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New vobasinyl-ibogan type bisindole alkaloids from *Tabernaemontana corymbosa*

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ABSTRACT

Ten vobasinyl-ibogan type bisindole alkaloids, including three new ones, tabercorines A–C (**1**–**3**), and a new natural product, 17-acetyl-tabernaecorymbosine A (**4**), were isolated from the twigs and leaves of *Tabernaemontana corymbosa*. Their structures were elucidated on the basis of spectroscopic data, and the NMR data of 17-acetyl-tabernaecorymbosine A (**4**) was assigned and reported for the first time. The absolute configurations of **1**–**4** were determined by CD exciton chirality method. All new compounds were evaluated for *in vitro* cytotoxicity against various human cancer cell lines. Compounds **1** and **4** showed significant inhibitory effects with IC_{50} values comparable to those of cisplatin.

1. Introduction

The monoterpenoid indole alkaloids are characteristic metabolites mainly elaborated by plants of the Apocynaceae family. They have long been of attractive objective for organic chemists due to their diverse structures and potent biological activities, such as catharanthine, vincristine and its derivatives [1]. The genus *Tabernaemontana* (Apocynaceae) comprises 99 species, and is distributed mainly over the tropical and subtropical areas of Asia, Africa, and America. Some of these species are used in folk medicine for the treatment of hypertension, snake poisoning, rheumatalgia, and fractures in southern of China [2]. In recent years, chemical investigation of this genus conducted in our lab and other research groups have led to the isolation of a series of new monoterpenoid indole and bisindole alkaloids with significant antitumor activities [3–8]. In a continuation of our search for structurally unique and bioactive indole alkaloids [9–12], ten vobasinyl-ibogan type bisindole alkaloids, including three new ones, tabercorines A–C (**1**–**3**), and a new natural product, 17-acetyl-tabernaecorymbosine A (**4**) were isolated from the twigs and leaves of *Tabernaemontana corymbosa*. The known alkaloids were identified as tabernaricatine A [5], tabernaricatine B [5], tabernaricatine D [5], 16-decarbomethoxyvoacamine [13], conodurine [14], and tabernaecorymbosine B [15]. Herein, isolation, structure elucidation, and cytotoxic properties of these alkaloids are reported.

2. Experimental

2.1. General experiment procedure

Optical rotations were measured on JASCO P-1020 digital polarimeter. UV spectra were recorded on a UV 210A spectrophotometer. IR spectra were taken on a Bio-Rad FTS-135 spectrophotometer with KBr pellets. ECD spectra were recorded with an Applied Photophysics Chirascan spectrometer. ESIMS data were obtained on a Finnigan MAT 90 spectrometer, while HREIMS data were measured on a VG Auto Spec-3000 spectrometer. NMR spectra were recorded on Bruker AM-400, DRX-500 and Avance III-600 NMR spectrometers using TMS as an internal standard. Silica

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gel (300–400 mesh, Qingdao Marine Chemical Inc., China), silica gel H (10–40 μm, Qingdao Marine Chemical Inc., China), Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany), and Sephadex LH-20 (40–70 μm, Amersham Biosciences, Sweden) were used for column chromatography (CC).

2.2. Plant material

The twigs and leaves of *T. corymbosa* were collected in Dec 2012 from Xishuangbanna, Yunnan Province, PR China, and were identified by Mr. Shun-Cheng Zhang, Xishuangbanna Tropical Plant Garden. A voucher specimen (no. 20121218) has been deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Science (CAS).

