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The Conformations of Several 1-Phenylethyl and 1-Phenylpropyl Aryl Sulfoxides. Evidence for Attractive Aryl/Aryl Interaction

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The conformations of the diastereoisomers of 1-phenylethyl phenyl (**1**), 1-phenylethyl *p*-tolyl (**2**), 1-phenylpropyl phenyl sulfoxides (**3**) were studied by NMR spectroscopy, largely by means of the computer simulation of the lanthanoid-induced shifts. It has been suggested that the rotamer in which the aromatic group (Ar) is

$C_6H_5CH(R)$-SO-Ar

	R	Ar
1:	$R=CH_3$,	$Ar=C_6H_5$
2:	CH_3,	$C_6H_4CH_3(p)$
3:	C_2H_5,	C_6H_5

gauche to the phenyl (Ph) and *anti* to the alkyl (R) group is most populated in the conformational equilibria of (*RS*/*SR*)-**1**, **2**, **3**, and (*RR*/*SS*)-**3**. For (*RR*/*SS*)-**1** and **2**, on the other hand, the most important contributor has been suggested to be the rotamer in which Ar is flanked by Ph and R. The results have been discussed in the light of the presence of attractive interactions between relevant groups.

In relation to our interest in the favored *gauche* interactions of flexible aliphatic systems,[1)] the conformations were studied for several compounds which have an aromatic group on each end of the molecules. This paper will deal with the diastereoisomeric pairs of 1-phenylethyl phenyl (**1**), 1-phenylethyl *p*-tolyl (**2**), and 1-phenylpropyl phenyl sulfoxides (**3**). The results allow us to conclude unequivocally that these compounds favor the folded (*gauche* aromatic groups) conformations in solution.

Experimental

Materials. The sulfoxides were prepared by the oxidation of the corresponding sulfides using (dichloroiodo)benzene and water in pyridine.[2)] The reaction was run at the rather high temperature of 50 °C, which enhanced the formation of the minor component in the diastereoisomeric pair. The isomeric sulfoxides were separated by repeated column chromatography on silica gel, with hexane–diethyl ether (4:1) as the eluent. The absolute configurations at the carbon and sulfur centers of optically active **1** and **2** have been rigorously determined.[3,4)] The NMR spectra of these sulfoxides allow us to make a configuration assignment for the racemic diastereomers of **1** and **2** studied in this work.

The stereochemical assignment of **3** is based on the similarity in the ^{13}C and ^{17}O chemical-shift patterns (see Table 1) between the 1-phenylethyl and 1-phenylpropyl derivatives: the sulfoxide with the higher mp and the smaller retention volume was assigned the (*RR*/*SS*) configuration.

(*RR*/*SS*)-**3**. Mp 142—143 °C. Found: C, 73.51; H, 6.56; S, 13.48%. Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60; S, 13.12%. (*RS*/*SR*)-**3**. Mp 90—93 °C. Found: C, 73.57; H, 6.61; S, 13.52%.

The ^{17}O-enriched sulfoxides were prepared by treating the sulfides with (dichloroiodo)benzene and ^{17}O-enriched water (10 atom%, Prochem) in dry pyridine, as has been described by Montanari *et al.* for unenriched sulfoxides.[2)]

NMR Spectra. The NMR spectra were obtained on a Varian EM-390 spectrometer for ^1H and on a JEOL FX-90Q spectrometer for ^{13}C NMR. The chemical shifts are given in ppm downfield from internal tetramethylsilane. The ^{17}O NMR spectra of the labelled sulfoxides were measured[5)] on a Varian FT-80A spectrometer: *ca.* (1—3)×10^5 transients were accumulated with a 90° pulse and an acquisition time of 0.03—0.04 s. The chemical shifts were measured as frequency shifts from the synthesizer frequency (8.53200 MHz) and expressed in ppm relative to the oxygen of water, which resonated at 10.78321 MHz when measured in a concentrically placed capillary tube. The chemical shifts are accurate to ±1 ppm. The sample temperature was 60 °C. Under these conditions, the half-band width was in the range of 150—200 Hz.

