Chinese Chemical Letters 24 (2013) 111–113

Contents lists available at SciVerse ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Original article

Two new guaianolide-type sesquiterpenoids from *Kadsura interior*

Ke Dong, Jian-Xin Pu *, Xue Du, Xiao-Nian Li, Han-Dong Sun *

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China

ARTICLE INFO

Article history:
Received 22 November 2012
Received in revised form 25 December 2012
Accepted 26 December 2012
Available online 4 February 2013

Keywords:
Kadsura interior
4β,9β-Dihydroxy-1α,5α-*H*-guaia-6,10(14)-dien
4β,9β,10α-Trihydroxy-1α,5α-*H*-guaia-6-en
X-ray technique

ABSTRACT

Two new guaianolide-type sesquiterpenoids, 4β,9β-dihydroxy-1α,5α-*H*-guaia-6,10(14)-dien (**1**) and 4β,9β,10α-trihydroxy-1α,5α-*H*-guaia-6-en (**2**), along with four known sesquiterpenoids (**3a**, **3b**, **4** and **5**), were isolated from *Kadsura interior*. Their structures and configurations were elucidated by spectroscopic methods including 2D-NMR and HR-MS techniques. Compounds **3a** and **3b** were obtained as a pair of enantiomers, and their structure and absolute configuration were established from their extensive NMR spectra and by single-crystal X-ray analysis.

1. Introduction

Kadsura interior A. C. Smith (Schizandraceae), a plant indigenous to southwestern Yunnan Province, is the main botanical components of the Chinese medicinal herb Ji-Xue Teng and has been used for the treatment of menstrual irregularities, blood deficiencies, and other feminine disorders [1–3]. Phytochemical investigations of plants belonging to the genus *Kadsura* have indicated that it is rich in dibenzocyclooctadiene lignans and some of them have shown antitumor and anti-HIV activities [4–10]. Although some cadinane and eudesmane-type sesquiterpenoids have been isolated from the stems of *K. longipedunculata* [11] and *K. ananosma* [12] before, there have been very few reports on sesquiterpenoids from these species. During our investigation on chemical constituents of *K. interior*, two new guaianolide-type sesquiterpenoids, 4β,9β-dihydroxy-1α,5α-*H*-guaia-6,10(14)-dien (**1**) and 4β,9β,10α-trihydroxy-1α,5α-*H*-guaia-6-en (**2**) and four known analogues, 4β,10β-dihydroxy-1β,5β-*H*-guaia-6-en (**3a**) [13], 4α,10α-dihydroxy-1α,5α-*H*-guaia-6-en (**3b**) [13], alismoxide (**4**) [14], and guaianediol (**5**) [15] were isolated from the stems of this species (Fig. 1). The structures of the known compounds were determined by comparing spectroscopic data with literature values, and the absolute configurations of **3a** and **3b** were determined by X-ray analysis (CCDC 911931).

2. Experimental

The stems of *K. interior* were collected in Fengqing county, Yunnan Province, China, and identified by Prof. Xi-Wen Li. Voucher specimens (KIB 20081006) were deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

The stems of *K. interior* (20 kg) were extracted with 70% aq. acetone (3 × 10 L) at room temperature and concentrated in vacuo to yield a residue, which was partitioned between H_2O and EtOAc. The EtOAc extract (70 g) was chromatographed over a silica gel, eluted in a step gradient manner with $CHCl_3$–$(CH_3)_2CO$ (1:0–0:1) to afford fractions A–G. Fraction C (2.3 g) was subjected to RP-18 column chromatography (40%–100% gradient CH_3OH–H_2O) to afford subfractions C1–C5. Fraction C3 (0.6 g) was chromatographed on silica gel (petroleum ether-Me_2CO, 40:1–2:1) to give six subfractions. Fraction C3.3 (0.13 g) was purified by semipreparative HPLC (65% CH_3CN–H_2O) to get **1** (7 mg), **3** (10 mg), Fraction C3.5 (0.22 g) was purified repeatedly by semipreparative HPLC (80% CH_3OH–H_2O) to give **2** (8 mg), **4** (12 mg), **5** (10 mg) (Fig. 1).

