Conformational Studies by Dynamic NMR. 79.[1] Dimesityl Sulfine Revisited: Detection of the Helical Antipodes and Determination of Their Enantiomerization Pathways

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By means of low-temperature NMR spectra, it is demonstrated that dimesityl sulfine ($Mes_2C{=}SO$) adopts in solution the same chiral propeller conformation (C_1 symmetry) determined by X-ray diffraction in the crystalline state. With the help of MM calculations, it has been also shown that a correlated rotation (cog wheel effect) of the two mesityl rings reverses the molecular helicity according to an enantiomerization process entailing a one-ring flip pathway with $\Delta G^{\ddagger} = 5.9$ kcal mol^{-1} and a two-ring flip pathway with $\Delta G^{\ddagger} = 13.8$ kcal mol^{-1}. On the contrary the *Z*- and *E*-isomers of mesityl phenyl sulfine ($MesPhC{=}SO$) adopt essentially achiral conformations (C_s symmetry), having the Ph−CSO rotation barriers equal to 5.2 and 5.8 kcal mol^{-1}, respectively, and the mesityl−CSO rotation barriers equal to 21.3 and 15.1 kcal mol^{-1}, respectively.

Introduction

The structure of dimesityl sufine (**1**) ($Mes_2C{=}SO$, where Mes = 2,4,6-trimethylphenyl) has been recently obtained by X-ray diffraction.[3] The molecule adopts in the crystal a propeller-like shape with the mesityl rings almost symmetrically twisted with respect to the plane of the bent (119°) C═SO moiety, the dihedral angles being 57° and 55° for the rings in the *E* and *Z* relationship, respectively. Lacking any element of symmetry, the crystal structure is therefore chiral (C_1 symmetry point group). The same authors proposed, however, that **1** adopts a different, achiral conformation (C_s symmetry point group) in solution, whereby one mesityl ring would be coplanar with and the other orthogonal to the CSO plane. This conclusion was essentially based on the observation that the low temperature (−40 °C) ^{1}H NMR spectrum displays anisochronous signals for the *ortho* methyls and for the *meta* hydrogens of one ring, whereas the corresponding signals of the other ring appear isochronous. This model entails the existence of two possible conformers of different stability (stereolabile diastereoisomers) having the mesityl which is coplanar with the CSO moiety either in a syn or in an anti relationship with respect to the SO group. On steric ground and on the basis of lanthanide-induced shifts (LIS) experiments,[3] the latter situation was considered to be that corresponding to the most stable of the two conformers, thus leading to the proposal that the *E*-ring was essentially coplanar with and the *Z*-ring essentially orthogonal to the CSO plane.

We wish to point out, however, that the reported experimental evidences could be interpreted equally well by means of a different model, which would not require the rejection of the chiral C_1 conformation observed in the crystal in favor of the achiral C_s conformation. The isochronicity of the signals of the *Z*-ring might be also accounted for by assuming that the compound adopts a propeller conformation in which both rings are twisted in the same sense but the *Z*-ring experiences a rotation process faster than the *E*-ring in the NMR time-scale. In other words, the two mesityl groups would exhibit two different topomerization barriers (i.e., rotational barriers resulting in the exchange of diastereotopic groups in a given ring) with the lesser one requiring temperatures lower than −40 °C to be detected. The time-averaged symmetry of this alternative model not only mimics the apparent C_s symmetry but also agrees with the results reported for an analogous compound having two mesityl rings bonded to the same trigonal carbon atom: in 2,2-dimesityl-1-ethenol ($Mes_2C{=}CHOH$) two such barriers were, in fact, observed. [4,5] The higher one (14.2 kcal mol^{-1}) was actually equal to that measured in **1** and corresponded to a disrotatory correlated rotation, resulting into a topomerization of the ring in the *E* relationship. The lower barrier (10.2 kcal mol^{-1}) was observed below −40 °C and corresponded to a process involving topomerization of the ring in the *Z* relationship. This compound thus displays the same chiral propeller-like conformation both in solution and in the crystalline state. On this basis it is quite possible that the lower of the two barriers had escaped observation in the case of dimesityl sulfine.

If the two mesityl rings of **1** are indeed twisted by the same amount with respect to the CSO plane, it is obviously impossible to have the two conformers hypothesized in ref 3. Dimesityl sulfine will exist, in this case, as a pair of helical antipodes with identical stability (stereolabile P and M enantiomers) that are displayed in Scheme 1. This assumption received further support when we carried out theoretical calculations predicting that **1** adopts a conformational ground state where both

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

[3] Kappert, W.; Sander, W.; Landgrafe, C. *Liebigs Ann. Recueil* **1997**, 2519.

[4] Nugiel, D. A.; Biali, S. E.; Rappoport, Z. *J. Am. Chem. Soc.* **1984**, *106*, 3357.

[5] Biali, S. E.; Nugiel, D. A.; Rappoport, Z. *J. Am. Chem. Soc.* **1989**, *111*, 846.

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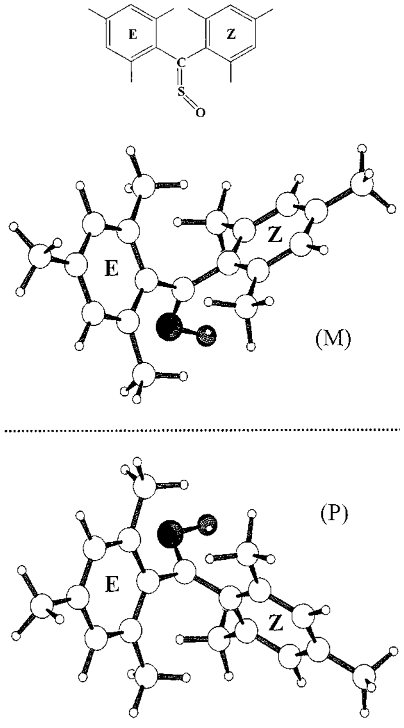
Scheme 1. MM Computed Structures of the M and P Stereolabile Antipodes (Conformational Enantiomers) of Dimesityl Sulfine (1). The Propeller-Like Shape of the M Enantiomer (top) Is Almost Exactly Superimposable to the X-ray Structure of Reference 3



the *E* and *Z* mesityl rings are equally twisted with respect to the CSO moiety (respectively by 57° and 60° according to PM3 [6a] and by 55° and 60° according to the MMFF force field[6b]). The near identity of the dihedral angles measured in the crystal with those computed for the isolated molecule makes difficult to believe that the chiral conformation of **1** in the solid has been modified into an achiral conformation in solution.

