Pergamon

Phytochemistry, Vol. 47, No. 7, pp. 1223 1226, 1998

0031 9422/98 $19.00+0.00

PII: S0031-9422(97)00698-5

SECOIRIDOID GLYCOSIDES AND AN ANTIFUNGAL ANTHRANILATE DERIVATIVE FROM *GENTIANA TIBETICA*

R. X. TAN,* L. D. KONG and H. X. WEI†

Institute of Biotechnology, Department of Biological Science & Technology, Nanjing University. Nanjing 210093, P.R. China

(*Received in revised form* 27 *June* 1997)

Key Word Index—*Gentiana tibetica*; Gentianaceae; sterols; triterpene; glycosides; iridoid; secoiridoids; 8-hydroxy-10-hydrosweroside; isomacrophylloside; ethyl N-docosanoylanthranilate; fungicide.

Abstract—Repetitive chromatography of the methanol extract of the roots of *Gentiana tibetica* afforded two new secoiridoid glycosides and a novel antifungal anthranilic acid derivative, together with β-sitosterol, daucosterol, oleanolic acid, loganic acid, gentiopicroside, sweroside, 2′-(2,3-dihydroxybenzoyl)sweroside, trifloroside, rindoside and macrophylloside A. The structures of the new products were determined mainly by spectroscopic methods as 8-hydroxy-10-hydrosweroside, isomacrophylloside and ethyl N-docosanoylanthranilate. Ethyl N-docosanoylanthranilate inhibited the growth of the human pathogenic fungi *Candida albicans* and *Aspergillus flavus*. The taxonomic significance of the constituent is discussed briefly.

INTRODUCTION

In China, a very famous traditional Chinese medicine, called "Qinjiao" in Chinese, is quite frequently used for the treatment of fungal and bacterial infections, hepatitis, constipation, rheumatism, pain and hypertension. As to the plant origin, "Qinjiao" is derived mainly from *Gentiana macrophylla* Pall., but also from other *Gentiana* species such as *G. tibetica* King, *G. crassicaulis* Duthie ex Burkill and *G. dahurica* Fisch [1]. However, little is known about the chemical constituent of *G. tibetica*. Furthermore, gentiopicroside, a main bitter secoiridoid glycoside widespread in the Gentianaceae family, was found to be capable of protecting against hepatitis by inhibiting the production of tumour necrosis factor [2]. As a follow-up to our phytochemical investigations of *G. scabra* [3], *G. macrophylla* [4], and *G. algida* [5], we have examined the constituent of the roots of *G. tibetica* to ascertain the presence of gentiopicroside in the title species, and to compare the secondary metabolites of *G. tibetica* with those of *G. macrophylla* reported recently [4]. The results are presented in this article.

RESULTS AND DISCUSSION

The coarsely powdered roots of *G. tibetica* was extracted exhaustively with methanol at room temperature. The extract obtained after removal of the solvent was repetitively fractionated by CC over silica gel and filtration over Sephadex LH-20 to afford a triterpene oleanolic acid, two sterols β-sitosterol and daucosterol, an iridoid glycoside loganic acid (**1**), six known (**2**, **3**, **5-8**) and two novel (**4** and **9**) secoiridoid glycosides as well as a new biologically active anthranilic acid derivative (**10**).

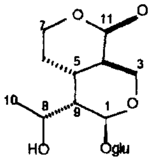
The spectral data of compound **1** (FABMS, ^{1}H and ^{13}C NMR, DEPT and ^{1}H-^{1}H COSY) indicated that it was loganic acid [6, 7]. Glycosides **2** and **3** were shown to be gentiopicroside and sweroside respectively by comparing their spectral data (^{1}H, ^{13}C and DEPT) with those of authentic materials [6]. The UV maxima of compound **5** was characteristic of a benzoylated sweroside [5]. Further scrutiny of the ^{1}H and ^{13}C NMR spectra of **5** established its identity with 2′-(2,3-dihydroxybenzoyl)sweroside, an acyl secoiridoid glycoside first characterized from *G. algida* [5] and reisolated very recently from *G. scabra* growing in China [3]. The UV absorption bands of compounds **6** and **7** showed that they were most probably acylated secoiridoid glycosides, too. This hypothesis was further substantiated by their spectral data (^{1}H, ^{13}C NMR, DEPT, ^{1}H-^{1}H COSY) which led to the identification of **6** and **7** as trifloroside and rindoside, respectively [8, 9]. Compound **8** was identified as macrophylloside A by comparing its spectral data (^{1}H, ^{13}C NMR, DEPT) with those reported [4].

