# *Triphenylmethane Derivatives from Condensations of Phenols with Hydroxybenzaldehydes.*

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The preparation of various trihydroxytriphenylmethanes by the acid-catalysed condensation of phenols with aromatic hydroxy-aldehydes is described. The mechanism of reactions of this type is considered, and evidence is given of the intermediate formation of a dihydroxydiarylmethanol in two condensations, and the reversibility of some of the changes involved.

RUSSANOW (*Ber.*, 1889, **22**, 1943) obtained 4 : 4′-dihydroxytriphenylmethane by the acid-catalysed condensation of phenol with benzaldehyde and thus showed that aromatic aldehydes could behave in these condensations in a similar way to those aliphatic aldehydes which yield the corresponding dihydroxydiphenylmethanes.

The resins formed by condensation of phenols with aldehydes are in general regarded as resulting from repeated reactions of types (1) and (2) on the initial products from (1) and (2). In phenol–formaldehyde condensations the diphenylmethane derivatives formed are regarded as true intermediates for resin formation (Megson, *J. Soc. Chem. Ind.*, 1939, 131); T. T. Jones (*ibid.*, 1946, 264) claims, however, that at lower temperatures and with equimolecular proportions of phenol and formaldehyde the resinification may also proceed through formation of dialcohols by the further addition of a molecule of formaldehyde to the phenolic alcohol formed by (1).

$$\mathrm{R{\cdot}CHO + C_6H_5{\cdot}OH = R{\cdot}CH(OH){\cdot}C_6H_4{\cdot}OH} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\mathrm{HO{\cdot}C_6H_5 + R{\cdot}CH(OH){\cdot}C_6H_4{\cdot}OH = HO{\cdot}C_6H_4{\cdot}CHR{\cdot}C_6H_4{\cdot}OH + H_2O} \quad . \quad . \quad . \quad (2)$$

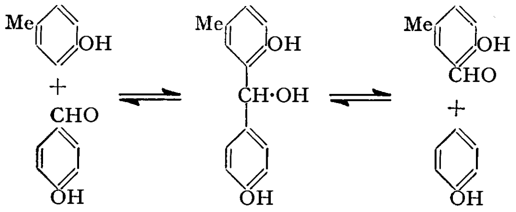
Isolation of the intermediate alcohol [as in (1)] is usually achieved only when the phenol is of lowered reactivity (Fishman, *J. Amer. Chem. Soc.*, 1920, **42**, 2288) or with special aldehydes (Balfe and Webber, *J.*, 1942, 718); various attempts have been made to prove the formation of the intermediate alcohol indirectly [Michael, *J. pr. Chem.*, 1898, (ii), 334; von Euler and Kispeczy, *Z. physikal. Chem.*, 1941, *A*, **189**, 109].

Previously, only resinous products have been obtained by the condensation of phenol with *o*- or *p*-hydroxybenzaldehyde (Liebermann and Schwarzer, *Ber.*, 1876, **9**, 800; Trzcinski, *Ber.*, 1883, **16**, 2835; Zulkowski, *Monatsh.*, 1884, **5**, 108; Driver, *J. Soc. Chem. Ind.*, 1927, 197T). It is now shown that, at relatively low temperatures and in a suitable medium, triphenylmethane derivatives can be readily prepared by the acid-catalysed condensation of phenol and the cresols with various aromatic hydroxy-aldehydes, although in most of the reactions amorphous resins remain the chief product. The reactions at comparable stages are more complex than those with aliphatic or simple aromatic aldehydes, since the intermediate alcohol (1) (for example) contains two phenolic hydroxyl groups so providing additional activated positions for further condensation.

A 12% yield of 4 : 4′ : 4″-trihydroxytriphenylmethane (leucaurin) was isolated from the resin resulting from the condensation of phenol with *p*-hydroxybenzaldehyde, but no crystalline compound could be isolated from the products from phenol with *o*- or *m*-hydroxybenzaldehyde. All three hydroxybenzaldehydes condensed with *o*-cresol to give triphenylmethane derivatives: notably, *o*-cresol and *p*-hydroxybenzaldehyde gave an 80% yield of 4 : 4′ : 4″-trihydroxy-3 : 3′-dimethyltriphenylmethane. Triphenylmethane derivatives were also obtained from the condensations of phenol and *o*-methoxybenzaldehyde, phenol and 2-hydroxy-5-methylbenzaldehyde, and *m*-cresol and *p*-hydroxybenzaldehyde.

