252. *The Isomerism of the Oximes. Part XLII. The Acid Hydrolysis of Acetyl-α-aldoximes.*

By O. L. Brady and J. Miller.

The acid-catalysed hydrolysis of nuclear substituted acetyl-benzaldoximes in aqueous acetone has been shown to take place by a bimolecular mechanism involving acyl–oxygen fission.

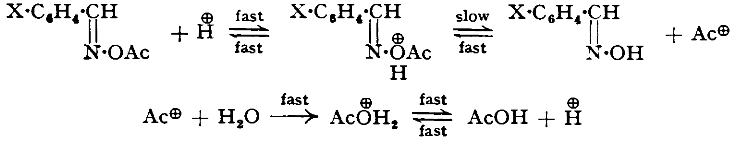
The rate constants for the reaction for varying nuclear substituents differ by only small amounts, as might be expected from the remoteness of the point of action from the electron-controlling substituent group, but are in the order *p*-OMe > *p*-Me > *o*-OMe > *m*-NO_2 > *p*-NO_2 > *o*-NO_2.

A secondary, but much slower, reaction between hydrogen chloride and acetone has been shown to take place when the concentration of water in the acetone is below 4%.

A study has been made of the acid-catalysed hydrolysis of some substituted acetyl-α-benzaldoximes, $X{\cdot}C_6H_4CH{:}N{\cdot}OAc$, in aqueous acetone.

The possibility of neutral hydrolysis was first eliminated by showing that no appreciable hydrolysis occurred in aqueous acetone under the conditions used.

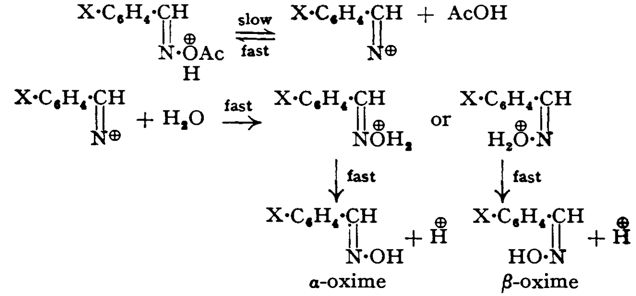
If the hydrolysis is analogous to ester hydrolysis (Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686) the possible reaction mechanisms may be represented :



$$\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{N{\cdot}OAc}\end{array} + \overset{\oplus}{\mathrm{H}} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\ \ \oplus\\ \mathrm{N{\cdot}OAc}\\ \mathrm{H}\end{array} \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{N{\cdot}OH}\end{array} + \mathrm{Ac}^{\oplus}$$

$$\mathrm{Ac}^{\oplus} + \mathrm{H_2O} \xrightarrow{\text{fast}} \mathrm{Ac\overset{\oplus}{O}H_2} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \mathrm{AcOH} + \overset{\oplus}{\mathrm{H}}$$

Unimolecular reaction with acyl–oxygen fission . . . . . (A′ 1)



$$\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\ \ \oplus\\ \mathrm{N{\cdot}OAc}\\ \mathrm{H}\end{array} \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{N}^{\oplus}\end{array} + \mathrm{AcOH}$$

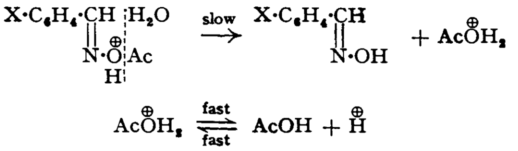
$$\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{N}^{\oplus}\end{array} + \mathrm{H_2O} \xrightarrow{\text{fast}} \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\ \oplus\\ \mathrm{NOH_2}\end{array} \text{ or } \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \oplus\ \|\\ \mathrm{H_2O{\cdot}N}\end{array}$$

$$\downarrow \text{fast} \qquad\qquad \downarrow \text{fast}$$

$$\underset{\alpha\text{-oxime}}{\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{N{\cdot}OH}\end{array}} + \overset{\oplus}{\mathrm{H}} \qquad \underset{\beta\text{-oxime}}{\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{HO{\cdot}N}\end{array}} + \overset{\oplus}{\mathrm{H}}$$

(this is analogous to alkyl–oxygen fission in the hydrolysis of esters)

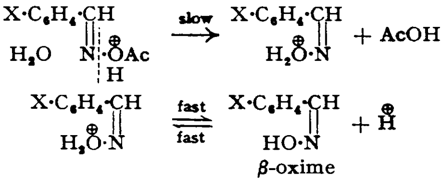
Unimolecular reaction with nitrogen–oxygen fission . . . . (A″ 1)



$$\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\ \vdots\ \mathrm{H_2O}\\ \|\ \ \oplus\vdots\\ \mathrm{N{\cdot}O}\vdots\mathrm{Ac}\\ \mathrm{H}\vdots\end{array} \xrightarrow{\text{slow}} \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{N{\cdot}OH}\end{array} + \mathrm{Ac\overset{\oplus}{O}H_2}$$

$$\mathrm{Ac\overset{\oplus}{O}H_2} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \mathrm{AcOH} + \overset{\oplus}{\mathrm{H}}$$

Bimolecular reaction with acyl–oxygen fission . . . . . (A′ 2)



$$\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\vdots\ \oplus\\ \mathrm{H_2O}\quad \mathrm{N}\vdots\mathrm{{\cdot}OAc}\\ \vdots\ \mathrm{H}\end{array} \xrightarrow{\text{slow}} \begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \oplus\ \|\\ \mathrm{H_2O{\cdot}N}\end{array} + \mathrm{AcOH}$$

$$\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \oplus\ \|\\ \mathrm{H_2O{\cdot}N}\end{array} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \underset{\beta\text{-oxime}}{\begin{array}{c}\mathrm{X{\cdot}C_6H_4{\cdot}CH}\\ \|\\ \mathrm{HO{\cdot}N}\end{array}} + \overset{\oplus}{\mathrm{H}}$$

