**Table XV.** Saponification of Esters of 2,4,6-Trimethylbenzoic Acid with Potassium Hydroxide Complex of Dicyclohexyl-18-crown-6

| No. | Solvent | Ester | Concn, $M^a$ Ester | Concn, $M^a$ Base | Temp, °C | Time, hr | Hydrolyzed, %[b] |
|---|---|---|---|---|---|---|---|
| 1 | Toluene | Methyl | 0.122 | 0.122 | 73.8 ± 0.2 | 31 | 58.4 |
| 2 | Benzene | Methyl | 0.061 | 0.154 | 80–80.1 | 5 | 39 |
| 3 | Toluene | Methyl | 0.120 | 0.120 | 99.9 ± 0.1 | 2 | 53.0 |
| 4 | Toluene | Methyl | 0.061 | 0.154 | 105–111 | 5 | 93 |
| 5 | Benzene | *t*-Butyl | 0.060 | 0.154 | 79.6–80.2 | 5 | 22 |
| 6 | Toluene | *t*-Butyl | 0.060 | 0.154 | 104–111 | 5 | 94 |
| 7 | Benzene | Neopentyl | 0.060 | 0.154 | 80.3–80.7 | 5 | 40 |

[a] The initial concentration. [b] No saponification measurable by this method occurred when the methyl ester was refluxed at 75.5–77° with excess potassium hydroxide in 1-propanol for 5 hr.

oxygen fission occurs in this saponification. It is likely that the activity of these solutions of the potassium hydroxide complex of XXXI is due to the presence of unsolvated hydroxyl ions which can attack the carbonyl groups of the hindered esters much more readily than the ordinary solvated hydroxyl ions.

**Toxicity.** Dicyclohexyl-18-crown-6 (XXXI) possesses unusual physiological properties which require care in its handling. It is likely that other cyclic polyethers with similar complexing power are also toxic, and should be handled with equal care.

**Oral Toxicity.** The approximate lethal dose for XXXI for ingestion by rats was 300 mg/kg. In a 10-day subacute oral test, the compound did not exhibit any cumulative oral toxicity when administered to male rats at a dose level of 60 mg/kg/day. It should be noted that dosage at the ALD level caused death in 11 min, but that a dose of 200 mg/kg was not lethal in 14 days.

**Eye Irritation.** XXXI produced some generalized corneal injury, some iritic injury, and conjunctivitis when introduced as a 10% solution in propylene glycol. Although tests are not complete, there may be permanent injury to the eye even if the eye is washed after exposure.

**Skin Absorption.** XXXI is very readily absorbed through the skin of test animals. It caused fatality when absorbed at the level of 130 mg/kg.

**Skin Irritation.** Primary skin irritation tests run on XXXI indicate the material should be considered a very irritating substance.

# Molecular Geometry. V. Evaluation of Functions and Conformations of Medium Rings[1]

**James B. Hendrickson**[2]

*Contribution from the Edison Chemical Laboratory, Brandeis University, Waltham, Massachusetts 02154. Received June 7, 1967*

**Abstract:** Constants in the functions used for the calculation of minimum-energy conformations for *n*-butane and cycloalkanes were varied so as to find the set which best reproduced a dozen items of experimental data (geometry and energies). The resultant best functions were then applied to obtain the geometry and energies of the symmetrical cycloalkane rings.

Calculations aimed at determining the conformational geometry of molecules[3] depend for their validity on the assumptions made and on the functions used to relate geometrical parameters to energy. Assumptions must be made partly because no clear physical mandate exists to guide the choice of selection of certain procedures and partly because the scale of the requisite computations usually demands some simplification even when employing contemporary high-speed computers. The functions used embody a number of constants, values for which are only available by extrapolation from experimental data. However, the experiments commonly either do not measure cases comparable to those on which the functions will be used in calculations or else they are not measurements of the pure, isolated effect for which a constant is required.[6] The calculations, however, allow variations

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(1) Paper IV: J. B. Hendrickson, *J. Am. Chem. Soc.*, **86**, 4854 (1964). Much of the present work was the subject of a lecture by the author at the Conformational Analysis Symposium at the National Meeting of the American Chemical Society, New York, N. Y., Sept 13, 1966. Support of this work by a grant from the National Institutes of Health is gratefully acknowledged, as is the opportunity afforded the author of using the computation facilities at the Massachusetts Institute of Technology (IBM 7094) and Brandeis University (IBM 1620).

(2) Alfred P. Sloan Foundation Fellow, 1962–1966.

(3) A general account of the procedures involved is available in E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, John Wiley and Sons, Inc., New York, N. Y., 1965, Chapter 7-2, which in turn derives largely from the discussions in ref 4 and 5.

(4) F. H. Westheimer in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 12.

(5) J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961).

(6) For example, spectroscopic determination of angle-bending constants must involve some 1–3 nonbonded interactions[7] and nonbonded potential functions are sought in many indirect ways.[3-5]

Table I. Geometrical Definition of Cycloalkanes

| Ring | Bond angles,[a,b] deg | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $\theta_1$ | $\theta_2$ | $\theta_3$ | $\theta_4$ | $\theta_5$ | $\theta_6$ | $\theta_7$ | $\theta_8$ | $\theta_9$ | $\theta_{10}$ |
| $C_6$: C | 111.6 | 111.6 | 111.6 | 111.6 | 111.6 | 111.6 | (exptl 111.6°[22]) | | | |
| TB | 112.2 | 111.6 | 111.6 | 112.2 | 111.6 | 111.6 | | | | |
| B | 112.0 | 112.5 | 112.5 | 112.0 | 112.5 | 112.5 | | | | |
| ‡[c] | 119.0 | 114.6 | 110.0 | 110.0 | 114.6 | 119.0 | | | | |
| $C_7$: TC | 116 | 115 | 113 | 115 | 115 | 113 | 115 | | | |
| C | 115 | 114 | 115 | 118 | 118 | 115 | 114 | | | |
| TB | 115 | 115 | 115 | 115 | 115 | 115 | 115 | | | |
| B | 115 | 115 | 115 | 116 | 116 | 115 | 115 | | | |
| $C_8$: BC | 117 | 116 | 116 | 116 | 117 | 116 | 116 | 116 | | |
| CC | 115 | 115 | 115 | 115 | 115 | 115 | 115 | 115 | | |
| BB | 118 | 119 | 118 | 119 | 118 | 119 | 118 | 119 | | |
| TC | 116 | 116 | 114 | 116 | 116 | 116 | 114 | 116 | | |
| C | 115 | 117 | 117 | 115 | 115 | 117 | 117 | 115 | | |
| B | 118 | 118 | 118 | 118 | 118 | 118 | 118 | 118 | | |
| Crown | 116 | 116 | 116 | 116 | 116 | 116 | 116 | 116 | | |
| TCC ($D_2$) | 116 | 115 | 115 | 116 | 116 | 115 | 115 | 116 | | |
| TBC | 116 | 116 | 116 | 115 | 115 | 116 | 116 | 116 | | |
| $S_4$ | 117 | 118 | 117 | 118 | 117 | 118 | 117 | 118 | | |
| $C_9$: TBC ($D_3$) | 116 | 115 | 115 | 116 | 115 | 115 | 116 | 115 | 115 | |
| TCB | 117 | 117 | 117 | 117 | 117 | 117 | 117 | 117 | 117 | |
| $C_{10}$: BCB | 118 | 118 | 116 | 116 | 118 | 118 | 118 | 116 | 116 | 118 |
| BCB (exptl) | 118 | 118 | 115 | 115 | 118 | 118 | 118 | 115 | 115 | 118 |
| CCC | 116 | 116 | 115 | 115 | 116 | 116 | 116 | 115 | 115 | 116 |
| Crown | 116 | 116 | 116 | 116 | 116 | 116 | 116 | 116 | 116 | 116 |

