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Dibenzocyclooctadiene-type lignans from *Magnolia pyramidata*

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Dedicated to Professor Dr. Otto R. Gottlieb on the occasion of his 80th birthday

Abstract

Eight dibenzocyclooctadiene-type lignans, pyramidatin A–H, were isolated from the leaves of *Magnolia pyramidata*. Their structures were established by spectral methods, mainly 2D NMR spectroscopic techniques, which involved combined applications of COSY, DEPT, ^{1}H, ^{13}C correlations, COLOC, INAPT and long-range inverse ^{1}H, ^{13}C NMR correlations. The molecular structures of pyramidatin A and B were determined by single crystal X-ray diffraction. The absolute configurations of all eight lignans were derived from CD spectral correlations with structurally related dibenzocyclooctadienes of known absolute configuration.

Keywords: Magnolia pyramidata; Magnoliaceae; Dibenzocyclooctadiene-type lignans; Pyramidatins A–H

1. Introduction

Eight species of the genus *Magnolia* are native to the United States. These evergreen or deciduous trees and shrubs are primarily found in the southeastern region of the country, with five species being native to Louisiana, where they form part of several types of pine hardwood communities. Members of this family are rich in a wide variety of biologically active compounds including lignans and neolignans (Song and Fischer, 1999). In continuation of our chemical investigations of members of the family Magnoliaceae from the southeastern United States (Song et al., 1998) for biologically active natural products, we have analysed aerial parts of the pyramid magnolia (*Magnolia pyramidata* Bartram). This is the rarest among the five native magnolias and is in danger of extinction in Louisiana and neighbouring states due to clear-cutting of native forests. We report below the isolation of eight new lignans, pyramidatin A to H (**1**–**8**), from *M. pyramidata* and their structure elucidation by spectral methods. Furthermore, the molecular structures of pyramidatin A (**1**) and B (**5**) were established by single crystal X-ray diffraction and the absolute configurations of **1**–**8** were determined by CD spectral correlations.

2. Results and discussion

Dried aerial parts of *M. pyramidata* were extracted with dichloromethane. VLC and HPLC separations of the crude extract afforded eight new lignans, pyramidatin A–H (**1**–**8**). Pyramidatin A (**1**) gave a molecular ion and base peak at m/z 430 which together with the ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) was consistent with the empirical formula $C_{24}H_{30}O_7$. Inspection of the ^{1}H NMR spectrum suggested that **1** was a biphenyl-type lignan, bearing six methoxy groups on the aromatic rings plus two aromatic protons which appeared as singlets at δ 6.39 and 6.46. This left a residual molecular fragment of $C_6H_{10}O$ for the structure of **1**. The absence of hydroxyl and carbonyl absorptions in the IR spectrum suggested the presence of another ether function in the molecule. In the COSY spectrum of **1**, a slightly broadened proton singlet at δ 4.75 (H-7) showed coupling to one of the aromatic proton absorptions at δ 6.39 (H-6). Chemical shift considerations and ^{1}H, ^{13}C HETCOR data indicated that the singlet at δ 4.75 had to be due to a proton attached to an oxygen-bearing benzylic carbon absorbing at δ 89.1(C-7). The presence of two geminally coupled methylene protons, one appearing as a doublet at δ 3.26 ($J = 8.5$ Hz; H-9′b) and

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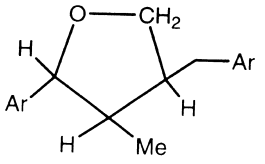
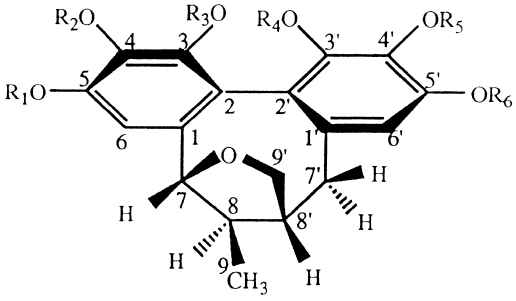
the other as a doublet of a doublet at δ 3.64 (J = 8.5, 4.2 Hz; H-9′a), was supported by ^{1}H, ^{13}C HETCOR experiments which showed that both protons correlated with the same carbon signal at δ 70.7. The ^{13}C chemical shift suggested that this had to be a methylene carbon bearing an oxygen, bridged to the other oxygen-bearing, C-7. The signal absorbing at δ 3.64 was coupled to two overlapping signals centered at δ 2.08. In benzene-d_6, these two signals separated into a quartet at δ 2.01, which in turn was coupled to a methyl doublet, centered at δ 1.06 ($CDCl_3$: δ 1.20; J = 7.2; H-9). The other signal, a doublet of a doublet at δ 1.78 showed coupling to the doublet of a doublet at δ 3.64 and was therefore assigned to H-8′. Another spin system was represented by a pair of geminally coupled protons. In $CDCl_3$, one appeared as a doublet at δ 2.35 (J = 14.0 Hz; H-7′b) and the other as a doublet of a doublet at δ 2.89 (J = 14.0; 10.9 Hz; H-7′a), the latter signal being further coupled to the overlapping signal centered at δ 2.08 (H-8′). These spectral features, which were further corroborated by 2D ^{1}H-^{1}H shift correlation (COSY), required a bonding as shown in partial structure **A**. This suggested a dibenzocyclooctadiene-type lignan which was supported by a characteristic UV spectrum with bands at λ_{max} 216, 254 and 292 nm (Chen et al., 1996).