The yields give some indication of the effect of orientation of phenolic hydroxyl groups on the course of the reaction. In no reaction in which the hypothetical intermediate alcohol or the triphenylmethane product has a free position *para* to a hydroxyl group was any other than a small yield of crystalline compound obtained. Diminution of yield as a result of resin formation is much less apparent where methoxyl groups are concerned: *o*-methoxybenzaldehyde and phenol gave a 21% yield of the expected triphenylmethane compound, and with *p*-methoxybenzaldehyde and anisole (no free positions *para* to methoxyl) a 95% yield of 4 : 4′ : 4″-trimethoxytriphenylmethane is readily obtained. That neither chelation nor steric hindrance can account for the apparent non-formation of triphenylmethane derivatives from, for example, phenol and salicylaldehyde is shown by the reaction between phenol and 2-hydroxy-5-methylbenzaldehyde, which is also chelated but has no free position *para* to the hydroxyl group.

In the condensations of phenol with 2-hydroxy-5-methylbenzaldehyde and of *p*-cresol with *p*-hydroxybenzaldehyde, where a common intermediate alcohol is postulated (only *ortho* condensation being possible in the second reaction), it was found possible to isolate in the early stages a compound, common to both reactions, which had the expected elementary composition and molecular weight. This provides the first clear indication that the formation of triphenylmethane derivatives in these reactions follows courses (1) and (2). In each condensation the aldehyde from the other reaction was also formed:



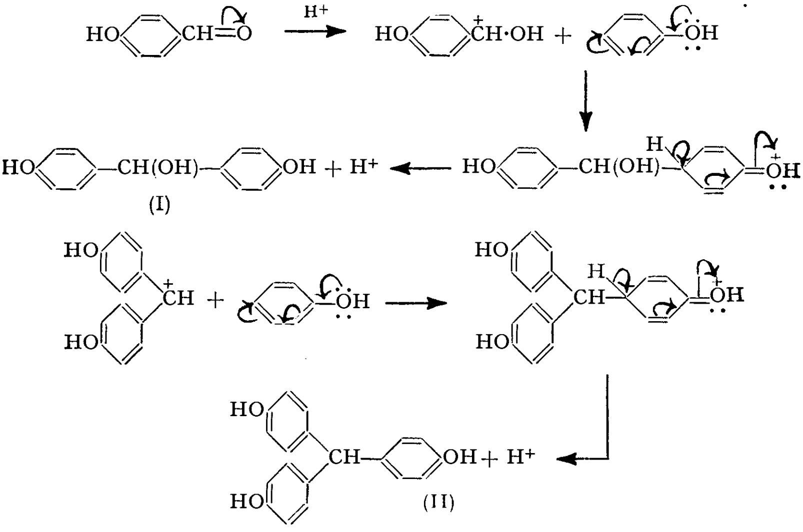
There is earlier evidence that reactions of this kind may be reversible, since Ziegler, Meralla, and Simmler (*Ber.*, 1943, **76**, *B*, 664) found that pure 2-hydroxymethyl-4 : 6-dimethylphenol in acid media gave some di-(2-hydroxy-3 : 5-dimethylphenyl)methane, a process which they accounted for by the supposed reversible fission of the first compound into 2 : 4-dimethylphenol and formaldehyde.

The behaviour in acid media of the intermediate alcohols is of considerable interest. A parallel series of alcohols (the methoxydiphenylmethanols) has been studied by Kenyon and his collaborators (*J.*, 1942, 605; 1951, 386; 1952, 790, 4964). These compounds tend to yield carbonium ions by alkyl–oxygen fission in acid media, a tendency enhanced by the mesomeric effects of *o*- and *p*-methoxyl substituents convergent on the carbinol carbon atom. In comparable dihydroxydiphenylmethanols the change would be:

$$(HO{\cdot}C_6H_4)_2CH{\cdot}OH + H_2SO_4 = (HO{\cdot}C_6H_4)_2\overset{+}{C}H + H_2O + HSO_4^-$$

In phenol–hydroxybenzaldehyde condensations the formation of deep colours on the addition of a few drops of sulphuric acid to glacial acetic acid solutions of the reactants may indicate the presence of carbonium ions.

