

## ITERATIVE FORCE-FIELD CALCULATIONS AND MOLECULAR DYNAMICS OF CYCLOOCTANONE

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(Received 12th March 1988)

## ABSTRACT

Boyd's iterative force - field computer program has been used to calculate strain energies in cyclooctanone (I). 348 MHz  $^1\text{H}$  NMR spectra of (I) have been investigated over the temperature range of 25° to 160° C. Two conformational processes effect the  $^1\text{H}$  NMR spectrum of (I). Iterative force-field calculations on the conformations and conformational inter-conversion paths of (I) give results consistent with the NMR findings.

## INTRODUCTION

One of the first attempts to determine the conformation of cyclooctanone goes back to 1959 when strain energy calculations led Allinger to conclude that cyclooctanone should exist as a mixture of the CC-1 and BC-1 conformations (1) (Numbering of these conformations is shown in Figure 1). In another study (1960) which made use of the dipole moment of 5-(p-chlorophenyl)-cyclooctanone, Allinger and his co-workers concluded that about 62% of this compound ex-

ists in a BC-1 and the remainder in the CC-1 conformation (2). Also, during the same year they reported that the dipole moment for 2-bromocyclooctanone and the change in the broad carbonyl stretching band in the ir spectrum of 2-bromocyclooctanone supported the existence of the two conformations (3).

In 1959, Chiurdoglu reported that the ir spectrum of cyclooctanone was essentially the same in the vapor, liquid, and solid phases (4). He concluded that cyclooctanone exists in a single conformation, a chair-chair with the carbonyl group at C-4.

Allinger confirmed that the ir spectra of cyclooctanone as a liquid at 62° and 120° C are the same as that of the solid at 20° C. Similarly the ir spectra of 5-(p-chlorophenyl)-cyclooctanone in carbon disulfide and in the solid phase (as a potassium bromide pellet) were found to be virtually the same (5). As a result, Allinger reinterpreted his data (2) as being consistent only with the CC-1 form. In addition, he reevaluated his data (3) on 2-bromocyclooctanone in terms of the same conformation. In 1960, Chiurdoglu and co-workers (6) reported an ir liquid phase study on cyclooctanone at different temperatures (+21° and +85° C). At 85° C they observed two absorption bands at  $1730\text{cm}^{-1}$  and  $1701-1689\text{cm}^{-1}$ . On the basis of this observation, they con-