To substantiate this hypothesis, the ^{13}C NMR spectrum of **1** was investigated at the lowest attainable temperature where the compound could still be maintained in a fluid solution.

Results and Discussion

Dimesityl Sulfine (1). The 100.6 MHz ^{13}C spectrum of **1** displays at ambient temperature a number of broad signals that sharpen on cooling, eventually yielding, below −30 °C, five lines for the methyl, three lines for the CH, and seven lines for the quaternary ring carbons (Table 1): within each group, one line is always twice as intense as the other, corresponding to a pair of carbons. In the top trace of Figure 1 are displayed the five lines due to the six methyl-bonded quaternary ring carbons, the line upfield having, as mentioned, a double integrated intensity. The same number of lines (five and three, respectively) are also observed for the methyl and CH hydrogens in the ^{1}H spectrum at −40 °C, as previously reported.[3] At this temperature the rate of topomerization involving the *E*-ring has become sufficiently slow[7] as to make the pairs of *ortho* and *meta* positions diastereotopic, whereas those of the other ring (in the *Z*-relationship) are still in a situation of rapid exchange, which accounts for the observed isochronicity of the corresponding signals. Only when the temperature is further lowered also the *ortho* and *meta* positions of the *Z*-ring can reveal their diastereotopicity. Indeed below −120 °C, the ^{13}C spectrum shows how the CH line (130.4 ppm), corresponding to the two *meta* carbons of the *Z*-ring, broadens and decoalesces, yielding two equally intense lines at −155 °C, one of which overlaps with one of the two CH lines of the *E*-ring (Table 1). Likewise the line (138.2 ppm) due to the pair of methyl-bonded ortho quaternary carbons of the *Z*-ring ($C_Z{}^o$ and $C_Z{}^{o'}$) broadens and eventually splits into two at −155 °C, so that six resolved lines (Figure 1) are now observed for the two para and for the four ortho carbons (Table 1).[8] These observations unambiguously prove that the apparent C_s symmetry has been unmasked and a chiral conformation (point group C_1, as in the crystal) is adopted by dimesitylsulfine in solution. Computer line shape simulation[9] in the appropriate temperature ranges yielded the rate constants, hence the free energy of activation, for the two observed dynamic processes. The one with the higher barrier has a $\Delta G^\ddagger$ of 13.8 ± 0.15 kcal mol^{-1}, that with the lower barrier a $\Delta G^\ddagger$ of 5.9 ± 0.2 kcal mol^{-1} (Table 2).

Table 1. ^{13}C Shifts (ppm) of 1 at −60 °C and −155 °C. The Single Star Identifies the Pairs of Exchanging Lines in the *Z*- and the Double Star the Pairs in the *E*-Ring[a]

quaternary carbons		methine carbons		methyl carbons	
−60 °C	−155 °C	−60 °C	−155 °C	−60 °C	−155 °C
190.0 (*C*=SO)	189.6 (*C*=SO)	131.2**	130.5	23.1**	22.7
141.1	140.2	130.8**	130.2	21.4 [2]	20.9*
141.0	140.0	130.4 [2]	130.2*	20.7	20.1
140.3**	139.0		129.1*	20.6	20.1
138.7**	138.4*			20.5**	20.1
138.2 [2]	137.6				20.0*
129.2 (*C*−CSO)	135.3*				
127.2 (*C*−CSO)	128.5 (*C*−CSO)				
	126.6 (*C*−CSO)				

[a] The number 2 in parentheses indicates that the corresponding line comprises two carbons (in the *Z*-mesityl ring) having dynamically averaged shift. The equal values reported in columns 4 and 6 are the shifts of lines that should be distinguishable in principle, but overlap accidentally.

The exchange processes observed in **1** might be described, in principle, by a π-radiant rotation of each mesityl ring taking place independently of the other and entailing the retention of the helicity.[10,11] This, however, is unlikely to occur in a crowded molecule like **1** since the motion of one ring would transmit a concomitant motion to the other, much in the same way as it happens in a macroscopic two-toothed gear (cog wheel effect). Indeed such a correlated motion had been shown to apply in the mentioned 2,2-dimesityl-1-ethenol which has quite similar steric properties.[5] If we compare **1** to a two-blades propeller, the enantiomerization process should then be

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(6) (a) PM3. (b) MMFF. Both as implemented in the PC Spartan-Pro 1.1 computer package.

(7) The assignment is that reported in ref 3, where LIS experiments indicated that the signals undergoing line broadening effect at ambient temperature are those of the *E*-ring.

(8) In the CHF_2Cl solution used for the low-temperature experiments the CH lines of the 400 MHz ^{1}H spectrum were not observed, being underneath those of the solvent. In the methyl region the intense ^{1}H line broadens considerably below −120 °C, but at −150 °C the line widths of the six expected methyl signals were too broad, with respect to their shift separation, to be meaningfully employed for a line shape analysis. The same problem was also encountered in the case of the ^{13}C methyl signals.

(9) PC version of the QCPE program 663, Indiana University, Bloomington, IN.

(10) Rappoport, Z.; Biali, S. E. *Acc. Chem. Res.* **1997**, *30*, 307.

(11) Rappoport, Z.; Biali, S. E. *Acc. Chem. Res.* **1988**, *21*, 441.

