Chinese Chemical Letters Vol. 10, No. 6, pp. 487–490, 1999

A Novel Sesquiterpene Polyol Ester from *Celastrus Angulatus* and its Antitumor Activities

Wei Ping YIN[1,*], Tian Zeng ZHAO[1], Ling Jie GAO[1], Da Peng ZOU[2], Jian Xun KANG[2]

[1] Institute of Chemistry, Henan Academy of Sciences, Zhengzhou 450003
[2]Centre of Instrumental Analysis, Zhengzhou University, Zhengzhou 450052

Abstract: A new sesquiterpene polyol ester was isolated from the leaves of *Celastrus angulatus*. Its structure was determined as 1 β , 2 β , 9 α -triacetoxy-8 α -(α -hydroxyl-isobutyryloxy)-15-benzoyloxy-4 α -hydroxy-dihydroagarofuran by means of NMR, MS and IR spectral analysis. Preliminary biological study on antitumor activity revealed that this compound showed strong nonselective cytotoxicity against four of the NCl panel cell lines.

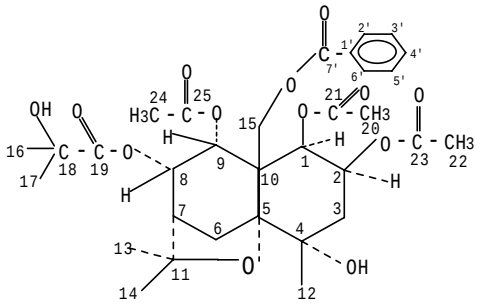
Keywords: *Celastrus angulatus*, sesquiterpene polyol ester, NMR, antitumor activities.

Chinese bittersweet (*Celastrus angulatus* M.) is widely distributed in China. It has been used as traditional plant insecticide and a medicinal herb for many years in the folk medicine of China[1-3]. In previous studies, β -dihydroagarofuran sesquiterpene polyol esters and sesquiterpene alkaloids were frequently found in the *celastrus* family of plants[4-8], It was reported that most of β - dihydroagarofuran sesquiterpene polyol esters from Chinese bittersweet have inhibitory effects on EBV and antitumor activity[9,10]. In our attempt to find novel bioactive compounds in the Chinese bittersweet, a new sesquiterpene polyol ester was isolated from the leaves. Its chemical structure was determined as 1 β , 2 β , 9 α -triacetoxy-8 α -(α -hydroxyl-isobutyryloxy)-15-benzoyloxy-4 α -hydroxy-dihydroagarofuran (**Scheme 1**). This compound contains an α -hydroxyl-isobutyryloxy group which has not been found in any other β - dihydroagarofuran sesquiterpene polyol esters. Biological study on antitumor activity revealed that this compound showed strong nonselective cytotoxicity against four of the NCl panel cell lines. Here, we wish to report the isolation, structure elucidation and antitumor activity of this compound.

C. angulatus leaves were extracted with acetone at room temperature. The extracts were chromatographed on the silica gel column to give a white amorphous powder. The molecular formula was determined to be $C_{32}H_{42}O_{13}$ from the HRMS. Its IR spectrum suggested the presence of an ester carbonyl group (1730 cm^{-1}), a phenyl group (1640, 1460 cm^{-1}), a isobutyry1 group (1753, 1375 cm^{-1}), an associated hydroxyl and free

hydroxyl groups (3545, 3500, 1045 cm^{-1}). Its ^{13}CNMR spectra indicated that this compound contained a β -dihydroagarofuran skeleton. A DEPT experiment revealed that there were three methy1 carbons (δ 25.0, 25.1 and 30.1 ppm), three methylene carbons (δ 31.5, 40.5 and 64.6 ppm), five methine carbons (δ 47.9, 68.3, 68.5, 70.1 and 71.1 ppm) and four quaternary carbons (δ 52.1, 69.5, 83.9 and 89.1 ppm) on the dihydroagarofuran skeleton. The signals at δ 165.6, 169.3, 169.6, 169.8 and 170.5 ppm indicated that there were three acetoxy, one α -hydroxyl-isobutyryloxy and one benzoyloxy groups. The characteristic fragments in its EIMS $[M]^+$ 634, m/z 573 $(M-18-Ac)^+$ and 43 $(Ac)^+$, 487 $(M-42-C_6H_5CO-)^+$ and 105 $(C_6H_5-CO)^+$, 513 $[(M-OH-(CH_3)_2C(OH)-COOH)]^+$ and 104 $[(CH_3)_2C(OH)COOH]^+$ further confirmed the above results.

Scheme 1



In HMBC spectrum, there are obviously correlations between δ c 170. 5 ppm and δ_H 5.69 ppm (H-8), between δ c 165.6 ppm and δ_H 4.54, 4.67 (H-15), 7.46, 8.06 ppm (aromatic protons), which indicated that (α -hydroxyl) isobutylate ester was connected to C-8 and the benzoate ester was joined to C-15. The remaining three acetate esters were obviously at C-1, C-2 and C-9 respectively.

The configurations of the substituted groups on the dihydroagarofuran skeleton were determined by the coupling constants in the proton NMR and NOESY spectra1[1-14]. From coupling constants, $J_{1,2}$=3.2 Hz (Hax-1, Heq-2), $J_{8,.9}$=6.4 Hz (Hax-8, Heq-9), $J_{7,8}$=4.0 Hz, we deduced that H-1 and H-2 are cis- configuration, H-8 and H-9 are cis- configuration as well[11,15].From above analysis, the structure of this compound was deduced as 1 β ,2 β ,9 α -triacetoxy-8 α -(α -hydroxyl-isobutyryloxy)-15-benzoyloxy-4 α -hydroxy-dihydroagaro-furan[16].