Lanthanoid-induced Shifts (LIS) Measurements. Weighted $Eu(fod)_3$ was added incrementally to a solution of a known amount of a substrate in $CDCl_3$ (*ca.* 0.2 M), and the chemical shifts were followed in the spectra. The induced shifts of each group of protons were found to be directly proportional to the $Eu(fod)_3$/substrate ratios up to a value of *ca.* 0.2 equiv. mol^{-1}. A least-squares analysis was performed on from four to six experimental points; correlation coefficients of 0.979 or better were thus obtained.

Results

Table 1 lists the ^1H, ^{13}C, and ^{17}O NMR parameters of the sulfoxides, **1**, **2**, and **3**. Table 2 summarizes the lanthanoid-induced shifts on proton resonances.

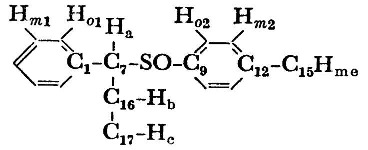
At first, we carried out a computer simulation of the LIS according to the procedure reported previously.[7)] Thus, the position of the lanthanoid shift-reagent (LSR) and the conformation of the molecule (with regard to the central C–S bond) were varied, step by step, in the search for a reasonable fit of the computed LIS's with the observed values [assuming the $(3\cos^2\chi_i-1)\ r_i^{-3}$ proportionality]. For the methyl (ethyl) and aromatic groups, the contribution of the individual protons in a number of conformers was calculated and then averaged. The crystallographic reliability factor (*AF*)[8)] was used in order to assess the agreement between the computed LIS's and the observed ones.

Figure 1 plots the *AF* against the O–S–C–C_6H_5 dihedral angle, ϕ, for compounds (*RS*/*SR*)-**1**, **2**, and

Table 1. ^{1}H, ^{13}C, and ^{17}O chemical shifts[a] of 1-phenylethyl (**1**), 1-phenylethyl *p*-tolyl (**2**) and 1-phenylpropyl phenyl sulfoxides (**3**)

	H_a	H_b	H_c	H_{me}	H_{o1}	H_{o2}	H_{m1}	H_{m2}	C_1	C_7	C_9	C_{12}	C_{15}	C_{16}	C_{17}	^{17}O
(*RS*/*SR*)-**1**	3.78 (0.34)	1.72 (0.27)[c]	—	—	7.06	7.33	7.27	7.39	135.6	67.1	142.1		—	14.1[b]	—	7[b]
2	3.75 (0.27)	1.68 (0.19)	—	2.36	7.11	7.16	7.24	7.13	135.7	67.0	141.3	138.9	21.4	14.1	—	5
3	3.55	2.03[d)] 2.39[e]	0.93	—	6.97	7.22	7.31	7.33	133.8	75.1	142.6		—	22.4[b]	11.6	11[b]
(*RR*/*SS*)-**1**	4.02 (0.48)	1.62 (0.23)	—	—	7.00	7.17	7.23	7.33	133.9	64.3	140.5		—	12.2[b]	—	3[b]
2	4.00 (0.39)	1.57 (0.14)	—	2.36	6.97	7.07	7.27	7.12	134.2	64.3	141.3	137.1	21.4	11.9	—	1
3	3.35	2.10[d] 2.33[e]	1.04	—	6.85	7.09	7.18	7.31	132.4	72.3	139.9		—	21.5[b]	12.0	3[b]

a) $\delta(^1H)$ and $\delta(^{13}C)$: Reported in ppm downfield from internal TMS in $CDCl_3$. The chemical shifts of the aromatic protons were determined by the extrapolation of the linear LIS plots to the intercept at the LSR concentration of zero. b) From Ref. 6. The ^{17}O data (ppm downfield from external D_2O in $CDCl_3$) reported previously for (*RS*/*SR*)-**3** (19 ppm) should be corrected to this. c) Data in parentheses are the aromatic solvent-induced shifts (ASIS): $\delta(CDCl_3)-\delta(C_6D_6)$. d) J_{ab}=11.4 Hz (*RS*/*SR*), 9.6 Hz (*RR*/*SS*); LIS is smaller for this proton than for the diastereotopic congener. c) J_{ab}=4.2 Hz (*RS*/*SR*), 6.0 Hz (*RR*/*SS*). The coupling constants are insensitive to the addition of the LSR.



