Haworth, Perkin and Rankin[10] in separating the benzoic acid formed simultaneously. From this, homoveratric acid was produced by oxidation with hydrogen dioxide, as already recorded by Cain, Simonsen and Smith;[11] and this acid, when treated with thionyl chloride in chloroform solution, gave the acid chloride desired, as has been shown by Haworth, Perkin and Rankin.[10]

The preparation of homoveratroylamino-veratraldehyde from the acid chloride and 6-amino-veratraldehyde was accomplished in a well-cooled 50% acetic acid solution, in the presence of sodium acetate; yield of crude product (m. p. 138.5–139.5°), 50%. Recrystallized from alcohol and decolorized by norite, it formed colorless needles, m. p. 141.2–142.2° (corr.).

Anal. Calcd. for $C_{19}H_{21}O_6N$: C, 63.48; H, 5.86. Found: C, 63.85; H, 6.16.

The Schotten–Baumann method was also employed, but was not satisfactory. Free acids or free bases, of course, must be carefully avoided in this reaction, because of the ease with which *o*-aminobenzaldehydes form condensation products.

(10) Haworth, Perkin and Rankin, *J. Chem. Soc.*, **125**, 1693 (1924).
(11) Cain, Simonsen and Smith, *ibid.*, **103**, 1036 (1913).

2-Veratryl-6,7-dimethoxyquinazoline (II).—A mixture of 1 g. of homoveratroylamino-veratraldehyde with 15 cc. of methanol saturated with ammonia was heated in a sealed tube for two hours at 100–120° and left in the furnace overnight, to cool to room temperature. From the tube contents, there was isolated 0.77 g. of crystals, which were recrystallized from ligroin until the melting point remained constant at 134–135° (corr.). The pure compound consisted of colorless needles, freely soluble in chloroform, carbon bisulfide, ethyl acetate, acetone or benzene, moderately soluble in water or methyl alcohol, very slightly in cold ligroin, and practically insoluble in petroleum ether.

Anal. Calcd. for $C_{19}H_{20}O_4N_2$: C, 67.02; H, 5.92; N, 8.24. Found: C, 67.47; H, 5.73; N, 8.00.

Summary

The synthesis of 2-veratryl-6,7-dimethoxyquinazoline is recorded, a compound structurally related to papaverine. Its pharmacological properties have not yet been studied.

NEW YORK, N. Y. RECEIVED MAY 18, 1935

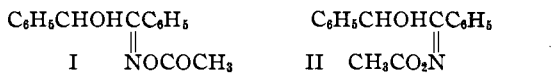
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HOWARD UNIVERSITY]

The Action of Alkali on Certain Acylated Ketoximes. I. The Effect of Structure and Configuration

BY R. P. BARNES AND A. H. BLATT

In an earlier communication[1] we reported that the acetate of α-benzoin oxime (I) on treatment with 5% aqueous sodium hydroxide was cleaved to benzaldehyde, benzonitrile and sodium acetate, while the stereoisomeric β-benzoin oxime acetate (II) under the same conditions was hydrolyzed without cleavage. Preparatory to a study of the mechanism of this cleavage process we thought it advisable to examine the behavior of a number of acylated ketoximes toward aqueous alkali. We chose first, in order to determine to what extent cleavage is conditioned by structure, a number of oxime acetates derived from structurally varied ketones. We chose next, in order to determine to what extent cleavage is conditioned by configuration, a series of acyl derivatives of α- and β-benzoin oximes. From our results, together with those already available in the literature, it is possible to define the limits of the cleavage reaction and, therefore, its usefulness. Since these features are quite independent of the mechanism proper we report on them briefly at this time.

(1) Blatt and Barnes, THIS JOURNAL, **56**, 1148 (1934).



