335. *Rottlerin. Part V. Tetrahydro*allo*rottlerin.*

By ALEXANDER MCGOOKIN, ALEXANDER ROBERTSON, and ERIC TITTENSOR.

Depending on the conditions employed, *iso*rottlerin (IV) on hydrogenation gives rise to dihydro*iso*rottlerin (VII, R = H) and/or tetrahydro*allo*rottlerin, $C_{30}H_{32}O_8$, of which the latter is analogous to tetrahydrorottlerin, forms a pentamethyl ether, and gives rise to 2 : 4 : 6-trihydroxy-5-acetyl-3-methylazobenzene and the azo-derivative (X, R = N:NPh). In consequence tetrahydro*allo*rottlerin has formula (VI, R = H) and in agreement with this expression undergoes the rottlerone change with warm alkali or boiling acetic acid, giving octahydro*allo*rottlerone (IX), the structure of which was established by synthesis from the keto-chroman (X, R = H).

The conversion of rottlerin (I) into tetrahydro*allo*rottlerin by way of *iso*rottlerin is explained and the structure which has been deduced for the latter compound is supported by its behaviour on hydrogenation and methylation. The relationship of the ethers obtained from *iso*rottlerin and its hydrogenation products has been determined and their orientations established.

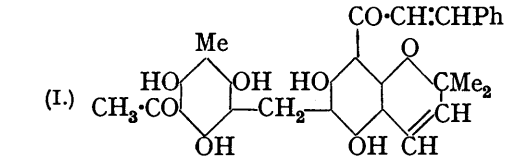
IN the course of the earlier work on the purification of rottlerin in these laboratories (Part I, J., 1937, 748) it was observed that the compound was unstable in high-boiling solvents (compare Ray and co-workers, J., 1938, 1862) and Brockmann and Maier (*Annalen*, 1938, **535**, 149), who have investigated the action of these agents in some detail, have shown that rottlerin is converted into its isomeride by means of boiling alcohol, acetic acid, or toluene. Ray and his co-workers (*loc. cit.*; *Current Science*, 1939, **8**, 165) appear to have isolated the same compound from extracts of kamala and claim that the isomeride occurs naturally. It must be observed, however, that clear evidence is lacking to prove *iso*rottlerin is a natural product and not an artefact formed by the action of boiling solvents employed in the isolation of rottlerin. We have prepared *iso*rottlerin by the alcohol and by the acetic acid methods of Brockmann and Maier (*loc. cit.*) and the present memoir deals with the chemistry and constitution of this important rottlerin derivative and related compounds.

The empirical formula $C_{30}H_{28}O_8$ for *iso*rottlerin, which was suggested by Brockmann and Maier (*loc. cit.*), has been substantiated in the present work, being in accordance with the analytical results obtained for a number of derivatives and supported by the close analogy in the behaviour and general properties observed between this substance and rottlerin (Part IV, preceding paper). Unlike rottlerin, however, the behaviour of *iso*-rottlerin on hydrogenation with a palladium–charcoal catalyst appears to depend to a large extent on the conditions employed and consequently these have been investigated in some detail. On hydrogenation in acetic acid with a palladium–charcoal catalyst and hydrogen at atmospheric or slightly elevated pressures *iso*rottlerin invariably yields dihydro*iso*rottlerin, m. p. 213°, which gives rise to benzaldehyde on being boiled with aqueous sodium hydroxide and appears to be identical with the product, m. p. 210—211°, described by Brookmann and Maier (*loc. cit.*). If, however, the reaction is carried out in alcohol, ethyl acetate (free from traces of acetic acid), or acetone with hydrogen at a pressure of 5—10 lb./sq. in. a tetrahydro-derivative is obtained which we have named *tetrahydro*allo*rottlerin*. When the hydrogenation is carried out in the same manner but the pressure of the hydrogen employed is approximately atmospheric, a mixture of tetrahydro*allo*- and dihydro*iso*-rottlerin is obtained, the proportions of which vary considerably. On hydrogenation in ethyl acetate dihydro*iso*rottlerin is quantitatively converted into tetrahydro*allo*rottlerin.

