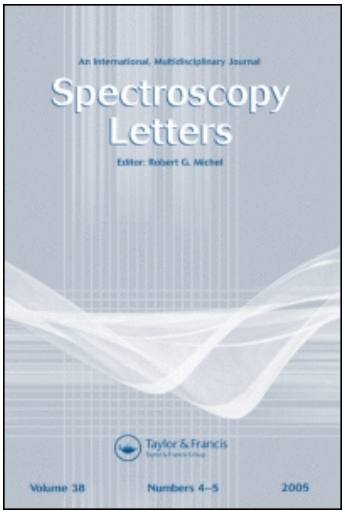
This article was downloaded by:
On: *30 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

NEW EUDESMENOIC ACID METHYL ESTER FROM *ARTEMISIA SELENGENSIS*

J. F. Hu[ab]; Y. Lu[a]; B. Zhao[a]; X. Z. Feng[a]; M. T. Hamann[c]
[a] Institute of Materia Medica (IMM), Chinese Academy of Medical Sciences and Peking Union Medical College (CAMS & PUMC), Beijing, People's Republic of China [b] Department of Pharmacognosy, School of Pharmacy, The University of Mississippi, University, Mississippi, U.S.A. [c] Department of Pharmacognosy and National Center for Natural Products Research, School of Pharmacy, The University of Mississippi, University, Mississippi, U.S.A.

Online publication date: 22 January 2001

To cite this Article Hu, J. F. , Lu, Y. , Zhao, B. , Feng, X. Z. and Hamann, M. T.(2001) 'NEW EUDESMENOIC ACID METHYL ESTER FROM *ARTEMISIA SELENGENSIS*', Spectroscopy Letters, 34: 1, 75 — 81
To link to this Article: DOI: 10.1081/SL-100001453
URL: http://dx.doi.org/10.1081/SL-100001453

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SPECTROSCOPY LETTERS, 34(1), 75–81 (2001)

NEW EUDESMENOIC ACID METHYL ESTER FROM *ARTEMISIA SELENGENSIS*

J. F. Hu,[1,*] Y. Lu,[1] B. Zhao,[1] X. Z. Feng,[1] and M. T. Hamann[2]

[1]Institute of Materia Medica (IMM), Chinese Academy of Medical Sciences and Peking Union Medical College (CAMS & PUMC), No. 1 Xian Nong Tan Street, Beijing 100050, People's Republic of China
[2]Department of Pharmacognosy and National Center for Natural Products Research, School of Pharmacy, The University of Mississippi, University, Mississippi 38677

Downloaded At: 03:13 30 January 2011

ABSTRACT

The aerial parts of *Artemisia selengensis* yielded a new eudesmenoic acid methyl ester together with a known eudesmanolide. The structures were elucidated by spectroscopic methods. The relative stereochemistry of the title compound was further supported by the result of a successful single-crystal X-ray diffraction analysis.

Key Words: *Artemisia selengensis*; Compositae; Sesquiterpene; Eudesmenoic acid methyl ester; Structural elucidation; X-ray diffraction analysis

*Address correspondence to Dr. J. F. Hu, Department of Pharmacognosy, School of Pharmacy, The University of Mississippi, University, Mississippi 38677.

Copyright © 2001 by Marcel Dekker, Inc. www.dekker.com

ORDER REPRINTS

INTRODUCTION

Artemisia selengensis Turcz (family Compositae, tribe Anthemideae), known in China as "Hong-Chen-Ai," is a species of the well-known traditional Chinese medicine (TCM) "Liu-Ji-Nu." It grows wild in the southwestern part of China and is used locally for anti-inflammation, hemostasis, invigorating the blood circulation, and relieving dysmenorrhea (1). In a preliminary communication (2), we have reported two new guaianolides from the ethanolic extract of the aerial parts of *A. selengensis.* In addition to a known eudesmanolide douglanine **1**, we hereby describe the isolation and structure identification of a new eudesmene **2**, which was obtained during our further chemical investigation of this plant species. The structure of the latter compound was determined to be 1α,6α-dihydroxyeudesma-3,11(13)-dien-12-carboxylic acid methyl ester by spectroscopic methods (IR, UV, EIMS, ^{1}H NMR, ^{13}C NMR, DEPT, and ^{1}H–^{1}H COSY). The relative stereochemistry of **2** was further supported by the result of a successful single-crystal X-ray diffraction analysis.

