[Contribution from the Chemical Laboratory of the State College of Washington]

SOME DIHYDROXYPHENONES AND DERIVATIVES[1]

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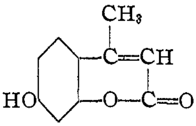
Introduction

In the course of an investigation of some highly colored crude products resulting from the condensation of resorcinol with acids, a number of new dihydroxyphenones and derivatives were prepared, and their properties compared with those of analogous compounds.

The general method of condensation applied by Nencki[2] and others[3] was used in a modified form, as zinc chloride was found to be so active that unless it was used with care charred products were produced. Hoesch,[4] prepared resacetophenone by the use of methyl cyanide and resorcinol, using dry hydrogen chloride as a condensing agent, but this method did not give satisfactory results in making the compounds described in this paper.

In introducing the acetyl group into resorcinol, Von Pechman and Duisberg[5] attempted to show that the entering group was in a position *ortho* and *para* to the hydroxyl groups. They fused β-methyl-umbelliferone,



with potassium hydroxide and obtained resacetophenone. In determining the position of the bromine atoms in dibromo-resacetophenone, Dahse[6] used chromic acid as oxidizing agent and obtained dibromo-dihydroxybenzoic acid, which was identical with the product obtained by the bromination of β-resorcylic acid. Meyer and Conzetti[7] had previously shown that the 2 bromine atoms in the latter compound were in the 3,5 positions. Since the carboxyl group was known to be in a position *ortho*

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[1] This paper is an abstract of a thesis presented by B. H. Gnagy in partial fulfilment of the requirements for the degree of Bachelor of Science at the State College of Washington, June, 1920. C. M. Brewster.

[2] Nencki and Sieber, *J. prakt. Chem.*, **23**, 147 (1881). Nencki and Schmid, *ibid.*, **23**, 546 (1881). Nencki and Sieber, *ibid.*, **23**, 1417 (1882). Nencki, *ibid.*, **25**, 273 (1882); *Monatsh.*, **10**, 906 (1889).

[3](a) Gukassiantz, *Ber.*, **11**, 1184 (1878). (b) Rasinski, *J. prakt. Chem.*, **26**, 53 (1882). (c) Crepieux, *Bull. soc. chim.*, [3] **6**, 151 (1891). (d) Goldzweig and Kaiser, *J. prakt. Chem.*, **43**, 86 (1891). (e) Frey and Horowitz, *ibid.*, **43**, 113 (1891).

[4] Hoesch, *Ber.*, **48**, 1128 (1915).

[5] Von Pechman and Duisberg, *Ber.*, **16**, 2121 (1883).

[6] Dahse, *Ber.*, **41**, 1619 (1908).

[7] Meyer and Conzetti, *Ber.*, **32**, 2106 (1899).

and *para* to the 2 hydroxyl groups already present, the orientation of 3,5-dibromo-2,4-dihydroxy-1-acetophenone was thus established.

The compound, 2,4-dihydroxy-1-propiophenone, was first described by Goldzweig and Kaiser,[8] who prepared it in small quantity by condensing resorcinol and propionic acid in the presence of zinc chloride. The same process was repeated with butyric acid, greater care being required to secure a good yield than with the propionic acid. These two compounds were brominated in acetic acid, the reaction taking place smoothly; the derivatives were more easily purified than was the case with the original phenones.

All of the 4 hydroxyphenones described in this paper are soluble in alkalies, in alcohol, and in acetic acid. They are insoluble or slightly soluble in water. As the side chains containing the ketone group increase in size, the melting points decrease; 2,4-dihydroxy-1-acetophenone melts at 141°, the propiophenone at 98° and the butyrophenone at 63–65°; and the corresponding dibromo derivatives melt at 173°, 148° and 113°, respectively. This accounts in part for the increasing difficulty experienced in purifying the hydroxyphenones with the larger side chains. The melting points of the dibromo derivatives are much higher than those of the respective compounds from which they were prepared. As might be expected, the introduction of the phenylhydrazone group raises the melting point of the compound.