2.3. Extraction and isolation

The dried twigs and leaves of *T. corymbosa* (16 kg) were extracted with CH_3OH, and the pH of the crude extract was adjusted with saturated tartaric acid to 2–3. The acidic mixture was then defatted with EtOAc. The aqueous phase was basified to pH 9–10 with saturated Na_2CO_3 and then extracted with $CHCl_3$ to obtain crude alkaloids. The crude alkaloids (80 g) were separated on a silica gel column (100–200 mesh; PE/acetone, 1:0 → 0:1), yielding four major fractions (I–IV). Fraction II (15.6 g) was subjected to a series of silica gel CC eluting with PE/acetone (15:1–7:1, *v*/*v*) and then purified by Sephadex LH-20 (acetone) to give compound **4** (12 mg), 16-decarbomethoxyvoacamine (8 mg), and tabernaricatine A (20 mg). Fraction III (14 g) was further purified by a reversed phase chromatography on a C_{18} column ($MeOH/H_2O$, 20:80 → 100:0, *v*/*v*) to give four subfractions (III_A–III_D). Subfraction III_B (1.8 g) was chromatographed over a silica gel CC (PE/acetone/Et_2NH, 10:1:0.1, *v*/*v*) to afford compound **1** (25 mg), and **3** (4 mg). Subfraction III_D (2.6 g) was further separated using a Sephadex LH-20 column (MeOH), followed by semipreparative HPLC using a Waters XBridge C_{18} (10 × 250 mm, 5 μm) column with $MeOH/H_2O$ (75:25, 0.1‰ *v*/*v* diethylamine) to give tabernaricatine B (11 mg) and conodurine (16 mg). Fraction IV (26.8 g) was subjected to a silica gel CC eluting with PE/acetone (8:1–0:1, *v*/*v*) and further separated by a Sephadex LH-20 column (MeOH) to give five subfractions (IV_A–IV_E). Subfraction IV_B (600 mg) was separated by semi-preparative HPLC using a Waters XBridge C_{18} (10 × 250 mm, 5 μm) column with $MeOH/H_2O$ (45:55, 0.1‰ *v*/*v* diethylamine) to afford compound **2** (28 mg), tabernaricatine D (25 mg), and tabernaecorymbosine B (70 mg).

2.4. Tabercorine A (*1*)

yellowish amorphous powder; $[\alpha]_D^{16}-79.2$ (*c* 0.18, CH_3OH); IR (KBr) ν_{max} 3446, 2926, 1717, 1635, 1457 and 1040 cm^{-1}; UV (CH_3OH) λ_{max} 222 (ε 41859), 285 nm (10313); CD (0.0010 M, CH_3OH) λ_{max} ($\Delta\varepsilon$) 223 (−11.99), 238 (+7.18) nm; ^1H and ^{13}C NMR data (Table 1); ESIMS *m*/*z* 789 $[M + H]^+$; HREIMS *m*/*z* 788.4162 ($[M]^+$; calcd for $C_{47}H_{56}N_4O_7$, 788.4149).

Table 1
^1H and ^{13}C NMR Data of **1** and **2** in acetone-d_6 (δ in ppm and *J* in Hz).

	1[a]		**2**[b]	
No.	δ_H	δ_C	δ_H	δ_C
2		137.9		138.6
3	5.34 (br d, 12.6)	36.0	5.23 (dd, 13.0, 4.0)	34.6
5	4.15 (t, 9.0)	61.7	4.02 (dd, 11.5, 7.5)	62.0
6a	3.75 (m)	26.4	4.18 (dd, 15.0, 11.5)	25.6
6b	3.60 (m)		3.24 (dd, 15.0, 8.0)	
7		109.5		109.3
8		130.8		131.0
9	7.77 (d, 7.2)	118.9	7.51 (dd, 6.5, 2.0)	118.2
10	7.10 (t, 7.2)	119.6	6.92 (m)	118.9
11	7.07 (t, 7.2)	122.6	6.91 (m)	121.4
12	7.16 (d, 7.2)	110.9	7.03 (br d, 6.5)	110.6
13		137.9		137.5
14a	2.61 (t, 13.8)	36.5	3.56 (m)[c]	36.2
14b	1.98 (m)		3.56 (m)[c]	
15	3.83 (t, 9.6)	40.4	3.61 (dd, 11.0, 5.5)	40.1
16		47.6		47.8
17a	3.63 (d, 10.6)	76.9	3.56 (d, 10.5)	77.4
17b	3.59 (d, 10.6)		3.48 (d, 10.5)	
18	1.64 (d, 6.6)	11.7	1.54 (dd, 6.5, 2.0)	11.8
19	5.12 (q, 6.6)	113.8	5.05 (q, 6.5)	112.3
20		142.6		144.1
21a	4.26 (br d, 16.3)	50.4	4.44 (d, 11.0)	50.7
21b	3.23 (br d, 16.3)		3.14 (d, 11.0)	
22a	4.69 (d, 10.2)	88.8	4.64 (d, 10.0)	88.8
22b	4.59 (d, 10.2)		4.53 (d, 10.0)	
CO_2Me	2.49 (s)	50.7	2.33 (s)	50.2
		174.0		173.9
2′		136.9		190.2
3′a	2.96 (t, 6.0)	55.4	2.50 (m)	49.9
3′b			2.28 (br d, 9.0)	
5′a	3.12 (m)[c]	51.9	3.40 (td, 13.5, 2.0)	49.7
5′b	3.12 (m)[c]		2.75 (m)[c]	
6′a	2.99 (dd, 16.8, 7.2)	22.6	1.75 (dt, 15.0, 2.0)	34.1
6′b	2.81 (dt, 16.8, 6.0)		1.53 (m)[c]	
7′		109.7		87.2
8′		125.6		136.4
9′	7.24 (d, 9.0)	117.6	7.04 (d, 8.5)	120.5
10′	6.87 (d, 9.0)	106.3	6.81 (d, 8.5)	108.7
11′		153.0		157.8
12′		116.1		127.3
13′		136.1		152.3
14′	1.23 (m)	31.5	1.58 (m)	28.0
15′a	1.31 (m)	27.6	1.67 (m)	32.8
15′b	1.10 (m)[c]		0.95 (m)	
16′		55.0		59.2
17′a	1.79 (br d, 13.8)	36.8	2.76 (m)	37.1
17′b	0.66 (br d, 13.8)		1.83 (dt, 15.0, 3.0)	
18′	0.83 (t, 7.2)	11.9	0.83 (t, 7.0)	11.9
19′a	1.48 (m)	27.4	1.44 (m)	27.7
19′b	1.32 (m)		1.33 (m)	
20′	1.09 (m)[c]	38.9	1.30 (m)	38.6
21′	3.38 (s)	59.0	3.91 (br s)	56.6
22′a	2.64 (dd, 16.2, 9.0)	46.6		
22′b	2.43 (dd, 16.2, 3.0)			
23′		208.4		
24′	2.02 (s)	30.7		
7′-OH			4.46 (br s)	
11′-OMe	3.99 (s)	57.5	3.92 (s)	56.6
CO_2Me'	3.73 (s)	52.8	3.56 (s)	52.8
		175.0		173.8

