

Halogenation of Ketones

XI.* Competitive Acid-Catalyzed
Halogenation and Deuteration of
2-Butanone

CHRISTOFFER RAPPE

*Institute of Chemistry, University of Uppsala,
Box 531, S-751 21 Uppsala 1, Sweden*

Enolization is generally accepted to be the rate determining step in the acid-catalyzed halogenation of ketones.¹⁻⁵ This means that the rate of halogenation should be the same for all halogens and equal to the rate of racemization. As another consequence of this it follows that the halogenating agent would be much more efficient in capturing the enol than the surrounding protonating solvent molecules. Thus as long as any halogenating agent is present, no re-ketonization of the enol takes place, or, if a deuterating solvent was used, no deuteration would take place. However, no experiments verifying this hypothesis seem to have been reported for acid-catalyzed reactions.

Recently it has been reported by Bell *et al.*^{6,7} that at very low halogen concentration (10^{-6} M or lower) the rate of acetone bromination was higher than the rate of chlorination, the rate determining step is not the halogenation of the enol. Therefore, it would be of interest to establish the existence of an eventual competitive halogenation and deuteration in various solvents with halogen concentration corresponding to synthetic conditions.

NMR-analyses of the reaction mixtures from halogenations performed in a deuterating medium provided a possibility for such studies. This method has previously been used to show that for base-catalyzed reactions of ordinary monoketones, *e.g.* 2-butanone, these two reactions are not competitive reactions.⁸ This is contradictory to the accepted view. In the present paper some results are given for the acid-catalyzed reactions of 2-butanone.

The reactions were studied in five deuterating solvents: deuterium oxide, acetic acid- d_4 , deuterium oxide-acetic acid- d_4

(4:1 by volume), acetic acid- d_4 -deuterium oxide (4:1 by volume), and methanol- d_4 -acetic acid- d_4 (4:1 by volume). Both bromine and iodine were tried as halogenating agent, but in the case of iodine the net reaction was very slow due to the reverse reaction (between iodoketone and hydrogen iodide). With the exception of the experiments in pure deuterium oxide, the reactions were performed in one phase systems at 20°C. The reaction mixtures were all about 2 M in 2-butanone and 0.3 M in bromine, and the concentration of the deuterating solvent is given in Table 1, [D], together with the results obtained.

Table 1. Competitive acid-catalyzed halogenation and deuteration of 2-butanone; 2.0 M $\text{CH}_3\text{CH}_2\text{COCH}_3$, 0.3 M Br_2 .

Solvent	% Halogen- ation	K_{Br}	[D] ^a mole l ⁻¹
D ₂ O	44	1.8	100
→→	38	2.1	100
CD ₃ COOD	17	7.0	16
→→	20	6.8	16
D ₂ O-CD ₃ COOD (4:1)	65	2.3	83
→→ (4:1)	50	2.2	83
→→ (1:4)	77	3.0	33
CD ₃ OD-CD ₃ COOD (4:1)	100	1.7	3

^a The concentration of available deuterium from D₂O being doubled.

Two samples were taken: one in the beginning of the reaction and the other when the bromine colour faded. The reaction mixtures were quenched by chilling to -50°C, and thereafter analyzed directly by NMR at -15°C. In the experiments with deuterium oxide only, acetic acid- d_4 was added to achieve a one phase system, and in the case of pure acetic acid- d_4 , deuterium oxide was added to lower the freezing point of the solvent. Samples kept at -50°C for several hours were analyzed and gave the same results, thus excluding the possibility of unwanted reactions during the chilling. The bromine colour still persisted after complete analyses. Only monobrominated products were observed.

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The percentage halogenation of the total amount of enolization (column two, Table 1) was calculated in the following way. The amount of bromination was calculated from the CH_3 -doublet in 3-bromo-2-butanone and the CH_2Br -singlet in the 1-bromo isomer, while the amount of total deuteration was estimated from the DOH-peak. From this latter value the amount of DOH in the starting sample was subtracted giving the total amount of proton exchange during the reaction. From this value and the total amount of halogenation the percentage of halogenation in the reaction could be calculated (Table 1).

The results stand in conflict to predictions based on accepted theories.¹⁻⁵ An obvious deuteration of the ketone was observed in most solvents, especially in the pure solvents deuterium oxide and acetic acid- d_4 , the mixture methanol- d_4 -acetic acid- d_4 with a rather low concentration of deuterating solvent being an exception.

The observed synchronous halogenation and deuteration can be explained in two ways. It is either due to the existence of different mechanisms for the two reactions as has recently been suggested in the case of base-catalyzed reactions,⁸ or to one common step, the enolization, followed by competitive halogenation and deuteration of the enol. Indication for the latter explanation is found in the observed orientation of the two reactions. The orientation of the reactions can be given as K_D - and K_{Hal} -values, which are defined as $[\text{3-substituted product}]/[\text{1-substituted product}]$; for a comprehensive discussion, see Ref. 9. Contrary to the base-catalyzed reactions, the observed K_D - and K_{Br} -values are close to each other and the small differences can be well understood by a difference in the efficiency of the halogenating agent in capturing the 1- and 3-enols compared with the deuterating agent.

The situation in pure acetic acid- d_4 and in the mixture methanol- d_4 -acetic acid- d_4 requires discussion in detail. For the deuteration in a mixture acetic acid-deuterium oxide (4:1 by volume) a K_D -value of 2.4 has previously been reported.¹⁰ The now observed K_{Br} -values varied between 7.0 for pure acetic acid- d_4 and 2.2 for a 1:4 mixture with deuterium oxide. How-

ever, it is also found that the K_D -value for the deuteration increased markedly when the amount of water decreased, and in pure acetic acid a value of 5.5-6 was observed.¹¹ However, in experiments with methanol as solvent, the K_D -value decreased, and in pure methanol- d_4 (DCl catalyst) a K_D -value of 1.5 was found.¹¹ In the mixture methanol- d_4 -acetic acid- d_4 (4:1 by volume) a K_D -value of 2.0 was obtained. Thus even in these solvents the K_D - and K_{Br} -values are close together.

The results reported above are in harmony with the observation by Bell *et al.*^{6,7} that at low halogen concentration the halogenation of the enol is the rate determining step. However, it is of interest to point out that even under "synthetic conditions" (dropwise bromine addition) and in solvents with a high concentration of protonating (or deuterating) species, enolization is not the rate determining step in the reaction.

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