Chinese Chemical Letters Vol. 16, No. 9, pp 1223-1226, 2005 1223
http://www.imm.ac.cn/journal/ccl.html

Two New Sesquiterpenes from *Eupatorium lindleyanum*

Nian Yun YANG[1, 2]*, Shi Hui QIAN[1], Jin Ao DUAN[1], Ping LI[2], Li Juan TIAN[3]

[1] Jiangsu Academy of Traditional Chinese Medicine, Nanjing 210028
[2] China Pharmaceutical University, Nanjing 21009
[3] Jinling Pharmaceutical Company Limited, Nanjing 210009

Abstract: Two new germacrane sesquiterpenes: 3,8,14-trihydroxy-1(10)E,4Z,11(13)-germacratrien-12, 6-olide, 8-(2-methyl-4-hydroxyl-2E-butenoyl), 3,14-diacetoxy (eupalinolide A, **1**), and 3,8,14-trihydroxy-1(10) E, 4E, 11(13)-germacratrien-12,6-olide, 8-2-methyl-4-hydroxyl-2E-butenoyl), 3,14-diacetoxy (eupalinolide B, **2**) were isolated from *Eupatorium lindleyanum*. Their structures were elucidated by means of ^{1}H and ^{13}C NMR spectroscopic analysis, including 2D NMR technique.

Keywords: *Eupatorium lindleyanum*, Eupatorium, sesquiterpene, eupalinolide A, eupalinolide B.

Various germacrane sesquiterpenes have been isolated from many species of the *Eupatorium*. In recent years these compounds have been increasing interest due to their insecticidal, cytotoxic, antitumor-promoting and insect-antifeedant activities[1]. In our present study, we have investigated the chemical constituents of *Eupatorium lindleyanum DC.*, which is a geo-authentic medicine of Jiangsu province. It is used as a antipyretic drug. Two novel germacrane sesquiterpenes (**Figure 1**) were found by us from this plant and named as eupalinolide A and eupalinolide B. In their structures there were a germacrranolide skeleton with three substituents, which were not reported in literature. In this paper, we deal with their structural elucidation.

Compound **1**, colorless gum, $[\alpha]_D^{20}$-167.4 (c 0.21, $CHCl_3$), its molecular formula was $C_{24}H_{30}O_9$ (HR-ESIMS: *m/z* 463.1960 $[M+H]^+$, calcd. for $C_{24}H_{31}O_9$ 463.1968) and its IR spectrum indicated the presence of carbonyl and hydroxyl groups. The ^{1}H and ^{13}CNMR spectra indicted that this compound has four quaternary methyl groups, two acetates, one (α-methyl)butenoate. Its parent structure is a germacranolide sesquiterpene.

The ring protons could be unequivocally assigned from its NOESY(**Figure 2**) and chemical shift correlated spectral data. By comparison of the ^{1}HNMR data of **1** with known sesquiterpenes[2-4], the signal at δ 4.30(d, J=6Hz) was assigned to H-4′ attached in the carbon atom bearing hydroxy group, and the signal at δ 6.76(t, J=6Hz) was assigned to H-3′. NOESY of **1** showed the correlation between H-4′ and a methyl group hydrogen atom with the signal at δ 1.80. In the HMBC spectrum of **1** (**Figure 2**), it showed the correlation between the hydrogen atom of methyl group and the carboxylic

* E-mail: nianyunyang@tom.com

carbon(δ_C 165.9), and the correlation between H-3′ and carbon of the methyl group(δ_C 12.4). These results together with the NMR data (**Table 1**) providedthe evidence of presence of an 2-methyl-4-hydroxyl-2(E)-butenoyloxyl group in the side chain. An AB quartet at δ 4.70 and 4.90 were assigned to two protons (H-14a, H-14b) attached to the carbon atom bearing ester group. The signal at δ 5.23 (brd, J=10Hz), 5.28 (dd, J=12, 5.5Hz) and 5.30 (dd, J=12, 6Hz) were assigned to H-5, H-1 and H-3 respectively, the signal at δ 5.83 (dd, J=12, 9Hz) was assigned to H-6. The assignments of H-2, H-8, H-9 and H-13 are more likely.

