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Experimental Evidence for a High Barrier to Internal Rotation in Hexaisopropylbenzene

Jay Siegel and Kurt Mislow*

Department of Chemistry, Princeton University
Princeton, New Jersey 08544

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Under conditions of intramolecular crowding, the arrangement of neighboring alkyl groups in the molecular ground state can be compared to a system of meshed gears (static gear effect).[1] A striking example is provided by hexaisopropylbenzene (**1**), in which the six isopropyl groups form a tightly interlocking tongue-and-groove arrangement "by virtue of cooperative nonbonded repulsions".[2,3] Inspection of space-filling models suggests that "rotation of the isopropyl groups is almost completely blocked" and further implies "the existence of stable enantiomers related to hexaisopropylbenzene in which the symmetry, with respect to the ring, is destroyed, provided that the average time for rotation is long enough to allow resolution".[2,4] We now present experimental evidence that **1** does indeed represent "an extreme case of hindered rotation"[2] and note the potential for conformational cycloenantiomerism in suitably substituted derivatives.

To measure the isopropyl group rotation barrier (E_r), the ground-state symmetry of **1** (C_{6h})[5] needs to be lowered in some appropriate manner, e.g., by π-complexation with a transition metal.[6] In order to minimize the effect of chemical perturbation on E_r, we chose to desymmetrize **1** through replacement of protium by deuterium in all but two ortho isopropyl groups. The desired compound, **1**-d_{28} (Figure 1), was obtained by cotrimerization of diisopropylacetylene (**2**) with a ca. tenfold excess of **2**-d_{14}[7] in the presence of $HgCo_2(CO)_8$.[9]

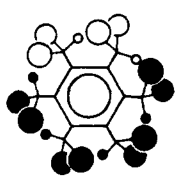

Figure 1. Schematic representation of **1**-d_{28}. Methyl groups and methine hydrogens are represented by large and small circles, respectively, and protium and deuterium atoms by open and filled circles, respectively.

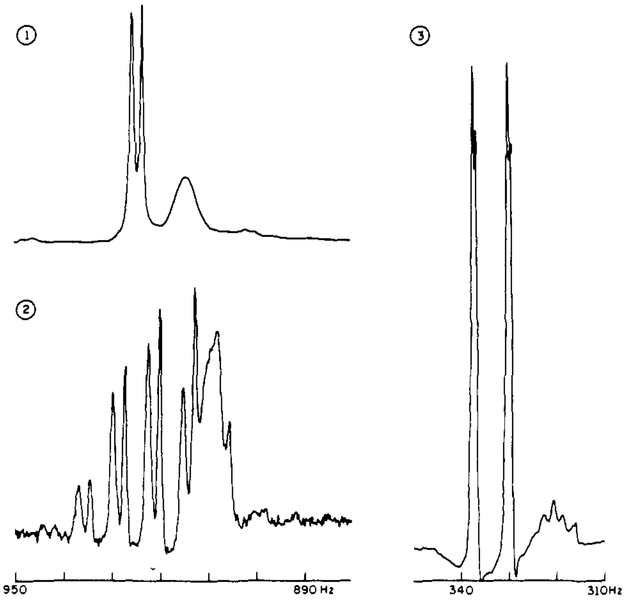

Figure 2. 250-MHz ^{1}H NMR spectrum of **1**-d_{28} (also containing other isotopomers[11]) in $CDCl_3$ at room temperature. (1) Methyl-decoupled methine signals. The sharp doublet and the broad singlet arise from **1**-d_{28} and from molecules containing $CH(CD_3)_2$ groups, respectively. (2) Convolution difference, resonance-enhanced methine signals. The CH signal of **1**-d_{28} is now a doublet of septets (J = 7.3 Hz) with the outer lines barely visible (the scales of 1 and 2 are the same). (3) Convolution difference, resonance-enhanced methyl signals (doublet of doublets, J = 7.3 Hz); the high-field multiplet arises from CD_2H groups.

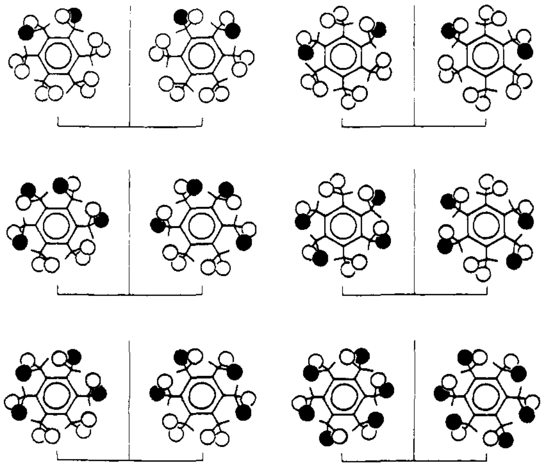

Figure 3. Conformational cycloenantiomerism based on hexaisopropylbenzene. The six possible substitution patterns are shown as racemic pairs, with filled circles representing modified methyl groups (e.g., CD_3). Enantiomers are related by vertical mirror lines.

