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Asymmetric hydrocyanation of olefins catalyzed by chiral diphosphite–nickel complexes

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Abstract

Chiral aryl diphosphite ligands derived from binaphthol were found to be effective in the nickel-catalyzed hydrocyanation of a variety of olefins. Enantioselective hydrocyanations of styrene, 4-substituted styrenes and norbornene were achieved with excellent regioselectivity and moderate enantioselectivity. The hydrocyanation of vinyl acetate gave 72.9% ee. The catalytic activity and the enantioselectivity of the Ni(0)–diphosphite complexes were found to be highly dependent on the structures of the ligands.

1. Introduction

Catalytic asymmetric carbon–carbon bond formation is of fundamental importance in organic synthesis. The asymmetric hydrocyanation of olefins catalyzed by transition metal complexes containing chiral phosphorus ligands provides a useful method for the preparation of optically active nitriles which can be easily converted to other useful compounds.[1] In spite of DuPont's successful industrial hydrocyanation process for the preparation of adiponitrile, research on asymmetric hydrocyanation is surprisingly rare.[2] Ni(0) and Pd(0) complexes of chiral diphosphite and phosphine–phosphite were examined in the hydrocyanation of norbornene with low enantioselectivity.[3,4] Highly enantioselective hydrocyanation of vinyl naphthalene was reported by RajanBabu et al. using phosphinite ligands with strong electron-withdrawing substituents.[5,6] In our pursuit of the synthesis and application of novel chiral diphosphite ligands, we prepared a series of diphosphite ligands based on binaphthol.[7,8] In this paper we report the enantioselective hydrocyanation of a variety of olefins using chiral diphosphite–nickel catalysts which gave promising enantioselectivities.

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2. Results and discussion

Diphosphites $\mathbf{L_a}$–$\mathbf{L_d}$ were prepared via the reaction of the corresponding chlorophosphite with aryl diols.[7,8] The hydrocyanation of styrene was carried out using the catalysts prepared in situ by mixing $Ni(COD)_2$ with the chiral diphosphites. Acetone cyanohydrin was used in the reactions and proved to be a more convenient and safer source of hydrogen cyanide than the extremely toxic free hydrogen cyanide. Nonpolar solvents such as hexane, benzene and toluene gave comparable reaction rates and ee values for the products. The reactions did not occur in chloroform and acetonitrile. Initially the Ni(0) complexes of ligands $\mathbf{L_a}$–$\mathbf{L_d}$ were examined in the hydrocyanation of styrene and the results are summarized in Table 1.

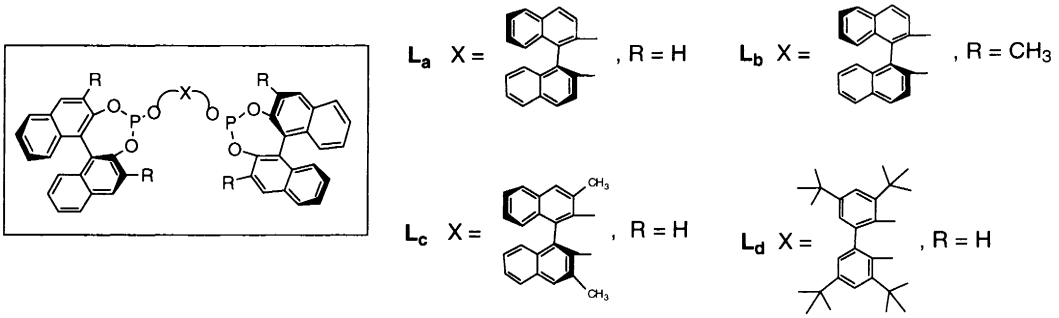
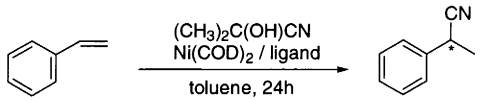


Table 1
The enantioselective hydrocyanation of styrene with Ni(0) complexes of $\mathbf{L_a}$–$\mathbf{L_d}$[a]



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Entry	Ligand	T (°C)	Conversion (%)[b]	Selectivity to **1** (%)[b,c]	E.e. (%)[d]
1	/	100	/	/	/
2	$\mathbf{L_a}$	20	12.6	92.0	23.4
3	$\mathbf{L_b}$	20	3.8	86.8	11.8
4	$\mathbf{L_c}$	20	<1	/	/
5	$\mathbf{L_d}$	20	10.5	89.5	65.0
6	$\mathbf{L_d}$	60	18.4	72.8	58.8
7	$\mathbf{L_d}$	100	47.6	70.3	49.1

a) The reactions were carried out in toluene for 24h; $Ni(COD)_2$: ligand : styrene: acetone cyanohydrin = 0.01 : 0.012 : 1 : 1.1.
b) The conversions of styrene and the selectivities to **1** were determined by GC using *n*-dodecane as internal standard. c) The balance was unidentified condensation products; no linear nitrile was observed. d) The ee values of **1** were determined by GC with a Chiraldex G-PN column (30m × 0.25mm).

