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A NEW TRITERPENOID ACID FROM *Schisandra henryi*

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*A new lanostane triterpenoid acid, nigranoic acid 3-ethyl ester (**1**), together with two known lanostane triterpenoid acids, isoschizandronic acid (**2**) and anwuweizic acid (**3**), was isolated from the stems of* Schisandra henryi *Clarke. The new compound was identified based on extensive spectroscopic studies including HR-ESI-MS and 2D NMR spectra, and the known compounds were identified by their spectroscopic data analysis and comparison with reports in the literature. Compounds **2** and **3** were isolated from the plant for the first time.*

Keywords: *Schisandra henryi*, nigranoic acid 3-ethyl ester, isoschizandronic acid, anwuweizic acid.

Fruits of *Schisandra henryi* Clarke, which belongs to the *Schisandra* genus (Schisandraceae), have been used in folk medicine as a substitute for Wu-Wei-Zi, fruits of *S. chinesis* (Yurcz.) Baill, a famous traditional Chinese tonic and sedative for over 2000 years. Its stems have been used to promote blood circulation and to treat fracture and irregular menstruation [1]. Previously, triterpenoid acids and lignans were isolated from *S. henryi* [2–8]. In the course of our search for new bioactive natural products from medicinal plants in Yunnan of China, we investigated the plant stems and isolated a new lanostane triterpenoid acid, nigranoic acid 3-ethyl ester (**1**), together with two known lanostane triterpenoid acids, isoschizandronic acid (**2**) and anwuweizic acid (**3**).

Compound **1** was obtained as a white amorphous powder. Its molecular formula was established as $C_{32}H_{50}O_4$ by HR-EI-MS, giving a molecular ion at *m/z* 498.3717 $[M]^+$ (calcd 498.3709). The ^{13}C NMR, DEPT, and ^1H NMR spectra revealed the presence of six methyls, thirteen methylenes, five methines, and eight quaternary carbons, indicating that **1** was a triterpenoid. The ^1H NMR spectrum showed an angelic acid unit [δ 6.09 (1H, t, J = 7.0, H-24) and 1.92 (3H, s, H-27)], a primary methyl [δ 1.22 (3H, t, J = 7.2, $OCH_2\underline{CH_3}$)], a secondary methyl [δ 0.89 (3H, d, J = 6.4, H-21), and three tertiary methyl groups at δ 1.68 (3H, s, H-29), 0.94 (3H, s, H-18), and 0.92 (3H, s, H-30), which closely resembled those of 3,4-*seco*-lanostene-3, 26-dioic acids isolated from plants of Schisandraceae [9, 10]. This deduction was proved by the appearance of two carbonyl signals at δ 174.0 (C-3) and 172.6 (C-26), the C-4 (28) terminal double bond signals at δ 4.81, 4.73 (each 1H, br.s, H-4), and the alkenyl methyl at C-29 [δ 1.68 (3H, s, H-29). The signals at δ 0.77, 0.40 (each 1H, d, J = 4.6, H-19) indicated that a cyclopropane unit exists among C-9, C-10, and C-19. Thus, the structure of **1** was determined to be very similar to the nigranoic acid previously isolated from *S. henryi* [8], except for the additional ethoxyl group [δ 4.09 (2H, q, J = 7.2, $O\underline{CH_2}CH_3$), 1.22 (3H, t, J = 7.2, $OCH_2\underline{CH_3}$); δ 60.3 ($O\underline{CH_2}CH_3$), 14.2 ($OCH_2\underline{CH_3}$)]. In the HMBC spectrum, correlation peaks between the proton signal at δ 4.09 and the carbonyl signals at δ 174.0 (C-3), δ 1.92 (H-27) and δ 172.6 (C-26), δ 147.2 (C-24) suggested the ethoxyl group was linked at C-3. Finally, **1** was determined to be 3,4-*seco*-cycloarta-4(28),24*Z*-diene-3,26-dioic acid 3-ethyl ester, i.e., nigranoic acid 3-ethyl ester.

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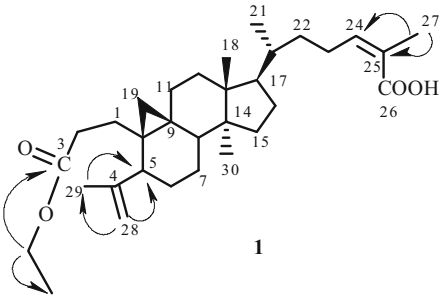

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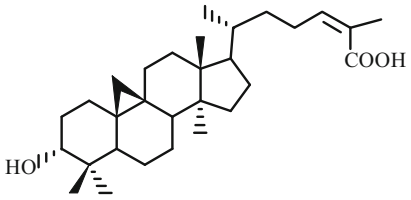

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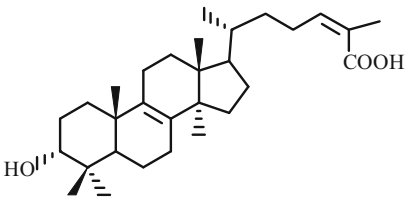

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On the basis of spectroscopic data analysis and comparison with reports in the literature [11–13], compounds **2** and **3** were identified to be isoschizandronic acid (**2**) and anwuweizic acid (**3**). Both were isolated from the plant for the first time.

EXPERIMENTAL

General Comments. MS were determined on an API Qstar Pulsa LC/TOF mass spectrometer. NMR spectra were measured on a Bruker DRX-500 spectrometer with TMS as an internal standard. Silica gel (200–300 mesh) was used for column chromatography and silica gel GF_{254} for TLC (Qingdao Marine Chemical Co., China). Solvents were of industrial purity and distilled prior to use.

