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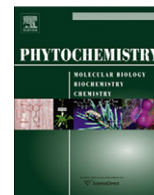

Chemical constituents from fruits of *Harrisonia perforata*

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ABSTRACT

Eight limonoids (**1–8**) including three A, B and D-seco-16-nor-type ones, 5,6-dehydrodesepoxyharperforin C2 (**1**), harrpernoid B (**2**), and its C-9S epimer, harrpernoid C (**3**), along with six known compounds (**9–14**), were isolated from fruits of *Harrisonia perforata*. Extensive spectroscopic analysis was used to elucidate their structures and stereochemistries. Further confirmation of structures of **1** and **2** were obtained by single-crystal X-ray diffraction. Limonoids (**1–8**) were evaluated for their anti-tobacco mosaic virus activity and in vitro cytotoxicity against A549 and HL60 cell lines; only compound **2** showed weak activity.

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1. Introduction

Limonoids are highly oxygenated nortriterpenoids found in the Meliaceae, Rutaceae, Cneoraceae and the *Harrisonia* of Simaroubaceae. They have attracted continuous interest for their large structural diversity and significant biological activities (Taylor, 1984; Champagne et al., 1992; Mulholland et al., 2000; Roy and Saraf, 2006). Approximately 1300 limonoids, more than 35 different carbon frameworks, have been isolated from all four families since the 1970s (Zhang et al., 2009).

The shrub *Harrisonia perforata* (Blanco) Merr. is the only species of *Harrisonia* grown in China (Chen et al., 1997). Previous chemical investigations of its leaves and branches led to isolation of quassinoids (Kamiuchi et al., 1996), chromones (Wang et al., 1983, 1984; Wei et al., 1985; Tanaka et al., 1995; Tuntiwachwuttikul et al., 2006), polyketides (Yin et al., 2009), and limonoids of tremendous structural diversity (Khuong-Huu et al., 2000, 2001; Rugutt et al., 2001; Kamiuchi et al., 1996; Sung et al., 1995). However, the fruits of *H. perforata* were not investigated phytochemically. A search for additional structurally diversified limonoids from plants (Di et al., 2007; Fang et al., 2008, 2009a,b), as well as for anti-tobacco mosaic virus (anti-TMV) bioactive components from the Simaroubeaceae (Chen et al., 2009; Yan et al., 2010), led us to investigate the fruits of *H. perforata* (Blanco) Merr. from the Hainan Province of China. This study has led to isolation of three novel limonoids compounds, **1**–**3**, with highly rearranged A, B and D-seco-16-nor skeletons, along with 11 known compounds, **4**–**14**. We describe the isolation, structural elucidation, anti-TMV and in vitro cytotoxicity of limonoids from the fruit of *H. perforata*.

2. Results and discussion

5,6-dehydrodesepoxyharperforin C2 (**1**) was obtained as colourless crystals (MeOH), and its HRESIMS showed a pseudo-molecular ion peak at m/z 445.1620 $[M + Na]^+$, consistent with the molecular formula $C_{25}H_{26}O_6$ (calcd. for 445.1627). The IR absorption bands at 1769, 1708, 1655 and 1628 cm^{-1} also indicated presence of carbonyls and double bonds. The ^1H and ^{13}C NMR spectroscopic data, in combination with an HMBC analysis indicated that **1** was very similar to harperforin C2 (Khuong-Huu et al., 2001). The only difference between the two was the presence of an additional double bond at C5–C6 in compound **1** instead of the epoxy group in harperforin C2, as suggested by the HMBC correlations from H-6 (δ 6.21) to C-5, C-10, C-7 and C-30. Its structure and relative configuration of **1** was further confirmed by X-ray diffraction, in which the seven-member rings, A and B, were shown to be in half-chair conformations and the six-member ring C exhibited a chair conformation. The γ-lactone ring D was also in an envelope conformation, while the furan ring E was planar. To determine the absolute configuration of **1**, the Flack parameter (Flack and Bernardinelli, 2000) of the crystal was refined to 0.00 (1) and its absolute configuration was depicted in Fig. 2. Thus, compound **1** was determined to be 5,6-dehydrodesepoxyharperforin C2 as shown in Fig. 1.

