g., m.p. 123–125°. The base recrystallized readily from either aqueous alcohol or from ethyl acetate, but the m.p., though sharp, was not easily reproducible and fell in the range 120–130°. A characteristic picrolonate was obtained in aqueous alcohol with m.p. 243–244°.

Anal. Calcd. for $C_{21}H_{20}O_6N$: C, 52.50; H, 4.20. Found: C, 52.72; H, 4.34.

The same substance (identified by mixed m.p. of bases and picrolonates) was obtained from the riboside XI after refluxing with 5 *N* ethanolic hydrogen chloride followed by appropriate isolation.

1-**Benzylhypoxanthine** (**VIII**).—4(5)-Amino-5(4)-imidazole-N-benzylcarboxamide was converted to the intermediate formamido derivative by heating the amine (0.15 g.) in 98% formic acid (2 ml.) and acetic anhydride (0.5 ml.) for three hours in a water-bath, removing the reagents *in vacuo*, and crystallizing the residue by addition of water. There was obtained 0.14 g., m.p. 175–177°. The formamido compound was refluxed for 90 minutes in formamide (3 ml.). When the major portion of the solvent was removed *in vacuo*, the residual sirup crystallized, was thinned with water and filtered, yielding 69 mg. of product. Recrystallization from 95% ethanol had little effect on the m.p., 268–270°.

Anal. Calcd. for $C_{12}H_{10}N_4O$: C, 63.70; H, 4.46; N, 24.77. Found: C, 63.52; H, 4.73; N, 25.25.

The same base (mixed m.p.) was obtained from 1-benzylinosine (III) after refluxing one hour in 5 *N* ethanolic hydrogen chloride followed by appropriate isolation.

5-Amino-4-imidazolecarboxamide β-Ribofuranoside (II).—It is advisable to adhere to the following conditions closely or over-reduction will occur with considerable loss of material. A piece of metallic sodium (0.65 g.) was cut into small chips which were added all at once to liquid ammonia (100 ml.) at −60° in an apparatus which provided stirring and protection from moisture. After 15 minutes, 5-amino-4-imidazole-N-benzylcarboxamide riboside (1.0 g.) was added to the blue solution. Six minutes later, powdered ammonium chloride (1.0 g.) was introduced to discharge the blue color. After evaporation of the ammonia, the residue was desiccated *in vacuo* over concd. sulfuric acid to remove last traces of the solvent and finally dissolved in water (40 ml.) for chromatography. This purification was based on the isolation of this substance by Greenberg and Spilman.[3] One-half of the solution was applied to a column (3 × 34 cm.) of Dowex 50 (200–400 mesh, 4% cross-linked) ammonium form, which had been washed with water. Elution was continued with water. After an alkaline band[19] (first 200 ml.), the eluate became neutral and the product, detectable by the Bratton–Marshall test,[15] emerged in a sharp band of about 100-ml. volume. The column retained some starting material which could be eluted with 0.01 *N* ammonium hydroxide and recovered if desired (about 20%).

The chromatographic fractions containing aminoimidazolecarboxamide riboside from both halves of a reduction product were combined and taken to dryness. The residual glass eventually crystallized; 0.12–0.14 g. was obtained, a yield of about 20%, based on unrecovered N-benzylamide. The recrystallized nucleoside did not depress the m.p. of an authentic sample kindly provided by Dr. G. R. Greenberg[3]; in addition, the infrared spectra of the samples were identical.

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(19) Products of further reduction were apparently contained in this fraction. The presence of dihydro-imidazoles was suggested by a study of the ultraviolet absorption spectra to be described later.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

Preparation of a Substituted 1,2-Benzofluorenone: An Unusual Perkin Reaction[1a]

BY JOHN C. GODFREY[1b] AND RODERICK A. BARNES

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The preparation, properties and proof of structure of the δ-lactone of 3-hydroxy-4-(2′-carboxyphenyl)-1,2-benzofluorenone are described. A study of the mechanism of the reaction by which it is produced from phthalic anhydride and homophthalic acid is reported.

Discussion

The preparation of 2,2′-dicarboxydesoxybenzoin by the pyrolysis of phthalic anhydride and homophthalic acid in the presence of a catalytic amount of sodium acetate has been described by Ephraim,[2] but in these laboratories the yield was found not to exceed *ca.* 50% although a variety of catalyst ratios, temperatures and rates of heating were investigated. Furthermore, the product was invariably accompanied by a small amount of orange by-product which gave a deep red color to the solution obtained by the hydrolysis of the whole product with warm, dilute potassium hydroxide.

