250. *The Isomerism of the Oximes. Part XL. The Hydrolysis of Acyl Halogenobenzaldoximes by Alkalis.*

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The relative amounts of nitrile and oxime formed in the alkaline hydrolysis of (1) acetyl derivatives of the *p*-halogeno-β-benzaldoximes and (2) carbethoxy-derivatives of *o*-, *m*-, and *p*-halogeno-α-benzaldoximes have been determined.
Interpreted in the light of the mechanisms of hydrolysis, the results confirm the electronic effects of the halogens reported by Baddeley, Bennett, Glasstone, and Jones and by Bird and Ingold.
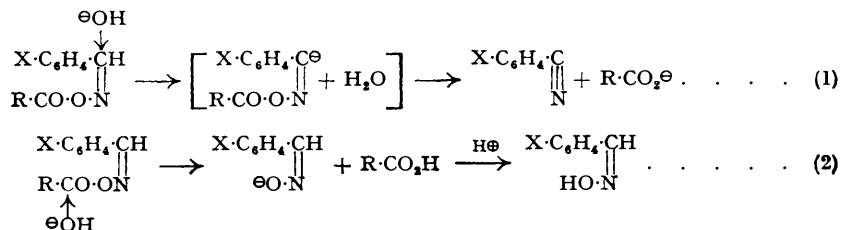
THE influence of nuclear substituents on the relative amounts of nitrile and oxime produced in the hydrolysis of an acyl-aldoxime having been established (Benger and Brady, preceding paper), it was of interest to investigate the complete series of halogenobenzaldoxime derivatives to correlate the previous results with the electronic behaviour of the halogens. By use of the technique previously described, a study has been made of the relative amounts of nitrile and oxime produced by the action of 2N-sodium hydroxide on the acetyl-β-halogenobenzaldoximes. Unfortunately only in the case of *o*-chlorobenzaldoxime and the four *p*-halogenobenzaldoximes has it been possible to prepare the β-acetyl derivatives sufficiently pure for investigation. The results are shown in Table I.

In the *para*-series F, Cl, and Br decrease the proportion of nitrile compared with the unsubstituted compound, whilst I increases it, the ratio of nitrile to oxime being in the order F ≪ Cl < Br < H ≪ I.

TABLE I.

X in β-X·C$_6$H$_4$·CH:N·OAc.	Temp.	Nitrile, %.	Oxime, %.	Total, %.	Nitrile, % of total.
p-F	0°	23	72	95	24
p-Cl	0	59	39	98	60
p-Br	0	58	33	91	64
H	0	61	30	91	67
p-I	0	90	8	98	92
p-F	25	50	45	95	53
p-Cl	25	92	3	95	97
o-Cl	0	79	11	90	88

Benger and Brady suggest that the principal mechanisms involved in the formation of nitrile and oxime at low temperatures are (1) and (2) :

$$X \cdot C_6H_4 \cdot \underset{R \cdot CO \cdot O \cdot N}{\overset{\overset{\ominus OH}{\downarrow}}{\overset{\|}{CH}}} \longrightarrow \left[X \cdot C_6H_4 \cdot \underset{R \cdot CO \cdot O \cdot N}{\overset{C\ominus}{\|}} + H_2O \right] \longrightarrow X \cdot C_6H_4 \cdot \underset{N}{\overset{C}{\|\|}} + R \cdot CO_2 \ominus \quad . \quad . \quad . \quad (1)$$

$$\underset{\overset{\uparrow}{\ominus OH}}{\underset{R \cdot CO \cdot ON}{X \cdot C_6H_4 \cdot \overset{\|}{CH}}} \longrightarrow X \cdot C_6H_4 \cdot \underset{\ominus O \cdot N}{\overset{\|}{CH}} + R \cdot CO_2H \xrightarrow{H\oplus} X \cdot C_6H_4 \cdot \underset{HO \cdot N}{\overset{\|}{CH}} \quad . \quad . \quad . \quad . \quad (2)$$

We will consider first the permanent polarisation due to the inductive ($-I_s$) and mesomeric ($+M$) effects which are generally accepted as being in the order F > Cl > Br > I (Baddeley, Bennett, Glasstone, and Jones, *J.*, 1935, 1827; Bird and Ingold, *J.*, 1938, 918). Now $-I_s$ would facilitate nitrile formation by mechanism (1) and oxime formation by mechanism (2), but the latter to a smaller degree as the point of attack by hydroxyl is more remote from the source of the effect; on the other hand $+M$ would retard both nitrile and oxime formation, the former probably more effectively than the latter where there is a break in the conjugation at the oxygen.

