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Thermal Rearrangements of Bicyclo[5.1.0]octa-2,4-diene and Its 8-Oxa, 6-Oxa, and 6,8-Dioxa Derivatives: An *ab Initio* Molecular Orbital Study[‡]

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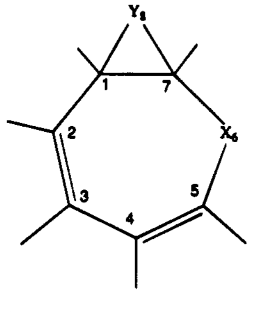
We have carried out calculations at the MP2/6-31G*//RHF/6-31G* level on bicyclo[5.1.0]octa-2,4-diene (BCOD), 8-oxabicyclo[5.1.0]octa-2,4-diene (8-oxaBCOD), 6-oxabicyclo[5.1.0]octa-2,4-diene (6-oxaBCOD), and 6,8-dioxabicylo[5.1.0]octa-2,4-diene (6,8-dioxaBCOD), otherwise 2,3-epoxyoxepin, to determine whether the remarkable instability of 6,8-dioxaBCOD with respect to the fission of both the three- and the seven-membered ring giving *eZzZz*-muconaldehyde—a key step in the metabolic oxidation of benzene—is already apparent in either or both monooxygen derivatives. The effect of oxygen substitution is traced from reactions in which the overall structure is conserved, i.e. the *cisoid/transoid* interconversion, the degenerate Cope rearrangement, and the 1,5-hydrogen shift in the bicyclic molecules, to the fission of both rings giving acyclic isomers. Oxygen substitution has little effect on the interconversion and the 1,5-hydrogen shift, but the Cope rearrangement of 6,8-dioxaBCOD is much slower than that of BCOD. On the other hand, oxygen substitution has an incremental destabilizing influence on the ring fission reaction with respect to both thermodynamic and kinetic parameters. Kinetically, the double substitution in 6,8-dioxaBCOD exerts a destabilizing influence over and above the combined effects of the single substitutions in 8-oxaBCOD and 6-oxaBCOD, decreasing the activation energy further by some 10 kcal mol^{-1}. The activation energies for the fission reactions of the three-membered ring in BCOD, in which cyclooctatriene and methylcycloheptatriene are formed, are far in excess of the activation energy for the fission of both rings. These results suggest that the fission of both rings of BCOD is a cooperative process.

Introduction

The hydrocarbon bicyclo[5.1.0]octa-2,4-diene (BCOD), **1** in Figure 1,[1] is[2−5] quite stable with respect to ring fission[6] (see Figure 2A), whereas the oxygen analog in which both CH_2 groups are replaced by O atoms, i.e. 6,8-dioxabicyclo[5.1.0]octa-2,4-diene, otherwise 2,3-epoxyoxepin,[3] **2** in Figure 1, has never been observed. It has,



Structure	X6	Y8	Abbreviation
1	CH_2	CH_2	BCOD
2	O	O	6,8-dioxaBCOD
3	O	CH_2	6-oxaBCOD
4	CH_2	O	8-oxaBCOD

Figure 1. Structures: **1**, bicyclo[5.1.0]octa-2,4-diene; **2**, 6,8-dioxabicyclo[5.1.0]octa-2,4-diene; **3**, 6-oxabicyclo[5.1.0]octa-2,4-diene; and **4**, 8-oxabicyclo[5.1.0]octa-2,4-diene. For brevity in the text, we shall employ the abbreviations set out in the grid.

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(1) The numbering scheme in Figure 1 follows the IUPAC 1957 Rules,[2] i.e. commencing with one of the bridgehead carbon atoms and proceeding by the longest possible path to the second bridgehead carbon atom with the double bond(s) having the lowest possible number(s). In previous publications,[3,4] a different numbering scheme was adopted which originated in an earlier study[5] of the benzene oxide/oxepin valence tautomerism in which the epoxide oxygen atom was taken as bridging C_1 and C_2 of the benzene ring.

(2) Definitive Rules for Nomenclature of Organic Chemistry. *J. Am. Chem. Soc.* **1960**, *82*, 5545. See A.31, p 5549, and A.31.1 and 31.2, p 5557.

(3) Greenberg, A.; Bock, C. W.; George, P.; Glusker, J. P. *Chem. Res. Toxicol.* **1993**, *6*, 701.

(4) Bock, C. W.; George, P.; Glusker, J. P.; Greenberg, A. *Chem. Res. Toxicol.* **1994**, *7*, 534.

(5) Bock, C. W.; George, P.; Stezowski, J. J.; Glusker, J. P. *Struct. Chem.* **1990**, *1*, 33.

(6) Grimme, W.; Doering, W. von E. *Chem. Ber.* **1973**, *106*, 1765.

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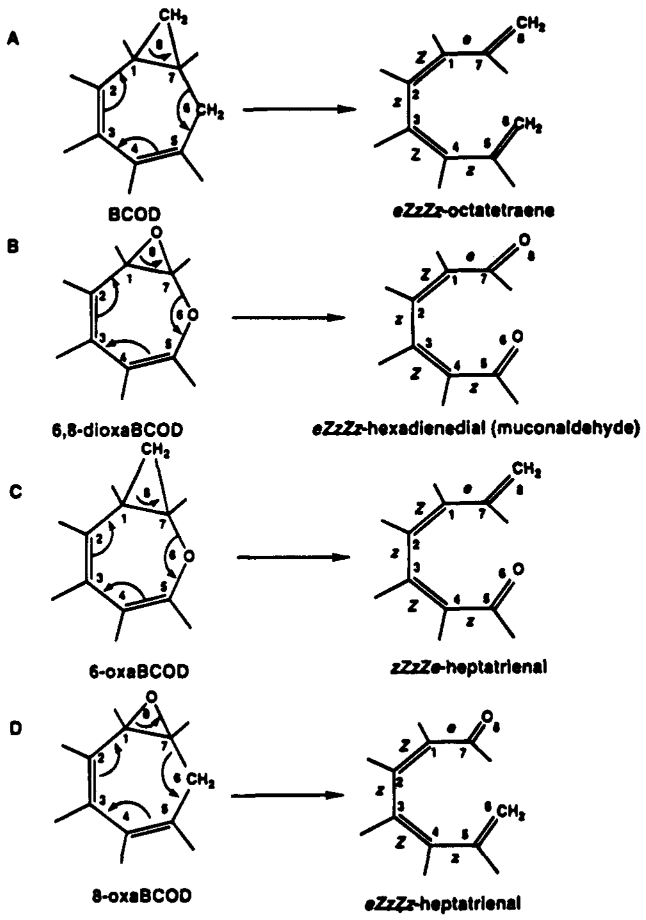

Figure 2. Ring fission reactions with a rearrangement of the double bonds giving acyclic isomers.

however, been suggested that this compound, **2**, is formed as a transient intermediate in the metabolic oxidation of benzene. Subsequent ring fission then gives *eZzZz*-muconaldehyde (see Figure 2B), which is finally oxidized to *E,E*-muconic acid via the *E,Z* and *E,E* isomers.[7] This reaction pathway is of great interest because there is good evidence that muconaldehyde is responsible for the hematotoxicity of benzene.[8,9] Furthermore, the presence of *E,E*-muconic acid in urine is widely used as a marker for exposure to benzene.[10] Recent molecular orbital calculations by us have confirmed that the oxygen analog is very unstable, finding the half-reaction time for ring fission to be only a few seconds at ambient temperatures.[3]

To gain some insight into the origin of this remarkable contrast in stability, we have carried out molecular orbital calculations on bicyclo[5.1.0]octa-2,4-diene, its monooxygen derivatives 6-oxabicyclo[5.1.0]octa-2,4-diene and 8-oxabicyclo[5.1.0]octa-2,4-diene, **3** and **4** in Figure 1, and the corresponding ring fission products shown in Figure 2. The effect of oxygen substitution is traced from reactions in which the structural changes are minimal to those in which they are maximal. These reactions are (i) the conversion of the *cisoid* conformer into the *transoid* conformer of the bicyclic structure,[6] (ii) the degenerate Cope rearrangement,[6] and the 1,5-hydrogen shift,[6] in which the overall structure is conserved[11] (see Figure 3A,B), and (iii) the ring fission reactions in which both the three-membered and the seven-membered rings are broken (e.g. Figure 2A). Of particular interest is the extent to which ring instability of disubstituted BCOD (6,8-dioxaBCOD) may already be apparent when only one methylene group has been replaced by oxygen (6-oxaBCOD or 8-oxaBCOD) and whether thermodynamic or kinetic parameters, or both, determine the stability or instability as the case may be. Finally, to get some indication as to whether the fission of both rings is a concerted process, we have also carried out calculations on the fission of the three-membered ring in bicyclo[5.1.0]octa-2,4-diene in which the monocyclic derivatives 2,4,7-cyclooctatriene and 1-methyl-2,4,6-cycloheptatriene are formed via 1,2- and 1,3-hydrogen shifts, respectively, (see Figure 3C,D).