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

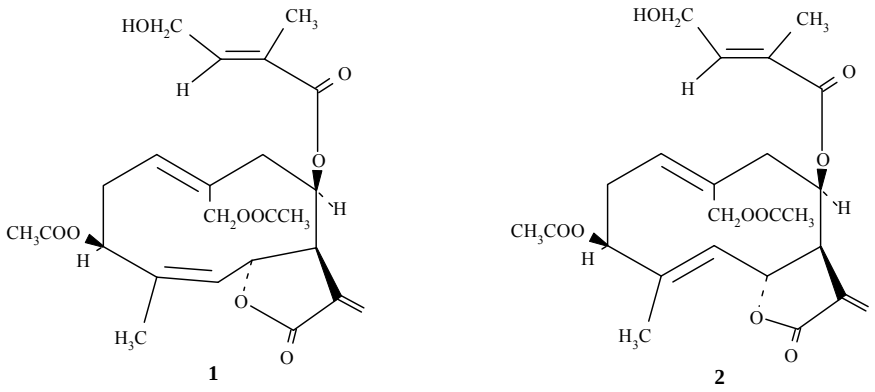

Figure 2 The key correlations in HMBC and NOESY spectra of **1** and **2**

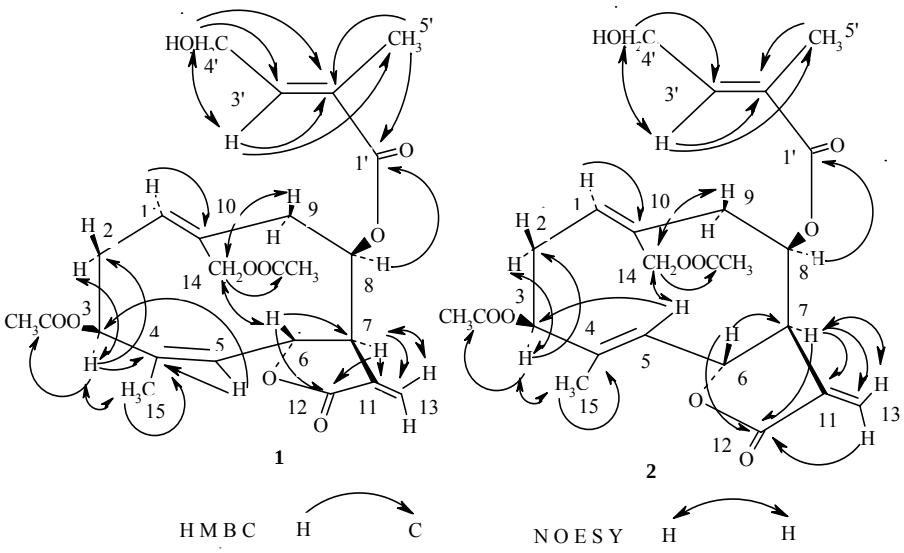

Table 1 ^{1}H (300MHz) and ^{13}CNMR(75MHz) data of **1** and **2** (in $CDCl_3$, δ ppm)

