Substituent Effects on Rates and Stereoselectivities of Conrotatory Electrocyclic Reactions of Cyclobutenes. A Theoretical Study

Satomi Niwayama, E. Adam Kallel, David C. Spellmeyer, Chimin Sheu, and K. N. Houk*

Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095

Received May 11, 1995 (Revised Manuscript Received January 25, 1996[⊗]*)*

Substituent effects on the geometries and conrotatory electrocyclic ring openings of cyclobutenes were studied. This work extends the original investigations to many more substituents and provides a comprehensive theory of substituent effects on geometries and reaction rates. The effects of substitution at the 1 position are minimal; donor substituents raise the activation energy slightly, and powerful acceptor substituents slightly lower the activation energy. Substituents on C_3 cause small distortions of the cyclobutene geometry, in the same direction as the favored stereochemistry of reaction. Donors prefer outward rotation, while strong acceptors prefer inward rotation. The activation energy changes and cyclobutene geometrical perturbations were found to correlate with Taft σ_R^0 parameters. Amino, hydroxy, fluoro, chloro, methyl, cyano, formyl, and vinyl substituents were studied in the 1 position. Boryl, dimethylboryl, nitroso, formyl, nitro, carboxyl (neutral, protonated, and deprotonated), cyano, trifluoromethyl, sulfoxyl, sulfonyl, sulfinic acid, imino, N-protonated imino, ammonio, ethynyl, methyl, mercapto, chloro, fluoro, hydroxyl, amino, lithium oxy, vinyl, and acetyl were calculated as substituents in the 3 position. Comparisons with experimental results are given when available, and predictions are made in other cases.

Introduction

Cyclobutenes undergo thermal electrocyclic reactions to produce butadienes via thermally allowed conrotatory processes.[1] Substituents at C_3 can rotate either inward to form a *cis* product or outward to form a *trans* product. In 1985, Rondan, Kirmse, and Houk proposed an electronic theory to account for the stereochemistry of ring openings and the large preference for outward rotation by some small substituents.[2] The theory explained why the larger group at C_3 sometimes rotates inward.[3] Subsequently, predictions about stereochemistry were made and verified experimentally.[4] A selection of these are shown in Figure 1. The stereoselectivity occurs due to a preferential direction of twisting of the breaking σ bonds in these reactions. This type of stereoselectivity has now been found to be operative in a variety of systems;[5] it has been termed "torquoselectivity".[6]

Figure 2 shows the frontier orbitals for cyclobutene and the ring-opening transition state as calculated with the 6-31G* basis set. The σ-bonding orbital rises in energy from −12.5 eV to −8.87 eV in the transition state. This makes the σ bond a very good donor in the transition state. The decrease in energy of the σ^* orbital from 8.95 to 3.91 eV causes the σ^* orbital to become a more efficient acceptor. The π bond is only elevated in energy by 0.35 eV, making it a slightly better donor than in the reactant. The π^* orbital comes down by only 0.07 eV and, consequently, is virtually unchanged as an acceptor.

Figure 3 shows how p or π orbitals on the substituent interact with the breaking σ-bond. Upon inward rotation, filled substituent donor orbitals overlap with the transition state HOMO of the cyclobutene transition state, which is primarily concentrated on the breaking C_3C_4 σ bond orbital. This overlap results in a destabilizing cyclic four-electron interaction, which substantially raises the activation energy for the inward rotation of a donor substituent. Conversely, outward rotation of a donor substituent lowers the activation energy substantially due to overlap of the donor substituent with the LUMO of the transition state (the anti-bonding orbital of the breaking C_3C_4 bond). There also exists less repulsion with the HOMO due to the remoteness of the substituent from the other terminus.

Acceptor substituents each possess a low-lying vacant orbital which, upon inward conrotation, overlaps with the HOMO of the transition state. This interaction is a two-electron interaction which stabilizes the transition state on inward rotation and consequently lowers the energy of activation for this process. Outward conrotation of the acceptor substituent produces a smaller stabilizing effect, since overlap with the HOMO is smaller.

Earlier, Houk and Rondan showed the effect of some substituents at the 3- and 4-positions.[2b] For example, in the case of *trans*-3,4-dihydroxycyclobutene, the HOMO

[⊗] Abstract published in *Advance ACS Abstracts,* March 15, 1996.

(1) (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie International: Deerfield Beach, FL, 1970. (b) Marvell, E. N. *Thermal Electrocyclic Reactions*; Academic Press: London, England, 1980.

(2) (a) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989. (b) Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099.

(3) (a) Curry, M. J.; Stevens, I. D. R. *J. Chem. Soc. Perkin Trans. 2* **1980**, 1391. (b) Dolbier, W. R.; Koroviak, H., *J. Am. Chem. Soc.* **1984**, *106*, 1872.

(4) (a) Rudolf, K.; Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 3708. (b) Buda, A. B.; Wang, Y.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 2264. (c) Niwayama, S.; Houk, K. N. *Tetrahedron Lett.* **1993**, *34*, 1251. (d) Hays, R.; Ingham, S.; Saengchantara, S. T.; Wallace. T. W. *Tetrahedron Lett.* **1991**, *32*, 2953.

(5) (a) Kallel, E. A.; Wang, Y.; Spellmeyer, D. C.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 6759. (b) Kallel, E. A.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 6006. (c) Thomas, B. E.; Evanseck, J. D.; Houk, K. N. *Isr. J. Chem.* **1993**, *33*, 287. (d) Finnochio, A. L.; Tezuka, H.; Evanseck, J. D.; Houk, K. N. Manuscript in preparation. (e) Evanseck, J. D. Ph. D. Dissertation, University of California, Los Angeles, 1990. (f) Evanseck, J. D.; Thomas, B. E., IV; Houk, K. N. *J. Am. Chem. Soc.* **1993**, *115*, 4165. (g) Houk, K. N.; Spellmeyer, D. C.; Jefford, C. W.; Rimbault, C. G.; Wang, Y.; Miller, R. D. *J. Org. Chem.* **1988**, *53*, 2125. (h) Nakamura, K.; Houk, K. N. *Heterocycles* **1993**, *35*, 631. (i) Evanseck, J. D.; Thomas, B. E., IV; Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1995**, *60*, 7134.

(6) Houk, K. N. in *Strain and Its Implications in Organic Chemistry*; de Meijere, A., Blechert, S., Eds.; Kluwer Academic Publishers: Dordrecht, 1989; p 25.

0022-3263/96/1961-2813$12.00/0 © 1996 American Chemical Society

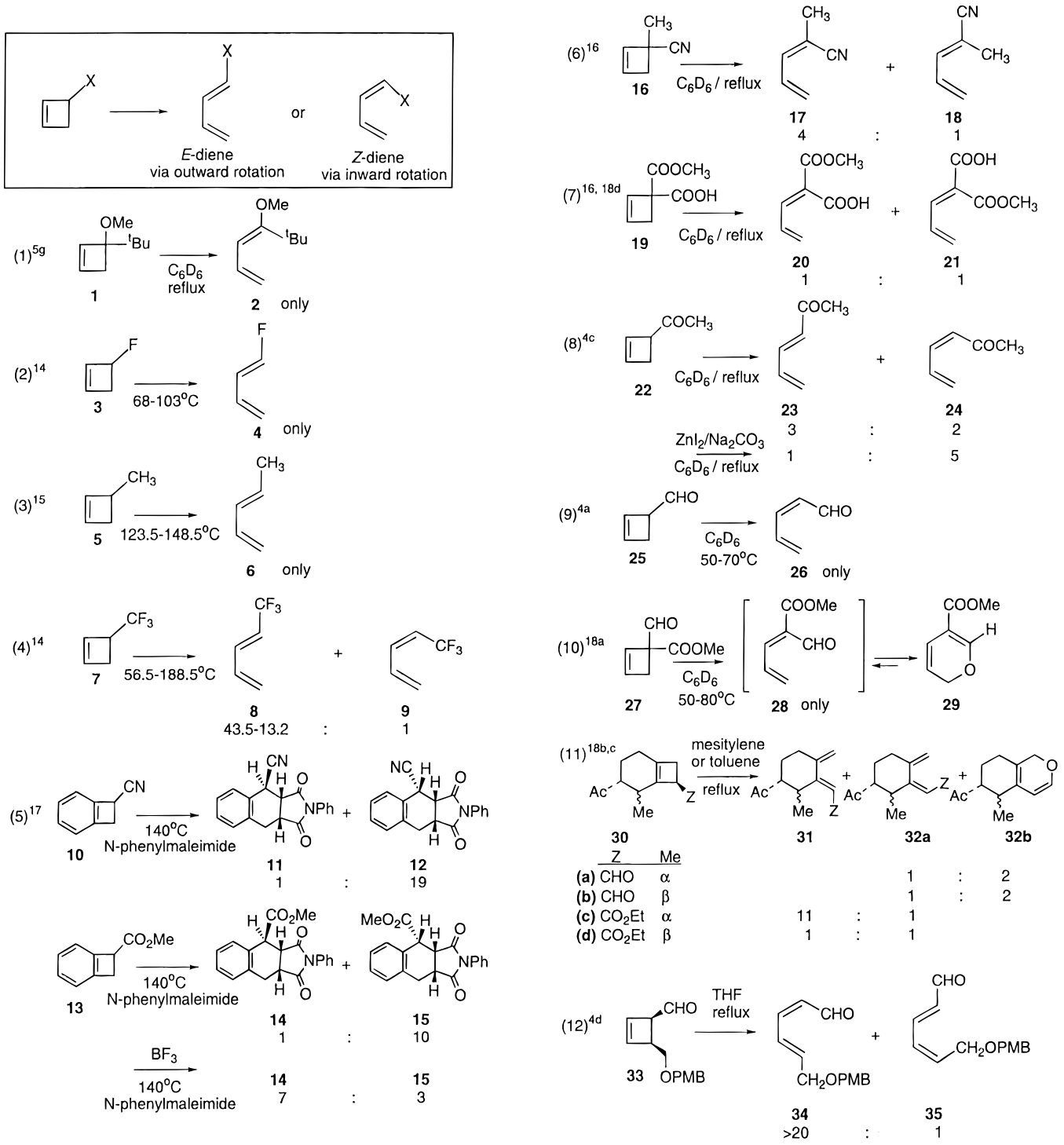


Figure 1. Possible products from a 3-substituted cyclobutene thermal opening.

in both inward and outward transition structures is the C_3C_4 σ orbital mixed with the C_1C_2 π^* orbital and with the oxygen lone pair. In addition, the outward HOMO (−8.11 eV) is lower in energy than the inward HOMO (−7.71 eV). This is due to the greater closed shell repulsive interaction in the inward rotation transition structure. The LUMO of both outward and inward rotation structures is mainly the C_3C_4 σ^* orbital mixed with the C_1C_2 π orbital and with the oxygen lone pair. The outward LUMO is 4.25 eV, while the inward LUMO is 3.52 eV. This higher energy of the outward LUMO arises from the larger overlap of donor orbitals with σ^*, the remote carbon has the opposite sign from the neighboring carbon, resulting in less net overlap in the inward rotation.

