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Isocoumarins. Part I. Synthesis of 4-Methylisocoumarins*

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Several 4-methylisocoumarin derivatives have been synthesised by cyclodehydration of the acetonyl esters of some of the *m*-methoxy- and *m*-hydroxy-benzoic acid derivatives, viz., 3-methoxybenzoic acid, 3-methoxy-4-methylbenzoic acid, 3-hydroxy-6-methylbenzoic acid, α-resorcylic acid, and its dimethyl ether, using 85% sulphuric acid.

Isocoumarins are an interesting class of compounds, expected to possess a marked physiological action[1]. Some of them are good anticoagulants, e.g. isocoumarin-3-carboxylic acid is half as effective as dicoumarol[2a]. The methods for the synthesis of isocoumarins, however, have been very little explored and comparatively few isocoumarins are known and these have been obtained by long and elaborate procedures[2].

In the present investigation, the syntheses of some 4-methylisocoumarins have been achieved by effecting internal condensation of acetonyl esters of some of the benzoic acid derivatives, using sulphuric acid as the condensing agent. 5,6,7-Trihydroxy-4-methylisocoumarin is the only 4-methylisocoumarin that has been reported in literature. It was obtained by Fritsch[3] by condensing acetonyl gallate, using sulphuric acid at 0° and this synthesis was later confirmed by Haworth *et al.*[4] Fritsch[3], however, reported that the condensation of acetonyl esters of the other acids were unsuccessful.

7-Methoxy-4-methylisocoumarin (II: R=Me; R′ = H), 7-methoxy-4,6-dimethylisocoumarin (II: R = R′ = Me), 5-hydroxy-4,8-dimethylisocoumarin (III: R = H; R′ = Me), 5,7-dihydroxy-4-methylisocoumarin (V: R=H) and 5,7-dimethoxy-4-methylisocoumarin (V: R = Me) have now been obtained by effecting internal condensation of the acetonyl esters of 3-methoxybenzoic acid (I: R = Me; R′ = R″ = H), 3-methoxy-4-methylbenzoic acid (I: R = R′ = Me; R″ = H), 3-hydroxy-6-methylbenzoic acid (I: R=R′ =H; R″=Me), 3,5-dihydroxybenzoic acid (IV: R=H), and 3,5-dimethoxybenzoic acid (IV: R=Me) respectively. It is interesting to note that the acetonyl ester of 3-methoxy-6-methylbenzoic acid (I:R=R″=Me; R′=H) failed to condense to provide the corresponding isocoumarin and the acetonyl ester of 3-hydroxybenzoic acid (I: R=R′= R″=H) afforded a mixture of isocoumarins (m. p. 160-85°), probably of 7-hydroxy-

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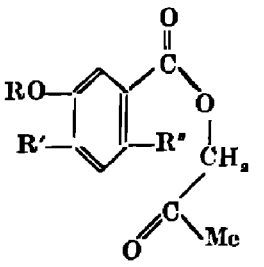
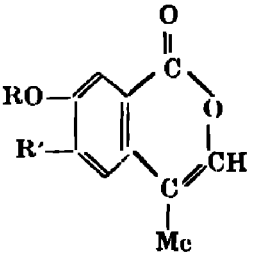
1. Haynes, *Quart. Rev.*, 1948, 2, 46.
2. (a) Johnston *et al.*, *J. Org. Chem.*, 1948, 13, 477.
(*b*) Kamal *et al.*, *J. Chem. Soc.*, 1950, 3375.
(*c*) Srivastav and Choudhury, *J. Org. Chem.*, 1962, 27, 4337; this *Journal*, 1963, 40, 865; Mukopadhaya and Choudhury, *ibid.*, p, 433.
3. *Ber.*, 1893, 26, 419.
4. *J. Chem. Soc.*, 1954, 3611.

