Mechanistic Aspects of Asymmetric Hydroformylation of Olefins Catalyzed by Chiral Phosphine−Phosphite−Rhodium(I) Complexes

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Effects of CO and H_2 partial pressures on the reaction rate and selectivity of asymmetric hydroformylation of 1-hexene and styrene were examined using an (*R,S*)-BINAPHOS−Rh^I complex as a catalyst ((*R,S*)-BINAPHOS = (*R*)-2-(diphenylphosphino)-1,1′-binaphthalen-2′-yl (*S*)-1,1′-binaphthalene-2,2′-diyl phosphite). For both substrates, the higher CO partial pressure inhibited the reaction, and the partial pressure of H_2 hardly affects the reaction rate (P_{H_2}, P_{CO} = 5−50 atm). In most cases, no serious change in the regio- and enantioselectivities was observed with variation of the H_2 and CO pressure. As an exception, the regioselectivity and enantioselectivity dropped to some extent for the reaction of styrene at 1 atm (H_2/CO = 1/1). Deuterioformylation experiments clearly demonstrate the irreversibility of the olefin-insertion step at total pressures of 20−100 atm (D_2/CO = 1/1). This fact proves that the regio- and enantioselectivity of the present hydroformylation should be controlled by the olefin-insertion step. This is the first example of highly enantioselective deuterioformylation under actual process conditions (30−60 °C, 1−100 atm). For the reaction of styrene at 1 atm, the olefin insertion becomes reversible to an extent, and the lower regioselectivity under these conditions can be rationalized by the degree of reversibility of olefin insertion to give the branched alkylrhodium intermediate, [Rh]$CH(CH_3)$Ph, being much greater than that to give the linear one, [Rh]CH_2CH_2Ph.

Introduction

Hydroformylation is one of the most important homogeneously catalyzed reactions for functionalization of C=C bonds. Among the transition metals employed for hydroformylation, rhodium is the most active one, and thus much effort has been devoted to elucidation of the mechanism of the rhodium-catalyzed hydroformylation.[1,2] Markó studied the reaction of 1-heptene catalyzed by $Rh_4(CO)_{12}$ and established that the hydrogenolysis of the acylrhodium intermediate is rate-determining at high CO pressure and that the coordination of CO to the alkylrhodium species becomes rate-determining at low CO pressure in the generally accepted Wilkinson mechanism.[4] Kinetic studies for the PPh_3−Rh^I system without excess triphenylphosphine demonstrate that hydrogenolysis is the rate-determining step, similar to the case of the unmodified system.[5] On the other hand, Cavalieri d'Oro investigated carefully the kinetics of the hydroformylation of propene catalyzed by a PPh_3−Rh^I complex in the presence of excess triphenylphosphine and established it to be zeroth order in both CO and H_2 concentrations.[6] This excludes the hydrogenolysis of the acyl intermediate as being rate-determining. Recently van Leeuwen studied the hydroformylation of 1-octene in the presence of an excess amount of bulky phosphite, tris(2-*tert*-butylphenyl) phosphite, as a ligand, for which the kinetics is similar to that for an unmodified system.[2] Thus, modified catalyst systems sometimes behave differently according to the nature and amount of the ligand employed.

In contrast to those achiral catalyst systems, the mechanistic aspects of asymmetric hydroformylation have not been adequately established, probably due to the lack of an efficient catalytic system. In addition, the effect of the hydrogen and carbon monoxide partial pressures have been carefully reported in only a few cases.[7] Recently, van Leeuwen reported the positive effect of H_2 and the negative effect of CO on the reaction rate of hydroformylation of styrene using bisphosphite ligands derived from 2,4-pentanediol[8a] and sugars.[8b]

Regio- and enantioselectivities of asymmetric hydroformylation are generally believed to be determined by an alkylrhodium-forming step. On the basis of this