While the orbital argument gives a compelling qualitative rationale of the observed effects, calculations are still necessary to give quantitative predictions. In this work, we have extended our earlier studies to a diverse range of substituents: lithium oxy, amino, hydroxyl, fluoro, chloro, ethynyl, methyl, ammonio, trifluoromethyl, carboxylate, cyano, sulfoxyl, sulfonyl, sulfinic acid, nitroso, imino, carboxylic acid, *N*-protonated imino, protonated carboxylic acid, nitro, formyl, acetyl, mercapto, boryl, and dimethylboryl. Substituents have been found to influence geometries of the cyclobutenes as well as transition

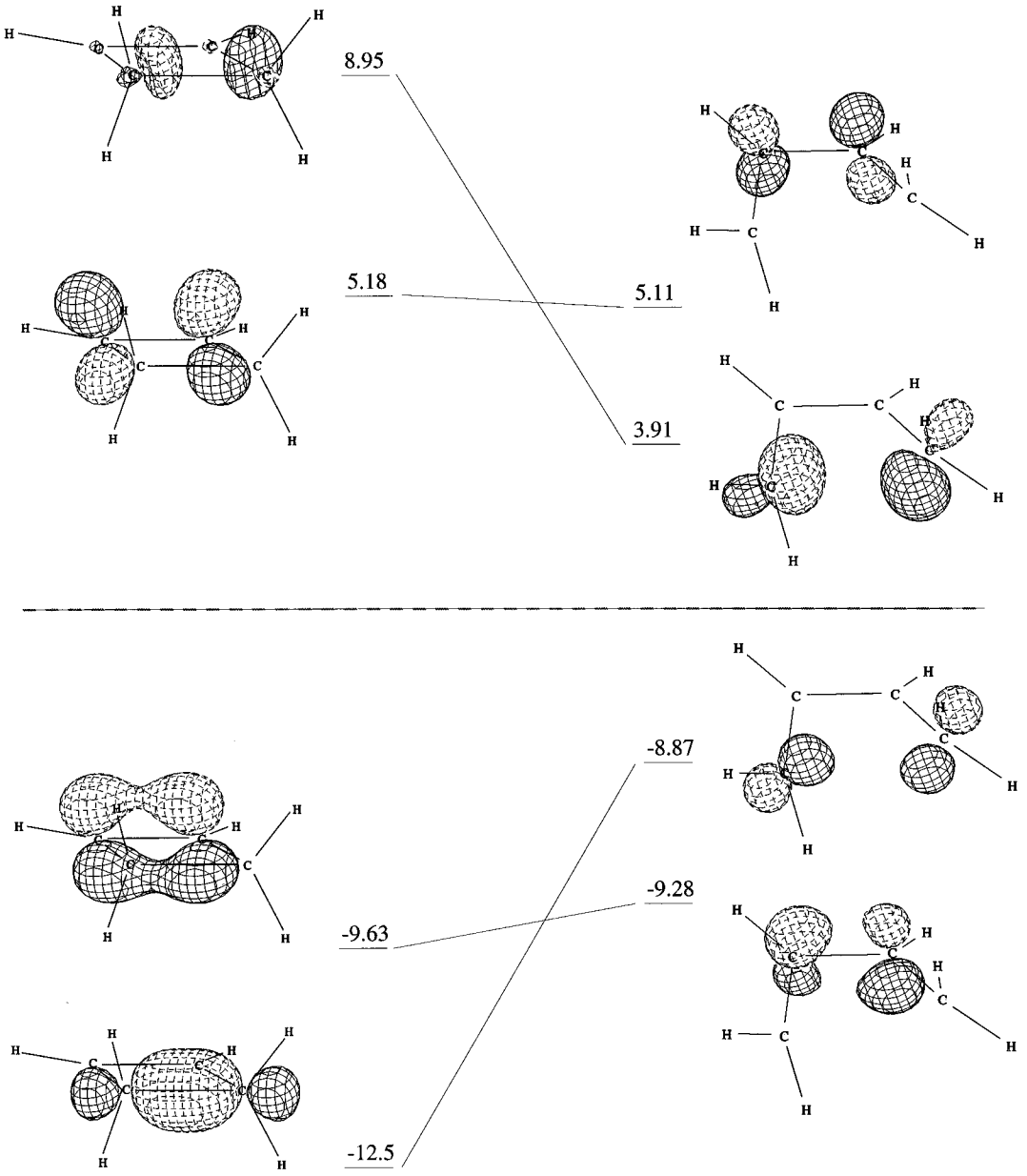


Figure 2. Orbital correlation between cyclobutene and the transition structure for electrocyclic opening (RHF/6-31G*, orbital energies in eV).

states. A correlation between the activation energy differences for inward and outward conrotation and the Taft σ_R^0 value was shown, allowing predictions of stereoselectivities of other groups for which quantum mechanical transition state calculations have not been performed. In addition, substituents at the 1-position were studied, and some interesting substituent effect patterns have been uncovered. The patterns found here are all in accord with the theory of torquoselectivity developed by Rondan and Houk[2] and do not fit an alternative theory proposed by Epiotis.[7]

Computational Methods

All calculations were performed with the GAUSSIAN 86 and GAUSSIAN 88 programs[8] using the 3-21G or 3-21G* basis sets with restricted Hartree−Fock theory for geometry optimizations. Frequency calculations were performed on all stationary points. Single point calculations were performed at the RHF/6-31G* level of theory on the optimized RHF/3-21G geometries. In some cases, 6-31G* optimizations and MP2/6-31G* single point calculations were also performed (−F, −Me, −CN, −CHO, −NO, $-BH_2$).

Results and Discussion

I. Geometries of Cyclobutenes. We describe first the effects of substituents on the geometries of cyclobutenes. A bond adjacent to a substituent can overlap with donor or acceptor orbitals on the substituent; consequently, the substituent may induce a twist of the

(7) Epiotis concluded that the lone pairs of these strong donating groups (−OH, $-NH_2$, −F, −Me) play no crucial role. He proposes that the σ bond by which these groups are attached is more important in influencing torquoselectivity. Epiotis, N. *THEOCHEM* **1990**, *66*, 225

(8) (a) GAUSSIAN 86: Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M. Kahn, L. R.; Defrees, D. J.; Seeger,R.; Whiteside, R. A.; Fox, D. J.; Fluder, E. M.; Pople, J. A. Carnegie-Mellon Quantum Chemistry Publishing Unit, Pittsburgh, PA, 1984. (b) GAUSSIAN 88: Frisch, M. J.; Head-Gordon, M.; Schlegel, H. B.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R.; Kahn, L. R.; Stewart, J. J. P.; Fluder, E. M.; Topiol, S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1988.

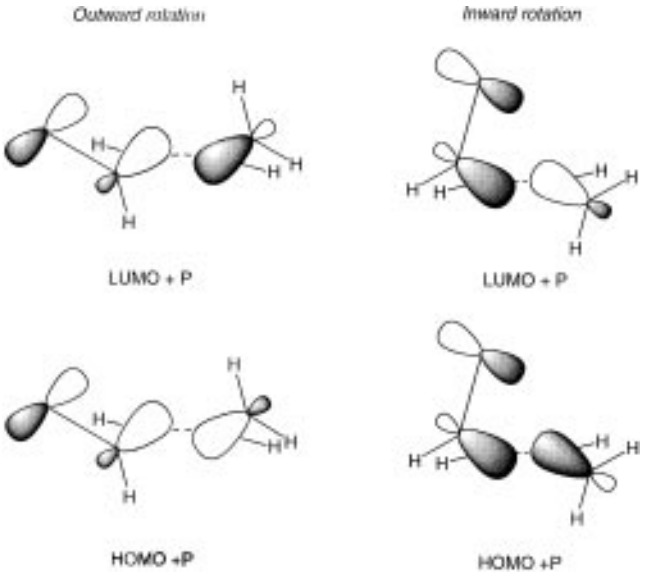


Figure 3. Orbital orientations upon inward and outward rotation.

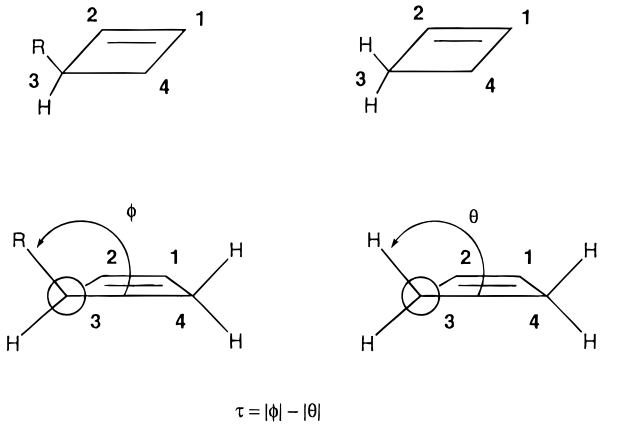


Figure 4. Pictorial representation of the inherent torque parameter τ.

