

Design of new phosphonium salt host compounds

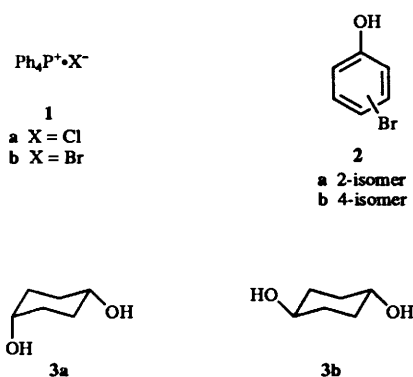
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A variety of phosphonium salts have been designed as new onium salt hosts and their ability to include phenols as guests has been studied. High inclusion ability was demonstrated by the salts together with high molecular recognition ability in the inclusion complex.

Earlier, we reported that some ammonium salts are effective hosts for phenols¹ and alcohols;² thus, the chiral salts *N*-benzylcinchonidium chloride includes (+)-1,1'-binaphthyl-2,2'-diol (+)-4 enantioselectively³ to form a 1:1 inclusion complex in which precise chiral recognition occurs.⁴ These results prompted us to design the corresponding phosphonium hosts and to investigate their ability to include phenols. The tetraphenylphosphonium halides 1 were found to be effective hosts for phenols with the occurrence of both molecular and chiral recognition. Isomers and enantiomers of the guest compounds were easily separated by this complexation procedure.

Tetraphenylphosphonium chloride 1a⁵ and bromide 1b,⁶ prepared according to reported procedures, are also commercially available. Inclusion complexation of 1 with phenol



derivatives was carried in an organic solvent. In a typical procedure, a solution of 1b (1.5 g, 3.6 mmol) and phenol (3.4 g, 3.6 mmol) in EtOH (2 cm³)–AcOEt (20 cm³) was kept at room temperature for 12 h to give the 1:1 inclusion complex as colourless prisms (4.5 g, 92%), mp 140–143 °C. Details for other similar complexes are summarised in Table 1. The host:guest ratios were determined by elemental analyses of the complex.† Upon complex formation, ν(OH) of the phenol guests shifted to lower frequencies probably as result of hydrogen bond formation between the halide ion of 1 and OH group of the guest; such behaviour has been established for the complex of (+)-4 and *N*-benzylcinchonidium chloride.‡⁴

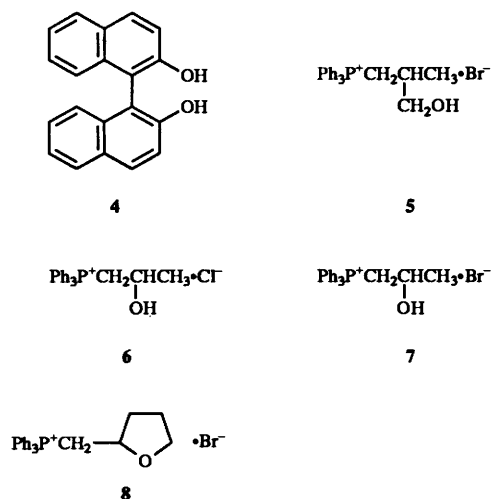
Although sterically bulky phenol derivatives such as 2,6- and 3,5-dichlorophenol, 2-phenylphenol and biphenyl-2,2'-diol

failed to form complexes with 1a or 1b, all the other phenols tested did (see Table 1).

The phosphonium salt host 1 shows efficient molecular recognition ability and this phenomenon can be used for the separation of isomers. In a typical example, a solution of 1b (1.5 g, 3.6 mmol) and a 1:1 mixture of 2-bromo- 2a and 4-bromo-phenol 2b (0.62 g, 3.6 mmol) in EtOH (2 cm³)–AcOEt (20 cm³) was kept at room temperature for 12 h to give a 2:1 inclusion complex of 1b and 2a as colourless prisms (1.4 g). Treatment of this with ether (50 cm³)–water (50 cm³) gave aqueous 1b and ethereal 2a. The latter was dried (MgSO₄) and evaporated to give 2a (>99% purity; 0.24 g, 77% yield). Unchanged 1b was recovered from the aqueous solution.

Since the host 1 also includes some alcohols selectively, their isomers too can be separated by selective inclusion with 1. A solution of 1b (1.0 g, 2.38 mmol) and a 1:1 mixture of *cis*- 3a and *trans*-cyclohexane-1,4-diol 3b (0.55 g, 4.77 mmol) in EtOH (5 cm³)–AcOEt (20 cm³) was kept at room temperature for 12 h to give a 1:1 inclusion complex of 1b and 3b as colourless prisms (0.73 g), mp 176–179 °C. Treatment of the complex with ether (50 cm³)–water (50 cm³) gave aqueous 1b and ethereal 3b; work-up of ethereal solution as above gave 3b (100% purity; 0.1 g, 36%).

