani, N. *J. Mol. Catal. A* **1998**, *133*, 289.
(12) Foca, C. M.; Barros, H. J. V.; dos Santos, E. N.; Gusevskaya, E. V.; Bayon, J. C. *New J. Chem.* **2003**, *27*, 533.
(13) Barros, H. J. V.; Guimarães, C. C.; dos Santos, E. N.; Gusevskaya, E. V. *Catal. Commun.* **2007**, *8*, 747.
(14) Barros, H. J. V.; Ospina, M. L.; Arguello, E.; Rocha, W. R.; Gusevskaya, E. V.; dos Santos, E. N. *J. Organomet. Chem.* **2003**, *671*, 150.
(15) Barros, H. J. V.; Hanson, B. E.; dos Santos, E. N.; Gusevskaya, E. V. *Appl. Catal., A* **2004**, *278*, 57.
(16) da Silva, J. G.; Barros, H. J. V.; dos Santos, E. N.; Gusevskaya, E. V. *Appl. Catal., A* **2006**, *309*, 169.

10.1021/om060994n CCC: $37.00
Publication on Web 03/27/2007

Chart 1. Structure of Hydrazones 2H−5H[a]



[a] R = $CH_2CH_2C(CH_3)=CH_2$ for **2H**, $CH=C(CH_3)CH_2CH_3$ for **3H**, $CH_2C(CH_3)=CHCH_3$ for **4H**, and $CH_2CH(CH_3)CH_2CH_3$ for **5H**.

phines were used as auxiliary ligands and the yields of identified products were usually quite low.[1−3,8,9,17]

Experimental Section

All chemicals were purchased from commercial sources and used as received, unless otherwise indicated. Isoprene (Fluka) was distilled before use. Benzene was purified under reflux with sodium wire/benzophenone for 8 h and then distilled under argon. Benzene rather than friendlier toluene was used as a solvent due to the overlapping of gas chromatography (GC) peaks of toluene and one of the aldehydes formed from isoprene. In a typical run, a benzene solution (15.0 mL) containing $[Rh(COD)(OAc)]_2$[18] (3.7×10^{-3} mmol), phosphorus ligand (0.014−3.7 mmol), substrate (3.0 mmol), and dodecane (1.5 mmol, internal standard) was transferred under argon into a stainless steel autoclave, which was pressurized to 20−80 atm of total pressure (CO/H_2 = 1/4 to 4/1), placed in an oil bath (60−120 °C), and magnetically stirred. After the reaction was carried out and cooled to room temperature, the excess CO and H_2 were slowly vented. Reactions were followed by GC using a sampling system (Shimadzu 17B, Carbowax 20M). Conversion and selectivity were determined by GC. The GC mass balance was based on the substrate charged using dodecane as an internal standard. The solution was also analyzed by GC/MS (Hewlett-Packard MSD 5890 instrument operating at 70 eV).

Aldehydes **2**−**5** were separated by column chromatography (hexane and CH_2Cl_2 as eluents) as the corresponding hydrazones **2H**−**5H** obtained by their reactions with 2,4-dinitrophenylhydrazine and identified by NMR (Bruker DRX-400, tetramethylsilane, $CDCl_3$). The carbon numbering used for isoprene is maintained for aldehydes and hydrazones to facilitate a comparison. The structure of the common part of hydrazones **2H**−**5H** and numbering are presented in Chart 1.

Data for Aldehyde 2: MS, EM [(*m*/*z*)/rel intens] 98/3 (M^+), 83/27 ($M^+ - CH_3$), 81/9, 79/8, 69/6 (M^+ − CHO), 67/8, 57/33, 56/35, 55/100 ($M^+ - CH_2CHO$), 53/10.

Data for Aldehyde 3: MS [(*m*/*z*)/rel intens] 98/71 (M^+), 97/22 (M^+ − H), 83/92 ($M^+ - CH_3$), 79/19, 69/49 (M^+ − CHO or $M^+ - C_2H_5$), 67/14, 55/100 ($M^+ - CH_2CHO$), 53/34, 51/15.

Data for Aldehyde 4: MS [(*m*/*z*)/rel intens] 98/81 (M^+), 97/22 (M^+ − H), 83/66 ($M^+ - CH_3$), 79/ 14, 69/57 (M^+ − CHO or $M^+ - C_2H_5$), 67/13, 55/100 ($M^+ - CH_2CHO$), 53/29, 51/14.

Data for Hydrazone 2H: ^{1}H NMR, δ_H (*J*, Hz) 1.79 (s, 3H, C^5H_3), 2.35 (t, 2H, C^3H_2, 7.6), 2.60 (td, 2H, C^4H_2, 7.6, 5.0), 4.77 (s, 1H, C^1HH), 4.82 (s, 1H, C^1HH), 7.53 (t, 1H, C^6HN, 5.0), 7.94 (d, 1H, $C^{12}H$, 9.6), 8.30 (dd, 1H, $C^{11}H$, 9.6, 2.5), 9.14 (d, 1H, C^9H, 2.5), 11.02 (br s), 1H, N*H*); ^{13}C NMR, δ_C 22.61 (C^5), 30.68 (C^4), 34.31 (C^3), 111.41 (C^1), 116.70 (C^{12}), 123.67 (C^9), 129.08 (C^8), 130.14 (C^{11}), 137.96 (C^{10}),143.94 (C^2), 145.32 (C^7), 152.10 (C^6).

Data for Hydrazone 3aH (*E*): ^{1}H NMR, δ_H (*J*, Hz) 1.05 (t, 3H, C^4H_3, 7.4), 1.89 (s, 3H, C^5H_3), 2.17 (q, 2H, C^3H_2, 7.4), 6.05 (d, 1H, C^1H, 9.7), 7.84 (d, 1H, $C^{12}H$, 9.6), 8.01 (d, 1H, C^6HN, 9.7), 8.20 (dd, 1H, $C^{11}H$, 9.6, 2.5), 9.01 (d, 1H, C^9H, 2.5), 11.04 (br s, 1H, N*H*); ^{13}C NMR, δ_C 12.21 (C^4), 17.80 (C^5), 33.31 (C^3), 116.83 (C^{12}), 119.81 (C^1), 123.73 (C^9), 129.08 (C^8), 130.09 (C^{11}), 137.96 (C^{10}), 144.92 (C^7), 147.76 (C^6), 153.64 (C^2).

