organic derivatives have been obtained in the course of the synthesis and are described.

New Haven, Connecticut

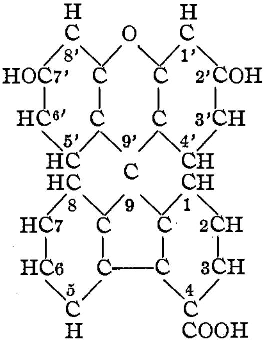
[Contribution from the Laboratory of Organic Chemistry of the University of Wisconsin]

THE CONDENSATION OF DIPHENIC ANHYDRIDE WITH RESORCINOL

By Fritz Bischoff and Homer Adkins

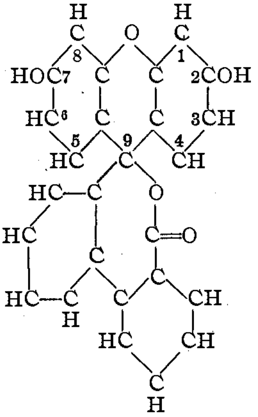
Received January 2, 1923

The compounds derived from diphenic anhydride and resorcinol as fluorescein is derived from phthalic anhydride and resorcinol have never been prepared. The possibility of their formation has been questioned because of the necessity of preventing the opening of a 7-membered ring. Graebe[1] attempted to condense diphenic anhydride with phenol and resorcinol but later discovered that he had used 9,10-diphenic-ketone-4-carboxylic acid (See Formula I).[2] The true condensation product of the anhydride (Formula II) has been obtained in this Laboratory, and its properties and some of its derivatives studied. The condensation of the ketone with resorcinol has also been carried out. The two condensation products are very similar in properties, but are not identical. Upon acetylation, the compound from the anhydride loses its alkali solubility because it can no longer tautomerize to the alkali-soluble form. Acetylation does not affect the alkali solubility of the compound from the ketone be-



I

2′,7′-Dihydroxy-*spiro* (9-fluorene-9′-xanthene)-4-carboxylic acid



II

9-lactone of *o*-[*o*-(2,7,9-trihydroxy-xanthenyl-)phenyl]benzoic acid

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[1] Graebe, *Ber.*, **13**, 1302 (1880).

[2] Graebe and Aubin, *Ann.*, **247**, 260 (1888).

cause the carboxyl group is free, even in the acetylated derivative. Two moles of resorcinol react quantitatively with one mole of diphenic anhydride when the temperature and amounts of condensing agent are properly adjusted. The resulting compound is fluorescent in alkaline solution, insoluble in acids and is itself a weaker acid than carbonic acid. The tetrabromo derivative corresponding to eosin was prepared. It is similar to eosin and has excellent dyeing properties. The acetylated derivative of the tetrabromo compound is also alkali-insoluble, as tautomerization is prevented. The metal content of the precipitated salts of the diphenic anhydride condensation products is greatly affected by the hydrogen-ion concentration of the solution of the salts. Baeyer[3] believed that the oxygen bridge in the xanthene ring of fluorescein opened up in strongly alkaline solution, though no experimental evidence was presented other than that the change of color under these circumstances could be accounted for. The sodium content of the condensation product of diphenic anhydride and resorcinol indicates that such a rupture of the ring does take place even in a rather weakly alkaline solution. This fact lends support to Baeyer's hypothesis as to the instability of fluorescence in strongly alkaline solutions.

Experimental Part

Phenanthraquinone.—The method described by Oyster and Adkins[4] was used. The oxidizing mixture should be cold before the hydrocarbon is added. After the completion of the oxidation it is feasible to filter the cold diluted solution on filter paper. The crude phenanthraquinone must be *thoroughly* dried before it is suspended in the ice-cold conc. sulfuric acid. A 15–20% solution of sodium or potassium bisulfite may be used instead of a concentrated solution of the salt. There must at all times be an excess of dichromate in the solution from which the pure phenanthraquinone is precipitated; otherwise the quinone is reduced. The presence of an excess of dichromate is easily observed by spotting out on filter paper. The yellow dichromate diffuses at a different rate than the green chromium sulfate; 100 g. of "80% phenanthrene" yielded 50 g. of phenanthraquinone; m. p., 202–204° (205–207° corr.).