A

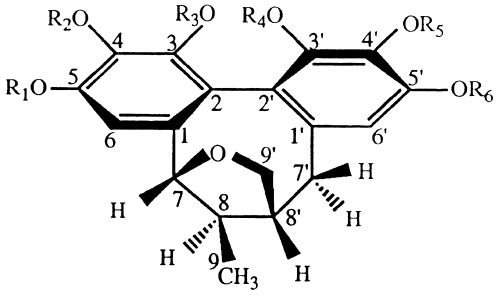


(**1**) $R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = CH_3$

(**2**) $R_1 = R_2 = R_3 = R_5 = R_6 = CH_3$; $R_4 = H$

(**3**) $R_1 = R_2 = R_4 = R_5 = R_6 = CH_3$; $R_3 = H$

(**4**) $R_3 = R_4 = CH_3$; $R_1, R_2 = -CH_2-$; $R_5 = R_6 = -CH_2-$



(**5**) $R_1 = R_2 = R_3 = R_5 = R_6 = CH_3$; $R_4 = H$

(**6**) $R_1 = R_2 = R_3 = R_4 = R_5 = CH_3$; $R_6 = H$

(**7**) $R_1 = R_2 = R_4 = CH_3$; $R_3 = H$; $R_5 = R_6 = -CH_2-$

(**8**) $R_1 = R_2 = R_3 = R_4 = CH_3$; $R_5, R_6 = -CH_2-$

The connectivity of the carbon framework in **1** was established by combined applications of ^{13}C–^{1}H shift correlation (HETCOR) and ^{13}C–^{1}H correlation via long-range ^{13}C–^{1}H coupling. In the COLOC spectrum of **1**, the aromatic proton signal at δ 6.39 (H-6) coupled with the quaternary carbons C-1, C-5 and C-4 of δ 138.24, 152.56 and 140.50, respectively. The benzylic methine proton at δ 4.75 (H-7) showed couplings with quarternary carbon signals assigned to C-1 (δ 138.2) and C-2 (δ 119.2), the chemical shifts of which indicated that they were not substituted with methoxy groups. The quaternary carbon signal at δ 151.6 (C-3) showed correlations to a methoxy absorption at δ 3.51. Based on model considerations, the upfield shift of this methyl signal must be due to shielding effect caused by the π-orbitals of the adjacent aromatic ring B. This provided further evidence that one of the three aromatic methoxy groups of ring A of the biphenyl system must be attached to C-3 instead of C-6. Two overlapping methoxy proton signals at δ 3.90 correlate with two methoxy carbon signals at δ 60.7 and 60.8. The two-proton signals at δ 2.08 (2H) must be due to protons attached to two different carbons absorbing at δ 42.0 (C-8) and 51.2 (C-8′), which indicated two overlapping proton signals consistent with previous assignments. The results of the COLOC experiment supported a skeletal arrangement for pyramidatin A as shown in **1**, except for its stereochemistry and absolute configuration.

The molecular structure of pyramidatin A (**1**) was established by single crystal X-ray diffraction, details of which will be presented at the end of this section. The CD spectrum of **1** was obtained to determine its absolute configuration by application of the chirality method (Ikeya et al., 1979) of the hexamethoxybiphenyl group of pyramidatin A (**1**). The Cotton effects are associated with the atropisomerism observed for biphenyls conjugation bands in the UV spectra, and allow determination of the absolute configuration of chiral hexamethoxybiphenyl groups by the following rule: a

Table 1
^{1}H NMR spectral data of **1**–**8**[a]

H	1	2	3	4	5	6	7[c]	8
6	6.39 *s*	6.43 *s*	6.23 *s*	6.36 *s*	6.77 *s*	6.40 *s*	6.22 *s*	6.40 *s* [b]
7	4.75 *s*	4.76 *s*	4.77 *s*	4.71 *s*	4.74 *s*	4.75 *s*	4.75 *s*	4.75 *s*
8	2.08 *m*[b]	2.09 *m*[b]	2.09 *m*[b]	2.03 *m*[b]	2.38 *q*	2.07 *m*[b]	2.07 *m*[b]	2.06 *m*[b]
9	1.20 *d* (7.2)	1.20 *d* (7.3)	1.21 *d* (7.2)	1.17 *d* (7.3)	0.96 *d* (7.0)	1.20 *d* (6.2)	1.20 *d* (7.2)	1.19 *d* (7.2)
6′	6.46 *s*	6.29 *s*	6.52 *s*	6.41 *s*	6.25 *s*	6.53 *s*	6.45 *s*	6.40 *s* [b]
7′a	2.89 *dd* (10.9, 14.0)	2.90 *dd* (10.9, 14.0)	2.90 *dd* (10.9, 14.0)	2.85 *dd* (10.9, 14.0)	2.77 *dd* (8.6, 13.1)	2.86 *dd* (10.9, 13.8)	2.87 *dd* (10.9, 14.1)	2.86 *dd* (10.9, 14.0)
7′b	2.35 *d* (14.0)	2.33 *d* (14.0)	2.38 *d* (14.0)	2.48 *d* (14.0)	2.56 *d* (13.1)	2.29 *d* (13.8)	2.31 *d* (14.1)	2.28 *d* (14.0)
8′	2.08 *m*[b]	2.09 *m*[b]	2.09 *m*[b]	2.03 *m*[b]	2.02 *m*[b]	2.07 *m*[b]	2.07 *m*[b]	2.06 *m*[b]
9′a	3.64 *dd* (4.3, 8.5)	3.64 *dd* (4.3, 8.5)	3.64 *dd* (4.3, 8.5)	3.62*dd* (4.1, 8.5)	4.03 *dd* (4.1, 8.7)	3.64 *dd* (4.2, 8.5)	3.65 *dd* (4.2, 8.5)	3.64 *dd* (4.2, 8.4)
9′b	3.26 *d* (8.5)	3.33 *d* (8.5)	3.26 *d* (8.5)	3.33 *d* (8.5)	3.90 *d* (8.7)	3.32 *d* (8.5)	3.34 *d* (8.5)	3.33 *d* (8.4)
OMe	3.51 *s*	3.56 *s*	3.56 *s*	3.75 *s*	3.53 *s*	3.49 *s*	3.81 *s*	3.43 *s*
	3.55.*s*	3.85 *s*	3.88 *s*	3.65 *s*	3.86 *s*	3.50 *s*	3.88 *s*	3.75 *s*
	3.84 *s*	3.88 *s*	3.88 *s*	–	3.89 *s*	3.85 *s*	3.90 *s*	3.86 *s*
	3.88 *s*	3.89 *s*	3.90 *s*	–	3.90 *s*	3.90 *s*	–	3.88 *s*
	3.90 *s*	3.91 *s*	3.90 *s*	–	3.92 *s*	3.94 *s*	–	–
	3.90 *s*	–	–	–	–	–	–	–
OCH_2O	–	–	–	5.96 *s*	–	–	5.97 *d*	5.94 *s*
	–	–	–	5.96 *s*	–	–	–	–
OH	–	5.73 *s*	5.77 *s*		5.87 *s*	–	5.79 *s*	–

[a] 200 MHz, $CDCl_3$, TMS as int. standard; δ ppm; *J* (Hz) in parentheses.
[b] Overlapping signals.
[c] Determined at 500 MHz.

