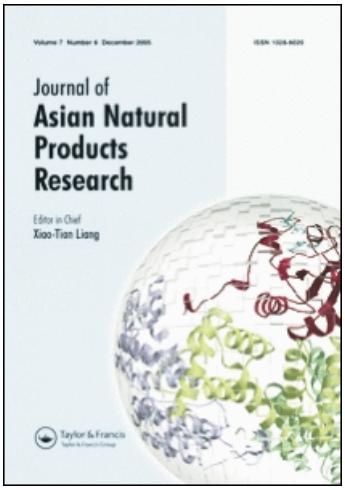

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OLIGOSTILBENES FROM THE ROOTS OF *VITIS AMURENSIS*

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Two new oligostilbenes, amurensin A (**1**) and amurensin B (**2**), were isolated from the roots of *Vitis amurensis* Rupr. together with five known oligostilbenes. Their structures were elucidated by means of spectroscopic evidence, and amurensin B was the first naturally occurring stilbene trimer with a *cis* dihydrobenzofuran moiety.

Keywords: *Vitis amurensis*; Vitaceae; Amurensin A; Amurensin B; Oligostilbenes; Resveratrol; *Cis*-dihydrobenzofuran moiety

INTRODUCTION

The roots and stems of *Vitis amurensis* Rupr. (Vitaceae) have been used to relieve pain from injury, rheumatalgia, stomachache, neuralgic pain and abdominal pain [1]. Phytochemical studies on some *Vitis* species revealed that they contained oligomers of resveratrol [2–6], but there were no reports about oligostilbenes from *Vitis amurensis*. As part of our research on oligostilbenes, the roots of *Vitis amurensis* have been studied carefully. Amurensin A (**1**) and amurensin B (**2**), two new compounds, have been isolated along with five known oligostilbenes: resveratrol (**3**) [7], (+)-ε-viniferin (**4**) [2], ampelopsin A (**5**) [8], ampelopsin D (**6**) and ampelopsin E (**7**) [9] (Structures 1–7). Amurensin B was the first naturally occurring stilbene trimer with a *cis* dihydrobenzofuran moiety.

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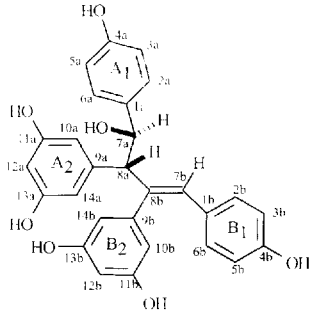

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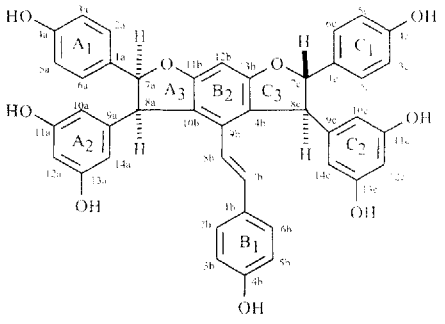

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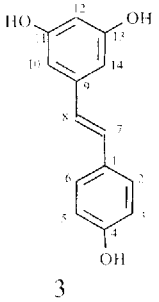

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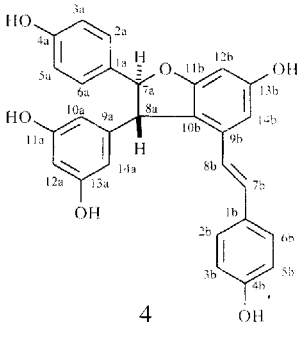

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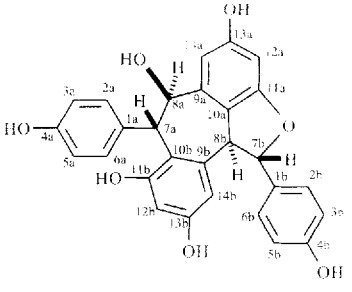

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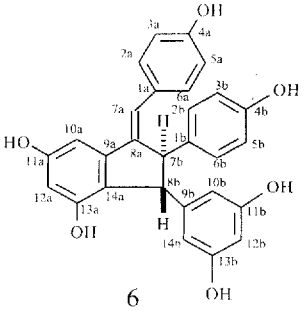