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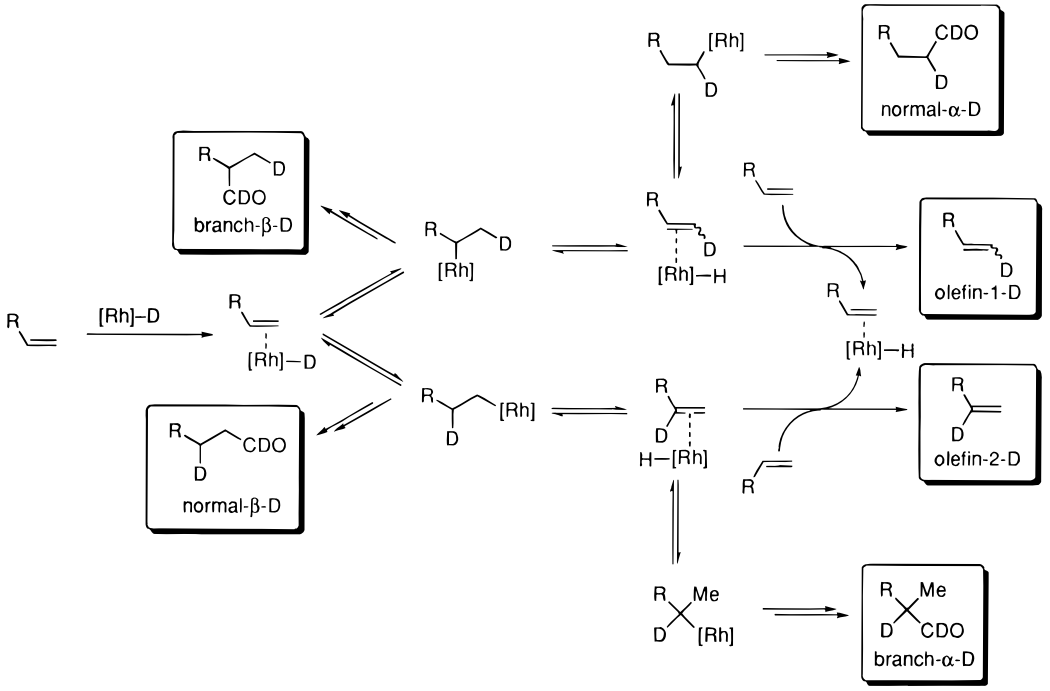
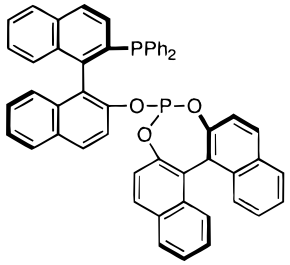
Scheme 1



consideration, the origin of the enantioselectivity of asymmetric hydroformylation has been discussed with the simple model proposed by Pino and Consiglio.[9] However, if this step is reversible, a difference in the reactivity of the intermediates would affect the selectivities of the hydroformylation. Deuterioformylation provides a very useful probe to distinguish whether alkylrhodium formation is reversible (Scheme 1).[10−12] Lazzaroni et al. studied deuterioformylation of various olefins catalyzed by $Rh_4(CO)_{12}$ and concluded that the formation of alkylrhodium species is irreversible at room temperature but that it becomes reversible at higher temperatures (≥80 °C), mainly for the branched species.[10] On the other hand, deuterioformylation with modified catalyst systems has been investigated to a much smaller extent.[11] To the best of our knowledge, there has been no report on rhodium-catalyzed asymmetric deuterioformylation under actual process conditions.[13]

We have demonstrated that the (*R*,*S*)-BINAPHOS−Rh^I complex is an excellent catalyst for enantioselective hydroformylation of a variety of prochiral olefins ((*R*,*S*)-BINAPHOS = (*R*)-2-(diphenylphosphino)-1,1′-binaphthalen-2′-yl (*S*)-1,1′-binaphthalene-2,2′-diyl phosphite; (*R*,*S*)-**1**).[14] In this article, we examined the reversibility



(*R*,*S*)-BINAPHOS [(*R*,*S*)-**1**]

of the alkylrhodium formation using this catalyst system to gain deeper insights into the mechanistic aspects of asymmetric hydroformylation, especially the origin of the regio- and enantioselectivity, in conjunction with the effect of the reaction conditions on the reaction rate and selectivity.

Results

Pressure Effect on Asymmetric Hydroformylation. For all substrates, a 100% conversion could eventually be reached. In order to compare the results properly, the reactions were stopped after a partial conversion of the substrate. The reaction rates were compared on the basis of the conversions after the same reaction time for each substrate.

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(13) Recently, we reported asymmetric deuterioformylation of 4,4,4-triphenyl-1-butene catalyzed by a (*R*,*S*)-**1a**−Rh^I complex.[11d] However, this compound is a rather unusual substrate that has a bulky substituent on the allylic position, and the reaction pressure was very low (P_{D_2}, P_{CO} = 0.5−5 atm).

