Journal of Natural Products
Vol. 52, No. 5, pp. 1177-1179, Sep-Oct 1989

PHENYLPROPANOIDS, SESQUITERPENES, AND ALKALOIDS FROM THE SEEDS OF *LIRIODENDRON TULIPIFERA*

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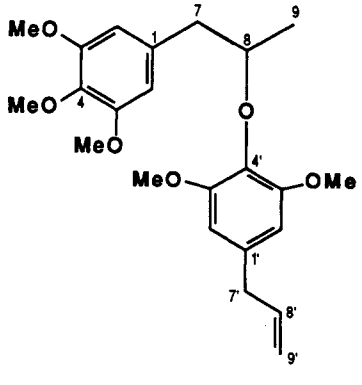
ABSTRACT.—From the seeds of *Liriodendron tulipifera*, commonly known as the tulip or yellow poplar tree, five known sesquiterpenes (lipiferolide, α- and β-liriodenolide, epitulipinolide diepoxide, and peroxyferolide), a known *N*-acetylnoraporphine alkaloid (tuliferoline), three known phenylpropanoids (lirioresinol B dimethylether, β-*O*-dilignol, and eudesmin) and a new lignan (liriolignal) have been isolated. Liriolignal [**2**] was characterized from spectroscopic data (2D nmr and ms) and was shown to be structurally related to β-*O*-dilignol [**1**].

Liriodendron tulipifera L. (Magnoliaceae), also known as the tulip poplar or yellow poplar tree, has been the subject of a number of investigations. Chemical studies of all parts of the plant have yielded a variety of different chemical entities including phenylpropanoids, sesquiterpenes, and alkaloids (1–6). The only plant part not yet investigated is the seeds, probably because of the difficulties encountered in collection.

The known sesquiterpenes, lipiferolide, epitulipinolide diepoxide, peroxyferolide, and α- and β-liriodenolide, the known *N*-acetylnoraporphine alkaloid, tuliferoline, and the known phenyl propanoid lirioresinol B dimethylether were isolated from the seeds; all have been previously isolated from this species (1–6). In addition, systematic cc yielded two other known phenylpropanoids, β-*O*-dilignol [**1**] and (+)-eudesmin, both of which have not been reported from *L. tulipifera*, and a new lignan, for which the trivial name liriolignal [**2**] has been chosen. This report describes the isolation and characterization of these compounds.

An EtOH extract of the seeds was partitioned between *n*-hexane and 10% aqueous MeOH. The aqueous MeOH fraction, by initial cc and subsequent purification on small Si gel columns, gave five sesquiterpenes, four phenylpropanoids, and one *N*-acetylnoraporphine alkaloid. The abundant sesquiterpenes were identified as lipiferolide, epitulipinolide diepoxide, peroxyferolide, α-liriodenolide, and β-liriodenolide (yields 0.03%, 0.008%, 0.006%, 0.006% and 0.02%, respectively). These sesquiterpenes were identified by comparing their spectral data with those previously published (1,5,6).

Four additional compounds were isolated and found to be phenylpropanoids. The most abundant one was identified as



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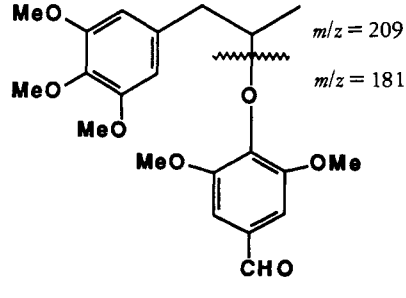

2

lirioresinol-B-dimethylether (0.05%), previously isolated from this species (2). Another phenylpropanoid was identified as eudesmin (0.003%), previously reported (7–10) but not from *Liriodendron*. Both compounds had spectral data identical to those reported previously. A third component was isolated as a colorless oil (0.005%), which after examination of the spectral data led to the formulation of structure **1**, which is the known β-*O*-dilignol, previously isolated from *Myristica fragrans* (11–13). Complete ^{13}C-nmr assignments of **1** not reported previously are reported here in Table 1. The assignments were aided by comparisons with other phenylpropanoids (14,15).

TABLE 1. ^{13}C-nmr Chemical Shift Assignments for **1** and **2**.[a]

Carbon	Compound	
	1	**2**
C-1	134.9(0)	134.6(0)
C-2, -6	106.6(1)	106.6(1)
C-3, -5	152.9(0)	152.9(0)
C-4	136.3(0)	136.5(0)
C-7	43.7(2)	43.7(2)
C-8	79.7(1)	80.2(1)
C-9	19.8(3)	19.3(3)
C-1′	135.5(0)	131.6(0)
C-2′, -6′	105.6(1)	106.7(1)
C-3′, -5′	153.6(0)	154.2(0)
C-4′	134.3(0)	141.9(0)
C-7′	40.5(2)	191.0(1)
C-8′	137.3(1)	—
C-9′	116.0(2)	—
3-, 5-OMe	56.0(3)[b]	56.1(3)[b]
4-OMe	60.8(3)	60.8(3)
3′-, 5′-OMe	56.1(3)[b]	56.2(3)[b]

[a]Numbers in parentheses refer to the number of attached protons as determined by APT and DEPTGL.

[b]Assignments may be interchanged.

