



## An unusual 9,11-*seco* limonoid from *Toona ciliata*



Jian-Jun Xia<sup>a,b,c,†</sup>, Xu-Yang Li<sup>b,d,†</sup>, Shao-Zhi Zhang<sup>b</sup>, Jie-Qing Liu<sup>b</sup>, Wei-Ming Zhang<sup>b,d</sup>, Yu-xin Yan<sup>b</sup>, Zhong-Tao Ding<sup>a</sup>, Ming-Hua Qiu<sup>b,d,\*</sup>

<sup>a</sup>School of Chemical Science and Technology, Yunnan University, Kunming 650091, PR China

<sup>b</sup>State Key Laboratory of Photochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, Yunnan, PR China

<sup>c</sup>R&D Center, HongyunHonghe Tobacco (Group) Co., Ltd, Kunming 650202, PR China

<sup>d</sup>University of Chinese Academy of Sciences, Beijing 100049, PR China

### ARTICLE INFO

#### Article history:

Received 28 October 2013

Revised 14 January 2014

Accepted 13 February 2014

Available online 24 February 2014

#### Keywords:

*Toona ciliata*

Meliaceae

Limonoids

Toonasecone A

### ABSTRACT

An unusual 9,11-*seco* limonoid, toonasecone A (**1**), had been isolated from the bark of *Toona ciliata*. The structure was elucidated on the basis of extensive spectroscopic data analysis. This is the first time the 9,11-*seco* limonoid has been isolated from the Meliaceae family.

© 2014 Elsevier Ltd. All rights reserved.

Plants of the Meliaceae family, which are rich in limonoids with fascinating structures and potential bioactivities, have been studied extensively in the past. Different types of limonoids, including meliacins, apoeuphors, trichilin, phragmalin and nimbolin have been isolated from Meliaceae species. *Toona ciliata* Roem (Meliaceae) is a timber tree which is distributed in China, India, Malaysia and so on.<sup>1</sup> The bark of this plant has historically been used as Chinese folk medicine to treat dysentery, fever and menstrual disorders.<sup>2</sup> Some studies have isolated limonoids,<sup>3</sup> norlimonoids,<sup>4</sup> coumarins and steroids<sup>5</sup> from the seeds,<sup>6</sup> leaves and stems of *T. ciliata*, however, very few chemical investigations<sup>7–13</sup> of the bark of *T. ciliata* have been carried out. In order to fully understand the potential uses of this plant, the chemical constituents of the bark were studied and an unusual 9,11-*seco* limonoid, named toonasecone A (Fig. 1), was found. Herein, we reported the isolation and determination of this new chemical structure by 1D- and 2D-NMR spectroscopy.

Compound **1**,<sup>14</sup> a white amorphous powder, was found to have a molecular formula of C<sub>31</sub>H<sub>42</sub>O<sub>8</sub> at *m/z* 542.2847 [M]<sup>+</sup> (calcd 542.2880) by HR-ESI-MS, with 11 degrees of unsaturation. The IR spectrum showed the presence of hydroxyl (3519 cm<sup>-1</sup>) and carbonyl (1733 cm<sup>-1</sup>) functionalities. Analysis of the NMR data (Table 1) for **1** revealed resonances for 31 carbons including eight

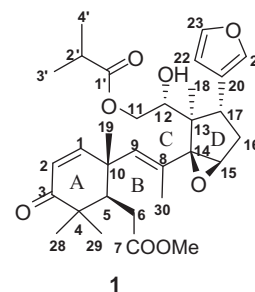


Figure 1. The structure of compound **1**.

methyls (one oxygenated), three methylenes (one oxygenated), eleven methines (two oxygenated and six olefins) and nine quaternary carbons (three carbonyls, two olefins, four sp<sup>3</sup>). In particular,  $\alpha,\beta$ -unsaturated carbonyl ( $\delta_{\text{H}}$  6.69 and 5.92;  $\delta_{\text{C}}$  156.5, 125.1 and 203.4), one carbonyl ( $\delta_{\text{C}}$  173.9) in the ester group, one isobutyryl ( $\delta_{\text{H}}$  1.11, 1.13, and 2.54;  $\delta_{\text{C}}$  19.1, 19.0, 33.9 and 177.5), a  $\beta$ -substituted furan ( $\delta_{\text{H}}$  6.23, 7.23, and 7.31;  $\delta_{\text{C}}$  111.5, 140.9, 142.9 and 123.1), the 14,15-epoxide ( $\delta_{\text{H}}$  3.34;  $\delta_{\text{C}}$  61.9 and 74.4) and one unsaturated bond ( $\delta_{\text{H}}$  5.45;  $\delta_{\text{C}}$  138.4 and 133.9) were also distinguished (Table 1). The above observations accounted for 9 of the 11 degrees of unsaturation suggestive of a limonoid analogue with two additional rings for **1**.

