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Four new C₁₉-diterpenoid alkaloids from *Delphinium elatum*

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Abstract

Diterpenoid alkaloids with remarkable chemical properties and biological activities are frequently found in plants of the genera *Aconitum*, *Delphinium*, and *Garrya*. Accordingly, several C₁₉-diterpenoid alkaloid components from *Delphinium elatum* cv. Pacific Giant, as well as their derivatives, exhibited cytotoxic activity against lung, prostate, nasopharyngeal, and vincristine-resistant nasopharyngeal cancer cell lines. Four new C₁₉-diterpenoid alkaloids, elapacigine (**1**), *N*-deethyl-*N*-formylpaciline (**2**), *N*-deethyl-*N*-formylpacinine (**3**), and *N*-formyl-4,19-secoyunnadelphinine (**4**), together with 11 known C₁₉-diterpenoid alkaloids were isolated in a phytochemical investigation on the seeds of *D. elatum* cv. Pacific Giant. Their structures were elucidated by extensive spectroscopic methods including NMR (1D and 2D), IR, and MS (HRMS). Three of the new C₁₉-diterpenoid alkaloids (**2–4**) and five of the known diterpenoid alkaloids were evaluated for cytotoxic activity against five human tumor cell lines.

Graphical Abstract

Four new C₁₉-diterpenoid alkaloids, elapacigine (**1**), *N*-deethyl-*N*-formylpaciline (**2**), *N*-deethyl-*N*-formylpacinine (**3**), and *N*-formyl-4,19-secoyunnadelphinine (**4**), together with 11 known C₁₉-diterpenoid alkaloids were isolated in a phytochemical investigation on the seeds of *D. elatum* cv. Pacific Giant.

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Keywords

Delphinium elatum; elapacigine; *N*-deethyl-*N*-formylpaciline; *N*-deethyl-*N*-formylpacinine; *N*-formyl-4; 19-secoyunnadelphinine

1. Introduction

Diterpenoid alkaloids with remarkable chemical properties and biological activities are frequently derived from plants of the genera *Aconitum*, *Delphinium*, and *Garrya* (Wang et al., 2010). In previous papers (Wada et al., 2016), the isolation and structure elucidation of 16 C₁₉-diterpenoid alkaloids from the seeds of *Delphinium elatum* cv. Pacific Giant were reported. In recent pharmacological studies, several diterpenoid alkaloid components from this plant and their derivatives exhibited cytotoxic activity against lung (A549), nasopharyngeal (KB), vincristine-resistant nasopharyngeal (KB-VIN), prostate (DU145), or triple-negative breast cancer (estrogen and progesterone receptors-negative/HER2-negative) (MDA-MB-231) cancer cell lines (Wada et al., 2012, Wada et al., 2015a). Continued investigations on the constituents of this plant have now resulted in the isolation of four new C₁₉-diterpenoid alkaloids, elapacigine (**1**), *N*-deethyl-*N*-formylpaciline (**2**), *N*-deethyl-*N*-formylpacinine (**3**), and *N*-formyl-4,19-secoyunnadelphinine (**4**), together with 11 known C₁₉-diterpenoid alkaloids, delpheline (**5**) (Pelletier et al., 1984), isodelpheline (**6**) (Pelletier et al., 1989), 19-oxoisodelpheline (**7**) (Wada et al., 2016), melpheline (**8**) (Wada et al., 2016), pacidine (**9**) (Wada et al., 1992), pacinine (**10**) (Bando et al., 1989), yunnadelphinine (**11**) (Luo et al., 1984), eladine (**12**) (Pelletier et al., 1989), 6-dehydroeladine (**13**) (Wada et al., 2015b), laxicyminine (**14**) (Tang et al., 2007), and delcorine (**15**) (Pelletier et al., 1984) (Fig. 1). Three new C₁₉-diterpenoid alkaloids **2–4** and five known C₁₉-diterpenoid alkaloids **6, 7, 9, 12**, and **15** were evaluated for cytotoxic activity against four human tumor cell lines (A549, MDA-MB-231, KB, and KB-VIN).

