Completely Stereoselective Synthesis of a Chiral Quadridentate Ligand with As_2NP Donor Atoms. Crystal and Molecular Structure of [OC-6,35-(*R**,*S**)]-(±)-Dichloro{1-[(2-dimethylarsinophenyl)methylarsino]-2-[(2-aminophenyl)methylphosphino]benzene-*As*, *As'*,*N*,*P*}cobalt(III) Chloride Dihydrate

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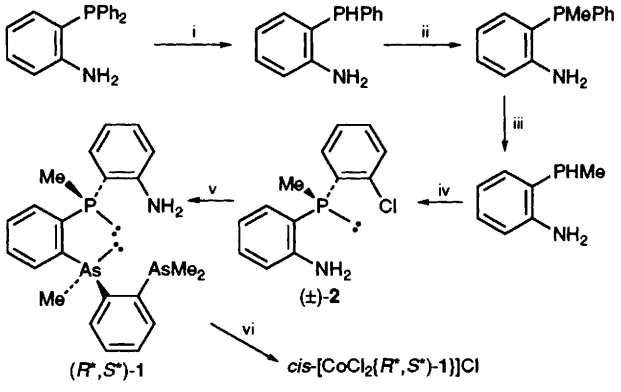
Reaction of (±)-(2-aminophenyl)(2-chlorophenyl)methylphosphine with sodium (2-dimethylarsinophenyl)methylarsenide is completely stereoselective giving (*R**,*S**)-1-[(2-dimethylarsinophenyl)methylarsino]-2-[(2-aminophenyl)methylphosphino]benzene, (*R**,*S**)-**1**; as confirmed by a crystal structure determination of *cis*-[$CoCl_2${(*R**,*S**)-**1**}]Cl·$2H_2O$.

Optically active quadridentate ligands have received little attention as chiral auxiliaries in asymmetric synthesis. Certain tetradentate ligands containing four nitrogen donor atoms have been used to effect the stereoselective synthesis of α-aminoacidates,[1] however, to our knowledge none containing phosphorus or arsenic donor atoms have been utilised in enantioselective synthesis, despite di(tertiary phosphines) being arguably the most successful chiral auxiliaries in asymmetric catalysis.[2] Appropriately designed optically active quadridentate lgiands bearing two or more stereogenic phosphorus or arsenic donor atoms and that selectively form *cis*-α complexes with transition metal ions offer an enormous potential as chiral auxiliaries in asymmetric synthesis, particularly in controlling the stereoselectivity of reactions involving substrates that bind in a bidentate fashion. A few examples of chiral tetradentate ligands containing arsenic or phosphorus stereocentres have appeared in the literature and include the racemic compounds (*R**,*R**)-1,2-bis{(diphenylphosphinoethyl)phenylphosphino}ethane, tetraphos; (*R**,*R**)-1,2-bis{(2-dimethylarsinophenyl)methylarsino}benzene, qars; (*R**,*R**)-1,2-bis{(dimethylarsinopropyl)methylarsino}benzene, fars; and (*R**,*R**)-1,2-bis{(dimethylarsinopropyl)phenylarsino}ethane, tetars.[3–5] The latter ligand has also been successfully resolved by Bosnich *et al.*[5] Furthermore, the racemic form of the ligand qars was found to coordinate to cobalt(III) to give the *cis*-α diastereomer exclusively.[4] This is a very important consideration in any rational approach towards the design and synthesis of chiral auxiliaries based on ligands of this type due to the relatively large number of isomeric possibilities.

Here we report on the stereoselective synthesis of a chiral quadridentate ligand (*R**,*S**)-(±)-1-[(2-dimethylarsinophenyl)methylarsino]-2-[(2-aminophenyl)methylphosphino]-benzene, (*R**,*S**)-**1**; the optically active forms of which have been specifically designed to be used as chiral auxiliaries in asymmetric synthesis. The basic strategy behind the synthesis of (*R**,*S**)-**1** involved the coupling of two suitably designed bidentate ligands, (±)-(2-aminophenyl)(2-chlorophenyl)-methylphosphine, (±)-**2**, and sodium (2-dimethylarsinophenyl)methylarsenide (Scheme 1). This approach has been undertaken for two reasons: firstly, the coupling of appropriately designed optically active bidentate ligands could provide a general synthetic route to optically active quadridentate ligands; and secondly, the resolution of chiral bidentate ligands *via* metal complexation is well established.[6]

Compound (±)-**2** was prepared in four relatively high yielding steps from (2-aminophenyl)diphenylphosphine (Scheme 1).† Chemoselective cleavage of a phenyl group from (2-aminophenyl)diphenylphosphine[7] by reaction with 3 equiv. of lithium in THF followed by hydrolysis gave secondary phosphine (±)-(2-aminophenyl)phenylphosphine.‡ Deprotonation of the secondary phosphine with sodium in THF followed by addition to a solution of methyl iodide in the same solvent at −78 °C gave (±)-(2-aminophenyl)methylphenylphosphine. Completely chemoselective cleavage of the phenyl group from the latter was achieved using lithium in THF to give (±)-(2-aminophenyl)methylphosphine, upon hydrolysis. Subsequent deprotonation of the secondary phosphine using sodium in THF followed by reaction with 1,2-dichlorobenzene gave (±)-**2**.

