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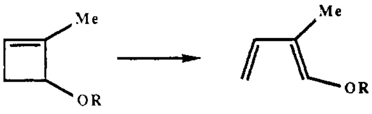
Electronic Control of the Stereoselectivities of Electrocyclic Reactions of Cyclobutenes against Incredible Steric Odds

Summary: Experimental studies of the electrocyclic reactions of 2- and 3-*tert*-butyl-3-(trimethylsiloxy)cyclobutene and of 3-methoxy-3-*tert*-butylcyclobutene confirm ab initio computational predictions.

Sir: Several years ago, two of us reported that the electrocyclic opening of 3-hydroxy, -deuteroxy, and -trimethylsiloxy derivatives of 2-methylcyclobutene (**1a–c**) gave only products **2** arising from outward rotation of the oxygen substituents even though these products appear to be less stable than those arising from inward rotation.[2] Subsequent experiments by Kirmse[3] and Dolbier[4] and calculations by Rondan and Houk[5] showed that donor substituents at C3 display a large preference for outward rotation in these electrocyclizations.



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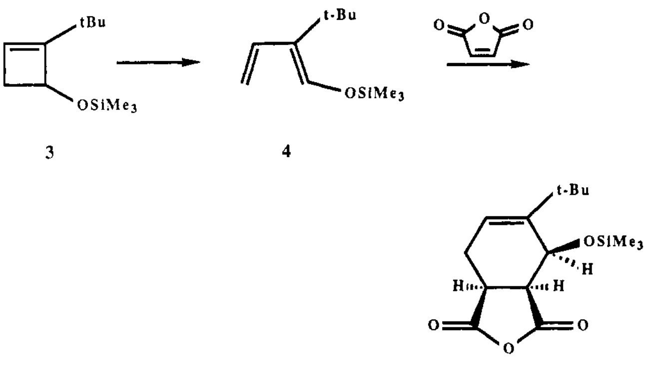
We now wish to report new experimental results which indicate that the preference of an oxygen substituent at C3 for outward rotation significantly exceeds that of a *tert*-butyl group. Calculations on the transition structures for electrocyclic reactions of various model systems and for 3-hydroxy-3-*tert*-butylcyclobutene provide an explanation of these results and confirm that substituent effects are approximately additive.

When 2-*tert*-butyl-3-(trimethylsiloxy)cyclobutene (**3**) is heated in deuteriochloroform at 95–100 °C for 1.5 h, a single silyl dienol ether, **4**, is obtained. When the reaction is carried out in the presence of maleic anhydride (1.1 molar equiv), a single Diels–Alder adduct, **5**, is formed. The cis configuration of the siloxy substituent and the anhydride grouping is established by the size of the vicinal coupling constant (2.8 Hz) of the respective methine protons. Their cis relationship is confirmed by NOE measurements.



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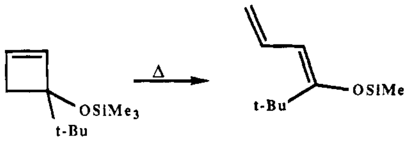
More telling is the thermal behavior of 3-*tert*-butyl-3-(trimethylsiloxy)cyclobutene (**6**) and 3-*tert*-butyl-3-methoxycyclobutene (**12**). Heating **6** in deuterochloroform for 4 h cleanly affords a single product, which must have the more hindered *E* geometry, **7**. Attempts to capture **7** with maleic anhydride are unavailing; polymerization predominates. Clearly, the cisoid conformation required for the Diels–Alder cycloaddition is inaccessible. Further support for the configuration of **7** is found by treating 2,2-dimethylhex-4-en-3-one (**8**) with LDA at −78 °C, followed by addition of trimethylsilyl chloride. Only one silyl ether, **9**, which is different from **7**, is found, indicating that the less encumbered *Z* dienolate **10** is formed rather than the *E* isomer **11**.[6] The structures of both **7** and **9** are unambiguously confirmed by their characteristic ^{13}C NMR spectra.[7] In **9**, the contiguous trimethylsiloxy group shields the γ carbon atom, (106.23 ppm) whereas in **7**, it does not (109.62 ppm). The effect is mutual and the silylmethyl ^{13}C shifts appear at 1.04 and 1.91 ppm, respectively.[8] The geometries of **7** and **9** were confirmed by NOE measurements.



