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Conformational Studies by Dynamic NMR. 94.[1] Cogwheel Pathway for the Stereomutations of Durene Derivatives Containing the Mesityl Ring

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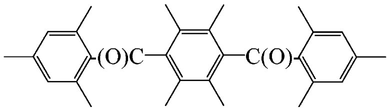
The low-temperature NMR spectra of 1,4-bis(mesitoyl)durene, **1**, and of 1,4-bis(mesitylethenyl)-durene, **2**, reveal the presence of syn and anti rotamers at the equilibrium, their relative proportions depending on the dielectric constant of the solvent. In solution the more stable rotamer of **1** is the anti whereas, in the case of **2**, the more stable is the syn. Depending on the crystallization solvent employed the more (anti) and the less stable (syn) rotamers were both observed (X-ray diffraction) in the solid state of **1**. On the other hand, only the less stable rotamer (anti) was found to be present in the solid state of **2**. As shown by MM calculations, the syn-to-anti interconversion occurs via a correlated process (cogwheel pathway) involving the mesityl-C and durene-C bond rotations: the dynamic NMR technique yields an experimental barrier of 8.2 kcal mol^{-1} for **1** and 13.1 kcal mol^{-1} for **2**. In the case of derivative **2** a second barrier, due to a second type of correlated rotation process (torsion), was also determined (8.6 kcal mol^{-1}). As a consequence of the restriction of this second torsional motion the anti rotamer of **2** displays two distinguishable NMR spectra at −133 °C, corresponding to a pair of conformers with different symmetry (anti C_i and anti C_2).

Introduction

Hindered aromatic ketones have the plane of the carbonyl group nearly orthogonal to that of the aromatic ring: the barriers for the corresponding aryl−CO bond rotation could be measured by variable-temperature NMR spectroscopy.[3] Durenes (2,3,5,6-tetramethylbenzene) substituted by two equal acyl moieties in positions 1,4 were shown, as a consequence, to display two conformational isomers (rotamers), depending on whether the two carbonyl groups are in an anti or in a syn relationship.[4] When the two acyl substituents are sufficiently bulky (e.g. in the case of the *t*-BuCO moieties) it even has been possible to achieve a physical separation of the two rotamers.[4] Recently we have reported that dimesityl ketones and related compounds adopt a propeller-like conformation that allows for the existence of conformational enantiomers interconverting into each other with a quite low barrier.[5]

We thus considered the possibility of combining these two features into the same molecule and for this purpose the 1,4-bis(mesitoyl)durene, **1**, was synthesized. This compound should in fact comprise a rotamer syn and a rotamer anti, each of which might also comprise a number of diastereomeric or enantiomeric helical conformers.



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Results and Discussion

1,4-Bis(mesitoyl)durene (1). Molecular Mechanics calculations (MMFF force field)[6] predict the existence of an energy minimum corresponding to the anti rotamer that is 0.36 kcal mol^{-1} lower than that corresponding to the minimum for the syn rotamer (Scheme 1, X = O). As shown in the scheme, the calculations also predict that in both rotamers the CO groups are symmetrically twisted with respect to the plane of durene (55° and 54° in the anti and syn rotamers, respectively) and likewise are twisted with respect to the mesityl rings (44° and 45° in the anti and syn rotamers, respectively) thus generating a propeller-like shape with a C_i symmetry for the anti and a C_2 symmetry for the syn. According to the nomenclature proposed by Biali et al.[7] they are referred to as A_u and S_u, respectively.

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[1] Part 93: Casarini, D.; Rosini, C.; Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2003**, *68*, 1815.

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

[3] Bonini, B. F.; Grossi, L.; Lunazzi, L.; Macciantelli, D. *J. Org. Chem.* **1986**, *51*, 517. Casarini, D.; Lunazzi, L.; Pasquali, F.; Gasparrini, F.; Villani, C. *J. Am. Chem. Soc.* **1992**, *114*, 6521. Casarini, D.; Lunazzi, L.; Verbeek, R. *Tetrahedron* **1996**, *52*, 2471. Leardini, R.; Lunazzi, L.; Mazzanti, A.; Nanni, D. *J. Org. Chem.* **2001**, *66*, 7879.

[4] Casarini, D.; Lunazzi, L. *J. Org. Chem.* **1996**, *61*, 6240.

[5] (a) Grilli, S.; Lunazzi, L.; Mazzanti, A.; Casarini, D.; Femoni, C. *J. Org. Chem.* **2001**, *66*, 488. (b) Casarini, D.; Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2001**, *66*, 2757. (c) Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2001**, *66*, 4444.

[6] MMFF force field, as implemented in the computer package PC-Model 7.5 (Serena Software: Bloomington, IN).

[7] Lindner, A. B.; Grynszpan, F.; Biali, S. E. *J. Org. Chem.* **1993**, *58*, 6662.

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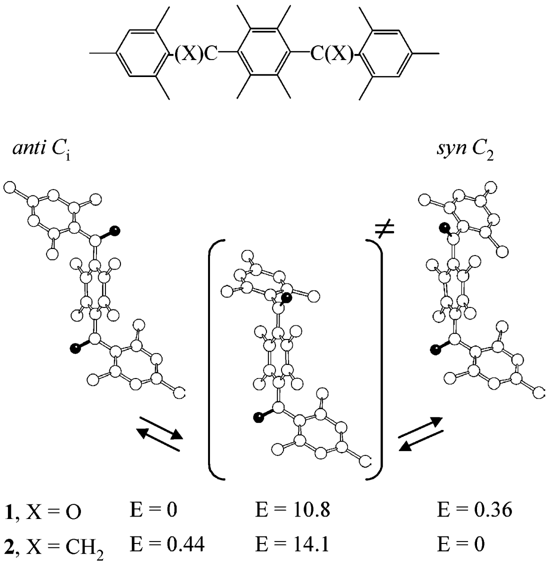
SCHEME 1. Representation of the Correlated Pathway Computed for the Anti-to-Syn Interconversion of 1 (X = O) and 2 (X = CH$_2$)[a]



[a] The hydrogen atoms are omitted for convenience and the black atoms can be either oxygen (**1**) or carbon (**2**). The computed relative energies are in kcal mol^{-1}.

