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LARICIRESINOL DERIVATIVES FROM *TURREA NILOTICA* AND *MONECHMA CILIATUM*

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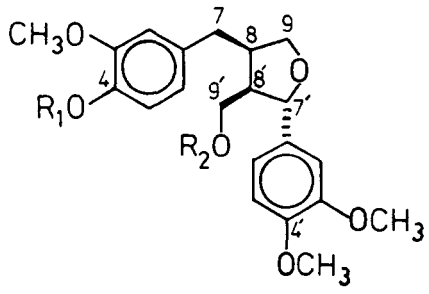
As part of an investigation of Sudanese plants for anticancer activity (1), we have investigated the constituents of *Turrea nilotica* Kotschy and Peyr. (Meliacae) and *Monechma ciliatum* Hochst. (Acanthaceae). Neither plant has been investigated previously for anticancer constituents.

Fractionation of *T. nilotica* leaves, guided by bioassay in the KB cell culture system, yielded a cytotoxic CH_2Cl_2-soluble fraction that was purified further by successive column chromatographic procedures to yield a small fraction with good cytotoxicity in KB cell culture (ED_{50} 0.02 μg/ml). Purification of this fraction by preparative tlc gave a pure compound identified as lariciresinol 4′-monomethyl ether (**1**). This compound has been prepared previously by methylation of lariciresinol (2), but it has not been reported from a natural source. Our compound has slightly different physical properties from those reported; for example, our compound is a crystalline solid, while the earlier report stated it to be an oil. The compound's pmr spectrum establishes that it is either lariciresinol-4′-monomethyl ether (**1**) or its isomer lariciresinol-4-monomethyl ether, and the compound's mass spectrum is conclusive for the former structure. Thus, ions at *m/z* 137 and 165 are assignable to the benzyl and benzoyl ions derived from **1**; its isomer would show both these ions at *m/z* 151. Finally, the cmr spectrum of our compound agrees very well with that published for **1** (2). Conversion of **1** to its diacetate **2** yielded a compound whose pmr and mass spectra also support the assigned structure. Direct comparison with an authentic sample of **1** was, unfortunately, not possible, but comparison of ir and mass spectra with those supplied by Dr. Fonseca indicated our compound to be identical to **1**. Compound **1** was inactive in the KB cell culture assay, indicating that the cytotoxicity of the fractions from which it was obtained must be due to other, as yet unidentified, components.

In a second investigation of a Sudanese plant, aerial parts of *M. ciliatum* were extracted, and the extract was purified without bioassay to yield a compound identified as lariciresinol dimethyl ether **3**. The pmr spectrum of the compound established its structure, and this was confirmed by its mass spectrum which showed intense ions at *m/z* 151 and 165, corresponding to the benzyl and benzoyl ions respectively generated by the expected cleavage of **3**. This compound has also been prepared previously by methylation of lariciresinol (3,4), but it has not been reported from a natural source.



1 $R_1=R_2=H$
2 $R_1=R_2=CH_3CO$
3 $R_1=CH_3$, $R_2=H$

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—

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Spectra were recorded with the following instruments: uv, Perkin-Elmer 330; pmr, IBM WP-200; ms, Varian-MAT 112. Adsorbents for tlc and cc were from E. Merck.

PLANT MATERIAL.—*T. nilotica* was collected in the southern Kordufan Province (Gibal Al-Nuba area) during the autumn of 1977, and *M. ciliatum* was grown from seed collected in the same province (Rashad area) during the autumn of 1975. Both plants were authenticated by faculty members of the Botany Department, University of Khartoum, and voucher specimens are preserved in this department and at the Department of Phytochemistry, Medicinal and Aromatic Herbs Research Unit, Khartoum.

EXTRACTION AND ISOLATION OF LARICIRESINOL 4′-MONOMETHYL ETHER (**1**).—Air-dried powdered leaves of *T. nilotica* were extracted with cold EtOH and the extract concentrated *in vacuo*. A total of 50 g of extract were partitioned between $CHCl_3$ and H_2O, and the $CHCl_3$ soluble portion (27 g) was partitioned between hexane and MeOH-H_2O (9:1). The MeOH-H_2O soluble fraction was diluted with H_2O to bring it to MeOH-H_2O (8:2), and was then extracted with CH_2Cl_2 to yield a cytotoxic CH_2Cl_2-soluble fraction (7.4 g; ED_{50} in KB cell culture less than 0.1 μg/ml). This fraction was further purified by two successive chromatographic separations on silica gel with elution by CH_2Cl_2-*i*PrOH to yield an active fraction (0.125 g; ED_{50} 0.02 μg/ml). Preparative tlc separation of this fraction [hexane-EtOAc (3:7) silica gel plates] yielded compound **1** (16 mg from 40 mg) as the major isolable product (ED_{50} greater than 10 μg/ml).

