Chinese Journal of Chemistry, **2004**, *22*, 203—206 **Article**

Asymmetric Hydroformylation of Olefins Catalyzed by a Chiral Diphosphite-Rhodium Complex

YAN, Ming*,[a](鄢明) LI, Xing-Shu[b](黎星术) CHAN, Albert Sun-Chi*,[b](陈新滋)

[a] *Department of Chemistry and Chemical Engineering, Suzhou University, Suzhou, Jiangsu 215006, China*
[b] *Open Laboratory of Chirotechnology of the Institute of Molecular Technology for Drug Discovery & Synthesis, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China*

A C_2-symmetrical aryl diphosphite derived from chiral binaphthol was prepared and its rhodium complex was used as catalysts in the asymmetric hydroformylation of olefins. High catalytic activity and good regioselectivity were observed. Up to 31.2% *ee* and 38.1% *ee* were achieved for the hydroformylation of 4-fluoro-styrene and vinyl acetate respectively. The influences of ligand-to-metal ratio, reaction temperature and the pressure of syn-gas on the enantioselectivity and regioselectivity were also studied.

Keywords diphosphite, chiral ligand, asymmetric hydroformylation, olefin, rhodium complex

Introduction

The catalytic asymmetric hydroformylation of olefins is a highly attractive reaction for the preparation of optically active aldehydes. Rhodium and platinum catalysts with diphosphine, diphosphinite, diphosphite and phosphine-phosphite ligands have been used for this reaction.[1]

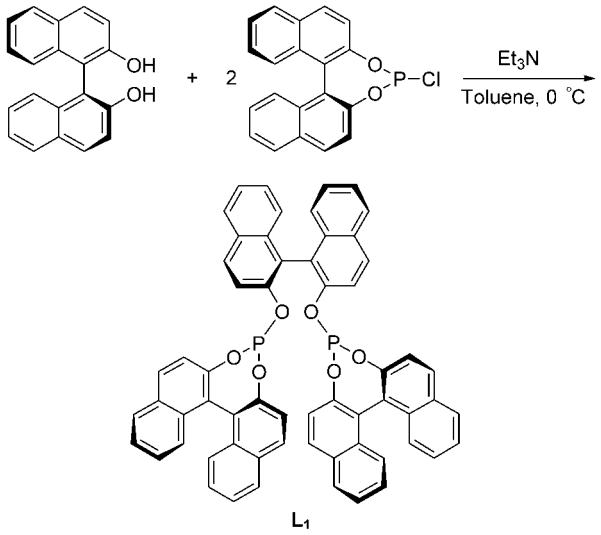
Although rhodium complexes with phosphine-phosphite ligands have been reported to give good enantioselectivities for several kinds of olefins, chiral diphosphite ligands are also attractive in rhodium and platinum catalyst systems due to their high catalytic activity and regioselectivity.[2] Continuous efforts have been made to develop highly enantioselective diphosphite-rhodium catalysts.[3] Recently we found that a C_2-symmetrical aryl diphosphite derived from chiral binaphthol was an efficient ligand in copper-catalyzed conjugate addition of diethylzinc to cyclic enones.[4] Here the application of the ligand in rhodium-catalyzed hydroformylation of olefins is reported.

Results and discussion

Optically pure aryl phosphite $\mathbf{L_1}$ was prepared by reaction of (*S*)-chlorophosphite and (*S*)-binaphthol in the presence of triethylamine and was purified by recrystallization in CH_2Cl_2-EtOH (Scheme 1).

The $\mathbf{L_1}$-rhodium complex is formed simply by mixing $\mathbf{L_1}$ with $Rh(acac)(CO)_2$ in benzene. The influences of the reaction conditions such as ligand-to-rhodium ratio, the pressure of syn-gas and the reaction temperature, on the catalytic activity and enantioselectivity in the hydroformylation of styrene were studied and these results are summarized in Tables 1—3.

