Novel Phenylpropanoids and Lignans from *Illicium verum*

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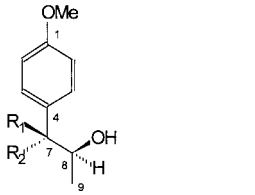
Nine new phenylpropanoids (**2**−**7**, **10**, **12**, and **14**) and two compounds representing novel structural classes of 7-*O*-8′ and 7-*O*-8′.8-*O*-7′ lignans (**8** and **9**, respectively) have been isolated from *Illicium verum* and their structures established by two-dimensional NMR. Most of these compounds appear to be biogenetically derived from *threo*-anethole glycol: relative stereochemistries for some members of this series were established by NOESY; absolute stereochemistries of others were determined by formation of Mosher esters.

Illicium verum Hook f. (Illiciaceae, Chinese star anise) is an evergreen tree indigenous to southern China, used by local people as a stimulant and carminative.[1] It is easily confused with the extremely posionous *I. anisatum* (containing the GABA antagonist anisatin, which is reported to be the most powerful poison of plant origin, and related sesquiterpenes), which is found in the same geographical region and which produces morphologically similar fruits.[2] Previous chemical investigations of *I. verum* have yielded 4-ethoxyphenol, anisyl ketone,[3] the phenylpropanoid, anisoxide,[4] and the sesquiterpenes veranisatins A and B,[5] as well as various cinnamic acid derivatives.[6]

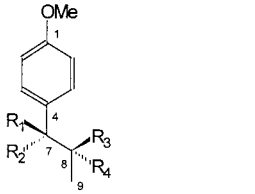
Results and Discussion

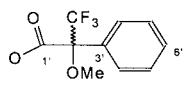
Extraction of the leaves of *I. verum* with CH_2Cl_2 yielded nine new phenylpropanoid derivatives (**2**−**7**, **10**, **12**, and **14**) and two new lignans (**8** and **9**). Many of these compounds are apparently derived from the simple phenylpropanoid diol, *threo*-anethole glycol (**1a**), which was also present as a significant component of the extract. ^{13}C and ^{1}H NMR assignments for **1a** and for all compounds reported in this paper were rigorously determined by means of 2D-NMR (HSQC, HMBC, and ^{1}H-^{1}H COSY) (Tables 1 and 2).

Compound **1** was isolated from *I. verum* predominantly as the *threo* form as shown by NMR; in particular, a $J_{7,8}$ coupling constant of 7.8 Hz in the ^{1}H NMR spectrum is considered diagnostic for this diastereoisomer.[7] Smaller amounts of the *erythro* isomer (**1b**) were also obtained, for which this coupling constant has been shown previously to have a consistently smaller value (ca. 4 Hz).[7] ^{1}H and ^{13}C chemical shifts for these two diastereoisomers of anethole glycol also agreed with those reported previously.[7] A pure sample of **1a** had a significant optical rotation ($[\alpha]_D$ +7.7°). Although both *threo* and *erythro* forms of anethole glycol have been reported from nature, there is apparently no data available in the literature concerning optical rotations of either the 7*R*,8*R* or 7*S*,8*S threo* isomers with which to make a comparison with our sample from *I. verum*. Consequently, we endeavored to determine the absolute configuration at the 7- and 8-positions of **1a** by formation of esters with the two enantiomers of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride ((*S*)-(+)-MTPCl and (*R*)-(−)-MTPCl).[8] In the event, treatment of **1a** with the (*S*)-(+) enantiomer of MTPCl yielded four compounds (**1c**−**f**), which were separable by HPLC; similarly, application of (*R*)-(−)-MTPCl yielded the corresponding four mirror image esters **1g**−**j**, respectively. (Note: *R*/*S* nomenclature for the α-methoxy-α-(trifluoromethyl)phenylacetate (MTPA) moiety of the esters so formed is reversed with respect to the acid chloride derivatizing agent.) Formation of four such distinct isomers from esterification with each enantiomer of



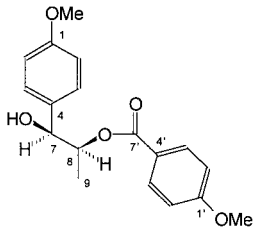
1a R_1 =OH; R_2 = H (*threo,* 7*S*, 8*S* form shown)
1b R_1 =H; R_2 = OH (*erythro*)





(*S*/*R*)-OMTP

1c R_1 = H; R_2 = OH; R_3 = H; R_4 = *R*-OMTP
1d R_1 = OH; R_2 = H; R_3 = *R*-OMTP; R_4 = H
1e R_1 = *R*-OMTP; R_2 = H; R_3 = OH; R_4 = H
1f R_1 = H; R_2 = *R*-OMTP; R_3 = H; R_4 = OH
1g R_1 = OH; R_2 = H; R_3 = *S*-OMTP; R_4 = H
1h R_1 = H; R_2 = OH; R_3 = H; R_4 = *S*-OMTP
1i R_1 = H; R_2 = *S*-OMTP; R_3 = H; R_4 = OH
1j R_1 = *S*-OMTP; R_2 = H; R_3 = OH; R_4 = H



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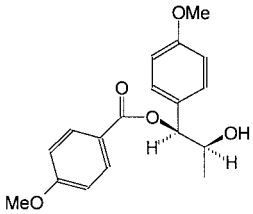

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Table 1. ^{13}C NMR Assignments (δ) for **1**−**7**

