The Synthesis of 7-Methoxy-5′,6′-methylenedioxy-benzofurano(3′,2′; 3,4)coumarin

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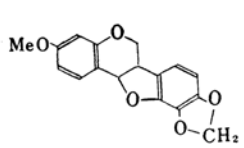
The structure of pterocarpin was proposed by McGookin et al. as 7-methoxy-6′, 7′-methylenedioxy-2′, 3′-dihydrobenzofurano(3′,2′; 3,4)-chroman (I).[1] Recently, on the basis of nuclear magnetic resonance spectral analysis, Bredenberg and Shoolery proposed the revised structure of 7-methoxy-5′, 6′-methylenedioxy-2′, 3′-dihydrobenzofurano(3′, 2′; 3, 4)chroman (II).[2] 7-Methoxy-5′, 6′-methylenedioxybenzofurano(3′, 2′; 3, 4)coumarin (III) has an oxygen pattern similar to that of II in the aromatic rings.

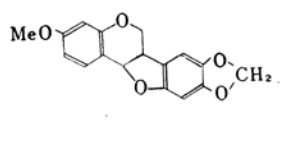
The synthesis of the coumarin (III) by the methylenation reaction of 7, 5′, 6′-trihydroxy compound (IV)[3] has, however, so far been unsuccessful. On the other hand, 7, 5′, 6′-trimethoxy compound (V)[3] has already been obtained by the methylation of IV.

In the present paper, we will describe the synthesis of III from 7-methoxy-4-hydroxycoumarin (VI)[4] by the Wanzlick method.[5]

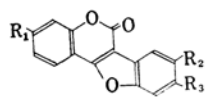
The dehydrogenatic condensation of catechol and VI in the presence of potassium ferricyanide gave a 40% yield of 7-methoxy-5′, 6′-dihydroxybenzofurano(3′, 2′; 3, 4)coumarin (VII) (m. p.> 300°C). VII gave a strong fluorescence in ethanol or acetone and a dark violet color reaction with alcoholic ferric chloride. A dimethyl ether (V) (m. p. 247~248°C) and a diacetate (VIII) (m. p. 225~226°C) of VII were prepared. The former showed no depression of the melting point on admixture with an authentic sample.[3] The methylenation of VII with methylene iodide afforded III (m. p. 269~270°C). III gave a green color reaction with gallic acid, and its infrared spectrum showed the absorption peaks at 1038 and 920 cm^{-1}, indicating the presence of a methylenedioxy group.[6] Moreover, the ultraviolet spectra of III and V are essentially identical (Fig. 1), and III gave a strong fluorescence in ethanol or acetone.



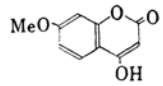
I



II



III



VI

R_1=OMe,
R_2-R_3=O−CH_2−O

IV R_1, R_2, R_3=OH
V R_1, R_2, R_3=OMe
VII R_1=OMe, R_2, R_3=OH
VIII R_1=OMe, R_2, R_3=OAc

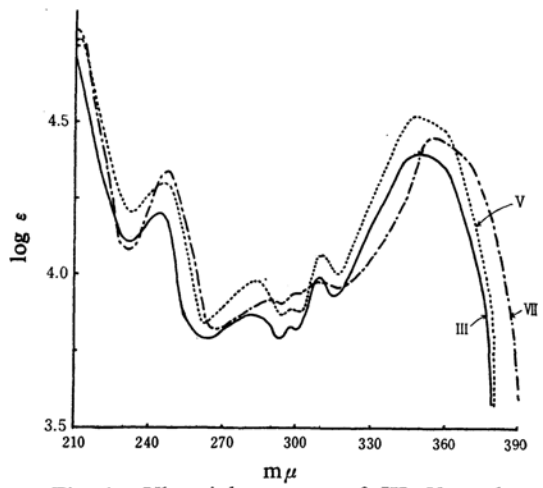


Fig. 1. Ultraviolet spectra of III, V, and VII (ethanol).

Experimental*

7-Methoxy-5′, 6′-dihydroxybenzofurano(3′, 2′; 3, 4)coumarin (VII).—To a solution of VI[4] (m. p. 255~256°C) (1.0 g.) and catechol (0.3 g.) in a mixture of acetone (90 ml.) and water (15 ml.), a solution of potassium ferricyanide (3.5 g.) and sodium acetate (18 g.) in water (30 ml.) was added.

