# X-Ray characterization of enantiomerically pure 1,1′-diphenyl-3,3′,4,4′-tetramethyl-2,2′-biphosphole: a ligand with axial and central chirality

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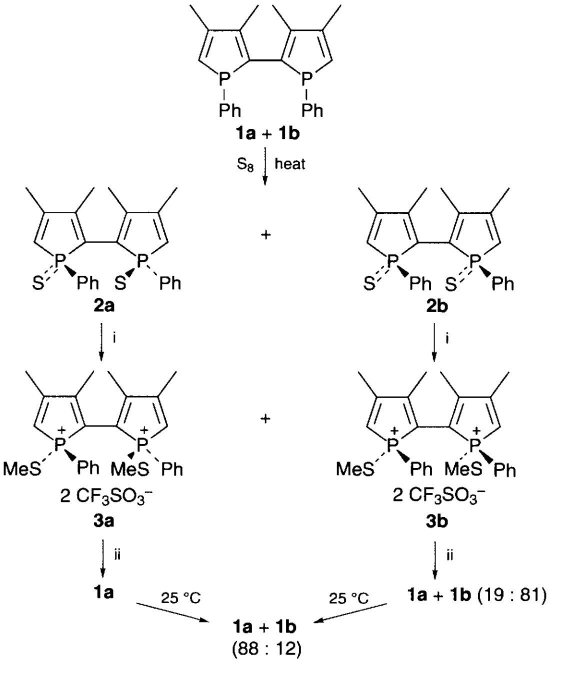
**The stereochemical analysis and characterization of diastereoisomers of 1,1′-diphenyl-3,3′,4,4′-tetramethyl-2,2′-biphosphole having axial and central chirality reveal the potential interest of this ligand for asymmetric catalysis.**

$C_2$-symmetric bidentate ligands with axial chirality, such as binap, are powerful chiral auxiliaries in catalytic asymmetric induction processes.[1] Mathey and coworkers[2] reported the first synthesis of 2,2′-biphospholes and their complexation to transition metals. Puzzled with the possible combination of axial chirality of the 2,2′-biphospholes and central chirality of the phosphorus atoms in these systems, we decided to explore their potential interest as ligands for asymmetric catalysis. We report here the stereochemical analysis, the structural characterization of the diastereoisomers and preliminary results concerning the use of 2,2′-biphosphole **1** in palladium complexes as catalysts. Using the procedure previously described by Mathey and coworkers,[2] we obtained the biphosphole **1** which we identified as a mixture of two isomers, **1a**, **b** in the ratio 88 : 12. Treatment of this mixture with sulfur in dichloromethane at 40 °C gave a mixture of **2a**, **b** in the same ratio 88 : 12 (Scheme 1). We were able to separate **2a** ($\delta_P$ 50.75) and **b** ($\delta_P$ 51.37) by column chromatography and they have been characterized by $^1H$, $^{31}P$ NMR spectroscopy, mass spectrometry and single-crystal X-ray diffraction† (Fig. 1, 2). In both compounds, the dihedral angle between the two phosphole rings (93.7° in **2a** and 99.4° in **2b**) generates an axial chirality. Both phosphorus atoms have the same absolute configurations [(*R*,*R*) or (*S*,*S*)] in the major isomer **2a** and opposite absolute configurations (*R*,*S*) in the minor compound **2b**. Since the sulfur addition to trivalent phosphorus compounds proceeds with retention of configuration,[3] these results suggest that biphosphole **1** exists also as a mixture of corresponding diastereoisomers. In order to isolate the two diastereoisomers **1a**, **b** we investigated a method reported by Mikolajczyk[4] to desulfurate stereospecifically **2a**, **b**. Compound **2a** was reacted with methyltrifluoromethane sulfonate to give compound **3a** ($\delta_P$ 52.95) in quantitative yield. Following the reaction of **3a** with *tert*-butyllithium sulfide by $^{31}P$ NMR, we observed at −70 °C the quantitative formation of **1a**. At −50 °C, the isomerisation proceeded giving a mixture of **1a** and **b** in a 98 : 2 ratio, rising to 88 : 12 at 25 °C. Similarly, **2b** was transformed into **3b** ($\delta_P$ 54.27), then **1b** was obtained as the main product at −70 °C (81%), with a small amount of **1a** (19%) (Scheme 1). Upon increasing the temperature to 25 °C the ratio **1a** : **b** of 88 : 12 was again obtained. The determination of kinetic parameters was



