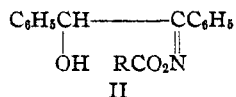
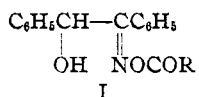


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HOWARD UNIVERSITY]

The Action of Alkali on Acylated Ketoximes. III. Hydrogen Bond Formation in Derivatives of the *o*-Hydroxybenzophenone Oximes

BY A. H. BLATT AND LILLIAN A. RUSSELL

In the earlier articles of this series¹ it was shown that, when hindrance does not intervene, the behavior of acylated benzoin oximes toward alkali is determined by their configuration. Acylated α -benzoin oximes (I) are cleaved by alkali while acylated β -benzoin oximes (II) are hydrolyzed. The mechanism of these two processes has been discussed but no explanation was advanced for the one-to-one correlation between configuration and mode of reaction. It is our purpose in this article to consider this latter point.



Since configuration is the determining factor, one seeks an explanation in terms of steric differences between the isomers. The most striking difference is the proximity in the α -series (I) of the unshared electron pair on the nitrogen atom to the hydroxyl group, and their separation in the β -series (II). We suggest, therefore, that the cleavage of acylated α -benzoin oximes is a consequence of incipient hydrogen bond formation (chelation) between the hydroxyl hydrogen atom and the spatially adjacent unshared electron pair on the nitrogen atom. The interaction between hydroxyl hydrogen and the unshared electron pair on nitrogen would be favored by their proximity in the α -series and it would be prevented in the β -series both by their separation and by the screening effect of the intervening acyl group. That such an interaction does take place is indicated by the infra-red absorption of the acetates of the benzoin oximes. The molal absorption area of β -benzoin oxime acetate (II, R = CH₃) approximates but is somewhat less than that of compounds containing a normal hydroxyl group, while the shape of the absorption curve shows some deviation from normal. α -Benzoin oxime acetate (I, R = CH₃), however, shows a marked suppression of hydroxyl group absorption and, more significant, a broad absorption curve.²

(1) Barnes and Blatt, *THIS JOURNAL*, **57**, 1330 (1935); Blatt and Barnes, *ibid.* **58**, 1900 (1936).

(2) The measurements of the infra-red absorption of these acetates have been published: Hilbert, Wulf, Liddel and Hendricks, *ibid.*, **58**, 548 (1936). We are indebted to Dr. Oliver Wulf and his

The acylated benzoin oximes, though useful as suggesting the explanation which we have just presented, are not of assistance in testing it. The requirements for complete hydrogen bond formation are well established: a system, capable of resonance, made up of a hydroxyl group and a conjugated system of double bonds terminating in oxygen or nitrogen. Such a system is not present in the acylated benzoin oximes though they contain one which approaches it and which constitutes a borderline case. Derivatives of the *o*-hydroxybenzophenone oximes, however, do meet exactly the requirements for hydrogen bond formation and, if our explanation is valid, stereoisomeric pairs of acylated *o*-hydroxybenzophenone oximes should show a difference in their chemical behavior comparable to that shown by stereoisomeric acylated benzoin oximes, while one isomer should show complete hydrogen bonding detectable by appropriate physical methods.

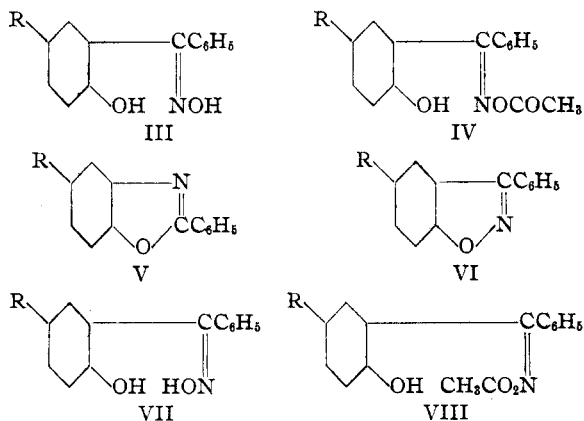
We have verified these consequences by an examination of the acetates of both oximes of *o*-hydroxybenzophenone and of both oximes of 2-hydroxy-5-methylbenzophenone. The isomeric oximes of *o*-hydroxybenzophenone were available as a result of the work of Kohler and Bruce,³ we were able to obtain the previously unknown isomer of 2-hydroxy-5-methylbenzophenone oxime by applying the method of conversion of Kohler and Bruce to the known oxime. Since the two pairs of isomeric oximes thus available show perfectly parallel behavior, it will only be necessary to describe one pair and we shall confine our discussion with few exceptions to the acetates of the oximes of *o*-hydroxybenzophenone.

