Tetrahedron 66 (2010) 2306–2310

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Pre-schisanartanins C–D and propintrilactones A–B, two classes of new nortriterpenoids from *Schisandra propinqua* var. *propinqua*

Chun Lei, Wei-Lie Xiao, Sheng-Xiong Huang, Ji-Jun Chen, Jian-Xin Pu *, Han-Dong Sun *

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, Yunnan, PR China

ARTICLE INFO

Article history:
Received 12 November 2009
Received in revised form 19 January 2010
Accepted 1 February 2010
Available online 4 February 2010

Keywords:
Schisandra
Nortriterpenoid
Lactone
Schisanartane
Wuweiziartane

ABSTRACT

Four new nortriterpenoids, pre-schisanartanins C and D (**1**–**2**) with pre-schisanartane backbone, and propintrilactones A and B (**3**–**4**) possessed wuweiziartane framework, were isolated from the acetone extract of the stems of *Schisandra propinqua* var. *propinqua*. Their structures were characterized by extensive spectroscopic analyses. Compounds **3** and **4** existed as a pair of slowly interconverting diastereomers at room temperature; their absolute configuration was established by CD methods. Compounds **1**–**4** showed no cytotoxicity against K562, A549, and HT–29 human cancer cells.

1. Introduction

During the past 10 years, great efforts of our group have been devoted to the phytochemical investigations on about 10 medicinal plants of the genus *Schisandra* in Schisandraceae family. Nearly 70 structurally attractive nortriterpenoids have been isolated so far, which can be mainly divided into two types, namely C_{29}[1–5] and C_{28}.[6] In the five classes of C_{29} type, compounds having schisanartane,[1a] schiartane,[1b] and 18(13→14)-*abeo*-schiartane[1c] skeletons account for >90%, while those possessing pre-schisanartane[1d] and wuweiziartane[1e] frameworks are rare. Only two members each have been firstly discovered from *Schisandra chinensis*.[1d,1e,3] In our continuing broad screening for novel bioactive triterpenoids among *Schisandra* species, *Schisandra propinqua* var. *propinqua*, a traditional Chinese medicinal plant indigenous in Yunnan province, was extensively studied. Except for the discovery of the characteristic dibenzocyclooctadiene lignans[4] and the nortriterpenoids with the main three C_{29} carbon skeletons,[5] two new compounds with pre-schisanartane carbon backbone (**1** and **2**) and a pair of new wuweiziartane-type nortriterpenoids (**3** and **4**) were isolated from the same plant. *S. propinqua* var. *propinqua* is the second plant reported heretofore, which can produce these two rare kinds of nortriterpenoids. In this paper, we report the isolation, the structure determination and cytotoxicity bioassay against K562, A549, and HT–29 human cancer cells of the new compounds.

2. Results and discussion

2.1. Structural elucidation of pre-schisanartanins C and D (1–2)

Pre-schisanartanin C (**1**) was isolated as an optically active, colorless powder. On the basis of HRESIMS data (found 531.2594 $[M-H]^-$), the molecular formula of **1** was defined as $C_{29}H_{40}O_9$, which indicated it contained 10 double-bond equivalents. This supposition was supported by the signals visible in the ^{13}C NMR (Table 1). In total 29 carbon resonances were observed in the ^{13}C NMR, DEPT, and HSQC spectra, which could be ascribed to five methyl, six methylene, 10 methine (four oxygenated ones), and eight quaternary carbons (three oxygenated ones). Sp^2 carbons including two lactones (C-3, δ_C 174.8; C-26, δ_C 175.3), a ketone (C-14, δ_C 215.3), and a double bond (C-24, δ_C 148.5; C-25, δ_C 130.4) accounted for four of total 10 degrees of unsaturation, which indicated that **1** contained six rings. The information mentioned above implied **1** maybe a highly oxygenated rearranged polycyclic nortriterpenoid derivative. Carbon signals at δ_C 22.3 (s, C-13), 31.8 (d, C-16), and 33.1 (d, C-17) indicated an evident three-membered carbon ring in **1**, which further suggested **1** could possess pre-schisanartane carbon skeleton as that of pre-schisanartanin.[4]

