First Resolution of a Linear Chelating Tetra(tertiary phosphine): Resolution and Absolute Configurations of Enantiomers of (*R**,*R**)-(±)-1,1,4,7,10,10-Hexaphenyl-1,4,7,10-tetraphosphadecane

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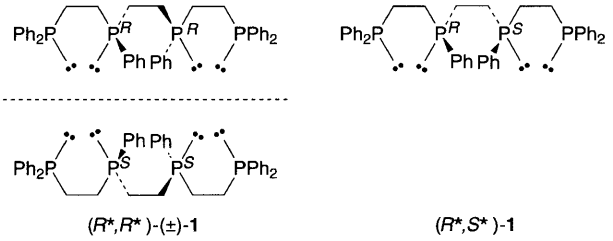
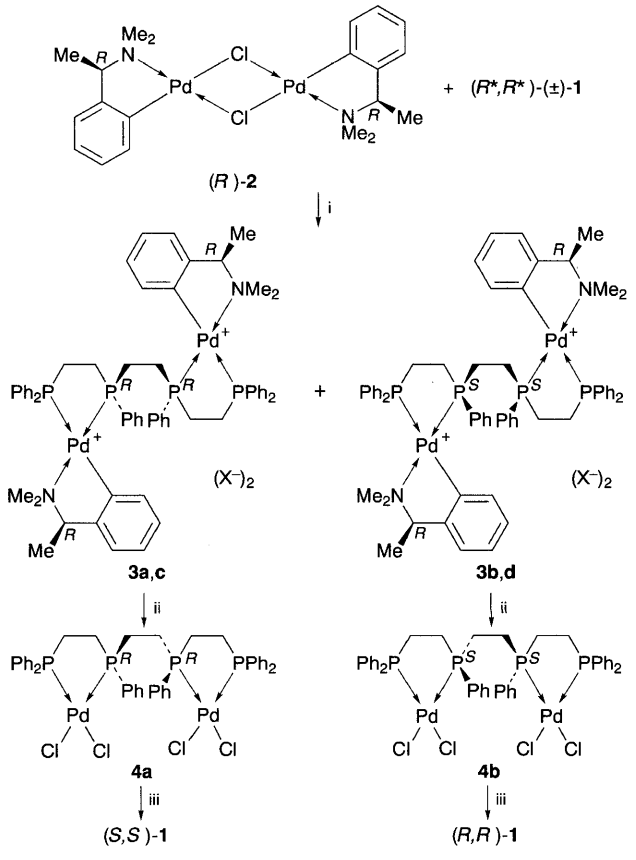
The important and commercially available linear tetra(tertiary phosphine) (*R**,*R**)-(±)/(*R**,*S**)-$Ph_2PCH_2CH_2P(Ph)CH_2CH_2P(Ph)CH_2CH_2PPh_2$ has been separated into diastereoisomers and the (*R**,*R**)-(±)-diastereoisomer resolved by the method of metal complexation giving the first optically active tetra(tertiary phosphine).

Despite extensive work on the synthesis and resolution of chiral unidentate and bidentate di(tertiary phosphines)[1] and arsines[2] for use as stereochemical probes of intra- and inter-molecular rearrangements in coordination complexes[3] and as auxiliaries for transition metal-mediated organic asymmetric synthesis,[4] little work has been directed toward the isolation of similar ligands of higher denticity in stereochemically homogeneous form. Of particular interest are C_2-quadridentates because of the almost universal capacity of similar C_2-bidentates to facilitate stereoselective reactions.[5] To our knowledge, the only linear C_2-quadridentate of this type to be separated into stereoisomeric forms is the tetra(tertiary arsine) (*R**,*R**)-(±)/(*R**,*S**)-1,1,12,12-tetramethyl-5,8-diphenyl-1,5,8,12-tetraarsadodecane, which was separated into diastereoisomers and resolved *via* dichlorocobalt(III) complexes.[6] Fourteen-membered cyclic *trans*-As_2S_2 and *trans*-As_2N_2 quadridentates have also been isolated in stereochemically pure forms.[7] Here we report the separation into diastereoisomers and resolution of the commercially available or readily prepared[8] linear C_2-tetra(tertiary phosphine) (*R**,*R**)-(±)/(*R**,*S**)-1,1,4,7,10,10-hexaphenyl-1,4,7,10-tetraphosphadecane **1**. Partial separation of the diastereoisomers of **1** has been achieved previously[9,10] and a number of stereospecific reactions of the individual diastereoisomers have been noted,[9,10,11] but the resolution of the (*R**,*R**)-(±) diastereoisomer has not been hitherto accomplished.

