

Intermediate Steps in Autoxidations

II. Autoxidation and Enolization of Acetophenone in Acetic Acid*

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The manganic acetate-catalyzed autoxidation (110°C, 1 atm of oxygen) of acetophenone (<0.7 M) in CH₃COOD as well as of acetophenone-*ω*-d₃ in CH₃COOH proceed at the same rates as the H/D exchange under the same conditions but in the absence of oxygen. In both oxidation reactions, the unoxidized ketones retain their isotopic compositions. Moreover, substituent effects on autoxidations of acetophenones are the same as observed for H/D exchange ($\rho \approx -0.7$). These data constitute definite evidence for enolization being the rate-determining step in these autoxidations. Arrhenius energies of activation are of the order of 15 kcal for autoxidation as well as for deuteration of acetophenone.

At higher concentrations, however, autoxidation rates fall *below* rates of H/D exchange; the unoxidized acetophenones show isotopic exchange. In these systems, reduction of trivalent manganese by the enol is probably so fast that its regeneration from Mn^{II} becomes (partly) rate-determining.

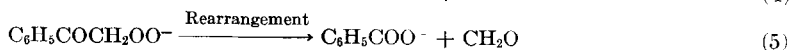
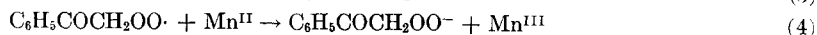
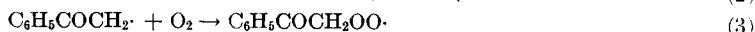
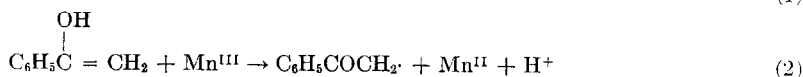
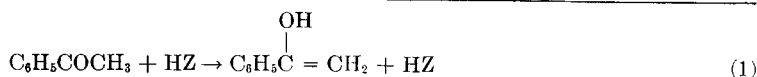
H/D isotope effects are small when changing the solvent from CH₃COOH to CH₃COOD, rates decreasing by a factor of 1.2 at 110°C. However, C₆H₅COCD₃ is oxidized in acetic acid at a three times lower rate than acetophenone.

INTRODUCTION

The present paper deals with the Mn-catalyzed autoxidation of acetophenone to benzoic acid and formaldehyde in acetic acid at temperatures of 50–110°C. In an earlier report (2) describing such autoxidations carried out in butyric acid (150°C), enolization of the ketone was proposed to be the rate-determining step. The following scheme was suggested:

Various qualitative and semiquantitative arguments were offered for the hypothesis that (1) should be rate-determining as well as for the plausibility of the other steps suggested.

If such a scheme were to hold for autoxidations in acetic acid at 110°C also, the rate of autoxidation should equal that of enolization in this solvent. In deuterated acetic acid (CH₃COOD), the regeneration



* Part I, ref. (1) (preceding paper).

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of ketone from the enol should lead to deuterium uptake in the ketone if the forward step (1) is rate-determining, the enol should be oxidized to benzoic acid as soon

as it is formed. Accordingly, the unoxidized ketone present should remain free from deuterium during the oxidation process.

Enolization of acetophenones followed by means of hydrogen/deuterium exchange has been dealt with in the first part of this series (1). We will now discuss the significance of enolization in the autoxidation of acetophenone, starting from the above reaction scheme.

METHODS

Rates of H/D exchange. These rates were determined as described in Part I (1). The experimental accuracies as regards rate constants are estimated to be within about 5%.

Starting materials. Acetophenone, CH_3COOD , acetophenone- ω - d_3 and Mn^{III} acetate used were the same as described in Part I (1) or ref. (2).

Autoxidation rates. These rates were measured as described earlier, viz., by titrimetric determinations of benzoic acid formed after different intervals of time, sometimes also by direct weighing (2). As in the case of autoxidations in butyric acid, rates were found to be first order with respect to the ketone.

RESULTS AND DISCUSSION

a. Comparison of rates of autoxidation and H/D exchange at 110°C. Table 1 pre-

TABLE 1
AUTOXIDATION (k_{aut}) AND H/D EXCHANGE
RATES (k_{exoh}) OF ACETOPHENONE IN
ACETIC ACID AT 110°C

Ketone ^a	Solvent	k_{aut}^b (hr ⁻¹)	k_{exoh}^b (hr ⁻¹)
Acetophenone	CH_3COOH	0.79	—
Acetophenone	CH_3COOD	0.68 ^c	0.66 ^c
Acetophenone- ω - d_3	CH_3COOH	0.25	0.22

^a Ketone concentration 0.56 mole/liter; acetic acid 16.8 mole/liter; Mn 20 mmoles/liter (as Mn^{III} acetate).

^b Mean values of first order rate constants derived from various runs; maximum deviations 5%.

^c Runs carried out with 95% CH_3COOD ; k_{exoh} extrapolated to 100% CH_3COOD [cf. Part I (1)]. For k_{aut} , the correction for 100% CH_3COOD amounts to less than 1%.

sents the data on rate constants for the autoxidations of acetophenone and acetophenone- ω - d_3 as well as for the H/D exchanges in acetic acid.

