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Conformations of Azocane (Azacyclooctane)

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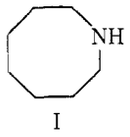
The ^{1}H and the natural-abundance ^{13}C NMR spectra of azocane (azacyclooctane) (I) have been measured from −10 to −180 °C. A dynamic NMR effect is observed in the ^{1}H NMR spectra of I in the vicinity of −120 °C, and is attributed to ring inversion in a boat–chair, which is the predominant conformation of I. The free energy of activation ($\Delta G^{\ddagger}$) for this process is 7.3 ± 0.2 kcal/mol. The ^{13}C NMR spectra of I show a dynamic NMR effect which does not arise from ring inversion in the boat–chair, but rather from the interconversion of this conformation with a small concentration (3% at −112 °C) of a crown–family conformation. The thermodynamic and kinetic parameters for the boat–chair to crown process are as follows: ΔG° = 1.2 ± 0.1 kcal/mol, $\Delta G^{\ddagger}$ = 10.5 ± 0.2 kcal/mol.

Lambert and Khan[1] have recently measured the ^{1}H and ^{13}C NMR spectra of azocane (I) and related compounds from room temperature to −120 °C. We have also studied the dynamic NMR behavior of I at low temperatures,[2] but our results, which we now report, differ in some important respects from those obtained by these authors.



I

Lambert and Khan[1] found that the α resonance of azocane in the 270 MHz ^{1}H NMR spectrum splits into two bands of equal intensities at low temperatures. The two bands were well resolved at −107 °C and coalesced to a single band at about −95 °C. These authors concluded that azocane has a boat–

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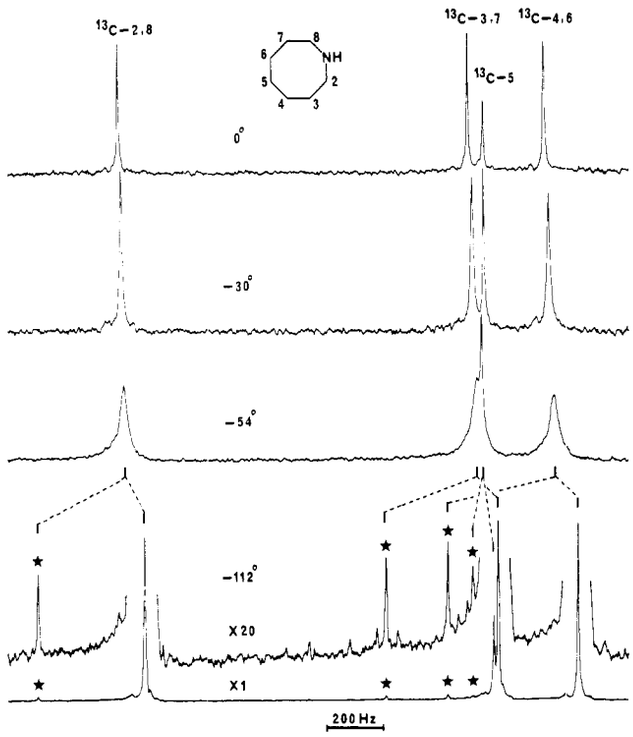
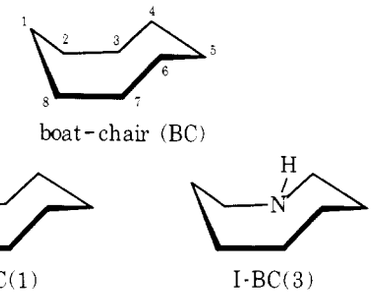


Figure 1. Proton-decoupled 63.1 MHz ^{13}C NMR spectra of azocane in $CHFCl_2$ at various temperatures. The spectrum at −112 °C is the Fourier transform of the sum of 6000 free induction decays. The peaks marked with stars belong to the crown-family conformation. The assignments of the C-3,7 and C-4,6 resonances are not certain and could be interchanged. The small peaks near the bases of the major signals are spinning side bands.

