HETEROCYCLES, Vol. 96, No. 9, 2018, pp. 1583 - 1591. © 2018 The Japan Institute of Heterocyclic Chemistry
Received, 12th July, 2018, Accepted, 1st August, 2018, Published online, 20th August, 2018
DOI: 10.3987/COM-18-13960

THREE NEW 5,6-DIHYDRO-α-PYRONES ISOLATED FROM *CRYPTOCARYA NITENS*

Koki Mori,[1,2] Aiko Shimogomi,[1] Naohito Abe,[1] Manami Haba,[1] Tomoaki Yoshimura,[2] Joko Ridho Witono,[3] Dedy Darnaedi,[4] Toshiyuki Tanaka,[5] Jin Murata,[6] and Masayoshi Oyama[1*]

[1] Laboratory of Pharmacognosy, Gifu Pharmaceutical University, 1-25-4 Daigaku-Nishi, Gifu 501-1196, Japan. [2] Department of Pharmacy, Ogaki Municipal Hospital, 4-86 Minaminokawa-Cho, Ogaki, Gifu 503-0864, Japan. [3] Center for Plant Conservation, Bogor Botanical Garden, Indonesian Institute of Sciences (LIPI), Jalan Ir. H. Juanda 13, Bogor 16122, Indonesia. [4] Faculty of Biology, Universitas Nasional, Jakarta, Jalan Sawo Manila No 61, Pejaten, Pasar Minggu, Jakarta Selatan 12520, Indonesia. [5] Laboratory of Natural Resources, Gifu Pharmaceutical University, Japan. [6] Botanical Gardens, Koishikawa, Graduate School of Science, University of Tokyo, 3-7-1 Hakusan, Bunkyo-Ku, Tokyo 112-0001, Japan. E-mail: oyama@gifu-pu.ac.jp (GPU)

Abstract – Three new 5,6-dihydro-α-pyrone derivatives, named cryptonitenones A–C (**1**–**3**), were isolated from the leaves of *Cryptocarya nitens* Koord. & Valeton. Their absolute structures were determined by means of the NMR and CD spectroscopic analyses. In addition, their deacetyl precursor, cryptomoscatone E3, was obtained from the twigs of the plant.

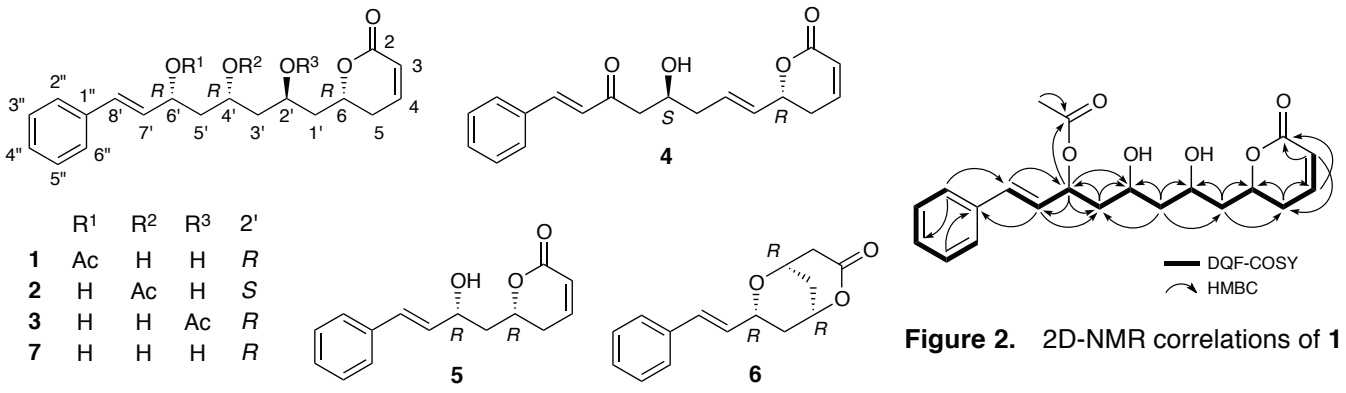
INTRODUCTION

The genus *Cryprocarya* (Lauraceae) contains approximately 350 species, most of which are distributed in the Indo-Malesian flora.[1,2] In Indonesia, they have been used for not only building timber but traditional medicines to treat diarrhea and skin diseases. Phytochemical researches have revealed that the genus contains 6-alkyl- or 6-aryl-5,6-dihydro-α-pyrones,[3,4] flavonoids produced by an irregular polyketide biosynthesis,[5] pavine-type alkaloids,[6] germacrane-type sesquiterpenoids,[7] and so on. Especially the α-pyrone derivatives exhibited a variety of biological activities such as antitumor,[8] anti-inflammatory,[9] antibacterial,[10] and antimalarial effects.[11] In the continuing studies of the Indonesian medicinal

plants,[12,13] we started to investigate the chemical constituents of *Cryptocarya* species cultivating in the Bogor Botanical Gardens. Herein, we describe about the structure elucidation of three new α-pyrone derivatives, cryptonitenones A–C (**1**–**3**), isolated from *C. nitens* Koord. & Valeton that originally grows in the regions from the Malay Peninsula to the Kalimantan and has the only report of a known lignan named yangambin.[2]

