data presented add both to the knowledge of naturally occurring pigments, and of substances with a quinoid structure as a group.

St. Louis, Missouri Received June 9, 1938

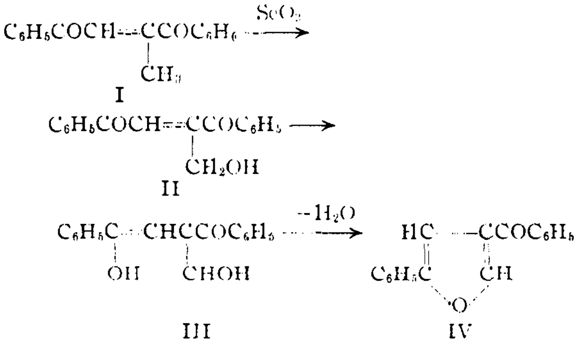
[Contribution from the Chemical Laboratory of the University of Illinois]

2-Phenyl-4-benzoylfuran

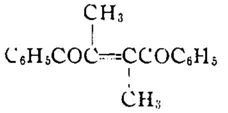
By Reynold C. Fuson, C. L. Fleming and Robert Johnson

Very few β-keto furans are known and of these none has an unsubstituted α-position. 2-Phenyl-4-benzoylfuran (IV) is, therefore, unique. In the study of the application of the principle of vinylogy to ketones we chanced to prepare this furan and noted that its properties reflected its unusual structure. This observation led us to examine these properties in some detail.

The furan was made by treating 1,2-dibenzoyl-1-propene (I) with selenium dioxide. Since the diketone is a vinylog of acetophenone it was expected that the methyl group would be attacked. Evidently this group is oxidized and the furan is formed by rearrangement and subsequent loss of water. Of especial interest in this connection is the observation that only one-half mole of selenium dioxide is required to convert one mole of the diketone (I) to the furan (IV). This corresponds to the amount of oxidation necessary to form the hydroxy compound (II). The latter could rearrange to the dienol (III) by a 1,5- or a double 1,3-shift. The dienol would be expected to lose water to form the furan.

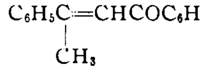


This mechanism suggests that the method might be general for ketones of the type $RCOC{=}C{-}CH_3$. To test this idea we subjected 2,3-dibenzoyl-2-butene (V), dypnone (VI) and crotonophenone (VII) to a similar treatment. Only dypnone yielded a furan; the other two ketones were recovered unchanged even after long treatment with the oxidizing agent. This indicates that this method of preparing furans is highly specific. It should be mentioned that 2,4-diphenylfuran (VIII), the product obtained from dypnone, had been prepared in low yields by the oxidation of dypnone with nitrobenzene.[1]



V

$C_6H_5COC(CH_3){=}C(CH_3)COC_6H_5$

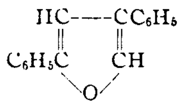


VI

$C_6H_5C(CH_3){=}CHCOC_6H_5$

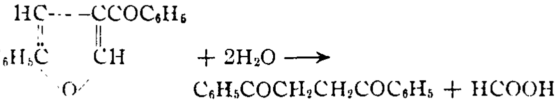
$C_6H_5COCH{=}CHCH_3$

VII

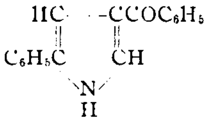


VIII

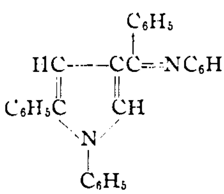
The most striking property of 2-phenyl-4-benzoylfuran is the ease with which it reacts with alkalies, ammonia or aniline. This appears less extraordinary if we consider that the compound is vinylogous with benzoic esters and might, therefore, be expected to be sensitive to hydrolytic and ammonolytic agents. Aqueous alkalies hydrolyze it rapidly to 1,2-dibenzoylethane and formic acid



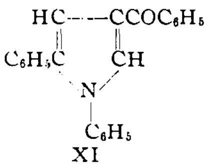
Ammonia and aniline convert the furan, respectively, into the pyrrole (IX) and the anil (X) of the expected phenylpyrrole.



