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BRUCEOSIDES D, E, AND F, THREE NEW CYTOTOXIC QUASSINOID GLUCOSIDES FROM *BRUCEA JAVANICA*

SATSUKI OHNISHI, NARIHIKO FUKAMIYA, MASAYOSHI OKANO,*

Department of Interdisciplinary Studies of Natural Environment, Faculty of Integrated Arts and Sciences, Hiroshima University, Higashihiroshima 724, Japan

KIYOSHI TAGAHARA,

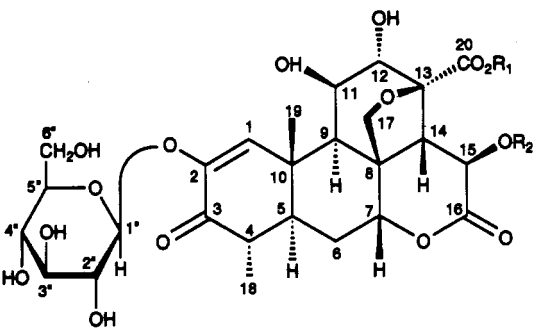
Faculty of Pharmaceutical Sciences, Kobe Pharmaceutical University, Kobe 658, Japan

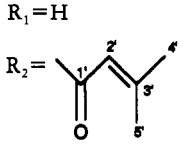
and KUO-HSIUNG LEE*

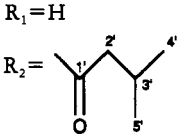
Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27599

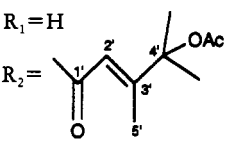
ABSTRACT.—Three new quassinoid glucosides, bruceosides D [**1**], E [**2**], and F [**3**], were isolated from *Brucea javanica*, and their structures were elucidated by spectral evidence and chemical transformation to known compounds. Compounds **1–3** show selective cytotoxicity in the leukemia and non-small cell lung, colon, CNS, melanoma, and ovarian cancer cell lines with log GI_{50} values in the range of −4.14 to −5.72.

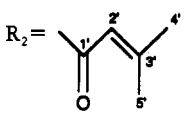
Following our earlier isolation of bruceosides A [**4**], B, and C, as well as brusatol and cleomiscosin A, from *Brucea javanica* (L.) Merr. (Simaroubaceae) ("Ya-Tan-Tzu") (1–3) and the isolation of 16 quassinoid glucosides from the same plant by Takahashi *et al.* (4–11), we have isolated three new quassinoid glucosides from this species. We report herein the isolation of the new cytotoxic quassinoid glucosides, bruceosides D [**1**], E [**2**], and F [**3**], and their structure elucidation by spectral evidence and chemical transformation to the known compounds, bruceoside A [**4**], yadanzioside A [**5**], and yadanzioside G [**6**], respectively.

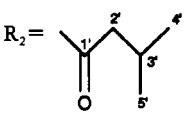


1 R_1=H, R_2= 

2 R_1=H, R_2= 

3 R_1=H, R_2= 

4 R_1=Me, R_2= 

5 R_1=Me, R_2= 

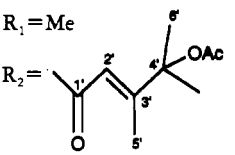
6 R_1=Me, R_2= 

TABLE 1. ^{1}H-Nmr Data[a] of Compounds **1–6**.

