

## Eupatoranolide, a New Sesquiterpene Lactone from *Eupatorium adenophorum*

Zhi Hui DING\*, Jing Kai DING

Laboratory of Phytochemistry, Kunming Institute of Botany, Academia Sinica, Kunming 650204

**Abstract:** A new sesquiterpene lactone eupatoranolide was isolated from the flowers of *Eupatorium adenophorum*, its structure was elucidated as 2 $\beta$ -acetoxy-(7 $\alpha$ , 9 $\beta$ H)-3,6(11)-cadinadien-12(7)-olide by spectral analysis.

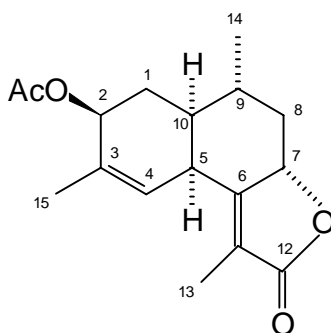
**Keywords:** *Eupatorium adenophorum*, cadinene sesquiterpene lactone, eupatoranolide.

In our investigation on the bioactive components from plants, the preliminary bioassay studies showed that the petroleum ether extract of *Eupatorium adenophorum* possessed potential insect antifeedant and insecticide activities. In the previous paper<sup>1</sup>, we isolated a new phenyl glucoside from the aerial parts of *E. adenophorum*. Further study on flowers of *E. adenophorum* led to the isolation of twelve compounds. Their structures were identified by spectral analysis and chemical reaction as a new sesquiterpene lactone named eupatoranolide, 2-acetoxy-3, 4, 6, 11-tetradecahydrocadinan-7-on<sup>2</sup>, 7-oxoageraphone<sup>3</sup>, an ant-repellent compound-kolavenol<sup>4</sup>, eugenyl-O- $\beta$ -D-glucopyranoside<sup>5-7</sup>, which was first isolated from this genus, 5, 4'-hydroxy-3, 6-dimethoxy-7-O- $\beta$ -D-glucopyrano-xyflavonone, 5, 4'-hydroxy-6, 7-dimethoxy-3-O- $\beta$ -D-glucopyranoxyflavonone<sup>1</sup>, 3, 5, 4'-trihydroxy-6, 7-dimethoxyflavone, stigmasterol,  $\beta$ -sitosterol, daucosterol and succinic anhydride.

Eupatoranolide was obtained as colorless plates, mp 182-184°C (from acetone),  $[\alpha]_D^{30.6} +173.7(\text{CHCl}_3, c 0.43)$ . The high resolution positive FABMS showed a molecular ion at  $m/z$  291.1606 (calcd. for  $\text{C}_{17}\text{H}_{22}\text{O}_4$ , 291.1596). Signals at  $\delta_H$  2.09 (3H, s),  $\delta_C$  170.7, 21.1 in  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra and ion peak at  $m/z$  230 ( $\text{M}^+-\text{CH}_3\text{COOH}$ ) in EIMS confirmed the presence of an acetoxy group. Signals at  $\delta_C$  120.3, 164.2, 174.6 in  $^{13}\text{C}$  NMR and IR absorption at  $1745\text{ cm}^{-1}$  implicated the presence of an  $\alpha$ ,  $\beta$ -unsaturated  $\gamma$ -lactone structure unit. So eupatoranolide could be deduced as a bicyclic sesquiterpene. Moreover,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra confirmed the presence of three methyl, two methylene, five methine, one trisubstituted double bond. The thorough study of 2D NMR spectra ( $^1\text{H}$ - $^1\text{H}$  COSY, NOESY, HMQC and HMBC) (see **Table1**) revealed the cadinene type skeleton for eupatoranolide. The cross peak between the

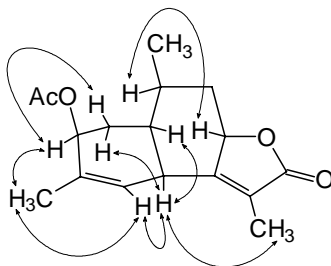
acetoxyl carbonyl at  $\delta_C$  170.7 and H-2 at  $\delta_H$  5.22 in HMBC suggested the location of acetoxyl group at C-2.

The investigation of NOESY spectrum established the relative stereochemistry of eupatoranolide. The correlation between H-5 and H-10 in NOESY spectrum suggested the *cis*-fusion of ring A and ring B. The correlations between H-2 and H-1 $\alpha$ , H-2 and H-1 $\beta$  implicated the  $\beta$ -orientation of acetoxyl group at C-2 and the half-chair conformation for ring A. The correlations between H-7 and H-8 $\beta$ , H-7 and H-9 showed the  $\beta$ -orientation of H-7; the correlations between H-9 and H-7, H-9 and H-10 suggested the  $\alpha$ -orientation of methyl group at C-9 and the chair conformation of ring B. The relative stereochemistry of eupatoranolide is similar to that of verocephol<sup>8</sup>. So the structure of eupatoranolide was deduced as 2 $\beta$ -acetoxyl-(7 $\alpha$ , 9 $\beta$ H)-3,6(11)-cadinadien-12(7)-olide.



