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Conformational Studies by Dynamic NMR. 81.[1] Cogwheeling Circuit for the Enantiomerization of the Propeller Antipodes of 2,2′,6,6′-Tetramethyldiphenyl Sulfide

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Compounds comprising two aryl groups connected to a single ligating atom (Ar−Z−Ar) can be considered the molecular analogues of macroscopic two-blade propellers and the internal rotations involving the two Ar-Z bonds can be described according to the so-called “cogwheeling circuit”, a concept introduced and discussed by Mislow[3] and further illustrated by Glaser.[4] Experimental examples are offered by very crowded ether (Z = O)[5] or sulfide derivatives (Z = S) [6] where, however, the two aryl rings either happened to be constitutionally heterotopic,[5] or contained edge-differentiating substituents.[6] Because of such a differentiation these examples do not correspond exactly to the proposed theoretical scheme of the cogwheeling circuit.

To obtain an experimental equivalent of the very same theoretical schemes reported in refs 3 and 4, we thus investigated a sulfide with two homotopic aryl groups bearing substituents that would not differentiate the edges of the rings. In addition, we wanted these substituents (to be placed in the *ortho* positions) to be small enough not to warp the molecular conformation but large enough as to allow an experimental detection of the cogwheel effect. Introduction of four methyl groups in the *ortho* positions of Ph_2S makes the resulting 2,2′,6,6′-tetramethyldiphenyl sulfide, **1** adopt the expected propeller arrangement.[3,4] According to a Molecular Mechanics model[7] each of the two rings of **1** makes in fact a dihedral angle with the C1−S−C1′ plane equal to 54° (or −126° if seen from the opposite direction): ab initio calculations[8] confirm this result, the mentioned angle being 56° in this case.

Since crystal structures of these types of sulfides are not available in the literature, we carried out an X-ray diffraction determination of the very similar dimesityl sulfide, **2** (Mes_2S, where Mes = 2,4,6-trimethylphenyl): the crystals of the latter turned out, in fact, to be more suited for this purpose than those of **1**. As shown in Figure 1, the structure of **2** (see Experimental Section) corresponds indeed to that of a propeller, where the dihedral angles of each of the two rings with the C1−S−C1′ plane (56.0° and 56.8°) are very close to that (54° or 56°) computed for **1** (the same 54° dihedral angle was also predicted for **2** on the basis of the MM calculations[7]).

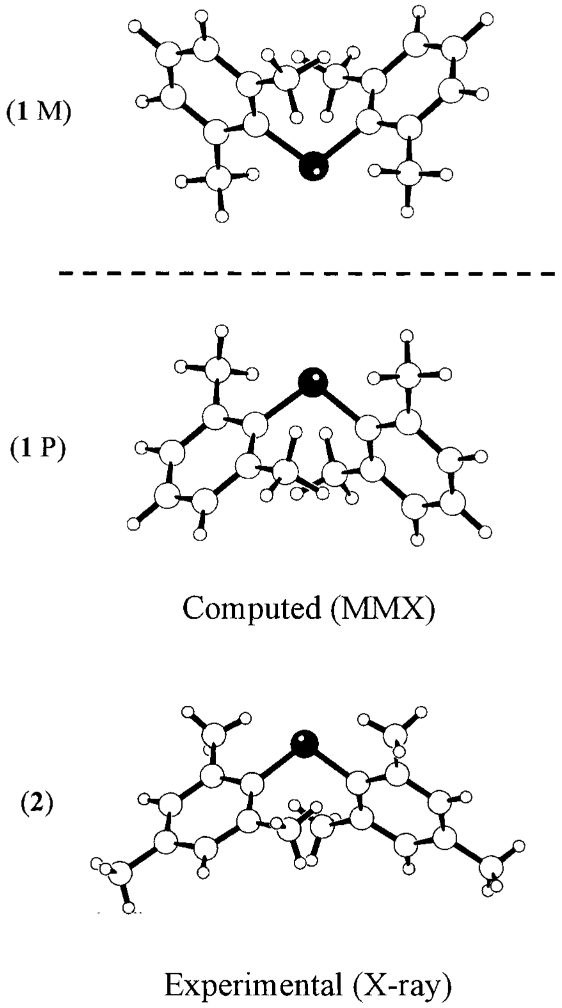

Figure 1. MM computed structures of the M and P antipodes of the 2,2′,6,6′-tetramethyldiphenyl sulfide **1**. Underneath is reported the X-ray structure of dimesityl sulfide, **2**.