Proton(s)	Compound					
	1	**2**	**3**	**4**	**5**	**6**
H-1	7.31 s	7.29 s	7.31 s	7.28 s	7.27 s	7.31 s
H-4	2.42 dq	2.40 dq	2.42 dq	2.40 m	2.40 m	2.43 m
H-5	[b]	[b]	[b]	3.35	[b]	[b]
H-6α	2.04 br d	2.02 br d	2.04 br d	2.02	2.00	2.03
H-6β	1.68 br d	1.67 br d	1.69 br d	1.64	1.64	1.65
H-7	4.99 br s	4.96 br s	5.00 br s	5.00	4.97	5.10
H-9	2.55 d (5.0)	2.52 d (4.5)	2.56 d (5.0)	2.52 d	2.50 d	2.54 d
H-11	5.23 d (5.0)	5.21 d (4.5)	5.23 br d	5.21	5.20	5.21
H-12	5.20 br d	5.14 br d	5.23 br d	5.13	5.13	5.18
H-14	[b]	[b]	[b]	[b]	[b]	[b]
H-15	[b]	[b]	[b]	6.90 br d	6.92 br d	6.90 br d
H-17α	3.95 m	3.94 m	3.95 d (7.0)	[b]	[b]	[b]
H-17β	5.12 d (7.5)	5.10 d (7.5)	5.11 m	[b]	[b]	[b]
Me-4	1.18 d (6.5)	1.16 d (6.5)	1.18 d (7.0)	1.18 d	1.15 d	1.17 d
Me-10	1.64 s	1.63 s	1.64 s	1.64 s	1.60 s	1.62 s
OMe-20	—	—	—	3.78 s	3.82 s	3.88 s
H-2′	5.79 m	2.32 d (7.5)	6.13 s	5.85 s	[b]	6.09 s
H-3′	—	2.21 dq	—	—	2.22 m	—
Me-3′	1.45 s	0.84 d (6.5)	2.25 s	1.68 s	0.95 d	2.25 s
	2.09 s	0.87 d (6.5)	—	2.17 s	0.97 d	—
Me-4′	—	—	1.27 s	—	—	1.40 s
	—	—	1.27 s	—	—	1.44 s
OAc-4′	—	—	1.86 s	—	—	1.93 s
H-1″	5.39 d (7.0)	5.36 d (7.5)	5.38 d (7.0)	5.38 d	5.36 d	5.39 d
H-2″	4.28 m	4.28 m	4.28 m	[b]	[b]	[b]
H-3″	4.27 m	4.27 m	4.26 m	[b]	[b]	[b]
H-4″	4.26 m	4.25 m	4.25 m	[b]	[b]	[b]
H-5″	3.94 m	3.92 m	3.94 m	[b]	[b]	[b]
H-6″	4.23 m	4.22 m	4.23 m	[b]	[b]	[b]
	4.49 dd	4.49 dd	4.49 dd			
	(12.3)	(12.3)				

[a]Measured at 500 MHz in C_5D_5N. Values are δ ppm. Coupling constants in Hz in parentheses.
[b]Not assignable.

RESULTS AND DISCUSSION

Compound **1** was obtained as a colorless amorphous solid. Its ir spectrum showed the presence of hydroxy (3400 cm^{-1}), δ-lactone and ester (1740 cm^{-1}), and α,β-unsaturated carbonyl (1680 and 1650 cm^{-1}) groups. The uv spectrum of **1** exhibited an absorption maximum at 380 nm due to a conjugated enone system. The hrsims showed the molecular formula of **1** to be $C_{31}H_{40}O_{16}$, and the eims showed a fragment ion peak $[M-C_6H_{10}O_5+H]^+$ at *m/z* 507, which suggested a glycoside structure.

^{1}H-Nmr (Table 1) assignments for **1** were based on ^{1}H-^{1}H and ^{13}C-^{1}H COSY spectra, and ^{13}C-nmr (Table 2) assignments were based on ^{13}C-^{1}H COSY and DEPT spectra. The ^{1}H-nmr spectrum of **1** disclosed the presence of a senecioyl [δ 1.45 (Me-3′), 2.09 (Me-3′), and 5.79 (H-2′)] and two methyl [δ 1.17 (Me-4) and 1.64 (Me-10)] groups. The ^{13}C-nmr spectrum of **1** also indicated the presence of a senecioyl group [δ 174.0 (C-1′), 116.3 (C-2′), 157.7 (C-3′), 26.9 (C-4′), and 20.1 (Me-3′)] and of a β-D-glucose moiety [δ 101.9 (C-1″), 74.7 (C-2″), 78.5 (C-3″), 71.2 (C-4″), 78.9 (C-5″), and 62.3 (C-6″)].