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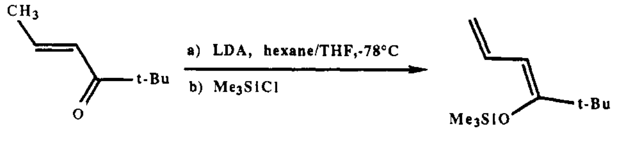

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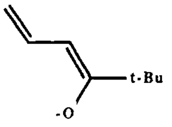

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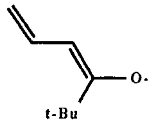

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(6) For related examples of the exclusive formation of *Z*-enolates, see: Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247. Fellman, P.; Dubois, J.-E. *Tetrahedron* **1978**, *34*, 1349.

(7) ^{13}C NMR ($CDCl_3$, 50 MHz): compound **7**, 161.05, 132.73, 111.87, 109.62, 37.83, 29.72, 1.91 ppm; compound **9**, 161.17, 132.48, 112.24, 106.23, 36.51, 28.39, 1.04 ppm.

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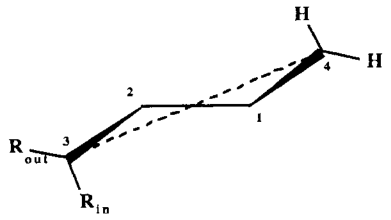
Table I. Transition-Structure Geometries for Ring Openings of 3-Hydroxy-, 3-Methyl-, and 3-Methyl-3-hydroxycyclobutenes



parameter	3-hydroxycyclobutane OH in	3-hydroxycyclobutane OH out	3-methylcyclobutene Me in	3-methylcyclobutene Me out	3-hydroxy-3-methylcyclobutene Me in, OH out	3-hydroxy-3-methylcyclobutene Me out, OH in
distances, Å						
C_1C_2	1.3702	1.3676	1.3715	1.3682	1.3682	1.3681
C_2C_3	1.4307	1.4242	1.4224	1.4232	1.4284	1.4360
C_1C_4	1.4208	1.4205	1.4144	1.4208	1.4147	1.4206
C_3C_4	2.1814	2.1252	2.1748	2.1425	2.1679	2.1921
angles, deg						
$R_{in}C_3C_2$	124.5	119.8	122.3	116.5	123.0	122.7
$R_{out}C_3C_2$	121.2	124.4	118.6	123.9	120.9	122.3
dihedral angles, deg						
$C_2C_3C_4C_1$	15.7	14.1	14.7	13.9	13.9	15.0
$R_{out}C_3C_2C_1$	−140.8	−145.3	−142.9	−144.9	−140.9	−139.1
$R_{in}C_3C_2C_1$	74.0	64.4	70.1	60.8	73.5	74.3
energies						
E, au	−228.38844	−228.41462	−192.77774	−192.78805	−267.23414	−267.21731
E_{rel}, kcal/mol[a,b]	48.7	32.3	47.3	40.9	36.8	47.4
E_{rel}, kcal/mol[c]	16.4	0.0	6.4	0.0	0.0	10.6

[a] Relative activation energy as compared to the substituted cyclobutene. [b] The calculated activation energy for the cyclobutene to butadiene electrocyclic reaction is 41.6 kcal/mol with the 3-21G basis set.[5] [c] Activation energy relative to the lower energy transition structure.

In order to determine if any steric effects are introduced by the large trimethylsilyl group, the methoxy derivative **12** was heated at 90–95° for 6.5 h in C_6D_6 in the dark. Only the (E)-diene **13** is observed. In all cases, the oxygen substituent rotates outward, regardless of the size of the alkyl or alkoxy group. Electronic effects clearly operate, since the thermolysis of 3-methyl-3-*tert*-butylcyclobutene is much less selective,[9] and there is a slight preference for outward rotation of a methyl group.