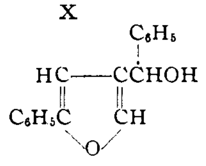
IX



X



XI



XII

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[1] Engler and Dengler, *Ber.*, **26**, 1446 (1893); *cf.* Delacre, *Bull. soc. roy. Belg.*, [3] **26**, 534 (1893).

Hydrolysis transforms the latter into the N-phenylpyrrole (XI) and aniline. It is of interest to note that the benzoylpyrrole (IX) does not show the sensitiveness to alkalies that characterizes the benzoylfuran (IV).

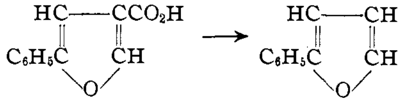
The furan was remarkably stable to acids. Long treatment with hot alcoholic hydrochloric acid partially transformed it into a high-melting derivative which appeared to be trimolecular. Its structure was not investigated further.

The behavior of the benzoylfuran under alkaline and acidic conditions is in distinct contrast with the usual reactions of the furan nucleus. In general this nucleus is characterized by stability to alkalies and extreme sensitiveness to acids, whereas the converse is true of the present furan. However, this is in harmony with the view already mentioned that β-keto furans are vinylogs of esters.

A number of reactions were carried out which affected only the carbonyl group. Oximes were prepared of the benzoylfuran (IV), the pyrrole (IX) and the N-phenylpyrrole (XI). Reduction of the furan gave a carbinol (XII) which was characterized by the formation of a benzoate and a *p*-nitrobenzoate. Attempts to effect differential oxidation were unavailing. Sodium chlorate in the presence of vanadium pentoxide gave only benzoic acid. Ozonolysis led to a similar result.

Confirmation of the structure of the benzoylfuran (IV) was obtained by degrading it to 2-phenylfuran (XIV). The furan formed an oxime which underwent the Beckmann rearrangement to give the corresponding anilide. The latter was hydrolyzed to 2-phenyl-4-furoic acid (XIII) which in turn was converted to 2-phenylfuran (XIV) by heating.

IV ⟶ oxime ⟶ anilide ⟶



XIII XIV

In contrast to the benzoylfuran (IV) the furoic acid (XIII) was very resistant to the attack of reagents. The ring was not attacked by alkalies or ammonia and decarboxylation could be effected only with difficulty.

Experimental

1,2-Dibenzoyl-1-propene (I).—This compound was prepared from mesaconyl chloride and benzene by a modification of the method described by Lutz and Taylor.[2] The following is a typical procedure. Twenty-five grams of mesaconyl chloride, prepared by the method of Meyer,[3] was added, with stirring, to an ice-cold suspension of 45 g. of aluminum chloride in 150 cc. of benzene. Fifteen minutes was required for the addition of the acid chloride. Stirring was continued for fifteen minutes after completion of the addition; the mixture was cooled in an ice-bath during the entire reaction period.

The reaction mixture was then hydrolyzed and worked up in the usual way. The solution was concentrated and cooled; a yellow solid separated and was collected on a filter. Two crystallizations from alcohol gave 32.0 g. of 1,2-dibenzoyl-1-propene; m. p. 52.0–52.5°. The yield was 85% of the theoretical amount. It was found necessary to work up the reaction mixture as rapidly as possible after hydrolysis. If this was not done the product was contaminated with a green oil which greatly retarded the separation of a crystalline product.

2-Phenyl-4-benzoylfuran (IV).—The oxidation was carried out in the usual way, using 60 cc. of dioxane, 2 cc. of water, 5.6 g. (0.05 mole) of selenium dioxide and 25.0 g. (0.10 mole) of the diketone. After eight hours the selenium was collected on a filter and washed with hot dioxane. The filtrate was poured into water; the brown solid which separated was collected on a filter and air dried. After crystallization from ether there was obtained 15.5 g. of 2-phenyl-4-benzoylfuran; the yield was 63% of the theoretical amount.

Anal. Calcd. for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87; mol. wt., 248. Found: C, 82.69, 82.31; H, 4.96, 5.15; mol. wt., 249, 254.

The furan is sparingly soluble in ether, from which it separates as colorless needles which melt at 113.7–114.0°. It is moderately soluble in alcohol and glacial acetic acid. It reduces a potassium permanganate solution readily and decolorizes a carbon tetrachloride solution of bromine with the evolution of hydrogen bromide.

