ON THE REACTION BETWEEN CRESOLS AND HYDROGEN PEROXIDE IN THE PRESENCE OF FERROUS SULPHATE.

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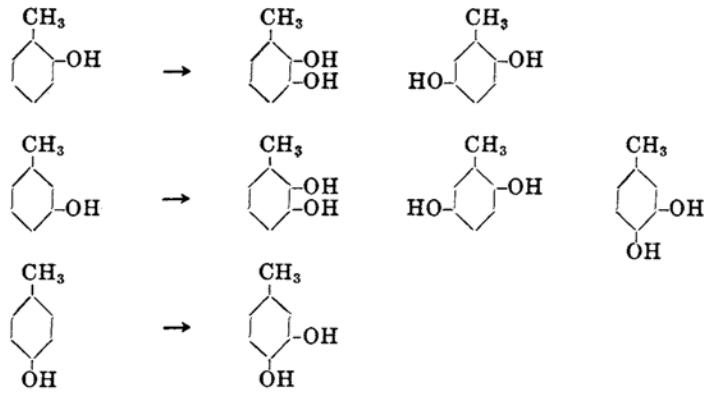
In 1900, Caross, Bevan, and Heiberg[1] reported that benzene when oxidised with hydrogen peroxide in the presence of ferrous sulphate yielded phenol (15%) and pyrocatechin (35%). Though this reaction seems to be interesting from the standpoint of pure chemistry as well as applied chemistry, only a few investigations on this subject have hitherto been carried out.[2]

The present authors extended this reaction to three isomeric cresols with the view to examining whether the direct introduction of a hydroxyl-group into a benzene nucleus is possible as in the case of benzene itself. If this reaction is always the case, it is expected that the following compounds, which are all important not only from a scientific, but also from a technological point of view, can be obtained:



As shown in details in the experimental part, the oxidation of *o*-cresol with hydrogen peroxide in the presence of ferrous sulphate was first conducted under various conditions and the chief product of the oxidation was a black substance, which is insoluble in water, partly soluble in ether and, on combusting, leaves iron oxide. Besides this substance *p*-toluhydroquinone

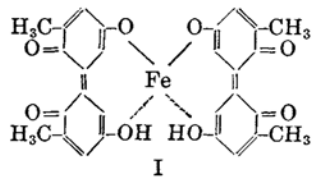
(1) *Ber.*, **33** (1900), 2015.

(2) Sommer, D.R.P. 155731. Bargellini and Monti, *Gazz. chim. ital.*, **45** (1915), 90. O. Magidson and N. Preobrashenski, *Trans. Sci.-Chem.-Pharm. Inst.* (*Moscow*), **16** (1926), 65.

was isolated in a small amount. Although some attempts were made to separate oxidation products, the oxidation products turned out to be nothing more than the above-mentioned substances, and the expected 1-methyl-2,3-dihydroxybenzene was not isolated.

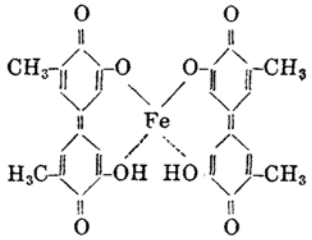
Now it is necessary to investigate the nature of this black substance in order to make clear the whole reaction. But, owing to the difficulty in purifying this substance, it was impossible to obtain a complete elucidation. After long and fruitless trials, however, it was found to be most probably a mixture of three or more substances. First, it was separated into an ether-soluble and an ether-insoluble parts. The ether-soluble part was separated into two compounds by gradual addition of petroleum ether. The precipitate first formed was represented by composition $C_{28}H_{22}O_8Fe$. On reduction with zinc dust and HCl in alcoholic solution, it gave a colourless compound melting at 202°, which was further converted into its acetate, melting at 135°, by heating with acetic anhydride and fused sodium acetate. This acetate was proved to be 2,5,2′,5′-tetracetoxy-3,3′-dimethyl-diphenyl by elementary analysis and mixed melting point test. Consequently, the reduction product which melts at 202° may be 2,5,2′,5′-tetrahydroxy-3,3′-dimethyl-diphenyl because of agreement in melting point and composition. From these results, it follows that the compound represented by $C_{28}H_{22}O_8Fe$ is probably a complex of Fe with two mol ditolydiquinone, represented by formula I.

The precipitate formed last was a yellow crystalline powder melting at 163–5° and found to be ditolydiquinone by analysis. Moreover, this was also ascertained to be the case by converting it into 2,5,2′,5′-teracetoxy-3,3′-dimethyl-diphenyl by means of reductive acetylation.



