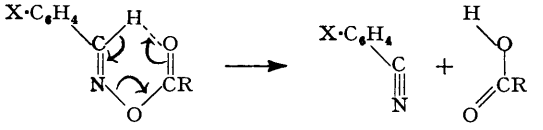
829. *The Isomerism of the Oximes. Part XLVI.* The Difference in Mechanism in the Pyrolysis of Acyl-α- and Acyl-β-aldoximes.*

By O. L. Brady and Hussein A. M. Sharawy.

A kinetic study of the pyrolysis of acyl-α- and -β-aldoximes in xylene has shown that the mechanism of decomposition is different in the two cases. The pyrolysis of the α-derivative is unaffected by acetic acid pre-added or formed during the decomposition but that of the β-derivative is strongly catalysed by pre-added acetic acid. The effect of the addition of acid in the latter case is not due to isomerisation, as might have been expected, since the rate constant for the catalysed reaction was about 10^3 times that of the pyrolysis of the acyl-α-aldoxime.

Acyl derivatives of α-aldoximes, when heated alone or in an aprotic solvent such as xylene, are decomposed almost quantitatively into nitriles and acid; Ambrose and Brady (*J.*, 1950, 1234) suggested that the most probable mechanism for this pyrolysis involved an electron shift in a structure containing hydrogen bonding:



No evidence was obtained of homolytic fission, and mechanisms involving a separation of charges appeared improbable in view of the energy barrier to be overcome in an aprotic solvent and the small effect on the rate constant of varying the substituent X. It was pointed out that further information on the validity of this hypothesis might be obtained by a kinetic study of the pyrolysis of acyl-β-aldoximes in which stereochemical considerations debar hydrogen bonding of the above type, although difficulties were expected on account of the isomerisation of acetyl-β-aldoximes by mineral acids and therefore possibly by the acetic acid formed in the reaction.

A study has now been made of the pyrolysis of acetyl- and propionyl-α- and -β-aldoximes in xylene at 120°, employing a technique which gave more concordant results than did that of Ambrose and Brady.

As before, the pyrolysis of the acyl-α-aldoximes showed first-order kinetics, the plot of $1 - \alpha_t$ (where α_t = extent of decomposition at time t) against time being linear, and it has now been found that the reaction is not catalysed by added acetic acid (Table 1).

* Part XLV, preceding paper.

The small increase in k in the case of acetyl-α-*m*-nitrobenzaldoxime is probably due to titration errors as the amount of added acetic acid was nearly four times the total acetic acid produced in the pyrolysis.

TABLE 1. *Pyrolysis of acetyl-α-aldoximes* X·C_6H_4·CH:N·OAc *in xylene at* 120°.

X	Concn. of acetyl compound (mole/l.)	Concn. of AcOH (mole/l.)	10^5k (sec.$^{-1}$)	X	Concn. of acetyl compound (mole/l.)	Concn. of AcOH (mole/l.)	10^5k (sec.$^{-1}$)
p-MeO	0·0330	0	2·89	3 : 4-CH_2O_2	0·0319	0	1·87
	0·0336	0	2·86		0·0299	0	1·88
	0·0336	0·0251	2·91		0·0319	0·0370	1·85
	0·0660	0	2·88	*m*-NO_2 ...	0·0381	0	0·72
	0·0660	0·0412	2·90		0·0376	0	0·74
					0·0381	0·1453	0·85

The rate constants for propionyl- and butyryl-α-3 : 4-methylenedioxybenzaldoxime under the same conditions are $k = 2·04$ and $2·29 \times 10^{-5}$ sec.$^{-1}$ respectively.

The pyrolysis of acyl-β-aldoximes presented a totally different picture to that of the

FIG. 1.

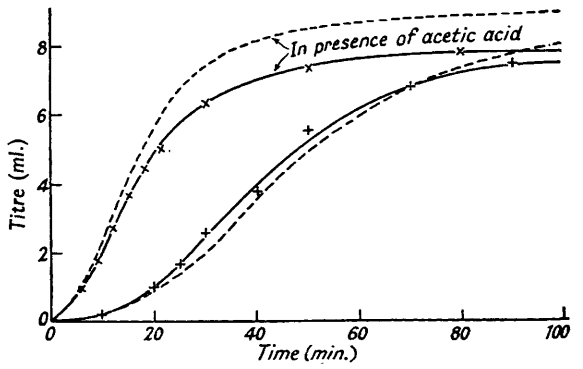


FIG. 2.

