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Gear Effects in Polycyclohexyl Systems: Tetracyclohexylethene

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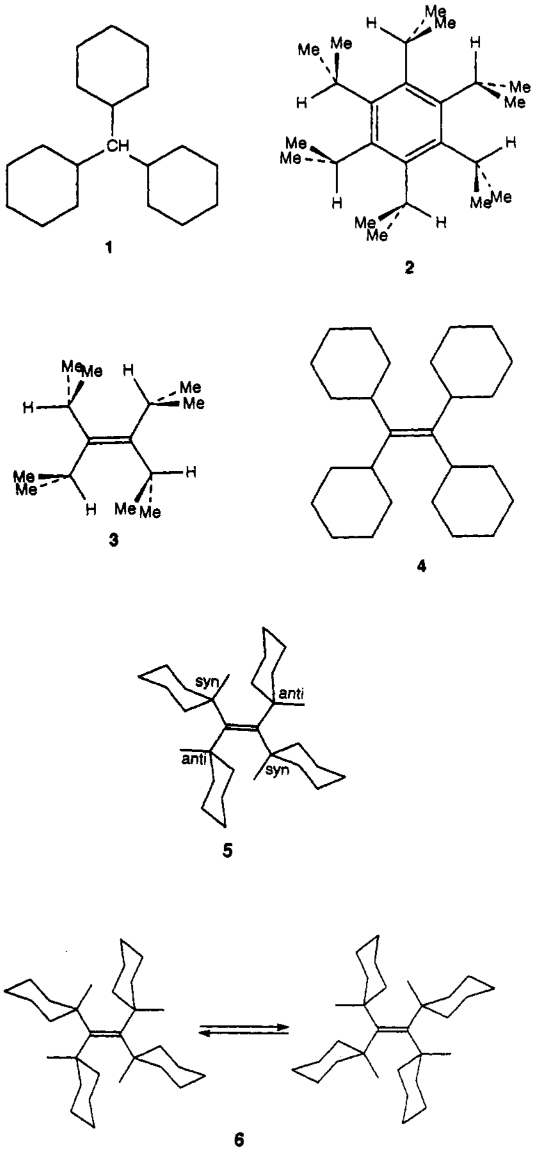
Tetracyclohexylethene (4) was synthesized by McMurry coupling of dicyclohexyl ketone. The ^{1}H and ^{13}C NMR spectra of 4 were analyzed by means of 2D NMR techniques. The compound exists both in solution and in the crystal in a conformation with a "tongue and groove" arrangement, i.e., in an arrangement in which the methine hydrogens are located in the notch provided by the methylene protons of a neighboring cyclohexyl ring. Molecular mechanics calculations reproduce satisfactorily the structural parameters found in the crystal structure of 4. The barrier for rotation of the cyclohexyl rings was measured by dynamic NMR from the exchange of *syn* and *anti* methine protons. This barrier is 18.7 kcal mol^{-1}, i.e., higher than that of tetraisopropylethene (ca. 16 kcal mol^{-1}). Molecular mechanics calculations of the rotational pathway suggest that the larger barrier observed for 4 is due to conformational restrictions imposed by the cyclohexyl rings.

Introduction

Cyclohexane represents a prototypical system which encompasses all the essential features of conformational analysis.[1,2] We have recently reported conformational studies of tricyclohexylmethane (1).[3] We found that in the lowest energy conformation the cyclohexyl rings are oriented in a chiral gauche–gauche–anti conformation. The enantiomerization of the system involves stepwise rotation of the rings and the rotational barrier is somewhat larger (7.3 ± 0.2 kcal mol^{-1}) than that for the related triisopropylmethane (6.6 kcal mol^{-1}).[4]

A substituted cyclohexane group should display in the region proximal to the substituent, a steric anisotropy similar to that found in an isopropyl group,[5] appearing "small" when encountered from the side of the methine hydrogen and "large" from the side of the two methylene groups attached to the methine carbon. Polyisopropyl systems in which several isopropyl groups are attached to a planar skeleton (e.g., hexaisopropylbenzene[6] (2) and tetraisopropylethene[7,8] (3)) exist in a conformation in which all isopropyl groups are oriented in the same direction (i.e., a homodirectional conformation)[9] and are bisected by the central plane. In this conformation the methine hydrogen of a given isopropyl group is tucked in the cleft of a pair of neighboring methyl groups while its two methyls provide the cleft for a neighboring isopropyl methine proton. This "tongue and groove" ("statically geared")[10] arrangement results in an appreciable barrier for internal rotation of the isopropyl groups.