RESULTS AND DISCUSSION

Compound **1**, $[\alpha]_D^{25}$ +78.6, was isolated as pale yellow oil. The HR-ESI-MS spectrum showed an $[M+Na]^+$ ion peak at *m/z* 397.1607, which established the quasi-molecular formula as $C_{21}H_{26}O_6Na$ (calcd. 397.1622). The ^{1}H-NMR spectrum exhibited a pair of *cis*-olefinic protons [δ 6.87 (1H, m), 5.98 (1H, d, *J* = 9.8 Hz)], a methylene [δ 2.31 (2H, m)], and an oxymethine [δ 4.73 (1H, m)], while the ^{13}C-NMR spectrum gave an ester or a lactone carbonyl carbon [δ 164.9 (s)]. These signals were assignable to a 5,6-dihydro-α-pyrone moiety found in various isolates from *Cryptocarya* species.[11] The ^{1}H-NMR spectrum also implied the presence of a phenyl group [δ 7.38 (2H, d, *J* = 7.6 Hz), 7.30 (2H, dd, *J* = 7.6, 7.4 Hz), 7.24 (1H, t, *J* = 7.4 Hz)], a pair of *trans*-olefins [δ 6.66 (1H, d, *J* = 15.7 Hz), 6.15 (1H, dd, *J* = 15.7, 7.7 Hz)], three methylenes [δ 2.03 (1H, m), 1.80 (2H, m), 1.71 (1H, m), 1.62 (2H, m)], three oxymethines [δ 5.60, 4.31, 4.03 (1H each, m)], as well as an acetyl methyl [δ 2.06 (3H, s)] (Table 1). The DQF-COSY and HMQC spectra achieved the complete NMR assignments and proposed the connectivity from C-1' to C-8' as illustrated in Figure 2. The significant HMBC correlations between H_2-2",6"/C-8' and H-7'/C-1" confirmed the substitutions of the phenyl at C-8'. In addition, both correlations of H-8'/C-6' and H-6'/C-1'" in the HMBC spectrum indicated that the acetyl function was substituted onto the hydroxy group at C-6'. Consequently, the spectral analyses suggested **1** to be a 5,6-dihydro-6-(2',4',6'-trihydroxy-8'-phenyl-7'-octenyl)-2-pyrone 6'-*O*-acetate.



	R1	R2	R3	2'
1	Ac	H	H	*R*
2	H	Ac	H	*S*
3	H	H	Ac	*R*
7	H	H	H	*R*

Figure 2. 2D-NMR correlations of **1**

Figure 1. Structures of the compounds **1**–**7** isolated from *C. nitens*

Table 1. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) data of compounds **1**–**3** in $CDCl_3$

