a solvent has been studied. The preparation of 3- and 4-bromofluorenes from the resulting fluorene mercury derivatives has been described.

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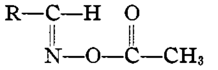
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

The Removal of Hydrogen and Acid Radicals from Organic Compounds by Means of Bases. II. The Removal of Acetic Acid from Acetyl-aldoximes by Alkalies

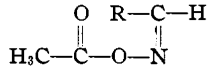
BY CHARLES R. HAUSER AND EARL JORDAN

As part of a general program on the removal of the elements of acids from organic compounds by means of bases it was of interest to study the removal of acetic acid from geometrically isomeric acetyl-aldoximes, (I) and (II).



$$\begin{array}{l}\text{R—C—H}\quad\text{O}\\ \quad\;\|\qquad\;\;\|\\ \text{N—O—C—CH}_3\end{array}$$

(I) *syn* (α)



$$\begin{array}{r}\text{O}\quad\text{R—C—H}\\ \|\qquad\;\;\;\|\\ \text{H}_3\text{C—C—O—N}\end{array}$$

(II) *anti* (β)

It is well known that in the presence of alkali one of these isomers eliminates acetic acid more readily than the other. Indeed, this reaction is used to distinguish a pair of geometrically isomeric aldoximes; the isomer whose acetyl derivative more readily forms nitrile is designated the β-, whereas the other is designated the α-isomer. Formerly, it was assumed that the unstable (β-) acetate had the *syn* configuration simply because the hydrogen atom and acetate group are in closer proximity in (I) than in (II); this view was based presumably on the assumption that the elements of acetic acid were removed simultaneously. At the present time, however, the unstable (β-) acetate is assigned the *anti* configuration (II), whereas the more stable (α-) isomer is assigned the *syn* (I). This view is based on a good deal of experimental evidence[1] accumulated during the past ten years. It is supported also on theoretical grounds on the basis of the hypothesis that, in the formation of nitrile, a proton is removed first by the action of alkali followed by the release of the acetate ion. According to Mills,[2] after the removal of a proton, the movement of the nitrogen nucleus to form the triple bond of the nitrile favors the release of the acetate ion, only in the case of the isomer with configuration (II). It should be pointed out also that the proximity of the acetate group to the hydrogen atom in (I) might offer some steric hindrance to the removal of the proton, thereby hindering the release of the acetate ion and formation of nitrile.

Although the reactions of acetyl aldoximes with alkalies have been studied extensively in connection with the determination of configurations of aldoximes there appears to have been relatively little quantitative work carried out under controlled conditions. In this investigation we have studied these reactions at definite temperatures and in most cases have isolated almost quantitative yields of products. The results are given in the following tables. The melting points of the crude products and those recorded in the literature are listed consecutively following the yields. In most cases the melting points of the crude products were either practically the same as those reported in the literature or were raised to these values after one recrystallization.

Discussion

It is often stated or implied in the literature that acetyl-α-, and acetyl-β-aldoximes react entirely differently toward alkali, that the α- give only oxime, and the β- only nitrile. Recently, however, it has been shown[3] that with sodium hydroxide certain acetyl-β-aldoximes give both nitrile and oxime, the yields of these products being dependent on the temperature, and now it has been found that at the temperature of the boiling water-bath at least certain acetyl-α-aldoximes with alkali give some nitrile in addition to the corresponding oxime.

It can be seen from Table I that, in general, acetyl-β-benzaldoximes with 2 *N* sodium hydroxide gave higher yields of oxime than nitrile at 0°, but greater yields of nitrile at 30°. These results confirm and extend those previously reported.[3]

In Table II are given the yields of products obtained from the reactions of certain acetyl-α-benzaldoximes with 2 *N* sodium hydroxide. It can be seen that at 61–64° the 2-nitro derivative

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[1] For review of evidence, see Freudenberg, *Stereochemie*, **7**, 974–979 (1933); Perkin and Kipping, "Organic Chemistry," Part III, 1934, pp. 661–663.

[2] Mills, *J. Soc. Chem. Ind.*, **51**, 755 (1932).

[3] Hauser and Sullivan, THIS JOURNAL, **55**, 4611 (1933).

