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CONFORMATIONAL ANALYSIS OF SOME ACYCLIC SYSTEMS BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Fritz Schweinsberg and James G. Traynham
Coates Chemical Laboratories, Louisiana State University
Baton Rouge, Louisiana 70803

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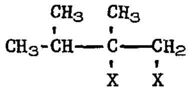
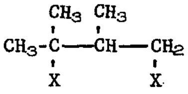
In connection with another study,[1] we prepared some 1,2-dihalo-, 1,3-dihalo-, and 1,2,3-trihalo-2,3-dimethylbutanes (I-III, X = Cl or Br). The nuclear magnetic resonance (nmr) spectra of these compounds reveal a surprising degree of conformational preference about C-C single bonds, such a preference, in fact, that the spectra are those one would expect with single conformations for each compound. We believe that some of the features of the conformational analysis of these compounds are of general interest.


$CH_3\text{-}\overset{CH_3}{CH}\text{—}\underset{X}{\overset{CH_3}{C}}\text{—}\underset{X}{CH_2}$

I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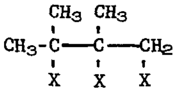
II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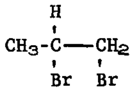
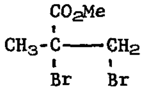
III


$CH_3\text{-}\underset{Br}{\overset{H}{C}}\text{—}\underset{Br}{CH_2}$

IV


$CH_3\text{-}\underset{Br}{\overset{CO_2Me}{C}}\text{—}\underset{Br}{CH_2}$

V

"A huge body of literature has accumulated about hindered internal rotation about single bonds,"[2] but few examples of effectively "locked" conformations in acyclic systems have been reported. Long-range nmr couplings (trans W-couplings)[3] between CH_3 and CH_2 in IV[4a] and V[4b], for example, have been recorded. Compounds I-III provide a closely related series amenable to conformational analysis by nmr methods; this analysis reveals some interesting non-bonded interactions of sufficient magnitude to make each compound appear to exist in a single conformation.

The 100 MHz spectrum of 1,2-dibromo-2,3-dimethylbutane (I, X=Br) is illustrated in Fig. 1.[5] The intrinsic magnetic non-equivalence of diastereotopic protons[6] is well-illustrated by the upfield pair of doublets for the two CH_3 groups in the isopropyl moiety and by the downfield pair of doublets for the protons in the CH_2Br group. H^A (most-downfield doublet) is long-range coupled to CH_3^C (confirmed by decoupling experiments; J_{AC} = 0.6 Hz), but the absorption for

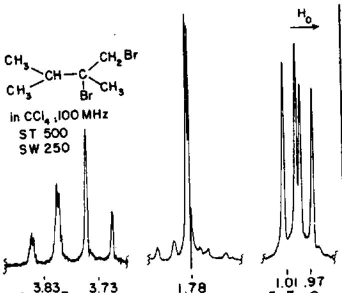


Fig. 1. Nmr spectrum of 1,2-dibromo-2,3-dimethylbutane

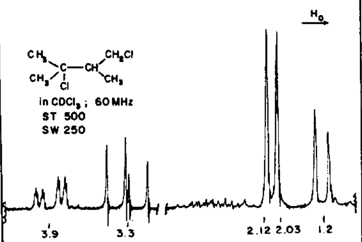


Fig. 2. Nmr spectrum of 1,3-dichloro-2,3-dimethylbutane

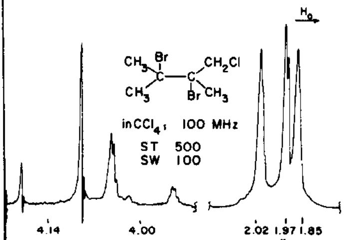
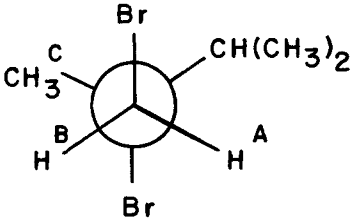
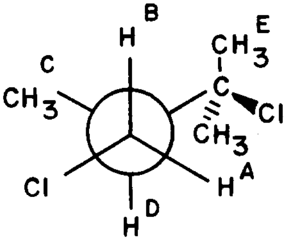


Fig. 3. Nmr spectrum of 1-chloro-2,3-dibromo-2,3-dimethylbutane



VI

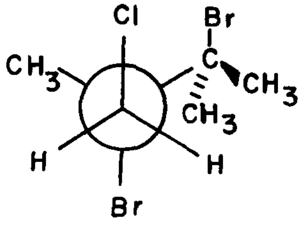


VII

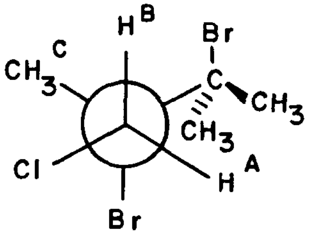
H^B (3.73 ppm) does not reveal any long range coupling. This W-coupling for only one of the CH_2Br protons strongly indicates that the molecule exists in one highly-favored conformation. Vincinal halogen substituents normally are trans to each other in a preferred conformation,[7] and this conformation (VI) is consistent with the nmr data. H^A, but not H^B, is ideally situated for W-coupling with H^C.[8] H^A and H^B are about equally deshielded by the halogen substituents, but H^B is more effectively shielded by CH_3^C than H^A is by the isopropyl group.

