J. Am. Chem. Soc. 1981, 103, 4458-4465

crystallized from the crude product mixture. Recrystallization as above gave a 69% yield of the ethyl ester: mp 90–90.5 °C; $[\alpha]_D^{20}$ +72° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) 7.6–7.1 (5 H), 5.58 (PhCH), 4.81 (H-1), 4.5–3.5 (m, 7 H), 3.41 (s, OCH_3), 2.67 and 2.58 (CH_2COO, AB spectrum, *J* = 14.6 Hz), 1.20 (t, 3 H).

Degradation of the Reformatsky product with permanganate was carried out as described above and **trimethyl (*S*)-[1,1-$^2H_2$]citrate**, obtained by reaction of the crude acid with diazomethane, was crystallized from ether to give 90 mg (35% yield calculated on the Reformatsky product): mp 76–77 °C; $[\alpha]_D^{20}$ –0.59°, $[\alpha]_{546}^{20}$ –0.73°, $[\alpha]_{365}^{20}$ –2.18° (*c* 6.3, methanol) (lit.[53] mp for trimethyl citrate, 78.5–79 °C); ^{1}H NMR ($CDCl_3$) δ 4.11 (s, 1 H), 3.84 (s, 3 H), 3.69 (s, 6 H), 2.91 and 2.81 (AB spectrum, *J* = 15.5 Hz); mass spectrum, *m/e* (rel intensity) M^+ 236 not observed, 177 (16), 176 (0.65), 145 (100), 144 (15), 103 (37), 101 (39), 59 (31). The abundance of the *m/e* 176 peak shows that a maximum of 3.5% monodeuterated ester is present.

(*S*)-[1,1-$^2H_2$]Citric acid was prepared from the trimethyl ester by hydrolysis with excess (60 mol equiv) aqueous sodium hydroxide (0.5 M, 24 h). Workup as described above for the acids yielded the product; $[\alpha]_D^{20}$ –0.96°, $[\alpha]_{546}^{20}$ –1.13°, $[\alpha]_{436}^{20}$ –1.94° (*c* 5.2, water) [lit.[54] value for the enantiomer, $[\alpha]_{546}^{20}$ +1.03° (*c* 12.6, water)]; optical rotation in saturated solution of ammonium molybdate(VI) as described by Martius and Schorre,[54] $[\alpha]_D^{20}$ –25.9°, $[\alpha]_{546}^{20}$ –31.6°, $[\alpha]_{436}^{20}$ –62.4° (lit.[54] values $[\alpha]_{546}^{20}$ –33.6° and $[\alpha]_{546}^{20}$ +31.9°); ^{1}H NMR (D_2O) δ 3.03 and 2.87 (AB spectrum, *J* = 15.9 Hz).

Acknowledgment. We thank Stiftelsen Bengt Lundvists Minne for a grant (to S.B.). CD spectra were kindly measured by Mr. Jan Glans, Kemicentrum, Lund, mass spectra by Mr. Per Persson, and NMR spectra by Mr. Anders Ericsson, Dr. Ulla Jacobsson (Royal Institute of Technology, Stockholm), and Ms. Lena Liedgren. Discussions with Professor Bengt Lindberg and several other colleagues are gratefully acknowledged.

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(53) Hunäus, P. *Ber. Dtsch. Chem. Ges.* **1876**, *9*, 1749–1752.

(54) Martius, C.; Schorre, G. *Justus Liebigs Ann. Chem.* **1950**, *570*, 140–143.

How Many Rings Can Share a Quaternary Atom?

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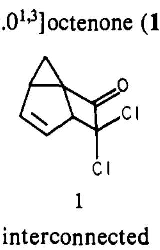
Abstract: With only primary branching, six rings may share a quaternary vertex; with secondary branching, 12 rings may be accommodated. There are two primary bicyclic systems (spiro and fused) and an additional (bridged) system when branching is considered. There are three primary tricyclic systems, termed monofuso, difuso, and trifuso (depending on the number of fusion bonds present); there are another six tricyclic systems involving secondary branching; and examples of all nine tricyclic classes are known. Without secondary branching there are two tetracyclic (trifuso and tetrafuso) and one each pentacyclic and hexacyclic classes. While the tetracyclic and higher classes with secondary branching have not been enumerated, T_d tetraadamantane is shown to possess 12 rings, the maximum possible for this class. Centropolycyclics with three-, four-, five-, and six-membered rings are enumerated and their strain energies are calculated. Although many of these polycyclic systems are known, some unknown ones are energetically accessible and should be stable. For the five-membered ring derivatives (polyquinanes), it is suggested that a small family of polydodecahedranes, analogous to the adamantanes, would be stable. When different ring sizes are allowed, a large number of polycyclics are possible. Strain calculations suggest that the five kinds of unbridged tricyclics containing three-, four-, and five-membered rings should all be reasonably stable. The proposed scheme may find use in categorizing the voluminous literature of polycyclic natural products, including alkaloids. Thus, despite a literature statement that difusotricyclics "remain rare", cephalotaxine, phytotuberin, and the cytochalasins fit this category.

Dichlorotricyclo[5.1.0.0^{1,3}]octenone (**1**), despite the ring strain inherent in this highly interconnected structure, proved to be surprisingly stable.[1] As we attempted to compare **1** with other possible tricyclooctanes, it became apparent that no convenient scheme for categorizing such polycyclic compounds existed. Thus, while the IUPAC rules[2a,b] and a recent graph-based nomenclature[2c] allow even the most complex ring system to be systematically named, it is usually necessary to sketch the skeleton to comprehend a given name; and it is not easy to find a given, say tricyclic, substructure buried in a higher cyclic structure. Certain groups of polycycles have been named and systematized[3] (e.g., adamantanes, polyquinanes, propellanes, fenestranes) but these are not extendable to other classes.



1

In considering how such molecules are assembled, it occurred to us to enumerate the ways that rings can share a common atom. This approach led to a novel way of categorizing such systems and uncovered some interesting and energetically accessible structures that have not yet been reported. Furthermore, we performed empirical force-field calculations and confirmed the potential stability of many of these systems.

How Many Rings Can Share a Vertex?

Consider a carbon atom with four valences directed toward the corners of a tetrahedron. How many rings, all containing that carbon atom, can be constructed? In order to make this problem

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(1) (a) L. A. Carpino, P. Gund, J. P. Springer, and T. Gund, *Tetrahedron Lett.*, **22**, 371 (1981); (b) P. Gund, Ph.D. Thesis, University of Massachusetts, Amherst, MA, 1967.

(2) (a) "Nomenclature of Organic Chemistry", 2nd ed., Butterworths, London, 1971; (b) T. Clark and M. A. McKervey in "Comprehensive Organic Chemistry", Vol. 1, J. F. Stoddart, Ed., Pergamon, Oxford, 1979, p 37; (c) A. L. Goodson, *J. Chem. Inf. Comput. Sci.*, **20**, 172 (1980).

(3) For an excellent review, see A. Greenberg and J. Liebman, "Strained Organic Molecules", Academic Press, New York, 1978.

tractable, we must impose certain restrictions on the analysis. First, we only consider simple rings;[4] clearly an infinite number of complex rings containing the same atom can be traced on the diamond lattice. Second, taking a topological approach,[5] we will consider links of zero to *n* atoms to be equivalent. Third, we initially restrict the analysis to a single branching point from each bond extending from the central carbon. In the final section, we will examine the consequences of removing the last restriction.

