Torquoselectivity in the Electrocyclic Conversion of Benzocyclobutenes to *o*-Xylylenes

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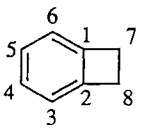
Abstract: The conrotatory electrocyclic opening of benzocyclobutene to *o*-xylylene was studied by means of ab initio molecular orbital calculations. The theory developed earlier to predict the torquoselectivity of ring opening of 3-substituted cyclobutenes was found to be applicable. Experimentally, the ring opening of several 7-substituted benzocyclobutenes, such as the cyano, methoxycarbonyl, and formyl derivatives was examined. *o*-Xylylenes were obtained in which cyano or ester groups had rotated outwards, whereas the formyl group turned inwards. *N,N*-Dimethylbenzocyclobutene-7-carboxamide exhibited 75% inward torquoselectivity upon ring opening. A reversal of mode was seen with the 7-methyl derivatives of benzocyclobutene-7-carbonitrile and methyl benzocyclobutene-7-carboxylate in that the 7-methyl substituent manifested overwhelming outward motion.

Introduction

The thermal conversion of cyclobutene to butadiene is the classic example of an electrocyclic reaction.[2] Although the preference for the conrotatory process has been amply proven experimentally in accordance with theoretical prediction, selection between the two possible conrotations has remained problematical.[3] In principle, the ring opening of 3-substituted cyclobutenes may proceed with either "outward" or "inward" rotation of the substituent. Recent ab initio calculations on the transition states of the electrocyclic reaction of 3-substituted cyclobutenes indicate that the tendency for outward rotation of substituents increases with the donor character of the substituent.[3,4] Predicted tendencies range from a pronounced preference for outward rotation for strong donors such as alkoxy or hydroxy groups to a net inward preference by good acceptors like formyl or dialkylboronyl groups. The selectivity for outward or inward twisting of the breaking C–C bond, or torquoselectivity, is due to an electronic effect arising from the interaction of molecular orbitals of the substituent and the breaking bond in the transition state. The same interaction also persists in the ground states of cyclobutenes and causes predictable distortions.[4]

In qualitative terms, the transition state for conrotation may be described by the HOMO and LUMO of the breaking C(3)–C(4) bond (Figure 1). When a donor group (D) is attached at the C-3 position, then outward rotation leads to favorable mixing with the LUMO, so stabilizing the transition state. Conversely, the doubly occupied orbital of the donor group (D) on inward rotation sets up an unfavorable interaction with the HOMO, thereby destabilizing the transition state. The result is that inward rotation will experience a higher activation energy than the outward motion. When acceptor groups (A) are attached, then the rotational preferences are reversed. The inward rather than the outward conrotatory transition state is better stabilized since the overlap of the empty acceptor orbital with the HOMO is more effective. In fact, inward rotation engenders an aromatic Hückel orbital array. Nonetheless it is worth remembering that, as many of the usual acceptors also possess doubly filled orbitals, only those having low-lying empty orbitals will be able to tip the balance in favor of inward rotation.

Table I. Optimized Bond Lengths and Angles[a] of Benzocyclobutene (1) Calculated by Different Methods



parameter	AM1	STO-3G	3-21G
C(1)C(2)	1.388	1.436	1.385
C(3)C(4)	1.368	1.390	1.396
C(4)C(5)	1.387	1.388	1.387
C(1)C(6)	1.374	1.368	1.371
C(1)C(7)	1.529	1.509	1.538
C(7)C(8)	1.571	1.577	1.599
C(1)C(7)C(8)	87	87	86
C(2)C(1)C(6)	122	122	122
C(2)C(1)C(7)	93	93	94
C(2)C(3)C(4)	116	116	116
C(3)C(4)C(5)	122	122	122
HC(7)C(1)	116	115	115

[a] Bond lengths and angles are expressed in Å and deg, respectively.

It is to be expected that the conversion of benzocyclobutene to *o*-xylylene will be governed by similar interactions.[3-5] However, the conversion can be viewed as a four- or eight-electron process.[2] Additionally, extra energy may be necessary to disrupt the resonance of the benzene ring. A MINDO-3 calculation has estimated a value of 100 kcal/mol for the activation energy.[6,7] Experimentally a much lower value is obtained. The enthalpy of activation for the thermal conversion of benzocyclobutene to *o*-xylylene is 39.9 kcal/mol.[8,9] Moreover, the process is endothermic by 13 kcal/mol. Consequently, cycloreversion is easy, making it difficult to determine the stereochemistry of the forward reaction. Despite this apparent drawback, we decided to synthesize various 7-substituted derivatives of benzocyclobutene[10] and to procure stereochemical information on the torquoselectivity of electrocyclization by trapping the first-formed *o*-xylylene products.

(1) On leave from the Jagiellonian University, Krakow, Poland.

(2) (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970. (b) Marvell, E. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980; pp 124–213.

(3) (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. (c) Spellmeyer, D. C.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 3412 and references therein.

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(6) Kametani, T.; Honda, T.; Ebisawa, Y.; Ichikawa, H. *Tetrahedron* **1985**, *41*, 3643.

(7) The charge distribution for *o*-xylylene and its 7-phenyl and 7-oxo derivatives has also been discussed (Charlton, J. L.; Alauddin, M. M.; Penner, G. H. *Can. J. Chem.* **1986**, *64*, 793).

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(10) The numbering used here for derivatives of benzocyclobutene (cf. Table I) is that adopted by W. Oppolzer: *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I.; Pergamon Press: Oxford, 1990; Vol. 5.

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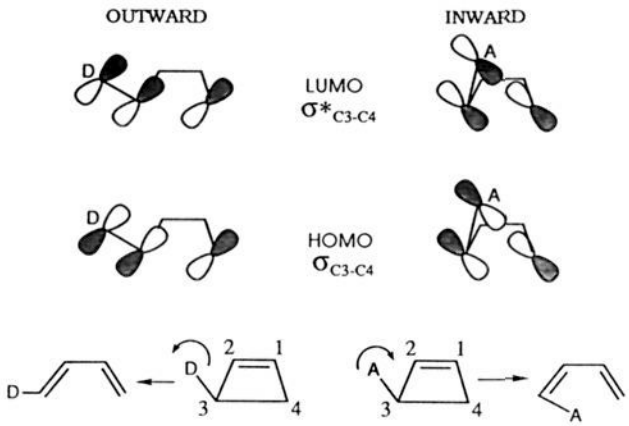
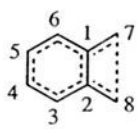


Figure 1. Frontier molecular orbitals of the two conrotatory transition structures arising from a 3-substituted cyclobutene. A donor (D) substituent by outward rotation stabilizes the LUMO, while an acceptor (A) substituent stabilizes the HOMO by inward rotation.

Table II. Optimized Bond Lengths and Angles[a] of the Transition Structure **2** Calculated by Different Methods



parameter	AM1	STO-3G	3-21G
C(1)C(2)	1.430	1.413	1.430
C(3)C(4)	1.379	1.348	1.333
C(4)C(5)	1.420	1.448	1.418
C(1)C(6)	1.409	1.438	1.453
C(1)C(7)	1.417	1.397	1.377
C(7)C(8)	2.243	2.208	2.241
C(1)C(7)C(8)	73	72	72
C(2)C(1)C(6)	120	120	119
C(2)C(1)C(7)	106	105	106
C(2)C(3)C(4)	118	117	118
C(3)C(4)C(5)	121	122	123
C(3)C(4)C(5)C(6)	4	5	5
C(3)C(2)C(1)C(6)	17	21	19
C(7)C(1)C(2)C(8)	18	25	20
C(1)C(7)C(8)C(2)	12	16	13
$H_{in}C(7)C(1)C(8)$	70	66	65
$H_{out}C(7)C(1)C(8)$	127	139	126

[a] See Table I.

We now report our experimental findings on the thermolytic behavior of the 7-cyano, dimethylaminocarbonyl, methoxycarbonyl, carboxyl, and formyl derivatives of benzocyclobutene together with the 7-cyano-7-methyl and 7-methoxycarbonyl-7-methyl derivatives. In order to complement the experimental results, calculations were performed at the restricted Hartree–Fock (RHF) level by using the semiempirical AM1 method[11] or ab initio using the STO-3G[12] and 3-21G[13] basis sets. Calculations on 7-cyanobenzocyclobutene (**4**) and its electrocyclic transition structures (**5** and **6**) were carried out at the RHF/3-21G level. All geometries were fully optimized with gradient techniques by using the GAUSSIAN 82[14] and GAUSSIAN 86[15] programs.

(11) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.
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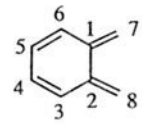
(13) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939.
(14) Binkley, J. S.; Frisch, M.; Raghavachari, K.; DeFrees, D. J.; Schlegel, H. B.; Whiteside, R.; Fluder, E.; Seeger, R.; Pople, J. A. GAUSSIAN 82: *Release E and H*; Carnegie-Mellon University: Pittsburgh, PA.
(15) Frisch, M.; 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.; Fox, D. J.; Fluder, E. M.; Pople, J. A. GAUSSIAN 86; Carnegie-Mellon Publishing: Pittsburgh, PA.

