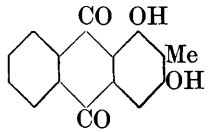
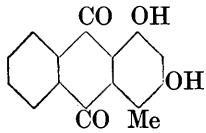
CCXXIII.—*Syntheses of Glucosides. Part V. Two New Syntheses of Rubiadin and Syntheses of 1-O-Methylrubiadin and of Rubiadin Glucoside.*

By ELFED THOMAS JONES and ALEXANDER ROBERTSON.

ALTHOUGH rubiadin was first isolated in 1853 by Schunck (*Phil. Trans.*, **143**, 72) from madder root, *Rubia tinctoria*, it was not until 1893 that Schunck and Marchlewski (*J.*, **63**, 969) isolated rubiadin glucoside from Dutch madder. These authors (*J.*, 1894, **65**, 182) showed that rubiadin was in all probability represented by either formula (I) or (II).

(I.)





(II.)

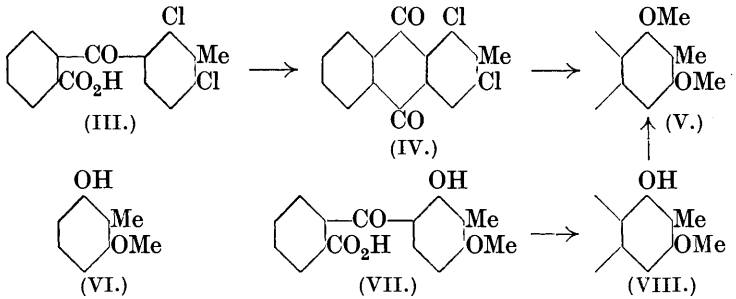
A synthesis of (I) gave a product which was not identical with the natural substance, and Schunck and Marchlewski concluded that rubiadin had formula (II). Barrowcliff and Tutin (*J.*, 1907, **91**, 1907) isolated from the root of *Morinda longiflora* a monomethyl ether of rubiadin which on demethylation yielded rubiadin identical with Schunck's product, but which, contrary to the views of Schunck and Marchlewski, they considered to be a derivative of (I). The same ether was obtained by Simonsen (*J.*, 1920, **117**, 561) from the root bark of *Morinda citrifolia*. As a result of the synthetical experiments of Schunck and Marchlewski, Simonsen concluded that the ether was derived from (II) and noted the anomaly in Barrowcliff and Tutin's communication.

The synthesis of the anthraquinone (II) by Stouder and Adams (*J. Amer. Chem. Soc.*, 1927, **49**, 2043) and by Mitter, Sen, and Paul (*J. Indian Chem. Soc.*, 1927, **4**, 535) definitely excluded the possibility that rubiadin had formula (II). Mitter and Gupta (*J. Indian Chem. Soc.*, 1928, **5**, 25), on repeating the synthesis of Schunck and Marchlewski (*loc. cit.*), obtained rubiadin (I) in small yield, but they do not appear to have made a direct comparison of their product with the natural material.

Syntheses of Rubiadin.—Of the following methods for the preparation of rubiadin in quantity, the second only proved suitable.

2 : 4-*Dichloro*-3-*methylbenzophenone*-2′-*carboxylic acid* (III), prepared by the condensation of phthalic anhydride and 2 : 6-dichlorotoluene by means of aluminium chloride, gave 1 : 3-*dichloro*-2-*methylanthraquinone* (IV) on ring closure by means of concentrated sulphuric acid and boric acid. The substance (IV) was converted by

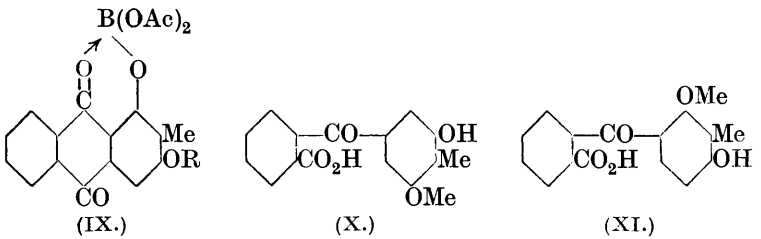
means of sodium methoxide and subsequent methylation of the crude product into 1 : 3-*dimethoxy*-2-*methylanthraquinone* (V), which on demethylation gave rubiadin (I). The synthetic rubiadin and its diacetate were identical with the natural product and its diacetate.



