ues, but it turned out to be poor with a high standard deviation.[26]

In fact, a reexamination of the data on the acetal hydrolysis[20] showed that a correlation of the type of eq 4 gave almost as good a fit as that used previously.[20,27] As pointed out by Dewar,[23a] both approaches (adjacent bond interaction and hyperconjugation) would be equivalent if hyperconjugation energies for C–H and C–C (and even C–Cl) bonds are similar. Indeed in recent publications C–C hyperconjugation is gaining more importance.[24,28]

It should be noted that solvation effects may also play a role in determining the equilibrium constant K_d. It is likely that in aqueous solutions, the aldehyde hydrates are stabilized by hydrogen bonding to solvent water relative to ketone hydrates. A more complete understanding of the factors influencing the reversible hydration of the carbonyl group could, no doubt, be obtained from heats of formation. Unfortunately, reliable data are available only for a limited number of compounds.[13]

Acknowledgment. We are gratefully indebted to Professor R. P. Bell for sending us a copy of his article prior to publication and to Professor E. Grunwald, Dr. S. Brownstein, and Dr. Z. Rappoport for helpful comments regarding the discussion of the results.

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[26] With the nomenclature of Kreevoy and Taft[20] the following best-fit parameters were obtained.

$$-\log K_d = (1.38 \pm 0.24)\Sigma\sigma^* - (0.53 \pm 0.12)(n - 6) - 2.83 \pm 0.51$$

$$d = 0.77 \quad r = 0.932$$

It is interesting to note that the coefficient of $(n - 6)$ that comes out of the present statistics, 0.53, is very close to the hyperconjugation energy per α hydrogen proposed by Kreevoy and Taft (0.54).[20]

[27] Using the data of Table I in ref 20, excluding those for neopentyl ketal and the α,β-unsaturated compounds, the equation of Kreevoy and Taft gave an over-all standard deviation of 0.31 while a correlation by eq 4 gave a standard deviation of 0.34. It is interesting to note that the B obtained (2.00 log units) is virtually the same as that in the present work (2.03 log units).

[28] Reference 22, pp 234, 349; see also R. S. Mulliken, *Tetrahedron*, 5, 253 (1959).

A Nuclear Magnetic Resonance Study of the Reversible Hydration of Aliphatic Aldehydes and Ketones. II. The Acid-Catalyzed Oxygen Exchange of Acetaldehyde

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Abstract: The rate constant for the acid-catalyzed oxygen exchange between acetaldehyde and solvent water was determined from the broadening of the acetaldehyde ^{17}O nuclear magnetic resonance lines as a function of HCl concentration. For solutions 1.9 to 5.7 *M* in acetaldehyde, the acid catalysis rate constant is ~470 M^{-1} sec^{-1}. This result is compared with the acid-catalysis rate constant for the hydration of acetaldehyde. It is concluded that the oxygen exchange can be accounted for by the hydration–dehydration process. The rate of oxygen exchange of methylene glycol in a neutral aqueous solution was also measured and found to be similar to that of the dehydration of this compound.

The reversible hydration of acetaldehyde (reaction 1) has been the subject of extensive studies by various workers. The reaction was shown to be acid and base catalyzed, the half-life at room temperature in neutral solutions being of the order of 1 min and much shorter in acidic or basic solutions. Therefore, methods for studying fast reactions must be employed. The various techniques including pmr, thermal maximum, and chemical scavenging have been thoroughly reviewed in a recent article by Bell.[1]

$$CH_3CHO + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CH_3CH(OH)_2 \qquad (1)$$

If the water or the acetaldehyde are labeled with either ^{17}O or ^{18}O, reaction 1 provides a route for isotopic exchange. When the exchange is measured by isolating one component of this system and analyzing for its isotopic oxygen content, the observed rate constant should be at least equal to half the hydration rate constant. The factor of 2 is due to the fact that only in half of the events in which a C–OH bond of the *gem*-diol is broken will isotopic exchange occur. Isotope effects in oxygen are very small[2] and can be ignored in reactions of this type.

The only reported data on the oxygen exchange of acetaldehyde in aqueous solutions are by Herbert and Lauder[3] using ^{18}O, who found a half-life of about 2 hr at room temperature, a result which is inconsistent with the rate of hydration[1] of this compound. Another attempt to measure the rate of oxygen exchange was recently made by Byrn and Calvin,[4] who found that the exchange of a slightly acidic solution of acetaldehyde in a tetrahydrofuran–water solution was complete within 5 min. In order to elucidate the mechanism of oxygen exchange and to resolve the inconsistencies

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[1] R. P. Bell, *Advan. Phys. Org. Chem.*, 4, 1 (1966).

