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Conformations of Cycloundecane

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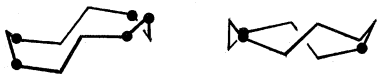

Cycloundecane (**1**) was shown to exist at −183.1 °C as a mixture of the [12323] (∼59%) and [335] (∼41%) conformations. Populations were determined from the ^{13}C NMR spectrum, and assignments were based on the ^{13}C spectra, calculated free energies and chemical shifts, and information from the literature, including X-ray studies of solid derivatives and calculated barriers.

Introduction

The conformations of the parent medium-ring cycloalkanes include many energy minima,[1] and determination of the conformational equilibria in solution is an interesting challenge. The even-membered rings including cyclodecane[2,3] have been studied more extensively than the odd-membered rings such as cycloundecane (**1**), which is the subject of this work. Early semiquantitative studies by Dale[4] predicted four conformations of **1** with relative strain energies of 0.0−0.6 kcal/mol and three substantially above this range. Anet and Rawdah[5] found the quinquangular [12323] and triangular [335] conformations to be essentially equal in strain energy according to MOLBUILD and 1.2 to 1.7 kcal/mol lower in energy than the other four conformations considered. Estimates of several barriers were also made.[5] Stochastic searches for **1** found 40 energy minima by MM2 and 29 by MM3.[2] Kolossvary and Guida[6] also reported 40 conformers by MM2, and barriers were calculated for 37 pairs of conversions involving 16 conformations.[6] Relative strain energies[2] for the [12323] (**1a**), [335] (**1b**), [13223] (**1c**), and [12314] (**1d**) conformations were 0.00, 0.26, 1.17, and 1.50 kcal/mol by MM3 and 0.00, 0.26, 1.02, and 0.93 kcal/mol by MM2. Both **1a** and **1b** have been found by X-ray crystallography for the ring conformations of solid derivatives of **1**. Cycloundecanone[7a] adopts a [335] conformation in the solid state at −165 °C, and low-temperature NMR spectra indicated[7b] that this ketone exists predominantly in a single, unsymmetrical conformation in solution, but the [12323] was reported[8] for the oxime in the solid state at −160 °C. Cycloundecanone-4-phenylsemicarbazone[9] in the solid state adopts a [335] conformation at −138 or −150 °C, but the major conformation is the [12323] at +20 °C. The conformation of cycloundecylmethyl-1-naphthylcarbamate[10] also changes with temperature in the solid state, from [12323] at −153 °C to [335] (major) at +20 °C.

Dynamic NMR spectroscopy, where applicable, can provide detailed information about conformational equilibria in solution, but only line broadening was observed in the published[11] 63.1 MHz ^{13}C and 251 MHz ^{1}H NMR spectra of **1** at −165 and −164 °C; decoalescence was not reported. The present study characterizes the populated conformations of **1** in solution by low-temperature ^{13}C NMR spectroscopy at higher field and

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(1) For example, eight conformers were found[2] for cyclononane by MM2 or MM3, and the numbers for cyclodecane were 18 and 16.
(2) Saunders, M. *J. Comput. Chem.* **1991**, *12*, 645.
(3) Pawar, D. M.; Smith, S. V.; Mark, H. L.; Odom, R. M.; Noe, E. A. *J. Am. Chem. Soc.* **1998**, *120*, 10715.
(4) (a) Dale, J. *Acta Chem. Scand.* **1973**, *27*, 1115, 1130. (b) Dale, J. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Eds.; Wiley-Interscience: New York, 1976; Vol. 9, p 199. In Dale's nomenclature system,[4a] corner positions are assigned, and the numbers of bonds between adjacent corners are given in brackets, beginning with the smallest number and continuing around the ring in the direction which puts the lower numbers first. The conformations of cycloundecane have three or five corners and the same number of sides. Nonadjacent corners have dihedral angles near 60° on either side, and of the same sign. Adjacent corners have gauche dihedral angles on either side, but of opposite sign.
(5) Anet, F. A. L.; Rawdah, T. N. *J. Am. Chem. Soc.* **1978**, *100*, 7810.
(6) Kolossvary, I.; Guida, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 2107.
(7) (a) Groth, P. *Acta Chem. Scand.* **1974**, *A28*, 294. (b) Anet, F. A. L.; St. Jacques, M.; Henrichs, P.; Cheng, A. K.; Krane, J.; Wong, L. *Tetrahedron* **1974**, *30*, 1629.
(8) Groth, P. Acta *Chem. Scand.* **1979**, *A33*, 503.
(9) (a) Groth, P. *Acta Chem. Scand.* **1980**, *A34*, 609. (b) Sim, G. A. *Acta Crystallogr.* **1991**, *C47*, 406.
(10) Russel, M. A.; Sim, G. A. *Acta Crystallogr.* **1990**, *B46*, 671.
(11) Cheng, A. K. Ph.D. Thesis, University of California, Los Angeles, 1973, p 227.