* Corresponding authors. Tel.: +86 871 5223251; fax: +86 871 5216343.
E-mail addresses: pujianxin@mail.kib.ac.cn (J.-X. Pu), hdsun@mail.kib.ac.cn (H.-D. Sun).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.02.002

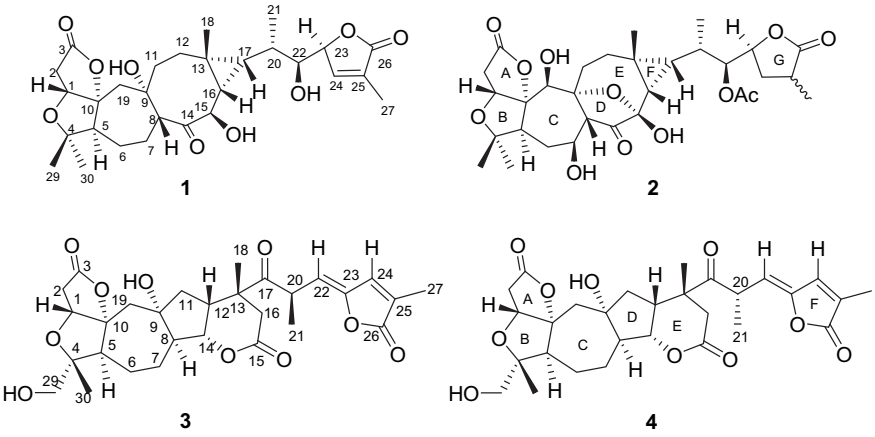

Table 1
^{13}C NMR Assignments of Compounds **1**–**4**[a]

No.	1	2	3	4	No.	1	2	3	4
1	81.8 (d)	79.5 (d)	81.6 (d)	81.7 (d)	16	31.8 (d)	31.5 (d)	34.8 (t)	34.5 (t)
2	36.0 (t)	35.4 (t)	35.6 (t)	35.5 (t)	17	33.1 (d)	34.5 (d)	211.1 (s)	211.2 (s)
3	174.8 (s)	175.5 (s)	174.6 (s)	174.6 (s)	18	28.1 (q)	28.5 (q)	22.4 (q)	22.1 (q)
4	84.3 (s)	84.4 (s)	88.0 (s)	87.8 (s)	19	47.8 (t)	70.5 (d)	41.0 (t)	41.1 (t)
5	60.3 (d)	58.1 (d)	53.7 (d)	54.9 (d)	20	34.6 (d)	31.0 (d)	39.8 (d)	39.0 (d)
6	25.5 (t)	36.0 (t)	22.1 (t)	22.1 (t)	21	17.2 (q)	17.9 (q)	18.7 (q)	19.8 (q)
7	27.1 (t)	69.0 (d)	24.3 (t)	24.3 (t)	22	75.0 (d)	80.0 (d)	113.0 (d)	114.1 (d)
8	56.1 (d)	64.0 (d)	56.7 (d)	57.9 (d)	23	83.1 (d)	76.8 (d)	149.0 (s)	148.4 (s)
9	75.1 (s)	81.3 (s)	80.2 (s)	79.4 (s)	24	148.5 (d)	33.3 (t)	139.0 (d)	139.2 (d)
10	98.7 (s)	97.9 (s)	99.7 (s)	99.4 (s)	25	130.4 (s)	34.4 (d)	130.9 (s)	131.0 (s)
11	43.2 (t)	38.1 (t)	44.5 (t)	44.5 (t)	26	175.3 (s)	180.4 (s)	170.7 (s)	171.0 (s)
12	26.1 (t)	25.6 (t)	38.5 (d)	38.2 (d)	27	10.7 (q)	16.6 (q)	10.5 (q)	10.6 (q)
13	22.3 (s)	24.8 (s)	50.5 (s)	50.1 (s)	29	22.0 (q)	22.0 (q)	68.5 (t)	68.3 (q)
14	215.3 (s)	213.6 (s)	83.9 (d)	83.1 (d)	30	28.7 (q)	28.5 (q)	17.8 (q)	17.8 (q)
15	75.3 (d)	99.0 (s)	169.9 (s)	169.7 (s)					