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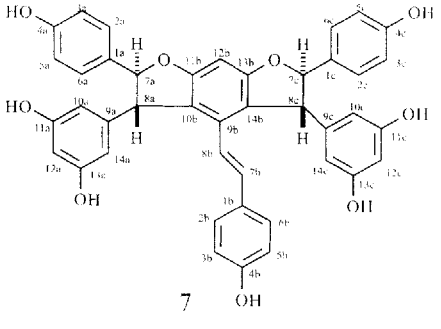

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STRUCTURES 1–7

RESULTS AND DISCUSSION

Amurensin A (**1**) was obtained as colorless amorphous powder, $[\alpha]_D^{19} = +16.9$ (c 0.068, MeOH). Its molecular formula $C_{28}H_{24}O_7$ was determined on the basis of FAB-MS *m/z* 472 and HRFAB-MS *m/z* 455.1517 $[M+H-H_2O]^+$ ($C_{28}H_{22}O_6$ required 455.1494), which together with ^{1}H-NMR of **1** suggested that it should be a resveratrol dimer. The UV spectrum showed absorption band at 270 nm ($\log\varepsilon = 4.29$), suggesting the absence of *trans* stilbene conjugated system in the molecule. The IR spectrum showed the presence of hydroxy (3369 cm^{-1}) and aromatic groups (1608, 1512 cm^{-1}). The ^{1}H-NMR spectrum of **1** showed signals for two 4-hydroxybenzene moieties at δ 7.08 (2H, d, $J = 8.6$ Hz) and δ 6.60 (2H, d, $J = 8.6$ Hz), δ 6.87 (2H, d, $J = 8.7$ Hz) and δ 6.55 (2H, d, $J = 8.7$ Hz); two 3,5-dihydroxybenzene moieties at δ 6.03 (2H, d, $J = 2.2$ Hz) and δ 6.00 (1H, t, $J = 2.2$ Hz), δ 6.04 (2H, d, $J = 2.2$ Hz) and δ 6.24 (1H, t, $J = 2.2$ Hz); two aliphatic methine proton doublets at δ 5.03 (1H, d, $J = 10.0$ Hz) and δ 3.70 (1H, d, $J = 10.0$ Hz) and an olefinic proton singlet at δ 6.75 (1H). The ^{13}C-NMR spectrum revealed signals of two aliphatic carbons at δ 75.7 and δ 64.8, two olefinic carbons at δ 128.0 and δ 141.6 besides twenty-four aromatic carbons. The HMBC spectrum (Fig. 1) showed long-range couplings of H-8a with C-1a, C-10(14)a, C-7b and C-9b, which suggested that two resveratrol units were connected by a linkage of C-8a and C-8b. Thus the structure of amurensin A was determined as shown in structure **1**.

In order to clarify the stereochemistry of **1**, NOESY (Fig. 1) experiment was carried out. The NOEs between H-7b and H-8a, H-7b and H-7a

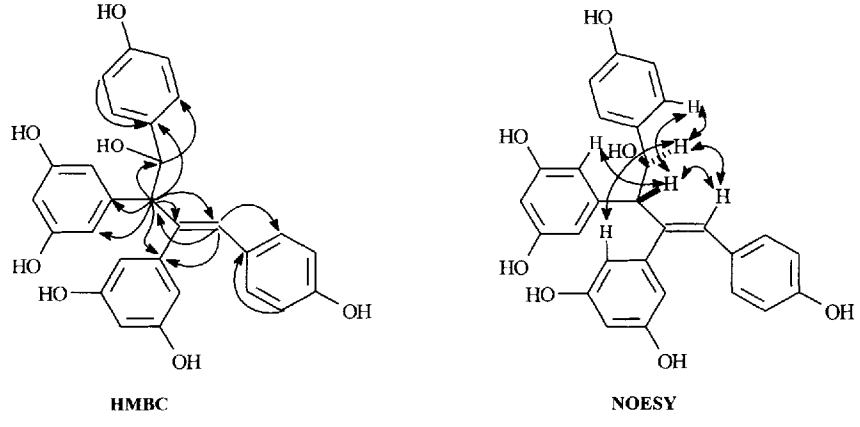

FIGURE 1 HMBC and NOESY for 1.

indicated a *cis* orientation of ring B_1 and B_2, the NOEs between H-8a and H-2(6)a, H-8a and H-10(14)a suggested that H-8a and H-7a should be *trans* oriented. Thus the stereochemistry was shown in structure **1**.

