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Registry No. 5a, 935-50-2; 5b, 64701-03-7; 5c, 72796-36-2; 5d, 57197-23-6; 5e, 72796-37-3; 6a, 72796-38-4; 6b, 72796-39-5; 6c, 72796-40-8; 6d, 72796-41-9; 7a, 72796-42-0; 7b, 72796-43-1; 7c, 72796-44-2; 8, 72796-45-3; 9, 72796-46-4; 10a, 72796-47-5; 10b, 72796-48-6; 11, 7287-51-6; 12a, 72796-49-7; 12b, 72796-50-0; 12c,

72811-85-9; 13, 72796-51-1; 14, 72796-52-2; 15, 72796-53-3; 16, 72796-54-4; 17, 72796-55-5; 18, 72796-24-8; 19, 72796-25-9; 20, 2033-89-8; 21, 72796-26-0; 22, 72796-27-1; 23, 50827-64-0; 2-methyl-3,4-dimethoxyphenol, 50827-64-0; 4,8-dimethoxy-1-naphthol, 3843-55-8; diethyl malonate, 105-53-3; ethyl 2-cyanopropionate, 1572-99-2; ethyl acetoacetate, 141-97-9; chloromethyl ethyl ether, 3188-13-4; methyl iodide, 74-88-4.

Conformation of 1-Thiacyclooctan-5-one

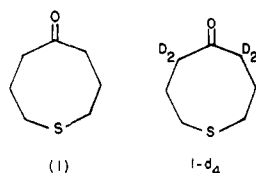
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Received August 10, 1979

¹H and ¹³C NMR spectra of 1-thiacyclooctan-5-one (1) have been measured from room temperature to -150 °C. One dynamic NMR effect is observed in the ¹³C spectra; on the other hand, the ¹H NMR spectra show the presence of two such effects. These results show that there are two conformational processes in 1 and that the free-energy barriers associated with these processes are 6.7 and 8.15 kcal/mol. 1 is deduced to have an unsymmetrical boat-chair conformation, and the lower and higher energy barriers are assigned to pseudorotation and ring inversion processes, respectively.

Medium-ring compounds containing carbonyl groups and suitably placed heteroatoms can exhibit transannular interactions.¹ Such interactions are very weak in eight-membered rings when the heteroatom is an ether function,^{1c} but are reported to be significantly stronger for the sulfur analogue.^{1c} In their original work on 1, Leonard and co-workers^{1c} interpreted the high dipole moment ($\mu = 3.80$) in terms of "folded" conformations, but at that time little was known about the relative energies of the conformations of eight-membered rings. Transannular interactions should be reflected in the barriers to conformational processes in these rings.² Since the conformations and conformational barriers in cyclooctanone³ and 1-oxacyclooctan-5-one² have been determined, it has become of interest to investigate the conformational properties of 1-thiacyclooctan-5-one (1) for comparison with these two compounds, and we now report a variable-temperature ¹H and ¹³C NMR study of 1 and of a tetradeuterio derivative of 1.



Experimental Section

1-Thiacyclooctan-5-one was synthesized by the Dieckmann cyclization of diethyl γ,γ' -thiabis(butyrate) using potassium *tert*-butoxide in xylene under high dilution conditions.¹ Sublimation of the compound (1 mm) gave white needles: mp 53-54 °C (lit.¹ 53-54 °C); ¹H NMR (CDCl₃, 348 MHz) δ 2.68 (2,8-CH₂),

Table I. ¹³C NMR Chemical Shifts in 1-Thiacyclooctan-5-one

| temp, °C | symmetry | chemical shifts, ppm ^a | | | |
|----------|-----------------------------|-----------------------------------|-----------------------|-----------------------|-----|
| | | CH ₂ (3,7) | CH ₂ (2,8) | CH ₂ (4,6) | C=O |
| -70 | C ₂ ^b | 28.8 | 32.0 | 41.9 | 219 |
| -140 | C ₁ ^b | 23.9, 33.3 | 30.0, 33.5 | 38.3, 45.2 | 219 |

^a In parts per million downfield from internal Me₄Si.

^b Time-averaged symmetry.

Table II. NMR Kinetic Parameters for Thiacyclooctan-5-one

| nucleus observed | chemical shift separation, Hz | coalescence temp (T _c), °C | k at T _c , s ⁻¹ | ΔG^\ddagger at T _c , kcal/mol |
|------------------|-------------------------------|--|---------------------------------------|--|
| ¹ H | 66 ^a | -105 ± 2 | 148 | 8.15 ± 0.1 |
| ¹ H | 238 ^b | -125 ± 2 | 530 | 6.7 ± 0.1 |
| ¹³ C | 488 ^c | -115 ± 2 | 1087 | 6.7 ± 0.1 |

^a For protons on C-3 and C-7. ^b For protons on C-2 and C-8. ^c For C-3 and C-7 carbons.