Although the yields of (III) and (IV) were good, that of (V) was disappointing and we were led to prepare rubiadin by the following route. 2-*Methoxy*-6-*nitrotoluene*, prepared by methylating 6-nitro-*o*-cresol (Noelting, *Ber.*, 1904, **37**, 1020), was reduced to 6-*methoxy*-o-*toluidine*, which on diazotisation and decomposition of the diazonium salt gave 6-*methoxy*-o-*cresol* (VI).

The condensation of (VI) with phthalic anhydride gave rise to only one product, 2-*hydroxy*-4-*methoxy*-3-*methylbenzophenone*-2′-*carboxylic acid* (VII), which on ring closure yielded 1-*hydroxy*-3-*methoxy*-2-*methylanthraquinone* (VIII). Methylation of (VIII) gave O-*dimethylrubiadin* (V) and demethylation afforded rubiadin (I).

It has been shown by Dimroth and Faust (*Ber.*, 1921, **54**, 3020) that α-hydroxyanthraquinones on treatment with boroacetic anhydride readily yield boroacetates. The properties of the ether (VIII) were found to be consistent with those of an α-hydroxyanthraquinone and the formation of the *diacetoborate* (IX, R = Me) afforded conclusive proof of the structure assigned to it.

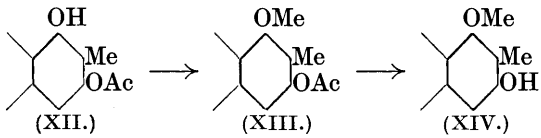


Further, it follows that the intermediate keto-acid which on ring closure can give rise to (VIII) must have either formula (VII) or (X). The constitution of this acid cannot be represented by (XI), since a

substance of this formula would give the ether (XIV). Formula (X) is excluded on general grounds, and, moreover, a compound of this structure would in all probability give rise to a mixture of (VIII) and (XIV) on ring closure. It seems certain, therefore, that the intermediate keto-acid has the structure (VII).

Barrowcliff and Tutin (*loc. cit.*) describe the preparation of a dimethylrubiadin, m. p. 181°, from natural *O*-monomethylrubiadin and from rubiadin by means of an alcoholic solution of sodium ethoxide and methyl iodide. The *O*-dimethyl ether prepared by us from (IV) and from (VIII) melted at 158° and under the microscope appeared to be homogeneous. In our hands the methylation of rubiadin by methods which involve the use of strong alkalis gave mixed products. Moreover, in compounds of this class alkylation of the hydroxyl in the *o*-position to carbonyl is difficult, and is frequently impossible by the method used by Barrowcliff and Tutin. On the other hand, we have found that the methylation of rubiadin and its derivatives in warm acetone by means of methyl iodide and silver oxide invariably gave pure products. Although it is possible that the compound described by these authors may have contained methyl attached to carbon, to us it seems probable that the substance was impure 3-*O*-methylrubiadin (VIII) (methoxyl determination not given). This ether we have found to melt at 187°.

Synthesis of 1-O-*Methylrubiadin.*—Rubiadin on treatment with boroacetic anhydride in acetic anhydride undergoes acetylation with the formation of the *diacetoborate* of 3-O-*acetylrubiadin* (IX, R = Ac). Decomposed with water, the boroacetate gave 3-*O*-acetylrubiadin (XII).



