Binaphthylidamine-Based Diazaphospholidines as a New Class of Chiral Monodentate P-Ligands

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Dedicated to Professor Wolfgang Steglich on the occasion of his 70th birthday.

Abstract: A new family of chiral diazaphospholidines is readily accessible by phosphorylating commercially available (S)-1,1′-binaphthyl-2,2′-diamine. NMR spectroscopy, mass spectrometry and X-ray crystallographic analysis reveal their unique structures. In preliminary studies these novel monodentate P-ligands were tested in Rh-catalyzed hydrogenation and hydroformylation (31% ee) reactions. The modular nature of the ligands allows for further structural diversity.

Key words: asymmetric catalysis, rhodium, phosphorus, hydrogenation, hydroformylation

Recently, we and others have shown that BINOL-based monodentate phosphites,1 phosphonites2,3 and phosphoramidites4 are excellent ligands in a number of transition metal catalyzed reactions. For example, in Rh-catalyzed olefin-hydrogenation unexpectedly high enantioselectivities were achieved in a number of cases (ee > 90%), which is of significant academic and industrial interest.1–4 As a consequence of these findings the long-standing dogma that chelating bidentate ligands are necessary in order to obtain high enantioselectivity no longer pertains.5 Moreover, these P-ligands are cheaper than the traditional chiral diphosphines by a factor of at least 50. In recent studies we extended the value of these compounds by demonstrating that mixtures of two different monodentate P-ligands can lead to dramatically enhanced enantioselectivities.6

In contrast to the extensive use of BINOL as a building block in a variety of chiral catalysts,1–5 little is known concerning similar ligands based on 1,1′-binaphthyl-2,2′-diamine (1), bis-ketimines derived thereof being one prominent example.7 This may be due to the distinctly higher price of 1 relative to that of BINOL. Nevertheless, we were interested in the synthesis of monodentate diazaphospholidines derived from 1. In this paper we describe the synthesis and characterization of the first representatives of this novel class of chiral P-ligands 2 (Figure 1). Moreover, preliminary results concerning their application in several asymmetric transition metal catalyzed reactions are presented. These ligands are modular in nature because the substituents at nitrogen (R) and at phosphorus (X) can be varied.

Figure 1 Diazaphospholidines 2 derived from binaphthylidiamine 1

The first step in the synthesis of compounds 2 from the starting material 1 involves the introduction of the R-substituents at nitrogen with formation of the secondary diamines 3 (Scheme 1). Compounds 3a,b were prepared by procedures described in the literature.7b,8,9 The new mesityl-derivative was synthesized by Pd-catalyzed arylation using the Buchwald–Hartwig method10 (94% yield).

Scheme 1 Synthesis of methyl- and aryl-substituted dinaphthyldiamines 3a (reductive amination using CH3O–NaCNBH4) and 3b,c (amination of arylbromides using the Buchwald–Hartwig procedure)

Ring-closing reaction of 3b with PCl3 in the presence of Et3N readily provided the sensitive chloride 4 in quantitative yield. This key compound was then used in the introduction of alkxy and amino groups, the products being isolated and purified as the BH3-adducts 5a,b, respectively. Compound 5b can be prepared even more conveniently by treating 3a with (Et3)2PdCl and protecting with BH3 (72% overall yield) (Scheme 2).

Unfortunately, these reactions failed to proceed smoothly with the aryl substituted derivatives 3b,c, possibly due to steric effects. Therefore, more forcing conditions had to be applied, specifically double deprotonation using n-bu-
tillithium followed by phosphorylation, as in the case of 5c (25% yield) (Scheme 3).

Along similar lines further derivatives 5d–g were prepared and isolated in pure form (Scheme 4). However, upon subjecting the mesityl-derivative 3c to the reaction conditions, mixtures of inseparable products were obtained. The synthesis of P-ligands based on 3c was therefore not pursued.

All compounds 5d–g were characterized by NMR spectroscopy and mass spectrometry (MS), and in two cases (5b and 5c) suitable crystals were grown for X-ray crystallographic analyses. Figures 2 and 3 show that chiral seven-membered P-heterocycles are indeed involved, the degree of puckering depending on the nature of R. In 5c all the N atoms are almost planar (R = C₆H₅, max. r.m.s. deviation 0.028 Å), whereas in 5b N1 lies 0.330 Å out of its coordination plane.