If $-I_s$ is the controlling factor, substitution by fluorine should give more nitrile than substitution by iodine; if $+M$ is the controlling factor, the effects would be the reverse. From the experimental results presence of fluorine depresses nitrile formation relative to the unsubstituted compound, so in this case $M > I_s$. On the other hand the iodo-oxime gives more nitrile than the unsubstituted oxime, so that in this case if only the above considerations are applied $I_s > M$. The positions of chlorine and bromine are less certain, as we hesitate to claim a degree of accuracy for our results which would clearly differentiate between, for example, 64 and 67% of nitrile formation.

These results are not at variance with the dissociation constants of the *p*-halogenophenols in 30% ethyl alcohol ($K_a \times 10^{10}$ = F 0·26, H 0·32, Cl 1·32, Br 1·55, I, 2·19; Bennett, Brooks, and Glasstone, *J.*, 1935, 1821) where permanent polarisation only is effective.

If it is accepted that the polarisability factor operates only at the moment of reaction to satisfy the demand of the attacking reagent it cannot retard a reaction but only favour it. The relative polarisability effects are usually accepted as being in the order I > Br > Cl > F, and as the attack is by a nucleophilic reagent they will be electron-withdrawing and more favourable to nitrile formation. The results given above show, therefore, that in the case of fluorine the inductive effect plus the polarisability factor are less than the mesomeric effect, whereas in the case of iodine the reverse holds. This conclusion is consonant with the evidence of the mesomeric moments (Groves and Sugden, *J.*, 1931, 1992) and G. N. Lewis's view that potential double-bond formation, inherent in mesomerism, is easier with the small fluorine atom than with the other halogen atoms. Pauling ("Nature of the Chemical Bond," Cornell Univ. Press, 1945, p. 236) concludes that the chlorine has about half the power of fluorine to form double bonds.

The increase in the proportion of nitrile formed in passing from the *para*- to the *ortho*-chloro-compound is to be expected from the relatively greater increase in the inductive and inductomeric effects which facilitate proton removal owing to the closer approach of the origin of the effect to the point of attack by the nucleophilic reagent.

Since acetyl-β-*p*-fluorobenzaldoxime gave on hydrolysis a smaller amount of nitrile than did acetyl-β-2 : 4- and acetyl-β-3 : 4-dimethoxybenzaldoxime it seemed probable that it would be stable, like these compounds and unlike most acetyl-β-benzaldoximes, to cold 2N-sodium

carbonate (Benger and Brady, *loc. cit.*). This proved to be the case, for no odour of nitrile was observable when acetyl-β-*p*-fluorobenzaldoxime was treated with 2N-sodium carbonate until the mixture was warmed to 50—60°.
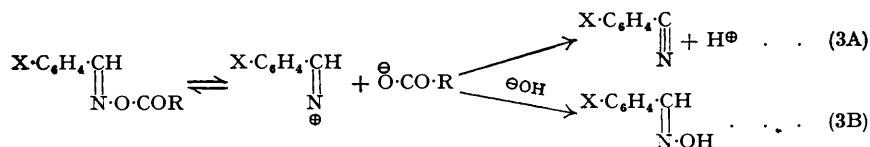
Our failure to prepare the acetyl derivatives of the β-halogenobenzaldoximes of the *ortho*- and *meta*-series led us to investigate the hydrolysis of the carbethoxy-derivatives of the α-halogenobenzaldoximes which, unlike the corresponding acetyl-α-benzaldoximes, give nitrile as well as α-oxime (Hauser, Jordan, and O'Connor, *J. Amer. Chem. Soc.*, 1935, 57, 2456). With these compounds it was necessary to carry out the hydrolysis at higher temperatures, with the introduction of complications of interpretation which will be mentioned later. At the higher temperatures used some of the nitrile formed was hydrolysed to acid and/or amide. The results are shown in Table II. The percentage of elimination reaction, that is initial nitrile formation, was calculated from the amount of carboxylic acid, nitrile, and amide isolated.