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Harrpernoid B (**2**) was obtained as colourless crystals (MeOH), and its formula was determined to be $C_{25}H_{28}O_7$ from the HRESIMS data ($[M + Na]^+$ at *m*/*z* 463.1724, calcd. for 463.1732). The molecular formula gave rise to 12° of unsaturation, and IR absorption bands at 1763, 1714 and 1196 cm^{-1} indicated presence of ester carbonyls and ether functionalities. The ^{13}C NMR and DEPT spectra of **2** (Table 1) showed 25 well-resolved resonances, including sp^3 carbons (5 quaternary carbons, 3 methines, 4 methylenes, and 4 tertiary methyls), and sp^2 carbons (5 methines and 5 quaternary carbons). The carbon resonances at δ_C 168.2 and δ_C 172.4 were assigned to ester carbonyls. Two sp^3 quaternary carbons (δ_C 83.7, δ_C 87.2) and one methine carbon (δ_C 77.9) were ascribed to those bearing an oxygen atom, while the sp^3 quaternary carbon at δ_C 111.4 was attributed to a ketal carbon bearing two oxygen atoms. Analysis of the ^1H and ^{13}C NMR spectroscopic data further indicated two α,β-unsaturated ester groups, and one characteristic β-furyl moiety [δ_H 7.44 (brs), H-21; δ_H 6.31 (brs), H-22; and δ_H 7.46 (brs), H-23; δ_c 119.9, C-20; δ_c 139.8, C-21; δ_c 108.2, C-22 and δ_c

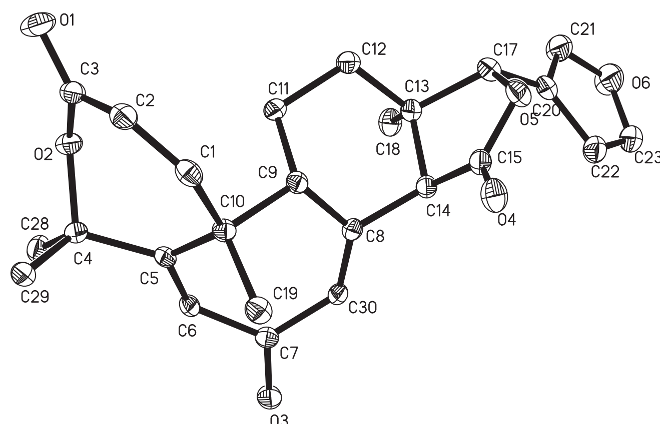


Fig. 2. Single-crystal X-ray structure of **1**.

Fig. 1. Structures of compounds **1**–**14**.

Table 1
^{1}H and ^{13}C NMR spectroscopic data of compounds **1–3** measured in $CDCl_3$.

Position	**1**[a]		**2**[b]		**3**[a]	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	6.01 (*d*,12.5)	149.5	7.40 (*d*,4.4)	160.9	7.41 (*d*,5.5)	160.8
2	6.17 (*d*,12.5)	123.7	6.03 (*d*,4.4)	119.9	6.03 (*d*,5.5)	119.9
3		166.0		172.4		172.3
4		83.1		83.7		83.6
5		154.1	2.64 (*dd*,9.6,6.0)	52.5	2.74 (*q*,6.5)	52.9
6a	6.21 (*s*)	130.1	1.97 (*m*,2H)	38.7	1.89 (*q*,6.5)	37.1
6b					2.04 (*t*,13.0)	
7		191.0		111.4		110.7
8		150.0		146.1		152.4
9	2.24 (*d*,12.0)	51.7	4.24 (*m*)	77.9	4.47 (*m*)	75.1
10		47.3		87.2		87.3
11α	1.58 (*m*)	26.6	1.82 (*brd*,7.6)	25.0	2.20 (*m*)	28.2
11β	1.78 (*m*)		2.15 (*m*)		1.35 (*m*)	
12α	1.84 (*m*)	36.2	1.86 (*m*)	30.6	1.51 (*m*)	28.7
12β			1.73 (*m*)		1.84 (*m*)	
13		48.6		43.5		43.7
14	3.21 (*s*)	58.0		125.6		126.6
15		174.4		168.2		168.4
17	5.10 (*s*)	82.7	4.94 (*s*)	83.4	4.95 (*s*)	81.9
18	0.92 (*s*,3H)	20.0	0.95 (*s*,3H)	21.2	0.88 (*s*,3H)	22.9
19	1.62 (*s*,3H)	32.2	1.56 (*s*,3H)	23.7	1.56 (*s*,3H)	23.8
20		120.7		119.9		119.8
21	7.45 (*brs*)	144.2	7.46 (*brs*)	139.8	7.47 (*brs*)	140.1
22	6.27 (*brs*)	108.5	6.31 (*s*)	108.2	6.36 (*brs*)	108.7
23	7.40 (*brs*)	140.1	7.44 (*brs*)	143.6	7.44 (*brs*)	143.5
28	1.73 (*s*,3H)	26.6	1.25 (*s*,3H)	24.8	1.28 (*s*,3H)	25.3
29	1.66 (*s*,3H)	29.6	1.47 (*s*,3H)	31.4	1.49 (*s*,3H)	31.8
30a	6.06 (*s*)	129.7	3.24 (*brd*,13.6)	38.2	2.97 (*dd*,19.5,2.5)	39.4
30b			2.75 (*dd*,13.6,1.6)		3.08 (*dd*,19.5,1.5)	

