J. Am. Chem. Soc. **1998,** *120,* 8241−8244

Conformational Studies of Oxacyclodecan-2-one and Oxacycloundecan-2-one by Dynamic NMR Spectroscopy and Computational Methods

Diwakar M. Pawar, Sumona V. Smith, Erica M. Moody, and Eric A. Noe*

Contribution from the Department of Chemistry, Jackson State University,
Jackson, Mississippi 39217-0510

Received February 6, 1998

Abstract: The ten-membered lactone, oxacyclodecan-2-one (**1**), was found by low-temperature ^{1}H and ^{13}C NMR spectroscopy to have two conformations with populations of 95.2 and 4.8% at −133.8 °C. Free-energy barriers of 9.09 ± 0.15 and 8.26 ± 0.15 kcal/mol for interconversion of conformations at −110.7 °C were calculated from ^{13}C NMR spectra, and a free-energy barrier of 9.1 ± 0.2 kcal/mol at −70.8 °C was determined for another process, observed only in the ^{1}H NMR spectra. The barrier for the process observed in the proton NMR spectra was suggested to be a lower limit for the barrier to rotation of the lactone group through the ring. Oxacycloundecan-2-one (**2**) has two conformations at −139.3 °C, with populations of 64.3 and 35.7% at this temperature and free-energy barriers to interconversion of 7.83 ± 0.15 and 7.67 ± 0.15 kcal/mol at −109.1 °C. The NMR results for both compounds are discussed in terms of the conformations predicted by Allinger's MM3 program. Ab initio calculations of electronic energies for three conformations of the 10-membered lactone were also carried out at the HF/6-311+G* and MP2/6-31G* levels.

Introduction and Background

The conformations of lactones, which occur widely in nature,[1] are of interest for comparison with those of related compounds such as the cycloalkanes. Force-field calculations have been reported for the parent lactones of six to eleven ring members,[2] and for oxacyclotetradecan-2-one,[3] but experimental evidence for many of these predictions is not available. In an early dynamic NMR study,[4] an AB quartet was found for the fluorines of γ,γ-difluoro-ϵ-caprolactone by −85 °C, and the spectra were interpreted in terms of a pair of enantiomeric chair conformations interconverting with a free-energy barrier of 10.0 kcal/mol. The small ring size of this compound requires the lactone group to be in the *E* conformation,[5] and pseudorotation requires at least partial breaking of the π−bond between the carbonyl carbon and the "ether" oxygen. Because cycloheptane prefers the twist-chair conformation and easily pseudorotates to the chair conformation, the results for the lactone indicated[4] a significant (ca. 10 kcal/mol or greater) barrier to interconversion of the *E* and *Z* conformations of an open-chain ester.[6]

More recently, the 10- and 14-membered lactones have been studied by X-ray crystallography.[3] A conformation resembling boat-chair-boat cyclodecane was found[3] for **1** in the solid state, and ^{13}C spectra were taken for the solid and in solution to −108 °C. Some of the ^{13}C peaks of the solution were found to broaden and then sharpen as the temperature was lowered, and the authors interpreted this result in terms of motion for some of the ring atoms of the solid-state conformation. However, the line shape changes are actually characteristic of exchange between one major and one or more minor conformations, with a large population difference and with slow exchange not yet reached. Varying chemical shift differences for the major and minor conformations would account for the different degrees of broadening observed above coalescence. The finding[7] of five conformations for *trans*-cyclodecene at low temperatures and the MM3 strain energies of **1**[2] also suggest that more than one conformation could be populated for the 10-membered lactone. *trans*-Cyclodecene has been shown to have a free-energy barrier of 12 kcal/mol[8] for rotation of the double bond through the ring, which is a necessary step in the interconversion of enantiomeric conformations. The barrier for the corresponding process in the lactone is also of interest, but this process can be studied only by proton NMR spectroscopy. We report here the results of a low-temperature ^{1}H and ^{13}C NMR study of oxacyclodecan-2-one (**1**) and the corresponding 11-membered lactone, oxacycloundecan-2-one (**2**). Free energies for conformations of both lactones were calculated for low temperatures by using Allinger's MM3 program,[9] and electronic energies for three conformations of the 10-membered lactone were obtained from ab initio calculations.

