328. *Condensation Products of Phenols and Ketones. Part VIII.* Proof of the Flavan Structure of the Dimerides of* o-iso*Propenylphenol, and of* 3-iso*Propenyl*-o- *and* -p-*cresol.*†

By Wilson Baker, R. F. Curtis, and J. F. W. McOmie.

The dimeride of 4-*iso*propenyl-*m*-cresol, which was proved in Part VI to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I), has been degraded by oxidation and partial decarboxylation to 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV). This acid has also been obtained by the degradation of the dimerides of *o-iso*propenylphenol and of 3-*iso*propenyl-*o*- and -*p*-cresol, proving that these compounds are all 2′-hydroxy-2 : 4 : 4-trimethylflavans.

Reaction of 2 : 4 : 4-trimethylchroman-2-carboxylic acid and homologues with copper chromite–quinoline is abnormal, as decarboxylation does not occur; instead, loss of the elements of carbon monoxide leads to 2-hydroxy-2 : 4 : 4-trimethylchromans, and simultaneous loss of the elements of carbon monoxide and water to 2 : 4 : 4-trimethylchromens. The tendency of 2′-hydroxy-2 : 4 : 4-trimethylflavans to form crystalline complexes (Part VII *) is further illustrated by the examples now given; an exception is provided by the dimeride of 3-*iso*propenyl-*o*-cresol, which is sterically hindered.

m-Cresol and acetone condense in presence of hydrogen chloride to give a compound $C_{20}H_{24}O_2$, which is also obtained by dimerisation of the intermediate 4-*iso*propenyl-*m*-cresol. A full account of this substance was given in Part VI (Baker, Curtis, and McOmie, *J.*, 1951, 76), where it was proved to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I) by an unambiguous synthesis of the oxidation product 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (II). It was desired to extend this investigation to other products obtained

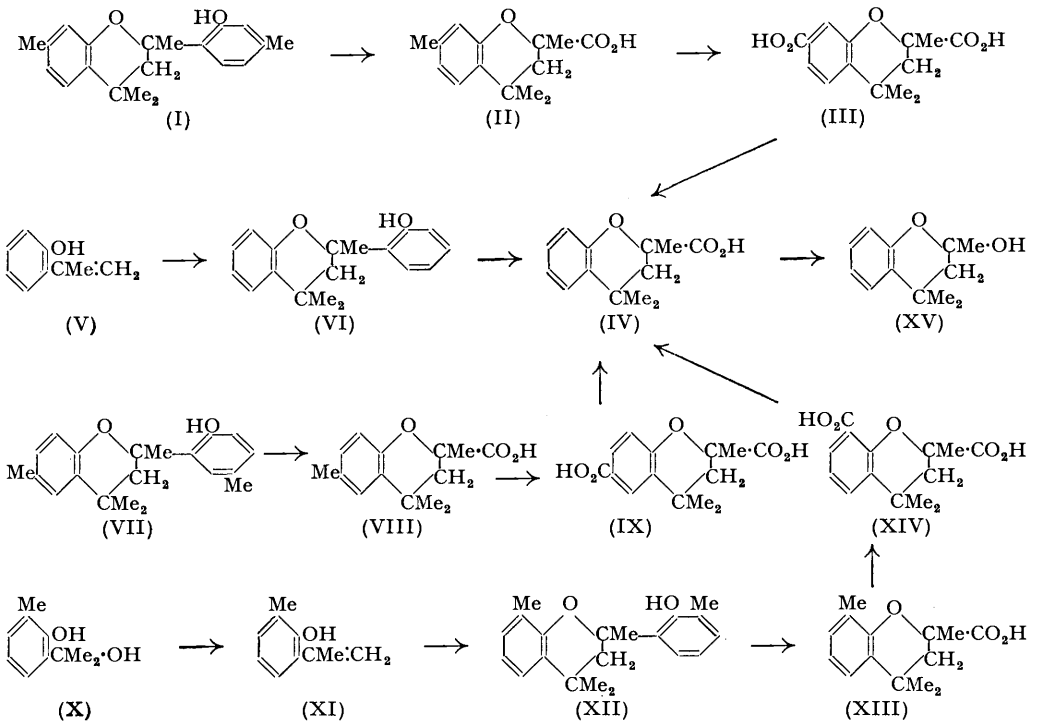
* Part VII, *J.*, 1951, 84.

† The nomenclature of cresols in this paper is based on Me = 1.

either by the direct condensation of acetone with certain phenols, or by the dimerisation of *o-iso*propenylphenols prepared in other ways. The probability that these compounds were all derived from 2′-hydroxy-2 : 4 : 4-trimethylflavan was first advanced by Baker and Besly (*Nature*, 1939, **144**, 865; Part V, *J.*, 1940, 1105), but factual evidence was then only available in the case of the dimeride of 4-*iso*propenyl-*m*-cresol. The suggestion that the dimerides had the same basic structure was made on the grounds that they were prepared by similar methods, that they were all saturated, monohydroxy-phenols possessing extremely weak phenolic functions, and that they reverted to the *o-iso*propenylphenols when distilled at atmospheric pressure. However, to adopt the method of proof employed in Part VI in the case of the dimeride of 4-*iso*propenyl-*m*-cresol would have involved a lengthy total synthesis of a separate substituted 2 : 4 : 4-trimethylchroman-2-carboxylic acid in each case.

The decision was therefore made to attempt the preparation from each of the supposed flavans of a common degradation product which would contain sufficient of the original structure to afford an unambiguous proof of the nature of the flavan. The obvious compound for this purpose was 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV), for the following reasons : (1) the carboxyl group would result from the oxidation of any hydroxyphenyl group in position 2, and a carboxyl group in this position is known to be very resistant towards decarboxylation (Part V, *loc. cit.*); (2) substituent groups of a wide variety of types, including methyl, would be capable of elimination from the benzo-ring, and even very vigorous methods might be used owing to the great stability of acids of the type (IV).

The acid (IV) was first prepared from the *m*-cresol–acetone condensation product (I) of established structure, *via* 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (II), the 7-methyl group of which was oxidised by boiling alkaline potassium permanganate to give 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III). This acid (III) lost the aromatic

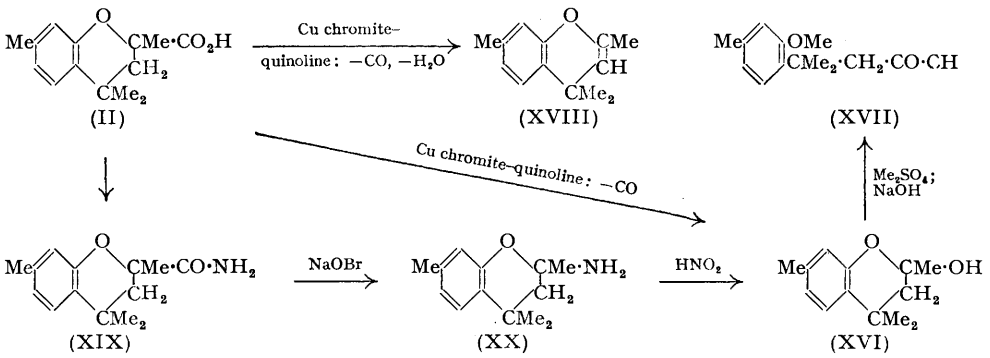


carboxyl group when boiled with copper chromite in quinoline and thus yielded the crystalline reference compound 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV) (for a by-product of this reaction see p. 1776).

