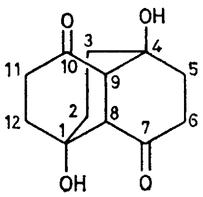
Application of Force Field Calculations to Organic Chemistry. Part 6.[1] Steric Analysis of Synthesis and Structure of 1,4-Dihydroxytricyclo-$[6.4.0.0^{4,9}]$dodecane-7,10-dione. Dynamic Conformational Calculations of its Hydrocarbon Skeleton and Related Systems (Bicyclo[3.3.1]nonane and Bicyclo[3.3.2]decane)

By **Eiji Ōsawa,*** Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060, Japan
Koji Aigami and **Yoshiaki Inamoto,** Industrial Research Laboratories, Kao Soap Company, Ltd., Minato-Yakushubata, Wakayama 64091, Japan

The product distribution for the double intramolecular condensation of cyclododecanetetraone (3) has been calculated by the MM1 force field and found to explain the unexpected isolation of 1,4-dihydroxytricyclo$[6.4.0.0,^{4,9}]$-dodecane-7,10-dione (1). Essential features of the detailed molecular structure of (1), as revealed by a previous *X*-ray analysis, can be reproduced by this force field. The hydrocarbon framework (9) of (1), which can be regarded as a triply fused twist-chair cyclohexane, an ethano-bridged *cis*-decalin, or a trimethylene-bridged bicyclo-[3.3.1]nonane, was subjected to detailed static and dynamic conformational calculations by the MM2 force field and recognized to be in a deep energy well as is bicyclo[3.3.1]nonane. Similar calculations on the homologue bicyclo[3.3.2]decane reveal that a boat chair conformation (13c) with an eclipsed two-carbon bridge and a twin twist-chair (13a) with a staggered bridge coexist at equilibrium.

POTENTIAL areas for the application of empirical force field calculations to organic chemistry include (1) prediction of product distributions based on comparison among calculated enthalpies of possible products, (2) generation of precise molecular structures, (3) interpretation of structures in terms of internal strain distributions, and (4) reproduction of mechanistic details in conformational transformations.[2] The recent synthesis and structure determination of 1,4-dihydroxytricyclo$[6.4.0.0^{4,9}]$dodecane-7,10-dione (1)[3] provide an ideal material for illustrating these potentialities of the force field method. In this paper, we first give a thermodynamic analysis of the unexpected isolation of (1), and then discuss its peculiar conformation and unique strain distribution in some detail, mainly in terms of its parent hydrocarbon in comparison to related systems involving *cis*-decalin, bicyclo[3.3.1]nonane, and bicyclo-[3.3.2]decane. Conformational calculations including the use of the bond-drive technique led to some insight into the origin of the apparent rigidity in bicyclo[3.3.1]-nonane and of flexibility in bicyclo[3.3.2]decane.



(1)

Throughout this work, the latest versions of the Allinger force field, MM1[4,5,]† and MM2,[6] are used unless otherwise noted.

Steric Aspects of Synthesis of Compound (1).—Musso[3] originally intended to obtain the potential tetra-asterane progenitor (2) (Figure 1) when he carried out the double aldol-type intramolecular cyclization of cyclododecane-1,4,7,10-tetraone (3). While only two intermediates are expected from the first cyclization, the second step theoretically can take place in as many as 20 ways! Among all possible products resulting from the double cyclization, the apparently highly strained (containing a three-membered ring) and/or labile ‡ structures A—I can be eliminated. This leaves seven tricyclic structures (1), (2), and (4)—(8) which can be reasonably expected to result from this reaction. An approximate but simple way of predicting the possibility of obtaining (2) is to compare calculated enthalpies among these possible products. Results of the MM1 force field calculations are included in Figure 1.

Two structures, (1) and (6), have enthalpies 10—20 kcal mol^{-1} lower than those of the other structures, and this difference is large enough to exclude the less stable structures as candidates for the products. Compound (2) is found among these unstable structures, its two potential conformers, (2a and b), having almost the same calculated enthalpy. Thus, on the basis of our calculations, compound (2) should never be isolated from this reaction. The calculated enthalpy of (1) is 1.5 kcal mol^{-1} lower than that of (6).§ If we neglect the entropy contribution,[7] this difference corresponds to a product ratio (1) : (6) of 12 : 1. Consequently, the isolation of

---

† Several modifications have been made on the original QCPE program by the present authors. Major changes are (a) dihedral angles are given conventional signs according to H. J. Geise, C. Altona, and C. Romers, *Tetrahedron*, 1967, **23**, 439, and (b) subroutine NDRIVE which rotates bonds according to the Wiberg–Boyd method is rewritten so that any number of selected bonds can be driven simultaneously.

‡ Labile structures tend to lose a water molecule to form unsaturated ketones. See ref. 3.

§ The uncertainty in the enthalpy calculations by the MM1 force field is ±1.2 kcal mol^{-1}, equal to three times the reported[7] standard deviation for a set of standard molecules. The calculated enthalpy difference between (1) and (6) is barely outside this uncertainty range, but the uncertainty usually diminishes when isomers and similar structures are compared because of the cancelling out of errors inherent in the force field employed.

(1) as the only $C_{12}H_{16}O_4$ product[3] is hardly surprising.*

If the calculations had been performed *before* experiments, this reaction would probably have been abandoned in favour of better ways of obtaining tetra-asterane.[8] The ignorance of the relative product stabilities at the outset of the experiments, however, led to the characterization of (1), the first derivative of an unknown but profoundly intriguing tricyclic hydrocarbon.