4-methylisocoumarin (II: R=R′=H) and of 5-hydroxy-4-methylisocoumarin (III:R=R′ =H) (condensation having taken place in position 6 and also in position 2 of the ester), from which 7-hydroxy isomer (II :R=R′ =H) was isolated by fractional crystallisation. The acetonyl ester of 3-hydroxy-4-methylbenzoic acid (I: R=R″=H; R′=Me) in the same manner was cyclodehydrated to provide a mixture of isocoumarins (m.p. 185-200°), but various attempts to separate the isomers so far met with failure.



(I)



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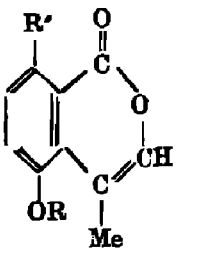

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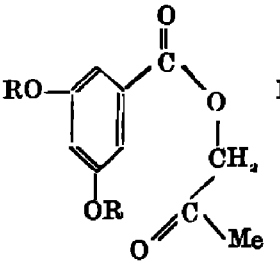

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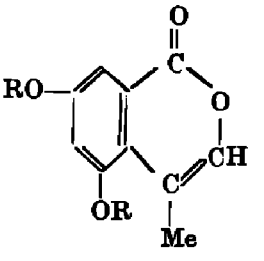

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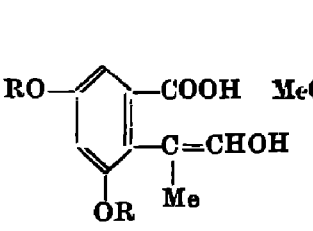

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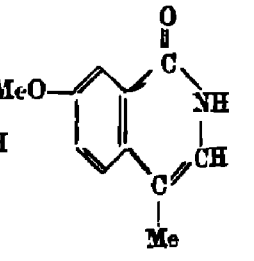

(VII)

The acetonyl esters of 3-methoxybenzoic acid (I:R=Me; R′=R″=H) and 3-methoxy-4-methylbenzoic acid (I:R=R′=Me; R″=H) can condense in the position either '2' or '6', leading to formation of either of the corresponding 5-methoxyisocoumarin derivative (III: R=Me) or of the corresponding 7-methoxyisocoumarin derivative (II: R=Me). The condensation in position 2 in both the cases, which is under steric hindrance of the bulky methoxy group, is ruled out as the acetonyl ester of 3-methoxy-6-methylbenzoic acid (I: R=R″=Me; R′=H), where position 6 is blocked by methyl group, failed to condense in position 2 to give rise to the corresponding isocoumarin. The observation by Haworth *et al.*[4] that acetonyl trimethoxygallate does not cyclise to provide isocoumarin derivative has been confirmed by the present authors. This shows that the methoxyl group in proximity hinders the condensation. It follows therefore that the condensation in case of both the above esters takes place in position 6, yielding the respective 7-methoxyisocoumarin derivatives. The structures of the other isocoumarins, viz., 5-hydroxy-4,8-dimethyl-, 5,7-dihydroxy-4-methyl-, and 5,7-dimethoxy-4-methyl-isocoumarins are unambiguous.

The isocoumarins exhibit the characteristic UV absorption curves (Fig. 1 and 2) with peaks between 230 and 245 mμ and between 330 and 360 mμ, which are characteristics of isocoumarins[4-5].

5. Hay and Haynes, *J. Chem. Soc.*, 1958, 2231.

The acetonyl esters of various acids were prepared by esterification of the corresponding acids with bromoacetone in presence of potassium carbonate in methanolic solution.