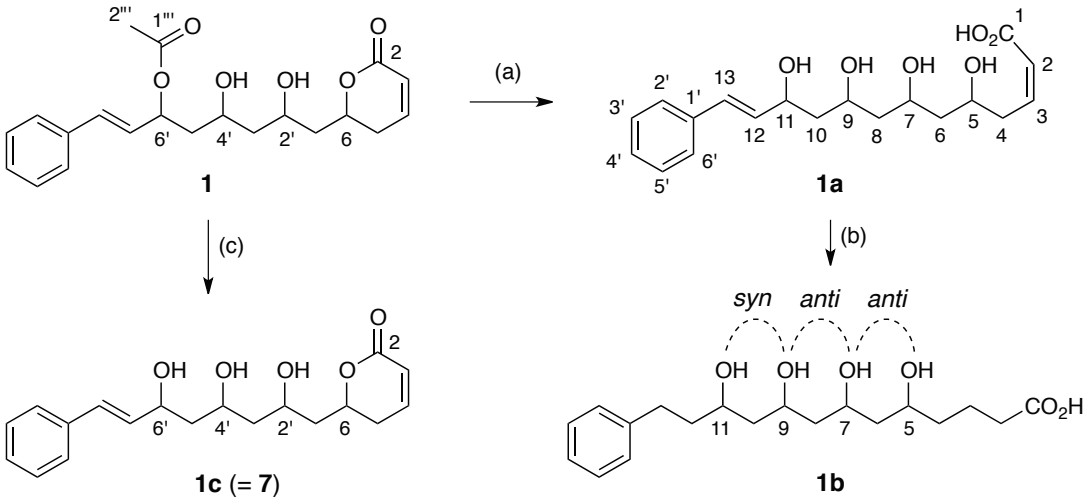
C No.	**1**		**2**		**3**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2		164.9		164.6		163.7
3	5.98 (d, 9.8)	121.0	5.98 (dd, 9.7, 2.3)	121.0	6.03 (d, 9.7)	121.4
4	6.87 (m)	145.9	6.84 (m)	145.5	6.87 (m)	144.7
5	2.31 (m)	29.7	2.30 (m)	29.8	2.35 (m)	29.5
6	4.73 (m)	74.9	4.71 (m)	74.8	4.49 (m)	74.3
1'	1.71, 1.80[a)] (m)	42.0	1.64[b)], 1.81[c)] (m)	42.2	1.94, 2.05 (m)	40.1
2'	4.31 (m)	63.9	3.87 (m)	62.7	5.33 (m)	67.7
3'	1.62 (2H, m)	43.7	1.64[b)] (2H, m)	42.9	1.68 (2H, m)	43.1
4'	4.03 (m)	65.9	5.24 (m)	68.9	3.85 (m)	67.9
5'	1.80[a)], 2.03 (m)	42.3	1.81[c)], 2.04 (m)	41.9	1.74 (2H, m)	43.6
6'	5.60 (m)	73.0	4.38 (m)	69.6	4.54 (m)	72.8
7'	6.15 (dd, 15.7, 7.7)	126.9	6.18 (dd, 16.1, 6.3)	131.4	6.20 (dd, 15.9, 6.1)	131.8
8'	6.66 (d, 15.7)	133.1	6.53 (d, 16.1)	130.2	6.61 (d, 15.9)	129.7
1"		136.1		136.3		136.7
2",6"	7.38 (d, 7.6)	126.6	7.35 (d, 6.9)	126.4	7.37 (d, 7.7)	126.4
3",5"	7.30 (dd, 7.6, 7.4)	128.5	7.30 (dd, 7.0, 6.9)	128.5	7.30 (dd, 7.7, 7.4)	128.5
4"	7.24 (t, 7.4)	128.0	7.23 (t, 7.0)	127.6	7.22 (t, 7.4)	127.5
1"'		170.4		172.4		172.1
2"'	2.06 (s)	21.4	2.05 (s)	21.2	2.10 (s)	21.0

The numbers in parentheses are coupling constants (*J*) in Hz. [a,b,c)]: overlapping signals.

The absolute stereochemistry at C-6 in the dihydro-α-pyrone ring is commonly determined by the Snatzke's rule: a positive Cotton effect at 254–272 nm corresponds to the *pseudo-equatorial* orientation of the side chain at C-6, and a negative one to the *pseudo-axial* orientation.[14,15] The CD spectrum of **1** showed a positive Cotton effect at 255 nm, indicating the *pseudo-equatorial* orientation, i.e. (6*R*)-configuration. Since **1** has the oxygen functions on alternate carbons (C-6, C-2', C-4', C-6'), the Kishi's universal ^{13}C-NMR database analysis was applied to determine the conformations around there. According to the database analysis,[16,17] an observed chemical shift of C-3 in a 1,3,5-triol motif predicts a preferable configuration as follows: (i) δ 66.3 ± 0.5 for an *anti*/*anti* configuration, (ii) δ 68.6 ± 0.5 for an *anti*/*syn* or a *syn*/*anti*, and (iii) δ 70.7 ± 0.5 for a *syn*/*syn* (Table 2). In order to apply the database analysis to both C-2' and C-4', **1** was treated with an alkali solution to afford the hydrolysate **1a** (Scheme 1). By means of the NMR spectroscopic analyses, the relevant C-7 and C-9 in **1a** were assigned to the carbon signals resonating at δ 66.2 and δ 67.6, respectively. The former chemical shift of the C-7 was close enough to determine the type-(i) *anti*/*anti*-configuration; however, the latter due to the C-9 was unable to discriminate between the type-(i) and type-(ii). As it was likely caused by the presence of the double bond between C-12 and C-13, a Pd/C-catalyzed hydrogenation of **1a** was performed to yield **1b**