Table 2
^{13}C NMR spectral data of lignans **1**–**8**[a,b,c]

C	1[c]	2	3	4	5	6	7	8
1	138.24 *s*	138.84	138.74	137.38	137.15	138.31	139.11	138.53
2	119.23 *s*	118.17	112.90	118.31	118.94	119.23	112.62	119.23
3	151.64 *s*	152.76	147.97	142.16	151.61	150.50	148.01	152.86
4	140.50 *s*	140.50	134.19	135.40	141.28	140.60	133.81	140.52
5	152.56 *s*	152.76	151.40	148.57	152.57	157.12	151.25	152.46
6	104.31 *d*	104.93	101.11	100.45	110.20	104.52	101.08	104.75
7	89.09 *d*	89.09	89.21	88.89	87.70	89.09	89.13	88.92
8	42.01 *d*	41.90	42.01	41.77	35.10	41.96	41.95	41.87
9	20.55 *q*	20.57	20.58	20.36	19.42	20.55	20.48	20.43
1′	133.01 *s*	133.42	133.63	131.65	134.26	133.74	132.02	131.43
2′	123.85 *s*	117.21	122.83	122.87	116.48	122.79	122.10	122.94
3′	152.78 *s*	146.83	151.57	141.36	147.38	157.12	141.50	141.32
4′	140.36	134.08	140.70	135.59	134.26	137.90	135.62	135.40
5′	151.27 *s*	150.17	151.57	147.18	151.79	147.16	147.49	147.23
6′	109.24 *d*	106.01	109.95	105.08	102.84	111.73	105.40	104.57
7′	39.00 *t*	39.03	39.13	38.70	37.52	38.63	38.86	38.70
8′	51.24 *d*	51.35	51.38	51.17	46.46	51.31	51.27	51.09
9′	70.68 *t*	70.57	70.72	70.64	74.33	70.73	70.68	70.60
OMe	55.84 *q*	55.80	55.75	59.65	55.61	55.87	55.69	55.79
	55.93 *q*	55.86	55.98	59.80	55.68	59.98	59.79	60.54
	60.34 *q*	60.79	60.82	–	60.79	60.62	60.94	60.86
	60.69 *q*	60.99	61.16	–	61.08	60.83	–	61.10
	60.75 *q*	60.99	60.98	–	61.08	61.16	–	–
	61.12 *q*	–	–	–	–	–	–	–
OCH_2O	–	–	–	100.77t	–	–	100.86	100.71
		–	–	101.01t	–	–	–	–

[a] (50.30 MHz, $CDCl_3$, δ, TMS as int. standard).
[b] Assignments based on ^{13}C–^{1}H HETCOR measurements.
[c] Peak multiplicities were determined by heteronuclear multipulse programs (DEPT); multiplicities are not repeated if identical with those in the preceding column.

negative Cotton effect near 225 nm associated with a positive band around 250 nm corresponds to the (*R*)-configuration and the positive band around 225 nm and negative band near 250 nm to the (*S*)-configuration (Ikeya et al., 1991). Therefore, the negative Cotton effect at 223 nm of pyramidatin A (**1**) with values of $[\theta]_{223}-20620$ and $[\theta]_{260}$ +8480 (Fig. 1) corresponds to the *R*-configuration of the biphenyl skeleton.

The ^{1}H and ^{13}C NMR spectra of pyramidatin B (**5**) revealed close structural similarities with pyramidatin A (**1**). The mass spectrum [M^+, 416] together with the ^{1}H, ^{13}C NMR data indicated an empirical formula $C_{23}H_{28}O_7$. IR absorptions at 3300–3400 cm^{-1} plus a proton chemical shift near δ 5.8 suggested the presence of a biphenyl group with five methoxy and one phenolic group. 1D INAPT and 2D COLOC experiments were carried out to locate the site of the phenolic group within the pyramidatin B skeleton. The phenolic hydroxyl proton was coupled via long range coupling with C-3′, C-2′ and C-4′, suggesting that it must be placed at C-3′. This was supported by the presence in the ^{1}H NMR spectrum of only one upfield methoxy signal at δ 3.53 and four three-proton absorptions near δ 3.9.

The structures of pyramidatin B (**5**), C (**2**), D (**3**) and E (**6**) were determined by detailed NMR spectral analyses involving 1D and 2D ^{1}H, ^{13}C correlation methods, as outlined above for pyramidatin A (**1**) and B (**5**). Their absolute configurations were established by CD spectra shown in Fig. 1. Cotton effects at 219–222 nm were assigned either the *R*-configuration (negative Cotton effect) or *S*-configuration (positive Cotton effect). Pyramidatin C (**2**) and B (**5**) represent diastereomers which differ only in the chirality of the biphenyl moiety.

Pyramidatin F (**7**), $C_{22}H_{24}O_7$, was isolated as an amorphous solid. The ^{1}H NMR spectra indicated that it contains three methoxy groups, one methylene dioxy group (O–CH_2–O) (δ_H5.97; δ_C 100.86) and one phenolic group. The locations of these substituents were assigned by the COLOC and INAPT experiments. The positive Cotton effect of its CD indicated that the biphenyl moiety of **7** has the *S*-configuration (Fig. 1).

^{1}H NMR spectra of pyramidatin G (**8**) ($C_{23}H_{26}O_7$) and pyramidatin H (**4**) ($C_{22}H_{22}O_7$) indicated the presences of mono-methylene dioxy and di-methylene dioxy groups, respectively. The locations of the substituents at the biphenyl group were assigned by the use of 2D COLOC experiments and the absolute configurations were determined by CD experiments as *S* and *R*, respectively (Fig. 1).

The crystal structures of pyramidatin A (**1**) and B (**5**) both contain two independent molecules in their asymmetric units. Aside from some major differences in conformations of methoxy groups in **5**, described below, the conformations of the A and B molecules are not in an atropisomeric relationship, but in each case are quite similar, exhibiting differences in torsion angles of 9° or less. One of the two independent molecules for each compound is illustrated in Figs. 2 and 3. The major difference in conformation between **1** and **5** is the twist about the central biphenyl bond C2–C2′. The endocyclic torsion angle about this bond has approximately the same magnitude for the two molecules, but with opposite signs. The average C1–C2–C2′–C1′ torsion angle for **1** is +64.6°, while for **5**, it is −62.3°. This opposite handedness of biphenyl twist, along with the constraints of the furan ring cause the eight-membered rings of the two compounds to have quite different conformations. Compound **1** has its eight-membered ring in a twist conformation, where the diad twist axis bisects the biphenyl central bond and the C8–C8′ bond. In compound **5**, the eight-ring is in a conformation such that there are two adjacent near-zero torsion angles, about C1′–C2′ and C1′–C7′. Thus five of the eight atoms, C2, C1′, C2′, C7′, and C8′, are nearly coplanar, while the other three lie out of this plane on the same side by 1–2 Å. The average deviation of the five atoms from their best plane is 0.031 Å for molecule A and 0.011 Å for molecule B. The conformation of the furan ring is the half chair with O1 on the twist axis for **1** and the envelope with C8′ at the flap position for **5**. The methoxy conformational differences mentioned above for **5** involve O3′–C11′ and O4′–C12′, both on the phenyl ring carrying three methoxy groups. The C3′–C4′–O3′–C11′

