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CHIRAL t-BUTYLPHENYLPHOSPHINOTHIOIC ACID: A NEW NMR SOLVATING AGENT FOR DETERMINATION OF ENANTIOMERIC EXCESSES OF SULFOXIDES

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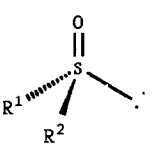
Abstract: *(-)-(S)-t-Butylphenylphosphinothioic acid forms with dialkyl and aralkyl sulfoxides diastereomeric dynamic systems the ^1H NMR spectra of which show typical anisochronism of the diastereotopic S-alkyl groups. The magnetic nonequivalence observed even for δ protons, is great enough to determine the e.e. values of sulfoxides having relatively long alkyl chains (e.g.* n*-butyl)*

Chiral sulfoxides play key role in the stereochemistry of organosulfur compounds[1] and asymmetric synthesis[2]. Therefore, there is a permanent interest in elaboration of convenient methods of their synthesis[3] as well as in determination of their enantiomeric purity. Among many methods applied for determination of the enantiomeric excess values of chiral sulfoxides, the NMR technique based on the nonequivalence of enantiomers induced by chiral solvating agents (CSA) or chiral shift reagents (CLSR) has found a widest application. However, this general method can be used only if the spectral patterns of the enantiotopic nuclei are simple and the NMR spectra of the sulfoxide diastereomeric dynamic systems show clear-cut differences. For these reasons, the best results have been obtained with structurally simple sulfoxides such as methyl aryl sulfoxides. Therefore, in connection with our current interest[4] in the synthesis of chiral sulfoxides we were searching for a new chiral solvating agent which would allow to determine e.e. of various sulfoxides **1**, especially those containing longer aliphatic substituents at sulfur. Here



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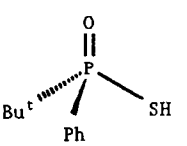

(-)-(S)-**2**

we wish to report that (-)-(S)-*t*-butylphenylphosphinothioic acid **2** can advantageously be used for such purposes. Both enantiomers of this acid may be easily obtained by the

classical resolution of the racemic **2**[5]. It is interesting to note that chiral **2** has already been applied as a solvating agent for phosphoryl compounds[6].

The standard conditions for enantiomer analysis are the following: the sulfoxide **1** is dissolved in C_6D_6, one or two equivalents of the acid (-)-(S)-**2** are added and ^1H NMR (300 Hz) spectrum is recorded. Selected results are listed in Table 1 and illustrative

Table 1. Enantiomeric excess of sulfoxides 1, $R^1S(O)R^2$, measured by ^1H NMR with (-)-(S)-*t*-butylphenylphosphinothioic acid 2 as a chiral solvating agent.

No	Sulfoxide			Chemical shift			Δδ	e.e.
	R^1	R^2	$[\alpha]_{589}$	δ[ppm] [a]	δ[ppm] [b]		[ppm]	[%]
1a	CH_3	$CH_2CH_2CH_2\underline{CH_3}$	-36.0 [c]	0.948	0.853	0.903	0.050	19.4
1a	$\underline{CH_3}$	$CH_2CH_2CH_2CH_3$	-36.0 [c]	2.080	2.228	2.306	0.078	24.7
1b	$pCH_3OC_6H_4$	$CH_2CH_2CH_2\underline{CH_3}$	-31.7 [d]	0.920	0.881	0.888	0.007	
1b	$p\underline{CH_3}OC_6H_4$	$CH_2CH_2CH_2CH_3$	-31.7 [d]	3.465	3.425	3.429	0.004	
1c	$(CH_3)_3C$	$CH_2CH_2CH_2\underline{CH_3}$	(-)	1.185	0.723	0.766	0.043	
1d	$(CH_3)_3C$	$CH_2\underline{CH_3}$	+23.6 [c]	1.354	1.254	1.300	0.046	20.0
1d	$(\underline{CH_3})_3C$	CH_2CH_3	+23.6 [c]	1.640	1.041	1.021	0.020	20.0
1e	$(CH_3)_3C$	$\underline{CH_3}$	-4.1 [c]	1.714	1.867	1.881	0.014	25.2
1f	C_6H_5	$\underline{CH_3}$	+43.1 [d]	2.279	2.426	2.429	0.003	28.5
1g	C_6H_5	$CH_2CH_2O\underline{CH_3}$	0.0	2.979	2.925	2.955	0.030	
1h	$pCH_3C_6H_4$	$CH_2\underline{CH_3}$	0.0	0.8707	0.701	0.710	0.009	

