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.

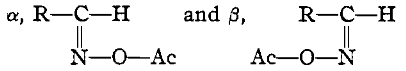
DURHAM, N. C. RECEIVED SEPTEMBER 11, 1935

[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



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

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.

TABLE I

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

Carbethoxy derivative	T, °C.	Nitrile Yield, %	Nitrile Melting point, °C. Obsd.	Nitrile Melting point, °C. Lit.	Acid Yield, %	Acid Melting point, °C. Obsd.	Acid Melting point, °C. Lit.	Oxime Yield, %	Oxime Melting point, °C. Obsd.	Oxime Melting point, °C. Lit.	Total, %
Benzal-	30				2	110–111	121	92	Oil	35	94
Benzal-	97–100				8	118–120	121	74	Oil	35	82
2-Nitro-	0	30	104–105	109–110	7	120–122	148	34	101–102	102–103	71
2-Nitro-	30	8	108–109	109–110	67	138–139	148	17	101–102	102–103	92
3-Nitro-	30	2	98– 99	118	6	122–124	140	65	120–121	123	73
3-Nitro-	97–100				50	120–122	140	45	120–121	123	95
4-Nitro-	0	3	146–147	147	2	225–227	238	90	129–131	133	95
4-Nitro-	30				8	225–226	238	78	129–131	133	86
4-Nitro-	97–100	40	140	147	8	233–234	238	51	132–133	133	99
2-Chloro-	30				5	118–120	139	94	72– 74	75– 76	99
2-Chloro-	97–100	54	42– 43	42– 43	20	136	139	16	74– 75	75– 76	90
4-Chloro-	30				2	235	236	95	107–108	110	97
4-Chloro-	97–100	81	76– 78	92	2	215–217	236	16	105–106	110	99
2-Methoxy-	30					Trace		80	90– 91	92	80
2-Methoxy-	97–100				12	97–98	98.5	60	91– 92	92	72
4-Methoxy-	30				1	160–162	184	92	63– 64	64	93
4-Methoxy-	97–100				31	175–177	184	52	62– 63	64	83
3,4-Methylene-	30	3	166[a]	166				96	110	110	99
dioxy-	97–100				34	220–221	228	59	108–109	110	93

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

TABLE II

PERCENTAGE YIELDS OF PRODUCTS FROM CARBETHOXY-α-BENZALDOXIMES AND POTASSIUM AMIDE IN LIQUID AMMONIA

Carbethoxy derivative	Nitrile Yield, %	Nitrile M. p. °C. Obsd.	Nitrile M. p. °C. Lit.	Oxime Yield, %	Oxime M. p., °C. Obsd.	Oxime M. p., °C. Lit.	Total, %
3-Nitro-	60	100–102	118	3	99–100	123	63
4-Methoxy-	70	53– 55	60	12	58– 60	64	82

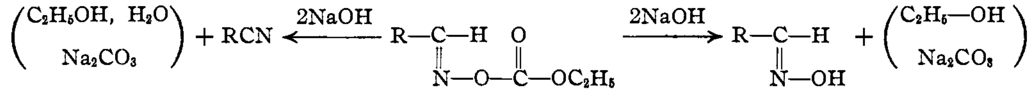
products were the same as those reported by Brady and McHugh. We were not able, however, to isolate the p-nitro derivative in two forms. Our product melted 108–109°, agreeing with that of the higher melting α-product reported by these earlier workers.

Reactions of Carbethoxy-α-benzaldoximes with 2 N Sodium Hydroxide.—A 1-g. sample of the carbethoxy-α-benzaldoxime was added to 15 cc. of 2 N sodium hydroxide at a definite temperature, and after the reaction was complete (usually two to seven days at 30° and one to two hours at 97–100°) the products were isolated according to the method previously used in the study of the reactions of acetyl-α-benzaldoximes with alkali.[1] The results are given in Table I. 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 obtained were either practically the same as those reported in the literature or were raised to these values after one recrystallization.

Reaction of Carbethoxy-α-benzaldoximes with Potassium Amide in Liquid Ammonia.—The reactions with potassium amide were carried out in a manner similar to that used in the study of the reactions of the acetyl-α-benzaldoximes with this reagent.[1]

Discussion

It can be seen from Table I that nitriles (or the corresponding acids) and α-oximes have been obtained from all of the carbethoxy derivatives. The fact that α-oximes[4] and not their β-isomers,[5] have been obtained by the hydrolysis of the carbethoxy derivatives, shows that these derivatives had also the α- or *syn*[6] configuration. Hence the reactions of carbethoxy-α-derivatives with alkali might be represented as follows



$$\begin{pmatrix} C_2H_5OH,\ H_2O \\ Na_2CO_3 \end{pmatrix} + RCN \xleftarrow{2NaOH} \underset{\displaystyle N—O—\overset{\displaystyle O}{\overset{\|}{C}}—OC_2H_5}{\overset{}{R—\underset{\|}{C}—H}} \xrightarrow{2NaOH} \underset{\displaystyle N—OH}{R—\underset{\|}{C}—H} + \begin{pmatrix} C_2H_5—OH \\ Na_2CO_3 \end{pmatrix}$$

