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# THREE ACYCLIC *BIS*-PHENYLPROPANE LIGNANAMIDES FROM FRUITS OF *CANNABIS SATIVA**

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**Key Word Index**—*Cannabis sativa*; Cannabidaceae; cannabisin E; cannabisin F; cannabisin G.

**Abstract**—Three new acyclic *bis*-phenylpropane lignanamides, named cannabisin E, F and G were isolated from the fruits of *Cannabis sativa*. Their structures have been elucidated based on spectral and chemical evidence.

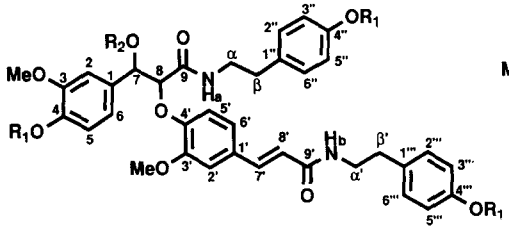
## INTRODUCTION

In the course of our investigation, we reported the isolation of cannabisin A–D from the fruits of *C. sativa*. In a continuation of this study, we now report the isolation and identification of three new acyclic *bis*-phenylpropane lignanamides from the same material.

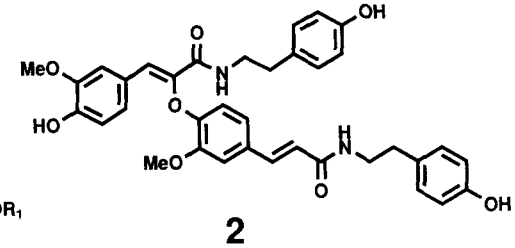
## RESULTS AND DISCUSSION

From the *n*-BuOH soluble fraction of the aqueous ethanol extract, cannabisin E (**1**), cannabisin F (**2**) and cannabisin G (**3**) were obtained. Cannabisin E (**1**) was obtained as an amorphous powder. The IR spectrum showed absorption bands for a hydroxyl group (3356 $cm^{-1}$), an amide group (1658 $cm^{-1}$) and an aromatic ring (1614 and 1514 $cm^{-1}$). The molecular formula of **1** was determined to be $C_{36}H_{38}N_2O_9$ by high-resolution FAB mass spectrometry (*m/z*: 643.2234, $[M + H]^+$). Acetylation of **1** gave tetraacetate (**1a**) ($\delta$2.12, 2.27, 2.29 and 2.30) (see Table 1) and methylation of **1** gave pentamethylether (**1b**) (**1** has originally two methoxyls). Thus **1** has three phenolic hydroxyls and an alcohol in its structure.

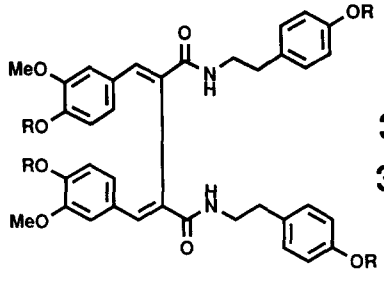
The NMR spectrum of **1** exhibited two tyramine moieties and two ABX-type coupled aromatic proton signals, along with $-CH(OH)-CH-$ moiety were observed (see Table 1). In the HMBC spectrum of **1**, there were cross peaks between benzylic methine proton signal at H-7 ($\delta$5.17) and C-2 and C-6 aromatic carbon signals ($\delta$111.6 and 120.4), respectively. A cross peak between



**1** $R_1$ $R_2$ =H
**1a** $R_1$ $R_2$ =Ac
**1b** $R_1$=Me $R_2$=H



**2**



**3** R=H
**3a** R=Ac

*Part 3 in the Series [1, 2].

Table 1. $^1$H NMR spectral data of **1**–**3**, **1a**, **1b** and **3a** (500 MHz, acetone-$d_6$)*

