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The Synthesis of Digicitrin

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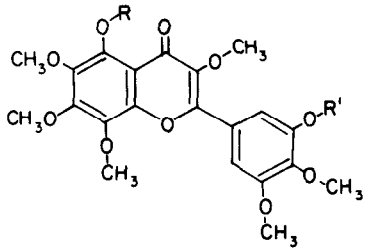
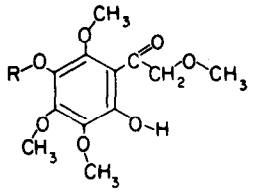
Digicitrin was isolated in 1962 by W. Meier and A. Fürst[1] from Digitalis purpurea L. and shown to be 3', 5-dihydroxy-3, 4', 5', 6, 7, 8-hexamethoxy-flavone (Ia)[1]. It thus is the most highly oxygenated naturally-occuring flavonoid substance.



Ia: R=R'=H
Ib: R=CH_3, R'=$C_6H_5CH_2$
Ic: R=CH_3, R'=H



IIa: R=CH_3
IIb: R=H

We now wish to report the total synthesis of Ia. Our key intermediate 2-hydroxy-3, 4, 5, 6, ω-pentamethoxyacetophenone[2](IIa) was prepared by partial methylation of 2, 5-dihydroxy-3, 4, 6, ω-tetramethoxyacetophenone[3](IIb). Allan-Robinson condensation of IIa with 3-benzyloxy-4, 5-dimethoxybenzoic anhydride (m.p. 121-122) prepared from the corresponding acid chloride of

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m.p. 70-72° in the presence of sodium salt of the same acid, gave rise to 3'-benzyloxy-3, 4', 5, 5', 6, 7, 8-heptamethoxyflavone (Ib), which was catalytically debenzylated to 3'-hydroxy-3, 4', 5, 5', 6, 7, 8-heptamethoxyflavone (Ic), m.p. 213-215°, λ_{max} 256 and 333 μm.

Partial demethylation of Ic with aluminum chloride in ether, followed by chromatography on silicic acid afforded 3,5-dihydroxy-3, 4', 5', 6, 7, 8-hexamethoxyflavone (Ia), identical in every respect with natural digicitrin, m.p. 177-179°, λ_{max} 282 and 338 μm, lit.[1] m.p. 178-179°, λ_{max} 282 and 337 μm. Details of the synthesis will be reported shortly in Chem. Ber.

References.

(1) W. Meier and A. Fürst, Helv. Chim. Acta 45, 232 (1962).

(2) No direct synthesis of IIa has been reported previously. It first was prepared by W. Karrer (Helv. Chim. Acta 17, 1560 /1934/), and later by T. R. Seshadry and Venkateswarlu (Proc. Indian Acad. Sci. 23 A, 192, 209 /1946/), who degraded calycopterin dimethyl ether, prepared either from natural calycopterin or by synthesis.

(3) V.V.V. Murti, L. R. Row and T. R. Seshadri, Proc. Indian Acad. Sci. 24A, 253 (1946).