Bimolecular reaction with nitrogen–oxygen fission . . . . . (A″ 2)

Of these possible mechanisms those involving nitrogen–oxygen fission, A″ 1 and A″ 2, can be eliminated on the following grounds. Only the α-oxime is produced in the hydrolysis; though the α-oxime is the more stable of the isomerides, the β-hydrochloride formed as an intermediate is more stable than the α-hydrochloride, and under the experimental conditions one would expect to be able to isolate some β-oxime if mechanisms A″ 1 or A″ 2 were operative. In absolute methyl alcohol acid-catalysed hydrolysis gives exclusively oxime and not the *O*-methyl ether as would be demanded by nitrogen–oxygen fission.

$$\mathrm{X{\cdot}C_6H_4CH{:}\overset{\oplus}{N}} + \mathrm{HOMe} \longrightarrow \mathrm{X{\cdot}C_6H_4CH{:}N{\cdot}\overset{\oplus}{O}HMe} \rightleftharpoons \mathrm{X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OMe} + \overset{\oplus}{\mathrm{H}} \quad . \quad \text{from A}''\ 1$$

$$\begin{tikzcd}
\mathrm{X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}\overset{\oplus}{O}HAc} \arrow[r] & \mathrm{X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}\overset{\oplus}{O}HMe} + \mathrm{AcOH} \arrow[d] \\
\mathrm{MeOH} \arrow[u] & \mathrm{X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OMe} + \overset{\oplus}{\mathrm{H}} \quad . \ . \ . \ . \quad \text{from A}''\ 2
\end{tikzcd}$$

Finally it would be expected that varying the substituent X in the benzene ring from, for example, nitro to methoxy, or replacing the methine-hydrogen atom by methyl would have a substantial effect on the rate constant, whereas, in fact, although an effect is observed it is small and is reasonably explicable by the influence of the substituents on the basicity of the oxygen atom at which proton is added (compare Day and Ingold, *loc. cit.*, for effect of electron-accession or -withdrawal in carboxylic ester hydrolysis).

It is not possible to decide from the experimental kinetics between the unimolecular and the bimolecular mechanism with acyl–oxygen fission since, although the kinetics are those for a first-order reaction, even in 99·5% acetone the initial ratio of water to acetate is not less than 6 : 1 and the bimolecular reaction is not, therefore, eliminated.

Other evidence is, however, in favour of a bimolecular mechanism. No mass-law effect was detected, such as would be expected in the unimolecular reaction; on the other hand "*ortho*-effects" were observed. The activation energies (14,000—18,000 cals./g.-mol.) are reasonable for a bimolecular, but low for a unimolecular, reaction and finally it seems unlikely that a reaction involving the separation of the cation would increase in velocity in acetone solution with decreasing amounts of water down to 2% (Table II). Mechanism A′ 2 seems, therefore, to be the correct one.

In the actual measurement of the rate constants certain complications arose. The oxime produced by the hydrolysis of the acetyl derivative undergoes further hydrolysis to aldehyde and hydroxylamine:

$$\mathrm{X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OH} + \mathrm{H_2O} \rightleftharpoons \mathrm{X{\cdot}C_6H_4{\cdot}CHO} + \mathrm{NH_2{\cdot}OH}$$

The rate of this secondary reaction was about one-fifth to one-tenth of the rate of the hydrolysis of the acetyl derivative, even with the highest acid concentrations used.

After 24 hours at 25° with 0·4N-hydrochloric acid in 80% acetone acetyl-α-*m*-nitrobenzaldoxime yielded 40—45% of α-*m*-nitrobenzaldoxime and 50—55% of *m*-nitrobenzaldehyde, whereas under these conditions the acetate is completely hydrolysed. After only 3¼ hours very little aldehyde was formed, although the acetyl compound was practically completely hydrolysed.

The formation of acetic acid was followed by titration with barium hydroxide using phenolphthalein, and it was found that hydroxylamine hydrochloride titrated as the equivalent of hydrochloric acid under these conditions, so that the secondary reaction is not evident in the measurements though it may have some effect towards the end of the primary reaction owing to competition for proton between the hydroxylamine aud the acetyl compound.

A further complication arose with reactions carried out in solutions containing a high percentage of acetone (>96%) owing, it is suggested, to the slow formation of mesityl oxide and phorone and combination of these compounds with the hydrogen chloride, thus reducing its effective concentration. This reaction has been shown to occur, not only in the presence of the acetyl-aldoximes, but also in the solutions of hydrogen chloride in acetone and water alone. The rate of this reaction is only one-fiftieth to one-hundredth of the rate of hydrolysis of the acetyl compound and a small correction can be applied where necessary to the titration values of the primary hydrolysis.

In all cases k has been calculated from the equation

$$k = \frac{1}{T}\ln\frac{a}{a-x} = \frac{2{\cdot}303}{T}\log\frac{a}{a-x}$$

Table I indicates the effect of different substituents in the benzene nucleus.

TABLE I.

80% Acetone,* $k \times 10^5$ in secs.$^{-1}$.

