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A lignan from *Daphne oleoides*

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Abstract

A new lignan has been isolated from the whole plant extract of *Daphne oleoides* besides the known taxiresinol and lariciresinol. The structure of the new lignan was established as 4,9′-dihydroxy-3′,4′,5-trimethoxy-7′,9-epoxylignan by spectroscopic methods. © 1998 Published by Elsevier Science Ltd. All rights reserved.

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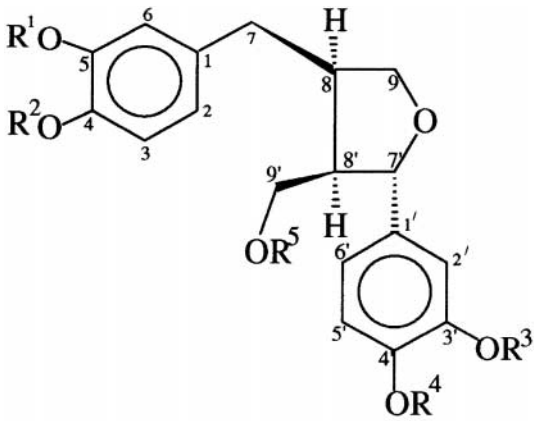
1. Introduction

Daphne oleoides L. is a xerophytic shrub. An infusion of the leaves is given in cases of gonorrhoea and applied to abscesses. The root is purgative, and the bark and leaves are used to treat cutaneous infections Baquer, 1989. As a part of our ongoing phytochemical studies on *D. oleoides* (Ullah, Ahmed, Anis, & Malik, 1997), we now wish to report the structure of a new lignan, daphneligin (**1**), along with the known taxiresinol (**3**) and lariciresinol (**4**) isolated for the first time from this species.

2. Results and discussion

Daphneligin (**1**) was assigned the molecular formula $C_{21}H_{26}O_6$ (EIMS and HRMS). Its IR spectrum showed absorption at 3550 cm^{-1} (OH), 1605, 1517 (aromatic). Acetylation of (**1**) with acetic anhydride and pyridine gave a diacetate (**2**). The ^1H NMR spectrum of (**1**) displayed the presence of six aromatic protons in a complicated pattern at δ 6.59–6.80, two methoxy groups at δ 3.71 (6H, s) and another methoxy group at 3.72 (3H, s). The remaining protons were found between δ 2.25 and 4.72. The ^{13}C NMR and DEPT experiments revealed the signals of three methylene, nine methine and three methyl carbon atoms. The quaternary carbons were determined by subtracting these from BB spectrum. The chemical shifts of individual carbon atoms are shown in Table 1. These



1 $R_1 = R_3 = R_4 = CH_3$, $R_2 = R_5 = H$

2 $R_1 = R_3 = R_4 = CH_3$, $R_2 = R_5 = Ac$

3 $R_1 = CH_3 = R_2 = R_3 = R_4 = R_5 = H$

4 $R_1 = R_3 = CH_3$ $R_2 = R_4 = R_5 = H$

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Table 1
^{13}C NMR spectral data of compounds **1**, **2** and **3**

Carbon	DEPT	1	2	3
1	C	133.5	138.0	133.9
2	CH	111.6	112.6	111.6
3	C	146.9	150.8	147.0
4	C	144.0	138.7	144.2
5	CH	114.6	122.8	114.6
6	CH	120.7	120.4	120.8
7	CH_2	32.3	33.4	32.3
8	CH	42.1	42.2	42.8
9	CH_2	72.2	72.8	72.0
1′	C	132.7	131.3	132.8
2′	CH	108.8	107.2	108.2
3′	C	149.0	148.6	145.7
4′	C	148.8	148.4	143.8
5′	CH	111.3	110.9	113.9
6′	CH	116.4	116.3	118.0
7′	CH	82.7	82.6	82.6
8′	CH	52.3	49.2	51.9
9′	CH_2	60.4	62.5	58.9
CH_3CO	CH_3	–	20.6	–
CH_3CO	CH_3	–	20.8	–
OCH_3	CH_3	55.6	55.6	55.5
OCH_3	CH_3	55.7	55.8	–
$COCH_3$	C	–	168.8	–
$COCH_3$	C	–	170.6	–

were assigned on the basis of the information given by Ferreira Fonseca, Paiva Campello, Lauro Barata, and Edmundo (1978). The ^{13}C NMR spectrum was very similar to that of lariciresinol except for the presence of an additional methoxy group. This fact was deduced from the EI mass spectrum which showed the same fragmentation pattern as (**3**) except the $[M]^+$ peak was at *m/z* 374, and in the ^1H NMR spectrum an additional peak appeared at δ 3.71. The relative position of the different aromatic residues followed from the fragmentation pattern in the mass spectrum. The fragment formed by fission of the 7–8 bond (*m/z* 137) confirmed that the additional methoxy group was on C-4′ rather than on C-4. The configuration of the chiral centers were confirmed by NOE difference measurements (NOEs between H-8 and H-8′ as well as between H-7′, H-7, and H-9′). Biogenetic evidence was provided by co-occurrence of lariciresinol, which has the same stereochemistry. Daphneligin is, therefore, assigned the structure 4,9′-dihydroxy-3′,4′,5-trimethoxy-7′,9-epoxylignan (**1**).