Since the central atom is invariant, we may neglect it, and the problem reduces to finding the number of ways of linking four equivalent centers, two at a time:

$$\binom{4}{2} \equiv \frac{4!}{2!(4-2)!} = 6$$

The possible ways rings may meet at a vertex are summarized in Scheme I. There are two topologically distinct ways that two rings may share a vertex: by sharing an atom (spirocyclic) or by sharing a bond (fused). (Bridged systems are topologically equivalent to fused systems; we will explicitly consider the effect of bridging in the last section.) There are three ways that tricyclic systems may share a common vertex: by sharing one fusion bond in common, by sharing two fusion bonds, or by sharing three fusion bonds. We introduce the notation "fuso" to refer to the number of fusion bonds: thus, monofuso-, bifuso-, and trifusotricyclic systems are possible. There are two ways for four rings to share a vertex: by sharing three or four fusion bonds (trifuso- and tetrafusotetracyclic, respectively). Five and six rings may share a common vertex only if there are four fusion bonds. Those systems with fusion atoms linked to only two rings (**2a**, **3b**, **3c**, **4b**) offer the complication of possible cis–trans isomerization.

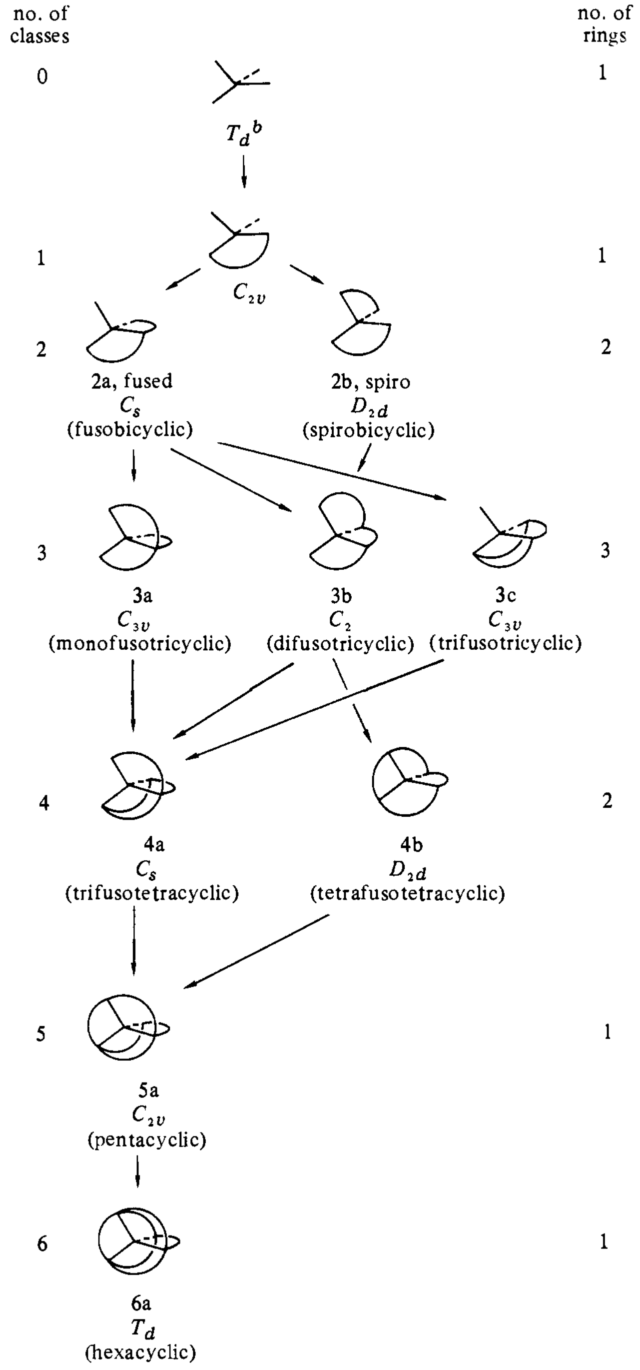
The bicyclic systems—fused and spiro—are well-known. Of the tricyclics, the monofuso systems (**3a**) have been named propellanes.[6] The tetrafusotetracyclics (**4b**) have been called fenestranes, after the four-membered ring derivative that resembles a window pane.[7] Greenberg and Liebman have also referred to the bifusotricyclics (**3b**) as [m.n.p.] fenestranes ("broken windows") and commented that they "remain rare".[8] As we shall see, this rarity has been somewhat exaggerated. Trifusotricyclics are well-known, and some examples are given in later sections. We have found no discussion of classes **4a** or **5a** in the literature; however, very recently interest has been directed to tetrafusohexacyclics **6a** as topologically nonplanar molecules,[9a,b] and the first example of this system has been prepared by two groups.[9b,c]

Classes of Centropolycyclic Structures: Centropolytrinanes

Structures of the types shown in Scheme I were derived by enumerating all arrangements of rings containing the same central atom. Consequently, they may be termed "centropolycyclic". In an attempt to find general rules about preferred isomers in this series, sets of structures having rings of the same size were subjected to strain-energy calculations.[10]

First we consider the class of compounds containing only three-membered rings, termed centropolytrinanes in analogy to Paquette's term, polyquinanes, for five-membered ring polycyclics.[11] The members of this class and their calculated strain energies are collected in Scheme II.

Scheme I. Analysis of Arrangements of Rings about a Central Carbon Atom[a]



[a] Straight lines connect adjacent atoms (vertices); curved lines represent links of 0-*n* atoms. The vertical symmetry, i.e., the pairing of (0,6), (1,5), (2,4), and (3,3) rings, occurs because the operation of adding links to the zero-ring structure is equivalent to removing links from the hexacyclic structure. [b] Symmetry group.

A word or two must be said about calculating strain energies of these highly strained systems. Firstly, we use the Hooke's law angle bending function, which is known to drastically overestimate the strain of cyclopropane; presumably the atom rehybridizes at drastic angle changes rather than acting like a classical rigid spring.[12] Since cyclopropane is assigned a strain energy of only 27.6 kcal,[13] a first-order correction can be made by subtracting

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[4] E. J. Corey and W. T. Wipke, *Science (Washington, D.C.)*, **166**, 178 (1969).

[5] A. T. Balaban, Ed., "Chemical Applications of Graph Theory", Academic Press, London, 1972.

[6] (a) Reference 3, p 343. (b) D. Ginsburg, "Propellanes: Structure and Reactions", Verlag Chemie, Weinheim/Bergstr., Germany, 1975.

[7] (a) Reference 3, p 373. (b) V. Georgian and M. Saltzman, *Tetrahedron Lett.*, 4315 (1972). See also W. T. Hoeve and H. Wynberg, *J. Org. Chem.*, **45**, 2925 (1980), and references therein.

[8] Reference 3, p 374.

[9] (a) H. E. Simons III, Ph.D. Thesis, Harvard University, Cambridge, MA, Nov 1980; (b) H. E. Simons III and J. E. Maggio, *Tetrahedron Lett.*, **22**, 287 (1981); (c) L. A. Paquette and M. Vazeux, *Tetrahedron Lett.*, **22**, 291 (1981).

