# Two New 2′-Oxygenated Flavones from *Andrographis elongata*

Galla JAYAKRISHNA,[a] Pennaka HARIKISHORE,[a] Chunduri VENKATA RAO,[a] Duvvuru GUNASEKAR,*[,a] Alan BLOND,[b] and Bernard BODO[b]

*Natural Products Division,[a] Department of Chemistry, Sri Venkateswara University, Tirupati-517 502, India and Laboratoire de Chimie des Substances Naturelles,[b] ESA 8041 CNRS-GDR 790 CNRS, Museum National d'Histoire Naturelle, 63 rue Buffon, 75005 Paris, France.* Received July 2, 2001; accepted September 19, 2001

**Two new 2′-oxygenated flavones, 5,2′,6′-trihydroxy-7-methoxyflavone (3) and skullcapflavone I 2′-*O*-β-D-(4″-*E*-cinnamyl) glucopyranoside (5), together with three known flavones, 7-*O*-methylwogonin (1), skullcapflavone I (2) and skullcapflavone I 2′-*O*-β-D-glucopyranoside (4) were isolated from the whole plant of *Andrographis elongata*, and the structures were elucidated by FAB-MS and one- and two-dimensional (1D- and 2D)-NMR spectral studies including $^1$H–$^1$H correlation spectroscopy (COSY), heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond connectivity (HMBC) and rotating frame Overhauser enhancement spectroscopy (ROESY) experiments, and chemical studies.**

**Key words** *Andrographis elongata*; Acanthaceae; 2′-oxygenated flavones

*Andrographis elongata* T. And (Acanthaceae) is an herbaceous plant distributed throughout the Western Ghats of South India.[1)] As part of our continuing investigation on the flavonoid constituents of *Andrographis* species,[2—6)] we have examined the whole plant of *A. elongata*, a plant hitherto not investigated for its chemical constituents and report here the isolation and structure elucidation of two new 2′-oxygenated flavones (**3**, **5**), in addition to three known flavones (**1**, **2**, **4**).

## Results and Discussion

Compound **3**, obtained as yellow crystals, mp 210—211 °C, showed the pseudomolecular ion at *m/z* 301.0714 in its positive high resolution chemical ionization mass spectrometry (HR-CI-MS) corresponding to the molecular formula $C_{16}H_{12}O_6$. This was corroborated by decoupled $^{13}$C-NMR spectrum which showed signals for all the sixteen carbons of the molecule. The UV absorption maxima of **3** in MeOH (258, 303 nm) and a bathochromic shift of 62 nm with $AlCl_3$/HCl suggested that it is a 5-hydroxyflavone.

The $^1$H-NMR spectrum of **3** showed the presence of a methoxyl ($\delta$ 3.83), a chelated hydroxyl ($\delta$ 12.88), two non-chelated hydroxyls ($\delta$ 9.88, 2H) and a singlet at $\delta$ 6.26 assigned to H-3. A set of *meta* coupled doublets ($J$=2.2 Hz) resonating at $\delta$ 6.38 and 6.61 were ascribed to H-6 and H-8 protons, respectively. From heteronuclear multiple bond connectivity (HMBC) and rotating frame Overhauser enhancement spectroscopy (ROESY) studies the methoxyl group at $\delta$ 3.83 was placed at C-7 as the methoxyl protons showed correlation with C-7 at 165.1 ppm in its HMBC spectrum (Fig. 1) and two strong nuclear Overhauser effects (NOEs) were observed between methoxyl protons at C-7 and H-6 ($\delta$ 6.38) and H-8 ($\delta$ 6.61) protons (Fig. 1). The presence of $AB_2$ type aromatic proton signals of ring B at $\delta$ 7.10 (1H, t, $J$=8.2 Hz) and 6.40 (2H, d, $J$=8.2 Hz) were typical of 4′, and 3′ and 5′ protons of 2′,6′-dihydroxy (or methoxy) flavones.[7—9)] The presence of 2′,6′-dioxygenation in **3** was also supported by the chemical shift values of the B-ring carbons which were very similar to those observed for the B-ring carbons of 2′,6′-dihydroxyflavones.[9,10)]