Methylation of tetrahydro*allo*rottlerin by the methyl sulphate–potassium carbonate method (George and Robertson, J., 1937, 1535) gives rise to a *pentamethyl* ether which does not contain a free hydroxyl group and is insoluble in aqueous sodium hydroxide, thus corresponding to *O*-pentamethylrottlerin. Though, as Brockmann and Maier have observed, *iso*rottlerin does not appear to react under the usual conditions with diazoaminobenzene, tetrahydro*allo*rottlerin reacts readily with this reagent, giving an almost theoretical yield of 2 : 4 : 6-trihydroxy-5-acetyl-3-methylazobenzene and the *azo*-derivative (X, R = N:NPh) of 5 : 7-dihydroxy-6-β-phenylpropionyl-2 : 2-dimethylchroman. The latter compound, which was identified by comparison with a synthetic sample, can be readily distinguished from the isomeride 6-*phenylazo*-5 : 7-*dihydroxy*-8-β-*phenylpropionyl*-2 : 2-*dimethylchroman*. By analogy with Boehm's work on the scission of polyhydroxydiphenylmethanes (*Annalen*, 1903, **329**, 310) this result clearly indicates that the tetrahydro*allo*rottlerin molecule is composed of a *C*-methylphloracetophenone residue attached to 5 : 7-dihydroxy-6-β-phenylpropionyl-2 : 2-dimethylchroman at the 8-position of the latter by a methylene radical and therefore tetrahydro*allo*rottlerin may be represented by the expression (VI, R = H) and its pentamethyl ether by (VI, R = Me).

Like rottlerin and its hydrogenation products, tetrahydro*allo*rottlerin readily undergoes the rottlerone change in warm alkali, and gives rise to *octahydro*allo*rottlerone*, the properties of which closely resemble those of octahydrorottlerone, including the insolubility in aqueous sodium hydroxide and the ferric reaction. Further, octahydro*allo*rottlerone is formed along with 2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-5 : 5′-diacetyl-3 : 3′-dimethyldiphenylmethane when tetrahydro*allo*rottlerin is boiled with acetic acid for 12 hours, this disproportionation being presumably strictly analogous to that obtaining in the case of tetrahydrorottlerin (Part IV, *loc. cit.*). By analogy with rottlerone and from the structure of the azo-compound (X, R = N:NPh) it appeared reasonably certain that octahydro*allo*rottlerone had formula (IX) and accordingly the synthesis of the latter was undertaken by the procedure employed for octahydrorottlerone. Interaction of the ketone (X, R = H) and formaldehyde in alcoholic sulphuric acid gave an almost quantitative yield of (IX) identical in every way with the compound from natural sources. Similarly, the analogous 5 : 7 : 5′ : 7′-*tetrahydroxy*-6 : 6′-*diacetyl*-2 : 2 : 2′ : 2′-*tetramethyl*-8 : 8′-*dichromanylmethane* was synthesised from the corresponding 6-acetylchroman. Although octahydro*allo*rottlerone and octahydrorottlerone closely resemble each other in general properties, they differ entirely in their behaviour towards warm alcoholic diazoaminobenzene. The former compound, though it reacts more slowly than tetrahydro*allo*rottlerin, ultimately gives an almost theoretical yield of the azo-derivative (X, R = N:NPh), whereas even on prolonged treatment octahydrorottlerone does not appear to react. This difference in reactivity is probably due to the fact that the 8-position of 5 : 7-dihydroxy-2 : 2-dimethylchroman is considerably

more active than the 6-position, *e.g.*, in Gattermann's reaction (Robertson and Subramanian, J., 1937, 286) and in the Hoesch reaction (Part III, this vol., p. 1257), and consequently the extrusion of the methylene group would be expected to take place more easily from the 8-position, thus allowing the scission of (IX) with the formation of two molecules of the azo-compound. The same factor may well account for the difference in behaviour between tetrahydro*allo*rottlerin and tetrahydrorottlerin towards alcoholic diazoaminobenzene, where in the latter case we have not yet been able to obtain the azo-derivative of the keto-chroman residue.