Table III. Optimized Bond Lengths and Angles[a] of *o*-Xylylene (**3**) Calculated by Different Methods



parameter	AM1	STO-3G	3-21G	4-31G[b]
C(1)C(2)	1.469	1.509	1.497	1.496
C(3)C(4)	1.349	1.322	1.327	1.328
C(4)C(5)	1.443	1.476	1.463	1.457
C(1)C(6)	1.458	1.491	1.474	1.469
C(1)C(7)	1.347	1.324	1.329	1.331
C(7)C(8)	2.938	2.981	2.983	
C(1)C(7)C(8)	57	56	56	
C(2)C(1)C(6)	117	116	116	117
C(2)C(1)C(7)	123	124	123	124
C(2)C(3)C(4)	122	123	122	123
C(3)C(4)C(5)	120	121	121	121
C(3)C(4)C(5)C(6)	2	0	4	0[b]
C(3)C(2)C(1)C(6)	7	0	15	
C(7)C(1)C(2)C(8)	9	0	20	

[a] See Table I. [b] From ref 8. The molecule was assumed to be planar.

Results and Discussion

Theoretical Studies. The optimized geometries of benzocyclobutene (**1**), the conrotatory transition structure (**2**), and *o*-xylylene (**3**) were calculated with the imposition of C_{2v} symmetry. They adequately describe the skeletal changes accompanying electrocyclization (Tables I–III). There is moderate bond length alternation present in the benzene ring of **1** with the C(1)C(6), C(3)C(4), and C(4)C(5) bond lengths equal to 1.371, 1.396, and 1.387 Å, respectively for the 3-21G calculation (Table I). With the exception of the C(4)C(5) bond, these values compare well with the C–C bond lengths determined by X-ray for 4,5-bis(trimethylsilyl)benzocyclobutene.[16] The dimensions of the cyclobutene moiety in **1**, by 3-21G calculation, are 1.599, 1.538, and 1.385 Å for the C(7)C(8), C(1)C(7), and C(1)C(2) bonds, respectively, and lie close to the values of 1.568, 1.526, and 1.384 Å found for the X-ray structure. The STO-3G and 3-21G calculated geometries of **1** are essentially the same but display some of the usual systematic differences. The AM1 optimized geometry of **1** resembles that calculated ab initio. The chief discrepancy is that the C(3)C(4) bond is shorter (1.368 Å) than that calculated by the other two methods. All the remaining features are quite similar to the 3-21G geometry. The present calculated values for **1** are similar to those found earlier.[6]

The calculated transition structure **2** is more like *o*-xylylene (**3**) than benzocyclobutene (**1**) at all levels of theory, which is a consequence of the endothermicity of the reaction, in keeping with the Hammond postulate.[17] The double bonds (C(3)C(4)) of the cyclohexadiene moiety of **2** are more fully formed at the 3-21G level (1.333 Å) than at the STO-3G (1.348 Å) or AM1 levels (1.379 Å) (Table II). Furthermore, there is much more conjugation throughout the benzene ring in the AM1 than in the 3-21G or the STO-3G calculated structures, as attested by the smaller bond length differences. It could just be a coincidence that the C(7)C(8) bond lengths are identical at the AM1 and the 3-21G levels. The angle of twist of the methylene termini (H_{in} C(7)C(1)C(8)) is 70° for the inner hydrogen atoms at the AM1 level, 66° for the STO-3G, and 65° for the 3-21G calculated structures. Thus, the inward rotating hydrogen atoms lie appreciably closer to the nearby carbon atom of the opening ring in **1** than in cyclobutene where the corresponding angle is 75° with the 3-21G basis set.

The geometry of *o*-xylylene (**3**) is also nonplanar (Table III). The expected bond alternation is seen, which is quite marked. The

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(17) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334. Farcasiu, D. J. *J. Chem. Educ.* **1975**, *52*, 76.

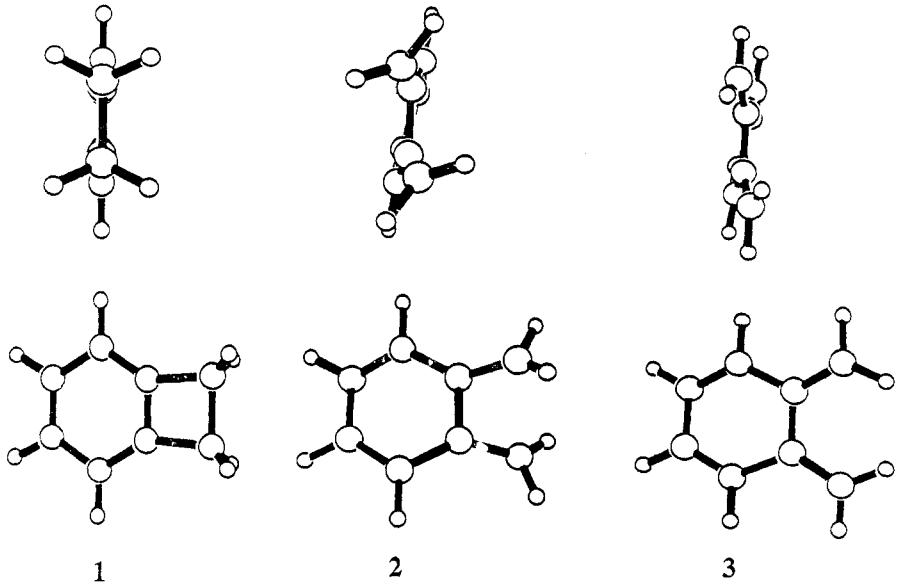


Figure 2. The 3-21G geometries of benzocyclobutene (**1**), the transition structure (**2**), and *o*-xylylene (**3**).

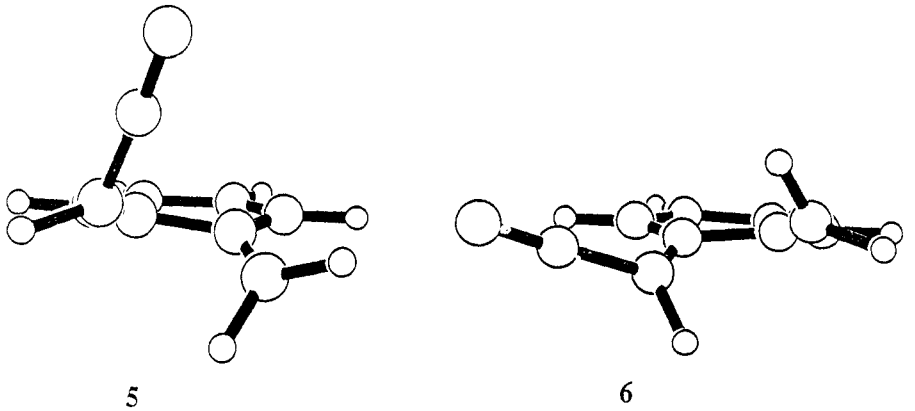
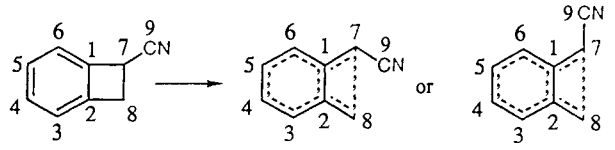


Figure 3. Inward (**5**) and outward (**6**) transition structures calculated (3-21G) for the electrocyclic opening of benzocyclobutene-7-carbonitrile (**4**).

Table IV. Some Calculated (3-21G) Geometric Parameters for Benzocyclobutene-7-carbonitrile (**4**) and the Inward (**5**) and Outward (**6**) Transition Structures[a]



4 5 6

parameter	4	5	6
C(1)C(2)	1.381	1.397	1.399
C(2)C(3)	1.371	1.411	1.411
C(3)C(4)	1.395	1.352	1.362
C(4)C(5)	1.386	1.416	1.422
C(5)C(6)	1.375	1.364	1.364
C(1)C(6)	1.396	1.408	1.408
C(2)C(8)	1.535	1.420	1.416
C(7)C(8)	1.605	2.307	2.270
C(7)C(9)	1.449	1.423	1.421
C(9)N	1.140	1.146	1.143
C(1)C(7)C(8)	86	70	71
C(2)C(1)C(6)	123	120	121
C(2)C(1)C(7)	94	107	106
C(1)C(6)C(5)	116	118	117
C(4)C(5)C(6)	116	122	122
C(3)C(4)C(5)C(6)	0	1	4
C(3)C(2)C(1)C(6)	0	16	17
C(7)C(1)C(2)C(8)	1	24	24

[a] See footnote to Table I.

C(3)C(2)C(1)C(6) dihedral angle of 15° is slightly less than that found (19°) for the 3-21G transition structure **2**. It is gratifying to note that the bond lengths and angles previously calculated by the 4-31G method assuming planarity are in good agreement with those now obtained for the nonplanar structure. However, the nonplanarity calculated for **3** is somewhat at odds with experimental reality, since the strong fluorescence characteristic of **3** must mean that the molecule is nearly planar in both the ground S_0 and excited S_1 states.[18] Whether or not the modest nonplanarity (Figure 2) is consistent with experiment would require extensive excited-state calculations.

In summary, the progress of the 3-21G calculated reaction is marked by a conrotatory twisting and elongation of the cyclobutyl C–C bond resulting in a sharp departure from planarity (**1** → **2**), which is only partially restored when the *o*-xylylene product is attained (**2** → **3**) (Figure 2).

The energies of activation (**1** → **2**) calculated at the STO-3G and 3-21G levels are 97.4 and 54.7 kcal/mol, respectively, and deviate widely from the experimental value (39.9 kcal/mol) (Table V). The heats of reaction (**1** → **3**), calculated by the two methods, are 43.0 and 14.5 kcal/mol, with the latter lying closer to the experimental value (13 kcal/mol).[19] Overall, the disparities observed resemble those found for the opening of cyclobutene.[3c] AM1 gives an excellent activation energy but a poor heat of reaction.