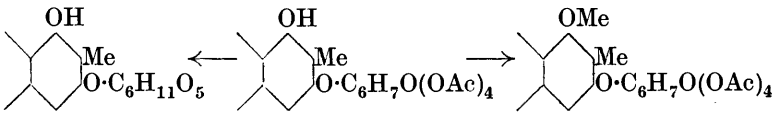
(XII.) (XIII.) (XIV.)

Methylation of (XII) by means of methyl iodide and silver oxide afforded 3-*acetoxy*-1-*methoxy*-2-*methylanthraquinone* (XIII), which on hydrolysis gave 1-*O*-methylrubiadin (XIV). This ether (XIV) and its acetate (XIII) have properties identical with those of the natural ether and its acetate described by Barrowcliff and Tutin (*loc. cit.*) and by Simonsen (*loc. cit.*).

Synthesis of Rubiadin Glucoside.—The glucoside isolated by Schunck and Marchlewski (*loc. cit.*) was shown by them to be a monoglucoside. The hexose obtained on hydrolysis was considered to be glucose.

3-O-*Tetra-acetyl*-β-*glucosidoxy*-1-*hydroxy*-2-*methylanthraquinone* (XV) was prepared by the procedure adopted by one of us (A. R.,

this vol., p. 1136) for the preparation of *O*-tetra-acetylglucoalizarin. Deacetylation of (XV) gave rubiadin glucoside (XVI). The synthetic glucoside and its penta-acetate were identical with the natural glucoside and its penta-acetate (obtained by Schunck).



(XVI.) (XV.) (XVII.)

By analogy with alizarin glucoside (*loc. cit.*) it was considered likely that the sugar residue in rubiadin glucoside was attached at the 3-position. The isolation of the substance (XIV) as a product of the hydrolysis of the *ether* (XVII), obtained by methylation of the glucoside (XV), afforded conclusive proof of the structure of (XV) and of rubiadin glucoside.

Application of Takahashi's procedure (*J. Pharm. Soc. Japan*, 1925, **525**, 4; compare Zemplén and Müller, *Ber.*, 1929, **62**, 2107; Müller, *ibid.*, p. 2793) for the preparation of hydroxyanthraquinone glucosides gave *octa-acetyl-β-diglucorubiadin* when the reagents were used in excess. With molecular proportions, the same reaction gave rise to an impure tetra-acetylglucoside. The latter substance, on deacetylation and treatment of the product with acetic anhydride and pyridine, afforded the penta-acetylglucoside of rubiadin.

EXPERIMENTAL.

2 : 4-*Dichloro*-3-*methylbenzophenone*-2'-*carboxylic Acid* (III).—To a mixture of phthalic anhydride (40 g.) and 2 : 6-dichlorotoluene (140 g.; Davies, J., 1921, **119**, 871), powdered aluminium chloride (100 g.) was added in 6 portions during 1 hour (agitation), and after the evolution of hydrogen chloride had almost ceased the mixture was heated on the steam-bath for 12 hours. The cooled reaction product was decomposed with ice (300 g.) and concentrated hydrochloric acid (60 c.c.), the excess of 2 : 6-dichlorotoluene removed by distillation in steam, and the residual solid extracted with warm 5% aqueous sodium carbonate. Acidified with concentrated hydrochloric acid, the filtered extract gave the acid (III) as a gum which quickly crystallised. Recrystallisation from acetic acid gave colourless rhombic prisms (54 g.), m. p. 144—145° (Found: C, 58·0; H, 3·2. $C_{15}H_{10}O_3Cl_2$ requires C, 58·2; H, 3·2%). This *acid* is moderately easily soluble in warm alcohol or benzene and insoluble in water. It is unaffected by potassium acetate or silver acetate in boiling acetic acid.