Scheme 1 Synthesis of chiral diphosphite $\mathbf{L_1}$

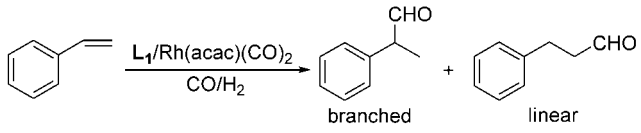


$\mathbf{L_1}$

For the phosphite-rhodium catalyst systems, excess ligands are usually used to prevent the formation of the achiral $Rh(CO)_4H$ species.[3c,3d] The use of two equivalents of $\mathbf{L_1}$ gave better enantioselctivity than the use of 1.1 equivalents of $\mathbf{L_1}$ (Table 1, Entry 2 vs. Entry 1). When 4 equivalents of $\mathbf{L_1}$ were used, slightly better regioselectivity but lower enantioselectivity were obtained.

* E-mail: yanm@suda.edu.cn
Received April 21, 2003; revised September 1, 2003; accepted October 9, 2003.
Project supported by the Suzhou University and the Hong Kong Polytechnic University ASD Fund and University Grants Committee Area of Excellence Scheme in Hong Kong (AoE P/10-01).

Table 1 Influence of ligand-to-rhodium ratio on the hydroformylation of styrene using $\mathbf{L_1}$-rhodium catalyst [a]



Entry	$\mathbf{L_1}$/Rh (mol/mol)	Conv.[b]/%	b/l [b]	*ee* [b,c]/%
1	1.1	100	81/19	17.9
2	2	100	83/17	25.3
3	4	100	85/15	15.1

[a] The reactions were carried out in benzene with 0.5 mol% $Rh(acac)(CO)_2$ (24 h, 60 ℃, 7.0 MPa syn-gas). [b] The conversions, b/l and *ee* values of products were determined by GC with a chiraldex B-TA column (30 m×0.25 mm). Only a small trace of ethylbenzene (<2%) was observed in the crude product. [c] The absolute configuration of the product was assigned as *S* by comparison of the optical rotation with reported value.

Table 2 Influences of pressure of syn-gas on the hydroformylation of styrene using $\mathbf{L_1}$-rhodium catalyst [a]

Entry	Pressure/MPa	Conv.[b]/%	b/l [b]	*ee* [b,c]/%
1	0.7	100	73/27	15.3
2	2.1	100	81/19	19.3
3	4.2	100	82/18	24.2
4	7.0	100	83/17	25.3

[a] The reactions were carried out in benzene with 0.5 mol% $Rh(acac)(CO)_2$ and 1 mol% $\mathbf{L_1}$ (24 h, 60 ℃). [b] The conversions, b/l and *ee* values of products were determined by GC with a chiraldex B-TA column (30 m×0.25 mm). [c] The absolute configuration of the product was assigned as *S* by comparison of the optical rotation with reported value.

Table 3 Influences of reaction temperature on the hydroformylation of styrene using $\mathbf{L_1}$-rhodium catalyst [a]

Entry	*t*/℃	Conv.[b]/%	b/l [b]	*ee* [b,c]/%
1	25	18.4	83/17	21.4
2	40	64.6	84/16	21.7
3	60	100	83/17	25.3
4	80	100	81/19	16.0

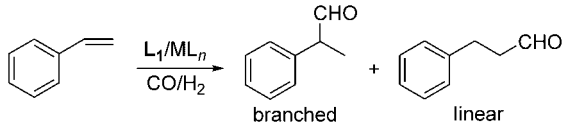
[a] The reactions were carried out in benzene (24 h, 0.5 mol% $Rh(acac)(CO)_2$, 1 mol% $\mathbf{L_1}$, 7.0 MPa syn-gas). [b] The conversions, b/l and *ee* values of products were determined by GC with a chiraldex B-TA column (30 m×0.25 mm). [c] The absolute configuration of the product was assigned as *S* by comparison of the optical rotation with reported value.

The regioselectivity and the enantioselectivity were improved as the pressure increased from 0.7 to 4.2 MPa (Table 2, Entries 1, 2, 3). Further increase of pressure showed slight effect on the reactions (Table 2, Entry 3 vs. Entry 4).

The hydroformylation of styrene proceeded very slowly at low temperature. Elevation of reaction temperature increased the conversion efficiently and also slightly improved enantioselectivity of the reactions (Table 3, Entries 1, 2, 3). The optimal reaction temperature was found to be about 60 ℃ and higher temperature decreased the enantioselectivity sharply (Table 3, Entry 3 vs. Entry 4).

