

ORGANIC AND BIOLOGICAL CHEMISTRY

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Molecular Geometry. I. Machine Computation of the Common Rings¹

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Computation of the energies of hydrocarbon molecule conformations as a function of various geometric parameters is discussed and machine computation advanced as a means of coping with the enormous calculations necessary for their solution. New functions for non-bonded interactions are developed and compared with several previous ones. The cycloalkanes, C_{5-7} , are taken as examples, their conformations of minimum energy computed, and these energies compared with experimental values. The conformations and pseudorotations of the flexible forms of these rings are discussed in the light of the calculations, and special attention is paid to a discussion of the more complex conformational analysis of cycloheptanes.

Introduction

The idea that one might calculate in detail the energy of a given molecular conformation has long intrigued chemists, as it offers promise of the prediction of most stable conformations or the intimate transition state geometry and energy in organic reactions. A number of such calculations has been made²⁻⁸ with varying success, and it is well at the outset of the present work to offer a brief summary of the problems involved in such calculations.² The first and most formidable difficulty is that of selecting the particular functions which relate energy to geometrical parameters of the molecular conformations being examined; such functions, discussed in more detail below, are generally derived indirectly from various empirical sources as spectroscopic or thermodynamic data. Secondly, one must choose a particular conformation on which to apply these functions. In order to ascertain the most stable conformation of a given molecule, it is theoretically necessary to calculate the sum of energies related to the various geometrical parameters of a given conformation, and to minimize this sum with respect to independent variation of each of these parameters (*i.e.*, by progressive distortion of the given conformation). This statement of approach to the problem serves to underscore the vast complexity of the calculations in any molecule of organic chemical interest, since the number of independent geometrical variables can be overwhelming while the calculation of the total energy of any *single* set of geometric parameters is itself extremely ponderous. In order to reduce the problem to workable dimensions, it is generally necessary to simplify it by certain assumptions of conformation or of parameter constancy, and frequently by simplifying or simply ignoring certain of the relevant energy functions themselves.

(1) This work was supported in part by a generous grant from the National Institutes of Health.

(2) An excellent review of the problems of calculating conformations is given by F. H. Westheimer, in Chap. 12, "Steric Effects in Organic Chemistry," ed., M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956.

(3) D. H. R. Barton, *J. Chem. Soc.*, 340 (1948).

(4) K. S. Pitzer and W. E. Donath, *J. Am. Chem. Soc.*, **81**, 3213 (1959).

(5) (a) E. A. Mason and M. M. Kreevoy, *ibid.*, **77**, 5808 (1955);

(b) M. M. Kreevoy and E. A. Mason, *ibid.*, **79**, 4851 (1957).

(6) P. Hazebroek and L. J. Oosterhoff, *Disc. Faraday Soc.*, **10**, 87 (1951).

(7) R. Pauncz and D. Ginsburg, *Tetrahedron*, **9**, 40 (1960).

(8) N. Allinger, *J. Am. Chem. Soc.*, **81**, 5727 (1959).

These simplifications, however, too often so drastically alter the complexion of the problem as to render the answers either suspect or unreasonable. The basis of the present work is accordingly an effort to break through this barrier of undue simplification by employing machine calculation, thus allowing a far greater magnitude of mathematical effort in a reasonable time with untiring accuracy, and a consequent capability of a more intimate probing into these problems than is possible with hand calculation.⁹ The choice of particular functions relating geometric variables with energies is discussed below.¹⁰

1. **Bond Angle Strain.**—The energy associated with bending a single bond angle, θ , from the tetrahedral angle ($\tau = 109.47^\circ$) is derived from spectroscopic evidence and has the form $E_\theta = K_\theta (\theta - \tau)^2$. Values of K_θ (in kcal./mole/rad.²) are taken from Westheimer's review²: H-C-H, 23.0; H-C-C, 39.6; C-C-C, 57.5. Since, on change of one angle at tetrahedral carbon, the others must reasonably also change to accommodate, the single assumption was made that this accommodation would occur such as to minimize the total energy of angle strain in the six involved angles. Computer programs were thus set up to locate the configuration of minimum strain energy in the total angle set when a C-C-C angle was given a value other than the tetrahedral angle¹¹; the geometry of such a set is shown in Fig. 1. It was generally found that in the minimum energy configuration, for changes of less than 10° from tetrahedral, the angles bore a substantially linear relation to each other, as indicated in Fig. 1. Qualitatively, then, a methylene angle in a cycloalkane can be changed from the

(9) The IBM 709 computer, used in the present work, is capable of 8000 additions or subtractions, 4000 multiplications or divisions or about 500 more complex functions (powers, roots and trigonometric functions) per second. The FORTRAN adaptation makes possible the submission to the computer of programs set out virtually in plain algebraic language, thus obviating the necessity of any special command of computer mathematics. The author wishes heartily to thank the Western Data Processing Center at UCLA for the generous facilities put at his disposal for the course of this work.

(10) Throughout this discussion, all energies are given in kcal./mole, all distances in Å.

(11) It is frequently convenient to solve complex equations by iterative trial-and-error with the computer, taking advantage of its immense capacity for arithmetic work. This approach was used in this instance and in most others in this work where not otherwise described in detail. Thus in this case, for a given value of α , a series of values for β were taken until the sum of bending strains for the six angles (Fig. 1) was a minimum, and so on for all useful values of α .

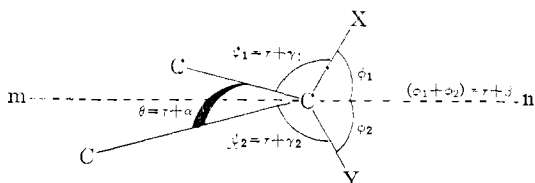


Fig. 1.—Angles around carbon: line \overline{mn} is common to the perpendicular planes \overline{CCC} and $\overline{XC\overline{Y}}$ and bisects angles \overline{CCC} and $\overline{XC\overline{Y}}$.

$$\cos \frac{1}{2}\theta \cos \theta_1 + \cos \psi_1 = 0$$

$$\cos \frac{1}{2}\theta \cos \phi_2 + \cos \psi_2 = 0$$

$$E_\theta = K_{CCC} \alpha^2 + 2K_{XCC} \gamma_1^2 + 2K_{YCC} \gamma_2^2 + K_{XC\overline{Y}} \beta^2$$

At minimum energy configuration

	X = Y = H		X = Y = C		X = C; Y = H	
	$\theta < \tau$	$\theta > \tau$	$\theta < \tau$	$\theta > \tau$	$\theta < \tau$	$\theta > \tau$
$\beta = -b\alpha$						
$\gamma_1 = -c\alpha$						
$\gamma_2 = -d\alpha$						
$E_\theta = K\theta\alpha^2$						
($K\theta$ in kcal./mole/rad ²)	63	65	68	71	66	68

tetrahedral by 5° with 0.5 kcal./mole strain, or by 10° with 1.9 kcal./mole. It is clear that much of the accommodation of a molecule to strain can be accomplished at relatively little cost by adjustments of bond angles, although this has been neglected or slighted in some previous calculations.^{5,7,8}

2. Bond Length.—It appears to be generally agreed that changes in bond length are much more costly of energy than the other geometrical changes discussed here² and accordingly the calculations have been made with invariant bond lengths; the values used were taken from the recent work of Bartell¹²: C-C, 1.533 Å. and C-H, 1.108 Å.

3. Torsional Strain.—In keeping with the estimates of the rotational barrier in ethane,^{4,13} a function $E_t = 1.40 (1 + \cos 3\omega)$ kcal./mole was adopted for the torsional strain due to rotation (*i.e.*, the extent of eclipsing of substituent hydrogens) around a single bond, in which ω is the dihedral angle as defined in the Appendix. This function derives an unfortunate uncertainty from the fact that its origins are not even qualitatively understood. It does not appear, however, to derive to any appreciable degree from non-bonded interactions¹⁴ so that its inclusion here as a separate function was deemed reasonable and some support for this is adduced below. In any event this function has been used in past calculations of this sort with a high order of success⁴ and its neglect⁷ probably introduces serious error.

4. Non-Bonded Interactions.—As discussed by Westheimer,² the choice of energy functions in this area is the most problematical. The potential between two atoms not bonded to each other consists of a repulsive and an attractive term so that the potential curves $E = E_R - E_A$ have the form seen

(12) R. A. Bonham and L. S. Bartell, *J. Am. Chem. Soc.*, **81**, 3491 (1959). It was generally found that use of the more common values, C-C, 1.54 Å., and C-H, 1.10 Å., caused only negligible differences.

(13) W. G. Dauben and K. S. Pitzer, Chap. 1 of "Steric Effects in Organic Chemistry," ed. M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956.

(14) (a) E. B. Wilson, Jr., *Adv. Chem. Phys.*, **2**, 367 (1959); (b) *Proc. Natl. Acad. Sci.*, **43**, 816 (1957).