Amurensin B (**2**) was obtained as brown amorphous powder, $[\alpha]_D^{30} = +164.0$ (c 0.056, MeOH). HRFAB-MS *m/z* 681.2119 $[M+H]^+$ gave a molecular formula of $C_{42}H_{32}O_9$ ($C_{42}H_{33}O_9$ required 681.2125), which in combination with the ^{1}H-NMR of **2** indicated that it was a resveratrol trimer. The UV (λ_{max} 284, 320 nm) and IR (3415, 1604, 1514, 1448, 1236, 1159, 1084, 999 cm^{-1}) were similar to those of other oligostilbenes. The ^{1}H-NMR spectrum of **2** showed signals as follows: three sets of signals for 4-hydroxybenzene moieties at δ 7.21 (2H, d, $J = 8.5$ Hz) and δ 6.84 (2H, d, $J = 8.5$ Hz), δ 7.02 (2H, d, $J = 8.4$ Hz) and δ 6.62 (2H, d, $J = 8.4$ Hz), δ 6.95 (2H, d, $J = 8.6$ Hz) and δ 6.61 (2H, d, $J = 8.6$ Hz); two sets of signals for 3,5-dihydroxybenzene moieties at δ 5.84 (2H, d, $J = 2.0$ Hz) and δ 5.95 (1H, t, $J = 2.0$ Hz), δ 6.23 (2H, d, $J = 2.1$ Hz) and δ 6.15 (1H, t, $J = 2.1$ Hz); one aromatic proton singlet at δ 6.47; two *trans* olefin protons at δ 6.72 (1H, d, $J = 16.7$ Hz) and δ 6.69 (1H, d, $J = 16.7$ Hz); two sets of signals for two dihydrobenzofuran moieties at δ 5.88 (1H, d, $J = 7.9$ Hz) and δ 4.68 (1H, d, $J = 7.9$ Hz), δ 5.42 (1H, d, $J = 5.0$ Hz) and δ 4.53 (1H, d, $J = 5.0$ Hz). The ^{1}H-NMR features of **2** were similar to those of gnetin H [10] and ampelopsin E [9], which revealed that **2** possessed the same plain structure with gnetin H and ampelopsin E, only with different stereochemistry. The HMBC spectrum (Fig. 2) confirmed our conclusion.

In the NOESY spectrum (Fig. 2), the NOEs between H-7a and H-8a suggested a *cis* orientation of H-7a and H-8a, the NOEs between H-7c and H-2(6)c, H-7c and H-10(14)c, H-8c and H-2(6)c, H-8c and H-10(14)c suggested a *trans* orientation of H-7c and H-8c, the NOEs between H-10(14)a and H-10(14)c suggested *cis* relations for ring A_2 and ring C_2 as well as for

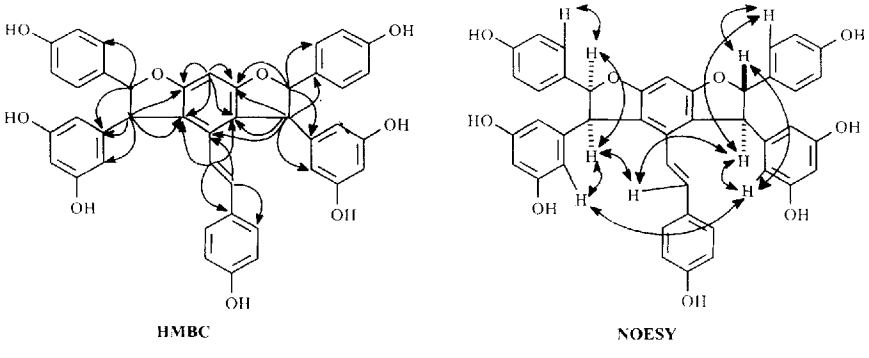

FIGURE 2 HMBC and NOESY for 2.