σ bond to reduce repulsion between the bond and a donor orbital or to increase stabilization from overlap of an acceptor. This twist should not be very large, since ground state σ and σ^* orbital energies are not compressed as they are in the transition states for bond breaking.[2] It is possible to quantify this ground state electronic effect.

To do so, we define a parameter, τ, as in Figure 4 which is the difference between the dihedrals $RC_3C_2C_4$ in substituted cyclobutenes and $HC_3C_2C_4$ in cyclobutene itself. This τ is the inherent torque of the system. This effect can be seen in substituted ethanes where substantial inherent torques are found when the C−C−R angle and C−C−H angle are compared.[9] For example, the substituent leans toward the C_3-C_4 bond in the formyl-substituted case and away from it in the amino and fluoro-substituted cases. The filled orbital of the donor repels the σ-bonding orbital and bends away from this bond to minimize repulsion.

Inherent torque values calculated for 3-substituted cyclobutenes (Table 1) correlate ($r = 0.97$) with the Taft σ_R^0 value. Figure 5 shows the relationship between the σ_R^0 of the substituent and its inherent torque. The Taft

(9) Spellmeyer, D. C.; Reiser, O.; Houk, K. N. unpublished results.

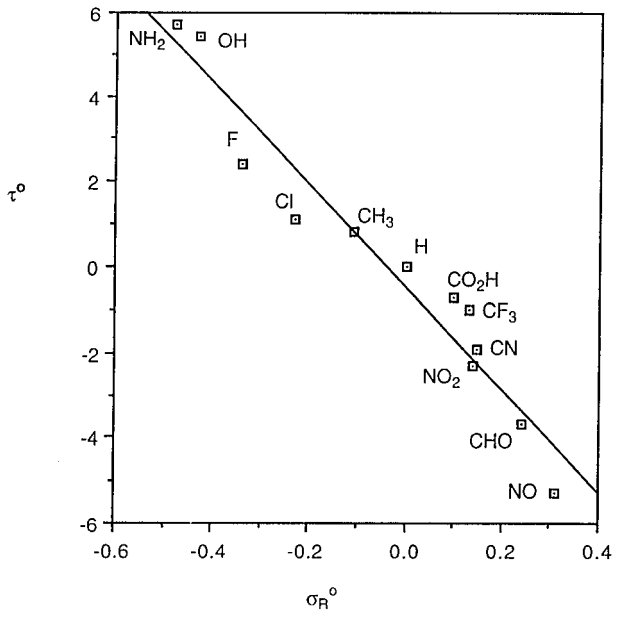


Figure 5. RHF/3-21G inherent torque plotted against Taft σ_R^0 values.

Table 1. Inherent Torque (τ) from 3-21G-Optimized Geometries

substituents	$\tau^{(o)}$	σ_R^o	substituents	$\tau^{(o)}$	σ_R^o
NH_2	5.7	−0.48	CF_3	−0.7	0.10
OH	5.4	−0.43	CN	−1.0	0.13
F	2.4	−0.34	NO_2	−1.9	0.15
Cl	1.1	−0.23	CO_2H	−2.3	0.14
CH_3	0.8	−0.11	CHO	−3.7	0.24
H	0.0	0.0	NO	−5.3	0.31

σ_R^0 parameter is an experimentally determined measure of the resonance, as opposed to inductive, electron-donor, or electron-acceptor character of the substituent.[10] Good π donors ($\sigma_R^0 < 0$) bend away from the adjacent bond, while π acceptors ($\sigma_R^0 > 0$) bend toward the adjacent bond.

II. Transition Structures of Substituted Cyclobutene Electrocyclic Reactions. 1. 1-Substituted Cyclobutenes. The transition structures for the conrotatory openings of 1-amino-, 1-hydroxy-, 1-fluoro-, 1-chloro-, 1-methyl-, 1-cyano-, 1-formyl-, and 1-vinylcyclobutene and the conjugate base of cyclobuten-1-ol were located; activation energies and geometries are listed in Table 2. Little effect of substitution was noted on geometry. Ordinary resonance electron donors raise the activation energy by 0.5−2.4 kcal/mol, while formyl, a resonance electron acceptor, lowers the activation energy by 1.1 kcal/mol. The very powerful donor, alkoxide, raises the activation energy by 6.9 kcal/mol. This is due to the large resonance donating power of a negatively charged oxygen, which experiences more repulsive interaction with the π bond in the transition state than in the reactant. A general description of the 1-substituent effects can be made on the basis of the orbital interactions. Figure 2 shows that the cyclobutene π orbital rises in energy to a small extent from cyclobutene to conrotatory transition state. Consequently, the vacant orbital of an acceptor substituent at C-1 stabilizes the transition state somewhat more than the

(10) (a) Taft, R. W.; Lewis, I. C. *J. Am. Chem. Soc.* **1958**, *80*, 2436. (b) Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W. *Prog. Phys. Org.Chem.* **1973**, *10*, 1.

Table 2. Selected Geometric Parameters for 3-21G 1-Substituted Cyclobutene Ring Opening Transition Structures[a]

R =	O^-	NH_2	OH	F	Cl	Me	$CHCH_2$	CN	CHO
C_4C_3	2.157	2.146	2.138	2.158	2.154	2.145	2.136	2.141	2.135
C_4C_1=C_3C_2	1.477	1.427	1.421	1.407	1.490	1.422	1.426	1.422	1.424
C_1C_2	1.403	1.417	1.419	1.419	1.412	1.418	1.416	1.412	1.415
$C_4C_1C_2$	104.4	104.6	74.3	74.2	103.1	73.5	73.7	104.4	73.7
HC_2C_3	125.4	126.8	126.6	127.5	127.6	126.1	126.4	126.9	124.5
$C_4C_1C_2C_3$	23.7	22.1	14.3	13.1	21.3	14.2	15.0	22.4	14.5
$H_{in}C_4C_1C_3$	79.7	76.9	82.1	74.0	75.0	75.0	81.5	76.0	76.6
$H_{out}C_3C_2C_4$	141.6	134.4	123.9	128.1	131.5	131.3	130.2	130.0	132.1
E_a(3-21G)	48.5	42.6	43.5	42.5	42.2	43.5	44.0	42.1	40.5
$E_a - E_a$(cyclobutene)	6.9	1.0	1.9	0.9	0.6	1.9	2.4	0.5	−1.1

[a] Distances are in angstroms, and angles are in degrees. 3-21G activation energies and relative activation energies ($E_a - E_a$(cyclobutene)) are given in kcal/mol.

reactant. The better the acceptor, the greater the acceleration, but the effects are very small.

There is a very small lowering of the cyclobutene π^* energy in the transition state. Consequently, there is no appreciable difference in stabilization of the reactant and transition states by donor substutituents. There is, however, an increase in closed shell repulsion between the donor filled orbitals and the cyclobutene π orbital as it rise in energy. Consequently, donors at C-1 retard the reaction.[11]

2. 3-Substituted Cyclobutenes. The transition structures for electrocyclic reactions of 3-substituted cyclobutenes are shown in Figure 6. Geometrical parameters are listed in Table 3. The results are discussed in order of increasing Taft σ_R^0. The geometries of all of the substituted cyclobutene transition structures are similar, except for the dihedral angle ($RC_3C_2C_4$) of the substituent in the transition structures for inward rotation. This parameter will be discussed for those substituted transition structures that exhibit unusual dihedral angles.

Table 4 summarizes activation energies for these 3-substituted cyclobutene ring openings calculated with RHF 3-21G, RHF 6-31G*//3-21G, and MP2/6-31G*//3-21G[5i] methods. From these values, substituent effects on the reaction rates can be predicted. Additionally, the torquoselectivities can be predicted from the activation energy differences between inward and outward rotations. The energies discussed in the text are those calculated at the 6-31G*//3-21G level. Some of them, in which the single point calculations were performed at the MP2/6-31G*//3-21G level (−F, −Me, −CN, −CHO, −NO, $-BH_2$), are also described in the text.

No transition structure for inward conrotation of the conjugate base of cyclobuten-3-ol anion could be located. Upon attempted optimization, the structure always collapsed to the 3-butenal anion. This is an extreme example of the effect of an alkoxide on weakening an α-CC bond.[12] Alkoxides are known to accelerate pericyclic reactions such as the Cope rearrangement to a large extent.[13] The lithoxy-substituted transition structures were located as examples of the effect of a somewhat less powerful donor. The Li−O−C angle was constrained to 180° for convenience. The outward transition state appears quite normal, and the activation energy is lowered by 17−18 kcal/mol. The inward transition state has a dihedral angle $OC_3C_2C_4$ of 94° as compared to 75° for the $H_{in}C_3C_2C_4$ of the parent cyclobutene system (see Table 3) due to the very strong repulsion between the anion and the breaking σ bond. The lithoxy system exhibits the largest outward preference found 24.4 kcal/mol.

−NH_2. For 3-aminocyclobutene, a large deviation in the dihedral angle for the amino group upon inward rotation was observed (95° versus 75° in the parent). The preference for outward rotation is 17.5 kcal/mol. This preference is due to a 6.0 kcal/mol destabilization of the inward rotation transition state and a 11.5 kcal/mol stabilization of the outward rotation transition state. In the transition structures the lone pair on the nitrogen is rotated away from the ring so as to be antiperiplanar with respect to the breaking bond. This diminishes the repulsive interaction by minimizing overlap of the lone pair with the HOMO and maximizes the $n_N-\sigma^*_{CC}$ interaction.

