PERGAMON

Phytochemistry 59 (2002) 767–777

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

Sesquiterpene pyridine alkaloids from *Hippocratea excelsa*

Masakatsu Furukawa[a], Mitsuko Makino[a], Taketo Uchiyama[a], Katsuhiro Ishimi[b],
Yoshiyuki Ichinohe[b], Yasuo Fujimoto[a,*]

[a]*College of Pharmacy, Nihon University, 7-7-1 Narashinodai, Funabashi, Chiba 274-8555, Japan*
[b]*College of Science and Technology, Nihon University, 7-24-1 Narashinodai, Funabashi, Chiba 274-8501, Japan*

Received 2 October 2001; received in revised form 26 December 2001

Abstract

Nineteen sesquiterpene pyridine alkaloids including 17 new compounds have been isolated from the 70% aq. EtOH extract of stem barks of *Hippocratea excelsa*. The structures of these compounds were elucidated by various spectroscopic means.

Keywords: Hippocratea excelsa; Hippocrateaceae; Stem bark; Sesquiterpene pyridine alkaloid

1. Introduction

Hippocratea excelsa H.B.K. (Hippocrateaceae) has been used for treating cancer, gastric ulcers, and as an insecticide (Palacios et al., 1989; Mata et al., 1990; Mata and Calzada, 1995). The dried stem barks of this plant are commonly called "cancerina" in Mexico (Palacios et al., 1989). We investigated the biological activities of the 70% aq. EtOH extract of this plant and found that this extract exhibited strong insecticidal activity on both *Nephotettix cincticeps* and *Nilaparvata lugens*. A bioassay guided fractionation of the extract led to the isolation of 19 alkaloids of which 17 were new sesquiterpene pyridine alkaloids (**1**–**7**, **10**–**19**, Fig. 1) and the remainder were the two known alkaloids, emarginatine A (**8**) (Mata et al., 1990; Kuo et al., 1989) and hippocrateine I (**9**) (Mata et al., 1990).

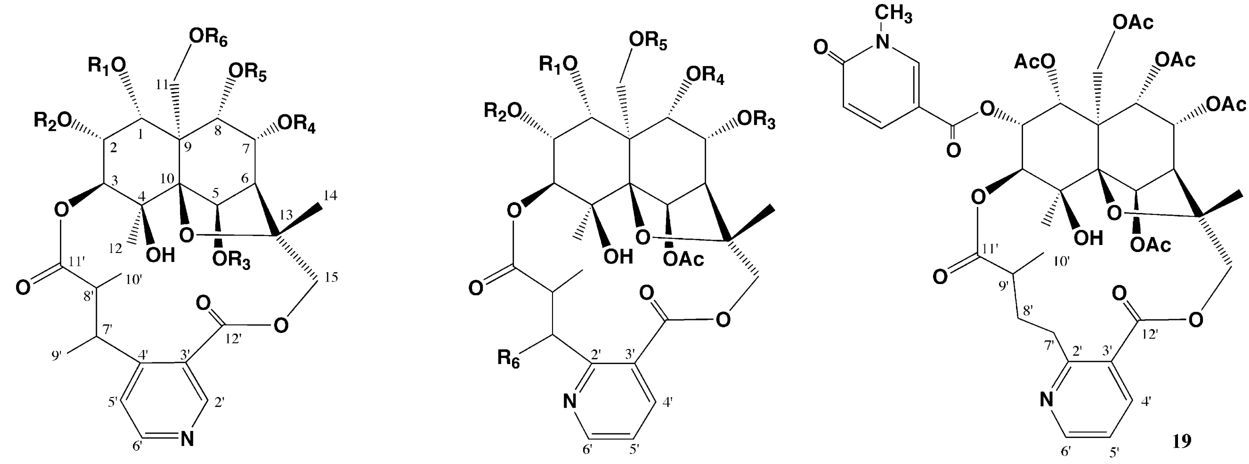
2. Results and discussion

Compound **1** gave a molecular ion peak at *m/z* 926.3321 corresponding to the molecular formula $C_{45}H_{54}N_2O_{19}$ in its high resolution (HR) EI–MS spectrum, whereas its UV spectrum showed the presence of an aromatic moiety (269 nm, log $\varepsilon = 3.97$). Its ^{1}H NMR spectrum (Table 1) showed the presence of four acetyl groups [δ_H 1.81, 1.97, 2.21 and 2.38 (each 3H, *s*)], an isobutyloyl group [δ_H 1.22, 1.23 (each 3H, *d*, $J = 7.0$ Hz), 2.67 (1H, *sep*, $J = 7.0$ Hz)], two secondary methyl groups [δ_H 1.10, 1.36 (each 3H, *d*, $J = 7.0$ Hz)], two primary methyl groups [δ_H 1.54, 1.74 (each 3H, *s*)], two sets of *O*-acylated methylene protons [δ_H 3.71, 6.06 (each 1H, *d*, $J = 12.0$ Hz), 4.18, 5.55 (each 1H, *d*, $J = 14.0$ Hz)], a 3,4-disubstituted pyridine ring [δ_H 7.37, 8.72 (each 1H, *d*, $J = 5.5$ Hz), 9.01(1H, *s*)], a 5-carboxy-*N*-methyl-2-pyridone (CNMP) ring [δ_H 6.59 (1H, *d*, $J = 10.0$ Hz), 7.87 (1H, *dd*, $J = 10.0$, 2.5 Hz), 8.44 (1H, *d*, $J = 2.5$ Hz), 3.72 (3H, *s*, *N*-methyl)], three methine protons [δ_H 2.36 (1H, *d*, $J = 4.5$ Hz), 2.47, 4.71 (each 1H, *q*, $J = 7.0$ Hz)], six *O*-acylated methine protons [δ_H 4.78 (1H, *d*, $J = 2.5$ Hz), 5.43 (1H, *d*, $J = 6.0$ Hz), 5.48 (1H, *dd*, $J = 4.5$, 2.5 Hz), 5.56 (1H, *dd*, $J = 6.0$, 4.5 Hz), 5.65 (1H, *d*, 4.5 Hz), 7.07 (1H, *s*)], and a proton signal due to a hydroxyl group [δ_H 4.93 (1H, *brs*)]. The ^{13}C NMR spectral data (Table 2) revealed the presence of ten methyl carbons, a *N*-methyl carbon (δ_C 38.1), two methylene carbons, sixteen methine carbons and sixteen quaternary carbons including nine carbonyl carbons. These spectral data suggested that this compound should be a *β*-dihydroagarofuran-type sesquiterpene pyridine alkaloid which has a 4-(2-carboxy-1-methylpropyl) nicotinic acid diester bridge such as in hippocrateine III (Mata and Calzada, 1995). The *O*-isobutyloyl group was located at the C-7 position, since the HMBC spectrum (Fig. 2) showed a long-range correlation between the proton signal at δ_H 5.56 (H-7) and the ester carbonyl carbon

---

* Corresponding author. Tel./Fax: +81-47-465-6470.
E-mail address: fujimoto@pha.nihon-u.ac.jp (Y. Fujimoto).

PII: S0031-9422(02)00020-1

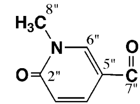


19

	R1	R2	R3	R4	R5	R6
1	Ac	CNMP	Ac	^{i}Pr-CO	Ac	Ac
2	Ac	CNMP	Ac	^{i}Pr-CO	Ac	^{i}Pr-CO
3	Ac	CNMP	Ac	^{i}Pr-CO	^{i}Pr-CO	^{i}Pr-CO
4	Ac	CNMP	H	^{i}Pr-CO	Ac	^{i}Pr-CO
5	H	CNMP	Ac	^{i}Pr-CO	^{i}Pr-CO	^{i}Pr-CO
6	Ac	Ac	Ac	^{i}Pr-CO	Ac	Ac
7	^{i}Pr-CO	CNMP	Ac	Ac	^{i}Pr-CO	^{i}Pr-CO

	R1	R2	R3	R4	R5	R6
8	Ac	CNMP	Ac	Ac	Ac	CH_3
9	Bz	CNMP	Ac	Ac	Ac	CH_3
10	Ac	CNMP	Ac	Ac	^{i}Pr-CO	CH_3
11	Ac	CNMP	^{i}Pr-CO	Ac	Ac	CH_3
12	^{i}Pr-CO	CNMP	Ac	^{i}Pr-CO	Ac	CH_3
13	H	CNMP	Ac	^{i}Pr-CO	Ac	CH_3
14	CNMP	Ac	Ac	Ac	Ac	CH_3
15	CNMP	H	Ac	Ac	Ac	CH_3
16	Ac	CNMP	Ac	Ac	Ac	H
17	Ac	CNMP	Ac	Ac	^{i}Pr-CO	H
18	Ac	CNMP	^{i}Pr-CO	Ac	^{i}Pr-CO	H

CNMP (5-carboxy-*N*-methylpyridonyl):



^{i}Pr-CO : $(H_3C)_2HC{-}\overset{O}{\overset{\|}{C}}{-}$

Bz :

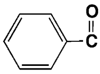


Fig. 1. Isolated compounds from *Hippocratea excelsa* H.B.K.

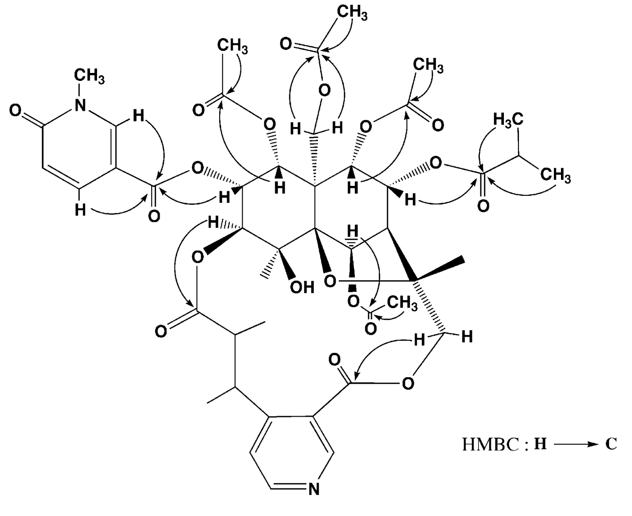


Fig. 2. HMBC correlations of compound **1**.

signal at δ_C 176.3 which in turn correlated with the proton signals (δ_H 1.22, 1.23 and 2.67) due to the isobutyloyl group. The pyridone group could be located at C-2 due to the long-range correlation between δ_H 5.48 (H-2) and the ester carbonyl carbon signal (δ_C 162.5). In addition, the proton signals at δ_H 5.65 (H-1), 7.07 (H-5), 5.43 (H-8) and 4.18, 5.55 (H_b-11) showed a long range correlation with the carbonyl carbon signals of the acetyl groups at δ_C 168.9, 169.9, 168.8 and 171.2, respectively. Furthermore, the HMBC spectrum of **1** showed cross peaks between the proton signal at δ_H 4.78 (H-3) and the signal at δ_C 173.4 (C-11′), and between δ_H 6.06 (H_b-15) and δ_C 168.0 (C-12′), indicating that the 4-(2-carboxy-1-methylpropyl) nicotinic acid moiety should be connected at C-3 and C-15 in β-dihydroagarofuran skeleton.