| H | 1 | 2 | 3 | 1a† | 1b‡ | 3a† |
|---|---|---|---|---|---|---|
| 2 | 7.16 (*d*, 2.0) | 7.27 (*d*, 2.0) | 7.28 (*d*, 2.1) | 6.90 (*d*, 1.9) | 7.02 (*d*, 2.0) | 7.14 (*d*, 2.0) |
| 5 | 6.78 (*d*, 8.1) | 6.75 (*d*, 8.4) | 6.83 (*d*, 8.4) | 7.01 (*d*, 8.5) | 6.28 (*d*, 8.4) | 6.99 (*d*, 8.3) |
| 6 | 6.94 (*dd*, 8.1, 2.0) | 7.03 (*dd*, 8.4, 2.0) | 7.08 (*dd*, 8.4, 2.1) | 7.06 (*dd*, 8.5, 1.9) | 6.90 (*dd*, 8.4, 2.0) | 7.09 (*dd*, 8.3, 2.0) |
| 7 | 5.17 (*brdd*, 6.7, 3.5) | 7.27 (*s*) | 7.89 (*s*) | 6.37 (*d*, 2.5) | 5.18 (*d*, 3.1) | 8.00 (*s*) |
| 8 | 4.59 (*d*, 3.5) | | | 4.61 (*d*, 2.5) | 4.54 (*d*, 3.1) | |
| 2′ | 7.14 (*d*, 2.0) | 7.35 (*d*, 2.0) | 7.28 (*d*, 2.1) | 7.09 (*d*, 1.9) | 7.11 (*d*, 2.0) | 7.14 (*d*, 2.0) |
| 5′ | 6.53 (*d*, 8.4) | 6.78 (*d*, 8.4) | 6.83 (*d*, 8.4) | 6.02 (*d*, 8.5) | 6.89 (*d*, 8.4) | 6.99 (*d*, 8.3) |
| 6′ | 6.96 (*dd*, 8.4, 2.0) | 7.14 (*dd*, 8.4, 2.0) | 7.08 (*dd*, 8.4, 2.1) | 6.87 (*dd*, 8.5, 1.9) | 6.98 (*dd*, 8.4, 2.0) | 7.09 (*dd*, 8.3, 2.0) |
| 7′ | 7.42 (*d*, 15.6) | 7.46 (*d*, 15.7) | 7.89 (*s*) | 7.47 (*d*, 15.5) | 7.39 (*d*, 15.7) | 8.00 (*s*) |
| 8′ | 6.53 (*d*, 15.6) | 6.57 (*d*, 15.7) | | 6.19 (*d*, 15.5) | 6.38 (*d*, 15.7) | |
| NHa | 7.50 (*t*, 6.0) | 7.22 (*t*, 6.1) | 7.11 (*brt*, 6.5) | 7.62 (*t*, 6.1) | | 6.10 (*t*, 6.1) |
| NHb | 7.21 (*t*, 6.0) | 7.25 (*t*, 6.1) | 7.11 (*brt*, 6.5) | 5.67 (*t*, 6.1) | | 6.10 (*t*, 6.1) |
| H-$\alpha$ | 3.39 (2H, *ddd*, 14.3, 7.3, 6.0) | 3.46 (2H, *dd*, 13.0, 6.0) | 3.26 (2H, *dddd*, 13.5, 8.3, 6.5, 2.0) | 3.47 (*dt*, 14.0, 6.8) 3.55 (*dt*, 14.0, 6.8) | 3.49 (*dd*, 13.4, 6.7) 3.36 (*dd*, 13.4 7.0) | 3.33 (2H, *dt*, 13.8, 6.9) |
| H-$\alpha'$ | 3.49 (2H, *ddd*, 13.1, 7.3, 6.0) | 3.49 (2H, *dd*, 13.0, 6.0) | 3.49 (2H, *dddd*, 13.5, 8.3, 6.5, 2.0) | 3.63 (2H, *dd*, 14.0, 6.8) | 3.47 (2H, *dd*, 7.4, 8.1) | 3.57 (2H, *dt*, 13.8, 6.9) |
| H-$\beta$ | 2.63 (2H, *dt*, 13.4, 7.3) | 2.65 (2H, *t*, 7.1) | 2.42 (2H, *ddd*, 13.5, 8.3, 2.0) | 2.71 (*dt*, 14.0, 6.8) 2.81 (*dt*, 14.0, 6.8) | 2.65 (*dt*, 13.4, 6.7) 2.67 (*dt*, 13.4, 6.7) | 2.51 (2H, *dt*, 13.8, 6.9) |
| H-$\beta'$ | 2.75 (2H, *t*, 7.3) | 2.75 (2H, *t*, 7.1) | 2.53 (2H, *ddd*, 13.5, 8.3, 2.0) | 2.87 (2H, *t*, 6.8) | 2.78 (2H, *t*, 7.4) | 2.63 (2H, *dt*, 13.8, 6.9) |
| 2″, 6″ | 6.93 (*d*, 8.6) | 6.90 (*d*, 8.6) | 6.84 (*d*, 8.6) | 7.07 (*d*, 8.6) | 6.95 (*d*, 8.8) | 6.95 (*d*, 8.6) |
| 3‴, 6‴ | 7.05 (*d*, 8.6) | 7.06 (*d*, 8.6) | 6.84 (*d*, 8.6) | 7.21 (*d*, 8.6) | 7.12 (*d*, 8.8) | 6.95 (*d*, 8.6) |
| 3″, 5″ | 6.70 (*d*, 8.6) | 6.68 (*d*, 8.6) | 6.68 (*d*, 8.6) | 6.91 (*d*, 8.6) | 6.69 (*d*, 8.8) | 6.90 (*d*, 8.6) |
| 3‴, 6‴ | 6.75 (*d*, 8.6) | 6.75 (*d*, 8.6) | 6.68 (*d*, 8.6) | 7.03 (*d*, 8.6) | 6.82 (*d*, 8.8) | 6.90 (*d*, 8.6) |
| OMe | 3.80 (2-OMe) 3.82 (3′-OMe) | 3.94 (3-OMe) 3.69 (3′-OMe) | 3.74 (3, 3′-OMe) | 3.64 (3-OMe) 3.78 (3′-OMe) | 3.80 (3-OMe) 3.82 (3′-OMe) 3.74 (4‴-OMe) 3.74 (4-OMe) | 3.71 (3,3′-OMe) |
| OAc | | | | 2.12 (7-OAc) 2.27, 2.29, 2.30 (4,4″,4‴-OAc) | 3.70 (4″-OMe) | 2.27 (4″, 4‴-OAc) 2.28 (4,4′-OAc) |

