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Mendeleev Commun., 2004, 14(6), 276–277
Mendeleev Communications

Chelating phosphines with C_2 and C_3 symmetry

Emilie Brulé, Yuxin Pei, Fredrik Lake, Fredrik Rahm and Christina Moberg*

Department of Chemistry, Royal Institute of Technology, SE 100 44 Stockholm, Sweden. Fax: +46 8 791 2333; e-mail: kimo@kth.se

DOI: 10.1070/MC2004v014n06ABEH002026

Amide formation between ring opened aziridines and 2-(diphenylphosphino)benzoic acid provides an easy access to chelating di- and triphosphines with C_2 and C_3 symmetry.

The tetrahedral carbon atom attached to four different groups is the most common reason for chirality in organic compounds. Asymmetric metal catalysis is a powerful method by which a large variety of chiral compounds can be prepared in enantiomerically pure forms. In the design of metal catalysts, the steric and electronic properties of the chiral ligands responsible for chirality transfer are crucial for the success of the catalytic system. The symmetry of the chiral ligands and their metal complexes is an additional factor that occasionally should be considered for efficient chiral recognition and transformation.

Rotational axes, C_n, are the only symmetry elements compatible with chirality. The presence of C_n elements of symmetry in the ligands responsible for chiral transfer in metal-catalysed reactions may be beneficial since symmetry can reduce the number of possible intermediates/transition states, thus increasing the probability of a successful result. Compounds belonging to point groups C_2 or D_2, having twofold rotational axes as their sole symmetry elements, have been extensively employed in asymmetric synthesis,[1] whereas examples of the use of those belonging to groups with threefold rotational symmetry axes, C_3 and D_3, are more scarce.[2] By definition, C_2 symmetry is characterised by the fact that an identical situation is obtained upon the rotation of C_2-symmetric species 180° about the rotation axis. In an event involving chiral recognition, this implies

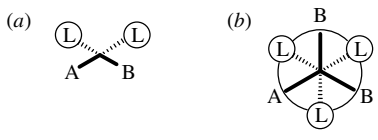
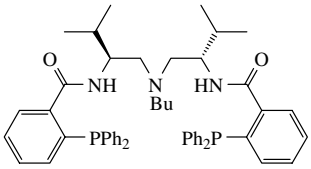


Figure 1 (*a*) In a square planar complex with a C_2-symmetric ligand, A and B are homotopic, and (*b*) A, B and C are homotopic in an octahedral complex with a C_3-symmetric tridentate ligand.



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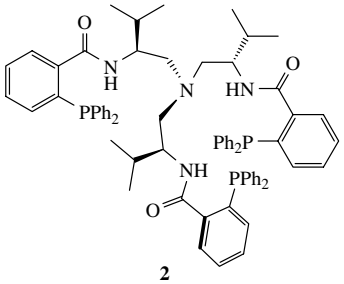

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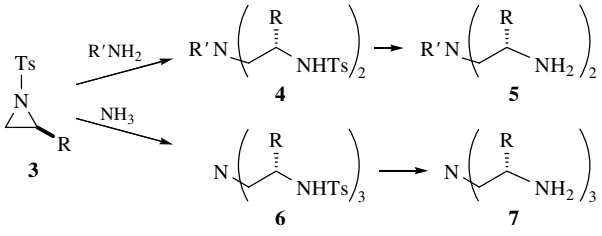
that two complexes, which are identical in the C_2 case, would be diastereomeric in the C_1 case. Thus, in a square-planar complex (Figure 1) containing a bidentate C_2-symmetric ligand, the two vacant coordination sites are homotopic. With threefold symmetry each rotation of 120° yields an identical situation, resulting in three homotopic coordination sites in an octahedral complex with a tridentate ligand having a threefold rotational axis (Figure 1). For this reason, the preparation of chiral ligands with rotational symmetry is an important issue.