*o-iso*Propenylphenol (V) is not formed by the condensation of phenol with acetone under acid conditions, as reaction occurs in the *p*-position to the hydroxyl group, giving 2 : 2′-di-*p*-hydroxyphenylpropane (Dianin, *J. Russ. Phys. Chem. Soc.*, 1891, **23**, 488, 523, 601). It was therefore prepared from the sodium salt of methyl salicylate and methylmagnesium iodide, followed by thermal dehydration of the resulting tertiary carbinol (Fries, Gross-Selbeck, and Wicke, *Annalen*, 1914, **402**, 305). Dimerisation was effected with anhydrous hydrogen chloride, and the crystalline dimeride (characterised as the acetyl derivative and the methyl ether) was then oxidised with potassium permanganate in boiling acetone, giving 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV). The dimeride of *o-iso*propenylphenol must therefore be 2′-hydroxy-2 : 4 : 4-trimethylflavan (VI).

With *p*-cresol the proof of structure of the condensation product with acetone followed exactly the steps used in the case of the derivative from *m*-cresol. The condensation product, finally proved to be 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII), was degraded by potassium permanganate in acetone to 2 : 4 : 4 : 6-tetramethylchroman-2-carboxylic acid (VIII), then further oxidised by boiling alkaline potassium permanganate to 2 : 4 : 4-trimethylchroman-2 : 6-dicarboxylic acid (IX), and finally partially decarboxylated with copper chromite in boiling quinoline to give once again 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV). The formation of the last acid proves the structures assigned to the compounds (VII), (VIII), and (IX).

The final case studied was that of the dimeride (XII) of 3-*iso*propenyl-*o*-cresol (XI). The dimeride (XII) is not obtained by condensation of acetone with *o*-cresol in presence of acid, as attack occurs in the *p*-position to the hydroxyl group, giving either 6 : 6′-dihydroxy-3 : 3 : 5 : 3′ : 3′ : 5′-hexamethylbis-1 : 1′-*spiro*indane, or 2 : 2-di-(4-hydroxy-3-methylphenyl)propane, according to the reaction conditions (see Part IV, Baker and Besly, *J.*, 1939, 1421). 3-*iso*Propenyl-*o*-cresol was obtained from the sodium salt of methyl *o*-cresotate by reaction with methylmagnesium iodide and thermal dehydration of the resulting (2-hydroxy-3-methylphenyl)dimethylcarbinol (X). Dimerisation of (XI) with hydrogen chloride proved very slow, but was conveniently carried out by treatment for a few minutes with a trace of iodine at 60°, and the crystalline dimeride was then proved to be 2′-hydroxy-2 : 4 : 4 : 8 : 3′-pentamethylflavan (XII) by reactions parallel to those employed in the *p*-cresol series, *i.e.*, *via* (XIII) and (XIV) to (IV).



During this work a second common degradation product of the four dimerides was unexpectedly encountered. It was produced during the decarboxylation of the three dicarboxylic acids (III), (IX), and (XIV) by means of copper chromite in boiling quinoline, and also in the same way from the monocarboxylic acid (IV) from which it is doubtless derived in all cases. From the acid (IV) this new compound, $C_{12}H_{16}O_2$, is formed by the loss of the elements of carbon monoxide, and, since it is neither phenolic nor acidic and is saturated, it must be 2-hydroxy-2 : 4 : 4-trimethylchroman (XV) which is a cyclic semiketal. As this compound was not available in quantity, its homologue, obtained similarly from the acid (II) derived from the *m*-cresol–acetone condensation product, was investigated, and was proved by its reactions to be 2-hydroxy-2 : 4 : 4 : 7-tetramethyl-

chroman (XVI). Methylation of (XVI) with methyl sulphate and alkali yielded 4-(2-methoxy-4-methylphenyl)-4-methylpentan-2-one (XVII), a ketone which had been previously synthesised and characterised as its 2 : 4-dinitrophenylhydrazone (Part VI, *loc. cit.*); and, as a semi-ketal, (XVI) reacted with ethanol and hydrogen chloride to give 2-ethoxy-2 : 4 : 4 : 7-tetramethylchroman. The analogous compounds, 2-hydroxy-2 : 4 : 4 : 6- and -2 : 4 : 4 : 8-tetramethylchroman, were obtained under similar reaction conditions from the acids (VIII) and (XIII). The ketone (XVII) undergoes a complex reaction with acetic–hydrobromic acids, giving 4 : 4 : 7 : 4′ : 4′ : 7′-hexamethylbis-2 : 2′-*spiro*chroman (Baker and Besly, *J.*, 1939, 199).

These 2-hydroxy-2 : 4 : 4-trimethylchromans differ widely in their properties from compounds claimed to have the same structures (Niederl, *J. Amer. Chem. Soc.*, 1929, **51**, 2426) which were prepared by the condensation of phenol or a cresol with mesityl oxide in presence of concentrated sulphuric acid. The melting points given by Niederl, except for that of the supposed 2-hydroxy-2 : 4 : 4-trimethylchroman (XV), differ from those which we obtain, and our 2-hydroxy-2 : 4 : 4-trimethylchromans, unlike Niederl's compounds, are stable to acids and alkalis and do not readily undergo dehydration. No proof of structure was advanced by Niederl, and moreover we have not been able to repeat his experiments, from which we have obtained only red tars; failure has also been reported by Smith and Prichard (*ibid.*, 1940, **62**, 771).

The observation that the carboxylic acids (II), (III), (IV), (IX), and (XIV), which resemble tertiary carboxylic acids in that they possess no α-hydrogen atom, lose the elements of carbon monoxide (the actual liberation of carbon monoxide has not been established) and yield 2-hydroxychromans when boiled in quinoline with copper chromite, may be a general reaction for this type of compound. Olefin formation has also been observed when the acids (II) and (XIII) are boiled with copper chromite in quinoline (the necessarily small scale of the reactions precluded the isolation of olefins in the other cases). From the acid (II) the liquid olefin, 2 : 4 : 4 : 7-tetramethylchromen (XVIII), was isolated and characterised as its tribromo-dibromide, and this derivative was also obtained by the action of bromine on 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI). Attempts to dehydrate the hydroxychroman (XVI) to the chromen (XVIII) by boiling it in quinoline either with or without copper chromite were unsuccessful, and it is concluded that these 2-methylchroman-2-carboxylic acids, when boiled with copper chromite–quinoline, undergo simultaneous decompositions to yield both the 2-hydroxychromans and the chromens. In connection with these reactions, tertiary acids are known to lose carbon monoxide when treated with concentrated sulphuric acid [see Bistrzycki and Mauron, *Ber.*, 1907, **40**, 4370 and references there cited; this behaviour is also shown by the acid (II), see Part VI, *loc. cit.*, p. 77], with formation of tertiary alcohols or olefins (Bistrzycki and Reintke, *Ber.*, 1905, **38**, 839), but a much closer analogy is provided by α-methoxy-acids, R·CH(OMe)·CO_2H (R = *n*-C_5H_{11}, *n*-$C_{10}H_{21}$, or *n*-$C_{16}H_{33}$) which, when distilled with copper, give carbon monoxide, methanol, and aldehydes R·CHO (Darzens and Levy, *Compt. rend.*, 1933, **196**, 348). This type of decomposition would be followed in the cases of the chroman-2-carboxylic acids by semi-ketal cyclisation to the 2-hydroxychromans.

Additional proof of the structure of 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) was obtained by its preparation from 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (II) by an alternative method. The amide (XIX) of the acid (II) was submitted to the Hofmann degradation with potassium hypobromite, giving 2-amino-2 : 4 : 4 : 7-tetramethylchroman (XX), and when this was treated with nitrous acid it gave in 10% yield 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) identical with that prepared previously.