3. Experimental

^1H and ^{13}C NMR were measured in $CDCl_3$ on a Bruker AM 400 Spectrometer. IR ($CHCl_3$) and UV (in EtOH) were recorded on Shimadzu IR 460 and Hitachi U-3200 Spectrometers. Optical rotation was measured in $CHCl_3$ using JASCO DIP-360.

The whole plant of *D. oleoides* was collected from Hazara division, in February, 1995. A voucher specimen was identified by Professor Iftikhar Hussain Shah and deposited in the Herbarium of the Faculty of Pharmacy, Gomal University, D. I. Khan, Pakistan.

3.1. Extraction and isolation

The shade dried plant material (16 kg) was extracted 3× with MeOH. The combined methanolic extract was evaporated under reduced pressure. The residue obtained was suspended in water and extracted successively with petrol, EtOAc, $CHCl_3$ and *n*-BuOH. The $CHCl_3$ was evaporated to give 70 g residue which was subjected to CC over silica gel using $CHCl_3$–MeOH as eluent. The fraction eluting with $CHCl_3$–MeOH (49:1) gave colorless amorphous (**1**) where as (**3**) and (**4**) were obtained using (13:7) and (7:3), respectively.

3.2. Daphneligin (1)

Amorphous powder, $C_{21}H_{26}O_6$; mp 136–138°C; $[\alpha]_D$ + 11.5° ($CHCl_3$; c 0.10); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 1605, 1517 (aromatic); UV λ_{max}^{EtOH} nm: 228; EIMS *m/z* (rel. int.): 374 $[M]^+$ (100) (calc. for $C_{21}H_{26}O_6$: 374.102) 360 (22), 342 (20), 192 (37), 137 (95). ^1H NMR (400 MHz, $CDCl_3$): δ 2.25 (dddd, H-8′), 2.70 (ddddd, H-8), 2.90 and 2.55 (dd, H-7), 3.71 (6H, s, OMe), 3.72 (3H, s), 3.95 and 3.76 (dd, H-9), 4.06 and 3.74 (dd, H-9′), 4.72 (d, H-7′), 6.80 br. s, 6.78 d, 6.76 br. s (2H), 6.61 br. d, 6.59 br. s (aromatic H); *J* (Hz) 8′, 7′ = 8′, 8 = 8′, 9′ = 7.1; 9, 9* = 8.1; 9, 8 = 6.5; 8, 7 = 5.0; 8, 7* = 10.5; 7, 7* = 13.1; 9′, 9′* = 11.1. ^{13}C NMR see Table 1.

3.3. Acetylation of daphneligin (1)

A mixture of 4 mg of (**1**), Ac_2O (1 ml) and pyridine (1 ml) was stirred overnight at room temp. and worked up in the usual way to afford (**2**) colorless oil (4.2 mg), $C_{25}H_{30}O_8$; $[\alpha]_D$ + 11.5°C ($CHCl_3$; c 0.10); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1605, 1510; UV λ_{max}^{EtOH} nm: 277, 228; EIMS *m/z* (rel. int.): 458 ($[M]^+$) (62), (cal. for $C_{25}H_{30}O_8$: 458.072), 416 (43), 398 (27), 356 (19), 137 (100). ^1H NMR (400 MHz, $CDCl_3$): δ 2.05 (3H, s, COMe), 2.31 (3H, s, COMe), 2.52 (1H, m, H-8′), 2.55 (1H, dd, *J* = 13.1 and 10.4 Hz, H-7), 2.68–2.80 (1H, m, H-8), 3.70 (6H, s, OMe), 3.84 (3H, s, OMe), 4.10 (1H, dd, *J* = 8.4 and 6.4 Hz, H-9), 4.22 (1H, dd, *J* = 11.4 and 7.4 Hz, H-9′), 4.35 (1H, dd, *J* = 11.4 and 7.4 Hz, H-9′), 4.75 (1H, d, *J* = 6.4 Hz, H-7′), 6.70–698 (6H, m, aromatic-H). ^{13}C NMR see Table 1.

3.4. Taxiresinol (**3**)

Colorless needles, mp 158°C, $[\alpha]_D^{EtOH}$ + 32.2°. The physical and spectral data agreed with the literature values Majumdar, Srinivasan, & Venkataraman, 1972. In the present work the ^{13}C NMR spectrum of (**3**) has been recorded and assigned for the first time.

3.5. Laricericinol (**4**)

Colorless needles, mp 167–168°C, $[\alpha]_D^{25}$ + 18° (*c*, 1.0 in Me_2CO). The physical and spectral data agreed with literature values Hawarth, 1937.

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