

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

A NEW OXIDATION PRODUCT FROM QUINONE

BY ETHEL M. TERRY AND NICHOLAS A. MILAS

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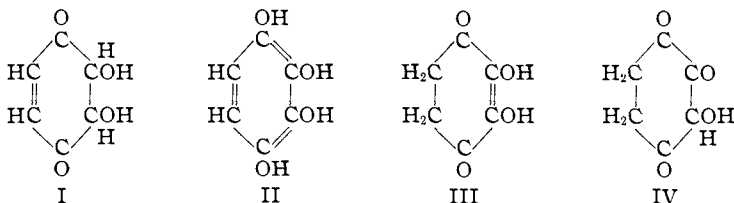
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The present paper is a preliminary report of the preparation and properties of a new substance tentatively called dihydroxy-dihydroquinone.

Either hydroquinol or quinone, treated at ordinary temperature with a mixture of sodium chlorate and osmium tetroxide,¹ preferably in dilute acid solution, will yield a white microcrystalline compound of empirical formula $C_6H_6O_2$. The molecular formula determined in water solution by the boiling-point method is $C_6H_6O_4$. The new substance is not soluble in the ordinary organic solvents but does dissolve slowly in boiling water. On long standing, the cooled solution gives up colorless crystals of the same composition and properties as the original material. These decompose, without melting, at 177–178°.

Structure of the New Substance.—The chemistry of the new substance indicates that it has a ring structure. In the first place, it forms colored compounds with an ease unknown to straight-chain compounds. For example, when suspended in glacial acetic acid and treated with bromine, it forms a brilliant red substance. When it is treated with acetone and aqueous ammonia and exposed to air, a deep blue compound² forms. In the second place, the properties of its derivatives resemble those of substituted benzene compounds.

The following ring structures will be considered.



Different arrangements of the groups about the ring are possible in each instance. In addition, bridge structures must finally be considered. For the present, however, discussion will be limited to the above four structures as they represent all that is at present known of the new compound.

Structures III and IV, or any alternative arrangements of the groups around the ring, are excluded by the fact that oxidation of the new substance with potassium permanganate in neutral solution failed to give either succinic or malonic acid. As a special precaution, it was proved

¹ See Milas and Terry [THIS JOURNAL, 47, 1412 (1925)] for details concerning the use of this reagent.

² The structures of these substances are being investigated.

by suitable tests that the two acids in question could survive the oxidation reaction as carried out by us.

Structures I and II represent closely related compounds. A substance of Structure I should undergo tautomeric change to Structure II swiftly on addition of alkali to its water solution, or slowly in acid solution. Any other arrangements of the same groups about the ring should represent compounds capable of the same type of tautomerism. Our substance forms both tetra-acetyl and tetrabenzoyl derivatives and should, therefore, be either a tetrahydroxybenzene or the closely related compound of structure like I.

A review of the properties of the known tetrahydroxybenzenes shows that they have nothing in common with our substance. For example, they are all easily soluble in water, alcohol or ether. They melt without decomposition and at temperatures widely removed from the decomposition point of our substance.

A study of the literature on the tetra-acetates of the tetrahydroxybenzenes shows that only one is at all comparable with our tetra-acetate. This is the tetra-acetate of 1, 2, 3, 4-hydroxybenzene or apionol reported by Einhorn, Cobliner and Pfeiffer.³

The melting point (with slight decomposition) of our tetra-acetate is 139°, whereas that of the apionol derivative is 136°. Both compounds are difficultly soluble in cold alcohol and in cold benzene. Our compound is little soluble in ether, is entirely stable when dry, and is slowly attacked by alkali. Apionol tetra-acetate is stated to be quite soluble in ether, not to be perfectly stable, and is also reported not to be attacked by dilute alkali. This description seems hardly consistent. If the tetra-acetate of apionol is unstable, it should be sensitive to alkali. If it is little soluble in alcohol and benzene, it should be little soluble in ether. Thus the reported differences between our tetra-acetate and that of Einhorn and co-workers seem to be due to impurities in the latter. This conclusion seems reasonable since our compound was made in 20g. lots, whereas that of Einhorn was made only in very small quantities. It is probable, therefore, that our substance forms the same tetra-acetate as does apionol and that its structure may be correctly represented by Structure I.

The tetra-acetate of the new substance is prepared by heating the latter on a water-bath for 48 hours in four times its weight of acetic anhydride. When the product is cooled and poured into water, crystals appear. These are collected, dried, recrystallized from acetone, etc. The mechanism of the reaction may be pictured as follows: under the conditions of preparation, a tautomeric change from Structure I to Structure II should occur with ease. Of the two forms, the phenolic should acetylate the more easily so that a good yield of the tetra-acetate should result, as is the case.

³ Einhorn, Cobliner and Pfeiffer, *Ber.*, **37**, 119 (1904).

The statement that phenolic hydroxyl should acetylate more readily than the secondary alcoholic groups is made on the basis of Menschutkin's⁴ measurements of the rates of acetylation of the two types of compounds under virtually the same conditions of acetylation as those used for the new substance, namely, acetic anhydride solution at 100°.