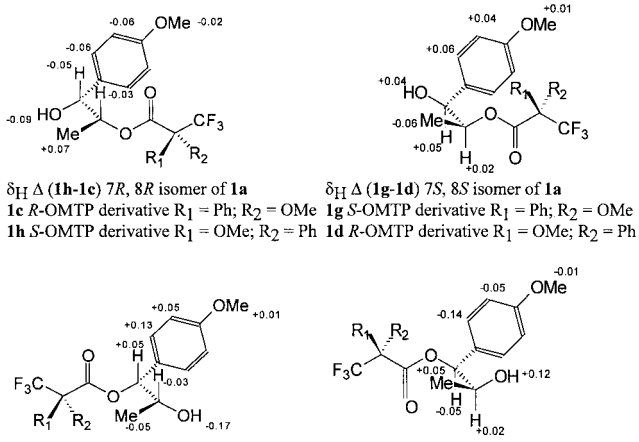
atom	**1a**	**1b**	**2**	**3**	**4**	**5**	**6**	**7**[a]
1	159.4	159.4	159.6	159.7	159.6	158.0	158.4	158.5
2/6	113.9	113.8	114.0	114.0	114.1	113.7	113.5	114.3
3/5	128.1	128.0	128.3	128.5	127.8	129.7	130.7	129.6
4	133.3	132.5	132.3	129.9	130.7	131.7	130.4	133.8
7	79.2	77.3	77.0	80.7	84.6	59.5	59.3	58.9
8	72.3	71.3	75.1	70.4	81.3	72.8	68.9	70.3
9	18.8	17.5	16.6	18.8	16.4	22.6	22.2	21.4
1′			163.5	163.6	160.4	158.8	158.9	158.2
2′/6′			113.7	113.7	113.8	113.4	113.4	114.0
3′/5′			131.7	131.8	128.0	128.0	128.0	129.0
4′			122.7	122.5	130.7	135.3	134.2	135.1
7′			166.2	165.7	104.0	80.4	75.2	
1-OMe	55.3	55.3	55.3	55.3	55.3	55.04	55.24	55.3
1′-OMe			55.5	55.5	55.4	55.14	55.18	55.2

[a] All assignments for 1−4 may be interchanged (as a group) with those for 1′−4′.

Table 2. ^{1}H NMR Assignments[a] (δ) for **1**−**7**

atom	**1a**	**1b**	**2**	**3**	**4**	**5**	**6**	**7**[b]
2/6	6.87 (d, 8.7)	6.90 (d, 8.6)	6.89 (d, 8.6)	6.88 (d, 8.7)	6.91 (d, 8.7)	6.63 (d, 8.8)	6.74 (d, 8.7)	6.86 (d, 8.7)
3/5	7.23 (d, 8.7)	7.29 (d, 8.6)	7.32 (d, 8.6)	7.34 (d, 8.7)	7.34 (d, 8.7)	6.74 (d, 8.8)	6.89 (d, 8.7)	7.28 (d, 8.7)
7	4.28 (d, 7.8)	4.60 (d, 4.5)	4.72 (d, 7.4)	5.71 (d, 7.2)	4.57 (d, 8.1)	2.75 (m)	2.87 (dd, 8.5, 4.5)	3.71 (d, 8.7)
8	3.82 (m)	4.00 (m)	5.30 (dq, 7.4, 6.4)	4.19 (dq, 7.2, 6.3)	4.04 (dq, 8.1, 6.1	4.36 (dq, 9.1, 6.2)	4.23 (dq, 8.5, 6.2)	4.45 (dq, 8.7, 6.1)
9	1.00 (d, 6.3)	1.10 (d, 6.4)	1.17 (d, 6.4)	1.13 (d, 6.3)	1.42 (d, 6.1)	0.94 (d, 6.2)	1.06 (d, 6.2)	1.18 (d, 6.1)
2′/6′			6.94 (d, 8.9)	6.92 (d, 8.9)	6.93 (d, 8.7)	6.66 (d, 8.7)	6.77 (d, 8.7	6.82 (d, 8.7)
3′/5′			8.02 (d, 8.9)	8.03 (d, 8.9)	7.48 (d, 8.7)	6.98 (d, 8.7)	6.99 (d, 8.7)	7.18 (d, 8.7)
7′					6.17 (s)	4.97 (d, 9.8)	5.16 (d, 4.5)	
1-OMe	3.81 (s)	3.81 (s)	3.81 (s)	3.80 (s)	3.82 (s)	3.70 (s)	3.78 (s)	3.78
1′-OMe			3.87 (s)	3.86 (s)	3.82 (s)	3.71 (s)	3.77 (s)	3.76

[a] Multiplicity and coupling constants (Hz) indicated in parentheses. [b] Assignments for 2−6 may be interchanged (as a group) with those for 2′−6′.



$\delta_H \Delta$ (**1h-1c**) 7*R*, 8*R* isomer of **1a**
1c *R*-OMTP derivative R_1 = Ph; R_2 = OMe
1h *S*-OMTP derivative R_1 = OMe; R_2 = Ph

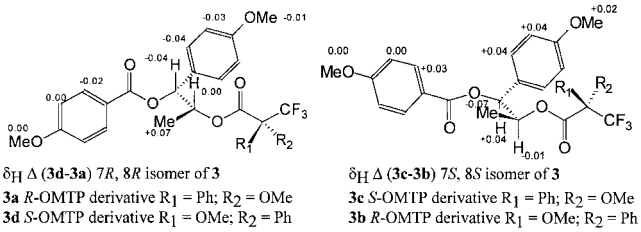
$\delta_H \Delta$ (**1g-1d**) 7*S*, 8*S* isomer of **1a**
1g *S*-OMTP derivative R_1 = Ph; R_2 = OMe
1d *R*-OMTP derivative R_1 = OMe; R_2 = Ph

$\delta_H \Delta$ (**1i-1f**) 7*R*, 8*R* isomer of **1a**
1f *R*-OMTP derivative R_1 = OMe; R_2 = Ph
1i *S*-OMTP derivative R_1 = Ph; R_2 = OMe

$\delta_H \Delta$ (**1j-1e**) 7*S*, 8*S* isomer of **1a**
1j *S*-OMTP derivative R_1 = OMe; R_2 = Ph
1e *R*-OMTP derivative R_1 = Ph; R_2 = OMe

Figure 1. Chemical shift differences between diastereoisomeric pairs of compounds formed from the derivatization of *threo*-anethole glycol (**1a**, 7*S*/8*S* and 7*R*/8*R*) by (*S*)-(+)- and (*R*)-(−)-MTPCl. From calculated differences ((*S*)-MTPA) −((*R*)-MTPA) **1c**, **1h**, **1f**, and **1i** are derivatives of the 7*R*,8*R* *threo* isomer (at the 7- and 8- positions), while **1g**, **1d**, **1j**, and **1e** are derived from the 7*S*, 8*S* isomer.