[a] Data were determined at 125 MHz in C_5D_5N with δ in parts per million.

The planar structure of **1** was established by comparing spectroscopic data with that of pre-schisanartanin, as well as by analysis of 2D NMR spectra. Close inspection of the spectroscopic data revealed similar 5/5/7 consecutive A/B/C rings in **1** on the basis of most similar ^{13}C NMR chemical shifts (Table 1), COSY, and HMBC correlations, except that one methine (δ_C 70.7, d, C-19) in pre-schisanartanin replaced by a methylene (δ_C 47.8, t, C-19) in **1**. The key COSY correlations H_3-21/H-20/H-22/H-23/H-24 (Fig. 1) and close carbon signals (Table 1) displayed identical ring G on the similar side chain without ethyl group connected at 22-OH in **1**. Considering there were six rings in **1**, only one more ring existed except the three-membered ring. An oxygenated methine carbon signal (δ_C 75.3, d, C-15) appeared in **1** rather than an oxygenated tertiary carbon (δ_C 99.1, s, C-15) in pre-schisanartanin suggested that the oxygen ring between C-9 and C-15 in pre-schisanartanin was open when in **1**. This suggestion was further confirmed by two group cross peaks observed in COSY spectrum, H_2-11/H_2-12 and H-15/H-16/H-17, coupled with those HMBC correlations starting with the carbon residues of the three-membered ring, from H-16 to C-13, C-15, and C-17, from H_3-18 to C-12, C-13, C-15, C-16, and C-17, from H-15 to C-9 and C-14, and from H_2-11 to C-9 (Fig. 1). Thus the 8/3 consecutive rings were established as that of pre-schisanartanin.

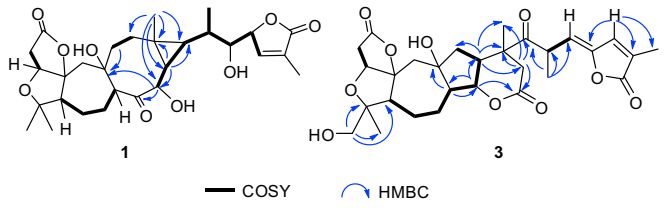

Figure 1. ^{1}H–^{1}H COSY and key HMBC correlations of **1** and **3**.

The relative configuration of **1** was assigned by analysis of proton coupling constants and ROESY correlations (Fig. 2). Two suites of ROESY correlations between H-16/H-8 and H-17/H_3-18 established the identical relative configuration of the chiral centers on three-membered ring with that of pre-schisanartanin, which was previously established by X-ray diffraction. While cross-peaks between H-15 with both H-20 and H_3-21 established the configuration of C-15 as *R**. The other spirocenters were elucidated the same as that of pre-schisanartanin with the similar coupling constants and ROESY correlations.

