Pergamon

Tetrahedron Letters, Vol. 37, No. 28, pp. 4933-4936, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00968-9

Chiral Tridentate C_2 Diphosphine Ligands for Enantioselective Catalysis.

Rafaël Sablong, Claire Newton, Peter Dierkes, and John A.Osborn*

Laboratoire de Metaux de Transition et de Catalyse, associé au C.N.R.S., Université Louis Pasteur, Institut Le Bel, 4 rue Blaise Pascal, 67070 Strasbourg Cedex, France.

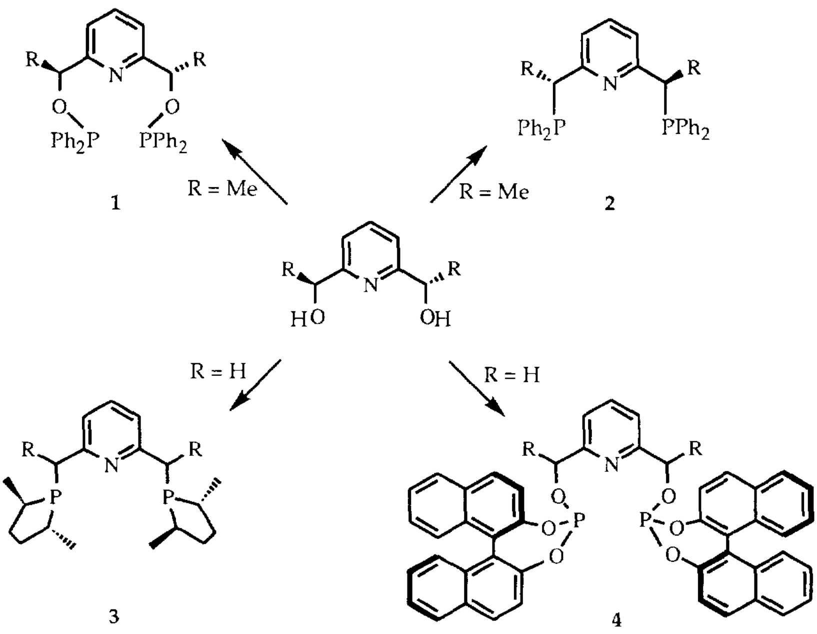
Abstract. We describe the synthesis of four ligands of a family of tridentate diphosphine ligands possessing C_2 symmetric chirality for use in transition metal complex asymmetric catalysis.

The synthesis of chiral diphosphine ligands (P-P donor set), particularly with C_2 symmetry, has been of crucial importance in the development of transition metal catalysed enantioselective reactions[1]. Triphosphine ligands[2] (P-P-P) and triamine (N-N-N)[3] with C_3 symmetry have also received much recent attention. However whereas chiral tridentate ligands possessing C_2 symmetry with donor sets such as O-N-O[4], N-N-N[5], and N-C-N[6] have been used in catalysis, those containing phosphine donors are less well known, which, until very recently[7], was limited to ligands of the type P-C-P[8] and P-O-P.[9]

We report here the synthesis of four examples (Figure 1) of a family of chiral ligands possessing the mixed donor set P-N-P, built about 2,6-substitution on the pyridine nucleus. These ligands possess C_2 symmetry where the chirality can be placed either on the backbone α to the pyridine nucleus (**1** and **2**), or on the pendant phosphine 'arms' (**3** and **4**), or eventually, both. One member of this family has very recently been described[7].

The syntheses of **1** and **2** are *via* the known[4] chiral pyridine diol but, like Zhang *et al.*[7], we find that reduction of the 2,6-diacetylpyridine is in preference carried out using Dip-Cl[10] instead of baker's yeast[11] which gave variable results in our hands. We have synthesised both the (S,S)-diol using (-)-Dip-Cl (THF, 6hrs. -78°C, then 10 days at 25°C, hydrolysis, 85% yield, 98% ee) and the (R,R)-diol similarly from the (+)-Dip-Cl. Treatment of the (S,S) diol with 2.4 eq. BuLi (THF, -78°C, 1hr.) followed by addition of Ph_2PCl (2eq.,THF, 0°C, 8h), removal of the solvent and chromatography over silica, leads to **1** as pale yellow oil (48%, δ $^{31}P\{^1H\}$ NMR: d 110.9). The synthesis of **2** was carried out by converting the (S,S) diol into the corresponding dimesylate (MsCl, NEt_3, CH_2Cl_2, 0°C, 90%) which was then treated with $KPPh_2$ (C_6H_6, 6°C) to yield after work up the R,R product as a viscous oil (30% , R,R / meso = 99 / 1, $^{31}P\{^1H\}$ NMR: δ 1.9).