C	**1**		**2**	
	δ_C	δ_H(J, Hz)	δ_C	δ_H(J, Hz)
1	126.6	5.28(1H, dd, 12, 5.5)	125.3	5.39(1H, dd, 12, 5)
2a	29.5	2.42(1H, m)	30.4	2.35(1H, m)
2b		2.75(1H, m)		3.05(1H, m)
3	71.4	5.30(1H, dd, 12, 6)	76.5	5.31(1H, dd, 12.5, 6)
4	136.4		135.5	
5	129.7	5.23(b1H, rd, 10)	130.0	5.38(1H, brd, 10.5)
6	78.2	5.83(1H, dd, 12, 9)	78.8	5.29(1H, dd, 10, 9)
7	48.3	2.96(1H, m)	48.3	3.02(1H, m)
8	73.9	5.48(1H, m)	73.9	5.55(1H, m)
9a	37.7	2.30(1H, m)	38.5	2.24(1H, m)
9b		3.14(1H, m)		2.94(1H, m)
10	134.3		133.9	
11	137.1		136.9	
12	169.3		169.0	
13a	124.6	6.37(1H, d, 3)	124.8	6.42(1H, d, 3.5)
13b		5.78(1H, d, 3)		5.83(1H, d, 3.5)
14a	63.2	4.98(1H, d, 13)	62.3	5.01(1H, d, 13)
14b		4.70(1H, d, 13)		4.74(1H, d, 13)
15	23.0	1.84(3H, brs)	17.9	1.85(3H, brs)
1'	165.9		166.4	
2'	127.6		127.7	
3'	142.5	6.76(1H, t, 6)	142.0	6.81(1H, t, 6)
4'	59.5	4.30(2H, d, 6)	59.5	4.37(2H, d, 6)
5'	12.4	1.80(3H, brs)	12.6	1.83(3H, brs)
CH_3COO	20.9	2.00(3H, s)	20.7	2.07(3H, s)
	171.0		171.8	
CH_3COO	21.0	2.12(3H, s)	20.9	2.13(3H, s)
	169.5		169.9	

By comparisons of ^{13}CNMR data of **1** with known sesquiterpenes[2-4], the carbons were assigned, and HMBC experiments also supported all these assignments. The HMBC spectrum of **1** showed the correlations between H-3 and H-14 with the carboxylic carbon of two acetate groups, H-8 has a correlation with the carboxylic carbon of α-methyl butenoate .

NOESY experiment allowed us to assign all the proton signals and established the stereochemistry for **1**. The lactones ring closed to C-6 was *trans* and the substituents at C-3 and C-8 were both β-oriented. Thus, compound **1** was identified as 3,8,14-trihydroxy-1(10) E, 4Z, 11(13)-germacratrien-12,6-olide, 8-(2–methyl-4-hydroxyl-2E-butenoyl), 3,14-diacetoxy, named eupalinolide A.

Compound **2**, colorless gum, $[\alpha]^{20}_{D}$ -93.1 (c 0.19, $CHCl_3$), has the molecular formula $C_{24}H_{30}O_9$ (HR-ESIMS: *m/z* 463.1958 $[M+H]^+$, calcd. for $C_{24}H_{31}O_9$ 463.1968). The ^{1}H and ^{13}CNMR spectral data (**Table1**) were very similar to that of **1**, except that C-15 showed a down-field shift and C-3 showed a up-field shift in the ^{13}CNMR spectrum compared with the same carbon atom in **1**, another significant change was observed for H-6 which also showed a down-field shift in the ^{1}HNMR spectrum. These results were from alkene bond anisotropic effect and space effect. By analysis of HMBC and NOESY spectrum, compound **2** was deduced as 3,8,14-trihydroxy–1(10) E, 4E, 11 (13)-

germacratrien-12, 6-olide, 8-(2-methyl-4-hydroxyl-2E-butenoyl), 3, 14-diacetoxy, named eupalinolide B.

Acknowledgment

This work was supported by the Natural Science Foundation of Jiangsu Science and Technology Department (No.BK2001185), which are gratefully acknowledged.

References

1. Z. H. Ding, J. K. Liu, J. K. Ding, *Natural Product Research and development*, **2001**, *13*(3), 76.
2. L. R. Hernandez, C. A. N. Catalan, C. M. Cerda, *Phytochemistry*, **1994**, *37*(5), 1331.
3. D. B. Stierle, *Phytochemistry*, **1986**, *25*(3), 743.
4. A. L. Perez, J. S. Mendoza, A. R. Vivar, *Phytochemistry*, **1984**, *23*(12), 2911.

Received 22 November, 2004