The electron impact-mass spectra (EI-MS) of compound **3** exhibited the molecular ion as the base peak at *m/z* 300, with the diagnostic peaks of *retro*-Diels–Alder cleavage of ring C at *m/z* 167 and 134 supporting the presence of a hydroxyl and a methoxyl in ring A, and two hydroxyls in ring B. From HMBC correlations the two non-chelated hydroxyls were located at C-2′ and C-6′ positions as both these hydroxyl bearing carbons at 156.6 ppm showed cross peaks with H-3′ and H-5′ ($\delta$ 6.40), and H-4′ ($\delta$ 7.10) protons (Fig. 1). Thus the structure of compound **3** was elucidated as 5,2′,6′-trihydroxy-7-methoxyflavone.

Compound **5**, obtained as yellow amorphous powder showed $[M+H]^+$ peak at *m/z* 607.1807 in its HR-FAB-MS corresponding to the molecular formula $C_{32}H_{30}O_{12}$, and was corroborated by $^{13}$C-NMR spectrum which showed signals for all the 32 carbons of the molecule. The UV spectrum exhibited absorption maxima at 272, 320 (sh) and 350 (sh) nm, typical of flavones with 5,7,8-trioxygenation.[11—13)] Addition of sodium acetate did not cause any change in band II absorption maximum indicating the absence of a free hydroxyl at C-7. The IR spectrum of **5** apart from hydroxyl (3391 $cm^{-1}$) and carbonyl (1615 $cm^{-1}$) absorption bands, showed an additional carbonyl absorption band at 1676 $cm^{-1}$ indicating the presence of an ester group conjugated with a double bond.[14,15)]

The $^1$H-NMR spectrum of **5** was very similar to skullcapflavone I 2′-*O*-β-D-glucopyranoside[16)] (**4**) with the excep-

