

# THE CONFORMATIONS OF 1- THIACYCLOOCTAN-3-ONE DYNAMIC NUCLEAR MAGNETIC RESONANCE AND FORCE-FIELD CALCULATION

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**ABSTRACT :** The  $^1\text{H}$  and natural- abundance  $^{13}\text{C}$ -NMR spectra of 1-thiacyclooctan-3- one (1) have been measured from 25 to  $-100^\circ\text{C}$ . Coalescence is observed in the  $^1\text{H}$ -NMR spectra of (1) at about  $-80^\circ\text{C}$ , and attributed to ring inversion in a boat- chair conformation, which is the predominant conformation of (1). The free energy of activation ( $\Delta G^\ddagger$ ) for this process is  $9.2 \pm 0.2$  kcal/mol. The  $^{13}\text{C}$ -NMR spectra of (1) is temperature independent.

**KEY WORDS :** Boat- chair conformation, Dynamic NMR, Ring inversion, Pseudorotation, Eight membered rings, Coalescence.

## INTRODUCTION :

The geometry of medium rings have been well studied theoretically [1] and experimentally [2]. The flexibility of these rings allows them to adopt a variety of shapes. In 1966, *Anet* and *Jacques* [3] reported the evidence that cyclo-octanone exists primarily in a boat-chair conformation with the carbonyl group at

position 3. Eight- membered ring compounds containing carbonyl groups and suitably placed heteroatoms that can exhibit transannular interactions have also been studied by *Anet* and coworkers [4,5], and they have obtained evidence which does fit nicely with the unsymmetrical boat-chair conformations.

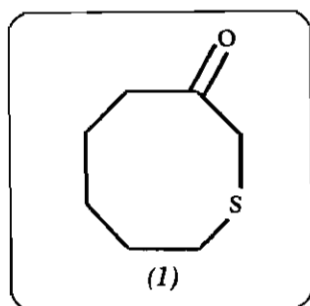
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**EXPERIMENTAL :**

The 1-thiacyclooctan-3-one (*1*) and 1,9-dithiacyclohexadecan-3,11-dione (*2*) have been synthesized by the *Dieckmann* cyclization of ethyl-6-(ethoxy-carbonylmethylthio)-hexanoate using potassium tert-butoxide in xylene under high dilution condition [6]. The *Dieckmann* cyclization products were hydrolyzed by the concentrated hydrochloric acid. Ether extraction followed by drying and evaporation operations furnished a residue, which was purified by column chromatography on silica gel (eluent: cyclohexane-ethylacetate): yield (20%); compound (*1*): b.p. 66-68°C(0.35 torr); IR(KBr):  $1694\text{cm}^{-1}$ (C=O);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ 3.2 (s, 2H,  $\text{CH}_2$ ), 2.6-2.85(m, 4H,  $\text{CH}_2$ ), 1.6-1.9(m, 6H,  $\text{CH}_2$ ); MS, m/e 144( $\text{M}^+$ ).

Compound (*2*): m.p. 79-80°C; IR(KBr):  $1694\text{cm}^{-1}$ (C=O);  $^1\text{H-NMR}$ ( $\text{CDCl}_3$ ) $\delta$ 3.15(s, 4H,  $\text{CH}_2$ ), 2.6-2.85(m, 8H,  $\text{CH}_2$ ), 1.6-1.9 (m, 12H,  $\text{CH}_2$ ); MS, m/e 288( $\text{M}^+$ ).



The variable temperature  $^1\text{H-NMR}$  spectra at different temperatures were measured on an NMR spectrometer (*Brucker*) operating at 400MHz (Fig. 1).  $\text{CD}_2\text{Cl}_2$  was used as the solvent and a deuterium line of the solvent was employed for lock purposes. The coalescence approximation was used for estimation of rate constant. At  $T_c$ , the unimolecular rate constant for the reaction is given by  $k_c = \pi\Delta\nu/\sqrt{2}$ , and the free energy of activation ( $\Delta G^\ddagger$ ) at the temperature of coalescence can be calculated from  $\Delta G_c = 2.3RT_c (10.32 + \log T_c / k_c)$ .