On treatment with excess sodium hydroxide the acetates of both *o*-hydroxybenzophenone oximes are hydrolyzed to the parent oximes. This perhaps means that under these conditions hydrolysis takes place more rapidly than cleavage. More likely, however, it indicates that salt formation occurs at the phenolic hydroxyl group and destroys the hydrogen bond. In either case,

associates of the Bureau of Chemistry and Soils of the U. S. Department of Agriculture for the measurements and for discussing with us their interpretation. We are, of course, responsible for the particular interpretation presented here.

(3) Kohler and Bruce, *ibid.*, **53**, 1569 (1931).

hydrolysis is most convenient for it permits one to relate the configurations of the acetates to those of the parent oximes by a chemical transformation. With sodium carbonate, that is, under conditions comparable in this series to the use of sodium hydroxide with the benzoin oxime acetates, differences in behavior are observed. The acetate (IV, R = H) undergoes a Beckmann rearrangement to furnish the benzoxazole (V, R = H)—a process which is the counterpart here of the cleavage of α -benzoin oxime acetate, for in both reactions the bond between the α -carbon atom and the carbon atom of the C=N group is broken. The acetate (VIII, R = H) on treatment with sodium carbonate undergoes hydrolysis to the parent oxime (VII, R = H) just as does β -benzoin oxime acetate. On pyrolysis, the acetate (IV, R = H) furnishes cleanly the benzisoxazole (VI, R = H). Pyrolysis of the stereoisomeric acetate (VIII, R = H) is not a smooth process; it furnishes in small yields a mixture of products from which it is possible to isolate the isoxazole (VI, R = H).



The behavior of the acetates (IV, R = H) and (VIII, R = H) on pyrolysis is particularly interesting in view of earlier attempts at ring closure made with the parent oximes. Meisenheimer and Meis,⁴ who were unable to dehydrate the oxime (VII, R = H) to the isoxazole (V, R = H), concluded that such a dehydration would take place only in the, then unknown, isomer (III, R = H) where it would result from the operation of residual valence forces. Kohler and Bruce,⁵ who first prepared the oxime (III, R = H), found that it could not be dehydrated to the isoxazole and this, together with the observation of v. Auwers and Jordan⁶ that the oxime of 2,2'-dihydroxybenzo-

phenone could not be converted to an isoxazole, seemed to discredit pretty thoroughly Meisenheimer's suggestion. However, Lindemann⁶ found that the acetates of a number of *o*-hydroxybenzaloximes and *o*-hydroxyacetophenone oximes furnished isoxazoles on pyrolysis. Lindemann in no case had isomeric oxime acetates. Our results with the acetates of the *o*-hydroxybenzophenone oximes and the 2-hydroxy-5-methylbenzophenone oximes show clearly that pyrolysis to an isoxazole is a smooth reaction only when the acylated oximino group is *anti* to the hydroxyl group. And, although no *trans* dehydration of an oxime to a heterocyclic compound has yet been observed, the assumption that a *trans* ring closure of an oxime *derivative* may take place, for example, in the Beckmann rearrangement of α -benzil dioxime⁷ becomes much more plausible.

