394. *Condensation Products of Phenols and Ketones. Part X.* The Structure of Dianin's Compound, a Unique Inclusion-forming Substance.*

By Wilson Baker, A. J. Floyd, J. F. W. McOmie, G. Pope, A. S. Weaving, and J. H. Wild.

A product, " Dianin's compound," first prepared in 1914 from phenol and mesityl oxide, is shown to be 4-*p*-hydroxyphenyl-2 : 2 : 4-trimethylchroman (III). Oxidation yields 2 : 2 : 4-trimethylchroman-4-carboxylic acid, and thermal degradation gives phenol and 2 : 2 : 4-trimethylchromen. The latter compound has been synthesised and yields Dianin's compound by addition of phenol.

Dianin's compound forms inclusion compounds with over fifty widely differing organic solvents, some inorganic gases, and with iodine. The large, separate cavities in the crystals are defined by six molecules of Dianin's compound, and the ratio of number of molecules of Dianin's compound to the number of included molecules is generally 6 : 1, though a ratio of 3 : 1, *i.e.*, 2 molecules per hole, is found with a number of small molecules.

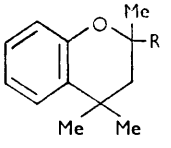
Previous papers [1,2] have described *inter al.* some derivatives of 2'-hydroxy-2 : 4 : 4-trimethylflavan prepared by condensing simple phenols with acetone, and these flavans formed inclusion compounds with a variety of organic solvents.[2,3] The condensation product of phenol with mesityl oxide was studied by Dianin,[4] and he observed that it formed crystalline adducts with certain organic solvents. We have now reinvestigated this substance, which will be referred to as " Dianin's compound " (see a preliminary note by Baker and McOmie [5]).

Dianin showed that phenol (2 mol.) reacted with mesityl oxide (1 mol.) in presence of hydrogen chloride to give a monohydric phenol, $C_{18}H_{20}O_2$, which formed a benzoate and a

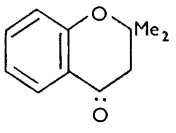
* Part IX, *J.*, 1952, 3796.

[1] Baker, Curtis, and McOmie, *J.*, 1951, 76.
[2] *Idem*, *J.*, 1952, 1774.
[3] Baker, Curtis, and Edwards, *J.*, 1951, 83; Baker, Downing, Hewitt-Symonds, and McOmie, *J.*, 1952, 3796.
[4] Dianin, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1310; *Chem. Zentr.*, 1915, I, 1063.
[5] Baker and McOmie, *Chem. and Ind.*, 1955, 256.

methyl ether; oxidation of the latter gave anisic acid. Dianin's compound gave salicylic acid when fused with alkali, and when distilled it gave phenol and an olefin, $C_{12}H_{14}O$, which recombined in presence of hydrogen chloride regenerating Dianin's compound. Dianin regarded the substance $C_{18}H_{20}O_2$ as 4'-hydroxy-2 : 4 : 4-trimethylflavan (I; R = *p*-HO·C_6H_4), and the olefin as 2 : 4 : 4-trimethylchromen. These experiments have now been confirmed, and in addition we have found that oxidation of Dianin's compound by potassium permanganate gives in low yield an acid, $C_{13}H_{16}O_3$, m. p. 124—125°, which is isomeric with 2 : 4 : 4-trimethylchroman-2-carboxylic acid (I; R = CO_2H), m. p. 172°, previously obtained[2] by the oxidative degradation of a number of 2'-hydroxy-2 : 4 : 4-trimethylflavans (I; R = *o*-HO·C_6H_4). This result disproves Dianin's suggested structures for his compound and for the derived olefin. A significant second product obtained also in low yield from the oxidation of Dianin's compound with potassium permanganate was 2 : 2-dimethylchromanone (II), isolated and characterised as its 2 : 4-dinitrophenylhydrazone.



(I)



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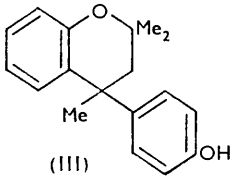
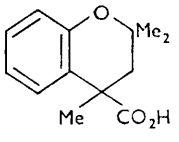
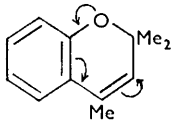


(III)

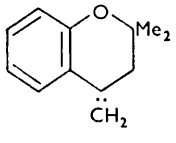
Consideration of the most likely course of the reaction between phenol and mesityl oxide, led to the expectation that Dianin's compound was 4-*p*-hydroxyphenyl-2 : 2 : 4-trimethylchroman (III), and consequently that the derived acid, $C_{13}H_{16}O_3$, was the tertiary acid 2 : 2 : 4-trimethylchroman-4-carboxylic acid (IV). In partial confirmation of this view, it was found that the acid behaved as a tertiary acid in that it rapidly evolved carbon monoxide when treated with concentrated sulphuric acid at 40°. Structure (III) was one of the alternatives rejected by Dianin, for reasons which are not clear, in favour of (I; R = *p*-HO·C_6H_4), but the present work proves that Dianin's compound is in fact correctly represented by (III).