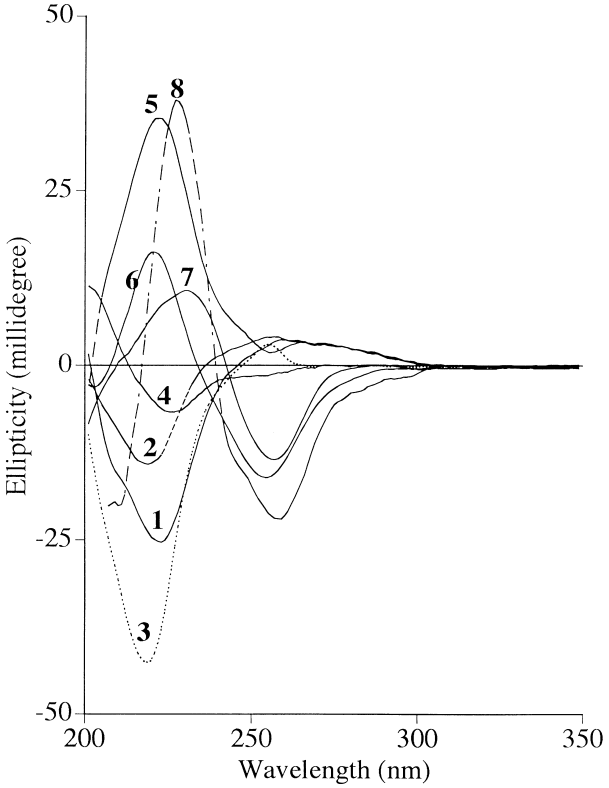


Fig. 1. CD spectra of compounds **1–8**.

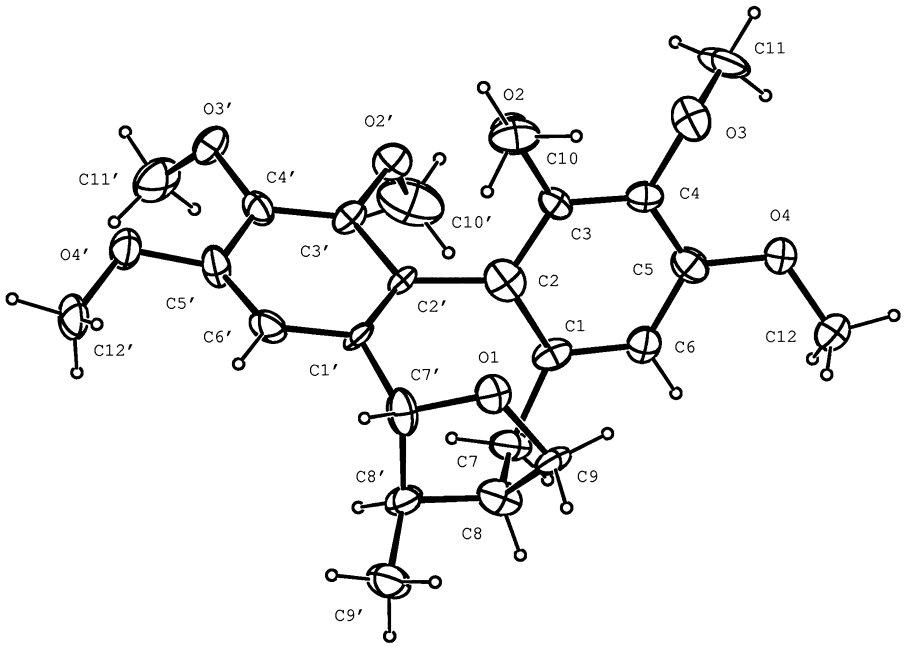


Fig. 2. One of the two independent molecules of pyramidatin A (**1**).

torsion angle differs by 29° between the A and B molecules, and torsion angle C6′–C5′–O4′–C12′ by 137°. Hydroxy groups O2 in **5** form intermolecular hydrogen bonds with furan oxygen atoms O1 as acceptor. The O···O distances are 2.873 (3) Å for O2A···O1A, and 2.781 (3) Å for O2B···O1B.

3. Experimental

3.1. General

^{1}H and ^{13}C NMR spectra were recorded at Bruker AC 200 MHz and Bruker AM 400 MHz spectrometers.

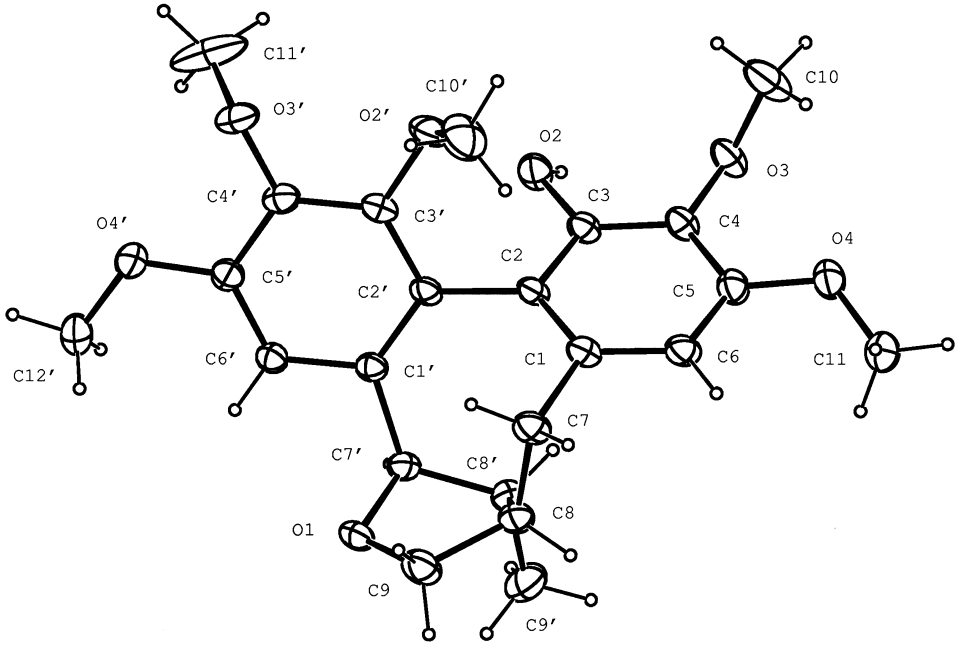


Fig. 3. One of the two independent molecules of pyramidatin B (**5**).