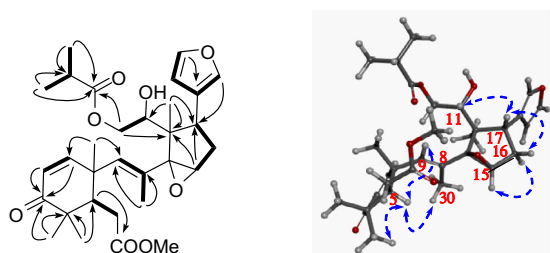
\* Corresponding author. Tel.: +86 0871 5223327; fax: +86 0871 5223255.

E-mail address: [mhchiu@mail.kib.ac.cn](mailto:mhchiu@mail.kib.ac.cn) (M.-H. Qiu).

<sup>†</sup> Jian-Jun Xia and Xu-Yang Li contributed equally to this work.

**Table 1**The NMR chemical shifts and assignments for **1** ( $^1\text{H}$  400 MHz,  $^{13}\text{C}$  100 MHz,  $\text{CDCl}_3$ ,  $\delta$  in ppm, TMS as a standard)

No.	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (mult, J in Hz)	No.	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (mult, J in Hz)
1	156.5 (d)	6.69 (d, 10.2)	17	33.7 (d)	3.17 (dd, 10.4, 7.3)
2	125.1 (d)	5.92 (d, 10.2)	18	17.2 (q)	0.83 (s)
3	203.4 (s)		19	23.5 (q)	1.26 (s)
4	45.7 (s)		20	123.1 (s)	
5	46.4 (d)	2.82 (dd, 4.3, 6.3)	21	140.9 (d)	7.23 (s)
6	32.2 (t)	2.43 (dd, 16.1, 6.3)	22	111.5 (d)	6.23 (s)
		2.37 (dd, 16.1, 4.3)	23	142.9 (d)	7.31 (s)
7	173.9 (s)		28	22.4 (q)	1.06 (s)
8	133.9 (s)		29	24.3 (q)	1.04 (s)
9	138.4 (d)	5.45 (s)	30	16.9 (q)	1.90 (s)
10	41.3 (s)		1'	177.5 (s)	
11	66.1 (t)	4.07 (dd, 10.0, 11.6)	2'	33.9 (d)	2.54 (m)
		4.36 (br d, 11.6)	3'	19.1 (q)	1.11 (d, 6.3)
12	74.6 (d)	3.88, (br d, 10.0)	4'	19.0 (q)	1.13 (d, 6.3)
13	49.1 (s)		7-OMe	52.0 (q)	3.60 (s)
14	74.4 (s)				
15	61.9 (d)	3.34 (s)			
16	32.9 (t)	2.22 (dd, 7.3, 14.3)			
		1.85 (dd, 10.4, 14.3)			

**Figure 2.** The  $^1\text{H}$ – $^1\text{H}$  COSY (—), key HMBC correlations (H  $\rightarrow$  C) and key ROESY correlations (---) of compound **1**.

The  $^1\text{H}$ – $^1\text{H}$  COSY and HSQC experiments further established six structural fragments: (i) (C-1–C-2), (ii) (C-5–C-6), (iii) (C-11–C-12), (iv) (C-15–C-17 via C-16), (v) (C-22–C-23), and (vi) (C-3'–C-4' via C-2' of isobutyryl) as shown in Figure 2. On the basis of fragments (ii) and (iii), and the HMBC cross-peaks (Fig. 2) of H<sub>2</sub>-6/C-4, C-5, C-7 and C-10; H<sub>3</sub>-30/C-8, C-9 and C-14; H-9/C-1, C-10, C-14 and C-30; H<sub>2</sub>-11/C-12, C-13 and C-1', it could be determined that **1** has a 7,8-*seco*-9,11-*seco* fragment. In addition, the multiple HMBC correlations of H-1/C-3; H-2/C-3; H<sub>3</sub>-28 (or/and H<sub>3</sub>-29)/C-3, C-4 and C-5; H<sub>3</sub>-19/C-1, C-5, C-9 and C-10; H<sub>3</sub>-18/C-12, C-13 and C-17; H-17/C-13 and C-16; H-15/C-13 and C-17 established rings A and D as shown. Furthermore, the HMBC correlations from H-17 ( $\delta_{\text{H}}$  3.17) to C-20 ( $\delta_{\text{C}}$  123.1) and C-22 ( $\delta_{\text{C}}$  111.5) revealed that the  $\beta$ -furyl group was attached to C-17 ( $\delta_{\text{C}}$  33.7). Based on the above information, **1** was defined as 9,11-*seco* limonoid, and probably derived from the limonoids, toonacilin or 12-deacetoxytoonacilin.<sup>15</sup>

The relative configuration of **1** was assigned by a ROESY spectrum (Fig. 2), in which the correlations of H-5 $\alpha$ /H<sub>3</sub>-28, H<sub>3</sub>-30 and H-9, of H-15 $\alpha$ /H-16 $\alpha$ , of H-16/H-17 and H-11, and of H<sub>3</sub>-18/H<sub>3</sub>-30 indicated that the 14,15-epoxy group was  $\beta$ -oriented. To our knowledge, the 12-hydroxyl group in the vast majority of limonoids from Meliaceae is  $\alpha$ -oriented.<sup>16</sup> Thus, the absolute configuration of C-12 in **1** was determined as R configuration.