(IV)



(V)



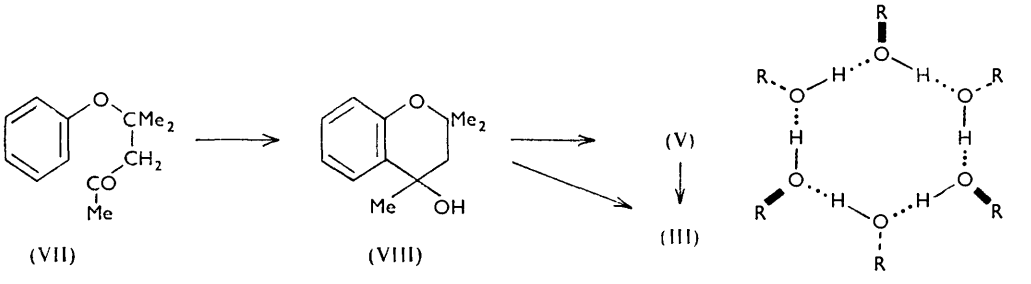
(VI)

The olefin, $C_{12}H_{14}O$, contains one olefinic bond as revealed by microhydrogenation and by the formation of a crystalline tribromo-dibromide, and the molar refractivity and ultraviolet absorption spectrum showed that the double bond was conjugated with the benzene ring. Controlled oxidative degradation of the olefin was difficult; oxidation of one sample by potassium permanganate gave a 1% yield of 2 : 2-dimethylchromanone, isolated and characterised as its 2 : 4-dinitrophenylhydrazone, but all other samples gave a 2% yield of a substance, isolated as a mono-2 : 4-dinitrophenylhydrazone, which may be *o*-(2-formyl-1-methylethoxy)acetophenone, *o*-Ac·C_6H_4·O·CMe_2·CHO. The latter was also produced in 17% yield by oxidation of the olefin with chromic acid. Ozonisation of the olefin gave a small yield of *o*-hydroxyacetophenone, but no formaldehyde could be detected. These experiments suggested that the olefin was probably 2 : 2 : 4-trimethylchromen (V) containing on the one occasion a trace of the isomeric 2 : 2-dimethyl-4-methylenechroman (VI) and this was confirmed by the synthesis of 2 : 2 : 4-trimethylchromen (V) from 4-methylcoumarin and methylmagnesium iodide. The synthetic chromen (V) had the same absorption spectrum and gave the same tribromo-dibromide as the chromen derived from Dianin's compound. Moreover, both specimens of the chromen gave practically the same yield of Dianin's compound when treated with excess of phenol and hydrogen

chloride, and in these experiments the *p*-hydroxyphenyl residue must become attached to carbon atom 4 of the chromen ring, because the related carboxylic acid is tertiary. Hence Dianin's compound must be 4-*p*-hydroxyphenyl-2 : 2 : 4-trimethylchroman (III) and the derived acid must be 2 : 2 : 4-trimethylchroman-4-carboxylic acid (IV).

The formation of Dianin's compound from phenol and mesityl oxide probably involves (*a*) the addition of phenol to the cationoid β-carbon atom of the mesityl oxide to give a β-phenoxy-ketone (VII), (*b*) cyclisation to 4-hydroxy-2 : 2 : 4-trimethylchroman (VIII), followed by *either* (*c*) condensation of the tertiary hydroxyl group with the *p*-hydrogen atom of the second molecule of phenol, or (*d*) elimination of water to give the chromen (V) to which the second molecule of phenol subsequently adds. All these reactions are likely to be acid catalysed. Steps (*c*) and (*d*) may both occur. Step (*a*) is much more probable than reaction of the ketonic carbon atom of the mesityl oxide with an *o*-hydrogen atom of the phenol, because such a reaction would be likely to occur almost exclusively in the *p*-position to the phenolic hydroxyl group (cf. the ready condensation of phenol with acetone to give 2 : 2-di-*p*-hydroxyphenylpropane), and because the cationoid reactivity of the carbonyl group in mesityl oxide is diminished by the presence of the αβ-double bond. The addition of the anionoid phenol to the chromen (V) to give Dianin's compound occurs, as expected, at the more cationoid of the two carbon atoms 3 and 4, the double bond being conjugated with the oxygen atom as shown in (V).