δ in ppm and J in Hz are in the parentheses.
[a] Recorded at 500 and 125 MHz for ^{1}H and ^{13}C NMR, respectively.
[b] Recorded at 400 and 100 MHz for ^{1}H and ^{13}C NMR, respectively.

143.6, C-23]. The four double bonds and two carbonyls accounted for six of the 12° of unsaturation, and the remaining 6° of unsaturation indicated compound **2** was hexacyclic. This aforementioned data supports the limonoid classification for **2**.

Detailed analysis of the 2D NMR spectroscopic data of **2**, especially using an HMBC analysis, confirmed that **2** was a limonoid. The C, D and E rings were established by comparison with compound **1**. However, HMBC correlations (Fig. 3) of H_3-18 to an olefinic carbon (δ_C 125.6, C-14), along with HMBC correlations from H-9 to a quaternary olefinic carbon (δ_C 146.1, C-8) and C-14, indicated the presence of a C8–C14 double bond in **2**. The β-furyl ring was attached to C-17 in the D ring, as confirmed by HMBC correlations from H-17 to C-20, C-21, and C-22. Analysis of the COSY

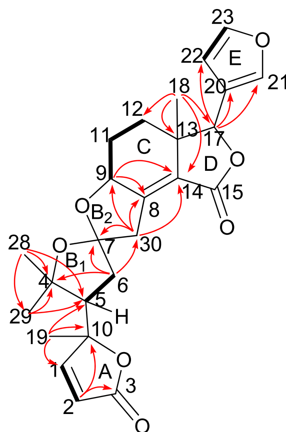


Fig. 3. ^{1}H–^{1}H COSY (––) and selected HMBC (→) correlations of **2**.

spectrum showed a connection from the proton at δ_H 7.40 (H-1) to the proton at δ_H 6.03 (H-2), indicating the presence of a C1–C2 spin system. HMBC correlations from H_3-19 to C-1 and C-10 and from H-2 to C-3 and C-10 were due to the contracted γ-lactone ring A. The presence of two methyl groups at C-4 was elucidated from the key HMBC correlations of H_3-28/H_3-29 to a quaternary carbon at δ_C 83.7(C-4) and to δ_C 52.5 (C-5, CH). The COSY connectivities (Fig. 3) between δ_H 2.64 (H-5) and δ_H 1.97 (H_2-6) indicated a C5–C6 spin system. The HMBC correlations from H_2-6 and H_2-30 to the ketal carbon (δ_C 111.4, C-7), together with the HMBC connectivities of H_2-6 with C-4 and C-30, and H_2-30 with C-8 and C-9, along with the downfield shifted C-9 (δ_C 77.9, oxygenated), indicated the rearranged B ring was a spirocyclic moiety. This spirocyclic moiety contained two oxygenated five-member rings, B_1 and B_2, with two oxygenated carbons C-4 and C-9 attached to the C-7 ketal. Compound **2** was thus determined to be an A, B and D-seco-16-nor-type limonoid bearing a rearranged spirocyclic ring B (Fig. 1). The relative conformation of **2** was determined by ROESY and confirmed by single-crystal X-ray diffraction. The stereochemical analysis from the X-ray diffraction showed that the γ-lactone ring A and the furan ring E were planar, while rings B_1, B_2 and D were in envelope conformations and the six-member ring C exhibited a half-chair conformation (Fig. 4). Biogenetically, harrpernoid B (**2**) might be derived from 5,6-dehydrodesepoxyharperforin C2 (**1**) as shown in Scheme 1. From a biosynthetic point of view, the absolute configuration of **2** should be the same as that of compound **1**.