| Ring | Dihedral angles,[a,b] deg | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $\omega_1$ | $\omega_2$ | $\omega_3$ | $\omega_4$ | $\omega_5$ | $\omega_6$ | $\omega_7$ | $\omega_8$ | $\omega_9$ | $\omega_{10}$ |
| $C_6$: C | 54.4 | −54.4 | 54.4 | −54.4 | 54.4 | −54.4 | | | | |
| TB | 30.1 | −62.8 | 30.1 | 30.1 | −62.8 | 30.1 | | | | |
| B | 52.1 | 0 | −52.1 | 52.1 | 0 | −52.1 | | | | |
| ‡[c] | 12.0 | 8.0 | −46.8 | 67.0 | −46.8 | 8.0 | | | | |
| $C_7$: TC | 39.1 | −88.1 | 72.3 | −54.3 | 72.3 | −88.1 | 39.1 | | | |
| C | 63.8 | −83.5 | 66.1 | 0 | −66.1 | 83.5 | −63.8 | | | |
| TB | 45.4 | −64.4 | −17.9 | 74.6 | −17.9 | −64.4 | 45.4 | | | |
| B | 57.5 | 30.9 | −69.9 | 0 | 69.9 | −30.9 | −57.5 | | | |
| $C_8$: BC | 65.0 | 44.7 | −102.2 | 65.0 | −65.0 | 102.2 | −44.7 | −65.0 | | |
| CC | 66.0 | −105.2 | 105.2 | −66.0 | 66.0 | −105.2 | 105.2 | −66.0 | | |
| BB | 52.5 | 52.5 | −52.5 | −52.5 | 52.5 | 52.5 | −52.5 | −52.5 | | |
| TC | 37.3 | −109.3 | 109.3 | −37.3 | −37.3 | 109.3 | −109.3 | 37.3 | | |
| C | 119.9 | −76.2 | 0 | 76.2 | −119.9 | 76.2 | 0 | −76.2 | | |
| B | −73.5 | 0 | 73.5 | 0 | −73.5 | 0 | 73.5 | 0 | | |
| Crown | 87.5 | −87.5 | 87.5 | −87.5 | 87.5 | −87.5 | 87.5 | −87.5 | | |
| TCC ($D_2$) | 56.2 | −82.4 | 114.6 | −82.4 | 56.2 | −82.4 | 114.6 | −82.4 | | |
| TBC | 88.0 | −93.2 | 51.9 | 44.8 | −115.6 | 44.8 | 51.9 | −93.2 | | |
| $S_4$ | 64.9 | 37.6 | −64.9 | −37.6 | 64.9 | 37.6 | −64.9 | −37.6 | | |
| $C_9$: TBC ($D_3$) | 56.0 | −124.8 | 56.0 | 56.0 | −124.8 | 56.0 | 56.0 | −124.8 | 56.0 | |
| TCB | 68.0 | −71.1 | −52.3 | 103.1 | −83.8 | 103.1 | −52.3 | −71.1 | 68.0 | |
| $C_{10}$: BCB | 66.0 | 54.9 | −152.0 | 54.9 | 66.0 | −66.0 | −54.9 | 152.0 | −54.9 | −66.0 |
| BCB (exptl) | 66.1 | 55.2 | −152.0 | 55.2 | 66.1 | −66.1 | −55.2 | 152.0 | −55.2 | −66.1 |
| CCC | 73.0 | −115.0 | 150.3 | −115.0 | 73.0 | −73.0 | 115.0 | −150.3 | 115.0 | −73.0 |
| Crown | 108.7 | −108.7 | 108.7 | −108.7 | 108.7 | −108.7 | 108.7 | −108.7 | 108.7 | −108.7 |

[a] All rings with an atom on a plane or axis of symmetry are numbered clockwise from that atom (bond angle $\theta_1$), $\omega_1$ being the dihedral angle of the first bond adjacent to atom 1 in a clockwise direction. With rings having no atom on a plane or axis, the bond bisected by the plane or axis is assigned dihedral angle $\omega_1$ and the first clockwise atom following it has bond angle $\theta_1$. The ring forms are named by the convention outlined in ref 1 and the following papers.[40] [b] Bond angles were normally varied by 1° in the calculations, except in *n*-butane and cyclohexanes in which they were varied by 0.2, or derived by calculation when not independently variable. Dunitz' bond angles are given to the same accuracy in the experimental values for cyclodecane.[9] Dihedral angles were varied by 1° when independently variable, $\omega_1$ usually being the one taken as independently variable. Repetition of angles in the table reflects the symmetry of the various rings. [c] The cyclohexane chair–twist-boat transition is described in the third paper; it is numbered here with $\omega_1$ assigned to the bond which is bisected by the axis of symmetry and is nearly eclipsed at the transition maximum in $C_2$ symmetry.

in these assumptions and comparison with known compounds. As both energy and geometry are obtained in the calculations, correlation of both with experimental values affords a stringent check on the procedure. The available experimental data are unfortunately still somewhat meager. Some information exists on the lower alkanes but their simplicity renders them less significant as models and to a lesser extent the same is true of the data on cyclohexane. The larger cycloalkane rings afford more conformational complexity and consequently provide a more critical test of the assumptions in calculation.[8] In particular the recent recognition by Dunitz[9] that the cyclodecane

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(7) L. S. Bartell, *J. Chem. Phys.*, **32**, 827 (1960).

(8) The highly strained small rings on the other hand pass into a region in which normal assumptions and functions are probably no longer adequate and hence are suspect as models. It is likely, for example, that some assessment of the interorbital angles as well as internuclear angles will be important in such strained cases.

