726. *Condensation Products of Phenols and Ketones. Part IX.* Dimerides of 4-Chloro- and 4-Bromo-2-isopropenylphenol.*

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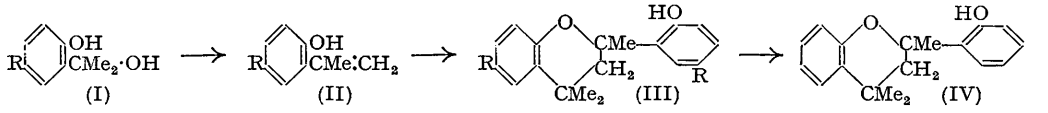
4-Chloro- and 4-bromo-2-*iso*propenylphenol (II; R = Cl and Br) have been prepared from methyl 5-chloro- and 5-bromo-salicylates by reaction with methylmagnesium iodide, and dehydration of the resulting alcohols (I; R = Cl and Br). The dimerides of these *o-iso*propenylphenols are shown to be 6 : 5′-dichloro- and 6 : 5′-dibromo-2′-hydroxy-2 : 4 : 4-trimethylflavan (III; R = Cl and Br respectively) by reduction to the known 2′-hydroxy-2 : 4 : 4-trimethylflavan (IV). The two halogenated flavans give crystalline adducts with dioxan and a number of organic bases.

In Parts VI and VIII of this series (Baker, Curtis, and McOmie, *J.*, 1951, 76; 1952, 1774) it has been proved that the dimerides of certain *o-iso*propenylphenols, namely, 4-*iso*propenyl-*m*-cresol, 3-*iso*propenyl-*o*-cresol, and 3-*iso*propenyl-*p*-cresol, are all derived from 2′-hydroxy-2 : 4 : 4-trimethylflavan (IV) which is itself obtained by dimerisation of *o-iso*propenylphenol. It is shown in the present paper that 4-chloro- and 4-bromo-2-*iso*propenylphenol (II; R = Cl and Br respectively) dimerise similarly to 6 : 5′-dichloro- and 6 : 5′-dibromo-2′-hydroxy-2 : 4 : 4-trimethylflavan (III; R = Cl and Br), the structure of both these products being established by catalytic reduction to the known 2′-hydroxy-2 : 4 : 4-trimethylflavan (IV).



The *iso*propenyl compounds (II; R = Cl and Br) cannot be obtained by direct condensation of *p*-chloro- and *p*-bromo-phenol with acetone owing to the weak reactivity of the aromatic nuclei in these compounds. They were, therefore, prepared by treating the

* Part VIII, *J.*, 1952, 1774.

sodium salts of methyl 5-chloro- and 5-bromo-salicylate with methylmagnesium iodide; the resulting alcohols (I; R = Cl and Br) were then dehydrated by heat. Dimerisation to the flavans (III; R = Cl and Br) was brought about either by hydrogen chloride or by iodine.

Like the other flavans encountered in this work (except that obtained by dimerisation of 3-*iso*-propenyl-*o*-cresol) (see Part VII, Baker, Curtis, and Edwards, *J.*, 1951, 84; Part VIII, Baker, Curtis, and McOmie, *loc. cit.*), these substances form crystalline adducts (all 1 : 1) with dioxan and many organic bases. Of these flavans, that derived from *m*-cresol and acetone, namely 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan, forms the greatest number of crystalline complexes.

Experimental

M. p.s are uncorrected. Microanalyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

2-(5-*Chloro*-2-*hydroxyphenyl*)*propan*-2-*ol* (I; R = Cl).—5-Chlorosalicylic acid (Hirwe, Rana, and Gavankar, *Proc. Indian Acad. Sci.*, 1938, **8**, *A*, 208) gave the methyl ester, b. p. 120°/12 mm., m. p. 47°, in 93% yield (Varnholt, *J. pr. Chem.*, 1887, **36**, 21, gives m. p. 48°).

A mixture of finely divided sodium (2·3 g., 1 mol.) and toluene (40 c.c.) was vigorously stirred in an oil-bath at 100° whilst a solution of methyl 5-chloro-2-hydroxybenzoate (18·7 g., 1 mol.) was slowly added; a vigorous reaction set in with the separation of an orange sodium salt, and heating was continued for 1 hour. The cooled mixture was stirred whilst a solution of methylmagnesium iodide, prepared from magnesium (8·5 g.), methyl iodide (49·7 g.), and ether (60 c.c.), was slowly added, stirring was continued for 2 hours at room temperature, and the mixture was then boiled for 16 hours, cooled, poured into 50% aqueous acetic acid (130 c.c.), and extracted with ether (3 × 25 c.c.). The organic layer was washed with water and with 2N-sodium hydroxide (4 × 50 c.c.), and the alkaline layer after being shaken with ether was heated on the water-bath for 4 hours (to hydrolyse any methyl 5-chloro-2-hydroxybenzoate) and saturated with carbon dioxide. The precipitated solid was collected, washed, dried, and crystallised from light petroleum (b. p. 100—120°), giving 2-(5-*chloro*-2-*hydroxyphenyl*)*propan*-2-*ol* as thick, highly-refracting, hexagonal prisms (17·3 g.), m. p. 100·5° (Found: C, 57·8; H, 6·1; Cl, 18·9. $C_9H_{11}O_2Cl$ requires C, 57·9; H, 5·9; Cl, 19·0%).