The final step in the synthetic sequence called for deprotection of the P-function, which in other cases is known to proceed best with DABCO. However, in the present cases the reaction generally failed to occur cleanly. Therefore, Et₂NH was used, which resulted in smooth deprotection and concomitant generation of the desired ligands 2a–g in essentially pure form as shown by NMR analyses. Since chromatography of the compounds for an-
alytical purposes led to excessive decomposition, the ligands were used directly in various transition metal catalyzed reactions.

Thus far only a few exploratory experiments to assess the P-compounds 2 as ligands in transition metal catalyzed reactions have been performed. In all cases the S-form was used. Upon treating Rh(cod)BF₄ (cod = 1,5-cyclooctadiene) with two equivalents of a P-ligand 2 and using the Rh-complexes RhL₂(cod)BF₄ as catalysts in the in situ hydrogenation of itaconic acid dimethyl ester (6) under standard conditions,¹⁻⁵ (Rh = 1000:1; 1.3 bar H₂; 20 h; CH₂Cl₂ as solvent) (Scheme 5), it became clear that the catalyst systems are considerably less active than the previously described Rh-catalysts using BINOL-based phosphites,¹ phosphonites₂,³ or phosphoramidites.⁴ Acceptable conversion under these conditions leading to a nearly quantitative conversion at room temperature and only 25 bar H₂/CO (Table 1, entry 7). The regioselectivity in favor of the branched isomer (9:10 = 80:20) and the ee-value of 31% [in favor of (S)-9] are remarkable for a monodentate ligand in asymmetric hydroformylation, but certainly far below the standard set by Takaya and Nozaki using their bidentate MOP-ligand.¹¹ However, due to the modular nature of the diazaphospholidines described in the present paper, further ligand tuning can be expected to be straightforward. Moreover, the concept of using mixtures of two different P-ligands recently introduced by us can now be extended to include the new chiral monodentate ligands prepared in the present study.

In the case of the Rh-catalyzed hydroformylation of styrene (8) (Scheme 6), a different picture evolved. Although not all of the ligands were tested, initial experiments using 2a–d, turned out to be promising (Table 1). Ligand 2d seems to be the most active, leading to a nearly quantitative conversion at room temperature and only 25 bar H₂/CO (Table 1, entry 7). The regioselectivity in favor of the branched isomer (9:10 = 80:20) and the ee-value of 31% [in favor of (S)-9] are remarkable for a monodentate ligand in asymmetric hydroformylation, but certainly far below the standard set by Takaya and Nozaki using their bidentate MOP-ligand.¹¹ However, due to the modular nature of the diazaphospholidines described in the present paper, further ligand tuning can be expected to be straightforward. Moreover, the concept of using mixtures of two different P-ligands recently introduced by us can now be extended to include the new chiral monodentate ligands prepared in the present study.

Thus, starting from commercially available 1,1’-binaphthyl-2,2’-diamine (1), we have prepared a number of novel diazaphospholidines 2a–g. They constitute a new class of chiral monodentate P-ligands. Characterization by

NMR spectroscopy and mass spectrometry has been performed in all cases, and two representative ligands were analyzed by X-ray crystallography. Some of the preliminary experiments applying these ligands in asymmetric transition metal-catalyzed reactions are promising, as for example, in enantioselective hydroformylation. It remains to be seen if the modular nature of these compounds can be exploited so that further ligand tuning will lead to efficient catalyst systems. Moreover, other types of transition metal catalyzed reactions need to be tested with the ligands described here, either in pure form or in mixtures.

Table 1 Rh-Catalyzed Hydroformylation of Styrene (8)²

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Rh-salt</th>
<th>H₂/CO Temp. (°C)</th>
<th>Conv. (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>Rh(acac)(CO)₂</td>
<td>50</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>Rh(cod)BF₄</td>
<td>50</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>2b</td>
<td>Rh(acac)(CO)₂</td>
<td>50</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>2b</td>
<td>Rh(cod)BF₄</td>
<td>50</td>
<td>60</td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td>2c</td>
<td>Rh(acac)(CO)₂</td>
<td>50</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>2c</td>
<td>Rh(cod)BF₄</td>
<td>50</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>7</td>
<td>2d</td>
<td>Rh(acac)(CO)₂</td>
<td>25</td>
<td>25</td>
<td>98</td>
</tr>
</tbody>
</table>

²Rh:substrate = 1:400; 20 h; H₂:CO = 1:1; toluene as solvent.
²Determined by GC.
²Determined by GC following oxidation to the acid.