12 13

Ab initio molecular orbital calculations with the 3-21G basis set[10] were carried out on the transition structures for several related conrotatory electrocyclizations of substituted cyclobutenes.[11] In earlier work, we determined that the relative activation energies of these electrocyclizations can be reproduced very well, even though the absolute activation energies are about 10 kcal/mol too high, due to the neglect of electron correlation energy.[5]

Table I shows the 3-21G transition structures for the conrotatory electrocyclic reactions of cyclobutanes with 3-hydroxy or 3-methyl substituents rotating both inward and outward. These transition structures were obtained by full gradient optimizations at the 3-21G level, and all have only one imaginary frequency in the harmonic frequency analysis, indicating that they are true transition structures at this level.[10]

The lowest energy transition structures of inward and outward rotation of the 3-hydroxyl group have the OH bond positioned over the ring to minimize the lone pair–π bond repulsion. Outward rotation is favored over inward rotation by 16.4 kcal/mol (E_a^{in} = 48.7 kcal/mol, E_a^{out} = 32.3 kcal/mol) because the four-electron destabilization of the oxygen lone pair and the breaking σ_{C-C} bond is greater for inward rotation than for outward rotation. The calculated substituent effect of −9.3 kcal/mol for outward rotation agrees quite well with the experimental value of −9.0 kcal/mol found for 3-methoxycyclobutene.[3]

Calculations on the transition structure for outward rotation of 3-methylcyclobutene imply that the activation energy should be lowered by 0.7 kcal/mol relative to the parent cyclobutene reaction. This is in very good agreement with the experimental stabilization of 0.9 kcal/mol.[3] Inward rotation of a methyl group is calculated to be destabilizing by 5.7 kcal/mol, higher than the 2–3 kcal/mol deduced by Kirmse.[3] The preference for outward rotation by methyl results from lesser closed-shell repulsion than occurs upon inward rotation.

We can use these values to predict that the relative activation energy for 3-hydroxy-3-methylcyclobutene opening in which the methyl rotates outward and the hydroxy rotates inward will be 6.4 kcal/mol above the activation energy for opening of the parent system. The activation energy corresponding to outward rotation of the hydroxy group and inward rotation of the methyl group is predicted to be 3.6 kcal/mol below that of the parent system, or 10.0 kcal/mol above the other transition structure.

We also have calculated directly the transition structures for both electrocyclic reactions of 3-hydroxy-3-methylcyclobutene. In good agreement with the predictions from the monosubstituted derivatives, we find the activation energy for hydroxy-in, methyl-out rotation is 10.6 kcal/mol above that for hydroxy-out, methyl-in rotation. The ac-

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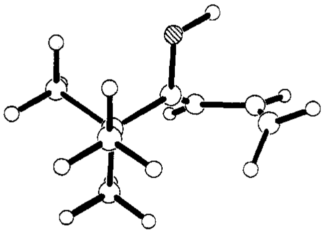
(11) All of these calculations were completed before the experiments were carried out.

tivation energy for inward rotation of the hydroxy group is 5.8 kcal/mol above that of the parent system. That of the hydroxy outward transition structure is 4.8 kcal/mol lower than the parent structure.