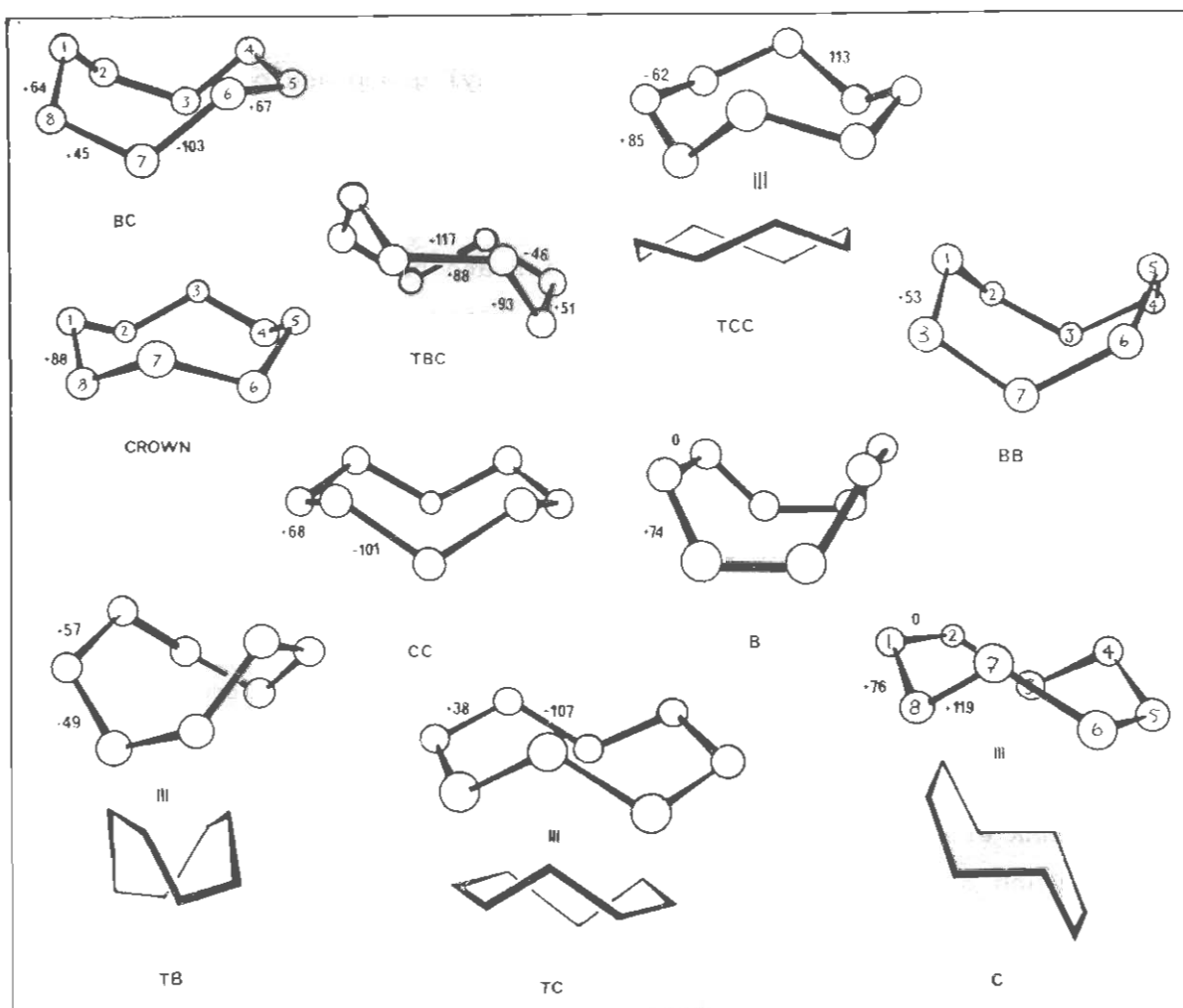


Figure 1. Various conformations of cyclooctane . Boat-Chair(BC), Twist-Boat-Chair(TBC),Crown,Chair-Chair(CC) , Twist-Chair-Chair(TCC),Boat-Boat(BB) Twist-Boat(TC),Boat(B), Chair(C) Twist-Chair (TC).

cluded that cyclooctanone exists in two conformation. But such a splitting could be due to fermi resonance (7), and thus this evidence cannot be regarded as proving that there is more than one conformation for cyclooctanone.

In 1966, F.A.L. Anet and St. Jacques (8) reported evidence that cyclooctanone exists primarily in a boat-chair conformation with the carbonyl group at the 3-position. They found

that cyclooctanone- $d_{13}$ -4-h has an NMR spectrum which consists of a single line at room temperature. This line splits into two lines of equal intensities below  $-123^{\circ}\text{C}$  ( $\delta = 1.343$  and  $1.577\text{ppm}$ ;  $\Delta U = 14\text{Hz}$  at  $60\text{MHz}$ ), and into four lines of equal intensities, below  $-147^{\circ}\text{C}$  at  $1.200$ ,  $1.403$ ,  $1.477$ , and  $1.737\text{ppm}$ . Thus, two separate dynamic NMR effects occur and the free energy of activation for the two corresponding

conformational processes are 7.6 kcal/mole and 6.3 kcal/mole. Anet and St.Jacques found that the spectrum of the deuterated cyclooctanone is consistent with an unsymmetrical conformation. To provide additional confirmatory evidence for the BC-3 conformation of cyclooctanone and to provide evidence that the four lines seen for cyclooctanone- $d_{13}$ -4-h at low temperatures were not due to a fortuitous mixture of two conformations in equal proportions, Anet and Henrichs(9) studied the dynamic properties of cyclooctanone- $d_{13}$ -5-h, cyclooctanone- $d_{13}$ -3-h, and cyclooctanone- $d_{13}$ -2-h. Two quite distinct dynamic NMR effects were observed in the  $\alpha$  and  $\beta$  isomers, but only a single dynamic NMR effect was seen in the  $\delta$  isomer. The  $\delta$  isomer (cyclooctanone- $d_{13}$ -5-h) had an NMR spectrum which consists of a single line at room temperature. This line splits into two equally intensive lines below  $-120^\circ\text{C}$ . One of these lines has an abnormally high-field chemical shift of 0.71ppm. These data are exactly those expected from a single conformation that has no symmetry. The high field position of one of the  $\delta$  protons was explained in terms of magnetic field anisotropy of the carbonyl group and requires that the proton be situated directly above the face of the double bond. The boat-chair form with the carbonyl group at position 3 or 7 posses-

ses exactly this relationship of the carbonyl group and one of the two  $\delta$  protons. Anet and Henrichs analyzed their experimental data on the basis of two processes, i.e., ring inversion and pseudorotation. The pseudorotation process was first recognized by Anet and St.Jacques in the cyclooctane(10). The NMR results of the  $\gamma$ -isomer have been interpreted in terms of four conformations, i.e., BC-3,6a., BC-7,2e'. , BC-3,8a' ., and BC-4,4e, as shown in Figure 2. Actually, the scheme shown applies strictly only to one enantiomer of the  $\gamma$  isomer. The other isomer follows a mirror-image scheme and thus gives rise to exactly the same NMR results as long as the solvent is achiral. The interconversion of BC-3,6a with BC-7,2e' on the one hand and BC-3,8a' with BC-7,4e on the other hand can occur by two different pseudorotation itineraries, namely BC-3  $\rightleftharpoons$  BC-6  $\rightleftharpoons$  BC-5  $\rightleftharpoons$  BC-4  $\rightleftharpoons$  BC-7 or proceeding in the alternate path around the ring, BC-3  $\rightleftharpoons$  BC-8  $\rightleftharpoons$  BC-1  $\rightleftharpoons$  BC-2  $\rightleftharpoons$  BC-7. The preferred pseudorotation path is the one with the BC-5 as intermediate. This point has been discussed in relation to the conformational barrier in 5-t-butylcyclooctanone by Anet and his co-workers (11) that we will discuss later. The pseudorotation just described accounts for the two lines at intermediate temperatures in the  $\gamma$ -isomer since this process is relative-

ly fast at these temperatures. In the  $\delta$ -isomer this process has no effect on  $\delta$  proton chemical shifts as it results in an interconversion of the type BC-3,7a(BC-7,3a). The higher temperature process in the  $\gamma$ -isomer and the only process observed in  $\delta$ -isomer are then ring inversion as shown in Figure 2.

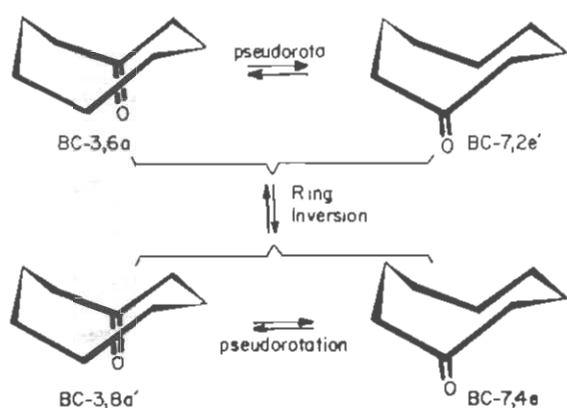


Figure 2. Conformational processes in  $\gamma$ -labelled isomer of cyclooctanone. This scheme applies strictly only to one enantiomer.

