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Stereomutations of Two-Bladed Propeller Derivatives: Ortho-Substituted Diaryl Ethylene and Diaryl Ketone

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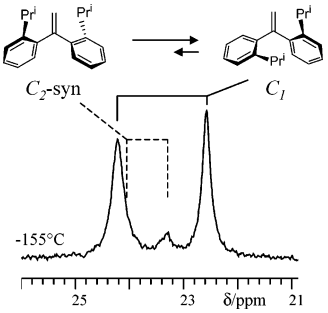

Stereochemical analysis, supported by ab initio computations, predicts the existence of three possible stable helical conformers for *o*,*o*′-diisopropyl-1,1′-diphenylethylene (**1**) and *o*,*o*′-diisopropylbenzophenone (**2**). At low temperature the NMR spectra of **1** showed distinct sets of signals for these conformers, thus allowing the measurement of the three barriers involved in the related stereomutation processes to be obtained ($\Delta G^{\ddagger} = 6.45$, 4.65, and ≤ 4.0 kcal mol^{-1}). The NMR spectra also indicate that the asymmetric conformer (C_1 point group) is the most stable one in solution, as anticipated by calculations. X-ray diffraction confirmed that this structure is that adopted in the crystalline state. On the other hand, *o*,*o*′-diisopropylbenzophenone (**2**) is predicted by calculations to exist essentially as a C_2-type conformer, a result that was confirmed by the low-temperature NMR spectra. The interconversion barrier for the enantiomeric forms of this conformer was also measured ($\Delta G^{\ddagger} = 6.3_5$ kcal mol^{-1}).

Introduction

It has been shown that compounds comprised of two mesityl substituents bonded to trigonal[2,3] or tetrahedral[4−6] moieties adopt conformations resembling a two-bladed propeller that entails the existence of a pair of conformational enantiomers. Their interconversion takes place via a correlated rotation process of the two mesityl rings, often referred to as cogwheel pathway.[7,8] When only one ortho substituent is present in each phenyl ring, rather than two as in mesitylene, three possible helical conformers can be, in principle, conceived owing to the lower molecular symmetry.

To study the stereodynamic consequences of such a situation, we investigated the 1,1-diaryl ethylene **1** and the diaryl ketone **2**, where the aryl group is a 2-isopropylphenyl moiety (Chart 1).

The isopropyl group was selected as a substituent because it is an appropriate NMR probe[9] (both at the ^{1}H and ^{13}C frequency) to detect the molecular dissymmetry and also because it is bulkier than the methyl groups of

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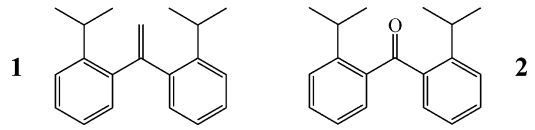
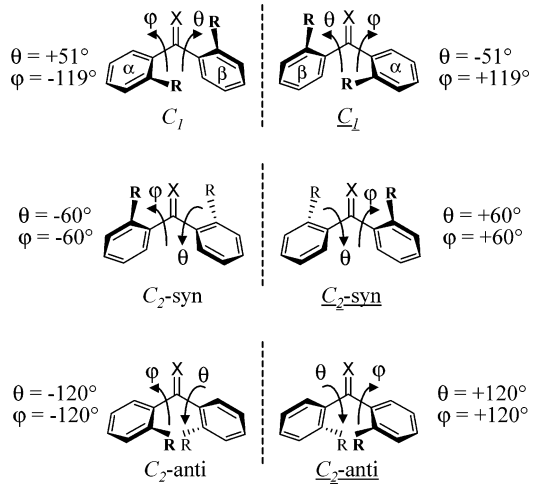
CHART 1



SCHEME 1. Schematic Representation of the Three Enantiomeric Pairs of Stable Conformers of 1 (X = CH_2, R = *i*-Pr) and 2 (X = O, R = *i*-Pr)[a]



[a] The reported θ and φ dihedral angles are those computed for **1**. The values computed for **2** are $\theta = |36°|$, $\varphi = |126°|$ for C_1; $\theta = \varphi = |40°|$ for C_2-syn; and $\theta = \varphi = |128°|$ for C_2-anti.

mesitylene, thus allowing the NMR investigation of the stereodynamic processes to be carried out at conveniently accessible low temperatures.

The lower symmetry of the aromatic substituent with respect to the mesityl substituent mentioned above[2−6] should allow the determination of not only the rotational threshold mechanism (in Mislow's terminology[7a−c,8a−c] this corresponds to the pathway of the lowest activation energy) but also higher energy processes as well.

Results and Discussion

The stereochemical analysis indicates that, in principle, three helical conformers might be populated (Scheme 1) and ab initio calculations[10] (see details in the Experimental Section and in the Supporting Information) confirm the existence of three energy minima for both **1** and **2**. Two such conformers belong to the C_2 point group: one (C_2-syn) has the isopropyl substituents close to and the other (C_2-anti) remote from the C=CH_2 or C=O moiety. The third conformer does not have any element of symmetry (C_1 point group). Each of these conformers exists as a pair of enantiomers, as shown in Scheme 1, where the ortho substituent corresponds, in this case, to the isopropyl group.

