Pergamon

PII: S0031-9422(97)00949-7

Phytochemistry, Vol. 49, No. 3, pp. 769–775, 1998

Printed in Great Britain
0031-9422/98/$—see front matter

LINEAR ACETOGENINS FROM *GONIOTHALAMUS DONNAIENSIS*

ZHONG JIANG,* YING CHEN, RUO-YUN CHEN and DE-QUAN YU

Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People's Republic of China

(*Received in revised form* 29 *September* 1997)

Key Word Index—*Goniothalamus donnaiensis*; Annonaceae; roots; linear acetogenins; donhepocin; 34-*epi*-donhepocin; donhexocin; donbutocin.

Abstract—Four linear acetogenins, donhepocin (**1**), 34-*epi*-donhepocin (**1′**), donhexocin and donbutocin, have been isolated from the roots of *Goniothalamus donnaiensis*. **1** and **1′**, isolated as an epimeric pair, contain a rare γ-hydroxymethyl-γ-lactone. Their structures have been established on the basis of spectral and chemical evidence.

INTRODUCTION

Since epoxyrollins A and B, the first two acetogenins without a THF ring were reported in 1990 [1], about 20 non-THF acetogenins have been isolated [2, 3]. These compounds are considered to be precursors in the formation of THF acetogenins. Our investigation on the ethanolic extract of the roots of *Goniothalamus donnaiensis* led to the isolation of several compounds [3, 4]. In the present paper, we report on the identification of four novel non-THF acetogenins, donhepocin (**1**), 34-*epi*-donhepocin (**1′**), donhexocin (**2**) and donbutocin (**3**); **1** and **1′** containing rare γ-hydroxymethyl-γ-lactone, was isolated as an epimeric pair.

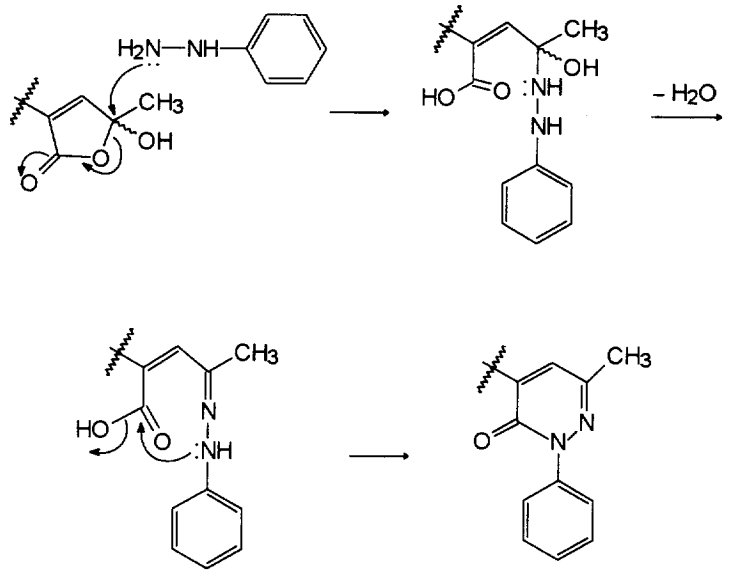
RESULTS AND DISCUSSION

Donhepocin (**1**), 34-*epi*-donhepocin (**1′**) were isolated as a white, amorphous powder. Mass spectrometry and elemental analysis indicated a molecular formula of $C_{35}H_{66}O_9$ and an identical skeleton (Fig. 1). Because of their high polarity, the NMR spectra of **1** (**1′**) was measured in CD_3OD, instead of in $CDCl_3$. Regarding the solvent effect, several proton signals (H-4, H-10, H-15, H-16, H-19, H-20, H-32 and H-35) of **1** (**1′**) shifted upfield by ca 0.05–0.15 ppm, in comparison with those previously reported for acetogenins in $CDCl_3$ [4, 5]. Though the duplication of several signals (H-3, H-4, C-2, C-4, C-33 and C-34) in the NMR spectra of **1** (**1′**) could not be observed, the existence of a lactol moiety in **1** (**1′**) was still ascertained by the disappearance of H-34 (ca δ 5.04), the observation of H-35 at δ 1.54 (*s*), instead of 1.42 (*d*), and the replacement of the signal at ca δ 77.9 by one at δ 105.0 (C-34). The lack of any THF ring along the aliphatic chain was elucidated from the absence of any corresponding THF ether proton and carbon signals in the NMR spectra. An isolated hydroxyl group was indicated by the ^{1}H NMR signal at δ 3.44 (*m*, 1H) and ^{13}C NMR signal at δ 72.4 (1C). Proton signals at δ 3.32 (*m*, 4H) and carbon signals at δ 75.2–75.7 (4C) showed that two 1,2 diols were present in **1** (**1′**). The locations of the hydroxyl groups were established by EI mass spectrometry (Fig. 1). The formation of acetonides **1a** (**1a′**) from **1** (**1′**) further confirmed the presence of two *vic*-diols. The duplication of several ^{1}H NMR signals (δ 2.23–2.38, 2.50–2.38, 3.83–3.76 and 6.94–6.95) and ^{13}C NMR signals (δ 69.4–71.1, 104.9–105.2, 131.8–132.4, 150.5–149.6 and 171.9–172.7) indicated that **1** and **1′** were epimeric at C-34, like the lactol-bearing acetogenins previously reported [4, 5]. This was confirmed by the formation of a phenylhydrazone derivative **1b** from **1** (**1′**) [6]. The ^{1}H NMR data (Table 1) and fragment ions (Fig. 2) of **1b** further confirmed the structures of **1** (**1′**). The mechanism for the formation of phenylhydrozone is illustrated in Scheme 1.