[a] ^1H NMR spectra were recorded at 600 MHz and ^{13}C NMR spectra at 150 MHz.
[b] ^1H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra at 125 MHz.
[c] Overlapped.

2.5. Tabercorine B (**2**)

yellowish amorphous powder; $[\alpha]_D^{16}$ −53.1 (*c* 0.195, CH_3OH); IR (KBr) ν_{max} 3431, 2923, 2854, 1727, 1621, 1462 and 1243 cm^{-1}; UV (CH_3OH) λ_{max} 202 (ε 36317), 232 (35984), 286 nm (11047); CD (0.00010 M, CH_3OH) λ_{max} ($\Delta\varepsilon$) 204 (−77.42), 242 (+19.58) nm; ^1H and ^{13}C NMR data (Table 1); ESIMS *m/z* 749 $[M + H]^+$; HREIMS *m/z* 748.3826 ($[M]^+$; calcd for $C_{44}H_{52}N_4O_7$, 748.3836).

2.6. Tabercorine C (**3**)

yellowish amorphous powder; $[\alpha]_D^{16}$ −41.0 (*c* 0.26, CH_3OH); IR (KBr) ν_{max} 3440, 2925, 2855, 1727, 1630, 1435, and 1243 cm^{-1}; UV (CH_3OH) λ_{max} 222 (ε 52373), 285 nm (13637); CD (0.00010 M, CH_3OH) λ_{max} ($\Delta\varepsilon$) 223 (−124.8), 238 (+117.3) nm; ^1H and ^{13}C NMR data (Table 2); ESIMS *m/z* 749 $[M + H]^+$; HREIMS *m/z* 748.3837 ($[M]^+$; calcd for $C_{44}H_{52}N_4O_7$,748.3836).

2.7. 17-Acetyl-tabernaecorymbosine A (**4**)

yellowish amorphous powder; $[\alpha]_D^{16}$ −78.8 (*c* 0.13, CH_3OH); IR (KBr) ν_{max} 3425, 2927, 2857, 1727, 1627, 1461, and 1242 cm^{-1}; UV (CH_3OH) λ_{max} 204 (ε 58247), 223 (68359), and 285 nm (17537); CD (0.000096 M, CH_3OH) λ_{max} ($\Delta\varepsilon$) 224 (−126.2), 239 (+99.4) nm; ^1H and ^{13}C NMR data (Table 2); ESIMS *m/z* 777 $[M + H]^+$; HRESIMS *m/z* 777.4220 ($[M + H]^+$; calcd for $C_{46}H_{57}N_4O_7$, 777.4227).

