ORGANIC
LETTERS

2008
Vol. 10, No. 21
4763−4766

Internal Dynamics and Optical Rotations Predicted for O_h- and O-Symmetric Cubanes

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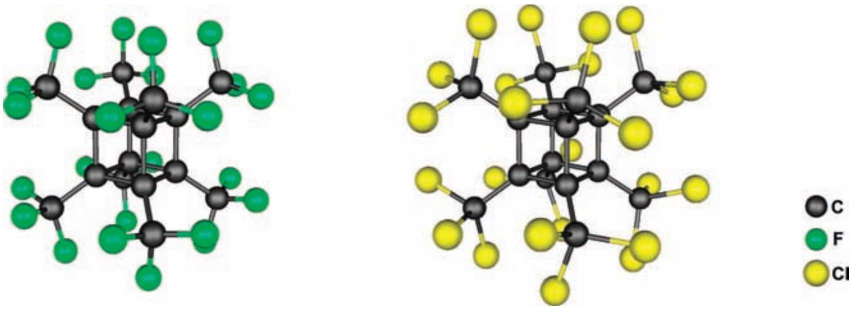
Received July 30, 2008

ABSTRACT



B3LYP/6-31G(d) calculations find that cubanes, persubstituted with NO_2 or BF_2 groups, are predicted to undergo near-barrierless, internal disrotations. However, as a consequence of the intrinsically higher energies of eclipsed conformations for threefold than for twofold rotors, the threshold mechanisms for octamethyl-, octakis(trifluoromethyl)-, octakis(trichloromethyl)-, octakis(tribromomethyl)-, octasilylcubane, and octakis(trichlorosilyl)cubane are calculated to be mono- or conrotation. The cubanes with the larger substituents are predicted to be *O*-symmetric, resolvable, and thus optically active.

Michl and co-workers, in their comprehensive review[1] of artificial molecular rotors, observed that complex molecular motions[2] can be irrationally mesmerizing. We previously fell under the spell of octanitrocubane (**1**),[3] not because of its explosive potential,[4] but because of the remarkably low barrier of only 0.078 kcal/mol that is computed for coupled disrotations of all eight nitro groups.[5]

We also predicted that, as a consequence of the desymmetrization that results from attaching twofold rotors to the body diagonal of an O_h cubic framework, correlated disrotation in **1** would be accompanied by a pseudorotation of the unique fourfold axis. On the other hand, cubanes that are persubstituted with threefold rotors can preserve the full rotational symmetry of the cubic frame, resulting in either achiral O_h- or chiral O-symmetric molecules. Here, we report the results of calculations on the extent to which the internal motions, calculated for **1**, can be generalized to another twofold rotor and to threefold rotors.

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10.1021/ol801762r CCC: $40.75

It has long been suspected that cubanes with eight threefold rotors could have *O*-symmetry,[6] in which the planes of symmetry in a cube are absent but the axes of symmetry remain. This point group has resisted representation by small molecules.[7,8] Our calculations predict (a) which threefold rotors should give cubanes with equilibrium conformations of *O*-symmetry, (b) whether the internal rotations of the substituents in such compounds are correlated, (c) whether such compounds would be configurationally stable, and (d) what would be the expected optical rotation of these chiral cubanes.

Density functional theory calculations were employed, using the three-parameter hybrid exchange functional of Becke[9a] and the correlation functional of Lee, Yang, and Parr (B3LYP).[9b] Geometry optimizations, vibrational analyses, potential energy surface scans, and optical rotation calculations were all carried out at the B3LYP/6-31G(d) level using the Gaussian 03[10] suite of programs.

Twofold Rotors: NO_2 and BF_2. We previously reported that correlated disrotation of the eight nitro groups in **1** is an essentially barrierless process.[5] Incremental rotations by 5° of a single nitro group gave a calculated barrier of just 0.078 kcal/mol for correlated disrotation of all eight nitro groups. Minima of D_4 symmetry and maxima of D_{2d} symmetry appear every 15° along the coordinate for internal rotation.