The synthesis of 2 : 2-dimethylchromanone, required for comparison with that obtained by degradation, has been the subject of controversy. Skraup and Beng [6] claimed to have prepared the chromanone by thermal rearrangement of phenyl ββ-dimethylacrylate alone or in presence of zinc chloride, but von Auwers and Mauss [7] were unable to repeat the Fries rearrangement even in the presence of aluminium chloride. In the present work it was found that the ester, conveniently prepared by heating phenol with ββ-dimethylacryloyl chloride, when heated with aluminium chloride gave a 45% yield of 2 : 2-dimethylchromanone. The same ester when treated with aluminium chloride in carbon disulphide is reported [8] to give 3 : 4-dihydro-4 : 4-dimethylcoumarin (67·5%) and a trace of 2 : 2-dimethylchromanone. A synthesis of 2 : 2-dimethylchromanone from 4-ethoxycoumarin gave a 57% yield of very crude material.[9]



(IX ; R = $C_{18}H_{19}O$)

With the object of preparing derivatives of Dianin's compound with substituents in the hydroxyphenyl nucleus, attempts have been made to add substituted phenols to 2 : 2 : 4-trimethylchromen (V). With *m*- and *p*-cresol, the chromen yielded non-phenolic resins which are probably cresol ethers. *o*-Cresol gave a phenolic crystalline homologue of Dianin's compound, which formed no complexes with solvents. Catechol also combined with the chromen, but the compound could not be crystallised and it gave no adducts; oxidation gave a low yield of 2 : 2 : 4-trimethylchroman-4-carboxylic acid (IV).

Inclusion Compounds.—Dianin's compound is remarkable in forming crystalline adducts with all the many organic solvents which have been tested. These adducts are

[6] Skraup and Beng, *Ber.*, 1927, **60**, 942; 1928, **61**, 1665.
[7] von Auwers and Mauss, *Ber.*, 1928, **61**, 416, 2545.
[8] Colonge and Chambard, *Bull. Soc. chim. France*, 1953, **20**, 581.
Wawzonek, Nagler, and Carlson, *J. Amer. Chem. Soc.*, 1954, **76**, 1080.

very stable and only lose their solvent when melted. Dianin described adducts with ethanol, acetone, acetic acid, and chloroform, which he stated had a ratio of four molecules of his compound to one of the solvent, and also an ether adduct with a ratio of 8 : 1.

The molecular ratios of Dianin's compound to included molecule as now determined do not agree with those recorded by Dianin (see Table in Experimental section). The ratio is 2 : 1 for methanol only, for somewhat larger molecules such as ethanol, acetone, or the butanols the ratio is 3 : 1, but for the majority of adducts, including aromatic compounds, the ratio is 6 : 1. These adducts are of the nature of inclusion compounds [10] (clathrates), and *X*-ray crystallographical studies by Powell and Wetters [11] show that six molecules of Dianin's compound surround a large, egg-shaped cavity, the ends being flat hexagons formed by six phenolic hydroxyl groups linked by hydrogen bonds; this feature is also found in the quinol clathrates. Each such hexagon, formally represented by (IX), is common to two cavities, and the sides of the cavity are defined by the $C_{18}H_{19}O$ parts of the molecules of Dianin's compound which are arranged alternately above and below the plane of the hexagon. A cavity can accommodate three molecules of methanol (ratio 2 : 1), two molecules of intermediate size (ratio 3 : 1), but only one molecule of the larger sizes (ratio 6 : 1). The Table shows some cases where other ratios are found, and these are to be explained by assuming that some of the holes are either incompletely filled or contain no enclosed molecule. Thus a 7 : 1 ratio is really a 6 : 1 ratio with every seventh hole unfilled. This phenomenon is known with other inclusion-forming substances, and is perhaps particularly likely to occur in cases like that of Dianin's compound which contain cavities rather than tunnels, and which crystallise alone in the same form as when an adduct is incorporated in the lattice; the ratio may vary according to the conditions of crystallisation. Dianin's compound is precipitated in a solvent-free, crystalline form from a hot solution in aqueous sodium hydroxide by passage of carbon dioxide, and the free substance may be sublimed under diminished pressure.

Inclusion compounds containing inorganic molecules have also been prepared, *e.g.*, crystallisation of Dianin's compound from liquid sulphur dioxide or from liquid ammonia gives the respective adducts. Powell and Wetters [11] prepared adducts with carbon dioxide and with argon by cooling solutions of Dianin's compound in decalin under about 40 atmospheres pressure of the appropriate gas. The argon clathrate had a ratio of 6 : 1. The iodine-containing adduct, prepared from decalin solution, is of particular interest. The colour of the crystals varies from light brown to reddish-brown according to the amount of iodine included. The ratio (7 : 1) indicates that the iodine is present in the crystal as separate molecules and not as long chains such as are present in the deep-blue inclusion compounds formed by iodine with starch and with the *cyclo*dextrins.[10]

Dianin's compound is very much more soluble in amines than in any other class of solvent. Approximate solubilities at 20° per 100 ml. of solvent are in triethylamine (17·5 g.), diethylamine (47·5 g.), pyridine (80 g.), 2 : 6-dimethylpyridine (70 g.), and piperidine (80 g.). The increased solubility is probably caused by strong hydrogen bonding with the solvent and possibly by salt formation. The adduct formed with piperidine is different from all the others in that the molecular ratio is nearly 1 : 1; the crystals are very unstable and become opaque through loss of solvent when exposed to the air for a few days (see Experimental). This behaviour is similar to the salt-like 1 : 1 piperidine adducts of quinol, pyrogallol, vanillin, etc., described by Rosenheim and Schidrowitz.[12] Crystallographical examination by Mr. H. M. Powell, Oxford, of the crystals of the adduct of piperidine with Dianin's compound show that it does not have the trigonal crystalline form of the normal series of inclusion compounds described in this paper.

