means of 2% potassium hydroxide in 70% methanol (refluxing) gave 50% yields of the hydroxyfuranone (III). The action of sodium methylate (at 25°), however, produced an unidentified compound melting at 119–121°.

The action of methanolic hydrogen chloride (twelve hours at room temperature) gave only 4-benzoyl-2,5-diphenyl-2-methoxyfuranone-3 (VIII).

Summary

4-Benzoyl-2,5-diphenyl-2-hydroxyfuranone-3 has been synthesized by carbon benzoylation of 1,4-diphenylbutane-1,2,4-trione sodium enolate. It is strongly acidic and remarkably stable toward alkali. The formation, interconversion and hydrolysis of the methyl and ethyl ethers and the acetyl and benzoyl derivatives, as well as the preparation and reactions of the chloride, have been described. The reactions of the silver salt take place in the sense of the hydroxyfuranone rather than the open-chain triketone enolate form.

Reaction with *o*-phenylenediamine gave an easily hydrolyzable quinoxalyl-β-diketone. The action of diazomethane produces an open-chain enol ether. Bromination gives the open-chain bromotetraketone.

The question of structure and the triketone enol–hydroxyfuranone tautomerism was discussed. The evidence was regarded as favoring the hydroxyfuranone formulation.

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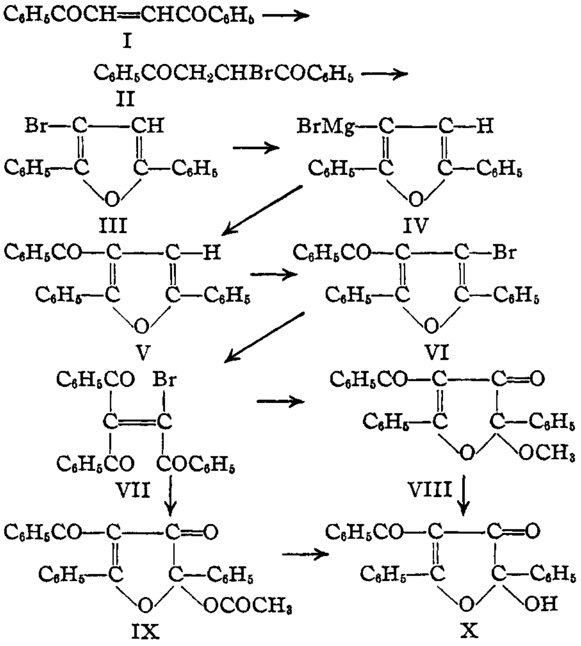
[Contribution from the Cobb Chemical Laboratory, University of Virginia]

The Synthesis of 4-Benzoyl-2,5-diphenyl-2-hydroxyfuranone-3 through Benzoyldiphenylfuran and Bromotribenzoylethylene

By Robert E. Lutz and James M. Smith, Jr.[1]

This synthesis by a second path[2] was carried out in order to demonstrate independently the nature of the benzoyl group attachment. The compounds and reactions involved are of interest in connection with the investigation now in progress on the unsaturated triketones and related substances.

The new synthesis started with dibenzoylethylene (I) which was converted through the bromodiketone (II) into the bromofuran (III). Diphenylfurylmagnesium bromide (IV) was then made according to the method described by Woodward,[3] and this, when treated with benzoic anhydride, gave β-benzoyldiphenylfuran (V, known[4]). Bromination in carbon tetrachloride gave the bromofuran (VI, also known[4]), and oxidation by nitric acid produced the corresponding unsaturated 1,4-diketone (VII, new). The latter compound was converted by methanolic hydrogen chloride into the methyl ether of the hydroxyfuranone (VIII) and by acetic anhydride and sulfuric acid into the acetate (IX). Analogy is to be found for these two reactions in the similar transformations of dibenzoylchloroethylene into 2,5-diphenyl-2-ethoxyfuranone-3[5] and of bromodibenzoylmethylethylene into 2,5-diphenyl-4-methyl-2-acetoxyfuranone-3.[6] These reactions evidently involve 1,4-addition of the reagent followed by hydrolysis and elimination of the hydrogen bromide, and cyclization. The two



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[1] Du Pont Service Fellow, University of Virginia (1936–1939); present location, Calco Chemical Division, American Cyanamid Company, Bound Brook, New Jersey.

[2] *Cf.* the preceding paper; Lutz, Smith and Stuart, This Journal, **63**, 1143 (1941).

[3] Woodward, Dissertation, Harvard University, 1937.

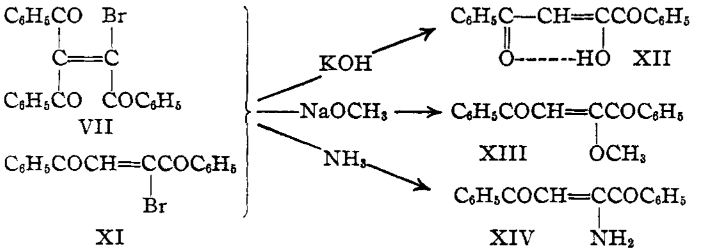
[4] Kohler and Jones, This Journal, **41**, 1249 (1919).