2. Results and discussion

Alkaloid **1** was obtained as a colorless amorphous solid, $[\alpha]_D^{25} -23.9$, with the molecular formula C₂₃H₃₁NO₆ as deduced from the molecular ion at m/z 417.2153 (calcd. 417.2151) in its HR-EIMS. The IR spectrum showed resonance for hydroxyl (3469 cm⁻¹) and carbonyl (1739 and 1695 cm⁻¹) groups. The ¹H NMR spectrum of **1** revealed the presence of an *N*-ethyl unit (δ_H 1.07, 3H, t, $J = 7.5$ Hz; 2.72 and 2.77, each 1H, m), a methoxy group at δ_H 3.37 (3H, s), two methine protons at δ_H 3.51 (1H, m, H-16 α) and 4.12 (1H, m, H-14 β), and

a methylenedioxy group at δ_{H} 5.15 and 5.62 (each 1H, s). Except for the absence of a resonance for a methoxy group at C-1, the ^1H NMR spectrum of **1** was very similar to that of yunnadelphinine (**11**) (Luo et al., 1984). The ^{13}C NMR spectrum of **1** indicated one methoxy carbon (δ_{C} 56.7), one methylenedioxy carbon (δ_{C} 95.8), four other oxygenated carbons (δ_{C} 73.6, 80.8, 81.8, 90.8) and two carbonyl moieties (δ_{C} 211.2 and 213.8). The assigned stereochemistry and relative configuration were corroborated by the ^1H and ^{13}C NMR spectra. In the HMBC spectra of **1**, correlation of a proton at δ_{H} 2.29 (1H, m, H-10), 3.22 (1H, m, H-2), and 3.59 (1H, s, H-17) with carbons at δ_{C} 211.2 (C-1) confirmed the presence of the carbonyl group. Correlations were also observed between signals at δ_{H} 2.24 (1H, s, H-5) and 3.59 (1H, s, H-17) with δ_{C} 213.8 (C-6), as well as δ_{H} 2.24 (1H, s, H-5) with δ_{C} 24.4 (C-18), 35.8 (C-4), 41.5 (C-10), 58.5 (C-19), and 65.2 (C-17), and δ_{H} 3.59 (1H, s, H-17) with δ_{C} 50.1 ($N\text{-CH}_2\text{CH}_3$), 56.1 (C-11), and 61.6 (C-5). Key two- and three-bond heteronuclear connectivities (Fig. 2) also substantiated the structure of **1**. All of the spectroscopic data of **1** were typical of those for a C_{19} -diterpenoid alkaloid and consistent with the structure shown for **1** (elapacigine).

Alkaloid **2** was obtained as a colorless amorphous solid, $[\alpha]_{\text{D}}^{25} -16.1$, with the molecular formula $\text{C}_{25}\text{H}_{37}\text{NO}_7$, as deduced from the molecular ion at m/z 463.2567 (calcd. 463.2571) in its HR-EIMS. The IR spectrum indicated the presence of an amide (1667 cm^{-1}) group. The ^1H NMR spectrum of **2** contained signals for an angular methyl (δ_{H} 1.02, 3H, s), four methoxy groups (δ_{H} 3.23, 3.37, 3.40, and 3.45, each 3H, s) and a methylenedioxy moiety (δ_{H} 5.10 and 5.12, each 1H, s). An IR absorption at 1667 cm^{-1} , ^1H NMR signal at δ_{H} 7.94, and ^{13}C NMR signal at δ_{C} 163.1 (s) suggested the presence of an *N*-formyl group, as also found in *N*-formyl-4,19-secopacine (Wada et al., 2015b). The ^1H NMR spectrum of **2** was very similar to that of paciline (Bando et al., 1989), except for the absence of a resonance for an *N*-ethyl unit. The ^{13}C NMR spectrum of **2** indicated six oxygenated carbons (δ_{C} 79.1, 81.3, 83.4, 83.8, 88.2, and 89.8), a methylenedioxy carbon (δ_{C} 94.1), and four methoxy carbons (δ_{C} 55.0, 56.4, 58.0, and 59.4). The assigned stereochemistry and relative configuration were supported by the ^1H and ^{13}C NMR spectra. In the HMBC spectrum of **2**, correlations were observed between signals at δ_{H} 7.94 (1H, s, *N*-CHO) with δ_{C} 47.1 (C-19) and 62.1 (C-17), δ_{H} 3.80 (1H, s, H-17) with δ_{C} 163.1 (*N*-CHO), 58.2 (C-5), 49.3 (C-11), and 47.1 (C-19), δ_{H} 2.76 and 3.86 (each 1H, d, H-19) with δ_{C} 163.1 (*N*-CHO), 58.2 (C-5), 36.2 (C-3), and 25.6 (C-18). Key two- and three-bond heteronuclear connectivities (Fig. 2) and the combined spectroscopic data verified the structure of **2** as *N*-deethyl-*N*-formylpaciline.