Preparation of o-iso*Propenylphenols and their Dimerides.*—The previous work on 4-*iso*propenyl-*m*-cresol and its dimeride was reviewed in Part VI (*loc. cit.*). The occasion of the establishment of the flavan structures of the dimerides mentioned in the title is an appropriate one on which to review the somewhat confused earlier work on these compounds.

o-iso*Propenylphenol* (V) *and its dimeride* (VI). *o-iso*Propenylphenol (V) has been reported to be preparable from: (1) methylmagnesium iodide and methyl salicylate followed by dehydration of the tertiary carbinol (Béhal and Tiffeneau, *Bull. Soc. chim.*,

1908, **3**, 315; details not given); (2) methyl salicylate methoxymethyl ether and methylmagnesium iodide, followed by acid hydrolysis (Hoering and Baum, D.R.-P. 208,886, 208,962; see *Chem. Zentr.*, 1909, I, 1522); (3) 2-hydroxy-β-methylcinnamic acid by the action of heat (Fries and Volk, *Annalen*, 1911, **379**, 95); (4) the sodium salt of methyl salicylate and methylmagnesium iodide (Fries, Gross-Selbeck, and Wicke, *ibid.*, 1914, **402**, 305); (5) phenol, allyl alcohol, and sulphuric acid (Niederl, Smith, and McGreal, *J. Amer. Chem. Soc.*, 1931, **53**, 3391); (6) phenyl *iso*propenyl ether by rearrangement (Niederl and Storch, *ibid.*, 1933, **55**, 284); (7) phenol, allyl chloride, and sulphuric acid (Smith and Niederl, *ibid.*, p. 4151); (8) phenol, allyl alcohol or trimethylene glycol, and phosphoric acid (Tchitchibabin, *Compt. rend.*, 1934, **198**, 1239; *Bull. Soc. chim.*, 1935, **2**, 517). There is considerable doubt whether methods (5)—(8) give *o-iso*propenylphenol; no characterisation of the products was attempted apart from the boiling points.

The dimeride, m. p. 97°, of *o-iso*propenylphenol was first prepared by reaction of the monomer with hydrogen chloride in ether (Fries, Gross-Selbeck, and Wicke, *loc. cit.*). It was probably also obtained by Smith and Prichard (*J. Amer. Chem. Soc.*, 1940, **62**, 777) as a product, m. p. 95—96°, from the action of hydrogen chloride on *o*-hydroxyphenyldimethylcarbinol in benzene; no opinion was expressed as to its structure. It has also been prepared from methylmagnesium iodide and *cis*-disalicylide (Baker, Ollis, and Zealley, *J.*, 1951, 201). Polymers of *o-iso*propenylphenol were reported to occur in the residue from the destructive distillation of 2 : 2-di-*p*-hydroxyphenylpropane prepared by condensation of acetone with phenol in presence of acids (von Braun, Anton, Haensel, and Werner, *Annalen*, 1929, **472**, 65). The ultra-violet absorption spectra measurements by Grumez (*Ann. Chim. Phys.*, 1938, **10**, 378, 388) require reinterpretation in terms of the flavan structure (VI) now established.

3-iso*Propenyl*-p-*cresol and its dimeride* (VII). 3-*iso*Propenyl-*p*-cresol has been prepared by the action of heat on β-(2-hydroxy-5-methylphenyl)-β-methylacrylic acid (Fries and Fickewirth, *Ber.*, 1908, **41**, 372; Fries and Volk, *Annalen*, 1911, **379**, 95). Guillaumin (*Bull. Soc. chim.*, 1910, **7**, 379) reported its preparation from methyl *p*-cresotate and methylmagnesium iodide, followed by dehydration of the tertiary alcohol with acetic anhydride and alkaline hydrolysis of the resulting *O*-acetyl derivative of the *iso*propenyl compound; Fries and Volk (*loc. cit.*) were, however, unable to confirm this work. The preparation of 3-*iso*propenyl-*p*-cresol from *p*-cresol, allyl alcohol, or allyl chloride, and sulphuric acid, and by rearrangement of *iso*propenyl *p*-tolyl ether, has been reported by Neiderl *et al.* (*loc. cit.*), but proof of their claims is lacking.

The dimeride (VII), formed from the monomer either on storage alone or by heating it with aqueous hydrochloric acid, is a resin, which distils unchanged *in vacuo*, but reverts to the monomer when distilled at atmospheric pressure (Fries and Fickewirth, *loc. cit.*); it possesses very weak phenolic properties (Fries, Gross-Selbeck, and Wicke, *loc. cit.*). Fries and Fickewirth (*Annalen*, 1908, **362**, 46) also obtained the dimeride from 4 : 6-dimethylcoumarin by reduction with zinc dust and alkali, followed by dehydration and dimerisation with acid.

Direct production of the dimeride from *p*-cresol, acetone, and hydrogen chloride is described in patents [Schering-Kahlbaum A.-G., B.P. 273,684, 279,856 (1927); F.P. 636,119 (1927); Swiss P. 127,522 (1927); U.S.P. 1,696,769 (1927)]; a crystalline *O*-acetyl derivative was obtained. The preparation now recorded, based on that given by Baker, Curtis, and McOmie (Part VI, *loc. cit.*) for the production of the *m*-cresol analogue, gives the pure compound in 25% yield; its isolation is greatly facilitated by the new observation that the non-crystalline dimeride very readily forms a well-crystallised adduct with one mol. of dioxan. Crystalline adducts with other solvents are mentioned on pp. 1781 and 1785. This dimeride–dioxan adduct loses some dioxan on exposure to the air and gives a powder, but this does not induce crystallisation of a solution of the free dimeride in light petroleum (contrast the behaviour of the related diethyl ether adduct of the dimeride of 4-*iso*propenyl-*m*-cresol; Part VI, *loc. cit.*). The pure dioxan adduct loses all solvent at 100° *in vacuo*, giving a resin which has failed to crystallise; the physical properties of this free dimeride, as are those of the *m*-cresol analogue, are being investigated at the Butterwick Research Laboratories of Imperial Chemical Industries Limited,

Welwyn. The previously described chemical properties of the dimeride (VII) have been confirmed.

In an attempt to improve the yield of 2 : 4 : 4 : 6-tetramethylchroman-2-carboxylic acid (VIII) by oxidation of the dimeride (VII), an amino-group was introduced into position 3′ in the hope that this *o*-aminophenol would be easily oxidised. Nitration of the acetyl derivative of (VII), followed by hydrolysis, gave 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethyl-3′-nitroflavan which showed the properties of an *o*-nitrophenol, and gave well-crystalline adducts with ethyl ether, methanol, and diethylamine. Reduction with tin and hydrochloric acid led to a very stable stannichloride, but reaction with hydrogen and Raney nickel gave 3′-amino-2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan, characterised as its *N*-acetyl derivative. This amino-compound gave crystalline adducts with methanol and diethylamine. Oxidation with potassium permanganate in acetone gave only yellow quinonoid material.

3-iso*Propenyl-o-cresol* (XI) *and its dimeride* (XII). 3-*iso*Propenyl-*o*-cresol (XI) was prepared by Béhal and Tiffeneau (*Bull. Soc. chim.*, 1910, **7**, 330) by the method used for *o*-*iso*propenylphenol (V) (above). Guillaumin (*loc. cit.*) described the preparation of (XI) from methyl *o*-cresotate by the process claimed to yield 3-*iso*propenyl-*p*-cresol (above), but doubts have been expressed as to the validity of this work (Fries and Volk, *loc. cit.*). The preparation of (XI) by several methods is reported by Niederl *et al.* (*loc. cit.*), but as with the similar claims to have prepared (V) and 3-*iso*propenyl-*p*-cresol, adequate evidence of success is lacking.

