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A complex of Ph_3PO with a chiral hydrogen-bond donor: X-ray crystal structures of the complexes with (*RS*)-(±)- and (*S*)-(−)-1,1′-bi-2,2′-naphthol: homochiral Ph_3PO

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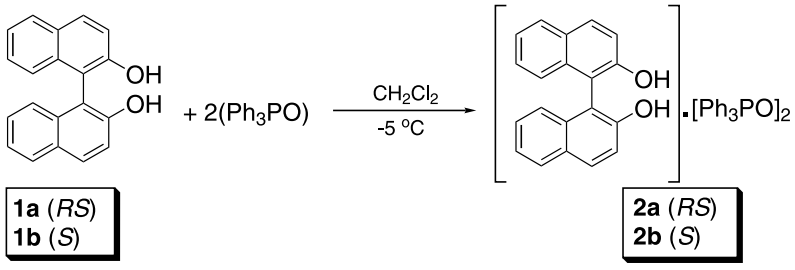
Abstract—The first complex of triphenylphosphine oxide (Ph_3PO) with a chiral substrate, formed by crystallising Ph_3PO in the presence of the synthetically important chiral auxiliary *S*-(−)-1,1′-bi-2,2′-naphthol (BINOL) is reported. The corresponding racemate form has also been prepared and the single-crystal X-ray diffraction structures of both reveal 1(BINOL):2(TPPO) stoichiometry. In the homochiral complex the TPPO molecules apparently exist in one enantiomeric form only. Crystal packing in both is dominated by intermolecular hydrogen bonding between a BINOL hydroxyl group and a TPPO oxygen atom (around 2_1 and 3_1 axes in the racemate and the chiral forms respectively). The crystalline racemate—a racemic compound rather than a conglomerate—is more densely packed than the homochiral form, thus apparently conforming to Wallach's rule.

The elegant work of Etter et al. has demonstrated that triphenylphosphine oxide (TPPO) complexes with hydrogen-bond donors such as alcohols, carboxylic acids and amides, etc., to afford large, well-defined crystals.[1] These observations are not only of considerable general interest in view of the relative rarity of the phenomenon of co-crystallisation, but could also lead to improved methods for resolving stereoisomeric mixtures as follows.

The present studies, in fact, were motivated by the possibility that TPPO complexes of racemates may afford large crystals amenable to Pasteur-type manual sorting ('triage').[2] However, as no crystalline complexes of TPPO with chiral substrates had been reported, the present investigations with (±)- and (*S*)-(−)-1,1′-bi-2,2′-naphthol ('BINOL', **1a** and **1b**, respectively, Scheme 1) were undertaken. Although two other noncentrosymmetric complexes of TPPO have been reported, these are with the achiral substrates 3,5-dinitrobenzoic acid and *N*-methylpyrrole-2-carboxylic acid.[3] Also, homochiral BINOL has found much application in current synthetic methodology,[4] hence the choice of **1b**.



Scheme 1. Formation of the racemate and chiral complexes (**2a** and **2b**, respectively) of the corresponding BINOL's **1a** and **1b**, respectively, with two molecules of TPPO.

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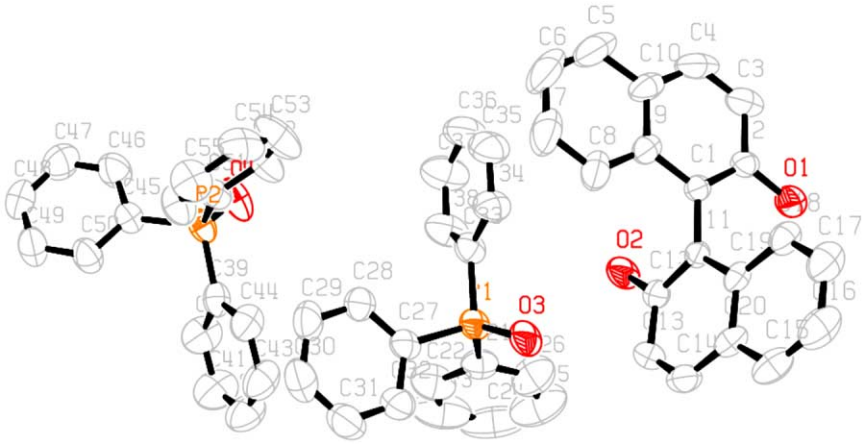

Figure 1. Crystal structure of the racemic TPPO·BINOL complex **2a**.

Crystalline complexes of **1a** and **1b** with TPPO, **2a** and **2b**, respectively, could be obtained by cooling dichloromethane solutions of the components for several days. The (single) crystal structures were determined by X-ray diffraction (cf. Figs. 1 and 2): full details have been deposited in the Cambridge Data Base[5] but relevant data are summarised in Table 1 and discussed below.[†] The crystal structures of (±)- and (*R*)-BINOL,[8] and TPPO[9] have been reported.

