- 87. Cycloreversion reactions are well-known processes in organic chemistry. Use molecular mechanics to calculate ΔH for the retro reactions of the carbocyclics having X = CH₂: (1) cyclohexane to three ethenes; (2) cyclohexene to 1,3-butadiene plus ethene (a retro Diels-Alder reaction); and (3) bicyclo[4.1.0]heptane to 1,4-pentadiene plus ethene; discuss the factors which are responsible for the quite different ΔH values obtained. Then, do calculations on the reversions of the three compounds with X = N in which the nitrogens are connected by a double bond (i.e., azo compounds); in these cases, molecular nitrogen is produced in place of ethene; compare these three values with one another and with those for the carbocyclic compounds; discuss why ΔH is so different for these azo compounds and for the corresponding hydrocarbons. [Berson, J. A. Acc. Chem. Res. 1991, 24, 215.]
- 88. The ene reaction can occur inter- (Eqn (I)) or intramolecularly (Eqn (2)). Calculate Δ H for Eqn (1) and for the intramolecular cases (Eqn (2)) in which n = 1, 2, or 3. Discuss the factors which lead to the variation observed for Δ H. Compare your answers with the calculate and experimental results in the cited article. [Berson, J. A. *Acc. Chem. Res.* **1991**, *24*, 215.]
- 89. Calculate Δ H for the thermal valence isomerization of 1,6-methano[10]annulene (the parent compound with both X's = H) to its tricyclic isomer. Do the same for the bridged compounds in which -X-X- is either -CH₂CH₂- or -CH=CH-. Discuss the variation in Δ H as a function of substituents; compare your answers with those given (calculated and experimental) in the cited article.

[Arnz, R.; Carneiro, J. W. de M.; Klug, W.; Schmickler, H.; Vogel, E.; Breuckmann, R.; Klärner, F.-G. Angew. Chem., Int. Ed. Engl. 1991, 30, 683.]

90. The kinetics of the solvolyses of some bridgehead allylic triflates (triflate = OSO₂CF₃, an excellent leaving group) have recently been reported. In order to account for the observed rate data and to see if "F-strain" in the reactant is a factor, MM2(87) calculations were performed on the corresponding bridgehead alcohols. Calculate the structures and heats of formation for the stereoisomeric [2.2.2] compounds: <u>Z</u> with R₁

= CH₃, R₂ = H and <u>E</u> with R₁ = H, R₂ = CH₃; do the same for the <u>Z</u> and <u>E</u> [3.2.2] compounds. Compare the heat differences for <u>Z</u> and <u>E</u> which you find with those in the article; discuss any differences.

[Takeuchi, K.; Ohga, Y.; Kitagawa, T. *J. Org. Chem.* **1991**, *56*, 5007; see also Takeuchi, K.; Kitagawa, T.; Ohga, Y.; Yoshida, M.; Akiyama, F.; Tsugeno, A. *Ibid.* **1992**, *57*, 280; Ohga, Y.; Munakata, M.; Kitagawa, T.; Konoshita, T.; Takeuchi, K.; Oishi, Y.; Fujimoto, H. *ibid.* **1994**, *59*, 4056.]









91. Heats of <u>hydration</u> of alkenes to alcohols provide the same information about the relative stability of alkenes as is obtained from heats of hydrogenation. Use MM to calculate Δ H for the following isomerizations, each of which is a measure of the relative energies of disubstituted vs. trisubstituted alkenes; do the calculation for the acyclic model and for the cyclic compounds in which n = 2, 3, or 4. Compare your answers with those in the article; discuss any differences.

[Wiberg, K. B.; Hao, S. J. Org. Chem. 1991, 56, 5108.]

- 92. Compound 1, (CH)₁₄, has recently been synthesized. It undergoes Cope rearrangement at 80°C and is completely transformed into isomer absolutely no 3 is detected. Upon irradiation, 1 is transformed into 4. Do MM calculations on these compounds; try to explain why the equilibrium between 1 and 2 is entirely on the side of product and why 1 gives no 3. Then do MM calculations on the related (CH)12 isomers 5-7. [Fessner, W.-D.; Rodriguez, M. Angew. Chem., Int. Ed. Engl. 1991, 30, 1020.]
- 93. In experiments designed to elucidate the stereo-chemistry of [1,3] sigmatropic carbon shifts, the trideuterio-substituted vinylcyclopropane (to the right) was pyrolyzed; migration of C_5 (or C_4) from C_3 to C_1 , with