Table 3
Fractional atomic coordinates and equivalent isotropic thermal parameters (Å^2) for **1**

	X	*Y*	*Z*	B_{eq}
O1A	−0.1295 (9)	0.8918 (3)	0.3371 (6)	3.4 (2)
O2A	0.2399(8)	0.8490 (3)	0.6017(6)	3.1 (2)
O3A	0.0936 (9)	0.8977 (3)	0.7905 (6)	4.4 (2)
O4A	−0.2563 (9)	0.8918 (3)	0.8264 (6)	4.6 (2)
O2′A	0.1854 (9)	0.7398 (3)	0.5719 (6)	3.6 (2)
O3′A	0.3783 (9)	0.6927 (3)	0.3998 (7)	4.2 (2)
O4′A	0.347 (1)	0.7197 (3)	0.1741 (6)	4.6 (2)
C1A	−0.232 (1)	0.8203 (4)	0.5455 (9)	3.1 (2)
C2A	−0.047 (2)	0.8210 (4)	0.5305 (9)	3.9 (3)
C3A	0.053 (1)	0.8461 (4)	0.6184 (8)	2.6 (2)
C4A	−0.017 (1)	0.8685 (4)	0.7135 (9)	2.9 (2)
C5A	−0.192 (1)	0.8670 (4)	0.7308 (9)	3.5 (3)
C6A	−0.300 (1)	0.8427 (4)	0.6461 (9)	3.4 (2)
C7A	−0.359 (1)	0.8004 (5)	0.453 (1)	4.0 (3)
C8A	−0.381 (1)	0.8396 (4)	0.348 (1)	4.1 (3)
C9A	−0.315 (1)	0.8933 (4)	0.3712 (9)	3.2 (2)
C10A	0.281 (1)	0.8951 (5)	0.540 (1)	4.7 (3)
C11A	0.118 (1)	0.8768 (6)	0.903 (1)	5.8 (4)
C12A	−0.439 (2)	0.9012 (7)	0.833 (1)	6.7 (4)
C1′A	0.028 (1)	0.8101 (4)	0.3072 (9)	2.6 (2)
C2′A	0.047 (1)	0.7954 (4)	0.4266 (8)	2.5 (2)
C3′A	0.167 (1)	0.7553 (4)	0.4532 (9)	2.6 (2)
C4′A	0.262 (1)	0.7303 (4)	0.3699 (9)	3.1 (2)
C5′A	0.237 (1)	0.7454 (4)	0.2509 (9)	3.6 (3)
C6′A	0.124 (1)	0.7848 (4)	0.2255 (9)	3.7 (3)
C7′A	−0.104 (2)	0.8487 (4)	0.2611 (9)	4.1 (3)
C8′A	−0.285 (1)	0.8259 (4)	0.2344 (9)	3.5 (3)
C9′A	−0.367 (2)	0.8513 (5)	0.123 (1)	5.0 (3)
C10′A	0.049 (2)	0.7052 (6)	0.617 (1)	8.4 (5)
C11′A	0.320 (2)	0.6419 (5)	0.373 (1)	6.0 (4)
C12′A	0.304 (2)	0.7251 (5)	0.0477 (9)	4.8 (3)
O1B	0.6202 (8)	0	0.0458 (6)	3.6 (2)
O2B	0.2571 (8)	0.0381 (3)	0.3012 (6)	3.4 (2)
O3B	0.3999 (9)	0.0008 (3)	0.5059 (6)	3.6 (2)
O4B	0.7447 (9)	0.0062 (3)	0.5482 (6)	4.0 (2)
O2′B	0.297 (1)	0.1489 (3)	0.2764 (6)	3.9 (2)
O3′B	0.1160 (9)	0.1988 (3)	0.1038 (7)	4.5 (2)
O4′B	0.1535 (9)	0.1740 (3)	-0.1275 (6)	4.4 (2)
C1B	0.720 (1)	0.0717 (4)	0.2542 (9)	2.6 (2)
C2B	0.536 (1)	0.0698 (4)	0.2329 (9)	3.0 (2)
C3B	0.426 (1)	0.0445 (4)	0.3187 (8)	2.6 (2)
C4B	0.499 (1)	0.0257 (4)	0.4282 (9)	3.1 (2)
C5B	0.688 (1)	0.0277 (4)	0.4423 (9)	3.5 (3)
C6B	0.789 (1)	0.0510 (4)	0.3579 (9)	3.4 (2)
C7B	0.838 (1)	0.0909 (4)	0.1593 (9)	3.5 (2)
C8B	0.876 (1)	0.0522 (4)	0.0610 (9)	3.0 (2)
C9B	0.804 (1)	−0.0007 (4)	0.0843 (9)	3.3 (2)
C10B	0.226 (2)	−0.0114 (5)	0.251 (1)	5.1 (3)
C11B	0.373 (2)	0.0279 (6)	0.605 (1)	5.9 (3)
C12B	0.928 (2)	−0.0054 (5)	0.552 (1)	5.8 (3)
C1′B	0.467 (1)	0.0824 (4)	0.0138 (9)	2.7 (2)
C2′B	0.444 (1)	0.0948 (4)	0.1334 (9)	2.8 (2)
C3′B	0.332 (1)	0.1347 (4)	0.1603 (9)	3.0 (2)
C4′B	0.234 (1)	0.1611 (4)	0.0691 (9)	2.9 (2)
C5′B	0.249 (1)	0.1459 (4)	−0.0472 (9)	3.2 (2)
C6′B	0.372 (1)	0.1089 (4)	−0.0744 (9)	3.2 (2)
C7′B	0.594 (1)	0.0426 (4)	−0.030 (1)	3.7 (3)
C8′B	0.782 (1)	0.0648 (4)	−0.0558 (9)	3.3 (2)
C9′B	0.862 (1)	0.0405 (5)	−0.165 (1)	4.3 (3)
C10′B	0.422 (2)	0.1828 (6)	0.329 (1)	7.2 (4)
C11′B	0.171 (2)	0.2496 (5)	0.085 (1)	6.1 (4)
C12′B	0.190 (2)	0.1681 (5)	−0.246 (1)	4.7 (3)

Table 4
Fractional atomic coordinates and equivalent isotropic thermal parameters (Å^2) for **5**

