[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Reactions of Aldoxime Derivatives with Bases. I. The Reactions of Certain Acetyl-β-aldoximes with Alkali[1]

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It seems to be rather generally agreed that when the acetyl derivatives of two geometrically isomeric aldoximes react with alkali, the β-isomer forms the nitrile,[2] and the α-isomer, the original oxime. Recently, however, Brady and McHugh[3] have isolated the corresponding β-oxime in addition to the nitrile from the reaction products of certain acetyl aldoximes and 2 *N* sodium hydroxide. They state, "The isolation of the β-aldoxime by treating with cold sodium hydroxide suggested that the supposed acetyl derivatives were contaminated with unchanged oxime. . . . An alternative explanation is that the hydrolysis of the acetyl-β-oxime gave partly nitrile and partly β-oxime, . . . Judging from experience in the hydrolysis of other acyl-β-aldoximes, we think the second contingency the less likely."

In connection with a study of the mechanism of decomposition of acyl-β-aldoximes in the presence of bases, we have determined the products formed when certain acetyl-β-aldoximes react with alkali. It has been found that when certain acetyl-β-aldoximes were decomposed by sodium hydroxide at 30°, yields of more than 50% of nitriles and 25–30% of β-oximes were obtained. At 0°, on the other hand, the yields of nitriles were only about 30%, while those of the β-oximes were more than 50% of the theoretical quantities (Tables II and III). Experimental evidence has been obtained which indicates that the acetyl compounds used in this work were essentially pure substances. These results show that acetyl-β-aldoximes react with alkali to form partly nitrile and partly β-oxime. Thus both α- and β-acetyl aldoximes are hydrolyzed by alkali to form the corresponding oxime; the β derivatives, however, in addition to the hydrolysis, undergo simultaneous decomposition leading to the formation of nitriles. The latter reaction apparently has the higher temperature coefficient since at 30° it is the predominant reaction, whereas at 0° the hydrolysis predominates.

Experimental

Acetyl-β-aldoximes.—These substances were prepared by a modification of the method described by Brady and McHugh.[3] A solution of 4 g. of β-4-methoxybenzaldoxime in a minimum (about 4.5 cc.) of acetic anhydride was kept at room temperature

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[2] A number of years ago Hantzsch [*Ber.*, **24**, 20 (1891)] reported that acetyl-β-aldoximes reacted with alkali carbonates to form nitriles, and with sodium or ammonium hydroxide to form the corresponding β-oxime. Later, Brady and Dunn [*J. Chem. Soc.*, **103**, 1625 (1913)] reported that certain acetyl-β-aldoximes reacted with alkali to form nitriles. See also Freudenberg "Stereochemie," 1933, [7] p. 975.

[3] Brady and McHugh, *J. Chem. Soc.*, **127**, 2423 (1925).

for five minutes and then cooled in an ice-bath until a solid formed. The suspension was dissolved in alcohol, the solution filtered, and cold water added to the filtrate until the cloudiness first produced just disappeared on shaking. On cooling, crystals were obtained. If the product possessed the odor of anhydride it was recrystallized from a cold acetone–alcohol–water mixture as described above. An alternative procedure was to shake the anhydride suspension with ice water until the anhydride was decomposed.[4] The precipitate was then filtered off and recrystallized as above. The acetyl derivative was obtained as white needles, melting at 64–65°. (A mixed m. p. determination with β-oxime was 54–57°, and one with nitrile, below 50°.) This acetyl aldoxime was prepared also according to the procedure of Brady and McHugh;[3] it melted at 64–65°. The acetyl compound evidently was not particularly sensitive to acetic acid at 0°. However, it is necessary to exclude bright light, halogen acid fumes, etc.[2]

The acetyl derivatives of β-3,4-methylenedioxybenzaldoxime (m. p. 84–85°), β-3-nitrobenzaldoxime (m. p. 97–98°), and β-4-chlorobenzaldoxime (m. p. 86–87°) have been prepared in a similar manner. The melting points of the first two agreed approximately with those reported by Brady and McHugh[3] and not with those reported by Hantzsch. In general these substances were dried on a porous plate over potassium hydroxide in a vacuum desiccator and used within a short time after preparation.