---

[1] For a review of medium-ring lactones, see: Rousseau, G. *Tetrahedron* **1995**, *51*, 2777.

[2] Saunders, M.; Jimenez-Vazquez, H. A. *J. Comput. Chem.* **1993**, *14*, 330.

[3] Wiberg, K. B.; Waldron, R. F.; Schulte, G.; Saunders: M. *J. Am. Chem. Soc.* **1991**, *113*, 971.

[4] Noe, E. A.; Roberts, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 7261.

[5] A dipole-moment study has shown that the parent lactones with eight or fewer ring members exist predominantly in the *E* conformation, and the lactones with larger rings exist mainly in the *Z* conformation: Huisgen, R.; Ott, H. *Tetrahedron* **1959**, *6*, 253.

[6] Free-energy barriers of 7.97 and 9.93 kcal/mol have been reported for methyl formate at −53 °C: Grindley, T. B. *Tetrahedron Lett.* **1982**, *23*, 1757.

[7] Pawar, D. M.; Noe, E. A. *J. Am. Chem. Soc.* **1996**, *118*, 12821.

[8] This free-energy barrier is calculated from the E_A and A values reported by: Binsch, G.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 5157.

[9] Version MM3(94) was used. The latest version of the MM3 program, which is referred to as MM3(96), is available to academic users from the Quantum Chemistry Program Exchange, and to commercial users from Tripos Associates, 1699 South Hanley St., St. Louis, MO 63144.

S0002-7863(98)00427-2 CCC: $15.00

Experimental Section

Baeyer–Villager oxidations[3,10] of cyclononanone and cyclodecanone with a mixture of pertrifluoroacetic acid and Na_2HPO_4 were used to prepare oxacyclodecan-2-one and oxacycloundecan-2-one. The two cyclic ketones were purchased from Aldrich Chemical Co., and 70% H_2O_2 for preparation of pertrifluoroacetic acid was obtained from FMC corporation. The lactones were purified by distillation under reduced pressure, followed by preparative gas chromatography with a 1/4 in. × 4 ft column containing 20% DC 200 on 80/100 chromosorb P. A column temperature of 131 °C was used. The structures of the lactones were established by the room-temperature ^{13}C and ^{1}H NMR spectra, and these spectra showed a satisfactory level of purity for both compounds (Figures 1–4). Small peaks found at δ 43.0 and 24.5 in the ^{13}C spectra of **2** at 18.9 °C did not interfere with the low-temperature study of this compound.

Five percent solutions of the lactones in a 3:1 mixture of $CHClF_2$ and $CHCl_2F$ were prepared in 5 mm thin-walled screw-capped NMR tubes from Wilmad Glass Co., and the sample temperatures were maintained below 0 °C most of the time. A small amount of TMS was added to provide an internal reference for ^{1}H and ^{13}C spectra, which were recorded on a General Electric Model GN-300 wide-bore NMR spectrometer, operating at a frequency of 75.58 MHz for carbons and 300.52 MHz for protons. Spectra were taken with a 5 mm dual probe, and spinning was discontinued below about −120 °C. Up to 800 acquisitions were used, with a sweep width of ±12000 Hz, data size of 64 K, and 3.0 Hz line broadening to increase the signal-to-noise ratio. For ^{13}C spectra, a pulse width of 6 μs, corresponding to a tip angle of 60°, and a pulse repetition period of 1 s were used at intermediate temperatures. The room-temperature and slow-exchange spectra were taken with a delay time of 10 s. For both samples, the ^{1}H NMR spectra were recorded with a pulse width, tip angle, and pulse repetition period of 5 μs, 45°, and 1 s, respectively, except for slow-exchange spectra, for which a delay time of 5 s was used.