(Scheme 1). Its NMR assignment was routinely achieved by a series of 2D-NMR experiments (Experimental). Both carbon signals assignable to C-7 and C-9 in **1b** were resonated at δ 66.2 and δ 68.5, respectively. This result deduced the type-(i) *anti*/*anti*-configuration at C-7 and the type-(ii) *anti*/*syn* (or *syn*/*anti*)-configuration at C-9. Taking the (6*R*)-configuration of **1** into account, the orientations of OH-5, OH-7, OH-9, OH-11 in **1b** were inferred to be α, β, α, α, respectively. Hence, the absolute stereochemistry of **1**, named cryptonitenone A, was demonstrated to be a (6*R*,2'*R*,4'*R*,6'*R*)-configuration as shown in Figure 1.

Based on the literature search, the structure of **1** was recognized as a 6'-*O*-acetyl metabolite of cryptomoscatone E3 (**7**), which was originally isolated form *C. moschata*[18] and then succeeded in total synthesis supported by a DP4 provability analysis.[19] When compared the ^{1}H- and ^{13}C-NMR spectral data of a hydrolysate **1c** with those of **7**,[19] the strong resemblance insisted on the accuracy of the absolute structure of **1**.



Scheme 1. Reagents and conditions: (a) KOH*aq*, reflux, 5 h, 66%; (b) H_2, 10%Pd/C, rt, 2 h, 77%; (c) KOH*aq*, rt, 72 h, 14%.

Table 2. ^{13}C-NMR (125 MHz) comparison of **1a** and **1b** with Kishi's database in MeOH-d_4

Compd.	Kishi's database		C-9		C-7	
	Comformation	$\delta_{exp.}$	$\delta_{obs.}$	Δ ($\delta_{exp.}$ - $\delta_{obs.}$)	$\delta_{obs.}$	Δ ($\delta_{exp.}$ - $\delta_{obs.}$)
1a	(i) *anti/anti*	66.3	67.6	-1.3	66.2	**0.1**
	(ii) *anti/syn, syn/anti*	68.5		0.9		2.3
	(iii) *syn/syn*	70.7		3.1		4.5
1b	(i) *anti/anti*	66.3	68.5	-2.2	66.2	**0.1**
	(ii) *anti/syn, syn/anti*	68.5		**0.0**		2.3
	(iii) *syn/syn*	70.7		2.2		4.5

$\delta_{exp.}$: Expected chemical shifts of C-3 in authentic compounds possessing a 1,3,5-triol motif.
$\delta_{obs.}$: Observed chemical shifts due to the relevant carbons in **1a** and **1b**.

Compound **2**, $[\alpha]_D^{25}$ +47.4, was isolated as pale yellow oil. The HR-ESI-MS spectrum gave a $[M+Na]^+$ ion peak at *m/z* 397.1597, showing the same quasi-molecular formula of $C_{21}H_{26}O_6Na$ (calcd. 397.1622) as **1**. The ^{1}H-NMR spectrum suggested that the only difference between **1** and **2** was an acetyl substitution at an alternate hydroxy group attaching to the octenyl chain [δ 6.53 (1H, d, *J* = 16.1 Hz), 6.18 (1H, dd, *J* = 16.1, 6.3 Hz), 5.24, 4.38, 3.87, 2.04 (1H each, m), 1.81 (2H, m), 1.64 (3H, m)]. In the HMBC spectrum, an oxymethine carbon signal at δ 69.6 (C-6') exhibited significant correlations between an olefinic proton signal at δ 6.53 (H-8') and an oxymethine proton signal at δ 5.24 (H-4') showing a $^3J_{HC}$ correlation to an acetyl carbonyl signal at δ 172.4 (C-1'''). Consequently, the acetyl substitution onto the OH-4' was substantiated. Although the planar structure of **2** looked identical to that of (6*R*,2'*S*,4'*R*,6'*S*)-cryptoconcatone B from *C. concinna*,[20] the hydrolyzation of **2** afforded **7** (Experimental), which confirmed **2** to be (6*R*,2'*S*,4'*R*,6'*R*)-4'-*O*-acetate of **7**, named cryptonitenone B.