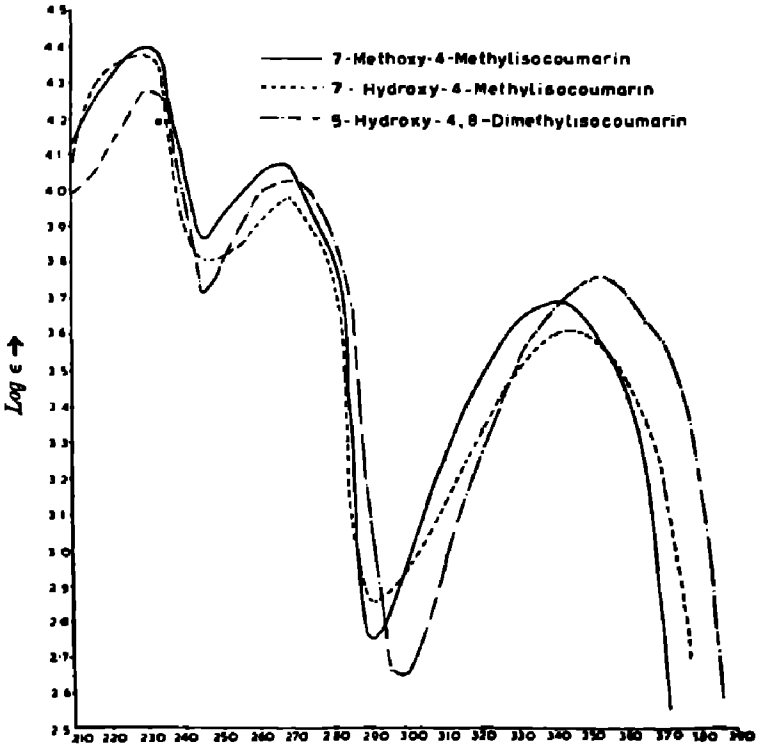

FIG. 1

7-Methoxy-4-methylisocoumarin (II: R = Me; R′ = H) and 7-methoxy-4,6-dimethylisocoumarin (II: R = R′ = Me) were successfully demethylated by refluxing with hydriodic acid in acetic anhydride solution to provide 7-hydroxy-4-methylisocoumarin (II: R=R′=H) and 7-hydroxy-4,6-dimethylisocoumarin (II: R=H; R′=Me) respectively. Demethylation of 5,7-dimethoxy-4-methylisocoumarin (V: R=Me), however, was not successful; a compound, m.p. 285-300°, was obtained. 5,7-Dihydroxy-4-methylisocoumarin (V: R=H) also yielded a similar compound (m.p. 300-320°) on refluxing it with hydriodic acid. Both these compounds have not been investigated further as these could not be obtained pure.

Hydroxyisocoumarins were characterised by preparing acetoxy derivatives. All the isocoumarins were easily attacked by caustic alkalis. These slowly dissolved in 10% caustic soda solution on warming, but could not be reprecipitated on acidification. Oily substances were obtained in the case of 7-methoxy-4-methylisocoumarin and 7-methoxy-4,6-dimethylisocoumarin, from which no pure substances could be isolated. 5,7-Dihydroxy-

6. Fritsch, D.R.P. 73700; Frdl., III, 970.
7. Maldrum and Perkin, *J. Chem. Soc.*, 1008, **93**, 1419.
8. Jacobson, *Ber.*, 1883, **16**, 1963; Baudisch and Perkin, *J. Chem. Soc.*, 1009, **95**, 1883.

4-methyl isocoumarin (V: R=H) and its dimethyl ether (V: R=Me) reacted readily with aqueous sodium hydroxide solution, even in cold, and these afforded ω,2,4-trihydroxy-α-methyl-6-carboxystyrene (VI: R = H) and ω-hydroxy-2,4-dimethoxy-α-methyl-6-carboxystryene (VI: R=Me), respectively, on acidification. A similar type of the compound was obtained by Chichibabin[9] by the action of alkali on 5,6,7-trimethoxyisocoumarin. 7-Methoxy-4-methylisocoumarin (II: R=Me; R′=H) on treating with ammonia furnished 7-methoxy-4-methylisoquinolone (VII), which is a characteristic reaction of the isocoumarins[10].