The acetonyl methyls of the acetonides derivative **1c** appeared at δ 1.37 and the dioxolane ring protons resonated at δ 3.59 and 3.61, suggesting that the two 1,2 diols have *threo*-configurations [7]. The absolute stereochemistry of C-4 was determined by using Mosher ester methodology [8]. Analysis of the chemical shifts differences of **1cs** and **1cr** (Table 3) allowed us to conclude that **1** (**1′**) have C-4*R*.

Donhexocin (**2**) was obtained as a white amorphous powder. The molecular formula was established to be $C_{35}H_{66}O_8$ on the basis of FAB mass spectrometry and elemental analysis. A prominent IR carbonyl absorp-

* Author to whom correspondence should be addressed.



Scheme 1. Mechanism for formation of phenylhydrazone derivative of compounds **1**(**1′**).

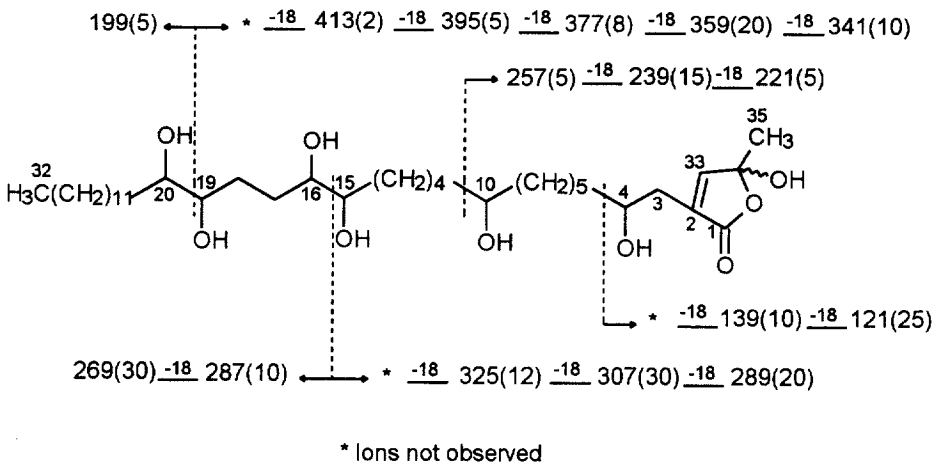


Fig. 1. Diagnostic EIMS fragment ions (*m*/*z*) of compounds **1**(**1′**). Numbers in parentheses are relative intensities.

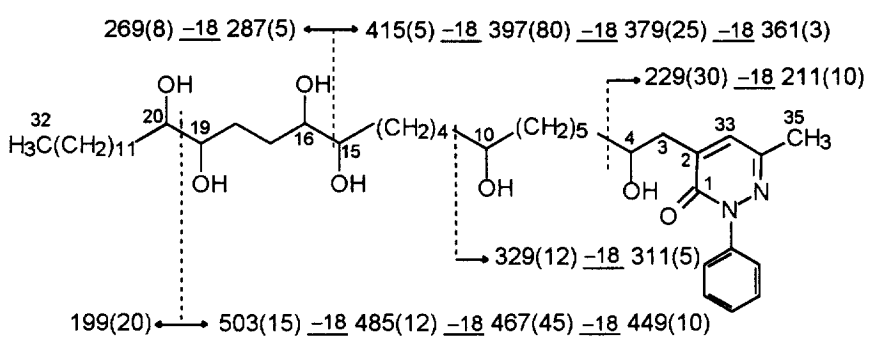


Fig. 2. Diagnostic EIMS fragment ions (*m*/*z*) of compounds **1b**. Numbers in parentheses are percent intensities.

