JOC Article

Conformational Studies by Dynamic NMR. 91.[1] Conformational Stereodynamics of Tetraethylmethane and Analogous $C(CH_2X)_4$ Compounds

Stefano Grilli, Lodovico Lunazzi,* Andrea Mazzanti, and Marco Pinamonti

Department of Organic Chemistry "A. Mangini", University of Bologna, Risorgimento, 4,
Bologna 40136, Italy

J. Edgar Anderson*

Chemistry Department, University College, Gower St., London, WC1E 6BT, UK

C. V. Ramana, Priti S. Koranne, and Mukund K. Gurjar

National Chemical Laboratory, Pune-411008, India

lunazzi@ms.fci.unibo.it

Received May 29, 2002

Variable-temperature NMR studies of tetraethylmethane (**1a**), tetrapropylmethane (**1b**), tetrachloromethylmethane (**1c**), tetrabromomethylmethane (**1d**), tetracyclopropylmethylmethane (**1e**), and tetrabenzylmethane (**1f**) show a range of dynamic behavior. Separate signals for two types of conformation are observed for **1a**, **1c,** and **1d** at low temperatures, with more than 95% of the molecules in a time-averaged D_{2d} conformation, and the S_4 conformation as the minor populated alternative. Compound **1e** populates only S_4-type conformations but equilibrates slowly between degenerate versions of these at low temperatures. Compounds **1b** and **1f** show a temperature-dependent spectrum but the low-temperature limit spectrum could not be observed. Ab initio calculations agree well with experiment on the conformational equilibria and suggest in particular that compounds **1b** and **1f** behave similarly to compounds **1a** and **1e**, respectively. A crystal structure of compound **1f** is reported.

Introduction

The conformational analysis of a quaternary carbon center with four radiating primary alkyl chains is potentially complex since each $C-CH_2$ bond, at least in acyclic molecules which are the subject of this paper, has three staggered conformations, so there are $3^4 = 81$ possible conformations. Fortunately with four identical alkyl groups, i.e., $C(CH_2X)_4$ **1**, symmetry reduces the 81 possible structures to 6 types with various levels of degeneracy. In important seminal work in this series for **1a** (X = Me) and **1b** (X = Et), Alder and his collaborators have shown[2-4] that two of these six types of conformation are of very similar stability and are much more stable than the other four. The relative instability of these latter four conformational types results from their having at least one parallel 1,3-interaction between X-groups (Scheme 1).

An electron diffraction study showed that for **1a**, both of the stable conformations are populated in the gas phase.[4] Calculations[2,3] confirm this observation and suggest a similar situation for **1b**. Crystal structure determination of a large range of analogous compounds centered on a quaternary nitrogen atom, i.e., $N^+(CH_2R)_4\ Y^-$, show many examples of these two stable conformational types.[3]

Scheme 1 shows the six conformational types in idealized form, and how they are related by successive 120° rotations of an appropriate CH_2X group. The two most stable conformations are labeled **T1** and **T3** since they are separated by ~120° rotations of **two** CH_2X groups, and **T2** is intermediate between these two. The set of conformations will be considered further in the Discussion.

We now want to report the dynamics of several molecules **1a**−**f** of this general type, using calculations

$C(CH_2X)_4$ **1**

1a X = Me, **1b** X = Et, **1c** X = Cl, **1d** X = Br, **1e** X =cyPr, **1f** X = Ph

and dynamic NMR spectroscopic observations to show what conformations are populated, how conformations

---

[1] Part 90: Grilli, S.; Lunazzi, L.; Mazzanti, A.; Pinamonti, M. *J. Org. Chem.* **2002**, *67*, 5733. See also Part 89: Gasparrini, F.; Grilli, S.; Leardini, R.; Lunazzi, L.; Mazzanti, A.; Nanni, D.; Pierini, M.; Pinamonti, M. *J. Org. Chem.* **2002**, *67*, 3089.

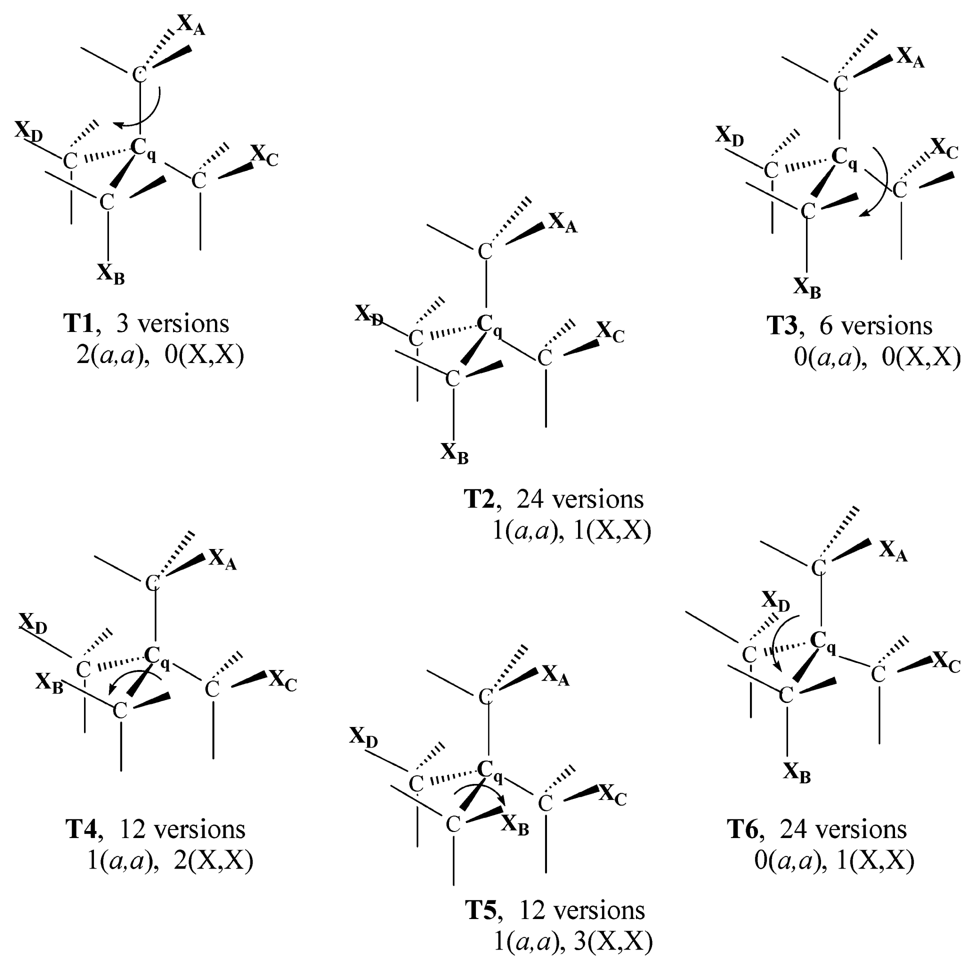
[2] Alder, R. W.; Maunder, C. M.; Orpen, A. G. *Tetrahedron Lett.* **1990**, *31*, 671.