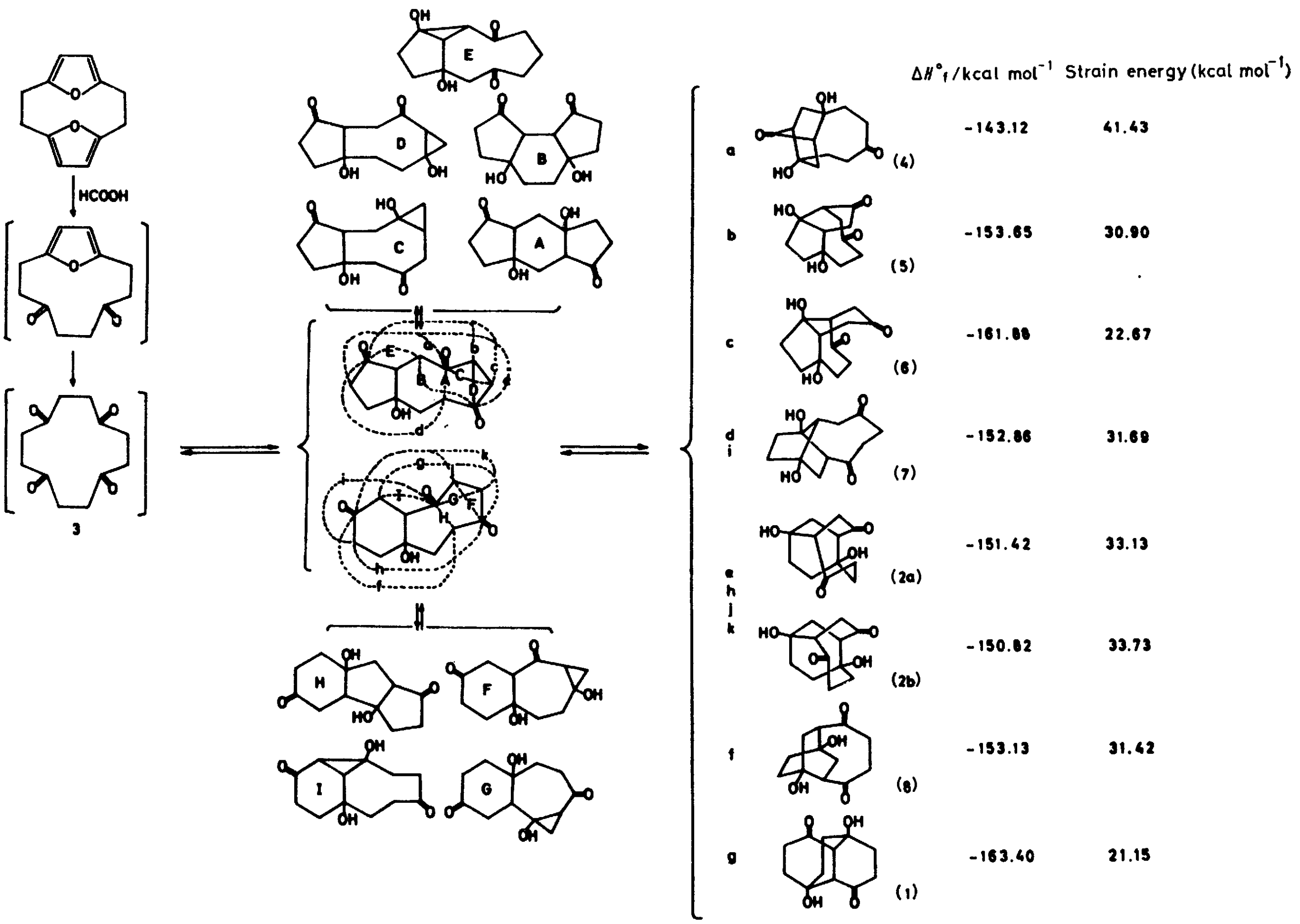


FIGURE 1 Possible intermediates and products of double aldol-type condensation of cyclododecatetraone (3), and heats of formation (ΔH_f^0) and strain energies of dihydroxytricyclododecanediones calculated by the MM1 force field

TABLE 1

Deviations of calculated structural parameters of (1) from those determined by *X*-ray analysis

	Standard deviation
Bond lengths	
C–C, C–O	0.015 Å
C–H, O–H	0.11 Å
Valence angles	
C–C–C, C–C–O	1.2°
C–C–H, C–O–H, H–C–H	2.4°
Dihedral angles	
C–C–C–C	3.9°

Comparison between X-Ray and Calculated Structures of Compound (1).—The structure of (1) has been determined by *X*-ray analysis.[3] We first take advantage of this to check the ability of the MM1 force field to reproduce the structure of a *polar* molecule like (1).†,‡ In terms of the standard deviation (Table 1), the agreement for bond lengths and valence angles not involving hydrogen atoms is quite satisfactory. The rather long C(1)—C(8) bond observed by *X*-ray analysis (1.561 Å) is calculated to have a normal value of 1.533 Å. The observed deviations are close to those reported for MM1 and other force fields on non-polar molecules.[2a,7,11] When hydrogen atoms are included, however, the error increases by 2—10 times. This is certainly due to experimental uncertainties in locating protons on a Fourier difference map, rather than to inaccuracies of

---

[*] It is likely that one of the two small spots in the t.l.c. of the equilibrium mixture with R_F slightly greater than that of (1)[3] is that for (6).

[†] While molecular mechanics structures refer to the gas phase, the structures of polar molecules are usually solved by *X*-ray analysis of crystals. Therefore, there is no *a priori* reason to expect good agreement between these two structures. For discussions of the effects of phase on molecular structure see ref. 9.

[‡] For another example of comparison between *X*-ray and molecular mechanics-calculated structure, albeit for a less polar molecule see ref. 10.

the hydrogen atom parameters of the force field.* The deviation of calculated C–C–C–C torsional angles from observed values is comparatively large (3.9°), reflecting the well recognized fact that the torsional energy is the ' softest ' among the intramolecular forces.[2] Nevertheless, this deviation is considerably smaller than the general deviation of torsional angles suggested by Allinger.[2b] This already indicates lower than usual flexibility for (1) (see below).

The *X*-ray analysis revealed that the three six-membered rings of (1) are all in twist-chair conformations.[3] Our force field calculations reproduce the complicated and uneven twisting and puckering of these rings with considerable precision. The first three colums of Table 2 compare observed with calculated cross angles, made by two opposing C–C bonds in a six-membered ring. Table 3 lists observed and calculated dihedral as well as valence angles in central and outer six-membered rings. The puckering of six-membered rings in (1) is deepest near the juncture of the three rings [(C(1)–C(8)–C(9)–C(4)] as shown by the large absolute dihedral angles and small valence angles, but shallowest at the outer periphery [C(2)–C(3), C(6)–C(7)] as shown by the small absolute dihedral angles and large valence angles. The complex but intriguing conformation of (1) undoubtedly arises as the result of the interplay of intramolecular forces trying to dissipate the strain at the ring junction. Unfortunately, (1) is too complicated for further analysis of the conformational consequences of the ring fusion because of the presence of substituents. For example, the flattening at C(7) may have been caused by the carbonyl group. Hence we now turn to the parent hydrocarbon (9) (Figure 2).

TABLE 2

Cross angles (°) of opposing C–C bonds in six-membered rings of 1,4-dihydroxytricyclo$[6.4.0.0^{4,9}]$dodecane-7,10-dione (1), tricyclo$[6.4.0.0^{4,9}]$dodecane (9), and *cis*-decalin (10)

	(1)		(9)			(10)	
	X-Ray [a]	MM1 [b]	MM1 [b]	MM2 [c]		MM1 [b]	MM2 [c]
Central ring							
C(2)–C(3), C(8)–C(9)	14.4	20.3	21.3	19.2			
C(1)–C(2), C(4)–C(9)	–7.0	–10.4	–10.9	–9.8			
Outer rings							
C(1)–C(8), C(10)–C(11)	19.6	17.9	12.4	12.7	C(3)–C(2), C(6)–C(5)	1.5 [d]	1.9 [d]
C(8)–C(9), C(11)–C(12)	–11.2	–8.1	–6.8	–7.4	C(1)–C(6), C(4)–C(3)	–1.6 [d]	–1.6 [d]
C(1)–C(12), C(9)–C(10)	–8.6	–9.9	–5.6	–5.5	C(1)–C(2), C(4)–C(5)	0.1 [d]	–0.3 [d]

[a] Ref. 3. [b] Calculations based on MM1 force field.[4,5] [c] Calculations based on MM2 force field.[6] [d] Conventional numbering based on that of (9). See illustration in (10).