Next, the effect of a substituent placed at C7 on the electrocyclization of benzocyclobutene was evaluated. The geometries for 7-cyanobenzocyclobutene (**4**) and the inward (**5**) and outward (**6**) transition structures as calculated by the 3-21G method (Table

Table V. Relative Energies Calculated (in kcal/mol) for the Electrocyclic Opening of Benzocyclobutene (**1**) and Its 7-Cyano Derivative (**4**)

molecule	AM1	STO-3G	3-21G
benzocyclobutene (**1**)	0.0	0.0	0.0
o-xylylene transition state (**2**)	33.7	97.4	54.7
o-xylylene (**3**)	−5.1	43.0	14.5
benzocyclobutene-7-carbonitrile (**4**)			0.0
inward transition structure (**5**)			54.9
outward transition structure (**6**)			50.4

Table VI. Summary of Crystal Data, Intensity Measurements, and Structure Refinement for Compounds **12**, **28**, and **52**

	12	**28**	**52**
formula	$C_{13}H_9NO_3$	$C_{15}H_{15}NO_4$	$C_{14}H_{11}NO_3$
mol wt	227.2	273.3	241.2
crystal system	orthorhombic	triclinic	orthorhombic
space group	$Pca2_1$	$P\bar{1}$	$Pna2_1$
crystal size [mm]	0.22 × 0.22 × 0.27	0.10 × 0.15 × 0.30	0.20 × 0.25 × 0.25
a [Å]	14.9067 (13)	7.7299 (9)	12.475 (3)
b [Å]	6.8114 (9)	9.136 (4)	7.848 (1)
c [Å]	20.719 (7)	10.202 (2)	23.666 (5)
α [deg]	90	78.91 (3)	90
β [deg]	90	78.65 (1)	90
γ [deg]	90	73.01 (1)	90
V [Å^3]	2103.7 (6)	668.5 (3)	2317.0 (8)
Z	8	2	8
F_{000}	944	288	1008
D_c [g·cm^{-3}]	1.44	1.36	1.38
μ [mm^{-1}]	0.097	0.093	0.092
$\sin(\theta/\lambda)_{max}$ [Å^{-1}]	0.58	0.58	0.58
no. measd reflcns	1938	2021	2134
no. obsd reflcns	1343	1487	1172
criterion for obsd	$\|F_o\| > 4\sigma(F_o)$	$\|F_o\| > 4\sigma(F_o)$	$\|F_o\| > 4\sigma(F_o)$
refinement (on F)	full-matrix	full-matrix	full-matrix
no. of params	307	181	325
weighting scheme	$\omega = 1/\sigma^2(F_o)$	$\omega = 1$	$\omega = 1$
max. and av Δ/σ	0.346, 0.093	0.0136, 0.009	0.540, 0.110
max. and min. $\Delta\rho$ [e.Å^{-3}]	0.27, −0.27	0.36, −0.50	0.48, −0.42
R, ωR (%)	5.1, 3.6	6.0, 6.0	5.9, 5.9

IV) are similar to those of the parent structures (Tables I–III). Apart from the disposition of the cyano group, there is little geometric difference between the inward (**5**) and outward (**6**) transition structures (Figure 3 and Table IV). However, the calculated energies of activation (Table V) for inward and outward rotation are significantly higher, namely 54.9 and 50.4 kcal/mol, than those calculated for 3-cyanocyclobutene (43.9 and 39.3 kcal/mol), although the difference between the two rotational modes is comparable for both molecules.[5] The influence of the 7-cyano substituent on the outward opening of **1** lowers the activation barrier by an amount (4.3 kcal/mol) greater than that noted for 3-cyanocyclobutene (2.3 kcal/mol).[19]

In light of these and previous calculations,[3c] it is reasonable to conclude that substituent effects on the opening of benzocyclobutenes should operate in the same sense as they do for cyclobutene.[5,20,21] Accordingly, electron donors such as alkoxy, amino, and alkyl groups will all strongly favor outward rotation. On the other hand, the formyl, the ketone, and iminium groups

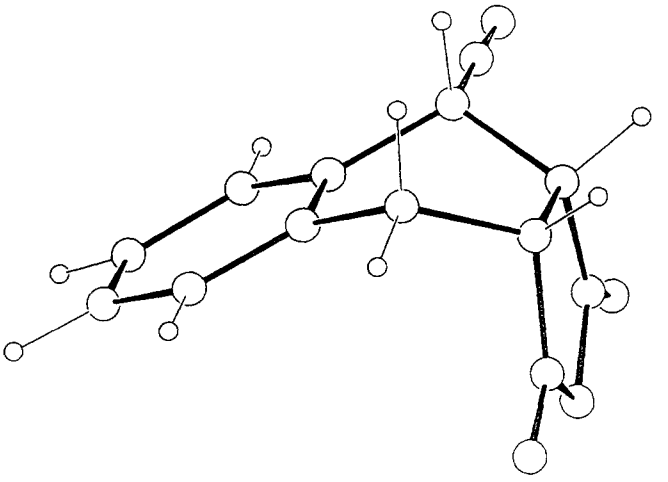
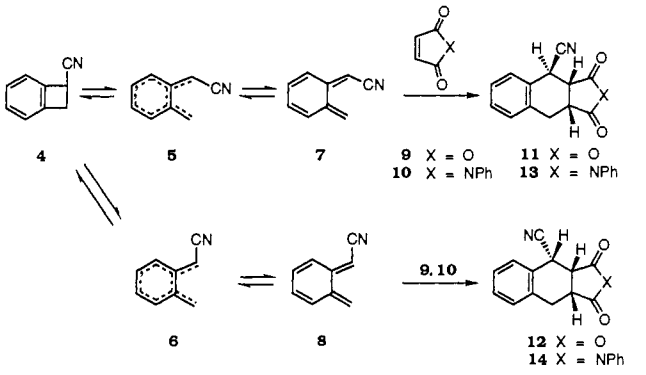


Figure 4. Perspective drawing of the X-ray structure of the adduct **12**.

Scheme I



as well as their Lewis acid complexed counterparts, since they are unequivocal electron acceptors, will all turn inwards. In contrast, the ester should be ambivalent and behave like the cyano group owing to the presence of nonbonding electrons and will usually, but not always, rotate outwards. Despite these expected trends, the electrocyclization of benzocyclobutenes may require higher temperatures than those needed for cyclobutene since an extra 8 kcal/mol of activation energy are anticipated.

Experimental Studies. Because of easy cycloreversion, the thermolysis of benzocyclobutene was carried out in the presence of efficient external trapping agents. When 7-cyanobenzocyclobutene (**4**) was heated with excess maleic anhydride (**9**) at 140 °C in benzene-d_6 for 3 days, a mixture of two adducts was obtained in a 1:19 ratio. The ratio remained constant during the reaction, and no other product was discerned on following the reaction by NMR spectroscopy. The use of *N*-phenylmaleimide (**10**) as dienophile under the same conditions also led to two new adducts in precisely the same ratio of 1:19 as before. The major adduct with **9** afforded a single crystal permitting its structure to be determined by X-ray as **12** (Figure 4). By comparison of the chemical shifts and coupling constants of **12**, the minor adduct derived from **9** was assigned as **11**, while the minor and major adducts from the reaction of **4** and **10** were identified as **13** and **14**, respectively (Scheme I).

Although the two dienophiles (**9** and **10**) in their previously reported Diels–Alder additions gave only endo adducts,[22] it cannot be assumed that they will behave in the same way with the *o*-xylylenes arising from 7-cyanobenzocyclobutene (**4**). Moreover the (*Z*)- and (*E*)-xylylenes (**7** and **8**) will be able to equilibrate by reversible electrocyclization through the corresponding transition states **5** and **6** to starting material **4**. However, in the presence of excess dienophile their capture, like that of the parent *o*-xylylene, will be fast and irreversible.[8,23] In principle, capture

(18) Miller, R. D.; Kolc, J.; Michl, J. *J. Am. Chem. Soc.* **1976**, *98*, 8510. Flynn, C. R.; Michl, J. *J. Am. Chem. Soc.* **1974**, *96*, 3280. Barton, J. W. *Ann. Rep. Prog.* **1970**, *70*, 405. Tewson, T. J. *Ann. Rep. Prog.* **1974**, *71*, 299. Dolbier, W. R., Jr.; McCullagh, D. R.; Robinson, D.; Anapolle, K. E. *J. Am. Chem. Soc.* **1975**, *97*, 934. Migirdicyan, E.; Baudet, J. *J. Am. Chem. Soc.* **1975**, *97*, 7400.

(19) The energy of activation for cyclobutene opening is calculated (3-21G) to be 7.1 kcal/mol higher than that found experimentally. This discrepancy is reduced by 8.6 kcal/mol when electron correlation is included. A similar correction should be applicable to the benzo derivatives (cf.: Spellmeyer, D. C.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 3412).

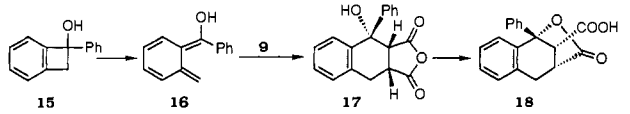
(20) Houk, K. N.; Spellmeyer, D. C.; Jefford, C. W.; Rimbault, C. G.; Wang, Y.; Miller, R. D. *J. Org. Chem.* **1988**, *53*, 2125.