1 : 3-*Dichloro*-2-*methylanthraquinone* (IV).—A mixture of the foregoing acid (20 g.), boric acid (4 g.), and concentrated sulphuric

acid (400 c.c.) was heated on the steam-bath for 4 hours. The cooled solution was poured on ice, and the precipitate of 1 : 3-*dichloro*-2-*methylanthraquinone* collected and washed with water. Crystallisation from alcohol gave pale yellow rhombic prisms, m. p. 172° (yield, about 90% of the theoretical) (Found : C, 61·8; H, 3·1; Cl, 23·8. $C_{15}H_8O_2Cl_2$ requires C, 61·9; H, 2·8; Cl, 24·4%). The substance is moderately easily soluble in warm alcohol or acetic acid.

1 : 3-*Dimethoxy*-2-*methylanthraquinone* (O-*Dimethylrubiadin*).—A solution of sodium methoxide was prepared by adding as much sodium to methyl alcohol (250 c.c.) as would dissolve in it at room temperature. 1 : 3-Dichloro-2-methylanthraquinone (6 g.) was then introduced, and the mixture refluxed for 12 hours; the almost colourless solution gradually became bright red. After dilution with water (250 c.c.) and acidification with acetic acid, the dark brown solid was collected. In subsequent experiments a more tractable product was obtained by diluting the cooled reaction mixture with water (50 c.c.) and gradually adding methyl sulphate until the colour changed to yellow. The crude product was extracted with methyl alcohol in a Soxhlet apparatus, and, on evaporation of the greater part of the solvent, a yellow crystalline solid separated from the cooled extract. Repeated crystallisation from methyl alcohol finally gave a product, m. p. about 176°, which appeared under the microscope to be a mixture and gave a red coloration with alcoholic sodium hydroxide. A mixture of this solid (7 g., collected from several experiments), silver oxide (8 g.), methyl iodide (10 c.c.), and acetone (250 c.c.) was refluxed for 3 hours. The silver salts were removed by filtration and washed with acetone and the solution was evaporated to 100 c.c.; on cooling, O-*dimethylrubiadin* (V) crystallised. Recrystallisation from methyl alcohol gave yellow needles (4 g.), m. p. 158° [Found : C, 72·5; H, 5·0; MeO, 21·9. $C_{15}H_8O_2(OMe)_2$ requires C, 72·3; H, 5·0; MeO, 22·0%]. The ether is readily soluble in warm acetic acid, from which it crystallises on cooling.

2-*Nitro*-6-*methoxytoluene*.—6-Nitro-*o*-toluidine (Ullmann and Panchaud, *Annalen*, 1906, **350**, 112) was converted into 6-nitro-*o*-cresol (Noelting, *Ber.*, 1904, **37**, 1020). Methylation of the nitrocresol (1 mol.) was effected by means of methyl sulphate (1·3 mols.) and 20% aqueous sodium hydroxide (1·5 mols.). The alkali-insoluble *ether* crystallised from methyl alcohol in colourless prisms (yield, 90%), m. p. 52° (Found : C, 57·4; H, 5·6. $C_8H_9O_3N$ requires C, 57·5; H, 5·4%). The compound is readily soluble in ether, acetone, and acetic acid.

6-*Methoxy*-o-*toluidine*.—A mixture of the foregoing nitro-com-

pound (32 g.), tin (40 g.), and concentrated hydrochloric acid (200 c.c.) was heated on the steam-bath until the solution cleared. The cooled reaction mixture was made alkaline with sodium hydroxide, and the product separated by distillation in steam. Extraction of the distillate with ether removed 6-methoxy-*o*-toluidine, which was obtained as a red-brown oil (20 g.) sufficiently pure to be used in the next stage. The *acetyl* derivative separated from warm water in silky needles, m. p. 117° (Found : C, 67·0; H, 7·3. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3%).