Harrpernoid C (**3**) was obtained as fine needle crystals (MeOH). It had the same molecular formula ($C_{25}H_{28}O_7$) and similar IR absorption bands as those of compound **2**. The same COSY and HMBC correlations showed compounds **3** and **2** had the overall structures, and ROESY experiments confirmed that they were C-9

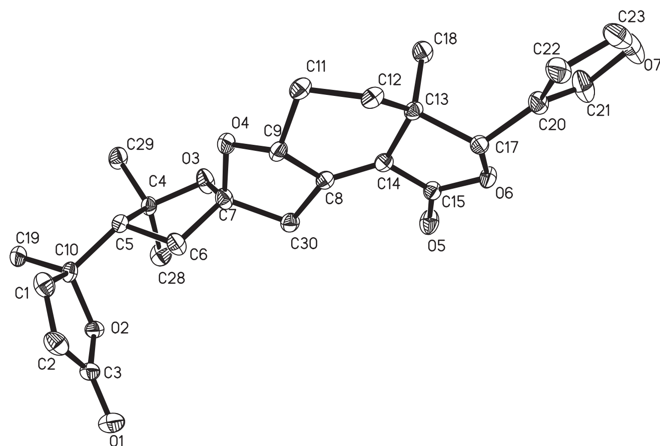


Fig. 4. Single-crystal X-ray structure of **2**.

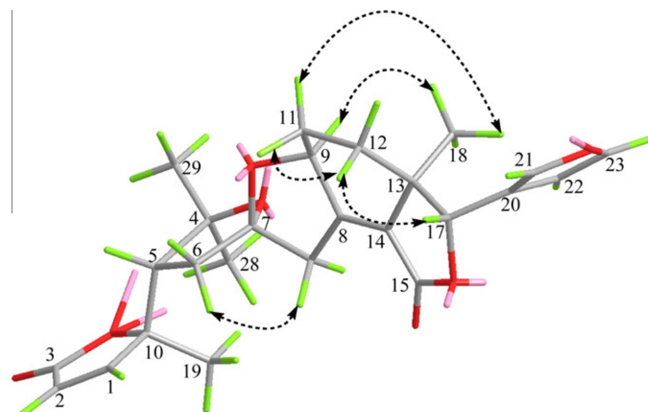


Fig. 5. Selected ROESY correlations of compound **3**.

epimers. In compound **3**, the ROESY correlation (Fig. 5) from H_3-18 to H-9 indicated that these protons were cofacial and were assigned in an α-orientation, while the ROESY correlations of the H-12β to the H-9 proton in compound **2** suggested that both protons were in a β orientation. Thus structure **3** was established as shown in Fig. 1.

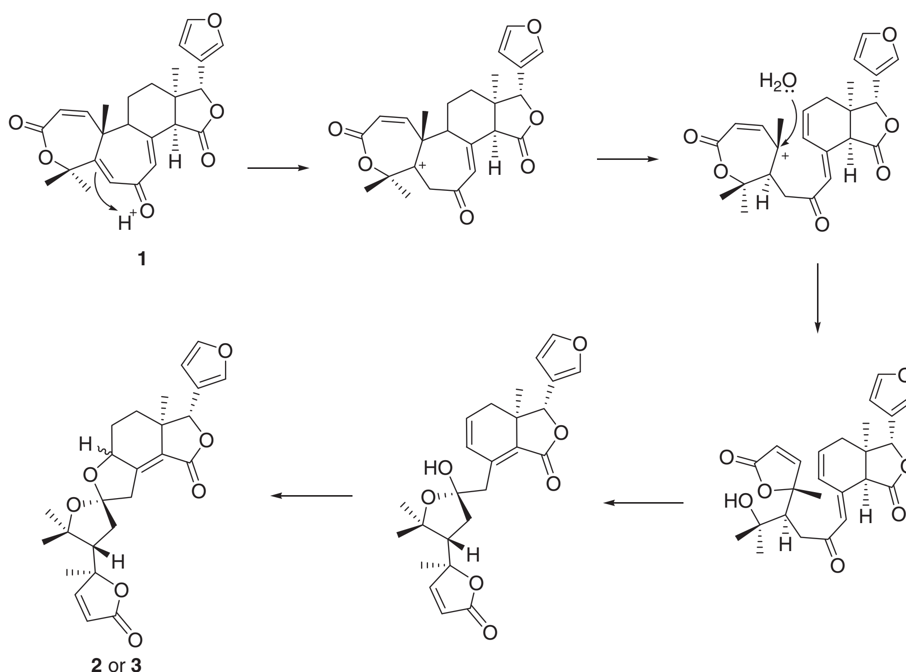
The five known limonoids were identified to be harperforin C2 (**4**) (Khuong-Huu et al., 2001), perforin A (**5**) (Kamiuchi et al., 1996), 12β-acetoxyharrisonin (**6**) (Rajab et al., 1999), 11β,12β-diacetoxyharrisonin (**7**) (Rajab et al., 1999) and rutaevine (**8**) (Sugimoto et al., 1988), by comparing their MS and 1D NMR spectroscopic data with those in the literature. In addition to limonoids, two chromones, umtatin (**9**) (Dean and Robinson, 1971) and greveichromenol (**10**) (Tuntiwachwuttikul et al., 2006), one triterpene, pachymic acid (**11**) (Zhou et al., 2008), one lignan, pinoresinol (**12**) (Ouyang et al., 2007), along with gallic acid (**13**) and methyl gallate (**14**) were also obtained.

