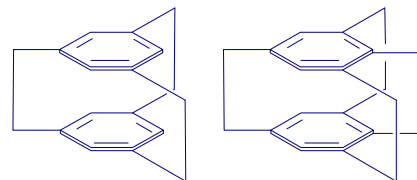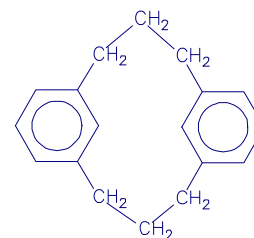52. Shown to the right are [2.2.2](1,3,5)-cyclophane and [2.2.2.2](1,2,3,5)-cyclophane. Do MM calculations of each of these as well as on <u>all</u> of the other two-carbon bridged structures: (1,2,3)-, (1,2,4)-, (1,2,3,4)-, (1,2,4,5)-, (1,2,3,4,5)-, and (1,2,3,4,5,6)-cyclophane; the latter is known as "superphane." Compare the computed angles and distances with those measured by X-ray crystallography (see the cited article).
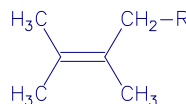[Sekine, Y.; Boekelheide, V. *J. Am. Chem. Soc.* **1991,** *103,* 1777 and references cited therein; also Gleiter, R.; Kratz, D. *Acc. Chem. Res.* **1993,** *26,* 311.]

53. Shown to the right is [3.3](1,3)-cyclophane. There are at least five reasonable conformations for this compound (see the cited article). Use molecular mechanics to calculate the energy and geometry of each of these five conformations; assess which factors are responsible for the energy differences among the conformations.
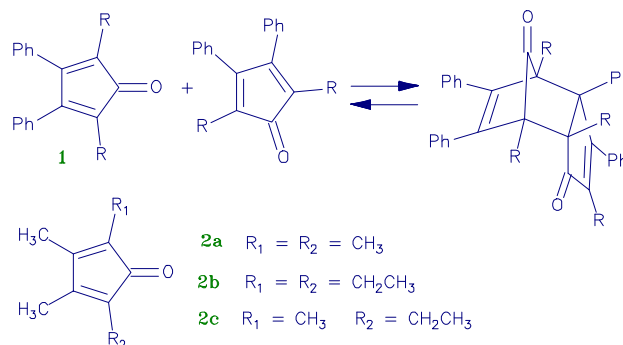[Biali, S. E. *J. Chem. Educ.* **1990,** *67,* 1039.]

54. Use molecular mechanics to calculate the energies and geometries of a series of tetrasubstituted alkenes where R is H, Me, Et, iPr, or tBu. Compare your answers with those in Chart I and Table III of the first-cited reference. (Don't bother trying to reproduce the rotational barriers of Chart II because these are in doubt, as indicated by the second-cited reference.)
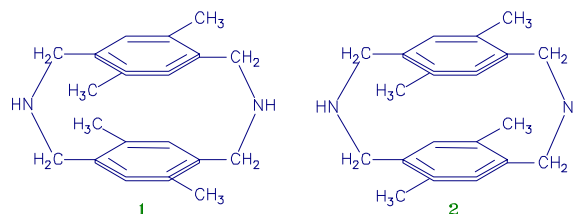[Clennan, E. L.; Chen, X.; Koola, J. J. *J. Am. Chem. Soc.* **1990,** *112,* 5193; Orfanopoulos, M.; Stratakis, M.; Elemes, Y.; Jensen, F. *J. Am. Chem. Soc.* **1991***, 113*, 3180.]

55. The Diels-Alder dimerization of cyclopentadienones has been well studied. A recent paper reports experimental work and molecular mechanics calculations on the dimerization of compound **1** where both R's are methyl, both are ethyl, or one is methyl and one ethyl. To make your calculation more manageable, compute the MMX energy of the dimer of tetramethyl compound **2a**, of dimethyldiethyl compound **2b**, and of the <u>four</u> possible dimers of trimethylethyl compound **2c**. Compare the energy trends in your answers with those obtained experimentally and computationally for the dimers of **1**.
[Weiss, H. M. *J. Chem. Soc., Perkin Trans. 2* **1991**, 439]

2a $R_1 = R_2 = CH_3$
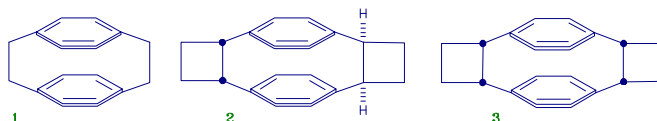2b $R_1 = R_2 = CH_2CH_3$
2c $R_1 = CH_3$ $R_2 = CH_2CH_3$

56. Tetramethyl para,para-cyclophane **1** is a chiral compound, capable of showing optical activity. Use molecular mechanics to calculate the energies of the two lowest energy conformations of chiral **1** and of the two lowest energy conformations of its meso diastereomer **2**; compare your energies and geometries with those in the reference.
[Finocchiaro, P.; Mamo, A.; Pappalardo, S.;

Weissensteiner, W.; Widhalm, M. *J. Chem. Soc., Perkin Trans. 2* **1991,** 449.]

57. Compute the geometry and degree of bending of the benzene rings in [2.2]-paracyclophane (**1**) and its cyclobutano-fused derivatives **2** and **3**. Compare your results with the experimental X-ray crystal structures for **1** and for a substituted version of **2** which are given in Table I of the reference. [Maekawa, Y.; Kato, S.; Hasegawa, M. *J. Am. Chem. Soc.* **1991***, 113,* 3867.]

