A Novel Norditerpene from *Eupatorium adenophorum*

Ming-Zhong Wang, Xiang-Hai Cai, Guo-Shun Du, and Xiao-Dong Luo

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, Yunnan 650204, PR China

Reprint requests to Prof. Dr. Xiao-Dong Luo. Fax: +86-871-5150227. E-mail: xdluo@mail.kib.ac.cn

Z. Naturforsch. **2007**, *62b,* 577 – 579; received October 3, 2006

A novel norditerpene was isolated from the flower of *Eupatorium adenophorum*, named (4a*R*,7*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-8-[3-methylenebut-4-alyl]-4,4a,7,8-tetramethylnaphthalen-2(1*H*)-one (**1**). Its structure was established by extensive NMR experiments. Based on the diversity of the side chains, a possible biodegradation pathway for the compound from the clerodane skeletone is proposed.

Key words: (4a*R*,7*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-Octahydro-8-[3-methylenebut-4-alyl]-4,4a,7,8-tetramethylnaphthalen-2(1*H*)-one, *Eupatorium adenophorum*, Biodegradation, Clerodane

Introduction

Eupatorium adenophorum Spreng, originating from Mexico, has invaded into the Yunnan Province of China from Burma since 1950s. It has resulted in much balefulness to agriculture and environment [1]. Many cadinene derivatives had been extracted by Ding *et al.* from the flowers of *E. adenophorum* [1]. This time a new compound named (4a*R*,7*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-8-[3-methylenebut-4-alyl] -4,4a,7,8-tetramethylnaphthalen-2(1*H*)-one (**1**) and two known compounds **2** – **3** were isolated from it [2, 3]. In this paper we mainly report the isolation and the structure elucidation of compound **1**. Its structure was established by extensive NMR spectroscopic experiments including HMQC, HMBC and NOESY techniques.

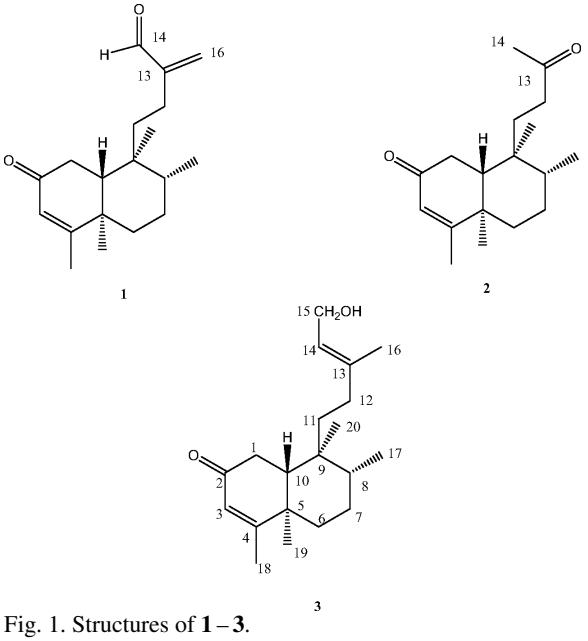

Fig. 1. Structures of **1** – **3**.

Results and Discussion

Compound **1** showed a quasimolecular ion peak at *m/z* = 288 in its EI mass spectrum. The molecular formula of **1** was revealed as $C_{19}H_{28}O_2$ by HRESIMS data $[M+H]^+$ (found 289.2164, calcd. 289.2167). The ^1H and ^{13}C NMR (Table 1) spectra showed the signals of six quaternary, four CH, five CH_2, and four methyl carbon atoms. Two C=O moieties are evident from the ^1H and ^{13}C NMR signals [δ_H = 9.51 (s, H-14) δ_C = 200.2 (s, C-2), δ_C = 194.6 (d, C-14)]. The signals δ_H = 1.95 (d, 2.4, H-10), δ_H = 1.59 (br, H-8), δ_C = 45.4 (d C-10), 35.9 (d, C-8), 39.7(s, C-5), 38.7 (s, C-9) suggest that **1** has a clerodane-type skeleton [4, 5]. The data also indicated that **1** is partially similar to **2** and **3**, except for the side chain at C-11 [6, 7], (Fig. 1).