6 : 5′-*Dichloro*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* (III; R = Cl).—The alcohol (I; R = Cl) (12·2 g.) was dehydrated by heating it for ½ hour at 180°/560 mm., and then distilled, giving 4-chloro-2-*iso*propenylphenol (II; R = Cl) as an oil (8·1 g.), b. p. 75—80°/1 mm. This compound was then dimerised by cooling it in ice-salt and passing in a little hydrogen chloride; a strongly exothermic reaction occurred and the mixture became very viscous and crystallised after being kept at 40° for 48 hours. Crystallisation from light petroleum (b. p. 100—120°) gave 6 : 5′-*dichloro*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* as rhombic crystals (7·6 g.), m. p 110° (Found: C, 64·1; H, 5·4; Cl, 20·6. $C_{18}H_{18}O_2Cl_2$ requires C, 64·1; H, 5·3; Cl, 21·1%). The *acetyl* derivative, prepared by boiling the flavan (II; R = Cl) (3 g.) for 4 hours with acetic anhydride (20 c.c.) and anhydrous sodium acetate (3 g.) and shaking the mixture with water, separated from ethanol in prismatic needles (2·9 g.), m. p. 130° (Found: C, 63·4; H, 5·6; Cl, 18·3. $C_{20}H_{20}O_3Cl_2$ requires C, 63·3; H, 5·3; Cl, 18·7%).

Reduction of 6 : 5′-*Dichloro*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan. Formation of* 2′-*Hydroxy*-2 : 4 : 4-*trimethylflavan* (IV).—The dichloro-flavan (III; R = Cl) (1·0 g.) in methanol was reduced with hydrogen at 5 atmospheres pressure in presence of powdered anhydrous sodium acetate (0·5 g.) and 2½% palladium–charcoal (1·0 g.) for 5 hours. The filtered solution was poured into water, and the halogen-free solid (0·7 g., 88%), m. p. 96—97°, was crystallised from light petroleum (b. p. 60—80°), giving prisms, m. p. 97°, undepressed when mixed with authentic 2′-hydroxy-2 : 4 : 4-trimethylflavan of the same m. p. (Baker, Curtis, and McOmie, *J.*, 1952, 1780).

2-(5-*Bromo*-2-*hydroxyphenyl*)*propan*-2-*ol* (I; R = Br).—Methyl 5-bromosalicylate was prepared according to Peratoner (*Gazzetta*, 1886, **16**, 405), but chloroform was used as solvent in place of carbon disulphide. A solution of the ester (115 g., 0·5 mol.) in toluene (300 c.c) was slowly added to a vigorously stirred mixture of powdered sodium (11·5 g., 0·5 mol.) and toluene (200 c.c.) heated in an oil-bath at 100°, giving the light yellow sodium salt of the phenolic ester. The cooled mixture was then treated with methylmagnesium iodide (2 mols.) and the product worked up as in the case of the chloro-compound (above), giving 2-(5-*bromo*-2-*hydroxyphenyl*)*propan*-2-*ol* (71 g., 62%) as hexagonal prisms [from light petroleum (b. p. 100—120°)],

m. p. 88—89° (Found: C, 46·5; H, 5·0; Br, 34·6. $C_9H_{11}O_2Br$ requires C, 46·7; H, 4·9; Br, 34·6%).

4-*Bromo*-2-iso*propenylphenol* (II; R = Br).—The alcohol (I; R = Br) (71 g.) was heated for ½ hour at 180°/560 mm., and then distilled, giving 4-*bromo*-2-iso*propenylphenol* as a viscous oil (45 g., 70%), b. p. 89—93°/2 mm. (Found: C, 50·4; H, 4·7; Br, 37·2. C_9H_9OBr requires C, 50·7; H, 4·2; Br, 37·6%).