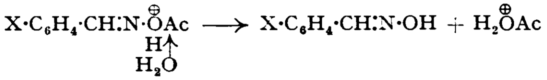
X in $X\cdot C_6H_4\cdot CH{:}N\cdot OAc$.	0·05N-HCl.	0·102N-HCl.	0·204N-HCl.	0·409N-HCl.
o-NO_2	—	1·537	—	6·226
p-NO_2	—	1·731	—	—
m-NO_2	0·901	1·916	3·834	8·707
o-OMe	—	2·004	—	9·20
p-Me	—	2·031	—	10·11
3 : 4-CH_2O_2	—	—	4·491	—
p-OMe	—	2·827	4·597	11·12
(*m*-$NO_2\cdot C_6H_4\cdot CMe{:}N\cdot OAc$)	—	—	—	10·93

* 80% Acetone and similar expressions indicate a mixture prepared by mixing 80 parts by volume of anhydrous acetone with 20 parts by volume of an appropriate mixture of hydrochloric acid and water to give a solution of the required normality with respect to hydrochloric acid, alteration in volume on mixing being ignored.

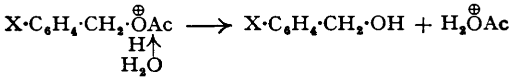
It will be seen that the effect of passing from groups of such different electron displacements as *p*-NO_2 to *p*-OMe produces but a small difference in rate constant.

The rate constants are in the order, *p*-OMe > *p*-Me > *o*-OMe >*m*NO_2 > *p*-NO_2 > *o*-NO_2, with the value for *o*-OMe not much higher than for *m*-NO_2; the value for *o*-NO_2 is considerably less than that for *p*-NO_2. The acid dissociation constants of the α-aldoximes at 25° in water are in the order, *p*-OMe < *o*-OMe < 3 : 4-CH_2O_2 < *m*-NO_2 < *o*-NO_2 < *p*-NO_2 (Brady and Goldstein, *J.*, 1926, 1918) and the basicity constants must run in the reverse order. If it be accepted that the effect of the substituent on the basicity of the oxime, *i.e.*, the oxime's attraction for proton, is paralleled in the acetyl derivatives, the rate constant for the hydrolysis of the latter compounds increases with increased affinity for proton if one excepts the *o*-compounds. The rate constants for the hydrion-catalysed hydrolysis of substituted benzyl acetates are *p*-Me > *p*-NO_2 > *m*-NO_2 (Tommila and Hinshelwood, *J.*, 1938, 1801) but, on the other hand, those for the hydrolysis of substituted ethyl benzoates are in the order *o*-NO_2 ⋘ *p*-OMe < *p*-Me < *m*-NO_2 < *p*-NO_2 (Timm and Hinshelwood, *J.*, 1938, 862).

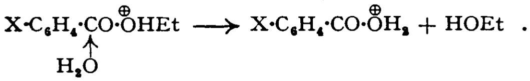
In the former case the mechanism is much more nearly parallel with the hydrolysis of the acetyl oximes :



$$X\cdot C_6H_4\cdot CH{:}N\cdot\underset{\substack{H\uparrow\\ H_2O}}{\overset{\oplus}{O}}Ac \longrightarrow X\cdot C_6H_4\cdot CH{:}N\cdot OH + H_2\overset{\oplus}{O}Ac \quad . \; . \; . \; . \; . \quad (i)$$



$$X\cdot C_6H_4\cdot CH_2\cdot\underset{\substack{H\uparrow\\ H_2O}}{\overset{\oplus}{O}}Ac \longrightarrow X\cdot C_6H_4\cdot CH_2\cdot OH + H_2\overset{\oplus}{O}Ac \quad . \; . \; . \; . \; . \quad (ii)$$



$$X\cdot C_6H_4\cdot\underset{\substack{\uparrow\\ H_2O}}{CO}\cdot\overset{\oplus}{O}HEt \longrightarrow X\cdot C_6H_4\cdot CO\cdot\overset{\oplus}{O}H_2 + HOEt \quad . \; . \; . \; . \; . \; . \quad (iii)$$

In (i) and (ii) electron-recession due to X will hinder oxonium-salt formation but is not likely, when X is in the *p*-position, to have much effect on the approach of the water molecule to the acetyl centre. In (iii), however, electron-recession, while hindering oxonium-salt formation, will exert a very favourable influence on the approach of the water molecule to the carbon atom directly attached to the nucleus. The *p*-nitro-group will accordingly hinder hydrolysis of acetyl-oximes and benzyl acetates, but favour hydrolysis of ethyl benzoates. The contrary effects will be observed with the methyl and the methoxy-group, though in the latter case some reservation may be necessary owing to the tendency of oxonium-salt formation by this group with a resulting inversion of its electronic effect.

There is a small " *ortho*-effect " since the reaction with the *o*- is slower than with the *p*-nitro-compound, and the dissociation constants of the aldoximes would lead one to expect the reverse order; further, it is slower with the *o*-methoxy-compound than one would expect from the dissociation constant which is only about 8% above that of the *p*-analogue. As, however, the point of attack by the water molecule is much more remote from the *ortho*-position in the acetyl-oximes than in the ethyl benzoates one does not get the very pronounced slowing effect of the *o*-nitro-group that one finds in the latter series where the rate constant is depressed below that of the *p*-methoxy-ester.

A comparison between the rate constants for acetyl-*m*-nitrobenzaldoxime and acetyl-*m*-nitroacetophenone oxime shows that the effect of replacing the methine-hydrogen atom by methyl is to increase the rate constant, as might be expected from the electronic effect of the methyl group weakening the acid dissociation constant or increasing the basic dissociation constant and facilitating attachment of proton. The acid dissociation constants of α-benzaldoxime and acetophenone oxime are approximately as 6·3 : 1 (Brady and Chokshi, *J.*, 1929, 946).