Commercially available **1** consists of an unequal mixture of (*R**,*R**)-(±)/(*R**,*S**) diastereoisomers with the (*R**,*S**) form predominating, presumably owing to the lower solubility and propensity for crystallisation of the higher melting (*R**,*S**) diastereoisomer.† The unequal mixture can be equilibrated into a 1:1 mixture by heating at 200 °C for 2 h [E_{inv} *ca.* 130 kJ mol^{-1} for phosphines of the type (±)-$PR^1R^2R^3$].[12] The pair of diastereoisomers was separated by stirring the 1:1 mixture in benzene–methanol (4:1) for several hours, leading to the almost exclusive extraction of the (*R**,*R**)-(±) diastereoisomer, which was subsequently isolated from methylene chloride–ethanol in *ca.* 95 % yield as colourless microcrystals having mp 117–117.5 °C (lit.[9] 118–119 °C). The less soluble (*R**,*S**) component of the mixture was similarly recrystallised, giving colourless needles of mp 179–180 °C (lit.[9] 189 °C). The ^{31}P NMR data for (*R**,*R**)-(±)- and (*R**,*S**)-**1** are given in ref. 10.

The resolution of (*R**,*R**)-(±)-**1** was achieved by the method of metal complexation. Thus, when allowed to react with 1 equiv. of the resolving agent **2** in methanol, (*R**,*R**)-(±)-**1** gave, in a completely regioselective bridge-splitting reaction, an equimolar mixture of the salts **3a,b** (X = Cl), which was precipitated quantitatively as **3c,d** (X = PF_6) with aqueous NH_4PF_6. Extraction of the latter mixture with chloroform, followed by fractional crystallisation of the two components thus separated, afforded **3c** (X = PF_6) as colourless prisms (less soluble) with *ca.* 90% recovery, and **3d** (X = PF_6) as the more soluble complex in similar yield and form.‡ The crystal and molecular structure of **3c** (X = PF_6) was determined.§ The structure of the dinuclear cation of the salt indicates *trans* arrangements of the inner tertiary phosphine-*P* stereocentres of the tetraphosphine of *R* configuration with respect to the (*R*)-1-(dimethylamino)ethyl groups of the resolving agents (Fig. 1). The coordination geometry around each palladium in **3c** (X = PF_6) is typical of such complexes.[13] When solutions of **3c** (X = PF_6) or **3d** (X = PF_6) were treated with hydrochloric acid, the respective sparingly soluble complexes **4a** and **4b** separated and the resolving amine was recovered from the mother liquors after neutralisation. The enantiomers of (*R**,*R**)-(±)-**1** were liberated from **4a** and **4b** by stirring the latter as a suspension in dichloromethane with an excess of sodium cyanide in water.¶ The pure complexes reacted in each case to give almost





Scheme 1 *Reagents and conditions*: i, MeOH (**3a,3b**) and then aq. NH_4PF_6 (**3c,3d**); ii, HCl in MeOH; iii, excess KCN in H_2O/CH_2Cl_2