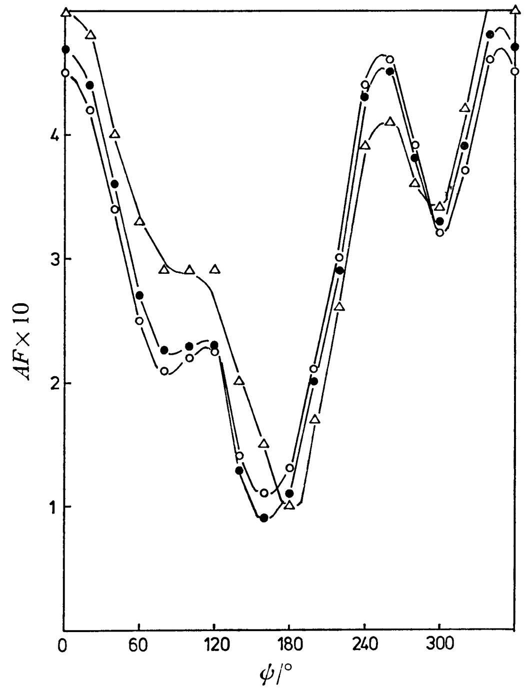


Fig. 1. Plots of *AF* *vs*. the O/Ph dihedral angle (ψ) for sulfoxides with the (*RS*/*SR*) configuration. ○—○: (*RS*/*SR*)-**1**. ●—●: (*RS*/*SR*)-**2**. △—△: (*RS*/*SR*)-**3**.

3; here, the values of *R* (LSR–O distance), θ (LSR–O–S angle), and *A* (index for the LSR-distribution)[7] are kept constant at 0.36 nm, 120°, and 0.8 respectively. The monitor nuclei are H_a, H_b, H_{o1}, H_{o2}, and H_{m1} in every case.

A notable feature of these profiles is the appearance of three minima at about the staggered geometries (ψ *ca*. 80°, 160—180°, and 300°) of the molecules. For reasons previously mentioned,[7] we believe that the values of ψ and *AF* at the extrema reflect, though in an indirect manner, the approximate geometries and the relative importance of the plausible rotamers.[9] In view of this, the most populated rotamer is suggested to have the O–S–C–Ph dihedral angle (ψ) *ca*. 160—180° for (*RS*/*SR*)-**1**, **2**, and **3** (**a** rotamer).[10] Note that in the **a** rotamer the aromatic group (Ar) is *gauche* to the phenyl group (Ph) and *anti* to the methyl group (Me). Also interesting is that the profiles suggest the second most stable one to be the **b** rotamer in every case. In this rotamer Ar is flanked by Me and Ph; the concentration of this rotamer appears to decrease in the 1-phenylpropyl derivative (*RS*/*SR*)-**3**.[11]

The profiles for the (*RR*/*SS*)-isomers are given in Fig. 2; in these cases also three minima are found. The most stable geometry is suggested to be the **b** rotamer for (*RR*/*SS*)-**1** and **2** (ψ *ca*. 200°; Ar is flanked by Me and Ph), the second most stable one being the **a** rotamer (ψ *ca*. 300°). The proportion of the **a** *vs*. **b** rotamer for the 1-phenylpropyl derivative (**3**, R=C_2H_5) seems to differ from that observed for **1** and **2** (R=CH_3); the most stable conformation is suggested to be the **a** rotamer for (*RR*/*SS*)-**3**.[11]