Sulfide **1** is thus expected to exist (Figure 1) as a pair of M and P antipodes (conformational enantiomers) whose presence in solution can be inferred by rendering slow the corresponding interconversion rate. In so doing, the two methyl groups within each aryl ligand would become diastereotopic yielding, as a consequence, anisochronous NMR signals. On the basis of these considerations sulfide **1** seems therefore to be an appropriate choice for obtaining an experimental verification of the mentioned cogwheeling circuit.

Indeed, below −150 °C the ^1H NMR spectra of **1** show how the single line due to the four methyl groups broadens considerably and eventually decoalesces, displaying ultimately two anisochronous lines at −179 °C. The computer line shape simulation of Figure 2 yields the rate constants for the M, P enantiomerization process that provides a value of 4.25 ± 0.15 kcal mol^{-1} for the corresponding free energy of activation.[9]

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[1] For Part 79 see ref 15 and for Part 80 ref 16.

[2] In partial fulfillment of the requirements for the Ph.D. in Chemical Sciences, University of Bologna.

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[7] MMX force field as implemented in the computer package PC Model 6, Serena Software, Bloomington, IN.

[8] These calculations were carried out at the HF 6-31G* level by using the Wave function Titan 1.0.5 computer package.

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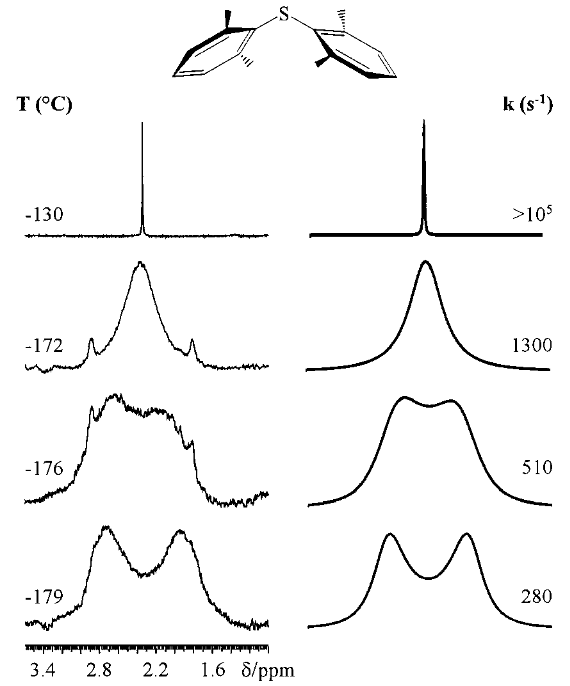


Figure 2. Experimental (left) ^{1}H NMR spectra (300 MHz) of the *ortho* methyl signals of **1** in CHF_2Cl/CH_2FCl as function of temperature. On the right are reported the line shape simulations obtained with the rate constants (k, in sec^{-1}) indicated.