58. Various meta- and para-cyclophanes with adamantane spacers have been prepared. Do MM calculations of the geometries and degree of benzene ring bending for dithia compounds **1** and **2** and for hydrocarbon **3**. Compare your values with the experimental X-ray crystal structure values given in the various figures and tables of the reference. [Dohm, J.; Nieger, M.; Rissanen, K.; Vögtle, F. *Chem. Ber.* **1991,** *124,* 915.]
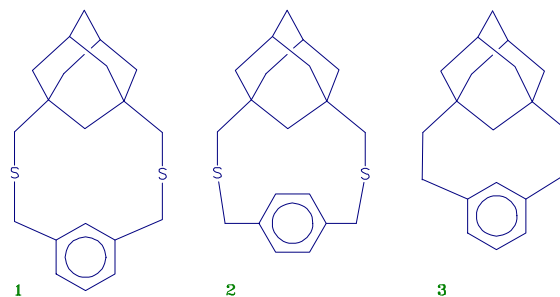
59. Calculate the torsion angles between the various aromatic rings in bimesityl (**1**), diphenylbimesityl (**2**), and dimesitylbimesityl (also known as quatermesityl) (**3**). Compare your answers with those from the X-ray crystal structures given in Table I of the reference.
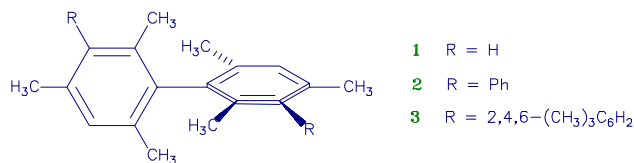
    1   R = H
    2   R = Ph
    3   R = 2,4,6−(CH₃)₃C₆H₂

    [Fischer, E.; Hess, H.; Lorenz, T.; Musso, H.; Rossnagel, I. *Chem. Ber.* **1991,** *124,* 783.]

The next two problems are designed to test the extent of van der Waals interactions when hydrogens are constrained to be near one another.

60. Two of the possible tetracyclic perhydropyrenes are shown below, once in planar form, once in its preferred conformation. Note that each isomer
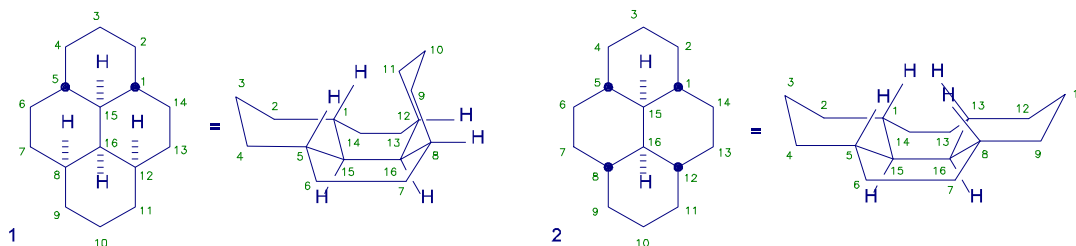
i
s constrained to have two boats (actually twists). Using molecular models as a guide when entering your structures, calculate the MM energies and structures of compounds **1** and **2**. <u>Then,</u> use the "delete" button to erase the C₁₅-C₁₆ bond; remove all of the H's, and re-add them; and do MM calculations of the energy and geometry of the dihydro derivatives of **1** and **2**. Be sure to

use molecular models in order to "locate" the most reasonable conformations of these dihydro compounds; be sure to try all of the likely rotations and flexings of the two remaining six-membered rings.

