Highly Enantioselective Hydroformylation of Olefins Catalyzed by Rhodium(I) Complexes of New Chiral Phosphine−Phosphite Ligands

Kyoko Nozaki,* Nozomu Sakai, Tetsuo Nanno, Takanori Higashijima, Satoshi Mano, Toshihide Horiuchi, and Hidemasa Takaya[†]

Contribution from the Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-01, Japan

Received January 6, 1997[⊗]

Abstract: A new chiral phosphine−phosphite ligand, (*R*)-2-(diphenylphosphino)-1,1′-binaphthalen-2′-yl (*S*)-1,1′-binaphthalene-2,2′-diyl phosphite [(*R*,*S*)-BINAPHOS, (*R*,*S*)-**2a**], was synthesized. Its Rh(I) complex was prepared, and its structure has been characterized by ^{1}H and ^{31}P NMR spectroscopy. Using Rh(I) complexes of (*R*,*S*)-**2a** and its enantiomer, highly enantioselective hydroformylation of styrene has been performed (94% ee, iso/normal = 88/12). The catalyst system was also effective for a variety of other olefins. Some other phosphine−phosphite ligands bearing 1,1′-binaphthyl and biphenyl backbones, such as (*S*)-3,3′-dichloro-6-(diphenylphosphino)-2,2′,4,4′-tetramethylbiphenyl-6′-yl (*R*)-1,1′-binaphthalene-2,2′-diyl phosphite [(*S*,*R*)-BIPHEMPHOS, (*S*,*R*)-**5a**], (*R*,*R*)-**2a**, (*R*,*S*)-**2b**, (*R*)-**2c**, and (*R*)-**5b**, were tested for asymmetric hydroformylation. The results indicate that the sense of enantioface selection for the prochiral olefins is mainly determined by the absolute configuration of the phosphine site, for example, the (*R*)-2-(diphenylphosphino)-1,1′-binaphthalen-2′-yl group in (*R*,*S*)-**2a**. The relative configurations of the two biaryl groups in the phosphine−phosphites play crucial roles in the degree of the enantioselectivities, that is, the (*R**,*S**)-isomer generally gives products in high ee's and the (*R**,*R**)-isomer does in low ee's. Treatment of Rh(acac)[(*R*,*S*)-**2a**] with a 1:1 mixture of carbon monoxide and hydrogen gave a hydridorhodium complex, RhH(CO)$_2$[(*R*,*S*)-**2a**], as a single species. Trigonal bipyramidal structure is suggested for this complex, in which the hydride and the phosphite moiety are located at the apical positions and the phosphine and the two carbonyls occupy the equatorial positions. The interchange of the phosphine and the phosphite sites with each other through rapid pseudorotations has not been observed in RhH(CO)$_2$[(*R*,*S*)-**2a**]. The structural deviations of the monohydride complexes from an ideal trigonal bipyramid seem to be larger in (*R**,*R**)-isomers than in the corresponding (*R**,*S**)-isomers. The existence of only one active species involved in the Rh(I)−(*R*,*S*)-**2a**-catalyzed hydroformylation has been manifested by the plot of ln([*R*]/[*S*]) of the hydroformylation product vs the reciprocals of the reaction temperatures. The higher thermodynamic stability of Rh(acac)[(*R*,*S*)-**2a**] than its diastereomer Rh(acac)[(*R*,*R*)-**2a**] is demonstrated in relation to the restricted configuration of (*R*)-**2c** to (*R*,*S*)-**2c** in its complex formation with Rh(I).

Introduction

Optically active aldehydes are very important as precursors not only for biologically active compounds but also for new materials such as biodegradable polymers and liquid crystals. Asymmetric hydroformylation has been attracting much attention as a potential synthetic tool for the preparation of enantiomerically pure aldehydes. Because hydroformylation seems to be attainable only with man-made catalysts, extensive efforts have been made to develop new chiral transition-metal catalysts.[1] Various chiral ligands are used in combination with transition metal ions, especially, Pt(II)[2] and Rh(I).[3−5]

The first highly enatioselective examples of asymmetric hydroformylation have been reported with styrene using Pt(II).[2a,b] In 1991, Consiglio and his coworkers achieved the highest level of optical purity up to 86% using a chiral bisphosphine complex of $PtCl_2$ as a catalyst in combination with $SnCl_2$. In spite of the high enantioselectivities established with

[†] Deceased on Oct 4, 1995.

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1997.

(1) Review articles for asymmetric hydroformylation: (a) Agbossou, F.; Carpentier, J.-F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485. (b) Gladiali, S.; Bayón, J. C.; Claver, C. *Tetrahedron: Asymmetry* **1995**, *6*, 1453. (c) Consiglio, G. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH Publishers Inc.: New York, 1993; p 273. (d) Botteghi, C.; Paganelli, S.; Schionato, A.; Marchetti, M. *Chirality* **1991**, *3*, 355. (e) Stille, J. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, p 927. (f) Ojima, I.; Hirai, K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Orlando, 1985; Vol. 5, p 126. (g) Consiglio, G.; Pino, P. *Top. Curr. Chem.* **1982**, *105*, 77. (h) Pino, P.; Consiglio, G.; Botteghi, C.; Salomon, C. *Adv. Chem. Ser.* **1974**, *132*, 295.

(2) Recent examples with Pt(II)−chiral phosphine complexes: (a) Consiglio, G.; Nefkens, S. C. A.; Borer, A. *Organometallics* **1991**, *10*, 2046. (b) Stille, J. K.; Su, H.; Brechot, P.; Parrinello, G.; Hegedus, L. S. *Organometallics* **1991**, *10*, 1183. (c) Consiglio, G.; Nefkens, S. C. A. *Tetrahedron: Asymmetry* **1990**, *1*, 417. (d) Kollár, L.; Kégel, T.; Bakos, J. *J. Organomet. Chem.* **1993**, *453*, 155. (e) Kollár, L.; Sandor, P.; Szalontai, G. *J. Mol. Catal.* **1991**, *67*, 191. (f) Tóth, I.; Guo, I.; Hanson, B. E. *Organometallics* **1993**, *12*, 848. (g) Gladiali, S.; Fabbri, D.; Kollár, L. *J. Organomet. Chem.* **1995**, *491*, 91. (h) Bandini, A. L.; Banditelli, G.; Cesarotti, E.; Minghetti, G.; Nowogrocki, G.; Wignacourt, J. P. *Inorg. Chem.* **1992**, *31*, 391. (i) Pottier, Y.; Mortreux, A.; Petit, F. *J. Organomet. Chem.* **1989**, *370*, 333. (j) Naili, S.; Carpentier, J.-F.; Agbossou, F.; Mortreux, A.; Nowogrocki, G.; Wignacourt, J. P. *Organometallics* **1995**, *14*, 401. (k) Parrinello, G.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7122. (l) Consiglio, G.; Kollár, L.; Kölliker, R. *J. Organomet. Chem.* **1990**, *396*, 375. (m) Kollár, L.; Consiglio, G.; Pino, P. *J. Organomet. Chem.* **1987**, *330*, 305. (n) Haelg, P.; Consiglio, G.; Pino, P. *J. Organomet. Chem.* **1985**, *296*, 281. (o) Pittman, C. U., Jr.; Kawabata, Y., Flowers, L. I. *J. Chem. Soc., Chem. Commun.* **1982**, 473. (p) Scrivanti, A.; Beghetto, V.; Bostianini, A.; Matteoli, U.; Menchi, G. *Organometallics* **1996**, *15*, 4687.

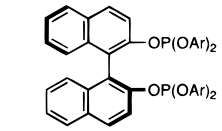
(3) Recent examples with Rh(I)−chiral phosphine complexes: (a) Hobbs, C. F.; Knowles, W. S. *J. Org. Chem.* **1981**, *46*, 4422. (b) Gladiali, S.; Pinna, L. *Tetrahedron: Asymmetry* **1990**, *1*, 693. (c) Gladiali, S.; Pinna, L. *Tetrahedron: Asymmetry* **1991**, *2*, 623. (d) Becker, Y.; Eisenstadt, A.; Stille, J. K. *J. Org. Chem.* **1980**, *45*, 2145. (e) Delogu, G.; Faedda, G.; Gladiali, S. *J. Organomet. Chem.* **1984**, *268*, 167. (f) Lee, C. W.; Alper, H. *J. Org. Chem.* **1995**, *60*, 499. (g) Stanley, G. In *Catalysis of Organic Reactions*; Scaros, M. G., Prunier, M. L., Eds.; Marcel Dekker, Inc.: New York, 1995; p 363.

S0002-7863(97)00049-8 CCC: $14.00

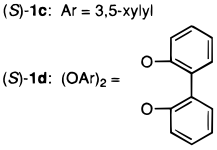
these systems, however, Pt(II)-catalyzed hydroformylation of arylethenes[2a−j] and some functionalized olefins[2k−m] still suffers from several disadvantages such as rather low reaction rates, a tendency for the substrates to undergo hydrogenation, unsatisfactory iso to normal ratios, and undesirable racemization of the products.

A chiral bisphosphine−Rh(I) complex has been another candidate for this purpose. With this system, high catalytic activity and a high iso/normal ratio have been realized,[3] but the ee's achieved so far have been less than 60%.[3b] In addition, enantioselectivities of Rh(I)-catalyzed hydroformylation often depend on the amount of the added chiral ligand because of much higher catalytic activity of phosphine-free rhodium species. Usually 4−6 equiv of the ligands to Rh(I) are used to obtain the maximum ee's at the expense of catalytic activity.[3a] Very recently, use of a tetraphosphine ligand which forms a chiral bimetallic complex has been reported by Stanley. Up to 85% ee has been achieved in the hydroformylation of vinyl esters, although the applicable substrates are still limited.[3g]

Lately, phosphite has attracted much attention as a ligand for Rh(I)-catalyzed hydroformylation because its complex often shows higher catalytic activity than phosphine complexes.[4] While bisphosphite ligands with bulky substituents are of much use to produce linear aldehydes from 1-alkenes,[4c,d] hydroformylation of styrene with these ligands results in a higher iso/normal ratio.[4e] Under these circumstances, several examples of asymmetric hydroformylation with Rh(I)−chiral phosphites have been reported.[5] We previously synthesized several new chiral bis(triaryl phosphite) ligands **1a**−**d** and used them for the Rh(I)-



(*S*)-**1a**: Ar = Ph
(*S*)-**1b**: Ar = 4-tolyl
(*S*)-**1c**: Ar = 3,5-xylyl

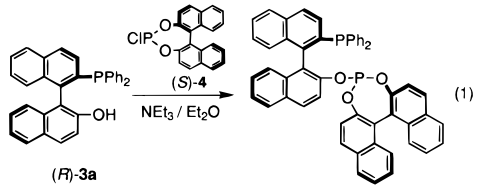


catalyzed asymmetric hydroformylation of vinyl acetate.[5c,6] These bis(triaryl phosphite)−Rh(I) catalyst systems showed comparable enantioselectivities and superior catalytic activities to those of chiral bisphosphine−Rh(I) catalysts at that time. The corresponding isoaldehyde, 2-acetoxypropanal, was given in 95% regioselectivity and in up to 49% ee. One of the characteristic features of the bisphosphite system is that less amount of the chiral ligand is required to attain the maximum ee compared with bisphosphine ligands. A ligand/Rh ratio of 1.1 is sufficient with this system. In the patent literature in 1992, Babin and Whiteker reported the hydroformylation of styrene in up to 90% ee using a chiral bisphosphite as a ligand.[5e] Nevertheless, the ee's observed with this catalyst for other substrates, such as 1-hexene or vinyl acetate, were not satisfactory (50% and 20%, respectively). Thus, at this stage, development of a truely efficient catalyst which is applicable to asymmetric hydroformylation of a wide variety of substrates has been eagerly desired.