The formation of triphenylmethane derivatives from phenols and hydroxybenzaldehydes *via* the intermediate alcohols may be represented as in the following example; the mechanism in the second stage [formation of (II) from (I)] is analogous to that suggested for the formation of 2 : 4 : 6 : 2′ : 4′ : 6′-hexamethoxytriphenylmethane from 1 : 3 : 5-trimethoxybenzene and 2 : 4 : 6-trimethoxydiphenylmethanol (Kenyon and Mason, *J.*, 1952, 4964) :



## EXPERIMENTAL

The sulphuric acid used was 36N.

*Condensation of Phenol and* p-*Hydroxybenzaldehyde*.—Sulphuric acid (30 ml.) in glacial acetic acid (50 ml.) was added to phenol (96·3 g.) and *p*-hydroxybenzaldehyde (50 g.) in glacial acetic acid (300 ml.) at 0° with constant stirring. A red colour developed (this was observed also in other condensations). The solution was kept at 10° for 70 hr. and then poured on a mixture of crushed ice and water. The red resin, after having been washed free from phenol and acid, formed a hard mass. Isolation of crystalline material was achieved by extraction with dilute ethanol. The extracts were cooled slowly, whereupon droplets of resin separated; rapid filtration and further cooling caused the deposition of feathery crystals of 4 : 4′ : 4″-trihydroxytriphenylmethane (leucaurin) (10·4 g.), m. p. 239—240°, which separated in large crystals from mixed solvents but persistently retained an orange tint (Found : C, 77·5; H, 5·3. Calc. for $C_{19}H_{16}O_3$ : C, 78·0; H, 5·4%). The triacetyl derivative had m. p. 128° (Found : C, 71·7; H, 5·5; Ac, 31·3%; *M* in benzene, 394. Calc. for $C_{25}H_{22}O_6$ : C, 71·7; H, 5·3; Ac, 30·9%; *M*, 418). The trimethyl ether, prepared by methylation with methyl sulphate and sodium hydroxide, had m. p. and mixed m. p. with an authentic sample 48—49° (Found : C, 78·2; H, 6·9; OMe, 25·2. Calc. for $C_{22}H_{22}O_3$ : C, 79·0; H, 6·6; OMe, 27·7%). Oxidation of the leucaurin with alkaline permanganate yielded traces of brown needles, m. p. 230—232° (possibly aurin, though there is no record of this reaction in the literature).

The resins obtained in the following condensations were treated in a similar way unless otherwise stated.

*Condensation of Phenol and* m-*Hydroxybenzaldehyde*.—Phenol (21·8 g.) was condensed with *m*-hydroxybenzaldehyde (10·7 g.) in glacial acetic acid (50 ml.) by means of sulphuric acid (6 ml.) in glacial acetic acid (12 ml.). The brittle olive-black resin isolated after 36 hr. at 10° yielded no crystalline compound, and the acetylated product (*M*, 590. Calc. : 418) also could not be crystallized.

*Condensation of Phenol and Salicylaldehyde*.—Phenol (50 g.) and salicylaldehyde (26 g.) in glacial acetic acid (125 ml.) were treated with sulphuric acid (15 ml.) in glacial acetic acid (25 ml.), and the mixture kept at 15° for 72 hr. Uncrystallizable red resin only was obtained, and the product on methylation yielded an uncrystallizable substance (*M*, 735. Calc. : 334). Condensations with larger proportions of phenol at 10° for times varied from 6 to 75 hr. yielded no crystalline product.

That the apparent non-formation of 2 : 4′ : 4″-trihydroxytriphenylmethane was not due to self-condensation of salicylaldehyde was shown by the following experiment. Salicylaldehyde (5 g.) in glacial acetic acid (25 ml.) was treated with sulphuric acid (3 ml.) in glacial acetic acid

(5 ml.). After 48 hr. at 10° the mixture was shaken with water, and phenol and salicylaldehyde were removed from the non-aqueous layer by extraction with chloroform. A small quantity (*ca.* 0·08 g.) of uncrystallizable red resin was obtained, most of the phenol and salicylaldehyde having been recovered.

*Attempted Condensation of Anisole and Salicylaldehyde.*—To anisole (24 g.) and salicylaldehyde (12·2 g.) in glacial acetic acid (50 ml.) was added sulphuric acid (6 ml.) in glacial acetic acid (10 ml.). After 72 hr. at 10° no appreciable change was visible. This condensation was not further investigated as reaction at suitably low temperatures was very slow.

