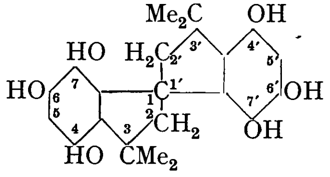
44. *Condensation Products of Phenols and Ketones. Part III. Hydroxyquinol, Pyrogallol, and* m- *and* p-*Cresols with Acetone.*

By Wilson Baker and D. M. Besly.

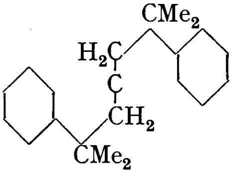
A condensation product of hydroxyquinol and acetone, $C_{21}H_{24}O_6$, has been shown to possess four hydroxyl groups and to yield phoronic anhydride on oxidation, thus proving it to be the bis-2 : 2'-*spiro*chroman derivative (III). An isomeric hexahydroxy-compound from pyrogallol and acetone has been proved by similar methods to be the bis-1 : 1'-*spiro*hydrindene (IV). The non-phenolic products, $C_{23}H_{28}O_2$, obtained from *m*- and *p*-cresol and acetone are to be represented by the formulæ (V) and (VI) as derivatives of bis-2 : 2'-*spiro*chroman. The rôle of certain less complex products derived from *m*-cresol and acetone in the formation of (V) is briefly discussed.

Hydroxyquinol.—The condensation of hydroxyquinol with acetone in presence of acetic and concentrated hydrochloric acids was described by Sükösd (*Acta Lit. Sci. Univ. Hung. Francisco-Josephinae*, 1932, **2**, 230; *Amer. Chem. Abstr.*, 1933, **27**, 1873). He isolated a compound $C_{21}H_{24}O_6$, equivalent to $2C_6H_6O_3 + 3COMe_2 - 3H_2O$, m. p. 267—268°, which yielded a so-called hexa-acetate, a hexabenzoate, and a hexapropionate. By analogy with the erroneous structure proposed by Fabinyi and Széki (*Ber.*, 1905, **38**, 2307) for the condensation product of catechol and acetone (see Baker, J., 1934, 1678; Baker and McGowan, J., 1938, 347) Sükösd assigned to the compound a constitution impossible on stereochemical grounds. The same condensation product was later prepared similarly from hydroxyquinol triacetate and acetone, or phorone, by Fisher, Furlong, and Grant (*J. Amer. Chem. Soc.*, 1936, **58**, 820), who formulated the compound as a hexahydroxy-3 : 3 : 3' : 3'-tetramethylbis-1 : 1'-*spiro*hydrindene (I), by analogy with the structure which had been proposed for the catechol–acetone product by Baker (*loc. cit.*).

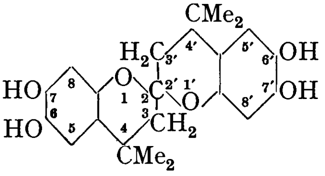
Reinvestigation of the substance $C_{21}H_{24}O_6$ has shown that structure (I) is incorrect. Oxidation with potassium permanganate led to the isolation of the anhydride of phoronic acid, $C(CH_2{\cdot}CMe_2{\cdot}CO{\cdot}O)_2$, which establishes the presence of the grouping (II), the argument being similar to that used in the case of the structure of the catechol–acetone product (*q.v.*, Baker and McGowan, *loc. cit.*). This partial structure (II) is consistent with the observation by Fisher, Furlong, and Grant that phorone may replace acetone in the condensation, and also with the structure (I). Methylation of $C_{21}H_{24}O_6$ with methyl sulphate and alkali, however, readily gave a completely non-phenolic *tetramethyl* ether, and not a hexamethyl ether as required by structure (I), and re-examination of the supposed hexa-acetate showed that it was really a *tetra-acetate*, which tenaciously retained one molecule of acetic acid of crystallisation. These facts prove that the condensation product contains only *four* free hydroxyl groups, and it can therefore only be a tetrahydroxy-4 : 4 : 4′ : 4′-tetramethylbis-2 : 2′-*spiro*chroman of the type (III). With regard to the hydroxyl groups,



(I.)