Alkaloid **3**, colorless amorphous solid, $[\alpha]_{\text{D}}^{25} -70.3$, has the molecular formula $\text{C}_{24}\text{H}_{33}\text{NO}_7$ (found m/z 447.2283, calcd. 447.2257) based on HR-EIMS data. The IR, ^1H NMR, and ^{13}C NMR spectra of **3** were also very similar to those of **2** and pacinine (**10**) (Bando et al., 1989). Significantly, an IR absorption at 1665 cm^{-1} and ^{13}C NMR signal at δ_{C} 162.0 (s, *N*-CHO) suggested the presence of a formyl amide group in **3** as also found in **2** and NMR signals for the *N*-ethyl group found in **10** were absent in the spectra of **3**. Meanwhile, an IR absorption at 1752 cm^{-1} and ^{13}C NMR signal at δ_{C} 213.9 (s, C-6) demonstrated the presence of an oxo carbonyl group as also found in **10**. The assigned stereochemistry and relative configuration were corroborated by the ^1H and ^{13}C NMR spectra. In the HMBC

spectrum of **3**, correlations were observed between signals at δ_{H} 1.88 (1H, s, H-5) and 4.16 (1H, s, H-17) with δ_{C} 213.9 (C-6), δ_{H} 2.51 and 4.04 (each 1H, d, H-19), and δ_{H} 4.16 (1H, s, H-17) with δ_{C} 163.1 (*N*-CHO). Key two- and three-bond heteronuclear connectivities also substantiated the structure of **3** as *N*-deethyl-*N*-formylpacinine.

Alkaloid **4**, a colorless amorphous solid, $[\alpha]_{\text{D}}^{25} -47.2$, exhibited a HR-EIMS molecular ion consistent with the composition $\text{C}_{24}\text{H}_{35}\text{NO}_7$ (found m/z 449.2399, calcd. 449.2414). The IR spectrum contained absorptions for hydroxy (3445 cm^{-1}), carbonyl (1738 cm^{-1}) and amide (1667 cm^{-1}) groups, and the ^{13}C NMR signals at δ_{C} 215.8 (s, C-6) and 163.8 (s, C-19) suggested the presence of carbonyl and amide groups, respectively, as also found in **2** and **3**. The ^1H NMR spectrum of **4** revealed the presence of an *N*-ethyl unit (δ_{H} 1.13; 3H, t, $J = 6.8$ Hz, 3.37; 2H, m), two methoxy groups (δ_{H} 3.34 and 3.39; each 3H, s), and a methylenedioxy moiety (δ_{H} 5.15 and 5.63; each 1H, s), and the ^{13}C NMR spectrum indicated the presence of five oxygenated carbons (δ_{C} 73.1, 80.8, 83.3, 85.1 and 89.8). The ^1H NMR and ^{13}C NMR spectra of **4** were very similar to those of *N*-formyl-4,19-secopacinine (Wada et al., 2015b) and yunnadelphinine (**11**) (Luo et al., 1984), except for the absence of a resonance for an angular methyl and the presence of a resonance for a secondary methyl (δ_{H} 1.16; 3H, d, $J = 6.1$ Hz, δ_{C} 21.6). The assigned stereochemistry and relative configuration were supported by the ^1H and ^{13}C NMR spectra. HMBC spectroscopic data also indicated key two- and three-bond heteronuclear connectivities, leading to the characterization of **4** as *N*-formyl-4,19-secoyunnadelphinine.

Three new C_{19} -diterpenoid alkaloids **2–4**, and five known C_{19} -diterpenoid alkaloids **6, 7, 9, 12**, and **15** were evaluated for cytotoxic activity against four human tumor cell lines [lung carcinoma (A549), triple-negative breast cancer (estrogen and progesterone receptors-negative/HER2-negative) (MDA-MB-231), nasopharyngeal (KB), and multidrug resistant KB subline expressing P-glycoprotein (KB-VIN)]. The new alkaloid **1** was not tested because of the extremely low quantity. However, the eight new and known alkaloids were inactive ($\text{IC}_{50} > 40\text{ }\mu\text{M}$) against the four tested cell lines.