TABLE II.

X in α-X·C₆H₄·CH:NO·O·CO₂Et.	65°. Elimination reaction, %.	Oxime, %.	Total, %.	100°. Elimination reaction, %.	Oxime, %.	Total, %.
o-F	21	78	99	40	57	97
o-Cl	35	64	99	82	16	98
o-Br	29	70	99	71	28	99
o-I	36	61	97	83	16	99
m-F	12	86	98	35	63	98
m-Cl	16	84	100	52	45	97
m-Br	16·5	83	99·5	65	34	99
m-I	19	80	99	76	21	97
p-F	6	92	98	31·5	66	97·5
p-Cl	8	90	98	42	57	99
p-Br	10	90	100	57	40	97
p-I	11	86	97	72	28	100
H	6	92	98	16	84	100

In the *para*-series, the amount of nitrile formed increases from fluorine to iodine, as with the acetyl-β-halogenobenzaldoximes, but less markedly, *p*-I/*p*-F at 65° = 1·71 and at 100° = 2·29 with the carbethoxy-α-halogenobenzaldoximes compared with *p*-I/*p*-F at 0° = 3·83 with the acetyl compounds.

The most interesting point, however, is the comparison between the decomposition of the carbethoxy-α-*p*-halogenobenzaldoximes at 65° and 100° and the corresponding acetyl-β-*p*-halogenobenzaldoximes at 0° with reference to the unsubstituted carbethoxy-α-benzaldoxime and acetyl-β-benzaldoxime under the same conditions. In the latter case fluorine depresses, and iodine favours, nitrile formation, chlorine and bromine having but small effect. In the former case at 65° fluorine has little effect whilst chlorine, bromine, and iodine slightly facilitate nitrile formation, but at 100° all the halogens markedly facilitate nitrile formation. This may be due to a differential temperature coefficient affecting the opposing electronic displacements, or to the third mechanism of decomposition of acyl aldoximes suggested by Benger and Brady (*loc. cit.*) coming into operation at the higher temperatures (cf. Ambrose and Brady, *J.*, 1950, 1243).

$$
X·C_6H_4·CH \underset{N·O·COR}{\|} \rightleftharpoons X·C_6H_4·CH \underset{\overset{N}{\oplus}}{\|} + \overset{\ominus}{O}·CO·R \xrightarrow{\ominus OH}
\begin{array}{l} X·C_6H_4·C \underset{N}{\overset{\|}{\|}} + H^{\oplus} \quad . \quad . \quad (3A) \\[2mm] X·C_6H_4·CH \underset{N·OH}{\|} \quad . \quad . \quad (3B) \end{array}
$$

As the oxime obtained from the carbethoxy-derivative is the stable α-isomeride this mechanism cannot be eliminated as it was in the alkaline hydrolysis of the acetyl-β-aldoximes (cf. Benger and Brady, *loc. cit.*). This mechanism will be favoured by the mesomeric effect of the halogens, and if it leads mainly to nitrile (3A) the proportion of nitrile to oxime in the decomposition of the fluoro-compound might well be greater than in the unsubstituted carbethoxy-derivative. This problem is being further investigated.

In the *meta*-series the amount of nitrile formed increases from fluorine to iodine at both temperatures and is greater than in the *para*-series. In this case the electromeric effect of the halogen will be much less marked and the inductive and inductomeric effects will be enhanced

compared with the *para*-substituted compounds because of the closer approach of the seat of the effect to the point of reaction. In the *ortho*-series a still greater amount of nitrile is produced at both temperatures owing to the still closer approach of the source of the inductive and inducto-meric effects. The retarding mesomeric effect may be less effective in the case of the *ortho*-substituted compounds as it has been suggested that for reasons of symmetry the mesomeric effect will be relayed more powerfully to the *para*- than to the *ortho*-position (Waters, *Trans. Faraday Soc.*, 1941, **37**, 746).