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TABLE 1. Calculated Energies (kcal/mol) for Conformations of Cycloundecane

				relative free energy at −190 °C		
conformer	Dale's nomenclature	symmetry	relative strain energy, MM3[a]	MM3	MM4	HF/6-311G*
1a	[12323]	C_1	0.00	0.01	0.00	0.00
1b	[335]	C_1	0.26	0.00	0.30	0.50
1c	[13223]	C_2	1.17	1.50	1.18	0.95
1d	[12314]	C_1	1.50	0.82	0.95	1.54
1e	[344]	C_2	1.65	1.30	1.81	2.38
1f	[344][b]	C_1	1.92	1.78	2.16	3.19[c]

[a] Relative MM3 strain energies were previously reported by Saunders (ref 2). [b] Conformation **1f** has C_1 symmetry but is not far from C_2 symmetry. [c] This conformation has one imaginary frequency at this level.

TABLE 2. Calculated Barriers in kcal/mol for Conformations of Cycloundecane

			barrier	
	process	mode[a]	MM2[a]	MOLBUILD[b]
1a → 1a	[12323] → [12323]	(F3F3K5)	8.67	
1a → 1b	[12323] → [335]	(K5F3F3)	5.72	8.0
1b → 1b	[335] → [335]	(F3k5F3)	2.64	2.0
1b → 1e	[335] → [344]	(K3)	9.19	4.2
1b → 1f	[335] → [344]	(K3)	4.20	
1e → 1f	[344] → [344]	(K3)	4.17	

[a] The mode describes the pathways for the conversions, as described by Kolossvary and Guida in ref 6. For example, K3 is their abbreviation for K3 kayaking, in which a dihedral angle goes to zero and then reverses sign. The first three conversions are complex and involve more than one elementary process. [b] Reference 5.

lower temperatures than used previously.[11] Also, relative free energies at −190 °C were obtained from MM3, MM4, and ab initio calculations. The ^{13}C chemical shifts were calculated by the GIAO method at the HF/6-311G* level for the [12323] and [335] conformations.

Results and Discussion

The symmetry, calculated strain energies, and relative free energies (−190 °C) for the first six conformations are shown in Table 1, and calculated barriers by MOLBUILD[5] and MM2[6] force fields are compared in Table 2.

The calculations predict that **1a** and **1b** are the most stable and are likely to be measurably populated, but do not rule out the possible presence of **1c** or **1d**.

Low-temperature ^{13}C NMR spectra of **1**[12] are shown in Figure 1. At +18 °C, a single averaged peak at δ 26.2 was observed. By −167.8 °C, this peak was replaced by 11 peaks of equal intensity and an additional intense, broad peak near δ 26. The broad signal decoalesces by −183.1 °C into two peaks, still broad, near δ 22 and δ 28. The 11 peaks, from a conformation of C_1 symmetry, have sharpened by this temperature. The additional absorption near δ 22 and δ 28 shows the presence of a second conformation. The calculations and X-ray studies of solid derivatives suggest that the [12323] and [335] conformations are likely to be populated, and the spectra are interpreted in terms of **1a** and **1b**. A few of the barriers calculated by Kolossvary and Guida[6] are shown in Table 2, and an extensive table of barriers is included in the Supporting Information. The lowest barrier for **1a** is 5.722 kcal/mol for conversion to **1b**. A process with a barrier of this magnitude should be stopped on the NMR time scale by −183.1 °C, and the 11 sharp peaks are