EXPERIMENTAL

All 1D and 2D NMR spectra were measured on a Bruker AM-500 spectrometer, at room temperature, using TMS as an internal standard; chemical shifts are expressed in ppm. IR spectra were recorded on a Perkin–Elmer 683 spectrometer. EIMS (at 70 eV) were collected on a direct probe on an Analytical VG ZAB-2F. UV spectra were scanned on a UV-240 (Shimadzu) spectrophotometer. Optical rotations were determined on a Perkin–Elmer 241 polarimeter. For elemental analysis, we used a Carlo Erba-1106 apparatus. Melting points were taken on a Kofler hot-stage apparatus and are uncorrected. Silica gel (200–300 mesh) was used for column chromatography (CC), and for TLC we used precoated with silica gel (0.25 mesh) F_{254}. Spots were visualized using UV light (254 nm) and 5% H_2SO_4–EtOH.

The aerial parts of *A. selengensis* were collected from Peng County in the Si-Chuan province of P. R. China in November 1990. They were identified by Prof. Y. H. Chen of the Department of Botany in our Institute (IMM). A voucher specimen was deposited at the herbarium of the Institute of Chinese Herb in Peng County.

The dried and pulverized aerial parts (5 kg) of *A. selengensis* were extracted with petroleum ether (60–90°C) in a percolator, and the defatted material was exhaustively extracted with hot 95% EtOH (10 L). Ethanol extract was concentrated under reduced pressure to give a black residue (300 g), 120 g of which was suspended in 0.5 L of boiling H_2O and filtered. Then the aqueous filtrate was extracted with petroleum ether (60–90°C), EtOAc and *n*-BuOH, respectively. The

Downloaded At: 03:13 30 January 2011

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

EtOAc extract (8 g) was chromatographed on a silica gel column (200–300 mesh, 250 g) eluted with $CHCl_3$–MeOH gradient as the developing solvent. The eluent was monitored by TLC and combined to give 11 fractions. Compound **1** (5 mg) and compound **2** (12 mg) were obtained from fr. 7 ($CHCl_3$/MeOH, 10:1) and purified by repeated silica gel CC and by preparative TLC.

Douglanine (1). Light yellow gum; IR (dry film) ν_{max} 3417 (OH), 2920, 2872, 1766 (C=O, α,β-unsaturated-γ-lactone), 1652 (C=C), 1456, 1375, 1249, 1137, 1045, 964 cm^{-1}; UV (MeOH) λ_{max} (log ε): 208 (3.85) nm; EIMS *m/z* (rel. int.): 248 ($[M]^+$, 5), 230 ($[M-H_2O]^+$, 100), 215 ($[M-H_2O–CH_3]^+$, 53); ^1H NMR spectral data: see Table 1.

1α,6α-Dihydroxyeudesma-3,11(13)-dien-12-carboxylic acid methyl ester (2). Colorless crystals (MeOH), m.p. 201–202°C; $[\alpha]_D^{16}$: +46° (*c* 0.04, MeOH); UV (MeOH) λ_{max} (log ε): 210 (3.91) nm; IR (KBr) ν_{max}: 3319 (OH), 2949, 2881, 1710 (C=O, α,β-unsaturated carboxylic acid ester), 1624 (C=C), 1436, 1326, 1149, 1043, 945 cm^{-1}; EIMS *m/z* (rel. int.): 280 $[M]^+$ (not found), 262 ($[M-H_2O]^+$, 7), 244 ($[M-2H_2O]^+$, 51), 230 (22), 215 (33), 197 (26), 185 (35), 169 (47), 107 (100), 91 (85), 79 (78), 67 (71), 55 (86), 53 (91), 43 (81); Elemental analysis (Anal. Calc. for $C_{16}H_{24}O_4$: C, 68.57; H, 8.57. Found: C, 68.45; H, 8.51%). ^1H NMR, ^{13}C NMR, and ^1H–^1H COSY spectral data: see Table 1.

