

Synthesis of 1-Hydroxy-4,6-dimethoxy-
8-methylxanthone

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1-Hydroxy-4,6-dimethoxy-8-methylxanthone (VII),
namely an isomer of lichexanthone (IIIb) was synthe-
sized from ethyl orsellinate, which is readily pre-
pared from diketene and ethyl acetoacetate.

Lichexanthone (IIIb) isolated from *Parmelia formosana* Zahlb.,
which grows in Formosa and the south of Japan, is known as the
unique xanthone compound found in lichen¹⁾. Recently, some pheno-
lic compounds having such xanthone structure were isolated from
fungi.²⁾ Observing these biological activities³⁾ we have studied
the synthesis of xanthone derivatives. In this communication we
wish to describe the synthesis of 1-hydroxy-4,6-dimethoxy-8-methyl-
xanthone (VII), an isomer of lichexanthone (IIIb), using ethyl
orsellinate (I) as a starting material, which is readily prepared
from diketene and ethyl acetoacetate⁴⁾.

Methylation of ethyl orsellinate (I) with excess diazomethane
in ether at room temperature followed by hydrolysis with a 5N solu-

tion of sodium hydroxide in 50% aqueous ethanol afforded everninic acid (II) in 60% yield.

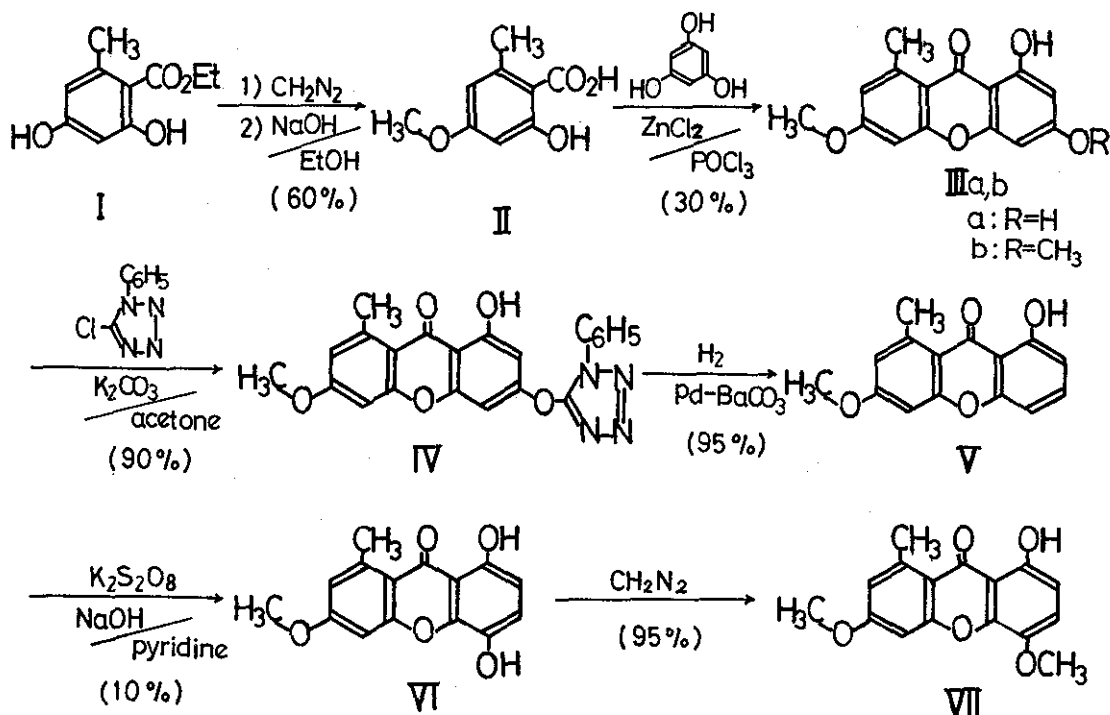
According to the procedure reported by Jayalakshmi⁵⁾, compound (II) was allowed to react with phloroglucinol in the presence of zinc chloride in phosphoryl chloride to give norlichexanthone (IIIa) in 30% yield (mp 260°, lit. mp 260°).

