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Optically Active 4,4',6,6'-Tetrachloro-2,2'-bis(hydroxydiphenylmethyl)-biphenyl As a Host for Optical Resolution and a Chiral Shift Reagent

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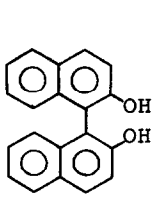
Abstract: The title biphenyl derivative was found to be useful as a host for optical resolution and as a chiral shift reagent for the determination of the optical purity and the absolute configuration of a wide variety of chiral compounds.

The axially asymmetric compounds such as 2,2'-dihydroxy-1,1'-binaphthyl (**1**)[1] and 10,10'-dihydroxy-9,9'-biphenanthryl (**2**)[1] have been known to be useful as chiral hosts for optical resolution and as chiral shift reagents for the determination of the optical purity and the absolute configuration of a wide variety of chiral compounds.[2] As a much simpler version host, we designed the title (**3**). The hydroxydiphenylmethyl group of **3** is important for inclusion of guest compounds such as optically active 1,6-bis(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**4**),[3] trans-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxacyclopentane (**5a**),[4] and its derivatives (**5b** and **5c**).[5] The hydroxyl and phenyl groups of the hydroxydiphenylmethyl moiety act to form hydrogen bonds with the guest and to surround the guest in the inclusion crystal, respectively.[6] The design of **3** is also based on the ability to encapsulate a guest molecule with the three phenyl groups of the hydroxytriphenylmethyl moiety of **3**.

4,4',6,6'-Tetrachlorobiphenyl-2,2'-dicarboxylic acid (**6a**) was resolved by a diastereoisomeric method.[7] Reaction of the Grignard PhMgBr and the (+)- and (-)-dimethyl esters of **6a** (**6b**) gave **3a** (mp 231-233 °C, $[\alpha]_D$ +110 (*c* 0.1 in $CHCl_3$)) and **3b** (mp 231-233 °C, $[\alpha]_D$ -110 (*c* 0.1 in $CHCl_3$)) respectively. Their optical purities were determined to be 100% by HPLC using a column containing an optically active solid phase, Chiralcel OC.[8] The hosts **3a** and **3b** showed a good inclusion ability for a wide variety of organic compounds such as methanol (1:2), ethanol (1:2), acetone (1:1), cyclopentanone (1:1), γ-butyrolactone (1:2), benzaldehyde (1:1), THF (1:1), dioxane (1:1), CCl_4 (1:1), DMF (1:1), DMSO (1:2), and pyridine (1:1), and formed inclusion compounds of the host-guest ratio shown in the parentheses.

Enantioselective inclusion by **3** was also observed. For example, when a solution of **3a** (1.5 g, 2.29 mmol) and 3-methyl-2-pyrrolidone (**7**) (0.45 g, 2.56 mmol) in benzene-hexane (1:1, 6 ml) was kept at room temperature for 24 h, a 1:1 inclusion complex of **3a** and **7b** was obtained as colorless prisms. Five recrystallisations of the crude crystals gave pure material (1.12 g, mp 213-214 °C, $[\alpha]_D$ +87.7 (*c* 0.1 in $CHCl_3$)), which upon heating in vacuo gave **7b** of 100% ee (0.14 g, 62%, $[\alpha]_D$ -60.6 (*c* 0.3 in benzene)). From the filtrate left after the separation of the crude inclusion complex of **3a** and **7b**, **7a** of 47% ee was obtained (0.25 g). Complexation of the crude **7a** with **3b** gave their 1:1 inclusion complex. Treatment of the complex as above finally gave **7a** of 100% ee (0.1 g, 43%, $[\alpha]_D$ +60.6 (*c* 0.3 in benzene)).

Enantioselective complexation between the host **3** and various guest compounds occurred even in solution allowing **3** to be used as a chiral shift reagent. The relationship between the chemical shift values and the host:guest ratio is shown in Table 1. In all cases, the signal of the italicised proton is split by addition of **3**, and the splitting is large enough to determine the enantiomeric purity of the guest compounds. Host **3** is effective for the guests containing 4B, 5B, and 6B elements of the periodical table in chiral compounds such as amines, alcohols, amine N-oxides, phosphinates, phosphine oxides, arsine oxides, sulfoxides, sulfoximines, and selenoxides. Previously we had reported that optically active **1** and **4** are effective as chiral shift reagents for the compounds containing 4B and 6B, and 4B and 5B elements, respectively.[2] Reagent **3** is effective for both types of compound, however.



