Application of monodentate secondary phosphine oxides, a new class of chiral ligands, in Ir(I)-catalyzed asymmetric imine hydrogenation


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Supporting information for:

Monodentate Secondary Phosphine Oxides, a New Class of Chiral Ligands. Their Application in Ir (I)-Catalyzed Asymmetric Imine Hydrogenation.

Xiao-bin Jiang a, Adriaan J. Minnaard a*, Bart Hessen a, Ben L. Feringa a*, Alexander L. L. Duchateau b, Jean G. O. Andrein b, Jeroen A. F. Boogers b and Johannes G. de Vries a, b*

Ligand Syntheses

Ligand 1 was prepared according to a literature procedure 1. The ligands 2-7 were prepared in a similar manner, modified to the extent that the Grignard reagent was added to the solution of the RPCl2 (reverse addition).

iso-propylphosphinoyl-benzene (2) 2

Colorless oil, isolated yield 36%. 31P (CDCl3, 75MHz) δ 39.38 (s) 1H(CDCl3, 300MHz) δ 1.08 (dd, 3H, CH3, J=7.33, 9.15Hz), 1.14 (dd, 3H, CH3, J=7.32, 9.16Hz), 2.03-2.21 (m, 1H), 7.22 (dd, 1H, P-H, J=2.2, 458.28 Hz), 7.3-7.74 (m, 5H) 13C(CDCl3, 121MHz) δ 129.81, 127.71, 127.56, 126.50 (d, J =94Hz), 126.12, 125.96, 25.70 (d, J = 69.59Hz), 12.34, 11.76
HRMS (EI+) M+ for C9H13OP, 168.07264, calcd. 168.07040

The enantiomerically pure ligands were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml/min, RT, UV 254nm, n-hexane/Ethanol=92.5/7.5, t1 =15.1min, [ ]D21 = -14.4° (C=0.25, CHCl3), t2 = 17.3min, [ ]D21 = +11.2° (C=0.285, CHCl3)

2-tert-butylphosphinoyl-naphthalene (3)

White powder, isolated yield 14%. 31P (CDCl3, 75MHz) δ 47.03 (s) 1H(CDCl3, 300MHz) δ 1.18 (d, 9H, 3CH3, J=16.6Hz), 7.17 (d, 1H, P-H, J P-H = 453.89Hz), 7.55-7.70 (m, 4H), 7.86-7.96 (m, 3H), 8.24 (d, 1H, J=14.41Hz) 13C(CDCl3, 121MHz) δ 133.54 (d, J=12.56Hz), 131.37, 130.65, 127.17, 126.72, 126.40, 125.54, 124.23, 124.02, 123.51, 30.72 (d, J = 69.05Hz), 21.96
HRMS (EI+) M+ for C14H17OP 232.10117, calcd. 232.10170

The enantiomerically pure ligands were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml/min, RT, UV 254nm, n-hexane/ethanol=67/33, t1 = 5.61min, mp 129-131°C, [ ]D21 = -38.8°(C=0.245, CHCl3), t2 = 7.91min, mp 138-140°C, [ ]D21 = +38.5° (C=0.275, CHCl3)

2-methoxy-tert-butylphosphinoyl-benzene (4)

Colorless oil, isolated yield 68%. 31P (CDCl3, 75MHz) δ 35.58 (s) 1H(CDCl3, 300MHz) δ 1.15 (d, 9H, 3CH3, J=17.09Hz), 3.83 (s, 3H, OCH3), 6.86-6.93 (m, 1H), 7.01-7.08 (m, 1H), 7.36 (d, 1H, P-H, J P-H= 484.4Hz), 7.43-7.51 (m, 1H), 7.63-7.73 (m, 1H) 13C(CDCl3, 121MHz) δ 159.35(d, J= 4.19 Hz), 132.42, 131.90, 119.14, 116.61, 109.05, 53.71, 30.92 (d, J=70.96Hz), 22.06
HRMS (EI+) M+ for C11H17O2P 212.09790, calcd. 212.09661
The enantiomerically pure ligands were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml/min, RT, UV 254nm, n-hexane/ethanol=67/33, t1 =3.99min, [ ]D\text{21} = -15.1° (C=0.35, CHCl3), t2 = 5.88min, [ ]D\text{21} = +11.8° (C=0.365, CHCl3).

(3,5-dimethyl)-tert-butylphosphinoyl-benzene (5)
White solid, isolated yield 65%. \( ^{31}P \) (CDCl3, 75MHz) \( \delta \) 47.76 (s) \( ^{1}H \)(CDCl3, 300MHz) \( \delta \) 1.13 (d, 9H, 3CH3, J=16.6Hz), 2.35 (s, 6H, 2CH3), 6.95 (d, 1H, P-H, J\_P-H = 452.42Hz), 7.17(s, 1H, CH), 7.28(s, 1H, CH), 7.22(s, 1H, CH) \( ^{13}C \)(CDCl3, 121MHz) \( \delta \) 136.65 (d, J =12.59 Hz), 132.77, 127.30, 127.00, 125.49, 30.24(d, J=69.05Hz), 21.87, 21.84, 19.62


The enantiomerically pure ligands were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml/min, RT, UV 254nm, n-hexane/Ethanol=92.5/7.5, t1 =7.23min, mp 144-147 oC, [ ]D\text{21} =+ 9.4° (C=0.265, CHCl3), t2 = 17.3min, mp 126-128°C, [ ]D\text{21} = -9.8° (C=0.275, CHCl3).