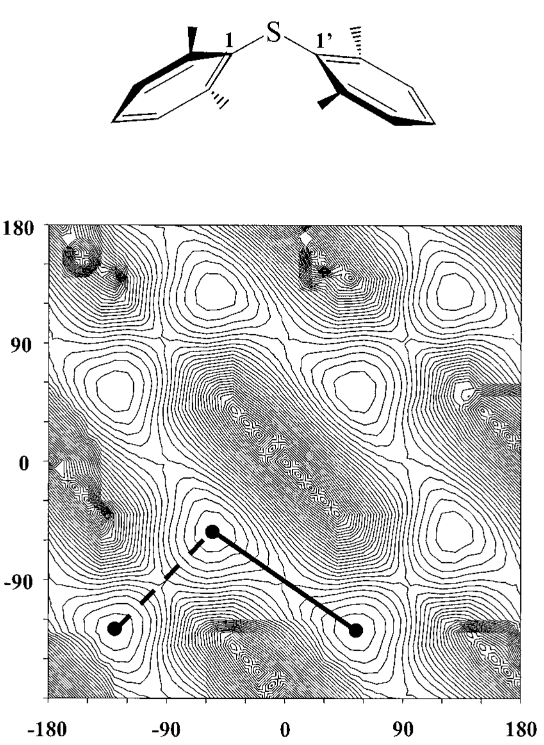
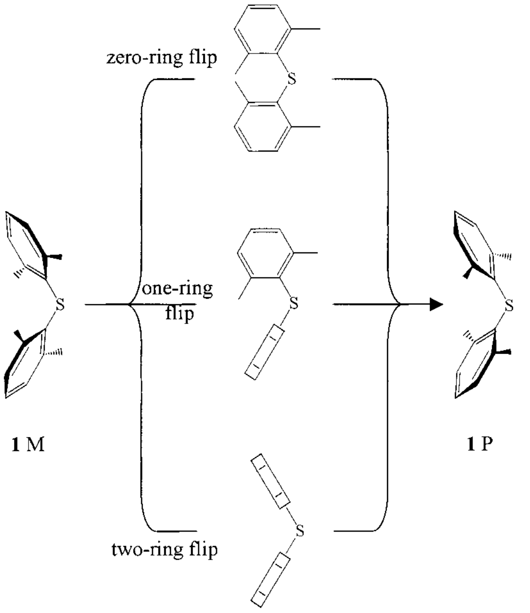


Figure 3. Contour plot of the energy levels of **1** computed as function of the two dihedral angles between the C1−S−C1′ and the aryl planes. The dotted and the full line represent, respectively, the two-ring flip and the one-ring flip pathway.

Scheme 1. Schematic Representation of the Transition States Corresponding to the Zero-, One- and Two-ring Flip Pathways for Sulfide 1



The enantiomerization might occur, in principle, via three possible correlated pathways, corresponding to the n-ring flip mechanisms displayed in Scheme 1, where n can be equal to 0, 1, or 2.[10]

The zero-ring flip pathway ($n = 0$) is a conrotatory motion leading to a transition state where both aryl rings are coplanar with the C1−S−C1′ plane. The corresponding barrier is consequently expected to be extremely high and unlikely to take place: in any case this process does not imply the exchange of the environment for the diastereotopic methyl groups and is thus unable to account for the spectral observation, being NMR invisible.[11,12]

The one-ring flip process ($n = 1$) is a disrotatory motion leading to a transition state where one ring is orthogonal to and the other coplanar with the C1−S−C1′ plane (gear-meshing). This transition state also has a degenerate form, where the disposition of the rings is interchanged.[13] Finally, the two-ring flip process ($n = 2$) is a conrotatory motion having a transition state where both rings are orthogonal to the C1−S−C1′ plane (gear-clashing). Both the latter pathways are, in principle, NMR visible in that require that the methyl groups exchange their positions, [11] and either of them might have sufficiently low rotation barriers as to be compatible with the value experimentally determined.

The two processes were therefore modeled[7] by computing the energy of **1** as function of the two dihedral angles between the aryl groups and the C1−S−C1′ plane. The two-dimensional contour plot, obtained (Figure 3) by slicing the resulting three-dimensional energy surface, shows how the enantiomerization of the two M and P antipodes can be accomplished, in principle, according to one or the other of these processes. The dotted line

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[9] The ^{1}H NMR spectrum of **2** displays, like **1**, two anisochronous lines for the diastereotopic *ortho* methyl substituents at −179 °C, although the superimposing line of the *para* methyl groups distorts the shape of these signals, making less accurate the determination of the free energy of activation (nonetheless a $\Delta G^{\ddagger}$ value of 4.3 ± 0.3 kcal mol^{-1} could be reasonably guessed also in the case of **2**).

