NUCLEAR MAGNETIC RESONANCE SPECTRA OF SIX-MEMBERED ALCYCLIC RING COMPOUNDS AT LOW TEMPERATURE

IV. PARTIALLY DEUTERATED 1,2-*trans*-CHLOROIODOCYCLOHEXANE

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ABSTRACT

A 50/50 mole% mixture of 1-iodo-2-chloro-1,3,3-trideutero-, and 1-chloro-2-iodo-1,3,3-trideutero-cyclohexane has been synthesized. At −93° C in a CS_2 solution iodochlorocyclohexane shows resolution into diaxial and diequatorial halogen forms. Analysis of the adjacent proton resonance signal intensities shows that this compound exists 68±3 mole% in the diaxial halogan form. This is quite similar to 1,2-dibromocyclohexane, which has 70 mole% in the diaxial form, and is in contrast to 1,2-dichlorocyclohexane, which has a more stable diequatorial form.

INTRODUCTION

In six-membered alcyclic ring compounds, axial and equatorial protons have been distinguished by chemical shift measurements (1). The indirect spin–spin coupling constants between the various protons have energies decreasing in the order $J\mathrm{e}_1\mathrm{a}_1 > J\mathrm{a}_1\mathrm{a}_2 > J\mathrm{e}_1\mathrm{a}_2 \simeq J\mathrm{e}_1\mathrm{e}_2$ (17). In this notation, e_1 corresponds to a proton equatorial on carbon 1, a_1 axial on carbon 1, e_2 equatorial on carbon 2, and a_2 axial on carbon 2.

Several other techniques have been used to determine the configurations in the six-membered ring compounds. In particular, electron diffraction methods (2) give the bond lengths and bond angles in some cases. The technique is limited to the gas phase and the method is not sensitive enough to give accurate populations of two chair forms in equilibrium. Infrared measurements have been made on these types of compounds, and the separation of the skeletal carbon vibrations from the vibrations of the >CH bonds have been made (3–5). The >CH stretching region of the infrared spectrum of these molecules is too complex to interpret in terms of the configurations of the rings. Selective deuteration of the rings and observation of the >CD stretching region have been carried out (15, 14). Axial and equatorial deuterium atoms in the rings have been distinguished by this means, but the method has not been accurate enough to determine an analysis of a compound with an unsymmetrical inverting ring system, chair to chair. The infrared method has also been used to distinguish axial and equatorial >CX groups from the region of the spectrum appropriate to the >CX stretching frequency (16, 13). Analysis of cyclohexyl chloride and cyclohexane thiol for axial and equatorial sulphur or halogen groups has been achieved by this technique.

Six-membered ring compounds which are not locked by the substitution of large groups around the ring into one configuration undergo chair-to-chair inversion. The rate of chair-to-chair inversion can be studied by proton resonance measurements. At room temperature these inverting ring compounds have a spectrum which is the weighted average of the equilibrium forms (18, 6, 12). Between room temperature and −150° C the two distinct forms in equilibrium become distinguishable in the n.m.r. spectrum so

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that it is possible to analyze the percentage of each chair form by either measuring the intensities under respective proton resonance peaks at low temperature or by the techniques suggested in the paper of Gutowsky and Saika (18). Measurements of chemical shifts and coupling constants of the two distinguishable chair forms at low temperature may be combined with average chemical shift and coupling constant measurements at room temperature to give an analysis of the rapidly interconverting mixture at room temperature. The proton resonance technique has already been used to study halogenated cyclohexane (6, 12), *trans*-disubstituted cyclohexanes (7), N,N-dimethylpiperazine (8), bicyclic systems such as decalins (9), cyclohexane (10), and perfluorocyclohexane (11).

The difficulties of the proton resonance method as applied to these molecules are the complexities of the proton resonance spectrum, which increase as the symmetry of the molecule is lowered by substitution. In most cases the energy barrier for chair-to-chair inversion has been estimated from the so-called "coalescence temperature", assuming a frequency factor of 10^{13}. It is apparent that substitution of the cyclohexane ring or the introduction of a hetero atom into the ring of carbons may result in the mechanism of chair-to-chair inversions being changed. The assumption of a frequency factor 10^{13} is then not justified, since in these different inversion mechanisms the entropy of activation will not be the same. In simple monosubstituted cyclohexanes the proton resonance adjacent to the substituted group is in general chemically shifted to low field from the rest of the ring protons, and indirect spin–spin interaction with the α protons renders the proton resonance spectrum of this adjacent proton quite complex and in many cases up to 12 cycles in apparent half-width. At low temperatures the resolution of the two chair forms into distinct n.m.r. spectra sometimes results in overlap between the axial and equatorial proton peaks. In order to overcome some of the difficulties of the n.m.r. technique in the study of these molecules, this paper will describe a selective deuteration around the cyclohexane ring so as to simplify the complex spectrum and obtain more accurate populations of chair forms.

EXPERIMENTAL

The variable-temperature n.m.r. apparatus is part of a 40 Mc/s Varian high-resolution spectrometer and is described in previous work (1). The verification of the structure of intermediates was greatly aided by the use of an A60 Varian spectrometer.