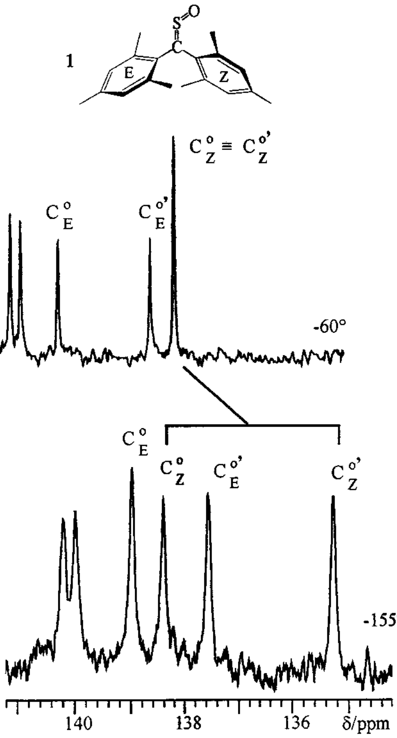


Figure 1. The ^{13}C spectrum (100.6 MHz in CHF_2Cl/acetone-d_6, 10:1 v/v) displays five lines for the six methyl-bonded quaternary ring carbons of dimesityl sulfine (**1**) at −60 °C (upper trace). At −155 °C (bottom trace) six lines are detected since the line comprising the two *ortho* *Z*-ring carbons (C_Z^o and $C_Z^{o'}$) has split.

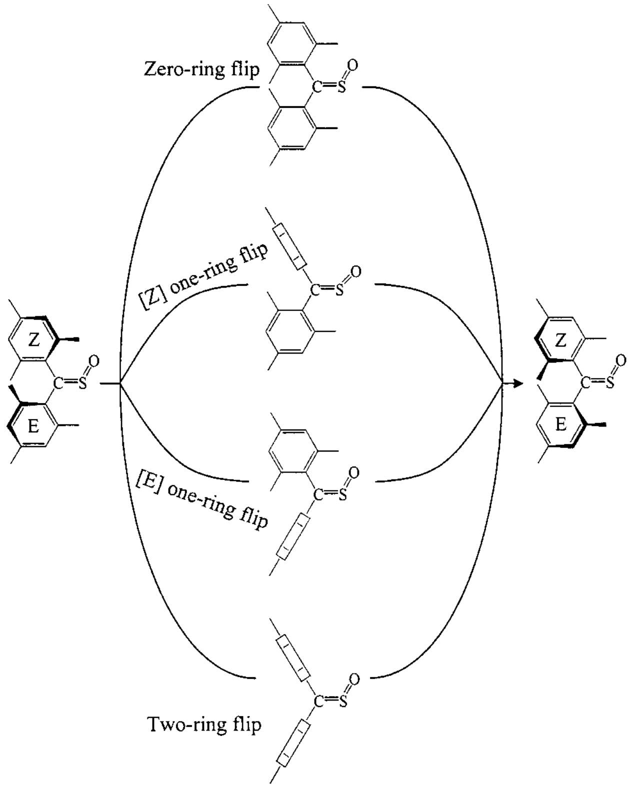
Table 2. Free Energies of Activation (kcal mol^{-1}) for the Rotations of the *Z*- and *E*-Rings ($\Delta G^{\ddagger}_Z$ and $\Delta G^{\ddagger}_E$, Respectively) in 1−3. $\Delta E^{\ddagger}_Z$ and $\Delta E^{\ddagger}_E$ Represents, Respectively, the Computed Energies Differences

	experimental		computed	
compd	$\Delta G^{\ddagger}_Z$	$\Delta G^{\ddagger}_E$	$\Delta E^{\ddagger}_Z$	$\Delta E^{\ddagger}_E$
1 (dimesitylsulfine)	5.9	13.8	10.8	11.6
2 (*Z*-mesitylphenylsulfine)	21.3	5.2	27.8	5.4
3 (*E*-mesitylphenylsulfine)	5.8	15.1	5.1	20.8

described by the so-called *n*-ring flip mechanisms (*n* being 0, 1, or 2)[10−12] where a reversal of the helicity takes place (Scheme 2). The zero-ring flip[13] pathway ($n = 0$) is a conrotatory motion which makes the two mesityl rings to reach a transition state where both their planes are coplanar with the reference plane of the CSO moiety (Scheme 2). The one-ring flip ($n = 1$) is a disrotatory motion leading to a transition state where one ring is orthogonal to and the other coplanar with the CSO plane (gear-meshing). In the case of **1** there are two such transition states, depending as to whether the ring orthogonal to the CSO moiety is the one in the *E* or in the *Z* relationship. Finally the two-ring flip pathway ($n = 2$) is a conrotatory motion which makes both rings to become simultaneously orthogonal to C=SO (gear-clashing).

The zero-ring flip mechanism is NMR invisible since it occurs without exchanging the diastereotopic environments of the meta and ortho positions of the mesityl ring and therefore cannot account for the observed dynamic process. However, it might still correspond to the threshold mechanism of enantiomerization if its barrier had a value lower than the lowest barrier measured experimentally. It is quite safe, however, to neglect such a possibility since in the corresponding transition state the two mesityl rings would be coplanar, thus leading to an overcrowded situation of extremely high energy which should be inaccessible. [4] Computations carried out on similar dimesityl derivatives showed indeed that the barriers for a zero-ring flip process are expected to lie in the range 40−60 kcal mol^{-1}.[1]

Scheme 2. Schematic Representation of the Possible Ring-Flip Pathways Available to Dimesityl Sulfine (1)



Of the two alternative routes left (i.e., $n = 1$ or $n = 2$), the one-ring flip involving the *Z*-ring (Scheme 2) is the only logical possibility to account for the process displaying the lower of the two barriers (threshold mechanism). In this pathway the *Z*-ring exchanges the pairs of diastereotopic groups (i.e., the methyls and quaternary carbons in position *ortho*, as well as the methine hydrogens and carbons in position *meta*) whereas the *E*-ring passes through the CSO plane, interchanging the edges but not the pairs of diastereotopic groups, whose signals still remain anisochronous.[1,5]

The second, higher barrier of 13.8 kcal mol^{-1} might correspond either to a second one-ring flip involving, now, the *E*-ring or to a two-ring flip process. A choice between these two possibilities cannot be easily made but a comparison with the case of the 2,2-dimesityl-1-ethenol could be helpful. Since the latter adopts the same ground state symmetry, experiences the same threshold mechanism, and exhibits a value for the barrier of interest essentially equal to that of **1** (14.2 and 13.8 kcal mol^{-1}, respectively), it is conceivable to assume that both molecules follow the same pathway for the higher energy process. The calculations of ref 5 strongly suggested the

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(12) Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26.