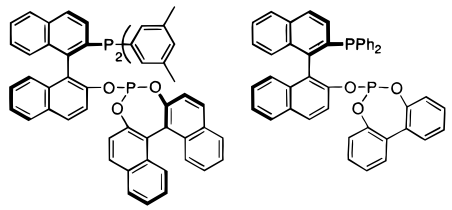
Encouraged by the advantages of the chiral bisphosphites, we designed a new type of chiral bidentate ligand, "phosphine−phosphite".[7] In this paper, we describe the highly enantioselective asymmetric hydroformylation of a wide variety of substrates catalyzed by chiral phosphine−phosphite−Rh(I) complexes.[8] Structures of the active species, $RhH(CO)_2$-(phosphine−phosphite) complexes, are also discussed in relation to the enantioselectivity of hydroformylation.

Results and Discussion

1. Asymmetric Hydroformylations Catalyzed by Rh(I) Complexes of Phosphine−Phosphite Ligands. Preparation of Chiral Phosphine−Phosphite Ligands. Chiral phosphine−phosphites **2** have been synthesized from optically active binaphthol. (*R*)-2-(Diphenylphosphino)-1,1′-binaphthalen-2′-ol [(*R*)-**3a**] was prepared according to the literature procedures.[9] The enantiomerically pure ligand (*R*,*S*)-**2a** was readily obtained in 90% yield from (*R*)-**3a** by the reaction with (*S*)-**4** in ether in the presence of triethylamine (eq 1). Similarly, (*S*,*R*)-**2a**, (*R*,*R*)-



(*R*)-**3a** (*R*,*S*)-**2a**: (*R*,*S*)-BINAPHOS



(*R*,*S*)-**2b** (*R*)-**2c**

2a, (*R*,*S*)-**2b**, and (*R*)-**2c** have also been prepared in high yields. For these ligands, the following characteristic features were observed in their ^{31}P NMR spectra:[10] (1) Ligand (*R*,*S*)-**2a** exhibits a signal of the phosphine moiety P^1 at δ −13.3, almost

(4) Recent examples with Rh(I)−achiral phosphite complexes: (a) van Leeuwen, P. W. N. M.; Roobeek, C. F. (Shell). Eur. Pat. Appl. EP 54986, 1982. (b) van Leeuwen, P. W. N. M.; Roobeek, C. F. *J. Organomet. Chem.* **1983**, *258*, 343. (c) Billig, E.; Abatjoglou, A. G.; Bryant, D. R. (Union Carbide). U.S. Pat. US 4769498, 1988. (d) Cuny, G. D.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 2066. (e) van Rooy, A.; Orij, E. N.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **1995**, *14*, 34.

(5) Recent examples with Rh(I)−chiral phosphite complexes: (a) Wink, D. J.; Kwok, T. J. Yee, A. *Inorg. Chem*. **1990**, *29*, 5006. (b) Kwok, J.; Wink, D. J. *Organometallics* **1993**, *12*, 1954. (c) Sakai, N.; Nozaki, K.; Mashima, K.; Takaya, H. *Tetrahedron: Asymmetry* **1992**, *3*, 583. (d) Buisman, G. J. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Tetrahedron: Asymmetry* **1993**, *4*, 1625. (e) Babin, J. E.; Whiteker, G. T. WO 93/03839, U.S. Pat. US 911518, 1992; *Chem. Abstr.* **1993**, *119*, 159872h. (f) Buisman, G. J. H.; Martin, M. E.; Vos, E. J.; Klootwijik, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Tetrahedron: Asymmetry* **1995**, *6*, 719. (g) Buisman, G. J. H.; Vos, E. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1995**, 409.

(6) (a) Podashova, G. M.; Smirnov, A. N.; and Khardin, A. P. *Chem. Abstr*. **1970**, *72*, 67309n. Related bis(triaryl phosphite) ligands have been reported for hydrocyanation of olefins. (b) Baker, M. J.; Harrison, K. N.; Orpen, A. G.; Pringle, P. G.; Shaw, G. *J. Chem. Soc., Chem. Commun*. **1991**, 803. (c) Baker, M. J.; Pringle, P. G. *J. Chem. Soc., Chem. Commun*. **1991**, 1292.

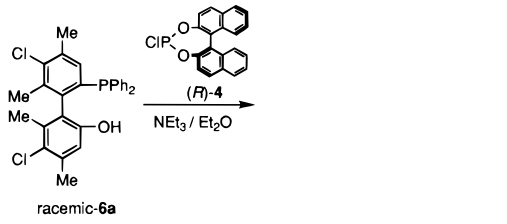
(7) Other hybrid-type ligands for asymmetric hydroformylation, for example: (a) Pottier, Y.; Mortreux, A.; Petit, F. *J. Organomet. Chem.* **1989**, *370*, 333. (b) Arena, C. G.; Nicoló, F.; Drommi, D.; Bruno, G.; Faraone, F. *J. Chem. Soc., Chem. Commun.* **1994**, 2251.

(8) Preliminary communications have been reported. (a) Sakai, N.; Nozaki, K.; Mano, S.; Takaya, H. *J. Am. Chem. Soc.* **1993**, *115*, 7033. (b) Sakai, N.; Nozaki, K.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1994**, 395. (c) Higashijima, T.; Sakai, N.; Nozaki, K.; Takaya, H. *Tetrahedron Lett.* **1994**, *35*, 2023.

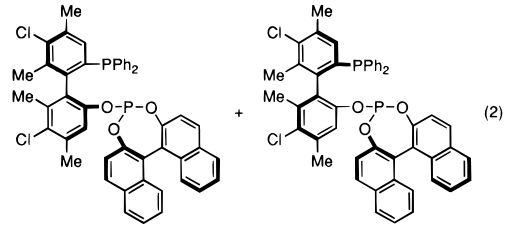
(9) (a) Kurz, L.; Lee, G.; Morgans, D., Jr.; Wa1dyke, M. J.; Ward, T. *Tetrahedron Lett*. **1990**, *31*, 6321. (b) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945.

the same value as those of a bis(triarylphosphine) BINAP (δ −12.8).[11a] The signal due to the phosphite moiety P^2 was observed at δ 146.2 (J_{P-P} = 29.0 Hz), almost the same value as that of bisphosphite (*S*)-**1d** (both δ 144.7). Thus, the phosphine and the phosphite in (*R*,*S*)-**2a** do not affect each other's chemical shift. (2) Compound (*R*,*R*)-**2a**, a diastereomer of (*R*,*S*)-**2a**, shows signals of P^1 and P^2 with almost the same chemical shifts as those of (*R*,*S*)-**2a** but with a much smaller J_{P-P} value (9.2 Hz). (3) For (*R*)-**2c**, in which the binaphthyl group of the phosphite moiety of (*R*,*S*)- or (*R*,*R*)-**2a** is replaced by a biphenyl group, the chemical shifts of P^1 and P^2 resemble those of (*R*,*S*)-**2a**. Due to the axial chirality of the biphenyl group, two pairs of signals for the two diastereomeric isomers could have seen. However, the existence of the single peak for each phosphorus atom suggests the rapid atropisomerization in the biphenyl moiety which is reported to occur on an NMR time scale.[5f] Thus, the J_{P-P} value of 19.0 Hz seems like the average of that of the atropisomeric two diastereomers, which are (*R*,*S*)- and (*R*,*R*)-**2c**.

Chiral phosphine−phosphite ligands bearing a biphenyl framework, (*S*,*R*)-**5a**, (*R*,*R*)-**5a**, and their enantiomers, have been synthesized by a similar procedure (eq 2). Treatment of racemic

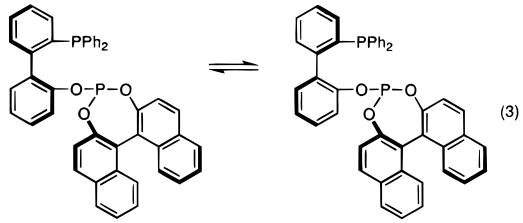


racemic-**6a**



(*S*,*R*)-**5a** (*R*,*R*)-**5a**

5,5′-dichloro-4,4′,6,6′-tetramethyl-2-diphenylphosphino-2′-hydroxybiphenyl (**6a**)[12a] with (*R*)-**4** gave a diastereomeric mixture of (*S*,*R*)- and (*R*,*R*)-**5a**, which was easily separated by silica-gel column chromatography to give pure (*S*,*R*)-**5a** (32% yield) and (*R*,*R*)-**5a** (21%).[8c] Similarly, (*R*)-**5b** was prepared starting



(*S*,*R*)-**5b** 55:45 (*R*,*R*)-**5b**

from biphenyl-2,2′-diol as a 55:45 mixture of two diasteromers (eq 3). On the basis of their P−P coupling constants (35.1 Hz for the major diastereomer and 21.4 Hz for the minor diastereomer), the major diastereomer was tentatively assigned to be (*S*,*R*)-**5b**. Attempted separation of each diastereomer by either recrystallization or column chromatography resulted in recovery of the mixture in the same composition. This result indicates that the rotation around the biphenyl axis of (*R*)-**5b** in solution is slower than the NMR time scale but that the diastereomers are not stable enough to be separated at room temperature.

Preparation of Rhodium(I) Complexes Bearing the Chiral Phosphine−Phosphite Ligands. The complex Rh(acac)[(*R*,*S*)-**2a**] was prepared by mixing $Rh(acac)(CO)_2$ and (*R*,*S*)-**2a** in dichloromethane. Similarly, the corresponding Rh(acac)(ligand) complexes of other phosphine−phosphites, (*R*,*R*)-**2a**, (*R*,*S*)-**2b**, (*R*)-**2c**, (*S*,*R*)-**5a**, (*R*,*R*)-**5a**, and (*R*)-**5b**, were prepared. The notable points observed by ^{31}P NMR are as follows:[10] (1) When the phosphine signals P^1 of Rh(acac)(phosphine-phosphite) complexes are compared with that of Rh(acac)[(*S*)-BINAP], smaller values are observed both in the chemical-shift change upon complex formation $\Delta\delta(P^1)$ (61.1−64.6 ppm for the phosphine−phosphites and 66.9 ppm for (*S*)-BINAP) and in the J_{Rh-P} (172.4−180.0 Hz for the phosphine−phosphites and 190.7 Hz for (*S*)-BINAP). (2) When the phosphite signals P^2 are compared with that of Rh(acac)[(*S*)-**1d**], larger values are observed both in the chemical-shift change $\Delta\delta(P^2)$ (6.7−15.6 ppm for the phosphine−phosphites and 0.6 ppm for (*S*)-**1d**) and in the J_{Rh-P} (325.0−332.6 Hz for the phosphine−phosphites and 300.0 Hz for (*S*)-**1d**).[13] Thus, the chemical shifts and J_{Rh-P} values of the phosphine and the phosphite moieties in the phosphine−phosphite complexes are considerably different from those of bis(triaryl phosphine) or bis(triarylphosphite) complexes. These data suggest that the phosphorus atoms of the phosphine and the phosphite influence each other in the complexes. These new complexes are therefore expected to show different catalytic properties from bisphosphine or bisphosphite complexes.

Interestingly, the ligand (*R*)-**2c** derived from biphenol provided a single species. Although the rapid atropisomerization of the biphenyl moiety might still be possible, we will propose in the latter part of this paper that the biphenyl is fixed to the *S* configuration to form Rh(acac)[(*R*,*S*)-**2c**]. The diastereomeric mixture of (*S*,*R*)- and (*R*,*R*)-**5b** (55:45 by ^{31}P NMR) also gave Rh(acac)[(*S*,*R*)-**5b**] as a sole product. Thus, the interconversion between (*S*,*R*)-**5b** and (*R*,*R*)-**5b** seems to be inhibited by the coordination to the Rh(I) center, and the ligand is in one configuration. Like (*R*)-**2c**, we will conclude that the configuration is (*S*,*R*) from the hydroformylation results (*vide infra*).

