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Synthesis of New Chiral Phosphinephosphites Having 2-Diphenylphosphino-biphenyl-2'-yl Backbone and Their Use in Rh(I)-Catalyzed Asymmetric Hydroformylations

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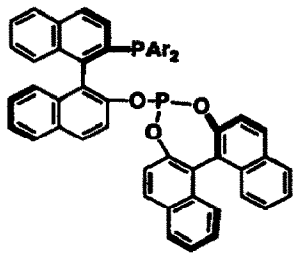
Abstract: New chiral phosphinephosphites (*R*)-(5,5'-dichloro-2-diphenylphosphino-4,4',6,6'-tetramethylbiphenyl-2'-yl)((*S*)-1,1'-binaphthalen-2,2'-diyl)phosphite [abbreviated (*R*,*S*)-BIPHEMPHOS] and its enantiomer (*S*,*R*)-BIPHEMPHOS have been synthesized from 5,5'-dichloro-4,4',6,6'-tetramethyl-2,2'-biphenyldiol in enantiomerically pure form. Their Rh(I) complexes have been shown to be highly efficient catalysts for asymmetric hydroformylations of a variety of olefinic substrates. The corresponding phosphinephosphites derived from 2,2'-biphenyldiol were also tested as ligands for asymmetric hydroformylation.

Recently we have reported that the Rh(I) complexes of phosphinephosphite ligand (*R*,*S*)-**1** and its enantiomer (*S*,*R*)-**1** are highly efficient catalysts for enantioselective hydroformylation of a variety of mono- and 1,2-disubstituted olefins.[1,2] In these ligands atropisomeric 1,1'-binaphthalene moieties are used as chiral elements. Since subtle alteration in structural and electronic properties of chiral ligands often brings about an important change in the efficiencies of asymmetric catalysis,[3] we have synthesized new phosphinephosphites **2** having biphenyl backbone.

New phosphinephosphite ligands (*S*,*R*)-**2a**, (*R*,*R*)-**2a**, and their enantiomers have been synthesized as shown in Scheme 1. Racemic 5,5'-dichloro-4,4',6,6'-tetramethyl-2,2'-biphenyldiol (**3a**) was prepared by a coupling of 4-chloro-3,5-dimethylphenol without solvent by using $FeCl_3$ as oxidizing agent in 30% isolation yield.[4] Compound **6a** was prepared in 53% overall yield from **3a** in three steps as we reported for the synthesis of **1**.[1] The reaction of racemic **6a** with enantiomerically pure (*R*)-**7** in the presence of NEt_3 gave a diastereomeric mixture of (*S*,*R*)-**2a** and (*R*,*R*)-**2a**, which could be easily separated by silica gel column chromatography to give pure (*S*,*R*)-**2a** (32%) and (*R*,*R*)-**2a** (21%). The absolute configurations of the two diastereomers of **2a**