To observe experimentally two different spectra for the anti and syn rotamers it is necessary to render the durene−CO bond rotation sufficiently slow in the NMR time scale. The barrier for this process would correspond to the energy difference between the transition state, having the carbonyl coplanar[8] with the durene ring, and the ground state of the more stable rotamer (i.e. A$_u$ with C_i symmetry). If this barrier is high enough as to be amenable to NMR observation at an accessible low temperature, all the signals of the anti would become distinguishable from those of the syn: the two sets of signals would obviously have a different intensity. An analogous barrier should also occur for the mesityl−CO bond rotation. The shape of the latter transition state would differ, however, from the previous one in that the carbonyl should be orthogonal to the mesityl ring.

Accordingly, if this rotation process is likewise frozen at an appropriate low temperature, the two *o*-methyl groups (positions 2,6) of the mesityl ring would become diastereotopic and should consequently display two anisochronous lines with the same intensity. Such a situation should be observable in both the anti and syn rotamers.

These two rotation processes, however, are unlikely to be independent of each other and are thus expected to undergo a correlated pathway,[7] sharing a common transition state, due to the crowding of the methyl substituents. Actually, when the three-dimensional energy surface is computed (MMFF force field[6]) as a function of these angles, it appears that driving the durene−CO dihedral angle forces also the mesityl−CO dihedral angle to be simultaneously driven in a disrotatory manner, according to the so-called "cogwheel" mechanism.[5c,9,10] As a consequence there is only a single transition state (shown in Scheme 1) and thus a single barrier for interconverting the anti (A$_u$) into the syn (S$_u$) rotamer. This pathway is conceptually the same as the correlated motion referred to as the "one-ring flip" process,[7,10,11] and the corresponding barrier is computed to be 10.8 kcal mol^{-1}, as in Table 1.

TABLE 1. Experimental and Computed (in Parenthesis) Barriers for the Stereomutation Processes in 1 and 2[a]

compd	syn/anti interconversion	torsional process
1 (X = O)	8.2 (10.8)	<5 (4.4)
2 (X = CH$_2$)	13.1 (14.1)	8.6$_5$ (11.1)[b]
		8.5 (10.5)[c]

[a] The values are in kcal mol^{-1} and refer to the exchange of the more into the less stable conformer. The errors are about ±0.15 kcal mol^{-1}. [b] These values refer to the torsional process in the major conformer syn. [c] These values refer to the torsional process in the minor conformer anti.

This value is high enough as to allow one to obtain an experimental verification, and in fact the variable-temperature NMR spectra of **1** show that the three ^{1}H methyl signals observed at ambient temperature broaden to a different extent when the temperature is lowered (Figure 1, top) and eventually split into a number of lines at −138 °C (Figure 1, bottom). Two closely spaced lines, having a different intensity, are observed for the methyl groups of durene as well as for those in the para position of the mesitylene ring. On the other hand the signal of the *o*-methyl groups of mesitylene[12] displays two pairs of lines, with the same unequal intensity as above: within each pair, however, these lines exhibit a 1:1 intensity ratio (Figure 1, bottom). Such features prove that the durene−CO bond rotation has become slow enough as to yield distinguishable spectra for the anti and syn rotamers, the intensity of the corresponding lines reflecting their different population. Furthermore the 1:1 ratio of the *o*- and *o′*-methyl lines of mesitylene also indicates that the mesityl−CO bond rotation has been frozen.

If the freezing of the latter motion had generated the A$_u$ and S$_u$ conformers of Scheme 1, the methyl signals of the durene moiety would also have appeared anisochronous. To reconcile the shape computed for these conformers with the experimental observation of a single line for the durene methyl groups in both the syn and anti rotamers, it is required that the mesityl rings still undergo a rapid rotation, with a less than 180° amplitude, about the mesityl−CO bond. For the sole purpose of distinguishing this lower rotation barrier from the previous one (i.e. the one interchanging the syn and anti rotamers) we dubbed it "torsion". Because of this rapid

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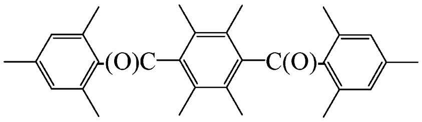
[8] This barrier is sometimes referred to as the π-barrier to indicate the possibility of conjugation, due to the planarity of the transition state. In the present case conjugation can occur in the transition state between the C=O substituent and the coplanar aromatic ring. See: Anderson, J. E.; Casarini, D.; Lunazzi, L. *Tetrahedron Lett.* **1988**, *29*, 3141.

[9] (a) Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26, (b) Mislow, K. *Chemtracts Org. Chem.* **1989**, *2*, 151. (c) Glaser, R. In *Acyclic Organonitrogen Stereochemistry*; Lambert, J. B., Takeuchi, Y., Eds.; VCH: New York, 1992; Chapter 4, p 123.

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

[11] Grilli, S.; Lunazzi, L.; Mazzanti, A.; Mazzanti, G. *J. Org. Chem.* **2001**, *66*, 748 and references quoted therein.

[12] This signal was unambiguously assigned by a 2D heteronuclear correlation (gHMBC sequence) showing the presence of a three-bond long-range coupling between these methyl hydrogens and the aromatic CH carbon of mesitylene. This coupling was not observed in the case of the methyl hydrogens of durene.