In contrast to the very low barrier computed for coupled disrotation, 180° rotation of a single nitro group, with all seven other nitro groups frozen at the equilibrium geometry, is computed to be energetically demanding. With a barrier height is computed to be 26.2 kcal/mol.[4] Rotation of negatively charged nitro oxygens past each other makes gear slippage in **1** energetically costly.

In order to test the generality of our findings on internal rotations in **1**, we replaced the eight NO_2 rotors in **1** with the eight BF_2 rotors in **2**. Like the NO_2 substituents in **1**, the BF_2 rotors in **2** have a twofold rotational axis of symmetry.

As for **1**, coupled disrotation is computed to be favored for **2**, although in **2** minima of D_2 symmetry are found to be very slightly lower in energy than those of D_4 symmetry. The calculated barrier in **2** of 0.059 kcal/mol is even closer to zero than the calculated barrier of 0.078 kcal/mol in **1**. As in **1**, gear slippage in **2** is energetically costly but not by nearly as much. Only 6.5 kcal/mol is required to rotate one BF_2 group by 180°, with all seven of the other BF_2 groups fixed at their equilibrium positions, compared to the barrier height of 26.2 kcal/mol for uncoupled rotation of just one NO_2 group in **1**.

Threefold Rotors: O_h- and Effectively O_h-Symmetric Cubanes. Persubstituted cubanes (cubane-L_8) with threefold rotors were also investigated computationally. Octamethylcubane (**3**) is predicted to be perfectly staggered with an O_h ground state (i.e., $H-C_{methyl}-C_{cubyl}-C_{cubyl)} = \pm 60°$). Octakis(trifluoromethyl)cubane (**4**), two views of which are shown in Figures 1a and 2a, is calculated to have a chiral *O* ground state, but barely so. A $F-C_{methyl}-C_{cubyl}-C_{cubyl}$ torsion angle of ±58.6° is computed, and a barrier to enantiomerization (via a transition structure of O_h-symmetry) of only 0.0003 kcal/mol is calculated. Octasilylcubane (**5**) is also computed to have a ground state of *O*-symmetry, with a $H-Si-C_{cubyl}-C_{cubyl}$ torsion angle of ±46.5° and a barrier to racemization of 0.51 kcal/mol.

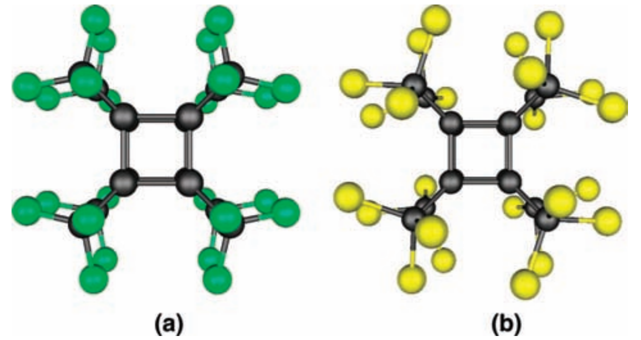

Figure 1. Face-on view of (a) O_h-symmetric octakis(trifluoromethyl)cubane (**4**) and (b) the *P* enantiomer of *O*-symmetric octakis(trichloromethyl)cubane (**6**).

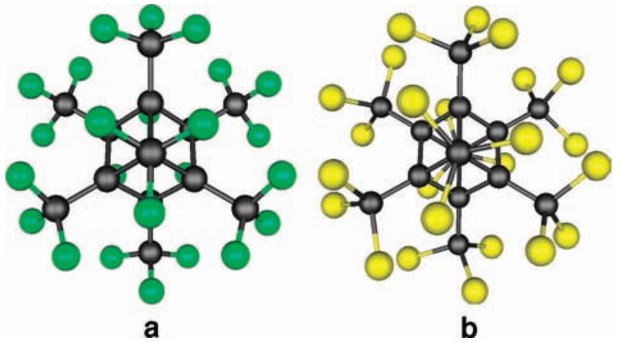

Figure 2. Views of (**a**) octakis(trifluoromethyl)cubane (**4**) and (**b**) the *P* enantiomer of octakis(trichloromethyl)cubane (**6**) along the body diagonals.