*Coupling constants (Hz) were given in parentheses. Assignments were based on the results of COLOC, HMBC, HMQC, COSY and NOESY spectral data.
†Measured in $CDCl_3$.
‡Measured in $CDCl_3$–MeOH (1:1).

the H-8 proton signal at $\delta$4.59 and quaternary aromatic carbon signal was assignable to C-4′ ($\delta$149.8). On the other hand, in the NOESY spectrum of **1**, there was a cross peak between H-5′ ($\delta$6.53) and the H-8 proton signal. These data supported the presence of an ether function connecting between the C-4′ and C-8. Thus **1** is a surinamensin-type lignan derivative [3], that has a 1-phenyl-2-phenoxyethanol moiety in its structure.

Furthermore, tyramine moieties were assigned on the basis of long-range couplings (HMBC experiment) between the NH proton signal at $\delta$7.21 and carbonylcarbon signals at $\delta$166.2, $\delta$7.50 and $\delta$169.9; those carbonylcarbon signals were assignable to C-9′ and the C-9, respectively (see Tables 1 and 2). The small $J_{7,8}$ values of **1**, **1a** and **1b** [**1** (3.5 Hz), **1a** (2.5 Hz) and **1b** (3.1 Hz)], were indicative of *erythro* derivatives [4–7]. These results led us to conclude the structure of cannabisin E to be **1** (see structure).

Cannabisin F (**2**) was obtained as an amorphous powder. The $^1$H NMR spectrum was similar to that of **1**, except for the presence of a conjugated olefinic proton ($\delta$7.27) in **2**, instead of $-$CH(OH) $-$ CH $-$ function in **1**, and its molecular formula $C_{36}H_{36}N_2O_8$ showed **2** was the dehydrate of **1**. Revealing the presence of an olefine moiety in **2**, **1** was subjected to a dehydration reaction

Table 2. $^{13}$C NMR spectral data of **1**–**3**, **1a**, **1b** and **3a** (125 MHz, acetone-$d_6$)*