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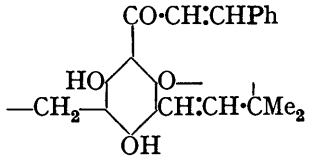

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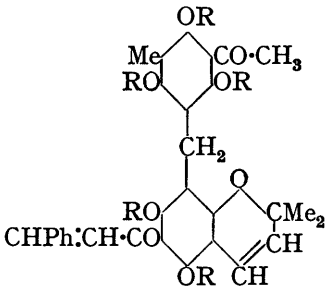

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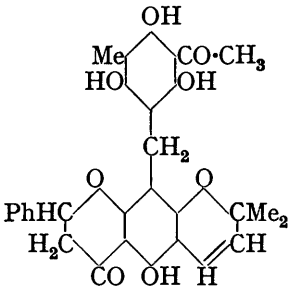

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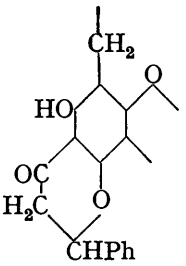

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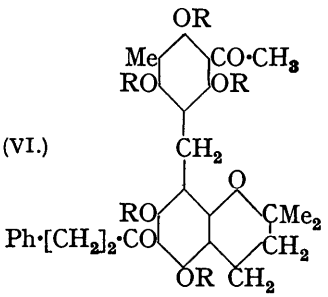

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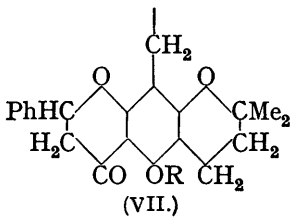

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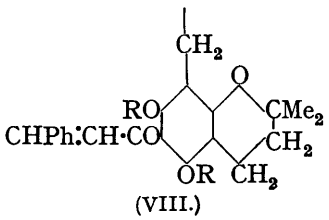

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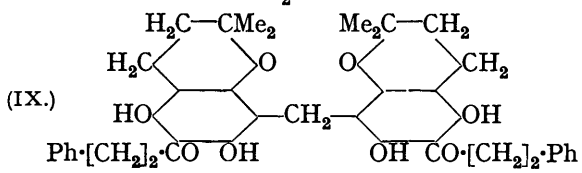

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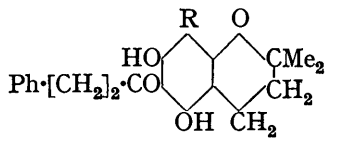

(X.)

To explain the isomerisation of rottlerin to *iso*rottlerin Brockmann and Maier (*loc. cit.*) suggested that the formation of the latter product was due to the cyclisation of the chalkone system to form the dihydro-γ-pyrone type, but it is clear from the foregoing results and the structure of tetrahydro*allo*rottlerin (VI, R = H) that this change is a more complex one than these authors envisaged and involves not only the cyclisation of the chalkone system but also the interchange of the cinnamoyl and the 2 : 4 : 6-trihydroxy-5-acetyl-3-methylphenylmethylene residues. It appears to us that the change can be best explained on the view that the first stage of the reaction is the conversion of rottlerin into the intermediate (II) by the opening of the chromen ring system and that this is followed by re-formation of the latter so as to produce (III, R = H), which is strictly analogous to rottlerin and hence may be termed *allo*rottlerin. At the same time the chalkone (III, R = H) is cyclised to the dihydro-γ-pyrone system with the production of type (IV), which we regard as repre-

senting Brockmann and Maier's *iso*rottlerin.* From the intermediate *allo*rottlerin (III, R = H), two formulæ (IV) and (V) for the cyclisation product are possible but owing to lack of evidence a final decision between the two orientations cannot be made at present. If the cyclisation of the chalkone system in rottlerin was to precede the scission of the chromen system, then it is reasonably certain that *iso*rottlerin would be the modification represented by (V). We are not at present inclined to accept this view of the reaction, however, because it would appear that the formation of the dihydro-γ-pyrone system involving the protection of a hydroxyl group in the chromen residue would tend to stabilise the latter unit.