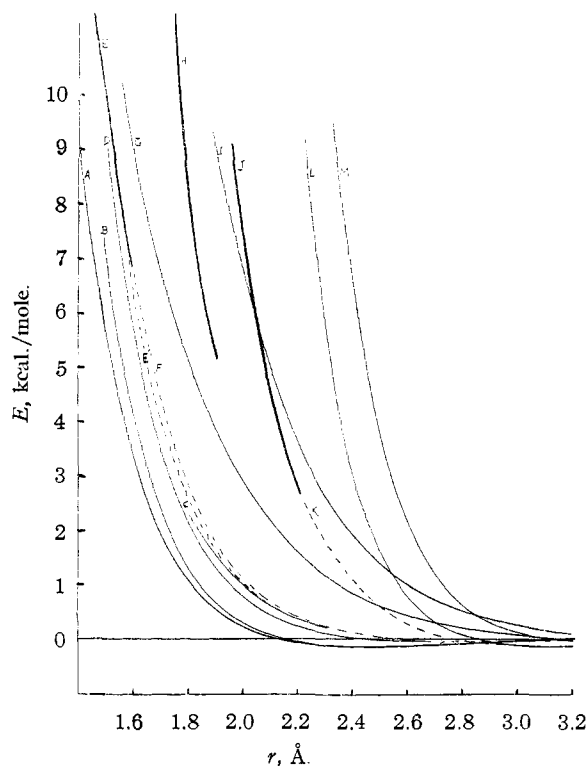


Fig. 2.—Non-bonded interaction energies: A, H-H, eq. 3; B, H-H, eq. i²³; C, He-He, Mason-Rice¹⁵; D, He-He, Slater-Kirkwood¹⁹; E, He-He experimental, Amdur²¹; E', best fit of (C + E), eq. 1²⁰; F, H-H, Bartell²³: $E = 6.60 \times 10^3 e^{-4.08r} - 49.2/r^6$ ($r_0 = 2.97$ Å.); G, H-H, Ginsburg⁷: $E = (166/r + 366 + 23.1r + 580r^2 + 1828r^3)e^{-4.35r}$; H, He-Ne, geometric mean of (E + J); I, H-H, Mason-Kreevov⁵: $E = 3.716 \times 10^3 e^{-3.07r} - 89.52/r^6$ ($r_0 = 4.4$ Å.); J, Ne-Ne experimental, Amdur,²¹ eq. 2; K, C-C, eq. 5; L, C-C, eq. ii²³; M, C-C, Bartell²³: $E = 3.00 \times 10^5 / r^{12} - 325/r^6$ ($r_0 = 3.50$ Å.).

in Fig. 2, with a shallow energy minimum at r_0 , the sum of the van der Waals radii of the interacting atoms. The attractive term arises from the London dispersion forces¹⁵ and is generally taken as $E_A = A/r^6$; the values of A used here are those of Pitzer¹⁶: $A_{H-H} = 49.2$, $A_{H-C} = 125$, $A_{C-C} = 325$.

The repulsive term, generally cast in the form $E_R = Be^{-\mu r}$ or $E_R = B/r^n$ ($n = 8-12$), is more difficult to estimate. Quite accurate calculations of the potential in the region of the minimum are available from gas-law deviations,¹⁷ but in the higher-energy region (0-5 kcal./mole), which figures decisively in estimating intramolecular non-bonded interactions of the sort desired here, these gas-law data are of little assistance. In order to obtain empirical entrée into this region, the functions of Amdur from the scattering of high-velocity

(15) F. London, *Trans. Faraday Soc.*, **33**, 8 (1937).

(16) K. S. Pitzer and E. Catalano, *J. Am. Chem. Soc.*, **78**, 4844 (1956).

(17) Curves C and D in Fig. 2 are examples for helium gas as derived by Mason and Rice¹⁸ and Slater and Kirkwood,¹⁹ respectively. Further discussion of potentials in this region will be found in "Molecular Theory of Gases and Liquids," by J. O. Hirschfelder, C. F. Curtiss and R. B. Bird, John Wiley and Sons, Inc., New York, N. Y., 1954.

(18) E. A. Mason and W. E. Rice, quoted in ref. 20.

(19) J. C. Slater and J. G. Kirkwood, *Phys. Rev.*, **37**, 682 (1931).

neutral atoms were utilized^{2,20,21}

$$\text{He-He: } E = 8.9 \times 10^3 e^{-4.56r} \text{ kcal./mole } (r = 1.27\text{--}2.30 \text{ \AA.}) \quad (1)$$

$$\text{Ne-Ne: } E = 7.2 \times 10^3/r^{10} \text{ kcal./mole } (r = 1.96\text{--}2.20 \text{ \AA.}) \quad (2)$$

Since the van der Waals radii of carbon and neon are approximately the same (3.15–3.2 Å),² a potential function for carbon-carbon interactions can be obtained by curve-fitting the experimental neon-neon curve in the repulsive region with a function of the form $E = Be^{-\mu r} - A/r^6$ with $A = 325$ and the minimum at $r_0 = 3.2$ Å. This yields eq. 5 and curve K, Fig. 2.

The same procedure, however, is not likely to produce a suitable curve for covalent hydrogen-hydrogen interaction by extending the helium-helium curve owing to the significant difference in van der Waals radii of these atoms. It is reasonable, however, to assume that in this repulsive region the curvature of the helium and hydrogen curves will be much the same, allowing the value of the helium parameter μ to be used in the hydrogen repulsive term. Thus, with $r_0 = 2.5$ Å., $A = 49.2$ and $\mu = 4.55$, a value of $B = 9.25 \times 10^3$ is derived from $dE/dr = 0$ at r_0 . A more convenient function, virtually indistinguishable from this, is given as eq. 3. The hydrogen-carbon interaction, eq. 4, is derived from the geometric mean of the repulsive terms.

$$\text{H-H: } E = 1.00 \times 10^4 e^{-4.60r} - 49.2/r^3 \quad (r_0 = 2.5 \text{ \AA.}) \quad (3)$$

$$\text{H-C: } E = 1.29 \times 10^4 e^{-4.12r} - 125/r^6 \quad (r_0 = 2.8 \text{ \AA.}) \quad (4)$$

$$\text{C-C: } E = 1.66 \times 10^4 e^{-3.63r} - 325/r^6 \quad (r_0 = 3.2 \text{ \AA.}) \quad (5)$$

The total energy due to non-bonded interactions in a hydrocarbon molecule should then be the sum of the above potentials taken between all pairs of non-bonded atoms in the molecule.²²

Various other proposals^{5,7,23} for these non-bonded potential functions have been made and it is an easy matter to incorporate each of them into the computer programs in order to ascertain how the final energies in each case compare with experimental results, thus affording in turn an empirical measure of their reasonableness. These functions are summarized for comparison in Fig. 2.

Discussion of the relative effectiveness of these various function is reserved for the next section. It should be noted that in the application of these equations to hydrocarbons, the largest energies in

(20) I. Amdur and A. L. Harkness, *J. Chem. Phys.*, **22**, 664 (1954).

(21) I. Amdur and E. A. Mason, *ibid.*, **23**, 415 (1955).

(22) In the application to the common cycloalkane rings discussed below, this total will consist of $n(2n - 1)$ H-H interactions, $n(n - 3)/2$ C-C interactions, and $2n(n - 1)$ H-C interactions, or a total of $9n(n - 1)/2$ non-bonded interactions for a ring of n carbons (*i.e.*, cycloheptane possesses 189 interactions), making manual calculations burdensome.

(23) C. S. Bartell, *J. Chem. Phys.*, **32**, 827 (1960). See curves F and M, Fig. 2. Another related set of functions can be derived from these using Bartell's starting datum of the slope at 1.36 Å. for the H-H curve and the r^{-12} repulsion for the C-C curve with $r_0 = 2.5$ Å. for H-H and $r_0 = 3.2$ Å. for C-C:

$$\text{H-H: } E = 1.36 \times 10^4 e^{-4.72r} - 49.2/r^6 \quad (r_0 = 2.5 \text{ \AA.}) \quad (i)$$

$$\text{C-C: } E = 1.75 \times 10^5/r^{12} - 325/r^6 \quad (r_0 = 3.2 \text{ \AA.}) \quad (ii)$$

most cases will arise from 1-3 interactions, *i.e.*, from interactions of two atoms bound to the same carbon, since these generally will afford the lowest values of r .²⁴

The assumption of spherical atoms which is implicit in these equations (no directional parameters) and the disregard of the effect of the bonding electrons on the repulsions of two atoms bound to the same carbon combine to make the use of such functions especially questionable for the 1-3 interactions. On the other hand, calculation of the energy differences between pairs of conformations of a given molecule is generally valid since the major non-bonded interaction differences in such pairs generally reside in hydrogen-hydrogen compressions in which the hydrogens are separated by three or more carbons and the large 1-3 interactions virtually cancel out. In such cases the hydrogens which are involved in such interpenetration usually meet much more nearly "head-on" so that the assumption of spherical symmetry implicit in the interaction functions is far more tenable. Finally, there is a serious question as to whether the inclusion of the rather large H-C and C-C terms results in the introduction of more refinement or more error in view of the uncertainty of the functions. Consideration is given below to using merely the sum of the H-H terms and discarding H-C and C-C interactions.