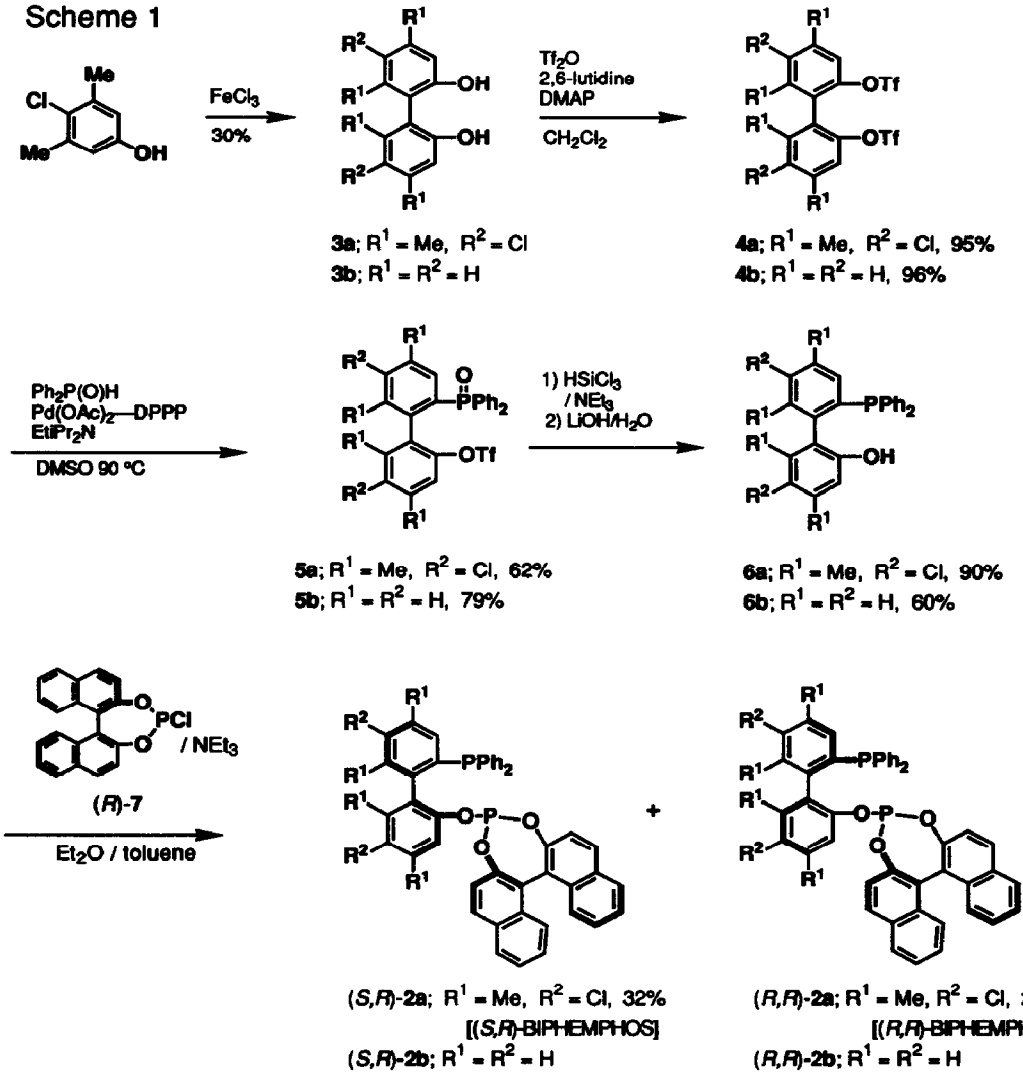


(*R*,*S*)-**1**: Ar = C_6H_5 [(*R*, *S*)-BINAPHOS]

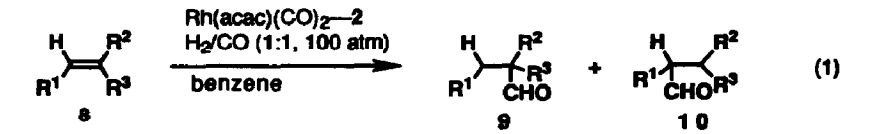
could be assigned by the comparison of P—P coupling constants of ^{31}P NMR spectra with those of (*S*,*R*)- and (*R*,*R*)-**1**.[5,6] Similarly, (*S*,*R*)-**2b** and (*R*,*R*)-**2b** were prepared starting from 2,2'-biphenyldiol (**3b**). ^{31}P NMR spectrum of the product mixture showed that two compounds were formed in 55:45 ratio, which were assigned to (*S*,*R*)-**2b** and (*R*,*R*)-**2b**, respectively.[6,7] Attempted separation of each diastereomer by either recrystallization or column chromatography resulted in recovery of the same mixture, which indicates that the rotation around the biphenyl axis of **2b** is restricted in solution at room temperature, but they are not stable enough to be separated.

Reaction of Rh(acac)$(CO)_2$ and 1.0 equiv of **2** in CH_2Cl_2 afforded complex Rh(acac)(**2**) in quantitative yield.[8] Interestingly, when the diastereomeric mixture of (*S*,*R*)-**2b** and (*R*,*R*)-**2b** (55:45 by ^{31}P NMR) was treated with Rh(acac)$(CO)_2$ in CH_2Cl_2, only one complex was obtained,[7] whose structure has not been elucidated yet (*vide infra*).