Chart 1



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(1) For reviews on conformational flexible molecules, see: Hoffmann, R. W. *Angew. Chem., Int. Ed. Eng.* **1992,** *31,* 1124. Anderson, J. E. In *The Chemistry of Alkanes and Cycloalkanes*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1992; Chapter 2.

(2) For a recent review on the stereochemistry of cyclohexanes, see: Mann, G. *Z. Chem.* **1990,** *30,* 1.

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(6) Arnett, E. M.; Bollinger, J. M. *J. Am. Chem. Soc.* **1964,** *86,* 4729. Hopff, H.; Gati, A. *Helv. Chim. Acta* **1965,** *48,* 509. Siegel, J.; Gutierrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* **1986,** *108,* 1569.

(7) (a) Bomse, D. S.; Morton, T. H. *Tetrahedron Lett.* **1975,** 781. (b) Langler, R. F.; Tidwell, T. T. *Tetrahedron Lett.* **1975,** *10,* 777. (c) McMurry, J. E.; Fleming, M. P. *J. Org. Chem.* **1976,** *41,* 896. (d) McMurry, J. E.; Leckta, T.; Rico, J. G. *J. Org. Chem.* **1989,** *54,* 3748.

(8) Casalone, G.; Pilati, T.; Simonetta, M. *Tetrahedron Lett.* **1980,** *21,* 2345.

(9) Mislow, K. *Chimia* **1986,** *40,* 395. Biali, S. E.; Buda, A. B.; Mislow, K. *J. Org. Chem.* **1988,** *53,* 1289.

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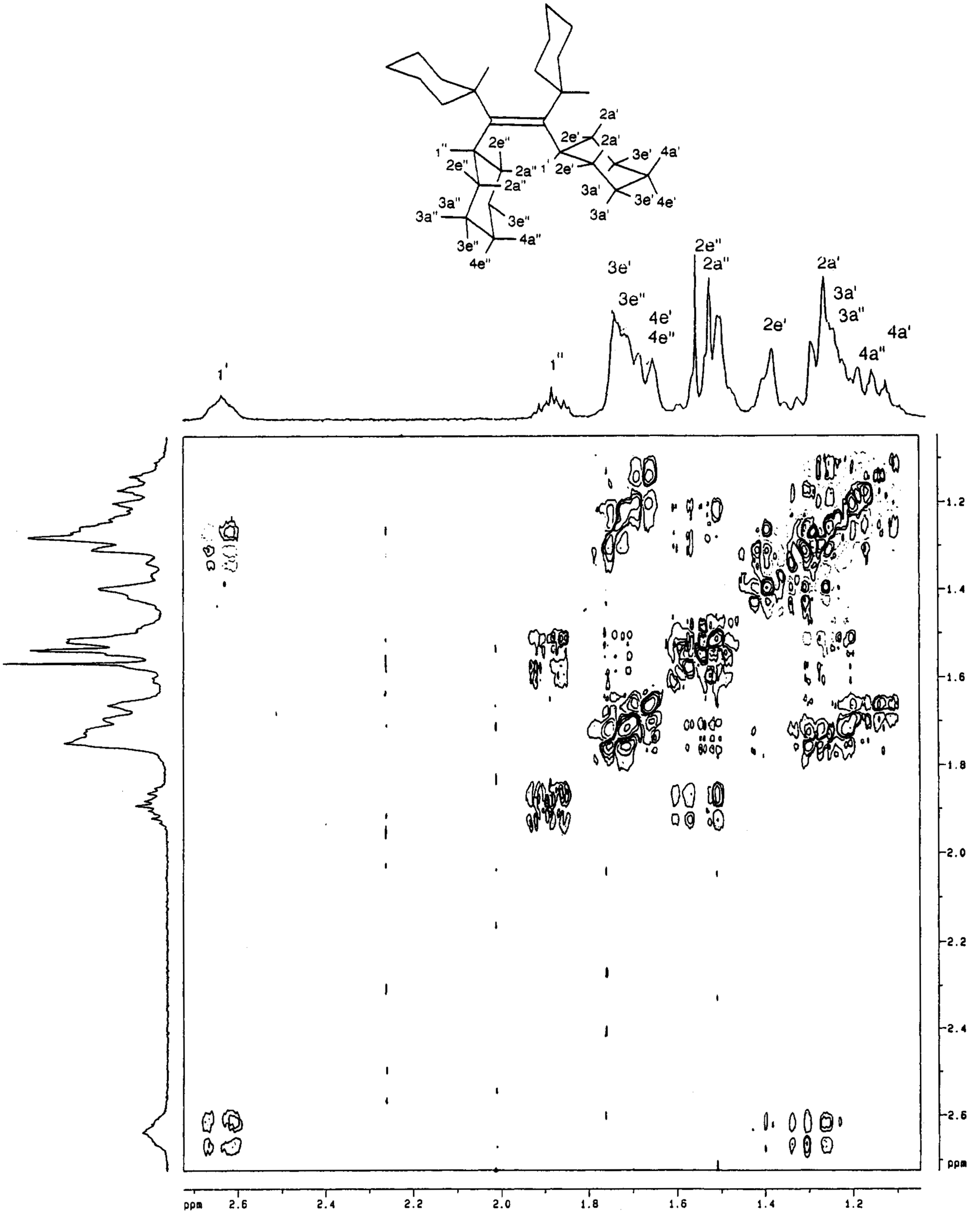