Preliminary biological study on antitumor activity revealed that this compound showed strong nonselective cytotoxicity against four of the NCl panel cell lines. The inhibitory activities *in vitro* human tumors were indicated in the **Table 1**.

Table 1. The cytotoxicities against four of the NCl panel cell lines

Cell Lines	GI50 Value(μ M)
Leukemia (PRMI-8226)	23
CNS cancer (U251)	32
prostate cancer (PC-3)	33
breast cancer (MDA-MB-231/ATCC)	17

Further biological studies of this compound are currently under way.

Acknowledgment

The authors thank the National Cancer Institute (NCI), Developmental Therapeutics Program (Bethesda, MD) for *in vitro* test of our compound for cytotoxicity .

References and Notes

1. Q. Q. Zhang, *Agric. Res* (teipei)., **1950**, *1*, 29.
2. W. J. Wu , G. J. Gao, *Acta phytochem Sin.*, **1985**, *12*, 57.
3. N. Wakbayashi, W. J. Wu, R. M. Waters, R. E. Redfern, Jr, G. D. Mills, A. B. Demilo, W. R. Lusby , D. Andrzejewski, *J. Nat. Prod.* **1988**, *51*, 537.
4. Y. Q. Tu, Q. B. Song, X. L. Wu, G. S. Huang, Y. X. Mu, Y. Z. Chen, *Acta Chim Sin.*, **1993**, *51*, 404.
5. J. K. Liu, S. W. Han, J. Z. Jia, Y. Yong, H. Q. Wang, *Phytochem.* **1991**, *30* (10), 3437.
6. Y. Q. Tu, G, S, Huang, Y. X. MA, X. L. Wu, Q. B. Song. *J. Nat. Prod.* **1992**, *55* (9), 1320.
7. C. Q .Cheng, D. G. Wu, J. K. Liu, *Phytochem.* **1992**, *31*, 2777.
8. M. T. Wang, H. L. Qin, M. Kong, Y. Z Li, *Phytochem.* **1991**, *30* (12) 3931.
9. Y. Takaishi, S. Ohshima, K. Nakano and T. Tomimatsu, *J. Nat. Prod.* **1992**, *56* (6), 815-824.
10. J. Liu, Z. Jia, D. Wu, J. Zhou, Z. Zhou, *Chin. Sci. Bull.* **1989**, *34*, 1693.
11. Y. Shizuy, H. Wada, K. Yama, Y. Hirata, *Tetrahedron*, **1973**, *29*, 1773.
12. H. Sang, H. Q. Wang, Y. Q. Tu, Y. Z. Chen, *Phytochem.* **1991**, *30*, 1574.
13. R. Bruning, H. Wagner, *Phytochem.* **1978**, *17*, 1821.
14. N. Waka Bayashi, W. J. Wu, R. M. Waters, *J. Nat. Prod.* **1988**, *51* (3), 537.
15. Y. H. Wang, L. Yang, Y. Q. Tu, K. Zhang, Y. Z. Chen, J. S. Fan, *J. Nat. Prod.* **1998**, *61* (7) 942.
16. ^{1}HNMR (400MHz, $CDCl_3$) δ 1.24 (s, 3H, Me-16), 1.34 (s, 3H, Me-17), 1.45 (s, 3H, Me-14), 1.58 (s, 3H, Me-13), 1.61 (s, 3H, Me-12), 1.70 (br. s, IH, 4-OH), 1.89 (s, 3H,MeCOO-), 2.02 (dd , *J*=14.4, 2.8Hz, 1H, H-3), 2.08 (s, 3H, MeCOO-), 2.15 (d, *J*=12.8Hz, 1H, H-6), 2.24 (dd , *J*=14.4, 4.4Hz, 1H, H-3), 2.27 (s, 3H, MeCOO-), 2.32 (dd, 1H, *J*=4.8, 4.0Hz, Heq-7), 2.59 (dd, *J*=12.8, 4.8Hz, 1H, H-6), 4.54 (d,1H, *J*=12.8Hz, H-15a), 4.67 (d, 1H, *J*=12.8Hz, H-15b), 5.51 (m, 1H, Heq-2), 5.58 (1H, d, *J*=3.2Hz, H-1), 5.69 (dd, 1H, *J*=6.4, 4.0Hz, Hax-8), 5.60 (d, *J*=6.4Hz, 1H, Heq-9), 7.46 (t, J=8.0Hz, 2H, H-3'&5'), 7.59 (d, J=8.0H, 1H, H-4'), 8.06 (d, J=8.0Hz, 2H, H-2'&6'); ^{13}CNMR (100MHz, $CDCl_3$) 170.5 (C-19), 169.8, 169.6, 169.3 (C-21, C-23, C-25), 165.6 (C-7'), 133.5 (C-4'), 130.2 (C-2',

C-6'), 129.5 (C-1'), 128.3 (C-3', C-5'), 89.1 (C-5), 83.9 (C-11), 78.3 (C-18), 71.1 (C-9), 70.1 (C-8), 69.5 (C-4), 68.5 (C-2), 68.3 (C-1), 64.6 (C-15), 52.1 (C-10), 47.9 (C-7), 40.5 (C-3), 31.5 (C-6), 30.1 (C-14), 25.1 (C-13), 25.0 (C-12), 20. 2(C-16), 20.2 (C-17), 21.3, 21.1, 20.8 (C-20, C-22, C-24).

Received 31 December 1998