The synthesis of apionol and the preparation of its tetra-acetyl derivative are now in progress. If apionol tetra-acetate and the tetra-acetate of our substance prove to be the same, the position of the oxygen atoms in the ring will be settled. Until this work is complete, the dihydroxy-dihydroquinone structure must be accepted only tentatively.

That the new substance undergoes tautomeric change is amply borne out, first, by the fact that the photographs of the absorption spectrum, taken with a Hilger quartz spectrograph and quartz sector spectrophotometer, using a high-tension spark under distilled water as a source of light, show a profound difference in the spectrum of the water solution of the original substance and that of the same solution made alkaline. The first shows only general absorption, while the second shows a pronounced band with a head located at a wave number of 35,000 cm.^{-1} . Evidence of tautomeric change is found also in the fact that the chemical properties of a freshly prepared water solution of the new substance differ greatly from those of a solution of the same material that has first been made alkaline and then acid. The fresh solution is only slowly attacked by bromine and shows no color with ferric salt. The same solution treated with alkali and then brought to the original hydrogen-ion concentration absorbs bromine quickly and develops a red color when treated with a very small proportion of ferric chloride. These phenomena parallel the well-known chemistry of acetoacetic ester⁵ and related compounds.

That the tautomer formed by treating the water solution of the new substance, first with alkali, and then with acid, is a polyhydric phenol is borne out by two facts: the first is that when ferric salts are added in quantities in excess of that needed for the red color test given above, an intense blue color develops; and the second is that the tautomer reduces silver nitrate *in acid solution*. Both phenomena are paralleled in the chemistry of pyrogallol. Their equivalent is not found in the chemistry of acetoacetic ester.

Summary of Evidence Concerning Structure of the New Substance.—

The chemistry of the new substance may thus be ascribed to a substance of Structure I. When the new substance undergoes reactions characteristic of a substance of Structure II, a preliminary tautomeric change is always indicated. We have, therefore, tentatively assigned the name dihydroxy-dihydroquinone to our product.

⁴ Menschutkin, *Z. physik. Chem.*, **1**, 611 (1887).

⁵ Meyer, *Ann.*, **380**, 212 (1911).

Although Structure I is satisfactory in many particulars, it leaves unexplained the very slow rate of solution of the new substance in water and the subsequent slow separation from the cooled solution. The failure of the fresh solution to absorb bromine may be due to a protective action of the two keto groups that flank the double bond. It is not impossible that they are able to shield one double bond, but not two double bonds as in quinone.

Miscellaneous Reactions.—When 5 g. of the new substance is suspended in 75 cc. of acetic anhydride and 5 cc. of concd. sulfuric acid is added, violent heating occurs. When the mixture has cooled and is poured into water, needle-shaped crystals appear. These have the following characteristics: m. p., 217–218°; composition, 57.66% of carbon, 4.07% of hydrogen; molecular weight, 416 (corresponding to the formula $C_{20}H_{16}O_{10}$). It is plain that in this compound two rings have united. Whether the union is between two carbon atoms, as in an aceto-acetic ester condensation, or is made through an oxygen atom, as in a phenol ether formation, has not yet been established. Discussion is postponed until the needed evidence is at hand.

If, in the above reaction, only a few drops of concentrated acid are used instead of the larger quantity specified above, and the mixture is heated, there will be found in the product not only the needle-like crystals of the above-mentioned substance, but rectangular crystals that have the composition of 55.45% of carbon and 4.4% of hydrogen (corresponding to an empirical formula of $C_{24}H_{22}O_{13}$). Presumably another linking of two rings has occurred and the question as to the type of linkage must also be decided in this case.

Thus, three different products may be formed on treating dihydroxy-dihydroquinone with acetic anhydride, according to the concentration of the free acid present. The substances of formulas $C_{20}H_{16}O_{10}$ and $C_{24}H_{22}O_{13}$ lend themselves easily to the formation of colored compounds in a variety of ways.

When a pyridine solution of the new substance, dihydroxy-dihydroquinone, is treated with benzoyl chloride, a tetrabenzoyl compound, forms having the following characteristics: m. p., 191–192°; composition, 73.17% of carbon, 3.97% of hydrogen; molecular weight, 526; empirical formula, $C_{34}H_{22}O_8$. A tetrabenzoyl compound of apionol is stated to have been prepared by Einhorn, Cobliner and Pfeiffer,³ but no detailed description of its properties is given.

If dihydroxy-dihydroquinone is dissolved in alkali, made acid, and allowed to stand mixed with sodium bromide and bromine, a yellow crystalline compound containing 77.4% of bromine is formed. It is soluble in the common organic solvents and has a melting point of 285°.