TABLE I

PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-β-BENZALDOXIMES AND 2 *N* SODIUM HYDROXIDE

		Nitrile			Acid			Oxime			
			M. p., °C.			M. p., °C.			M. p., °C.		
Acetyl derivative	Temp., °C.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.	Total, %
4-Nitro-	0	38	139–140	147	13	228	238	45	164	184	96
4-Nitro-	30	1	126–127	147	57	232	238	27	158–160	184	85
3,4-Methylenedioxy-	0	33	85–88	94–95				66	143–145	146	99
3,4-Methylenedioxy-	30	48	93–94	94–95				38	130–132	146	86
4-Methoxy-[a]	0	25	56–57	60				71	131	133	96
4-Methoxy-[a]	30	41	53–54	60	25	180	184	25	61[c]	64	91
4-Methoxy-[b]	30	45	54–55	60	10	171	184	32	63[c]	64	87

[a] The previously reported[3] yields of products from this derivative were: at 0°, nitrile 25%, oxime 63%; at 30°, nitrile 55%, oxime 30%. [b] 0.48 *N* NaOH used. [c] On standing this oxime had changed to the α-isomer.

TABLE II

PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-α-BENZALDOXIMES AND 2 *N* SODIUM HYDROXIDE

		Nitrile			Acid			Oxime			
			M. p., °C.			M. p., °C.			M. p., °C.		
Acetyl derivative	Temp., °C.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.	Total, %
2-Nitro-	30				9	128–130	148	86	97–98	102	95
2-Nitro-	61–64	24	91–93	109–110	12	148	148	57	99–100	102	93
Blank	61–64				[3 gum]			[93	102	102]	[93]
4-Nitro-	30				2	205	238	95	130	133	97
4-Nitro-	97–100				16	237	238	76	128–129	133	92
Blank	97–100				[5	190–193	238]	[90	130–132	133]	[95]
3-Nitro-	30					Trace		96	122	123	96
3-Nitro-	97–100				11 gum			86	121–122	123	86
2-Chloro-	30				Trace	132	139	97	73–74	75–76	97
2-Chloro-	97–100				25	137	139	74	73–75	75–76	99
Blank	97–100				[5	137	139]	[94	74–75	75–76]	[99]
3,4-Methyl-	30				Trace			98	108–109	110	98
enedioxy-	97–100				5	220	228	94	108–109	110	99
Blank	97–100				[3	224	228]	[90	109–110	110]	[93]
4-Methoxy-	30				3	145–148	184	94	60–63	64	97
4-Methoxy-	97–100				10	180	184	87	62–64	64	97
Blank	97–100				[3	173–175	184]	[93	62–63	64]	[96]

TABLE III

PERCENTAGE YIELDS OF PRODUCTS FROM THE ACETYL DERIVATIVES OF α- AND β-3,4-$CH_2O_2C_6H_3CH{=}NOH$ AND ALKALIES AFTER CERTAIN TIME INTERVALS

				Oxime			Nitrile			Recovered acetate		
					M. p., °C.			M. p., °C.			M. p., °C.	
Isomeric form	Alkali	Temp., °C.	Time, min.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.
α	Aq. NaOH	0	6	4	105–107	110				95	105	105
β	Aq. NaOH	0	6	35	144–146	146	(60% of mixture of acetate and nitrile)					
α	Alc. NaOH	0	3	69	109–110	110						
β	Alc. NaOH	0	3	70	125–129	146						
α	Alc. NaOH	−8	3	53	109–110	110						
β	Alc. NaOH	−8	3	64	145–146	146						
α	Na_2CO_3 (aq. acetone soln.)	0	6	15	110	110						
α	Na_2CO_3 (aq. acetone soln.)	0	60 hrs.	75	109–110	110				13	105	105
β	Na_2CO_3 (aq. acetone soln.)	0	6	12	143–145	146						
β	Na_2CO_3 (aq. acetone soln.)	0	52 hrs.	30	144–145	146	63	92–93	94–95			

TABLE IV

PERCENTAGE YIELDS OF PRODUCTS FROM THE ACETYL-β-BENZALDOXIMES AND 10% AQ. Na_2CO_3

		Nitrile			Oxime			
			M. p., °C.			M. p., °C.		
Acetyl derivative	Temp., °C.	Yield, %	Obsd.	Lit.	Yield, %	Obsd.	Lit.	Total, %
3,4-Methylenedioxy-	0	75	92–93	94–95	21	145–146	146	96
3,4-Methylenedioxy-	30	88	92–93	94–95	9	134–135	146	97
4-Methoxy-	30	86	53–55	60	13	63[a]	64	99

[a] On standing this oxime had changed to the α-isomer.