On the basis of the structure type (IV) or (V) for *iso*rottlerin the formulation of the two hydrogenation products of this compound clearly follows and further, it would appear that the failure of the compound to react with alcoholic diazoaminobenzene is due to the suppression of a hydroxyl group in the formation of the dihydro-γ-pyrone ring as in the case of the dimethyl ethers of rottlerin and tetrahydrorottlerin (Part IV, *loc. cit.*). The production of tetrahydro*allo*rottlerin from *iso*rottlerin in which two molecules of hydrogen are absorbed clearly arises by the hydrogenation of the ethylenic linkage in the chromen ring with the simultaneous opening of the dihydro-γ-pyrone system to the chalkone type (VIII, R = H) and subsequent saturation of the double bond thus formed, giving (VI, R = H); alternatively, the second stage might simulate the opening of the dihydrofuran system in tubaic acid under the same conditions and the oxygen bridge of the dihydro-γ-pyrone system undergo a direct reductive fission. On the other hand, the formation of dihydro*iso*rottlerin type (VII, R = H) takes place by the saturation of the double bond in the chromen system, but the acetic acid used as a solvent apparently inhibits the opening of the dihydro-γ-pyrone ring. It may be noted here that dihydro*iso*rottlerin may have a corresponding structure derived from the alternative formula (V) for *iso*rottlerin.

The foregoing explanation of the behaviour of *iso*rottlerin on hydrogenation is amply supported by the following methylation experiments: On methylation by the methyl sulphate–potassium carbonate method dihydro*iso*rottlerin type (VII, R = H) gave rise to a mixture of O-*tetramethyldihydro*iso- and O-*pentamethyldihydro*allo-*rottlerin*. Of these the former behaves as a saturated compound towards hydrogen and a palladium catalyst, is insoluble in cold aqueous sodium hydroxide and gives a negative ferric reaction and hence this substance has retained the dihydro-γ-pyrone ring system intact, being represented by the formula type (VII, R = Me) (the protection of the hydroxyl groups presumably stabilises the dihydro-γ-pyrone system). The second product, a pentamethyl ether, which contains an ethylenic linkage and on hydrogenation gives rise to *O*-pentamethyltetrahydro*allo*rottlerin (VI, R = Me), must arise by the opening of the dihydro-γ-pyrone ring in type (VII, R = H) and consequently has the structure (VIII, R = Me). Though in agreement with the formula type (IV) *iso*rottlerin contains four hydroxyl groups according to Zerewitinoff's method, this compound on methylation gave only O-*pentamethyl*allo*rottlerin*, which clearly arises by the opening of the dihydro-γ-pyrone ring in (IV) to give the intermediate *allo*rottlerin (III, R = H) and is therefore represented by the expression (III, R = Me). In agreement with this structure the ether (III, R = Me) on hydrogenation absorbs two mols. of hydrogen, giving *O*-pentamethyltetrahydro*allo*rottlerin (VI, R = Me).

Since the completion of the analytical work in the present communication our attention has been directed to a recent communication by Brockmann and Maier (*Naturwiss.*, 1939, **27**, 259) (compare Ray and co-workers, *Current Science*, 1939, **8**, 165), but owing to considerable discrepancies between the melting points of some of our products and those given by the German authors it is not possible at present to be certain of the identity of the respective series of derivatives. It would seem reasonably certain, however, that the "transformation products" of *iso*rottlerin and of dihydro*iso*rottlerin are respectively *allo*rottlerin (III, R = H), m. p. 194°, and dihydro*allo*rottlerin (VIII, R = H), m. p. 215°.

* At present for the sake of clarity we have retained this name, which was originally suggested by Brockmann and Maier (*loc. cit.*), but in this connexion it must be noted that by cyclisation of the chalkone system in rottlerin (I) a dihydro-γ-pyrone type (one only) is possible which we think should be named *iso*rottlerin. On the other hand, by the same change *allo*rottlerin (III, R = H) can give rise to two isomerides, α- and β-*iso*allorottlerin.