61. The complicated structure shown to the right is related to compounds **1** and **2** from the problem above, as can be seen from its conformational drawing. In fact, it has been numbered from 1 to 16, exactly as is compound **2**. There are 24 carbons in all, but only the first 22 are numbered in the two drawings. As in Problem No. 60, do the MM calculation of the given structure. <u>Then</u>, use "delete" to erase the C_{15}-C_{16}, C_{17}-C_{22}, and C_{19}-C_{20} bonds. The resulting hexahydro derivative is not only related to the dihydro derivatives of **1** and **2** from the previous problem, but also to compound **3** from Problem 58. But unlike the old compound **3** which can relieve the internal van der Waals interactions from the CH_2 group, <u>this</u> compound has <u>two</u> such CH_2 groups near one another. Use models to try to find "reasonable" conformations which can then be subjected to MM calculations.
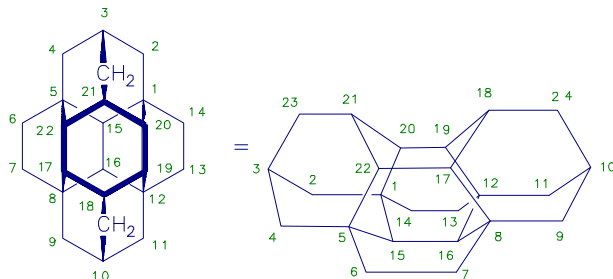
62. Intramolecular Diels-Alder reaction of a thia-substituted acyclic triene can give either a fused or bridged bicyclic structure; each of these can have either cis or trans stereochemistry. Calculate the energies of the four possible product structures and compare your heats of formation with those in the cited reference. Also, calculate the energy of the reactant, and estimate ΔH for the reaction.
[Harano, K.; Ono, K.; Nishimoto, M.; Eto, M.; Hisano, T. *Tetrahedron Lett.* **1991,** *32,* 2387.]
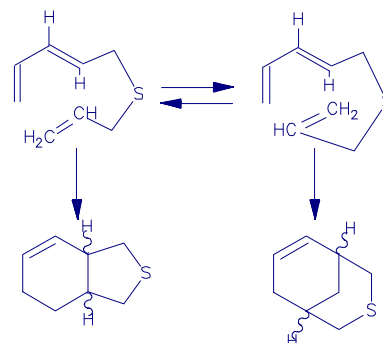
63. A series of orthoparacyclophanes has recently been prepared. Do MM calculations on hydrocarbons **1** and **2a**, and on dithia analog **2b**. Compare your calculated geometries with those suggested by the NMR data of **1** and **2a**, and the X-ray crystal structure for **2b**.
[Asami, M.; Krieger, C.; Staab, H. A. *Tetrahedron Lett.* **1991***, 32,* 2117.]
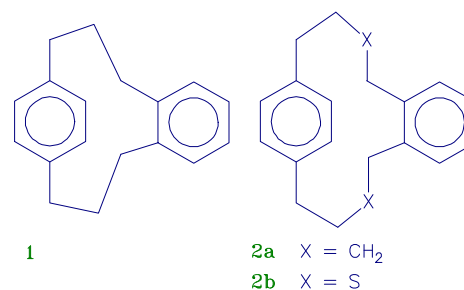
64. Non-bonded interactions in certain polycyclic aromatic compounds can cause a twisting of the rings, resulting in a non-planar structure. Compound **1** with R = Ph (see next page) has been synthesized; its X-ray crystal structure indicates that the phenanthrene rings at the left and right are 65° tilted from one another. Compound **2**, R = Ph, has not been made, but calculations suggest that here the phenanthrenes are orthogonal. These two compounds with R = Ph give the message "too many pi-atoms" when entered into our MMX
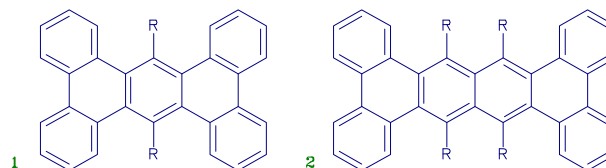
program. However, calculations <u>can</u> be done on **1** with R = H and with R = CH$_3$; and on **2** with R = H and with R = CH$_3$. Carry out these calculations to see if the alleged twisting occurs. Compare your calculated geometries with those reported (experimental or calculated) for the phenyl-substituted compounds.
[Plummer, B. F.; Russell, S. J.; Reese, W. G.; Watson, W. H.; Krawiec, M. *J. Org. Chem.* **1991***, 56,* 3219; Smyth, N.; Van Engen, D.; Pascal, R. A., Jr. *J. Org. Chem.* **1990,** *55,* 1937 and references therein.]

The next four questions are derived from a recent review article on the possibility of creating molecules with planar (or nearly planar) sp^3-hybridized carbon atoms. The structures shown in Problem 65 are called triquinacenes; those in Problems 66-68 are [5.5.5.5]-fenestranes. [This name is derived from the Latin word for window, and was originally assigned to [4.4.4.4]-fenestrane which looks like a window pane.] Be <u>sure</u> to use molecular models for all of these questions; the closer your input structure is to "reality," the better and quicker it will minimize,
[Gupta, A. K.; Fu, X.; Snyder, J. P.; Cook, J. M. *Tetrahedron* **1991***, 42,* 3665.]

