Diastereoisomeric *ent*-Labdane Diterpenoids from *Andrographis paniculata*

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Four C(8),C(12)-diastereoisomers, (8*S*,12*S*)-isoandrographolide (**1**), (8*S*,12*R*)-isoandrographolide (**2**), (8*R*,12*R*)-isoandrographolide (**3**), and (8*R*,12*S*)-isoandrographolide (**4**) were isolated from the aerial parts of *Andrographis paniculata.* The structures of the new compounds **1**–**3** were established on the basis of the spectroscopic data including UV, IR, NMR, HR-ESI-MS, and X-ray diffraction analysis.

Introduction. – The plant *Andrographis paniculata* (BURM. f.) NEES (Acanthaceae), a well known herbal medicine distributed throughout India, Southeast Asia, and South China, has been widely used as an anti-inflammatory and antimicrobial [1][2] agent with a satisfactory clinical efficacy. Extensive chemical and pharmaceutical investigations on this plant had demonstrated that the *ent*-labdane diterpenoids [3–7] were the main constituents responsible for its therapeutic properties. The crude extracts and *ent*-labdane diterpenoids from the plant had been reported to display various bioactivities [8–11]. In our previous work, three new *ent*-labdane diterpenoids [12] and a unique diterpene [13] had been isolated from the aerial parts of *A. paniculata*. In this work, four diastereoisomeric *ent*-labdane diterpenoids, (8*S*,12*S*)-isoandrographolide (**1**), (8*S*,12*R*)-isoandrographolide (**2**), (8*R*,12*R*)-isoandrographolide (**3**), and (8*R*,12*S*)-isoandrographolide (**4**) (*Fig. 1*) were isolated from the 95% EtOH extract of *A. paniculata*. Among them, **1**–**3** were new compounds with different configurations at the C(8) and C(12) positions, and their structures were elucidated by chemical and spectroscopic methods. Their configurations were inferred from the known andrographolide in combination with the analysis of NOESY data and X-ray diffraction.

Results and Discussion. – The powder of the air-dried aerial parts of *A. paniculta* was percolated with 95% EtOH at room temperature. The concentrated residue was subsequently suspended in H_2O and partitioned with cyclohexane, AcOEt, and BuOH. The AcOEt extract was subjected to column chromatography (silica gel, *Sephadex LH-20*) and semi-prep. HPLC to afford compounds **1**–**4**.

Compound **1** was obtained as colorless needles (MeOH). The HR-ESI-MS of **1** with the quasimolecular-ion peak at *m/z* 349.2021 ($[M-H]^-$) gave the molecular

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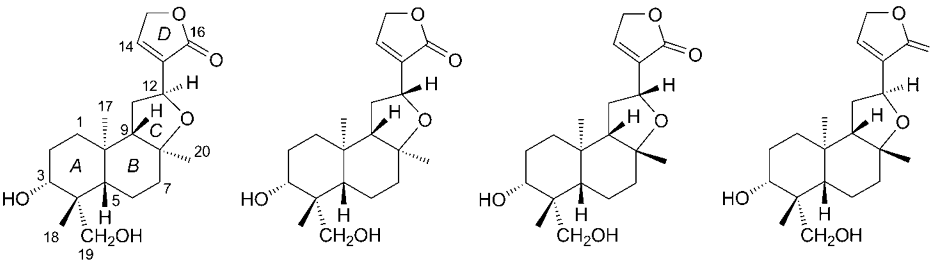
[1]) The authors contributed equally to this work.