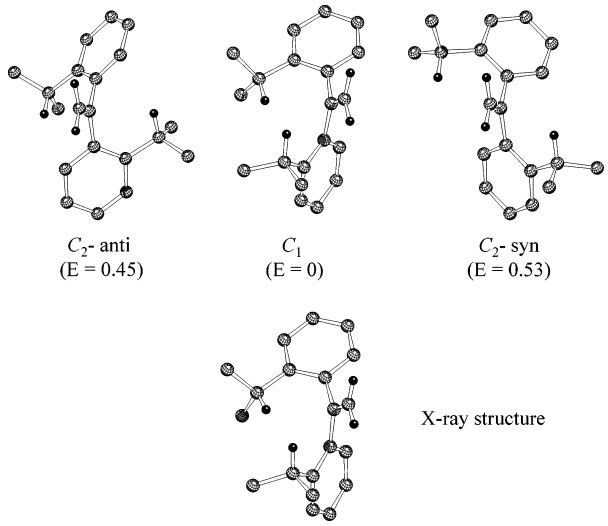


FIGURE 1. Top: Ab initio computed structures of the three possible energy minima of **1** with the relative energies (E) in kcal mol^{-1}. Bottom: X-ray crystal structure of **1** (for convenience only the methine isopropyl and the ethylenic hydrogens are displayed).

TABLE 1. Experimental and Computed Barriers (kcal mol^{-1}) for the Dynamic Processes Occurring in 1

	[α] one-ring flip of C_1[a]	two-ring flip of C_1[b]	two-ring flip[c] of C_2-syn and C_2-anti
exptl	$6.4_5 \pm 0.15$	$4.6_5 \pm 0.15$	≤4.0
calcd	8.0	5.4	2.9

[a] Barrier required for the interconversion of C_1 into the pair of C_2 conformers as well as for the enantiomerization of the conformers C_2-syn and C_2-anti (see text). [b] Barrier corresponding to the enantiomerization of C_1. [c] Barrier corresponding to the interconversion of C_2-syn into C_2-anti.

Ab initio calculations also predict that the asymmetric C_1 conformer of **1** is the most stable, whereas the less stable C_2-anti and C_2-syn conformers should have essentially the same population, their relative energies (computed with respect to that of C_1) being 0.45 and 0.53 kcal mol^{-1}, respectively (Figure 1).

X-ray diffraction (Supporting Information) shows that in the crystal cell of **1** there are two molecules in the enantiomeric relationship and that the compound adopts the same asymmetric conformation that the theory had predicted to be the most stable. The experimental structure obtained from X-ray (Figure 1, bottom) analysis is essentially equal to that derived from calculations.

Inspection of molecular models, supported by the results of calculations, indicates that the barrier for the reciprocal interconversion of the C_2-syn and C_2-anti conformers of **1** is quite low, the computed value for this two-ring flip process being 2.9 kcal mol^{-1} (Table 1). The transition state for this process, labeled TS-D, is sketched in Scheme 2, together with its enantiomeric

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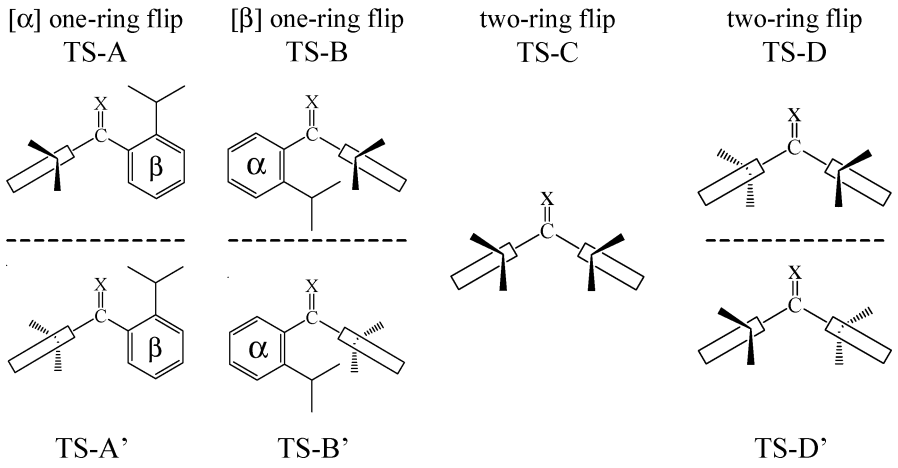
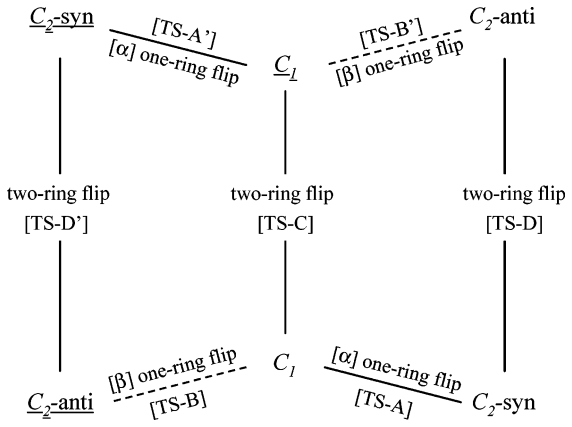
SCHEME 2. Representation of the Transition States of 1 (X = CH_2) and 2 (X = O)



