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Fischeria A, a Novel Norditerpene Lactone from *Euphorbia fischeriana*

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Abstract A novel norditerpene lactone possessing a new skeleton, named fischeria A, was isolated from the rhizomes of *Euphorbia fischeriana* Steud.. Its structure and relative configuration were determined on the basis of extensive NMR studies and X-ray crystallography.

Euphorbia fischeriana Steud.(Langdu Daji in Chinese) is a well known traditional Chinese herbal medicine and mainly used as remedy for oebema, ascites and cancer[1]. Previous chemical investigation demonstrated the presence of diterpenoid constituents in *Euphorbia fischeriana* which had irritant, cocarcinogenic and antitumor activies.[1-3] We now wish to report the isolation and structural elucidation of fischeria A, a novel norditerpene lactone possessing a new carbon skeleton from *E. Fischeriana.*

The powdered rhizomes of *E. Fischeriana*[4] were extracted with 95% ethanol and the extracts were concentrated. The residue was chromatographed on a silica gel column and eluted with cyclohexane/ethyl acetate (29/1) to gain fischeria A, as colorless needles, mp 120-121°C, $[\alpha]^{20}_{D}$+51.8 (*c* 2.4,$CHCl_3$).The molecular formula ($C_{19}H_{28}O_2$) was determined by high resolution EI-MS(*m/z* 288,2080 for the molecular ion). The DEPT spectrum showed 4 methyl groups, 6 methylene groups,4 methine groups and 5 quaternary carbon atoms. The ^{1}H-NMR spectrum displayed a vinyl group (4.89 ppm, dd, *J*=11.0Hz and 0.9Hz; 4.94 ppm, dd, *J*=17.7Hz and 0.9Hz; 5.79 ppm, dd, *J*=11.0Hz and 17.7Hz), olefinic methine group(5.90 ppm, d, *J*=1.5Hz), a proton attached to an oxygenated tertiary carbon atom(4.93, d, *J*=1.5Hz),and 4 quaternary methyl groups. The ^{13}C-NMR spectrum indicated an α,β-unsaturated γ-lactone (183.9,117.4, 173.3,89.9ppm). The IR spectrum (KBr) exhibited absorption at 1742 cm^{-1} further supporting the presence of the α,β-unsaturated γ-lactone. The overall structure and the relative configuration of fischeria A were established by 2D-NMR (Table1 and Fig.1) and X-ray analysis (Fig. 2).

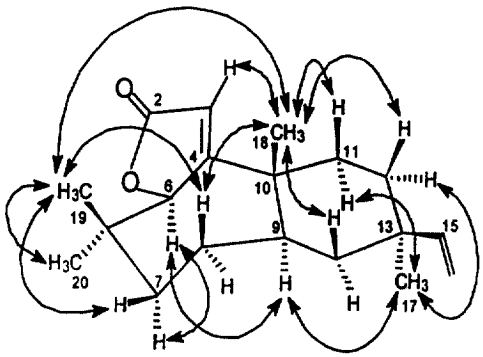

Fig. 1. The relative stereochemistry based on NOE relationship from a phase-sensitive NOESY

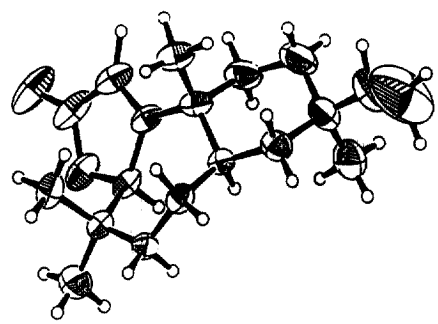

Fig. 2 The ORTEP drawing of fischeria A

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Table 1. ^{13}C,^{1}H-NMR and HMBC data of Fischeria A†