It is clear from the foregoing description that the difference in chemical behavior—hydrolysis *vs.* cleavage—which was observed with the isomeric benzoin oxime acetates is also found in the isomeric *o*-hydroxybenzophenone oxime acetates. It remains to be shown that cleavage is associated with the presence of a hydrogen bond in the molecule. Our evidence on this point is from two sources: infra-red absorption and solubility. Dr. Oliver Wulf and his associates at the Bureau of Chemistry and Soils of the U. S. Department of Agriculture, have determined the infra-red absorption of the four acetates (IV, R = H and CH₃) and (VIII, R = H and CH₃). They find that the acetates (IV, R = H and CH₃), in which the hydroxyl group and acetylated oximino group are spatially distant with respect to each other, show no absorption in the hydroxyl region. The acetates (VIII, R = H and CH₃), in which the hydroxyl group and acetylated oximino group are spatially adjacent with respect to each other, show normal hydroxyl group absorption. Their data for the acetate (VIII, R = CH₃) are shown graphically in Fig. 1.⁸ Since the work of these investigators⁹ has shown that the disappearance of hydroxyl group absorption is a criterion of hydrogen bond formation between hydroxyl hydrogen

(6) Lindemann and co-workers, *Ann.*, **449**, 63 (1926); **456**, 275, 284 (1927); *J. prakt. Chem.*, [II] **122**, 214 (1929).

(7) Compare Blatt, *Chem. Rev.*, **12**, 229 (1933).

(8) The data for the acetates (IV, R = H and CH₃) and (VIII, R = H) are presented in an article by Hendricks, Wulf, Hilbert and Liddel, *This Journal*, **58**, 1991 (1936).

(9) Hilbert, Wulf, Liddel and Hendricks, *Nature*, **135**, 147 (1935). See also references 2 and 8.

(4) Meisenheimer and Meis, *Ber.*, **57**, 289 (1924).

(5) Von Auwers and Jordan, *ibid.*, **58**, 26 (1925).

and either carbonyl oxygen or trivalent nitrogen, their results establish definitely the existence of hydrogen bonds in the acetates (IV, $R = H$ and CH_3) and their absence in the acetates (VIII, $R = H$ and CH_3).

In connection with this discussion of the infra-red absorption data we wish to point out that it furnishes a new and absolute method for determining the configuration of oximes of the type under consideration. The results obtained by this method as applied to the oxime acetates can be related to the parent oximes by the fact that each oxime furnishes a single acetate from which the parent oxime can be cleanly regenerated. When the configurations of the oxime acetates, as determined by their infra-red absorption, are related back to the parent oximes, it is found that the configurations thus obtained are in complete agreement with those obtained from the Beckmann rearrangement of the oximes on the assumption of a *trans* shift of groups during rearrangement.

The conclusions from infra-red absorption are supported by the solubilities of the four acetates under discussion. The acetates (IV, $R = H$ and CH_3) are soluble in carbon tetrachloride to the extent of forming one-tenth molar solutions at room temperature. The stereoisomeric acetates (VIII, $R = H$ and CH_3) are so sparingly soluble that it is not possible to prepare one one-hundredth molar solutions in this solvent under the same conditions. While we realize that the use of solubility in assigning structure must be made with proper caution, in a case such as this where the solubilities of stereoisomers are being compared it seems legitimate to conclude that the tenfold greater solubility of the acetates (IV, $R = H$ and CH_3) in a non-polar solvent like carbon tetrachloride indicates the disappearance of the polar hydroxyl group in these acetates. Corroborating the solubilities in carbon tetrachloride are those in alcohol where the acetates (VIII, $R = H$ and CH_3) possessing a polar hydroxyl group are more soluble than their stereoisomers (IV, $R = H$ and CH_3).

The material presented in this article furnishes a firm foundation for the suggestion that the alkaline cleavage of acylated oximes of the α -benzoin and *o*-hydroxybenzophenone types is a consequence of hydrogen bond formation in these substances. In addition, it makes possible a study of the chemical effects which accompany

hydrogen bond formation. It is obvious from our results that hydrogen bond formation between oxygen and nitrogen is completely conditioned by steric factors. Because of this and because of the existence in isomeric forms of compounds containing an unsaturated trivalent nitrogen atom, it is possible for the first time to secure and study isomers which differ from each other only in that one contains a hydrogen bond while the other does not.¹⁰ It has already been shown that occurrence of hydrogen bonding is accompanied by ease of cleavage of the molecule.