Data for Hydrazone 3bH (*Z*): ^{1}H NMR, δ_H (*J*, Hz) 1.05 (t, 3H, C^4H_3, 7.4), 1.89 (s, 3H, C^5H_3), 2.28 (q, 2H, C^3H_2, 7.6), 6.01 (d, 1H, C^1H, 9.8), 7.83 (d, 1H, $C^{12}H$, 9.6), 7.98 (d, 1H, C^6HN, 9.8), 8.20 (dd, 1H, $C^{11}H$, 9.6, 2.5), 9.01 (d, 1H, C^9H, 2.5), 11.04 (br s, 1H, N*H*); ^{13}C NMR, δ_C 12.21 (C^4), 24.25 (C^5), 25.37 (C^3), 116.83 (C^{12}),120.98 (C^1), 123.73 (C^9), 129.08 (C^8), 130.09 (C^{11}), 137.96 (C^{10}), 144.92 (C^7), 147.10 (C^6), 153.65 (C^2).

Hydrazone 4H (*E*): ^{1}H NMR, δ_H (*J*, Hz) 1.65 (d, 3H, C^4H_3, 6.8), 1.69 (s, 3H, C^5H_3), 3.08 (d, 2H, C^1H_2, 6.0), 5.38 (q, 1H, C^3H, 6.8), 7.46 (t, 1H, C^6HN, 6.0), 7.99 (d, 1H, $C^{12}H$, 9.6), 8.32 (dd, 1H, $C^{11}H$, 9.6, 2.5), 9.12 (d, 1H, C^9H, 2.5), 11.20 (br s, 1H, N*H*); ^{13}C NMR δ_C 13.48 (C^4), 16.32 (C^5), 42.73 (C^1), 116.70 (C^{12}), 123.67 (C^9), 129.08 (C^8), 130.14 (C^{11}),123.11 (C^3), 130.43 (C^2), 137.96 (C^{10}), 145.32 (C^7), 151.15 (C^6).

Data for Hydrazone 5H: ^{1}H NMR, δ_H (*J*, Hz) 0.95 (t, 3H, C^4H_3, 7.4), 1.00 (d, 3H, C^5H_3, 6.4), 1.25−1.35 (m, 1H, C^3HH), 1.40−1.50 (m, 1H, C^3HH), 1.75−1.80 (m, 1H, C^2H), 2.33−2.43 (m, 2H, C^1H_2), 7.54−7.58 (m, 1H, C^6HN), 7.95 (d, 1H, $C^{12}H$, 9.6), 8.32 (dd, 1H, $C^{11}H$, 9.6, 2.5), 9.14 (d, 1H, C^9H, 2.5), 11.02 (br s, 1H, N*H*); ^{13}C NMR, δ_C 11.52 (C^4), 19.49 (C^5), 29.53 (C^3), 33.22 (C^2), 39.40 (C^1), 116.70 (C^{12}), 123.67 (C^9), 129.08 (C^8), 130.14 (C^{11}), 137.96 (C^{10}), 145.32 (C^7), 152.41 (C^6).

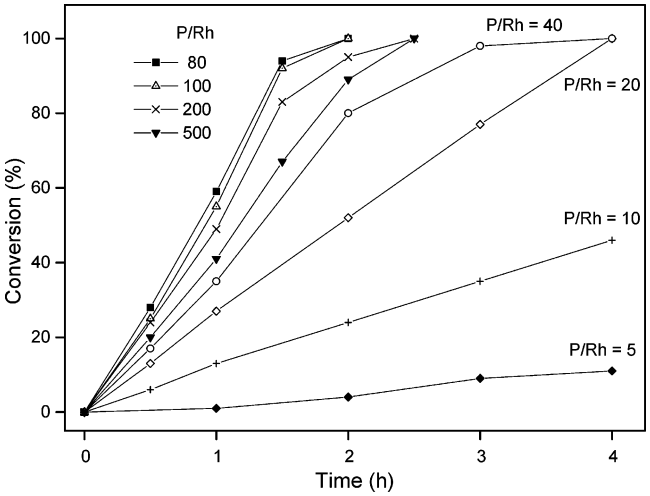


Figure 1. Hydroformylation of isoprene catalyzed by $[Rh(COD)(OAc)]_2/PPh_3$ at different P/Rh ratios. Conditions: isoprene (0.20 M), $[Rh(COD)(OAc)]_2$ (0.25 mM), 80 atm (CO/H_2 = 1/1), 100 °C.

Results and Discussion

Isoprene Hydroformylation with Rh/PPh_3 Systems: Effects of the PPh_3 Concentration and Temperature. At P/Rh = 5, the hydroformylation of isoprene with Rh/PPh_3 occurs rather slowly: a 48% conversion for 24 h at 100 °C (Table 1, run 1). However, the reaction is highly chemo- and regioselective. Three unsaturated aldehydes (**2**−**4**) are formed in a 95% combined selectivity, with two of them, **3** and **4**, having the same carbon skeleton and corresponding to ca. 80% of the total amounts of the aldehydes (Scheme 1). We have found that the increase in the ligand concentration produces a remarkable accelerating effect on this process: at P/Rh = 20, isoprene is completely converted into aldehydes within 4 h (Table 1, run 3). At P/Rh = 80, the reaction is even faster, resulting in a complete conversion within 1.5 h (Table 1, run 4). Kinetic curves for the reactions at 100 °C at various P/Rh ratios are

(17) Chen, L.; Chew. W.; Garland, M. *Appl. Spectrosc.* **2003**, *57*, 491.
(18) Giordano, G.; Crabtree, R. H. *Inorg. Synth.* **1990**, *28*, 88.

