Highly Enantioselective Hydroformylation of Olefins Catalyzed by New Phosphinephosphite–Rh(I) Complexes

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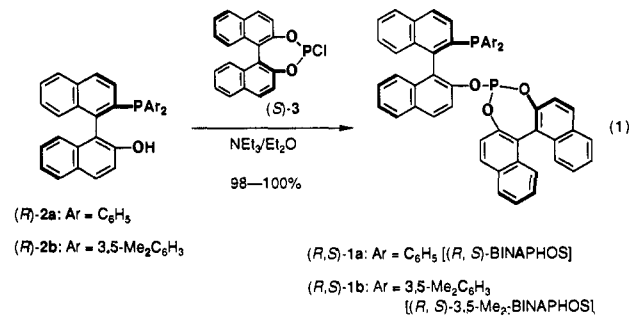
Hydroformylation is one of the most versatile methods for the functionalization of C=C bonds. Despite recent extensive investigations, however, highly enantioselective hydroformylation catalyzed by chiral metal complexes has rarely been attained.[1-3] We now report that the Rh(I) complexes of new chiral phosphinephosphite ligands, (*R*)-(2-(diphenylphosphino)-1,1′-binaphthalen-2′-yl)-((*S*)-1,1′-binaphthalen-2,2′-yl)phosphite [(*R*,*S*)-**1a**] (hereafter abbreviated (*R*,*S*)-BINAPHOS) and its enantiomer (*S*,*R*)-**1a**, are highly efficient catalysts for asymmetric hydroformylation of both arylethenes and functionalized olefins such as vinyl acetate and *N*-vinylphthalimide.[6]

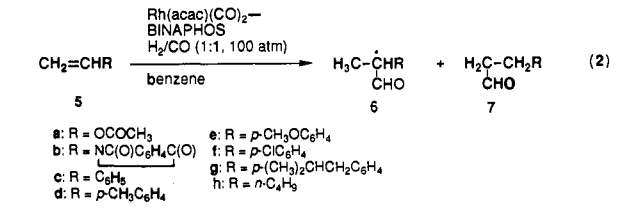
The enantiomerically pure ligand (*R*,*S*)-**1a**[7] was readily obtained in 98% yield from (*R*)-**2a** by the reaction with (*S*)-**3** in ether in the presence of triethylamine (eq 1). Similarly, (*S*,*R*)-**1a**, (*R*,*R*)-**1a**, (*R*,*S*)-**1b**, and (*R*)-(2-(diphenylphosphino)-1,1′-binaphthalen-2′-yl)-diphenylphosphite [(*R*)-**4**] have also been prepared in high yields.[7] Since the starting compounds **2**[8] are easily accessible from enantiomerically pure 1,1′-binaphthalene-2,2′-diol,[11] the present procedure is suitable for the synthesis of optically pure **1** and the related phosphinephosphite ligands on a preparative scale.



(*R*)-**2a**: Ar = C_6H_5
(*R*)-**2b**: Ar = 3,5-$Me_2C_6H_3$
(*R*,*S*)-**1a**: Ar = C_6H_5 [(*R*, *S*)-BINAPHOS]
(*R*,*S*)-**1b**: Ar = 3,5-$Me_2C_6H_3$ [(*R*, *S*)-3,5-Me_2-BINAPHOS]

The catalyst precursors Rh(acac)(binaphos) and Rh(acac)(**4**) have been prepared by the reaction of Rh(acac)$(CO)_2$ and **1** or **4** in dichloromethane.[12] For the catalytic reactions, 1–3 equiv of free ligand were added to Rh(acac)(binaphos). Sometimes, it is more convenient to prepare the catalytic species *in situ* by simply mixing Rh(acac)$(CO)_2$ and 2.0–4.0 equiv of **1** or **4**.

Some representative results are given in Table I. A solution of vinyl acetate (**5a**) (6.19 mmol), Rh(acac)$(CO)_2$ (1.55×10^{-2} mmol), and (*R*,*S*)-**1a** (3.34×10^{-2} mmol) in benzene (1.0 mL) placed in a Schlenk tube was degassed by freeze–thaw cycles. It was then transferred into a 50-mL autoclave, and the mixture was stirred at 60 °C for 36 h under hydrogen and carbon monoxide pressure (1:1 ratio, total 100 atm). ^{1}H NMR analysis of the reaction mixture showed that the conversion was >99% and the branched and normal aldehydes, (*S*)-**6a** and **7a**, were formed in 86:14 ratio. The enantiomeric excess of (*S*)-**6a** (92% ee) was determined by GLC using a chiral capillary column. Ethyl acetate, the hydrogenation product of **5a**, was not detected. The asymmetric hydroformylation has also been extended to another functionalized olefin **5b** and arylethenes **5c–g** to give the corresponding aldehydes **6b–g** in high ees (eq 2 and Table I).