MTPCl is only possible if compound **1** is actually present as a mixture of 7*R*,8*R* and 7*S*,8*S* forms and if MTPA esters are formed at both the 7-OH and 8-OH positions. Detailed analysis of ^{1}H chemical shift differences between (*S*)-MTPA and (*R*)-MTPA derivatives for each of the four possible products (i.e., $\Delta\delta^{1}H$ ((*S*)-MTPA) − ((*R*)-MTPA) for **1g**−**1d**, **1j**−**1e**, **1h**−**1c** and **1i**−**1f**), according to the preferred conformations normally assumed for MTPA esters[8] (Figure 1), confirmed this supposition and



$\delta_H \Delta$ (**3d-3a**) 7*R*, 8*R* isomer of **3**
3a *R*-OMTP derivative R_1 = Ph; R_2 = OMe
3d *S*-OMTP derivative R_1 = OMe; R_2 = Ph

$\delta_H \Delta$ (**3c-3b**) 7*S*, 8*S* isomer of **3**
3c *S*-OMTP derivative R_1 = Ph; R_2 = OMe
3b *R*-OMTP derivative R_1 = OMe; R_2 = Ph

Figure 2. Chemical shift differences ((*S*)-OMTP − (*R*)-OMTP) between diastereoisomeric pairs of compounds formed in the derivatization of *threo*-7-(4-methoxybenzoloyl)anethole glycol (**3**, 7*S*/8*S* and 7*R*/8*R*) by (*S*)-(+)- and (*R*)-(−)-MTPCl. Compounds **3a** and **3d** derived from threo 7*R*,8*R* isomer; compounds **3b** and **3c** derived from 7*S*,8*S* isomer.

demonstrated unambiguously that compound **1a** from *I. verum* is indeed the *threo* form of anethole glycol (as previously supposed from the value of $J_{7,8}$) and is an approximately 2:1 mixture of *7S,8S* and *7R,8R* isomers.

Compound **2** is the 8-(4-methoxybenzoloyl) derivative of anethole glycol as shown by a correlation between C-7′ of the benzoyl substituent and H-8 of the anethole glycol moiety in the HMBC spectrum. The coupling constant between H-7 and H-8 in ^{1}H NMR suggests *threo* stereochemistry for this natural product, consistent with **2** being derived from **1a**. Compound **3** is the 7-(4-methoxybenzoloyl) derivative of anethole glycol (as shown by a correlation in HMBC from the benzoyl carbonyl to H-7). An attempt was made to establish the absolute stereochemistry of the 8-secondary hydroxyl in **3** by formation of Mosher esters using both (*S*)-(+)- and (*R*)-(−)-MTPCl as previously.[8] Derivatization with (*S*)-(+)-MTPCl yielded two diastereiosmers (**3a** and **3b**), while use of (*R*)-(−)-MTPCl yielded the two corresponding mirror images (**3c** and **3d**). Analysis of chemical

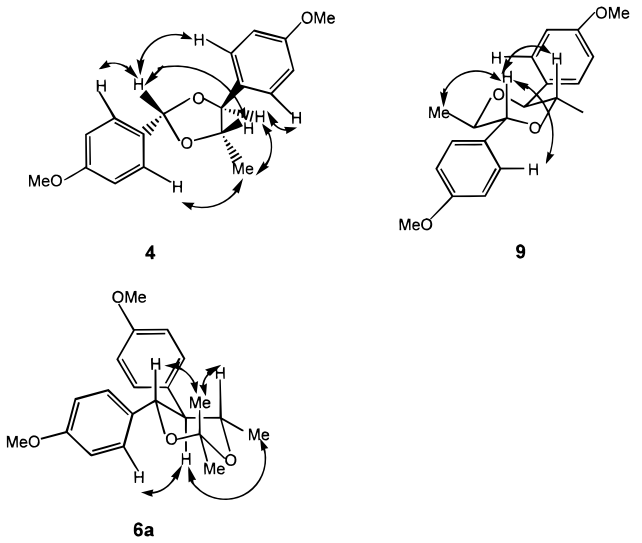
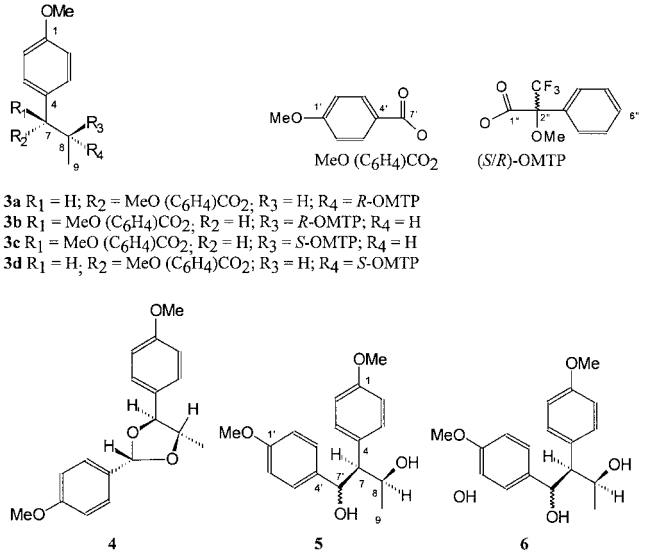


