A Synthesis of Endocrocin, Endocrocin-9-anthrone, and Related Compounds

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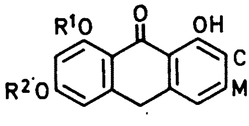
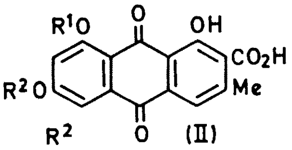
Summary Endocrocin-9-anthrone and endocrocin, the biogenetic precursors of emodin-type anthraquinones, have been synthesized by a method easily adaptable to the synthesis of radioactively labelled compounds.

ENDOCROCIN-9-ANTHRONE (Ia) and endocrocin (IIa) are considered to be important intermediates in the biosynthesis of emodin and related anthraquinones.[1] In order to study the details of the decarboxylation step in emodin biosynthesis we needed radioactively labelled (Ia) and (IIa). Compound (IIa) has previously been prepared by a rather tedious procedure,[2] not easily adaptable to the synthesis of [^{14}C]-labelled compounds.[3] We report here an efficient synthesis of (Ia) and (IIa), based on a modification of Mühlemanns' emodin synthesis.[4]

Treatment of Mühlemanns' dicarboxylic acid (III)[4] with polyphosphoric acid or anhydrous HF gave a quantitative yield of the anthrone (Ib), m.p. 156° (with decarboxylation); λ_{max} (MeOH) 342 nm (ϵ 15,500); ν_{max} (KBr) 3450—2780, 1733, and 1600 cm^{-1}. Oxidation of (Ib) with H_2O_2 in 1N-NaOH afforded endocrocin 6,8-dimethyl ether (IIb), m.p. 271—273° (decomp.), yield 75%. *O*-Demethylation of (IIb) with BBr_3 in refluxing CH_2Cl_2, followed by chromatography of the product on polyamide, gave endocrocin (IIa) in 50% yield, in every respect identical with the natural pigment.[5]

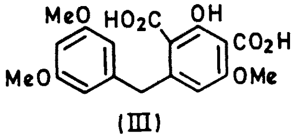


(I)

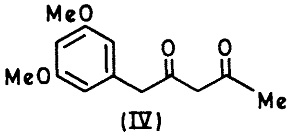


(II)

	R^1	R^2
(a)	H	H
(b)	Me	Me
(c)	H	Me



(III)



(IV)

Demethylation of (Ib) by the same procedure yielded a mixture of (Ia), (Ib), and (Ic), which was separated by chromatography on acetylated polyamide (eluant acetone) in the dark. Compound (Ia) forms a beige yellow powder, m.p. 259—260° (decomp., after shrinking); λ_{max} (MeOH) 354 nm (ϵ 15,000); ν_{max} (KBr) 3450—2630, 1721, and 1616 cm^{-1}; M^+, *m/e* 300 (0·6%); 256 (100%), 241 (16%), 228 (10%), 227 (12%), and 213 (14%). It is stable as a solid, but readily undergoes changes in solution. On dissolving in aqueous $NaHCO_3$ (Ia) quickly develops a red colour. The purity of (Ia) was checked by t.l.c. on acetylated polyamide (Macherey, Nagel & Co.; $C_6H_6:HCO_2H:HCO_2Et$, 13 : 2 : 5; colour after spraying with *p*-nitrosodimethylaniline[6]): R_F (Ia) = 0·11 (dark gray), R_F (Ib) = 0·33 (brown gray), R_F (Ic) = 0·36 (dark gray). Demethylation of (Ib) in sulpholane–CH_2Cl_2 (1 : 1) gave the monoether (Ic), m.p. 196° (decomp.), as the only anthrone carboxylic acid. On oxidation with CrO_3 (Ia) and (Ic) yielded the corresponding anthraquinones (IIa) and (IIc). Compound (IIc) was identical with the pigment cinnalutein, recently isolated from *Dermocybe cinnabarina*.[7]

The dicarboxylic acid (III), [^{14}C]-labelled at both carboxy-groups, was synthesized by condensation of the diketone (IV)[4] with dimethyl [1,5-$^{14}C_2$]acetonedicarboxylate. The synthesis of radioactive (Ia) and (IIa) and its use in feeding experiments is under active investigation and will be published in the full paper.

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