In the hope of obtaining an improved yield of uncontaminated product, the procedure employed by Buckles and Bremer[3] in the preparation of stilbene was applied to the present problem. When phthalic anhydride was condensed with homophthalic acid in the presence of acetic anhydride and triethylamine, no 2,2′-dicarboxydesoxybenzoin was obtained. The product which formed in good yield was bright orange needles, m.p. 250°. The structure I was assigned to this compound on the basis of the following evidence.

Elemental analyses were in excellent agreement with the empirical formula C_8H_4O. The compound was neutral, and its infrared spectrum exhibited carbonyl absorption at 5.75 and 5.89 μ. Its complex ultraviolet spectrum, λ_{max} 226 mμ (log ε 4.60), 267 (4.62), 320 (4.32) and 397 (3.60), suggested a polynuclear aromatic system. Compound I slowly dissolved on refluxing with dilute, aqueous potassium hydroxide, giving an intensely purple solution. Acidification of the hydrolysate precipitated red-orange prisms (II), which reverted to I above 170°. The infrared spectrum of II showed general, diffuse absorption in the 3 μ region characteristic of carboxylic acids and phenols, and a single, intense carbonyl band at 5.95 μ. The two expected carbonyl absorptions are undoubtedly superimposed. Potentiometric titration of II gave pK_1 6.75 and pK_2 9.75, and an equivalent weight of 187 (calcd. 183 for II). Comparison of the pK values with a large number of dicarboxylic acids and phenols[4]

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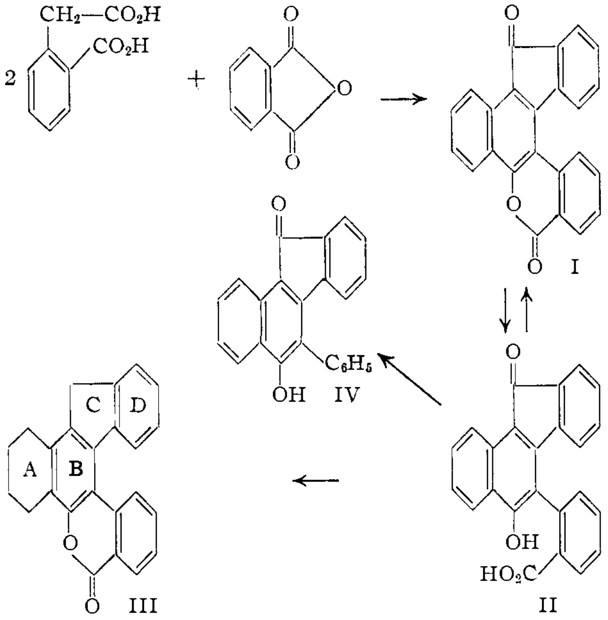
(1) (a) Presented before the Division of Organic Chemistry, Second Delaware Valley Regional Meeting, American Chemical Society, Philadelphia, Pa., February 5, 1958. (b) Smith, Kline and French Postdoctoral Fellow, 1955–1957.

(2) J. Ephraim, *Ber.*, **24**, 2820 (1891).

(3) R. E. Buckles and K. Bremer, *Org. Syntheses*, **33**, 70 (1953).

(4) N. A. Lange and G. M. Forker, "Handbook of Chemistry," 8th edition, Handbook Publishers, Inc., Sandusky, Ohio, 1952, pp. 1229–1233.

CHART I

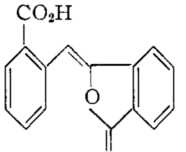


demonstrated unequivocally that pK_1 corresponds to a carboxylic acid, and that pK_2 corresponds to a phenol. Finally, elemental analyses of II yielded the empirical formula $C_{12}H_7O_2$.

