

The Acetate-Catalyzed Enolization of 2-Butanone

Some Remarks on Some Recent Papers by J. Warkentin and
Co-workers

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The acetate-catalyzed deuteration of 2-butanone has been studied. The orientation of exchange was found to be the same as in the deuterioxide-catalyzed deuteration. This is in agreement with previous results of the present author but deviate from results recently reported by Warkentin and co-workers.

NMR-Spectroscopy has proven to be an excellent tool with which to follow the deuteration of ketones. The rate of reaction and the orientation of reaction for unsymmetric ketones can be estimated in one experiment.¹⁻¹¹

2-Butanone, the simplest unsymmetric ketone, has been most extensively studied. It has been suggested that the orientation of deuteration can be given as K_D -values,⁴ which are defined as 3-deuteration/1-deuteration ($2k_{CH_3}^{obs}/3k_{CH_2}^{obs}$). In 1966 the present author reported that no significant differences in the K_D -values could be observed when either weaker bases such as sodium acetate or sodium bicarbonate were used, or when the stronger base, sodium deuterioxide, was used. The K_D -values varied between 0.6 and 0.75, and the solvent was throughout D_2O . About the same K_D -value was obtained in an acetate buffer.^{1,2}

In 1967 Bothner-By and Sun reported similar K_D -values for a series of experiments with sodium acetate in D_2O , the mean value was 0.66,³ and the same year Rappe and Sachs reported $K_D=0.61$ for sodium carbonate in a D_2O /dioxane mixture.⁴

However, in a series of papers Warkentin and collaborators are of the opposite opinion: The K_D -values vary with the base used.⁵⁻⁸ In two papers in 1966 Warkentin and Tee report a series of experiments with sodium acetate in D_2O .^{5,6} If the rate constants were treated according to the definition above in calculating K_D , values of 0.75-0.8 were obtained. However, Warkentin and Tee consider that in these observed rate constants there is a substantial contribution from catalysis by OD^- . In order to calculate the rate constants for acetate only, Warkentin *et al.* introduced an extrapolation technique in

which they plot observed catalytic rate constants against $[\text{OAc}^-]^{-1/2}$, and the value found for $[\text{OAc}^-]^{-1/2}=0$ was given as the true catalytic constants for sodium acetate. The K_D -value calculated from these extrapolated rate constants is 1.44; thus there is a significant variation in the orientation due to the base used.^{5,6}

The extrapolation to obtain the catalytic constants implies that $[\text{OAc}^-] \rightarrow \infty$. Such a procedure is always open to question; the more so in this case as the relationship between the catalytic constant and the acetate concentration has been derived on the basis of laws which are valid only for very dilute, ideal solutions.

In addition to the objections raised above and in Ref. 2 there is another serious objection to the catalytic rate constants given by Warkentin and Tee. They state that their observed rate constants are the sum of acetate and deuterioxide catalyzed reactions, the other terms in eqn. (1) being neglected:

$$k^{\text{obs}} = k^{\text{OAc}^-} [\text{OAc}^-] + k^{\text{OD}^-} [\text{OD}^-] + k^{\text{D}_2\text{O}^+} [\text{D}_2\text{O}^+] + k^{\text{DOAc}} [\text{DOAc}] + k^{\text{DOAc, OAc}^-} [\text{DOAc}] [\text{OAc}^-] + k_0 \quad (1)$$

If we now use the catalytic constants for acetate obtained from the extrapolation technique, it is possible to calculate the term $k^{\text{OD}^-} [\text{OD}^-]$ for the CH_3 - and the CH_2 -groups from the values of k^{obs} , see Table 1. Here it is

Table 1. Rate constants calculated from the values given by Warkentin and Tee.⁶

[OAc ⁻]	$k^{\text{obs}} \times 10^7 \text{sec}^{-1}$		$k^{\text{OAc}^-} \times 10^7 \text{sec}^{-1}$		$k^{\text{OD}^-} \times 10^7 \text{sec}^{-1}$	
	CH ₂	CH ₃	CH ₂	CH ₃	CH ₂	CH ₃
0.104	3.60	3.19	1.23	0.57	2.37	2.62
0.136	4.34	3.88	1.60	0.74	2.74	3.14
0.260	6.56	5.75	3.07	1.42	3.49	4.33
0.468	10.8	8.68	5.5	2.56	5.3	6.12
0.490	11.0	5.94 (!)	5.8	2.68	5.2	3.26 (!)
0.630	14.6	12.0	7.4	3.4	7.2	8.6
0.930	19.1	13.4	11.0	5.1	8.1	8.3
0.946	19.7	13.9	11.2	5.2	8.5	8.7
1.310	21.3	14.3	15.5	7.2	5.8	7.1
1.310	20.6	14.8	15.5	7.2	5.1	7.6
1.500	26.7	21.5	17.7	8.2	9.0	13.3

obvious that in all experiments $k_{\text{CH}_2, \text{OD}^-}$ is 10–50 % larger than $k_{\text{CH}_3, \text{OD}^-}$. In separate experiments Warkentin and Tee have determined $k_{\text{CH}_2, \text{OD}^-}$ and $k_{\text{CH}_3, \text{OD}^-}$.^{5,6} (This has also been done by Rappe in Ref. 1, and later by Warkentin and Barnett;⁷ the results in these series are in agreement). Here it is found that $k_{\text{CH}_2, \text{OD}^-}$ is 10–20 % smaller than $k_{\text{CH}_3, \text{OD}^-}$. Thus it is apparent that the treatment of the experimental data according to Warkentin and Tee is not correct.