Figure 1. 400-MHz ^{1}H NMR DQF COSY spectrum of tetracyclohexylethene 4.

In order to study the static gearing effects of cyclohexyl rings, we decided to prepare and study a polycyclohexyl system displaying this conformational phenomenon. The chosen system was tetracyclohexylethene (**4**) since inspection of space filling models suggested that the system may exist in a tongue and groove arrangement.[11]

Results and Discussion

Preparation and Solution NMR Spectra of the System. For the preparation of **4**, we reacted dicyclohexyl ketone with $TiCl_3$ under the conditions reported for the

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[10] Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynsky, R. J.; Mislow, K. *Isr. J. Chem.* **1980**, *20*, 65.

[11] The saturated analogue of **4** (1,1,2,2-tetracyclohexylethane) has been synthesized and stereochemically analyzed. See: Baxter, S. G.; Fritz, H.; Hellmann, G.; Kitschke, B.; Lindner, H. J.; Mislow, K.; Rüchardt, C.; Weiner, S. *J. Am. Chem. Soc.* **1979**, *101*, 4493.

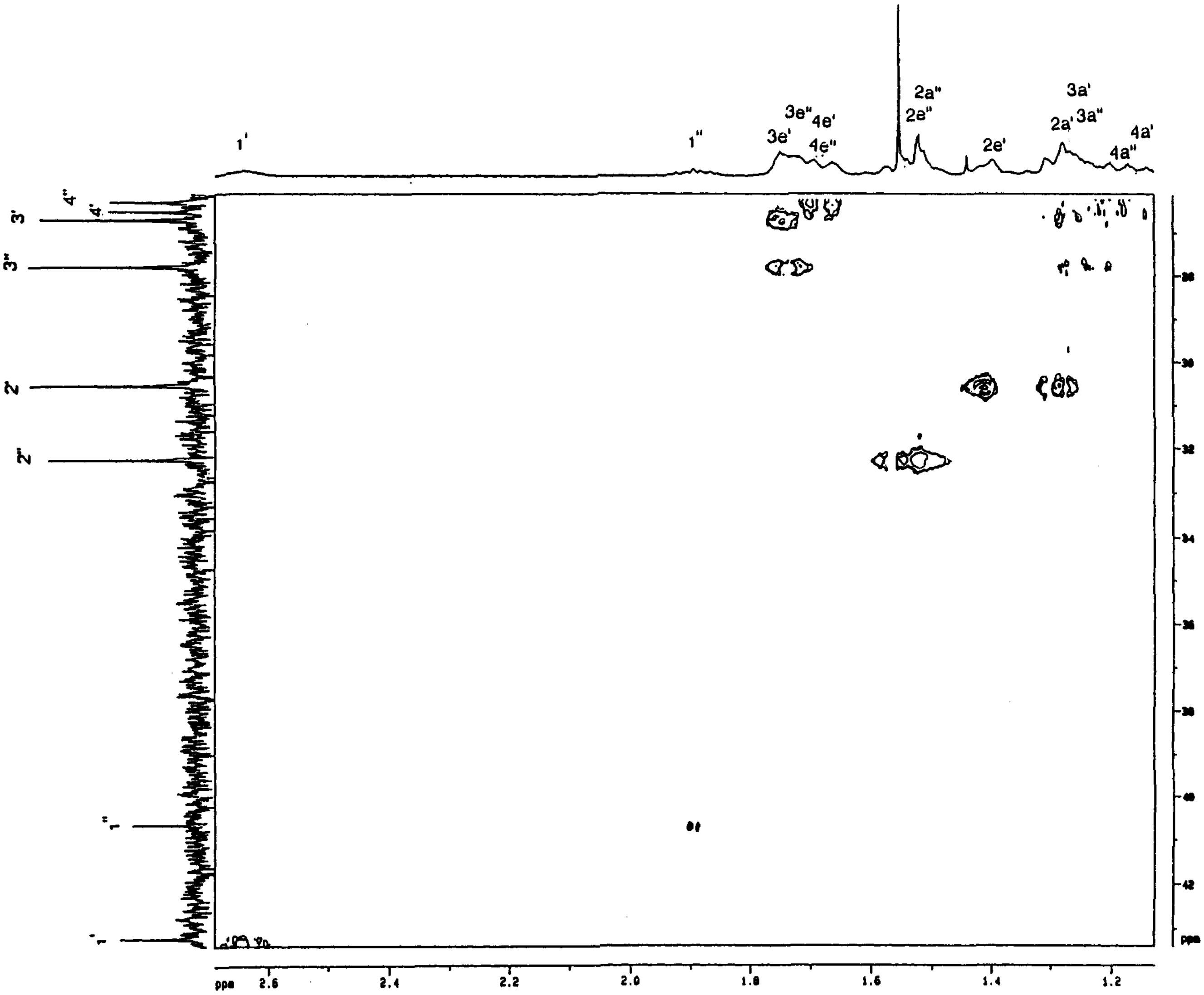

Figure 2. Inverse H/C correlation spectrum of 4, using the BIRD pulse sequence.

preparation of tetraisopropylethene in ref 7c. The reaction resulted in the isolation of 4 in 20% yield. 4 displays in the ^{13}C NMR ($CDCl_3$) one signal at 143.0 ppm, corresponding to the ethylenic carbons and eight signals in the aliphatic region. This NMR pattern is consistent with a frozen homodirectional conformation of C_{2h} symmetry with two symmetry nonequivalent rings, each bisected by the double-bond plane. For nomenclature purposes a ring will be dubbed *syn* and *anti* depending whether its methine proton is oriented *syn* or *anti* to the C=C bond (cf. 5). Ethene 4 displayed in the ^1H NMR ($CDCl_3$, rt, 400 MHz) a very complex spectrum in the δ 1.1–1.8 region resulting from the presence of several overlapping methylene protons and two separate signals at δ 1.85 and 2.6, which were assigned to the methine protons. The chemical shift difference between the two methine protons ($\Delta\delta$ = 0.75 ppm) is somewhat larger than the reported difference for 3 (($\Delta\delta$ = 0.67 ppm)).