concontant reorganization of the π electrons, produces the substituted cyclopentene (numbered so as to agree with the carbon numbers in the reactant). In order to determine the relative stereochemistry of the deuterium-labeled carbons, the alkene was epoxided, giving a mixture of epoxides (50% from above the plane, 50% from below); ¹H-NMR spectroscopy was used to assign stereochemistry. Your tasks are: (a) to confirm or disprove the authors' assertion that this epoxide exists preferentially in a boat rather than in a chair conformation; (b) to decide if this boat preference is or is not caused by the t-butyl group (i.e., do MM calculations on cyclopentenoxide itself); (c) to use MM to determine all of the vicinal coupling constants (between H's on C₁ and C₅, and between H's on C₅ and C₄) in the two product epoxides and to compare these with the experimental values cited in the paper; (d) to decide if the authors were justified in the relative stereochemistry which they assigned to the three stereogenic centers. [Do your calculations of energy and of J values on the non-deuteriated cyclopentenoxides.] [Gajewski, J. J.; Olson, L. P. J. Am. Chem. Soc. **1991**, *113*, 7432. NOTE: the senior author of this article lives on <u>Serena Lane</u> in Bloomington, IN - does this ring a bell?]

94. The ability of a series of ene-diynes to undergo thermal closure to a fused aromatic product (in a stepwise process via a diradical which abstracts hydrogens from solvent) depends critically on the distance between the termini of the two triple bonds. Use MM to calculate the bond distances, bond angles, dihedral angles, etc. of the



22

5







hydrocarbons with X = CH₂ and n = 0 or 1 or 2; of the hydrocarbon with X absent and n = 0; and of the heterocycle with X = S and n = 1. Compare your results with the calculated and experimental (X-Ray crystal structure) results in the cited article. [Sakai, Y.; Nishiwaki, E.; Shishido, K.; Shibuya, M.; Kido, M. *Tetrahedron Lett.* **1991**, *3*2, 4363; see also Sakai, Y.; Bando, Y.; Shishido, K.; Shibuya, M. *Ibid.* **1992**, *33*, 957; Nicolaou, K. C.;

Zuccarello, G.; Riemer, C.; Estevez, V. A.; Dai, W.-M. J. Am. Chem. Soc. 1992, 114, 7360.]

- 95 Kasallene is an optically active brominated allene which is isolate from a red alga. Shown to the right is the acetonide derivative of the diol (OH groups at C₉ and C₁₀ in the natural product). The ¹H-NMR vicinal coupling constants were used to establish the stereochemistry at C₉ and C₁₀. Use MM to calculate the energy and all of the coupling constants expected for the 9α,10α and of the 9β,10β derivatives. Compare your results with both the calculate and experimental results in the cited reference. Indicate whether or not you agree with the authors' assignment of structure. [Öztunç, A.; Imre, S.; Wagner, H.; Norte, M.; Fernández, J. J.; González, R. *Tetrahedron Lett.* **1991**, *32*, 4376.]
- 96. Intramolecular aza Diels-Alder reaction gave exclusively <u>one</u> stereoisomeric product. The relative configuration at the three stereogenic centers was determined by ¹H-NMR vicinal coupling constants. For three stereogenic centers, there are (of course) eight possible stereoisomers; do MM calculations on <u>four</u> of

these (keeping the H at C_{9a} down, for example, and varying the configurations at C_8 and C_2 . Calculate relative energies and vicinal coupling constants; compare your results with the calculated and experimental results in the cited article.

 $(CH_2)_n$

[Uyehara, T.; Chiba, N.; Suzuki, I.; Yamamoto, Y. Tetrahedron Lett. 1991, 32, 4371.]

- 97. Consider the series of lactones, n = 3 through n = 8. Do MM calculations on the heats of formation, stable conformations, bond distances, bond angles, dihedral angles, etc. Compare your results with the experimental and theoretical results (Tables VI and VIII, Figures 1 and 2) of the cited reference.
 [Wiberg, K. B.; Waldron, R. F.; *J. Am. Chem. Soc.* **1991**, *113*, 7697.]
- 98. The 2,3-dihalobutanes have two stereogenic centers. Do MM calculations of the energies and dihedral angles (between the C-CH₃ bonds) of all three staggered conformations for <u>both</u> the R,S (meso if X = Y, erythro if X ≠ Y) and R,R compounds (dl or threo); do the calculations for the five compounds X = Y = F; X = F, Y = Cl; X = F, Y = Br; X = Y = Cl; X = Y = Br; compare your results with the experimental and calculated results in the cited reference. [Meyer, R. J.; Kingsbury, C. A.; Rack, E. P. J. Mol. Struct. **1991**, *248*, 179.]
- 99. The natural product 3-carene (next page) is alleged to have a planar (or nearly planar) six-membered ring, rather than the (expected?) boat. Do MM calculations on the boat and planar forms to see which, in fact, is more stable; compare your dihedral angles with those in the cited article. Then, in order to understand <u>why</u> the six-membered ring is flattened, do MM calculations on: the non-methylated compound; on all of the possible <u>mono</u>-methyl compounds (methyl at C₃ or at C₇, either endo or exo); and on the various <u>di</u>-methyl compounds. [Tkachev, A. V.; Denisov, A. Y. *J. Chem. Soc., Mendel Commun.* **1991**, 98.]