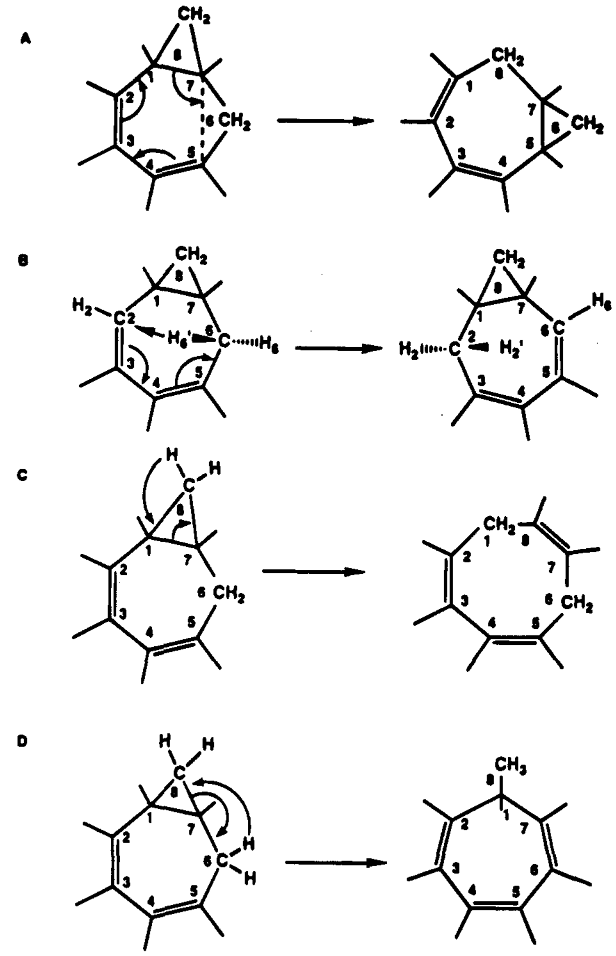

Figure 3. BCOD: (A) the degenerate Cope rearrangement in which C_1-C_7 breaks and C_5-C_7 is formed with a concomitant shift of the double bonds; (B) the 1,5-hydrogen shift in which H_6 moves from C_6 to C_2 with a concomitant shift of the double bonds, and (C and D) fission of the three-membered ring giving 2,4,7-cyclooctatriene and 1-methyl-2,4,6-cycloheptatriene, respectively.

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[7] Davies, S. G.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1346.

[8] Bleasdale, C.; Golding, B. T.; Kennedy, G.; MacGregor, J. O.; Watson, W. P. *Chem. Res. Toxicol.* **1993**, *6*, 407.

[9] Kline, S. A.; Xiang, Q.; Goldstein, B. D.; Witz, G. *Chem. Res. Toxicol.* **1993**, *6*, 578.

[10] Bechtold, W. E.; Lucier, G.; Birnbaum, L. S.; Yin, S. N.; Henderson, R. F. *Am. Ind. Hyg. Assoc. J.* **1991**, *52*, 473.

[11] This special class of isomerization reactions in which individual groups or atoms become mixed, but in which the overall structure is conserved, has been termed autoisomerization.[12,13]

[12] Balaban, A. T.; Fărcaşiu, D. *J. Am. Chem. Soc.* **1967**, *89*, 1958.

[13] Leone, R. E.; Schleyer, P. von R. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 860.

Table 1. E_{298} Values,[a] in Hartrees, S_{298} Values,[b] in Calories per Mole per Kelvin, and $\Delta H_f^\circ(g)$ Values,[c] in Kilocalories per Mole

		MP2/6-31G*//RHF/6-31G*				
molecule	isomer	E_{298}	S_{298}	MM2 $\Delta H_f(g)$	MM2Pi $\Delta H_f(g)$	AM1 $H_f(g)$
BCOD	*cisoid*	−309.540 95	78.15	+53.69	+48.84	+48.04
	transoid	−309.540 76	78.80	+55.84	+51.16	+48.72
6,8-dioxaBCOD	*cisoid*	−381.309 01	77.59	+0.01	−15.81	
	transoid	−381.307 15	79.24	+0.83	−14.74	
6-oxaBCOD	*cisoid*	−345.420 16	77.81	+26.43	+11.84	+24.79
	transoid	–	–	+27.91	+13.32	+24.93
8-oxaBCOD	*cisoid*	−345.426 19	77.38	+24.79	+21.29	
	transoid	−345.424 88	78.20	+26.47	+22.61	
1,3,5,7-octatetraene	*eZzZz*	−309.510 34	90.95		+58.44	
	eEeEe	−309.527 43	89.00		+49.31	
2,4-hexadienedial	*eZzZz*	−381.334 30	87.46		−31.11	
(muconaldehyde)	*eEeEe*	−381.349 92	88.71		−38.44	
2,4,6-heptatrienal	*eZzZz*	−345.422 12	89.57		+14.66	
	zZzZe	−345.423 26	89.30			
	eEeEe	−345.440 48	89.35		+6.40	
2,4,7-cyclooctatriene		−309.540 13	85.96			
1-methyl-2,4,6-cycloheptatriene		−309.562 34	83.05			

[a] The sum of the MP2/6-31G*//RHF/6-31G* electronic energy and the thermal energy at 298 K evaluated from the vibrational frequencies calculated at the RHF/6-31G* level. [b] The entropy from the vibrational frequencies. [c] Calculated using the molecular mechanics method, PCMODEL, MMX,[23] and the semiempirical quantum mechanical model, AM1.[24]

Computational Methods

The calculations were performed at the Advanced Scientific Computing Laboratory, NCI-FCRF, using the GAUSSIAN 90 and GAUSSIAN 92 series of programs[14,15] on a Cray computer. All structures were fully optimized using the split-valence RHF/6-31G* basis set.[16] The effects of electron correlation were included by performing single point Møller-Plesset perturbation calculations[17-19] at the MP2/6-31G*//RHF/6-31G* (frozen core, valence orbitals active) level. Vibrational frequencies were calculated at the RHF/6-31G*//RHF/6-31G* level to determine whether the computed structures correspond to local minima on the potential energy surface or to transition states[20-22] and to evaluate total thermal energies and entropies at 298 K. The total molecular energies, MP2/6-31G*//RHF/6-31G*, plus the total thermal energies, together with the entropies are listed in Tables 1 and 2. *Z*-matrix orientations for all the structures are available as supporting information. To explore the effect of extending the basis set, additional single point energy calculations including polarization functions on the hydrogen, MP2 (frozen core)/6-31G**, with the full core taken into account, MP2 (full core)/6-31G**, and with diffuse functions on all atoms, MP2(full core)/6-311++G** were carried out on the *cisoid* and *transoid* conformers of BCOD (see Table 3).

Values of $\Delta H_f^\circ(g)$ at 298 K for the *cisoid* and *transoid* conformers of BCOD and the 6-oxa, 8-oxa, and 6,8-dioxa derivatives calculated using the molecular mechanics PCMODEL and the MMX parameter set (with extended π calculations for conjugated systems having four or more π centers[23]) are also listed in Table 1, together with values for the *cisoid* and *transoid* conformers of BCOD and 6-oxaBCOD calculated using the AM1 semiempirical quantum mechanical model.[24] Energy changes, activation barriers, and half-reaction times, based on *ab initio* results, for the reactions discussed below have been calculated from these values and would thus correspond to experimental gas phase data.[25] Judging from calculations on the benzene oxide oxepin valence tautomerism,[26] solvent interactions would probably modify these calculated gas phase values by no more than 3 kcal mol^{-1}. Total atomic charges were calculated using Mulliken population analysis[27] from the SCF densities.