TABLE 3

Endocyclic dihedral and valence angles (°) in central and outer six-membered rings of (1)

Dihedral angles						Valence angles					
Central ring			Outer ring			Central ring			Outer ring		
	X-Ray [a]	Calc.[b]		*X*-Ray [a]	Calc.[b]		*X*-Ray [a]	Calc.[b]		*X*-Ray [a]	Calc.[b]
C(1)–C(8) [c]	59.0	60.0	C(7)–C(8)	–39.7	–37.8	C(1)	111.5	109.6	C(7)	119.4	118.8
C(8)–C(9)	–65.8	–72.2	C(8)–C(9)	58.0	54.4	C(8)	108.4	108.4	C(8)	111.5	113.8
C(9)–C(4)	59.0	60.0	C(9)–C(4)	–65.9	–63.9	C(9)	108.4	108.4	C(9)	108.4	108.4
C(4)–C(3)	–45.3	–40.0	C(4)–C(5)	56.1	57.7	C(4)	111.5	109.6	C(4)	107.1	108.9
C(3)–C(2)	39.0	31.3	C(5)–C(6)	–37.1	–39.0	C(3)	115.3	117.0	C(5)	114.6	114.5
C(2)–C(1)	–45.3	–40.0	C(6)–C(7)	28.3	28.9	C(2)	115.3	117.0	C(6)	115.3	113.8

[a] Ref. 3. [b] According to MM1 force field.[4,5] [c] An expression such as C(1)–C(8) is an abbreviation of C(2)–C(1)–C(8)–C(9) comprising a four-atom unit.

Static Conformation of Tricyclo$[6.4.0.0^{4,9}]$*dodecane* (9) *in Comparison with* cis-*Decalin* (10) *and Bicyclo*[3.3.1]-*nonane* (11).—Calculations of (9) and other hydrocarbons to be discussed hereafter are performed using Allinger's new force field MM2 [6] while MM1 is used only for comparison purposes. In contrast to MM1 which adopts a ' too hard ' hydrogen nucleus,[13] MM2 uses a reasonably sized proton and is believed to be more suitable for studying the steric energy distribution in congested molecules.[6]

The structure of (9) reveals several intriguing stereochemical features.† As seen in Figure 2 where the calculated minimum energy conformation of (9) ‡ is viewed from various angles, it is composed of three twist chair cyclohexane rings constrained in a rigid cage framework to give a chiral composite [14] and as such may be contrasted to twistane [15] which incorporates three fused twist boat cyclohexane rings.

Comparison of cross angles between (1) and (9) (Table 2) reveals that twisting in cyclohexane rings becomes more pronounced at the ring junction and less severe at the outer periphery of (9) compared with (1). The sites of calculated maximum and minimum dihedral

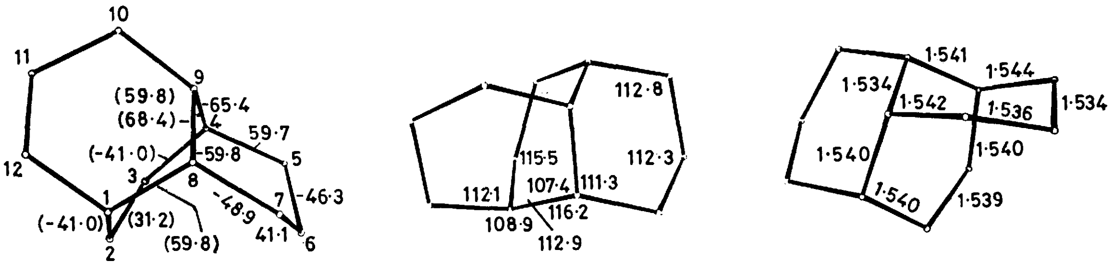
---

* In fact, force field calculations are sometimes more reliable and convenient than experimental methods for determining the position and accompanying stereochemical consequences of proton nuclei in organic molecules, if the proton force field parameters are correctly chosen. Regarding this last point, see ref. 12.

† (9) has been prepared from (1). (1) has been resolved into enantiomers, H. Buding and H. Musso, personal communication.

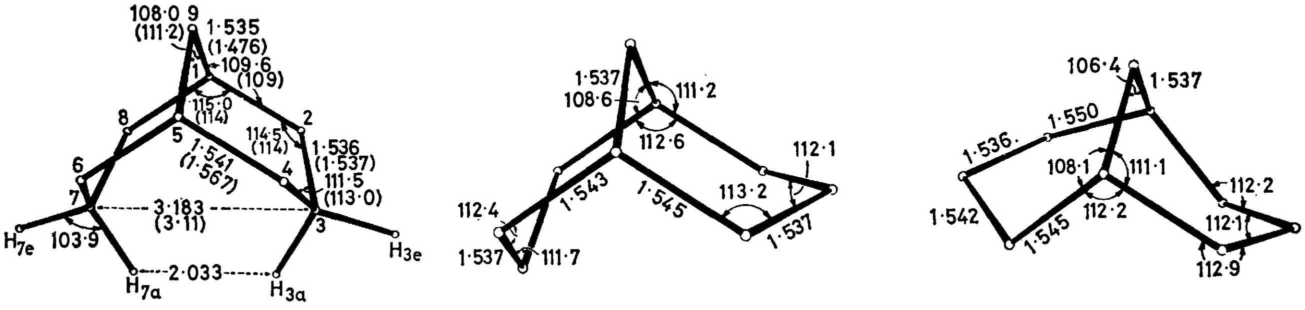
‡ MM2 calculations of (9) were repeated twice, starting from a ' diamond lattice ' conformation as well as from the *X*-ray carbon skeleton of (1). The two sets of starting co-ordinates gave identical final structures, believed to be at the global energy minimum.

and valence angles of (9) are identical with those of (1) given in Table 3. Thus, the peculiarly deformed skeletal conformation of (1) is inherent to its hydrocarbon skeleton (9), and the substituents in (1) act rather to weaken the twisting and puckering.



(9c) (9a) (9b)

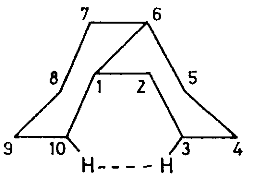
FIGURE 2 ORTEP drawing of tricyclo[6.4.0.0^{4,9}]dodecane (9) according to the MM2 force field. Calculated C–C–C bond angles (°) (9a), C–C bond lengths (Å) (9b), and C–C–C–C dihedral angles along inner (in parentheses) and outer six-membered rings (9c) are given



(11a) (11b) (11c)

FIGURE 3 ORTEP illustration of twin chair (11a) (point group C_{2v}), boat-chair (11b) (C_s), and twin boat (11c) (C_2) conformers of bicyclo[3.3.1]nonane calculated by the MM2 force field. Numbers refer to calculated C–C bond lengths (Å), C–C–C bond angles (°), and H–H nonbonded distances (Å). Electron diffraction values (in parentheses) are taken from ref. 23

Compound (9) can be regarded as an ethano-bridged *cis*-decalin (9b) or a trimethylene-bridged, twin chair bicyclo[3.3.1]nonane (9c). In order to assess the effects of bridging on the conformation of (9), it appeared helpful to study the conformation of *cis*-decalin (10) and bicyclo[3.3.1]nonane (11) (Figure 3).[16] Inspection of the calculated structure of *cis*-decalin (10) [6,*] reveals that the six-membered rings take an almost perfect chair form with the junction only slightly flattened (Table 2, last two columns). The calculated closest nonbonded H-H distance in the concave space of (10) is 4.41 Å.