NMR spectra of 8a: 1H NMR (CDCl₃): δ = 2.1 (s, 12 H, 4 CH₃), 2.27 (s, 6 H, 2 CH₂), 5.18 (br s, 2 H, NH), 6.72 (d, J = 8.9 Hz, 2 H, Ar), 6.88 (s, 4 H, Ar), 7.16–7.32 (m, 4 H, Ar), 7.67–7.83 (m, 4 H, Ar).
13C NMR: 7.16–7.32 (m, 4 H, Ar), 7.67–7.83 (m, 4 H, Ar).

Scheme 5 Rh-catalyzed hydrogenation of 6

Scheme 6 Rh-catalyzed hydroformylation of 8

(5S,5S)-5,5-Bis(2,4,6-trimethylphenyl)dinaphthyl diamine (3c)
The mixture of (S),1,1’-binaphthyl-2,2’-diamine ([S]-1) (284 mg, 1.0 mmol), 2-bromomesitylene (0.33 mL, 436 mg, 2.2 mmol), Pd₂(dba)₃ (22 mg, 0.04 mmol Pd), (±)-BINAP (25 mg, 0.04 mmol) and sodium tert-butoxide (270 mg, 2.8 mmol) was suspended in anhyd xylene (8 mL) and stirred at 150 °C for 24 h. To the dark brown reaction mixture was added H₂O (20 mL) and the mixture was extracted with tert-butyl methyl ether (3 × 30 mL). The combined organic phases were washed with H₂O, then with brine and dried (MgSO₄). Evaporation of the solvents gave an orange oil (ca. 700 mg), which was purified by chromatography (SiO₂; hexane–EtOAc, 20:1).

Yield: 490 mg (94%); colorless solid.

¹H NMR (CDCl₃): δ = 2.1 (s, 12 H, 4 CH₃), 2.27 (s, 6 H, 2 CH₂), 5.18 (br s, 2 H, NH), 6.72 (d, J = 8.9 Hz, 2 H, Ar), 6.88 (s, 4 H, Ar), 7.16–7.32 (m, 4 H, Ar), 7.67–7.83 (m, 4 H, Ar).
¹³C NMR: δ = 18.6, 20.9, 111.3, 114.3, 122.0, 124.2, 126.6, 128.0, 128.1, 129.1, 129.5, 134.0, 134.9, 135.7, 136.6, 143.3.
MS (EI): m/z = 520 [M⁺], 386.

(5S)-5a
A stirred mixture of diamine (5)-3a (146 mg, 0.467 mmol) and Et₃N (0.5 mL, 360 mg, 3.6 mmol) in CH₂Cl₂ (7 mL) in a Schlenk flask was treated with an Et₃O solution of PCl₃ (0.5 M; 1.05 mL, 0.525

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mmol) dropwise at 0 °C. After stirring for 16 h, anhyd MeOH (25 μL, 0.6 mmol) was added and the mixture was stirred for 2 h. All volatiles were removed under reduced pressure and the resultant solid was suspended in toluene. A portion did not dissolve, and was filtered off by a pad of Celite® under argon. The yellowish orange filtrate was treated with a THF solution of BH₃·THF (1 M; 1 mL, 1 mmol) and the mixture stirred at r.t. for 2 h. All volatiles were removed and the resultant colorless solid was purified by chromatography (5 g neutral alumina; EtOAc).

Yield: 184 mg (99%); colorless solid.

1H NMR (CDCl₃): δ = 0.02–1.4 (br, 3 H, BH₃), 2.9–3.1 (m, 6 H, 2 NCH₃), 3.62 (d, J = 11.5 Hz, 3 H, OCH₃), 7.0–8.1 (m, 12 H, Ar).

13C NMR: δ = 130.9 (d), 126–132 (Ar), 141.0 (d), 144.3 (d).

13P NMR: δ = 134.9 (m).

MS (EI): m/z = 469 [M⁺ – BH₃], 343.