TABLE II.

0·204N-HCl, $k \times 10^5$ in secs.$^{-1}$.

X in $X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OAc$.	80% Acetone.	90% Acetone.	96% Acetone.	98% Acetone.	99·5% Acetone.
o-NO_2	(3·074)	—	—	12·08	—
m-NO_2	3·834	5·266	11·85	15·14	4·779
o-OMe	(4·008)	—	—	20·0	—
p-Me	(4·062)	—	—	18·32	—
p-OMe	4·597	6·952	16·67	20·36	—

Figures in parenthesis are calculated by doubling the constant for 0·1N-HCl in Table I. The rate constants in 98 and 99·5% acetone are corrected for phorone formation.

TABLE III.

$k \times 10^5$ in secs.$^{-1}$.

	0·102N-HCl.			0·14N-HCl.
	80% Acetone.	98% Acetone.	99% Acetone.	99·5% Acetone.
m-NO_2	1·916	6·938 *	5·312 *	3·533 *

* Corrected for phorone formation.

Tables II and III show the effect on the rate constant of altering the concentration of water. Decreasing the water content of the solution from 20% to 2% causes a rate increase, slowly at first, then more rapidly, and finally more slowly. A further decrease in water content down to 0·5% produces a marked decrease in the rate.

The ratio of the rate in 80% acetone to that at other concentrations, with 0·2N-hydrochloric acid, for acetyl-α-*m*-nitrobenzaldoxime is 80% 1, 90% 1·37, 96% 3·09, 98% 3·95, and 99·5% 1·25, and for acetyl-α-*p*-methoxybenzaldoxime is 80% 1, 90% 1·51, 96% 3·63, and 98% 4·43.

At very low water concentration the hydrogen chloride is little ionised and the rate constant is low. Brownson and Cray (*J.*, 1925, **127**, 2923) found that the ionisation of 0·1N-hydrochloric acid in aqueous acetone fell from 47·2% to 19·8% when the water content fell from 20% to 10%, and that of 0·02N-hydrochloric acid from 66·8% to 17·6% when the water content fell from 20% to 5%.

Passing from 0·5% to 2% of water considerably increases the ionisation of the hydrochloric acid and a rapid increase in the rate constant occurs but, with >2% of water, a competition effect between water molecules and the acetyl compound for available protons causing a rate reduction begins to outweigh the still increasing concentration of hydrogen ions. Thus the drop for 2% to 4% of water is small, but as the rate of increase of dissociation drops, the competition effect shows more strongly in solutions containing 4—10% of water.

Above 10% of water the competition shows a " saturation " effect decreasing the relative influence of increasing water concentration.

The rate constants are independent of the concentration of the acetyl compound (in 80% acetone with 0·2N-hydrochloric acid, 0·0475M-acetyl-α-*m*-nitrobenzaldoxime $k = 3{\cdot}830 \times 10^{-5}$ secs.$^{-1}$, 0·0931M-acetyl-α-*m*-nitrobenzaldoxime $k = 3{\cdot}792 \times 10^{-5}$ secs.$^{-1}$), and, as can be seen from Table I, are approximately proportional to the concentration of hydrochloric acid though in the stronger acid there is a marked " over-acid effect."

Since the hydrogen-ion concentration cannot be identified with the concentration of hydrogen chloride in these solutions the former has been determined potentiometrically by using the platinum–quinhydrone electrode and standard procedure. A 0·0028N-hydrochloric acid solution in 80% acetone was used as reference solution and its pH was estimated from the data of Brownson and Cray (*loc. cit.*) to be 2·73. By use of the formula pH $= E/0{\cdot}0591$ the following data for solutions of hydrogen chloride in 80% acetone at 25° were obtained :

Normality of HCl	0·051	0·102	0·205	0·409
E (mv.)	74·5	84	95	107
H^+ activity, moles/l.	0·0337	0·0486	0·0746	0·1190

These were confirmed by intercomparison of the half-cells.

Conductivities of hydrogen chloride in 80% acetone at 25° were measured by using the normal procedure with the following results :

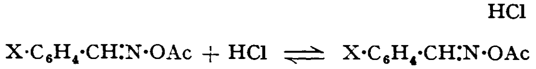
Normality of HCl	0·051	0·102	0·205	0·409
Equiv. conductivity	59·2	42·7	34·2	23·6

The ratios between the various values are :

Normality of HCl	0·051	0·102	0·205	0·409
Ratio of H activity	1·00	1·44	2·21	3·53
Ratio of equiv. conductivity	1·00	0·72	0·63	0·40

As might be expected in this solvent, there was no increase in conductivity when 0·051N-acetic acid was added to 0·102N-hydrochloric acid.

As hydrogen chloride in 80% acetone showed the properties of a weak electrolyte it follows from the results in Table I that undissociated hydrogen chloride also catalyses the reaction, probably by hydrogen bonding (Rolfe and Hinshelwood, *Trans. Faraday Soc.*, 1934, **30**, 935; Fairclough and Hinshelwood, *J.*, 1939, 593) :



$$X\cdot C_6H_4\cdot CH{:}N\cdot OAc + HCl \rightleftharpoons \overset{HCl}{X\cdot C_6H_4\cdot CH{:}N\cdot OAc}$$

The oxime formed in the primary reaction and the hydroxylamine formed in the secondary reaction will compete with the acetyl-aldoxime for the available protons and, if no counter-effect operates, there should be a gradual diminution in the rate constant as the reaction proceeds; as this is not observed the acetic acid produced in the reaction must also act as a catalyst to counteract the above competition effect. The addition of further acetic acid has a pronounced effect on the rate constant, that for 0·1N-hydrochloric plus 0·05N-acetic acid being about 11% greater than that for 0·1N-hydrochloric acid alone.