The other oily phenylpropanoid **2** was pure by tlc and nmr analysis. After examination of its spectral data, it appeared to be a new phenylpropanoid related to **1**, and the trivial name lirioligNal [**2**] was chosen. The formula $C_{21}H_{26}O_7$ was established by hrms analysis. The uv spectrum was similar to that of **1** and was characteristic for a simple phenylpropanoid (14). The 300-MHz ^{1}H-nmr spectrum revealed four aromatic protons at δ 6.45 (2H, s) and δ 7.12 (2H, s), one aldehydic proton at δ 9.86 (1H, s), signals for five methoxyl groups at δ 3.88 (6H, s), 3.83 (6H, s) and 3.81 (3H, s), a characteristic ABX pattern at δ 4.60 (1H, dd), 3.09 (1H, dd), and 2.79 (1H, dd), and a secondary methyl at δ 1.25 (3H, d). The mass spectrum showed an intense ion at *m/z* 181 $[C_9H_9O_4]^+$ (32%) and the base peak at *m/z* 290 $[M-181]^+$ (100%). These fragmentations are also seen for **1**. The aldehydic group was confirmed by ir (ν max 1690 cm^{-1}) and ^{13}C-nmr (δ 191.0, d) data. The remaining ^{13}C-nmr spectral data (Table 1) were very similar to those of **1** except for the side chain. Based on these data the structure for lirioligNal was formulated as **2**. The 2D-nmr data (COSY and HETCOR) were in complete agreement with structure **2**.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The ^{1}H-nmr spectra were run at 300 MHz and ^{13}C-nmr spectra at 75 MHz in $CDCl_3$ on a VXR-300 spectrometer. Multiplicity determinations (APT, DEPTGL) and 2D-nmr spectra (COSY, HETCOR) were run using standard Varian pulse sequences. Tlc was performed on Si gel GF 254 and cc on Si gel G. Compounds were visualized by spraying with 1% vanillin in H_2SO_4. Optical rotations were recorded on a Perkin-Elmer 141 polarimeter as solutions in a 1-dm cell.

PLANT MATERIAL.—The seeds of *L. tulipifera* were collected from a large tree on the campus of The University of Mississippi during November of 1986 and 1987 with aid of a hydraulic bucket truck. The seeds were separated from the fruit stalk, dried and ground. A voucher specimen has been deposited in the herbarium at the Department of Pharmacognosy, The University of Mississippi.

EXTRACTION AND ISOLATION OF PHENYLPROPANOIDS, SESQUITERPENES, AND ALKALOID.—The dried ground seed (1 kg) was percolated with 95% EtOH (3 × 5 liters). The EtOH extract (56.7 g) was subjected to solvent partitioning between *n*-hexane and 10% aqueous MeOH. The aqueous MeOH fraction (10.6 g)

was subjected to cc over Si gel (750 g). Elution with toluene and increasing amounts of EtOAc in toluene (containing a small amount of HOAc) separated the components. Elution with toluene-EtOAc-HOAc (92:8:0.1) gave 35 mg of **1** followed by 45 mg of **2**. Elution with 90:10:0.1 composition yielded a mixture of compounds. This mixture was separated over another cc over Si gel [same solvent mixture (82:18:0.1)] and gave 300 mg of lipiferolide, 60 mg of peroxyferolide, 25 mg of eudesmin, and 75 mg of epitulipinolide diepoxide.

Elution with an 80:20:0.1 solvent composition yielded another mixture which was further separated by cc over Si gel using $CHCl_3$–*n*-hexane (1:1) to give 450 mg of lirioresinol β dimethylether, 60 mg of tuliferoline, and 55 mg of α-liriodenolide. Further elution with toluene-EtOAc-HOAc (78:22:0.1) yielded 200 mg of β-liriodenolide. Known compounds were established by direct comparisons with authentic samples or by comparison with published physical and spectral data.

Liriolignal [**2**].—Compound **2** was obtained as a colorless oil: $[\alpha]^{25}D + 10.6°$ ($c = 0.01$, $CHCl_3$); uv (λ max, nm, EtOH) (log ε) 292 (3.86), 230 (3.92), 218 (3.98); ir (ν max, cm^{-1}, $CHCl_3$) 2940–3010, 1690, 1590, 1510, 1490; ^{1}H-nmr δ 9.86 (1H, s, CHO), 7.12 (2H, s, H-2′, -6′), 6.45 (2H, s, H-2, -6), 4.60 (1H, qdd, $J = 6.0$, 7.5, 7.5, H-8), 3.88 (6H, s, OMe), 3.83 (6H, s, OMe), 3.81 (3H, s, 4-OMe), 3.09 (1H, dd, $J = 6.0$, 13.5, H-7), 2.79 (1H, dd, $J = 7.2$, 13.5, H-7), 1.25 (3H, d, $J = 6.0$, Me); ^{13}C-nmr see Table 1; hrms for $C_{21}H_{26}O_7$ found 390.1667, calcd 390.1677; ms $[M]^+$ 390 (5), 279 (2), $[M - 181]^+$ 209 (100), 194 (24), 181 (32).

ACKNOWLEDGMENTS

The authors thank Dr. R.W. Doskotch for authentic samples of lipiferolide, epitulipinolide diepoxide, and γ-liriodenolide (samples of α- and β-liriodenolide were not available). Samples of tuliferoline and lirioresinol β dimethylether were previously isolated in these laboratories.

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Received 11 April 1989