Based on HMBC, the correlations between H-12 [δ_H = 1.96 (br), 2.25 (m)] and C-13, C-14, C-16 [δ_C = 150.2 (s, C-13), 194.6 (d, C-14), 133.8 (t, C-16)], between H-16 [δ_H = 6.24 (s), 5.97 (s)] and C-12, C-13, C-14, [δ_C = 20.9 (t, C-12), 150.2 (s, C-13), 194.6 (d, C-14)], and between H-14 [δ_H = 9.51 (s)]

Table1. NMR spectral data of **1**, **2**, and **3** in $CDCl_3$ (500 MHz for ^1H and 125 MHz for ^{13}C, *J* in Hz).

	1		**2**		**3**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	2.37 (s)	34.8 (t)	2.29 (s)	34.8(t)	2.29 (s)	34.9 (t)
	2.38 (d, 2.4)		2.36 (d, 3.6)		2.37(d, 4.4)	
2		200.2 (s)		200.1(s)		200.5 (s)
3	5.72 (s)	125.5 (d)	5.71 (s)	125.4(d)	5.69 (s)	125.4 (d)
4		172.5 (s)		172.4(s)		172.7 (s)
5		39.7 (s)		39.8(s)		39.8 (s)
6	1.40 (br)	35.4 (t)	1.34 (m)	35.4(t)	1.35 (br)	35.5 (t)
	1.82 (m)		1.81 (m)		1.79 (br)	
7	1.50 (m)	26.8 (t)	1.49 (m)	26.7(t)	1.45 (m)	26.8 (t)
8	1.59 (br)	35.9 (d)	1.48 (br)	36.1(d)	1.48 (br)	36.1 (d)
9		38.7 (s)		38.1(s)		38.6 (s)
10	1.95 (d, 2.4)	45.4 (d)	1.76 (dd, 3.6, 13.6)	46.0(d)	1.85 (m)	45.6 (d)
11	1.40 (br)	35.4 (t)	1.52 (br)	30.6(t)	1.49 (br)	35.7 (t)
			1.56 (br)		1.35 (br)	
12	1.96 (br)	20.9 (t)	2.23 (m)	37.0(t)	1.73 (m)	32.1 (t)
	2.25 (m)				1.84 (m)	
13		150.2 (s)		208.4(s)		139.6 (s)
14	9.51 (s)	194.6 (d)	2.11(s)	30.1(q)	5.34 (d, 6.8)	123.3 (d)
15					4.09 (d, 6.8)	59.3 (t)
16	6.24 (s)	133.8 (t)			1.63 (s)	16.6 (q)
	5.97 (s)					
17	0.85 (d, 6.0)	15.7 (q)	0.82 (d, 6.4)	15.7(q)	0.80 (d, 4.8)	15.7 (q)
18	1.89 (d, 1.1)	18.9 (q)	1.87 (d, 1.2)	18.9(q)	1.86 (s)	19.0 (q)
19	1.11 (s)	18.3 (q)	1.10 (s)	18.2(q)	1.08 (s)	18.2 (q)
20	0.80 (s)	17.7 (q)	0.81 (s)	17.7(q)	0.78 (s)	17.7 (q)