The  $^1\text{H-NMR}$  spectrum of (*1*) at 400MHz shows well-separated signals for the six chemically different  $\text{CH}_2$  groups. A dynamic NMR effect can be observed over the temperature

range of +25 to  $-100^\circ\text{C}$  (Fig. 2). Free energy barrier of  $9.2 \pm 0.2\text{kcal/mol}$  has been calculated for this dynamic effect. In order to calculate the free energy of activation ( $\Delta G^\ddagger$ ) we have used the triplet centered at 2.7ppm ( $T_c = -80^\circ\text{C}$ ).

Carbon-13 NMR spectra of (*1*) have been obtained over the temperature range of +25 to  $-100^\circ\text{C}$ , and typical spectra are displayed in Fig.1. The spectrum is temperature independent and shows six sharp methylene carbon resonances. The chemical shifts and assignments are given in Table 1. There is a change of 0.7 to 1.0ppm in the chemical shifts when changing the solvent from  $\text{CDCl}_3$  to  $\text{CD}_2\text{Cl}_2$ , which can be attributed to different solute-solvent interaction and the difference in the viscosity of solutions at 25 and  $-96^\circ\text{C}$ .

Boyd's iterative force-field computer program has been used to calculate strain energies in 1-thiacyclooctan-3-one (*1*) [7]. In order to carry out force-field calculations on(*1*), it is necessary

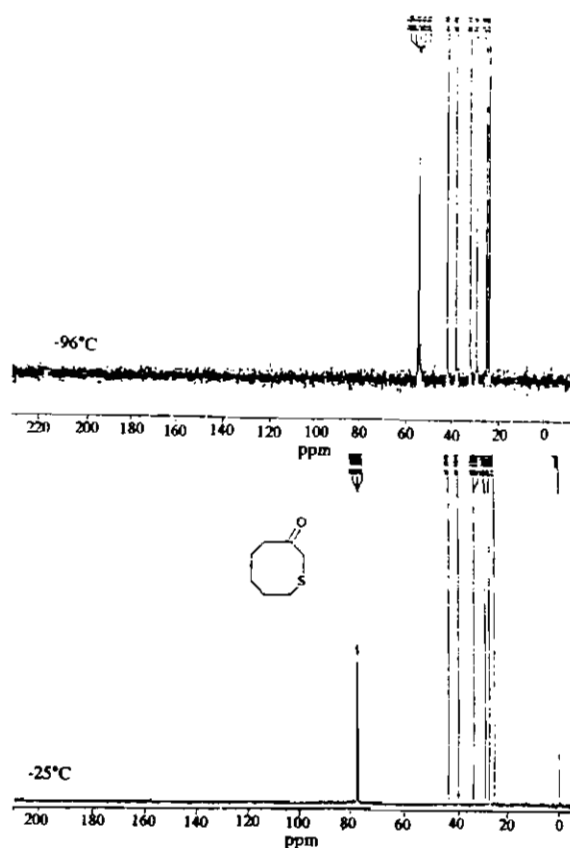


Fig. 1: Carbon-13 NMR spectra (100MHz) of (*1*) at various temperatures.

Table 1:  $^{13}\text{C}$ -NMR Chemical shifts in 1- thiacyclooctan-3-one

Chemical Shifts, ppm <sup>(a)</sup>							Symmetry	Temp., °C	Solvent
C=O	C <sub>8</sub>	C <sub>7</sub>	C <sub>6</sub>	C <sub>5</sub>	C <sub>4</sub>	C <sub>2</sub>			
215	32.8	26.9	25.0	28.4	38.6	42.4	C <sub>1</sub> <sup>(b)</sup>	25°C	CDCl <sub>3</sub>
216	32.1	25.3	24.0	29.4	37.8	41.6	C <sub>1</sub> <sup>(b)</sup>	-96°C	CD <sub>2</sub> Cl <sub>2</sub>

(a) In part per million downfield from internal Me<sub>4</sub>Si.