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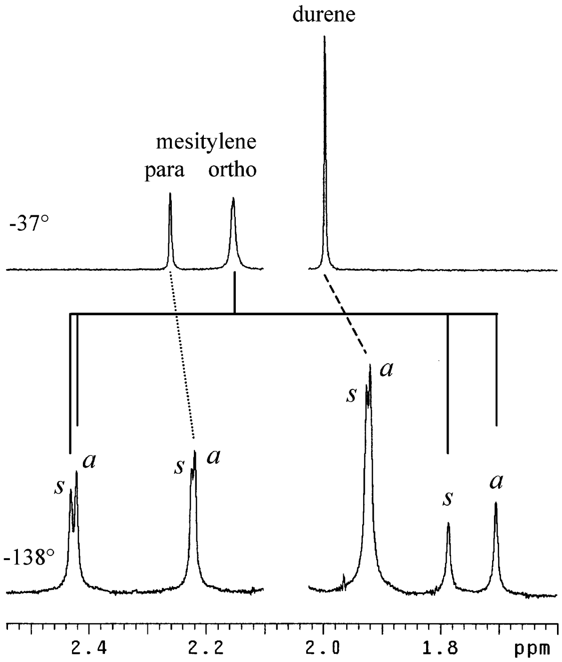

FIGURE 1. ^{1}H NMR spectrum (400 MHz in CHF_2Cl/acetone-d_6) of the methyl region of **1**. The three methyl lines observed at −37 °C (top trace) split at −138 °C (bottom trace), showing the presence of the anti (*a*) and syn (*s*) rotamers in a 55:45 proportion (the signal of acetone at about 2.06 ppm has been omitted for the sake of clarity).

torsional process the dynamic symmetry for the anti rotamer should be actually considered of C_{2h} type and that for the syn of C_{2v} type.

To assign the more intense of the two low-temperature NMR spectra to the anti or to the syn structure we considered that the proportion of the latter would increase with the dielectric constant of the environment because the dipole moment of the syn rotamer is expected to be larger than that of its anti companion. Indeed we observed that in a CHF_2Cl/C_6D_6 solution the rotamer ratio is 1.8:1 at −138 °C, whereas in the more polar CHF_2Cl/acetone-d_6 solution the ratio becomes 1.2:1 at the same temperature (Figure 1). Having increased its population in a more polar medium, the minor rotamer should correspond to the syn structure:[13] this conclusion agrees with the prediction of the MM calculations for A_u and S_u of Scheme 1.

Satisfactory line shape simulation of the spectra of **1** could be achieved,[14] in the temperature range −80 to −110 °C, by using the same value for the rate constant that exchanges the signals involved in the mesityl−CO rotation (i.e. the 1:1 lines for the *o*- and *o′*-methyl groups of mesitylene) as well as the signals involved in the anti-to-syn exchange (i.e. all other lines having a different intensity ratio). This confirms, within the experimental uncertainty, that the two processes are not independent but share a common transition state and thus exhibit a unique barrier, as expected on the basis of the correlated pathway predicted by computations. The experimental $\Delta G^‡$ value for this process (Table 1) was found to be 8.2 kcal mol^{-1}:[15] in the Eyring equation a transmission coefficient of $^1/_2$ was used to account for the fact that rotation of either of the two durene−CO bonds allows interconversion[13,16] (although the computations overestimate this barrier by 2.6 kcal mol^{-1}, the difference is quite acceptable given the approximations involved in the MM approach). It should also be mentioned that the $\Delta G^‡$ value measured for **1** is lower than that reported for the same type of anti-to-syn interconversion occurring in less hindered durene derivatives:[4] for instance in the 1,4-diacetyl durene the barrier is 10.9 kcal mol^{-1}. This further supports the existence of correlated rotations in **1** since this type of pathway renders more facile the interconversion processes.

The low-temperature NMR spectra of **1** do not show evidence of the propeller shape that, according to calculations, is adopted by the two rotamers of **1**. To observe this situation both the lower barrier motion (torsion) about the mesityl−CO bond and that about the durene−CO bond should be frozen. The first type of motion has a transition state with the mesityl and carbonyl planes parallel with each other whereas the second has a transition state with the plane of durene orthogonal to that of carbonyl. If the torsional process about the durene−CO bond is frozen, the methyl groups of durene in position 2,6 will become diastereotopic in both the syn and anti rotamers (the same will also occur for the methyl in positions 3,5). As a consequence the corresponding NMR signals would split into a 1:1 pair, providing evidence for the helical shape. If also the torsional process about the mesityl−CO bond is simultaneously frozen, additional conformers are expected to be obtained.

According to MM calculations,[6] these so-called torsional processes are also correlated and, as a consequence, two possible energy minima for the anti and two for the syn rotamer are expected. In other words, in addition to the meso A_u rotamer (C_i) of Scheme 1, the freezing of the two correlated torsional processes would yield a second anti conformer (A_l, C_2 racemic),[7] which is 3.4 kcal mol^{-1} less stable. Likewise, in addition to the racemic S_u rotamer (C_2) it is also possible to have a second syn conformer (S_l, C_s meso)[7] that is 3.5 kcal mol^{-1} less stable.