The figures demonstrate that autoxidation and exchange proceed at the same rates within the limits of experimental error. Beyond a certain limit (10 mmole/liter), the manganic acetate concentration had no effect on rates of autoxidation—as had been found earlier for the autoxidation of acetophenone in butyric acid at 150°C (2).

b. Effect of temperature on rates of autoxidation. Rate constants (cf. Table 2) were determined at temperatures of 50°, 70°, 90°, and 110°C and concentrations of acetophenone in acetic acid of 0.56 mole/liter. The usual Arrhenius plot led to an energy of activation of 14.5 ± 1 kcal, close to that obtained (1) for the deuteration of acetophenone in CH_3COOD (16 kcal). Considering that the two processes were carried out in different solvents (CH_3COOH and CH_3COOD , respectively), the agreement is very satisfactory, the "lower" activation energy (14.5 kcal) corresponding to the "faster" solvent (CH_3COOH). The Arrhenius plots are given in Fig. 1.

c. H-D exchange in unoxidized acetophenone. NMR analyses (1) of unconverted ketones (acetophenone oxidized in CH_3COOD ; acetophenone- ω - d_3 in CH_3COOH) indicated that no isotopic exchange had occurred under conditions leading to appreciable proportions of benzoic acid. Taken together with the identity of autoxidation and H/D exchange rates this definitely demonstrates enolization to be the rate-determining step in autoxidation at 110°C. It may be noted that this also precludes direct formation of phenacyl radicals ($\text{PhCOCH}_2\cdot$) from the ketone and Mn^{III} as an initiating step.

However, this conclusion appeared to be limited to ketone concentrations below about 0.65 mole/liter. At higher concentrations, the rates of autoxidation were lower than the rates of deuterium exchange; the unoxidized acetophenones then did show hydrogen-deuterium exchange. A typical example of this situation is given

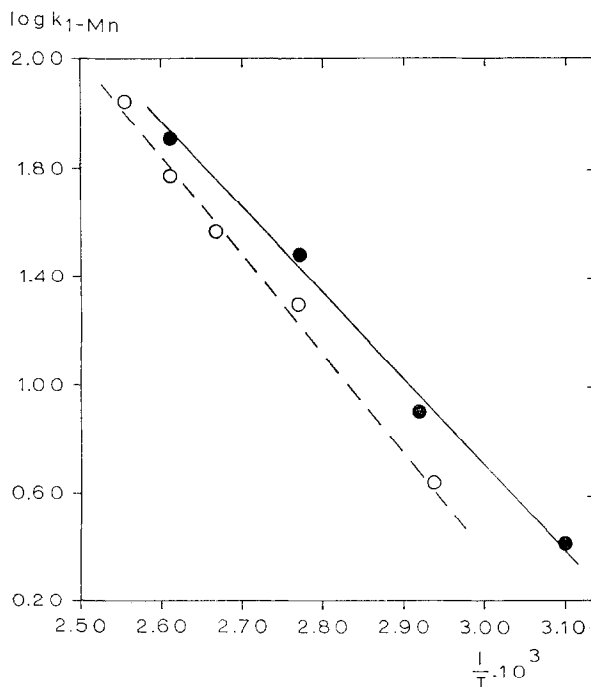


Fig. 1. Arrhenius plot for autoxidation in CH_3COOH (●) and H/D exchange [95% CH_3COOD ; (○)].

by the result of an oxidation experiment run at an initial concentration of acetophenone of 3.5 mole/liter and of acetic acid of 10.5 mole/liter. After a reaction time of 3 hours at 110°C , 34% of the acetophenone intake had not undergone any reaction, the sum total of benzoic acid formed (15%) and of deuterium uptake (51%) amounting to 66%; a deuteration run under otherwise identical conditions gave 38% unreacted ketone. The latter percentage is only slightly higher than may be calculated from the rate constants observed at higher dilutions. These aspects are further discussed in Section f.

d. Isotope effects in the exchange reactions acetophenone/ CH_3COOD versus acetophenone- ω - d_3 / CH_3COOH . Now that it has been shown that, under certain conditions, autoxidation and deuteration (= enolization) proceed at identical rates, the isotope effect of 3.0 observed (1) for the ratio of exchange rates in the systems acetophenone/ CH_3COOD and acetophenone- ω - d_3 / CH_3COOH can be further interpreted. Thus, since $k_{\text{aut}} = k_{\text{enolization}} = 0.79$ for the

system acetophenone/ CH_3COOH , whereas $k_{\text{aut}} = 0.25$ for acetophenone- ω - d_3 / CH_3COOH , we find for the isotope effect in the *same solvent* CH_3COOH the value $0.79/0.25 = 3.2$ (cf. Table 1). Accordingly, the former isotope effect of 3.0 is probably composed of two competing effects, viz. an acceleration by a factor of 3.2 due to the removal of a proton from the methyl group being faster than that of a deuterium and a decrease by a factor of $3.2/3.0 = 1.07$ due to the stronger complexing properties of CH_3COOH as compared with CH_3COOD . Considering the large effect of dilution of CH_3COOD by CH_3COOH (Part I, Table 4), this value is unexpectedly close to unity. However, it was derived from four independent rate constants and may therefore contain an appreciable experimental error.