(b) Time- average symmetry.

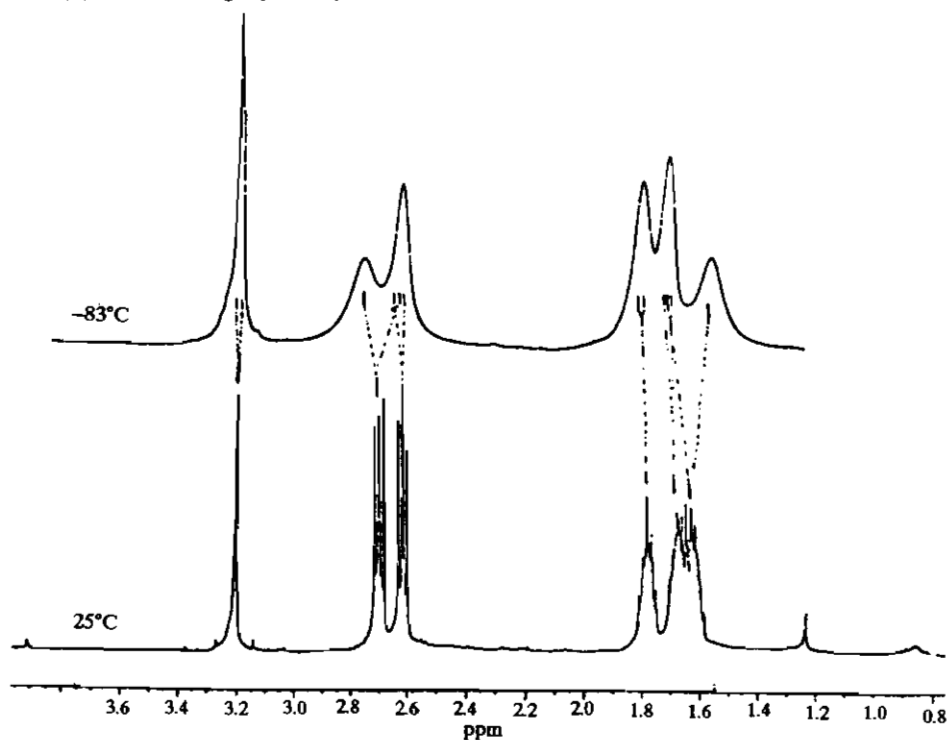


Fig. 2: Proton NMR spectra (400MHz) of (1) at various temperatures.

to have the appropriate parameters for the carbonyl group and the sulfur moiety in addition to those for hydrocarbon molecules. Some force-field calculations have been carried out with ketones, and the parameters for this class of compounds have been extensively tested [8], especially in medium rings. For the sulfur moiety we have used the parameters that Allinger [9] has applied to calculate the strain energies of different sulfur compounds.

## RESULTS AND DISCUSSION :

As shown in previous works, cyclooctane

[10], cyclooctanone [3], 1- oxacyclooctan-5- one [5] and 1- thiacyclooctan-5- one [4] exist as boat-chair with the carbonyl group situated at the 3 or 7 position. By analogy, we propose that (1) exists as a boat- chair stereoisomer. In this respect we have calculated the strain energies of different stereoisomers of the boat- chair family (Fig. 3). In the nomenclature of these stereoisomers, the first and the second subscripts show the position of the sulfur atom and the carbonyl group respectively. The excess strain energies for different stereoisomers are listed in Table 2.