When compound (IIIa) was allowed to react with 1-phenyl-5-chlorotetrazole in the presence of potassium carbonate in acetone, 1-hydroxy-3-(1-phenyl-5-tetrazolyloxy)-6-methoxy-8-methylxanthone (IV) was obtained in quantitative yield. (mp 199°, pale yellow needles from dioxane) IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2400-3600, 1650, 1605. UV $\lambda_{\text{max}}^{\text{ethanol}}$ nm (log ϵ): 339 (3.88), 303 (4.26), 245 (4.56), 239 (4.55). NMR (DMSO, ppm): 2.84 (3H, s, CH₃), 3.99 (3H, s, OCH₃), 6.88 (1H, br, s, ring H), 6.98 (2H, d, J=2 Hz, ring H), 7.21 (1H, d, J=2 Hz, ring H), 7.60-7.92 (5H, m, benzenè ring H), 12.99 (1H, s, OH). MS m/e: 416 (M⁺), 272.

Hydrogenolysis of compound (IV) in dioxane in the presence of 6% Pd/BaCO₃ as a catalyst afforded a quantitative yield of 1-hydroxy-6-methoxy-8-methylxanthone (V), yellow needles (from acetone), mp 162°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2400-3600, 1650, 1600. UV $\lambda_{\text{max}}^{95\% \text{ ethanol}}$ nm (log ϵ): 349 (3.78), 301 (4.21), 266 (4.16), 248 (4.32), 234 (4.46). NMR (CDCl₃, ppm): 2.88 (3H, s, CH₃), 3.90 (3H, s, OCH₃), 6.65 (2H, br, s, ring H), 6.68 (1H, d, J=8 Hz, ring H), 6.77 (1H, d, J=8 Hz, ring H), 7.43 (1H, t, J=8 Hz, ring H), 13.00 (1H, s, OH). MS m/e: 256 (M⁺).

To a solution of compound (V) and potassium hydroxide in pyridine was added a solution of K₂S₂O₈ in H₂O dropwise. The mixture

was stirred at room temperature for 2 days, and sodium thiosulfate was added to decompose excess potassium persulfate ($K_2S_2O_8$). Product obtained was purified by extraction with ether followed by silica gel preparative thin layer chromatography (Merk Kiesel gel 60F) using a mixture of benzene-ethyl acetate (5:1) as an eluant to give yellowish substance ($R_f=0.42$). Purification by crystallization from acetone-ethyl acetate gave 1,4-dihydroxy-6-methoxy-8-methylxanthone (VI) as yellow needles, mp 236-237° in 60% recovery of starting material. IR $\nu_{max}^{KBr} \text{ cm}^{-1}$: 2400-3600, 1640, 1610, 1595. UV $\lambda_{max}^{95\% \text{ ethanol}}$ nm (log ϵ): 379 (3.61), 3.00 (4.13), 279 (4.33), 256 (4.13), 236 (4.39). NMR ($CDCl_3$, ppm): 2.91 (3H, s, CH_3), 3.97 (3H, s, OCH_3), 5.50 (1H, br.s, OH), 6.60-7.14 (4H, m, ring H), 11.93 (1H, s, OH). MS m/e: 272 (M^+), 257 (M^+-CH_3).



Treatment of VI with excess diazomethane in ether at room temperature afforded a quantitative yield of 1-hydroxy-4,6-dimethoxy-8-methylxanthone (VII), yellow prisms (from ethyl acetate), mp 167-169°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2400-3600, 1650, 1610. UV $\lambda_{\text{max}}^{95\% \text{ ethanol}}$ nm (log ϵ): 371 (3.54), 298 (4.05), 277 (4.20), 253 (4.06), 235 (4.38). NMR (CDCl_3 , ppm); 2.90 (3H, s, CH_3), 3.93 (3H, s, OCH_3), 3.99 (3H, s, OCH_3), 6.60-7.12 (4-H, m, ring H), 12.15 (1H, s, OH). MS m/e: 286 (M^+), 271 ($\text{M}^+ - \text{CH}_3$).

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