TABLE 1 ^{1}H and ^{13}C-NMR assignments for **1** and **2** (in CD_3COCD_3, TMS as internal standard)

No.	**1**		**2**	
	^{1}H*	^{13}C**	^{1}H*	^{13}C**
1a		135.9		128.9
2(6)a	7.08 d (8.6)	129.2	7.02 d (8.4)	129.0
3(5)a	6.60 d (8.6)	115.2	6.62 d (8.4)	116.1
4a		157.0		157.4
7a	5.03 d (10.0)	75.7	5.88 d (7.9)	90.6
8a	3.70 d (10.0)	64.8	4.68 d (7.9)	53.9
9a		143.9		143.0
10(14)a	6.03 d (2.2)	108.8	5.84 d (2.0)	108.6
11(13)a		158.5		158.6
12a	6.00 t (2.2)	101.5	5.95 t (2.0)	101.6
1b		130.1		130.0
2(6)b	6.87 d (8.7)	131.3	6.95 d (8.6)	128.5
3(5)b	6.55 d (8.8)	115.4	6.61 d (8.6)	115.0
4b		156.6		158.2
7b	6.75 s	128.0	6.72 d (16.7)	133.7
8b		141.6	6.59 d (16.7)	122.3
9b		145.0		133.1
10b	6.04 d (2.3)	108.4		121.7
11b		159.3		162.3
12b	6.22 t (2.3)	102.0	6.47 s	91.7
13b		159.3		162.0
14b	6.04 d (2.3)	108.4		120.3
1c				133.8
2(6)c			7.21 d (8.5)	127.7
3(5)c			6.84 d (8.5)	116.1
4c				158.2
7c			5.42 d (5.0)	94.0
8c			4.53 d (5.0)	57.7
9c				147.3
10(14)c			6.23 d (2.1)	106.7
11(13)c				159.7
12c			6.15 t (2.1)	101.9

*500 MHz, δ in ppm, J in Hz;
**125 MHz, δ in ppm.

H-8a and H-8c. For the reason that only (+)-ε-viniferin was isolated from this plant, we surmised that H-7c should be in β position and H-8c in α position on the basis of biosynthetic considerations. Therefore amurensin **B** should have relative configuration as shown in structure **2**. Amurensin B was the first naturally occurring oligostilbene with a *cis* dihydrobenzofuran group.

EXPERIMENTAL SECTION

General Experimental Procedures Melting points were measured on a micromelting apparatus and are uncorrected. UV spectra were taken on a Shimadzu UV-300 spectrophotometer. IR spectra were run on a Perkin

Elmer 683 infrared spectrometer in KBr pellets. Optical rotations were measured on Perkin Elmer 241 spectrometer. NMR spectra were carried out on Bruker AM-500 and Mercury 300 using TMS as internal standard. FAB-MS spectra were taken on an Autospec-Ultima-Tof mass spectrometer and HPLC on Waters 411.

Plant Material The roots of *Vitis amurensis* Rupr. were collected from Huairou Beijing in May 1997, identified as *Vitis amurensis* Rupr. by Prof. W.Z. Song. A voucher specimen (97021) was deposited in the herbarium of the Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College.

Extraction and Isolation Dried and powdered roots of *Vitis amurensis* Rupr. (20 kg) were refluxed with 95% EtOH. The extract was concentrated *in vacuo* to yield 2.2 kg gum, which was mixed with silica gel (60–100 mesh), then eluted with $CHCl_3$, Me_2CO, MeOH respectively to give four fractions. The acetone fraction (640 g) was subjected to silica gel chromatography and elution with $CHCl_3$–MeOH (100 : 1–100 : 30) to give A (27.5 g), B (30 g), C (25 g), D (230 g) and E (210 g) fractions. We obtained **3** (8 g) from A, **4** (10 g) from B, **7** (80 mg) from C by repeated column chromatography (silica gel, 100–200 mesh, cyclohexane–acetone). Fraction D was divided into D_1–D_4 by column chromatography (silica gel, 100–200 mesh, cyclohexane–acetone). D_1 was passed through an ODS RP-18 column eluted with MeOH–H_2O = 4 : 6–6 : 4, then purified by MPLC to afford **1** (15 mg), **2** (54 mg), **5** (3 g) and **6** (12 mg).