Dypnone.—This ketone was made by the method of Calloway and Green.[4] The oxidation of 22.3 g. (0.10 mole) of dypnone with 5.6 g. (0.05 mole) of selenium dioxide was carried out in the usual way. No crystalline material could be isolated from the tarry product and so it was distilled *in vacuo*. The 2,4-diphenylfuran (VIII) distilled at about 200° under 3 mm. pressure and solidified in the side-arm. After two crystallizations from alcohol there was obtained 2.3 g. of colorless plates; m. p. 110.7–111.0°. A solution of the pyran in concentrated sulfuric acid exhibited an intense violet fluorescence; this was reported also by Engler and Dengler.[1] The furan changed on standing, in the solid state or in solution, to an insoluble colorless powder which did not melt below 250°; this change was also noted by Delacre.[1]

Crotonophenone and 2,3-Dibenzoyl-2-butene.—Each of these compounds was recovered unchanged after long treatment with selenium dioxide.

Reactions of 2-Phenyl-4-benzoylfuran

Cleavage with Alkali.—A solution of 2.5 g. of the furan, 75 cc. of alcohol and 30 cc. of a 10% sodium hydroxide solution was heated under reflux for forty-five minutes. The resulting mixture was steam distilled; no product

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[2] Lutz and Taylor, THIS JOURNAL, **55**, 1177 (1933).

[3] Meyer, *Monatsh.*, **22**, 423 (1901).

[4] Calloway and Green, THIS JOURNAL, **59**, 810 (1937).

other than alcohol was found in the distillate. The residue was acidified with phosphoric acid and again steam-distilled; the clear distillate was acidic.

This distillate was neutralized with sodium hydroxide and evaporated to dryness. An aqueous solution of this salt reduced a solution of potassium permanganate immediately. A portion of the dry salt was heated with *p*-bromoaniline; after crystallization from dilute alcohol the product melted at 115.8–116.8°. A mixture of the product with an authentic specimen of *p*-bromoformanilide also melted at 115.8–116.8°.

The solid residue which remained in the flask after the steam distillation was collected on a filter and recrystallized from alcohol. There was thus obtained 0.7 g. of colorless needles; m. p. 145.2–146.2°. A mixture of this product with an authentic specimen of 1,2-dibenzoylethane also melted at 145.2–146.2°.

The same products were formed when the furan was treated with potassium carbonate under similar conditions.

Reaction with Hydrochloric Acid.—A solution of 1.0 g. of the furan, 20 cc. of concentrated hydrochloric acid and 50 cc. of alcohol was heated under reflux for eighty hours. The solution was diluted with water and cooled; a solid product separated. This material was collected on a filter and purified by recrystallization from alcohol. A portion of the product was insoluble in boiling alcohol and was removed. The solid which separated when the filtrate was cooled was isolated by filtration; there was obtained in this way 0.5 g. of unchanged starting material.

The insoluble product separated above was purified by several recrystallizations from aqueous acetone; it becomes brown at 211.5° and melts with decomposition at 214.8–215.8°.

Anal. Calcd. for $C_{51}H_{34}O_5$: C, 84.28; H, 4.72; mol. wt., 727. Found: C, 84.24, 84.10; H, 4.73, 4.65; mol. wt. (Rast), 686.

The compound separates from dilute acetone as colorless fluffy needles. It is insoluble in dilute acids and bases and forms a green solution in concentrated sulfuric acid. It does not contain chlorine.

The same product was formed by treating the furan with a methyl alcoholic solution of dry hydrogen chloride.

Reaction with Ammonium Hydroxide.—A mixture of 1.0 g. of the furan, 5 cc. of concentrated ammonium hydroxide and 10 cc. of alcohol was heated at 130–140° for eighteen hours. The reaction was carried out in a stainless steel bomb. A solid product was isolated from the reaction mixture by filtration and washed with water. This material was then extracted several times with boiling alcohol; the extract was discarded. After two crystallizations of the residue from dilute acetone there was obtained 0.5 g. of 2-phenyl-4-benzoylpyrrole (IX) in fine yellow needles which melted at 213.7–215.5°.

