NATURAL PRODUCT COMMUNICATIONS
An International Journal for Communications and Reviews Covering all Aspects of Natural Products Research

ISSN 1934-578X (printed); ISSN 1555-9475 (online)
www.naturalproduct.us
EDITOR-IN-CHIEF
DR. PÅWAN K. AGRAWAL
Natural Product Inc.
7963, Anderson Park Lane,
Westerville, Ohio 43081, USA
agrawal@naturalproduct.us

EDITORS
PROFESSOR ALEJANDRO F. BARRERO
Department of Organic Chemistry,
University of Granada,
Campus de Fuentenueva, s/n, 18071, Granada, Spain
afbarre@ugr.es

PROFESSOR ALESSANDRA BRACA
Dipartimento di Chimica Biororganica Biofarmacia,
Università di Pisa,
via Bonanno 33, 56126 Pisa, Italy
braca@farm.unipi.it

PROFESSOR DEAN GUO
State Key Laboratory of Natural and Biomimetic Drugs,
School of Pharmaceutical Sciences,
Peking University,
Beijing 100083, China
gdsg5958@163.com

PROFESSOR YOSHIHIRO MIMAKI
School of Pharmacy,
Tokyo University of Pharmacy and Life Sciences,
Hortinsouchi 1432-1, Hachioji, Tokyo 192-0392, Japan
mimaki@gps.touyasaki.ac.jp

PROFESSOR STEPHEN G. PYNE
Department of Chemistry,
University of Wollongong,
Wollongong, New South Wales, 2522, Australia
spyne@uow.edu.au

PROFESSOR MANFRED G. REINECKE
Department of Chemistry,
Texas Christian University,
Forts Worth, TX 76129, USA
m.reinecke@tcu.edu

PROFESSOR WILLIAM N. SETZER
Department of Chemistry,
The University of Alabama in Huntsville
Huntsville, AL 35809, USA
wssetzer@chemistry.uah.edu

PROFESSOR YASUHIRO TEZUKA
Institute of Natural Medicine
Institute of Natural Medicine, University of Toyama,
2630-Sugitani, Toyama 930-0194, Japan
tezuka@inn.u-toyama.ac.jp

PROFESSOR DAVID E. THURSTON
Department of Pharmaceutical and Biological Chemistry,
The School of Pharmacy,
University of London, 29-39 Brunswick Square,
London WC1N 1AX, UK
david.thurston@pharmacy.ac.uk

HONORARY EDITOR
PROFESSOR YASUHIRO TEZUKA
Institute of Natural Medicine
The School of Pharmacy & Biomedical Sciences,
University of Portsmouth,
Portsmouth, PO1 2DT U.K.
axuf64@dsl.pipex.com

PROFESSOR ALEJANDRO F. BARRERO
Department of Organic Chemistry,
University of Granada,
Campus de Fuentenueva, s/n, 18071, Granada, Spain
afbarre@ugr.es

PROFESSOR YOSHIHIRO MIMAKI
School of Pharmacy,
Tokyo University of Pharmacy and Life Sciences,
Hortinsouchi 1432-1, Hachioji, Tokyo 192-0392, Japan
mimaki@gps.touyasaki.ac.jp

PROFESSOR DEAN GUO
State Key Laboratory of Natural and Biomimetic Drugs,
School of Pharmaceutical Sciences,
Peking University,
Beijing 100083, China
gdsg5958@163.com

INFORMATION FOR AUTHORS

Full details of how to submit a manuscript for publication in Natural Product Communications are given in Information for Authors on our Web site http://www.naturalproduct.us.

Authors may reproduce/republish portions of their published contribution without seeking permission from NPC, provided that any such republication is accompanied by an acknowledgment (original citation)-Reproduced by permission of Natural Product Communications. Any unauthorized reproduction, transmission or storage may result in either civil or criminal liability.