LARICIRESINOL 4′-MONOMETHYL ETHER (**1**).—The isolated compound had the following properties: mp 125-127° [lit (2) viscous oil]; $[\alpha]^{25}D$ +12.90° (*c* 0.8, $CHCl_3$) [lit (2)+8° (*c* 1.0, $CHCl_3$)]; ms *m/z* 374(99), 250(16), 233(16), 208(35), 194(17), 190(12), 180(13), 167(49), 160(22), 165(51), 163(11), 151(34), 150(15), 137(100); pmr ($CDCl_3$) 2.4-2.6 (2H, m), 2.73 (1H, m), 2.92 (1H, dd, *J*=6,2 Hz), 3.76 (1H, dd, *J*=8,6 Hz, 9b-H), 3.8 (2H, m, 9′-H), 3.87 (6H, s, 2 x OCH_3), 3.89 (3H, s, OCH_3), 4.06 (1H, dd, *J*=8, 6 Hz, 9a-H), 4.81 (1H, d, *J*=6 Hz, 7′-H), 5.49 (1H, s, O*H*, 6.7 (2H, m), 6.85 (4H, m) ppm; cmr ($CDCl_3$) 33.3, 42.5, 52.6, 55.9 (3), 61.0, 72.9, 82.8, 109.1, 111.2 (2), 114.4, 118.0, 121.2, 132.3, 135.6, 144.0, 146.6, 148.5, 149.2 ppm; uv (EtOH) λ max (log ε) 202(4.15), 229(3.45), 278(3.00).

LARICIRESINOL 4′-MONOMETHYL ETHER DIACETATE (**2**).—A solution of **1** (5 mg) in Ac_2O and pyridine (0.5 ml each) was allowed to stand at room temperature for 24 h. Usual work-up and purification by preparative tlc [$CHCl_3$-MeOH (9:1)] yielded the diacetate **2** as a viscous oil. The isolated material had the following properties: $[\alpha]^{25}D$ +18.2° (*c* 0.4, $CHCl_3$) [lit. (2) +5° (*c* 1.0, $CHCl_3$)]; ms, *m/z* 458(41), 416(19), 356(39), 233(36), 219(67), 192(23), 191(18), 190(30), 167(20), 166(30), 165(97), 151(44), 149(22), 137(100), 113(24), 57(40); pmr ($CDCl_3$) 2.02 (3H, s, $OCOCH_3$), 2.31 (3H, s, $OCOCH_3$), 2.5-3.0 (4H, m, 7, 8, 8′-H), 3.75 (1H, dd, *J*=8, 6Hz, 9a-H), 3.82 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.10 (1H, dd, *J*=8, 6Hz, 9b-H), 4.18 (1H, dd, *J*=10, 7Hz, 9′a-H), 4.36 (1H, dd, *J*=10, 7Hz, 9′b-H), 4.79 (1H, d, *J*=6Hz, 7′-H), 6.7-7.0 (6H, c, ArH) ppm.

LARICIRESINOL DIMETHYL ETHER (**3**).—Extraction of deseeded aerial parts of *M. ciliatum* and solvent partitioning as described above yielded a MeOH-H_2O (9:1) fraction that was subjected to chromatography on silica gel and preparative tlc to yield lariciresinol dimethyl ether (**3**). The isolated compound had the following properties: viscous oil [lit. (3) mp 78-80°]; $[\alpha]^{25}D$ +19.4° (*c* 0.6, $CHCl_3$) [lit. +12° (*c* 1.0, Me_2CO) (3); +22° (*c* 2.05, Me_2CO) (4)]; ms, *m/z* 388(91), 250(18), 235(24), 233(17), 220(15), 208(34), 205(14), 194(27), 191(12), 184(17), 181(11), 178(12), 177(13), 167(28), 165(38), 152(23), 151(100); pmr ($CDCl_3$) 2.4-2.6 (2H, m), 2.70 (1H, m), 2.88 (1H, dd, *J*=6, 2Hz), 3.65-3.95 (3H, m), 3.80-3.86 (12H, 4 x 3H, OCH_3), 4.02 (1H, dd, *J*=7, 6Hz), 4.75 (1H, d, *J*=6Hz, 7′-H), 6.6-6.9 (6H, m) ppm.

LARICIRESINOL DIMETHYL ETHER ACETATE.—A solution of **3** (6 mg) in Ac_2O and pyridine (1.0 ml each) was allowed to stand at room temperature for 24 h. After usual work-up and purification by preparative tlc [$CHCl_3$-MeOH (9:1)], the product was obtained as a viscous oil: $[\alpha]^{25}D$ +17.8° (*c* 0.4, $CHCl_3$), [lit. (2) +16° (*c* 1.0, $CHCl_3$)].

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LITERATURE CITED

1. S.M.H. Ayoub and D.G.I. Kingston, *Fitoterapia*, **53**, 119 (1982).
2. S.F. Fonseca, L.T. Nielsen, and E.A. Rúveda, *Phytochemistry*, **18**, 1703 (1979).
3. S.F. Fonseca, J. deP. Campello, L.E.S. Barata, and E.A. Rúveda, *Phytochemistry*, **17**, 499 (1978).
4. R.D. Haworth and W. Kelly, *J. Chem. Soc.*, 384 (1937).

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