X-ray structure analysis of 2. $C_{16}H_{24}O_4$: A colorless crystal of **2** with dimensions $0.2 \times 0.3 \times 1.0$ mm^3 was selected for X-ray analysis, orthorhombic, space group $P2_12_12_1$, unit cell dimensions: $a = 7.7870\,(1)$ Å, $b = 9.3530\,(2)$ Å, $c = 21.0570\,(1)$ Å, $V = 1533.6\,(4)$ $Å^3$, $Z = 4$. Single-crystal X-ray diffraction data were collected by using a MAC Science DTP 2030K Image Plate with graphite monochromate, Moka radiation. There were 1555 reflections of which 1184 were observed; the position of 20 nonhydrogen atoms was obtained directly from E-map. The structure was solved with NOMCSDP software package; thereafter the positions of the nonhydrogen atoms were obtained and the kind of atoms was determined by using the least square calculation and the difference Fourier method in turn. Position of all hydrogen atoms was obtained by geometric calculation and difference Fourier method. The final reliable factors were $R_f = 0.061$, $R_w = 0.060$, GOF = 5.837.

RESULTS AND DISCUSSION

The minor component (**1**) gave rise to a clear molecular-ion peak at *m/z* 248, and the IR as well as the UV spectra displayed the presence of hydroxyl (IR: 3417 cm^{-1}) and α-methylene-γ-lactone (IR: 1766 cm^{-1}; UV λ_{max}: 208 nm) groups. Its ^1H NMR spectrum (Table 1), reported here in detail for the first time, established the structure of **1** to be 1α-hydroxyeudesma-3,11(13)-dien-12,6α-olide. The structure of douglanine (**1**) was reported earlier (3).

Downloaded At: 03:13 30 January 2011

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Downloaded At: 03:13 30 January 2011

Table 1. ^{1}H (500 MHz) NMR Data for **1**, **2** and ^{13}C- (125 MHz) NMR Data for **2**

Proton	δ, mult., J (Hz), int.		Observed ^{1}H–^{1}H COSY, **2**[b]	Carbon	δ (DEPT), **2**[b]
	1[a]	**2**[b]			
H-1β	3.34, brd, 4.0, 1H	3.32, brd, 4.7, 1H	H-2β	C-1	72.07 (CH)[c]
H-2α	2.05, brd, 19.1, 1H	2.05, brd, 18.8, 1H	H-2β	C-2	34.85 (CH_2)[d]
H-2β	2.37, brd, 19.1, 1H	2.48, brd,[e] 18.8, 1H	H-1β, H-2α	C-3	121.17 (CH)
H-3	5.25, brs, 1H	5.29, brs, 1H	H-2α, H-2β, H-5α	C-4	136.68 (C)
H-5α	2.70, brd, 11.4, 1H	2.29, brd, 10.1, 1H	H-3, H-6β	C-5	52.13 (CH)
H-6β	4.00, dd, 10.8, 11.4, 1H	3.95, dd, 10.1, 10.5, 1H	H-5α, H-7α	C-6	74.43 (CH)[c]
H-7α	2.51, ddt, 10.8, 5.1, 3.2, 3.0, 1H	2.48, m,[e] 1H	H-6β, H-8α, H-8β	C-7	46.56 (CH)
H-8α	1.68, m, 1H	1.87, m,[f] 1H	H-8β, H-9α, H-9β	C-8	26.98 (CH_2)
H-8β	1.24, m,[e] 1H	1.63, ddt, 14.5, 11.1, 5.7, 1H	H-8α, H-9α, H-9β	C-9	33.04 (CH_2)[d]
H-9α	1.91, m, 1H	1.90, m,[f] 1H	H-8α, H-8β, H-9β	C-10	40.97 (C)
H-9β	1.24, m,[e] 1H	1.16, ddd, 13.3, 5.7, 2.3, 1H	H-8α, H-8β, H-9α	C-11	144.64 (C)
H-13	5.90, d, 3.2, 1H	6.27, d, 1.1, 1H	H-13′	C-12	169.22 (C)
H-13′	5.43, d, 3.0, 1H	5.75, brs, 1H	H-13	C-13	126.35 (CH_2)
H-14	0.81, s, 3H	0.88, s, 3H		C-14	17.23 (CH_3)
H-15	1.80, brs, 3H	1.88, brs, 3H		C-15	23.69 (CH_3)
OMe		3.78, s, 3H		OMe	52.93 (CH_3)