The publication of each of the articles contained herein is protected by copyright. Except as allowed under national “fair use” laws, copying is not permitted by any means or for any purpose, such as for distribution to any third party (whether by sale, loan, gift, or otherwise); as agent (express or implied) of any third party; for purposes of advertising or promotion; or to create collective or derivative works. Such permission requests, or other inquiries, should be addressed to the Natural Product Inc. (NPI). A photocopy license is available from the NPI for institutional subscribers that need to make multiple copies of single articles for internal study or research purposes.

To Subscribe: Natural Product Communications is a journal published monthly. 2012 subscription price: US$1,995 (Print, ISSN# 1934-578X); US$1,995 (Web edition, ISSN# 1555-9475); US$2,495 (Print + single site online); US$595 (Personal online). Orders should be addressed to Subscription Department, Natural Product Communications, Natural Product Inc., 7963 Anderson Park Lane, Westerville, Ohio 43081, USA. Subscriptions are renewed on an annual basis. Claims for nonreceipt of issues will be honored if made within three months of publication of the issue. All issues are dispatched by airmail throughout the world, excluding the USA and Canada.
Glucosylated Sesquiterpene Alcohols from *Fraxinus griffithii*

Rene Angelo Macahig, Liva Harinantenaina, Sachiko Sugimoto, Katsuyoshi Matsunami, Hideaki Otsuka, Yoshiro Takeda and Takakazu Shinzato

aDepartment of Chemistry, School of Science and Engineering, Ateneo de Manila University, Katipunan Avenue, Loyola Heights, Quezon City 1108, Philippines
bDepartment of Chemistry, Virginia Polytechnic Institute and State University, 107 Davidson Hall Blacksburg, Virginia 24061-0001, USA
cDepartment of Pharmacognosy, Graduate School of Biomedical Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8553, Japan
dFaculty of Pharmacy, Yasuda Women’s University, 6-13-1 Yasuhigashi, Asaminami-ku, Hiroshima 731-0153, Japan
eSubtropical Field Science Center, Faculty of Agriculture, University of the Ryukyus, I Sembaru, Nishihara-cho, Nakagami-gun, Okinawa 903-0213, Japan

rmacahig@ateneo.edu

Received: February 6th, 2012; Accepted: March 10th, 2012

Phytochemical investigation of the leaves of *Fraxinus griffithii* has led to the isolation of two new glucosylated acyclic sesquiterpene alcohols, griffithosides D (1) and E (2), along with iridoid and secoiridoid glycosides. The molecular structures of these compounds were elucidated using NMR, MS and other spectroscopic techniques, as well as comparison with literature data. The isolated compounds were tested for radical-scavenging activity and cytotoxicity against A549 human lung adenocarcinoma cells and *Leishmania major* parasites.

Keywords: *Fraxinus griffithii*, Oleaceae, Sesquiterpene alcohol.

Belonging to the Oleaceae family, *Fraxinus* species consist of around forty species distributed in temperate and subtropical regions. These species are widely used as timber, ornamentals and garden plants. Also used in traditional medicine, *Fraxinus* species are mainly indicated for inflammatory ailments such as arthritis, rheumatic pain, gout and rhinitis. In China, the roots of *F. malacophylla* are used to treat malaria and excretory organ infection. The bark of *F. japonica* is used for diuretic, anti-febrile and analgesic purposes [1-3]. A formulation of the cortex of various *Fraxinus* species- cortex fraxini in English or qinpi in Chinese- is used as an antibacterial, analgesic and anti-inflammatory agent for the treatment of diarrhea, bacillary dysentery, arthritis and hyperuricemia. It has also been shown to have diuretic, anticoagulant, antiallergic and antioxidant effects [4-8]. Air-dried leaves of *F. griffithii* were extracted with MeOH and the resulting extract was concentrated and then successively extracted with n-hexane, EtOAc and n-BuOH. The EtOAc-soluble fraction afforded two new glucosylated sesquiterpene alcohols (1-2), along with an iridoid and secoiridoid glycosides.