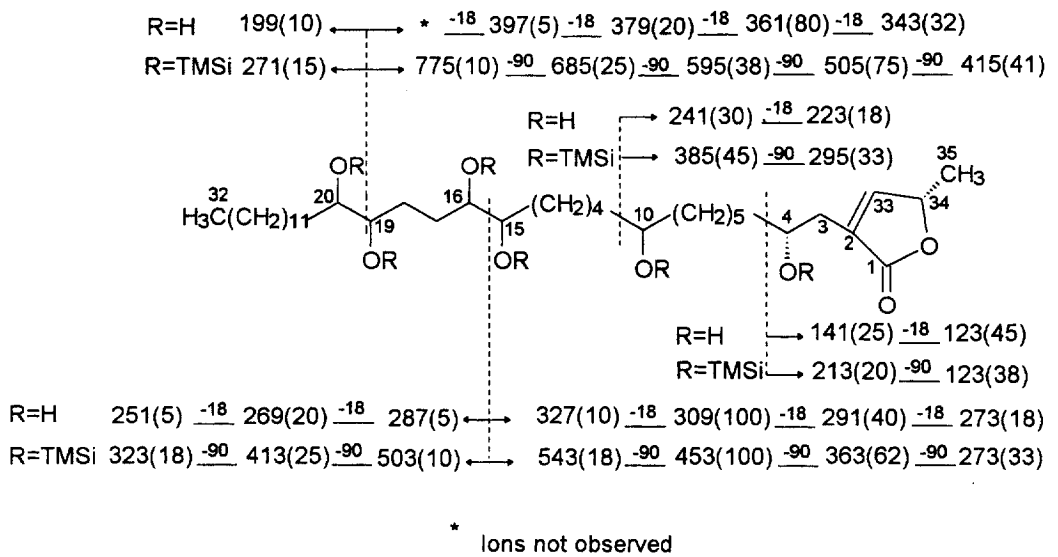


Fig. 3. Diagnostic EIMS fragment ions (*m/z*) of compounds **2** (R=H) and **2a** (R=TMSi). Numbers in parentheses are relative intensities.

Table 1. ^{1}H NMR (500 MHz) data of compounds **1** (**1′**), **1a**, **1a′** and **1b**

No.	**1** (**1′**) (CD_3OD)	**1a** ($CDCl_3$)	**1a′** ($CDCl_3$)	**1b** ($CDCl_3$)
3a	2.24 *dq* (14.9, 8.3)	2.23 *dq* (14.2, 9.1)	2.38 *m*	2.71 *dq* (13.9, 8.2)
3b	2.34 *dd* (14.9, 4.1)	2.50 *dd* (14.2, 4.1)	2.38 *m*	2.87 *dd* (13.9, 4.0)
4	3.71 *m*	3.83 *m*	3.76 *m*	3.92 *m*
5–9	1.2–1.5 *m*	1.2–1.6 *m*	1.2–1.6 *m*	1.2–1.6 *m*
10	3.44 *m*	3.61 *m*	3.61 *m*	3.61 *m*
11–14	1.2–1.5 *m*	1.2–1.6 *m*	1.2–1.6 *m*	1.2–1.6 *m*
15, 16	3.32 *m*	3.58 *m**	3.58 *m*†	3.40 *m*
17, 18	1.2–1.5 *m*	1.2–1.6 *m*	1.2–1.6 *m*	1.2–1.6 *m*
19, 20	3.32 *m*	3.61 *m**	3.61 *m*†	3.40 *m*
21–31	1.2–1.5 *m*	1.2–1.6 *m*	1.2–1.6 *m*	1.2–1.6 *m*
32	0.82 *t* (6.9)	0.87 *t* (6.9)	0.87 *t* (6.9)	0.88 *t* (6.8)
33	6.96 *bs*	6.94 *s*	6.95 *s*	7.07 *s*
35	1.54 *bs*	1.65 *s*	1.65 *s*	2.38 *s*
38–41	—	1.37 *s*	1.37 *s*	—
ArH	—	—	—	7.34-7.58 *m*

*† Assignment with same superscript may be interchangeable.

