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New Chiral Shift Reagents, Optically Active 2,2'-Dihydroxy-1,1'-binaphthyl and 1,6-Di(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol

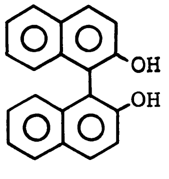
Fumio TODA,* Koji MORI, Jyōji OKADA,
Manabu NODE,† Akichika ITOH,† Kyoko OOMINE,† and Kaoru FUJI*†
Department of Industrial Chemistry, Faculty of Engineering,
Ehime University, Matsuyama 790
†Institute for Chemical Research, Kyoto University, Uji, Kyoto 611

The title compounds were found to be useful as a chiral shift reagent in ^1H NMR spectroscopy to determine enantiomeric purity of amines, alcohols, sulfoxides, selenoxides, phosphine oxides, phosphinates, and arsenoxides. It is also reported that the induced chemical shift difference increases when the title compound is used together with the typical chiral shift reagent, Eu(hfc)$_3$.

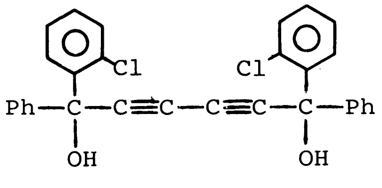
Previously, we reported that the optically active host compounds, 2,2'-dihydroxy-1,1'-binaphthyl (**1**) and 1,6-di(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**2**), recognize the chirality of a wide variety of guest compounds in the host-guest complex, and the host compounds can be used for an efficient optical resolution of a guest compound by complex formation.[1)]

Recently, we have found that the complex formation and the chiral recognition occur not only in the solid state but also in solution. The chiral recognition in solution was detected by ^1H NMR spectroscopy. Finally we found that **1** and **2** are useful as chiral shift reagents for determining the enantiomeric purity of a wide variety of organic compounds. It was also disclosed that the induced chemical shift difference increases when **1** or **2** is used together with the typical chiral shift reagent, Eu(hfc)$_3$ compared to the case when the host compounds or Eu(hfc)$_3$ is used separately.

The relationship between chemical shift values and host:guest molar ratio is shown in Tables 1 and 2. In all cases except the entry 8 in Table 1, signal is splitted by addition of one or two molar amounts of the shift reagent, and the splitting is large enough to determine enantiomeric purity of the guest compounds. Even in the case of the entry 8 in Table 1, a splitting occurs by addition of three molar amounts of **1a** (Table 1). Of course, **1b** and **2b** can also be used instead of **1a** and **1b**, respectively. The host **1** is effective to the guest compounds


1

a: (*S*)-(-)-form
b: (*R*)-(+)-form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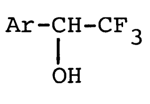
a: (*R*,*R*)-(-)-form
b: (*S*,*S*)-(+)-form


$$\underset{\displaystyle OH}{Ar\text{-}CH\text{-}CF_3}$$
3

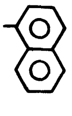
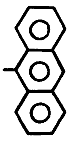
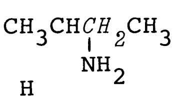
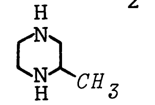
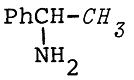
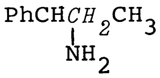
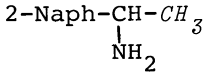
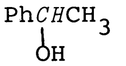
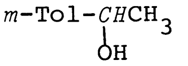
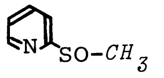
a: Ar=Ph; **b**: Ar= ; **c**: Ar= 

Table 1. Relationship Between Chemical Shift Value[a] and Molar Ratio of the Host Compound 1a to the Guest Compound[2]