Table 1. Hydroformylation of Isoprene Catalyzed by [Rh(COD)(OAc)]$_2$/PPh$_3$[a]

						selectivity (%)		
run	P/Rh	*T* (°C)	time (h)	conversion (%)	S_{ald}[b] (%)	**2**	**3**	**4**
1	5	100	24	48	95	18	47	30
2	10	100	10	98	95	17	47	29
3	20	100	4	100	96	17	48	31
4	40	100	3	98	93	12	50	31
5	80	100	1.5	98	97	16	50	31
6	100	100	2	100	94	17	49	28
7	500	100	2.5	100	95	18	48	29
8	10	60	13	74	98	14	53	31
9	20	60	13	80	98	15	53	30
10	20	80	8	98	98	16	51	32
11	40	80	5	100	97	17	49	31
12[c]	20	120	2	100	97	15	50	28
13[c]	60	120	1.5	98	98	14	50	29
14[c]	100	120	1	100	98	18	48	28
15[d]	80	100	6	100	96	24	49	23

[a] Conditions: solvent benzene, isoprene (0.20 M), [Rh(COD)(OAc)]$_2$ (0.25 mM), 80 atm (CO/H$_2$ = 1/1). [b] Selectivity for products **2**−**4**. [c] Aldehyde **5** was also formed (included in S_{ald}). [d] Pressure 40 atm (CO/H$_2$ = 1/1).

shown in Figure 1. The effect of the P/Rh ratio is also illustrated in Figure 2c, which shows the conversion of isoprene at 100 °C for 1 h. A strong increase in the reaction rate can be seen when the P/Rh ratio increases from 5 to 80. Further addition of the ligand slows the reaction; however, even at a large excess of PPh$_3$ (P/Rh = 500), it remains reasonably fast, resulting in a complete conversion in 2.5 h (Table 1, run 7). It is noteworthy that, for P/Rh ratios up to 20, the kinetic curves are nearly straight lines from 0% to 100% conversion. This means that under these conditions the rate is virtually independent of the concentration of the substrate! Even at P/Rh ratios as high as 500 the linearity range is quite high (up to 80−95% conversions), indicating that a ligand vs isoprene competition for the catalyst sites does not play a significant role. In other words, the substrate reacts with rhodium quite readily, and most of the metal centers always, even at high conversions and high PPh$_3$ concentrations, contain strongly coordinated isoprene or fragments derived from isoprene.

At any P/Rh ratio within the range studied, the combined yield of three main aldehydes is high: 93−97%, from which ca. 80% are aldehydes **3** and **4**. It should be mentioned that unsaturated aldehydes are very useful compounds in organic synthesis, hardly accessible by conventional synthetic routes. It is also noteworthy that α−β-unsaturated aldehyde **3** obtained here in ca. 50% yield has not been reported in previous works on the hydroformylation of isoprene.

The accelerating effect of PPh$_3$ in hydroformylation at such high P/Rh ratios is quite unusual. In most Rh systems modified by arylphosphines, an inverse reaction rate dependence on their concentration is commonly observed, at least under "normal" hydroformylation conditions, due to the competition between the P ligand and the substrate for the coordination sites on the metal center.[4] Some works on the hydroformylation of 1-alkenes reported an increase in activity of rhodium catalysts with the addition of small amounts of PPh$_3$ (up to P/Rh < 10).[19−21] However, this effect was usually observed at high metal concentrations and/or low CO pressures and was associated with the production of monometallic species from inactive bi- or polynuclear complexes and/or their stabilization. In other works describing the accelerating effect of PPh$_3$ (also at low P/Rh ratios), the substrates were technical-grade methyl oleate and/or soybean oil, which might well contain conjugated dienes in their compositions.[22,23] Recently,[16] we have also observed an unusual accelerating effect of phosphorus ligands in the hydroformylation of linalool, which was explained by the structure of this substrate.

We studied the effect of the P/Rh ratio on the hydroformylation of isoprene at different temperatures (Figure 2). It has been revealed that the PPh$_3$ addition up to a limit value significantly accelerates the reaction at any temperature, with the following tendency being observed: the higher the temperature, the greater the ligand excess which starts to inhibit the hydroformylation. In other words, the limit value, i.e., the maximum on the "conversion vs P/Rh ratio" curves (Figure 2), strongly depends on the temperature. For example, at 120 °C, increasing the P/Rh ratio to 150−200 (Figure 2d) still positively affects the reaction rate. On the other hand, at 100, 80, and 60 °C, the limit P/Rh value, after which the ligand addition is not advantageous anymore, gradually decreases to 80, 60, and 20, respectively (parts c, b, and a, respectively, of Figure 2).

We believe that the results obtained with isoprene are consistent with the hypothesis that its hydroformylation can be accelerated by promoting the rearrangement of η^3-allyl- into η^1-allylrhodium complexes. This can be done by increasing the ligand to rhodium ratio. At PPh$_3$/Rh = 20−100 (depending on the reaction temperature), a complete and selective conversion of isoprene into aldehydes can be performed in 1.5−2 h (Table 1, runs 5, 6, and 12−14). However, too high PPh$_3$ concentrations slowly decrease the reaction rate. This seems to occur due to the competition of PPh$_3$ for the catalyst sites not with isoprene but with CO, as the reaction rate is virtually independent of the substrate concentration. On the other hand, the η^1-allylrhodium intermediate complex must have at least one CO molecule for the CO insertion to occur, and this CO ligand must be in a *cis* position to the η^1-allyl group. Too high PPh$_3$ concentrations could result in the formation of trisligand [Rh(η^1-allyl)](PPh$_3$)$_3$(CO)] complexes, which may not be catalytically active at all if three phosphines are in the equatorial positions and CO and η^1-allyl groups are in the apical positions. Thus, the CO insertion is more probable if the complex contains two CO molecules: one of them will surely be *cis* to the η^1-allyl group. In addition, we believe that the substitution of PPh$_3$ by CO on rhodium is probably an endothermic reaction, because the PPh$_3$ concentration, which begins to decelerate the reaction, increases with temperature. In other words, the increase in temperature shifts the equilibrium toward rhodium carbonyl complexes; thus, the decelerating effect of phosphine appears at higher P/Rh ratios.