e. Substituent effects on autoxidation and H/D exchange. Rates of autoxidation were measured for a small number of substituted acetophenones in CH_3COOH at 110°C , using ketone concentrations of 0.5 *M*. These rates were then compared with the H/D exchange rates in 95% CH_3COOD (col-

umns 1 and 2, Table 3). For unsubstituted acetophenone, the ratio of autoxidation in CH_3COOH (= rate of enolization in the same solvent) and H/D exchange in 95% CH_3COOD amounts to $0.79/0.59 = 1.34$ (Table 1). For simplicity, it has been assumed that the same ratio will also hold for the case of substituted acetophenones; the figures given in column 3 were obtained by

TABLE 2
VARIATION OF RATE CONSTANTS OF AUTOXIDATION OF ACETOPHENONE IN ACETIC ACID (CH_3COOH) WITH TEMPERATURE

Temperature (°C)	$k_1 \times 10$ (hr ⁻¹)
50	0.27
70	0.78
90	3.2
110	7.9

[Acetophenone]: 0.56 mole/liter
[CH_3COOH]: 16.8 mole/liter
[$\text{Mn}(\text{OAc})_2$]: 0.012 mole/liter

correcting the exchange rates by 1.34 to account for the difference in solvent. Accordingly, they should represent rates of enolization in CH_3COOH ; the figures are close to those observed for autoxidation, as anticipated on the basis of analogy.

f. Effects of acetophenone concentration on autoxidation and H/D exchange. As mentioned in Section c, autoxidation rates drop far below those of enolization when ketone concentrations are increased beyond 0.7 M. Rates of enolization, however, do not

undergo much change. This is illustrated in Fig. 2, points for enolization having been corrected by the factor 1.34 to account for the difference in solvent (Tables 1, 3). Thus, at high concentrations of the ketone, autoxidation becomes slower than enolization, meaning that one or more of the subsequent steps becomes rate-determining.

TABLE 3
SUBSTITUENT EFFECTS^a

Substituent	k_{aut}^b (hr ⁻¹)	k_{exch}^c (hr ⁻¹)	$k_{\text{enol}}^{\text{calc}}$ (hr ⁻¹)
<i>p</i> -CH ₃	1.45	1.02	1.37
H	0.79	0.59	0.79
<i>p</i> -Br	0.55	0.44	0.59
<i>p</i> -CN	0.34	0.30	0.40
<i>p</i> -NO ₂	0.31	0.26	0.35

^a 110°C; ketones about 0.5 mole/liter; acetic acid about 17 moles/liter.

^b In CH_3COOH .

^c 95% CH_3COOD [cf. Part I (1)].

The inadequacy of the simple scheme represented by steps (1)–(4) also follows from several other facts, e.g., the lower rate of autoxidation observed when using air rather than oxygen as the oxidant (even at low ketone concentrations) and the rapid disappearance of added Mn^{III} in autoxidations at high ketone concentrations.

Evidently, the rapid formation of enol molecules at high ketone concentrations leads to termination processes. The lower rate of autoxidation in the presence of air

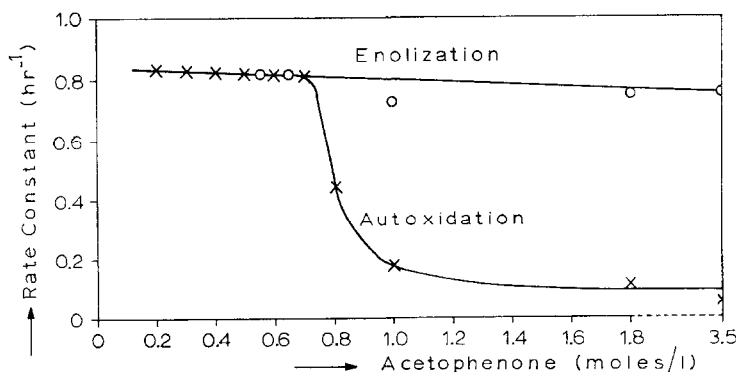


Fig. 2. First order rate constants for autoxidation (X) and for enolization (O) of acetophenone in acetic acid at 110°C.

may suggest that step (3) (addition of oxygen to the phenacyl radical) becomes rate-determining as a result of combination and/or disproportionation reactions involving the phenacyl radical. The latter suggests that regeneration of Mn^{III} due to steps 3 and/or 4 becomes too slow. In view of the high efficiency of alkyl peroxy radicals in the oxidation of Mn^{II} (3), the most plausible explanation would seem to be the failure of step (3), viz., the addition of oxygen to the phenacyl radicals. Some support for this assumption is given by the fact that the Mn-catalyzed autoxidation of ω -phenylacetophenone in butyric acid at 150°C gives an appreciable proportion of the dimers of the

corresponding ω -phenylphenacyl radicals (1,2-dibenzoyl-1,2-diphenylethane) (2).

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