6-*Methoxy*-o-*cresol* (VI).—Sodium nitrite (5 g.), dissolved in water (20 c.c.), was added to a solution of 6-methoxy-*o*-toluidine (10 g.) in 10% sulphuric acid (500 c.c.) cooled to — 3° (with agitation). After 2 hours, the filtered diazonium solution was diluted with 10% sulphuric acid (100 c.c.) and heated on the steam-bath until the evolution of nitrogen had ceased. The product was separated from tar by distillation in steam and extracted from the distillate with ether. After removal of the solvent, the residual semi-solid on distillation under diminished pressure gave the *phenol* (VI) as an oil, b. p. 164—165°/20 mm., which quickly solidified. Crystallised from light petroleum, it formed colourless hexagonal plates, m. p. 47° (Found : C, 69·2; H, 7·4. $C_8H_{10}O_2$ requires C, 69·5; H, 7·2%). The substance is readily soluble in alcohol, ether, and benzene and does not give a ferric chloride reaction.

2-*Hydroxy*-4-*methoxy*-3-*methylbenzophenone*-2′-*carboxylic Acid* (VII).—To a solution of phthalic anhydride (10 g.) and 2-hydroxy-6-methoxytoluene (11 g.) in acetylene tetrachloride (70 c.c.), aluminium chloride (30 g.) was added in portions of 5 g. during 1 hour. The temperature of the mixture was then gradually raised to 125° (oil-bath) and a copious evolution of hydrogen chloride ensued. After 2 hours, ice and water (200 g.) were added to the cooled reaction mixture, and the acetylene tetrachloride and unchanged phenol removed in steam. The solid was extracted with aqueous sodium bicarbonate and the extract, after filtration from the insoluble residue, was acidified with concentrated hydrochloric acid. The *acid* (VII) separated as a gum which gradually crystallised. Recrystallised from benzene and then from acetic acid, it formed colourless rhombic plates (16 g.), m. p. 161—162° (Found : C, 66·9; H, 5·0. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%). The substance is moderately easily soluble in warm alcohol. The ferric chloride reaction in alcohol is cherry-red.

1-*Hydroxy*-3-*methoxy*-2-*methylanthraquinone* (3-O-*Methylrubiadin*) (VIII).—A solution of the acid (VII) (4·5 g.) and boric acid (8 g.) in concentrated sulphuric acid (50 c.c.) was heated on the steam-bath for 25 minutes, cooled, and poured on crushed ice (200 g.). The

yellow solid was extracted with sodium bicarbonate solution to remove unchanged acid, washed with water, and dissolved in warm acetic acid. On cooling, 3-O-*methylrubiadin* separated in yellow, elongated, rectangular plates (2·7 g.); when recrystallised (charcoal), it melted at 186° (Found: C, 71·5; H, 4·4. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). The substance is sparingly soluble in cold alcohol or acetic acid. It does not give a coloration with aqueous sodium carbonate but dissolves in alcoholic sodium hydroxide to a bright red solution. Acetylation with acetic anhydride and sodium acetate on the steam-bath during 10 hours gave the *acetyl* derivative, which crystallised from acetic acid–methyl alcohol in pale yellow needles, m. p. 200° (Found: C, 69·4; H, 4·6. $C_{18}H_{14}O_5$ requires C, 69·7; H, 4·5%).

3-*O*-Methylrubiadin (1 g.) was dissolved in acetone (40 c.c.) and methylated by means of methyl iodide (5 c.c.) and silver oxide (5 g.) during 40 hours on the water-bath; a test then showed that methylation was complete. The dimethyl ether (V) crystallised from methyl alcohol in yellow needles, m. p. and mixed m. p. 158° (Found: C, 72·3; H, 5·0%).