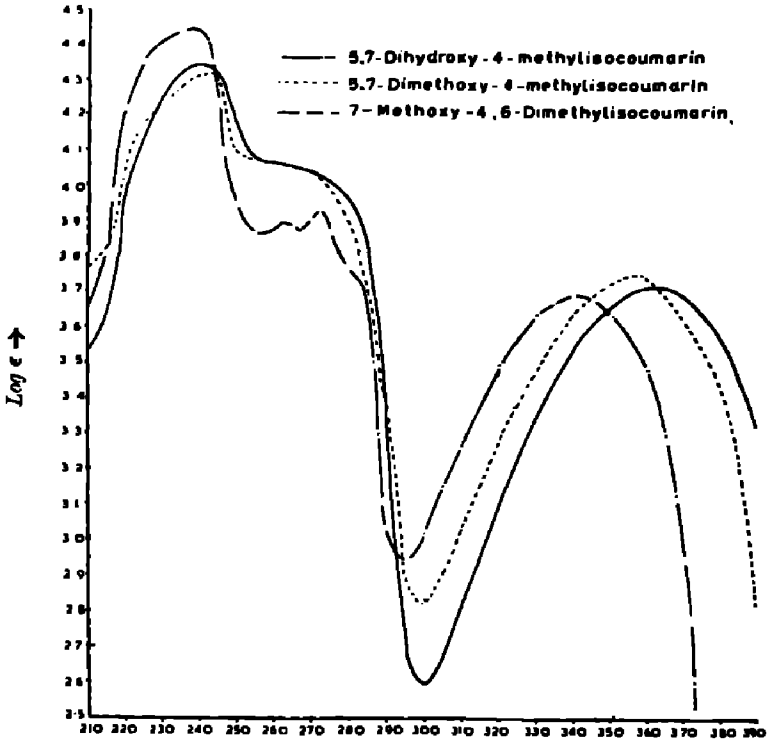

FIG. 2

The main difficulty in effecting the condensation of acetonyl esters to yield isocoumarins is the susceptibility of the acetonyl esters to easy hydrolysis to acids by alkaline and acidic reagents. This restricted the choice to the use of 85% sulphuric acid as the only condensing agent, as it was found that with other condensing agents, like phosphorus oxychloride, anhydrous aluminium chlorides, etc., only the hydrolysed products could be isolated. Even in presence of sulphuric acid, the reaction was accompanied with a large amount of hydrolysed product. Thus in the synthesis of 7-methoxy-4-methylisocoumarin (II: R=Me; R′=H) from acetonyl 3-methoxybenzoate (I: R=Me; R′=R″=H), nearly 60% of the crude product isolated was 3-methoxybenzoic acid. The condensations, however, took place more readily with acetonyl esters of the acids having more activated

9. *Annalen*, 1929, **469**, 93.
10. Ungande *et al.*, *J. Org. Chem.*, 1945, **10**, 533.

nucleus; thus the yield of 5,7-dihydroxy-4-methylisocoumarin (V: R=H) from acetonyl 3,5-dihydroxybenzoate (IV: R=H) was as high as 73% and the product was accompanied with very little of the hydrolysed product, *i.e.*, 3,5-dihydroxybenzoic acid, and the reaction took place even at 5°. It is also interesting to note that acetonyl 3,5-dimethoxybenzoate (IV: R=Me) condensed smoothly in spite of the steric hindrance of the methoxyl group to provide the isocoumarin (V: R=Me) in good yield. This shows that the activity of nuclear hydrogen atom plays a great part in bringing this condensation.

Attempts to effect the condensation of the acetonyl esters of benzoic acid, salicylic acid, veratric acid, vanillic acid, *m*-toluic acid, and *m*-acetamidobenzoic acid met with failures. In all cases the corresponding acids were isolated.

EXPERIMENTAL

Acetonyl 3-Methoxybenzoate (I: R=Me; R′=R″=H).—Bromoacetone (13.5 ml) was added to a mixture of 3-methoxybenzoic acid (19 g.), potassium carbonate (10 g.) in methanol (127 ml), and water (27 ml) and the reaction mixture was refluxed on a water bath for 16 hr. Potassium bromide separating from the mixture was filtered and methanol and unchanged bromoacetone etc. were removed by distilling under reduced pressure. The residue after treatment with a saturated solution of sodium bicarbonate was extracted with ether. The oil, left behind after removing ether, distilled at 138°/4 mm, yield 16 g. (Found: C, 63.2; H, 6.0. $C_{11}H_{12}O_4$ requires C, 63.46; H, 5.76%).