	X	*Y*	*Z*	B_{eq}[a]
O1A	0.5141 (2)	0	0.9102 (2)	3.36 (4)
O2A	0.5563 (2)	0.3738 (1)	0.9392 (2)	3.36 (4)
O3A	0.3624 (2)	0.4680 (1)	0.8532 (2)	3.51 (4)
O4A	0.1999 (2)	0.3998 (2)	0.7090 (2)	4.12 (5)
O2′A	0.7551 (2)	0.3213 (1)	0.7970 (2)	4.01 (5)
O3′A	0.9700 (2)	0.2459 (2)	0.8761 (2)	3.71 (4)
O4′A	0.9537 (2)	0.1081 (2)	1.0004 (2)	3.72 (4)
C1A	0.4277 (3)	0.2244 (2)	0.7467 (2)	2.73 (5)
C2A	0.5084 (3)	0.2591 (2)	0.8242 (2)	2.46 (5)
C3A	0.4826 (3)	0.3410 (2)	0.8596 (2)	2.62 (5)
C4A	0.3821 (3)	0.3865 (2)	0.8164 (2)	2.86 (5)
C5A	0.2988 (3)	0.3504 (2)	0.7422 (2)	3.06 (6)
C6A	0.3234 (3)	0.2689 (2)	0.7070 (2)	3.11 (6)
C7A	0.4445 (3)	0.1332 (2)	0.7158 (2)	3.16 (6)
C8A	0.3738 (3)	0.0729 (2)	0.7921 (2)	3.10 (5)
C9A	0.4446 (3)	−0.0094 (2)	0.8119 (3)	3.92 (7)
C10A	0.3956 (5)	0.5316 (2)	0.7792 (3)	5.29 (9)
C11A	0.1021 (4)	0.3608 (3)	0.6488 (3)	5.57 (9)
C1′A	0.6137 (3)	0.1378 (2)	0.9259 (2)	2.35 (5)
C2′A	0.6212 (3)	0.2127 (2)	0.8693 (2)	2.46 (5)
C3′A	0.7427 (3)	0.2477 (2)	0.8541 (2)	2.85 (5)
C4′A	0.8525 (3)	0.2125 (2)	0.8972 (2)	2.80 (5)
C5′A	0.8421 (3)	0.1390 (2)	0.9578 (2)	2.71 (5)
C6′A	0.7249 (3)	0.1019 (2)	0.9700 (2)	2.56 (5)
C7′A	0.4955 (3)	0.0847 (2)	0.9493 (2)	2.56 (5)
C8′A	0.3646 (3)	0.1077 (2)	0.9043 (2)	2.81 (5)
C9′A	0.2609 (3)	0.0649 (3)	0.9668 (3)	4.54 (8)
C10′A	0.7460 (4)	0.3113 (3)	0.6859 (3)	5.50 (9)
C11′A	1.0258 (4)	0.2956 (3)	0.9542 (4)	8.5 (1)
C12′A	0.9445 (3)	0.0371 (3)	1.0686 (3)	4.35 (7)
O1B	−0.0749 (2)	0.5996 (1)	0.4063 (2)	3.46 (4)
O2B	0.0123 (2)	0.2302 (1)	0.4553 (2)	3.40 (4)
O3B	0.2152 (2)	0.1551 (1)	0.3618 (2)	3.61 (4)
O4B	0.3339 (2)	0.2335 (2)	0.2007 (2)	3.95 (4)
O2′B	−0.1959 (2)	0.2503 (1)	0.3013 (2)	3.90 (5)
O3′B	−0.4372 (2)	0.2967 (2)	0.3547 (2)	4.03 (5)
O4′B	−0.4736 (2)	0.4505 (2)	0.4633 (2)	4.95 (6)
C1B	0.0823 (3)	0.3888 (2)	0.2582 (2)	2.79 (5)
C2B	0.0196 (3)	0.3457 (2)	0.3376 (2)	2.64 (5)
C3B	0.0690 (3)	0.2685 (2)	0.3726 (2)	2.70 (5)
C4B	0.1729 (3)	0.2325 (2)	0.3249 (2)	2.95 (5)
C5B	0.2339 (3)	0.2745 (2)	0.2436 (2)	3.06 (6)
C6B	0.1894 (3)	0.3537 (2)	0.2127 (2)	3.07 (6)
C7B	0.0399 (3)	0.4765 (2)	0.2290 (2)	3.36 (6)
C8B	0.0944 (3)	0.5441 (2)	0.3064 (2)	3.13 (6)
C9B	0.0035 (3)	0.6185 (2)	0.3167 (3)	3.86 (7)
C10B	0.1887 (5)	0.0877 (2)	0.2897 (3)	5.6 (1)
C11B	0.4015 (3)	0.2762 (3)	0.1212 (3)	4.41 (7)
C1′B	−0.1283 (3)	0.4533 (2)	0.4295 (2)	2.62 (5)
C2′B	−0.1053 (3)	0.3759 (2)	0.3791 (2)	2.65 (5)
C3′B	−0.2123 (3)	0.3246 (2)	0.3566 (2)	2.99 (5)
C4′B	−0.3345 (3)	0.3448 (2)	0.3854 (2)	2.98 (5)
C5′B	−0.3543 (3)	0.4217 (2)	0.4380 (2)	3.11 (6)
C6′B	−0.2521 (3)	0.4735 (2)	0.4573 (2)	2.98 (6)
C7′B	−0.0305 (3)	0.5219 (2)	0.4550 (2)	2.89 (5)
C8′B	0.1065 (3)	0.5143 (2)	0.4209 (2)	3.10 (6)
C9′B	0.1957 (3)	0.5702 (2)	0.4870 (3)	4.42 (7)
C10′B	−0.2076 (5)	0.2611 (3)	0.1903 (3)	6.0 (1)
C11′B	−0.4495 (4)	0.2173 (3)	0.4061 (4)	5.61 (9)
C12′B	−0.5628 (5)	0.3990 (4)	0.5036 (5)	7.5 (1)

[a] $B_{eq=}(8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \boldsymbol{a_i a_j}$

IR spectra were obtained on a Perkin-Elmer 1760X FT-IR spectrometer as a film on KBr plates. Mass spectra were determined on a Hewlett-Packard 5971A GC–MS spectrometer. UV and CD spectra were recorded at AVIS 118DS UV–Vis Spectrometer and AVIS 62DS Circular Dichroism Spectrometer using MeOH as solvent. Semi-preparative HPLC separations were performed on a 10 cm C18 reversed phase column (250×10 mm, Alltech) coupled to a LDC/Milton Roy CM 4000 multi-solvent delivery system and an ISCO UV detector using an absorption wavelength at 260 nm. Analytical HPLC were carried out on a 10 m C8 or C18 reversed phase column (250×4.6 mm, Alltech) coupled to a Hewlett-Packard 1090 HPLC system with diode array detection at 260 nm. Vacuum liquid chromatographic (VLC) separations (Coll and Bowden, 1986) were run on silica gel (MN Kieselgel G). TLC were run on precoated MN Sil-G 25 UV254 plates (thickness 0.25 mm).