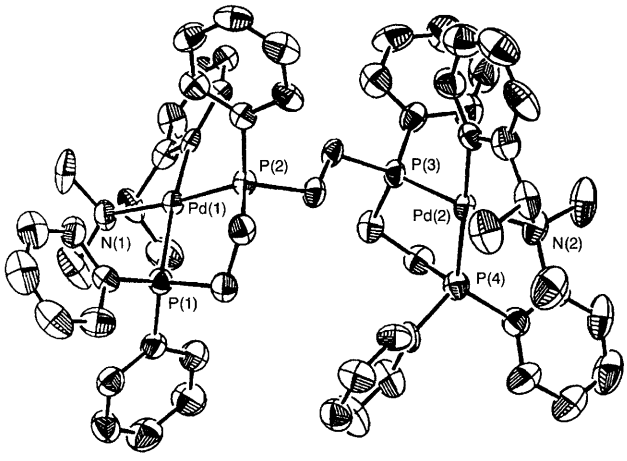


Fig. 1 An ORTEP plot of the cation of **3c** with key atoms numbered. Hydrogen atoms have been omitted for clarity. Selected interatomic distances (Å) and angles (°) are as follows: P(1)–Pd(1) 2.363(3), P(2)–Pd(1) 2.247(3), P(3)–Pd(2) 2.227(3), P(4)–Pd(2) 2.356(3), P(1)–Pd(1)–P(2) 84.97(9), P(3)–Pd(2)–P(4) 84.7(1).

colourless solutions from which the respective optically active phosphines were isolated in crystalline form from the organic phases by evaporation of the dichloromethane in the presence of ethanol. The pure enantiomers, (*S*,*S*)-(+)- and (*R*,*R*)-(–)-**1**, have, respectively, $[\alpha]_D^{21}$ +22 and −22 (c 1.0, CH_2Cl_2), and mp 88 °C after recrystallisation from acetone–ethanol. The optical purities of the enantiomers were confirmed by the quantitative re-preparation of **3c** (X = PF_6) and **3d** (X = PF_6) from the respective enantiomeric phosphines and (*R*)-**2**; the diastereoisomers **3c** (X = PF_6) and **3d** (X = PF_6) were found to be pure within the limits of detectability of the NMR spectrometer.

The ready availability of the various forms of **1** opens up the prospect of interesting new chemistry. For example, the enantiomers of (*R**,*R**)-(±)-**1** react with silver(I) to give optically active double-stranded disilver(I) complexes with double-helix and side-by-side helix structures.[13]

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Footnotes

† Purchased from the Aldrich Chemical Co. Inc., Milwaukee, Wisconsin, 53233, USA. The material supplied had (*R**,*R**)-(±):(*R**,*S**) *ca.* 1:4.

‡ *Selected physical and spectroscopic data* for **3c** (X = PF_6): mp 214 °C, $[\alpha]_D^{21}$ − 104 (*c* 1.0, acetone). ^{31}P NMR (CD_2Cl_2): δ 64.37 , 43.25. Satisfactory elemental analyses were obtained for all compounds.

For **3d** (X = PF_6): mp 205 °C, $[\alpha]_D^{21}$ + 96 (*c* 1.0, Me_2CO). ^{31}P NMR (CD_2Cl_2): δ 65.69, 43.25.

For **4a** and **4b**: mp 289 °C. ^{31}P NMR (CD_2Cl_2): δ_P 72.35, 66.04 (J_{AB} = 5.41 Hz).

§ *Crystal data* for **3c** (X = PF_6): $C_{62}H_{70}F_{12}N_2P_6Pd_2$; M_r = 1469.89 g mol^{-1}; colourless prisms from methanol–dichloromethane; space group $P2_1$, *a* = 10.841(3), *b* = 13.668(2), *c* = 22.330(3) Å, β = 103.09(1)°, *U* = 3222.8(10) Å^3, D_c = 1.515 g cm^{-3} for *Z* = 2; λ(Mo–Kα) = 0.71069 Å; Philips PW 1100/20 diffractometer (20 °C); ω–2θ scan method. A total of 5941 unique data were collected in the range 4 ≤ 2θ ≤ 50° of which 4418 were refined [$I > 3\sigma(I)$]. The structure was solved by heavy-atom and difference-Fourier techniques; subsequent refinement (full matrix least-squares) converged at *R* and R_w values of 0.036 and 0.033, respectively. The absolute configuration was established with use of a Flack enantiomorph-polarity parameter [final value *x* = 0.00(4)][14] and concurred with the known configuration of the resolving agent. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No.1.

¶ The coordination of the phosphine to the metal is stereospecific with retention of configuration at phosphorus: the apparent inversion is a consequence of the Cahn–Ingold–Prelog (CIP) rules for assigning absolute configurations.[15]

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