TABLE III

PERCENTAGE YIELDS OF PRODUCTS FROM BENZOYL DERIVATIVES OF SUBSTITUTED *syn*-BENZALDOXIMES IN PYRIDINIUM ION SOLUTION

Substituent	Recovered derivative Yield, %	M. p., °C. Found[a]	Lit. m. p., °C.	Nitrile Yield, %	M. p., °C. Found[a]	Lit. m. p., °C.
4-Chloro-	18	141–143	143–144	65	89–92	92
3-Nitro-	35	162–163	164	55	110–113	115
4-Nitro-	35	186–188	196	52	133–137	147

[a] The melting points of products were raised by recrystallization to those reported in the literature.

are found in both Tables II and III it is possible to arrange all of the derivatives studied in the order of their stabilities.

Summary

1. The relative ease of conversion of the benzoyl derivatives of a series of substituted *syn*-benzaldoximes to nitrile in the presence of pyridine and pyridinium ion has been determined.

2. The mechanism of the conversion has been discussed.

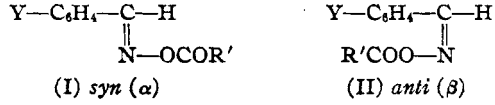
DURHAM, N. C. RECEIVED DECEMBER 23, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

The Relative Ease of Elimination of the Elements of Benzoic Acid from Para Substituted *syn*-Benzaldoxime Benzoates in the Presence of Triethylamine

BY GERTRUDE VERMILLION AND CHARLES R. HAUSER

It has been shown that *syn*- or *anti*-benzaldoxime esters, (I) or (II), respectively, may undergo two types of reaction in the presence of a base like sodium hydroxide[1] or potassium amide[1a]; one type of reaction involves the elimination of the elements of acid to form nitrile, while the other type involves the usual hydrolysis or ammonolysis at the carbonyl group of the ester, leading to the formation of the corresponding *syn*- or *anti*-aldoxime.



(I) *syn* (α) (II) *anti* (β)

Since tertiary amines are incapable of effecting the usual hydrolytic type of reaction at the carbonyl group of esters, it might be expected that if tertiary amines react with *syn*- or *anti*-benzaldoxime esters they would effect only the elimination reaction. Actually, it has already been shown[2] that with pyridine, *anti*-benzaldoxime esters (II) readily eliminate the elements of acid to form nitrile, whereas all of the *syn*-benzaldoxime esters (I) that have been studied thus far are relatively stable in pyridine solution at room temperatures; in fact, this base serves as a convenient reagent for distinguishing *syn*- and *anti*-isomers.[2]

In the present paper it is shown that in the presence of the stronger base, triethylamine, even *syn*-benzaldoxime benzoates (I in which R′ is phenyl) eliminate the elements of benzoic acid to form nitrile (apparently quantitatively) and that the ease of this reaction is dependent upon the activation of the aldehydic hydrogen atom. In Table I are given the yields of unchanged *syn*-benzaldoxime benzoates recovered and the yields of nitriles (and benzoic acid) formed after heating the esters in pyridine solutions in the presence of two equivalents of triethylamine at 89° for three hours.

TABLE I

PERCENTAGE YIELDS OF PRODUCTS FROM PARA SUBSTITUTED *syn*-BENZALDOXIME BENZOATES WITH TWO EQUIVALENTS OF TRIETHYLAMINE IN PYRIDINE SOLUTION FOR THREE HOURS AT 89°

Para substituent	*syn*-Benzoate recovered Yield, %	M. p., °C. Found[a]	Lit.	Yield,[b] %	Nitrile formed M. p., °C. Found[a]	Lit.
Methoxy	78	106–108	109–110	12	55–57	60–61
Chloro	41	139–141	143–144	48	83–85	92
Nitro	0	.....	.....	95	145–146	147

[a] These melting points were raised by recrystallization to those reported in the literature. [b] The yields of benzoic acid obtained corresponded to within 2% of the yield of the nitrile.

It can be seen from Table I that the ease of elimination of the elements of benzoic acid from the *syn*-benzaldoxime benzoates in the presence of the tertiary amines decreases in the following order as the para substituent, Y, is varied: $NO_2 > Cl > OCH_3$. This order is related directly to the strengths of the corresponding carboxylic acids. Hence, it may be concluded that in the presence of the base, the elimination reaction is

(1) See especially (a) Hauser and Jordan, THIS JOURNAL, **57**, 2450 (1935); (b) Vermillion, Rainsford and Hauser, *J. Org. Chem.*, **5**, 68 (1940).