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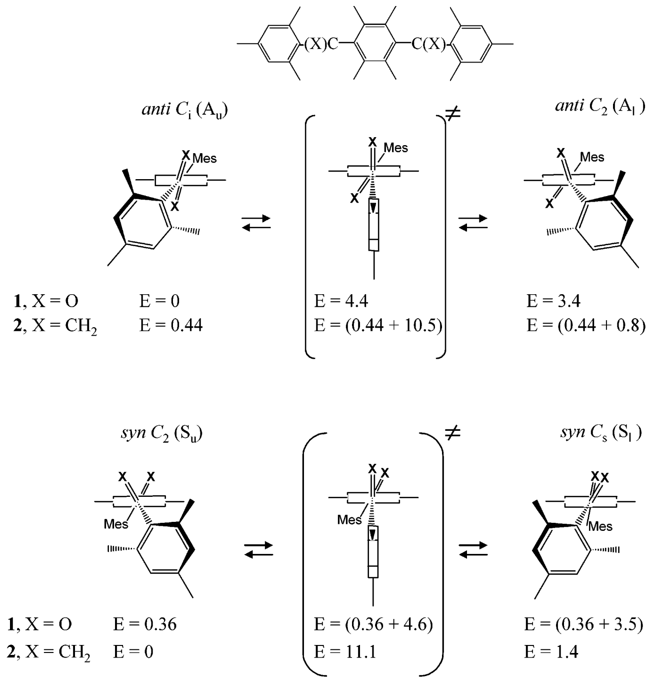
[13] Casarini, D.; Lunazzi, L. *J. Org. Chem.* **1996**, *61*, 6240.

[14] QCPE program no. 633, Indiana University: Bloomington, IN.

[15] As was often observed in conformational processes the $\Delta G^‡$ value is independent of temperature, indicating a negligible $\Delta S^‡$ value. See: Hoogosian, S.; Bushweller, C. H.; Anderson, W. G.; Kigsley, G. *J. Phys. Chem.* **1976**, *80*, 643. Lunazzi, L.; Cerioni, G.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7484. Bernardi, F.; Lunazzi, L.; Zanirato, P.; Cerioni, G. *Tetrahedron* **1977**, *33*, 1337. Lunazzi, L.; Magagnoli, C.; Guerra, M.; Macciantelli, D. *Tetrahedron Lett.* **1979**, 3031. Anderson, J. E.; Tocher, D. A.; Casarini, D.; Lunazzi, L. *J. Org. Chem.* **1991**, *56*, 1731. Cremonini, M. A.; Lunazzi, L.; Placucci, G.; Okazaki, R.; Yamamoto, G. *J. Am. Chem. Soc.* **1992**, *114*, 6521. Borghi, R.; Lunazzi, L.; Placucci, G.; Cerioni, G.; Foresti, E.; Plumitallo, A. *J. Org. Chem.* **1997**, *62*, 4923.

[16] Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **1997**, *62*, 7592. Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **1998**, *63*, 4991. Bonini, B. F.; Fochi, M.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2000**, *65*, 2596. Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2000**, *65*, 3563. Dell'Erba, C.; Gasparrini, F.; Grilli, S.; Lunazzi, L.; Mazzanti, A.; Novi, M.; Pierini, M.; Tavani, C.; Villani, C. *J. Org. Chem.* **2000**, *65*, 1663. Grilli, S.; Lunazzi, L.; Mazzanti, A.; Pinamonti, M. *J. Org. Chem.* **2002**, *67*, 5733.

SCHEME 2. Schematic Representation of the Correlated Torsional Processes Occurring in the Anti and Syn Forms of 1 (X = O) and 2 (X = CH$_2$)[a]



[a] The second mesitylene ring has been indicated as Mes for simplicity. The computed relative energies are in kcal mol^{-1}.

These conformers, and the computed transition states through which their exchange takes place, are displayed in Scheme 2. The large energy difference between the ground states predicted by calculations (3.4 kcal mol^{-1}) suggests, however, that only the more stable rotamers A$_u$ and S$_u$ are likely to be populated in the case of **1**. Accordingly, the only detectable feature due to the freezing of the torsional process would be the 1:1 splitting of the durene methyl line.

Computations predict, however, that the energy of the transition state for the correlated torsion pathway is only 4.4 kcal mol^{-1} higher than that of the ground state (Table 1), a value conceivably too low to produce any detectable effect on the NMR spectra. Thus the absence of 1:1 splitting of the methyl durene lines in the NMR spectrum of **1**, even at −180 °C, suggests an experimental barrier of less than 5 kcal mol^{-1} (Table 1).[17]

In view of the inconclusive result of the latter NMR experiment in solution, the proof that this molecule actually adopts a propeller-like shape had to be searched by X-ray diffraction in the solid state. When the compound was crystallized from ethanol, which has a high dielectric constant, the structure observed is that of the more polar conformer S$_u$ (C_2 racemic). The diffraction data also indicate that there are two independent syn (racemic) structures having slightly different angles and bond lengths (Figure 2).

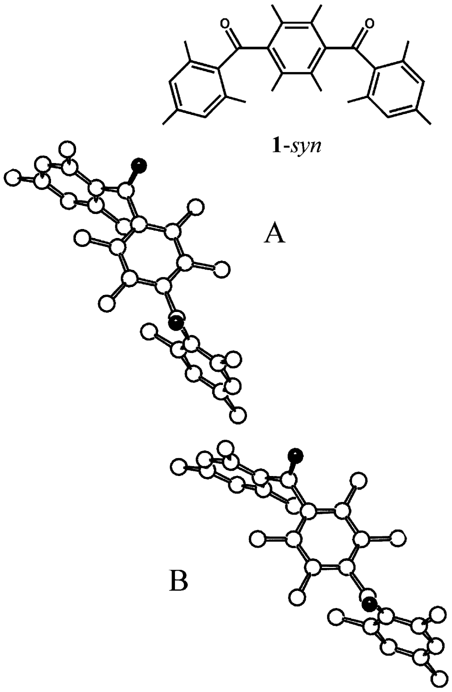


FIGURE 2. X-ray diffraction (single crystals obtained from ethanol) shows that the crystal cell of **1** comprises two slightly different syn helical structures (S$_u$ type), identified as A and B (see text).

