A Determination Method of Absolute Configuration

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Synopsis. A determination method of absolute configuration of sulfoxides, amines, and aminoalcohols by measuring their ^{1}H NMR spectra in the presence of optically active 2,2′-dihydroxy-1,1′-binaphthyl and 1,6-di(*o*-chlorophenyl)-1,6-diphenyl-2,4-hexadiyne-1,6-diol, was reported.

There are mainly three determination methods of absolute configuration of chiral compounds, CD- and X-ray analyses and chemical conversion to a configurationally known compound. However, each method has own problem. We report a simple method of determining the absolute configuration by a combination of host–guest complexation and ^{1}H NMR spectra measurement. Previously, it was reported that optically active 2,2′-dihydroxy-1,1′-binaphthyl (**1**) and 1,6-di(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**2**) form complex with a wide variety of organic compounds not only in the solid state[1] but also in solution,[2] and these host compounds can be used as chiral shift reagents.[2]

We recently found that the direction and magnitude of shifts of the proton signals of the complex depend on the difference of absolute configuration of the host and guest compounds, and that the phenomena are applicable to determining the absolute configuration of the guest compounds. Although a similar determination method of the absolute configuration of sulfinate esters[3] and γ-lactones[4,5] by using optically active 1-phenyl- (**3a**), 1-(1-naphthyl)- (**3b**), and 1-(9-anthryl)-2,2,2-trifluoroethanol (**3c**) has been known, application of this method to sulfoxides, amines, and aminoalcohols has not been reported.

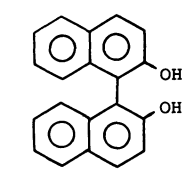
Experimental

General. All the ^{1}H NMR spectra were measured in $CDCl_3$ by JEOL-PMX 60 Spectrometer. All the host (**1** and **2**) and the guest compounds (**4**—**18**) were prepared according to the reported method in the literature cited.[1]

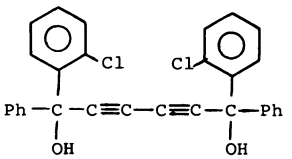
Results and Discussion

For example, the methyl signal (δ 2.717) of racemic methyl phenyl sulfoxide (**4**) is split into two signals at δ 2.654 and 2.667 in the presence of an equimolar amount of (*S*)-(−)-**1** (**1a**) (Table 1). The optically pure (*R*)-(+)- and (*S*)-(−)-**4**[6] show the former and the latter signals, respectively, under the same conditions. In the case of other alkyl aryl sulfoxides, **6**[7] and **7**,[8] the methyl signals of (*S*)-(−)-enantiomers are also in higher field than those of (*R*)-(+)-ones (Table 1). (*S*)-(+)-Enantiomer of butyl methyl sulfoxide (**7**)[9] showed its methyl signal at higher field than did (*R*)-(−)-one. Although the configuration of other dialkyl sulfoxides **8**—**10** has not been determined, their (+)-enantiomers which show the methyl signal at higher field probably have (*S*)-configuration. This assignment is probably correct because (+)-enantiomers of many alkyl methyl sulfoxides such as ethyl methyl,[9] methyl propyl, isopropyl methyl,[10,11] isobutyl methyl,[11] and *t*-butyl methyl sulfoxides[9] have been reported to have (*S*)-configuration. In the case of dialkyl sulfoxides, however, more than two molar amounts of **1a** are necessary for a splitting of the methyl signal (Table 1).

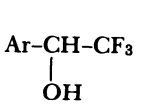
In the case of amines, **11**,[12] **12**,[13] **13**,[14] and **14**, the methyl signals of their (*R*)-enantiomers appeared at higher field than did those of (*S*)-ones in the presence of **1a** (Table 1). However, the methine signal of **15**[15] or **16** appeared at higher field when the configuration is (*S*). Although the methine signals of **12** (δ 4.117) and **13** (4.217) were not split by **1a**, these were split to δ 3.801 and 3.843, and 4.040 and 4.067, respectively, in the presence of (*R*,*R*)-(−)-**2** (**2a**), and the signal of (*S*)-enantiomers appeared at higher field. Methyl signals of aminoalcohols **17**[16] and **18**[17] were also split by **1a**, and those of (*S*)-enantiomers appeared at higher field (Table 1). These data clearly show again the presence of a correlation between the manner of shift in



1
a: (*S*)-(−)-enantiomer
b: (*R*)-(+)-enantiomer



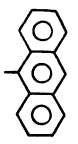
2
a: (*R*,*R*)-(−)-enantiomer
b: (*S*,*S*)-(+)-enantiomer