tion at 1740 cm^{-1} suggested the presence of an α,β-unsaturated γ-lactone group. The NMR spectra of **2** showed ^{1}H NMR (CD_3OD) resonances at δ 7.39 (*d*, H-33), 5.13 (*q*, H-34), 3.83 (*m*, H-4), 2.46 (*dd*, H-3a), 2.38 (*dd*, H-3b), 1.43 (*d*, H-35), and six ^{13}C NMR (CD_3OD) resonances at δ 176.5 (C-1), 154.3 (C-33), 131.5 (C-2), 79.7 (C-34), 70.4 (C-4) and 19.1 (C-35), confirming the existence of a γ-methyl α,β-unsaturated γ-lactone with a C-4-OH moiety, in common with most of the annonaceous acetogenins [2, 9–11]. The presence of six OH groups in **2** was evidenced by signals at δ 3.83 (1H), 3.57 (1H), 3.44 (4H) in the ^{1}H NMR (CD_3OD) spectrum and resonances due to oxygenated carbons at δ 70.4, 72.4, 75.2, 75.3, 75.4 and 75.7 in ^{13}C NMR (CD_3OD) spectrum. However, the lack of a THF ring along the aliphatic chain was indicated by the absence of any corresponding THF ether proton and carbon signals in the NMR spectra. The locations of the hydroxyl groups were established by EI mass fragmentation analyses of **2** and its TMSi derivative **2a** (Fig. 3). This compound contained two 1,2-diols in the aliphatic chain. The formation of the acetonide derivative **2b** from **2** further supported this conclusion. The ^{1}H NMR ($CDCl_3$) signals for the dioxolane ring protons at δ 3.59 (*m*, 2H), 3.61 (*m*, 2H) and the signals for the acetonyl methyl protons at δ 1.377 (*s*, 6H) and 1.378 (*s*, 6H), suggested the *threo*-configuration for the two diols [7]. The absolute stereochemistry of C-4 was determined using Mosher ester methodology [8]. Analysis of the chemical shift

Table 2. ^{13}C NMR (125 MHz) data of compounds **1** (**1'**), **1a** and **1a'**

No.	**1** (**1'**) (in CD_3OD)	**1a** (in $CDCl_3$)	**1a'** (in $CDCl_3$)
1	174.0	171.9	172.7
2	132.2	131.8	132.4
3	33.0	33.1	32.1
4	70.4	69.4	71.1
5–9	23–39	22–38	22–38
10	72.4	71.8	71.8
11–14	23–39	22–38	22–38
15	75.2*	80.6†	80.6‡
16	75.3*	80.7†	80.8‡
17–18	23–39	22–38	22–38
19	75.4*	81.0†	81.0‡
20	75.7*	81.1†	81.1‡
21–31	23–39	22–38	22–38
32	14.4	14.1	14.1
33	151.6	150.5	149.6
34	105.0	104.9	105.2
35	24.9	24.2	24.2
36, 37	—	107.8	107.8
38–41	—	24.2	24.2

*–‡Assignment with same superscript may be interchangeable.

and 74.4 (2C) in the ^{13}C NMR spectrum, indicated the existence of four OH groups and the absence of any THF ring. The location of the hydroxyl groups was established by EI mass spectrometry of **3** and its TMSi derivative **3a** (Fig. 4) To determine the relative configuration at C-17/C-18, the acetonide derivative **3b** of **3** was prepared. The acetonyl methyls appeared at δ 1.38 and 1.39, and the dioxolane ring protons appeared at δ 3.59, indicating that the 1,2-diol has the *threo*-configuration [6]. The absolute stereochemistry at C-4 in **3** was assigned by studying the per-Mosher ester derivatives (**3brs**, **3br**) of **3b** [7]. The ^1H NMR chemical shifts (Table 3) showed that C-4 in **3** possessed the *R*-configuration. The values 0.23 ppm and 0.04 ppm of $\Delta\delta_{S-R}$ for H-33 and H-34, respectively, indicated that the C-34 chiral centre is of the usual *S*-configuration [11].

Compounds **1** (**1'**) gave cytotoxic IC_{50} values against HCT-8 and Bel 7402 human tumour cell lines, and L1210 mouse tumour cell lines of > 10 $\mu g\ ml^{-1}$, whereas IC_{50} values of compound **2** against HCT-8, Bel 7402 and L1210 were 0.82, > 10, > 10 $\mu g\ ml^{-1}$, respectively, and IC_{50} values of compound **3** were 4.8, 5.7, 0.81 $\mu g\ ml^{-1}$, respectively. The replacement of H-34 by OH in compound **1** (**1'**) decreases the cytotoxic potency significantly. Also, a certain median level of polarity may be important for biological activity in acetogenins.