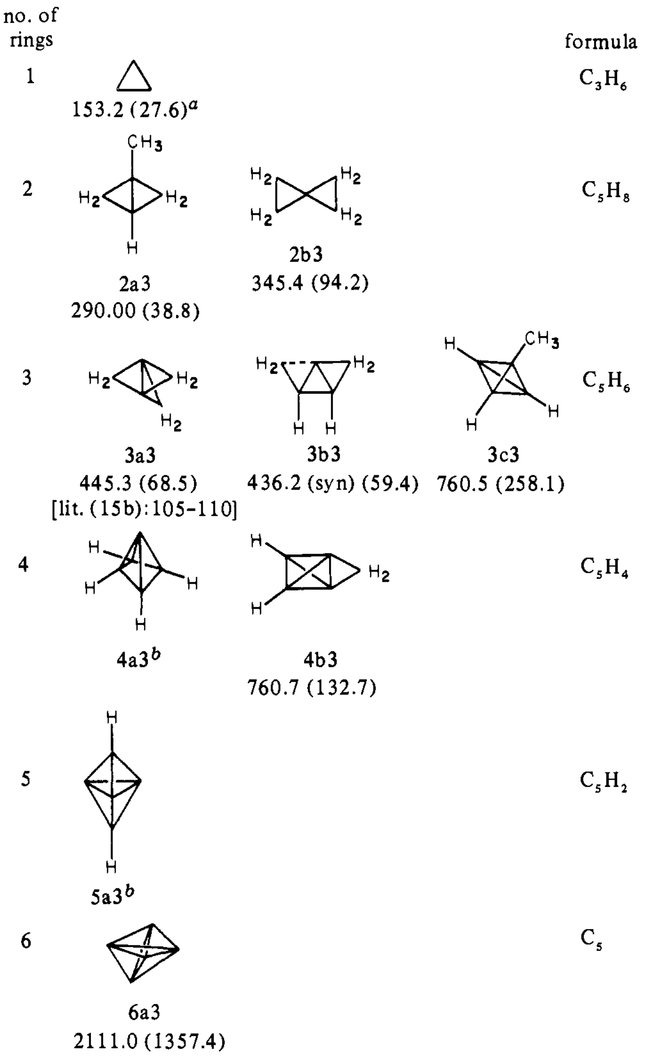
[10] Using the Merck Molecular Modeling System: P. Gund, J. D. Andose, J. B. Rhodes, and G. M. Smith, *Science (Washington, D.C)*, **208**, 1425 (1980). Strain calculations used Boyd's MODBLD II program: R. H. Boyd, S. M. Breitling, and M. Mansfield, *AIChEJ*, **19**, 1016 (1973).

[11] L. A. Paquette, *Top. Curr. Chem.*, **79**, 41 (1979).

[12] Many classical force fields exclude cyclopropanes from consideration: see, for example, N. L. Allinger, *Adv. Phys. Org. Chem.*, **13**, 1 (1976).

[13] L. N. Ferguson, "Highlights of Alicyclic Chemistry", Part I, Franklin Publishers, Palisade, NJ, 1973, p 94.

Scheme II. Centropolytrinanes and Their Strain Energies (kcal)[a]



1 C_3H_6: 153.2 (27.6)[a]

2 C_5H_8: 2a3 290.00 (38.8); 2b3 345.4 (94.2)

3 C_5H_6: 3a3 445.3 (68.5) [lit. (15b): 105-110]; 3b3 436.2 (syn) (59.4); 3c3 760.5 (258.1)

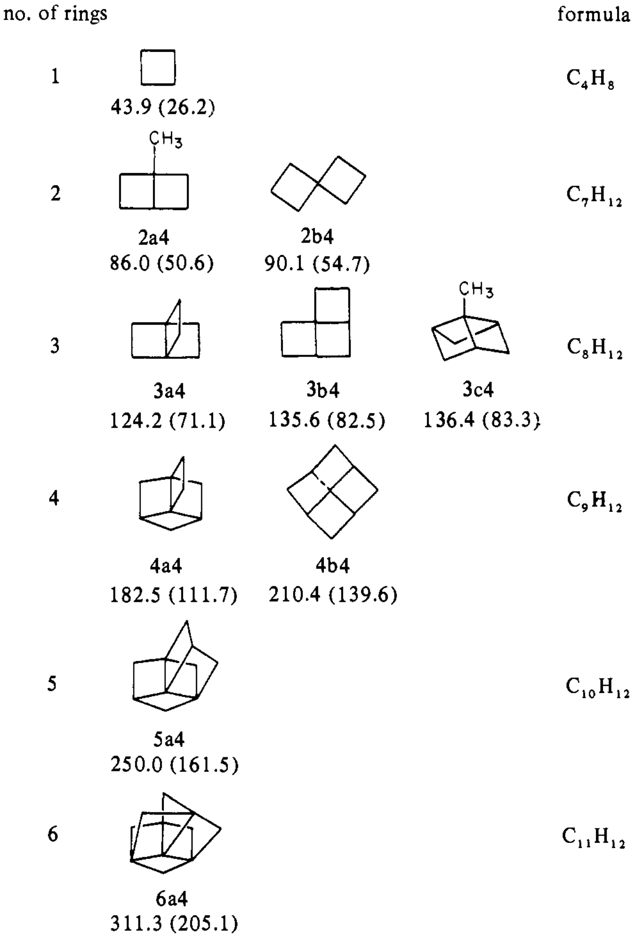
4 C_5H_4: 4a3[b]; 4b3 760.7 (132.7)

5 C_5H_2: 5a3[b]

6 C_5: 6a3 2111.0 (1357.4)

[a] Corrected values in parentheses are obtained by subtracting 125.6 kcal per 3-membered ring. The strain energies should only be used as rough guides of relative stabilities (see text). [b] A strain energy could not be computed.

Scheme III. Centropolyquadranes and Their Strain Energies (kcal)[a]



1 C_4H_8: 43.9 (26.2)

2 C_7H_{12}: 2a4 86.0 (50.6); 2b4 90.1 (54.7)

3 C_8H_{12}: 3a4 124.2 (71.1); 3b4 135.6 (82.5); 3c4 136.4 (83.3)

4 C_9H_{12}: 4a4 182.5 (111.7); 4b4 210.4 (139.6)

5 $C_{10}H_{12}$: 5a4 250.0 (161.5)

6 $C_{11}H_{12}$: 6a4 311.3 (205.1)

[a] Corrected values in parentheses are obtained by subtracting 17.7 kcal per 4 -membered ring (see text). The numbers should only be used as a rough estimate of relative stabilities.

125.6 kcal (153.2 - 27.6) for each cyclopropane ring in the molecule: these are the parenthetical values in Scheme II. Secondly, it is not widely appreciated that the Hooke's law angle bending function is really an inadequate measure of angle strain because it treats each angle independently, whereas motions of angles around an atom are interdependent.[14] For most of the molecules shown in Scheme II, the classical strain-energy program tends to make the atoms square pyramidal (all attachments on the same side, as the top atom in **4a3**) rather than tetrahedral. The calculated strain energies are thus too low for derivatives having all of an atom's attachments on one side of a plane passing through that atom.[15] Finally, for the above and other reasons, the strain energies of these small-ring systems should be taken as very rough measures of relative stabilities and no confidence should be placed in the actual numerical values.

Of the compounds listed in Scheme II, those with two rings (**2a3**, **2b3**) or less (cyclopropane) are the only stable compounds. Compound **3a3** is the simplest propellane and has been studied theoretically[14,16] but remains unknown. Methyltetrahedrane (**3c3**) is unknown and is calculated to be by far the highest in strain energy of the three tritrinanes; it actually contains four three-membered rings. Nonetheless the tetra-*tert*-butyl derivative has been prepared as a stable compound.[17] The difusotritrinane (**3b3**) appears to be the least strained of these three isomers, although our strain-energy program tended to make the central carbon atom square pyramidal. Although we were able to find no mention of **3b3** in the literature, this molecule may yield to synthesis.