Amurensin A (**1**) was obtained as colorless amorphous powder. $[\alpha]_D^{19}$ = +16.9 (c 0.068, MeOH). FAB-MS *m/z* 472 $[M]^+$ and HRFAB-MS *m/z* 455.1517 $[M+H-HO]^+$; UV (MeOH) λ_{max}: 270 nm ($\log\varepsilon = 4.29$); IR (KBr) ν_{max}: 3369, 1608, 1512, 1446, 1331, 1238, 1153, 999 and 831 cm^{-1}; ^{1}H-NMR and ^{13}C-NMR data see Table I.

Amurensin B (**2**) was obtained as brown amorphous powder. $[\alpha]_D^{30}$ = +164.0 (c 0.056, MeOH). HRFAB-MS *m/z* 681.2119 $[M+H]^+$; UV (MeOH) λ_{max}: 284 ($\log\varepsilon = 4.40$) nm, 320 ($\log\varepsilon = 4.49$) nm; IR (KBr) ν_{max}: 3415, 1604, 1514, 1448, 1236, 1159, 1084 and 999 cm^{-1}; ^{1}H-NMR and ^{13}C-NMR data see Table I.

Resveratrol (**3**): colorless needles, m.p. 254–255°C. ^{1}H-NMR (300 MHz, in CD_3COCD_3): δ 7.38 (2H, d, J = 8.7 Hz, H-2,6), 6.82 (2H, d, J = 8.7 Hz, H-3,5), 7.00 (1H, d, J = 16.5 Hz, H-8), 6.83 (1H, d, J = 16.5 Hz, H-7), 6.52 (2H, d, J = 2.2 Hz, H-10,14), 6.27 (1H, t, J = 2.2 Hz, H-12).

(+)-ε-Viniferin (**4**): colorless amorphous powder, $[\alpha]_D^{28}$ = +136.9 (c 0.098, MeOH). EI-MS *m/z* 454 $[M]^+$, 360, 347, 331, 267, 107; ^{1}H-NMR (300 MHz, in CD_3COCD_3): δ 7.21 (2H, d, J = 8.7 Hz, H-2a,6a), 7.19 (2H, d, J = 8.4 Hz,

H-2b,6b), 6.85 (2H, d, $J=8.7$ Hz, H-3a,5a), 6.75 (2H, d, $J=8.4$ Hz, H-3b,5b), 6.94 (1H, d, $J=16.2$ Hz, H-8b), 6.73 (1H, d, $J=16.2$ Hz, H-7b), 6.75 (2H, brs, H-12b,14b), 6.34 (1H, t, $J=2.2$ Hz, H-12a), 6.26 (2H, d, $J=2.2$ Hz, H-10a,14a), 5.44 (1H, d, $J=5.1$ Hz, H-7a), 4.46 1H, d, $J=$ 5.1 Hz, H-8a).

Ampelopsin A (**5**): colorless amorphous powder, $[\alpha]_D^{30} = +209.2$ (c 0.071, MeOH). EI-MS *m/z* 452 $[M-H_2O]^+$, 347, 215, 197; UV (MeOH) λ_{max}: 284 nm; IR (KBr) ν_{max}: 3386, 1612, 1516, 1450, 1340, 1234, 1134, 993, 835 cm^{-1}; ^{1}H-NMR (500 M Hz, in CD_3COCD_3): δ 6.83 (2H, d, $J=8.6$ Hz, H-2a,6a), 6.60 (2H, d, $J=8.6$ Hz, H-3a,5a), 5.36 (1H, d, $J=4.9$ Hz, H-8a), 5.39 (1H, d, $J=4.9$ Hz, H-7a), 6.12 (1H, d, $J=2.2$ Hz, H-12a), 6.58 (1H, d, $J=2.2$ Hz, H-14a), 7.07 (2H, d, $J=8.5$ Hz, H-2b,6b), 6.77 (2H, d, $J=$ 8.5 Hz, H-3b,5b), 5.72 (1H, d, $J=11.4$ Hz, H-7b), 4.10 (1H, d, $J=11.4$ Hz, H-8b), 6.39 (1H, d, $J=2.2$ Hz, H-12b), 6.19 (1H, d, $J=2.2$ Hz, H-14b). ^{13}C-NMR (125 MHz, in CD_3COCD_3): δ 132.5 (C-1a), 128.6 ($\times$ 2, C-2a,6a), 115.3 ($\times$ 2, C-3a,5a), 156.0 (C-4a), 71.1 (C-8a), 43.7 (C-7a), 140.2 (C-9a), 116.7 (C-10a), 160.0 (C-11a), 97.0 (C-12a), 158.9 (C-13a), 110.4 (C-14a), 130.7 (C-1b), 129.9 ($\times$ 2, C-2b,6b), 115.9 ($\times$ 2, C-3b,5b), 158.5 (C-4b), 88.4 (C-7b), 49.5 (C-8b), 143.0 (C-9b), 116.1 (C-10b), 158.9 (C-11b), 101.4 (C-12b), 157.2 (C-13b), 105.3 (C-14b).