3.2. Plant material

Magnolia pyramidata Bartram was collected on 30 April, 1991 in the Ragland Hill, ca 15 miles south of Hattiesburg, MS and its voucher specimen (Fischer No 411) is deposited at the Herbarium of Louisiana State University, Baton Rouge, LA.

3.3. Extraction and isolation

The air-dried leaves (1.8 kg) were ground and extracted with CH_2Cl_2 at room temp. for 24 h, providing 17g of crude extract. Part of the extracts (8.2 g) was sepd. by VLC on silica-gel using *n*-hexane–EtOAc mixtures of increasing polarity, 45 frs of 25 ml each being collected. Combined frs 22–24 (766.5 mg) were rechromatographed by VLC (petrol–EtOAc mixtures of increasing polarity) and afforded 40 subfractions of 25 ml each. Further prep. TLC of subfrs 15′–19′ ($CHCl_3$–EtOAc, 9:1, ×2) gave pyramidatin A (**1**) (54.6 mg) and G (**8**) (17.2 mg). Subfrs 20′–26′, after prep. TLC ($CHCl_3$: EtOAc, 17:3, ×2), provided 11.4 mg of pyramidatin E (**6**) plus additional pyramidatin A (**1**). The combined subfrs 27′–29′ were purified by prep. TLC ($CHCl_3$–EtOAc, 9:1, ×4) to give 24.3 mg of pyramidatin B (**5**) and 16.7 mg of pyramidatin D (**3**). Pyramidatin C (**2**) (11.8 mg) was obtained from subfrs 30′–32′ after purification by prep. TLC ($CHCl_3$–EtOAc, 9:1, ×3). Rechromatography of fr 21 (791.3 mg) by VLC with petrol–EtOAc mixtures of increasing polarity produced 35 subfrs of 25 ml each. In addition to pyramidatin A (**1**), pyramidatin C (**2**), pyramidatin E (**6**), and pyramidatin G (**8**), pyramidatin H (**4**) (21.2 mg) was isolated from subfrs 12′–14′ by further prep. TLC ($CHCl_3$–EtOAc, 19:1). Subfrs 23′–24′ gave pyramidatin F (**7**) (12.6 mg) by prep. TLC ($CHCl_3$–EtOAc, 9:1, ×2), which was further purified by HPLC (H_2O–MeOH, 1:3).

3.4. Pyramidatin A (*1*)

Colorless crystal, mp 152–154°C ($CHCl_3$–EtOAc, 9:1) IR : 1595 (aromatic ring), 1332 (Ar–OMe), 1103 (ether). UVλ_{max}^{MeOH}nm (log ϵ): 216(4.58), 254(4.06), 292(3.09). CD (MeOH; c 3.45×10^{-5} M): $[\theta]_{223}$ −20620, $[\theta]_{260}$ +8480. MS (70 eV) *m*/*z* (rel. int.): 430 $[M]^+$ (100), 415 $[M–Me]^+$ (2.5), 399 $[M–OMe]^+$ (5.0), 371 (5.0), 359 (5.0), 328 (8.9), 316 (6.3), 215 (3.8), 181 (5.0), 55 (5.0). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.5. Pyramidatin C (**2**)

Colorless oil. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1601 (aromatic ring), 1336 (Ar–OMe), 1103 (C–O–C). UVλ_{max}^{MeOH} nm (log ϵ): 211 (4.54), 256 (3.90), 290 (3.36); CD (MeOH; c 2.82×10^{-5} M): $[\theta]_{219}$–9830, $[\theta]_{258}$ +8710. MS (70 eV) *m*/*z* (rel. int.): 416 $[M]^+$ (100), 385 $[M-OMe]^+$ (7.6), 384 $[M-HOMe]^+$ (4.5), 359 (6.0), 345 (12.1), 331 (4.5), 313 (4.5), 302 (7.6), 115 (2.3), 55 (3.0). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.6. Pyramidatin D (*3*)

Amorphous solid. IR ν_{max}^{KBr} cm^{-1}: 3418 (OH), 1602 (aromatic ring), 1336 (Ar–OMe), 1105 (C–O–C). UVλ_{max}^{MeOH} nm(log ϵ): 217 (4.53), 256 (3.88), 290 (3.40). CD (MeOH; c 5.91×10^{-5} M): −42690, $[\theta]_{254}$ +3150. MS (70 eV) *m*/*z* (rel. int.): 416 $[M]^+$ (100), 401 $[M–Me]^+$ (3.0), 384 $[M-HOMe]^+$ (3.8), 359 (3.8), 341 (5.3), 325 (4.5), 302 (6.0), 282 (4.5), 181 (9.0), 55 (2.3). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.7. Pyramidatin H (*4*)

Colorless crystal, mp 208–211°C (hexane–EtOAc). IR ν_{max}^{KBr} cm^{-1}: 1619 (aromatic ring), 1367 (Ar–OMe), 1267, 1208 (Ar–OCH_2O–Ar), 1049 (C–O–C). UVλ_{max}^{MeOH} nm (log ϵ): 217 (4.45), 262 (3.78), 296 (3.38); CD (MeOH; c 1.96×10^{-5} M): $[\theta]_{225}$ −6660, $[\theta]_{257}$ −1170. MS (70 eV) *m*/*z* (rel. int.): 398 $[M]^+$ (100), 381 $[M–OH]^+$ (1.9), 370 $[M–CH_2=CH_2]^+$ (3.8), 327 (8.8), 313 (10.1), 297 (12.6), 269 (5.0), 233 (3.8), 207 (4.5), 165 (7.6), 55 (2.5). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.8. Pyramidatin B (*5*)

Colorless crystal, mp 198–199°C ($CHCl_3$–EtOAc, 9:1). IR ν_{max}^{KBr} cm^{-1}: 3393 (OH), 1601 (aromatic ring), 1333 (Ar–OMe), 1121 (C–O–C). UVλ_{max}^{MeOH} nm (log ϵ): 218 (33 850), 256(8408), 290 (2243); CD (c 3.97×10^{-5} M, MeOH): $[\theta]_{222}$: +40 550, $[\theta]_{265}$ +8170. MS (70 eV) *m*/*z* (rel. int.): 416 $[M]^+$ (100), 401 $[M–Me]^+$ (2.3), 385