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Table 1. Pressure Effect on Hydroformylation of 1-Hexene (2a) Catalyzed by (*R,S*)-BINAPHOS−Rh^{I} Complexes[a]

run no.	P_{H_2}, atm	P_{CO}, atm	conversion,[b] %	**3a**/**4a**[b]	ee of **3a**,[c] % (confign)
1	50	50	16	24/76	82 (*R*)
2	30	30	26	25/75	82 (*R*)
3	10	10	44	25/75	83 (*R*)
4	5	5	56	25/75	82 (*R*)
5[d]	0.5	0.5	38	23/77	81 (*R*)
6	10	50	19	22/78	83 (*R*)
7	50	10	48	25/75	82 (*R*)
8	5	10	37	26/74	83 (*R*)

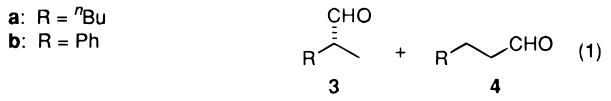
[a] Reactions were carried out with 9.6 mmol of **2a** in benzene (1.5 mL) in a 50 mL autoclave at 30 °C for 24 h. Each run was duplicated to ensure consistency. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by GLC analysis of the corresponding acids using a chiral capillary column. [d] Carried out in a 20 mL Schlenk tube.

Table 2. Pressure Effect on Hydroformylation of Styrene (2b) Catalyzed by (*R,S*)-BINAPHOS−Rh^{I} Complexes[a]

run no.	P_{H_2}, atm	P_{CO}, atm	conversion,[b] %	**3b**/**4b**[b]	ee of **3b**,[c] % (confign)
1	50	50	15	89/11	94 (*R*)
2	20	20	30	89/11	93 (*R*)
3	10	10	40	90/10	94 (*R*)
4	5	5	52	90/10	94 (*R*)
5[d]	0.5	0.5	15	83/17	89 (*R*)
6	10	50	16	89/11	94 (*R*)
7	50	10	43	90/10	94 (*R*)
8	5	10	45	88/12	94 (*R*)

[a] Reactions were carried out with 9.6 mmol of **2b** in benzene (1.5 mL) in a 50 mL autoclave at 40 °C for 5 h. Each run was duplicated to ensure consistency. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by GLC analysis of the corresponding acids using a chiral capillary column. [d] Carried out in a 20 mL Schlenk tube.

First, 1-hexene (**2a**) was chosen as a standard simple olefin substrate (eq 1 and Table 1). Side reactions such



as hydrogenation and isomerization of the substrate did not take place in all runs. No serious change in the regio- or enantioselectivity was observed. With a 1:1 mixture of H_2 and CO, decrease in the total pressure causes a significant enhancement of the reaction rate in the pressure range of 10−100 atm (runs 1−4). At 1 atm, the reaction is rather slow (run 5).

The higher CO partial pressure obviously slows down the reaction at constant H_2 pressures (runs 1 and 7, 3 and 6, 4 and 8). The reaction rate is enhanced only slightly by increasing H_2 partial pressure at 10 atm of CO (runs 3, 7, and 8) and is almost independent of the H_2 pressure at 50 atm of CO (runs 1 and 6).

Next, we employed styrene (**2b**) as a substrate, which favors the branched aldehyde formation from hydroformylation (Table 2). Again, products from hydrogenation or polymerization were not formed in any of the runs. Similar to the case of **2a**, the reaction rate is decreased with increasing CO partial pressure and is

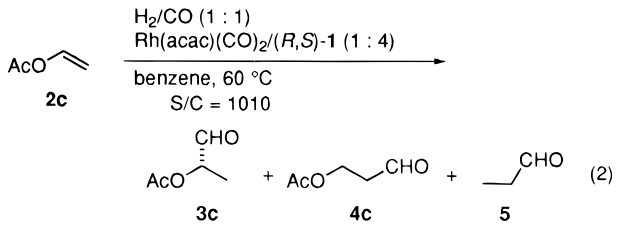
Table 3. Asymmetric Hydroformylation of Vinyl Acetate (2c) Catalyzed by (*R,S*)-BINAPHOS−Rh^{I} Complexes[a]

run no.	*P*, atm	time, h	conversion,[b] %	**3c**/**4c**/**5**[b]	ee of **3c**,[c] % (confign)
1	100	6	16	87/13/0	91 (*S*)
2	20	6	62	87/12/1	92 (*S*)
3	20	13	94	88/8/4	91 (*S*)
4[d]	1	6	7	90/3/7	89 (*S*)

[a] Reactions were carried out with 9.7 mmol of **2c** in benzene (1.5 mL) under a 1:1 mixture of H_2 and CO in a 50 mL autoclave at 60 °C. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by ^{1}H NMR spectroscopy in chloroform-*d* using Eu(hfc)$_3$ as the chiral shift reagent. [d] Carried out in a 20 mL Schlenk tube.