(II.)

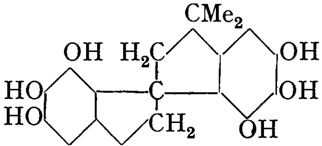


(III.)

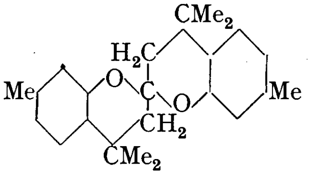
these must occupy positions 6, 7, 6′, and 7′ if the hydroxyquinol exhibits its usual reactivity in position 5, and it may therefore be assumed with some certainty that the condensation product is 6 : 7 : 6′ : 7′-tetrahydroxy-4 : 4 : 4′ : 4′-tetramethylbis-2 : 2′-*spiro*chroman (III). When treated with oxidising agents, lead peroxide, silver oxide, nitric acid, etc., the compound gives brilliant red solutions, doubtless due to the formation of a double *o*-quinone (cf. the catechol–acetone product, which possesses four similarly placed hydroxyl groups), but the product is very unstable and has not been isolated in an analytically pure state. Treatment with bromine in acetic acid gives a red product, probably a dibromo-diquinone, which when reduced and acetylated gives 8 : 8′ (or less likely 5 : 5′)-*dibromo*-6 : 7 : 6′ : 7′-*tetra-acetoxy*-4 : 4 : 4′ : 4′-*tetramethylbis*-2 : 2′-spiro*chroman.*

Pyrogallol.—Wittenberg in 1882 (*J. pr. Chem.*, **26**, 76) condensed acetone with pyrogallol in presence of phosphorus oxychloride and obtained a product, " gallacetonin ", which turned brown at 250°. He regarded the substance as the simple acetal of pyrogallol and acetone, $C_6H_3(OH)O_2CMe_2$, and mentions an uncharacterised crystalline acetyl derivative. Acetone and pyrogallol were condensed in presence of acetic and hydrochloric acids by Fabinyi and Széki (*Ber.*, 1905, **38**, 3527), who isolated a substance $C_{21}H_{24}O_6$, m. p. 260—265° with previous darkening, which yielded a hexa-acetate, a hexabenzoate, and a dibromo-derivative. The proposed structure for the compound, based on their erroneous formula for the catechol–acetone product, is stereochemically impossible and inconsistent with its chemical properties. The same product $C_{21}H_{24}O_6$ was later obtained by Ghiglieno (*Atti R. Accad. Sci. Torino*, 1912, **47**, 16), who showed that phorone could replace acetone in the condensation; he suggested the structure $(CMe_2{:}CH)_2C[C_6H_2(OH)_3]_2$, but this may be rejected as it would not yield a dibromo-derivative, but at least a tetrabromo-derivative. Finally Fisher, Furlong, and Grant (*loc. cit.*) mention the condensation product of pyrogallol and acetone as " a high-melting solid as yet not properly characterised."