SCHEME 3. Possible Pathways for the Stereomutations of 1 (X = CH_2)



partner TS-D′. As indicated in Scheme 3 these transition states are visited respectively when the C_2-syn conformer exchanges with the C_2-anti. Because of such a low interconversion barrier, this pair of conformers can be treated, for many purposes, as a single averaged conformation having a "dynamic" C_2 symmetry. Such a fast process, in fact, would become slow enough to reveal the existence of the two static C_2-syn and C_2-anti conformers in a NMR spectrum only at extremely low temperatures.

On the other hand, a higher barrier is expected to occur for the interconversion of the asymmetric C_1 into the pair of C_2 conformers since this pathway corresponds to the one-ring flip process requiring that one aryl ring crosses over the plane containing the $=CH_2$ moiety. This pathway can be achieved, in principle, by visiting either of two alternative transition states: (i) TS-A (and its enantiomeric form TS-A′), where the dihedral angle θ between the β ring and the C=CH_2 plane (as defined in Scheme 1) has become about 0° (see Scheme 2), and (ii) TS-B (and its enantiomeric form TS-B′), where the dihedral angle φ between the α ring and the C=CH_2 plane (as defined in Scheme 1) has become about 180° (see Scheme 2).

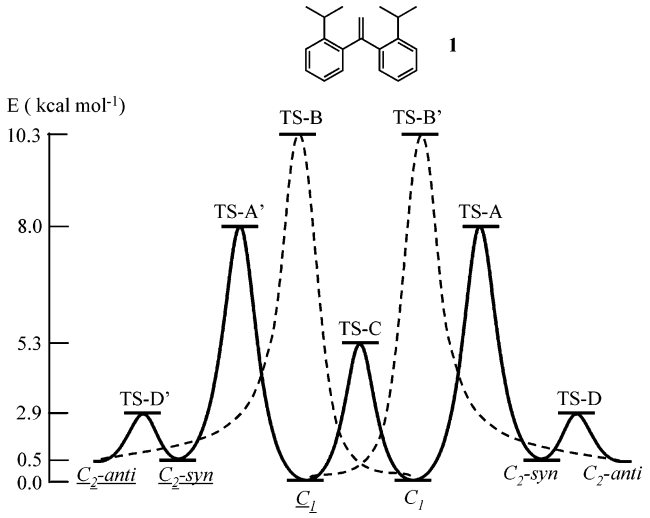
In the case of **1** (X = CH_2) the energy values, computed with respect to the C_1 ground state, are 8.0 and 10.3 kcal mol^{-1} for TS-A and TS-B, respectively: this suggests that the actual pathway should take place through the lower energy transition state TS-A. In the one-ring flip process via TS-A/TS-A′, the ring syn to the C=CH_2 moiety (labeled β) crosses over the C=CH_2 plane, thus exchanging the sign of its dihedral angle θ, whereas the absolute value remains essentially the same. In the course of this motion the α ring anti to C=CH_2 is driven in a correlated fashion, eventually assuming a syn relationship: in this way the corresponding dihedral angle φ changes its value keeping, however, the same sign. At the end of this pathway, therefore, the asymmetric C_1 conformer has exchanged with the C_2-syn conformer (Scheme 3).

On the contrary, the direct exchange of C_1 with C_2-anti cannot take place: such an exchange would in fact require the passage of the ring α through the transition states TS-B/TS-B′ with a change of the sign of the corresponding dihedral angle φ. This motion would be accompanied by the correlated rotation of the β ring, which would change the value of its θ dihedral angle, keeping the same sign. As mentioned, however, the TS-B transition state has a higher computed energy than TS-A (10.3 vs 8.0 kcal mol^{-1}) so that the corresponding pathway cannot take place. The C_2-anti conformer can be populated, nevertheless, owing to the extremely facile interconversion of C_2-syn into C_2-anti via the two-ring flip process involving the low-energy TS-D/TS-D′ transition state. In Scheme 3 this has been indicated by a full line for the "allowed" interconversion of C_1 into C_2-syn and for the subsequent interconversion of the latter into C_2-anti, whereas a dashed line has been used to identify the "not allowed " direct interconversion of C_1 into C_2-anti.