Ampelopsin D (**6**): brown amorphous powder. EI-MS *m/z* 454 $[M]^+$; ^{1}H-NMR (500 MHz, in CD_3COCD_3): δ 7.17 (2H, d, $J=8.6$ Hz, H-2a,6a), 6.65 (2H, d, $J=8.6$ Hz, H-3a,5a), 7.03 (1H, s, H-7a), 6.79 (1H, d, $J=2.0$ Hz, H-10a), 6.29 (1H, d, $J=2.0$ Hz, H-12a), 7.11 (2H, d, $J=8.4$ Hz, H-2b,6b), 6.74 (2H, d, $J=8.4$ Hz, H-3b,5b), 6.10 (2H, d, $J=2.0$ Hz, H-10b,14b), 6.14 (1H, t, $J=2.0$ Hz, H-12b), 4.27 (1H, s, H-7b), 4.14 (1H, s, H-8b).

Ampelopsin E (**7**): colorless amorphous powder, $[\alpha]_D^{19} = 0$. FAB-MS *m/z* 680 $[M]^+$; UV (MeOH) λ_{max}: 284, 320 nm; IR (KBr) ν_{max}: 3386, 1604, 1514, 1446, 1236, 1159, 997, 833 cm^{-1}; ^{1}H-NMR (500 MHz, in CD_3COCD_3): δ 7.21 (4H, d, $J=8.5$ Hz, H-2a,6a,2c,6c), 6.83 (4H, d, $J=8.5$ Hz, H-3a,5a, 3c,5c), 6.90 (2H, d, $J=8.6$ Hz, H-2b,6b), 6.59 (2H, d, $J=8.6$ Hz, H-3b,5b), 6.62 (1H, d, $J=16.7$ Hz, H-7b), 6.52 (1H, d, $J=16.7$ Hz, H-8b), 6.43 (1H, s, H-12b), 6.23 (4H, d, $J=2.2$ Hz, H-10a,14a,10c,14c), 6.17 (2H, t, $J=2.2$ Hz, H-12a,12c), 5.40 (2H, d, $J=5.1$ Hz, H-7a,7c), 4.52 (2H, d, $J=5.1$ Hz, H-8a,8c); ^{13}C-NMR (125 MHz, in CD_3COCD_3): δ 127.8 ($\times$ 4, C-2a,6a,2c,6c), 116.1 ($\times$ 4, C-3a,5a,3c,5c), 128.5 ($\times$ 2, C-2b,6b), 116.1 ($\times$ 2, C-3b,5b), 133.9 (C-7b), 122.0 (C-8b), 106.7 ($\times$ 4, C-10a,14a,10c,14c), 102.0 (C-12a,12c), 91.2 (C-12b), 94.1 ($\times$ 2, C-7a,7c), 57.9 ($\times$ 2, C-8a,8c), 162.5 ($\times$ 2, C-11b,13b), 159.7 ($\times$ 4, C-11a,13a,11c,13c), 158.2 ($\times$ 3, C-4a,4b,4c), 147.2 ($\times$ 2, C-9a,9c), 133.6 ($\times$ 2, C-1a,1c), 133.3 (C-9b), 129.9 (C-1b), 119.8 ($\times$ 2, C-10b,14b).

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