[2] L. Melander, "Isotope Effects in Reaction Rates," Ronald Press Co., New York, N. Y., 1960.

[3] J. B. M. Herbert and I. Lauder, *Trans. Faraday Soc.*, 34, 433 (1938).

[4] M. Byrn and M. Calvin, *J. Am. Chem. Soc.*, 88, 1916 (1966).

found[5] in previous work, we have studied the oxygen exchange of acetaldehyde in acidic aqueous solutions by oxygen-17 nuclear magnetic resonance (omr).

Omr may be employed to study isotopic oxygen exchange in two ways. (i) When the half-life for the exchange reaction is longer than 1 to 2 min, the rate can be determined from peak intensity measurements as a function of time. (ii) When the specific rate of exchange (in $\sec^{-1}$) is of the order of, or exceeds, the nmr line width (in rads/sec), line broadening of the nmr signals occurs, and from the excess widths it is possible to derive rates.[6] Since ^{17}O line widths[7] are usually of the order of 10^2 $\sec^{-1}$, the rates of the exchange reaction must equal orexc eed 10^2 $\sec^{-1}$ in order to be measurable by omr. In this case the rate measured is that at which the ^{17}O nucleus leaves its particular magnetic environment. Assuming that reaction 1 is the only one occurring, line broadening of the carbonyl group will give the rate of hydration, while line broadening of the *gem*-diol oxygens yields the rate of dehydration.

The omr spectrum of an aqueous solution of acetaldehyde has been described previously.[8] It consists of, in addition to the water resonance, two lines at -558 and -71 ppm[9] corresponding to the unhydrated and hydrated forms of acetaldehyde. The rate of oxygen exchange in neutral solutions is of the order of 1 min and thus falls in a range which cannot be studied conveniently by either of the above two nmr techniques. However, in acidic solutions the exchange rate can be enhanced enough to broaden the omr resonances of acetaldehyde and thus provide a convenient means of studying the oxygen exchange rate in acidic solutions directly. In the present paper we shall describe the results of such measurements.

Formaldehyde is almost completely hydrated in water to form methylene glycol and shows only a single omr peak at -51 ppm.[8] The rate of oxygen exchange of this compound is sufficiently slow in neutral solutions to follow by method i outlined above. The results are described in the last section of the present paper.

The pseudo-first-order rate constant for the noncatalyzed hydration of acetaldehyde, k_1^0, has been measured by Bell, *et al.*,[10,11] by the thermal maximum method, and by chemical scavenging, and found to be about 5×10^{-3} $\sec^{-1}$ at room temperature. For methylene glycol the rate of dehydration in neutral solution has been measured by several workers. The most recent determination is by Bell and Evans,[11] who obtained the value 5×10^{-3} $\sec^{-1}$.[12]

The pseudo-second-order acid-catalysis rate constant for acetaldehyde, k_1^H, has been studied by various methods.[10,11,13-15] The results of five different determinations at room temperature fall between 480 and 810 M^{-1} $\sec^{-1}$ depending on the method used and the value taken for the equilibrium constant of reaction 1. Four of these results fall between 480 and 670 M^{-1} $\sec^{-1}$. Despite this scatter, it is felt that the true value of k_1^H lies within the limits of these two figures.

The results of the present work show that the rate of oxygen exchange of the carbonyl and *gem*-diol oxygen in the compounds studied can be accounted for by assuming that the exchange proceeds *via* the hydration reaction 1. Thus within our experimental accuracy there is no other important mechanism for the exchange of the carbonyl and *gem*-diol oxygens.

Nmr Measurements

The nmr spectrometer was the same as that used in the previous work.[8] The probe temperature was 27 ± 1°.

For the determination of the exchange rate from line broadening it is necessary to know accurately the transverse relaxation rate $1/T_2$ of the nmr resonances. In the present work the signals were obtained by low-frequency (20 or 40 cps) sweep-field modulation and phase detecting the signal. Under these conditions, provided the sweep-field amplitude is small compared to the line width, and the radiofrequency field is kept below saturation level, the output signal is recorded as the derivative of the absorption mode. The peak-to-peak separation ($\Delta\nu$ in cps) between the two extrema of the derivative line is then related to the transverse relaxation rate, $1/T_2$, by

$$1/T_2 = \sqrt{3}\pi\Delta\nu \tag{2}$$

In order to obtain optimal conditions and a high signal-to-noise ratio, it is sometimes necessary to use high modulation and radiofrequency fields. Under such conditions, distortion and broadening of the observed signals may result, and proper corrections must be employed. We have applied these corrections in two steps: first for overmodulation and then, if necessary, for saturation.