Experimental Part

2,4-Dihydroxy-1-propiophenone, $C_6H_3(OH)_2.CO.C_2H_5$.—This compound was first prepared by Goldzweig and Kaiser,[8] but their method gives low yields and much charring. Better results were obtained, after numerous trials, by use of the following procedure: 100 g. of freshly fused granular zinc chloride was heated with 100 g. of propionic acid, using an oil-bath and reflux condenser and keeping the mixture at boiling temperature until all of the zinc chloride was dissolved. The mixture was then lifted from the oil-bath and, when nearly cool, 50 g. of resorcinol was added and the contents again heated on the oil-bath until the mixture began to boil, when it was kept at this temperature for 15 minutes, for completion of the reaction. The contents of the flask were poured into a liter of cold water, and the deep red, tarry product was washed by decantation until all of the zinc chloride was removed. The residue was dissolved in dil. sodium hydroxide solution, diluted to 1 liter in volume, and poured slowly into a liter of dil. hydrochloric acid. The acid solution was allowed to stand for several hours, and was kept below 10°, during which time the product slowly separated in a crystalline mass. The process of solution in alkali and acidification was again repeated, and upon standing overnight yellow needles of the substance separated. Some of the crystals were 5 cm. in length. This product melts at 85–90°, and may be used directly for preparing the dibromo derivative. To obtain the pure compound, it was twice purified by treatment with animal charcoal while in alcoholic solution; this solution was added to hot water in large volume. On cooling, the solution remained clear, but upon standing for several days beautiful transparent needles separated; these were of a pale cream color when dry and melted at 98°. The mother liquor, upon evaporation, gave more crystals of the same melting point.

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[8] Ref. 3d, p. 90.

Properties.—The alkaline solution of the crude product has a red color and a very marked green fluorescence, which is not possessed by the pure compound. The latter is soluble in alcohol, ether, benzene, and readily soluble in alkalies. From a water solution of the pure substance silver nitrate precipitates light yellow needles. A water solution is turned red by ferric chloride solution. Lead acetate gives a rose-red precipitate and barium hydroxide a yellow precipitate.

2,4-Dihydroxy-3,5-dibromo-1-propiophenone, $C_6H(OH)_2(Br)_2.CO.C_2H_5$.—Propioresorcinol, twice purified by neutralization, was dissolved in 5 volumes of glacial acetic acid, and an acetic acid solution of 2 molecules of bromine added in small portions. The solution became very warm and a partial separation of yellow crystals occurred. The mixture was allowed to stand for 2 hours, then was poured into water and filtered. The light yellow needles were dissolved in boiling alcohol and the solution was boiled with animal charcoal. A second purification with charcoal yielded pure white crystals melting at 148°. The compound is readily soluble in alkalies, alcohol, benzene, or acetic acid; it is only slightly soluble in water. The crude product shows green fluorescence when in alkaline solution, but the pure compound gives no color or fluorescence.

Analyses. Subs., 0.1645, 0.1784: AgBr, 0.1841, 0.2068. Calc. for $C_6H(OH)_2Br_2.CO.C_2H_5$: Br, 49.33. Found: 49.19, 49.33. Mol. wt. Calc.: 323.8. Found: 319, 325.

2,4-Dihydroxy-3,5-dibromo-1-propiophenone Phenylhydrazone, $C_6H(OH)_2Br_2C(C_2H_5)NNHC_6H_5$.—This compound was prepared by dissolving the above propiophenone in 90% alcohol, adding the equivalent amount of phenylhydrazine and heating the mixture on a water-bath for 1/2 hour, by which time some of the phenylhydrazone had separated. Enough hot alcohol was added to redissolve the compound, and the solution was then boiled with animal charcoal for 10 minutes, filtered and allowed to cool. Light greenish-yellow crystals were separated; these were again boiled with charcoal in alcoholic solution, and the filtrate set away overnight. The phenylhydrazone separated as small short greenish-yellow needles grouped in roset clusters, melting with decomposition at 173°. The compound is soluble in alcohol and in acetic acid, but insoluble in water. It dissolves in alkali, but not so readily as the compound from which it is derived. Sunlight seems to have but slight darkening effect on it. Attempts to analyze it for bromine were not very satisfactory because of the fact that the substance is decomposed with difficulty. It was heated for 6 hours in the bomb furnace at 230° to 250°; one determination was discarded due to incomplete oxidation, and the other resulted as follows.

Analysis. Subs., 0.1684: AgBr, 0.1512. Calc. for $C_6H(OH)_2Br_2C(C_2H_5)NNHC_6H_5$: Br, 38.63. Found: 38.19.

