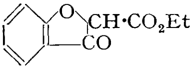
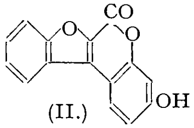
339. *Analogues of Rotenone and Related Compounds. Part II. Coumarono-(2′ : 3′ : 3 : 4)-coumarins.*

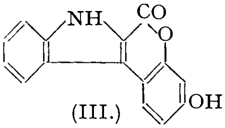
By H. I. King, R. H. Holland, F. P. Reed, and Alexander Robertson.

A number of coumarono-(2′ : 3′ : 3 : 4)-coumarins have been synthesised by the condensation of β-ketonic esters (type I) and *m*-dihydroxyphenols according to von Pechmann's method. The indolocoumarin (III) has been prepared by the same procedure.

In pursuit of the objective defined in Part I (*J.*, 1936, 423) we have synthesised by a general method a series of coumarono-(2′ : 3′ : 3 : 4)-coumarins, type (II), which are closely analogous to the chromeno-(2′ : 3′ : 3 : 4)-coumarins previously described; as an example, the condensation of the ester (I) with resorcinol according to the method of von Pechmann gave rise to 7-*hydroxycoumarono*-(2′ : 3′ : 3 : 4)-*coumarin* (II). When the ester (I) was replaced by methyl


(I.)


(II.)


(III.)

3-hydroxyindole-2-carboxylate, the *indolocoumarin* (III) was obtained. Attempts to condense esters (type I) with phenol or the cresols by the general method gave negative results or only traces of the desired products.

EXPERIMENTAL.

7-*Hydroxycoumarono*-(2′ : 3′ : 3 : 4)-*coumarin* (II). (With W. H. DAVIS.)—A mixture of ethyl β-coumaranone-2-carboxylate (Friedländer, *Ber.*, 1899, **32**, 1868) (6·8 g.) and resorcinol (12 g.) in 85% sulphuric acid (90 c.c.) was kept at room temperature for 2 days and treated with ice–water. The *product* was repeatedly triturated with much water and then with a little alcohol, and crystallised from a large volume of hot alcohol or acetic acid, forming tiny prisms (7·2 g.), m. p. 311° (decomp.) (Found : C, 71·4; H, 3·4. $C_{15}H_8O_4$ requires C, 71·4; H, 3·4%). Prepared by the pyridine method, the *acetate* formed slender prisms, m. p. 235—236°, from ethyl acetate (Found : C, 69·5; H, 3·7. $C_{17}H_{10}O_5$ requires C, 69·5; H, 3·7%). Methylation of the hydroxycoumarin by the potassium carbonate–acetone method gave the *methyl ether* which separated from much methanol in needles, m. p. 186—187° (Found : C, 72·3; H, 3·5. $C_{16}H_{10}O_4$ requires C, 72·2; H, 3·8%).

7 : 8-*Dihydroxycoumarono*-(2′ : 3′ : 3 : 4)-*coumarin*.—A solution of ethyl β-coumaranone-2-carboxylate (2 g.) and pyrogallol (2 g.) in methanol saturated with hydrogen chloride at room temperature slowly deposited the coumarin (1·1 g.), m. p. 274—276°, having a green ferric reaction, which could not be economically purified and was converted into the *diacetate*. This derivative formed colourless, elongated, rectangular prisms, m. p. 228—231°, from acetic acid (Found : C, 64·7; H, 3·4. $C_{19}H_{12}O_7$ requires C, 64·8; H, 3·4%). The *dimethyl ether* separated from acetic acid in elongated plates, m. p. 210·5—211·5° (Found : C, 69·1; H, 4·3. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%).

5 : 7-Dihydroxycoumarone-(2′ : 3′ : 3 : 4)-coumarin (hydrogen chloride method) was crystallised from nitrobenzene and then from aqueous glycol, forming tiny prisms, m. p. above 300°, which have a negative ferric reaction. On methylation the compound gave the *dimethyl ether* which separated from acetic acid in colourless needles, m. p. 267—268° (Found : C, 68·9; H, 4·0. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%).