Diphosphite $\mathbf{L_1}$ combined with different rhodium and platinum precursors were also examined in the hydroformylation of styrene and the results are summarized in Table 4. When a cationic rhodium precursor was used, lower enantioselectivity was obtained (Table 4, Entry 1 vs. Entry 2). Cserepi-Szucs and Bakos[5] reported that diphosphite/Pt-$SnCl_2$ catalysts gave much better enantioselectivity than the corresponding diphosphite/rhodium catalysts in the hydroformylation of styrene. In this study we found that the $\mathbf{L_1}$-$Pt(PhCN)_2Cl_2$-$SnCl_2$ catalyst system provided similar enantioselectivity and regioselectivity, but lower catalytic activity compared with the $\mathbf{L_1}$-rhodium catalyst system (Table 4, Entry 1 vs. Entry 3). It is noticeable that no ethylbenzene was formed using the $\mathbf{L_1}$-$Pt(PhCN)_2Cl_2$-$SnCl_2$ catalyst, while a large amount (>50%) of ethylbenzene was observed with Bakos' diphosphite/Pt-$SnCl_2$ catalyst.[5]

Table 4 Hydroformylation of styrene catalyzed by $\mathbf{L_1}$ combined with different rhodium and platinum precursors



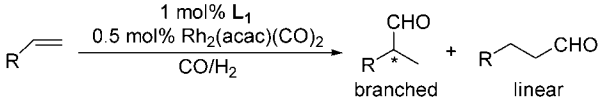
Entry	ML_n	*t*/℃	Conv.[b]/%	b/l [b]	*ee* [b,c]/%
1	$Rh(acac)(CO)_2$	60	100	83/17	25.3
2	$Rh(COD)BF_4$	60	100	82/18	18.4
3	$Pt(PhCN)_2Cl_2$-$SnCl_2$	80	81.0	79/21	22.6

[a] The reactions were carried out in benzene with 0.5 mol% rhodium or platinum precursor and 1 mol% $\mathbf{L_1}$ (24 h, 7 MPa syn-gas). [b] The conversions, b/l and *ee* values of products were determined by GC with a chiraldex B-TA column (30 m×0.25 mm). Only a small trace of ethylbenzene (<2%) was observed in the crude product. [c] The absolute configuration of the product was assigned as *S* by comparison of the optical rotation with reported value.

To explore the scope of applicable substrates, asymmetric hydroformylation of several other olefins was also examined and the results are summarized in Table 5.

Electronic property of 4-substitution of styrene displayed effects on the enantioselectivity and regioselectivity. Electron-withdrawing group provided beneficial influence on enantioselectivity and regioselectivity, in contrast electron-donating group gave lower enantioselectivity and regioselectivity (Table 5, Entry 2 vs. Entry 1). Bulky 2-vinyl naphthalene showed lower reactivity and regioselectivity, but the enantioselectivity was comparable with that obtained using styrene (Table 5, Entry 3).

Table 5 Asymmetric hydroformylation of olefins using $\mathbf{L_1}$-rhodium catalyst [a]



Entry	Olefin	Conv.[b]/%	b/l [b]	*ee* [b]/%
1	4-Methyl-styrene	100	85/15	21.1
2	4-Fluoro-styrene	100	89/11	31.2
3	2-Vinyl-naphthalene	95	79/21	27.5[c]
4	Vinyl acetate	100	92/8	38.1[d]

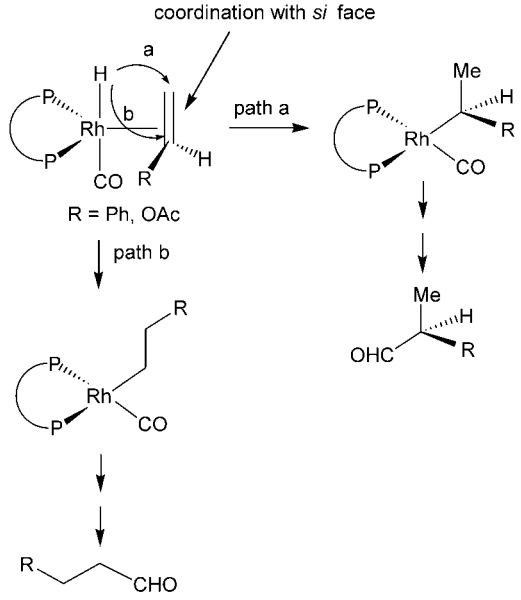
[a] The reactions were carried out in benzene with 0.5 mol% $Rh(acac)(CO)_2$ and 1 mol% $\mathbf{L_1}$ (24 h, 60 ℃, 7.0 MPa syn-gas). [b] The conversions, b/l and *ee* values of products were determined by GC with a chiraldex B-TA column (30 m×0.25 mm). [c] The *ee* value was determined by comparison of the optical rotation with reported value. [d] The absolute configuration of the product was assigned as *R* by comparison of the optical rotation with reported value.[6]

