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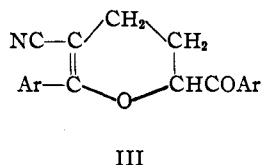
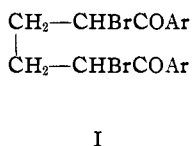
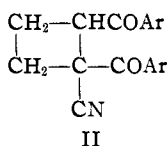
DIHYDRO-1,4-PYRANS. II. DEGRADATION BY USE OF THE BECKMANN REARRANGEMENT

BY TSI YU KAO AND REYNOLD C. FUSON

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It has been reported¹ that when 1,4-dibromo-1,4-diaroylbutanes (I) are treated with sodium cyanide in a mixture of absolute alcohol and ethyl acetate they do not yield the 1-cyano-1,2-diaroylcyclobutanes (II) to be expected by analogy with the results obtained when this method was applied to α, α' -dibromo-adipic esters.² Instead, they are transformed into dihydro-1,4-pyrans of the type 2-aryl-3-cyano-6-aroyl-5,6-dihydro-1,4-pyran (III).



Actually, the two compounds (of types II and III) are in each case unknown, and the properties of those actually obtained are such as to make it difficult to decide which type of formula should be assigned to them.

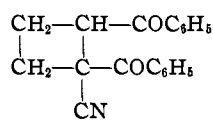
The present paper is a report of a study of this question. For this work the product obtained from 1,4-dibromo-1,4-dibenzoylbutane has been chosen. It should be either 1-cyano-1,2-dibenzoylcyclobutane (IVa) or 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran (IV).

In view of the close similarity between this case and that of the α, α' -dibromo-adipic ester cyclization to cyclobutane derivatives, it seemed likely that formula IVa would be found to be correct. Accordingly, in order to form a plan of attack on the problem of structure, this formula was assumed. The plan devised was to prepare the dioxime and by means of the Beckmann rearrangement, followed by hydrolysis and loss of carbon dioxide, to arrive at cyclobutane-1,2-dicarboxylic acid—a known compound.

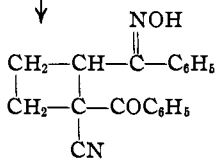
The attempt to carry out this plan led to the preparation of a series of compounds corresponding rather closely to those to be expected on the basis of the original assumption. However, certain developments, to be mentioned presently, pointed to the 1,4-pyran type of structure (IV) and the problem resolved itself into an attempt to discover unequivocal evidence in favor of one or the other of the two proposed structures. Since

¹ Fuson, Kuykendall and Wilhelm, *THIS JOURNAL*, **53**, 4187 (1931).

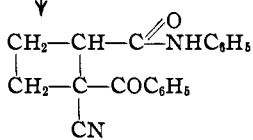
² Fuson and Kao, *ibid.*, **51**, 1536 (1929); Fuson, Kreimeier and Nimmo, *ibid.*, **52**, 4074 (1930).



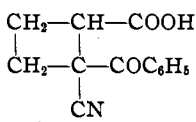
IVa



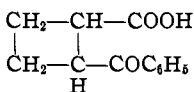
Va



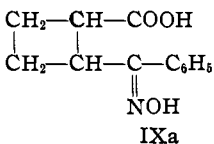
VIa



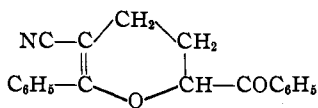
VIIa



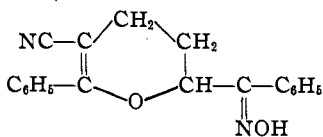
VIIIa



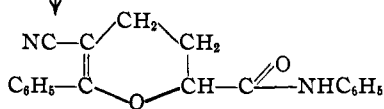
IXa



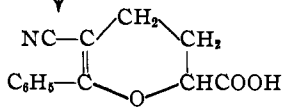
IV



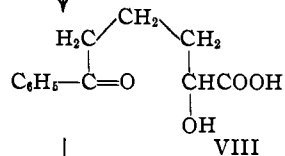
V



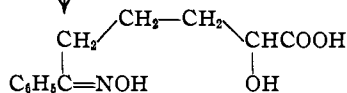
VI



VII



VIII



IX

the weight of evidence now at hand is strongly in favor of formula IV, it will be convenient to assume this structure in order to expedite the presentation of the facts upon which the decision rests.

In the first place, the original cyano compound (IV) was a colorless solid melting at 105–106°. Under no conditions has it been found possible to open the ring. It did not decolorize an acetone solution of alkaline permanganate and took up bromine very slowly to form an unstable derivative which appeared to be a monobromo derivative. The original cyano compound formed a monoxime and a monosemicarbazone but under no circumstances could any evidence be obtained of the presence of a second ketone

group. This was the first evidence which strongly favored the monoketone structure (IV) as compared with the diketone structure (IVa).