In two recent papers this year Warkentin and co-workers report further experimental data for the base-catalyzed deuteration of 2-butanone.^{7,8}

In the article by Warkentin and Cox⁸ there is an extensive discussion of the so-called uncatalyzed reaction k_0 in eqn. (1). In 1966 it was reported by

Rappe that a sample of 2-butanone in D_2O was deuterated very slowly, the reaction being noticeable first after several months.¹ It seems a little peculiar that Warkentin and Cox can refer to this extremely slow reaction as a reaction with "an appreciable rate" or as a reaction with "a high rate". In the 1966-experiment the reaction was followed by the decrease in the CH_3 - and CH_2 -peaks as well as by the increase in the DOH-peak.¹ The experiment was repeated later with similar results. — Warkentin and Cox, on the other hand, studied the integrals and the splitting of the peaks. Since the integral over the CH_3 - and CH_2 -peaks did not change and since no new splitting was observed they conclude that there does not exist any "uncatalyzed" reaction.⁸ It has recently been reported by Rappe and Sachs for the deuteration of cycloalkyl methyl ketones, that although the starting ketones were purified by preparative VPC, some of them contained base-consuming impurities resulting in errors in the base-catalyzed deuteration.⁹ Therefore it is difficult to establish whether the observed, extremely slow "uncatalyzed" reaction originates from impurities or not; impurities may be present in the purified starting ketone or formed during the reaction.

Warkentin and Cox⁸ reported that they obtained the same catalytic rate constants for acetate as for those reported previously by Warkentin and Tee:^{5,6} $k_{CH_3}^{OAc^-} = 11.47 \times 10^{-7}$ and 11.8×10^{-7} , $k_{CH_2}^{OAc^-} = 6.03 \times 10^{-7}$ and 6.47×10^{-7} . Of course this is a good agreement but the authors seem to have overlooked the *difference in temperature*, 54.8°C respectively 59.2°C. Data from the investigation of Bothner-By and Sun make it possible to estimate the rate difference for a 5°C variation as about 1.5–2 in the acetate-catalyzed deuteration of 2-butanone.³ Thus the agreement reported by Warkentin and Cox seems to be of minor importance and only fortuitous.

The experiments earlier reported by Rappe, Bothner-By and by Warkentin *et al.* are all performed using 1H -acetate and 1H -acetic acid.¹⁻⁸ The CH_3 -singlets of these compounds are very close to the CH_3 -singlet of 2-butanone, and it is overlapped by the multiplets of partially deuterated 2-butanone,¹² resulting in difficulties in a careful estimation of the rate of CH_3 -deuteration. In order to avoid these difficulties experiments are now reported in a 1:10 DOAc/OAc⁻ buffer of fully deuterated acetic acid and sodium acetate. As already has been pointed out,^{2,8} in an acetate buffer all other factors in eqn. (1) can be neglected except $k^{OAc^-} [OAc^-]$. The experiments were performed at the same temperature (54.8°C) and within the same concentration region as has been studied by Warkentin and Cox.⁸

The deuteration was followed as usual: by the decrease in the integrals of the α -groups as well as in the increase of the DOH-singlet.^{1,2,4,10} The integrals from the CH_2 -quartet and the CH_3 -singlet were separated in the inflexion point. In Figs. 1 and 2 are spectra for the starting sample ($[OAc^-] = 0.2$ M) and the same sample after 15 days at 54.8°C. The rate constants for the CH_2 - and CH_3 -deuteration were calculated using a linear least-squares program, see Table 2. The orientation of the deuteration (K_D) can be calculated in each analysis as well as from the ratio of the rate constants, the latter calculation gave $K_D = 0.80 \pm 0.04$ and $K_D = 0.79 \pm 0.06$, see Table 2.

