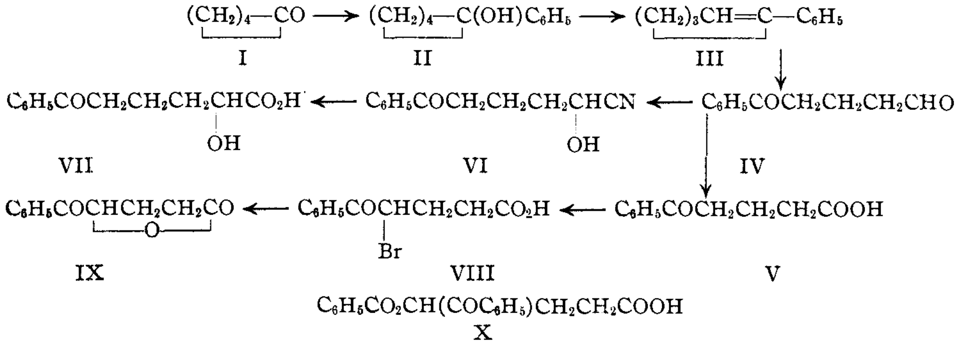
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF ILLINOIS AND THE OHIO STATE UNIVERSITY]

Dihydro-1,4-pyrans. IV. The Synthesis of γ-Benzoyl-γ-butyrolactone and α-Hydroxy-δ-benzoylvaleric Acid

BY REYNOLD C. FUSON, M. E. DAVIS, B. H. WOJCIK AND J. A. V. TURCK

The dihydro-1,4-pyran structure proposed for the compounds obtained from 1,4-dibromo-1,4-diaroylbutanes by ring closure[1] has been supported by certain degradation studies[2] in which the end products obtained were thought to be the benzoate of γ-hydroxy-γ-benzoylbutyric acid (X) and α-hydroxy-δ-benzoylvaleric acid (VII). The latter has now been prepared by a method which leaves no doubt as to its identity and has made possible the identification of the degradation product in question. This paper is a report of this synthesis and of the results of an attempt to prepare the benzoate.



α-Hydroxy-δ-benzoylvaleric Acid (VII).—γ-Benzoylbutyraldehyde, which served as the starting material in both of the syntheses being reported, was prepared from cyclopentanone (I) by way of 1-phenylcyclopentanol (II) and 1-phenylcyclopentene (III). For the preparation of the pentanol and the pentene the method of Bauer[3] was modified somewhat. The crude 1-phenylcyclopentanol obtained by treating cyclopentanone with phenylmagnesium bromide was not purified but was treated directly with formic acid.

From 1-phenylcyclopentene the aldehyde was prepared by ozonization according to the general method of Helferich[4] in which the ozonide is decomposed in the presence of zinc dust. γ-Benzoylbutyraldehyde was obtained as an oil which could not be purified by distillation. With the temperature of the bath at 300° the aldehyde came over at 154–190° (7 mm.). Moreover, the aldehyde both before and after distillation reacted sluggishly with sodium bisulfite. It seems likely that the compound tends to polymerize and that the distillation process may involve depolymerization. However, the bisulfite addition compound was found to react normally and served for the preparation of the cyanohydrin. It reacted with sodium cyanide to give α-hydroxy-δ-benzoylvaleronitrile (VI). Hydrolysis converted the hydroxy-nitrile into the desired acid, α-hydroxy-δ-benzoylvaleric acid (VII), which melted at 118–119.5° and proved to be identical with the compound obtained by the degradation of 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran.

γ-Benzoyl-γ-butyrolactone (IX).[5]—The γ-benzoylbutyric acid which was used in making the lactone was prepared in several ways. As has already been stated, it was always obtained along with the ketoaldehyde by ozonization of 1-phenylcyclopentene. Also, the ketoaldehyde was found to yield the acid when oxidized with potassium permanganate. Finally, when 1-phenylcyclopentene was oxidized with potassium permanganate by the method of Bauer[3] δ-benzoylbutyric acid was obtained in good yield.

γ-Benzoylbutyric acid reacted very rapidly with bromine to yield the monobromo derivative, γ-bromo-γ-benzoylbutyric acid (VIII). When

---

[1] Fuson, Knykendall and Wilhelm, THIS JOURNAL, **53**, 4187 (1931).

[2] Kao and Fuson, *ibid.*, **54**, 313 (1932); Brock and Fuson, unpublished work.

[3] Bauer, *Ann. chim.*, [9] 1, 367 (1914).

[4] Helferich, *Ber.*, **52**, 1123 (1919).

[5] Since this work was done Allen and Cressman [THIS JOURNAL, **55**, 2953 (1933)] have prepared the lactone by another method.

the bromo acid was treated with aqueous alkali or merely boiled with water, it passed smoothly into the corresponding lactone, γ-benzoyl-γ-butyrolactone. This compound was found to be a solid melting at 78–79°. Attempts to prepare the benzoate of γ-hydroxy-γ-benzoylbutyric acid (X) were unsuccessful. The bromo compound when treated with silver benzoate gave the lactone (IX).