[3] Alder, R. W.; Allen, P. R.; Anderson, K. R.; Butts, C. P.; Khosravi, E.; Martin, A.; Maunder, C. M.; Orpen, A. G.; St. Pourçain, C. B. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2083.

[4] Alder; R. W.; Allen, P. R.; Hnyk, D.; Rankin, D. W. H.; Robertson, H. E.; Smart, B. A.; Gillespie, R. J.; Byetheway, I. *J. Org. Chem.* **1999**, *64*, 4226.

10.1021/jo025984k CCC: $22.00

SCHEME 1. One Version Each of the Six Conformational Types (T1−T6) of $C(CH_2X)_4$ Derivatives (1a−1f)[a]



T1, 3 versions
2(*a*,*a*), 0(X,X)

T2, 24 versions
1(*a*,*a*), 1(X,X)

T3, 6 versions
0(*a*,*a*), 0(X,X)

T4, 12 versions
1(*a*,*a*), 2(X,X)

T5, 12 versions
1(*a*,*a*), 3(X,X)

T6, 24 versions
0(*a*,*a*), 1(X,X)

[a] Types actually populated are **T1** and **T3**. The versions shown for types **T1** and **T3**−**T6** can each be converted to **T2** by rotation of the one CH_2X group indicated. Structures are drawn with the labels for hydrogen atoms omitted and with idealized staggered conformations although minimum energy forms may have torsion angles skewed. Each type is uniquely defined by two criteria: (i) the number of anti,anti arrangements (a,a) of $X-C-C_q-C-X$ chains that can be identified, thus **T1** has two of these, $X_A-C-C_q-C-X_B$ and $X_C-C-C_q-C-X_D$, and (ii) the number of 1,3-parallel arrangements of substituents (X,X), thus **T6** has one of these, X_A with X_C. For each type, the number of degenerate/enantiomeric versions that exist is indicated.

interconvert, and what the barrier to these interconversion processes are.

Results

All compounds showed relatively simple NMR spectra at room temperature with dynamic broadening of signals at considerably lower temperatures. For compounds **1a**−**d**, signals sharpened at even lower temperatures and, except for **1b**, two sets of signals of different intensity were seen. For **1e** resharpening at lowest temperatures produced 1:1 doubling of the three ^1H signals arising from methylene protons, but for **1f**, which by calculation is conformationally similar, resharpening of signals was not observed at the lowest temperatures attainable. Because of solubility problems at very low temperatures, useful ^{13}C NMR data were obtained only for compounds **1a** and **1b**, so ^{13}C NMR of **1c**−**f** will not be mentioned. Each compound will now be discussed in turn.

Tetraethylmethane ($C(CH_2Me)_4$, 1a). The ^{13}C NMR spectrum of Et_4C features three signals at ambient temperature. On progressively lowering the temperature, broadening of the C_q and CH_2 signals occurs, followed by a resharpening as in Figure 1. Such an effect is not noticeable for the Me signal. The C_q signal was too weak for quantitative determinations, but the CH_2 signal shows maximum incremental broadening of 10 Hz (i.e. 13−3 Hz) at −138 °C. From the relationship[5,6] $k = 2\pi(10)$, the rate constant for the conformational process is 63 s^{-1}, hence $\Delta G^{\ddagger} = 6.6$ kcal mol^{-1} (Table 1). At −155 °C a CH_2 signal due to the minor conformer was detected, 166 Hz (1.65 ppm) to lower field of the major one, with ~3% relative intensity. By allowing for the degeneracy of types **T3** and **T1** (see Scheme 1) and assuming $\Delta S° = 0$ this proportion should become 5% at −138 °C. Using this value, the computer line shape simulation provides, at −138 °C, $\Delta G^{\ddagger} = 6.6$ kcal mol^{-1}, in agreement with the approximate formula above.

The 400 MHz ^1H NMR spectrum also shows incremental broadening of 3.3 Hz at −142 °C for the CH_2 quartet whereas the CH_3 triplet is essentially unaffected. This corresponds, as above,[5,6] to $k = 21$ s^{-1} and thence to

---

(5) (a) Anet, F. A. L.; Basus, V. J. *J. Magn. Reson.* **1978**, *32*, 339. (b) Sandström, J. *Dynamic NMR Spectroscopy*; Academic Press: London, New York, 1982; p 84.

(6) Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2001**, *66*, 4444.

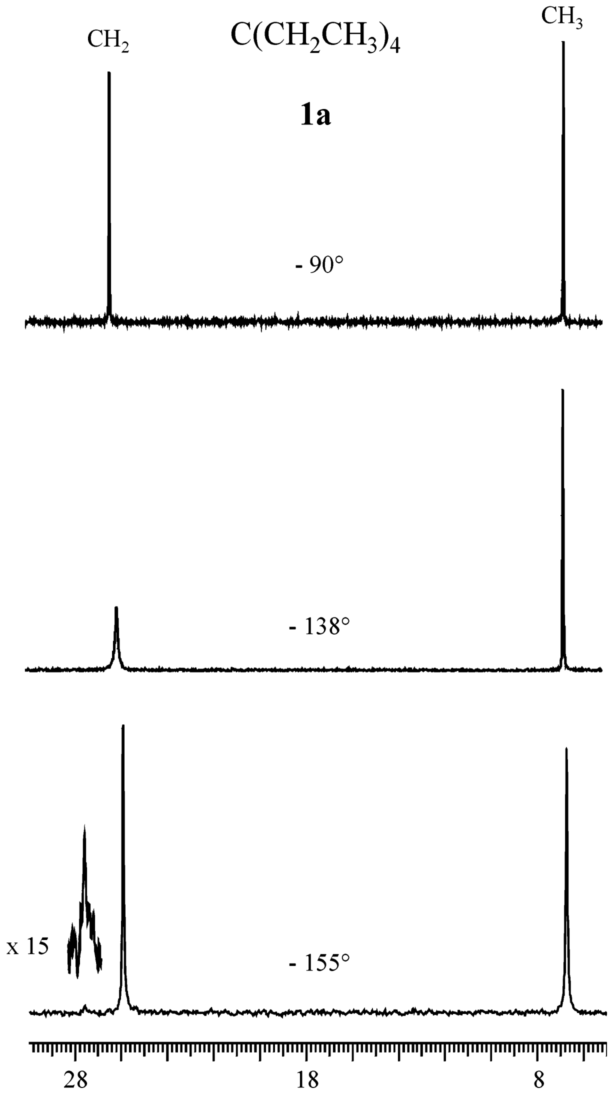


FIGURE 1. Methyl and methylene ^{13}C NMR (100.6 MHz) lines of tetraethylmethane (**1a**) in CHF$_2$Cl/CHFCl$_2$ as function of temperature. The inset at −155 °C displays the 15-fold amplified CH$_2$ line of the minor conformer.