The presence of a diphosphite ligand was essential for the occurrence of the reaction (entry 1) and excellent regioselectivities for branched nitrile **1** were achieved with $Ni(COD)_2/\mathbf{L_a}$–$\mathbf{L_d}$ complexes. The previous studies on the hydrocyanation of olefins with chiral phosphite ligands and various achiral phosphorus ligands demonstrated significant steric and electronic effects of the ligands.[5,9] In this study the structures of the chiral diphosphite ligands also showed profound influence on the catalytic activity and enantioselectivity. $Ni(COD)_2/\mathbf{L_b}$ and $Ni(COD)_2/\mathbf{L_c}$ gave very low catalytic activity and enantioselectivity (entries 3 and 4). $Ni(COD)_2/\mathbf{L_a}$ provided branched nitrile with 23.4% ee and 12.6%

conversion (entry 2). Ni(COD)$_2$/**L$_d$** gave 65% ee and 10.5% conversion at 20°C (entry 5) and a 47.6% conversion was achieved at 100°C with 49.1% ee (entry 7). Further studies of the Ni(COD)$_2$/**L$_d$** complex uncovered a remarkable increase of conversion using higher ligand-to-nickel ratios and the results are summarized in Table 2.

Table 2
The influence of the ligand-to-nickel ratio on the conversion and enantioselectivity in the hydrocyanation of styrene with Ni(COD)$_2$/**L$_d$**[a]

Entry	Ligand/Ni (mol/mol)	Conversion (%)[b]	Selectivity to **1** (%)[b,c]	E.e. (%)[d]
1	0.8	30.6	78.4	51.3
2	1.2	47.6	70.3	49.1
3	2.0	72.7	68.7	50.3
4	5.0	92.4	73.3	51.7
5	7.0	>98	79.7	51.1

a) The reactions were carried out in toluene at 100 °C for 24h [Ni(COD)$_2$: styrene: acetone cyanohydrin = 0.01: 1 : 1.1]. b) The conversions of styrene and the selectivities to **1** were determined by GC using *n*-dodecane as internal standard. c) The balance was unidentified condensation products; no linear nitrile was observed. d) The ee values of **1** were determined by GC with a Chiraldex G-PN column (30m × 0.25mm).

The enantioselectivity was essentially independent of the ligand-to-nickel ratio, but the increase of ligand-to-nickel ratio significantly improved the conversion (Table 2, entries 1–5). The catalyst deactivation was found to be a serious problem in many phosphine–nickel and phosphite–nickel catalyst systems.[9,10] A deactivation pathway of Ni(0) catalysts via the formation of the inactive Ni(CN)$_2$ species was proposed by Goertz et al.[10] With the Ni(COD)$_2$/**L$_d$** catalyst system the excess ligand **L$_d$** may be beneficial in shifting the balance toward the active catalytic species.

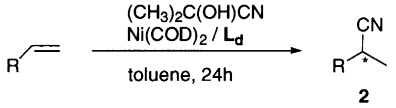
The nickel complex of **L$_d$** was further examined in the hydrocyanation of other olefins and the results are listed in Table 3. The hydrocyanation of 4-fluorostyrene gave complete conversion and the enantioselectivity was comparable to that of the hydrocyanation of styrene (Table 3, entry 3). Electron-rich substitutents such as methoxyl group gave somewhat lower enantioselectivity (Table 3, entry 2). The hydrocyanation of vinyl acetate led to α-hydroxyl propylnitrile with promising enantioselectivity (Table 3, entry 5). The hydrocyanation of vinylnaphthalene afforded low conversion and enantioselectivity (Table 3, entry 6).