(13) One of the reviewers suggested that the term "zero-ring flip" used in the literature[10−12] should be substituted either by "coplanar ring flip" or by "bis-coplanar ring flip".

two-ring flip to be the preferred mechanism, so that the same conclusion should also hold for dimesitylsulfine, **1**.

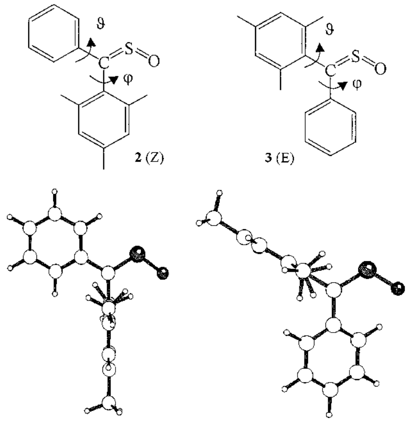
To gain support to this hypothesis we carried out an analogous calculation (the MMFF force field[6b] was used) also in the case of dimesitylsulfine. Being that the C=SO is a rather "exotic" moiety, however, the corresponding parametrization cannot be considered as reliable as that for dimesitylethenol (especially for what concerns the torsional transition states) so that only an approximate, qualitative indication has to be expected. Despite these limitations, the lower computed barrier corresponded indeed to the one-ring flip process involving the *Z*-ring and the subsequent higher barrier was that for the two-ring flip, whereas the highest value corresponded to the one-ring flip process involving the *E*-ring which, accordingly, is unlikely to take place.[14]

Mesitylphenyl Sulfines 2 and 3. We have shown that, as in the crystal, the ground state conformation of dimesityl sulfine (**1**) in solution belongs to the C_1, rather than to the C_s point group. On the other hand, the latter is the one adopted by the allowed transitions states (corresponding to the $n = 1$ and $n = 2$ ring flip pathways) where a plane of symmetry is always present (Scheme 2). It should be possible, in principle, to obtain sulfines that adopt a ground state C_s symmetry by interfering with the correlated motion of the two aromatic rings.

If in a macroscopic two-toothed gear the "teeth" are eliminated from one of the two components, each one should be able to rotate independently of the other. The *ortho* methyl groups of **1** play somehow the same role as the teeth of a gear, so that their elimination from one of the two rings might change the molecular symmetry, [15a] allowing each ring to find the more convenient conformational arrangement without interference by its companion.[15b]

With the purpose of ascertaining whether such a situation can be realized in practice, we substituted one of the two mesityl rings of **1** with a phenyl group, obtaining the two isomeric mesitylphenyl sulfines: MesPhC=SO (**2**) with mp 101 °C**,** and **3** with mp 59 °C.[16] MM calculations[6b] predict that in the *Z*-isomer the mesityl is essentially perpendicular to and the phenyl nearly coplanar with the C=SO plane (Scheme 3), the calculated dihedral angles being, respectively, 81° and 23°. Within the framework of the computational approximations,[17] this isomer seems therefore to be a good candidate for exhibiting a non chiral C_s symmetry, particularly if the low energy libration process, consequences of thermal vibrations, is also taken into account.

Scheme 3. MM Computed Structures of the Two Isomeric Mesitylphenyl Sulfines (2, *Z* and 3, *E*). the Dihedral Angles Are Labeled ϑ and φ for the Ring in the *E* and in the *Z* Relationship to the SO Moiety, Respectively



Owing to the lacking of any indication, in the previous literature,[16] of the method used to attribute the *Z* and *E* configuration to the isomers **2** and **3**, we checked anew this assignment by monitoring the displacements of the ^{13}C signals of the *meta* carbons of the phenyl and of the mesityl ring as function of increasing amounts of Eu $(fod)_3$.[18a] The meta ^{13}C signal of the mesityl ring of **2** was unambiguously identified by means of a 2D heteronuclear correlation (see Experimental Section) where this line appears to be connected with the mesityl CH single line, clearly detectable in the ^{1}H spectrum. Since this approach could not be used to identify the meta ^{13}C signal of the phenyl ring (the ortho and meta lines overlap in the ^{1}H spectrum, making the process of disentangling the latter from the former quite uncertain), an alternative method, relying upon low temperature observations, was employed for this purpose, as described in a subsequent paragraph (vide infra).

Eventually it was found that the *meta* ^{13}C line of mesityl undergoes a much larger lanthanide-induced shift (LIS)[18b] than the corresponding line of phenyl (further details are given in the Experimental Section), thus proving that the mesityl ring must be syn and the phenyl anti to the SO moiety. Such a method gives an internally consistent assignment, totally independent of any conclusion concerning the structure of **3** and confirms that the higher melting isomer **2** has the *Z*-configuration. Although it is quite obvious to assign, as a consequence, the alternative configuration to the lower melting isomer **3**, an analogous, independent LIS experiment (reported in the Experimental Section) was nonetheless performed to ascertain that the latter has indeed the *E*-configuration.

On lowering the temperature below −120 °C, the ^{13}C spectrum of **2** shows how one of the three CH lines

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(14) The three computed barriers are 10.8, 11.6, and 19.0 kcal mol^{-1}, respectively, for the [*Z*] one-ring, for the two-ring and for the [*E*] one-ring flip mechanism. As mentioned, only the trend should be considered meaningful, since the values of the two experimental barriers are very different, whereas those of the two lowest computed barriers are quite similar.