TABLE 1. Interconversion Barriers as Determined by NMR for C(CH$_2$X)$_4$, 1a−1f

	1a	**1b**	**1c**	**1d**	**1e**	**1f**
X	Me	Et	Cl	Br	cyPr	Ph
$\Delta G^{\ddagger\,a}$	6.6 (6.6)^b	6.3$_5$	6.9 (10.0)^c	8.0 (10.4)^c	5.8	4.3

[a] Experimental free energies of activation (kcal mol^{-1}) of the interconversion of **T1** (D_{2d} symmetry) to **T3** (S$_4$ symmetry) for compounds **1a**−**1d** and of the degenerate **T3** interconversion for **1e** and **1f**. [b] Computed barrier by the MM2 force field as in ref 3. [c] Computed barrier by the MM3 force field assuming successive CH$_2$X rotations (present work).[11]

$\Delta G^{\ddagger}$ = 6.65 kcal mol^{-1} at −142 °C, in agreement with the ^{13}C experiments. At −157 °C the minor species signal (3% relative intensity) is seen 60 Hz (0.15 ppm) downfield from that for the major species. While the major CH$_2$ signal is seen as a quartet (J = 7.2 Hz and line width 6.5 Hz) at −157 °C, the minor signal is a broad line 30 Hz wide. This much broader minor signal is compatible with the **T3** structure of S_4 symmetry, whose diastereotopic CH$_2$ protons provide the AB part of an ABX$_3$ spectrum, too complex to be resolved at low temperature.

The $\Delta G°$ derived from the 3% population for **T3** at about −155 °C is 0.97 kcal mol^{-1}, which is not far from that obtained at 293 K by electron diffraction[4] (0.79 kcal mol^{-1}). The former value suggests that if $\Delta S° = 0$, the population ratio in solution at ambient temperature should be 73:27, which compares satisfactorily with the 66:34 ratio derived by electron diffraction measurements in the gas phase.[4] The NMR barrier of 6.6 kcal mol^{-1} for the **T1** to **T3** interconversion agrees well with the MM2 computed value (6.6 kcal mol^{-1}) of Alder and co-workers.[3]

Tetra-*n*-propylmethane (C(CH$_2$Et)$_4$, 1b). In a similar way, all signals (except that of Me) in the C-13 spectrum of **1b** show dynamic broadening as the temperature is lowered, followed by a resharpening. It was only in the case of the downfield CH$_2$ signal (i.e. that next to the quaternary carbon) that the effect was large enough to allow reasonably accurate measurements. A maximum incremental broadening of 24 Hz (i.e. 31−7 Hz) was observed at −138 °C, corresponding to a $\Delta G^{\ddagger}$ value of 6.3$_5$ kcal mol^{-1}, for the major to minor interconversion, a value only slightly lower than the 6.6 kcal mol^{-1} barrier for **1a**.

At −155 °C all the lines are equally sharp, but the solubility had decreased dramatically, so that a minor conformer with a proportion lower than 10−15% could not be observed above the noise. Assuming a conceivable shift difference for conformers in the range 1.5−2.50 ppm, (i.e. a range that includes the 1.65 ppm separation found above for **1a**), the experimental maximum line broadening suggests a proportion of the minor conformer of 12 ± 3% at −138 °C. Corrected to −155 °C with allowance for the greater degeneracy of **T3**, there should be about 8% of this latter conformation, a proportion too small to be detected in the experimental conditions we have described, but significantly greater than the 3% observed at the same temperature for tetraethylmethane (**1a**). This agrees with our ab initio computations (see Table 2) predicting energy differences between these conformers of 0.70 and 0.75 kcal mol^{-1} for **1b** and **1a**, respectively

Tetrachloromethylmethane (C(CH$_2$Cl)$_4$, 1c). The 400-MHz ^{1}H NMR spectrum of C(CH$_2$Cl)$_4$ comprises two signals at −158 °C as shown in Figure 2, which allows a confident assignment of the conformational equilibrium.

The major signal (96%) is a single line (3.58 ppm), as expected for the **T1** conformer, while the minor signal (4%) is an AB-multiplet (δ 3.92 and 3.77, J = −11 Hz) characteristic of the **T3** conformer. Allowing for degeneracy, the free energy difference between conformers is 0.88 kcal mol^{-1} at −158 °C. Spectral simulations carried out at −146° and −138 °C indicate an interconversion barrier of the major into the minor conformer of 6.9 ± 0.2 kcal mol^{-1}.

Tetrabromomethylmethane (C(CH$_2$Br)$_4$, 1d). The 400-MHz ^{1}H NMR spectrum at −150 °C comprises a single line for the **T1** conformer (≈98.5%) and an (≈1.5%) AB-multiplet ($\delta\nu$ = 16 Hz, $J \sim -11$ Hz) for the **T3** conformer. Of the four lines expected for the latter spectrum, three are clearly visible, whereas the fourth is overlapped by the downfield ^{13}C satellite ($J_{C,H}$ = 154 Hz) of the major **T1** conformer singlet line. There is a free energy difference of 1.02 kcal mol^{-1} between any one **T1** and **T3** conformer. The barrier, as obtained by line

TABLE 2. Relative Computed Energies (kcal mol^{-1}) for the Two Most Stable Conformers of C(CH$_2$X)$_4$, 1a–f

	1a (X = Me)		**1b** (X = Et)		**1c** (X = Cl)		**1d** (X = Br)		**1e** (X = cyPr)		**1f** (X = Ph)[a]	
	ab initio	MM3	ab initio	MM3	ab initio	MM3	ab initio	MM3	ab initio	MM3	ab initio	MM3
T1	0.0	0.0	0.0	0.0	0.0	0.31	0.0	0.18	1.34	0.77	3.01	3.30
T3	0.75	0.20	0.70	0.29	0.3	0.0	0.63	0.0	0.0	0.0	0.0	0.25

[a] In this case both ab initio and MM3 calculations predict that the two most stable conformers are **T3** and **T6** (C_2 symmetry as in Scheme 1), with **T1** being only the third (ab initio) or the fourth (MM3) most stable. Ab initio calculations found **T3** to be the most stable, with **T6** having a 1.4 kcal mol^{-1} higher energy (an opposite trend is indicated by MM3 calculations, which predict **T6** to be the most stable, with **T3** having a 0.25 kcal mol^{-1} higher energy).