The centrosymmetric space group in the case of the racemate **2a** confirms it as a racemic compound rather than a conglomerate, analogously to (±)-BINOL.[8] Although this rules out resolution by triage,[2] the present results remain of considerable significance as **2b** is apparently the only known complex of TPPO with a homochiral substrate. Furthermore, a comparison of the crystal packing features of **2a** and **2b** offers interesting insight into the nature of the interactions that apparently drive **2a** preferentially to form a racemic compound. In fact, there is much current interest in understanding the nature of the crystalline forces that determine whether a conglomerate or a racemate is formed in a given case:[2] Clearly, crystal structures of both the racemate and homochiral forms would be invaluable thereby, so the present studies contribute towards that end (vide infra for further discussion).

The dominant feature of each of the crystal structures is the extensive hydrogen bonding pattern, formed between the BINOL hydroxyl groups and the TPPO oxygen atom. Each hydroxyl group bonds with a separate TPPO molecule, so the stoichiometry of complex formation is 1(BINOL):2(TPPO) in both the racemate **2a** and the homochiral **2b** cases. The intermolecular hydrogen bonding is formed around either a 2_1 axis (**2a**) or a 3_1 axis (**2b**) between BINOL and TPPO: interestingly, these two symmetry features also characterise and distinguish between (±)- and (*R*)-BINOL,[8]

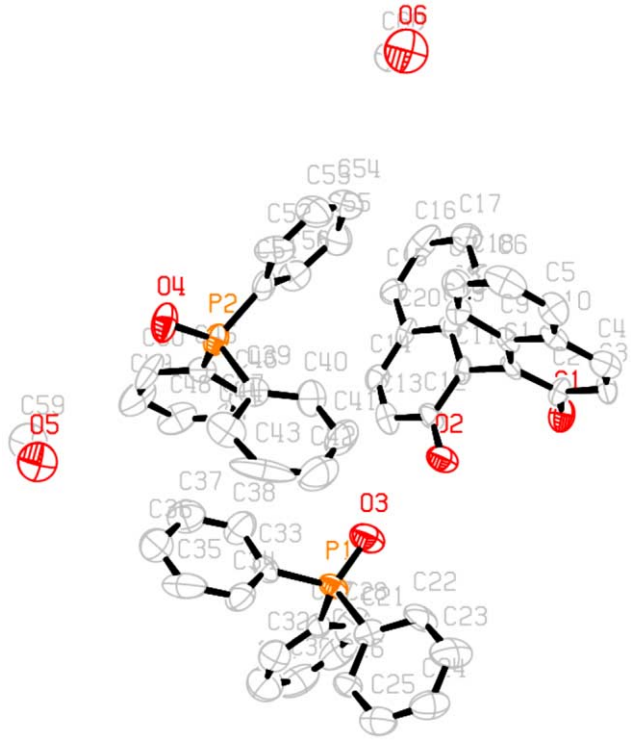

Figure 2. Crystal structure of the chiral TPPO·BINOL complex **2b**.

[†] It is interesting to compare the melting points of **2a** and **2b** with those of the components [TPPO[6] 152.5°C, (±)-BINOL[4,7] 216°C and (*S*)-BINOL[4,7] 208°C]: whereas **2a** is a racemic compound of lower mp than one of its components,[2] **2b** melts lower than both its components. Therefore, the isolation of both **2a** and **2b** in crystalline form despite their relatively low mp's, apparently indicates that their solubilities and mp's (relative to their components) follow different trends.[2] (This implies that **1** and TPPO are more solvated than **2**.)

Table 1. Selected crystallographic data for the BINOL.$(TPPO)_2$ complexes **2a** (racemate) and **2b** (chiral). Atom numbering follows the crystallographic scheme in Figures 1 and 2

Item	Data	**2a**	**2b**
1	Melting point (°C)	173	73
2	Crystal system	Monoclinic	Trigonal
3	Space group	$P2_1/n$	$P3_1$
4	No. of molecules in unit cell[a]	4	3
5	*R* factor	0.058	0.0982
6	Crystal density	1.21	1.17
7	O (1)···O (4) (Å)	2.610 (2)	2.735 (12)
8	O (2)···O (3) (Å)	2.664 (3)	2.714 (7)
9	O (1)–H (1)···O (4)	175.42° (15)	115.15° (1)
10	O (2)–H (2)···O (3)	161.61° (15)	120.86° (1)
11	C (2)–C (1)–C (11)–C (12)	75.02° (31)	−98.06° (1)

[a] Refers to the number of molecules of the complex.

although in these cases the hydrogen bonding may involve only the hydroxyl groups. The O–H–O bond angles are considerably wider, and the corresponding O–O distances marginally shorter, relatively in **2a** (items 7–10 in Table 1). The immediate space around the 3_1 axis in **2b** is apparently occupied by disordered molecules of methanol, as indicated by the rather high residual electron density. (The MeOH was employed during the preparation of **1b** and is presumed to have been carried over via its solvate. Attempts to remove the MeOH in vacuo from **2b** failed.)

