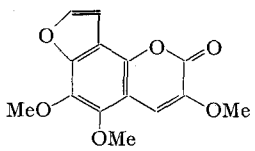

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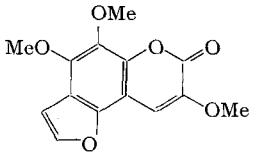

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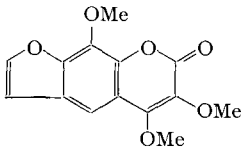

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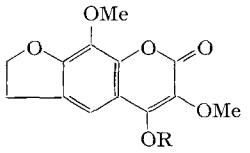
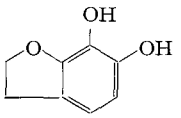
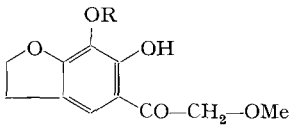


VII R = H
VIII R = Me



IV



V R = H
VI R = Me

153.5–155°, UVλ_{max}^{EtOH} nm (log ε): 240 (4.33), 245$_i$ (4.33), 259$_i$ (4.19), 299 (4.11), IR 1700, 1623, 1595 cm^{-1} (Nujol), NMR δ ppm: 7.79$_d$ (J = 2.5 Hz), 7.76$_s$, 6.90$_d$ (J = 2.5 Hz), 4.40$_s$, 4.31$_s$, 3.97$_s$ ($CDCl_3$). Found: C, 61.01; H, 4.41. $C_{14}H_{12}O_6$ requires: C, 60.87; H, 4.38%) (lit. m.p.[1] 151–152°, NMR[2] δ ppm: 7.76$_d$ (J = 2.5 Hz), 7.68$_s$, 6.88$_d$ (J = 2.5 Hz), 4.37$_s$, 4.30$_s$, 3.97$_s$). The properties of the synthetic III were in accordance with the reported ones[1,2] of the natural isohalfordin.

Zusammenfassung. Die Synthese von Isohalfordin (3,4,8-Trimethoxyfuro[3′,2′:6,7]cumarin) aus 6,7-Dihydroxy-2,3-dihydrobenzo[*b*]furan wird beschrieben.

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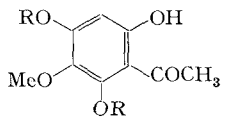
S. FUJIMOTO and O. FUKUDA

Department of Chemistry, Faculty of Science, Hiroshima University, Hiroshima (Japan), 2 January 1969.

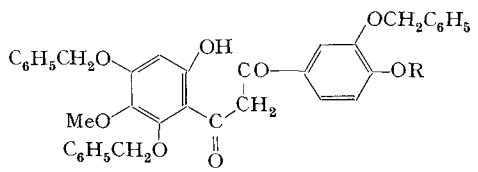
The Syntheses of 6-Methoxyluteolin and Desmethoxycentaureidin

Recently, 6-methoxyluteolin (5,7,3′,4′-tetrahydroxy-6-methoxyflavone) (I) and desmethoxycentaureidin (5,7,3′-trihydroxy-6,4′-dimethoxyflavone) (II) were isolated from *Rosmarinus officinalis* L.[1] and *Centaurea nigrescens* Willd.[2], respectively. These compounds have the closely related structures to axillarin and centaureidin. In previous papers[3], the authors reported the synthetic studies of the 5,7-dihydroxy-6-methoxyflavone derivatives. The present paper reports the syntheses of I and II from 3-methoxy-2,4,6-trihydroxyacetophenone (III)[4] via 2,4-dibenzyloxyl derivative (IV)[5].