Discussion

A remarkable feature of the above results is that the rotamers which have the aromatic groups *gauche*

Table 2. The lanthanoid-induced shifts[a] of (*RS*/*SR*)- and (*RR*/*SS*)-**1**, **2**, and **3**

Compound	H_a	H_b	H_c	H_{me}	H_{o1}	H_{o2}	H_{m1}	H_{m2}
(*RS*/*SR*)-**1**	1.37	0.89	—	—	0.60	1.00	0.15	0.14
2	1.33	0.89	—	0.09	0.54	1.00	0.16	0.16
3	1.41	0.73 1.36	0.31	—	0.53	1.00	0.09	0.12
(*RR*/*SS*)-**1**	0.87	0.87	—	—	0.47	1.00	0.16	0.19
2	0.96	0.94	—	0.11	0.42	1.00	0.14	0.20
3	0.69	0.86 1.10	0.31	—	0.63	1.00	0.16	0.17

a) Relative values.

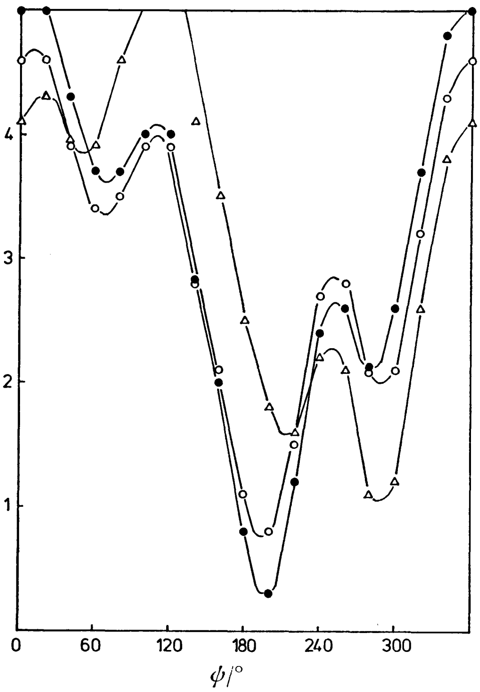


Fig. 2. Plots of *AF* *vs.* the O/Ph dihedral angle (*φ*) for sulfoxides with the (*RR*/*SS*) configuration. ○—○: (*RR*/*SS*)-**1**. ●—●: (*RR*/*SS*)-**2**. △—△: (*RR*/*SS*)-**3**.

to each other (**a** and **b**) are present predominantly in the conformational equilibria for all of the compounds studied. Evidence was, therefore, sought in the present NMR data to support this suggestion.

^{13}C and ^{17}O γ-Effects. Significant differences are found between the diastereoisomers of **1** and **2** with regard to the chemical shifts of the methyl carbon [C(16)] and the oxygen of the sulfoxide. This can be understood well on the basis of the rotameric equilibria suggested by the LIS method (Fig. 3). In the cases of (*RS*/*SR*)-isomers, the oxygen is *gauche* to Me in the **a** rotamer, but is *anti* in the **b** rotamer. For the (*RR*/*SS*)-sulfoxides, on the other hand, O is *gauche* to Me in both of the preferred rotamers. We can, therefore, expect a more profound *γ-gauche* effect to be observed for the (*RR*/*SS*)-isomers.[7] The data in Table 1 support this. An essentially similar, but somewhat different, trend is observed for the 1-phenylpropyl derivatives[6] (**3**). We will refrain from discussing this problem in more detail, however, until more exact knowledge about the conformational equilibria becomes available.[12]

