ADDENDUM TO MOLECULAR MECHANICS PROBLEM SET
Fall semester, 2005

A number of recent journal articles and review articles contain information that is relevant to a significant number of examples in the problem set. If you choose one of the following problems for your MMX project, you should be sure to consult the appropriate review article(s) (as well as the cited references where the problem is first presented).

There are three relevant review articles from the series "Advances in Strain in Organic Chemistry";
Halton, B., Ed.; JAI: London (available in the library):

for anti Bredt compounds and small-ring propellanes (Nos. 1, 13, others?): Szeimies, G.; 1992,
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for cyclophanes (Nos. 3, 27, 34, 52, 53, 56-58, 63, 119, 125, 181, 187, 189, 193, 197, 220, others?):


Dodziuk, H. Top. Stereochem. 1994, 21, 351: this is a review article on inverted or pyramidalized sp³ hybridized carbons in strained compounds (Nos. 78, 149, 352, others?) A very recent paper from this same research group elaborates on several of the compounds calculated in 352 and suggests a new structure with only one inverted carbon: Dodziuk, H.; Dolgones, G.; Leszczynski, J. Tetrahedron 2003, 59, 10013.


Marchand, A. P.; Xing, D.; Bott, S. G. Tetrahedron 1996, 52, 825 presents new information about the
crowded molecules (Z)- and (E)-1,2-di(1-adamantyl)ethene; cf Problem 198.


Alder, R. W.; East, S. P. Chem. Rev. 1996, 96, 2097 presents an extensive review of the experimental and computational details on bicyclo [m.n.o] compounds in which the bridgehead substituents are either both outside the ring (the normal situation) or one inside/one outside or both inside. This will be relevant to Problems 14 and 35 (both of which are mentioned in this review) and to other problems that you might devise on your own. Especially interesting are the MM2 calculated data in Table 1.

Gwaltney, S. L.; Sakata, S. T.; Shea, K. J. J. Org. Chem. 1996, 61, 7438 is the full paper of the 1992 communication that was the basis for Problem 142.

Sakamoto, Y.; Miyoshi, N.; Hirakida, M.; Kusumoto, S.; Kawase, H.; Rudzinski, J. M.; Shinmyozy, T. J. Am. Chem. Soc. 1996, 118, 12267 is the full paper related to the communication that served as the basis for Problem 257; for work on the mechanism by which this "pinwheel" molecule inverts, see Hori, K.; Sentou, W.; Shinmyozu, T. Tetrahedron Lett. 1997, 52, 8955. See, also, the recent calculations on these compounds, reported by Bettinger, H. F.; Schleyer, P. von R.; Schaefer, H. F., III J. Am. Chem. Soc. 1998, 120, 1074.

Li, W.; Fox, M. A. J. Am. Chem. Soc. 1996, 118, 11752 presents data on dimers, trimers, tetramers, etc. from substituted cyclobutadienes; these "ladder" compounds are related to those in Problem 164. (See, also, Hopf's 2003 article on "ladderanes" that is mentioned on p. 4 of this addendum.)


For further work on bridgehead allylic cations that are incapable of resonance stabilization (see Problems 90 and 112), there is a recent paper by Tokunaga, K.; Ohtsu, T.; Ohga, Y.; Takeuchi, K. J. Org. Chem. 1998, 63, 2209.


Much work has been done on the Bergman cyclization of enediynes to six-membered ring aromatic diradicals (see Problem 94, for example), a reaction of interest not only for its mechanistic but also for its biological connotations. For an update and for recent calculations on the product (a p-benzyne), see Schreiner, P. R. J. Am. Chem. Soc. 1998, 120, 4184.


Conformational analysis of the crowded 1-alkyl-2,2,6,6-tetramethylpiperidines was addressed in Problems 150 and 180. Now there are new calculations that shed some doubt on the earlier interpretations. See Belostotskii, A. M.; Gottlieb, H. E.; Aped, P.; Hassner, A. Chem. Eur. J. 1999, 5, 449.

For a follow-up on the conformations of tetraethylmethane (3,3-diethylpentane) from Problem 330, see Alder, R. W.; Allen, P. R.; Hnyk, D.; Rankin, D. W. H.; Robertson, H. E.; Smart, B. A.; Gillespie, R. J.; Bytheway, I. J. Org. Chem. 1999, 64, 4226.
A recent article describes the stereochemical relationship of the aromatic rings in the \([n,n]\)metaparacyclopahnes (where \(n=2, 3, \) or \(4\)); these are related to Problems 193 and 220; see Hong, B. H.; Lee, J. Y.; Cho, S. J.; Yun, S.; Kim, K. S. J. Org. Chem. 1999, 64, 5661.