Scheme 1 *Reagents and conditions*: i, $CF_3SO_3Me$, $CH_2Cl_2$, 25 °C; ii, $Bu^tSLi$ −70 °C, $Et_2O–CH_2Cl_2$

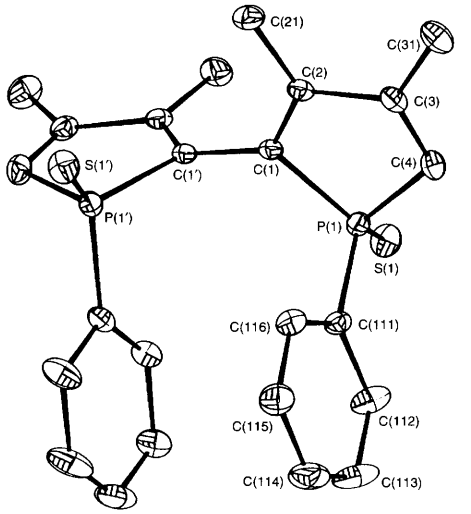


**Fig. 1** Molecular structure of **2a** (thermal ellipsoids at 30%)

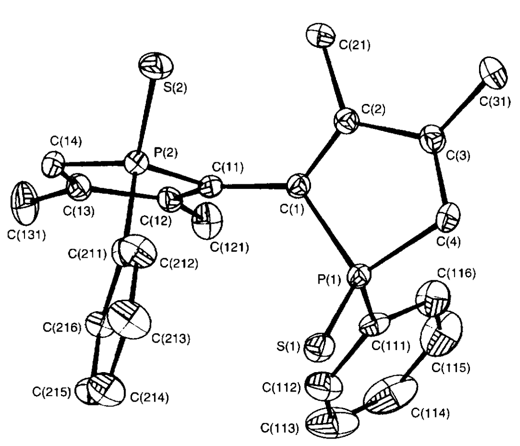
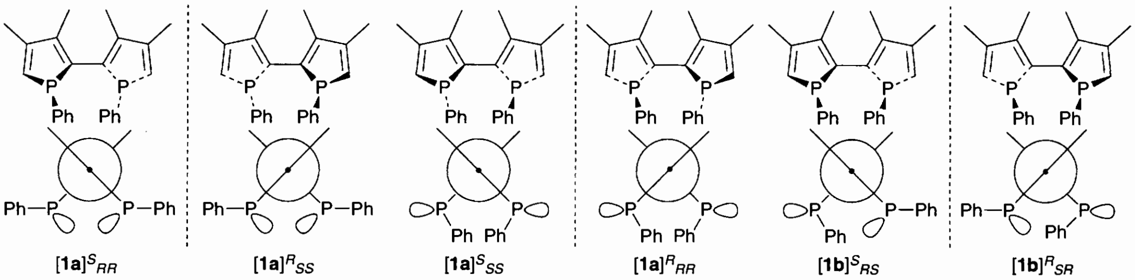


**Fig. 2** Molecular structure of **2b** (thermal ellipsoids at 30%)



**Scheme 2** Projection is along the C–C axis; superscript refers to axial chirality, subscript refers to central chirality