Compound **3**, $[\alpha]_D^{25}$ +54.0, was isolated as pale yellow oil. The HR-ESI-MS spectrum exhibited a $[M+Na]^+$ ion peak at *m/z* 397.1628, indicating that **3** was a structure isomer of **1** and **2**. In the HMBC spectrum, an oxymethine proton signal at δ 4.49 (H-6) in an α-pyrone ring was correlated to a carbon signal at δ 67.7 (C-2'); furthermore, the relevant proton signal at δ 5.33 (H-2') was correlated to an acetyl carbonyl at δ 172.1 (C-1'''). It is certain that the acetoxy group adheres to C-2'. Since **3** was assumed to be a diastereomer of (6*R*,2'*R*,4'*R*,6'*S*)-cryptoconcatone A,[20] the deacetylation of **3** was carried out to yield **7** (Experimental), therefore, the structure of **3** was demonstrated to be (6*R*,2'*R*,4'*R*,6'*R*)-2'-*O*-acetate of **7**, named cryptonitenone C.

During the current phytochemical study, (+)-6'-keto-cryprofolione (**4**),[21] (+)-deacetylcryprocaryalactone (**5**),[22,23] (1*R*,5*R*,7*R*)-7-styryl-2,6-dioxabicyclo[3.3.1]nonan-3-one (**6**)[22,23] were isolated from the leaves of *C. nitens* as well. Cryptomoscatone E3 (**7**), which was a possible precursor of **1**–**3**, was isolated from the twig but not the leaves.

EXPERIMENTAL

General. ^{1}H- and ^{13}C-NMR spectra were measured on a JEOL JNM-ECA-500 spectrometer (^{1}H at 500 MHz and ^{13}C at 125 MHz). Chemical shifts are given in δ values (ppm) relative to tetramethylsilane as an internal standard. DART-MS and HR-ESI-MS were obtained using a JEOL JMS-DX300 and a Shimadzu LCMS-IT-TOF spectrometers, respectively. UV spectra were recorded using a Shimadzu UV-3100 spectrophotometer (in MeOH solution). Optical rotations were recorded using a Jasco P-1020 polarimeter (in $CHCl_3$ solution). CD spectra were measured using a JASCO J-820 spectrometer (in MeOH solution). Silica gel 60 (70-230 mesh, Merck) and Sephadex LH-20 (GE Healthcare) were used for column chromatography (CC). Vacuum liquid chromatography (VLC) was performed using silica gel 60H (Merck). TLC analysis was performed using silica gel $60F_{254}$ and silica gel RF-$18F_{254S}$ (Merck).

Preparative HPLC was performed on a Shimadzu HPLC system equipped with LC-10AT pump, SCL-10A system controller, SPD-10AV UV-Vis detector, and Nacalai Cosmosil 5SL-II column (5 μm, 10 mm i.d. x 250 mm).

Plant Material. The dried leaves and twigs of *Cryptocarya nitens* were collected at the Bogor Botanical Gardens, Indonesia, in September 2007, and identified by two of the authors (J.R.W. and D.D.). Voucher specimens were deposited at Gifu Pharmaceutical University, Gifu, Japan.

Extraction and Isolation. The dried leaves (372 g) were extracted with an equivalent mixture of $CHCl_3$ and MeOH at room temperature. The extract (41.3 g) was partitioned into a $CHCl_3$-soluble portion (20.7 g) and a water-soluble portion (20.6 g). The $CHCl_3$-soluble portion was subjected to silica gel CC (Si CC) eluting with $CHCl_3$–acetone (50:1 to 1:1) to give 11 main fractions (Fr. A–K). Fr. D was purified by Si CC (*n*-hexane–acetone, 20:1) to obtain 13 subfractions, and Fr. D7 was identified to be **6** (109.3 mg). Fr. D10 yielded **5** (13.1 mg) and **6** (46.1 mg) after the following VLC (*n*-hexane–EtOAc, 8:1). Fr. D11 was subjected to Sephadex LH-20 CC ($CHCl_3$–MeOH, 1:2) and successive VLC (*n*-hexane–*n*-PrOH, 40:1) to afford **4** (6.3 mg). Fr. J was purified repetitively using Si CC (*n*-hexane–acetone, 5:1) and HPLC (*n*-hexane–*n*-PrOH, 65:35) to afford **1** (73.5 mg, t_R = 10.3 min), **2** (82.3 mg, t_R = 12.2 min), and **3** (28.9 mg, t_R = 14.1 min).

The dried twigs (520 g), extracted with the same solvent as above, produced its extract (23.8 g). After the extract was poured into water, $CHCl_3$ was added to make a $CHCl_3$-soluble portion (8.2 mg). The $CHCl_3$-soluble portion was subjected to Si CC ($CHCl_3$–acetone, 100:1) to give 9 main fractions (Fr. A'–I'). Fr. H' yielded **7** (61.1 mg) after the successive Si CC ($CHCl_3$–MeOH, 100:1) and Sephadex LH-20 CC ($CHCl_3$–MeOH, 1:1).