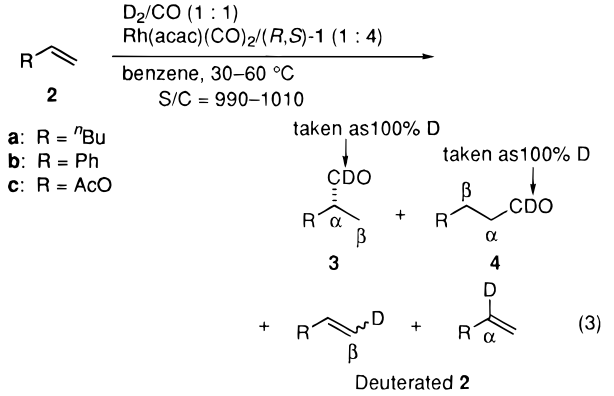
hardly affected by variation of H_2 partial pressure (P_{H_2}, P_{CO} = 5−50 atm). No significant change in the regio- or enantioselectivity is observable in this pressure range. However, in contrast to the case of **2a**, both the regio- and enantioselectivities have dropped to some extent in the reaction at 1 atm (run 5). The reaction rate is also lowered under this condition.

The hydroformylation of vinyl acetate (**2c**) is also faster at 20 atm than at 100 and 1 atm (eq 2 and Table 3). At a lower pressure, decomposition of **4c** took place



to give acetic acid and acrolein. Acrolein was hydrogenated to propanal (**5**) under the reaction conditions.[7c] The content of **5** is increased by a prolonged reaction time (run 3). The decomposition of **4c** is also significant in the reaction at 1 atm (run 4). At 100 atm, **5** was not observed even at a longer reaction time.[14a,e] The regioselectivity, **3c**/(**4c** + **5**), and enantioselectivity of the reaction are not significantly changed by variation of the total pressure.

Deuterioformylation. Deuterioformylation experiments were carried out in a way similar to that for hydroformylation using a 1:1 mixture of D_2 and CO (eq 3). The conversion and selectivity of the deuterioformy-



lation of **2a**−**c** are summarized in Table 4. In all runs, the reaction rate is lower than that of hydroformylation under identical conditions. It might be attributed to the kinetic isotope effect of deuterium. The regio- and enantioselectivities of the deuterioformylation of **2b** are

Table 4. Deuterioformylation of Olefins 2a−c Catalyzed by (*R,S*)-BINAPHOS−Rh^{I} Complexes[a]

run no.	substrate	temp, °C	*P*, atm	time, h	conversion,[b] %	**3**/**4**[b]	ee of **3**,[c] % (confign)
1	**2a**	30	100	48	18	18/82	77 (*R*)
2	**2a**	30	20	24	19	21/79	77 (*R*)
3[d]	**2a**	30	1	24	22	19/81	77 (*R*)
4	**2b**	40	100	13	12	88/12	92 (*R*)
5	**2b**	40	20	5	15	88/12	93 (*R*)
6[d]	**2b**	40	1	5	6.4	82/18	90 (*R*)
7	**2c**	60	100	17	13	81/19	ND[e]
8	**2c**	60	20	6	36	81/19	ND[e]

[a] Reactions were carried out with 9.6 mmol of **2a**,**b** or 9.7 mmol of **2c** in benzene (1.5 mL) in a 50 mL autoclave under a 1:1 mixture of D_2 and CO. Each run was duplicated to ensure consistency. [b] Determined by GLC analysis. [c] Determined by GLC analysis of the corresponding acids using a chiral capillary column. [d] Carried out in a 20 mL Schlenk tube. [e] Not determined.

