Syntheses of Two Cytotoxic Sinapyl Alcohol Derivatives and Isolation of Four New Related Compounds from *Ligularia nelumbifolia*

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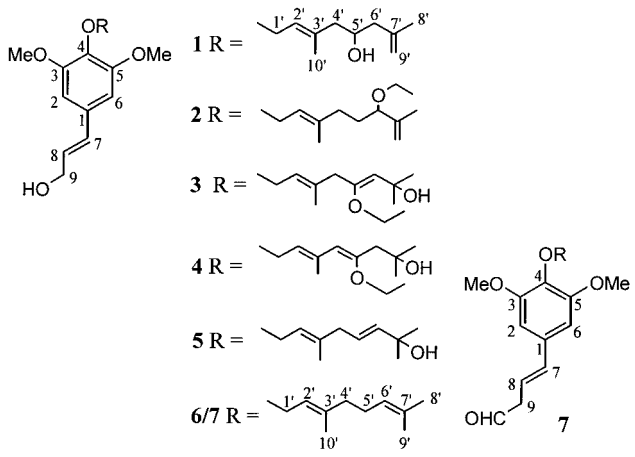
Phytochemical reinvestigation on *Ligularia nelumbifolia* afforded four novel sinapyl alcohol analogues named nelumols B−E (**1**−**4**) and three known sinapyl alcohol derivatives (**5**−**7**). Their structures were elucidated by NMR techniques. Total syntheses of cytotoxic geranyloxy sinapyl alcohol (**6**) and geranyloxy sinapyl aldehyde (**7**) were carried out via two different paths. The 4-*O*-benzyl-substituted analogues (**20** and **27**) as well as the 4-*O*-(2-methylbutenyl) derivatives (**34** and **35**) were also synthesized. The cytotoxicities of **6** and **7** were measured using A-549, HL-60, and KB cancer cell lines.

The genus *Ligularia* has been used medicinally for a long time in China. Distributed in damp shadowy regions beside brooks and sloping fields, the whole plant of *Ligularia nelumbifolia* [(Bur. Et Franch) Hand.-Mazz] (family Compositae, Chinese folk name Lian Ye Tuo Wu) has been used as folk medicine for pulmonary tuberculosis and apoplexy.[1] Previous phytochemical examination of *Ligularia* species revealed eremophilane derivatives.[2−6] Interestingly, no eremophilane derivatives were found in the species investigated by us; however, several sinapyl alcohol derivatives and aromatic components were isolated.[3] Thorough examination of this species has now afforded five further sinapyl alcohol derivatives (**1**−**5**), four of which (**1**−**4**) are new compunds. In the course of our continuing search for pharmacologically active compounds, two major principles of this species, geranyloxy sinapyl alcohol (**6**)[3,7] and geranyloxy sinapyl aldehyde (**7**), were found to be cytotoxic to KB cell with an IC_{50} of 3.0×10^{-6} and 2.6×10^{-6} M, respectively. This prompted us to reinvestigate further analogues in this plant and to synthesize compounds **6** and **7** as well as several analogues for further pharmacological activity studies.



Results and Discussion

Nelumol B (**1**) was obtained as colorless gum. EIMS and elemental analysis indicated its molecular formula to be $C_{21}H_{30}O_5$. Showing the molecular ion peak at *m*/*z* 362, the EIMS of **1** also exhibited a base peak due to a sinapyl alcohol fragment at *m*/*z* 210. The ^{1}H and ^{13}C NMR spectra of **1** showed close similarities with those of the geranyloxy sinapyl alcohol (**6**).[3,7] In the ^{1}H NMR spectrum (Table 1), the only differences were the presence in **1** of an olefinic methylene multiplet (H-9′) at δ 5.00 (1H, brs) and 4.98 (1H, brs), as well as an olefinic methyl signal (H-8′) at δ 1.73 (brs, 3H) in place of the olefinic H-6′ and Me-9′ signals of **6**. Furthermore, a signal was detected at δ 3.88 (m, 1H), suggesting a secondary OH group at the C-5′ position. This was supported by an OH absorption band at 3399 cm^{-1} in the IR spectrum of **1**. The ^{13}C NMR spectrum of **1** was in complete accord with the proposed structure (Table 2).

Comparison of the ^{1}H and ^{13}C NMR spectra of **2** with those of **1** indicated that **2** had an oxygenated C-6′, since H-6′ was shifted downfield (from δ 2.06 to 4.55) when compared to **1**, thus disclosing that H-6′ was vicinal to the 7′(9′) double bond in the case of **2**. Furthermore, the ^{1}H NMR spectrum of **2** revealed the presence of an ethoxy group at C-6′. EIMS gave the molecular ion peak at *m*/*z* 390, which was consistent with the molecular formula $C_{23}H_{34}O_5$. Since ethanol was exclusive during the extraction and isolation procedure, compound **2** might be derived biosynthetically from precursor **6**.

The ^{1}H NMR spectrum of nelumol D (**3**) exhibited some differences from that of geranyloxy sinapyl alcohol **6**. The methylene proton (H-5′) of **6** could not be found in the ^{1}H NMR spectrum of **3**, while two olefinic hydrogens were observable at δ 5.58 (m, 2H). Furthermore, the methyl singlets appeared at δ 1.33 (s, 6H), somewhat higher field than those of **6** in the ^{1}H NMR spectrum, suggesting that an OH group was most likely connected to C-7′, in agreement with the corresponding ^{13}C resonance appearing at δ 82.04 (s, C-7′). The olefinic carbons attributable to a trisubstituted double bond at δ 140.16 (s) and 127.88 (d)

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Table 1. ^{1}H NMR Spectral Data [400 MHz, δ_H (J, Hz)] for Nelumols B−E (**1**−**4**) in $CDCl_3$

position	**1**	**2**	**3**	**4**
2	6.59 s	6.60 s	6.61 s	6.61 s
6	6.59 s	6.60 s	6.61 s	6.61 s
7	6.52 dt (15.8, 1.4)	6.52 dt (15.9, 1.4)	6.55 dt (15.9, 1.4)	6.55 dt (16.0, 1.5)
8	6.28 dt (15.8, 5.8)	6.28 dt (15.9, 5.8)	6.30 dt (15.9, 6.0)	6.30 dt (16.0, 6.0)
9	4.32 dd (5.8, 1.4)	4.32 dd (5.8, 1.4)	4.32 dd (6.0, 1.4)	4.33 dd (6.0, 1.5)
1′	4.54 br d (7.2)	4.54 br d (7.1)	4.55 br d (7.0)	4.54 br d (7.2)
2′	5.66 tq (7.2, 1.0)	5.58 tq (7.1, 1.0)	5.58 m	5.61 tq (7.1, 1.0)
4′	2.06 m	2.02 m	2.74 m	5.47 dt (2.0, 1.5)
5′	3.88 m	2.00 m		
6′	2.06 m	4.55 br dt (7.0, 1.5)	5.58 m	2.74 dd (6.6, 2.0)
8′	1.73 br s	1.63 br s	1.31 s	1.26 s
9′	5.00 br s	4.92 br dd (1.5, 1.5)	1.31 s	1.26 s
	4.98 br s	4.83 br dd (1.5, 1.5)		
10′	1.65 d (1.0)	1.65 d (1.0)	1.63 d (0.9)	1.63 d (1.0)
OMe	3.86 s	3.87 s	3.87 s	3.86 s
OEt		3.65 q (7.0)	3.49 q (7.0)	3.32 q (7.0)
		1.24 t (7.0)	1.22 t (7.0)	1.14 t (7.0)