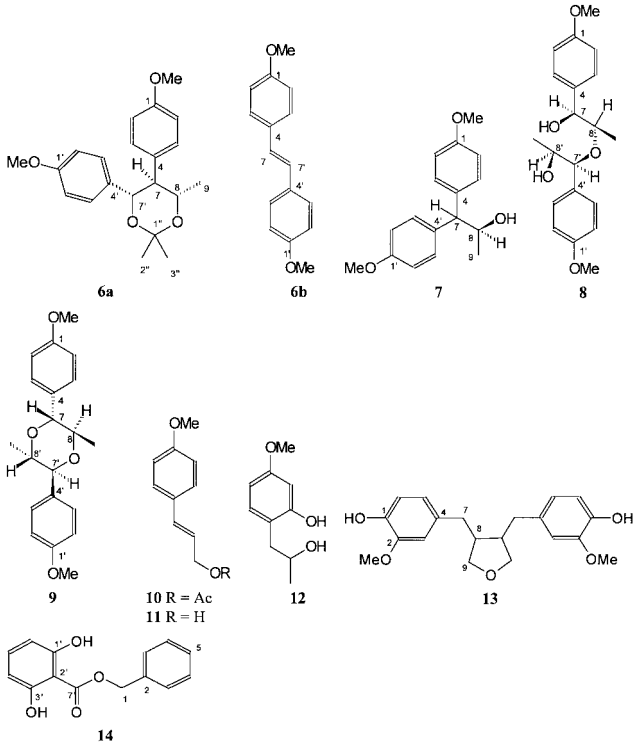
Figure 3. NOESY correlations used in assigning relative configuration of **4**, **6a**, and **9** indicated by arrows from ^{1}H to ^{1}H.

shift differences between the two diastereoisomeric pairs[8] (i.e., $\Delta\,\delta^1$H ((*S*)-MTPA) − ((*R*)-MTPA) for **3d**−**3a** and **3c**−**3b**) confirmed the presumed *threo* stereochemistry and indicated that compound **3** was an approximately 1:1 mixture of *7R,8R* and *7S,8S* isomers (Figure 2). Given the tendency to partial or complete racemization observed for compounds **1** and **3**, no further attempts were made to establish the absolute stereochemistry of other novel phenylpropanoid and derived compounds (**2**, **4**−**10**, and **12**) described in this paper; relative stereochemistry only, as determined by NMR, is reported. It is proposed that most of these compounds are at least partially racemic; for simplicity, structures are drawn with relative stereochemistry corresponding to the *7S,8S* stereoisomer of *threo*-anethole glycol only.



Compound **4** can be envisaged as being formed from either **2** or **3** by reduction of the benzoyl ester linkage accompanied by intramolecular ketal formation with a free −OH group in the phenylpropanoid moiety. Relative stereochemistry about the new five-membered ring in **4** was determined from NOESY experiments (Figure 3) and was consistent with *threo* stereochemistry previously determined for proposed biogenetic precursors **1**−**3**.

Compounds **5** and **6** are diastereoisomers that apparently arise from direct linkage of a C_6C_1 substituent at the reduced 7-position of anethole glycol. Derivatization of either of the 1,3-diols **5** or **6** with 2,2-dimethoxypropane[9]) yielded an identical cyclic product **6a**, for which relative stereochemistry around the new six-membered ring could be determined by NOESY (Figure 3). This surprising result may be due to the ease of formation of a phenyl-stabilized carbocation at the 7′ position under the acid conditions of the derivatization, which would favor rapid ring opening and closing of the ketal and accompanying epimerization at C-7′ to yield the thermodynamically more stable all-equatorially substituted 1,3-dioxan (Figure 3). Formation of the stilbene **6b** as a major byproduct of this reaction is also simply explained by the above mechanism and lends support to this hypothesis. Derivatization of **5** and **6** as ketals thus seemed to show that these compounds are diastereoisomeric at the 7′-position; this is consistent with their formation from the nonstereospecific addition of a C_6C_1 unit to a C_6C_3 phenylpropanoid derived from anethole glycol, as proposed above. Compound **7** is a one-carbon-deficient homologue of **5/6**, possibly formed by the analogous addition of a C_6 unit. The two aromatic rings in **7** are diastereotopic and gave similar but distinguishable NMR resonances, which were confidently assigned using 2D-NMR methodology employed throughout this paper.



Compound **8** is apparently formed by ether linkage of two units of *threo*-anethol glycol. Significant upfield shifts were observed in the ^{13}C resonances for C-7 and C-8′ ($\Delta\delta$ +0.21 ppm and +0.10 ppm, respectively) of **8** following a D_2O shake, indicating that these carbons bear −OH groups (the upfield shift is a consequence of secondary isotope effects following replacement of an

Table 3. ^{13}C and ^{1}H Assignments for Compounds **8** and **9**

	δ ^{13}C		δ ^{1}H[a]	
atom	**8**	**9**	**8**	**9**
1	159.1	159.6		
2/6	113.7	113.9	6.88 (d, 8.7)	6.89 (d, 8.7)
3/5	127.7	128.3	7.27 (d, 8.7)	7.33 (d, 8.7)
4	133.0	131.3		
7	74.8	84.2	4.82 (d, 4.1)	4.27 (d, 9.0)
8	78.3	76.9	3.62 (m)	3.72 (dq, 9.0, 6.3)
9	15.8	17.3	0.84 (d, 6.4)	1.00 (d, 6.3)
1′	159.5	159.6		
2′/6′	113.8	113.9	6.87 (d, 8.7)	6.89 (d, 8.7)
3′/5′	128.7	128.3	7.20 (d, 8.7)	7.33 (d, 8.7)
4′	131.8	131.3		
7′	86.9	84.2	4.06 (d, 8.4)	4.27 (d, 9.0)
8′	71.8	76.9	3.82 (m)	3.72 (dq, 9.0, 6.3)
9′	18.3	17.3	0.91 (d, 6.4)	1.00 (d, 6.3)
1-OMe	55.29	55.3	3.81 (s)	3.81 (s)
1′-OMe	55.27	55.3	3.80 (s)	3.81 (s)

[a] Multiplicity and coupling constants (Hz) indicated in parentheses.