Pre-schisanartanin D (**2**) was obtained as colorless powder in MeOH. The molecular formula of **2** was defined as $C_{31}H_{42}O_{12}$ by the HR-FABMS data (found 605.2578 $[M-H]^-$). The ^{13}C NMR spectrum (Table 1) displayed 31 carbon signals. In corporation with ^{1}H NMR data (Table 2), a ketone (δ_C 213.6), two ester groups (δ_C 180.4, 175.5),

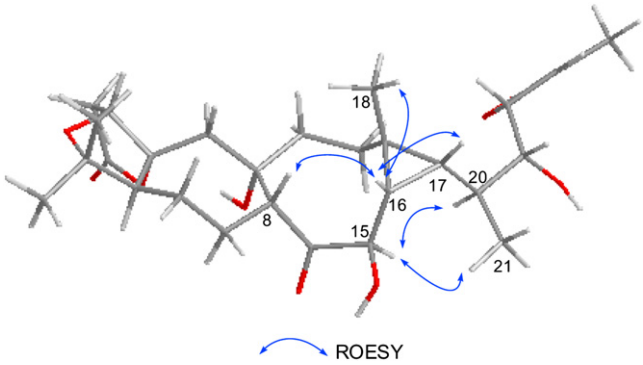

Figure 2. Selected ROESY correlations of **1**.

an acetyl (δ_C 170.8 and 21.6; δ_H 2.13, s) and a three-membered carbon ring (δ_C 24.8, s, C-13; 31.5, d, C-16; and 34.5, d, C-17; δ_H 1.52, d, H-16; 0.91, m, H-17) were appeared in **1**. Side by side comparison the ^{13}C NMR with those of pre-schisanartanin suggested the identical A/B and D/E rings. In ring G, the signals of the double bond was absent in ^{13}C NMR spectrum (Table 1) of **1**, where three signals at δ_C 33.3(t), 34.4(d), and 180.4(s) suggested the saturated lactone moiety in **1**. This assignment was supported by the long COSY spin system of H_3-21/H-20/H-22/H-23/H_2-24/H-25/H_3-27 and the key HMBC correlations of H_3-27 with C-24, C-25, and C-26. As to ring C, a methylene carbon signal was replaced by an oxygenated methine one (δ_C 69.0, d), and the ^1H–^1H COSY spin system of H-5/H_2-6/H-7/H-8 corroborated an hydroxyl attributed to C-7. In ROESY spectrum, H-7 showed no cross peak with H-8 indicating the β orientation of 7-OH. Due to the lack of convincible correlations in ROESY spectrum, the stereochemistry of C-25 was not determined. The other spirocenters were the same as that of pre-schisanartanin.

2.2. Structural elucidation of propintrilactones A and B (3–4)

Propindilactones A and B (**3** and **4**) were obtained as white solid. They showed the same pseudo-molecular ion peak $[M-H]^-$ at *m*/*z* 543.2237 in HRESIMS spectra, corresponding to the molecular formula $C_{29}H_{36}O_{10}$, which required 12 degrees of unsaturation. The analysis of ^{13}C (Table 1) and ^1H NMR (Table 2) spectra of them indicated the identical carbon signals and similar proton information, whereas their optical rotation properties were contrary. This information suggested **3** and **4** were a pair of epimers. They slowly interconverted in MeOH and showed stable as solid. Their ^{13}C NMR (Table 1) spectra displayed six sp^2 carbon signals including three ester groups, a ketone carbon, and two double bonds, which occupied six of in total 12 double-bond equivalents and suggested six rings in them. Closely investigation on their spectroscopic data with those of wuweiziartane-type members [5] revealed they were 29-hydroxymethyl analogies of schintrilactones A and B. This suggestion can be further corroborated by the key HMBC correlations of H_2-29 with C-4, C-5, and C-30, as well as ^1H–^1H COSY signals and other HMBC information depicted in Figure 1.

The absolute configurations of this epimers were elucidated by CD experiments and ROESY information. The measured CD behavior of **3** and **4** were, respectively, similar with that of schintrilactones A and B (Fig. S26),[5] which assigned the absolute configurations of C-20 in **3** and **4** as *R* and *S*, respectively. The cross peak between H_3-30 and H_β-1 in the ROESY spectrum of **3** (Fig. 3) defined C-4 as *S* configuration. The other spirocenters showed the same absolute configuration as that of schintrilactones (Fig. 3).