*Condensation of Phenol and* o-*Methoxybenzaldehyde.*—Phenol (19 g.) and *o*-methoxybenzaldehyde (11 g.) in glacial acetic acid (60 ml.), kept at 10° for 70 hr. with sulphuric acid (6 ml.) in glacial acetic acid (10 ml.), yielded 6·5 g. of 4 : *4′-dihydroxy-2″-methoxytriphenylmethane*, m. p. 181—183° (Found: C, 78·7; H, 5·7; OMe, 9·0. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9; OMe, 10·1%). The *diacetyl* derivative, after recrystallization from 95% ethanol, had m. p. 105—106° (Found: C, 73·4; H, 5·5; Ac, 22·4. $C_{24}H_{22}O_5$ requires C, 73·8; H, 5·6; Ac, 22·1%).

*Condensation of Phenol and 2-Hydroxy-5-methylbenzaldehyde.*—(*a*) Phenol (8·7 g.) and 2-hydroxy-5-methylbenzaldehyde (5·4 g.) were condensed by sulphuric acid (3 ml.) in glacial acetic acid (5 ml.) at 10° for 70 hr. From the product was isolated 0·51 g. of 2 : 4′ : *4″-trihydroxy-5-methyltriphenylmethane*, m. p. 209—210° after recrystallization from dilute ethanol from which it separated in rosettes (Found: C, 78·0; H, 5·6. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%).

(*b*) To phenol (15·3 g.) and 2-hydroxy-5-methylbenzaldehyde (9·65 g.) in glacial acetic acid (50 ml.) was added sulphuric acid (4·8 ml.) in glacial acetic acid (5 ml.). After 20 hr. at 0° the solution was diluted with water. The resinous layer was dissolved in ether, the ether removed, and the residue steam-distilled. The distillate contained 2-hydroxy-5-methylbenzaldehyde and traces of anhydrobis-6-*m*-hydroxytolualdehyde, m. p. 141° (insoluble in alkali). The residual aqueous solution (with resin) was filtered rapidly; the filtrate when allowed to cool slowly deposited crystals (0·2 g.) of 2 : *4′-dihydroxy-5-methyldiphenylmethanol*, m. p. 175—180° (decomp.) raised to 183—184° (decomp.) by three recrystallizations from dilute ethanol (Found: C, 73·4; H, 6·1%; *M* in benzene, 225. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%; *M*, 230).

(*c*) Phenol (6·9 g.) and 2-hydroxy-5-methylbenzaldehyde (4·9 g.) in glacial acetic acid (25 ml.) were kept with sulphuric acid (2·4 ml.) in glacial acetic acid (6·1 ml.) at 6° for 14 hr. After treatment similar to that in the previous experiment there was obtained a crystalline deposit which by fractional crystallization was separated into 2 : 4′ : 4″-trihydroxy-5-methyltriphenylmethane, m. p. 209—210°, and a small quantity of 2 : 4′-dihydroxy-5-methyldiphenylmethanol, m. p. 183—184° (decomp.). Concentration of the filtrate from the first recrystallization yielded prisms (0·093 g.) of *p*-hydroxybenzaldehyde, m. p. 114—115° undepressed in admixture with an authentic sample of m. p. 115—116°.

*Condensation of* o-*Cresol and* p-*Hydroxybenzaldehyde.*—To *o*-cresol (30 g.) and *p*-hydroxybenzaldehyde (15·5 g.) in glacial acetic acid (50 ml.) was added sulphuric acid (6 ml.) in glacial acetic acid (10 ml.). The mixture set to a sludgy mass within an hour. It was kept for a further 12 hr. at the same temperature (10°) and filtered. The residue was boiled thrice with water, and then yielded 4 : 4′ : *4″-trihydroxy-3* : *3′-dimethyltriphenylmethane* (32·5 g.), m. p. 245—246° (Found: C, 78·7; H, 6·6. $C_{21}H_{20}O_3$ requires C, 78·7; H, 6·2%). The *triacetyl* derivative had m. p. 185° after recrystallization from 95% ethanol (Found: C, 72·9; H, 5·8; Ac, 28·9. $C_{27}H_{26}O_6$ requires C, 72·6; H, 5·8; Ac, 28·9%).