The monomer (XI) and the dimeride (XII) were obtained as described above; the latter has not previously been prepared. The dimeride yielded an *O*-acetyl derivative, but possessed only very weak phenolic properties.

Crystal Complexes formed by 2′-Hydroxy-2 : 4 : 4-trimethylflavans.—The property of forming crystalline adducts with many solvents is characteristic of these compounds. Those formed by 2-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I) were described by Baker, Curtis, and Edwards (Part VII, *loc. cit.*). Crystal complexes given by 2′-hydroxy-2 : 4 : 4-trimethylflavan (VI) and by 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII) are given on pp. 1781 and 1785.

2′-Hydroxy-2 : 4 : 4 : 8 : 3′-pentamethylflavan (XII) has failed to give any such adducts, and this is attributed mainly to the steric effect of the methyl group in position 8. Since all the solvents with which complexes are formed are proton acceptors (bases, ethers, and ketones, although the last two are very weak acceptors), salt formation involving the 2′-hydroxyl group may play a part in the formation of the adducts; hydrogen bonding between the two oxygen atoms may also be involved. It is probable that the solvent molecules in the crystal have their functional groups close to the two oxygen atoms of the 2′-hydroxyflavan, and scale models show that in this case a methyl group in position 8 would exert a considerable, if not a prohibitive, effect against the formation of such complexes. Support for this general structure is derived from the fact that the adducts (over 40 are now known) containing monofunctional molecules are all of the 1 : 1 type, whilst the difunctional molecules dioxan and morpholine give more than usually stable adducts with a flavan : solvent ratio of 2 : 1 in the cases of flavans (I) and (VI), although the adducts from (I) contain, in addition, two molecules of water. However, adducts given by the flavan (VII) with dioxan or morpholine have the 1 : 1 ratio of the components.

Experimental

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

2 : 4 : 4-*Trimethylchroman-2 : 7-dicarboxylic Acid* (III).—2 : 4 : 4 : 7-Tetramethylchroman-2-carboxylic acid (II) (2·0 g.; Part VI, p. 80) in 5% aqueous sodium carbonate (100 c.c.) was boiled, and potassium permanganate (*ca.* 10 g.) added during 15 minutes. Boiling was continued for 20 minutes, sulphur dioxide passed in, and the solid collected at 0°, washed, and dried (yield 1·96 g.; m. p. 248—250°). Two recrystallisations from light petroleum (b. p. 60—80°)–ethyl acetate gave 2 : 4 : 4-*trimethylchroman-2 : 7-dicarboxylic acid* (III) as fine, colourless

needles (1·7 g.), m. p. 261° (Found: C, 63·6; H, 6·1%; equiv., 133. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%; equiv., 132).

Reaction of 2 : 4 : 4-*Trimethylchroman*-2 : 7-*dicarboxylic Acid* (III) *with Copper Chromite–Quinoline.* 2 : 4 : 4-*Trimethylchroman*-2-*carboxylic Acid* (IV) *and* 2-*Hydroxy*-2 : 4 : 4-*Trimethylchroman* (XV).—The acid (III) could not be decarboxylated by (1) soda–lime at 370°, (2) potassium hydroxide at 260° or 300°, (3) heating it with copper chromite in dimethyl- or diethyl-aniline. Success was achieved as below, but the time of heating is critical.

The acid (III) (200 mg.), freshly distilled quinoline (4 c.c.), and copper chromite (400 mg.) were placed in a metal-bath at 260° and boiled for 20 minutes; liberated water caused vigorous bumping. The cooled mixture was poured into concentrated hydrochloric acid (15 c.c.), digested on the water-bath for 15 minutes, diluted with water (20 c.c.), and filtered through sand. The residue was washed with ether (30 c.c.), and the ether combined with the filtrate, shaken, and separated. The aqueous layer was extracted with ether (10 c.c.), and the combined organic extracts were then shaken with saturated sodium hydrogen carbonate which, on acidification, yielded colourless acidic material (47 mg.; m. p. 162—164°). Sublimation at 170°/360 mm. gave colourless needles (29 mg.), m. p. 167—168°, and recrystallisation from benzene–light petroleum (b. p. 60—80°) (1 c.c.) gave 2 : 4 : 4-*trimethylchroman*-2-*carboxylic acid* (IV) as thin rhombs, m. p. 172° (Found: C, 71·0; H, 7·3%; equiv., 216. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%; equiv., 220). The residue from the sublimation (15 mg.; m. p. 258°) had m. p. 258—261° on admixture with a specimen of 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III), m. p. 261°.

The ethereal layer containing neutral material yielded a yellow oil which solidified, and crystallised from light petroleum (b. p. 40—60°) in stout prisms, m. p. 90° (28 mg.). A further crystallisation raised the m. p. of this 2-*hydroxy*-2 : 4 : 4-*trimethylchroman* (XV) to 91° (Found: C, 75·3; H, 8·5. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%).

o-iso*Propenylphenol* (V) *and* 2′-*Hydroxy*-2 : 4 : 4-*trimethylflavan* (VI).—This compound was prepared as described by Fries, Gross-Selbeck, and Wicke (*Annalen*, 1914, **402**, 305), the intermediate *o*-hydroxyphenyldimethylcarbinol being conveniently dehydrated by heating it in an oil-bath at 180°/560 mm. for ½ hour. The residue was distilled twice through a column, giving *o-iso*propenylphenol (V) as an oil, b. p. 39°/0·4 mm. (Found: C, 80·2; H, 7·3. Calc. for $C_9H_{10}O$: C, 80·6; H, 7·5%). The flavan (VI) was prepared from *o-iso*propenylphenol (V) (30·2 g.) by treatment with a little anhydrous hydrogen chloride while being cooled in water. An exothermic reaction occurred and after 20 minutes the product had become resinous; crystallisation occurred after it had been kept at 40° for 12 hours. The solution in ether (60 c.c.), after extraction with 2N-sodium hydroxide (2 × 30 c.c.), left a viscous oil which gave the flavan (VI) by crystallisation from light petroleum (30 c.c.; b. p. 60—80°) as thin prisms (26·7 g.) (dimorphic, also separates as rhombs), m. p. 97° (Found: C, 80·8; H, 7·5. Calc. for $C_{18}H_{20}O_2$: C, 80·6; H, 7·5%). This compound was characterised as the acetyl derivative, which separated from light petroleum (b. p. 60—80°) in hexagonal prisms, m. p. 97° (Found: C, 77·4; H, 7·1. Calc. for $C_{20}H_{22}O_3$: C, 77·4; H, 7·1%).

2′-*Methoxy*-2 : 4 : 4-*trimethylflavan.*—The flavan (VI) (0·5 g.) and methyl iodide (2 c.c.) were added to a solution of sodium (0·1 g.) in dry methanol (10 c.c.), and the mixture boiled for 2 hours. Excess of methyl iodide and methanol was distilled off, and the residue diluted with water, giving an oil which solidified. Two recrystallisations from aqueous methanol gave the methyl ether as fine prisms (0·275 g.), m. p. 116—117° (Found: C, 80·8; H, 7·7. Calc. for $C_{19}H_{22}O_2$: C, 80·8; H, 7·8%).

