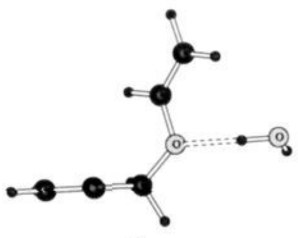
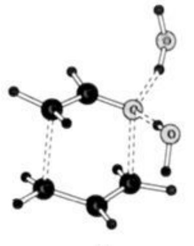
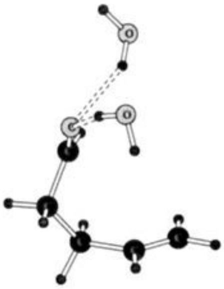


**6**



**7**



**8**

bond to 1.92 Å in the TS from 1.41 Å in AVE also increases the solvent accessibility of the O. Simultaneously, the dipole moment increases from 1.9 *D* for **1** to 2.5 *D* for the TS; it continues to increase to the product, while $\Delta\Delta G_{\text{hyd}}$ levels off (Figure 1). Overall, the results promote catalyst designs that incorporate two or more hydrogen-bond-donating groups positioned to interact with the oxygen in the TS (**7**).

**Acknowledgment**. This work was sponsored by the National Science Foundation.

**Supplementary Material Available:** Listings of 6-31G(d) geometries in *Z*-matrix format and the potential function parameters for the reactant, TS, and product (2 pages). Ordering information is given on any current masthead page.

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## Cation Radical Probes. Development and Application to Metalloporphyrin-Catalyzed Epoxidation

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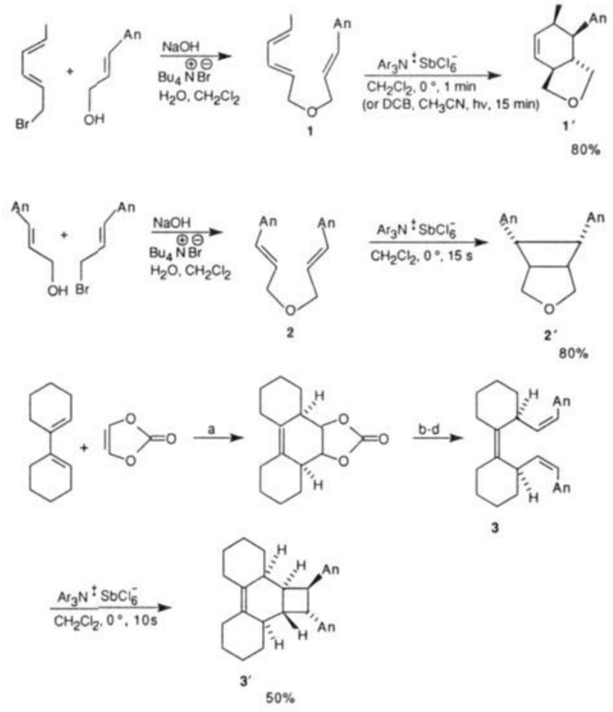
Radical probes such as the cyclization of the 5-hexenyl radical have proved highly effective in diagnosing free radical mechanisms.[1] Analogous cation radical probes would constitute a powerful tool for detecting short-lived cation radical intermediates in the burgeoning area of hole catalytic chemistry.[2,3] The synthesis of conveniently accessible cation radical probe substrates and the characterization and calibration of their rapid intramolecular probe reactions as cation radical clocks are now reported. The new probes have further been used to investigate the hypothetical electron-transfer mechanism for metalloporphyrin-catalyzed epoxidation.[4,5]