The interconversion of the enantiomers of the asymmetric conformer C_1 is expected to have a barrier lower than that involving the TS-A transition state since the corresponding two-ring flip pathway can be achieved via the transition state TS-C (Schemes 2 and 3) without the need for the aromatic ring to cross over the plane containing the $=CH_2$ moiety. The corresponding enantiomerization barrier was calculated to have a value (5.4 kcal mol^{-1} for **1**, X = CH_2) intermediate between the barriers involving the transitions state TS-D and TS-A mentioned above (see Table 1). The computed stereomutation pathways of **1** are described in Scheme 4: the dashed line represents the theoretical pathway which, in practice, is not followed, due to the higher computed energy for the transition state TS-B.

The temperature-dependent NMR spectra of **1** agree well with this theoretical model. For **1**, the ^{13}C single

SCHEME 4. Stereomutation Pathways Computed for 1



signal of the methyl groups broadens on cooling and eventually splits into a pair of almost equally intense lines below −130 °C (Figure 2). In addition, a minor signal (14% at 23.3 ppm), which exchanges with the upfield major line (86% at 22.6 ppm), is observed at −155 °C. The corresponding minor signal for the downfield major line at 24.2 ppm is not resolved, but its presence is revealed by the larger width of this line with respect to that at 22.6 ppm. At this temperature a number of aromatic carbons also display two signals with a 14:86 proportion.

The line shape simulation (Figure 2, right) requires the use of rate constants for the mutual exchange of the two major methyl lines and for the mutual exchange of the two minor methyl lines, as well as rate constants for the exchange of the two major into the two minor lines. A very satisfactory line shape simulation (Figure 2) could be obtained, however, by using the same value for these constants, a result that implies that the same motion is responsible for the mutual exchange of the methyl lines and for the interconversion of the two conformers. The measured barrier ($\Delta G^{\ddagger} = 6.4_5$ kcal mol^{-1})[11] corresponds to that computed for the [α] one-ring flip pathway occurring via the transition state TA-A/TS-A′ (Table 1). The reason for having a single rate constant is a consequence of the fact that the barrier which must be overcome to achieve the interconversion of C_1 into C_2-syn corresponds, as mentioned, to the passage through the transition state TS-A/TS-A′: this passage is the same required to complete the mutual exchange of the enantiomers of C_2-syn, as shown in Scheme 3. Since the latter enantiomerization process exchanges the diastereotopic methyl groups, they become dynamically equivalent

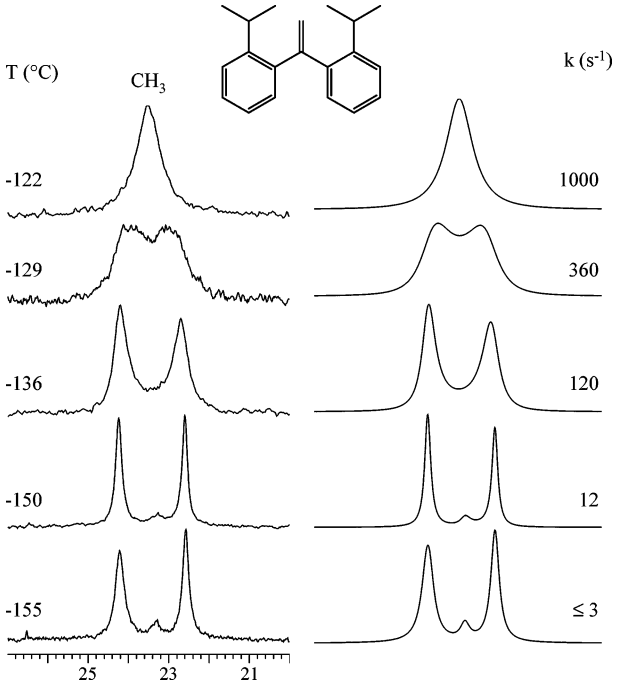


FIGURE 2. Left: Temperature dependence of the ^{13}C NMR (150.8 MHz) methyl signal of **1** in $CHF_2Cl/CHFCl_2$. Right: Line shape simulation obtained with the rate constants indicated (see text).

(enantiotopic), with the same rate that exchanges the lines of the C_1 and C_2-syn conformers (Figure 2).