The monoxime was found to exist in two forms melting at 156.6–157° and 141–142°. However, when treated with thionyl chloride both oximes gave the anilide VI—a compound melting at 156–156.5°. When hydrolyzed, the anilide gave the corresponding acid (VII), melting at 155–156°. This acid did not form an oxime—a fact which militates in favor of formula VII as compared with VIIa since the latter does have a ketone group.

By careful hydrolysis in alkaline solution the cyano acid was converted into the corresponding dicarboxylic acid. This acid gave the calculated neutral equivalent but its instability prevented a satisfactory analysis being made. When this acid was treated with hydrochloric acid it lost carbon dioxide and gave a ketonic acid whose analysis corresponded to formula VII (=VIIIa + H₂O). The monoxime of this acid corresponded to formula IX (=IXa + H₂O).

It would seem certain that formulas VIIIa and IXa would have to be discarded in favor of VIII and IX, respectively. To settle this point definitely an independent synthesis of δ -benzoyl- α -hydroxyvaleric acid (VIII) has been carried out. This compound, whose preparation will be described elsewhere, has been found to be identical with the degradation product obtained from VII.

It is evident, in the light of this result, that the ring must have opened in the transformation of VII into VIII. This is easily explained by reference to formula VII and seems to exclude the cyclobutane type of structure (VIIa) as a possibility. Also, there is every reason to believe that compounds IV, V and VI are of the same type as VII, an assumption which leads to the conclusion that the formula III (and not formula II) correctly represents the cyclization products obtained by the cyanide treatment of the 1,4-dibromo-1,4-diaroylbutanes.

Experimental Part

2-Phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran (IV).—This compound was prepared from 1,4-dibromo-1,4-dibenzoylbutane by the method of Fuson, Kuykendall and Wilhelm.¹ The yields were about 50% of the theoretical. The closure evidently is accompanied by side reactions. A sticky red liquid was always obtained as by-product and from this has been isolated a bromine-containing compound melting at 138–139°. This compound is under investigation.

Mono-oximes.—Two and nine-tenths grams of 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran was dissolved in a mixture of 30 cc. of ethyl alcohol and 10 cc. of water. To this solution were added 3 g. of hydroxylamine hydrochloride and 6 g. of potassium acetate in 15 cc. of water. The mixture was heated on a steam-bath for thirty minutes under a reflux condenser. The reaction mixture was stirred continuously throughout the period of heating and then for an hour or two longer. When allowed to stand at room temperature for twelve hours, the solution deposited crystals melting at 130 to 155°. The mother liquor after the crystals had been removed by filtration was then diluted with water; a precipitate was obtained which set to a gummy mass. Both

this and the first crop of crystals were repeatedly recrystallized from 70% alcohol. In this way two compounds were obtained melting at 156.5–157° (A) and 141–142° (B). In the separation of these compounds much difficulty was encountered; it was comparatively easy in those runs in which the crude product melted above 145° to separate the high-melting compound (A) but in other runs the separation was very difficult and was not always accomplished. Fortunately, as will be seen in the sequel, the separation proved to be unnecessary for the purpose in view. That the two compounds were mono-oximes was shown by the analyses.

Anal. Calcd. for $C_{19}H_{16}O_2N_2$: C, 75.0; H, 5.3; N, 9.2. Found for Compound A: C, 75.0; H, 5.3; N, 9.6. Found for Compound B: C, 74.8; H, 5.4.

The Anilide of 2-Phenyl-3-cyano-6-carboxy-5,6-dihydro-1,4-pyran (VI).—Both of the mono-oximes (A and B) were subjected to the Beckmann rearrangement. One gram of the dry oxime was added in small portions to a mixture of 3 cc. of thionyl chloride and 7 cc. of chloroform contained in a 50-cc. Erlenmeyer flask surrounded by an ice-bath. After the addition was completed the reaction mixture was allowed to stand for a few minutes in the ice-bath and then for about an hour at room temperature. The temperature gradually rose to 30° and the color of the mixture changed from a light yellow to a pink or faint purple.

The excess thionyl chloride was decomposed by adding cracked ice to the reaction mixture. After the evolution of sulfur dioxide had ceased, 20 cc. of chloroform was added and the chloroform layer was separated and washed twice with water. After the chloroform solution had been dried over anhydrous magnesium sulfate, the chloroform was evaporated under diminished pressure. The residue set to a colorless solid which was washed on a filter with a little cold alcohol and then recrystallized three times from 95% alcohol.