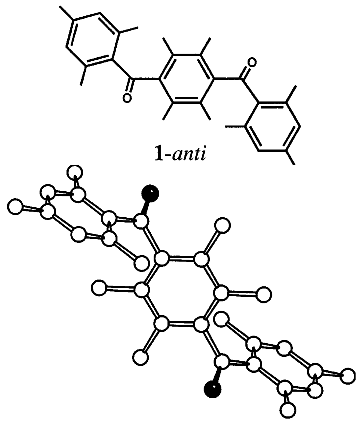


FIGURE 3. X-ray diffraction structure of **1** (single crystals obtained from chloroform) showing the anti (C_i meso) helical structure (A$_u$ type).

Both structures have dihedral angles extremely similar to the computed ones, thus giving evidence of a propeller-like shape, which consequently entails the existence of two nonsuperimposable antipodes: in the crystal cell of **1** there are in fact two pairs of enantiomerically related molecules (see Supporting Information).

On the other hand, when the crystals of **1** are obtained from chloroform, which has a much lower dielectric constant, the X-ray diffraction indicates that the structure is that of a meso anti (C_i symmetry), also displaying a propeller-like shape (Figure 3), very similar to the computed one. The possibility of detecting the structures of both rotamers by using different crystallization solvents is probably a consequence of the fact that in more polar solutions the rotamer syn is definitely more abundant that in the less polar solutions, whereas the opposite occurs for the rotamer anti.

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(17) Obviously it cannot be excluded that the negative results might be a consequence of a separation of the corresponding lines being smaller than the line width, which is quite large at −180 °C (about 40−50 Hz in a CHF$_2$Cl/CHFCl$_2$/C$_6$D$_6$ solution) owing to the increased viscosity.

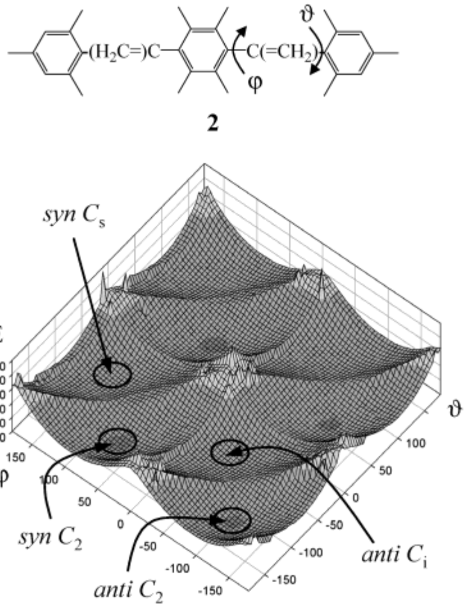
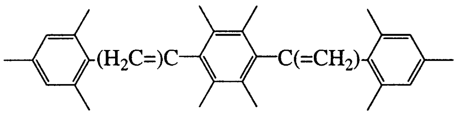


FIGURE 4. MM computed energy (kcal mol^{-1}) surface of **2** as function of the angles ϑ and φ. The four minima, corresponding to the four possible conformers, are indicated. The three bent arrows refer to the three conformers whose spectra were experimentally observed.

1,4-Bis(mesitylethenyl)durene (2). It is conceivable to predict that substitution of the C=O with the bulkier C=CH$_2$ moiety should greatly increase the barrier for all the stereomutation processes, and for this purpose we synthesized 1,4-bis(mesitylethenyl)durene, **2**.



2

As shown in Schemes 1 and 2, the MM computed[6] barrier for the syn-to-anti interconversion is 14.1 kcal mol^{-1} and those for the so-called torsional process are 11.1 and 10.5 kcal mol^{-1} for the syn and anti rotamers, respectively. As it appears from the computed tridimensional energy surface reported in Figure 4, all these are correlated processes (cogwheel pathway[7,9]) because they follow a diagonal pathway. In particular both the higher energy syn-to-anti interconversion and the lower energy correlated torsional processes are predicted to follow a disrotatory one-ring-flip pathway,[5c,9–11] since the latter appears to have a computed barrier that is lower than the barrier of the other possible process (i.e. the two-ring-flip mechanism).[5c, 9–11]

That the correlated torsional process of compounds **1** and **2** corresponds to a one-ring-flip pathway, as predicted by the theory, also can be deduced from experimental evidence. In fact the observation of anisochronous lines for the *o*-methyl groups of the mesitylene ring is compatible only with the dynamic symmetry of the one-ring-flip process: in the case of a two-ring-flip process these lines would have appeared isochronous. Although these computations might have the tendency of overestimating the barriers, the computed values for **2** are predicted to be high enough as to be amenable to an experimental verification. It is thus expected that also the correlated torsion, which had escaped detection in the case of **1**, should become NMR visible in the more hindered compound **2**.