Griffithoside D (1) was isolated as an amorphous solid with a molecular formula of C21H36O8, as determined by HR-ESI-MS. The IR spectrum showed absorption bands characteristic for hydroxyl groups (3365 cm⁻¹), as well as olefinic groups (1654 and 1559 cm⁻¹). The ¹H NMR spectrum showed an anomeric proton resonance at δH 4.36 (1H, d, J = 8 Hz) indicating the presence of a glucosyl moiety, olefinic resonances at δH 5.20 (1H, dd, J = 11, 1.5 Hz), δH 5.24 (1H, dd, J = 18, 1.5 Hz), and δH 5.94 (1H, dd, J = 18, 11 Hz) indicating a terminal alkene moiety, as well as an overlapped olefinic resonance at δH 5.36 (2H, td, J = 7, 1 Hz), indicating the presence of two more alkene groups (Table 1).

The ¹³C NMR spectral data showed 21 resonances (Table 1), six of which were attributable to a β-glucopyranosyl moiety. COSY, HSQC and HMBC showed the remaining signals to be attributable to a 15-carbon unit of an acyclic sesquiterpene with three olefinic moieties and three oxygenated carbon atoms. The presence of long-range correlations from the methyl protons (H-13) at δH 1.38 to the olefinic resonance at δC 144.5 and the oxygenated carbon resonance at δC 81.4 in the HMBC spectrum established the position of the terminal olefinic moiety. This was further supported by the presence of a long-range correlation between the terminal olefinic protons (H-1) at δH 5.20 and δH 5.24 and the oxygenated carbon resonance (C-3) at δC 81.4, as well as the presence of a COSY correlation between these protons and the olefinic proton (H-2) at δH 5.94. The position of the other alkene group was substantiated by the following 2D-NMR correlations: long-range HMBC correlation

![Figure 1: Sesquiterpene alcohols from *F. griffithii*.](image-url)
between the vinylic methyl protons (H-14) at δH 1.60 and the olefinic resonance (C-6) at δC 127.7 and a COSY correlation between the olefinic proton (H-6) at δH 5.36 and the methylene protons (H-2-5) at δH 2.10. The position of the third olefinic moiety was substantiated by the following 2D-NMR correlations: a long-range correlation between the vinylic methyl protons (H-15) at δH 1.65 and the olefinic resonance (C-10) at δC 123.2, a long-range correlation between the oxygenated methylene protons (H-12) at δH 3.91 and the same olefinic resonance (C-10) and a COSY correlation between the olefinic proton (H-10) at δH 5.36 and the methylene protons (H-9) at δH 2.27. The presence of a hydroxyl moiety at position 8 was established by the presence of long-range correlations from the vinylic methyl protons (H-14) at δH 1.60 and the methylene protons (H-2-9) at δH 2.27 to the oxygenated carbon resonance (C-8) at δC 77.7. The attachment of the glucosyl moiety at the 3-position was deduced from the observation of a long-range correlation between the anomeric proton (H-1') at δH 4.36 and the quaternary resonance (C-3) at δC 81.4 (Figure 1). The presence of a correlation between the olefinic proton (H-6) at δH 5.36 and the methine proton (H-8) at δH 3.18 in the NOE spectrum showed the stereochemistry of the olefinic group at the 6-position to be E. Similarly, the presence of an NOE correlation between the olefinic proton (H-10) at δH 5.36 and the methylene protons (H-12-15) at δH 3.91 established the stereochemistry of the olefinic group at the 10-position to be E. Hence the structure of I was elucidated as shown in Figure 1.