In the Meliaceae family, previous studies have reported that ring A was open between C-3 and C-4<sup>17</sup> and the breakage between C-7 and C-8 occurred in ring B.<sup>18</sup> The most common opening in ring C occurred at C-11 and C-12.<sup>19</sup> Ring D was generally broken between C-16 and C-17.<sup>20</sup> However, other than the common breakage at ring C, compound **1**, isolated from the bark of *T. ciliata*,

was found to be a novel 9,11-*seco* limonoid type and is the first example of a structure with 9,11-*seco* limonoid from Meliaceae. The discovery of this unusual 9,11-*seco* limonoid will hopefully promote further research into the chemical diversity and bioactive components of Meliaceae.

### Acknowledgments

The authors are grateful to Prof. Wang Zong-Yu in Kunming Institute of Botany, Chinese Academy of Sciences for identification of the plant. This work was supported financially by the National Special Program of Basic Research (SB2007FY400), the Knowledge Innovation Program of CAS (Grant No. KSCX2-YW-G-038, Qian-2011), as well as Foundation of Yunnan Tobacco Industry Group (2010.2012) and State Key Laboratory of Phytochemistry and Plant Resources in West China (P2010-ZZ14).

### Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2014.02.057>.

### References and notes

- Chen, S. K.; Chen, B. Y.; Li, H. *In Flora Reipublicae Popularis Sinicae (Zhongguo Zhiwu Zhi)*; Science Press: Beijing, 1997. Vol. 43, pp 239–240.
- The Editorial Committee of the Administration Bureau of Traditional Chinese Medicine Chinese *Materia Medica (Zhonghua Bencao)*; Shanghai Science and Technology Press: Shanghai, 1999, pp 44–45.
- Liao, S. G.; Yang, S. P.; Yuan, T.; Zhang, C. R.; Chen, H. D.; Wu, Y.; Xu, Y. K.; Yue, J. M. *J. Nat. Prod.* **2007**, *70*, 1268–1273.
- Oiano Neto, J.; Fatima Das, G. F.; Da Silva, M.; Fo, E. R.; Fernandes, J. B.; Vieira, P. C.; Pinheiro, A. L. *Phytochemistry* **1998**, *49*, 1369–1373.
- Chowdhury, R.; Rashid, R. B.; Sohrab, M. H.; Hasan, C. M. *J. Bangladesh Acad. Sci.* **2002**, *26*, 219–222.
- Jiang, S. Y.; Liu, J. Q.; Xia, J. J.; Yan, Y. X.; Qiu, M. H. *Helv. Chim. Acta* **2012**, *95*, 301–307.
- Kraus, W.; Grimminger, W.; Sawitzki, G. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 452–453.
- Kraus, W.; Grimminger, W.; Sawitzki, G. *Chem. Nat. Compd.* **1978**, *2*, 115–116.
- Kraus, W.; Grimminger, W. *Nouveau J. Chim.* **1980**, *4*, 651.
- Chowdhury, R.; Ahmed, A.; Rahman, M. Z. *Nat. Prod. Sci.* **2004**, *10*, 99–100.
- Chowdhury, R. *Biochem. Syst. Ecol.* **2004**, *32*, 103–105.
- Chowdhury, R.; Rashid, R. B.; Hasan, C. M.; Rashid, M. A. *J. Bangladesh Acad. Sci.* **2002**, *26*, 219–222.
- Zhang, F.; Wang, J. S.; Gu, Y. C.; Kong, L. Y. *J. Nat. Prod.* **2012**, *75*, 538–546.
- Toonasecone A (1)*: White powder (CHCl<sub>3</sub>); UV in CHCl<sub>3</sub>  $\lambda_{\text{max}}$  (log  $\epsilon$ ): 240 (3.68), 226 (3.15); [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +36.78 (c 1.3, CHCl<sub>3</sub>); IR (KBr)  $\nu_{\text{max}}$  3519, 2974, 2938, 1733, 1672, 1469, 1264, 1193, 1161, 1026 cm<sup>-1</sup>;  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR data: see

Table 1; positive ESI-MS:  $m/z$  565  $[M+Na]^+$ ; positive HREIMS:  $m/z$  542.2847  $[M]^+$  (calcd for  $C_{31}H_{42}O_8$ , 542.2880).

15. Oiano Neto, J.; Agostinho, S. M. M.; Fatima Das, G. F.; Da Silva, M.; Vieira, P. C.; Fernandes, J. B.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1995**, *38*, 397–401.
16. Tan, Q. G.; Luo, X. D. *Chem. Rev.* **2011**, *111*, 7437–7522.
17. Maclachlan, L. K.; Taylor, D. A. H. *Phytochemistry* **1982**, *21*, 1701–1703.
18. Liu, J.; Yang, S. P.; Su, Z. S.; Lin, B. D.; Wu, Y.; Yue, J. M. *Phytochemistry* **2011**, *72*, 2189–2196.
19. Kraus, W.; Cramer, R. *Chem. Ber.* **1981**, *114*, 2375–2381.
20. Taylor, D. A. H. *J. Chem. Soc. (C)* **1969**, 2439–2442.