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THE REACTION OF ALDOXIMES WITH ALKALI

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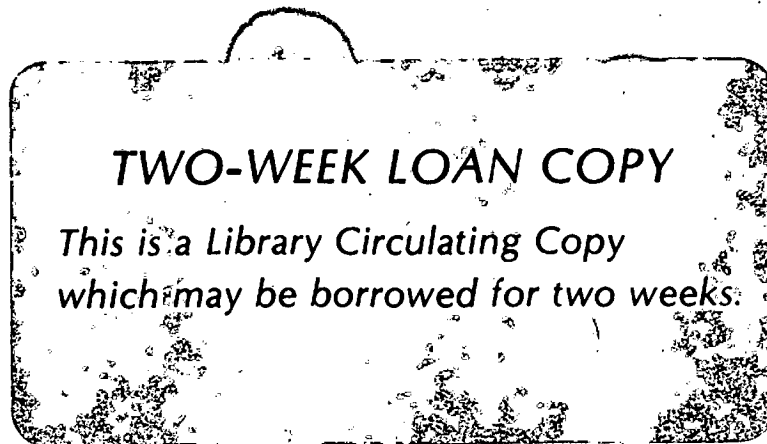
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THE REACTION OF ALDOXIMES WITH ALKALI

Henry Rapoport and William Nilsson

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The Reaction of Aldoximes With Alkali<sup>1</sup>

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(1) Sponsored in part by the United States Atomic Energy Commission.

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by Henry Rapoport and William Nilsson

During the course of another investigation<sup>2</sup> it was

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(2) H. Rapoport and W. Nilsson, J. Am. Chem. Soc., 83, 0000 (1961).

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found that phenylacetaldoxime, when subjected to the action of alkali at 170°, was converted in 78% yield to phenylacetic acid. This reaction seemed to have sufficient potential as a synthetic tool to merit further investigation, and its application to a variety of aldoximes is the subject of the present report.

The only similar case of such a conversion of an aldoxime to an acid by means of hot alkali<sup>3</sup> involved the conversion of

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(3) E. Jordan and C. R. Hanser, J. Am. Chem. Soc., 58, 1304 (1936).

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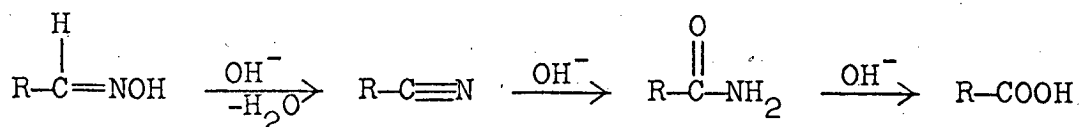
benzaldoxime and several substituted benzaldoximes, as well as furfuraldoxime, to the corresponding acids by heating in 2 N aqueous sodium hydroxide at 100°. The syn-oximes were trans-

formed to acids in considerably lower yields than were the anti-isomers, and the unreacted oximes were recovered in considerable quantity. The anti-oximes were converted to acids in 38-62% yield, the remainder being converted to the more stable syn-isomer.

In the present work the reaction conditions most frequently employed have been diethylene glycol as solvent at a temperature of 170-190°. Under these conditions, all the aldoximes tested were converted by potassium hydroxide to carboxylic acids in good yields except for pivalic acid which was obtained in 38% yield. Here, however, high volatility may account for loss of material during the reaction and isolation.

The reaction has been found to be quite general for aliphatic aldoximes as well as aromatic aldoximes. It may offer a useful alternative to the commonly employed conversion of aldehydes to acids through dehydration of aldoximes under acidic conditions followed by hydrolysis of the resulting nitrile. The results of the various reactions are presented in Table I.

The reaction appears to be a base catalyzed dehydration of the aldoxime to the nitrile followed by hydrolysis of the nitrile through the amide to the acid. This sequence is borne out by the detection of both the nitrile and the amide as intermediates in those cases where the reaction was incomplete.



Alkali is needed, since heating syn-benzaloxime at 120° for

TABLE I

Products Resulting from the Action of  
Potassium Hydroxide on Aldoximes

Aldoxime	M.P., °	Sol-vent <sup>a</sup>	Time, hrs.	Temp., °C	Yield of (%) of Products	
					Acid	Other
Phenylacetal- doxime	101-102 <sup>b</sup>	A	3	190	80	--
Enanthaldoxime	57 <sup>c</sup>	A	3	190	63 <sup>d</sup>	--
		C	16	80	21 <sup>d</sup>	50, oxime 20, amide <sup>d</sup>
Isobutyral- doxime	b.p. 141-142 <sup>e</sup>	A	3	170	88 <sup>f</sup>	--
		B	8	120	89 <sup>f</sup>	--
Pivaldoxime	38-39 <sup>g</sup>	A	3	170	38 <sup>h</sup>	15, amide
		A	6	120	4	42 <sup>i</sup>
<u>anti</u> -Cinnamal- doxime	131-132 <sup>j</sup>	A	3	190	68	--
<u>syn</u> -Benzaldoxime	30-32 <sup>k</sup>	A	3	170	95	--
		B	6	120	15	40, oxime 30, amide 4, nitrile

<sup>a</sup>Solvents: A, diethylene glycol; B, 2-methoxyethanol; C, 80% aqueous ethanol.