The treatment of the kinetic data obtained revealed the temperature dependence for this reaction. The data on the reaction rates (runs 3, 9, 10, and 12, Table 1) expressed by means of the Arrhenius equation yield an activation energy of ca. 40 kJ mol^{-1} in the range of 60−120 °C. The reaction selectivity and product distribution vary quite slightly, with the combined yield of aldehydes **2**−**4** reaching 93−99%. We suppose that the use of high concentrations of PPh$_3$, together with relatively mild conditions, favors the reaction selectivity, since in hydroformylation, phosphorus ligands are known to

(19) Kalck, P. *Polyhedron* **1988**, *7*, 2441.
(20) Aubry, D. A.; Monteil, A. R.; Peng, W. -J.; Stanley, G. G. *C. R. Chim.* **2002**, *5*, 473.
(21) Diéguez, M.; Claver, C.; Masdeu-Bultó, A. M.; Ruiz, A.; Leeuwen, P. W. N. M.; Schoemaker, G. C. *Organometallics* **1999**, *18*, 2107.
(22) Kandanarachchi, P.; Guo, A.; Demydov, D.; Petrovic, Z. *J. Am. Oil Chem. Soc.* **2002**, *79*, 1221.
(23) Mendes, A. N. F.; Gregório, J. R.; Rosa, R. G. *J. Braz. Chem. Soc.* **2005**, *16*, 1124.

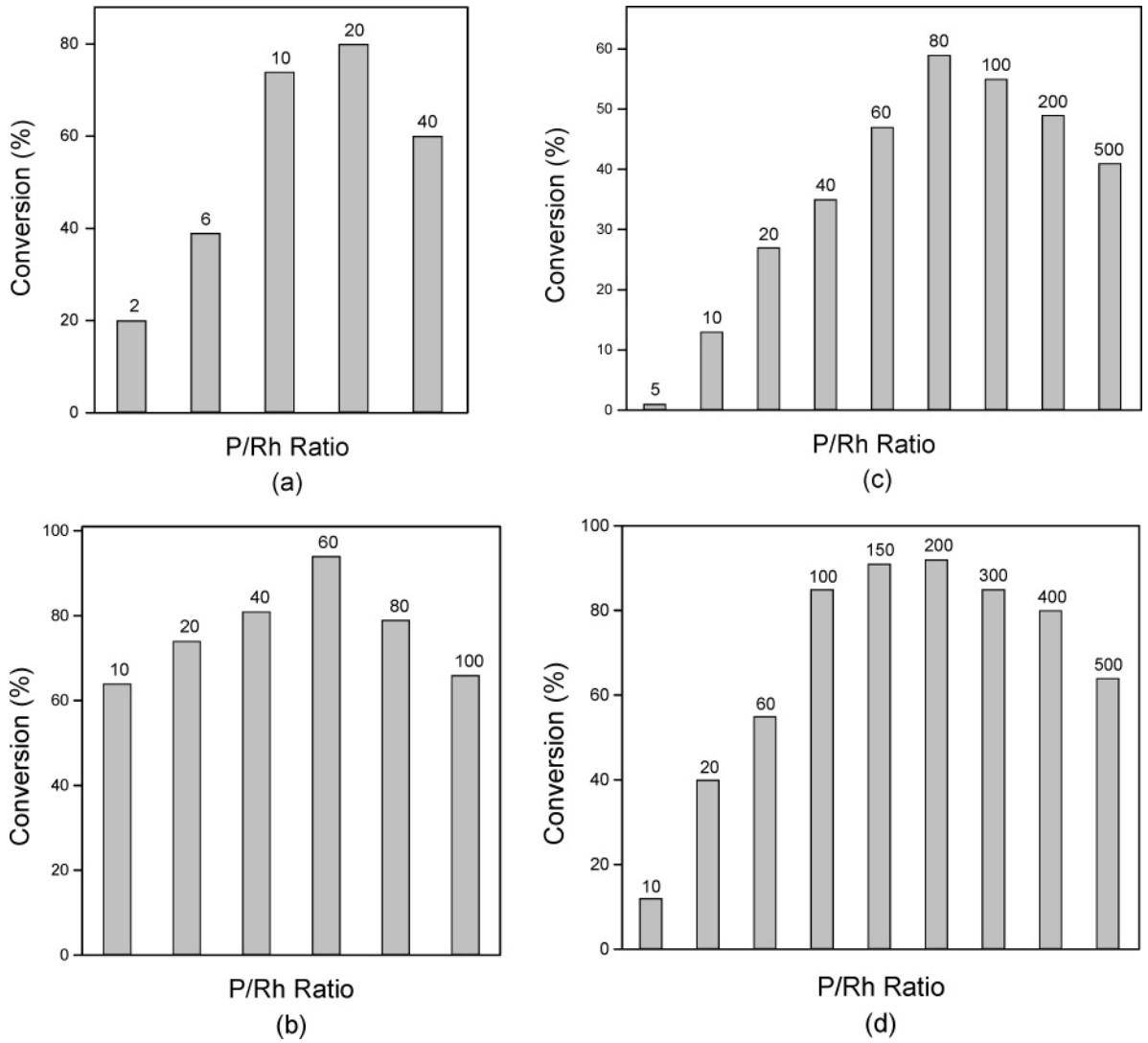
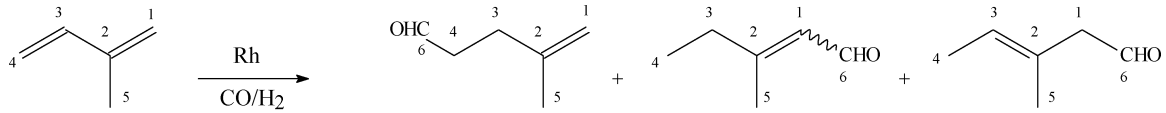


Figure 2. Hydroformylation of isoprene catalyzed by $[Rh(COD)(OAc)]_2/PPh_3$ at different P/Rh ratios: (a) 60 °C, conversions for 13 h; (b) 80 °C, conversions for 4 h; (c) 100 °C, conversions for 1 h; (d) 120 °C, conversions for 0.75 h. Conditions: isoprene (0.20 M), $[Rh(COD)(OAc)]_2$ (0.25 mM), 80 atm (CO/H_2 = 1/1).

Scheme 1



1 **2** **3a/3b** **4**

disfavor undesirable isomerization and hydrogenation side reactions.[4] In addition, as all rhodium centers are "trapped" by isoprene, a possibility of secondary rhodium-catalyzed reactions until a complete isoprene conversion is low.