There is some evidence that the tautomeric change of dihydroxy-dihydroquinone may go a stage further than that of apionol formation,

namely, that of Structure III. If an alkaline solution of the new substance is allowed to stand at room temperature for some time, and the excess of alkali is then determined by titration in the usual way, using phenolphthalein as indicator, it will be found that instead of binding no alkali as at first, it becomes capable of binding two equivalents. This represents an enormous increase in affinity for alkali. It will be seen that Structure III has two hydroxyl groups attached to the carbon atoms of a double bond. These should show stronger acid properties than either the secondary alcohol groups of Structure I or the phenol groups of Structure II. The properties should resemble those of rhodizonic acid, croconic acid hydride or croconic acid, all of which are pronounced salt formers. Further evidence is needed to show that the change is as simple as reported, that is, that it involves only one molecule. However, since it is rapid even at great dilution of the dihydroxy-dihydroquinone, there is a high degree of probability that the change is monomolecular with respect to the latter.

Attempts have been made to oxidize the rearranged substance and thus secure succinic acid, as would be possible if Structure III were formed. However, they have been unsuccessful so far.

Structures III and IV are, of course, closely related. Should the rearrangement in question be effected, it should be possible to prepare derivatives of either structure from the product.

With phenylhydrazine the new substance forms a variety of yellow, crystalline compounds. Efforts to make the reaction as complete as possible resulted in the preparation of a crystalline precipitate of constant nitrogen composition, namely, 22.9%. Although it was possible to produce this precipitate at will, it is not yet proved that it is a single substance, for at temperatures suitable for recrystallization in common solvents, extensive decomposition occurs. Examination under the microscope proved that the crystals were all of the same shape. It is probable, therefore, that the material is a single substance. Its composition corresponds to that of a dihydrazone-dihydrazide. Since no aniline or ammonia was found in the filtrate from the preparation described above, no osazone could have been formed.

Crystalline compounds are formed on treatment of the new substance with hydroxylamine, aniline or mercuric acetate, etc. These have not been analyzed. Heavy metal ions precipitate insoluble salts of dihydroxy-dihydroquinone from alkaline solution. When the ammonium salt is fused with zinc dust and a match stick is first dipped in acid and then in the vapor issuing from the fused mass, the red pyrrole test is given. Nitric acid in excess oxidizes the new substance to oxalic acid. However, intermediate substances (not succinic acid) can be isolated.

Many other reactions have been investigated and will be reported on shortly. The above are given as representative of the great variety of activities of the new substance.

Detail of the Preparation of Dihydroxy-dihydroquinone.—A mixture of 100 g. of hydroquinol, 400 cc. of water, 150 g. of sodium chlorate, 50 cc. of *N* hydrochloric acid and 10 cc. of a 1% osmium tetroxide solution is made in a 1-liter flask. The change to quinhydrone is observed to occur rapidly and it is found necessary to cool the mixture. After the evolution of heat has ceased, the flask is closed with a stopper carrying a tube equipped with a Bunsen valve (slit rubber tube closed at the outer end) so that the carbon dioxide which forms during the change may escape. The mixture is then shaken during about 54 hours. By this time all quinone will have disappeared and abundant white crystals will have formed. These are removed, washed with water, alcohol and finally with ether. The yield is better than 50%. The product may be recrystallized from boiling water. Oxalic acid and at least one other product not yet fully identified are present in the water solution left from the preparation.

Summary

A new oxidation product of quinone is reported. Its molecular formula is $C_6H_6O_4$. Tentatively it is called dihydroxy-dihydroquinone. Its preparation and representative reactions are described.

CHICAGO, ILLINOIS

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE
UNIVERSITY OF IOWA]

THE EFFECT OF SUBSTITUENTS IN THE FORMATION AND REACTIONS OF CERTAIN ETHERS¹

BY L. CHARLES RAIFORD AND JAMES C. COLBERT

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Though chloro- and bromobenzenes do not give up halogen readily by double decomposition,² the nitro radical in the *ortho* or *para* position increases the activity.³ Thus, Heumann⁴ and Laubenheimer⁵ found that

¹ An abstract of part of a thesis presented by James C. Colbert to the Graduate College of the State University of Iowa in partial fulfilment of the requirements for the degree of Doctor of Philosophy. Reported in abstract at the Tulsa meeting of the American Chemical Society, April, 1926.

² Fittig, *Ann.*, **133**, 49 (1865). Jungfleisch, *Ann. chim. phys.*, [4] **15**, 224 (1868). Weber and Wolf, *Ber.*, **18**, 335 (1885). Blau, *Monatsh.*, **7**, 621 (1886).

³ Fry [THIS JOURNAL, **38**, 1329 (1916)] heated the three isomeric chloronitrobenzenes in separate sealed tubes with sodium methylate for five hours at 100°. Chlorine was removed from the *ortho* and *para* positions, but the *meta* isomer did not react. The activating effect of the *ortho* nitro group may sometimes fail, for Borsche found [*Ber.* **50**, 1343 (1917)] when 1,3-dichloro-4,6-dinitrobenzene was heated with potassium phenolate, that it gave 2,4-dinitro-5-chlorodiphenyl ether instead of the expected triphenyl ether.

⁴ Heumann, *Ber.*, **5**, 910 (1872).

⁵ Laubenheimer, *Ber.*, **8**, 1626 (1875); Ger. pat. 140,133, 1903.