According to calculations the major conformer belongs to the C_1 point group and this asymmetry should make the NMR signals of one ring distinguishable from those of the other: this, however, was not observed, since even at −155 °C the major spectrum displays a ^{13}C line for each pair of carbon atoms of **1**. This can be explained by considering that the enantiomerization process of C_1 occurs via a two-ring flip process that, according to calculations, has a barrier (computed value 5.3 kcal mol^{-1}) lower than that (computed value 8.0 kcal mol^{-1}) required to render the methyl groups diastereotopic and to make simultaneously distinguishable the C_1 from the pair of C_2 conformers (see Scheme 4). This faster enantiomerization process (the corresponding transition state is the TS-C of Scheme 2) creates, in fact, a dynamic plane of symmetry orthogonal to the plane of the C═CH_2 moiety of C_1, making the two rings apparently equivalent, but leaving diastereotopic the geminal methyl groups of the isopropyl substituents. This is because the local symmetry plane of the isopropyl group (i.e., the plane passing through the prochiral isopropyl methine carbon center) is not coincident with the (dynamic) plane of symmetry of the whole molecule.[9b] To provide experimental evidence for the asymmetry of the major conformer it is therefore necessary to reach even lower temperatures that would make sufficiently slow the exchange of the enantiomers of C_1. In Figure 3 the ^{1}H NMR signal of the isopropyl CH hydrogen is displayed in a range of temperatures lower than −150 °C (at these temperatures the viscosity broadened lines do not exhibit the fine structure due to the coupling with the methyl hydrogens). The trace at −152 °C shows two partially overlapped CH lines,

(11) Within the experimental errors (±0.15 kcal mol^{-1}) the $\Delta G^{\ddagger}$ values were found independent of temperature, as is often observed in conformational processes, 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. Cremonini, M. A.; Lunazzi, L.; Placucci, G.; Okazaki, R.; Yamamoto, G. *J. Am. Chem. Soc.* **1990**, *112*, 2915. Anderson, J. E.; Tocher, D. A.; Casarini, D.; Lunazzi, L. *J. Org. Chem.* **1991**, *56*, 1731. Borghi, R.; Lunazzi, L.; Placucci, G.; Cerioni, G.; Foresti, E.; Plumitallo, A. *J. Org. Chem.* **1997**, *62*, 4924.

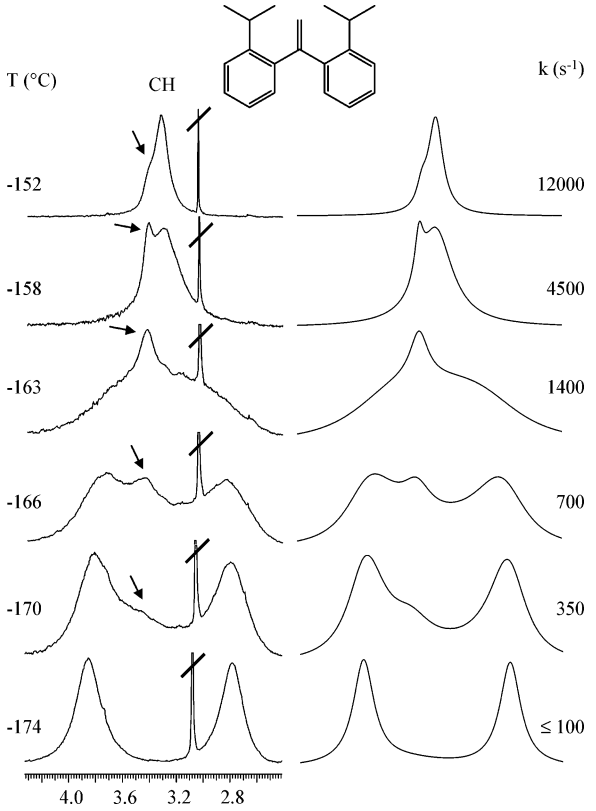


FIGURE 3. Left: Temperature dependence of the ^{1}H NMR (600 MHz) isopropyl methine signal of **1** in $CHF_2Cl/CHFCl_2$ (the arrow indicates the signal of the minor conformer, whereas the sharp line at 3.05 ppm is an impurity of the solvent). Right: Line shape simulation obtained with the rate constants indicated (see text).

corresponding to the major (86%) and to the minor (14%) conformer.

On further lowering the temperature the major signal broadens considerably and decoalesces into a pair of equally intense lines at −174 °C ($\Delta\nu$ = 645 Hz at 600 MHz). This observation supports the prediction that the major conformer is indeed asymmetric since the two aliphatic CH hydrogens become diastereotopic when the exchange of the C_1 enantiomers is rendered slow in the NMR time scale.

The rate constants derived by line shape simulation provide a free energy of activation ($\Delta G^{\ddagger} = 4.6_5$ kcal mol^{-1}),[11] which is in keeping with the theoretical prediction (Table 1), and it is of course lower than the one previously measured (i.e., $\Delta G^{\ddagger} = 6.4_5$ kcal mol^{-1}). At −174 °C also the major signal of the ethylenic hydrogens splits into a pair of equally intense lines ($\Delta\nu$ = 165 Hz at 600 MHz) since the diastereotopicity of the aryl rings renders diastereotopic also these hydrogens. The barrier determined by exploiting the coalescence of the $=CH_2$ signal must be the same as that derived from the signals of the isopropyl methine hydrogens: indeed the appropriate simulation provided an equal $\Delta G^{\ddagger}$ value (4.6$_5$ kcal mol^{-1}).