Table 2. E_{298} Values,[a] in Hartrees, and S_{298} Values,[b] in Calories per Mole per Kelvin,

transition state	E_{298}	S_{298}
BCOD		
TS: Cope rearrangement	−309.495 32	76.37
TS: 1,5-hydrogen shift	−309.498 14	75.17
TS: *transoid* conformer → *eZzZz*-octatetraene	−309.464 90	80.17
6,8-dioxaBOCD		
TS: Cope rearrangement	−381.246 66	75.66
TS: *transoid* conformer → *eZzZz*-heptadienedial	−381.280 88	77.74
6-oxaBOCD		
TS: *cisoid* conformer → *zZzZe*-heptatrienal	−345.368 08	78.90
8-oxaBOCD		
TS: 1,5-hydrogen shift	−345.384 35	74.38
TS: *transoid* conformer → *eZzZz*-heptatrienal	−345.358 95	79.79
BCOD		
TS: 2,4,7-cyclooctatriene formation	−309.396 76	85.46
TS: 1-methyl-2,4,6-cycloheptatriene formation	−309.319 45	82.29

[a] The sum of the MP2/6-31G*//RHF/6-31G* electronic energy and the thermal energy at 298 K evaluated from the vibrational frequencies calculated at the RHF/6-31G* level for the transition state structures. [b] The entropy evaluated from the vibrational frequencies, for the transition state structures.

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(14) Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; DeFrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. *GAUSSIAN 90*, Revision J; Gaussian, Inc.: Pittsburgh, PA, 1990.

(15) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Repogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *GAUSSIAN 92*, Revision C; Gaussian, Inc.: Pittsburgh, PA, 1992.

(16) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(17) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(18) Binkley, J. S.; Pople, J. A. *Int. J. Quantum Chem.* **1975**, *9*, 229.

(19) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quantum Chem., Symp.* **1976**, *10*, 1.

(20) McIver, J. W., Jr.; Kormornicki, A. *J. Am. Chem. Soc.* **1972**, *94*, 2625.

(21) Pople, J. A.; Krishnan, R.; Schlegel, H. B.; Binkley, J. S. *Int. J. Quantum Chem., Quantum Chem. Symp.* **1979**, *13*, 225.

(22) Schlegel, H. B. In *New Theoretical Concepts for Understanding Organic Reactions;* Bertran, J., Csizmadia, I. G., Eds.; Kluwer Academic Publishers: Dordrecht, 1989; pp 33−53.

(23) *PCMODEL* (using "q-q" electrostatic approximation and extended π calculations); Serena Software, Bloomington, IN.

(24) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(25) Del Bene, J. E. In *Molecular Structure and Energetics;* Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: Deerfield Beach, FL, 1986; Vol. 1, Chapter 9, pp 319−349.

(26) Thieme, R.; Weiss, C. *Stud. Biophys.* **1983**, *93*, 273.

Table 3. E_{298} Values, in Hartrees, for the *Cisoid* and *Transoid* Conformers of Bicyclo[5.1.0]octa-2,4-diene, 1, and the *Cisoid* → *Transoid* Energy Difference, in Kilocalories per Mole

entry	basis set	E_{298} (*cisoid*)	E_{298} (transoid)	ΔE_{298}
i	RHF/6-31G*//RFH/6-31G*	−308.52213	−308.52105	+0.68
ii	MP2 (frozen core)/6-31G*//RHF/6-31G*	−309.54095	−309.54076	+0.12
iii	MP2 (frozen core)/6-31G**//RHF/6-31G*	−309.62175	−309.62157	+0.11
iv	MP2 (full core)/6-31G**//RHF/6-31G*	−309.66303	−309.66285	+0.11
v	MP2 (full core)/6-311^{++}G**//RHF/6-31G*	−309.88108	−309.88089	+0.12

Table 4. Reaction Energies, ΔE_{298} and $\delta\Delta H_f^\circ$(g), in Kilocalories per Mole^{-1}, and Reaction Entropies, ΔS_{298}, in Calories per Mole per Kelvin, Calculated from the Data in Table 1

	MP2/6-31G*				
reaction	ΔE_{298}	ΔS_{298}	MM2 $\delta\Delta H_f$(g)	MM2Pi $\delta\Delta H_f$(g)	AM1 $\delta\Delta H_f$(g)
A. *cisoid* → *transoid* conformer					
BCOD	+0.12	+0.65	+2.15	+2.32	+0.68
6,8-dioxaBCOD	+1.17	+1.65	+0.72	+1.07	
6-oxaBCOD	–	–	+1.48	+1.48	+0.14
8-oxaBCOD	+0.82	+0.82	+1.68	+1.32	
B. *transoid* conformer → acyclic isomer					
BCOD	+19.1	+12.2			
6,8-dioxaBCOD	−17.0	+8.2			
6-oxaBCOD[a]	−2.0	+11.5			
8-oxaBCOD	+1.7	+11.4			
C. *eZzZz* → *eEeEe* acyclic isomer					
octatetraene	−10.7	−2.0		−9.1	
hexadienedial (muconaldehyde)	−9.8	+1.3		−7.3	
heptatrienal[b]	−10.8	+0.1			
heptatrienal	−11.5	−0.2		−8.3	
D. *transoid* BCOD → 2,4,7-cyclooctatriene	+0.4	+7.2			
E. *cisoid* BCOD → 1-methyl-2,4,6-cycloheptatriene	−13.4	+4.9			

[a] *Cisoid* conformer. [b] *zZzZe* conformer.

Table 5. Energies of Activation, $\Delta E^{\ddagger}_{298}$, in Kilocalories per Mole, and Entropies of Activation, $\Delta S^{\ddagger}_{298}$, in Calories per Mole per Kelvin, Calculated from the Data in Tables 1 and 3, Together with the Rate Constants *k* at 25 °C,[31] in s^{-1}, Evaluated from These Activation Parameters, and the Half-Reaction Times, $t_{1/2}$ = ln 2/*k*, in Seconds

reaction	$\Delta E^{\ddagger}_{298}$	$\Delta S^{\ddagger}_{298}$	*k*[a]	$t_{1/2}$[a]	*k*[b]	$t_{1/2}$[b]
BCOD						
transoid conformer → TS (Cope rearrangement)	+28.5	−2.4	1.84×10^{-10}	3.8×10^{9}	3.94×10^{-4}[c]	1.8×10^{3}
cisoid conformer → (1,5-hydrogen shift)	+26.9	−3.0	2.03×10^{-9}	3.4×10^{8}	1.95×10^{-3}[d]	3.6×10^{2}
transoid conformer → TS (*eZzZz*-octatetraene)	+47.6	+1.4	1.22×10^{-23}	5.7×10^{22}	3.60×10^{-13}	1.9×10^{12}
6,8-dioxaBCOD						
transoid conformer → TS (Cope rearrangement)	+38.0	−3.6	1.09×10^{-7}	6.4×10^{16}	2.66×10^{-9}	2.6×10^{8}
transoid conformer → TS (*eZzZz*-hexadienedial)	+16.5	−1.5	1.84×10^{-1}	3.8	9.38×10^{2}	7.4×10^{-4}
6-oxaBCOD						
cisoid conformer → TS (*zZzZe*-heptatrienal)	+32.7	+1.1	8.92×10^{-13}	7.8×10^{11}	1.55×10^{-5}	4.5×10^{4}
8-oxaBCOD						
cisoid conformer → TS (1,5-hydrogen shift)	+26.3	−3.0	5.60×10^{-9}	1.2×10^{8}	3.99×10^{-3}	1.7×10^{2}
transoid conformer → TS (*eZzZz*-heptatrienal)	+41.4	+1.6	4.77×10^{-19}	1.5×10^{18}	6.37×10^{-10}	1.1×10^{9}
BCOD						
transoid conformer → TS (2,4,7-cyclooctatetraene)	+90.4	+6.7				
cisoid conformer → TS (1-methyl-2,4,6-cycloheptatriene)	+139.0	+4.1				

[a] At 25 °C. [b] The last two columns give estimates for the rate constants and half-reaction times at 150 °C, assuming that the activation parameters remain the same at this higher temperature. [c,d] Experimental values for *k* determined at 150 °C[6] are 3.1×10^{-4} and 3.5×10^{-4} s^{-1}, respectively.