100. Bromine adds to alkenes in stereospecific anti fashion. Consider the bromination of steroids 2-cholestene (1) and cholesterol ($\mathbf{2}, X = OH$), shown as partial structures to the right. Anti addition of Br₂ to each can (in principle) produce either of two diastereomers; in fact, only one diastereomer is initially formed (for reasons which will be discussed later in lecture), but it



can rearrange to the other. Your job is to determine which diastereomer predominates for the case of trans-2,3-dibromocholestane and for three cases of addition to 2: X = H, OH, or Br.

2

3

101. Hexaprismane (1) is a highly strained molecule, but various derivatives such as seco-[6]-prismane (2), homo-[6]-prismane (3), and various bis-homo-[6]-prismanes (such as 1.3-bishomo compound 4) have been made. Do MM calculations on the geometry and

> energy of these structures and structures related to them. Alternatively, one could do calculations on the heptaprismane and its various seco-, homo-, and bishomo-derivatives. [Mehta, G.; Padma, S. Tetrahedron 1991, 47, 7783, 7807; Mehta, G.; Krishna Reddy, S. H.; Padma, S. Ibid. 1991, 47, 7821]

102. For bicyclo[5.1.0]decane-2.6-dione (shown to the right), there are five reasonable conformations; see the cited reference for the names and structures of them. Do MM calculations of their energies, and compare these with the experimental and calculated values in the article.

[Abraham, R. J.; Rowan, A. E.; Bakke, J. M.; Braeden, J. E. J. Chem. Soc., Perkin Trans. 2 1991, 1471.]

- 103. (R)-(-)- α -Phellandrene (shown to the right) can have its isopropyl group axial or equatorial; for each of these situations, there are three staggered conformations for rotation about the ring carbon to isopropyl carbon bond. Calculate the energy of all six conformations as well as the "skew" angle for the diene unit; compare your results with those in the cited article. [Araki, S.; Sakakibara, K.; Hirota, M.; Nishio, M.; Tsuzuki, S.; Tanabe, K. Tetrahedron Lett. 1991, 32, 6587.]
- 104. Consider the cyclic divnes whose general structure is shown to the right. Calculate the energy, bond angles at the sp carbons, and distance between $(CH_2)_m$ acetylene units for the symmetrical molecules m = n = 2, 3, 4; and for the unsymmetrical molecules with m = 2, n = 3, 4, or 5; and m = 3, n = 4 or 5. Compare your answers with those obtained either experimentally or by calculation in the cited reference. [Gleiter, R.; Kratz, D.; Schäfer, W.; Schehlmann, V. J. Am. Chem. Soc. 1991, 113, 9258; also Gleiter, R. Angew. Chem., Int. Ed. Engl. 1992, 31, 27.]
- 105. The next four problems are based on the numbers (experimental and calculated) found in a recent compilation. Any one of these four would constitute a reasonable MM problem set. [Roth, W. R.; Adamczak, O.; Brueckmann, R.; Lennartz, H.-W.; Boese, R.; Chem. Ber. 1991, 124, 2499.1

A. 1,3-Butadiene is the simplest conjugated hydrocarbon. Calculate the energy and structure (including bond angles, bond lengths, and degree of nonplanarity of the diene system) as substituents are introduced; compare your answers with those in the article. Do calculations on the parent; on the three possible monomethyl derivatives; on the 2,3-dimethyl and 2,3-di-t-butyl derivatives; and on the three stereoisomeric 1,2,3,4-tetramethyl compounds

$$H_{2}C \xrightarrow{C} C \xrightarrow{3} CH_{2}$$



4





(i.e., 3,4-dimethyl-2,4-hexadiene).

B. Do calculations on the various cis- fused bicyclo[n.1.0]alkanes (\mathbf{A} , n = 1, 2, 3, 4, 5); on those molecules which "might" be able to have trans ring fusion/s (\mathbf{B} , n = 3, 4, 5); and on the cis- and transfused alkenes \mathbf{C} ; compare your answers with those in the article.