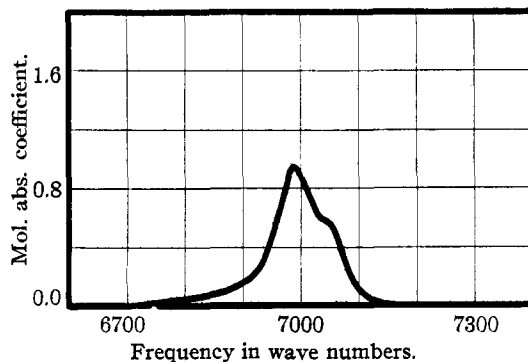


Fig. 1.—Infra-red absorption of *anti* phenyl 2-hydroxy-5-methylphenyl ketoxime acetate.

It is also true that hydrogen bond formation in the *o*-hydroxybenzophenone oxime acetates is accompanied by a decrease in the acidity of the phenolic hydrogen atom. It is our intention to continue the study of systems where hydrogen bonding between oxygen and nitrogen can take place so as to secure additional information about the chemical effects which accompany it. It is our hope that a more complete knowledge of these chemical effects will be of use in the development of a physical interpretation of the hydrogen bond.

Experimental

A. Derivatives of *o*-Hydroxybenzophenone

Preparation of *syn*-Phenyl 2-Hydroxyphenyl Ketoxime Acetate (IV, $R = H$).—To 5.0 g. of the oxime (III, $R = H$)¹¹ was added 10 cc. of acetic anhydride. On gentle warming the oxime dissolved and on cooling the acetate

(10) The existence of isomers of this type has been postulated by Pauling, *THIS JOURNAL*, **58**, 94 (1936), in connection with the infra-red absorption of certain ortho substituted phenols. However, the isomerism predicted by Pauling would result from two different configurations of the hydroxyl group while the isomers with which we are dealing result from different configurations of the atom to which the hydroxyl hydrogen atom is bonded.

(11) The preparation of this oxime is much more satisfactory if twice the quantity of hydroxylamine hydrochloride recommended by Kohler and Bruce,³ is employed. Compare the directions given below for *syn*-phenyl 2-hydroxy-5-methylphenyl ketoxime.

crystallized. Decomposition of the excess anhydride with water and crystallization of the product from alcohol furnished 3.5 g. of pure acetate, melting at 96–97°.

Anal. Calcd. for $C_{15}H_{13}O_3N$: C, 70.6; H, 5.1. Found: C, 70.6; H, 4.9.

Action of Sodium Hydroxide on the Acetate (IV, R = H).—When 0.5 g. of the acetate was shaken with 10 cc. of 5% sodium hydroxide a slight yellow color developed but much of the solid did not dissolve. On addition of 20 cc. of alcohol a clear yellow solution was obtained. After five minutes it was diluted with water, iced and acidified with dilute hydrochloric acid. The resulting colorless precipitate, which weighed 0.35 g., melted at 110–125°. Mixed with the *syn* oxime (III, R = H), m. p. 142–143°, it melted at 133–138°, and mixed with the *anti* oxime (VII, R = H), m. p. 140–141°, it melted below 105°. A single crystallization of the product from benzene and ligroin furnished the pure *syn* oxime (III, R = H).

Action of Sodium Carbonate on the Acetate (IV, R = H).—When a solution of 0.5 g. of sodium carbonate in 5.0 cc. of water was added to 0.5 g. of the acetate in 25 cc. of alcohol there was a transient yellow color while a small amount of material precipitated. After five minutes, the addition of 70 cc. of water precipitated 0.35 g. of a colorless solid which melted at 80–85°; mixed with 2-phenylbenzoxazole (V, R = H)¹² it melted at 95–100°, and mixed with 3-phenylbenzisoxazole (VI, R = H)¹³ it melted below 65°. Crystallization from alcohol furnished the pure benzoxazole, m. p. and mixed m. p. 102–103°.

Pyrolysis of the Acetate (IV, R = H).—When 0.2 g. of acetate was slowly heated in a Späth bulb connected to an oil pump it began to decompose at about 65° while between 140–150° a pale yellow oil distilled. There was almost no charring in the bulb. The distillate dissolved in 2 cc. of hot alcohol, gave on cooling 0.1 g. of 3-phenylbenzisoxazole (VI, R = H) melting at 83–84°. The melting point of the product was not lowered by admixture with a synthetic sample of the benzisoxazole but a mixture of the product and 2-phenylbenzoxazole (V, R = H) melted below 70°.