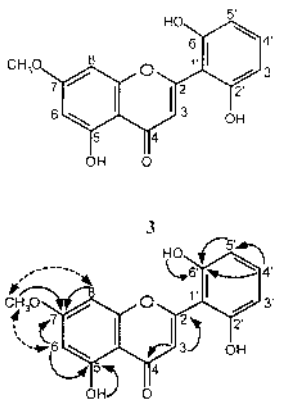


Fig. 1. Significant HMBC (→) and ROESY (↔) Correlations for **3**

* To whom correspondence should be addressed. e-mail: duvvurusekar@usa.net

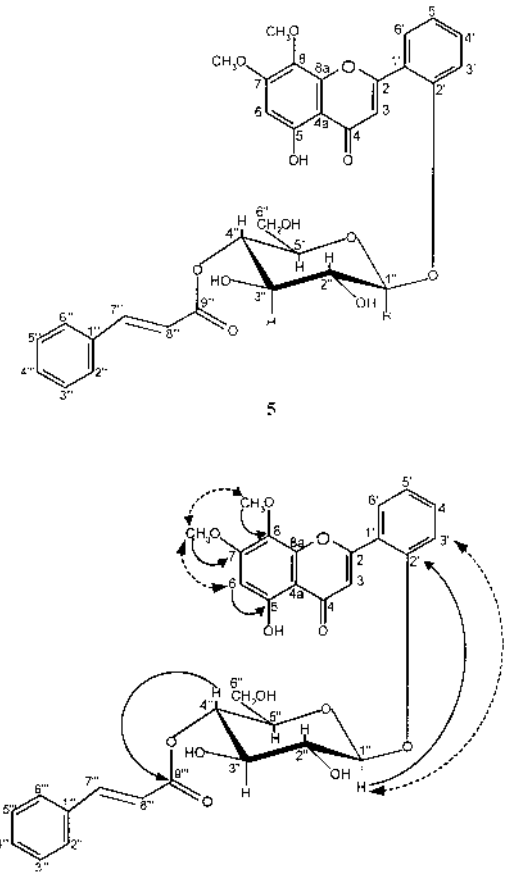

Fig. 2. Significant HMBC (→) and ROESY (↔) Correlations for **5**

tion of additional signals at $\delta$ 7.43 (m, 3H) and 7.74 (m, 2H) together with two olefinic doublets at $\delta$ 6.68 and 7.68 with large coupling constant ($J$=16 Hz) revealed the presence of a *trans*-cinnamyl moiety. The presence of a cinnamyl residue in **5** was further evidenced by the formation of *trans*-cinnamic acid, D-glucose and skullcapflavone I[17] (**2**) when compound **5** was subjected to total acid hydrolysis. From HMBC and ROESY studies the glucose residue in **5** was found to be linked to C-2′ as a strong NOE was observed between H-1″ and H-3′ in its ROESY spectrum (Fig. 2), and a cross peak between H-1″ and C-2′ in its HMBC spectrum (Fig. 2). Alkaline hydrolysis of **5** gave *trans*-cinnamic acid and skullcapflavone I 2′-*O*-$\beta$-D-glucopyranoside[16] (**4**) indicating that the cinnamyl moiety was attached to glucosyl residue. Comparison of $^{13}$C-NMR spectral data of **5** with **4**[4] (Table 1) showed that the cinnamyl residue in **5** was found to be linked to C-4″ hydroxyl of the glucose residue as this carbon signal (70.6 ppm) was shifted to downfield[18] by 1.20 ppm, while the C-3″ and C-5″ signals at 74.5 and 75.5 ppm were shifted to upfield by 2.0 and 1.5 ppm, respectively. The site of esterification in **5** was also revealed by a downfield shift[19] of 1.90 ppm observed for H-4″ ($\delta$ 5.10) in its $^1$H-NMR spectrum compared with that of **4** ($\delta$ 3.20). The attachment of cinnamyl moiety at C-4″ in **5** was further supported by the presence of a cross peak between H-4″ ($\delta$ 5.10) of the glucose and carbonyl carbon (165.6 ppm) of the cinnamyl residue in its HMBC spectrum (Fig. 2).

Thus from the foregoing spectral studies compound **5** was elucidated as skullcapflavone I 2′-*O*-$\beta$-D-(4″-*E*-cinnamyl) glucopyranoside as shown in Fig. 2.

Table 1. $^{13}$C-NMR Data (75 MHz, DMSO-$d_6$) of **4** and **5**

| Carbon | **4** | **5** |
|---|---|---|
| 2 | 160.7 | 160.9 |
| 3 | 110.0 | 110.1 |
| 4 | 182.1 | 182.3 |
| 4a | 103.9 | 104.0 |
| 5 | 156.4 | 156.5 |
| 6 | 95.6 | 95.8 |
| 7 | 158.3 | 158.4 |
| 8 | 128.2 | 128.4 |
| 8a | 149.0 | 149.0 |
| 1′ | 120.2 | 120.3 |
| 2′ | 155.3 | 155.2 |
| 3′ | 115.4 | 115.5 |
| 4′ | 132.8 | 133.0 |
| 5′ | 122.1 | 122.3 |
| 6′ | 128.8 | 128.9 |
| 7-OMe | 56.2 | 56.4 |
| 8-OMe | 61.0 | 61.1 |
| 1″ | 99.8 | 99.5 |
| 2″ | 73.2 | 71.3 |
| 3″ | 76.5 | 74.5 |
| 4″ | 69.4 | 70.6 |
| 5″ | 77.0 | 75.5 |
| 6″ | 60.3 | 60.1 |
| 1‴ | — | 134.1 |
| 2‴,6‴ | — | 128.2 |
| 3‴,5‴ | — | 128.9 |
| 4‴ | — | 130.3 |
| 7‴ | — | 144.1 |
| 8‴ | — | 118.6 |
| 9‴ | — | 165.6 |