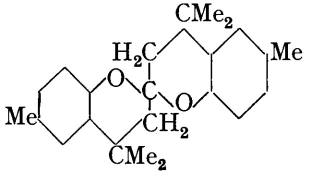
It was suggested in Beilstein's " Handbuch der Organischen Chemie " (4th ed., 1923, **6**, 1080) that the product described by Wittenberg was identical with the substance isolated by Fabinyi and Széki, and we have now confirmed this suggestion. Specimens of the compound prepared by the two methods showed no divergence in properties, and the derived acetyl derivatives were proved to be identical by a mixed melting-point determination. The acetyl derivative was moreover shown to contain six acetoxyl groups. Oxidation of the compound $C_{21}H_{24}O_6$ with potassium permanganate gave phoronic anhydride, thus proving the presence of the partial structure (II), and the presence of six hydroxyl groups was further established by the formation of a *hexamethyl* ether. These facts prove that the compound is a hexahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene (IV) analogous to the catechol–acetone product. The positions assigned to the hydroxyl groups, 5, 6, 7, 5′, 6′, and 7′, are based on the probability that condensation first occurs between the tertiary carbon atoms of phorone (*via* its dihydrochloride) and the pyrogallol nuclei in position 5, followed by ring closure; if the initial condensation occurred in position 4, *i.e.*, ortho to a hydroxyl group, it is probable that a bis-2 : 2′-*spiro*chroman would result as in the case of hydroxyquinol. The alternative positions of the hydroxyl groups, 4, 5, 6, 4′, 5′, and 6′, would involve the less likely assumption that the first step in the condensation was between the carbonyl group of phorone and position 5 in the two pyrogallol nuclei. We, therefore, regard the pyrogallol–acetone condensation product as 5 : 6 : 7 : 5′ : 6′ : 7′-*hexahydroxy*-3 : 3 : 3′ : 3′-*tetramethylbis*-1 : 1′-spiro*hydrindene* (IV). Aerial oxidation in alkaline solution led to no definite results (contrast catechol–acetone product). An alternative structure for the compound showing two dissimilarly placed aromatic nuclei analogous to that shown in a footnote to the paper of Baker and McGowan (*loc. cit.*, p. 349) cannot be seriously considered.



(IV.)



(V.)



(VI.)

m- *and* p-*Cresols.*—Zincke and Gaebel (*Annalen*, 1912, **388**, 299; Gaebel, Dissert., Marburg, 1903) heated solutions of *m*- and *p*-cresols in acetone saturated with hydrogen chloride to 100° and isolated crystalline non-phenolic products, melting at 126° (and 132°, dimorphous), and 138° respectively, regarded as $C_{20}H_{24}O_2$. Formulæ which do not merit discussion were suggested for these compounds and were later revived by Böttcher (Dissert., Berlin, 1930). Niederl (*J. Amer. Chem. Soc.*, 1928, **50**, 2230) and Niederl and Casty (*Sitzungsber. Akad. Wiss. Wien*, 1928, **137**, II*b*, 1038) treated *m*- and *p*-cresols with acetone in presence of cold concentrated sulphuric acid and obtained the same products, but they were found not to possess the molecular formulæ ascribed to them by Zincke and Gaebel but to be $C_{23}H_{28}O_2$ (subsequently fully confirmed by Niederl, *Sitzungsber. Akad. Wiss. Wien*, 1932, **141**, II*b*, 150), *i.e.*, $2C_7H_7{\cdot}OH + 3C_3H_6O - 3H_2O$. As the *m*-cresol product was prepared from *m*-cresol and phorone in much better yield than from *m*-cresol and acetone, and gave dimethylmalonic acid on oxidation, Niederl assumed a phorone grouping in these compounds and, after having put forward certain unlikely formulæ, ultimately suggested for them the bis-*spiro*chroman structures (V) and (VI) (*Z. angew. Chem.*, 1931, **44**, 467).

In the present work we have degraded both the *m*- and *p*-cresol products to phoronic anhydride by oxidation with potassium permanganate in acetic acid, thus, as before, proving the partial structure (II). Since, moreover, the compounds are non-phenolic, they can only be 4 : 4 : 7 : 4′ : 4′ : 7′-hexamethylbis-2 : 2′-*spiro*chroman (V) and 4 : 4 : 6 : 4′ : 4′ : 6′-hexamethylbis-2 : 2′-*spiro*chroman (VI) respectively, as suggested by Niederl.