Preparation of *anti*-Phenyl 2-Hydroxyphenyl Ketoxime Acetate (VIII, R = H).—To 2.4 g. of the oxime (VII, R = H)¹⁴ 8 cc. of acetic anhydride was added. The reaction was worked up as with the *syn* acetate (IV, R = H) and crystallization of the product from 15 cc. of alcohol and 10 cc. of water furnished 2.1 g. of pure acetate which melted at 156°.

Anal. Calcd. for $C_{15}H_{13}O_3N$: C, 70.6; H, 5.1. Found: C, 70.57; H, 4.9.

Action of Sodium Hydroxide on the Acetate (VIII, R = H).—When 0.5 g. of the acetate was shaken with 10 cc. of 5% sodium hydroxide all save a trace of the material

dissolved. After fifteen minutes the solution was filtered, diluted, iced and acidified. It furnished 0.4 g. of the *anti* oxime (VII, R = H), melting at 140–141°, and whose melting point was not lowered by admixture with the *anti* oxime.

Action of Sodium Carbonate on the Acetate (VIII, R = H).—A solution of 0.5 g. of sodium carbonate in 5 cc. of water was added to 0.5 g. of the acetate in 25 cc. of alcohol. A pale yellow color developed and a slight precipitate, apparently inorganic, was formed. After fifteen minutes, the addition of 70 cc. of water gave a clear solution. Careful acidification with dilute hydrochloric acid furnished 0.35 g. of the *anti* oxime melting at 140–141°. The melting point of the product was not lowered by admixture with the *anti* oxime (VII, R = H) but it was lowered to 115–120° by admixture with the *syn* oxime (III, R = H).

Pyrolysis of the Acetate (VIII, R = H).—When 0.2 g. of the acetate was distilled in vacuum there was much charring. The yellow oily distillate dissolved in 1 cc. of alcohol and diluted with water furnished 0.07 g. of a colorless solid which melted at 72–78° and whose melting point was raised by admixture with 3-phenylbenzisoxazole and with 2-phenylbenzoxazole. The solid behaved like a mixture of the oxazole and isoxazole. Crystallization from alcohol and water furnished 0.03 g. of 3-phenylbenzisoxazole (VI, R = H) melting at 79–81° with preliminary softening. Mixed with pure benzisoxazole (83–84°) the recrystallized material melted at 82–84°, mixed with the pure benzoxazole (102–103°) it melted at 67–70°.

B. Derivatives of 2-Hydroxy-5-methylbenzophenone

Preparation of *syn*-Phenyl 2-Hydroxy-5-methylphenyl Ketoxime (III, R = CH₃).—Since the preparation and purification of this oxime are reported to be quite troublesome,¹⁵ we present the following procedure based on that of Kohler and Bruce for the unmethylated analog. Ten grams of 2-hydroxy-5-methylbenzophenone is shaken with 80 cc. of 40% potassium hydroxide. The solid dissolves and an orange-yellow potassium derivative separates. The reaction mixture is then cooled and shaken while 15.0 g. of hydroxylamine hydrochloride is added over a period of forty-five minutes. When no more heat is evolved the flask is stoppered and shaken mechanically for four hours or left to stand overnight. The resulting clear yellow solution is then diluted, iced and acidified with dilute hydrochloric acid. The crude oxime, thus precipitated, weighs 10.1 g. and melts at 127–135°. Crystallization from 25 cc. of benzene and an equal volume of ligroin (70–90°) furnishes 8.2 g. of pure oxime melting at 135–136°. The oxime develops a bright yellow color on exposure to direct sunlight.

Preparation of *syn*-Phenyl 2-Hydroxy-5-methylphenyl Ketoxime Acetate (IV, R = CH₃).—To 2.0 g. of the oxime (III, R = CH₃) there was added 4 cc. of acetic anhydride. Solution was effected by warming and the acetate crystallized on cooling. Purified by crystallization from 25 cc. of alcohol the acetate melted at 125–126°; yield, 1.8 g.