Experimental

γ-Benzoylbutyraldehyde.—By use of the general method of Helferich[4] 48 g. of 1-phenylcyclopentene was ozonized in acetic acid solution. Following the decomposition of the ozonide with water in the presence of zinc dust the crude aldehyde was taken up in ether. The ether solution was washed with water followed by a solution of sodium carbonate to remove the γ-benzoylbutyric acid. Acidification of the carbonate solution gave 6.3 g. of this acid.

After the ether solution of the keto-aldehyde had been dried the ether was allowed to evaporate in a vacuum desiccator. There was obtained 22 g. of a golden yellow oil which could not be purified by distillation. Attempts to distil the compound gave a distillate which came over at 154–190° (7 mm.) with the temperature of the bath at 300°. The *sodium bisulfite derivative* of the keto-aldehyde formed very slowly when the aldehyde was shaken with a saturated solution of sodium bisulfite.

α-Hydroxy-γ-benzoylvaleronitrile (VI).—The bisulfite addition compound obtained from the keto-aldehyde was treated with an equivalent amount of sodium cyanide in aqueous solution. A brown oil formed and crystallized after several days to a sticky mass. This was pressed on a clay plate and recrystallized repeatedly from alcohol. The colorless crystals of the cyanohydrin melted at 151–151.5°.

Anal. Calcd. for $C_{12}H_{13}O_2N$: N, 6.9. Found: N, 6.8.

α-Hydroxy-γ-benzoylvaleric Acid (VII).—Treatment of the cyanohydrin with concentrated hydrochloric acid in the usual way gave the hydroxy acid which, after recrystallization from very dilute alcohol, melted at 117.5–118.5°. A mixture of this with a specimen of the acid prepared by Kao and Fuson[2] melted at 117.5–118.5°.

γ-Benzoylbutyric Acid. (a) By Oxidation of 1-Phenylcyclopentene with Potassium Permanganate.—The method of Bauer was used. It was found that the temperature and the concentration of the oxidizing agent must be carefully controlled in order to obtain good yields. The temperature of the reaction mixture must be kept below 50° and the amount of permanganate must not be more than 40 cc. of a 5% solution for each gram of pentene. The γ-benzoylbutyric acid when recrystallized from hot water melted at 126°. The yield was 59% of the theoretical amount.

(b) **By Oxidation of γ-Benzoylbutyraldehyde with Potassium Permanganate.**—To 17.6 g. of the crude γ-benzoylbutyraldehyde in a beaker was added 300 cc. of a 5% potassium permanganate solution, a little at a time, with stirring. The reaction mixture became very warm but cooling was not necessary. After the addition of the permanganate solution had been completed, 30 cc. of a 20% solution of potassium hydroxide was added. The manganese dioxide was filtered from the cold mixture and the filtrate was extracted twice with 200-cc. portions of ether and then treated with dilute hydrochloric acid until the organic acid was completely precipitated. The solution was cooled and the crude acid was separated by filtration. After recrystallization from water 11 g. of γ-benzoylbutyric acid was obtained which melted at 125–126°.

(c) **By Oxidation of 1-Phenylcyclopentene with Ozone.**—The acid was also prepared directly from the ozonide of phenylcyclopentene by treating it with water. However, the yield of acid was only slightly greater than the yield obtained when the ozonide was treated with zinc in the presence of acetic acid.

γ-Bromo-γ-benzoylbutyric Acid.—To a suspension of 3.8 g. of γ-benzoylbutyric acid in 100 cc. of carbon tetrachloride, bromine was added drop by drop, with stirring, until a bromine color persisted in the solution. During the course of the reaction the γ-benzoylbutyric acid, which was only slightly soluble in carbon tetrachloride, went entirely into solution. The solvent was removed by evaporation under reduced pressure. The brown solid remaining was recrystallized from carbon tetrachloride. The bromo acid was found to melt at 97–98°; the yield was 80% of the theoretical amount.

Anal. Calcd. for $C_{11}H_{11}O_3Br$: Br, 29.5. Found: Br, 29.8.

γ-Benzoyl-γ-butyrolactone.—A mixture of 2.7 g. of γ-bromo-γ-benzoylbutyric acid and 75 cc. of water was boiled until the acid which at first formed an oily layer on the bottom of the flask had completely disappeared. When the solution was cooled a yellow solid separated. The solid was removed by filtration and was recrystallized first from water and then from an ethyl acetate–petroleum ether mixture. The colorless crystalline lactone was found to melt at 78–79°. The yield was 84% of the theoretical amount.

The lactone was also obtained by heating 2.8 g. of γ-bromo-γ-benzoylbutyric acid with 50 cc. of a 10% solution of sodium hydroxide for fifteen minutes. After the reaction mixture was acidified with dilute hydrochloric acid and cooled, the lactone was separated by filtration and then purified as described above. Practically the same yield of the lactone was obtained.