(9) J. D. Dunitz, personal communication. See also E. Huber-Buser and J. D. Dunitz, *Helv. Chim. Acta*, **43**, 760 (1960); **44**, 2027 (1961); **45**, 1036 (1962); J. D. Dunitz and K. Venkatesan, *ibid.*, **44**, 2033 (1961);

**Table II.** Energies of the Cycloalkanes[a,b]

| Ring | | $E_\theta$ | $E_t$ | $E_{HH}$ | $E_{HC}$ | $E_{CC}$ | $E_{NB}$ | $\Sigma E$ | $E_0$ | $E_{exp}$ | $\Delta E$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| C$_6$: | C | 0.02 | 0.34 | 1.27 | −0.70 | 0.14 | 0.71 | 1.08 | 0.0 | 0.0 | 0.0 |
| | TB | 0.02 | 5.31 | 1.75 | −0.88 | 0.50 | 1.38 | 6.70 | 5.6 | 5.5 ± 0.3[3] | 5.6 |
| | B | 0.02 | 5.75 | 1.66 | −0.37 | 0.46 | 1.75 | 7.52 | 6.4 | | 6.4 |
| | ‡ | 2.75 | 8.16 | 2.15 | −0.98 | 0.06 | 1.19 | 12.10 | 11.0 | 10.8[c] | 11.0 |
| C$_7$: | TC | 1.24 | 4.41 | 2.12 | −0.51 | −0.16 | 1.45 | 7.10 | 6.0 | 6.3 ± 0.3[d] | 0.0 |
| | C | 2.46 | 4.60 | 2.21 | −0.60 | −0.15 | 1.46 | 8.52 | 7.4 | | 1.4 |
| | TB | 1.45 | 5.39 | 3.15 | −0.70 | 0.22 | 2.66 | 9.50 | 8.4 | | 2.4 |
| | B | 1.77 | 5.55 | 2.88 | −0.73 | 0.27 | 2.42 | 9.74 | 8.7 | | 2.7 |
| C$_8$: | BC | 3.36 | 5.22 | 3.92 | −0.67 | −0.72 | 2.52 | 11.10 | 10.0 | 10.0 ± 0.4[d] | 0.0 |
| | CC | 1.66 | 9.35 | 2.90 | −0.12 | −0.78 | 2.00 | 13.00 | 11.9 | | 1.9 |
| | BB | 7.82 | 0.81 | 6.59 | −2.05 | −0.65 | 3.89 | 12.53 | 11.4 | | 1.4 |
| | TC | 2.39 | 13.12 | 4.39 | 0.37 | −0.47 | 4.30 | 19.81 | 18.7 | | 8.7 |
| | C | 3.13 | 12.40 | 4.57 | −0.11 | −0.57 | 3.90 | 19.44 | 18.3 | | 8.3 |
| | B | 6.62 | 11.87 | 4.82 | −1.45 | −0.46 | 2.91 | 21.40 | 20.3 | | 10.3 |
| | Crown | 2.94 | 9.22 | 3.13 | −0.40 | −0.97 | 1.76 | 13.92 | 12.8 | | 2.8 |
| | TCC (D$_2$) | 2.30 | 8.49 | 3.10 | −0.30 | −0.82 | 1.98 | 12.77 | 11.7 | | 1.7 |
| | TBC | 2.62 | 7.93 | 3.71 | −0.43 | −0.70 | 2.58 | 13.13 | 12.0 | | 2.0 |
| | S$_4$ | 5.61 | 3.43 | 5.09 | −1.43 | −0.72 | 2.94 | 11.98 | 10.9 | | 0.9 |
| C$_9$: | TBC (D$_3$) | 2.35 | 8.00 | 4.92 | −0.25 | −1.06 | 3.61 | 13.96 | 12.9 | 12.9 ± 0.4[d] | 0.0 |
| | TBC | 5.17 | 6.11 | 6.92 | −0.72 | −1.24 | 4.96 | 16.24 | 15.1 | | 2.2 |
| C$_{10}$: | BCB | 6.44 | 2.82 | 7.66 | −1.15 | −1.44 | 5.06 | 14.32 | 13.2 | 13.4 ± 0.5[d] | 0.0 |
| | CCC | 3.04 | 14.21 | 5.91 | 0.14 | −1.49 | 4.57 | 21.82 | 20.7 | | 7.5 |
| | Crown | 3.68 | 24.23 | 6.70 | 0.61 | −1.46 | 5.85 | 33.76 | 32.7 | | 19.5 |

[a] The rings listed are those of Table I. Energies are given in kcal/mole. $E_\theta$ = bond angle bending strain; $E_t$ = torsional strain; $E_{HH}$ = interactions of nonbonded hydrogens; $E_{HC}$ = interactions of nonbonded hydrogens and carbons; $E_{CC}$ = interactions of nonbonded carbons; $E_{NB}$ = sum of nonbonded interactions; $\Sigma E = E_\theta + E_t + E_{NB}$ = sum of calculated strain energy; $E_0 = \Sigma E - E_{C_6}$ = energy relative to cyclohexane chair; $E_{exptl}$ = experimental value relative to cyclohexane chair; $\Delta E$ = energy relative to that calculated for lowest member of the cycloalkane in question (*e.g.*, for C$_8$, $\Delta E = E_0 - 10.0$). [b] Calculated energies are shown to two decimal places but the final energies for comparison ($E_0$) are only shown to one since no more accuracy is warranted. [c] F. A. L. and A. J. R. Bourn, *J. Am. Chem. Soc.*, **89**, 760 (1967), and other work cited therein. We are grateful to Professor Anet for correspondence on this value prior to publication. [d] J. Coops, H. von Kamp, W. A. Lamregets, J. Visser, and H. Dekker, *Rec. Trav. Chim.*, **79**, 1226 (1960).

ring retains a virtually fixed geometry in four differently substituted derivatives afforded a model with a high order of complexity in which both the geometry[10] and energy are known. Thus cyclodecane presents a test capable of stringent discrimination among the assumptions employed in calculation, and, taken with the other alkane data (energies and geometry), provided the impetus for a reassessment of previous assumptions.[1,5]

The procedure taken here was to calculate the minimum energy and consequent geometry of the *n*-butane conformations and the medium-ring cycloalkanes from C$_6$ to C$_{10}$, carrying out a systematic search for the lowest minimum within each symmetrical conformation of each ring.[11] There is apparently no proof that symmetrical forms of cycloalkanes will be more stable than unsymmetrical forms,[12] but Wiberg's[13] minimization method does proceed through unsymmetrical forms and in his cases only symmetrical minima result. The disadvantage of his method lies in the fact that although many energy minima occur for a given cycloalkane, only the one nearest the starting model conformation is actually located; the procedure used here assures locating the lowest energy minimum in every symmetrical conformation.

The programs for *n*-butane[14] and the rings were written so that the assumptions made and the seven constants in the energy functions discussed below could be treated as independent variables. These were then varied systematically in a search for a set which would reproduce the known empirical data for these compounds, about a dozen independent pieces of information, both energies and geometries, as listed in Tables I, II, and III. As the comparisons in these tables testify, the search was quite successful and the final functions and constants obtained, which produced the values in these tables, are summarized in Table IV.

In general, the strain energy for a given conformation is taken to be the sum of independent energy terms, each related to a single geometrical parameter; the discussion which follows is concerned with the choice of these relating functions and their behavior in the search for a best set of constants.