Results

1. *Cisoid* and *Transoid* Conformers. Schematic three-dimensional structures for the *cisoid* and *transoid* conformers of BCOD, 6,8-dioxaBCOD, and 8-oxaBCOD and for the *cisoid* conformer of 6-oxaBCOD, calculated at the RHF/6-31G* level, are depicted in Figure 4. The orientation of the three- and seven-membered rings is such that the *cisoid* conformer has a more "open" structure compared to the "closed" or "compact" structure of the *transoid* conformer.[6] But, even though the C−O bond lengths are much shorter than the corresponding C−C bond lengths, there is relatively little change in these bond lengths in going from the *cisoid* to the *transoid* conformer (see Figure 4A,B,D). In keeping with this finding, there is very little difference in energy. The *cisoid* conformer is consistently the more stable one (see Table 4A), in accord with the assignment of the *cisoid* conformation for BCOD on the basis of NMR measurements.[6] However, it would appear that the *ab initio* calculations tend to underestimate the energy difference a little in the case of BCOD. The small value of ΔE_{298} at the RHF/6-31G*//RHF/6-31G* level and the even smaller values at higher levels of calculation with electron correlation included and with more extended basis sets (see Table 3, entries ii−iv), coupled with the small but positive value for ΔS_{298} (+0.65 eu, see Table 1), predict a detectable concentration of the *transoid* conformer, contrary to observation. It is unclear how this discrep-

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(27) Mulliken, R. S. *J. Chem. Phys.* **1955**, *23*, 1833.

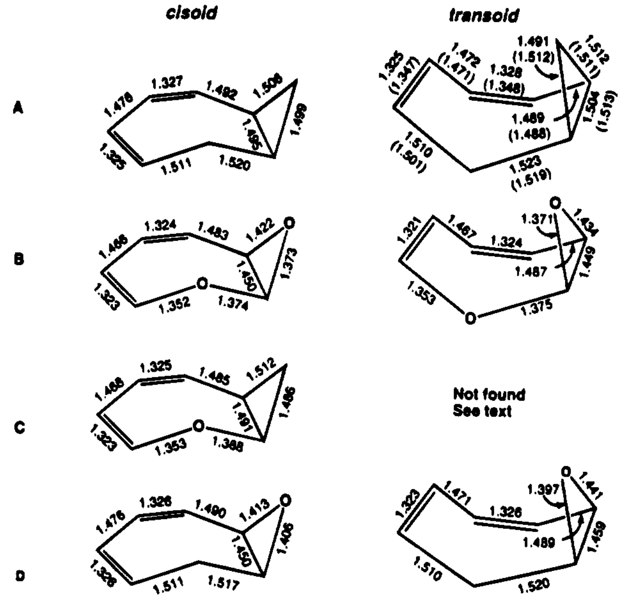

Figure 4. Schematic three-dimensional structures, with bond lengths in angstroms, for the *cisoid* and *transoid* conformers of (A) BCOD, (B) 6,8-dioxaBCOD, (C) 6-oxaBCOD, and (D) 8-oxaBCOD at the RHF/6-31G*//RHF/6-31G* level. Bond lengths determined by the MM2Pi method are given in parentheses.

ancy arises. With $\delta\Delta H_f^\circ$(g) values of about 2 kcal mol^{-1}, the molecular mechanics calculations are more in line with experiment.

A comparison of the two structures for BCOD suggests that there is stronger conjugation between the cyclopropane moiety and the olefinic linkage in the *transoid* conformer. Relative to the *cisoid* conformer, there is a shortening of 0.003 Å of the exocyclic bond, C_1-C_2, linking the two groups, a lengthening of 0.009 and 0.006 Å of both vicinal cyclopropane bonds, C_1-C_7 and C_1-C_8, respectively, and a shortening of 0.008 Å of the distal cyclopropane bond, C_7-C_8. These bond length changes are consistent with those anticipated by Hoffmann[28,29] for a π acceptor substituent attached to cyclopropane and furthermore reflect the tendency of cyclopropane to be a stronger π donor than a π acceptor.[30] Although the *transoid* conformer of 6-oxaBCOD was found to be a stable species using the molecular mechanics and semiempirical AM1 methods, repeated attempts to locate it on the RHF/6-31G* potential energy surface failed, all the calculations reverting back to the *cisoid* structure.

2. Degenerate Cope Rearrangement. Oxygen substitution has a marked effect on the energy of the transition state relative to that for the *transoid* conformer. With BCOD, $\Delta E^{\ddagger}_{298}$ is found to be 28.5 kcal mol^{-1}, compared to 38.0 kcal mol^{-1} for 6,8-dioxa BCOD,[3] although the $\Delta S^{\ddagger}_{298}$ values are both small and negative, showing that the structures have tightened up slightly (see Table 5). The rate constant for BCOD in the gas phase, determined at 150 °C,[6] is 3.1 × 10^{-4} s^{-1}. Assuming that the same values of $\Delta E^{\ddagger}_{298}$ and $\Delta S^{\ddagger}_{298}$ hold at this higher temperature, the calculated rate constant[31] is 3.9 × 10^{-4} s^{-1}, in close agreement with experiment.

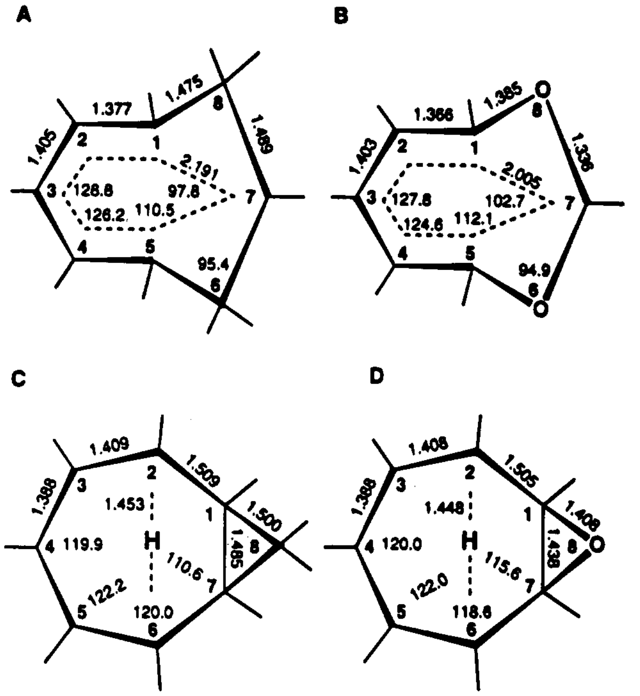

Figure 5. Bond lengths in angstroms and bond angles in degrees in the transition state structures for the degenerate Cope rearrangement in (A) BCOD and (B) 6,8-dioxaBOCD and for the 1,5-hydrogen shift in (C) BCOD and (D) 8-oxaBCOD. The structures in parts A and B have C_2 symmetry, and the structures in parts C and D have C_s symmetry.

Table 6. Torsional Angles, in Degrees, in the Six-Membered Ring ($C_7C_1C_2C_3C_4C_5$) and in the Eight-Membered Ring ($C_8C_1C_2C_3C_4C_5C_6C_7$)[a] in the Transition States for the Cope Rearrangement in BCOD and 6,8-dioxaBCOD and in the Seven-Membered Ring ($C_7C_1C_2C_3C_4C_5C_6$) in the Transition States for the 1,5-Hydrogen Shift in BCOD and 8-oxaBCOD

TS: Cope rearrangement[b]			TS: 1,5-hydrogen shift[c]		
bonding pattern	BCOD τ	6,8-dioxa-BCOD τ	bonding pattern	BCOD τ	8-oxaBCOD τ
$C_7C_1C_2C_3$	+5.1	+8.9	$C_7C_1C_2C_3$	−73.7	−74.0
$C_1C_2C_3C_4$	+27.0	+23.2	$C_1C_2C_3C_4$	+56.8	+56.2
$C_2C_3C_4C_5$	+27.0	+23.2	$C_2C_3C_4C_5$	+14.6	+14.7
$C_3C_4C_5C_7$	+5.1	+8.9	$C_3C_4C_5C_6$	−14.6	−14.7
$C_4C_5C_7C_1$	+17.5	+16.3	$C_4C_5C_6C_7$	−56.8	−56.2
$C_5C_7C_1C_2$	+17.5	+16.3	$C_5C_6C_7C_1$	+73.7	+74.0
			$C_6C_7C_1C_2$	0	0
$C_4C_5C_6C_7$	−88.1	−94.4			
$C_5C_6C_7C_8$	+56.8	+61.9			
$C_6C_7C_8C_1$	+56.8	+61.9			
$C_7C_8C_1C_2$	−88.1	−94.4			

[a] In 6,8-dioxaBCOD, C_8 is replaced by O_8. [b] C_2 symmetry. [c] C_s symmetry.

The structures of the two transition states are nevertheless very similar (see Figure 5A,B). There are 2-fold axes of symmetry passing through C_3 and C_7, (see Table 6). The six-membered rings, $C_7C_1C_2C_3C_4C_5$, are more nearly planar than the eight-membered $C_8C_1C_2C_3C_4C_5C_6C_7$ rings, and compared to the *transoid* conformers, there are similar changes in bond length, namely the long bonds C_1-C_2 and C_3-C_4 become shorter and the short

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(28) Hoffmann, R. *Tetrahedron Lett.* **1970**, 2907.