The ^{1}H and ^{13}C NMR spectral data of the minor

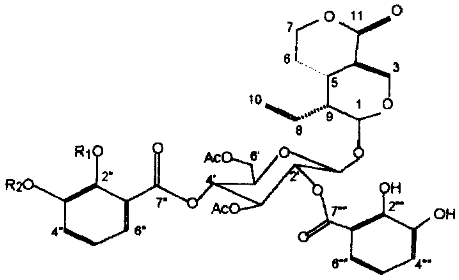
---

* Author to whom correspondence should be addressed.

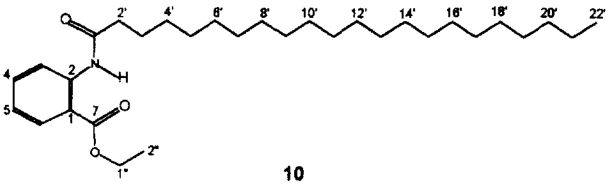
† Present address: Department of Chemistry, University of Lausanne, BCH, CH-1015 Lausanne-Dorigny, Switzerland.



4



8 $R_1 = H$, $R_2 = glu$
9 $R_1 = glu$, $R_2 = H$



10

glucoside **4** were close in part to those of sweroside [6]. All carbon and proton resonances were assigned by comparing them with those of sweroside and its analogues reviewed elsewhere [6]. However, the signals due to the vinyl group in the ^1H NMR spectrum of sweroside [6] were replaced in that of compound **4** by a three-proton doublet (J = 6.8 Hz) at δ 1.30 and a double quartet (J = 6.5, 6.8 Hz) at δ 3.21. Accordingly, the presence of an 1-hydroxyethyl group was most likely. This assumption was confirmed by the carbon resonance lines at δ 24.2 (CH_3) and 70.0 (CH). In the CI mass spectrum of **4**, an intense quasimolecular ion was exhibited at *m/z* 394 $[M+NH_4]^+$, together with a strong fragment peak at *m/z* 214 produced through elimination of glucosyl from the molecular ion. The stereochemistry of C-8 was not determined with certainty due to the lack of sufficient amounts of the sample. However, the formulated configurations at other chiral centres were based on: (i) the magnitude of couplings of H-1 with H-9 and of H-5 with H-3, and (ii) the chemical shifts arising from H-1, H-5 and C-1 through C-7 [6]. In conclusion, glycoside **4** was 8-hydroxy-10-hydrosweroside, a hitherto unknown secoiridoid glycoside.

The UV spectrum of compound **9** was very similar to that of macrophylloside A (**8**) [4]. The FAB mass spectrum in positive mode gave quasimolecular ions at *m/z* 899 $[M+Na]^+$ and 877 $[M+H]^+$. These findings, together with the ^1H and ^{13}C NMR data, indicated that the molecular formula of glycoside **9** was $C_{40}H_{44}O_{22}$, identical to that of **8** [4]. Accordingly, glycoside **9** was probably an isomer of macrophylloside A. This proposal was reinforced by the ^1H and ^{13}C NMR spectral data (Experimental), which were unequivocally assigned by ^1H-^1H COSY, HETCOR and COLOC techniques. Most of the proton and carbon signals well resembled those of macrophylloside A (**8**). The shift difference between both sets was less than 0.09 (^1H) and 0.5 (^{13}C) ppm, respectively. However, the resonances arising from the glucosyloxybenzoyl moiety in **9** were strikingly different from those of the 2-hydroxy-3-(1-β-D-glucopyranosyl)oxybenzoyl residue in trifloroside and rindoside [8, 9] as well as in macrophylloside A and B [4]. Obviously, a set of three mutually coupled double doublets at δ 7.15 (J = 7.2, 2.2 Hz), 7.11 (J = 8.2, 2.2 Hz), 7.07 (J = 7.2, 8.2 Hz) demonstrated the presence of 1,2,3-trisubstituted benzene nucleus, namely, 1,2- or 2,6-dioxygenated benzoyl function. However, a group of sp^2 carbon resonance lines at δ 126.2 (*s*, C-1″), 151.8 (*s*, C-2″), 144.9 (*s*, C-3″), 126.4 (*d*, C-4″), 122.7 (*d*, C-5″), 122.4 (*d*, C-6″) and 167.1 (*s*, C-7″) excluded the possibility for the presence of any 2,6-disubstituted benzoyl group [10]. Thus, these observations could only be rationalized by assuming that glycoside **9** possessed a (2-β-D-glucopyranosyloxy-3-hydroxy)benzoyl moiety [10]. The pronouced deviation between both sets of carbon shift values of 2-glycopyranosyloxy-3-hydroxy- and 2-hydroxy-3-glucopyranosyloxy-benzoyl residues (particularly those of C-1″, C-7″ and C-1‴) was discerned. This was presumably due to the fact that the carbonyl of the former, closer to C-1‴ and not well conjugated with the benzene ring because of the steric hindrance, could not be hydrogen-bonded by an *ortho*-hydroxy group. This deduction was reinforced by comparisons among ^{13}C NMR spectral data of a group of hydroxybenzoic acids [10]. Finally, the structure of glycoside **9** was also confirmed by its COLOC spectrum in which the anticipated long-range correlation of C-7″ with H-6″ and H-4′ was discerned. We have named glycoside **9** isomacrophylloside.