(15) (a) An indication that this was a reasonable possibility was obtained by the X-ray structure of the *E*-isomer of the *O*-tolylphenyl sulfine. There the *o*-tolyl, although less bulky than the mesityl group, is nonetheless twisted more (dihedral angle with the C=SO moiety = 66°) and the phenyl group is twisted less (dihedral angle with the C=SO moiety = 15°) than observed for the mesityl rings in **1.** See: Dahn, H.; Pechy, P.; Van Toan, V.; Bonini, B. F.; Lunazzi, L.; Mazzanti, G.; Cerioni, G.; Zwanenburg, B. *J. Chem. Soc. Perkin Trans. 2* **1993**, 1881. (b) A non propeller arrangement seems to be the intrinsically preferred conformation for a Mes−C(sp^2)−Ph moiety. See: Yamataka, H.; Alesiuk, O.; Biali, S. E.; Rappoport, Z. *J. Am. Chem. Soc.* **1996**, *118*, 12580.

(16) (a) Tangerman, A.; Thijs, L.; Anker, A. P.; Zwanenburg, B. *J. Chem. Soc., Perkin Trans. 2* **1973**, 458. (b) Zwanenburg, B.; Janssen, W. A. J. *Synthesis* **1973**, 617. (c) Tangerman, A.; Zwanenburg, B. *Recueil*, **1977**, *96*, 196.

(17) The computed energy for a conformer with the phenyl perfectly coplanar with and the mesityl exactly orthogonal to the C=SO plane is almost identical to that computed for the conformation of **2** having the minimum energy, the difference between the two situations being less than 0.1 kcal mol^{-1}. Within the approximations of this theory the two cases are, in practice, indistinguishable.

(18) (a) The term (fod) stays for 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedioanate. (b) von Ammon, R.; Fischer, R. D. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 675. Cockerill, A.F.; Davies, G. L. O.; Harden, R. C.; Rackham, D. M. *Chem. Rev.* **1973**, *73*, 553. Reuben, J. *Prog. NMR Spectrosc.* **1973**, *9*, 1. Hofer, O. *Top. Stereochem.* **1976**, *9*, 111. Peters, J. A. *Prog. NMR Spectrosc.* **1996**, *28*, 283.

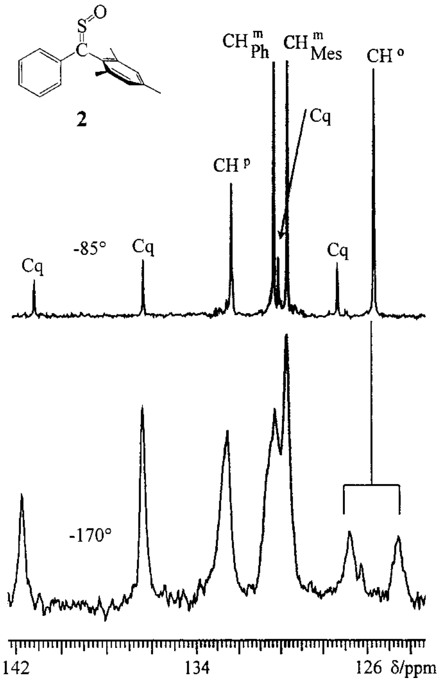

Figure 2. Aromatic region of the ^{13}C spectrum (75.5 MHz in CHF_2Cl /CD_2Cl_2, 2:1 v/v) of the *Z*-mesitylphenyl sulfine (**2**) at −85 °C (top) and −170 °C (bottom). The CH signals for the *ortho* and *para* positions of phenyl, as well as those for the *meta* positions of phenyl and mesityl, are identified, whereas the quaternary carbons lines (Cq) are not assigned. At −170 °C the exchange process makes the phenyl ring to split the CH line of the *ortho* carbons and to broaden that of the *meta* carbons. The CH line of the mesityl ring is not affected by the exchange process.

comprising two carbons (that at 125.6 ppm in Figure 2, top) broadens considerably and, after having reached the coalescence point (at −156 °C), splits (at −170 °C) into two widely separated lines ($\Delta\nu = 168$ Hz at 75.5 MHz): spectral simulation yielded a $\Delta G^\ddagger$ value of 5.2 ± 0.2 kcal mol^{-1} for the barrier to rotation about the Ph−CSO bond (Table 2). This result agrees with MM calculations [6] that predict for the phenyl ring rotation a barrier equal to 5.4 kcal mol^{-1}. On the basis of the large splitting displayed at low temperature, this line could be confidently assigned to the *ortho* carbons (CH° in Figure 2, top).[19] Also the line at 130.3 ppm was broadened by the exchange process below −150 °C, but could not be resolved into the expected pair of lines at −170 °C (Figure 2, bottom) because the shift separation was essentially equal to the line width. On the contrary, the CH line, previously assigned (by 2D experiment) to mesityl (CH^m_{Mes} at 129.7 ppm as in Figure 2 top), does not exhibit line splitting, nor exchange broadening effect (likewise behaved all the other ^1H and ^{13}C lines of the mesityl ring).

The evidence collected from these low-temperature experiments allowed the *meta* ^{13}C line of the phenyl ring to be unambiguously identified[19] as that at 130.3 ppm (CH^m_{Ph} in Figure 2, top).