[7a] The assignment of the signals in the ^1H and ^{13}C NMR spectra was carried out by a combination of the DQF/COSY and inverse H/C correlation techniques (Figures 1 and 2).[12] In the DQF/COSY spectra mutually coupled signals can be spotted by the appearance of cross-peaks. As shown previously for 1,[3] pairs of protons in a 1,2-diaxial or geminal relationship display strong cross-peaks while pairs of protons in axial/equatorial or diequatorial arrangements display small cross-peaks. The H/C correlation allows us to assign pairs of protons attached to a given carbon. Based on this assignment, it can be concluded that the methine protons involved in the tongue and groove arrangement are located at axial positions and therefore the cyclohexyl rings are attached to the central ethylene by their equatorial positions. In the positions not involved in the tongue and groove arrangement (positions 3 and 4 of the cyclohexane rings), the equatorial protons resonate at a lower field than the axial ones, as generally observed for cyclohexane systems.[13] The assignment provided by the 2D spectra allows us to sort the signals into two sets, each set belonging to one of the two symmetry nonequivalent cyclohexyl rings. However, based on the NMR alone, one cannot conclude whether it is the methine *syn* or the one *anti* to the double bond which is the one more strongly deshielded. Petterson and Berg[14] assigned the lower field methine signal of 3 to the *syn* protons on the basis of comparison with several di- and triisopropylethylene systems and double-bond anisotropy arguments. Assuming that similar effects are

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[12] For a review on 2D NMR techniques, see: Kessler, H.; Gehrke, M.; Griesinger, M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 490.

[13] Günther, H. *NMR Spectroscopy*; Wiley: Chichester, 1980; p 72.

[14] Petterson, I.; Berg, U. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1365.