Preparation of Cyclohexanone-2,6-D_4

Cyclohexanone was treated with D_2O from Stuart Oxygen Co. (99.8% deuterium). Twenty milliliters of cyclohexanone and a solution of 1–2 g of sodium carbonate in 10 ml D_2O were refluxed overnight. The D_2O layer was then frozen and separated. The cyclohexanone layer was dried over sodium sulphate. The exchange was repeated four times until the A60 spectra showed, from integrated intensity measurements, that only 2% of the α protons remained.

Reduction of 2,6-Tetradeuterocyclohexanone

A typical reduction was carried out with lithium aluminum hydride in the following manner. A saturated solution of lithium aluminum hydride in dry ether was placed into a two-necked, round-bottomed flask. The flask was cooled with ice and the reaction mixture stirred magnetically. A reflux was set up and cyclohexanone-D_4 was added dropwise from a separatory funnel. When the reduction was complete, excess of lithium aluminum hydride was destroyed with slow addition of moist ether. Ice-cold 10% sulphuric acid was then added gradually, until all of the precipitated aluminum hydroxide dissolved. The ether layer was then separated out and dried over anhydrous sodium sulphate. The ether was removed by distillation and the fraction boiling at 155–157° C collected. On a 10-g preparation, yield of cyclohexanol-D_4 (2,6-tetradeuterocyclohexanol) was 7.2 g.

Dehydration of Cyclohexanol-D_4 to 1,3,3-Trideuterocyclohexene

The conventional dehydration of cyclohexanol with phosphoric acid was used. Phosphoric acid (85%) was added dropwise to 6.33 g of cyclohexanol-D_4 until a homogeneous mixture resulted (2.5 ml of phosphoric acid). The reaction mixture was then subjected to distillation using a small glass-bead column and the fraction distilling at 82–83° C collected. A good yield of 3.4 g or 65.6% of pure deuterated cyclohexene was thus obtained.

Addition of Iodine–Chloride across the Double Bond of Cyclohexene-D_3

Cyclohexene-D_3 (1.23 g) was dissolved in 3 cc of ice-cold glacial acetic acid. Iodine–chloride (2.3 g) dissolved in 6 ml of glacial acetic acid was then added dropwise to this solution. The reaction mixture was cooled throughout. At the end of the reaction, the product containing a slight excess of iodine–chloride was transferred into a separatory funnel, and then shaken well with 5 ml of saturated sodium thiosulphate. The oily chloroiodocyclohexane was allowed to separate out, treated further with sodium bicarbonate, and dried over anhydrous sodium sulphate. The almost quantitative yield of the mixture of 1-iodo-2-chloro-1,3,3-trideuterocyclohexane and 1-chloro-2-iodo-1,3,3-trideutero cyclohexane was then subjected to n.m.r. studies.

RESULTS

Figure 1 shows 60 Mc/s spectra of 1-chloro-2-iodo-cyclohexane and the 50/50 mole% mixture of 1-iodo-2-chloro-1,3,3-trideutero cyclohexane and 1-chloro-2-iodo-1,3,3-trideuterocyclohexane. The chemical shift between the —CHI— proton and the —CHCl— is small and can be measured directly from the mixture of deuterated molecules (0.12 p.p.m. = 7.2 c.p.s.).

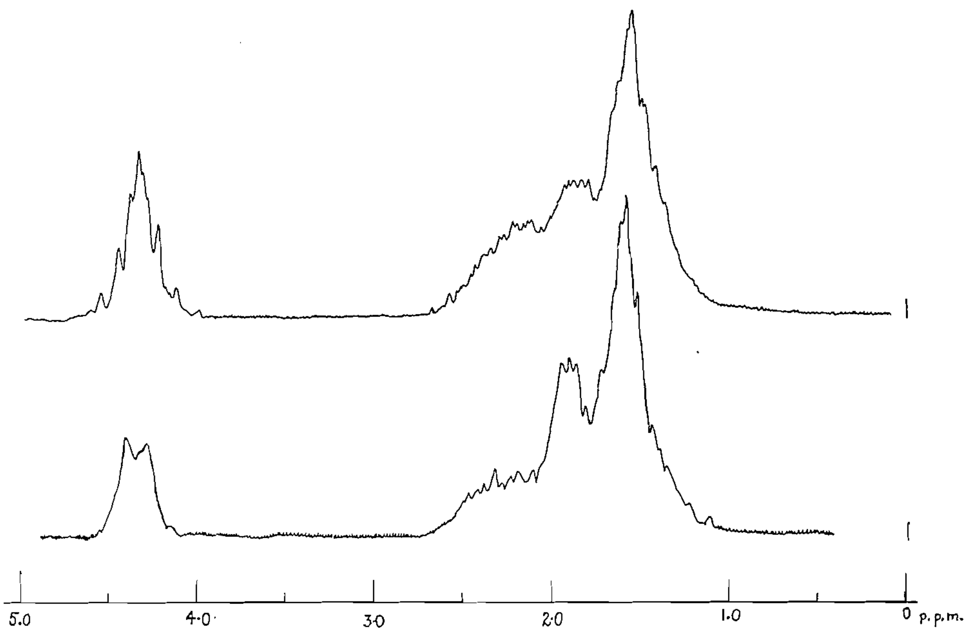

FIG. 1. Sixty-megacycle spectra of 1,2-*trans*-chloroiodocyclohexane (upper) and the 50/50 mixture of 1-iodo-2-chloro-1,3,3-trideuterocyclohexane and 1-chloro-2-iodo-1,3,3-trideuterocyclohexane. Both were diluted to 20 mole% in CS_2.

