

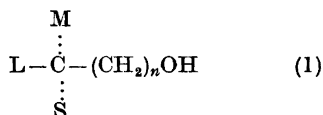
Studies on the Reaction between Chloral and Alcohols

VI. NMR-Investigations of the Epimerization of Diastereomeric Chloral Hemiacetals

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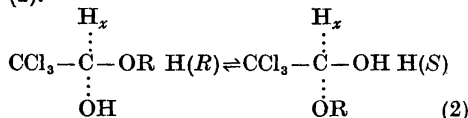
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It was reported in our previous publications¹⁻⁴ that chloral hemiacetals prepared from chloral and optically active alcohols of



L, M, and S mean large, medium and small with respect to steric bulk.

type (1) were able to mutarotate, if $n \leq 1$. The mutarotation was followed by polarimetry and UV-spectroscopy. Heptane was used as solvent, and it was found that the rate of the reaction was increased by adding small amounts of acetic acid. The mutarotation was explained as resulting from an equilibrium asymmetric transformation (epimerization) between the two possible diastereomeric hemiacetals, H(R) and H(S), (2).



This explanation was supported by two types of observations. A plot of $\log [([\varphi]_t - [\varphi]_\infty)]$ versus time where $[\varphi]_t$ is the molecular rotation of the hemiacetal mixture at the time t and $[\varphi]_\infty$ at equilibrium, gave a straight line; a similar relationship has been observed by Hudson⁵ for the α - β isomerization of glucose. Also, by investigating the hemiacetals from fifty-six optically active alcohols it was found that the value of $d[\varphi]/dt$ was determined solely by the spatial arrangement

of the groups L, M, S, and $(\text{CH}_2)_n\text{OH}$ in the alcohol. It was shown that a negative value of $d[\varphi]/dt$ corresponds to a right-handed sequence of L, M, and S (noted as L→M→S when L, M, and S follow a clockwise sequence when viewed from the asymmetric carbon atom) and a positive value of $d[\varphi]/dt$ corresponds to a left-handed sequence. Exceptions to this rule were found for alcohols containing polar or aromatic groups. A more definite proof of this epimerization theory could not be realized because hemiacetals from alcohols more complex than ethanol or other straight-chain alcohols were not stable; thus these complex hemiacetals could not be separated into their respective diastereomers and studied in the same manner as those from α - and β -glucose.

It has now been found that NMR-spectroscopy of hemiacetals in CCl_4 solution gives a more direct proof of this theory of epimerization. An additional advantage of this NMR method is that the hemiacetals can be prepared from racemic alcohol. By recording the NMR spectra of the hemiacetals, the signal from the methine protons (H_x in eqn. (2)) in most cases appears as a singlet. However, in the spectra of hemiacetals of sterically hindered alcohols like, *e.g.*, 3,3-dimethyl-2-butanol the signal appeared as two closely spaced

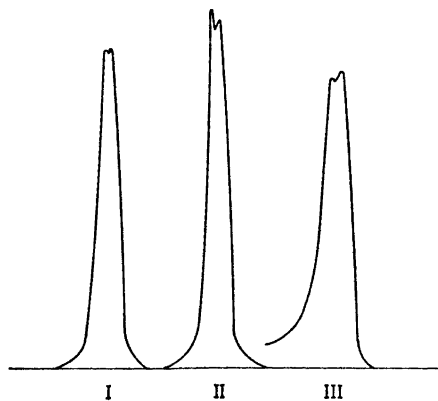


Fig. 1. The NMR-signal at approximately 4.0 τ of the H_x proton (eqn. (2)) in the chloral hemiacetals prepared from: I. 3-methyl-2-butanol, II. 2-cyclohexylethanol and III. 3,3-dimethyl-2-butanol. These spectra were recorded with a sweep width of 50 cps, and show a splitting of the signal due to H_x because of the existence of the two possible diastereomeric hemiacetals. $1 \text{ mm} = 8.35 \times 10^{-3} \tau$.

singlets (Fig. 1). In cases where this signal could not be resolved at 60 Mc/s (hemiacetals of less sterically hindered alcohols such as 2-butanol) it was possible to resolve this signal into two components by use of 100 Mc/s spectra. The occurrence of epimerization was demonstrated by recording the NMR-spectrum of the previously mentioned hemiacetal of 3,3-dimethyl-2-butanol as a function of time (Fig. 2). As shown in the figure, the mole fraction X_A of the most shielded H_x -proton changed from 0.72 to 0.50 in 1440 min. No further change in the mole fraction was observed after 1440 min, in contrast to the reaction followed by UV which was complete after 10 min. The mole fraction of the two diastereomers was determined by measuring (by use of a planimeter) the areas of the two signals. To make this measurement possible the signals were separated from each other by drawing a vertical line from the crossing point between the two signals to the base line. It is interesting to observe (Fig. 1) that the mole fraction at equilibrium for three different hemiacetals is approximately 0.5. This means that the free energy difference between the two

diastereomeric hemiacetals is approximately zero, contrary to the energy difference between their corresponding transition states. In order to obtain a better understanding of the epimerization process, a study of the half lives of various hemiacetals as a function of the steric bulk of the groups surrounding the asymmetric centre is planned.

Experimental. NMR Spectra were recorded on a Varian A-60 A spectrophotometer in CCl_4 solution with TMS as internal standard at 25°. The concentration of chloral and the alcohols were both 5×10^{-1} M and the concentration of acetic acid was 10^{-2} M in the experiments shown in Fig. 1. For the experiments shown in Fig. 2, no acetic acid was added and the concentrations of chloral and 3,3-dimethyl-2-butanol were both 5×10^{-1} M.

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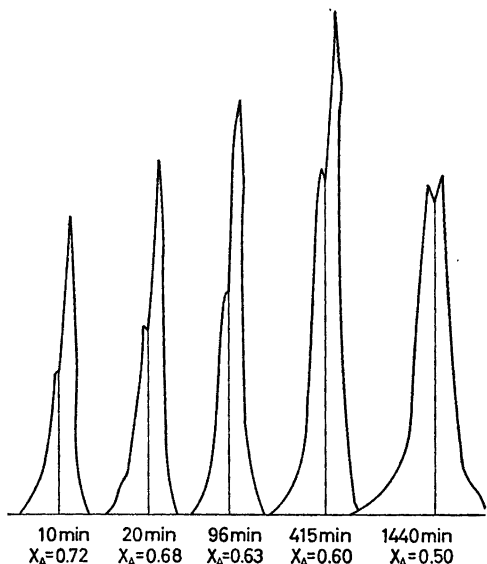


Fig. 2. Time dependence of the NMR-signal at 4.0 τ of the chloral hemiacetal of 3,3-dimethyl-2-butanol. These spectra were recorded with a sweep-width of 50 cps. 1 mm = 8.35×10^{-3} τ . X_A is the mole fraction of the most shielded diastereomer.

An SCF MO Study of Two Isomeric Thiadiazoles

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From a theoretical point a view the electronic structure of the monocyclic thiadiazoles is of considerable interest.¹⁻³ Previous calculations, performed within the Hückel-approximation, have made possible a discussion of some of the molec-

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