Experimental.

iso*Rottlerin*.—This compound has been prepared by a number of procedures, including that of Brockmann and Maier (*loc. cit.*) and the following modification of it: On being gently boiled (oil bath at 120—130°) with acetic acid (450 c.c. of 95% by vol.), rottlerin (30 g.) dissolved in about 15 minutes; ½ hour later the solution was allowed to cool and the buff precipitate (29 g.) obtained by the addition of much water was washed, dried, and triturated with methyl alcohol (150 c.c.). Next day the insoluble product was collected, washed, and boiled with alcohol (150 c.c.) for 20 minutes; the extract was rejected, and the solid was purified from acetic acid–alcohol and then alcohol, giving *iso*rottlerin in yellow diamond-shaped plates, m. p. 182° (Found: C, 69·8; H, 5·4. Calc. for $C_{30}H_{28}O_8$: C, 69·8; H, 5·4. Calc. for $C_{31}H_{30}O_8$: C, 70·2; H, 5·7%) (Brockmann and Maier and Ray and co-workers, *locc. cit.*, give m. p. 180°). A further quantity of impure material was isolated from the alcoholic liquors.

Hydrogenation of iso*Rottlerin*.—(A) Hydrogenation of the compound (2 g.), dissolved in absolute acetic acid (200 c.c.), with a palladium–charcoal catalyst (from 0·2 g. of palladium chloride and 2 g. of charcoal) and hydrogen at 10 lb./sq. in. during 2 hours gave the dihydro-derivative (VII, R = H), which, on isolation by addition of water, separated from alcohol, then benzene, and finally alcohol in light yellow prisms (1 g.), m. p. 213°, soluble in acetone, ethyl acetate, or acetic acid and insoluble in light petroleum, and having a brownish-green ferric reaction in alcohol (Found: C, 69·5; H, 5·9. Calc. for $C_{30}H_{30}O_8$: C, 69·5; H, 5·8%). On being boiled, a solution of this substance in 8% aqueous sodium hydroxide gave rise to benzaldehyde. The quantitative hydrogenation of *iso*rottlerin (1 g.) was effected in ethyl acetate (200 c.c.) containing a little acetic acid with a palladium–charcoal catalyst and hydrogen at atmospheric pressure (approximately 1 mol. absorbed), giving the dihydro-compound (0·7 g.), m. p. 213° after purification.

(B) Hydrogenation of *iso*rottlerin (1 g.) in absolute ethyl acetate (200 c.c.) with a palladium–charcoal catalyst (from 0·1 g. of palladium chloride and 1 g. of charcoal) and hydrogen at 5 lb./sq. in. during 2 hours furnished *tetrahydro*allo*rottlerin* (VI, R = H), which separated from a little benzene and then alcohol in long, slender, bright yellow prisms (0·8 g.), m. p. 241°, sparingly soluble in acetone, ethyl acetate, or hot methyl alcohol and giving a brown ferric reaction in alcohol (Found: C, 69·45, 69·4; H, 6·3, 6·2. $C_{30}H_{32}O_8$ requires C, 69·2; H, 6·15%). The same compound was obtained when acetone or alcohol was employed as the solvent for the hydrogenation with hydrogen at 5—10 lb./sq. in.

When dihydro*iso*rottlerin (VII, R = H) (1 g.), dissolved in ethyl acetate (250 c.c.), was hydrogenated under the same conditions (2 g. of catalyst), tetrahydro*allo*rottlerin was obtained; on purification from alcohol it formed slender prisms (0·6 g.), m. p. and mixed m. p. 241°, identical with the foregoing specimen.

When the hydrogenation was carried out in absolute ethyl acetate, acetone, or alcohol with a palladium catalyst and hydrogen at atmospheric pressure, the product invariably consisted of a mixture, m. p. about 200°, of tetrahydro*allo*- and dihydro*iso*-rottlerin which was extremely difficult to separate. Fractional crystallisation of the mixture (3 g.) from acetone gave three main fractions: (a) m. p. 234°, (b) m. p. 223°, and (c) m. p. 209°. On repeated purification from alcohol fractions (a) and (b) each gave tetrahydro*allo*rottlerin (about 1·5 g.), m. p. 241°; fraction (c), on being combined with the residue left on evaporation of the acetone liquors and recrystallised from alcohol, gave dihydro*iso*rottlerin (0·5 g.), m. p. 213°.