In this series although the fluoro-compound gives least nitrile and the iodo-compound gives most, the behaviour of the chloro-compound is anomalous, as it gives more nitrile than the bromo-compound. This abnormal behaviour of chlorine, especially in the *ortho*-position, is not unknown; it appears, for example, in the action of potassium iodide on the halogenobenzyl chlorides (Bennett and Jones, *J.*, 1935, 1815).

<div align="center">EXPERIMENTAL.</div>

α-*Fluorobenzaldoximes.*—The *o*- and *p*-fluorobenzaldoximes were obtained by preparing the aldehydes by the method of Rinkes (*Chem. Weekbl.*, 1919, **16**, 206) by chlorination of the fluorotoluenes and hydrolysis. The mixture of aldehyde and alcohol so obtained was not separated, but treated with aqueous hydroxyl-amine hydrochloride and enough 4N-sodium hydroxide to form the soluble sodium salt of the oxime; the fluorobenzyl alcohol was removed by extraction with a mixture of benzene and light petroleum, and the oxime precipitated from the aqueous layer with carbon dioxide. Rinkes gives no yields, but from 70 g. of fluorotoluene 44—50 g. of oxime were obtained.

o-*Fluorobenzaldoxime*, after crystallisation from light petroleum, melts at 64·5—65° (Found : C, 60·2; H, 4·5. C_7H_8ONF requires C, 60·4; H, 4·3%), and p-*fluorobenzaldoxime* at 88·5° (Found : C, 60·4; H, 4·3%). Rinkes gives m. p.'s 62·6° and 81·2° respectively and publishes no analyses, but his method of preparation of the oximes would not eliminate fluorobenzoic acids, and it has been found that small quantities of these depress the m. p. of the oximes and are not readily removed by crystallisation from light petroleum.

m-Fluorobenzaldehyde has not been previously described and has been prepared as follows. *m*-Nitro-benzaldehyde (50 g.), suspended in concentrated hydrochloric acid (250 c.c.), was reduced with stannous chloride (225 g.), and the reddish-brown solution was cooled to 0°, diluted with water (50 c.c.), and diazo-tised with sodium nitrite (23 g. in 100 c.c. water). The yellowish-brown solution containing a slight deposit of amorphous material which need not be removed was kept for 30 minutes, and powdered ice was then added (100 g.), followed by borofluoric acid (100 c.c.); the diazonium borofluoride soon separated as brownish needles and was washed with water, alcohol, and ether and dried over concentrated sulphuric acid in a vacuum. The diazonium borofluoride, mixed with an equal bulk of sand, was decomposed in 2 portions in a flask fitted with a long condenser tube leading to a stoppered bottle connected to a water-pump. After evacuation, decomposition was started by heating the flask at one point. The boron trifluoride evolved dissolved in the pump water, and a greenish crystalline sublimate appeared in the condenser and was driven over into the receiver. When stronger heating was applied, an oil distilled. On addition of water to the contents of the receiver, the solid portion decomposed, with the liberation of boron trifluoride. The oil was purified by conversion into the oxime by the addition of hydroxyl-amine hydrochloride (15 g. in water) and enough 2N-sodium hydroxide to give a clear solution. After cooling and filtration, the solution was saturated with carbon dioxide, and the precipitated oxime (15 g.) collected, dried, and crystallised from light petroleum containing a little benzene. The oxime (10 g.) was heated in steam with N-hydrochloric acid (100 c.c.), the aldehyde distilling as a colourless oil which was extracted with ether. *m*-*Fluorobenzaldehyde* is a colourless liquid with a benzaldehyde-like odour, b. p. 170°/760 mm. (Found : C, 67·4; H, 4·0. C_7H_5OF requires C, 67·7; H, 4·0%); on oxidation it gave *m*-fluorobenzoic acid, m. p. 123° (Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 31). The aldehyde was re-oximated as before and α-*m*-*fluorobenzaldoxime* crystallised from light petroleum as colourless prisms, m. p. 67—67·5° (Found : C, 61·1; H, 4·3. C_7H_6ONF requires C, 60·4; H, 4·3%).