The 2,4-*DNP* was prepared by adding a hot ethanolic solution of dinitrophenylhydrazine hydrochloride to a hot ethanolic solution of the ester. It was crystallised from acetic acid in needles, m.p. 169-70°. (Found: C, 52.90; H, 4.00; N, 14.30. $C_{17}H_{16}O_7N_4$ requires C, 52.58; H, 4.12; N, 14.43%).

7-Methoxy-4-methylisocoumarin (II: R=Me; R′=H).—Acetonyl 3-methoxybenzoate (3 g.) was well mixed with 90% H_2SO_4 (27 ml) and the reaction mixture was kept at the room temperature (28-31°) for 65 hr. On adding crushed ice to it, a pasty mass was obtained which solidified on keeping overnight. It was filtered, washed well with water, and dried in vacuum; m.p. 69-80°, yield 2.8 g. The crude product was triturated with sodium bicarbonate solution in cold and was immediately filtered, washed well with water, and dried; m.p. 90-93°, yield 1.2. It was crystallised repeatedly from dilute acetone (200 ml, 20%) in fine needles, m.p. 101-102°, yield 0.7g. It sublimed at 100°/4 mm. (Found: C, 69.6; H, 5.5. $C_{11}H_{10}O_3$ requires C, 69.47; H, 5.26%). U V absrption: λ_{max}^{MeOH} 230, 268, 341 mμ (log ε, 4.40, 4.08, 3.69). 3-Methoxybenzoic acid (1.5 g.) was recovered after acidification of the sodium bicarbonate solution; m.p. and mixed. m.p. with the authentic specimen, 105-107°.

7-Hydroxy-4-methylisocoumarin (II: R=R′=H).—7-Methoxy-4-methylisocoumarin (1 g.) was demethylated by heating with HI (7 ml) in acetic anhydride (2 ml) at 130-40° in an oil bath for 3hr. The crude solid, obtained after pouring the reaction mixture in

sodium bisulphite solution, was dried and sublimed in vacuum. Two sublimates were collected: one at 100-10°/4mm, m.p. 175-190°, and the second sublimate at 110-20°/4 mm, m.p. 202-204°. The second sublimate on resublimation at 120°/4 mm melted sharply at 204-205°. (Found: C, 68.1; H, 4.3. $C_{10}H_8O_3$ requires C, 68.18; H, 4.54%). UV absorption: λ_{max}^{MeOH} 230, 267, 345mμ (log ε, 4.38, 3.99, 3.61).

The first sublimate was found to contain some unchanged isocoumarin together with the demethylated product. A negligible residue (m.p. 305-15°) remained behind without being sublimed. It did not crystallise from any solvent. It was soluble in cold alkali.

7-Methoxy-4-methylisoquinolone (VII).—7-Methoxy-4-methylisocoumarin (0.5 g.) was refluxed with liquor ammonia (42 ml) for 1½ hr. and then left overnight at the room temperature. The solid separating (m.p. 180-205°, yield 0.2 g.) was repeatedly crystallised from benzene as plates, m.p. 220-21°. (Found: C, 69.80; H, 6.00; N, 7.20. $C_{11}H_{11}O_2N$ requires C, 69.84; H, 5.82; N, 7.40%). UV absorption: λ_{max}^{MeOH} 223, 255, 278, 345 mμ (log ε, 4.38, 3.83, 4.00, 3.76).

Acetonyl 3-Hydroxybenzoate (I : R = R′ = R″ = H).—A mixture of bromoacetone (8.5 ml), 3-hydroxybenzoic acid (11 g.), potassium carbonate (7g.) in methanol (90 ml), and water (17 ml) was refluxed for 16 hr. The reaction mixture was worked up as in the case of acetonyl 3-methoxybenzoate. It separated as an oil which solidified on cooling. It was crystallised from a mixture of benzene and petroleum (40-60°) in prismatic needles, m.p. 66-68°, yield 11 g. (Found: C, 62.2; H, 5.4. $C_{10}H_{10}O_4$ requires C, 61.9; H, 5.19%).

