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DYNAMICS OF SEVEN- AND EIGHT-MEMBERED 1,5-CYCLOALKANE-FUSED SEMIBULLVALENE DERIVATIVES

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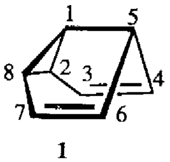
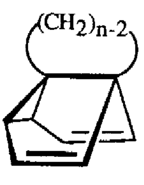
Abstract: The conformations and conformational dynamics of the two title hydrocarbons have been determined by ^1H 500 MHz NMR and molecular mechanics calculations; barriers for the Cope rearrangements are also reported.

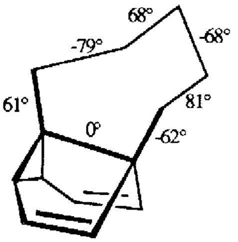
The semibullvalene (SBV) molecule (**1**) has a rigid tricyclic structure (C_s point group symmetry) and thus any cycloalkane ring fused to it at C(1) and C(5), such as occurs in **2** and **3**, is forced to have an eclipsed or nearly eclipsed bond at the ring junction. As a result of this near-zero torsional angle, the SBV-fused cycloalkane ring is expected to show conformational similarities to the corresponding *cis*-cycloalkene and its epoxide rather than to the parent cycloalkane, at least as far as the geometries of the local energy-minimum conformations are concerned.[2] Thus, the lowest energy conformations of the cycloalkane ring should be a chair (**2a**) in **2** and one of the two possible distorted boat-chairs (**3a** and **3b**) in **3** (the torsional angles shown in these structures arise from the molecular mechanics calculations described below). These three conformations are chiral so that their mirror images have to be considered. It is also useful to view the chair in **2a** as being similar in geometry to the transition state for pseudorotation of the twist-chair in cycloheptane. Similarly, the distorted boat-chair in **3a** or **3b** is similar to the transition state for pseudorotation of the boat-chair to the twist-boat-chair in cyclooctane. Conformational barriers in **2** and **3**, it should be noted, need not resemble closely those in the *cis*-cycloalkenes because of differences in the torsional potentials of single bonds at saturated and unsaturated carbon atoms.[2]



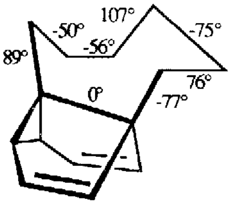
1



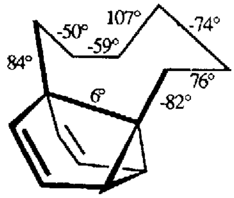
2, n = 7
3, n = 8



2a

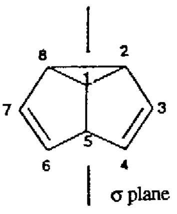


3a



3b

The Cope rearrangement of SBV (**4** ⇆ **5**) has a low free-energy barrier (5.6 ± 0.1 kcal/mol at -140 °C)[3a, 3d] which is expected to be lowered by about 1 kcal/mol by the cycloalkyl methylene substituents in **2** and **3**.[3c, 3d, 4, 5] The symmetry of the transition state for the Cope rearrangement of SBV is not completely clear and the most symmetrical arrangement (**6**), which belongs to the C_{2v} point group, could correspond to a local energy minimum, a twodimensional energy hill, or a saddle point (i.e., a true transition state).[3,4,6] In any case the *time-averaged* symmetry when the Cope rearrangement is fast must be C_{2v}. Structure **6** not only has a plane of symmetry (σ_1) related to σ shown in **4** and **5** but also a second plane of symmetry (σ_2), which is perpendicular to the first plane. The intersection of the two planes defines a C_2 axis (heavy dot in **6**), as required by the C_{2v} point group. These symmetry element designations will also be used for the 1,5-cycloalkane-fused SBV's. There is no reason for the Cope and ring conformational rearrangements to be concerted. To first order these processes should occur independently of one another because if both processes took place simultaneously the energy barriers would add and become prohibitive.