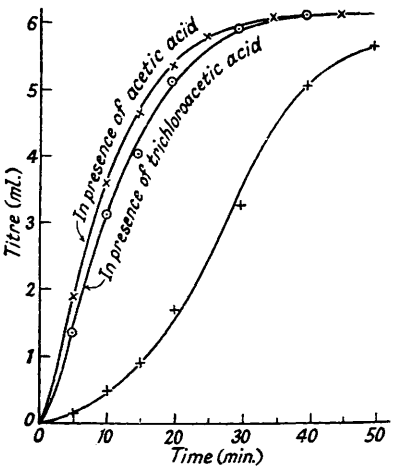


FIG. 1. *Pyrolysis of acetyl-β-*m*-nitrobenzaldoxime* (——) *and acetyl-β-*p*-anisaldoxime* (– – –) *at* 120°.
FIG. 2. *Pyrolysis of acetyl-β-piperonaldoxime at* 120°.

acyl-α-aldoximes. The reaction is slow at first but, after an induction period, becomes much faster. Moreover, pre-addition of some of the carboxylic acid formed in the pyrolysis greatly reduces the induction period (Figs. 1 and 2).

In the presence of added acid the reaction is of the second order, the results being shown in Table 2. In the examples given, the time required for the maximum amount

TABLE 2. *Pyrolysis of* β-X·C_6H_4·CH:N·O·COR *in xylene at* 120°.

X	R	Concn. of acyl aldoxime (mole/l.)	Concn. of added R′·CO_2H (mole/l.)	10^2k (sec.$^{-1}$ mole^{-1} l.)	Decomp. (%)
p-MeO	Me	0·0437	0·0222 (R′ = Me)	2·31	91·4
		0·0404	0·0332 (R′ = Me)	2·25	92·8
3 : 4-CH_2O_2	Me	0·0290	0·0341 (R′ = Me)	2·77, 2·92	91·8, 92·5
	Me	0·0290	0·0315 (R′ = CCl_3)	2·55	92·7
	Et	0·0290	0·0393 (R′ = Me)	5·00	90·1
	Et	0·0210	0·0393 (R′ = Et)	4·77	90·5
m-NO_2	Me	0·0369	0·0246 (R′ = Me)	2·06, 2·24	93·4, 93·6

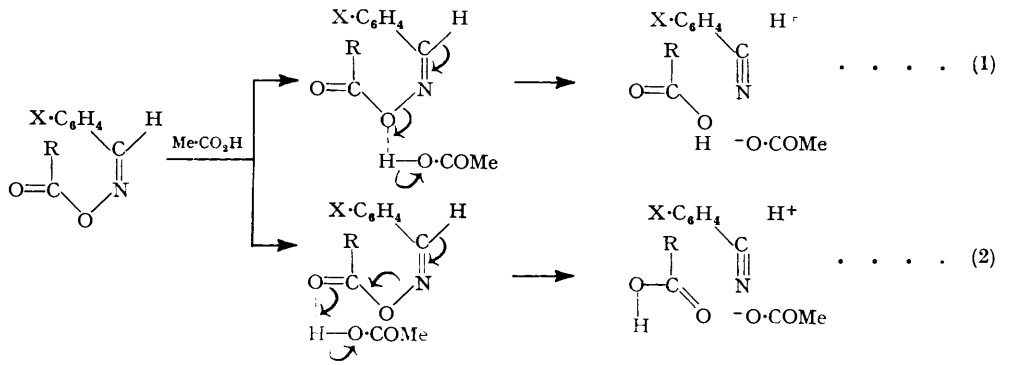
of acid to be liberated was, for acetyl-β-*p*-methoxybenzaldoxime and -β-*m*-nitrobenzaldoxime, reduced from 150—180 to 80—100 min. by pre-addition of the acetic acid; for acetyl-β-3 : 4-methylenedioxybenzaldoxime from 100—120 to 55—75 min. by pre-addition of the acetic or trichloroacetic acid; and for propionyl-β-3 : 4-methylenedioxy-