1-*Hydroxy*-3-*methoxy*-2-*methylanthraquinone Diacetoborate* (IX, R = Me).—A mixture of 3-*O*-methylrubiadin (1 g.), boroacetic anhydride (2 g.), and acetic anhydride (10 c.c.) was heated on the steam-bath for 5 minutes. Orange-red hexagonal prisms of the *diacetoborate* began to separate almost at once from the warm solution. On cooling, the crystals were collected, washed with a cold solution of boroacetic anhydride in acetic anhydride and with ether, and dried over sulphuric acid for 2 hours. Analysis of the diacetoborate was made by decomposing the compound with warm water and weighing the 3-*O*-methylrubiadin [Found: $C_{16}H_{12}O_4$, 67·8. $C_{16}H_{11}O_4$,$B(O{\cdot}CO{\cdot}CH_3)_2$ requires $C_{16}H_{12}O_4$, 67·8%)]. The substance is but slowly decomposed by cold water.

1 : 3-*Dihydroxy*-2-*methylanthraquinone* (*Rubiadin*) (I).—(A) A suspension of 3-*O*-methylrubiadin (2 g.) in a mixture of concentrated hydrobromic acid (50 c.c.) and acetic acid (150 c.c.) was heated under reflux for 12 hours. The solid gradually dissolved and after several hours the demethylated product partly separated. After having been kept overnight, the solid was collected; a further quantity of less pure material was obtained on diluting the filtrate with water. Rubiadin crystallised from acetic acid in lustrous, yellow, rectangular plates and from alcohol in slender, elongated, rectangular plates, m. p. 290°, alone or mixed with a natural specimen (Found: C, 71·1; H, 4·0. Calc. for $C_{15}H_{10}O_4$: C, 70·9; H, 3·9%). Schunck and Marchlewski (*loc. cit.*) state that rubiadin crystallised from alcohol in "lustrous, yellow needles." Examin-

ation of their material under the microscope revealed the same crystalline form as that of the synthetic material. The behaviour of synthetic rubiadin towards solvents, warm baryta water, and aqueous sodium hydroxide is identical with that of the natural substance described by Schunck and Marchlewski. Acetylation with acetic anhydride and sodium acetate (or pyridine) afforded the diacetyl derivative, which crystallised from alcohol in pale yellow needles, m. p. 225°, alone or mixed with a specimen prepared from natural rubiadin (Found : C, 67·4; H, 4·2. Calc. for $C_{19}H_{14}O_6$: C, 67·5; H, 4·1%).

(B) Demethylation of *O*-dimethylrubiadin (V) gave rubiadin, m. p. (after crystallisation from acetic acid) and mixed m. p. 290° (Found : C, 70·6; H, 3·9%). The diacetate melted at 225° (Found : C, 67·6; H, 4·2%).

1-*Hydroxy*-3-*acetoxy*-2-*methylanthraquinone Diacetoborate* (IX, R = Ac).—A mixture of rubiadin (1 g.), boroacetic anhydride (2·5 g.), and acetic anhydride (10 c.c.) was refluxed for 5 minutes. The *diacetoborate* crystallised from the cooled, dark red solution in rosettes of slender orange needles. After filtration, the crystals were washed with a cold solution of boroacetic anhydride in acetic anhydride and then with ether, and dried over sulphuric acid for 2 hours. In contact with water during 12 hours, the substance was decomposed quantitatively, yielding 3-O-*acetylrubiadin* (XII), which crystallised from alcohol–acetic acid in yellow needles, m. p. 191° after sintering at 187° (Found : C, 69·1; H, 3·9. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%). Analysis of the diacetoborate was made by decomposing it with cold water and weighing the acetyl rubiadin [Found : $C_{17}H_{12}O_5$, 69·4. $C_{17}H_{11}O_5$,$B(O{\cdot}CO{\cdot}CH_3)_2$ requires $C_{17}H_{12}O_5$, 69·8%].

3-*Hydroxy*-1-*methoxy*-2-*methylanthraquinone* (1-O-*Methylrubiadin*) (XIV).—3-*O*-Acetylrubiadin (0·8 g.), dissolved in acetone (30 c.c.), was methylated with methyl iodide (3 c.c.) and silver oxide (4 g.) on the steam-bath during 10 hours. The product (XIII) crystallised from methyl alcohol–acetone in long yellow needles, m. p. 174° (Found : C, 69·7; H, 4·4. Calc. for $C_{18}H_{14}O_5$: C, 69·7; H, 4·5%), and appears to be identical with the acetyl derivative of the natural *O*-monomethylrubiadin described by Barrowcliff and Tutin (*loc. cit.*) and by Simonsen (*loc. cit.*).