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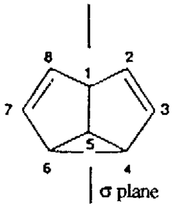

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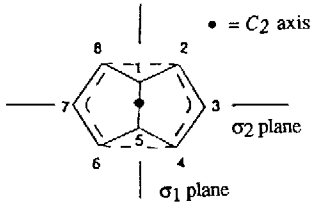

6

Samples of **2** and **3** were prepared in the manner described previously.[7] The thermodynamic and kinetic data as determined by variable temperature ^{1}H NMR measurements at 500 MHz have been compiled in Tables I and II, which also show molecular mechanics results obtained with the Delphi program[8] and three different force fields.[9] The free energy barrier to the Cope rearrangement in **2a** is ca 4.5 kcal/mol as determined from the signals of the 2, 4, 6, and 8 protons at -160 °C, which is the coalescence and lowest temperature reached (a chemical shift difference of 2.8 ppm, as in SBV, is assumed). The Cope equilibrium in **3a**, and **3b** becomes one sided at very low temperatures so that the lines never become extremely broad; at -138 °C the broadening is ca 110 Hz, giving k(minor → major) = 30,000 s^{-1} and $\Delta G^{\ddagger}$(minor → major) = ca 5.0 kcal/mol. Clearly, the Cope rearrangements in **2** and **3** are always fast on the NMR time scale down to at least -130 °C. The $\Delta G^{\ddagger}$'s in **2** and **3** are distinctly lower than the $\Delta G^{\ddagger}$ in SBV itself, but similar to the recently reported $\Delta G^{\ddagger}$ of 4.8 kcal/mol in 1,5-dimethylsemibullvalene at -140 °C.[3d]

Table I. Ring Inversion Barriers[a] (kcal/mol) in the Chair Seven-Membered Ring of **2** as Calculated with Various Force Fields, and Measured by NMR in CF_2Cl_2-$CDCl_2F$

Boyd		Ermer-Lifson		MM2	NMR
ΔSE[b]	$\Delta G^{\ddagger}$	ΔSE	$\Delta G^{\ddagger}$	ΔSE	$\Delta G^{\ddagger}$
12.6	12.2	12.4	12.2	11.3	11.9

[a] The mean sequential ring torsional angles in degrees for the transition state, starting with the two bonds at the cyclopropane carbon, are: -1, -72, 59, -2, -3, -55, and 71.
[b] ΔSE is the difference in steric energy between the ground and the transition state.

The ring inversion in the chair seven-membered ring of **2a** takes place via the following local energy minima: boat (**2b**), twist-boat (**2c**), and inverted twist-boat, where **2b** and **2c** are both about 4.0 kcal/mol above the chair in energy and are thus not significantly populated. When the Cope rearrangement is fast, **2b** and **2c** have C_s and C_2 time-averaged symmetries respectively. The ring inversion path is similar to that in cycloheptene,[2d] with the exception that the chair-to-boat process involves a local inversion of the staggered rather the eclipsed part of the chair. The highest points (i.e., the transition states) on the ring inversion energy path lie between adjacent **2a** and **2b** conformations.

Because of its conformational rigidity, the chair in **2a** has torsional angles that differ from C_s symmetry by only ±1°, whereas the boat in **2b** and the twist-boat in **2c** are flexible and their torsional angles differ from C_s and C_2 symmetry respectively by up to ±5°. The NMR spectrum in the CH_2 region of **2** at -55 °C shows six first-order multiplets in the ratio of 1:2:2:2:2:1 in order of increasing shielding; the SBV resonances are at δ 4.09 (superposed 2H + 2H), 4.99 (1H), and 5.10 (1H). The number of CH_2 shifts and the values of the vicinal coupling constants prove that the seven-membered ring is a chair. Because of the relatively high barrier to ring inversion in **2**, the NMR spectrum (in $CDCl_3$) becomes sharp only above 50 °C. Although this barrier is much higher than that in cycloheptene (5.0 kcal/mol),[2c] it is comparable to that in benzocycloheptene (10.9 kcal/mol).[2a]

Table II. Conformational Equilibrium and Barriers (kcal/mol) in the Boat-Chair Eight-Membered Ring of **3** as Calculated with Various Force Fields, and Measured by NMR in CF_2Cl_2-$CDCl_2F$