$[M–OMe]^+$ (9.0), 359 (6.0), 345 (12.1), 331 (6.0), 302 (8.3), 287 (3.8), 208 (4.5), 55 (3.0); ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.9. Pyramidatin E (**6**)

Amorphous solid. IR ν_{max}^{KBr} cm^{-1}: 3413 (OH), 1590 (aromatic ring), 1334 (Ar–OMe), 1122, 1094 (C–O–C). UV λ_{max}^{MeOH} nm (log ϵ): 214 (4.68), 258 (3.84), 219 (3.28); CD (MeOH; c 2.14×10^{-5} M): $[\theta]_{221}$ +16294, $[\theta]_{255}$ −16075. MS (70 eV) *m/z* (rel. int.): 416 $[M]^+$ (100), 401 $[M–Me]^+$ (1.5), 388 $[M–CH_2=CH_2]^+$ (4.5), 356 (3.0), 345 (4.5), 327 (3.8), 302 (6.0), 287 (3.0), 208 (4.5), 55 (3.0). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.10. Pyramidatin F (**7**)

Amorphous solid. IR ν_{max}^{KBr} cm^{-1}: 3389 (OH), 1596 (aromatic ring), 1333 (Ar–OMe), 1120, 1093 (C–O–C). UV λ_{max}^{MeOH} nm (log ϵ): 219 (4.54), 256 (3.87), 293 (3.49); CD (MeOH; c 1.91×10^{-5} M): $[\theta]_{231}$ +10 834, $[\theta]_{257}$ −13512; MS (70 eV) *m/z* (rel. int.): 400 $[M]^+$ (100), 385 $[M–Me]^+$ (0.76), 369 $[M–OMe]^+$ (4.5), 329 (3.0), 315 (3.8), 281 (4.5), 267 (4.5), 239 (1.5), 165 (4.5), 55 (3.0). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.11. Pyramidatin G (**8**)

Colorless oil. IR ν_{max}^{KBr} cm^{-1}: 1618,1597 (aromatic ring), 1334 (Ar–OMe), 1106, 1081 (C–O–C). UV λ_{max}^{MeOH} nm (log ϵ): 216 (4.60), 268 (3.72), 298 (3.06); CD (MeOH; c $3.35x10^{-5}$ M): $[\theta]_{229}$ +36 000, $[\theta]_{259}$ −25 000; MS (70 eV) *m/z* (rel. int.): 414 $[M]^+$ (100), 399 $[M–Me]^+$ (1.5), 386 $[M–CH_2=CH_2]^+$ (3.8), 355 (4.5), 343 (6.0), 326 (6.0), 312 (9.0), 300 (7.6), 285 (3.0), 55 (2.3). ^{1}H NMR see Table 1. ^{13}C NMR see Table 2.

3.12. X-Ray data of pyramidatin A (**1**)

A colorless needle of dimensions $0.40\times0.10\times0.10$ mm was used for data collection on an Enraf-Nonius CAD4 diffractometer equipped with CuK_α radiation (λ = 1.54184 Å), and a graphite monochromator. Crystal data are: $C_{24}H_{30}O_7$, $M_r = 430.5$, monoclinic space group $P2_1$, $a = 7.597$ (1), $b = 25.966$ (3), $c = 11.261$ (2) Å, $\beta = 90.68$ (1)°, $V = 2221$ (1) Å^3, $Z = 4$, $d_c = 1.287$ g cm^{-3}, T = 25°C. Intensity data were measured by ω-2θ scans of variable rate, 1.37–3.30° min^{-1}. A quadrant of data was collected within the limits $2 < \theta < 60°$. Data reduction included corrections for background, Lorentz, polarization, and absorption effects. Absorption corrections ($\mu = 7.4$ cm^{-1}) were based on ψ scans, with minimum relative transmission coefficient 76.25%. Standard reflections did not decrease in intensity during data collection. Of 3322 unique data, 2767 had $I > 1\sigma(I)$ and were used in the refinement. The structure was solved by direct methods using SHELXS (Sheldrick, 1990) and refined by full-matrix least squares based on F with weights $w = \sigma^{-2}(F_o)$, using the Enraf-Nonius MolEN programs (Fair, 1990). Nonhydrogen atoms were refined anisotropically, while hydrogen atoms were placed in calculated positions. An extinction coefficient refined to a final value of 4.9 $(14)\times10^{-7}$. Convergence was achieved with $R = 0.090$, $R_w = 0.086$ using 559 variables, with maximum residual electron density 0.36 eÅ^{-3}. The fractional atomic coordinates of **1** are given in Table 3. Bond distances and angles, as well as anisotropic thermal parameters are given in supplementary material.

3.13. X- ray data of pyramidatin B (**5**)

A colorless crystal fragment of dimensions $0.55\times0.50\times0.38$ mm was used for data collection on an Enraf-Nonius CAD4 diffractometer equipped with MoK_α radiation (λ = 0.71073 Å), and a graphite monochromator. Crystal data are: $C_{23}H_{28}O_7$, $M_r = 416.5$, monoclinic space group $P2_1$, $a = 10.4898$ (6), $b = 15.8450$ (11), $c = 12.6757$ (8) Å, $\beta = 91.30$ (1)°, $V = 2106.3$ (4) Å^3, $Z = 4$, $d_c = 1.313$ g cm^{-3}, $T = 23°$. Intensity data were measured by ω-2θ scans of variable rate, 0.66–3.30° min^{-1}. A quadrant of data was collected within the limits $1 < \theta < 27°$. Data reduction included corrections for background, Lorentz, and polarization effects. Absorption effects ($\mu = 0.90$ cm^{-1}) were negligible, and standard reflections did not decrease in intensity during data collection. Of 4763 unique data, 4156 had $I > 3\sigma(I)$ and were used in the refinement. The structure was solved by direct methods and refined by full-matrix least squares based on F with weights $w = \sigma^{-2}(F_o)$, using the Enraf-Nonius MolEN programs (Fair, 1990). Nonhydrogen atoms were refined anisotropically, while hydrogen atoms were included in calculated positions, except for those of the OH groups, which were refined isotropically. An extinction coefficient refined to a final value of 6.6 $(8)\times10^{-7}$. Convergence was achieved with $R = 0.041$ $R_w = 0.051$ using 549 variables, with maximum residual electron density 0.41 eÅ^{-3}. The fractional atomic coordinates of **5** are given in Table 4. Bond distances and angles, as well as anisotropic thermal parameters are given in supplementary material. All data have been deposited at the Cambridge Crystallographic Data Center.

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