[5] Lutz, Wilder and Parrish, *ibid.*, **56**, 1980 (1934).

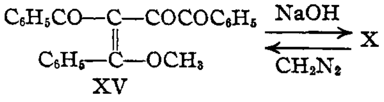
[6] Lutz and McGinn, unpublished results obtained subsequent to this research.

products (VIII and IX) were readily hydrolyzed to the hydroxyfuranone (IX).

It is noteworthy that the alkaline reagents, alcoholic potassium hydroxide, sodium methoxide and alcoholic ammonia, reacted with bromotribenzoylethylene (VII) but did not give the expected 4-benzoylhydroxyfuranone (X) which, once it is formed, is stable under these various conditions. Instead, there was produced, respectively, diphenylbutanetrione enol (XII), the enol ether, XIII, and the ammono analog, XIV. The reactions involved in each case elimination of a benzoyl group, and except for cleavage they are strictly comparable with the analogous reactions of bromodibenzoylethylene (XI) where the same products were obtained under similar conditions. The facility of cleavage is of the same order as that of β-di- and triketones which cannot cyclize to stable products, *e. g.*, acetyldibenzoylmethane,[7] tribenzoylmethane[8] and dibenzoylphenylmethane.[9]



In connection with the cleavage during hydrolysis of bromotribenzoylethylene (VII) attention should be called to the alkali hydrolysis of the supposed enol ether, XV,[2] which took place under comparable conditions *without* cleavage. Perhaps the loss of the benzoyl group in the case of bromotribenzoylethylene is a direct β-diketone cleavage and occurred first; or possibly there exists some difference in mechanism with cyclization in the one case competing successfully with hydrolytic fission.


XV

The reduction of bromotribenzoylethylene (VII) by catalytic hydrogen produced directly benzoyldiphenylfuran (V). The facile closure of the furan ring in this case was not unexpected in view of the probable intermediate formation of a β-diketone enol system in the presence of an unhindered γ-carbonyl group.

Experimental[10]

Bromodibenzoylethane (II) was prepared directly from dibenzoylethylene (I) by the action of hydrogen bromide in concd. acetic acid solution, the product crystallizing directly from this solvent in sufficient purity for immediate use.

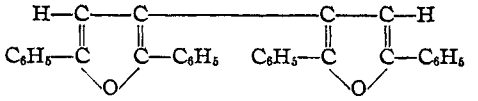
3-Bromo-2,5-diphenylfuran (III) was made by suspending the bromodiketone (II) in acetic anhydride, adding a few drops of sulfuric acid and allowing the mixture to stand for twenty minutes. Hydrolysis in ice and crystallization at least twice from ethanol gave a product sufficiently pure for preparation of the Grignard reagent.

Attempts to carry out a Friedel–Crafts reaction on this compound in the hope of substituting the benzoyl group directly into the remaining β-position failed.

2,5-Diphenyl-3-furylmagnesium bromide (IV) was prepared according to the directions of Woodward[3] with the following precautions: the bromodiphenylfuran was carefully purified, the materials and apparatus were thoroughly dried, and methylmagnesium iodide was used to complete the drying of the ether.

In many of the subsequent reactions, the difficultly soluble 3,3'-bis-2,5-diphenylfuran (XVI) was obtained in varying amounts and separated by its slight solubility in methanol. It was identified by mixture melting point with an authentic sample prepared from the dimolecular reduction product of dibenzoylethylene.[11] This product evidently arises from coupling in the formation of the Grignard reagent.[12]

As a check on the quality of the Grignard reagent obtained, a rapid stream of dry carbon dioxide was passed through a solution prepared from 5 g. of the bromofuran and 0.5 g. of magnesium in ether at 5°. Upon hydrolysis, 3.5 g. of 2,5-diphenyl-3-furoic acid was obtained (m. p. 219°; 80%).


XVI

3-Benzoyl-2,5-diphenylfuran (V).—The Grignard reagent was prepared from 19 g. of bromodiphenylfuran (III) in 400 cc. of dry ether. This solution was added over a period of one and one-half hours to a solution of 16 g. of benzoic anhydride in 100 cc. of absolute ether, the mixture being kept at 0° and mechanically stirred. The mixture was allowed to come to room temperature overnight and was poured into ice. From the ether solution an oil was obtained which did not crystallize. This was dissolved in 75 cc. of methanol, treated with 200 cc. of 5% potassium hydroxide and the mixture boiled for thirty minutes. Upon cooling and extracting with ether, an oil was obtained which crystallized on standing. Recrystallization from methanol gave 13 g. of V (65%).

In similar experiments using benzoyl chloride or benzonitrile, the products were much harder to isolate and the

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[7] Meyer, *Monatsh.*, **28**, 1231 (1907).

[8] Meyer, *ibid.*, **28**, 1211 (1907).

[9] Prinz, *J. prakt. Chem.*, **24**, 353 (1881).

[10] All melting points are corrected. We are indebted to Mrs. James A. L. Mathers for several of the microanalyses.

[11] Lutz and Palmer, THIS JOURNAL, **57**, 1947, 1953 (1935).