Cyclodehydration of Acetonyl 3-Hydroxybenzoate.—Acetonyl 3-hydroxybenzoate (3 g.) was mixed with 90% H_2SO_4 (37 ml) and was kept at the room temperature (28-31°) for 65 hr. On adding crushed ice to the mixture, a pasty product separated. It solidified on keeping overnight (yield 1.6 g.). It was triturated with a sodium bicarbonate solution in cold and was immediately filtered, washed well, and dried. It was crystallised from water in plates, m.p. 160-85°, yield 0.4 g. Repeated crystallisations did not improve the m.p. 3-Hydroxybenzoic acid (1.5 g.) was recovered from the sodium bicarbonate extract on acidification. 7-Hydroxy-4-methylisocoumarin (II : R=R′=H) was isolated from the product (m.p. 160-85°) by dissolving it in ethyl acetate and allowing it to crystallise slowly (10 days). The prismatic compound (m.p. 200-203°) separating sublimed at 120°/4 mm, m.p. 204-205°. Mixed m.p. with an authentic specimen of 7-hydroxy-4-methylisocoumarin showed no lowering. Attempts to separate the mixture further met with failures.

Acetonyl 3-Methoxy-4-methylbenzoate (I : R=R′ = Me; R″ = H).—A mixture of 3-methoxy-4-methylbenzoic acid[7] (10 g.), bromoacetone (7.5 ml), potassium carbonate (5 g.) in methanol (126 ml), and water (11 ml) was refluxed for 17 hr. The reaction mixture was worked up as in previous cases. The crude solid separating was treated with sodium bicarbonate solution and crystallised from dilute methanol in needles, m.p. 65-67°, yield 10g. (Found: C, 64.4; H, 6.5. $C_{12}H_{14}O_4$ requires C, 64.3; H, 6.6%).

7-Methoxy-4,6-dimethylisocoumarin (II: R=R′=Me).—The preceding acetonyl ester (3 g.) was well mixed with H_2SO_4 (conc., 41 ml) and left at the room temperature (28-31°) for 40 hr. when a violet colour developed. On adding crushed ice to it, a pasty mass was obtained which solidified on keeping. It was triturated with sodium bicarbonate solution in cold and immediately filtered, washed well, dried, and dissolved in ether. The ether

solution was charcoaled. The solid obtained after removing the ether was crystallised from dilute acetone in prismatic plates, m.p. 203-204°, yield 0.4 g. (Found: C, 70.40; H, 6.20. $C_{12}H_{12}O_3$ requires C, 70.58; H, 5.88%). UV absorption: λ_{max}^{EtOH} 240, 262, 272, 340 mμ (log ε, 4.44, 3.89, 3.93, 3.69).

7-Hydroxy-4,6-dimethylisocoumarin (II: R=H; R′=Me).—7-Methoxy-4,6-dimethylisocoumarin (0.7 g.) was demethylated by heating it with HI (7ml) in acetic anhydride (1ml) at 130-40° in an oil bath for 3 hr. The crude product, obtained after pouring the reaction mixture in water, was filtered and washed with an aqueous sodium bisulphite solution. It was sublimed in vacuum at 165-70°/0.3mm; m.p. 274-75°, yield 0.4 g. (Found: C, 69.40; H, 5.30. $C_{11}H_{10}O_3$ requires C, 69.47; H, 5.26%).

Acetonyl 3-Hydroxy-4-methylbenzoate (I: R=R″ =H; R′=Me).—A mixture of 3-hydroxy-4-methylbenzoic acid[7] (3.1g.), bromoacetone (2.5 ml), potassium carbonate (1.6 g.) in methanol (24 ml), and water (3 ml) was refluxed for 17 hr. The reaction mixture was worked up as usual. The crude oily residue after trituration with sodium bicarbonate solution was extracted with ether. The ether was removed and the residue was crystallised from petroleum (80-100°) in needles, m.p. 93-95°, yield 3.3 g. (Found: C, 64.10; H, 5.60. $C_{11}H_{12}O_4$ requires C, 63.46; H, 5.76%).

