Tetrahedron 73 (2017) 2931–2937

Contents lists available at ScienceDirect

Tetrahedron

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

Lanostane-type triterpenoids from *Kadsura coccinea*

Zheng-Xi Hu [a, b], Xiao-Nian Li [b, c], Yi-Ming Shi [b, c], Wei-Guang Wang [b, c], Xue Du [b, c], Yan Li [b, c], Yong-Hui Zhang [a, **], Jian-Xin Pu [b, c, *], Han-Dong Sun [b, c]

[a] *Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, People's Republic of China*

[b] *State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, People's Republic of China*

[c] *Yunnan Key Laboratory of Natural Medicinal Chemistry, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, People's Republic of China*

ARTICLE INFO

Article history:
Received 21 February 2017
Received in revised form
29 March 2017
Accepted 31 March 2017
Available online 2 April 2017

Keywords:
Kadsura coccinea
Lanostane-type triterpenoids
Cytotoxicity

ABSTRACT

Systematic phytochemical investigation on the stems of *Kadsura coccinea* resulted in the isolation of eleven new lanostane-type triterpenoids, named kadcoccinones G–Q (**1**–**11**), together with two known structural analogues, kadpolysperin M (**12**) and abiesatrine D (**13**). Their structures were characterized on the basis of comprehensive spectroscopic methods, and the absolute configuration of **1** was ascertained by single-crystal X-ray diffraction. Structurally, compounds **1**/**2**, **4**/**5**, and **6**/**7** were three pairs of C-12 epimers, respectively. Additionally, compounds **1**–**11** were evaluated for their in vitro cytotoxicity against the human tumor HL-60, SMMC-772, A-549, MCF-7, SW-480, and HeLa cell lines using the MTS viability assay.

1. Introduction

Plants of the Schisandraceae family, consisting of two genera *Schisandra* and *Kadsura*, are well-known not only for the beneficial pharmacological activities, but also for their powerful abilities to produce architecturally attractive triterpenoids.[1,2] Referring to their different carbon frameworks, Schisandraceae triterpenoids are classified into three categories: lanostane-type, cycloartane-type, and schinortriterpenoids (SNTs).[1,2] Over the past decades, a series of studies have showed that SNTs were almost the chemotaxonomic markers for *Schisandra* species, and hitherto very few *Kadsura* species, such as *K. coccinea*[3] and *K. ananosma*,[4] involved the examples of SNTs, these results implied their intimate connections and huge differences. To further search for the relevance of these two genera, our research group has devoted itself to the discovery of structurally fascinating and bioactive secondary metabolites from the *Kadsura* species. Several highly oxygenated and rearranged lanostane-type or cycloartane-type triterpenoids with new structural types were reported, such as kadlongilactones A and B,[5] kadcoccitones A and B,[6] kadcotriones A–C,[7] kadcoccinic acids A and B,[8] and ananosins A–C,[9] some of which showed cytotoxic or anti-HIV activities.

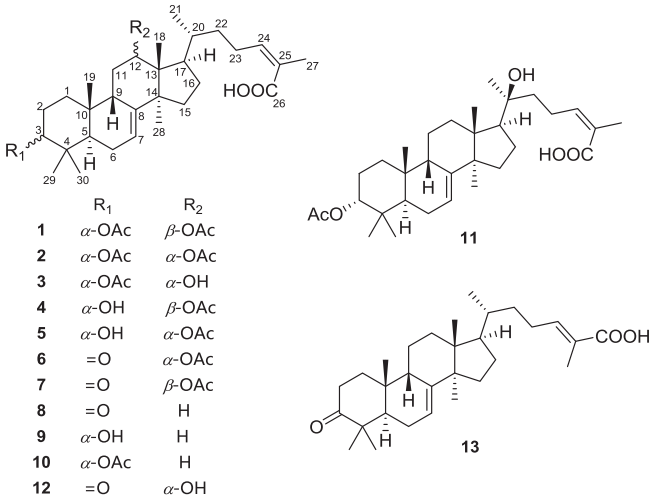
Kadsura coccinea (Lem.) A. C. Smith, distributed in southwest China, was commonly used in the Traditional Chinese Medicine (TCM) for the treatment of gastroenteric disorders and rheumatoid arthritis.[3] Following a preliminary chemical investigation of the structurally novel and bioactive components of this species,[10–12] eleven new lanostane-type triterpenoids (**1**–**11**) and two known structural analogues (**12** and **13**) were obtained from an EtOAc-soluble extract. In this report, the isolation, structure elucidation, and cytotoxicity for these compounds (Fig. 1) are described.