−OH. A total of five transition structures was found for 3-hydroxycyclobutene, two for outward conrotation, and three for inward conrotation. As in Figure 6, among the five transition structures, the lowest outward structure has the OH bond syn to the C_3C_2 bond, so that an oxygen lone-pair orbital, perpendicular to the HOC plane, can have maximum overlap with the breaking C_3C_4 σ bond. The lowest energy inward transition structure has the OH bond oriented inside the cyclobutene ring. This arrangement has one oxygen lone pair anti to the breaking C_3C_4 bond and the other lone pair pointing outward from the ring. The dihedral angle of the inward rotating hydroxy group is 90° compared with 75° in the parent. A smaller degree of rotation diminishes overlap of the oxygen with the breaking σ bond; consequently, the oxygen does not rotate as far inward to take advantage of this distortion. The in−out preference is 17.2 kcal/mol, resulting from a 8.8 kcal/mol stabilization of the outward transition structure and 8.4 kcal/mol destabilization of the inward rotating structure. This prefer-

(11) Carpenter predicted that any substituent at the 1-position of cyclobutene should destabilize the transition structure causing an elevation of activation energy and concomitant deceleration of the reaction. However, this prediction was derived from Hückel calculations of Möbius cyclobutadiene as a model of the conrotatory transition structure, which is based on assumption of complete delocalization in the transition state. It does not differentiate the effects we have observed between donor and acceptor substituents. (Carpenter, B. *Tetrahedron* **1978**, *34*, 1877).

(12) Steigerwald, M. L.; Goddard, W. A., III; Evans, D. A. *J. Am. Chem. Soc.* **1979**, *101*, 1994

(13) (a) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 1476. (b) Bronson, J. J.; Danheiser, R. L. *Compr. Org. Synth.* **1991**, *5*, 999. (c) Sprules, T. J.; Galpin, J. D. Macdonald, D. *Tetrahedron Lett.* **1993**, *34*, 243.

Substituents	Outward	Inward	σ_R^o
-H	<R(=H)C$_3$C$_2$C$_4$=131.6°, <R'(=H)C$_4$C$_1$C$_3$=75.3°, R, R', 1, 2, 3, 4, 2.138 Å		0.0
-OLi	127.0°, 2.130 Å, 0.0 (0.0)	94.0°, 2.239 Å, +21.1 (+24.4)	-0.60 (O$^-$)
-NH$_2$	129.9°, 2.128 Å, 0.0 (0.0)	94.9°, 2.227 Å, +19.5 (+17.5)	-0.48
-OH	130.9°, 2.125 Å, 0.0 (0.0)	90.9°, 2.181 Å, +16.4 (+17.2)	-0.43
-CF$_3$	127.8°, 2.133 Å, 0.0 (0.0)	81.8°, 2.174 Å, +1.9 (+2.6)	0.10
-SO$_2$H	126.9°, 2.127 Å, +1.3 (+0.3)	76.1°, 2.179 Å, 0.0 (0.0)	0.19 (SO$_2$Me)
-NO$_2$	130.1°, 2.123 Å, 0.0 (0.0)	79.8°, 2.171 Å, +6.9 (+7.3)	0.15
-F	132.5°, 2.154 Å, 0.0 (0.0) <0.0>	84.1°, 2.118 Å, +17.3 (+16.9) <+15.2>	-0.34
-Cl	132.0°, 2.122 Å, 0.0 (0.0)	86.0°, 2.175 Å, +14.8 (+13.6)	-0.23
-SH	132.3°, 2.135 Å, 0.0 (0.0)	79.3°, 2.174 Å, +13.1 (+13.7)	-0.15
-Me	130.1°, 2.143 Å, 0.0 (0.0) <0.0>	85.1°, 2.175 Å, +6.9 (+6.8) <+5.3>	-0.11
-CH=CH$_2$	127.4°, 2.145 Å, 0.0 (0.0)	82.0°, 2.167 Å, +4.7 (+4.9)	-0.03
-NH$_3^+$	127.9°, 2.141 Å, 0.0 (0.0)	84.9°, 2.203 Å, +7.7 (+7.9)	-0.04
-CCH	128.9°, 2.139 Å, 0.0 (0.0)	82.0°, 2.175 Å, +7.3 (+7.6)	0.07

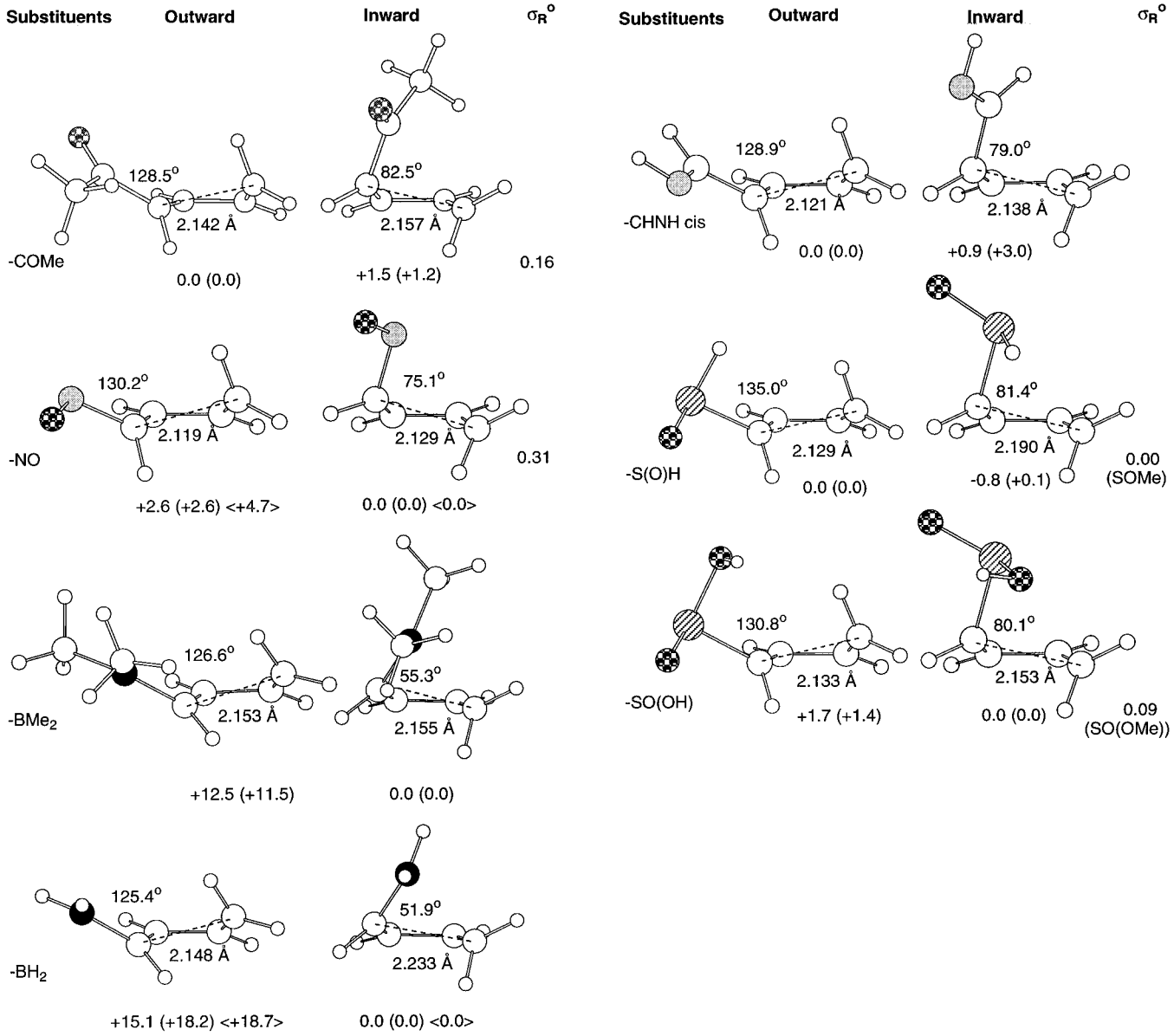


Figure 6. Transition structures of 3-substituted cyclobutene with RHF/3-21G(*) calculations. Relative energies (kcal/mol) with 3-21G(6-31G*//3-21G) <MP2/6-31G*//3-21G>[5i] calculations are shown.

ence is illustrated in the thermolysis of 3-methoxy-3-*tert*-butylcyclobutene, **1**, which affords exclusively the diene **2**, formed by the outward rotation of methoxy group and inward rotation of the bulky *tert*-butyl group (Figure 1, eq 1).

−F. A slightly smaller effect is found upon inward rotation in 3-fluorocyclobutene, **3**; a deviation of 9° is calculated for the substituent dihedral angle. The outward preference for 3-fluorocyclobutene is 16.9 kcal/mol at the 6-31G*//30-21G level or 15.1 kcal/mol at the MP2/6-31G*//3-21G theory level. Upon outward rotation there is 4.2 kcal/mol (6-31G*//3-21G) or 6.0 kcal/mol (MP2/6-31G*//3-21G) stabilization, and upon inward rotation there is 12.7 (6-31G*//3-21G) or 9.1 kcal/mol (MP2/6-31G*//3-21G) destabilization. Dolbier et al. reported that thermolysis of 3-fluorocyclobutene, **3**, afforded only the *E*-diene, **4** (Figure 1, eq 2).[14] The activation energy for this ring opening was experimentally measured to be 28.1 kcal/mol by them.

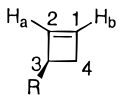
(14) Dolbier, W. R.; Gray, T. A.; Keaffaber, J. J.; Calewicz, L.; Koroniak, H. *J. Am. Chem. Soc.* **1990**, *112*, 363.