Compounds **1**–**8** were tested for their in vitro cytotoxicities against the HL-60 (human leukaemia) and A-549 (human lung adenocarcinoma) cell lines using the methyl-thiazol-tetrozolium (MTT) (Alley et al., 1988) and sulforhodamine B (SRB) (Skehan et al., 1990) methods, respectively. Compound **2** showed weak activity (inhibition rates of 63.6% and 64.9%, respectively, at the concentration of 10 μM), but the other compounds were inactive. None of the isolated limonoids showed activity against tobacco mosaic virus (TMV) using the half-leaf method (Yan et al., 2010).

3. Conclusions

Three new limonoids, Harpernoids A–C (**1**–**3**), together with 11 known compounds (**4**–**14**), were isolated from fruits of *H. perforata*. Known compounds perforin A (**5**), rutaevine (**8**), pachymic acid (**11**), and pinoresinol (**12**) were also found in *H. perforata* for the first time. All isolated limonoids (**1**–**8**) were screened for cytotoxicity in vitro, as well as anti-tobacco mosaic virus activities only compound **2** showed very weak cytotoxicity to A-549 and HL-60 cell lines.

It is interesting to note that compounds **2**–**3** showed a great deal of similarity with the cneorins and tricoccins, the limonoids



Scheme 1. Hypothetical biosynthetic relationship between compounds **1**–**3**.

isolated from *Cneorum tricoccum* (Cneoraceae) (Mondon and Epe, 1983), as well as with cedkathryn A–B from *Cedrelopsis gracilis* (Ptaeroxylaceae) (Mulholland et al., 2004). They all have a rearranged spirocyclic moiety which was formed by incorporation of the C-30 methyl group between C-8 and C-7; oxidative cleavage of the C-3/C-4 bond followed by recyclisation to form a 4,7-ether linkage and a C-3, C-10 lactone (Mulholland et al., 2004). The prominence difference between them was whether the C-18 formed an additional ring moiety. Specifically, limonoids in *Harrisonia* all had a C-18 methyl group, whereas the C-18 in limonoids of *Cneorum tricoccum* (Cneoraceae) and *Cedrelopsis grevei* (Ptaeroxylaceae) have an additional 13,14,18-cyclopropyl group. Mulholland previously noted structural similarity of limonoids isolated from the Cneoraceae and Ptaeroxylaceae (Mulholland and Mahomed, 2000). The structural similarity of the limonoids in *H. perforata*, and those in the species of Ptaeroxylaceae and Cneoraceae further suggest that these taxa are closely related, and this is in agreement with the conclusion by Waterman that there are close links among the Ptaeroxylaceae, Cneoraceae and the genus *Harrisonia* of the Simaroubaceae (Waterman, 1983, 2007).

4. Experimental

4.1. General experimental procedures

Melting points were obtained on an X-4 apparatus and was uncorrected. Optical rotations were determined using a Perkin–Elmer 241 polarimeter. IR spectra were recorded on a Bio-Rad FTS-135 spectrometer with a KBr disc, whereas 1D NMR and 2D NMR spectra were acquired on a Bruker AM-400 spectrometer and a Bruker DRX-500 instrument. ESIMS and HRESIMS spectra were measured with a Finnigan MAT 90 instrument and a VG Auto Spec-3000 spectrometer, respectively. Semi-preparative HPLC was performed on a Merck column (i.d. 100–10 mm; Merck, Darmstadt, Germany). Column chromatography (CC) was performed on silica gel (90–150 μm; Qingdao Marine Chemical Inc. Qingdao, China), MCI gel (75–150 μm; Mitsubishi Chemical Corporation, Tokyo, Japan), Sephadex LH-20 (40–70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden), and Lichroprep RP-18 gel (40–63 μm; Merck, Darmstadt, Germany). Precoated silica gel GF254 and HF254 plates (QingdaoHaiyang Chemical Plant, Qingdao, People's Republic of China) were used for TLC and the spots were visualised by spraying the plates with 10% H_2SO_4 in EtOH.

4.2. Plant material

Fruits of *H. perforata* were collected from the Hainan province of China in November 2008, and were authenticated by Dr. Hao-Fu Dai of the Chinese Academy of Tropical Agricultural. A voucher specimen (accession number KIB-20081102) was deposited at the Kunming Institute of Botany.