O-*Pentamethyl*allo*rottlerin* (III, R = Me).—A mixture of *iso*rottlerin (2 g.), potassium carbonate (40 g.), methyl sulphate (10 c.c.), and acetone (100 c.c.) was heated on the steam-bath until the deep red colour of the original solution had almost disappeared (2½ hours); it was then cooled and treated with water (300 c.c.). Next day the yellow plastic solid was collected, dried, and triturated with a little cold methyl alcohol, and the resulting pale yellow product crystallised several times from light petroleum (b. p. 60—80°), then aqueous alcohol, and finally light petroleum, yielding the *pentamethyl* ether in pale greenish-yellow (almost colourless) rhombic prisms (1 g.), m. p. 136°, which had a negative ferric reaction and were insoluble in aqueous sodium hydroxide [Found: C, 71·6, 71·7; H, 6·5, 6·5; OMe, 26·4, 26·6; *M*, 546. $C_{30}H_{23}O_3(OMe)_5$ requires C, 71·7; H, 6·5; OMe, 26·45%; *M*, 586. $C_{31}H_{25}O_3(OMe)_5$ requires C, 72·0; H, 6·7; OMe, 25·8%; *M*, 600].

O-*Pentamethyltetrahydro*allo*rottlerin* (VI, R = Me).—(A) Hydrogenation of the foregoing ether (1 g.), dissolved in absolute alcohol (150 c.c.), with a palladium–charcoal catalyst (2 g.) and hydrogen at 20 lb./sq. in. during 2 hours and subsequent removal of the catalyst and the alcohol gave a colourless oil. On slow evaporation of the solvent a solution of this material

in light petroleum (b. p. 40—60°) gradually deposited an almost theoretical yield of the *tetrahydro*-derivative in large prisms, m. p. 101° after purification from aqueous alcohol and light petroleum [Found: C, 71·2, 71·2; H, 7·1, 7·3; OMe, 26·1, 26·4; *M* (Rast), 540. $C_{30}H_{27}O_3(OMe)_5$ requires C, 71·2; H, 7·1; OMe, 26·3%; *M*, 590]. This compound had a negative ferric reaction and was readily soluble in benzene, ethyl acetate and warm alcohol. When the hydrogenation was carried out at atmospheric pressure in the same solvent, approximately 2 mols. of hydrogen were absorbed, giving a similar yield of the same ether, m. p. 101°.

(B) A mixture of tetrahydro*allo*rottlerin (VI, R = H) (1 g.), potassium carbonate (20 g.), methyl sulphate (5 c.c.), and acetone (50 c.c.) was heated on the water-bath until the deep yellow colour of the original solution had almost disappeared (1½ hours), and then treated with water (200 c.c.). Next day the product was isolated with ether and purfied by the procedure employed in method (A), giving *O*-pentamethyltetrahydro*allo*rottlerin in colourless prisms (0·5 g.), m. p. and mixed m. p. 101°.

*Methylation of Dihydro*iso*rottlerin.*—When this compound (2 g.) was heated on the water-bath with methyl sulphate (10 c.c.), potassium carbonate (40 g.), and acetone (75 c.c.) for 4½—5 hours, with the addition of more carbonate (10 g.) and more sulphate (5 c.c.) after 3 hours, the mixture became almost colourless; the oil which separated on the addition of water (300 c.c.) solidified in the course of 2 days. The product obtained by crystallisation of this material from light petroleum (b. p. 60—80°) was a mixture and after having been twice purified from the same solvent it was then recrystallised from alcohol and obtained in crystals sufficiently large to be separated manually into (a) colourless and (b) pale yellow prisms.

The colourless material was repeatedly crystallised from light petroleum (b. p. 60—80°), a few pale yellow crystals were separated, and the residue recrystallised from aqueous alcohol and then light petroleum, giving O-*tetramethyldihydro*iso*rottlerin* (type VII, R = Me) in colourless prisms, m. p. 149°, readily soluble in benzene, acetone, or ethyl acetate and having a negative ferric reaction [Found: C, 71·2, 71·1; H, 6·6, 6·5; OMe, 20·6, 21·0; *M* (Rast), 552. $C_{30}H_{26}O_4(OMe)_4$ requires C, 71·1; H, 6·6; OMe, 21·6%; *M*, 574]. Attempts to hydrogenate this ether (0·5 g.), dissolved in alcohol (100 c.c.), with hydrogen at 8 lb./sq. in. and a palladium–charcoal catalyst gave unchanged material.