The total strain energy of a given conformation is thus the sum of the components discussed above and may be summarized as in eq. 6.²⁵ Zero-point energies have not been included, the assumption being made⁴ that they will, like bond energies, cancel in the comparison of two conformations of a given molecule. Similarly, only hydrocarbons have been employed in calculation so that no further error need be introduced by inclusion of coulombic terms.² Hence

$$E = E_\theta + E_t + E_R - E_A \quad (6)$$

$$\text{OR}$$

$$E = K_\theta \sum_{\theta} (\theta_1 - \tau)^2 + K_t \sum_{\omega} (1 + \cos 3\omega_1) + \sum_{r_{HH}} (B_{HH} e^{-\mu_{HH}r_1} - A_{HH}/r_1^6) + \sum_{r_{HC}} (B_{HC} e^{-\mu_{HC}r_1} - A_{HC}/r_1^6) + \sum_{r_{CC}} (B_{CC} e^{-\mu_{CC}r_1} - A_{CC}/r_1^6)$$

(24) See the discussion of Bartell in ref. 23 of the effect of these large 1-3 interactions on other molecular properties.

(25) The use of models in assessing conformation is widespread and convenient, but the models also lend themselves to deception in their mechanical reproduction of these various kinds of molecular strain. Thus the Hirshfelder models overrate both non-bonded interactions (inflexible spheres) and angle strain, but give a fair notion of torsional barriers, whereas the Dreiding models afford a rather stiff simulation of angle strain but not the slightest mechanical sense of torsional barriers and, of course, no non-bonded interactions. The "ball and spring" models are fair on angle strain but overrate torsional barriers badly, although both of the latter two transmit strains from one portion of the molecule to another, as Hirshfelder models do not. The incorporation of a reasonable mechanical simulation of these several kinds of strain into molecular models would be a great boon to qualitative conformational assessments and poses an engineering challenge of a high order.

Of existing models the Dreiding models are probably the best, with the reservations noted, for following the conformational arguments advanced here. For the estimation of distances to be used in non-bonded energy calculations they are not sufficiently accurate since the exponential functions seriously distort distance errors. These models are obtainable from G. M. Instrument Co., P. O. Box 167, Greenville, Ill., or W. Büchi, Flawil, Switzerland.

TABLE I
GEOMETRICAL DEFINITION AND ENERGIES OF CYCLOALKANES

	Bond angles, deg.							Dihedral angles, deg.							Energies, kcal./mole ^a					
	θ_1	θ_2	μ_3	θ_4	θ_5	θ_6	θ_7	ω_1	ω_2	ω_3	ω_4	ω_5	ω_6	ω_7	E_θ	E_t	$(E_R - E_A)$	$(E_R - E_A)_{HH}$	ΣE_H	ΣE_{HH}
Planar cyclopentane	108.0	108.0	108.0	108.0	108.0			0.0	0.0	0.0	0.0	0.0			0.2	14.0	13.5	3.2	27.7	17.3
Cyclopentanes: minima for $\omega_1 = 0-60^\circ$	105.9	105.9	103.5	101.4	103.5			0.0	26.4	-42.4	42.4	-26.3			2.8	7.2	13.4	2.4	23.5	12.4
	105.6	106.1	104.1	101.5	103.0			5.0	22.1	-40.6	43.6	-30.2			2.8	7.2	13.4	2.4	23.5	12.4
	105.3	106.2	104.6	101.8	102.4			10.0	17.6	-38.2	44.2	-33.6			2.8	7.3	13.4	2.4	23.5	12.4
	104.9	106.2	105.1	102.2	102.0			15.0	12.6	-35.3	44.3	-36.7			2.8	7.3	13.4	2.4	23.5	12.4
	104.3	106.2	105.5	102.7	101.7			20.0	9.3	-31.7	43.8	-39.4			2.8	7.3	13.4	2.4	23.5	12.4
	103.7	106.0	105.8	103.4	101.4			25.0	1.6	-27.6	42.8	-41.8			2.8	7.2	13.4	2.4	23.5	12.4
	102.9	105.7	106.1	104.0	101.6			30.0	-4.8	-22.3	40.7	-43.5			2.8	7.2	13.4	2.4	23.5	12.4
	102.3	105.1	106.2	104.8	101.8			35.0	-12.0	-15.6	37.2	-44.4			2.8	7.2	13.4	2.4	23.5	12.4
	101.7	104.1	106.2	105.6	102.7			40.0	-20.9	-6.3	31.1	-43.8			2.8	7.3	13.4	2.4	23.5	12.4
	102.0	101.9	104.8	106.3	104.8			45.0	-36.7	-14.3	13.7	-36.3			2.9	7.2	13.4	2.4	23.5	12.5
	100.5	100.5	103.8	106.0	103.9			50.0	-40.6	-15.7	15.3	-40.4			4.1	6.2	13.8	2.2	24.1	12.6
	99.0	99.0	102.5	106.1	102.4			55.0	-44.2	-16.8	17.2	-44.4			5.8	5.5	14.3	2.1	25.6	13.3
	97.3	97.3	101.0	106.2	100.9			60.0	-47.9	-18.3	18.5	-48.1			7.9	4.9	15.4	2.0	28.2	14.8
Cyclopentanes: Pitzer C ₅ ^{4,34}	100.4	102.4	105.6	105.6	102.4			46.1	-28.6	0.0	28.6	-46.1			3.7	6.5	13.6	2.3	23.9	12.5
Cyclopentanes: Pitzer C ₂	105.0	105.0	100.7	100.7	105.0			15.1	-39.4	48.1	-39.4	15.1			3.8	6.5	13.6	2.3	23.9	12.5
Cyclohexanes: Planar	120.0	120.0	120.0	120.0	120.0	120.0		0.0	0.0	0.0	0.0	0.0	0.0		13.3	16.8	17.7	5.8	47.8	35.9
Chair Ia	τ	τ	τ	τ	τ	τ		60.0	-60.0	60.0	-60.0	60.0	60.0		0.0	0.0	14.0	2.9	14.0	2.9
Boat IIa	τ	τ	τ	τ	τ	τ		60.0	0.0	-60.0	60.0	0.0	-60.0		.0	5.6	16.8	4.2	22.4	9.8
Twist-boat Ic	τ	τ	τ	τ	τ	τ		33.2	-70.6	33.2	33.2	-70.6	33.2		.0	5.1	14.6	3.1	19.7	8.2
C ₂ barrier Ib	113.5	118.3	118.3	113.5	106.2	106.2		19.1	0.0	19.1	-56.2	75.0	-56.2		4.1	7.6	15.6	3.9	27.3	15.6
C ₅ barrier IIB	119.9	117.2	τ	τ	τ	117.2		0.0	30.0	-60.0	60.0	-30.0	0.0		4.5	8.4	15.4	4.2	28.3	17.0
Cycloheptanes: Planar	128.6	128.6	128.6	128.6	128.6	128.6	128.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50.5	19.6	24.4	9.1	94.5	79.2
Chair III	τ	τ	τ	τ	τ	τ	τ	62.0	-99.6	81.7	0.0	-81.7	99.6	-62.0	0.0	8.6	43.5	22.1	52.0	30.7
(Tetrahedral Twist-chair V angles)	τ	τ	τ	τ	τ	τ	τ	-42.8	103.2	-79.8	55.1	-79.8	103.2	-42.8	.0	7.1	20.4	5.4	27.4	12.4
Boat IV	τ	τ	τ	τ	τ	τ	τ	62.0	38.3	-81.7	0.0	81.7	-38.3	-62.0	.0	6.1	45.3	22.8	51.4	28.9
Twist-boat VII	τ	τ	τ	τ	τ	τ	τ	-51.4	72.5	20.7	-85.5	20.7	72.5	-51.4	.0	6.0	39.9	17.9	45.9	23.9
Cycloheptanes: Chair III	τ	112.0	111.0	116.0	116.0	111.0	112.0	69.9	-91.8	70.6	0.0	-70.6	91.8	-69.9	2.0	6.8	16.9	4.4	25.8	13.3
(Preferred Twist-chair V forms)	112.0	112.0	112.0	112.0	112.0	112.0	112.0	-41.2	97.0	-75.8	52.9	-75.8	97.0	-41.2	0.9	6.1	16.7	4.2	23.6	11.1
Boat IV	114.0	114.0	114.0	114.0	114.0	114.0	114.0	56.7	34.4	-73.7	0.0	73.7	-34.4	-56.7	2.9	5.7	18.0	5.6	26.5	14.2
Twist-boat VII	113.0	113.0	113.0	113.0	113.0	113.0	113.0	-47.8	67.7	19.0	-78.9	19.0	67.7	-47.8	1.7	5.7	18.8	6.2	26.2	13.6
C ₂ barrier VI	106.7	106.0	113.3	117.8	117.8	113.3	106.0	-48.6	101.1	-40.6	0.0	-40.6	101.1	-48.6	4.0	8.9	23.4	6.7	36.3	19.6

^a The sum of all non-bonded interactions listed as $(E_R - E_A)$; $\Sigma E = E_\theta + E_t + E_R - E_A$. The sum of all non-bonded H-H interactions listed as $(E_R - E_A)_{HH}$; $\Sigma E_{HH} = E_\theta + E_t + (E_R - E_A)_{HH}$.