W. Nowacki and M. H. Mladeck, *Helv. Chim. Acta*, **47**, 1280 (1964). The data quoted for the experimental geometry of cyclodecane in Table I is a grand average of the four compounds cited in these papers; the four cyclodecanes are so close in conformation that over 90% of the atomic coordinates lie within 0.03 A of the average values. The author is very grateful to Professor Dunitz for making these values available prior to full publication.

(10) Four independently variable angles must be correctly assigned (in this program $\theta_1$, $\theta_2$, $\theta_3$, $\omega_1$) to specify a particular BCB cyclodecane such as Dunitz's average conformation.

(11) A scheme for locating all the possible symmetrical forms is outlined in ref 1. The more detailed calculations reported here provided somewhat different energies and geometries from those in ref 1 (with more limiting assumptions), but they are generally similar.

(12) One general argument can be made that favors symmetrical forms. If a given atom or group is moved to a new position with geometrical parameters (bond and dihedral angles and nonbonded distances) corresponding to lower energy, other atoms or groups must also be moved more or less equivalently to maintain the condition of a closed ring. Both the bond angle bending curve and the nonbonded interaction curve in the critical (repulsive) region, however, are unsymmetrical so that a pair of equivalent shifts of the relevant geometrical parameter ($\theta$ or $r$) in each direction results in more raising of energy for one than lowering for the other and a net increase in energy. Only by maintaining the symmetry of a symmetrical form can a pair of shifts (one on each side of the symmetry plane or axis) both move to lower energy and retain a closed ring. As stated, however, this argument only implies that asymmetrical deformation of a symmetrical conformation must cause an energy increase but does not show that after an initial rise over a barrier this asymmetrical deformation may not ultimately proceed to an unsymmetrical form of lower energy.

(13) K. B. Wiberg, *J. Am. Chem. Soc.*, **87**, 1070 (1965).

(14) A program for the *n*-butane results was devised and carried out by Mr. Larry Temkin on a summer National Science Foundation undergraduate research grant in 1966.

Table III. Geometrical Definition and Energies of Simple *n*-Alkanes

| Alkane | Bond angles at $CH_2$,[a] deg CCC | HCH | Dihedral angles,[a] deg $CH_2CH_3$ | $CH_2CH_2$ | Energies[b] $E_\theta$ | $E_t$ | $E_{NB}$ | $\Sigma E$ | $E_0$ | $E_{exptl}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Propane[18] | 112.4 ± 0.2 | 106.1 ± 0.2 | | | | | | | | |
| *n*-Alkanes (mean)[19,37] | 112.6 ± 0.2 | 104 ± 2 | | 61 ± 3[17]<br>67.5 ± 1[c] | | | | | | |
| *n*-Butane (*trans*) | 112.8 | 106.4 | 60 | 180 | 0.03 | 0.00 | 0.67 | 0.70 | 0.0 | 0.0 |
| *n*-Butane (120°) | 113.2 | 106.1 | 60 | 120 | 0.07 | 2.65 | 1.20 | 3.91 | 3.2 | 3.2–3.6[3,37] |
| *n*-Butane (*gauche*) | 113.2 | 106.1 | 65 | 63 | 0.07 | 0.21 | 0.99 | 1.26 | 0.6 | 0.7 ± 0.2[3,37] |
| *n*-Butane (eclipsed) | 115.8 | 104.2 | 60 | 0 | 0.66 | 2.65 | 1.72 | 5.03 | 4.3 | |

[a] Bond angles were varied by 0.2°, dihedral angles by 1°. [b] Energies are defined as in Table II. [c] K. Kuchitsu, *J. Chem. Soc. Japan*, **32**, 748 (1959).

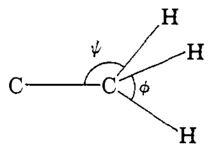
Table IV. Final Functions for Calculations[a]

$$\Sigma E = \Sigma E_\theta + \Sigma E_t + \Sigma E_{HH} + \Sigma E_{HC} + \Sigma E_{CC}$$
$$E_\theta = 0.0230(\theta - 112)^2$$
$$E_t = 1.325(1 + \cos 3\omega)$$
$$E_{HH} = 2300e^{-3.6r} - 49.2/r^6$$
$$(E_{min} = -0.023;\ r_{min} = 3.15)$$
$$E_{HC} = 4012e^{-3.4r} - 125/r^6$$
$$(E_{min} = -0.043;\ r_{min} = 3.30)$$
$$E_{CC} = 7000e^{-3.2r} - 325/r^6$$
$$(E_{min} = -0.083;\ r_{min} = 3.48)$$

[a] Energies in kcal/mole, angles in degrees, distances in A.

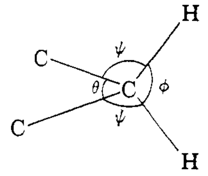
**Bond Stretching.** The energy required to stretch or compress a bond from its optimum length is very much more severe than the other strain energies below and where it has been employed in calculations turns up usually to contribute only a very small fraction of the total energy. Furthermore, the optimum lengths (C–C and C–H) to be used as norms in the calculations are obtained from X-ray and electron-diffraction evidence on selected "unstrained" models and these experimental norms often differ among themselves more than variations from a selected norm that arise in calculations which employ them.[15–18] Since incorporation of bond-length variation into the minimization procedure also involves many more independent variables, seriously lengthening computation time, bond lengths have been assumed to be invariant in this work. As before,[1,5] the C–C length is taken at 1.533 A and C–H as 1.109 A. (The new cyclodecane data[9] show C–C to be 1.532 ± 0.005 A.)

**Bond-Angle Bending.** In assessing bond-angle strains one must take into account six interdependent angles ($\theta$) around each carbon atom, for each of which the energy is related by $E = K(\theta - \theta_0)^2$ in which $\theta_0$ represents the optimum unstrained angle; both $K$ and $\theta_0$ must then be specified for use in calculation. The correct specification of bond angles is especially important since it not only affects the angle-bending portion of the total strain but also determines the positions of atoms and hence their distances from other, nonbonded atoms, and the derived van der Waal's interactions. The cases of interest for us are the angles around carbon at the methyl, methylene, and methine carbon; the geometrical interdependence of these angles is delineated in Figure 1 along with the full angle-bending energy for the set. Granting the symmetry restrictions implicit in the figures, it is clear that specification of one angle (CCH or HCH) at methyl determines all six while in the other cases specification of two of the six is required to define the set fully. In these cases it was assumed in the previous work[1,5] that, if the CCC angle ($\theta$) were once assigned, the others would be related by minimizing the sum of the energies for the six angles and thus determining not only a single total energy for the whole set of six at any given CCC angle ($\theta$) but also, implicitly, the CCH ($\psi$) and HCH ($\phi$) angles obtaining for that $\theta$ at the energy minimum.[5] For this process values of $K$ were taken from West-



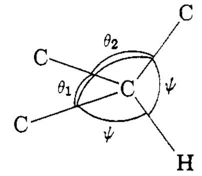
(a) methyl

$$2\cos\phi - 3\cos^2\psi + 1 = 0$$
$$E = 3[K_{CCH}(\psi - \psi_0)^2 + K_{HCH}(\phi - \phi_0)_0^2]$$