The relative stereochemistry of the acyloxyl and hydroxyl groups on the β-dihydroagarofuran skeleton were determined by analysis of the NOESY spectrum. In the NOESY spectrum of **1**, correlations were observed between the following proton signals as shown in Fig. 3: δ_H 5.43 (H-8) and δ_H 5.65 (H-1), δ_H 1.74 (H_3-14); δ_H 1.54 (H_3-12) and δ_H 4.78 (H-3), 7.07 (H-5), 5.55 (H_b-11), 8.44 (H-6″); δ_H 2.36 (H-6) and δ_H 7.07 (H-5). These results and the coupling constants of protons on β-dihydroagarofuran skeleton indicated that the relative stereochemistry of the acyloxyl and hydroxyl groups could be assigned to 1α, 2α, 3β, 4β, 5β, 7α, and 8α configurations. Thus, the structure of **1** was confirmed as shown in Fig. 1. The NOESY spectra of all new compounds described in the text showed that the relative stereochemistry on the β-dihydroagarofuran moiety was the same as that of **1**.

Compound **2** had a $[M+H]^+$ ion peak at *m*/*z* 955.3694 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{47}H_{58}N_2O_{19}$. The spectral data were similar to those of **1** except for the presence of another isobutyloyl group in place of an acetyl group. The HMBC spectrum of **2** exhibited cross peaks due to

Table 1
^{1}H NMR chemical shifts for compounds **1**–**7**, **10, 11** (CDC1$_3$, 400 MHz)

Proton	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**10**	**11**
1-H	5 65 (*d*, 4.5)	5 66 (*d*, 4.0)	5.70 (*d*, 4.0)	5.66 (*d*, 4.0)	4.52 (*dd*, 6.0, 4.0)	5.54 (*d*, 4.0)	5.72 (*d*, 4.0)	5.68 (*d*, 4.0)	5.66 (*d*, 4.0)
2-H	5.48 (*dd*, 4.5, 2.5)	5.47 (*dd*, 4.0, 2.5)	5.46 (*dd*, 4.0, 2.5)	5.52–5.56[a]	5.38 (*dd*, 4.0, 2.5)	5.22 (*dd*, 4.0, 2.5)	5.50 (*dd*, 4.0, 2.5)	5.48 (*dd*, 4.0, 2.5)	5.48 (*dd*, 4.0, 2.5)
3-H	4.78 (*d*, 2.5)	4.78 (*d*, 2.5)	4.78 (*d*, 2.5)	4.79 (*d*, 2.5)	4.80 (*d*, 2.5)	4.71 (*d*, 2.5)	4.77 (*d*, 2.5)	4.79 (*d*, 2.5)	4.79 (*d*, 2.5)
4-OH	4.93 (*brs*)	4.92 (*d*, 1.0)	4.91 (*brs*)	6.04[d] (*brs*)	4.76 (*d*, 1.0)	4.86 (*d*, 1.5)	4.86 (*d*, 1.0)	4.58 (*d*, 1.0)	4.59 (*brs*)
5-H	7.07 (*s*)	6.92 (*s*)	6.91 (*s*)	5.59 (*d*, 3.0)	6.74 (*s*)	7.04 (*s*)	6.87 (*s*)	6.89 (*s*)	7.06 (*s*)
6-H	2.36 (*d*, 4.5)	2.39 (*d*, 4.0)	2.37 (*d*, 4.0)	2.47[b]	2.41 (*d*, 4.0)	2.33 (*d*, 4.0)	2.42 (*d*, 4.0)	2.40 (*d*, 4.0)	2.34 (*d*, 4.0)
7-H	5.56 (*dd*, 6.0, 4,5)	5.55 (*dd*, 6.0, 4.0)	5.56 (*dd*, 6.0, 4.0)	5.52–5.56[a]	5.56 (*dd*, 6.0, 4.0)	5.51 (*dd*, 6.0, 4.0)	5.57 (*dd*, 6.0, 4,0)	5.54 (*dd*, 6.0, 4.0)	5.56 (*dd*, 6.0, 4.0)
8-H	5.43 (*d*, 6.0)	5.42 (*d*, 6.0)	5.40 (*d*, 6.0)	5.43 (*d*, 6.0)	5.63 (*d*, 6.0)	5.67 (*d*, 6.0)	5.34 (*d*, 6.0)	5.41 (*d*, 6.0)	5.41 (*d*, 6.0)
11-Ha	4.18 (*d*, 14.0)	4.24 (*d*, 14.0)	4.21 (*d*, 14.0)	4.22 (*d*, 14.0)	4.46 (*d*, 13.0)	4.39 (*d*, 13.5)	4.22 (*d*, 14.0)	4.20 (*d*, 13.5)	4.16 (*d*, 13.5)
11-Hb	5.55 (*d*, 14.0)	5.49 (*d*, 14.0)	5.48 (*d*, 14.0)	5.49 (*d*, 14.0)	5.34 (*d*, 13.0)	5.21 (*d*, 13.5)	5.51 (*d*, 14.0)	5.49 (*d*, 13.5)	5.55 (*d*, 13.5)
12-H$_3$	1.54 (*brs*)	1.53 (*d*, 1.0)	1.54 (*brs*)	1.76 (*brs*)	1.52 (*d*, 1.0)	1.52 (*d*, 1.0)	1.55 (*d*, 1.0)	1.55 (*d*, 1.0)	1.54 (*brs*)
14-H$_3$	1.74 (*brs*)	1.74 (*brs*)	1.73 (*brs*)	1.54 (*brs*)	1.74 (*brs*)	1.71 (*brs*)	1.72 (*brs*)	1.70 (*s*)	1.71 (*brs*)
15-Ha	3.71 (*d*, 12.0)	3.69 (*d*, 12.0)	3,69 (*d*, 12.0)	3.77[c]	3.68 (*d*, 12.0)	3.67 (*d*, 12.0)	3.67 (*d*, 12.0)	3.70 (*d*, 12.0)	3.69 (*d*, 12.0)
15-Hb	6.06 (*d*, 12.0)	6.02 (*d*, 12,0)	5.99 (*d*, 12.0)	6.06[d]	6.00 (*d*, 12.0)	6.02 (*d*, 12.0)	6.02 (*d*, 12.0)	5.94 (*d*, 12,0)	5.98 (*d*, 12.0)
2′-H	9.01 (*s*)	9.00 (*s*)	9.00 (*s*)	9.05 (*s*)	8.99 (*s*)	8.99 (*s*)	8.99 (*s*)		
4′-H								8.07 (*dd*, 8.0, 2.0)	8.07 (*dd*, 8.0, 2.0)
5′-H	7.37 (*d*, 5.5)	7.37 (*d*, 5.0)	7.37 (*d*, 5.0)	7.36 (*d*, 5.0)	7.37 (*d*, 5.0)	7.35 (*d*, 5.0)	7.36 (*d*, 5.0)	7.26 (*dd*, 8.0, 5.0)	7.27 (*dd*, 8.0, 5.0)
6′-H	8.72 (*d*, 5.5)	8.71 (*d*, 5.0)	8.71 (*d*, 5.0)	8.71 (*d*, 5.0)	8.71 (*d*, 5.0)	8.70 (*d*, 5.0)	8.70 (*d*, 5.0)	8.70 (*dd*, 5.0, 2.0)	8.70 (*dd*, 5.0, 2.0)
7′-H	4.71 (*q*, 7.0)	4.69 (*q*, 7.0)	4.70 (*q*, 7.0)	4.78 (*q*, 7.0)	4.66 (*q*, 7.0)	4.68 (*q*, 7.0)	4.67 (*q*, 7.0)	4.66 (*q*, 7.0)	4.65 (*q*, 7.0)
8′-H$_3$	2.47 (*q*, 7.0)	2.45 (*q*, 7.0)	2.46 (*q*, 7.0)	2.46[b]	2.33 (*q*, 7.0)	2.42 (*q*, 7.0)	2.46 (*q*, 7.0)	2.57 (q, 7.0)	2.57 (*q*, 7.0)
9′-H$_3$	1.36 (*d*, 7.0)	1.36 (*d*, 7.0)	1.36 (*d*, 7.0)	1.35 (*d*, 7.0)	1.36 (*d*, 7.0)	1.07 (*d*, 7.0)	1.35 (*d*, 7.0)	1.39 (*d*. 7.0)	1.39 (*d*, 7.0)
10′-H$_3$	1.10 (*d*, 7.0)	1.09 (*d*, 5.0)	1.10 (*d*, 7.0)	1.10 (*d*, 7.0)	1.07 (*d*, 7.0)	1.35 (*d*, 7.0)	1.10 (*d*, 7.0)	1.20 (*d*, 7.0)	1.19 (*d*,7.0)
3″-H	6.59 (*d*, 10.0)	6.58 (*d*, 9.5)	6.59 (*d*, 9.5)	6.59 (*d*, 10.0)	6.56 (*d*, 9.5)		6.59 (*d*, 9.5)	6.59 (*d*, 9.5)	6.58 (*d*, 9.5)
4″-H	7.87 (*dd*, 10.0, 2.5)	7.87 (*dd*, 9.5, 2.5)	7.87 (*dd*, 9.5, 2.5)	7.88 (*dd*, 10.0, 2.5)	7.85 (*dd*, 9.5, 2.5)		7.87 (*dd*, 9.5, 2.5)	7.89 (*dd*, 9.5, 2.5)	7.89 (*dd*, 9.5, 3.0)
6″-H	8.44 (*d*, 2.5)	8.45 (*d*, 2.5)	8.46 (*d*, 2.5)	8.46 (*d*, 2.5)	8.39 (*d*, 2.5)		8.49 (*d*, 2.5)	8.46 (*d*, 2.5)	8.43 (*d*, 3.0)
8″-H	3.72 (*s*)	3.73 (*s*)	3.73 (*s*)	3.74[c] (*s*)	3.70 (*s*)		3.74 (*s*)	3.73 (*s*)	3.72 (*s*)
1-OAc	1.81 (*s*)	1.81 (*s*)	1.82 (*s*)	1.80 (*s*)		1.98 (*s*)		1.82 (*s*)	1.81 (*s*)
1-OiBu							0.93 (*d*, 7.0) 1.01 (*d*, 7.0) 2.17 (*sep*, 7.0)		
1-OH					2.37 (*d*, 6.0)				
2-OAc						1.83 (*s*)			
2-OH									
5-OAc	2.21 (*s*)	2.20 (*s*)	2.19(*s*)		2.19 (*s*)	2.20 (*s*)	2.19 (*s*)	2.21 (*s*)	2.22 (*s*)
5-OH				5.98 (*d*, 3.0)					
7-OAc							2.16 (*s*)	2.17(*s*)	
7-OiBu	1.22 (*d*, 7.0) 1.23 (*d*, 7.0) 2.67 (*sep*, 7.0)	1.20 (*d*, 7.0) 1.24 (*d*, 7.0) 2.66 (*sep*, 7.0)	1.18 (*d*, 7.0) 1.26 (*d*, 7.0) 2.64 (*sep*, 7.0)	1.18 (*d*, 7.0) 1.21 (*d*, 7.0) 2.60 (*sep*, 7.0)	1.20 (*d*, 7.0) 1.25 (*d*, 7.0) 2.67 (*sep*, 7.0)	1.20 (*d*, 7.0) 1.22 (*d*, 7.0) 2.63 (*sep*, 7.0)			1.219 (*d*, 7.0) 1.22 (*d*, 7.0) 2.67 (*sep*, 7.0)
8-OAc	1.97 (*s*)	1.97 (*s*)		1.95 (*s*)		2.16 (*s*)		1.98 (*s*)	1.97 (*s*)
8-OiBu			1.10 (*d*, 7.0) 1.11 (*d*, 7.0) 2.46 (*sep*, 7.0)		1.07 (*d*, 7.0) 1.09 (*d*, 7.0) 2.46 (*sep*, 7.0)		1.09 (*d*, 7.0) 1.11 (*d*, 7.0) 2.48 (*sep*, 7.0)		
11-OAc	2.38 (*s*)					2.32 (*s*)			2.37 (*s*)
11-OiBu		1.24 (*d*, 7.0) 1.29 (*d*, 7.0) 2.93 (*sep*, 7.0)	1.25 (*d*, 7.0) 1.30 (*d*, 7.0) 2.95 (*sep*, 7.0)	1.22 (*d*, 7.0) 1.33 (*d*, 7.0) 2.68 (*sep*, 7.0)	1.16 (*d*, 7.0) 1.23 (*d*, 7.0) 2.82 (*sep*, 7.0)		1.28 (*d*, 7.0) 1.32 (*d*, 7.0) 2.95 (*sep*, 7.0)	1.26 (*d*, 7.0) 1.31 (*d*, 7.0) 2.93 (*sep*, 7.0)	