Because of the difficulty in ejecting the sample at lower temperatures, the temperature calibration was performed separately, using a copper–constantan thermocouple immersed in the same solvents contained in a nonspinning dummy sample tube and under conditions as nearly identical as possible. The emf's were measured with a Leeds and Northrup Model 8690-2 millivolt potentiometer. The uncertainty in the temperatures was estimated to be ±2 °C.

The rate constants from the carbon spectra were obtained by line shape matching on an Apple computer with a two-site exchange program written by R. A. Newmark.[11] For **1** at −70.8 °C, the rate constant was obtained from the spectrum of the CH_2O hydrogens by use of the approximate equation $[k_c = (\pi/\sqrt{2}) \times \Delta\nu]$.

Coordinates and strain energies[2] for **1** and **2** calculated with Allinger's MM3 force field were provided by Saunders and Jimenez-Vazquez[12] and the coordinates were used as input for an MM3 program purchased from the Quantum Chemistry Program Exchange at Indiana University.[9] Drawings of the structures were made with Spartan, and free energies were obtained for the conformers at the slow-exchange temperatures and used to estimate populations. The MM3 geometries for three conformations of **1** were used as input for Gaussian 94[13] to calculate optimized structures at the HF/3-21G* and MP2/3-21G* levels. These geometries in turn were used as the starting point for full geometry optimizations at the HF/6-311+G* and MP2/6-31G* levels.

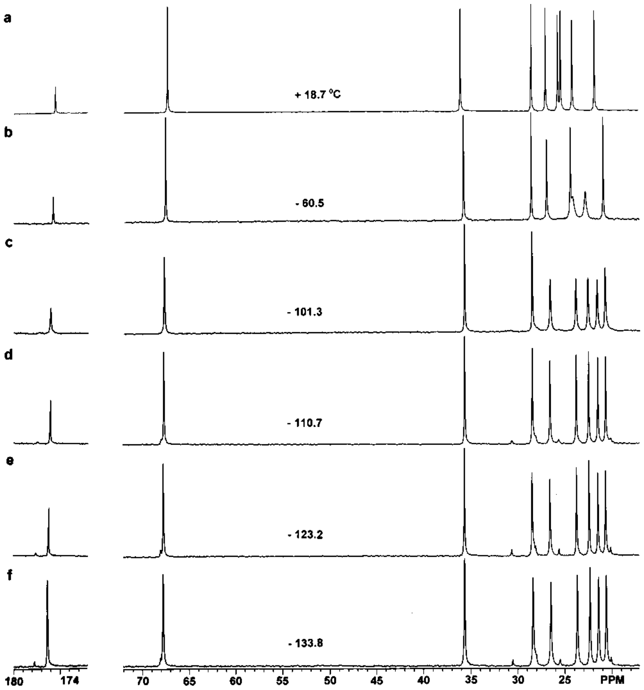

Figure 1. Low-temperature ^{13}C NMR spectra of oxacyclodecan-2-one.

Results and Discussion

The ^{13}C NMR spectrum of a 5% solution of **1** in 3:1 $CHClF_2/CHCl_2F$ at +18.7 °C shows the expected 9 peaks at δ 175.57 (C=O), 67.37 (CH_2O), 36.06, 28.55, 27.04, 25.72, 25.42, 24.18, and 21.80 (Figure 1). By −133.8 °C, signals for two conformations, with populations of 95.2 and 4.8%, corresponding to a free-energy difference of 0.83 kcal/mol, have appeared. The coalescence temperature for the CH_2O peak was −110.7 °C, and coalescence for the carbonyl carbon peak occurs at a somewhat higher temperature (near −101.3 °C), as a consequence of the larger chemical shift difference between minor and major conformations for the latter carbon. Several small signals for the minor conformation can also be seen between δ 20 and δ 31. The carbons of the two conformations which absorb in spectrum **1a** at δ 36.06 have a very small chemical shift difference and appear to be unresolved at −133.8 °C. Populations of 92.9 and 7.1% at −110.7 °C were estimated with the assumption that $\Delta G°$ is constant, and free-energy barriers of 9.09 ± 0.15 and 8.26 ± 0.15 kcal/mol were obtained at this temperature by line shape matching.