(b) methylene

$$\cos {}^1\!/_2\theta \cos {}^1\!/_2\phi + \cos\psi = 0$$
$$E = K_{CCC}(\theta - \theta_0)^2 + 4K_{CCH}(\psi - \psi_0)^2 + K_{HCH}(\phi - \phi_0)^2$$



(c) methine

$$\cos^2\psi = \frac{2\cos^2\theta_2 - \cos\theta_1 - 1}{4\cos\theta_2 - \cos\theta_1 - 3}$$
$$E = K_{CCC}(\theta_1 - \theta_0)^2 + 2K_{CCC}(\theta_2 - \theta_0)^2 + 3K_{CCH}(\psi - \psi_0)^2$$

Figure 1. Bond angle interdependence: (a) methyl group, (b) methylene group, (c) methine group. The total bond angle bending energy for each group is subtended in terms of separate bending constants for the CCC angle ($\theta$), the CCH angle ($\psi$), and the HCH angle ($\phi$).[4]

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(15) M. J. S. Dewar, *Tetrahedron*, **17**, 125 (1962).

(16) L. S. Bartell and D. A. Kohl, *J. Chem. Phys.*, **39**, 3097 (1963).

(17) D. R. Lide, Jr., *ibid.*, **33**, 1514, 1519 (1960).

(18) L. S. Bartell, submitted for publication. The author is grateful to Professor Bartell for correspondence on bond lengths and angles prior to publication.

heimer's discussion,[4] and the optimum unstrained angles were assumed to be tetrahedral ($\theta_0 = \psi_0 = \phi_0 = 109.5°$); it was found that a plot of $E$ *vs.* $(\theta - \theta_0)^2$ obtained by this minimization was quite close to a straight line which could be expressed as $E_\theta = K_\theta(\theta - \theta^0)^2$.[19]

However, it has become increasingly clear that the angles at carbon are a function of the hybridization in effect there and that the optimum angle will not necessarily be tetrahedral but rather a function of the substituents bonded to the carbon.[20] This is supported by CCC angles at methylene of around 112° (rather than 109.5°) found experimentally for presumably "unstrained" cases such as the lower alkanes (112.5 ± 0.3°; see Table III)[16–18] and cyclohexane (111.6°).[21] Thus, if the optimal angle ($\theta_0$) for CCC in methylene is to be 112°, those for CCH ($\psi_0$) and HCH ($\phi_0$) will be obtainable from the equations relating the mixing coefficients by hybridization.[22] It seems reasonable in fact to depend on hybridization control of the angles around the carbon and use the equations of footnote 22 to relate the CCH ($\psi$) and HCH ($\phi$) angles to the CCC angle ($\theta$) not only for obtaining the optimum angles of each kind for the $E_\theta$ minimization process above but also in actually determining $\psi$ and $\phi$ directly from $\theta$ for cases in which $\theta$ differs from 112°.[23] When the Westheimer force constants[4] were used to evaluate a plot of $E$ *vs.* $(\theta - \theta_0)^2$ this plot was also found to be virtually a straight line for values of $\theta_0$ between 111 and 113° and up to $\Delta\theta$ of 10–12°. The plot expressed by $E_\theta = K_\theta(\theta - 112)^2$ was very similar to that obtained by the minimization procedure above,[19] with a resultant $K_\theta = 0.0215$.

Thus the over-all angle-bending energy for a set of six carbon resulting from either of the two approaches to interrelating $\theta$, $\psi$, and $\phi$ is very similar. However, the actual values of $\psi$ and $\phi$ obtained from $\theta$ by the two methods differed somewhat, smaller values being obtained by the hybridization procedure. Experimental values for mean angles to hydrogens are rare, the most accurate apparently being the HCH angle at methylene in propane (see Table III) determined by microwave spectroscopy as 106.1 ± 0.2° with a CCC angle at that carbon of 112.4 ± 0.2°.[16] The minimization process above yields $\phi = 108.7°$ while the hybridization approach gives $\phi = 106.7°$. Both approaches were applied in the search for best functions but only the hybridization method led to a set of functions reproducing all the empirical data and it is this method which was finally used in obtaining the values in Table I–IV. The evident correlation of hybridization and bond angle reported by Foote[24] also lends support to this procedure.

Variation of $K_\theta$ in the angle-bending energy term $E_\theta = K_\theta(\theta - 112)^2$ was independently carried out in the search for the most appropriate constants. In general, of course, larger values of $K_\theta$ tended to depress the final CCC bond angles ($\theta$) which were found and *vice versa;* also variations more than about ±0.03 from the final value (0.0230) produced sets of cyclodecane angles inconsistent with the X-ray results. Finally, variations in $K_\theta$ had differential effects on the total calculated ring energies, a moderate increase in $K_\theta$ (near 0.230) producing virtually no effect on the TB-cyclohexane or cyclooctane energies, a modest increase in cycloheptane and cyclononane energies, and a large increase in cyclodecane energy. The final value chosen for $K_\theta$ (0.0230) from these variations is only somewhat larger than that calculated *via* the Westheimer force constants (0.0215). After this work was completed, the author's attention was drawn to the more recent force constants of Shachtschneider and Synder[25] (average values of $K_{\mathrm{CCC}} = 0.0215$, $K_{\mathrm{CCH}} = 0.0115$, $K_{\mathrm{HCH}} = 0.0067$); when $(\theta - 112)^2$ is plotted against $E_\theta$ obtained from these constants and hybridization interrelation of angles, a straight-line is also obtained yielding a value of $K_\theta = 0.025$, also very close to the final value obtained in this study.

**Torsional Strain.** Although the source of the barrier to free rotation around single bonds remains controversial,[26] considerable success has attended conformational calculations made by assuming the torsional strain to be a cosine function of the dihedral angle $\omega$, *i.e.*, $E_t = {}^1/_2K_t(1 + \cos 3\omega)$, in which the constant $K_t$ is the value (2.8 kcal/mole) for the ethane barrier.[3] Actually, since nonbonded interactions make up a small but real portion of the ethane barrier, $K_t$ should be somewhat less than 2.8 so that these van der Waal's forces will make up the difference. There is, however, no significant basis for using a simple cosine function here, since only the positions of maxima and minima are known. A more general expression would be the expanded form,[28] $E_t = {}^1/_2K_t(1 + \cos 3\omega + K_t' \cos 6\omega)$, and in the search for proper functions by empirical correlation values of $K_t'$ as well as $K_t$ were also examined.[29] The results of this search provided a pre-

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[19] In units of kcal/(mole deg²), Westheimer's individual constants are $K_{\mathrm{CCC}} = 0.0175$, $K_{\mathrm{CCH}} = 0.0121$, and $K_{\mathrm{HCH}} = 0.0070$. The single constant derived[5] by the minimization procedure for all six angles at methylene as a function of CCC ($\theta$) alone was $K\theta = 0.020$. This is not much more than the $K_{\mathrm{CCC}}$ value since the HCH constant is small and the CCH angles at methylene remain near the optimum value (109.5°) as CCC and HCH are changed so that their energy contribution is small even though there are four of them.