2.8. Cytotoxicity bioassays

Five human cancer cell lines, human myeloid leukemia HL-60, hepatocellular carcinoma SMMC-7721, lung cancer A-549, breast cancer MCF-7, and colon cancer SW480 cells, were used in the cytotoxic assay. All the cells were cultured in RPMI-1640 or DMEM medium (Hyclone, USA), supplemented with 10% fetal bovine serum (Hyclone) in 5% CO_2 at 37 °C. The cytotoxicity assay was performed according to the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) method in 96-well microplates [16]. Briefly, 100 μL of adherent cells was seeded into each well of 96-well cell culture plates and allowed to adhere for 12 h before drug addition, while suspended cells were seeded just before drug addition with an initial density of 1×10^5 cells/mL. Each tumor cell line was exposed to the test compound dissolved in DMSO at concentrations of 0.0625, 0.32, 1.6, 8, and 40 μM in triplicates for 48 h with cisplatin (Sigma, USA) as the positive controls. After compound treatment, cell viability was measured and a cell growth curve was plotted. IC_{50} values were calculated by Reed and Muench's method [17].

3. Results and discussion

3.1. Structure elucidation

Tabercorine A (**1**) was obtained as a yellowish amorphous powder, and possessed a molecular formula of $C_{47}H_{56}N_4O_7$ with 22 degrees of unsaturation, as established by HREIMS (*m/z* 788.4162 $[M]^+$, calcd 788.4149) and ^{13}C NMR spectroscopic data (Table 1). Its UV spectrum showed the characteristic absorptions of an indole chromophore at 222 and 285 nm [18]. The IR absorptions at 3446 and 1717 cm^{-1} implied the presence of amino or hydroxyl and ester carbonyl functions, respectively. The ^{13}C NMR and DEPT spectrum suggested that **1** possessed 47 carbon signals, which was classified as six methyls, 11 methylenes, 14 methines, and 16 quaternary carbons. Direct comparison of its NMR data (Table 1) with those of tabernaricatine D indicated that **1** was also an

Table 2
^1H and ^{13}C NMR Data of **3** and **4** in acetone-d_6 (δ in ppm and *J* in Hz).

	3[a]		**4**[a]	
No.	δ_H	δ_C	δ_H	δ_C
2		138.4		137.6
3	5.11 (br d, 12.0)	35.5	5.33 (dd, 13.0, 3.5)	36.0
5	3.56 (t, 8.4)	62.7	3.85 (t, 8.5)	61.7
6a	4.14 (dd, 13.8, 9.0)	31.5	3.56 (d, 15.0)	18.6
6b	3.31 (m)		3.50 (dd, 15.0, 8.0)	
7		109.2		109.6
8		130.1		130.4
9	7.74 (d, 7.2)	118.9	7.68 (dd, 7.5, 1.5)	118.8
10	7.08 (t, 7.2)	119.6	7.03 (td, 7.5, 1.5)	119.4
11	7.05 (t, 7.2)	122.6	7.01 (td, 7.5, 1.5)	122.2
12	7.13 (d, 7.2)	110.8	7.09 (dd, 7.5, 1.5)	110.6
13		137.5		138.7
14a	2.95 (m)	35.5	2.74 (td, 15.0, 12.0)	34.8
14b	2.01 (m)		1.89 (ddd, 15.0, 7.0, 3.5)	
15	2.64 (dd, 12.0, 5.4)	44.2	3.74 (m)[b]	35.7
16		50.0		51.8
17a	3.75 [b]	73.5	4.53 (d, 11.0)	70.6
17b	3.75[b]		4.12 (d, 11.0)	
18	1.27 (d, 5.6)	14.5	1.62 (dd, 7.0, 1.5)	12.1
19	3.31 (q, 5.6)[b]	56.8	5.37 (q, 7.0)	120.1
20		66.1		137.9
21a	3.96 (s)[b]	85.8	3.59 (m)	52.3
21b			2.92 (m)[b]	
NH	9.70 (br s)		9.65 (br s)	
CO_2Me	2.34 (s)	50.5	2.32 (s)	50.1
		172.0		172.0
NMe	2.78 (s)	41.3	2.60 (s)	42.4
17-OAc			1.92 (s)	20.7
				170.4
2′		136.8		136.5
3′a	2.69 (m)	52.3	2.65 (m)	52.6
3′b	2.46 (br d, 7.2)		2.38 (br d, 8.5)	
5′a	3.27(m)	53.8	3.24 (m)	53.7
5′b	3.02 (m)[b]		2.94 (m)[b]	
6′a	3.01 (m)[b]	22.6	2.93 (m)[b]	22.5
6′b	2.87 (m)		2.83 (m)	
7′		109.9		109.6
8′		125.6		125.5
9′	7.27 (d, 9.0)	117.8	7.21(d, 8.5)	117.6
10′	6.88 (d, 9.0)	106.2	6.85 (d, 8.5)	106.2
11′		153.0		152.9
12′		115.9		116.0
13′		135.9		136.1
14′	1.42 (m)	28.1	1.35 (m)	28.1
15′a	1.53 (m)	32.9	1.47 (m)	32.8
15′b	0.93 (m)		0.88 (m)	
16′		55.3		55.1
17′a	1.86 (br d, 12.6)	35.6	1.76 (dt, 14.0, 2.0)	35.5
17′b	0.66 (br d, 12.6)		0.59 (ddd, 14.0, 4.0, 2.5)	
18′	0.85 (t, 7.2)	11.9	0.81 (t, 7.0)	11.8
19′a	1.49 (m)	27.6	1.43 (m)	27.3
19′b	1.35 (m)		1.30 (m)	
20′	1.20 (m)	39.5	1.14 (m)	39.5
21′	3.40 (br s)	57.9	3.37 (s)	57.4
11′-OMe	3.96 (s)[b]	57.4	3.96 (s)	57.4
CO_2Me'	3.77 (s)[b]	52.7	3.72 (s)	52.8
		174.9		174.8