All quassinoids previously isolated from this plant contain a $COOCH_3$ group at C-

TABLE 2. ^{13}C-Nmr Data[a] of Compounds **1–6**.

Carbon	Compound					
	1	**2**	**3**	**4**	**5**	**6**
C-1 ...	129.3 (CH)	129.2 (CH)	129.4 (CH)	129.1 (CH)	128.9 (CH)	129.0 (CH)
C-2 ...	148.4 (C)	148.8 (C)	148.8 (C)	148.6 (C)	148.6 (C)	148.7 (C)
C-3 ...	194.6 (C=O)	194.6 (C=O)	194.7 (C=O)	194.6 (C=O)	194.4 (C=O)	194.4 (C=O)
C-4 ...	41.4 (CH)	41.4 (CH)	41.4 (CH)	41.1 (CH)	41.0 (CH)	43.9 (CH)
C-5 ...	43.8 (CH)	43.7 (CH)	43.8 (CH)	43.5 (CH)	43.4 (CH)	43.5 (CH)
C-6 ...	30.1 (CH_2)	30.1 (CH_2)	30.1 (CH_2)	29.8 (CH_2)	29.7 (CH_2)	29.8 (CH_2)
C-7 ...	83.7 (CH)	83.8 (CH)	83.6 (CH)	83.2 (CH)	83.3 (CH)	83.5 (CH)
C-8 ...	46.7 (C)	46.7 (C)	46.7 (C)	46.4 (C)	46.4 (C)	46.4 (C)
C-9 ...	40.6 (CH)	40.7 (CH)	40.6 (CH)	40.2 (CH)	40.1 (CH)	40.4 (CH)
C-10 ..	39.7 (C)	39.6 (CH)	39.7 (C)	39.4 (C)	39.3 (C)	39.4 (C)
C-11 ..	73.2 (CH)	73.3 (CH)	73.2 (CH)	73.2 (CH)	73.2 (CH)	73.3 (CH)
C-12 ..	76.7 (CH)	76.6 (CH)	76.8 (CH)	75.8 (CH)	75.6 (CH)	76.0 (CH)
C-13 ..	82.5 (C)	82.6 (C)	82.7 (C)	82.4 (C)	82.4 (C)	82.3 (C)
C-14 ..	50.2 (CH)	50.2 (CH)	50.2 (CH)	50.5 (CH)	50.2 (CH)	50.5 (CH)
C-15 ..	68.3 (CH)	68.5 (CH)	69.0 (CH)	68.0 (CH)	68.3 (CH)	68.5 (CH)
C-16 ..	168.2 (C=O)	168.4 (C=O)	168.4 (C=O)	168.1 (C=O)	168.0 (C=O)	168.0 (C=O)
C-17 ..	73.8 (CH_2)	73.7 (CH_2)	73.7 (CH_2)	73.5 (CH_2)	73.5 (CH_2)	73.7 (CH_2)
C-18 ..	12.6 (CH_3)	12.6 (CH_3)	12.6 (CH_3)	12.5 (CH_3)	12.2 (CH_3)	12.3 (CH_3)
C-19 ..	18.0 (CH_3)	17.9 (CH_3)	18.0 (CH_3)	17.6 (CH_3)	17.6 (CH_3)	17.6 (CH_3)
C-20 ..	173.5 (C=O)	173.4 (C=O)	173.4 (C=O)	171.0 (C=O)	171.0 (C=O)	171.0 (C=O)
OMe ..	—	—	—	52.1 (CH_3)	52.1 (CH_3)	52.6 (CH_3)
C-1′ ...	174.0 (C=O)	174.0 (C=O)	162.6 (C=O)	165.1 (C=O)	171.5 (C=O)	165.6 (C=O)
C-2′ ...	116.3 (CH)	43.3 (CH)	113.9 (CH)	115.7 (CH)	43.0 (CH)	113.3 (CH)
C-3′ ...	157.7 (C)	25.6 (C)	169.5 (C)	158.2 (C)	25.6 (C)	169.3 (C)
C-4′ ...	26.9 (CH_3)	22.4 (CH_3)	82.3 (C)	26.8 (CH_3)	22.2 (CH_3)	82.0 (CH_3)
Me-3′..	20.1 (CH_3)	22.5 (CH_3)	14.5 (CH_3)	19.9 (CH_3)	22.1 (CH_3)	14.2 (CH_3)
Me-4′..	—	—	25.8 (CH_3)	—	—	26.4 (CH_3)
	—	—	25.8 (CH_3)	—	—	25.8 (CH_3)
OAc-4′	—	—	166.0 (C=O)	—	—	162.3 (C=O)
	—	—	21.4 (CH_3)	—	—	21.1 (CH_3)
C-1″ ...	101.9 (CH)	101.9 (CH)	101.9 (CH)	101.7 (CH)	101.7 (CH)	101.8 (CH)
C-2″ ...	74.7 (CH)	74.7 (CH)	74.7 (CH)	74.4 (CH)	74.4 (CH)	74.4 (CH)
C-3″ ...	78.5 (CH)	78.5 (CH)	78.5 (CH)	78.6 (CH)	78.7 (CH)	78.7 (CH)
C-4″ ...	71.2 (CH)	71.2 (CH)	71.2 (CH)	71.0 (CH)	71.0 (CH)	71.0 (CH)
C-5″ ...	78.9 (CH)	78.9 (CH)	78.9 (CH)	78.2 (CH)	78.2 (CH)	78.2 (CH)
C-6″ ...	62.3 (CH_2)	62.3 (CH_2)	62.3 (CH_2)	62.1 (CH_2)	62.0 (CH_2)	62.0 (CH_2)

