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A novel alkaloid from *Fluggea virosa*: 14,15-epoxynorsecurinine

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Abstract

Fluggea virosa contains 14,15-epoxynorsecurinine (**2**) in addition to norsecurinine (**1**). The former compound has been characterized for the first time.

Keywords: *Fluggea virosa*; Euphorbiaceae; 14,15-epoxynorsecurinine; Fluggeainol; Fluggeaine ether

1. Introduction

In the course of a screening of South African supposed medicinal plants, we are taking interest in the title species [subsp. *virosa* (Euphorbiaceae)]. From this plant, (−)-norsecurinine (**1**) has been isolated twice, in 1964 and 1985 [from *Securinega virosa* Pax et Hoffm. (identical to *Fluggea virosa* subsp. *virosa*) (Saito et al., 1964) and from *Fluggea virosa* (Chen & Hou, 1985, 1986) It is known that **1** is present in various species either as its (+) or as its (−) enantiomer (Saito et al., 1964); Chen and Hou (1985, 1986); (−) isomer also from *Securinega virosa* Baill., Iketubosin and Mathieson (1963); (+) isomer from *Phyllanthus niruri* (Euphorbiaceae), Rouffiac and Parello (1969); Joshi, Gawad, Pelletier, Kartha and Bhandary (1986); Hassarajani and Mulchandani (1990)]. Both isomers have been synthesized (Jacobi, Blum, DeSimone, & Udodong, 1991) and the absolute configuration has been established (Joshi et al., 1986).

Chromatography of the raw alkaloid concentrate from *Fluggea* furnished a less polar first compound in addition to the more polar main alkaloid. Both compounds were relatively sensitive and decomposed to brown tars within days, even in solution. The major (later eluted) compound could be identified as **1** on the basis of its ^{1}H NMR signals. H,H and H,C COSYs allowed to make safe ^{13}C NMR signal assignments for the first time (Chen & Hou, 1985, 1986). The other, first eluted compound had a MS mol peak of 219 corresponding to $C_{12}H_{13}NO_3$, thus containing one oxygen more than **1**. Most of the ^{1}H and ^{13}C signals of **2** were positioned similarly to the ones of **1**, but instead of two olefinic signals for the carbon atoms (14) and (15), there were indications for two structural elements –CH–O–. Therefore an epoxide must be present. This was corroborated by a H,C COSY. Furthermore, high field shifts of the signals for C(8) in the ^{13}C and for one of the C(8) hydrogens in the ^{1}H NMR spectra showed conclusively that the relative configuration of the epoxide ring must be *syn* to the C(8)H_2 bridge. As the configuration of **1** is known the absolute stereochemistry of **2** must be as indicated in Scheme 1.

Take note that the conventional numbering of norsecurinine (having a pyrrolizidine skeleton) follows the one of securinine (an indolizidine), so that there is no (6) position in **1**.

Careful control experiments showed that **2** was not an artefact of the workup. Both contact with air (and silica gel) under neutral, basic or acidic conditions and attempted H_2O_2 oxidation under these circumstances did not give **2**.

We notice that Chen and Hou have isolated flug-

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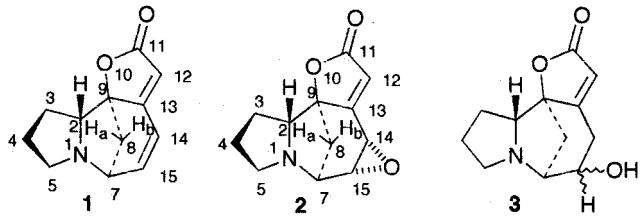

Scheme 1.

geainol (**3**) out of *Fluggea virosa* from China together again with (−) norsecurinine. In addition, the respective difluggeainyl ether ("fluggeaine ether") was found (Chen & Hou, 1985, 1986). The authors could not assign configurations at C(15) in these compounds. No indications for **3** and its ether were observed in our plant material. Our **2** could conceivably be the biosynthetic link between **1** and **3**, but other biosynthetic processes cannot be excluded, of course.

2. Experimental

The plant was identified and material was collected at the University of Venda (South Africa) by T.v.R. in 1998.