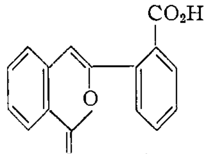
The structure of II, and therefore of the primary product I, was established beyond doubt by the conversion of II to the known 3-hydroxy-4-phenyl-1,2-benzofluorenone (IV).[5] Compound II was inert to the usual procedures for decarboxylation, but was converted to IV in satisfactory yield by refluxing the dipotassium salt with excess potassium hydroxide in dimethylsulfolane (b.p. 278°) for five hours. The properties of IV thus obtained were in agreement with those reported by Koelsch and Geissman,[5] and on bromination it yielded an X-bromo derivative identical in all respects with a sample kindly supplied by Professor Koelsch.

Additional evidence for the benzofluorenone structure was obtained by catalytic hydrogenation of II. The colorless, neutral product which resulted had, by analysis, the formula $C_{24}H_{18}O_2$, in agreement with structure III. The infrared spectrum showed no hydroxyl absorption, but had a single carbonyl band at 5.80 μ (δ-lactone). On refluxing with ethanolic potassium hydroxide, the neutral product slowly dissolved, and the material remaining after removal of the solvent was completely soluble in cold water, again indicating the presence of a lactone structure in III. The reduction of ring A is considered to be more likely than either B or D. Ring B is fully substituted, and addition of two molecules of hydrogen to ring D would lead to a vinyl naphthalene derivative, whereas the ultraviolet spectrum of III [λ_{max} 211 (log ϵ 4.43), 256 (4.24), 264 (4.22), 291 (3.98), 309 (4.01) and 330 (4.02)] is quite similar to that of ethyl fluorenone-1-carboxylate.[6]

The primary condensation product of phthalic anhydride and homophthalic acid must (after decarboxylation) be the γ-enol lactone of 2,2′-dicarboxydesoxybenzoin (V). Attempts to isolate V or the corresponding δ-lactone VI from the sodium acetate catalyzed Perkin reaction results in the isolation, in low yields, of impure δ-lactone VI (carbonyl absorption at 5.80 μ) and the spiro-γ,δ-bislactone of 2,2′-dicarboxydesoxybenzoin.[7] Attempts to condense VI or pure 2,2′-dicarboxydesoxybenzoin with homophthalic acid in acetic anhydride and triethylamine led only to recovery of starting materials and homophthalic anhydride. It may thus be concluded that neither of these compounds is an intermediate in the formation of I.



V



VI

A likely mechanism involving the condensation of homophthalic acid with the γ-lactone V (2′-carboxybenzalphthalide) was tested by attempting to condense benzalphthalide[8] with homophthalic acid under the same conditions as in the preparation of I. The expected product was the known compound IV. Partial rearrangement of benzalphthalide to 2-phenylindane-1,3-dione was the only reaction which occurred. It is therefore considered unlikely that the γ-lactone V gives rise to I by condensation with homophthalic acid.

Considering the facile rearrangement of benzalphthalide to 2-phenylindane-1,3-dione, the most likely mechanism for the formation of I is the rapid rearrangement of 2′-carboxybenzalphthalide (V) to 2′-carboxyphenylindane-1,3-dione followed by condensation with homophthalic acid and the necessary ring-closures to the benzofluorenone system. Rigorous proof of this mechanism waits upon the preparation of 2′-carboxyphenylindane-1,3-dione, a compound which has not been described.

Experimental[9]

2,2′-Dicarboxydesoxybenzoin.[2]—An intimately ground mixture of phthalic anhydride, 15.0 g., homophthalic acid,

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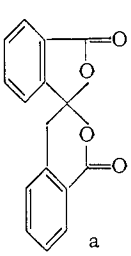
[5] C. F. Koelsch and T. A. Geissman, *J. Org. Chem.*, **3**, 480 (1938).

[6] R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, serial no. 326.

[7] S. Gabriel and E. Leupold, *Ber.*, **31**, 2646 (1898). We have determined that the colorless, neutral by-product, m.p. 255°, obtained during the fusion of phthalic anhydride and homophthalic acid with sodium acetate is actually the spiro-γ,δ-bislactone (a), as suggested by Gabriel and Leupold. Its infrared spectrum exhibits strong carbonyl bands at 5.61 and 5.76 μ, and it therefore cannot possess either the nine-membered cyclic anhydride structure (ref. 2) or the γ,γ-bislactone structure as claimed by P. Ruggli and R. E. Meyer (*Helv. Chim. Acta*, **5**, 28 (1922)).



a

[8] R. Weiss, J. R. Johnson and H. R. Snyder, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 61. In a total of four preparations, the product was obtained as long prisms or large, colorless plates, but both forms invariably melted sharply at 90–91°, rather than 100–101° as reported. The product was therefore thought to be "isobenzalphthalide" (3-phenylcoumarin) described by S. Gabriel (*Ber.*, **18**, 2433 (1885)). That our product actually was benzalphthalide was demonstrated by its infrared spectrum (λ_{max} 5.85–5.92 μ) and by its facile conversion to 2-phenylindane-1,3-dione (λ_{max} 5.72 and 5.84 μ). The rearrangement of benzalphthalide has been described by F. Nathanson, *ibid.*, **26**, 2576 (1893).