C. Consider the stepwise hydrogenation of the triene shown to the right. Calculate the energy of the triene; of the three possible dienes; of the monoene; and of the saturated final



(CH₂)_n

Α

product. Discuss differences and similarities in the energy changes as each double bond is hydrogenated; compare your answers with those in the article.

D. Similarly, consider the stepwise hydrogenation of "birdcage" dienes A, B, and
C. Calculate the energies of these molecules as well as of the resulting monoenes and saturated hydrocarbons. Discuss differences and similarities in the energy changes as each double bond is hydrogenated; compare your answers with those in the article. (See, als



 $(CH_2)_n$

В

C

your answers with those in the article. (See, also, Turner, R. B.; Jarrett, A. D.; Goebel, P.; Mallon, B. J. *J. Am. Chem. Soc.* **1973**, *95*, 790.)

- 106. A recent article relates assesses steric effects on reaction rates. The following problems are quite similar to those described in Problems 38 and 39. Solving either Part A or Part B would constitute a satisfactory molecular mechanics project. [Müller, P.; Millin, D. *Helv. Chim. Acta* **1991**, *74*, 1809.]
 - A. Compute the MMX energy for the series of 2-alkyl-2-bromoadamantanes shown to the right (where R = methyl, ethyl, isobutyl, tert-butyl, and neopentyl); also compute the MMX energy of the tertiary carbocation obtained by S_N 1 reaction of the halide. Plot the difference in energy between R-Br and R⁺ vs. the log of the solvolysis rates of such compounds (see the cited article) and discuss similarities/differences between your correlation and the published one.
 - B. Similarly, compute the MMX energy for a series of 1-bromo bridged bicyclic molecules and for the resulting cation. Do the calculations on the [3.3.3], [3.3.2], [3.3.1], [3.2.1], and [2.2.2] systems. Plot the difference in energies between R-Br and R⁺ vs. the log of the solvolysis rates of such compounds (see the cited article) and discuss similarities/differences between your correlation and the published one.
- 107. Calculate the conformational energies of the relatively stable conformations of oxocane (C₇H₁₄O) and compare your results with those in the cited reference (Table I). Do your calculations on the conformations called BC-1, BC-3, BC-4, TBC-1, and TCC-1 (those which are within 2 kcal/mol of each other). If desired, you can then use the dihedral driver program to try to reproduce the barriers to conformational change in Table II.







[Meyer, W. L.; Taylor, P. W.; Reed, S. A.; Leister, M. C.; Schneider, H.-J.; Schmidt, G.; Evans, F. A.; Levine, R. A. J. Org. Chem. 1992, 57, 291.]

108. Cyclization by intramolecular nucleophilic substitution of the anion to the right and produce either fused (1,2) or bridged (1.4) products, each of which can be either cis or trans in stereochemistry. One MM



project would be to calculate the energies and structures of all of the 1,2-products for n =2 through n = 5. Another project would be to do the same for the 1,4-products (n = 2 through 5). For either project, compare your results with those found in the cited article. [Auchter-Krummel, P.; Krummel, G.; Lex, J.; Müllen, K. Chem. Ber. 1991, 124, 2819.]

109. By calculating the energies of the alkenes and alkanes shown to the right, determine the heat of hydrogenation for each case; compare your results with those in the cited reference. Do calculations on the systems where n = 0, 1, and 2 and, forreference purposes, on the "unstrained" parent system where there is no bridge (i.e., bicyclo[3.3.0]-1(5)-octene). Discuss the strain energy as a function of pyramidalization of the alkene unit.



[Branan, B. M.; Paquette, L. A.; Hrovat, D. A.; Borden, W. T. J. Am. Chem. Soc. 1992, 114. 774.1

110. Calculate the energies, bond angles, bond distances, etc. for adamantane (shown to the right), diadamantane (C₁₄H₂₀), triamantane (C₁₈H₂₄), isotetramantane (C₂₂H₂₈), cyclohexamantane (C₂₆H₃₀), and "super-adamantane" (C₃₅H₃₆); see the article for the structures of these hydrocarbons. Compare your results with those found by other versions of MM and by various quantum mechanical methods, as listed in the tables of the cited reference. [Shen, M.; Schaefer, H. F., III; Liang, C.; Lii, J.-H.; Allinger, N. L.; Schleyer, P. von R. J. Am. Chem. Soc. 1992, 114, 497.1

