Available online at www.sciencedirect.com
ScienceDirect
Chinese Journal of Natural Medicines 2016, **14**(6): 0457–0461
Chinese Journal of Natural Medicines

Two new cyclic bisbibenzyl derivatives from *Hebertus dicranus*

XU Chang-Long [1], WANG Jin-Xin [2Δ], LI Hui-Liang [2*]

[1]*School of Pharmacy and Life Science, Jiujiang University, Jiujiang 332000, China;*
[2]*School of Pharmacy, Second Military Medical University, Shanghai 200433, China*

Available online 20 June, 2016

[ABSTRACT] In the present study, two new cyclic bisbibenzyls (**1**, **2**) co-occuring with a known compound, isoplagiochins C (**3**) were isolated from *Hebertus dicranus*. The structures were determined mainly by extensive 1D and 2D NMR experiments, and the absolute configurations of **1** and **2** were established by the circular dichroism spectrum. Furthermore, all these three rare compounds were tested *in vitro* for inhibitory activity against the growth of human cancer cell lines (A549, HCT116, MDA-MB-231, and BEL7404) by the MTT assay, and compound **2** exhibited moderately inhibitory activity with IC_{50} values ranging from 13.89 to 31.62 μmol·L^{-1}. In conclusion, our results provided a basis for future development and modification of these compounds for cancer therapy.

[KEY WORDS] *Hebertus dicranus*; Cyclic bisbibenzyl; Circular dichroism spectrum

[CLC Number] R284.1 **[Document code]** A **[Article ID]** 2095-6975(2016)06-0457-05

Introduction

Liverworts, the lower plants, have been increasingly studied, owing to their chemical constituents' diversity and varying biological activities [1]. Many characteristic compounds have been isolated from liverworts, and the most special class is the cyclic bisbibenzyls. These compounds are valuable for chemotaxonomic classification of bryophytes and exhibit remarkable antitumor, antibacterial, and antimycotic activities [2]. Since 1996, a series of unique bisbibenzyls, including the chlorinated, possessing two C6-C2′ and C14-C12′ coterminous bisbibenzyl carbon skeletons, such as isoplagiochins C and D, have been found from different bryophytes collected in Japan, Taiwan, New Zealand, Costa Rica, Argentine, and European [3]. Exemplarily for the mcrocyclic bisbibenzyls, the isoplagiochin skeleton is of substantially structural interest, because of the chirality of the entire molecule. The absolute configuration of a cyclic bisbibenzyl, isoplagiochin C (**3**) has been investigated with quantum chemical CD calculations, and its enantiomeric purity is determined by HPLC-CD analysis [4-5]. These methods are also used to determine the absolute configuration of other optically active bisbibenzyls from *Bazzania trilobata*.

In the present study, we isolated three cyclic bisbibenzyls from *Herbertus dicranus* collected in Guizhou Province of China and elucidated their structures. In addition, compound **2** exhibited moderately inhibitory activity on human cancer cell lines (A549, HCT116, MDA-MB-231, and BEL7404) with IC_{50} values ranging from 13.89 to 31.62 μmol·L^{-1}.

Results and Discussion

Structure elucidation and identification

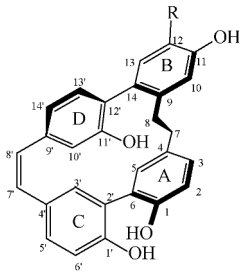
The methanol extract of *Herbertus dicranus* was repeatedly chromatographed on silica gel and sephadex LH20 and further purified by pre-TLC to give two new cyclic bisbibenzyls, 12-hydroxyloisoplagiochin C (**1**) and 12-chloroisoplagiochin C (**2**) (Fig. 1).

The HR-ESI-MS data (439.1547 $[M + H]^+$) of compound

[Received on] 08-Sep.-2015
[Research funding] This work was supported by program NCET Foundation, National Natural Science Foundation of China (Nos. 81230090, 81102335, and 81473109), Shanghai Leading Academic Discipline Project (B906), Key Laboratory of Drug Research for Special Environments, PLA, Shanghai Engineering Research Center for the Preparation of Bioactive Natural Products (10DZ2251300), the Scientific Foundation of Shanghai China (Nos. 12401900801, 13401900101), National Major Project of China (No. 2011ZX09307-002-03), the National Key Technology R&D Program of China (No. 2012BAI29B06), the National Natural Science Foundation of China (No. 21161009), the Natural Science Foundation of Jiangxi Province (No. 20132BAB203004).
[*Corresponding author] Tel/Fax: 86-21-81871245, E-mail: faranli@hotmail.com
[Δ]Co-first author
These authors have no conflict of interest to declare.
Published by Elsevier B.V. All rights reserved

1, a yellow powder, established the molecular formula as $C_{28}H_{22}O_5$ with eighteen degrees of unsaturation. The IR (3 407, 1 654, 1 592, 1 514, 1 458, 1 292, and 1 030 cm^{-1}) and UV (244 nm) spectra showed the presence of a hydroxyl group and a benzene ring.