An interesting preparation of (V) is described by Fries and Fickewirth (*Annalen*, 1908, **362**, 40), who obtained it by heating 3-hydroxy-*p*-tolyldimethylcarbinol (hydroxythymol), $C_6H_3Me(OH){\cdot}CMe_2{\cdot}OH$, with concentrated hydriodic acid (*d* 1·7), and, in view of the supposed formula, $C_{20}H_{24}O_2$, of the final product (Gaebel, *loc. cit.*), regarded the change as a simple loss of two molecules of water from two molecules of the hydroxythymol, a view also held by Böttcher (*loc. cit.*). Hydroxythymol is also dehydrated by hydrochloric or hydrobromic acid in the cold into an intermediate compound, the dimeric form of 2-hydroxy-4-methyl*iso*propenylbenzene, $[C_6H_3Me(OH){\cdot}CMe{:}CH_2]_2$ (see Fries and Fickewirth, *Ber.*, 1907, **41**, 367), and this is further converted into (V) by heating with concentrated hydriodic acid (this paper). These reactions cannot now be regarded as simple, since the final product is known to be $C_{23}H_{28}O_2$, and it seemed likely that the formation of (V) must be accompanied by the loss of *m*-cresol. Investigation of the conversion of the dimeric form of 2-hydroxy-4-methyl*iso*propenylbenzene into (V) by the action of hydriodic acid has shown that this is actually the case, an 81% yield of *m*-cresol and a 91% yield of (V) being obtained according to the equation:

$$3(C_{10}H_{12}O)_2 \longrightarrow 2C_{23}H_{28}O_2 + 2C_7H_7{\cdot}OH$$

In view of the fact that the dimeric form of 2-hydroxy-4-methyl*iso*propenylbenzene may be directly prepared by the condensation of *m*-cresol with acetone in presence of hydrogen chloride at 40° (Eng. Pat., 273,684), the dimer must be regarded as an intermediate in the "direct" production of (V) from *m*-cresol and acetone in the presence of hydrogen chloride (Zincke and Gaebel), and probably also in the presence of sulphuric acid (Niederl), since it is known that the dimer is converted into (V) at 180° in presence of a little sulphuric acid (Böttcher, *loc. cit.*). The same mechanism doubtless operates in the condensation of *p*-cresol with acetone to give the *spiro*chroman (VI). The condensation of phenols with phorone must proceed in a more direct manner.

EXPERIMENTAL.

6 : 7 : 6′ : 7′-*Tetrahydroxy*-4 : 4 : 4′ : 4′-*tetramethylbis*-2 : 2′-spiro*chroman* (III) (cf. Fisher, Furlong, and Grant, *loc. cit.*).—Hydroxyquinol triacetate (176 g.) was dissolved in a warm mixture of acetone (77 c.c.), acetic acid (184 c.c.), and concentrated hydrochloric acid (140 c.c.). After 24 hours the red solid was collected, washed with water (yield, 115 g.), and crystallised from dilute acetone as follows. It was dissolved in excess of hot acetone containing glacial acetic acid (1 c.c.), a solution of sodium metabisulphite (1 c.c.) added to prevent oxidation, and the mixture diluted with water at 50° to four times its volume. On rubbing, the condensation product separated in small, colourless, glistening plates, m. p. 270° (decomp.) after darkening at about 260°. The compound gave a bright green ferric chloride reaction, and dissolved in aqueous alkalis with a green colour which soon changed to bright red.

Oxidation. To the *spiro*chroman (III) (20 g.) was slowly added a warm saturated aqueous solution of potassium permanganate with constant shaking until the oxidising agent was in excess. After 24 hours sulphur dioxide was passed into the mixture, and the resulting liquid yielded to ether a partly solid product (4 g.) possessing a rancid odour. After pressing on porous earthenware the solid (3 g.) crystallised from light petroleum (b. p. 60—80°) in colourless needles, m. p. 127·5—129°, not depressed by authentic phoronic anhydride. A convenient method for the isolation of phoronic anhydride in these experiments is to boil the oxidation product with a little water: the anhydride crystallises on cooling.