For further work on compounds related to the annelated benzenes of Problem 274, see the review by Komatsu, K. Eur. J. Org. Chem. 1999, 1495.


A recently published book on hydrocarbon chemistry has discussions of many of the types of compounds that are found throughout these problem sets: prismanes, Platonic solids, twisted alkenes, cyclic alkynes, bridgehead alkenes, cyclophanes, etc. If you are doing a project that involves some sort of unique or strained or implausible hydrocarbon, a brief "stroll" through this book should prove rewarding: Hopf, H. Classics in Hydrocarbon Chemistry; Wiley-VCH: Weinheim, 2000.

If you are working any of the exercises involving fenestranes (66-70, 161, 273), you might be interested in some recent MM3 and MMX calculations on a naturally occurring 5/5/5/7 fenestrane system: Weavers, R. T. J. Org. Chem. 2001, 66, 6453.

Problem 249 called for calculations on the major conformations of \(\text{Et}_2\text{N-CH(CH}_3\text{)}_2\). This molecule has been examined, again, this time using MM3 (instead of MM2) and very careful low temperature \(^{13}\text{C}\)NMR analysis. Be sure to include the new energy data from Figure 1, if you choose to work on this problem: Sebag, A. B.; Forsyth, D. A.; Plante, M. A. J. Org. Chem. 2001, 66, 7967.

If you are working on any of the problems (310, 341, 362, 374) concerning polyalkylated aromatic compounds (like hexaethylbenzene) that come from the Biali and Gottlieb research groups, you should consult a very recent review article: Marks, V.; Gottlieb, H. E.; Biali, S. E. Eur. J. Org. Chem. 2003, 1825.

"Ladderanes" are the subject of three earlier problems (164, 213, and 244) and are mentioned briefly on p. 2 of this handout. One of the leading practitioners, Henning Hopf, has published a brief review on the preparation and characterization of these molecules, including a discussion of the ladderanes that are found in Nature. If you decide to do an MMX project in this area, you need to look at this recent review: Hopf, H. Angew. Chem., Int. Ed. Engl. 2003, 42, 2822. See, also, a very recent article on construction of ladderanes in the solid state: Gao, X.; Friscic, T.; MacGillivray, R. Angew. Chem., Int. Ed. Engl. 2004, 43, 232.

A number of problems (e.g., 2, 9, 10, 269, 302, and 368) have explored the use of alkynes as spacers in rings of moderate size. For the latest word on these and others not yet set as problems, be sure to consult Marsden, J. A.; Palmer, G. J.; Haley, M. M. Eur. J. Org. Chem. 2003, 2355.
Problem 339 was concerned with the structure and reactivity of polyspirocyclobutanes. A recent article by the same research group describes the synthesis and stereochemistry (racemic or meso) for several of these compounds: Fitjer, L.; Kanschik, A.; Gerke, R. *Tetrahedron* **2004**, *60*, 1205.

Problem 387 focused on a series of compounds with a central benzene ring, fused to which were various bicyclic units. A related series of molecules has recently been synthesized; someone who chooses to do this problem should also consult the more recent work: Dastan, A.; Fabris, F.; De Lucchi, O.; Güney, M.; Balci, M. *Helv. Chim. Acta* **2003**, *86*, 3411.

A review article covering all sorts of strained hydrocarbons has recently appeared. If you are doing calculations on propellanes (Problem 13), trans-fused bicyclo[n.1.0]alkanes (Problem 105), anti-Bredt bridgehead alkenes (Problems 1 and 117), etc., you should compare your MMX calculations with the experimental and *ab initio* results reported by Wiberg, K. B. In *Reactive Intermediate Chemistry*; Moss, R. A.; Platz, M. S.; Jones, Jr., M. Eds.; Wiley, 2004; Chapter 15.

For a recent research article and for a review article on the strained pyramidalized alkenes of Problems 279, 306, and 363, see: Camps, P.; Fernández, J. A.; Font-Bardia, M.; Solans, X.; Vázquez, S. *Tetrahedron* **2005**, *61*, 3593; Vázquez, S.; Camps, P. *Tetrahedron* **2005**, *61*, 5147. Another type of pyramidalization is found in strained polycyclic alkenes (e.g., Problems 26, 109, 113, 270, 383, 386, 400); many of these and many new ones are found in a recent article: Williams, R. V.; Margetic, D. *J. Org. Chem.* **2004**, *69*, 7135.


For problems involving [2,2]cyclophanes, whether p,p or p,m or m,m (e.g., 23, 58, 183, 227, 2412, 248, 316, 355, 375, 395) see the most recent calculations in Caramori, G. F.; Galembeck, S. E.; Laali, K. K. *J. Org. Chem.* **2005**, *70*, 3242.