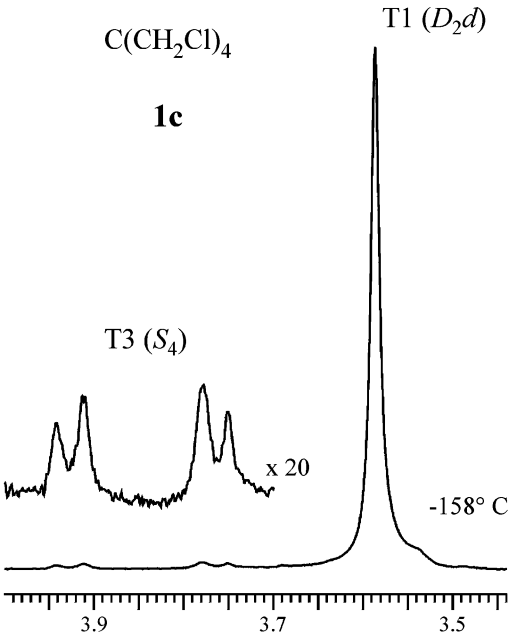
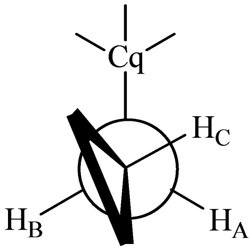


FIGURE 2. ^{1}H NMR (400 MHz) spectrum of tetrachloromethylmethane (**1c**) in CHF$_2$Cl/CHFCl$_2$ at −158 °C, showing signals for type **T1** (D_{2d} symmetry) and type **T3** (S_4 symmetry) conformations, i.e., a singlet and an AB multiplet, respectively (the latter appears in the inset with a 20-fold amplification).

shape simulation at −138 °C, is about 8 kcal mol^{-1}, higher than in **1a**–**c** in agreement with the prediction of the MM3 calculations. The differences between the values for the bromine and chlorine derivatives (**1c** and **1d**, respectively) are a consequence of the larger steric effects of bromine with respect to chlorine.

Tetracyclopropylmethylmethane (C[CH$_2$CH(CH$_2$)$_2$]$_4$, 1e). The temperature dependence of the 400-MHz ^{1}H spectrum is shown in Figure 3. The signal of the two exocyclic methylene hydrogens (which at ambient temperature is a doublet at 1.4 ppm with a J = 6.6 Hz due to the coupling with the CH hydrogen) broadens considerably below −110 °C and decoalesces into a pair of equally intense integrated signals, separated by 368 Hz at −161 °C. Such a feature indicates the existence of a single conformer having diastereotopic methylene hydrogens, due to the CH$_2$–C$_q$ rotation being slow in the NMR time scale at such a low temperature. This also implies that the conformer has S_4 symmetry, in agreement with the crystal structure shape,[7] whose C_2 static symmetry becomes S_4 with fast cyclopropyl–CH$_2$ bond rotation in solution. Indeed our ab initio calculations (see further) predict that the **T3**-type conformer of Scheme 1 is more stable than all the other five possible conformers of **1e**, and the corresponding computed structure reported in Figure 4 appears almost identical with the experimental one.

SCHEME 2



The anisochronous signals for the exocyclic methylene hydrogens observed at δ 0.92 and 1.84 (Figure 3, trace at −161 °C) are too broadened to show the fine structure expected for an ABX-type spectrum. However, the upfield line is broader than its downfield companion, the half-height line widths being 36 and 32 Hz, respectively. This is a consequence of two different ^3J vicinal couplings between the methine and diastereotopic methylene protons. Both experimental (X-ray) and computed (ab initio) structures indicate that the H–C–C–H dihedral angles of the CH$_2$–CH moiety (see Scheme 2) are +68° (H$_A$–C–C–H$_C$) and −176° (H$_B$–C–C–H$_C$), so the ^3J vicinal couplings are expected to be respectively 2.1 and 10.4 Hz according to a Karplus-type equation.[8]

Computer simulation with these values and assuming a geminal J_{AB} = −12 Hz, with an intrinsic width of about 20 Hz, matched satisfactorily the two experimental line widths (Figure 3, trace at −161 °C). Accordingly, the upfield signal corresponds to that of the two methylene hydrogens having the larger dihedral angle with the CH hydrogen of the ring. Line shape simulations at various temperatures (Figure 3) provided a set of rate constants for the CH$_2$–C$_q$ rotation process, yielding a free energy of activation of 5.8 ± 0.15 kcal mol^{-1}.

The S_4 symmetry adopted by **1e** in solution implies that, even in the presence of a fast cyclopropyl–CH$_2$ bond rotation, the four endocyclic methylene hydrogens must all become anisochronous when the CH$_2$–C$_q$ rotation rate becomes slow. Indeed the 400-MHz spectrum at −161 °C shows how both the cis and trans ring proton signals centered at −0.02 and +0.35 ppm appear to be split, their separation being 36 and 47 Hz, respectively (Figure 3, trace at −161 °C). The barrier obtained by computer simulating these signals (Figure 3) is equal to that

---

[7] Ramana, C. V.; Baquer, S. M.; Gonnade, R G.; Gurjar, M. K. *Chem. Commun.* **2002**, 614.

[8] This equation takes the form $J = 7.76 \cos^2\theta - 1.1 \cos\theta + 1.40$, as in: Haasnoot, C. A. G.; Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

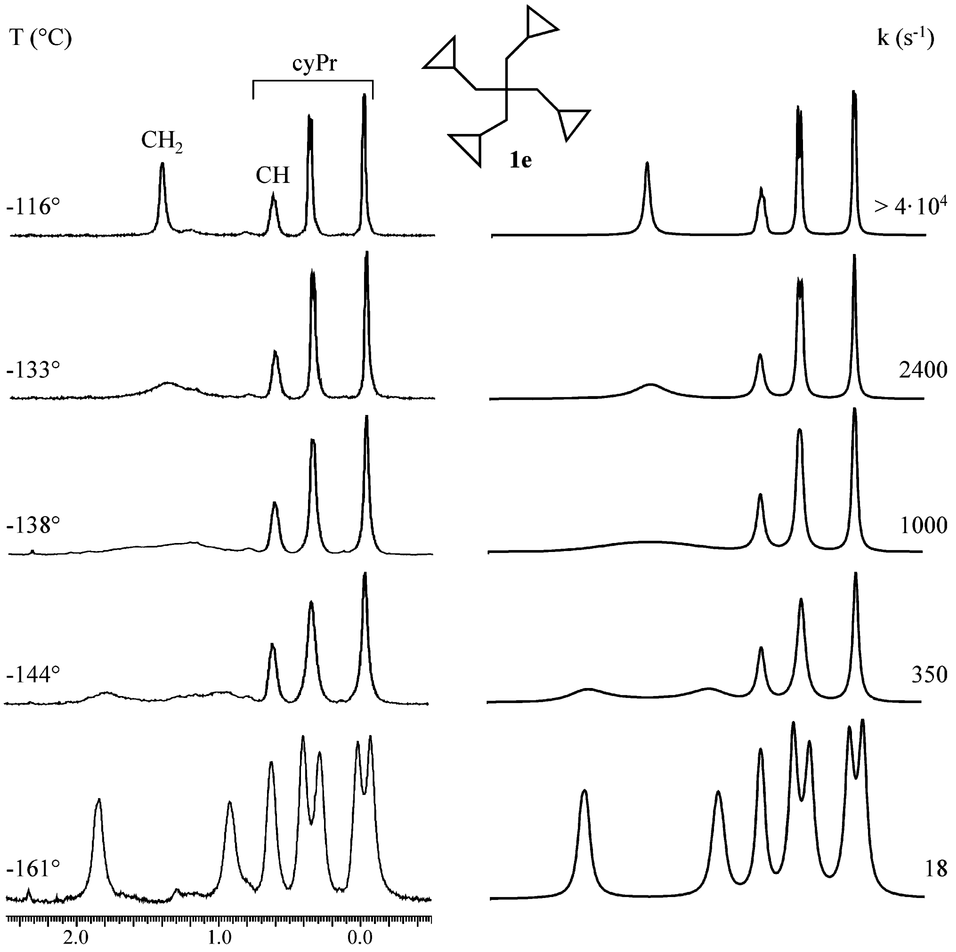


FIGURE 3. Temperature dependence of the experimental ^{1}H NMR spectrum (400 MHz) of **1e** in $CHF_2Cl/CHFCl_2$ (left). On the right is displayed the simulation obtained with the rate constants shown.