In view of the uncertainty of the strain energy calculations for systems other than hydrocarbons, Anet and his co-workers (11) came to the conclusion that another possible way of determining which of the two possible pseudorotation paths is lower in energy is to study substituent effects.

They investigated the NMR spectrum of 5-t-butyl-cyclooctanone as a function of temperature (11,12). The observations showed evidence at low temperatures for restricted rotation about the t-butyl ring bond and for

a conformational process with a  $\Delta G$  of 8.0 kcal/mole.

They suggested that if the conformation is BC-3 and the t-butyl group is at the 7 equatorial position (the axial position at 7 is extremely hindered), the process seen at low temperature cannot be ring inversion, as this leads to equatorial-axial interconversion of the large t-Bu group. Pseudorotation, however, is possible and if the path BC-3  $\rightleftharpoons$  BC-8  $\rightleftharpoons$  BC-1  $\rightleftharpoons$  BC-2  $\rightleftharpoons$  BC-7 is chosen, the t-Bu group finally resides in an equatorial position, and as well remains unhindered at all stages of the process. Pseudorotation in the alternate way, requires that the t-butyl group be placed in a highly hindered position during the change from BC-3 to the BC-7 form, and this is essentially forbidden. yet, the pseudorotation barrier is appreciably higher in 5-t-butylcyclooctanone than it is in cyclooctanone itself. They reasoned that this difference could be explained if cyclooctanone pseudorotate more easily via BC-5 than via BC-1. Pseudorotation in 5-t-butyl-cyclooctanone is forced to occur by the less favorable pathway for the carbonyl group, i.e., via the BC-1 form since the t-butyl group controls the direction of the pseudorotation. It is necessary to mention that there are errors in the discussion of this point in references (11) and (12). These

errors are the result of confusion of the conformational labelling for the position of the carbonyl and t-butyl group.

#### A. Conformational labelling

The labelling of hydrogen in the important boat-chair conformations of cyclooctanone and cyclooctane is shown in the perspective drawings in Figure 3. Ignoring for the moment the distinction between a and a' or e and e', we can see from this figure that vicinal trans substituents are either diaxial or diequatorial (as in the cyclohexane chair) except when the substituents are on C-2 and C-3 (or the equivalent C-7 and C-8), in which case one substituent is axial and the other equatorial. We have also given the calculated and conformational processes in cyclooctane (Table 1 and 2) that might be helpful as a background for comparison with cyclooctanone case.

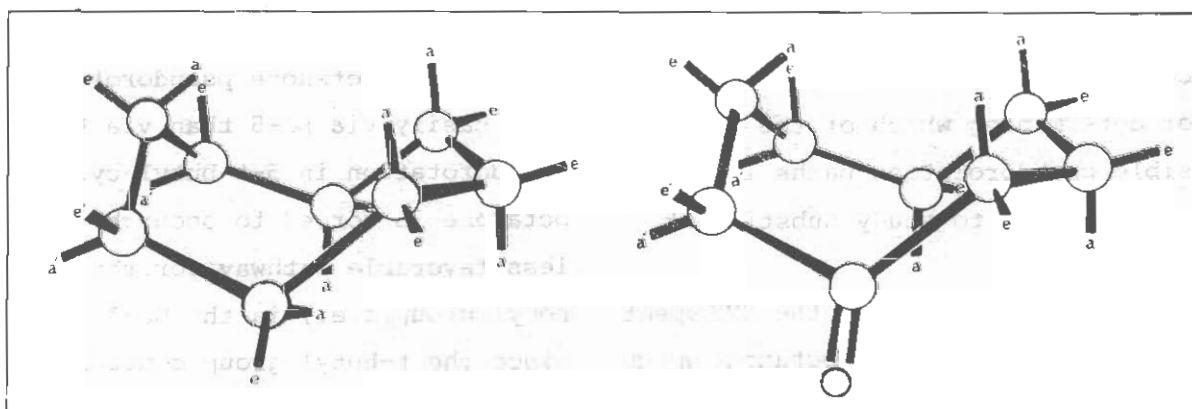


Figure 3. Axial (a), equatorial (e), quasi-axial (a') and quasiequatorial (e') positions in the boat-chair conformation of cyclooctane and cyclooctanone (BC-3).

Table 1. Conformational energies for cyclooctane.

Family and name	Symmetry group	Relative Strain Energies (kcal/mole) <sup>a</sup>					
		1	2	3	4	5	6
Boat-chair		0	0	0	0	0	
Boat-chair (BC)	C <sub>2v</sub>	0	0	0	0	0	
Twist-boat-chair (TBC)	C <sub>2</sub>	1.7	2.0	-	-	-	
Crown							
Twist-chair-chair (TCC)	D <sub>2</sub>	0.8	1.7	1.09	0.25	2.20	1.7
Crown	D <sub>4d</sub>	1.5	2.8	3.62	0.25	2.09	
Chair-chair (CC)	C <sub>2v</sub>	1.8	1.9	-	-	2.25	
Boat							
Boat-boat (BB)	D <sub>2d</sub>	2.8	1.4	-	4.44	-	2.0
Twist-boat (TB)	S <sub>4</sub>	2.8	0.9	-	-	-	
Boat (B)	D <sub>2d</sub>	11.2	10.8	-	8.96	-	
Chair							
Chair (C)	C <sub>2h</sub>	7.5	8.3	-	-	-	
Twist-chair (TC)	C <sub>2h</sub>	7.7	6.7	-	6.09	-	

<sup>a</sup>References: (1)Anet and Krane(1); (2)Hendrickson(4); (3)Bixon and Lifson(15); (4)Wiberg(16)

Table 2. Maximum-energy conformations for various interconversion paths in cyclooctane.