1[2]) **2** **3** **4**

Fig. 1. *Compounds* **1**–**4**, *isolated from* Andrographis paniculata

formula $C_{20}H_{30}O_5$. The IR spectrum showed the presence of OH groups (3489 and 3425 cm^{-1}) and an α,β-unsaturated γ-lactone ring (1758 and 1650 cm^{-1}). In the ^1H-NMR spectrum (*Table*), the *s* at δ(H) 0.90, 1.19, and 1.20 indicated the presence of three Me groups at quaternary C-atoms. The H-atom signal at δ(H) 7.43 with a small coupling constant ($J = 1.5$ Hz) was assigned to the endocyclic-olefine H-atom of the α,β-unsaturated γ-lactone ring [14]. Two characteristic geminal H-atoms at δ(H) 3.46 and 4.03 (each *d*, $J = 11.1$ Hz, 1 H), and an oxymethine H-atom at δ(H) 3.30 (*dd*, $J =$ 11.9, 4.7 Hz) were also observed in the ^1H-NMR spectrum. In the ^{13}C-NMR spectrum (*Table*), the signals of twenty C-atoms including a characteristic lactonic C=O at δ(C) 174.8, two olefinic C-atoms at δ(C) 146.4 and 137.1, and five O-bearing C-atoms at δ(C) 83.3, 81.2, 72.4, 72.0, and 65.0 were observed. All the above data were similar to those of the known compound isoandrographolide (= 3-[(2*S*,3a*R*,5a*S*,6*R*,7*R*,9a*R*,9b*S*)-dodecahydro-7-hydroxy-6-(hydroxymethyl)-3a,6,9a-trimethylnaphtho[2,1-*b*]furan-2-yl]furan-2(5*H*)-one) [15], suggesting **1** has the same molecular skeleton as isoandrographolide. In the NOESY plot of **1**, the correlations H–C(9) (δ(H) 1.51)/H–C(5) (δ(H) 1.10), H–C(5)/H–C(3) (δ(H) 3.30), H–C(3)/Me(18) (δ(H) 1.20), H–C(12) (δ(H) 4.80)/ Me(20) (δ(H) 1.19), as well as Me(20)/Me(17) (δ(H) 0.90) assigned the relative configuration of **1**. The above result was further confirmed by the X-ray crystallographic analysis (*Fig. 2*). The absolute configuration of **1** was established on the basis of the configurations of andrographolide and isoandrographolide, which were confirmed by X-ray diffraction [15][16] and ORD studies [17][18]. Considering the biogenetic pathway of these diterpenoids, the configurations of C(3), C(4), C(5), C(9), and C(10) of **1** were determined as (*R*), (*R*), (*S*), (*S*), and (*R*), respectively. Thus, the absolute configurations of C(8) and C(12) were determined as (*S*) and (*S*), respectively, and **1** was elucidated as (8*S*,12*S*)-isoandrographolide[2]).

Compound **2** was obtained as colorless crystals. The IR absorptions (1755 and 1647 cm^{-1}) indicated the presence of an α,β-unsaturated γ-lactone ring. The HR-ESI-MS with a quasimolecular-ion peak at *m/z* 349.2015 ($[M - H]^-$) revealed the presence of the molecular formula $C_{20}H_{30}O_5$. The ^{13}C-NMR data of **2** (*Table*) were similar to those of **1**, except for the downfield shifts of C(9) (δ(C) 62.2), C(12) (δ(C) 74.5), and C(17) (δ(C) 25.0) by +2.8, +2.5, and +3.2 ppm, respectively. These data indicated

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[2]) Trivial atom numbering; for systematic names, see *Exper. Part.*

Table. *^{13}C- and ^{1}H-NMR Data* (CD_3OD) *of* **1**–**4**. δ in ppm, J in Hz.