65. Calculate the relative energies of the three 1,10-dimethyl-triquinacenes and compare your answers with those obtained by other versions of molecular mechanics (see Table 6 of the cited reference).
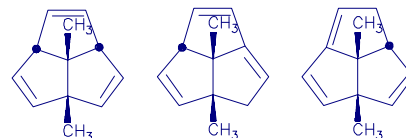
66. For this set of [5.5.5.5]-fenes-tra**tetra**enes, compute their heats of formation, strain energy, and bond angles; compare your results with those shown in Table 8 and in Figure 7 of the cited article.
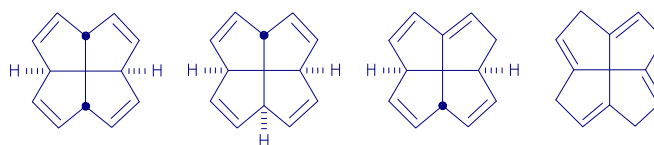
67. For this set of [5.5.5.5]-fenestra-**penta**enes, compute their energies and bond angles; compare your results with those in Table 9 (and accompanying text) in the cited article.
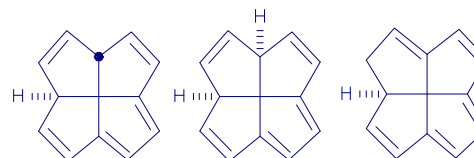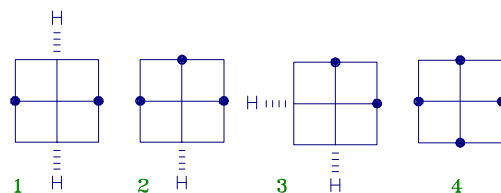
68. The first two structures represent the most stable of the **tetra**enes and **penta**enes (Problems 66 and 67); the third structure is a [5.5.5.5]-fenestra**hexa**ene. Compute the change in strain energy which occurs as each double bond is introduced; compare your answers with those in Table 10 of the cited article.
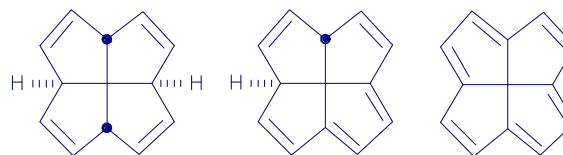
And speaking of fenestranes, the next two problems are concerned with the strain energy and geometry of [4.4.4.4]-fenestrane (a.k.a. "windowpane," an appropriate name with an appropriate ending for an alk<u>ane</u>).
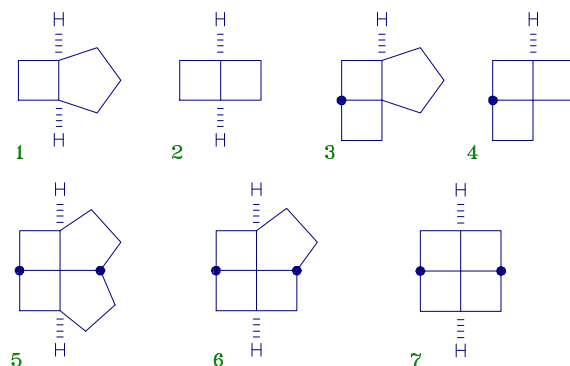
69.   Using molecular models (careful - they <u>can</u> break if they are abused too much) to enter the approximate structure, calculate the heats of formation, strain energies, and geometries of the various [4.4.4.4]-fenestranes. Note that each of these structures has a central C which is forced to adopt some rather unfavorable bond angles; compound **4** is especially interesting in that the central C has all four bonds on <u>one</u> side of a plane. Compare your energies and geometries with those in the cited articles.
[Würthwein, E.-U.; Chandrasekar, J.; Jemmis, E. D.; Schleyer, P. von R. *Tetrahedron Lett.* **1981***, 22*, 843; *Ibid.* **1982,** *23,* 3306 (correction); Wiberg, K.; Olli, L. K.; Golembeski, N.; Adams, R. D. *J. Am. Chem. Soc.* **1980,** *102,* 7467.]
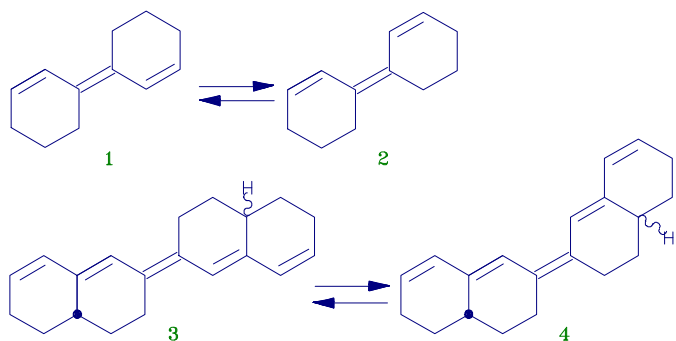
70.   This exercise is concerned with assessing the increase in strain on going from a five- to a four-membered ring in certain compounds. For each of these molecules, compute their heats of formation, strain energies (SE), and bond angles; compare your answers with those in Figure 3 in the cited article. Calculate ΔSE for the pair **1/2**; for the pair **3/4**; for the pair **5/6**; and for the pair **6/7**; compare your values with the published numbers.
[Wiberg, K.; Olli, L. K.; Golembeski, N.; Adams, R. D. *J. Am. Chem. Soc.* **1980,** *102,* 7467.]

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71.   A recent article focuses on the energy required to rotate about a C=C bond. <u>Kinetics</u> studies give the activation enthalpy and entropy of the processes shown. [Note: rotation about the central double bond is made feasible by resonance stabilization of the 90°-twisted biradical.] Your task is to calculate the <u>thermodynamics</u> (ΔH) for **1** going to **2** and for **3** going to **4**. Compare your calculated ΔH values with those in Tables III and IV of the reference. Note that structure **3** represents <u>two</u> compounds: a racemic isomer (in which the squiggle H is up) and a meso isomer (H down); these give, respectively, racemic **4** (H down) and meso **4** (H up).
[Doering, W. von E.; Kitagawa, T. *J. Am. Chem. Soc.* **1991,** *113,* 4288; see also Doering, W. von E.; Sarma, K. *ibid.* **1992***, 114,* 6037.]

A delightful book to read (and to learn from) is Nickon, A.; Silversmith, E. F. *Organic Chemistry: The Name Game*; Pergamon: New York, 1987. It tells the stories (using first-hand accounts as much as possible) of how some organic molecules were given their unusual names (e.g., 18[crown]6, snoutene, basketane, bullvalene, etc.). It is also an excellent source of structures for MM calculations, as the next four problems will indicate; the references are to page numbers in this book.

72.   The name **peristylane** (p. 51, 295) comes from the Greek word for roof. An [n]-peristylane "has an n-membered base joined by n bonds to alternate atoms of a 2n-membered cycle." Confused? Sure. But pictures help. Shown here are [3]- and [5]-peristylane (two perspectives). Your task is to calculate the energies and geometries of [3]-, [4]-, and [5]-peristylane. Then, use the SSADD command to bring a horizontal five-membered ring close to the five "points" of [5]-peristylane ($C_{15}H_{20}$); delete five H's from each molecule, join the carbons, and construct the exquisitely symmetrical dodecahedrane ($C_{20}H_{20}$) for which you should then do the MM calculation.