Asymmetric Hydroformylation of Olefins. The oxoaldehydes derived from aryl-substituted olefins can be converted to the various pharmaceuticals such as anti-inflammatory agents.[1d,14] We have first tested the asymmetric hydroformylation of styrene (**7a**) and its derivatives (**7b**−**e**) using the complexes Rh(acac)(phosphine−phosphite) as catalysts (eq 4). In order to prevent the reaction catalyzed by unmodified rhodium species,[3] 3.0 equiv of free ligands was added to the Rh(acac)(phosphine−phosphite) complexes for catalytic reactions. It is more convenient to prepare the catalytic species *in situ* by simply mixing $Rh(acac)(CO)_2$ and 4.0 equiv of the ligands. The results are summarized in Table 1. The corresponding aldehyde 2-phenylpropanal (**8a**) and its derivatives

(10) A table summarizing the ^{31}P NMR NMR data of the ligands and their rhodium(I) complexes is deposited as Supporting Information.

(11) (a) Miyashita, A.; Takaya, H.; Souchi, T.; Noyori, R. *Tetrahedron* **1984**, *40*, 1245. (b) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

(12) (a) Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem.* **1989**, *54*, 3007. (b) Toda, F.; Tanaka, K. *J. Org. Chem.* **1988**, *53*, 3607. (c) Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem.* **1994**, *59*, 5748.

(13) A similar tendency in $J\{\text{metal}-P\}$ has been observed in Pt complexes. For example, in $PtCl_2$[(*R*,*S*)-**2a**], the $J\{Pt-P\}$ of the phosphine (3243 Hz) is smaller than that in $PtCl_2$(BINAP) (3665 Hz) and the $J\{Pt-P\}$ of the phosphite site in $PtCl_2$[(*R*,*S*)-**2a**] (6270 Hz) is larger than that in $PtCl_2$[(*S*)-**1a**] (5672 Hz). Nozaki, K.; Sato, N.; Tonomura, Y.; Yasutomi, M.; Takaya, H. Submitted for publication.

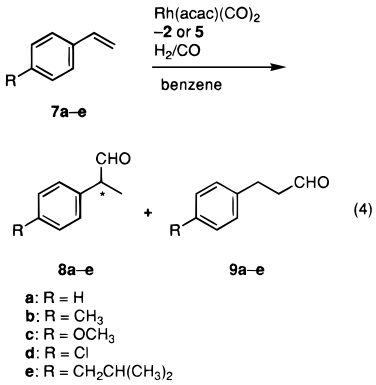
(14) Siegel, H.; Himmele, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 178.

Table 1. Asymmetric Hydroformylation of Styrene and Its Derivatives **7** Catalyzed by Rh(acac)(L) Complexes[a]

run	substrate	CO/H_2, atm/atm	solvent	ligand, L	temp, °C	time, h	conv, %	**8**/**9**	% ee of **8**[b]
1	**7a**	50/50	C_6H_6	(*S*,*R*)-**2a**	60	43	>99	88/12	94 (*S*)
2		50/50	C_6H_6	(*R*,*S*)-**2a**	80	16	>99	86/14	89 (*R*)
3		50/50	C_6H_6	(*R*,*S*)-**2a**	rt	39	24	92/8	95 (*R*)
4		50/50	C_6H_6	(*R*,*S*)-**2a**	60	59	>99	90/10	45 (*R*)
5		63/8	C_6H_6	(*R*,*S*)-**2a**	60	40	93	88/12	92 (*R*)
6		10/90	C_6H_6	(*R*,*S*)-**2a**	60	40	>99	88/12	92 (*R*)
7		50/50	cyclohexane	(*R*,*S*)-**2a**	60	40	>98	87/13	89 (*R*)
8		50/50	CH_2Cl_2	(*R*,*S*)-**2a**	60	41	>99	89/11	84 (*R*)
9		50/50	THF	(*R*,*S*)-**2a**	60	41	>99	92/8	41 (*R*)
10		50/50	MeOH	(*R*,*S*)-**2a**	60	98	98	92/8[c]	25 (*R*)
11		50/50	C_6H_6	(*R*,*S*)-**2b**	60	37	>99	90/10	85 (*R*)
12		50/50	C_6H_6	(*R*,*R*)-**2a**	60	38	>99	86/14	25 (*R*)
13		50/50	C_6H_6	(*R*)-**2c**	60	43	>99	91/9	83 (*R*)
14		50/50	C_6H_6	(*S*,*R*)-**5a**	60	42	>99	90/10	94 (*S*)
15		50/50	C_6H_6	(*R*,*R*)-**5a**	60	40	95	92/8	16 (*R*)
16		50/50	C_6H_6	(*R*)-**5b**	60	40	98	89/11	69 (*S*)
17	**7b**	50/50	C_6H_6	(*S*,*R*)-**2a**	60	20	97	86/14	95 (+)
18	**7c**	50/50	C_6H_6	(*S*,*R*)-**2a**	60	34	>99	87/13	88 (+)
19	**7d**	50/50	C_6H_6	(*S*,*R*)-**2a**	60	34	>99	87/13	93 (+)
20	**7e**[d]	50/50	C_6H_6	(*S*,*R*)-**2a**	60	66	>99	88/12	92 (*S*)[e]

[a] The reaction conditions are described in the Experimental Section. [b] The ee's were determined by GLC analysis using a chiral capillary column (Chrompack β-236M, 0.25 mm × 25 m) of the corresponding 2-arylpropionic acids derived by Jones oxidation of the products. Optical rotations or absolute configurations are drawn in parentheses. [c] The product distribution: **8a**, 27%, **9a**, 1%, dimethyl acetal of **8a**, 65%, dimethyl acetal of **9a**, 7%. [d] Substrate/Rh = 300. [e] The absolute configuration was determined by oxidation of the product aldehyde and comparison of the optical rotation with the authentic sample. The carboxylic acid is Ibuprofen which is commercially available from Aldrich.

(**8b**−**e**) have been obtained in the highest level of enantioselectivity among the previous catalyst systems. The regioisomers **9** were also given. The byproducts from hydrogenation or polymerization of **7a** were not detected.



First, the reaction conditions have been optimized (runs 1−10). A satisfactory **8a**/**9a** ratio (88/12) and the highest ee (94%, >99% conversion) were achieved in benzene, under CO/H_2 = 50 atm/50 atm, at 60 °C for 43 h (run 1). The ee of the product decreased with increasing temperature (runs 1, 2, and 3). The prolonged reaction time after completion of the reaction resulted in a substantial decrease in the ee (run 4), which should be due to racemization of the product **8a**. The ratio of CO to H_2 did not affect regio- and enantioselectivity (runs 5 and 6). As a solvent, cyclohexane gave a comparable result (run 7), but the use of dichloromethane or THF resulted in the loss of ee (runs 8 and 9). In methanol, most of the product aldehydes were obtained as the corresponding dimethyl acetals (run 10). This suggests that the reaction condition is fairly acidic in methanol and that the low ee results from racemization of **8a**. The precursor $Rh(acac)(CO)_2$ was the best choice. Other precursors, $[RhCl(CO)_2]_2$, $[Rh(cod)_2]BF_4$, and $RhH(CO)(PPh_3)_3$, gave (*R*)-**8a** in 80%, 25%, and 69% ee, respectively, when they were used with (*R*,*S*)-**2a**.

Next, each phosphine−phosphite ligand was evaluated in the hydroformylation of **7a** (runs 11−16). The results are summarized in the following two facts: (1) Remarkably high ee's were obtained with (*R**,*S**)-ligands (runs 11 and 14) and much lower ee's were obtained with (*R**,*R**)-ligands (runs 12 and 15). (2) The absolute configuration of the major enantiomer of **8a** was always *R* when the ligands have an (*R*)-2-diphenylphosphino-1,1′-biaryl group. Thus, the sense of enantiofacial selection is predominantly controlled by the phosphine moiety. It is noteworthy that the ee acomplished with (*R*)-**2c** is fairly high considering the possible exchange between the (*R*,*S*)- and (*R*,*R*)-forms (run 13). This may be explained by the fixation of the biphenyl ring to be in the (*S*)-form. The existence of a single active species will be discussed later. In the literature, other examples are seen for similar fixation of biphenyl rings upon the coordination to a transition metal center using biphenol-derived bisphosphites.[6b] Similar discussion is possible for the biphenyl ligand (*R*)-**5b**. With (*R*)-**5b**, (*S*)-**8a** was obtained in 69% ee (run 16). The ee of 69% (run 16) is lower than that with (*S*,*R*)-**5a** (94% ee, run 14) but much higher than that with (*R*,*R*)-**5a** (16% ee, run 15). Thus, this hydroformylation result suggests the (*S*,*R*)-configuration of (*R*)-**5b** in the Rh complex (*vide supra*). With bisphosphines, such as BINAP and DIOP, the $PtCl_2-SnCl_2$ system is reported to give higher ee's than their corresponding Rh(I) systems in the hydroformylation of styrene.[2e,o,p] In contrast, hydroformylation using the present phosphine−phosphite ligands in combination with $Pt(II)-SnCl_2$ was unsuccessful. The complex $PtCl_2$[(*R*,*S*)-**2a**] was used as a catalyst for asymmetric hydroformylation of styrene (**7a**) in the presence of $SnCl_2$ (S/C = 500, CO/H_2 = 50 atm/50 atm, in benzene, 60 °C, 40 h) to give (*R*)-**8a** (12% yield, 33% ee), **9a** (75% yield), and ethylbenzene (13% yield). Hydroformylations of *para*-substituted styrene derivatives **7b**−**e** with the $Rh(acac)(CO)_2$−(*S*,*R*)-**2a** catalyst system also gave aldehydes **8b**−**e** in high regio- and enantioselectivities (runs 17−20).[8a] In particular, (*S*)-2-(4-isobutylphenyl)propanal (**8e**), derived from **7e** in 92% ee, is the precursor of the anti-inflammatory (*S*)-ibuprofen.[1d]

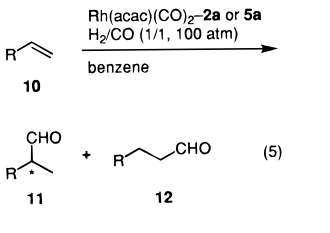
The phosphine−phosphite−Rh(I) complexes were next applied to functionalized olefins. Hydroformylation of vinyl carboxylates **10a**−**e** with (*R*,*S*)-**2a**/$Rh(acac)(CO)_2$ gave 2-car-

Table 2. Asymmetric Hydroformylation of Heteroatom-Substituted Olefins (**10a**−**g**) Catalyzed by Rh(acac)(L)[a]

run	substrate	S/C	ligand[b]	temp, °C	time, h	conv, %	**11**/**12**	% ee of **11**[c]
1	**10a**	400	(*R*,*S*)-**2a**	60	36	>99	86/14	92 (*S*)
2	**10a**	2000	(*R*,*S*)-**2a**	80	78	97	84/16	88 (*S*)
3	**10a**	200	(*R*,*R*)-**2a**	50	37	46	92/8	73 (*S*)
4	**10a**	400	(*R*,*S*)-**2b**	60	36	72	85/15	90 (*S*)
5	**10a**	1000	(*S*,*R*)-**5a**	60	40	65	85/15	90 (*R*)
6	**10b**	500	(*R*,*S*)-**2a**	60	74	>99	88/12	93 (*S*)
7	**10b**	500	(*R*,*S*)-**2a**	40	47	38	88/12	98 (*S*)
8	**10c**	500	(*R*,*S*)-**2a**	60	78	>99	85/15	90 (*S*)
9	**10c**	500	(*R*,*S*)-**2a**	40	47	45	88/12	93 (*S*)
10	**10d**	500	(*R*,*S*)-**2a**	60	71	>99	91/9	89 (*S*)
11	**10e**	500	(*R*,*S*)-**2a**	60	72	>99	88/12	80 (*S*)
12	**10f**	300	(*S*,*R*)-**2a**	60	90	98	89/11	85 (*R*)
13	**10g**	1000	(*R*,*S*)-**2a**	40	20	96	96/4	74 (*S*)[d]