Asymmetric hydroformylation of functionalized alkenes can serve as an useful method for the synthesis of valuable intermediates to biologically active compounds and materials. Nozaki *et al.*[2] reported that the excellent enantioselectivity and regioselectivity had been achieved in the hydroformylation of vinyl acetate using a chiral phosphine-phosphite/Rh(I) catalyst. A Rh(I) complex of bulky chiral diphosphite ligand was examined in the asymmetric hydroformylation of vinyl acetate by Babin *et al.*[7] and provided exclusively branched aldehyde with moderate enantioselectivity (50% *ee*). The rhodium complex of $\mathbf{L_1}$ was also tested in the hydroformylation of vinyl acetate (Table 5, Entry 4). Complete conversion of vinyl acetate and excellent yield of aldehyde products were obtained with a good regioselectivity (branch/linear = 92/8). The enantioselectivity (38.1% *ee*) was moderate but still promising.

In previous studies of reaction mechanism, the coordination of olefin with Rh(P-P)(CO)H species and consequent hydride transfer were proposed in P/Rh complex catalyzed hydroformylation of olefins.[1b,1c] The transfer of hydride to olefin can proceed via two pathways (Scheme 2, path a and path b). The regioselectivity of the hydroformylation depends on the relative rate of path a and path b. Due to bigger electron withdrawing ability of the acetoxy group in vinyl acetate, the path a is more favored in hydroformylation of vinyl acetate comparing with in hydroformylation of styrene, so better regioselectivity for branched aldehyde was observed in the hydroformylation of vinyl acetate.

In conclusion rhodium complex of chiral aryl diphosphite $\mathbf{L_1}$ has been found to be active catalysts for the hydroformylation of olefins. Excellent chemoselectivity and good regioselectivity for the desired branch aldehydes were achieved. The ratio of ligand to rhodium, the pressure of syn-gas, the reaction temperature and the rhodium precursors showed significant effects on the enantioselectivities and regioselectivities of the reaction. Introduction of electron-withdrawing group improved the enantioselectivity and regioselectivity efficiently in the hydroformylation of styrene. A working model was proposed to explain the regioselectivity observed in the reactions.

Scheme 2 Proposed working model for regioselectivity



Experimental

General information

All reactions were carried out in oven-dried glassware using standard Schlenk technique under nitrogen atmosphere. Toluene was distilled from sodium/benzophenone and triethylamine was distilled from CaH_2. PCl_3 was distilled before use. ^{31}P, ^{1}H, and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer. Mass analysis was performed on a Finnigan Model Mat 95 ST mass spectrometer. Optical rotations were measured on a Perkin-Elmer Model 341 polarimeter. GC analysis was performed on an HP 4890 apparatus equipped with FID.

Synthesis of diphosphite $\mathbf{L_1}$

(*S*)-Binaphthol (1.0 g, 3.4 mmol) was azeotropically dried with toluene (3×5 mL) and was dissolved in toluene (6 mL) and triethylamine (1.7 mL, 12 mmol). This solution was added dropwise to a solution of PCl_3 (0.32 mL, 1.8 mmol) and triethylamine (1.7 mL, 12 mmol) in toluene (6 mL) in an ice bath. The reaction mixture was stirred at reflux temperature for 8 h. After the $Et_3N \cdot HCl$ was filtered off, the solvent and excess of PCl_3 were removed under vacuum to give a colorless oil. Toluene (5 mL) was added and evaporated under vacuum. This procedure was repeated three times to remove any trace of PCl_3. The resulting chlorophosphite was dissolved in toluene (10 mL). ^{31}P NMR (toluene-d^8) δ: 181.