TABLE V

PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-α-BENZALDOXIMES WITH 2 *N* $NaOC_2H_5$ IN ABSOLUTE C_2H_5–OH

Acetyl derivative	Acid Yield, %	Acid M. p., °C. Obsd.	Acid M. p., °C. Lit.	Oxime Yield, %	Oxime M. p., °C. Obsd.	Oxime M. p., °C. Lit.	Total, %
2-Chloro-	2	133	139	66	73–74	75–76	68
3,4-Methylenedioxy-	1	174	228	90	109–110	110	91
4-Methoxy-	Trace			91	63–64	64	91

PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-α-BENZALDOXIMES WITH 2 *N* NaOH IN 50% ALCOHOL

Acetyl derivative	Acid Yield, %	Acid M. p., °C. Obsd.	Acid M. p., °C. Lit.	Oxime Yield, %	Oxime M. p., °C. Obsd.	Oxime M. p., °C. Lit.	Total, %
2-Chloro-	3	124	139	94	75–76	75–76	97
3,4-Methylenedioxy-	2	220–221	228	97	109–110	110	99
4-Methoxy-	1	158–160	184	95	61–62	64	96

TABLE VI

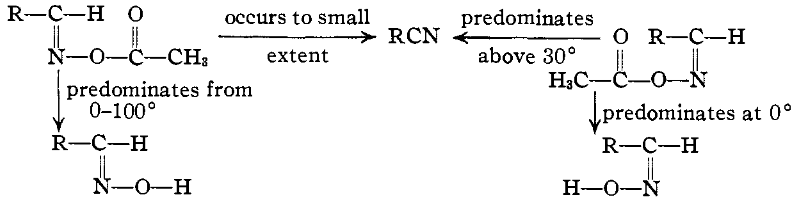
PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-α-BENZALDOXIMES WITH POTASSIUM AMIDE

Acetyl derivative	Nitrile Yield, %	Nitrile M. p., °C. Obsd.	Nitrile M. p., °C. Lit.	Acid Yield, %	Acid M. p., °C. Obsd.	Acid M. p., °C. Lit.	Oxime Yield, %	Oxime M. p., °C. Obsd.	Oxime M. p., °C. Lit.	Total, %
4-Methoxy-	47	145–147	162[a]	Trace	150–154	184	43	61–62	64	90
3-Nitro-	23	95–97	118	60 gum			8	108–112	123	31
2-Chloro-	80	42	42–43				9	66–68	75–76	89
Blank				[2 gum]			[88	74–75	75–76]	[88]
3,4-Methylenedioxy-	58	85–87	94–95	2	185–187	228	39	110	110	99
Blank				[1	192–193	228]	[96	110	110]	[97]

[a] The corresponding amide was obtained in this case.

gave some nitrile and acid in addition to the corresponding oxime, and at the temperature of the boiling water-bath several of the other acetyl-α-derivatives also gave appreciable yields of the acid. Even at 30° it has been possible to isolate small quantities of acid from the nitro derivatives. Although most of the yield of the carboxylic acid reported in each case in Table II was probably produced by the hydrolysis of the corresponding nitrile formed from the acetyl derivative by elimination of acetic acid, a small percentage of it was apparently produced, directly or indirectly, by a reaction of alkali with the α-oxime which was formed by the hydrolysis of the acetate. The yields of acid obtained from blanks determined with α-oximes are given in brackets in Table II. The actual yields of acid obtained from the acetyl derivatives through the intermediate formation of nitrile may be calculated by subtracting the blanks from the yields reported in this table. The small quantities of acid obtained from the oximes were probably also produced through the intermediate formation of nitrile formed from the oxime by elimination of water.

Since it is unlikely that these acetyl-α-derivatives rearranged[4] to the corresponding β-isomers previous to elimination of acetic acid, these results indicate that acetyl-α- and acetyl-β-benzaldoximes undergo fundamentally the same types of reaction with sodium hydroxide; they form oxime by hydrolysis and nitrile by elimination of acetic acid as represented by the scheme.



The yields of products in each case depend on the relative rates of the two competing reactions. It is obvious that with acetyl-β-aldoximes at 0° the hydrolysis proceeds more rapidly than the elimination of acetic acid, but at 30° or above, the elimination process is more rapid; whereas with the α-isomers,[5] the hydrolysis is more rapid than the elimination reaction even at 100°. At 30°, most acetyl-α-derivatives form an almost negligible yield of nitrile.[6] It is noteworthy that the elimination reaction apparently has a higher temperature coefficient than the hydrolysis.