dodecahedrane
$C_{20}H_{20}$
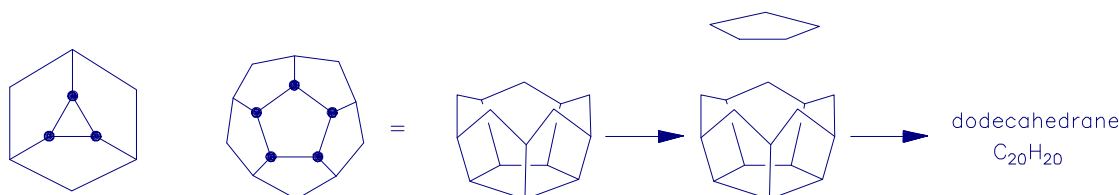
73.   The **asteranes** (p. 93) are also beautifully symmetrical molecules. Shown here are triasterane and hexaasterane. Your task is to do MM calculations on the energies and geometries of tri-, tetra-, penta-, and hexaasterane. Discuss the variations in strain energy as the ring size changes; explain clearly why hexaasterane is not the least strained of the series. [Ahlquist, B.; Almenningen, A.; Benterud, B.; Traetteberg, M.; Bakken, P.; Lüttke, W. *Chem. Ber.* **1992**, *125,* 1217.]
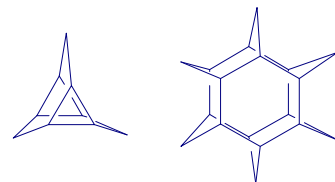
74.   **Israelane** and **Helvetane** (p. 87) [Why are these names used?] are $(CH)_{24}$ molecules. Do MM calculations on both of them. What you will discover is that although these structures are aesthetically pleasing, they are disasters chemically. The latter structure has not only the strain of the four-membered rings but also has four H's from the "front" 12-membered ring and four more from the "rear" ring pointing toward one another; nevertheless, it minimizes to a structure not too different from that shown. Israelane, on the other hand, has six H's on the "front" and six more on the "rear" ring, all pointing to the center; neither RMM nor JEB has managed to get a minimized structure whose geometry is close to that shown. Try the MM procedure on israelane, and see what you get. Then, try various "tricks" to hold the ring system in this geometry; for example, connect the interior carbons to an added single carbon or to the carbons of added three-membered or six-membered rings; be creative!
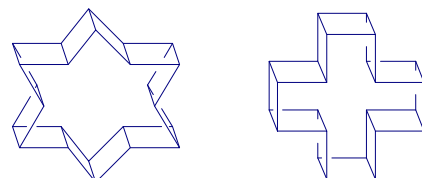

75.   The name **triblattane** (p. 269) is derived from the German word for "leaf" and is used to describe the distorted bicyclo[2.2.2]octane nucleus which results when various short chains
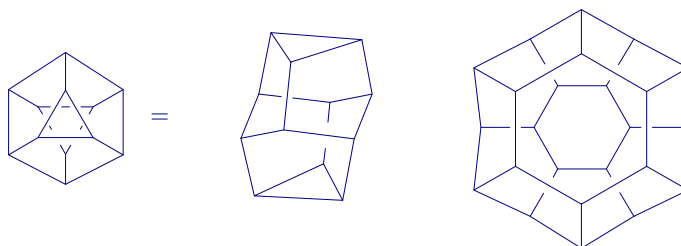

$(CH_2)_n$ $(CH_2)_m$

$(CH_2)_p$
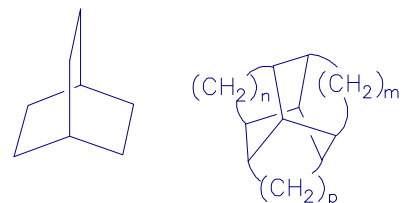
are introduced. The exercise, here, is to calculate the energy and geometry of the parent compound; pay special attention to the dihedral angle C_1-C_2-C_3-C_4. Then do calculations on three molecules with just <u>one</u> bridge; let m = 2, 1, and 0. Then do calculations on three molecules with <u>two</u> bridges; let m = p = 2, 1, and 0. Finally, do calculations on three molecules with <u>three</u> bridges; let m = p = n = 2, 1, and 0; the last compound is the beautifully symmetrical "cubane." Discuss the strain energy and the variation in the dihedral angle as the number and length of the bridges are changed.

Thoughts of one beautifully symmetrical structure beget thoughts of others. The next several problems (76 to 80) concern structures which are related to some from the Nickon-Silversmith set above.

76.   Problem 75 was concerned with the increasing strain of a bicyclic octane as bridges of ever-shorter length were incorporated into it. The present problem starts with an analogous molecule, but with <u>two cyclopropane rings</u> instead of the <u>two bridgehead carbons</u>. Models (and MM) suggest that unlike bicyclo[2.2.2]octane itself, there is already significant twist in the parent structure, the one with no bridges; models also suggest the cyclopropane rings are not quite orthogonal and also that introduction of the bridges does not lead to a large increase in strain. Do MM calculations on the energy, geometry, and dihedral angles for the parent compound; for the singly-bridged compounds with m = 1 or 0; for the doubly-bridged compounds with m = p = 1 or 0; and for the triply-bridged compounds with m = p = n = 1 or 0. This last compound, a wonderfully symmetrical structure, is identical to the first bis-peristylane of the next problem.
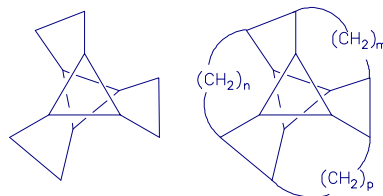
77.   Problem 72 asked for an analysis of the [n]-peristylanes from n = 3 through 5. One can also imagine a set of bis-[n]-peristylanes for which structures are shown for n = 3 (two perspectives) and n = 6. Do MM calculations on the complete set from n = 3 through n = 6; discuss the large variation in strain energy (and the principal reasons for it) along this series; as in Problem 73, note that the n = 6 compound is not the least strained. Also note that n = 3 is identical to the last compound calculated in Problem 76 and that n = 5 is identical to dodecahedrane from Problem 72.
[Lee, C.-H.; Liang, S.; Haumann, T.; Boese, R.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1993,** *32,* 559.]