Model transition structure calculations have also been performed on both modes of opening of 3-*tert*-butyl-3-hydroxycyclobutene. In both cases, the *tert*-butyl group is placed in the position of the methyl group in the transition structures discussed above. The *tert*-butyl conformation is fully staggered and was given the CC and CH bond lengths and CCH bond angles of the STO-3G-optimized neopentane.[12] The calculations indicate that the *tert*-butyl group prefers to rotate inward, even though it is extremely large. The activation energy at the 3-21G level of the hydroxy-in, *tert*-butyl-out transition structure, **14**, is 4.0 kcal/mol higher than that of the hydroxy-out, *tert*-butyl-in transition structure, **15**. Since the hydroxy outward preference is 16 kcal/mol, the inherent preference for *tert*-butyl to rotate outward must be approximately 12 kcal/mol, although Curry and Steven have shown that this value is more nearly 7 or 8 kcal/mol.[9] In spite of this incredible steric effect, the *tert*-butyl is predicted and found to rotate inward due to the electronic effect of the small hydroxy group.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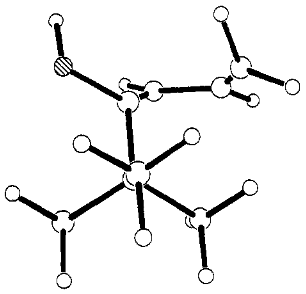
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Acknowledgment. We are grateful to the U. S. and Swiss National Science Foundations for financial support of this research and to the former for computer time at the San Diego Supercomputer Center and to the Harris Corporation for the grant of a H800 computer at UCLA.

Registry No. **3**, 113747-61-8; **4**, 113747-62-9; **5**, 113747-63-0; **6**, 113747-64-1; **7**, 113747-65-2; **8**, 20971-19-1; **9**, 113747-66-3; **12**, 113747-60-7; **13**, 113747-68-5; maleic anhydride, 108-31-6; 3-hydroxycyclobutene, 113747-67-4; 3-methylcyclobutene, 1120-55-4; 3-hydroxy-3-methylcyclobutene, 77931-77-2; 3-*tert*-butyl-3-hydroxycyclobutene, 77931-78-3.

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[12] Carnegie-Mellon University Quantum Chemistry Archive, Carnegie-Mellon University, Pittsburgh, PA 15260.

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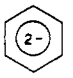
A Conformational Criterion for Aromaticity and Antiaromaticity

Summary: A conformational criterion for aromaticity and antiaromaticity is suggested: relative to planar reference geometries, folding of aromatic and antiaromatic systems results in large endothermic and exothermic changes, respectively. A series of 8π-electron heterocyclic systems were found to be highly flexible and are therefore classified as nonaromatic rather than antiaromatic.

Sir: The concept of aromaticity has evolved dramatically over the last two centuries into a cornerstone for modern theories of chemical structure and reactivity.[1-3] In particular, the π-electron analysis originated by Huckel[4] allows predictions of physical and chemical behavior of cyclic conjugated systems. The extension of Huckel's work by Frost[5] and by Breslow[6] led to the $(4n + 2)\pi$-electron criterion for aromaticity and the $4n\pi$-electron criterion for antiaromaticity, which are so widely accepted that they have achieved the level of dogma in modern organic chemistry. However, there are classes of compounds whose properties are not correctly predicted by using these criteria, and there remains a need for an unambiguous operational definition of aromaticity and antiaromaticity.[7] We report here the preliminary details of a novel computational approach that allows direct evaluation of aromaticity and antiaromaticity.

Inherent in all definitions of aromaticity and antiaromaticity is the notion that a planar ring system maximizes overlap of the atomic p orbitals contributing to the π-system. This π-interaction is highly stabilizing for aromatic systems but destabilizing for antiaromatic systems. Deviations from planarity of the molecular framework will disrupt the π-overlap and consequently affect the energy. Therefore probing the potential energy hypersurface for various geometries should permit determination of the aromatic or antiaromatic nature of a species. We have carried out an ab initio (Hartree–Fock) molecular orbital study[8] of a series of potentially antiaromatic 8π-electron, six-membered ring systems (**1**–**6**), of which the singlet benzene dianion, $C_6H_6^{2-}$ (**1**), is the prototype. Energies were calculated for a series of geometries with varying distortions from planarity (see Table I). For a series of folding angles (the 2–1–4–5 dihedral angle),[9]



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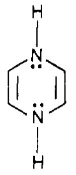

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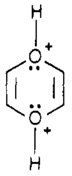

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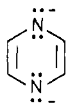

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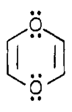

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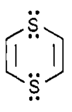

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