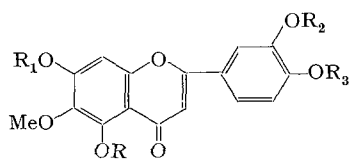
The ketone IV was esterified with 3,4-dibenzyloxybenzoyl chloride in the presence of anhydrous pyridine and then the resulting ester was converted to 4,6-dibenzyloxy-2-hydroxy-5-methoxy-ω-(3,4-dibenzyloxybenzoyl)-acetophenone (V, m.p. 136.5–137.5°. Found: C, 76.26; H, 5.47. $C_{44}H_{38}O_8$ requires: C, 76.06; H, 5.51%) by the BAKER-VENKATARAMAN transformation[6]. Cyclization of the diketone V with anhydrous sodium acetate in acetic acid afforded 5-hydroxy-6-methoxy-7,3′,4′-tribenzyloxyflavone (VI, m.p. 158–159° (143–145° sinter), UVλ_{max} nm (log ε): (EtOH) 242.5 (4.31), 277.5 (4.25), 337 (4.43); (EtOH-$AlCl_3$) 258.5 (4.21), 295 (4.28), 360 (4.38). Found: C, 75.98; H, 5.47. $C_{37}H_{30}O_7$ requires: C, 75.75; H, 5.16%). The debenzylation of VI with hydrogen gave the desired flavone (I, m.p. 264–266°, IR 3380, 1658, 1615, 1577, 1500 cm^{-1} (KBr), UVλ_{max} nm (log ε): (EtOH) 255 (4.21), 273 (4.21), 350 (4.42); (EtOH-AcONa) 276 (4.34), 366 (4.28). Found: C, 60.75; H, 3.63. $C_{16}H_{12}O_7$ requires: C, 60.76; H, 3.82%) (lit.[1], m.p. 258–262°, IR 3390, 1655, 1600, 1570, 1490 cm^{-1}, UV λ_{EtOH}^{max} nm: 256, 273, 348) (tetra-acetate: m.p. 202.5–203°, UV λ_{EtOH}^{max} nm (log ε): 265 (4.37), 302 (4.39). Found: C, 59.25; H, 4.44. $C_{24}H_{20}O_{11}$ requires: C, 59.50; H, 4.16%). Its triethyl derivative (VII, m.p. 152.5–153.5°, UVλ_{max} nm (log ε): (EtOH) 243.5 (4.26), 277 (4.15), 342 (4.42); (EtOH-$AlCl_3$) 261.5 (4.15), 293 (4.26), 368 (4.42). Found: C, 65.76; H, 6.18. $C_{22}H_{24}O_7$ requires: C, 65.99; H, 6.04%), obtained with diethyl sulfate, was also prepared from 2,4-diethoxy-3-methoxy-6-hydroxyacetophenone (VIII)[7] with 3,4-diethoxybenzoyl chloride via 6-methoxy-5,7,3′,4′-tetraethoxyflavone (IX, m.p. 142.5–143.5°. Found: C, 67.27;



III R = H
IV R = $C_6H_5CH_2$
VIII R = C_2H_5



V R = $C_6H_5CH_2$
X R = Me



I R = R_1 = R_2 = R_3 = H
II R = R_1 = R_2 = H, R_3 = Me
VI R = H, R_1 = R_2 = R_3 = $C_6H_5CH_2$
VII R = H, R_1 = R_2 = R_3 = C_2H_5
IX R = R_1 = R_2 = R_3 = C_2H_5
XI R = H, R_1 = R_2 = $C_6H_5CH_2$, R_3 = Me

H, 6.44. $C_{24}H_{28}O_7$ requires C, 67.27; H, 6.59%), by an unambiguous method.

On the other hand, II has now been obtained from IV by a modification of the above method. The ketone IV with 3-benzyloxy-4-methoxybenzoyl chloride gave 4,6-dibenzyloxy-2-hydroxy-5-methoxy-ω-(3-benzyloxy-4-methoxybenzoyl)-acetophenone (X, m.p. 183–184°. Found: C, 73.69; H, 5.59. $C_{38}H_{34}O_8$ requires C, 73.77; H, 5.54%), which was then converted to 7,3′-dibenzyloxy-6,4′-dimethoxy-5-hydroxyflavone (XI, m.p. 145–146.5°, UV λ_{max} nm (log ε): (EtOH) 243.5 (4.29), 277 (4.24), 339 (4.39); (EtOH-$AlCl_3$) 261 (4.16), 293 (4.25), 364 (4.38). Found: C, 72.84; H, 5.20. $C_{31}H_{26}O_7$ requires: C, 72.93; H, 5.13%) was prepared. The catalytic debenzylation of XI gave II (m.p. 264–266°, IR 3390, 1650, 1615, 1585, 1555, 1518 cm^{-1} (KBr), UV λ_{max} nm (log ε): (EtOH) 245 (4.24), 275 (4.23), 344 (4.40); (EtOH-AcONa) 241 (4.37), 277 (4.36), 356 (4.23). Found: C, 61.56; H, 4.05. $C_{17}H_{14}O_7$ requires: C, 61.82; H, 4.27%) (lit.[2], m.p. 269–272°, IR 3430, 1670, 1630, 1600, 1530, 1514 cm^{-1}, UV λ_{max} nm: 273, 342) (triacetate, m.p. 186.5–187°, UV λ^{max}_{EtOH} nm (log ε): 262 (4.17), 320 (3.93). Found: C, 60.52; H, 4.29. $C_{23}H_{20}O_{10}$ requires: C, 60.52; H, 4.42%) (lit.[2], m.p. 189–190°). The properties of the synthetic samples of I and II were superimposable with those recorded in the literature[1,2] for 6-methoxyluteolin and desmethoxycentaureidin.