[a] Reactions were carried out in benzene (solvent/substrate ratios were 0.5−1) in a 50-mL autoclave under a 1:1 mixture of H_2 and CO at an initial total pressure of 100 atm. [b] Ligand/[Rh] ratios were 4.0. [c] Determination of the ee's is as follows. For **11a**, **11d**, and **11f**, ^{1}H NMR spectroscopy using Eu(hfc)$_3$. For **11b** and **11c**, GLC analysis with a chiral capillary column (Chrompack β-236M, 0.25 mm × 25 m) of acids derived by Jones oxidation of the products. For **11e**, HPLC analysis (Daicel Chiralcel OD) of the amide obtained from Jones oxidation of **11e** followed by the reaction with aniline. Absolute configurations were determined by comparing the signs of optical rotation of acids with reported data. For **11a**−**d**, see ref 3a. For **11e**, (*S*)-2-(octanoyloxy)propanoic acid was prepared from (*S*)-lactic acid and octanoyl chloride: (*S*)-2-(octanoyloxy)propanoic acid, $[\alpha]^{26}_D$ 21.1 (*c* 1.94, toluene). [d] These data have been reported in ref 16.

boxypropanals **11a**−**e** and 3-carboxypropanals **12a**−**e** (eq 5 and Table 2). Vinyl acetate (**10a**) was converted to (*S*)-2-acetoxy-



propanal [(*S*)-**11a**] (86% yield, 92% ee) and 3-acetoxypropanal (**12a**) (14% yield) (run 1). The combined yield of **11a** and **12a** was quantitative from **10a**, and no byproduct such as ethyl acetate and acrolein was observed.[2,3a] This result is the first example of successful asymmetric hydroformylation of heteroatom-functionalized olefins. The substrate/catalyst ratio can be raised up to 2000 (run 2). Hydroformylation of **10b**, bearing a bulky alkyl group on the carboxyl group, gave **11b** in high ee, and the absolute configuration of **11b** was the same as that of **11a** (run 6). At a lower temperature of 40 °C, (*S*)-**11b** was obtained and the highest level of ee, 98%, was achieved (run 7). Hydroformylation of other vinyl esters **10a**−**e** also proceeded in high regio- and enantioselectivities (runs 8−11). Chiral aldehydes **11a**−**e** can be readily converted to lactic acid and threonine.[1d] (*S*)-Lactic acid has been attracting much interest as a monomer of biodegradable polymers.[15] Hydroformylation of *N*-vinylphthalimide (**10f**)[3d] catalyzed by Rh-

(15) Ikada, Y. In *Polymers and Biomaterials*; Feng, H., Han, Y., Huang, L., Eds.; Elsevier Science Publishers B.V.: New York, 1991; p 273 and references cited therein.

Table 3. Asymmetric Hydroformylation of Fluorinated Olefins (**10h**−**k**) Catalyzed by Rh(acac)(L)[a]

run	substrate	S/C	ligand[b] L	temp, °C	time, h	yield,[c] %	**11**/**12**[d]	% ee of **11**[e]
1	**10h**	1000	(*R*,*S*)-**2a**	30	44	85	87/3	96 (*R*)[f]
2	**10h**	1000	(*R*,*S*)-**2a**	35	24	72	96/4	98 (*R*)[f]
3	**10h**	1000	(*R*,*S*)-**2a**	35	40	>99	96/4	87 (*R*)[f]
4	**10i**	*g*	(*S*,*R*)-**2a**	35	42	*h*	96/4	92 (*R*)[i]
5	**10i**	*g*	(*R*,*S*)-**2a**	35	46	*j*	95/5	93 (*S*)[i]
6	**10j**	2000	(*R*,*S*)-**2a**	40	30	52	91/9	95 (−)
7	**10k**	2000	(*R*,*S*)-**2a**	40	39	43	89/11	92 (−)

[a] Reactions were carried out in benzene (solvent/substrate ratios were 0.5−1 unless otherwise stated) in a 50-mL autoclave under a 1:1 mixture of H_2 and CO at an initial total pressure of 100 atm. [b] Ligand/[Rh] ratios were 4.0. [c] Yields were determined on the basis of ^{1}H NMR using Ph_2CH_2 as an internal standard. [d] Determined by ^{1}H NMR. [e] The ee's were determined by GLC analysis with a chiral capillary column (Chrompack β-236M, 0.25 mm × 25 m) of acids derived by Jones oxidation of the products **11h**−**k**. Optical rotations or the absolute configurations are shown in parentheses. [f] See ref 35a for the absolute configuration. [g] A large excess of substrate was used. [h] Turnover number 366 (8.72 h^{-1}). [i] See ref 35b for the absolute configuration. [l] Turnover number 380 (8.26 h^{-1}).

(acac)[(*S*,*R*)-**2a**] gave (*R*)-**11f** (89% selectivity, 85% ee) and **12f** (11% selectivity) (run 12). The product **11f** is a precursor of alanine, one of the essential amino acids.[1d] Asymmetric hydroformylation was successfully applied to sulfur-containing olefins, and the results have been reported elsewhere.[16] For example, vinyl 4-methylphenyl sulfide (**10g**) gave (*S*)-**11g** with (*R*,*S*)-**2a** (**11g**/**12g** = 96/4, 74% ee). It should be noted that the sense of enantioface selection for those heteroatom-substituted olefins **10a**−**g** is the same as that observed for styrene (**7a**). It was reported that hydroformylation of methyl α-acetamidoacrylate with RhH(CO)(PPh$_3$)$_3$−DIOP gave methyl 2-acetamido-2-formylpropanoate in >99% yield and in 60% ee.[3b] Attempted hydroformylation of this substrate catalyzed by the RhH(CO)(PPh$_3$)$_3$−(*R*,*S*)-**2a** system (60 °C, 65 h, H_2/CO = 50 atm/50 atm) afforded methyl 2-acetamido-2-formylpropanoate in low ee (53% yield, 13% ee). A significant amount of hydrogenated product was formed (30% yield).

The discovery that introducing a pentafluorophenyl or a trifluoromethyl group into a biologically active compound often prompts unique physiological activities[17] stimulated the studies on the synthesis of various building blocks embodying polyfluorinated moieties. Hydroformylation of fluorinated olefins is a convenient way to synthesize such compounds. Hydroformylation of 2,3,4,5,6-pentafluorostyrene (**10h**) and 3,3,3-trifluoropropene (**10i**) was reported to give isoaldehydes **11h** and **11i** in high regioselectivities, respectively.[18] To our knowledge, no asymmetric hydroformylation of this type of substrate has been reported until now. Hydroformylation of **10h** with Rh(acac)[(*R*,*S*)-**2a**] proceeded under very mild conditions (turnover number 19.4 h^{-1} at 30 °C) to give **11h** in high regioselectivity (**11h**/**12h** = 97/3) and in high ee (96%) (eq 5 and Table 3, run 1). The regioselectivity to **11h** with Rh(acac)-[(*R*,*S*)-**2a**] is comparable to that with other Rh(I) complexes.[18] It is necessary to stop the reaction at moderate conversion to obtain high enantioselectivities, probably because of the racemization of **11h** (runs 2 and 3). Similarly, hydroformylation of 3,3,3-trifluoropropene (**10i**) with Rh(acac)[(*R*,*S*)-**2a**] also resulted in high regio- and enantioselectivities for **11i** (runs 4

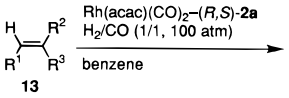
(16) Nanno, T.; Sakai, N.; Nozaki, K.; Takaya, H. *Tetrahedron: Asymmetry* **1995**, *6*, 2583.

(17) (a) Smith, F. A. CHEMTECH **1973**, 422. (b) Filler, R. CHEMTECH **1974**, 722. (c) Lin, T.-S.; Chai, C.; Prusoff, W. H. *J. Med. Chem.* **1976**, *19*, 915.

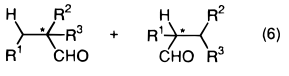
(18) (a) Ojima, I. *Chem. Rev.* **1988**, *68*, 1011. (b) Ojima, I.; Kato, K.; Okabe, M.; Fuchikami, T. *J. Am. Chem. Soc.* **1987**, *109*, 7714.

and 5). *Ortho*- and *para*-monofluorinated styrenes, **10j** and **10k**, gave the corresponding isoaldehydes in high ee's (runs 6 and 7). The regioselectivity is the same level as that for styrene (**7a**) and is lower than that for **10h**.

The present catalyst system was successfully applied to the asymmetric hydroformylation of a wide variety of olefins, both internal ones **13a**−**f** and terminal ones **13g**−**j** (eq 6). Most of



13



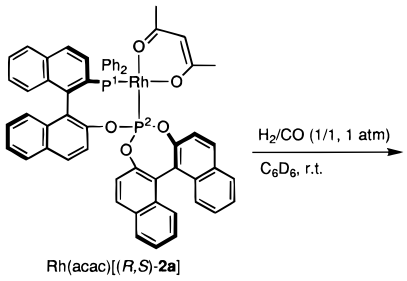
14 **15** (6)

	R^1	R^2	R^3	**14**/**15**	%*ee* of **14**
a:	CH_3	C_6H_5	H	98/2	80(*R*)
b:	CH_3	H	C_6H_5	78/22	79(*R*) (from **13a**/**13b** = 1/1)
c:	CH_3	H	CH_3	–	82(*S*)
d:	CH_3	CH_3	H	–	48(*S*)
e:	C_2H_5	H	C_2H_5	–	79(*S*)
f:	C_2H_5	C_2H_5	H	–	69(*S*)
g:	H	n-C_4H_9	H	24/76	82(*R*)
h:	H	C_2H_5	H	21/79	83(*R*)
i:	H	$CH(CH_3)_2$	H	8/92	83(*R*)
j:	H	1-cyclohexenyl	H	88/12	96(*R*)

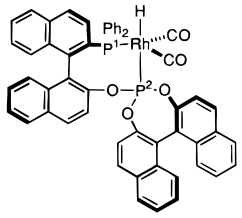
the data are shown in our previous papers.[8,19,20] In addition to the results shown in eq 6, the reaction of indene and 1,2-dihydronaphthalene also gave the corresponding aldehydes in high ee's, in which the formyl groups are introduced at the α-position of the aromatic rings.[8b,c,20] On the other hand, hydroformylation of 2,3-dimethyl-1-butene, a 1,1-disubstituted olefin, gave racemic 3,4-dimethylpentanal. This is in sharp contrast to the fact that hydroformylation of 2,3-dimethyl-1-butene catalyzed by $PtCl_2-SnCl_2-$(*R*,*R*)-Bco-dbp gave (*S*)-3,4-dimethylpentanal in moderate ee, 48%.[2a] Hydroformylation of 2,3-dimethyl-1-butene with $PtCl_2-SnCl_2-$(*R*,*S*)-**2a** gave 3,4-dimethylpentanal in even low ee (25%). In this case, the chiral center is created at the *β*-position of the formyl group, and the present chiral phosphine−phosphite system may be unsuitable for this type of enantioselection.