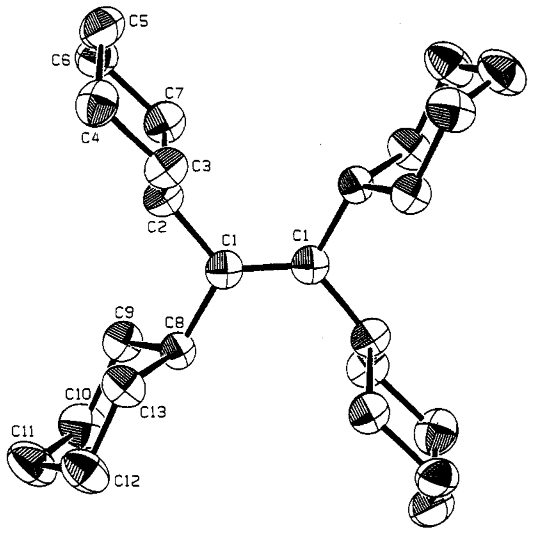

Figure 3. Numbering scheme of of the crystal conformation of 4. One-half of the molecule is related by the crystallographic inversion center to the second half.

operative in 4, a complete assignment of the ^{1}H and ^{13}C NMR signals can be made as shown in Figures 1 and 2.

Rotational Barrier. Rotation of all rings by 180° should mutually exchange pairs of signals at the *syn* and *anti* rings and therefore should result in topomerization (cf. 6). The more convenient probe for following the process is the exchange of the methine protons since they are well separated from the rest of the signals. The temperature dependence of the 400-MHz ^{1}H NMR spectrum of 4 in 1,1,2,2-tetrachloroethane-d_2 was examined. Upon raising the temperature, the two diastereotopic cyclohexyl methines broadened and coalesced at 406 K. From the chemical shift separation of the methines ($\Delta\nu$ = 303.2 Hz), the exchange rate at the coalescence temperature was calculated using the Gutowsky–Holm approximation.[15] The barrier for the rotation of the cyclohexyl rings is $\Delta G^{\ddagger}$ = 18.7 kcal mol^{-1}. For the corresponding tetraisopropyl system 3, this barrier was reported[7a] as 17.0 kcal mol^{-1} but a better estimate is 16.0 kcal mol^{-1}.[16] Clearly, the rotational barrier for a system with statically geared cyclohexyl groups is higher than the corresponding barrier for a system with statically geared isopropyl groups.

X-ray Structure. A single crystal of 4 was grown from benzene and submitted to X-ray crystallography. The molecule crystalizes in the $C2/c$ space group with four molecules in the unit cell. The numbering scheme of the crystal conformation and a stereoscopic view are shown in Figures 3 and 4. The molecule is located in a crystallographic inversion center. As shown in the Figures, 4 exists in a conformation in which all cyclohexyl groups are approximately bisected by the double bond, the C═C—CH torsional angles being 0.5 and 179.4°. All cyclohexyl rings exist in chair conformations and are attached to the ethene moiety through their equatorial positions. The axial protons of the rings are involved in the tongue and groove arrangement, either providing the tongue (the methine protons) or delimiting the groove (the axial protons in the 2 position). Of special interest are the nonbonded distances between these two sets of protons. This distance is somewhat smaller for two rings in a *cis* relationship than for two rings in a geminal arrangement (2.02 and 2.18 Å, respectively), suggesting that the mutual interlocking between two *cis* groups is somewhat more efficient than for a pair of geminally related rings. Selected bond lengths and angles are collected in Table 1. The conformation adopted is similar to that reported for the crystal structure of 3 (Table 1), although in the latter case the molecule displayed disorder in the crystal.[8]

Table 1. Selected Experimental (X-ray) and Calculated Structural Parameters for 4 and 3[a,b]

parameter	4 (exp)	4 (calcd)	3 (exp)	3 (calcd)
C1–C1′	1.348(3)	1.369	1.347(2)	1.367
C1–C2	1.532(2)	1.540	1.531(3)	1.540
C1–C8	1.519(3)	1.525	1.520(3)	1.525
C1′–C1–C2	124.7(2)	125.3	125.2(2)	125.2
C1′–C1–C8	122.3(2)	122.8	122.2(2)	122.8
C1–C8–C13	113.1(1)	112.9	112.5(2)	112.3
C1–C2–C3	115.6(1)	113.9	114.3(1)	113.6
C1′–C1–C2–H2	0.5	0.0	−0.9/3.1	0.0
C1′–C1–C8–H8	179.4	180.0	193.9/180.6	180.0
C2–C1–C8	113.0(1)	111.9	112.6(1)	112.0
H3–H8[c]	2.18	2.09	2.20/2.22	2.13
H13–H2′ [c]	2.02	1.93	2.06/2.12	1.96

[a] X-ray structural parameters of 3 taken from ref 8. [b] Bond lengths in angstroms, bond and dihedral angles in degrees. [c] Nonbonded distance.