(21) Jefford, C. W.; Wang, Y.; Houk, K. N., manuscript in preparation.

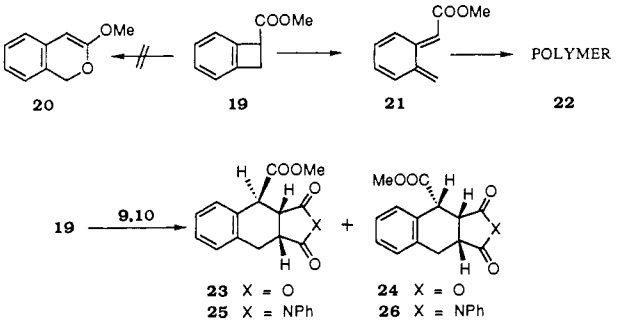
(22) Martin, J. G.; Hill, R. K. *Chem. Rev.* **1961**, *61*, 537.

(23) Huisgen, R.; Seidl, H. *Tetrahedron Lett.* **1964**, 3381.

Scheme II



Scheme III



could occur with endo or exo orientation. Consequently, four different conclusions could be drawn from the ratio of Diels–Alder adducts. First, addition could have taken place exclusively endo, in which case the major electrocyclic event is the formation of (*E*)-*o*-xylylene **8**. Second, the sole intermediate formed could have been **8** which is mainly trapped by endo addition with some exo addition occurring as well. Third, addition could have occurred entirely in the exo sense, in which case the major electrocyclic intermediate is the (*Z*)-*o*-xylylene **7**. Fourth, **7** could have been the only intermediate formed which reacts with dienophile in the exo and endo orientations to major and minor extents, respectively.

Sufficient evidence exists to show that the first conclusion is the correct one. The simplest instance, where exo–endo preferences might be expected to be less marked,[24] is provided by the single diene obtained by thermolysis of (*Z*)-2-*tert*-butyl-3-(trimethylsiloxy)cyclobutene.[21] By NOE measurements, its *Z* configuration was determined as well as the endo configuration of its adduct with maleic anhydride.

3*H*-2-Benzopyran-3-ones provide a good model for *o*-xylylene as they contain this element configurationally fixed within the ring. They undergo endo addition with *N*-phenylmaleimide.[25]

Most convincing is the behavior of 7-phenylbenzocyclobutan-7-ol (**15**), which on heating with maleic anhydride gave the acid lactone **18** as the sole product of addition (Scheme II).[26] As the intermediate *o*-xylylene is known to have the *E* configuration (**16**), addition must have occurred endo to give the anhydride **17**, which subsequently isomerized to **18**.

In interpreting the present series of Diels–Alder experiments, it will be assumed that the dienophiles behave consistently. Therefore, the ratio of the two adducts (e.g., **11**:**12** and **13**:**14**), even if the transition states for capture of the (*Z*)- and (*E*)-xylylenes (**7** and **8**) are not energetically equivalent, can be taken as an index of inward versus outward torquoselectivity. Consequently, the cyano group displays an outward torquoselectivity of 95%. This ratio expressed as $\Delta\Delta G^{\ddagger}$, corresponds to 2.4 kcal/mol, which is a little less than predicted by calculation. Previously, the reaction of **4** and **10** was reported to give only **14**; its formation being ascribed to the steric preference for outward rotation to give **8**. Presumably, the minor adduct **13** was formed but not isolated.[27]

Methyl benzocyclobutene-7-carboxylate (**19**) was next considered. In principle, it could avail itself of inward rotation to rearrange to 3-methoxyisochromene (**20**) as other acyl derivatives do (Scheme III).[28] Unaccountably, **19** was reported to give

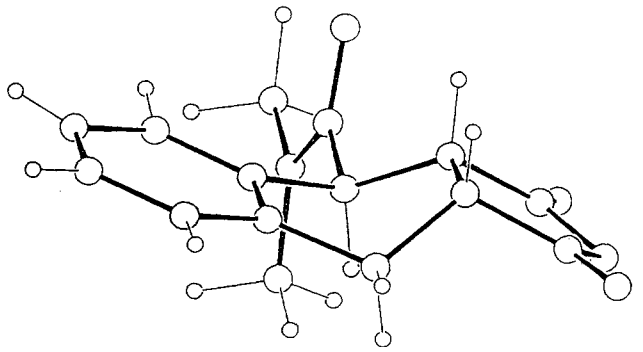
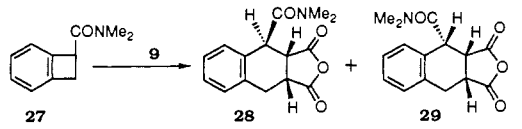
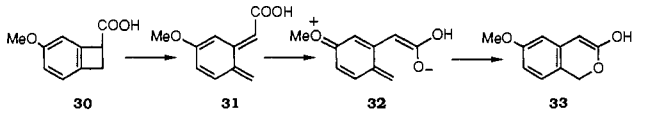


Figure 5. Perspective drawing of the X-ray structure of the adduct **28**.

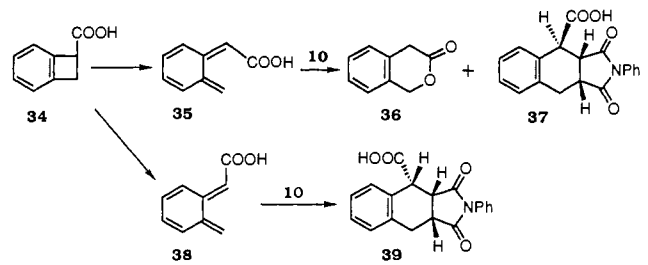
Scheme IV



Scheme V



Scheme VI



polymeric material (**22**), presumably by further reaction of the resulting (*E*)-xylylene (**21**). Reexamination of the thermolytic behavior of **19** was obviously necessary. When it was heated at 140 °C for 10 days with an excess of maleic anhydride, reaction was essentially complete affording a mixture of two adducts in a 1:10 ratio (Scheme III). The same course was followed when *N*-phenylmaleimide was used as a trap. The configurations of the minor (**23** and **25**) and major adducts (**24** and **26**) were readily distinguishable by comparing their NMR spectra with those of the adducts obtained from **4**. Thus the outward torquoselectivity of the ester group is marked (80%) but is less than that of the nitrile group.

Although the intramolecular Diels–Alder reaction of benzocyclobutene-7-carboxamides has been usefully exploited for synthetic ends,[29] the intermolecular variant has not been studied so far. With maleic anhydride, the 7-dimethylaminocarbonyl derivative **27** on heating at 140 °C for 7 days gave two adducts (**28** and **29**), this time in a 7:3 ratio (Scheme IV). The structure of the major adduct **28** was elucidated by X-analysis (Figure 5) and reveals its provenance as the inner substituted (or *Z*) amidoxylylene.

The role of the carboxylic acid function as substituent at C7 also needs to be defined. The thermal conversion of 5-methoxybenzocyclobutene-7-carboxylic acid (**30**) into the isochromanone (**33**) was ingeniously explained[30] by supposing that

(24) Stephenson, L. M.; Smith, D. E.; Current, S. P. *J. Org. Chem.* **1982**, *47*, 4171.

(25) Van Broeck, P. I.; Vanderzande, D. J.; Kiekens, E. G.; Hoornaert, G. J. *J. Chem. Soc., Perkin Trans. I* **1991**, 639.

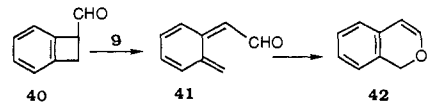
(26) (a) Arnold, B. J.; Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. I* **1974**, 415. (b) Arnold, B. J.; Mellows, S. M.; Sammes, P. G. *J. Chem. Soc., Perkin Trans. I* **1974**, 401.

(27) Jones, D. W.; Kneen, G. *J. Chem. Soc., Perkins Trans. I* **1976**, 1647.

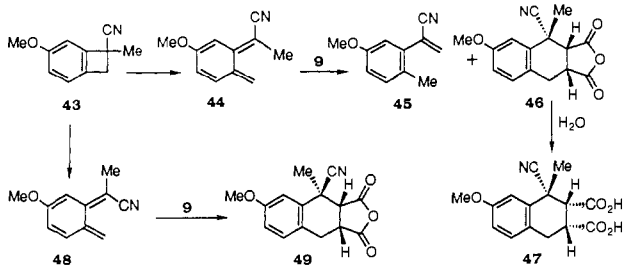
(28) Hug, R.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 10. Bowne, A. T.; Levin, R. H. *Tetrahedron Lett.* **1974**, 2043. Shikido, K.; Ito, M.; Shimada, S.; Fukumoto, K.; Kametani, T. *Chem. Lett.* **1984**, 1943.

(29) For reviews see: (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Oppolzer, W. *Synthesis* **1978**, 793. (c) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187 and references therein.