Cryptonitenone A [(6*R*,2'*R*,4'*R*,6'*R*)-5,6-dihydro-6-(2',4',6'-trihydroxy-8'-phenyl-7'-octenyl)-2-pyrone 6'-*O*-acetate] (**1**): Pale yellow oil; $[\alpha]_D^{25}$ +78.6 (*c* 0.1, $CHCl_3$); UV (log ε, MeOH): 245 (3.63); CD (*c* 0.001, MeOH) nm (**Δ**ε): 255 (+4.36); ^{1}H-NMR ($CDCl_3$, 500 MHz) and ^{13}C-NMR ($CDCl_3$, 125 MHz): see Table 1. HR-ESI-MS (pos.): 397.1607 ($[M+Na]^+$, $C_{21}H_{26}O_6Na$, calc. 397.1622).

Preparation of 1a. **1** (11.4 mg) was added to an aqueous solution of KOH (11 mL, 0.05% w/v), and refluxed for 5 h. The mixture was neutralized with a cold HCl solution, and then partitioned with EtOAc. The EtOAc layer was subjected to Si CC (benzene–EtOH, 3:1) to yield **1a** (7.0 mg): Pale yellow oil; $[\alpha]_D^{25}$ –33.0 (*c* 0.1, MeOH); UV (log ε, MeOH): 248 (3.89); ^{1}H-NMR (MeOH-d_4, 500 MHz) δ: 7.31 (2H, d, *J* = 7.7 Hz, H-2', 6'), 7.19 (2H, dd, *J* = 7.7, 7.5 Hz, H-3', 5'), 7.11 (1H, t, *J* = 7.5 Hz, H-4'), 6.51 (1H, d, *J* = 16.0 Hz, H-13), 6.14 (1H, dd, *J* = 16.0, 6.9 Hz, H-12), 5.85 (1H, d, *J* = 11.5 Hz, H-2), 5.79 (1H, m, H-3), 4.35 (1H, m, H-11), 3.98 (1H, m, H-7), 3.88 (1H, m, H-9), 3.79 (1H, m, H-5), 2.54 (2H, m, H_2-4), 1.72, 1.57 (1H each, m, H_2-10), 1.46 (4H, m, H_2-6, 8); ^{13}C-NMR (MeOH-d_4, 125 MHz) δ: 175.9 (s, C-1), 138.4 (s, C-1'), 136.0 (d, C-3), 133.2 (d, C-12), 131.5 (d, C-13), 130.8 (d, C-2), 129.6 (d,

C-3', 5'), 128.5 (d, C-4'), 127.5 (d, C-2', 6'), 72.1 (d, C-11), 69.1 (d, C-5), 67.6 (d, C-9), 66.2 (d, C-7), 46.6 (t, C-6), 46.4 (t, C-8), 46.1 (t, C-10), 37.8 (t, C-4); HR-ESI-MS (pos.): 373.1601 ($[M+Na]^+$, $C_{19}H_{26}O_6Na$, calc. 373.1622).

Preparation of 1b. A solution of **1a** (7.0 mg) in MeOH (10 mL) was stirred with Pd/C (equiv.) under H_2 atmosphere at room temperature for 4 h. The reaction mixture was filtrated to give **1b**: Pale yellow oil; $[\alpha]_D^{25}$ –6.6 (*c* 0.1, MeOH); UV (log ε, MeOH): 207 (3.85); ^{1}H-NMR (MeOH-d_4, 500 MHz) δ: 7.24 (2H, dd, *J* = 7.2, 6.9 Hz, H-3', 5'), 7.20 (2H, d, *J* = 6.9 Hz, H-2', 6'), 7.13 (1H, t, *J* = 7.2 Hz, H-4'), 4.07 (1H, m, H-7), 4.01 (1H, m, H-9), 3.81 (1H, m, H-5), 3.79 (1H, m, H-11), 2.77, 2.64 (1H each, m, H_2-13), 2.18 (2H, m, H_2-2), 1.79, 1.67 (1H each, m, H_2-12), 1.72, 1.62 (1H each, m, H_2-3), 1.63 (2H, m, H_2-10), 1.54 (2H, m, H_2-6) 1.45 (4H, m, H_2-4,8); ^{13}C-NMR (MeOH-d_4, 125 MHz) δ: 182.6 (s, C-1), 143.7 (s, C-1'), 129.4 (d, C-3', 5'), 129.3 (d, C-2', 6'), 126.7 (d, C-4'), 70.8 (d, C-11), 69.0 (d, C-5), 68.5 (d, C-9), 66.2 (d, C-7), 46.3 (t, C-8), 46.2 (t, C-6), 45.7 (t, C-10), 40.6 (t, C-12), 39.1 (t, C-4), 38.8 (t, C-2), 32.8 (t, C-13), 23.7 (t, C-3); HR-ESI-MS (neg.): 353.1971 ($[M-H]^-$, $C_{19}H_{29}O_6$, calc. 353.1970).