We present here the syntheses of C_2-symmetric diphosphine **1** and C_3-symmetric triphosphine **2** starting from dipodal and tripodal amines. The required amines were prepared by a previously developed modular approach, whereby a chiral *N*-activated aziridine, in turn obtained from easily available enantiopure amino alcohols, reacted with a primary amine or ammonia to give chelating bis(tosylamides) and tris(tosylamides), respectively (Scheme 1).[3] After deprotection, the desired C_2- and C_3-symmetric amines are obtained.

For the preparation of ligand **1**, (*S*)-*N*-tosyl-2-isopropylaziridine (**3**, R = Pr^i) was reacted with butylamine to give dipodal tosylamide **4** (R = Pr^i, R′ = Bu) with time averaged C_2 symmetry in 85% yield, using a procedure analogous to that used for the corresponding triflates.[4] Deprotection of the amino groups using aqueous HBr and phenol gave **5** (with two primary amino groups) in 83–92% yield. The analogous ring opening with ammonia has been shown to proceed in high yield using microwave irradiation to yield **6** (R = Pr^i). Deprotection, forming **7**, was performed by the same procedure as that used for **4**.

In order to finally obtain phosphine ligands **1** and **2**, amines **5** and **7** were reacted with 2-(diphenylphosphino)benzoic acid. In the reaction with **5**, amide coupling was performed using *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)-pyridine (DMAP), providing the C_2-symmetric ligand in 64% yield.† Use of the same procedure for the preparation of C_3-symmetric **2** gave an impure compound, which proved difficult to purify. However, by changing to 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC) and *N*-hydroxybenzotriazole (HOBt),[5] the desired product was obtained in 30% yield.‡

The symmetry of the ligands is evident from their NMR spectra. The two ligands exhibited one set of ^{1}H, ^{13}C and ^{31}P signals for the phosphorus-containing substituents on the central nitrogen atoms, clearly demonstrating the identity of the substituents. However, whereas **2** has true inherent threefold symmetry and is expected to give C_3-symmetric metal complexes, **1** has only time-averaged symmetry; in the latter compound, there is no single stable conformation with C_2 symmetry. In contrast to the situation in **2**, metal complexes of **1** where the central nitrogen atom takes part in coordination to the metal are devoid of symmetry due to the tetrahedral nitrogen. The rotational symmetry of the ligand is advantageous, however, in that complex formation is restricted to form one single complex.



Scheme 1

With the present method for the synthesis of phosphine ligands, a wide variety of derivatives are easily accessible. We have recently demonstrated that, in addition to ammonia and aliphatic primary amines, diamines and primary amines containing a variety of functional groups and primary amines with central, axial and planar chirality can be employed in the reaction with differently substituted aziridines.[3] Therefore, the electronic and steric properties of the ligands can be easily varied while maintaining their symmetry. By analogy to the Trost diphosphine ligand prepared by amidation of (*R**,*R**)-1,2-diaminocyclohexane,[6] **1** and **2** are expected to exhibit interesting catalytic properties.

We are grateful to Delphine Marches and Richard Holzwarth for synthetic work. The project was supported by EU (grant no. HPRN-CT-2001-00187).

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Received: 7th September 2004; Com. 04/2351