The ^{1}H NMR spectrum for the CH_2O protons of **1** decoalesces into two bands of equal intensity, as shown in Figure 2, and in an overlapping process, peaks for the minor conformation also appear by −133.1 °C. At slow exchange, two doublets (major and minor) and two triplets (major and minor) are found. A free-energy barrier of 9.1 ± 0.2 kcal/mol was determined for **1** at the coalescence temperature of −70.8 °C.

The ^{13}C spectrum of 5% **2** in 3:1 $CHClF_2/CHCl_2F$ at +18.7 °C shows 10 peaks at δ 175.82, 65.95, 36.37, 27.39, 26.57, 26.42, 25.91, 25.29, 23.54, and 22.45 (Figure 3). The coalescence temperature for the carbonyl carbon is −109.1 °C, and slow exchange is observed by −139.3 °C. Populations of 64.3 and 35.7% were obtained at slow exchange, and the corresponding free-energy difference is 0.16 kcal/mol. Populations of 61.8 and 38.2% at −109.1 °C were estimated with the assumption of a constant $\Delta G°$, and free-energy barriers at this temperature of 7.83 ± 0.15 and 7.67 ± 0.15 kcal/mol were obtained by complete line shape matching. The proton NMR

---

(10) Emmons, W. D.; Lucas, G. B. *J. Am. Chem. Soc.* **1955**, *77*, 2287.

(11) Newmark, R. A. *J. Chem. Educ.* **1983**, *60*, 45.

(12) We thank Professor Saunders and Mr. Jimenez-Vazquez for sending a complete set of calculations for **1** and **2**.

(13) Gaussian 94: Rev. E. 2, Frisch M. J.; Trucks, G. W.; Gill, P. M. W.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Cheesman, J. R.; Gomperts, R.; Keith, T.; Petersson, G. A.; Montgomary, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, J. V. O.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Fox, D. J.; Head-Gordon, M.; Binkley, J. S.; Gonzales, C.; Martin, R. L.; Defrees, D. J.; Baker, J.; Stewart, J. J.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1995.

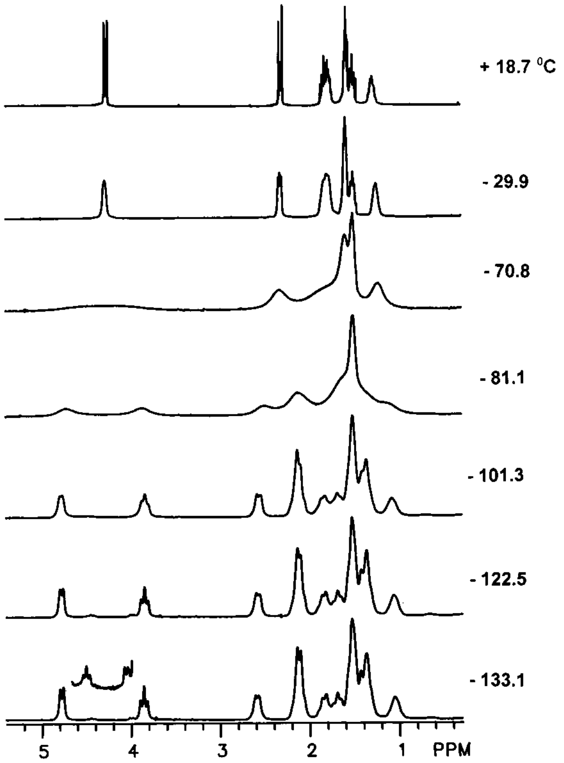

Figure 2. ^{1}H NMR spectra of oxacyclodecan-2-one.