Anal. Calcd. for $C_{17}H_{13}ON$: C, 82.57; H, 5.30; N, 5.66; mol. wt., 247. Found: C, 82.73; H, 5.51; N, 5.42, 5.59; mol. wt. (Rast), 256.

The pyrrole is sparingly soluble in alcohol and readily soluble in ether and benzene. It is insoluble in dilute acids and bases; it forms an orange solution in concentrated sulfuric acid. It reduces a potassium permanganate solution readily and decolorizes a bromine solution with the evolution of hydrogen bromide. It was recovered unchanged after treatment with sodium hydroxide under conditions similar to those used in the cleavage of the parent furan. It forms an **oxime** which separates from dilute alcohol as fine, faintly pink needles which soften at 171° and melt with decomposition at 188.5–191.5°.

Anal. Calcd. for $C_{17}H_{14}ON_2$: N, 10.68. Found: N, 10.89.

Reaction with Aniline.—A solution of 5.0 g. of the furan in 50 cc. of dry aniline was heated under reflux for seventy-two hours. The solution was then cooled and concentrated under a pressure of 3 mm.; absolute alcohol was added to the residue. The solid product which separated was collected on a filter, washed with absolute alcohol and recrystallized from a mixture of dry benzene and petroleum ether (b. p. 60–90°). There was thus obtained 2.3 g. of a solid in the form of clumps of colorless needles. After further crystallization the anil (X) melted at 230.5–231.0°.

Anal. Calcd. for $C_{29}H_{22}N_2$: C, 87.40; H, 5.57; N, 7.03. Found: C, 87.59; H, 5.61; N, 7.08.

The anil is readily soluble in benzene and moderately so in absolute alcohol. In contact with concentrated sulfuric acid it turns yellow but does not dissolve.

The hydrolysis of the anil was carried out by adding 20 cc. of dilute hydrochloric acid to a suspension of 1.5 g. of the anil in 75 cc. of alcohol. A yellow color appeared instantly and the mixture became slightly warm. The reaction mixture was allowed to stand at room temperature for forty-eight hours and then was diluted with water. The solid product was isolated by filtration, dried and recrystallized from ethyl acetate. There was obtained in this way 0.8 g. of 1,2-diphenyl-4-benzoylpyrrole (XI) which melted at 240.0–241.0°. Further crystallization did not alter the melting point.

Anal. Calcd. for $C_{23}H_{17}ON$: C, 85.42; H, 5.30; N, 4.33. Found: C, 85.68, 85.87; H, 5.58, 5.37; N, 4.53.

The pyrrole (XI) separates from ethyl acetate or from a benzene–petroleum ether (b. p. 60–90°) mixture as colorless silky needles. It is practically insoluble in alcohol, sparingly soluble in acetone, ether or ethyl acetate and moderately soluble in benzene. It forms a straw-yellow solution in concentrated sulfuric acid. The **oxime** of the pyrrole was prepared in the usual way; it separates from dilute alcohol as colorless needles which melt at 215.5–218.5°.

Anal. Calcd. for $C_{23}H_{18}ON_2$: N, 8.28. Found: N, 8.13.

Reduction to the Carbinol.—A solution of the furan in ethyl acetate was treated with hydrogen in the presence of a nickel catalyst.[5] The solid residue obtained by evaporating the solution to dryness was crystallized from alcohol. The **carbinol** was thus obtained as colorless needles which melted at 128.1–129.1°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.57; H, 5.64. Found: C, 81.82; H, 5.62.

The carbinol is readily soluble in ethyl acetate and in ether. It forms a wine-colored solution in concentrated sulfuric acid.

The benzoate, prepared in pyridine solution, separates from alcohol as colorless needles which melt at 123.1–124.1°.

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[5] Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.32; H, 5.12. Found: C, 81.11; H, 5.15.

The *p*-nitrobenzoate separates from alcohol as rosets of colorless needles which melt at 109.5–109.8°.

Anal. Calcd. for $C_{24}H_{17}O_5N$: N, 3.51. Found: N, 3.49.

Conversion to 2-Phenylfuran.—The oxime of 2-phenyl-4-benzoylfuran was prepared in absolute alcohol solution in the presence of pyridine. It is readily soluble in the common organic solvents and separates from dilute alcohol as colorless needles which melt at 149.0–149.4°.