benzaldoxime from 70—80 to 35—45 min. by pre-addition of acetic acid and to 40—50 min. by pre-addition of propionic acid. Further, whereas pyrolysis of acetyl-α-aldoximes gave ultimately not less than 98% of the calculated amount of acetic acid, pyrolysis of acetyl-β-aldoximes gave amounts of acetic acid varying from 92·1 to 93·6% of the calculated quantity; the amount of acid liberated was the same within 0·5% for each individual acetyl-β-aldoxime whether it was heated alone or with pre-added acid. The amount of acid liberated from propionyl-β-3 : 4-methylenedioxybenzaldoxime was somewhat less, namely, 90·4%.

The pyrolysis is clearly catalysed by acetic acid; in the absence of pre-added acid a slow reaction takes place at first, giving rise to nitrile and acetic acid, and as the latter accumulates the much faster acid-catalysed reaction is superimposed.

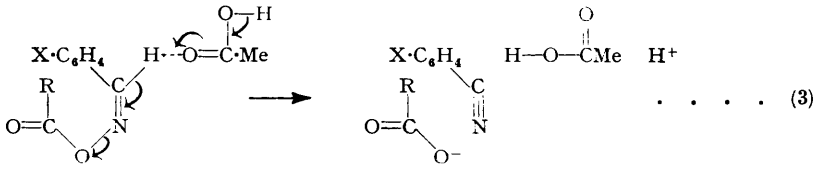
Considering first, the second-order acid-catalysed, reaction it is clear that it is not a preliminary isomeric change from the acyl-β-aldoxime to the acyl-α-aldoxime, followed by pyrolysis of the latter, since the rate constant is nearly 1000 times that of the pyrolysis of the acyl-α-aldoxime which is unaffected by acetic acid. In representing the possible mechanisms one has the choice between catalysis by protons and by the un-ionised acid by hydrogen bonding, as suggested by Hinshelwood and his co-workers (*Trans. Faraday Soc.*, 1934, **30**, 935; *J.*, 1939, 593). Since it has been shown that the hydrogen chloride-catalysed hydrolysis of acyl oximes in aqueous acetone is due partly to un-ionised hydrogen chloride (Brady and Miller, *J.*, 1950, 1234), and the reaction was carried out in an aprotic solvent, we have adopted the latter representation, but the former could be used equally well [compare mechanisms (4) and (5) below].

There are several places in the acylaldoxime molecule where such hydrogen bonding could occur :



The fractional positive charge induced on either oxygen atom would favour the rupture of the oxygen–nitrogen bond and bring about the elimination of acetic acid as shown. Weakening of the oxygen–nitrogen bond in ketoximes by oxonium-salt formation has been suggested as the initial stage in the Beckmann rearrangement (Bennett, quoted by Chapman, *J.*, 1935, 1226).

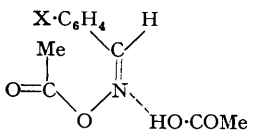
On the other hand, the acetic acid could function as a weak base, giving potential hydrogen bonding with the methine-hydrogen atom :



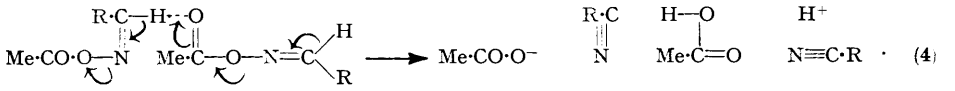
Against mechanism (1) it can be argued that one might expect the acyl-α-aldoxime to form a similar hydrogen bond unless the power of the hydroxyimino-oxygen atom to accept a

proton is reduced by the hydrogen bonding of the carbonyl oxygen of the acyl group with the methine-hydrogen. On the other hand, mechanism (2) is free from this objection since in the acyl-α-aldoxime the carbonyl-oxygen atom already takes part in hydrogen bonding. It will account for the negligible effect of changing the substituent X in the pyrolysis of the acyl-β-aldoximes compared with the effect of similar changes in X in the pyrolysis of the acyl-α-aldoximes (Table 1) since the seat of the initiation of the reaction is, in the former case, far removed from the substituent X. As the reaction is one of general acid catalysis the slight reduction in the rate constant when trichloroacetic acid is substituted for acetic acid is not disturbing in view of possible steric-hindrance effects and of other anomalous properties of trichloroacetic acid in aprotic solvents (LaMer and Downes, *J. Amer. Chem. Soc.*, 1933, **55**, 1840; Wooten and Hammett, *ibid.*, 1935, **57**, 2289).