Griffithside E (2) was isolated as an amorphous solid with a molecular formula of C21H16O6, as determined by HR-ESI-MS. The IR spectrum displayed the same absorption pattern as I, showing characteristic bands for hydroxyl and olefinic moieties. The 1H NMR spectrum of 2 also showed a similar pattern to I with an anomeric proton resonance at δH 4.24 (1H, d, J = 8 Hz), indicating the presence of a glucosyl moiety, olefinic resonances at δH 5.02 (1H, dd, J = 11, 1.5 Hz), δH 5.19 (1H, dd, J = 18, 1.5 Hz), and δH 5.91 (1H, dd, J = 18, 11 Hz), indicating a terminal alkene moiety, and δH 5.36 (1H, td, J = 7, 1 Hz) and δH 5.44 (1H, td, J = 7, 1 Hz) indicating the presence of two more olefinic groups (Table 1). The 13C NMR spectral data also showed a similar pattern to I displaying 21 resonances (Table 1), six of which were attributable to a β-glucopyranosyl moiety with the remaining fifteen signals attributable to an acyclic sesquiterpene similar to I.

COSY, HSQC and HMBC experiments showed 2 to be an isomer of I, the main difference being the position of attachment of the sugar moiety. This was further supported by the upfield shift of the carbon signal at the 3-position at δC 73.8 and the downfield shift of the signal at the 12-position at δC 75.9 in comparison with I, consistent with a glucosylation shift trend. The attachment of the glucosyl moiety at the 12-position was confirmed by the observation of a long-range correlation between the anomeric proton (H-1') at δH 4.24 and the oxymethylene resonance (C-12) at δC 75.9 (Figure 1).

Similar to I, the observation of correlations between the olefinic proton (H-6) at δH 5.36 and the methine proton (H-8) at δH 3.23 and between the olefinic proton (H-10) at δH 5.44 and the methylene protons (H-12-15) at δH 4.03 and δH 4.19 in the NOE spectrum of 2 established the stereochemistry of the olefinic groups at the 6 and 10-positions to be both E, allowing the structure of 2 to be elucidated as shown in Figure 1.

While the stereochemistry at positions 3 and 8 could not be determined for I and 2, it is noteworthy that in most acyclic terpenes isolated from natural sources, the 3S stereochemistry is much more common. However, as this is the first report of acyclic sesquiterpenes from F. griffithii, such a generalization is difficult to make.

In a previous work, we reported the isolation and identification of some secoiridoids: griffithside A-C (3-5) and 7-epi-7-O-(E)-caffeoylloganic acid (6) [9]. Other known secoiridoids isolated from this plant were identified as formoside (9) [10,11], isoligustroside (10) [12], 1′′-O-β-glucosylformoside (9) [10], isoligustrosideic acid (10) [13], isoligustroside (11) [12], safghanoside C (12) [14], safghanoside D (13) [14], oleoside dimethyl ester (14) [13] and syringalactone A (15) [15].

Assay results showed that 5, 6 and 13 exhibited significant radical scavenging activity (IC50: 42.4, 17.4 and 26.2 μM, respectively). Structurally, a common feature among these compounds was the presence of the 1,2-dihydroxystyrenyl moiety, which appeared to be important for radical scavenging activity. Compounds 9 and 11 showed moderate cytotoxic activity against A549 cells (IC50: 46.5 and 40.8 μM, respectively). None of the isolated compounds showed selective cytotoxicity against L. major parasites.

**Experimental**

**General:** IR spectra were obtained on a Horiba Fourier transform infrared spectrophotometer FT-710. Optical rotation data were measured on a JASCO P-1030 polarimeter. 1H and 13C NMR spectra were recorded on a JEOL JNM α-400 spectrometer at 400 MHz and 100 MHz, respectively, with tetramethylsilane as an internal standard. HR-FAB mass spectra (negative-ion mode) and HRFAB mass spectra (positive-ion mode) were taken on a JEOL JMS-SX 102 mass spectrometer and an Applied Biosystems QSTAR XL System, respectively.

