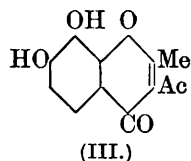
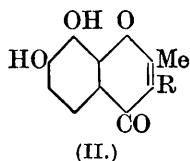
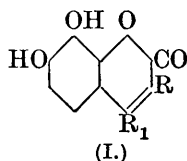


CCLII.—*Hydroxy-carbonyl Compounds. Part IV. The Preparation of Coumarins and 1:4-Benzopyrones from Pyrogallol.*

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IN Part III of this series (this vol., p. 1255) it was shown that the condensation of resorcinol and of phloroglucinol with esters of acylacetic acids according to the method of Simonis (*Ber.*, 1913, **46**, 2014) gives rise to coumarins and not to the expected 1:4-benzopyrones. This investigation has been extended to pyrogallol, with similar results.

The products from the interaction of pyrogallol with ethyl acetoacetate, α -methylacetoacetate, and benzoylacetate in the presence of phosphoric oxide have been shown to be respectively the coumarins (I; R = H, R₁ = Me) (Pechmann and Duisberg, *Ber.*, 1883, **16**, 2127), (I; R = Me, R₁ = Me), and (I; R = H, R₁ = Ph) (Kostanecki and Weber, *Ber.*, 1893, **26**, 2906). Compared with those from resorcinol or phloroglucinol, the yields obtained from pyrogallol were poor. A similar contrast was observed on applying the Hoesch reaction. The condensation of pyrogallol with acetonitrile, with propionitrile, and with benzonitrile in the presence of zinc chloride, and subsequent hydrolysis of the ketimines, gave meagre yields of respective ketones.



By ring closure of gallacetophenone with acetic anhydride and sodium acetate at 160—170°, Venkataraman (*J.*, 1929, 2219) claims to have obtained a mixture of 7:8-dihydroxy-2-methyl-1:4-benzopyrone (II; R = H) and its *O*-diacetate, but on attempting to prepare the pyrone by this method, we found that the product (isolated as the diacetate) was not identical with an authentic specimen (Blumberg and Kostanecki, *Ber.*, 1903, **36**, 2192). The same lack of identity was observed on comparing the respective diacetates and dimethyl ethers. The only other product which we were able to isolate from the reaction mixture was *O*-triacetyl-gallacetophenone. The compound obtained by us appears to contain a *C*-acetyl group and, by analogy with resacetophenone (Nagai, *Ber.*, 1892, **25**, 1284; Kostanecki and co-workers, *Ber.*, 1901, **34**, 102,

2942; compare Part II of this series, this vol., p. 1245), we consider that ring closure of gallacetophenone is accompanied by acetylation in the 3-position, yielding the 1 : 4-pyrone (III). On the other hand, for reasons already enumerated (this vol., p. 1247), we believe that gallopropiophenone furnishes the 1 : 4-pyrone (II; R = Me) on ring closure with sodium acetate and acetic anhydride.

EXPERIMENTAL.

7 : 8-Dihydroxy-4-methylcoumarin (I; R = H, R₁ = Me).—An excess of phosphoric oxide was added in small portions with stirring to a mixture of pyrogallol (1 g.) and ethyl acetoacetate (1 g.), and the reaction completed by heating on the steam-bath for 10 minutes. The mixture was kept at room temperature for 1 hour and then extracted with water, and the insoluble product collected. Crystallised from dilute alcohol, the coumarin formed clusters of colourless needles (0.5 g.), m. p. 238° (Found, in specimen dried at 120° : C, 62.6; H, 4.5. Calc. for C₁₀H₈O₄ : C, 62.5; H, 4.2%). Mixed with 7 : 8-dihydroxy-2-methyl-1 : 4-benzopyrone (Blumberg and Kostanecki, *loc. cit.*), it showed a depression of about 40°.

An authentic specimen of the coumarin was prepared by the method of Pechmann and Duisberg (*loc. cit.*) and found to melt at 237° (these authors give m. p. 235°). A mixture of the two specimens melted at 237—238°. The diacetate prepared from either specimen crystallised from alcohol in rhombic plates, m. p. 178°.