3. Conclusion

The present paper describes the isolation of four new lycoctonine-type C_{19} -diterpenoid alkaloids (**1–4**) from the seeds of *D. elatum* cv. Pacific Giant. The structures of **1–4** were elucidated from 1D and 2D NMR spectroscopic data. To our knowledge, elapacigine (**1**) is the first reported lycoctonine-type C_{19} -diterpenoid alkaloid with 1,6-diketo moieties. *N*-Deethyl-*N*-formylpacinine (**2**) and *N*-deethyl-*N*-formylpacinine (**3**) are the first reported lycoctonine-type C_{19} -diterpenoid alkaloids with a 7,8-dioxymethylene moiety and *N*-CHO group. *N*-Formyl-4,19-secoyunnadelphinine (**4**) is the second reported C_{19} -diterpenoid alkaloid with both *N*-ethyl and *N*-formyl groups and a cleaved C-4-C-9 bond. *N*-Formyl-4,19-secopacinine is the only previously reported C_{19} -diterpenoid alkaloid with both *N*-ethyl and *N*-formyl groups and a cleaved C-4-C-9 bond (Wada et al., 2015b). Three new C_{19} -diterpenoid alkaloids **2–4** and five known C_{19} -diterpenoid alkaloids **6, 7, 9, 12**, and **15** were inactive ($\text{IC}_{50} > 40\text{ }\mu\text{M}$) against four human tumor cell lines (A549, MDA-MB-231, KB, and KB-VIN).

4. Experimental Section

4.1. General experimental procedures

Optical rotations were measured on a Jasco Model P-2300 polarimeter. IR spectra were recorded using a Perkin-Elmer Model Spectrum100 spectrometer. NMR spectra were recorded in CDCl₃ on a JEOL Model AL-400 or ECA600 spectrometer with TMS as an internal standard. MS and HRMS were recorded on a JEOL Model JMS-700 mass spectrometer.

4.2. Isolation procedure

In a previous paper (Wada et al., 2016), 16 alkaloids were extracted and isolated from the seeds of the title plant. Purification of the B6 fraction by repeated column chromatography (5% MeOH-CHCl₃ saturated with 28% aq. NH₃) gave four new C₁₉-diterpenoid alkaloids, elapacigine (**1**, 1 mg), *N*-deethyl-*N*-formylpaciline (**2**, 2 mg), *N*-deethyl-*N*-formylpacinine (**3**, 5 mg), and *N*-formyl-4,19-secoyunnadelphinine (**4**, 25 mg), together with 11 known C₁₉-diterpenoid alkaloids; delpheline (**5**, 15 mg) (Pelletier et al., 1984), isodelpheline (**6**, 6 mg) (Pelletier et al., 1989), 19-oxoisodelpheline (**7**, 14 mg) (Wada et al., 2016), melpheline (**8**, 9 mg) (Wada et al., 2016), pacidine (**9**, 47 mg) (Wada et al., 1992), pacinine (**10**, 2 mg) (Bando et al., 1989), yunnadelphinine (**11**, 7 mg) (Luo et al., 1984), eladine (**12**, 34 mg) (Pelletier et al., 1989), 6-dehydroeladine (**13**, 2 mg) (Wada et al., 2015b), laxicyminine (**14**, 4 mg) (Tang et al., 2007), and delcorine (**15**, 22 mg) (Pelletier et al., 1984).

4.2.1. Elapacigine (1)—Colorless amorphous solid; $[\alpha]_D^{25} -23.9$ (*c* 0.072, CHCl₃); IR (ATR) $\nu_{\max}$ cm⁻¹: 3469, 2922, 2876, 1739, 1695, 1085; ¹H NMR (CDCl₃, 600 MHz) and ¹³C NMR (CDCl₃, 150 MHz) spectroscopic data, see Table 1; EIMS *m/z* 417 [M]⁺, 402 [M-CH₃]⁺; HR-EIMS *m/z* 417.2153 [M]⁺ (calcd. for C₂₃H₃₁NO₆, 417.2151).

4.2.2. N-Deethyl-N-formylpaciline (2)—Colorless amorphous solid; $[\alpha]_D^{25} -16.1$ (*c* 0.18, CHCl₃); IR (ATR) $\nu_{\max}$ cm⁻¹: 2922, 2853, 1667, 1080; ¹H NMR (CDCl₃, 600 MHz) and ¹³C NMR (CDCl₃, 150 MHz) spectroscopic data, see Table 1; EIMS *m/z* 463 [M]⁺, 448 [M-CH₃]⁺, 434 [M-CHO]⁺; HREI-MS *m/z* 463.2567 [M]⁺ (calcd for C₂₅H₃₇NO₇; 463.2571).