Trifusotetrinane (**4b3**) has a strain energy essentially no greater than tetrahedrane; the other tetra-, penta-, and hexatrinanes gave no valid geometry on strain minimization[10] or were impossibly strained. However it has been reported on the basis of MINDO/3 calculations[18] that tetrafusotetrinane (**4a3**) is a true minimum on the C_5H_4 potential energy surface and possesses some kinetic stability.

Centropolyquadranes. Our strain-energy calculations are less in error for cyclobutanes than for cyclopropanes, but a Hooke's law angle bending function still overemphasizes the strain.[12]

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(14) K. B. Wiberg, G. B. Ellison, and J. J. Wendolowski, *J. Am. Chem. Soc.*, **98**, 1212 (1976).

(15) A program developed some time ago at Princeton overcame this problem: W. T. Wipke in "Computer Representation and Manipulation of Chemical Information", W. T. Wipke, S. R. Heller, R. J. Feldmann, and E. Hyde, Eds., Wiley, NY, 1974, p 147; W. T. Wipke, P. Gund, T. M. Dyott, and J. Verbalis, Abstr. 7th Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, PA, Feb 1972, p 42. Tetrahedral hybridization of carbon in small ring strained systems was enforced by two empirical functions. A *chirality* function preserved given chirality at an atom by adding a strain penalty if the fourth substituent was not on the proper side of a plane containing the other three substituents. A *hybridization* function optimized the sum of the four *smallest* angles (out of six around carbon) to ≥380°. These functions are also used in Jurs' MOLMEC program: A. J. Stuper, W. E. Brügger, and P. C. Jurs, "Computer Assisted Studies of Chemical Structure and Biological Function", Wiley, NY, 1979, p 83.

(16) (a) Reference 3, p 348; (b) M. D. Newton and J. M. Schulman, *J. Am. Chem. Soc.*, **94**, 773 (1972).

(17) G. Maier, S. Pfriem, U. Schäfer, and R. Matusch, *Angew. Chem., Int. Ed. Engl.*, **17**, 520 (1978).

(18) V. I. Minkin and R. M. Minyaev, *Zh. Org. Khim.*, **15**, 225 (1979).

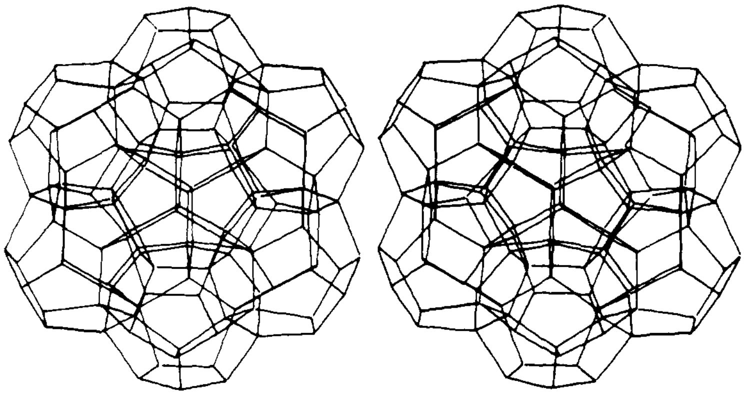


Figure 1. Stereoscopic view of a tridecadodecahedrane model. Twelve dodecahedra surround the central one.

Consequently we have corrected the strain energies in Scheme III by subtracting 17.7 kcal (43.9 - 26.2[13]) for each cyclobutane ring: the corrected values are shown in parentheses.

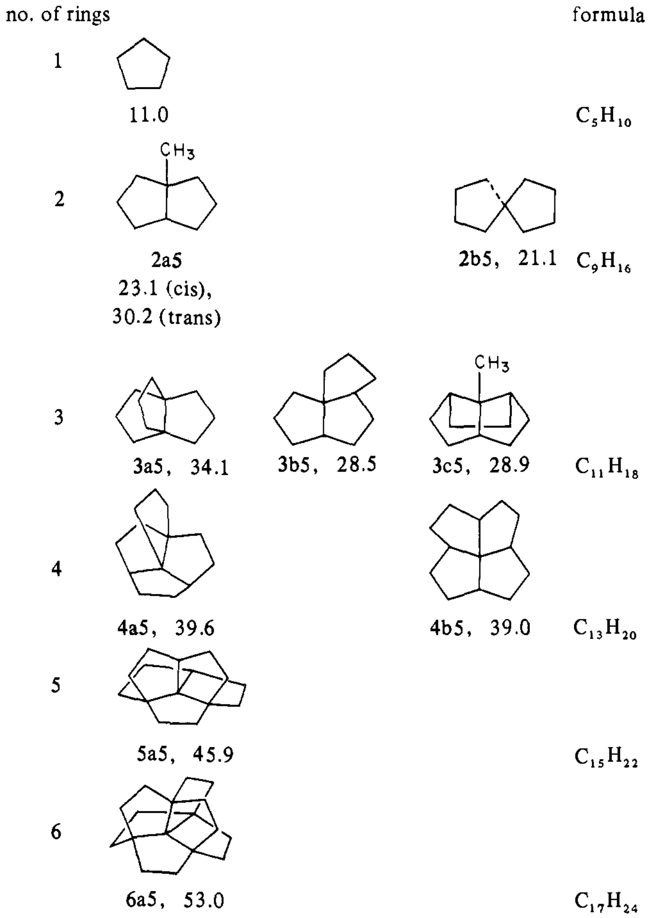
The biquadranes (**2a4**[19] and **2b4**[20]) are known compounds. Monofusotriquadrane or tricyclo[2.2.2]octane (**3a4**) has been studied extensively from a theoretical perspective[21] and has been prepared as an unstable intermediate by several routes.[22] A stable amide derivative is known.[22d] Greenberg and Liebman report estimates of 74–110 kcal/mol for the strain energy of **3a4**, depending on the method.[21a] The more highly strained difusotriquadrane **3b4** ([4.4.4] fenestrane[8] or tricyclo[4.2.0.0^{1,4}]octane) was very recently prepared.[23] The trifusotriquadrane **3c4** (tricyclo[3.1.1.0^{3,6}]heptane) may be formally derived by replacing the three axial hydrogens on one side of chair cyclohexane with bonds to a central carbon; it is at least as strained as **3b4**, but derivatives have been reported.[24]

Of the tetraquadranes, the trifuso isomer (**4a4**) is the lower in energy but appears to be unreported. The tetrafuso isomer (**4b4**) (fenestrane) remains unknown as discussed by Greenberg and Liebman.[7a,b] It is interesting that Georgian and Saltzman originally proposed that it might contain a planar central carbon, but our strain-minimized structure has a decidedly nonplanar central carbon (bond angles 102 and 132°, out-of-plane angles 40 and 60°). For comparison Wiberg[23] recently reported molecular mechanics calculations for **4b4** (bond angles 100 and 130°, strain energy 183 kcal) and **3b4** (strain energy 91 kcal). Stereoisomers of **4b4** having three or four cis hydrogens would have a more planar central atom but would be much higher in strain energy.

The pentacyclic (**5a4**) and hexacyclic (**6a4**) structures appear too strained to exist; amusingly the latter is formally obtained by removing the hydrogens from the four methine carbons of adamantane and inverting and bonding these carbons to a bare carbon atom in the center.