[20] The argument is lucidly presented in K. Mislow, "Introduction to Stereochemistry," W. A. Benjamin, Inc., New York, N. Y., 1964, Chapter 1.

[21] M. Davis and O. Hassel, *Acta Chem. Scand.*, **17**, 1181 (1963).

[22] Following Mislow,[20] the hybridization indices, $\lambda^2$, for CH and CC bonds are related to the CCC angle ($\theta$) and HCH angle ($\phi$)

$$2\left(\frac{1}{1 + \lambda^2{}_{\mathrm{CC}}} + \frac{1}{1 + \lambda^2{}_{\mathrm{CH}}}\right) = 1$$

hence $\lambda^2{}_{\mathrm{CH}} = (\lambda^2{}_{\mathrm{CC}} + 3)/(\lambda^2{}_{\mathrm{CC}} - 1)$.

$$1 + \lambda^2{}_{\mathrm{HC}} \cos \phi = 0 \qquad 1 + \lambda^2{}_{\mathrm{CC}} \cos \theta = 0$$

Hence, $\cos \phi = (\cos \theta + 1)/(3 \cos \theta - 1)$. (From Figure 1, then, $\cos \psi = -\sqrt{\cos \theta \cos \phi}$.) In principal, these equations only relate *interorbital* angles, not the *internuclear* angles implied in molecular geometry, but the two parallel each other so closely that these correlating equations are probably valid for either in the moderately unstrained range of interest to us here.

[23] Implicit in the procedure is the maintenance of $C_{2v}$ symmetry for the methylene groups in the cycloalkane rings. In cases of severe nonbonded H–H interactions, this assumption may be incorrect and strain relief may be afforded by bending the H–C–H angle asymmetrically. However, some crude comparisons made by incorporating this distortion did not reveal much change in the total energy in cyclodecane.

[24] C. S. Foote, *Tetrahedron Letters*, 579 (1963).

[25] J. H. Shachtschneider and R. G. Snyder, *Spectrochim. Acta*, **19**, 117 (1963).

[26] E. B. Wilson, Jr., *Advan. Chem. Phys.*, **2**, 367 (1959); for more recent discussions see ref 27 and references quoted therein.

[27] R. A. Scott and H. A. Scheraga, *J. Chem. Phys.*, **42**, 2209 (1965).

[28] This function retains the threefold barrier form of the simple cosine function, while introduction of cos 9ω or higher terms leads to new secondary maxima and so these were not considered.

ferred value for $K_t = 2.65$ and $K_t' = 0$. Thus the empirical correlation carried out here appears to support a simple cosine function for the torsional barrier.

Simmons and Williams[30] have recently adapted a molecular orbital treatment of Hoffman[31] to provide a nonbonded H–H interaction potential "hard" enough to account for the barrier in ethane completely by nonbonded H–H interactions with no separate torsional energy term. This approach has been used before by Mason and Kreevoy[32] and will be discussed in the next section.

**Nonbonded Interactions.** Any pair of nonbonded atoms at an internuclear distance, $r$, possesses a mutual interaction, which may be cast in the form $E_{\mathrm{NB}} = Be^{-\mu r} - A/r^6$, the first term being a repulsive interaction, the second attractive; the constants $B$, $\mu$, and $A$ are characteristic of the kind of atoms involved in the pair and the curve has a minimum (slightly attractive) at the sum of the van der Waal's radii of the two atoms. The attractive portion of the curve (relatively large $r$) may be studied reasonably accurately and acceptable values of $A$ are available, but the repulsive potentials are very difficult to evaluate experimentally.[5] Thus in the present work values of $B$ and $\mu$ were varied independently for both HH and CC interactions and the HC interactions were evaluated from a function the repulsive component of which was taken as the geometric mean of the HH and CC values. The interactions must be evaluated over all pairs of atoms in the molecule with the exception of the necessarily large 1–3 interactions which are presumed to be incorporated in the angle-bending terms.[7] Although H–H repulsions between a few critical hydrogens account for a very large proportion of the total nonbonded interactions in most cases, the other interactions, while usually insignificant separately, take on real importance in the mass (there are 405 nonbonded interactions in cyclodecane) and may not be ignored.[33]

In the course of the empirical correlation search, it was first found that the original function[5] for H–H interactions was somewhat too soft (this arises in part because the optimum bond angles are now taken at 112° instead of tetrahedral) and the attractive component of the total nonbonded energy was too large in the larger rings owing to the rapid increase in the number of these nonbonded interactions with ring size. At first the only curves considered were also those which minimized at the sum of the traditionally quoted van der Waal's radii of the atoms (*cf.* for hydrogen, 1.2–1.3 A); none of these served to provide both the energies of the rings and the angles of cyclodecane in agreement with experimental values. The final curve (Table IV) for the H–H potential shows a minimum at 3.15 A implying a van der Waal's radius of nearly 1.6 A for hydrogen covalently bound to carbon. These radii have been commonly assessed in the past from the intermolecular distance between hydrogens in various covalent molecules, but it may be argued that such distances are likely to be less than the minimum in the nonbonded H–H potential since the other atoms in the molecules measured are likely to have net intermolecular attraction at these distances and so squeeze the abutting hydrogens closer than their minimum-energy distance.

The final curve for the important H–H potential is very similar to that offered by Bartell,[7] which also reproduces most of the ring energies quite well, the $C_{10}$ angles less well. These curves are also similar to the helium potentials of Amdur[34] and to several other "soft" functions for H–H used with success in other calculations.[27,35–38] Potentials substantially "harder" were used by Mason and Kreevoy[32] and by Simmons and Williams[30] in an effort to incorporate the effect of torsional strain into the H–H potential. Such functions only perform well in those cases in which there is no substantial nonbonded repulsion, such as the simple alkanes or cyclohexane (note ref 33), but fail badly where these repulsions are serious as in the medium rings; in eclipsed ethane the H–H distances are about 2.3 A so that any function which provides about 1 kcal/mole at 2.3 A (to yield an ethane barrier of 3 kcal/mole) must be of much higher energy at the 2.0-A distances encountered in the medium rings.

Cyclodecane affords an excellent qualitative test of nonbonded potential functions for H–H interactions. From Table II it is clear that the strain energy of cyclodecane, after subtracting bond angle bending, is 6.8 of the total 13.2 kcal/mole. There are six H–H interactions in the molecule which are critical and account for almost all of the repulsion strain: two at 1.9 A and four at 2.0 A. In the present work these alone afford 6.28 kcal/mole of total H–H energy. Hence any H–H interaction function yielding much more than about 1 kcal/mole per H–H interaction at 2.0 A cannot reproduce the strain energy of cyclodecane. Simmons' function[30,39] requires 7.4 kcal/mole per H–H interaction at 2.0 A and that of Mason and Kreevoy, 6.9 kcal/mole.