78.   There are five possible "Platonic solids," polyhedra in which all faces are identical rings. Three of these are the **tetrahedron, cube,** and **dodecahedron**, all of which have been "built" in the form of saturated organic molecules: **tetrahedrane** (C_4H_4), **cubane** (C_8H_8, Problem 75), and **dodecahedrane** ($C_{20}H_{20}$, Problems 72 and 77). The other two cannot be "built" as organic structures, either because they would require five bonds to carbon or because they would require inverted sp^3-hybridized carbons. There are, however, <u>many</u> other molecules which are nearly spherical, which have symmetry almost as high as the Platonic solids, but which contain two (or more) different-sized rings (rather than all rings the same). Any <u>one</u> of the following five sections will constitute a reasonable MM problem set for solution.

A.   Do MM calculations on compounds **1** and **2** which consist of three- and six-membered rings. The latter, despite its lovely shape, is a <u>very</u> strained molecule (make a model!); perhaps the best way to do its MM structure is first to enter compound **3**; minimize it;
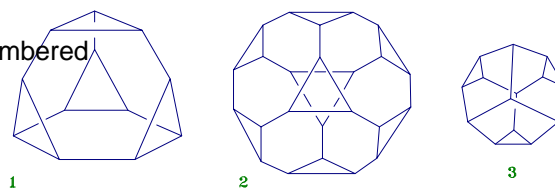
replace one of the five CH groups by a C_3H_3 group; minimize; and continue the process so that eventually all five CH groups of **3** are replaced by the three-membered rings needed for **2**. Report the MM structures and energies for **1**, for **3**, for <u>each</u> of the cyclopropane-substituted materials, and finally for **2**. You'll note that introduction of the first cyclopropane raises the energy somewhat; introducing the second, third, and fourth raises it a little; and introducing the final one leads to a large increase.

B. Do MM calculations on this set of compounds which consists of molecules containing various combinations of three-, four-, five-, and six-membered rings. Note that the first two structures have, respectively, two and one inverted sp^3-hybridized carbons; note, also, that the third compound is geometrically constrained to have planar four-membered rings. As a result, the first set of three structures is much more strained than the second set of three.
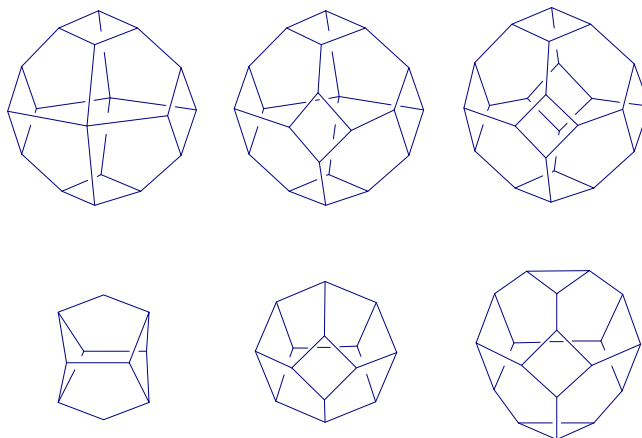
C. A compound much in the news lately is "buckminsterfullerene" or "buckyball," a form of carbon having the formula C_{60} and consisting of fused five- and six-membered rings in a nearly spherical array. Its saturated version, $C_{60}H_{60}$ ("soccerane"), consisting of 12 regular pentagons and 20 regular hexagons, has never been made. Because that structure has too many atoms for an MMX calculation, you should do MM calculations on two smaller molecules (shown) which contain 12 pentagons but only three or two hexagons; the second of these is also found in Problem 77.

$C_{26}H_{26}$ $C_{24}H_{24}$
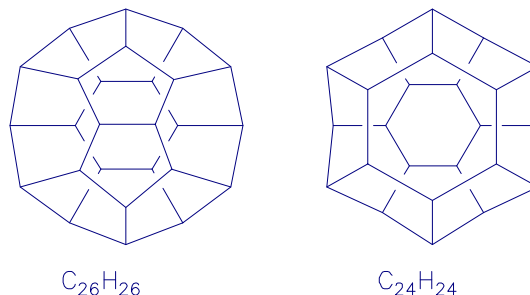
D. Do MM calculations on this set of structures which contain four-membered rings in combination with rings of varying sizes. The third compound is also found in Part B; the fourth compound is also calculated (although not shown) in Problem 77.
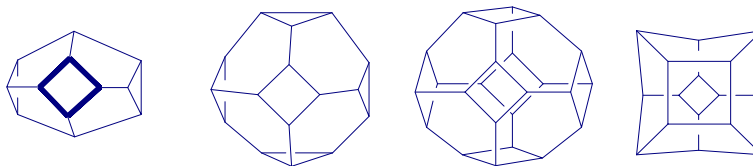
E. Replacement of any one of the CH groups of cubane by a C_3H_3 unit generates a compound called "lampane." From lampane, replacement of one or another of the three different CH groups by a C_3H_3 unit gives three different $C_{12}H_{12}$ compounds. Compute the MM energy and structure of these five compounds.