The structures of known compounds **1**, **2**, and **4** were established by comparison of their spectral data with literature values.[16,17]

## Experimental

**General Procedures** Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded in KBr discs on a Bio-Rad win Fourier transform (FT)-IR spectrophotometer and UV spectra on a Shimadzu UV-240 spectrophotometer. Optical rotations were measured in MeOH at 25 °C on a Perkin-Elmer 241 polarimeter. $^1$H- and $^{13}$C-NMR spectra were determined on a Bruker AC 300 spectrometer operating at 300.13 and 75.43 MHz, respectively using tetramethylsilane (TMS) as an internal standard. $^1$H–$^1$H COSY, HSQC, HMBC and the phase-sensitive ROESY (with 150 ms mixing time) spectra were recorded using the standard pulse sequences. FAB and HR-FABMS were obtained on a 700 JEOL mass spectrometer in thioglycerol matrix. Column chromatography (CC) was performed on Acme silica gel finer than 200 mesh (0.08 mm).

**Plant Material** The whole plant of *A. elongata* T. And was collected in September 1998 at Pachaimalai Hills, Salem, Tamilnadu, India. A voucher specimen (DG-989) has been deposited in the Herbarium of the Department of Botany, Sri Venkateswara University, Tirupati, India.

**Extraction and Isolation** The air-dried and powdered whole plant (2.5 kg) of *A. elongata* was successively extracted with *n*-hexane, $Me_2CO$ and MeOH. The *n*-hexane extract was purified over a silica gel column using *n*-hexane and EtOAc and their step gradient mixtures as eluents. The *n*-hexane–EtOAc (1 : 1, 2 : 8) eluates yielded **1** (20 mg) and **2** (15 mg), respectively.

The $Me_2CO$ extract was defatted with *n*-hexane and the residue obtained was purified over a silica gel column using *n*-hexane and EtOAc and their step gradient mixtures as eluents. The *n*-hexane–EtOAc (3 : 7, 2 : 8, 1 : 9) eluates yielded **3** (25 mg), **4** (18 mg) and **5** (30 mg), respectively.

7-*O*-Methylwogonin (**1**): Yellow needles, mp 181—182 °C (hexane). UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 272 (4.52), 345 sh (3.78); (NaOAc) 272, 345 sh; ($AlCl_3$) 290, 330, 413; ($AlCl_3$+HCl) 290, 330, 413. IR (KBr) $\nu_{max}$ cm$^{-1}$: 3432 (OH), 2938, 1713 (>C=O), 1610, 1511, 1449. $^1$H-NMR ($Me_2CO$-$d_6$) $\delta$: 12.65 (1H, s, OH-5), 8.10 (2H, m, H-2′, 6′), 7.61 (3H, m, H-3′, 4′, 5′), 6.80 (1H, s, H-3), 6.51 (1H, s, H-6), 3.98 (3H, s, OMe-7), 3.90 (3H, s, OMe-

8). $^{13}$C-NMR ($Me_2CO$-$d_6$) $\delta$: 183.5 (C-4), 164.7 (C-2), 160.0 (C-7), 158.4 (C-5), 150.3 (C-8a), 132.8 (C-4′), 132.3 (C-8), 130.0 (C-1′), 130.1 (C-3′, 5′), 127.2 (C-2′, 6′), 105.8 (C-3), 105.4 (C-4a), 96.7 (C-6), 61.6 (OMe-8), 56.8 (OMe-7). EI-MS *m/z* (%) 298, ($M^+$, 46), 283 (100), 255 (8), 181 (12), 153 (32), 105 (4), 102(6).