These observations are compatible with a conformer having the phenyl essentially coplanar with and the mesityl orthogonal to the plane of the CSO moiety, even though they do not constitute yet an unambiguous proof of **2** adopting a C_s symmetry. It might be argued, in fact, that the mesityl signals appear isochronous at −170 °C as a consequence of a rotation process being fast even at that temperature. However, this and other similar barriers had been reported[16c] to be quite large, and also our MM calculations[6] predicted this value (27.8 kcal mol^{-1}) to be much higher than that computed for the phenyl ring rotation. Thus the situation where the mesityl is orthogonal to the CSO planes should be very long living, making the *ortho* methyl groups to appear enantiotopic even at ambient temperature. They should become therefore diastereotopic in a chiral environment, where anisochronous NMR signals would be, accordingly, detected.[16c]

In the presence of a chiral solvating agent (CSA)[20] in large excess, the single line of the two *ortho* methyl hydrogens of **2** appears indeed as a doublet at 25 °C, whereas the signal of the *para* methyl group remains a singlet. The existence of three equally intense ^1H lines for the three methyl groups in a chiral environment, in conjunction with the previous observation of diastereotopic phenyl *ortho* carbons at low temperature, conclusively demonstrates that the *Z*-mesitylphenyl sulfine **2**, contrary to **1**, does adopt an achiral C_s ground state conformation in solution.

At +121 °C the two anisochronous signals for the *ortho* methyl groups of **2** coalesce, so that a barrier of 21.3 ± 0.2 kcal mol^{-1} for the rotation about the mesityl−CSO bond (Table 2) could be derived by computer line shape simulation (see Experimental Section). This value coincides with that previously obtained (using a different chiral agent) for this compound[16c] and is of the same order of magnitude as that (27.8 kcal mol^{-1}) computed by MM calculations.[6b]

Similarly to the *Z*-isomer **2**, the *E*-isomer **3** displays a ^{13}C spectrum (75.5 MHz) exhibiting, at −158 °C, two widely separated lines ($\Delta\nu = 263$ Hz) for the phenyl carbons in the *ortho* positions and two closely spaced lines ($\Delta\nu = 14$ Hz) for those in the *meta* positions.[19] The line shape simulation yielded a value ($\Delta G^\ddagger = 5.8 \pm 0.2$ kcal mol^{-1}) very close to that of **2** for the rotation barrier about the Ph−CSO bond (Table 2).

The ^1H signal of the *ortho* methyl groups of the mesitylphenyl sulfine **3** also splits into a pair of lines in a chiral environment (see Experimental Section), but this occurs in a temperature range (Figure 3) lower than in the case of **2**, so that the coalescence temperature (about +15 °C) and, consequently, the rotation barrier about the mesityl−CSO bond ($\Delta G^\ddagger = 15.1 \pm 0.2$ kcal mol^{-1}) are also lower (Table 2).

The decreasing of the latter barrier in the case of **3** with respect to **2** ($\Delta\Delta G^\ddagger = 6.2$ kcal mol^{-1}) is a consequence of the lower hindrance experienced by the mesityl group in the *E*- with respect to the *Z*-configuration.[21] The

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(19) When, at low temperature, the Ph−X rotation of monosubstituted phenyl derivatives (e.g., X = −CHO, −NHMe, −NO, −NHNH$_2$, −COMes) is frozen, the two diastereotopic carbons in the *meta* positions always display ^{13}C shift separations much smaller (from a factor of 6 up to a factor of 30) than the separations of the corresponding pair of *ortho* carbons, due to the latter being closer to the source of diastereotopicity. See: Lunazzi, L.; Macciantelli, D.; Boicelli, A. C. *Tetrahedron Lett.* **1975**, 1205. Lunazzi, L.; Magagnoli, C.; Guerra, M.; Macciantelli, D. *Tetrahedron Lett.* **1979**, 3031. Lunazzi, L.; Macciantelli, D. Placucci, G. *Tetrahedron Lett.* **1980**, 975. Casarini, D.; Lunazzi, L.; Verbeek, R. *Tetrahedron* **1996**, *52*, 2471.

(20) (*R*)-*l*-1-(9-anthryl)-2, 2, 2,-trifluoroethanol, as in Pirkle, W. H. *J. Am. Chem. Soc.* **1966**, *88*, 1837.

(21) The computed[6b] conformation of **3** having the minimum energy has the dihedral angles equal to 78° and 34° for the mesityl and phenyl rings, respectively, and only differs by 1 kcal mol^{-1} from the conformation corresponding to the perfect C_s symmetry, where these angles are 90° and 0°.

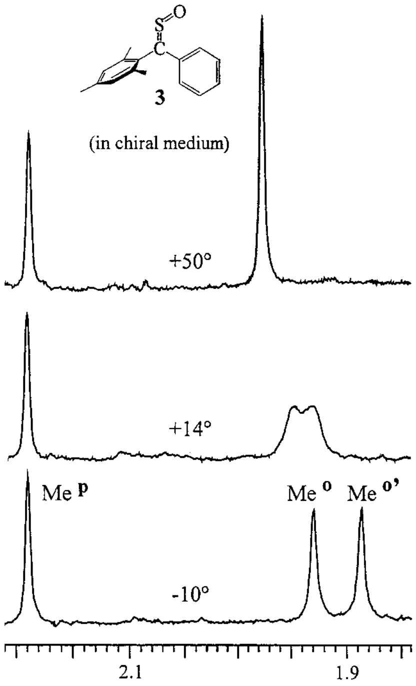

Figure 3. Temperature dependence of the 400 MHz methyl signals (in C_2Cl_4/C_6D_6 6:1 v/v) of the *E*-mesitylphenyl sulfine (**3**) in the presence of a 420:1 molar excess of a chiral solvating agent (see Experimental Section.)

rotation process forces the mesityl group to become coplanar with an anti SO moiety in the transition state of **3**, a situation entailing a barrier much lower than that of **2**, where the mesityl in the transition state is coplanar with a syn SO moiety. This interpretation is also reflected in the MM calculations[6b] that predict for the mesityl–CSO rotation barrier of **3** a value 7 kcal mol^{-1} lower (Table 2) than that computed for **2** (this difference matches satisfactorily the experimental $\Delta\Delta G^{\ddagger}$ of 6.2 kcal mol^{-1}).