The fact that at a given temperature the acetyl-β-aldoximes give much higher yields of nitrile, and correspondingly lower yields of oxime than

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(4) It should be pointed out that aldoximes tend to undergo the reverse change in alkaline solution. At 30° β-oximes are relatively stable but at the temperature of the boiling water-bath they are converted within a few hours to the α-isomers and corresponding carboxylic acids.

(5) There is a possibility that at 100° certain α-aldoxime acetates might give more nitrile than oxime.

(6) This is not the case, however, with certain carbethoxy-α-benzaldoximes; at 30°, the 2-nitro derivative gives a higher yield of nitrile than oxime (see following paper).

the α-isomers indicates, that the β-isomers eliminate acetic acid much more rapidly than the α-, or that the latter are hydrolyzed much more readily. Actually, β-3,4-methylenedioxybenzaldoxime acetate undergoes hydrolysis somewhat more rapidly than the corresponding α-isomer; therefore the β-derivative must eliminate the elements of acetic acid much more readily than the α-isomer in order to account for the much higher yield of nitrile produced. From Table III it can be seen that with aqueous[7] or alcoholic sodium hydroxide the β-acetate is hydrolyzed more rapidly than the α-isomer. The 64 and 70% yields of oxime obtained from the β-acetate after three minutes at −8 and 0°, respectively, correspond to practically complete decomposition of this derivative (see Table I). On the other hand, the α-acetate was only 53 and 69% decomposed under the same conditions.[8]

On the basis of the hypothesis proposed for the formation of nitrile it should be expected that the rate of removal of acetic acid from an acetyl aldoxime would be dependent on the activity of the aldehydic hydrogen atom and on the strength of the base used. The activity of the hydrogen atom is apparently dependent on at least two factors, (a) on polarity, as influenced by the presence of so-called negative atoms or groups, and (b) on a steric factor.

Since the acetate group and the aldehydic hydrogen atom are closer in a *syn* acetate (I) than in the *anti* isomer (II), it would appear that the relative unreactivity of the hydrogen atom in the former is at least in part due to a steric factor.

Of the *syn* (α-) acetates studied in this investigation, only the *o*-nitro derivative gave nitrile fairly readily (36% at 61–64°). It is probable that the greater yield of nitrile obtained in this case is due primarily to an increased rate of elimination of acetic acid rather than to a retarded hydrolysis, since the presence of the nitro group in *o*-nitrobenzalchlorimine ($RCH{=}NCl$) greatly facilitates the removal of hydrogen chloride by alkali.[9] Apparently the nitro group in the ortho position in both the aldchlorimine and the acetyl aldoxime greatly enhances the reactivity of the aldehydic hydrogen atom.

It was of interest to study the reactions of acetyl aldoximes with certain other alkaline reagents. Sodium carbonate has often been used instead of sodium hydroxide to distinguish α- and β-isomers;[10] the β- gives mostly nitrile, whereas the α- is either unattacked or is hydrolyzed to the corresponding oxime. Contrary to the results recently reported[11] it has now been found possible to isolate low yields of oxime in addition to high yields of nitrile from the reaction products of certain acetyl-β-benzaldoximes and sodium carbonate. These results are given in Tables III and IV. From Table III it can be seen that, similar to the results obtained with sodium hydroxide, β-3,4-methylenedioxybenzaldoxime acetate is hydrolyzed by excess sodium carbonate in aqueous acetone solution more rapidly than the corresponding α-isomer. After six minutes at 0°, approximately the same yields (12–15%) of oxime were obtained from both isomers. Since a 30% yield of oxime was obtained from the β-acetate on complete decomposition, the 12–15% yield of oxime obtained after six minutes corresponds to approximately 50% decomposition of the β-acetate. On the other hand, the α-acetate was only 12–15% decomposed under the same conditions.

It is to be observed that the yields of oxime obtained with sodium carbonate are much lower, and the yields of nitrile correspondingly higher, than those obtained with sodium hydroxide (see Table I). This rather striking fact suggests that the carbonate ion is capable of removing the elements of acetic acid from β-acetates to form nitrile, but has relatively little if any effect on the hydrolysis, whereas the hydroxyl ion brings about both reactions. The high concentration of carbonate ion and low concentration of hydroxyl ion in the carbonate solution would then cause the elimination reaction to proceed at a relatively rapid rate, and the hydrolysis at a relatively slow rate.