In summary, then, the procedure here of searching for the best assumptions (including the seven constants required by the functions) by attempting to match calculated values with empirical results for about 12 independent pieces of data has led to a very good reproduction of experimental results, as tabulated in Table I, II, and III, with the final selection of functions and constants used being listed in Table IV. As noted with $K_\theta$ above, variation of all these seven constants had differential effects on the calculated energies and angles being matched with experiment, so that the final set

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(29) Wiberg[13] used a trial expression, $E_t = K_t(1 + \cos^2 3\omega)$, but this is actually identical with the simple cosine function (with $K_t' = 0$).

(30) H. E. Simmons and J. K. Williams, *J. Am. Chem. Soc.*, **86**, 3222 (1964).

(31) R. Hoffman, *J. Chem. Phys.*, **39**, 1397 (1963); Simmons and Williams actually quoted the reference to the similar work of R. M. Pitzer and W. N. Lipscomb, *ibid.*, **39**, 1995 (1963).

(32) E. A. Mason and M. M. Kreevoy, *J. Am. Chem. Soc.*, **77**, 5808 (1955); **79**, 4851 (1957).

(33) As an example of the idea above that the simpler alkanes are not of themselves adequate tests of the various functions used in calculation, the results on the energies of cyclohexane (chair, twist-boat, and interconversion barrier) in the first paper of the series[5] reproduced the experimental values about equally well whether the full set of nonbonded interactions was employed or merely the H–H potentials. This in turn suggested the validity of computing the more complex medium rings using only the few critical H–H interactions instead of the full set,[1] but the present study shows this assumption to have been in significant error in the medium rings while it was not in cyclohexane.

(34) I. Amdur and A. L. Harkness, *J. Chem. Phys.*, **22**, 664 (1954); see also ref 5.

(35) F. J. Adrian, *ibid.*, **28**, 608 (1958).

(36) L. R. Snyder, *J. Phys. Chem.*, **67**, 240 (1963).

(37) A. Abe, R. L. Jernigan, and P. L. Flory, *J. Am. Chem. Soc.*, **88**, 631 (1966).

(38) G. J. Gleicher and P. von R. Schleyer, *ibid.*, **89**, 582 (1967).

(39) In a personal communication, Snyder[36] notes that Simmons function "predicts a total H–H interaction energy in planar biphenyl of 35 kcal/mole."

represents a rough convergence. This convergence and the number of matched data lend strong support to the final functions of Table IV and confidence in their use in application of these conformational calculations to unknown systems. Furthermore, newer X-ray data have since offered gratifying support for these calculations in several cases described below.

## Discussion of Results

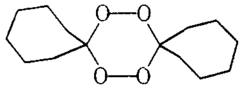
This paper is intended primarily to derive the preferred functions for calculation and to list the characteristics of preferred conformations. In the next paper[40] are discussed the energies of methyl-substituted cycloalkanes and perspective drawings of the rings tabulated here are presented only in the next paper (with methyl-substitution energies added) to avoid duplication. Since the forms of *n*-butane constitute a classical model for the strain in axial *vs.* equatorial methylcyclohexane, discussion of this hydrocarbon is also reserved for the second paper.[40] In the third paper[41] the modes of interconversion, and the energy barriers involved, are taken up for the several cycloalkanes with a view to developing a system for their conformational analysis.

Although the details of geometry and energy for the various cycloalkane conformers differ somewhat from those in the previous studies[1,5] in no case was the stability order reversed and the qualitative discussion there is still valid. The difference in energy favoring the twist-chair form of cycloheptane over the chair is small (1.4 kcal/mole) but since the chair form represents an energy maximum on the pseudo-rotation itinerary[5,41] it would only be expected to have a transient existence. The analogous situation is found with boat cyclohexane, which also represents a maximum on the energy profile. Evidence from nmr studies on fluorocycloheptanes supports the twist-chair form as the most stable cycloheptane conformation.[42] A small proportion of cycloheptane molecules should be in the twist-boat form ($\Delta E_{\mathrm{TC-TB}}$ = 2.4 kcal/mole) as a (smaller) proportion of cyclohexane is expected to be in the twist-boat form.

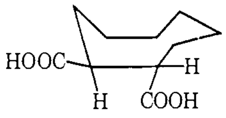
Values for the angles in a simple *gem*-disubstituted cycloheptane, "dimeric cycloheptanone peroxide" (I), have recently been obtained by Groth[43] at Oslo and show bond angles less than 1° higher than those calculated in Table I except for the C-1 value, at the disubstituted site, which is 1.4° higher; in short, the pattern of variation in $\theta$ parallels that in Table I but all the X-ray values are slightly higher. The dihedral angles, averaged to $C_2$ symmetry,[43] differ by less than 2° from those calculated, except for $\omega_3$, which differs by 15°, although the calculated value still lies within the range of distortion of the X-ray $\omega_3$ values from $C_2$ symmetry (these show the largest distortion from symmetry, of 17°). The over-all comparison is very favorable to the accuracy of the present calculations.

Cyclooctane is unquestionably the conformationally most complex cycloalkane owing to the existence of so many forms of comparable energy and this fact has caused great difficulty in the interpretation of physical data. Anet's nmr studies on cyclooctane and alkylcyclooctanes,[44] however, are best understood in terms of the boat–chair form in consonance with the present calculations. Three X-ray studies of crystalline cyclooctane derivatives have come to light since this work was undertaken; all have the boat–chair form of the ring. The *cis*- and *trans*-cyclooctanedicarboxylic acids (II and III) were examined by Dunitz;[9] the bond and dihedral angles down each side of the ring in each case vary on the average about 2° from average symmetrical values. The five calculated bond angles ($\theta$) in Table I are identical with those of the five average angles for the *cis* acid and 1–2° off for the *trans* (the observed rings themselves differ that much), while the dihedral angles vary less than 2° at each of the four positions for each ring (with one exception = 5°), the calculated four angles in fact lying between the averages for the two experimental cases.

The third determination is a recently completed study of "dimeric cyclooctanone peroxide" (IV) by Groth,[45] which also reveals a boat–chair conformation in both cyclooctane rings and which shows bond angles again about 1° higher than those calculated in Table I and dihedral angles 2° or less below the calculated ones. (Variations of experimental values from plane symmetry are $\Delta\theta$ = 1.5° and $\Delta\omega$ = 3.3° on the average.)



I



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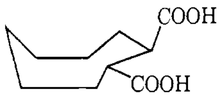
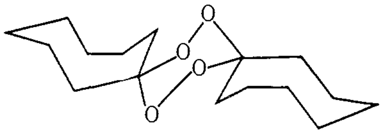


III



IV

The only previous X-ray determination of a cyclooctane was that of a salt of azacyclooctane, said to resemble an extended crown conformation after partial refinement;[46] subsequent work[9] has indicated, however, that there is too much molecular oscillation in the crystal to provide a significant structure. Over-all the experimental results to date are in remarkable agreement not only with the boat–chair form but also with the particular boat–chair geometry calculated here.