(2) Hauser and Jordan, THIS JOURNAL, **58**, 1772 (1936).

dependent upon the activation (acidity) of the aldehydic hydrogen atom. The elimination is also dependent upon the strength of base used, since in the presence of only the relatively weak base, pyridine, even *syn*-*p*-nitrobenzaldoxime benzoate (the most active, acidic, of those studied) is decomposed to only a relatively small extent within three hours at 90°. The mechanism of the elimination is considered to involve the removal of the aldehydic hydrogen atom as a proton, accompanied or followed by the release of the benzoate ion, thus

$$Y{-}C_6H_4{-}\underset{\underset{N{-}OCOC_6H_5}{\|}}{C}{-}H \xrightarrow{\text{Base}} Y{-}C_6H_4{-}\underset{\underset{N{-}OCOC_6H_5}{\|}}{C}{:}^- \longrightarrow Y{-}C_6H_4{-}C{\equiv}N + C_6H_5COO^-$$

It has been shown previously[3] that the ease of elimination of hydrogen chloride from the corresponding para substituted benzalchlorimines, $Y{-}C_6H_4CH{=}N{-}Cl$, in the presence of alcoholic alkali likewise decreases in the following order as the para substituent, Y, is varied: NO_2 > Cl > OCH_3. Many years ago Hantzsch[4] reported that the ease of elimination of acetic acid from the corresponding para substituted *anti*-benzaldoxime acetates in the presence of sodium carbonate decreases in the following order: NO_2 > OCH_3 > Cl. Since the positions of the chloro and methoxy groups are reversed to what one might expect, Hantzsch's work should be repeated. Of course it is possible that the ease of elimination from *anti*-compounds might follow a different order than that found for *syn*-compounds.

The results presented in this paper are of interest in connection with the belief sometimes expressed[5] that *syn*-benzaldoxime esters do not directly eliminate the elements of acid in the presence of a base, but first rearrange to their *anti*-isomers which then undergo the elimination reaction. It is true that *anti*-benzaldoxime esters undergo the elimination reaction much more readily than their *syn*-isomers and under certain conditions isomerization doubtless precedes the elimination, but in the presence of a sufficiently strong base it seems very probable that *syn*-esters eliminate the elements of acid directly, especially since the isomerization is not favored by the presence of the base. This point of view is supported by the fact that the order found for the ease of elimination of benzoic acid in the presence of triethylamine (Table I) is the reverse of that found for the conversion of *syn*-benzaldoxime benzoates to nitriles[6] in the presence of pyridine and pyridinium ion in which the isomerization to *anti*-benzaldoxime benzoates undoubtedly precedes the elimination.

(3) Hauser, Le Maistre and Rainsford, THIS JOURNAL, **57**, 1056 (1935).

(4) Hantzsch, *Z. physik. Chem.*, **13**, 509 (1894).

(5) See, for example, "Gilman's Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938, p. 387.

Experimental

***syn*-Benzaldoxime Benzoates with Triethylamine and Pyridine.**—Eight-tenths gram of the benzoyl derivatives of *syn*-4-methoxy-, *syn*-4-chloro-, and *syn*-4-nitro-benzaldoximes, prepared as described previously,[6] was dissolved in two equivalents of dry triethylamine and 8 cc. of dry pyridine and the solution heated on a steam-bath (at approximately 89°). After three hours the solutions were allowed to cool to room temperature and then poured on a mixture of 12 cc. of cold concentrated hydrochloric acid and 60 g. of crushed ice. The precipitate was filtered with suction on a sintered glass crucible and washed with cold water. In order to remove any benzoic acid, the solid in the crucible was washed with 10 cc. of cold 2 *N* sodium hydroxide followed by 10 cc. of cold water. Nitrile was separated from unchanged *syn*-benzoate in the following manner. After sucking the water from the solid, the vacuum was turned off and 10 cc. of 95% ethyl alcohol allowed to run slowly through it; the vacuum was again turned on to remove the remainder of the alcohol. Practically all of the unchanged *syn*-benzoate remained in the crucible; evaporation (*in vacuo*) of the alcohol filtrate gave practically pure nitrile. In certain cases further treatment with alcohol was required to separate completely the products. Benzoic acid and an additional amount of nitrile were obtained from the original aqueous hydrochloric acid filtrate by extracting it three times with 40-cc. portions of ether and extracting the ether solution with two 20-cc. portions of cold 2 *N* sodium hydroxide. Nitrile was obtained by evaporation of the dried ether solution, and benzoic acid, by acidifying the alkaline solution and extracting it with ether. The yields of products and the melting points on which the yields are based are given in Table I.

Two grams of *syn*-4-methoxybenzaldoxime benzoate dissolved in 12 cc. of dry pyridine, was heated on a steam-bath at approximately 90°. After three hours the mixture was worked up as described above. A yield of only 2% of nitrile was obtained, 93% of the unchanged *syn*-benzoate being recovered.

syn-4-Nitrobenzaldoxime benzoate (0.11 g.) mixed with 8 cc. of dry pyridine (a portion of the benzoate remaining undissolved) was allowed to stand at room temperature for three days and then heated at 90° for three hours; at this temperature all of the solid went into solution. On working up the mixture as described above, a yield of only 4% of nitrile was obtained, 88% of the original *syn*-benzoate being recovered unchanged.