[12] *Cf.* Marshall, *J. Chem. Soc.*, **107**, 509 (1915).

yields were inferior (32% in the former case and very small in the latter).

Upon purification from methanol, the compound was obtained as rosets of yellow needles melting at 76–77°. It was identical in properties with the compound described by Kohler and Jones[4] which was prepared in an entirely different manner and which melted at 77°. It gave an oxime melting at 173–176° (K. and J.[4] reported 174°).

Anal. Calcd. for $C_{23}H_{16}O_2$: C, 85.2; H, 5.0. Found: C, 84.84; H, 4.9.

Attempts to oxidize V with concd. nitric and acetic acid mixtures at 25, 50, and 75° gave only non-crystalline products. The *semicarbazone* was prepared from 0.2 g. of V in the usual way in methanol (refluxing for two hours). Feathery colorless needles were obtained (0.23 g.) and crystallized from ethanol; melting point 225°.

Anal. Calcd. for $C_{24}H_{19}O_2N_3$: C, 75.6; H, 5.0. Found: C, 75.3; H, 5.2.

3-Benzoyl-4-bromo-2,5-diphenylfuran (VI).—Attempts to prepare this compound by the directions of Kohler and Jones[4] were unsuccessful. It was obtained in 60% yield by treatment of 3 g. of the benzoyldiphenylfuran (V) at *room temperature (forty-eight hours)* in carbon tetrachloride with 1.5 g. of bromine. The oily product was finally induced to crystallize (yield 2.6 g.) and was purified from methanol; melting point 119.5–120° (K. and J.[4] reported the melting point 120°). This bromo derivative was obtained also by treatment of V with an excess of phosphorus pentabromide at 25° (one hour).

Bromotribenzoylethylene (VII).—A mixture of 2 cc. of concd. nitric and 5 cc. of concd. acetic acids was added to a solution of 1.6 g. of VI in 15 cc. of concd. acetic acid, both solutions being preheated to 50°. The temperature rose to 52° with evolution of oxides of nitrogen and was maintained at 50° for one hour. Dilution with water precipitated a gum which crystallized from methanol; yield 0.9 g. or 54%. Upon repeated crystallization from ethanol, it was obtained as colorless prisms melting at 101°.

Anal. Calcd. for $C_{23}H_{15}O_3Br$: C, 66.0; H, 3.6. Found: C, 66.2; H, 3.7.

Reduction of 0.6 g. in 40 cc. of ethanol by means of hydrogen and 0.4 g. of palladium–barium sulfate catalyst involved absorption of two molecules. Upon filtering and evaporating, an oil was obtained which upon standing in methanol slowly deposited crystals of benzoyldiphenylfuran (V) which was identified by mixture melting point; yield 0.2 g. (42%). Reduction with zinc dust and concd. acetic acid at 25 or 50° gave resinous materials and a smaller amount of solid of melting point 167–169° which has not yet been investigated.

Conversion into Benzoyldiphenylhydroxyfuranone was accomplished in two ways as follows: (a) A solution of 0.1 g. of VII in 10 cc. of saturated methanolic hydrogen chloride was allowed to stand for forty-eight hours and evaporated at room temperature. The residue was nearly pure benzoyldiphenylmethoxyfuranone (VIII) which was purified by crystallization from methanol and identified; yield 0.09 g. (practically quantitative). This compound has already been hydrolyzed[2] to the hydroxyfuranone (X).

(b) A suspension of 0.2 g. of VII in 5 cc. of acetic anhydride and one drop of concd. sulfuric acid was allowed to stand at 25° for thirty minutes. Upon hydrolysis in 100 cc. of water and extraction of the product by means of ether, an oil was obtained which crystallized from a ligroin–ethyl acetate mixture; yield 0.14 g. (73%). This was identified by mixture melting point as nearly pure acetoxybenzoyldiphenylfuranone (IX) which has already been hydrolyzed[2] to the hydroxyfuranone (X).

The Action of Alkaline Reagents.—(a) The action of refluxing 2% potassium hydroxide in 70% methanol (fifteen minutes) converted VII into diphenylbutanetrione enol (XII) *in good yield.*

(b) When VII was treated with an excess of sodium methylate in methanol at 25° for two hours, dibenzoylmethoxyethylene (XIII) was obtained in almost quantitative yield and identified.

(c) A solution of 0.1 g. of VII in 3 cc. of saturated ammoniacal methanol was allowed to stand for two hours at room temperature, and on cooling deposited 0.6 g. (95%) of aminodibenzoylethylene (XIV) which was identified by mixture melting point with an authentic sample.

Summary

The synthesis of 4-benzoyl-2,5-diphenyl-2-hydroxyfuranone-3 was carried out through diphenylfurylmagnesium bromide, benzoyldiphenylfuran and bromotribenzoylethylene. The latter compound is converted into the methoxy and acetoxyfuranones by means of, respectively, methanolic hydrogen chloride, and acetic anhydride and concd. sulfuric acid.

Facile cleavage occurs in the alkaline hydrolysis of bromotribenzoylethylene. Reduction produces benzoyldiphenylfuran.

Charlottesville, Virginia Received January 23, 1941