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a: R = $OCOCH_3$
b: R = $NC(O)C_6H_4C(O)$
c: R = C_6H_5
d: R = p-$CH_3C_6H_4$
e: R = p-$CH_3OC_6H_4$
f: R = p-ClC_6H_4
g: R = p-$(CH_3)_2CHCH_2C_6H_4$
h: R = n-C_4H_9

Reaction of a simple olefin **5h** afforded **6h** in 75% ee, but the regioselectivity was not satisfactory. No noticeable racemization of the product aldehydes was observed under the reaction conditions.

A marked dependence of the enantioselectivities on the structures of the phosphite moieties relative to that of the 2-(diphenylphosphino)-1,1′-binaphthyl backbone in **1** has been observed. The highest ees have always been obtained with (*R*,*S*)-**1a** and its enantiomer (*S*,*R*)-**1a**, while reactions with (*R*,*R*)-**1a** and (*R*)-**4** resulted in much lower enantioselectivities. The results also show that the absolute configurations of the 2-phosphino-1,1′-binaphthyl backbone are of primary importance in determining the sense of asymmetric inductions.

Several striking features of the present catalysis are revealed. For the substrates reported herein, the present catalytic system

(1) A recent review: Botteghi, C.; Paganelli, S.; Schionato, A.; Marchetti, M. *Chirality* **1991**, *3*, 335.

(2) Highly enantioselective hydroformylation of arylethenes catalyzed by diphosphine-$PtCl_2$-$SnCl_2$ have been reported: (a) Stille, J. K.; Su, H.; Brechot, P.; Parrinello, G.; Hegedus, L. S. *Organometallics* **1991**, *10*, 1183. (b) Consiglio, G.; Nefkens, S. C. A.; Borer, A. *Organometallics* **1991**, *10*, 2046.

(3) In spite of high enantioselectivities, hydroformylations of arylethenes and some functionalized olefins catalyzed by the chiral diphosphine-Pt(II)-$SnCl_2$ systems still seem to have, in many cases, several disadvantages such as fairly low reaction rates, a tendency for the substrates to undergo competitive hydrogenation, unsatisfactory branched to normal ratios, and undesirable racemization of the products. For the hydroformylations of functionalized olefins, chiral diphoshpine-Rh(I) or diphosphite-Rh(I) complexes have mostly been used, but the highest ees so far achieved have been less than 60%.[4] In addition, enantioselectivities are often reported to be proportional to the amount of added chiral ligand.[5] Usually 4–6 equiv of the ligands to Rh(I) have been used.

(4) To our knowledge, the highest reported ee (60%) in Rh(I)-catalyzed hydroformylation is that of methyl α-acetamidoacrylate catalyzed by DIOP-Rh(I) complexes (substrate/Rh(I) = 100, 30 °C, 575 h, 75% conversion, 87% selectivity): Gladiali, S.; Pinna, L. *Tetrahedron: Asymmetry* **1990**, *1*, 693 and a private communication from the author (S.G.).

(5) Hobbs, C. F.; Knowles, W. S. *J. Org. Chem.* **1981**, *46*, 4422.

(6) In a previous paper we reported an asymmetric hydroformylation of vinyl acetate catalyzed by Rh(I) complexes of bis(triarylphosphite) ligands, giving the branched aldehyde in up to 49% ee: Sakai, N.; Nozaki, K.; Mashima, K.; Takaya, H. *Tetrahedron: Asymmetry*, **1991**, *3*, 583. Rhodium(I) complexes of bis(triarylphosphite) ligands derived from 1,1′-binaphthalene-2,2′-diol have also been used as catalysts for hydroformylation of arylethenes: Baker, M. J.; Pringle, P.G. *Abstracts of the 8th International Symposium on Homogeneous Catalysis*, August 2–7, 1992, Amsterdam; p 12.

(7) All new compounds gave satisfactory analytical and spectroscopic data. (*R*,*S*)-**1a**: 98% yield, colorless solid; ^{31}P NMR ($CDCl_3$) δ −13.3 (d, J_{P-P} = 29.0 Hz) and 146.2 (d). (*R*,*R*)-**1a**: 99% yield, pale yellow solid; ^{31}P NMR ($CDCl_3$) δ −12.7 (d, J_{P-P} = 9.2 Hz) and 145.8 (d). (*R*,*S*)-**1b**: 98% yield, pale yellow solid; ^{31}P NMR ($CDCl_3$) δ −12.4 (d, J_{P-P} = 30.5 Hz) and 145.5 (d). (*R*)-**4**: 77% yield, pale yellow solid; ^{31}P NMR ($CDCl_3$) δ −13.1 (d, J_{P-P} = 13.7 Hz) and 126.8 (d).