2.44 (4,6-CH₂), and 2.23 (3,7-CH₂); ¹³C NMR (CDFCl₂-CF₂Cl₂, 50 MHz, ¹H noise decoupled) δ 28.8 (3,7-¹³CH₂), 32.0 (2,8-¹³CH₂), 41.9 (4,6-¹³CH₂), and 219 (¹³C=O).

¹H NMR spectra measured on a superconducting solenoid NMR spectrometer operating at 82 kG.⁴ The proton spectra were obtained with standard 5-mm sample tubes in a frequency-sweep mode. The ¹³C spectra were measured on a Bruker WP-200 operating at 47 kG and are Fourier transforms of accumulated free induction decays obtained with 10-mm tubes under the following conditions: 30° pulse angle, 16 K data points, 12500-Hz spectrum width, and an exponential broadening function corresponding to a 2-Hz broadening. A mixture of CDFCl₂/CHF₂Cl (1:2) was used as the solvent and a deuterium line of the solvent was employed for lock purposes. All temperatures were measured with a copper-constantan thermocouple situated in the probe a few centimeters below the sample.

Line-shape calculations were carried out with a Fortran program on a Data General Corp. Nova computer.

Results and Discussion

NMR Data. Carbon-13 NMR spectra of 1 have been obtained over the temperature range of -50 to -150 °C,

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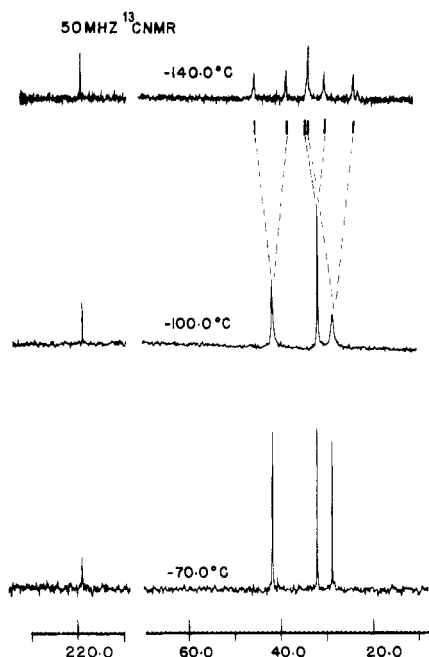


Figure 1. ^{13}C NMR spectra (50 MHz, ^1H noise decoupled) of **1** in $\text{CDFCl}_2/\text{CF}_2\text{Cl}_2$ (1:2).

and typical spectra are displayed in Figure 1. Above -90°C , the spectrum shows three sharp methylene carbon resonances with the chemical shifts and assignments given in Table I. A single dynamic NMR effect is observed in the temperature range -90 to -140°C . The three methylene carbon resonances split into 1:1 doublets, but the carbonyl carbon signal remains a singlet. This behavior is consistent with a single unsymmetrical conformation (not counting mirror image forms) for **1**. From the coalescence temperature of the C-3,7 doublet (Table II), a conformational barrier of 6.7 ± 0.1 kcal/mol at -115°C can be calculated.

The ^1H NMR spectrum of **1** at 348 MHz shows well-separated multiplets for the three chemically different CH_2 groups. Two dynamic NMR effects can be observed over the temperature range -90 to -140°C , but because of peak overlaps even at 348 MHz, the spectra are quite complex. Much simpler spectra (Figure 2) are obtained from I-d_4 , where the protons α to the carbonyl group have been replaced by deuterons. Calculated spectra based on the exchange scheme discussed below fit the observed spectra quite well. Free-energy barriers of 6.7 ± 0.1 and 8.15 ± 0.1 kcal/mol were used in the calculation of the rate constants, and it was assumed that ΔS^\ddagger was zero. The spectra are not suitable for reliable measurements of ΔH^\ddagger and ΔS^\ddagger . However, it is expected that ΔS^\ddagger should be close to zero in these conformational processes and that ΔG^\ddagger should be approximately the same as ΔH^\ddagger and be virtually temperature independent.⁵