[9] Elemental analyses by G. Robertson, Florham Park, N. J.

15.0 g., and anhydrous sodium acetate, 1.5 g., was heated at 200–210° for 1 hour, when the evolution of gas was observed to cease. The cooled, orange mass was warmed with 100 ml. of 10% aqueous potassium hydroxide solution until it was almost completely dissolved, and the resulting deep red solution was filtered. The base-insoluble material was recrystallized from ethyl acetate, 1.6 g. (7%), m.p. 254–256°, and was found to be the spiro-γ,δ-bislactone of 2,2'-dicarboxydesoxybenzoin (see footnote 7). The red filtrate was acidified and filtered, and the orange product so obtained was purified by triturating with 75 ml. of boiling absolute ethanol, colorless crystals, 9.9 g. (42%); this substance changes crystal form at about 210° and melts 235–237°. The yield of the desired product was raised to 49% by refluxing the spiro-γ,δ-bislactone with potassium hydroxide in aqueous ethanol.

Lactone of 3-Hydroxy-4-(2'-carboxyphenyl)-1,2-benzofluorenone (I).—A mixture of 5.0 g. (0.034 mole) of phthalic anhydride, 5.0 g. (0.028 mole) of homophthalic acid and 10.5 ml. of triethylamine was warmed at 40–50° for 5 min., 50 ml. of acetic anhydride was added and the purple mixture was heated at 100° until evolution of carbon dioxide subsided and a voluminous orange precipitate formed. An additional 30 ml. of acetic anhydride was added and the mixture was refluxed for 0.5 hr. It was cooled thoroughly, filtered and washed with cold ethanol; orange needles, 3.8 g. (79%), m.p. 225–230°. Recrystallization from chloroform gave 3.1 g. (64%), m.p. 249–251°.

Anal. Calcd. for $C_{24}H_{12}O_3$: C, 82.75; H, 3.47. Found: C, 82.85, 82.60; H, 3.47, 3.52.

3-Hydroxy-4-(2'-carboxyphenyl)-1,2-benzofluorenone (II).—A mixture of 114 mg. of I, 4 potassium hydroxide pellets and 12 ml. of water was refluxed for 12 hours. The cooled solution was acidified with hydrochloric acid, filtered and the product was dissolved away from the silicic acid with ethanol. Removal of the solvent left a red residue which was purified by 5 reprecipitations from aqueous medium; the deep orange prisms thus obtained changed to needles above 170° and melted at 249–250°.

Anal. Calcd. for $C_{24}H_{14}O_4$: C, 78.68; H, 3.85; equiv. wt., 183. Found: C, 78.78; H, 4.02; equiv. wt., 186, 188; pK_1, 6.75; pK_2, 9.75.

The anilide of 3-hydroxy-4-(2'-carboxyphenyl)-1,2-benzofluorenone (II) was obtained by refluxing 51 mg. of II in 1 ml. of purified aniline under nitrogen for 5 hours. The mixture was dissolved in 20 ml. of ether and extracted with 6 *N* hydrochloric acid. The ether layer, which contained suspended orange solid, was then extracted with 4 × 10 ml. of 5% ammonium hydroxide, removing an acid which was deep purple in base. Filtration of the ether layer then yielded 27 mg. of I. The acid was precipitated with hydrochloric acid; 6 mg., m.p. 244–245°. It was recrystallized twice from ethanol–water, m.p. 244–245°. The infrared spectrum (Nujol) showed a broad band at 3.1–3.2 μ, and carbonyl absorptions at 5.89 and 6.12 μ.

Anal. Calcd. for $C_{30}H_{19}O_3N$: C, 81.62; H, 4.34. Found: C, 81.60; H, 4.70.