	Boyd		Ermer-Lifson		MM2	NMR
Equilibrium	ΔSE[a]	ΔG°	ΔSE	ΔG°	ΔSE	ΔG°
3a $\leftrightarrows$ **3b**	0.35	0.30	0.51	0.45	0.31	±0.38
Transition State	ΔSE	$\Delta G^\ddagger$	ΔSE	$\Delta G^\ddagger$	ΔSE	$\Delta G^\ddagger$
3a $\leftrightarrows$ **3a***[b, c]	6.7	6.4	8.3	8.0	6.6	8.6
3a $\leftrightarrows$ **3a'**[b, d]	8.8	8.6	10.8	10.6	9.2	9.8

[a] ΔSE is defined in Table I. [b] **3a*** and **3a'** differ from **3a** in the labelling of protons. [c] This process, which introduces the time-averaged σ_2 plane shown in **6** when the Cope rearrangement is fast, has a transition state with the following mean ring torsional angles (given as in Table I): -5, 70, -92, 101, 74, -6, 92, and -83. [d] This process, which introduces a time-averaged C_2 axis when the Cope rearrangement is fast, has a transition state defined[c] by: 1, -70, 107, -73, 69, -108, 82, and -8.

The geometries of the distorted boat-chairs in **3a** and **3b** are similar to each other and to the geometry in cyclooctene or in the cyclooctane boat-chair to twist-boat-chair transition state.[6] The ΔG° for **3a**$\leftrightarrows$**3b** is ±0.38 kcal/mol as determined from chemical shift differences of the SBV protons at -113 °C (fast Cope rearrangement), in good agreement with the molecular mechanics results given in Table II. When the Cope rearrangement is fast, the time-averaged σ_2 plane shown in **6** is introduced by a path where the nearly symmetrical form is a chair, which is a transition state between two high-energy twist-chairs, but the actual transition state (i.e. highest point along this path) is very unsymmetrical (Table II, footnote c). The alternate boat path, which gives the same time-averaged symmetry is kinetically insignificant. Finally, the maximum time-averaged symmetry (C_{2v}) is achieved with a process that involves an intermediate with a time-averaged C_2 axis, and the transition state for this process is also very unsymmetrical (Table II, footnote d). The NMR spectrum of **3** shows two dynamic NMR processes between -20 and -125 °C.[10] As shown in Table II, the barriers for the C_s and the C_2 paths are reproduced significantly better by the Ermer-Lifson than by the Boyd or the MM2 force field. For comparison, the C_s and C_2 barriers in *cis*-cyclooctene are 8.2 and 5.3 kcal/mol respectively;[2a] barriers in benzocyclooctene do not appear to be known.

The twelve-membered analog of **2** and **3** was also synthesized, but its NMR spectrum showed that it was a complex mixture of conformations and no molecular mechanics calculations were done on this compound.[11]

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REFERENCES AND NOTES

(1) Philips Petroleum Fellow 1986-1987.

(2) (a) Anet, F. A. L.; Anet, R. in *Dynamic Nuclear Magnetic Resonance Spectroscopy*, Jackman, L. M.; Cotton, F. A., Eds., Academic Press: New York, 1975, p 543. (b) Dale, J. *Top. Stereochem.* **1976**, *9*, 199. (c) St-Jacques, M.; Vaziri, C. *Can. J. Chem.* **1971**, *49*, 1256 (d) St-Jacques, M.; Vaziri, C. *Can. J. Chem.* **1973**, *51*, 1192. (e) Anet, F. A. L. *Top. Curr. Chem.* **1974**, *45*, 169. (f) Anet, F. A. L. in *Conformational Analysis of Medium-Sized Heterocycles*, Glass, R. S., Ed., VCH Publishers: New York, 1988, p 35, and references therein.