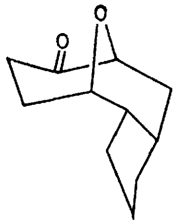
(10)

On the other hand, it is well established experimentally that the most favourable conformation of bicyclo[3.3.1]nonane in solid,[18] in solution,[19,†] and in the vapour phase,[23] is an *eclipsed* twin chair (11a) (Figure 3), despite the severe repulsion between the two close methylene groups (at positions 3 and 7) and the consequent skeletal angle deformations.[16] Equilibration of 3-hydroxy and 3-methoxycarbonyl derivatives of (11) has led to an estimate that (11a) is 2.9—3.2 kcal mol^{-1} more stable than a boat-chair form (11b).[24] Our MM2 calculations on three basic forms of (11) (Table 4 and Figure 3) rationalize these experimental observations: (11a) is

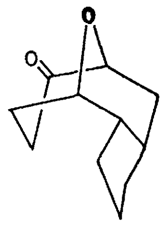
---

[*] To our knowledge, experimental information on the molecular structure of *cis*-decalin is scarce. A preliminary gas-phase electron diffraction study reports only average C–C bond lengths and C–C–C angles.[17]

[†] The recent discovery [20] by *X*-ray analysis of a partial boat-chair bicyclo[3.3.1]nonyl structure in the fused oxa-analogue (A) represents a notable exception. However, several solution reactions of this molecule involving transannular 1,6-hydride shifts can best be explained on the basis of chair-chair conformation (B) rather than (A).[20,21] MM1 calculations indicate (B) to be 1.45 kcal mol^{-1} more stable than (A).[21] Recently an example of the coexistence of chair and twist-boat cyclohexanones in the unit cell has been reported.[22]



(A)



(B)

TABLE 4

MM2 Calculations of three basic conformers of bicyclo[3.3.1]nonane

	ΔH_f° [a]/ kcal mol^{-1}	Strain energy (kcal mol^{-1})	Point group
Twin chair (11a)	−30.48	12.33	C_{2v}
Boat-chair (11b) [b]	−28.16	14.66	C_s
Twin boat (11c) [c]	−23.13	19.68	C_2

[a] Latest experimental heat of formation, −30.5 ± 0.6 kcal mol^{-1}: W. Parker, W. V. Steele, and I. Watt, *J. Chem. Thermodynamics*, 1977, **9**, 307. For previous calculations, see ref. 25. [b] For a recent *X*-ray observation of boat-chair conformer in an oxa-analogue, see ref. 22. [c] Twisted. See text.

2.3 kcal mol^{-1} more stable than (11b).* Hence, the twist conformation of the corresponding bicyclo[3.3.1]-nonane portion of (9) [see (9c), Figure 2] clearly contrasts with (11). The effect of twisting in (9) and (11) upon the steric energy will be discussed later.

TABLE 5

Steric energy distribution on unique atoms of tricyclo[6.4.0.0^{4,9}]dodecane (9) by MM2 force field

	Stretch	Bending	Stretch–bend	Torsion	v.d.W.[a]	Sum
C(1)	0.1695	0.2814	0.0356	1.050	0.1078	1.6443
C(2)	0.0919	0.6245	0.0602	0.737	0.1268	0.6404
C(5)	0.0910	0.2136	0.0345	0.681	0.2187	1.2388
C(6)	0.0485	0.2775	0.0272	0.736	0.0337	1.1229
C(7)	0.0874	0.5388	0.0496	0.568	0.1193	1.3631
C(8)	0.1321	0.6724	0.0474	2.112	0.0506	3.0145
H(1e) [b]	0.0054			0.060	0.4954	0.5608
H(2e)	0.0016			0.180	0.2272	0.4088
H(2a)	0.0000			0.196	0.4684	0.6644
H(5e)	0.0020			0.029	0.2353	0.2663
H(5a)	0.0021			0.061	0.3054	0.3685
H(6e)	0.0027			0.069	0.3209	0.3926
H(6a)	0.0001			0.160	0.5140	0.6741
H(7e)	0.0016			0.061	0.1216	0.1842
H(7a)	0.0027			0.094	0.1932	0.2899
H(8) [c]	0.0055			0.046	0.6687	0.7202
Sum	0.6441	2.6082	0.2545	6.840	4.2070	14.5534 [d]

[a] van der Waals interactions. [b] Equatorial with regard to both the central and outer rings. [c] Axial with regard to an outer ring [C(1)–C(8)–C(9)–C(10)–C(11)–C(12)] but equatorial to the other two rings. [d] Twice this value is equal to the total steric energy of (9).

Thus, the minimum-energy structures of the reference molecules (10) and (11) demonstrate that the unique twisting and puckering in (9) are caused by the bridging.

Internal Strain Distribution in Compound (9).—The calculatetotal strad in energy † of (9) (21.15 kcal mol^{-1}) is considerably higher than those of *cis*-decalin (7.57 kcal mol^{-1}) and bicyclo[3.3.1]nonane (12.33 kcal mol^{-1}).‡ In view of the possible relation between the means of dissipating this large amount of strain within the molecule and the peculiar conformation of (9), the steric energy distribution in (9) is analysed. For this purpose, it is convenient if the steric energies, initially calculated for interacting atom pairs, can be partitioned between atoms. The following terms are summed to obtain steric energy ' per atom ': (1) one half of stretch energy involving the atom in question; (2) combined bending and stretch-bend energies of an angle system if the atom in question comprises the central atom (A–*B*–C); (3) one half of torsion energy of a torsional system if the atom in question comprises an end of a system (*A*–B–C–D); and (4) one half of van der Waals energy of a pair of nonbonded atoms involving the atom in question.

The results of the analysis are summarized in Table 5. As expected, C(8) [and the equivalent C(9)] at the three-ring junction is by far the most strained of all atoms in (9). The major contributor to the strain at this carbon atom as well as at C(1) [and C(4)], the next most strained

---

* Bicyclo[3.3.1]nonane has frequently been the subject of force field calculations.[25] However, it is now clear that these results are not suitable for detailed analysis of internal H–H interaction energies.

While the boat-boat conformer (11c) is decidedly disfavoured, it is interesting to note that this conformer is twisted at its energy minimum, *i.e.* each half of the boat cyclohexane ring is displaced in opposite directions sideways parallel to the plane of the central bridge. The dihedral angle between planes C(2)–C(1) · · · C(5) and C(4)–C(5) · · · C(1) is 21.1°. The same structure is reached no matter whether the energy minimization is started from eclipsed or severely twisted starting conformations. These results appear to reflect the inherent flexibility of the boat cyclohexane ring. In contrast, the boat-chair form (11b) has C_{2v} symmetry at its energy minimum. Here the boat cyclohexane ring is fixed into non-twisted form apparently by virtue of its fusion with a rigid chair cyclohexane ring.