The corrections for overmodulation were done according to Wahlquist.[16] He obtained a closed expression relating the peak-to-peak separation of the observed line $(H_\delta)_p$, with the amplitude of the modulation field, H_ω, and the true half-width of the resonance, $H_{1/2}$. $H_{1/2}$, if expressed in cps, is related to $1/T_2$ by $1/T_2 = \pi H_{1/2}$. The amplitudes of the modulation field, H_ω, for the different settings of the field-sweep knob were determined by the method of Smith[17] using the deuterium resonance of D_2O. Except for the lowest settings, the H_ω's determined were in good agreement with those given by Varian in the instruction manual. From eq 13 and 15 of ref 16, a plot was constructed relating $(H_\delta)_p/H_\omega$ and $H_\omega/H_{1/2}$. From this plot, knowing H_ω and the measured $(H_\delta)_p$, $H_{1/2}$ and thus $1/T_2$ could be determined. The range of $H_\omega/H_{1/2}$ did not exceed 0.2 and was usually lower. The corrections due to overmodulation were always below 10%. To check this procedure we have reconstructed some of the experimental lines using eq 10 of ref 16 and compared them with the recorded spectra. In

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(5) D. Samuel and B. L. Silver, *Advan. Phys. Org. Chem.*, 3, 123 (1965).

(6) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chapter 10.

(7) H. A. Christ, D. Diehl, H. R. Schneider, and H. Dahn, *Helv. Chim. Acta*, **44**, 865 (1961).

(8) P. Greenzaid, Z. Luz, and D. Samuel, *J. Am. Chem. Soc.*, **89**, 749 (1967).

(9) These figures are for a 3 M solution. As discussed in ref 8 the chemical shifts are slightly concentration dependent.

(10) R. P. Bell, M. H. Rand, and K. M. A. Wynne-Jones, *Trans. Faraday Soc.*, **52**, 1093 (1956).

(11) R. P. Bell and P. G. Evans, *Proc. Roy. Soc.* (London), **A291**, 297 (1966).

(12) For discussion of previous work and results, see ref 11.

(13) L. C. Gruen and P. T. McTigue, *J. Chem. Soc.*, 5224 (1963).

(14) M.-L. Ahrens and H. Strehlow, *Discussions Faraday Soc.*, 112 (1965).

(15) P. G. Evans, G. R. Miller, and M. M. Kreevoy, *J. Phys. Chem.*, **69**, 4325 (1965).

(16) H. Wahlquist, *J. Chem. Phys.*, **35**, 1708 (1961).

(17) G. W. Smith, *J. Appl. Phys.*, **35**, 1217 (1964).

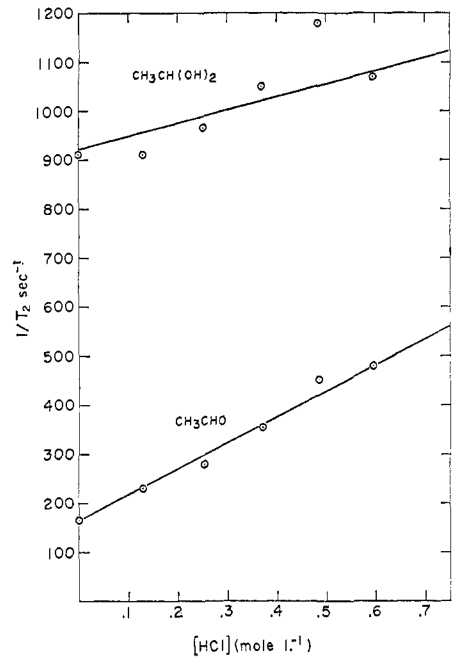

Figure 1. $1/T_2$ of carbonyl and *gem*-diol oxygen resonances plotted *vs.* acid concentration for solution no. 3 of Table I.

general, a good fit between the experimental and reconstructed lines was found. However, the amplitudes at the ends of the wings of the experimental lines were slightly more intense than those of the calculated ones.

Under conditions of saturation, $1/T_2$ is related to the experimental full width at half-maximum absorption, $H_{1/2}^{\text{sat}}$, expressed in cps by

$$1/T_2 = \pi H_{1/2}^{\text{sat}}[1 + (\gamma H_1)^2 T_1 T_2]^{-1/2} \tag{3}$$

where H_1 is the radiofrequency field intensity. In most measurements $(\gamma H_1)^2 T_1 T_2$ could be neglected compared to unity, but in some cases a slight correction due to this factor was necessary. To calculate the saturation factor we have assumed that $T_1 = T_2^0$, where T_2^0 is T_2 of the resonance not broadened by exchange (see below). H_1 was calibrated by the method of Anderson[18] using the proton signal of water.[19] The corrections due to the saturation factor did not exceed 8%.