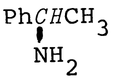
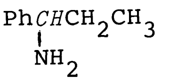
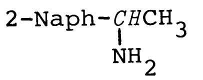
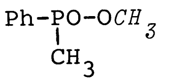
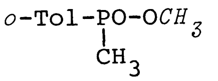
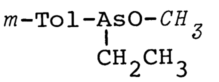
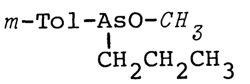
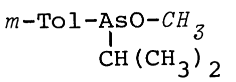
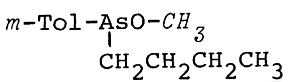
Entry	Guest compound	Chemical shift δ (ppm) Molar ratio of the host to the guest		
		0	1	2
1	 $\mathrm{CH_3}\underset{\mathrm{NH_2}}{\mathrm{CH}}\mathit{CH}_2\mathrm{CH_3}$	2.806	2.317 2.367	
2		0.958	0.640 0.683	
3	 $\mathrm{Ph}\underset{\mathrm{NH_2}}{\mathrm{CH}}\text{-}\mathit{CH}_3$	1.377	1.124 1.167	
4	 $\mathrm{Ph}\underset{\mathrm{NH_2}}{\mathrm{CH}}\mathit{CH}_2\mathrm{CH_3}$	1.833	1.467 1.483	
5	 $\text{2-Naph-}\underset{\mathrm{NH_2}}{\mathrm{CH}}\text{-}\mathit{CH}_3$	1.450	1.235 1.267	
6	 $\mathrm{Ph}\underset{\mathrm{OH}}{\mathit{CH}}\mathrm{CH_3}$	4.860	4.783	4.680 4.720
7	 $m\text{-Tol-}\underset{\mathrm{OH}}{\mathit{CH}}\mathrm{CH_3}$	4.747	4.700	4.627 4.663
8	Bu-SO-CH_3	2.367	2.367	2.344[b]
9	Am-SO-CH_3	2.517	2.500	2.413 2.433
10	Hex-SO-CH_3	2.517	2.483	2.417 2.433
11	Hep-SO-CH_3	2.583	2.500	2.453 2.470
12	Ph-SO-CH_3	2.717	2.654 2.667	
13	*m*-Tol-SO-CH_3	2.717	2.667	2.616 2.633
14	*p*-Tol-SO-CH_3	2.700	2.667 2.680	
15		2.883	2.673 2.713	
16	Ph-SeO-CH_3	2.627	2.463 2.483	
17	*o*-Tol-SeO-CH_3	2.567	2.433 2.467	
18	*m*-Tol-SeO-CH_3	2.600	2.439 2.467	

a) Of protons italicized. b) The signal is splitted into two signals at δ 2.315 and 2.333 ppm when the molar ratio is increased to 3.

containing group 6B elements of the periodical table such as alcohols, sulfoxides, and selenoxides. Contrarily, the host 2 is effective to the guest compounds containing group 5B elements such as phosphinates and arsenoxides. Both the host compounds are effective for amines.

The host compounds 1 and 2 probably work in the similar manner to the known shift reagents, 1-phenyl- (3a),[3-5] 1-(1-naphthyl)- (3b),[3-5] and 1-(9-anthryl)-2,2,2-trifluoroethanol (3c).[3-5] For example, methyl *m*-tolyl sulfoxide would form a complex with 1 in such a way that the methyl signal is shifted to a higher

Table 2. Relationship Between Chemical Shift Value[a] and Molar Ratio of the Host Compound **2a** to the Guest Compound[2]

Entry	Guest compound	Chemical shift δ (ppm) Molar ratio of the host to the guest 0	 1	 2
1	 $\mathrm{Ph}\underset{\mathrm{NH_2}}{\underset{\vert}{\mathit{CH}}}\mathrm{CH_3}$	4.117	3.801 3.843	
2	 $\mathrm{Ph}\underset{\mathrm{NH_2}}{\underset{\vert}{\mathit{CH}}}\mathrm{CH_2CH_3}$	3.783	3.529 3.567	
3	 $\text{2-Naph-}\underset{\mathrm{NH_2}}{\underset{\vert}{\mathit{CH}}}\mathrm{CH_3}$	4.217	4.040 4.067	
4	 $\mathrm{Ph{-}}\underset{\mathrm{CH_3}}{\underset{\vert}{\mathrm{P}}}\mathrm{O{-}O}\mathit{CH_3}$	3.909	3.671	2.970 3.154
5	 $o\text{-Tol-}\underset{\mathrm{CH_3}}{\underset{\vert}{\mathrm{P}}}\mathrm{O{-}O}\mathit{CH_3}$	3.909	3.600	3.397 3.597
6	 $m\text{-Tol-}\underset{\mathrm{CH_2CH_3}}{\underset{\vert}{\mathrm{As}}}\mathrm{O{-}}\mathit{CH_3}$	2.300	1.667	1.440 1.493
7	 $m\text{-Tol-}\underset{\mathrm{CH_2CH_2CH_3}}{\underset{\vert}{\mathrm{As}}}\mathrm{O{-}}\mathit{CH_3}$	2.167	1.583 1.600	1.408 1.440
8	 $m\text{-Tol-}\underset{\mathrm{CH(CH_3)_2}}{\underset{\vert}{\mathrm{As}}}\mathrm{O{-}}\mathit{CH_3}$	2.117	1.583 1.600	1.450 1.493
9	 $m\text{-Tol-}\underset{\mathrm{CH_2CH_2CH_2CH_3}}{\underset{\vert}{\mathrm{As}}}\mathrm{O{-}}\mathit{CH_3}$	2.150	1.500 1.516	1.427 1.467

a) Of protons italicized.