The values in parentheses represent the coupling constant in Hz.

[a] These signals overlapped respectively.

[b] These signals overlapped respectively.

[c] These signals overlapped respectively.

[d] These signals overlapped respectively.

Table 2
^{1}H NMR chemical shifts for compounds **12**–**19** ($CDCl_3$, 400 MHz)

Proton	**12**	**13**	**14**	**15**[a]	**16**[a]	**17**	**18**	**19**
1-H	5.72 (*d*, 4.0)	4.52 (*m*)	5.79 (*d*, 4.0)	5.68 (*d*, 4.0)	5.70 (*d*, 4.0)	5.72 (*d*, 4.0)	5.71 (*d*, 4.0)	5.72 (*d*, 4.0)
2-H	5.42 (*dd*, 4.0, 2.0)	5.37 (*dd*, 4.0, 2.5)	5.27 (*dd*, 4.0, 2.5)	4.08 (*m*)	5.47 (*dd*, 4.0, 2.5)	5.47 (*dd*, 4.0, 2.5)	5.47 (*dd*, 4.0, 2.5)	5.39 (*dd*, 4.0, 2.5)
3-H	4.78 (*d*, 2.0)	4.80 (*d*, 2.5)	4.76 (*d*, 2.5)	4.79 (*d*, 2.5)	4.90 (*d*, 2.5)	4.91 (*d*, 2.5)	4.90 (*d*, 2.5)	5.00 (*d*, 2.5)
4-OH	4.54 (*brs*)	4.43 (*d*, 1.0)	4.57 (*brs*)	4.52 (*d*, 1.0)	5.08 (*brs*)	5.06 (*brs*)	5.08 (*d*, 1.0)	5.09 (*d*, 1.0)
5-H	6.99 (*s*)	6.95 (*s*)	7.05 (*s*)	7.07 (*s*)	7.04 (*s*)	6.90 (*s*)	6.91 (*s*)	7.01 (*s*)
6-H	2.39 (*d*, 4.0)	2.37 (*d*, 4.0)	2.36 (*d*, 4.5)	2.35 (*d*, 4.0)	2.35 (*d*, 4.0)	2.39 (*d*, 4.0)	2.37 (*d*, 4.0)	2.32–2.35
7-H	5.57 (*dd*, 6.0, 4.0)	5.56 (*dd*, 6.0, 4.0)	5.52 (*dd*, 6.0, 4.5)	5.52 (*dd*, 6.0, 4.0)	5.53 (*dd*, 6.0, 4.0)	5.55 (*dd*, 6.0, 4.0)	5.54 (*dd*, 6.0, 4.0)	5.55 (*dd*, 6.0, 4.0)
8-H	5.34 (*d*, 6.0)	5.60 (*d*, 6.0)	5.40 (*d*, 6.0)	5.38 (*d*, 6.0)	5.41 (*d*, 6.0)	5.41 (*d*, 6.0)	5.41 (*d*, 6.0)	5.42 (*d*, 6.0)
11-Ha	4.23 (*d*, 13.5)	4.32 (*d*, 13.5)	4.53 (*d*, 14.0)	4.68 (*d*, 14.0)	4.15 (*d*, 13.5)	4.19 (*d*, 14.0)	4.24 (*d*, 14.0)	4.15 (*d*, 14.0)
11-Hb	5.50 (*d*, 13.5)	5.35 (*d*, 13.5)	5.25 (*d*, 14.0)	5.39 (*d*, 14.0)	5.51 (*d*, 13.5)	5.51 (*d*, 14.0)	5.50 (*d*, 14.0)	5.53 (*d*, 14.0)
12-H$_3$	1.55 (*brs*)	1.52 (*d*, 1.0)	1.57 (*d*, 1.0)	1.61 (*d*, 1.0)	1.55 (*brs*)	1.56 (*brs*)	1.54 (*d*, 1.0)	1.55 (*d*, 1.0)
14-H$_3$	1.70 (*brs*)	1.70 (*brs*)	1.71 (*brs*)	1.70 (*brs*)	1.69 (*brs*)	1.68 (*brs*)	1.69 (*brs*)	1.69 (*brs*)
15-Ha	3.70 (*d*, 11.5)	3.72 (*d*, 12.0)	3.70 (*d*, 12.0)	3.69 (*d*, 11.5)	3.75 (*d*, 12.0)	3.74 (*d*, 12.0)	3.74 (*d*, 12.0)	3.75 (*d*, 12.0)
15-Hb	5.92 (*d*, 11.5)	5.94 (*d*, 12.0)	5.97 (*d*, 12.0)	5.98 (*d*, 11.5)	5.87 (*d*, 12.0)	5.86 (*d*, 12.0)	5.85 (*d*, 12.0)	5.78 (*d*, 12.0)
4′-H	8.07 (*dd*, 8.0, 2.0)	8.05 (*dd*, 8.0, 2.0)	8.08 (*dd*, 8.0, 2.0)	8.05 (*dd*. 8.0, 2.0)	8.19 (*dd*, 8.0, 2.0)	8.20 (*dd*, 8.0, 2.0)	8.19 (*dd*, 8.0. 2,0)	8.33 (*dd*, 8.0, 2.0)
5′-H	7.28 (*dd*, 8.0, 5.0)	7.28 (*dd*, 8.0, 5.0)	7.28 (*dd*, 8.0, 5.0)	7.25 (*dd*, 8.0, 5.0)	7.30 (*dd*, 8.0, 5.0)	7.31 (*dd*, 8.0, 5.0)	7.30 (*dd*, 8.0, 5.0)	7.27 (*dd*, 8.0, 5.0)
6′-H	8.70 (*dd*, 5.0, 2.0)	8.70 (*dd*, 5.0, 2.0)	8.70 (*dd*, 5.0, 2.0)	8.69 (*dd*, 5.0, 2.0)	8.67 (*dd*, 5.0, 2.0)	8.68 (*dd*, 5.0, 2.0)	8.67 (*dd*, 5.0, 2.0)	8.76 (*dd*, 5.0, 2.0)
7′-Ha	4.65 (*q*, 7.0)	4.60 (*q*, 7.0)	4.67 (*q*, 7.0)	4.65 (*q*, 7.0)	2.78 (*dd*, 13.0, 8.5)	2.81 (*dd*, 14.0, 7.0)	2.78 (*dd*, 13.0, 8.5)	2.91 (*m*)
7′-Hb					4.44 (*d*, 13.0)	4.44 (*d*, 14.0)	4.44 (*d*, 13.0)	3.96 (*m*)
8′-Ha	2.57 (*q*, 7.0)	2.46 (*q*, 7.0)	2.58 (*q*, 7.0)	2.54 (*q*, 7.0)	2.48 (*m*)	2.48 (*m*)	2.48 (*m*)	1.95 (*m*)
8′-Hb								2.32–2.35
9′-H	1.38 (*d*, 7.0)	1.38 (*d*, 7.0)	1.39 (*d*, 7.0)	1.37 (*d*, 7.0)				2.32–2.35
10′-H$_3$	1.21 (*d*, 7.0)	1.19 (*d*, 7.0)	1.19 (*d*, 7.0)	1.15 (*d*, 7.0)	1.35 (*d*, 7.0)	1.36 (*d*, 7.0)	1.35 (*d*, 7.0)	1.18 (*d*, 6.5)
3″-H	6.58 (*d*, 9.5)	6.56 (*d*, 9.5)	6.48 (*d*, 10.0)	6.49 (*d*, 10.0)	6.58 (*d*, 9.5)	6.55 (*d*, 10.0)	6.58 (*d*, 10.0)	6.57 (*d*, 9.5)
4″-H	7.90 (*dd*, 9.5, 2.5)	7.87 (*dd*, 9.5, 2.5)	7.49 (*dd*, 10.0, 2.5)	7.71 (*dd*, 10.0, 2.5)	7.88 (*dd*, 9.5, 2.5)	7.89 (*dd*, 10.0, 2.5)	7.87 (*dd*, 10.0, 2.5)	7.86 (*dd*, 9.5, 2.5)
6″-H	8.43 (*d*, 2.5)	8.41 (*d*, 2.5)	8.07 (*d*, 2.5)	8.11 (*d*, 2.5)	8.42 (*d*, 2.5)	8.46 (*d*, 2.5)	8.45 (*d*, 2.5)	8.43 (*d*, 2.5)
8″-H	3.73 (*s*)	3.70 (*s*)	3.55 (*s*)	3.57 (*s*)	3.72 (*s*)	3.73 (*s*)	3.73 (*s*)	3.71 (*s*)
1-OAc					1.82 (*s*)	1.83 (*s*)	1.82 (*s*)	1.84 (*s*)
1-OiBu	0.93 (*d*, 7.0) 1.00 (*d*, 7.0) 2.19 (*m*)							
1-OH		2.20 (*d*, 5.5)						
2-OAc			2.14 (*s*)					
2-OH				2.71 (*d*, 5.0)				
5-OAc	2.21 (*s*)	2.20 (*s*)	2.22 (*s*)	2.22 (*s*)	2.17 (*s*)	2.18 (*s*)	2.18 (*s*)	2.18 (*s*)
7-OAc	2.17 (*s*)	2.17 (s)	*2.15* (*s*)	2.12 (*s*)	2.19 (*s*)	2.17 (*s*)		2.18 (*s*)
7-OiBu							1.19 (*d*, 7.0) 1.23 (*d*, 7.0) 2.65 (*sep*, 7.0)	
8-OAc			1.70 (*s*)	1.68 (*s*)	1.95 (*s*)	1.98 (*s*)	1.97 (*s*)	1.99 (*s*)
8-OiBu	1.09 (*d*, 7.0) 1.11 (*d*, 7.0) 2.47 (*sep*, 7.0)	1.07 (*d*, 7.0) 1.09 (*d*, 7.0) 2.47 (*sep*, 7.0)						
1l-OAc	2.37 (*s*)	2.32 (*s*)	2.35 (*s*)	2.32 (*s*)	2.37 (*s*)			2.35 (*s*)
11-OiBu						1.16 (*d*, 7.0) 1.23 (*d*, 7.0) 2.82 (*sep*, 7.0)	1.22 (*d*, 7.0) 1.28 (*d*, 7.0) 2.92 (*sep*, 7.0)	