Figure 1

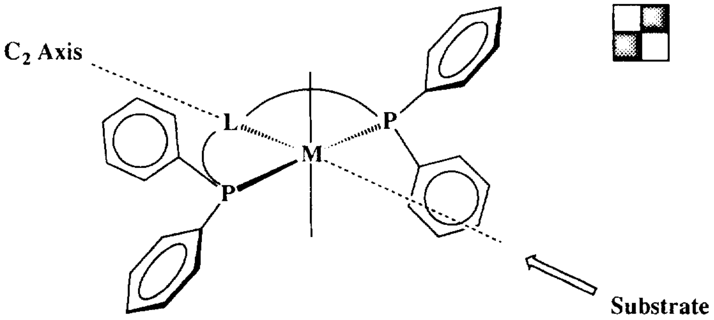


The ligands **3** and **4** were synthesised from the achiral pyridine diol (Figure 1, R = H). The synthesis of **3** involves the conversion of the achiral 2,6 pyridine diol into the dichloro derivative ($SOCl_2$, 0°C, then reflux 6hrs., then $NaHCO_3$), which was recrystallised from hot heptane. A THF solution of the Li^+ salt of (2R,5R)-dimethylphospholanate (2eq., synthesised according to Burk[2]) was added to the 2,6-bis(chloromethyl)pyridine (THF, 25°C, 1hr.), then treated with MeOH, and after work up, gave a pale yellow oil, which was distilled at 10^{-4} mbar and 200°C (40%, $^{31}P\{^1H\}$ NMR: δ 7.85).

In the first step of the synthesis of **4** in a modification of the literature procedure,[9] a THF solution of PCl_3 was added dropwise to optically pure (R)-(+)-1,1'-bi-2-naphthol (0.9 eq. in THF, -40°C, 10 mins.) followed by 2 eq. NEt_3, yielding the naphtolatochlorophosphite as a white solid (92%, $^{31}P\{^1H\}$ NMR: δ 179.0); 2eq. of this chlorophosphite in THF was added dropwise to the pyridine diol in THF (1eq., -40°C) and after 15 mins NEt_3 (2eq.) was added. After work-up, **3** was obtained as a white solid (65%,$^{31}P\{^1H\}$ NMR: δ 141.1).

Complexes of the type Rh(diene)(PNP)$^+$ and Ir(COD)(PNP)$^+$ have been synthesised and characterised for these ligands and their achiral analogues[12] and will be reported separately along their catalytic activity in the catalytic hydrogenation of olefins, ketones and imines.

The principle interest of this class of ligands is twofold. Firstly the ligands **1** and **4** (and to a lesser extent **2** and **3**, as a result of the rigidity of the backbone and chelate ring size, should prefer a *mer* coordination geometry about the metal. This would then place the phosphine donors *trans* to each other. Indeed in X-ray structure determinations[12] of complexes of achiral analogues of **1** and **2** we have found this to be the case in several octahedral structures although in pentacoordinate complexes such as Rh(diene)(PNP)$^+$, the P- M -P angle has been found surprisingly to be considerably less than 180°. However in the *mer* arrangement it is possible for the substrate to approach and bind along the C_2 axis (which is most unlikely to be the case for C_2 bidentate chelates) thus interacting directly with the substituents on the phosphorus donor atoms and experiencing the 'quadrant effect' as shown below. This is illustrated by the face- edge arrangement of the phenyl groups imposed by the chirality on the backbone in **1** and **2** but, of course, the same effect will be found for **3** and **4** resulting from the chiral substituents on phosphorus.



