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THE SYNTHESIS AND ANTIFUNGAL ACTIVITY OF 6-HYDROXY-11-THIOPTEROCARPANS

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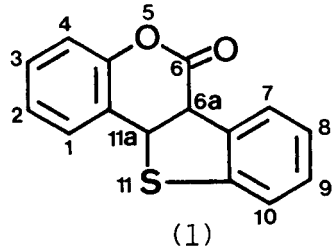
Pterocarpans (benzofuro [3,2-c] benzopyrans) are a group of naturally occurring compounds of flavonoid origin some of which are known to possess antifungal activity (Grisebach and Ebel 1978). 11-Thiopterocarpan derivatives have been shown to possess moderate antifungal activity (Meegan and Tyndall 1981). To study the effect on the activity of the introduction of a hydroxyl group at C-6, a series of 6-hydroxy-11-thiopterocarpans was prepared.

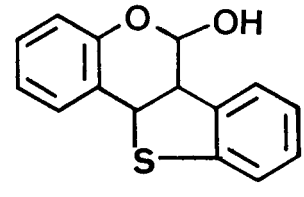
Treatment of the 11-thiopterocarpan-6-one (1) with diborane (B_2H_6/THF) or diisobutylaluminium hydride at low temperature afforded the corresponding lactol product (2) in good yield. This compound was identified by spectroscopic data and elemental analysis. [ν max (KBr) 3200 (OH) cm^{-1}, δ ($CDCl_3$) 5.70,d, J6.2Hz,H-6 δ5.31,d, J7.3Hz H-11a δ3.58,t, J6.6 Hz H-6a, M^+256]. In the ^{13}C nmr spectrum of (2) carbons 6,6a and 11a were identified at 92.3, 50.4 and 48.1 ppm respectively. The corresponding hydroxy-aldehyde tautomer was not detected in solution in the IR spectrum of the reaction mixture or product.

2-3,- and 4-methoxy substituted 6-hydroxy-11-thiopterocarpans were also similarly prepared. On acetylation of (2) a monoacetate was formed. [ν max KBr 1760 (C=O) cm^{-1}, δ($CDCl_3$) 2.13,s,$COOCH_3$, δ3.68,t, J6.9Hz, H-6a, δ5.15, d, J7.OHz. H-11a, δ6.72, J5.4Hz,d, H-6, M^+298]. The 11-thiopterocarpan (3) and also the 2,3-dihydrobenzo{b} thiophen (4) were obtained as minor products in the diborane reduction of the 11-thiopterocarpan-6-one (1).

The 6-hydroxy-11-thiopterocarpans prepared showed moderate antifungal activity against Fomes annosus (LD_{50} 50-75 μg/ml), while the 2,3-dihydrobenzo{b} thiophens showed activity against both Fomes annosus and Candida albicans (LD_{50} 50 -100 μg/ml).



(1)



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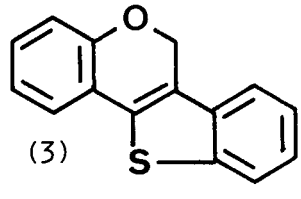

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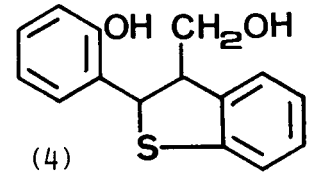

(4)

Grisbach, M., Ebel, J. (1978) Angew.Chem.Int.Ed. Engl. 17: 635-647.
Meegan, M.J., Tyndall, D.V. (1981) J.Chem.Research (S) 239.