Conformation	Leiven angle	Symmetry group	Energy (kcal/mole) <sup>a</sup>		
			1	2	Observed
(BC $\rightleftharpoons$ TBC) <sup>b</sup>	w <sub>2</sub> or w <sub>3</sub>	C <sub>1</sub>	3.3	-	4 <sup>b</sup>
(TBC $\rightleftharpoons$ TC) <sup>b</sup>	w <sub>2</sub> or w <sub>3</sub>	C <sub>1</sub>	7.9	(11.6)	-
(TBC $\rightleftharpoons$ C) <sup>b</sup>	w <sub>1</sub> and w <sub>5</sub>	C <sub>2h</sub>	7.5	8.3	8.1 <sup>c</sup>
(BC $\rightleftharpoons$ TB) <sup>b</sup>	w <sub>4</sub>	C <sub>1</sub>	10.8	-	-
(BC $\rightleftharpoons$ BB) <sup>b</sup>	w <sub>4</sub> and w <sub>5</sub>	C <sub>2v</sub>	10.7	-20	-
(TBC $\rightleftharpoons$ TCC) <sup>b</sup>	w <sub>3</sub>	C <sub>2</sub>	10.3	(11.4)	10.5 <sup>d</sup>
(BB $\rightleftharpoons$ B) <sup>b</sup>	w <sub>1</sub> , w <sub>3</sub> , w <sub>5</sub> and w <sub>7</sub>	D <sub>2d</sub>	11.2	-	-
(BB $\rightleftharpoons$ TB) <sup>b</sup>	w <sub>1</sub> and w <sub>5</sub>	S <sub>4</sub>	<0.2	-	-

<sup>a</sup>All energies are above the energy of the BC; (1)Anet and Krane(13); (2)Hendrickson (18) <sup>b</sup>Anet(12); <sup>c</sup>Anet and Hartman(20); <sup>d</sup>Anet and Ravus(19).

#### EXPERIMENTAL

In the present work, the <sup>1</sup>H

NMR spectrum of cyclooctanone was also studied at very high spectrometer frequency (348 MHz), where the chemical shifts are well resolved at room temperature, but still show a good deal of overlap at both intermediate and low temperatures (Figure 4). Chemical shifts of cyclooctanone at different temperatures are given in Table 3. The spectral lines are a good deal wider than in the deuterated compounds because of the presence of spin-spin coupling, and at low temperature because of dipole-dipole relaxation in  $\text{CH}_2$  groups. Such effects have previously been reported for cyclohexanone-3,3,4,5,5- $\text{d}_5$  where the much greater broadening of the proton line as compared to the  $\gamma$ -proton lines at low temperature was ascribed to faster intermolecular dipole-dipole relaxation in the  $\text{CH}_2$  group as compared to the CHD group (17).

It is known that in systems like cyclooctane (18), azacane (19), and oxacane (to be published) (20), that crown forms exist as minor conformation. Therefore, we did a careful study on the  $^{13}\text{C}$  NMR of the cyclooctanone between  $25^\circ$  and  $40^\circ\text{C}$ . But the lines stay very sharp and show only a small temperature dependence of their chemical shifts. Thus, there is no evidence for crown forms. It is possible that a few percent of BC-4 and BC-6 conformations may become populated in the

region of  $-40^\circ\text{C}$  to room temperature. This would be expected to lead to a small temperature dependence of the chemical shifts in the temperature range, but would not give rise to a dynamic NMR effects since the relevant barriers are too low.

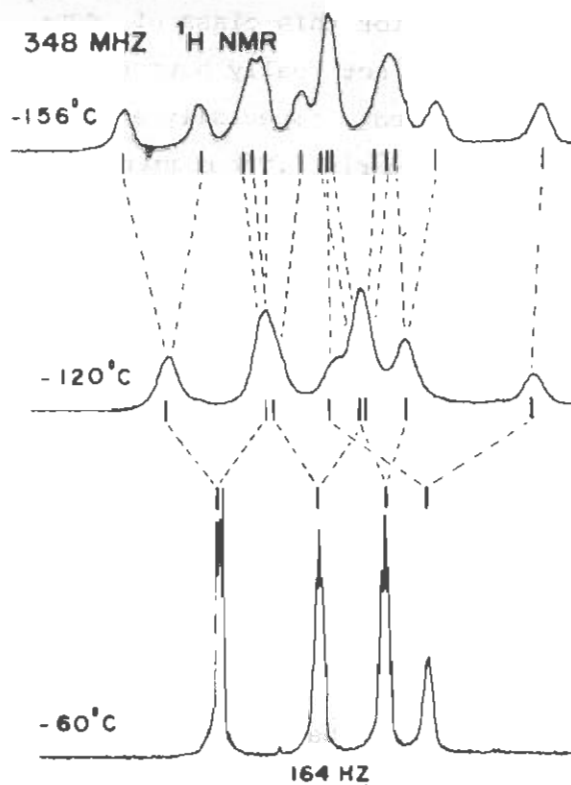


Figure 4. The 348 MHz  $^1\text{H}$  NMR of cyclooctanone in  $\text{CHFC}_2-\text{CHF}_2\text{Cl}$  (1:2) at various temperatures.

Table 3.  $^1\text{H}$  NMR chemical shifts of cyclooctanone.