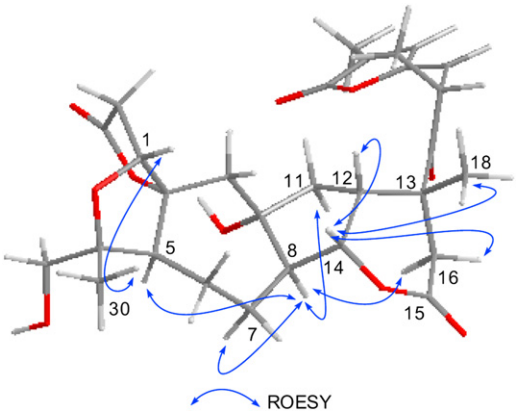

Figure 3. Key ROESY correlations of **3**.

Table 2
^1H NMR Assignments of Compounds **1**–**4**[a]

No.	1	2	3	4
1β	4.26 (d, 5.5)	5.07 (d, 5.5)	4.31 (d, 5.5)	4.28 (d, 5.5)
2α	2.73 (d, 18.0)	2.72 (d, 18.0)	2.46 (d, 18.0)	2.44 (d, 18.0)
2β	2.96 (dd, 18.0, 5.5)	3.36 (dd, 18.0, 5.5)	2.88 (dd, 18.0, 5.5)	2.79–2.83[b]
5α	2.40–2.45[b]	2.38 (dd, 13.0, 3.5)	2.70 (dd, 8.0, 4.0)	2.65 (dd, 8.0, 4.5)
6α	1.77 (m)	2.92 (m)	1.69 (m)	1.64 (m)
6β	1.41 (m)	1.96 (dd, 11.5, 3.0)	1.58–1.61[b]	1.57 (m)
7α	2.33–2.42[b]	4.87 (t like, 10.0)	1.83–1.87[b]	1.83 (m)
7β	2.06–2.15[b]		1.83–1.87[b]	1.89 (m)
8	3.64 (dd, 11.0, 3.0, H_β)	3.12 (d, 10.0, H_β)	2.23 (m, H_α)	2.13 (m, H_α)
11α	1.93 (m)	1.57 (br d, 15.0)	1.87–1.92[b]	1.51 (t like, 12.5)
11β	2.08–2.15[b]	2.77–2.80[b]	1.54–1.58[b]	1.34 (dd, 12.5, 7.5)
12α	1.87–1.94[b]	1.40 (m)	3.04 (m)	2.91 (m)
12β	2.24–2.30[b]	2.47 (t like, 13.0)		
14β			5.01 (dd, 8.5, 6.5)	5.07 (dd, 8.0, 7.5)
15α	4.76 (d, 7.5)			
16α			2.81–2.84[b]	2.83–2.86[b]
16β	1.24–1.29[b]	1.52 (d, 9.0)	2.31 (dd, 17.0, 2.0)	2.31 (d, 17.5)
17	1.04–1.10[b]	0.91 (m)		
18	1.27 (s)	0.97 (s)	1.26 (s)	1.46 (s)
19α	2.11–2.17[b]	4.26 (d, 6.5)	2.08 (ABd, 15.5)	1.76 (ABd, 15.5)
19β	2.38–2.44[b]		2.38 (ABd, 15.5)	2.22 (ABd, 15.5)
20	2.22–2.30[b]	3.58 (m)	4.26 (m)	4.33 (m)
21	1.59 (d, 6.5)	1.70 (d, 7.0)	1.19 (d, 6.5)	1.26 (d, 6.5)
22	3.92 (br s)	5.01 (dd, 8.0, 2.0)	5.11 (d, 11.5)	5.34 (d, 11.5)
23	5.18 (br s)	4.98 (m)		
24	7.19 (br s)	1.92 (m, H_a), 2.18 (m, H_b)	7.34 (br s)	7.39 (br s)
25		2.79–2.84[b]		
27	1.81(br s)	1.18 (d, 7.0)	1.95 (br s)	1.96 (br s)
29	1.08 (s)	1.34 (s)	3.49 (dd, 11.5, 8.0, H_a), 3.38 (dd, 11.5, 8.0, H_b)	3.47 (d, 11.5, H_a), 3.37 (d, 11.5, H_b)
30	1.23 (s)	1.17 (s)	1.09 (s)	1.10 (s)

[a] Data were determined at 500 MHz in C_5D_5N with δ in parts per millions and *J* in hertz.
[b] Overlapped.