3. Results and discussion

Compound (**1**), $[\alpha]_D^{15.2}$ – 13.1 (*c* 1.21, CH_3OH), was obtained as a white powder, and its HR-ESI-MS (*m/z* 259.1670 $[M+Na]^+$,

* Corresponding authors.
E-mail addresses: pujianxin@mail.kib.ac.cn (J.-X. Pu), hdsun@mail.kib.ac.cn (H.-D. Sun).

1001-8417/$ – see front matter © 2013 Jian-Xin Pu. Published by Elsevier B.V. on behalf of Chinese Chemical Society. All rights reserved.
http://dx.doi.org/10.1016/j.cclet.2013.01.024

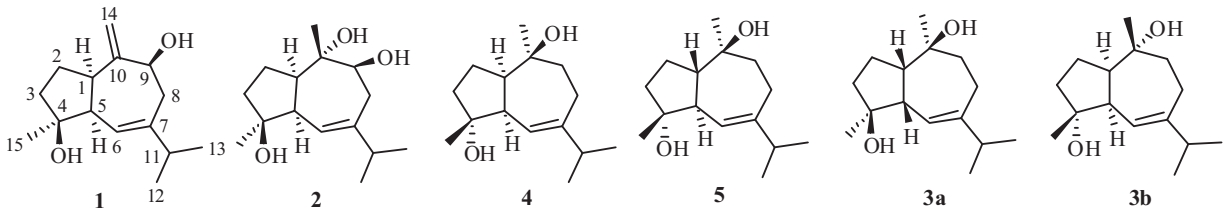

Fig. 1. Structures of compounds **1**–**5**.

Table 1
^{1}H and ^{13}C NMR data of compounds **1** and **2** in CD_3Cl (400 MHz, δ in ppm, J in Hz).

No.	**1**		**2**	
	δ_C	δ_H	δ_C	δ_H
1α	46.4 (d)	2.16 (m)	49.9 (d)	1.65 (overlap)
2α	24.5 (t)	1.70 (m)	21.2 (t)	1.65 (overlap)
2β		1.97 (m)		1.81 (m)
3α	40.2 (t)	1.73 (m)	40.2 (t)	1.65 (overlap)
3β		1.78 (m)		1.72 (m)
4	80.7 (s)		80.1 (s)	
5α	55.8 (d)	2.22 (d, 11.5)	49.9 (d)	2.26 (overlap)
6	122.8 (d)	5.65 (d, 1.2)	122.5 (d)	5.56 (d, 0.7)
7	144.4 (s)		145.8 (s)	
8α	38.6 (t)	2.26 (m)	33.7 (t)	2.25 (overlap)
8β		2.43 (d, 14.6)		2.12 (dd, 14.8, 1.1)
9α	73.5 (d)	3.94 (d, 9.3)	77.5 (d)	3.26 (dd, 11.1, 2.2)
10α	155.8 (s)		78.5 (s)	
11	37.7 (d)	2.29 (m)	37.4 (d)	2.27 (overlap)
12	21.1 (q)	1.01 (d, 6.9)	20.9 (q)	0.99 (d, 6.8)
13	21.2 (q)	0.99 (d, 6.9)	21.0 (q)	0.97 (d, 6.8)
14a	104.7 (t)	5.16 (s)	13.7 (q)	1.26 (s)
14b		4.91 (s)		
15α	24.4 (q)	1.24 (s)	22.6 (q)	1.22 (s)

calcd. 259.1673) gave the molecular formula, $C_{15}H_{24}O_2$, indicating four degrees of unsaturation. The ^{1}H NMR and ^{13}C NMR spectra (Table 1) contained signals for a trisubstituted double bond δ_H 5.65 (d, J = 1.2 Hz), δ_C 122.8 (d) and 144.4 (s), an exocyclic double bond δ_H 5.16 (s) and 4.91 (s), δ_C 155.8 (s) and 104.7 (t), an isopropyl group δ_H 2.29 (m), 1.01 (d, J = 6.9 Hz), 0.99 (d, J = 6.9 Hz), δ_C 37.7 (d), 21.1 (q), and 21.2 (q), and a tertiary methyl group δ_H 1.24 (s), δ_C 24.4 (q). The locations of these groups were confirmed by the HMBC correlations of (Fig. 2) H-6 with C-1, C-4, C-5, and C-11, of H_2-14 with C-1, C-9, and C-10, of H_3-12, H_3-13 with C-7, and of H_3-15 with C-3, C-4 and C-5. The ^{1}H-^{1}H COSY of **1** (Fig. 2) implied the connectivities H-1/H_2-2/H_2-3, H-1/H-5/H-6, and H_2-8/H-9. These evidences indicated that **1** was a guaiane-type sesquiterpenoid [16]. The