C_8H_8 $C_{10}H_{10}$
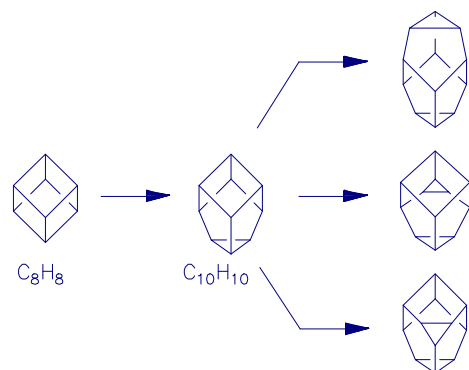
79. The asteranes (Problem 73) consisted of parallel identical rings, separated by a series of one-carbon bridges. Shown below are two sets of related molecules, either with zero-carbon or with two-carbon bridges. Do MM calculations on the four compounds (from cyclopropane to cyclohexane) from either Set A or Set B. The first two members of Set A are prismane (shown) and cubane. The first member of Set B also appeared in Problem 76; all of the members of Set B have severe non-bonded interactions between C-H bonds.

A through   B through
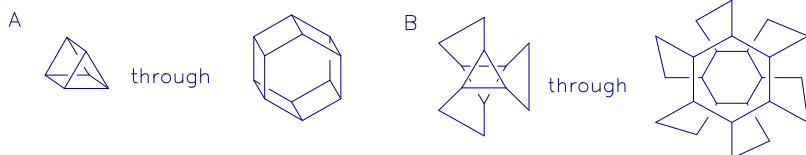
80. One can imagine the triple intramolecular [2 + 2] cycloaddition shown here, giving a saturated molecule which is drawn with deliberately ridiculous-looking long bonds. Do MM calculations on this cyclized compound, $C_{21}H_{18}$, and on the analogous compounds which one would get from the quadruple and pentuple cyclization of related compounds with a central four- or five-membered ring; these will have formulas $C_{28}H_{24}$ and $C_{35}H_{30}$, respectively.

UV light
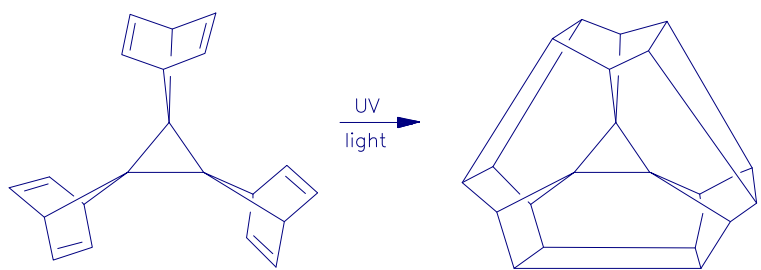
81. A recent article describes ab initio and molecular mechanics (with the new MM3 program) calculations on a series of methylenecyclobutanes. Do MM calculations on the parent compound ($R_1 = R_2 = H$), on the monomethyl compounds ($R_1 = CH_3$ or $R_2 = CH_3$ in its axial and equatorial conformations) and on the dimethyl compound in both axial and equatorial conformations. Compare your energies, bond distances, bond angles, and dihedral angles with those in Tables III and IV of the reference.
[Pasto, D. J.; Sugi, K. D.; Malandra, J. L. *J. Org. Chem.* **1991***, 56,* 3781.]
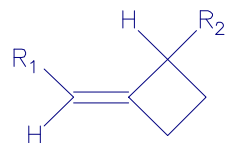
82. Starting in late 1989, Allinger has published a series of articles on MM3, a new version of molecular mechanics with a new force field and new parameters. The most recent article concerns calculations on various aldehydes and ketones. Suitable projects would be: (a) calculate the energies and structures of the conformations of methyisopropyl ketone and of diisopropyl ketone and compare the results with those in Tables XII and XIII; (b) calculate the energies and structures of the important conformations of cyclopentanone, cyclohexanone, and cycloheptanone (Tables XVI, XVII, and XX); (c) calculate the energies of the several