[a] ^1H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra at 125 MHz.
[b] Overlapped.

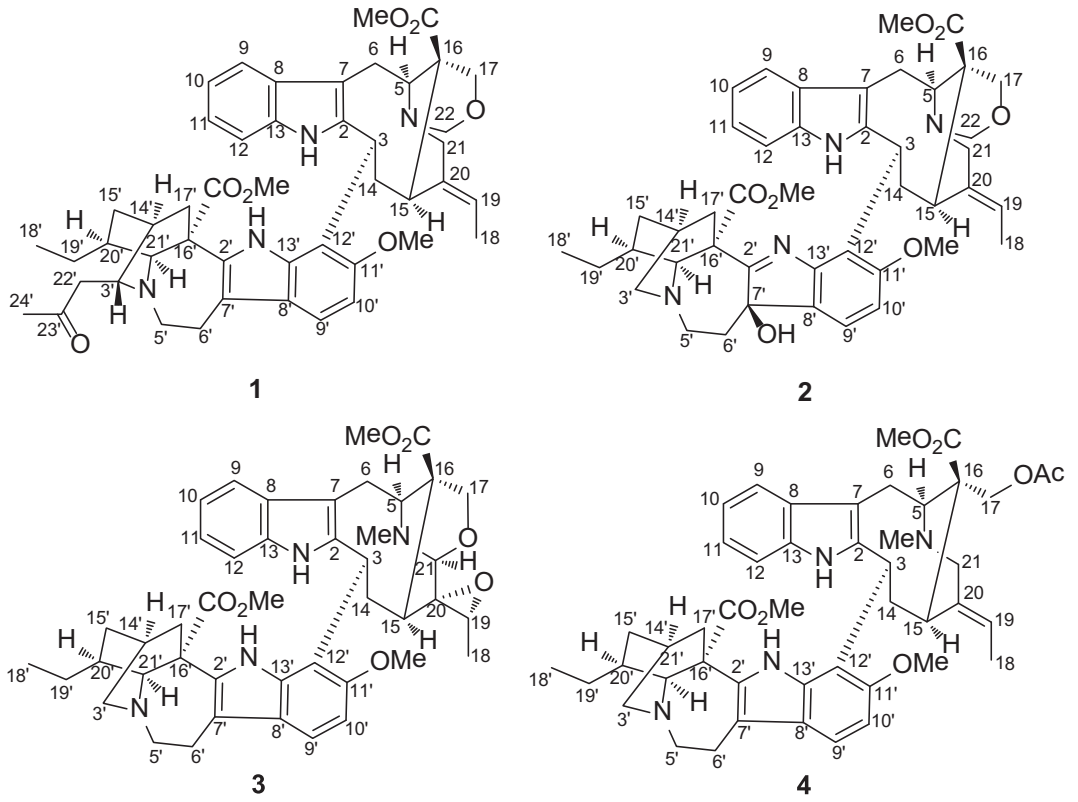


Fig. 1. Molecular structures of **1**–**4** isolated from *Tabernaemontana corymbosa*.