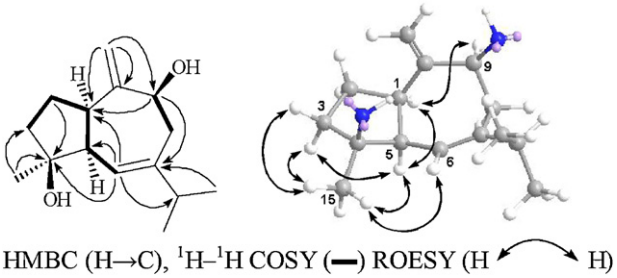

Fig. 2. Key HMBC, ^{1}H–^{1}H COSY, and ROESY correlations of 1.

locations of the two hydroxy groups at C-4 and C-9 was deduced from the HMBC correlations of H-2, H-3, H-5, H-6, and H-15 with C-4, and of H-9 with C-1, C-7, C-8, C-10 and C-14 (Fig. 2).

The relative configurations of **1** were deduced from the ROESY data. H-1 was supposed to be α-oriented [16], in the ROESY spectrum, H-5 showed correlation to H-1α, H-3α, and H_3-15, H-9 correlated to H-1α, and H_3-15 correlated to H-3α, H-3β, and H-6, revealing H-5, H-9, and H_3-15 to be all α-oriented. On the basis of the above evidence, the structure of **1** was determined to be 4β,9β-dihydroxy-1α,5α-*H*-guaia-6,10(14)-dien.

Compound (**2**), $[\alpha]_D^{15.3}$ – 22.5 (*c* 1.59, CH_3OH), was isolated as a white solid. The molecular formula was established as $C_{15}H_{26}O_3$ by HR-ESI-MS (*m/z* 277.1777 $[M+Na]^+$, calcd. 277.1779), which was supported by ^{13}C NMR and DEPT spectroscopic data. Intense analysis of ^{1}H and ^{13}C NMR data disclosed that **2** had two tertiary methyl groups: δ_H 1.26 (s), δ_C 13.7 (q); δ_H 1.22 (s), δ_C 22.6 (q), together with an isopropyl and a trisubstituted olefin-moieties. These spectral features suggested **2** had the same guaiane-type skeleton as **1**. The only significant difference between **1** and **2** was a tertiary methyl group δ_H 1.26 (s), δ_C 13.7 (q) appeared in **2**, instead of an exocyclic double bond between C-10 and C-14 in **1**. A hydroxyl

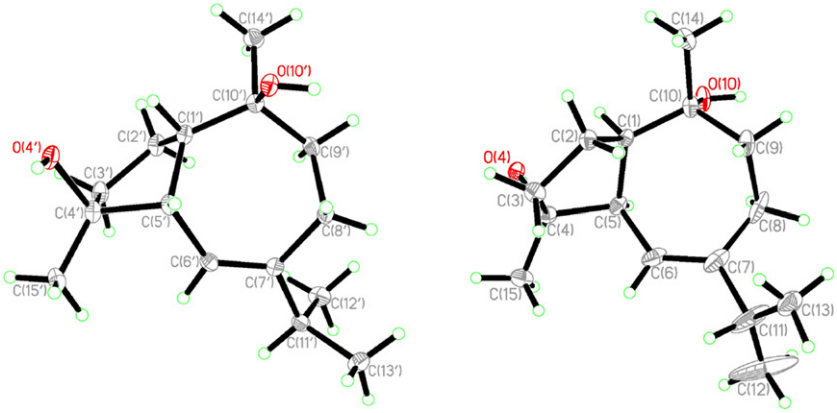

Fig. 3. X-ray crystal structures of **3a** and **3b**.

group was located at C-10, which was confirmed by the HMBC correlations of H-2, H-5, H-8, H-9, and H-14 with C-10. In the ROESY spectrum, the correlations between H_3-14 and H-2β, H-8β indicated that H_3-14 was β-oriented. The rest of the relative configurations of **2** were determined to be the same as those of **1** from further analysis of the ROESY spectrum. Consequently, the structure of **2** was identified as 4β,9β,10α-trihydroxy-1α,5α-H-guaia-6-en.