The rate constants have been measured at two different temperatures, and the approximate activation energy and frequency constant calculated from the Arrhenius equation, the results being given in Table IV.

TABLE IV.

X in $X\cdot C_6H_4\cdot CH{:}N\cdot OAc$.	Solvent.	Normality of HCl.	$T°$, K.	$k \times 10^5$, secs.$^{-1}$.	E, cals. per g.-mol.	$\log_{10}$ H, sec.$^{-1}$.
m-NO_2	80%	0·409	284·38	2·577	15,100	7·02
	80%	0·409	298·00	8·707		
m-NO_2	98%	0·204	284·38	4·331	15,500	7·57
	98%	0·204	298·00	15·14		
p-OMe	80%	0·409	284·38	2·848	17,000	8·47
	80%	0·409	298·00	11·12		
o-OMe	80%	0·409	284·38	2·780	14,900	6·86
	80%	0·409	298·00	9·200		
p-Me	80%	0·409	284·38	2·193	18,990	9·92
	80%	0·409	298·00	10·11		
o-NO_2	80%	0·409	288·18	2·658	14,900	6·68
	80%	0·409	298·00	6·226		

The side reaction mentioned above has been investigated in so far as it might affect the rate constants of the hydrolysis of the acetyl derivatives in acetone containing low concentrations of water. The formation of mesityl oxide and phorone from acetone under the influence of hydrogen chloride is well known, but little work has been done on the addition of hydrogen chloride to these compounds. Vorlander and Hayakawa (*Ber.*, 1903, **36**, 3536) prepared a compound containing two proportions of hydrogen chloride to one of phorone; they give no structural formula but it is presumably $CO(CH_2\cdot CMe_2Cl)_2$. It is stated that with cold water it loses hydrogen chloride very slowly but with warm water more rapidly, and that the loss of hydrogen chloride can be followed by titration with warm baryta solution. Rupe and Kessler (*Ber.*, 1909, **42**, 4715) prepared $Me_2CBr\cdot CH_2\cdot COMe$ by the action of hydrogen bromide on mesityl oxide cooled in ether–solid carbon dioxide and Thayer and McElvain (*J. Amer. Chem. Soc.*, 1928, **50**, 3353) prepared the corresponding chloro-compound by the action of thionyl chloride on diacetone alcohol. From the descriptions given both these compounds seem moderately stable to cold dilute alkali.

We have found that, in the presence of hydrogen chloride, acetone containing less than 4% of water undergoes a slow reaction which involves the disappearance of protons which can be followed by diluting the reaction mixture with a large excess of ice-cold water and titration with baryta. In the initial period (up to 24 hours at 25°) the rate constant fell progressively but thereafter (up to 40 days) a good first-order constant was obtained. With acetone containing

4% of water this side reaction could only just be detected after 4 days, but the rate constant increases at least until the water content is reduced to 1%.

In view of the possibility of the formation of both mesityl oxide and phorone, and of the addition to the former of one molecule of hydrogen chloride and to the latter of one or two molecules of hydrogen chloride, it is not possible to decide from this kinetic study alone what reaction or combination of reactions the rate constant represents; we were interested in it, however, only as an item to be allowed for in the determination of the rate constants for the hydrolysis of acetyl-aldoximes in acetone containing small amounts of water. From the work of others it seems that the addition of hydrogen chloride is rapid, so it has been assumed that the rate constant measured corresponds at first to mesityl oxide and phorone formation and later to phorone formation.

The rate constants for phorone formation are given in Table V. This rate constant is decreased by the presence of the products of hydrolysis of acetyl-aldoximes as shown in Tables VI and VII owing, probably, to their competition for protons.

TABLE V.

Phorone formation from acetone at 25°.

H_2O, %.	Normality of HCl.	$k \times 10^6$, secs.$^{-1}$.	% Reaction at $t = \infty$, HCl absorbed/HCl taken.
2	0·102	1·13	31·3
2	0·204	1·92	40·6
1	0·102	1·65	57·1
0·5	0·102	1·53	66·6
0·5	0·204	2·19	66·6

TABLE VI.

Phorone formation in 98% *acetone at* 25° *in presence of* 0·204N-HCl, 0·044N-*acetic acid, and aldoxime.*

Oxime $X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OH$ where X is	Molecular concn. of oxime.	$k \times 10^6$, secs.$^{-1}$.
m-NO_2	0·0635	1·125
p-OMe	0·0630	1·124
o-OMe	0·0635	1·130
p-Me	0·0545	1·304

TABLE VII.

Phorone formation in 98% *acetone at* 25° *in presence of products of hydrolysis of acetyl-aldoximes.*

Compound hydrolysed, $X{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OAc$ where X is	Normality of HCl.	$k \times 10^6$, secs.$^{-1}$.
p-OMe	0·204	1·323
o-OMe	0·204	1·437
p-Me	0·204	1·234
o-NO_2	0·204	1·459
m-NO_2	0·102	1·087
m-NO_2 (99·5% acetone)	0·139	1·338

EXPERIMENTAL.

Preparation of Materials.—The acetyl derivatives of aldoximes were prepared in the usual way from the oxime and acetic anhydride and purified by crystallisation either from acetone and water or from light petroleum.