4.2.3. N-Deethyl-N-formylpacinine (3)—Colorless amorphous solid; $[\alpha]_D^{25} -70.3$ (*c* 0.13, CHCl₃); IR (ATR) $\nu_{\max}$ cm⁻¹: 2924, 1752, 1665, 1084; ¹H NMR (CDCl₃, 600 MHz) and ¹³C NMR (CDCl₃, 150 MHz) spectroscopic data, see Table 1; EIMS *m/z* 447 [M]⁺, 432 [M-CH₃]⁺, 418 [M-CHO]⁺; HREI-MS *m/z* : 447.2283 [M]⁺ (calcd for C₂₄H₃₃NO₇; 447.2257);.

4.2.4. N-Formyl-4,19-secoyunnadelphinine (4)—Colorless amorphous solid; $[\alpha]_D^{25} -47.2$ (*c* 0.13, CHCl₃); IR (ATR) $\nu_{\max}$ cm⁻¹: 3445, 2931, 2867, 1738, 1667, 1073; ¹H NMR (CDCl₃, 600 MHz) and ¹³C NMR (CDCl₃, 150 MHz) spectroscopic data, see Table 1; EIMS *m/z* 449 [M]⁺, 434 [M-CH₃]⁺, 418 [M-OCH₃]⁺; HREI-MS *m/z* 449.2399 [M]⁺ (calcd for C₂₄H₃₅NO₇; 449.2414).

4.3. Cell culture and cytotoxicity analysis

All cell lines were obtained from American Type Culture Collection (ATCC, Virginia, USA) or UNC Lineberger Comprehensive Cancer Center (North Carolina, USA), except KB-VIN (vincristine-resistant KB subline), which was a gift from Professor Y.-C. Cheng (Yale University, Connecticut, USA). Cells were cultured in RPMI 1640 medium containing 25 mM HEPES and 2 mM L-glutamine (Corning, New York, USA), supplemented with 10% heat-inactivated fetal bovine serum (Sigma-Aldrich, Missouri, USA), 100 IU penicillin, 100 µg/mL streptomycin, and 0.25 µg/mL amphotericin B (Corning, New York, USA). KB-VIN cells were maintained in media containing 100 nM vincristine (Sigma-Aldrich, Missouri, USA). Cells were maintained at 37 °C in a humidified 5% CO₂ atmosphere. The cells were passaged every 3–4 days.

Cytotoxicity was evaluated by the sulforhodamine B method as described before (Nakagawa-Goto et al., 2015). In brief, all compounds were prepared at 10 mM with DMSO, and the highest concentration of DMSO in the cultures (0.4% v/v) used for the cytotoxicity assay had no effect on cell growth. All stock cell lines were cultured in T-75 flasks at 37 °C with 5% CO₂ in air. Freshly trypsinized cell suspensions were seeded in 96-well microtiter plates at densities of 4,000–7,500 cells per well with compounds. After 72 h in culture with test compounds, cells were fixed in 10% trichloroacetic acid followed by staining with 0.04% sulforhodamine B. The protein-bound dye was solubilized by 10 mM Tris base and absorbance was measured at 515 nm using a ELx800 microplate reader with Gen5 software (BioTek, Vermont, USA). The IC₅₀ was calculated from at least three independent experiments performed in duplicate.

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Highlights

- New C₁₉-diterpenoid alkaloids were isolated from *Delphinium elatum* cv. Pacific Giant.
- Elapacigine is the first reported lycoctonine-type C₁₉-diterpenoid alkaloid with 1,6-diketo moieties.
- *N*-Deethyl-*N*-formylpaciline and *N*-deethyl-*N*-formylpacinine are the first reported lycoctonine-type C₁₉-diterpenoid alkaloids with a 7,8-dioxymethylene moiety and *N*-CHO group.

Fig. 1.
Structures of new compounds 1–4.

Fig. 2.

Key ¹H-¹H COSY and HMBC correlations of compounds 1 and 2.

Table 1

^{13}C and ^1H NMR spectroscopic data for compounds **1–4**, **11** in CDCl_3 (δ_{C} and δ_{H} in ppm; J in Hz)^a.