The product, (*R**,*S**)-**1**, from the reaction of (±)-**2** with sodium (2-dimethylarsinophenyl)methylarsenide in THF was



Scheme 1 Only one of the enantiomers of (*R**,*S**)-**1** and (±)-**2** is depicted. *Reagents and conditions*; i, 3Li, THF then H_2O; ii, Na, THF then MeI, THF; iii, 3Li, THF then H_2O; iv, Na, THF then 1,2-dichlorobenzene, THF; v, sodium(2-dimethylarsinophenyl)methylarsenide, THF; vi, $[Co(H_2O)_6]Cl_2$, MeOH, air.

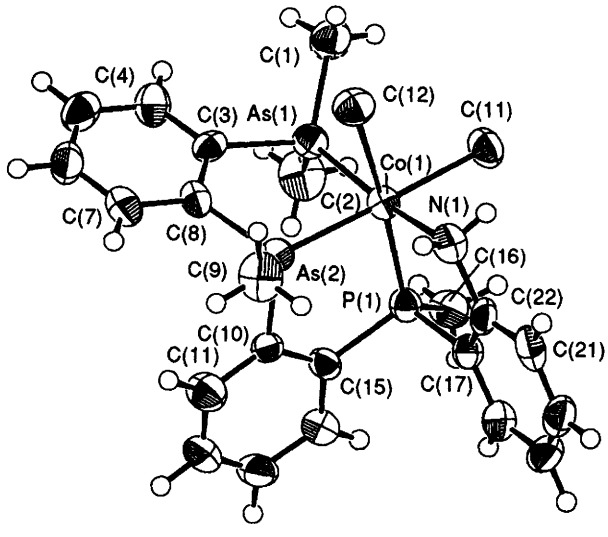


Fig. 1 Molecular structure of the cation *cis*-(±)-[$CoCl_2${(*R**,*S**)-**1**}]$^+$. Selected bond distances and angles are as follows: Co–As(1) 2.311(2), Co–As(2) 2.258(2), Co–P 2.173(4), Co–N 2.008(10), Co–Cl(1) 2.279(4), Co–Cl(2) 2.296(4) Å; As(1)–Co–As(2) 86.07(8), As(1)–Co–Cl(2) 85.7(1), As(2)–Co–Cl(2) 85.8(1), As(2)–Co–N 96.8(3), Cl(1)–Co–P 91.2(1), P–Co–N 86.1(3), As(1)–Co–Cl(1) 88.5(1), As(1)–Co–P 100.4(1), As(2)–Co–P 87.0(1), Cl(1)–Co–Cl(2) 96.5(1), Cl(1)–Co–N 88.9(3) and Cl(2)–Co–N 88.1(3)°.

treated with a solution of hexaaquacobalt(II) chloride in methanol and oxidised in air to yield a single complex, *cis*-(±)-[$CoCl_2${(*R**,*S**)-**1**}]Cl·$2H_2O$,§ the structure of which has been confirmed by an X-ray analysis (Fig. 1).¶ The complex is a racemic compound with the Δ-(R_{As},S_P) and Λ-(S_{As},R_P) forms of the cation being present in the unit cell. Only the former is shown in Fig. 1. It is clear from the structural data that the *cis*-α diastereomer has been formed exclusively and that the stereogenic arsenic and phosphorus atoms of the quadridentate ligand have opposite relative configurations. Furthermore, the data show that the coupling reaction between (±)-**2** and sodium (2-dimethylarsino- phenyl)methylarsenide was completely stereoselective. This result augurs well for the role of the optically active forms of (*R**,*S**)-**1** as potential chiral auxiliaries in enantioselective synthesis. Resolution of (±)-**2** *via* the method of metal complexation is currently in progress. The optically active bidentate (*S*)-**2** [or (*R*)-**2**] should again react with sodium (2-dimethylarsinophenyl)methylarsenide in a completely stereoselective manner to give (*R*,*S*)-**1** [or (*S*,*R*)-**1**] the cobalt(III) complex of which is to be used as a chiral auxiliary in the stereoselective derivatisation of the glycinate ion.

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Footnotes

† Yields for the first three steps in the synthesis of (±)-**2** were >80%. The final step is a relatively slow reaction that proceeds in *ca.* 40% yield. [Some 30% of the starting material (±)-(2-aminophenyl)-methylphosphine was recovered from the reaction].

‡ When less than 3 equiv. of lithium were used some unreacted starting material was recovered from the reaction. Presumably deprotonation of the amino group accompanied the chemoselective cleavage of a phenyl moiety from (2-aminophenyl)diphenylphosphine.

§ Small quantities of *trans*-[$CoCl_2$(diars)$_2$]Cl[8] and [$CoCl_2$(PN)$_2$]Cl [diars = 1,2-phenylenebis(dimethylarsine), PN = (±)-(2-aminophenyl)methylphenylphosphine] were also isolated.

¶ *Crystal data* for *cis*-(±)-[$CoCl_2${(*R***S**)-**1**}]Cl·$2H_2O$, $C_{22}H_{30}As_2Cl_3CoNPO_2$, M = 686.59, triclinic, space group $P\bar{1}$ (no. 2), a = 9.261(2), b = 12.129(1), c = 12.397(1) Å, α = 94.908(9), β = 97.84(1), γ = 94.34(1)°, U = 1369.1(4) Å^3, D_c = 1.655 g cm^{-3} for Z = 2, F(000) = 688, μ(Cu-Kα) = 110.12 cm^{-1}. Of 4081 measured intensities, 2490 were considered observed [$I > 3\sigma(I)$]. After Lorentz-polarisation and absorption corrections, the structure was solved by direct methods and expanded using Fourier techniques. Subsequent refinement (full-matrix least squares) afforded R and R_w values of 0.054 and 0.055, respectively. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Data Centre. See Information for Authors, Issue No. 1.

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