Thus, the energy is a function of the geometrical parameters θ , ω and r , which are in turn interrelated by the nature of the skeletal geometry of the molecular conformation under consideration. The very useful equations given in the Appendix were derived to compute these geometrical interrelations for any set of points in space; the usefulness of these equations is enhanced by the lack of necessity for placing the molecule onto a coordinate system. In their most general form, as given in the Appendix, they are rather forbidding for hand calculation but often can be simplified drastically in practice by substitution of such constants as bond length and, frequently, the tetrahedral bond angle.

Results and Discussion

When the bond and dihedral angles of a given cycloalkane conformation have been defined, the computation of angle and torsional energies is a simple matter, but the computation of all the non-bonded distances and corresponding energies is more complex.²² A program was designed for the computer in which the computer is essentially given the initial data of angles and bond distances and told to move from one carbon to the next around the ring, computing each time the 1-3 interactions around that carbon and then the interactions back to previous methylenes (1-4, 1-5 and 1-6), in a logical system that does not allow duplication of any interactions. The interaction distances are then all printed out and the energies summed and printed as well (the computer time for computation of all these values for any given cycloheptane is about 15 seconds). The results of these calculations for a variety of cycloalkanes are detailed in Table I and discussed in the succeeding paragraphs.

Energy Calculations.—A number of proposals have been made,^{5,14} to account for the rotational barrier in ethane (and hence the E_t values here) by non-bonded interactions of the eclipsing hydrogens. A simple calculation of all non-bonded H-H interactions can be made for ethane with eq. 3 used here, giving a difference of 0.14 kcal./mole between the staggered and eclipsed forms, or only about 5% of the experimental value. If the H-H function has any validity, and it is hard to believe it off by a factor of 20 in the region of the van der Waals radius, this supports the thesis of Wilson¹⁴ that steric factors are a small portion of this potential and strengthens the usage in the present work of a component, E_t , entirely separate from the calculated non-bonded potentials.

The calculated angles and energies for the cyclopentanes given here are quite commensurate with those of Pitzer and Donath,⁴ making allowance for the fact that they did not employ any estimate of van der Waals repulsions, but utilized only the attractive non-bonded forces. This procedure seems logically unbalanced, particularly since a large portion of the attractive energies calculated in their work is from 1-3 interactions, where repulsion must play a comparable major role,²⁴ and in fact if any repulsive terms are incorporated in their cyclopentane energies it will have the effect of enlarging the discrepancies between experimental and calculated heats of formation.²⁶

Several of these calculations can be compared with empirical data. Thus, the energy barrier to boat-chair interconversion recently has been derived from low-temperature nuclear magnetic resonance data and found to be 9.7 kcal./mole.²⁷ Also, Allinger recently has observed $\Delta H = 5.9 \pm 0.6$ kcal./mole for the *cis*- and *trans*-1,3-di-*t*-butylcyclohexanes, which is a reasonable approximation to the energy difference between the chair and boat forms of cyclohexane.²⁸

By a quite different procedure Johnson²⁹ has obtained a value of $\Delta H = 5.5 \pm 0.3$ kcal./mole and the similarity of the two results is heartening. The calculated values are found by subtracting the energies of the two conformations involved from Table I. The calculations were duplicated with each of the various sets of van der Waals functions (Fig. 1) and it was found that calculations most in accord with the empirical data were obtained with the "softest" non-bonded interactions, *i.e.*, eq. 3-5, which are also those most similar to the neutral-atom scattering data, and which are consequently employed in Table I.³⁰ The largest portion of the energy in the cyclohexane conformer differences arises from ($E_\theta + E_t$) but is relatively less important in the cycloheptane cases, as might be expected. With regard to non-bonded interactions there is a suggestion in these comparisons that more error may be introduced by summing all these interactions than simply by summing the H-H interactions, so that such sums are listed separately in Table I.

The boat-chair cyclohexane difference (twist-boat *vs.* chair; *vide infra*) is thus calculated as 5.71 kcal./mole utilizing all non-bonded interactions (eq. 3-5) or 5.33 using H-H interactions only; the agreement with experiment is excellent.³⁰ For the energy difference between the chair form and the transition barrier (*vide infra*) the agreement is less good: 13.29 kcal./mole for all interactions; 12.66 for H-H only. The latter value is preferable and in error by 30%, whereas other functions yield even higher values.³⁰ Nevertheless, in view of the uncertainty here of the conformation as well as the functions used, this is probably satisfactory. In any event the sum ($E_t + E_\theta$) is itself higher than the empirical value and suggests that, for conformations necessitating strain of this magnitude, a molecular assemblage may achieve some energy accommodation different from or more subtle than those calculated here.

(26) When Pitzer's procedure, using only attractive forces between non-bonded atoms, is applied to the boat-chair energy difference in cyclohexane a value of only 3.9 kcal./mole is obtained. See also footnote 32.

(27) F. R. Jensen, D. S. Noyce, C. H. Sederholm and A. J. Berlin, *J. Am. Chem. Soc.*, **82**, 1256 (1960).

(28) N. L. Allinger and L. A. Freiberg, *ibid.*, **82**, 2393 (1960); see also the discussion in ref. 29.

(29) W. S. Johnson, J. L. Margrave, V. J. Bauer, M. A. Frisch, L. H. Dreger and W. N. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).

(30) ($E_\theta + E_t$) added to total (H-H, H-C and C-C) non-bonded interactions for the other curves of Fig. 1 yielded the following boat-chair differences: (B) + (L), 6.20; (F) + (M), 7.79; with H-H interactions only: (B), 5.38; (F), 6.00; (G), 6.75; (I), 8.84. Total energies for the cyclohexane barrier to chair-chair interconversion,²⁷ similarly, are: (B) + (L), 13.82; (F) + (M), 15.01; (B), 12.87; (F), 13.93; (G), 16.43; (I), 19.09. The values calculated for $\Delta H/\text{CH}_2$ for cycloheptane-cyclohexane³¹ are similarly too high, ranging from 1.25 to 5.83.

Another comparison may be obtained in the difference in enthalpy for cyclohexane and cycloheptane, an experimental value of 6.4 kcal./mole, or 0.91 kcal./mole per CH_2 , having been reported recently by Kaarsemaker and Coops.³¹ The use again of the "softest" curve for non-bonded interactions, and using H-H interactions only, yields 1.17 kcal./mole/ CH_2 (28% high), other functions again yielding higher values.^{30,32} In any event the results in these comparisons lend confidence in the general approach and in the use of such computations of particular conformers are discussed below.

Cyclopentane.—Pitzer and Donath⁴ have made calculations of the preferred cyclopentane conformations assuming C_2 or C_s symmetry and found that the most stable conformations of each symmetry were of essentially the same energy. The approach taken here was to ignore symmetry restrictions and attempt to calculate the preferred cyclopentane by a minimization of the total energy with respect to each independent geometric variable. Any general cyclopentane (carbon skeleton only) is defined by four independently variable angles, the other six (bond and dihedral) angles being then derivable from these by use of the equation in the Appendix. A computer program was set up to calculate the conformation and energy for a cyclopentane with ω_1 , θ_1 , θ_2 and θ_3 defined, and the bond angles were then all independently varied through a range near the tetrahedral (by 0.1° increments) until a conformation of minimum energy was found for each value of ω_1 . The minimization procedure used here requires that N^3 different conformations (with their energies in each case) be computed to produce a minimum energy conformation for one given value of ω_1 , where N = no. of values taken in each range of θ 's explored, *i.e.*, if each θ is varied from 110° to 100° in 0.1° increments, 100^3 or a million conformations must be computed. The incorporation of non-bonded interactions into E for this calculation is beyond the time-scale even of the computer, so that the minimization was done only as a minimum in $(E_\theta + E_t)$,³³ with calculations of $E_R - E_A$ made of the minimum-energy conformers so obtained (Table I). The calculations show that for *all* values of ω_1 below about 45° , there is a cyclopentane conformation of equal, minimum energy. These conformations include the symmetrical C_2 and C_s forms and presumably represent the entire circuit of conformers on the pseudorotation itinerary, *i.e.*, the passage of the out-of-plane pucker from carbon to carbon around the ring.³⁴ The list in Table I allows selection of the most stable conformation containing any desired dihedral angle, a feature

(31) S. Kaarsemaker and J. Coops, *Rec. trav. chim.*, **71**, 261 (1952).

(32) Use of attractive (dispersion) forces only^{4,26} in this calculation yields a negative value (-1.04 kcal./mole), implying a cycloheptane more stable than cyclohexane. In general this procedure favors more contracted conformers energetically, whereas it is more likely that *repulsions* figure larger in the more contracted forms and that they are destabilized, not stabilized.