Comparison of the NMR and MS data of **3** and those of known compounds [13] indicated that these two compounds had the same structure, and both of them had the same ORD value with zero. We speculated that **3** was probably a pair of enantiomers, and the single-crystal X-ray diffraction verified this conclusion, a pair of enantiomers (**3a**, **3b**) in the asymmetric unit (Fig. 3).

4. Conclusion

Up to now, there have been very few reports on sesquiterpenoids from *Kadsura* species. This research led to the isolation of two new sesquiterpenoids, together with four known ones, from the stems of *K. interior*, and also further riched the natural product library of the species of the genus *Kadsura*.

Acknowledgments

This work was supported financially by the NSFC (Nos. 30830115 and 20902093), the foundation of State Key Laboratory of Phytochemistry and Plant Resources in West China (No. P2008-ZZ13), and the Reservation-talent Project of Yunnan Province (No. 2011CI043).

References

[1] J.S. Yang, Y.L. Zeng, Chinese medicine Jixueteng Gao and its original plant investigation, Chin. Pharmaceut. J. 9 (1963) 127–131.
[2] D.F. Chen, G.J. Xu, L.S. Xu, R.L. Jin, The original botanical investigation and commodity identification of traditional Chinese medicine Ji-Xue-Teng, Chin. Herb. Med. 24 (1993) 34–37.
[3] The State Pharmacopoeia Commission of P. R. China, Pharmacopoeia of the People's Republic of China, vol. I, Chemical Industry Press, Beijing, 2000, pp. 522–523.
[4] S. Luo, Z.H. Din, R. Mayer, et al., Interiorin, ein neolignan mit einem neuen Grundgerüst aus *Kadsura interior*, Planta Med. 54 (1988) 440–443.
[5] Z.H. Ding, S.D. Luo, Study on lignans from *Kadsura interior* A. C. Sm, Acta Chim. Sin. 48 (1990) 1075–1079.
[6] Y. Lu, D.F. Chen, Kadsutherins A–C: three new dibenzocyclooctane lignans from the stems of *Kadsura* species, Helv. Chim. Acta 89 (2006) 895–901.
[7] Z.W. Jia, Z.X. Liao, D.F. Chen, Two new dibenzocyclooctene lignans from the water extract of *Kadsura* spp, Helv. Chim. Acta 88 (2005) 2288–2293.
[8] D.F. Chen, S.X. Zhang, K. Chen, et al., Two new lignans, interiotherins A and B, as anti-HIV principles from *Kadsura interior*, J. Nat. Prod. 59 (1996) 1066–1068.
[9] D.F. Chen, S.X. Zhang, L. Xie, et al., Anti-aids agents – XXVI. Structure-activity correlations of Gomisin-G-related anti-HIV lignans from *Kadsura interior* and of related synthetic analogues, Bioorg Med. Chem. 8 (1997) 1715–1723.
[10] D.F. Chen, S.X. Zhang, M. Kozuka, et al., Interiotherins C and D, two new lignans from *Kadsura interior* and antitumor-promoting effects of related neolignans on Epstein-Barr virus activation, J. Nat. Prod. 65 (2002) 1242–1245.
[11] J.X. Pu, X.M. Gao, C. Lei, et al., Three new compounds from *Kadsura longipedunculata*, Chem. Pharm. Bull. 56 (2008) 1143–1146.
[12] C. Zou, X.Y. Pu, J. Zhou, Sesquiterpenoids from *Kadsura ananosma*, Acta Bot. Yunnanica 15 (1993) 196–200.
[13] F. Bohlmann, J. Jakupovic, Neue labdan-derivate und sesquiterpene aus *Silphium*-arten, Phytochemistry 18 (1979) 1987–1992.
[14] Y. Oshima, T. Iwakawa, H. Hikino, Alismol and alismoxide, sesquiterpenoids of *Alisma* rhizomes, Phytochemistry 22 (1983) 183–185.
[15] K.A.E.I. Sayed, M.T. Hamann, A new norcembranoid dimer from the red sea soft coral *Sinularia gardineri*, J. Nat. Prod. 59 (1996) 687–689.
[16] B.F. Bowden, J.C. Coll, S.J. Mitchell, Studies of Australian soft corals. XXI. A new sesquiterpene from *Nephthea chabrolii* and an investigation of the common clam *Tridacna maxima*, Aust. J. Chem. 33 (1980) 1833–1839.