Experimental

Preparation of Dianin's Compound (III).—The procedure described has been developed as a routine method for the preparation of Dianin's compound in quantity. It is much simpler than the original and takes 4 days instead of 4 weeks. A mixture of phenol (400 g.) and mesityl

[10] See Cramer, " Einschlussverbindungen," Springer-Verlag, Berlin, 1954.
[11] Powell and Wetters, *Chem. and Ind.*, 1955, 256.
[12] Rosenheim and Schidrowitz, *J.*, 1898, **73**, 139.

oxide (100 g.) was saturated (8 hr.) with a stream of anhydrous hydrogen chloride, the flask being cooled in a vessel of (initially) cold water. The red, viscous mixture was kept ($CaCl_2$ tube) at about 38° for 4 days (or at room temperature for 14 days), giving a red-brown crystalline mass. Boiling water (1 l.) was added, and the mixture was well shaken and heated on the water-bath. The top aqueous layer was decanted and the lower layer similarly treated with a further 1 litre of hot water. After being decanted, the damp, oily product was now shaken with hot ethanol (250 ml.), cooled and shaken, and after ½—1 hr. the crystalline ethanol adduct was collected, drained, and twice stirred with cold ethanol (150 ml.) and drained (large sintered-glass funnel). The product (130—155 g.) was crystallised from ethanol (1200—1300 ml.), collected, washed well with cold ethanol and dried, giving hexagonal needles (115—130 g.; 40—45% calc. on the mesityl oxide), m. p. 165—166° (Found: C, 79·6; H, 7·8. Calc. for $3C_{18}H_{20}O_2,C_2H_5{\cdot}OH$: C, 79·1; H, 7·8%). Dianin gave m. p. 163—164°.

Preparation of Unsolvated Dianin's Compound.—(*a*) The ethanol complex (30 g.) was dissolved in hot 2N-sodium hydroxide (200 ml.), boiled for 15 min., and carbon dioxide passed through the hot solution for 30 min. The collected solid was boiled twice with water (200 ml.) and dried *in vacuo* over phosphoric anhydride. This unsolvated compound (26 g., 89%) formed fine needles, m. p. 156—157° (Found: C, 80·8; H, 7·6. Calc. for $C_{18}H_{20}O_2$: C, 80·6; H, 7·5%). Dianin recorded m. p. 157·5°.

(*b*) The ethanol complex was slowly sublimed at 140°/0·1 mm. giving the unsolvated material as large irregular prisms, m. p. 155—156°; at higher temperatures the product was a white powder [Found: C, 80·7; H, 7·5%; *M*, 266 (ebullioscopic in benzene, the Menzies–Wright apparatus being used with the refinements described by Baker, Ollis, and Zealley [13]). Calc. for $C_{18}H_{20}O_2$: *M*, 268].

Dianin's compound is soluble in hot aqueous sodium or potassium hydroxide; on cooling the alkali salts crystallise. In concentrated sulphuric acid it gives an orange-red colour. No coloration is obtained with aqueous or alcoholic ferric chloride.

Oxidation of Dianin's Compound. 2 : 2 : 4-*Trimethylchroman-4-carboxylic Acid* (IV) *and* 2 : 2-*Dimethylchromanone* (II).—An excess of saturated solution of potassium permanganate in boiling acetone (in all *ca.* 1200 ml.) was added rapidly to a solution of the ethanol adduct of Dianin's compound (3 g.) in boiling acetone (100 ml.) containing a few crystals of ferrous sulphate. The acetone was removed by distillation and the residue was shaken with water (100 ml.), sodium pyrosulphite (20 g.), and 2N-hydrochloric acid (20 ml.), and sulphur dioxide passed until all manganese dioxide had dissolved. The mixture was extracted with ether (3 × 50 ml.), and the extracts were shaken three times with saturated aqueous sodium carbonate. Acidification of the alkaline solutions gave a product which was boiled with light petroleum (b. p. 60—80°; 4 × 30 ml.); concentration of the extracts to 5 ml. and cooling to 0° gave a sticky solid (0·22 g.). Two recrystallisations from the same solvent (charcoal) gave 2 : 2 : 4-*trimethylchroman-4-carboxylic acid* (IV) as irregular prisms (0·16 g., 6%), m. p. 124—125° (Found: C, 70·9; H, 7·2; equiv., 216. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3; equiv., 220).

On treatment with cold, concentrated sulphuric acid, the carboxylic acid dissolved slowly to an orange-red solution with evolution of carbon monoxide. At 40° the reaction was brisk. The gas was identified by reduction of 1% palladous chloride in dilute hydrochloric acid on filter paper.