It seemed possible that acetyl-α-aldoximes might form considerable nitrile when treated with

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[7] A part of the difference in rate with aqueous sodium hydroxide might be due to a difference in solubility. Although the α-aldoxime acetate is more soluble in ether or benzene, the β-isomer appears to be more soluble in water. This is being studied.

[8] It is possible that certain α-aldoxime acetates might be hydrolyzed more rapidly than the corresponding β-isomers, but it is not likely that there would be any great difference in their rates.

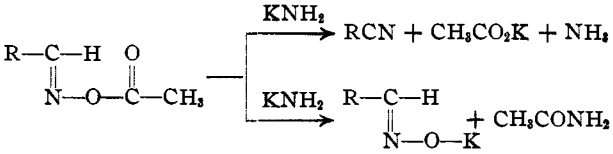
[9] The rates of removal of hydrogen chloride from $RCH{=}NCl$ by alkali in alcoholic solution are in general in the same relative order as the ionization constants of the corresponding acids ($RCOOH$). In this reaction nitrile is formed almost quantitatively. Hauser, LeMaistre and Rainsford, THIS JOURNAL, **57**, 1056 (1935).

[10] Brady has found that certain acetyl-β-aldoximes are relatively stable in sodium carbonate. See *J. Chem. Soc.*, **117**, 1045 (1920); **123**, 1800 (1923); **125**, 1419 (1924).

[11] It has usually been considered that acetyl-β-aldoximes with sodium carbonate give only nitrile. Also in a recent paper[3] it was reported that it was not possible to isolate oxime from the reaction products of certain acetyl-β-aldoximes and sodium carbonate.

sodium ethylate or potassium amide, which are stronger bases than sodium hydroxide. However, when certain acetyl-α-aldoximes were added to sodium ethylate[12] in absolute alcohol at the refluxing temperature, the sodium salt of the corresponding oxime precipitated almost immediately, very little acid being produced (see Table V). Apparently the rate of the reaction leading to the formation of the oxime (alcoholysis) was more rapid than the elimination reaction.

As was expected the reaction of potassium amide in liquid ammonia with acetyl-α-aldoximes formed considerable nitrile, in addition to the corresponding oxime. The yields of products are given in Table VI. It is probable that the reaction took place as represented by the equations



$$\begin{aligned} \mathrm{R{-}CH{=}N{-}O{-}C({=}O){-}CH_3} &\xrightarrow{\mathrm{KNH_2}} \mathrm{RCN + CH_3CO_2K + NH_3} \\ &\xrightarrow{\mathrm{KNH_2}} \mathrm{R{-}CH{=}N{-}O{-}K + CH_3CONH_2} \end{aligned}$$

Evidently, the rate of removal of acetic acid from the α-acetate was more rapid than the reaction leading to the formation of oxime (ammonolysis).

Finally, it should be mentioned that the products of reaction of acetyl aldoximes with alkalies at 100° often had the isocyanide odor. However, it has not been possible to isolate an isocyanide; even attempts to obtain a positive test for an isocyanide failed. It is evident, therefore, that the reactions of an acetyl aldoxime with alkali yield not more than a trace if any of an isocyanide (which would be a rearrangement product), but form almost quantitative yields of the non-rearrangement products, nitrile, acid and oxime. According to the mechanism proposed for the formation of nitrile from an acetyl aldoxime, it should not be expected that the elimination of acetic acid would be accompanied by rearrangement of the molecule, since the negative fragment that is formed by the removal of a proton should be stabilized most readily by the release of acetate ion and shift of an electron pair, thus

$$\left(\mathrm{R:\underset{\cdot\cdot}{\overset{\cdot\cdot}{C}}::N:\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}:Ac}\right)^- \longrightarrow \mathrm{R:C:::\underset{\cdot\cdot}{N} + :\underset{\cdot\cdot}{\overset{-}{\ddot{O}}}:Ac}$$

it should be expected that an electron pair would shift more readily than the group (R).