Crystal data for 5c

\[ \text{[C₃₃H₂₈BN₂OP]} \text{, from toluene–pentane, } M_r = 510.35, \text{ crystal size: } 0.04 \times 0.15 \times 0.16 \text{ mm; } a = 9.1778(1), b = 10.1788(1), c = 28.8611(3) \\ \text{Å, } V = 2696.17(5) \\ A^3, T = 100 \text{ K, orthorhombic, space group } P 2 1 2 1 2 1 \text{ (No. 19), } Z = 4, \rho_{\text{calc}} = 1.257 \text{ g cm}^{-3}, \text{ Nonius KappaCCD diffractometer, } \lambda(\text{MoK}\alpha) = 0.71073 \ \text{Å, } \mu = 0.13 \text{ mm}^{-1}, \text{ 49894 measured and 10319 independent reflections (R}_{int} = 0.0899, 8392 with } I > 2 \sigma(I), \ \delta_{max} = 33.20, T_{min} = 0.981, T = 0.995, \text{ index委托 (SHELXS-97) and least-squares refinement (SHELXL-97) on } F^2, \text{ both programs from G. Sheldrick, University of Göttingen, } H \text{ atoms riding, Flack parameter -0.11(7), Chebychev weights, } R_I = 0.055 [I > 2\sigma(I)], \ \text{wR}_2 = 0.122 (all data), \ \Delta\rho_{max/min} = 0.386/–0.391 \text{ eÅ}^{-3}, \text{ CCDC 213917.}

Compounds (S)-5d-g: General Procedure

In a Schlenk flask a solution of (S)-3a or (S)-3b (0.6 mmol) in Et₂O (7 mL) was treated with a hexane solution of BuLi (1.6 M; 0.9 mL, 1.44 mmol) at −78 °C. After stirring at r.t. for 20 min, the solution was cooled once more to −78 °C and then treated with the appropriate RPCl₂ (0.72 mmol). The suspension was stirred at r.t. for 24 h and then treated with a THF solution of BH₃·THF (1 M; 1 mL, 1 mmol) at r.t. After 2 h all volatiles were removed and the solid material was purified by chromatography (SiO₂; hexane–EtOAc, 3:1).

Yield: 160 mg (84%).

1H NMR (CDCl₃): δ = 0.1–1.6 (br, 3 H, BH₃), 1.65 (d, J = 7.3 Hz, 3 H, CH₃), 6.7–8.1 (m, 22 H, Ar).

13C NMR: δ = 133.4 (m), 129.0–134 (m), 141.0 (d), 144.3 (d).

13P NMR: δ = 120.4 (m).

MS (EI): m/z = 480 [M⁺ – BH₃], 465.

(S)-5e

Yield: 184 mg (70%).

1H NMR (CDCl₃): δ = 0.1–1.4 (br, 3 H, BH₃), 0.53 (dd, J = 7.2, 12.6 Hz, 3 H, CH₃), 1.48 (dd, J = 7.2, 18.7 Hz, 3 H, CH₃), 2.51 (m, 1 H, PCH), 6.7–8.0 (m, 22 H, Ar).

13C NMR: δ = 16.1 (d, J = 6.6 Hz), 17.1 (d, J = 4.0 Hz), 29.8 (d, J = 36.6 Hz), 125–133 (Ar), 141–146 (Ar).

13P NMR: δ = 131.1 (m).

MS (EI): m/z = 508 [M⁺ – BH₃], 465.

(S)-5f

Yield: 142 mg (50%).

1H NMR (CDCl₃): δ = 0.1–1.5 (br, 3 H, BH₃), 0.5–2.45 (m, 11 H, c-C₆H₁₅), 6.7–8.0 (m, 22 H, Ar).

13P NMR: δ = 128.3 (m).

MS (EI): m/z = 548 [M⁺ – BH₃], 465.
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S.5g
Yield: 141 mg (53%).

1H NMR (CDCl3): δ = 0.3–1.5 (br, 3 H, BH3), 1.07 (d, J = 14.3 Hz, 9 H, 3 CH3), 6.7–8.0 (m, 22 H, Ar).

13C NMR: δ = 27.8, 38.0 (d, J = 31.5 Hz), 122–135 (Ar), 142–145 (Ar).

31P NMR: δ = 139.0 (m).

MS (EI): m/z = 522 [M+–BH3], 465.