7-*Hydroxy*-5′-*methylcoumarono*-(2′ : 3′ : 3 : 4)-*coumarin*.—When a solution of ethyl 5-methyl-β-coumaranone-2-carboxylate (Auwers, *Annalen*, 1913, **393**, 366) (1 g.) and resorcinol (1 g.) in methyl alcohol was slowly saturated at room temperature with hydrogen chloride, a yellow solid gradually separated. Two days later the mixture was heated on the steam-bath for ½ hour, and on cooling the resulting *coumarin* (0·6 g.) was collected, washed, and crystallised from alcohol, forming needles which have a negative ferric reaction, m. p. above 300° (Found : C, 72·0; H, 3·8. $C_{16}H_{10}O_4$ requires C, 72·2; H, 3·8%). The *acetate* separated from alcohol in long slender needles, m. p. 233° (Found : C, 70·0; H, 3·9. $C_{18}H_{12}O_5$ requires C, 70·1; H, 3·9%).

5 : 7-*Dihydroxy*-5′-*methylcoumarono*-(2′ : 3′ : 3 : 4)-*coumarin*.—Prepared by the hydrogen chloride method this substance, m. p. > 300°, could not be economically obtained pure for analysis and was converted into the *diacetate* which formed tiny needles, m. p. 218°, from acetic acid, sparingly soluble in organic solvents (Found : C, 66·0; H, 4·1. $C_{20}H_{14}O_7$ requires C, 65·6; H, 3·9%).

7 : 8-*Dihydroxy*-5′-*methylcoumarono*-(2′ : 3′ : 3 : 4)-*coumarin* separated from alcohol in needles, m. p. above 300°, which give a green coloration with alcoholic ferric chloride (Found : C, 68·1; H, 3·7. $C_{16}H_{10}O_5$ requires C, 68·1; H, 3·6%). The *diacetate* formed colourless needles, m. p. 267°, from acetic acid (Found : C, 65·4; H, 3·9. $C_{20}H_{14}O_7$ requires C, 65·6; H, 3·9%).

Ethyl 7-*Methyl*-β-*coumaranone*-2-*carboxylate*.—Interaction of ethyl 2-hydroxy-*m*-toluate (10 g.), ethyl bromoacetate (20 g.), and potassium carbonate (15 g.) in boiling acetone (75 c.c.) for 13 hours gave *ethyl* 3-*carbethoxy*-o-*tolyloxyacetate* (15 g.), b. p. 184°/16 mm., m. p. 39°, after purification by distillation 3 times in a vacuum (Found : C, 63·5; H, 6·7. $C_{14}H_{18}O_5$ requires C, 63·1; H, 6·8%). When the vigorous reaction between this ester (20 g.) and sodium (2·5 g.) in benzene (100 c.c.) had ceased, the mixture was heated on the steam-bath for 1·5 hours and next day the sodio-derivative was collected and decomposed with dilute acetic acid. The resulting *carbethoxycoumaranone* separated from light petroleum (b. p. 80—100°) in colourless prisms (13 g.), m. p. 80—81°, which gave a dark green coloration with alcoholic ferric chloride (Found : C, 65·3; H, 5·4. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·5%). The slow spontaneous transformation of this crystalline coumaranone into a viscous oil is probably due to partial formation of the ketonic form.

7-*Hydroxy*-7′-*methylcoumarono*-(2′ : 3′ : 3 : 4)-*coumarin* (3·1 g.) was obtained by the interaction of the foregoing carbethoxycoumaranone (3·5 g.) and resorcinol (5 g.) in 85% sulphuric acid during 2 days; it separated from warm alcohol as a microcrystalline powder (2·7 g.) which did not melt below 300° (Found : C, 71·8; H, 3·7. $C_{16}H_{10}O_4$ requires C, 72·2; H, 3·8%). The *acetate* formed long slender needles, m. p. 251°, from ethyl acetate (Found : C, 70·4; H, 4·1. $C_{18}H_{12}O_5$ requires C, 70·2; H, 3·9%). Prepared by methylation of the coumarin (0·15 g.) with excess of silver oxide and methyl iodide (2 c.c., added in 5 portions) in boiling ether (20 c.c.) during 8 hours, the *methyl ether* separated from methanol in small needles, m. p. 234° (Found : C, 73·0; H, 4·6. $C_{17}H_{12}O_2$ requires C, 72·9; H, 4·3%).

When resorcinol was replaced by phloroglucinol or pyrogallol in the foregoing condensation, crystalline products could not be isolated. With these phenols the hydrogen chloride method also gave negative results.