The cation radical probe reactions developed in this study are based upon the intramolecular cation radical Diels–Alder reaction[6] and analogous intramolecular cyclobutanation.[7] The choice of substrates **1** and **2** was based upon synthetic accessibility and reactivity considerations. Both are conveniently prepared by phase-transfer-catalyzed coupling of readily available alcohols and bromides (Scheme I). Although the probe reaction of **2** (cyclobutanation) would appear to be inherently less favorable than that of **1** (Diels–Alder addition), it is significant that the trapping moiety of $\mathbf{2}^{\bullet+}$ (a neutral moiety of the *trans*-anethole type) is much more reactive toward a cation radical moiety than is the neutral diene moiety of $\mathbf{1}^{\bullet+}$.[8] In both instances the cation radical moiety is of the *trans*-anethole type. Further, $\mathbf{1}^{\bullet+}$, but not $\mathbf{2}^{\bullet+}$, requires prior s-trans to s-cis isomerization of the diene moiety.[9] Conformational contributions to the activation free energy of cyclization are further minimized in the preorganized probe molecule **3**. The efficient cyclizations of $\mathbf{1}^{\bullet+}$, $\mathbf{2}^{\bullet+}$, and $\mathbf{3}^{\bullet+}$ were characterized synthetically under standard aminium salt conditions [tris(4-bromophenyl)aminium hexachloroantimonate, $CH_2Cl_2$, 0 °C]. The already well-characterized Diels–Alder cycloaddition of 1,3-cyclohexadiene (**4**) has also been exploited as a bimolecular probe reaction.[10]

**Scheme I.** Synthesis of Probe Substrates and Characterization of the Probe Reactions



An = 4-MeOC$_6$H$_4$- ; Ar = 4-BrC$_6$H$_4$- ; DCB = 1,4-Dicyanobenzene

a. Δ, 24h, 270°C ; b. LAH, Et$_2$O, 1 h, r.t. ; c. Pb(OAc)$_4$, benzene, 1h, r.t.;

d. AnCH$_2$PPh$_3^+$ Cl$^-$, n-BuLi, THF, 3 hr, r.t.

Calibration of the probe reaction of $\mathbf{1}^{\bullet+}$ was accomplished via standard quenching studies, using 1,4-dicyanobenzene as the photosensitizer and 1,2,4-trimethoxybenzene as the quencher in acetonitrile ($k_{\text{DA1}} = 3 \times 10^7\ \text{s}^{-1}$).[11] The intramolecular cyclobutanation of $\mathbf{2}^{\bullet+}$ (rate constant $\equiv k_{\text{CB2}}$) was then calibrated via

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[1] Wilt, J. W. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, pp 420–424.

[2] Bauld, N. L. *Tetrahedron* **1989**, *45* (17), 5307–5363.

[3] Bauld, N. L. *Advances in Electron Transfer Chemistry*; Mariano, P. M., Ed.; JAI Press: Greenwich, CT, 1992; Vol. 2, pp 1–66.

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[5] Traylor, T. G.; Nakano, T.; Dunlap, B. E. *J. Am. Chem. Soc.* **1986**, *108*, 2782–2784.

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[7] Courtneidge, J. L.; Davies, A. G.; Tollerfield, S. M.; Rideout, J.; Symons, M. C. R. *J. Chem. Soc., Chem. Commun.* **1985**, 1092.

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[9] Kim, T.; Pye, R. J.; Bauld, N. L. *J. Am. Chem. Soc.* **1990**, *112*, 6285–6290.

[10] Calhoun, G. C.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 6871–6872.

[11] A detailed description of this study is included in the supplementary material. The kinetic scheme assumed is essentially that of Calhoun and Schuster,[10] and the experimental conditions (quencher, sensitizer) are essentially those of Lewis and Kojima in their study of *trans*-anethole dimerization.[12]

[12] Lewis, F. D.; Kojima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8664–8670.