Anal. Calcd. for $C_{16}H_{15}O_3N$: C, 71.4; H, 5.6. Found: C, 71.6; H, 5.6.

(12) Prepared according to Ladenburg, *Ber.*, **9**, 1526 (1876), and melting at 102–103°.

(13) Prepared according to Kohler and Bruce, *THIS JOURNAL*, **53**, 646 (1931), and melting at 83–84°.

(14) The gummy by-products formed in the conversion of the *syn* to the *anti* oxime (*cf.* ref. 3) can be removed conveniently by incompletely neutralizing the strongly alkaline reaction mixture, after dilution with water, with carbon dioxide. This precipitates the by-products so that on acidification of the filtered solution with dilute hydrochloric acid the *anti* oxime is obtained as a colorless, crystalline solid.

(15) (a) Von Auwers and Jordan, *Ber.*, **58**, 34 (1925); (b) Von Auwers and Czerny, *ibid.*, **31**, 2694 (1898).

Action of Sodium Hydroxide on the Acetate (IV, R = CH₃).—When 0.5 g. of the acetate was shaken with 10 cc. of 5% sodium hydroxide, the material dissolved in part to furnish a yellow solution. Addition of 20 cc. of alcohol effected solution, and on dilution with water and acidification with hydrochloric acid 0.4 g. of crude *syn* oxime was obtained. The crude product melted at 110–120°; mixed with the *syn* oxime it melted at 120–133° and, on crystallization from benzene and ligroin, furnished pure *syn* oxime melting at 135–136°.

Action of Sodium Carbonate on the Acetate (IV, R = CH₃).—A solution of 0.5 g. of sodium carbonate in 5 cc. of water was added to 0.5 g. of the acetate in 25 cc. of alcohol. A slight yellow color developed and a small amount of material precipitated. After fifteen minutes the addition of 70 cc. of water precipitated 0.35 g. of a colorless solid which melted at 80–88°. A mixture of this material and 2-phenyl-5-methylbenzoxazole (V, R = CH₃)¹⁶ melted at 90–95°, while a mixture with 3-phenyl-5-methylbenzisoxazole (see below) melted below 65°. Crystallization from alcohol furnished the pure benzoxazole, m. p. and mixed m. p. 102–103°.

Pyrolysis of the Acetate (IV, R = CH₃).—When 1.0 g. of the acetate was pyrolyzed the product distilled at about 160° in an oil pump vacuum. Taken up in 4 cc. of alcohol the solution deposited on cooling 0.5 g. of impure 3-phenyl-5-methylbenzisoxazole (VI, R = CH₃). On crystallization from alcohol the pure benzisoxazole, melting at 92–93°, was obtained. Identification was made by a mixed melting point with a synthetic sample.

Synthesis of 3-Phenyl-5-methylbenzisoxazole (VI, R = CH₃).—A mixture of 2-chloro-5-methylbenzophenone and 2-methyl-5-chlorobenzophenone was prepared from *p*-chlorotoluene according to the directions of Heller.¹⁷ Since the 2-chloro-5-methylbenzophenone did not crystallize, the mixture of isomers was treated with hydroxylamine and then with alkali according to the procedure of Köhler and Bruce for the preparation of 3-phenylbenzisoxazole.¹⁸ The reaction mixture was then extracted with ether, the ether removed and the residue vacuum distilled. The fraction boiling at about 160° when dissolved in alcohol slowly deposited the characteristic large crystals of the isoxazole which melted at 92–93° and which were identical with the previously described pyrolysis product.

Anal. Calcd. for C₁₄H₁₁ON: C, 80.4; H, 5.26. Found: C, 80.2; H, 5.3.