Preparation of 1c. Deacetylation of **1** (5.9 mg) was performed in an aqueous solution of KOH (19 mL, 0.07% w/v) at room temperature for 72 h. After the neutralization, the solution was partitioned with EtOAc. The EtOAc layer was subjected to Si CC (benzene–MeOH, 4:1) to yield **1c** (0.7 mg): Pale yellow oil; $[\alpha]_D^{25}$ +67.4 (*c* 0.1, $CHCl_3$); UV (log ε, MeOH): 248 (4.15); ^{1}H-NMR (MeOH-d_4, 500 MHz) δ: 7.40 (2H, d, *J* = 7.5 Hz, H-2", 6"), 7.29 (2H, dd, *J* = 7.5, 7.3 Hz, H-3", 5"), 7.20 (1H, t, *J* = 7.3 Hz, H-4"), 7.04 (1H, m, H-4), 6.61 (1H, d, *J* = 15.8 Hz, H-8'), 6.24 (1H, dd, *J* = 15.8, 6.9 Hz, H-7'), 5.97 (1H, dd, *J* = 9.7, 2.9 Hz, H-3), 4.71 (1H, m, H-6), 4.45 (1H, dt, *J* = 6.9, 6.9 Hz, H-6'), 4.14 (1H, m, H-2'), 4.00 (1H, m, H-4'), 2.43, 2.34 (1H each, m, H_2-5), 1.87 (1H, m, H-1'), 1.83 (1H, m, H-5'), 1.67 (2H, m, H-1', 5'), 1.58 (2H, m, H-3'); ^{13}C-NMR (MeOH-d_4, 125 MHz) δ: 167.0 (s, C-2), 148.5 (d, C-4), 138.4 (s, C-1"), 133.2 (d, C-7'), 131.6 (d, C-8'), 121.4 (d, C-3), 129.6 (d, C-3", 5"), 128.6 (d, C-4"), 127.5 (d, C-2", 6"), 72.0 (d, C-6'), 76.7 (d, C-6), 67.4 (d, C-4'), 64.8 (d, C-2'), 46.5 (t, C-3'), 46.1 (t, C-5'), 44.2 (t, C-1'), 30.9 (t, C-5); HR-ESI-MS (pos.): 355.1488 ($[M+Na]^+$, $C_{19}H_{24}O_5Na$, calc. 355.1516).

Both **2** (4.5 mg) and **3** (6.0 mg) were deacetylated in the same manner to afford **1c** in yields of 15% (0.8 mg) and 27% (1.4 mg), respectively.

Cryptonitenone B [(6*R*,2'*S*,4'*R*,6'*R*)-5,6-dihydro-6-(2',4',6'-trihydroxy-8'-phenyl-7'-octenyl)-2-pyrone 4'-*O*-acetate] (**2**): Pale yellow oil; $[\alpha]_D^{25}$ +47.4 (*c* 0.1, $CHCl_3$); UV (log ε, MeOH): 244 (3.62); CD (*c* 0.001, MeOH) nm (**Δ**ε): 267 (+1.51); ^{1}H-NMR ($CDCl_3$, 500 MHz) and ^{13}C-NMR ($CDCl_3$, 125 MHz): see Table 1. HR-ESI-MS (pos.): 397.1597 ($[M+Na]^+$, $C_{21}H_{26}O_6Na$, calc. 397.1622).

Cryptonitenone C [(6*R*,2'*R*,4'*R*,6'*R*)-5,6-dihydro-6-(2',4',6'-trihydroxy-8'-phenyl-7'-octenyl)-2-pyrone 2'-*O*-acetate] (**3**): Pale yellow oil; $[\alpha]_D^{25}$ +54.0 (*c* 0.1, $CHCl_3$); UV (log ε, MeOH): 245 (3.62); CD (*c* 0.001, MeOH) nm (**Δ**ε): 268 (+1.06); ^{1}H-NMR ($CDCl_3$, 500 MHz) and ^{13}C-NMR ($CDCl_3$, 125 MHz): see

Table 1. HR-ESI-MS (pos.): 397.1628 ($[M+Na]^+$, $C_{21}H_{26}O_6Na$, calc. 397.1622).