In conclusion, diphosphite **L$_d$** was an effective ligand in the nickel-catalyzed enantioselective hydrocyanation of styrene, norbornene and vinyl acetate. The enantioselectivities achieved so far are moderate but still superior to those obtained with other chiral diphosphite and phosphine–phosphite ligands. Further studies directed toward the synthesis of more efficient diphosphite ligands and the expansion of the scope of the substrates are in progress.

3. Experimental

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 analyses were performed on a Finnigan Model Mat 95 ST mass spectrometer.

Table 3
The hydrocyanation of olefins with $Ni(COD)_2/\mathbf{L_d}$[a]



Entry	Substrate	Conversion (%)[b]	Selectivity to **2** (%)[b,c]	E.e. (%)
1	4-Methyl-styrene	>98	80.0	40.6[d]
2	4-Methoxyl-styrene	>98	82.9	39.7[e]
3	4-Fluoro-styrene	>98	94.0	49.3[d]
4	Norbornene	89.1	84.2	55.0[f]
5	Vinyl acetate	24.2	83.4	72.9[d]
6	2-Vinyl-naphthalene	20.0[g]	93.5	38.3[h]

a) The reactions were carried out in toluene at 100 °C for 24h; $\mathbf{L_d}$: $Ni(COD)_2$: styrene: acetone cyanohydrin = 0.07: 0.01: 1: 1.1. b) The conversions of olefins and the selectivities to **2** were determined by GC using *n*-dodecane as internal standard. c) The balance was unidentified condensation products; no linear nitrile was observed. d) The ee value was determined by GC with a Chiraldex G-PN column (30m × 0.25mm). e) The ee value was determined by GC with a Chiropack CP-Chirasil-Dex CB column (50m × 0.25mm). f) *Exo*-2-cyanonorbornane was the sole product and the ee value was determined by GC with a Chiraldex B-TA column (30m × 0.25mm). g) The conversion of 2-vinyl-naphthalene and the selectivity to **2** were determined by HPLC using naphthalene as internal standard. h) The ee value was determined by HPLC with a Diacel-OD column.

Optical rotations were measured on a Perkin–Elmer Model 341 polarimeter. GC analyses were performed on an HP 4890 apparatus equipped with a FID.

3.1. *Synthesis of diphosphites* L_a–L_d

(*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 refluxed 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 re-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) and placed in an ice bath. To this solution was added dropwise a solution of (*S*)-binaphthol (0.5 g, 1.7 mmol), triethylamine (1.2 ml, 8.5 mmol) and 4-dimethylaminopyridine (42 mg, 0.34 mmol) in toluene (10 ml). The reaction mixture was stirred for 8 h at 0°C and 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 1.0 g of pure $\mathbf{L_a}$. Yield 64.5%. Elemental analysis for $C_{60}H_{36}O_6P_2{\cdot}0.5C_2H_6O$ (crystalline solvent), calcd: C, 78.12; H, 4.16. Found: C, 78.13; H, 4.16. ^{31}P NMR ($CDCl_3$): δ 145.7 ppm. ^1H 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 Hz, J_2 8.8 Hz, 4H), 7.73 (d, J 8.0 Hz), 7.52 (d, J 8.8 Hz, 2H), 7.37 (m, 8H), 7.16–7.31 (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 ($CDCl_3$): 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 ppm. MS (ESI): 915 (M^++1, 100%). Mp: 196–198°C (decomp.). $[\alpha]_D^{20}$=+346.6 (c 1.085, THF).

$\mathbf{L_b}$, $\mathbf{L_c}$ and $\mathbf{L_d}$ were synthesized via a similar procedure and the crude $\mathbf{L_d}$ was purified by column chromatography:

L_b: ^{31}P NMR ($CDCl_3$): δ 142.3 ppm. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.67 (s, 6H), 2.29 (s, 6H), 7.09 (m, 10H), 7.33 (m, 10H), 7.49 (d, J 8.8 Hz, 2H), 7.64 (s, 2H), 7.68 (d, J 8.0 Hz, 2H), 7.75 (d, J 8.0 Hz, 2H), 7.83 (d, J 8.0 Hz, 2H), 7.87 (d, J 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 16.9, 17.3, 120.6, 120.7, 122.0, 123.0, 124.5, 124.8, 124.9, 125.1, 125.8, 126.0, 126.8, 126.9, 127.4, 127.47, 128.0, 129.2, 129.6, 130.0, 130.08, 130.2, 130.9, 131.0, 131.3, 131.5, 133.8, 146.0, 147.5, 147.7 ppm. MS (ESI): 971 (M^++1, 10%). Mp: 202–204°C. $[\alpha]_D^{20}$=+459.7 (c 0.81, benzene).