chair conformation analogous to that of oxocane[3] and cyclooctane.[4] The dynamic NMR effect was ascribed to a ring reversal process in the boat–chair, which is undergoing a rapid degenerate pseudorotation at these temperatures. Although we are in general agreement with these conclusions, our NMR data, which were obtained at 251 MHz, show that the coalescence temperature for the α protons is −118 °C, i.e., 23 °C lower than that reported.[1] The difference in coalescence temperatures resulting from the different spectrometer frequencies should be less than 1 °C. We have carefully checked the calibration of the temperature of the probe in our spectrometer.[5] Also, the same coalescence temperature for azocane was obtained in separate experiments carried out 6 years apart.

The free-energy barrier for ring inversion in the boat–chair conformation of azocane is calculated to be 7.3 ± 0.2 kcal/mol, which is lower than the 8–9 kcal/mol given by Lambert and Khan,[1] as a result of the temperature differences discussed above. The ring inversion barrier in azocane is similar to that of oxocane (7.4 kcal/mol)[3] and a little smaller than that of cyclooctane (8.1 kcal/mol).[6]

The ^1H NMR spectrum of azocane does not show any additional dynamic NMR effect between −140 and −180 °C, and thus there is no evidence for nitrogen inversion or ring pseudorotation in the boat–chair conformation. As in the case of oxocane and cyclooctanone, and as is discussed in detail by Lambert and Khan, the position of the nitrogen atom in the boat–chair should be such as to relieve nonbonded transannular repulsions, and therefore positions 1, 3, and 7 (a mirror-image position to 3) in the boat–chair conformation are possible for the nitrogen atom. This requires that the lone pair of electrons on the nitrogen atom be in an inside orientation, and therefore the configuration at the nitrogen atom should be strongly biased, with the NH proton placed in an outside, or equatorial, position, as in I-BC(1) or I-BC(3). In



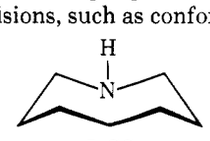
any case, ring pseudorotation of the boat–chair and nitrogen inversion are probably rapid at the temperatures investigated, so that the effective (time-averaged) symmetry of azocane in the boat–chair conformation should be C_s from the NMR point of view at, say, −140 °C, and this is consistent with the experimental data.

Lambert and Khan[1] reported that the ^{13}C NMR spectrum of azocane was temperature independent at 22.6 MHz over the temperature range of 25 to −120 °C. In our initial study,[2] we also did not detect any dynamic NMR effect in the ^{13}C spectrum of azocane. The finding[7] that cyclooctane itself is a 95:5 mixture of boat–chair and crown–family conformations prompted us to reinvestigate the ^{13}C NMR spectrum of azocane.

As shown in Figure 1, the ^{13}C NMR spectrum of azocane at 63.1 MHz is distinctly temperature dependent and shows a dynamic NMR effect characteristic of a strongly one-sided conformational equilibrium. The four sharp lines in the ^{13}C NMR spectrum of azocane at room temperature broaden below about −20 °C, reaching a maximum width between −50 and −60 °C.

The lines become sharp again at about −80 °C or below, but the spectrum now has the β- and δ-^{13}C resonances in an opposite order from that found at room temperature. This spectrum also shows the presence of four weak bands which are quite broad at −80 °C but become sharp at somewhat lower temperatures, e.g., −112 °C (Figure 1). Thus, there are two different conformations of azocane, and their ratio is about 97:3 at −112 °C, corresponding to a $\Delta G°$ of 1.2 ± 0.1 kcal/mol. The observed line shapes at −54 °C were well reproduced by calculations based on the exchange scheme shown in Figure 1, with a rate constant for the change from the major to the minor conformation of 150 s^{-1}. The free energy of activation ($\Delta G^{\ddagger}$), as calculated from the absolute rate theory, is 10.5 ± 0.2 kcal/mol. The values of $\Delta G°$ and $\Delta G^{\ddagger}$ for azocane are very similar to those observed[7] for cyclooctane (1.7 and 10.5 kcal/mol, respectively) for the equilibrium between the boat–chair and a crown–family conformation.