Further evidence that these acetyl derivatives were essentially pure substances has been obtained in the following manner. When ether solutions of the acetyl derivatives of β-4-methoxybenzaldoxime and of β-3,4-methylenedioxybenzaldoxime were extracted with cold sodium hydroxide, and the alkaline layers saturated with carbon dioxide, only very small amounts of the corresponding oximes were obtained, whereas, when an ether solution of a β-oxime was extracted by alkali in a similar manner 80% of it was recovered. It was shown also that these acetyl derivatives neutralized approximately equivalents of standard alkali. After samples of the acetyl compounds in alcoholic solutions were allowed to stand with excess of standard alkali for twenty hours, the excess base was titrated with acid using phenolphthalein as indicator. The results in terms of 0.1 *N* alkali are given in Table I. The amounts of alkali neutralized were approximately equivalent to the quantities of acetic acid that would have been formed by the decomposition of pure samples of the acetyl compounds. Blanks were run with nitrile and oxime, the latter being too weak an acid to interfere with the titration for acetic acid under the conditions used. Also, a mixture consisting of two-thirds acetyl-β-4-methoxybenzaldoxime and one-third of the corresponding oxime neutralized an amount of standard alkali approximately equivalent to the amount of acetyl compound present in the mixture. The total error in this method of analysis was less than 3%.

TABLE I

Calcd. 0.3914 g. $CH_3OC_6H_4CH{=}NOCOCH_3$ = 20.3 cc. 0.1 *M* NaOH. Found, 20.1 cc.
Calcd. 0.1485 g. $CH_3OC_6H_4CH{=}NOCOCH_3$ = 7.69 cc. 0.1 *M* NaOH. Found, 7.70 cc.
Calcd. 0.8100 g. 3,4-$CH_2O_2C_6H_3CH{=}NOCOCH_3$ = 39.1 cc. 0.1 *M* NaOH. Found, 38.4 cc.

Yields of Products from Acetyl-β-aldoximes and Alkali.—Following the general procedure of Brady and McHugh[3] certain acetyl derivatives were shaken with 2 *N* aqueous sodium hydroxide at 0°, kept for twenty to forty minutes and filtered. The solid was the corresponding nitrile. The corresponding β-oxime was precipitated from the filtrate by passing in carbon dioxide or by adding concentrated ammonium chloride. The experiments were repeated at 30°. The average yields of nitriles and oxime obtained from several runs together with the melting points of the products are given in Table II. The products were identified by determining mixed melting points with authentic specimens of the nitrile and β-oxime.

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(4) See Hantzsch, *Z. physik. Chem.*, **13**, 511 (1894).

The yields of products have been determined also from the reaction of 0.125–0.25 *M* acetyl aldoxime with 0.5 *M* alkali in 95% alcoholic solution. After standing for twenty to twenty-four hours the solution was evaporated to dryness at room temperature by means of a hood draft. The residue was triturated with 10 cc. of 2 *N* sodium hydroxide and filtered through a Gooch crucible. The oxime was precipitated from the filtrate with carbon dioxide, and filtered through another Gooch crucible. No appreciable amount of organic acid was obtained by acidifying the bicarbonate solution. The products were washed, dried and weighed. The yields are given in Table III.

TABLE II

PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-β-BENZALDOXIMES AND AQUEOUS ALKALI

Acetyl derivative	Temp., °C.	Nitrile	Oxime	Total
4-Methoxy-	0	25 (m. p. 56–57°)	63 (m. p. 125–128°)	88
3-Nitro-	0	33 (m. p. 114–116°)	40 (m. p. 108–112°)	73
4-Methoxy-	30	55 (m. p. 56–57°)	30 (m. p. 125–128°)	85
3-Nitro-	30	52 (m. p. 114–116°)	25 (m. p. 108–113°)	77

TABLE III

PERCENTAGE YIELDS OF PRODUCTS FROM ACETYL-β-BENZALDOXIMES AND ALKALI IN ALCOHOLIC SOLUTION

Acetyl derivative	Temp., °C.	Nitrile	Oxime	Total
4-Methoxy-	0	35 (m. p. 57–59°)	56 (m. p. 124°)	91
4-Chloro-	0	35 (m. p. 83°)	60 (m. p. 146°)	95
3,4-Methylenedioxy-	0	22 (m. p. 87–90°)	56 (m. p. 135–138°)	78
4-Methoxy-	30	68 (m. p. 57°)	31 (m. p. 123–124°)	99
4-Chloro-	30	67	30 (m. p. 147°)	97
3,4-Methylenedioxy-	30	64 (m. p. 87–90°)	25 (m. p. 132–134°)	89

Reaction of Acetyl-β-aldoximes with Sodium Carbonate.—The only product that could be isolated from the reaction of acetyl-β-4-methoxybenzaldoxime or acetyl-β-3-nitrobenzaldoxime with aqueous sodium carbonate at 0 or 30° was the corresponding nitrile, in yields of 70–90% of the theoretical quantities.

Summary

It has been shown that certain acetyl-β-aldoximes react with sodium hydroxide to form partly nitrile and partly β-oxime.

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