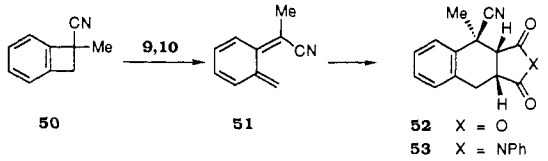
Scheme VII



Scheme VIII



Scheme IX



the (*E*)-xylylene (**31**) formed initially and subsequently cyclized to **33** through the configurationally mobile dipolar resonance form **32** (Scheme V). However, the same cyclization proceeded even when the methoxy group was absent.[26a] The experiment was repeated, and it was found that the parent acid **34** gave the benzopyranone **36** as the only product, clearly arising from the (*Z*)-xylylene intermediate **35** (Scheme VI). Nevertheless, according to its electronic properties, carboxyl as a substituent should behave like the ester group and rotate mainly outwards. External trapping confirmed this expectation. Heating **34** with *N*-phenylmaleimide in deuterated benzene gave **36** and the cis-fused, trans adduct **37** which arose from the (*Z*)-xylylene **35** in 19 and 13% yields, respectively, and the cis-fused, cis adduct **39** in 68% yield stemming from the (*E*)-xylylene **38**. Clearly, intermolecular capture (**34** → **37**) competes well with electrocyclization (**35** → **36**). Heating **37** or **39** separately under the reaction conditions caused no equilibration; accordingly the figure of 68% represents the extent of outward torquoselectivity.

On the basis of precedent,[5,31] benzocyclobutene-7-carboxaldehyde (**40**) should display overwhelming inward torquoselectivity. Heating **40** with excess maleic anhydride proved to be of no avail in trapping the supposed (*Z*)-xylylene **41** (Scheme VII). Only a trace of adduct (~2%) was detected; the main event being the formation of benzopyran (**42**) undoubtedly arising from **41**. The brief duration of the reaction (2.5 h) at 130 °C indicates that ring opening of **40** is much easier than that seen for other 7-substituted derivatives.

Lastly, we report on the competition between two C7 substituents and how they influence the conrotatory modes. A classic example is provided by 5-methoxy-7-methylbenzocyclobutene-7-carbonitrile (**43**), which on heating with maleic anhydride at 240 °C for 5 h gave 2-(2′-methyl-5′-methoxyphenyl)acrylonitrile (**45**, 12% yield), tetralin-2,3-dicarboxylic acid (**47**, 24%), and the anhydride **49** (41%) (Scheme VIII).[32] The origin of these products was attributed to the intermediacy of the (*E*)- and (*Z*)-xylylenes. Most of the *E*-isomer **44** reacted as such by cycloaddition to give **46**, which on adventitious hydrolysis gave the diacid **47**. Some escaped capture by undergoing 1,5 sigmatropic rearrangement to **45**. The (*Z*)-xylylene **48**, only having one option,

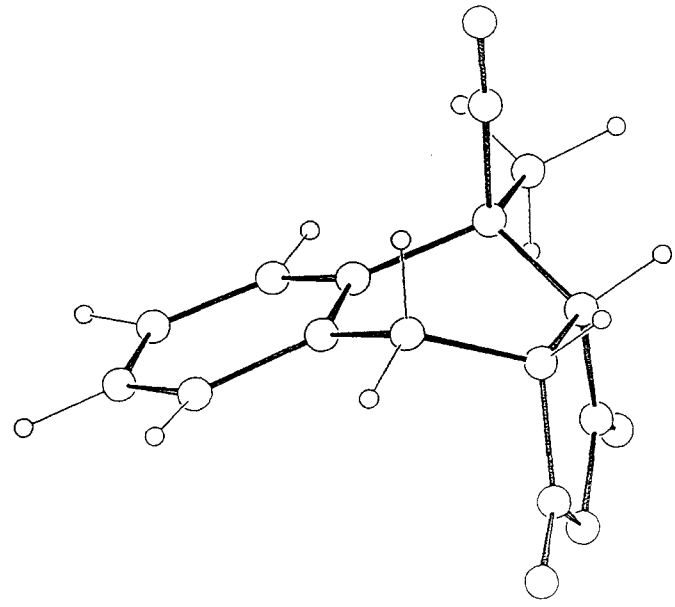
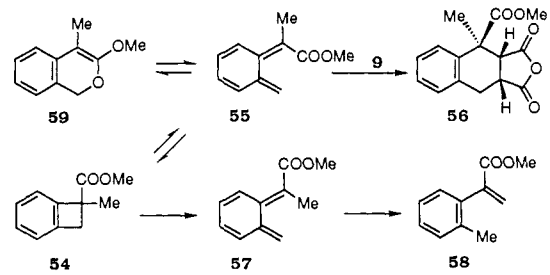
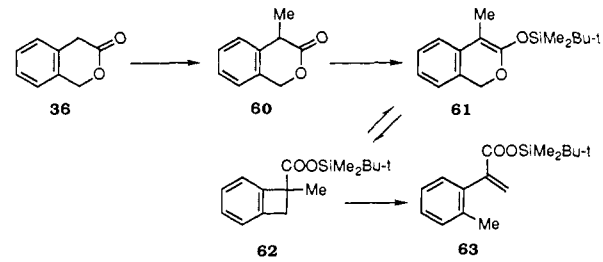


Figure 6. Perspective drawing of the X-ray structure of the adduct **52**.

Scheme X



Scheme XI

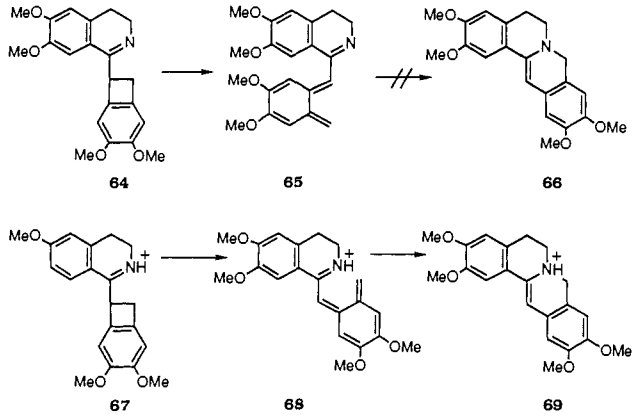


simply gave the adduct **49**. The proportions of these products were ascribed to the roughly equal amounts of **44** and **48** which were thought to be due to the contending bulkiness of the C7 substituents. We now know that steric effects alone are unlikely to be responsible for controlling product composition in these reactions.[33] Our studies[3,21] with 3-methylcyclobutene point to an electronic effect and portend an overriding outward motion for the 7-methyl substituent in **43**. Examination of 7-methylbenzocyclobutene-7-carbonitrile (**50**) shows that this is so (Scheme IX). Heating **50** with maleic anhydride for 5 days or with *N*-phenylmaleimide for 7 days at 140 °C afforded in each case a single adduct, **52** and **53**, respectively. The structure of **52** was unambiguously determined by X-ray (Figure 6) and correlated with that of **53** by their NMR spectra, thereby establishing that the ring-opened intermediate had the *Z* geometry **51**.

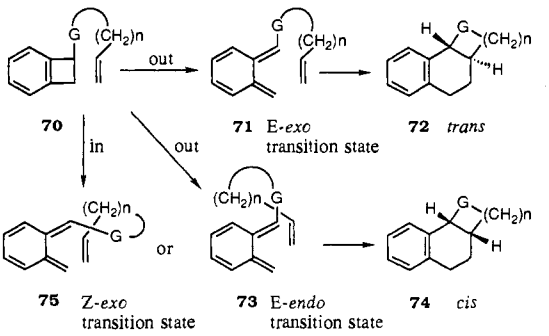
The same reaction propensity should characterize the ester analogue **54**. In similar fashion, **54** completely reacted with maleic anhydride and gave only one adduct (**56**) after 10 days at 130 °C (Scheme X). Under the same conditions, but without dienophile, thermolysis afforded the acrylate **58**, although conversion

(30) Kametani, T.; Enomoto, Y.; Takahahshi, K.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. I* **1979**, 2836.
(31) Ingham, S.; Turner, R. W.; Wallace, T. W. *J. Chem. Soc., Chem. Commun.* **1985**, 1664.
(32) Kametani, T.; Tsubuki, M.; Shiratori, Y.; Kato, Y.; Nemoto, H.; Ihara, M.; Fukumoto, K. *J. Org. Chem.* **1977**, *42*, 2672.
(33) Curry, M. J.; Stevens, I. D. R. *J. Chem. Soc., Perkin Trans. II* **1980**, 1391.

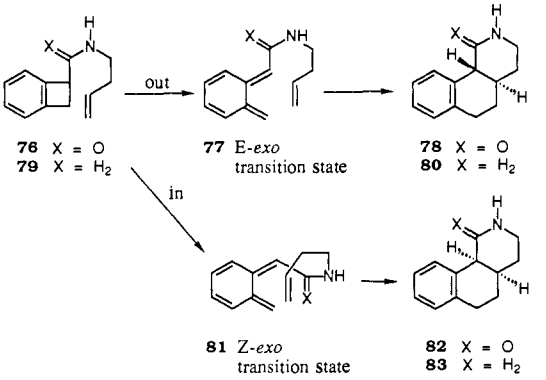
Scheme XII



Scheme XIII



Scheme XIV



was only some 10%. Repeating this experiment at higher temperature (190 °C) brought about complete conversion to **58** in just 2 days. These results indicate that it is energetically more expensive to rotate the methyl and ester groups inwards and outwards, respectively, than the converse. In other words, the (*Z*)-xylylene **55** is easier to generate than the *E*-isomer **57**. Moreover, as soon as the latter is formed, it promptly undergoes 1,5-hydride shift isomerizing irreversibly to the acrylate **58**. The more accessible (*Z*)-xylylene **55** also has the option of rapidly isomerizing by electrocyclization to the benzopyran **59**. Curiously enough, this event remains invisible, which suggests that it must be a reversible process. Proof for this interpretation was secured by preparing the ketene acetal **61** from the methyl lactone **60** obtained in turn from benzopyranone **36** (Scheme XI). When **61** was pyrolyzed in benzene at 170 °C overnight, the NMR spectrum showed that the resulting mixture contained **61**, the benzocyclobutene **62**, and the acrylate **63**. On continued heating at 170 °C for 5 days, **61** was entirely transformed to **63**.