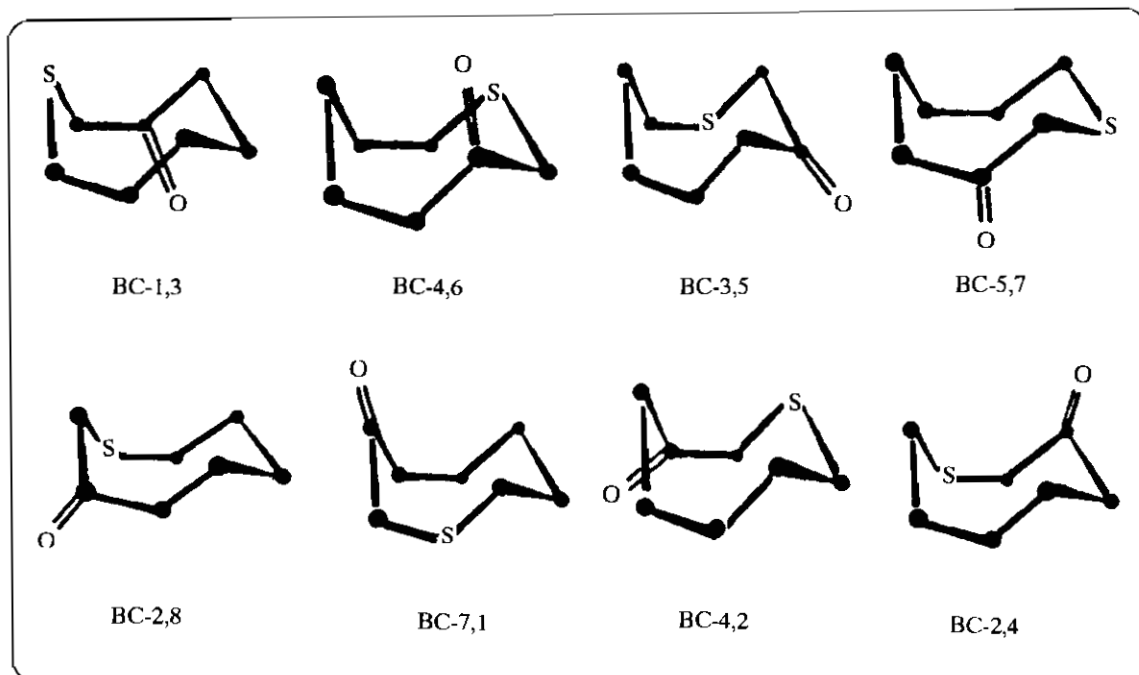


Fig. 3: Different stereoisomers of the boat-chair family of (1)

Table 2 : Relative strain energies of the boat-chair family stereoisomers.

Stereoisomers	Relative strain energy (kcal/mol)(Calculated)
BC-1,3	0.00
BC-5,7	1.40
BC-2,4	1.45
BC-4,6	1.60
BC-7,1	1.70
BC-4,2	2.70
BC-2,8	3.00
BC-3,5	3.20

In these calculations, the BC-1,3- conformation of 1- thiacyclooctan-3- one turned out to be of the lowest energy and on the basis of the  $^{13}\text{C}$ -NMR spectra the population of the other BC family conformation should be less than 5%. But the calculations on the basis of the MM2 force- field [11] are in disagreement with our calculations where it is predicted that 1- thiacyclooctan-3- one would be a mixture of at least four conformations.

The conformational process in (1) having  $\Delta G^\ddagger = 9.2\text{kcal/mol}$  is assigned to the ring inversion of the boat- chair conformation. The BC-1,3 can undergo this process through BB-1,3 or through a TC or a chair transition state (Fig. 4).