Temperature ( $^\circ\text{C}$ )	Chemical Shifts (PPM from TMS)
-60	2.43, 1.92, 1.58, 1.36,
-120	2.70, 2.19, 1.83, 1.70, 1.46, 0.81
-156	2.91, 2.53, 2.22, 2.02, 1.87, 1.53, 1.34, 0.80

## RESULTS AND DISCUSSION

### A. Force-field parameters

In carrying out force - field

calculations on cyclooctanone it is necessary to have parameters for the C=O group in addition to those used for hydrocarbon molecule. Although some force-field calculations have been carried out with ketones, the parameters for this class of compounds have not really been extensively tested, especially as concerns medium rings. The required parameters are those for stretching, bending, torsional and van der Waals interactions associated with a carbonyl group. At first, we treated cyclooctanone like methylenecyclooctane, by applying the same force-field parameters that have been used for unsaturated systems (21), except for the torsional parameter for rotation about the single bond adjacent to the carbonyl group. It is known that the barrier to internal rotation in acetone (0.8 kcal/mole) is substantially lower than in isobutylene (2.2 kcal/mole).

In these calculations, the BC-3 conformation of cyclooctanone turned out to be of the lowest energy, as required by the experimental data, but the barrier to pseudorotation in this conformation was somewhat too low (5.2 kcal/mole versus an experimental value of 6.3 kcal/mole). This can be compared with the corresponding process in methylenecyclooctane where the experimental and calculated barriers are 4.2 and 4.7

kcal/mole respectively. Additionally, we tried the same parameters used before to reproduce the conformational data on 1,3-cyclooctandione and cyclononanone. These parameters reproduce poorly the conformational data on these compounds.

The reason for the significantly different behavior of the ketone and its methylene analog may arise from different electron densities at the ring  $sp^2$  hybridized carbon. This should give rise to different non-bonded repulsions in the two systems, and since the BC-3 conformation has the C-5 methylene group in close proximity of the ring  $sp^2$  carbon, the non-bonded interactions are of critical importance in a correct description of the strain energies of the two systems. A change in the ground state energy can, of course, be important in affecting a conformational barrier, and the reason for the higher barrier in cyclooctane would then arise from a lower ground state strain energy in the ketone than in the olefin.

With these considerations in mind, we considered modifying the van der Waals terms for the carbon of a carbonyl group so as to reduce the repulsive contribution of a normal carbon by a significant amount. Of course, the modification of the force-field in order to improve the fit for a specific system may be

considered to be objectionable. However, if a new set of parameters can reproduce well the experimental data for several compounds they can be considered to be useful at least at an empirical level. The van der Waals parameters associated with the carbonyl group were modified as shown in Figure 5. The magnitude of the changes made were guessed to be reasonable from the point of view of changing the total strain energy in a molecule by an amount of the order of a few kcal/mole. Figure 5 shows a comparison of the van der Waals interactions between a normal carbon and a carbon that is a part of a carbonyl group with hydrogen and other carbon atoms in molecules. Such curves show the distance at which the strain energy crosses the zero strain energy line. For a carbon-hydrogen non-bonded interaction this distance is 2.45 Å when the carbon is part of a carbonyl group, rather than 2.75 Å for the case that carbon is normal. Similarly, for the carbon-carbon non-bonded term, the zero strain energy distance becomes 3.05 Å when the carbon is part of a carbonyl group, as compared to 3.4 Å when neither carbon is part of a carbonyl group. These new non-bonded parameters together with the normal carbon parameters are given in Table 4. For convenience we have called the new non-bonded parameters, set B.

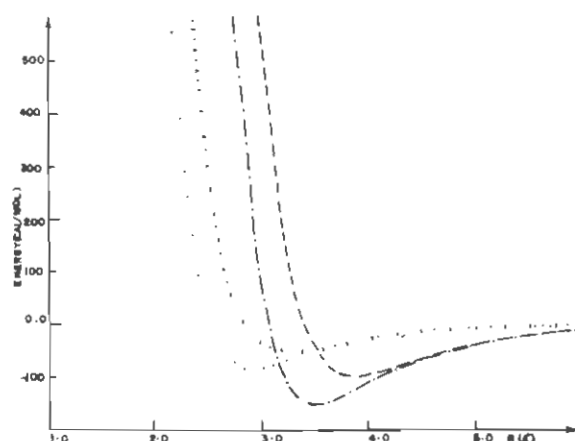


Figure 5. Non-bonded potential energy diagram.  $E(\text{kcal/mole}) = 144 \left[ A \exp(-Br) - C/r^6 \right]$

----- C-----C  
 - - - - - C - - C (Carbonyl)  
 ..... H-----C  
 ..... H----C (Carbonyl)

Table 4. Non-bonded Interaction parameters for carbonyl group.

Set A			
Interaction	A	B	C
C---C (Carbonyl)	104	3.05	4.45
H---C (Carbonyl)	30	3.145	0.96
Set B			
Interaction	A	B	C
C---C (Carbonyl)	120	3.30	4.0
H---C (Carbonyl)	35	3.7	0.8

#### B. Energy minimum conformations of cyclooctanone.

Force-field calculations were carried out with the modified non-bonded parameters (set B) described above for the conformations given in Table 5. For the boat-chair all conformations have been investigated. For the twist-chair-chair, and boat-boat, the carbonyl group was placed



Table 5. Conformational energies for cyclooctanone.