| C | 1 | 2 | 3 | 1a† | 1b‡ | 3a† |
|---|---|---|---|---|---|---|
| 1 | 133.7 | 125.5 | 127.8 | 135.8 | 134.4 | 132.6 |
| 2 | 111.6 | 112.3 | 113.3 | 111.4 | 111.3 | 113.4 |
| 3 | 148.1 | 148.3 | 149.2 | 151.3 | 149.6 | 151.3 |
| 4 | 146.9 | 147.1 | 148.3 | 139.9 | 149.5 | 141.3 |
| 5 | 115.2 | 115.1 | 116.0 | 122.9 | 111.8 | 123.4 |
| 6 | 120.4 | 121.5 | 125.9 | 119.5 | 119.9 | 123.5 |
| 7 | 74.4 | 123.7 | 140.5 | 74.5 | 74.3 | 140.1 |
| 8 | 86.5 | 142.3 | 127.9 | 85.4 | 86.9 | 128.4 |
| 9 | 169.9 | 166.1 | 166.2 | 168.0 | 171.2 | 164.1 |
| 1′ | 131.3 | 131.7 | 127.8 | 130.7 | 131.1 | 132.6 |
| 2′ | 112.0 | 113.6 | 113.3 | 111.1 | 112.0 | 113.4 |
| 3′ | 151.2 | 150.2 | 149.2 | 149.9 | 150.8 | 151.3 |
| 4′ | 149.8 | 148.8 | 148.3 | 148.6 | 149.8 | 141.3 |
| 5′ | 117.7 | 115.9 | 116.0 | 117.6 | 117.4 | 123.4 |
| 6′ | 121.8 | 125.5 | 125.9 | 121.5 | 120.5 | 123.5 |
| 7′ | 139.7 | 139.6 | 140.5 | 140.2 | 140.8 | 140.1 |
| 8′ | 121.8 | 122.0 | 127.9 | 120.0 | 122.2 | 128.4 |
| 9′ | 166.2 | 163.3 | 166.2 | 165.8 | 168.2 | 164.1 |
| α | 41.5 | 41.8 | 42.6 | 40.6 | 41.6 | 41.3 |
| α′ | 41.9 | 42.0 | 42.6 | 40.7 | 42.1 | 41.3 |
| β | 35.5 | 35.5 | 35.5 | 35.0 | 35.1 | 34.8 |
| β′ | 35.7 | 35.7 | 35.5 | 35.0 | 35.4 | 34.8 |
| 1″ | 130.8 | 130.8 | 130.9 | 136.4 | 131.6 | 135.9 |
| 2″ | 130.5 | 130.5 | 130.4 | 129.6 | 130.4 | 129.5 |
| 3″ | 116.1 | 116.1 | 116.0 | 121.6 | 114.6 | 121.7 |
| 4″ | 156.7 | 156.7 | 156.6 | 149.3 | 159.1 | 149.3 |
| 5″ | 116.1 | 116.1 | 116.0 | 121.6 | 114.6 | 121.7 |
| 6″ | 130.5 | 130.5 | 130.4 | 129.6 | 130.4 | 129.5 |
| 1‴ | 131.1 | 131.1 | 130.9 | 136.5 | 132.0 | 135.9 |
| 2‴ | 130.5 | 130.5 | 130.4 | 129.8 | 130.4 | 129.5 |
| 3‴ | 116.1 | 116.1 | 116.0 | 121.8 | 114.6 | 121.7 |
| 4‴ | 156.7 | 156.7 | 156.6 | 149.3 | 159.2 | 149.3 |
| 5‴ | 116.1 | 116.1 | 116.0 | 121.8 | 114.6 | 121.7 |
| 6‴ | 130.5 | 130.5 | 130.4 | 129.8 | 130.4 | 129.5 |
| Methoxyl | 56.2 (C-3)<br>56.3 (C-3′) | 56.0 (C-3′)<br>56.2 (C-3) | 56.1 (C-3)<br>56.1 (C-3′) | 55.6 (C-3)<br>56.0 (C-3′) | 55.6 (C-4)<br>56.2 (C-3)<br>56.2 (C-4″)<br>56.3 (C-3′) | 55.8 (C-3)<br>55.8 (C-3′) |
| Acetoxyl | | | | 20.6 168.8<br>20.9 169.3<br>21.1 169.6<br>21.1 169.7 | 56.4 (C-4‴) | 20.6 168.5<br>(C-4,4′)<br>21.1 169.4<br>(C-4″, 4‴) |

*All assignments were based on COLOC, HMBC and HMQC experiments.
†Measured in $CDCl_3$.
‡Measured in $CDCl_3$–MeOH (1:1).

with *p*-toluenesulphonic acid in THF, giving a dehydrant which was identified with cannabisin F. In the COLOC spectrum of **2**, the conjugated olefinic proton ($\delta$ 7.27) has two cross peaks with C-2 ($\delta$112.3) and C-6 ($\delta$121.5), respectively. These results showed that the olefine moiety was located at the C-7 and C-8 position. From the above observations, the structure of cannabisin F was concluded as **2** (see structure).