2. Mechanistic Considerations. Configuration of the Rh-H(CO)$_2$(phosphine−phosphite) Complexes. The generally accepted mechanism of monophosphine−Rh(I)-catalyzed hydroformylation was first proposed by Wilkinson and his co-workers.[21] The most important intermediates in this mechanism are five-coordinate bis(phosphine)rhodium complexes, although complexes with one or three phosphine ligands may also be involved. In the trigonal bipyramidal bis(phosphine)rhodium species, two phosphine ligands occupy either two equatorial sites or one equatorial and one apical site. Recently, Casey and his co-workers reported a bidentate bisphosphine which was designed to realize a P−Rh−P angle near 120°.[22] With this ligand, a complex $RhH(CO)_2$(bisphosphine) was formed in which both phosphorus atoms of the ligand occupy equatorial positions. They concluded that this is essential to achieve high normal/iso selectivity in the hydroformylation of 1-hexene. With a chiral bisphosphite system, complexes $RhH(CO)_2$(bisphosphite) bearing both of the two phosphorus atoms at equatorial positions have been reported by van Leeuwen and his co-workers as active species to achieve high iso/normal selectivity[23] and enantioselectivity.[5g]

In contrast to these studies, we have revealed that $RhH(CO)_2$-[(*R*,*S*)-**2a**] exists as a single species in which the phosphine occupies an equatorial position and the phosphite an apical position as follows.[8a] When a solution of Rh(acac)[(*R*,*S*)-**2a**] in benzene-d_6 was treated with a 1:1 mixture of hydrogen and carbon monoxide at atmospheric pressure, a monohydride complex, $RhH(CO)_2$[(*R*,*S*)-**2a**] was formed.[23,24] The structure shown in eq 7 has been determined for the monohydride



Rh(acac)[(*R*,*S*)-**2a**]



RhH(CO)$_2$[(*R*,*S*)-**2a**] (7)

complex on the basis of the following data. (1) The IR spectrum of $RhH(CO)_2$[(*R*,*S*)-**2a**] in benzene-d_6 has absorption bands at 1969 (strong) and 2014 (medium) cm^{-1} due to ν_{CO} and ν_{Rh-H}, respectively. No shift in the ν_{CO} upon deuteration established that the hydride and CO ligands of $RhH(CO)_2$[(*R*,*S*)-**2a**] are *cis* to one another.[25] (2) In NMR studies, the coupling constant between the phsophorus atom in the phosphite (P^2) and the hydride ($J\{P^2-H\}$) of 160 Hz was observed (Table 4). The magnitude of $J\{P^2-H\}$ is similar to that reported for the apical hydride with the apical phosphite $J\{$P of apical phosphite−H$\}$ (152 Hz) rather than with the equatorial phosphite $J\{$P of equatorial phosphite−H$\}$ (5 Hz) in trigonal bipyramidal $HRh[P(OEt)_3]_4$ at −134 °C.[26] These NMR data suggest the hydride orientation *cis* to phosphine (P^1) and *trans* to phosphite (P^2). This complex $RhH(CO)_2$[(*R*,*S*)-**2a**] also exhibited catalytic activity for hydroformylation of *p*-methylstyrene (**7b**) in the presence of 2.3 equiv of (*R*,*S*)-**2a** (S/C = 300, in benzene, 60 °C, 20 h) to give (−)-**8b** (82% yield, 94% ee) and **9b** (18% yield), which demonstrates that $RhH(CO)_2$[(*R*,*S*)-**2a**] is an active species involved in the catalytic cycle.

(19) (a) Horiuchi, T.; Ohta, T.; Nozaki, K.; Takaya, H. *Chem. Commun.* **1996**, 155. (b) Nozaki, K.; Nanno, T.; Takaya, H. *J. Organomet. Chem.*, in press.

(20) Details are deposited as Supporting Information.

(21) (a) Evans, D.; Osborn, J. A.; Wilkinson, G. *J. Chem. Soc. A* **1968**, 3133. (b) Yagupsky, G.; Brown, C. K.; Wilkinson, G. *J. Chem. Soc. A* **1970**, 1392. (c) Brown, C. K.; Wilkinson, G. *J. Chem. Soc. A* **1970**, 2753.

(22) (a) Casey, C. P.; Whiteker, G. T.; Melville, M. G.; Petrovich, L. M.; Gavney, J. A., Jr.; Powell, D. R. *J. Am. Chem. Soc.* **1992**, *114*, 5535. The natural bite angle was proposed by the same authors. (b) Casey, C. P.; Whiteker, G. T. *Isr. J. Chem.* **1990**, *30*, 299.

(23) van Rooy, A.; Kamer, P. C. J.; van Leewen, P. W. N. M.; Veldman, N.; Spek, A. L. *J. Organomet. Chem.* **1995**, *494*, C15. See also ref 5f, 5g.

(24) (a) Moasser, B.; Gladfelter, W. L.; Roe, D. C. *Organometallics* **1995**, *14*, 3832. (b) Moasser, B.; Gladfelter, W. *Inorg. Chim. Acta* **1996**, *242*, 125.

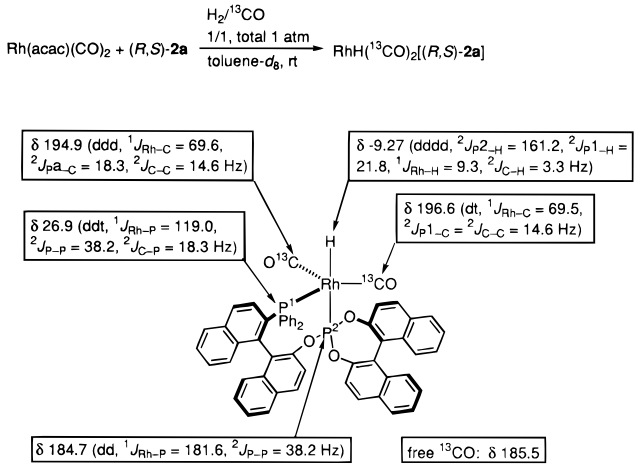
(25) Infrared spectroscopy allows an easy distinction between *cis* and *trans* structures in metal−carbonyl hydrides. Vaska, L. *J. Am. Chem. Soc.* **1966**, *88*, 4100.

(26) Meakin, P.; Muetterties, E. L.; Jesson, J. P. *J. Am. Chem. Soc.* **1972**, *94*, 5271.

Table 4. Spectral Data of the Complexes $RhH(CO)_2$(phosphine−phosphite) in C_6D_6

	phosphine			phosphite				hydride		IR (C_6D_6)	
ligand	$\delta(P^1)$ (ppm)	$J\{P^1-H\}$ (Hz)	$J\{P^1-Rh\}$ (Hz)	$\delta(P^2)$ (ppm)	$J\{P^2-H\}$ (Hz)	$J\{P^2-Rh\}$ (Hz)	$J\{P^1-P^2\}$ (Hz)	$\delta(H)$ (ppm)	$J\{H-Rh\}$ (Hz)	$\nu(CO)$ (cm^{-1})	$\nu(Rh-H)$ (cm^{-1})
(*R*,*S*)-**2a**	26.92	23.2	119.0	184.86	159.9	181.6	39.7	−8.85	9.8	1969	2014
(*R*,*R*)-**2a**	30.26	33.6	119.8	179.52	134.3	193.0	32.8	−9.08	9.1	1971	2012
(*R*)-**2c**	26.87	23.8	119.8	184.01	158.1	182.3	40.5	−8.85	9.2	1968	2012
(*R*,*S*)-**5a**	24.97	17.1	120.5	183.46	173.4	177.0	42.7	−8.85	8.7	1968	2014
(*R*,*R*)-**5a**	26.20	22.1	122.1	179.31	155.0	187.7	33.6	−9.18	8.5	1972	2016

Chart 1



We have also prepared the ^{13}C-labeled hydride complex $RhH(^{13}CO)_2$[(*R*,*S*)-**2a**]. The NMR data in toluene-d_8 are summarized in Chart 1. In the literature, three other examples have so been far reported for $RhH(^{13}CO)_2$(ligand) complexes with *cis* bidentate ligands, two kinds of bisphosphines,[22a,27] and a bisphosphite.[24a] The characteristic feature of the present complex $RhH(^{13}CO)_2$[(*R*,*S*)-**2a**] is the existence of the C−C coupling between the two carbonyls. In a reported example,[22a] the two carbonyls are under a rapid interchange between the apical and the equatorial positions via pseudorotation so that the averaged signal could be observed. In $RhH(^{13}CO)_2$[(*R*,*S*)-**2a**], on the other hand, the two carbonyls seem to occupy the two equatorial positions. Thus, it is suggested that all the ligands in $RhH(^{13}CO)_2$[(*R*,*S*)-**2a**] form a rigid environment which is favorable for the asymmetric hydroformylation (*vide infra*).

The hydride complexes of the other phosphine−phosphite ligands were also prepared, and their structures were characterized by spectroscopic data. When NMR spectra of $RhH(CO)_2$-(phosphine−phosphite) complexes of (*R*,*S*)-**2a** and (*S*,*R*)-**5a** are compared with those of (*R*,*R*)-**2a** and (*S*,*S*)-**5a**, several common tendencies are recognized. (1) The $J\{P^2$(phosphite)−H$\}$ values in (*R**,*S**)-isomers are always larger than those in their corresponding (*R**,*R**)-isomers. (2) On the other hand, the $J\{P^1$(phosphine)−H$\}$ values in (*R**,*S**)-isomers are always smaller than those in their corresponding (*R**,*R**)-isomers. On the basis of the much larger $J\{$P(apical)−H$\}$ (=152 Hz) than $J\{$P(equatorial)−H$\}$ (=5 Hz) in the trigonal bipyramidal $HRh[P(OEt)_3]_4$,[26] it may be expected that the $J\{$P−H$\}$ increases with increasing P−Rh−H bond angle in the range of 90−180°. If this is the case, the above observations might suggest that the structural deviations of the monohydride complexes from an ideal trigonal bipyramid are larger in (*R**,*R**)-isomers than in the corresponding (*R**,*S**)-isomers. (3) In addition, the $J\{$Rh−P(phosphite)$\}$ values in (*R**,*S**)-isomers are smaller than those of (*R**,*R**)-isomers. The smaller $J\{$Rh−P(phosphite)$\}$ may reflect the weakened bond due to the larger *trans* influence of the hydride. The maximal *trans* influence would be observed when the bond angle of P(phosphite)−Rh−H is 180°. Hence, we think that a structure closer to the ideal trigonal bipyramid has been attained in the (*R**,*S**)-isomers rather than in the (*R**,*R**)-isomers.

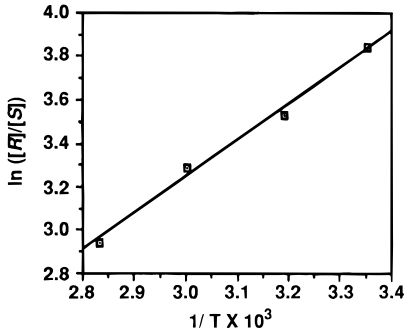


Figure 1. ln([*R*]/[*S*]) vs 1/*T* for asymmetric hydroformylation of styrene catalyzed by Rh(acac)[(*R*,*S*)-**2a**].

Existence of a Single Species and Its Fluxional Nature of $RhH(CO)_2$[(*S*,*R*)-2a]. Brown and Kent have reported that $RhH(CO)_2(PPh_3)_2$ exists as an 85:15 mixture of two isomers in which the two phosphines are placed on equatorial−equatorial and equatorial−apical positions, respectively.[28] At room temperature, these two isomers are in rapid equilibrium. It is considered essential to form a single catalytically active species in order to achieve high selectivity,[29] because multiple species would give different products via different reaction pathways. We have examined the existence of a single active species in the Rh(I)−(*R*,*S*)-**2a**-catalyzed hydroformylation of styrene (**7a**), changing the reaction temperature. The plot of ln([*R*]/[*S*]) of the product **8a** vs the reciprocals of the reaction temperatures shows a straight-line relationship (Figure 1). This manifests that a single active species is involved in this hydroformylation.[30]

Regarding the diequatorial complex $RhH(CO)_2$(bisphosphine), Casey suggested that the two phosphine parts of the bidentate ligand interchange with each other through rapid pseudorotations via equatorial−apical isomers.[22a] Such exchange was also observed in $RhH(CO)_2$(bisphosphite) by van Leeuwen.[5f,g] In both studies, low-temperature NMR spectroscopy revealed the existence of the pseudorotations. In contrast, such pseudorotation has not been observed in $RhH(CO)_2$[(*R*,*S*)-**2a**]. Phosphorus-31 NMR spectroscopy shows the complex $RhH(CO)_2$[(*S*,*R*)-**2a**] as a single species at 60 °C and at 25 °C (in toluene-d_8 under 1 atm of CO). On cooling, the resonances due to the two phosphorus atoms broadened around −50 °C. These signals then sharpened again at −90 °C to give substantially the same signal patterns as those observed at 25 °C. Because the chemical

(27) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer. P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081.