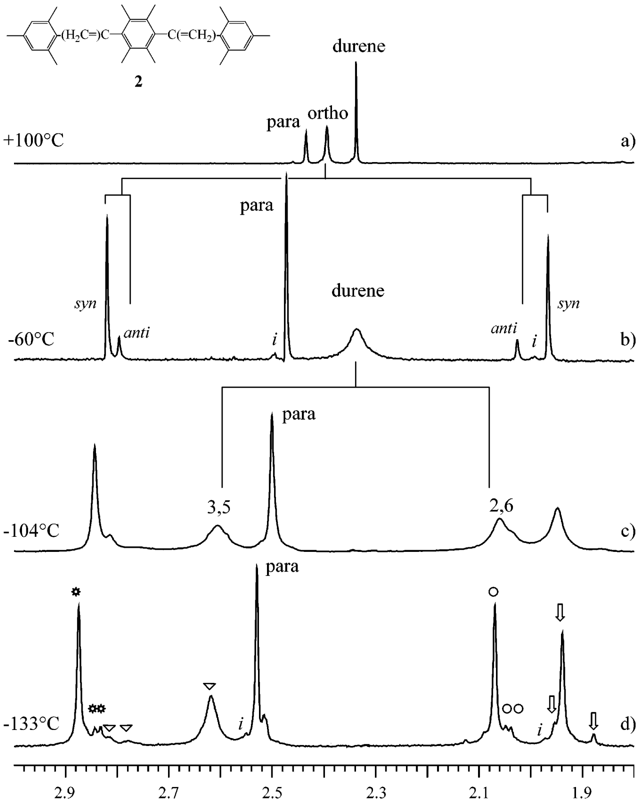


FIGURE 5. (a) ^{1}H NMR (400 MHz) methyl region spectra of **2** in C_2Cl_4 at +100 °C. The *o*- and *p*-methyl signals are those of the mesitylene moiety. (b–d) Temperature dependence of the same region in $CHF_2Cl/CHFCl_2/C_6D_6$. At −60 °C (trace b) the *o*-methyl signal of mesitylene splits into a pair of more intense and of less intense lines (rotamers syn and anti, respectively). At −104 °C (trace c) the signals of the four methyl groups in positions 2,3,5,6 of durene split into a pair of lines arbitrarily identified as 3,5 and 2,6. At −133 °C (trace d) the lines with the same symbol refer to the same type of methyl group: the major lines are singlet (syn C_2) and the minor lines doublets of slightly unequal intensity (anti C_2 and anti C_i). Impurities are identified by the letter *i*.

Even at ambient temperature the ^{1}H NMR spectrum of **2** shows a number of exchange-broadened signals. On cooling to about −60 °C the single signal of the four *o*-methyl groups of mesitylene[12] splits into a 1:1 pair of more intense lines and a 1:1 pair of less intense lines (Figure 5). This indicates that the correlated rotation about the durene−CCH$_2$ and mesityl−CCH$_2$ single bonds has been frozen, generating the anti (C_i symmetry) and syn (C_2 symmetry) rotamers displayed in Scheme 1 for X = CH$_2$ (however, the occurrence at this temperature of a rapid torsional process would make the dynamic symmetry of the anti be considered of C_{2h} type and that of the syn rotamer of C_{2v} type). This feature is the same as observed in the case of **1**, but it occurs at a higher temperature, in agreement with the expectation of a larger syn−anti interconversion barrier in the case of **2**. The methyl groups of durene and the methyl groups in the para position of mesitylene yield single signals since the corresponding shift differences for the two rotamers are lower than the line width.[18]

Contrary to the case of **1**, calculations had predicted that the S_u rotamer of **2** is more stable (by 0.44 kcal mol^{-1}) than its A_u companion (see Scheme 1, X = CH_2) and for this reason the more intense pair of *o*-,*o*′-methyl lines of mesitylene in Figure 5 were labeled syn and the less intense were labeled anti. This assignment was confirmed by the observation that the rotamer ratio is 1.8 in toluene-d_8 and 1.75 in CS_2 at −60 °C but 2.9 and 3.2 in CD_2Cl_2 and acetone-d_6, respectively, at the same temperature.

This trend is opposite to that found in the case of **1** in that the proportion of the major rotamer increases with an increase in the dielectric constant[19] of the solvent, as expected if the predominant rotamer has the syn structure.

Line shape analysis allowed us to obtain the rate constants for the syn-to-anti interconversion at various temperatures [15] that yielded an activation energy of 13.1 kcal mol^{-1} (again a $^1/_2$ transmission coefficient was employed[13,16]), in fair agreement with the theoretical prediction of 14.1 kcal mol^{-1}. As anticipated, this barrier is definitely higher than that measured for the analogous process in **1**.

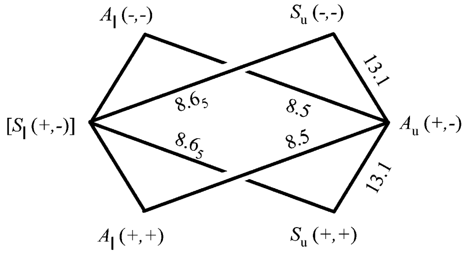
When the spectrum of **2** is obtained at temperatures lower than −60 °C, the signal of the four methyl groups of durene broadens considerably and eventually splits into a pair of 1:1 lines at −104 °C (Figure 5) due to the torsional process about the durene−CCH_2 bond becoming slow in the NMR time scale (as discussed for the case of **1** this process is conceivably correlated with the analogous torsional process occurring about the mesityl−CCH_2 bond).

Such a feature is in keeping with the propeller-like conformation predicted by theory, where the pair of methyl groups in positions 2,6 of durene (and likewise those in positions 3,5) are expected to be diastereotopic in the ground state conformation.

At about −133 °C a further splitting of some of the minor signals also becomes visible. This is a consequence of the same correlated torsional process mentioned above. This effect is visible at a lower temperature, with respect to the 1:1 separation of the methyl durene signals, because the corresponding chemical shift differences are much smaller. As shown in Scheme 2, when the correlated torsional process is frozen, not only the methyl groups of durene become diastereotopic but also a pair of conformers is expected to be generated for the anti (C_i and C_2 symmetry) and for the syn (C_2 and C_s symmetry) arrangement. In other words the dynamic anti symmetry (C_{2h}) and the dynamic syn symmetry (C_{2v}) are broken at low temperature so that the static symmetries of the ground state conformers can be revealed.