Table 2. ^{13}C NMR Spectral Data [100 MHz, δ (ppm)] for Nelumols B−E (**1**−**4**) in $CDCl_3$[a]

C no.	**1** (mult)	**2** (mult)	**3** (mult)	**4** (mult)
1	136.5 s	136.3 s	136.6 s	138.0 s
2	103.5 d	103.3 d	103.3 d	103.4 d
3	153.7 s	153.6 s	153.7 s	153.7 s
4	139.8 s	141.0 s	139.8 s	140.0 s
5	153.7 s	153.6 s	153.7 s	153.7
6	103.5 d	103.3 d	103.3 d	103.4 s
7	131.2 d	131.1 d	131.2 d	131.2 d
8	129.0 d	127.8 d	127.9 d	127.9 d
9	63.6 t	63.5 t	63.7 t	63.7 t
1′	69.2 t	69.2 t	69.3 t	69.4 t
2′	121.4 d	120.6 d	121.2 d	121.2 d
3′	132.4 s	132.3 s	132.3 s	132.3 s
4′	39.5 t	35.4 t	42.2 t	126.9 d
5′	88.9 d	32.5 t	140.2 s	140.2 s
6′	28.7 t	75.2 d	127.9 d	42.6 t
7′	143.8 t	147.2 s	70.8s	74.8 s
8′	17.1 q	17.4 q	29.7 q	26.4 q
9′	114.1 t	111.0 t	29.7 q	26.4 q
10′	16.1 q	16.1 q	16.3 q	16.2 q
OMe	56.1 q	56.0 q	56.0 q	56.0 q
OEt		63.8 t	56.0 t	57.7 t

[a] Assignment in the same column could be exchangeable.

were assigned to C-5′ and C-6′, respectively. This side chain is similar to that of the sinapyl alcohol derivative **5**, previously isolated from *Ligularia duciformis*.[8] However, the molecular ion peak of **3** appearing at *m*/*z* 406, i.e., 44 mass units higher than that of **5**, as well as the NMR data all indicated that **3** was an C-5′-OEt derivative of **5** (Tables 1 and 2). Compound **3** might be another artifact or the enzymatic derivative of **5**, as mentioned above.

Nelumol E (**4**) had a molecular ion peak and NMR data similar to those of **3**. Elemental analysis and a DEPT spectrum revealed its molecular formula to be $C_{23}H_{34}O_6$, apparently isomeric with **3**. Scrutiny of its ^{1}H and ^{13}C NMR spectra with those of **3** led to the assignment of a 2′(3′),4′-(5′)-diene system in compound **4** (Tables 1 and 2). A COLOC experiment on **4** exhibited correlations of olefinic H-4′ with C-2′ and C-10′, consistent with the presence of a conjugated diene moiety in **4**. This enol ether could be either an artifact or a biosynthetic derivative, as discussed above.

As **6** and **7** were cytotoxic to KB cells (Table 3) and appeared as principle metabolites in *L. nelumbifolia*, syntheses of further sinapyl alcohol derivatives become interesting. Thus, **6** and **7** were selected to be totally synthesized.

The first path used commercially available sinapinic acid **8** as starting material. After esterification,[9] a Mitsunobu reaction of the resulting methyl ester **9** with geranyl alcohol led to the geranyl derivative **10**.[10] Reduction of **10** by DIBAH afforded geranyloxy sinapyl alcohol **6** in an 86% yield, while oxidation of **6** by magnesium dioxide gave geranyloxy sinapyl aldehyde **7** in 92% yield (Scheme 1).

Table 3. IC_{50} of **6** and **7** on Some Selected Pharmacological Models

	A-549 cell	HL-60 cell	KB cell
6	3.4×10^{-5} M	6.7×10^{-6} M	3.0×10^{-6} M
7	2.2×10^{-5} M	1.2×10^{-5} M	2.6×10^{-6}M

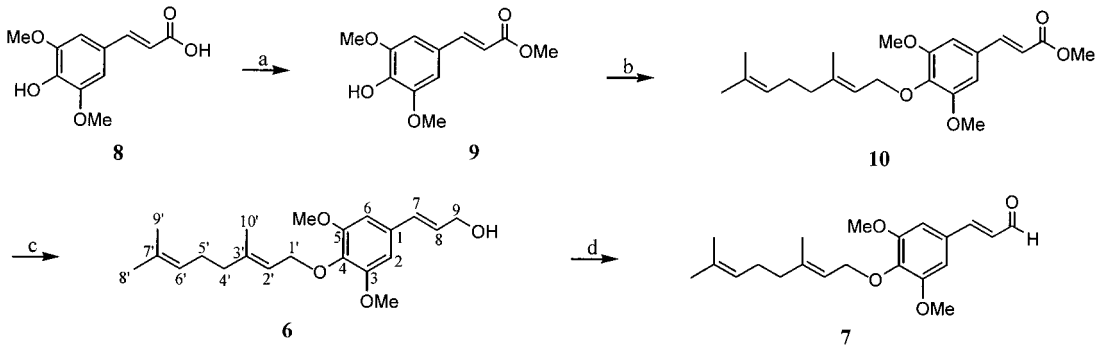
Another synthetic path started from methyl gallate (**11**) (Scheme 2) Acetylation led to product **12**, which was subjected to a selective substitution reaction,[11] during which the 4-acetoxy group was replaced by a geranyl moiety to yield compound **13b**. The unexpected mono-deacetylated product **13a** was also formed in the reaction. The reaction time and the temperature influenced the yields of **13a** and **13b**. The mixture of **13a** and **13b** was treated with aqueous K_2CO_3 to give **14**, which was then transformed to the methoxy derivative **15** (82% yield over two steps). Reduction of **15** by LAH afforded primary alcohol **16**, which was oxidized to aldehyde **17** by pyridinium chlorochromate in 86% yield. A Knoevenagel condensation of **17** with malonic acid in the presence of piperidine afforded the *E*-form of acid **18**. Reduction of **18** by LAH afforded, apart from the 80% yield of expected target molecule **6**, the 1,4-addition product **19** in 5% yield. Finally, geranyloxy sinapyl aldehyde **7** was obtained by manganese dioxide oxidation in 92% yield. The total yield of **8** was 28%. Cytotoxic screening results of synthetic **6** and **7** against A-549, HL-60, and KB cell lines are shown in Table 3.