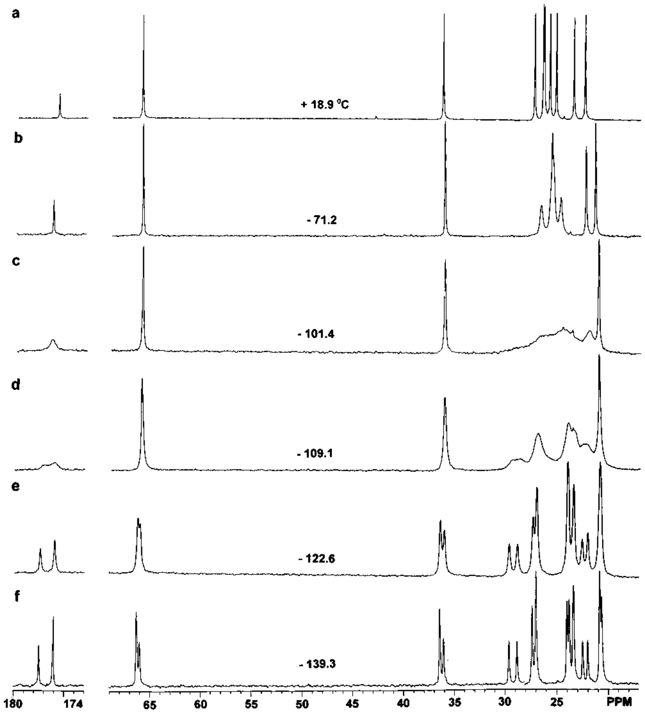

Figure 3. Low-temperature ^{13}C NMR spectra of oxacycloundecan-2-one.

spectra (Figure 4) also correspond to two conformations, and again two triplets and two doublets are found at slow exchange.

Relative strain energies, relative free energies, and estimated populations for six conformations of **1**, calculated by Allinger's MM3 program with the use of geometries provided by Saunders and Jimenez-Vazquez,[12] are listed in Table 1. The strain energies obtained in this way are in agreement within 0.04 kcal/mol of the values reported in ref 2, which are identical to the strain energies provided by Saunders and Jimenez-Vazquez.[12] However, the relative strain energies of Table 1 differ greatly in some cases from the energies reported in ref 3. The most stable conformation in each case is **1a** (**N-I** in ref 3), but **N-II**, for example, corresponds to **1f** and is reported to have an energy of 0.59 kcal/mol relative to **N-I**, while **1f** has a strain energy of 3.00 kcal/mol relative to **1a**. Electronic energies for **1a**−**1c** from ab initio calculations are also shown in Table 2, and drawings for conformations **1a**−**1f** are shown in Figure 5. The calculated free energies and populations predict that the major and minor conformations are **1a** and **1c**, respectively, and the electronic energies of Table 2 are consistent with this conclusion, although the possibility that **1b** is the minor conformation is not excluded. Conformation **1a** resembles the boat-chair-boat conformation of cyclodecane, and conformations **1b** and **1c** both resemble the boat-chair-chair conformation of cyclodecane. Slowing of the process with a free-energy barrier of 9.1 ± 0.2 kcal/mol, which was obtained from the ^{1}H NMR spectra, results in loss of a time-averaged plane of symmetry. The process is

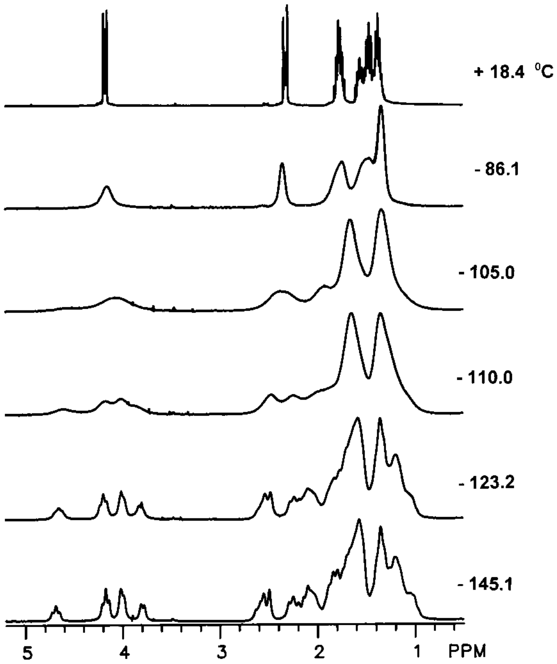

Figure 4. ^{1}H NMR spectra of oxacycloundecan-2-one.