Molecular Mechanics Calculations. For the evaluation of the relative energies of the different conformers of the system, we used the MM3(92) program.[17] In principle the different conformations of 4 arise from the different possible orientations of the cyclohexyl rings with regard to the double bond (*syn* or *anti*), the conformation adopted by the ring, and the point of attachment of the ring (an axial or equatorial position). In the following discussion we will restrict ourselves to conformations in which the cyclohexyl rings exist in a chair conformation and are attached to the double bond by their equatorial positions, since these are expected to be the lower energy conformations. The different conformations of 4 will be described by a four-letter descriptor which describes, in a clockwise order, the relative orientations (*syn* (s) or *anti* (a)) of the cyclohexyl rings. For example, in the homodirectional conformation the four rings are oriented in *anti*, *syn*, *anti*, *syn* arrangements and therefore the descriptor is "sasa".[18] We generated all possible conformations resulting from different arrangements of cyclohexanes existing in chair conformations and evaluated their energies by the MM calculations. Input conformations were based on standard geometries of the cyclohexyl rings oriented either with C═C—C—H torsional angles of 0° or 180°. The calculated relative steric energies of the

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[15] Gutowsky, H. S.; Holm, C. H. *J. Chem. Phys.* **1956**, *25*, 1228.

[16] The rotational barrier height of 3 was obtained in ref 7a according to Gupta, R. K.; Pitner, T. P.; Wasylishen, R. *J. Magn. Reson.* **1974**, *13*, 383. It was reported that the two unequivalent methyl groups resonate in the ^{1}H NMR at δ 0.94 and 1.13 and that these signals coalesce at 35 °C. Assuming that the NMR spectrum was run on a 60-MHz instrument, the Gutowsky–Holm equation ($k_c = \pi\Delta\nu/2$) affords a value of 25.3 s^{-1} for the exchange rate at the coalescence temperature, and therefore a barrier of 16.0 kcal mol^{-1}. Reference 7b reports that at 60 MHz the two isopropyl doublets (δ 0.91 and 1.10) coalesce at 35 °C, which affords a barrier of 16.1 kcal mol^{-1}.

[17] Allinger, N. L. *Molecular Mechanics. Operating Instructions for the MM3 program, 1989 Force Field (updated 5/6/92)*. Technical Utilization Corporation.

[18] Depending of its symmetry, a conformation can be described by one, two, or four descriptors. For example, the homodirectional conformation can be described either by sasa or asas while a conformation with three rings *anti* and one *syn* can be described by either saaa, asaa, aasa, or aaas. However, although there may be more than one descriptor for a conformation, a given descriptor describes the conformation unequivocally.