The foregoing model experiments prove that the methyl group shows a strong preference for outward movement which overrides that of the nitrile and ester groups and obliges them to turn inwards. Indeed, these findings clarify the body of results previously acquired from 7-alkyl-7-carbonyl derivatives of benzocyclobutene.[34,35]

The present findings have relevance to certain intramolecular reactions of benzocyclobutene derivatives that have been used for synthesizing alkaloids.[36] The benzocyclobutenylisoquinoline **64** did not rearrange on heating to the protoberberine **66** but gave another unidentified product (Scheme XII).[37] The simple expedient of protonating **64** to give **67** delivered the desired product **69**. This difference in reactivity can be nicely explained in terms of torquoselective principles. The conjugated imine function in **64** is a weak acceptor like the cyano and ester groups and will prefer to twist outward breaking the cyclobutene moiety to form the (*E*)-xylylene **65** which cannot close to the six-membered ring. However, **64** on protonation produces the positively charged iminium entity (**67**), which is a powerful π acceptor. Consequently, it turns inwards with facility just like the formyl group, so creating the (*Z*)-xylylene **68** and ultimately **69** by cyclization.

Other intramolecular cyclizations may entail similar inwardly turned rotations. Conventionally, a benzocyclobutene precursor exemplified by **70** was always assumed for steric reasons to give the (*E*)-xylylene regardless of the nature of the linkage (G) to the olefinic side chain (Scheme XIII). Subsequently, the conformational preferences of the group G were supposed to favor either an exo (**71**) or endo orientation (**73**) of the pendant olefin, thereby accounting for the formation of the trans- (**72**) and cis-fused (**74**) products.[29] Another possibility is that the cis-fused ring could arise from the capture of an exo-oriented olefin side chain in an intermediate (*Z*)-xylylene (**75**). For example, the finding[38] that the olefinic carboxamide **76** on heating gave the trans- and cis-fused products **78** and **82** in a 1:5.2 ratio reflects the intermolecular inward torquoselectivity of 70% observed for **27**. Evidently, the trans- and cis-fused rings could originate from the *E*-exo and *Z*-exo arrangements **77** and **81**, respectively. This rationale finds credence since, when the carboxamide function is absent[38b] as exemplified by **79**, the ratio of trans-to-cis products (**80** and **83**) is reversed, becoming 2.7:1. As a methyl or methylene substituent at C7 in benzocyclobutene exhibits pronounced outward torquoselectivity, the predominance of the trans product **80** becomes understandable. Clearly, other factors are undoubtedly implicated in the transition state, but arguments based on exclusive outward rotation, particularly of carboxamide groups, are probably too simplistic.

Conclusion

The present study shows that benzocyclobutenes behave in much the same way as cyclobutenes in manifesting the same torquoselectivity pattern. It is also seen that the temperature chosen for thermolysis is crucial. Although reactions proceed more slowly at 120–140 °C, greater discrimination between the conrotatory modes is exercised. The concept of steric control in deciding the course of intramolecular cyclization of 7-benzocyclobutene derivatives appears not to be relevant. Rather, the proportion of (*E*)- and (*Z*)-xylylenes is dictated by electronic factors and determines the stereochemical outcome. It is to be expected that complexation of the 7-substituent with Lewis acids or bases will enable subsequent cycloadditions, both inter- and intramolecular, to be stereochemically modulated. Such experiments are under way, and the results will be reported elsewhere.

(34) Shishido, K.; Shitara, E.; Fukumoto, K.; Kametani, T. *J. Am. Chem. Soc.* **1985**, *107*, 5810. Shishido, K.; Hiroya, K.; Fukumoto, K.; Kametani, T. *Tetrahedron Lett.* **1986**, *27*, 971. Shishido, K.; Shitara, E.; Komatsu, H.; Hiroya, K.; Fukumoto, K.; Kametani, T. *J. Org. Chem.* **1986**, *51*, 3007. Shishido, K.; Yamashita, A.; Hiroya, K.; Fukumoto, K.; Kametani, T. *Chem. Lett.* **1987**, 2113.

(35) An extensive amount of work has been reported on 7-hydroxy and related derivatives of benzocyclobutene. The hydroxy group is strongly outward torquoselective (Arnold, B. J.; Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. II* **1974**, 409. See also ref 26).

(36) Review: Kametani, T.; Fukumoto, K. *Heterocycles* **1975**, *3*, 29.

(37) Kametani, T.; Ogasawara, K.; Takahashi, T. *J. Chem. Soc., Chem. Commun.* **1972**, 675.

(38) (a) Oppolzer, W. *J. Am. Chem. Soc.* **1971**, *93*, 3834. (b) Oppolzer, W. *Tetrahedron Lett.* **1974**, 1001.

Experimental Section

General Methods. IR spectra were taken on a Perkin-Elmer 681 spectrometer or a Perkin-Elmer 1310 infrared spectrophotometer. ^1H NMR spectra were recorded on Bruker AM or WM 360 instruments. The residual proton peak of the deuterated solvent was taken as standard. Mass spectra were obtained on a Finnigan-GC/MS-4023 instrument. Melting points were measured on a Fisher-Johns melting point apparatus and were uncorrected. Elemental analyses were carried out by Dr. H. J. Eder, Service de Microchimie, Institut de Chimie Pharmaceutique, University of Geneva. All thermolyses were conducted in NMR tubes. Deuterated benzene was dried over sodium. Maleic anhydride was freshly sublimed before use. The tubes containing samples were sealed after degassing, wrapped in aluminum foil, and immersed in a deep, well-stirred oil bath kept at constant temperature. The temperature deviation was about ~2 °C. Thermolyses were periodically interrupted as necessary by quenching in chilled water and then examined by NMR spectroscopy.

Preparation of Starting and Reference Materials. *N,N*-Dimethylbenzocyclobutene-7-carboxamide (27). Benzocyclobutenecarbonyl chloride was prepared from the corresponding acid (300 mg, 2 mmol) by mixing with thionyl chloride (8 mL) and letting stand at room temperature for 2 h and then heating the mixture at 80 °C for 45 min.[39] After evaporation at low pressure the residue was diluted with anhydrous benzene. Aqueous dimethylamine (40%, 100 mL) was extracted with benzene (3 × 40 mL). The extracts were combined and dried (Na_2SO_4). The dimethylamine solution, after filtration, was cooled to 10 °C, and the acid chloride solution was added from a funnel in several portions. The reaction mixture was stirred at room temperature overnight and evaporated. The residue was dissolved in ethyl acetate and washed with water and brine. The crude product obtained after drying and evaporation of the solvent was purified by preparative TLC using ether as eluent to give a colorless oil (298 mg, 84%); IR ($CHCl_3$) 300, 2930, 1635, 1495, 1455, 1400, 1140, 1000 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.26–7.13 (m, 3 H), 7.08 (m, 1 H), 4.47 (d, d, J = 3. 5.5 Hz, 1 H), 3.57 (d, d J = 3, 13.5 Hz, 1 H), 3.41 (d, d, J = 5.5, 13.5 Hz, 1 H), 3.16 (s, 3 H), 2.96 (s, 3 H); MS, m/z 175 ($M^{\cdot+}$), 160, 131, 118, 103, 72. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.47; H, 7.43; N, 7.94.

Methyl 7-Methylbenzocyclobutene-7-carboxylate (54). To a solution of LDA (7.8 mmol, 1 M in cyclohexane) in THF (12 mL) cooled at −78 °C under N_2 was added benzocyclobutene-7-carboxylic acid (480 mg, 3.24 mmol) in THF (5 mL). The solution was kept at −78 °C for 2 h, and MeI (1.4 g, 11 mmol) was added. The mixture was stirred at room temperature for 24 h and then poured into saturated aqueous NH_4Cl. Acidification with 5% HCl to pH 5, extraction with ether, drying of the extract (Na_2SO_4), filtration, and evaporation of the solvent afforded crude 7-methylbenzocyclobutene-7-carboxylic acid. The acid was purified by dissolving in 15% NaOH and extracting with ether. The aqueous solution was then reextracted with ether after acidification. The acid was obtained as a pale yellow oil (346 mg, 83%). Methylation with excess diazomethane in ether at 0 °C, followed by evaporation, gave **54** in 100% yield, having the same spectrum as that reported.[40]

3,4-Dihydro-4-methyl-(3*H*)-2-benzopyran-3-one (60). To LDA (1.49 mmol, 1 M in cyclohexane) in THF cooled at −78 °C was added (3*H*)-2-benzopyran-3-one (**36**) (200 mg, 1.35 mmol) in THF (2 mL). The resulting mixture was stirred for 1 h, and MeI (213 mg, 1.5 mmol) was added. The mixture was allowed to reach room temperature and then stirred for 2 more h. The crude product after workup was purified by preparative TLC using hexane and ethyl acetate as eluent (8:2). On cooling **60** was obtained as a solid, mp 47–48 °C (141 mg, 62%), accompanied by some dimethyl derivative (**60a**) (38 mg, 16%) and starting material. **60**: IR (thin film) 2980, 1740, 1485, 1460, 1380, 1240, 1150, 1120, 1024 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.40–7.21 (m, 4 H), 5.32 (d, J = 14 Hz, 1 H), 5.25 (d, J = 14 Hz, 1 H), 3.62 (q, J = 7 Hz, 1 H), 1.62 (d, J = 7 Hz, 3 H); MS, m/z 162 ($M^{\cdot+}$), 118 (100%), 117; HRMS calcd for $C_{10}H_{10}O_2$ 162.0681, found 162.0699. **60a**: IR (thin film) 2980, 1760, 1490, 1465, 1390, 1240, 1150, 1105, 1050, 1030 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 7.05–6.92 (m, 3 H), 6.63 (m, 1 H), 4.83 (s, 2 H), 1.29 (s, 3 H); MS, m/z 176 ($M^{\cdot+}$), 133, 132 (100%), 131; HRMS calcd for $C_{11}H_{12}O_2$ 176.0837, found 176.0823.