Diphenic Acid.—The method of Schmitz[5] was used; 50 g. of phenanthraquinone was added to a cold solution of 200 g. of potassium dichromate, 300 g. of conc. sulfuric acid, 500 cc. of water, contained in a round-bottom flask attached to an air condenser. The mixture was heated very slowly for an hour to avoid oxidation to carbon dioxide and water. It was then heated at 105–110° for about 20 hours, with occasional agitation; yield, 85%; m. p., 228° (uncorr.).

Diphenic Anhydride.—The method of Graebe and Aubin[6] gave a yield of 92%; m. p., 219° (corr.).

9,10-Diphenyl-ketone-4-carboxylic Acid.[7]—Finely powdered diphenic acid was mixed with conc. sulfuric acid to form a thick paste and heated for 10 minutes at 130°.

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[3] Baeyer, *Ann.*, **183**, 22 (1873).

[4] Oyster and Adkins, THIS JOURNAL, **43**, 208 (1921).

[5] Schmitz, *Ann.*, **193**, 116 (1878).

[6] Ref. 2, p. 263. Ref. 4, p. 208.

[7] Graebe and Mensching, *Ber.*, **13**, 1302 (1880).

After complete solution had taken place the reaction mixture was poured into water, washed free from acid and dried at 100°. It was soluble in alkali, and after recrystallization from alcohol it melted at 217° (uncorr.).

Condensation of Diphenic Acid Anhydride and Resorcinol. Formation of 9-Lactone of *o*-(*o*-(2,7,9-Trihydroxy-xanthenyl)phenyl)-Benzoic Acid

Thirty g. of diphenic anhydride, 32 g. of resorcinol and 22.5 g. of fused zinc chloride were heated at 135–150° for 11 hours. When less zinc chloride is used, rather more complex products are formed. The cold, glassy, ruby-red product was ground and extracted with water. The main product (all but zinc oxide) was dissolved in cold caustic solution and precipitated with dil. hydrochloric acid. This process was repeated several times. The solutions of the soluble salts of the condensation product are yellowish-brown in color and have a green fluorescence. The compound is sticky and spongy. It is very soluble in alcohol, commercial ether, glacial acetic acid or amyl alcohol; it is insoluble, or almost so, in toluene, benzene, carbon tetrachloride, carbon disulfide, water, hydrochloric acid or pure ether. It retains alcohol at 100° but may be obtained as a solid at 108° from commercial ether. It could not be crystallized from any common solvent or combination of solvents.

The ammonium salt was obtained by exposing the compound in a thin layer for 36 hours to ammonia as in the preparation of eosin. The yellow powder became red and soluble in water. It contained 6.02% of ammonia, according to a titration with 0.2 *N* acid, using congo red as an indicator. Carbon dioxide acts either upon the solid or upon its solution to give the original compound. No ammonium salt could be obtained by evaporating a solution of the compound in ammonium hydroxide.

The sodium salt of the compound was prepared by adding an excess of a strong alcoholic solution of sodium hydroxide to an approximately 10% solution of the compound in absolute alcohol. A precipitate which forms at first dissolved on the addition of more alkali. Evaporation of $^1/_3$ of the volume of the solution caused a brown, slimy precipitate to form. It was washed with alcohol four times and dried at 100°. A sodium determination by conversion to the sulfate gave 15.9% of sodium; calc. for $C_{26}H_{14}O_6Na_4$: 17.8%.

Acetylation of the condensation product was accomplished at the boiling point by the use of acetic anhydride. A yellow compound was precipitated when the reaction mixture was poured into water. This acetylated product was soluble in carbon tetrachloride and insoluble in alkalies.