The pale yellow fraction (b) was repeatedly crystallised from light petroleum (b. p. 60—80°), a few colourless crystals removed by hand, and the residual O-*pentamethyldihydro*allo*rottlerin* (VIII, R = Me) purified from aqueous alcohol and then light petroleum, forming pale greenish-yellow, tiny hexagonal plates, m. p. 135°, having solubilities similar to those of *O*-tetramethyldihydro*iso*rottlerin and a negative ferric reaction [Found: C, 71·5, 71·5; H, 6·9, 6·8; OMe, 27·2, 27·0; *M* (Rast), 569. $C_{30}H_{25}O_3(OMe)_5$ requires C, 71·4; H, 6·8; OMe, 26·4%; *M*, 588]. A mixture of this substance and *O*-pentamethyl*allo*rottlerin melted at about 130—132°. On hydrogenation with the aid of a palladium–charcoal catalyst (1 g.) this ether (0·3 g.), dissolved in alcohol (100 c.c.), gave rise to *O*-pentamethyltetrahydro*allo*rottlerin (VI, R = Me), m. p. and mixed m. p. 101°.

*Action of Diazoaminobenzene on Tetrahydro*allo*rottlerin.*—When a solution of diazoaminobenzene (1·83 g.) in hot alcohol (30 c.c.) was added to boiling alcohol (80 c.c.) containing a suspension of tetrahydro*allo*rottlerin (2·6 g.), the solid rapidly dissolved and the solution then became dark red. On cooling, the reaction mixture deposited orange-red crystals, and on slow evaporation of the solvent three further fractions were obtained, finally leaving a small amount of a resinous residue which smelt of aniline. The combined products, which were obtained in almost theoretical amount, were separated into two fractions, (a) and (b), by fractional crystallisation from acetic acid, in which (a) was less soluble, and then from methyl alcohol, in which (b) is sparingly soluble. In this way (a) was obtained in red plates, m. p. 202°, identical in every way with an authentic specimen of 2 : 4 : 6-trihydroxy-5-acetyl-3-methylazobenzene, m. p. 202° (Part IV, *loc. cit.*) (Found: N, 9·5. Calc. for $C_{15}H_{14}O_4N_2$: N, 9·8%). Repeated crystallisation of fraction (b) finally gave 8-*phenylazo*-5 : 7-*dihydroxy*-6-β-*phenylpropionyl*-2 : 2-*dimethylchroman* (X, R = N:NPh) as a felted mass of slender orange-red needles, m. p. 162°, identified by direct comparison with an authentic specimen (Found: C, 72·2; H, 6·2; N, 6·6. $C_{26}H_{26}O_4N_2$ requires C, 72·6; H, 6·1; N, 6·5%).

An authentic specimen of this azo-compound was prepared in good yield by boiling a solution of 5 : 7-dihydroxy-6-β-phenylpropionyl-2 : 2-dimethylchroman (X, R = H) (0·5 g.) and diazoaminobenzene (0·5 g.) in alcohol (20 c.c.) for 2 minutes. The product, which quickly began to separate from the cooled dark red solution, was collected 2 days later and purified from acetic acid and then acetic acid–alcohol, forming orange-red needles, m. p. 162°, sparingly soluble in alcohol, benzene, or light petroleum (Found: C, 72·6; H, 6·1; N, 6·9%).

Prepared in a similar manner from 5 : 7-dihydroxy-8-β-phenylpropionyl-2 : 2-dimethylchroman, the isomeride *6-phenylazo-5 : 7-dihydroxy-8-β-phenylpropionyl-2 : 2-dimethylchroman* separated from the reaction mixture on spontaneous evaporation of the solvent and then formed dark red, rectangular plates, m. p. 181°, from acetic acid and then alcohol, sparingly soluble in light petroleum (Found : C, 72·7; H, 6·1; N, 6·7%). A mixture of this compound and the isomeride from tetrahydro*allo*rottlerin melted at about 140°.

By the same procedure 5 : 7-dihydroxy-8-acetyl-2 : 2-dimethylchroman gave the *6-phenylazo*-derivative, which formed deep red plates, m. p. 232°, from alcohol (Found : N, 8·0. $C_{19}H_{20}O_4N_2$ requires N, 8·2%).