Rectified acetone (2½ l.) was heated under reflux for 4 hours with potassium permanganate (40 g.) and calcium oxide (40 g.) and then distilled through a column packed with glass helices and fitted with a Whitmore still head. The head and the tail fractions were rejected. Distilled water was boiled in a Pyrex flask, cooled, and kept in an atmosphere free from carbon dioxide. The amount of water in the purified acetone was determined by its refractive index: n_D^{25} = 1·3560, 1·3561, 1·3560, 1·3559; average 1·3560. The average value for the distilled water measured at the same time was n_D^{25} 1·3324. From the graph constructed by plotting % of water against *n* for acetone–water mixtures from data in International Critical Tables the purified acetone was found to contain 99·7% of acetone.

Method.—A water-bath was used, the temperature being held constant to ±0·01° by a thermostat. The reactions were carried out in stoppered graduated flasks.

A weighed quantity of the acetyl derivative, equivalent to approx. 0·05M-solution in the volume used (usually 100 c.c. in all), was dissolved in slightly less than the final volume of acetone and allowed to reach 25° in the bath. The requisite volumes of aqueous hydrochloric acid and distilled water were then added, the mixture was well shaken, and the volume made up with acetone to the mark. After further shaking the flask was placed in the thermostat; portions (5 c.c.) were withdrawn at suitable intervals, poured into ice-cold CO_2-free distilled water and immediately titrated against standard (approx. 0·05N.) barium hydroxide using phenolphthalein. The barium hydroxide was kept out of contact with carbon dioxide and was standardised twice daily with approx. 0·2N-hydrochloric acid, checked at intervals against borax. The zero reading was taken 7—10 minutes after mixing and the infinity reading after ten half-times. Pure concentrated hydrochloric acid (10·23N.) was used in making up solutions containing more than 90% of acetone, the same acid diluted five-fold with water was used for making up mixtures containing 80—90% of acetone. For experiments with acetone containing less than 1% of water pure dry hydrogen chloride was passed into a small volume of well-cooled aqueous acetone and the required volume of this added to the main solution.

The following are typical results :

0·0477M-*m*-$\mathrm{NO_2{\cdot}C_6H_4{\cdot}CH{\colon}N{\cdot}OAc}$, 0·102N-HCl; 25·00°. Solvent: 5 vols. of 2N-HCl + 15 vols. of H_2O made up to 100 vols. with acetone.

Titration $= r$.	$\infty - r = (a - x)$.	$1 + \log_{10} (a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^5$, secs.$^{-1}$.	Titration $= r$.	$\infty - r = (a - x)$.	$1 + \log_{10} (a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^5$, secs.$^{-1}$.
5·68	1·97	1·2945	0	—	7·12	0·53	0·7243	702	1·871
5·81	1·84	1·2648	36	1·900	7·30	0·35	0·5441	918	1·883
5·95	1·70	1·2304	78	1·893	7·38	0·27	0·4314	1,026	1·937
6·07	1·58	1·1987	117	1·886	7·55	—	—	(45)*	—
6·17	1·48	1·1703	153	1·870	7·58	—	—	(52)*	—
6·25	1·40	1·1461	180	1·899	7·64	—	—	(70)*	—
6·50	1·15	1·0607	279	1·930	7·65 (∞)	—	—	(84)*	—

Average : $k = 1{\cdot}896 \times 10^{-5}$ sec.$^{-1}$. * *t* (hrs.).

0·0480M-*m*-$\mathrm{NO_2{\cdot}C_6H_4{\cdot}CH{\colon}N{\cdot}OAc}$, 0·205N-HCl; 25·00°. Solvent: 10 vols. of 2N-HCl + 10 vols. of H_2O, made up to 100 vols. with acetone.

8·54	1·71	1·2330	0	—	9·23	1·02	1·0086	1,404	3·681
8·62	1·63	1·2122	12	3·992	9·39	0·86	0·9345	1,800	3·820
8·76	1·49	1·1732	36	3·824	9·90	0·35	0·5441	4,080	3·889
8·89	1·36	1·1335	60	3·819	10·20	0·05	—	(28·5) *	—
9·04	1·21	1·0828	90	3·844	10·25	—	—	(214) *	—

Average : $k = 3{\cdot}838 \times 10^{-5}$ secs.$^{-1}$. * *t* (hrs.).

0·0959M-*m*-$\mathrm{NO_2{\cdot}C_6H_4{\cdot}CH{\colon}N{\cdot}OAc}$, 0·205N-HCl; 25·00°. Solvent : 5 vols. of 2N-HCl and 5 vols. of H_2O, made up to 50 vols. with acetone.

8·83	3·32	1·5211	0	—	10·39	1·76	1·2455	168	3·759
9·12	3·03	1·4814	24	3·808	11·44	0·71	0·8513	402	3·836
9·38	2·77	1·4425	48	3·772	12·07	—	—	(28·25) *	—
9·68	2·47	1·3927	78	3·792	12·15(∞)	—	—	(214) *	—
10·07	2·08	1·3181	126	3·710					

Average : $k = 3{\cdot}779 \times 10^{-5}$ secs.$^{-1}$. * *t* (hrs.).

0·0463M-*m*-$\mathrm{NO_2{\cdot}C_6H_4{\cdot}CMe{\colon}N{\cdot}OAc}$, 0·409N-HCl; 25·00°. Solvent : 20 vols. of 2N-HCl, made up to 100 vols. with acetone.