The peaks obtained for the —CHCl—CHI— group arise as follows. The two protons within this group comprise an AB spectrum requiring second-order theory in order to evaluate δ_{AB} and J_{AB}. The value for δ_{AB} is 7.2 c.p.s. (The —CH_2— groups adjacent to the —CHI—CHCl— group form a set of four inequivalent protons all of which are at least 120 c.p.s. removed to higher field.) There should be 16 lines in all, some of which may be coincident. Ten lines have been resolved in spectra taken under slower sweep conditions than those illustrated in Fig. 1. It has not been possible to satisfactorily assign these transitions to obtain coupling constant data.

Low-temperature Studies at 40 Mc/s

Figure 2 shows two spectra, at −44° C and −107° C, of the mixture of deuterated iodochlorocyclohexanes. There was no detectable change in the proton resonance spectra between room temperature and −80° C so the spectrum at −44° C is typical of this temperature range. It can be related to the spectrum described in Fig. 1 at 60 Mc/s for the same sample. The low-field peak in spectrum I, Fig. 2, does not show complete resolution into the —CHI— and —CHCl— components. These are labelled (*a*) for the —CHI— proton resonance and (*b*) for the —CHCl— signal. Signals (*c*) and (*d*) marked in spectrum I, Fig. 2, correspond to the distinguishable peaks in the high-field spectra at 60 Mc/s in Fig. 1. The low-field tail of these peaks is barely distinguishable in the 40 Mc/s spectrum. The internal standard hexamethyldisiloxane appears in Fig. 2 marked as 0 c.p.s. The compound was dissolved in CS_2 at a concentration of 40 mole%.

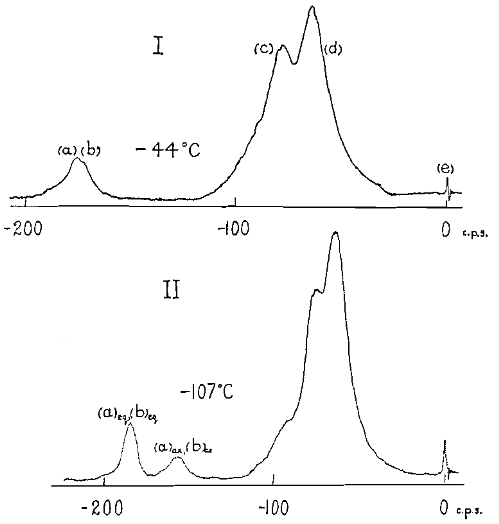

FIG. 2. Forty-megacycle spectra at −44° C and −107° C of the deuterated iodochlorocyclohexane at 40 mole% in CS_2.

The broadening of the low-field signals occurs below −80° C and they become clearly resolved into two peaks at −100° C. A single broad peak (the "coalescence temperature") is observed at −93° C. The two resolved low-field peaks are in fact composite so that at lowest field $(a)_{eq}(b)_{eq}$ are made up of equatorial proton signals geminal to chlorine in one half of the sample and to iodine in the rest. The corresponding axial proton resonances $(a)_{ax}(b)_{ax}$ are also designated in spectrum II of Fig. 2. The protons geminal to chlorine and iodine are not distinguishable at 40 Mc/s and so the spectra at low temperature can be analyzed into the percentage of the diaxial halogen chair form. Analysis of the spectra below −95° C shows that 68±3 mole% of this iodo–chloro compound exists in the diaxial halogen form. This result is based on the intensities obtained from 18 low-temperature spectra. The deviation from the mean is a maximum value. The mean chemical shift of $>$CHI and $>$CHCl protons at room temperature is −174.8 c.p.s. (−4.37 p.p.m.) from an internal hexamethyldisiloxane reference. At low temperature the mean of the two diaxial proton shifts adjacent to the halogens is −158.2 c.p.s. (−3.96 p.p.m.) and the mean of the diequatorial protons is found at -185.2 c.p.s. (-4.66 p.p.m.). These values can be compared with earlier studies on dichloro- and dibromo-cyclohexane (7).

DISCUSSIONS

The difference in free energy, which is approximately the same as the energy content difference (6, 7) between diaxial and diequatorial halogen forms, is almost the same for iodochlorocyclohexane ($+241$ cal mole^{-1}) as for dibromocyclohexane ($+305$ cal mole^{-1}) (7). The repulsions of diequatorially substituted groups and the halogen with 3,5-diaxial hydrogens are almost exactly the same for iodochloro- as for dibromo-cyclohexane. The sum of the van der Waals radii of 1,2-*trans*-disubstituted groups appears to be the dominant effect in determining the stability of the configurations in the halogenated series of cyclohexanes.

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