Unlike the case for the twofold rotors in **1** and **2**, enforced rotation of a single threefold rotor in **3**−**5** does

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(6) Iroff, L. D.; Mislow, K. *J. Am. Chem. Soc.* **1978**, *100*, 2121–2126.

(7) In their book on optical activity, Caldwell and Eyring went to great lengths in their conception of a molecule with *O* symmetry. See: Caldwell, D. J.; Eyring, H. *The Theory of Optical Activity*; Wiley-Interscience: New York, 1971; pp 156−157. Narasimhan et al. have likewise used DFT to design *T*-symmetric compounds. See: Narasimhan, S. K.; Lu, X.; Luk, Y.-Y. *Chirality* **2008**, *20*, 878–884.

(8) On the other hand, the protein ferritin, an aggregate of 24 subunits, was shown to have *O* symmetry. (a) Lawson, D. M.; Artymiuk, P. J.; Yewdall, S. J.; Smith, J. M. A.; Livingstone, J. C.; Treffry, A.; Luzzago, A.; Levi, S.; Arosio, P.; Cesareni, G.; Thomas, C. D.; Shaw, W. V.; Harrison, P. M. *Nature* **1991**, *349*, 541–544. More recently, chiral, octahedral, supramolecular nanoballs were synthesized. See: (b) Moon, D.; Kang, S.; Park, J.; Lee, K.; John, R. P.; Won, H.; Seong, G. H.; Kim, Y. S.; Kim, G. H.; Rhee, H.; Lah, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 3530–3531. (c) Ghosh, S.; Mukherjee, P. S. *J. Org. Chem.* **2006**, *71*, 8412–8416. The synthesis of a chiral nanocube has just been reported. (d) Xu, D.; Warmuth, R. *J. Am. Chem. Soc.* **2008**, *130*, 7520.

(9) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *B37*, 785–789.

(10) Frisch, M. J.; et al. *Gaussian 03*, *revision D.02*; Gaussian, Inc.: Wallingford CT, 2004. For the full references, see the Supporting Information.

not result in coupled rotation of the other seven substituents. Instead, transition structures for the rotation of just one substituent were located. Table 1 shows that as a single substituent is rotated against the seven others, energy barriers of 2.3, 5.4, and 1.7 kcal/mol, respectively, are encountered in **3**−**5**.

Table 1. Energy Barriers (kcal/mol) for C−L Rotations

	cubane-L_8			
L	monorotation[a]	T_d[b]	O_h[c]	cubane-L[d]
NO_2 (**1**)	*e*	0.078	—	0.023
BF_2 (**2**)	*e*	0.059	—	0.010
CH_3 (**3**)	2.3[f]	8.8[i]	0	3.1
CF_3 (**4**)	5.4[f]	22.4[i]	3.1×10^{-4}	3.2
SiH_3 (**5**)	1.7[f]	5.1[i]	0.51	1.8
CCl_3 (**6**)	—[f,g,h]	129.8[i,j]	43.0[i]	8.0
CBr_3(**7**)	—[f,g,h]	133.8[i,j]	72.9[i]	8.9
$SiCl_3$(**8**)	—[f,g,h]	76.9[i,j]	26.0[i]	1.8

[a] A scan in which only a single substituent is forced to rotate. [b] Transition structure or maximum energy structure for coupled disrotation. [c] Maximum energy structure for coupled conrotation. [d] The energy difference between the staggered and eclipsed conformations. [e] When a single substituent is forced to rotate, the remaining seven substituents undergo correlated disrotation. [f] When a single substituent is forced to rotate, the remaining seven substituents do not rotate at all. [g] No stationary point, corresponding to a monorotation transition structure, could be located. [h] $C_{cubyl}-C_{cubyl}$ and M−X bond cleavage occurs. [i] Structure has multiple imaginary frequencies. [j] $C_{cubyl}-M$ bond cleavage occurs.