(33) Following Pitzer, no account was taken here of the added strain of the H-C angles so that the values of E_θ represent only C-C-C bending; they may be corrected for this additional strain by multiplying E_θ by $63/57.5 = 1.1$ (*cf.* Fig. 1).

(34) The C_2 and C_s forms obtained compare favorably with those calculated by Pitzer, which are also included in Table I, with their energies computed by the present method for comparison.

that is useful in ascertaining the best five-ring form for bicyclic ring fusions, placement of substituents, etc.

Cyclohexane.—The chair form of cyclohexane (Ia) owes its unique stability to the fact that it is the only cycloalkane in which each of the energy components discussed above is a minimum, *i.e.*, all angles are tetrahedral, all dihedral angles are 60° , and the H-H interactions (other than 1-3) are all ≥ 2.5 Å. The boat form of cyclohexane is commonly represented as IIa with a plane of symmetry,¹³ and often a tacit assumption made that it is equally rigid, *i.e.* occupies a potential minimum like the chair form. However, the boat form, unlike the chair, is flexible in that it can exist in an entire spectrum of conformations all possessing unstrained tetrahedral angles. This idea is not new^{6,8,35} but *it should be recognized that the most stable conformation of this boat or flexible form is readily and logically defined.* Of the continuum of conformations, all have equal E_θ ; the traditional boat has a serious H-H interaction (1.83 Å.) which, however, widens as it is rotated through the continuum and another pair of hydrogens approaches each other until it is at 1.83 Å. in the next true boat form. At the half cycle the approaching and receding H-H pairs have a common separation of 2.30 Å. and hence a conformation of minimum non-bonded repulsions. Finally, this conformation has a lower value of $\sum \cos 3\omega$, hence of E_t , than the traditional boat as well, so that in all respects it commands the position of minimum energy (see Table I). This conformation, Ic, called the *twist-boat*,³⁵ possesses three mutually perpendicular 2-fold symmetry axes, and its geometry is readily defined from the symmetry by hand calculation.

The form of the transition state for boat-chair interconversion has been assumed tacitly to be the bent-chair form IIb, the direct plane-symmetrical transition from Ia to IIa.³⁶ However, this form has five carbons in one plane, a situation of considerable strain owing to torsional eclipsing as well as excessive spreading of bond angles (in this connection, the possible transition state with all six carbons planar is clearly unlikely, energetically). A better model would thus be a form with only four carbons planar, as in Ib, which is similar to the half-chair cyclohexene³⁷ in shape. *This form, furthermore, is also the direct intermediate conformation between the chair and the twist boat forms, all of C_2 symmetry, and so is reasonable from that point of view as well.* The interconversion of chair to twist-boat then takes place by a rotation of one bond around the 2-fold axis (mn) that passes through its mid-point, as shown in I and Fig. 3.

In detail, the computation of the actual geometry of the half-chair (four carbons planar) transition is similar to, though less complex than, that for cyclopentane. In Fig. 3 any three of the angles shown define the entire conformation, the rest

(35) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger and W. N. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).

(36) *Cf.* C. W. Shoppee, *J. Chem. Soc.*, 1138 (1946); C. S. Beckett, K. S. Pitzer and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 2488 (1947).

(37) C. W. Beckett, N. K. Freeman and K. S. Pitzer, *ibid.*, **70**, 4227 (1948); M. W. Lister, *ibid.*, **63**, 147 (1941); D. H. R. Barton, R. C. Cookson, W. Klyne and C. W. Shoppee, *Chemistry & Industry*, 21 (1954).

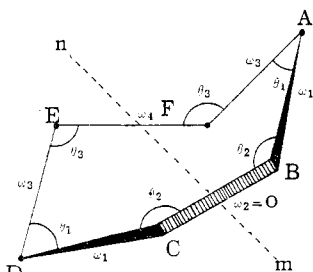
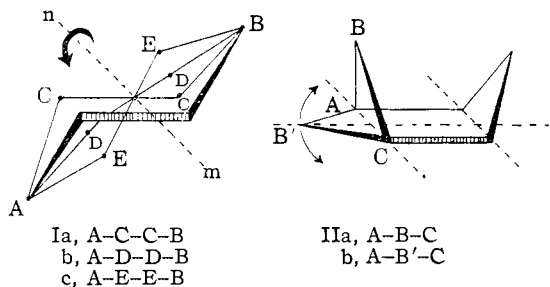


Fig. 3.—Half-chair transition state for chair to skew-boat cyclohexane.

arising from these by the equations in the Appendix. Since $\omega_2 = 0^\circ$ at the transition, one has only to vary, say, θ_2 and θ_3 through a range of values near tetrahedral to locate the geometry of minimum energy, which is that entered in Table I (as with cyclopentane, this was done with respect to $(E_\theta + E_t)$, varying θ_2 and θ_3 by 0.1° increments). In the chair-twist-boat interconversion, ω_2 passes from 60° to 0° to -70.64° . Since this is the most economical route for boat-chair conversion, it is probably also the most economical pathway for



smaller-scale deformations of cyclohexane to conform to strained molecular circumstances, *cf.* fusion to a five-membered ring, and the same computational program then suffices to provide the minimum-energy form for any desired value of ω_2 . From Table I, the difference between the chair and plane-symmetrical boat cyclohexanes is then 6.93 kcal./mole and the corresponding (5-C planar) barrier 14.13 kcal./mole (H-H interactions only). The twist-boat is thus 1.60 kcal./mole more stable than the traditional boat form. These data are summarized in Fig. 4.

Cycloheptane.—Just as with cyclohexane, there are two forms of cycloheptane which can only be interconverted through major deformations of bond angles from tetrahedral, and it is convenient to call the plane-symmetrical forms chair (III) and boat (IV) by analogy. However, in cycloheptane, unlike cyclohexane, *both* forms are flexible with respect to their bond angles and may undergo pseudorotation, so that both must be considered in the same light as the flexible form of cyclohexane in probing for the conformation of lowest energy. Thus, the chair III has an extremely serious H-H repulsion (1.28 Å.) across the axial C_3 -positions, which it may relieve by pseudorotation; as with the boat cyclohexane, the half-cycle position equalizes the approaching and receding H-H pair (at 1.86 Å. each), providing minimum repulsion energy, and this form is similarly a form with a

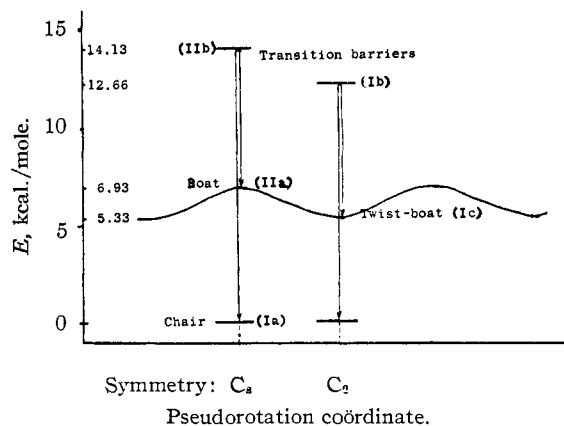
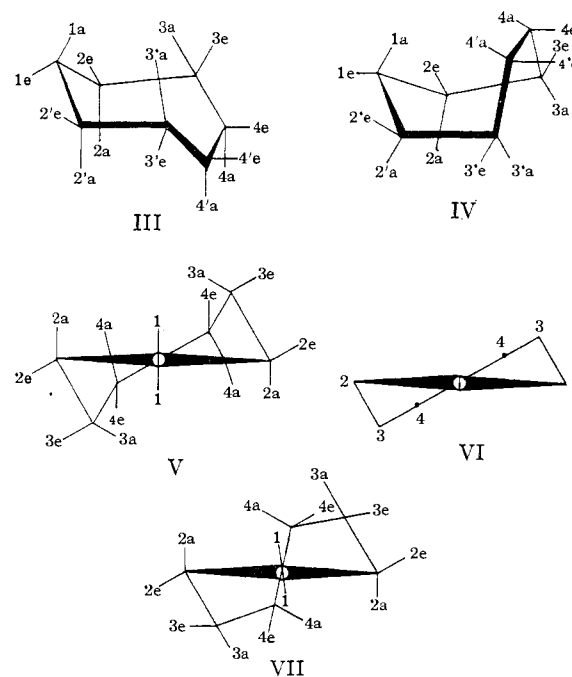


Fig. 4.—Calculated energies and pseudorotation of cyclohexanes.

2-fold symmetry axis, called the *twist-chair* conformation (V). Since, as with cyclohexane, this form also has lower E_t than the plane-symmetrical chair, it is certainly the stable form of "chair cycloheptane." In similar wise, the other conformational family, entered only by bond-angle deformation from the chair forms, contains a boat III (C_s symmetry) and a *twist-boat* VII (C_2 symmetry) conformation, the latter again preferred on grounds of torsional strain as well as non-bonded repulsions.³⁸ As before, the logic of energy preference for the C_2 form is essentially independent of the detailed functions utilized.