Eupatoranolide

**Figure 1** Key NOE's observed for eupatoranolide



**Table 1.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data for eupatoranolide

Position	$\delta_{\text{C}}$ (DEPT)	$\delta_{\text{H}}$	HMBC	$^1\text{H}$ - $^1\text{H}$ COSY	NOESY
1	29.8(CH <sub>2</sub> )	1.89 <i>m</i> H $\alpha$ 2.33 <i>dd</i> 2.8, 15.5 H $\beta$		H-1 $\beta$ , H-2, H-10 H-1 $\alpha$ , H-2, H-10	H-1 $\beta$ , H-2, H-5, H-10 H-1 $\alpha$ , H-2, H-10, H-14
2	68.0(CH)	5.22 <i>brd</i> 5.0	H-1 $\beta$ , H-4, H-15	H-1 $\alpha$ , H-1 $\beta$ , H-15	H-1 $\alpha$ , H-1 $\beta$ , H-15
3	133.8(C)		H-1 $\beta$ , H-2, H-15		
4	125.4(CH)	5.32 <i>s</i>	H-2, H-15	H-5, H-15	H-5, H-7, H-13, H-15
5	38.1(CH)	3.54 <i>brs</i>	H-1 $\alpha$ , H-1 $\beta$ , H-4	H-4, H-10, H-15	H-1 $\alpha$ , H-4, H-10, H-13
6	164.2(C)		H-4, H-13		
7	78.5(CH)	4.71 <i>m</i>	H-8 $\alpha$ , H-13	H-8 $\alpha$ , H-8 $\beta$ , H-13	H-8 $\beta$ , H-9
8	41.9(CH <sub>2</sub> )	0.98 <i>m</i> H $\alpha$ 2.34 <i>m</i> H $\beta$	H-14	H-7, H-8 $\beta$ , H-9 H-7, H-8 $\alpha$	H-8 $\beta$ , H-10 H-7, H-8 $\alpha$ , H-9, H-14
9	27.4(CH)	2.13 <i>m</i>	H-8 $\alpha$ , H-14	H-8 $\alpha$ , H-10, H-14	H-7, H-8 $\beta$ , H-10, H-14
10	39.6(CH)	1.47 <i>m</i>	H-1 $\alpha$ , H-2, H-4, H-8 $\alpha$ , H-14	H-1 $\alpha$ , H-1 $\beta$ , H-5, H-9	H-1 $\alpha$ , H-1 $\beta$ , H-5, H-14
11	120.3(C)		H-13		
12	174.6(C)		H-13		
13	8.2(CH <sub>3</sub> )	1.84 <i>s</i>		H-7	H-5
14	19.1 (CH <sub>3</sub> )	0.96 <i>d</i> 6.5	H-8 $\alpha$	H-9	H-1 $\beta$ , H-9, H-10
15	20.3(CH <sub>3</sub> )	1.71 <i>s</i>	H-4	H-4, H-5	H-2, H-4
COCH <sub>3</sub>	170.7(C)		H-2, COCH <sub>3</sub>		
COCH <sub>3</sub>	21.1(CH <sub>3</sub> )	2.09 <i>s</i>			

### Acknowledgment

The authors are grateful for financial support from Natural Sciences Foundation of Yunnan (NSFY) (project No. 96B081M).

### References

1. R T. Li, Zh. H. Ding and J. K. Ding, *Acta Botanica Yunnanica*, **1997**, 19(2), 196.
2. F. Bohlmann, J. Jakupovic and M. Lonitz, *Chem. Ber.*, **1977**, 110, 301.
3. F. Bohlmann and R. K. Gupta, *Phytochem.*, **1981**, 20(6), 1432.
4. T. D. Hubert and D. F. Wiemer, *Phytochem.*, **1985**, 24(6), 1197.
5. A. Sawabe, Y. Matsubara, H. Kumamoto, Y. Iizuka and K. Okamoto, *Nippon Nogeikagaku Kaishi*, **1986**, 60(8), 593.
6. T. Fujita and M. Nakayama, *Phytochem.*, **1992**, 31(9), 3265.
7. T. Fujita, A. Funayoshi and M. Nakayama, *Phytochem.*, **1994**, 37(2), 543.

8. M. Salmon, M. Soriano-Garcia, R. A. Toscano and J. Cardenas, *J. Org. Chem.*, **1985**, 50(21), 4171.

Received 4 January 1999