Carbon	^{13}C(ppm)	^{1}H(ppm)	HMBC
2	183.9 s	—	3-H,5-H
3	117.3 d	5.90 d(1.5Hz)	—
4	173.3 s	—	3-H,5-H
5	89.9 d	4.93 d(1.5)	3-H,6α-CH_3,6β-CH_3
6	39.1 s	—	5-H,6α-CH_3,6β-CH_3,
7	43.3 t	1.63 m	6α-CH_3,6β-CH_3
8	39.3 t	1.52(β) m 1.69(α) m	14α-H
9	39.3 d	1.65 m	10-CH_3,14-H
10	39.6 s	—	5-H,10-CH_3
11	28.5 t	1.14(α) ddd (13.2,2.7,6.2) 1.50(β) m	10-CH_3,12β-H
12	31.6 t	1.27(α) ddd (13.1,5.5,2.8) 1.60(β) m	11β-H,15-H,13-H
13	35.9 s	—	11β-H,12β-H,15-H,13-CH_3,
14	41.0 t	1.13(α) dt(13.5,2.8) 1.45(β) t(13.5)	13-CH_3,12α-H,15-H
15	150.0 d	5.79 dd(17.7,11.0)	16-H,13-CH_3
16	109.5 t	4.89 dd(11.0,0.9) 4.94 dd(17.7,0.9)	—
17	22.6 q	1.03 s	14-H,15-H,12β-H
18	18.8 q	1.22 s	11β-H
19	18.9 q	0.70 s	5-H,6β-CH_3,7β-H
20	30.0 q	1.21 s	5-H,6β-CH_3

† Recorded in $CDCl_3$ on a JEOL α-500(500MHz) spectrometer. The ^{1}H and ^{13}C assignments were based upon COSY, HOHOHA, DEPT, HETCOR, HMBC and phase-sensitive NOESY.

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References and Notes

1. Liu,G.F.; Yang,S.S.;Yang,Z.Q. Zhongyao Tongbao **1987**,12,484-486.
2. Liu,G.F.; Yang,Z.Q. Zhongcaoyao **1989**,20,290-292.
3. Liu,G.F.; Fu, Y.Q.; Yang,Z.Q.Zhongyao Tongbao **1988**,13,291-292.
4. *Euphorbia fischeriana* was identified by Prof. Chunquan Xu, Teaching and Research Section of Pharmacognosy, Shenyang Pharmaceutical University.
5. Fischeria A: $C_{19}H_{28}O_2$, colorless needles, mp 120-121°C $[\alpha]^{20}_D$+51.8 (*c* 2.4,$CHCl_3$).HR EI-MS: *m/z* 288.2080 [M^+]($C_{19}H_{28}O_2$,Δ-0.2 mmu of the calcd.), 273.1853 [M^+-CH_3]. EI-MS (rel. int.): 288[M^+](83), 273 [M^+-CH_3](40), 245 (69), 244 (57), 95 (100). IR(KBr)$\nu_{max}$$cm^{-1}$: 3457, 2925, 1742, 1611, 1457, 1383, 1327, 1180, 1004.
6. Crystal of 1. Crystallized from methanol, belong to an orthorhombic space group $P2_1P2_1P2_1$. Lattice constants and intensity data were measured on a Rigaku AFC-7R diffractometer equipped with a device for graphite-monochromated CuKα radiation. Crystal data: $C_{19}H_{28}O_2$, a=12.2855(7), b=22.254(1), C=6.3921(5)Å,Z=4, Dc=1.0096 g/cm^3, μ(CuKα)=5.35 cm^{-1}, A total of 970 independent reflections with I>3.00σ(I) was used for structural analysis. Structure was determined by a direct method SAPI91[7] extended using Fourier techniques and refined by full-matrix least square. Final refinement cycle gave R=0.04J (Rw=0.059). The final Fourier difference synthesis showed a maximum and minimum of +0.16 and –0.12 e/Å, respectively. Atomic coordinates, bond lengths, bond angles, thermal parameters and structure factors have been entered into the Cambridge Crystallographic Data Center.
7. SAPI91: Fan,H.F. (1991) Structural analysis program with intelligent control, Rigaku Corporation Tokyo, Japan