−OH group by an −OD group[10]). Consequently, the ether linkage in compound **8** is between oxygenated carbons C-7′ and C-8. The value of the ^{1}H coupling constant for H-7/H-8 ($J_{7,8}$ = 4.1 Hz) suggested *erythro* stereochemistry for this half of the lignan, while that for H-7′/H-8′ (8.4 Hz) suggested *threo* stereochemistry. We propose that **8** is formed by S_N2-type attack of the 7′-OH group of one molecule of *threo*-anethole glycol at the 8-position of a second such molecule with consequent inversion of configuration at the 8-position accompanying formation of the 7′-*O*-8 bond. The 7-*O*-8′ lignan skeleton of **8** apparently represents a new structrual class.[11]

The 1,4-dioxane lignan **9** demonstrated only nine carbon resonances in the ^{13}C NMR, indicating a symmetry element in the structure of this dimer. The coupling constant between H-7/H-8 (and H-7′/H-8′) in ^{1}H NMR (J = 9.0 Hz) was indicative of a *trans* diaxial relationship between these protons. We propose that **9** is formed from **8** by a second attack of the 8′-OH group at the 7-center with an accompanying second inversion at the 7-position. NOESY spectra for **9** (Figure 3) demonstrated the expected "*threo*" stereochemistry for each biogenetic phenylpropanoid moiety and a correlation across the oxygen bridge (H7 → H8′) provided evidence for the proposed double inversion of absolute stereochemistry in one of the biogenetic phenylpropanoid units. Zero optical rotation was recorded for compound **9**, which was consistent with the foregoing proposals. Compound **9** is a representative of a second new structural class of 7-*O*-8′.8-*O*-7′ lignans.[11]

Two other simple novel phenylpropanoids were also isolated from the extract. Compound **10** is the acetate of the known compound *p*-coumaryl alcohol **11** (compound **11** was also present in the extract and was identified from its NMR spectrum[12]); compound **12** incorporates a 3-hydroxyl group. Compound **13** is a known lignan[13,14] belonging to the well-established furan class.[11]

Known compounds from the extract which were identified from their 1D-NMR spectra included *trans*-anethole,[15,16] (4-hydroxyphenyl)ethanol,[17] anisyl alcohol,[18] *p*-anisaldehyde,[19] and *p*-anisic acid.[20]

Experimental Section

General Experimental Procedures. Chemical shifts are expressed in ppm (δ) relative to TMS as internal standard. All NMR experiments were run on a Bruker DRX 500 instrument. HSQC and HMBC spectra were recorded with 1024 data points in F_2 and 256 data points in F_1. High-resolution MS were recorded in EI mode at 70 e.v. on a Finnigan-MAT 95 MS spectrometer. IR spectra were recorded in $CHCl_3$ on a BIO-RAD FT S-7 IR spectrometer. Column chromatography was performed using silica gel 60−200 μm (Merck). HPLC separations were performed using a Varian chromatograph equipped with RI star 9040 and UV 9050 detectors and a Intersil PREP-SIL 20 mm × 25 cm column, flow rate 8 mL/min.

Plant Material. Leaf tissue of *I. verum* was obtained from the South China Botanical Garden (plant material originally collected in Guangxi province by the Guangxi Institute of Botany). A voucher specimen (Hao Gang103) has been deposited in the University of Hong Kong Herbarium (HKU).

Extraction and Isolation. The fresh sample (1.2 kg) was ground to a fine powder under liquid N_2 in order to ensure complete rupture of plant cell walls and liberation of intracellular contents and then extracted with CH_2Cl_2 over several days. The organic extract was then dried and evaporated under reduced pressure to yield a dark green oil (26.5 g; 2.2% w/w). Compounds **1**−**14** were isolated by column chromatography using hexane and ethyl acetate (TLC plates used to monitor the column were visualized using *p*-anisaldehyde). In most cases, further purification was required by HPLC, using ethyl acetate/hexane: **1a** (161 mg); **1b** (59 mg); **2** (16 mg); **3** (26 mg); **4** (23 mg); **5** (87 mg); **6** (58 mg); **7** (51 mg); **8** (567 mg); **9** (16 mg); **10** (12 mg); **11** (24 mg); **12** (6 mg); **13** (540 mg); **14** (15 mg); *trans*-anethole (1.28 g); (4-hydroxyphenyl)ethanol (24 mg); anisyl alcohol (75 mg); *p*-anisaldehyde (83 mg); *p*-anisic acid (26 mg).

***threo*-Anethole glycol (1a):** oil; $[\alpha]_D$ = +7.7° (*c* 2.22, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3420 (br), 3011, 2970, 2932, 2856, 1612, 1514, 1250 cm^{-1}; ^{1}H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS *m*/*z* 182.0945 (calcd for $C_{10}H_{14}O_3$, Δ −0.2 mmu) (10), 137 (100), 109 (30), 94 (15).

***erythro*-Anethole glycol (1b)** isolated as a mixture with **1a**: ^{1}H NMR and ^{13}C NMR, Tables 1 and 2.

Derivatization of 1a with (*S*)-(+)-MTPCl To Form (*R*)-MTPA Esters 1c−f. To a solution of *threo*-anethole glycol **1a** (19.4 mg) in pyridine (0.36 mL) was added (*S*)-(+)-MTPCl (0.02 mL). The solution was allowed to stand at room temperature for 13 h, and then *N*,*N*-diisopropylethylamine (0.02 mL) was added and the mixture allowed to stand for 10 min. Solvent was evaporated, and the products were separated by HPLC in 15% ethyl acetate/hexane yielding compounds **1c**−**f**.