Summary

1. The relative ease of elimination of ben-

(6) Hauser and Vermillion, THIS JOURNAL, **63**, 1224 (1941).

zoic acid from a series of para substituted *syn*-benzaldoxime benzoates in the presence of triethylamine and pyridine has been determined.

2. The mechanism of the elimination reaction is discussed.

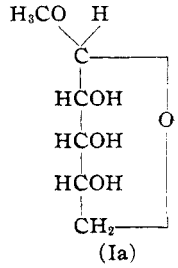
DURHAM, N. C. RECEIVED JANUARY 13, 1941

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

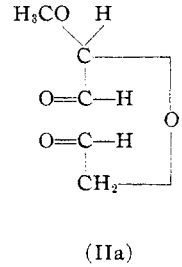
Crystalline β-Methyl-D-ribopyranoside[1]

BY ERNEST L. JACKSON AND C. S. HUDSON

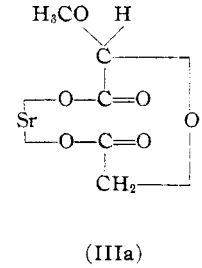
The isolation of a crystalline methyl-D-riboside by J. Minsaas[2] in 1934 made available for structural study a pure isomer of this methylpentoside. Levene and Tipson[3] had obtained evidence for the pyranoside ring structure of "normal methyl-riboside" through methylation of a sirup, which was presumably a mixture of isomeric methyl-D-ribosides. Although Minsaas made no study of the ring structure of his crystalline riboside, he inferred it to be a beta form because of the pronounced levorotation ($[\alpha]^{20}D$ $-113.6°$ in water) as compared with the rotation of the sirupy portion of his product, which he presumed to contain a large proportion of the alpha form. With the aid of seed crystals, kindly supplied by Dr. Minsaas, we have prepared the riboside in pure crystalline condition, with melting point 83° and $[\alpha]^{20}D$ $-105.0°$ in water, and by oxidation with periodic acid have proved it to be β-methyl-D-ribopyranoside (Ia or Ib).



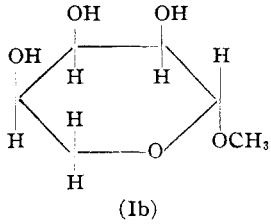
(Ia)



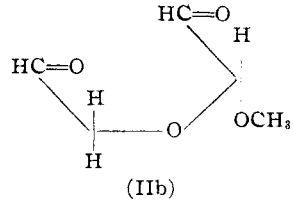
(IIa)



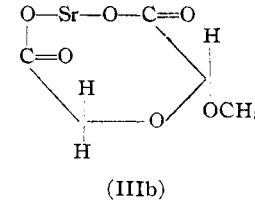
(IIIa)



(Ib)
β-Methyl-D-ribopyranoside



(IIb)
L′-Methoxy-diglycolic aldehyde



(IIIb)
Strontium L′-methoxydiglycolate

The crystalline riboside, upon oxidation by periodic acid or sodium metaperiodate, consumed two moles of the oxidant and produced one mole of formic acid. These data have been shown by us[4] to be typical of the oxidation of the methyl-aldopentopyranosides with periodic acid, and accordingly are in agreement with the oxidation of the ribopyranoside (Ia or Ib) to L′-methoxydiglycolic aldehyde (IIa or IIb). The final proof is based upon the oxidation of the product from the periodic acid reaction with bromine water kept neutral with strontium carbonate to produce in good yield the same crystalline strontium L′-methoxydiglycolate (IIIa or IIIb), which we had obtained in a similar way from β-methyl-D-arabinopyranoside and β-methyl-D-xylopyranoside.[4] These oxidation results not only prove the pyranoside ring structure and the beta classification of the crystalline riboside, but also show it to be substantially homogeneous[5] since the end rotation of the periodic acid oxidation solution, as indicated in Table I, was in agreement with the rotation of L′-methoxydiglycolic aldehyde derived from β-methyl-D-arabinopyranoside, β-methyl-D-xylopyranoside and β-methyl-D-lyxopyranoside.[6]

Experimental

Preparation of β-Methyl-D-ribopyranoside.—The procedure of Minsaas[2] was modified, principally by shortening

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) J. Minsaas, *Ann.*, **512**, 286 (1934).

(3) Levene and Tipson, *J. Biol. Chem.*, **93**, 623 (1931); **92**, 109 (1931).

(4) Jackson and Hudson, THIS JOURNAL, **59**, 994 (1937); **61**, 1530 (1939).

(5) Jackson and Hudson, *ibid.*, **61**, 959 (1939).

(6) Isbell and Frush, *J. Research Natl. Bur. Standards*, **24**, 125 (1940).