6 : 7 : 6′ : 7′-*Tetramethoxy*-4 : 4 : 4′ : 4′-*tetramethylbis*-2 : 2′-spiro*chroman*.—The tetrahydroxy-compound (III) (15 g.), methyl alcohol (25 c.c.), and methyl sulphate (40 c.c.) were shaken during the gradual addition of 20% aqueous sodium hydroxide (70 c.c.); further similar quantities of methyl sulphate and alkali were subsequently added. After boiling and cooling, the solid was collected and crystallised thrice from glacial acetic acid. The *tetramethyl* ether separated as a microcrystalline powder, m. p. 214—216° [Found in material dried in a vacuum over potassium hydroxide at 100°: C, 70·2; H, 7·6; OMe, 29·8. $C_{21}H_{20}O_2(OMe)_4$ requires C, 70·1; H, 7·5; OMe, 29·0%].

6 : 7 : 6′ : 7′-*Tetra-acetoxy*-4 : 4 : 4′ : 4′-*tetramethylbis*-2 : 2′-spiro*chroman*.—The tetrahydroxy-compound (III) (25 g.) was refluxed for 4 hours with acetic anhydride (150 c.c.) and anhydrous sodium acetate (20 g.), and the cooled mixture stirred into water. The pink solid product was crystallised four times from glacial acetic acid and obtained in small colourless crystals, m. p. 205—206° (previous workers record the same m. p.) [Found: Ac, 35·9. Calc. for $C_{21}H_{20}O_2(OAc)_4,HOAc$: Ac, 35·8%], which evolved acetic acid at the m. p. After three further crystallisations from alcohol the compound still retained the molecule of acetic acid and formed thick needles, m. p. 205—206° (Found: Ac, 36·3%), but the acetic acid was lost when the substance was dried in a vacuum over potassium hydroxide at 160° for 4 hours, or when distilled to dryness with toluene, the product in both cases being subsequently crystallised from alcohol [Found: C, 64·2; H, 5·9; Ac, 27·9, 29·3; *M*, 490. Calc. for $C_{21}H_{20}O_2(OAc)_4$: C, 64·5; H, 5·9; Ac, 31·9%; *M*, 540].

8 : 8′(or 5 : 5′)-*Dibromo*-6 : 7 : 6′ : 7′-*tetra-acetoxy*-4 : 4 : 4′ : 4′-*tetramethylbis*-2 : 2′-spiro*chroman*.—The tetrahydroxy-compound (III) (15 g.), suspended in acetic acid (120 c.c.) at 40°, was treated with a solution of bromine (15 c.c.) in acetic acid (30 c.c.). After ½ hour the solution was poured into water, the red solid collected, washed with water, and dried in a desiccator, and its solution in acetic acid decolourised by the addition of a little zinc dust, and then boiled with the addition of acetic anhydride. The solid obtained on the addition of water separated

from alcohol in small crystals, m. p. 227—230° [Found: C, 49·1; H, 4·5; Br, 22·1; Ac, 25·8. $C_{21}H_{18}O_2Br_2(OAc)_4$ requires C, 49·8; H, 4·3; Br, 22·9; Ac, 24·6%].

5 : 6 : 7 : 5′ : 6′ : 7′-*Hexahydroxy*-3 : 3 : 3′ : 3′-*tetramethylbis*-1 : 1′-spiro*hydrindene* (IV).—(A) *Fabinyi and Széki.* The modification adopted by Baker (*loc. cit.*) gives considerably improved yields. Pyrogallol (42 g.), acetone (33 g.), acetic acid (80 c.c.), and concentrated hydrochloric acid (64 c.c.) were heated on the water-bath for 48 hours and cooled. The solid was collected, washed with acetic acid, boiled with water, and dried (yield, 53 g.). (B) *Wittenberg.* The reaction is best carried out as follows. To pyrogallol (10 g.) in acetone (16 c.c.) was added phosphorus oxychloride (1 c.c.), and, after the reaction had subsided, the solid product was boiled with 15% alcohol (200 c.c.), collected, washed with dilute alcohol and water, and dried (yield, almost quantitative). After two crystallisations from acetic acid containing a little dilute hydrochloric acid both specimens melted at 260—265° after darkening from 240°, and gave a greenish-purple ferric chloride reaction in alcoholic solution. The acetyl derivative (excess of acetic anhydride and anhydrous sodium acetate for 4 hours) from both products was crystallised several times from alcohol and from acetic acid; the m. p. of both specimens and a mixed m. p. was 247° (rapid heating) [Found : Ac, 42·3. Calc. for $C_{21}H_{18}(OAc)_6$: Ac, 41·3%].