Compound 1c: t_R 21.5 min (23.7% of total reaction product); ^{1}H NMR ($CDCl_3$) δ 7.49 (2H, m, H-4′/8′), 7.37 (3H, m, H-5′-7′), 7.27 (2H, d, J = 8.0 Hz, H-3/5), 6.90 (2H, d, J = 7.7 Hz, H-2/6), 5.31 (1H, dq, J = 7.3, 6.3 Hz, H-8), 4.62 (1H, dd, J = 7.3, 4.2 Hz, H-7), 3.82 (3H, s, 1-OMe), 3.54 (3H, q, J = 1.0 Hz, 2′-OMe), 2.17 (1H, d, J = 4.3 Hz, 7-OH), 1.12 (3H, d, J = 6.3 Hz, H-9).

Compound 1d: t_R 24.8 min (47.5% of total reaction product); ^{1}H NMR ($CDCl_3$) δ 7.53 (2H, m, H-4′/8′), 7.40 (3H, m, H-5′-7′), 7.21 (2H, d, J = 8.0 Hz, H-3/5), 6.85

(2H, d, J = 8.7 Hz, H-2/6), 5.29 (1H, dq, J = 7.5, 6.4 Hz, H-8), 4.57 (1H, dd, J = 7.5, 3.4 Hz, H-7), 3.80 (3H, s, 1-OMe), 3.57 (3H, q, J = 1.1 Hz, 2′-OMe), 2.11 (1H, d, J = 3.4 Hz, 7-OH), 1.19 (3H, d, J = 6.4 Hz, H-9).

Compound 1e: t_R 32.4 min (18.4% of total reaction product); ^{1}H NMR ($CDCl_3$) δ 7.42 (2H, m, H-4′/8′), 7.38 (3H, m, H-5′-7′), 7.29 (2H, d, J = 8.7 Hz, H-3/5), 6.89 (2H, d, J = 8.7 Hz, H-2/6), 5.63 (1H, d, J = 8.1 Hz, H-7), 4.07 (1H, m, H-8), 3.82 (3H, s, 1-OMe), 3.44 (3H, q, J = 0.7 Hz, 2′-OMe), 1.90 (1H, d, J = 3.7 Hz, 8-OH), 1.00 (3H, d, J = 6.4 Hz, H-9).

Compound 1f: t_R 35.4 min (10.4% of total reaction product); ^{1}H NMR ($CDCl_3$) δ 7.41−7.34 (5H, m, H-4′-8′), 7.15 (2H, d, J = 8.7 Hz, H-3/5), 6.84 (2H, d, J = 8.7 Hz, H-2/6), 5.58 (1H, d, J = 8.1 Hz, H-7), 4.09 (1H, m, H-8), 3.81 (3H, s, 1-OMe), 3.53 (3H, q, J = 1.0 Hz, 2′-OMe), 2.05 (1H, d, J = 2.5 Hz, 8-OH), 1.05 (3H, d, J = 6.4 Hz, H-9).

Derivatization of 1a with (*R*)-(−)-MTPCl To Form (*S*)-MTPA Esters 1g−j (1g Is Mirror Image of 1c, 1h Is Mirror Image of 1d, 1i Is Mirror Image of 1e, 1j Is Mirror Image of 1f). The same experimental procedure was adopted as for (*S*)-(+)-MTPCl. Chromatographic data were identical to within 0.1 min (2% peak area) for **1g** and **1c**. NMR data for **1g** were identical to within 0.01 ppm with **1c** (except 7-OH). Chromatographic data were identical to within 0.1 min (2% peak area) for **1h** and **1d.** NMR data for **1h** were identical within 0.01 ppm with **1d** (except 7-OH). Chromatographic data were identical to within 0.1 min (2% peak area) for **1i** and **1e.** NMR data for **1i** were identical within 0.01 ppm with **1e** (except 8-OH). Chromatographic data were identical to within 0.1 min (2% peak area) for **1j** and **1f**. NMR data for **1j** were identical within 0.01 ppm with **1f** (except 8-OH).

8-(4-Methoxybenoloyl)anethole glycol, verimol A (2): oil; IR ($CHCl_3$) ν_{max} 3400 (br), 3013, 2936, 2841, 1707, 1607, 1514, 1254, 1169 cm^{-1}; ^{1}H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS m/z 255 (10), 227 (20), 165 (30), 148 (35), 135.0444 (calcd for $C_8H_7O_2$, Δ 0.2 mmu, i.e., MeO(C_6H_4)CO^+) (100).

7-(4-Methoxybenzoloyl)anethole glycol, verimol B (3): oil; IR ($CHCl_3$) ν_{max} 3612, 3443 (br), 3013, 2974, 2928, 1713, 1607, 1514, 1252 cm^{-1}; ^{1}H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS m/z 272 (12) [$M^+ - C_2H_4O$], 227 (8), 148 (10), 135.0444 (calcd for $C_8H_7O_2$, Δ 0.2 mmu, i.e., MeO(C_6H_4)CO^+) (100).

Derivatization of 3 with (*S*)-(+)-MTPCl To Form (*R*)-MTPA Esters 3a and 3b. To a solution of **3** (15.0 mg) in pyridine (0.16 mL) was added (*S*)-(+)-MTPCl (0.016 mL). The solution was allowed to stand at room temperature for 13 h, and then *N*,*N*-diisopropylethylamine (0.016 mL) was added and the mixture allowed to stand for 10 min. The solvent was evaporated to yield a crude product that was purified by HPLC in 15% ethyl acetate/hexane, yielding compounds **3a** and **3b**.