[a] in a free sulfoxide [b] in a complex with (-)-(S)-2 [c] in ethanol [d] in acetone.

spectra are shown in Figure 1. The experimental results quoted in Table 1 clearly demonstrate the most interesting feature of the acid **2** as a CSA, namely, its ability to induce magnetic nonequivalence of the enantiotopic β and δ methyl protons of an alkyl chain in sulfoxides **1**. For example, the peak separations (expressed in ppm) of the δ methyl protons of the *n*-butyl group in sulfoxides **1a**, **1b**, **1c** and **1g** are 0.05, 0.007, 0.043, and 0.03, respectively. These values are much higher than those observed for the α-methyl sulfinyl protons in the presence of (-)-(R)-N-(3,5-dinitrobenzoyl)(α-phenylethyl)amine ($\Delta\delta < 0.025$ ppm)[7a], 1-trifluoromethyl-α-aryl ethanols ($\Delta\delta < 0.03$ ppm)[7b] or 2,2'-dihydroxy-1,1'-binaphthyl ($\Delta\delta < 0.016$ ppm)[7c]. It should also be noted that the above mentioned CSAs fail to induce nonequivalence of the δ protons in sulfoxides **1a-c**

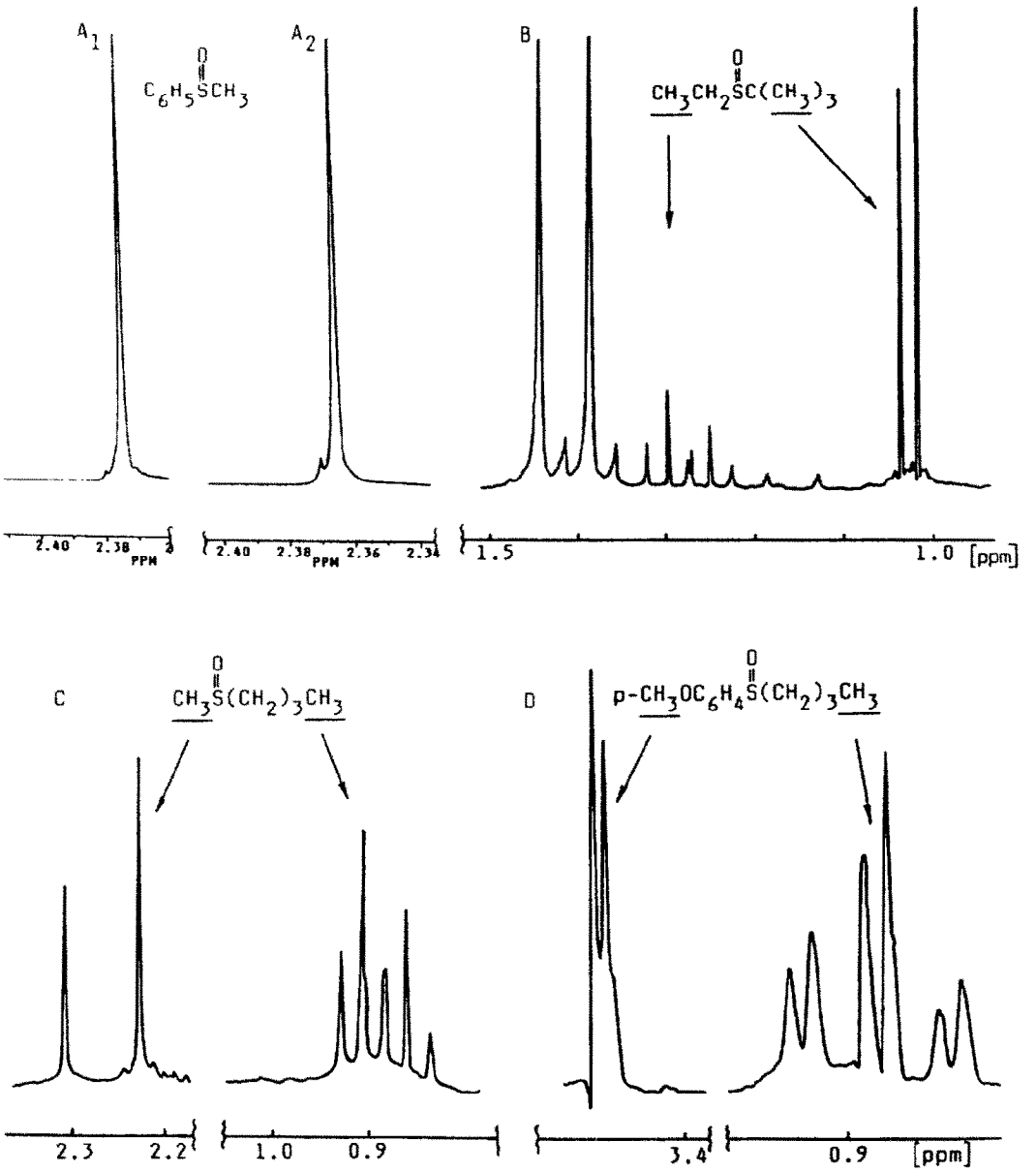

Figure 1. ^{1}H-NMR spectra of the complexes of (-)-(S)-**2** with sulfoxides **1**: A_1: **1f**, $[\alpha]_D$=+154.5 ; A_2:**1f** $[\alpha]_D$=+154.5 + 1.25% of (±)-**1f**; B: **1d** $[\alpha]_D$=+23.6 C: **1a** $[\alpha]_D$=-36.0 ; D: **1b** $[\alpha]_D$=-31.7 .

and **1g**. On the other hand, the magnetic nonequivalence, $\Delta\delta$, of the α-methyl sulfinyl protons induced by **2** is larger than those observed with other CSAs. For instance, whereas the $\Delta\delta$ value for the α-methyl protons in the complex of **1a** with Kagan's reagent[7a] is 0.0097 ppm[7a], it is 8 times greater