Centropolyquinanes. Paquette has recently reviewed the chemistry of the polyquinanes,[11] culminating in the challenging synthetic objective, dodecahedrane ($C_{20}H_{20}$).[25] The centropolyquinanes and their strain energies are collected in Scheme IV. The strain energies are expected to be quite accurate for this series, which in some ways is the most interesting group; none of the members of this series is intolerably strained. The bicyclic derivatives are comparable to energy, and both are known. All three tricyclics are comparable in energy (the difusotricyclic is lowest), and all are known, at least as derivatives.[26]

Scheme IV. Centropolyquinanes and Their Strain Energy (kcal)



The unreported tetrafusotetraquadrane (**4b5**), dubbed "staurane",[27] and the corresponding tetraene are highly sym-

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(19) B. Andersen and R. Srinivasan, *Acta Chem. Scand.*, **26**, 3468 (1972).

(20) B. Weinstein, A. H. Fenselau, and J. G. Thoene, *J. Chem. Soc.*, 2281 (1965).

(21) (a) Reference 3, p 357; (b) "Modern Theoretical Chemistry", Vol. 4, H. F. Schaefer, Ed., 1977, pp 223–68; (c) W. D. Stohrer and R. Hoffmann, *J. Am. Chem. Soc.*, **94**, 779 (1972).

(22) (a) K. B. Wiberg, G. A. Epling, and M. Jason, *J. Am. Chem. Soc.*, **96**, 912 (1974); (b) J. J. Dannenberg, T. M. Prociv, and C. Hutt, *Ibid.*, **96**, 913 (1974); (c) K. B. Wiberg, W. E. Pratt, and W. F. Bailey, *Ibid.*, **99**, 2297 (1977); (d) P. E. Eaton and G. H. Temme III, *Ibid.*, **95**, 7508 (1973).

(23) K. B. Wiberg, L. K. Olli, N. Golembeski, and R. D. Adams, *J. Am. Chem. Soc.*, **102**, 7467 (1980).

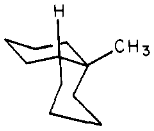
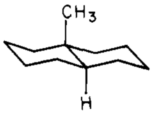
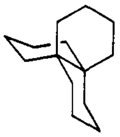
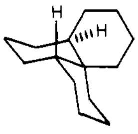
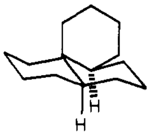
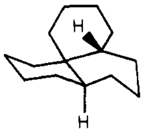
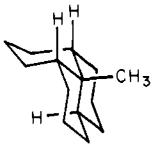
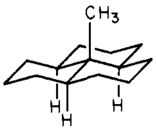
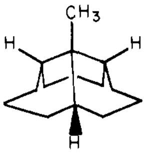
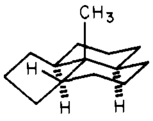
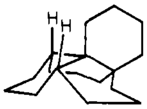
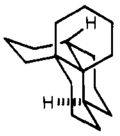
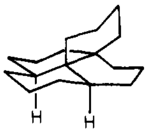
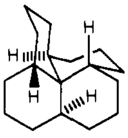
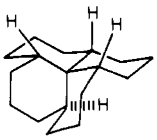
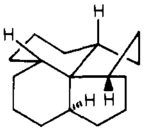
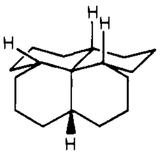
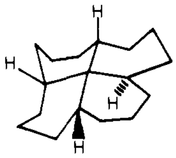
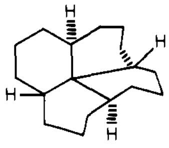
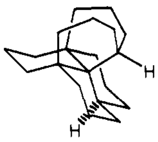
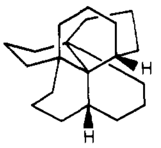
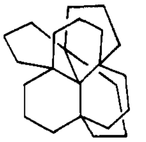
(24) (a) J. M. Harless and S. A. Monti, *J. Am. Chem. Soc.*, **96**, 4714 (1974); (b) S. A. Monti and J. M. Harless, *Ibid.*, **99**, 2690 (1977).

(25) P. E. Eaton, *Tetrahedron*, **35**, 2189 (1979).

(26) (a) Monofusotricyclic: J. Altman, E. Cohen, T. Maymon, J. B. Petersen, N. Reschef, and D. Ginsburg, *Tetrahedron*, **25**, 5115 (1969); R. W. Weber and J. M. Cook, *Can. J. Chem.*, **56**, 189 (1978); T. Prange, J. Drouin, F. Leyendecker, and J. M. Conia, *J. Chem. Soc., Chem. Commun.*, 430 (1977); see also ref 6b. (b) Difusotricyclic: A. Alexakis, M. J. Chapdelaine, and G. H. Posner, *Tetrahedron Lett.*, 4209 (1978); J. Oehldrich, J. M. Cook, and U. Weiss, *Tetrahedron Lett.*, 4549 (1976). Dibenzo derivative: W. T. Hoeve and H. Wynberg, *J. Org. Chem.*, **45**, 2930 (1980). (c) Trifusotricyclic (perhydroquinacene): I. T. Jacobson, *Acta Chem. Scand.*, **21**, 2235 (1967); L. A. Paquette, G. V. Meehan, and S. J. Marshall, *J. Am. Chem. Soc.*, **91**, 6779 (1969); T. Clark, T. McO. Knox, H. Mackle, and M. A. McKervey, *J. Chem. Soc., Chem. Commun.*, 666 (1975).

(27) R. Mitschka, J. M. Cook, and U. Weiss, *J. Am. Chem. Soc.*, **100**, 3973 (1978).

Scheme V. Centropolysexanes and Their Strain Energies (kcal)[a]

no. of rings					formula	no. of isomers
1	 4.0				C_6H_{12}	1
2	 cc,[b] 2a6 (cis), 8.0	 cc, 2a6′ (trans), 6.2	 tt,[c] 2b6, 18.8		$C_{11}H_{20}$	3
3	 ccc, 3a6 (cis), 17.2	 ccc, 3b6 (cis,cis), 15.6	 ccc, 3b6′ (trans,cis), 15.9	 cct,[c] 3b6″ (trans,trans), 27.8	$C_{14}H_{24}$	8
	 ccc, 3c6 (cis,cis,trans), 30.9	 ccc, 3c6′ (trans,trans,trans), 14.7	 cct,[c] 3c6″ (cis,cis,cis), 23.7	 cct,[c] 3c6‴ (cis,trans,trans), 23.7		
4	 cctc,[c] 4a6 (cis,cis,cis), 35.1	 cccc, 4a6′ (cis,cis,trans), 36.6	 cctc,[c] 4a6″ (cis,trans,trans), 35.9	 ccct,[c] 4b6 (cis,cis,cis,cis), 37.0	$C_{17}H_{28}$	9
	 ctct,[c] 4b6′ (cis,cis,cis,trans), 40.4	 cttt,[c] 4b6″ (cis,cis,trans,trans), 50.5	 cctt,[c] 4b6‴ (cis,trans,cis,trans), 64.9	 bttt,[c] 4b6⁗ (cis,trans,trans,trans), 76.7		
	 tttt,[c] 4b6^{v} (trans,trans,trans,trans), 114.9					
5	 ccctt,[c] 5a6 (cis,cis,cis,trans), 49.7		 ccttt,[c] 5a6′ (cis,cis,cis,cis), 60.2		$C_{20}H_{32}$	2
6		 cttttt,[c] 6a6 (all cis), 89.7			$C_{22}H_{36}$	1

[a] Cis,trans refers to configuration at each ring fusion bond. [b] Computed conformation (c = chair, b = boat, t = twist boat) of component rings. [c] Does not fit the diamond lattice.