(29) Hoffmann, R.; Stohrer, W.-D. *J. Am. Chem. Soc.* **1971**, *93*, 6941.

(30) Greenberg, A.; Stevenson, T. A. *J. Am. Chem. Soc.* **1985**, *107*, 3488.

(31) Kondratiev, V. N.; Nikitin, E. E. *Gas-Phase Reactions;* Springer-Verlag: New York, 1981; pp 60 and 104.

(32) Cremer, D.; Kraka, E.; Slee, T. S.; Bader, R. F. W.; Lau, C. H. D.; Nguyen-Dang, T. T.; MacDougall, P. J. *J. Am. Chem. Soc.* **1983**, *105*, 5069.

(33) Dewar, M. J. S. In *Modern Models of Bonding and Delocalization;* Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: New York, 1988; Chapter 1, pp 1−59.

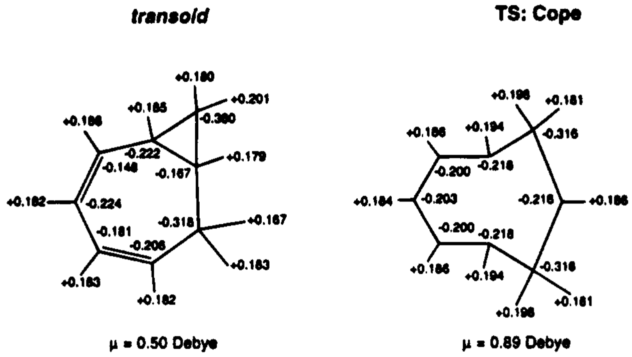

Figure 6. Distribution of total atomic charges, calculated using Mulliken population analysis,[27] in the *transoid* conformer and in the transition state for the degenerate Cope rearrangement of BCOD.

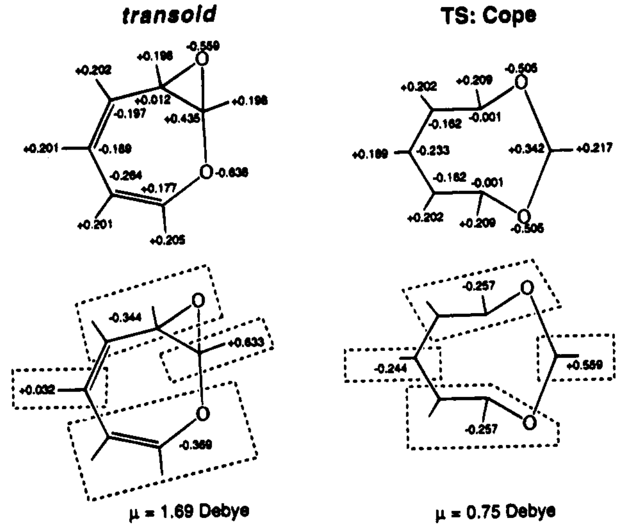

Figure 7. Distribution of total atomic charges, calculated using Mulliken population analysis,[27] in the *transoid* conformer and in the transition state for the degenerate Cope rearrangement of 6,8-dioxaBCOD.

bonds C_2-C_3 and C_4-C_5 become longer. These features are indicative of homoaromatic stabilization.[32,33]

With BCOD, the total atomic charge on the carbon atoms in the six-membered ring becomes more evenly distributed in going from the *transoid* conformer to the transition state (see Figure 6). Notably, there is no marked difference between the charges on C_3 and C_7, −0.203 and −0.216, respectively, and the charges on the other four carbon atoms, mean value of −0.209 ± 0.010. The dipole moment is a little larger for the transition state, 0.89 D compared to 0.50 D for the transoid conformer, which suggests that the rearrangement may be somewhat more favored in polar solvents than in the gas phase.

The presence of the two O atoms in 6,8-dioxaBCOD profoundly affects the charge distribution (see Figure 7). But, although C_7, lying between the O atoms, is more positively charged than C_3, the comparison of the net charges on corresponding structural elements in the lower part of the figure shows the *transoid* conformer to be more polar than the transition state. This is further borne out by the dipole moments, 1.69 D for the *transoid* conformer compared to 0.75 D for the transition state. It is therefore unlikely that the rate constant would be enhanced in polar solvents (unless there is a marked change in the charge distribution in the transition state), and the conclusion still holds that the rearrangement is too slow (see Table 5) to permit labeling experiments which could otherwise demonstrate the role of 6,8-dioxaBCOD as an intermediate in the metabolic oxidation of benzene.[3]

Finally, it may be noted that, although it is possible to envisage the interconversion of 8-oxaBCOD and 6-oxaBCOD, a process closely related to the above Cope rearrangements, there was no indication that 6-oxaBCOD was formed in the pyrolysis of 8-oxaBCOD.[34] Calculations have failed to locate a transition state for this interconversion, but since the 6-oxa structure is less stable than the 8-oxa structure by a few kilocalories per mole (see Table 1), it could be that the former passes into the latter with very little if any activation.

3. 1,5-Hydrogen Shift. Transition states have been identified for the 1,5-hydrogen shift in the *cisoid* conformers of BCOD and 8-oxaBCOD; the absence of a CH_2 group in position 6 obviously rules out the possibility of such a shift in the 6-oxa and 6,8-dioxa derivatives. Oxygen substitution has scarcely any effect. The energies of the transition states relative to the energies of the *cisoid* conformers differ by only 0.6 kcal mol^{-1}, and the changes in entropy are identical (see Table 5).

The structures of the two transition states are very similar with regard to both the C−C bond lengths and the CCC bond angles in the seven-membered ring (see Figure 5C,D). As expected, there is a plane of symmetry passing through C_4 and C_8 and C_4 and O_8 (see Table 6). The hydrogen atom involved in the shift, H_6', lies equidistant between C_2 and C_6 with $\angle C_2H_6C_6$ = 122.6 and 123.0° for BCOD and 6,8-dioxaBCOD, respectively. In the transition state for BCOD, the total atomic charge on this hydrogen atom is significantly less than that on the other hydrogen atoms, +0.157 compared to +0.189 ± 0.007, although for 8-oxaBCOD, there is no appreciable difference.

The rate constant for the shift in BCOD in the gas phase, determined at 150 °C,[6] is 3.5×10^{-4} s^{-1}. Assuming that the values of $\Delta E^{\ddagger}_{298}$ and $\Delta S^{\ddagger}_{298}$ in Table 5 hold at this higher temperature, the calculated rate constant is 2.0×10^{-3} s^{-1}.

4. Acyclic Isomers. As in the case of 6,8-dioxaBCOD[3,4] the acyclic isomers with the *eEeEe* configuration are more stable than the *eZzZz* (*zZzZe*) isomers formed initially in the ring fission reactions (see Figure 2). Oxygen substitution has very little influence on the energy difference; ΔE_{298} ranges from −9.8 to −11.5 kcal mol^{-1}, (see Table 4, C), and the changes in entropy are all very small.

The C−C and C=C bond lengths and the CCC bond angles in the *eZzZz (zZzZe)* isomers are scarcely affected by the oxygen substitution (see Figure 8). All four structures are nonplanar with respect to the "*z*" bonds. There is a pronounced twist about the central *z* bonds, with the torsional angle $\tau C_1{=}C_2{-}C_3{=}C_4$ of about 61°. The twist about the terminal *z* bonds is rather less. The torsional angle $\tau C_3{=}C_4{-}C_5{=}C_6$ is about 46° and between 13 and 23° for $\tau C_3{=}C_4{-}C_5{=}O_6$. Otherwise, the CCCC segments are nearly planar (see Table 7).