(8) Palladium-catalyzed reaction of the ditriflate of 1,1′-binaphthalene-2,2′-diol and diarylphosphine oxides gave 2-(diarylphosphinyl)-1,1′-binaphthalen-2′-ols,[9] which were then reduced to the corresponding phosphines with $SiHCl_3$-$N(C_2H_5)_3$[10] followed by hydrolysis of the products with LiOH in aqueous THF to afford **2** in good yields.

(9) Kurtz, L.; Lee, G.; Morgans, D., Jr.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321.

(10) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

(11) Toda, F.; Tanaka, K. *J. Org. Chem.* **1988**, *53*, 3607.

(12) Rh(acac)[(*R*,*S*)-**1a**]: ^{31}P NMR ($CDCl_3$) δ 48.3 (dd, J_{P-P} = 83.9 Hz, J_{Rh-P} = 174.0 Hz) and 161.8 (dd, J_{Rh-P} = 331.1 Hz). Rh(acac)[(*R*,*R*)-**1a**]: ^{31}P NMR ($CDCl_3$) δ 51.9 (dd, J_{P-P} = 80.8 Hz, J_{Rh-P} = 178.5 Hz) and 152.5 (dd, J_{Rh-P} = 325.1 Hz). Rh(acac)[(*R*,*S*)-**1b**]: ^{31}P NMR ($CDCl_3$) δ 48.7 (dd, J_{P-P} = 82.4 Hz, J_{Rh-P} = 172.4 Hz) and 160.9 (dd, J_{Rh-P} = 332.6 Hz). Rh(acac)[(*R*)-**4**]: ^{31}P NMR ($CDCl_3$) δ 49.4 (dd, J_{P-P} = 82.4 Hz, J_{Rh-P} = 175.5 Hz) and 136.2 (dd, J_{Rh-P} = 328.0 Hz).

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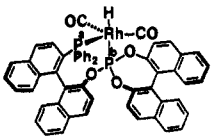
Table I. Hydroformylations of Olefins 5 Catalyzed by Phosphinephosphite–Rh(I) Complexes[a]

substrate	S/C[b]	ligand[c]	t, °C	time, h	% conv[d]	6/7[d]	% ee of 6[e]	config[f]
5a	400	(*R*,*S*)-**1a**	60	36	>99	86/14	92	*S*-(−)
5a[g]	2000	(*R*,*S*)-**1a**	80	78	97	84/16	88	*S*-(−)
5a[g]	200	(*R*,*R*)-**1a**	50	37	46	92/8	73	*S*-(−)
5a	400	(*R*,*S*)-**1b**	60	36	72	85/15	90	*S*-(−)
5b	300	(*S*,*R*)-**1a**	60	90	98	89/11	85	*R*-(+)
5c	2000	(*S*,*R*)-**1a**	60	43	>99	88/12	94	*S*-(+)
5d	1000	(*S*,*R*)-**1a**	60	20	97	86/14	95	(+)
5e	1000	(*S*,*R*)-**1a**	60	34	>99	87/13	88	(+)
5f	1000	(*S*,*R*)-**1a**	60	34	>99	87/13	93	(+)
5g	300	(*S*,*R*)-**1a**	60	66	>99	88/12	92	*S*-(+)
5h	1000	(*R*,*S*)-**1a**	30	93	90	24/76	75	*R*-(−)

[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 initial total pressure of 100 atm. [b] Substrate/[Rh] ratio. [c] Ligand/[Rh] ratios were 2.0–4.0. [d] Conversions were determined on the basis of ^{1}H NMR using $CHPh_3$ as internal standard. The ratios of **6**/**7** together with the conversions reflect the actual yields. [e] Determined by GLC analysis with a chiral capillary column (CHROMPACK Cp-Cyclodex β 236M) of aldehyde **6a** or acids derived by Jones oxidation of the products **6c–6h** or by ^{1}H NMR spectroscopy of **6b** using Eu(hfc)$_3$. [f] Determined by the signs of optical rotation, which were given in parentheses where possible. [g] Solvent/substrate ratios were 5–10.

exhibited the highest levels of enantioselectivities.[1,2,4] Moreover, use of a relatively small excess of chiral ligands (1.0–3.0 equiv to Rh(acac)(binaphos)) is sufficient for obtaining high enantioselectivities.[3] Branched to normal ratios are always satisfactorily high, except for the simple terminal olefin **5h**, and no trace of hydrogenation products was detected.[13] Turnover numbers as high as 2000 have been attained in reasonable reaction time at slightly elevated temperatures without substantial loss of enantioselectivities.