The crown family in cyclooctane includes the highly symmetrical (D_{4d} point group) crown and distorted crowns of lower symmetries, namely, the chair–chair (C_{2v}) and the twist-chair–chair (D_2). The members of the crown family do not necessarily represent distinct conformations, since calculations show that pseudorotation between these members may be almost free. In the case of azocane, the presence of a nitrogen atom with a lone pair of electrons should lead to a conformation with the nitrogen placed to give the minimum trans-annular repulsions, such as conformation I-CC. Other



I-CC

conformations in the crown family, however, are not excluded. In any case, either because of rapid pseudorotation and nitrogen inversion or because of symmetry, the effective (time-averaged) symmetry of the crown–family conformation is C_s. Thus the ^{13}C spectrum of azocane in this conformation

Table I. Carbon-13 Resonances[a] in Azocane

temp, °C	conformation	^{13}C-2,8	^{13}C-3,7	^{13}C-5	^{13}C-4,6
0	*b*	49.1	29.8	29.0	25.6
−54	*b*	(48.7)[c]	(29.3)[c]	(28.9)[d]	(24.9)[c]
−112	boat–chair	48.4	28.8	29.0	24.3
−112	crown	54.3	35.3	30.2	31.6

[a] In parts per million with respect to internal tetramethylsilane. [b] Boat–chair and crown. [c] Line width at half-height is 30 ± 5 Hz. [d] Sharp line.

should consist of four lines in the ratio of 2:2:2:1, as observed.

The four strong ^{13}C lines in the spectrum at −112 °C are assigned to the boat–chair and are consistent with the time-averaged C_s symmetry that is expected at this temperature, as was discussed previously. The assignments of the boat–chair and crown–family conformations are supported by ^{13}C chemical shifts (Table I). Carbons are shielded in the major conformation when compared with corresponding nuclei in the minor conformation, as is found in the case of cyclooctane, and as is also expected from the presence of shielding gauche butane interactions (γ effects)[8] in the boat–chair but not the crown–family conformations.

The ^{13}C NMR spectrum of azocane did not show any further dynamic NMR effect between −110 and −180 °C. The crown–family conformation is difficult to observe at very low temperatures, because of its small population. These spectra are consistent with rapid nitrogen inversion and ring pseudorotation in the boat–chair above −180 °C.[9]

Conclusions

The conformational properties of azocane are similar to those of cyclooctane and the dominant conformation is a boat–chair. As in cyclooctane, the crown–family conformation in azocane can be detected fairly easily by ^{13}C NMR, but it is virtually impossible to observe with ^{1}H NMR, at least without the use of massive deuteration to simplify the spectrum.

Experimental Section

The azocane was obtained from Aldrich Chemical Co. and used without further purification.

All NMR spectra were measured on a superconducting solenoid spectrometer operating at 59 kG.[10] The proton noise-decoupled ^{13}C NMR spectra are Fourier transforms of accumulated free induction decays and were obtained under the following conditions: 45° pulse angle, 8K data points, and 4000 Hz spectrum width and an exponential broadening function corresponding to 4 Hz broadening. For variable temperature NMR spectra, $CHFCl_2$ or a mixture of $CHFCl_2$ and CHF_2Cl (1:1) was used as the solvent and a source of an ^{19}F resonance for lock purposes. Tetramethylsilane was used as an internal reference for both the ^{1}H and ^{13}C NMR spectra. All temperatures were measured with a copper–constantan thermocouple situated a few centimeters below the sample. Temperature calibrations were made by inserting another thermocouple in an NMR tube containing a standard amount of solvent and with the probe outside of the magnetic field.

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