The anilides obtained by the above procedure from the two mono-oximes proved to be identical. The melting point was 156–156.5°; a mixture of the two samples showed no depression of the melting point. Mixtures of the anilide with the original oximes showed a marked depression of the melting point.

Anal. Calcd. for $C_{19}H_{16}O_2N$: C, 75.0; H, 5.3; N, 9.2. Found: C, 75.3; H, 5.6; N, 9.5.

2-Phenyl-3-cyano-6-carboxy-5,6-dihydro-1,4-pyran (VII).—Two grams of the anilide was heated under a reflux condenser with 40 cc. of a solution of alcoholic potassium hydroxide (1 part potassium hydroxide, 1 part water and 8 parts alcohol) for thirty minutes and allowed to stand for a few hours at room temperature. The reaction mixture was diluted with two or three times its volume of water and concentrated somewhat by evaporation under diminished pressure to remove the alcohol. The aqueous solution remaining was then cooled to 0° and treated with an excess of dilute hydrochloric acid to precipitate the cyano acid. This compound after a few recrystallizations from 50% alcohol separated in the form of yellowish cubical crystals melting at 155–155.5°. It was soluble in dilute alkalis.

Anal. Calcd. for $C_{18}H_{14}O_2N$: C, 88.1; H, 4.8; N, 6.1. Found: C, 88.0; H, 5.1; N, 6.4.

2-Phenyl-3,6-dicarboxy-5,6-dihydro-1,4-pyran.—One-half gram of the cyano acid (VII) was heated under a return condenser with a 20% solution of sodium hydroxide. The evolution of ammonia was noticeable after a half hour and continued for twenty hours. When ammonia ceased to be evolved, the heating was discontinued and the reaction mixture, after being cooled to 0°, was acidified with dilute hydrochloric acid. The precipitated silicic acid was removed by filtration and the filtrate, after being saturated with sodium sulfate, was extracted repeatedly with ether. The ether extract

was dried over anhydrous sodium sulfate and evaporated under diminished pressure. There was obtained a residue which, when recrystallized from hot water, separated as colorless crystals melting at 144–144.5°, with evolution of gas. The neutral equivalent was found to be 123; that calculated for 2-phenyl-3,6-dicarboxy-5,6-dihydro-1,4-pyran is 124.

When the hot alkaline reaction mixture was acidified with hydrochloric acid the product obtained was the mono-carboxylic acid (see below).

δ -Benzoyl- α -hydroxyvaleric Acid (VIII).—One gram of the cyano acid (VII) was heated under a reflux condenser with 60 cc. of a 50% solution of sulfuric acid. After fifteen minutes of boiling the cyano acid was completely dissolved. The solution darkened rapidly and at the end of an hour dark crystals began to separate. The heating was then discontinued and the reaction mixture was diluted with an equal volume of water. This solution was cooled to 0° and allowed to stand for several hours. The crystals obtained in this way were removed by filtration and recrystallized first from hot water and then from ethyl acetate. The δ -benzoyl- α -hydroxyvaleric acid thus obtained was shown to be identical with that prepared from the dicarboxylic acid as indicated in the preceding section. It melted at 120–120.5°; the yield was 88% of the theoretical.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.2; H, 6.3. Found: C, 64.3; H, 6.0.

Oxime.—The oxime was a colorless crystalline compound, melting at 144–145.5°; the yield was 63% of the theoretical.

Anal. Calcd. for $C_{12}H_{16}O_4N$: C, 60.8; H, 6.4. Found: C, 60.7; H, 6.4.

Summary

Evidence has been presented in support of a dihydro-1,4-pyran structure for the cyano ketone obtained by the cyanide ring-closure of 1,4-dibromo-1,4-dibenzoylbutane. The anilide obtained by rearrangement of the oxime of the cyano ketone has been found to hydrolyze to δ -benzoyl- α -hydroxyvaleric acid. This result furnishes convincing evidence that the cyano compound is 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

PENTOSE REACTIONS. I. FURFURAL FORMATION

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It is generally known that pentoses yield furfural on distillation with mineral acids. This is the basis for the determination² of pentoses. Furthermore, the commercial production of furfural³ depends on the pentosan content of oat hulls. In proportion to the general familiarity with the reaction, detailed study on it has been quite limited.

To ascertain whether or not the reaction of pentose into furfural was merely one of dehydration, xylose was heated with phosphorus pentoxide

¹ Quaker Oats Fellow at Northwestern University, 1927–1929.

² Pervier and Gortner, *Ind. Eng. Chem.*, 15, 1167, 1255 (1923).

³ Miner and Brownlee, British Patent, 203,691, Dec. 4, 1924; *Chem. Abstracts*, 18, 692 (1924).