2 : 4 : 4-*Trimethylchroman*-2-*carboxylic Acid* (IV).—2′-Hydroxy-2 : 4 : 4-trimethylflavan (VI) (3 g.) in acetone (30 c.c.) was oxidised by rapid addition of a solution of potassium permanganate in acetone (900 c.c.; saturated at the b. p.). The mixture boiled spontaneously and reduction of the permanganate was complete in 1 minute. The acetone was then distilled from the reaction mixture and the residue was shaken with water (100 c.c.), sodium pyrosulphite (metabisulphite) (*ca.* 40 g.), and 2N-hydrochloric acid (40 c.c.), and sulphur dioxide was passed in until the solution was colourless. Two similar oxidations were carried out, and the united products extracted with ether (300 c.c., then 100 c.c.). The ethereal solution was washed with water and shaken 4 times with saturated sodium hydrogen carbonate solution, and the alkaline layer washed with ether and then acidified with hydrochloric acid, giving a pale yellow solid, which was collected at 0° and dried (yield 4·3 g.). Two recrystallisations from benzene (15 c.c.) gave the acid (IV) as rhombs (2·6 g., 35%), m. p. 171—172° alone or mixed with the specimen previously prepared. The identity of the two specimens was also confirmed by *X*-ray powder photographs kindly taken by Dr. T. H. Beavan of this Department.

2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII).—*p*-Cresol (324 g.) in acetone (116 g.) was saturated with hydrogen chloride at 0°, and the mixture was left in the ice-bath and slowly allowed to reach room temperature. After 2 days the dark product was stirred into 2N-aqueous sodium hydroxide (1 l.), and then became colourless. Dioxan (200 g.) was added, the mixture stirred on the water-bath for 20 minutes and left overnight at 0°, and the solid collected dried over phosphoric anhydride *in vacuo*, and recrystallised from light petroleum (300 c.c.; b. p. 60—80°) with the addition of dioxan (5 c.c.), giving the pure *flavan–dioxan* complex (145 g., 25%) as minute rhombs, m. p. (dissociation, rapid heating) 88—90° (Found : C, 75·3; H, 8·3. $C_{20}H_{24}O_2,C_4H_8O_2$ requires C, 75·0; H, 8·3%).

2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII), obtained from the dioxan complex by heating it *in vacuo* at 100°, is a colourless resin, b. p. 168°/0·5 mm. without decomposition (Found : C, 80·8; H, 8·2. Calc. for $C_{20}H_{24}O_2$: C, 81·1; H, 8·1%). The phenolic function is very weak; the substance dissolves slightly in aqueous-alcoholic, but not in aqueous, sodium hydroxide, and does not give a ferric chloride reaction. When diethylamine is added to a solution of (VII) in light petroleum the *flavan–diethylamine* complex separates in short, thick needles, m. p. (dissociation) 86—88° [Found : C, 78·1; H, 9·1; N, 3·7; $NH(C_2H_5)_2$ (by loss in weight at 100°), 19·5. $C_{20}H_{24}O_2,NH(C_2H_5)_2$ requires C, 78·1; H, 9·5; N, 3·8; $NH(C_2H_5)_2$, 19·8%]. 2′-Acetoxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan was prepared from the hydroxyflavan (VII) by boiling it with excess of acetic anhydride and sodium acetate for 4 hours. It separated from ethanol in stout needles, m. p. 151° (Found : C, 78·3; H, 7·6. Calc. for $C_{22}H_{26}O_3$: C, 78·1; H, 7·7%). Hydrolysis with alcoholic potassium hydroxide regenerated the hydroxyflavan (VII).

Oxidation of 2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII). *2 : 4 : 4-Trimethylchroman-2 : 6-dicarboxylic Acid* (IX) *and 2 : 4 : 4 : 6-Tetramethylchroman-2-carboxylic Acid* (VIII).—The flavan (VII) was oxidised in 3 portions of 3 g. each as described for the flavan (VI). The acidic products were obtained as a pale yellow, slightly resinous material (2·3 g.) which was dissolved in ethylene dichloride (50 c.c.; charcoal), the solution filtered, distilled to a small bulk (5 c.c.), and cooled to 0°, and the solvent decanted from the crystals which separated. This solid was washed with ice-cold light petroleum (b. p. 60—80°) containing a trace of ethanol and dissolved in benzene (25 c.c.), and light petroleum (5 c.c.) was added, whereupon a sparingly soluble acid separated, m. p. 261°. Recrystallisation of this from ethyl acetate–light petroleum (20 c.c.) gave *2 : 4 : 4-trimethylchroman-2 : 6-dicarboxylic acid* (IX) as microcrystalline rhombs (0·22 g.), m. p. 266° (Found : C, 63·7; H, 6·1%; equiv., 133. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%; equiv., 132).

The mother-liquors after removal of the dicarboxylic acid were concentrated (to 2 c.c.), ethylene dichloride (1 c.c.) added, and the dark brown, sticky mass kept overnight at 0°, crystalline material being deposited. This was collected, washed with a few drops of ice-cold ethylene dichloride, and recrystallised from benzene (3 c.c.), giving needles, m. p. 138°. Recrystallisation from aqueous methanol gave *2 : 4 : 4 : 6-tetramethylchroman-2-carboxylic acid* (VIII) as clusters of fine needles (0·23 g.), m. p. 143° (Found : C, 71·9; H, 7·7%; equiv., 238. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%; equiv., 234).

Oxidation of 2 : 4 : 4 : 6-Tetramethylchroman-2-carboxylic Acid (VIII). *2 : 4 : 4-Trimethylchroman-2 : 6-dicarboxylic Acid* (IX).—The acid (VIII) (0·05 g.) in a solution of sodium carbonate (1 g.) in water (10 c.c.) was boiled, and powdered potassium permanganate slowly added until present in excess for 15 minutes. The solution was cooled, excess of sulphur dioxide passed in, and the precipitated acid collected, washed, and dried (0·049 g.; m. p. 264°). Recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave microcrystalline rhombs, m. p. 266°, showing no depression on admixture with the specimen of 2 : 4 : 4-trimethylchroman-2 : 6-dicarboxylic acid (IX) isolated from the oxidation described above.

Reaction of 2 : 4 : 4-Trimethylchroman-2 : 6-dicarboxylic Acid (IX) *with Copper Chromite–Quinoline. 2 : 4 : 4-Trimethylchroman-2-carboxylic Acid* (IV) *and 2-Hydroxy-2 : 4 : 4-trimethylchroman* (XV).—The acid (IX) (0·200 g.), freshly distilled quinoline (4 c.c.), and copper chromite (0·400 g.) were heated under reflux (metal-bath at 260°) for 20 minutes. The product was then worked up as described for the partial decarboxylation of 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III). The acidic product (0·055 g.), m. p. 158—160°, was sublimed (160°/360 mm.), giving colourless needles (0·029 g., 20%), m. p. 162—164°. Two recrystallisations from benzene–light petroleum (b. p. 60—80°) (1 c.c.) gave a product, m. p. 172°, alone or mixed with a previous specimen of 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV), m. p. 172°. The residue from the sublimation (0·022 g.), m. p. 262°, was the unchanged acid (IX). The neutral fraction yielded pale yellow prisms (0·006 g.), m. p. 86—87°, which sublimed

(120°/10 mm.) in needles, m. p. 90°, undepressed when mixed with the previous specimens of 2-hydroxy-2 : 4 : 4-trimethylchroman (XV), m. p. 91°.