−Cl. Behavior similar to 3-fluorocyclobutene was observed for 3-chlorocyclobutene; however, the dihedral angle of the inward rotating chlorine is only enlarged to 86° which is almost identical to the one for fluorine (84°). This is due to the decreased ability of chlorine to function as a π donor. Chloro substitution produces an outward preference of 13.6 kcal/mol. An outward rotating chlorine destabilizes the transition structure by 0.4 kcal/mol relative to the parent, while an inward rotating chlorine destabilizes the transition structure by 14.0 kcal/mol.

−SH. Mercapto substitution produces inward and outward transition states that are similar (Table 4) to the hydroxycyclobutene transition states. The outside preference is only 13.7 kcal/mol as compared to 17.2 kcal/mol for hydroxy substitution. Mercapto is a weaker π donor than hydroxy as measured by σ_R^0 values of −0.15 and −0.43, respectively. The inward transition structure is destabilized by 8.8 kcal/mol, but the outward transition structure is stabilized by 4.9 kcal/mol. There are no examples where this has been tested.

−CH_3. Few changes from the parent are noted for the

Table 3. Selected 3-21G Geometric Parameters for 3-Substituted Cyclobutene Electrocyclc Ring Opening Transition Structures



	OLi		NH_2		OH			OLi		NH_2		OH	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.239	2.130	2.227	2.128	2.181	2.125	H_a−2−3	126.1	127.0	126.2	125.2	125.1	1.420
2−3	1.431	1.433	1.442	1.428	1.431	1.424	H_b−1−2	124.4	125.4	124.4	126.9	126.4	126.2
1−4	1.462	1.436	1.419	1.440	1.421	1.420	R−3−2−4	94.0	127.0	94.9	129.9	90.0	130.9
	F		Cl		SH			F		Cl		SH	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.118	2.154	2.175	2.122	2.188	2.128	H_a−2−3	125.7	126.6	125.6	126.3	125.3	125.6
2−3	1.408	1.411	1.412	1.405	1.413	1.423	H_b−1−2	125.8	126.4	125.6	126.2	126.2	128.5
1−4	1.417	1.417	1.413	1.421	1.423	1.425	R−3−2−4	84.1	132.5	86.0	132.0	88.0	129.0
	Me		$CHCH_2$		CCH			Me		$CHCH_2$		CCH	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.175	2.143	2.167	2.145	2.183	2.139	H_a−2−3	125.4	125.7	129.3	129.9	125.6	125.6
2−3	1.423	1.422	1.431	1.433	1.419	1.432	H_b−1−2	126.6	126.2	129.1	128.9	125.6	125.6
1−4	1.421	1.414	1.431	1.423	1.426	1.420	R−3−2−4	85.1	130.1	82.0	127.4	82.0	128.9
	CO_2^-		NH_3^+		t-CHNH			CO_2^-		NH_3^+		t-CHNH	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.152	2.126	2.203	2.141	2.159	2.132	H_a−2−3	126.7	123.9	126.1	125.2	125.6	126.1
2−3	1.419	1.422	1.425	1.412	1.420	1.435	H_b−1−2	125.8	126.6	126.1	126.9	125.9	126.1
1−4	1.468	1.427	1.427	1.434	1.422	1.434	R−3−2−4	79.5	130.4	84.9	127.9	79.4	128.9
	c-CHNH		SO_2H		SO(OH)			c-CHNH		SO_2H		SO(OH)	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.121	2.138	2.179	2.123	2.174	2.133	H_a−2−3	124.9	125.9	125.9	126.0	125.8	125.1
2−3	1.467	1.433	1.417	1.436	1.406	1.424	H_b−1−2	125.0	125.9	125.0	125.7	125.4	125.0
1−4	1.463	1.427	1.419	1.436	1.412	1.423	R−3−2−4	79.0	128.9	76.1	126.9	77.4	127.2
	SHO		CF_3		CN			SHO		CF_3		CN	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.184	2.126	2.174	2.133	2.175	2.140	H_a−2−3	125.3	126.1	125.8	125.1	125.1	125.9
2−3	1.410	1.419	1.406	1.424	1.431	1.423	H_b−1−2	126.2	125.6	125.4	125.0	125.4	125.8
1−4	1.413	1.422	1.412	1.423	1.421	1.428	R−3−2−4	76.6	127.9	81.8	127.8	76.0	129.9
	CO_2H		NO_2		COMe			CO_2H		NO_2		COMe	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.167	2.132	2.171	2.123	2.157	2.139	H_a−2−3	125.8	125.8	125.1	126.8	129.3	129.0
2−3	1.422	1.421	1.407	1.411	1.431	1.427	H_b−1−2	125.3	125.8	125.1	126.8	129.1	129.3
1−4	1.424	1.431	1.412	1.424	1.431	1.423	R−3−2−4	78.2	130.4	79.8	130.1	82.0	128.5
	CHO		NO		$CO_2H_2^+$			CHO		NO		$CO_2H_2^+$	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.152	2.143	2.129	2.119	2.212	2.182	H_a−2−3	125.1	126.3	125.1	126.4	124.9	125.5
2−3	1.427	1.426	1.427	1.423	1.447	1.463	H_b−1−2	125.4	125.9	125.4	125.8	124.0	123.8
1−4	1.425	1.427	1.423	1.429	1.441	1.450	R−3−2−4	76.0	115.4	75.1	130.2	73.5	125.2
	BMe_2		$CHNH_2^+$		BH_2			BMe_2		$CHNH_2^+$		BH_2	
	in	out	in	out	in	out		in	out	in	out	in	out
3−4	2.155	2.153	2.190	2.152	2.233	2.148	H_a−2−3	125.5	125.9	125.9	124.6	126.1	125.6
2−3	1.453	1.428	1.456	1.459	1.425	1.437	H_b−1−2	128.7	129.5	123.8	124.7	124.4	125.6
1−4	1.442	1.440	1.437	1.463	1.445	1.432	R−3−2−4	55.3	126.6	70.5	125.2	51.9	125.4

transition structure geometries of 3-methylcyclobutene, **5**. The degree of rotation of the methyl group is similar to the parent system for both inward and outward conrotation. Outward rotation is preferred by 5.3 kcal/mol (MP2/6-31G*//3-21G). Inward rotation is destabilized by 3.6 kcal/mol and outward is stabilized by 1.7 kcal/mol compared to the parent system, which is in good agreement with the experimental lowering of the activation energy of 1.0 kcal/mol by a methyl measured by Frey et al. (Figure 1, eq 3).[15] We interpret this as a steric effect which, in part, involves repulsion between filled orbital of the methyl and the σ orbital of the breaking bond. There are some experimental results reported which illustrate the preference for outward rotation for methyl or alkyl groups in 3,3-disubstituted cyclobutenes as

(15) Frey, H. M.; Marshall, D., C. *Trans. Faraday Soc.* **1965**, *61*, 1715.

Table 4. 3−21G (6−31G*//3−21G) [MP2/6−31G*//3−21G+ZPE][5i] Activation Energies for 3- Substituted Cyclobutene Ring Openings