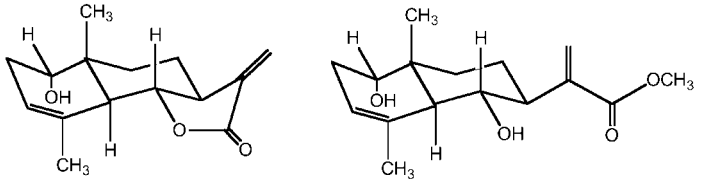
[a]Recorded in acetone-d_6.
[b]Recorded in CD_3OD.
[c,d]Assignments in the same column with the same superscript may be interchangeable.
[e,f]Proton signals were hidden or overlapped with the same superscript in the same column.

ORDER REPRINTS

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Copyright © Marcel Dekker, Inc. All rights reserved.

ORDER REPRINTS



1 **2**

Figure 1. The structures of **1** and **2**.

The EI mass spectrum of compound **2** showed a clear $[M - H_2O]^+$ peak at *m/z* 262. This, together with its ^1H and ^{13}C NMR (DEPT) spectral data (Table 1) and an elemental analysis, indicated the molecular formula to be $C_{16}H_{24}O_4$. The prominent mass spectral fragments and the ^1H NMR spectrum data showed general features similar to those of 6α,8α-dihydroxyisocostic acid methyl ester obtained earlier by us from *A. mongolica* (4,5). This indicated that the structure of **2** is also an eudesmen-12-oic acid methyl ester skeleton: δ 0.88 (3H, brs, H-14), 1.88 (3H, brs, H-15), 6.27 (1H, d, $J = 1.1$ Hz, H-13), 5.75 (1H, brs, H-13′) and 3.78 (3H, s, COOMe). A proton signal geminal to a hydroxyl group showed a broad doublet with a small coupling constant ($J = 4.7$ Hz) at δ 3.32. This clearly indicated that this proton was equatorial and β-orientated at C-1 on the basis of analogies with similar compounds such as douglanine (**1**) ($J_{1\beta,2\beta} = 4.0$ Hz) and 11β,13-dihydrodouglanin acetate ($J_{1\beta,2\beta} = 4.5$ Hz) (6).

For the presence of a double bond at C-3, ring A required a semichair conformation (Figs. 1 and 2). The downfield shift of H-2β at δ 2.48 is in agreement with the proposed stereochemistry, and this proton is in the deshielding zone of the C-3 double bond. H-2α proton signal at δ 2.05 is in the shielding zone of this double bond. Therefore, the dihedral angle between H-2α and H-1β is almost 90° ($J_{1\beta,2\alpha} = \sim 0$ Hz), so the proton signal of H-1β showed a broad doublet coupling with H-2β. The structure feature of H-1β and its chemical shift assignment was further confirmed by ^1H–^1H COSY spectrum, which revealed no

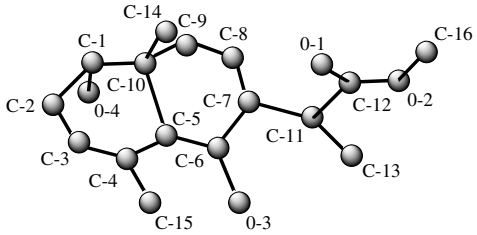


Figure 2. The X-ray structure of **2**.