Family and name	Conformation		Relative strain energies(kcal/mole)	
	Symmetry group		Calculated	
<b>Boat-chair</b>				
BC-3	C <sub>1</sub>		0.0	
BC-4	C <sub>1</sub>		1.38	
BC-1	C <sub>S</sub>		1.64	
BC-2	C <sub>1</sub>		3.1	
BC-5	C <sub>S</sub>		3.51	
<b>Crown</b>				
Twist-chair-chair	C <sub>1</sub>		1.51	
Crown	C <sub>S</sub>		—	
Twist-chair	C <sub>S</sub>		1.70	
<b>Boat-boat</b>				
Twist-boat	C <sub>1</sub>		2.39	
<b>Chair</b>				
Chair-1	C <sub>3</sub>		8.07	
Chair-2	C <sub>3</sub>		8.96	
Twist-chair-1 <sup>a</sup>	C <sub>2</sub>		9.99	
Twist-chair-2 <sup>b</sup>	C <sub>2</sub>		8.09	

<sup>a</sup>BC-3 TC BC-7;<sup>b</sup>BC-6 TC BC-8.

at the most favorable position in each case and other conformations in these families were not investigated. The conformations chosen give the maximum relief of non-bonded strain and, in the case of TCC and CC also have the maximum relief of torsional strain. Calculated torsional and internal angles in various conformations of this compound are also given in Figure 6.

The most stable conformation as expected, is the boat-chair with the carbonyl group at the 3 position (BC-3). Since the next lowest energy conformation is BC-4 which is calculated to be 1.4 kcal/mole above the BC-3, the BC-3 is therefore expected to be major conformation (> 90%) at room temperature and to be virtually the only populated conformation at low temperatures, in agreement with experimental data presented above.

## Conformational processes in boat - chair cyclooctanone

### A. Pseudorotation processes

The boat-chair conformation can undergo several exchange processes similar to those undergone by cyclooctane and its derivatives. One process is pseudorotation of the boat chair with the twist-boat-chair as a high energy intermediate.

BC-3 and TBC are chiral and hence there are actually two mirror-image or enantiomeric conformations. Consequently there are two mirror-image pseudorotation paths conveniently labelled by the mirror-image letters b and d. If we arbitrarily assign the letter b to the process shown in Figure 7, and if we use the carbonyl group in the position 3 and the protons in the  $\gamma$  position relative to the carbonyl group as labels, we can write down the effect of pseudorotation in the two mirror-image paths as shown in Figure 8.

As shown in Figure 8, pseudorotation through twist-boat-chair gives rise to either a BC-6 or BC-8 depending on the direction of pseudorotation. Further pseudorotation steps ultimately lead to BC-7. Calculated potential energy profiles for conformational enantiomerization are shown in Figures 9 and 10. Each path has a boat-chair intermediate which has a plane of symmetry (BC-1 or BC-5).

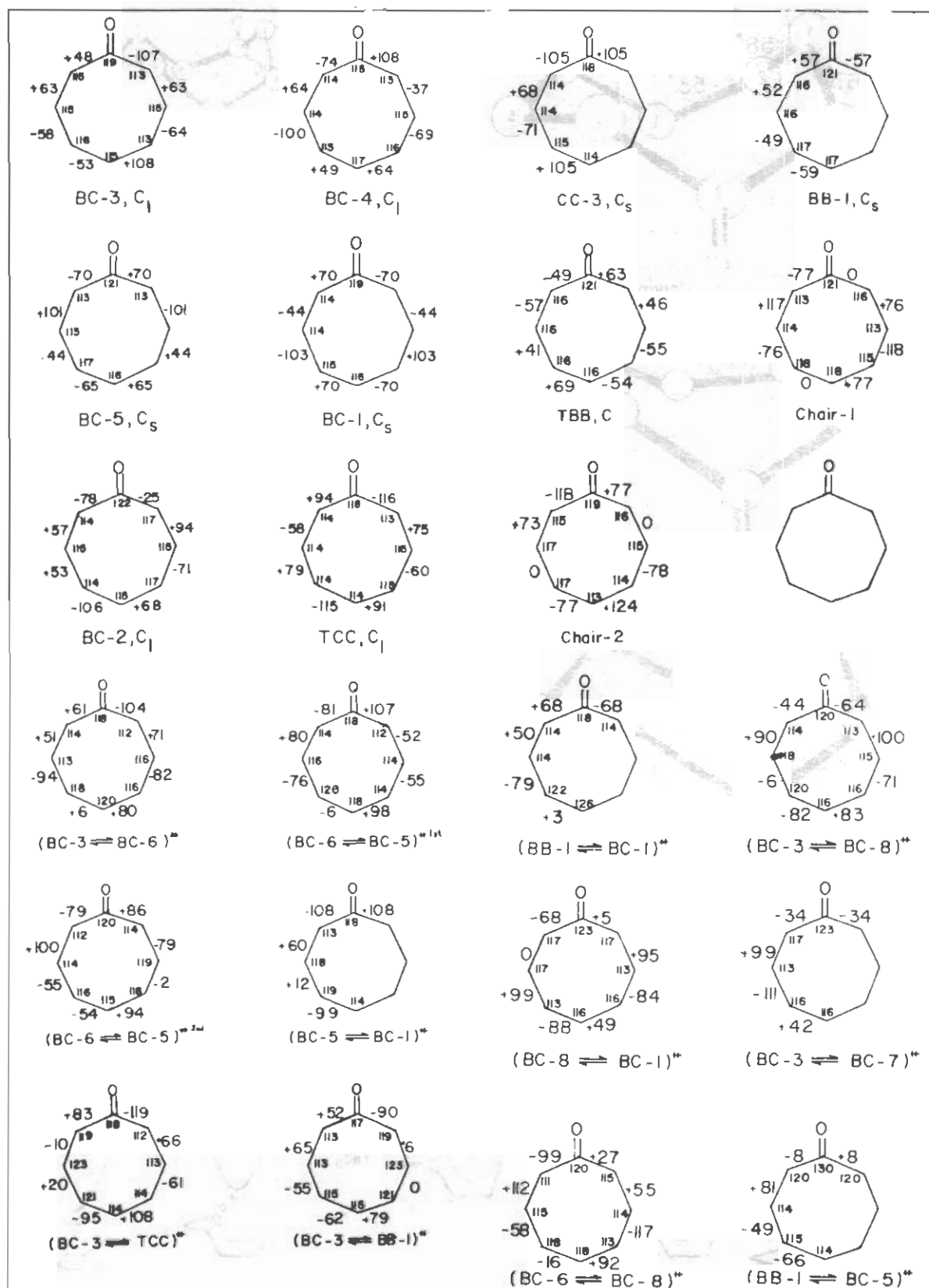


Figure 6. Calculated torsional and internal angles in various conformations of cyclooctanone.