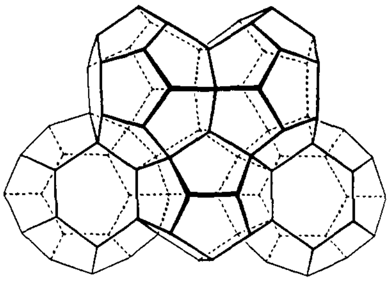


Figure 2. A space-filling arrangement of dodecahedra and tetrakaidecahedra which could be assumed by carbon (taken from ref 32b with permission).

metrical (D_{2d}) and might have interesting properties. A tetraketone[27] and tetraaza analogue[28] have been described. While the trifusotetra- and pentacyclic derivatives appear not to have been reported, they should all be stable compounds. A trioxahexaquinane has very recently been prepared.[9]

Contemplating the hexaquinane (**6a5**), it appeared that this structure might be extensible in three dimensions to fill space in an alternative to the diamond structure of carbon. When this was tried with models, it became apparent that four dodecahedra can join at the central carbon of **6a5**. This structure can repeat but only with distortion of the dodecahedra. A crude model of the structure with 13 dodecahedra is shown as Figure 1.[29]

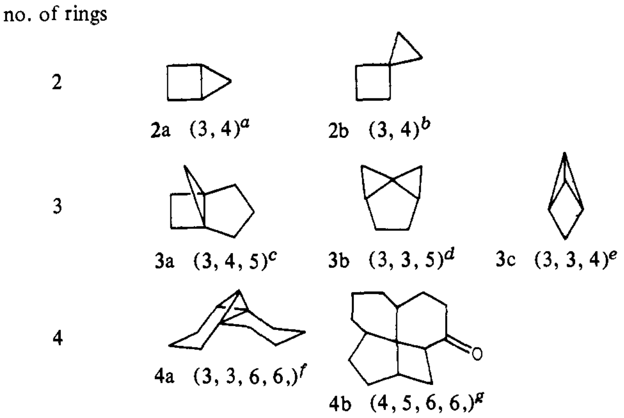
In principle, multiple dodecahedra may be generated just as multiple adamantane units form the members of the diamondoid family,[30] although the distortion of the dodecahedra (108° internal angle) will eventually limit the size attainable. Wells[31] described this system as an infinite radiating net, of point symbol 5^6, centered on a pentagonal dodecahedron and "surrounded by a shell of 12 dodecahedra, which is succeeded by further shells of dodecahedra". A less regular space-filling arrangement of dodecahedra is also possible; this arrangement, sketched in Figure 2, appears in the $Cl_2{:}8H_2O$ clathrate crystal.[32] This may represent an alternative form of solid carbon which should not be impossibly strained—although the diamond lattice is less strained.

Centropolysexanes. These structures tend to be more crowded, more flexible, and more strained than the corresponding polyquinanes. In several cases, they offer the further complication of stereoisomerism. Scheme V displays the centropolysexanes and their computed strain energies (since no exhaustive search of alternative conformations was attempted, it is possible that lower energy conformations could exist for some of the species).

The cis and trans decalins (**2a6**, **2a6′**) are well-known, as is the [5.5]spiroundecane (**2b6**).[33] Other known systems include fusotricyclic (**3a6**),[34] difusotricyclic (e.g., **3b6**),[35] and trifusotricyclic (e.g., **3c6′**)[36] derivatives.

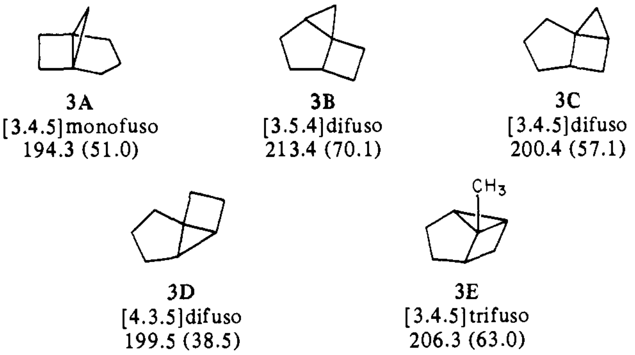
Many of the lower members can be made to fit the diamond lattice; however, most of the higher members cannot. Polyadamantanes do not fit the present scheme because carbons β to the central atom are involved in additional rings (β branching); in the last section, Scheme I is extended to embrace such branched structures.

Scheme VI. Small-Ring Mixed Centropolycyclanes of Each Type (Component Ring Sizes in Parentheses)



[a] R. Criegee and A. Rimmelin, *Chem. Ber.*, 90, 414 (1957); [b] D. E. McGreer, *Can. J. Chem.*, 38, 1638 (1960); [c] reference 37a; [d] L. Skatteboel, *J. Org. Chem.*, 31, 2789 (1966); [e] G. D. Andrews and J. E. Baldwin, *J. Am. Chem. Soc.*, 99, 4851 (1977); [f] R. Vaidyanathaswamy and D. Devaprabhakara, *Chem. Ind. (London)*, 515 (1968); [g] Reference 8.

Scheme VII. Tricyclics with Three-, Four-, and Five-Membered Rings and Their Strain Energies (kcal)[a]

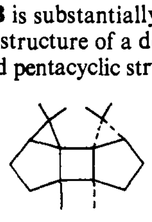


[a] Strain energies in parentheses were corrected by subtracting 143.3 and 17.7 kcal for the presence of the three- and four-membered rings, respectively (see text). These strain energies are only rough indications of relative stabilities.

Mixed Centropolycyclics. Allowing different sized rings gives rise to a large number of new systems possessing moderate strain energy. In Scheme VI are collected the lowest ring size members of each type of system that we were able to find. We know of no examples of mixed centropenta- or sexacyclic compounds.

We have a particular interest in tricyclics containing three-, four-, and five-membered rings.[1] The five possible isomers of this type are shown in Scheme VII, with their computed strain energies. As in Schemes II and III, the strain values are corrected by subtracting the errors for three- and four-membered rings. The monofusotricyclic **3A** is a stable compound, and the crystal structure of a derivative has been reported.[37] The strain energy of **3A** was previously estimated to be 85 kcal/mol.[37]

The difusotricyclic **3B** is substantially higher in strain energy; nevertheless, the crystal structure of a derivative (**1**) has recently been reported.[1] A related pentacyclic structure (**2**) is also stable.[38]



2

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(28) J. E. Richman and H. E. Simmons, *Tetrahedron*, **30**, 1769 (1974).

(29) We thank Dr. Graham Smith for creating this structure.

(30) (a) R. C. Fort, Jr., "Adamantane: The Chemistry of Diamondoid Molecules", Marcel Dekker, New York, 1976; (b) A. T. Balaban and P. v. R. Schleyer, *Tetrahedron*, **34**, 3599 (1978).

(31) A. F. Wells, "Three-dimensional Nets and Polyhedra", Wiley, New York, 1977, p 19.

(32) (a) L. Pauling and R. E. Marsh, *Proc. Natl. Acad. Sci. U.S.A.*, **38**, 112 (1952); (b) L. Pauling, "Nature of the Chemical Bond", 3rd ed., Cornell University Press, Ithaca, NY, 1960, p 469. (c) Clathrate structures involving dodecahedra and other polyhedra have been reviewed: G. A. Jeffrey and R. K. McMullan, *Progr. Inorg. Chem.*, **8**, 43 (1967).

(33) J. A. Dixon and P. A. Naro, *J. Org. Chem.*, **25**, 2094 (1960).