In tandem with the above-described chiral recognition optical resolution also occurs. Thus, upon inclusion complexation with (–)-4, *rac*-(3-hydroxy-2-methylpropyl)triphenylphosphonium bromide (*rac*)-5 was efficiently resolved. Thus a solution of (–)-4 (0.5 g, 1.75 mmol) and (*rac*)-5 (1.45 g, 3.5 mmol) in EtOH (10 cm³) stored at room temperature for 12 h gave a 1:1 inclusion complex as colourless prisms (1.05 g, 86; mp 227–229 °C). This was treated with ether–water, and the resulting aqueous solution evaporated to give (–)-5 (88% ee; 0.61 g, 84%), [α]_D –0.94 (c 0.35, MeOH).§ Recrystallisation of the partially resolved (*rac*)-5



† Satisfactory elemental analyses were obtained for all new inclusion complexes.

‡ For example, ν(OH) of *o*-cresol at 3250 cm⁻¹ (neat) shifted to 3040 cm⁻¹ (Nujol) upon the formation of a 1:1 inclusion complex with 1b.

§ [α]_D Values recorded in units of 10⁻¹ deg cm² g⁻¹.

Table 1 Host: guest molar ratio^a and mps of inclusion complexes of **1** with phenol guest compounds

Phenol	Host			
	1a		1b	
	host: guest	mp (°C)	host: guest	mp (°C)
C ₆ H ₅ OH	1:1	169–170	1:1	140–143
2-MeC ₆ H ₄ OH	1:1	<i>b</i>	1:1	127–130
3-MeC ₆ H ₄ OH		<i>c</i>	1:1	114–118
4-MeC ₆ H ₄ OH	1:2	105–110	1:1	103–106
2,5-Me ₂ C ₆ H ₃ OH	2:1	<i>b</i>	2:1	<i>b</i>
2-ClC ₆ H ₄ OH		<i>c</i>	1:1	123–126
4-ClC ₆ H ₄ OH	1:2	94–96		<i>c</i>
2-BrC ₆ H ₄ OH	1:2	64–67	2:1	145–147
4-BrC ₆ H ₄ OH	1:1	102–103		<i>c</i>
2-PhC ₆ H ₄ OH		<i>c</i>		<i>c</i>
4-PhC ₆ H ₄ OH		<i>c</i>	2:1	182–185
1,1'-Biphenyl-2,2'-diol		<i>c</i>		<i>c</i>
1,1'-Biphenyl-4,4'-diol	2:1	200–202	2:1	196–198
1-Naphthol	1:1	88–89	1:1	108–111
2-Naphthol	2:1	<i>b</i>	2:1	<i>b</i>
Naphthalene-2,6-diol	2:1	242–245	2:1	238–239
Naphthalene-2,7-diol	2:1	242–243	2:1	234–236
Naphthalene-1,5-diol	2:1	237–240	2:1	237–238

^a Host: guest molar ratios were determined by elemental analysis. ^b Showed no clear mp. ^c Inclusion complex not formed.

from EtOH gave a product of 100% ee (0.23 g, 37%), $[\alpha]_D -1.68$ (*c* 0.35, MeOH). The optical purity of (–)-**5** was determined by comparison of the $[\alpha]_D$ value with that reported.⁷ Other phosphonium salts were similarly resolved. For example, 2-hydroxypropyl(triphenyl)phosphonium chloride (*rac*)-**6**, 2-hydroxybutyl(triphenyl)phosphonium bromide (*rac*)-**7** and tetrahydro-2-furylmethyl(triphenyl)phosphonium bromide (*rac*)-**8** were resolved by complexation with (–)-**4**, (–)-**6** {36% ee, 65% yield, $[\alpha]_D -22.8$ (*c* 0.1, MeOH)}, (–)-**7** {44% yield, $[\alpha]_D -12.3$ (*c* 1.0, MeOH)} and (+)-**8** {81% yield, $[\alpha]_D + 45.4$ (*c* 0.8, H₂O)}, respectively; the optical purity of (–)-**7** and (+)-**8** was not determined. Although optically active phosphonium halides are important as precursors of optically active Wittig reagents, preparation of the reagents is not easy.^{8–12}

In contrast, (*rac*)-**4** was resolved by complexation with (–)-**5** or (+)-**5**. Thus, a solution of (*rac*)-**4** (0.69 g, 2.4 mmol) and (+)-**5** (0.5 g, 1.2 mmol) in EtOH (10 cm³) was kept at room temperature for 12 h to give a 1:1 complex after three recrystallisations from EtOH as colourless prisms (0.47 g, 55%), mp 227–229 °C. Treatment of the complex with ether (50 cm³)-water (50 cm³) gave ethereal (+)-**4** and aqueous (+)-**5**. The former was dried (MgSO₄) and evaporated to give (+)-**4** (97% ee) as colourless prisms (0.19 g, 55%), whilst the latter gave unchanged (+)-**5** (0.28 g, 55% yield). The optical purity of (+)-**4c** was determined by HPLC on the chiral solid phase Chiralpak AS[†] using hexane–EtOH (95:5) as eluent.

This work suggests that there is considerable potential

for the design of a variety of new phosphonium salt host compounds.

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[†] Chiralpak AS is available from Daicel Chemical Industries, Ltd., Himeji, Japan.