<sup>b</sup>Reported<sup>5</sup> m.p. 99-100°.

<sup>c</sup>Reported m.p. 57° [E. Bamberger and F. Elger, Ann., 475, 288 (1929)].

<sup>d</sup>Enanthic acid was identified as its amide, m.p. 93°; reported m.p. 93-94° [O. Aschan, Ber., 31, 2344 (1898)].

<sup>e</sup>Reported b.p. 141-142° [J. Petraczek, Ber., 15, 2783 (1882)].

<sup>f</sup>Identified as the amide, m.p. 128°; reported m.p. 128° [A. W. Hofmann, Ber., 15, 977 (1882)].

<sup>g</sup>Reported m.p. 41° [A. Richard, Ann. chim. (Paris), [8], 21, 371 (1910)].

<sup>h</sup>Identified as the anilide, m.p. 135°; reported m.p. 131-132° [G. Schroeter, Ber., 44, 1201 (1911)].

<sup>i</sup>This was separated into oxime (mostly) plus amide and nitrile.

<sup>j</sup>Reported m.p. 135° [O. L. Brady and R. F. Goldstein, J. Chem. Soc., 1918 (1926)].

<sup>k</sup>Reported m.p. 35° [O. L. Brady and R. F. Goldstein, J. Chem. Soc., 1918 (1926)].

twelve hours in the absence of alkali in 2-methoxyethanol yielded no nitrile, amide, or acid. The oxime was quantitatively recovered. Also, the reaction is sensitive to steric factors. As seen from the table, lowering the reaction temperature from 190° to 120° does not affect the high yield of isobutyric acid from isobutyraldoxime, but it drastically reduces the yields of pivalic acid from the more highly hindered pivaldoxime, which remains largely unchanged at this lower temperature.

At 120°, syn-benzaloxime reacts slowly, only a 15% yield of benzoic acid being isolated after 6 hours. About 40% of the oxime is recovered, while the yields of nitrile and amide are about 4% and 30%, respectively. Hauser and Jordan<sup>3</sup> similarly report only a 10% yield of acid at 100° from syn-benzaloxime. The reaction gives a virtually quantitative yield of benzoic acid at 170°. Thus, it appears that a relatively high activation energy is associated with the dehydration of aldoxime to nitrile; a somewhat lower energy is required for conversion of amide to acid; and a much lower activation energy is associated with hydrolysis of the nitriles to the amides. Also, the reaction is not merely a thermal dehydration followed by alkaline hydrolysis of the resulting nitrile, since thermal dehydration requires significantly higher temperatures and longer reaction times.

It should be mentioned that the recently reported<sup>4</sup> con-

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(4) L. Field, P. B. Hughmark, S. H. Shumaker, and W. S. Marshall, J. Am. Chem. Soc., 83, 1983 (1961).

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version of aldoximes to amides by means of nickel tetraacetate in xylene involves an entirely different mechanism, since the nitrile has been shown not to be intermediat in that case.

#### Experimental

Oximes were prepared by heating the aldehyde with hydroxylamine hydrochloride and sodium acetate in aqueous ethanol, except for phenylacetaldoxime which was made by the method of Weerman.<sup>5</sup> The aldehydes were all commercially avail-

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(5) R. A. Weerman, Ann., 401, 1 (1913).

able except for pivalaldehyde, prepared according to the method of Roberts and Teague.<sup>6</sup>

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(6) T. G. Roberts and P. C. Teague, J. Am. Chem. Soc., 77, 6258 (1955).

The Reaction of Aldoximes with Alkali.--The general procedure used was as follows: The aldoxime (10 mmoles) was heated in 100 ml. of the solvent indicated at the temperature indicated in the table above with about 50 mmoles of potassium hydroxide, and the heating was carried out under a nitrogen atmosphere.

At the end of the reaction time, the cooled mixture was diluted with water and extracted four times with half volumes of methylene chloride, these combined extracts being washed with 100 ml. of aqueous sodium chloride solution. Drying the organic extracts over sodium sulfate, filtering, and evaporating the



the solvent left as a residue the neutral fraction of the reaction mixture. The original aqueous alkaline solution then was acidified with hydrochloric acid to pH 7, and again extracted with methylene chloride. A similar treatment of the organic phase yielded the weakly acidic products. Finally, acidification of the aqueous solution to pH 2 and similar extraction with methylene chloride yielded the strongly acidic products. The products were then identified by mixed m.p. and infrared comparison with authentic samples

The Thermal Dehydration of *syn*-Benzaldoxime.--A solution of 1.09 g. of *syn*-benzaldoxime in 80 ml. of 2-methoxyethanol was heated at 120° for 12 hrs. under a nitrogen atmosphere with no alkali present. The product was isolated as described above and found to consist entirely of unreacted oxime.

A solution of 1.04 g. benzaldoxime in 50 ml. of diethylene glycol was heated 10 hrs. at 200° under a nitrogen atmosphere. The product was entirely neutral and consisted of nitrile and amide. No unreacted oxime or acid was present.

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