*Condensation of* o-*Cresol and* m-*Hydroxybenzaldehyde.*—To *o*-cresol (35 g.) and *m*-hydroxybenzaldehyde (17·6 g.) in glacial acetic acid (55 ml.) was added sulphuric acid (6 ml.) in glacial acetic acid (12 ml.), and the mixture was kept at 10° for 36 hr. The resin yielded prisms of 3 : 4′ : *4″-trihydroxy-3′* : *3″-dimethyltriphenylmethane* (0·8 g.), m. p. 162° after recrystallization from dilute ethanol (Found: C, 78·8; H, 6·5%).

*Condensation of* o-*Cresol and Salicylaldehyde.*—*o*-Cresol (34·9 g.) and salicylaldehyde (19·5 g.) in glacial acetic acid (60 ml.) were kept with sulphuric acid (10 ml.) in glacial acetic acid (20 ml.) at 10° for 70 hr. The resin yielded yellowish crystals of 2 : 4′ : *4″-trihydroxy-3′* : *3″-dimethyltriphenylmethane* (0·07 g.), m. p. 236° (Found: C, 77·7; H, 6·4%).

*Condensation of* m-*Cresol and* p-*Hydroxybenzaldehyde.*—*m*-Cresol (25·6 g.) and *p*-hydroxybenzaldehyde (12·75 g.) were kept with sulphuric acid (6 ml.) in glacial acetic acid (10 ml.) at 11° for 40 hr. Excess of *m*-cresol was removed by steam-distillation. From the residual resin was isolated 4 : 4′ : *4″-trihydroxy-2* : *2′-dimethyltriphenylmethane* (0·69 g.) in crystals, m. p. 205°, which became red on exposure to air (Found: C, 78·0; H, 6·6%). The *triacetyl* derivative had m. p. 185° after recrystallization from 95% ethanol (Found: C, 72·5; H, 5·7%).

*Condensation of* p-*Cresol and* p-*Hydroxybenzaldehyde*.—(*a*) *p*-Cresol (10·5 g.) and *p*-hydroxybenzaldehyde (5 g.) in glacial acetic acid (30 ml.) were kept with sulphuric acid (3 ml.) in glacial acetic acid (5 ml.) at 10° for 70 hr. Traces of a substance, m. p. 173—175°, were isolated (Found : C, 74·1; H, 6·5. Calc. for $C_{21}H_{20}O_3$ : C, 78·7; H, 6·2. Calc. for $C_{14}H_{14}O_3$ : C, 73·0; H, 6·1%).

(*b*) A solution of *p*-cresol (45 g.) and *p*-hydroxybenzaldehyde (10·2 g.) in glacial acetic acid (50 ml.) was kept with sulphuric acid (5·5 ml.) in glacial acetic acid (4·5 ml.) at 4·5° for 70 hr. It was then diluted with ice-water, and the resinous layer was steam-distilled. The distillate contained 2-hydroxy-5-methylbenzaldehyde, which was isolated (0·331 g.), after extraction with ether, *via* the sodium bisulphite compound; it then had m. p. 55—56°, unchanged in admixture with an authentic sample.

The aqueous liquid remaining from the steam distillation was separated from most of the resin and extracted with ether. After removal of the ether, slow cooling of a hot solution of the residue in 10% ethanol yielded first a little resin, and then faintly pink crystals (0·18 g.) of 2 : 4′-dihydroxy-5-methyldiphenylmethanol, m. p. 179—181° (decomp.) raised by recrystallization to 181—183° (decomp.) undepressed in admixture with the compound obtained in the condensation of phenol with 2-hydroxy-5-methylbenzaldehyde. A further small quantity of the same compound was obtained by extracting with dilute ethanol the residual resin from the steam-distillation.

*Condensation of Anisole and Anisaldehyde*.—Anisole (18 g.) and anisaldehyde (9·5 g.) in glacial acetic acid (40 ml.) were kept with sulphuric acid (18 ml.) and glacial acetic acid (15 ml.) at 11° for 2 weeks : by this time the whole mass had become semi-solid. Vacuum-distillation of the product made in this way is unnecessary (cf. Baeyer and Villiger, *Ber.*, 1902, **35**, 1197). After having been shaken successively with water, sodium hydroxide solution, and water, the product was recrystallized from 95% ethanol, yielding 4 : 4′ : 4″-trimethoxytriphenylmethane (20 g.), m. p. 48—49° after two recrystallizations.

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