To examine the importance of the C-4 side chain on cytotoxicity, we designed another target molecule (**20**) with a benzyl group attached to O-C(4). Furthermore, a five-carbon side chain (compound **34**) was also introduced to extend the SAR concept. Two paths were examined to synthesize these analogues, which are shown in Schemes 2 and 3. Cytotoxicity screening of **20**, **27**, **34**, and **35** is shown in Table 4. It was seen that compounds **20** and **27** were less cytotoxic to KB cells than **6** and **7**, while the five-carbon side chain derivatives **34** and **35** had cytotoxicities to KB cells similar to those of **1** and **2**.

Experimental Section

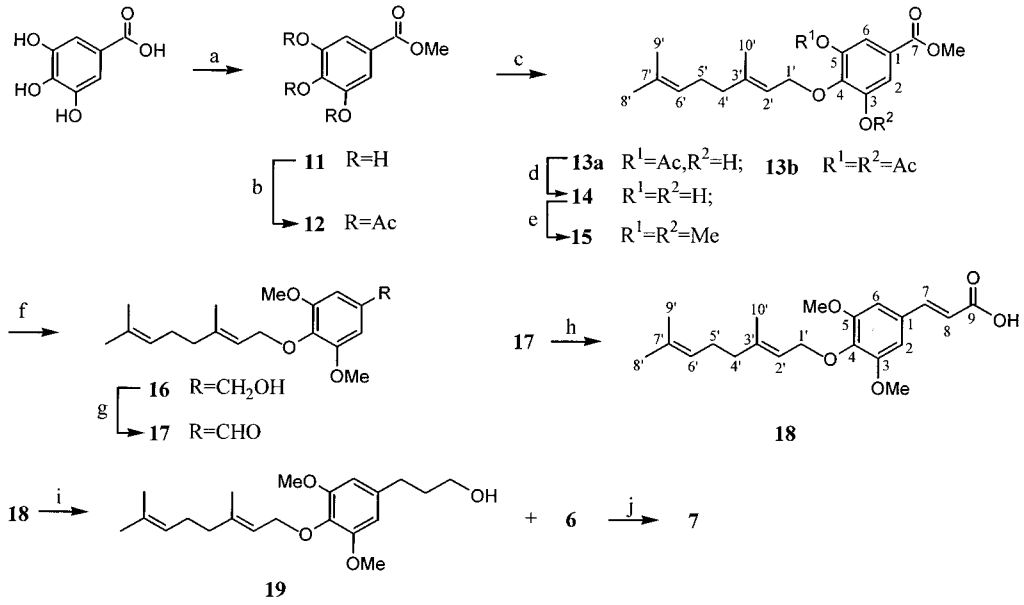
General Experimental Procedures. ^{1}H NMR and ^{13}C NMR spectra were measured on Bruker AM-400 MHz and Bruker AC-300 MHz NMR instruments, with TMS as internal

Scheme 1[a]



[a] (a) H_2SO_4, MeOH, reflux, 2 h, 98%; (b) geranyl alcohol, Ph_3P, DEAD, 24 h, 50%; (c) DIBAH, THF, −78 °C, 2 h, 86%; (d) 1: PCC, CH_2Cl_2, rt, 6 h, 81%; 2: MnO_2, EtOAc, rt, 92%.

Scheme 2[a]



[a] (a) H_2SO_4, MeOH, reflux, 2 h, 96%; (b) Ac_2O, Py, rt, 12 h, 93%; (c) geranyl bromide, K_2CO_3, DMF, 0 °C, 24 h, 50% of **13b**, 29% of **13a**; (d) K_2CO_3, MeOH−H_2O, rt, 0.5 h, 90%; (e) MeI, K_2CO_3, reflux, 3 h, 91%; (f) LAH, ether, 0 °C, 90%; (g) PCC, CH_2Cl_2, rt, 6 h, 86%; (h) malonic acid, piperidine, Py, reflux, 4 h, 86%; (i) LAH, ether, 0 °C, 80% of **6**, 5% of **19**; (j) MnO_2, EtOAc, rt, 2 h, 92%.

Table 4. IC_{50} of Compounds **20**, **27**, **34**, and **35** on KB Cells (mol/L)

20	27	34	35
8.6 × 10−4	6.4 × 10−4	7.8 × 10−6	5.3 × 10−6

standard. HREIMS and EIMS were performed on a VG Auto Spec-3000 MS instrument. EIMS: direct inlet, 70 eV. Solvents and reagents were purified according to standard laboratory techniques. IR spectra were recorded on a Perkin-Elmer 577 spectrometer.

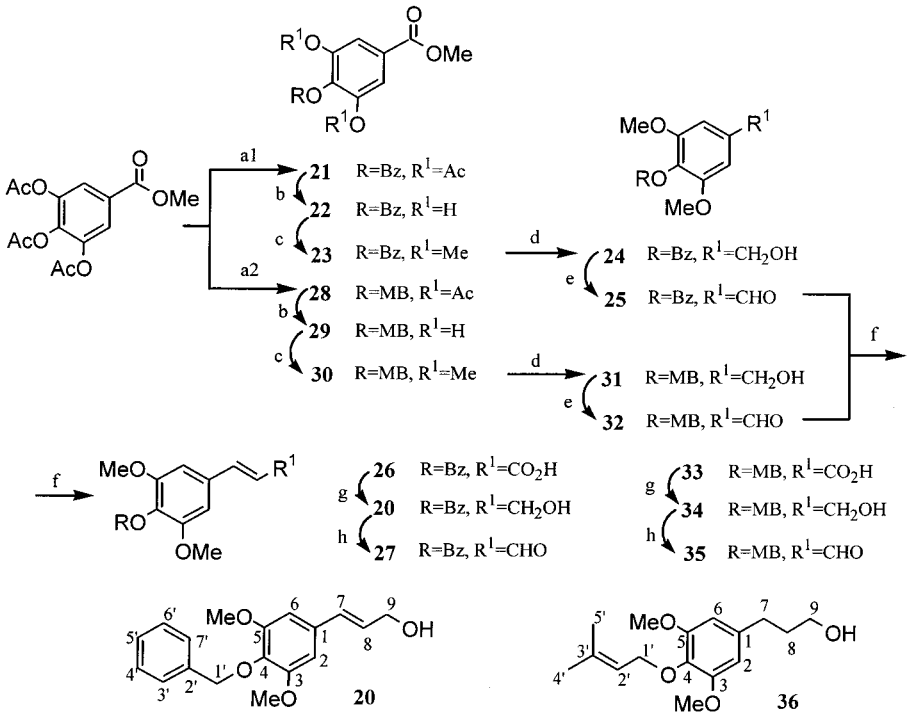
Plant Material. The material plant was collected in August 2000, Zhaotong County, Yunnan Province, China, and identified by Prof. Hua Peng. A voucher specimen (no. 20000806) is deposited in the Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, Yunan Province, China.