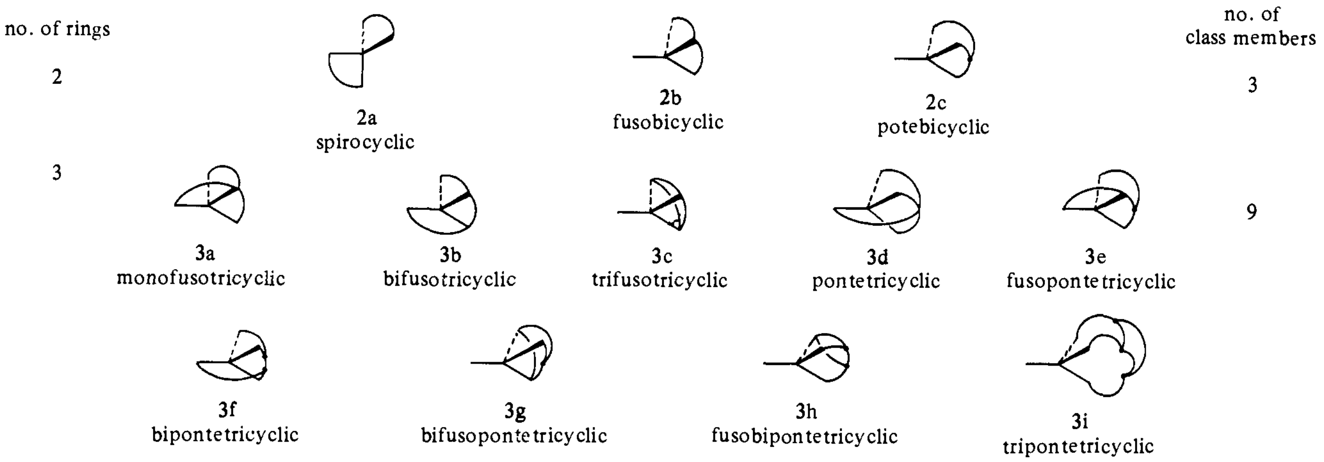
(34) J. Altman, D. Becker, D. Ginsburg, and H. J. E. Leewenthal, *Tetrahedron Lett.*, 757 (1967).

(35) Reference 3, p 374.

(36) 1*H*-Phenalene: G. Lock and G. Gergely, *Chem. Ber.*, **77**, 461 (1944).

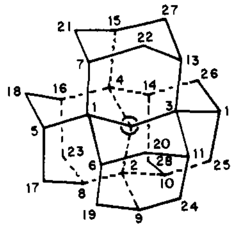
(37) (a) K. B. Wiberg and G. J. Burgmaier, *J. Am. Chem. Soc.*, **94**, 7396 (1972); (b) K. B. Wiberg, G. J. Burgmaier, K. W. Shen, S. J. LaPlaca, and W. C. Hamilton, *Ibid.*, **94**, 7402 (1972).

Scheme VIII. Extended Analysis of Arrangements of Rings about a Central Carbon, Allowing Secondary Branching



2a spirocyclic
2b fusobicyclic
2c potebicyclic
3a monofusotricyclic
3b bifusotricyclic
3c trifusotricyclic
3d pontetricyclic
3e fusopontetricyclic
3f bipontetricyclic
3g bifusopontetricyclic
3h fusobipontetricyclic
3i tripontetricyclic

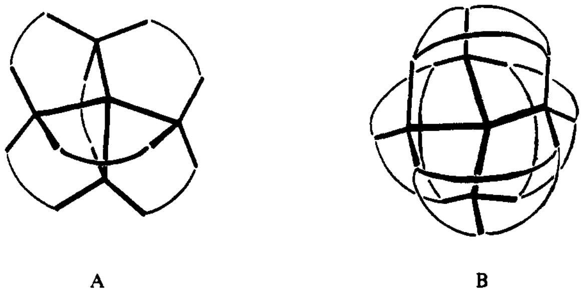
Scheme IX. Rings (12) Sharing a Common Vertex in a T_d Tetraadamantane



rings sharing vertex 0:

(1)	0	1	6	20	11	3
(2)	0	1	6	19	9	2
(3)	0	1	5	18	16	4
(4)	0	1	5	17	8	2
(5)	0	1	7	22	13	3
(6)	0	1	7	21	15	4
(7)	0	2	10	25	12	3
(8)	0	2	9	24	11	3
(9)	0	2	10	28	14	4
(10)	0	2	8	23	16	4
(11)	0	3	13	27	15	4
(12)	0	3	12	26	14	4

Scheme X. Construction of Centropolycyclic and Diamondoid Series from Different Isomers of Tetra-*tert*-butylmethane


A B

The alternative difusotricyclic structures (**3C** and **3D**) surprisingly are substantially lower in strain energy than **3B** but are unknown; a report of an unsaturated derivative of **3D**[39] is clearly a typographical error. The trifusotricyclic isomer (**3E**) is also known.[40] It would thus appear that many more small-ring tricyclics are capable of existence than have heretofore been reported and may prove to be quite stable; Wiberg[23] attributed the surprising lack of reactivity of **3b4** to steric hindrance to attack on the fusion bonds—an argument that may apply to most difusotricyclics.

Allowing Secondary Branching, How Many Rings Can Share a Common Vertex? Returning to Scheme I, it is apparent that a common class of bicyclic structures is missing—namely, bridged bicyclics. Such structures (**2c** in Scheme VIII) may be constructed by two equivalent operations: (1) elongating the fusion bond with a vertex atom and an arc (link of 0–*n* atoms) or (2) breaking a link to the vertex and reconnecting it to a new vertex in the middle of an arc. (Note that the resulting new vertex is no longer adjacent to the central vertex.) We call **2c** pontebicyclic after the French "ponte", meaning "bridging bonds or atoms".

Similarly, bridged tricyclic isomers may be systematically generated by transforming each of the three simple tricyclics by all combinations of bond elongation and vertex reconnection, repeating the operations on any new structures and eliminating duplicates. In this way there was generated **3d** (from **3a**), **3e** (from **3a** and **3b**), **3f** (from **3d** and **3e**), **3g** and **3h** (from **3c**), and **3i** (from **3h**), as summarized in Scheme VIII. Similar construction of bridged tetra-, penta-, and hexacyclics should be straightforward and is left as an exercise for the industrious reader.

It is clear from inspection of, e.g., structure **3i** of Scheme VIII that additional rings to the central carbon may be formed by linking to the unappended vertex. Similarly, elongation of the four fusion bonds of structure **4b** (Scheme I) affords new vertices which may be connected by six new links. The resulting, ultimate centrododecacyclic system is shown as the prototypical T_d tetraadamantane structure of Scheme IX, which has not been reported in the literature.

An alternative way to differentiate the primary and the secondary branched centropolycyclics is shown in Scheme X. Joining the various carbons of the all eclipsed conformation of tetra-*tert*-butylmethane (A) gives rise to the simple centropolycyclics. Twisting the *tert*-butyl groups to the all-staggered conformation and joining the ends pairwise (B) lead to the branched centropolycyclics. The differentiation is lost for the centropolysexanes, which are flexible enough to often adopt the staggered conformation, even for the simple series.

Surprisingly, examples of all of the branched tricyclic classes are known. Representative structures are shown in Scheme XI. The pontetricyclics (**3d**) are called "paddlanes" and a small number of examples are known.[41] The other classes do not appear to have been systematically named.

Many natural products are conveniently classified by these schemes. The difusotricyclics appear to be more prevalent and important than might have been expected from the comment of Greenberg and Liebman;[8] phytotuberin[42] (**3**), cephalotaxine[43] (**4**), and the cytochalasins [e.g., cytochalasin B[44] (**5**)] all fall into this

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[38] M. Rule and J. A. Berson, *Tetrahedron Lett.*, 3191 (1978).