Table 1. Relative Strain Energies,[a] Relative Free Energies, and Populations of Different Conformations of Oxacyclodecan-2-one, Calculated with Allinger's MM3 Program[b]

		25 °C		−133.1 °C	
conformer	rel strain energies (kcal/mol)	rel free energies (kcal/mol)	popul-ations	rel free energies (kcal/mol)	popul-ations
1a	0.00	0.00	0.655	0.00	0.962
1b	1.57	1.16	0.092	1.24	0.011
1c	1.64	0.76	0.182	1.01	0.026
1d	2.64	1.60	0.044	1.83	0.001
1e	2.90	2.30	0.013	2.49	0.000
1f	3.00	2.29	0.013	2.49	0.000

[a] Previously calculated in ref 2. [b] Conformations are numbered according to increasing relative strain energy.

Table 2. Relative Electronic Energies (kcal/mol) of Different Conformations of Oxacyclodecan-2-one, Calculated with Gaussian 94[13]

conformer	HF/6-311+G*	MP2/6-31G*
1a	0.00	0.00
1b	2.32	2.33
1c	0.69	1.67

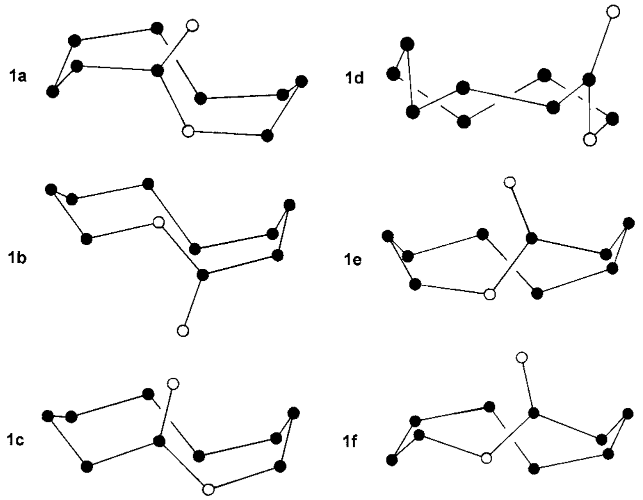

Figure 5. Conformations of oxacyclodecan-2-one.

Table 3. Relative Strain Energies,[a] Relative Free Energies, and Populations of Different Conformations of Oxacycloundecan-2-one, Calculated with Allinger's MM3 Program[b]

		25 °C		−145.1 °C	
con- former	rel strain energies (kcal/mol)	rel free energies (kcal/mol)	populations	rel free energies (kcal/mol)	populations
2a	0.00	0.00	0.688	0.00	0.923
2b	0.42	0.92	0.146	0.69	0.061
2c	0.69	2.20	0.017	1.23	0.007
2d	1.02	2.36	0.013	1.37	0.004
2e	1.17	2.33	0.013	1.55	0.002
2f	1.75	2.03	0.022	2.04	0.000
2g	2.26	1.42	0.063	1.70	0.001
2h	2.26	2.69	0.007	2.52	0.000
2i	2.31	2.30	0.014	2.38	0.000
2j	2.37	2.22	0.016	2.30	0.000

[a] Previously calculated in ref 2. [b] Conformations are numbered according to increasing relative strain energy.

likely to be rotation of the lactone group through the ring, although other equivalent processes may exist. The barrier should be a lower limit for the free-energy barrier to rotation of the lactone group through the ring. Free-energy barriers have been reported for the corresponding process in *trans*-cyclodecene ($\Delta G^{\ddagger} = 12.0$ kcal/mol)[8] and in (*Z*)-azacyclodecan-2-one (11.0 kcal/mol).[14] The lactam was also reported[14] to have two conformations.