Enforced disrotation in **3**−**5** leads to T_d energy maxima with multiple imaginary frequencies. As shown in Table 1, these maxima are three to four times higher in energy than the transition structures for rotation of a single substituent.[11]

Table 1 also gives the calculated barriers to rotation for monosubstituted cubanes (cubane-L) with the same rotors as in **1**−**5**. Like the energy barriers to disrotation in cubane-L_8, the energy barriers for single substituent group rotation in cubane-L are more than 2 orders of magnitude smaller for the twofold rotor groups in **1** and **2** than for the threefold rotor groups in **3**−**5**. In fact, rotation of a single NO_2 or BF_2 group in cubane-L is computed to be nearly barrierless. The nearly barrier-free rotation of the individual NO_2 rotors in **1** and the BF_2 rotors in **2** allows coupled rotation of all eight twofold rotors in these two cubane-L_8 molecules also to be nearly barrier-free.

As described in ref 1, the difference in the barriers to rotation of twofold and threefold rotors has its origin in the fact that, when the axial symmetries of the groups moving past one another are not matched, the number of minima are multiplicative. More importantly, the barrier heights are suppressed because no purely staggered conformations are accessible.

Comparison of the barrier heights for rotation of one of the threefold rotor substituents in cubane-L_8 and in monosubstituted cubane-L shows the monorotation barrier height in cubane-L_8 is actually sightly lower for L = CH_3, about the same for L = SiH_3, and somewhat higher only for L = CF_3. Thus, in **3**, **4**, and **5**, the barriers to rotation of one substituent in cubane-L_8 are apparently dominated by the same eclipsing interactions between the substituent and the cubane skeleton that are present in the corresponding monosubstituted cubane-L. Interactions between the substituents appears to be of lesser importance in **3**−**5**.

This conclusion makes it easy to understand why monorotation is preferred to coupled rotation in **3**−**5**. At the T_d energy maximum for enforced disrotation of eight threefold rotors in cubane-L_8, the bonds of four of the rotors eclipse the cubane skeleton. Since the steric environment around each eclipsed rotor at the T_d energy maximum for enforced disrotation is similar to that around the single eclipsed rotor in the transition structure for monorotation, one might naively expect that the barrier to enforced, disrotation in cubane-L_8 would be about four times higher than the barrier to monorotation. As already noted, Table 1 shows that this is, in fact, the case for **3** and **4**; although, for **5**, the barrier to disrotation is a factor of 3, not 4, greater than that for monorotation.

Threefold Rotors: *O*-Symmetric Cubanes. In order to identify a persubstituted cubane with a more robust preference for *O* symmetry than **4** or **5**, we considered threefold rotors, larger than CF_3, which would interact more strongly with each other when attached to adjacent cubane vertices. We were thus led to compute the ground-state conformations of octakis(trichloromethyl)cubane (**6**), octakis(tribromomethyl)cubane (**7**), and octakis(trichlorosilyl)cubane (**8**). These compounds were indeed found to have *O*-symmetry with $X-M-C_l-C_c$ torsion angles of ±42.4, ±41.3, and ±41.9° (see Table 2) for the pairs of *M* (negative dihedral angles) and *P* (positive dihedral angles) enantiomers. Two views of the *P* enantiomer of **6** are shown in Figures 1b and 2b.