substituent	E_{act}	E_{rel} (to parent)	$E_{in} - E_{out}$	σ_R^0
OLi in	45.5 (52.2)	3.9 (6.0)		
OLi out	24.4 (27.8)	−17.2 (−18.4)	21.1 (24.4)	−0.60(O^-)
NH_2 in	46.5 (52.2)	4.9 (6.0)		
NH_2 out	27.0 (34.7)	−14.6 (−11.5)	19.5 (17.5)	−0.48
OH in	48.7 (54.6)	7.1 (8.4)		
OH out	32.3 (37.4)	−9.3 (−8.8)	16.4 (17.2)	−0.43
F in	52.8 (58.9) [44.3]	11.2 (12.7) [9.1]		
F out	35.5 (42.0) [29.2]	−6.1 (−4.2) [−6.0]	17.3 (16.9) [15.1]	−0.34
Cl in (3-21G*)	53.4 (60.2)	11.8 (14.0)		
Cl out (3-21G*)	38.6 (46.6)	−3.0 (0.4)	14.8 (13.6)	−0.23
SH in (3-21G*)	50.0 (55.0)	8.4 (8.8)		
SH out (3-21G*)	36.9 (41.3)	−4.7 (−4.9)	13.1 (13.7)	−0.15
Me in	47.3 (51.3) [38.8]	5.7 (5.1) [+3.6]		
Me out	40.4 (44.5) [33.5]	−1.2 (−1.7) [−1.7]	6.9 (6.8) [5.3]	−0.11
$HCCH_2$ in	41.7 (45.3)	0.1 (−0.9)		
$HCCH_2$ out	37.0 (40.4)	−4.6 (−5.8)	4.7 (4.9)	−0.03
CO_2^- in	42.1 (47.1)	0.5 (0.9)		
CO_2^- out	37.2 (39.8)	−4.4 (−6.4)	4.9 (7.3)	
NH_3^+ in	49.8 (54.2)	8.2 (8.0)		
NH_3^+ out	42.1 (46.3)	0.5 (0.1)	7.7 (7.9)	−0.04
H	41.6 (46.2)	0.0 (0.0)		0.0
CHNH trans in	38.9 (39.3)	−2.7 (−6.9)		
CHNH trans out	38.7 (42.3)	−2.9 (−3.9)	0.2 (−3.0)	
CHNH cis in	39.4 (45.6)	−2.2 (−0.6)		
CHNH cis out	38.5 (42.6)	−3.1 (−3.6)	0.9 (3.0)	
S(O)H in (3−21G*)	40.2 (45.4)	−1.4 (−0.8)		
S(O)H out (3−21G*)	41.0 (45.3)	−0.6 (−0.9)	−0.8 (0.1)	0.00(S(O)Me)
CCH in	45.5 (48.2)	3.9 (2.0)		
CCH out	38.2 (40.6)	−3.4 (−5.6)	7.3 (7.6)	0.07
SO(OH) in (3−21G*)	39.7 (45.2)	−1.9 (−1.0)		
SO(OH) out (3−21G*)	41.4 (46.6)	−0.2 (0.4)	−1.7 (−1.4)	0.09(SO(OMe))
CF_3 in	47.0 (50.9)	5.4 (4.7)		
CF_3 out	45.1 (48.3)	3.5 (2.1)	1.9 (2.6)	0.10
SO_2H in (3−21G*)	39.6 (42.2)	−2.0 (−4.0)		
SO_2H out (3−21G*)	40.9 (42.5)	−0.7 (−3.7)	−1.3 (−0.3)	0.19(SO_2Me)
CN in	43.9 (47.2) [35.2]	2.3 (1.0) [0.0]		
CN out	39.3 (42.9) [31.0]	−2.3 (−3.3) [−4.2]	4.6 (4.3) [4.2]	0.13
CO_2H in	40.0 (44.2)	−1.6 (−2.0)		
CO_2H out	38.5 (41.9)	−3.1 (−4.3)	1.5 (2.3)	0.14
NO_2 in	45.2 (50.1)	3.6 (3.9)		
NO_2 out	38.3 (42.8)	−3.3 (−3.4)	6.9 (7.3)	0.15
COMe in	40.5 (42.6)	−1.1 (−3.6)		
COMe out	39.0 (41.4)	−2.6 (−4.8)	1.5 (1.2)	0.16
CHO in	34.7 (38.0) [26.5]	−6.9 (−8.2) [−8.7]		
CHO out	39.2 (42.6) [31.2]	−2.4 (−3.6) [−4.0]	−4.5 (−4.6) [−4.7]	0.24
NO in	34.5 (39.1) [25.1]	−7.1 (−7.1) [−10.1]		
NO out	37.1 (41.7) [29.8]	−4.5 (−4.5) [−5.4]	−2.6 (−2.6) [−4.7]	0.31
$CO_2H_2^+$ in	23.3 (30.4)	−18.3 (−15.8)		
$CO_2H_2^+$ out	29.6 (35.2)	−12.0 (−11.0)	−6.3 (−4.8)	
$B(Me)_{2\ in}$	24.6 (29.0)	−17.0 (−17.2)		
$B(Me)_2$ out	37.1 (40.5)	−4.5 (−5.7)	−12.5 (−11.5)	
$CHNH_2^+$ in	22.1 (24.7)	−19.5 (−21.5)		
$CHNH_2^+$ out	32.6 (34.8)	−9.0 (−11.4)	−10.5 (−10.1)	
BH_2 in	17.1 (20.8) [10.8]	−24.5 (−25.4) [−24.4]		
BH_2 out	32.2 (39.0) [29.5]	−9.4 (−7.2) [−5.7]	−15.1 (−18.2) [−18.7]	

shown in Figure 1 (eq 5).[16] A full discussion of the alkyl group effects on torquoselectivity has been given.[5]

−CH=H₂. The transition structure for outward rotation of 3-vinylcyclobutene is normal, and the activation energy is lowered by ∼5 kcal/mol. There is little effect on the inward transition structure. This is consistent with the behavior of a vinyl group as weak donor ($\sigma_R^0 = -0.03$). The preference for outward conrotation is only 4.9 kcal/mol. In both the inward and outward transition structures, the vinyl group is anti to the ring. The transition structures with the vinyl group syn to the ring are both approximately 2 kcal/mol higher in energy than their respective anti conformers.

−C≡CH. The ethynyl group behaves much like the vinyl group. Although small, the ethynyl group causes some distortion upon inward rotation, having a substituent dihedral of 82°. The σ_R^0 implies this group is an acceptor but the repulsion upon inward rotation is larger than for vinyl, propably due to the better overlaps of the π orbitals with the breaking σ bond orbitals. The outward rotating substituent dihedral angle is identical to the value of the outward rotating hydrogen in cyclobutene. The ethynyl substituent causes outward rotation to be preferred by 7.6 kcal/mol. The preference arises from 5.6 kcal/mol of stabilization for outward rotation and 2.0 kcal/mol of destabilization for inward rotation.

−NH_3^+. The 3-ammonio results provide good evidence for the importance of π substituent orbitals on torquoselectivity. In 3-ammoniocyclobutene, a destabilization of 8.0 kcal/mol is predicted on inward rotation and 0.1 kcal/mol on outward rotation. Epiotis[7] postulated an expla-

(16) Niwayama, S.; Wang, Y.; Houk, K. N. *Tetrahedron Lett.* **1995**, *36*, 6201.

nation of the torquoelectronic behavior of fluorine which predicts ammoniocyclobutene should behave similarly to fluorocyclobutene, since their inductive power is similar; however, according to our results, the ammonio group behaves more like a methyl substituent than a fluorine, even though it is a powerful inductive electron-withdrawing substituent.

−CH=NH. In 3-iminocyclobutene, the imine may be either *cis* or *trans* and be a *syn* or *anti* conformer with respect to the cyclobutene ring. The lowest energy transition structure is the outward *anti-trans*. The lowest energy transition structure for the *cis* isomer is also *anti*. Both the in-*anti-trans* and the in-*anti-cis* isomers are very similar to the parent transition state; their substituent dihedrals are both 79°. Slight deviation is expected as there is only slight preference for outward conrotation, indicating that the substituent has little effect on the transition structure. The preference of out over in is 3.0 kcal/mol for the *cis* isomer, but inward rotation is preferred for the *trans* isomer by 3.0 kcal/mol. The *cis* imino group provides 0.6 kcal/mol of stabilization on inward rotation and 3.6 kcal/mol on outward rotation. *Trans* imino substitution provides 6.9 kcal/mol of stabilization on inward rotation and 3.9 kcal/mol on outward rotation.

$-CH=NH_2^+$. Protonation of 3-iminocyclobutene gives the 3-immoniocyclobutene. This substituent exhibits a dramatic preference for inward conrotation (10.1 kcal/mol). Separation into the components yields 21.5 kcal/mol of stabilization on inward rotation and 11.4 kcal/mol of stabilization on outward rotation. The dihedral angle of the protonated imino group upon inward rotation is consequently decreased to 71°, signaling the increased interaction of the acceptor orbital of the imino group with the breaking σ bond. The π^* acceptor orbital of the imine group is lowered substantially by the protonation, and enhanced interaction between the π^* orbital and breaking σ-orbital favors inward rotation. This prediction of reversed torquoselectivity upon protonation has not yet been tested experimentally.

$-SO_2H$. The sulfonyl group, SO_2H, is a moderate electron withdrawer ($\sigma_R^0 = 0.19$ for SO_2Me), causing a 0.3 kcal/mol preference for inward rotation. The activation energy for inward rotation is lowered by 4.0 kcal/mol relative to the parent, and outward rotation is stabilized by 3.7 kcal/mol. The sulfonyl ($-SO_2H$) group does not lean inward toward the breaking bond appreciably during inward conrotation. The dihedral for the inward rotating sulfonyl is 76°, which is almost unchanged from the parent dihedral angle. One of the two SO groups is directed toward the cyclobutene ring in both inward (dihedral angle for the $O-S-C_3-C_2$ is −11°) and outward rotation (−19°) transition structures.

−SO(OH). The sulfinic acid group, −SO(OH), functionality should function as an attenuated carboxylic acid functionality, since the sulfone functions essentially as an attenuated carbonyl group. However, the activation energies are lowered slightly for inward rotation (by 1.0 kcal/mol) and raised for outward rotation (by 0.4 kcal/mol). A 1.4 kcal/mol preference for inward rotation over outward rotation results. The inward rotating sulfinic acid substituent has a dihedral angle of 77°, an increase of 2° over the parent system. The conformation of the sulfinic acid in the transition state is that of the SO double bond anti to the ring.

−S(O)H. The sulfoxyl substituent, −SOH, has very little effect, consistent with its value of $\sigma_R^0 = 0.00$ (for SOMe). The activation energy for inward rotation for SOH is 0.8 kcal/mol lower than in the unsubstituted system. The outward activation energy is also lowered by 0.9 kcal/mol. Consequently, the sulfoxyl group shows essentially no preference for either rotation. The group adopts a conformation with the SO bond rotated away from the ring, in the reactant and both transition structures.

These three −SOX substituents are predicted to exhibit very weak torquoselectivity, which is consistent with the nearly unchanged dihedral angle of $SC_3C_2C_4$ compared to the parent system. Only the sulfinic acid, −SO(OH), shows a small preference for inward rotation by 1.4 kcal/mol, while the two other substituents have essentially no effect on torquoselectivity: the sulfonyl group, $-SO_2H$, has a preference for inward rotation of only 0.3 kcal/mol and sulfoxyl group, while −SOH has a preference for outward rotation of 0.1 kcal/mol.