The spectra of Figure 3 also show that, on lowering the temperature, the minor methine isopropyl line (indicated by an arrow) broadens considerably more than expected on the basis of the increased viscosity of the solution and, apparently, disappears in the spectrum taken at −174 °C. This effect could be attributed to a

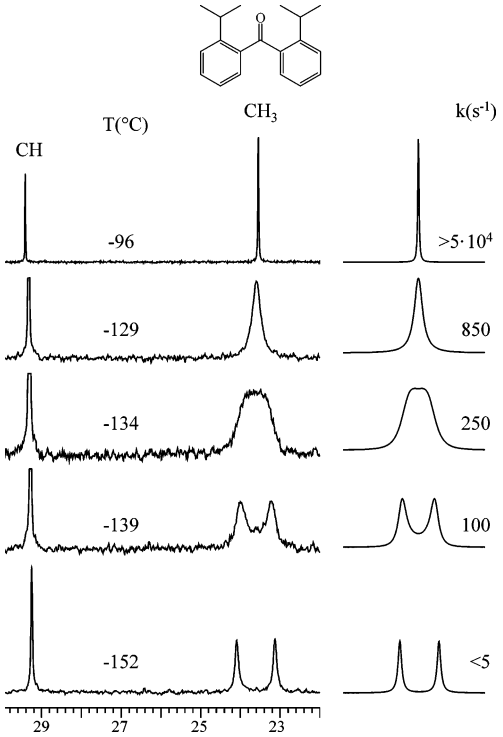


FIGURE 4. Temperature dependence of the ^{13}C NMR spectrum (150.8 MHz) of the aliphatic region of **2** in $CHF_2Cl/CHFCl_2$. The simulation of the methyl signal, obtained with the rate constants indicated, is shown on the right.

pair of exchanging lines having similar intensity that yield signals so broad as to be invisible because they are approaching the coalescence point[12] (at even lower temperatures the solubility was insufficient for obtaining spectra showing the decoalescence of these lines). The simulated trace at −174 °C was actually obtained by assuming that the minor (14%) signal at 3.45 ppm has not disappeared but is still present, its line width being at least 450 Hz, or broader.

These two "invisible" lines might plausibly be due to the similarly populated C_2-anti and C_2-syn conformers predicted by the ab initio calculations and displayed in Figure 1. On the reasonable assumption that the shift separation of their CH lines is analogous to that of the corresponding lines of the major C_1 conformer (i.e., $\Delta\nu$ in the range 600−700 Hz at 600 MHz), a coalescence near −174 °C, or slightly below this temperature, entails a barrier equal to or lower than 4.0 kcal mol^{-1}. The trend experimentally determined for these three barriers thus parallels the sequence predicted by the theory (Table 1).

As in the case of **1**, the variable-temperature ^{13}C spectrum of ketone **2** (Figure 4) shows a broadening of the methyl signal, which likewise splits into two equally intense lines (trace at −152 °C). The rate constants derived from the line shape simulations provide a free energy of activation ($\Delta G^{\ddagger} = 6.3_5 \pm 0.15$ kcal mol^{-1}),[11] which, notably, is equal to that of **1** within the experimental uncertainty. Contrary to the case of **1**, however, no evidence of signals due to a second conformer was

(12) An analogous situation was observed in the case of tetrabenzylmethane, $C(CH_2Ph)_4$ (see: Grilli, S.; Lunazzi, L.; Mazzanti, A.; Pinamonti, M.; Anderson, J. E.; Ramana, C. V.; Koranne, P. S.; Gurjar, M. K. *J. Org. Chem.* **2002**, *67*, 6387).

obtained, nor did any line (both at the ^1H and ^{13}C frequencies) display additional broadening and decoalescence when the sample was further cooled from −152 to −170 °C. The absence of minor signals suggests that only one conformer is essentially populated and the observation of a single ^{13}C line for each pair of carbons at any temperature seems to indicate that its structure cannot be asymmetric as that of C_1.

Ab initio calculations actually show that the C_2-syn conformer of **2** is the most stable species, with C_1 and C_2-anti having much higher energies (1.6 and 5.3 kcal mol^{-1}, respectively). The 6.3_5 kcal mol^{-1} value obtained from the analysis of the methyl signal of **2** thus corresponds to the interconversion barrier of the two enantiomers of C_2-syn (Scheme 1). This process, as mentioned, requires the passage through the C_1 conformer but, being the energy of the latter quite high in **2**, its proportion is too low to be experimentally detected (the computed relative energy of 1.6 kcal mol^{-1} entails in fact a population as low as 0.1% at −152 °C, and, of course, the population expected for C_2-anti is even lower).

