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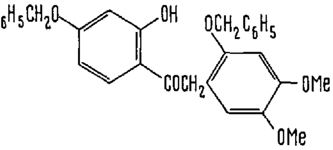
SPECIALIA

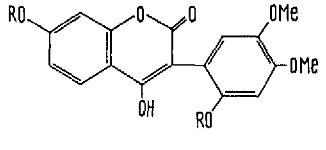
A New Synthetic Method of Coumestan Derivatives

Synthesis of naturally occurring coumestan and its derivatives have been described[1]. Attempts have now been made to prepare the compounds following possible routes of their biogenesis. The coumestans have an oxygen pattern similar to that of several 2'-hydroxyisoflavones and are thought probably to arise by the oxidation of the latter in the path of biogenesis. In the present paper a conventional conversion of a 2'-hydroxyisoflavone into the corresponding coumestan derivative is described.

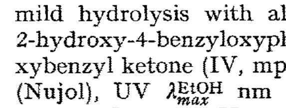
The reaction of 7, 2'-dihydroxy-(I)[2] or 7-benzyloxy-2'-hydroxy-4', 5'-dimethoxyisoflavone (II)[2] with benzyl chloride in the presence of potassium iodide and potassium carbonate provided 7, 2'-dibenzyloxy compound (III, mp 142–143°, IR cm^{-1}: 1640 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 248 (4.40), 296.5 (4.29). Found: C, 75.07; H, 5.39. $C_{31}H_{26}O_6$ requires: C, 75.29; H, 5.30%). Upon mild hydrolysis with alkali III was transformed into 2-hydroxy-4-benzyloxyphenyl 2-benzyloxy-4, 5-dimethoxybenzyl ketone (IV, mp 133–134°, IR cm^{-1}: 1635 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 279 (4.29), 314i (4.01). Found: C, 74.64; H, 5.86. $C_{30}H_{28}O_6$ requires: C, 74.36; H, 5.83%). According to the Robertson coumarin synthesis, the condensation of IV with diethyl carbonate and sodium gave 4-hydroxy-7-benzyloxy-3-(2'-benzyloxy-4', 5'-dimethoxyphenyl)coumarin (V, mp 210–211°, IR cm^{-1}: 3300 (OH), 1690 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 285 (4.09), 315 (4.30). Found: C, 73.20; H, 5.29. $C_{31}H_{26}O_7$ requires: C, 72.93; H, 5.13%) (acetate; mp 190–191°, IR cm^{-1}: 1765, 1720 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 293 (4.13), 328 (4.29)). The debenzylation of V with hydrochloric acid or with hydrogen over 10% palladium charcoal afforded 4, 7, 2'-trihydroxycoumarin derivative (VI, mp 293–296°, IR cm^{-1}: 3400, 3250 (OH), 1680 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 285 (4.01), 326 (4.27). Found: C, 61.72; H, 4.35. $C_{17}H_{14}O_7$ requires: C, 61.82; H, 4.27%) (triacetate; mp 202–203°, IR cm^{-1}: 1770, 1720 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 277 (4.10), 321 (4.13)). The intramolecular dehydration of VI with hydrogen chloride-methanol readily led to a coumestan, 7-hydroxy-5', 6'-dimethoxybenzofurano-[3', 2': 3, 4]coumarin (VII, mp 306–308° (lit.[3] 303–305°), IR cm^{-1}: 3130 (OH), 1690 (C=O) (Nujol), UV λ_{max}^{EtOH} nm (log ε): 246.5 (4.32), 275i (3.90), 281.5 (3.91), 295 (3.91), 306.5 (4.05), 348 (4.45)) which was isolated from alfalfa (Medicago)[3] and was synthesized by BICKOFF et al.[3] and by present authors[4]. Its acetate (mp 219–220°) and methyl ether (mp 255–256°) were prepared and identical in all respects with the authentic samples. This new method is thought to be adaptable to synthesize coumestan derivatives.



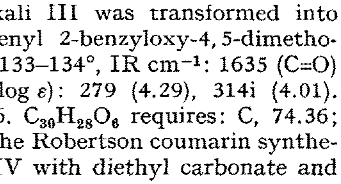
VII



I $R_1=R_2=H$
II $R_1=CH_2C_6H_5$ $R_2=H$
III $R_1=R_2=CH_2C_6H_5$



IV



V $R=CH_2C_6H_2$
VI $R=H$

Zusammenfassung. Die Synthese von 7-Hydroxy-5', 6'-dimethoxybenzofurano[3', 2': 3, 4]coumarin aus 7, 2'-Dihydroxy- oder 7-Benzyloxy-2'-hydroxy-4', 5'-dimethoxyisoflavon wird beschrieben.

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[1] K. FUKUI and M. NAKAYAMA, Nippon Kagaku Zasshi (J. chem. Soc. Japan, Pure chem. Sect.) *85*, 790 (1964) and references cited therein. – K. FUKUI and M. NAKAYAMA, Tetrahedron Lett. *1965*, 2559, and references cited therein.

[2] K. FUKUI, M. NAKAYAMA and T. HARANO, Bull. chem. Soc. Japan *42*, 233 (1969).

[3] E. M. BICKOFF, A. L. LIVINGSTON, S. C. WITT, B. E. KNUCKLES, J. GUGGOLZ and R. R. SPENCER, J. Am. pharm. Ass. *53*, 1496 (1964). – R. R. SPENCER, B. E. KNUCKLES and E. M. BICKOFF, J. org. Chem. *31*, 988 (1966). – A. L. LIVINGSTON, S. C. WITT, R. E. LUNDIN and E. M. BICKOFF, J. org. Chem. *30*, 2353 (1965).

[4] K. FUKUI, M. NAKAYAMA and H. SESITA, Bull. chem. Soc. Japan *37*, 1887 (1964).