The structure of compound **10** followed from its spectral data. The presence of an anthraniloyl nucleus was indicated by the carbon resonance lines at δ 114.6 (C), 120.3 (CH), 122.4 (CH), 131.5 (CH), 134.9 (CH), 141.9 (C) and 170.6 (C) as well as a group of ^{1}H NMR signals at δ 8.71 (*dd*, J = 8.0, 2.0 Hz), 8.07 (*dd*, J = 8.0, 2.0 Hz), 7.53 (*ddd*, J = 8.0, 8.0, 2.0 Hz), 7.07 (*ddd*, J = 8.0, 8.0, 2.0 Hz) [11]. Furthermore, a two-proton quartet (J = 6.8 Hz) at δ 3.72 coupling to a methyl triplet (J = 6.8 Hz) at δ 1.25 required an ethoxy group. A quaternary carbon signal at δ 172.6 demonstrated the presence of another carbonyl function. The above assigned spectral features, together with a protonated molecular ion at *m/z* 488 and a total of 20 methylene resonances in the upper-field region of the ^{1}H and ^{13}C NMR spectra, revealed that compound **10** was ethyl N-docosanoylanthranilate.

All isolates were subjected to antifungal tests as outlined earlier [12, 13]. Compound **10** inhibited the growth of *Candida albicans* and *Aspergillus flavus* with minimal inhibition concentrations (MIC) being 80 and 60 μg/ml, respectively.

This phytochemical attention to *G. tibetica* shows, in addition to its relationships to other *Gentiana* species mentioned in references [4, 5], that *G. tibetica* is closely similar in chemical constituents to *G. macrophylla* [4]. Furthermore, the characterization of anthramilate **10**, which has never been detected before in representatives of the Gentianaceae, indicated again the chemical diversity of the family. On the other hand, this plant was found to be another rich source (Experimental) of gentiopicroside, a biologically significant bitter principle [2].

EXPERIMENTAL

General.

^{1}H and ^{13}C NMR: 500 and 125 MHz, respectively. DEPT and 2D NMR experiments were carried out following the usual procedures. Other apparatus and chemicals used in this study was as described elsewhere [14]

Plant material.

Roots of *G. tibetica* were collected in July 1996 in the Gannan Tibetan Prefecture, Gansu Province, P.R. China. The material was identified by Dr. L. X. Zhang. A voucher specimen (LXZ-96708) was deposited in the Herbarium of the Department of Biological Science and Technology, Nanjing University.

Extraction and isolation.

