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Asymmetric synthesis. Part 29: Asymmetric hydroformylation of styrene catalyzed by chiral spiro diphosphite–rhodium(I) complexes

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Abstract

Chiral diphosphite ligands L_1–L_3 were prepared by the reaction of (1*S*,5*S*,6*R*)-(*cis*,*trans*)-spiro[4.4]nonane-1,6-diol with chlorophosphites. These ligands were tested in the rhodium catalyzed hydroformylation of styrene and enantioselectivities up to 69% were achieved. High regioselectivities (97%) to 2-phenylpropanal and high yields (98%) were obtained under mild reaction conditions. The influence of reaction conditions is also discussed. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Asymmetric hydroformylation is a method for the preparation of homochiral aldehydes, which are important precursors for the synthesis of pharmaceuticals and food ingredients. Much effort has been made to develop chiral catalysts, especially in the design of novel chiral ligands, which are expected to provide high regio- and stereoselectivity in the hydroformylation of olefins. Rh(I)-catalysts containing chiral phosphine–phosphite or diphosphite have provided 50–94% ee in the hydroformylation of styrene with excellent chemo- and regioselectivity.[1–3]

$$\mathrm{PhCH{=}CH_2} \xrightarrow[\mathrm{Rh(acac)(CO)_2+L^*}]{\mathrm{CO/H_2}} \underset{\mathrm{b}}{\mathrm{PhCH(CH_3)CHO}} + \underset{\mathrm{n}}{\mathrm{PhCH_2CH_2CHO}}$$

Recently, a bisphosphinite containing a spiro backbone has been found to be an efficient chiral ligand for the catalytic asymmetric hydrogenation of enamides in our laboratory.[4] Since phosphite–Rh(I) complexes often show high catalytic activity in hydroformylation,[5,6] and the phosphites are easily prepared

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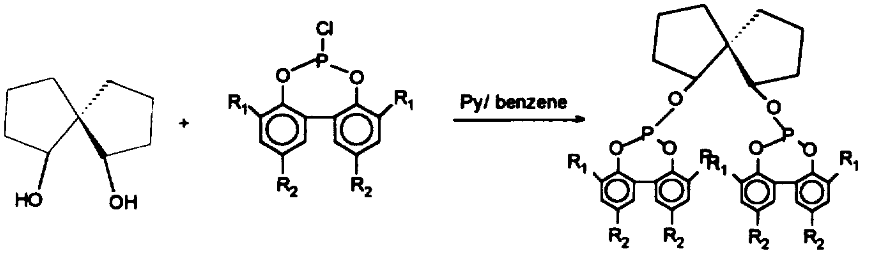
from spiro-diol, we have synthesised diphosphites derived from (1*S*,5*S*,6*R*)-(*cis,trans*)-spiro[4.4]nonane-1,6-diol **1** and investigated them in the asymmetric hydroformylation of styrene.

2. Results and discussion

The chiral phosphites were readily prepared by the reaction of (1*S*,5*S*,6*R*)-(*cis,trans*)-diol **1** with the corresponding chlorophosphites **2a–c**, which were formed *in situ* according to the literature procedure,[6] in benzene in the presence of pyridine. Compounds L$_{1-3}$ are stable in air and can be easily purified by flash column chromatography using toluene as the eluent.



(1*S*,5*S*,6*R*)-(*cis,trans*)-diol
1

2a: $R_1=R_2=H$
2b: $R_1=R_2=Bu^t$
2c: $R_1=Bu^t$, $R_2=OMe$

L$_1$
L$_2$
L$_3$

The catalyst species were prepared *in situ* by simply mixing Rh(acac)(CO)$_2$ and diphosphites. The results of the asymmetric hydroformylation of styrene are given in Table 1. In run 1, the substrate was immediately added after the autoclave had been heated to the desired reaction temperature and a low yield of aldehyde resulted. Since an incubation period is necessary for the formation of RhH(L)(CO)$_2$[6,7] from Rh(acac)(CO)$_2$ and diphosphite, the catalyst was prepared under typical conditions [40°C, 10 atm of syn gas (CO:H$_2$=1:1), 10 h] before the substrate was added. Little influence on the enantioselectivity was observed on varying the pressure of syn gas (runs 2–6), however, the yield of product decreased markedly when the pressure of syn gas was increased. This catalyst was also tested at low pressure, even at atmospheric pressure of syn gas and 98% yield of aldehyde was obtained at 5 atm of syn gas with 61% ee (run 6). It is noteworthy that only 47% ee was obtained at 1 atm of syn gas with moderate yield (77%, run 7). Moreover, the reaction rate decreased dramatically when the complex was incubated under the conditions (40°C, 1 atm of syn gas, 10 h) with the same reaction conditions (run 8 versus 7) and the result implies that the intermediates RhH(L)(CO)$_2$ can be partially formed at an atmospheric pressure of syn gas. Thus, to achieve high yield, a higher pressure of syn gas (10 atm) is necessary for the efficient formation of RhH(L)(CO)$_2$ while the catalyst was prepared. When the reaction temperature was decreased from 40 to 25°C, the enantiomeric excess was slightly increased, but yield of product decreased markedly (run 2 versus 9). An increase of the ee value was achieved by using a small excess of diphosphite (run 2 versus 12). However, the enantiometric excess did not improve and the yield of product decreased when the ratio of P/Rh was increased to 5. High b/n ratios were obtained in this reaction (runs 1–6, 9–14) and this might be attributed to the presence of the spiro backbone and large bulky substituents on the bis(phenol) group of the catalyst.[8]