In the spectrum of Figure 5 at −133 °C, however, the more intense signals due to the syn rotamer do not display such additional splitting, which is detectable only for the minor signals of the rotamer anti. This splitting is particularly evident for the minor signal of the *o*′-methyl groups of mesitylene (starred lines at 2.83, 2.85 ppm), for the minor signal of the methyl group of durene (lines at 2.78, 2.82 ppm arbitrary labeled as positions 3,5), for the minor signal of the methyl groups of durene (lines at 2.04, 2.05 ppm arbitrarily labeled as positions 2,6), and for the minor signal of the *o*-methyl groups of mesitylene (arrowed lines at 1.88, 1.95 ppm).[20]

SCHEME 3[a]



[a] The numbers refer to the experimental barriers (in kcal mol^{-1}) for the interconversion of the more into the less stable conformers of compound **2**.

On the basis of the theoretical predictions concerning the relative stability of the conformers of **2**, as reported in Scheme 2, the computed energy difference between the two syn conformers S_u, S_l is quite high (1.4 kcal mol^{-1}), indicating that only S_u should be essentially populated. As a consequence, when the correlated torsional process is frozen, the major signals would correspond only to those of S_u, the population of S_l being negligible. In this case evidence of the frozen torsional process is given solely by the anisochronicity of the durene methyl lines. On the other hand, the computed energy difference between the two anti conformers A_u, A_l is significantly lower (its value is almost halved, being 0.8 kcal mol^{-1}) and this makes plausible that, in addition to the anisochronicity of the durene methyl signals, the signals of both species become visible when the correlated torsional process is frozen at low temperature.

Line shape analysis provided a barrier of 8.6_5 kcal mol^{-1} for the correlated torsional process involving the major rotamer syn (Table 1) and 8.5 kcal mol^{-1} for the same process involving the minor rotamer anti. Within the experimental uncertainty these values are obviously equal: the difference of 0.6 kcal mol^{-1} predicted by the theory for these two barriers (i.e. 11.1 and 10.5 kcal mol^{-1}, as in Table 1) is thus slightly overestimated and is a consequence of the approximations involved in the computations. The values computed for this process, however, are in the same range as those determined experimentally and correctly predict that this barrier is lower than that for the syn-to-anti interconversion, as observed experimentally.

Borrowing from the theoretical scheme proposed by Biali et al,[7] the results obtained for **2** are represented (see Scheme 3) as an experimental version of their graph, where each vertex corresponds to a conformer and each edge to a barrier (S_l is placed in square brackets to indicate that it was not experimentally detected).

The single-crystal X-ray structure of **2** shows that the rotamer observed in the solid state is A_u, with a C_i symmetry (see Figure 6). The structure present in the

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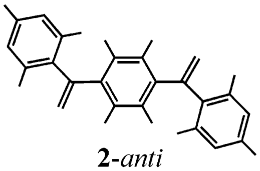
(18) In the case of **1** these separations were barely detectable, being only 0.005 ppm for the *p*-methyl signals of mesitylene and 0.006 ppm for the methyl signals of durene (see Figure 1).

(19) *Landolt-Börnstein*, Band II, Teil 6; Springer-Verlag: Berlin, Germany, 1959.

(20) The two minor lines of the *p*-methyl group of mesitylene (at 2.55 ppm) are so close as to make their separation barely distinguishable.



2-*anti*

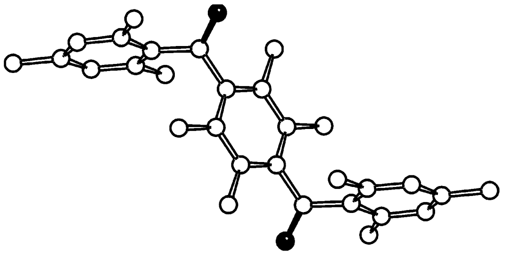


FIGURE 6. Single-crystal X-ray structure of **2** showing the propeller-like shape of the anti C_i rotamer (A_u type).

crystal corresponds to that of the less abundant rotamer observed at the equilibrium in solution.

The X-ray structural determination, combined with the knowledge of the syn-to-anti interconversion barrier (13.1 kcal mol^{-1}), offers the opportunity of testing in an independent way the assignment of the syn structure to the more abundant rotamer in solution. From the measured barrier, in fact, the half-lifetimes of the rotamers are estimated to be close to 5 min at about −85 °C. Thus the very same crystal of **2** used for X-ray diffraction (which contains only the rotamer anti) was dissolved in CD_2Cl_2 at this temperature[21] and the sample transferred as quickly as possible into the probe of the NMR spectrometer, cooled to −90 °C. In this way the system should not have sufficient time to reach a complete equilibrium and a proportion of the anti rotamer, greater than that expected at the equilibrium, would consequently be observed.

Indeed we measured in this experiment an initial 3.5:1 ratio, and observed a decreasing of the proportion of the minor rotamer with time, until a 5.2:1 ratio[22] was obtained when the equilibrium conditions were finally achieved. This allowed us to identify the minor rotamer as that having the same structure (anti) observed in the single crystal by X-ray crystallography, a result in agreement with the previous assignment.

Conclusions

In both compounds **1** and **2** we have been able to observe, by X-ray diffraction, the crystal structure of the less stable of the two rotamers (syn and anti, respectively) detected in solution by low-temperature NMR spectroscopy. Although other examples of this type have been reported,[23] such a feature is not that usually observed. MM calculations confirm that the structures of the more and of the less stable rotamers correspond to those determined by NMR in solution. The syn−anti interconversion barriers of rotamers of **1** and of **2** were experimentally determined by line shape analysis of the temperature-dependent NMR spectra, and the corresponding pathways are believed to occur via a cogwheel mechanism, identified as the one-ring-flip process. In the case of the hydrocarbon **2** it was observed that at lower temperatures another motion (dubbed correlated torsion) takes place with the same mechanism, and a value for this second barrier was experimentally determined.