The non-acidic material obtained in the oxidation was treated with 2 : 4-dinitrophenylhydrazine in ethanolic phosphoric acid, thereby yielding the 2 : 4-dinitrophenylhydrazone of 2 : 2-dimethylchromanone (II) as orange-red needles (0·078 g., 2%), m. p. 222—223° undepressed by admixture with an authentic specimen (Found: C, 57·0; H, 4·5; N, 15·5. Calc. for $C_{17}H_{16}O_5N_4$: C, 57·3; H, 4·5; N, 15·7%).

Methyl Ether of Dianin's Compound.—Methylation of the ethanol adduct, suspended in acetone, with excess of methyl sulphate and potassium hydroxide gave the ether, b. p. 140—141°/0·2 mm. (87%), which solidified after 4 weeks; recrystallisation from light petroleum (b. p. 40—60°) gave rectangular tablets, m. p. 50—51° (Found: C, 80·6; H, 8·0. Calc. for $C_{19}H_{22}O_2$: C, 80·0; H, 7·8%). The ether is probably dimorphic; our first preparation had m. p. 34—36°, and Dianin gave m. p. 36°. The *tribromo*-derivative, prepared by reaction at room temperature with excess of bromine in acetic acid for 18 hr., was twice crystallised from ethanol giving needles (1·51 g., 82%), m. p. 103—104° (Found: C, 43·8; H, 3·9; Br, 47·0. $C_{19}H_{19}O_2Br_3$ requires C, 43·9; H, 3·7; Br, 46·2%).

Pyrolysis of Dianin's Compound. 2 : 2 : 4-*Trimethylchromen* (V).—The ethanol adduct of Dianin's compound (40 g.) was heated at 300° under reflux for 2 hr., giving an oil which was

[13] Baker, Ollis, and Zealley, *J.*, 1951, 207.

distilled twice at atmospheric pressure, shaken with 10% sodium hydroxide (100 ml.), and extracted into ether (3 × 50 ml.), giving finally the chromen (V), b. p. 114—115°/17 mm. (18·5 g., 73%), n_D^{20} 1·5502 (Found: C, 83·1; H, 7·9. Calc. for $C_{12}H_{14}O$: C, 82·8; H, 8·0%). Dianin recorded d_D^{20} 1·0084, n_D^{20} 1·5450. Light absorption in ethanol: $\lambda_{max.}$ 218·5, 262, 307·5; $\lambda_{min.}$ 241, 280·5 ($\log_{10}\varepsilon$ 4·38, 3·60, 3·52, 3·33, 3·04).

Tribromo-dibromide of 2 : 2 : 4-*Trimethylchromen.*—The above chromen (0·5 g.) was treated dropwise (vigorous reaction) at room temperature with bromine (3 ml.). Next day the semi-solid product was dissolved in chloroform, the solution shaken with aqueous sodium hydrogen sulphite, and dried, and the residue crystallised twice from light petroleum (b. p. 60—80°) giving 3 : 3 : 4 : 6 : 8-*pentabromo*-2 : 2 : 4-*trimethylchroman* as rectangular prisms (1·18 g., 72%), m. p. 145—146° (Found: C, 25·5; H, 1·7; Br, 70·3. $C_{12}H_{11}OBr_5$ requires C, 25·3; H, 1·9; Br, 70·0%). A mixture with authentic material (see below) had the same m. p.

Oxidation of 2 : 2 : 4-*Trimethylchromen* (V) *prepared from Dianin's Compound.*—(*a*) *With potassium permanganate.* Saturated aqueous potassium permanganate was dropped into a stirred suspension of the chromen (2 g.) in 1% aqueous potassium hydroxide (20 ml.) until the permanganate remained in excess. The solution was acidified and decolorised with sulphur dioxide, and then saturated with sodium chloride and extracted with ether. The resulting oil (1·63 g.) gave a 2 : 4-*dinitrophenylhydrazone* (0·084 g.) as orange-red plates, m. p. 203—204°, from methanol (Found: C, 56·0; H, 4·1; N, 15·0. $C_{18}H_{18}O_6N_4$ requires C, 56·0; H, 4·7; N, 14·5%). The compound may be the mono-2 : 4-dinitrophenylhydrazone of *o*-(2-formyl-1-methylethoxy)acetophenone.

A similar oxidation with chromen from an earlier pyrolysis gave 2 : 2-dimethylchromanone 2 : 4-dinitrophenylhydrazone (0·046 g.), m. p. and mixed m. p. with authentic material 221° (Found: C, 57·1; H, 4·6; N, 15·8. Calc. for $C_{17}H_{16}O_5N_4$: C, 57·3; H, 4·5; N, 15·7%).

(*b*) *With chromic acid.* Chromic oxide (3 g.) in water (10 ml.) was added gradually to the chromen (1 g.) in acetic acid (20 ml.). Next day the neutral material was isolated as an oil which gave a 2 : 4-dinitrophenylhydrazone (1·13 g.); after two recrystallisations from methanol it had m. p. 194—195°, mixed m. p. with the above 2 : 4-dinitrophenylhydrazone (m. p. 203—204°) 197—200° (Found: C, 56·1; H, 4·0; N, 14·7, 15·3%).