$-CF_3$. In 3-(trifluoromethyl)cyclobutene, **7**, the bulky trifluoromethyl group has a 2.6 kcal/mol preference for outward rotation. In the inward transition structure, the trifluoromethyl group dihedral angle is 82°. The inward transition structure is destabilized by 4.7 kcal/mol with respect to the parent. The outward structure is destabilized by 2.1 kcal/mol. Dolbier has measured $E_{in} - E_{out}$ to be 1.2 kcal/mol for trifluoromethyl, **7**.[14] As mentioned above, the thermolysis of both 3-fluoro- and 3-methylcyclobutene afforded only *E*-dienes, while **7** is accompanied by a small amount of *Z*-diene, **9** (Figure 1, eq 4).[14]

−CN. Outward rotation is predicted to be favored by 4.3 (6-31G*//3-21G) or 4.2 (MP2/6-31G*//3-21G) kcal/mol for cyano. Inward rotation is destabilized by 1.0 kcal/mol (6-31G*//3-21G) or remains the same as the parent at the MP2/6-31G*//3-21G level, but outward rotation is stabilized by 3.3 (6-31G*//3-21G) or 4.2 (MP2/6-31G*//3-21G) kcal/mol. Cyano is only a weak resonance acceptor and, consequently, does not stabilize inward rotation. Upon inward rotation the substituent dihedral angle shows less deviation from the parent than do the donor substituents discussed previously (5° larger than that of the parent inward hydrogen). $E_{in} - E_{out}$ has been measured for cyanobenzocyclobutene, **10**, to be 2.4 kcal/mol (Figure 1, eq 5).[17] The ring opening of 3-cyano-3-methylcyclobutene, **16**, at 140 °C gives both dienes **17** and **18** with inward rotation of the cyano group preferred in a 4:1 ratio (Figure 1, eq 6).[16] This is consistent with predictions made by our calculated activation energies.

$-CO_2H$, $-CO_2^-$, $-CO_2H^+$, and $-CO_2Me$. Cyclobutene-3-carboxylic acid and its conjugate base and acid have been studied earlier.[4b] The preferences for outward rotation are 7.3 kcal/mol for the carboxylate and 2.3 kcal/mol of the acid, while there is a 4.8 kcal/mol preference for inward rotation for the protonated acid. The acid exhibits 4.3 kcal/mol stabilization for inward rotation and 2.0 kcal/mol for outward, resulting in the net preference for inward rotation. Consequently, only the protonated species is predicted to favor inward rotation among these three species. Although no direct experimental verification has been reported for cyclobutenes, in benzocyclobutenes, Jefford, Bernardinelli, Wang, Spellmeyer, Buda, and Houk observed that thermolysis of methyl benzocyclobutene-7-carboxylate, **13**, in the presence of BF_3 and *N*-phenylmaleimide preferentially afforded the Diels−Alder adduct **14** that arises from

(17) Jefford, C. W.; Bernardinelli, G.; Wang, Y.; Spellmeyer, D. C.; Buda, A.; Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 1157.

inward rotation of the benzocyclobutene.[17] Without BF_3, the main product is **15**, which was formed from the outward rotation of the COOMe group.

The carboalkoxy group is expected to exhibit almost the same behavior as a carboxylic acid. Therefore, the $E_{in} - E_{out}$ of methyl cyclobutene-3-carboxylate was approximated by replacing the hydrogen of the acid with a methyl group. The energy difference was found to be 1.7 kcal/mol with 3-21G basis set, which is almost identical with that calculated for the −COOH group.[4b] The torquoselectivity was illustrated in the thermolysis of 3,3-disubstituted cyclobutene **19**[16,18d] as in Figure 1, eq 7. As expected, the two dienes, **20** and **21**, were observed in a 1:1 ratio.

−NO_2. Nitro is a relatively poor resonance acceptor, as can be seen in its small positive σ_R^0 of 0.15, the same as a carboxylic acid. Outward rotation is preferred for nitro by 7.3 kcal/mol. Outward rotation stabilizes the transition structure by 3.4 kcal/mol, but inward rotation destabilizes the structure by 3.9 kcal/mol. Nitro substitution perturbs the geometry slightly, and the slight resistance to inward conrotation is evidenced by the substituent dihedral angle of 80°.

−$COCH_3$. Acetyl is a resonance electron-withdrawing substituent of the same strength as a carboxylic acid. Outward rotation is predicted to be preferred by 1.2 kcal/mol. The ring opening of 3-acetylcyclobutene, **22**, shown in Figure 1, eq 8, produces outward and inward rotation products, **23** and **24**, in a ratio of 3:2.[4c,e] The preferred conformation calculated for outward rotation has the carbonyl oxygen syn to the ring. This conformation is 1.1 kcal/mol more stable than the anti conformer. Inward rotation prefers the O anti conformation over O syn conformation by 1.7 kcal/mol in energy (Figure 6).

Both computationally and experimentally it has been shown that the addition of a soft Lewis acid reverses this torquoselectivity: inward rotation is now better, due to the enhanced electron-withdrawing character as predicted above for the protonated 3-carboxylic acid (Figure 1, eq 8).[4c] The calculation of the ring opening with the Lewis acid, BH_3, complexed with the carbonyl results in a prediction of the preference for inward rotation over outward rotation by 2.7 kcal/mol with the 3-21G level. Experimentally, in the presence of ZnI_2, the formation ratio for the *E*- and *Z*-dienes was observed to be 1:5 (*E*:*Z*).[4c]

−CHO. Formyl is a more powerful acceptor than acetyl. It was first predicted, and then shown experimentally, that formyl will rotate inward to give the less stable product.[4a] Inward and outward rotations are both stabilized, by 8.2 and 3.6 kcal/mol, respectively, at the 6-31G*//3-21G level, or 8.7 kcal/mol and 4.0 kcal/mol, respectively, at the MP2/6-31G*//3-21G level. Inward rotation is preferred by 4.6 (6-31G*//3-21G) or 4.7 (MP2/6-31G*//3-21G) kcal/mol. Experimental studies which verify this torquoselectivity toward inward rotation were reported by Houk and Rudolf (Figure 1, eq 9).[4a] In addition, Niwayama and Houk observed that methyl 1-formyl-2-cyclobutene-1-carboxylate, **27**, opens with inward rotation of the formyl group to produce the cyclized **29** (Figure 1, eq 10).[16a] Piers et al. also showed similar torquoselectivity of the formyl and carboethoxy groups in more complicated systems, **30a**−**d** (Figure 1, eq 11).[18b,c] A theoretical study was carried out to explain the stereoselectivity observed by Piers.[18e] Wallace's result is also a good example of the preference of inward rotation of the formyl group (Figure 1, eq 12).[4d] The substituent dihedral angle deviation for the lowest energy outward transition state is −17°. This substantial deviation results in order to maintain overlap of the formyl π system with the breaking bond. The lowest energy inward transition state exhibits only a 3° positive deviation from that of the parent inward hydrogen.

−NO. The acceptor substituent, 3-nitroso, is predicted to exhibit an inward conrotatory preference. The σ_R^0 value, 0.32, indicates strong resonance electron-withdrawing character. Both transition structures are stabilized, the inward by 7.1 (6-31G*//3-21G) or 10.1 (MP2/6-31G*//3-21G) kcal/mol and the outward by 4.5 (6-31G*//3-21G) or 5.4 (MP2/6-31G*//3-21G) kcal/mol. In this case the substituent dihedral exhibits a negative deviation (−2°), which shows quite clearly the favorable overlap upon inward rotation.

Although cyano and nitro groups are powerful electron acceptors, outward rotation is predicted to be favored over inward rotation for both substituents ($E_{in} - E_{out} = 4.3$ or 4.2 for CN, 7.3 for NO_2). Why do the cyano and nitro groups prefer outward rotation while the formyl and nitroso groups prefer inward rotation?

Acceptors prefer to maximize overlap of the acceptor π^* orbitals and the cyclobutene σ HOMO upon inward rotation if the π^* orbital is low enough in energy. In the absence of other orbital and steric interactions, acceptor substituents should cause inward rotation. However, in addition to low-lying vacant orbitals, acceptors have filled orbitals that can interact with the σ HOMO in the same manner as donor orbitals. The four-electron destabilizing interaction of the filled π orbitals with the HOMO is the largest upon inward rotation, and two-electron stabilizing interaction of the filled π orbitals with the LUMO should be the largest upon outward rotation, since the filled orbitals are donor orbitals. The two-electron stabilizing interactions of the vacant π^* orbitals with the HOMO is the largest upon inward rotation. There is a competition set up between the HOMO−π filled orbital interaction and the HOMO−π^* interaction upon inward rotation. Inward rotation should occur when the π^*−HOMO stabilizing interaction exceeds the π−HOMO destabilizing interaction. The results of the calculations of the outward and inward transition structures of 3-cyano- and 3-formylcyclobutene show that this competition is subtle. The cyano group has relatively high-lying π orbitals, causing the π^*_{CN}−HOMO interaction, which is favored upon inward rotation, to be overwhelmed by the π_{CN}−HOMO destabilization, which is disfavored upon inward rotation. Outward rotation maximizes the π_{CN}−LUMO interaction and minimizes the π_{CN}−HOMO interaction. On the other hand, the formyl group has lower-lying vacant orbitals, and the π^*_{CO}−HOMO- and π_{CO}−LUMO-stabilizing interactions are enough to counterbalance the π_{CO}−HOMO destabilizing interaction; inward rotation becomes favored. Similarly, the nitroso group is a better resonance acceptor($\sigma_R^0 = 0.24$), than nitro ($\sigma_R^0 = 0.14$), and the latter have several filled orbitals which resist inward rotation.

−BH_2 and −BMe_2. Boryl is the most powerful electron acceptor studied. A huge deviation from the parent system is seen upon inward conrotation of the substituent. Boryl has a dihedral of 52°, an inward deviation of

(18) (a) Niwayama, S.; Houk, K. N.; *Tetrahedron Lett.* **1992**, *33*, 883. (b) Piers, E.; Lu, Y.-F. *J. Org. Chem.* **1989**, *54*, 2268. (c) Piers, E.; Ellis, K. A. *Tetrahedron Lett.* **1993**, *34*, 1875. (d) Niwayama, S.; Houk, K. N.; Kusumi, T. *Tetrahedron Lett.* **1994**, *35*, 527. (e) Nakamura, K.; Houk, K. N. *J. Org. Chem.* **1995**, *60*, 686.