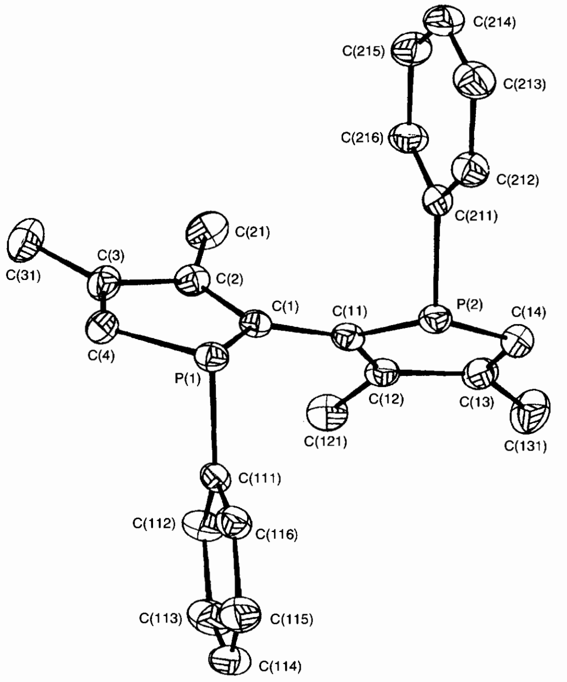


**Fig. 3** Molecular structure of **1a** (thermal ellipsoids at 30%)

carried out by $^{31}$P NMR in the temperature range of −60 to −50 °C in which the isomerisation process **1b** ⟶ **1a** is slow on the NMR timescale. It is a first-order reaction with $\Delta H^{\ddagger}$ = 63.48 kJ mol$^{-1}$ and $\Delta S^{\ddagger}$ = −25 J mol$^{-1}$ K$^{-1}$ evaluated from plotting log $k/T$ *vs.* $1/T$ (correlation coefficient 0.999) The free enthalpy of activation ($\Delta G^{\ddagger}$ 218 = 68.9 kJ $\Delta G^{\ddagger}_{298}$ mol$^{-1}$) can be compared to the pyramidal inversion barrier of phosphorus observed for the monophosphole series (*ca.* 66.88 kJ mol$^{-1}$).[5] Between −50 and +30 °C, the ratio **1a** : **b** is still temperature dependent but the equilibrium mixture is rapidly obtained. These results indicate that even with a low pyramidal inversion barrier, biphosphole **1** exists in solution as a mixture of two diastereoisomers, the energetically preferred isomer being **1a**. Crystals of **1a** suitable for X-ray analysis (Fig. 3) were obtained by slow evaporation from a dichloromethane solution and belong to the chiral non-centrosymmetric space group $P2_1$. Structural data of **1a** are in good agreement with related published structures.[6] The phosphorus atoms in **1a** retains a pyramidal geometry Σ(CPC angles) = 301.6° inducing a central chirality. The dihedral angle between the two phosphole rings (46.63°), much lower than in compounds **2a** and **b**, generates an axial chirality. In the crystal examined, obtained by spontaneous resolution, the (*R,R*) central chirality is associated with the (*S*) axial chirality of the biphosphole. Surprisingly in **2a**, the (*R,R*) phosphorus stereochemistry is associated with the (*R*) axial chirality. The different possibilities of combining axial and central chiralities are represented in Scheme 2. In the isomers ([**1a**]$^S_{RR}$ + [**1a**]$^R_{SS}$), the phosphorus lone pairs are in the right direction to coordinate to metal atoms. Starting with the mixture of the racemic biphospholes **1a,b** (88 : 12), several metal complexes have been quantitatively obtained and fully characterized.[7] Once coordinated to the metal, the stereochemistry of the biphosphole ligands is stable ([**1a**]$^S_{RR}$, [**1a**]$^R_{SS}$) and some of these complexes are shown to be effective catalysts. For example, the palladium complex generated from [{Pd($\eta_3$-$C_3H_5$)Cl}$_2$] and a slight excess of biphosphole **1** was used in catalytic allylic substitution of 1,3-diphenylprop-2-enylacetate with the anion of the dimethyl malonate. The 2,2′-biphosphole palladium complex proved to be as effective as the best reported catalytic systems for this reaction.[8] At 35 °C in dichloromethane, working on a 2 mmol scale and using 0.02 equiv. of catalyst, the formation of $PhCH{=}CHCHPhCH(CO_2Me)_2$ is quantitative (99%) in 10 min. We are presently investigating the optical resolution of these chiral biphosphole metal complexes in order to explore their performance in asymmetric catalysis.

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## Footnote

† *Crystal data*: **2a**. $C_{24}H_{24}P_2S_2$, $M$ = 438.6, monoclinic, space group $C2/c$, $a$ = 9.525(1), $b$ = 17.491(1), $c$ = 14.236(2) Å, β = 109.36(1)°, $U$ = 2237.6(1) Å$^3$, $Z$ = 4. $R$ = 0.0395, $R_w$ = 0.0456.

**2b**. $C_{24}H_{24}P_2S_2$, $M$ = 438.6, orthorhombic, space group $Pcab$, $a$ = 14.642(3), $b$ = 17.578(4), c = 17.737(2) Å, $U$ = 4566(2) Å$^3$, $Z$ = 8. $R$ = 0.0391, $R_w$ = 0.0478.

**1a**. $C_{24}H_{24}P_2$, $M$ = 374.4, monoclinic, space group $P2_1$, $a$ = 8.529(1), $b$ = 15.120(2), $c$ = 8.728(1) Å, β = 110.21(1)°, $U$ = 1055.9(3) Å$^3$, $Z$ = 2. $R$ = 0.0404, $R_w$ = 0.0475. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/205.

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