Compounds L$_{1-2}$ were also evaluated under the typical hydroformylation reaction conditions (40°C, 20 atm of syn gas, 10 h). Compound L$_2$ showed relatively high catalytic activity and 92% yield was found with up to 59% ee (run 15). Compound L$_1$ with no substituents on the ortho and para positions of the biaryl moiety showed very low catalytic activity and only gave very low enantioselectivity (run

Table 1
Asymmetric hydroformylation of styrene catalyzed by diphosphite–Rh(I) complexes[a]

run	ligand	P/Rh	temp,°C	P, atm	time, h	ee, %[b]	yield, %[c]	b/n[c]	config.[d]
1[e]	L_3	3/1	40	20	10	63	49	97/3	S
2		3/1	40	20	10	65	85	97/3	S
3		3/1	40	40	10	66	71	97/3	S
4		3/1	40	58	10	65	44	97/3	S
5		3/1	40	10	10	62	89	97/3	S
6		3/1	40	5	10	61	98	97/3	S
7		3/1	40	1	10	47	77	88/12	S
8		3/1	40	1	10	43	18	91/9	S
9		3/1	25	20	10	69	21	97/3	S
10		3/1	25	5	10	67	60	97/3	S
11		3/1	40	20	5	63	50	97/3	S
12		2/1	40	20	10	56	76	97/3	S
13		5/1	40	20	10	66	75	97/3	S
14		5/1	40	40	10	64	50	97/3	S
15	L_2	3/1	40	20	10	59	92	98/2	S
16	L_1	3/1	40	20	10	3	30	87/13	R

a) Reactions were carried out in toluene in a 40 ml autoclave under syn gas ($CO/H_2=1/1$); styrene/catalyst=500; the complex was incubated under 10 atm of syn gas at 40°C for 10 h before substrate was added unless otherwise stated. b) Determined by GC analysis (β-236M, 0.25mmx25m) of the corresponding acid. c) Yields and b/n ratios were determined by GC (β-236M, 0.25mmx25m) using cis-decahydronaphthalene as an internal standard. d) Determined by the sign of optical rotation of the corresponding aldehyde. e) The complex was not incubated before styrene was added. f) The complex was incubated under the condition (40°C, 1 atm of syn gas, 10 h) before styrene was added.

16). These results demonstrate that the enantioface discriminating ability of this type of catalyst may be steered by a bulky phenol moiety.[9]

In conclusion, novel chiral diphosphites L_{2-3} derived from (1*S*,5*S*,6*R*)-(*cis,trans*)-spiro[4.4]nonane-1,6-diol **1** are good ligands in the rhodium-catalyzed hydroformylation of styrene providing high regio- and chemoselectivity for branched aldehydes, and moderate enantioselectivity.

3. Experimental

3.1. General

All reactions were carried out in oven-dried glassware using Schlenk techniques under pure nitrogen. Benzene and toluene were distilled from sodium–benzophenone, pyridine from CaH_2. PCl_3 and styrene were distilled before use and stored under pure nitrogen. 2,2′-Dihydroxybiphenyl was purchased from Sigma Chemical Co. 4,4′,6,6′-Tetra-*tert*-butyl-2,2′-bis(phenol) and 6,6′-di-*tert*-butyl-4,4′-dimethoxy-2,2′-bis(phenol) were prepared according to literature procedures.[10,11] Melting points were determined on a Southend SS25PH apparatus and are uncorrected. Elemental analyses were recorded on a Carlo Erba-1106 instrument. Gas chromatographic analyses were performed by SC-7 gas chromagraphy. ^{31}P-NMR spectra were obtained on a Varian FT-80A using H_3PO_4 (85%) as an internal standard and ^{1}H-NMR spectra on a Bruker 300 spectrometer. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Enantiomeric excesses were measured after Jones oxidation of the aldehyde to the corresponding acids on a SC-7 gas chromatograph with a Chrompack β-236M, 0.25×25 m chiral capillary column. Hydroformylation reactions were carried out in a laboratory-made stainless-steel autoclave (40 ml).