Extraction and Isolation. Air-dried roots of *Ligularia nelumbifolia* [(Bur. Et Franch) Hand.-Mazz] (2.0 kg) were powdered and extracted with petroleum ether (60−90 °C)−Et_2O−MeOH (1:1:1) at room temperature (3 days × 3) to give 85 g of crude extract, which was subjected to column chromatography on 1 kg of silica gel with petroleum ether containing gradually increasing amounts of EtOAc (1:0−1:1). Ten crude fractions (F_1−F_{10}) were obtained. F_1−F_7 contained, by TLC, mainly the same products reported previously.[3] F_8 (2.1 g) afforded, after repeated column chromatography, 86 mg of **6** and 35 mg of **7**. F_9 (3.2 g) was chromatographed (200 g of silica gel gel, 200−300 mesh) using a $CHCl_3$−Me_2CO (20:1−1:1) step gradient. Eluates 25−28 (150 mL each) were combined and purified by PTLC ($CHCl_3$−Me_2CO, 3:1) to give 14 mg of **1** (R_f = 0.46). Eluate 14 (120 mL) was evaporated and purified by PTLC (C_6H_6−Me_2CO, 4:1) to give 21 mg of **2**. Eluate 17 (80 mL) contained 26 mg of **5**, which was obtained by PTLC with C_6H_6−Me_2CO, 8:1 (R_f = 0.65). F_{10} (6.6 g) was rechromatographed over silica H (200 g) with a $CHCl_3$−EtOAc (10:1−1:2) solvent system. Eluates 16−17 (125 mL each) were combined and evaporated, and the residue (86 mg) was purified through PTLC ($CHCl_3$−MeOH, 8:1) to afford 17 mg of **3** (R_f = 0.57) and 15 mg of **4** (R_f = 0.49).

4-*O*-[(2*E*)-3,7-Dimethyl-2,7-octadien-5-ol]sinapyl alcohol (1): gum; IR (KBr) ν_{max} 3399 (OH), 3349 (OH), 2977, 1659, 1583, 1504, 1459, 1420, 1332, 1241, 1127, 963 cm^{-1}; EIMS *m/z* (rel int) 362 $[M]^+$ (16), 347 (3), 344 (5), 329 (6), 306 (14), 277 (10), 252 (18), 238 (50), 210 (100), 182 (36), 167 (42), 154 (18); ^1H NMR ($CDCl_3$) data, see Table 1; ^{13}C NMR ($CDCl_3$) data, see Table 2; *anal.* C 69.56%, H 8.27%, calcd for $C_{21}H_{30}O$, C 69.61%, H 8.29%.

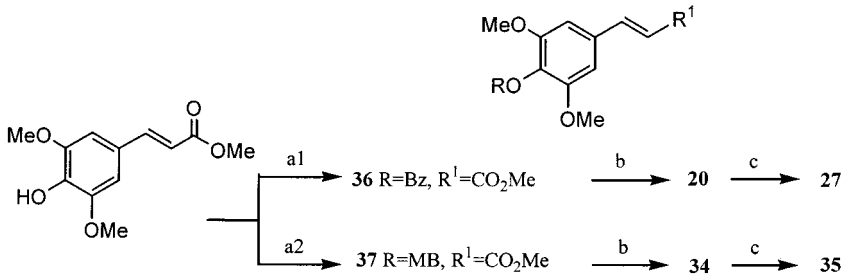
4-*O*-[(2*E*)-3,7-Dimethyl-6-ethoxy-2,7-octadiene]-sinapyl alcohol (2): gum; IR (KBr) ν_{max} 3398 br (OH), 3072, 2939, 1653, 1583, 1504, 1456, 1418, 1333, 1241, 1128, 992, 904, 629 cm^{-1}; EIMS *m/z* (rel int) 390 $[M]^+$, (15), 375 (22), 349 (18), 344 (16), 277 (10), 210 (100), 182 (55), 167 (43), 137 (16), 121 (14), 113 (20), 69 (72), 46 (23); ^1H NMR ($CDCl_3$) data, see Table

Scheme 3[a]



[a] (a1) Benzyl bromide, DMF, 0 °C, 24 h; (a2) 2-methylbutenyl bromide, K_2CO_3, DMF, 0 °C, 10 h; (b) K_2CO_3, MeOH−H_2O, rt, 0.5 h; (c) MeI, K_2CO_3, reflux, 3 h; (d) LAH, ether, 0 °C; (e) PCC, CH_2Cl_2, rt, 6 h, (f) malonic acid, piperidine, Py, reflux, 4 h; (g) LAH, ether, 0 °C; (h) MnO_2, EtOAc, rt, 2 h (MB = 2-methylbutenyl).

Scheme 4[a]



[a] (a1) Benzol, Ph_3P, DEAD, 24 h, 65%; (a2) 2-methylbutenol, Ph_3P, DEAD, 24 h, 60%; (b) DIBAH, THF, −78 °C, 2 h; 88% of **20**, 80% of **34**; (c) 1: PCC, CH_2Cl_2, rt, 6 h; 83% of **27**, 81% of **35**; 2: MnO_2, EtOAc, rt, 92% of **27**, 94% of **35** (MB = 2-methylbutenyl).

1; ^{13}C NMR ($CDCl_3$) data, see Table 2; *anal.* C 70.73%, H 8.72%, calcd for $C_{23}H_{34}O_5$, C 70.77%, H 8.72%.

4-*O*-[(2*E*,5*E*)-3,7-Dimethyl-5-ethoxy-2,5-octadiene-7-ol]-sinapyl alcohol (3): gum; IR (KBr) ν_{max} 3408 br (OH), 2967, 2926, 1665, 1582, 1504, 1459, 1417, 1332, 1240, 1127, 969, 914, 744 cm^{-1}; EIMS *m*/*z* (rel int) 406 [M]$^+$, (8), 391 (2), 389 (5), 360 (6), 314 (15), 264 (3), 210 (100), 197 (3), 182 (25), 167 (42), 154 (16), 69 (18), 46 (48); ^{1}H NMR ($CDCl_3$) data, see Table 1; ^{13}C NMR ($CDCl_3$) data, see Table 2; *anal.* C 67.90%, H 8.31%, calcd for $C_{23}H_{34}O_6$, C 67.98%, H 8.37%.

4-*O*-[(2*E*,4*E*)-3,7-Dimethyl-5-ethoxy-2,4-octadien-7-ol]-sinapyl alcohol (4): gum, IR (KBr) ν_{max} 3402 br (OH), 3349, 2973, 2933, 1673, 1582, 1503, 1457, 1418, 1333, 1240, 1128, 969, 844 cm^{-1}; EIMS *m*/*z* (rel int) 406 [M]$^+$, (12), 391 (4), 389 (8), 374 (4), 360 (2), 343 (5), 210 (100), 197 (6), 182 (38), 167 (44), 154 (23), 128 (6), 69 (18), 46 (36); ^{1}H NMR ($CDCl_3$) data, see Table 1; ^{13}C NMR ($CDCl_3$) data, see Table 2; *anal.* C, 67.90%, H, 8.31%, calcd for $C_{23}H_{34}O_6$, C, 67.98%, H, 8.37%.

Sinapic Acid Methyl Ester (9). NMR and physical data were identical with a previous publication.[9] EIMS: *m*/*z* 238 [M]$^+$ (100), 223 (9), 207 (95), 175 (33), 163 (11), 119 (10), 91 (6). HREIMS: 238.0856 (calcd for $C_{12}H_{14}O_5$, 238.0841).