In sharp contrast, the oxygen substitution brings about a dramatic decrease in the thermodynamic stability of the ring structure relative to the *eZzZz (zZzZe)* acyclic isomer. The differences in free energy, ΔG_{298}, calculated from the values of ΔE_{298} and ΔS_{298} in Table 4 range from

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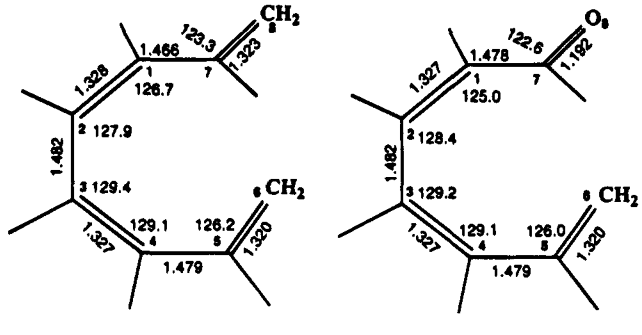
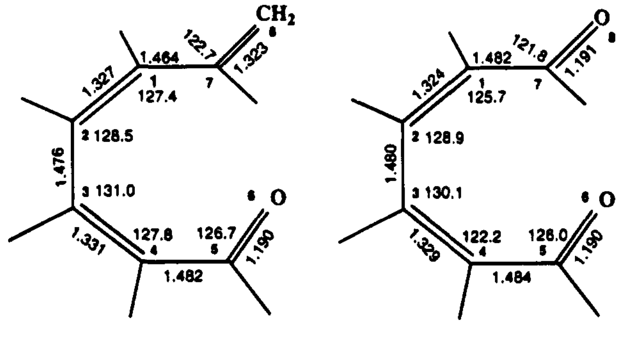
[34] Schiess, P. W.; Wisson, M. *Tetrahedron Lett.* **1971**, 2389.



eZzZz-octatetraene *eZzZz*-heptatrienal



zZzZe-heptatrienal *eZzZz*-hexadienal

Figure 8. Bond lengths, in angstroms, and bond angles, in degrees, in the *eZzZz*(*zZzZe*) isomers.

+15.5 kcal mol^{-1} for BCOD, the most stable, to −19.4 kcal mol^{-1} for 6,8-dioxaBCOD, the least stable, with the values for 8-oxaBCOD and 6-oxaBCOD, −1.7 and −5.4 kcal mol^{-1}, respectively, lying in between. The substantial endothermicity of +19.1 kcal mol^{-1} for the fission of the ring in BCOD does not, however, by itself account for the known stability in pyrolysis experiments.[6] With no additional energy of activation, i.e. putting $\Delta E^{\ddagger}_{298} = \Delta E$ and $S^{\ddagger}_{298} = +1.4$ cal mol^{-1} K^{-1}, the half-reaction time at 25 °C is 71 s.

5. Ring Structures → Acyclic Isomers. Transition states have been identified for the fission of the ring in all four structures. Kinetic parameters, and half-reaction times at 25 and 150 °C, are listed in Table 5. The energies of the transition state, the *eZzZz (zZzZe)* isomer, and the *eEeEe* isomer relative to the energy of the ring structure are plotted in Figure 9 for BCOD and 6,8-dioxaBCOD and in Figure 10 for 6-oxaBCOD and 8-oxaBCOD.

The thermal stability of BCOD is clearly due to the high energy of activation, +47.6 kcal mol^{-1}, far in excess of the endothermicity, which results in a half-reaction time of 1.9×10^{12} s. As with the thermodynamic data, oxygen substitution has a greater destabilizing influence in the seven-membered as opposed to the three-membered ring; i.e. the activation energy is 32.7 kcal mol^{-1} for 6-oxaBCOD compared to 41.4 kcal mol^{-1} for 8-oxaBCOD, and the half-reaction times at 150 °C are 4.5×10^4 and 1.9×10^9 s, respectively. The double substitution in 6,8-dioxaBCOD, however, exerts a destabilizing influence over and above a combined effect of these single substitutions by some 10 kcal mol^{-1}. For 6-oxaBCOD, the destabilization amounts to a decrease in $\Delta E^{\ddagger}_{298}$ of $47.6 - 32.7 = 14.9$ kcal mol^{-1}, and for 8-oxaBCOD, the destabilization is a decrease of $47.6 - 41.4 = 6.2$ kcal mol^{-1}, giving a total for both compounds of 21.1 kcal mol^{-1}, compared to the decrease of $47.6 - 16.5 = 31.1$ kcal mol^{-1} for 6,8-dioxaBCOD.

Despite these reactivity differences, the structures of the four transition states are very similar. Selected internuclear distances in the ring structure, the transition state, and the *eZzZz* (*zZzZe*) isomer are listed in Table 8, together with the percentage increments in going from the ring structure to the transition state. The changes in the C_8-C_1 and O_8-C_1 bond lengths in the three-membered rings are well-advanced in the transition states, by 73% on average, whereas the changes in the C_6-C_7 and O_6-C_7 bond lengths in the seven-membered rings are far less advanced, by only 14% on average. Evidently, considerable relaxation of the heavy atom chain follows the formation of the transition state.

With the exception of C_1-C_7, all the other carbon–carbon bonds, and carbon–oxygen bonds, change from single to double or *vice versa* as ring fission occurs (see Figure 2). Although there is quite a considerable variation in the percentage increments in bond length, the changes from single to double (C_1-C_2, C_3-C_4, C_5-C_6, C_7-C_8, and C_7-O_8) appear to be more advanced than the changes from double to single (C_2-C_3 and C_4-C_5), by 58% on average compared to 42%. The increments in the C_1-C_7 bond length present an interesting anomaly. Although the percentage increments for BCOD and 6,8-dioxaBCOD fall into line, decreasing progressively in going from the ring structure (single bond) to the transition state to the *eZzZz* isomer (double bond), the increments for 6-oxoBCOD and 8-oxaBCOD pass through a minimum and a maximum, respectively.

These percentage increments, greater for C_8-C_1 (O_8-C_1) in the three-membered ring than for C_1-C_2, C_3-C_4, C_5-C_6, and C_7-C_8 (C_7-O_8) and greater for C_2-C_3 and C_4-C_5 in the seven-membered ring, suggest that partial fission of the three-membered ring destabilizes the seven-membered ring and helps bring about its fission in a cooperative process.

In contrast to these trends in bond length and internuclear distance, the changes in total atomic charge on the atoms directly involved in the fission reactions are far less systematic. Even though the charges on corresponding atoms in some of the structures are almost identical—e.g. O_8 in *transoid* 8-oxaBCOD and *transoid* 6,8-dioxaBCOD, C_8 in *eZzZz*-octatetraene and *zZzZe*-heptatrienal, and C_5 and O_6 in *zZzZe*-heptatrienal and *eZzZz*-hexadienedial—the changes in charge in going from the ring structures to the transition states and then to the acyclic structures increase progressively in some cases, decrease in others, pass through a maximum in some cases, but pass through a minimum in others (see Table 9). The changes in charge on C_7 exemplify all four possibilities.

6. 2,4,7-Cyclooctatriene (IUPAC 1,3,6-Cyclooctatriene) and 1-Methyl-2,4,6-cycloheptatriene (IUPAC 7-Methyl-3,5-cycloheptatriene). In the search for the transition state for the fission of both rings in BCOD, two other transition states were identified in which only the three-membered ring was broken, i.e. one for the formation of cyclooctatriene via a 1,2-hydrogen shift from C_8 to C_1 and the other for the formation of methylcycloheptatriene via a 1,3-hydrogen shift from C_6 to C_8 (see Figure 3C,D). Compared to $\Delta E^{\ddagger}_{298}$ for the fission of both rings, 47.6 kcal mol^{-1}, the $\Delta E^{\ddagger}_{298}$ values for these reactions are much greater, 90.4 and 137.0 kcal mol^{-1}, respectively (see Table 5). Hence, BCOD is

Table 7. Torsional Angles, in Degrees, about the Bonds along the Heavy Atom Chain in the Ring Fission Products from BCOD, 6,8-dioxaBCOD, 6-oxaBCOD, and 8-oxaBCOD[a]

	structural element				
molecule	*e* terminal	*eZz*	*ZzZ*	*zZz*	*z* terminal
eZzZz-octatetraene	$C_8{=}C_7{-}C_1{=}C_2$ +178.1	$C_7{-}C_1{=}C_2{-}C_3$ +1.1	$C_1{=}C_2{-}C_3{=}C_4$ −62.2	$C_2{-}C_3{=}C_4{-}C_5$ −1.7	$C_3{=}C_4{-}C_5{=}C_6$ −44.9
eZzZz-muconaldehyde	$O_8{=}C_7{-}C_1{=}C_2$ +178.6	$C_7{-}C_1{=}C_2{-}C_3$ +0.9	$C_1{=}C_2{-}C_3{=}C_4$ +61.8	$C_2{-}C_3{=}C_4{-}C_5$ +0.4	$C_3{=}C_4{-}C_5{=}O_6$ −23.3
zZzZe-heptatrienal	$C_8{=}C_7{-}C_1{=}C_2$ +177.4	$C_7{-}C_1{=}C_2{-}C_3$ −1.1	$C_1{=}C_2{-}C_3{=}C_4$ +61.3	$C_2{-}C_3{=}C_4{-}C_5$ +2.9	$C_3{=}C_4{-}C_5{=}O_6$ −12.7
eZzZz-heptatrienal	$O_8{=}C_7{-}C_1{=}C_2$ +184.4	$C_7{-}C_1{=}C_2{-}C_3$ −0.1	$C_1{=}C_2{-}C_3{=}C_4$ +60.6	$C_2{-}C_3{=}C_4{-}C_5$ +0.9	$C_3{=}C_4{-}C_5{=}C_6$ +46.6

[a] See Figure 2.