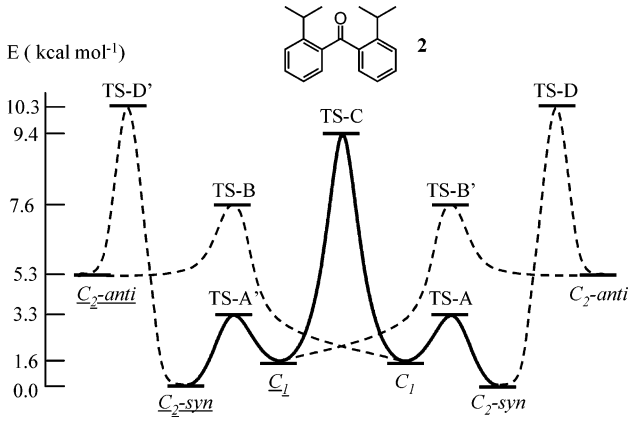
It seems quite surprising that the measured enantiomerization barrier, which interchanges the methyl signals of **1** (6.4_5 kcal mol^{-1}), is essentially equal to that observed for the same type of exchange in **2** (6.3_5 kcal mol^{-1}): in both cases, in fact, a passage through the transition state TS-A (Scheme 2) is required, which seems more facile for the less hindered ketone **2** than for the ethylene **1**. Indeed this barrier was computed to be much lower (3.3 kcal mol^{-1}) for **2** than for **1** (8.0 kcal mol^{-1}, as in Table 1). This suggests that the barrier measured in **2** does not correspond, as in **1**, to the transition state TS-A but reflects another type of transition state.

The pathway for interconverting the C_2 enantiomers is the same, as mentioned, as that required to obtain the C_1 conformer (invisible in the case of **2** because it has too low a population): the latter conformer, however, must itself enantiomerize to bring about the overall enantiomerization of C_2-syn. Whereas in **1** this process, which takes place through the transition state TS-C (Scheme 3), is computed to have a lower energy than that of TS-A of Scheme 2 (5.4 vs 8.0 kcal mol^{-1}, as in Table 1), the opposite occurs in the case of **2**. Calculations predict, in fact, a barrier of 9.4 kcal mol^{-1} for passage through the transition state TS-C, i.e., a value much larger than the 3.3 kcal mol^{-1} for the passage through the transition state TS-A. The computed interconversion pathways for **2** are displayed in Scheme 5.

The measured barrier of 6.3_5 kcal mol^{-1} in **2** corresponds, therefore, to the passage through the TS-C transition state, which has an energy comparably high to that (8.0 kcal mol^{-1}) computed for the TS-A transition state of **1**. This might account for the similarity of the two measured barriers: 6.4_5 (experimental) corresponds in fact to 8.0 kcal mol^{-1} (computed) in the case of **1** and 6.3_5 (experimental) corresponds to 9.4 kcal mol^{-1} (computed) in the case of **2**.

It should be pointed out that the interconversion of the enantiomers of C_2-syn, which has been indicated to take place (full line of Scheme 5) via the transition states TS-A, TS-C, and TS-A′, might alternatively occur via the transition states TS-A, TS-B, and TS-D′, as represented by the dashed lines of Scheme 5. Since the rate determining step of this second process involves a barrier

SCHEME 5. Stereomutation Pathways Computed for 2



larger than that of the former (10.3 vs 9.4 kcal mol^{-1} for TS-D and TS-C, respectively) the stereomutation is expected to occur via the more facile pathway comprising the TS-C transition state. Contrary to the case of **1**, however, the difference between these two computed barriers (0.9 kcal mol^{-1}) is quite small and, for this reason, the choice of the preferred interconversion pathway proposed for derivative **2** cannot be considered completely unambiguous, since this conclusion might be affected by the approximations involved in the computational approach.

Conclusions

Derivatives comprising two equal aryl rings bonded to an sp^2 carbon give rise, in principle, to three types of conformers if each ring bears a single substitutent in the ortho position (in the present example an isopropyl group). In the case of the ethylenic derivative **1**, experimental evidence for the existence of such conformers has been obtained and the corresponding interconversion barriers determined. These results are in agreement with the ab initio calculations describing their stereomutation pathways. In the analogous ketone **2** only one conformer was experimentally observed because the relative energies of the other two are computed to be exceedingly high. Whereas in **1** the most stable conformer is asymmetric (C_1 point group, as confirmed also by X-ray diffraction), that of **2** has C_2 symmetry, in agreement with the theoretical prediction.

Experimental Section

Materials: Bis(2-isopropylphenyl)methanone (2). To a cooled (−78 °C) solution of 2-isopropylbenzene lithium, prepared by addition of butyl lithium (14 mmol) to a solution of 1-bromo-2-isopropylbenzene (2.98 g, 15 mmol in 50 mL of THF) was added a solution of 2-isopropylbenzaldeyde (2.0 g, 13.5 mmol in 10 mL of THF). After 30 min the solution was allowed to warm and quenched with aqueous NH_4Cl. The product was extracted with Et_2O and dried (Na_2SO_4) and the solvent was removed at reduced pressure. The crude was washed with Et_2O to give 3.25 g (90%) of pure bis(2-isopropylphenyl)methanol. Oxidation with pyiridinium chlorochromate (4.70 g, 18.2 mmol in 50 mL of CH_2Cl_2) at room temperature, followed by filtration on silica, yielded 3.50 g (88%) of bis(2-isopropylphenyl)-methanone, which yielded 3.20 g of the product pure (purified by chromatography on silica gel, petroleum ether/Et_2O 10/1). Mp 38.2−39.0 °C. ^1H NMR (400 MHz, $CDCl_3$, 22 °C, TMS) δ