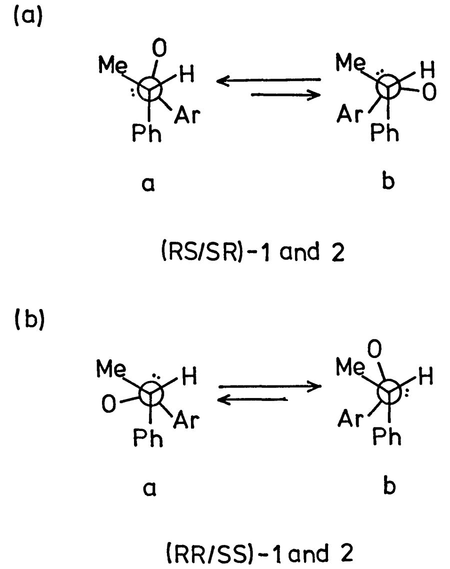


Fig. 3. Conformational equilibria suggested for (a) (*RS*/*SR*)-**1** and **2**, (b) (*RR*/*SS*)-**1** and **2**.

Chemical Shifts of the Aromatic Protons. A common aspect of the NMR spectra of **1**—**3** is that the aromatic protons give multiplets which cover a rather wide range of magnetic fields. Figure 4 illustrates this for a representative case of (*RR*/*SS*)-**2**. In contrast, the aromatic protons of the alkyl analogues (in which Ar is replaced by an alkyl group) gave rise to broad singlets (or narrow multiplets) centered at δ *ca.* 7.25.[7b] In the present cases (Ar=C_6H_5 or $C_6H_4CH_3$), the signals ascribable to the *ortho* protons of the 1-phenylethyl (or 1-phenylpropyl) moiety (H_{o1}), have been shown to resonate at considerably higher magnetic fields [δ 6.97—7.11 for (*RS*/*SR*), 6.85—7.00 for (*RR*/*SS*)]; this was shown by extrapolating the linear LIS plots to the intercept at the LSR concentration of zero (see Fig. 5). This is reasonable, since, in the **a** and **b** rotamers, the aromatic groups are close to each other; H_{o1} (and H_{o2}) can be expected to be effectively shielded by the opposing aromatic ring.

Aromatic Solvent-induced Shifts (ASIS). In Fig. 3, the sulfoxide oxygen in (*RS*/*SR*)-isomers is flanked by H_a in both of the predominant rotamers (**a** and **b**), but in the (*RR*/*SS*)-sulfoxides O approaches H_a only in the **b** rotamer. The reverse is true for the orientation of Me with respect to the oxygen. According to the theory,[13] the upfield shifts induced

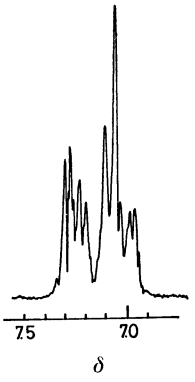


Fig. 4. The aromatic part of the ^{1}H NMR spectrum for (*RR*/*SS*)-**2**.

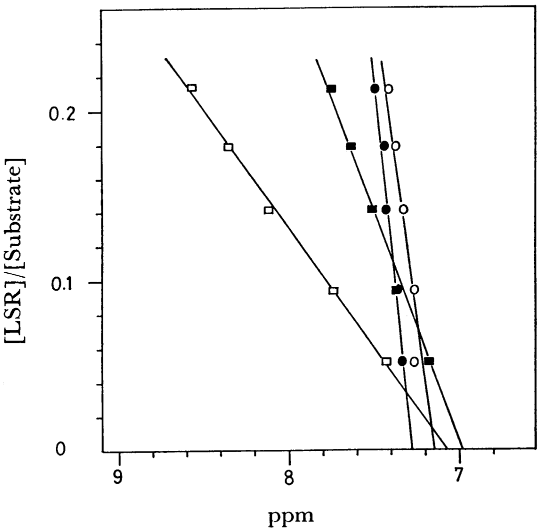


Fig. 5. Plots of the ^{1}H chemical shifts *vs*. LSR concentration for the aromatic protons of (*RR*/*SS*)-**2**. ■: H_{o1}, □: H_{o2}, ●: H_{m1}, ○: H_{m2}.

by benzene (ASIS) are expected to decrease if the relevant nuclei lie close to the negative end of the molecule. The trend observed in ASIS (Table 1) is consistent with the LIS results. Thus, ASIS for the methyl protons (H_b) is larger in (*RS*/*SR*)-**1** and **2** than in the respective (*RR*/*SS*)-isomer. ASIS for H_a, in contrast, is larger in (*RR*/*SS*)-sulfoxides.