3-((Dimethyl-*tert*-butyl)siloxy)-4-methyl-(1*H*)-2-benzopyran (61). A solution of **60** (40 mg, 0.25 mmol) in THF (1.5 mL) was added to LDA (0.38 mmol, 1 M in cyclohexane) in THF (5 mL) cooled at −78 °C. After 30 min, chlorodimethyl-*tert*-butylsilane (50 mg, 0.33 mmol) was added, followed by HMPA (0.2 mL). The mixture was allowed to warm to room temperature and stirred for 3 more h and poured into ice–water (30 mL). Ether (25 mL) and cold diluted HCl (0.5 N, 5 mL) were added. The organic phase was separated and washed thoroughly first with ice–water and then with brine and dried (Na_2SO_4). After evaporation of ether, the crude product was dissolved in *n*-pentane and cooled to −78 °C. The clear solution was separated from the precipitate, concentrated to a small volume, and cooled to −78 °C again. The pentane solution, after it turned clear, was evaporated to give a colorless oil (35 mg, 52%): ^1H NMR (360 MHz, C_6D_6) δ 6.97–6.89 (m, 3 H), 6.66 (d, J = 7 Hz, 1 H), 4.70 (s, 2 H), 1.98 (s, 3 H), 0.99 (s, 9 H), 0.20 (s, 6 H).

Thermolyses. Benzocyclobutene-7-carbonitrile (4)[41] in the Presence of Maleic Anhydride (9). A solution of **4** (25 mg, 0.19 mmol) and **9** (39 mg, 0.4 mmol) in C_6D_6 (0.5 mL) was heated for 3 days at 140 °C. Only two adducts (**11** and **12**) were detected. The conversion was virtually quantitative. The isomer ratio was 1:19 and remained constant throughout the reaction. Solvent was evaporated, and the residue was recrystallized from ethyl acetate and hexane. The major isomer (**12**) was obtained as a crystalline solid, mp 158–160 °C. A sample for X-ray was obtained by recrystallization from an acetone/hexane mixture. The minor adduct (**11**) remained in the mother liquor: ^1H NMR (360 MHz, $CDCl_3$) **11** δ 7.46–7.20 (m, 4 H), 4.42 (d, J = 2.5 Hz, 1 H), 3.95 (d, d J = 2.5, 10 Hz, 1 H), 3.80 (d, d, d, J = 2.5, 7, 10 Hz, 1 H), 3.42 (d, d, J = 7, 15.5 Hz, 1 H), 3.29 (d, d, J = 15.5 Hz, 1 H). ^1H NMR (360 MHz, $CDCl_3$) **12** δ 7.60 (m, 4 H), 7.41 (m, 2 H), 7.29 (m, 1 H), 4.15 (d, J = 5 Hz, 1 H), 3.89 (d, d, J = 5, 10 Hz, 1 H).

Benzocyclobutene-7-carbonitrile (4) in the Presence of *N*-Phenylmaleimide (10). A solution of **4** (20 mg, 0.16 mmol) and **10** (57 mg, 0.32 mmol) in C_6D_6 (0.5 mL) was heated at 140 °C for 3.5 days. Two adducts (**13** and **14**) formed in a 1:19 ratio as determined by integration of the signal of the methine proton (C(7)–H). The ratio remained constant during the reaction. The adducts were not spearated: ^1H NMR (360 MHz, C_6D_6) **13** δ 7.52–6.80 (m, 9 H), 4.12 (d, 3 Hz, 1 H), 3.06 (d, d, J = 7, 15 Hz, 1 H), 3.02 (d, d, J = 3 Hz, 1 H), 2.81 (d, d, d, J = 3, 7, 10 Hz, 2 H). ^1H NMR (360 MHz, C_6D_6) **14** δ 7.52–6.80 (m, 9 H), 3.39 (d, J = 5 Hz, 1 H), 2.97 (d, d, J = 3.5, 15 Hz, 1 H), 2.96 (d, d, J = 5, 9.5 Hz, 1 H), 2.72 (d, d, d, J = 3.5, 7, 9.5 Hz, 1 H), 2.24 (d, d, J = 6.5, 15 Hz, 1 H).

Methyl Benzocyclobutene-7-carboxylate (19) in the Presence of 9. Heating **19**[42] (25 mg, 0.15 mmol) in C_6D_6 in the presence of **9** (35 mg, 0.36 mmol) at 140 °C for 10 days gave two adducts (**23** and **24**) in a ratio of 1:10, as indicated by integration of the methyl signals. No ratio change was seen during thermolysis. No attempt was made to separate the adducts: ^1H NMR (360 MHz, C_6D_6) **23** δ 7.15–6.90 (m, 4 H), 4.02 (d, J = 2 Hz, 1 H), 3.45 (d, d, J = 2, 10.5 Hz, 1 H), 3.29 (s, 3 H), 2.78–2.50 (m, 3 H). ^1H NMR (360 MHz, C_6D_6) **24** δ 7.15–6.90 (m, 4 H), 4.00 (d, J = 6 Hz, 1 H), 2.97 (d, d, J = 10, 15 Hz, 1 H), 2.90 (s, 3 H), 2.78 (d, d, J = 8, 15 Hz, 1 H), 2.56 (d, d, d, J = 8, 10, 11.5 Hz, 1 H), 2.50 (d, d, J = 6, 11.5 Hz, 1 H).

Methyl Benzocyclobutene-7-carboxylate (19) in the Presence of 10. A solution of **19** (20 mg, 0.12 mmol) and **10** (52 mg, 0.29 mmol) in C_6D_6 (0.5 mL) was heated at 140 °C for 11 days. The ratio of two adducts (**25** and **26**) remained constant (1:10) as shown by integration of the methyl signals: ^1H NMR (360 MHz, C_6D_6) **25** δ 7.60–6.85 (m, 9 H), 4.31 (d, J = 2 Hz, 1 H), 3.55 (d, d, J = 2, 9 Hz, 1 H), 3.22 (s, 3 H), 2.82 (d, d, J = 7, 14.5 Hz, 1 H), 2.62 (m, 2 H). ^1H NMR (360 MHz, C_6D_6) **26** δ 7.58 (m, 2 H), 7.42–6.85 (m, 7 H), 4.24 (d, J = 7 Hz, 1 H), 3.17 (d, d, J = 10.5, 15 Hz, 1 H), 3.03 (d, d, J = 7, 15 Hz, 1 H), 2.93 (s, 3 H), 2.73 (m, 2 H).

***N,N*-Dimethylbenzocyclobutene-7-carboxamide (27) in the Presence of 9.** A solution of **27** (18 mg, 0.1 mmol) and **9** (35 mg, 0.36 mmol) in C_6D_6 (0.5 mL) was heated at 140 °C for 7 days. A mixture of two adducts (**28** and **29**) was formed in 2:1 ratio as shown by the integration of the signal of methine proton (C(7)–H). After removing solvent, the residue was recrystallized from ethyl acetate and hexane. The major product (**28**) was obtained pure as a crystalline solid, mp 133–135 °C. No attempt was made to separate the minor adduct (**29**) from the mother liquor: ^1H NMR (360 MHz, C_6D_6) **28** δ 7.01–6.69 (m, 4 H), 4.12 (d, J = 3 Hz, 1 H), 3.63 (d, d, J = 3, 10 Hz, 1 H), 3.29 (d, d, J = 7.5, 15 Hz, 1 H), 3.20 (d, d, d, J = 3.5, 7.5, 10 Hz, 1 H), 2.73 (d, d, J = 3.5, 15 Hz, 1 H), 2.42 (s, 3 H), 2.25 (s, 3 H). ^1H NMR (360 MHz, C_6D_6) **29** δ 7.01–6.69 (m, 4 H), 4.21 (d, J = 6 Hz, 1 H), 3.40 (d, d, J = 10, 15 Hz, 1 H), 2.82 (d, d J = 8, 15 Hz, 1 H), 2.62 (d, d, d, J = 8, 10, 11 Hz, 1 H), 2.55 (d, d, J = 6, 11 Hz, 1 H), 2.23 (s, 3 H), 2.19 (s, 3 H).