It can be seen from Table I that at 30° the yields of oxime were much greater than those of

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(4) The configurations of these oximes have previously been established from a study of the reactions of alkali with their acetyl derivatives and with the acetyl derivatives of the corresponding β-isomers. See previous paper.[1]

(5) The hydrolysis of acetyl-β-aldoximes at 30° gives the corresponding β-oximes. The latter in alkaline solution are relatively stable at 30°. Therefore if the carbethoxy derivatives listed in Table I had had the β-configuration, the corresponding β-oximes should have been formed on hydrolysis.

(6) See previous paper[1] for references to the evidence supporting the view that the α-oximes and their derivatives have the *syn* configuration.

nitrile with the exception of the *o*-nitro derivative, which gave considerable nitrile even at 0°. At 97–100°, the yields of nitrile were higher than those obtained at 30°, and in several cases even greater than those of oxime. As with the acetyl derivatives, the elimination reaction appears to have a higher temperature coefficient than the hydrolysis.

It should be pointed out that the yields of nitrile obtained from these carbethoxy derivatives are higher, and those of oxime correspondingly lower, than those obtained from the analogous acetyl-α-aldoximes under the same conditions.[1] Evidently, a carbethoxy-α-aldoxime eliminates the elements of acid to form nitrile more readily, and/or undergoes hydrolysis less rapidly, than the corresponding acetyl-α-derivatives.

In Table II are given the yields of products obtained from the reactions of potassium amide in liquid ammonia with certain carbethoxy-α-derivatives. It can be seen that high yields of nitrile and low yields of oxime were produced.

Summary

1. The relative yields of nitriles and oximes formed in the reactions of carbethoxy-α-benzaldoximes with sodium hydroxide are a function of the temperature.

2. Contrary to the previously accepted view, that certain carbethoxy derivatives of α-benzaldoximes have β-configurations, it has been shown that they are all of the α-type.

3. The carbethoxy-α-benzaldoximes with sodium hydroxide give higher yields of nitrile, and lower yields of oxime, than the corresponding acetyl-α-benzaldoximes.

DURHAM, N. C. RECEIVED SEPTEMBER 11, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Dehalogenation of β-Bromo Acids. IV. β-Bromophenylpyruvic Acid

BY BEN SOBIN AND G. BRYANT BACHMAN

In the present work an effort has been made to extend the β-bromo acid synthesis of olefin derivatives to the preparation of ketenes. It seemed probable from previous studies[1] that α-keto-β-bromo acids ought to dehalogenate predominantly as follows

$$\mathrm{RCHBrCOCOOH} \longrightarrow \mathrm{RCH{=}C{=}O + HBr + CO_2} \quad (1)$$

in view of the strongly electronegative character of the α-carbonyl group. In order to test this hypothesis, β-bromophenylpyruvic acid was prepared and its dehalogenation studied under a variety of conditions.

The difficulty of selecting a suitable solvent and a suitable dehalogenating agent for the proposed study was immediately apparent, for no substance could be present at any time which would react with the ketene formed. This of course eliminated a good many common solvents and bases from consideration. At first sight, tertiary amines seemed ideally suited for the purpose both as solvents and as dehalogenating agents. When the reaction was tried, however, with pyridine and dimethylaniline the results were unsatisfactory. Carbon dioxide was evolved as expected but the products were tars which were apparently complex in nature and which contained no ketene.

An endeavor was next made to adapt the method to the synthesis of ketene derivatives. It was hoped that primary or secondary amines either in the presence or absence of other solvents would react to form substituted amides of phenylacetic acid. Here again, however, in addition to carbon dioxide only tars were obtained, and no evidence was found of the presence of simple ketene derivatives. Fortunately, we were able to secure decomposition in the desired manner by simply boiling the bromo acid with water. Carbon dioxide was evolved and phenylacetic acid in 77% yield was recovered from the solution. Furthermore, when an aqueous solution of the acid was shaken with silver oxide the same product was obtained in 94% yields. It is difficult to account for the product formed other than by assuming the intermediate formation of phenylketene which then reacted further with water to form phenylacetic acid.

$$\mathrm{C_6H_5CHBrCOCOOH} \longrightarrow \mathrm{C_6H_5CH{=}C{=}O + HBr + CO_2} \quad (2)$$

$$\mathrm{C_6H_5CH{=}C{=}O + H_2O} \longrightarrow \mathrm{C_6H_5CH_2COOH} \quad (3)$$

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(1) Bachman, THIS JOURNAL, **55**, 4279 (1933); Farrell and Bachman, *ibid.*, **57**, 1281 (1935); Alberts and Bachman, *ibid.*, **57**, 1284 (1935).