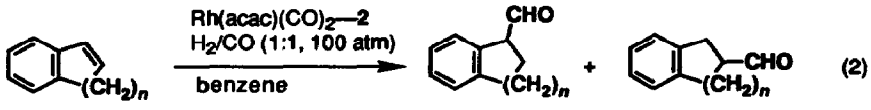
Scheme 1



Hydroformylations catalyzed by Rh(acac)(2) were carried out in the presence of three fold excess of free ligands. In most cases, however, the catalyst species were prepared *in situ* by simply mixing Rh(acac)$(CO)_2$ and 4.0 equiv of 2. Some selected results are given in Table 1. The results obtained with ligand 1 are also listed in parentheses.[1,2] When (*R*,*S*)- or (*S*,*R*)-**2a** was used as ligand, high regio- and enantioselectivities have been obtained. For all of the substrates listed, the values are almost the same or even higher compared with those



a; $R^1 = R^2 = H$, $R^3 = C_6H_5$
b; $R^1 = R^2 = H$, $R^3 = OCOCH_3$
c; $R^1 = R^2 = H$, $R^3 = n\text{-}C_4H_9$
d; $R^1 = CH_3$, $R^2 = H$, $R^3 = CH_3$



a: $n = 1$
b: $n = 2$

Table 1. Hydroformylations of olefins **8** and **11** catalyzed by phosphinephosphite—Rh(I) complexes[a]

Substrate	Ligand[b]	Temp ℃	Time h	S/C	Convs[c] %	9/10[c,d] or 12/13	9 or 12[d,e] % *ee*	Config[f]
8a	(*S*,*R*)-**2a**	60	42	1000	>99	90/10 (88/12)	94 (94)	*S*-(+)
8a	(*R*,*R*)-**2a**	60	40	1000	95	92/8	16	*R*-(-)
8a	(*S*,*R*)-**2b**+ (*R*,*R*)-**2b**	60	40	1000	98	89/11	69	*S*-(+)
8b	(*S*,*R*)-**2a**	60	40	1000	65	85/15 (86/14)	90 (92)	*R*-(+)
8c	(*S*,*R*)-**2a**	30	40	1000	51	23/77 (24/76)	85 (75)	*S*-(+)
8d	(*S*,*R*)-**2a**	60	40	3500	—[g]	—	85 (82)	*R*-(-)
11a	(*S*,*R*)-**2a**	60	20	200	62	92/8 (92/8)	88 (83)	(+)
11b	(*R*,*S*)-**2a**	60	12	500	74	95/5 (96/4)	96 (97)	(-)

[a] Reactions were carried out in benzene (solvent/substrate ratios were 0.5—1) in a 50-mL autoclave under 1:1 mixture of H_2 and CO at initial total pressure of 100 atm. [b] Catalysts were prepared *in situ* by addition of 4.0 equiv of 2 to Rh(acac)$(CO)_2$ unless otherwise stated. [c] Conversions and 9/10 or 12/13 ratio were determined based on ^1H NMR using Ph_2CH_2 as internal standard. The ratios of 9/10 or 12/13 together with the conversions reflect the actual yield. [d] The results obtained with (*S*,*R*)- or (*R*,*S*)-1 are given in parentheses. [e] Determined by GLC analysis with a chiral capillary column (CHROMPACK Cp-Cyclodex β-236M (**9a**, **9c**, **9d**) or astec Chiraldex B-PH (**12a**, **12b**)) of acids derived by Jones oxidation of the products, or ^1H NMR of **9b** using Eu(hfc)$_3$. [f] Determined by the sign of optical rotation. [g] Since **8d** is very volatile, only turnover number / hour (3.7) was determined by ^1H NMR using Ph_2CH_2 as an internal standard.

obtained by use of (*R*,*S*)- or (*S*,*R*)-**1**. On the other hand, the reaction using (*R*,*R*)-**2a**—Rh(acac)$(CO)_2$ system as catalyst resulted in much lower *ee* (16%) as has also been observed for the reaction with (*R*,*R*)-**1**.[1] Notably, reaction of **8a** with the catalytic system derived from a mixture of (*S*,*R*)-**2b** and (*R*,*R*)-**2b** (55:45) and Rh(acac)$(CO)_2$ afforded (*S*)-**9a** in 69% *ee* whose absolute configuration is the same with that of the product obtained using (*S*,*R*)-**1** and (*S*,*R*)-**2a**. Since only one **2b**—Rh(I) complex has been formed by the reaction of a chirally flexible mixture of (*S*,*R*)-**2b** and (*R*,*R*)-**2b** with Rh(acac)$(CO)_2$, the result suggests that the catalyst formed *in situ* is a (*S*,*R*)-**2b**—Rh(I) complex.