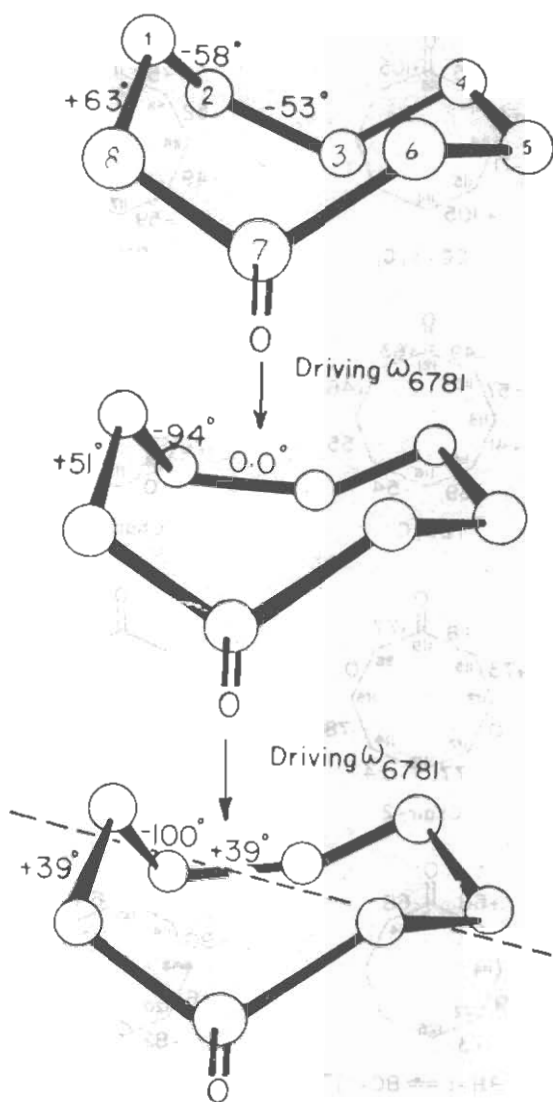


Figure 7. Interconversion of the boat-chair conformation to the twist-boat-chair.

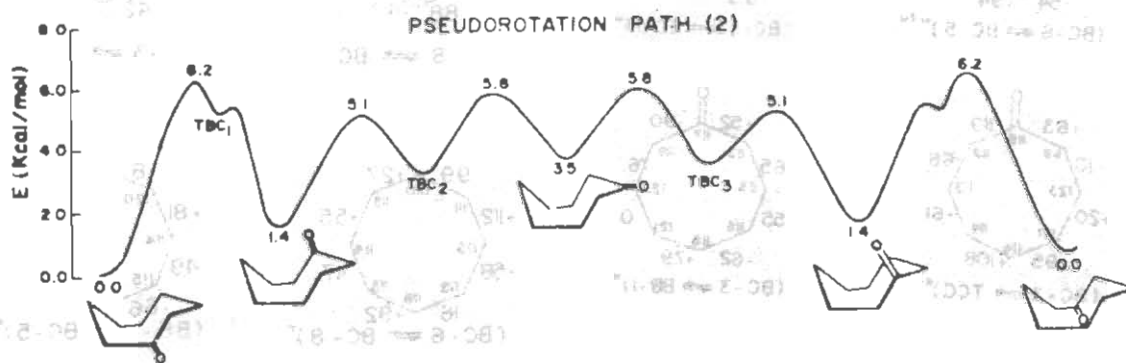


Figure 9. Calculated strain energy profile for pseudorotation process in BC-3 with BC-5 as symmetrical intermediate.

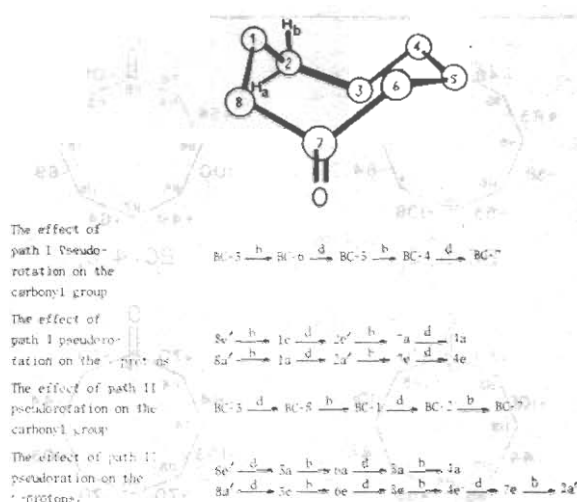


Figure 8. Effects of the two mirror-image pseudorotation paths on the carbonyl group and the protons in the  $\gamma$  position relative to the carbonyl group in BC-3 conformation.

