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ABOUT METABOLIC PRODUCTS OF PENICILLIUM VIRIDICATUM WESTLING AND PENICILLIUM CYCLOPIUM WESTLING; SYNTHESIS OF VIRIDICATOL, 3'-O-METHYLVIRIDICATOL AND N-METHYL-3'-O-METHYLVIRIDICATOL

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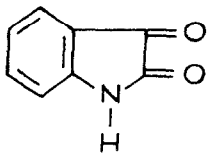
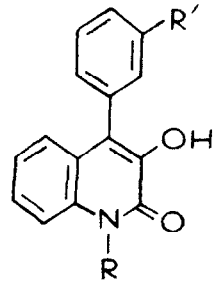
VIRIDICATOL, $C_{15}H_{11}NO_3$ (II; R=H; R'=OH) was first isolated together with viridicatin (II; R=R'=H) by Luckner and Mothes[1] from a strain of Penicillium viridicatum Westling. It was also obtained as a hydrolysis product of cyclopenol, $C_{17}H_{14}N_2O_4$, a metabolite of Penicillium viridicatum and of Penicillium cyclopium[2,3]. Degradative studies have indicated that viridicatol is 3'-hydroxyviridicatin (3-hydroxy-4-(3-hydroxyphenyl)-2-quinolone)[2]. This structure is now confirmed by the synthesis of viridicatol, 3'-O-methylviridicatol (II; R=H; R'=OCH_3) and N-methyl-3'-O-methylviridicatol (II; R=CH_3; R'=OCH_3)

Synthetic 3'-O-methylviridicatol (II; R=H; R'=OCH_3) was obtained by the condensation of m-methoxyphenyldiazomethane with isatin (I). This type of condensation was first successfully carried out for the synthesis of viridicatin from phenyldiazomethane and isatin by Eistert and Selzer[4].

m-Methoxybenzaldehyde was converted to m-methoxyphenyldiazomethane by the method of Gutsche and Jason[5], then condensed with isatin (I) in the usual way. The resulting 3'-O-methylviridicatol (II; R=H; R'=OCH_3) was separated and crystallised from ethanol, m.p. 257°. Its ethanolic solution gives the green colour with ferric chloride characteristic for 3-hydroxycarbostyrils.



(I)



(II)

3'-O-methylviridicatol was demethylated by heating at 130-140° with hydroiodic acid for 2 hours. After recrystallisation from ethylacetat and methanol-water pure viridicatol was obtained, m.p. 274°. The identity of authentic and synthetic viridicatol was confirmed by a mixed melting point (274°), and identical I.R. spectra.

Acetylation of 3'-O-methylviridicatol gave a labile acetyl derivative, crystallising in needles from ethyl acetate-petroleum ether (40-60°), m.p. 174°. The compound was treated with diazomethane and the resulting product was deacetylated by mild alkali. On acidification of the reaction mixture synthetic N-methyl-3'-O-methylviridicatol (II; R=CH_3, R'=OCH_3) separated out; m.p. after sublimation 235°.

N-methyl-3'-O-methylviridicatol also was obtained from dimethylcyclopenol, $C_{19}H_{18}N_2O_4$[2], by acid hydrolysis, together with methylamine, carbon dioxide and a little m-methoxybenzoic acid (Found: C, 72.9; H, 5.5; N, 5.1; $-OCH_3$, 11.0 %. Calc. for $C_{17}H_{15}NO_3$: C, 72.6; H, 5.3; N, 5.0; one $-OCH_3$ 11.1 %).

The identity of both preparations of N-methyl-3'-O-methylviridicatol was established by a mixed melting point (235°) and comparison of the I.R. spectra. N-methyl-3'-O-methylviridicatol was optically inactive. Its ethanolic solution gave a green colour with ferric chloride.

This work was carried out at the Microbiology Unit, Medical Research Institute, Hadara, Alexandria, Egypt, U.A.R.

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