The nmr spectrum of 1,3-dichloro-2,3-dimethylbutane (II, X = Cl), illustrated in Fig. 2,[9] is similar to that of the 1,2-dihalide. Again, long-range W-coupling is evident in the downfield absorption pattern for the non-equivalent CH_2Cl, but barely discernable in the upfield one. The chemical shift difference ($\Delta\delta$) for the two protons in CH_2Cl is quite substantial[6] (0.6 ppm) and larger than is found for CH_2X in I. We believe this increase in $\Delta\delta$ is an important clue to conformation. Formula VII depicts a conformation which accommodates the nmr data particularly well. H^A, the proton which is long-range coupled to H^C(J_{AC}=0.6 Hz), is actually diastereotopic with H^A in VI. This conformation is supported by the substantially different vicinal coupling constants for H^A and H^B: J_{AD} (gauche) = 3.4 and J_{BD} (anti) = 8.7 Hz. It also reduces unfavorable interactions between Cl on C-1 and the $C(CH_3)_2Cl$ group and produces sufficiently different magnetic environments for H^A and H^B to account for the substantial difference in chemical shifts. H^B is shielded by CH_3^C, while H^A and H^B may be affected equally or unequally by the $C(CH_3)_2Cl$ group, depending on how freely that group rotates. If rotation were restricted, the conformation shown (VII) would lead to deshielding of H^A by Cl and shielding of H^B by CH_3, and the large $\Delta\delta$ may favor this interpretation. Long-range coupling is evident in the absorption signals for the terminal CH_3 groups, but the proximity of the chemical shifts involved prevented us from ascertaining whether the two CH_3 groups are coupled only with each other or one (CH_3^E) is coupled with H^D.

The third compound in the series, 1-chloro-2,3-dibromo-2,3-dimethylbutane, VIII, gives the nmr spectrum illustrated in Fig. 3. Long-range coupling is apparent in the upfield absorptions for the three non-equivalent CH_3 groups, but it is apparent in only one of the two downfield absorptions for CH_2Cl. Unlike the first two compounds discussed (VI and VII), this one exhibits this splitting in the more upfield rather than the more downfield absorption for CH_2Cl. Decoupling experiments revealed that this downfield proton is coupled with the CH_3 (J_{AC} = 0.5 Hz) responsible for the middle upfield absorption. Again, these data are taken to reveal a strongly-preferred conformation for the trihalide. If the vicinal halogens in each pair are arranged trans to each other[6] (VIIa), strong, unfavorable interaction between the halogens at C-1 and C-3, similar to 1,3-diaxial interactions in cyclohexane derivatives, results. We rotate C-1 to give a gauche interaction for the two halogens on C-1 and C-2, leave C-3 unchanged, and obtain a conformation (VIIIb) which uniquely accommodates the nmr data. H^A is again W-coupled with H^C, but H^B is now deshielded by the 1,3-eclipsed interaction with Br at C-3 and H^A is shielded by a terminal CH_3 group. The relative chemical shifts of H^A and H^B change in VII and VIIIb as a



VIIIa



VIII b

result of the preferred conformations at C-3. Were C-3 in VIIIb to rotate freely (on the nmr time scale), the shielding contribution of $C(CH_3)_2Br$ to H^A and H^B would be the same, and the cause of the inversion of chemical shifts for H^A and H^B would not be apparent.

The nmr data for these acyclic compounds clearly imply that one conformation for each compound is exceptionally favored over all others. They further indicate that gauche-vicinal interactions between halogens are less unfavorable than 1,3-eclipsed ones.

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3. L.M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed., Pergamon Press, New York, N.Y., 1969, pp 334-341.
4. a) R. Freeman and N.S. Bhacca, J. Chem. Phys., **38**, 1088 (1963); b) D.R. Davis, R.P. Lutz, and J.D. Roberts, J. Amer. Chem. Soc., **83**, 246 (1961).
5. Except for small differences in chemical shifts and coupling constants, the nmr spectra of 1-bromo-2-chloro-2,3-dimethylbutane and 1,2-dichloro-2,3-dimethylbutane are essentially the same as Fig. 1.
6. K. Mislow and M. Raban, in "Topics in Stereochemistry", Vol. 1, N.L. Allinger and E.L. Eliel, eds., Interscience Publishers, New York, N.Y., 1967, Chapter 1.
7. E.L. Eliel, N.L. Allinger, S.J. Angyal, and G.A. Morrison, "Conformational Analysis", Interscience Publishers, New York, N.Y., 1966, pp 13-16.
8. In effect, H^A is substantially coupled to only one H^C at a time, and the rotation of CH_3^C results in an average J_{AC}.
9. The nmr spectrum of II, X = Cl, was recently published without conformational analysis; K. Griesbaum and Z. Rehman, J. Amer. Chem. Soc., **92**, 1416 (1970).