[a]Measured at 125.7 MHz in C_5D_5N. Values are δ ppm.

13, which shows ^{1}H- and ^{13}C-nmr signals at δ ca. 3.8 and ca. 52, respectively. However, these signals were not present in the spectra of **1**. From these results, the C-13 moiety of **1** was assumed to be a free COOH. Except for this moiety, the ^{1}H- and ^{13}C-nmr spectra of **1** coincided with those of bruceoside A [**4**] (1). Therefore, compound **1** was methylated with CH_2N_2 to afford bruceoside A [**4**] (1,3), confirming the structural assignment of **1**. Compound **1** is a new quassinoid glycoside and has been named bruceoside D.

The ir, uv, ms, and nmr spectra of **2** and **3** were similar to those of **1** and again suggested glycoside structures with free carboxylic acid groups at C-13. The only differences in the structures of compounds **1–3** occurred at the C-15 ester group. The ^{1}H- and ^{13}C-nmr spectra indicated a 3-methylbutanoyl group in **2** [δ_H 0.84 (Me-3′), 0.87 (Me-3′), 2.21 (H-3′), 2.32 (H-2′) and δ_C 174.0 (C-1′), 43.3 (C-2′), 25.6 (C-3′), 22.4 (C-4′), 22.5 (Me-3′)] and a 4-acetoxy-3,4-dimethyl-2-pentenoyl group in **3** [δ_H 1.27 (Me-4′), 1.86 (OAc-4′), 2.25 (H-3′), 6.13 (H-2′) and δ_C 162.6 (C-1′), 113.9 (C-2′), 169.5

TABLE 3. Inhibition of In Vitro Cancer Cell Growth by Compounds **1–3** [Cytotoxicity Log GI_{50} (M)].[a,b]