The resonance of the *gem*-diol grouping falls quite close to the solvent $H_2{}^{17}O$ peak, and there is a slight amount of superposition of the two peaks. However, a close examination showed that this slight superposition did not affect the observed line widths.

Rate Measurements

As noted above, the analysis of the nmr line shape provides a method of determining the rate of exchange reactions involving magnetic nuclei. A complete analysis requires the solution of the Bloch equation in which terms representing the transfer of nuclei due to chemical exchange are included and which depend on the details of the mechanism assumed.[20] Under conditions in which the average time between successive exchanges, τ, is long compared to the reciprocal chemical shift (in rads/sec) between the resonances of the exchanging nuclei

$$\tau\delta > 1 \tag{4}$$

it is possible to use the approximate relation ("slow exchange approximation")[6]

$$\frac{1}{\tau} = \frac{1}{T_2} - \frac{1}{T_2^0} \tag{5}$$

where T_2^0 is the transverse relaxation time under conditions of no exchange and δ is the chemical shift. Condition 4 holds in our case and eq 5 has been used throughout. For the calculation of $1/\tau$, it was assumed that the values of T_2^0 equal those of T_2 for the corresponding peaks in neutral solutions where the exchange is too slow to affect the line width.

Preparation of Solutions

For the omr measurements, solutions containing acetaldehyde (E. Merck AG, Puriss Grade) and varying concentrations of HCl in water enriched with ^{17}O isotope (~8 atom %) were prepared. The ^{17}O-enriched water was obtained from the Institute's enrichment plant. Final volumes of the solutions used were about 2 ml.

Results and Discussion

$1/T_2$ values were measured for the carbonyl, *gem*-diol, and water resonances as a function of acid concentration for three solutions: 1.9, 3.7, and 5.7 *M* in acetaldehyde. Within experimental accuracy no broadening of the water line could be detected over the whole range of acid concentration studied (0 to 0.72 *M*), while appreciable broadening of the carbonyl and *gem*-diol resonances occurred. Since $1/T_2^0$ for the carbonyl resonance is much smaller than that for the *gem*-diol resonance (*cf.* Table I), the additional broadening of the carbonyl peak could be determined much more accurately. We shall discuss the results for the carbonyl resonance first.

Table I. $1/T_2^0$ Values and $k_H^{C=O}$ for Solutions of Acetaldehyde in Water

No.	Acetaldehyde, *M*	$1/T_2^0$, sec⁻¹ Carbonyl	$1/T_2^0$, sec⁻¹ *gem*-Diol	Range of acid concn, *M*	$k_H^{C=O}$, M^{-1} sec⁻¹
1	1.9	138	580	0–0.40	410 ± 60
2	3.7	160	740	0–0.72	480 ± 70
3	5.7	165	910	0–0.60	525 ± 80

In Figure 1, $1/T_2$ of the carbonyl oxygen resonance is plotted *vs.* acid concentration for solution no. 3. It is seen that $1/T_2$ and thus $1/\tau$ of the carbonyl oxygen, $1/\tau^{C=O}$, depends linearly on the concentration of acid, *i.e.*

$$1/\tau^{C=O} = k_H{}^{C=O}[H^+] \tag{6}$$

where $k_H{}^{C=O}$, is the acid-catalysis second-order rate constant for the exchange of carbonyl oxygen. From the slope of the line in Figure 1, $k_H{}^{C=O} = 525\ M^{-1}$ sec⁻¹. Similar values were obtained for the other two solutions and are listed in Table I.

The value of $k_H{}^{C=O}$ so obtained may now be compared with the rate constant for the acid-catalyzed hydration. Although the omr results were obtained in much more acidic solutions than those used in the hydration studies

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[18] "NMR & EPR Spectroscopy, Varian 3rd Annual Work Shop," Pergamon Press, Oxford, 1960, p 164.

[19] We are indebted to J. Reuben for performing the radiofrequency field calibration.

[20] H. M. McConnell, *J. Chem. Phys.*, **28**, 430 (1958).

and although the results seem to depend on the molarity of acetaldehyde, they do fall within the range of rate constants (480–670 M^{-1} sec^{-1}) determined for the acid-catalyzed hydration. Thus within the experimental accuracy both rate constants are equal and the oxygen exchange of the carbonyl group can be completely accounted for by the hydration reaction 1.