	1		**2**		**3**		**4**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
CH_2(1)	1.15–1.18, 1.48–1.50 (2*m*)	39.1	1.15–1.18, 1.46–1.49 (2*m*)	39.3	1.07–1.10, 1.74–1.77 (2*m*)	40.8	1.06–1.09, 1.75–1.78 (2*m*)	40.4
CH_2(2)	1.70–1.73, 1.80–1.83 (2*m*)	28.3	1.72–1.75, 1.83–1.86 (2*m*)	28.5	1.68–1.71, 1.77–1.79 (2*m*)	28.2	1.69–1.72, 1.77–1.79 (2*m*)	28.4
H–C(3)	3.30 (*dd*, J = 11.9, 4.7)	81.2	3.30 (*dd*, J = 11.7, 4.6)	81.2	3.40 (*dd*, J = 8.4, 3.0)	81.3	3.40 (*dd*, J = 10.0, 4.8)	81.5
C(4)	–	43.7	–	43.8	–	43.4	–	43.5
H–C(5)	1.10 (*dd*, J = 13.2, 3.0)	57.7	1.07 (*dd*, J = 13.1, 3.0)	57.7	1.00 (*dd*, J = 11.4, 2.4)	53.5	1.00 (*dd*, J = 11.4, 2.4)	53.7
CH_2(6)	1.45–1.48, 1.87–1.90 (2*m*)	22.0	1.45–1.48, 1.89–1.91 (2*m*)	22.2	1.50–1.53, 1.58–1.61 (2*m*)	19.4	1.52–1.55, 1.57–1.62 (2*m*)	19.5
CH_2(7)	1.44–1.47, 1.96–1.99 (2*m*)	41.1	1.44–1.47, 1.96–1.99 (2*m*)	41.3	1.56–1.59, 2.14–2.17 (2*m*)	35.9	1.54–1.57, 2.14–2.17 (2*m*)	37.2
C(8)	–	83.3	–	83.2	–	83.5	–	84.4
H–C(9)	1.51 (*dd*, J = 13.2, 4.8)	59.4	1.52 (*dd*, J = 12.2, 2.8)	62.2	1.60 (*dd*, J = 8.6, 2.2)	59.5	1.60 (*dd*, J = 10.2, 6.8)	59.6
C(10)	–	37.0	–	37.3	–	36.9	–	36.9
CH_2(11)	1.62–1.66, 2.16–2.19 (2*m*)	29.7	1.74–1.76, 2.15–2.18 (2*m*)	30.3	2.06–2.09, 2.43–2.46 (2*m*)	32.9	2.06–2.09, 2.36–2.39 (2*m*)	33.9
H–C(12)	4.80 (*t*, J = 6.7)	72.0	4.66 (*dd*, J = 11.5, 4.7)	74.5	4.68 (*dd*, J = 10.0, 2.8)	72.4	4.60 (*dd*, J = 11.8, 4.8)	74.3
C(13)	–	137.1	–	137.9	–	135.4	–	138.5
H–C(14)	7.43 (*t*, J = 1.5)	146.4	7.46 (*t*, J = 1.5)	147.3	7.40 (*s*)	147.3	7.40 (*s*)	146.5
CH_2(15)	4.83–4.86 (*m*)	72.4	4.83–4.86 (*m*)	72.6	4.83–4.87 (*m*)	71.7	4.83–4.87 (*m*)	72.4
C(16)	–	174.8	–	175.1	–	174.8	–	175.0
Me(17)	0.90 (*s*)	15.9	0.88 (*s*)	16.5	0.75 (*s*)	18.8	1.00 (*s*)	17.0
Me(18)	1.20 (*s*)	23.5	1.20 (*s*)	23.5	1.20 (*s*)	23.2	1.22 (*s*)	23.5
CH_2(19)	3.46, 4.03 (2*d*, each J = 11.1)	65.0	3.45, 4.02 (2*d*, each J = 11.1)	65.0	4.17, 3.40 (2*d*, each J = 11.2)	65.0	4.20, 3.40 (2*d*, each J = 11.2)	65.2
Me(20)	1.19 (*s*)	21.8	1.15 (*s*)	25.0	1.19 (*s*)	28.4	1.13 (*s*)	32.0

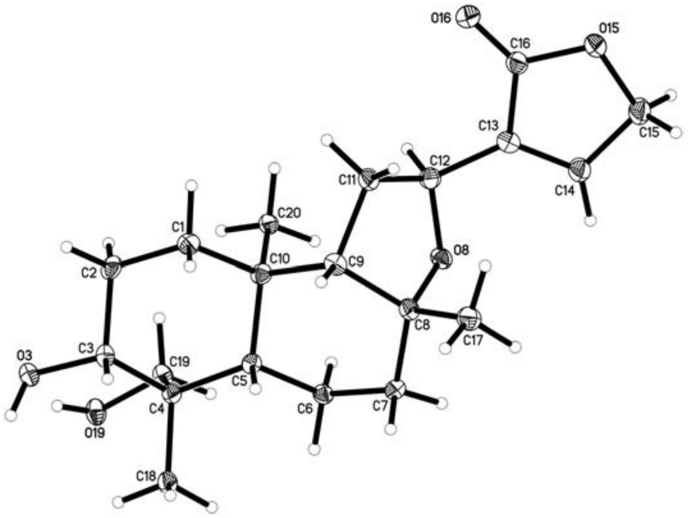

Fig. 2. *Perspective ORTEP view of compound* **1**. Arbitrary atom numbering.