Highly porous synthetic resin Diaion HP-20 was purchased from Mitsubishi Chemical Co., Ltd. (Tokyo, Japan). Silica gel column chromatography (CC) was performed on silica gel 60 [(E. Merck, Darmstadt, Germany) 70-230 mesh]. Reversed-phase ODS open CC (RPCC) was performed on Cosmosil 75 C18-OPN (Nacalai

| Table 1: NMR spectroscopic data for I and 2. |
|------|------|--|------|--|
| 1    | 2    |
|δC   | δH   |δC   | δH   |
|1    | 115.8 |5.20 dd 11,1.5 |112.1 |5.02 dd 11,1.5 |
|2    | 144.5 |5.94 dd 17,1.5 |146.4 |5.91 dd 17,1.5 |
|3    | 81.4  | --           | 73.8  | --           |
|4    | 42.3  |1.66 m        | 43.1  |1.55 m        |
|5    | 23.3  |2.10 dt 11,7  | 23.4  |2.07 m        |
|6    | 127.7 |5.36 td 7,1   | 127.5 |5.36 td 7,1   |
|7    | 137.5 | --           | 134.4 | --           |
|8    | 77.7  |3.18 dd 7,3   | 77.9  |3.23 dd 7,3   |
|9    | 34.6  |2.27 dd 10,7  | 34.6  |2.28 dd 7,7   |
|10   | 123.2 |5.36 td 7,1   | 126.4 |5.44 dd 7,1   |
|11   | 137.9 | --           | 137.9 | --           |
|12   | 69.0  |3.91 s        | 75.9  |4.03 dd 12,4  |
|13   | 23.4  |1.38 s        | 27.6  |1.26 s        |
|14   | 11.6  |1.60 br s     | 11.6  |1.61 br s     |
|15   | 14.0  |1.65 br s     | 14.4  |1.69 br s     |
|1′   | 99.6  |4.36 d 8      | 102.6 |4.24 d 8      |
|2′   | 75.3  |3.16 dd 9,8   | 75.1  |3.19 dd 9,8   |
|3′   | 78.4  | m            | 78.3  | m            |
|4′   | 71.9  |3.27 d 9      | 71.8  |3.27 d 9      |
|5′   | 78.5  |3.95 d 17     | 78.3  |3.96 d 17     |
|6′   | 62.9  |3.63 dd 12,6  | 62.9  |3.66 dd 12,6  |
|     | 3.80 dd 12,2 | 3.85 dd 12,2 |

\( J \) in ppm from TMS as internal standard. \( J \) in Hz. Assigned by HSQC. m = multiplet or overlapped signal.
Glycosylated sesquiterpene alcohols from *Fraxinus griffithii*

**Plant material:** The leaves of *F. griffithii* C. B. Clarke were collected in Okinawa, Japan in June, 2005, and a voucher specimen was deposited in the Herbarium of Pharmaceutical Sciences, Graduate School of Biomedical Sciences, Hiroshima University (05-FG-Okinawa-0628).