(*c*) *With ozone.* Ozonised oxygen was passed at −20° through the chromen (1 g.) in dry carbon tetrachloride (20 ml.) for 1 hr. The solvent was removed under reduced pressure, and the oil, isolated in the usual way, gave *o*-hydroxyacetophenone 2 : 4-dinitrophenylhydrazone (0·34 g.), which after twice crystallising from ethanol had m. p. and mixed m. p. with authentic material, 212—213°.

Synthesis of 2 : 2-*Dimethylchromanone* (II).—ββ-Dimethylacryloyl chloride (7·5 g.) was added dropwise to phenol (6 g.), the mixture heated on the steam-bath for 4 hr. and then cooled, water (100 ml.) added, and the oily product extracted into ether giving phenyl ββ-dimethylacrylate (8·8 g., 79%), b. p. 127°/11 mm. This ester (2 g.) was added slowly to powdered aluminium chloride (2·1 g.), and the mixture kept at 90° for 2 hr. When cool, 2N-hydrochloric acid (25 ml.) was added, and the ethereal solution of the product washed with 1% sodium hydroxide and with water, yielding 2 : 2-dimethylchromanone (II) (0·9 g., 45%; m. p. 70—75°). Recrystallisation from light petroleum (b. p. 40—60°) gave prisms, m. p. 87—88° (Skraup and Beng[6] give m. p. 88°). The 2 : 4-dinitrophenylhydrazone, after 3 recrystallisations from ethanol, had m. p. 220—221°.

Synthesis of 2 : 2 : 4-*Trimethylchromen* (V).—4-Methylcoumarin (10 g.) in ether (200 ml.) was added during 1 hr. to methylmagnesium iodide [from magnesium (12·2 g.) and methyl iodide (71 g.)] in ether (100 ml.), and the mixture boiled for 10 hr., and then poured into 20% hydrochloric acid (200 ml.) containing crushed ice (200 g.). Extraction with ether gave a brown oil (10·8 g.) which partially solidified. The separated solid was crystallised from light petroleum (b. p. 60—80°) giving 4-*o*-*hydroxyphenyl*-2-*methylpent*-3-*en*-2-*ol* (1·2 g., 10%) as needles, m. p. 97—98° (Found: C, 75·1; H, 8·4. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). This product dissolved in sodium hydroxide solution, and rapidly decolorised a solution of bromine in carbon tetrachloride.

The above-mentioned brown oil was distilled giving 2 : 2 : 4-trimethylchromen (V) (7·9 g., 73%), b. p. 124—126°/28 mm., n_D^{20} 1·5511 (Found: C, 82·5; H, 8·1. Calc. for $C_{12}H_{14}O$: C, 82·8; H, 8·0%). Light absorption in ethanol: $\lambda_{max.}$ 219, 262, 307·5; $\lambda_{min.}$ 241, 280·5 ($\log_{10}\varepsilon$ 4·4, 3·66, 3·59, 3·37, 3·07). It yielded the same tribromo-dibromide (79% yield), m. p. and mixed m. p. 145—146° (Found: C, 25·6; H, 1·7; Br, 70·0%), as that from the chromen derived from Dianin's compound.

Cyclisation of 4-o-*Hydroxyphenyl*-2-*methylpent*-3-*en*-2-*ol*.—The carbinol (0·8 g.), acetic acid (10 ml.), and concentrated sulphuric acid (0·25 ml.) were boiled for ½ hr., the solution diluted with water, and the product collected in ether. Distillation then gave 2 : 2 : 4-trimethylchromen (0·48 g., 66%), 114—116°/17 mm., characterised as the tribromo-dibromide, m. p. 145—146°.

Addition of Phenol to 2 : 2 : 4-*Trimethylchromen. Formation of Dianin's Compound*.—Dry hydrogen chloride was slowly bubbled (1 hr.) through a cooled mixture of phenol (1·65 g.) and 2 : 2 : 4-trimethylchromen (1·5 g.). After 5 days the crystalline mass was worked up as previously described giving Dianin's compound as the ethanol adduct (1·23 g., 53%), m. p. 163—164°. The benzoate, crystallised from ethanol, had m. p. 160—161°, not depressed by admixture with an authentic specimen.

An experiment with the chromen obtained by pyrolysis of Dianin's compound similarly regenerated Dianin's compound (58%) (adduct with ethanol, m. p. 163—164°; benzoate, m. p. 160—161°).

Addition of o-*Cresol to* 2 : 2 : 4-*Trimethylchromen*. 4-(4-*Hydroxy*-3-*methylphenyl*)-2 : 2 : 4-*trimethylchroman*.—A mixture of *o*-cresol (2·25 g.) and the chromen (2·5 g.) was saturated with hydrogen chloride (1 hr.), and after 12 days the partly crystalline mass was extracted with boiling water (5 × 20 ml.) and the residue steam distilled until the distillate was clear. The residue was collected in ether which then yielded a pale yellow solid. Two crystallisations from light petroleum (b. p. 60—80°) gave 4-(4-*hydroxy*-3-*methylphenyl*)-2 : 2 : 4-*trimethylchroman* as needles (2·4 g., 60%), m. p. 135—136° (Found: C, 80·9; H, 8·1. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·8%). The chroman gave no colour with alcoholic ferric chloride, but dissolved in warm 2N-sodium hydroxide. It gave a red solution in concentrated sulphuric acid. The *acetate*, crystallised twice from light petroleum (b. p. 60—80°), formed irregular prisms, m. p. 121—122° (Found: C, 78·0; H, 7·2. $C_{21}H_{24}O_3$ requires C, 77·7; H, 7·4%).

