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CONFORMATIONAL ANALYSIS OF AMINOCYCLOHEXANE USING ^{15}N NUCLEAR MAGNETIC RESONANCE AT LOW TEMPERATURE

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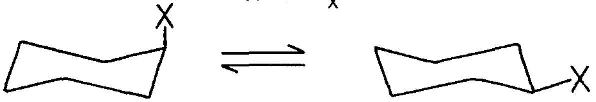
Abstract: The axial form of ^{15}N enriched aminocyclohexane has been detected at 173K, permitting the first direct measurement of the conformational free energy of the NH_2 group.

Relative intensities of individual conformer resonances in NMR spectra at low temperature, where ring inversion is slow on the spectral timescale, permit the most direct estimates of the conformational free energy ($-\Delta G^o_X$) for a substituent X bonded to cyclohexane.



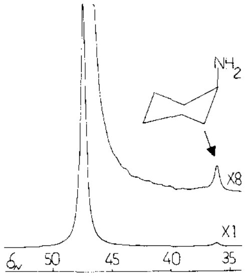
For X = NH_2, small differences in methine proton shifts have precluded such a measurement via ^1H NMR(1), although determinations of $-\Delta G^o_{NH_2}$ were made via additivity using cis-4-methylcyclohexylamine.(1)

^{13}C NMR at low temperature has also been applied to this problem(2), but no spectrum of the axial form of aminocyclohexane could be obtained. It was suggested(2) that dimer formation occurs in the relatively concentrated solutions needed for natural abundance ^{13}C studies, thus increasing the effective size of the NH_2 group and rendering observation of the axial conformer more difficult. In more recent work(3) an analysis of the ^{13}C NMR lineshape at the coalescence temperature (193K) has led to an indirect estimate of 1.23 kcal/mol for $-\Delta G^o_{NH_2}$.

We wish to report the first detection of the axial conformer at 173K using 99.9% ^{15}N enriched material and ^{15}N NMR at 20.28 MHz.(4) Under conditions of complete ^1H noise decoupling in the ^{15}N spectrum, there is a beneficial nuclear Overhauser enhancement (n.O.e.) near the theoretical maximum of -3.93(5) for aminocyclohexane. This, combined with the high level of isotopic enrichment, allows clear detection of the axial conformer resonance after only 500-800 spectral accumulations at 173K for 1.0 M solutions in toluene-d_8 and CD_2Cl_2.

At 293K in C_7D_8, the ^{15}N resonance of aminocyclohexane appears at δ_N = 42.7(6). Upon cooling to 173K, two resonances are evident at δ_N = 43.4 and 32.9. These lines have relative intensities of 67.1:1.0, and correspond to the equatorial and axial conformers respectively. The chemical shift difference of 10.5 ppm is similar to that reported previously(7) for the model compounds cis- and trans-4-t-butylcyclohexylamine.

For CD_2Cl_2 solutions, the axial conformer appears at $\delta_N = 35.9$ and the equatorial at $\delta_N = 47.4$. The relative intensity of these resonances at 173K is 1.0:60.4 as computed electronically, (spectrum shown below, 754 accumulations).



On the basis of the relative peak areas(8) and by using the equation $-\Delta G^o = RT\ln K$, one can obtain values for $-\Delta G^o_{NH_2}$ of 1.44 ± 0.07 and 1.41 ± 0.07 kcal/mol for C_7D_8 and CD_2Cl_2 solutions respectively. Other estimates of this parameter range from 1.1 to 1.8 kcal/mol(9) depending on the solvent and method employed for determination. Apparently dimer formation, if indeed it occurs in the present solutions does not substantially alter the effective size of the NH_2 moiety.

The ^{15}N labelled aminocyclohexane was prepared via $^{15}NH_4OH$ treatment of the organoborane derived from cyclohexene, according to published methods.(10)

References and Notes

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2. H.-J. Schneider and V. Hoppen. Tetrahedron Lett. 579 (1974).
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4. Spectra were recorded using a Varian XL-200 NMR spectrometer under conditions of complete ^1H noise decoupling. Sweep width was 10,000 Hz, acquisition time 1.6 seconds with 32K data points. Pulse repetition rate was 5.0 seconds, with 60^o observe pulses.
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6. Chemical shifts were measured relative to external saturated aqueous NH_4Cl and then converted to the standard ^{15}N scale in ppm relative to NH_3 using a conversion constant of +27.3 ppm (p. 32 of ref. 5).
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8. One is assuming that the n.O.e.'s for axial and equatorial nitrogen are equal, as are the ^{15}N T_1's. Both factors are dominated by directly bonded protons, rendering the assumption valid at least to a first approximation.
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