Table 5. Deuterium Content of the Products 3 and 4 and the Recovered Substrate 2 from the Deuterioformylation of 2a−c[a]

				4[b]		**2**	
run no.	substrate	*P*, atm	**3**[b,c] % D on β	% D on β	% D on α	% D on β[d]	% D on α[e]
1	**2a**	100	103 (98)	103 (99)	<0.1	1	3
2	**2a**	20	90 (97)	100 (101)	<0.1	2	5
3	**2a**	1	91	98	<0.1	2	5
4	**2b**	100	101	94	<0.1	1	1
5	**2b**	20	101	97	<0.1	1	2
6	**2b**	1	78	69	4	27	3
7	**2c**	100	98	92	<1	<1	<1
8	**2c**	20	105	97	<1	<1	<1

[a] Determined by $^2H\{^1H\}$ NMR spectroscopy of the crude reaction mixture. The values obtained by ^2H NMR of the isolated samples are shown in parentheses. [b] Based on the formyl group as 100% D. [c] Deuterium content on the α-carbon of **3a**,**b** was estimated to be <0.1%, and that of **3c** was estimated to be <1% (see text). [d] Based on the formyl group of **3**. [e] Based on the formyl group of **4**.

similar to those of hydroformylation, but selectivity to **3** and enantioselectivity are slightly lower for **2a** and **2c**. The reason for such a deviation of the selectivities is unclear. These results are different from those with bisphosphine ligands reported by Casey and Petrovich, in which the reaction rate and selectivity of deuterioformylation of 1-hexene are similar to those for hydroformylation.[11c]

The crude reaction mixture was directly analyzed by ^2H NMR spectroscopy without any handling or treatment, as described by Lazzaroni.[10e] Deuterium distribution in the products **3** and **4** was evaluated by integration of the respective signals, using the resonance of the formyl groups of the products as internal references. Absence of the formyl proton was confirmed by ^1H NMR analysis. As shown in Table 5, deuterium label was incorporated exclusively in the formyl group and the position β to the formyl group of all products from the deuterioformylation at total pressures of 20 and 100 atm. For **3a** and **4a**, deuterium distribution was also measured for the isolated samples, and the results are shown in parentheses. Deuterium incorporation in the position α to the formyl group was not detected by ^2H NMR for **3a**,**b** and **4a**−**c** and was estimated to be less than 0.1%. The deuterium incorporation in the α-carbon of **3c** was estimated to be less than 1% (see Experimental Section).

In the case of **2a**, deuterium label was also not observed on the α-carbon of the products **3a** and **4a** from the deuterioformylation at 1 atm (run 3). On the other hand, from the deuterioformylation of styrene at 1 atm, the deuterium enrichment on the β-carbon of both products is significantly lower than on the formyl group (run 6). A small amount of deuterium was also detected on the α-carbon of **4b** (4%). No enrichment of deuterium was observed on the α-carbon of **3b**. Deuterioformylation of **2c** was not carried out at 1 atm because the decomposition of **4c** to **5** predominated under this condition (*vide supra*).

For the recovered substrate **2a**−**c**, only the vinyl resonance in ^2H NMR showed deuterium enrichment. Since deuterium label on the carbon β to R (β-carbon) of **2** should come from β-elimination of the branched alkylrhodium species and that on the α-carbon (α to R) should come from the linear one (Scheme 1), the amount of deuterium on the β-carbon is described according to moles of **3** formed and that on the α-carbon according to moles of **4**. As shown in Table 5, only a small amount of incorporation of deuterium in the recovered **2a**−**c** was observed from the deuterioformylation at 20 and 100 atm. In contrast, a large amount (27% to **3b**) of deuterium was observed on the β-carbon of **2b** from the deuterioformylation at 1 atm (run 6). Notably, such a large deuterium enrichment was observed only on the β-carbon. Similar amounts of deuterium were incorporated in the recovered **2a** from the deuterioformylations at 1−100 atm. For **2a**,**b**, the amount of the deuterated substrate is much larger than that of the α-deuterated aldehydes in all runs.