The values reported here are in perfect agreement with the rate constants reported in Ref. 2 for the deuteration in a 1:1 acetate buffer at 60°C (Table 2)

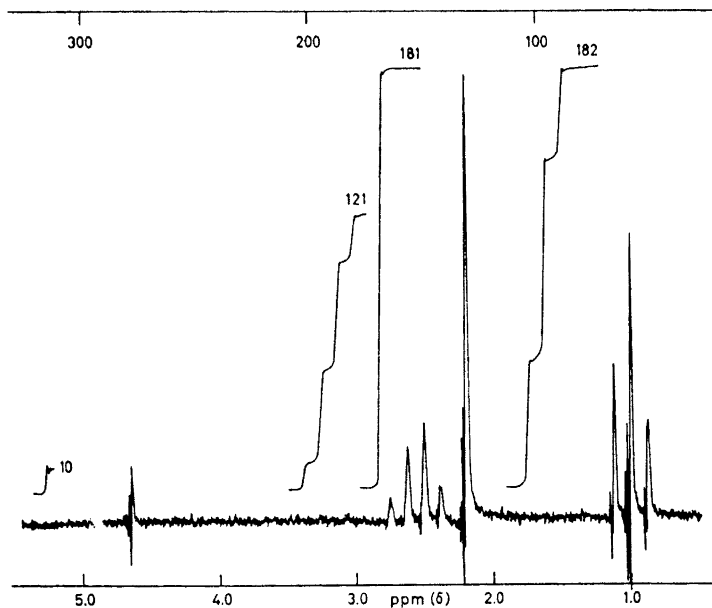


Fig. 1. Starting sample of 2-butanone in acetate buffer in D_2O .

Table 2. Rate constants for the deuteration of 2-butanone in a 1:10 acetic acid- d_4 -sodium acetate- d_3 buffer in D_2O at $54.8 \pm 0.1^\circ C$.

$[OAc^-] M$	$k_{CH_3}^{obs} \times 10^7$	$k_{CH_3}^{obs} \times 10^7$	$k_{CH_3} \times 10^7$	$k_{CH_3} \times 10^7$
0.2	1.17 ± 0.02	1.41 ± 0.05	5.8 ± 0.1	7.1 ± 0.3
0.1	0.58 ± 0.03	0.69 ± 0.02	5.8 ± 0.3	6.9 ± 0.2

and, what is more important, with the proposal in Refs. 1 and 2 that *no significant difference* exists between the orientation of the deuteration of 2-butanone using sodium acetate, a weak oxygen base, and sodium deuterioxide, a strong oxygen base. On the other hand, the K_D -values and the rate constants for the CH_2 -deuteration are in obvious disagreement with the results by Warkentin *et al.*⁵⁻⁸ At the present state no explanation can be given for this remarkable difference in results.

EXPERIMENTAL

NMR-Measurements were carried out on a Varian A-60 spectrometer. Acetic acid- d_4 and D_2O were used as supplied (CIBA). Sodium acetate- d_3 was prepared by neutralizing acetic acid- d_4 followed by thorough drying. Stock solutions of acetic acid- d_4 and sodium

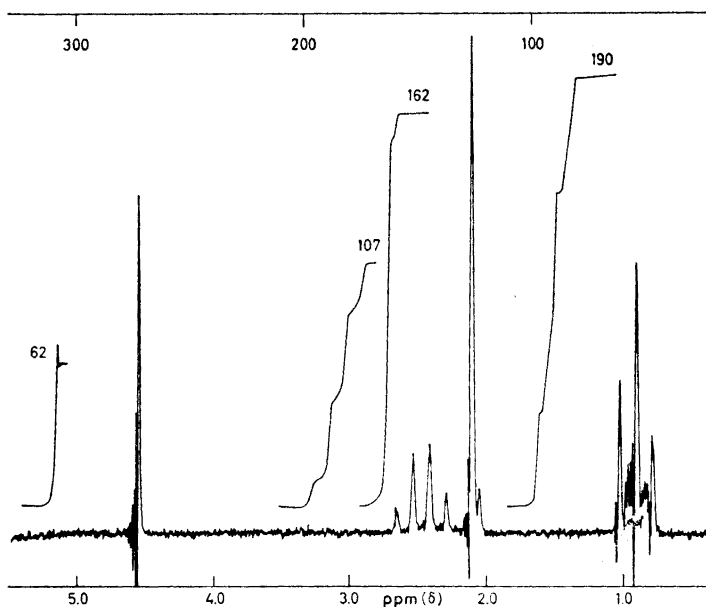


Fig. 2. Sample after 15 days at $54.8 \pm 0.1^\circ\text{C}$ in acetate buffer in D_2O .

acetate- d_3 were made up gravimetrically, and the buffer solutions were prepared from these.

Kinetic runs. Kinetic runs were carried out in one-phase systems in duplicate directly in NMR-tubes. In one experiment 0.1 ml of 2-butanone (>99.5 according to VPC) and 0.5 ml of the buffer were pipetted in, and the tubes were carefully sealed by melting the open end. If ordinary caps were used the ketone was found to evaporate. The tubes were kept at constant temperature at $54.8 \pm 0.1^\circ\text{C}$. NMR-Integrals were recorded until a predominant trace was apparent, thus averaging to zero temporary instabilities within the instrument. Each analysis was internally referenced by integrating over the protons of the unreacting methyl group of the ketone, and/or by integrating over the DOH-peak, which gives a constant when summed with the remaining area of the deuterating groups.

The pseudo-first-order rate constants were calculated on a control Data 3600 computer using a linear least-squares program designed to accept the integral values from the NMR-spectra. The values are given in Table 2.

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