The values in parentheses represent the coupling constant in Hz.

[a] Measurements performed in $CDCl_3$ at 500 MHz.

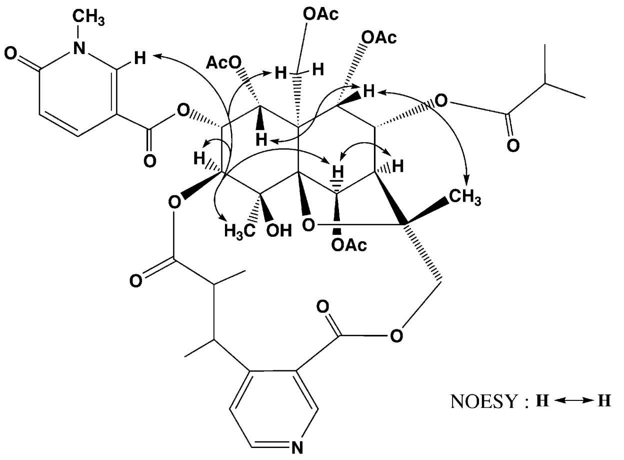


Fig. 3. NOESY correlations of compound **1**.

the long-range correlations between the proton signals at δ_H 5.55 (H-7), 1.20, 1.24, 2.66 and the ester carbonyl carbon signal at δ_C 176.5 $[(CH_3)_2CH\underline{C}OO]$, and between the proton signals at δ_H 5.49 (H_b-11), 1.24, 1.29, 2.93 and the carbonyl carbon signal at δ_C 178.2 $[(CH_3)_2CH\underline{C}OO]$. These correlations indicated that two *O*-isobutyloyl groups should be located at C-7 and 11 positions. Thus the structure of compound **2** was represented as **2** shown in Fig. 1.

Compound **3** gave a $[M+H]^+$ ion peak at *m/z* 983.4015 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{49}H_{62}N_2O_{19}$, and the spectral data were similar to those of **2** except for the presence of an additional isobutyloyl group in place of an acetyl group. The HMBC spectrum of **3** exhibited cross peaks due to the long-range correlations between the proton signals at δ_H 5.40 (H-8), 1.10, 1.11, 2.46 and the ester carbonyl carbon signal at δ_C 174.5 $[(CH_3)_2CH\underline{C}OO]$, between the proton signals at δ_H 5.56 (H-7), 1.18, 1.26, 2.64 and the ester carbonyl carbon signal at δ_C 176.4 $[(CH_3)_2CH\underline{C}OO]$, and between the proton signals at δ_H 5.48 (H_b-11), 1.24, 1.29, 2.95 and the ester carbonyl carbon signal at δ_C 178.2 $[(CH_3)_2CH\underline{C}OO]$. These correlations indicated that three *O*-isobutyloyl groups should be located at C-7, 8 and 11 positions. Therefore, the structure of compound **3** was confirmed as shown in Fig. 1.

Compound **4** had $[M+H]^+$ ion peak at *m/z* 913.3582 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{45}H_{56}N_2O_{18}$, and its molecular weight was 42 mass units (C_2H_2O) lower than that of **2**. The ^1H and ^{13}C NMR spectra of **4** were similar to those of **2**, except for the loss of the signals due to an acetyl group and the large upfield shift of H-5 signal (δ_H 6.92 in **2** and 5.59 in **4**). The HMBC spectrum of **4** exhibited cross peaks due to long-range correlations between the proton signals at δ_H 5.54 (H-7), 1.18, 1.21, 2.60 and the ester carbonyl carbon signal at δ_C 176.4 $[(CH_3)_2CH\underline{C}OO]$, and between the proton signals at δ_H 5.49 (H_b-11), 1.22, 1.33, 2.68 and the ester carbonyl carbon signal at δ_C 177.4 $[(CH_3)_2CH\underline{C}OO]$. These observations indicated that compound **4** should be a hydroxyl derivative at C-5 in **2**.

Compound **5** gave a $[M+H]^+$ ion peak at *m/z* 941.3934 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{47}H_{60}N_2O_{18}$, and the molecular weight was 42 mass unit lower than that of **3**. The ^1H and ^{13}C NMR spectra of **5** were similar to those of **3**, except for the loss of the signals due to an acetyl group and the large upfield shift of H-1 signal (δ_H 5.70 in **3** and 4.52 in **5**). These facts indicated that the C-1 acetoxyl group in **3** must be replaced for a hydroxyl group in **5**.

Compound **6** had a $[M+H]^+$ ion peak at *m/z* 834.3134 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{40}H_{51}NO_{18}$. The UV spectrum of **6** did not show the specific absorption band (269 nm), suggesting the absence of the pyridone moiety. The ^1H and ^{13}C NMR spectra of **6** showed the presence of one isobutyloyl and five acetyl and one isobutyloyl groups. The HMBC spectrum of **6** exhibited cross peaks due to the long-range correlations between the proton signals at δ_H 5.51 (H-7), 1.20, 1.22, 2.63 and the ester carbonyl carbon signal at δ_C 176.4 $[(CH_3)_2CH\underline{C}OO]$. These facts indicated that the compound **6** should have an acetoxyl group in place of the pyridone group at C-2 in **1**.

Compound **7** gave a $[M+H]^+$ ion peak at *m/z* 983.4008 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{49}H_{62}N_2O_{19}$, which was the same to that of **3**. The ^1H and ^{13}C NMR spectra were also very similar to those of **3**, except for signals in the high-field region. The HMBC spectrum of **7** exhibited cross peaks due to long-range correlations between the proton signals at δ_H 5.34 (H-8), 1.09, 1.11, 2.48 and the ester carbonyl carbon signal at δ_C 174.3 $[(CH_3)_2CH\underline{C}OO]$, between the proton signals at δ_H 5.51 (H_b-11), 1.28, 1.32, 2.95 and the ester carbonyl carbon signal at δ_C 178.0 $[(CH_3)_2CH\underline{C}OO]$, and between the proton signals at δ_H 5.72 (H-1), 0.93, 1.01, 2.17 and the ester carbonyl carbon signal at δ_C 175.2 $[(CH_3)_2CH\underline{C}OO]$. These facts indicated that an *O*-isobutyloyl group should be located at the C-1, 8 and 11 positions. Thus, the structure of **7** was confirmed as shown in Fig. 1.

Compounds **8** and **9** were identified to be emarginatine A (Kuo et al., 1989; Mata et al., 1990) and hippocrateine I (Mata et al., 1990), respectively, by comparison of their spectral data with those described in the literature. These compounds contain macrocyclic ring with an evoninate diester bridge between C-3 and 15 position.