2,4-Dihydroxy-1-butyrophenone, $C_6H_3(OH)_2.CO.C_3H_7$.—To make this compound the same general method was used as for making propioresorcinol. The pure compound is obtained as colorless needles which gave neither color nor fluorescence when treated with alkali. The dark red reaction mixture was found very difficult to purify. It was washed free from zinc chloride, then purified twice by solution in alkali and neutralization with acid. After each neutralization several hours is required for complete separation. When the salt is allowed to stand for several days in cold water, reddish-brown needles form. To obtain the pure product, the brown needles were dissolved in a large volume of hot water, in which they are sparingly soluble, boiled with animal charcoal for 15 minutes, and the process repeated until a colorless filtrate was obtained. If the filtrate becomes cloudy upon cooling, it must be reheated and diluted just enough to produce a clear solution when cold. After the solution has stood for several days, large, colorless needles separate; m. p., 63–65°. The substance is readily soluble in alkali, alcohol, ether, benzene or acetic acid, sparingly soluble in water or carbon tetrachloride.

The brown crystals were sufficiently pure for use in preparing the dibromo derivative described below.[9]

2,4-Dihydroxy-1-butyrophenone Phenylhydrazone, $C_6H_3(OH)_2.C(C_3H_7)NHHC_6H_5$.—Crude butyryl-resorcinol was dissolved in 90% alcohol, and an approximately equivalent quantity of phenylhydrazone added. The mixture was heated upon a water-bath for an hour, but upon cooling it no crystals were formed. A portion diluted with water gave only a tarry mass. About 25% of acetic acid was then added and the heating repeated. After this mixture had stood for about a week a small quantity of fine brown crystals was obtained, which after recrystallization melted with decomposition at 191° to 193°. The quantity was too small to allow further study, but when additional butyryl-resorcinol is available it is expected that the reaction will be studied more extensively, for apparently several compounds are produced.

2,4-Dihydroxy-3,5-dibromo-1-butyrophenone, $C_6H(OH)_2Br_2.CO.C_3H_7$.—Ten g. of crude butyryl-resorcinol, twice purified by neutralization as in the purification of propio-resorcinol, was dissolved in 50 cc. of glacial acetic acid by heat. To the cooled solution was slowly added a solution of 6 cc. of bromine in 20 cc. of glacial acetic acid. The mixture should be stirred during the addition of the bromine solution. Large volumes of hydrogen bromide were given off, and upon cooling the mixture a light yellow crystalline mass separated. Dilution increased the yield. The suspension was filtered, boiled in acetic acid with animal charcoal, and diluted. The pinkish-white crystalline precipitate was filtered out, dissolved in alcohol and again boiled with charcoal for 15 minutes. As the solution cooled, fine silky, colorless needles separated; these were washed with dil. alcohol, then with hot water, and dried. The substance is readily soluble in alkali, alcohol, benzene or acetic acid, and melts sharply at 113°.

Analyses. Subs., 0.1803, 0.1911: AgBr, 0.2018, 0.2120. Calc. for $C_6H(OH)_2Br_2.CO.C_3H_7$: Br, 47.31. Found: 47.78, 47.18.

2,4-Dihydroxy-3,5-dibromo-1-butyrophenone Phenylhydrazone, $C_6H(OH)_2Br_2C(C_3H_7)NNHC_6H_5$.—To make this compound, dibromobutyryl-resorcinol was dissolved in 90% alcohol and an equivalent quantity of phenylhydrazine added. The mixture was then heated on a water-bath for 45 minutes. As it cooled, fine yellow crystals separated. These were again dissolved in alcohol, boiled with animal charcoal for 10 minutes, and filtered. As the solution cooled, pure yellow hexagonal crystals separated, melting at 155°. The substance is readily soluble in alcohol and acetic acid, and insoluble in water; it is soluble in alkali, but not as readily as the compound from which it is derived.

Summary

1. The condensation method of Nencki for the preparation of hydroxyphenones has been modified to give better yields in the preparation of propiophenone.

2. Five new compounds have been prepared and described.

3. The bromine derivatives of the hydroxyphenones are more easily purified and are obtained in better yield than the original hydroxyphenones.

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[9] Since the completion of the above work, preparation of this compound has been described by Treat B. Johnson and Frederick W. Lane [THIS JOURNAL, **43,** 357 (1921)] who purified the crude product by fractional distillation, and crystallization from a mixture of benzene and carbon tetrachloride, obtaining colorless crystals melting at 69° to 70°.