The specific rate of exchange of the *gem*-diol oxygens, $1/\tau^{C(OH)_2}$, is related to $1/\tau^{C=O}$.

$$\frac{1/\tau^{C(OH)_2}}{1/\tau^{C=O}} = \frac{[CH_3CHO]}{2[CH_3CH(OH)_2]} \tag{7}$$

The experimental points of $1/T_2$ for the *gem*-diol oxygen of solution no. 3 are also shown in Figure 1. Since $1/T_2^0$ for this line is quite large, there is a relatively small change in $1/T_2$ and therefore a large error in determining $1/\tau^{C(OH)_2}$. Instead of obtaining this quantity from the experimental results, we have plotted in Figure 1 the calculated $1/T_2$ for the *gem*-diol resonance from eq 6 and 7. It is seen that this line gives a satisfactory fit with the experimental points. The same holds for solutions 1 and 2.

No broadening of the solvent $H_2{}^{17}O$ resonance was detected. The maximum broadening of the water resonance $1/\tau^{H_2O}$, due to reaction 1, can be calculated from the relation

$$\frac{1/\tau^{C=O}}{1/\tau^{H_2O}} = \frac{[H_2O]}{[CH_3CHO]} \tag{8}$$

From this equation the maximum calculated broadening of the water line in our experiments should not exceed 10% of the natural line width of water, which is within the experimental accuracy of the determination of line widths.

Ahrens and Strehlow[14] studied the reversible hydration of acetaldehyde in aqueous solutions containing up to 57 mole % of acetaldehyde and varying concentrations of HCl (up to ~0.1 *M*). They used pmr spectroscopy and calculated the exchange rates from the broadening of the methyl resonances. At low concentration of acetaldehyde the broadenings of the methyl peaks corresponding to free and hydrated molecules were found to be reciprocally related to their concentrations, as expected. However, at high concentrations of acetaldehyde, upon addition of HCl, it was found that the methyl resonances due to the unhydrated molecules broadened while the peaks located at the position of the hydrated molecules did not. To explain this phenomenon these authors proposed that at high acetaldehyde concentrations new species, presumably the hemihydrate or some higher polymers, are formed and their peaks, which are narrow, merge with the broad methyl peaks of the hydrated acetaldehyde.[21]

To shed more light on this problem we had originally hoped to detect signals of the suggested new species by omr. However, no new signal appeared in the spectra of concentrated acetaldehyde solutions. Thus if new species were indeed formed, their omr resonances must have merged with those of the water or *gem*-diol peaks. When sufficient HCl (0.1–1.0 *M*) was added to concentrated solution of acetaldehyde (above 20 mole %) to cause broadening of the omr peaks, the solution separated into two layers apparently because of formation of paraldehyde, which is insoluble in water.[22]

Oxygen Exchange in a Neutral Aqueous Solution of Methylene Glycol

As mentioned above, oxygen exchange of methylene glycol is sufficiently slow to be followed by the change of the ^{17}O peak height upon dissolving methylene glycol in enriched water. One such experiment was carried out: 0.3 ml of formaldehyde solution (36% w/v) was added to 0.7 ml of $H_2{}^{17}O$ (~9 atom % ^{17}O) and the mixture placed in the nmr spectrometer. The increase of the signal due to methylene glycol could easily be followed and gave a first-order plot with $k = 2 \times 10^{-3}$ sec^{-1}. In order to compare this value with the rate constant for dehydration of methylene glycol it should be multiplied by two since only one of the two oxygens is involved in a dehydration event. Therefore, 4×10^{-3} sec^{-1} should be compared with the rate constant for dehydration of methylene glycol,[11] which is 5×10^{-3} sec^{-1}. An uncertainty in the rate of exchange is due to the presence of polymers. However, the rate of depolymerization is very much slower than the oxygen exchange measured here.[23] Thus within the experimental accuracy the oxygen exchange of formaldehyde can be completely accounted for by the dehydration–hydration reaction.

[21] Reference 14 and private communication.

[22] The paraldehyde was identified by its ^{17}O chemical shift. The upper layer was extracted into CCl_4, and this solution gave an omr signal at − 104 ppm; *cf.* Christ, *et al.*,[7] − 102 ppm for paraldehyde.

[23] J. F. Walker, "Formaldehyde," 3rd ed, American Chemical Society Monograph Series, Reinhold Publishing Corp., New York, N. Y., 1964, p 72.