vobasinyl-ibogan type bisindole alkaloid [5], except for the presence of an additional 2-oxopropyl group at δ_C 208.4 (s), 46.6 (t), 30.7 (q) in the ^{13}C NMR spectrum. The molecular weight of **1** is larger than that of tabernaricatine D by 56 units, suggesting that **1** was a 2-oxopropyl derivative of tabernaricatine D, and the additional 2-oxopropyl group was located at C-3′, which was further confirmed by the HMBC correlations of H-21′ (δ_H 3.38, s) and H_2-22′ (δ_H 2.64, dd, J = 16.2, 9.0 Hz; δ_H 2.43, dd, J = 16.2, 3.0 Hz) to C-3′ (δ_C 55.4). Thus, the planar structure of tabercorine A was assigned as **1**, which was further verified by a combination analysis of the HSQC, ^1H–^1H COSY, and HMBC spectra (Fig. 2). The ROESY spectrum showed that tabercorine A (**1**) had the same relative configuration as tabernaricatine D. Especially, the β-orientation of H-3′ was established by the ROESY correlations of H-3′ (δ_H 2.96, t, J = 6.0 Hz) with H-17′β (δ_H 0.66, br d, J =

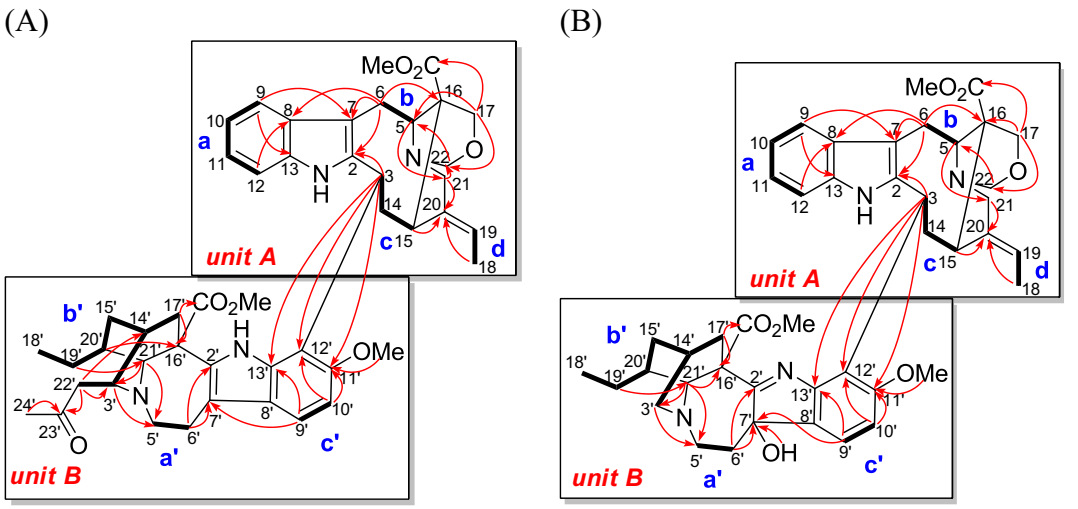


Fig. 2. ^1H–^1H COSY (bold) and key HMBC (arrow, H → C) correlations for tabercorine A (**1**) (A) and tabercorine B (**2**) (B).