Cell Line	Compound		
	1	**2**	**3**
Leukemia			
CCRF-CEM	−4.44	−4.61	−4.36
HL-60 (TB)	−4.45	−4.38	−4.32
K-562	−4.59	−4.62	−4.40
MOLT-4	−4.65	−4.72	−4.47
SR	−4.51	−4.47	−4.31
Non-Small Cell Lung Cancer			
A549/ATCC	−4.26	−4.38	—[c]
EKVX	—[c]	—[c]	—[c]
HOP-62	−4.48	−4.35	−4.16
HOP-92	−4.50	−4.43	−4.18
NCI-H226	−4.55	−4.53	−4.14
NCI-H23	—[c]	—[c]	—[c]
NCI-H322M	—[c]	—[c]	—[c]
NCI-H460	−4.49	−4.56	−4.40
NCI-H522	−4.54	−5.66	−4.73
Colon Cancer			
COLO-205	—[c]	—[c]	—[c]
HCC-2998	−4.61	−4.69	−4.44
HCT-116	−4.53	−4.48	−4.42
HCT-15	—[c]	—[c]	—[c]
HT 29	−4.45	−4.47	—[c]
KM 12	−4.31	—[c]	—[c]
SW 620	—[c]	—[c]	—[c]
CNS Cancer			
SF-268	—[c]	—[c]	—[c]
SF-539	−4.58	−4.69	−4.25
SNB-19	−4.50	−4.50	—[c]
SNB-75	—[c]	—[c]	—[c]
U 251	−4.40	−4.50	—[c]
Melanoma			
LOX1MVI	−4.39	−4.41	—[c]
MALME-3M	−4.62	−4.64	−4.25
M14	−4.49	—[c]	—[c]
SK-MEL-2	—[c]	—[c]	—[c]
SK-MEL-28	−4.43	−4.60	—[c]
SK-MEL-5	−4.37	−4.55	—[c]
UACC-257	—[c]	—[c]	—[c]
UACC-62	—[c]	—[c]	—[c]
Ovarian Cancer			
IGROV1	—[c]	−4.45	—[c]
OVCAR-3	−4.69	−4.44	−4.59
OVCAR-4	−4.60	−5.72	—[c]
OVCAR-5	—[c]	—[c]	—[c]
OVCAR-8	—[c]	—[c]	—[c]
SK-OV-3	—[c]	—[c]	—[c]
Renal Cancer			
786-0	—[c]	—[c]	—[c]
A 498	—[c]	—[c]	—[c]
ACHN	—[c]	—[c]	—[c]
CAKI-1	—[c]	—[c]	—[c]
RXF-393	−4.60	−4.97	−4.43

TABLE 3. Continued.

Cell Line	Compound		
	1	2	3
SN12C	—[c]	—[c]	—[c]
TK-10	—[c]	—[c]	—[c]
UO-31	−4.50	—[c]	—[c]
Prostate Cancer			
PC-3	—[c]	—[c]	—[c]
DU-145	—[c]	—[c]	—[c]
Breast Cancer			
MCF-7	−4.65	−4.55	−4.56
MCF7/ADR-RES	—[c]	—[c]	—[c]
MDA-MB-231/ATCC	—[c]	—[c]	—[c]
HS 578T	—[c]	−4.40	—[c]
MDA-MB-435	—[c]	—[c]	—[c]
MDA-N	—[c]	—[c]	—[c]
BT-549	—[c]	—[c]	—[c]
T-47D	—[c]	—[c]	—[c]

[a]Data obtained from NCI's in vitro disease-oriented human tumor cells screen [see Grever *et al.* (12) and Monks *et al.* (13) for details].

[b]Log concentrations which reduced cell growth to 50% of level at start of experiment. The average log GI_{50} values were calculated from all cell lines tested.

[c]"—" means log GI_{50} is greater than −4.

(C-3′), 82.3 (C-4′), 14.5 (Me-3′), 25.8 (Me-4′), 166.0 (C=O)]. Methylation of **2** and **3** with CH_2N_2 gave yadanzioside A [**5**] (3,8), and yadanzioside G [**6**] (3,8), respectively. The new quassinoids **2** and **3** were designated as bruceosides E and F, respectively.