The Configuration of Aldoximes and their Acyl Derivatives.—In the determination of the configurations of aldoximes no difficulty should be encountered. However, both geometrical isomers should be isolated and their acetyl derivatives treated with alkali under the same conditions, preferably at about 30°. If only one isomer is known its configuration might be determined at least in some cases by comparing the alkaline decomposition products of its acetyl derivative with those of similarly constituted acetyl derivatives which are known in two isomeric forms. Although most acetyl α-benzaldoximes with sodium hydroxide even at the temperature of the water-bath give high yields of oxime and relatively little nitrile or acid, certain other acyl-α-derivatives produce considerable nitrile under the same conditions, and accordingly have been erroneously assigned the β-configuration. Certain of these are discussed in the following paper.

Experimental

Preparation of Acetyl Benzaldoximes.—The acetyl-α-benzaldoximes were prepared by a modification of the method of Brady and Dunn.[13] The pure α-oxime was dissolved in about equal weight of acetic anhydride and the solution allowed to stand at room temperature for five to ten minutes. Sufficient ice and sodium carbonate solution was then added to decompose the excess acetic anhydride and precipitate the α-acetate. The mixture was filtered through a Büchner funnel and the solid washed with cold water until free from the odor of acetic anhydride. After sucking the precipitate practically dry, the α-acetate was dissolved by pouring through the funnel small portions of acetone or alcohol. To this solution was added about 3 volumes of finely crushed ice and the mixture vigorously shaken. The α-acetate separated as small white crystals which were filtered off and dried. In most cases a pure product was obtained by this procedure in 70–80% yields. If the melting points were low, the compound was recrystallized.

The acetyl-β-benzaldoximes were prepared by the method recently described.[3]

Reaction of Acetyl Benzaldoximes with 2 N Sodium Hydroxide.—The reactions of acetyl-α-benzaldoximes were carried out usually at 30 ± 0.1° in a thermostat, and at 97–100° in a boiling water-bath; the reactions of the β-derivatives at 0° in an ice-bath and at 30°. The products were filtered through sintered glass crucibles of the Gooch type.

In general, a 1.0-g. sample of acetate was added to 15 cc. of 2 N sodium hydroxide which had previously been brought to the desired temperature. For the reactions at 97–100°, the samples were made into pellets and introduced into the hot solution through a short reflux condenser. After the reactions were complete (forty-five to ninety minutes at 97–100°, one to four days at 30° and two to

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[12] In this connection it is of interest to note that Segaller [*J. Chem. Soc.*, **103**, 1430 (1913)] found that more isobutylene was formed from tertiary butyl iodide in the presence of potassium hydroxide than in the presence of sodium ethylate under the same conditions.

[13] Brady and Dunn, *J. Chem. Soc.*, **103**, 1619 (1913).

seven days at 0°), the mixture was filtered and the solution extracted with ether. This procedure removed nitrile. The alkaline solution was then saturated with carbon dioxide to precipitate oxime. After filtering off the oxime and extracting the filtrate with ether, the aqueous solution was acidified with hydrochloric acid to precipitate carboxylic acid. This was filtered off and the solution extracted again with ether. These ether extracts were dried with sodium sulfate and evaporated in tared beakers. Even in cases where no precipitate formed, the solution was extracted with ether. The residue from the first ether extract contained small amounts of oxime and nitrile. These were separated by dissolving the oxime in a small amount of cold alkali. All products were dried, weighed, and their melting points taken. After recrystallization mixed melting points with authentic specimens were determined.

Relative Rates of Hydrolysis of the Acetyl Derivatives of α- and β-3,4-Methylenedioxybenzaldoximes

With Aqueous Sodium Hydroxide.—After a given time the reaction mixture of 15 cc. of 2 *N* sodium hydroxide and 1 g. of the acetate was filtered rapidly with suction and the filtrate saturated with carbon dioxide. The extent of hydrolysis was then calculated from the amount of oxime obtained.

With Alcoholic Sodium Hydroxide.—A 1-g. sample of the acetate was dissolved in 60 cc. of 80% alcohol at 0°, and the solution added to an equal volume of 1.3 *N* sodium hydroxide in the same solvent, also at 0°. After a certain time the solution was poured into an excess of acetic acid containing ice. Most of the alcohol was then quickly evaporated in an air draft and the mixture extracted with benzene, which in turn was extracted with 100 cc. of ice cold 1 *N* alkali to remove the oxime. The oxime was precipitated with carbon dioxide in the usual way. During the extraction of the benzene solution with alkali, a small amount of the unchanged acetate was hydrolyzed. Therefore the extraction process was standardized, each extraction being shaken ten times, using 100 cc. of 1 *N* sodium hydroxide at 0°. Under these conditions 80–90% of the free oxime in the benzene solution was extracted as the sodium salt, whereas when a 0.6-g. sample of either the α- or β-acetate in benzene solution was extracted with alkali under the same conditions only 3–5% of oxime was obtained. The yields of oximes reported in Table III are those obtained as described above minus this blank (3–5%).