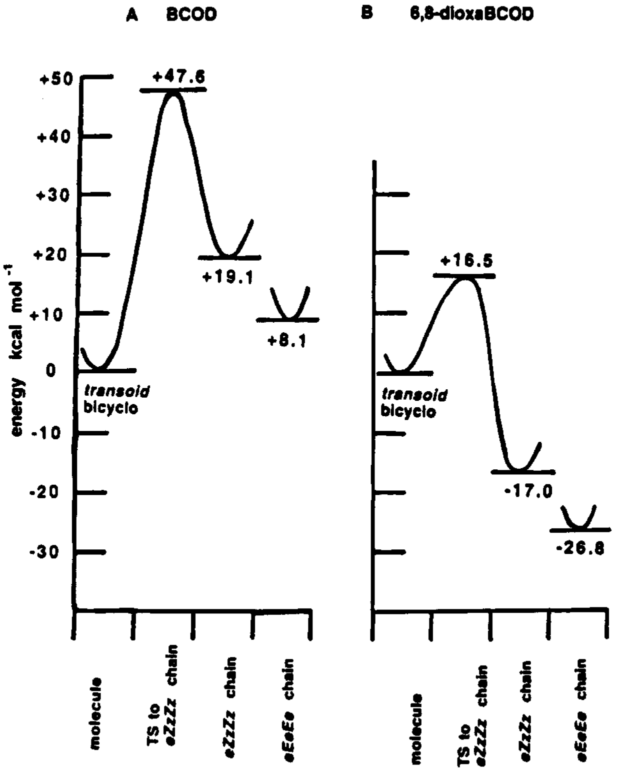


Figure 9. Energy profile for (A) the *transoid* conformer of BCOD, the transition state for the ring fission giving *eZzZz*-octatetraene, and *eZzZz*- and *eEeEe*-octatetraene and (B) the *transoid* conformer of 6,8-dioxaBCOD, the transition state for the ring fission giving *eZzZz*-hexadienedial, and *eZzZz*- and *eEeEe*-hexadienedial.

thermally stable not only with respect to the *eZzZz* chain isomer but also with respect to the more limited ring fission giving these cyclooctatriene and methylcycloheptatriene derivatives. The difficulty in breaking only the three-membered ring compared to the more favorable (less unfavorable) fission of both rings is additional presumptive evidence that the fission of both rings is a concerted process. It is interesting to observe that, despite the formidable activation barriers, both cyclooctatriene and methylcycloheptatriene are actually more stable thermodynamically than BCOD. The values of ΔG_{298} for their formation from BCOD, calculated from the ΔE_{298} and ΔS_{298} values in Table 4, are −1.8 and −14.9 kcal mol^{-1}, respectively.

The bond lengths and angles in these structures are shown in Figure 11 A,B, and the torsional angles around the rings are listed in Table 10. In cyclooctatriene, there is a 2-fold axis of symmetry passing through the midpoints of $C_3{-}C_4$ and $C_7{-}C_8$, whereas methylcycloheptatriene has a plane of symmetry passing through $C_8{-}C_1$ and the midpoint of $C_4{-}C_5$.

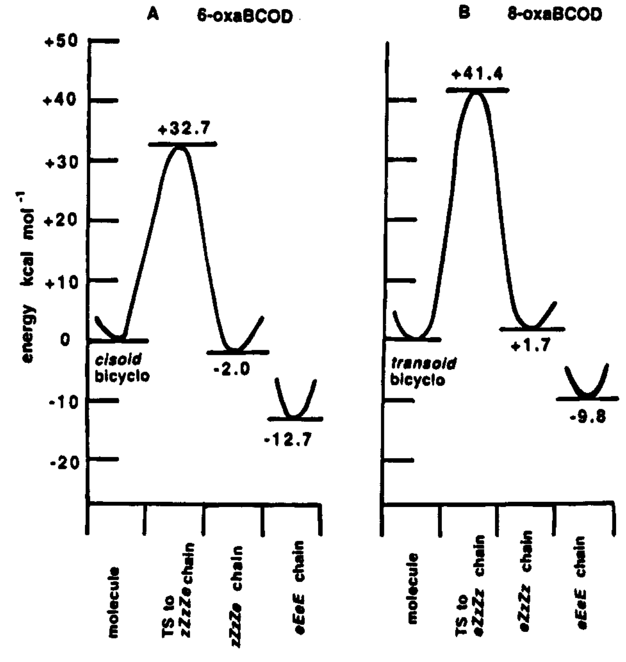


Figure 10. Energy profile for (A) the *cisoid* conformer of 6-oxaBCOD, the transition state for the ring fission giving *zZzZe*-heptatrienal, and *zZzZe*- and *eEeEe*-heptatrienal and (B) the *transoid* conformer of 8-oxaBCOD, the transition state for the ring fission giving *eZzZz*-heptatrienal, and *eZzZz*- and *eEeEe*-heptatrienal.

Conclusions

The remarkable contrast between the facile ring fission of 6,8-dioxaBCOD (2,3-epoxyoxepin) and the thermal stability of the parent hydrocarbon BCOD, as described in the Introduction, has been shown in the present study to involve both thermodynamic and kinetic factors.

Both factors favor the fission of 6,8-dioxaBCOD. ΔG_{298} is large and negative, −19.4 kcal mol^{-1}, so on thermodynamic grounds, the molecule is very unstable. With regard to the kinetics, the activation energy is not very large, +16.5 kcal mol^{-1}, so that, with a small entropy of activation of −1.5 cal mol^{-1} K^{-1}, the half-reaction time for the fission reaction is only some 15 s at the experimental temperature of 10 °C.[3]

On the other hand, BCOD owes its stability in the pyrolysis experiments[6] entirely to the extremely large energy of activation, ΔE_{298}, of +47.6 kcal mol^{-1}, commensurate with a half-reaction time of 1.9×10^{12} s at 150 °C. Although the free energy change is positive, indicative of an inherent stability with respect to the

Table 8. A Comparison of Selected Internuclear Distances, in Angstroms, in the Ring Structure, the Transition State and the Acyclic Structure Resulting from Ring Fission, for BCOD, 6,8-dioxaBCOD, 6-oxaBCOD, and 8-oxaBCOD.

internuclear distance	*transoid*	TS[a]	*eZzZz*	internuclear distance	*transoid*	TS[a]	*eZzZz*
	BCOD				6,8-dioxaBCOD		
C_8-C_1	1.512	2.198 (73%)	2.456	O_8-C_1	1.434	2.016 (64%)	2.340
C_6-C_7	1.523	1.924 (17%)	3.879	O_6-C_7	1.375	1.508 (9%)	2.930
C_8-C_7	1.491	1.381 (66%)	1.323	O_8-C_7	1.371	1.274 (54%)	1.191
C_7-C_1	1.504	1.479 (66%)	1.466	C_7-C_1	1.449	1.477 (85%)	1.482
C_1-C_2	1.489	1.370 (74%)	1.328	C_1-C_2	1.487	1.385 (63%)	1.324
C_2-C_3	1.328	1.410 (47%)	1.482	C_2-C_3	1.324	1.378 (35%)	1.480
C_3-C_4	1.472	1.387 (59%)	1.327	C_3-C_4	1.467	1.405 (45%)	1.329
C_4-C_5	1.325	1.385 (61%)	1.479	C_4-C_5	1.321	1.365 (27%)	1.484
C_5-C_6	1.510	1.400 (58%)	1.320	C_5-O_6	1.353	1.281 (44%)	1.190
	6-oxaBCOD[b]				8-oxaBCOD		
C_8-C_1	1.512	2.123 (65%)	2.447	O_8-C_1	1.411	2.250 (90%)	2.346
O_6-C_7	1.388	1.708 (19%)	3.090	C_6-C_7	1.520	1.748 (10%)	3.823
C_8-C_7	1.486	1.388 (60%)	1.323	O_8-C_7	1.397	1.259 (67%)	1.192
C_7-C_1	1.491	1.437 (min)	1.464	C_7-C_1	1.459	1.510 (max.)	1.478
C_1-C_2	1.485	1.396 (56%)	1.327	C_1-C_2	1.489	1.358 (81%)	1.327
C_2-C_3	1.325	1.380 (36%)	1.476	C_2-C_3	1.326	1.417 (58%)	1.482
C_3-C_4	1.468	1.408 (44%)	1.331	C_3-C_4	1.471	1.382 (62%)	1.327
C_4-C_5	1.323	1.373 (31%)	1.482	C_4-C_5	1.323	1.383 (39%)	1.479
C_5-O_6	1.353	1.268 (52%)	1.190	C_5-C_6	1.510	1.421 (47%)	1.320

[a] The percentage increments in the internuclear distances in going from the ring structure to the transition state are in parentheses.
[b] *Cisoid* 6-oxaBCOD.