obtained from the exocyclic methylene signals, meaning that the same process (i.e. CH_2-C_q rotation) is responsible for the dynamic features observed for all the methylene hydrogen signals of **1e**.

Tetrabenzylmethane ($C(CH_2Ph)_4$, 1f). In the 300-MHz ^{1}H NMR spectrum the CH_2 singlet significantly broadens below −120 °C and shows a line width of more than 70 Hz at about −165 °C. On further cooling the sample, in the −170 to −175 °C range, the line becomes so broad as to disappear under the noise, whereas the lines of the solvents are still only 15 Hz wide. To account for such changes, the diastereotopic hydrogens must have a very large shift separation of 300 Hz or more. At even lower temperature, the compound precipitates so, contrary to the case of **1e**, we could not detect two individual signals. In any case, since the above experiment indicates that the line separation must be similar to that of **1e**, a coalescence temperature in the range −170 to −175 °C implies[5,6] a particularly low free energy of activation between 4.2 and 4.5 kcal mol^{-1}.[9] The exchange process observed might be, in principle, attributed to slow rotation about the $Ph-CH_2$ bond but no dynamic broadening of the benzene ring signals was observed, so the process is concluded to involve the bonds to the quaternary center. The molecular asymmetry that renders methylene protons diastereotopic is averaged out for both ortho and meta positions by fast rotation of the phenyl ring.

The crystal structure (see Experimental Section) of $C(CH_2Ph)_4$ shows that this molecule adopts a single conformation in the solid state that is matched by the ab initio computations. This has a C_2 static symmetry (Figure 4) that would become S_4 when the $Ph-CH_2$ rotation is fast, thus corresponding, in solution, to the **T3**-type conformation of Scheme 1.

Calculations. The calculated energies of conformational types **T1** and **T3** for compounds **1a**−**f** are shown in Table 2. Some calculated interconversion barriers based on successive rotations of CH_2X groups are also included in Table 1. Ab initio calculations at the RHF 6.31G* level[10] and empirical Molecular Mechanics (MM3 force field) calculations[11] were employed (see Experimental Section).

Particular care had to be taken with empirical calculations of the tetracyclopropylmethyl and tetrabenzyl compounds **1e** and **1f** to ensure that best minima had been found, since conformational variation about one cyclo-

---

[9] Anderson, J. E.; de Meijere, A.; Kozhushkov, S. I.; Lunazzi, L.; Mazzanti, A. *J. Am. Chem. Soc.* **2002**, *124*, 6706.

[10] As in the computer package Titan 1.0.5; Wavefunction Inc.: Irvine, CA.

[11] Allinger, N. L.; Yuh, Y. H.; Lii, J. H. *J. Am. Chem. Soc.* **1989**, *111*, 8552.

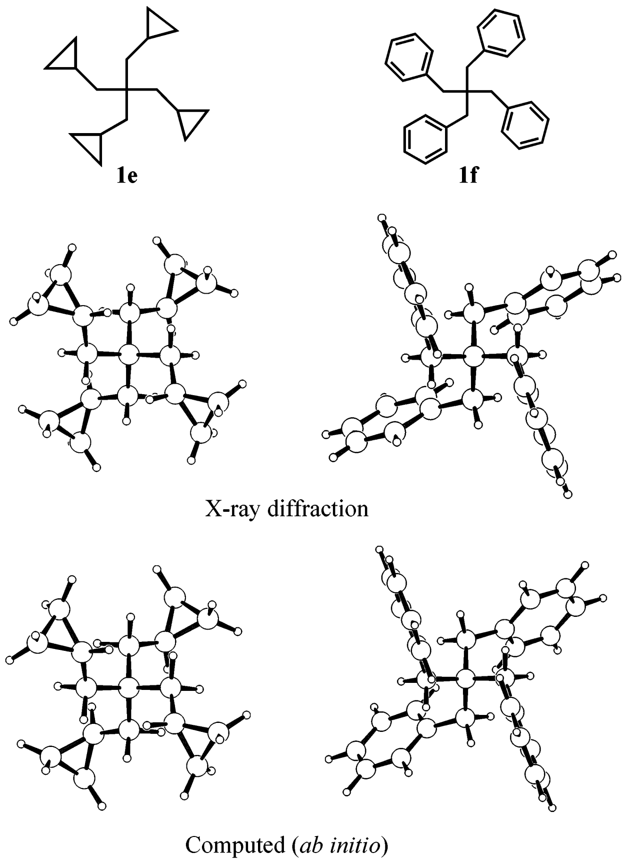


FIGURE 4. X-ray diffraction (top) and ab initio computed (bottom) structures of the most stable conformer **T3** of compounds **1e** and **1f**. The crystallographic data of **1f** are reported in the Experimental Section, for those of **1e** see ref 7.

propyl−CH_2 or Ph−CH_2 bond affects the minimum about all CH_2 bonds. Interconversion of conformations is a much more complicated process in these molecules. The **T1**−**T3** transformation in **1e**, for example, requires −120° of rotation about two C_q−CH_2 bonds, and two cyclopropyl−CH_2 bonds, so we made no attempt to simulate this process.

Ab initio calculations[10] for **1a**−**d** indicate that in all four cases a conformation of type **T1** conformation is the most stable, followed by the type **T3** conformation, with energy differences lower than 1 kcal mol^{-1}. This should lead to a minor (a few percent) population for the latter, in agreement with experimental observations.

Molecular Mechanics calculations[11] suggest that the easiest pathway for **T1** to **T3** interconversion is via **T2**, although the last conformation is too high in energy to be significantly populated. We can thus imagine a succession of **T1**−**T2**−**T3**−**T2′**−**T1′** interconversions with molecules spending most of their lifetimes in **T1** conformations.