Anal. Calcd. for $C_{17}H_{13}O_2N$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.70; H, 5.13; N, 5.46, 5.40.

The Beckmann rearrangement was carried out by adding phosphorus pentachloride to a solution of the oxime in absolute ether. After crystallization from alcohol with the aid of Norite the **anilide** of 2-phenyl-4-furoic acid was obtained as colorless plates which melted at 192.0–193.0°.

Anal. Calcd. for $C_{17}H_{13}O_2N$: N, 5.32. Found: N, 5.44.

The anilide was hydrolyzed with alcoholic potassium hydroxide; it was necessary to heat the solution under reflux for twenty-four hours to cause complete reaction. The aniline was separated by steam distillation and identified as 1-phenylazo-2-naphthol, m. p. 128–129°. The residue was treated with Norite and acidified. Crystallization from alcohol produced colorless needles of **2-phenyl-4-furoic acid** which melted at 208.0–209.0°.

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.25; H, 4.25; neut. equiv., 188. Found: C, 70.20; H, 4.49; neut. equiv., 191, 190.

The acid is readily soluble in acetone, moderately soluble in alcohol, sparingly soluble in benzene, xylene, ether and chloroform. It forms a yellow solution in concentrated sulfuric acid.

The acid was not converted to the corresponding pyrrole when treated with ammonium hydroxide in a bomb at 180°. Decarboxylation did not occur when it was subjected to the following treatments:

1. A mixture of the acid and copper bronze was heated to 250°.
2. A mixture of the acid and copper bronze in quinoline was heated at 225° in a stream of nitrogen.
3. A mixture of the acid and copper bronze in benzylmethylaniline was heated at 280° for one hour.
4. A mixture of the sodium salt of the acid and soda-lime was heated for two hours at 375° under a pressure of 10 mm.

The reaction was finally carried out by heating the acid overnight at 275° in a high-pressure bomb. The **2-phenylfuran** obtained in this way had the following properties: b. p. 107–108° (18 mm.); n^{20}_D 1.5968; d^{20}_4 1.083. These data are in agreement with those found for a sample prepared by the method described by Kondo and Suzuki.[6]

Summary

1,2-Dibenzoyl-1-propene is transformed into 2-phenyl-4-benzoylfuran by treatment with selenium dioxide. The furan is readily hydrolyzed by aqueous alkalies to give 1,2-dibenzoylethane and formic acid. Ammonia and aniline react to give the corresponding pyrroles. By a series of reactions the benzoylfuran was degraded to the known 2-phenylfuran.

[6] Kondo and Suzuki, *J. Pharm. Soc. Japan*, No. **544**, 501 (1927); *C. A.*, **21**, 3362 (1927).

URBANA, ILLINOIS RECEIVED MAY 31, 1938

NOTES

The Structure of Cholesteryl Chloride

BY ERNST BERGMANN

In work with cholesteryl chloride, as carried out in various laboratories and also in this Institute, certain conflicting evidence has accumulated with regard to its usual formula (I). The main point is the following one: while the two epimeric cholestyl chlorides react with sodium acetate under Walden inversion,[1] cholesteryl chloride has been found in our laboratory to give the same cholesteryl acetate which is obtained by direct acetylation of cholesterol.[2] Recently, Marker and co-workers[3] have reported that 7-oxocholesteryl chloride, the constitution of which follows from the characteristic absorption band at 270 mμ of α,β-unsaturated ketones[4] behaves "normally" toward sodium acetate, giving an acetate under configurational inversion. Besides that, Marker and his co-workers have pointed out that cholesteryl chloride reacts under much less drastic conditions than the other chlorides mentioned.[5]

Reactions of halogenides with acetate ions are

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[1] Marker and co-workers, THIS JOURNAL, **57**, 1755, 2358 (1935).

[2] That cholesterol and cholesteryl chloride have identical configuration, has been discussed in *Helv. Chim. Acta*, **20**, 590 (1937).

[3] Marker and co-workers, THIS JOURNAL, **59**, 619 (1937).

[4] Unpublished results from our laboratory (Miss F. Goldschmidt); compare for 7-oxocholesteryl acetate, Eckhardt, *Ber.*, **71**, 461 (1938).

[5] Compare Mauthner, *Chem. Central.*, **80**, II, 1537 (1909).