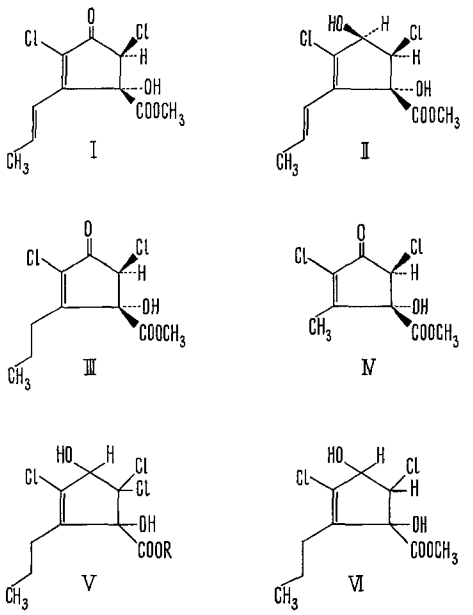
Synthesis of (±) Dihydrocryptosporiopsin

The dichlorocyclopentenone I is a metabolite, possessing antifungal activity, produced by the coprophilous fungus *Sporormia affinis* Sacc., Bomm and Rouss[1] and by a *Cryptosporiopsis* sp.[2], an imperfect fungus isolated from yellow birch, *Betula alleghaniensis* Britt. The name cryptosporiopsin has been advanced for I[2a]. Isolation of the related metabolite II from *Periconia macrospinosa* has recently been reported[3].

Hydrogenation of cryptosporiopsin in ethyl acetate solution with a palladium-charcoal catalyst gives rise to a dihydro-product III, mp 90–96°, in which the *trans*-allyl side chain is reduced to a *n*-propyl group[2b,c]. In a previous paper[4], we have described the conversion of *m*-cresol to the dichlorocyclopentenone IV, suggesting that it should be feasible to synthesize cryptosporiopsin derivatives by hypochlorite-induced rearrangement of appropriately substituted phenols[5–7]. We now report the successful application of the hypochlorite-phenol rearrangement in the synthesis of racemic dihydrocryptosporiopsin III.



Meta-propyl phenol (prepared by reduction of isosafrole with sodium in alcohol[8]) was treated with chlorine in alkaline solution under conditions based on earlier studies[4–7]. The hydroxy acid V (R=H) could be isolated from the mixture of acidic products by partition chromatography on silica gel[9]. Alternatively, the methyl ester V ($R=CH_3$) could more readily be obtained in a pure state, mp 144–145°[10], on chromatography of the mixture resulting from treatment of the hypochlorite products with diazomethane. For the purposes of the synthesis, it was found expedient to effect purification at a later stage. Accordingly the crude acidic mixture was treated with sodium amalgam to effect reduction of the *gem*-dichloro grouping in V (R=H)[4–7]. Following esterification with diazomethane, chromatography afforded the desired dichlorodihydroxy ester VI[11], mp 178–180° (1.5% overall yield from *m*-propyl phenol).

Finally, conversion of VI to racemic dihydrocryptosporiopsin III, mp 101–103°, was accomplished quantitatively by oxidation with Jones' reagent in acetone. The identity of synthetic and naturally derived material was established by IR-, UV-, nuclear magnetic resonance and mass-spectrometry.

Zusammenfassung. Die Synthese von (±) Dihydrocryptosporiopsin aus 3-Propylphenol wird beschrieben.

G. M. STRUNZ and A. S. COURT

Canada Department of Fisheries and Forestry, Forest Research Laboratory, Fredericton (New Brunswick, Canada), 12 January 1970.

[1] W. J. MCGAHREN, J. H. VAN DEN HENDE and L. A. MITSCHER, J. Am. chem. Soc. *91*, 157 (1969).

[2] [a] M. A. STILLWELL, F. A. WOOD and G. M. STRUNZ, Can. J. Microbiol. *15*, 501 (1969). – [b] G. M. STRUNZ, A. S. COURT, J. KOMLOSSY and M. A. STILLWELL, Can. J. Chem. *47*, 2087 (1969). – [c] G. M. STRUNZ, A. S. COURT, J. KOMLOSSY and M. A. STILLWELL, Can. J. Chem. *47*, 3700 (1969).

[3] D. GILES and W. B. TURNER, J. chem. Soc. (C) (*1969*), 2187.

[4] G. M. STRUNZ, A. S. COURT and J. KOMLOSSY, Tetrahedron Letters (*1969*), 3613.

[5] A. HANTZSCH, Chem. Ber. *20*, 2780 (1887); *22*, 1238 (1889).

[6] C. J. MOYE and S. STERNHELL, Tetrahedron Letters (*1964*), 2411; Aust. J. Chem. *19*, 2107 (1966).

[7] A. W. BURGSTAHLER, T. B. LEWIS and M. O. ABDEL-RAHMEN, J. org. Chem. *31*, 3516 (1966).

[8] S. G. COUSIN and F. LYONS, J. Proc. R. Soc. N. S. Wales *70*, 413 (1937). (C.A. *31*, 6637[5].)

[9] C. S. MARVEL and R. D. RANDS JR., J. Am. chem. Soc. *72*, 2642 (1950).

[10] All compounds for which melting points are reported gave satisfactory analytical results by microanalysis and/or mass-spectrometry.

[11] The observed coupling constant (6.4 Hz) of the *vicinal* protons at carbons 4 and 5 of VI[3,6,7], in conjunction with the established stereochemistry of III, its oxidation product (vide infra), suggests that the relative stereochemistry of VI and the *Periconia* metabolite (II) may be identical. In accord with this tentative assignment, BURGSTAHLER[7] has suggested, on the basis of different evidence, that the *phenol*-hypochlorite product is probably a *trans*-diol.

Identification of the Drug Darvon and its Metabolites in the Urine of a Comatose Patient Using a Gas Chromatograph-Mass . Spectrometer-Computer System[1]

High- and low-resolution mass-spectrometry, in conjunction with data obtained from a gas-chromatograph low-resolution mass-spectrometer computer system, were used in the analysis of urine from a patient suspected of ingestion of an overdose of Librium[2]. No indication of this drug could be found in the urine, but instead the drug Darvon (IV)[3] could be detected, together with several of its metabolites.

In patients suffering from drug overdose, therapy is best administered with a thorough knowledge of the