Reaction of 2 : 4 : 4 : 6-*Tetramethylchroman-2-carboxylic Acid* (VIII) *with Copper Chromite–Quinoline.* 2-*Hydroxy*-2 : 4 : 4 : 6-*tetramethylchroman.*—The acid (VIII) (0·20 g.), copper chromite (0·2 g.), and quinoline (4 c.c.) were boiled under reflux for 6 hours. The product was worked up as before, giving unchanged acid (0·059 g.), m. p. 142—143°. The ethereal layer gave neutral material, which was crystallised from light petroleum (2 c.c.; b. p. 60—80°) (charcoal). 2-*Hydroxy*-2 : 4 : 4 : 6-*tetramethylchroman* separated as thin rhombs (0·010 g.), which after rapid sublimation (115°/13 mm.) had m. p. 100° (Found : C, 75·7; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

2′-*Acetoxy*-2 : 4 : 4 : 6 : 5′-*pentamethyl*-3′-*nitroflavan.*—2′-Acetoxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (above) (20 g.) in glacial acetic acid (200 c.c.) at 50° was treated dropwise (cooling and vigorous stirring) with concentrated nitric acid (20 c.c.; *d* 1·41) during 2 hours. The deep red solution was poured into water, and the solid collected and recrystallised from ethanol, giving the *nitro*-compound as thick, pale yellow plates (18·5 g.), m. p. 136—137° (Found : C, 68·5; H, 6·5; N, 3·6. $C_{22}H_{25}O_5N$ requires C, 68·9; H, 6·3; N, 3·7%).

2′-*Hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethyl*-3′-*nitroflavan.*—The preceding acetoxy-compound (16 g.) was stirred with ethanol (160 c.c.) and 2N-sodium hydroxide (40 c.c.) for 2 hours at 40°. Acidification of the deep orange solution gave a yellow solid which was crystallised twice from aqueous methanol, giving the *methanol* complex of 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethyl-3′-nitroflavan as thin, yellow prisms (15·3 g.), m. p. 88—89° (dissociation with loss of methanol) (Found : C, 67·4; H, 7·3; N, 4·0. $C_{20}H_{23}O_4N,CH_4O$ requires C, 67·6; H, 7·2; N, 3·8%). Crystallisation from light petroleum (b. p. 80—100°) gave very pale yellow prisms of the free 2′-*hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethyl*-3′-*nitroflavan*, m. p. 100—101° (Found : C, 70·1; H, 6·4; N, 4·4. $C_{20}H_{23}O_4N$ requires C, 70·4; H, 6·7; N, 4·1%). When crystallised from ether, the *diethyl ether* complex separated as pale yellow rhombs, m. p. (rapid heating with loss of ether) 73—74° (Found : C, 69·4; H, 8·0; N, 3·0; $C_4H_{10}O$, by loss of weight at 100°, 17·8. $C_{20}H_{23}O_4N,C_4H_{10}O$ requires C, 69·4; H, 7·95; N, 3·4; $C_4H_{10}O$, 17·8%). From light petroleum containing diethylamine the substance crystallised as the *diethylamine* complex, large, pale yellow rhombs, m. p. (rapid heating with loss of $NHEt_2$) 116—117° (Found : C, 69·6; H, 8·2; N, 6·8; $C_4H_{11}N$, by loss of weight at 120°, 17·7. $C_{20}H_{23}O_4N,C_4H_{11}N$ requires C, 69·6; H, 8·2; N, 6·8; $C_4H_{11}N$, 17·6%).

2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethyl-3′-nitroflavan gives a reddish-orange solution in alcoholic potassium hydroxide, and when boiled with acetic anhydride and anhydrous sodium acetate regenerated the acetyl derivative, m. p. and mixed m. p. 136—137°.

3′-*Amino*-2′-*hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethylflavan.*—The methanol complex of the preceding nitro-compound (10·2 g.) in methanol (150 c.c.) was hydrogenated (5 atm.) with a Raney nickel catalyst (*ca.* 10 g.) for 6 hours. The filtrate (Filtercel used) was concentrated (to 50 c.c.) and diluted with water. 3′-*Amino*-2′-*hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethylflavan* separated from methanol with methanol of crystallisation in microcrystalline rhombs (9·0 g.; m. p. 126—127° with loss of methanol), which after recrystallisation from the same solvent had m. p. 130—131° (Found: C, 73·2; H, 8·2; N, 4·2. $C_{20}H_{25}O_2N,CH_4O$ requires C, 73·5; H, 8·45; N, 4·1%). Removal of the methanol under diminished pressure gave a resin which when dissolved in light petroleum (b. p. 40—60°) containing diethylamine deposited the *diethylamine* complex, m. p. (with loss of $NHEt_2$) 109—110° (Found : C, 74·7; H, 9·0; N, 7·3. $C_{20}H_{25}O_2N,C_4H_{11}N$ requires C, 75·0; H, 9·4; N, 7·3%). The amine gave under normal conditions a diazonium salt which coupled with alkaline β-naphthol. The N-*acetyl* derivative, prepared from the amine (0·200 g.) and acetic anhydride (5 c.c.) at 60° for 10 minutes, followed by addition of water (yield 0·194 g.), separated from ethanol (charcoal) in rhombs, m. p. 214° (Found : C, 74·7; H, 7·6; N, 3·8. $C_{22}H_{27}O_3N$ requires C, 74·8; H, 7·65; N, 4·0%).

(2-*Hydroxy*-3-*methylphenyl*)*dimethylcarbinol* (X).—The preparation of the sodium salt of methyl *o*-cresotate from the ester (84 g.), and sodium (11·5 g.) in toluene (150 c.c.), its reaction with methylmagnesium iodide, and the isolation of the product was carried out as for the preparation of *o-iso*propenylphenol (p. 1780). After saturation of the alkaline solution with carbon dioxide the solid was collected, washed, dried (P_4O_{10}), and crystallised from light petroleum (300 c.c.; b. p. 60—80°) (charcoal) at 0°. (2-Hydroxy-3-methylphenyl)dimethylcarbinol (X) separated as long (*ca.* 3 cm.) needles (63·0 g., 75%), m. p. 77° (Found : C, 72·5; H, 8·6. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·4%).

3-iso*Propenyl*-o-*cresol* (XI).—(2-Hydroxy-3-methylphenyl)dimethylcarbinol (5 g.) was heated for 20 minutes in an oil-bath at 200°/460 mm. Water was rapidly lost and the 3-*iso*-

propenyl-*o*-cresol distilled at 54°/0·5 mm. (Found: C, 81·4; H, 8·4. Calc. for $C_{10}H_{12}O$: C, 81·1; H, 8·1%) (yield 3·6 g.; 81%). Iodine may not be used as a catalyst in this reaction as it causes immediate dimerisation of the *iso*propenyl compound (see below).

2'-Hydroxy-2 : 4 : 4 : 8 : 3'-pentamethylflavan (XII).—3-*iso*Propenyl-*o*-cresol (XI) undergoes dimerisation to the flavan (XII) in 72% yield when saturated with hydrogen chloride and kept at 40° for 5 days. The dimerisation is, however, much more rapidly caused by iodine. 3-*iso*-Propenyl-*o*-cresol (3·1 g.) was treated at 60° with iodine (8 mg.); a strongly exothermic reaction occurred and the oil became very viscous within 5 minutes. After 15 minutes the product was dissolved in ether (20 c.c.), washed with aqueous sodium sulphite, then with water, and dried, and the ether distilled, leaving a pale yellow resin which was crystallised from light petroleum (10 c.c.; b. p. 40—60°) at 0°. *2'-Hydroxy-2 : 4 : 4 : 8 : 3'-pentamethylflavan* (XII) separated as stout prisms (2·4 g.), m. p. 70—71° (Found: C, 80·7; H, 8·2. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·1%). The flavan distils unchanged at 162—163°/0·5 mm., and, like the other flavans of the series, it shows only very weak phenolic properties and gives no ferric chloride reaction. The *acetyl* derivative crystallised from aqueous methanol in prisms, m. p. 103° (Found: C, 78·4; H, 7·8. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%).