2. Results and discussion

Kadcoccinone G (**1**) was originally obtained as a white, amorphous powder. Its molecular formula was determined to be $C_{34}H_{52}O_6$ based on a $[M + Na]^+$ ion at *m/z* 579.3658 in the HRESIMS analysis (calcd for $C_{34}H_{52}O_6Na$, 579.3656), indicative of nine degrees of unsaturation. The ^1H NMR spectroscopic data (Table 1) of **1** showed resonances characteristic for one doublet methyl (δ_H 0.98, d, J = 6.3 Hz), eight singlet methyls (δ_H 0.87, 0.90, 0.98, 1.03, 1.16, 2.01, 2.16, and 2.18), two olefinic protons (δ_H 5.66 and 6.05), and two

* Corresponding author.State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, People's Republic of China.
** Corresponding author.
E-mail address: pujianxin@mail.kib.ac.cn (J.-X. Pu).

http://dx.doi.org/10.1016/j.tet.2017.03.087
0040-4020/



	R_1	R_2
1	α-OAc	β-OAc
2	α-OAc	α-OAc
3	α-OAc	α-OH
4	α-OH	β-OAc
5	α-OH	α-OAc
6	=O	α-OAc
7	=O	β-OAc
8	=O	H
9	α-OH	H
10	α-OAc	H
12	=O	α-OH

Fig. 1. Chemical structures of compounds **1**–**13**.

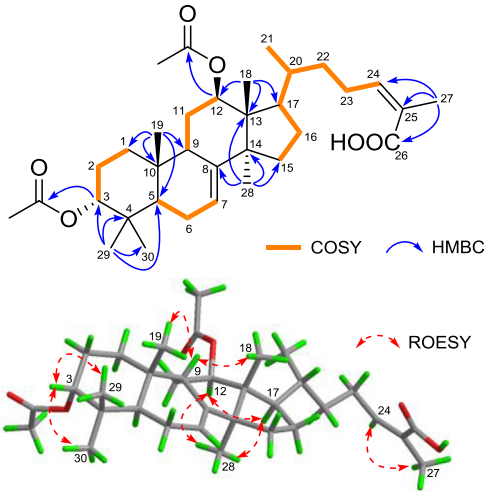


Fig. 2. Selected 2D NMR correlations of compound **1**.

oxygenated methines (δ_H 4.82 and 5.28). Its ^{13}C NMR and DEPT data (Table 3) revealed 34 carbon resonances, corresponding to seven methyls, eight sp^3 methylenes, eight methines (two oxygenated and two olefinic), seven quaternary carbons [two olefinic and one carboxyl (δ_C 171.2)], and two acetyl groups (δ_C 170.8 C, 21.5 CH_3; 171.0 C, 22.2 CH_3). Apart from five degrees of unsaturation occupied by two double bonds and three carbonyls, the remaining ones required a tetracyclic structure for **1**.

These evidence indicated that compound **1** was an intact lanostane-type triterpenoid, whose ^1H and ^{13}C NMR spectroscopic data were very similar to those of kadcoccinone F,[10] differing only in that **1** possessed an acetyl group instead of a ketone group at C-12. This speculation was further supported by the 2D NMR spectra (Fig. 2), including ^1H–^1H COSY cross-peaks of H-9/H_2-11/H-12 and HMBC correlations from Me-18 to C-12 and from H-12 to the acetyl carbonyl (δ_C 171.0). Similar ROESY correlations clarified that the relative configuration of **1** was identical to that of kadcoccinone F. Additionally, the apparent ROESY interactions (Fig. 2) of H-12, H-17α, and Me-28 revealed that 12-OAc should be β-direction. Therefore, the relative configuration of **1** was determined.