Etherification of 9. To a stirred solution of 313 mg (1.2 mmol) of Ph_3P and 240 mg of **9** (1.0 mmol) in dry THF (10 mL) was added 150 mg of geraniol (1.0 mmol) and DEAD (262 μL, 1.2 mmol) at room temperature under nitrogen. The solution was stirred overnight and then refluxed for 0.5 h. The cooled solution was partitioned between H_2O (30 mL) and EtOAc (30 mL × 3) and dried ($MgSO_4$). After filtration, the solvent was evaporated and the residue was subjected to CC (petroleum ether−Et_2O, 5:1−2:1); 186 mg of **10** was isolated (50%).

4-Geranyl sinapic acid methyl ester (10): gum; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.57 (1H, d, *J* = 16.0 Hz, H-7), 6.72 (2H, s, H-2, H-6), 6.32 (1H, d, *J* = 15.8 Hz, H-8), 5.53 (1H, brt, *J* = 7.0 Hz, H-2′), 5.05 (1H, m, H-6′), 4.55 (2H, d, *J* = 7.1 Hz, H-1′), 3.86 (6H, s, O*Me*-3, O*Me*-5), 3.79 (3H, s, CO_2*Me*), 2.03 (4H, m, H-4′, H-5′), 1.65 (3H, s, H-8′), 1.63 (3H, s, H-9′), 1.57 (3H, s, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.3 (s, C-9), 153.82 (s, C-3, C-5), 144.90 (d, C-7), 141.6 (s, C-4), 139.0 (s, C-2), 131.5 (s, C-3′), 129.7 (s, C-7), 123.92 (d, C-6′), 119.97 (d, C-2′), 116.77 (d, C-8), 105.17 (d, C-2, C-6), 69.50 (t, C-1′), 56.09 (q, O*Me*-3, O*Me*-5), 51.62 (q, CO_2*Me*), 39.57 (t, C-4′), 26.39 (t, C-5′), 25.62 (t, C-8′), 17.61 (q, C-9′), 16.31 (q, C-10′); EIMS *m*/*z* 374 [M]$^+$ (1), 343 (1), 305 (2), 266 (1), 248 (1), 238 (100), 223 (3), 207 (8), 175 (3), 163 (2), 135 (2), 69 (13); HREIMS *m*/*z* 374.2082 (calcd for $C_{22}H_{30}O_5$, 374.2093).

Reduction of 10. To a stirred solution of 374 mg (1.0 mmol) of **10** in dry Et_2O (10 mL) was added DIBAH (1.0 mL, 1.0 M in hexane) at −78 °C under nitrogen. The solution was stirred for 0.5 h, 3 mL of H_2O was added at −78 °C to quench the reaction, and the solution was allowed to warm to room

temperature. Ten milliliters of 1 M HCl was added, and the solution was extracted with EtOAc (15 mL × 3). The organic layers were combined and dried ($MgSO_4$). Purification by flash column afforded 299 mg of **6** (86%). Physical and NMR data for compound **6** have been reported in an earlier publication.[3]

Allylic Oxidation of 6 by MnO_2. To a stirred suspension of 105 mg (1.2 mmol) of MnO_2 in EtOAc (15 mL) was added 345 mg (1.0 mmol) of **6** in EtOAc (5 mL) at room temperature, and the solution was stirred for 4 h. After filtration, the eluate was evaporated to dryness and was partitioned between H_2O (20 mL) and Et_2O (60 mL). The organic layer was combined and dried ($MgSO_4$), and the solvent was evaporated to afford **7** (317 mg, 92%). Physical and NMR data for compound **7** have been reported in an earlier publication.[3]

Deacetylation of 12. To a stirred solution of 15.5 g of **12** (50 mmol) in dry DMF (150 mL) was added 20.7 g of K_2CO_3 (150 mmol) at 0 °C. The solution was stirred for 20 min and 10.85 g (9.9 mL) of geranyl bromide (60 mmol) in dry DMF (60 mL) was added in 10 min. The solution was stirred for 10 h. After suction filtration, 300 mL of H_2O was added. The mixture was extracted with EtOAc (600 mL), followed by Et_2O (600 mL). The organic layers were combined, washed with brine (100 mL), and dried ($MgSO_4$). The solution was evaporated, and the residue was subjected to CC (hexane−Et_2O, 5:1) to afford 10.11 g (25 mmol) of **13b** (50%) and 5.25 g (14.5 mmol) of **13a** (29%). Also, 925 mg (3.0 mmol) of **12** (6%) was recovered.

4-Geranoyl-3,5-diacetoxybenzoic acid methyl ester (13b): gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (2H, s, H-2, H-6), 5.42 (1H, brt, J = 7.0 Hz, H-2′), 5.09 (1H, m, H-6′), 4.59 (2H, d, J = 7.2 Hz, H-1′), 3.89 (3H, s, CO_2Me), 2.36 (3H, s, OCOCH_3), 2.09 (4H, m, H-4′, H-5′), 1.70 (3H, s, H-8′), 1.68 (3H, s, H-9′), 1.62 (3H, s, H-10′); HREIMS m/z 404.1818 (calcd for $C_{22}H_{28}O_7$, 404.1835).

4-Geranoyl-3-acetoxy-5-hydroxysinapic acid methyl ester (13a): gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (1H, brs, H− 2), 7.36 (1H, brs, H-6), 5.90 (1H, brs, O*H*-5), exchanged in D_2O), 5.48 (1H, t, J = 7.0 Hz, H-2′), 5.08 (1H, m, H-6′), 4.63 (1H, d, J = 7.1 Hz, H-1′), 3.90 (3H, s, CO_2Me), 2.36 (3H, s, OCOCH_3), 2.10 (4H, m, H-4′, H-5′), 1.70 (3H, s, H-8′), 1.66 (3H, s, H-9′), 1.61 (3H, s, H-10′); HREIMS m/z 362.1709 (calcd for $C_{20}H_{26}O_6$, 362.1729).

Deacetylation of 13 (13a and 13b) (e.g., 13a). To a stirred solution of **13a** (2.91 g, 8.0 mmol) in MeOH (200 mL) at 0 °C was added 5.66 g (43.2 mmol) of K_2CO_3 in H_2O (60 mL) in 10 min. The solution was stirred for 20 min, and the solvent was evaporated. Then 1 M HCl was added to adjust the pH value to 2, and the aqueous solution was extracted by EtOAc (300 mL). The organic layers were combined and dried ($MgSO_4$), and the solvent was evaporated to afford 2.32 g (7.2 mmol) of **14** (90%).