that **2** was a *C*-ring geometric isomer of **1**. The NOE correlations H–C(5)/H–C(9), H–C(9)/H–C(12), and Me(17)/Me(20), as well as the absence of the correlation H–C(12)/Me(20) indicated that H–C(12) has β-orientation, which is opposite to the α-orientation of H–C(12) in **1**. The configurations of C(8) and C(12) in **2** were then assigned as (*S*) and (*R*), respectively. Thus, **2** was determined as (8*S*,12*R*)-isoandrographolide2)).

Compound **3** was isolated as colorless needles. The molecular formula of **3** was deduced as $C_{20}H_{30}O_5$ from its HR-ESI-MS at (*m*/*z* 349.2021 ($[M-\mathrm{H}]^-$)). The IR spectrum also showed the characteristic absorptions of OH groups (3435 and 3350 cm^{-1}) and an α,β-unsaturated γ-lactone ring (1760 and 1648 cm^{-1}). Although most of the ^{13}C-NMR data of **3** (*Table*) were similar to those of **1**, obvious variations in the chemical shifts of C(5), C(6), C(7), C(11), C(17), and C(20) were observed, indicating that **3** was another *C*-ring geometric isomer of **1**. The NOE correlations H–C(9)/H–C(5), H–C(12), and Me(20) suggested the presence of the β-orientation of H–C(9), H–C(12) and Me(20), and a *cis*-fusion mode between rings *B* and *C*. The X-ray crystallographic analysis of **3** confirmed the above result (*Fig. 3*). Thus, compound **3** was elucidated as (8*R*,12*R*)-isoandrographolide2)).

Compound **4** was obtained as colorless needles. The HR-ESI-MS of **4** displayed the quasimolecular-ion peak at *m*/*z* 349.2027 ($[M-\mathrm{H}]^-$), corresponding to the molecular formula $C_{20}H_{30}O_5$. All spectroscopic evidences indicated that **4** was a C(12) geometric isomer of **3**. The molecular structure and relative configuration of **4** were unambiguously confirmed by 2D-NMR spectra and X-ray analysis (*Fig. 4*). The absolute configuration of **4** was assumed on the basis of the structure of **3**. Thus, **4** was elucidated as (8*R*,12*S*)-isoandrographolide2)), which had been previously reported by *Mukhopadhyay* and co-workers and named isoandrographolide [15].

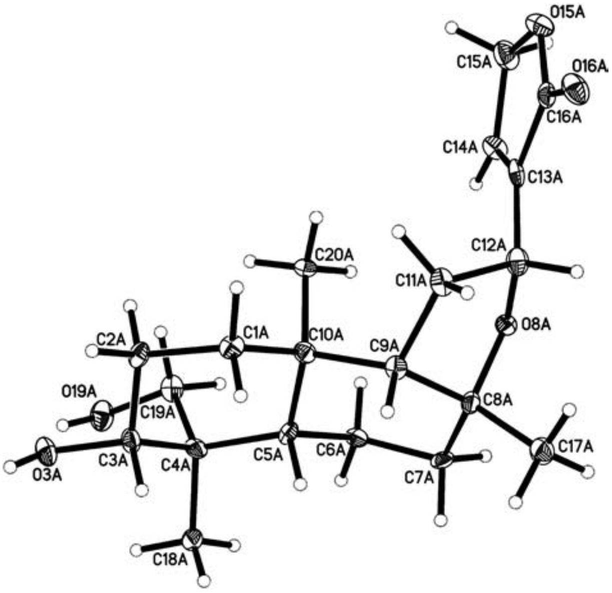

Fig. 3. *Perspective ORTEP view of compound* **3**. Arbitrary atom numbering.