(28) Brown, J. M.; Kent, A. G. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1597.

(29) (a) Noyori, R.; Takaya, H. *Chem. Scr.* **1985**, *25*, 83. (b) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345.

(30) (a) Enders, D. CHEMTECH **1981**, 504. (b) Tóth, I.; Guo, I.; Hanson, B. E.; *Organometallics* **1993**, *12*, 848.

Table 5. Asymmetric Hydroformylations of Styrene (**7a**) Catalyzed by Rh(acac)$(CO)_2$−Mixed Ligand Systems[a]

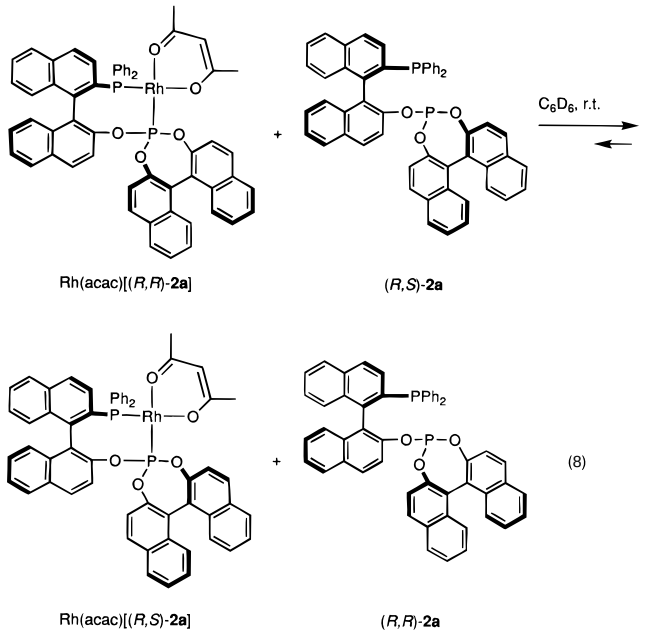
run	catalyst	conditions	conv, %	turnover, h^{-1}	**8a**/**9a**	% ee of **8a**
1	(*R*,*S*)-**2a**−(*R*,*R*)-**2a**−Rh(acac)$(CO)_2$ (2:2:1)	25 °C/42 h	26	12.4	90/10	85 (*R*)
2	(*R*,*S*)-**2a**−(*R*,*R*)-**2a**−Rh(acac)$(CO)_2$ (2:2:1)	60 °C/39 h	98		89/11	72 (*R*)
3	(*R*,*S*)-**2a**−(*R*,*R*)-**2a**−Rh(acac)$(CO)_2$ (2:2:1)	80 °C/15 h	>99		88/12	75 (*R*)
4	(*R*,*R*)-**2a**−Rh(acac)$(CO)_2$ (4:1)	25 °C/43 h	21	9.8	85/15	26 (*R*)
5	(*R*,*S*)-**2a**−Rh(acac)$(CO)_2$ (4:1)	25 °C/39 h	24	12.3	92/8	95 (*R*)
6	(*R*,*S*)-**2a**−Rh(acac)$(CO)_2$ (2:1)	25 °C/45 h	27	12.0	91/9	95 (*R*)
7	(*R*,*S*)-**2a**−PPh_3−Rh(acac)$(CO)_2$ (2:2:3:1)	25 °C/45 h	29	12.9	91/9	95 (*R*)

[a] The determination of the **8a**/**9a** ratio and the *ee*'s was carried out in the same way as that in Table 1. S/C = 2000.

shift of each phosphorus atom is constant with changing temperature, no apical−equatorial interchange should exist at any temperature. The reason for the peak broadening observed at −50 °C is unclear.

Ligands without C_2 symmetry have been believed to be unsuitable for asymmetric catalysis because several catalytically active species may compete with each other to give a product with the opposite absolute configurations.[29] As described above, however, a sole active species is formed and is involved in the hydroformylation catalyzed by Rh(I) complexes of phosphine−phosphites. The unique dissymmetric environments created by phosphine−phosphites coupled with the formation of a single catalytically active species seem to be the important factors for giving high enantioselectivity.[31]

Preferred (*R*,*S*)- and (*S*,*R*)-Configurations of the Phosphine−Phosphite Ligands for the Complex Formation. Thermodynamic stability of the (*R**,*S**)-phosphine−phosphite−Rh(I) complex over the (*R**,*R**)-diasteromer has been demonstrated as follows. When 1 equiv of (*R*,*S*)-**2a** was added to a solution of Rh(acac)[(*R*,*R*)-**2a**] in C_6D_6, a ligand exchange occurred. Phosphorus-31 NMR of the resulting mixture showed that the ratio of free ligands (*R*,*R*)-**2a**/(*R*,*S*)-**2a** that remained in the solution was about 7.0 at room temperature. Almost the same composition of the free ligands and the complexes was observed starting from Rh(acac)[(*R*,*S*)-**2a**] and (*R*,*R*)-**2a**. These facts show the existence of a fast equilibrium as shown in eq 8.



(8)

The difference in coordinating abilities between (*R*,*S*)- and (*R*,*R*)-**2a** was reflected in the enantioselectivity of asymmetric hydroformylation. Some runs of the hydroformylation of styrene catalyzed by mixed-ligand systems were conducted (Table 5). First, the catalytic activity of Rh(acac)[(*R*,*S*)-**2a**] in the presence of 3 equiv of free ligand (run 5) is comparable to that of Rh(acac)[(*R*,*R*)-**2a**] (run 4). Second, we assume that the Rh(I) complexes of (*R*,*S*)- and (*R*,*R*)-**2a** are formed in a 7:1 ratio when the two ligands are mixed with Rh(acac)$(CO)_2$ in a ratio of (*R*,*S*)-**2a**:(*R*,*R*)-**2a**:Rh = 2:2:1. The ee's of the reactions with (*R*,*S*)-**2a**:(*R*,*R*)-**2a**:Rh = 2:2:1 can then be estimated from runs 4 and 5 (or 6) to be 83%. The experimental result of 85% ee in run 1 shows good agreement with the calculated values. The nonlinear behavior of ln([*R*]/[*S*]) vs the reciprocal of the reaction temperature observed in runs 1−3 consists with the fact that this reaction is catalyzed by more than two active species. Addition of achiral phosphine PPh_3 did not affect the ee (run 7).

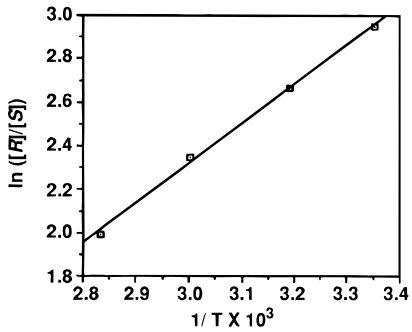


Figure 2. ln([*R*]/[*S*]) vs 1/*T* for asymmetric hydroformylation of styrene catalyzed by Rh(acac)[(*R*)-**2c**].

Such thermodynamic stability of the (*R**,*S**)-phosphine−phosphite−Rh(I) over the (*R**,*R**)-isomer nicely explains the behavior of (*R*)-**2c**. When (*R*)-**2c** is used as a ligand, two isomers of $RhH(CO)_2$[(*R*)-**2c**] can exist in solution, namely, $RhH(CO)_2$[(*R*,*S*)-**2c**] and $RhH(CO)_2$[(*R*,*R*)-**2c**]. The chemical shifts and coupling constants for $RhH(CO)_2$[(*R*)-**2c**] in ^{31}P and ^1H NMR spectra resemble those of $RhH(CO)_2$[(*R*,*S*)-**2a**] very closely (Table 4). Hydroformylation of styrene (**7a**) gave (*R*)-**8a** in 83% ee with (*R*)-**2c**. This is slightly lower than that with (*R*,*S*)-**2a** (92%) but much higher than that with (*R*,*R*)-**2a** (25%) (Table 1). The results suggest that (*R*)-**2c** coordinates to Rh(I) in the (*R*,*S*)-form. We have elucidated the existence of only one active species by the plot of ln([*R*]/[*S*]) of the product **8a** against the reciprocals of the reaction temperatures (Figure 2). As was the case for (*R*,*S*)-**2a**, a straight-line relationship is observed. Thus, it is suggested that $RhH(CO)_2$[(*R*,*S*)-**2c**] is formed as an exclusive species and that this species affords the product in much higher ee than the corresponding (*R*,*R*)-isomer would give. We can deny the existence of $RhH(CO)_2$[(*R*,*R*)-**2c**] with much lower catalytic activity because the activity of Rh(acac)[(*R*,*R*)-**2a**] is similar to that of Rh(acac)[(*R*,*S*)-**2a**] (Table 1). We think that $RhH(CO)_2$[(*S*,*R*)-**5b**] is similarly formed predominantly from (*R*)-**5b** on the basis of the hydroformylation result (*vide supra*).

(31) Such formation of a single active species from a chiral unsymmetrical bidentate ligand was also reported in the aminophosphine−phosphinite−Rh(I) system. See ref 7a.

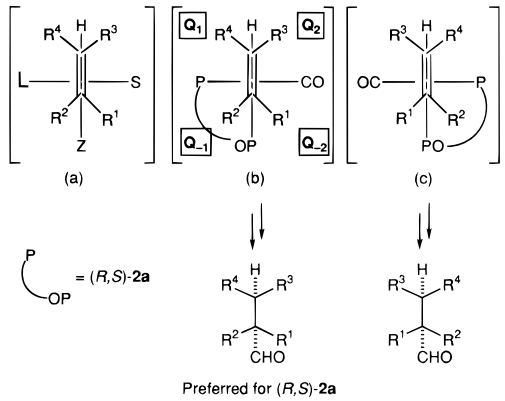


Figure 3. Models for the transition state determining asymmetric induction: (a) A simplified general model proposed by Consiglio and Pino.[1g] Olefin approach or coordinate from the front side. L, S, and Z represent a large, a small, and an apical ligand, respectively. (b) and (c) (*R*,*S*)-**2a**−Rh(I) system. All the experimental results can be predicted by (b).

Proposed Models for the Transition States. Figure 3a is a model of the transition state proposed by Consiglio and Pino that differentiates the enantiofaces of prochiral olefins.[1g] It has been considered that the asymmetric induction occurs before or during the metal−alkyl formation from the metal−olefin π complex.[32] L, S, and Z represent a large, a small, and an apical ligand, respectively. Isoaldehydes are produced from α-olefins via transition states where either R^1 or R^2 is occupied by the substituent. Substituents would prefer the R^1 position because of steric demand. On the basis of the structure of $RhH(CO)_2$-[(*R*,*S*)-**2a**], it is reasonable to assume that the "large" group is the phosphine site of (*R*,*S*)-**2a** and the "small" group is the carbonyl. The apical position Z is occupied by the phosphite site. Accordingly, two transition states, Figure 3b, c, can be drawn for the (*R*,*S*)-**2a**−Rh(I) system.