Table 3. Characteristic ^1H NMR data of compounds **1cs**, **1cr**, **2bs**, **3bs** and **3br**

Derivative	MTPA configuration	Proton chemical shifts H-5	H-4	H-3a	H-3b	33	34	35
1c	*S*	1.62	5.52	2.68	3.04	6.76	—	2.19
	R	1.60	5.50	2.74	3.07	6.91	—	2.23
	$\Delta\delta_{S-R}$	+0.02	*R*	−0.06	−0.03	−0.15	—	−0.04
2b	*S*	1.55	5.33	2.56	2.58	6.73	4.87	1.28
	R	1.53	5.35	2.59	2.65	6.96	4.91	1.31
	$\Delta\delta_{S-R}$	+0.02	*R*	−0.03	−0.07	−0.23	−0.04	−0.03
3b	*S*	1.54	5.33	2.55	2.58	6.73	4.87	1.28
	R	1.52	5.35	2.59	2.65	6.96	4.91	1.31
	$\Delta\delta_{S-R}$	+0.02	*R*	−0.04	−0.07	−0.23	−0.04	−0.03

differences of **2bs** and **2br** around the γ-lactone ring moiety showed negative results for H-3, H-33, H-34 and H-35, suggesting the *R*-configuration for C-4 (Table 3). The magnitude of the $\Delta\delta_{S-R}$ values for H-33 and H-34 were 0.23 ppm and 0.04 ppm, respectively, showing that C-34 has the usual *S*-configuration [12].

Donbutocin (**3**) was also obtained as a white, amorphous powder. The molecular formula $C_{35}H_{66}O_6$ was determined by FAB mass spectrometry and elemental analysis, and it showed spectral features characteristic of the α,β-unsaturated γ-lactone with a C-4-OH group in annonaceous acetogenins [2, 9–11]. The signals at δ 3.84 (1H), 3.58 (1H), 3.44 (2H) in the ^1H NMR spectrum and the corresponding resonances due to oxygenated carbons at δ 69.8 (1C), 71.7 (1C)

EXPERIMENTAL

General

Mps: uncorr. IR: KBr. ^1H NMR and ^{13}C NMR: Bruker AM500 spectrometer.

Plant material

Roots of *G. donnaiensis* Finet et Gagnep were collected from Long Jin county, Guangxi Province, People's Republic of China, in August 1994. Identification was confirmed by Prof. Shou-Yang Liu, Department of Medicinal Plants, Guangxi College of Traditional

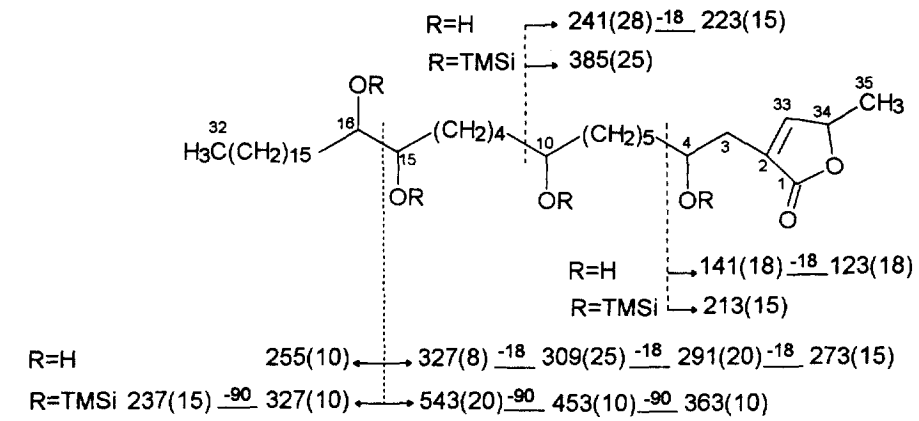


Fig. 4. Diagnostic EIMS fragment ions (*m/z*) of compounds **3** (R = H) and **3a** (R = TMSi). Numbers in parentheses are relative intensities.

Chinese Medicine, where a voucher specimen has been deposited.

Extraction and isolation

Dried and pulverized roots (9.5 kg) were extracted exhaustively with 95% EtOH and the solvent removed to yield extract F001 (2.05 kg), which was partitioned between H_2O and $CHCl_3$ (1:1), giving the H_2O-sol. fr. F002 (448 g) and the $CHCl_3$-sol. fr. F003 (820 g) and the insoluble interface fr. F004 (201 g). F003 was then partitioned between 90% aq. MeOH and petrol (1:1) to yield a petrol-sol. fr. F006 (42 g) and an aq. MeOH-sol. fr. F005 (638 g). F005 (91 g) was applied to a column of silica gel (120–180 mesh), eluted with $CHCl_3$ containing gradually increasing amounts of MeOH. Impure components were obtained according to their similar appearance on TLC analysis, and these were again subjected to repeated chromatography (300–400 mesh silica gel gradients of $CHCl_3$–MeOH) to yield donhepocin and 34-*epi*-donhepocin (**1**, **1'**) (75 mg), donhexocin (**2**) (90 mg) and donbutocin (**3**) (30 mg).

Bioassays

Cytotoxicity against human and mouse solid tumour cells was measured in 5-day MTT tests at the Department of Pharmacology, Institute of Materia Medica, Chinese Academy of Medical Sciences, for HCT-8 colon adenocarainoma, Bel 7402 hepatoma and L1210 mouse leukaemia cell lines.