Table 9. Total Atomic Charges on C_1, $C_8(O_8)$, C_7, $C_6(O_6)$, and C_5 in *Transoid* BCOD, *Transoid* 8-oxaBCOD, *Cisoid* 6-oxaBCOD, and *Transoid* 6,8-dioxaBCOD, in the Transition States, and in the Acyclic Structures that Result from the Fission of the Three- and Seven-Membered Ring

molecule	C_1	$C_8(O_8)$	C_7	$C_6(O_6)$	C_5
transoid BCOD	−0.222	−0.360	−0.167	−0.318	−0.206
TS	−0.200	−0.340	−0.201	−0.421	−0.128
eZzZz-octatetraene	−0.166	−0.412	−0.130	−0.369	−0.163
transoid 8-oxaBCOD	+0.060	−0.557	+0.107	−0.375	−0.172
TS	−0.080	−0.688	+0.272	−0.534	+0.022
eZzZz-hepatrienal	−0.270	−0.500	+0.320	−0.367	−0.178
cisoid 6-oxaBCOD	−0.239	−0.381	+0.162	−0.622	+0.159
TS	−0.112	−0.462	+0.065	−0.638	+0.303
zZzZe-heptatrienal	−0.134	−0.407	−0.115	−0.482	+0.316
transoid 6,8-dioxaBCOD	+0.012	−0.559	+0.435	−0.638	+0.177
TS	−0.053	−0.682	+0.488	−0.629	+0.318
eZzZz-hexadienedial	−0.236	−0.495	+0.342	−0.479	+0.316

[a] A listing of the total atomic charges on all the heavy atoms is given in Table 16S of the supporting information.

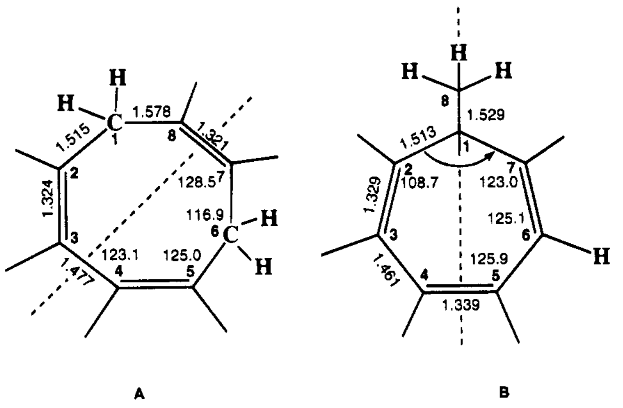


Figure 11. Bond lengths, in angstroms, and bond angles in degrees, in (A) 2,4,7-cyclooctatriene (IUPAC 1,3,6-cyclooctatriene) and (B) 1-methyl-2,4,6-cycloheptatriene (IUPAC 7-methyl-1,3,5-cycloheptatriene). The structure in part A has C_2 symmetry, and the structure in part B has C_s symmetry.

fission product, the energy change, ΔE_{298}, of +19.1 kcal mol^{-1} is not in itself sufficient to account for the stability in practice since, were there no additional energy for activation, the half-reaction time would be about 1 min even at 25 °C.

Table 10. Torsional Angles, in Degrees, in 2,4,7-Cyclooctatriene and 1-Methyl-2,4,6-cycloheptatriene

bonding pattern	τ	bonding pattern	τ
2,4,7-cyclooctatriene[a]		1-methyl-2,4,6-cycloheptatriene[b]	
$C_8C_1C_2C_3$	−83.5	$C_7C_1C_2C_3$	−63.5
$C_1C_2C_3C_4$	+6.4	$C_1C_2C_3C_4$	+6.1
$C_2C_3C_4C_5$	+57.5	$C_2C_3C_4C_5$	+32.1
$C_3C_4C_5C_6$	+6.4	$C_3C_4C_5C_6$	0
$C_4C_5C_6C_7$	−83.5	$C_4C_5C_6C_7$	−32.1
$C_5C_6C_7C_8$	+45.1	$C_5C_6C_7C_1$	−6.1
$C_6C_7C_8C_1$	−3.9	$C_6C_7C_1C_2$	+63.5
$C_7C_8C_1C_2$	+45.1		

[a] C_2 symmetry. [b] C_s symmetry.

The onset of ring instability is already apparent in the monooxygen derivatives. For 8-oxaBCOD and 6-oxaBCOD, ΔG_{298} = −1.7 and −5.4 kcal mol^{-1}, respectively, so, relative to ΔG_{298} for BCOD, +15.5 kcal mol^{-1}, these derivatives are 17.2 and 20.9 kcal mol^{-1} less stable, 38.1 kcal mol^{-1} *in toto*. ΔG_{298} for 6,8-dioxaBCOD is −19.4 kcal mol^{-1}; hence relative to BCOD, it is 34.9 kcal mol^{-1} less stable. Thus, on this accounting, the thermodynamic instability of the 6- and 8-monooxygen derivatives, taken together, slightly exceeds that of the 6,8-dioxa derivative.

The kinetic instability, however, is enhanced in 6,8-dioxaBCOD relative to that in the monooxygen derivatives. For 8-oxaBCOD and 6,8-oxaBCOD, $\Delta E^{\ddagger}_{298}$ = +41.4 and +32.7 kcal mol^{-1}, respectively, so, relative to $\Delta E^{\ddagger}_{298}$ for BCOD, +47.6 kcal mol^{-1}, these derivatives are 6.2 and 14.9 kcal mol^{-1} less stable, respectively, 21.1 kcal mol^{-1} *in toto*. $\Delta E^{\ddagger}_{298}$ for 6,8-dioxaBCOD is +16.5 kcal mol^{-1}; hence, relative to BCOD, it is kinetically 31.1 kcal mol^{-1} less stable, an enhancement of some 10 kcal mol^{-1}.

These results, together with the finding that the $\Delta E^{\ddagger}_{298}$ values for the three-ring fission reactions of BCOD giving cyclooctatriene and methylcycloheptatriene are far in excess of $\Delta E^{\ddagger}_{298}$ for the fission of both rings, suggest that the fission of both rings is a cooperative process.

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Supporting Information Available: *Z*-matrix orientations: Tables 1S–4S, *cisoid* and *transoid* BCOD, *cisoid* and *transoid* 6,8-dioxaBCOD, *cisoid* 6-oxaBCOD, and *cisoid* and *transoid* 8-oxaBCOD; Table 5S, *eZzZz*- and *eEeEe*-octatetraene; Table 6S, *eZzZz*- and *eEeEe*-hexadienedial (muconaldehyde); Tables 7S and 8S, *zZzZe*-, *eZzZz*-, and *eEeEe*-heptatrienal; Table 9S, 2,4,7-cyclooctatriene and 1-methyl-2,4,6-cycloheptatriene; Tables 10S and 11S, BCOD, TS for the Cope rearrangement, TS for the 1,5-hydrogen shift, and TS for the fission giving *eZzZz*-octatetraene; Table 12S, 6,8-dioxaBCOD, TS for the Cope rearrangement, and TS for the fission giving *eZzZz*-hexadienedial; Table 13S, 6-oxaBCOD, TS for the fission giving *zZzZe*-heptatrienal; Table 14S, 8-oxaBCOD, TS for the 1,5-hydrogen shift, and TS for the fission giving *eZzZz*-heptatrienal; and Table 15S, BCOD, TS for the formation of 2,4,7-cyclooctatriene, and TS for the formation of 1-methyl-2,4,6-cycloheptatriene. Total atomic charges:[27] Table 16S, total atomic charges on the C and O atoms in *transoid* BCOD, *transoid* 6,8-dioxaBCOD, *cisoid* 6-oxaBCOD, and *transoid* 8-oxaBCOD, in the transition states, and in the acyclic structures which result from the fission of the three- and seven-membered rings (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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