In the isomer **2** the topomerization barrier involving the *Z*-mesityl ring is much higher ($\Delta\Delta G^{\ddagger} = 15.4$ kcal mol^{-1}) than that measured for the *Z*-mesityl ring in **1** (Table 2), although the latter is, apparently, more crowded. Since **2** is a less-hindered compound, the motion of the two rings is likely to be less correlated than in **1**: a correlated process, in fact, is expected to be energetically favored over an uncorrelated one,[1,10,22] thus explaining the lower barrier observed in **1** with respect to **2**.

To understand which type of mechanism drives the two rings (i.e., mesityl and phenyl) in sulfines **2** and **3**, a three-dimensional energy surface was computed as a function of the two dihedral Ar–CSO angles (Ar = phenyl and mesityl). On this surface the interconversion process will follow different pathways depending on whether the two rings rotate in a correlated or in an independent manner. This can be made evident by taking a two-dimensional slice of such a surface (contour map): the allowed pathways (i.e., those passing through a transition state with the lowest possible energy) connecting the energy minima (enantiomers in the case of **1**, topomers in the case of **2**, **3**) will appear as a line parallel to one of the axes in the case of an independent motion or as a diagonal line in the case of a correlated motion. As shown in Figure 4, the latter situation applies to the rotation of both the mesityl rings[23] in sulfine **1**, thus confirming that we are dealing with a wholly correlated mechanism. On the other hand, in the case of isomeric mesitylphenyl sulfines the rotation of the phenyl ring is not a correlated process since the corresponding trace is parallel to the *x*-axis (in **2**) or to the *y*-axis (in **3**), where the phenyl–CSO dihedral angles (labeled ϑ in **2** and φ in **3**, as in

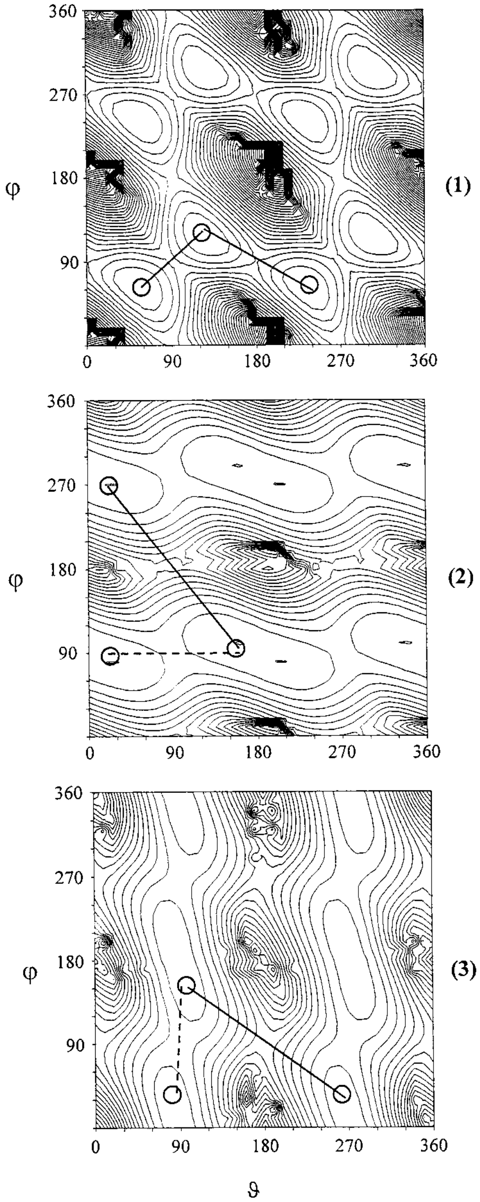

Figure 4. Two-dimensional contour map of the energy surface of **1**–**3**, computed as function of the dihedral angles ϑ and φ made by the CSO moiety with the rings in the *E* and *Z* relationship, respectively (see Scheme 3). The diagonal full lines represent correlated pathways, the parallel broken lines uncorrelated pathways. Each compound has two pathways for the interconversion process, corresponding to the two barriers experimentally determined. In the top picture the full line on the right corresponds to the [*Z*] one-ring flip and that on the left to the two-ring flip pathway described in Scheme 2 for dimesityl sulfine **1**.

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(22) Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 1535. Cremonini. M. A.; Lunazzi, L.; Placucci, G.; Okazaki, R.; Yamamoto, G. *J. Am. Chem. Soc.* **1990**, *112*, 2915.

(23) For the sake of simplicity, the high energy pathway due to the [*E*] one-ring flip correlated mechanism (shown in Scheme 2) has not been drawn on this surface since it does not correspond [14] to either of the two experimentally observed barriers.

Scheme 3) are, respectively, reported. On the contrary, the rotation of the mesityl ring corresponds in both cases to a correlated process since the related pathway follows a diagonal trace. In other words, the lower barrier process (which involve the Ph−CSO rotation) is independent of the position of mesityl, which stays essentially locked in a plane almost orthogonal to that of the CSO moiety, thus leaving sufficient room for the independent rotation of phenyl. Conversely, when the mesityl begins to rotate, the phenyl is forced to move alongside: only this second motion, responsible for the higher barrier, corresponds therefore to a correlated process in **2** and **3**.

Conclusions

Dimesityl sulfine **1** adopts a chiral conformation in solution (C_1 symmetry, as in the crystal), and the enantiomerization process, which interconverts the helical M and P antipodes, takes place via correlated pathways involving a [*Z*] one-ring flip and a two-ring flip mechanism displaying, respectively, a lower and a higher free energy of activation. The isomeric *Z* and *E* mesitylphenyl sulfines (**2** and **3**, respectively) adopt, on the contrary, an achiral C_s symmetry in solution. The corresponding topomers intercovert with a noncorrelated lower barrier rotation about the Ph−CSO bond and with a correlated higher barrier rotation about the Mes−CSO bond.

Experimental Section

Material. Dimesityl Sulfine, [**Dimesityl methanethial *S*-oxide**], (**1**)[3] and the isomeric sulfines **2** and **3**[16a,b] were prepared according to the literature.