(3) (a) Cheng, A. K.; Anet, F. A. L.; Mioduski, J.; Meinwald, J. *J. Am. Chem. Soc.* **1974**, *96,* 2887. (b) Askani, R.; Kalinowski, H.-O.; Weuste, B. *Org. Magn. Reson.* **1982**, *18*, 176. (c) Schneiders, C.; Müllen, K.; Braig, C.; Schuster, H.; Sauer, J. *Tetrahedron Lett.* **1984**, *25*, 749. (d) Moskau, D.; Aydin, R.; Leber,W.; Günther, H.; Quast, H.; Martin, H.-D.; Hassenrück, K.; Miller, L. S.; Grohmann, K. *Chem. Ber.* **1989**, *122*, 925.

(4) Miller, L.S.; Grohmann, K.; Dannenberg, J. J. *J. Am. Chem. Soc.* **1983**, *105*, 6862 and references cited therein.

(5) (a) Quast, H.; Christ, J.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1985**, *118*, 1154, 1176 and earlier references. (b) Paquette, L. A.; Volz, W. E. *J. Am. Chem. Soc.* **1976**, *98*, 2190. (c) See also Iyengar, R.; Piña, R.; Grohmann, K.; Todaro, L. *ibid.* **1988**, *110*, 2643. (d) Jackman, L. M.; Benesi, A.; Mayer, A.; Quast, H.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *ibid.* **1989**, *111*, 1512.

(6) (a) Hoffmann, R.; Stohrer, W. D. *J. Am. Chem. Soc.* **1971**, *93*, 6941. (b) Dewar, M. J. S.; Jie, C. *ibid.* **1987**, *109*, 5893.

(7) (a) Paquette, L. A.; Trova, M. P. *Tetrahedron Lett.* **1987**, *28*, 2795; errata p 4354. (b) Paquette, L. A.; Trova, M. P.; Luo, J.; Clough, A. E.; Anderson, L. B. submitted for publication.

(8) (a) van de Graaf, B.; Baas, J. M. A.; van Veen, A. *Recl. Trav. Chim. Pays-Bas*, **1980**, *99*, 175. (b) van de Graaf, B.; Baas, J. M. A. *J. Comput. Chem.* **1984**, *5*, 314. (c) Anet, F. A. L.; Anet, R. *Tetrahedron Lett.* **1985**, *26*, 5355.

(9) The force field used were: (a) Boyd (Chang, S.; McNally, D.; Shary-Tehrany, S.; Hickey, M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109; Anet, F. A. L.; Yavari, I. *Tetrahedron* **1978**, *34*, 2879), (b) Ermer-Lifson[8c] (Ermer, O. *Structure and Bonding* **1976**, *27*, 161-211; Ermer, O.; Lifson, S. *J. Am. Chem. Soc.* **1973**, *95*, 4121; Ermer, O. *Aspekte von Kraftfeldrechnungen*, Wolfgang Baur: München, 1981), and (c) MM2 (Allinger, N. L. QCPE Program No 395; Burkert, U.; Allinger, N. L. *Molecular Mechanics*, American Chemical Society: Washington, 1982). The following parameter modifications were made: (i) special θ_0 parameters were used at C(1) and C(5) to reproduce the semibullvalene geometry; (ii) the torsional potential about the cyclopropane-ethylenic bond was evaluated from vinylcyclopropane (Klahn, B.; Dyczmons, V. *J. Mol. Struct. (Theochem)* **1985**, *122*, 75); (iii) the Boyd parameters for cyclopropane were used in the Ermer-Lifson force field.

(10) The ^{1}H NMR shifts of **3** at -20 °C are: (a) CH_2: δ 1.30, 1.40, 1.70, (b) SBV_{2468}: δ 4.28, and (c) SBV_{37}: δ 5.1. At -73 °C the SBV lines have split symmetrically (δ 4.20, 4.40, 5.10, 5.18). At -113 °C the SBV_{2468} lines have again split symmetrically, δ 3.50, 3.60, 5.02, 5.32, and the shifts are temperature dependent in the way expected from the equilibrium **3a**$\leftrightarrows$**3b.** The change in the CH_2 resonances are complex but consistent with those of the SBV moiety.

(11) *cis*-Cyclododecene is conformationally complex, Anet, F. A. L.; Rawdah, T. *Tetrahedron Lett.* **1979**, 1943.

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