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studies of the reactions of **1**$^{\bullet+}$ and **2**$^{\bullet+}$ with a common reactant, ethyl diazoacetate, under aminium salt conditions, which effects the cyclopropanation of **1**$^{\bullet+}$ and **2**$^{\bullet+}$ (with second-order rate constants $k_{\mathrm{CP1}}$ and $k_{\mathrm{CP2}}$, respectively) in competition with the respective intramolecular cycloadditions.[13] The experimentally determined ratio $k_{\mathrm{DA1}}/k_{\mathrm{CP1}} = 20$ affords $k_{\mathrm{CP1}} = 1.5 \times 10^6\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$. If we assume $k_{\mathrm{CP1}} = k_{\mathrm{CP2}}$ (the hole sites in **1**$^{\bullet+}$ and **2**$^{\bullet+}$ are essentially identical), the observed minimum ratio $k_{\mathrm{CB2}}/k_{\mathrm{CP2}} \geq 2000$ affords $k_{\mathrm{CB2}} \geq 3 \times 10^9\ \mathrm{s}^{-1}$. The accuracy of this latter estimate of the minimum cyclobutanation rate constant rests upon the assumption that the *relative* rate ratios $k_{\mathrm{DA1}}/k_{\mathrm{CP1}}$ and $k_{\mathrm{CB2}}/k_{\mathrm{CP2}}$ (hence $k_{\mathrm{DA1}}/k_{\mathrm{CB2}}$), which are measured in dichloromethane, are not substantially different in acetonitrile, the solvent in which $k_{\mathrm{DA1}}$ was measured. This key assumption is supported by additional studies of the competitive dimerization($k_{\mathrm{CB5}}$)/cyclopropanation($k_{\mathrm{CP5}}$) of *trans*-anethole (**5**). The rate ratio $k_{\mathrm{CB5}}/k_{\mathrm{CP5}} = 2$ affords $k_{\mathrm{CB5}} = 3 \times 10^6\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$, in reasonable agreement with the value previously derived from quenching studies in acetonitrile.[12] In like manner, the lower limit estimated for the rate constant for the cyclization of **3**$^{\bullet+}$ is $k_{\mathrm{CB3}} \geq 3 \times 10^9\ \mathrm{s}^{-1}$. The reaction **4**$^{\bullet+}$ + **4** has previously been found to have a rate constant $k_{\mathrm{DA4}} = 3 \times 10^8\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$.

Substrates **1–4** were then used to investigate the hypothetical electron-transfer (ET) mechanism of metalloporphyrin (MP)-catalyzed epoxidation. According to this mechanism, an alkene molecule undergoes ET to the metal oxene to give the corresponding alkene cation radical, which is then rapidly epoxidized by the reduced metal oxene. The ease of ionization of **1–3** should make them especially amenable to an ET mechanism if this were operable, and the cation radicals **1**$^{\bullet+}$–**3**$^{\bullet+}$ should be *relatively* long lived and thus especially susceptible to detection. The monoepoxides of **1–3** and of the cyclized form **1′** were first characterized by MCPBA epoxidation. The MP-catalyzed epoxidations of **1–3** were then examined using M = Fe(III) and Mn(III) (as the chlorides) and P = 5,10,15,20-tetraphenylporphyrin and also 5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrin in dichloromethane and in acetonitrile/water (90:10) with iodosylbenzene as the oxidant. Reactions were carried out to ~10% conversions to the epoxides, and material balances were ≥99%. In every instance only unreacted **1–3** and the corresponding (uncyclized) epoxides were found. Specifically, no **1′–3′** or their corresponding epoxides or other oxidation or dehydrogenation products were formed. It was established that such products would have been detectable in amounts at least as small as 0.5% of the uncyclized epoxide product. Similarly, the MP-catalyzed epoxidation of 1,3-cyclohexadiene (M = Mn, Fe) yielded only 3,4-oxidocyclohexene and none of the Diels–Alder dimer of **4** or the epoxide of the latter even when carried out in a 2.0 M solution of **4** in acetonitrile/dichloromethane solution.

Free cation radicals are clearly not formed in these epoxidations, even in the relatively more polar solvent. To the extent that cation radicals in the coordination sphere of iron resemble free cation radicals in their reactivity (this should be especially true in polar solvents), narrow limits can be defined for the maximum lifetime of any such cation radical intermediate. Using **1** as a probe ($k_{\mathrm{DA1}} = 3 \times 10^7\ \mathrm{s}^{-1}$) and the indicated detectability limits of cation radical products (0.5%), a cation radical intermediate would have been detected if its rate constant for epoxidation were $\leq 6 \times 10^9\ \mathrm{s}^{-1}$. With **2** or **3** as the probe ($k_{\mathrm{CB2}}, k_{\mathrm{CB3}} \geq 3 \times 10^9\ \mathrm{s}^{-1}$), a cation radical process with a rate constant of up to $6 \times 10^{11}\ \mathrm{s}^{-1}$ would have been detected. Finally, with **4** as the probe a cation radical process of rate constant $3 \times 10^{11}\ \mathrm{s}^{-1}$ would have been detected. For comparison, the rate constant for the quasi-intramolecular hydroxylation of alkyl radicals in P-450-catalyzed hydroxylation is just $2 \times 10^{10}\ \mathrm{s}^{-1}$.[14]

The failure to detect cation radical intermediates using rather sensitive intramolecular clock probes which present relatively ionizable functionalities significantly limits the tenable role of cation radicals in MP-catalyzed epoxidation.