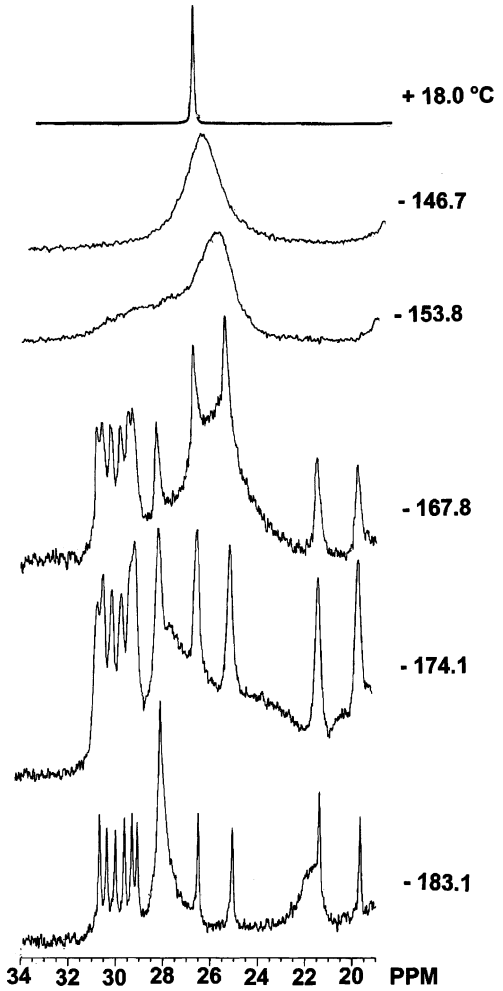

FIGURE 1. Low-temperature ^{13}C NMR spectra for a 2% solution of cycloundecane in propane.

assigned to **1a**. The barrier of only 2.636 kcal/mol for the [335] to [335] conversion ensures that this process will be rapid on the NMR time scale at all experimentally accessible temperatures, resulting in a time-averaged 2-fold axis of symmetry; thus, a maximum of six peaks, with one of half the intensity of the other five, could be observed for **1b**. The next higher barrier of 4.195 kcal/mol, for the **1b → 1f** conversion, suggests that this process is responsible for the line shape changes of the second conformer between −167.8 and −183.1 °C.[13]

(12) Cycloundecane was prepared by hydrogenation of 1,2-cycloundecadiene. A dynamic NMR and computational study of the diene was reported: Brown, J., II; Pawar, D. M.; Noe, E. A. *J. Org. Chem.* **2003**, *68*, 3420.

(13) A reviewer has suggested that an approximate barrier for this process could be obtained from the chemical shift difference for the two lines of about 500 Hz at −183 °C and from the approximate coalescence temperature (around −174 °C). The reviewer calculated a $\Delta G^{\ddagger}$ of about 4.2 kcal/mol, in good agreement with theory.[6]

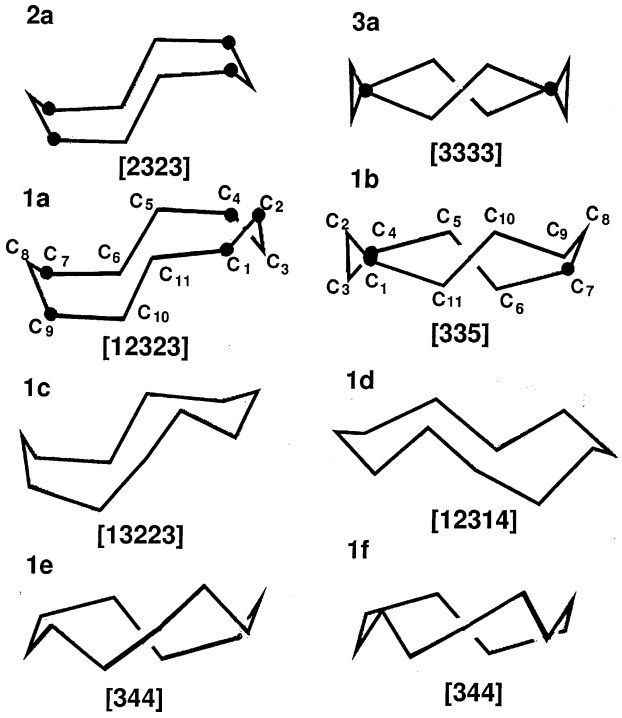

FIGURE 2. Low-energy conformations of cycloundecane (**1a**−**f**), cyclodecane (**2a**), and cyclododecane (**3a**).

In Figure 2, structures are shown for conformations **1a**−**f** of cycloundecane and for the most stable conformations of cyclodecane ([2323], **2a**)[3] and cyclododecane ([3333], **3a**).[14] As noted by Dale,[4] the quinquangular [12323] conformation of **1** is related to the preferred rectangular BCB [2323] conformation of cyclodecane, and the triangular [335] conformation can be formally derived from the most stable [3333] conformation of cyclododecane. The corner positions are marked by filled circles for **1a**, **1b**, **2a**, and **3a**, and the carbons are numbered for **1a** and **1b**.