***Z*-Mesitylphenyl methanethial *S*-oxide (2)**, mp 101 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), 7.50−7.25(5H, mult, Ph), 7.00 (2H, s, CH mes), 2.34 (3H, s, CH_3), 2.17 (6H, s, CH_3). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 195.3 (CSO), 139.5 (q), 135.4 (q), 132.8 (q), 131.1 (CH *para*), 129.4 (CH *meta*, Ph), 128.9 (CH, mes), 126.4 (q), 124.8 (CH *ortho*), 21.1 (CH_3), 20.0 (CH_3).

***E*-Mesitylphenyl methanethial *S*-oxide (3),** mp 59 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), 8.0 (2H, mult, CH ortho), 7.35−7.55 (3H, mult, Ph), 7.00 (2H, s, CH mes), 2.36 (3H, s, CH_3), 2.19 (6H, s, CH_3). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 183.5 (CSO), 140.1 (q), 139.5 (q), 134.7 (q), 131.7 (CH para), 128.8 (CH meta, Ph), 128.7 (CH, mes.), 128.2 (q), 125.2 (CH orto), 21.2 (CH_3), 20.1 (CH_3).

NMR Measurements. The ^{13}C lines at 100.6 MHz were identified by DEPT and by two-dimensional (2D) gradient heteronuclear single quantum coherence (gHSQC) pulse sequence. The configuration assignment was carried out by adding appropriate amounts of $Eu(fod)_3$[18a] to a $CDCl_3$ solution of the isomer **2** (mp 101 °C), so that a number of solutions, with increasing [**2**]/[$Eu(fod)_3$] molar ratios (up to a maximum of 1/0.6), were obtained. A linear dependence (correlation coefficient = 0.998) was observed between these ratios and the low-field displacements of the ^{13}C lines, due to the binding of the europium atom to the oxygen of the SO moiety.[3,24] The slope of the straight line correlating the displacements of the mesityl *meta* carbons signal (LIS effect[18b]) was found much larger (2.96 ppm) than that (1.12 ppm) of the signal due to the phenyl *meta* carbons. The distance between the oxygen of the SO moiety and the phenyl *meta* carbons in the *E*-isomer is equal to the corresponding distance of the mesityl *meta* carbons in the *Z*-isomer. The larger LIS effect observed for the latter proves, therefore, that the oxygen atom is closer to the mesityl than to the phenyl ring: the *Z*, rather than the *E*, configuration must be consequently assigned to the higher melting isomer **2**. Also the isomer **3** (mp 59 °C) was investigated by the same LIS method, after having identified both the *meta* ^{13}C lines of phenyl and mesityl using the previously mentioned 2D experiment. This because in the ^{1}H spectrum of **3** the *ortho* and *meta* multiplets of phenyl, as well the *meta* singlet of mesityl, were widely separated (identical assignment was also obtained by applying to **3** the same ^{13}C low-temperature experiment described for **2**). The LIS displayed by the *meta* mesityl ^{13}C line of **3** is now lower (1.65 ppm) than that of the corresponding line of phenyl (1.97 ppm), thus confirming, again in an independent manner, the *E*-configuration for the lower melting isomer. It should also be stressed that the LIS ratio $2.96/1.65 = 1.79$ (due the *meta* mesityl carbons of **2** and **3**) is essentially equal to the ratio $1.97/1.12 = 1.76$ (due to the *meta* phenyl carbons of **3** and **2**): this proves the internal consistency of the method because the ratios of the distances involved are essentially the same in both isomers. Finally the ^{1}H and ^{13}C LIS effects, experienced by the *ortho* methyl signals, were measured in both **2** and **3**. In the case of the higher melting isomer **2** the values were found much larger (3.82 ppm for ^{1}H and 4.17 ppm for ^{13}C ppm) than in the case of the lower melting isomer **3** (2.21 ppm for ^{1}H and 2.01 ppm for ^{13}C). Accordingly, **2** must have the *ortho* methyl groups in a syn and **3** in an anti relationship to the SO moiety, further establishing the *Z*-configuration for the former and the *E*-configuration for latter.

The barrier for the mesityl rotation in the *Z*-isomer **2** was measured in a C_2Cl_4/C_6D_6 (6:1 v/v) solution containing a 260:1 molar excess of Pirkle's alcohol.[20] At +65 °C the 400 MHz ^{1}H spectrum of the two *ortho* methyl lines displays a 15.8 Hz separation which, on rising the temperature from +65 to +95 °C, decreases according to a linear equation (correlation coefficient 0.995). At further high temperatures the separation increasingly deviates from linearity and simultaneously displays a line broadening indicative of an exchange process taking place. The coalescence point was eventually reached at +121 °C, and the corresponding trace was reproduced by line shape simulation (rate constant = 16 s^{-1}) using as shift difference the one extrapolated from the mentioned linear equation and as intrinsic line width that for the line of the *para* methyl group (the *ortho* methyl lines exhibit in fact the same width as that of the *para* methyl line at temperatures lower than 95 °C, where the exchange broadening effect is not yet observable). Using the method reported above, the barrier for the mesityl rotation in the *E*-isomer **3** was measured in the same solvent, using a 420:1 molar excess of Pirkle's alcohol.[20] The *ortho* methyl ^{1}H signals displayed a 17.2 Hz separation (400 MHz) at −10 °C, and simulation of the line shape at +14 °C yielded a $\Delta G^{\ddagger}$ value of 15.1 ± 0.2 kcal mol^{-1} (Table 2).

The samples for the low-temperature measurements were prepared by connecting to a vacuum line the NMR tubes containing the desired compound dissolved in a deuterated solvent (CD_2Cl_2 or acetone-d_6 for locking purpose) and condensing therein the appropriate amount of gaseous CHF_2Cl by means of liquid nitrogen. The tubes were subsequently sealed in vacuo and introduced into the precooled probe of a 300 or of a 400 MHz spectrometer operating, respectively, at 75.45 or 100.6 MHz for ^{13}C. The temperatures were calibrated by substituting the sample with a precision Cu/Ni thermocouple before the measurements.

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