Because nmr spectra for the known compounds bruceoside A [**4**], yadanzioside A [**5**], and yadanzioside G [**6**] either have not been previously reported (^{13}C-nmr data for **4**) or were obtained at lower-field strengths [100 MHz for ^{1}H-nmr data for **4** (1); 90 MHz ^{1}H-nmr data for **5** and **6** (8); 22.5 MHz ^{13}C-nmr data for **5** and **6** (8)] than those used in this study, we have included such values in Table 1. We determined the ^{1}H- and ^{13}C-nmr spectra of these compounds at 500 MHz and 100 MHz, respectively, and assigned all signals by 2D nmr techniques (^{1}H-^{1}H COSY, ^{13}C-^{1}H COSY, and DEPT).

Bruceosides D, E, and F [**1–3**] were evaluated for cytotoxicity in the National Cancer Institute's in vitro human tumor cell line panel, which included 58 cell lines representing nine cancer types. These compounds showed selective cytotoxicity in cell lines from leukemia, melanoma, and non-small cell lung, colon, CNS, and ovarian cancers. The log GI_{50} values ranged from −4.14 to −5.72 as shown in Table 3.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps were determined on an MRK air-bath type melting-point apparatus and are uncorrected. Specific rotations were obtained on a Jasco DIP-370 digital polarimeter (length=0.5 dm). Ir and uv spectra were recorded on a Jasco IR-810 spectrometer and Hitachi 320-S spectrometer, respectively. ^{1}H- and ^{13}C-nmr spectra were determined on a Varian VXR-500 or JEOL JNM-A400 spectrometer in C_5D_5N using TMS as an internal standard. Mass spectra were recorded on a Hitachi M80 instrument. Hrsims were obtained in a mixture of glycerol and thioglycerol. Si gel (Merck, type 60, 70–230 mesh) was used for cc. Precoated Si gel plates (Merck, $60F_{254}$ of 0.25 mm thickness) were used for analytical tlc, and plates of 1-mm and 2-mm thickness were used for prep. tlc; $CHCl_3$-MeOH-H_2O (50:14:3, v/v, lower phase) was used as the tlc solvent. Components on tlc plates were detected using a uv lamp and the indicator bromocresol green (0.3% solution of 80% MeOH). Analytical hplc was performed on a Tosoh liquid chromatograph equipped with a uv detector at 254 nm and a reversed-phase column (TSK-gel ODS-

8OTM) using a mixed solvent of MeOH/H_2O. Prep. hplc was carried out on a Gilson liquid chromatograph equipped with a reversed-phase column (Lichrosorb RP-18 and/or Dynamax-60A) at 245 nm using the same solvents as for analytical hplc.

PLANT MATERIAL.—As described previously (3).

EXTRACTION AND ISOLATION.—A part (445 g) of the crude *n*-BuOH fraction, which has been previously described (3), was subjected to Si gel cc using EtOAc-Et_2O (1:1) to give four fractions, then $CHCl_3$-MeOH-H_2O (50:14:3, lower phase) to yield eleven fractions, and finally MeOH to afford two fractions. The first MeOH fraction (104 g) contained acidic components as indicated by analytical tlc using bromocrescol green.

The first MeOH fraction (104 g) was dissolved in MeOH and filtered. The filtrate was evaporated to afford a brown resinous substance (8.71 g), which contained three major components as shown by analytical hplc (MeOH-H_2O, 1:1). The resinous substance (8.71 g) was subjected first to cc using Sephadex LH-20 to remove polymeric compounds and then to prep. hplc (H_2O-MeOH-AcOH, 70:30:1, 60:40:1, and 55:45:1) to afford bruceosides D (**1**, 102 mg, 0.00022%), E (**2**, 60.9 mg, 0.00013%), and F (**3**, 49.9 mg, 0.00011%).

Bruceoside D [**1**].—Colorless amorphous solid; mp 189–191°; $[\alpha]^{22}D$ +16.4° (c=0.049, MeOH); uv λ max (MeOH) 380 (ε 18500) nm; ir ν max (KBr) 3400 (OH), 1740 (δ-lactone and ester C=O), 1680, 1650 (α,β-unsaturated C=O) cm^{-1}; ^{1}H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; eims *m/z* 506 ($[M-C_6H_{10}O_5]^+$, 3%), 83 ($[C_5H_7O]^+$, 100) (side-chain); sims *m/z* 507 ($[M-C_6H_{10}O_5+H]^+$, 2%), 83 ($[C_5H_7O]^+$, 100%) (side-chain); hrsims *m/z* $[M+Na]^+$ 691.2250 (error 3.9, $C_{31}H_{40}O_{16}Na_1$).