I

The ether-insoluble black substance was also represented by formula $C_{28}H_{22}O_8Fe$ (although the analytical data was unsatisfactory) and, on reductive acetylation, gave an acetate melting at 194–6° in a small amount. On the other hand, Prof. Majima,[3] in his series of researches on urushiol, tried to oxidise 1-methyl-2,3-dihydroxybenzene with $FeCl_3$ and then observed the formation of a complex compound (II).



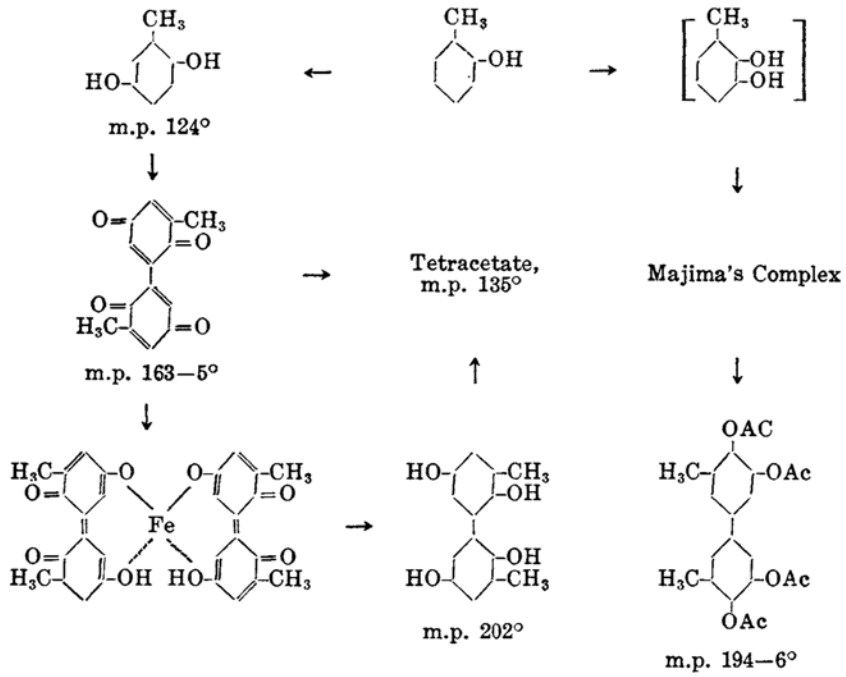
II

The complex obtained by the present authors seems to be in agreement with Majima's complex in appearance, composition, and the melting point of

(3) *Ber.*, **53** (1920), 1907.

the reductively acetylated product, so they may be assumed to be in all probability the same compound. Thus, 1-methyl-2,3-dihydroxybenzene which could not be isolated may be considered to have once been formed and to have undergone subsequent oxidation and condensation.

The above-described results can be summarised in the following manner:



Such a direct introduction of the hydroxyl-group into the benzene nucleus has been demonstrated already in the case of the anodic oxidation of aromatic compounds by various investigators. For instance, F. Fichter and Franz Ackermann[4] obtained *p*-toluhydroquinone and 4,4′-dihydroxy-3,3′-dimethyldiphenyl from *o*-cresol by anodic oxidation. It is of interest to note that the oxidation with H_2O_2 in the presence of $FeSO_4$ takes place in a manner somewhat similar to that of electrolytic oxidation.

Under the same conditions as described above *m*- and *p*-cresols were oxidised. In the former case, a large amount of a black substance together with a little *p*-toluhydroquinone was isolated as in the case of *o*-cresol, and the black substance, on close examination, was proved to be a mixture of ditolydiquinone and a complex containing Fe. From the oxidation products of

(4) *Helv. Chim. Acta*, **2** (1919), 596.

p-cresol, no definite crystalline compound except a black substance was isolated. This black substance was treated in the same way as in the case of *o*-cresol. From the ether soluble part, on reductive acetylation, an acetate which melts at 145° was obtained but owing to the small quantity, a further investigation could not be carried out. From the ether insoluble part, on reduction and subsequent acetylation, an acetate melting at 250° was obtained which also could not be identified owing to the scarcity of the substance.

Experimental Part.

I. **Oxidation of *o*-cresol with H_2O_2 in the presence of $FeSO_4$.** (a) To a mixture of 40 g. of *o*-cresol and 100 c.c. of water containing 6 g. of $FeSO_4$, 300 c.c. of 2% aqueous solution of H_2O_2 was added in portions with frequent shaking and the mixture was allowed to stand overnight, when the solution became brownish red and a black resinous oil separated out. In order to drive off unacted cresol the whole oxidised mixture was subjected to steam distillation and 19 g. of *o*-cresol was obtained from the distillate. On cooling, a resinous mass solidified in the residue of the steam treatment and was collected on a filter. The filtrate separated from the black substance was thoroughly extracted with ether and then the ethereal solution evaporated, when about 2.5 g. of a reddish substance remained and gradually crystallised which was dried on a porous plate and recrystallised from benzene. It forms colourless needles melting at 124° and was identified with *p*-toluhydroquinone by elementary analysis and mixed melting point test. (Found: C, 67.68; H, 6.86. Calc. for $C_7H_8O_2$: C, 67.8; H, 6.4%.)