Recent gas-phase electron diffraction analysis of (11)[23] provides a further check on the accuracy of the MM2 calculations: average C–C length 1.538 ± 0.001 Å by electron diffraction, 1.538 Å by calculation; average C–C–C angle 111.5 ± 1.0° (exp.), 112.3° (calc.); dihedral angle C(3)–C(2)–C(1)–C(9) 53 ± 2° (exp.), 53.6° (calc.). Further comparisons are given in structure (11a) (Figure 3). The characteristic features of (11a), namely the expanded valence angles at the bridgehead position and the drastic flattening of the lower half of the cyclohexane ring are reasonably reproduced by calculations. However, MM2 calculations gave too long a C(3) · · · C(7) distance despite the smaller, softer hydrogen atoms as opposed to MM1. This suggests that still more adjustment may be required for MM2. It may be noted here that not only MM2 but also CFF (O. Ermer and S. Lifson, *J. Amer. Chem. Soc.*, 1973, **95**, 4121) which uses softer hydrogen atoms and harder carbon atoms compared to MM2[6] still gives too long C · · · C and H · · · H distances in highly congested *endo,endo*- and *exo,exo*-tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodecane [MM2 values: H(4) · · · H(10) 1.947 Å, C(4) · · · C(10) 3.342 Å for *endo,endo*-isomer; H(11) · · · H(12) 1.893 Å, C(11) · · · C(12) 3.212 Å for *exo,exo*-isomer].

† For a definition of strain energy, see ref. 4*b*.

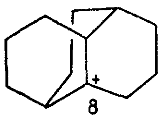
‡ The calculated ΔH_f^0 of (9) (−32.34 kcal mol^{-1}) is much higher than the experimental ΔH_f^0 (−52.3 ± 0.7 kcal mol^{-1})[26] of 1,3-dimethyladamantane, the stabilomer of tricyclododecanes.[27]

atom at the two-ring junction, is the torsional term.[*] The second largest strain source at C(8) is angle bending [see Figure 2 (9a)].

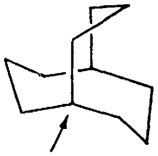
Two salient features regarding internal strain involving hydrogen atoms merit attention. First, 1,4-gauche H–H nonbonded interactions, the controversial strain source recently recognized by Wertz and Allinger,[4a] are largely responsible for the strain in two of the most strained protons, H(1e) and H(8) [and also for a part of strain of H(6a)]. Although the role of this interaction in organic molecules is not likely to be as important as first proposed,[13,†] it is strong in this particular instance in which twisted and puckered rigid component rings produce ' favourable ' circumstances for close 1,4 H–H interactions. Additional examples of strong gauche H–H interactions in the bicyclo[3.3.2]decane system (13) will be mentioned below. Secondly, there is a remarkably strong repulsive interaction between H(2a) and H(6a) over a calculated distance of 2.07 Å, quite short for a H–H nonbonded distance.[‡,§] This interaction resembles that of H(3a)–H(7a) in twin chair bicyclo[3.3.1]nonane (11a) (calculated 2.03 Å, 1.07 kcal mol^{-1}).[¶]

Thus, the following picture emerges. The molecular strain is concentrated at the ring junction in the form of ' soft ' torsional and bending energies while some of the strain is spread out to hydrogen atoms attached to the junction and even far into the outer rings.

Predicted Carbonium Ion Reactivity of Compound (9).—As mentioned above, C(8) of (9) is the most strained atom in the molecule and two of its C–C–C angles are much larger than the tetrahedral value (Figure 2). The steric circumstances of this carbon atom are similar to those of bridgehead carbon atom of manxane (12) which is so flattened that it is already close to the sp^3 configuration in the ground state.[32] The hydrocarbon — carbonium ion strain energy difference, a measure of the activation energy of carbonium ion formation introduced by Bingham and Schleyer,[33,34] is 4.69 kcal mol^{-1} for $(9)^+$,[35,**] as calculated by the Engler force field.[25c] We thus predict that $(9)^+$ will be formed with considerable ease, probably only slightly slower than t-butyl cation.[36,37]



$(9)^+$



(12)

Bond-drive Calculations for Compounds (9) *and* (11).—More information on the subtle balance between nonbonded H–H repulsion, angle bending, and other strain components, expected to play a crucial role to the total energy level, can be obtained by dynamic molecular mechanics calculations on (9) and (11). In order to achieve any desired deformation of less symmetrical molecules such as (9), the original Wiberg–Boyd technique of bond-driving[38] is modified so that a selected multiple number of bonds can be driven simultaneously.

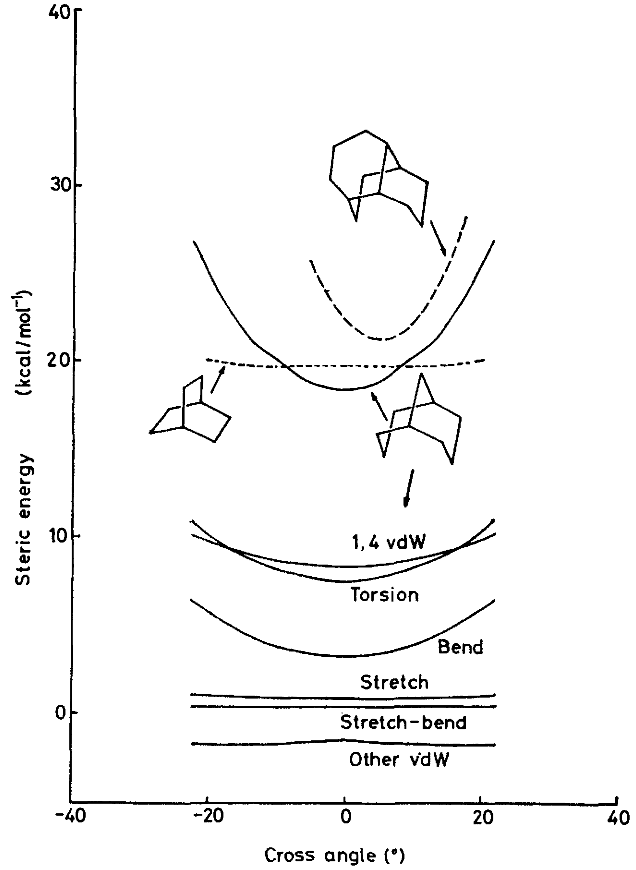


FIGURE 4 Dependence of steric energy upon twisting of twin chair bicyclo[3.3.1]nonane (11a) (solid line), tricyclo[$6.4.0.0^{4,9}$]-dodecane (9) (broken line), and bicyclo[2.2.2]octane (dotted line) to both sides of central bridge in opposite directions. Twist angle means dihedral angle between planes C(2)–C(1) · · · C(5) and C(4)–C(5) · · · C(1) for (11a), between planes C(3)–C(2) · · · C(6) and C(5)–C(6) · · · C(2) for (9), and in C(1)–C(2)–C(3)–C(4) for bicyclo[2.2.2]octane

Figure 5 (solid lines) shows the changes in steric energy of twin chair bicyclo[3.3.1]nonane (11a) as two dihedral angles, C(3)–C(2)–C(1)–C(9) and C(7)–C(6)–C(5)–C(9), are given by equal increments so that the *endo*-hydrogen atoms at C(3) and C(7) move sideways in opposite direc-

---

[*] This is partly the result of adding one- and two-fold torsional components for the C–C–C–C system in the MM2 force field which inevitably leads to high torsional strain at the ring junction.

[†] The energy minimization procedure (pattern search) employed in our previous paper[13] has recently been criticized.[28] In this paper, we used a modified Newton–Raphson approach with occasional preliminary minimization by pattern search for both MM1 and MM2.