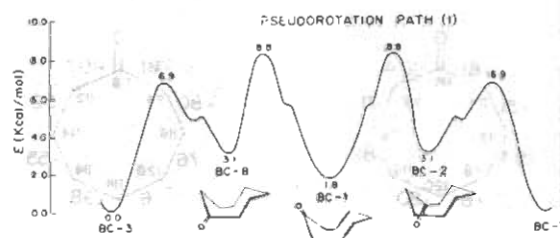


Figure 10. Calculated strain energy profile for pseudorotation process in BC-3 with BC-1 as symmetrical intermediate.

The path proceeding through BC-5 is calculated to be distinctly lower in energy than that proceeding through BC-1. When either of these pseudorotation processes is fast the time average symmetry of the molecule becomes  $C_s$ . Another mechanism which achieves the same averaging effect is an interconversion of BC-3 and BC-7 via a BB intermediate as shown below. The strain energy barrier (9.3kcal/mole) calculated for this process is substantially larger than that of either mechanism involving twist-boat-chair as intermediate. This energy difference is 3.1 kcal/mole when compared with the pseudorotation through BC-5 as an intermediate and 0.9 kcal/mole when the BC-1 is the intermediate. Thus, the calculated barrier for the best interconversion path linking the BC-3 and BC-7 is 6.2 kcal/mole and this path is a BC-TBC pseudorotation proceeding via the plane-symmetrical BC-5. In Table 6 are listed maximum energy conformations for various interconversion.

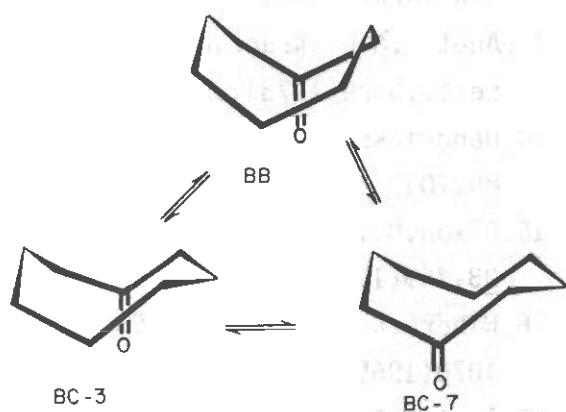
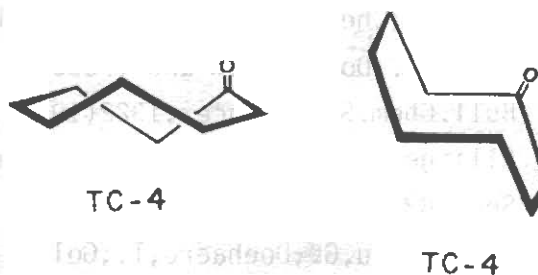


Table 6. Maximum-energy conformations for various interconversion paths in cyclooctanone.

Conformation	Driven Torsional angle	Relative Strain energy (Kcal/mole)
(BC-3 $\rightleftharpoons$ TCC) <sup>*</sup>	$\omega_7$ or $\omega_2$	11.57
(BC-3 $\rightleftharpoons$ BB) <sup>*</sup>	$\omega_4$ and $\omega_5$	9.30
(BC-5 $\rightleftharpoons$ BB) <sup>*</sup>	$\omega_4$ and $\omega_5$	8.84
(BC-1 $\rightleftharpoons$ BB) <sup>*</sup>	$\omega_4$ and $\omega_5$	13.80
BC-6 $\rightleftharpoons$ BC-8	$\omega_2, \omega_3, \omega_6,$ and $\omega_7$	8.2
BC-3 $\rightleftharpoons$ BC-7	$\omega_2, \omega_3, \omega_6$ and $\omega_7$	9.99
BC-5 $\rightleftharpoons$ BC-1	$\omega_2, \omega_3, \omega_6$ and $\omega_7$	10.06
BC-3 $\rightleftharpoons$ BC-6		6.2
BC-6 $\rightleftharpoons$ BC-5		5.07 and 5.83
BC-3 $\rightleftharpoons$ BC-8		6.90
BC-8 $\rightleftharpoons$ BC-1		8.43

### B. Ring Inversion Processes

There is a second type of process which occurs in the BC-3 and BC-7 that can be called a RING INVERSION and involves the introduction of a  $C_2$  time-average symmetry. This process can involve the chair or twist chair as transition state, as in cyclooctane. Force-field calculations show that the strain energy difference between the best chair and the best twist-chair is virtually zero. The TC and C can be reached as they link the BC-2 and BC-4 or BC-6 and BC-8. Since the strain energy barriers (pseudorotation) separating the BC-8 and BC-6 from the BC-3 are 6.9 and 6.2 kcal/mole respectively, the transition state for ring inversion



in the BC-3 is probably the chair and the calculated strain energy barrier is 8.1 kcal/mole. (Figure 11).

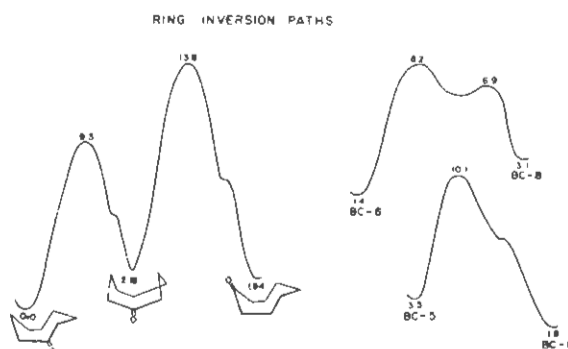


Figure 11. Calculated energy profile for ring inversion process in cyclooctanone

The energy profile for ring inversion in BC-7 is just the mirror-image of the BC-3 process. Since the BC-3 to BC-7 pseudorotation is always much faster than ring inversion, one cannot view ring inversion of the BC-3 in isolation from the BC-7.

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