Compounds **10** and **11** have the same molecular formula $C_{45}H_{54}N_2O_{19}$ confirmed by their HR–FAB MS spectra (**10**: HR–FAB MS: *m/z* 927.3402 $[M+H]^+$, **11**: HR–FAB MS: *m/z* 927.3381 $[M+H]^+$). The ^1H and ^{13}C NMR spectra of these compounds were very similar to those of **8** except for the presence of an isobutyloyl group in place of an acetyl group. The HMBC spectrum of **10** exhibited cross peaks due to the long-range correlations between the proton signals at δ_H 4.20, 5.49 (H_2-11), 1.26, 1.31, 2.93 and the ester carbonyl carbon signal at δ_C 178.0 [$(CH_3)_2CH\underline{C}OO$]. On the other hand, the HMBC spectrum of **11** exhibited cross peaks between the proton signals at δ_H 5.56 (H-7), 1.22, 1.22, 2.67 and the ester carbonyl carbon signal at δ_C 176.4 [$(CH_3)_2CH\underline{C}OO$]. These facts indicated that the *O*-isobutyloyl group should be located at C-11 position in **10**, and should be located at C-7 position in **11**. The other correlations observed in the HMBC spectra of **10** and **11** were satisfactorily explained by the structures **10** and **11** shown in Fig. 1.

Compound **12** had a $[M+H]^+$ ion peak at *m*/*z* 955.3711 in its HR–FAB MS spectrum corresponding to molecular formula $C_{47}H_{58}N_2O_{19}$. The ^1H and ^{13}C NMR spectra showed the presence of two isobutyloyl groups and three acetyl groups on the β-dihydroagarofuran skeleton. The HMBC spectrum of **12** exhibited cross peaks due to long-range correlations between the proton signals at δ_H 5.72 (H-1), 0.93, 1.00, 2.19 and the ester carbonyl carbon signal at δ_C 175.2 [$(CH_3)_2CH\underline{C}OO$], and between the proton signals at δ_H 5.34 (H-8), 1.09, 1.11, 2.47 and the ester carbonyl carbon signal at δ_C 174.4 [$(CH_3)_2CH\underline{C}OO$]. These facts indicated that an *O*-isobutyloyl group should be located at C-1 and 8 positions. Therefore, the structure of **12** was confirmed as shown in Fig. 1.

Compound **13** gave a $[M+H]^+$ ion peak at *m*/*z* 885.3290 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{43}H_{52}N_2O_{18}$. The ^1H and ^{13}C NMR spectra were very similar to those of **12** except for the loss of an isobutyloyl group. The ^1H NMR spectrum of **13** exhibited the large upfield shift of H-1 signal as compared with that of **12** (δ_H 5.72 in **12** and 4.52 in **13**), suggesting the presence of a hydroxyl group at C-1 position. The HMBC spectrum of **13** exhibited cross peaks between the proton signals at δ_H 5.60 (H-8), 1.07, 1.09, 2.47 and the ester carbonyl carbon signal at δ_C 175.9 [$(CH_3)_2CH\underline{C}OO$]. Thus, the compound **13** should be the hydroxy derivative at C-1 position in **12**.

Compound **14** had a $[M+H]^+$ ion peak at *m*/*z* 899.3078 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{43}H_{50}N_2O_{19}$, which was the same as that of **8**. However, in the ^1H NMR spectrum of **14**, the chemical shifts values of the proton signals due to CNMP moiety [δ_H 6.47 (1H, *d*, $J=10.0$ Hz), 7.49 (1H, *dd*, $J=10.0$, 2.5 Hz), 8.07 (1H, *d*, $J=2.5$ Hz), 3.55 (3H, *s*, *N*-methyl)] were different from those of **8**. Furthermore, the HMBC spectrum of **14** exhibited cross peaks due to the long-range correlations between the proton signal at δ_H 5.79 (H-1) and the ester carbonyl carbon signal at δ_C 162.4 which was correlated with the proton signals at δ_H 7.49 (H-4″) and 8.07 (H-6″). These observations indicated that the *O*-CNMP moiety should be located at C-1 position of β-dihydroagarofuran skeleton. Thus, the structure of **14** was represented as shown in Fig. 1.

Compound **15** gave a $[M+H]^+$ ion peak at *m*/*z* 857.3008 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{41}H_{48}N_2O_{18}$. The ^1H and ^{13}C NMR spectra were very similar to those of **14** except for the loss of an acetyl group. The proton signal due to H-2 showed large upfield shift as compared with that of **14** (δ_H 5.27 in **14** to 4.08 in **15**), and this proton signal correlated with the signal due to hydroxyl group at δ_H 2.71 (1H, *d*, $J=5.0$ Hz) in the ^1H–^1H COSY spectrum. This fact indicated that the C-2 acetoxyl group in **14** was replaced for a hydroxyl group in **15**.

Compound **16** had a molecular ion peak at *m*/*z* 884.2855 in its HR–EI MS spectrum corresponding to the molecular formula $C_{42}H_{48}N_2O_{19}$, which is 14 unit smaller than that of **8**. The ^1H and ^{13}C NMR spectra were similar to those of **8** except for the presence of signals due to a methylene group [δ_H 2.78 (1H, *dd*, $J=13.0$, 8.5 Hz) and 4.44 (1H, *d*, $J=13.0$ Hz), δ_C 40.3] and the loss of a doublet methyl signal (H-9′). The HMBC spectrum of **16** exhibited cross peaks due to the long-range correlations between the proton signal at δ_H 2.78 (H-7′) and the carbon signals at δ_C 124.4 (C-3′) and 174.7 (C-11′). These facts indicated that the secondary methyl group at C-7′ in **8** is replaced for a proton in **16**. Thus, the structure of **16** was confirmed as shown in Fig. 1.

Compound **17** gave a $[M+H]^+$ ion peak at *m*/*z* 913.3250 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{44}H_{52}N_2O_{19}$. The ^1H and ^{13}C NMR spectra were similar to those of **16** except for the presence of an isobutyloyl group in place of an acetyl group. The HMBC spectrum of **17** exhibited cross peaks due to the long-range correlations between the proton signals at δ_H 5.51 (H_b-11), 1.16, 1.23, 2.82 and the ester carbonyl carbon signal at δ_C 178.0 [$(CH_3)_2CH\underline{C}OO$]. These facts indicated that the acetoxyl group at C-11 in **16** must be replaced with an *O*-isobutyloyl group in **17**.

Compound **18** had a $[M+H]^+$ ion peak at *m*/*z* 941.3579 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{46}H_{56}N_2O_{19}$. The ^1H and ^{13}C NMR spectra were similar to those of **17** except for the presence of additional isobutyloyl group in place of an acetyl group. The HMBC spectrum of **18** exhibited cross peaks due to the long-range correlations between the proton signals at δ_H 5.54 (H-7), 1.19, 1.23, 2.65 and the ester carbonyl carbon signal at δ_C 176.6 [$(CH_3)_2CH\underline{C}OO$], and between the proton signals at δ_H 5.50 (H_b-11), 1.22, 1.28, 2.92 and the ester carbonyl carbon signal at δ_C 178.2 [$(CH_3)_2CH\underline{C}OO$]. These facts indicated that the acetoxyl group at C-7 in **17** must be replaced with an *O*-isobutyloyl group in **18**.

Compound **19** gave a $[M+H]^+$ ion peak at *m*/*z* 899.3089 in its HR–FAB MS spectrum corresponding to the molecular formula $C_{43}H_{50}N_2O_{19}$, which was the same as that of **8**. The ^1H and ^{13}C NMR spectra were also similar to those of **8** except for the presence of two sets of methylene groups [δ_H 1.95 (1H, *m*), 2.32–2.35 (1H, overlapping with H-9′) and δ_H 2.91, 3.96 (each 1H, *m*)] and the loss of a secondary methyl group and a methine proton which coupled with the methyl group. The ^1H–^1H COSY spectrum of **19** exhibited the correlation between H_b-8′ [δ_H 2.32–2.35 (1H, overlapping with H-9′)] and H_a-8′ [δ_H 1.95 (1H, *m*)] which correlated with H_a-7′ [δ_H 2.91(1H, *m*)]. The HMBC spectrum of **19** exhibited cross peaks due to long-range correlations between the proton signals at δ_H 1.95 (H_a-8′), 2.91 (H_a-7′) and 3.96 (H_a-7′) with the carbon signal at δ_C 164.4 (C-2′). Furthermore, comparison of the ^1H and ^{13}C NMR spectral data with euonine (Itokawa et al., 1993) and wilforine (Li et al., 1990) suggested that the structure of **19** is a macrocyclic diester derivative as shown in Fig. 1.

3. Experimental

3.1. General

Melting points: Yanagimoto micro melting-point apparatus (uncorr.). ^1H NMR: 400 or 500 MHz, ^{13}C NMR: 100 or 125 MHz using Jeol JNM lambda-400 and 500 spectrometer with $CDCl_3$ as solvent and TMS as int. standard. MS: Jeol JMS-GCMATE. $[\alpha]_D$: JASCO DIP-360 digital polarimeter. UV: Shimadzu UV-160 spectrophotometer. CC: Diaion HP-20 (Nippon Rensui). SiO_2 gel CC: Wakogel C-200 (Wako). TLC: SiO_2 gel 60 F_{254} plates (Merck), and alkaloids were detected by spraying with Dragendorff's reagent. HPLC: normal phase (Shodex SIL-5E, 250×10 mm, Showa Denko), reverse phase [Senshu pak PEGASIL ODS 250×20 mm (A), 250×10 mm (B), Senshu Scientific. CAPCELL PAK C_{18} UG120Å 5 μm 250×20 mm (C), 250×10 mm (D), CAPCELL PAK Ph UG120Å 5 μm 250×10 mm (E), Shiseido].

3.2. Plant material

The plant material was identified by Dr. G. O. Calderón (Herbario Nacional de Mexico, Instituto de Biologia, UNAM) and herbarium specimens have been deposited at the Instituto de Biologia, UNAM and the herbarium of College of Pharmacy, Nihon University, respectively.