Discussion

Effect of Partial Pressures of Hydrogen and Carbon Monoxide on the Reaction Rate and Selectivity. A plausible mechanism for (*R,S*)-**1**−Rh^{I} complex-catalyzed hydroformylation is proposed in Scheme 2 based on Wilkinson's mechanism.[4] As mentioned above, the reaction rate of the present hydroformylation showed an inverse dependence on the CO partial pressure at more than 5 atm for both **2a** and **2b**. According to the presented mechanism, the inhibition by CO can be attributed to the deactivation of the catalytically active species by forming **I′** and **V′**. For all the substrates tested, the reaction was slow at 0.5 atm of CO, particularly for **2b** and **2c**. This fact suggests that the coordination of CO to **III** may become rate-determining at a low CO pressure.[1,3] It has been pointed out that the 1-phenylethyl group in **III** (R = Ph) from **2b** can coordinate in an η^3 fashion (**IIIa**) (*vide infra*).[7b,15] In the case of **2c**, the carbonyl group can coordinate to the metal in **III** (R = AcO).[16] For these reasons, the coordination of CO to **III** should be prevented at a low CO partial pressure, particularly in the reaction of **2b** and **2c**.

The effect of H_2 partial pressure indicates no participation of H_2 in the rate-determining step; that is, hydrogenolysis of the acylrhodium species (**V** → **I**) may be excluded as being rate-determining. The regio- and enantioselectivities were not affected by variation of the H_2 and CO partial pressures, except for the reaction of

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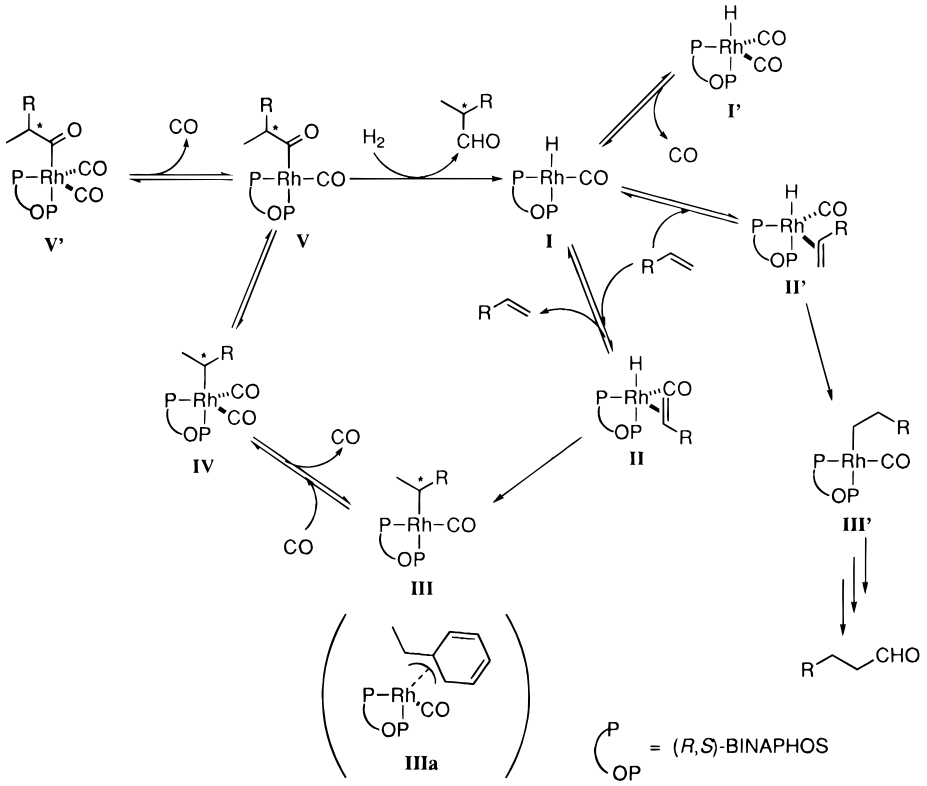
Scheme 2. Proposed Mechanism of Hydroformylation Catalyzed by the (*R,S*)-BINAPHOS−Rh^{I} Complex



2b at 1 atm. These results on the pressure effect are different from those with chiral bisphosphite ligands reported by van Leeuwen, in which the higher H_2/CO ratio caused significant rate enhancement and decrease in the selectivities.[8] This can be accounted for by the difference in the structure and electronic properties of the ligands. In particular, these bisphosphite ligands are established to form the hydridorhodium complexes $RhH(CO)_2$(bisphosphite), with both phosphorus atoms coordinating to the equatorial sites.[8,17] On the other hand, (*R,S*)-**1** forms the related hydridorhodium complex **I′** (Scheme 2), in which the phosphine moiety is located at the equatorial site and the phosphite moiety at the apical site.[14a,e] Therefore, the difference in the ligand orientation in the intermediates should cause these differences in the behavior of the catalysts.