7 : 8-Diacetoxy-3-acetyl-2-methyl-1 : 4-benzopyrone.—A mixture of gallacetophenone (5 g.), sodium acetate (10 g.), and acetic anhydride (50 g.) was heated at 160—170° (oil-bath) for 6 hours. After removal of excess of anhydride in a vacuum, the residue was poured into water, and next day the semi-solid product was crystallised from alcohol. The *diacetate* formed almost colourless plates (2 g.), m. p. 132°, which did not lose weight on heating at 110° for 2½ hours (Found : C, 60.4; H, 4.6. C₁₆H₁₄O₇ requires C, 60.4; H, 4.4%). The compound did not give a ferric chloride reaction. Mixed with a specimen of 7 : 8-diacetoxy-2-methyl-1 : 4-benzopyrone (needles, m. p. 122°) (*loc. cit.*), it melted at 95—100°. After the separation of the diacetate, the alcoholic mother-liquors were diluted with water and *O*-triacetyl gallacetophenone gradually separated, m. p. 85° after crystallisation from dilute alcohol. Mixed with an authentic specimen, it gave an undepressed melting point.

When the ring closure was effected at 170—180° during 20 hours, the same diacetate, m. p. and mixed m. p. 132°, was obtained.

7 : 8-Dihydroxy-3-acetyl-2-methyl-1 : 4-benzopyrone (III).—(A) The foregoing diacetate was hydrolysed by boiling with a mixture of methyl alcohol (45 c.c.) and concentrated hydrochloric acid (5 c.c.)

for 1 hour. After distillation of the greater part of the alcohol in a vacuum, the mixture was diluted with water, and the precipitate was collected and washed with water. Crystallised from alcohol (charcoal), the *pyrone* formed colourless needles, m. p. 247° (Found, in a specimen dried at 110° : C, 61.1; H, 4.7. $C_{12}H_{10}O_5$ requires C, 61.5; H, 4.3%). Unlike 7:8-dihydroxy-2-methyl-1:4-benzopyrone (*loc. cit.*), this compound is sparingly soluble in cold ethyl or methyl alcohol and in hot water. With alcoholic ferric chloride it gives a green coloration. Mixed with 7:8-dihydroxy-2-methyl-1:4-benzopyrone and with 7:8-dihydroxy-4-methylcoumarin, it showed m. p. depressions of about 35° and 45° respectively. Acetylation with acetic anhydride and sodium acetate (or pyridine) regenerated the diacetate, m. p. and mixed m. p. 132° .

(B) A solution of the diacetate (1 g.) in 5% methyl-alcoholic potassium hydroxide was boiled for 3 minutes, cooled, and neutralised with mineral acid (Congo-red). After 12 hours the precipitate of 7:8-dihydroxy-3-acetyl-2-methyl-1:4-benzopyrone was collected and crystallised from alcohol, forming needles, m. p. 245° . Mixed with a specimen prepared by method (A), it melted at 245 – 246° . The same product, m. p. and mixed m. p. 245° , was obtained in poor yield when the deacetylation was effected by means of warm 5% aqueous sodium hydroxide for $\frac{3}{4}$ -hour.

7:8-Dimethoxy-3-acetyl-2-methyl-1:4-benzopyrone.—The *pyrone* (0.5 g.) was dissolved in acetone (30 c.c.), and methylated by means of methyl iodide (2 c.c.) and anhydrous potassium carbonate (1 g.) during 5 hours on the steam-bath. On isolation, the *dimethyl* ether crystallised from water in colourless elongated, rectangular prisms, m. p. 148° [Found: C, 64.2; H, 5.2; OMe, 23.6. $C_{12}H_8O_3(OMe)_2$ requires C, 64.1; H, 5.3; OMe, 23.7. Calc. for $C_{10}H_6O_2(OMe)_2$: C, 65.5; H, 5.5; OMe, 28.2%. Loss on drying at 110° for 15 hours: nil]. This ether is readily soluble in methyl or ethyl alcohol and does not give a ferric chloride reaction. Mixed with 7:8-dimethoxy-2-methyl-1:4-benzopyrone (Blumberg and Kostanecki, *loc. cit.*), it showed a depression in m. p. of about 60° .

7:8-Dihydroxy-2:3-dimethyl-1:4-benzopyrone (II; R = Me).—A mixture of gallopropiophenone (5 g.), sodium acetate (5 g.), and acetic anhydride (40 c.c.) was heated at 170 – 180° for 20 hours. On isolation in the usual manner, the *diacetate* crystallised from dilute acetic acid in almost colourless rectangular prisms (2.5 g.), m. p. 150° (Found: C, 62.2; H, 5.0. $C_{15}H_{14}O_6$ requires C, 62.1; H, 4.8%). The compound is readily soluble in alcohol and insoluble in ether.