Importance of Attractive Ar/Ar Interaction. From the considerations raised above, we conclude that these molecules favor the folded (*gauche* aromatic groups) conformations in solution. The preference of the folded conformation has been demonstrated in 1967 by Dewar for 2-arylethyl *p*-toluenesulfonates ($C_7H_7SO_2OCH_2CH_2Ar$; Ar=1-pyrenyl and 9-phenanthryl)[14] and more extensively by Engberts *et al.*[15] for several sulfonyl compounds, $ArSO_2CH_2Ar$, $ArSO_2CH_2NMeCO_2Ar$, and $(ArSO_2CHPhNH)_2CO$. Their conclusions were drawn mainly on the basis of the X-ray,[15] UV, (appearance of the intramolecular charge-transfer band),[15] and NMR data (upfield shifts of the aromatic protons as compared with those of reference compounds).[14,15] The predominance of the *gauche* rotamers has been argued also for several sulfoxides similar to **1** and **2**[3a,6] and structurally related sulfides.[16] The present findings provide strong support for this and, further, suggest that the favored interaction between aromatic groups is rather general in other kinds of molecules. Also noteworthy in the above results is the importance of the rotamer with the aromatic group (Ar) flanked by Ph and Me (**b** rotamer); in some cases, this becomes the main contributor.

In view of this and other evidence,[17] we conclude that the conformations of these molecules are determined principally by the interaction between aromatic groups, which must be attractive, at least in the framework of the molecules presently studied. Superimposed on this effect is probably the dipole(SO)/quadrupole(Ph) interaction (repulsive, if parallelly oriented).[13,17]

The nature of the attractive Ar/Ar interaction remains open, but we feel it likely that the London dispersion force is mainly responsible, since the phenomenon appears to be rather general for a variety of compounds.[14–19] The CH/π[1,20] (CH_3 *vs*. Ar; C–H_o *vs*. Ar) and quadrupole/quadrupole (Ph *vs*. Ar)[21] interactions may also play some parts in determining the molecular structures of these compounds. In order to obtain insight into this problem, theoretical calculations are currently being made in these laboratories; the results will appear in a future paper.

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8) $AF=[\sum_i(\text{LIS}_i^{\text{obsd}}-\text{LIS}_i^{\text{calcd}})^2/\sum_i(\text{LIS}_i^{\text{obsd}})^2]^{1/2}$. The calculated shifts were normalized to the average experimental LIS in the computational process.[1,7a] The normalization was made to the largest LIS in Ref. 7b.

9) Perturbation to the conformational equilibria by the complex formation has been shown to be unimportant in these cases.[7] This is shown also by the insensitivity of $^3J_{H_aH_b}$ in **3** to the addition of the LSR.

10) In view of the limitation of the present methodology (a number of approximations were introduced in the computational procedure), we do not wish to imply that the values of ϕ at the *AF* minima correspond exactly to the molecular shapes of these compounds. Earlier work on similar subjects, however, has shown that the LIS method gave results which agreed quite well with those obtained by other means, including the X-ray crystallographic work.

See Ref. 7b and Y. Kodama, K. Nishihata, M. Nishio, and Y. Iitaka, *J. Chem. Soc., Perkin Trans. 2*, **1976**, 1490.

11) The results are compatible with our stereochemical intuition.

12) Differences are also found between the diastereomers of **1** and **2** (and **3**) for chemical shifts of H_a, H_b(methyl), C(1), and C(7). These may be conformational effects, but at present we have no clear explanation.

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