4-Geranoyl-3,5-hydroxybenzoic acid methyl ester (14): gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (2H, s, H-2, H-6), 5.91 (1H, s, exchanged in D_2O, ArO*H*), 5.60 (1H, brt, J = 7.0 Hz, H-2′), 5.09 (1H, m, H-6′), 4.66 (2H, d, J = 7.1 Hz, H-1′), 3.90 (3H, s, CO_2Me), 2.08 (4H, m, H-4′, H-5′), 1.70 (3H, s, H-8′), 1.66 (3H, s, H-9′), 1.61 (3H, s, H-10′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9 (s, C-7), 149.2 (s, C-3, C-5), 145.2 (s, C-1), 137.4 (s, C-4), 132.1 (s, C-3′), 126.1 (s, C-7′), 123.5 (s, C-6′), 118.7 (s, C-2′), 109.5 (d, C-2, C-6), 69.9 (t, C-1′), 52.2 (q, CO_2Me), 39.6 (t, C-4′), 26.2 (t, C-5′), 25.6 (q, C-8′), 17.7 (q, C-9′), 16.4 (q, C-10′); HREIMS δ 320.1622 (calcd for $C_{18}H_{24}O_5$, 320.1624).

4-Geranoyl-3,5-methoxybenzoic acid methyl ester (15). To a stirred solution of **14** (320 mg, 1.0 mmol) in dry DMF (30 mL) was added 8 mg of K_2CO_3 (6.0 mmol) at room temperature under argon, then 0.312 mL (5.0 mmol) of MeI in DMF (5 mL) was added. The solution was heated at 100 °C for 3 h and was cooled to 25 °C. After suction filtration, the filtrate was partitioned between H_2O (120 mL) and EtOAc−ether (100 mL/100 mL). The organic layers were combined and dried ($MgSO_4$). The solution was evaporated under reduced pressure, and the residue was subjected to PTLC; 315 mg (0.91 mmol) of **15** was obtained (91%): gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (2H, s, H-2, H-6), 5.55 (1H, brt, J = 7.0 Hz, H-2′), 5.05 (1H, m, H-6′), 4.59 (1H, d, J = 7.0 Hz, H-1′), 3.93 (3H, s, H-9′), 3.89 (6H, s, O*Me*-3, O*Me*-5), 2.04 (4H, m, H-4′, H-5′), 1.66 (3H, s, C-8′), 1.64 (3H, s, C-9′), 1.60 (3H, s, C-10′); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.8 (s, C-7), 153.4 (s, C-3, C-5), 141.9 (s, C-1), 141.2 (s, C-4), 131.6 (s, C-3′), 125.1 (s, C-7′), 123.9 (d, C-6′), 119.9 (s, C-2′), 109.6 (d, C-2, C-6), 69.4 (t, C-1′), 56.2 (q, O*Me*-3, O*Me*-5), 52.2 (q, CO_2Me), 39.6 (t, C-4′), 26.4 (t, C-5′), 25.6 (q, C-8′), 17.6 (q, C-9′), 16.3 (q, C-10′); HREIMS δ 348.1925 (calcd for $C_{20}H_{28}O_5$, 348.1937).

4-Geranoyl-3,5-dimethoxybenzyl Alcohol (16). To a stirred suspension of LAH (49 mg, 1.28 mmol) in Et_2O (50 mL) at 0 °C was added a solution of **15** (280 mg, 0.8 mmol) in dry Et_2O (20 mL) under argon atmosphere. The solution was stirred for 10 min and was quenched by H_2O (8 mL). Then 50 mL of 1 N HCl was added, and the mixture was extracted by Et_2O (150 mL). The ether layers were combined and dried ($MgSO_4$). Evaporation of the solvent followed by PTLC afforded 230 mg of **16** (0.72 mmol, 90%): gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.62 (2H, brs, H-2, H-6), 5.60 (1H, brt, J = 7.0 Hz, H-2′), 5.05 (1H, m, H-6′), 4.69 (2H, brs, H-7), 4.52 (2H, d, J = 7.1 Hz, H-1′), 3.89 (6H, s, O*Me*-3, O*Me*-5), 2.10 (4H, m, H-4′, H-5′), 1.70 (3H, s, H-8′), 1.68 (3H, s, H-9′), 1.63 (3H, s, H-10′); HREIMS m/z 320.1966 (calcd for $C_{19}H_{28}O_4$, 320.1988).

4-Geranoyl-3,5-dimethoxybenzaldehyde (17). To a stirred suspension of PCC (225 mg, 1.04 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added 208 mg of **16** (0.65 mmol) in CH_2Cl_2 (10 mL). The solution was stirred at 0 °C for 5 h. The suspension was filtered and washed by Et_2O (60 mL) and partitioned between Et_2O (90 mL) and H_2O (30 mL). The ether layers were combined, dried ($MgSO_4$), and evaporated to afford a residue. PTLC of the residue afforded finally 178 mg of **17** (0.56 mmol, 86%): gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.86 (1H, s, H-7), 7.13 (2H, s, H-2, H-6), 5.60 (1H, brt, J = 6.9 Hz, H-2′), 5.05 (1H, m, H-6), 4.77 (2H, brd, J = 7.0 Hz, H-1′), 3.94 (6H, s, O*Me*-3, O*Me*-5), 2.04 (4H, m, H-4′, H-5′), 1.64 (3H, s, H-8′), 1.63 (3H, s, H-9′), 1.57 (3H, s, H-10′); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.2 (s, C-7), 154.2 (s, C-3, C-5), 142.5 (s, C-1), 142.3 (s, C-4), 131.7 (s, C-3′), 131.8 (s, C-7′), 123.9 (d, C-6′), 119.78 (d, C-2′), 106.6 (d, C-2, C-6), 69.6 (t, C-1′), 56.3 (q, O*Me*-3, O*Me*-5), 39.6 (t, C-4′), 26.4 (t, C-5′), 25.7 (q, C-8′), 17.7 (q, C-9′), 16.4 (q, C-10′); HREIMS m/z 318.1822 (calcd for $C_{19}H_{26}O_4$, 318.1831).

4-Geranoylsinapic Acid (18). To a stirred solution of malonic acid (156 mg, 1.5 mmol) in Py (15 mL) at room temperature was added 475 mg (1.5 mmol) of **17** in Py (10 mL). Piperidine (20 mg) was added to the solution. The mixture was heated at 120 °C for 4 h. The solvent was evaporated and dried ($MgSO_4$), evaporated, and followed by CC ($CHCl_3$−MeOH, 8:1) to afford 463 mg of **18** (1.3 mmol, 86%): gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69 (1H, d, J = 15.9 Hz, H-7), 6.75 (2H, s, H-2, H-6), 6.34 (d, J = 15.8 Hz, H-8), 5.53 (1H, brt, J = 7.2 Hz, H-2′), 5.05 (1H, m, H-6′), 4.57 (2H, brd, J = 7.1 Hz, H-1′), 3.87 (6H, s, O*Me*-3, O*Me*-5), 2.03 (4H, m, H-4′, H-5′), 1.65 (3H, s, H-8′), 1.64 (3H, s, H-9′), 1.57 (3H, s, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1 (s, C-9), 154.0 (s, C-3, C-5), 147.1 (d, C-7), 141.8 (s, C-4), 139.4 (s, C-1), 131.6 (s, C-3′), 129.4 (s, C-7′), 134.0 (d, C-6′), 120.0 (d, C-2′), 116.2 (d, C-8), 105.5 (d, C-2, C-6), 69.6 (t, C-1′), 56.2 (q, O*Me*-3, O*Me*-5), 39.6 (t, C-4′), 26.4 (t, C-5′), 25.7 (q, C-8′), 17.7 (q, C-9′), 16.4 (q, C-10′); EIMS m/z 360 $[M]^+$, (3), 345 (1), 331 (11), 316 (3), 224 (100), 209 (4), 198 (26), 181 (4), 69 (23); HREIMS m/z 360.1927 (calcd for $C_{21}H_{28}O_5$, 360.1937).