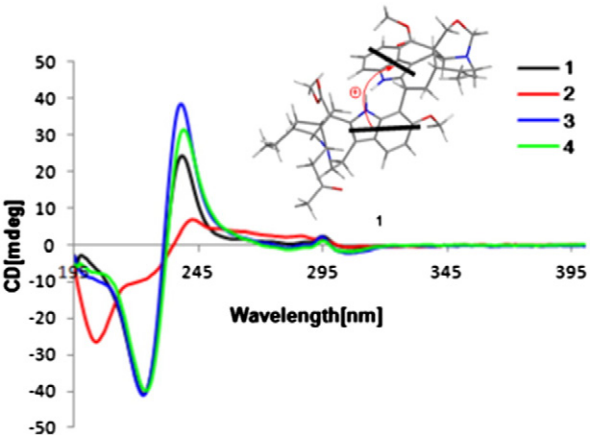
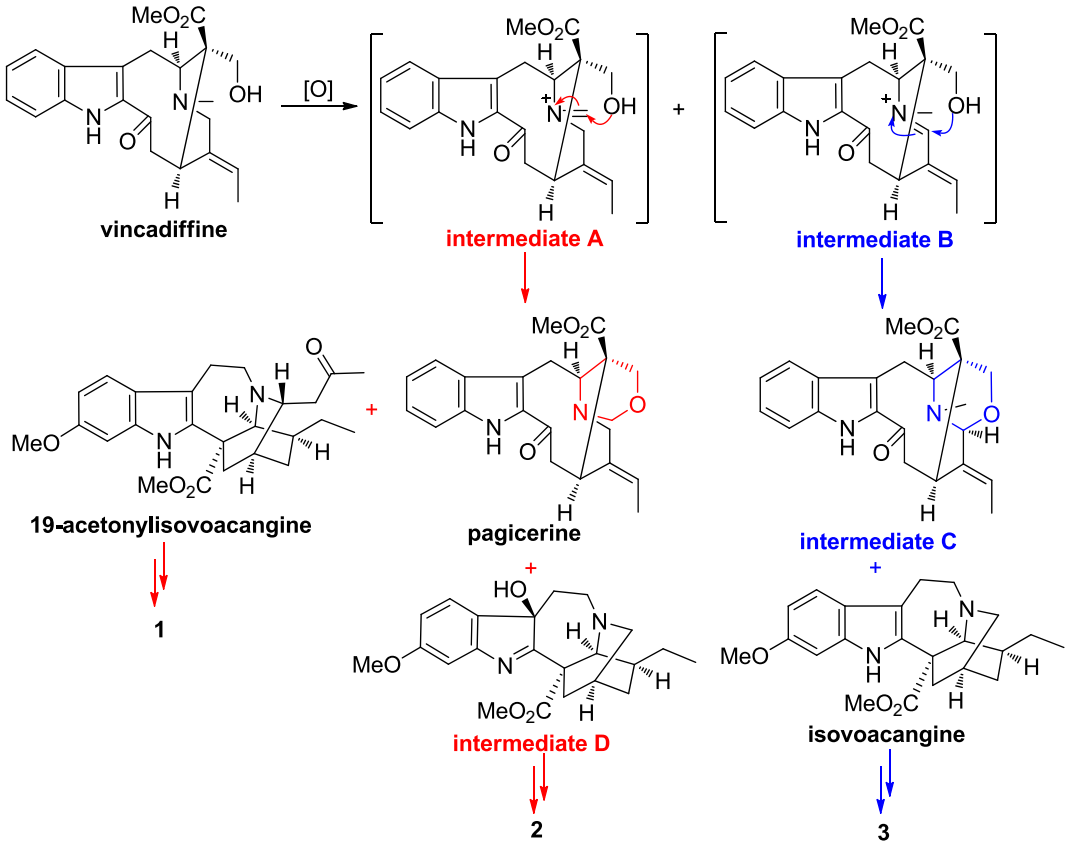


Fig. 3. ECD spectra of compounds **1**–**4**.

13.8 Hz), which was identical with those of tabernaricatines E–G [5].

Tabercorine B (**2**) was obtained as a yellowish amorphous powder, and its HREIMS signal at *m/z* 748.3826 ($[M]^+$, calcd 748.3836) established the molecular formula $C_{44}H_{52}N_4O_7$ with 21 degrees of unsaturation. The IR spectrum displayed absorptions at 3431, 1727 and 1621 cm^{-1} due to amino or hydroxyl and conjugated ester carbonyl functions, respectively. The ^{13}C and DEPT spectral data (Table 1) of **2** showed 44 carbon signals including five methyls, 11 methylenes, 13 methines, and 15 quaternary carbons, which were analogous to those of tabernaricatine D [5]. The major difference was the presence of an iboga indolenine alkaloid (unit B) instead of the common iboga indole unit in **2**. HMBC correlations of 7′-OH (δ_H 4.46, br s), H-6′a (δ_H 1.75, dt, J = 15.0, 2.0 Hz), and H-9′ (δ_H 7.04, d, J = 8.5 Hz) to C-7′ (δ_C 87.2), and H-6′a to C-2′ (δ_C 190.2) verified the above elucidation. Detailed analysis of the 2D NMR spectra (HSQC, ^1H–^1H COSY, HMBC, and ROESY) confirmed that the other parts of the molecule were the same as those of tabernaricatine D. Though ROESY correlations of 7′-OH with other proton signals were not observed, C-7′ might display the *R* configuration as those of voacangine hydroxyindolenine by comparison of their nearly identical NMR data [19]. The structure of alkaloid **2** was thereby characterized as shown in Fig. 1.