The symmetry nonequivalence of the isopropyl groups in **1**-d_{28} (open circles, Figure 1) is expressed in an intrinsic steric isotope effect,[10] as manifested by resonance doubling in the methyl and methine regions ($\Delta\nu$ = 0.5 and 2.4 Hz at 250 MHz, respectively) of the ^{1}H NMR spectrum (Figure 2).[11,12] The doubling remains

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[1] Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynski, R. J.; Mislow, K. *Isr. J. Chem.* **1980**, *20*, 65 and references therein.

[2] Arnett, E. M.; Bollinger, J. M. *J. Am. Chem. Soc.* **1964**, *86*, 4729. See also: Hopff, H. *Chimia* **1964**, *18*, 140. Hopff, H.; Gati, A. *Helv. Chim. Acta* **1965**, *48*, 509.

[3] A 0.7 ppm downfield shift of the methine septet (relative to cumene) and the presence of a sharp C–H stretch at 3070 cm^{-1} in the IR spectrum provide evidence for intramolecular crowding in the ground state.[2]

[4] Molecular models are often quite useful in the assessment of conformational ground-state properties. However, they cannot be reliably used to gauge the magnitude of conformational interconversion barriers. See: Blount, J. F.; Finocchiaro, P.; Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 7019. Guenzi, A.; Johnson, C. A.; Cozzi, F.; Mislow, K. *Ibid.* **1983**, *105*, 1438.

[5] This symmetry, suggested by inspection of molecular models,[2,4] was found by molecular mechanics calculations using Allinger's MM2 force field. The same calculations indicate that the D_{3d} conformation is more than 50 kcal mol^{-1} higher in energy.

[6] The ethyl group rotation barrier in hexaethylbenzene was determined in this way. See: Iverson, D. J.; Hunter, G.; Blount, J. F.; Damewood, J. R., Jr.; Mislow, K. *J. Am. Chem. Soc.* **1981**, *103*, 6073. However, **1** resists complexation [Iverson, D. J. Ph.D. Dissertation, Princeton University, 1981, p 113], presumably because the ring is protected on both sides by crowns of methyl groups; by the same token, steric crowding in such a π-complex, once formed, would be expected to lower E_r significantly because of an increase in ground-state energy. See: Iverson, D. J.; Mislow, K. *Organometallics* **1982**, *1*, 3.

[7] This compound (97 atom % D) was synthesized in 50–60% yield by $NaBD_4$ reduction of $(CD_3)_2C(OD)C{\equiv}CC(OD)(CD_3)_2{\cdot}Co_2(CO)_6$ in CH_2Cl_2/CF_3COOH at 0 °C followed by $Fe(NO_3)_3$ oxidation of the resulting complex. Details of this general procedure for the synthesis of acetylenes will be published separately.[8]

[8] Siegel, J.; Nicholas, K. M., manuscript in preparation.

[9] For reviews on the oligomerization of acetylenes, see: Bird, C. W. "Transition Metal Intermediates in Organic Synthesis"; Logos Press: London, 1967; Chapter 1. Yur'eva, L. P. *Russ. Chem. Rev.* (*Engl. Transl.*) **1974**, *43*, 48.

[10] Anet, F. A. L.; Dekmezian, A. H. *J. Am. Chem. Soc.* **1979**, *101*, 5449.

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apparent even at elevated temperatures (to 125 °C, in decalin-d_{18}). From these data, and using the Gutowsky–Holm approximation, a lower limit for E_r of ca. 22 kcal mol^{-1} was established. This value is also a lower limit for E_r of **1** since CD and CD$_3$ have smaller steric requirements than CH and CH$_3$.[13]

These findings indicate that **1** may exhibit conformational rigidity even on the laboratory time scale and suggest the possibility of separating cycloenantiomers[14] of a novel type (Figure 3), in which the direction of the ring is dictated by the conformational orientation of modified isopropyl groups, rather than by the directed sequence of bonded atoms (e.g., peptide linkages). Work is under way to test this prediction.

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[11] Cyclotrimerization produces four products from a mixture of **2** and **2**-d_{14}: **1**, **1**-d_{14}, **1**-d_{28}, and **1**-d_{42}. Given a starting mole ratio of **2**:**2**-d_{14} = 1:11, and disregarding possible isotope effects, the calculated percent product distribution is 0.06:1.9:20.9:77.1, respectively. It follows that 84% of the available protons are incorporated in **1**-d_{28}, in fair agreement with a value of 89% calculated from relative MS intensities. The relative integrated intensities of the methyl-decoupled methine proton signals indicate that the observed resonance doubling is virtually entirely due to **1**-d_{28}.

[12] Resonance doubling of the methine proton signal is consistent with C_s symmetry for **1**-d_{28}, but not with C_2 symmetry. This observation provides experimental evidence against the D_{3d} structure for **1**, in support of our calculations.[5]

[13] Mislow, K.; Graeve, R.; Gordon, A. J.; Wahl, G. H., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 1733.