When 15 mg. of II was heated on a Kofler block, the transition from prisms to needles was complete at 235°. The infrared spectrum of the heated product confirmed its identity with I.

Tetrahydro-δ-lactone of 3-Hydroxy-4-(2'-carboxyphenyl)-1,2-benzofluorene (III).—A solution of 468 mg. (1.25 millimoles) of II in 85 ml. of ethanol was reduced at 22° and atmospheric pressure with hydrogen over 100 mg. of Adams catalyst. The originally red solution became colorless when two equivalents of hydrogen had been absorbed, and reduction ceased after 54 hours, at a total hydrogen uptake of 3 equivalents. Filtration from the catalyst, acidification with acetic acid and removal of solvent left a gray mass of soft crystals which was partly soluble in hot absolute ethanol. As the solution was boiled, more precipitate formed until a total of 250 mg. (55%) of small prisms was collected, m.p. 260–264°; after recrystallization several times from chloroform–ethanol, m.p. 271–272°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.21; H, 5.32.

3-Hydroxy-4-phenyl-1,2-benzofluorenone (IV).—A mixture of 0.7 g. of II, 1.0 g. of 85% potassium hydroxide and 25 ml. of dimethylsulfolane (b.p. 278°) contained in a 1.5-inch black iron pipe fitted with a cold finger was refluxed for 4.5 hours. The solution was poured into 400 ml. of water, made strongly basic with potassium hydroxide and extracted with 8 × 50 ml. of chloroform. The solution was then acidified and extracted with 5 × 50 ml. of chloroform. Extraction of the latter solution with 5×50 ml. of 5% sodium bicarbonate removed any carboxylic acid. Further extraction with 4 × 40 ml. of 10% potassium hydroxide removed the desired phenol which was recovered on acidification; 80 mg. (12%), m.p. 230–240°. It was treated with charcoal in benzene and then crystallized several times from benzene–hexane for analysis, m.p. 241.0–242.5°. The infrared spectrum (chloroform) showed hydroxyl absorption at 2.92 μ and a single carbonyl band at 5.94 μ. The ultraviolet and visible spectrum in acidified ethanol had λ_{max} 252 mμ (log ε 4.53), 260 (4.52), 313 (4.27), 339 (4.23), 385 (3.61) and 460 (3.42), while in strongly basic solution the values were shifted to λ_{max} 260.5 (4.67), 339 (4.53), 397 (3.68) and 524 (3.95).

Anal. Calcd. for $C_{23}H_{14}O_2$: C, 85.70; H, 4.38. Found: C, 85.48; H, 4.25.

X-Bromo-3-hydroxy-4-phenyl-1,2-benzofluorenone.—Twenty mg. of analytically pure IV was dissolved in 1.0 ml. of concd. sulfuric acid, giving a deep green solution, and 15–20 mg. of bromine in 0.1 ml. of glacial acetic acid was added. The mixture was stirred for 10 minutes, diluted to 8 ml. with water, and the orange crystals so obtained were recrystallized several times from benzene, m.p. 290–295°. A sample of authentic X-bromo derivative obtained from Dr. Koelsch melted at 295–299°, and the mixed melting point was 294–297°. The ultraviolet spectra of the samples were found to be identical in acidified ethanol; λ_{max} 256 mμ (log ε 4.53), 281 (4.63), 385 (3.57) and 455 (3.34); as well as in base, λ_{max} 262 (log ε 4.62), 340 (4.52), 397 (3.68) and 525 (3.97). Furthermore, the infrared spectra of the two samples were completely superimposable, with major absorption bands at 3.05 and 5.93 μ (Nujol).

Direct Preparation of 2-Phenylindane-1,3-dione.—A mixture of 1.5 g. of phthalic anhydride, 1.0 g. of phenylacetic acid and 4 ml. of triethylamine was warmed to 70° for 3 minutes, and 10 ml. of acetic anhydride was added. The mixture became red, and it was heated on the steam-bath until evolution of carbon dioxide ceased. The solvent was removed under vacuum and the residue was warmed at 90° with 100 ml. of water. Cooling precipitated yellow leaflets, m.p. 124–130°. Two recrystallizations from ethanol–water raised the melting point to 145–147° (lit.[9] m.p. 145°). The infrared spectrum in chloroform solution exhibited sharp carbonyl absorptions at 5.72 and 5.84 μ.

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