From our results (Table I) and those already published by other workers it follows that the structural factor in an acylated ketoxime[2] which determines the occurrence of cleavage is the presence α to the C=N linkage of an hydroxyl group, a carboxyl group[3] or a carbonyl group[4]—

(2) The type of cleavage which we are considering has long been known to occur with acylated aldoximes [Hantzsch, *Ber.*, **24**, 36 (1891)], but we are limiting the present discussion to ketoximes where a carbon–carbon linkage is broken in the cleavage process.
(3) Hantzsch, *ibid.*, **24**, 43 (1891).
(4) Meisenheimer, (a) *ibid.*, **54**, 3213 (1921); (b) *Ann.*, **446**, 228 (1926). See also Reference 1.

TABLE I

	Substance	Method of preparation	Crystallized from	M. p., °C.	Analyses, % Calcd.	Found	Reaction with alkali
1	$C_6H_5C(CH_3)(OH)CC_6H_5$ ‖ $NOCOCH_3$	A	Ether–pet. ether	73–74	C, 72.1 H, 6.0	72.3 5.85	Cleavage
2	$(CH_3)_2>CHCHOHCCH(CH_3)_2$ ‖ $NOCOCH_3$	A	(This acetate could not be crystallized.)				Cleavage
3	$C_6H_5CHOHCC_6H_4OCH_3$-p ‖ $NOCOCH_3$	A	(This acetate could not be crystallized.)				Cleavage
4	o-$ClC_6H_4CHOHCC_6H_4OCH_3$-p ‖ $NOCOCH_3$	A	Ethanol	139	OCH_3, 9.3	9.0	Cleavage
5	$C_6H_5CHOHCC_6H_5$ ‖ $NOCOC_2H_5$	A	Ether–pet. ether	110–111	C, 72.1 H, 6.0	72.0 6.2	Cleavage
6	$C_6H_5CHOHCC_6H_5$ ‖ $NOCOC_6H_5$	B	Ether–pet. ether	117–118	C, 76.1 H, 5.1	76.3 5.3	Cleavage
7	$C_6H_5CHOHCC_6H_5$ ‖ $NOCOCH=CHC_6H_5$	B	Ethanol	123	C, 77.3 H, 5.3	77.9 4.8	Cleavage
8	$C_6H_5CHOHCC_6H_5$ ‖ C_2H_5COON	A	Ether–pet. ether	104	C, 72.1 H, 6.0	71.8 6.1	Hydrolysis
9	$C_6H_5CHOHCC_6H_5$ ‖ C_6H_5COON	B	Ethanol	170	C, 76.1 H, 5.1	75.9 5.2	Hydrolysis
10	$C_6H_5CHOHCC_6H_5$ ‖ $C_6H_5CH=CHCOON$	B	Ethanol–ether	163	C, 77.3 H, 5.3	77.1 5.6	Hydrolysis
11	$C_6H_5COCC_6H_5$ ‖ C_2H_5CON ‖ O	A	Ether–pet. ether	88–89	C, 72.6 H, 5.4	72.4 5.6	Hydrolysis
12	$C_6H_5COCC_6H_5$ ‖ $C_6H_5CH=CHCON$ ‖ O	B	Ethanol	137	C, 77.7 H, 4.8	77.6 4.9	Hydrolysis

all groups which either contain a hydroxyl group or which may be hydrated in aqueous solution to furnish an hydroxyl group. The ethylene double bond[5] which is not readily hydrated does not bring about cleavage. The other groups present in the ketoxime are of little significance; they may be either aliphatic, as in diacetyl monoxime acetate[6] and isobutyroin oxime acetate, or aromatic.

When one is dealing with the stereoisomeric acyl derivatives of ketoximes which meet the above structural requirements for cleavage, it follows from the data in Table I, from our earlier results and from the work of Meisenheimer on the acyl derivatives of α-benzil monoxime,[4] that only those isomers will cleave whose configurations are similar to that of α-benzoin oxime—that is, those isomers in which the acylated oximino group is *anti* to the structurally significant group on the α-carbon atom. In the case of acylated ketoximes having the α-configuration cleavage is usually accompanied by very slight amounts of hydrolysis. With acylated ketoximes having the β-configuration hydrolysis is not accompanied by cleavage.