Interpretation of NMR Data. A crown-family conformation for **1** can be ruled out as the pseudorotation barrier in this family is known to be very small,^{6,7} and thus only one conformational process should be observable by dynamic NMR. The experimental observation of an unsymmetrical conformation and of two conformational processes is reminiscent of the behavior of cyclooctanone³ and 1-oxacyclooctan-5-one.² These two compounds exist as boat-chairs with the carbonyl group situated at the 3

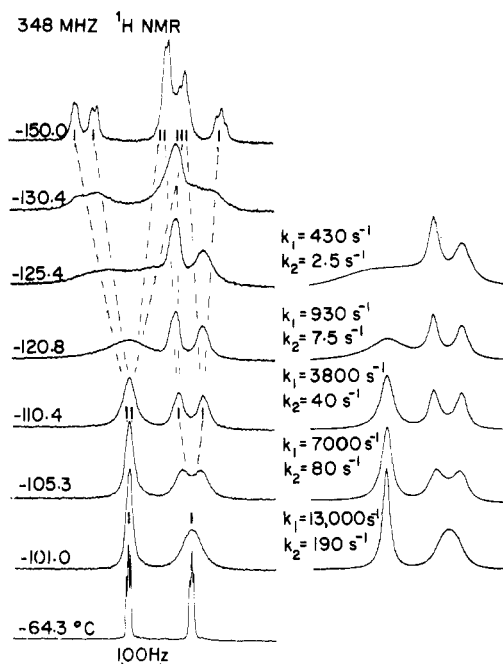
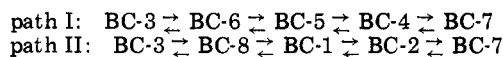


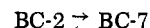
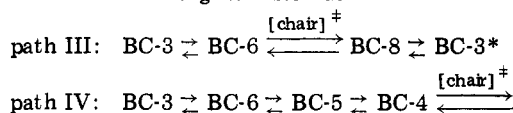
Figure 2. ^1H NMR spectra (348 MHz) of I-d_4 in $\text{CDFCl}_2/\text{CF}_2\text{Cl}_2$ (1:2). The calculated line shapes shown on the right were obtained with the rate constants shown and the exchange scheme given in Table IV.

Scheme I. Conformations

Pseudorotation in 1



Ring Inversion in 1



or 7 position. By analogy, we propose that **1** exists as a 1:1 mixture of the mirror-image chiral boat-chairs 1-BC-3 and 1-BC-7 (Figure 3).

The conformational process in **1** having $\Delta G^\ddagger = 6.7$ kcal/mol is assigned to a pseudorotation of the boat-chair (Figure 3). This process interconverts 1-BC-3 with its mirror image (1-BC-7) via other boat-chairs as intermediates. Between pairs of boat-chairs there are also high-energy twist-boat-chairs,⁷ but these latter conformations are not shown in Figure 3. If the energy profile in **1** is similar to that in cyclooctanone (which is not certain, however), the pseudorotation itinerary shown in Figure 3 (also shown as path I in Scheme I) should be preferred over the alternative itinerary, path II. When pseudorotation is fast on the NMR time scale, the time-averaged symmetry of the boat-chair becomes C_s .

The higher energy conformational process in **1** has a ΔG^\ddagger of 8.15 kcal/mol and is expected, in analogy with cyclooctanone, to be a ring inversion having a chair transition state (1-chair). In its simplest form the ring inversion proceeds by path III. Because the interconversions of BC-6 and BC-4 are expected to be fast with respect to the overall inversion process, path IV is nearly equally probable. The scheme (Table III) used to calculate the line shapes in Figure 2 assumes that the ring inversion process starting with BC-3 can give with equal probability BC-3* or BC-7. The asterisk in the name BC-3* is used to indicate that BC-3 and BC-3* differ in the position of the labeled pro-

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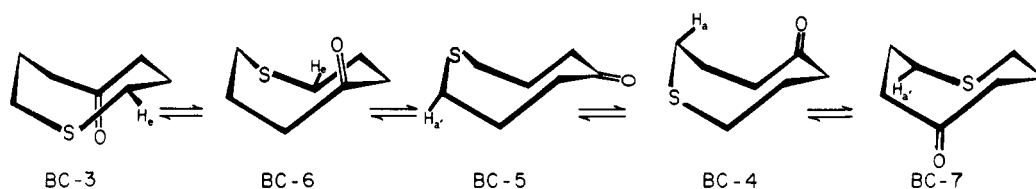


Figure 3. Pseudorotation (path I in Scheme I) in the boat-chair conformation of 1. BC-4, BC-5, and BC-6 are high-energy intermediates separating BC-3 from its mirror image, BC-7. One hydrogen (α to the sulfur) only is explicitly shown. The (conformational) labeling refers to the CO group.