Only at 120 °C, one more carbonylated product—the saturated aldehyde **5** resulting from the hydrogenation of aldehydes **3** and **4**—was detected in appreciable amounts (ca. 5%). When the mixture was kept under the reaction conditions after the complete conversion of isoprene, the yield of **5** strongly increased at the expense of **3** and **4**. It is important to note that no changes in the **3/4** ratio occurred, which implies that, contrary to what might be expected, the rhodium catalyst did not promote the isomerization of aldehyde **4** into more stable conjugated aldehyde **3**. The amounts of the other unsaturated aldehyde, **2**, also declined; however, no corresponding hydrogenated or dicarbonylated products were observed. Instead, the difference in the GC mass balance increased, which was attributed to the formation of not GC determinable high molecular weight products.

Product Stereochemistry. The reaction is highly stereoselective. Aldehyde **4** is formed almost exclusively as a single stereoisomer having CH_3 and CH_2CHO groups in a *trans* position (*E* isomer). Only trace amounts of the corresponding *Z* isomer were detected by NMR in the isolated product. The stereochemistry of **4** was determined using the following approach. It is known that ^{13}C NMR spectroscopy is a particularly valuable tool for the configurational assignment of trisubstituted alkenes ($RR^1C{=}CHR^2$). The principle involved is that the carbon nucleus *cis* to the R^2 group will be shielded (5−7 ppm), through a "γ compression effect", relative to the same carbon nucleus positioned *cis* to hydrogen.[24] In the spectra of compound **4H**, resonances for carbons C-1 and C-5 attached

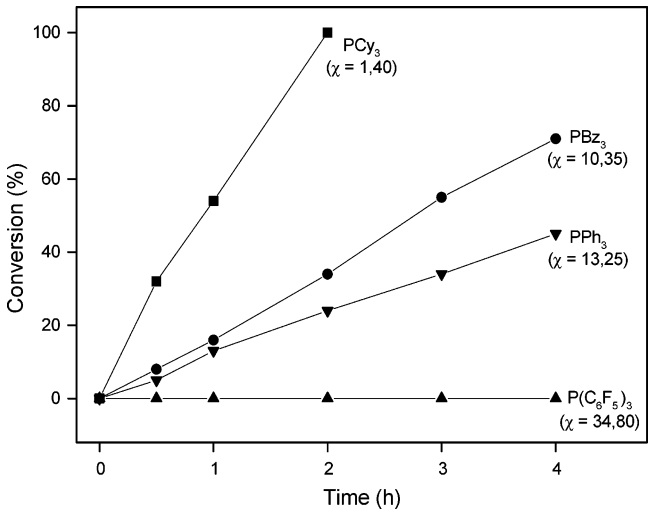


Figure 3. Hydroformylation of isoprene catalyzed by $[Rh(COD)(OAc)]_2$ with different monophosphines. Conditions: isoprene (0.20 M), $[Rh(COD)(OAc)]_2$ (0.25 mM), P/Rh = 10, 80 atm (CO/H_2 = 1/1), 100 °C (Bz = CH_2Ph; Cy = cyclohexyl).

to olefinic carbon C-2 in the major isomer appear at 42.73 and 16.32 ppm, respectively, whereas in the minor isomer they appear at 34.10 and 21.09 ppm. Thus, in the major isomer of **4**, CH_3 and CH_2CHO groups are in *trans* positions, while in the minor isomer they are *cis* to each other.

Aldehyde **3** is formed as a pair of GC-distinguishable stereoisomers in a ratio of ca. 80/20. These two isomers were completely characterized by NMR as hydrazones. Using the approach described above, we have attributed to major isomer **3b** a *Z* configuration, where the CHO and C_2H_5 groups are in a *cis* position. Resonances for carbons C-3 and C-5 attached to olefinic carbon C-2 in **3bH** appear at 25.37 and 24.25 ppm, respectively, whereas in the minor isomer **3aH** (*E*) they appear at 33.31 and 17.80 ppm.

Isoprene Hydroformylation with Rh/Monophosphine Systems: Effect of the Ligand Basicity. In a further study, we varied the nature of the monophosphine ligand. The cone angles, θ, and χ value were taken as quantitative measures of steric and electronic effects, respectively, as proposed by Tolman.[25] The higher the cone angle, the greater steric crowding the ligand introduces to rhodium. The χ value is determined by IR and becomes lower with an increase in the ligand basicity.

The data on the activity of various rhodium/monophosphine systems at P/Rh = 10 are presented in Figure 3. Selectivities and product distributions are very similar for all monophosphines studied (for PPh_3 the data are given in Table 1). It can be seen that the rate of the isoprene hydroformylation strongly depends on the ligand basicity: the more basic ligands (lower χ) show much higher activity. With the most basic ligand in this series, PCy_3 (χ = 1.40) (Cy = cyclohexyl), the reaction is ca. 3 times faster than with PPh_3 (χ = 13.25). On the other hand, with the less basic $P(C_6F_5)_3$ ligand (χ = 34.80) the hydroformylation does not occur. The ligand effect in the hydroformylation of isoprene seems to be more electronic than steric because two ligands with similar cone angles, PBz_3 (θ = 165°) (Bz = CH_2Ph) and PCy_3 (θ = 170°),[25] show very different catalytic activities. In should be mentioned that, in the case of $P(C_6F_5)_3$, its steric bulk (θ = 184° vs 145° for PPh_3)[25] also has to be taken into account because this also can contribute to lowering the activity. In this system, most rhodium complexes contain no phosphorus ligands, as $P(C_6F_5)_3$ is a very poorly coordinating ligand, especially under the reaction conditions used (40 atm of CO and sterically highly demanding substrate). Mono- and bisligand species, if formed, are virtually not involved in the isoprene transformations for steric reasons.