38·70	3·77	1·5763	0	—	41·32	1·15	1·0607	108	11·00
39·17	3·30	1·5185	12	11·09	41·78	0·69	0·8388	154	10·97
39·57	2·90	1·4624	24	10·93	41·92	0·55	0·7404	177	10·88
39·94	2·53	1·4031	36	11·08	42·48 } 42·47(∞)	—	—	(22) *	—
40·35	2·12	1·3263	54	10·66	42·46	—	—	(28) *	—
40·85	1·62	1·2095	78	10·83					

Average : $k = 10{\cdot}93 \times 10^{-5}$ secs.$^{-1}$. * *t* (hrs.).

The following are examples of the interaction of acetone and hydrochloric acid. In the earlier stages where it is supposed that mesityl oxide and phorone are formed a falling rate constant is obtained but the final stage, where it is supposed that phorone formation only takes place, was isolated by taking *t* at 756×10^2 secs.

0·102N-HCl; 25·00°. Solvent : 1 vol. of 10N-HCl + 1 vol. of H_2O, made up to 100 vols. with acetone.

Titration $= r$.	$\infty - r = (a - x)$.	$1 + \log_{10} (a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^6$, secs.$^{-1}$.	$t \times 10^{-2}$, secs.	$k \times 10^6$, secs.$^{-1}$.
10·46	3·18	1·5024	0	—	—	—
10·41	3·13	1·4955	42	3·783	—	—
10·30	3·03	1·4814	180	2·687	—	—
10·08	2·80	1·4472	756	1·682	0	—
9·98	2·70	1·4314	1,044	1·566	288	1·263
9·80	2·52	1·4014	1,728	1·346	972	1·085
9·37	2·09	1·3201	3,384	1·241	2,628	1·114
8·86	1·58	1·987	5,940	1·176	5,184	1·104
8·29	1·01	1·0043	9,576	1·198	8,820	1·156
7·81	0·47	0·6721	17,208	1·111	16,452	1·084
7·42	—	—	(769)*	—	—	—
7·28(∞)	—	—	(1032)*	—	—	—

Average for phorone formation : $k = 1{\cdot}134 \times 10^{-6}$ secs.$^{-1}$. * *t* (hrs.).

0·204N-HCl; 25·00°. Solvent : 2 vols. of 2N-HCl, made up to 100 vols. with acetone.

Titration = r.	$\infty - r$ = $(a - x)$.	$1 + \log_{10}$ $(a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^6$, secs.$^{-1}$.	$t \times 10^{-2}$, secs.	k × 10^6, secs.$^{-1}$.
20·51	8·23	1·9154	0	—	—	—
20·44	8·16	1·9117	27	3·156	—	—
20·38	8·10	1·9055	54	2·943	—	—
20·05	7·77	1·8904	198	2·907	—	—
19·93	7·65	1·8837	261	2·797	—	—
19·13	6·85	1·8357	756	2·428	0	—
18·75	6·47	1·8109	1,044	2·358	288	1·983
17·98	5·70	1·7559	1,656	2·218	900	2·042
15·63	3·35	1·5250	4,356	2·064	3,600	1·988
14·53	2·25	1·3522	16,840	1·896	6,084	1·830
12·86	0·58	0·7634	14,004	1·894	13,248	1·864
12·49	0·21	0·3222	19,980	1·836	19,234	1·812
12·28(∞)	—	—	(1008) *	—	(987) *	—

Average for phorone formation : $k = 1{\cdot}920 \times 10^{-6}$ secs.$^{-1}$. * t (hrs.).

The following is an example of an experiment where phorone hydrochloride formation was followed after the main reaction was completed, that is, in the presence of the hydrolysis products of the acetyl derivative (Table VII). The conditions were: 0·0478M-*m*-$NO_2{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OAc$; 0·102 N-HCl; 25·00°; solvent : 1 vol. of 10N-HCl + 1 vol. of H_2O, made up to 100 vols. with acetone. The reaction was allowed to proceed for 50 hours to complete hydrolysis and the titration at that point was that for zero time in the side reaction.

Titration = r.	$\infty - r = (a - x)$.	$1 + \log_{10} (a - x)$.	t, hrs.	$k \times 10^6$, secs.$^{-1}$.
12·72	2·18	1·3385	0	—
12·36	1·82	1·2601	44	1·140
11·34	0·80	0·9031	269	1·035
10·82	0·28	0·4472	525	1·086
10·54	—	—	1,110	—

Average : $k = 1{\cdot}087 \times 10^{-6}$ secs.$^{-1}$.

Experiments were also conducted on phorone formation in the presence of added oxime and acetic acid, the hydrolysis products in the first reaction. The following is an example.

0·204N-HCl; added 0·0635M-*m*-$NO_2{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}OH$; 0·044M-AcOH; 25·00°. Solvent: 2 vols. of 10N-HCl, made up to 100 vols. with acetone.

Titration = r.	$\infty - r$ = $(a - x)$.	$1 + \log_{10}$ $(a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^6$, secs.$^{-1}$.	$t \times 10^{-2}$, secs.	$k \times 10^6$, secs.$^{-1}$.
21·01	6·01	0·7789	0	—	—	—
21·90	5·90	0·7709	81	2·275	—	—
21·84	5·84	0·7664	144	1·999	—	—
21·79	5·79	0·7627	198	1·884	—	—
21·37	5·37	0·7300	870	1·294	0	—
20·82	4·82	0·6830	1,809	1·221	939	1·153
19·64	3·64	0·5611	4,322	1·142	3,522	1·105
18·69	2·69	0·4298	7,020	1·145	6,150	1·124
17·84	1·84	0·2648	10,447	1·133	9,577	1·119
16·00(∞)	—	—	(1,032)*	—	—	—

Average for phorone formation : $k = 1{\cdot}125 \times 10^{-6}$ secs.$^{-1}$. * t (hrs.).