Table III. Chemical Shifts and Exchange Scheme Used in the Line Shape Calculations

| chemical origin | conformational sites | chemical shifts, ppm |
|---------------------|----------------------|----------------------|
| 2,8-CH ₂ | I | 2.019 |
| 2,8-CH ₂ | II | 2.241 |
| 2,8-CH ₂ | III | 2.300 |
| 2,8-CH ₂ | IV | 2.400 |
| 3,7-CH ₂ | V | 2.283 |
| 3,7-CH ₂ | VI | 2.486 |
| 3,7-CH ₂ | VII | 2.973 |
| 3,7-CH ₂ | VIII | 3.119 |

| | exchange scheme |
|--------------------------|---|
| pseudorotation (k_1) | I \rightleftharpoons II, III \rightleftharpoons IV, V \rightleftharpoons VIII, VI \rightleftharpoons VII |
| ring inversion (k_2) | I \rightleftharpoons III, I \rightleftharpoons IV, II \rightleftharpoons III, II \rightleftharpoons IV, V \rightleftharpoons VI V \rightleftharpoons VII, VI \rightleftharpoons VIII, VI \rightleftharpoons V |

^a The designations I, II, etc. are given in order of decreasing shielding and do not imply any particular conformational assignment.

Table IV. Conformational Barriers in 8-Membered-Ring Ketones

| compd | ΔG^\ddagger , kcal/mol ring inversion | ΔG^\ddagger , kcal/mol pseudo-rotation |
|------------------------|---|--|
| cyclooctanone | 7.6 | 6.3 |
| 1-thiacyclooctan-5-one | 8.15 | 6.7 |
| 1-oxacyclooctan-5-one | 9.0 | 7.8 |

ton, as shown in Figure 4, which also shows the labeled proton in the BC-7 conformation. The time-averaged symmetry when both pseudorotation and ring inversion are fast is C_{2v} , which is the maximum time-averaged symmetry which a molecule of the chemical structure of 1 can possess.

A comparison of the conformational barriers in 1, cyclooctanone, and 1-oxacyclooctan-5-one is given in Table IV. It can be seen that 1 is more similar to cyclooctanone than to oxacyclooctan-5-one, at least as far as the magnitude of conformational barriers are concerned. This is

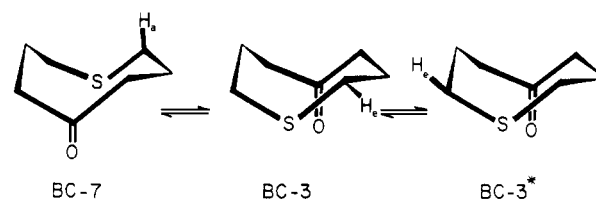
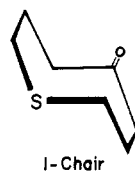


Figure 4. Ring inversion in the BC-3 conformation of 1. The resulting conformation can be either BC-3* (path III) or BC-7 (path IV). See Scheme I. One hydrogen (α to the sulfur) only is explicitly shown.

in contrast to previous deductions made on the basis of infrared spectra that transannular interactions are stronger in 1 than in its oxygen analogue.¹ One difficulty in interpreting the NMR data is that the bond lengths and bond angles at C, O, and S are significantly different. The observed changes in conformational barriers therefore may reflect these differences as well as those due to changes in transannular interactions. Because of the potential presence of transannular interactions in 1, we have not tried to carry out force-field calculations of this molecule. Such force-field calculations are quite successful in describing the conformational behavior of medium-ring hydrocarbons⁸ and ketones.⁹

One remaining point concerning the conformation of 1 should be made. The ¹³C NMR spectrum of 1 gives no evidence for line broadening in the vicinity of -50 °C. Such a broadening is diagnostic for the presence of small (1–10%) amounts of a crown conformation and is found on cyclooctane¹⁰ and oxacyclooctane (oxacane),¹¹ but not in cyclooctanone. Thus 1, like cyclooctanone, does not appear to have significant proportions (<1% at -50 °C) of crown conformations in equilibrium with the boat-chair conformations.

Acknowledgment. We thank the National Science Foundation for their support of this work both directly (CHE76-01738) and for the purchase of a Bruker WP-200 NMR spectrometer used in part of this work (Grant No. CHE76-05926).

Registry No. 1, 20701-80-8; diethyl γ,γ' -thiabis(butyrate), 72844-59-8; cyclooctanone, 502-49-8; 1-oxacyclooctan-5-one, 37727-93-8.

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