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corresponds to the two-ring flip pathway ($n = 2$), with a barrier of 5.8 kcal mol^{-1}, and the full line to the one-ring flip pathway ($n = 1$), with a barrier of 4.8 kcal mol^{-1}. The latter value is the lowest of the two and, in addition, matches better the experimental free energy of activation.[14] Additional support to this conclusion was obtained by computing the energy of the two saddle points of Figure 3 (corresponding to the one- and two-ring pathways) by means of an ab initio method.[8] Frequency calculations proved that they were indeed transitions states, since there is only one imaginary frequency for each of them. The ab initio barrier for the two-ring process (11.5 kcal mol^{-1}) was found higher than that computed by Molecular Mechanics whereas that computed for the one ring flip process (4.3 kcal mol^{-1}) was found quite similar. Furthermore, the latter value turned out to be even closer to the experimental barrier ($\Delta G^{\ddagger} = 4.25$ kcal mol^{-1}), thus confirming that the cogwheeling circuit of **1** is properly described by this mechanism, which thus represents the experimental realization of the circuit previously hypothesized[3,4] for the general case Ar−Z−Ar.

To connect the energy minima corresponding to the M and P conformational enantiomers in the contour plot of Figure 3, the lines describing the ring flip processes appear diagonal with respect to the axes. This is an evidence that we are dealing with a cogwheel mechanism: the latter, in fact, requires that the motion of the two rings is correlated, in that the torsion of on ring drives a concomitant torsion of the second one.[12,13] Had the rotation of the two rings been independent of each other, the connecting lines would have had a trend parallel or orthogonal to the axes.[15,16]

Experimental Section

2,2′,6,′6′-Tetramethyldiphenyl Sulfide (1).[17] To a suspension of LiAlH$_4$ (2.2 mmol) in Et$_2$O (10 mL) was added a solution of 2,2′,6,′6′-tetramethyldiphenyl sulfoxide[16] (0.190 g, 0.74 mmol in 10 mL of THF) in about 10 min. The suspension was allowed to reflux for 2 h. The cooled suspension was carefully quenched with aqueous NH$_4$Cl. The product was extracted (Et$_2$O) and dried (Na$_2$SO$_4$) and the solvent removed at reduced pressure. The crude was purified on a silica gel column (eluent 10:1 petroleum ether/Et$_2$O) to give 0.075 g of **1**. ^{1}H NMR (200 MHz, CDCl$_3$, 22 °C, TMS): $\delta = 2.21$ (s, 12H, Me), 6.95−7.05 (m, 6H, CH); ^{13}C NMR (50.3 MHz, CDCl$_3$, 22 °C, TMS): $\delta = 21.7$ (CH$_3$), 126.9 (CH), 128.4 (CH), 134.3 (q), 140.4 (q).

2,2′,4,4′,6,′6′-Hexamethyldiphenyl sulfide (dimesityl sulfide**)**, (**2**)[18] was prepared according to the previous methodology, starting from dimesityl sulfoxide.[16] Crystals suitable for X-ray analysis were obtained by slow crystallization in ethanol. ^{1}H NMR (200 MHz, CDCl$_3$, 22 °C, TMS): $\delta = 2.2$ (s, 12H, Me), 2.25 (s, 6H, CH$_3$), 6.82 (s, 4H, CH); ^{13}C NMR (50.3 MHz, CDCl$_3$, 22 °C, TMS): $\delta = 21.0$ (CH$_3$), 21.8 (CH$_3$), 129.7 (CH), 131.2 (q), 136.2 (q), 140.1 (q).