Cyclodehydration of Acetonyl 3-Hydroxy-4-methylbenzoate.—The above ester (1g.) was mixed with 85% H_2SO_4 (11ml) and kept at the room temperature (28-31°) for 40hr. On adding crushed ice to the mixture, a pasty product separated that solidified on keeping overnight. It was then triturated with sodium bicarbonate solution and was immediately filtered, washed, and crystallised from water (charcoal); m.p. 185-200°. Repeated crystallisations of the same did not improve the m.p. 3-Hydroxy-4-methylbenzoic acid was recovered by acidification of the sodium bicarbonate extract.

Acetonyl 3-Hydroxy-6-methylbenzoate (I: R = R′ = H, R″ = Me).—A mixture of 3-hydoxy-6-methylbenzoic acid[8] (6.1 g.), bromoacetone (5.2 ml), potassium carbonate (3.2 g.) in methanol (70 ml), and water (11 ml) was refluxed for 17 hr. and was worked up as usual. The crude solid was triturated with sodium bicarbonate solution, washed, and then crystallised from petroleum (60-80°), m.p. 86-87, yield 6.5 g. (Found: C, 63.80; H, 5.60. $C_{11}H_{12}O_4$ requires C, 63.46; H, 5.76%).

5-Hydroxy-4,8-dimethylisocoumarin (III: R=H; R′=Me).—Acetonyl 3-hydroxy-6-methylbenzoate (2 g.) was well mixed with 95% H_2SO_4 (27ml) and kept at the room temperature (31°) for 5 hr. On adding crushed ice to the mixture a solid separated. It was triturated with sodium bicarbonate solution and was filtered immediately; m.p. 240-43°. yield 0.75 g. It was crystallised from dilute acetone in prisms, m.p. 243-44°, yield 0.6g. (Found: C, 69.70; H, 5.50. $C_{11}H_{10}O_3$ requires C, 69.47; H, 5.26%). UV absorption: λ_{max}^{EtOH} 230,267,353 mμ (log ε, 4.28, 4.03, 3.76).

The *acetyl derivative* was prepared by refluxing the isocoumarin (III: R=H; R′=Me) (0.5 g.) with acetic anhydride (7 ml) and pyridine (3-4 drops) for 3 hr. It was crystallised from ethanol in plates, m.p. 158°, yield 0.45 g. (Found: C, 67.00; H, 5.40. $C_{13}H_{12}O_4$ requires C, 67.24; H, 5.20%).

Acetonyl 3-Methoxy-6-methylbenzoate (I: R = R″ = Me; R′ = H).—A mixture of 3-methoxy-6-methylbenzoic acid[8] (3.3 g.), bromoacetone (2.6 g.), potassium carbonate (1.6 g.) in methanol (37 ml), and water (5 ml) was refluxed for 16 hr. The reaction mixture was worked up as usual. The crude oily product was triturated with sodium bicarbonate

solution and was extracted with ether. The ether was removed and the oily residue was distilled in vacuum at 170-72°/1 mm, yield 3.g (Found: C, 64.70; H, 6.70. $C_{12}H_{12}O_5$ requires C, 64.85; H, 6.35%).

Attempted Condensation of Acetonyl 3-Methoxy-6-methylbenzoate.—A mixture of acetonyl 3-methoxy-6-methylbenzoate (1 g.) and H_2SO_4 (11 ml, 85%) was kept at the room temperature for 24 hr. On adding crushed ice to the mixture, a pasty compound separated which remained in semisolid state even after keeping it overnight. The product was triturated with sodium bicarbonate solution when it dissolved with only a few traces of an oily substance floating on the surface, which were removed by extraction with ether. The sodium bicarbonate extract furnished pure 3-methoxy-6-methylbenzoic acid (0.9 g.); m.p. and mixed m.p. with the authentic specimen, 145-46°.