[14] Prelog, V.; Gerlach, H. *Helv. Chim. Acta* **1964**, *47*, 2288. Cruse, R., in Eliel, L. "Stereochemie der Kohlenstoffverbindungen"; Verlag Chemie: Weinheim, 1966; pp 215–225.

Photochemical and Chemical Reduction of Vicinal Dibromides via Phase Transfer of 4,4′-Bipyridinium Radical: The Role of Radical Disproportionation

Zafrir Goren and Itamar Willner*

Department of Organic Chemistry
The Hebrew University of Jerusalem
Jerusalem 91904, Israel

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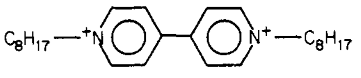
Fundamental processes in nature such as CO$_2$ and N$_2$ fixation involve multielectron reduction reactions. Yet, the primary events in these processes involve single-electron-transfer reactions. Thus, the transformation of a one-electron reductant to multielectron reducing products seems to be a basic problem. Phase-transfer catalysis[1,2] has found significant synthetic applications, including oxidations and reductions of organic substrates.[3,4] Electron acceptors might be used as electron carriers between the two phases, leading to the reduction of substrates in the organic phase. Yet, by generating a single-electron reductant in a two-phase system and designing opposite solubility properties of the disproportionation products in the two phases (eq 1), one might

$$2A^{+\cdot} \rightleftharpoons A^{2+} + A: \qquad (1)$$

anticipate the transformation into a two-electron reducing product and its utilization in chemical routes.

4,4′-Bipyridinium salts (viologens) have been widely explored as electron acceptors and electron carriers.[5,6] Presently, the photosensitized reduction of these compounds is being intensively studied,[2] in particular as a means of solar energy conversion and storage.[7,8] The utilization of the photoproducts in chemical routes and in particular as a synthetic tool is an unexplored field. Among the different alkylviologens, *N,N′*-dioctyl-4,4′-bipyridinium dibromide (I), C$_8$V^{2+}, shows interesting solubilization properties, depending on its oxidation state.[9] The oxidized form, C$_8$V^{2+}, is soluble only in an aqueous media, while the reduced form, C$_8$V$^{+\cdot}$, due to its lipophilic character, is extracted into organic phases. Here we wish to report on the chemical and photochemical debromination of 1,2-dibromodiarylethanes to 1,2-diarylethylenes in a two-phase system. This debromination process is mediated by C$_8$V^{2+} (**1**), as a phase-transfer catalyst. The active species in the reduction process is the two-electron reductant C$_8$V, which is formed by an induced disproportionation of the singly reduced product C$_8$V$^{+\cdot}$ in the two-phase system.



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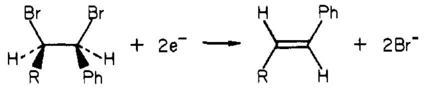
The system is composed of an aqueous sodium dithionite solution and ethyl acetate as an organic phase that includes the dibromide. Introduction of a catalytic amount of C$_8$V^{2+} to the deaerated system results in the blue color of C$_8$V$^{+\cdot}$ (in the H$_2$O). Upon stirring the two-phase system, the radical is extracted into the organic phase and the reduction of the dibromide to the corresponding alkene proceeds quantitatively. In such a system the reduction of dibromostilbenes **2** and **3** to the corresponding *trans*-stilbenes **4** and **5** is afforded in quantitative yields (>95%). Similarly, 1,2-dibromo-2-stilbazole (**6**) and 1,2-dibromo-4-stilbazole (**7**) undergo debromination to **8** and **9** (yield >90%). The net reaction (eq 2) corresponds to the two-electron reduction of the 1,2-dibromodiarylethane to the corresponding *trans*-diarylethylene.



(2)

2, R = Ph
3, R = 4-MeOPh
6, R = 2-Py
7, R = 4-Py

4, R = Ph
5, R = 4-MeOPh
8, R = 2-Py
9, R = 4-Py

No reduction of the dibromides occurs when C$_8$V^{2+} is excluded from the system. Thus, C$_8$V^{2+} mediates the debromination reaction, and since the molar ratio of C$_8$V^{2+} to the dibromide substrate is 1:15, the reducing species is recycled in the system. Similarly, the mediated reduction of the dibromides was accomplished when glucose was substituted for dithionite as the reductant in the aqueous phase.[10] Under these conditions glucose is oxidized by C$_8$V^{2+}, and the resulting C$_8$V$^{+\cdot}$ is extracted into the organic phase.

The reduction of C$_8$V^{2+} and the effect of added dibromostilbene on its reduction products was followed by cyclic voltammetry. The cyclic voltamogram of C$_8$V^{2+} shows two reversible one-electron reduction waves at $E_{1/2}{}^1 = -0.47$ and $E_{1/2}{}^2 = -0.90$ V (vs. NHE), corresponding to the formation of the radical cation C$_8$V$^{+\cdot}$ and the biradical C$_8$V. Addition of dibromostilbene to C$_8$V^{2+} does not affect the reversibility of the first reduction wave, while the reoxidation wave of C$_8$V is depleted, pointing to its rapid chemical consumption. These results indicate that the active species in the

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