In Figure 3, ^{13}C chemical shifts from ab initio calculations for the [12323] and [335] conformations are shown graphically and compared with the experimental spectrum at −183.1 °C.

The carbon numbers from Figure 2 are included. The corner carbons of **1a** (7, 2, 9, 4, and 1) are calculated to absorb at the lowest field, as observed for **2a** [3] and **3a**.[14]

The corner carbons of **1b** (7, 4, and 1) are also expected to absorb at low field, although a noncorner carbon (no. 8) is calculated to absorb between carbons 7 and 4. As noted above, the [335] to [335] process has a very low barrier, resulting in time-averaged C_2 symmetry for the conformation at all attainable temperatures, and a graphic representation for the averaged spectrum ([335]av) is also shown in Figure 3. This spectrum indicates that the broad peak near δ 22 is from four carbons and would split into two peaks of equal intensity at slightly lower temperatures. The broad absorption near δ 28 is expected to contain the intensity for the other seven carbons.

Integration by a cut-and-weigh method[15] of the spectrum at −183.1 °C gave populations of ∼59% **1a** and ∼41% **1b**. No evidence was found for any additional conformations.

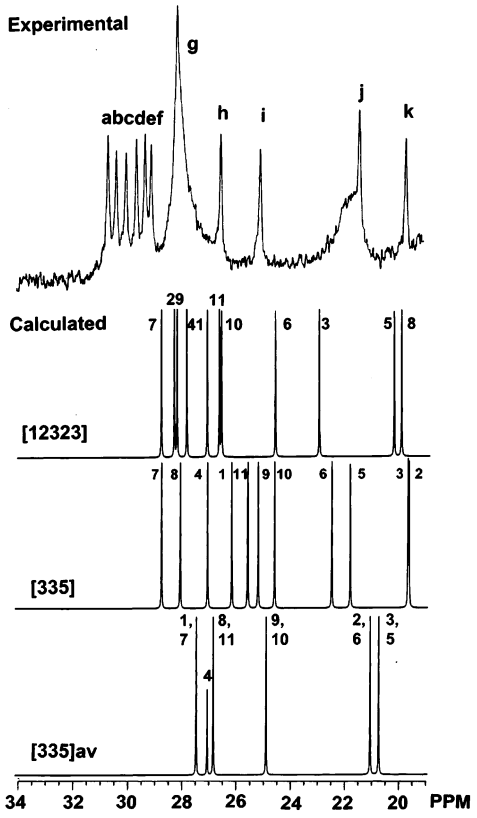

FIGURE 3. Experimental (at −183.1 °C) and calculated (GIAO, HF/6-311G*) ^{13}C NMR spectra of cycloundecane.

Conclusions

The ^{13}C spectrum of cycloundecane at −183.1 °C includes 11 peaks of equal intensity for a conformation of C_1 symmetry and two broad, additional peaks for a second conformation. Based on calculations and the results of X-ray studies, the most likely conformations are the [12323] and the [335]. Calculated barriers[6] for cycloundecane conversions make possible the assignment of the [12323] conformation to the 11 peaks and the [335] to the conformation for which exchange of carbon sites is not stopped on the NMR time-scale by −183.1 °C.

Experimental and Methods Section

Cycloundecane was synthesized by complete reduction of 1,2-cycloundecadiene. The diene (1.87 g) and 90 mg of 10% Pd/C in 30.7 mL of methanol were placed in a flask equipped with a hydrogen-filled balloon, and the mixture was stirred at room temperature for 24 h. The resulting solution was filtered, extracted with pentane, and dried over Drierite. Solvent was removed by rotary evaporator to give 1.15 g (59.9%) cycloundecane. The purity of the compound was determined by the room-temperature ^{13}C NMR spectrum.

A 2% solution of **1** in propane was prepared in a 5 mm thin-walled screw-capped NMR tube, and a small amount of TMS was added for an internal reference. *Caution:* high pressure. The sample tube was stored and handled below 0 °C most of the time. Spectra were recorded on a wide-bore NMR spectrometer at Jackson State University, operating at 75.57 MHz for carbon. The ^{13}C spectra

(14) Anet, F. A. L.; Cheng, A. K.; Wagner, J. J. *J. Am. Chem. Soc.* **1972**, *94*, 9250.