α-*Chloro-*, α-*Bromo-*, and α-*Iodo-benzaldoximes.*—*o*-Bromo- and *o*-iodo-benzaldehyde were prepared by a Sandmeyer reaction (Stuart, *J.*, 1888, **53**, 1401; Weitzenbock, *Monatsh.*, 1913, **34**, 206) from *o*-aminobenzaldehyde prepared by the reduction of *o*-nitrobenzaldehyde with hydrogen using a nickel catalyst (Ruggli and Schmid, *Helv. Chim. Acta*, 1935, **18**, 1235). These authors do not specify the nature of the catalyst, but it was found that Raney nickel kept in contact with the alkaline sodium aluminate solution overnight was suitable : the more active form promoted a rapid reduction to *o*-aminobenzyl alcohol.

m-Bromo- and *m*-iodobenzaldehyde were obtained from *m*-aminobenzaldehyde, and *p*-bromo- and *p*-iodobenzaldehydes were prepared from the *p*-aminobenzaldehyde "polymer" (Willgerodt and Ucke, *J. pr. Chem.*, 1912, **86**, 276). The α-bromobenzaldoximes were prepared by adding the aldehyde to an equivalent amount of hydroxylamine hydrochloride in water to which three equivalents of 2N-sodium hydroxide had been added with cooling, and precipitating the oxime with carbon dioxide. The iodo-benzaldoximes were prepared by Patterson's method (*J.*, 1896, **69**, 1006). α-*m*-Bromobenzaldoxime melted at 74—75°; Einhorn and Gernsheim (*Annalen*, 1895, **284**, 141) give m. p. 71·5°. The α-chloro-benzaldoximes were prepared in the same way as the α-bromobenzaldoxime from purchased chlorobenz-aldehydes. Except where specially mentioned, the m. p.s of the oximes were those given by previous workers.

β-*Halogenobenzaldoximes.*—The β-oximes of the *para*-series were prepared by dissolving the α-oxime in hot dry benzene, precipitating the hydrochloride with dry hydrogen chloride, collecting, drying, and decomposing the salt with excess of 2N-sodium carbonate. β-*p*-Fluorobenzaldoxime melted at 120—121°; Rinkes (*loc. cit.*) gives m. p. 116—117°.

This method was not successful with the *ortho-* and *meta*-compounds, but when the hydrogen chloride was replaced by hydrogen bromide, prepared by dropping fuming hydrobromic acid on phosphoric oxide and dried by passage through a U-tube containing phosphoric oxide, conversion was brought about. So prepared, β-*o*-chlorobenzaldoxime melted at 100°. Brady and McHugh (*J.*, 1924, **125**, 547) obtained a compound of this m. p. by the action of ultra-violet light on the α-isomeride, but Brady, Cosson, and Roper (*J.*, 1925, **127**, 2427), using the hydrochloride method, obtained a product melting at 101—103°. β-*o*-*Iodobenzaldoxime*, obtained for the first time by this method and crystallised from benzene, had m. p. 135° (Found : C, 34·3; H, 2·3. C₇H₆ONI requires C, 34·0; H, 2·4%). β-*m*-Iodobenzaldoxime (from benzene), m. p. 121°, and β-*m*-fluorobenzaldoxime (from light petroleum containing a little benzene), m. p. 103—104°, have also been obtained for the first time by this method.

