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SECONDARY α-DEUTERIUM ISOTOPE EFFECTS ON ALDEHYDE HYDRATE AND HEMIACETAL FORMATION

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Recent interest in secondary α-deuterium isotope effects on carbonyl reactions[1-3] prompts us to present a preliminary report of our findings for hydrate and hemiacetal formation from pentanal-1-d.[4]

Equilibrium isotope effects for addition of water or ethanol were determined by observation of the n → π* absorption of free aldehyde in dilute aqueous or ethanolic solution.[5] The equilibrium constant is defined as K = [adduct]/[aldehyde]. For hydration in ~ 4 × 10^{-3} M aqueous solution, we found $K_H = 0.402 \pm 0.008$; $K_D = 0.560 \pm 0.008$; $K_H/K_D = 0.718 \pm 0.019$ (or 1/1.39). Hemiacetal formation (in 1.5 × 10^{-2} M solution) was studied in the presence of a 10^{-2} M acetate buffer to assure complete attainment of equilibrium. The results were: $K_H = 5.17 \pm 0.10$; $K_D = 7.07 \pm 0.11$; $K_H/K_D = 0.728 \pm 0.021$ (or 1/1.37). These equilibrium isotope effects are similar to those previously reported for addition of nitrogen and carbon nucleophiles to benzaldehydes (~ 0.73 and 0.78),[1] but substantially greater than for some thermal rearrangements (0.92 per D) which might be regarded as additions to C=C.[8]

The *rate* of hemiacetal formation was also studied. In 1:1 acetate buffer (3.2 × 10^{-3} to 2.6 × 10^{-2} M), the rate law had the form: Rate = [aldehyde](k_1 + k_2 [buffer]). For the buffer-catalyzed portion of the reaction, $(k_2)_H = 0.212 \pm 0.003\ M^{-1}\ sec^{-1}$, $(k_2)_D = 0.273 \pm 0.002\ M^{-1}\ sec^{-1}$, and $(k_2)_H/(k_2)_D = 0.777 \pm 0.012$. Utilizing the relationships among K, k_{obs}, k_f, and k_r, isotope effects for hemiacetal formation and decomposition are derived as $(k_{2f})_H/(k_{2f})_D = 0.74$ (or 1/1.35) and $(k_{2r})_H/(k_{2r})_D = 1.02$.

$$\mathrm{RCHO} + \mathrm{C_2H_5OH} \underset{k_r}{\overset{k_f}{\rightleftharpoons}} \mathrm{RCH(OH)OC_2H_5}$$

The isotope effect for addition is again slightly greater than that reported for nitrogen nucleophiles with benzaldehydes (0.86 to 0.76).[1] For decomposition of the tetrahedral species, small isotope effects are observed for hydrolyses of ethyl orthoformate and p-methoxybenzaldehyde diethyl acetal[9] and mutarotation of glucose[10] (~ 1.04-1.1), and somewhat larger ones for hydrolyses which are most clearly A-1.[9]

The isotope effects we observe for the hemiacetal reaction indicate that the carbonyl carbon must be very close to tetrahedral in the transition state. They would be consistent with a mechanism with rate-determining proton transfer in a dipolar adduct, resembling an "intimate stepwise" mechanism recently discussed.[11]

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4. Pentanal-1-d was prepared by the method of Walborsky. Spectrometric results reported for deuterated aldehyde are corrected for its content of several percent of isotopically normal compound, as determined by integration of the nmr spectrum.
5. In agreement with earlier literature,[6] deuterium substitution produces a decrease in molar absorptivity of aldehyde; in hydrocarbon solution, $\varepsilon_H = 22.45 \pm 0.09$; $\varepsilon_D = 21.04 \pm 0.30$. The molar absorptivity of free aldehyde in water and ethanol, determined by extrapolation of the observed value back to the time of mixing ($\varepsilon^0_{\text{ethanol}} = 21.8 \pm 0.10$; $\varepsilon^0_{H_2O} = 19.0 \pm 0.8$), is in accord with the pattern reported for other aliphatic aldehydes.[7] The ratio $\varepsilon^0_H/\varepsilon^0_D$ in ethanol and water was taken equal to that in hydrocarbon.
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