Unlike the flexible forms of cyclohexane, however, the H-H repulsions in the cycloheptanes are still

(38) Twist-chair and twist-boat cycloheptane configurations are completely defined by their C_2 symmetry and tetrahedral angles, but actual solution of the relevant geometrical equations is extremely tedious; the solutions given in Table I were produced by the computer using an iterative process. The "twist" nomenclature is applied to cycloheptane, as to cyclohexane, to mean the form with C_2 (axial) symmetry only.

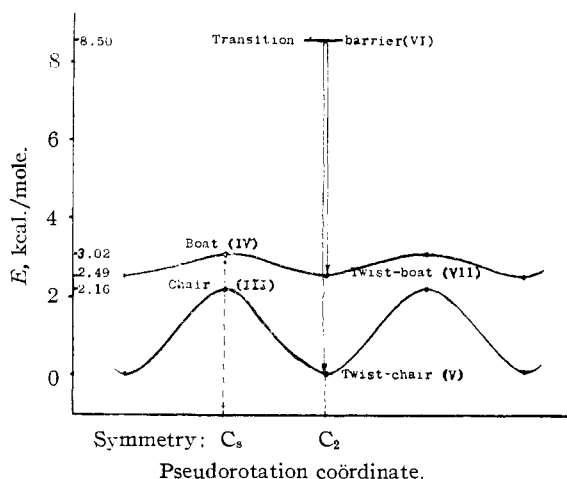


Fig. 5.—Calculated energies of pseudorotation of cycloheptanes.

serious even in the twist forms, the twist-chair having two interactions of 1.86 Å., these being the ones approaching and receding from the 1.28 Å. separation in the chair; the comparable pairs in the skew-boat are still at only 1.45 Å. Hence, pseudorotation by itself is not sufficient to eliminate these serious repulsions and the molecules must resort to some opening of bond angles to render these minimal.³⁹ Computation of the conformations and energies attendant on bond angle enlargement is a rather lengthy chore involving independent variation of each of the four different bond angles and computation from each bond angle set so obtained of the dihedral angles and then total energies for each of the four symmetrical forms of cycloheptane discussed above. When these calculations were made, it was found that in the C_3 chair form, a minimum is obtained by differential altering of bond angles, the most significant alteration for minimizing the serious C_3 axial hydrogen repulsions being a spreading of the C_4 angle. In the other three forms, however, a simple uniform enlargement of the bond angles sufficed to produce the best balance of strains and repulsions. Thus, the best conformation energetically is the twist-chair with bond angles opened to 112° ; by pseudorotation this may pass to the chair ($\theta = 109.5^\circ, 112^\circ, 111^\circ, 116^\circ$) at a cost of 2.16 kcal./mole, or flip over a barrier of 8.50 kcal./mole to a twist-boat ($\theta = 113^\circ$), which is 2.49 kcal./mole less stable than the twist-chair; it is the last figure which compares to the 5.33 kcal./mole boat-chair difference in cyclohexane. These data are summarized in Table I and Fig. 5.

Thus it may be seen that pseudorotation in the cycloheptanes is accompanied by a slight regular flexing of bond angles, *i.e.*, a general "breathing" of the ring. This is nevertheless a qualitatively different deformation from the angle bending required to flip from one of the chair forms to one of the boat forms. The form of the barrier to chair-

(39) In his calculations neglecting these H-H repulsions, Allinger in fact concluded, on the basis of E_t alone, that the boat cycloheptane was the more stable.⁹ This is confirmed by the column of E_t values in Fig. 1, but non-bonded interactions in the boats are clearly much more serious than in the chairs so that the latter are in fact the more stable conformational family.

boat transition was taken as analogous to that in the cyclohexane series: the bond perpendicular to the rotation axis in the twist-chair is rotated to a dihedral angle of 0° (*i.e.*, four consecutive ring carbons coplanar), as in VI, then on to the skew boat, VII. The computation of the detailed form of VI was carried out as with the cyclohexane barrier and, like that conformation, VI must represent roughly the geometry of cycloheptene.

Conformational Analysis of Cycloheptane Derivatives.—The realization of a detailed conformational analysis of cycloheptanes has been hampered in the past by a lack of reasonable values for the strain energies in the various possible conformers. The values obtained here are sufficiently accurate to allow some confidence in a detailed conformational treatment. Furthermore, the rapidly increasing number of complex natural cycloheptanes (particularly the perhydroazulenic sesquiterpenes) makes imperative an extension of the scope of conformational analysis to these compounds with the aim of realizing a theoretical framework of comparable predictive power to that which has been so successful in the six-ring terpenes and steroids.

It rapidly becomes clear that there are more variables in cycloheptane conformational analysis than in the familiar chair-cyclohexane. The high symmetry of the chair form of cyclohexane allows the distinguishing of only two kinds of position for substituents, *viz.*, equatorial and axial. By contrast there are seven substituent positions distinguishable in the twist-chair cycloheptane and eight in the chair form, with a corresponding seven and eight in the twist-boat and boat, respectively, so that conformational analysis of substituted cycloheptanes is notably more complex than that in cyclohexane. On the other hand, these do fall into equatorial (e) and axial (a) types, analogous to the chair cyclohexane in that the former lie more in the plane of the molecule, the latter more perpendicular to it⁴⁰; therefore, nomenclature assignments can conveniently be made as shown in III, IV, V and VII. The relative steric hindrance encountered by substituents in these positions is qualitatively

Twist-chair (TC)	2e, 3e, 4e < 1 < 4a < 2a, 3a
Chair (C)	1e, 2e, 3e < 4e < 1a, 2a, 4a << 3a
Twist-boat (TB)	2e, 3e < 4e < 1 < 3a << 2a, 4a
Boat (B)	1e, 2e, 3e < 4e < 2a < 1a < 4a << 3a

If a substituent be placed in one position in either chair or boat family it will pass from that position to every other in turn in the course of the pseudorotation, its detailed itinerary being indicated in Fig. 6, which is an extension of Fig. 5 (the prime numbers refer to the mirror-image configuration or position).

A monosubstituted cycloheptane will preferentially exist with the substituent in one of the twist-chair positions 2e, 3e or 4e and the barrier to its pseudorotation will be 2.16 kcal./mole if it is no

(40) The term "axial" is more unfortunate here because of the possible confusion it may cause with the rotational axis of the C_2 forms which lies of course in the plane of the molecule; the term is retained to emphasize the analogy with chair cyclohexane in matters of the steric hindrance, and to minimize unwarranted proliferation of terminology.

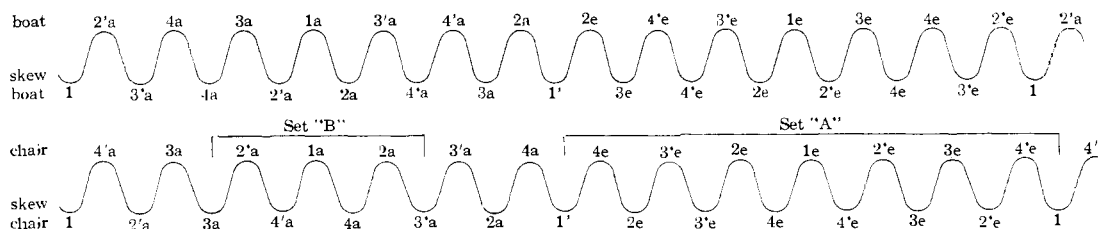


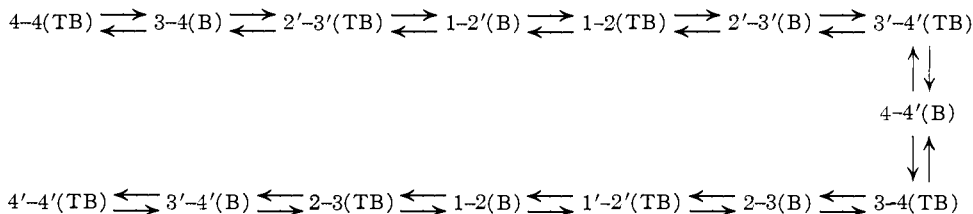
Fig. 6.—Pseudorotation itineraries in cycloheptane.

larger than hydrogen. Larger substituents will experience larger barriers which will be especially bad for passage of the substituent through the 3a(C) and 3a(B) positions. With a sufficiently bulky substituent pseudorotation past these high-energy axial barriers could be substantially prevented so that the conclusion might be drawn that two isomeric monosubstituted cycloheptanes could exist, partially pseudorotating through the conformations labeled set "A" and set "B" on the chair family of positions but not interconvertible because of the 3a barrier between them. This is not in fact the case, however, since any of the chair family conformers may flip into a boat form *via* VI, pseudorotate in this family and then flip back to a chair conformer elsewhere on the itinerary. This is possible because the *order of position changes* in the two family itineraries is different, as seen in Fig. 6. When the twist-chair flips to a twist-boat