MM3 relative strain energies, relative free energies, and calculated populations for 10 conformations of **2** are listed in Table 3, and drawings for six of these conformations are shown in Figure 6. The relative free energies at −145.1 °C suggest that the major and minor conformations may correspond to **2a** and **2b**. Strain-energy calculations[15,16] for cycloundecane predict two low-energy conformations, the [335] and the [12323],[17] and NMR spectra[15] were interpreted in terms of a mixture of these conformations. Cycloundecanone in the solid state has been shown[18] by X-ray crystallography to exist in a [335] conformation, with the carbonyl group within the five-bond segment. Conformation **2a** of the lactone is also similar to [335] cycloundecane, with the lactone group occupying part of the five-bond segment. Dale[17b] has noted that the [335] conformation of cycloundecane can be viewed as derived from [3333] cyclododecane by dropping a carbon, and the [12323] conformation can be regarded as boat-chair-boat cyclodecane with a carbon added at one end. Conformation **2b** bears some resemblence to twist-boat-chair-chair cyclodecane with an additional carbon.

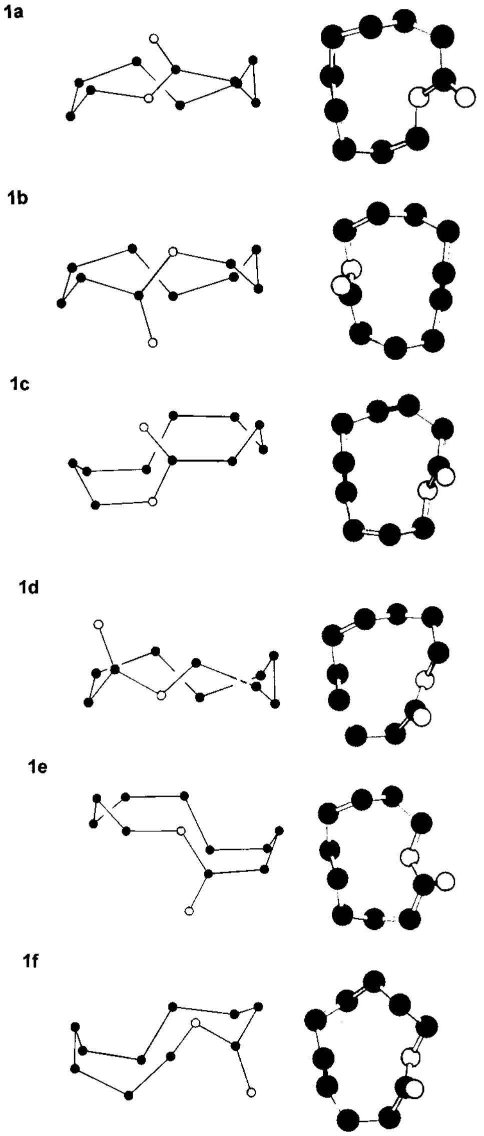

Figure 6. Conformations of oxacycloundecan-2-one.

Acknowledgment. We thank the National Institutes of Health (Grant No. SO6GM08047) for support of this work.

JA980427U

---

(14) Borgen, G.; Dale, J.; Rise, F.; Gunderson, L.-L. *Magn. Reson. Chem.* **1995**, *33*, 252.

(15) Anet, F. A. L.; Rawdah, T. N. *J. Am. Chem. Soc.* **1978**, *100*, 7810.

(16) Saunders, M. *J. Comput. Chem.* **1991**, *12*, 645.

(17) For the nomenclature used here, see: (a) Dale, J. *Top. Stereochem.* **1976**, *9*, 199. (b) Dale, J. *Acta Chem. Scand.* **1973**, *27*, 1115−1130.

(18) Groth, P. *Acta Chem. Scand. Ser. A* **1974**, *28*, 294.