As shown in our calculations, the BC-5,7 is not a stable stereoisomer relative to BC-1,3. So there should be some way by which this stereoisomer could revert to BC-1,3 or its mirror

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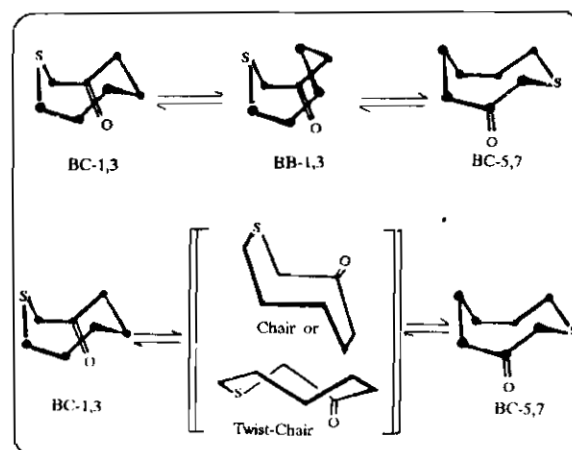


Fig. 4: Different paths for the ring inversion of (1).

there should be some way by which this stereoisomer could revert to BC-1,3 or its mirror image, BC-1,7. In Fig. 5 we have shown two paths for pseudorotation in (1), by which BC-5,7 could complete the interconversion of BC-1,3 and its mirror image conformation, BC-1,7. Previous force-field calculations on cyclooctanone show that the path 1 is the preferred path for the pseudorotation process.

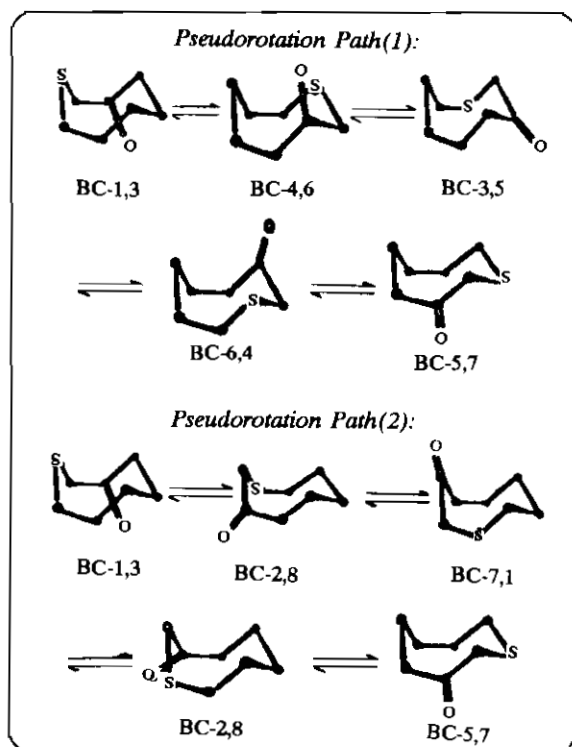


Fig. 5: Different paths for the pseudorotation of (1).

It is interesting to compare the ring inversion barriers and the carbonyl vibrational frequencies of the compounds 1,1- thiacyclooctan-5- one and cyclooctanone (Table 3). The NMR data are in good agreement with the idea that the difference in the ring inversion barriers of cyclooctanone and 1- thiacyclooctan-5- one may result from the transannular interaction and the change in the structural parameters including bond lengths, bond angles and non- bonded interactions. If we assume that the 1- thiacyclooctan-3- one has the BC-1,3 conformation, we would expect that decreasing the non- bonded interaction by

replacing a methylene group with a sulfur atom, the barrier to ring inversion should increase. However, the interpretation of the IR frequencies is not so straightforward and discussion of the NMR data is probably more reliable.

Table 3: Ring inversion barriers and vib. frequencies.

Compounds	$\Delta G^\ddagger$ (kcal/mol)	(C=O) ( $\text{cm}^{-1}$ )
Cyclooctanone	7.60	1694
1- thiacyclooctan-5-one	8.15	1680
1- thiacyclooctan-3-one	9.22	1694

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[11] Calculation of the strain energies of

different conformations of 1- thiacyclooctan- 3- one using the MM2 force-field as implemented in the program MacroModel V3.0 shows a decidedly different order of stability.