A NEW SESQUITERPENE LACTONE GLUCOSIDE OF *IXERIS CHINENSIS*

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Abstract-A new sesquiterpene lactone glucoside, 8-epicrepioside 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-epicrepioside 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-epicrepioside 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 ($[M-H]^-$, $C_{29}H_{33}O_{11}$). 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 cm^{-1}). The uv spectrum showed absorptions at λ_{max} (MeOH) 278 and 286 nm. The ^{1}H-nmr spectrum showed the presence of characteristic signals of exocyclic α-methylene-γ-lactone[6] at δ 5.53 (1H, d, J= 2.9 Hz, H-13a) and 6.29 (1H, d, J= 3.4 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 Hz) and signals at δ 3.57 (2H, br s) which were due to a *p-hydroxyphenylacetic acid moiety.*[7] *The* ^{13}*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,

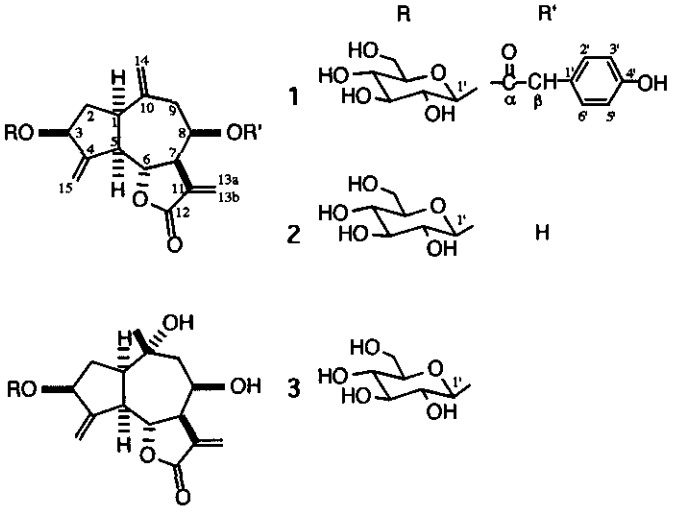

Table 1 ^{13}C-Nmr spectral data of 1 and 2

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. ^{1}H- 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-H_2O (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° (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 υ_{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(ε) 278 (3.35), 286(sh) nm. ^{1}H-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, Ar$\underline{CH_2}$). ^{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 H_2O, and concentrated and chromatographed on a silica gel column with $CHCl_3$-MeOH-H_2O (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, H_2O-MeOH (9:1); flow rate, 2.0 ml/min; detector, uv 254 nm; t_R 12.5 min].

Acid Hydrolysis of 8-Epicrepioside 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, N_2; t_R 8.89, 9.65 min].

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