Bruceoside E [**2**].—Colorless amorphous solid; mp 188–190°; $[\alpha]^{23}D$ 0° (c=0.045, MeOH); uv λ max (MeOH) 345 (ε 7820) nm; ir ν max (KBr) 3400 (OH), 1735 (δ-lactone and ester C=O), 1680, 1630 (α,β-unsaturated C=O) cm^{-1}; ^{1}H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; eims *m/z* 508 ($[M-C_6H_{10}O_5]^+$, 1), 85 ($[C_5H_9O]^+$, 40%) (side-chain); sims *m/z* 508 ($[M-C_6H_{10}O_5+H]^+$, 100%), 85 ($[C_5H_9O]^+$, 100%) (side-chain); hrsims *m/z* $[M+Na]^+$ 693.2356 (error −1.2, $C_{31}H_{42}O_{16}Na_1$).

Bruceoside F [**3**].—Colorless amorphous solid; mp 196–199°; $[\alpha]^{22}D$ +5.0° (c=0.040, MeOH); uv λ max (MeOH) 380 (ε 20200) nm; ir ν max (KBr) 3400 (OH), 1735 (δ-lactone and ester C=O), 1680, 1640 (α,β-unsaturated C=O) cm^{-1}; ^{1}H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; sims *m/z* 533 ($[M-C_6H_{10}O_5+H-AcOH]^+$, 100%); hrsims *m/z* $[M+Na]^+$ 777.2598 (error 2.0, $C_{35}H_{46}O_{18}Na_1$).

METHYLATION OF **1**, **2**, AND **3**.—A MeOH (1 ml) solution of **1** (5.0 mg, 0.00075 mmol) was added to an Et_2O (10 ml) solution of CH_2N_2 prepared from *N*-nitroso-*N*-methylurea (500 mg, 3.8 mmol) at 0°. The reaction mixture was stirred at 0° for 2.5 h; the solvent was then evaporated to give a crude product. Purification using prep. hplc [Lichrosorb RP-18, MeOH-H_2O (1:1)] afforded compound **4** (4.9 mg, 97% yield). Methylations of **2** (5.0 mg) and **3** (5.0 mg) were carried out in the same manner described above and afforded compounds **5** (4.3 mg, 84% yield) and **6** (5.0 mg, 98% yield), respectively. The physical and spectral data of compounds **4**–**6** were identical with those of the known compounds bruceoside A (1,3), yadanzioside A (3,8), and yadanzioside G (3,8), respectively.

Bruceoside A [**1**].—Colorless amorphous solid; mp 184–189°; ir ν max (KBr) 3400 (OH), 1740 (δ-lactone and ester C=O), 1680, 1645 (α,β-unsaturated C=O) cm^{-1}; ^{1}H-nmr data, see Table 1.

Yadanzioside [**2**].—Colorless amorphous solid; mp 223–226°; ir ν max (KBr) 3425 (OH), 1740 (δ-lactone and ester C=O), 1680, 1630 (α,β-unsaturated C=O) cm^{-1}; ^{1}H-nmr data, see Table 1.

Yadanzioside G [**3**].—Colorless amorphous solid; mp 178–181°; ir ν max (KBr) 3400 (OH), 1740 (δ-lactone and ester C=O), 1680, 1635 (α,β-unsaturated C=O) cm^{-1}; ^{1}H-nmr data, see Table 1.

CYTOTOXICITY ASSAYS.—Based on significant cytotoxicity found in an initial in-house cytotoxicity screen, bruceosides D, E, and F [**1**–**3**] were submitted to the National Cancer Institute (NCI) for evaluation in their in vitro human tumor cell line panel. Details of the assay procedures have been reported (12,13). The results are shown in Table 3.

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