(With James Matchet) *Octahydro*allo*rottlerone* (IX).—(A) For the preparation of this compound the following practical directions must be closely adhered to : On being gently heated (oil bath) in nitrogen, the clear yellow solution of tetrahydro*allo*rottlerin (1·8 g.) in 4% aqueous sodium hydroxide (75 c.c.) became opaque at about 40° and an almost colourless solid began to separate. When the temperature had reached 55°, heating was discontinued, the hot reaction mixture was kept for 5 minutes and then rapidly cooled, and the precipitate (0·6 g.) collected, washed, and dried. Crystallised from acetone containing a little acetic acid and then from alcohol, *octahydro*allo*rottlerone* formed pale yellow, squat prisms or elongated rectangular prisms, m. p. 175—175·5°, having a dark violet ferric reaction in alcohol (Found : C, 74·3, 74·2; H, 6·6, 6·7. $C_{41}H_{44}O_8$ requires C, 74·1; H, 6·6%). On being saturated with carbon dioxide, a further small amount of this compound separated from the alkaline liquors and after its removal acidification of the filtrate with hydrochloric acid gave an intractable red-brown resin which has not so far yielded crystalline material. Prepared by the acetic anhydride–pyridine method at room temperature and then on the water-bath, the tetra-acetate of octahydro*allo*rottlerone formed pearly leaflets, m. p. 163°, from aqueous alcohol and then aqueous acetone.

When a hot solution of diazoaminobenzene (0·3 g.) in alcohol (20 c.c.) was added to octahydro*allo*rottlerone (0·1 g.) dissolved in a little warm dioxan, and the mixture heated on the steam-bath for ½ hour, an almost quantitative yield of the azo-derivative (X, R = N:NPh) separated in the course of 48 hours, m. p. 161° after purification, identical with an authentic specimen.

(B) On being boiled with acetic acid (200 c.c.) for 12 hours, tetrahydro*allo*rottlerin (2 g.) gradually dissolved and a yellow precipitate gradually separated from the resulting reddish solution. On cooling, the solid (0·96 g.) was collected and crystallised from much acetone and then dioxan, giving 2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-5 : 5′-diacetyl-3 : 3′-dimethyldiphenylmethane, m. p. 291°, identical in every way with a synthetical specimen (Part IV, *loc. cit.*). Evaporation of the acetone liquors gave unchanged tetrahydro*allo*rottlerin, m. p. 241° after purification from alcohol.

Addition of excess of water to the acetic acid liquor left on separation of the foregoing compound gave a pinkish precipitate (0·88 g.), which on repeated crystallisation from alcohol gave octahydro*allo*rottlerone, m. p. 175°, identical with a synthetical specimen.

(C) On being treated with 12 drops of concentrated sulphuric acid, a solution of 5 : 7-dihydroxy-6-β-phenylpropionyl-2 : 2-dimethylchroman (X, R = H) (Part III, *loc. cit.*) (0·12 g.) in alcohol (5 c.c.) containing 40% formaldehyde (0·5 c.c.) almost immediately gave a nearly colourless crystalline precipitate. Next day the product was collected, washed, and recrystallised from acetone–alcohol and then alcohol, giving octahydro*allo*rottlerone in pale yellow, squat prisms (sometimes elongated rectangular prisms), m. p. 175°, undepressed by admixture with a natural specimen, with which it was identical in every way (Found : C, 74·0; H, 6·8%).

In the same way the interaction of 5 : 7-dihydroxy-6-acetyl-2 : 2-dimethylchroman (0·1 g.), 40% formaldehyde (0·5 c.c.), and 6 drops of concentrated sulphuric acid in alcohol (2 c.c.) furnished an almost theoretical yield of *5 : 7 : 5′ : 7′-tetrahydroxy-6 : 6′-diacetyl-2 : 2 : 2′ : 2′-tetramethyl-8 : 8′-dichromanylmethane*, which separated from alcohol in greenish-yellow, squat prisms, m. p. 209°, readily soluble in acetone or aqueous sodium hydroxide and having a dark purple-brown ferric reaction in alcohol (Found : C, 67·0; H, 6·7. $C_{27}H_{32}O_8$ requires C, 67·0; H, 6·6%).

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