

A NEW SESQUITERPENE LACTONE GLUCOSIDE OF *IXERIS CHINENSIS*Shwu-Woan Lee^a, Zong-Tsi Chen^a, and Chiu-Ming Chen^{*b}^aDepartment of Applied Chemistry, Chia-Nan Junior College of Pharmacy, Tainan, 71710, Taiwan, R.O.C.^bDepartment of Chemistry, National Tsing Hua University, Hsinchu, Taiwan, R.O.C.

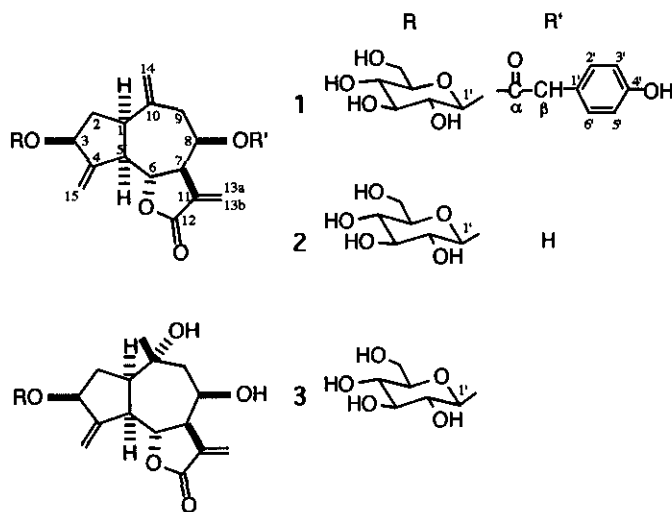
Abstract—A new sesquiterpene lactone glucoside, 8-epicrepiside G(1) together with two known compounds, 8-epidesacylcynaropicrin glucoside (2) and ixerin D (3) were isolated from the whole plant of *Ixeris chinensis*. Their structures were determined on the basis of chemical and spectroscopic evidence. Compounds 1, 2 and 3 taste of strong bitterness.

Ixeris chinensis Nakai, Compositae, is used as a folk medicine in Taiwan with antipyretic, analgesic and anti-inflammatory actions.¹ Bauerenyl acetate, luteolin and luteolin 7-*O*-glucoside have been previously isolated from the same species.² As part of a search for bitter principles from medicinal plants,³ we here describe the isolation and structural elucidation of a new sesquiterpene lactone glucoside, 8-epicrepiside G (1), together with two known compounds, 8-epidesacylcynaropicrin glucoside (2) and ixerin D (3). These compounds show strong bitterness.

The ethanol extract of the whole plant was concentrated, and then suspended in water. The suspension was extracted with ethyl acetate and *n*-butanol, successively. The ethyl acetate extract was chromatographed to give a new sesquiterpene lactone glucoside. The *n*-butanol extract was chromatographed to give two known sesquiterpene lactone glucosides. The known compounds were identified as 8-epidesacylcynaropicrin glucoside (2)⁴ and ixerin D (3)⁵ by comparison with the reported data.

Compound (1), named 8-epicrepiside G, was the main bitter principle of this plant. The high-resolution negative ion FAB ms showed an ion peak at *m/z* 557.1998 ([M-H]⁻, C₂₉H₃₃O₁₁). The ir spectrum of 1

showed the presence of a hydroxyl (3400 cm^{-1}), an unsaturated γ -lactone (1760 cm^{-1}), an ester carbonyl (1740 cm^{-1}) and aromatic groups ($1580, 1520, 1460\text{ cm}^{-1}$). The uv spectrum showed absorptions at λ_{max} (MeOH) 278 and 286 nm. The $^1\text{H-nmr}$ spectrum showed the presence of characteristic signals of exocyclic α -methylene- γ -lactone⁶ at δ 5.53 (1H, d, $J = 2.9\text{ Hz}$, H-13a) and 6.29 (1H, d, $J = 3.4\text{ Hz}$, H-13b) which were coupled with H-7, two terminal methylene groups at δ 4.82, 5.14 (each 1H, br s, H-14) and δ 5.61, 5.93 (each 1H, br s, H-15), as well as A_2B_2 type signals at δ 7.12 and 7.24 (each 2H, d, $J = 8.3\text{ Hz}$) and signals at δ 3.57 (2H, br s) which were due to a *p*-hydroxyphenylacetic acid moiety.⁷ The $^{13}\text{C-nmr}$ spectrum (Table 1) of 1 was similar to that of 2, except for eight additional signals due to the *p*-hydroxyphenylacetic acid moiety. The signal at δ 68.2 due to C-8 showed downfield shift by 2.1 ppm whereas the signals at δ 48.4 and 40.4 due to C-7 and C-9 showed upfield shift by 1.5 and 3.7 ppm, respectively, in comparison with those of 2. On saponification of 1, compound (2) and *p*-hydroxyphenylacetic acid were obtained. These facts indicated that the hydroxyl group at C-8 of compound (2) was esterified by *p*-hydroxyphenylacetic acid. On acid hydrolysis of 1,

Table 1 $^{13}\text{C-Nmr}$ spectral data of 1 and 2

Carbon	1	2
1	44.4(d)	45.0(d)
2	38.2(t)	38.5(t)
3	80.7(d)	80.9(d)
4	150.6(s)	151.3(s)
5	50.1(d)	50.5(d)
6	78.9(d)	78.5(d)
7	48.4(d)	49.9(d)
8	68.2(d)	66.1(d)
9	40.4(t)	44.1(t)
10	143.6(s)	145.2(s)
11	136.1(s)	137.8(s)
12	169.4(s)	170.7(s)
13	123.1(t)	121.6(t)
14	117.2(t)	116.3(t)
15	111.9(t)	111.7(t)
1'	104.8(d)	104.9(d)
2'	75.4(d)	75.4(d)
3'	78.6(d)	78.6(d)
4'	71.8(d)	71.8(d)
5'	78.5(d)	78.5(d)
6'	62.9(t)	62.9(t)
α	171.6(s)	
β	40.7(t)	
1''	125.0(s)	
2'',6''	131.1(d)	
3'',5''	116.4(d)	
4''	158.2(s)	

Assignments were made with the aid of DEPT experiments.