The effect of the ligand basicity on the hydroformylation of isoprene is also completely opposite most of the previously reported results for alkenes.[4,14] Usually, the more basic the phosphines, the less active they are in hydroformylation because they "block" the metal active center due to their strong coordination. The results obtained confirm once again that the hydroformylation of isoprene can be accelerated by favoring the $\eta^3-\eta^1$ rearrangement. This can be done by increasing either the ligand to rhodium ratio or ligand basicity, which turns stronger the competition for the coordination sites on rhodium. In addition, phosphine ligands on rhodium, especially more donating phosphines, shift the equilibrium to the η^1-allyl form, probably for both electronic and steric reasons. For example, it was reported that although allylic complexes of rhodium usually are very resistant to CO insertion, an electron-rich tetraphosphine dirhodium bridged η^3-allyl complex, $[Rh_2(\eta^3\text{-allyl})_2L]$ (L = $(Et_2PCH_2CH_2)PhPCH_2PPh(CH_2CH_2PEt_2)$, can be readily carbonylated under mild conditions.[26]

Table 2. Hydroformylation of Isoprene Catalyzed by $[Rh(COD)(OAc)]_2$/Diphosphines[a]

					selectivity (%)		
run	ligand	P/Rh	conversion (%)	S_{ald}[b] (%)	**2**	**3**	**4**
1	dppe	10	90	96	25	44	27
2	dppe	20	57	90	12	48	30
3	dppp	20	45	95	13	48	34
4	dppb	20	59	98	33	39	26
5	dppb	4	12	98	18	48	32
6	dppb	10	90	96	25	44	27
7	dppb	30	40	98	35	40	23
8[c]	dppb	20	100	90[c]	29	33	21

[a] Conditions: solvent benzene, isoprene (0.20 M), $[Rh(COD)(OAc)]_2$ (0.25 mM), 100 °C, 80 atm (CO/H_2 = 1/1); reaction time 4 h. dppe = 1,2-bis(diphenylphosphino)ethane, dppp = 1,4-bis(diphenylphosphino)propane, and dppb = 1,4-bis(diphenylphosphino)butane. [b] Selectivity for hydroformylation products **2**−**4**. [c] Temperature 120 °C. Aldehyde **5** was also formed (7%, included in S_{ald}).

Isoprene Hydroformylation with Rh/Diphosphine Systems. The substitution of PPh_3 by 1,2-bis(diphenylphosphino)ethane (dppe) also showed interesting results (Table 2). As mentioned in the Introduction, only diphosphines were reported to be used as auxiliary ligands in the rhodium-catalyzed hydroformylation of isoprene so far. Indeed at P/Rh = 10, the reaction is faster in the presence of diphosphine: the complete conversion occurs in 4 h instead of 10 h with PPh_3. However, at P/Rh = 20, the use of PPh_3 results in a much more efficient catalytic system (run 3 in Table 1 vs run 2 in Table 2). At higher ligand concentrations, the advantage of using PPh_3 over dppe for the catalyst activity becomes even more pronounced. To the best of our knowledge, all the previous attempts to hydroformylate isoprene in the presence of phosphorus ligands were carried out at P/Rh ratios not higher than 10 (mostly at P/Rh = 2−4).[2,8,9]

We also tested other diphosphines: 1,4-bis(diphenylphosphino)propane (dppp) and 1,4-bis(diphenylphosphino)butane (dppb) (Table 2). The results are quite similar to those with dppe, on both activity and selectivity. Nevertheless, the increased amounts of $\gamma-\delta$-unsaturated aldehyde **2** among the products

(24) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994.
(25) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.
(26) Peng, W. -J.; Train, S. G.; Howell, D. K.; Fronczek, F. R.; Stanley, G. G. *Chem. Commun.* **1996**, 2607.

Table 3. Hydroformylation of Isoprene Catalyzed by $[Rh(COD)(OAc)]_2/PPh_3$: Effect of Pressure[a]

run	$P(H_2)$ (atm)	$P(CO)$(atm)	rate[b] ($M\ h^{-1}$)
1	10	10	0.010
2	10	40	0.040
3	40	10	0.040
4	20	20	0.036
5[c]	40	40	0.152

[a] Conditions: solvent benzene, isoprene (0.20 M), $[Rh(COD)(OAc)]_2$ (0.25 mM), P/Rh = 80, 100 °C. [b] Initial rate of the conversion of isoprene. [c] A kinetic curve for this run (typical for all others) is presented in Figure 1 (P/Rh = 80).

with Rh/dppb should be mentioned. For this system, the effect of the ligand concentration was investigated in more detail.

At low P/Rh ratios, the addition of dppb significantly enhances the hydroformylation: 90% of isoprene was converted at P/Rh = 10, while only 12% was converted at P/Rh = 4 for the same period of 4 h. With a further dppb addition to P/Rh = 20 and then to P/Rh = 30, the reaction rate declines, resulting in 59% and 40% conversions, respectively (Table 2, runs 4−7). Thus, as in the case of PPh_3, there is a pronounced maximum on the "activity vs P/Rh ratio" correlation in the Rh/dppb system. However, the optimal P/Rh value, after which the ligand excess negatively affects the hydroformylation, is much lower with dppb (ca. 10) than with PPh_3 (ca. 80) at the same temperature of 100 °C. As a result, more active catalysts can be developed with PPh_3, a ligand of much better choice for industry than diphosphines.

Diphosphines as bidentate ligands usually give an enhanced preference for the formation of bis(phosphine)rhodium complexes. Therefore, they are expected to be more efficient than monophosphines in favoring the conversion of η^3-allyl- into η^1-allylrhodium complexes, where the CO insertion occurs easier. The accelerating effect of diphosphine ligands was observed in the hydroformylation of butadiene by van Leeuwen and coworkers,[2] and it was similarly rationalized. It has been suggested that with bidentate phosphine the formation of rhodium complexes with a geometry favorable for both η^1 coordination and acyl formation, i.e., phosphorus in a position *trans* to the η^3-allyl ligand and the η^1-allyl ligand *cis* to CO and *trans* to phosphorus, is much more probable. Thus, at relatively low P/Rh ratios the accelerating effect of diphosphines is greater than that of PPh_3. On the other hand, the inhibition effect due to blocking the coordination sites appears with chelating diphosphines at lower concentrations compared to that of PPh_3.