In the experiments carried out at −0.8°, 1 g. of the acetate in 80 cc. of 95% alcohol was mixed with an equal volume of 0.6 *N* sodium hydroxide in 95% alcohol.

With Sodium Carbonate.—The sodium carbonate used in this work was prepared from pure sodium bicarbonate. A 1-g. sample of the acetate was dissolved in 60 cc. of acetone at 0°, and added with stirring to 250 cc. of a 2% aqueous sodium carbonate solution also at 0°. A slight turbidity was produced, but no precipitate was formed. After standing at 0° for a certain time the solution was poured into an excess of cold acetic acid and then extracted with benzene. The benzene solution was extracted with ice cold alkali. The oxime was precipitated from the alkaline solution in the usual manner. In cases where some unchanged acetate was present, blanks of 3–5% have been subtracted from the yields of oxime obtained. These are given in Table III.

Reaction of Acetyl-β-benzaldoximes with 10% Sodium Carbonate.—A 1-g. sample of the acetate was added to 15 cc. of a 10% aqueous sodium carbonate solution at 0 or 30°. After three to six days the solid was filtered off. When the filtrate was saturated with carbon dioxide and extracted with ether a very small amount of oxime was obtained. It was shown that the solid consisted mostly of nitrile mixed with a small amount of oxime. When cold sodium hydroxide was poured over the solid the oxime dissolved, leaving the nitrile in the funnel. The oxime was isolated by saturating the alkaline solution with carbon dioxide and extracting with ether.

In order to show that the oxime obtained in this manner had not been produced by the action of the sodium hydroxide on some unchanged acetate, the following experiment was carried out. The solid, obtained after filtering off the carbonate, was dissolved in benzene and the solution extracted with cold alkali. The yield of oxime obtained by saturating the alkaline solution with carbon dioxide was approximately the same as that obtained in the manner described above. It has been shown that even if as much as 0.6 g. of acetate in benzene solution is extracted with alkali in the manner employed yields of oxime of only 3–5% are obtained.

Reaction of Acetyl-α-benzaldoximes with Alkali in Alcoholic Solution.—A 1-g. sample of an acetate was introduced through a reflux condenser into 15 cc. of 2 *N* sodium ethylate in absolute alcohol at the refluxing temperature of the solution. The acetate reacted immediately, forming a precipitate of the sodium salt of the oxime. After refluxing for forty-five minutes the mixture was cooled and an equal volume of water added. After evaporating most of the alcohol in an air draft the products were isolated from the alkaline solution in the usual manner.

The experiment was repeated with 2 *N* sodium hydroxide in 50% alcohol.

Reaction of Acetyl-α-benzaldoximes with Potassium Amide in Liquid Ammonia.—The potassium amide in liquid ammonia was prepared[14] by suspending a rusty nail in a 2 *N* potassium solution in liquid ammonia until the blue color disappeared.

A 1-g. sample of an acetate was dissolved in a minimum of dry ether (20–50 cc.). To this solution was added with rapid shaking, about 50 cc. of the potassium amide solution of liquid ammonia. After the ammonia had evaporated cold water was added and the mixture extracted with ether. The nitrile was obtained by evaporation of the ether solution. The oxime and acid were isolated in the usual manner.

Summary

1. The products of the reactions of certain acetyl-β-benzaldoximes with 2 *N* sodium hydroxide have been determined at 0 and 30°. Both nitrile and oxime were formed at these temperatures, the yields of oxime in most cases predominating at 0°, and those of the nitrile at 30°.

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(14) See Bergstrom and Fernelius, *Chem. Rev.*, **12**, 59 (1933); and Coleman and Maxwell, THIS JOURNAL, **56**, 133 (1934).

2. The products of the reactions of certain acetyl-α-benzaldoximes with 2 *N* sodium hydroxide have been determined at 30 and 100°. Both nitrile (or the corresponding acid) and oxime were formed at 100°, and in certain cases, even at 30°. With the exception of the *o*-nitro derivative, the yields of oxime were much greater than those of the acid; at 30°, the yields of acid were extremely small.