The above results show that (*S*,*R*)- and (*R*,*S*)-**2** are highly efficient ligands for Rh(I)-catalyzed asymmetric hydroformylations. The starting 2,2'-biphenyldiol derivatives are easily accessible by oxidative coupling of a variety of substituted phenols. Thus, new unsymmetrical phosphinephosphites **2** will become versatile chiral ligands for asymmetric hydroformylations. Optical resolution of **3a** is now underway.

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REFERENCES AND NOTES

1. Sakai, N.; Mano, S.; Nozaki, K.; Takaya, H., *J. Am. Chem. Soc.*, **1993**, *115*, 7033.
2. Sakai, N.; Nozaki, K.; Takaya, H., *J. Chem. Soc., Chem. Commun.*, in press.
3. For chiral diphosphines having binaphthyl and biphenyl backbones, see, for example: Takaya, H.; Ohta, T.; Noyori, R. "Catalytic Asymmetric Synthesis", Ojima, I., Ed. VCH Publishers, Inc. New York, NY, 1993, Chapter 1.
4. For phenol coupling reactions in solid state, see: Toda, F.; Tanaka, K., *J. Org. Chem.* **1988**, *53*, 3607.
5. The P—P coupling constant of (*S*,*R*)-**1** (29.2 Hz) is considerably larger than that of (*R*,*R*)-**1** (9.2Hz).[1]
6. All new compounds **2**—**6** gave satisfactory elemental analyses and consistent spectral data. (*S*,*R*)-**2a**: pale yellow solid, mp 155—162 °C (dec), $[\alpha]_D^{25}$ = -281 (*c* 1.0, toluene), ^{31}P NMR (toluene-d_8) δ -13.4 (d, $J_{P\text{-}P}$ = 35.1 Hz) and 146.7 (d). (*R*,*R*)-**2a**: pale yellow solid, mp 153—159 °C, $[\alpha]_D^{22}$ = -252 (*c* 1.0, toluene), ^{31}P NMR (toluene-d_8) δ -12.6 (d, $J_{P\text{-}P}$ = 12.2 Hz) and 145.8 (d). A 55:45 mixture of (*R*,*S*)-**2b** and (*S*,*S*)-**2b**: pale yellow solid, mp 150—156 °C, $[\alpha]_D^{22}$ = 324 (*c* 1.0, toluene), ^{31}P NMR (toluene-d_8) (*S*,*R*)-isomer: δ -11.9 (d, $J_{P\text{-}P}$ = 35.1 Hz) and 146.8 (d), (*R*,*R*)-isomer: δ -11.5 (d, $J_{P\text{-}P}$ = 21.4 Hz) and 146.8 (d).
7 A mixture of (*S*,*R*)-**2b** and (*R*,*R*)-**2b** was obtained in 62% yield from **6b**.
8. Rh(acac)[(*S*,*R*)-**2a**]: ^{31}P NMR (toluene-d_8) δ 49.4 (dd, $J_{P\text{-}P}$ = 84.0 Hz, $J_{Rh\text{-}P}$ = 175.5 Hz) and 159.8 (dd, $J_{Rh\text{-}P}$ = 330.4 Hz). Rh(acac)[(*R*,*R*)-**2a**]: ^{31}P NMR (toluene-d_8) δ 51.2 (dd, $J_{P\text{-}P}$ = 82.4 Hz, $J_{Rh\text{-}P}$ = 180.0 Hz) and 154.7 (dd, $J_{Rh\text{-}P}$ = 325.0 Hz). The complex derived from a mixture of (*S*,*R*)-and (*R*,*R*)-**2b** and Rh(acac)$(CO)_2$)(tentatively assigned to Rh(acac)[(*S*,*R*)-**2b**]): ^{31}P NMR ($CDCl_3$) δ 50.4 (dd, $J_{P\text{-}P}$ = 87.0 Hz, $J_{Rh\text{-}P}$ = 174.0 Hz) and 160.2 (dd, $J_{Rh\text{-}P}$ = 328.1 Hz).

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