Preparation of anti-Phenyl 2-Hydroxy-5-methylphenyl Ketoxime (VII, R = CH₃).—Strongly alkaline solutions at the boiling point convert the *syn* oxime (III, R = CH₃) into a mixture of the *syn* and *anti* forms. Fortunately the *syn* modification is precipitated from its alkaline solutions by carbon dioxide before the *anti*, so that the isolation of the *anti* form from the mixture presents no special difficulties. Our preferred procedure consists in boiling for two hours 1.0 g. of the pure *syn* oxime with 40 cc. of 40% sodium hydroxide. At the end of the first hour a clear yellow solution is obtained; at the end of the second hour a precipitate is suspended in the alkaline liquid. The hot alkaline reaction mixture is diluted with cold water to

300 cc., 50 g. of crushed ice added and a rapid stream of carbon dioxide passed in for from an hour to an hour and a quarter. At this point the yellow solution is filtered from a small flocculent precipitate of the *syn* oxime which is rejected. To the filtrate, 150 g. of crushed ice is added and then dilute hydrochloric acid is added with stirring until a vigorous evolution of carbon dioxide occurs. At this point the precipitation of the *anti* oxime is complete and it is unnecessary to add additional acid. The reaction mixture at no time is acid to litmus. If no seed is available the *anti* oxime precipitates as a gray curdy mass; once seed is available, the precipitate is lighter in color and granular in form. From three such runs 2.0 g. of crude *anti* oxime is obtained. The material is purified by crystallization from benzene (using 2.5 cc. per gram of solid) by diluting with an equal volume of ligroin (70–90°). The pure *anti* oxime melts at 136–137°, almost the same point as the *syn* modification, but mixtures of the two melt below 115°. The *anti* oxime precipitated from alkaline solutions picks up an electric charge very readily and is difficult to handle.

Anal. Calcd. for C₁₄H₁₃O₂N: C, 74.0; H, 5.7. Found: C, 74.5; H, 5.65.

Beckmann Rearrangement of the anti Oxime (VII, R = CH₃).—A solution of 1.0 g. of the *anti* oxime in 25 cc. of absolute ether was cooled while 1.0 g. of phosphorus pentachloride was added. After one hour, after which time there was no increase in the amount of precipitate, the reaction mixture was poured on ice and the ether layer was separated. Evaporation of the ether, after appropriate washing and drying, left a sticky brownish residue which dissolved completely in 5% sodium hydroxide. Acidification of the alkaline solution and crystallization of the precipitate from dilute alcohol furnished *p*-cresotinic anilide melting at 160–162° and whose melting point was not lowered by mixture with a synthetic sample of the anilide (m. p. 162–163°).¹⁸

Preparation of anti-Phenyl 2-Hydroxy-5-methylphenyl Ketoxime Acetate (VIII, R = CH₃).—Two grams of crude *anti* oxime was warmed with 4 cc. of acetic anhydride for half a minute. The oxime dissolved and the reaction mixture while still warm solidified. After cooling, water was added and the crude acetate was crystallized from dilute alcohol; yield 2.1 g. The pure *anti* acetate melted at 157–158°.

Anal. Calcd. for C₁₆H₁₅O₃N: C, 71.4; H, 5.6. Found: C, 71.24; H, 5.9.

Action of Sodium Hydroxide on the Acetate (VIII, R = CH₃).—When 0.5 g. of the acetate was shaken with 10 cc. of 5% sodium hydroxide, all save a few specks dissolved. After thirty minutes the pale yellow solution was diluted, iced and acidified with dilute hydrochloric acid. The precipitate thus obtained weighed 0.4 g. and melted at 135–136° and its identity as the *anti* oxime was established by mixed melting points with the *syn* and *anti* oximes.

Action of Sodium Carbonate on the Acetate (VIII, R = CH₃).—When 0.5 g. of sodium carbonate was added to 0.5 g. of the acetate in 25 cc. of alcohol, there was a transient deep yellow color and a slight inorganic precipitate. After fifteen minutes, the addition of 70 cc. of

(16) Prepared by a Beckmann rearrangement of the *syn* oxime, compare ref. 15, and melting at 102–103°.

(17) Heller, *Ber.*, **46**, 1500 (1913).

(18) *p*-Cresotinic acid, Zeltner, *J. Chem. Soc.*, **104**, 726 (1913); *p*-cresotinic anilide, reference 15(a), p. 34.

water formed a clear pale yellow solution. Acidification with dilute hydrochloric acid gave 0.4 g. of the *anti* oxime melting at 120–125°; mixed with the *anti* oxime it melted at 128–133° and mixed with the *syn* oxime it melted below 110°. Crystallization from benzene and ligroin gave the pure *anti* oxime.