2.3. Bioactivity evaluation of compounds 1–4

Compounds **1**–**4** were tested for cytotoxicity against A549, HT–29, and K562 cells according to the method described previously.[6] All were inactive with IC_{50} values greater than 100 μM.

3. Experimental section

3.1. General

All solvents including petroleum ether (60–90 °C) were distilled prior to use. Column chromatography (CC) was performed on silica gel (200–300 mesh; Qingdao Marine Chemical Inc., Qingdao, People's Republic of China), Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany), MCI gel (75–150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan), and Sephadex LH-20 (Pharmacia). Semi-preparative HPLC was performed on an Agilent 1100 liquid chromatograph with a Zorbax SB-C_{18}, 9.4 mm×25 cm column. Optical rotations were carried out on a JASCO DIP-370 digital polarimeter. IR spectra were obtained on a Bio-Rad FtS-135 spectrophotometer with KBr pellets, and UV data were obtained using a UV-210A spectrometer. CD spectra were measured on a JASCO J-810 spectropolarimeter. High-resolution electrospray-ionization (HRESIMS), and fast atom bombardment (FABMS) mass spectra were acquired on an API QSTAR time-of-flight mass spectrometer and a VG Autospec-3000 mass spectrometer, respectively. 1D and 2D NMR spectra were taken on a Bruker DRX-500 NMR spectrometer with TMS as internal standard.

3.2. Plant material

Stems of *S. propinqua* var. *propinqua* were collected in Tengchong County, Yunnan Province, PR China, in July 2006, and identified by Prof. Xi-Wen Li, Kunming Institute of Botany, Chinese Academy of Sciences. A voucher specimen (No.20050823) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, PR China.

3.3. Extraction and isolation

The air-dried stems of *S. propinqua* var. *propinqua* (8 kg) were extracted with 70% aqueous acetone (4×15 L, three days each) at room temperature. The solvent was removed in vacuo to afford a crude extract (560 g), which was dissolved in H_2O, and then extracted successively with petroleum ether and EtOAc. The EtOAc-soluble part (250 g) was separated by CC (on SiO_2 with $CHCl_3$/acetone 1:0, 9:1, 8:2, 2:1, 1:1, 0:1) to afford six main fractions (A–F). Fraction C ($CHCl_3$/acetone 9:1 to 8:2, 29 g) was subjected to repeated CC, first on Sephadex LH-20 eluted with MeOH, then on silica gel eluted by PE/*i*-PrOH in a gradient system, followed by semi-prep. HPLC (40% MeOH in H_2O) to afford **3** (1 mg) and **4** (3 mg). Fraction D ($CHCl_3$/acetone 8:2 to 2:1, 45 g) was separated by CC on silica gel with $CHCl_3$/acetone 4:1 to obtain fractions of D1, D2, and D3. Fraction D2 was then subjected to RP-18 in C using a 30–60% aqueous MeOH gradient system, then separated further on Sephadex LH-20 eluted with MeOH to afford five fractions (D2.1–D2.5). Fraction D2.2 (40% aqueous MeOH) was chromatographed on silica gel with PE/*i*-PrOH 5:1 followed by semi-prep. HPLC (45% MeOH in H_2O) to yield **1** (4 mg) and **2** (15 mg).