Zusammenfassung. Die Synthese von 6-Methoxyluteolin und Desmethoxycentaureidin aus 2,4-Dibenzyloxy-3-Methoxy-6-Oxyacetophenon wird beschrieben.

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Faculty of Science, Hiroshima University and
Department of Applied Chemistry,
Faculty of Engineering,
University of Tokushima (Japan),
19 November 1968.

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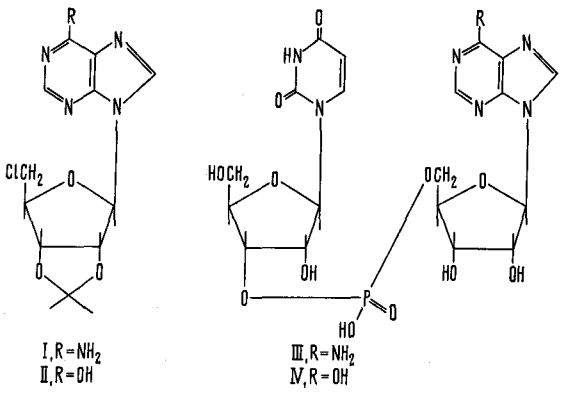
Synthesis of Dinucleoside Phosphates by Reaction of 5′-Chloro-5′-deoxynucleosides with Nucleotide Anions

The use of purine cyclonucleosides in the synthesis of internucleotide bonds was recently reported from this laboratory. The dinucleoside phosphate obtained by treatment of 8,5′-*O*-anhydro-2′,3′-isopropylideneadenosine with uridine-3′-phosphate anion had on OH function at position 8 of the purine moiety[1], while the product obtained from 8,5′-*S*-anhydrognanosine had an SH group, which required treatment with Raney Ni for its removal[2]. In this communication we report the synthesis of uridylyl-(3′-5′)-adenosine and uridylyl-(3′-5′)-inosine by a method which allows the isolation of the products with no substituents. This method involves the treatment of the appropriate 5′-chloro-5′-deoxy-2′,3′-*O*-isopropylidene purine nucleoside with the nucleoside phosphate anion.

5′-Chloro-5′-deoxynucleosides. The required 5′-chloro-5′-deoxynucleosides were conveniently obtained by treating the corresponding 2′,3′-*O*-isopropylidene nucleoside with thionyl chloride as exemplified by the preparation of 5′-chloro-5′-deoxy-2′,3′-*O*-isopropylidene adenosine (I).

A solution of dry 2′,3′-*O*-isopropylidene adenosine (500 mg) in thionyl chloride[3] (1.5 ml) was allowed to stand at room temperature for 12 h in a stoppered flask. Thionyl chloride was removed under reduced pressure and benzene (8 ml) added and evaporated. The residue so obtained was dissolved in an ice-cold mixture of triethylamine (2.5 ml), water (0.5 ml) and alcohol (2.0 ml) and the solution set aside for 30 min before being evaporated to dryness in vacuo. Water was then added to the residue, the whole extracted with benzene (5 × 25 ml) and the benzene extract washed with water (20 ml). Removal of solvent and crystallization of the residue from water yielded the product (316 mg, 60%), m.p. 255–256° (dec., softens at 175°). Rf (B)[4], 0.92; Found: C, 47.71; H, 5.02; N, 22.01; Cl, 10.46. Anal. calcd. for $C_{13}H_{16}N_5O_3Cl$: C, 47.92; H, 4.91; N, 21.50; Cl, 10.90%. λ_{max}, H_2O-260 nm (ε, 13,450); 0.1 *N* HCl-258 nm (ε, 17,500); 0.1 *N* NaOH-261 nm (ε, 16,450). Formic acid treatment of I at room temperature for 48 h yielded the deblocked product, 5′-chloro-5′-deoxyadenosine[5], m.p.



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[3] Thionyl chloride was distilled over quinoline and linseed oil.
[4] Solvent A, isopropanol – ammonia – water (7:1:2) ascending. Solvent B, butanol-acetic acid-water (4:1:5) descending.
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