Deprotection of Ligands; General Procedure
Removal of BH3 from the P-ligands is best performed by treatment with a large excess (> 10 equiv) of diethylamine at 75 °C overnight without a solvent. Excess diethylamine and amine–borane adduct were removed under reduced pressure (< 0.02 bar) at 45 °C for 3–4 h. Since the resulting P-ligands cannot be chromatographed without extensive degradation, they were used as such in catalysis. Characteristic NMR data could be obtained routinely.

(S)-2a
1H NMR (CDCl3): δ = 2.85 (d, J = 9.7 Hz, 3 H, NCH3), 3.00 (d, J = 13.8 Hz, 3 H, NCH3), 3.25 (d, J = 9.5 Hz, 3 H, OCH3), 6.9–7.9 (m, 12 H, Ar).

13C NMR: δ = 33.9 (d, J = 7.2 Hz, 11.6 Hz, 3 H, CH3), 1.92–2.08 (m, 1 H, PCH), 6.5–8.0 (m, 22 H, Ar).

31P NMR: δ = 165.9 (m).

(S)-2b
31P NMR: δ = 149.0 (m).

(S)-2c
1H NMR (CDCl3): δ = 3.14 (d, J = 10.0 Hz, 3 H, OCH3), 6.7–7.9 (m, 22 H, Ar).

13C NMR: δ = 51.6 (d, J = 2.7 Hz), 123–147 (Ar).

31P NMR: δ = 147.9 (m).

(S)-2d
1H NMR (CDCl3): δ = 1.22 (d, J = 9.2 Hz, 3 H, CH3), 6.5–8.0 (m, 22 H, Ar).

13C NMR: δ = 16.5 (d, J = 24.8 Hz), 116–147 (Ar).

31P NMR: δ = 135.0 (m).

(S)-2e
1H NMR (CDCl3): δ = 0.59 (dd, J = 7.2 Hz, 11.6 Hz, 3 H, CH3), 0.82 (dd, J = 7.2, 14.5 Hz, 3 H, CH3), 1.92–2.08 (m, 1 H, PCH), 6.5–8.0 (m, 22 H, Ar).

13C NMR: δ = 15.6 (d, J = 10.7 Hz), 16.4 (d, J = 15.4 Hz), 30.3 (d, J = 26.0 Hz), 125–133 (Ar), 141–146 (Ar).

31P NMR: δ = 150.5 (m).

(S)-2f
31P NMR: δ = 148.8 (m).

(S)-2g
1H NMR (CDCl3): δ = 0.65 (d, J = 11.9 Hz, 9 H, 3 CH3), 6.6–8.0 (m, 22 H, Ar).

13C NMR: δ = 27.8, 36.9 (d, J = 32.2 Hz), 118–150 (Ar).

31P NMR: δ = 160.4 (m).

Hydrogenation of 6; General Procedure
A 25 mL Schlenk flask was charged with a CH2Cl2 stock solution of Rh(cod)BF4 (2 mM; 0.5 mL, 0.001 mmol), additional CH2Cl2 (7.3 mL), a CH2Cl2 solution of a chiral P-ligand 2 (10 mM; 0.2 mL, 0.002 mmol) and a CH2Cl2 solution of 6 (0.5 M; 2 mL, 1.0 mmol) at r.t. The argon gas was evacuated until bubbles could be observed in the solution, then H2 gas was introduced until 1 bar was reached. The evacuation/introduction cycle was carried out three times, then the H2 pressure was adjusted to 1.3 bar. The mixture was stirred at r.t. for 20 h. Conversion and the ee were determined by GC.

Hydroformylation of 8; General Procedure
A 4 mL reaction vessel equipped with a rubber septum was charged with a toluene solution of a rhodium precursor [Rh(acac)(CO)2 or Rh(cod)BF4] (2 mM; 1.25 mL, 0.025 mmol) and a toluene solution of a monodentate P-ligand 2 (10 mM; 0.75 mL, 0.0075 mmol) under argon. After stirring for 1 h at r.t., styrene (6) (a) was then introduced at the desired pressure, and the reaction carried out with stirring at the desired temperature for 20 h (Table 1).

Conversion and regioselectivity were determined by GC. In order to determine the ee-value, oxidation by CrO3 to the corresponding acid according to a literature procedure13 was performed following GC analysis.

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(11) See experimental section.