The usefulness of the cleavage process is threefold. It enables one to assign configurations to several classes of ketoximes by analogy with the acylated benzoin oximes and benzil monoximes. It enables one to obtain β-oximes from otherwise difficultly separable mixtures of α- and β-isomers. By way of illustration it may be mentioned that acetylation of the crude oxime mixture and subsequent treatment with 5% aqueous sodium hydroxide is the only convenient method we have found for the preparation of pure β-benzoin oxime and β-benzil monoxime. And, finally, treatment of an oxime acetate with alkali is a

(5) Blatt and Stone, THIS JOURNAL, **53**, 4142 (1931).
(6) Diels and Stern, *Ber.*, **40**, 1629 (1907).

much more convenient and clean method of effecting the second order Beckmann cleavage for determining the structure of ketones than is the usual phosphorus pentachloride or benzenesulfonyl chloride process. The practical usefulness of the alkali cleavage method is increased by the fact that the isolation of the ketoxime acetate is not necessary.

Experimental Part

Preparation and Properties of the Acylated Oximes.—The acylated oximes were prepared by one of two methods. A. The oxime was warmed slightly with an excess of the appropriate acid anhydride until it dissolved. In most cases the reaction mixture solidified on cooling. B. The oxime dissolved in pyridine was treated with the acid chloride. The yields, except in the case of the cinnamate of α-benzoin oxime which was difficult to crystallize, were excellent. The pertinent factual details concerning the products are given in Table I. The oximes used as starting materials have all been previously described.

All of the acylated oximes decomposed on standing. We pyrolyzed the acyl derivatives of the α- and β-benzoin oximes and found that the α-derivatives decomposed more readily than the β-derivatives. Both the α- and the β-derivatives pyrolyzed in the same manner to furnish acid, aldehyde and nitrile. The β-derivatives, however, developed a slight isonitrile odor on heating.

Treatment of the Acylated Oximes with Alkali.—The procedure used, except for the cinnamates, consisted of shaking the material at room temperature with an excess of 5% aqueous sodium hydroxide (20 cc. per hundredth mole of substance). In the case of the α-oximes the acyl derivatives usually liquefied in a few minutes while the odor of nitrile and aldehyde was very pronounced. In the case of the β-oximes the acyl derivatives dissolved slowly and without the development of any odor. After a half hour, or longer if necessary, the reaction mixture was shaken out with ether and the aqueous layer separated, acidified and then made alkaline with carbonate solution. Any precipitate at this point consisted of oxime resulting from hydrolysis. With the derivatives of the α-oximes there was either no precipitate at this point or an insignificantly small precipitate. With the derivatives of β-oximes the precipitate consisted of pure β-oxime in an almost quantitative yield. As a further check on the occurrence of cleavage with the acyl derivatives of the α-oximes the ether layer, after shaking with bisulfite solution to remove aldehyde, was concentrated and the residue was hydrolyzed with alkaline hydrogen peroxide. In each case the amide corresponding to the nitrile produced by the cleavage was obtained and identified by comparison with an authentic specimen. In the two instances where the acetates were liquid (Numbers 2 and 3, Table I), both cleavage products, aldehyde and nitrile, were identified through solid derivatives.

The cinnamates of α- and β-benzoin oxime were not affected by aqueous alkali so they were dissolved in alcohol, then treated with the 5% aqueous alkali. The remainder of the treatment paralleled the cases already described.

Summary

The facts available in the literature dealing with the action of sodium hydroxide on certain types of acylated ketoximes have been collected and new facts dealing with the same subject are presented. From these facts it is pointed out that the acyl derivatives of ketoximes having an hydroxyl, carboxyl or carbonyl group α to the C=N linkage, on treatment with 5% sodium hydroxide, undergo hydrolysis if the acylated oximino group is *syn* to the α standing group, and undergo a second order Beckmann cleavage if the acylated oximino group is *anti* to the α standing group. The usefulness of this cleavage process is discussed.

WASHINGTON, D. C. RECEIVED MAY 27, 1935