The torsion angle between the naphthyl moieties is not only negative but also considerably greater in the homochiral case **2b** relative to the racemate **2a** [–98.06 (1)° versus +75.02 (31)°] (item 11, Table 1); thus, the BINOL moieties deviate considerably from planarity in both the cases, but more so in the homochiral case **2b** in which the naphthyl moieties are not only almost mutually orthogonal but also *transoid*: all this apparently indicates relatively greater steric congestion in the case of **2b**. (Closely similar trends have been reported in the crystal structures of BINOL itself.[8]) Interestingly, both the above crystal structures are rich in C–H–O interactions (numbering 15 and 10 in **2a** and **2b**, respectively), but only around half of these are intermolecular.[5] The intermolecular C–H–O interactions may involve either a BINOL O–H group (preferred) or a TPPO oxygen atom, whereas the intramolecular ones invariably involve TPPO molecules.

The relative stability of the racemic compound form **2a** over the homochiral form **2b** is thus supported by the following features in **2a:** the higher melting point, the more congenial torsion angles between the naphthyl moieties, the less strained O–H–O angles and the greater preponderance of the C–H–O interaction, as mentioned in Table 1 and at appropriate junctures above. These features apparently rule out the formation of the conglomerate under the conditions employed.[2] Interestingly, the density of the racemate crystal **2a** is considerably higher (by 3.4%) than that of the chiral one **2b** (Table 1, item 6): The difference is of the order generally expected and thus supports Wallach's rule,[2,10] by which the crystalline density of a racemic compound is greater than that of the corresponding homochiral form. In fact, the question of whether the relative preponderance of racemic compounds is due to enthalpic or entropic effects—or even whether it reflects a greater stability—is a matter of current debate.[2,10] In the present case, a strong enthalpic contribution to the observed relative stability of the racemic compound form **2a** is indicated—by virtue of its better crystal packing as revealed by X-ray crystallography.

Most interestingly perhaps, in the case of **2b** all the molecules of TPPO are apparently present in one enantiomeric form, as revealed by the three corresponding O–P–C–C dihedral angles which are all of the same sign (Table 2: note that both positive and negative torsion angles are present in equal numbers, in the case of the racemate **2a**). It is known that the TPPO molecule adopts a propeller form and is hence chiral, although the energy barrier to the interconversion of the enantiomeric propeller forms is estimated to be far too low to permit their resolution in solution.[11] In **2b**, however, it appears TPPO has been dynamically resolved into a homochiral form that is sustained in the crystal lattice under the influence of the chiral BINOL auxiliary. Apparently, the observation of homochiral TPPO is practically unprecedented (although it is indicated in the previous reports on the noncentrosymmetric TPPO complexes mentioned above.[3])

Further work to extend the above results to other chiral substrates is planned.

Experimental procedures. (±)-BINOL **1a** was prepared by oxidising naphth-2-ol with $FeCl_3$, and resolved via the (+)-cinchonine salt of the phosphoric acid derivative as reported.[4,7] A solution of the BINOL **1a** or **1b** and TPPO (both 0.2 mM in CH_2Cl_2) was allowed to stand at −5°C for several days, when the deposited crystals of the corresponding complex **2a** or **2b** were harvested. Crystals suitable for X-ray diffraction were obtained by

Table 2. Torsion angles around O–P–C–C in **2a** (racemate) and **2b** (homochiral)[a]

Complex:	Torsion angles (°): O–P–C–C (*transoid*)		
2a/**2b**	Ph(1)	Ph(2)	Ph(3)
2a	±106.8	±167.3	±146.5
2a	±118.9	±147.7	±151.3
2b	−140.2	−153.3	−171.5

[a] The two sets of data in the case of **2a** apparently indicate different conformational forms for the two TPPO molecules. The values for the two TPPO molecules are nearly identical in the case of **2b**. The *cisoid* torsion angles (not included) possess the opposite sign to the *transoid* ones. The following torsion angles were considered (atom numbering as in Fig. 2): $O_3P_1C_{21}C_{22}$, $O_3P_1C_{27}C_{28}$, $O_3P_1C_{33}C_{38}$, and $O_4P_2C_{39}C_{40}$, $O_4P_2C_{45}C_{46}$, $O_4P_2C_{51}C_{55}$ (**2a**); $O_3P_1C_{21}C_{26}$, $O_3P_1C_{27}C_{32}$, $O_3P_1C_{33}C_{34}$ (**2b**).

recrystallisation via the slow evaporation of a CH_2Cl_2 solution at 25°C. (A Bruker AXS SMART APEX CCD diffractometer employing 0.7107 Å radiation was used. The structure was solved by direct methods using SHELXS and refined with SHELXL using the WINGX suite.[5b])

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