Skullcapflavone I (**2**): Pale yellow needles, mp 254—255 °C (MeOH). UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 270 (4.03), 340 sh (3.76); (NaOMe) 275, 398; (NaOAc) 270, 340; ($AlCl_3$) 280, 290, 350, 362 sh; ($AlCl_3$+HCl) 275, 293, 315, 355. IR (KBr) $\nu_{max}$ cm$^{-1}$: 3434 (OH), 2937, 1651 (>C=O), 1611, 1575, 1508, 1453. $^1$H-NMR (DMSO-$d_6$) $\delta$: 12.75 (1H, s, OH-5), 9.70 (1H, s, OH-2′), 8.01 (1H, dd, *J*=8.0, 1.7 Hz, H-6′), 7.43 (1H, ddd, *J*=8.0, 7.3, 1.7 Hz, H-4′), 7.14 (1H, s, H-3), 7.11 (2H, m, H-3′, 5′), 6.49 (1H, s, H-6), 3.97 (3H, s, OMe-7), 3.88 (3H, s, OMe-8). $^{13}$C-NMR (DMSO-$d_6$) $\delta$: 182.2 (C-4), 161.7 (C-2), 158.4 (C-7), 157.5 (C-2′), 156.6 (C-5), 149.5 (C-8a), 133.0 (C-4(), 128.3 (C-8), 128.2 (C-6(), 119.2 (C-5′), 117.3 (C-3′), 117.2 (C-1′), 108.6 (C-3), 103.5 (C-4a), 95.8 (C-6), 61.1 (OMe-8), 56.7 (OMe-7). EI-MS *m/z* (%) 314 ($M^+$, 44), 299 (100), 284 (1), 271 (8), 257 (2), 196 (2), 181 (19), 168 (3), 153 (45), 121 (4), 118 (9).

5,2′,6′-Trihydroxy-7-methoxyflavone (**3**): Yellow needles, mp 210—211 °C (MeOH). UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 258 (4.55), 303 (4.20); (NaOMe) 257 sh, 290 sh, 357; (NaOAc) 258, 305; (NaOAc+$H_3BO_3$) 258, 305; ($AlCl_3$) 267, 286 sh, 318, 365; ($AlCl_3$+HCl) 267, 286 sh, 318, 365. IR (KBr) $\nu_{max}$ cm$^{-1}$: 3376 (OH), 3072, 2924, 1647 (>C=O), 1618, 1562, 1456. $^1$H-NMR (DMSO-$d_6$): see text. $^{13}$C-NMR (DMSO-$d_6$) $\delta$: 181.9 (C-4), 165.1 (C-7), 162.8 (C-2), 161.2 (C-5), 158.2 (C-8a), 156.6 (C-2′, 6′), 131.9 (C-4′), 112.1 (C-3), 108.1 (C-1′), 106.4 (C-3′, 5′), 104.8 (C-4a), 97.9 (C-6), 92.4 (C-8), 56.0 (OMe-7). EI-MS *m/z* (%) 300 ($M^+$, 100), 283 (5), 272 (11), 167 (60), 166 (12), 137 (16), 134 (7). HR-CI-MS *m/z* 301.0714 $[M+H]^+$ (Calcd for $C_{16}H_{13}O_6$: 301.0711).

**Acetylation of 3** Compound **3** was acetylated with $Ac_2O/C_5H_5N$ by the usual procedure to give triacetate as colourless needles, mp 183—185 °C. IR (KBr) $\nu_{max}$ cm$^{-1}$: 2928, 1771 (>C=O of OAc), 1645, 1619, 1434. $^1$H-NMR ($CDCl_3$) $\delta$: 7.48 (1H, t, *J*=8.2 Hz, H-4′), 7.07 (1H, d, *J*=2.2 Hz, H-8), 6.65 (2H, d, *J*=8.2 Hz, H-3′, 5′), 6.57 (1H, d, *J*=2.2 Hz, H-6), 6.17 (1H, s, H-3), 3.81 (3H, s, OMe-7), 2.38 (3H, s, OAc-5), 2.13 (6H, s, OAc-2′, 6′).