(15) The weight of **1a** was obtained as 11 times the weight of peak i in Figure 3, and the weight of **1b** was obtained by subtracting the weight of peak i from the combined weights of peak j and the overlapping broad peak near δ 22 and multiplying this difference by 11/4.

for **1** were obtained from +17.0 to −183.1 °C with a 5 mm dual probe over a period of many months. A pulse width of 8.2 μs was used, corresponding to a tip angle of 83°, and the repetition rate was 1 s for all recorded temperatures. Spinning was discontinued below about −140 °C. Because ejecting the sample at lower temperatures was difficult, due to the ice formation on the inner wall of the stack, the temperature calibrations were performed separately, using a copper−constantan thermocouple immersed in propane solvent contained in a nonspinning dummy sample tube and under conditions as nearly identical as possible. The emf's were measured with a millivolt potentiometer. The uncertainty in the temperatures was estimated to be ±2 °C, although differences in temperatures are more accurate (perhaps ±1 °C).

The initial structure for cycloundecane was generated using Spartan 5.0,[16] and the geometry was exported into the MM3 program.[17] A default method for searching conformational space was used with a kick size of 2 Å and 1000 pushes. The structures obtained were organized in increasing order of strain energy and matched the published results of Saunders.[2] The free energies and lowest frequencies were obtained at 25 °C and −190 °C for the first 19 conformations (nos. 1−19) which included four transition states (nos. 7, 9, 14, and 18) and 15 minima. The 15 minimum energy structures in increasing order of MM3 steric energies are designated as conformations **1a**−**o** in Table S1 (Supporting Information). A search of conformational space was done by MM4, and the strain energies for the conformations within a 5 kcal/mol window are included in Table S2 (Supporting Information), along with strain energies from other force fields. The free energies at two temperatures for the 11 conformations in this window are shown in Table S3 (Supporting Information).

The MM3-optimized geometries were used as inputs for ab initio calculations. Full-geometry optimizations were performed subsequently at the HF/3-21G*, HF/6-31G*, and HF/6-311G* levels.[18] These calculations were followed by calculations of vibrational frequencies (analytical method), and all structures were characterized by the absence of imaginary frequencies except for **1f**, which was a minimum energy conformation in MM3 but was characterized by an imaginary frequency (−30.89 cm^{-1}) at the HF/6-311G* level. Our results for the highest Hartree−Fock level are shown in Table S4 (Supporting Information), and calculations at the MP2/3-21G* level[19] for **1a**−**e** are included in Table S5 (Supporting Information).

Kolossvary and Guida[6] reported 17 minima within a 25 kJ/mol window by MM2, and 37 saddle points were found within a 50 kJ/mol window. However, the associated Supporting Information provides details for 16 (not 17) local minima. A geometry comparison between these 16 MM2 structures and our 15 MM3 structures (**1a**−**o**) showed 14 matches. Our conformation **1o** is not found among Kolossvary and Guida's 16 conformations, and their twelfth and thirteenth conformations in order of increasing MM2 energies are not among our 15. Barriers from these workers[6] and several from Anet and Rawdah[5] are included in Table S6 (Supporting Information). Three conversion numbers (4, 12, and 22)[6] do not appear because they involve one of the two conformations of their 16 not found among our 14. The corresponding dihedral angles for the conversions are shown in Table S7 (Supporting Information).

Table S8 (Supporting Information) shows that the dihedral angles obtained for conformations of **1** by different methods are very similar.

The chemical shifts (GIAO, HF/6-311G*) calculated for **1a** and **1b** and used for Figure 3 are shown in Table S9 (Supporting Information).

All ab initio calculations were done at the Mississippi Center for Supercomputing Research (MCSR), University of Mississippi, Oxford, MS, using the Gaussian 94 and 98 series of programs. The MM3 calculations and geometry visualizations were done at the molecular modeling laboratory, Jackson State University, funded by the Army High Performance Computing Research Center. The MM4 calculations were done using the computational facilities at the University of Georgia, Athens, GA.

Acknowledgment. We thank the National Science Foundation (NSF-CREST Grant No. HRD-9805465, to Jackson State University) for financial support and the Mississippi Center for Supercomputing Research for a generous amount of computing time. Some calculations were done using the molecular modeling laboratory at Jackson State University, funded by the Army High Performance Computing Research Center. The NMR facility at Jackson State University used for this study was supported by the National Institutes of Health (RCMI Grant No. G12RR13459).

Supporting Information Available: Optimized geometries, calculated energies, dihedral angles, and magnetic shielding tensors are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) *Spartan version 5.10*.; Wavefunction, Inc.: Irvine, CA.

(17) Molecular mechanics (MM3) program version 2000 was used. The latest version of this program is available to academic users from the University of Georgia, Athens, GA.

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