**Extraction and isolation:** Air-dried leaves of *F. griffithii* (5.64 kg) were extracted 3 times with MeOH (45 L × 3) for one week at ambient conditions, and then the MeOH extract was concentrated to 6 L *in vacuo*. The extract was washed with *n*-hexane (6 L) and then the methanolic layer was concentrated to a viscous gum (*n*-hexane-soluble fraction: 46.8 g). The residue was suspended in H2O (6 L) and then extracted with EtOAc (6 L), 500 mL fractions being collected. The residue (1.5 g) in fractions 42-52 was suspended in CHCl3 and then extracted with EtOAc (6 L), 500 mL fractions being collected. The final water-layer was concentrated to 242 g of a water-soluble fraction. An aliquot of the *n*-BuOH-soluble fraction (209 g) was applied to Diaion HP-20 CC (Φ=60 mm, L=65 cm) and eluted with a stepwise-gradient of MeOH-H2O (1:4, 2:3, 3:2 and 4:1, 6 L each) and MeOH (6 L), 500 mL fractions being collected. The residue (63.4 g) eluted with 40% MeOH in fraction 4 obtained on HP-20 CC was subjected to silica gel CC (750 g) using CHCl3 (3 L), CHCl3:MeOH (49:1, 24:1, 23:2, 9:1, 17.3, 4:1, 3:1 and 7:3, 4.5 L each), and CHCl3:MeOH:H2O (70:30:4, 4.5 L), 500 mL fractions being collected. The residue (515 mg) in fractions 42-52 of the 10% MeOH in CHCl3 eluate was further subjected to RPCC to afford 9 fractions, the eighth of which (19.3 mg) was further purified by HPLC (47.5% MeOH in H2O) to afford 4.20 mg of 1 and 3.77 mg of 2 from the peaks at 29.7 and 31.8 min, respectively. The residue (33.3 g) eluted with 40% MeOH in fraction 5 obtained on HP-20 CC was subjected to silica gel CC (750 g) using CHCl3 (3 L), CHCl3:MeOH (49:1, 24:1, 23:2, 9:1, 17.3, 4:1, 3:1 and 7:3, 4.5 L each), and CHCl3:MeOH:H2O (70:30:4, 4.5 L), 500 mL fractions being collected. The residue (1.09 g) in fractions 30-41 of the 8% MeOH in CHCl3 eluate was further subjected to RPCC to afford 14 fractions, the fourth being (65.5 mg) subsequently purified by HPLC (50% MeOH in H2O) to give 23.6 mg of 14 from the peak at 12.6 min, and the sixth fraction (52.6 mg) was also purified by HPLC (50% MeOH in H2O) to afford 11.0 mg of 3 from the peak at 15.6 min. From the same RPCC experiment, the ninth and 11th fractions were identified as 7 (179 mg) and 4 (32.8 mg), respectively. The residue (1.72 g) in fractions 70-79 of the 30% MeOH in CHCl3 eluate was further subjected to RPCC affording a residue (165 mg) in fractions 112-117, which was subsequently purified by DCCC to afford 36.0 mg of 12 from the peak at 41.6 min. From the same RPCC experiment, the residue (94.6 mg) in fractions 138-144 was subsequently purified by DCCC to afford 23.7 mg of 9 from fractions 38-44. From the same RPCC experiment, the residue (363 mg) in fractions 145-152 was subsequently purified by DCCC to afford 68.4 mg of 10 in fractions 42-52. The residue (1.92 g in fractions 42-49) of the 10% MeOH in CHCl3 eluate was further subjected to RPCC affording a residue (191 mg) from fractions 134-139 that was subsequently purified by DCCC to yield 22.5 mg of 15 from fractions 94-102. From the same RPCC experiment, the residue (50.1 mg) from fractions 157-162 was subsequently purified by DCCC to afford 10.7 mg of 5 in fractions 91-107 and 12.0 mg of 11 in fractions 108-120. Also, the residue (98.9 mg) from fractions 163-169 was subsequently purified by HPLC (45% MeOH in H2O) to give 39.1 mg of 13 from the peak at 33.6 min. The residue (235 mg) from fractions 176-179 was identified as 8.

**DPPH radical-scavenging assay:** The antioxidant activity was evaluated using the DPPH radical-scavenging system as described previously [9]. Into a 96-well plate, 2 µL aliquots of the DMSO solution of the compounds were diluted with 98 µL of MeOH in triplicate. A 100 µL aliquot of the methanolic solution of DPPH was added to each well to a final concentration of 100 µM. The compounds were tested at final concentrations of 50, 30, 10 and 5 µM. The mixture was incubated in the dark for 30 min at room temperature, followed by measurement of the absorbance at 515 nm using a Molecular Devices Versamax tunable microplate reader. DMSO was used as a negative control and Trolox as a positive one. Radical scavenging activity was expressed as the inhibition percentage.