Nevertheless, within 2 kcal/mole of the boat–chair form in energy exist five more symmetrical forms: chair–chair (extended crown), boat–boat (saddle), twist-chair–chair[41] ($D_2$), twist-boat-chair,[41] and $S_4$; the latter appears somewhat preferred over the first four and is in fact the twist-tub or twist-boat of Roberts,[42] favored in his work on the nmr spectra of fluorinated cyclooctanes. These six conformations of

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(40) J. B. Hendrickson, *J. Am. Chem. Soc.*, **89**, 7043 (1967).

(41) J. B. Hendrickson, *ibid.*, **89**, 7047 (1967).

(42) J. D. Roberts, Chemical Society Centenary Lecture, 1966; *cf. Chem. Brit.*, 529 (1966).

(43) P. Groth, *Acta Chem. Scand.*, **18**, 1801 (1964). Since publication of this preliminary account refinement has proceeded to $R$ = 7.4% and reveals two clearly twist-chair cycloheptane rings, distorted from $C_2$ symmetry by an average of 1° in bond angles and 10° in dihedral angles.

(44) F. A. L. Anet and M. St. Jacques, *J. Am. Chem. Soc.*, **88**, 2585, 2586 (1966).

(45) P. Groth, *Acta Chem. Scand.*, **19**, 1497 (1965). The author is very grateful to Dr. Groth for the detailed geometrical data on this derivative, as well as that of ref 43, in advance of publication.

(46) J. D. Dunitz and V. Prelog, *Angew. Chem.*, **72**, 896 (1960).

nearly equal energy all represent energy minima (unlike chair cycloheptane, above) on the complex interconversion profiles discussed in the third paper[41] and so there is no surprise if substitution of fluorine atoms should tip the energy balance toward the $S_4$ form.[47]

With cyclononane the several $C_2$ forms of ref 1 were reinvestigated only roughly and the best of them (TCB form in the third paper[41]) found to be still about 2.2 kcal/mole less stable than the favored $D_3$ form listed here; as this parallels the previous situation, there is nothing significant to add to the discussion there. The same is true of other cyclodecane forms: rough calculation of the other plane- and axial-symmetric $C_{10}$ conformers showed none to be preferred over the favored BCB form listed here. The all-chair (CCC) conformation is less favored by 7.5 kcal/mole. A more detailed discussion of these rings is reserved for the last paper in this group.[41]

[47] The $S_4$ form was not considered in the previous study[1] since the system devised there for identifying all the possible symmetrical rings was created to locate only planes and axes of symmetry passing through the ring of which the $S_4$ form (uniquely) has neither.

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# Molecular Geometry. VI. Methyl-Substituted Cycloalkanes[1]

**James B. Hendrickson**[2]

*Contribution from the Edison Chemical Laboratory, Brandeis University, Waltham, Massachusetts 02154. Received June 7, 1967*

**Abstract:** The strain energies of the methylcycloalkanes of six- to ten-membered rings have been computed for all possible substituent positions on each symmetrical conformation. The results provide a basis for conformational analysis of substituted cycloalkanes.

For purposes of conformational analysis of the medium-ring cycloalkanes it is necessary to obtain the strain energies characteristic of substituents on the various possible positions of the several conformations of the cycloalkanes of six to ten members. In the familiar, highly symmetrical chair form of cyclohexane there are only two distinguishable positions for a substituent, *i.e.*, equatorial and axial, implying respectively one substituent lying more or less in the plane of the ring and the other perpendicular to that plane. With less symmetrical rings the situation is made more complex by the fact that since the steric environments at the various ring carbons are different, so will the energies of the pairs of substituent positions on these carbons also differ. Thus in a ring of $N$ carbons and no symmetry elements there will be $2N$ possible substituent positions. Nevertheless, models reveal that at all these atoms the equatorial–axial distinction defined above remains clear enough for this convenient nomenclature to be carried over into rings larger and less symmetrical than the chair cyclohexane. The one exception to this procedure is the necessity of distinguishing the pair of substituents on a ring carbon lying on a twofold axis of symmetry (the axis carbon), which, by virtue of that symmetry, experience identical steric environments; such identical substituent positions, being neither axial nor equatorial, are labeled "isoclinal."[3]

The functions developed in the preceding paper[1] for saturated hydrocarbons have been used here to evaluate the energies of methyl substituents on each possible position of the symmetrical rings determined previously.[1] The procedure taken is identical with that used in an earlier discussion of methylcyclohexanes and cycloheptanes[4] with the exception that the newer functions were used and all nonbonded interactions (HH, HC, and CC) were included in the analysis. As before, both the CCC angle ($\phi_M$) of methyl to ring carbons and the rotation ($\omega_M$) of the methyl relative to a fully staggered orientation were allowed to vary independently in seeking the minimum.[5] The optimum CCC angle ($\theta_{min}$) for use in the bond angle bending strain calculation for the methine carbon was taken as the mean of 112° for methylene[1] and 109.5° for $C(CH_3)_4$, or 110.7°, from which is derived the corresponding HCC optimum angle of 108.2°. The full equation for $E_\theta$ at the methine carbon was used (eq 1) and values for $K_{CC} = 0.0188$ and $K_{HC} = 0.0129$ kcal/(mole deg$^2$) were derived by breakdown of the over-all $K_\theta = 0.0230$ derived previously for the methylene group[1] ($\psi_M$ = HCC angle at methine carbon).

$$E_{\theta-\text{methine}} = K_{CC}[(\theta - 110.7)^2 + 2(\phi_M - 110.7)^2] + 3K_{HC}(\psi_M - 108.2)^2 \quad (1)$$

This procedure has been applied to substituents on the major cycloalkane conformations with the results tabulated in Table I, the designation of substituents "down" or "up" at a given carbon when the ring is viewed from above being respectively $\alpha$ and $\beta$, as in the steroid convention. The relevant views and ring numbers are shown in Chart I.

The value for methylcyclohexane in the chair form ($\Delta E = 0.7$) must be compared to an average of empirical values[6] showing about 1.7 kcal/mole for the

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(1) Paper V (preceding paper): J. B. Hendrickson, *J. Am. Chem. Soc.*, **89**, 7036 (1967). The author wishes gratefully to acknowledge financial support by a research grant from the National Institutes of Health as well as the opportunity to use the computation facilities of the Massachusetts Institute of Technology (IBM 7094) and Brandeis University (IBM 1620).

(2) Alfred P. Sloan Foundation Fellow, 1962–1966.

(3) J. B. Hendrickson, *J. Am. Chem. Soc.*, **86**, 4854 (1964).

(4) J. B. Hendrickson, *ibid.*, **84**, 3355 (1962).

(5) $\phi_M$ was varied by 1° increments, $\omega_M$ by 20°.

(6) A general discussion of these values is available in E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, John Wiley and Sons, Inc., New York, N. Y., 1965.