NMR Measurements. The samples for the low-temperature measurements were prepared by connecting to a vacuum line the NMR tubes containing the desired compounds dissolved in some C$_6$D$_6$ for locking purpose and condensing therein the gaseous solvents (CHF$_2$Cl and CH$_2$FCl in a 5:1 v/v ratio) by means of liquid nitrogen. The tubes were subsequently sealed in vacuo and introduced into the precooled probe of the 300 MHz spectrometer. The temperatures were calibrated by substituting the sample with a precision Cu/Ni thermocouple before the measurements. Total line shape simulations were achieved by using a PC version of the DNMR-6 program.[19] Since at the low temperatures required to observe the dynamic process, the intrinsic width of the methyl line was significantly temperature dependent, its value was obtained by multiplying that of the most intense solvent line by a 1.6 factor. This occurs, because at higher temperatures, where the exchange process is rapid, the intrinsic methyl line width of **1** was constantly 60% broader. We also checked that errors as large as 50% on this value affected the activation energy by less than 0.05 kcal mol^{-1} in the temperature range investigated.[20]

X-ray Diffraction. Crystal Data for 2,2′,4,4′,6,6′-Hexamethyldiphenyl sulfide (2): C$_{18}$H$_{22}$S (270.42), monoclinic, space group $P2_1/c$, $Z = 4$, $a = 8.5791(3)$, $b = 9.6893(3)$, $c = 18.9776(7)$ Å, $\beta = 97.1110(10)$, $V = 1565.39(17)$ Å^3, $D_c = 1.147$ g cm^{-3}, $F(000) = 584$, $\mu_{\mathrm{Mo}} = 0.192$ cm^{-1}, $T = 293$ K; data were collected using a graphite monochromated Mo−Kα X-radiation ($\lambda = 0.71073$ Å) range $2.16° < \theta < 30.00°$. Of 20409 reflections measured, 4568 were found to be independent ($R_{\mathrm{int}} = 0.0253$), 2905 of which were considered as observed [$I > 2\sigma(I)$], and were used in the refinement of 172 parameters leading to a final R_1 of 0.0450 and a R_{all} of 0.0683. The structure was solved by direct method and refined by full-matrix least squares on F^2, using SHELXTL 97 program packages. In refinements were used weights according to the scheme w = [$\sigma^2(F_o{}^2) + (0.0867P)^2 + 0.0000P]^{-1}$ where $P = (F_o{}^2) + 2\,F_c2)/3$. The hydrogen atoms were located by geometrical calculations and refined using a “riding” method. wR_2 was equal to 0.1324. The goodness of fit parameters S was 1.006. Largest difference density between peak and hole was 0.240 and −0.322 eÅ^{-3}. Crystallographic data (excluding structure factors and including selected torsion angles) have been deposited with the Cambridge Crystallographic Data Center, CCDC 161609.

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[14] When the sulfur is substituted by the oxygen atom to yield the 2,2′,6,6′-tetramethyldiphenyl ether, the MM computations [7] predict an enantiomerization barrier higher than in the case of **1** for the two-ring flip (12.0 instead of 5.8 kcal mol^{-1}) but lower (3.0 instead of 4.8 kcal mol^{-1}) for the one-ring flip mechanism (the same results were obtained for the analogous dimesityl ether). Accordingly, when we looked for the enantiomerization process in the case of dimesityl ether, which was preferred for synthetic convenience (Bottino, F.; Foti, S.; Pappalardo, S, *J. Chem. Soc. Perkin Trans 1* **1977**, 1652), we were unable to determine the experimental barrier by ^{1}H NMR spectroscopy. Although the *ortho* broadened more than that *para* methyl line (an indication that the motion had begun to slow in the NMR time scale), not even at −180 °C we could detect anisochronous *ortho* signals, as expected for a barrier that theory predicts to be lower than 4 kcal mol^{-1}.

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