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*ISO*PICROPODOPHYLLONE FROM *PODOPHYLLUM PLEIANTHUM*

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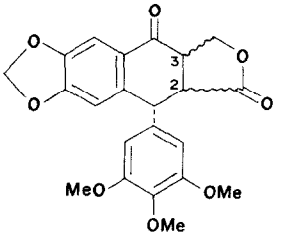
Key Word Index—*Podophyllum pleianthum*; Berberidaceae; novel keto lignan; 2α, 3α-configuration.

Podophyllum pleianthum Hance (Berberidaceae), highly prized by the mountain tribes of Taiwan for its medicinal properties, was investigated by Shibata *et al.*, who reported [1] the isolation of a number of compounds, among them several lignans previously known to have antitumor activity [2].

We have isolated from a benzene extract of the roots and rhizomes of the plant other known compounds [3] in addition to the new keto lignan described in this report.

The new compound **(1)** was obtained by column chromatography of the extract as a minor component (0·013% of dried plant) in a fraction the major product of which was desoxypodophyllotoxin [1]. Following preparative TLC, crystallization from MeOH yielded colorless needles, $C_{22}H_{20}O_8$† (M^+, 412.1130), mp 170–172°, $[\alpha]_D$ −273° ($CHCl_3$); UV, λ_{max}(EtOH) 235 nm (ε 23 100), 259 (10 600), 318 (6500); IR, λ_{max}($CHCl_3$) 5·62 and 5·99 μ. Its NMR spectrum exhibits singlets at 6·27τ (6H, 2-OMe), 6·18 (3H, -OMe), 3·92 (2H, OCH_2O), 3·67 (2H, C-2′,6′), 3·28 (1H, C-8), 2·53 (1H, C-5), perturbed multiplets at 6·62–5·92τ (3H) and 5·79–5·28 (2H). *M/e* of major ions in the MS are 412 (100), 367 (26), 297 (29), 188 (92), and 168 (12).

Thus **1** and the known synthetic keto lignans, podophyllotoxone [5] (**2**; 2α, 3β) and picropodophyllone [4] (**3**; 2β, 3β), are isomeric and have markedly similar spectrometric characteristics [6],



(1) 2α, 3α
(2) 2α, 3β
(3) 2β, 3β
(4) 2β, 3α

suggesting that **1** might be one of the two other ketones stereoisomeric at positions **2** and **3**, namely *iso*picropodophyllone (2α, 3α) or *iso*podophyllotoxone (**4**; 2β, 3α) [6]. The identity of **1** was confirmed by direct comparison (mmp, UV, NMR, mass) with a synthetic sample of *iso*picropodophyllone (unpublished) provided by Dr. A. von Wartburg‡.

Neither **2** nor **3** was detected in the total plant extract; *iso*picropodophyllone is the first naturally occurring lignan lactone to be reported from plants of the *Podophyllum* species which does not have the 2α, 3β-configuration as in podophyllotoxin. Assays§ for inhibitory activity *in vitro* against cells from human carcinoma of the nasopharynx (KB) on the three ketones gave the following ED_{50} results in μg/ml: **1**, 3·2; **2**, 0·26; **3**, >100.

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† Confirmed by elemental analysis and high resolution mass spectrometry.

‡ This compound was first synthesized in the Pharmaceutical Chemical Laboratories, Sandoz Ltd., Basle, Switzerland, by Max Kuhn, by isomerization of podophyllotoxone (private communication from Dr. A von Wartburg).

§ Assayed under the auspices of the National Cancer Institute, Drug Evaluation Branch. *In vivo* assays for tumor inhibitory activity are in process.