A solution of the acetyl derivative (0·6 g.) in 5% methyl-alcoholic potash (20 c.c.) was kept at room temperature for 2·5 hours and then acidified with acetic acid. The mixture was diluted with water (60 c.c.) and, after 1 hour, the solid was collected. 1-*O*-Methylrubiadin (XIV) crystallised from alcohol in yellow needles and from acetic acid in yellow diamond-shaped plates, m. p. 291° [Found :

C, 71·7; H, 4·4; OMe, 11·1. Calc. for $C_{15}H_9O_3(OMe)$: C, 71·6; H, 4·5; OMe, 11·5%]. This ether is sparingly soluble in cold alcohol or acetic acid. With dilute sodium carbonate solution it gives a red solution.

3-O-*Tetra-acetyl-β-glucosidoxy-1-hydroxy-2-methylanthraquinone* (XV).—Rubiadin (2·5 g.) was dissolved in a mixture of 2·8% aqueous sodium hydroxide (20 c.c.) and acetone (20 c.c.). A solution of *O*-tetra-acetyl-α-glucosidyl bromide (4 g.) in ether (10 c.c.) was then introduced, and the mixture agitated for 12 hours. Potassium hydroxide (0·5 g.), dissolved in water (5 c.c.), and a further quantity of bromide (3·5 g.) were then added (agitation). Next day, the faintly alkaline reaction mixture was acidified with acetic acid and diluted with water (100 c.c.), and the ether allowed to evaporate spontaneously. The yellow solid was then collected, washed with water, and dissolved in boiling acetic acid. On cooling, unchanged rubiadin crystallised and, after 4 hours at room temperature, was removed by filtration. The filtrate was poured into water (300 c.c. at 50°) and the *tetra-acetyl glucoside* (XV), contaminated with traces of rubiadin, separated as a yellow solid. After several crystallisations from alcohol it was obtained in slender yellow needles (0·9 g.), m. p. 230° (Found: C, 59·7; H, 5·1. $C_{29}H_{28}O_{13}$ requires C, 59·6; H, 4·8%). The glucoside is sparingly soluble in cold alcohol and moderately easily soluble in acetic acid. With alcoholic sodium hydroxide it gives a bright red solution. Acetylation with pyridine and acetic anhydride during 2·5 hours on the water-bath gave the penta-acetyl derivative of rubiadin glucoside, which crystallised from alcohol in slender, pale yellow needles, m. p. 237° (Found: C, 59·4; H, 5·0. Calc. for $C_{31}H_{30}O_{14}$: C, 59·5; H, 4·8%). This specimen was identical in every way with a specimen of the natural penta-acetyl compound. A mixture of the natural and the synthetic compound gave an undepressed melting point.

3-β-*Glucosidoxy-1-hydroxy-2-methylanthraquinone* (*Rubiadin Glucoside*) (XVI).—The above tetra-acetyl glucoside (0·5 g.), suspended in warm methyl alcohol (40 c.c.), was treated with 5% aqueous sodium hydroxide (20 c.c.) at 55° for 20 minutes. The warm, dark red solution was acidified with acetic acid, and on cooling rubiadin glucoside separated as a yellow crystalline solid. Recrystallised from alcohol, it formed slender yellow needles (0·3 g.), m. p. 270—271°, alone or mixed with a specimen of the natural glucoside [Found: in material dried at 130° for 24 hours (compare Schunck and Marchlewski, *loc. cit.*): C, 60·3; H, 5·0. Calc. for $C_{21}H_{20}O_9$: C, 60·6; H, 4·8%]. The behaviour of the synthetic glucoside towards solvents, aqueous potassium carbonate, aqueous potassium hydroxide, baryta water, alcoholic cupric

acetate, alcoholic lead acetate, and boiling dilute mineral acids is identical with that of the natural substance described by Schunck and Marchlewski (*loc. cit.*).