30 g of air dried and ground bark of *Fluggea virosa* were extracted with methanol in a Soxhlet apparatus until the eluate became colorless. The brownish green extract was refrigerated over night, then filtered and concentrated to a volume of <10 ml. The sirupy residue was taken up in 100 ml of 4% aqueous acetic acid. This solution was extracted thrice with 20 ml of ether each time to remove neutral components. The aqueous solution was made alkaline with 30 ml of aqueous ammonia, and the mixture was extracted again ten times with 10 ml of ether each time (until the last extract did not give a positive Dragendorff test on thin layer chromatography). The combined etheral extracts were dried over Na_2SO_4, whereafter the solvent was removed in vacuo. 500 mg of raw alkaloid were obtained. Thin layer chromatography (silica gel 60 F_{254} of Merck, Darmstadt) showed two spots at R_f 0.56 and 0.40 with chloroform/methanol 4:1 and detection by Dragendorff's reagent. These could be separated preparatively on column chromatography on silica gel 60 (0.063–0.2 mm particle size) with the same eluent mixture. 58 mg **2** and 307 mg **1** were obtained.

Norsecurinine, **1**: ^{1}H NMR (500 MHz, CD_3OD): δ 1.72 (m, $\Sigma J = 31$ Hz; 1H; H-4β), 1.75 (d, $J_{8a,8b} = 10.8$ Hz; 1H; H-8a), 1.85 (m, $\Sigma J = 32$ Hz; 1H; H-3α), 1.96 (m, $\Sigma J = 27$ Hz; 1H; H-3β), 2.02 (m, $\Sigma J = 24$ Hz; 1H; H-4α), 2.65 (m, $\Sigma J = 29$ Hz; 1H; H-5α), 2.67 (dd, $J_{8b,8a} = 11$, $J_{8b,7} = 4.7$ Hz; 1H; H-8b), 3.16 (dd, $J_{2,3\beta} = 8.9$, $J_{2,3\alpha} = 7.6$ Hz; 1H; H-2), 3.22 (m, $\Sigma J = 16$ Hz; 1H; H-5β), 3.75 (dd, $J_{7,15} = 6$, $J_{7,8b} = 5$ Hz; 1H; H-7), 5.79 (s; 1H; H-12), 6.62 (d, $J_{14,15} = 9.1$ Hz; 1H; H-14), 6.81 (dd, $J_{15,14} = 9.0$, $J_{15,7} = 6.5$ Hz; 1H; H-15). (for the ^{1}H NMR in $HCCl_3$-d_1, see Joshi et al. (1986)) — ^{13}C NMR (125.8 MHz, CD_3OD): δ 27.6 (C-4), 30.1 (C-3), 36.7 (C-8), 55.9 (C-5), 60.8 (C-7), 66.3 (C-2), 92.8 (C-9), 108.7 (C-12), 121.9 (C-14), 145.2 (C-15), 170.4 (C-13), 174.3 (C-11).

14,15-Epoxynorsecurinine, **2**, $C_{12}H_{13}NO_3$ (219), MS (70 eV, EI): m/z 219 (M^+, 25),190 (24), 126 (17), 96 (100), 70 (40), 41 (19).— ^{1}H NMR (500 MHz, CD_3OD): δ 1.69 (d, $J_{8a,8b} = 11.3$ Hz; 1H; H-8a), 1.71 (m, $\Sigma J = 27$ Hz; 1H; H-4β), 1.78 (m, $\Sigma J = 28$ Hz; 1H; H-3α), 1.92 (m, $\Sigma J = 25$ Hz; 1H; H-3β), 2.00 (m, $\Sigma J = 23$ Hz; 1H; H-4α), 2.24 (dd, $J_{8b,8a} = 11.4$, $J_{8b,7} = 5.3$ Hz; 1H; H-8b), 2.70 (m, $\Sigma J = 26$ Hz; 1H; H-5α), 3.23 (dd, $J_{2,3\beta} = 9.0$, $J_{2,3\alpha} = 7.4$ Hz; 1H; H-2), 3.30 (m, $\Sigma J = 16$ Hz; 1H; H-5β), 3.60 (t, $J_{15,14} = J_{15,7} = 3.7$ Hz; 1H; H-15), 3.65 (dd, $J_{7,8b} = 4.8$, $J_{7,15} = 4.2$ Hz; 1H; H-7), 3.87 (d, $J_{14,15} = 3.5$ Hz; 1H; H-14), 6.23 (s; 1H; H-12). —^{13}C NMR (125.8 MHz, CD_3OD): δ 26.3 (C-8), 27.5 (C-4), 30.4 (C-3), 45.6 (C-14), 55.5 (C-15), 57.1 (C-5), 61.9 (C-7), 67.6 (C-2), 92.3 (C-9), 118.6 (C-12), 168.7 (C-13), 173.6 (C-11).

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