The mechanism suggested in (3) represents, in effect, the normal proton removal from an acylaldoxime by, for example, hydroxyl ions which in acyl-β-aldoximes is extremely rapid (Mills, British Ass. Report, 1932, p. 47; Benger and Brady, *J.*, 1950, 1221); but it is unlikely because the reaction is catalysed by trichloroacetic acid which has a negligible basic strength, being un-ionised in concentrated sulphuric acid (Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1708). In addition, one would expect the effects of variation in X to be greater and to operate in the opposite direction, *i.e.*, electron withdrawal from the methine group should favour proton removal, as shown by Benger and Brady (*loc. cit.*). Finally, hydrogen bonding could take place at the nitrogen atom (as inset), but such an intermediate provides no simple mechanism for the pyrolysis, which must therefore occur through hydrogen bonding with oxygen even if this species is present in only small amounts.

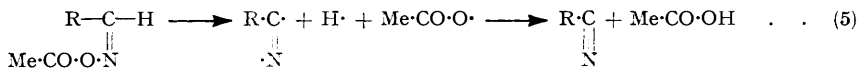


Turning now to a consideration of the early stage of the pyrolysis of acyl-β-aldoximes without added acid and before enough has been formed in the decomposition to act as catalyst, it is clear that the reaction may be initiated by a kind of autocatalysis, in the sense that the acyl-β-aldoxime can act as a feeble proton donor to another acylaldoxime molecule :



(4)

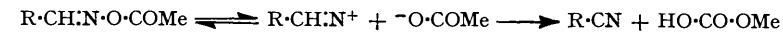
Another possibility is that in the absence of an acid catalyst homolytic fission may occur :



(5)

Such a reaction could continue slowly after the liberated acid had initiated the acid-catalysed reaction and throughout the reaction when acid was pre-added; it would, therefore, account for the fact that pyrolysis of acyl-β-aldoximes differs from that of acyl-α-aldoximes in not going to completion in the sense that not more than 93·0% of the theoretical amount of acetic acid is liberated; for it has been shown (Kharasch, *J. Org. Chem.*, 1949, **14**, 91) that the free acetoxy-radical produced in the pyrolysis of diacetyl peroxide partly breaks down to Me· and CO_2. The lack of appreciable effect of the addition of benzoyl peroxide on the pyrolysis is, however, rather unfavourable to this interpretation.

Heterolytic fission of the acyl derivative



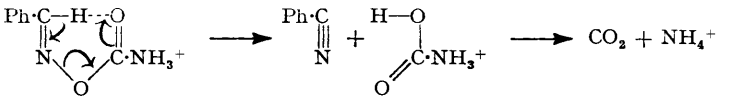
seems unlikely in view of the energy barrier to be surmounted in xylene.

Of these three possibilities we are of opinion that the first mechanism (4) is the most likely.

In conclusion, something must be said about the suggestion by Grammaticakis (*Bull. Soc. chim.*, 1941, [*ve*], **8**, 106) that the acetyl derivatives of α-aldoximes are *N*-acyl derivatives, Ph·CH:N(COMe)→O. His argument is based on the similarity in absorption