[‡] Examples of remarkably short intramolecular H–H distances: (a) 1.954 Å in 2,2′-bisadamantylidene;[29] (b) 1.82 in *exo,exo*- and 1.85 Å in *endo,endo*-tetracyclo[$6.2.1.1^{3,6}.0^{2,7}$]dodecane;[30] (c) 1.84 Å in *syn*-4,13;6,11-dimethano[15]annulenone.[31]

[§] Because of C_2 symmetry in (9), the same strong interaction exists between H(9a) and H(12a).

[¶] It should also be noted that the two geminal hydrogen atoms at C(3) [and C(7) in (11a)] are pressed towards each other with a resultant H–C–H angle of 103.9° by our calculation.

[**] The corresponding $\Delta H_f{}^0$ difference for bicyclo[3.3.1]non-1-yl cation is 8.91 by the Engler force field[25c] and 8.3 kcal mol^{-1} by the Bingham–Schleyer force field.

tions while keeping C_2 symmetry throughout.* The *endo*-H–H distance reaches 2.4 Å at a twist angle of 20°, and the total van der Waals energy *versus* twist angle curve shows a barely discernible maximum for the eclipsed conformation. However, the decrease in van der Waals repulsion with twisting is not so large as to effectively compete with the rapid increase in bending and torsional strain. As twisting proceeds, the bridgehead C(8)–C(1)–C(2) angle decreases slowly but the angles at C(1)–C(2)–C(3) [and C(5)–C(6)–C(7)] and C(2)–C(3)–C(4) [and C(6)–C(7)–C(8)] expand rapidly, and the flattening of the cyclohexane ring is increased. Regarding torsional strain, unfavourable torsion angles involving C–C–C–H and H–C–C–H appear and the accompanying small strain accumulates in the course of twisting. As a whole, the combined steric energy increases rather sharply with twisting, with the consequence that the eclipsed form (11a) is located at the bottom of a relatively sharp energy well. This is the answer, albeit entirely within the limitation of MM2 parameterization, to the long standing question of why bicyclo[3.3.1]nonane does not take a twist conformation despite the energetically expensive transannular H–H nonbonded repulsion and extensive angle deformation in the eclipsed form.

The corresponding energy *versus* angle curve for (9) is prepared by driving the dihedral angles C(6)–C(5)–C(4)–C(9) and C(8)–C(1)–C(12)–C(11) simultaneously. The curve is steeper near the energy minimum than that of (11a) with the minimum displaced by a twist angle of 5.5°. This twist conformation is calculated to be 1.3 kcal mol^{-1} more stable than the eclipsed conformer (Figure 4, broken line).

Bond-drive Calculations of the Flexible Molecules Bicyclo[2.2.2]*octane and Bicyclo*[3.3.2]*decane.*—The steepness of steric energy *versus* twist angle curve near the energy minimum may be considered as a measure of conformational rigidity. For example, those of (9) and (11) are clearly much sharper than that of bicyclo[2.2.2]octane, the simplest of 'flexible' bicyclic hydrocarbons with a two-carbon bridge (Figure 4).[39,†]

The multi-bond drive technique is applied here also to another flexible hydrocarbon, bicyclo[3.3.2]decane (13). This molecule is of particular interest from the dynamic conformational standpoint because of the question of whether there is a staggered or eclipsed ethano bridge conformation at the energy minimum and the possibility of twin chair $\rightleftharpoons$ boat chair equilibrium proposed recently.[40] Figure 5 summarises the steric energy-twist angle relations for three basic conformations of (13): twin chair, boat-chair, and twin boat. Minimum and maximum points in these curves are reiterated in Table 6 and Figure 6.

Doyle *et al.*[40] compared twist and eclipsed forms of each of these basic conformations for Dreiding models and Schleyer and his co-workers[39] described the results of preliminary calculations on these conformers using the Bingham force field.[33] Our MM2 results agree with most of these previous investigations, but we predict that the twist boat-chair does not correspond to an energy minimum. A gradual twisting of the eclipsed form (13c) leads to a continuous increase in the total steric energy (Figure 5). Two main sources responsible for the continuous increase are C–C–C angle bending and transannular repulsion between the hydrogen atoms on C(3) and C(10), as well as those on C(4) and C(7). The shallow energy minimum of the eclipsed boat-chair (13c) is the lowest of all possible conformers of bicyclo[3.3.2]decane calculated in this study. A careful look at the relaxed structure of (13c) indicates that all the C–C–C angles are widened (from 113 to 118°) to keep nonbonded the H–H distances between hydrogen atoms in

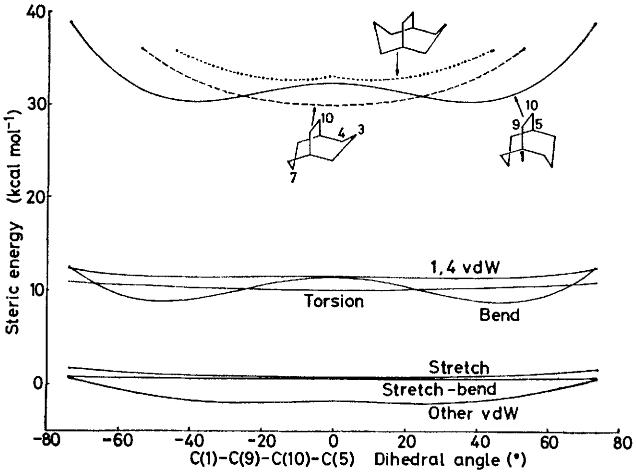


FIGURE 5 Dependence of steric energy upon twisting of twin chair, boat-chair, and twin boat conformers of bicyclo[3.3.2]decane (13). Twist angle means C–C–C–C dihedral angle involving two-carbon bridge in the centre of the four-atom unit

TABLE 6

MM2 Calculations of three basic conformers of bicyclo[3.3.2]decane (13)

	ΔH_f° [a]/ kcal mol^{-1}	Strain energy (kcal mol^{-1})	ϕ [b]
Twin twist chair [c] (13a)	−24.81	23.76	37.5°
Eclipsed twin chair [d] (13b)	−22.79	25.78	0.0
Eclipsed boat-chair [c] (13c)	−25.20	23.38	0.0
Twin twist boat [c] (13d)	−22.45	26.12	11.1
Eclipsed twin boat [d] (13e)	−22.09	26.49	0.0

[a] Experimental value, 25.3 ± 1.8 kcal mol^{-1}: W. Parker, W. V. Steele, and I. Watt, *J. Chem. Thermodynamics*, 1977, **9**, 307. [b] C–C–C–C Dihedral angle of ethano bridge. [c] Energy minimum. [d] Energy maximum.