Ab initio and MM calculations predict that a different conformational situation holds for compounds **1e** and **1f**. Conformations of type **T1** are much *less* stable than type **T3** for these compounds. Whereas in **1e** ab initio computations predict **T1** to be the second most stable conformer (with an energy higher than **T3** by 1.3 for compounds **1e** and **1f**, as in Table 2), in **1f** the second most stable conformer is the **T6** type (C_2 symmetrry as in Scheme 1), with energy 1.4 kcal mol^{-1} higher than **T3**. The prediction of **T3** to be the most stable conformer in **1e** and **1f** agrees well with the X-ray structure (Figure 4) in the solid state as well as with the low-temperature NMR observations in solution.

Conformational energies calculated with MM3 are expected to be sensitive to the dielectric constant used, at least for compounds **1c**, **1d**, and **1f**. In the first two of these compounds there is, contrary to the experimental observation, a small calculated preference, 0.31 and 0.18 kcal mol^{-1}, respectively, for the **T3** conformation over **T1** (with the default dielectric constant of 1.5). This preference reduces to 0.07 and 0.03 kcal mol^{-1}, respectively, when the default dielectric constant of 1.5 is increased modestly to 5.0. The **T1** conformation is eventually calculated to be more stable than **T3** at higher values of the dielectric constant.

Discussion

Electron diffraction studies of compounds **1a**, **1c**, and **1d** in the gaseous phase have been reported[4,12,13] and both **T1** and **T3** conformation types are found in all three compounds. The **T1**:**T3** population ratio for tetraethylmethane **1a** is 66:34[4] while for the chloride **1c** it is 50:50[12] and for the bromide **1d** it is 58:42.[13]

There have been several crystal structure determinations of acyclic compounds $C(CH_2X)_4$ (**1**), and only conformations of type **T1** or **T3** are found. Those adopting a **T1** conformation are **1**, X = Br,[14,15] Cl,[14,15] CH_2CH_2Br,[14] or CH═CH_2.[16] Those adopting a **T3** conformation are **1**, X = CH_2Br,[14] cyclopropyl,[7] and COOH.[17] There are in addition eight examples of Pentaerythritol derivatives **1**, X = OR, of which six have a **T1** structure[18] and two have a **T3** structure.[19]

The characteristic of the other conformational types **T2** and **T4**−**T6** is that each has at least one X,X parallel-1,3 interaction, see Scheme 1. Such interactions are destabilizing both for steric and for dipole/dipole reasons and are plausibly the reasons for the higher energy of these conformations. Bushweller and his collaborators[20,21] have studied some compounds quite similar to our present ones but with only two or three CH_2X groups. The conformational analysis is dominated by conforma-

---

[12] Stølvek, R. *Acta Chem. Scand.* **1974**, *28A*, 327.

[13] Rustad, S.; Stølvek, R. *Acta Chem. Scand.* **1976**, *30 A*, 209.

[14] Newkome, G. R.; Arai, S.; Fronczek, F. R.; Moorefield, C. N.; Lin, X.; Weis, C. D. *J. Org. Chem.* **1993**, *58*, 898.

[15] Klaeboe, P.; Klewe, B.; Martinsen, K.; Nielsen, G. J.; Powell, D. L.; Stubbles, D. J. *J. Mol. Struct.* **1986**, *140*, 1.

[16] Bunz, U.; Vollhardt, K. P. C.; Ho, J. S. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1648.

[17] Ermer, O.; Eling, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 829.

[18] (a) Chao, L. C. F.; Decken, A.; Britten, J. F.; McGlinchey, M. J. *Can. J. Chem.* **1995**, *73*, 1196. (b) Quast, L.; Nieger, M.; Dotz, K. H. *Organometallics* **2000**, *19*, 2179. (c) Uechi, T.; Fuchita, Y. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2831. (d) Ladd, M. F. C. *Acta Crystallogr. Sect. B* **1979**, *35*, 2375. (e) Newkome, G. R.; Weis, C. D.; Xiaofeng, L.; Fronczek, F. R. *Acta Crystallogr. Sect. C* **1993**, *49*, 998. (f) Bormann, L. M.; Baughman, R. G.; Mumba, P.; Meloan, C. E. *Acta Crystallogr. Sect. C* **1993**, *49*, 1982.

[19] (a) Marsh, R. E. *Acta Crystallogr. Sect. B* **1997**, *53*, 317. (b) Cady, H. H.; Larson, A. C. *Acta Crystallogr. Sect. B* **1975**, *31*, 1864.

[20] Bushweller, C. H.; Whalon, M. R.; Fleischmann, S. H.; Rithner, C. D.; Sturges, J. S. *J. Am. Chem. Soc.* **1979**, *101*, 4703.

[21] Bushweller, C. H.; Whalon, M. R.; Laurenzi, B. J. *Tetrahedron Lett.* **1981**, *22*, 2945.

tions which have no such X−X parallel-1,3 interactions. In the compound $CH_3C(CH_2Cl)_3$, for example,[21] there are three conformational types with no such interactions, and the low-temperature spectrum shows (at −171 °C) three sets of signals of different intensity.

The spectral appearance, at low temperatures, for **1c** and **1d** and, by implication, **1a**, namely a singlet and an AB spectrum for **T1** and **T3** conformations respectively, implies that interconversion of **T1** with **T3** and also interconversion between degenerate conformations of **T3** are slow on the NMR time scale. The modes of conformational interconversion of other molecules of the type $C(CX_2Y)_4$ have recently been analyzed in detail,[9] and suggest that the **T1**−**T3** interconversion is by way of **T2**. This implies rotation of about 120° by two appropriate CX_2Y groups, and calculations for CX_2Y = isopropyl suggested that a certain degree of cooperativity in these rotations lowers the overall barrier to rotation, so that the best minimum energy **T2** conformation may not be exactly on the easiest interconversion pathway. Our present MM3 calculations for **1a** to **1d** suggest that rotation of less-branched CH_2X groups does not require significant cooperation from neighboring groups, so a straightforward **T1**−**T2**−**T3** pathway seems likely. It is surprising that MM3 calculations for the barrier in the two halides give results more than 2 kcal mol^{-1} higher than experiment. Use of a higher dielectric constant lowers these **T1**−**T3** interconversion barriers: the 10.0 kcal mol^{-1} barrier quoted for **1c** in Table 1, for example, is reduced to 9.3 kcal mol^{-1} when a dielectric constant $\epsilon = 10$ (rather than the standard $\epsilon = 1.5$) is used, a value nearer to the experimental one, although hardly in good agreement with it.