Isoprene Hydroformylation with Rh/PPh_3 Systems: Effect of Pressure. The remarkable difference in the behavior of isoprene vs alkenes and nonconjugated dienes in hydroformylation has become particularly pronounced in studying the effects of the gas pressure (Table 3). In general, under "common" hydroformylation conditions (10−50 atm, 70−120 °C), the reaction is zeroth order in hydrogen and a negative order in the concentration of CO, the ligand competing with alkene for a place on rhodium, likewise phosphine.[4] On the other hand, at low pressure, high rhodium concentrations, and low temperatures, a positive order in the hydrogen pressure can be observed due to the hydrogen requirement to cleave inactive dirhodium species and enter the catalytic cycle.[4]

Surprisingly, under the conditions we used, the increase in the pressure of both CO and hydrogen significantly accelerated the hydroformylation of isoprene. The reaction is ca. 16 times faster at 80 atm of the equimolar mixture of CO/H_2 than at 20 atm (cf. runs 1 and 5, Table 3). The kinetic data show that the reaction is roughly first order in both hydrogen and CO. Really, a 4-fold increase in the partial pressure of either hydrogen (run 1 vs run 3; run 2 vs run 5) or CO (run 1 vs run 2; run 3 vs run 5) leads to a 4-fold increase in the reaction rate. The positive order in hydrogen observed at relatively high pressures used in this work suggests that, in the case of isoprene, the oxidative addition of the hydrogen to the rhodium acyl intermediate seems to be the most likely rate-determining step (similarly to what was observed for linalool[16]). The effect of CO can be rationalized similarly to that of phosphorus ligands. As for dienes the ability of the catalyst to promote the $\eta^3-\eta^1$ rearrangement is of great importance for its catalytic activity, the concentration of any coordinating ligand is expected to positively affect the reaction rate. No substantial changes in the product distribution have been observed with varying pressure.

Reaction Mechanism. The reaction network is presented in Scheme 2. The structure of major aldehydes **2**−**4** and the dynamics of their accumulation show that they are primary reaction products resulting from the reaction of the rhodium catalyst with the less substituted C═C bond of isoprene. In a subsequent migration step, either *n*-alkyl or isoalkyl intermediates are formed as a result of anti-Markovnikov and Markovnikov additions of the metal hydride. The first, reacting with CO and hydrogen, evolves to "linear" aldehyde **2** (route A). Aldehydes **3** and **4** arise from η^3-allyl intermediate **a** formed by the rearrangement of the isoalkyl intermediate (route B). Since the aldehyde derived from the isoalkyl intermediate was not detected in reaction mixtures, it should be inferred that this rearrangement is faster than the CO insertion. This is consistent with the observation that a rhodium-catalyzed deuteroformylation of 1,3-butadiene has resulted in the formation of *1,5-d*$_2$-3-pentenal.[9] Furthermore, it has been found that rhodium η^3-allyl complexes are stable enough to be characterized by X-ray diffraction.[26−28]

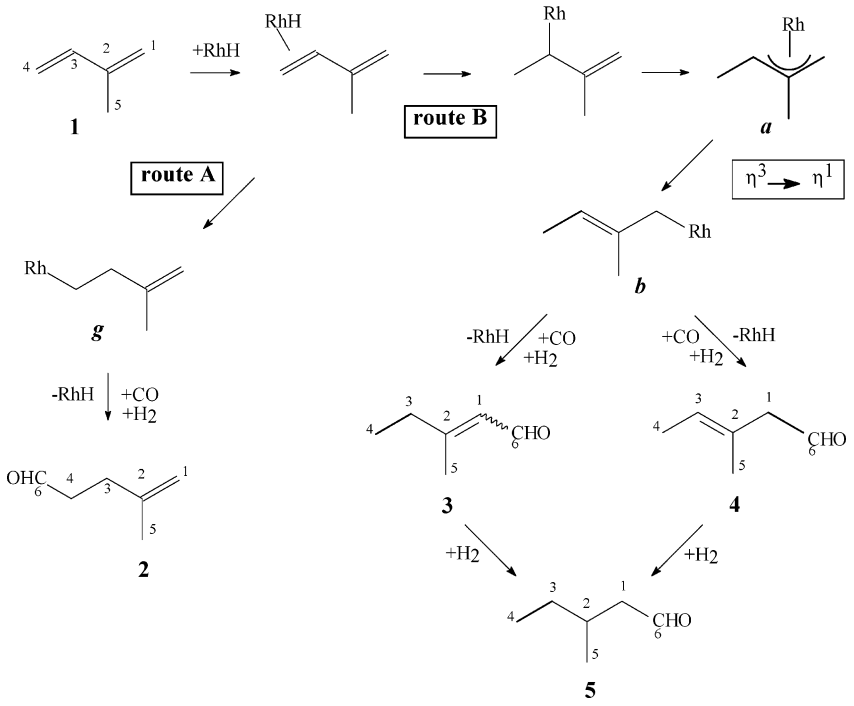
Although η^3-allylrhodium complexes are known to be rather resistant to the CO insertion, they can form η^1-allylrhodium species.[2,10] Thus, the products seem to be generated through η^1-allyl intermediate **b** instead of the direct carbonylation of η^3-allyl intermediate **a**. The formation of η^3-allyl-, η^1-allyl-, and acylrhodium complexes has been recently observed by HPIR in situ in the hydroformylation of some conjugated dienes including isoprene.[3,29]

A migratory insertion of CO in intermediate **b** followed by hydrogenolysis produces aldehyde **4**. The stereochemistry of the latter is determined in the $\eta^3-\eta^1$ rearrangment step or even earlier: at the formation of intermediate **a**. It seems reasonable that intermediates **a** and **b** with bulk rhodium-containing fragments *trans* to methyl group C-4 (as shown in Scheme 2) are sterically much more favorable. Expectedly, aldehyde **4** is formed almost exclusively as the *trans* isomer (*E*).