L_c: ^{31}P NMR ($CDCl_3$): δ 145.7 ppm. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.55 (s, 6H), 6.52 (d, J 8.8 Hz, 2H), 7.16–7.27 (m, 12H), 7.29–7.42 (m, 8H), 7.51 (d, J 8.8 Hz, 2H), 7.73 (d, J 8.0 Hz, 2H), 7.79 (d, J 8.8 Hz, 2H), 7.83 (d, J 8.0 Hz, 2H), 7.89 (d, J 8.0 Hz, 2H), 7.97 (d, J 8.8 Hz, 2H). MS (ESI): 943 (M^++1, 17%). Mp: 168–170°C. $[\alpha]_D^{20}$=+138.0 (c 0.56, benzene).

L_d: ^{31}P NMR $CDCl_3$): δ 141.6 (s), 143.0 (s) ppm. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.17 (s, 9H), 1.32 (s, 9H), 1.43 (s, 9H), 1.55 (s, 9H), 6.77 (d, J 8.4 Hz, 1H), 7.12 (d, J 8.4 Hz, 1H), 7.19–7.23 (m, 8H), 7.31–7.40 (m, 8H), 7.53 (d, J 2.4 Hz, 1H), 7.60–7.63 (m, 2H), 7.67 (d, J 8.4 Hz, 1H), 7.75 (d, J 8.4 Hz, 1H), 7.81–7.86 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 30.52, 31.02, 31.30, 31.69, 34.52, 34.68, 35.46, 35.72, 122.06, 122.30, 122.52, 122.76, 122.88, 124.51, 124.58, 124.88, 124.95, 125.71, 125.90, 125.99, 127.09, 128.15, 128.24, 128.33, 129.17, 129.33, 129.42, 129.76, 130.12, 130.74, 130.93, 131.34, 131.42, 132.39, 132.45, 132.66, 132.71, 140.49, 140.78, 145.04, 145.40, 146.84, 147.12, 147.77, 148.38, 148.71 ppm. HRMS for $C_{68}H_{64}O_6P_2$, calcd: 1038.4178. Found: 1038.4150. Mp: 250–252°C. $[\alpha]_D^{20}$=+170.9 (c 1.0, benzene).

3.2. Typical procedure for the asymmetric hydrocyanation of olefins

$Ni(COD)_2$ (2 mg, 7.3×10^{-3} mmol), **L_d** (53 mg, 51.1×10^{-3} mmol) and toluene (2 ml) were added to a Schlenk vessel and the mixture was stirred for 5 minutes. After olefin (0.73 mmol) and acetone cyanohydrin (0.073 ml, 0.80 mmol) were added, the reaction mixture was placed in an oil bath at 100°C and stirred for 24 h. *n*-Dodecane (61 mg, 0.36 mmol) as internal standard was added and the reaction solution was filtered through a thin layer of silica gel and the filtrate was analyzed by GC for the determination of conversion, selectivity and enantiomeric excess according to the methods reported in the text.

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References

1. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; VCH: New York, 1993; Chapter 4, p. 169.
2. Tolman, C. A.; Mckinney, R. J.; Seidel, W. C.; Druliner, J. D.; Stevens, W. R. *Adv. Catal.* **1985**, *33*, 1.
3. Baker, M. J.; Pringle, P. G. *J. Chem. Soc., Chem. Commun.* **1991**, 1292.
4. Horiuchi, T.; Shirakawa, E.; Nozaki, K.; Takaya, H. *Tetrahedron: Asymmetry* **1997**, *8*, 57.
5. Casalnuovo, A. L.; RajanBabu, T. V.; Ayers, T. A.; Warren, T. H. *J. Am. Chem. Soc.* **1994**, *116*, 9869.
6. RajanBabu, T. V.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 6325.
7. Yan, M.; Yang, L. W.; Wong, K. Y.; Chan, A. S. C. *Chem. Commun.* **1999**, 11.
8. Yan, M.; Chan, A. S. C. *Tetrahedron Lett.* **1999**, *40*, 6645.
9. Tolman, C. A. *J. Chem. Educ.* **1986**, *63*, 199.
10. Goertz, W.; Keim, W.; Vogt, D.; Englert, U.; Boele, M. D. K.; van der Veen, L. A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1998**, 2981.