Downloaded At: 03:13 30 January 2011

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

cross peak between H-1 and other protons except for H-2β (δ 2.48). We could assign unambiguously all the ^{1}H NMR signals by ^{1}H–^{1}H COSY experiment (Table 1).

Furthermore, an evident explanation of this fact is that the molecule has a 1α-hydroxyl group that is responsible for the lowfield shifts of the H-5α (δ 2.29) and H-9α (δ 1.90) signals because 1,3-diaxial steric compression effect between 1α-OH and 5α-H, as well as between 1α-OH and 9α-H. The *trans*-decalin of the bicyclo (4,4,0) system followed from the biogenetic point of view. Therefore, the H-14 signal showed a singlet broadened by long range *W*-coupling between H-5 and H-14. The ^{13}C NMR and DEPT measurements were in full agreement with the proposed structure 1α,6α-dihydroxyeudesma-3,11(13)-dien-12-carboxylic acid methyl ester **2**. Finally, the relative stereochemistry of **2** was confirmed by X-ray diffraction for single crystals. Analysis results indicated that in the molecular skeleton of compound **2**, ring A (semichair) and ring B (chair) is linked by *trans*. Its relation configuration is displayed in Figure 1 and the X-ray structure in Figure 2. The absolute configuration remains unassigned. We went back to check the petroleum ether extract of the dried and pulverized material using TLC and NMR methods and found that both **1** and **2** are naturally occurring products.

Downloaded At: 03:13 30 January 2011

ACKNOWLEDGMENTS

This project was supported by the China Postdoctoral Science Foundation. The authors thank Associate Professor He, W. Y., and his colleagues in the Department of Instrumental Analysis in IMM for spectral measurements.

REFERENCES

1. Institum Botanicum Austro-Sinense Academiae Sinicae. *Delectis Florae Reipublicae Popularis Sinicae Agendae Academiae Sinicae Edita*. Florae Reipublicae Popularis Sinicae, Beijing: Science Press, 1991, Tomus **76** (2): 144–145.
2. Hu, J.F.; Feng, X.Z. New Guaianolides from *Artemisia selengensis*. J. Asia. Nat. Prod. Res. **1999**, *1*, 169–76.
3. Lee, K.H.; Geissman, T.A. Sesquiterpene Lactones of *Artemisia* Constituents *of A. ludoviciana ss. Mexicana.* Phytochemistry **1970**, *9*, 403–408.
4. Hu, J.F.; Zhu, Q.X.; Bai, S.P.; Jia, Z.J. New Eudesmane Sesquiterpene and other Constituents from *Artemisia mongolica.* Planta Medica **1996**, *62*, 477–78.

Copyright © Marcel Dekker, Inc. All rights reserved.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

5. Hu, J.F.; Feng, X.Z.; Jia, Z.J. Spectral Features of a Typical Sesquiterpene Eudesmane in The Genus *Artemisia* and *Senecio*. Nat. Prod. Res & Dev. **1999**, *11*, 95–102.
6. Marco, J.A. Sesquiterpene Lactones from *Artemisia Herba-Alba subsp. Herba-Alba*. Phytochemistry **1989**, *28*, 3121–26.

Received May 25, 2000
Accepted July 15, 2000

Downloaded At: 03:13 30 January 2011

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Downloaded At: 03:13 30 January 2011

Request Permission or Order Reprints Instantly!

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the U.S. Copyright Office for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on Fair Use in the Classroom.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our Website User Agreement for more details.

Order now!

Reprints of this article can also be ordered at

http://www.dekker.com/servlet/product/DOI/101081SL100001453