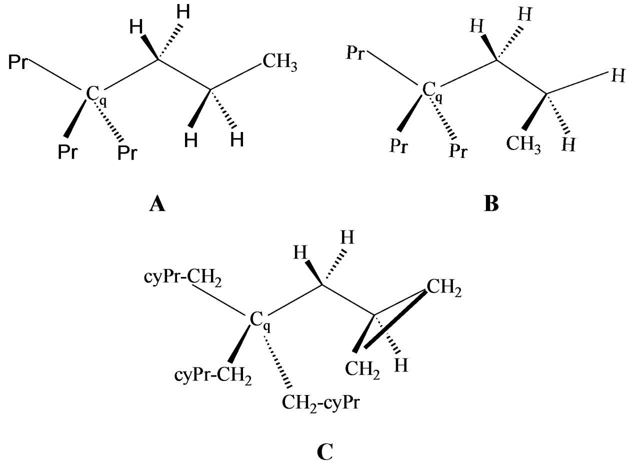
MM3 calculations suggest that interconversion of degenerate versions of the **T3** conformation, the only observed process for **1e** and **1f**, and the minor process for **1a**−**d**, takes place via the **T6** conformation, rather than by what is now the relatively high-energy **T1** conformation. This **T6** is followed by a second **T6** conformation, or a **T2** conformation, i.e., **T3**−**T6**−**T6′**−**T3′** or **T3**−**T6**−**T2**−**T3′** with only **T3** conformations of **1e** and **1f** detectably populated.

The contrasting preferences for the **T1** conformation in **1a**−**d** and for the **T3** conformation in **1e** and **1f** can be understood in light of an earlier observation of Alder and co-workers.[3] They found that in tetrapropylmethane, **1b**, the second bond from the quaternary center in each propyl group adopts the anti conformation completely.

As Scheme 3 shows the quaternary center requires this anti arrangement **A** for the $C_q{-}CH_2{-}CH_2{-}CH_3$ torsion angle, rather than the gauche **B** in which the methyl group has marked interactions with one other propyl chain. With the more branched cyclopropylmethyl groups, such an anti conformation free of interaction with other groups is not possible (see structure **C**).

In the tetrabenzyl compound **1f**, the preferred conformation for an individual benzyl group would have the $C_q{-}CH_2$ bond orthogonal to the plane of the benzene ring as in neopentyl benzene.[22] The consequence of this is that phenyl rings interfere with each other so, as with **1e**, there is no particularly stable **T1** conformation. Even in the preferred **T3** structure of tetrabenzyl derivative **1f** there is a conformational compromise since the $C_q{-}CH_2{-}C{-}C_{ortho}$ torsion angles are not 90° in the crystal but, alternately, 96.3° and −107.2° and are calculated to be, alternately, +80° and −106° (ab initio). A **T3** conformation is perhaps to be favored for $C(CH_2X)_4$ when any substantial group X occurs β to the quaternary center and cannot avoid interactions with it.

SCHEME 3[a]



[a] Structures **A** and **B** show one side chain of the **T1** conformation of compound **1b**, where the second bond is in an anti or a gauche conformation, respectively. In the latter, the end of the chain interferes with another propyl group. Structure **C** shows that in compound **1e**, where the chain branches at the β-position, interference with another side chain is inevitable.

The biased position of the equilibrium in **1a**, **1c**, and **1d** produces very little detail in the exchange-broadened NMR spectra, so it is not possible to distinguish whether in these compounds there is any involvement of interconversions of the **T3**−**T6**−**T6′**−**T3′** type as well as of the **T3**−**T2**−**T1**−**T2′**−**T3′** type.

In the earlier work[9,23,24] on compounds of the type $C(CX_2Y)_4$ with one hydrogen atom Y and two larger groups, a type **T1** or a type **T3** conformation is always adopted rather than the other four types. Tetracyclohexylmethane,[23] tetraisopropylmethane,[9,24] and tetracyclopropylmethane[9,24] have been studied, and once again the stability of conformational types is governed by parallel-1,3 interactions of large X-groups. In contrast to the present study such interactions cannot be absent, but in conformation types **T1** and **T3** there are only four such interactions, while there are five or six in the remaining four types. Bearing on our present results for compounds **1e** and **1f**, there is an interesting contrast between tetraisoproylmethane and tetracyclopropylmethane. The former adopts a type **T1** for preference over the **T3**, the population ratio being 93:7 at −110 °C.[9] When the flexible isopropyl group is replaced by a more rigid cyclopropyl group to give the latter compound, molecules are 100% in a type **T3** conformation, and the **T1** conformation is

---

(22) (a) Andersson, S.; Drakenberg T. *J. Magn. Reson.* **1983**, *21*, 730. (b) Anderson, J. E.; Barkel, D. J. D. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1053. (c) Schaefer, T.; Penner, G. H.; Takeuchi, C. S.; Beaulieu, C. *Can. J. Chem.* **1989**, *67*, 1283.

(23) Columbus, I.; Biali, S. E. *J. Org. Chem.* **1994**, *59*, 8132.

(24) Kozhushkov, S. I.; Kostikov, R. R.; Molchanov, A. P.; Boese, R.; Benet-Buchholz, J.; Schreiner, P. R.; Rinderspacher, C.; Ghiviriga, I.; De Meijere, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 180.

calculated to be at least 10 kcal mol^{-1} less stable.[9] Calculations for **1e** and **1f** show that here likewise the **T1**-type conformation is significantly destabilized.

Experimental Section

Materials: 3,3-Diethylpentane (tetraethylmethane, 1a) was prepared as described in the literature.[4]

4,4-Dipropylheptane (tetrapropylmethane, 1b) was prepared[25] by reacting dipropyl ketone with propylmagnesium bromide. The resulting tripropylmethanol was treated with concentrated HCl to obtain the corresponding chloride (bp 81−83 °C at 13 mbar), which was subsequently reacted with allylmagnesium bromide. Reduction of the resulting 4,4-dipropyl-1-heptene (bp 78−79 °C at 8 mbar) by means of H_2 on Pd/C (alternatively ammonium formiate on Pd/C also can be used) yielded the final compound **1b**. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.12(t, 12H, $J = 6.5$ Hz), 1.30−1.45 (m, 16H). ^{13}C NMR ($CDCl_3$, 75.45 MHz) δ 14.51 (CH_3), 16.21 (CH_2), 37.39 (Cq), 39.32 (CH_2). Anal. Calcd for $C_{13}H_{28}$: C, 84.69; H, 15.31. Found: C, 84.66; H, 15.38.

1,3-Dichloro-2,2-bis(chloromethyl)propane (1c) and 1,3-dibromo-2,2-bis(bromomethyl)propane (1d) were commercially available and were further purified by recristallization (absolute ethanol).

1,3-Dicyclopropyl-2,2-bis(cyclopropylmethyl)propane (tetracyclopropylmethylmethane, 1e) was prepared as described in the literature.[7]

1-(2,2-Dibenzyl-3-phenylpropyl)benzene (tetrabenzylmethane, 1f) was prepared as described in the literature.[26] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.75(s, 8H), 7.15−7.35 (m, 20H). ^{13}C NMR ($CDCl_3$, 75.45 MHz) δ 42.06 (CH_2), 42.26 (Cq), 126.05 (CH), 127.90 (CH), 131.65 (CH), 139.34 (Cq). Anal. Calcd for $C_{29}H_{28}$: C, 92.50; H, 7.50. Found: C, 92.45; H, 7.55.