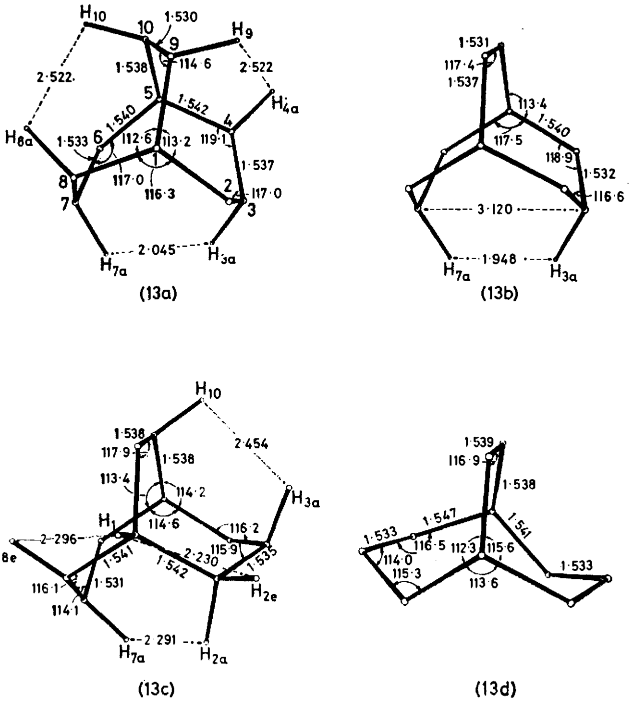
---

* Two other modes of bond drive, namely the two-bond drive at C(3)–C(2)–C(1)–C(8) and C(4)–C(5)–C(6)–C(7) as well as the one-bond drive at C(3)–C(2)–C(1)–C(9) were also performed. The mode discussed in the text moved the congested *endo*-hydrogen atoms apart most effectively.

† In bicyclo[2.2.2]octane, with the progress of twisting starting from eclipsed conformation, stretch, bend, and van der Waals energies increase while stretch-bend and torsion energies decrease, and compensation between these two groups takes place effectively.

the pairs H(3)–H(9),(10) and H(2),(4)–H(7) in the 2.3—2.4 Å range.*

In the twin chair form, the eclipsed conformer (13b) is an energy maximum † with a calculated H(3a)–H(7a) nonbonded distance of only 1.948 Å and widened C–C–C angles (from 113 to 119°). Note that these nonbonded and angle strains are severer in (13b) than the corresponding values in (11a) (Figure 3), which is the energy minimum. The contrast between (13b) and (11a) demonstrates a remarkable effect upon switching from the one- to the two-carbon bridge on the geometry and steric energy. The energy minimum of twin chair bicyclo[3.3.2]decane is found in a twist form (13a). A single contributor to the appearance of this shallow minimum is the angle bending term; many C–C–C angles *decrease* in going from (13b) to (13a). In the course of this twisting process, the H(3a)–H(7a) distance increases to 2.045 Å but H(8a) and H(10) [as well as H(4a) and H(9)] approach each other to 2.522 Å with a consequence that the total nonbonded interaction does not change essentially: 9.67 for eclipse (13b) and 9.50 kcal mol^{-1} for twist (13a).



(13a) (13b)

(13c) (13d)

FIGURE 6 ORTEP illustration of twin twist chair (13a) (point group C_2), eclipsed twin chair (13b) (C_{2v}), eclipsed boat-chair (13c) (C_s), and twin twist boat (13d) (C_s) conformers of bicyclo[3.3.2]decane calculated by the MM2 force field

The energy profile during twisting of the twin boat form is somewhat similar to that of the twin chair conformer, but throughout the extensive driving process, the total steric energy is always *ca.* 2 kcal mol^{-1} higher than the other two conformers and therefore we exclude the twin boat conformer from further consideration.

Our computational finding that eclipsed boat-chair (13c) has significantly lower steric energy than eclipsed twin chair (13b) agrees well with the accumulating evidence [42] indicating that, when the C(9)–C(10) bridge is constrained into the eclipsed form (by introducing sp^2 hybridization, for example), the bicyclo[3.3.2]decyl system prefers to take a boat-chair conformation. Furthermore, Doyle's suggestion [40] of a twin chair $\rightleftharpoons$ boat-chair equilibrium, heavily biased to the left, is at least qualitatively compatible with our results which indicate the possibility of cross-over from boat-chair to twin chair taking place at twist angles of *ca.* 25° (Figure 6). According to our calculations, the equilibrating species will essentially be eclipsed boat-chair (13c) and twin twist chair (13a).

Finally, a mention should be made of the apparent importance of the gauche H–H interactions [4a] in the bicyclic hydrocarbons treated here. In fact, the sum of 1,4-nonbonded interactions for C–C, C–H, and H–H types constitute the largest (for boat-chair and twin chair bicyclo[3.3.2]decane, Figure 6) or the second largest (for twin boat bicyclo[3.3.2]decane and twin chair bicyclo[3.3.1]nonane, Figure 3) contributor to the calculated total steric energy. Further analysis reveals that 1,4-H–H interactions always occupy *ca.* 25—35% of the total steric energy of the bicyclic hydrocarbons calculated in this work. In eclipsed boat-chair bicyclo-[3.3.2]decane (13c), some gauche H–H interactions, including H(1)–H(2e) and H(1)–H(8e), are even stronger than the transannular H–H interactions in H(3a)–H(9),(10) and H(7a)–H(2a),(4a) (Figure 6).[40] While the main roles. in deciding the relative energies among various conformers of (13) and (11) are played by bending and torsional terms as mentioned above, a consistently high, albeit not a predominant,[13] contribution of the gauche interactions to the total steric energy emerging from the MM2 force field calculations should not be overlooked.

We are indebted to Professor H. Musso for suggesting this problem and for drawing the first sketch of Figure 1, to Professor N. L. Allinger for a preprint and additional information of his new force field MM2, to Professor V. S. Mastryukov for providing details of electron diffraction analysis of bicyclo[3.3.1]nonane, and to Professor H. Shirahama for communicating unpublished results quoted in footnote * on p. 176. Financial support from Alexander von Humboldt-Stiftung which made possible E. O.'s stay at Universität Karlsruhe is gratefully acknowledged. Computations were performed at Hokkaido University Computing Center, Rechenzentrum der Universität Karlsruhe, Kao Soap Company, and Hokkaido Takushoku Bank, Ltd. We thank a referee for a number of helpful comments.

[8/190 *Received, 6th February,* 1978]

---

* Calculated closest H–H nonbonded distances in eclipsed boat-chair (13c) (2.3 Å), and twin twist-chair (13a) (2.0 Å), conformations suggest the high frequency ν_{C-H} and δ_{C-H} absorption bands observed by Doyle *et al.*[40] are likely to arise from (13a), in agreement with their reasoning.

† This provides another illustration that molecules with eclipsed butane fragments often lead to an energy maximum rather than a minimum by the conventional energy minimization method.[41] Automatic bond driving as has been done in this instance is a safe method to avoid this difficulty, albeit time consuming.

REFERENCES

[1] Part 5, E. Ōsawa, K. Aigami, and Y. Inamoto, *Tetrahedron*, 1978, **34**, 509.

[2] Reviews: (*a*) S. R. Niketic and K. Rasmussen, 'The Consistent Force Field,' Springer-Verlag, Berlin, 1977; (*b*) N. L. Allinger, *Adv. Phys. Org. Chem.*, 1976, **13**, 1; (*c*) O. Ermer, *Structure and Bonding*, 1976, **27**, 161.

[3] H.-G. Fritz, H. Henke, and H. Musso, *Chem. Ber.*, 1974, **107**, 3164; H.-G. Fritz, Dissertation, Universität Karlsruhe, 1972.