From a consideration of the change in rate constant, in the experiment quoted above, of the action of hydrochloric acid on acetone leading to mixed mesityl oxide and phorone formation at first and then to phorone formation only, it was assumed that while the hydrolysis was taking place the secondary reaction proceeded at a rate $k = 2(1{\cdot}087 \times 10^{-6})$ during the first 90×10^2 secs., $k = 1{\cdot}5(1{\cdot}087 \times 10^{-6})$ up to 243×10^2 secs., and $k = 1{\cdot}087 \times 10^{-6}$ for from 24 to 50 hours. From this it is possible to calculate the amount of hydrochloric acid removed from the system by mesityl oxide and phorone formation during the hydrolysis in terms of barium hydroxide used for titration. These corrections must be added to the actual titre to follow the kinetics of the hydrolysis. In this case they were :

t, × 10^2 secs. ...	12	24	42	54	72	90	117	153	198	243	24 hrs.	50 hrs.
Correction, c.c. ...	0·01	0·01	0·02	0·03	0·04	0·06	0·07	0·09	0·10	0·13	0·39	0·62

A run was then performed using the same concentration of acetyl derivative, hydrochloric acid, and water, and these corrections were applied.

0·0478M-*m*-$NO_2\cdot C_6H_4\cdot CH{:}N\cdot OAc$; 0·102N-HCl. Solvent: 1 vol. of 10N-HCl + 1 vol. of H_2O, made up to 100 vols. with acetone.

Actual titration.	Corrected titration = r.	$\infty - r = (a - x)$.	$1 + \log_{10} (a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^5$, secs.$^{-1}$.
9·40	9·40	3·56	1·5539	0	—
9·68	9·69	3·29	1·5172	12	7·044
9·94	9·95	3·03	1·4814	24	6·956
10·28	10·30	2·68	1·4281	42	6·898
10·46	10·49	2·49	1·3962	54	6·724
10·78	10·82	2·16	1·3345	72	7·018
11·00	11·06	1·92	1·2833	90	6·925
11·34	11·41	1·57	1·1959	117	7·011
11·64	11·73	1·25	1·0969	153	6·878
11·99	12·09	0·89	0·9494	198	7·030
12·18	12·31	0·67	0·8261	243	6·898
12·58	12·97	—	—	(24)*	—
12·36	12·98 ∞	—	—	(50)*	—

Average: $k = 6\cdot938 \times 10^{-5}$ secs.$^{-1}$. * t (hrs.).

The attainment of a steady infinity reading is regarded as a justification for the application of the correction.

Another example using a different acetyl derivative gave the following figures.

0·0507M-*p*-$MeO\cdot C_6H_4\cdot CH{:}N\cdot OAc$; 0·204N-HCl; 25·00°. Solvent: 2 vols. of 10N-HCl, made up to 100 vols. with acetone.

Actual titration.	Corrected titration = r.	$\infty - r = (a - x)$.	$1 + \log_{10} (a - x)$.	$t \times 10^{-2}$, secs.	$k \times 10^5$, sec.$^{-1}$.
21·09	21·09	3·85	1·5855	0	—
21·91	21·93	3·01	1·4786	12	20·51
22·56	22·60	2·34	1·3692	24	20 76
23·02	23·08	1·86	1·2695	36	20·22
23·40	23·48	1·46	1·1644	48	20·21
23·69	23·79	1·15	1·0607	60	20·14
24·03	24·16	0·78	0·8921	78	20·47
24·32	24·48	0·46	0·6628	105	20·23
24·64	24·83	—	—	132	—
24·66	24·90	—	—	168	—
24·67	24·94	—	—	204	—
24·64	24·94(∞)	—	—	252 (7)*	—
24·64	—	5·94	1·7738	0	—
24·18	—	5·48	1·7388	(18)*	0·1244
23·01	—	4·91	1·6911	(40)*	0·1322
21·75	—	3·05	1·4843	(144)*	0·1286
20·57	—	1·87	1·2718	(240)*	0·1338
19·53	—	0·83	0·9191	(406)*	0·1347
18·70(∞)	—	—	—	(954)*	—

Average for hydrolysis: $k = 20\cdot36 \times 10^{-5}$ secs.$^{-1}$.
Average for side reaction: $k = 1\cdot323 \times 10^{-6}$ secs.$^{-1}$.

* t (hrs.).

Examination of End-products.—The reaction mixture from the acetyl-*m*-nitrobenzaldoxime hydrolysed by 0·4N-hydrochloric acid in 80% acetone was poured into excess of aqueous 2N-sodium carbonate and extracted several times with ether. The ethereal layers were evaporated in a current of air, dried in a vacuum, and weighed. The product was redissolved in ether and extracted several times with sodium hydrogen sulphite solution to remove aldehyde. The ethereal layer was evaporated at room temperature, and the product dried, weighed, and identified as α-*m*-nitrobenzaldoxime. The aqueous layer was treated with excess of sodium carbonate and again extracted with ether, and after evaporation the *m*-nitrobenzaldehyde was recovered and identified. In two experiments, each starting with 1 g. of acetyl derivative, the total yield of product isolated was 92·7% and 90·6% respectively and the yield of oxime recovered was 41·4% and 40·7% respectively.

From oxime instead of the acetyl derivative, hydrolysed under the same conditions, a similar mixture of oxime and aldehyde was recovered.

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