Experimental Section

Materials. 1,4-Bis(mesitoyl)-2,3,5,6-tetramethylbenzene (1). 1,4-Dibromodurene (7 mmol in 40 mL of dry THF) was first reacted with *n*-BuLi at −78 °C (7 mmol, solution 1.6 M in hexane), then with mesitylaldehyde (10 mmol in 5 mL of dry THF). After the temperature was raised, the mixture was treated with NH_4Cl, extracted with ether, and dried (Na_2SO_4) to give the 1-bromo-4-methylhydroxymesityl-2,3,5,6-tetramethylbenzene. The intermediate was treated again with *n*-BuLi at −78 °C and then with mesitylaldehyde to give, after workup, 1,4-bis(methylhydroxymesityl)-2,3,5,6-tetramethylbenzene. The diol (4 mmol in 40 mL of CH_2Cl_2) was then treated with PCC (10 mmol). After 1 h, Et_2O was added to the mixture and the solution was filtered on decalite and concentrated at reduced pressure. The crude product was purified by use of silica gel chromatography (petroleum ether/Et_2O 30/1) to give **1** (2.5 mmol, overall yield over 1,4 dibromodurene 35%). Single crystals suitable for X-ray diffraction were obtained by slow evaporation from absolute ethanol or chloroform.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03 (12H, s), 2.19 (12H, s), 2.29 (6H, s), 6.87 (4H, s). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 17.63 (CH_3), 21.71 (CH_3), 22.24 (CH_3), 130.56 (CH), 132.19 (Cq), 137.23 (Cq), 138.2 (Cq), 141.13 (Cq), 144.22 (Cq), 202.6 (CO). Anal. Calcd for $C_{30}H_{34}O_2$: C, 83.79; H, 9.23. Found: C, 83.84; H, 9.15. Mp 184−186°C (from ethanol).

1,4-Bis(mesitilvinyl)-2,3,5,6-tetramethylbenzene (2). A solution of **1** (2.5 mmol in 15 mL of dry hexane) was treated with MeLi (8 mmol in Et_2O) and heated to reflux for 3 h.[24] The mixture was subsequently quenched with water, extracted with Et_2O, dried (Na_2SO_4), and purified on a silica gel chromatography column (petroleum ether/Et_2O 10/1) to obtain 1,4-bis(1-hydroxyethylmesityl)-2,3,5,6-tetramethylbenzene. The intermediate diol (0.35 mmol in 20 mL of $CHCl_3$) was then treated with P_2O_5 (5 mmol) for 15 h and the solution was filtered and concentrated at reduced pressure. Crystallization from acetone yielded **2** as a white solid. Single crystals suitable for X-ray diffraction were obtained by slow evaporation from acetone.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.10 (12H, s), 2.22 (6H, s), 5.50 (2H, d, $J = 4.0$ Hz), 5.60 (2H, d, $J = 4.0$ Hz), 6.81 (4H, s). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 18.95 (CH_3), 20.83 (CH_3), 22.0 (CH_3), 125.37 (CH_2), 129.61 (CH), 132.78 (Cq), 135.83 (Cq), 136.33 (Cq), 141.28 (Cq), 144.91 (C_q). Anal. Calcd for $C_{32}H_{38}$: C, 89.80; H, 10.20. Found: C, 89.82; H, 10.18. Mp 190−192 °C.

NMR Measurements. The assignment of the ^{13}C spectra was carried out by DEPT and 2D heteronuclear correlation (gHMBC sequence). The samples for the low-temperature measurements were prepared by connecting the NMR tubes containing the compound and some deuterated solvent for

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[21] Methylene chloride was selected because, even at temperatures in the range −80 to − 85 °C, it is capable of dissolving compound **2** quite rapidly and is still fluid enough as to yield sufficiently resolved spectra for distinguishing the signals of the syn from those of the anti form. At lower temperatures the time required to dissolve the compound was too long, thus allowing the equilibrium to be established before the sample could be transferred into the NMR probe.

[22] The conformer ratio for the equilibrium in CD_2Cl_2 increases from 2.9:1 to 5.2:1 by lowering of the temperature from −60 to −90 °C. The more stable species increases its proportion not only according to the Boltzamann equation but also because of the larger value of the dielectric constant at lower temperatures.[19]

[23] Taha, M.; Marks, V.; Gottlieb, H. E.; Biali, S. E. *J. Org. Chem.* **2000**, *65*, 8621. Marks, V.; Gottlieb, H. E.; Melman, A.; Byk, G.; Cohen, S.; Biali, S. E. *J. Org. Chem.* **2001**, *66*, 6711. Marks, V.; Nahmany, M.; Gottlieb, H. E.; Biali, S. E. *J. Org. Chem.* **2002**, *67*, 7898.

[24] Roberts, R. M.; El-Khawaga, A. M.; Roengsumram, S. *J. Org. Chem.* **1984**, *49*, 1380.

locking purpose to a vacuum line and condensing therein the gaseous solvents (CHF_2Cl and $CHFCl_2$) by means of liquid nitrogen. The tubes were subsequently sealed in vacuo and introduced into the precooled probe of the spectrometer. The temperatures were calibrated by substituting the sample with a precision Cu/Ni thermocouple before the measurements. Complete fitting of the dynamic NMR line shape was carried out with use of a PC version of the DNMR-6 program.[14]

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Supporting Information Available: Crystallographic data and ORTEP drawings for compounds **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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