(b) To a mixture of 40 g. of *o*-cresol and 100 c.c. of water containing 10 g. of $FeSO_4$, 300 c.c. of 2% aqueous hydrogen peroxide solution was added drop by drop with ice-cooling and vigorous stirring. After being allowed to stand for several hours at room temperature, the excess of H_2O_2 was decomposed by the addition of MnO_2. With the intention of isolating the expected 1-methyl 2,3-dihydroxybenzene, the whole mixture was first treated with a solution of lead acetate when a brown precipitate of a lead salt was deposited. The precipitate thus obtained was washed with water, alcohol, and ether succesively, decomposed with dilute sulphuric acid, and extracted with ether. From the ethereal extract a brown resinous matter was obtained, from which no definite compound could be isolated. The mixture was treated with lead acetate solution, mixed together with the washings and submitted to steam distillation, and 25 g. of unchanged *o*-cresol was recovered. The residue was filtered from the black viscous resinous matter and extracted with ether. From the ethereal solution *p*-toluhydroquinone was obtained in a small amount. The aqueous solution which had been treated with ether was evaporated to dryness under reduced pressure, from which no definite organic compound was isolated.

(c) To a mixture of 30 g. of *o*-cresol and 100 c.c. water containing 6 g. of $FeSO_4$, 300 c.c. of 2% aqueous hydrogen peroxide solution was added in small portions and the temperature was maintained at 80° during the oxidation.

The investigation of oxidation products was carried out just as in case (a) and about 1 g. *p*-toluhydroquinone and a large amount of the black material were obtained.

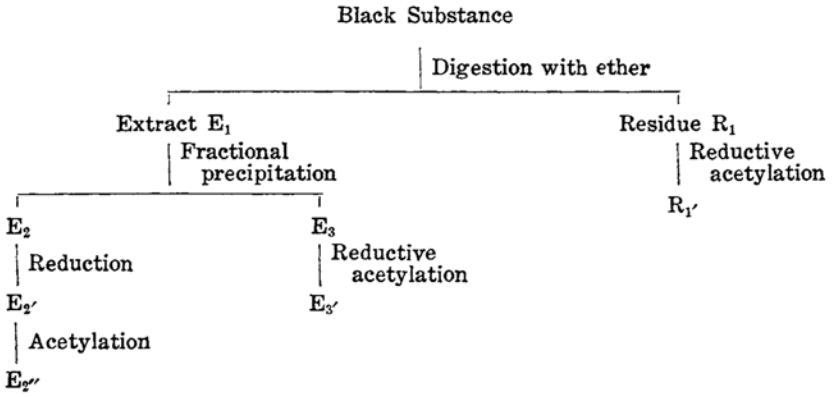
(d) A solution of 30 g. of *o*-cresol in acetone was mixed with a solution of ferrous sulphate in 100 c.c. water and the mixture heated with constant stirring on the water-bath. Three hundred c.c. of 2% aqueous solution of H_2O_2 was added to the mixture

drop by drop. From the oxidation products nothing other than the above-mentioned materials was isolated.

(e) When a large amount of $FeSO_4$ was used, the chief oxidation product was obtained as a black powder instead of an oily substance. Aside from this, *p*-toluhydroquinone was found in a small amount as in the above cases.

To a mixture of 30 g. of *o*-cresol and 100 c.c. of water containing 40 g. of $FeSO_4$, 300 c.c. of 2% aqueous solution of H_2O_2 was added in portions with vigorous shaking. Twenty grams of a black substance and 2 g. of *p*-toluhydroquinone were obtained from the oxidation products.

II. **The investigation of the black substance.** As already stated, the chief oxidation product was a black substance insoluble in water. For a further investigation of this substance, it was treated as follows:



Of course, a complete separation was by no means attained in this way, but it was possible to speculate that it would be a mixture of the substances described in the introduction.

(A) *Part soluble in ether.* The black substance was thoroughly extracted with ether in a Soxhlet apparatus. On addition of petroleum ether to the ethereal solution, E_2 first and then E_3 separated out.

(a) *Complex salt* (E_2). E_2 was again dissolved in ether and fractionally reprecipitated by addition of petroleum ether. By the repetition of this process, E_2 was purified and used in a further experiment as below. (Found: C, 61.05; H, 5.13; Fe, 9.67. Calc. for $C_{28}H_{22}O_8Fe$: C, 61.99; H, 4.06; Fe, 10.14%.)