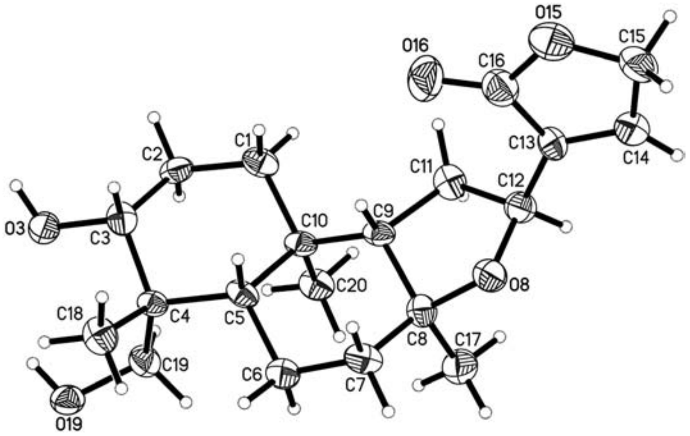

Fig. 4. *Perspective ORTEP view of compound* **4**. Arbitrary atom numbering.

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Experimental Part

General. Column chromatography (CC): silica gel (SiO_2, 200–300 mesh; *Qingdao Marine Chemical Factory*, Qingdao, P. R. China); *Sephadex LH-20* (*Pharmacia*). TLC: precoated SiO_2 GF_{254} plates

(*Qingdao Marine Chemical Factory*, Qingdao, P. R. China). M.p.: *X-4* microscope melting-point apparatus; uncorrected. Optical rotation: *Jasco-P-1020* polarimeter. UV Spectra: *Perkin-Elmer Lambada 2* UV/VIS spectrophotometer; $\lambda_{\max}$ (log ε) in nm. IR Spectra: *Nicolet-Impact-410* spectrometer; KBr; $\tilde{\nu}$ in cm^{-1}. ^{1}H-, ^{13}C-, and 2D-NMR Spectra: *Bruker-AV-400* spectrometer; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. ESI-MS: *HP-1100 HPLC/EST*; in *m/z*. HR-ESI-MS: *Biosystems-Mariner*^{TM}*-5140* spectrometer; in *m/z*.

Plant Material. The aerial parts of *Andrographis paniculata* were collected in Ganzhou City, Jiangxi Province of China, in September 2002, and were authenticated by Prof. *Min-Jian Qin*, China Pharmaceutical University. A voucher specimen (No. 020036) had been deposited with the Herbarium of the China Pharmaceutical University, Nanjing, P. R. China.

Extraction and Isolation. The powder of the air-dried aerial parts (10 kg) of *A. paniculta* was percolated with 95% EtOH at r.t. The concentrated residue was subsequently suspended in H_2O and partitioned with cyclohexane, AcOEt, and BuOH. The AcOEt extract (258 g) was subjected to CC (SiO_2, CH_2Cl_2/MeOH 100 : 1 → 7 : 3; then *Sephadex LH-20*, 60% → 100% MeOH): *Fractions 1–6*. *Fr. 5* was further purified by semi-prep. HPLC (*Cosmosil*, 10 × 250 mm, 5 μm, MeOH/H_2O 3 : 2): **1** (38.6 mg), **2** (26.0 mg), **3** (36.2 mg), and **4** (33.6 mg).

*(8*S*,12*S*)-Isoandrographolide (=3-[(2*S*,3a*S*,5a*S*,6*R*,7*R*,9a*R*,9b*S*)-Dodecahydro-7-hydroxy-6-(hydroxymethyl)-3a,6,9a-trimethylnaphtho[2,1-*b*]furan-2-yl]furan-2(5*H*)-one*; **1**): Colorless needles (MeOH). M.p. 179–181°. $[\alpha]_D^{25} = -21.4$ ($c = 0.12$, MeOH). IR (KBr): 3489, 3425, 1758, 1650, 1153, 1028, 993, 790. ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS: 349.2019 ($[M-H]^-$, $C_{20}H_{29}O_5^-$; calc. 349.2020).