REFERENCES

1. P. F. Stevens (2001 onwards), Angiosperm Phylogeny Website, Ver. 14, July 2017, http://www.mobot.org/MOBOT/research/APweb/, (accessed 2018-06-26).
2. L. D. Juliawaty, N. Aimi, E. L. Ghisalberti, M. Kitajima, L. Makmur, Y. M. Syah, J. Siallagan, H. Takayama, S. A. Achmad, and E. H. Hakim, 'Chemistry of Indonesian *Cryptocarya* plants (Lauraceae)', Chemistry of Natural Products: Recent Trends & Developments, ed. by G. Brahmachari, Research Signpost, India, 2006, pp. 399-423.
3. T. Grkovic, J. S. Blees, N. H. Colburn, T. Schmid, C. L. Thomas, C. J. Henrich, J. B. McMahon, and K. R. Gustafson, *J. Nat. Prod.*, 2011, **74**, 1015.
4. T. L. Meragelman, D. A. Scudiero, R. E. Davis, L. M. Staudt, T. G. McCloud, J. H. Cardellina II, and R. H. Shoemaker, *J. Nat. Prod.*, 2009, **72**, 336.
5. T.-H. Chou, J.-J. Chen, S.-J. Lee, M. Y. Chiang, C.-W. Yang, and I.-S. Chen, *J. Nat. Prod.*, 2010, **73**, 1470.
6. F.-W. Lin, J.-J. Wu, and T.-S. Wu, *Chem. Pharm. Bull.*, 2002, **50**, 157.
7. S. A. Achmad, H. Azmina, Y. Effend, E. L. Ghisalberti, E. H. Hakim, L. Makmur, and A. H. White, *Aust. J. Chem.*, 1992, **45**, 445.
8. B.-Y. Yang, Y.-M. Shi, J.-G. Luo, and L.-Y. Kong, *Nat. Prod. Res.*, 2017, **31**, 1409.
9. M. E. S. B. Barros, J. C. R. Freitas, J. M. Oliveira, C. H. B. da Cruz, P. B. N. da Silva, L. C. C. de Araújo, G. C. G. Militão, T. G. da Silva, R. A. Oliveira, and P. H. Menezes, *Eur. J. Med. Chem.*, 2014, **76**, 291.
10. M. B. Nodwell, H. Menz, S. F. Kirsch, and S. A. Sieber, *ChemBioChem*, 2012, **13**, 1439.
11. Y. Liu, L. H. Rakotondraibe, P. J. Brodie, J. D. Wiley, M. B. Cassera, J. S. Miller, F. Ratovoson, E. Rakotobe, V. E. Rasamison, and D. G. I. Kingston, *J. Nat. Prod.*, 2015, **78**, 1330.
12. K. Nakashima, M. Oyama, T. Ito, Y. Akao, J. R. Witono, D. Darnaedi, T. Tanaka, J. Murata, and M. Iinuma, *Tetrahedron*, 2012, **68**, 2421.
13. K. Nakashima, M. Oyama, T. Ito, J. R. Witono, D. Darnaedi, T. Tanaka, J. Murata, and M. Iinuma, *Chem. Biodives.*, 2012, **9**, 2195.
14. G. Snatzke, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 14.
15. M. T. Davies-Coleman, and D. E. A. Rivett, *Prog. Chem. Org. Nat. Prod.*, 1989, **55**, 1.
16. Y. Kobayashi, C.-H. Tan, and Y. Kishi, *Helv. Chim. Acta*, 2000, **83**, 2562.
17. Y. Kobayashi, C.-H. Tan, and Y. Kishi, *Angew. Chem. Int. Ed.*, 2000, **39**, 4279.
18. A. J. Cavalheiro and M. Yoshida, *Phytochemistry*, 2000, **53**, 811.

19. L. F. T. Novaes, A. M. Sarotti, and R. A. Pilli, *J. Org. Chem.*, 2015, **80**, 12027.
20. B.-Y. Yang, L.-Y. Kong, X.-B. Wang, Y.-M. Zhang, R.-J. Li, M.-H. Yang, and J.-G. Luo, *J. Nat. Prod.*, 2016, **79**, 196.
21. B. M. Sehlapelo, S. E. Drewes, and R. Scott-Shaw, *Phytochemistry*, 1994, **37**, 847.
22. S. E. Drewes, M. M. Horn, and R. Scott-Shaw, *Phytochemistry*, 1995, **40**, 321.
23. S. E. Drewes, M. M. Horn, N. S. Ramesar, D. Ferreira, R. J. J. Nel, and A. Hutchings, *Phytochemistry*, 1998, **49**, 1683.