3-O-*Tetra-acetyl-β-glucosidoxy-1-methoxy-2-methylanthraquinone* (XVII).—Silver oxide (3 g.) and methyl iodide (3 c.c.) were added to a solution of the tetra-acetyl glucoside (XV) (0·6 g.) in acetone (30 c.c.), and the mixture refluxed for 3 hours; a test with alcoholic sodium hydroxide then showed that methylation was complete. The silver salts were removed by filtration and the solvent was distilled under diminished pressure. The residual solid on crystallisation from methyl alcohol gave the *methyl* ether (XVII) in pale yellow, slender rods (0·5 g.), m. p. 185° (Found: C, 59·9; H, 5·2. $C_{30}H_{30}O_{13}$ requires C, 60·2; H, 5·0%).

A suspension of the foregoing ether (0·3 g.) in a mixture of methyl alcohol (16 c.c.) and concentrated hydrochloric acid (8 c.c.) was heated under reflux for 2 hours. The solid rapidly dissolved and after ¾ hour 1-*O*-methylrubiadin began to separate. After dilution with water (20 c.c.), the mixture was cooled and the substance collected, m. p. (after crystallisation from alcohol) and mixed m. p. 291°. Acetylation with acetic anhydride and pyridine on the water-bath during 2 hours gave the acetyl compound (XIII), which crystallised from methyl alcohol in yellow needles, m. p. and mixed m. p. 174° (Found: C, 69·5; H, 4·8%).

1:3-O-*Octa-acetyl-β-diglucosidoxy-2-methylanthraquinone*.—Dry "active" silver oxide (2 g.) was added with stirring to a thick paste of rubiadin (0·5 g.), *O*-tetra-acetyl-α-glucosidyl bromide (3 g.), and freshly distilled quinoline (4 c.c.). The mixture, which became warm and less viscous, was agitated for 15 minutes and then kept in a desiccator for 2 hours. The dark brown paste was digested with boiling acetic acid (70 c.c.) for 2 minutes and, after the addition of charcoal, the digest was filtered. The almost colourless filtrate was poured into water (200 c.c. at 50°) and the *diglucoside* thus precipitated was collected. Crystallised from alcohol–acetic acid, it formed sheaves of pale yellow, slender needles (0·8 g.), m. p. 248° (Found: C, 56·7; H, 5·2. $C_{43}H_{46}O_{22}$ requires C, 56·5; H, 5·0%). The substance does not give a coloration with cold alcoholic sodium hydroxide.

By the interaction of rubiadin (0·5 g.), *O*-tetra-acetyl-α-glucosidyl bromide (0·8 g.), and silver oxide (1 g.) in quinoline (4 c.c.) a solid (A) (isolation as before) was obtained which crystallised from alcohol in slender yellow needles (0·4 g.), m. p. 220—224°. This product (A), which appeared to be a mixture, could not be purified and on acetylation gave an acetyl derivative, which crystallised from alcohol in pale yellow needles, m. p. 218—220°. Deacetylation of

(A) by means of warm methyl-alcoholic sodium hydroxide gave a yellow solid (B), which crystallised from alcohol in slender needles. Treatment of (B) with acetic anhydride and pyridine on the water-bath gave the penta-acetate of rubiadin glucoside, m. p. (after crystallisation from alcohol) and mixed m. p. 237°. The product (A) dissolved in cold alcoholic sodium hydroxide to a red solution and there can be little doubt that it consisted of a mixture of the two possible monoglucosides. The ultimate isolation of the penta-acetate of rubiadin glucoside probably depends on the decomposition of the 1-glucoside in the deacetylation process.

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