Skullcapflavone I 2′-*O*-$\beta$-D-Glucopyranoside (**4**): Yellow needles, mp 260—262 °C (MeOH). $[\alpha]^{25}_D$ −24.6° (*c*=0.3, MeOH). UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 270 (4.05), 315 sh (3.42); (NaOAc) 270, 315; ($AlCl_3$) 280, 330, 380 sh; ($AlCl_3$+HCl) 278, 320, 370 sh. IR (KBr) $\nu_{max}$ cm$^{-1}$: 3431 (OH), 3305, 2923, 1658 (>C=O), 1610, 1574, 1508, 1450, 1372. $^1$H-NMR (DMSO-$d_6$) $\delta$: 12.70 (1H, s, OH-5), 7.89 (1H, dd, *J*=7.8, 1.5 Hz, H-6′), 7.58 (1H, dt, *J*=7.3, 1.5 Hz, H-4′), 7.37 (1H, d, *J*=7.3 Hz, H-3′) 7.25 (1H, dt, *J*=7.8, 1.5 Hz, H-5′), 7.08 (1H, s, H-3), 6.61 (1H, s, H-6), 5.33 (1H, d, *J*=7.0 Hz, H-1′), 3.71 (1H, m, H-6′a), 3.49 (1H, m, H-6′b), 3.42 (1H, ddd, *J*=9.0, 8.0, 2.0 Hz, H-5′), 3.32 (1H, dd, *J*=9.0, 7.0 Hz, H-2′), 3.30 (1H, dd, *J*=9.0, 9.0 Hz, H-3′), 3.20 (1H, dd, *J*=9.0, 9.0 Hz, H-4′), 3.91 (3H, s, OMe-7), 3.81 (3H, s, OMe-8). $^{13}$C-NMR (DMSO-$d_6$): See Table 1. FAB-MS (positive ion mode) *m/z* 477 $[M+H]^+$, 315 $[M+H-glucosyl]^+$.

Skullcapflavone I 2′-*O*-$\beta$-D-(4″-*E*-Cinnamyl)glucopyranoside (**5**): Yellow amorphous powder, mp 247—249 °C (MeOH). $[\alpha]^{25}_D$ −0.12° (*c*=4.0, MeOH). UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 272 (4.80), 320 sh (4.46), 350 sh (4.29); (NaOMe) 273, 380; (NaOAc) 271, 318 sh, 351 sh; (NaOAc+$H_3BO_3$) 271, 318 sh, 351 sh; ($AlCl_3$) 278, 332, 390 sh; ($AlCl_3$+HCl) 278, 332, 390 sh. IR (KBr) $\nu_{max}$ cm$^{-1}$: 3391 (OH), 1676 (>C=O ester), 1615 (>C=O), 1565, 1518. $^1$H-NMR (DMSO-$d_6$) $\delta$: 12.69 (1H, s, OH-5), 7.89 (1H, dd, *J*=7.9, 1.5 Hz, H-6′), 7.74 (2H, m, H-2‴, 6‴), 7.68 (1H, d, *J*=16.0 Hz, H-7‴), 7.60 (1H, ddd, *J*=8.4, 8.0, 1.5 Hz, H-4′), 7.43 (4H, m, H-3′, 3‴, 4‴, 5‴), 7.27 (1H, ddd, *J*=8.0, 7.9, 0.9 Hz, H-5′), 7.02 (1H, s, H-3), 6.68 (1H, d, *J*=16.0 Hz, H-8‴), 6.60 (1H, s, H-6), 5.36 (1H, d, *J*=7.9 Hz, H-1″), 5.10 (1H, dd, *J*=9.1, 9.1 Hz, H-4″), 3.92 (3H, s, OMe-7), 3.81 (3H, s, OMe-8), 3.73 (1H, m, H-6″a), 3.53 (4H, m, H-2″, 3″, 5″, 6″b). $^{13}$C-NMR (DMSO-$d_6$): see Table 1. FAB-MS (positive ion mode) *m/z*: 607 $[M+H]^+$, 477 $[M+H-cinnamyl]^+$, 315 $[M+H-cinnamyl\ glucosyl]^+$. HR-FAB-MS (positive ion mode) *m/z*: 607.1807 $[M+H]^+$ (Calcd for $C_{32}H_{31}O_{12}$: 607.1815).