3.3. Extraction and isolation

The dried stem barks of *Hippocratea excelsa* H.B.K (1 kg, purchased in Mexico City) was crushed and extracted ultrasonically with *n*-hexane (6 l) and 70% aq. EtOH (15 l), successively. The 70% aq. EtOH extracts were concd. in vacuo to give a crude extract (104 g). The crude extract was subjected on Diaion HP-20 CC (1.5 l) and eluted with water (4 l), 40% MeOH (6 l), 70% MeOH (7 l), MeOH (7 l), and acetone (6 l), respectively. The MeOH fraction was concd in vacuo to give the MeOH eluate (30 g). The MeOH eluate (29 g) was subjected to CC SiO_2 gel eluting successively with solvent of increasing polarity [*n*-hexane:EtOAc = 1:3 (frs. 1–4), 1:4 (fr. 5), EtOAc (fr. 6), MeOH (fr. 7), 50% aq. Me_2CO (fr. 8) and H_2O (fr. 9)] to give 9 fractions. Fr. 4 (1.3 g) was separated by reverse phase (rp)-HPLC (system C, 70% MeOH) to give 17 fractions (fr. 10–26). Fr. 14 was purified by rp-HPLC (system E, 45% CH_3CN) to give **13** (11 mg) and **8** (3.7 mg). Fr. 15 was separated by rp-HPLC (system E, 50% CH_3CN) to give 5 fractions (frs. 27–31), whereas fr. 31 was purified using rp-HPLC (system E, 45% CH_3CN) to give **6** (9.1 mg). Frs. 17, 19, and 24 were purified by rp-HPLC (system E, 50% CH_3CN) to give from: fr. 17, compound **10** (36.5 mg), fr. 19, compound **9** (25.3 mg), and fr. 24, compounds **5** (9.0 mg) and **12** (11.1 mg). Fr. 18 was purified by rp-HPLC (system E, 43% CH_3CN) to give **11** (10.2 mg) and **18** (4.2 mg), whereas fr. 5 (1.6 g) was separated by normal phase HPLC (*n*-hexane:EtOAc = 1:4) to give 8 fractions (frs. 32–39). Of these, fr. 34 was purified by rp-HPLC (system B, 70% MeOH) to give **3** (8 mg). Fr. 35 was purified by rp-HPLC (system B, 65% MeOH) to give **2** (77 mg), **4** (8 mg) and **7** (11 mg). Fr. 6 (1.0 g) was separated by rp-HPLC (system A, 70% MeOH) to give 15 fractions (frs. 40–54). Frs. 41 and 42 were purified by rp-HPLC (system B, 55% MeOH). Fr. 41 gave **15** (7 mg) and **16** (3 mg), and fr. 42 gave **14** (20 mg). Frs. 44 and 49 were purified by rp-HPLC (system B, 60% MeOH). Fr. 44 gave **17** (30.4 mg), and fr. 49 gave **1** (10 mg). Fr. 7 (7.1 g) was applied to a HP-20 column eluted with H_2O, 20, 40, 60, 80, 100% MeOH, and Me_2CO, to give 7 fractions (frs. 55–61). Fr. 61 (1.9 g) was separated by rp-HPLC (system C, 60% MeOH) to give 17 fractions (fr. 62∼78). Fr. 69 was purified by rp-HPLC (system D, 55% MeOH) to give **19** (13 mg).

3.4. 1,5,8,11-Tetraacetoxy-2-(5′-carboxy-N-methyl-pyridonyl)-4-hydroxy-7-isobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (1)

Colorless powder, mp: 189–196 °C; $[\alpha]_D$ +2.3° ($CHCl_3$, *c* 1.10); UV λ_{max} nm (log ε): 269 (3.97); HR–EIMS: *m*/*z* 926.3321 $[M]^+$ (calc. for $C_{45}H_{54}N_2O_{19}$, requires 926.3320); for ^1H: and ^{13}C NMR spectra data, see Tables 1 and 3.

3.5. 1,5,8-Triacetoxy-2-(5′-carboxy-N-methyl-pyridonyl)-4-hydroxy-7,11-diisobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (2)

Colorless powder, mp: 179–187 °C; $[\alpha]_D$ +6.6° ($CHCl_3$, *c* 1.10); UV λ_{max} nm (log ε): 269 (4.39); HR–FAB MS: *m*/*z* 955.3694 $[M+H]^+$ (calc. for

Table 3
^{13}C NMR chemical shifts for compounds **1**–**7**, **10**, **11** (100 MHz, $CDCl_3$)

Carbon	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**10**	**11**
1	73.2 *d*	73.2 *d*	73.0 *d*	73.2 *d*	72.9 *d*	73.5 *d*	72.6 *d*	73.0 *d*	73.1 *d*
2	69.1 *d*	68.9 *d*	69.2 *d*	68.9 *d*	72.6 *d*	68.7 *d*	69.0 *d*	69.3 *d*	69.2 *d*
3	75.7 *d*	75.7 *d*	75.7 *d*	75.1 *d*	75.8 *d*	75.9 *d*	75.5 *d*	75.5 *d*	75.5 *d*
4	70.5 *s*	70.5 *s*	70.5 *s*	72.2 *s*	70.5 *s*	70.8 *s*	70.4 *s*	70.3 *s*	70.3 *s*
5	73.6 *d*	74.0 *d*	74.0 *d*	74.5 *d*	74.1 *d*	73.8 *d*	73.8 *d*	74.0 *d*	73.7 *d*
6	50.7 *d*	50.6 *d*	50.7 *d*	52.0 *d*	50.6 *d*	50.6 *d*	50.6 *d*	50.6 *d*	50.6 *d*
7	68.2 *d*	69.2 *d*	68.5 *d*	68.6 *d*	69.2 *d*	68.5 *d*	68.7 *d*	68.9 *d*	68.2 *d*
8	70.6 *d*	70.6 *d*	70.3 *d*	70.8 *d*	71.7 *d*	70.7 *d*	70.3 *d*	70.4 *d*	70.6 *d*
9	51.9 *s*	51.8 *s*	52.3 *s*	50.9 *s*	52.0 *s*	51.9 *s*	52.6 *s*	52.1 *s*	51.9 *s*
10	94.1 *s*	93.9 *s*	93.9 *s*	92.7 *s*	93.8 *s*	94.2 *s*	94.0 *s*	93.8 *s*	93.9 *s*
11	60.4 *t*	60.9 *t*	60.7 *t*	60.8 *t*	61.8 *t*	60.2 *t*	60.8 *t*	60.6 *t*	60.4 *t*
12	23.0 *q*	22.9 *q*	23.1 *q*	22.8 *q*	23.2 *q*	22.7 *q*	23.3 *q*	23.3 *q*	23.1 *q*
13	84.4 *s*	84.7 *s*	84.2 *s*	84.7 *s*	84.4 *s*	84.4 *s*	84.1 *s*	84.2 *s*	84.3 *s*
14	18.8 *q*	18.5 *q*	18.5 *q*	18.7 *q*	18.6 *q*	18.5 *q*	18.5 *q*	18.6 *q*	18.6 *q*
15	70.1 *t*	70.1 *t*	70.0 *t*	70.9 *t*	70.2 *t*	70.1 *t*	69.9 *t*	69.8 *t*	69.8 *t*
2′	150.9 *d*	150.9 *d*	150.9 *d*	151.4 *d*	150.8 *d*	150.4 *d*	150.9 *d*	165.3 *s*	165.4 *s*
3′	125.2 *s*	125.1 *s*	125.2 *s*	124.6 *s*	125.2 *s*	125.2 *s*	125.2 *s*	125.0 *s*	125.0 *s*
4′	156.4 *s*	156.4 *s*	156.4 *s*	156.6 *s*	156.2 *s*	156.4 *s*	156.3 *s*	137.8 *d*	137.8 *d*
5′	121.5 *d*	121.5 *d*	121.5 *d*	121.4 *d*	121.7 *d*	121.5 *d*	121.4 *d*	121.1 *d*	121.1 *d*
6′	153.0 *d*	152.9 *d*	152.9 *d*	153.2 *d*	152.9 *d*	152.9 *d*	152.9 *d*	151.5 *d*	151.6 *d*
7′	33.2 *d*	33.2 *d*	33.2 *d*	33.0 *d*	33.4 *d*	33.2 *d*	33.2 *d*	36.4 *d*	36.4 *d*
8′	45.7 *d*	45.6 *d*	45.6 *d*	45.9 *d*	45.7 *d*	45.7 *d*	45.6 *d*	44.9 *d*	45.0 *d*
9′	11.3 *q*	11.3 *q*	11.3 *q*	11.1 *q*	11.4 *q*	11.3 *q*	11.3 *q*	11.9 *q*	11.8 *q*
10′	10.0 *q*	9.9 *q*	10.0 *q*	9.8 *q*	9.6 *q*	9.8 *q*	10.0 *q*	9.7 *q*	9.7 *q*
11′	173.4 *s*	173.4 *s*	173.5 *s*	173.2 *s*	173.4 *s*	173.6 *s*	173.4 *s*	173.9 *s*	173.9 *s*
12′	168.0 *s*	168.0 *s*	168.0 *s*	168.5 *s*	168.0 *s*	168.0 *s*	168.0 *s*	168.5 *s*	168.5 *s*
2″	163.0 *s*	163.0 *s*	162.9 *s*	162.9 *s*	162.9 *s*		163.0 *s*	163.0 *s*	163.0 *s*
3″	119.8 *d*	119.8 *d*	119.8 *d*	119.9 *d*	119.8 *d*		119.9 *d*	119.8 *d*	119.8 *d*
4″	138.9 *d*	138.9 *d*	139.0 *d*	138.9 *d*	138.8 *d*		138.9 *d*	139.0 *d*	139.0 *d*
5″	108.1 *s*	108.3 *s*	108.1 *s*	108.0 *s*	108.2 *s*		108.0 *s*	108.2 *s*	108.1 *s*
6″	144.1 *d*	144.1 *d*	144.2 *d*	144.1 *d*	144.3 *d*		144.0 *d*	144.1 *d*	144.1 *d*
7″	162.5 *s*	162.5 *s*	162.5 *s*	162.5 *s*	163.5 *s*		162.4 *s*	162.5 *s*	162.5 *s*
8″	38.1 *q*	38.0 *q*	38.1 *q*	38.1 *q*	38.1 *q*		38.0 *q*	38.0 *q*	38.1 *q*
l-OAc	20.4 *q*	20.4 *q*	20.6 *q*	20.4 *q*		20.5 *q*		20.4 *q*	20.4 *q*
	168.9 *s*	168.9 *s*	169.0 *s*	168.9 *s*		168.8 *s*		169.0 *s*	168.9 *s*
1-OiBu							17.9 *q*		
							19.1 *q*		
							33.7 *d*		
							175.2 *s*		
2-OAc						20.4 *q*			
						169.1 *s*			
5-OAc	21.6 *q*	21.6 *q*	21.6 *q*		21.6 *q*	21.6 *q*	21.6 *q*	21.6 *q*	21.7 *q*
	169.9 *s*	169.7 *s*	169.7 *s*		169.7 *s*	169.8 *s*	169.8 *s*	169.8 *s*	169.9 *s*
7-OAc							21.1 *q*	20.9 *q*	
							169.9 *s*	170.1 *s*	
7-OiBu	18.5 *q*	19.4 *q*	18.7 *q*	18.6 *q*	19.0 *q*	18.8 *q*			18.7 *q*
	19.3 *q*	19.9 *q*	19.3 *q*	19.4 *q*	19.1 *q*	19.2 *q*			19.3 *q*
	34.1 *d*	34.0 *d*	34.0 *d*	34.2 *d*	34.0 *d*	34.1 *d*			34.1 *d*
	176.3 *s*	176.5 *s*	176.4 *s*	176.4 *s*	176.3 *s*	176.4 *s*			176.4 *s*
8-OAc	20.5 *q*	20.5 *q*		20.5 *q*		21.0 *q*		20.5 *q*	20.5 *q*
	168.8 *s*	168.8 *s*		168.8 *s*		168.7 *s*		168.9 *s*	168.8 *s*
8-OiBu			18.5 *q*		18.6 *q*		18.1 *q*		
			19.6 *q*		18.7 *q*		18.8 *q*		
			33.8 *d*		34.1 *d*		33.9 *d*		
			174.5 *s*		176.0 *s*		174.3 *s*		
1l-OAc	21.2 *q*					21.1 *q*			21.2 *q*
	171.2 *s*					170.5 *s*			171.2 *s*
11-OiBu		19.3 *q*	18.8 *q*	18.8 *q*	19.2 *q*		19.0 *q*	19.0 *q*	
		19.3 *q*	19.2 *q*	19.5 *q*	19.3 *q*		19.7 *q*	19.7 *q*	
		34.0 *d*	34.0 *d*	34.2 *d*	34.0 *d*		34.0 *d*	34.0 *d*	
		178.2 *s*	178.2 *s*	177.4 *s*	177.6 *s*		178.0 *s*	178.0 *s*	