Reversibility of Alkylrhodium Formation. The exclusive incorporation of the deuterium label in the formyl group and the position β to the formyl group of the products clearly exhibits the largely irreversible olefin insertion in the present hydroformylation at 20−100 atm. It proves that the regio- and enantioselectivities of the reaction are set by the insertion of the olefin into Rh−H bond.[18] The amount of the deuterated substrates was very small but was much larger than that of the α-deuterated aldehydes for **2a**,**b**. This fact indicates that the olefin insertion is reversible and that the interconversion of the rhodium-olefin complexes **II** and **II′** (Scheme 2) may require the dissociation of the coordinated olefin.

In the reaction of **2a**, olefin insertion was still virtually irreversible also at 1 atm. From the deuterioformylation of **2b** at 1 atm, however, a considerable amount of deuterium (27% to **3b**) on the β-carbon of **2b** was observed. This fact demonstrates that at least 27% of the branched alkylrhodium intermediate **III** reverts to the olefin complex **II** under this condition (Scheme 2). The important feature of this result is that the reversibility is significant only for the formation of the branched isomer, as demonstrated by much more deuterium enrichment on the β-carbon than on the α-carbon of **2b**. Thus, the lower regioselectivity of the hydroformylation of **2b** at 1 atm can be rationalized by a much higher reversibility for the formation of the branched alkylrhodium intermediate. The lower enantioselectivity under this condition indicates that the rate of the β-elimination or the steps after olefin insertion may be different between the diastereomeric intermediates.

Such a greater degree of reversibility of the branched alkylrhodium formation was also seen for the other catalytic systems.[10,11c] van Leeuwen explained the susceptibility toward the β-elimination of the (1-phenylethyl)rhodium intermediate at a low CO pressure in relation to a resonance-stabilized species such as **IIIa** (Scheme 2),[2] which is considered to be responsible for the strong preference of **2b** to form the branched aldehyde **3b**.[7b,15] When the olefin insertion leads to a coordinatively unsaturated alkylrhodium species such as **III**, the vacant site will be rapidly occupied by CO, and thus the intermediate cannot revert to the olefin complex **II**. For the 1-phenylethyl complex, this unsaturation can be released by coordination in an η^3 fashion (**IIIa**). Thus, the coordination of CO may be retarded

(17) Recently, an X-ray crystallographic study was reported for the related hydridorhodium complex of a bisphosphite ligand: van Rooy, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Veldman, N.; Spek, A. L. *J. Organomet. Chem.* **1995**, *494*, C15.

(18) In many cases, insertion of CO into a metal−alkyl bond proceeds with retention of stereochemistry at a carbon atom of the migrating alkyl group.[19] For the present hydroformylation, the possibility of racemization can be ruled out by the high enantioselectivity of the reaction.

(19) (a) Bock, P. L.; Boschette, D. J.; Rasmussen, J. R.; Demers, J. P.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 2814. (b) Lau, K. S.; Wong, P. K.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 5232.

at a low CO partial pressure, and deinsertion of **2b** may be facilitated.

Conclusion

The reaction was not accelerated by the high pressure of H_2 in the present hydroformylation. This result is different from that with the chiral bisphosphite ligands reported by van Leeuwen. Deuterioformylation results clearly demonstrate almost no reversibility of the alkylrhodium-forming step at 20−100 atm. Thus, it is established that the regio- and enantioselectivities are set by the alkylrhodium-forming step. For the reaction of 1-hexene, alkylrhodium formation was irreversible also at 1 atm. On the other hand, alkylrhodium formation becomes reversible in the reaction of styrene at 1 atm, mainly for the branched species. It accounts for the lower regioselectivity from the reaction under this condition. The lower enantioselectivity under this condition indicates that the rate of the β-elimination or the steps after alkylrhodium formation may be different between the diastereomeric intermediates. Thus, irreversibility of the alkylrhodium formation should be essential in achieving the high enantioselectivity in the asymmetric hydroformylation.