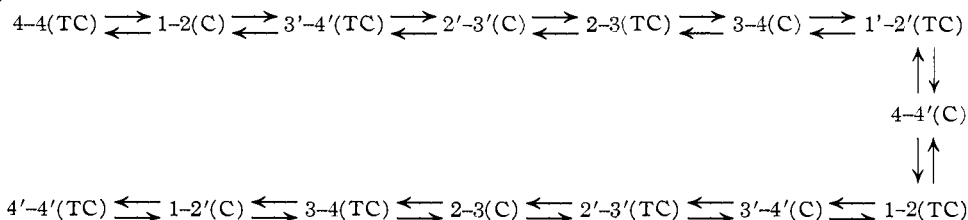
flipping from one family to the other, the possibility of isolating isomeric species is remote even with bulky substituents. It may be noted that most of the conformations of substituted cycloheptanes are asymmetric, but the above argument assures that isolation of optically active material is unlikely to be feasible. The notation developed above also serves as a convenient shorthand in following substituents through the various complex conformational interconversions that are open to them.²⁵

Centering attention now on the kinds of *bonds* in cycloheptane, we may distinguish four bonds by their different dihedral angles (as against only one, 60°, for all bonds in cyclohexane chair); these are shown in Table I for the four conformations. As with the substituents it is convenient to map an itinerary for passage of a given *bond* through the various positions in pseudorotation, which follows from Fig. 6:

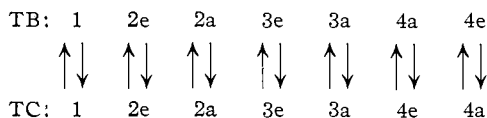
Boat family:



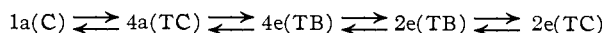
Chair family:



(V \rightleftharpoons VI \rightleftharpoons VII) or *vice versa*, these positional changes occur



Therefore, the two presumed isomers above can interconvert, without having to pseudorotate through the high-energy 3a(C) barrier, by flipping from the twist-chair axial set ("B") to the twist-boat equatorial set at positions 4, in particular by the route



Thus, since all the conformations are interconvertible, either *via* pseudorotation within one family or

In 1,2-disubstituted chair cyclohexanes we can distinguish three conformational isomers: *cis* (e, a), *trans* (e, e) and *trans* (a, a). In 1,2-disubstituted cycloheptanes we can distinguish two *cis* and two *trans* forms for each of the four kinds of bonds, thus with the 2,3-disubstitution in the twist-chair, the *cis* forms (2e-3a) and (2a-3e), are different molecules, as are the *trans* forms (2e-3e) and (2a-3a). The dihedral angle between *cis* substituents is the same as the dihedral angle (ω) of the bond itself in the ring (*cf.* Table I), while the dihedral angles of the *trans* forms are ($\omega + 120^\circ$) and ($\omega - 120^\circ$). The various conformations of the *cis* isomer may interconvert freely, through pseudorotation and/or flipping back and forth between families, subject to the same conditions discussed above for monosubstituted cycloheptanes and

based on the steric hindrance to passage of a substituent in certain critical conformations on the itinerary. The same may be said for the *trans* isomers, of course, and, whereas in chair cyclohexane the *trans* (a, a) can only convert to *trans* (e, e) by slipping to a boat and back, in chair cycloheptane most such interconversions of *trans* forms may occur merely by pseudorotation. The dihedral angles noted for the symmetrical forms are not, however, the only possible dihedral angles between 1,2-substituents, for all the intermediate unsymmetrical conformers (on the pseudorotation between chair and twist-chair or boat and twist-boat) provide a smoothly varying set of angles between the two extremes. Thus, *cis* isomer dihedral angles range from 0° to 97.0° and the *trans* from 23.0° to 217.0° , the latter range for example including the 180° angle deemed ideal for 1,2-eliminations,⁴¹ which occurs in a conformation very near to (4a-4a) and another near to (1-2a) in the twist-chair.

The recent work of Huffman⁴² on deamination of *cis*- and *trans*-aminocycloheptanols provides an interesting illustration. The *trans* compound would be expected to lie largely in one of the three roughly equivalent conformations 2e-3e(TC), 3e-4e(TC) or 4e-4e(TC), which represent energy minima; the dihedral angles of the ring at these bonds are, respectively, 97.0° , -75.8° and 52.9° , and the latter represents a situation close to ideal (60°) for ring contraction to cyclohexylmethanal, the only observed product. In the *cis* case the groups can take up the 1-2e(TC) positions, a situation energetically more favorable than any of the various axial-equatorial pairs analogous to the cyclohexane case and may, furthermore, pseudorotate directly back and forth from 1-amino-2e-hydroxycycloheptane to the 2e-amino-1-hydroxy derivative. These two conformers are likely to be of almost identical energy and their interconversion by pseudorotation through the 4e-4'e(C) intermediate represents a barrier of only 2-3 kcal./mole. The ring dihedral angle at the 1-2 bond is 41.2° which slight pseudorotation will carry to the 60° angle that is stereoelectronically suited both for ring contraction of the 2e-amino conformer or formation of cycloheptanone from the 1-amino conformer. Both products are in fact obtained as expected, the proportion depending on the relative rates of these two reactions, as discussed by Huffman.⁴²

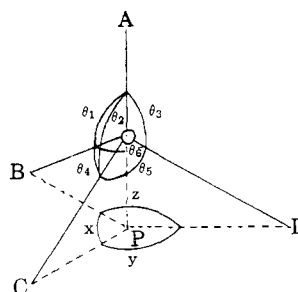
We may likewise assess the best conformations for fusion of another ring across one bond of cycloheptane to form bicyclic systems. *cis* fusion of a cyclopentane should be most favored at 1-2e (41.2°) of the twist-chair; the other *cis* fusion angles available, being over 45° , would strain the cyclopentane system (Table I). However, *trans* fusion across either 2e-3e (23.0°) or 3e-4e (4.2°) is to a first approximation equally favored, more precise definition of the difference lying with the differences in interannular H-H repulsions which will be small since all the involved positions are equatorial; the two *trans* fusions are readily interconvertible by pseudorotation. The energy difference between

these *cis*- and *trans*-perhydroazulenes is therefore likely to be virtually negligible, by contrast with the isomeric decalins, which differ by some 2.4 kcal./mole.¹³ The rigidity of chair cyclohexane makes ring fusion conditions much more stringent, resulting in marked differences in *cis* and *trans* isomers not found in comparable cycloheptane examples. Fusion of a chair cyclohexane to cycloheptane requires a dihedral angle of 60° in both *cis* and *trans* fusions, which lies easily in the two ranges noted for cycloheptane above. Both *cis* and *trans* fusions are best accommodated by having the 4-4 bond (52.9°) very close to the twist-chair conformation, but since the *cis* fusion includes an axial orientation, it will be somewhat less stable than the *trans* isomer.

The question of isomers in *cis* ring-fusion to cycloheptane is an interesting one and best illustrated with *cis*-perhydroazulene, selected above as a (1-2e)(TC) fusion of cyclopentane. The different and somewhat less stable *cis* isomer (1-2a)(TC) may be capable of separate existence since the pseudorotation interconverting the two carries the ring through the high-energy 3a(C) position and, more important, requires of the cyclopentane ring internal dihedral angles up to 97.0° during the pseudorotation. Furthermore, in this case, flipping to the boat family offers little assistance so that the energies required to accommodate (by severe angle bending, etc.) the conditions noted above for pseudorotation will likely be severe enough to allow the separate existence of these two *cis*-perhydroazulenes. Computations of the detailed energies of these various bicyclic systems are in process.

Appendix

A. Relations of angles in the irregular tetrahedron.



Definition: Extend \overline{AO} to P and distance $\overline{OP} = 1$; plane \overline{BCD} is defined as passing through P $\perp \overline{AP}$. Thus x , y and z are the projection angles of θ_4 , θ_5 and θ_6 .

$$x + y + z = 2\pi \quad (1)$$

$$\cos x = \frac{\cos \theta_4 - \cos \theta_1 \cos \theta_2}{\sin \theta_1 \sin \theta_2} \quad (2)$$

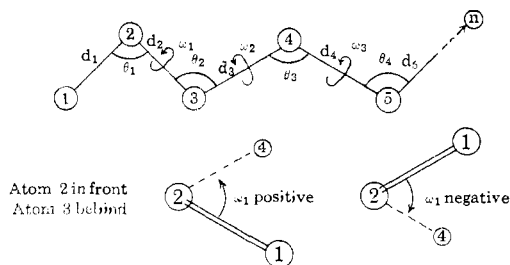
$$\cos y = \frac{\cos \theta_5 - \cos \theta_2 \cos \theta_3}{\sin \theta_2 \sin \theta_3} \quad (3)$$

$$\cos z = \frac{\cos \theta_6 - \cos \theta_1 \cos \theta_3}{\sin \theta_1 \sin \theta_3} \quad (4)$$

B. Calculation of the distance, r , between atom 1 and atom n in any linear chain of atoms. Let d be the internuclear distance, θ the bond angle and ω the dihedral or torsional angle around any bond, in the general chain

(41) D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 65 (1956).