[39] L. A. Paquette and J. C. Philips, *J. Am. Chem. Soc.*, **91**, 3973 (1969); *Chem. Abstr.*, **71**, 90909 (1969), indexed erroneously as a **3D** structure.

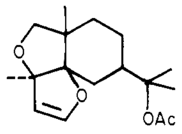
[40] D. D. Davis and H. T. Johnson, *J. Am. Chem. Soc.*, **96**, 7576 (1974).

[41] (a) Reference 3, p 366; (b) E. H. Hahn, H. Bohm, and D. Ginsberg, *Tetrahedron Lett.*, 507 (1973).

[42] D. L. Hughes and D. T. Coxon, *J. Chem. Soc., Chem. Commun.*, 822 (1974).

[43] R. G. Powell, D. Weisleder, C. R. Smith, Jr., and I. A. Wolff, *Tetrahedron Lett.*, 4081 (1969).

category. The often tortuously complex alkaloids may sometimes be classified by these schemes; thus, lycopodine[45] (**6**) is trifusopontetracyclic; lycoflexine[46] (**7**) is trifusopontetetracyclic at the internal tetrasubstituted carbon; and lycopecurine[47] (**8**) is trifusodipontepentacyclic.



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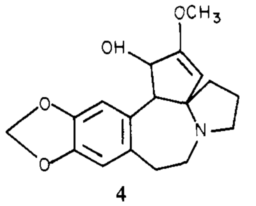

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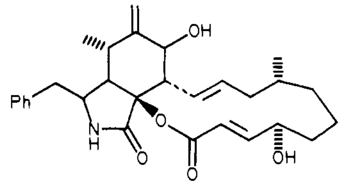

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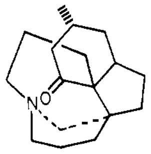
6



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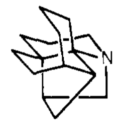


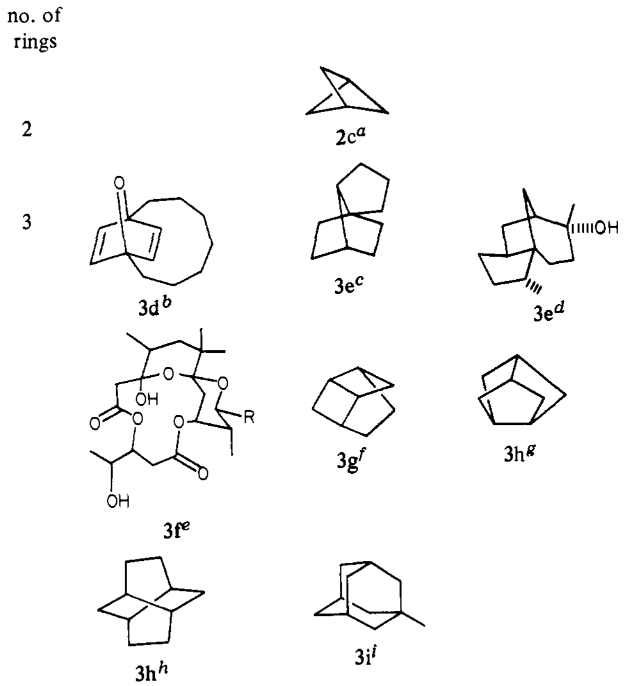
8

This classification system may also be useful in other areas involving tetracoordinate central atoms in polycycles: for example, tetracoordinate borate and transition metals. Finally, it is possible that this scheme could be extended to pentacoordinate systems, such as tricyclic phosphoranes,[48] and hexacoordinate systems.

Conclusions

Without secondary branching, there are two bicyclic, three centrotricyclic, and two centrotetracyclic isomers as well as one centropentacyclic and one centrohexacyclic structure. The structures composed of three-membered rings (polytrinanes) appear to be unstable with more than two rings. The four-membered ring system (polyquadranes) are mostly known through the tricyclics, as are the five-membered ring system members (polyquinanes). It appears that polydodecahedranes could exist although some distortion of the structure is required. Due to increased flexibility stereoisomers must be considered for the centropolysexanes: three bicyclic, eight tricyclic, two pentacyclic, and one hexacyclic isomers were enumerated and their strain computed; derivatives through the tricyclics are mostly known. The first example of a hexacycloquadrane has just been reported.

Scheme XI. Examples of Secondary Branched Centropolycyclics



[a] J. F. Chiang and S. H. Bauer, *J. Am. Chem. Soc.*, 92, 1614 (1970); [b] R. Helder and H. Wynberg, *Tetrahedron Lett.*, 4321 (1973); [c] F. J. Jäggi and C. Ganter, *Helv. Chem. Acta*, 63, 214 (1980); [d] cedrol: G. Stork and F. H. Clarke, *J. Am. Chem. Soc.*, 83, 3114 (1961); [e] Y. Kato and P. J. Scheuer, *J. Am. Chem. Soc.*, 96, 2245 (1974); [f] R. Askani and W. Schwertfeger, *Chem. Ber.*, 110, 3046 (1971); [g] bisnoradamantane: P. K. Freeman, V. N. Mallikarjuna Rao, and G. E. Bigam, *J. Chem. Soc., Chem. Commun.*, 511 (1965); J. A. Jenkins, R. E. Doehner, Jr., and L. A. Paquette, *J. Am. Chem. Soc.*, 102, 2131 (1980); [h] ditwistane: K. Hirao, T. Iwakuma, M. Taniguchi, E. Abe, O. Yonemitsu, T. Date, and K. Kotera, *J. Chem. Soc., Chem. Commun.*, 691 (1974); [i] Methyladamantane: see ref 28.

When different ring sizes are allowed, a large number of polycyclics may be categorized according to this scheme. We consider explicitly the five unbridged tricyclics containing three-, four-, and five-membered rings and suggest all should be stable.

When secondary branching is allowed, up to 12 rings may share the same vertex, as demonstrated for the T_d tetraadamantane (Scheme IX). The expanded scheme accommodates three bicyclic (the new isomer is bridged) and nine tricyclic isomers; examples of all of these classes are known. Finally, the scheme is suggested to be useful for categorizing polycyclic natural products and tetracoordinate bridged complexes.

Certainly in the literature there is a mass of tricyclic and polycyclic compounds of diverse structure. It is our hope that the present scheme will help categorize and organize that mass.

Acknowledgment. We thank Drs. Regina Mladineo, Bernhard Schlegel, Graham Smith, and Jim Springer for helpful discussions and Drs. Leo Paquette and Howard E. Simmons III for supplying useful preprints.

Supplementary Material Available: Stereoscopic views of the centropolycyclic compounds modeled for this study (9 pages). Ordering information is given on any current masthead page.

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(44) For example, G. M. McLaughlin, G. A. Sim, J. R. Kiechel, and Ch. Tamm, *J. Chem. Soc., Chem. Commun.*, 1398 (1970).

(45) M. U. Haque and D. Rogers, *J. Chem. Soc., Perkin Trans. 2*, 93 (1975).

(46) W. A. Ayer, Y. Fukazawa, P. P. Singer, and B. Altenkirk, *Tetrahedron Lett.*, 5045 (1973).

(47) W. A. Ayer and N. Masaki, *Can. J. Chem.*, **49**, 524 (1971).

(48) D. B. Denney, D. Z. Denney, P. J. Hammond, C. Huang, and K. S. Tseng, *J. Am. Chem. Soc.*, **102**, 5073 (1980).