Ethyl 6-*Methoxy-β-coumaranone*-2-*carboxylate.*—Condensation of ethyl 4-methoxysalicylate (Gomberg and Johnson, *J. Amer. Chem. Soc.*, 1917, **39**, 1687) (51 g.) with ethyl bromoacetate (75 ml.) in the presence of potassium carbonate (85 g.) in boiling acetone (350 ml.) in the course of 6 hours (until a sample gave a negative ferric reaction) gave *ethyl* 5-*methoxy*-2-*carbethoxyphenoxyacetate* (53 g.) as an oil, b. p. 152—155°/0·1 mm. (Found: C, 59·2; H, 6·1. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%). Interaction of this compound (21 g.) with pulverised sodium (3·2 g.) in boiling benzene (150 ml.) during 2 hours gave a solid (27·5 g.) which on decomposition with warm acetic acid (40 ml.) and subsequent addition of water (400 ml.) gave the *carbethoxycoumaranone* (13 g.), forming rectangular plates, m. p. 112°, from alcohol (Found: C, 61·1; H, 5·0. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1%). This substance has a green ferric reaction in alcohol.

7-*Hydroxy*-6′-*methoxycoumarono*-(2′ : 3′ : 3 : 4)-*coumarin* was prepared from the foregoing ester and resorcinol by the hydrogen chloride method; on crystallisation from hot nitrobenzene it formed micaceous plates, m. p. > 300°, almost insoluble in the usual organic solvents (Found: C, 68·3; H, 3·7. $C_{16}H_{10}O_5$ requires C, 68·1; H, 3·5%). Methylation of the coumarin by the methyl iodide–potassium carbonate method gave the *methyl ether* which separated from acetic acid or much alcohol in tiny rods, m. p. 224·5—225° (Found: C, 68·9; H, 4·2. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%). The *acetate* crystallised from acetic acid in small needles, m. p. 248—249° (Found: C, 66·5; H, 3·9. $C_{18}H_{12}O_6$ requires C, 66·7; H, 3·7%).

7 : 8-*Dihydroxy*-6′-*methoxycoumarono*-(2′ : 3′ : 3 : 4)-*coumarin* (hydrogen chloride method) separated from nitrobenzene in rod-like prisms, m. p. > 300°, having a pale green ferric reaction in alcohol (Found: C, 63·9; H, 3·5. $C_{16}H_{10}O_6$ requires C, 64·4; H, 3·4%). The *diacetate* formed small needles, m. p. 237—238°, from aqueous acetic acid (Found: C, 62·6; H, 4·0. $C_{20}H_{14}O_8$ requires C, 62·8; H, 3·7%), and the *dimethyl ether* crystallised from acetic acid in tiny prisms, m. p. 237—238° (Found: C, 66·2; H, 4·4. $C_{18}H_{14}O_6$ requires C, 66·3; H, 4·3%). A mixture of the ether and the acetate began to melt at 218°.

5 : 7-Dihydroxy-6′-methoxycoumarono-(2′ : 3′ : 3 : 4)-coumarin (hydrogen chloride method), which could not be satisfactorily purified, gave a *dimethyl ether* forming tiny prisms, m. p. 257—258°, from acetic acid (Found: C, 66·5; H, 4·5. $C_{18}H_{14}O_6$ requires C, 66·3; H, 4·3%).

Attempts to condense ethyl 6-methoxy-β-coumaranone-2-carboxylate with *o*-, *m*-, or *p*-cresol were unsuccessful.

7-*Hydroxyindolo*-(2′ : 3′ : 3 : 4)-*coumarin* (III).—The dark-brown solution of methyl 3-hydroxyindole-2-carboxylate (1 g.) and resorcinol (3 g.) in 90% sulphuric acid gradually deposited a yellow solid. After 2 days ice was added, and the yellow precipitate on being isolated and well washed with water became dark green. Crystallised several times from 50% alcohol (charcoal), this product gave the *indolocoumarin* as a colourless microcrystalline solid (1·2 g.) which did not melt below 315° (Found: C, 71·3; H, 3·7; N, 5·4. $C_{15}H_9O_3N$ requires C, 71·7; H, 3·6; N, 5·6%). Acetylation of this compound by the pyridine method gave the *diacetyl* derivative which separated from ethyl acetate in long, slender, colourless needles, m. p. 232° (Found: C, 68·1; H, 4·0. $C_{19}H_{13}O_5N$ requires C, 68·1; H, 3·9%).

UNIVERSITY OF LIVERPOOL.

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