Tabercorine C (**3**) had the molecular formula of $C_{44}H_{52}N_4O_7$ as established by HREIMS at *m/z* 748.3837 ($[M]^+$; calcd 748.3836). Comparison of the NMR data of **3** (Table 2) with those of tabernaricatine A, showed that both alkaloids are closely related [5], except for the obvious downfield shifts of H-19 (δ_H 3.31, $\Delta\delta_H$ +0.29) and H-21 (δ_H 3.96, $\Delta\delta_H$ +0.34), as well as upfield shifts of C-18, C-19, and C-21 observed in **3**. Further analysis of 2D NMR (HSQC, ^1H–^1H COSY, HMBC, and ROESY) data suggested the same connectivity as for tabernaricatine A. The large chemical shift differences of C-18 (δ_C 14.5, $\Delta\delta_C$ −2.1), C-19 (δ_C 56.8, $\Delta\delta_C$ −2.3), and C-21 (δ_C 85.8, $\Delta\delta_C$ −4.3) indicated that **3** might be an epimer of tabernaricatine A at the position of oxirane ring involving C-19 and C-20 due to its steric effect. The lack of key ROESY correlations of H-19 and



Scheme 1. Biogenetic pathway proposed for compounds **1**–**3**.

Table 3
Cytotoxicity of compounds **1**–**4** (IC_{50}[a], μM).

Compounds	HL-60	SMMC-7721	A-549	MCF-7	SW480
1	2.98	3.53	4.14	8.10	9.24
2	14.79	13.31	10.34	4.70	16.93
3	14.95	31.52	33.16	>40	>40
4	2.90	4.67	3.83	4.75	4.70
Cisplatin[b]	1.05	4.46	6.57	13.13	11.07

[a] IC_{50}: 50% inhibitory concentration.
[b] Positive control.

H-21 further confirmed the α-orientation of the oxirane ring. Therefore, tabercorine C (**3**) was assigned as shown.

Compound **4** exhibited a molecular formula of $C_{46}H_{56}N_4O_7$ as determined by HRESIMS ($[M + H]^+$ at *m/z* 777.4220, calcd 777.4227) and ^{13}C NMR spectroscopic data (Table 2). Detailed analysis of the NMR data of **4** suggested that it shared the same basic skeleton with those of tabernaecorymbosine A [15]. The presence of an acetoxy group (δ_H 1.92 (3H, s) and δ_C 20.7 and 170.4) suggested that **4** might be 17-acetyl-tabernaecorymbosine A [15], which was obtained from tabernaecorymbosine A by chemical method. 2D NMR (HSQC, ^1H–^1H COSY, HMBC, and ROESY) were firstly performed to complete the full assignments of ^1H and ^{13}C NMR signals and verified the structure of the new natural product of 17-acetyl-tabernaecorymbosine A.

The absolute configurations of alkaloids **1**–**4** were determined by applying the CD exciton chirality method [20]. The sign of the first Cotton effect (λ_{max} ca. 238 nm) was positive, while that of the second one (λ_{max} ca. 220 nm) was negative, indicating that the transition dipole moments of the two indole chromophores in **1**–**4** were oriented in a clockwise manner (Fig. 3). The absolute configurations of **1**–**4** were thus assigned as shown in Fig. 1.

Tabercorines A–C (**1**–**3**) are new vobasinyl-ibogan type bisindole alkaloids possessed a rare 1, 3-oxazinane moiety within alkaloid category. Biogenetically, compounds **1**–**3** might originate from the common precursor vincadiffine [21], with nucleophilic attack onto iminium ion by hydroxyl group as the key step (Scheme 1). Alternatively, compounds **1**–**3** might also be derived from tabernaecorymbosines A and B through the identical mechanism for the formation of 1, 3-oxazinane moiety [15].

3.2. Cytotoxic activity

Compounds **1**–**4** were evaluated for cytotoxicity against five human cancer cell lines, HL-60, SMMC-7721, A-549, MCF-7 and SW480 using the MTT method, with cisplatin as a positive control [16]. Compounds **1** and **4** showed significant inhibitory effects against five human cancer cell lines with IC_{50} values similar to those of cisplatin, while compounds **2** and **3** showed moderate and weak inhibitory effects (Table 3), respectively.

Conflict of interest

Authors declare that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.fitote.2014.11.016.

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