*(8*S*,12*R*)-Isoandrographolide (=3-[(2*R*,3a*S*,5a*S*,6*R*,7*R*,9a*R*,9b*S*)-Dodecahydro-7-hydroxy-6-(hydroxymethyl)-3a,6,9a-trimethylnaphtho[2,1-*b*]furan-2-yl]furan-2(5*H*)-one*; **2**): Colorless crystals (MeOH). M.p. 128–130°. $[\alpha]_D^{25} = +14.8$ ($c = 0.11$, MeOH). IR (KBr): 3429, 3354, 1755, 1647, 1123, 1025, 896. ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS: 349.2015 ($[M-H]^-$, $C_{20}H_{29}O_5^-$; calc. 349.2020).

*(8*R*,12*R*)-Isoandrographolide (=3-[(2*R*,3a*R*,5a*S*,6*R*,7*R*,9a*R*,9b*S*)-Dodecahydro-7-hydroxy-6-(hydroxymethyl)-3a,6,9a-trimethylnaphtho[2,1-*b*]furan-2-yl]furan-2(5*H*)-one*; **3**): Colorless needles (MeOH). M.p. 189–191°. $[\alpha]_D^{25} = +18.6$ ($c = 0.1$, MeOH). IR (KBr): 3435, 3350, 1760, 1648, 1230, 1159, 965. ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS: 349.2021 ($[M-H]^-$, $C_{20}H_{29}O_5^-$; calc. 349.2020).

*(8*R*,12*S*)-Isoandrographolide (=3-[(2*S*,3a*R*,5a*S*,6*R*,7*R*,9a*R*,9b*S*)-Dodecahydro-7-hydroxy-6-(hydroxymethyl)-3a,6,9a-trimethylnaphtho[2,1-*b*]furan-2-yl]furan-2(5*H*)-one*; **4**): Colorless needles (MeOH). M.p. 199–200°. $[\alpha]_D^{25} = -36.7$ ($c = 0.08$, MeOH). IR (KBr): 3489, 3425, 1758, 1665, 1203, 1078, 984, 765. ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS: 349.2027 ($[M-H]^-$, $C_{20}H_{29}O_5^-$; calc. 349.2020).

X-Ray Crystallography of **1**, **3**, *and* **4**. Data were collected on a *Bruker-APEX-CCD* diffractometer with graphite monochromated MoK_α radiation (λ 0.71073 Å). Lattice determination and data collection with SMART v. 5.625, data reduction and absorption correction by empirical methods were performed by SAINT v. 6.26 and SADABS v. 2.03. Structure solution and refinement by SHELXTL v. 610, the crystal structure was solved by direct methods, expanded by difference *Fourier* syntheses, and refined by full-matrix least-squares on F^2.

Crystallographic Data of **1**: $C_{20}H_{32}O_6$, M_r 368.46; crystal size 0.30 × 0.25 × 0.10 mm^3; space group monoclinic, *C*2; *T* 298(2) K; $a = 13.216(2)$ Å, $b = 6.3512(12)$ Å, $c = 22.587(4)$ Å, $\beta = 91.860(4)°$, $V =$ 1894.9 (6) Å^3; $F(000) = 800$, $Z = 4$, $D_x = 1.292$ Mg/m^3; 6655 reflections collected with 3178 independent $R_{int} = 0.0574$, data/restraints/parameters 3178/0/237; goodness-of-fit on $F^2 = 1.002$, final indices $R_1 =$ 0.0508, $wR_2 = 0.0797$; largest difference peak and hole 0.141 and -0.129 e · Å^{-3}, resp.

Crystallographic Data of **3**: $C_{20}H_{30}O_5 \cdot 0.067\ H_2O$, M_r 351.57; crystal size 0.40 × 0.35 × 0.30 mm^3; space group orthorhombic, $P2_12_12_1$; $T = 100(2)$ K; $a = 12.2994(13)$ Å, $b = 13.1192$ (14) Å, $c =$ 22.113(2) Å, $V = 3568.1(7)$ Å^3; $F(000) = 1525$, $Z = 8$, $D_x = 1.309$ Mg/m^3; 17983 reflections collected with 6204 independent $R_{int} = 0.0346$, data/restraints/parameters 6204/0/461; goodness-of-fit on $F^2 = 1.038$, final indices $R_1 = 0.0525$, $wR_2 = 0.1124$; largest difference peak and hole 0.220 and -0.236 e · Å^{-3}, resp.