Cannabisin G (**3**) was obtained as an amorphous powder. The $^1$H NMR spectrum of **3** was similar to that of *N-trans*-feruloyltyramine, except for the presence of a singlet olefinic proton signal ($\delta$7.89), instead of trans olefine proton signals in *N-trans*-feruloyltyramine. The molecular formula of **3** ($C_{36}H_{36}N_2O_8$) showed that **3** was a dimer of *N-trans*-feruloyltyramine. Acetylation of **3** gave tetraacetate **3a** (FAB-MS *m/z*: 793 $[M + H]^+$), supporting its dimeric structure. In the COLOC spectrum of **3a**, there were cross peaks between this singlet olefine proton signal ($\delta$8.00, 2H) and an aromatic methine carbon signal ($\delta$113.4, C-2 and C-2′), another aromatic methine carbon signal ($\delta$123.4, C-6 and C-6′) and a carbonylcarbon signal ($\delta$164.1), respectively. These data suggested that this singlet signal was assignable to the H-7 and the H-7′. Therefore these feruloyl-tyramine units were connected between the C-8 and the C-8′ positions. From these findings, cannabisin G has a biphenylbutadiene moiety and its structure was elucidated as **3** (see structure).

All these cannabisins were presumed to be synthesized during the process of oxidative coupling according to the biosynthesis of lignan [8–10] *N-trans*-feruloyltyramine was subjected to a catalytic condensation with aqueous $FeCl_3$ solution and acetone, affording cannabisin E, F and G as minor products, along with cannabisin D and grossamide as major products. Cannabisin E, F and G are the first naturally occurring acyclic *bis*-phenylpropane lignanamides.

## EXPERIMENTAL

Mps: uncorr; $^1$H and $^{13}$C NMR were measured at 500 MHz and 125 MHz, respectively, with TMS as int. standard; 2D NMR: 500 MHz under the same conditions: EI-MS: 70 eV; prep. TLC: prepacked CIG Si-10 column (silica gel, 2.2 cm i.d. × 30 cm); prep. HPLC: YMC R-354 (ODS, 5 cm i.d. × 50 cm): CC: Silica gel 60 (70–230 mesh). Acetylation was conducted with $Ac_2O$ and pyridine. Methylation was conducted by methyliodide with $K_2CO_3$ and $Me_2CO$. Plant material was purchased from a Japanese market and a voucher specimen stored in the Herbarium stock room of our Laboratory.

*Extraction and isolation.* Fruits of *C. sativa* L. (10 kg) were extracted with boiling $H_2O$–EtOH (1:1) (8 l × 3). The extract was concd to 4 l, which was then extracted with $CHCl_3$ (20 l), and *n*-BuOH (20 l), successively. The *n*-BuOH extract was concd to dryness to give a brown mass (239 g), which was chromatographed on Diaion HP-20 eluted with $H_2O$ (40 l), followed by MeOH (50 l). The MeOH eluate was concd to give a yellow mass (172 g), which was chromatographed on silica gel, eluted with $CHCl_3$–MeOH [4:1 (2 l)], then purified by prep. HPLC [$H_2O$–MeCN–MeOH (7:2:2)] to give **1** (120 mg), **2** (45 mg) and **3** (20 mg), respectively.