The decomposition of the hydrobromide from α-*o*-fluorobenzaldoxime with ice-cold 2N-sodium carbonate and crystallisation from benzene gave a product, m. p. 57—62°, which gives an intense red colour with alcoholic ferric chloride, a diagnostic test for β-aldoximes (Beck and Hase, *Annalen*, 1907, **355**, 37). When dissolved in acetic anhydride and warmed with sodium carbonate, a strong odour of nitrile was produced. Addition of an equal amount of α-*o*-fluorobenzaldoxime (m. p. 64—65°) depressed the m. p. to <30°. The compound undoubtedly consists largely of the β-isomeride, but is probably not pure in view of the range over which it melts; further crystallisation lowered the m. p. β-*o*-Methoxybenzaldoxime has never been isolated pure, and as the methoxy- and fluoro-substituents have in common a large mesomeric displacement, the difficulty in obtaining pure β-*o*-fluorobenzaldoxime is not surprising.

A quicker method of obtaining the β-isomerides from *o*-iodo,- *m*-iodo- and *m*-fluoro-α-aldoximes consists in dissolving these in the minimum amount of warm ether and adding a slight excess of hydrobromic acid (*d* 1·7) from a measuring pipette. Crystals of hydrobromide soon separate, and the mixture solidifies with evolution of heat and some ether boils off; the rest is removed in a current of dry air, and the addition of 2N-sodium carbonate liberates the β-aldoxime. The crude material so obtained is, however, not very pure and the yield of pure β-aldoxime obtained from it by crystallisation is not as high as when gaseous hydrogen bromide is used.

β-*Acetyl-halogenobenzaldoximes.*—These were prepared by the method of Hauser and Sullivan (*J. Amer. Chem. Soc.*, 1933, **55**, 4611). It is essential that the acetic anhydride should be free from traces of acetyl chloride or hydrogen chloride, and acid fumes and bright light should be excluded during the preparation. The compounds are very unstable and must be prepared immediately before use. The acetyl derivatives of the β-aldoximes frequently melt at temperatures close to those of the α-aldoximes, so in order to be sure that inversion had not occurred during the preparation, mixed m. p.s were determined with samples of the acetyl-α-aldoxime; in every case there was a depression of >20°.

Acetyl-β-*p*-fluorobenzaldoxime has m. p. 82—83°, acetyl-β-*p*-iodobenzaldoxime m. p. 76—77°, and acetyl-β-*o*-chlorobenzaldoxime, m. p. 45—46° (Found : C, 44·5; H, 4·0. The acetyl derivatives of β-*p*-chlorobenzaldoxime and β-*p*-bromobenzaldoxime have been previously described; our specimen of the latter melted at 69—70°, though Hantzsch (*Z. physikal. Chem.*, 1894, **13**, 520) gives 91—92°. Acetyl derivatives of β-*o*-bromobenzaldoxime and β-*o*-iodobenzaldoxime could not be obtained pure, as mixtures of the α- and β-isomerides were always formed; the *m*-halogeno-β-benzaldoximes gave mainly nitrile. Hantzsch (*loc. cit.*) experienced similar difficulties with these compounds.

Carbethoxy-α-halogenobenzaldoximes.—The following O-*carbethoxy-halogenobenzaldoximes* were prepared by the method of Brady and Dunn (*J.*, 1916, **109**, 678) who describe the carbethoxy-α-chlorobenzaldoximes : *o*- (from light petroleum), m. p. 41—42° (Found : C, 57·6; H, 4·9. C₁₀H₁₀O₃NF requires C, 56·9; H, 4·9%), *m*- (from light petroleum), m. p. 37—39° (Found : C, 57·2; H, 4·9%), and *p-fluoro-* (from aqueous alcohol), m. p. 76—77° (Found : C, 57·3; H, ·5·0%); *o*- (from light petroleum and benzene), m. p. 78° (Found : C, 44·5; H, 4·0. C₁₀H₁₀O₂NBr requires C, 44·2; H, 3·7%), *m*- (from light petroleum and benzene), m. p. 46—48° (Found : C, 44·5; H, 3·8%), and p-*bromo-* (from aqueous alcohol), m. p. 90—91° (Found : C, 44·2; H, 3·7%); *o*- (from aqueous alcohol), m. p. 109·5° (Found : C, 38·1; H, 3·1. C₁₀H₁₀O₂NI requires C, 37·6; H, 3·1%), *m*- (from light petroleum), m. p. 59—61° (Found : C, 38·0; H, 3·3%), and p-*iodo-* (from aqueous alcohol), m. p. 93—94° (Found : C, 37·9; H, 3·1%).