spectra between the acetyl and the carbamyl derivatives to which Conduche (*Ann. Chim.*, 1907, **12**, 554; 1908, **13**, 26, 41), adopting the Beckmann rather than the Hantzsch–Werner structures for the isomeric oximes, formulated as Ph·CH—N·CO·NH_2. Conduche based this structure only on the evidence that hydrolysis of the carbamyl derivatives with hydrochloric acid gave nitriles, although hydrolysis with alkali gave the α-aldoxime. Nitrile formation in those days was taken as evidence of Beckmann's " iso-oxime " structure R·C——N·COMe, although alkaline hydrolysis was usually employed, and such structures were assigned to the derivatives of β-aldoximes rather than to the α-isomerides. Doubt has already been thrown on Conduche's structure for the carbamyl derivatives (Brady and Dunn, *J.*, 1913, **103**, 1613), and Brady and Grayson (*J.*, 1933, 1037), from evidence of absorption spectra, concluded that acetyl-α- and acetyl-β-aldoximes were both *O*-acetyl derivatives. Grammaticakis makes no reference to either of these papers and takes Conduche's structure as established; in fact, his absorption curves in no way contradict Brady and Grayson's view and only go to show that the carbamyl compounds also have the structure Ph·CH:N·O·CO·NH_2.

Hydrolysis to nitriles by hydrochloric acid is readily explicable if one realises that the compound undergoing hydrolysis, in this case, is Ph·CH:N·O·CO·NH_3^+. Electron withdrawal due to the positive charge will favour the rupture of the N–O bond, resulting in pyrolytic decomposition according to the mechanism of Ambrose and Brady (*loc. cit.*):



Trichloroacetylbenzaldoximes, where CCl_3 replaces NH_3^+ above, rapidly undergo such decompositions at room temperature (Benger and Brady, *loc. cit.*). In alkali the compound undergoing hydrolysis is Ph·CH:N·O·CO·NH_2 where the electron displacement will hinder rather than favour the rupture of the N–O bond, so oxime is formed.

Experimental

Preparation of Materials.—α-Aldoximes were prepared from hydroxylamine hydrochloride, the aldehyde, and excess of 2N-sodium hydroxide, to give a homogeneous solution. The oxime was then precipitated with carbon dioxide. β-Aldoximes were prepared by the usual methods, except in the case of β-*m*-nitrobenzaldoxime where only that described by Forster and Dunn (*J.*, 1909, **95**, 430) was satisfactory. β-*p*-Methoxybenzaldoxime, crystallised from warm benzene, had m. p. 133—134° (lit., 133°); β-3 : 4-methylenedioxybenzaldoxime, crystallised first from acetone and water and then from methanol and water, had m. p. 142° (lit., 145°). β-*m*-Nitrobenzaldoxime, crystallised from warm ethyl acetate and light petroleum, had m. p. 123° (lit., 123°). Satisfactory acetyl derivatives cannot be prepared from β-aldoximes unless the oximes used are pure; it is much easier to purify the β-oxime than its acetyl derivative.

The α- and the β-acetyl derivatives were prepared by dissolving the aldoximes in the minimum amount of pure acetic anhydride (2·5 c.c. for 2 g. of oxime), with cooling so that the temperature did not rise above 25°. After 10 min. the solution was cooled in solid carbon dioxide–ethanol, and the crystals which separated were rapidly collected in a well-cooled Hirsch funnel. In the case of α-*m*-nitrobenzaldoxime more acetic anhydride was required for solution (10 c.c.) and nothing separated on cooling; so the excess of anhydride was decomposed by 2N-sodium carbonate (cooling); the acetyl derivative then separated. The acetyl derivatives were first crystallised by addition of water drop by drop to the cold acetone solution, with scratching until crystallisation occurred, then dropwise addition of more water with vigorous shaking until about two-thirds of the compound was precipitated. This was collected, rapidly dried on a porous tile, and recrystallised in a similar manner from cold benzene and light petroleum (b. p. 60—80°). Acetyl-α-aldoximes are relatively stable and can be kept for some days in a desiccator over solid sodium hydroxide, but acetyl-β-aldoximes must be placed in a desiccator over solid sodium hydroxide at once and used within a few hours. Mineral-acid vapour must

be rigorously excluded from the room when β-aldoximes or their acetyl derivatives are made or used, or isomerisation will occur.

The m. p.s of the compounds Ar·CH:N·OAc used (previous values in parentheses) were: Ar = *p*-C_6H_4·OMe, α-, 48—49° (48°), β-, 64—65° (64°); 3 : 4-CH_2O_2:C_6H_3, α-, 105° (105°, 108°), β-, 87° (85°, 86°); *m*-C_6H_4·NO_2, α-, 129° (128°), β-, 99° (96—98°).