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**Supplementary Material Available:** Experimental details of the epoxidation reactions mentioned in the text (14 pages). Ordering information is given on any current masthead page.

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[13] Bauld, N. L.; Stufflebeme, G. W.; Lorenz, K. T. *J. Phys. Org. Chem.* **1989**, *2*, 585–601.

[14] Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5687–5698.

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# On the Potential Energy Surface for Ring Inversion in Cyclohexene and Related Molecules

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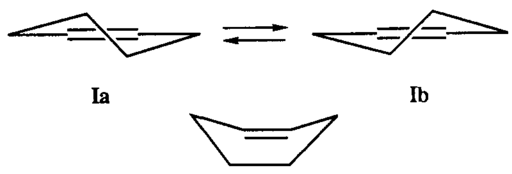
The conformations of cyclohexene and related monounsaturated heterocyclic six-membered rings have been extensively investigated by spectroscopic and molecular mechanics methods.[1] Cyclohexene (**I**) itself exists in the half-chair conformation ($C_2$ point group) and undergoes ring inversion (**Ia** ⇄ **Ib**) with the boat form (**II**, $C_s$ point group) as a presumed transition state. The barrier for this process is 4.2–7.9 kcal/mol as calculated by molecular mechanics with more than half a dozen different force fields.[1] The free energy barrier ($\Delta G^{\ddagger}$) has been measured to be 5.3 ($\mathrm{CBrF_3}$ solution) and 5.4 kcal/mol (vinyl chloride–chlorotrifluoroethylene solution) by dynamic NMR of partially deuteriated **I** at −165 °C.[1,2] In a recent paper,[3] Laane and co-workers have deduced a potential energy surface for ring inversion in **I** from an analysis of the ring bending and twisting vibrations in the gas-phase infrared spectrum of **I**. The analysis is based on a two-dimensional model describing the ring inversion energy surface as a quartic in ring bending and twisting coordinates.[4] The potential energy barrier for ring inversion in cyclohexene corresponding to this surface is 10.3 kcal/mol.[3] These authors discount the much lower barriers obtained previously by NMR and molecular mechanics for reasons that are unconvincing to us.[5,6] We now present results from (i)



**Ia** **Ib**

**II**

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[1] For a review, see Anet, F. A. L. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P. W., Ed.; VCH Publishers: New York, 1987; Chapter 1.

[2] (a) Anet, F. A. L.; Haq, M. Z. *J. Am. Chem. Soc.* **1965**, *87*, 3147–3150. (b) Jensen, F. R.; Bushweller, C. H. *J. Am. Chem. Soc.* **1969**, *91*, 5774–5782.

[3] Rivera-Gaines, V. E.; Leibowitz, S. J.; Laane, J. *J. Am. Chem. Soc.* **1991**, *113*, 9735–9742. These authors discuss the possibility that the barrier might be 1–2 kcal/mol lower than their best estimate, but they do not seem to put much weight on such a possibility, and no such qualification is made in the abstract or conclusion sections of their paper.

[4] This model has been applied previously to related heterocyclic molecules. (a) Tecklenberg, M. M. J.; Laane, J. *J. Am. Chem. Soc.* **1989**, *111*, 6920–6926. (b) Tecklenberg, M. M. J.; Villarreal, J. R.; Laane, J. *J. Chem. Phys.* **1989**, *91*, 2771–2775.

[5] Molecular mechanics force fields are, with a few exceptions, parametrized as much on energy as on geometry and generally reproduce conformational barriers, including gas-phase values (Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, 1982), in contrast with the views expressed by Laane and co-workers.[3] The geometry and barriers to planarity and pseudorotation in four- and five-membered rings are reasonably well predicted by MM2 (Rasas, R. L.; Cooper, C.; Laane, J. *J. Phys. Chem.* **1990**, *94*, 1830–1836).

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