(2,4,6-trimethyl)-tert-butylphosphinoyl-benzene (6)
Colorless oil, isolated yield 21% over 2 steps. \( ^{31}P \) (CDCl3, 75MHz) \( \delta \) 38.16 (s) \( ^{1}H \)(CDCl3, 300MHz) \( \delta \) 1.16 (d, 9H, 3CH3, J\_P-H = 16.6Hz), 2.22 (s, 3H, CH3), 2.49 (br, 6H, 2CH3), 6.83 (br, 2H, 2CH), 7.55 (d, 1H, P-H, J\_P-H = 455.59Hz) \( ^{13}C \)(CDCl3, 121MHz) \( \delta \) 139.81, 139.77, 128.67, 128.12, 120.23 (d, J=88.12Hz), 32.70 (d, J= 69.05Hz), 22.78, 22.72, 20.45, 20.35, 19.12 HRMS (EI+) M⁺ for C13H21OP 224.13412, calcd. 224.13299

The enantiomerically pure ligands were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml /min, RT, UV 254nm, n-Heptane/2-propanol=95/5, t1=8.971min, mp 109.5-112°C, [ ]D\text{21} = -16.9 ° (C=0.255, CHCl3), t2=13.728min, mp 105-107°C, [ ]D\text{21} = +20.4° (C=0.275, CHCl3).

2-phenylphosphinoyl-naphthalene (7)
White solid, isolated yield 35%. \( ^{31}P \) (CDCl3, 75MHz) \( \delta \) 21.38 (s) \( ^{1}H \)(CDCl3, 300MHz) \( \delta \) 6.85-7.00 (m, 5H), 7.01-7.35 (m, 6H), 7.72 (d, 1H, P-H, J\_P-H = 483.18Hz), 7.90 (d, 1H, J=15.63Hz) \( ^{13}C \)(CDCl3, 121MHz) \( \delta \) 133.07 (d, J=2.29Hz), 130.92, 130.71, 130.43, 128.91, 128.68, 127.74, 127.19, 126.94, 126.88, 126.57, 126.12, 125.73, 125.33, 123.09, 123.07 HRMS (EI+) M⁺ for C16H13OP 252.06907, calcd.252.07039

The enantiomerically pure ligands were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml /min, RT, UV 254nm, n-Hexane/2-propanol=95/5, t1=8.971min, mp 109.5-112°C, [ ]D\text{21} = -16.9 ° (C=0.255, CHCl3), t2=13.728min, mp 105-107°C, [ ]D\text{21} = +20.4° (C=0.275, CHCl3).

\((IR, 7R)-9,9\text{-Dimethyl}-4\text{-hydrido}-4\text{-oxo}-2, 2, 6, 6\text{-tetraphenyl}-3, 5, 8, 10\text{-tetraoxa}-4\text{-phosphabicyclo}[5.3.0]\text{decane}\) (8)
In a 100ml Schlenk vessel, was placed (4R, 5R)-4,5-bis-(hydroxy-diphenylmethyl)-[1,3]dioxolane)(R,R-Taddol) (2mmol, 0.94g) and 5ml dry toluene. The solution was cooled down to -78°C, and PCl₃ (3.0mmol, 0.26ml) was added over 20mins. The solution was
allowed to come to RT and stirring was continued for 3h. After cooling down to 0°C, 5ml H2O was added slowly. After warming up to RT stirring was continued for 30mins. The mixture was extracted with CH2Cl2 (3x10 ml), with brine (3x) and dried over MgSO4. After removal of the solvent the residue was purified by flash chromatography (SiO2, EtOAc/Hexane=1/1) to obtain a white powder; isolated yield 75%. Mp 224-226°C (dec.), [ ]D21 =-268.4° (C=0.275, CHCl3), (lit. mp 226-227°C, dec., [ ]D = -289.9 °, C=1.56, CHCl3), 31P (CDCl3, 75MHz) δ -4.73, -4.79 (we presume the double peak is due to the presence of two slowly interconverting conformers) 1H(CDCl3, 300MHz) δ 0.56 (s, 3H, CH3), 0.76 (s, 3H, CH3), 5.21 (d, 1H, CH, J=7.82Hz), 5.36 (d, 1H, CH, J=8.06Hz), 7.08 (d, 1H, P-H, JP-H =726.85Hz), 7.23-7.46 (m, 16H), 7.56-7.63 (m, 4H) 13C(CDCl3,121MHz) δ 142.16 (d, J=2.68Hz), 141.65 (d, J=2.25Hz), 137.66 (d, J=8.78Hz), 137.45 (d, J=6.48Hz), 127.31, 127.22, 127.00, 126.83, 126.70, 126.51, 126.40, 126.04, 125.86, 125.38, 125.30, 112.90, 87.31, 87.14, 78.57, 78.30, 25.28, 24.79 MS(Cl+,%) 530(M+NH4+,100).