3. It has been shown that β-3,4-methylenedioxybenzaldoxime acetate is hydrolyzed somewhat more rapidly than the corresponding α-isomer, but it is probable that there is no very great difference in these rates.

4. It has been concluded that α- and β-aldoxime acetates undergo fundamentally the same types of reaction with alkali; they form oxime by hydrolysis, and nitrile by elimination of acetic acid. They differ primarily in the ease with which they eliminate acetic acid, the β-isomers undergoing this reaction much more readily than the corresponding α-isomers.

5. These results are discussed on the basis of the hypothesis that the formation of nitrile from acetyl aldoximes consists of the removal of a proton by alkali, followed by the release of acetate ion.

6. It has been shown that in the presence of sodium carbonate certain acetyl-β-benzaldoximes give high yields of nitrile and low yields of the corresponding oxime.

7. It has been found that certain acetyl-α-benzaldoximes with potassium amide in liquid ammonia form both nitriles and oxime, the yields of nitrile being greater.

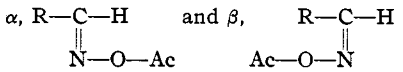
DURHAM, N. C. RECEIVED SEPTEMBER 11, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

The Reactions of Aldoxime Derivatives with Bases. II. The Reactions of Carbethoxy-α-benzaldoximes with Sodium Hydroxide

BY CHARLES R. HAUSER, EARL JORDAN AND RUTH O'CONNOR

In the previous paper[1] it has been shown that the acetyl derivatives of a pair of geometrically isomeric aldoximes



$$\alpha,\ \begin{array}{l}\mathrm{R{-}C{-}H}\\ \quad\ \|\\ \quad\mathrm{N{-}O{-}Ac}\end{array} \qquad \text{and } \beta,\ \begin{array}{r}\mathrm{R{-}C{-}H}\\ \|\quad\ \\ \mathrm{Ac{-}O{-}N}\quad\end{array}$$

undergo fundamentally the same types of reaction with sodium hydroxide; they form oxime by hydrolysis, and nitrile by elimination of acetic acid. They differ primarily in the ease with which they eliminate the elements of acetic acid, and therefore can be readily distinguished. At 30° the β-isomer gives a high yield of nitrile, whereas the α-isomer gives a high yield of oxime, with only a trace or a very small yield of nitrile. At the temperature of the boiling water-bath, however, certain acetyl-α-benzaldoximes[2] give considerable nitrile or corresponding acid, in addition to the α-oxime. Since the yields of products are dependent upon the relative rates of the two competing reactions it appeared not improbable that certain other acyl-α-derivatives might eliminate the elements of acid sufficiently rapidly, relative to their rates of hydrolysis, to give high yields of nitrile at ordinary temperatures, and if the acyl derivative is known in only one isomeric form it might readily be mistaken for the β-isomer. It seemed worth while therefore to reinvestigate the reactions of alkali with various acyl derivatives prepared from α-aldoximes, especially those that have been assigned the β-configuration. In this paper are reported the results obtained with carbethoxy derivatives, certain of which have been previously assigned the β-configuration.[3]

Experimental

Preparation of the Carbethoxy-α-benzaldoximes.—These compounds were prepared from the α-oxime in cold alkaline solution and ethyl chlorocarbonate (ethyl chloroformate), and recrystallized from acetone, alcohol and water according to the method of Brady and McHugh.[3] The yields were about 70%. The melting points of our

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(1) Hauser and Jordan, THIS JOURNAL, **57**, 2450 (1935).

(2) Acetyl-α-*o*-nitrobenzaldoxime gives 36% nitrile and acid even at 61–64°.

(3) Brady and McHugh [*J. Chem. Soc.*, **123**, 1190 (1923)] have reported that of fourteen carbethoxy derivatives prepared from α-aldoximes and ethyl chlorocarbonate, ten had the α-configuration, but, contrary to what was expected, four of them (2-nitro-, 4-nitro-, 4-methoxy- and 3,4-methylenedioxybenzaldoxime derivatives), appeared to have the β-configuration since nitrile (or acid) was obtained when they were heated with alkali on the water-bath. They point out that an explanation is required for the formation of β-derivatives from α-oximes in the presence of alkali, especially since, under the same conditions, β-oximes yield nitriles.