Acetonyl 3,5-dihydroxybenzoate (IV: R= H) was prepared by refluxing a mixture of 3,5-dihydroxybenzoic acid (12.5 g.), bromoacetone (11.5 ml), potassium carbonate (7g.) in methanol (125 ml), and water (20 ml) for 16 hr. The mixture was worked up as usual. The solid obtained after treating the residue with sodium bicarbonate solution was crystallised from water in prisms, m.p. 95-97°, yield 10 g. On drying at 100° it melted at 134-35°. Fritsch[6] recorded the same m.p.

5,7-Dihydroxy-4-methylisocoumarin (V: R= H).—The above ester (9 g.) was mixed with cooled H_2SO_4 (100ml, 85%) and after shaking well it was kept at 5° for 42 hr. when a dark green colour developed. It was then decomposed by adding crushed ice and the solid separating was filtered, washed, and dried; m.p. 248-52°, yield 7.5 g. It was crystallised from rectified spirit in prisms, m.p. 262-64°, yield 6 g. (Found: C, 62.10; H, 4.60. $C_{10}H_8O_4$ requires C 62.50; H, 4.16%). UV absorption: λ_{max}^{EtOH} 237, 365mμ (log ε, 4.34, 3.71).

The *diacetyl derivative* was prepared by refluxing the isocoumarin (V: R=H) (1 g.) with acetic anhydride (7 ml) and pyridine (3-4 drops) for 3 hr. It was crystallised from ethanol in shining plates, m.p. 148-49°, yield 1.1 g. (Found: C, 61.10; H, 4.60. $C_{14}H_{12}O_6$ requires C, 60.87; H, 4.37%).

ω.2.4-Trihydroxy-α-methyl-6-carboxystyrene (VI: R=H) : *Action of* NaOH *on 5,7-Dihydroxy-4-methylisocoumarin.*—The *isocoumarin* (0.3 g.) was dissolved in 10% aqueous NaOH solution (20 ml) and left overnight at the room temperature. The solid separating on acidification was repeatedly crystallised from water in prisms, m.p. 214-15°. (Found: C, 57.30; H, 4.80. $C_{10}H_{10}O_5$ requires C, 57.24; H, 4.76%). It dissolved in sodium bicarbonate solution and reduced silver nitrate solution.

Acetonyl 3,5-dimethoxybenzoate (IV: R=Me) was prepared by refluxing the mixture of 3,5-dimethoxybenzoic acid (5.7 g.), bromoacetone (3.5 ml), potassium carbonate (2.4 g.) in methanol (100 ml), and water (7 ml) for 15 hr. and worked up as usual The viscous oil separating after revoming the ether solidified on cooling. It was crystallised from petroleum (60-80°) in needles, m.p. 64-65°, yield 4.5 g. (Found: C, 60.20; H, 6.00. $C_{12}H_{14}O_5$ requires C, 60.37; H, 5.88%).

5,7-Dimethoxy-4-methylisocoumarin (V: R=Me).—A mixture of acetonyl 3,5-dimethoxybenzoate (1g.) and H_2SO_4 (14 ml, 85%) was kept at the room temperature (31°) for 3 hr., when slowly a dark green colour developed. On adding crushed ice to the mixture a solid (0.7 g.) separated. It was crystallised from rectified spirit in silky needles, m.p.

175-76°, yield 0.6 g. (Found: C, 65.30; H, 5.60. $C_{12}H_{12}O_4$ requires C, 65.45; H, 5.45%). UV absorption : λ_{max}^{EtOH} 242, 357 mμ (log ε, 4.33, 3.71).

ω-Hydroxy-2,4-dimethoxy-α-methyl-6-carboxystyrene (VI : R = Me) : *Action of* NaOH *on* 5, 7-*Dimethoxy-4-methylisocoumarin*.—The isocoumarin (0.3 g.) was dissolved in 10% aqueous NaOH soluion (20 ml) by warming and the solution kept overnight at the room temperature On acidiffication a solid was obtained. It was repeatedly crystallised from water in tiny prisms, m.p. 148°. (Found: C, 60.10; H, 6.00. $C_{12}H_{14}O_5$ requires C, 60.37; H, 5.88%).

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