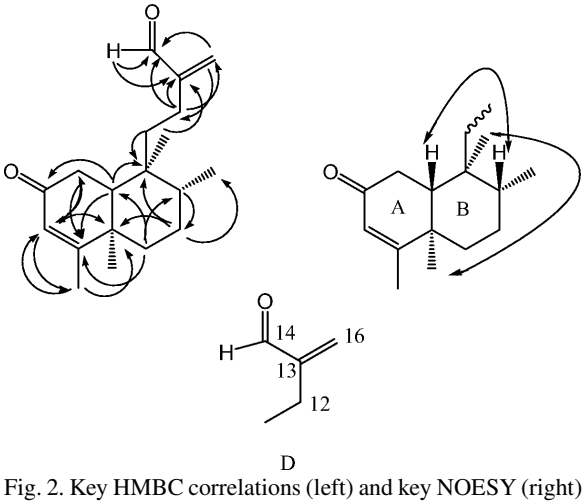

Fig. 2. Key HMBC correlations (left) and key NOESY (right) correlations of **1**.

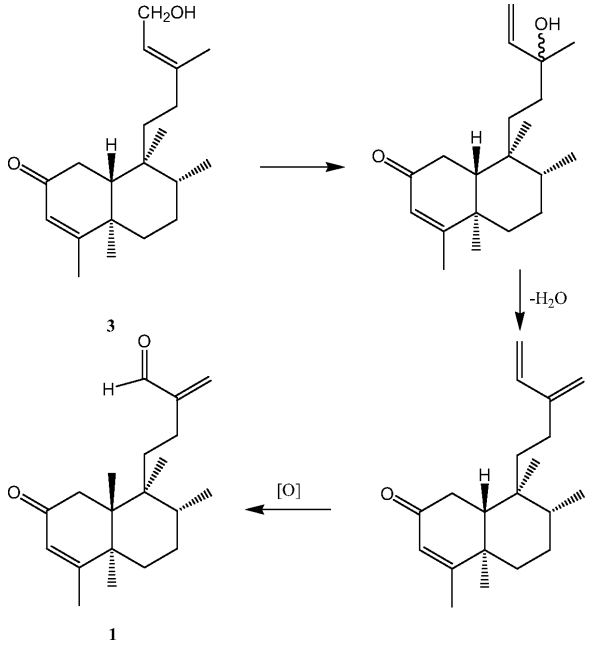

Fig. 3. Possible biodegradation pathway from **3** to **1**.

and C-12, C-13, C-16 [δ_C = 20.9 (t, C-12), 150.2 (s, C-13), 133.8 (t, C-16)] indicated that the side chain at C-11 is a D group (Fig. 2). The NOESY spectra, with correlations between H-10 [δ_H = 1.95 (d, 2.4, H-10)] and H-8 [δ_H = 1.59 (br, H-8)], and between H-19 [δ_H = 1.11 (s, H-19)] and H-20 [δ_H = 0.80 (s, H-20)], together with the resonances of C-5 [δ_C = 39.7(s)] and C-10 [δ_C = 45.4 (d)] bear out that **1** has a AB/*trans* junction and that H-10 is in a β orientation [6–9] (Fig. 2). Therefore, this structure was deduced to be (4a*R*,7*R*,8*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-8-[3-methylenebut-4-alyl]-4,4a,7,8-tetramethylnaphthalen-2(1*H*)-one.

A possible biosynthesis pathway is proposed in Fig. 3.

Experimental Section

General

NMR spectra were run on a BRUKER DRX-500 (500 MHz for ^{1}H NMR and 2D NMR, 125 MHz for ^{13}C NMR) instrument with TMS as internal standard; IR spectra were measured on a Bio-Rad FTS-135 spectrometer with KBr pellets; EI-MS spectra were recorded on a VG Auto Spec-3000 spectrometer; UV spectra were obtained on a Shimadzu double-beam 210A spectrophotometer. EI-MS: 70 eV; Silica gel (200 – 300 mesh).

Plant material

The whole flower of *E. adenophorum* was collected and identified by Prof. Xiao-Dong Luo in June 2005 in Kunming Yunnan Province, P. R. China. A Voucher specimen has been deposited in the herbarium of the Department of Taxonomy, Kunming Institute of Botany, Chinese Academy of Science.