The coarsely pulverized air-dried plant material (2 kg) was extracted with MeOH at room temp. The extract (45 g) afforded after evaporation of the solvent was subjected to silica gel CC to yield seven CC fractions (F-1: 3.3 g, F-2: 2.7 g, F-3: 4.5 g, F-4: 5.1 g, F-5: 4.7 g, F-6: 2.2 g and F-7: 11.4 g). F-1 contained fatty materials, and F-7 saccharides as indicated by spray agents. Rechromatography of F-2 over a silica gel (200 g) column with petrol-Me$_2$CO gradient yielded β-sitosterol (230 mg) and a complex mixture of no interest. F-3 was further fractionated by CC (silica gel, 300 g) into three parts (F-3a: 0.2 g, F-3b: 0.5 g, F-3c: 1.5 g). F-3a contained mainly β-sitosterol. Fractionation of F-3b over a silica gel (50 g) column with a CHCl$_3$-MeOH gradient afforded compound **10** (23 mg) and β-sitosterol (29 mg). F-4, after combining with F-3c, was separated over a silica gel (400 g) column using a CHCl$_3$-MeOH gradient to afford four parts (F-4a: 1.7 g, F-4b: 0.2 g, F-4c: 0.7 g, F-4d: 1.8 g). F-4a and F-4d contained mainly pigments and gummy materials. Gel filtration of F-4b with CHCl$_3$-MeOH (1:1) gave a mixture (95 mg) of β-sitosterol and compound **10** (*ca* 2:1) as well as a fraction of no interest (pigment). Fractionation of F-4c through gel filtration with CHCl$_3$-MeOH (1:2) afforded oleanolic acid (51 mg). Separation of F-5 over a silica gel (400 g) column with a CHCl$_3$-MeOH gradient gave five parts (F-5a: 0.7 g, F-5b: 0.4 g, F-5c: 0.5 g, F-5d: 0.6 g, F-5e: 0.9 g). Successive gel filtration of F-5a with MeOH, MeOH-CHCl$_3$ (9:1), MeOH-CHCl$_3$ (5:1) gave glycosides **6** (28 mg) and **7** (21 mg). Gel filtration of F-5b in the same way afforded a mixture which was repeatedly fractionated by gel filtration with MeOH-EtOAc (5:1) to give **8** (22 mg) and **9** (14 mg). Repetitive gel filtration of F-5c with MeOH yielded mainly compound **5** (35 mg). Repeated gel chromatography of F-5d with MeOH gave gentiopicroside (**2**, 55 mg) and a mixture which yielded 4 mg of **4** (R_f = 0.47) by prep TLC using CHCl$_3$-MeOH (7:1). F-6 was combined with F-5e, and the mixture obtained was separated by CC (silica gel, 250 g) using a CHCl$_3$-MeOH-H$_2$O gradient of increasing polarity to afford four parts (F-6a: 0.7 g, F-6b: 0.5 g, F-6c: 0.3 g, F-6d: 0.6 g). Repetitive gel filtration of F-6a with CHCl$_3$-MeOH (1:1) gave daucosterol (130 mg) and a fraction containing mainly glycoside **5**. About 450 mg of gentiopicroside (**2**) was obtained from F-6b by repeated chromatography over a Sephadex LH-20 column with MeOH. Gel filtration of F-6c with MeOH gave again gentiopicroside (**2**, 150 mg) and a fraction which afforded sweroside (**3**, 25 mg) by prep TLC using CHCl$_3$-MeOH (7:1). Repetitive gel filtration of F-6d gave loganic acid (**1**, 15 mg) and a complex saccharide mixture of no interest.

Bioassays.

Tests for antifungal activity were performed as described previously [12, 13].

8-*Hydroxy*-10-*hydrosweroside* (**4**).

Colourless gum; $[\alpha]^{20}$ -13° (MeOH; *c* 0.012). UV λ_{max} (MeOH) (log ε): 253 (3.73); IR ν_{max} (KBr) cm^{-1}: 3570–3230 (OH), 1675 (α,β-unsaturated ester); CI MS *m/z*: 394 $[M+NH_4]^+$, 214 [M-glucosyl]$^+$; ^{1}H NMR (CD$_3$OD) δ: 5.92 (1H, *d*, J = 1.7 Hz, H-1), 7.59 (1H, *d*, J = 2.7 Hz, H-3), 3.05 (1H, *m*, H-5), 2.01 (1H, *m*, H-6a), 1.90 (1H, *m*, H-6b), 4.35 (1H, *m*, H-7a), 4.21 (1H, *br dd*, J = 11.3, 11.5 Hz, H-7b), 3.21 (1H, *dq*, J = 6.5, 6.8 Hz, H-8), 1.98 (1H, *m*, H-9), 1.30 (3H, *d*, J = 6.8 Hz, H-10), 4.67 (1H, *d*, J = 7.8 Hz, H-1′), 3.45 (1H, *dd*, J = 7.8, 9.0 Hz, H-2′), 3.41 (1H, *t*, J = 9.0 Hz, H-3′), 3.35 (1H, *t*, J = 9.0 Hz, H-4′), 3.12 (1H, *m*, H-5′), 3.89 (1H, *dd*, J = 12.1, 2.1 Hz, H-6′a), 3.63 (1H, *dd*, J = 12.1, 4.4 Hz, H-6′b). ^{13}C NMR (CD_3OD, multiplicities by DEPT pulse sequences) δ: 95.7 (*d*, C-1), 154.8 (*d*, C-3), 106.5 (*s*, C-4), 28.7 (*d*, C-5), 26.3 (*t*, C-6), 65.2 (*t*, C-7), 70.0 (*d*, C-8), 44.5 (*d*, C-9), 24.2 (*q*, C-10), 167.8 (*s*, C-11), 99.9 (*d*, C-1′), 74.7 (*d*, C-2′), 78.3 (*d*, C-3′), 71.5 (*d*, C-4′), 77.9 (*d*, C-5′), 62.8 (*t*, C-6′).