X-ray Diffraction: Crystal data of 1-(2,2-dibenzyl-3-phenylpropyl)benzene (Tetrabenzylmethane, 1f): $C_{29}H_{28}$ (376.51), trigonal, space group $P3_221$, $Z = 3$, Z primary $= 0.5$, $a = 9.9127(4)$ Å, $c = 18.9110(9)$ Å, $V = 1609.27(12)$ Å^3, $D_c = 1.166$ g cm^{-3}, $F(000) = 606$, $\mu_{Mo} = 0.065$ mm^{-1}, $T = 293$ K, Crystal size 1.2 × 1.2 × 1.0 mm^3. Data were collected by using a graphite monochromated Mo Kα X-radiation ($\lambda = 0.71073$ Å) range $2.37° < \theta < 25.00°$. Of 14577 reflections collected, 1907 were found to be independent ($R_{int} = 0.0311$), 1846 of which were considered as observed [$I > 2\sigma(I)$], and were used in the refinement of 133 parameters leading to a final R_1 of 0.0330 and a R_{all} of 0.0342. The structure was solved by direct method and refined by full-matrix least squares on F^2, using SHELXTL 97 program packages. In refinements were used weights according to the scheme $w = [\sigma^2(F_o{}^2) + (0.0441P)^2 + 0.1825P\,]^{-1}$, where $P = (F_o{}^2) + 2F_c{}^2)/3$. The hydrogen atoms were located by geometrical calculations and refined by using a “riding” method. wR_2 was equal to 0.0874. The goodness of fit parameter S was 1.094. The largest differences between the peak and hole were 0.162 and −0.105 eÅ^{-3}. Crystallographic data (excluding structure factors and including selected torsion angles) have been deposited with the Cambridge Crystallographic Data Center, CCDC no. 188152.

NMR Measurements. The samples for the low-temperature determinations were prepared by connecting to a vacuum line the NMR tubes containing the desired compounds and some C_6D_6 or CD_2Cl_2 for locking purpose. The gaseous solvents (CHF_2Cl and $CHFCl_2$ in about a 4:1 v/v proportion) were subsequently condensed therein by means of liquid nitrogen. The tubes were then sealed in a vacuum and introduced in the precooled probe of the spectrometers. The temperature was calibrated by means of a Ni/Cu thermocouple inserted in the NMR probe before the measurements. The computer simulation of the line shape was performed by a PC version of the computer program based on DNMR6 routines[27] and the best fit was visually judged by superimposing the plotted and experimental traces. As often reported in the case of conformational processes,[28]the free energies of activation were found essentially independent of the temperature in the examined range, thus indicating that the $\Delta S^{\ddagger}$ values are negligible within the experimental uncertainty.

TABLE 3. Selected Torsion Angles (deg) for 1e and 1f in the Preferred Conformation Type T3 As Found in the Crystal, by Ab Initio and Molecular Mechanics Calculations with Calculations for the T1-Type Conformation Shown for Comparison[a]

		conformation **T3**			conformation **T1**	
	dihedral	crystal	ab initio	MM3	ab initio	mm3
1e[b]	$X_A-C_A-C_q-C_B$	61.9	65.8	62.3	175.1	175.4
	$X_B-C_B-C_q-C_A$	179.2	173.1	177.5	175.1	175.7
	$X_C-C_C-C_q-C_D$	62.6	65.7	62.6	−175.1	−175.6
	$X_D-C_D-C_q-C_C$	177.8	173.2	177.7	−175.1	−175.9
	C_q-C_A-C-H	51.4	54.7	55.8	47.7	48.4
	C_q-C_B-C-H	−50.2	−54.7	−56.2	47.8	48.5
	C_q-C_C-C-H	54.2	54.7	56.0	−47.7	−48.7
	C_q-C_D-C-H	−55.3	−54.7	−56.1	−47.7	−48.9
1f	$X_A-C_A-C_q-C_B$	51.1	48.2	63.7	167.6	170.4
	$X_B-C_B-C_q-C_A$	179.7	−179.5	175.9	167.5	175.1
	$X_C-C_C-C_q-C_D$	51.1	48.2	66.0	−175.2	169.5
	$X_D-C_D-C_q-C_C$	179.7	−179.5	173.0	−175.2	174.1
	$C_q-C_A-C-C_{ortho}$	−86.7	−101.8	−76.1	35.9	66.5
	$C_q-C_B-C-C_{ortho}$	79.5	79.3	76.2	36.0	70.3
	$C_q-C_C-C-C_{ortho}$	−86.7	−101.8	−76.4	83.8	64.4
	$C_q-C_D-C-C_{ortho}$	79.5	79.3	76.5	83.9	68.4

[a] Atom labeling for **T1** and **T3** is indicated in Scheme 1. [b] The crystal structure data for **1e** are taken from ref 7.

Computations. The Molecular Mechanics (MM3 force field[11]) approach was used for all the conformational types **T1**−**T6** of each compound and, for the three conformers with the lower energy, also by ab initio (at the RHF 6.31G* level[10]) methods. For compounds **1c**−**f**, not previously calculated by Alder and co-workers, the relative MM3 energies of the six conformational types **T1**−**T6** are the following: **1c** 0.31, 3.48, 0.00, 6.86, 9.53, 2.98; **1d** 0.18, 3.68, 0.00, 7.38, 10.20, 3.20; **1e** 0.77, 1.76, 0.00, 3.58, 6.34, 1.71; and **1f** 3.30, 2.41, 0.25, 4.45, 8.08, 0.00. For compounds **1e** and **1f** various versions of each conformational type were found, depending on the disposition about cyclopropyl−CH_2 or phenyl−CH_2 bonds, respectively, but only the lowest energy value is reported. Significant torsion angles found for compounds **1e** and **1f** which adopt a **T3**-type conformation in the crystal are shown in Table 3 along with ab initio and molecular mechanics (MM3) calculated values for that conformation and for **T1**.

Acknowledgment. One of the authors (M.P.) thanks CINMPIS for a fellowship. L.L. and A.M. received financial support from MURST, Rome (national project “Stereoselection in Organic Synthesis”), and from the University of Bologna (Funds for selected research topics 2001−2002). A research fund for young researchers from the University of Bologna is also acknowledged by S.G.

JO025984K

---

(25) Petrov, A. D.; Tschernyschev, E. A. *Izv. Akad. Nauk SSSR Ser. Khim.* **1952**, 1082; *Chem. Abstr.* **1954**, *48*, 565e.

(26) Trotman, E. R. *J. Chem. Soc.* **1925**, *127*, 88. For the preparation of the intermediates see: Hill, G. A.; Nelson, W. C.; Dunnell, R. L.; Moody, L. S. *J. Am. Chem. Soc.* **1941**, *63*, 1367. Rodriguez, G.; Bazan, G. C. J. *Am. Chem. Soc.* **1997**, *119*, 343.

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

(28) Hoogasian, S.; Bushweller, C. H.; Anderson, W. G.; Kingsley, 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.