4.3. Extraction and isolation

Dried powder from fruits of *H. perforata* (2.1 kg) were extracted with 5L MeOH under conditions of reflux. The corresponding extracts were then combined and concentrated, after which they were suspended in H_2O, with one latter extracted successively with petroleum ether, 5L EtOAc and 5L *n*-BuOH at 60–90 °C. The EtOAc extract was next subjected to silica gel CC and eluted with petroleum ether/Me_2CO (from 1:0 to 0:1) to give 10 fractions (A1–A10). Fraction A4 (petroleum ether/Me_2CO 4:1, 5 g) was further fractionated via MCI gel CC and eluted with a MeOH/H_2O gradient from 5:5 to 9:1 to obtain five fractions (B1–B5). Fraction B1 (1.3 g) was first subjected to Sephadex LH-20 CC to afford **13** (110 mg) and **14** (230 mg), and further separated by semi-preparative HPLC afford to **9** (7 mg) and **10** (8 mg). Fraction B2 (2.4 g) was then subjected to Sephadex LH-20 CC eluted with MeOH to afford four fractions (C1–C4). Fraction C1 was recrystallised from methanol to afford **5** (120 mg). C2 was further purified by silica gel CC (petroleum ether/EtOAc, 5:1) to afford **6** (45 mg), **7** (37 mg), **8** (43 mg), and **11** (17 mg), whereas fraction C3 was further subjected to silica gel CC (petroleum ether/EtOAc, 4:1) to give **1** (23 mg), **4** (56 mg) and **12** (28 mg). The remaining fraction (C4) was further separated by semi-preparative HPLC (MeOH/H_2O, 65:35, 2 ml/min) affording **2** (22 mg) and **3** (15 mg).

4.3.1. 5,6-dehydrodesepoxyharperforin C2

5,6-dehydrodesepoxyharperforin C2 (1): colourless crystals (MeOH); mp, 235–237 °C; $[\alpha]_D^{16}$ −422.2 (c 0.08, MeOH); IR (KBr) vmax 2934, 1769, 1708, 1628, 1310, 1125, 1002, and 821 cm−1; positive-ion ESIMS m/z 423 [M + H]+ and 445 [M + Na]+; HR-ESIMS m/z 445.1620 [M + Na]+, calcd. 445.1627; for ^{1}H NMR and ^{13}C NMR spectroscopic data, see Table 1.

4.3.2. Harrpernoid B

Harrpernoid B (2): colourless crystals; mp, 194–196 °C; $[\alpha]_D^{16}$ −6.9 (c 0.12, MeOH); IR (KBr) vmax 2971, 2938, 1763, 1453, 1196, 1090, 1020, and 978 cm−1; positive-ion ESIMS m/z 441.3 [M + H]+, 463.4[M + Na]+ and 903.0 [2 M + Na]+; HR-ESIMS m/z 463.1724 [M + Na]+, calcd. 463.1732; for ^{1}H NMR and ^{13}C NMR spectroscopic data, see Table 1.

4.3.3. Harrpernoid C

Harrpernoid C (3): colourless needles (MeOH); mp, 202–205 °C; $[\alpha]_D^{16}$ −92.6 (c 0.08, MeOH); IR (KBr) vmax 2941, 1753, 1442, 1195, 1059, 1024, 956 cm−1; positive-ion ESIMS m/z 441.09 [M + H]+, 463.30[M + Na]+ and 903.01 [2 M + Na]+; HR-ESIMS m/z 463.1721 [M + Na]+, calcd. 463.1732; for ^{1}H NMR and ^{13}C NMR spectroscopic data, see Table 1.

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Appendix A. Supplementary data

Supplementary data (IR, HRESIMS, 1D and 2D NMR spectra of compounds 1–3). Crystallographic data for 5,6-dehydrodesepoxyharperforin C2 (1) and harrpernoid B (2) have been deposited at the Cambridge Crystallographic Data Centre (deposition No. CCDC-764966 and 764967). These data can be obtained free of charge at via www.ccdc.cam.ac.uk/conts/retrieving.html. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.phytochem.2011.01.010.

References

Alley, M.C., Scudiero, D.A., Monks, A., Hursey, M.L., Czerwinski, M.J., Fine, D.L., Abbott, B.J., Mayo, J.G., Shoemaker, R.H., Boyd, M.R., 1988. Feasibility of drug screening with panels of human tumor cell lines using a microculture tetrazolium assay. Cancer Res. 48, 589–601.