Extraction and isolation

The air-dried and powdered flowers (10 kg) were extracted with methanol (4 × 25 L) at r. t. and the solution concentrated in vacuum to give a crude extract (800 g), which was partitioned in H_2O and extracted with petroleum ether and EtOAc three times each. The petroleum ether layer (170 g) was chromatographed over silica gel using petroleum ether/acetone (10 : 0 – 0 : 10) as an eluent to give 7 fractions; the EtOAc layer (178 g) was partitioned into 9 fractions in the same way. Fraction 6 of the petroleum ether layer and fraction 2 of the EtOAc layer are similar according to the TLC detection. They were mixed to give a total of 27 g. The mixture was repeatedly chromatographed over silica gel using petroleum ether/Me_2CO (20 : 1 – 0 : 20) as an eluent to give 5 fractions. Fraction 1 (5.8 g) was subjected to RP-18 ($MeOH/H_2O$, 50 : 50 – 100 : 0), then repeatedly subjected to silica gel using petroleum ether/EtOAc (30 : 1) as an eluent to yield **1** (3 mg) and **3** (100 mg). Fraction 3 (4.0 g) was subjected to the same procedure as above to yield **2** (53 mg).

*Physical and spectroscopic data: compound **1***, colorless oil. – $[\alpha]_D^{25} = -14.2$ ($c = -0.5$, $CHCl_3$). – UV ($CHCl_3$): $\lambda(\log \varepsilon_{max}) = 241$ (4.21) nm. – IR (film): $\nu = 2871$, 2698, 1687, 1622, 1873, 947, 1668 cm^{-1}. – EI-MS (70 eV): *m/z* (%) = 288 (3) $[M]^+$, 273 (10), 245 (18), 205 (26), 189 (35), 135 (49), 121 (100), 109 (86), 95 (45). – HRESIMS: *m/z* = 289.2164 $[M+H]^+$ (found 289.2164, calcd. 289.2167). – ^{1}H and ^{13}C NMR spectral data: see Table 1.

Acknowledgements

The authors are grateful to the Chinese Academy of Science (XiBuZhiGuang Project) and the Natural Science Foundation of Yunnan (2004C0009Z) and the National Science Foundation of China (30670214) for financial support, and to the members of the analytical group of the State Key Laboratory of Phytochemistry and Plant Resource in West China, Kunming Institute of Botany, Chinese Academy of Science, for spectral measurements.

[1] Z. H. Ding, U. B. Guo, J. K. Ding, *Acta Bot.Yunnan*. **1999**, *21*, 505 – 510.
[2] H. P. He, Y. M. Shen, G. Y. Zuo, X. S. Yang, X. J. Hao, *Helv. Chim. Acta* **2003**, *86*, 3187 – 3193.
[3] S. M. Yang, S. H. Wu, X. D. Qin, X. D. Luo, D. G. Wu, *Helv. Chim. Acta* **2004**, *87*, 1279 – 1286.
[4] J. G. Urones, P. Basabe, I. S. Marcos, A. Jimenez, A. M. Lithgow, M. Lopez, R. F. Moro, A. Gomez, *Tetrahedron* **1994**, *50*, 10791 – 10802.
[5] L. M. X. Lopes, V. Bolzani, L. M. V. Trevisan, *Phytochemistry* **1987**, *26*, 2781 – 2784.
[6] M. D. Bomm, J. Zukerman-Schpector, L. M. X. Lopes, *Phytochemistry* **1999**, *50*, 455 – 461.
[7] D. Avila, J. D. Medina, *Phytochemistry* **1991**, *30*, 3474 – 3475.
[8] F. Bohlmann, C. Zdero, R. K. Gupta, R. M. King, H. Robinson, *Phytochemistry* **1980**, *19*, 2695 – 2705.
[9] A. C. Pinto, W. S. Garcez, P. P. S. Queiroz, N. G. Fiorani, *Phytochemistry* **1994**, *37*, 1115 – 1117.