Tetrabromo Derivative of Resorcinol-diphenic-anhydride Condensation Product. Formation of 9-Lactone of *o*(*o*(1,3,6,8-Tetrabromo-2,7,9-trihydroxy-xanthenyl)phenyl)-benzoic Acid

On adding an excess of bromine to a concentrated solution of the resorcinol-diphenic-anhydride condensation product in alcohol, a brisk reaction ensued. The pinkish-yellow precipitate which formed on cooling was filtered, washed with a little alcohol, finally with water, and dried at 100°. The considerable quantity of material which does not separate from the alcohol on cooling may be precipitated with water. A bromine determination by the peroxide fusion method gave 43.5%. On drying a sample of the substance at 125°, a loss of 1.89% of moisture was found, so that the corrected bromine content should be 44.3%; calc. for $C_{26}H_{12}O_6Br_4$: 44.4%. The difficulty of removing the last molecule of water from our compound is similar to that observed by Gomberg[8] with erythrosin.

The compound dyes silk and wool pink from a faintly acid bath. It dissolves in alkalies with an intense purple-red color. A sample was acetylated by boiling for 15

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[8] Gomberg, *J. Ind. Eng. Chem.*, **14**, 1115 (1922).

minutes in acetic anhydride. The acetylated product was obtained by precipitating with water. It dried to a semi-crystalline, reddish powder, insoluble in alkalies.

Condensation of 9,10-Diphenic-ketone-4-carboxylic Acid with Resorcinol. Formation of 2′,7′-Dihydroxy-*spiro*(9-fluorene-9′-xanthene)4-carboxylic Acid

Fifteen g. of the ketonic acid, 16 g. of resorcinol and 25 g. of fused zinc chloride[9] were heated 5 hours at 115–120°. The melt was boiled with hydrochloric acid, dissolved in dil. caustic soda solution and precipitated with hydrochloric acid. The product so obtained was not so sticky as that from the anhydride. It was dissolved in boiling alcohol and reprecipitated with water. The resinous solid was dried at 105° and powdered. Its alkaline solution was brownish-yellow and had a green fluorescence; 22.17% of silver was found in the silver salt. A sample was acetylated at 135° for 2 hours, as in the case of the condensation product from the diphenic anhydride. The product was soluble in alkali.

Summary

Diphenic anhydride has been condensed with resorcinol to form a compound similar in structure and properties to fluorescein. The condensation product was brominated to give a compound analagous to eosin.

Madison, Wisconsin

[Contribution from the Division of Agricultural Biochemistry, University of Minnesota]

THE DETERMINATION OF SULFUR IN ORGANIC COMPOUNDS[1]

By Walter F. Hoffman and Ross Aiken Gortner

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The quantitative determination of sulfur in organic compounds is based on the oxidation of the sulfur to sulfate, under such conditions that the remainder of the molecule is completely decomposed. The sulfate is then precipitated as barium sulfate. In carrying out this oxidation two methods are, in general, used by the organic chemist, the Carius and the peroxide fusion methods. Besides these there is a third method which is occasionally employed, consisting in burning the compound in a stream of oxygen.

The Carius method quantitatively oxidizes the sulfur in all but a very few compounds. It is, however, a difficult determination and requires the technique of a trained chemist to yield satisfactory results. The peroxide fusion method is disagreeable, demands extreme care and is not quantitative for any volatile substance or for a compound that sublimes unless the oxidation is carried out in a calorimetric bomb as described by v. Konek.[2]

The biochemists have developed a number of methods for the determination of total sulfur in body fluids, especially urine. These are likewise based on the oxidation of the sulfur to the sulfate. One of the most

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[9] Ref. 1. Ref. 2, p. 288.

[1] Published with the approval of the Director as Paper No. 363, Journal Series of the Minnesota Agricultural Experiment Station.

[2] v. Konek, *Z. angew. Chem.*, **16**, 518 (1903).