Donhepocin (**1**) *and 34-epi-donhepocin* (**1'**). White, amorphous powder, mp 102–104°. $[\alpha]_D^{18}$ 0° (*c* 0.10, CH_3OH). IR (KBr) ν_{max}: 3373, 2918, 2848, 1743, 1470 cm^{-1}. FABMS *m/z* $[M+Na]^+$ 653, $[M+H]^+$ 631, $[MH-H_2O]^+$ 613, $[MH-2H_2O]^+$ 595, $[MH-3H_2O]^+$ 577; EIMS: Fig. 1. ^1H NMR and ^{13}C NMR: Tables 1 and 2. Anal. calc. for $C_{35}H_{66}O_9$: C 66.67, H 10.48 (found: C 66.42, H 10.55).

Acetonide derivative of **1** (**1'**). To **1** (**1'**) (15 mg in 10 ml of dry CH_2Cl_2) was added 0.5 ml of 2,2-dimethoxypropane and a few of crystals of *p*-toluenesulfonic acid, and the mixt. stirred at room temp. for 2 h. The product **1a** (**1a'**) was purified by prep. TLC. Compound **1a** (**1a'**). Colourless oil. ^1H NMR and ^{13}C NMR: Tables 1 and 2.

Phenylhydrazone derivative of **1** (**1'**). A mixt. of a 20 mg sample and 5 mg of phenylhydrazine in 10 ml of EtOH was refluxed for 2 h. The viscous mass (**1b**) which was obtained after removal of solvent *in vacuo* was purified by prep. TLC. Compound **1b**. Colourless oil. EIMS: Fig. 2. ^1H NMR: Table 1.

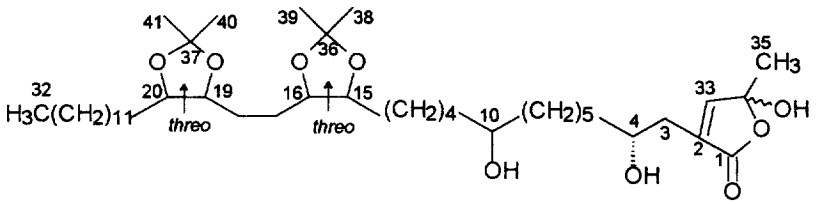
Acetonide derivative of **1b**. **1b** (15 mg) was treated as described previously to give acetonide derivative **1c**. *Compound* **1c**. Colourless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 0.88 (3H, *t*, J = 6.8 Hz, H-32), 1.37 (*s*, 12H, 4 × CH_3), 2.38 (3H, *s*, H-35), 2.70 (1H, *dq*, J = 14.0, 8.1 Hz, H-3a), 2.86 (1H, *dd*, J = 14.0, 4.0 Hz, H-3b), 3.59 (2H, *m*, H-15, 16), 3.61 (3H, *m*, H-10, 19, 20), 3.92 (1H, *m*, H-4), 7.07 (1H, *s*, H-35), 7.34–7.58 (5H, *m*, ArH).

MTPA derivatives of **1c**. (*R*)−(+)− or (*S*)−(−)-α-Methoxyl-α-(trifluoromethyl) phenylacetic acid (MTPA, 25 mg) and *N,N*-dicyclohexylcarbodiimide (DCC, 15 mg) were added to a 5-mg sample of **1c** dissolved in dry CH_2Cl_2 with a few crystals of (dimethylamino)pyridine (DMAP). Each mixt. was stirred at room temp. for 6 h and the product (**1cs** or **1cr**) was purified by prep. TLC. **1cs** and **1cr**, both colourless oils. ^1H NMR: Table 3.

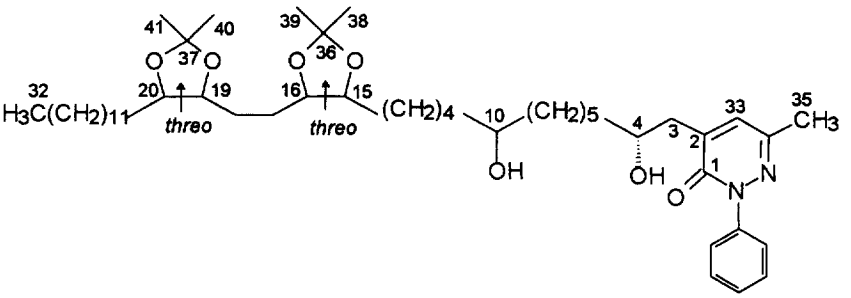
Donhexocin (**2**). Amorphous, mp 96–98°. $[\alpha]_D^{18}$ +8.0° (*c* 0.10, MeOH). IR (KBr) ν_{max}: 3362 (OH), 2918, 2849, 1740 (C=O), 1469 cm^{-1}. FABMS: *m/z* $[M+H]^+$ 615. EIMS: Fig. 3. ^1H NMR and ^{13}C NMR: Table 4. Anal. calc. for $C_{35}H_{66}O_8$: C, 68.40; H, 10.75 (Found: C, 68.13; H, 10.64).