Champagne, D.E., Koul, O., Isman, M.B., Scudder, G.G.E., Towers, G.H.N., 1992. Biological activity of limonoids from the Rutales. Phytochemistry 31, 377–394.

Chen, S.K., Chen, B.Y., Li, H., 1997. Flora of China (Zhongguo ZhiwuZhi), vol. 433. VCH, Beijing. p. 16.
Chen, J., Yan, X.H., Dong, J.H., Sang, P., Fang, X., Di, Y.T., Zhang, Z.K., Hao, X.J., 2009. Tobacco mosaic virus (TMV) inhibitors from *Picrasma quassioides* Benn. J. Agric. Food Chem. 57, 6590–6595.
Dean, F.M., Robinson, M.L., 1971. Heartwood chromones of *C. Grevei*. Phytochemistry 10, 3221–3227.
Di, Y.T., He, H.P., Liu, H.Y., Yi, P., Zhang, Z., Ren, Y.L., Wang, J.S., Sun, Q.Y., Yang, F.M., Fang, X., Li, S.L., Zhu, H.J., Hao, X.J., 2007. Trijugin-type limonoids from the leaves of *Cipadessa cinerascens*. J. Nat. Prod. 70, 1352–1355.
Fang, X., Di, Y.T., He, H.P., Liu, H.Y., Zhang, Z., Ren, Y.L., Gao, Z.L., Gao, S., Hao, X.J., 2008. Cipadonoid A, a novel limonoid with an unprecedented skeleton, from *Cipadessa cinerasecns*. Org. Lett. 10, 1905–1908.
Fang, X., Di, Y.T., Li, C.S., Geng, Z.L., Zhang, Z., Zhang, Y., Lu, Y., Zheng, Q.T., Yang, S.Y., Hao, X.J., 2009a. Tetranortriterpenoids from the leaves of *Cipadessa cinerascens*. J. Nat. Prod. 72, 714–718.
Fang, X., Zhang, Q., Tan, C.J., Mu, S.Z., Lu, Y., Lu, Y.B., Zheng, Q.T., Di, Y.T., Hao, X.J., 2009b. Cipadonoids B–G, six new limonoids from *Cipadessa cinerascens*. Tetrahedron 65, 7408–7414.
Flack, H.D., Bernardinelli, G., 2000. Reporting and evaluating absolute-structure and absolute-configuration determinations. J. Appl. Cryst. 33, 1143–1148.
Kamiuchi, K., Mitsunaga, K., Koike, K., Ouyang, Y., Ohmoto, T., Nikaido, T., 1996. Quassinoids and limonoids from *Harrisonia perforata*. Heterocycles 43, 653–664.
Khuong-Huu, Q., Chiarona, A., Riche, C., Nguyen-Ngoc, H., Nguten-Viet, K., Khuong-Huu, F., 2000. New rearranged limonoids from *Harrisonia perforata*. J. Nat. Prod. 63, 1015–1018.
Khuong-Huu, Q., Chiaroni, A., Riche, C., Nguyen-Ngoc, H., Nguyen-Viet, K., Khuong-Huu, F., 2001. New rearranged limonoids from *Harrisonia perforata* III. J. Nat. Prod. 64, 634–637.
Mondon, A., Epe, B., 1983. Bitter principles of the Cneoraceae. Prog. Chem. Nat. Prod. 44, 101–187.
Mulholland, D.A., Mahomed, H., 2000. Isolation of Cneorubin X, an unusual diterpenoid from *Ptaeroxylon obliquum* (Ptaeroxylaceae). Biochem. Syst. Ecol. 28, 713–716.
Mulholland, D.A., Parel, B., Coombes, P.H., 2000. The chemistry of Meliaceae and Ptaeroxylaceae of southern and eastern Africa and Madagascar. Curr. Org. Chem. 4, 1011–1054.
Mulholland, D.A., McFarland, K., Randrianarivelojosia, M., Rabarison, H., 2004. Cedkathryns A and B, pentanortriterpenoids from *Cedrelopsis gracilis* (Ptaeroxylaceae). Phytochemistry 65, 2929–2934.
Ouyang, M.-A., Wein, Y.-S., Zhang, Z.-K., Kuo, Y.-H., 2007. Inhibitory activity against tobacco mosaic virus (TMV) replication of pinoresinol and syringaresinol lignans and their glycosides from the root of *Rhus javanica* var. Roxburghiana. J. Agric. Food Chem. 55, 6460–6465.
Rajab, M.S., Fronczek, F.R., Mulholland, D.A., Rugutt, J.K., 1999. 11β, 12β-Diacetoxyharrisonin, a tetranortriterpenoid from Harrisonia abyssinica. Phytochemistry 52, 127–133.