Generous financial support from the Supermolecules Joint Research Project of the Research Development Corporation of Japan and University Louis Pasteur is gratefully acknowledged. The Deutsche Forschungsgemeineschaft is thanked for the post-doctoral Fellowship to P.D.

References.

1. For example, see: (a) Kagan, H. B., *Comprehensive Organometallic Chemistry, Vol. 8*, Wilkinson, G.; Stone, F. G. A. (Editors), Pergamon, Oxford, **1982**. (b) Brunner, H., *Angew. Chem. Int. Ed. Engl.*, **1983**, *17* , 897-1012. (c) Knowles, W. S., *Acc. Chem. Res.*, **1983**, *16* , 106-112. (d) Whitesell, J.K., *Chem. Rev.*, **1989**, *89*, 1581-1590. (e) Noyori, R., Asymmetric Catalysis in Organic Synthesis, Wiley, New York, **1994**.

2. (a) Burk, M. J.; Harlow, R. L., *Angew. Chem. Int. Ed. Engl.*, **1990**, *29*, 1462-1464. (b) Burk, M. J.; Easter, J. E.; Harlow, R. L.,*Tetrahedron: Asymm.*, **1991**, *2*, 569-592. (c) Johnson, C. R.; Imamoto,T., *J. Org. Chem.*, **1987**, *52*, 2170-2174. (d) Ward, T. R.; Venanzi, L. M.; Albinati, A.; Lianza, F.; Gerfin, T.; Gramlich, V.; Ramos Tombo, G.M., *Helv. Chim. Acta*, **1991**, *74*, 983-988. (e) Barbaro, P.; Togni, A., *Organometallics*, **1995**, *14*, 3570-3573.
3. LeCloux, D. C.; Tolman, W. B., *J. Am. Chem. Soc.*, **1993**, *115*, 1153-1154.
4. Hawkins, J. M.; Sharpless, K. B., *Tetrahedron Lett.* **1987**, *28*, 2825-2828.
5. (a) Nishiyama, H.; Yamaguchi, S.; Kondo, M.; Itoh, K., *J. Org. Chem.*, **1992**, *57*, 4306-4309. (b) Park, S.-B.; Murata, K.; Matsumo, H.; Nishiyama, H., *Tetrahedron: Asymm.*, **1995**, *6*, 2487-2494, and references therein.
6. De Martin, S.; Zassinovich, G.; Mestroni, G., *Inorg.Chim. Acta*, **1990**, *174*, 9-11.
7. Jiang, Q.; Van Plew, D.; Murtuza, S.; Zhang, X., *Tetrahedron Lett.*, **1996**, *37*, 797-800.
8. van de Kuil, L. A.; Veldhuizen, Y. S. J.; Grove, D. M.; Zwikker, J. W.; Jenneskens, L. W.; Drent, W.; Smeets, W. J. J.; Spek, A. L.; van Koten, G., *Recl. Trav. Chim. Pays-Bas*, **1994**, *113*, 267-277.
9. a) Descotes, G.; Lafont, D.; Sinou, D.; Brown, J. M.; Chaloner, P. A.; Parker, D., *New J. Chem.*, **1981**, *5*, 167-173. b) Descotes, G.; Lafont, D.; Sinou, D., *J. Organomet. Chem.*, **1978**, *150*, C14-16.
10. Brown, H. C.; Ramachandran, P. V., *J. Organomet.Chem.*, **1995**, *500*, 1-19.
11. (a) Bailey, D.; O'Hagan, D.; Dyer, U.; Lamont, R. B., *Tetrahedron: Asymm.*, **1993**, *4*, 1255-1258. (b) Nakamura, K.; Kawai, Y.; Oka,S.; Ohno, A., *Bull. Chem. Soc. Jpn*, **1989**, *62*, 875-879. (c) Nakamura, K.; Inoue, K.; Ushio, K.; Oka, S., *Chem. Letts.*, **1987**, 679-682.
12. See following communication and the Ph.D. Theses of C. Newton (**1995**), and R. Sablong (**1996**), Université Louis Pasteur, Strasbourg, France. This research was first presented at the MMCOS Meeting, Rocamadour, France, **1994**.

(*Received in France* 14 *March* 1996; *accepted* 17 *May* 1996)