Compound 3a: t_R 29.1 min (51.7% of total reaction product); ^{1}H NMR ($CDCl_3$) δ 7.97 (2H, d, J = 8.8 Hz, H-3′/5′), 7.38 (2H, d, J = 8.0 Hz, H-4″/8″), 7.34 (2H, d, J = 8.6 Hz, H-3/5), 7.28 (1H, t, J = 8.0 Hz, H-6″), 7.16 (2H, t, J = 8.0 Hz, H-5″/7″), 6.90 (2H, d, J = 8.8 Hz, H-2′/6′), 6.86 (2H, d, J = 8.6 Hz, H-2/6), 5.91 (1H, d, J = 7.8 Hz, H-7), 5.67 (1H, dq, J = 7.8, 6.4 Hz, H-8), 3.86 (3H, s, 1′-OMe), 3.79 (3H, s, 1-OMe), 3.42 (3H, s, 2″-OMe), 1.17 (3H, d, J = 6.4 Hz, H-9).

Compound 3b: t_R 32.2 min (48.3% of total reaction product); ^{1}H NMR ($CDCl_3$) δ 7.95 (2H, d, J = 8.9 Hz, H-3′/5′), 7.42 (2H, d, J = 7.8 Hz, H-4″/8″), 7.30 (2H, d, J = 8.7 Hz, H-3/5), 7.27 (1H, t, J = 7.8 Hz, H-6″), 7.15 (2H, t, J = 7.8 Hz, H-5″/7″), 6.90 (2H, d, J = 8.9 Hz, H-2′/6′), 6.83 (2H, d, J = 8.7 Hz, H-2/6), 5.87 (1H, d, J = 7.7 Hz, H-7), 5.67 (1H, dq, J = 7.7, 6.5 Hz, H-8), 3.86 (3H, s, 4′-OMe), 3.77 (3H, s, 1-OMe), 3.46 (3H, d, J = 0.7 Hz, 2″-OMe), 1.24 (3H, d, J = 6.5 Hz, H-9).

Derivatization of 3 with (*R*)-(−)-MTPCl To Form (*S*)-MTPA Esters 3c and 3d. The same procedure was adopted as for **3** with (*S*)-(+)-MTPCl. Chromatographic data for **3c** were identical with **3a** within 0.1 min (2% peak integral). NMR data for **3c** were identical to **3a** within 0.01 ppm. Chromatographic data for **3d** were identical with **3b** within 0.1 min (2% peak integral). NMR data for **3d** were identical to **3b** within 0.01 ppm.

Verimol C (4): oil; $[\alpha]_D$ +2.1° (*c* 0.08, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3013, 2961, 2934, 2839, 1614, 1516, 1248 cm^{-1}; ^{1}H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS m/z 300.1357 (5) (calcd for $C_{18}H_{20}O_4$, Δ 0.5 mmu), 256 (10), 227 (50), 164 (100), 135 (30), 120 (45).

Verimol D (5): oil; $[\alpha]_D$ −1.5° (*c* 0.58, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3393 (br), 3009, 2966, 2936, 2839, 1612, 1514, 1248 cm^{-1}; ^{1}H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS m/z 302.1508 (5) (calcd for $C_{18}H_{22}O_4$, Δ 1.0 mmu), 301 (30), 255 (30), 240 (100), 225 (55), 165 (90), 137 (100), 119 (60).

Verimol E (6): oil; $[\alpha]_D$ +7.0° (*c* 0.43, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3609, 3420 (br), 3011, 2970, 2936, 2840, 1612, 1514, 1250 cm^{-1}; ^{1}H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS m/z 302.1511 (35) (calcd for $C_{18}H_{22}O_4$, Δ 0.7 mmu) (30), 301 (100), 284 (35), 137 (100).

Derivatization of 6 with 2,2-Dimethoxypropane. Compound **6** (20.2 mg) was dissolved in benzene (3 mL) and 2,2-dimethoxypropane (0.16 mL) added with a trace of *p*-toluenesulfonic acid. The mixture was stirred under reflux for 90 min and 0.32 mg K_2CO_3 added and then stirred for a further 4 h at room temperature. The mixture was extracted with CH_2Cl_2 and dried ($MgSO_4$). Purification of the crude product yielded **6a** (2.1 mg).

Compound 6a: ^{1}H NMR ($CDCl_3$) δ 7.00 (2H, d, J = 8.7 Hz, H-2′/6′), 6.85 (2H, br d, H-2/6), 6.71 (2H, d, J = 8.7 Hz, H-3/5), 6.68 (2H, d, J = 8.7 Hz, H-3′/6′), 4.87 (1H, d, J = 10.5 Hz, H-7′), 4.29 (1H, dq, J = 10.5, 6.0 Hz, H-8), 3.74 (3H, s, 1-OMe), 3.71 (3H, s, 1′-OMe), 2.46 (1H, t, J = 10.5 Hz, H-7), 1.71 (3H, s, H-2″), 1.56 (3H, s, H-3″), 1.02 (3H, d, J = 6.0 Hz, H-9); ^{13}C NMR ($CDCl_3$) δ 158.8 C (C-1′), 158.2 (C-1), 132.7 C (C-4′), 130.5 C (C-4), 129.5 CH × 2 (br) (C-3/5), 128.3 CH × 2 (C-3′/5′), 113.8 CH × 2 (C-2/6), 113.3 CH × 2 (C-2′/6′) 98.7 C (C-1″), 76.9 CH (C-7′), 70.0 CH (C-8), 55.5 CH (C-7), 55.15 CH_3 (1′-OMe), 55.11 CH_3 (1-OMe), 30.3 CH_3 (C-3″), 20.1 CH_3 (C-9), 19.9 CH_3 (C-2″).

Compound 6b: ^{1}H NMR ($CDCl_3$) δ 7.43 (4H, d, J = 8.8 Hz, H-3/3′/5/5′), 6.93 (2H, s, H-7/7′), 6.88 (4H, d, J = 8.8 Hz, H-2/2′/6/6′), 3.83 (6H, s, 1-OMe, 1′-OMe);^{13}C NMR ($CDCl_3$) δ 150.9 C × 2 (C-1/1′), 130.5 C × 2 (C-4/4′), 127.4 CH × 4 (C-3/3′/5/5′), 126.2 CH × 2 (C-7/7′), 114.1 CH × 4 (C-2/2′/6/6′), 55.3 CH_3 × 2 (1-OMe/1′-OMe).