Isolation of 1–3 from *S. henryi*. The stems of *S. henryi* were collected in December 1999 from Tonghai County of Yunnan Province, China. The extracts were prepared as described in the previous report [8]. The EtOAc extract (107 g) was applied to a silica gel column, eluting with petroleum ether containing increasing amounts of EtOAc. The fractions obtained from petroleum ether–EtOAc (4:1) elution were combined and subjected to repeated column chromatography (silica gel, petroleum ether–EtOAc 4:1; then Sephadex LH-20, MeOH–$CHCl_3$ 9:1) to yield **1** (15 mg), **2** (10 mg), and **3** (6 mg).

Nigranoic acid 3-ethyl ester (1), amorphous powder. EI-MS *m/z* (%): 498 (M^+, 68), 483 (60), 454 (11), 395 (17), 357 (8), 261 (12), 173 (22), 159 (11), 131 (25), 119 (47), 105 (56), 91 (95). ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 6.09 (1H, t, J = 7.0, H-24), 4.81, 4.73 (each 1H, br.s, H-28), 4.09 (2H, q, J = 7.2, $OC\underline{H}_2CH_3$), 1.92 (3H, s, H-27), 1.68 (3H, s, H-29), 1.22 (3H, t, J = 7.2, $OCH_2C\underline{H}_3$), 0.94 (3H, s, H-18), 0.92 (3H, s, H-30), 0.89 (3H, d, J = 6.4, H-21), 0.77, 0.40 (each 1H, d, J = 4.6, H-19). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 174.0 (C-3), 172.6 (C-26), 149.5 (C-4), 147.2 (C-24), 125.8 (C-25), 111.5 (C-28), 60.2 ($O\underline{C}H_2CH_3$), 52.2 (C-17), 49.0 (C-14), 47.8 (C-8), 45.8 (C-13), 45.1 (C-5), 36.0 (C-20), 35.8 (C-11), 35.6 (C-12), 33.1 (C-15), 33.0 (C-2), 31.6 (C-1), 30.0 (C-19), 29.0 (C-16), 28.1 (C-10), 27.9 (C-6), 27.8 (C-22), 26.9 (C-23), 25.0 (C-7), 21.3 (C-27), 20.9 (C-29), 20.5 (C-9), 19.8 (C-30), 19.3 (C-21), 18.1 (C-18), 14.2 ($OCH_2\underline{C}H_3$). HR-ESI-MS: *m/z* 498.3717 $[M]^+$, $C_{32}H_{50}O_4$ requires 498.3709.

Isoschizandronic acid (2), amorphous powder; mp 159–161°C. EI-MS *m/z* (%): 456 (M^+, 40), 441 (75), 423 (100), 327 (25), 301 (26), 287 (12), 255 (15), 241 (22), 227 (17), 175 (60), 107 (42), 95 (62), 81 (24), 69 (15). ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 6.06 (1H, t, J = 7.4), 3.45 (1H, br.s), 1.90 (3H, s), 0.97 (3H, s), 0.95 (3H, s), 0.91 (3H, s), 0.90 (3H, s), 0.89 (3H, d, J = 6.5), 0.55 (1H, d, J = 4.0), 0.34 (1H, d, J = 4.0).

Anwuweizic acid (3), amorphous powder; mp 160–161°C. EI-MS *m/z* (%): 456 (M^+, 70), 441 (61), 423 (100), 327 (7), 301 (11), 287 (4), 255 (6), 241 (5), 227 (6), 175 (12), 107 (13), 95 (34), 81 (10), 69 (11). ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 6.06 (1H, t, J = 7.4), 3.41 (1H, br.s), 2.54 (1H, m), 2.45 (1H, m), 1.91 (3H, s), 0.97 (3H, s), 0.95 (3H, s), 0.93 (3H, d, J = 6.3), 0.91 (3H, s), 0.86 (3H, s), 0.67 (3H, s).

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REFERENCES

1. Yunnan Provincinal Crude Drugs Company, *Name Lists of Chinese Herbal Medicine Resources in Yunnan*, Science Press, Beijing, 151 (1993).
2. L. Li and H. Xue, *Planta Med.,* **52**, 493 (1986).
3. J. Liu, M. Huang, and Y. Gao, *Acta. Chim. Sin.,* **38**, 361 (1980).
4. J. Liu, M. Huang, W. Ayer, and T. Nakashima, *Phytochemistry*, **23**, 1143 (1984).
5. J. Liu, Y. Tao, and M. Huang, *Acta. Chim. Sin.,* **46**, 483 (1988).
6. Y. Tao, J. Liu, and M. Huang, *Chin. Trad. Herb. Drugs*, **22**, 51 (1991).
7. Y. Chen, Z. Wu, S. Gui, Y. Lv, X. Liao, and F. Halaweish, *Fitoterapia*, **76**, 370 (2005).
8. Y. Chen, Z. Wu, Y. Lv, S. Gui, J. Wen, X. Liao, L. Yuan, and F. Halaweish, *Arch. Pharm. Res.*, **26**, 912 (2003).
9. H. Sun, S. Qiu, L. Lin, Z. Wang, Z. Lin, T. Pengsuparp, J. Pezzuto, H. Fong, G. Cordell, and N. Farnsworth, *J. Nat. Prod*., **59**, 525 (1996)
10. Y. Chen, G. Qin, L. Cao, Y. Leng, and Y. Xie, *Fitoterapia*, **72**, 434 (2001).
11. J. Liu, W. Wang, and M. Huang, *Chin. Trad. Herb. Drugs*, **21**, 294 (1990).
12. J. Liu and M. Huang, *Acta. Chim. Sin*., **42**, 264 (1984).
13. Y. Chen, X. Song, L. Hai, F. A, Y. Bi, and X. Liao, *Pol. J. Chem*., **80**, 1677 (2006).