6 : 5′-*Dibromo*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* (III; R = Br).—4-Bromo-2-*iso*propenylphenol (II; R = Br) (4·6 g.) was dimerised (*a*) by addition of a crystal of iodine and warming on a water bath, the dimeride (III; R = Br) solidifying, after cooling, to a sticky mass, or (*b*) by passing in dry hydrogen chloride whilst cooling the whole in ice-salt [the dimeride separated after 5 minutes as in (*a*)]. In each case the product was first crystallised from light petroleum (b. p. 100—120°) (25 c.c.) and dioxan (1 c.c.) as the dioxan adduct, which was then heated (100°/1 mm.) till no further loss in weight occurred, and the free 6 : 5′-*dibromo*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* (III; R = Br) recrystallised from light petroleum (b. p. 100—120°) as rhombic crystals, m. p. 96° (Found: C, 50·6; H, 4·3; Br, 37·3. $C_{18}H_{18}O_2Br_2$ requires C, 50·6; H, 4·2; Br, 37·6%). The *acetyl* derivative, prepared by refluxing the flavan (III; R = Br) (0·5 g.) for 4 hours with acetic anhydride (2 c.c.) and pouring into water, separated from light petroleum (b. p. 100—120°) in prisms (0·48 g., 87%), m. p. 134° (Found: C, 51·0; H, 4·1; Br, 34·3. $C_{20}H_{20}O_3Br_2$ requires C, 50·3; H, 4·3; Br, 34·9%). The hydroxyflavan (III; R = Br) was insoluble in dilute aqueous sodium hydroxide, and did not give a colour with alcoholic ferric chloride. In concentrated sulphuric acid it gave a deep orange solution.

Reduction of 6 : 5′-*Dibromo*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* (III; R = Br). *Formation of* 2′-*Hydroxy*-2 : 4 : 4-*trimethylflavan* (IV).—The flavan (III; R = Br) (0·4 g.) in ethanol (30 c.c.) was reduced with hydrogen at 5 atmospheres in the presence of powdered anhydrous sodium acetate (0·2 g.) and palladium black (0·05 g.) for 6 hours. The product, isolated as before, proved to be 2′-hydroxy-2 : 4 : 4-trimethylflavan (IV), m. p. and mixed m. p. 97° (yield of recrystallised material 0·2 g., 80%) (Found: C, 80·1; H, 7·3. Calc. for $C_{18}H_{20}O_2$: C, 80·4; H, 7·4%).

Adducts.—The *adducts* (all 1 : 1) obtained are listed in the Table. Neither compound forms adducts with the usual laboratory solvents or with quinoline, diethyl ketone, di*iso*propyl ketone, mesityl oxide, di*iso*butylamine, or β-picoline. The chloro-compound does not form adducts with di-*n*-propyl ketone, γ-picoline, or 2 : 4- or 2 : 6-lutidene; neither does the bromo-compound with di-*n*-butyl ether, di*iso*butyl ketone, di-*n*-propyl-, di-*n*-butyl-, or diethyl-amine, di*iso*propylamine, *cyclo*hexylamine, α-picoline, or 2-bromopyridine.

Addenda	M. p.*	Found, %				Required, %			
		C	H	N	Loss*	C	H	N	Loss
6 : 5′-*Dichloro*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* (III; R = Cl).									
Dioxan	97°	62·4	6·3	—	20·3 [a]	62·1	6·1	—	20·7
Diethylamine	95—96	—	—	3·0	17·8	—	—	3·3	17·8
Di-*n*-propylamine	87—88	65·3	7·5	3·5	23·0 [b]	65·7	7·5	3·2	22·8
Di*iso*propylamine	97—98	—	—	2·8	22·8	—	—	3·2	22·8
Di-*n*-butylamine	66	—	—	2·9	27·3	—	—	3·0	27·7
*cyclo*Hexylamine	94	—	—	3·0	23·1	—	—	3·2	23·0
Morpholine	134	—	—	4·0	20·9	—	—	3·5	20·5
Piperidine	124	—	—	3·2	19·9	—	—	3·3	20·0
Pyridine	105	—	—	3·2	19·4	—	—	3·3	19·0
α-Picoline	86—87	—	—	3·2	22·0	—	—	3·3	21·8
6 : 5′-*Dibromo*-2′-*hydroxy*-2 : 4 : 4-*trimethylflavan* (III; R = Br).									
Tetrahydrofuran	125—126	53·0	5·5	—	14·3 [c]	53·0	5·3	—	14·4
Dioxan	114	52·0	5·1	—	17·0 [d]	51·5	5·1	—	17·1
Morpholine	146	—	—	2·7	16·7	—	—	2·7	16·9
Piperidine	141	—	—	2·6	16·2	—	—	2·7	16·3
Pyridine	120	—	—	2·9	15·8	—	—	3·1	15·6
3-Bromopyridine	93—94	—	—	2·0	26·6	—	—	2·3	27·0

* Dissociation. † At 100°/1 mm.

[a] Found: Cl, 16·6. Reqd.: Cl, 16·7%. [b] Found: Cl, 16·0. Reqd.: Cl, 16·2%. [c] Found: Br, 31·8. Reqd.: Br, 32·0%. [d] Found: Br, 32·3. Reqd.: Br, 31·3%.

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