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

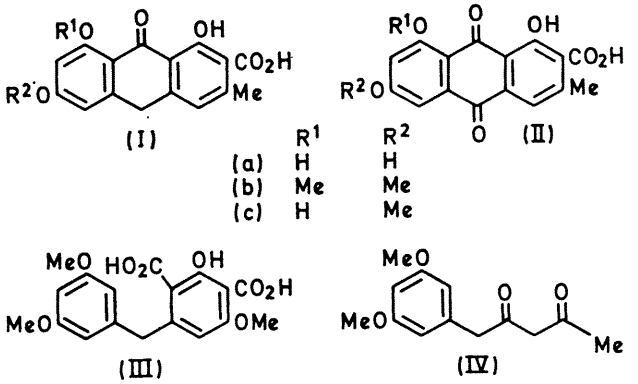
By WOLFGANG STEGLICH* and WOLFGANG REININGER

(*Organisch-Chemisches Institut der Technischen Hochschule, München, Germany*)

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 carboxygroups, 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.

We thank the Deutsche Forschungsgemeinschaft for financial support.

(*Received, December 19th*, 1969; *Com.* 1903.)

[1] A. J. Birch and F. W. Donovan, *Austral. J. Chem.*, 1953, **6**, 360; R. Robinson, "Structural Relations of Natural Products," Clarendon Press, Oxford, 1955, p. 10.
[2] B. S. Joshi, S. Ramanathan, and K. Venkataraman, *Tetrahedron Letters*, 1962, 951.
[3] U. Ohnsorge, Dissertation, Kiel, 1967.
[4] H. Mühlemann, *Pharm. Acta Helv.*, 1951, **26**, 195.
[5] Y. Asahina and F. Fuzikawa, *Ber.*, 1935, **68**, 1558; S. Shibata and S. Natori, *Pharm. Bull.* (*Tokyo*), 1953, **1**, 160; B. Franck and T. Reschke, *Chem. Ber.*, 1960, **93**, 347; S. Gatenbeck, *Svensk kem. Tidskr.*, 1960, **72**, 188; W. Steglich, W. Lösel, and V. Austel, *Chem. Ber.*, 1969, **102**, 4104.
[6] T. Kariyone, K. Tsukida, and N. Suzuki, *J. Pharm. Soc.* (*Japan*), 1954, **74**, 234.
[7] W. Steglich and W. Reininger, *Chem. Ber.*, in preparation.