By recrystallization with various organic solvents, a suitable crystal of **1** was obtained from $CHCl_3$ (with six drops of MeOH), which was then submitted to a single-crystal X-ray diffraction experiment (Fig. 3). A Flack parameter of 0.01(10) (CCDC 1470163) not only verified our speculation for its planar structure, but also undisputedly allowed an explicit assignment of its absolute structure as 3*R*,5*R*,9*S*,10*R*,12*R*,13*R*,14*S*,17*R*,20*R*, and a *Z*-geometry of the double bond between C-24 and C-25.

Table 1
^1H NMR spectroscopic data (δ in ppm, *J* in Hz) for compounds **1**–**5** in pyridine-d_5.

no.	1[a,b]	2[a,b]	3[a,b]	4[a,b]	5[a,b]
1	1.03 m; 1.69 m	1.14 m; 1.74 m	1.22 m; 1.89 m	1.12 m; 2.30 m	1.17 m; 2.29 m
2	1.66 m; 1.80 m	1.68 m; 1.85 m	1.71 m; 1.89 m	1.78 m; 1.98 m	1.80 m; 2.01 m
3	4.82 br s	4.85 br s	4.85 br s	3.64 br s	3.65 br s
5	1.38 dd (10.0, 5.3)	1.43 br d (9.7)	1.50 dd (10.4, 5.0)	1.66 m	1.69 dd (11.0, 4.2)
6	1.89 m	1.91 m	1.94 m	1.99 m	2.01 m
7	5.66 m	5.72 m	5.75 m	5.71 m	5.76 m
9	2.59 br d (14.4)	2.33 br d (14.2)	2.41 m	2.62 m	2.33 m
11	1.87 m; 2.36 m	1.54 m; 2.82 m	1.91 m; 2.63 m	1.94 m; 2.37 m	1.46 m; 2.86 m
12	5.28 br d (7.2)	5.14 dd (9.8, 7.1)	4.20 t (7.9)	5.23 br d (7.2)	5.11 dd (9.0, 7.1)
15	1.58 m; 1.68 m	1.59 m	1.66 m	1.58 m; 1.70 m	1.60 m
16	1.41 m; 2.07 m	1.34 m; 2.11 m	1.41 m; 2.20 m	1.41 m; 2.06 m	1.32 m; 2.11 m
17	1.71 m	2.24 m	2.63 m	1.68 m	2.23 m
18	1.16 s	0.96 s	1.03 s	1.17 s	0.97 s
19	0.98 s	1.01 s	1.06 s	1.08 s	1.10 s
20	1.51 m	1.50 m	1.61 m	1.50 m	1.50 m
21	0.98 d (6.3)	0.94 m	1.36 d (6.6)	0.97 d (6.9)	0.93 d (6.7)
22	1.24 m; 1.69 m	1.29 m; 1.69 m	1.40 m; 1.80 m	1.25 m; 1.68 m	1.30 m; 1.69 m
23	2.78 m; 2.86 m	2.80 m; 2.87 m	2.89 m; 2.97 m	2.77 m; 2.86 m	2.78 m; 2.88 m
24	6.05 t (6.9)	6.07 t (6.2)	6.08 t (6.9)	6.05 t (7.0)	6.07 t (7.4)
27	2.16 s	2.15 s	2.14 s	2.15 s	2.15 s
28	1.03 s	1.17 s	1.47 s	1.01 s	1.14 s
29	0.87 s	0.89 s	0.90 s	0.96 s	0.98 s
30	0.90 s	0.93 s	0.93 s	1.24 s	1.26 s
–OAc	2.01 s	1.94 s	1.98 s	2.13 s	2.08 s
–OAc	2.18 s	2.07 s	–	–	–

[a] Recorded at 600 MHz.
[b] "m" means overlapped or multiplet with other signals.