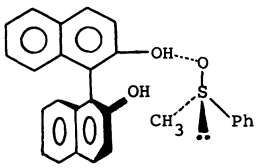


3

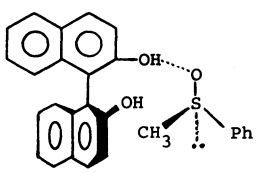
a: Ar=Ph
b: Ar=

c: Ar=





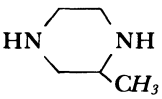
1a·(*S*)-(−)-**4**
19



1a·(*R*)-(+)-**4**
20

Fig. 1. Shielding effect in the complex.

Table 1. Chemical Shift Values of the Italicized Protons of Guest Compounds in the Absence and Presence of **1a**, and Assignment of Absolute Configuration to the Shifted Signal to Relatively Higher Magnetic Field[a)]

Guest compound	Chemical shift δ/ppm			Absolute configuration
	Molar ratio of **1a** to the guest			
	0	0.5—3		
Ph-SO-C*H*$_3$ (**4**)	2.717	1	2.654 2.667	(*S*)-(−)
m-Tol-SO-C*H*$_3$ (**5**)	2.717	2	2.616 2.633	(*S*)-(−)
p-Tol-SO-C*H*$_3$ (**6**)	2.700	1	2.667 2.680	(*S*)-(−)
Bu^n-SO-C*H*$_3$ (**7**)	2.367	3	2.315 2.333	(*S*)-(+)
Am^n-SO-C*H*$_3$ (**8**)	2.517	2	2.413 2.433	(*S*)-(+)
Hex^n-SO-C*H*$_3$ (**9**)	2.517	2	2.417 2.433	(*S*)-(+)
Hep^n-SO-C*H*$_3$ (**10**)	2.583	2	2.453 2.470	(*S*)-(+)
 (**11**)	0.958	1	0.640 0.683	(*R*)-(−)
Ph-CH(NH$_2$)-C*H*$_3$ (**12**)	1.377	1	1.124 1.167	(*R*)-(+)
2-Naph-CH(NH$_2$)-C*H*$_3$ (**13**)	1.450	1	1.235 1.267	(*R*)-(+)
C*H*$_3$-CH(NH$_2$)-COOCH$_3$ (**14**)	1.333	0.5	1.170 1.200	(*R*)-(−)
CH$_3$CH$_2$-C*H*(NH$_2$)-CH$_3$ (**15**)	2.806	1	2.317 2.367	(*S*)-(+)
(CH$_3$)$_2$CHCH$_2$-C*H*(NH$_2$)-COOCH$_3$ (**16**)	3.500	0.5	3.250 3.317	(*S*)-(+)
C*H*$_3$-CH(OH)-CH$_2$-NH$_2$ (**17**)	1.150	0.5	0.900 0.917	(*S*)-(+)
HO-CH$_2$-CH(NH$_2$)-CH(C*H*$_3$)$_2$ (**18**)	0.917	0.5	0.583 0.665	(*S*)-(+)

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.

^{1}H NMR spectra and absolute configuration. Using the relation, absolute configuration of amines and aminoalcohols can be determined.

Of course, the two signals at higher and lower fields take turn when **1b** and **2b** are used instead of **1a** and **2a**, respectively.

The regular correlation between the configuration and the manner of shift of signal is probably due to the shielding effect in the complex of the components (Fig. 1). For example, **1a** forms complexes with (*S*)-**4** (**19**) and with (*R*)-**4** (**20**). In **19**, the methyl is shielded by the naphthyl group of **1a** and its signal appears at higher field than that of **20** (Fig. 1).

In all complexes, hydrogen bond may play an important role as is shown in Fig. 1. Since amines and aminoalcohols form relatively stronger hydrogen bond with **1a** than do dialkyl sulfoxide, smaller amount of **1a** is probably enough for the splitting of the former's signal. Nevertheless, the complex formation in solution does not always support the formation of crystalline inclusion complex. For example, **4**, **5**, and **7** form crystalline complex with **1**, and these are effectively resolved.[1)] However, **6**, **8**, **9**, and **10** do not form complex with **1**. Contrarily, **7**—**10** form complex with **2** and these are resolved.[1)] Although **11** forms complex with **2** and is efficiently resolved,[18)] **12**—**18** do not from comlex with **2**. Nevertheless, **17** and **18** form complex with **1** and are resolved.[19)]

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