Verimol F (7): oil; $[\alpha]_D$ +5.5° (*c* 0.52, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3583, 3458 (br), 3011, 2974, 2936, 2847, 1609, 1510, 1250 cm^{-1}; ^1H NMR and ^{13}C NMR, Tables 1 and 2; HREIMS *m/z* 272.1414 (2) (calcd for $C_{17}H_{20}O_3$, Δ −0.2 mmu), 227 (100), 212 (5).

Verimol G (8): oil; $[\alpha]_D$ +1.6° (*c* 1.67, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3620, 3420 (br), 3013, 2976, 2930, 2899, 1610, 1510, 1250 cm^{-1}; ^1H NMR and ^{13}C NMR, Table 3; HREIMS *m/z* 301.1438 [$M^+ - C_2H_5O$] (10) (calcd for $C_{18}H_{21}O_4$, Δ 0.2 mmu), 165 (35), 148 (100), 137 (95), 121 (20).

Verimol H (9): oil; $[\alpha]_D$ 0.0° (*c* 1.23, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3007, 2932, 2857, 1612, 1516, 1464, 1250 cm^{-1}; ^1H NMR and ^{13}C NMR, Table 3; HREIMS *m/z* 328.1670 (10) (calcd for $C_{20}H_{24}O_4$, Δ 0.4 mmu), 148 (100).

Verimol I (10): oil; ^1H NMR ($CDCl_3$) δ 7.33 (2H, d, J = 8.7 Hz, H-3/5), 6.86 (2H, d, J = 8.7 Hz, H-2/6), 6.60 (1H, d, J = 15.9 Hz, H-7), 6.15 (1H, dt, J = 15.9, 6.6 Hz, H-8), 4.70 (2H, d, J = 6.6 Hz, H-9), 3.81 (3H, s, 1-OMe), 2.10 (3H, s, *Me*CO); ^{13}C NMR ($CDCl_3$) δ 170.9 C (C=O), 159.6 C (C-1), 134.1 CH (C-7), 129.0 C (C-4), 127.9 CH × 2 (C-3/5), 120.9 CH (C-8), 114.1 CH × 2 (C-2/6), 65.4 CH_2 (C-9), 55.3 CH_3 (1-OMe), 21.1 CH_3 (*Me*CO).

Verimol J (12): oil; IR ($CHCl_3$) ν_{max} 3419 (br), 3011, 2974, 1610, 1510, 1220 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.91 (1H, d, J = 8.3 Hz, H-5), 6.51 (1H, d, J = 2.6 Hz, H-2), 6.41 (1H, dd, J = 8.3, 2.6 Hz, H-6), 4.20 (1H, m, H-8), 3.77 (3H, s, 1-OMe), 2.82 (1H, dd, J = 14.7, 2.6 Hz, H-7a) 2.69 (1H, dd, J = 14.7, 7.2 Hz, H-7b), 1.26 (3H, d, J = 6.2 Hz, H-9); ^{13}C NMR ($CDCl_3$) δ 160.0 C (C-1), 156.7 C (C-3), 132.1 CH (C-5), 117.5 C (C-4), 106.2 CH (C-6), 102.8 CH (C-2), 70.7 CH (C-8), 55.3 CH_3 (1-OMe), 39.9 CH_2 (C-7), 23.2 CH_3 (C-9); HREIMS *m/z* 182.0945 (35) (calcd for $C_{10}H_{14}O_3$, Δ −0.2 mmu), 164 (45), 137 (100).

Compound (13): oil; IR ($CHCl_3$) ν_{max} 3531, 3003, 2932, 2855, 1610, 1514, 1269 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.79 (2H, d, J = 7.9 Hz, H-6/6′), 6.58 (2H, dd, J = 7.9, 1.9 Hz, H-5/5′), 6.49 (2H, d, J = 1.9 Hz, H-3/3′), 3.91 (2H, dd, J = 8.6, 6.6 Hz, H-9a/9a′), 3.82 (6H, s, 2-OMe, 2′-OMe), 3.56 (2H, dd, J = 8.6, 5.3 Hz, H-9b/9b′), 2.58 (2H, dd, J = 13.7, 7.7 Hz, H-7a/7a′); 2.52 (2H, dd, J = 13.7, 7.7 Hz, H-7b/7b′), 2.16 (2H, m, H-8/8′); ^{13}C NMR ($CDCl_3$) δ 146.4 C (C-2/2′), 143.9 C (C-1/1′), 132.3 C (C-4/4′), 121.4 CH (C-5/5′), 114.1 CH (C-6/6′), 111.1 CH (C-3/3′) 73.3 CH_2 (C-9/9′), 55.8 CH_3 (2/2′-OMe), 46.5 CH (C-8/8′) 39.2 CH_2 (C-7/7′); HREIMS *m/z* 344.1619 (100) (calcd for $C_{20}H_{24}O_5$, Δ 0.5 mmu), 165 (5), 148 (20), 138 (60).

Verimol K (14): oil; ^1H NMR ($CDCl_3$) δ 9.69 (2H, br s, 1′/3′-OH), 7.43 (5H, m, H-3−7), 7.31 (1H, t, J = 8.3 Hz, H-5′), 6.46 (2H, d, J = 8.3 Hz, H-4′/6′), 5.50 (2H, s, H-1); ^{13}C NMR ($CDCl_3$) δ 169.5 C (C-7′), 161.0 C (C-1/3), 136.8 CH (C-5′), 133.9 C (C-2), 129.4 CH (C-5), 129.1 CH (C-4/6), 128.8 CH (C-3/7), 108.3 CH (C-4′/6′), 100.1 C (C-2′), 68.3 CH_2 (C-1); HREIMS *m/z* 244.0737 (15) (calcd for $C_{14}H_{12}O_4$, Δ −0.2 mmu), 91 (100).

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