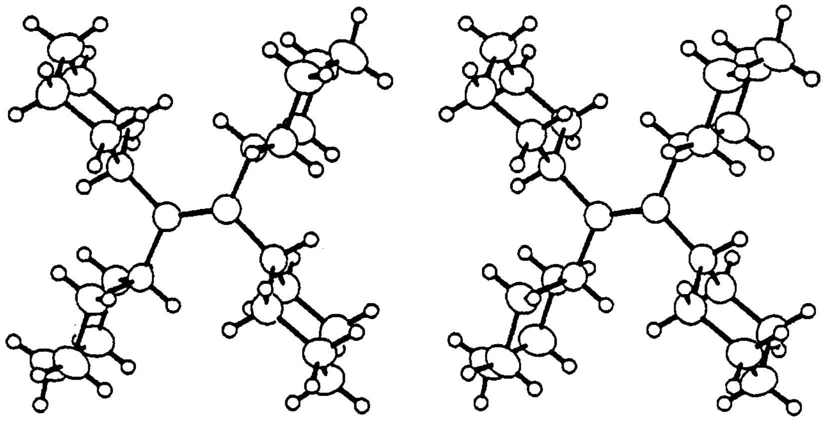


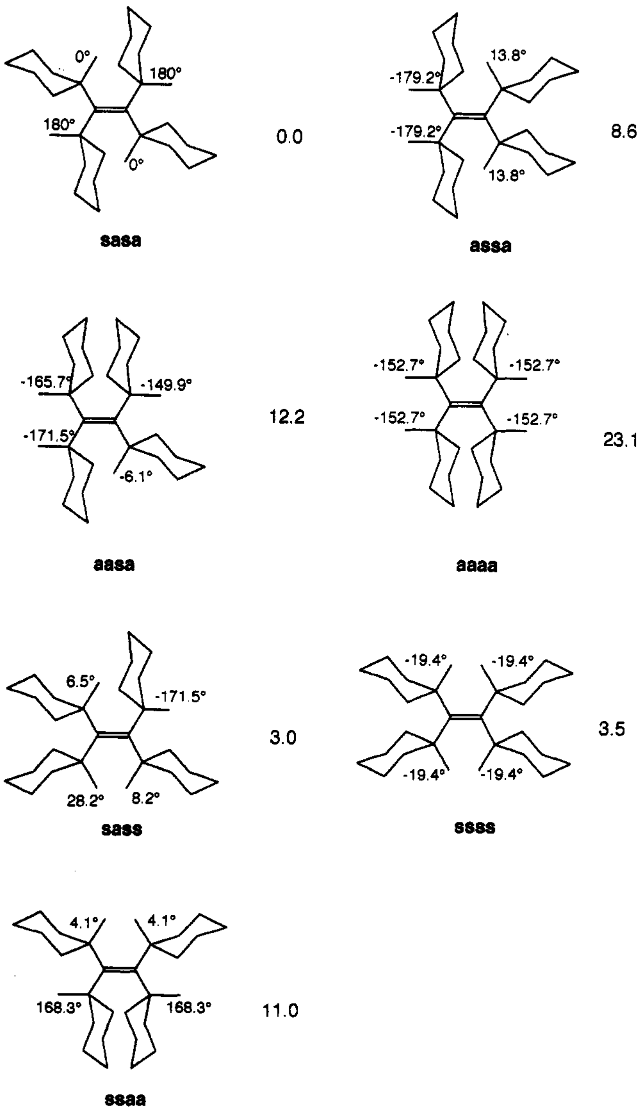
Figure 4. Stereoscopic view of the crystal conformation of 4.

conformations and the calculated torsional angles are collected in Scheme 1. As shown in Scheme 1, the crystallographic sasa conformation represents the minimum energy conformation. The calculations reproduce satisfactorily the structural parameters of the system (Table 1) although they seem to overestimate the length of the $C{=}C$ bond. Only in the sasa conformation are the rings exactly bisected by the double bond ($C{=}C{-}CH$ torsional angles of 180° and 0°). According to the calculations, sasa conformations with one axial *syn* ring, one axial *anti* ring, a pair of axial rings in geminal or vicinal relationships, and four axial rings lie 7.1, 11.2, 12.5, 12.5, and 24.9 kcal mol^{-1} above the all-equatorial conformation, respectively.[19] Ethene 3 was previously calculated by two groups[20,21] and for comparison purposes we decided to recalculate its structure with the state-of-the-art MM3 program. As in the case of 4, the program reproduces the geometry satisfactorily (Table 1), but the $C{=}C$ length is overestimated.

As shown in Scheme 1, the energy of the conformations increases with the number of gear-clashing interactions. As shown by the calculations, the clashing interaction of two *anti* rings in a *cis* relationship is substantially more repulsive than the corresponding interaction between two *syn* rings in a geminal disposition.

The rotation of the cyclohexyl rings may involve a stepwise rotation of the cyclohexyl rings or a correlated rotation through a single transition state. For the related tetraisopropylethene 3, Ermer showed that the preferred rotational pathway involves stepwise rotation of the rings.[21] The topomerization barrier of 4 was calculated starting from the sasa conformer by driving either the *anti* or the *syn* ring leading to the sass and aasa conformations, respectively. Since the two rings are symmetry nonequivalent, two different barriers were obtained. The different rotational barriers calculated by driving the different cyclohexyl rings are displayed in Figure 5. The lowest energy pathway which results in topomerization corresponds to the sasa → sass → saas with barriers of 17.8 and 19.7 kcal mol^{-1}, respectively. This process involves the consecutive rotations of two ring in a *cis* relationship.

Scheme 1. Calculated (MM3) Relative Steric Energies of the Conformers of 4. The $C{=}C{-}CH$ Torsional Angles (in Degrees) Are Denoted on the Different Structures



The rotational barriers for 3 were calculated by Ermer using the consistent force field[21] which gave barriers of 14.9 and 17.6 kcal mol^{-1} for the sasa ⇄ sass and sass ⇄ saas interconversions, respectively. By inclusion of entropy terms, the corresponding ΔG were calculated as 17.5 and 19.5 kcal mol^{-1}.[21] For comparison purposes with the calculated barrier of 4, we recalculated 3 using the MM3 program and obtained values of 15.1 and 16.6 kcal mol^{-1}, respectively, which are in better agreement with the

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[19] Conformations with an *anti* axial cyclohexyl displayed severe distortions of the chair conformation.

[20] Favini, G.; Simonetta, M.; Todeschini, R. *J. Comput. Chem.* **1981**, 2, 149.

[21] Ermer, O. *Angew. Chem. Suppl.* **1983**, 1353.