Multiplicities were obtained from DEPT spectra.

$C_{47}H_{59}N_2O_{19}$, requires 955.3711); for ^1H and ^{13}C NMR spectal data, see Tables 1 and 3.

*3.6. 1,5-Diacetoxy-2-(5′-carboxy-N-methylpyridonyl)-4-hydroxy-7,8,11-triisobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (**3**)*

Colorless powder, mp: 186–190 °C; $[\alpha]_D$ −18.6° ($CHCl_3$, *c* 0.86); UV λ_{max} nm (log ε): 268 (3.83); HR–FAB MS: *m*/*z* 983.4015 $[M+H]^+$ (calc. for $C_{49}H_{63}N_2O_{19}$, requires 983.4024); for ^1H: and ^{13}C NMR spectral data, see Tables 1 and 3.

*3.7. 1,8-Diacetoxy-2-(5′-carboxy-N-methylpyridonyl)-4,5-dihydroxy-7,11-diisobutyl-oyloxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (**4**)*

Colorless powder, mp: 171–176 °C; $[\alpha]_D$ +12.5° ($CHCl_3$, *c* 0.73); UV λ_{max} nm (log ε): 270 (4.44); HR–FAB MS: *m*/*z* 913.3582 $[M+H]^+$ (calc. for $C_{45}H_{57}N_2O_{18}$, requires 913.3606); ^1H and ^{13}C NMR spectral data, see Tables 1 and 3.

*3.8. 5-Acetoxy-2-(5′-carboxy-N-methylpyridonyl)-1,4-dihydroxy-7,8,11-triisobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (**5**)*

Colorless powder, mp: 189–194 °C; $[\alpha]_D$ −21.7° ($CHCl_3$, *c* 0.90); UV $\lambda?_{max}$ nm (log ε):269 (4.38); HR–FAB MS:*m*/*z* 941.3934 $[M+H]^+$ (calc. for $C_{47}H_{61}N_2O_{18}$, requires 941.3919); ^1H NMR: and ^{13}C NMR: spectral data, see Tables 1 and 3.

*3.9. 1,2,5,8,11-Pentaacetoxy-4-hydroxy-7-isobutyl-oyloxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)-propanoic acid]dicarbolactone-dihydroagarofuran (**6**)*

Colorless powder, mp: 162–164 °C; $[\alpha]_D$ −36.8° ($CHCl_3$, *c* 0.50); UV λ_{max} nm (log ε):266 (3.46), 242 (3.52); HR–FAB MS *m*/*z* 834.3184 $[M+H]^+$ (calc. for $C_{40}H_{52}NO_{18}$, requires 834.3184); for ^1H and ^{13}C NMR spectral data, see Tables 1 and 3.

3.10. 5,7-Diacetoxy-2-(5′-carboxy-N-methylpyridonyl)-4-hydroxy-1,8,11-triiso-butyloyloxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-4″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (7)

Colorless powder, mp: 206–210 °C; $[\alpha]_D$ −16.0° ($CHCl_3$, *c* 1.09); UV $\lambda?_{max}$ nm (log ε):268 (4.35); HR–FAB MS *m*/*z* 983.4008 $[M+H]^+$ (calc. for $C_{49}H_{63}N_2O_{19}$, requires 983.4024); for ^1H NMR: and ^{13}C NMR spectral data, see Tables 1 and 3.

*3.11. 1,5,7,8-Tetraacetoxy-2-(5′-carboxy-N-methyl-pyridonyl)-4-hydroxy-11-isobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (**10**)*

Colorless powder, mp: 246–249 °C; $[\alpha]_D$ +15.5° ($CHCl_3$, *c* 3.05); UV λ_{max}nm (log ε): 268 (4.34); HR–FAB MS *m*/*z* 927.3402 $[M+H]^+$ (calc. for $C_{45}H_{55}N_2O_{19}$, requires 927.3398); for ^1H and ^{13}C NMR spectral data, see Tables 1 and 3.

*3.12. 1,5,8,11-Tetracetoxy-2-(5′-carboxy-N-methyl-pyridonyl)-4-hydroxy-7-isobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (**11**)*

Colorless powder, mp: 300–307 °C; $[\alpha]_D$ +15.3° ($CHCl_3$, *c* 0.99); UV λ_{max} nm (log ε): 268 (4.30); HR–FAB MS *m*/*z* 927.3381 $[M+H]^+$ (calc. for $C_{45}H_{55}N_2O_{19}$, requires 927.3398); for ^1H and ^{13}C NMR spectral data, see Tables 1 and 3.

*3.13. 5,7,11-Triacetoxy-2-(5′-carboxy-N-methyl-pyridonyl)-4-hydroxy-1,8-diisobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (**12**)*

Colorless powder, mp: 177–183 °C; $[\alpha]_D$ −2.3° ($CHCl_3$, *c* 0.89); UV λ_{max}nm (log ε): 268 (4.37); HR–FAB MS *m*/*z* 955.3711 $[M+H]^+$ (calc. for $C_{47}H_{59}N_2O_{19}$, requires 955.3711); for ^1H and ^{13}C NMR: spectral data, see Tables 2 and 4.

*3.14. 5,7,11-Triacetoxy-2-(5′-carboxy-N-methyl-pyridonyl)-1,4-dihydroxy-8-isobutyl-oyloxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]-dicarbolactone-dihydroagarofuran (**13**)*

Colorless powder, mp: 194–198 °C; $[\alpha]_D$ −4.3° ($CHCl_3$, *c* 1.00); UV λ_{max} nm (log ε): 269 (4.31); HR–FAB MS *m*/*z* 885.3290 $[M+H]^+$ (calc. for $C_{43}H_{53}N_2O_{18}$, requires 885.3293); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

*3.15. 2,5,7,8,11-Pentaacetoxy-1-(5′-carboxy-N-methyl-pyridonyl)-4-hydroxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (**14**)*

Colorless powder, mp: 154–178 °C; $[\alpha]_D$ −11.6° ($CHCl_3$, *c* 0.70); UV λ_{max} nm (log ε): 268 (4.10); HR–FAB MS *m*/*z* 899.3078 $[M+H]^+$ (calc. for $C_{43}H_{51}N_2O_{19}$, requires 899.3085); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

Table 4
^{13}C NMR chemical shifts for compounds **12**–**19** (100 MHz, $CDC1_3$)