Preparation of Crystalline Adducts.—(a) *With liquids*. These were prepared by crystallisation of unsolvated Dianin's compound from the various solvents. A modification of this method was used with methyl iodide in which Dianin's compound is sparingly soluble. The unsolvated compound was placed in the thimble of a Soxhlet apparatus and extracted with methyl iodide; the adduct separated as the solvent became saturated.

(b) *With solids*. The iodine adducts were prepared by using decalin as solvent. Although decalin forms an adduct with Dianin's compound, it shows less tendency to do this than any other solvent examined, the ratios varying from 9 : 1 to 17 : 1 (see Table). It is likely that the iodine adducts made in this way contain very little decalin, the holes being filled preferentially by the smaller molecules. The amount of iodine included depends upon its concentration in the decalin. In three different preparations the iodine content of the adducts was 3·5, 5·0, and 12·2%.

(c) *With ammonia and sulphur dioxide*. Dianin's compound was dissolved in the liquefied gases; the solutions were decanted from undissolved solid and allowed to evaporate. The solubility in liquid sulphur dioxide was very low.

(d) *With piperidine*. The *adduct* was made as in (a) and the well-drained crystals were kept in a desiccator without a drying agent until they just showed signs of becoming opaque (8 weeks) [Found: loss in weight with heat (see below), 21·9. $C_{18}H_{20}O_2,C_5H_{11}N$ requires loss, 24·1%]. After exposure to air for 2, 5, 8, and 12 days, the subsequent loss in weight of samples with heat was 17·4, 12·9, 10·4 and 8·3% respectively. The melting point is not determinable owing to ready loss of solvent.

Methods for the Analysis of the Adducts.—(a) *Elementary analysis*. The ratio of the components can be determined by elementary analysis only when the adduct contains a relatively high proportion of nitrogen, sulphur, or halogen, because the values for carbon and hydrogen are not usually sufficiently different to distinguish between ratios of, *e.g.*, 5 : 1, 6 : 1, and 7 : 1.

(b) *Loss in weight with heat*. This reliable and rapid method was used, though less accurately, by Dianin. When the unsolvated compound was heated a clear mobile liquid was first obtained which tended to sublime on to the cold neck of the flask. The temperature must not be taken much above 200° because of decomposition of the Dianin's compound. The complexes were dried at 100°/0·1 mm. for 4 hr., then weighed samples (*ca.* 0·5 g.) were heated in an oil-bath at 190—200° for 5 min. Melting began after about ½ min. with evolution of the solvent vapour, and after 3 min. a clear mobile liquid was obtained. The slight sublimate remained in the upper parts of the flask.

With solvents whose b. p. exceeds 100°, reduced pressure was necessary. This resulted in increased sublimation and a longer necked (7·5 cm.) 10-ml. flask was used. A longer period

Crystalline adducts formed by Dianin's compound (III).