*3.3.1. Pre-schisanartanin C (**1**).* White powder; $[\alpha]_D^{25.7}$ −37.80 (*c* 0.23, MeOH); IR(KBr) ν_{max} 3596, 3475, 2978, 2926, 2872, 1749, 1703, 1340, 1216, 1053 cm^{-1}; ^{13}C NMR see Table 1; ^1H NMR, see Table 2; negative FABMS *m*/*z* 531 $[M-H]^-$; HRESIMS (neg.) $[M-H]^-$ *m*/*z*: 531.2594 (calcd for $C_{29}H_{39}O_9$, 531.2564).

*3.3.2. Pre-schisanartanin D (**2**).* White powder; $[\alpha]_D^{24.6}$ +26.7 (*c* 0.35, MeOH); IR(KBr) ν_{max} 3455, 2956, 2925, 2855, 1765, 1640, 1462, 1376, 1240, 1069, 907 cm^{-1}; ^{13}C NMR see Table 1; ^1H NMR, see Table 2; OAc, δ_H 2.13 (s), δ_C 170.8, 21.6; negative FABMS *m*/*z* 605 $[M-H]^-$; HR-FABMS (neg.) $[M-H]^-$ *m*/*z*: 605.2578 (calcd for $C_{31}H_{41}O_{12}$, 605.2598).

*3.3.3. Propintrilactone A (**3**).* White solid; $[\alpha]_D^{20.3}$ −25.60 (*c* 0.04, MeOH); CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 309.4 (−155.56), 269.6 (+108.3), 219.4 (−3.63), 210.6 (−4.03), 200.2 (−19.9); UV (MeOH) λ_{max} nm (log ε): 272.2 (4.20), 201.2 (4.32); IR (KBr) ν_{max} 3439, 2930, 1770, 1771, 1622, 1456, 1384, 1203, 1067 cm^{-1}. ^{13}C NMR see Table 1; ^1H NMR, see Table 2; negative FABMS *m*/*z* 543 $[M-H]^-$; HRESIMS (neg.) $[M-H]^-$ *m*/*z*: 543.2237 (calcd for $C_{29}H_{35}O_{10}$, 543.2230).

*3.3.4. Propintrilactone B (**4**).* White solid; $[\alpha]_D^{20.4}$ +142.20 (*c* 0.04, MeOH); CD (MeOH) λ_{max} nm ($\Delta\varepsilon$) 304.0 (+90.17), 271.0 (−47.07), 248.6(−11.09), 220.8 (−22.63), 197.6 (+13.26); UV (MeOH) λ_{max} nm (log ε): 275.0 (4.20), 202.2 (4.45); IR (KBr) ν_{max} 3439, 2930, 1770, 1771, 1622, 1456, 1384, 1203, 1067 cm^{-1}; ^{13}C NMR see Table 1; ^1H NMR, see Table 2; negative FABMS *m*/*z* 543 $[M-H]^-$; HRESIMS (neg.) $[M-H]^-$ *m*/*z*: 543.2237 (calcd for $C_{29}H_{35}O_{10}$, 543.2230).

3.4. Cytotoxicity assay

Cytotoxicity of compounds **1**–**4** against suspended tumor cells was determined by the trypan blue exclusion method, and against adherent cells by sulforhodamine B (SRB) assay. Cells were plated in a 96-well plate 24 h before treatment and continuously exposed to different concentrations (100, 10, 1, and 0.1 μM) of compounds for 72 h. After compound treatment, cells were counted (suspended cells) or fixed and stained with SRB (adherent cells) as described in the literature.[6] Amrubicin hydrochloride was used as a positive control with IC_{50} values of 0.82 (A549), 4.36 (HT–29), and 1.26 μM (K562), respectively.

Acknowledgements

This work was supported financially by the NSFC (No. 30830115 and 2008GA031 to H.-D. Sun), the Major State Basic Research Development Program of China (Nos. 2009CB522300, and 2009CB940900), the project of Chinese Academy of Sciences (XiBuZhiGuang to W.-L. Xiao), the Natural Science Foundation of Yunnan Province (2007BC004) and from the Yong Academic and Technical Leader Raising Foundation of Yunnan Province (2006PY01-47).