when (-)-(S)-**2** is used ($\Delta\delta$=0.078 ppm). The usefulness of **2** as a CSA is furthermore illustrated by the determination of e.e. of *t*-butyl ethyl sulfoxide **1d**. In contrast to the α methylene protons of **1d** which are not affected by formation of the diastereomeric complexes with (-)-(S)-**2**, the β methyl protons of the ethyl grup show typical nonequivalence ($\Delta\delta$=0.009 ppm), thus providing a basis for the e.e. measurements.

A very high detection limit of the present method is illustrated by comparison of the spectrum of a 1:1 mixture of **1f** $[\alpha]_{589}$=+154.5 ($CHCl_3$) and **2** with that of the same sample to which 1,25% of the racemic **1f** is added (Figure 1). Moreover, the first spectrum clearly indicates that the value $[\alpha]_{589}$=+145 ($CHCl_3$), commonly accepted for the sulfoxide **1f** enantiomers, is too low. It should also be noted that, for methyl n-butyl sulfoxide **1a** the value $[\alpha]_{589}$=-145.7 (EtOH) calculated according to the data from Table 1 exceeds substantially the value $[\alpha]_{589}$=~110 (EtOH) already ascribed to the pure enantiomers of **1a**.

In our opinion the relatively big differences in values of specific rotation given for various sulfoxides, especially for aliphatic ones, are mainly due to contamination with solvent which is very difficult to remove.

The spectral nonequivalence observed for the sulfoxide **1** enantiomers in the presence of(-)-(S)-**2** is undoubtedly due to the formation of hydrogen bonded complexes of the type $R_2S{=}O\cdots HOSP<$ or salts $R_2S^+OH\cdots {}^-OSP<$[8].

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