4-Geranoyl-7,8-dihydrosinapic Acid (19). To a stirred solution of LAH (41 mg, 1.09 mmol) in dry Et_2O (15 mL) at 0 °C was added 195 mg (0.54 mmol) of **18** in dry Et_2O (10 mL) under argon. The mixture was stirred for 1 h at 0 °C and was quenched by H_2O (6 mL). Then 1 N HCl (10 mL) was added and extracted by Et_2O (30 mL). The ether layer was dried ($MgSO_4$), evaporated, and subjected to CC (petroleum ether−Et_2O, 1:2) to afford 150 mg of **7** (0.43 mmol, 80%) and 10 mg of **19** (0.03 mmol, 5%): gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.46 (2H, brs, H-2, H-6), 5.58 (1H, brt, J = 7.0 Hz, H-2′), 5.07 (1H, m, H-6′), 4.55 (2H, brd, J = 7.0 Hz, H-1′), 3.86 (2H, brt, J = 7.6 Hz, H-9), 3.90 (6H, s, O*Me*-3, O*Me*-5), 2.79 (2H, brt, J = 7.6 Hz, H-7), 2.01−1.94 (2H, *m*, H-8); HREIMS m/z 348.2298 (calcd for $C_{21}H_{32}O_4$, 348.2300).

4-*O*-Benzyl-3,5-diacetoxybenzoic Acid Methyl Ester (21). The method of preparation of **21** was similar to that used

for the preparation of **13**. The yield **21** from **12** was 67%. This compound was identical to that reported by Pearson et al.[11] It was noticeable that no mono-deacetylated compound was obtained in this reaction.

4-*O*-Benzyl-3,5-dihydroxybenzoic Acid Methyl Ester (22). The method of preparation of **22** was similar to that used for the preparation of **14**. The yield of **22** from **21** was 92%: gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43−7.36 (5H, m, H-3′−H-7′), 7.25 (2H, s, H-2, H-6), 5.80 (brs, exchanged in D_2O, ArO*H*), 5.16 (2H, s, H-1′), 3.90 (3H, s, CO_2*Me*); HREIMS *m*/*z* 274.0870 (calcd for $C_{15}H_{14}O_4$, 274.0841). This compound was first reported by Pearson et al.[16]

4-*O*-Benzyl-3,5-dimethoxybenzoic Acid Methyl Ester (23). The method of preparation of **23** was similar to that used for the preparation of **15**. The yield of **23** from **22** was 90%: gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25−7.5 (5H, m, H-2′−H-7′), 5.10 (2H, s, H-1′), 3.93 (3H, s, Me-8), 3.90 (3H, s, O*Me*-3, O*Me*-5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.8 (s, C-7), 153.3 (s, C-3, C-5), 141.0 (s, C-1), 137.5 (s, C-4), 128.5 (d, C-3′, C-7′), 128.27 (d, C-4′, C-6′), 128.1 (d, C-5′), 125.4 (s, C-2′), 106.9 (d, C-2, C-6), 75.0 (t, C-1′), 56.3 (q, O*Me*-3, O*Me*-5), 52.3 (q, CO_2*Me*); HREIMS *m*/*z* 302.1133 (calcd for $C_{17}H_{18}O_5$, 302.1154). This compound was first reported by Jurd et al.[14]

4-*O*-Benzyl-3,5-dimethoxybenzyl Alcohol (24). The method of preparation of **24** was similar to that used for the preparation of **16**. The yield of **24** from **23** is 94%. This compound was identical to that reported by Battersby et al.[15]

4-*O*-Benzyl-3,5-dimethoxybenzaldehyde (25). The method of preparation of **25** was similar to that used for the preparation of **17**. The yield of **25** from **24** was 88%. This compound was identical to that reported by Battersby et al.[16]

4-*O*-Benzylsinapic Acid (26). The method of preparation of **26** was similar to that used for the preparation of **18**. The yield of **26** from **25** was 90%. This compound was identical to that reported by Kametani et al.[17]

4-*O*-Benzylsinapyl Alcohol (20). The method of preparation of **20** was similar to that used for the preparation of **7**. The yield of **20** from **26** was 87%: gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51−7.20 (5H, m, H-3′−H-7′), 6.56 (2H, brs, H-2, H-6), 6.50 (1H, d, J = 15.8 Hz, H-7), 6.28 (1H, dt, J = 15.8, 5.7 Hz, H-8), 5.06 (2H, brs, H-1′), 3.88 (6H, s, O*Me*-3, O*Me*-5); HREIMS *m*/*z* 300.1341 (calcd for $C_{18}H_{20}O_4$, 300.1362).

4-*O*-Benzylsinapaldehyde (27). The method of preparation of **27** was similar to that used for the preparation of **7**. The yield of **27** from **20** was 94%: gum; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.68 (1H, d, J = 7.5 Hz, H-9), 7.52−7.22 (6H, m, H-3′−H-7′, H-7), 6.74 (2H, brs, H-2, H-6), 6.61 (1H, dd, J = 15.8, 7.5 Hz, H-8), 5.09 (2H, brs, H-1′), 3.90 (6H, s, O*Me*-3, O*Me*-5); HREIMS *m*/*z* 298.1229 (calcd for $C_{18}H_{18}O_4$, 298.1205).

4-*O*-(2-Methyl-2-butenyl)-3,5-diacetoxybenzoic Acid Methyl Ester (28). The method of preparation of **28** was similar to that used for the preparation of **13**. The yield of **28** from **12** was 60%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (2H, s, H-2, H-6), 5.37 (1H, t, J = 7.0 Hz, H-2′), 4.48 (2H, d, J = 7.25 Hz, H-1′), 3.86 (3H, s, CO_2*Me*), 2.31 (6H, s, OCOCH_3-3, OCOCH_3-5), 1.74 (3H, s, H-4′), 1.64 (3H, s, H-5′); EIMS m/*z* 336 $[M]^+$ (1), 321 (1), 295 (1), 281 (2), 286 (6), 253 (2), 237 (4), 226 (41), 195 (3), 184 (60), 153 (5), 121 (4), 85 (14), 69 (100); HREIMS *m*/*z* 336.1208 (calcd for $C_{17}H_{20}O_7$, 336.1209).