Crystallographic Data of **4**: $C_{20}H_{30}O_5$, M_r 350.44; crystal size 0.40 × 0.20 × 0.15 mm^3; space group orthorhombic, $P2_12_12_1$; *T* 100(2) K; $a = 6.9717(7)$ Å, $b = 11.4183(12)$ Å, $c = 22.466(4)$ Å, $V = 1788.4$ (3) Å^3; $F(000) = 760$, $Z = 4$, $D_x = 1.302$ Mg/m^3; 9138 reflections collected with 3130 independent $R_{int} =$ 0.0313, data/restraints/parameters 3130/0/226; goodness-of-fit on $F^2 = 1.041$, final indices $R_1 = 0.0359$, $wR_2 = 0.0814$; largest difference peak and hole 0.255 and -0.161 e · Å^{-3}, resp.

CCDC-676897 (**1**), -676898 (**3**), and -676899 (**4**) contain the supplementary crystallographic data for this article. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

REFERENCES

[1] W. L. Deng, *Drug Future* **1990**, *15*, 809.

[2] J. Sinha, S. Mukhopadhyay, N. Das, M. K. Basu, *Drug Delivery* **2000**, *7*, 209.

[3] T. Fujita, R. Fujitani, Y. Takeda, Y. Takaishi, T. Yamada, M. Kido, I. Miura, *Chem. Pharm. Bull.* **1984**, *32*, 2117.

[4] I. Jantan, P. G. Waterman, *Phytochemistry* **1994**, *37*, 1477.

[5] T. Matsuda, M. Kuroyanagi, S. Sugiyama, K. Umehara, A. Ueno, K. Nishi, *Chem. Pharm. Bull.* **1994**, *42*, 1216.

[6] M. K. Reddy, M. V. B. Reddy, D. Gunasekar, M. M. Murthy, C. Caux, B. Bodo, *Phytochemistry* **2003**, *62*, 1271.

[7] Y. K. Rao, G. Vimalamma, C. V. Rao, Y.-M. Tzeng, *Phytochemistry* **2004**, *65*, 2317.

[8] P. K. S. Visen, B. Shukia, G. K. Patnaik, B. N. Dhawan, *J. Ethnopharmacol.* **1993**, *40*, 131.

[9] A. Puri, A. Saxena, R. P. Saxena, K. C. Saxena, V. Srivastava, J. S. Tandon, *J. Nat. Prod.* **1993**, *56*, 995.

[10] P. Misra, N. L. Pal, P. Y. Guru, J. C. Katiyar, V. Srivastava, J. S. Tandon, *Pharm. Biol.* **1992**, *30*, 263.

[11] S.-S. Handa, A. Sharma, *Indian J. Med. Res.* **1990**, *92*, 284.

[12] X.-Q Zhang, G.-C. Wang, W.-C. Ye, Q. Li, G.-X. Zhou, X.-S. Yao, *J. Integr. Plant Biol.* **2006**, *48*, 1122.

[13] G.-C. Wang, Y. Wang, I. D. Williams, H. H-Y. Sung, X.-Q. Zhang, D.-M. Zhang, R.-W. Jiang, X.-S. Yao, W.-C. Ye, *Tetrahedron Lett.* **2009**, *50*, 4824.

[14] S. J. Zhang, A. Masayoshi, *Chin. J. Med. Chem.* **1997**, *7*, 270.

[15] S. Pramanick, S. Baberjee, B. Achari, B. Das, A. K. Sen, Sr., S. Mukhopadhyay, A. Neuman, T. Prangé, *J. Nat. Prod.* **2006**, *69*, 403.

[16] X. He, J. Li, H. Gao, F. Qiu, X. Cui, X. Yao, *Chem. Pharm. Bull.* **2003**, *51*, 586.

[17] M. P. Cava, W. R. Chan, L. J. Haynes, L. F. Johnson, B. Weinstein, *Tetrahedron* **1962**, *18*, 397.

[18] M. P. Cava, W. R. Chan, R. P. Stein, C. R. Willis, *Tetrahedron* **1965**, *21*, 2617.

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