	1		2		3		4		11 ^b
Position	δ_{C}	δ_{H}	δ_{C}	δ_{H}	δ_{C}	δ_{H}	δ_{C}	δ_{H}	δ_{C}
1	211.2 s	–	79.1 d	3.11 dd (9.6, 7.6)	79.6 d	3.33 m	85.1 d	3.25 dd (11.3, 4.8)	83.6
2	40.4 t	3.22 m, 2.39 m	26.0 t	2.12 m, 1.35 m	25.8 t	2.16 dd (13.0, 6.2), 1.59 m	25.4 t	1.95 m, 1.21 m	26.4 ^c
3	39.4 t	1.91 m, 1.82 m	36.2 t	1.64 m, 1.26 m	36.7 t	1.71 m, 1.33 m	32.5 t	1.74 m, 0.88 m	37.9
4	35.8 s	–	32.7 s	–	34.2 s	–	33.3 d	1.56 m	35.1
5	61.6 d	2.24 s	58.2 d	1.41 s	61.2 d	1.88 s	58.7 d	1.73 d (11.7)	60.7
6	213.8 s	–	89.8 d	3.61 s	213.9 s	–	215.8 s	–	215.9
7	90.8 s	–	88.2 s	–	87.2 s	–	89.8 s	–	91.7
8	81.8 s	–	83.8 s	–	83.0 s	–	83.3 s	–	81.1
9	44.9 d	2.20 m	40.2 d	3.77 m	41.9 d	2.42 dd (6.2, 4.8)	44.7 d	2.35 t (4.8)	45.5
10	41.5 d	2.29 m	48.4 d	2.22 m	47.5 d	2.17 m	53.2 d	2.15 m	47.5
11	56.1 s	–	49.3 s	–	46.2 s	–	49.5 s	–	46.2
12	28.6 t	2.42 m, 1.34 m	27.3 t	2.45 m, 1.72 m	27.1 t	2.37 dd (14.5, 5.5), 1.96 m	26.5 t	2.66 m, 1.84 dd (15.8, 7.6)	26.5 ^c
13	36.5 d	2.52 m	38.7 d	2.40 m	38.6 d	2.50 dd (8.9, 4.8)	37.7 d	2.56 m	36.0
14	73.6 d	4.12 m	83.4 d	3.68 t (5.5)	82.0 d	3.68 t (4.8)	73.1 d	4.16 t (4.8)	73.6
15	32.4 t	2.42 m, 1.85 m	34.7 t	2.47 m, 1.99 dd (15.1, 8.2)	32.7 t	2.51 dd (15.8, 8.9), 1.95 dd (15.8, 6.2)	33.2 t	2.59 dd (17.1, 8.9), 1.95 m	31.1
16	80.8 d	3.51 m	81.3 d	3.28 m	81.1 d	3.32 m	80.8 d	3.55 d (8.9)	81.1
17	65.2 d	3.59 s	62.1 d	3.80 s	59.0 d	4.16 s	59.5 d	3.34 s	63.2
18	24.4 q	1.05 s	25.6 q	1.02 s	24.2 q	1.00 s	21.6 q	1.16 d (6.1)	24.6
19	58.5 t	2.77 m, 2.42 m	47.1 t	3.86 d (15.1), 2.76 d (15.1)	46.0 t	4.04 d (14.4), 2.51 d (14.4)	163.8 d	8.09 s	57.1
$N\text{-CH}_2\text{CH}_3$	50.1 t	2.77 m, 2.72 m	–	–	–	–	40.3 t	3.37 m	50.2
$N\text{-CH}_2\text{CH}_3$	13.7 q	1.07 t (7.5)	–	–	–	–	12.7 q	1.13 t (6.8)	13.8
$N\text{-CHO}$	–	–	163.1 s	7.94 s	162.0 s	8.04 s	–	–	–
1-OCH ₃	–	–	55.0 q	3.23 s	55.6 q	3.29 s	56.0 q	3.34 s	56.1
6-OCH ₃	–	–	59.4 q	3.40 s	–	–	–	–	–
14-OCH ₃	–	–	58.0 q	3.45 s	58.1 q	3.40 s	–	–	–
16-OCH ₃	56.7 q	3.37 s	56.4 q	3.37 s	56.6 q	3.38 s	56.6 q	3.39 s	56.6

Position	1		2		3		4		δ_C
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	
OCH ₃ O	95.8 t	5.62 s, 5.15 s	94.1 t	5.12 s, 5.10 s	95.9 t	5.54 s, 5.13 s	95.6 t	5.63 s, 5.15 s	95.7

^a : The assignments were based on ¹H-¹H COSY, HSQC, and HMBC experiments.

^b : The data were cited from a previous study (Wada et al., 1992).

^c : Assignments may be interchanged.