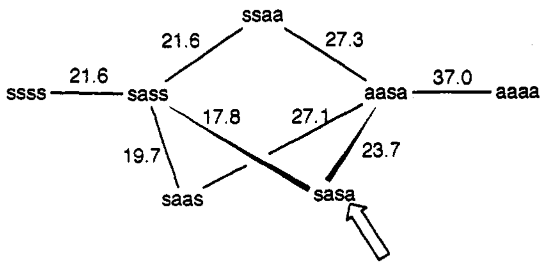

Figure 5. Calculated (MM3) interconversion graph for the internal rotations of 4. All numbers represent relative steric energies (steric energy of the transition-state energy of the sasa conformation) in kcal mol^{-1}.

experimental value. According to the MM3 calculations, the topomerization barrier of 4 is 3.1 kcal mol^{-1} higher than the corresponding barrier for 3. This barrier difference is in agreement with the experimental values ($\Delta\Delta G^{\ddagger} = 2.7$ kcal mol^{-1}), which indicates that the barrier difference is mostly due to enthalpic reasons.

Gear Meshing in Polycyclohexyl Systems. There is one important conformational restriction in a cyclohexyl group which is not present in an isopropyl group: whereas the two methyls in an isopropyl group are capable to adopt any conformation, the presence of a ring limits the possible orientations of the two methylene units attached to the methine carbon (i.e, those delimiting the "groove" involved in the static gearing process). Examination of the crystallographic and calculated lower energy conformations of 4 and 3 shows that the methine hydrogens of the *syn* rings in 4 are more deeply introduced in their corresponding grooves than the methines of 3, as judged from the H3/H8 and H13/H12 nonbonded distances. However this ground-state effect is not sufficient to account for the difference in rotational barriers. The main influence probably occurs in the transition state. Examination of the calculated rotational transition states of 4 and 3 shows that the main steric interactions between the groups are between the hydrogens at the 1 and 2 positions of the cyclohexyl or isopropyl groups. For 4, the nonbonded distances between the methylene protons at the 2 position of the rotating ring and the protons at the 1 or 2 positions of the neighboring rings are shorter than the corresponding distances in the case of 3. Due to the conformational restrictions imposed by the cyclohexyl rings, the methylene groups at the 2 positions of 4 are not free to adopt a conformation attainable by 3 which minimizes partially the steric interactions. This effect results in the higher barrier observed for 4.

Experimental Section

Dicyclohexyl ketone was purchased from Aldrich. The X-ray diffraction data were measured with an ENRAF-NONIUS CAD-4 automatic diffractometer. Cu Kα ($\lambda = 1.54178$ Å) radiation with a graphite crystal monochromator in the incident beam was used. Intensities were corrected for Lorentz and polarization effects. All non-hydrogen atoms were found by using the results of the SHELXS-86 direct method analysis. After several cycles of refinements the positions of the hydrogen atoms were calculated and added to the refinement process. All crystallographic computing was done on a VAX 9000 computer using the TEXSAN structure analysis package.

Crystal data for 4:[22] $C_{26}H_{44}$ space group $C2/c$, $a = 19.641(3)$ Å, $b = 6.419(1)$ Å, $c = 17.693(2)$ Å, $\beta = 94.83(1)°$, $V = 2222.7(8)$ Å^3, $z = 4$, $\rho_{calc} = 1.07$ g cm^{-3}, μ(Cu Kα) = 3.99 cm^{-1}, no. of unique reflections = 1638, no. of reflections with $I \geqslant 3\sigma_I = 1364$, $R = 0.055$, $R_w = 0.072$.

Tetracyclohexylethene. $TiCl_3$ (3.1 g, 0.028 mol) and 2.5 g of K were added under an argon atmosphere to 130 mL of dry THF, and the mixture was refluxed for 1h. Dicyclohexyl ketone (0.65 g) in 20 mL of dry THF was added, the mixture was refluxed for 10 h, and then the reaction was quenched with EtOH, yielding 150 mg of 4 (20%): mp 273–275 °C; IR (KBr) ν 2927, 2858, 1447 cm^{-1}; MS m/z 356 (M); ^{13}C NMR ($CDCl_3$, rt) δ 26.28, 26.50, 26.70, 27.81, 30.55, 32.27, 40.67, 43.23, 142.99. Anal. Calcd for $C_{26}H_{44}$: C, 87.56; H, 12.44. Found: C, 87.75; H, 12.06.

Acknowledgment. We thank Dr. Shmuel Cohen for the crystal structure determination and Dr. Roy E. Hoffman for his assistance in the NMR experiments and helpful discussions. This work was supported by the Niedersachsen Foundation.

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[22] The authors have deposited atomic coordinates for structure 4 with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.