Roy, A., Saraf, S., 2006. Limonoids: overview of significant bioactive triterpenes distributed in plants kingdom. Biol. Pharm. Bull. 29, 191–201.
Rugutt, J.K., Rugutt, K.J., Berner, D.K., 2001. Limonoids from Nigerian *Harrisonia abyssinica* and their stimulatory activity against *Striga hermonthica* seeds. J. Nat. Prod. 64, 1434–1438.
Skehan, P.A., Storeng, R., Monks, A., McMahon, J., Vistica, D., Warren, J.T., Bokesch, H., Kenney, S., Boyd, M.R., 1990. New colorimetric cytotoxicity assay for anticancer-drug screening. J. Nat. Can. Inst. 82, 1107–1112.
Sugimoto, T., Miyase, T., Kuroyanagi, M., Ueno, A., 1988. Limonoids and quinolone alkaloids from *Evodia rutaecarpa* Bentham. Chem. Pharm. Bull. 36, 4453–4461.
Sung, T.V., Phung, N.M., Kamperdick, C., Adam, G., 1995. Perforatinolone, a limonoid from *Harrisonia perforata*. Phytochemistry 38, 213–215.
Tanaka, T., Koike, K., Mitsunaga, K., Narita, K., Takano, S., Kamioka, A., Sase, E., Ouyang, Y., Ohmoto, T., 1995. Chromones from *Harrisonia perforata*. Phytochemistry 40, 1787–1790.
Taylor, D.A.H., 1984. The chemistry of the limonoids from Meliaceae. In: Herz, W., Grisebach, H., Kirby, G.W. (Eds.), Progress in the Chemistry of Organic Natural Products, vol. 45. Springer-Verlag, New York, pp. 1–102.
Tuntiwachwuttikul, P., Phansa, P., Pootaengon, Y., Taylor, W.C., 2006. Chromones from the branches of *Harrisonia perforata*. Chem. Pharm. Bull. 54, 44–47.
Wang, M.X., Zhang, M.S., Zhu, Y.L., 1983. Studies on the chemical constituents of a Chinese folk medicine Niu-Jin-Guo (*Harrisonia perforata* Blano Merr). Acta pharmaceutica Sinica. 18, 113–118.
Wang, M.X., Zhang, M.S., Liu, W.Z., Zhu, Y.L., 1984. Isolation and structural determination of perforatic acid from Chinese folk medicine niu-jin-guo (*Harrisonia perforata*). Acta pharmaceutica Sinica. 19, 760–763.
Waterman, P.G., 1983. Phylogenetic implications of the distribution of secondary metabolites in the Rutales. In: Waterman, P.G., Grundon, M.F. (Eds.), Chemistry and Chemical Taxonomy of the Rutales. Academic Press, London, pp. 377–400.
Waterman, P.G., 2007. The current status of chemical systematics. Phytochemistry 68, 2896–2903.
Wei, X.C., Pan, Z.H., Gu, X.C., Wang, M.X., Zhu, Y.L., 1985. Chemical constituents of the Chinese medicine Niu-Jin-Guo (*Harrisonia perforata* Blanco Merr.). IV. Molecular and crystal structure on Niu-Jing V. Jiegou Huaxue 4, 281–287.
Yan, X.H., Chen, J., Di, Y.T., Fang, X., Dong, J.H., Sang, P., Wang, Y.H., He, H.P., Zhang, Z.K., Hao, X.J., 2010. Anti-tobacco mosaic virus (TMV) quassinoids from *Brucea javanica* (L.) Merr.. J. Agric. Food Chem. 58, 1572–1577.
Yin, S., Chen, X., Su, Z.S., Yang, S.P., Fan, C.Q., Ding, J., Yue, J.M., 2009. Harrisotones A–E, five novel prenylated polyketides with a rare spirocyclic skeleton from *Harrisonia perforata*. Tetrahedron 65, 1147–1152.
Zhang, H.P., Tan, J.J., VanDerveer, D., Wang, X., Wargovich, M.J., Chen, F., 2009. Khayanolides from African mahogany *Khaya senegalensis* (Meliaceae): a revision. Phytochemistry 70, 294–299.
Zhou, L., Zhang, Y.C., Gapiter, L.A., Ling, H., Agrwal, R., NG, K.-Y., 2008. Cytotoxic and anti-oxidant activities of lanostane-type triterpenes isolated from *Poria cocos*. Chem. Pharm. Bull. 56, 1459–1462.