Carbon	**12**	**13**	**14**	**15**[a]	**16**[a]	**17**	**18**	**19**
1	72.6 *d*	72.5 *d*	73.7 *d*	*75.5 d*	73.1 *d*	73.1 *d*	73.4 *d*	73.2 *d*
2	69.2 *d*	72.5 *d*	69.1 *d*	69.9 *d*	69.5 *d*	69.6 *d*	69.6 *d*	69.8 *d*
3	75.4 *d*	75.7 *d*	75.7 *d*	78.3 *d*	*75.5 d*	75.5 *d*	75.6 *d*	75.7 *d*
4	70.3 *s*	70.2 *s*	70.5 *s*	70.5 *s*	70.5 *s*	70.6 *s*	70.6 *s*	69.6 *s*
5	73.7 *d*	73.8 *s*	73.7 *d*	73.8 *d*	73.6 *d*	73.9 *d*	74.1 *d*	73.5 *d*
6	50.6 *d*	50.6 *s*	50.5 *d*	50.4 *d*	50.8 *d*	50.8 *d*	50.8 *d*	51.3 *d*
7	68.7 *d*	69.2 *d*	68.8 *d*	68.8 *d*	68.8 *d*	68.9 *d*	68.5 *d*	68.9 *d*
8	70.5 *d*	71.2 *d*	71.2 *d*	71.5 *d*	70.5 *d*	70.5 *d*	70.9 *d*	70.6 *d*
9	52.6 *s*	52.4 *s*	52.4 *s*	52.8 *s*	52.0 *s*	52.1 *s*	51.9 *s*	52.1 *s*
10	93.9 *s*	93.8 *s*	94.1 *s*	94.5 *s*	94.1 *s*	93.9 *s*	93.9 *s*	93.8 *s*
11	60.7 *t*	60.7 *t*	59.8 *t*	60.2 *t*	60.3 *t*	60.6 *t*	60.7 *t*	60.3 *t*
12	23.4 *q*	22.3 *q*	22.9 *q*	23.0 *q*	23.0 *q*	23.1 *q*	22.9 *q*	23.0 *q*
13	84.1 *s*	84.1 *s*	84.4 *s*	84.2 *s*	84.5 *s*	84.4 *s*	84.5 *s*	84.5 *s*
14	18.6 *q*	18.5 *q*	18.4 *q*	18.4 *q*	18.3 *q*	18.4 *q*	18.3 *q*	18.0 *q*
15	69.7 *t*	69.9 *t*	69.9 *t*	70.0 *t*	70.3 *t*	70.3 *t*	70.3 *t*	70.3 *t*
2′	165.4 *s*	165.1 *s*	165.3 *s*	165.1 *s*	163.3 *s*	163.2 *s*	163.2 *s*	164.4 *s*
3′	125.0 *s*	125.2 *s*	125.0 *s*	125.3 *s*	124.4 *s*	124.5 *s*	124.5 *s*	124.2 *s*
4′	137.8 *d*	137.7 *d*	137.8 *d*	137.7 *d*	138.4 *d*	138.4 *d*	138.4 *d*	138.7 *d*
5′	121.1 *d*	121.2 *d*	121.1 *d*	121.1 *d*	121.7 *d*	121.6 *d*	121.6 *d*	121.2 *d*
6′	151.6 *d*	151.5 *d*	151.5 *d*	151.4 *d*	152.1 *d*	152.1 *d*	152.1 *d*	153.3 *d*
7′	36.4 *d*	36.5 *d*	36.4 *d*	36.4 *d*	40.3 *t*	40.2 *t*	40.3 *t*	33.3[a] *t*
8′	44.9 *d*	45.0 *d*	45.0 *d*	45.0 *d*	42.5 *d*	42.4 *d*	42.4 *d*	33.3[a] *t*
9′	12.0 *q*	11.9 *q*	11.9 *q*	11.9 *q*				38.3 *d*
10′	9.7 *q*	9.7 *q*	9.8 *q*	9.4 *q*	17.6 *q*	17.6 *q*	17.6 *q*	18.9 *q*
11′	173.8 *s*	173.8 *s*	174.0 *s*	174.6 *s*	174.7 *s*	174.7 *s*	174.7 *s*	175.1 *s*
12′	168.5 *s*	168.5 *s*	168.5 *s*	168.5 *s*	167.9 *s*	167.9 *s*	167.9 *s*	166.8 *s*
2″	163.0 *s*	163.0 *s*	162.4 *s*	162.6 *s*	163.0 *s*	163.0 *s*	163.0 *s*	163.0 *s*
3″	119.9 *d*	119.8 *d*	119.5 *d*	119.6 *d*	119.8 *d*	119.8 *d*	119.8 *d*	119.8 *d*
4″	138.9 *d*	138.9 *d*	137.3 *d*	138.0 *d*	138.9 *d*	138.9 *d*	138.9 *d*	138.8 *d*
5	108.2 *s*	108.3 *s*	108.4 *s*	108.6 *s*	108.1 *s*	108.1 *s*	108.1 *s*	108.1 *s*
6″	143.9 *d*	144.2 *d*	144.6 *d*	144.2 *d*	144.1 *d*	144.2 *d*	144.2 *d*	144.1 *d*
7″	162.3 *s*	163.6 *s*	162.6 *s*	162.6 *s*	162.6 *s*	162.6 *s*	162.4 *s*	162.6 *s*
8″	38.2 *q*	38.2 *q*	38.4 *q*	38.4 *q*	38.2 *q*	38.1 *q*	38.0 *q*	38.2 *q*
1-OAc					20.4 *q* 168.9 *s*	20.4 *q* 168.9 *s*	20.5 *q* 168.8 *s*	20.5 *q* 169.1 *s*
1-OiBu	18.0 *q* 19.2 *q* 33.7 *d* 175.2 *s*							
2-OAc			20.9 *q* 167.0 *s*					
5-OAc	21.6 *q* 170.0 *s*	21.6 *q* 167.0 *s*	21.6 *q* 169.9 *s*	21.7 *q* 169.9 *s*	21.1 *q* 169.9 *s*	21.6 *q* 169.7 *s*	21.6 *q* 169.7 *s*	21.1 *q* 167.0 *s*
7-OAc	21.2 *q* 169.8 *s*	21.1 *q* 169.9 *s*	21.0 *q* 168.5 *s*	20.9 *q* 170.1 *s*	21.6 *q* 170.0 *s*	20.9 *q* 170.1 *s*		21.6 *q* 170.0 *s*
7-OiBu							18.9 *q* 19.5 *q* 34.0 *d* 176.6 *s*	
8-OAc			20.4 *q* 168.9 *s*	20.4 *q* 169.0 *s*	20.5 *q* 169.0 *s*	20.5 *q* 169.0 *s*	20.4 *q* 168.9 *s*	20.5 *q* 169.0 *s*
8-OiBu	18.2 *q* 18.9 *q* 33.9 *d* 174.4 *s*	18.5 *q* 18.7 *q* 34.0 *d* 175.9 *s*						
11-OAc	21.2 *q* 171.0 *s*	21.3 *q* 170.9 *s*	21.4 *q* 170.3 *s*	21.5 *q* 170.2 *s*	21.3 *q* 171.0 *s*			21.3 *q* 171.0 *s*
11-OiBu						19.0 *q* 19.7 *q* 34.0 *d* 178.0 *s*	19.3 *q* 19.3 *q* 34.0 *d* 178.2 *s*	

Multiplicities were obtained from DEPT spectra.

[a] Measurements performed in $CDCl_3$ at 125 MHz.

*3.16. 5,7,8,11-Tetraacetoxy-1-(5′-carboxy-N-methylpyridonyl)-2,4-dihydroxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (**15**)*

Colorless powder, mp: 192–199 °C; $[\alpha]_D$ −22.8° ($CHCl_3$, *c* 0.29); UV λ_{max} nm (log ε): 268 (4.34); HR–FAB MS *m/z* 857.3008 $[M+H]^+$ (calc. for $C_{41}H_{49}N_2O_{18}$, requires 857.2980); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

*3.17. 1,5,7,8,11-Pentaacetoxy-2-(5′-carboxy-N-methylpyridonyl)-4-hydroxy-3,15-[2′-methyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (**16**)*

Colorless powder, mp: 177–184 °C; $[\alpha]_D$ +1.8° ($CHCl_3$, *c* 0.66); UV λ_{max}nm (log ε): 269 (4.43); HR–EI MS *m/z* 884.2855 $[M]^+$ (calc. for $C_{42}H_{48}N_2O_{19}$, requires 884.2850); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

*3.18. 1,5,7,8-Tetraacetoxy-2-(5′-carboxy-N-methylpyridonyl)-4-hydroxy-11-isobutyloyl-oxy-3,15-[2′-methyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]-dicarbolactone-dihydro-agarofuran (**17**)*

Colorless powder, mp: 178–192 °C; $[\alpha]_D$ +4.2° ($CHCl_3$, *c* 0.70); UV λ_{max}nm (log ε): 269 (4.39); HR–FAB MS *m/z* 913.3250 $[M+H]^+$ (calc. for $C_{44}H_{53}N_2O_{19}$, requires 913.3242); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

*3.19. 1,5,8-Triacetoxy-2-(5′-carboxy-N-methylpyridonyl)--4-hydroxy-7,11-diisobutyloyl-oxy-3,15-[2′,3′-dimethyl-3′(3″-carboxy-2″-pyridyl)propanoic acid]dicarbolactone-dihydroagarofuran (**18**)*

Colorless powder, mp: 161–164 °C; $[\alpha]_D$ +2.6° ($CHCl_3$, *c* 0.39); UV λ_{max} nm (log ε): 268.5 (4.33); HR–FAB MS *m/z* 941.3579 $[M+H]^+$ (calc. for $C_{46}H_{57}N_2O_{19}$, requires 941.3555); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

*3.20. 1,5,7,8,11-Pentaacetoxy-2-(5′-carboxy-N-methylpyridonyl)-4-hydroxy-3,15-[2′-methyl-4′(3″-carboxy-2″-pyridyl)butanoic acid]dicarbolactone-dihydroagarofuran (**19**)*

Colorless powder, mp: 178–182 °C; $[\alpha]_D$ +23.6° ($CHCl_3$, *c* 1.00); UV λ_{max} nm (log ε): 269 (4.30); HR–FAB MS *m/z* 899.3089 $[M+H]^+$ (calc. for $C_{43}H_{51}N_2O_{19}$, requires 899.3085); for ^1H and ^{13}C NMR spectral data, see Tables 2 and 4.

References

Itokawa, H., Shirota, O., Morita, H., Tanaka, K., Iitaka, Y., 1993. Isolation, structural elucidation and conformational analysis of sesquiterpene pyridine alkaloids from *Maytenus ebenifolia*. J. Chem. Soc. Perkin Trans. 1, 1247.

Kuo, Y.H., Chen, C.H., Kuo, Y.L.M., King, M.L., Wu, T.S., Lu, S.T., Chen, I.S., McPhail, A.T., Lee, K.H., 1989. Structure and stereochemistry of emarginatine-A, a novel cytotoxic sesquiterpene pyridine alkaloid from *Maytenus Emarginata*: X-ray crystal structure of emarginatine-A monohydrate. Heterocycles 29, 1465.

Li, Y., Strunz, G.M., Calhoun, L.A., 1990. Sesquiterpene alkaloids from *Triptrerygium wilfordii* (Hook): a nuclear magnetic resonance study of 1-desacetylwilfordine, 1-desacetylwilfortine, and 2-debenzoyl-2-nicotinoylwilforine. Can. J. Chem. 68, 371.

Mata, R., Calzada, F., Diaz, E., Toscano, R.A., 1990. Chemical studies on Mexican plant used in traditional medicine, XV. Sesquiterpene evoninoate alkaloids from *Hippocratea excelsa*. J. Nat. Prod. 53, 1212.

Mata, R., Calzada, F., 1995. Hippocrateine III, a sesquiterpene alkaloid from *Hippocratea excelsa*. Phytochemistry 40, 583.

Palacios, J., Mata, R., Lopez, R., Bye, R., Linares, E., 1989. *Hippocratea excelsa* (Hippocrateaceae), a new source of *trans* polyisoprene. Economic Botany 43, 508.