A solution of the acetyl derivative (2 g.) in 5% methyl-alcoholic potassium hydroxide (60 c.c.) was kept at room temperature for 2

hours, and then acidified with acetic acid. The *pyrone* was precipitated by the addition of water (200 c.c.) and, on crystallisation from dilute alcohol (charcoal), formed colourless needles, m. p. 234° (Found in material dried at 130°: C, 64.2; H, 5.2. $C_{11}H_{10}O_4$ requires C, 64.1; H, 4.9%). The compound is readily soluble in alcohol and sparingly soluble in water. It forms an orange-yellow solution in dilute sodium hydroxide, and with aqueous-alcoholic ferric chloride gives a green coloration.

7 : 8-*Dihydroxy-3 : 4-dimethylcoumarin* (I; R = Me, R₁ = Me).—(A) The condensation of pyrogallol (5 g.) and ethyl α -methylacetoacetate (5.5 g.) was effected by means of concentrated sulphuric acid (14 c.c.) at 0° during 12 hours. Addition of ice precipitated the *coumarin*, which crystallised from alcohol in microscopic, pale yellow, rhombic plates (2.5 g.), m. p. 272—273° (Found: C, 64.5; H, 5.0. $C_{11}H_{10}O_4$ requires C, 64.1; H, 4.9%). The compound is insoluble in ether and benzene and gives a green ferric chloride reaction. It forms an orange-yellow solution in dilute sodium hydroxide. The *diacetate* separated from alcohol in tiny, colourless, rhombic prisms, m. p. 202° (Found: C, 62.4; H, 4.9. $C_{15}H_{14}O_6$ requires C, 62.1; H, 4.8%). This derivative does not give a ferric chloride reaction.

(B) Excess of phosphoric oxide was added in portions with stirring to a mixture of pyrogallol (2 g.) and ethyl α -methylacetoacetate (2.2 g.). After having been heated on the steam-bath for $\frac{1}{2}$ hour, the mixture was kept at room temperature for 1 hour and then extracted with water. The product, which was obtained as a reddish oil, gradually solidified, and after 3 days was collected and washed with water. Crystallised from alcohol, it formed pale yellow, rhombic plates, m. p. and mixed m. p. 272° (Found: C, 64.2; H, 5.2%). The *diacetate* had m. p. and mixed m. p. 202°.

Mixed with a specimen of the isomeric 1 : 4-pyrone (II; R = Me), the coumarin (prepared by either method) showed an m. p. depression of about 55°. A mixture of the corresponding *diacetates* melted at about 140°.

7 : 8-*Dihydroxy-4-phenylcoumarin* (I; R = H; R₁ = Ph).—The condensation of pyrogallol (1.2 g.) and ethyl benzoylacetate (1.8 g.) was effected by means of phosphoric oxide (5 g.). At intervals during the addition of the reagent, the mixture was heated for short periods on the water-bath. The reaction was finally completed by heating for 10 minutes, and after having been kept for 1 hour at room temperature, the mixture was extracted with water. The insoluble oily product partly solidified and, on crystallisation from dilute alcohol, gave the coumarin as the hydrate in pale yellow, prismatic needles, m. p. 189—190° (Found: C, 66.3; H, 4.7. Calc.

for $C_{15}H_{10}O_4 \cdot H_2O$: C, 66.2; H, 4.4%). Mixed with an authentic specimen (Kostanecki and Weber, *Ber.*, 1893, **26**, 2906), it showed no depression in m. p. The diacetate had m. p. and mixed m. p. 127°.

Methylation of this coumarin by means of methyl iodide and potassium carbonate in boiling acetone afforded the *dimethyl* ether, which separated from 70% alcohol in almost colourless prisms, m. p. 138° (Found: C, 72.3; H, 5.1; OMe, 22.5. $C_{17}H_{14}O_4$ requires C, 72.4; H, 5.0; OMe, 22.0%).

The ring closure of gallobenzophenone with sodium acetate and acetic anhydride was effected by Bargellini and Leonardi (*Gazzetta*, 1911, **41**, 742), but they did not state the temperature employed. On repeating the acetylation at 170–180°, the only product which we obtained was *O*-triacetyl gallobenzophenone, m. p. and mixed m. p. 119°. We found, however, that when the temperature of the mixture is maintained at about 215° for 20 hours, the diacetyl derivative of the coumarin is obtained, m. p. 127°, which, on hydrolysis, furnished the coumarin, m. p. and mixed m. p. 190°.

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