D-glucose was obtained as the sugar moiety. The anomeric structure of **1** was assigned to be β -anomer on the basis of C_1 - H_1 coupling parameter ($J = 159$ Hz).⁸ These evidence enabled us to determined the structure of **1**.

EXPERIMENTAL

Mp was uncorrected. Optical rotations were measured on a JASCO DIP-360 digital polarimeter. Ir spectra were measured on a Hitachi 270-30 spectrophotometer and uv spectra were measured on a Hitachi 200 spectrophotometer. 1H - and ^{13}C -Nmr spectra were recorded on a Bruker AM-400 spectrometer. FAB mass spectra were measured on a JEOL JMS-HX-110 mass spectrometer. Hplc was done on a Waters ALC/GPC-244/M-6000A instrument. Glc was done on a Hewlett-Packard 5890 gas chromatography.

Extraction and Isolation. The fresh whole plants of *I. chinensis* Nakai (7.2 kg) were extracted with EtOH (5L x 6) under reflux for 6 h. The concentrated EtOH extract was suspended in water. The suspension was partitioned with EtOAc and *n*-BuOH, successively. The EtOAc fraction (16.8 g) was chromatographed on a silica gel column with $CHCl_3$ as gradients of MeOH as eluent and 250 ml were collected for each fraction.

Fractions 45-51 (2.2 g) were collected and chromatographed on a silica gel column with EtOAc-MeOH (20:1) as eluent to give 8-epicrepioside G (1, 1.02 g). The *n*-BuOH fraction (12.0 g) was chromatographed on a Sephadex LH-20 column with EtOH-H₂O (1:1) as eluent and 20 ml were collected for each fraction.

Fractions 42-52 (1.8 g) were collected and chromatographed on a silica gel column with EtOAc as gradients of MeOH as eluent to give 8-epidesacylcynaropicrin glucoside (2, 65 mg) and ixerin D (3, 12 mg).

8-Epicrepioside G (1). Colorless amorphous powder, mp 116-119°C, $[\alpha]_D^{27} -28.5^\circ$ (c 1.68, MeOH).

Negative ion FAB ms (matrix: diethanolamine) m/z 557 $[M-H]^-$. High-resolution FAB ms m/z : 557.1998 ($[M-H]^-$, Calcd for $C_{29}H_{33}O_{11}$: 557.1973). Ir ν_{max} (KBr) 3400, 2950, 1760, 1740, 1650, 1620, 1580, 1520, 1460, 1420, 1370, 1330, 1260, 1160, 1080, 1040, 920, 820 cm^{-1} . Uv λ_{max} (MeOH) $\log(\epsilon)$ 278 (3.35), 286 (sh) nm. 1H -Nmr (C_5D_5N) δ 7.24 (2H, d, $J = 8.3$ Hz, H-2", 6"), 7.12 (2H, d, $J = 8.3$ Hz, H-3", 5"), 6.29 (1H, d, $J = 3.4$ Hz, H-13b), 5.93 (1H, br s, H-15), 5.66 (1H, m, H-8), 5.61 (1H, br s, H-15), 5.53 (1H, d, $J = 2.9$ Hz, H-13a), 5.14 (1H, br s, H-14), 4.82 (1H, br s, H-14), 4.35 (2H, m, H-3, 6), 3.57 (2H, br s, ArCH₂). ^{13}C -Nmr (C_5D_5N , δ ppm): See Table 1.

Saponification of 8-Epicrepioside G (1). A solution of **1** (35 mg) in 2% NaOH (3 ml) was stirred under a

nitrogen atmosphere for 1h at room temperature. The mixture was neutralized with 6% HCl and extracted with *n*-butanol. The extract was washed with H₂O, and concentrated and chromatographed on a silica gel column with CHCl₃-MeOH-H₂O (10:2:0.1) as eluent to afford **2** (8 mg) and *p*-hydroxyphenylacetic acid (1.5 mg). The latter was identified by hplc with authentic sample [column, Lichrosorb RP-18, 4mm x 25cm; solvent, H₂O-MeOH (9:1); flow rate, 2.0 ml/min; detector, uv 254 nm; t_R 12.5 min].

Acid Hydrolysis of 8-Epicrepiside G (1). A solution of **1** (3 mg) in 2% HCl (3 ml) was heated on a boiling water bath for 4 h. The mixture was evaporated *in vacuo*. The residue was dissolved in dry pyridine (0.5 ml) and the trimethylsilyl ethers were prepared by addition of hexamethyldisilazane (0.4 ml) and trimethylchlorosilane (0.2 ml) successively. The mixture was evaporated *in vacuo*; 0.5 ml of *n*-heptane was added. The insoluble material was filtered off. The filtrate was shown to contain TMS-glucitol by glc [packed glass column, 3% OV-101 on Chromosorb W-HP 80-100 mesh, 2mm x 2m; column temperature, 150-250°C at 10°C/min; carrier gas, N₂; t_R 8.89, 9.65 min].

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