(42) J. W. Huffman and C. E. Engle, *J. Org. Chem.*, **24**, 1844 (1959).



The angle, ω , is defined by the projection along the bond around which ω represents the torsional angle, looking from the lower-numbered to the higher-numbered atom. ω is negative if taken clockwise, positive if taken counterclockwise, from the projection of the front bond to that of the rear bond, as shown in the diagram. In any formula for the distance, r , between atoms 1 and n there will be $(3n-6)$ variables (d , θ and ω terms).

$$n = 3$$

$$r^2 = d_1^2 + d_2^2 - 2d_1d_2\cos\theta_1 \quad (1)$$

$$n = 4$$

$$r^2 = d_1^2 + d_2^2 + d_3^2 - 2d_1d_2\cos\theta_1 - 2d_2d_3\cos\theta_2 + 2d_1d_3(\cos\theta_1\cos\theta_2 - \sin\theta_1\sin\theta_2\cos\omega_1) \quad (2)$$

$$n = 5$$

$$r^2 = (x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2$$

$$(x_2 - x_1) = (d_3 - d_4\cos\theta_3)\cos\theta_2 + d_4\sin\theta_2\sin\theta_3\cos\omega_2 - (d_2 - d_1\cos\theta_1)$$

$$(y_2 - y_1) = (d_3 - d_4\cos\theta_3)\sin\theta_2 - d_4\cos\theta_2\sin\theta_3\cos\omega_2 - d_1\sin\theta_1\cos\omega_1$$

$$(z_2 - z_1) = -d_4\sin\theta_3\sin\omega_2 - d_1\sin\theta_1\sin\omega_1 \quad (3)$$

$$n = 6$$

$$r^2 = (x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2$$

$$(x_2 - x_1) = d_5[\cos\theta_4(\cos\theta_2\cos\theta_3 - \sin\theta_2\sin\theta_3\cos\omega_2) -$$

$$\sin\theta_4(\sin\theta_2\sin\omega_2\sin\omega_3 + \cos\theta_2\sin\theta_3\cos\omega_3 + \sin\theta_2\cos\theta_3\cos\omega_2\cos\omega_3)] - d_4(\cos\theta_2\cos\theta_3 - \sin\theta_2\sin\theta_3\cos\omega_2) + d_3\cos\theta_2 - d_2 + d_1\cos\theta_1$$

$$(y_2 - y_1) = d_5[\cos\theta_4(\sin\theta_2\cos\theta_3 + \cos\theta_2\sin\theta_3\cos\omega_3) + \sin\theta_4(\cos\theta_2\sin\omega_2\sin\omega_3 - \sin\theta_2\sin\theta_3\cos\omega_3 + \cos\theta_2\cos\theta_3\cos\omega_2\cos\omega_3)] - d_4(\sin\theta_2\cos\theta_3 + \cos\theta_2\sin\theta_3\cos\omega_2) + d_3\sin\theta_2 - d_1\sin\theta_1\cos\omega_1$$

$$(z_2 - z_1) = d_5[-\sin\theta_4\cos\theta_3\sin\omega_2 + \sin\theta_4(\cos\omega_2\sin\omega_3 - \cos\theta_3\sin\omega_2\cos\omega_3)] + d_4\sin\theta_3\sin\omega_2 + d_1\sin\theta_1\sin\omega_1 \quad (4)$$

$$n = 7$$

$$r^2 = (x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2$$

$$(x_2 - x_1) = d_6[\cos\theta_5(\cos\theta_3\cos\theta_4 - \sin\theta_3\sin\theta_4\cos\omega_3) - \sin\theta_5(\sin\theta_3\sin\omega_3\sin\omega_4 + \cos\theta_3\sin\theta_4\cos\omega_4 + \sin\theta_3\cos\theta_4\cos\omega_3\cos\omega_4)] - d_5(\cos\theta_3\cos\theta_4 - \sin\theta_3\sin\theta_4\cos\omega_3) + d_4\cos\theta_3 - d_3 + d_2\cos\theta_2 - d_1(\cos\theta_1\cos\theta_2 - \sin\theta_1\sin\theta_2\cos\omega_1)$$

$$(y_2 - y_1) = d_6[\cos\theta_5(\sin\theta_3\cos\theta_4 + \cos\theta_3\sin\theta_4\cos\omega_3) + \sin\theta_5(\cos\theta_3\sin\omega_3\sin\omega_4 - \sin\theta_3\sin\theta_4\cos\omega_4 + \cos\theta_3\cos\theta_4\cos\omega_3\cos\omega_4)] - d_5(\sin\theta_3\cos\theta_4 + \cos\theta_3\sin\theta_4\cos\omega_3) + d_4\sin\theta_3 - d_2\sin\theta_2\cos\omega_2 + d_1[\cos\omega_2(\cos\theta_1\sin\theta_2 + \sin\theta_1\cos\theta_2\cos\omega_1) + \sin\theta_1\sin\omega_1\sin\omega_2]$$

$$(z_2 - z_1) = d_6[-\sin\theta_4\cos\theta_5\sin\omega_3 + \sin\theta_5(\cos\omega_3\sin\omega_4 - \cos\theta_4\sin\omega_3\cos\omega_4)] + d_5\sin\theta_4\sin\omega_3 + d_2\sin\theta_2\sin\omega_2 - d_1[\sin\omega_2(\cos\theta_1\sin\theta_2 + \sin\theta_1\cos\theta_2\cos\omega_1) - \sin\theta_1\sin\omega_1\cos\omega_2] \quad (5)$$

Alternatively, computation of the distance between any number of atoms may be accomplished in an iterative process, progressing one atom at a time using these equations to derive the coordinates of the new (n th) atom from those of the last; the over-all distance from atom 1 to n is then $r = \sqrt{x_n^2 + y_n^2 + z_n^2}$.

$$x_n = d_{n-1} - x_{n-1}\cos\theta_{n-2} - y_{n-1}\sin\theta_{n-2}\cos\omega_{n-3} + z_{n-1}\sin\theta_{n-2}\sin\omega_{n-3}$$

$$y_n = x_{n-1}\sin\theta_{n-2} - y_{n-1}\cos\theta_{n-2}\cos\omega_{n-3} + z_{n-1}\cos\theta_{n-2}\sin\omega_{n-3}$$

$$z_n = y_{n-1}\sin\omega_{n-3} + z_{n-1}\cos\omega_{n-3}$$

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, N. Y.]

Contraction of Medium Size Rings¹

BY A. T. BLOMQUIST AND F. W. SCHLAEFER

RECEIVED JULY 5, 1961

With the object of providing an auxiliary sequence to the acyloin cyclization, irradiation of α -diazo ketones derived from simple nine-, ten- and eleven-membered rings have been studied. In solvent aqueous dioxane they all have been found to contract smoothly and in fair yield to the corresponding cycloalkylcarboxylic acids, which contain one ring member less than the starting diazo ketone. This simple ring contraction thus provides an entree to strained carbocycles unavailable directly *via* the acyloin cyclization. Degradation of the cycloalkylcarboxylic acids, thus formed, to the related simple cycloalkanones has been done easily and in good yield with cyclononancarboxylic acid to give cyclononane.

Although the acyloin cyclization has proved to be a superior method for obtaining many cyclic systems, including the medium size rings, it has been found to fail in efforts to realize certain rather interesting cyclic systems. Illustrative of the latter are carbocycles such as [8]paracyclophane, 1,6-cyclodecadiyne and *trans*-5-cyclononane. It seemed desirable, therefore, to examine a synthetic route which could be used to prepare cyclic compounds of the type mentioned.

In view of the fact that little, if any, attention has been given to contraction of medium sized rings, it seemed useful here to study the photolysis

(1) This is the twenty-fourth publication concerned with the chemistry of large carbon rings. For the preceding paper in this series see A. T. Blomquist, R. E. Stahl, Y. C. Meinwald and B. H. Smith, *J. Org. Chem.*, **26**, 1687 (1961).

of α -diazo ketones of such rings as a synthetic method. In smaller ring systems it has been possible to obtain very highly strained rings by this method.²⁻⁴

Contraction of simple nine-, ten- and eleven-membered carbon rings has been done with fair success as outlined (Fig. 1).

Preparation of the tosylhydrazones, compounds IV, was straightforward. The α -diazoketones, compounds V, were irradiated with an ultraviolet source immediately following their preparation. The yields of pure distilled carboxylic acids were: VIa, 23%; VIb, 33%; VIc, 31%.

(2) L. Horner and E. Spietscka, *Ber.*, **88**, 934 (1954).

(3) M. P. Cava, R. L. Little and R. D. Napier, *J. Am. Chem. Soc.*, **80**, 2257 (1958).

(4) J. Meinwald and P. Gassman, *ibid.*, **82**, 2857 (1960).