Isomacrophylloside (**9**).

Colourless gum; $[\alpha]^{20}$ −12° (MeOH; *c* 0.003). UV λ_{max} (MeOH) (log ε): 240 (4.5), 254 (3.9), 326 (1.2); IR ν_{max} (KBr) cm^{-1}: 3510–3220 (OH), 1735, 1675 (ester carbonyl), 1595, 1485 (benzene ring); FAB MS (positive) *m*/*z*: 899 $[M+Na]^+$, 877 $[M+H]^+$; ^{1}H NMR (CD_3OD) δ: 5.36 (1H, *d*, J = 1.0 Hz, H-1), 7.24 (1H, *d*, J = 1.9 Hz, H-3), 2.66 (1H, *m*, H-5), 1.65 (1H, *m*, H-6a), 1.52 (1H, *dddd*, J = 12.9, 12.0, 11.8, 3.4 Hz, H-6b), 4.27 (1H, *m*, H-7a), 4.00 (1H, *ddd*, J = 11.8, 12, 1.7 Hz, H-7b), 5.42 (1H, *ddd*, J = 17.2, 10.1, 9.3 Hz, H-8), 2.66 (1H, *m*, H-9), 5.23 (1H, *dd*, J = 10.1, 2.0 Hz, H-10a), 5.29 (1H, *dd*, J = 17.2, 2.1 Hz, H-10b), 5.40 (2H, *m*, H-1′ and H-2′), 5.76 (1H, *t*, J = 9.5 Hz, H-3′), 5.38 (1H, *t*, J = 9.5 Hz, H-4′), 4.23 (1H, *m*, H-5′), 4.34 (1H, *dd*, J = 12.5, 1.7 Hz, H-6′a), 4.25 (1H, *dd*, J = 12.5, 4.4 Hz, H-6′b), 7.15 (1H, *dd*, J = 7.2, 2.2 Hz, H-4″), 7.07 (1H, *dd*, J = 7.2, 8.2 Hz, H-5″), 7.11 (1H, *dd*, J = 8.2, 2.2 Hz, H-6″), 4.86 (1H, *d*, J = 7.7 Hz, H-1‴), 3.49 (1H, *dd*, J = 7.7, 9.3 Hz, H-2‴), 3.43 (1H, *dd*, J = 9.3, 9.0 Hz, H-3‴), 3.40 (1H, *t*, J = 9.0 Hz, H-4‴), 3.30 (1H, *m*, H-5‴), 3.84 (1H, *dd*, J = 12.1, 2.3 Hz, H-6‴a), 3.71 (1H, *dd*, J = 12.1, 5.3 Hz, H-6‴b), 7.00 (1H, *dd*, J = 8.0, 1.5 Hz, H-4⁗), 6.70 (1H, *t*, J = 8.0, H-5⁗), 7.21 (1H, *dd*, J = 8.0, 1.5 Hz, H-6⁗), 2.07, 1.93 (3H each, *s*, OAc × 2); ^{13}C NMR (CD_3OD, multiplicities by DEPT pulse sequences) δ: 97.7 (*d*, C-1), 153.1 (*d*, C-3), 106.0 (*s*, C-4), 28.7 (*d*, C-5), 25.7 (*t*, C-6), 69.4 (*t*, C-7), 132.6 (*d*, C-8), 43.2 (*d*, C-9), 121.4 (*t*, C-10), 166.9 (*s*, C-11), 96.6 (*d*, C-1′), 72.8 (*d*, C-2′), 72.9 (*d*, C-3′), 70.8 (*d*, C-4′), 73.3 (*d*, C-5′), 63.4 (*t*, C-6′), 126.2 (*s*, C-1″), 151.8 (*s*, C-2″), 144.9 (*s*, C-3″), 126.4 (*d*, C-4″), 122.7 (*d*, C-5″), 122.4 (*d*, C-6″), 167.1 (*s*, C-7″), 106.1 (*d*, C-1‴), 75.1 (*d*, C-2‴), 77.7 (*d*, C-3‴), 70.9 (*d*, C-4‴), 78.8 (*d*, C-5‴), 62.2 (*t*, C-6‴), 113.0 (*s*, C-1⁗), 151.3 (*s*, C-2⁗), 147.3 (*s*, C-3⁗), 121.0 (*d*, C-4⁗), 120.7 (*d*, C-5⁗), 123.0 (*d*, C-6⁗), 170.5 (*s*, C-7⁗), 20.7 (2C, *q* each, OAc × 2), 172.5, 171.6 (*s*, OAc × 2).