1) A. McGookin, A. Robertson and W. B. Whalley, *J. Chem. Soc.*, **1940**, 787.
2) J. B-Son Bredenberg and J. N. Shoolery, *Tetrahedron Letters*, No. 9, 285 (1961).
3) K. Fukui and M. Nakayama, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), to be published.
4) J. Boyd and A. Robertson, *J. Chem. Soc.*, **1948**, 174.
5) H. W. Wanzlick, R. Gritzky and H. Heidepriem, *Chem. Ber.*, **96**, 305 (1963).
6) L. H. Briggs, L. D. Colebrook, H. M. Fales and W. C. Wieldmann, *Anal. Chem.*, **29**, 904 (1957).

* All melting points are uncorrected; the infrared spectra were measured in Nujol, while the ultraviolet spectra were measured in an ethanol solution.

After 1.5 hr., the resulting mixture was filtered from the precipitates (inorganic salts). The residue was washed with a solution (acetone : water=3 : 1). The combined filtrate was then treated with 46% formic acid (10 ml.), concentrated to ca. 80 ml. in vacuo, and then left overnight. The precipitates were collected and recrystallized from acetone to given VII in the form of pale yellow needles; m. p.> 300°C; yield 0.65 g. (40%). This gave a blue fluorescence in ethanol or acetone and a dark violet color with an alcoholic ferric chloride solution. IR: 3310 (broad) (OH); 1725 (α-pyrone) cm^{-1}. UV: λ_{max} mμ (log ε); 210 (4.80), 250 (4.34), 288 (3.92), 301_1 (3.94), 310 (3.97), 355 (4.45).

Found: C, 64.69; H, 3.11. Calcd. for $C_{16}H_{10}O_6$: C, 64.43; H, 3.38%.

The diacetate (VIII): acetic anhydride-pyridine method; m. p. 225~226°C (colorless needles from acetone). IR: 1776, 1759, 1730 (acetate, α-pyrone) cm^{-1}. UV: λ_{max} mμ (log ε); 240 (4.34), 266 (3.90), 288.5_1 (3.90), 299 (4.12), 335 (4.54), 342_1 (4.44), 351 (4.45).

Found: C, 62.58; H, 3.54. Calcd. for $C_{20}H_{14}O_8$: C, 62.83; H, 3.69%.

7, 5', 6'-Trimethoxybenzofurano (3', 2'; 3, 4) coumarin (V).—A mixture of VII (0.5 g.) methyl iodide (1.0 g.) and anhydrous potassium carbonate (3.0 g.) in anhydrous acetone (300 ml.) was refluxed for 5 hr. on a steam bath. The reaction mixture was then filtered from the precipitates. The filtrate was distilled and the residue was recrystallized from acetone to give V in the form of colorless needles; m. p. 247~248°C; yield 0.5 g. (88%). This was identical with an authentic sample[3] (m. p. 248~249°C) and gave a blue fluorescence in ethanol or acetone. IR: 1730 (α-pyrone) cm^{-1}. UV: λ_{max} mμ (log ε); 211 (4.77), 246 (4.30), 283.5 (3.98), 297 (3.89), 310 (4.06), 348 (4.52).

Found: C, 66.21, H, 4.42. Calcd. for $C_{18}H_{14}O_6$: C, 66.25; H, 4.32%.

7-Methoxy-5', 6'-methylenedioxybenzofurano (3', 2'; 3, 4) coumarin (III).—A mixture of VII (0.5 g.), methylene iodide (1.0 g.) and anhydrous potassium carbonate (3.0 g.) in acetone (300 ml.) was refluxed for 30 hr. on a steam bath; then the solvent was evaporated. The water was added to the residue. The resulting precipitates were collected and recrystallized from acetone to give III in the form of colorless microcrystals; m. p. 269~270°C; yield 0.25 g. (47%). This gave a green color reaction with gallic acid and a blue fluorescence in ethanol or acetone. IR: 1746 (α-pyrone); 1038, 943 (O-CH_2-O). UV: λ_{max} mμ (log ε); 245 (4.25), 283 (3.87), 297 (3.83), 309 (3.99), 347 (4.40).

Found: C, 65.52; H, 3.14. Calcd. for $C_{17}H_{10}O_6$: C, 65.81; H, 3.25%.

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