(b) *Reduction of* E_2 ($E_{2'}$). To a mixture of 1 g. of E_2 in alcohol (20 c.c.) and 5 g. of zinc dust, 5 c.c. of concentrated HCl was slowly added. After an hour, the reaction mixture was filtered by suction and the solution was poured into 150 c.c. of cold water, when an almost colourless precipitate separated out. It was recrystallised from alcohol, crystalline powder melting at 202°, and giving data agreeing with 2,5,2′,5′-tetrahydroxy-3,3′-dimethyl-diphenyl. (Found: C, 68.03; H, 6.10. Calc. for $C_{14}H_{14}O_4$: C, 68.29; H, 5.69%.)

(c) *Acetylation of* $E_{2'}$ ($E_{2''}$). One gram of $E_{2'}$ was boiled with 10 c.c. of acetic anhydride together with 2 g. fused sodium acetate under reflux for an hour. After cooling, it was poured into cold water, when a colourless precipitate separated out.

The precipitate was recrystallised from alcohol, a colourless crystalline substance melting at 135° and showing no depression of melting point by admixture with 2,5,2′,5′-tetra-acetoxy-3,3′-dimethyl-diphenyl synthesized from *p*-toluhydroquinone. (Found: C, 63.56; H, 6.10. Calc. for $C_{22}H_{22}O_8$: C, 63.8; H, 5.3%.)

(d) *Purification of* E_3. E_3 was also dissolved in ether and petroleum ether was added until a yellow precipitate was just separating out. To the filtrate a large amount of petroleum ether was added to complete the precipitation, when a yellow substance was deposited. By repeating such a treatment several times, a yellow crystalline powder melting at 163-5° was obtained. The analytical data and the melting point agree with those of ditolydiquinone. This was, moreover, ascertained also by converting it into its acetate. (Found: C, 68.98; H, 4.68. Calc. for $C_{14}H_{10}O_4$: C, 69.42; H, 4.13%.)

(e) *Reductive acetylation of* E_3. Two grams of E_3 was dissolved in 15 c.c. of acetic anhydride and 5 g. of zinc dust and 3 g. of fused sodium acetate were added and the whole was boiled under reflux for an hour, when the brownish red colour of the initial mixture faded. After removal of the excess of zinc dust, the mixture was poured into cold water and left to stand. A yellowish mass separating out therefrom, and after recrystallisation from alcohol it showed a melting point 135°, agreeing with the data for 2,5,2′,5′-tetracetoxy-3,3′-dimethyl-diphenyl. It was moreover identified by the mixed melting point test with a synthetical specimen which had been prepared by the reductive acetylation of ditolydiquinone, prepared from *p*-toluhydroquinone according to Brunner.

(B) *Part insoluble in ether* (R_1). (a) *Reductive acetylation of* R_1. Twelve grams of R_1 was boiled with 20 c.c. of acetic anhydride together with 14 g. of fused sodium acetate and 10 g. of zinc dust under reflux for an hour. While hot, excess of zinc was filtered off and the solution thus obtained was poured into cold water, when a yellowish mass separated. On recrystallisation from alcohol, a colourless substance melting at 193-5° was obtained. This melting point coincides with that of 3,3′-dimethyl-4,4′,5,5′-tetracetoxy-diphenyl. (Found: C, 61.25; H, 5.20; Fe, 9.56. Calc. for $C_{28}H_{22}O_8Fe$: C, 61.99; H, 4.06; Fe, 10.14%.)

III. **Oxidation of *m*-cresol with H_2O_2 in the presence of $FeSO_4$.** Thirty grams of *m*-cresol was oxidised under the same conditions as in case (a) for *o*-cresol. The formation of *p*-toluhydroquinone and the black material were also observed here. The investigation of the black material was carried out exactly in the same way as in the case of *o*-cresol. (A) *Part soluble in ether*. By the treatment as in the case of *o*-cresol, ditolydiquinone and the complex of Fe with it were detected. (B) *Part insoluble in ether*. From this part, no definite compound could be isolated.

IV. **Oxidation of *p*-cresol with H_2O_2 in the presence of $FeSO_4$.** The oxidation and the separation of the resulting products were carried out as in the above two cases. (A) *Part soluble in ether*. On reductive acetylation by means of acetic anhydride and zinc dust, it gave an acetate melting at 145° in a very small amount. (B) *Part insoluble in ether*. By reductive acetylation, an acetate melting at 250° was obtained in a small amount. These two acetates could not be identified owing to the small amounts of the substances available.

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