1.02 (d, 12H, Me), 3.23 (m, 2H, CH), 7.12−7.24 (m, 4H); 7.40−7.48 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 22 °C, TMS) δ 23.0 (CH_3), 29.0 (CH), 124.6 (CH), 126 (CH) 129.4 (CH) 130.9 (CH) 138.8 (q), 148.6 (q), 202.4 (CO).

1-Isopropyl-2-[1-(2-isopropylphenyl)vinyl]benzene (1). To a cooled (0 °C) solution of bis(2-isopropylphenyl)methanone (**2**) (536 mg, 2 mmol) in *n*-hexane (20 mL) was added 1.88 mL (3 mmol) of methyl lithium (1.6 M in Et_2O). When the addition was terminated the reaction was refluxed for 2 h and then quenched with water (15−20 mL). The product was extracted with Et_2O and dried (Na_2SO_4) and the solvent was removed at reduced pressure: 540 mg (1.91 mmol) of pure 1,1-bis(2-isopropylphenyl)-1-ethanol were obtained. The crude was treated with HCl (0.5 M, 20 mL) in THF (30 mL), and the solution was allowed to warm for 1 h. The product was extracted with Et_2O and dried (Na_2SO_4) and the solvent was removed at reduced pressure to obtain 520 mg (98%) of 1-isopropyl-2-[1-(2-isopropylphenyl)vinyl]benzene. Crystals suitable for X-ray analysis were obtained by slow crystallization in hexane. Mp 63.5−64.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, TMS) δ 1.07 (d, 12H, Me), 3.23 (m, 2H, CH), 7.08−7.14 (m, 4H); 7.23−7.30 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 22 °C, TMS) δ 24.0 (CH_3), 29.4 (CH), 119.1 (CH_2), 125.2 (CH), 125.9 (CH), 127.5 (CH), 129.8 (CH), 141 7 (q), 146.2 (q), 149.4 (q).

Computations. A complete conformational search, using Molecular Mechanics (MM3 Force Field[13]), was performed to locate the potential minima of **1** and **2**. For each of the three mentioned structures C_1, C_2-syn, and C_2-anti, other local minima also can be reached by rotation of the isopropyl groups. The latter minima, however, have energies higher than those of the corresponding ground states appearing in Schemes 4 and 5, so that their populations can be considered negligible. In the case of **1** the MM3 approach predicted that the C_2-anti was 0.3 kcal mol^{-1} more stable than the C_1 conformer, a result in obvious disagreement with the experimental observation (spectrum at −174 °C in Figure 3). Such a result suggests that theoretical methods more sophisticated than Molecular Mechanics are needed in the present case.[14] For this reason ab initio computations were carried out at the RHF/6-31G level by means of the Gaussian 03 series of programs (the standard Berny algoritm in redundant internal coordinates, and a 10^{-4} au criteria of convergence were employed):[10] this approach actually predicted C_1 to be the most stable conformer of **1** (see Figure 1), as experimentally observed. The choice of an unpolarized basis set was due to the need for reducing the computation time. Harmonic vibrational frequency were calculated to ascertain the nature of all the stationary points. For each optimized ground state the frequency analysis showed the absence of imaginary frequencies, whereas for each transition state the frequency analysis showed a single imaginary frequency. The corresponding optimized structures are reported in the Supporting Information.

NMR Measurements. The samples for the ^{13}C NMR low-temperature measurements were prepared by connecting to a vacuum line the NMR tubes containing the compound and some C_6D_6 for locking purposes and condensing therein the gaseous CHF_2Cl and $CHFCl_2$ under cooling with liquid nitrogen. The tubes were subsequently sealed in vacuo and introduced into the precooled probe of a spectrometer operating at 600 MHz for ^{1}H and 150.8 MHz for ^{13}C. The temperatures were calibrated by substituting the sample with a precision Cu/Ni thermocouple before the measurements. Complete fitting of dynamic NMR line shapes was carried out with use of a PC version of the DNMR-6 program.[15]

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

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(13) Computer package PC Model v 7.5; Serena Software: Bloomington, IN.

(14) Also the MMX[13] force field yielded an analogous inconsistency in the case of **1**, indicating C_2-anti to be more stable (by 0.38 kcal mol^{-1}) than C_1. Likewise the MMFF[13] force field yielded C_2-syn, which was erroneously predicted to be more stable (by 0.64 kcal mol^{-1}) than C_1.

(15) QCPE program no. 633, Indiana University: Bloomington, IN.