In attempts to prepare the benzoate of γ-hydroxy-γ-benzoylbutyric acid nearly quantitative yields of the lactone were obtained. The reaction was carried out in the following manner. To 2.7 g. of γ-bromo-γ-benzoylbutyric acid suspended in 250 cc. of dry ether was added 2.8 g. of silver benzoate. The mixture was heated under reflux for eight hours. The solution was filtered and the crude lactone was obtained after the ether had been distilled from the filtrate. The crude lactone was then put into a beaker which was set on a steam-bath and heated for one hour in order to remove the benzoic acid by sublimation. The lactone was finally purified by recrystallization as indicated above.

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.5; H, 5.3. Found: C, 69.4; H, 5.4.

Summary

γ-Benzoyl-γ-butyrolactone and α-hydroxy-δ-benzoylvaleric acid have been synthesized. The latter has been identified with the end-product obtained by degradation of the compound obtained by the ring closure of 1,4-dibromo-1,4-dibenzoylbutane. This result confirms the identification of this compound as 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran.

URBANA, ILL. RECEIVED OCTOBER 16, 1933

[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS, U. S. DEPARTMENT OF AGRICULTURE]

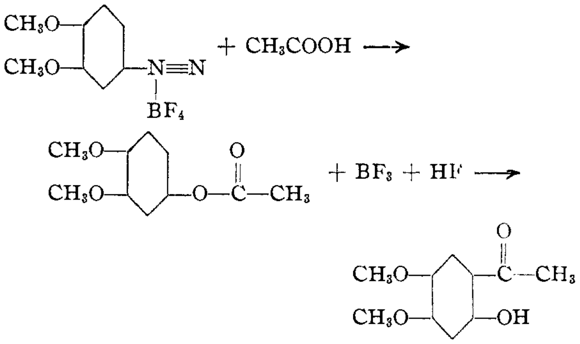
The Action of Acetic Acid on 3,4-Dimethoxyphenyldiazonium Borofluoride

BY L. E. SMITH AND H. L. HALLER

It has been shown recently[1] that acetic acid interacts with *m*-chlorophenyldiazonium borofluoride to give *m*-chlorophenyl acetate in a yield of about 50%. As the acetate is readily saponified to the phenol, the method appeared to be useful for the preparation of phenols when the normal decomposition of the diazo compound in water does not take place readily. Accordingly, the reaction suggested itself for the preparation of 1-hydroxy-3,4-dimethoxybenzene, a degradation product of rotenone and related substances, that is obtained only in poor yield through the usual diazo reaction on veratrylamine.

When this reaction was carried out, instead of yielding the expected acetate of 1-hydroxy-3,4-dimethoxybenzene, it yielded a product of the same empirical formula as the desired acetate, but soluble in alkali. This product contained two methoxyl groups, yielded an oxime and a semicarbazone, and with dimethyl sulfate and sodium hydroxide it was methylated to give an alkali-insoluble product. On oxidation with an aqueous solution of potassium permanganate the methylated product gave a keto acid, which on treatment with hydrogen peroxide yielded asaronic acid.

These reactions identified the original compound as a hydroxydimethoxyacetophenone, and its melting point and the melting points of its derivatives showed it to be identical with 2-hydroxy-4,5-dimethoxyacetophenone. The formation of this substance can be accounted for by the assumption that the acetate which is first formed is rearranged by the boron fluoride produced in the reaction. The exact mechanism of the reaction is not known, but the following is suggested.



Boron fluoride has been shown to rearrange alkyl phenyl ethers to the isomeric nuclei substituted phenols,[2] but the writers found no record of boron fluoride producing a wandering of an acyl group. However, the wandering of an acyl group under the influence of aluminum chloride is well known. The solid product obtained was homogeneous, and there was no evidence that a methyl group had migrated.

In addition to the 2-hydroxy-4,5-dimethoxyacetophenone, there was obtained a small quantity of a fluorine compound which contained two methoxyl groups. It is probably 3,4-dimethoxyfluorobenzene.

Experimental Part

Veratrylamine.—Veratrol was nitrated by the method of Cardwell and Robinson.[3] The yield was 99% of the theoretical. The nitroveratrol was suspended in ethyl alcohol at 50° and reduced with hydrogen, platinum oxide being used as a catalyst. The reduction proceeded rapidly with the evolution of sufficient heat to keep the solution warm. When the absorption of hydrogen had ceased, the solution was filtered from the catalyst into alcohol containing the theoretical amount of hydrochloric acid. The alcoholic solution was then concentrated to a small volume under reduced pressure, ether was added, and the

---

(1) Haller and Schaffer, THIS JOURNAL, **55**, 4954 (1933).

(2) Sowa, Hinton and Nieuwland, *ibid.*, **54**, 2019 (1932); *ibid.*, **55**, 3402 (1933).

(3) Cardwell and Robinson, *J. Chem. Soc.*, **107**, 257 (1915).