conformations and stereoisomers of cis and trans "dimethyl decalin-1,4-dione" (Table XXVII); (d) calculate the energies of various other aldehydes and ketones for comparison with the experimental heats of formations in Tables XXX-XXXII).
[Allinger, N. L.; Chen, K.; Rahman, M.; Pathiaseril, A. *J. Am. Chem. Soc.* **1991,** *113,* 4505.]
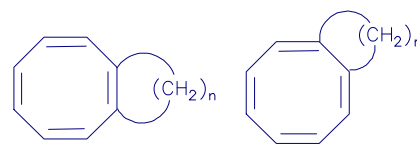
83. The highly symmetrical "pagodane" ($C_{20}H_{20}$, **A**) is another strained molecule. Shown here are several possible synthetic entries to it, including [2 + 2] cycloaddition from dienes **B** or
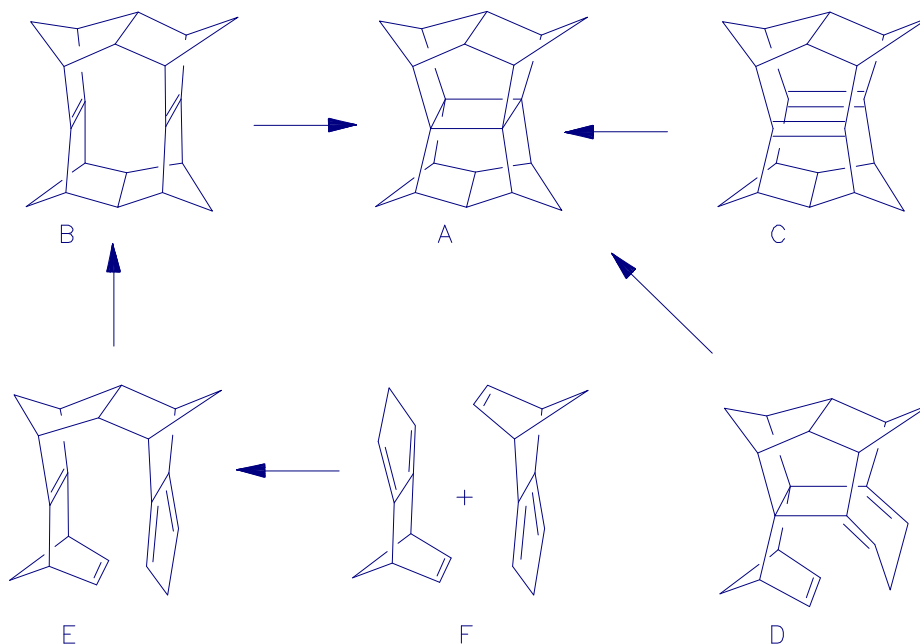
C and [2 + 2 + 2] reaction from triene **D**. Also shown is a potential route to **B** via Diels-Alder dimerization of **F** followed by intramolecular Diels-Alder reaction of the initially formed **E**.   Do calculations on all six structures, and assess the likelihood of synthetic procedures involving them. Pay particular attention to the "similar-looking" dienes **B** and **C** which differ markedly in strain energy; what is the origin of this difference?
[Melder, J.-P.; Prinzbach, H. *Chem. Ber.* **1991***, 124,* 1271 and references therein.]

84. Unlike its planar "vinylog" benzene, cyclooctatetraene is a tub-shaped molecule. Do MM calculations on the parent compound, on its monocarboxy derivative, and on its two types of fused derivatives with n = 2, 3, and 4. Compare the MMX energies of the isomeric 1,2-bridged and 1,8-bridged compounds. Determine the "flap angle" (a measure of non-planarity; see the cited reference for its definition) of each compound; compare your results with those reported for MMX and X-ray crystal structures.
[Pirrung, M. C.; Krishnamurthy, N.; Nunn, D. S.; McPhail, A. T. *J. Am. Chem. Soc.* **1991***, 113*, 4910.]

85. In order to understand the stereo- and regiochemical aspects of various cyclization steps used for synthesis, MMX calculations were performed on the cis-2-oxabicyclo[4.n.0] compounds where n = 4 or 3 or 2. For all three of these compounds, do MMX calculations on the equilibrating chair conformations of the six-membered ring; evaluate boat conformations where necessary. Compare your results with those shown in Figures 4 and 5 of the reference. Decide which factors are important in determining the energy differences between conformations.
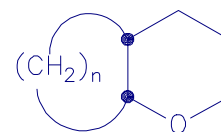
[Brown. M. J.; Harrison, T.; Herrington, P. M.; Hopkins, M. H.; Hutchinson, K. D.; Mishra. P.; Overman, L. E. *J. Am. Chem. Soc.* **1991,** *113,* 5365.]

86.   The following exercises are drawn from one article. Either one will constitute a reasonable MM problem set.

A.   Upon heating (<u>E</u>)-1,3,5-hexatriene cyclizes to 1,3-cyclohexadiene, presumably by first undergoing electrocyclic ring closure to 3-vinylcyclobutene which then opens to (<u>Z</u>)-1,3,5-hexatriene, the immediate precursor to the six-membered ring. (Note: neither acyclic triene is shown in the conformation needed for ring closure to occur.) Calculate the heats of formation of all four compounds and compare your results with those shown in Figure 1 and Table 3 of the reference.
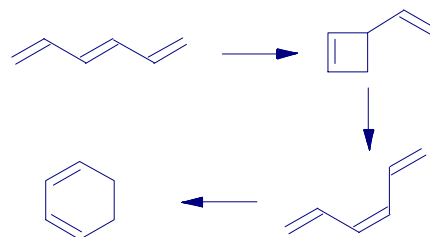
B.   Similarly, (<u>E</u>,<u>E</u>)-1,3,5-heptatriene cyclizes to a six-membered cyclic diene. Unlike the case above, this initial diene can undergo a set of [1,5] sigmatropic shifts of H to give two isomeric cyclic dienes. Calculate the heats of formation of the four structures, and compare your results with those in Tables 2 and 3 of the reference.
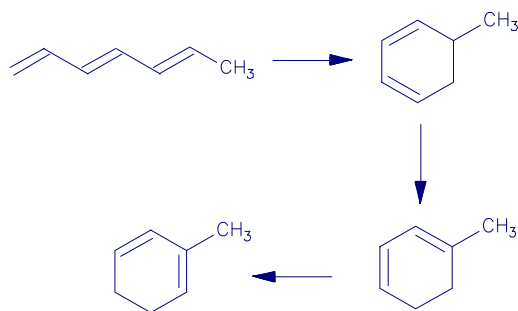
[Doering, W. von E.; Roth, W. R.; Bauer, F.; Boenke, M.; Breuckmann, R.; Ruhkamp, J.; Wortmann, O. *Chem. Ber.* **1991***, 124,* 1461.]