Component	M. p.	Mole ratio *	Analysis: Found, % (reqd., %, in parentheses) C	H	Other elements	Loss in weight	Acid by titration
With organic compounds							
Methanol	155—156°	2 : 1	77·9 (78·2)	7·8 (7·7)	—	5·2 (5·6)	—
Ethanol	163—164	3 : 1	—	—	—	5·4 (5·7)	—
Propan-2-ol	160—161	3 : 1	—	—	—	7·3 (6·9)	—
n-Butanol	159—160	3 : 1	—	—	—	8·5 (8·4)	—
tert.-Butanol	166—167	3 : 1	—	—	—	8·4 (8·4)	—
Acetone	159—160	3 : 1	—	—	—	6·3 (6·7)	—
Carbon tetrachloride	159—160	3 : 1	—	—	Cl, 14·2 (13·6)	—	—
Methylene chloride	167—168	3 : 1	74·4 (74·2)	7·2 (7·0)	—	9·1 (9·5)	—
Methyl iodide	166—167	3 : 1	70·1 (69·8)	6·7 (6·4)	I, 14·1 (13·5)	15·2 (15·0)	—
Nitromethane	164—165	3 : 1	75·8 (76·3)	7·3 (7·3)	N, 1·3 (1·6)	—	—
Formic acid	159—160	3 : 1	77·3 (77·6)	7·2 (7·3)	—	5·4 (5·4)	5·2 (5·4)
Acetic acid	161—162	3 : 1	77·2 (77·7)	7·4 (7·7)	—	7·2 (6·9)	7·5 (6·9)
Propionic acid	156—157	4 : 1	—	—	—	6·3 (6·5)	6·6 (6·5)
Chloroform	161—162	4 : 1	74·1 (73·6)	7·0 (6·8)	Cl, 9·5 (8·9)	9·6 (10·0)	—
Carbon disulphide	164—165	4 : 1	—	—	S, 5·4 (5·6)	—	—
n-Butyric acid	162—163	5 : 1	—	—	—	6·3 (6·3)	6·0 (6·3)
n-Pentanol	169—170	6 : 1	—	—	—	5·2 (5·2)	—
n-Heptanol	162—163	6 : 1	—	—	—	6·5 (6·7)	—
Diethyl ether	172—173	6 : 1	—	—	—	4·2 (4·4)	—
1 : 3-Dibromopropane	168—169	6 : 1	73·6 (73·6)	7·0 (7·0)	Br, 9·5 (8·9)	—	—
Ethylene dichloride	163—164	6 : 1	77·5 (77·2)	7·4 (7·3)	Cl, 4·1 (4·2)	—	—
Ethylene dibromide	165—166	6 : 1	73·3 (73·5)	6·9 (6·9)	Br, 9·5 (8·9)	—	—
Tetrachloroethylene	153—154	6 : 1	74·3 (74·4)	6·7 (6·8)	Cl, 8·1 (8·0)	—	—
n-Butyl bromide	169—170	6 : 1	76·9 (77·1)	7·5 (7·4)	Br, 5·0 (4·7)	—	—
Diacetyl	162—163	6 : 1	—	—	—	5·2 (5·1)	—
Valeric acid	169—170	6 : 1	—	—	—	6·1 (6·0)	6·3 (6·0)
Hexanoic acid	169—170	6 : 1	—	—	—	6·6 (6·7)	7·1 (6·7)
Diethylamine	164—165	6 : 1	—	—	—	4·3 (4·3)	—
Ethyl chloroacetate	171—172	6 : 1	—	—	—	7·0 (7·1)	—
Benzene	160—161	6 : 1	—	—	—	4·5 (4·6)	—
Toluene	155—156	6 : 1	—	—	—	5·1 (5·4)	—
o-Xylene	154—155	6 : 1	—	—	—	6·5 (6·2)	—
m-Xylene	153—155	6 : 1	—	—	—	6·1 (6·2)	—
p-Xylene	152—153	6 : 1	—	—	—	5·9 (6·2)	—
Bromobenzene	158—159	6 : 1	—	—	Br, 4·6 (4·5)	—	—
Iodobenzene	153—154	6 : 1	—	—	I, 8·6 (7·0)	11·5 (11·2)	—
o-Dichlorobenzene	150—151	6 : 1	—	—	Cl, 3·5 (4·0)	8·7 (8·4)	—
Di*iso*butylene	157—158	7 : 1	—	—	—	5·9 (5·6)	—
tert.-Pentyl alcohol	161—162	7 : 1	—	—	—	4·6 (4·5)	—
Ethyl acetate	167—168	7 : 1	—	—	—	4·3 (4·5)	—
*iso*Pentyl valerate	160—161	7 : 1	—	—	—	8·0 (8·4)	—
p-Bromoanisole	154—155	7 : 1	—	—	Br, 3·9 (3·9)	—	—
m-Dichlorobenzene	158—159	7 : 1	—	—	Cl, 3·3 (3·5)	7·7 (7·3)	—
2-Bromopyridine	154—155	7 : 1	—	—	Br, 3·8 (3·9)	—	—
2 : 6-Lutidine	164—165	7 : 1	—	—	—	5·5 (5·4)	—
3-Methylheptane (tech.)	174—175	8 : 1	—	—	—	4·7 (5·0)	—
1-Methylnaphthalene	157—158	8 : 1	—	—	—	6·4 (6·2)	—
Pyridine	159—160	8 : 1	—	—	—	3·7 (3·5)	—
Triethylamine	158—159	9 : 1	79·9 (80·2)	7·3 (7·9)	N, 1·0 (0·8)	3·9 (4·0)	—
Decalin	157—158	9 : 1	—	—	—	4·7 (4·7)	—
„	156—157	17 : 1	—	—	—	2·9 (2·9)	—
With inorganic compounds							
Sulphur dioxide	152—153	4 : 1	—	—	S, 3·0 (2·8)	—	—
Ammonia	161—162	6 : 1	80·9 (79·8)	7·4 (7·6)	N, 0·86 (0·86)	1·2 (1·05)	—
Iodine	154—155	7 : 1	71·1 (70·9)	6·6 (6·6)	I, 12·2 (12·5)	—	—

* Mole ratio, Dianin's compound : component.

of heating (up to 10 min.) was necessary with high-boiling solvents such as *n*-heptanol (b. p. 176°) and decalin (b. p. 190°).

(c) *By titration.* Samples of the adducts with aliphatic acids were dissolved in ethanol and titrated with 0·02N-sodium hydroxide, a blank being performed on an equal volume of the ethanol used. The iodine-adduct in ethanol was titrated with 0·01N-sodium thiosulphate.

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