*Cannabisin E* (**1**). Amorphous powder. FAB-MS *m/z*: 643.2631 ($[M + H]^+$, calcd for $C_{36}H_{39}N_2O_9$; 643.2656). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3356 (OH), 1658 (C=O), 1614, 1514 (benzene ring). UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 226 (4.16), 283 (4.43), 313 (4.31). $^1$H NMR: see Table 1. $^{13}$C NMR: see Table 2. *Cannabisin F* (**2**). Amorphous powder. FAB-MS *m/z*: 625.2532 ($[M + H]^+$, calcd for $C_{36}H_{37}N_2O_8$; 625.2550). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3408 (OH), 1658 (C=O), 1614, 1514 (benzene ring). UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 287 (4.55), 320 (4.57). $^1$H NMR: see Table 1. $^{13}$C NMR: see Table 2. *Cannabisin G* (**3**). Amorphous powder. FAB-MS *m/z*: 625.2533 ($[M + H]^+$, calcd for $C_{36}H_{37}N_2O_8$; 625.2550). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3356 (OH), 1658 (C=O), 1614, 1514 (benzene ring). UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 283 (4.48), 316 (4.28). $^1$H NMR: see Table 1. $^{13}$C NMR: see Table 2. *Cannabisin E trimethyl ether* (**1a**). Amorphous powder. FAB-MS *m/z*: 625.2522 ($[M + H]^+$, calcd for $C_{39}H_{45}N_2O_9$; 685.3125). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1650, 1614, 1594, 1512. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 225 (4.67), 280 (4.43), 284 (4.45), 314 (4.34). $^1$H NMR: see Table 1. $^{13}$C NMR: see Table 2. *Cannabisin E tetraacetate* (**1b**). Needles mp 123–125°. FAB-MS *m/z*: 811 ($[M + H]^+$.IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1760, 1658, 1606, 1536, 1218. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 282 (4.37), 290 (4.35), 313 (4.29). $^1$H NMR: see Table 1. $^{13}$C NMR: see Table 2. *Cannabisin G tetramethyl ether* (**3a**). Amorphous powder. FAB-MS *m/z*: 793 $[M + H]^+$. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1768, 1642, 1600, 1536, 1194. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 283 (4.44), 316 (4.32). $^1$H NMR: see Table 1. $^{13}$C NMR: see Table 2.

*Dehydration of* **1** *with* p-*toluenesulphonic acid.* To a soln of **1** (8.4 mg) with THF (10 ml) was added *p*-toluenesulphonic acid (2 mg). The reaction mixt. was refluxed overnight. The reaction mixt. was diluted with $H_2O$ and then extracted with EtOAc. The EtOAc layer was evapd and then purified by prep. LC [$CHCl_3$–MeOH (1:2, 180 ml)] to give an amorphous powder (5.5 mg), which was identified by direct comparison ($^1$H, $^{13}$C NMR, IR, UV) with an authentic sample of cannabisin F (**2**).

*Catalytic condensation of N-trans-feruloyltyramine.* To a soln of *N-trans*-feruloyltyramine (isolated from this material, 4.13 g) in $Me_2CO$ (25 ml) was added aq. $FeCl_3$ soln (10%, 25 ml) kept at room temp. for 2 days. The reaction mixt. was treated with 2M HCl soln (10 ml), then extracted with EtOAc (100 ml, twice). The EtOAc layer was washed with $H_2O$ and then purified by prep. HPLC ($H_2O$–MeOH–MeCN, 7:2:2, 4 l) to afford cannabisin D (832 mg), grossamide (535 mg), cannabisin E (22 mg) and cannabisin G (14 mg). Cannabisin F could not be isolated, but was identified by co-TLC and co-injection on analytical HPLC.

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## REFERENCES

1. Sakakibara, I., Katsuhara, T., Ikeya, Y., Hayashi, K. and Mitsuhashi, H. (1991) *Phytochemistry* **30**, 3013.

2. Sakakibara, I., Ikeya, Y., Hayashi, K. and Mitsuhashi, H. (1992) *Phytochemistry* **31**, 3219.
3. Agrawal, P. K. and Thakur, R. S. (1985) *Magn. Reson. Chem.* **23**, 389.
4. Miyase, T., Ueno, A., Tanizawa, N., Kobayashi, H. and Karasawa, H. (1987) *Chem. Pharm. Bull.* **35**, 1109.
5. Hattori, M., Hada, S., Shu., Y., Kakiuchi, N. and Namba, T. (1987) *Chem. Pharm. Bull.* **35**, 668.
6. Charles, H. L., Nist, B. J. and McCarthy, J. L. (1964) *J. Am. Chem. Soc.* **86**, 1186.
7. Hattori, M., Yang, X., Shu, Y., Kakiuchi, N., Tezuka, Y., Kikuchi, T. and Namba, T. (1988) *Chem. Pharm. Bull.* **36**, 648.
8. Sarkanen, K. V. and Wallis, A. F. A. (1973) *J. Chem. Soc. Perkin I* 1878.
9. Sarkanen, K. V. and Wallis, A. F. A. (1973) *J. Chem. Soc. Perkin I* 1869.
10. Kuo, Y., Kuo, P. and Lin, S. (1983) *Proc. Natl Sci. Counc. B. ROC.* **7**, 28.