Table 2. Geometric Parameters for $C_8(MX_3)_8$

	$C_{cubyll}-C_{cubyl}$ (Å)	$C_{cubyl}-M$ (Å)	M−X (Å)	$C_{cubyl}-C_{cubyl}-M-X$ (°)
3	1.578	1.508	1.098	60.0
4	1.571	1.508	1.344	58.6
5	1.590	1.889	1.488	46.5
6	1.640	1.615	1.801	42.4
7	1.652	1.612	1.976	41.3
8	1.616	1.953	2.052	41.9

The MX_3 substituents in **6**−**8** are large enough to enforce geometries of *O* symmetry, with high barriers to enantiomerization (Table 1).[12] However, the MX_3 substituents in

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(11) We also carried out a few calculations with the recently developed MO6-2X functional, which is purported to give better results than B3LYP in describing main group thermochemistry and noncovalent interactions (Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157167). The entries in Table 1 for cubane-L_8, with L = CH_3, were reduced from 2.3 and 8.8 kcal/mol with B3LYP to, respectively, 2.0 and 8.2 kcal/mol with by MO6-2X. Thus, although repeating all of our calculations with the MO6-2X functional would certainly change the numbers in Table 1, it seems unlikely that the qualitative results in Table 1 would be significantly altered.

6−**8** are too large to permit coupled disrotation. Instead, C−MX_3 bond breaking occurs on enforced disrotation, in order to relieve the crushing nonbonded interactions between the substituents. Similarly, monorotation results in steric interactions so severe as to lead to bond cleavage being the predicted outcome (Table 1).

On the other hand, coupled conrotation does not lead to bond breaking in **6**−**8**. This motion proceeds through staggered maxima of O_h-symmetry with barriers of 43.0, 72.9, and 26.0 kcal/mol, respectively. These maxima have multiple imaginary frequencies, and attempts to locate true transition structures for enantiomerization of **6**−**8** have, to this point, been unsuccessful. Therefore, these calculated barrier heights to racemization by conrotation should be regarded as upper limits.

Nevertheless, we predict that **6**, **7**, and possibly **8** are likely to have configurationally stable and resolvable *O* conformations at room temperature. Given the predicted configurational stability of **6**, **7**, and **8**, we computed their optical rotations.[10] Frequency-dependent linear response (LR) theory calculations were performed at the sodium-D wavelength of light ($\omega = 0.0773$ atomic units = 589.3 nm). The computed LR-B3LYP/6-31G(d) rotations in degrees/(dm·g/cm^3) are −110.5, +162.5, and −114.5, respectively, for the *P* enantiomers.

It is certainly noteworthy that homochiral compounds **6** and **7** are calculated to have opposite signs of optical rotation. Although this prediction might seem surprising, homochiral crystals of $NaClO_3$ and $NaBrO_3$ have been found experimentally to have opposite signs of rotation.[13] Surprise that substitution of bromine for chlorine can change the sign of rotation of chiral compounds reflects the stubborn desire of chemists to correlate configuration and sign of rotation, even though we teach our undergraduates not to expect such correlations.

The computed optical rotation of compound **8** is similar in both magnitude and sign to that of compound **6**. This similarity is consistent with the classical expectation that the halogens in the −1 oxidation state should have much larger polarizabilities than C^{4+} and Si^{4+} atoms.[13] Thus changing the M atom from carbon to silicon in the MX_3-substituted cubanes does not have nearly as great an effect on the optical rotation as changing the X atom from chlorine to bromine.

Of the compounds listed in Table 1, other than **1**, only **3** has been synthesized.[14] It has D_{3d} symmetry in the crystalline state.[15]

Synthesis of **6**, and **7**, followed by a chromatographic resolution, would serve as a test of our prediction that both compounds should be stable toward racemization at room temperature. With optically active samples of **6** and **7** in hand, our prediction that enantiomers with the same configuration should have opposite signs of rotation could be tested.

Acknowledgment. B.K. and W.T.B. thank the National. Science Foundation for the support of this research. W.T.B also thanks the Robert A. Welch Foundation. C.M.I was supported by a UIF nanotechnology fellowship.

Supporting Information Available: Optimized geometries, energies, thermal corrections, and frequencies for substituted cubanes **1** − **8** and the analogous monosubstituted cubanes, and the complete list of authors for reference 10. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) The dependence of correlated rotation on rotor size was previously described. Bürgi, H.-B.; Hounshell, D. W., Jr.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 1427–1438.

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