Experimental Section

General Comments. All manipulations of oxygen- and moisture-sensitive materials were conducted under a purified argon atmosphere (deoxygenated by BASF catalyst RC-11 at 80 °C and dried by molecular sieves 3A) by use of standard Schlenk techniques. Chemical shifts of NMR spectra were referred to tetramethylsilane (^{1}H) and benzene-d_6 (^{2}H) as internal standards. Benzene was purified by distillation over sodium benzophenone ketyl or calcium hydride under argon and degassed by three freeze−thaw cycles before use. 1-Hexene (**2a**) was distilled over calcium hydride and degassed by freeze−thaw cycles. Styrene (**2b**) and vinyl acetate (**2c**) were purified by vacuum distillation prior to use. (*R*,*S*)-BINAPHOS ((*R*,*S*)-**1a**) was prepared by a known procedure.[14a,e] Commercial Rh(acac)(CO)$_2$ (Aldrich) was used as received.

Asymmetric Hydroformylation of 1-Hexene (2a). Representative Procedure for the Asymmetric Hydroformylation at High Pressures (10−100 atm). A 50-mL stainless-steel autoclave equipped with a stirbar was charged with Rh(acac)(CO)$_2$ (2.5 mg, 0.0097 mmol) and (*R*,*S*)-**1** (29.8 mg, 0.0388 mmol) under argon. To this was added benzene (1.5 mL), and the system was pressurized to 20 atm with a 1:1 mixture of H_2 and CO. After the mixture was stirred by magnetic stirrer at 30 °C for 1 h, the pressure was released, and then **2a** (1.2 mL, 9.6 mmol) was introduced with a gastight syringe. The mixture was stirred at 30 °C for 24 h under an atmosphere of H_2 and CO. The conversion and regioselectivity of the reaction were determined by ^{1}H NMR spectroscopy of the crude reaction mixture without evaporation of the solvent. Enantiomeric excesses of **3a** and **3b** were determined by GLC analysis of the corresponding carboxylic acid derived by treatment of the product with CrO_3 in aqueous acetone (Jones oxidation) using a chiral capillary column (Chrompack Cp-Cyclodex β-236M; 0.25 mm × 25 m). The enantiomeric excess of **3c** was determined by ^{1}H NMR spectroscopy in chloroform-*d* using Eu(hfc)$_3$ as a chiral shift reagent.

Asymmetric Hydroformylation of 1-Hexene at 1 atm. Representative Procedure for the Asymmetric Hydroformylation at 1 atm. A 20 mL Schlenk tube, equipped with a magnetic stirring bar and a three-way stopcock, was charged with benzene (1.5 mL), Rh(acac)(CO)$_2$ (2.5 mg, 0.0097 mmol), and (*R*,*S*)-**1** (29.8 mg, 0.0388 mmol) under argon. The resulting solution was degassed by three freeze−thaw cycles, and finally the Schlenk tube was refilled with H_2/CO (1 atm). After the solution was stirred at 30 °C for 12 h, **2a** (1.2 mL, 9.6 mmol) was introduced, and then the solution was stirred at 30 °C for 24 h.

Deuterioformylation Procedure. Deuterioformylation was performed in the same manner as hydroformylation, using a 1:1 mixture of D_2 and CO in place of H_2 and CO. The conversion and regioselectivity of the reaction were determined by GLC analysis of the crude reaction mixture using a 40 m × 1.2 mm PEG capillary column. Deuterium contents of the aldehydes and the recovered substrates were determined by ^{2}H{^{1}H} NMR spectroscopy of the crude reaction mixture without any handling or treatment.[10e] Recovery and purification of 2-methylhexanal (**3a**) and heptanal (**4a**) were carried out by preparative gas chromatography (3 m × $^1/_4$ in. 15% poly(propylene glycol adipate) on 60/80 Uniport B column) as described by Casey and Petrovich.[11c]

NMR Analysis of 2-(Acetyloxy)propanal (3c) and 3-(Acetyloxy)propanal (4c) from Deuterioformylation of Vinyl Acetate (2c). ^{2}H{^{1}H} NMR (C_6H_6, 61.3 MHz): δ 0.94 (s, AcOCH(CH_2D)CDO, **3c**), 3.98 (s, AcOCH*D*CH_2CDO, **4c**), 9.12 (s, AcOCH(CH_2D)C*D*O, **3c**), 9.25 (s, AcOCHDCH_2C*D*O, **4c**). Because of the incomplete separation of the signals of deuterium on the α-carbon of **3c** in ^{2}H NMR, deuterium enrichment on the α-carbon of **3c** and on the β-carbon of **2c** cannot be strictly excluded, but they were estimated to be less than 1% on the basis of the integration value of the unresolved signals.

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