3.2. *Preparation of 1,6-bis(2,2′-bisphenoxyphosphinoxy)spiro[4.4]nonane, L_1*

2,2′-Dihydroxybiphenyl (600 mg, 3.2 mmol) dried under reduced pressure at 80°C for 30 min was dissolved in benzene (10 ml) and pyridine (0.5 ml). This solution was added dropwise to a cooled solution (0°C) of PCl_3 (0.3 ml) and pyridine (0.5 ml). The reaction mixture was stirred for 6 h at 60°C. The solvent and excess of PCl_3 were removed under vacuum. The last trace of PCl_3 in the residue was removed by benzene (3 ml) under reduced pressure and this procedure was repeated three times. Compound **2a** formed *in situ* was dissolved in benzene (10 ml) and pyridine (1.0 ml). (1*S*,5*S*,6*R*)-(*cis,trans*)-Spiro[4.4]nonane-1,6-diol (210 mg, 1.3 mmol) dissolved in benzene was added dropwise to the solution of compound **2a** at 0°C. The reaction mixture was stirred overnight at room temperature. The resulting pyridine salts were filtered off. Evaporation of the solvent gave a white plaster which was purified by flash column chromatography using toluene as eluent. A white foam (460 mg, 58%) was obtained. $[\alpha]_D^{20}=-8.4$ (0.35, CH_2Cl_2); mp=58–59°C; ^{31}P-NMR (CD_3COCD_3, δ) 145.72, 140.69 ppm; ^{1}H-NMR (CD_3COCD_3, δ) 7.56–7.20 (m, 16H), 4.97 (m, 1H), 4.38 (m, 1H), 2.07–1.47 (m, 12H). Elemental analysis, calcd: C, 67.82; H, 5.14. Found: C, 67.71; H, 5.15.

3.3. *Preparation of 1,6-bis(4,4′,6,6′-tetra-*tert*-butyl-2,2′-bisphenoxyphosphinoxy)spiro[4.4]nonane, L_2*

Treatment of 4,4′,6,6′-tetra-*tert*-butyl-2,2′-bis(phenol) (950 mg, 2.3 mmol) and (1*S*,5*S*,6*R*)-(*cis,trans*)-spiro[4.4]nonane-1,6-diol (120 mg, 0.77 mmol) as described for compound L_1 afforded compound L_2 (380 mg, 48%). $[\alpha]_D^{20}=-15.6$ (0.52, CH_2Cl_2); mp=139–140°C; ^{31}P-NMR (CD_3COCD_3, δ) 146.59, 144.90 ppm; ^{1}H-NMR (CD_3COCD_3, δ) 7.50–7.45 (m, 4H), 7.23–7.17 (m, 4H), 4.92 (m, 1H), 4.39 (m, 1H), 1.71–0.83 (m, 84H). Elemental analysis, calcd: C, 75.33; H, 9.07. Found: C, 75.59; H, 9.17

3.4. *Preparation of 1,6-bis(6,6′-di-*tert*-butyl-4,4′-dimethoxy-2,2′-bisphenoxyphosphinoxy)spiro[4.4]nonane, L_3*

Treatment of 6,6′-di-*tert*-butyl-4,4′-dimethoxy-2,2′-bis(phenol) (900 mg, 2.5 mmol) and (1*S*,5*S*,6*R*)-(*cis,trans*)-spiro[4.4]nonane-1,6-diol (130 mg, 0.83 mmol) as described for compound L_1 afforded compound L_3 (510 mg, 66%). $[\alpha]_D^{20}=+13.8$ (0.44, CH_2Cl_2); mp=81–82°C; ^{31}P-NMR (CD_3COCD_3, δ) 145.83, 144.81 ppm; ^{1}H-NMR (CD_3COCD_3, δ) 6.96–6.93 (m, 4H), 6.83–6.76 (m, 4H), 4.93 (m, 1H), 4.41 (m, 1H), 3.84 (s, 6H), 3.82 (s, 6H), 1.82–0.83 (m, 48H). Elemental analysis, calcd: C, 68.52; H, 7.29. Found: C, 69.22; H, 7.64.

3.5. *General procedure for the asymmetric hydroformylation*

The autoclave filled with $Rh(acac)(CO)_2$ (0.0085 mmol) and diphosphite (0.025 mmol) was purged three times with syn gas ($CO:H_2=1:1$), then toluene (1.5 ml) was added and pressurised to 10 atm of syn gas. The reaction mixture was stirred for 10 h at 40°C to form the active catalyst. Styrene (4.25 mmol) and toluene (1 ml) were placed in the autoclave and the syn gas was introduced until the desired pressure was reached. After the desired reaction time, the autoclave was cooled to room temperature and depressurised. *cis*-Decahydronaphthalene as an internal standard was added. The mixture was filtered on silica gel and the filtrate was analysed by GC for the yield and regioselectivity. A sample of the filtrate was oxidised to acid by Jones oxidation and analysed by GC for determination of the enantiomeric excess.

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