**Acid Hydrolysis of 5** Compound **5** (10 mg) on acid hydrolysis with 2 N HCl in MeOH for 2 h after usual workup gave skullcapflavone I[17] (**2**), *trans*-cinnamic acid and glucose identified by co-PC in BAW.

**Alkaline Hydrolysis of 5** Compound **5** (5 mg) in 1% KOH was refluxed for 2 h. The reaction mixture on usual workup gave skullcapflavone I 2′-*O*-$\beta$-D-glucopyranoside[16] (**4**) and *trans*-cinnamic acid.

## References


1) Gamble J. S., "Flora of the Presidency of Madras," Botanical Survey of India, Calcutta, 1956, Vol. 2, p. 1048.
2) Damu A. G., Jayaprakasam B., Gunasekar D., *J. Asian Nat. Products Res*., **1**, 133—138 (1998).
3) Damu A. G., Jayaprakasam B., Rao K. V., Gunasekar D., *Phytochemistry*, **49**, 1811—1813 (1998).
4) Damu A. G., Jayaprakasam B., Gunasekar D., Blond A., Bodo B., *Phytochemistry*, **52**, 147—151 (1999).
5) Jayaprakasam B., Damu A. G., Gunasekar D., Blond A., Bodo B., *Phytochemistry*, **52**, 935—937 (1999).
6) Jayaprakasam B., Gunasekar D., Rao K. V., Blond A., Bodo B., *J. Asian Nat. Products Res*., **3**, 43—48 (2001).
7) Garratt P. J., Scheinmann F., Sondheimer F., *Tetrahedron*, **23**, 2413—2416 (1967).
8) Tomimori T., Miyaichi Y., Imoto Y., Kizu H., Namba T., *Chem. Pharm. Bull*., **34**, 406—408 (1986).
9) Kikuchi Y., Miyaichi Y., Yamaguchi Y., Kizu H., Tomimori T., Vetschera K., *Chem. Pharm. Bull*., **39**, 199—201 (1991).
10) Tomimori T., Miyaichi Y., Kizu H., *Yakugaku Zasshi*, **102**, 388—391 (1982).
11) Geissman T. A. (ed.), "The Chemistry of Flavonoid Compounds," Pergamon Press, London, 1962, pp. 111—113.
12) Govindachari T. R., Parthasarathy P. C., Pai B. R., Kalyanaraman P. S., *Tetrahedron*, **24**, 7027—7031 (1968).
13) Gupta K. K., Taneja S. C., Dhar K. L., Atal C. K., *Phytochemistry*, **22**, 314—315 (1983).
14) Karl C., Muller G., Pedersen P. A., *Phytochemistry*, **15**, 1084—1085 (1976).
15) Aritomi M., *Chem. Pharm. Bull*., **11**, 1225—1228 (1963).
16) Gupta K. K., Taneja S. C., Dhar K. L., *Indian J. Chem*., **35B**, 512—513 (1996).
17) Jalal M. A. F., Overton K. H., Rycroft D. S., *Phytochemistry*, **18**, 149—151 (1979).
18) Agrawal P. K., Bansal M. C., "Carbon-13 NMR of Flavonoids," ed. by Agrawal P. K., Elsevier, Amsterdam, 1989, p. 313.
19) Markham K. R., Geiger H., "The Flavonoids: Advances in Research since 1986," ed. by Harborne J. B., Chapman & Hall, London, 1994, p. 467.