Benzocyclobutene-7-carboxylic Acid (34) in the Presence of 10. A solution of **34** (20 mg, 0.14 mmol) and **10** (120 mg, 0.7 mmol) in C_6D_6 (0.5 mL) was heated at 140 °C for 3 days. Each time the NMR tube was cooled for NMR analysis, crystals separated. After the reaction, solvent was removed under reduced pressure, and the solid residue was

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dissolved in deuterated acetone. NMR spectra showed the mixture contained the minor (**37**) and major (**39**) adducts as well as benzopyranone (**36**) in 13, 68, and 19%, respectively, together with a small amount of starting material. The solution was then diluted with benzene. The major adduct **39** was obtained as white crystals, mp 250–253 °C dec, only slightly soluble in benzene at room temperature: ^{1}H NMR (360 MHz, CD_3COCD_3) **39** δ 7.50–7.29 (m, 9 H), 4.52 (d, J = 6.3 Hz, 1 H), 3.51–3.39 (m, 2 H), 3.22 (d, d, J = 7, 14.5 Hz, 1 H), 3.04 (d, d, J = 10, 14.5 Hz, 1 H). ^{1}H NMR (360 MHz, CD_3COCD_3) **37** δ 7.50–7.29 (m, 9 H), 4.36 (d, J = 2 Hz, 1 H), 4.03 (d, d, J = 2, 9 Hz, 1 H), 3.66 (d, d, d, J = 2.4, 7, 9 Hz, 1 H), 3.18 (d, d, J = 2.4, 15 Hz, 1 H), 3.06 (d, d, J = 7, 15 Hz, 1 H). Pure **39** (2 mg) was placed in an NMR tube with benzene and was heated at 140 °C for 15 h. After cooling, the solvent was replaced with deuterated acetone. No trace of **37** was detected.

Benzocyclobutene-7-carboxaldehyde (40). Oxidation of benzocyclobutene-7-methanol[43] with PDC at 0 °C or reduction of **4** with DIBAL[44] gave **40**: ^{1}H NMR (360 MHz, C_6D_6) δ 9.30 (d, J = 3 Hz, 1 H), 7.02–6.96 (m, 2 H), 6.83–6.77 (m, 2 H), 3.68 (m, 1 H), 2.94 (d, d, J = 2.4, 14.4 Hz, 1 H), 2.76 (d, d, J = 5.4, 14.4 Hz, 1 H); ^{13}C NMR (90 MHz, C_6D_6) δ 197.90, 144.56, 141.43, 128.51, 127.65, 123.18, 123.03, 53.99, 30.59. A solution of **40** (12 mg, 0.09 mmol) in C_6D_6 (0.5 mL) was heated at 130 °C. After 2 h, 95% conversion to a single product, (1*H*)-2-benzopyran (**42**), had occurred: ^{1}H NMR (360 MHz, C_6D_6) δ 7.01–6.86 (m, 2 H), 6.73 (d, J = 7.4 Hz, 1 H), 6.53 (d, J = 7 Hz, 1 H), 6.37 (d, J = 5.7 Hz, 1 H), 5.55 (d, J = 5.7 Hz, 1 H), 4.75 (s, 2 H).[45] In another experiment, **40** (10 mg, 0.076 mmol) was heated at 130 °C in C_6D_6 (0.5 mL) with **9** (38 mg, 0.39 mmol), **42** was formed in >98% yield together with ~2% of an unknown product as revealed by NMR.

7-Methylbenzocyclobutene-7-carbonitrile (50) in the Presence of 9. A solution of **4** (200 mg, 1.55 mol) in THF (0.5 mL) was added to LDA, prepared from diisopropylamine (196 mg, 1.94 mmol) and BuLi (1.94 mmol, 1.6 M in hexane, Aldrich) in THF (7 mL) at 0 °C, at −78 °C. After 1 h, MeI (382 mg, 2.7 mmol) was added, and the reaction mixture was stirred overnight at room temperature. Workup gave **50** (204 mg) in 92% yield after chromatography.[40]

A solution of **50** (18 mg, 0.13 mmol) and **9** (28 mg, 0.29 mmol) in C_6D_6 containing 2 crystals of hydroquinone was heated at 140 °C for 5 days. A single adduct formed (**52**). A crystal suitable for X-ray analysis was obtained by recrystallization of **52** from benzene and hexane, mp 139–140 °C: ^{1}H NMR (360 MHz, C_6D_6) δ 6.94–6.80 (m, 3 H), 6.66 (m, 1 H), 3.10 (d, d, J = 8.5, 16.5 Hz, 1 H), 2.76 (d, d, J = 3, 16.5 Hz, 1 H), 2.74 (d, d, d, J = 3, 8.5, 10 Hz, 1 H), 2.57 (d, J = 10 Hz, 1 H), 1.56 (s, 3 H).

7-Methylbenzocyclobutene-7-carbonitrile (50) in the Presence of 10. A solution of **50** (20 mg, 0.14 mmol) and **10** (63 mg, 0.35 mmol) in C_6D_6 (0.5 mL) was heated for 6 days and 18 h at 140 °C until the reaction was complete. Only one adduct (**53**) was formed: ^{1}H NMR (360 MHz, C_6D_6) δ 7.33–6.77 (m, 9 H), 3.35 (d, d, J = 15.5 Hz, 1 H), 3.01 (d, d, J = 3, 15.5 Hz, 1 H), 2.83 (d, d, d, J = 3, 8, 10 Hz, 1 H), 2.75 (d, J = 10 Hz, 1 H), 1.75 (s, 3 H).

Methyl 7-Methylbenzocyclobutene-7-carboxylate (54) in the Presence of 9. A solution of **54** (10 mg, 0.06 mmol) and **9** (15 mg, 0.15 mmol) in C_6D_6 (0.5 mL) containing 3 crystals of hydroquinone was heated at 130 °C for 10 days. Only one adduct (**56**) formed: ^{1}H NMR (360 MHz, C_6D_6) δ 7.14 (d, J = 7.5 Hz, 1 H), 7.00 (t, J = 7.5 Hz, 1 H), 6.92 (t, J = 7.5 Hz, 1 H), 6.81 (d, J = 7.5 Hz, 1 H), 3.61 (d, J = 10 Hz, 1 H), 3.17 (d, d, d, J = 2, 8, 10 Hz, 1 H), 3.07 (s, 3 H), 2.92 (d, d, J = 2, 15.5 Hz, 1 H), 2.45 (d, d, J = 8, 15.5 Hz, 1 H), 1.81 (s, 3 H). In a control experiment, the same amount of sample was heated for the same period without dienophile. After 10 days reaction only 10% conversion to methyl 2-(2′-methylphenyl)acrylate (**58**) had occurred. On further heating at 185 °C for 36 h conversion to **58** was complete: ^{1}H NMR (360 MHz, C_6D_6) δ 7.10–6.95 (m, 4 H), 6.43 (d, J = 2 Hz, 1 H), 5.32 (d, J = 2 Hz, 1 H), 3.28 (s, 3 H), 2.12 (s, 3 H). In another experiment **58** was obtained when the reaction was conducted at 190 °C for 2 days in the presence of hydroquinone.

3-((Dimethyl-*tert*-butyl)siloxy)-4-methyl-(1*H*)-2-benzopyran (61). A solution of **61** (35 mg, 0.12 mmol) in benzene (0.7 ml) was heated at 170 °C for 17 h. A mixture of **61**, 7-((dimethyl-*tert*-butyl)siloxy)-7-methylbenzocyclobutene (**62**) and dimethyl-*tert*-butylsily 2-(2′-methylphenyl)acrylate (**63**) was formed in a 9:5:1 ratio. On continued heating for 5 days, conversion of **61** to **63** was complete: ^{1}H NMR (360 MHz, C_6D_6) **62** δ 7.15–6.85 (m, 4 H), 3.76 (d, J = 7 Hz, 1 H), 2.80 (d, J = 7 Hz, 1 H), 1.60 (s, 3 H), 0.95 (s, 9 H), 0.20 (s, 6 H). ^{1}H NMR (360 MHz, C_6D_6) **63** 7.20–6.90 (m, 4 H), 6.47 (s, 1 H), 5.38 (s, 1 H), 2.23 (s, 3 H), 0.90 (s, 9 H), 0.29 (s, 6 H).

Crystallographic Data for Compounds 12, 28, and 52. Cell parameters and reflection intensities were measured at room temperature on Nonius CAD-4 (**12** and **28**) and Philips PW100 (**52**) diffractometers with graphite monochromated Mo Kα radiation. The structures were solved by direct methods (MULTAN-80) and refined by least-square analysis with the XTAL program (Table VI).

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Supplementary Material Available: Tables of atomic coordinates, anisotropic and isotropic thermal parameters, and bond distances and angles for **12**, **28**, and **52** (21 pages); tables of observed and calculated structure factors for **28** and **52** (20 pages). Ordering information is given on any current masthead page.

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Is Triquinacene Homoaromatic? An MM3 Study of Triquinacene and Its Hydrogenation Products

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Abstract: MM3 energies of triquinacene and di-, tetra-, and perhydrotriquinacene are in reasonable accord with the thermochemical measurements reported by Liebman, Paquette, Peterson, and Rogers (*J. Am. Chem. Soc.* **1986**, *108*, 8267). An analysis of the optimized structures shows the origin of the "differential relaxation" postulated for this series by Dewar and Holder (*J. Am. Chem. Soc.* **1989**, *111*, 5384). The anomalously low heat of hydrogenation of triquinacene can be explained without invoking homoaromaticity.

Introduction

Liebman, Paquette, Peterson, and Rogers have measured the heats of hydrogenation of triquinacene (**1**), dihydrotriquinacene (**2**), and tetrahydrotriquinacene (**3**) to the fully saturated perhydrotriquinacene (**4**). The reported values are shown in Figure 1.[1] The heat of hydrogenation of triquinacene to dihydrotriquinacene (**1** → **2**) is 4.5 ± 2 kcal/mol smaller than for **2** → **3**

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