5 : 6 : 7 : 5′ : 6′ :7′-*Hexamethoxy*-3 : 3 : 3′ : 3′-*tetramethylbis*-1 : 1′-spiro*hydrindene*.—The hexahydroxy-compound (IV) (20 g.) in acetone (30 c.c.) was stirred in coal gas during the gradual addition of potassium hydroxide (50 g.) in water (150 c.c.) and methyl sulphate (84 c.c.), the mixture being finally allowed to boil. After 2 hours the sticky material was collected, boiled with a little alcoholic potassium hydroxide, again collected, washed with alcohol, and finally boiled with water (yield, 7 g.). It was crystallised three times from alcohol and obtained in faintly yellow needles, m. p. 135—137° [Found C, 71·2; H, 7·8; OMe, 41·3. $C_{21}H_{18}(OMe)_6$ requires C, 71·0; H, 7·9; OMe, 40·8%].

Oxidation of 5 : 6 : 7 : 5′ : 6′ : 7′-*Hexahydroxy*-3 : 3 : 3′ : 3′-*tetramethylbis*-1 : 1′-spiro*hydrindene* (IV).—The oxidation of (IV) (24 g.) was carried out as described under the oxidation of (III). The syrupy product (2 g.) was boiled with a little water and then yielded phoronic anhydride (0·3 g.), m. p. 129—130°, undepressed on admixture with an authentic specimen.

Oxidation of the m-*Cresol and* p-*Cresol–Acetone Condensation Products* (V) *and* (VI).—The compounds were prepared according to the directions of Niederl and Niederl and Casty (*locc. cit.*), the yields being about 10%. After careful purification the former had m. p. 128° (after solidification, 136°, dimorphous), and the latter had m. p. 136° (after solidification, m. p. 144°, dimorphous). The condensation products (5 g.) were dissolved in hot acetic acid (300 c.c.) under reflux on the steam-bath, and warm saturated aqueous solutions of potassium permanganate slowly added in excess. The cooled solutions were now treated with excess of sulphur dioxide, filtered, and extracted with ether, and the extracts dried and evaporated on the water-bath under diminished pressure. The partly solid residues were boiled with a little water, and the crystals which separated on cooling were collected and recrystallised from light petroleum. In each case they melted at 128·5—129·5°, and did not depress the m. p. of phoronic anhydride.

Conversion of the Dimeric Form of 2-*Hydroxy*-4-*methyl*iso*propenylbenzene into* (V).—The dimeric compound was prepared according to Eng. Pat. 273,684, and purified as its ether addition compound, $(C_{10}H_{12}O)_2,Et_2O$, by crystallisation from light petroleum (b. p. 40—60°) containing a little ether. The addition compound was obtained as colourless, highly refracting, rhombic prisms, melting when fairly rapidly heated at 76—77° [Found : Et_2O by loss of weight at 100°, 20·3. Calc. for $(C_{10}H_{12}O)_2,Et_2O$: Et_2O, 20·0%]. The ether-containing substance (4·5 g.) was refluxed for 7 hours with hydriodic acid (100 c.c.; *d* 1·7), diluted with water (500 c.c.), and steam-distilled. The distillate yielded to ether a non-phenolic product (0·3 g.) having an odour of thymol, and a phenolic product which by treatment with benzoyl chloride and alkali gave a solid benzoyl derivative (1·4 g.), m. p. 55—56° after crystallisation from light petroleum. The m. p. was not altered on admixture with a specimen of *m*-cresol benzoate. The crystalline material not volatile in steam (2·5 g.) was isolated by ether extraction and, after crystallisation from alcohol, was identified as (V) by m. p. and mixed m. p. determination, and by its characteristic dimorphism.

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