When a solution of Rh(acac)[(*S*,*R*)-**1a**] in benzene was treated with a 1:1 mixture of hydrogen and carbon monoxide at atmospheric pressure, a monohydrido complex was formed which has been tentatively assigned a trigonal bipyramidal structure ((*S*,*R*)-**8**).[14–16] This complex also exhibited catalytic activity for hydroformylation of **5d** in the presence of 2.3 equiv of (*S*,*R*)-**1a** (S/C = 300, in benzene, 60 °C, 20 h) to give (*S*)-**6d** (82% yield, 94% ee) and **7d** (18% yield), which suggests that (*S*,*R*)-**8** is a catalytically active species involved in the catalytic cycle. Complex (*S*,*R*)-**8** appears to exist as a single isomer at 60 °C, as shown by ^{31}P NMR spectroscopy.[18,19] Although dissymmetric structure around the Rh(I) catalytic center seems to be the most



(*S*,*R*)-**8**

important factor in achieving high enantioselectivity, the formation of a single catalytic species may also contribute.[20]

The results establish the Rh(I) complexes of phosphinephosphites **1**, a new class of unsymmetrical chiral bidentate ligands, as highly efficient catalysts for asymmetric hydroformylation. The product aldehydes are very important synthetic precursors to various physiologically active compounds. For example, (*S*)-**6a** can readily be converted to lactic acid and threonine.[5,21] Thus, the present catalysis has potential by wide application to asymmetric hydroformylation of a variety of olefins and provides a powerful new tool in organic synthesis. Studies on the scope and mechanistic aspects of the catalytic process are continuing.

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(13) Attempted reaction of methyl α-acetamidoacrylate catalyzed by the RhH(CO)(PPh$_3$)$_3$ and (*R*,*S*)-**1a** system (60 °C, 65 h, H_2/CO 100 atm (1:1)) afforded methyl 2-acetamido-2-formylpropanoate in 53% yield (13% ee) in addition to the corresponding hydrogenation product in 30% yield.

(14) 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.

(15) The IR spectrum of **8** in benzene-d_6 had bands at 1970 and 2010 cm^{-1} due to ν_{CO} and ν_{Rh-H}, respectively. No shift of ν_{CO} upon deuteration established that the hydride and CO ligands of **8** are cis to one another. The complex exhibited ^{31}P NMR ($CDCl_3$, 25 °C) signals at δ 25.5 (ddd, P^a, $J_{P^a-P^b}$ = 36.6, J_{Rh-P^a} = 119.0, J_{P^a-H} = 21.3 Hz) and 183.5 (ddd, P^b, J_{Rh-P^b} = 183.1, J_{P^b-H} = 158.7 Hz), and ^{1}H NMR ($CDCl_3$, 25 °C) signals at δ −9.70 (ddd, Rh-H, J_{Rh-H} = 8.5 Hz). These data led us to assign structure **8** to the complex. Specifically, the magnitude of J[P^b-H] is similar to that observed for J[P$_{ax}$-H] (152 Hz) in trigonal-bipyramidal HRh{P(OEt)$_3$}$_4$ at −134 °C: Meakin, P.; Muetterties, E. L.; Jesson, J. P. *J. Am. Chem. Soc.* **1972**, *94*, 5271.

(16) The natural bite angle (β_n)[17] of (*R*,*S*)-**1a** was determined to be 90.37° by molecular mechanics calculations using the CACHE system and bond distance of 2.315 Å for two Rh-phosphorus bonds.

(17) Casey, C. P.; Whiteker, G. T. *Isr. J. Chem.* **1990**, *30*, 299.

(18) The corresponding complex with two unidentate phosphines, HRh(CO)$_2$(PPh$_3$)$_2$, has been shown to be an 85:15 mixture of diequatorial and apical-equatorial isomers: Brown, J. M.; Kent, A. G. *J. Chem. Soc., Perkin Trans.* **1987**, *2*, 1597.

(19) In the ^{31}P NMR spectrum taken in toluene-d_8 under 1 atm of CO atmosphere, resonances due to the two phosphorus atoms broadened around −50 °C and then sharpened again below −90 °C to give substantially the same signal patterns as those observed at room temperature. This suggests the presence of a fluxional process.

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

(21) (*S*)-Lactic acid has also been attracting much interest as a monomer of biodegradable or bioabsorbable polymers: Ikada, Y. In *Polymers and Biomaterials*; Feng, H., Han, Y., Huang, L., Eds.; Elsevier Science Publishers B. V.: 1991; Amsterdam, p 273 and references cited therein.