† Ligand **1**: compound **5** (1 mmol, 43 mg), 2-(diphenylphosphino)-benzoic acid (2.1 mmol, 643 mg), DCC (2.2 mmol, 454 mg), and DMAP (0.11 mmol, 13.4 mg) in CH_2Cl_2 (6.4 ml) were stirred at room temperature for 14 h. The reaction mixture was filtered through celite, the filter cake was washed with CH_2Cl_2, and the solvent was removed *in vacuo*. Purification by flash chromatography [hexane/EtOAc (3:1) to which 0.5% Et_3N and 0.5% MeOH were added] afforded compound **1** as a white foam-like solid. Yield 64%; R_f 0.23 (30% ethyl acetate in hexane); $[\alpha]_{24}$ = +30.6 (*c* 1.37, $CHCl_3$); mp 166.2–166.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.43 (dd, 2H, *J* 7.6 and 4.0 Hz), 7.19–7.35 (m, 20H), 7.16 (dt, 2H, *J* 7.6 and 1.0 Hz), 7.00 (dt, 2H, *J* 7.6 and 1.0 Hz), 6.91 (dd, 2H, *J* 7.8 and 4.0 Hz), 6.24 (d, 2H, *J* 8.3 Hz), 4.04–4.15 (m, 2H), 2.40–2.53 (m, 1H), 2.23–2.40 (m, 1H), 2.47 (dd, 2H, *J* 12.6 and 9.1 Hz), 2.29 (dd, 2H, *J* 12.7 and 5.9 Hz), 1.81–1.94 (m, 2H), 1.18–1.40 (m, 4H), 0.72–0.81 (t, 3H), 0.85 (d, 6H, *J* 7.05 Hz), 0.73 (d, 6H, *J* 7.05 Hz). ^{13}C NMR ($CDCl_3$, 500 MHz) δ: 169.5, 142.5 (d, *J* 26.5 Hz), 138.2 (d, *J* 12.1 Hz), 137.9 (d, *J* 11.3 Hz), 135.8 (d, *J* 21.2 Hz), 134.7, 134.4, 134.25, 134.20, 134.0, 130.2, 129.1, 128.9 (several signals), 128.41, 128.38, 55.5, 54.0, 52.2, 29.9, 28.9, 21.1, 19.5, 17.6, 14.7. ^{31}P NMR ($CDCl_3$, 500 MHz) δ: –9.51. Found (%): C, 75.94; H, 7.29; N, 5.09. Calc. for $C_{52}H_{59}N_5O_2P_2$ (%): C, 76.17; H, 7.25; N, 5.12.

‡ Ligand **2**: a solution of **7** (1 mmol, 0.27 g) and 2-(diphenylphosphino)-benzoic acid (3.1 mmol, 950 mg) in CH_2Cl_2 (20 ml) was added dropwise to a solution of EDC (4.5 mmol, 860 mg) and HOBt (4.5 mmol, 600 mg) in CH_2Cl_2 (20 ml) at 0 °C. Ethyldiisopropylamine (5 mmol, 0.68 ml) was added dropwise to the resulting mixture. After being stirred at 0 °C for 4 h, the reaction mixture was allowed to stir overnight at room temperature. The mixture was then extracted with water, 1 M HCl, 1 M NaOH, and $NaHCO_3$ (sat aq.). The organic layer was dried over $MgSO_4$, and the solvent was evaporated. The crude product obtained as a yellow oil was purified by flash chromatography (hexane/ethyl acetate, 7:3) to give **2** as a white solid (30%). R_f = 0.25 (hexane/ethyl acetate, 7:3). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.32 (dd, 3H, *J* 6.8 and 3.8 Hz), 7.22–7.03 (m, 33H), 6.86 (dt, 3H, *J* 7.5 Hz, *J* 1.0 Hz), 6.79 (dd, 3H, *J* 8.0 and 4.8 Hz), 6.10 (d, 3H, *J* 9.4 Hz), 4.05 (m, 3H), 2.55–2.61 (m, 3H), 2.19–2.24 (m, 3H), 1.69–1.76 (m, 3H), 0.75 (d, 9H, *J* 6.8 Hz), 0.64 (d, 9H, *J* 6.8 Hz). ^{13}C NMR ($CDCl_3$, 400 MHz) δ: 169.3, 141.9 (d, *J* 25.5 Hz), 138.2 (d, *J* 10.1 Hz), 138.1 (d, *J* 8.8 Hz), 136.5 (d, *J* 21.1 Hz), 134.7, 134.6, 134.4, 134.2, 134.0, 130.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.2, 128.1, 56.2, 52.0, 30.0, 20.2, 17.3. ^{31}P NMR ($CDCl_3$, 500 MHz) δ: –8.77.