TMSi derivative of **2**. Dry microamount samples of **1** were treated with *N,O-bis*(trimethylsilyl) acetamide (BSA) and pyridine (10:1) and heated at 70° for 30 min. EIMS: Fig 3.

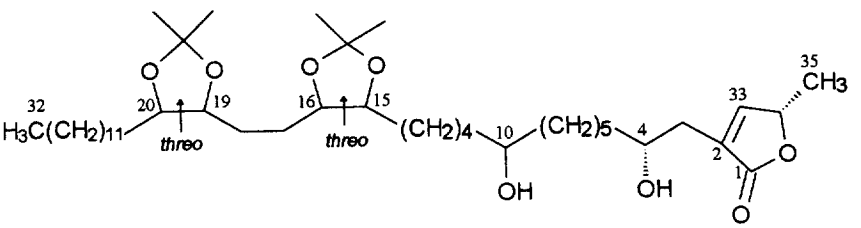
Acetonide derivative of **2**. **2** (15 mg) was treated as



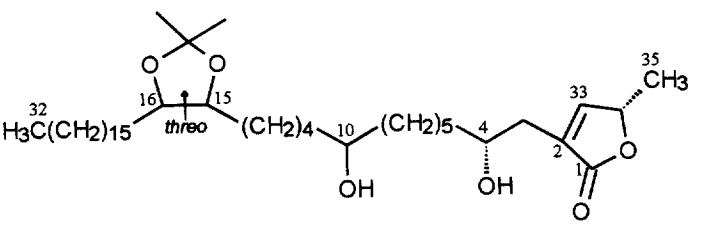
1a (1a')



1c



2b



3b

described previously to gave the acetonide derivative **2b**. *Compound* **2b**. Colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (3H, *t*, J = 6.8 Hz, H-32), 1.37 (*s*, 12H, 4 × CH_3), 1.43 (3H, *d*, J = 7.0 Hz, H-35), 2.40 (1H, *dq*, J = 15.0, 8.1 Hz, H-3a), 2.52 (1H, *ddd*, J = 15.0, 1.5 Hz, H-3b), 3.59 (2H, *m*, H-15,16), 3.61 (3H, *m*, H-10, 19, 20), 3.84 (1H, *m*, H-4), 5.05 (1H, *dq*, J = 1.1, 6.7 Hz, H-34), 7.18 (1H, *d*, J = 1.0 Hz, H-33).

MTPA derivatives of **2b**. After work-up as described previously, the Mosher esters **2bs** and **2br** were obtained as colorless oils. ^{1}H NMR: Table 3.

Donbutocin (**3**). Amorphous, mp 90–92°. $[\alpha]_D^{18}$ +16.3° (*c* 0.10, MeOH). IR (KBr) ν_{max}: 3370 (OH), 2920, 2850, 1739 (C=O), 1467 cm^{-1}. FABMS: *m/z* $[M+H]^+$ 583. EIMS: Fig. 4. ^{1}H NMR and ^{13}C NMR: Table 4. Anal. calc. for $C_{35}H_{66}O_6$: C, 72.16; H, 11.34 (Found: C, 71.98; H, 11.41).

TMSi derivative of **3**. Dry microamount samples of

Table 4. ^{1}H NMR and ^{13}C NMR data of compounds **2** and **3**

	2 (CD_3OD)		**3** ($CDCl_3$)	
No.	δ_H	δ_C	δ_H	δ_C
1		176.4		174.2
2		131.5		131.1
3a	2.38, *dq* (14.8, 8.1)	33.0	2.39, *dq* (15.0, 8.1)	33.3
3b	2.46, *dd* (14.8, 3.0)		2.51, *dd* (15.0, 4.2)	
4	3.83, *m*	70.4	3.84, *m*	69.8
5–9	1.2–1.6, *m*	22–39	1.2–1.6, *m*	22–39
10	3.57, *m*	72.4	3.57, *m*	71.7
11–14	1.2–1.6, *m*	22–39	1.2–1.6, *m*	22–38
15	3.44, *m*	75.2*	3.40, *m*	74.4
16	3.44, *m*	75.3*	3.40, *m*	74.4
17a, 18a	1.71, *m*	25.6	1.2–1.6, *m*	22–38
17b, 18b	1.62, *m*		1.2–1.6, *m*	
19	3.44, *m*	75.4*	1.2–1.6, *m*	22–38
20	3.44, *m*	75.7*	1.2–1.6, *m*	22–38
21–31	1.2–1.6, *m*	22–39	1.2–1.6, *m*	22–38
32	0.94, *t* (6.8)	14.4	0.88, *t* (6.8)	14.1
33	7.39, *d* (1.3)	154.3	7.20, *s*	152.0
34	5.13, *dq* (1.3, 6.8)	79.7	5.06, *m*	78.1
35	1.43, *d* (6.8)	19.1	1.43, *d* (6.8)	19.1