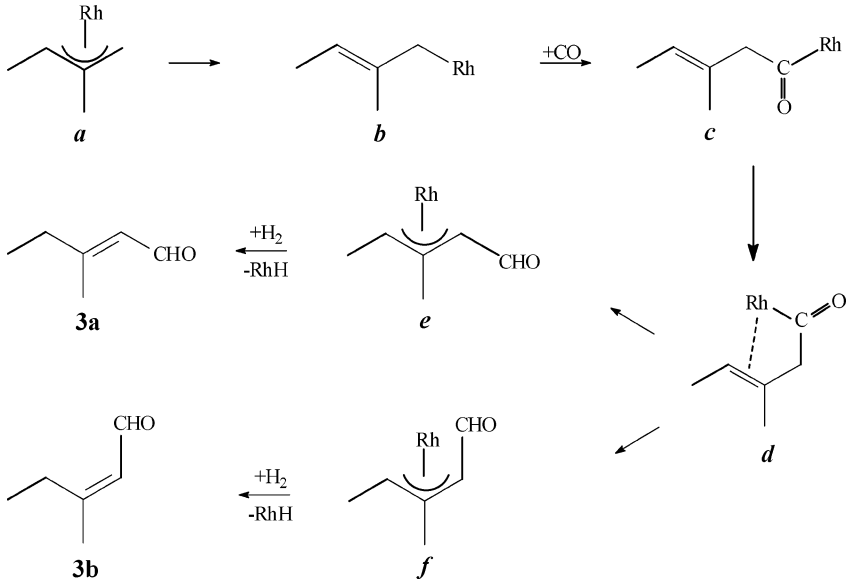
Although $\alpha-\beta$-unsaturated aldehyde **3** has the same carbon skeleton as $\beta-\gamma$-unsaturated aldehyde **4**, it is hardly formed by the isomerization of the latter, as it would require a highly unlikely *tert*-alkyl intermediate with rhodium bound to C-2. The isomerization of aldehyde **4**, in principle, could occur via a π-allylic mechanism. However, this alternative is also unlikely as the ratio between aldehydes **3** and **4** barely varies in all the runs as well as in the course of each reaction: they are accumulated simultaneously. Their ratio remained virtually unchanged even when the mixture was kept under the reaction

(27) Osakada, K.; Choi, J. C.; Koimuzi, T.; Yamaguchi, I.; Yamamoto, T. *Organometallics* **1995**, *14*, 4962.
(28) Choi, J. C.; Osakada, K.; Yamamoto, T. *Organometallics* **1998**, *17*, 3044.
(29) Chen, L.; Chew, W.; Garland, M. *Appl. Spectrosc.* **2003**, *57*, 491.

Scheme 2



Scheme 3



conditions after the complete conversion of isoprene, i.e., when the rhodium became available for substrates other than isoprene (the run described above). Therefore, aldehyde **3** does not appear to arise from a secondary reaction. We believe that it is also formed from η^1-allyl intermediate **b** via the same acyl intermediate, which gives both aldehydes **4** and **3** by parallel routes. A possible mechanism for the formation of **3** is shown in Scheme 3.

The migratory insertion of CO in intermediate **b** releases the vacant site on rhodium. The proximity of the alkene functionality in acyl intermediate **c** to rhodium opens the possibility of its coordination on this vacant site, forming chelate **d**, which then evolves to other η^3-allyl complexes **e** and **f**. Although the organometallic chemistry of this rearrangement is not clear so far and looks quite unusual, it can be formally rationalized as a hydrogen transfer from C-1 to carbonylic C-6. This transfer should be favored by the enhanced acidic character of the hydrogen at C-1 due to the neighborhood of the carbonyl group. A connection of rhodium with the carbonyl group in the course of this rearrangement makes the formation of isomer **f** more probable. Really, the major isomer of aldehyde **3** is *cis* compound **3b** (>80%) with the two bulkiest groups on the same side of the double bond. *Cis* isomer **3b** results from intermediate **f**, while intermediate **e** gives *trans* isomer **3a** (the minor one). Thus, we suppose that although aldehydes **3** and **4** are formed via common intermediate **c**, aldehyde **4** results from the direct hydrogenolysis of **c**, whereas the formation of aldehyde **3** requires previous rearrangement of **c** followed by hydrogenolysis.

We have observed that more than 80% of the products are formed by the "allylic" route B. In this route, the most critical step seems to be the $\eta^3-\eta^1$ rearrangment, which converts a resistant to CO insertion η^3-allyl complex **a** into the much more reactive η^1 intermediate **b**. The results of the present work

clearly show that this step can be strongly accelerated by the increase in the ligand (phosphine or CO) concentration and/or phosphine basicity. As conjugated dienes are highly reactive toward complex formation with rhodium (much more reactive than alkenes), isoprene successfully competes for rhodium even under such conditions. However, the formation of η^1 complexes becomes more favorable than that of η^3-allyl ones, since it requires only one coordination site.

It is noteworthy that in all the runs the distribution of aldehydes **2**−**4** remains roughly the same (**2**/(**3** + **4**) ≈ 20/80), indicating that route A also benefits from the presence of enhanced amounts of coordinating ligands. To rationalize this observation, we can consider at least two arguments. First, the ligand excess expectedly favors the formation of *n*-alkyl intermediate **g** from isoprene (route A) rather than the more sterically demanding isoalkyl complex (route B) (Scheme 2). Second, we suppose that intermediate **g** can be formed as a chelate, in which the alkene moiety is bound to the vacant site released during the previous migration step (likewise chelate **d** in Scheme 3). This chelate intermediate is expected to suffer certain restrictions for the CO insertion because the chelation would hinder the η^1-allyl fragment from migration to CO. The excess of coordinating ligands would prevent chelation by trapping the vacant sites released during the formation of intermediate **g** or would favor the cleavage of the chelating η^2-alkene−rhodium bond. Thus, both routes A and B (Scheme 2) benefit from the excess of coordinating ligands (up to a limit value), and the rate of the formation of all aldehydes increases to roughly the same extent.

Conclusions

The hydroformylation of isoprene can be readily performed under mild conditions (80−100 °C, 40−80 atm) with [Rh(COD)OAc]$_2$ as a catalyst precursor using a large excess of PPh_3 (P/Rh = 20−500). The study of the effects of the reaction variables revealed remarkable trends, opposite those usually observed with simple alkenes. The systems with more basic ligands show higher activities, and an increase in the P/Rh ratio to a limit value, which depends on the ligand nature and temperature, significantly accelerates the reaction. Moreover, the reaction shows unusual kinetics, being first order in both hydrogen and CO under common hydroformylation conditions. The data obtained confirm that the η^3−η^1 rearrangement, which converts a resistant to CO insertion η^3-allylrhodium complex into the much more reactive η^1 intermediate, is really the most critical step of this reaction.

Acknowledgment. We acknowledge CNPq, CAPES, and FAPEMIG for financial support and scholarships (H.J.V.B. and C.C.G.).

OM060994N