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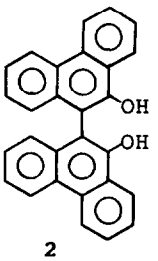

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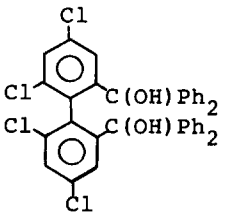

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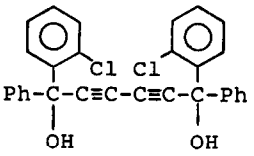
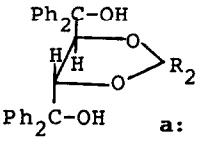


4

a: (+)-form

b: (-)-form

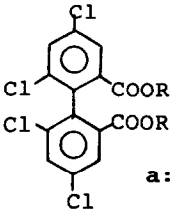


5

a: R_2=Me_2

b: R_2= 

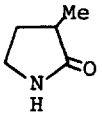
c: R_2= 



6

a: R=H

b: R=Me

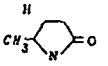
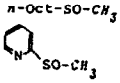


7

a: (+)-form

b: (-)-form

Table 1. Relationship Between Chemical Shift Value and Molar Ratio of 3 to the Guest Compound[a]

Entry	Guest compound	Chemical shift (ppm) Molar ratio of 3 to the guest 0	1	2
1	PhCH(NH$_2$)-CH$_3$	1 377	1 234 1 251	1 065 1 096
2		1 038	0 979 1 000	0 938 0 983
3		1 196	1 081 1 100	0 958 1 017
4		1 220	1 033 1 058	0 956 0 998
5	Ph-C(OH)H-CH$_3$	4 860	4 779	4 635 4 676
6	CH$_3$-C(OH)H-C≡N	4 605	4 295 4 441	
7	i-Pr-C(CH$_3$)(OH)-C≡N	1 552	1 467 1 483	1 407 1 440
8	n-Oct-SO-CH$_3$	2 550	2 227 2 280	
9		2 853	2 623 2 667	
10	Ph-SO-CH$_3$ (NH)	2 703	2 444 2 500	
11	p-Tol-SaO-CH$_3$	2 587	2 167 2 283	
12	p-Tol-NO-CH$_3$ (CH$_2$CH$_3$)	3 483	2 910 2 943	2 743 2 813
13	p-Tol-PO-OCH$_3$ (CH$_3$)	1 643 3 588	1 414 1 432 3 430 3 450	1 313 1 336 3 335 3 365
14	Ph-PO-C≡CH (CH$_3$)	1 928	1 610 1 661	
15	Ph-AsO-CH$_3$	1 807	1 433 1 457	1 284 1 329

[a]All the spectra were measured in $CDCl_3$ at a concentration of guest compound 0.02 g in 1 ml solvent.

It was also found that 3 is effective for the determination of the absolute configuration of sulfoxides. The italicised proton of the (R)-sulfoxides[2] of entries 1-4 in Table 2 appeared at relatively higher magnetic field in the presence of 3. By this method, previously unknown configurations for (-)-sulfoxides of entries 5-8 were assigned as (R) (Table 2). Although 1 and 4 are also useful for the determination of absolute configuration,[2] 3 is very effective for sulfoxides, about one fifth~one tenth molar the amount compared to 1 or 4 being enough.

Table 2. Chemical Shift Values of the Italicised Protons of Guest Compounds in the Absence and Presence of **3b** and Assignment of Absolute Configuration to the Shifted Signal to Relatively Higher Magnetic Field[a)]

Entry	Guest compound	Chemical shift δ/ppm: Molar ratio of **3b** to the guest 0	Chemical shift δ/ppm: Molar ratio of **3b** to the guest 1	Absolute configuration
1	Ph-SO-*CH*$_3$	2.717	2.446 2.498	(R)-(+)
2	*m*-Tol-SO-*CH*$_3$	2.717	2.375 2.480	(R)-(+)
3	*p*-Tol-SO-*CH*$_3$	2.700	2.513 2.561	(R)-(+)
4	*n*-Bu-SO-*CH*$_3$	2.540	2.217 2.297	(R)-(-)
5	*n*-Am-SO-*CH*$_3$	2.537	2.300 2 388	(R)-(-)
6	*n*-Hex-SO-*CH*$_3$	2.517	2.286 2.334	(R)-(-)
7	*n*-Hep-SO-*CH*$_3$	2.537	2.318 2.358	(R)-(-)
8	*n*-Oct-SO-*CH*$_3$	2.550	2.227 2.280	(R)-(-)

a) All the spectra were measured at a concentration of guest compound 0.02 g in 1 ml $CDCl_3$ When the signal is multiplet,chemical shift value at a center of the signal is indicated.

References and Notes

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