(*S*)-Binaphthol (0.5 g, 1.7 mmol) was azeotropically dried with toluene (3×5 mL) and was dissolved in triethylamine (0.5 mL, 2 mmol) and toluene (5 mL). The solution was cooled with an ice-bath and the toluene solution of chlorophosphite prepared above was added dropwise in a period of 0.5 h. The mixture was stirred for 8 h at 0 ℃. The reaction solution was filtered through a layer of alkaline alumina. The filtrate was evaporated under vacuum to give a white solid which was recrystallized from CH_2Cl_2-EtOH to give pure **L_1** 1.0 g, Yield 64.5%. m.p. 196—198 ℃ (decomp.), $[\alpha]_D^{20}$ +346.6 (*c* 1.085, THF); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 145.7; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.97 (d, J=8.8 Hz, 2H), 7.90 (d, J=8.0 Hz, 2H), 7.82 (dd, J_1=8.0, J_2=8.8 Hz, 4H), 7.73 (d, J=8.0 Hz, 2H), 7.52 (d, J=8.8 Hz, 2H), 7.42—7.33 (m, 8H), 7.31—7.16 (m, 14H), 6.53 (d, J=8.8 Hz, 2H), 3.72 (q, J=6.8 Hz, 1H), 2.36 (s, 0.5H), 1.24 (t, J=6.8 Hz, 1.5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 147.2, 147.0, 146.5, 134.2, 132.7, 132.2, 131.4, 131.0, 130.8, 130.2, 130.0, 129.5, 128.3, 128.2, 128.1, 126.9, 126.8, 126.2, 126.0, 125.8, 125.1, 124.9, 124.6, 124.2, 122.4, 121.8, 121.7, 121.1; MS (ESI) *m*/*z* (%): 915 (M^++1, 100). Anal. calcd for $C_{60}H_{36}O_6P_2 \cdot 0.5C_2H_6O$ (crystalline solvent): C 78.12, H 4.16; found C 78.13, H 4.16.

General procedure for the asymmetric hydroformylation

Rh(acac)$(CO)_2$ (2 mg, 7.7×10^{-3} mmol), diphosphite **L_1** (14 mg, 15.4×10^{-3} mmol) and benzene (2 mL) were added to an autoclave and the mixture was stirred for 5 min to give a light yellow solution. After olefin (1.54 mmol) and benzene (2 mL) was added, the reaction mixture was heated to the desired temperature and pressurized with syn-gas [V(CO) ∶ $V(H_2)$=1 ∶ 1)] to the appropriate initial pressure. When the reaction was stopped, the mixture was filtered through a thin layer of silica gel and the filtrate was analyzed by GC for determination of the conversion, regioselectivity and enantiomeric excess.

References

1 (a) Lin, G. Q.; Li, Y. M.; Chan, A. S. C. *Principles and Applications of Asymmetric Synthesis*, Wiley & Sons, New York, **2000**.
(b) Gladiali, S.; Bayon, J.; Claver, C. *Tetrahedron: Asymmetry* **1995**, *7*, 1453.
(c) Agbossou, F.; Carpentier, J.-F.; Mortreux, A. *Chem. Rev*. **1995**, *95*, 2485.

2 Nozaki, K.; Sakai, N.; Nanno, T.; Higashijima, T.; Mano, S.; Horiuchi, T.; Takaya, H. *J. Am. Chem. Soc.* **1997**, *119*, 4413.

3 (a) Dieguez, M.; Pamies, O.; Ruiz, A.; Claver, C. *New J. Chem*. **2002**, *26*, 827.
(b) Freixa, Z.; Bayon, J. C. *J. Chem. Soc., Dalton Trans.* **2001**, 2067.
(c) Buisman, G. J. H.; Vos, E. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1995**, 409.
(d) Kadyrov, R.; Heller, D.; Selke, R. *Tetrahedron: Asymmetry* **1998**, *9*, 329.
(e) Jiang, Y. Z.; Xue, S.; Li, Z.; Deng, J. G.; Mi, A. Q.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1998**, *9*, 3185.

4 Yan, M.; Yang, L. W.; Wong, K. Y.; Chan, A. S. C. *Chem. Commun.* **1999**, 11.

5 Cserepi-Szucs, S.; Bakos, J. *J. Chem. Soc., Chem. Commun.* **1997**, 635.

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

7 Babin, J. E.; Whiteker, G. T. *US 5360938*, **1994** [*Chem. Abstr*. **1994**, *122*, 186609].

(E0304219 PAN, B. F.)