**A549 growth inhibition assay:** Human lung cancer cells (A549) were cultured in Dulbecco’s modified Eagle medium supplemented with 10% heat-inactivated fetal bovine serum and 100 µg/mL of kanamycin and 0.5 µg/mL amphotericin. Into a 96-well plate, aliquots of the DMSO solution of the test compounds (1% final concentration) were incubated with A549 cells (5 × 10^4) for 24 h in the same medium without the test compounds [9]. The viability was compared to that of control cells incubated in the same medium without the test compounds [9].

**Anti-Leishmania major assay:** *Leishmania major* promastigotes were cultured in M199 medium supplemented with 10% heat-inactivated fetal bovine serum and 100 µg/mL of kanamycin. Into a 96-well plate, aliquots of the DMSO solution of the test compounds (1% final concentration) were incubated with *L. major* cells (1 × 10^5) for 24 h in the same medium without the test compounds [9].

**Giffithoside D (1)**

Amorphous solid. [α]_D^n = −22.9 (c = 0.28, MeOH).

IR ν_{max} (film) cm⁻¹: 3365, 1654, 1559, 1507, 1072, 1037.
1H NMR (400 MHz, CD3OD): Table 1.
13C NMR (100 MHz, CD3OD): Table 1.
HR-ESI-MS (positive-ion mode) m/z: 439.2309 [M+Na]+ (Calcd for C21H36O8Na: 439.2308).

Griffithoside E (2)
Amorphous solid.
[α]D: −11.1 (c 0.25, MeOH).
IR νmax (film) cm−1: 3368, 1653, 1559, 1507, 1072, 1037.

Acknowledgments - The authors are grateful for access to the superconducting NMR instrument and the HR-ESI-MS at the Analytical Center of Molecular Medicine and the Analysis Center of Life Science, respectively, of the Graduate School of Biomedical Sciences, Hiroshima University. RAM expresses his gratitude to the Ministry of Education, Sports, Culture and Technology (MEXT) of Japan, the Japan Student Services Organization (JASSO) and the Kumahira Scholarship and Cultural Foundation for the financial assistance.

References
Alexandra S. Silchenko, Anatoly I. Kalinovsky, Sergey A. Avilov, Pelageya V. Andryjaschenko, Pavel S. Dmitrenok, Ekaterina A. Martyyas and Vladimir I. Kalinin

A New Geranylated Aromatic Compound from the Mushroom *Hericium erinaceum*
Yasunori Yaoita, Shiori Yonezawa, Masao Kikuchi and Koichi Machida

Formation of Tetrahydrocurcumin by Reduction of Curcumin with Cultured Plant Cells of *Marchantia polymorpha*
Kei Shimoda, Naoji Kubota, Hirotaka Hirano, Masahiro Matsumoto, Hatsuyuki Hamada and Hiroki Hamada

Regioselective Formation of Silybin-23-β-D-glucoside by Glucosylation of Silybin with Cultured Plant Cells of *Eucalyptus perriniana*
Kei Shimoda, Hiroya Imai, Tadakatsu Mandai and Hiroki Hamada

**Review/Account**

Terpenoids and Related Compounds from Plants of the Family Compositae (Asteraceae)
Yasunori Yaoita, Masao Kikuchi and Koichi Machida

Diversity of Furanoeremophilanes in Major *Ligularia* Species in the Hengduan Mountains
Chiaki Kuroda, Ryo Hanai, Hajime Nagano, Motoo Tori and Xun Gong
Contents

Original Paper Page

Determination of the Absolute Stereochemistry of Limonene and α-Santalol by Raman Optical Activity Spectroscopy
Akira Sakamoto, Nao Ohya, Toshih Hasegawa, Hiroaki Izumi, Nakako Tokita and Yoshiaki Hamada 419