*Assignments may be interchangeable.

1 were treated with *N,O-bis*(trimethylsilyl) acetamide (BSA) and pyridine (10:1) and heated at 70° for 30 min. EIMS: Fig 4.

Acetonide derivative of **3**. **3** (15 mg) was treated as described previously to gave the acetonide derivative **3b**. *Compound* **3b**. Colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (3H, *t*, J = 6.8 Hz, H-32), 1.38, 1.39 (each *s*, 3H, 2 × CH_3), 1.43 (3H, *d*, J = 6.8 Hz, H-35), 2.40 (1H, *dq*, J = 15.0, 8.2 Hz, H-3a), 2.53 (1H, *ddd*, J = 15.0, 1.5, 1.5 Hz, H-3b), 3.59 (2H, *m*, H-15, 16), 3.65 (1H, *m*, H-10), 3.86 (1H, *m*, H-4), 5.06 (1H, *m*, H-34), 7.18 (1H, *s*, H-33).

MTPA derivatives of **3b**. After work-up as described previously, the Mosher esters **2bs** and **2br** were obtained as colourless oils. ^{1}H NMR: Table 3.

Acknowledgements—This work is supported by the Science Foundation of Chinese Academy of Medical Sciences. The authors express their gratitude to Mr W.-Y. He and Mrs M. Kong for NMR measurements and to Mr L.-J. Li for help in acquiring MS data. thanks are also expressed to Miss Y. M. Ye for cytotoxicity testing.

REFERENCES

1. Laprévote, O., Roblot, F., Hocquemiller, R. and Cavé, A., *Tetrahedron Letters*, 1990, **31**, 2283.
2. Zeng, L., Ye, Q., Oberlies, N. H., Shi, G.-E., Gu, Z.-M., He, K. and McLaughlin, J. L., *Natural Product Reports*, 1996, **13**, 275.
3. Cavé, A., Figadère, B., Laurens, A. and Cortes, D., in *Progress in the Chemistry of Organic Natural Products*, Vol. 70, ed. W. Herz, Springer, Wien, 1997, pp. 81–288.
4. Jiang, Z. and Yu, D.-Q., *Journal of Natural Products*, 1997, **60**, 122.
5. Jiang, Z., Chen, Y., Chen, R.-Y. and Yu, D.-Q., *Phytochemistry*, 1997, in press.
6. Kocienski, P. J., Ansell, J. M. and Ostrow, R. W., *Journal of Organic Chemistry*, 1976, **41**, 3625.
7. Gu, Z. M., Fang, X. P., Zeng, L., Kozlowski, J. F. and McLaughlin, J. L., *Bioorganic and Medicinal Chemistry Letters*, 1994, **4**, 473.
8. Rieser, M. J., Hui, Y. H., Rupprecht, J. K., Kozlowski, J. F., Wood, K. V., McLaughlin, J. L., Hanson, P. R., Zhuang, Z. P. and Hoye, T. R., *Journal of the American Chemical Society*, 1992, **114**, 10203.
9. Cavé, A., Cortes, D., Figadère, B., Hocquemiller, L. O., Laprévote, O. and Leboeuf, M., in *Recent Advances in Phytochemistry*, Vol. 27, ed. K. R. Downum, J. T. Romeo and H. A. Stafford, Plenum Press, New York, 1993, pp. 167–202.
10. Gu, Z. M., Zhao, G. X., Oberlies, N. H., Zeng, L. and McLaughlin, J. L., in *Recent Advances in Phytochemistry*, Vol. 29, ed. J. T. Arnason, R. Mata and J. T. Romeo, Plenum Press, New York, 1995, pp. 249–310.
11. Zafra-Polo, M. C., González, M. C., Estornell, E., Sahpaz, S. and Cortes, D., *Phytochemistry*, 1996, **42**, 253.
12. Hoye, T. R., Hanson, P. R., Hasenwinkel, L. E., Ramirez, E. A. and Zhuang, Z. P., *Tetrahedron Letters*, 1994, **35**, 8529.