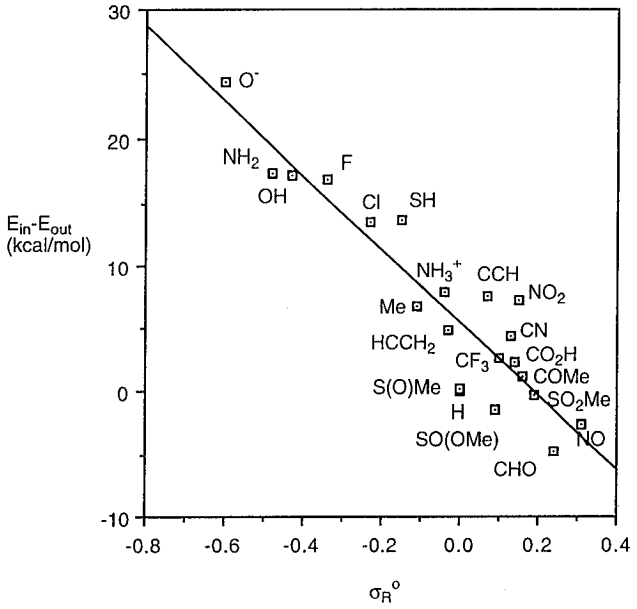


Figure 7. 6-31G*//3-21G activation energy difference plotted against Taft σ_R^0 values.

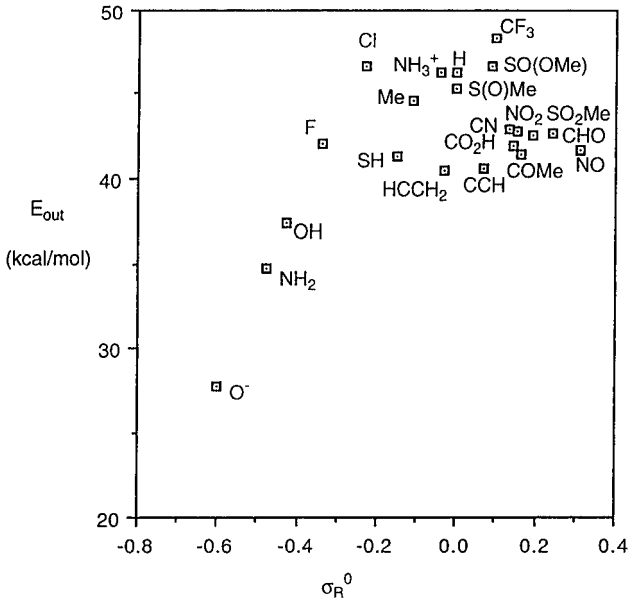


Figure 8. 6-31G*//3-21G outward conrotatory activation energies plotted against Taft σ_R^0 values.

23°. The high degree of stabilization produced by the cyclic two-electron array is shown by this amount of distortion. The large preference for inward rotation exhibited by boryl substitution (18.2 kcal/mol with the 6-31G*//3-21G or 18.7 kcal/mol with the MP2/6-31G*//3-21G) is decreased by adding methyl groups. Dimethylborylcyclobutene has transition structures very similar in geometry to those of borylcyclobutene; however, the preference for inward rotation has decreased to 11.5 kcal/mol. Substitution on the boron to produce dimethylborylcyclobutene attenuates the electron-withdrawing ability of the boron slightly. Stabilization of both transition structures is still large. The inward transition structure is stabilized by 17.2 kcal/mol, but the outward is stabilized by only 5.7 kcal/mol. The favorable overlap of the vacant orbital with the rupturing bond can be inferred from the decreased dihedral angle (55.3°) of the dimethylboryl group upon inward rotation.

III. Systematics of Substituent Effects on Torquoselectivity. Figure 7 shows the relationship between $E_{rel} = E_{act}(\text{in}) - E_{act}(\text{out})$ and σ_R^0 ($R = 0.92$). Reasonable correlations are found.

This correlation is in keeping with the general explanation of torquoselectivity given here. The effects of substituents on C_3 are correlated with the resonance capabilities of the substituent. If other factors (bond polarity, inductive effects, etc.) were more important, this correlation would not occur. In fact, no significant correlation exists when E_{rel} is graphed versus σ_I^0.

A poorer correlation is obtained when the activation energies for inward and outward rotation are plotted against the Taft σ_R^0 parameter[19] (Figures 8 and 9). Outward rotation of either type of substituent is stabilizing (Figure 8). A donor can overlap with the LUMO, which drops in energy at the transition state, and this filled-vacant interaction stabilizes the transition state. An acceptor will overlap with the HOMO, and the filled-vacant interaction produced there will also stabilize the transition state. Indeed, in Figure 8, the plot shows that almost all the substituents stabilize outward rotation with the exception of CF_3 and SO_2Me.

(19) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

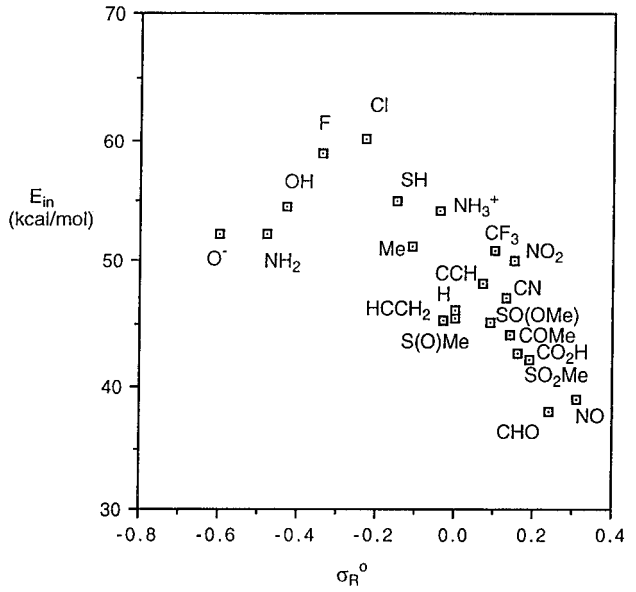


Figure 9. 6-31G*//3-21G inward conrotatory activation energies plotted against Taft σ_R^0 values.

Figure 9 shows the plot of the inward activation energy versus the σ_R^0 value of the substituent.[19] Inward rotation will be destabilizing for donor substituents, since the donor orbital is brought into close contact with the breaking σ-bonding orbital as the reaction proceeds. This results in a closed shell interaction which will be destabilizing. Therefore, the magnitude of the destabilization is related to the resonance electron-donating ability of the substituent. Conversely, a resonance electron acceptor stabilizes the transition structure by the filled-vacant interaction produced upon inward rotation of the acceptor substituent. The destabilizing effect of a donor rotating inward can be clearly seen from this plot. As the resonance-donating ability increases (σ_R^0 large and negative) the activation energy increases; however, hydroxyl and amino can rotate the electron-donating lone pair away to minimize overlap and thereby diminish destabilization. This accounts for their abnormally low destabilization.

Radical stabilization energies should also be related to the lowering of outward activation energies by substituents. This is because at the transition state the C−C bond is stretching toward a diradical geometry. A plot of Pasto's radical stabilization energies[20] versus E_{rel}, E_{act}(in), and E_{act}(out) yield in the first two cases no correlation ($r = 0.22, 0.30$) and some correlation in the third ($r = 0.80$). The outward conrotatory transition states should provide the most favorable correlation, and they do. Inward conrotation produces an effect which results from the interplay of the electronic interaction with the breaking bond and the minor steric effect of forcing the substituent inward; consequently, only outward conrotation should show direct correlation. The plot of outward activation energy against Pasto's radical stabilization energies is shown in Figure 10. It can be concluded that those factors which stabilize radicals also stabilize the cyclobutene electrocyclic transition state.

Conclusion

Substitution at the 1-position has only a small effect on the ground states and transition structures for the electrocyclic openings. Electron acceptors may accelerate the reaction rate, while electron donors retard the reaction, although both effects are small.

The preference for outward or inward rotation in the electrocyclic openings of 3-substituted cyclobutenes is caused by electronic effects related to the resonance π donor or acceptor ability of the substituent. The effective overlap of a donor or acceptor substituent orbital with the C_3-C_4 bond was also found to influence the cyclobutene geometries. Correlations were discovered between the E_{rel} for the reactions and σ_R^0 and radical stabilization energies. The torquoselectivity expected for a wide range of substituents can be predicted simply from the σ_R^0 values values of the substituents.

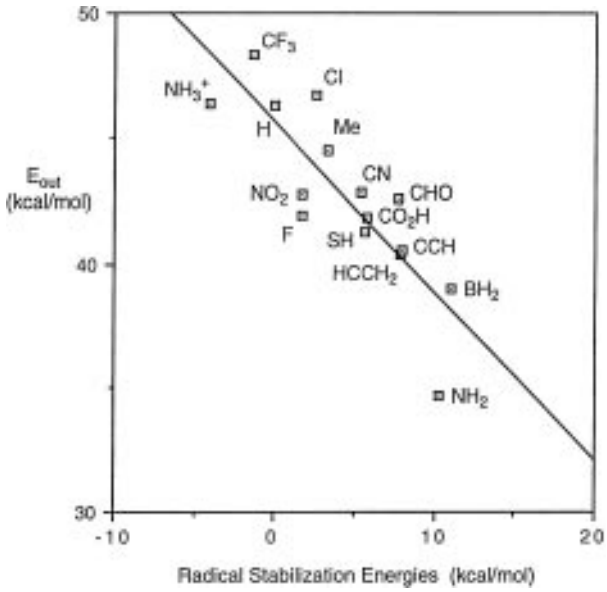


Figure 10. 6-31G*//3-21G outward activation energies plotted against radical stabilization energies.

Acknowledgment. We are grateful to the National Science Foundation for financial support of this work and to the San Diego Supercomputing Center and the UCLA Office of Academic Computing for computer time used in this research.

JO950884I

(20) Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062.