[4] (*a*) D. H. Wertz and N. L. Allinger, *Tetrahedron*, 1974, **30**, 1579; (*b*) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Amer. Chem. Soc.*, 1971, **93**, 1637.

[5] N. L. Allinger and Y. H. Yuh, Quantum Chemistry Program Exchange, 1977, No. 318.

[6] N. L. Allinger, *J. Amer. Chem. Soc.*, 1977, **99**, 8127.

[7] (*a*) Ref. 2*b*; (*b*) D. H. Wertz, Ph.D. Thesis, University of Georgia, 1974.

[8] H. M.Hutmacher, H.-G. Fritz, and H. Musso, *Angew. Chem.*, 1975, **87** 174.

[9] (*a*) R. A. Ford and N. L. Allinger, *J. Org. Chem.*, 1970, **35**, 3178; (*b*) R. J. Quellette and S. H. Williams, *J. Amer. Chem. Soc.*, 1971, **93**, 466.

[10] G. J. Kent, S. A. Godleski, E. Ōsawa, and P. von R. Schleyer, *J. Org. Chem.*, 1977, **41**, 3582.

[11] D. N. J. White and M. J. Bovill, *J.C.S. Perkin II*, 1977, 1610.

[12] (*a*) L. S. Bartell, *J. Amer. Chem. Soc.*, 1977, **99**, 3279; (*b*) N. L. Allinger, D. Hindman, and H. Hönig, *ibid.*, p. 3282; (*c*) R. H. Boyd, *ibid.*, 1975, **97**, 5353; (*d*) D. N. J. White and M. J. Bovill, *J. Mol. Struct.*, 1976, **33**, 273.

[13] E. Ōsawa, J. B. Collins, and P. v. R. Schleyer, *Tetrahedron*, 1977, **33**, 2667.

[14] K. Mislow, 'Introduction to Stereochemistry,' Benjamin, New York, 1966, p. 113.

[15] W. H. Whitlock, jun., and M. W. Siefken, *J. Amer. Chem. Soc.*, 1968, **90**, 4929.

[16] (*a*) G. L. Buchanan, *Topics Carbocyclic Chem.*, 1969, **1**, 199; (*b*) N. S. Zefirov, *Uspkhi Khim.*, 1975, **44**, 413 (*Chem. Abs.*, 1975, **82**, 154579a).

[17] M. Davis and O. Hassel, *Acta Chem. Scand.*, 1964, **18**, 813.

[18] (*a*) W. A. C. Brown, J. Martin, and G. A. Sim, *J. Chem. Soc.*, 1965, 1844; (*b*) N. C. Webb and M. R. Becker, *J. Chem. Soc.* (*B*), 1967, 1317; (*c*) M. Dobler and J. D. Dunitz, *Helv. Chim. Acta*, 1964, **47**, 695; (*d*) W. D. K. Macrosson and G. Ferguson, *J. Chem. Soc.* (*B*), 1968, 242.

[19] G. Eglinton, J. Martin, and W. Parker, *J. Chem. Soc.*, 1965, 1243.

[20] S. Misumi, Y. Ohfune, A. Furusaki, H. Shirahama, and T. Matsumoto, *Tetrahedron Letters*, 1976, 2865.

[21] S. Misumi, Y. Ohfune, A. Furusaki, H. Shirahama, and T. Matsumoto, personal communication.

[22] J. Sayers, D. Schindler, and M. Sundaralingam, *J. Amer. Chem. Soc.*, 1977, **99**, 3848.

[23] (*a*) E. L. Osina, V. S. Mastryukov, L. V. Vilkov, and N. A. Belikova, *J.C.S. Chem. Comm.*, 1976, 12; (*b*) E. L. Osina, Dissertation, Moscow State University, 1976.

[24] E. N. Marvell and R. S. Knutson, *J. Org. Chem.*, 1970, **35**, 388; R. A. Appleton, C. Egan, J. M. Evans, S. H. Graham, and J. R. Dixon, *J. Chem. Soc.* (*C*), 1968, 1110.

[25] (*a*) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. A. Van-Catledge, *J. Amer. Chem. Soc.*, 1968, **90**, 1199; (*b*) G. J. Gleicher and P. v. R. Schleyer, *ibid.*, 1967, **89**, 582; (*c*) E. M. Engler, J. D. Andose, and P. v. R. Schleyer, *ibid.*, 1973, **95**, 8005; (*d*) E. N. Marvell, G. J. Gleicher, D. Sturmer, and K. Salisbury, *J. Org. Chem.*, 1968, **33**, 3393.

[26] W. V. Steele and I. Watt, *J. Chem. Thermodynamics*, 1977, **9**, 843.

[27] S. A. Godleski, P. v. R. Schleyer, E. Ōsawa, and W. T. Wipke, *Progr. Phys. Org. Chem.*, in the press.

[28] J. M. A. Baas, B. van de Graaf, A. v. Veen, and B. M. Wepster, *Tetrahedron Letters*, 1978, 819.

[29] S. C. Swen-Walstra and G. J. Visser, *Chem. Comm.*, 1971, 82.

[30] O. Ermer, *Angew. Chem.*, 1977, **89**, 833.

[31] W. Wagemann, K. Müllen, E. Vogel, T. Pilati, and M. Simonetta, *Angew. Chem.*, 1977, **89**, 176.

[32] (*a*) Footnote 50 in J. C. Coll, D. R. Crist, M. del C. G. Barrio, and N. J. Leonard, *J. Amer. Chem. Soc.*, 1972, **94**, 7092; (*b*) P. v. R. Schleyer, personal communication.

[33] R. C. Bingham and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1971, **93**, 3189.

[34] For recent arguments on this and a related approach, see J. S. Lomas, P. K. Luong, and J.-E. Dubois, *J. Amer. Chem. Soc.*, 1977, **99**, 5478.

[35] Corrected for α and β branching according to E. M. Engler, M. Farcasiu, A. Sevin, J. M. Cense, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1973, **95**, 5769.

[36] For the latest compilation of relative carbonium ion stabilities, see R. C. Fort, jun., 'Adamantane, the Chemistry of Diamond Molecules,' Dekker, New York, 1976, p. 151.

[37] For the latest example of carbonium ion energy calculations as applied to reactivity problems, see, N. Takaishi, Y. Inamoto, K. Aigami, Y. Fujikura, E. Ōsawa, M. Kawanisi, and T. Katsushima, *J. Org. Chem.*, 1977, **42**, 2041.

[38] K. B. Wiberg and R. H. Boyd, *J. Amer. Chem. Soc.*, 1972, **94**, 8426.

[39] E. M. Engler, L. Chang, and P. v. R. Schleyer, *Tetrahedron Letters*, 1972, 2525.

[40] M. Doyle, R. Hafter, and W. Parker, *J.C.S. Perkin I*, 1977, 364.

[41] O. Ermer, *Tetrahedron*, 1975, **31**, 1849.

[42] (*a*) E.s.r.: G. A. Russell and R. G. Keske, *J. Amer. Chem. Soc.*, 1970, **92**, 4460; (*b*) *X*-ray: J. Murray-Rust and R. Murray-Rust, *Acta Cryst.*, 1975, **B31**, 310; (*c*) i.r.: ref. 40.