Regioselection to iso over normal strongly depends on the nature of the substrate olefins, and this selectivity is beyond the discussion here. An olefin is expected to approach and coordinate to the Rh center to minimize the steric repulsion between substituents on the olefin and the ligands on the metal. If we assume the enantioface of the olefin is discriminated either at this stage or at the following olefin insetion to Rh−H in a similar conformation,[33] the absolute configuration of the product aldehyde can be predicted using the model of Figure 3b (Table 6). The transition state drawn in Figure 3c would give the opposite configurations. The prediction was made on the basis of the following rules. (1) For a monosubstituted olefin (**7**, **10**, and **13g**−**j**), the substituent occupies R^1 to give the isoaldehyde. (2) For a *cis*-disubstituted olefin (**13c** and **13e**), the substituents are placed at R^1 and R^3. (3) For a *trans*-disubstituted olefin (**13a**, **13d**, and **13f**) the substituents occupy R^1 and R^4. Assignment of R^1 and R^4 for **13a** is based on the regioselectivity of the experimental result. As a result, the model in Figure 3b is consistent not only with the experimental results of the hydroformylation of simple olefins but also with those of functionalized olefins and 1,2-disubstituted olefins. Because of the rigid equatorial−apical conformation of (*R*,*S*)-**2a**, the quadrants Q_{-1} and Q_{-2} in Figure 3b seem to be strictly distinguished. On the other hand, the difference in steric hinderance between Q_1 and Q_2 may not be large in the (*R*,*S*)-**2a** system. This is consistent with the low ee's observed for 1,1-disubstituted olefins for which the substituents occupy R^3 and R^4 in the transition state.

Table 6. Absolute Configuration of the Prevailing Enantiomers in Asymmetric Hydroformylation Catalyzed by Rh(I)−(*R*,*S*)-**2a**:[a] Predicted from Model b vs Observed

olefin	absolute configuration: predicted	absolute configuration: observed	% ee
styrene and its derivatives (**7a**,**e** and **10h**)	*R*	*R*	88−95
vinyl carboxylate (**10a**−**e**)	*S*	*S*	80−98
N-vinylphthalimide (**10f**)	*S*	*S*	85
vinyl 4-methylphenyl sulfide (**10g**)	*S*	*S*	74
3,3,3-trifluoropropene (**10i**)	*S*	*S*	92
(*E*)-1-propenylbenzene (**13a**)	*R*	*R*	92
(*Z*)-2-butene (**13c**) and (*Z*)-3-hexene (**13e**)	*S*	*S*	79−82
(*E*)-2-butene (**13d**) and (*E*)-3-hexene (**13f**)	*S*	*S*	48−69
monosubstituted aliphatic olefins (**13g**−**i**)	*R*	*R*	82−83
1-vinylcyclohexene (**13j**)	*R*	*R*	96

[a] When the experiment was carried out with (*S*,*R*)-**2a**, the *ee*'s were given as they are here and the opposite absolute configurations were given.

Conclusions

Rhodium(I) complexes of chiral phosphine−phosphite, a new class of chiral bidentate ligands, are highly efficient catalysts for asymmetric hydroformylations of a very wide range of prochiral olefins, including heteroatom-functionalized olefins and 1,2-disubstituted olefins. The reason for the exceptionally high enantioselectivities is attributed to the exclusive formation of a single active species, $RhH(CO)_2$(phosphine−phosphite) in which the phosphine occupies the equatorial position and the phosphite the apical position. The unique dissymmetric structure is considered to be a very important factor in retaining this structure. Because derivatives of the phosphine−phosphite seem to be easily prepared from various chiral biphenols and binaphthols, it would be possible to select the best ligand according to the type of substrate. Thus, we believe that our new catalyst systems have high potential use for industrial preparation of biologically active compounds via asymmetric hydroformylation.

Experimental Section

General Procedures. All manipulations involving the air- and moisture-sensitive compounds were carried out using standard Schlenk techniques under argon purified by passing through a hot column packed with BASF-Catalyst R3-11. All NMR spectra were recorded using a JEOL EX-270 (^{1}H, 270 MHz; ^{31}P, 109 MHz; ^{13}C, 67.8 MHz) spectrometer. Tetramethylsilane (^{1}H and ^{13}C) and H_3PO_4 (^{31}P) were employed as internal and external standards, respectively. Gas chromatographic (GLC) analyses were conducted on a Hitachi 263-30 or a Shimadzu GC-15A equipped with a flame ionization detector. Optical rotations were measured on a JASCO DIP-360 spectrometer. Melting points were measured in sealed tubes on a Yanagimoto-Seisakusho micro melting point apparatus, MP-500D, and uncorrected. Column chromatography was conducted on silica gel (Wakogel C-200) from Wako Pure Chemical Industries Ltd. Elemental analyses were performed at the Microanalytical Center, Kyoto University. Most reagents were purchased from Wako Pure Chemical Industries Ltd., Nacalai Tesque, or Aldrich Chemical Co., Inc., and were used without further purification unless otherwise specified. Solvents were purified by distillation under argon after drying over calcium hydride (xylene and dimethyl sulfoxide), P_2O_5 (dichloromethane), or sodium benzophenone ketyl (toluene, benzene, THF, and ether). Benzene-d_6 and toluene-

(32) Consiglio, G.; Botteghi, C.; Salomon, C.; Pino, P. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 669.

(33) Deuterioformylation with the present catalyst system suggests the olefin insertion is mostly irreversible. Horiuchi, T.; Shirakawa, E.; Nozaki, K.; Takaya, H. Submitted for publication.

d_8 for NMR spectroscopy of oxygen- and moisture-sensitive materials were distilled over Na−K alloy. Triethylamine was distilled under argon after drying over calcium hydride. Vinyl acetate and styrene were distilled before use. Carbon monoxide (99.9%) and hydrogen (99.9999%) were obtained from Teisan Co. (*S*)-(−)-Binaphthol and its enantiomer came from Mitubishi Gas Chemical Co. Inc.

Prepration of (*S*)-(1,1′-Binaphthalene-2,2′-dioxy)chlorophosphine [(*S*)-4]. A mixture of (*S*)-2,2′-dihydroxy-1,1′-binaphthyl (3.5 g, 12 mmol) and phosphorus trichloride (25 g, 0.18 mol) was heated at reflux with stirring under an argon overnight. The excess phosphorus trichloride in the reaction mixture was removed under reduced pressure. The last trace of phosphorus trichloride in the residue was removed by azeotropic distillation with toluene (25 mL) under reduced pressure, and this procedure was repeated three times. A yellow solid (4.4 g, 100%) was obtained after freeze-drying of the benzene solution of the residue *in vacuo*. The crude product (*S*)-**4** was used for the next reaction without further purification: ^{31}P NMR ($CDCl_3$) δ 174.0 (s).

General Procedure for Preparation of Phosphine−Phosphite Ligands Consisting of 2-(Diarylphosphino)-1,1′-binaphthyl Groups [(*R*,*S*)-2a, (*R*,*R*)-2a, (*R*,*S*)-2b, and (*R*)-2c]. Hydroxyphosphines (*R*)- and (*S*)-**3a** were prepared according to the literature procedure.[9] To a solution of (*R*)-**3a** (3.4 g, 7.5 mmol) and (*S*)-**4** (4.7 g, 13 mmol) in ether (170 mL) was added triethylamine (1.4 g, 14 mmol) in ether (40 mL) at 0 °C. The mixture was stirred at room temperature for 10 h, and then quenched with cold brine (200 mL). The phases were separated, and the aqueous phase was extracted with ether (200 mL). The combined organic phases were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (*n*-hexane/dichloromethane = 2/1 → 5/3) to afford (*R*,*S*)-BINAPHOS [(*R*,*S*)-**2a**] as a white solid (5.2 g, 90%). Data for (*R*,*S*)-**2a**: mp 159−175 °C (unclear); ^{31}P NMR ($CDCl_3$) δ −13.3 (phosphine, J_{P-P} = 29.0 Hz), 146.2 (phosphite); $[\alpha]^{23}_D$ = +339° (*c* 1.3, toluene). Anal. Calcd for $C_{52}H_{34}O_3P_2$: C, 81.24; H, 4.46. Found: C, 81.16; H, 4.66. Other phosphine−phosphite ligands (*R*,*R*)-**2a**, (*R*,*S*)-**2b**, and (*R*)-**2c**, were similarly prepared. Data for (*R*,*R*)-**2a**: 99% yield, pale yellow solid (hexane−CH_2Cl_2), mp 168−173 °C (unclear); ^{31}P NMR ($CDCl_3$) δ −12.7 (phosphine, J_{P-P} = 9.2 Hz), 145.8 (phosphite); $[\alpha]^{23}_D$ = −214° (*c* 1.2, toluene). Anal. Calcd for $C_{52}H_{34}O_3P_2$: C, 81.24; H, 4.46. Found: C, 80.76; H, 5.53. Data for (*R*,*S*)-**2b**: 98% yield, pale yellow solid (hexane−CH_2Cl_2): mp 158−162 °C (unclear); ^{31}P NMR ($CDCl_3$) δ −12.4 (phosphine, J_{P-P} = 30.5 Hz), 145.5 (phosphite); $[\alpha]^{23}_D$ = +228° (*c* 1.0, toluene). Anal. Calcd for $C_{56}H_{42}O_3P_2$: C, 81.54; H, 5.13. Found: C, 81.33; H, 5.31. (*R*)-**2c**: 77% yield, pale yellow solid (hexane−CH_2Cl_2): mp 102−109 °C (unclear); ^{31}P NMR ($CDCl_3$) δ −13.1 (phosphine, J_{P-P} = 13.7 Hz), 126.8 (phosphite); $[\alpha]^{23}_D$ = +92.4° (*c* 1.0, toluene). Anal. Calcd for $C_{44}H_{30}O_3P_2$: C, 79.04; H, 4.52. Found: C, 79.21; H, 4.78.

Preparation of 2,2′-Bis[[(trifluoromethylsulfonyl]oxy]biphenyls. To a solution of (±)-5,5′-dichloro-4,4′,6,6′-tetramethylbiphenyl-2,2′-diol (6.22 g, 20.0 mmol),[12a] 2,6-lutidine (4.72 g, 44.0 mmol), and 4-(dimethylamino)pyridine (732 mg, 6.00 mmol) in CH_2Cl_2 (30 mL) was added trifluoromethanesulfonic anhydride (12.4 g, 44.0 mmol) at 0 °C under argon. The mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated and chromatographed on silica gel (hexane/CH_2Cl_2 = 1/1) to give (±)-5,5′-dichloro-4,4′,6,6′-tetramethyl-2,2′-bis[[(trifluoromethylsulfonyl]oxy]biphenyl (10.9 g, 18.9 mmol, 95%). mp 90−91 °C. Anal. Calcd for $C_{18}H_{14}Cl_2F_6O_6S_2$: C, 37.58; H, 2.45. Found: C, 37.77; H, 2.39. Similary, 2,2′-bis-[[(trifluoromethyl)sulfonyl]oxy]biphenyl was prepared from biphenyl-2,2′-diol (96%): mp 33−34 °C. Anal. Calcd for $C_{14}H_8F_6O_6S_2$: C, 37.34; H, 1.79. Found: C, 33.76; H, 1.59.

Preparation of 2-(Diphenylphosphinyo)-2′-[[(trifluoromethyl)-sulfonyl]oxy]biphenyls. The title compounds were prepared in the same manner as their binaphthyl analogs. Data for (±)-3,3′-Dichloro-6-(diphenylphosphino)-2,2′,4,4′-tetramethyl-6′-[[(trifluoromethyl)sulfonyl]oxy]biphenyl (62% yield): mp 159−160 °C; ^{31}P NMR ($CDCl_3$) δ 27.75. Anal. Calcd for $C_{29}H_{24}F_3O_4SPCl_2$: C, 55.51; H, 3.86. Found: C, 55.57; H, 3.89. Data for (±)-2-(diphenylphosphino)-2′-[[(trifluoromethylsulfonyl]oxy]biphenyl (77%): mp 123−124 °C; ^{31}P NMR ($CDCl_3$) δ 27.78. Anal. Calcd for $C_{25}H_{18}F_3O_4PS$: C, 59.76; H, 3.61. Found: C, 60.48; H, 3.66.