Hydrolysis of Acetyl-β-halogenobenzaldoximes.—The pure, freshly prepared, acetyl derivative (1 g.) was added to 2N-sodium hydroxide (15 c.c.) previously cooled to 0° or heated in a thermostat to 25°. After 120 minutes at 0° or 45 minutes at 25°, with frequent shaking, the acetyl derivative was completely decomposed to nitrile and oxime, the latter dissolving in the excess of sodium hydroxide. The nitrile was collected in a tared sintered-glass crucible, the filtrate saturated with carbon dioxide, and the precipitated oxime likewise collected. After being washed with water the solids were dried in a desiccator to constant weight. No indication of the formation of carboxylic acid by hydrolysis of the nitrile was detected and no correction was made for the slight solubility of the compounds in water. The m. p.s of the products were taken to ascertain whether α- or β-aldoximes were recovered. The crude nitriles melted as follows : *p*-F- 33° (34·8°); *p*-Cl- 89—91° (91—92°); *p*-Br 108—110° (113°); *p*-I- 122° (124°); *o*-Cl- 45° (45°); the figures in brackets are the m. p.s of the nitriles recorded in the literature. In the following list the m. p. of the oxime recovered is given followed by the correct m. p.s of the β- and α-oximes : *p*-F- 115—118°, β- 121°, α- 87°; *p*-Cl- 134—138°, β- 149°, α- 108°; *p*-Br- 150°, β- 157°, α- 115°; *p*-I- 148°, β- 150°, α- 118°; *o*-Cl- 87—95°, β- 110°, α- 75—76°. The relative amount of nitrile and oxime produced are shown in Table I.

Hydrolysis of Carbethoxy-α-halogenobenzaldoximes.—The hydrolyses were carried out at 65° and 100°. In the first case a rubber-stoppered flask (50 c.c.) containing 2N-sodium hydroxide (15 c.c.) was heated at 65° (thermostat) and the carbethoxy-compound (1 g.) introduced. The mixture was shaken periodically until complete dissolution occurred (1—3 days); in these circumstances the insoluble nitrile first formed is hydrolysed to the corresponding acid; it was more satisfactory to adopt this procedure than to heat for a shorter time and determine the nitrile and acid separately. For experiments at 100°, the 2N-sodium hydroxide (15 c.c.) and the carbethoxy-compound (1 g.) were introduced into a small bulb (30—40 c.c.), which was sealed, weighted with lead, and submerged in boiling water. The bulbs

were shaken during the first few minutes and then left for 45 minutes; in this instance some nitrile remained insoluble, contaminated in some cases with a small amount of amide.

In the reactions at 65° the cooled solution was diluted to 30 c.c. with water, saturated with carbon dioxide, and the precipitated oxime collected in a tared sintered-glass crucible, washed with a little water, dried, and weighed. The filtrate and washings were extracted once with ether to remove dissolved oxime, the ethereal solution, after washing, evaporated in a tared beaker, and the oxime dried in a desiccator and weighed. The aqueous solution was acidified with hydrochloric acid and the carboxylic acid extracted twice with ether; the ethereal extracts were washed with a little water and evaporated in a tared beaker, and the residue dried in a desiccator and weighed.

When the reaction was carried out at 100°, the cooled solution was extracted with ether, which removed nitrile and some oxime, the latter was removed by washing the ethereal extracts twice with small quantities of 2N-sodium hydroxide. The alkaline solution and washings were saturated with carbon dioxide, and the precipitated oxime was collected or extracted with ether according to its amount; when it was collected, the filtrate was extracted with ether. The hydrogen carbonate solution was acidified and the carboxylic acid extracted with ether. The various ethereal solutions were evaporated in tared beakers, and the products dried and weighed. In no case was the recovery less than 97% calculated on the material used.