4-*O*-(2-Methyl-2-butenyl)-3,5-dihydroxybenzoic Acid Methyl Ester (29). The method of preparation of **29** was similar to that used for the preparation of **14**. The yield of **29** from **28** was 91%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.20 (2H, s, H-2, H-6), 5.96 (1H, brs, exchanged in D_2O, ArO*H*), 5.50 (1H, t, J = 7.0 Hz, H-2′), 4.60 (2H, d, J = 7.0 Hz, H-1′), 3.86 (3H, s, CO_2*Me*), 1.75 (3H, s, H-4′), 1.63 (3H, s, H-5′); EIMS *m*/*z* 252 $[M]^+$ (21), 235 (8), 226 (75), 211 (33), 205 (18), 184 (44), 167 (5), 153 (46), 149 (8), 69 (100); HREIMS *m*/*z* 252.0978 (calcd for $C_{13}H_{16}O_5$, 252.0998).

4-*O*-(2-Methyl-2-butenyl)-3,5-dimethoxybenzoic Acid Methyl Ester (30). The method of preparation of **30** was similar to that used for the preparation of **15**. The yield of **30** from **29** was 92%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26 (2H, s, H-2, H-6), 5.52 (1H, brt, J = 7.2 Hz, H-2′), 4.55 (2H, d, J = 7.3 Hz, H-1′), 3.89 (3H, s, CO_2*Me*), 3.88 (3H, s, O*Me*-3, O*Me*-5), 1.72 (3H, s, H-4′), 1.64 (3H, s, H-5′); HREIMS *m*/*z* 280.1300 (calcd for $C_{15}H_{20}O_5$, 280.1311).

4-*O*-(2-Methyl-2-butenyl)-3,5-dimethoxybenzyl Alcohol (31). The method of preparation of **31** was similar to that used for the preparation of **16**. The yield of **31** from **30** was 89%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.53 (2H, s, H-2, H-6), 5.51 (1H, brt, J = 7.1 Hz, H-2′), 4.56 (2H, s, H-7), 4.42 (1H, d, J = 7.2 Hz, H-1′), 3.79 (6H, s, O*Me*-3), O*Me*-5), 1.69 (3H, s, H-5′), 1.62 (3H, s, H-4′); EIMS *m*/*z* 252 $[M]^+$ (6), 239 (6), 235 (5), 226 (28), 211 (10), 205 (33), 184 (100), 182 (2), 167 (14), 155 (12), 153 (8), 127 (8), 123 (12), 109 (9), 69 (18); HREIMS δ 252.1374 (calcd for $C_{14}H_{20}O_4$, 252.1362).

4-*O*-(2-Methyl-2-butenyl)-3,5-dimethoxybenzaldehyde (32). The method of preparation of **32** was similar to that used for the preparation of **17**. The yield of **32** from **31** was 85%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.81 (1H, s, H-7), 7.07 (2H, s, H-2, H-6), 5.49 (1H, t, J = 7.1 Hz, H-2′), 4.56 (2H, d, J = 7.3 Hz, H-1′), 3.87 (6H, s, O*Me*-3, O*Me*-5), 1.69 (3H, s, H-4′), 1.62 (3H, s, H-5′); EIMS *m*/*z* 250 $[M]^+$ (1), 235 (1), 226 (16), 196 (2), 182 (100), 167 (8), 153 (2), 139 (4), 125 (5), 110 (6), 95 (7); HREIMS *m*/*z* 250.1199 (calcd for $C_{14}H_{18}O_4$, 250.1205).

4-*O*-(2-Methyl-2-butenyl)sinapic Acid (33). The method of preparation of **33** was similar to that used for the preparation of **18**. The yield of **33** from **32** was 88%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (1H, d, J = 15.7 Hz, H-7), 6.75 (1H, s, H-2, H-6), 6.34 (1H, d, J = 15.8 Hz, H-8), 5.53 (1H, dt, J = 7.2, 1.3 Hz, H-2′), 4.57 (2H, d, J = 7.2 Hz, H-1′), 3.86 (6H, s, O*Me*-3, O*Me*-5), 1.72 (3H, s, H-4′), 1.65 (3H, s, H-5′); EIMS *m*/*z* 292 $[M]^+$ (6) 277 (2), 265 (5), 250 (3), 224 (100), 209 (40), 197 (3), 195 (3), 181 (10), 163 (12), 149 (8), 135 (9), 121 (15), 69 (69); HREIMS *m*/*z* 292.1303 (calcd for $C_{16}H_{20}O_5$, 292.1311).

4-*O*-(2-Methyl-2-butenyl)sinapyl Alcohol (34). The method of preparation of **34** was similar to that used for the preparation of **6** from **18**. The yield of **34** from **33** was 81%, while the yield of byproduct **36** was 8%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.59 (2H, s, H-2, H−C6), 6.52 (1H, d, J = 16.0, H-7), 6.27 (1H, dt, J = 15.6, 5.7 Hz, H-8), 5.54 (1H, m, H-2′), 4.47 (2H, brd, J = 7.1 Hz, H-1′), 4.30 (2H, brd, J = 5.7 Hz, H-9), 3.84 (6H, s, O*Me*-3, O*Me*-5), 1.72 (3H, H-4′), 1.65 (3H, s, H-5′); HREIMS *m*/*z* 278.1532 (calcd for $C_{16}H_{22}O_4$, 278.1518).

4-*O*-(2-Methyl-2-butenyl)sinapaldehyde (35). The method of preparation of **35** was similar to that used for the preparation of **7** from **6**. The yield of **35** from **34** was 91%: gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.66 (1H, d, J = 7.6 Hz, H-9), 7.40 (1H, d, J = 15.9 Hz, H-7), 6.77 (2H, br. s, H-2, H-6), 6.60 (1H, dd, J = 15.9, 7.6 Hz, H-8), 5.54 (1H, brt, J = 7.2 Hz, H-2′), 4.56 (2H, brd, J = 7.2 Hz, H-1′), 3.89 (6H, s, O*Me*-3, O*Me*-5), 1.72 (3H, s, H-4′), 1.65 (3H, s, Me-5′); HREIMS *m*/*z* 276.1351 (calcd for $C_{16}H_{20}O_4$, 276.1362).

4-*O*-(2-Methyl-2-butenyl)-7,8-dihydrosinapyl alcohol (36): gum; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.48 (2H, brs, H-2, H-6), 5.53 (1H, brt, J = 7.2 Hz, H-2′), 4.51 (2H, brd, J = 7.1 Hz, H-1′), 3.90 (2H, brt, J = 7.5 Hz, H-9), 3.88 (6H, s, O*Me*-3, O*Me*-5), 2.81 (2H, brt, J = 7.5 Hz, H-7), 2.03−1.96 (2H, m, H-8), 1.71 (3H, s, H-4′), 1.65 (3H, s, H-5′); HREIMS *m*/*z* 278.1509 (calcd for $C_{16}H_{22}O_4$, 278.1518).

Cytotoxicity Assay. KB cells were obtained from the American type culture collection.[12] Effects of compounds on the growth of the cells were monitored at the Laboratoire de Cultures Cellulaires, ICSN, Gif-sur-Yvette, France. The IC_{50} values refer to the concentration of drug corresponding to 50% growth inhibition after 72 h incubation.[13] The assays of A-549 and HL-60 were carried out at the Institute of Shanghai Material Medica and were performed according to published techniques.[18−20]

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