magnetic field by a shielding effect with the naphthyl group of **1** (Fig. 1). X-Ray crystal structural study of a 1:1 complex of (−)-methyl *m*-tolyl sulfoxide and **1a** shows that both the groups are in positions for an efficient shielding.[6] Nevertheless, the host-guest complex formation in solution does not always lead to the formation of crystalline complex. For example, the guest compounds of entries 12, 13, and 16-18[1] in Table 1 and entries 4-5,[7] 6,[8] and 8[8] in Table 2 form crystalline complex with **1**, and these are effectively resolved. The guest compounds of entries 8-11[8] in Table 1 form crystalline complex with **2**, and these are also effectively resolved. But, other guest compounds in Tables 1 and 2 do not form crystalline complex with **1** and **2**.

Induced chemical shift difference due to Eu(hfc)$_3$ increases on addition of **1** or **2** in some cases. Thus, the methyl signal of ethyl phenyl selenoxide (**4**), poorly separated (1.483 and 1.450 ppm) in the presence of 0.25 mol equivalent of Eu(hfc)$_3$, splitted into two triplets centered at 1.367 and 1.084 ppm on addition of 1 mol equivalent of **1a** (Fig. 2). Similarly, the methyl doublet of ethynylmethylphenylphosphine oxide (**5**) at 2.467 and 2.447 ppm moved to 2.284 and 2.234 ppm, respectively, on addition of **2a** as shown in Fig. 3. However, the methyl signals of **4** and **5** are not splitted in the presence of **1a** and **2a** only, respectively. Though the reason for the additive effect remains to be clarified, it is useful for determination of enantiomeric purity of optically active compounds. A similar additive effect of an achiral europium salt, $Eu(fod)_3$ to the chiral shift reagent 3c in a measurement of enantiomeric purity of γ-butyrolactones has been reported.5)

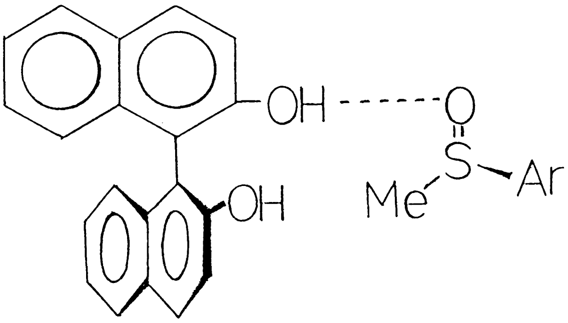


Fig. 1. Complex formation and shielding effect

Fig. 2. Methyl signal of $Ph-SeO-CH_2CH_3$ (4) in the presence of $Eu(hfc)_3$ (0.25 mol equiv.) (A), and of $Eu(hfc)_3$ (0.25 mol equiv.) and 1a (1 mol equiv.) (B).

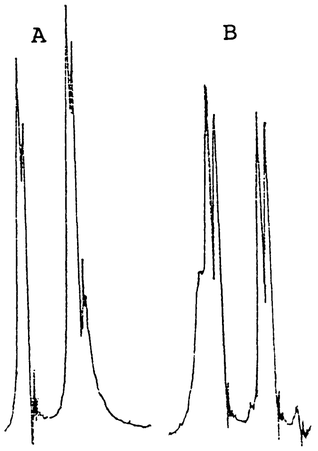


Fig. 3. Methyl signal of Ph-PO(Me)-C≡CH (5) in the presence of $Eu(hfc)_3$ (0.25 mol equiv.) (A), and of $Eu(hfc)_3$ (0.25 mol equiv.) and 2a (1 mol equiv.) (B).

References

1) F. Toda, Top. Curr. Chem., 140, 43 (1987).
2) All the ^1H NMR spectra were measured by JEOL JNM-PMX 60 Spectrometer in $CDCl_3$ at the concentration of guest compound 0.02 g in 1 ml solvent. When a signal is multiplet, chemical shift value at the center of the signal is indicated.
3) W. H. Pirkle and M. S. Hoekstra, J. Am. Chem. Soc., 98, 1832 (1976).
4) W. H. Pirkle, D. L. Sikkenga, and M. S. Pavlin, J. Org. Chem., 42, 384 (1977).
5) W. H. Pirkle and D. L. Sikkenga, J. Org. Chem., 42, 1370 (1977).
6) F. Toda, K. Tanaka, and T. C. W. Mak, Chem. Lett., 1984, 2085.
7) M. Kaftory, K. Mori, and F. Toda, J. Org. Chem. in press.
8) F. Toda and K. Mori, unpublished data.

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