Oxidation of 2'-Hydroxy-2 : 4 : 4 : 8 : 3'-pentamethylflavan (XII). *2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic Acid* (XIV) *and 2 : 4 : 4 : 8-Tetramethylchroman-2-carboxylic Acid* (XIII).—The flavan (XII) was oxidised in 3 portions of 3 g. each as described above for the oxidation of 2'-hydroxy-2 : 4 : 4-trimethylflavan (VI), and the acidic products (2·2 g.) were isolated in the same way. Fractional crystallisation from benzene (7 c.c.) gave the less soluble 2 : 4 : 4-trimethylchroman-2 : 8-dicarboxylic acid (XIV), which was finally crystallised from ethyl acetate–light petroleum (b. p. 60—80°), giving microcrystalline rhombs (0·028 g.), m. p. 198°, undepressed on admixture with the specimen prepared as described below. Concentration of the mother-liquors gave *2 : 4 : 4 : 8-tetramethylchroman-2-carboxylic acid* (XIII) as clusters of thin needles (1·2 g., 25%), m. p. 143—144°, which after recrystallisation from benzene–light petroleum (b. p. 60—80°) had m. p. 151° (Found: C, 71·9; H, 7·7%; equiv., 238. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%; equiv., 234).

Oxidation of 2 : 4 : 4 : 8-Tetramethylchroman-2-carboxylic Acid (XIII). *2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic Acid* (XIV).—The acid (XIII) (1·0 g.) in sodium carbonate (2·5 g.) and water (50 c.c.) was boiled under reflux and powdered potassium permanganate (*ca.* 5 g.) added during 15 minutes. Boiling was continued for 20 minutes, sulphur dioxide passed in until the solution was colourless, and the precipitated acidic material collected and crystallised twice from ethyl acetate–light petroleum (b. p. 60—80°). *2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic acid* (XIV) separated as rhombs (0·87 g.), m. p. 198° (Found: C, 63·3; H, 6·0%; equiv., 127. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%; equiv., 132).

Reaction of 2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic Acid (XIV) *with Copper Chromite–Quinoline. 2 : 4 : 4-Trimethylchroman-2-carboxylic Acid* (IV) *and 2-Hydroxy-2 : 4 : 4-trimethylchroman* (XV).—The dicarboxylic acid (XIV) (0·200 g.) was boiled with quinoline and copper chromite and the products were isolated as described for the partial decarboxylation of 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III). The acidic material, m. p. 170—171° (0·071 g.), was recrystallised from benzene–light petroleum (b. p. 60—80°) (1 c.c.), giving rhombs, m. p. 172° alone or mixed with a specimen of 2 : 4 : 4-trimethylchroman-2-carboxylic acid, m. p. 172°.

The neutral ethereal extract yielded a yellow oil which separated from light petroleum (1 c.c.; b. p. 60—80°) in pale yellow prisms (0·012 g.), m. p. 88—89°; recrystallisation gave 2-hydroxy-2 : 4 : 4-trimethylchroman (XV), m. p. 91°, alone or mixed with the material, m. p. 91°, previously prepared.

Reaction of 2 : 4 : 4 : 8-Tetramethylchroman-2-carboxylic Acid (XIII) *with Copper Chromite–Quinoline. 2-Hydroxy-2 : 4 : 4 : 8-tetramethylchroman and 2 : 4 : 4 : 8-Tetramethylchromen.*—The acid (XIII) (2·8 g.), copper chromite (1·4 g.), and quinoline (10 c.c.) were boiled under reflux in a rotating flask for 2 hours. The product was worked up as previously described, giving unchanged acid (1·10 g.), m. p. 150°, and a neutral oil which partly crystallised. The solid was separated and washed with light petroleum (b. p. 40—60°), giving *2-hydroxy-2 : 4 : 4 : 8-tetramethylchroman* as hexagonal prisms (0·104 g.), m. p. 60°. Two further crystallisations from light petroleum raised the m. p. to 62—63° (Found: C, 75·5; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

The non-crystalline material from the separation was distilled, giving *2 : 4 : 4 : 8-tetramethylchromen* as a liquid (0·046 g.), b. p. 56—58°/0·3 mm. (Found: C, 83·1; H, 8·5. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%), and a residue from which a further quantity of 2-hydroxy-2 : 4 : 4 : 8-tetramethylchroman (0·044 g.) was obtained.

Reaction of 2 : 4 : 4-*Trimethylchroman-2-carboxylic Acid* (IV) *with Copper Chromite–Quinoline. 2-Hydroxy*-2 : 4 : 4-*trimethylchroman* (XV).—The acid (IV) (0·500 g.), quinoline (5 c.c.), and copper chromite (0·5 g.) were boiled (metal-bath at 260°) for 4 hours, and the products isolated as previously described. The acidic fraction yielded unchanged acid (IV) (0·081 g.), m. p. and mixed m. p. 172°. The neutral fraction was distilled, giving a greenish-yellow oil which crystallised from light petroleum (1 c.c.; b. p. 60—80°) in thin prisms, m. p. 87—89° (0·062 g.). Recrystallisation from light petroleum (b. p. 40—60°) gave 2-hydroxy-2 : 4 : 4-trimethylchroman (XV) as prisms, m. p. 91°, either alone or mixed with the specimens previously prepared.

Reaction of 4-(2-*Methoxy*-4-*methylphenyl*)-4-*methylpentan*-2-*one* (XVII) *with Hydrobromic and Acetic Acids.*—The ketone (XVII) (2·0 g.), hydrobromic acid (5 c.c.; *d* 1·48), and acetic acid (15 c.c.) were boiled for 6 hours, poured into water, and extracted with ether, and the extract was shaken with 2N-sodium hydroxide, which on acidification yielded a trace of phenolic material. The ethereal layer was distilled, giving a resin which crystallised from aqueous methanol. 4 : 4 : 7 : 4′ : 4′ : 7′-Hexamethylbis-2 : 2′-*spiro*chroman separated as hexagonal plates (0·409 g.), m. p. and mixed m. p. with an authentic specimen (see Baker and Besly, *J.*, 1939, 199) 132° (Found: C, 82·2; H, 8·3. Calc. for $C_{23}H_{28}O_2$: C, 82·2; H, 8·3%).

Reaction of 2 : 4 : 4 : 7-*Tetramethylchroman-2-carboxylic Acid* (II) *with Copper Chromite–Quinoline. 2-Hydroxy*-2 : 4 : 4 : 7-*tetramethylchroman* (XVI) *and* 2 : 4 : 4 : 7-*Tetramethylchromen* (XVIII).—The statement (Part V, p. 1105) that 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid is not decarboxylated in boiling quinoline in presence of copper chromite is correct, but the reaction was not then continued long enough to enable the hydroxy-compound (XVI) to be isolated. The acid (II) (2·0 g.) and copper chromite (1·0 g.) were boiled in quinoline (8 c.c.) for 6 hours. The product was worked up as described in earlier reactions, giving unchanged acid (0·48 g.), m. p. and mixed m. p. 148°. The ethereal layer containing neutral material yielded a greenish oil which solidified and was crystallised from light petroleum (b. p. 60—80°), giving 2-*hydroxy*-2 : 4 : 4 : 7-*tetramethylchroman* (XVI) as rectangular prisms (0·62 g.), m. p. 76—80°. A second crystallisation raised the m. p. to 80—81° (Found: C, 75·4; H, 8·5. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

The mother-liquors and the residue after separation of the hydroxychroman were distilled, giving 2 : 4 : 4 : 7-*tetramethylchromen* (XVIII) (0·149 g.), b. p. 46—47°/0·1 mm. (Found: C, 83·5; H, 8·8. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%). It slowly reduced a cold solution of potassium permanganate in acetone, and instantly decolourised a solution of bromine in chloroform.