α- and β-3 : 4-Methylenedioxypropionylbenzaldoxime, prepared in a similar manner, had m. p. (α-) 94—95° (95°), (β-) 72·5° (71°); n-*butyryl*-α-3 : 4-*methylenedioxybenzaldoxime* had m. p. 72·5° (Found: C, 61·2; H, 5·3. $C_{12}H_{13}O_4N$ requires C, 61·3; H, 5·6%).

Purification of Xylene.—Commercial xylene (2¼ l.) was shaken successively with concentrated sulphuric acid (8 × 100 c.c.), 5N-sodium hydroxide (5 × 100 c.c.), and mercury (twice). After being kept for 24 hr. over phosphoric oxide it was distilled twice over fresh pentoxide and finally over sodium. The solvent was kept in a vessel with a guard tube of silica gel and connected to a burette with an ungreased 3-way mercury-sealed tap.

Procedure.—The pyrolysis was investigated in xylene at 120°, by sealed tube technique. The extent of reaction was determined by titration of the acetic or propionic acid formed with barium hydroxide (phenolphthalein). Titration of the organic acid in a mixture of water and xylene presented difficulties but when the tirrations were carried out under carefully controlled conditions results were concordant.

A sample of the compound was weighed into a 100-c.c. flask fitted with a ground-glass stopper, and a known weight of dry xylene was introduced in such a way that the solvent did not come into contact with moist air. The flask was shaken until dissolution was complete and the liquid was transferred to an automatic pipette through ground-glass connections without exposure to the atmosphere. Clean dry tubes were then charged with known weights of the solution and immediately sealed. The tubes were heated at 120° ± 0·05°. After 5—10 min. one tube was chilled rapidly in carbon dioxide–ethanol. This was taken as the zero-time tube but in very slow reactions a longer interval was necessary. The remaining tubes were removed after various time intervals, cleaned (carbon tetrachloride), washed with ether, then water, broken under water, and titrated against 0·02—0·04N-barium hydroxide.

Cleaning of the reaction tubes presented some difficulty as the usual acid mixtures were unsatisfactory and contact with metal had to be avoided since both acids and metals acted as catalysts in some cases. Ultimately the tubes were steamed for 2 hr. on glass jets of an all-glass steaming-apparatus, dried in an oven, and kept in a desiccator over solid sodium hydroxide.

The tubes were broken under water in which the carbon dioxide had been neutralised with barium hydroxide, this being the most satisfactory method of removing carbon dioxide. Nitrogen from a cylinder was bubbled through the mixture of water and xylene, preventing absorption of atmospheric carbon dioxide and providing stirring. A blue daylight lamp was used as a standard source of light, and a burette reading to 0·01-c.c. with a lens was employed.

Identification of the Products.—No decomposition product other than the nitrile and acid was detected in any of the pyrolyses. These tests were carried out as were the kinetic experiments, but with larger amounts. The xylene solution, either as obtained or after evaporation to small bulk under reduced pressure, was diluted with a large excess of light petroleum which precipitated most of the solute which, when the reaction was allowed to go to completion, was almost pure nitrile. With acetyl-β-aldoximes an attempt was made to detect acetyl-α-aldoxime after the action had proceeded half way, by warming the precipitated solid with 2N-sodium carbonate. This would have converted unchanged acetyl-β-aldoxime into nitrile and hydrolysed acetyl-α-aldoxime to α-aldoxime which could be extracted with cold 2N-sodium hydroxide, but no α-oxime was found.

Calculations.—The pyrolysis of acetyl-α-aldoximes showed first-order kinetics. The extent (α) of reaction = $TNM/1000W$ where T = titre, N = normality of barium hydroxide, M = molecular weight, and W = weight of compound in each tube. The rate constant was then calculated from: $k = 2{\cdot}303[\log(1 - \alpha_0) - \log(1 - \alpha_t)]/(t - t_0)$.

The experiment tabulated is typical.

*Pyrolysis of acetyl-α-*p*-methoxybenzaldoxime in xylene at* 120°.

Concn., 0·0330 mole/l. W = 0·0341 g. M, 193·2. N = 0·0245.