Four New Eremophilane-Type Alcohols from Cremanthodium helianthus Collected in China
Yoshinori Saito, Mayu Ichihara, Yasuko Okamoto, Xun Gong, Chikai Kuroda and Motoo Tori 423

Culcitolides A-D, Four New Eremophilane-Type Sesquiterpene Derivatives from Senecio culcitoides
Hiroshi Nozaki, Ken-ichiro Hayashi, Mikiko Kawai, Taich Matsui, Masahiro Kido, Hiroky Tani, Daisuke Takaoka, Hidenitsu Uno, Susumu Ohira, Atsuto Kaboki and Nobuyasu Matsunara 427

Complex Diversity in Ligularia kanaitzensis
Anna Shimizu, Yurika Suzuki, Atsushi Torihata, Ryo Hanai, Yoshinori Saito, Motoo Tori, Xun Gong, and Chiaki Kuroda 431

Chemical Constituents from Farfugium japonicum var. formosanum
Sung-Fei Hsieh, Tain-Jye Hsieh, Mohamed El-Shazly, Ying-Chi Du, Chin-Chung Wu, Tsong-Long Hwang, Yang-Chang Wu and Fang-Rong Chang 435

Transannular Cyclization of (4S,5S)-Germacrone-4,5-epoxide into Guaiane and Secoguaine-type Sesquiterpenes
Masanori Kuroyanagi, Osamu Shirota, Setsuko Sekita and Takahisa Nakane 441

Four New Guianolides and Acetylenic Alcohol from Saussurea katochaete Collected in China
Yoshinori Saito, Yuko Iwamoto, Yasuko Okamoto, Xun Gong, Chiaki Kuroda and Motoo Tori 447

Four New Bisabolane-type Sesquiterpenes from Ligularia lankongensis
Hiroshi Hirota, Yurie Horiguchi, Satoru Kawaii, Chiaki Kuroda, Ryo Hanai and Xun Gong 451

Enantioselective Synthesis of the Bisabolane Sesquiterpene (+)-1-Hydroxy-1,3,5-bisabolatrien-10-one and Revision of its Absolute Configuration
Stefano Serra 455

Stereoselective Synthesis of Bicyclo[3.1.1]heptane Derivatives via Intramolecular Photocycloaddition Reaction
Kiyoshi Honda, Mari Kanishi, Manabu Kawai, Akira Hishida, Yasuhiko Takahashi, Yajiro Hoshino and Seiichi Inoue 459

Glucosylated Sesquiterpenes Alcohols from Fraxinus griffithii
Rene Angelo Macahig, Liva Harinantenaina, Sachiko Sugimoto, Katsuyoshi Matsunami, Hideaki Otsuka, Yoshiho Takeda and Takazaku Shizato 467

Acaricidal and Repellent Activity of Terpenoids from Seaweeds Collected in Pernambuco, Brazil
Flavia Souza Born, Everson Miguel Bianco and Claudio Augusto Gomes da Camara 473

Competitive and Repellent Activity of Terpenoids from Seaweeds Collected in Pernambuco, Brazil
Yung-Husan Chen, Chia-Ying Tai, Tsong-Long Hwang and Ping-Jyun Sung 481

A New Diterpene from the Leaves of Andrographis paniculata Nees
Parvataneni Radhika, Yejella Rajendra Prasad and Kattupalli Sowjanya 485

New Meroterpenoids from the Marine Sponge Aka coralliphaga

New Triterpenoid Saponins from Leaves of Panax japonicus (3). Saponins of the Specimens Collected in Miyazaki Prefecture
Kouichi Yoshizaki and Shoji Yahara 497

Orophicayunnol, an Unusual 22,23-epoxy Apotirucallane Triterpenoid from Orophea yunnanensis
Wen-Jian Du, Zhihong Cheng and Daofeng Chen 503

New Metabolites from the Marine-derived Fungus Aspergillus fumigatus

Continued inside backcover