Pyrolysis of the Acetate (VIII, R = CH₃).—When 0.2 g. of the acetate was vacuum distilled, it charred badly and the yield of distillate, a yellow oil, was poor. Dissolved in alcohol and diluted with water it gave 0.1 g. of a solid melting by 70° and whose melting point was raised by admixture with either the isoxazole (VI, R = CH₃) or the oxazole (V, R = CH₃). Careful crystallization from alcohol gave a small amount of 3-phenyl-5-methylbenzisoxazole (VI, R = CH₃) melting at 91–92° and whose melting point was not lowered by mixing with the pure benzisoxazole, m. p. 92–93°, but which was lowered to 70° by mixing with the oxazole, m. p. 102–103°.

Summary

It has been suggested that the cleavage of acylated α -benzoin oximes by alkali is a consequence of incipient hydrogen bond formation in these compounds. By an examination of acylated *o*-hydroxybenzophenone oximes it has been shown that hydrogen bond formation, sterically conditioned, does take place and that its occurrence is accompanied by behavior comparable to that observed in the acylated α -benzoin oximes. It is pointed out that the existence of stereoisomers, only one of which contains a hydrogen bond, makes possible a study of the chemical effects associated with hydrogen bonding.

WASHINGTON, D. C.

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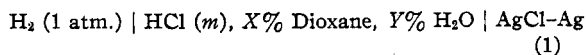
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

The Thermodynamics of Hydrochloric Acid in Dioxane–Water Mixtures from Electromotive Force Measurements. I. Standard Potentials

BY HERBERT S. HARNED AND JOHN OWEN MORRISON¹

The further development of the physical chemistry of ionized solutes and ionic equilibria requires a knowledge of the variation of the fundamental thermodynamic property, the relative partial molal free energy, as a function of all the intensive variables. Such a comprehensive study of many electrolytes by different methods of measurement is a tremendous task, only to be carried out by many investigators over a long period of time. As a part of this general scheme, we have undertaken in this Laboratory a comprehensive study of the relative partial molal free energy of a single electrolyte as a function of its concentration, the temperature and dielectric constant of the solvent medium over as wide a range of values of these variables as will be found possible.

To achieve this purpose, the cell



is peculiarly adapted. The cell reaction is well known and the electrodes are very reproducible. Dioxane–water mixtures because of their complete miscibility and because of the low dielectric constant of pure dioxane (~ 2) afford a wide

range of variation of the dielectric constant. These properties have been shown to be of great value by Kraus and Fuoss² and Fuoss and Kraus,³ who measured conductances of some electrolytes in these mixtures.

As part of this program, Åkerlöf and Short⁴ have determined the dielectric constant of dioxane–water mixtures from 0 to 80°. The present communication contains electromotive force measurements of the above cells containing 20, 45 and 70% dioxane, respectively. Measurements have been made from 0 to 50° at 5° intervals, and from them the standard potentials of the cell from 0 to 50° inclusive have been calculated.

Experimental Procedure

In order to obtain electromotive forces in these mixtures with an accuracy equal to that obtained by Harned and Ehlers in water⁵ and Harned and Thomas⁶ in methanol–water mixtures, it was necessary to develop a new type of cell and a specialized technique. It was found that complete air elimination in all-glass apparatus was essential. Any contact of vapor or liquid in the cells with rubber rendered the measurements erratic and uncertain. Upon elimination of these difficulties, very accurate results may be obtained with a potentiometer circuit and a high sen-

(2) Kraus and Fuoss, *THIS JOURNAL*, **55**, 21 (1933).

(3) Fuoss and Kraus, *ibid.*, **55**, 1019 (1933).

(4) Åkerlöf and Short, *ibid.*, **58**, 1241 (1936).

(5) Harned and Ehlers, *ibid.*, **55**, 2179 (1933).

(6) Harned and Thomas, *ibid.*, **57**, 1666 (1935); **58**, 761 (1936).

(1) This communication contains material from a dissertation presented by John Owen Morrison to the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1936.