Time, secs., ...	0	2400	6000	9600	13,200	16,800	20,400	24,000	60 hrs.
Titre, c.c., ...	0·73	1·15	1·76	2·34	2·83	3·25	3·66	3·93	7·10
$k \times 10^5$, sec.$^{-1}$	—	2·78	2·88	2·97	2·96	2·92	2·94	2·80	—

Mean 10^5k = 2·89 sec.$^{-1}$; decomposition after 60 hr. = 98·3%. The plot of (1 − α) against time was linear.

If, in the pyrolysis of acyl-β-aldoximes in the presence of added acid, two simultaneous reactions occur and the first is very slow compared with the acid-catalysed one, the former can be neglected and the reaction represented at time t by

$$(a - x) + b \longrightarrow x + (b + x)$$

where a = initial concentration of acyl-β-aldoxime, b = concentration of added acid, and x = concentration of nitrile or acid formed at time t. If the rate of pyrolysis is proportional to the first power of the concentrations of the acyl-β-aldoxime and the acid present, the rate will be proportional to $(a - x)(b + x)$, and the rate equation takes the form $dx/dt = k(a - x)(b + x)$ since b is a constant. On integration we have

$$k = \frac{2{\cdot}303}{t(a + b)}\left[\log \frac{b + x}{a - x} + \log \frac{a}{b}\right]$$

It was found that in all cases the plot of $\log (b + x)(a - x)$ against t was linear for at least 75—80% of the reaction.

If no acid was added at the beginning of the reaction, $b = 0$ and $dx/dt = k(a - x)x$ and $k = 2{\cdot}303\{\log [x/(a - x)] + \text{const.}\}/at$. The plot of $\log x/(a - x)$ against time should be a straight line but this was found not to be so, as would be expected since the first reaction would not be negligible until sufficient acid had accumulated to start the acid-catalysed reaction. For this reason the rate constant was calculated only where acid was added at the beginning of the reaction.

Typical experiments are tabulated.

*Pyrolysis of acetyl-*β*-*m*-nitrobenzaldoxime in xylene at* 120°.

W = 0·0411 g. N = 0·0233. M = 208·17. Initial concn. of acetyl derivative (a) = 0·0369 mole/l., and acetic acid (b) = 0·0246 mole/l. Selected zero-time tube removed after 360 sec. Original titre = 5·65 c.c. of 0·0233N-$Ba(OH)_2$; titre after 360 sec. = 6·60 c.c., giving, at selected zero time, a = 0·0328 and b = 0·0287.

Time (sec.)	Titre	$b + x$	x	$a - x$	10^2k (sec.$^{-1}$ mole^{-1} l.)
0	6·60	0·0287	0	0·0328	—
180	7·45	0·9324	0·0037	0·0291	2·17
360	8·35	0·0363	0·0076	0·0252	2·26
540	9·30	0·0404	0·0117	0·0211	2·36
720	10·05	0·0437	0·0150	0·0178	2·33
900	10·65	0·0463	0·0176	0·0152	2·25
1440	12·00	0·0522	0·0235	0·0093	2·10
2640	13·05	0·0567	0·0280	0·0048	(1·62)
120 min.	13·60	0·0591	0·0304	0·0024	—
180 min.	13·60	0·0591	0·0304	0·0024	—

Mean $k = 2{\cdot}24 \times 10^{-2}$ sec.$^{-1}$ mole^{-1} l. Decomp. at the end of the reaction = 93·6%.

*Pyrolysis of acetyl-*β*-*m*-nitrobenzaldoxime in xylene at* 120° *without the pre-addition of acid.*

a = 0·374 mole/l. W = 0·0417 g. N = 0·0245. M = 208·17.

Time (min.)	10	20	25	30	40	50	70	90	150	20 hr.
Titre (c.c.)	0·20	1·00	1·65	2·55	3·80	5·60	6·85	7·60	8·05	8·05

Decomp. after 20 hr. = 93·5%.

Addition of Benzoyl Peroxide.—The pyrolysis of identical solutions of acetyl-β-*p*-methoxybenzaldoxime, without the pre-addition of acid, was measured with and without the addition of 3% of benzoyl peroxide; in both cases the reaction was complete in from 150 to 180 min. Addition of as much as 50% of benzoyl peroxide reduced the time of completion of the reaction only to 100—120 min.

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