Preparation of Hydroxyphosphines with Biphenyl Frameworks. The above triflates were hydrolized by NaOH in dioxane−MeOH−H_2O and then were reduced by trichlorosilane in the same manner as their binaphthyl analogs.[9b] Data for (±)-**6a** (90% yield): mp 71−79 °C; ^{31}P NMR ($CDCl_3$) δ −13.37. Anal. Calcd for $C_{28}H_{25}Cl_2OP$: C, 70.15; H, 5.26. Found: C, 70.08; H, 5.27. Data for (±)-2-(diphenylphosphino)-2′-hydroxybiphenyl (**6b**) was prepared in 60% yield by the same method: mp 122−123 °C; ^{31}P NMR ($CDCl_3$) δ −12.01. Anal. Calcd for $C_{24}H_{19}OP$: C, 81.34; H, 5.40. Found: C, 80.88; H, 5.30.

General Procedure for the Preparation of Phosphine−Phosphite Ligands Consisting of 2-(Diphenylphosphino)biphenyl Groups [(*S*,*R*)-5a, (*R*,*R*)-5a, and (*R*)-5b]. The racemic **6a** was allowed to couple with (*R*)-**4** in the presence of triethylamine as for its binaphthyl analog **3**. The crude reaction mixture was purified by silica-gel chromatography (hexane/CH_2Cl_2 = 20/1 → 3/1) to give (*S*,*R*)-**5a** (32% yield) and (*R*,*R*)-**5a** (21% yield). The isomeric phosphine−phosphites (*R*,*S*)-**5a** and (*S*,*S*)-**5a** were also prepared. Data for (*S*,*R*)-**5a**: mp 155−162 °C; ^{31}P NMR ($CDCl_3$) δ −13.4 (phosphine, J_{P-P} = 35.1 Hz), 146.7 (phosphite); $[\alpha]_D^{25}$ = −281° (*c* 1.0, toluene). Anal. Calcd for $C_{48}H_{36}Cl_2O_3P_2$: C, 72.64; H, 4.57. Found: C, 72.71; H, 5.14. Data for (*S*,*S*)-**5a**: mp 147−151 °C; ^{31}P NMR ($CDCl_3$) δ −12.6 (phosphine, J_{P-P} = 12.2 Hz), 145.8 (phosphite); $[\alpha]_D^{21}$ = +253 (*c* 1.0, toluene). Anal. Calcd for $C_{48}H_{36}Cl_2O_3P_2$: C, 72.64; H, 4.57. Found: C, 71.98; H, 5.14. (*R*)-**5b** was given as a mixture of diastereomers (*S*,*R*)-**5b** and (*R*,*R*)-**5b** via a method similar to that for **6b**. Separation of the diasteromers by either column chromatgraphy or recrystallization was unsuccessful. Data for (*S*,*R*)- and (*R*,*R*)-**5b** (55:45, 871 mg, 62% yield): the mixture melted in the range 150−156 °C; ^{31}P NMR ($CDCl_3$) δ for major, −11.9 (phosphine, J_{P-P} = 35.1 Hz), 146.8 (phosphite); for minor, −11.5 (phosphine, J_{P-P} = 21.4 Hz), 146.8 (phosphite); $[\alpha]_D^{22}$ (as a mixture) = +324° (*c* 1.0, toluene). Anal. Calcd for $C_{44}H_{30}O_3P_2$: C, 79.04; H, 4.52. Found: C, 79.18; H, 4.55.

Preparation of Rh(acac)(phosphine−phosphite). In a 20-mL Schlenk tube were dissolved (*R*,*S*)-**2a** (50.0 mg, 0.0651 mmol) and $Rh(CO)_2(acac)$ (16.8 mg, 0.0651 mmol) in CH_2Cl_2 (5 mL). The solution was stirred at room temperature for 5 min. The reaction mixture was concentrated under reduced pressure to give Rh(acac)-[(*R*,*S*)-**2a**] as a yellow solid. Purification of the complex by recrystallization was unsuccessful: ^{31}P NMR ($CDCl_3$) δ 48.9 (phosphine, J_{Rh-P} = 174.0 Hz, J_{P-P} = 83.9 Hz), 161.8 (phosphite, J_{Rh-P} = 331.1 Hz). Rh(acac) complexes of (*R*,*R*)-**2a**, (*R*,*S*)-**2b**, (*R*)-**2c**, (*S*,*R*)-**5a**, and (*R*,*R*)-**5a** were also prepared, and the formations of these complexes were confirmed by ^{31}P NMR. A mixture of (*S*,*R*)-**5b** and (*R*,*R*)-**5b** gave a single species by an admixture with $Rh(CO)_2(acac)$, which was assigned to be Rh(acac)[(*S*,*R*)-**5b**] (see the text). ^{31}P NMR ($CDCl_3$) of Rh(acac)(ligand) complexes are as follows: (*R*,*R*)-**2a**, δ 51.9 (phosphine, J_{Rh-P} = 178.5 Hz, J_{P-P} = 80.4 Hz), 152.5 (phosphite, J_{Rh-P} = 325.1 Hz); (*R*,*S*)-**2b**, δ 48.7 (phosphine, J_{Rh-P} = 172.4 Hz, J_{P-P} = 82.4 Hz), 160.9 (phosphite, J_{Rh-P} = 332.6 Hz); (*R*)-**2c**, δ 49.4 (phosphine, J_{Rh-P} = 175.5 Hz, J_{P-P} = 82.4 Hz), 136.2 (phosphite, J_{Rh-P} = 328.0 Hz); (*S*,*R*)-**5a**, δ 49.4 (phosphine, J_{Rh-P} = 175.5 Hz, J_{P-P} = 84.0 Hz), 159.8 (phosphite, J_{Rh-P} = 330.4 Hz); (*R*,*R*)-**5a**, δ 51.2 (phosphine, J_{Rh-P} = 180.0 Hz, J_{P-P} = 82.4 Hz), 154.7 (phosphite, J_{Rh-P} = 325.0 Hz); (*S*,*R*)-**5b** (from a mixture of (*S*,*R*)-**5b** and (*R*,*R*)-**5b**), δ 50.4 (phosphine, J_{Rh-P} = 174.0 Hz, J_{P-P} = 87.0 Hz), 160.2 (phosphite, J_{Rh-P} = 328.1 Hz).

General Procedure for the Asymmetric Hydroformylation of Olefins Catalyzed by Rhodium(I) Complexes of Phosphine−Phosphite Ligands. A solution of styrene (**7a**) (2.08 g, 20.0 mmol), dicarbonyl(2,4-pentanedionato)rhodium (2.6 mg, 0.010 mmol), and (*R*,*S*)-**2a** (31 mg, 0.040 mmol) in benzene (1 mL) was degassed by freeze−pump−thaw cycles and transferred into a 50-mL stainless-steel autoclave. Carbon monoxide (50 atm) and dihydrogen (50 atm) were charged, and the solution was stirred at 60 °C for 43 h. Conversion to aldehydes (>99%) and the regioselectivity of the reaction (2-phenylpropanal (**8a**)/3-phenylpropanal (**9a**) = 88/12) were determined by ^{1}H NMR spectroscopy of the crude reaction mixture without evaporation of the solvent. Chromatography on silica gel followed by short pass distillation of the reaction mixture gave a pure sample of (*R*)-(+)-2-phenylpropanal [(*R*)-**8**]. Optical rotation was used to determine the absolute configuration.[34] The enantiomeric excess of the product **8a** was determined to be 94% ee by oxidation of **8a** to the corresponding

carboxylic acid by Jones oxidation followed by GLC analysis using a chiral capillary column (Chrompack β-236M, 0.25 mm × 25 m, 135 °C, He 2 kg·cm^{-2}). Other olefins except for extremely volatile ones were subjected to hydroformylation by a similar procedure. The determination of the ee of other products is shown in the corresponding tables or Supporting Information.

Hydroformylation of Highly Volatile Olefins. In a 20-mL Schlenk tube was dissolved (*Z*)-2-butene (**13c**) (5.0 mL, excess), Rh(acac)(CO)$_2$ (2.6 mg, 0.010 mmol), and (*R*,*S*)-**2a** (31 mg, 0.040 mmol). As an internal standard to calculate turnover number by ^{1}H NMR, Ph_2CH_2 was added (5−10 equiv to the catalyst). The solution was degassed by three freeze−thaw cycles and was transferred into a 50-mL autoclave. The mixture was stirred under the pressure of H_2 (50 atm) and CO (50 atm) at 60 °C for 40 h. The ee's were determind by GLC analysis of the corresponding acid using a chiral capillary column (Chrompack β-236M, 0.25 mm × 25 m, for **14c** (= **14d** = **15c** = **15d**) , 80 °C; for **14e** (= **14f** = **15e** = **15f**), at 100 °C). Absolute configurations are given in parentheses. See ref 32 for the assignment. Hydroformylations of other highly volatile olefins 1-butene (**13h**), (*E*)-2-butene (**13d**), and 3,3,3-trifluoropropene (**10i**) were conducted in the same way. The determination of the ee's of other products are shown in the corresponding tables.

Asymmetric Hydroformylation of Styrene (7a) Catalyzed by PtCl$_2$[(*R*,*S*)-2a]. In a 20-mL Schlenk tube were dissolved PtCl$_2$[(*R*,*S*)-**2a**] (21.0 mg, 0.0203 mmol), $SnCl_2$ (3.8 mg, 0.020 mmol), (*R*,*S*)-**2a** (24 mg, 0.0301 mmol), and styrene (**7a**) (1.01 g, 10.2 mmol) in benzene (3 mL). The solution was degassed by freeze−thaw cycles and transferred into a 50-mL autoclave. Dihydrogen (50 atm) and carbon monoxide (50 atm) were charged, and the mixture was stirred at 60 °C for 40 h. The analyses were conducted in the same way as the Rh(I)-catalyzed reaction.

Preparation of the Hydride Complexes RhH(CO)$_2$(phosphine−phosphite). A solution of the complex Rh(acac)(phosphine−phosphite) (50−100 mg/1 mL in benzene-d_6 or toluene-d_8) was stirred under a 1:1 mixture of H_2 and CO (1−100 atm) at room temperature for 12 h. The resulting solution was tranferred into an NMR tube under CO (1 atm) to record ^{31}P and ^{1}H NMR spectra. IR spectra were also measured for the same solution. Spectral data are shown in Table 4.

Acknowledgment. This work was supported by the Grant-in-Aid for Scientific Research on Priority Area of Reactive Organometallics No. 05236106 from the Ministry of Education, Science and Culture, Japan.

Supporting Information Available: A table summarizing the ^{31}P NMR data of the ligands and their complexes, experimental details for the hydroformylation of **13**, and ^{31}P NMR spectra of RhH(CO)$_2$[(*R*,*S*)-**2a**] at 60, 25, −50, and −90 °C (5 pages). See any current masthead page for ordering and Internet access instructions.

JA970049D

(34) Consiglio, G.; Pino, P.; Flowers, L. I.; Pittman, C. U., Jr. *J. Chem. Soc., Chem. Commun*. **1983**, 612.

(35) (a) Iseki, K.; Kuroki, Y.; Nagai, T.; Kobayashi, Y. *J. Fluorine Chem.* **1994**, *69*, 5. (b) Fukumasa, M.; Furuhashi, K.; Umezawa, J.; Takahashi, O.; Hirai, T. *Tetrahedron Lett.* **1991**, *32*, 1059.