2, 5-diphenyl-phospholane-1-oxide (9)
This ligand was prepared according to a literature method. The pure enantiomers were obtained by preparative HPLC, chiralpak AD column, Preparative 250x20 mm ID flow 20 ml/min, RT, UV 254nm, n-heptane/isopropanol=75/25, t1=10.486min, t2=13.071min.

Imines
Imines were prepared from the ketones and the amines by azeotropic reflux in toluene using molecular sieves 4Å. All imines are known compounds with the exception of 13.

(4-chlorophenyl)-N-[(E)-1-phenylethylidene]methanamine (13)
Isolated yield 44%, yellow oil, 1H (CDCl3, 300MHz) major isomer: δ 2.28 (s, 3H, CH3), 4.63 (s, 2H, CH2), 7.20-7.39 (m, 6H), 7.79-7.82 (m, 2H), 7.91 (d, 1H, J=7.32Hz) minor: δ 2.33, 4.88, 13C(CDCl3, 121MHz) major isomer: δ 165.53, 137.98, 130.78, 127.76, 127.29, 127.09, 126.91 125.40, 53.48, 16.83 minor: 164.69, 139.41, 127.83, 126.43, 124.45, 54.74, 14.44. In the 1HN M Ra nd the 13C NMR some resonances of the minor isomer are obscured. HRMS (EI+) C15H14NCl 243.08030, calcd. 243.08147

Typical procedure for imine hydrogenation
In a 5ml glass vial provided with a magnetic stirrer, a mixture of [Ir(COD)Cl]2 (3.4mg, 0.005mmol), SPO ligand (0.02 mmol), imine (0.5mmol) and pyridine (2eq. w.r.t. Ir, 2 l) were dissolved in dry toluene (3ml). 7 of these vials were placed in an autoclave, which was closed, purged 3 times with N2 and 3 times with H2. The autoclave was pressurized with H2 to 20-25bar and the reactions were magnetically stirred at room temperature (unless noted otherwise). After the desired time, the autoclave was opened. The solvent in each vial was transferred to a 10ml round bottle and the solvent was removed under vacuum. Degree of conversion and selectivity was determined by 1H NMR (CDCl3). For the e.e. determination the amines were converted to their N-acetyl derivatives with 50 1 Ac2O. After filtration on a short silica gel column the filtrate was analysed by HPLC (chiralpak AD or OD column). The absolute configuration was determined by comparing
with commercially available enantiomerically pure products. Racemic samples were prepared by NaBH₄ reduction of imines in ethanol as solvent for 30 minutes.

**Table 1 HPLC data of N-acetyl derivatives of hydrogenation products**

<table>
<thead>
<tr>
<th>Name</th>
<th>Column</th>
<th>Condition</th>
<th>t₁ (min)</th>
<th>t₂ (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amine 10(N-acetyl)</td>
<td>OD 250x4.6</td>
<td>Hep/IPA 95/5</td>
<td>t₁=11.573 t₂=14.101</td>
<td></td>
</tr>
<tr>
<td>Amine 11(N-acetyl)</td>
<td>AD 250x4.6</td>
<td>Hep/IPA 95/5</td>
<td>t₁=16.821 t₂=18.955</td>
<td></td>
</tr>
<tr>
<td>Amine 12(N-acetyl)</td>
<td>AD 250x4.6</td>
<td>Hep/IPA 95/5</td>
<td>t₁=14.827 t₂=17.173</td>
<td></td>
</tr>
<tr>
<td>Amine 13(N-acetyl)</td>
<td>AD 250x4.6</td>
<td>Hep/IPA 95/5</td>
<td>t₁=11.403 t₂=13.685</td>
<td></td>
</tr>
<tr>
<td>Amine 14(N-acetyl)</td>
<td>AD 250x4.6</td>
<td>Hep/IPA 95/5</td>
<td>t₁=12.544 t₂=13.803</td>
<td></td>
</tr>
<tr>
<td>Amine 15(N-acetyl)</td>
<td>OD 250x4.6</td>
<td>Hep/IPA 95/5</td>
<td>t₁=10.731 t₂=15.307</td>
<td></td>
</tr>
<tr>
<td>Amine 16(free amine)</td>
<td>Wh01 250x4.6</td>
<td>Hep/EtOH 90/10</td>
<td>t₁=6.603 t₂=8.651</td>
<td></td>
</tr>
<tr>
<td>Amine 17(free amine)</td>
<td>OD 250x4.6</td>
<td>Hep/IPA 90/10</td>
<td>t₁=6.843 t₂=8.122</td>
<td></td>
</tr>
</tbody>
</table>

*General conditions for HPLC: flow rate 1.0ml/min, RT, UV 220 nm*

**References**