Ethyl N-docosanoylanthranilate (**10**).

White gum; IR ν_{max} (KBr) cm^{-1}: 3310 (NH), 2924, 2855 (CH_2, CH_3), 1690 (carbonyl), 1605, 1585, 1450; CI MS *m*/*z*: 488 $[M+H]^+$; ^{1}H NMR ($CDCl_3$) δ: 11.15 (1H, *br s*, NH chelated with the ester carbonyl), 8.71 (1H, *dd*, J = 8.0, 2.0 Hz, H-3), 7.53 (1H, *td*, J = 8.0, 2.0 Hz, H-4), 7.07 (1H, *td*, J = 8.0, 2.0 Hz, H-5), 8.07 (1H, *dd*, J = 8.0, 2.0 Hz, H-6), 2.44 (2H, *m*, H-2′), 1.25 (38H, *m*, H-3′ ~ H-21′), 0.86 (3H, *m*, H-22′), 3.72 (2H, *q*, J = 6.8 Hz, H-1″), 1.25 (3H, *t*, J = 6.8 Hz, H-2″); ^{13}C NMR ($CDCl_3$, multiplicities by DEPT pulse sequences) δ: 114.6 (*s*, C-1), 141.9 (*s*, C-2), 120.3 (*d*, C-3), 134.9 (*d*, C-4), 122.4 (*d*, C-5), 131.5 (*d*, C-6), 170.6 (*s*, C-7), 172.6 (*s*, C-1′), 38.7 (*t*, C-2′), 25.5 (*t*, C-3′), 29.9–29.1 (16C, *t*, C-4′ ~ C-19′), 31.9 (*t*, C-20′), 22.7 (*t*, C-21′), 14.1 (*q*, C-22′), 58.4 (*t*, C-1″), 18.3 (*q*, C-2″).

Acknowledgements—This study was co-supported by grants to RXT from the National Natural Science Foundation (No: 39670873) and the Doctoral Training Programme (No: 9628418).

REFERENCES

1. Jiangsu College of New Medicine (1977) *A Comprehensive Dictionary of the Traditional Chinese Medicine*, pp. 1764–1767. Suzhou Jiangsu, China.
2. Kondo, Y., Takano, F. and Hojo, H., *Planta Med.*, 1994, **60**, 414.
3. Tang, H. Q. and Tan, R. X., *Planta Med.*, 1997 (in press).
4. Tan, R. X., Wolfender, J.-L., Zhang, L. X., Ma, W. G., Fuzzati, N., Marston, A. and Hostettmann, K., *Phytochemistry*, 1996, **42**,1305.
5. Tan, R. X., Wolfender, J.-L., Ma, W. G., Zhang, L. X. and Hostettmann, K., *Phytochemistry*, 1996, **41**, 111.
6. Boros, C. A. and Stermitz, F. R., *J. Nat. Prod.*, 1991, **54**, 1173.
7. Çaliş, I., Lahloub, M. F. and Sticher, O., *Helv. Chim. Acta*, 1984, **67**, 160.
8. Çaliş, I., Ruegger, H., Chun, Z. and Sticher, O., *Planta Med.*, 1990, **56**, 406.
9. Ikeshiro, Y., Mase, I. and Tomita, Y., *Planta Med.*, 1990, **56**, 101.
10. Scott, K. N., *J. Am. Chem. Soc.*, 1972, **94**, 8564.
11. Barrero, A. F., Sánchez, J. F. and Rodriguez, I., *Phytochemistry*, 1990, **29**, 1967.
12. Rahalison, L., Hamburger, M., Hostettmann, K., Monod, M. and Frenk, E., *Phytochem. Anal.*, 1991, **2**, 199.
13. Zheng, W. F., Tan, R. X., Yang, L. and Liu, Z. L., *Planta Med.*, 1996, **62**, 160.
14. Tan, R. X., Hu, Y. H., Liu, Z. L. and Pan, X., *J. Nat. Prod.*, 1993, **56**, 1917.