Supplementary data

The HRESIMS, ^1H, ^{13}C and DEPT NMR, HSQC, ^1H–^1H COSY, HMBC and ROESY spectra of compounds **1**–**3**, ^1H, ^{13}C NMR, HSQC, and ROESY spectra of compound **4**, UV and CD spectra of **3** and **4** are available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.02.002.

References and notes

1. (a) Li, R. T.; Zhao, Q. S.; Li, S. H.; Han, Q. B.; Sun, H. D.; Lu, Y.; Zhang, L. L.; Zheng, Q. T. *Org. Lett.* **2003**, *5*, 1023–1026; (b) Li, R. T.; Han, Q. B.; Zheng, Y. T.; Wang, R. R.; Yang, L. M.; Lu, Y.; Sang, S. Q.; Zheng, Q. T.; Zhao, Q. S.; Sun, H. D. *Chem. Commun.* **2005**, 2936–2938; (c) Huang, S. X.; Yang, L. B.; Xiao, W. L.; Lei, C.; Liu, J. P.; Lu, Y.; Weng, Z. Y.; Li, L. M.; Li, R. T.; Yu, J. L.; Zheng, Q. T.; Sun, H. D. *Chem.—Eur. J.* **2007**, *13*, 4816–4822; (d) Huang, S. X.; Li, R. T.; Liu, J. P.; Lu, Y.; Chang, Y.; Lei, C.; Xiao, W. L.; Yang, L. B.; Zheng, Q. T.; Sun, H. D. *Org. Lett.*

2007, *9*, 2079–2082; (e) Huang, S. X.; Yang, J.; Huang, H.; Li, L. M.; Xiao, W. L.; Li, R. T.; Sun, H. D. *Org. Lett.* **2007**, *9*, 4175–4178.
2. Li, R. T.; Li, S. H.; Zhao, Q. S.; Lin, Z. W.; Sun, H. D.; Lu, Y.; Wang, C.; Zheng, Q. T. *Tetrahedron Lett.* **2003**, *44*, 3531–3534.
3. Huang, S. X.; Han, Q. B.; Lei, C.; Pu, J. X.; Xiao, W. L.; Yu, J. L.; Yang, L. M.; Xu, H. X.; Zheng, Y. T.; Sun, H. D. *Tetrahedron* **2008**, *64*, 4260–4267.
4. Lei, C.; Huang, S. X.; Chen, J. J.; Pu, J. X.; Yang, L. B.; Zhao, Y.; Liu, J. P.; Gao, X. M.; Xiao, W. L.; Sun, H. D. *Chem. Pharm. Bull.* **2007**, *55*, 1281–1283.
5. (a) Lei, C.; Huang, S. X.; Chen, J. J.; Pu, J. X.; Li, L. M.; Xiao, W. L.; Liu, J. P.; Yang, L. B.; Sun, H. D. *Helv. Chim. Acta* **2007**, *90*, 1399–1405; (b) Lei, C.; Huang, S. X.; Chen, J. J.; Yang, L. B.; Xiao, W. L.; Chang, Y.; Lv, Y.; Huang, H.; Pu, J. X.; Sun, H. D. *J. Nat. Prod.* **2008**, *71*, 228–1232; (c) Lei, C.; Pu, J. X.; Huang, S. X.; Chen, J. J.; Liu, J. P.; Yang, L. B.; Ma, Y. B.; Xiao, W. L.; Li, X. N.; Sun, H. D. *Tetrahedron* **2009**, *65*, 164–170.
6. Monks, A.; Scudiero, D.; Skehan, P.; Shoemaker, R.; Paull, K.; Vistica, D.; Hose, C.; Langley, J.; Cronise, P.; Vaigro-Wolff, A. *J. Natl. Cancer Inst.* **1991**, *83*, 757–766.