In the ^{1}H NMR spectrum of compound **1**, three groups ABX coupling systems, a 1,3,4,6-tetrasubstituted benzene,



1: R=OH
2: R=Cl
3: R=H

Fig. 1 Structures of compounds 1−3

a *cis* double bond (δ_H 6.62 and 6.53, each d, J = 11.9 Hz, H-8′ and H-7′) as well as two adjacent methylenes were observed. The ^{13}C NMR spectrum of compound 1 (Table 1) revealed the presence of 28 carbon resonances, which were sorted via the DEPT data into 2 methylenes, 13 unsaturated methines, and 13 unsaturated quarternary carbons. On the basis of the ^{1}H-^{1}HCOSY (Fig. 2), HMQC and the HMBC correlations of H-14′/C-10′, H-5′/C-3′, and H-3/C-5, those aforementioned signals were distinguished to be two contiguous methylene groups (δ_H 2.52, 2H, m, H-8 and 2.64, 2H, m, H-7; δ_C 38.6 and 38.5, C-8 and C-7), a *cis* double bond (δ_H 6.62 and 6.53, each d, J = 11.9 Hz, H-8′ and H-7′; δ_C 130.4 and 129.4, C-7′and C-8′), and four benzene rings (24 benzene ring carbons, including eleven aromatic protons, which can be identified as three ABX couple systems and a *para*-4-substituted pattern). The four benzene rings and one double bond accounted for seventeen of the eighteen units of unsaturation. Therefore, compound 1 was identified as a macrocyclic compound.

Table 1 ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectral data for compounds 1–3 (CD_3OD)

Position	1		2		3	
	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1		151.7 s		151.9 s		151.8 s
2	6.71 d (8.0)	116.5 d	6.72 d (8.0)	116.4 d	6.73 d (8.0)	116.4 d
3	6.95 dd (8.0, 2.2)	128.3 d	6.97 dd (8.0, 2.2)	128.4 d	6.97 dd (8.0, 2.2)	128.4 d
4		136.9 s		136.4 s		136.7 s
5	6.57 d (2.2)	134.1 d	6.55 d (2.2)	134.0 d	6.57 d (2.2)	134.1 d
6		127.5 s		127.6 s		127.6 s
7	2.55−2.68 m (2H)	38.5 t	2.60−2.70 m (2H)	38.6 t	2.55−2.68 m(2H)	39.1 t
8	2.45−2.55 m (2H)	38.6 t	2.45−2.60m (2H)	38.0 t	2.45−2.55 m (2H)	38.2 t
9		134.5 s		131.6 s		144.2 s
10	6.75 s	116.5 d	6.88 s	117.3 d	6.77 d (2.6)	116.1 d
11		145.2 s		153.0 s		157.4 s
12		143.6 s		118.2 s	6.69 dd (8.2, 2.6)	113.4 d
13	6.64 s	118.3 d	7.08 s	132.1 d	7.00 d (8.2)	132.2 d
14		130.0 s		143.0 s		130.2 s
1′		153.5 s		153.6 s		153.5 s
2′		126.9 s		126.8s		126.8s
3′	7.21 d (2.2)	133.8 d	7.19 d (2.2)	133.8 d	7.21 d (2.2)	133.9 d
4′		130.2 s		130.2 s		130.3 s
5′	7.13 dd (8.2, 2.2)	131.0 d	7.14 dd (8.2, 2.2)	131.0 d	7.13 dd (8.2, 2.2)	131.0 d
6′	6.85 d (8.2)	117.3 d	6.86 d (8.2)	117.4 d	6.85 d (8.2)	117.3 d
7′	6.53 d (12.0)	130.4 d	6.55 d (12.0)	130.6 d	6.53 d (12.0)	130.4 d
8′	6.62 d (12.0)	129.4 d	6.63 d (12.0)	129.3 d	6.62 d (12.0)	129.4 d
9′		140.6 s		141.2 s		140.7 s
10′	6.82 d (1.5)	116.0 d	6.84 d (1.5)	116.2 d	6.83 d (1.5)	116.1 d
11′		155.7 s		155.8 s		155.8 s
12′		128.7 s		127.5 s		128.8 s
13′	7.08 d (7.6)	132.8 d	7.09 d (7.6)	132.8 d	7.08 d (7.6)	133.0 d
14′	6.79 dd (7.6, 1.5)	120.2 d	6.81 dd (7.6, 1.5)	120.3 d	6.79 dd (7.6, 1.5)	120.3 d

Download English Version:

https://daneshyari.com/en/article/2526156

Download Persian Version:

https://daneshyari.com/article/2526156

Daneshyari.com