2 : 3 : 5 : 6 : 8-*Pentabromo*-2 : 4 : 4 : 7-*tetramethylchroman.*—(*a*) 2 : 4 : 4 : 7-Tetramethylchromen (XVIII) (0·123 g.) was treated at room temperature with bromine (1 c.c.), a vigorous reaction occurring. After 2 hours the semi-solid product was crystallised twice from light petroleum (2 c.c.; b. p. 60—80°) containing a trace of benzene (charcoal), giving 2 : 3 : 5 : 6 : 8-*pentabromo*-2 : 4 : 4 : 7-*tetramethylchroman* as clusters of nacreous blades, m. p. 167° (*ca.* 50%) (Found: C, 26·9; H, 1·9; Br, 68·0. $C_{13}H_{13}OBr_5$ requires C, 26·7; H, 2·2; Br, 68·4%).

(*b*) 2-Hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) (0·05 g.) in chloroform (0·5 c.c.) was treated with bromine (0·2 c.c.) at room temperature. Next day, the residue after evaporation to dryness was crystallised twice from light petroleum (2 c.c.; b. p. 60—80°; charcoal), giving the pentabromotetramethylchroman, m. p. and mixed m. p. 166° (yield *ca.* 48%).

Methylation of 2-*Hydroxy*-2 : 4 : 4 : 7-*tetramethylchroman* (XVI). 4-(2-*Methoxy*-4-*methylphenyl*)-4-*methylpentan*-2-*one* (XVII).—The hydroxychroman (XVI) (0·400 g.) was boiled with a solution of sodium hydroxide (8 g.) in water (10 c.c.) for 5 minutes, then cooled, and methanol (5 c.c.) added. Methyl sulphate (5 c.c.) was then added during 5 minutes, boiling continued for 15 minutes, water (50 c.c.) added, and the solution extracted with ether (2 × 20 c.c.), giving an oil (0·260 g.), b. p. 132°/4 mm. This oil was dissolved in ethanol (5 c.c.) and added at *ca.* 60° to a solution of 2 : 4-dinitrophenylhydrazine (0·300 g.) in ethanol (10 c.c.) and concentrated sulphuric acid (2 c.c.). The solution was boiled for a few minutes, then cooled, and the solid finally crystallised from ethanol (15 c.c.), giving deep orange needles (0·380 g.), m. p. 143° (Found: C, 60·4; H, 6·1. Calc. for $C_{20}H_{24}O_5N_4$: C, 60·0; H, 6·0%) alone or mixed with a specimen similarly prepared from 4-(2-methoxy-4-methylphenyl)-4-methylpentan-2-one (XVII) which had been synthesised by a different method (Part VI, *loc. cit.*). The m. p. of 138° previously recorded for this 2 : 4-dinitrophenylhydrazone is that of a second form crystallising in thin plates which was prepared at room temperature.

2-*Ethoxy*-2 : 4 : 4 : 7-*tetramethylchroman.*—2-Hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) (0·400 g.) in dry ethanol (5 c.c.) was saturated with hydrogen chloride and then boiled for

4 hours. The diluted product yielded to ether *2-ethoxy-2 : 4 : 4 : 7-tetramethylchroman* as a viscous oil (0·201 g., 44%), b. p. 74°/0·2 mm. (Found : C, 77·4; H, 9·0. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%).

2-Amino-2 : 4 : 4 : 7-tetramethylchroman (XX).—Bromine (0·8 g.) was added to a solution of potassium hydroxide (1·12 g.) in water (11·2·c.c.) at −10°. 2 : 4 : 4 : 7-Tetramethylchroman-2-carboxyamide (XIX) (1·16 g.; Baker, Curtis, and McOmie, Part VI, *loc. cit.*) in dioxan (7 c.c.) was now added with efficient stirring to the solution at 0°, and stirring was continued at 0° for 15 minutes and then for 1½ hours at 80°, and the cooled solution was diluted and extracted with ether (2 × 30 c.c.). The extract was shaken with excess of dilute hydrochloric acid, and the acid layer when neutralised gave an oil which solidified (the ether yielded unchanged amide, 0·197 g., m. p. 146—147°). After being dried *in vacuo* this *2-amino-2 : 4 : 4 : 7-tetramethylchroman* (XX) (0·497 g.) had m. p. 74°, raised to 76° by recrystallisation from aqueous methanol (charcoal) (Found : C, 75·9; H, 9·3; N, 6·7. $C_{13}H_{19}ON$ requires C, 76·1; H, 9·3; N, 6·8%). The amine (XX) (0·04 g.) in acetic acid (0·2 c.c.) and acetic anhydride (0·5 c.c.) was kept for 1½ hours, then diluted and shaken; the solid was collected, and finally crystallised from benzene–light petroleum (b. p. 60—80°) (2 c.c.). *2-Acetamido-2 : 4 : 4 : 7-tetramethylchroman* separated in fine needles (0·031 g.), m. p. 134° (Found : C, 72·5; H, 8·4; N 5·85. $C_{15}H_{21}O_2N$ requires C, 72·9; H, 8·5; N, 5·7%).

2-Hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) *from 2-Amino-2 : 4 : 4 : 7-tetramethylchroman* (XX).—Sodium nitrite (0·024 g.) in water (2 c.c.) was added to the amine (XX) (0·069 g.) in dilute hydrochloric acid (10 c.c.; 10%) at room temperature, and after 6 hours the whole was diluted with water and extracted with ether. The extracts were shaken with hydrochloric acid in excess, then with water, dried, and distilled, giving an oil which was dissolved in light petroleum (b. p. 60—80°) (charcoal); the solution was filtered and concentrated to 2 c.c. The resulting solid was sublimed (100°/13 mm.), giving prisms (0·007 g.), m. p. 80° not depressed by a specimen of 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI), m. p. 80—81°.

Crystalline Complexes formed by the Flavans (VI) *and* (VII).—These *complexes* were prepared by dissolving the flavan in light petroleum (b. p. 40—60°) and adding the other component of the complex (see Part VII, *loc. cit.*). In connection with the annexed list it is to be understood that, except for those mentioned, complexes are not formed with organic solvents usually found in the laboratory, with other solvents mentioned in this list, or with solvents listed in Part VII as forming complexes with 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I).

Crystalline complexes formed by flavans (VI) *and* (VII).

Component	M. p. (dissociation)	Ratio, flavan : component	Analyses : Found, % (required % in parentheses) Carbon	Hydrogen	Nitrogen
	2′-Hydroxy-2 : 4 : 4-trimethylflavan (VI) *				
Dioxan	142—144°	2 : 1	76·7 (76·9)	7·6 (7·7)	—
Morpholine	146—148	2 : 1	76·7 (77·0)	7·9 (7·9)	—
	2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII) †				
Tetrahydrofuran	77—79	1 : 1	78·2 (78·3)	8·8 (8·7)	—
Morpholine	109—111	1 : 1	75·2 (75·2)	8·6 (8·6)	3·7 (4·0)
Pyridine	101—103	1 : 1	80·4 (80·0)	7·7 (7·7)	—
Piperidine	100—102	1 : 1	—	—	3·6 (3·7)
*cyclo*Hexylamine	69—71	1 : 1	—	—	3·5 (3·5)

* Crystalline complexes (uncharacterised) are also formed with diethylamine, di*iso*propylamine, aniline, *cyclo*hexylamine, pyridine, and 2-bromopyridine.

† Complexes are also formed with dioxan and diethylamine (already described in this paper), di-*n*-propylamine, di*iso*propylamine, di-*n*-butylamine, di*iso*butylamine, 3-methylpyridine, 4-methylpyridine, 2 : 6-dimethylpyridine.

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