Indian Journal of Chemistry
Vol. 36B, February 1997, pp. 206-207

Note

Securinega alkaloids: Reinvestigation on the fresh leaves of *Breynia coronata* (Euphorbiaceae)

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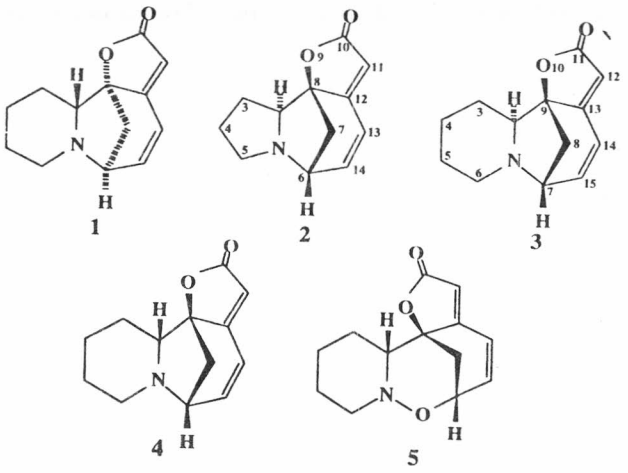
Received 14 May 1996; revised and accepted 16 August 1996

From the fresh leaves of *Breynia coronata*, the securinega alkaloids securinine **1**, *ent*-norsecurinine **2** and virosecurinine **3** have been isolated. These constituents are different from those isolated from the same species earlier which was collected from a different population in peninsular Malaysia.

Securinine, the major alkaloid of the securinega group of alkaloids, has been isolated from a number of species from the family Euphorbiaceae[1-3]. We have been working on the isolation of alkaloids from *Breynia coronata* and in the process, securinine was isolated from the fresh leaves collected from Langkawi Island in Malaysia. Investigation on the fresh leaves collected from the state of Selangor (in the middle part of peninsular Malaysia) however yielded only viroallosecurinine **4** and *ent*-phyllanthidine **5**[4]. Our failure to detect securinine from the latter prompted us to reinvestigate the identity of its alkaloid constituents.

Securinine has been reported as a crystalline solid and stable, while norsecurinine as an oil which is rather unstable on storage[4]. In our investigation compound NA1 (see Experimental) also appeared as a light brown oil and was found to be unstable on storage. Its mass spectrum gave M^+ peak at m/z 203 which was consistent with the molecular formula $C_{12}H_{13}NO_2$. The major fragments in the mass spectrum strongly suggested that the alkaloid belongs to the securinega type with ring-A consisting of a pyrrolidine ring as in norsecurinine[4,5]. The ^{1}H NMR spectrum was in agreement with gross formulation of *ent*-norsecurinine **2**[4].

From the ^{1}H NMR spectra of securinine, allosecurinine[6], (4β)-4-methoxysecurinan-11-one



(phyllanthine), (2α,4α)-4-methoxysecurinan-11-one (securitinine)[7], *ent*-norsecurinine, 4-methoxynorsecurinine[8] and *ent*-phyllanthidine[9] it is apparent that the signals for β-H2 should appear at δ 2.10-2.79 and that of α-H2 at 3.24-3.90 ppm, both as dd. If the configurational relationship of the proton at C2 is α, the signal for H14(d) will appear at higher field than that for H15 (dd) while the reverse is true if the same proton is in β-configuration. These ^{1}H NMR spectral characteristics indicated NA1 to be *ent*-norsecurinine **2**. It is interesting to note that the reported chemical shifts for H2, H14 and H15 in norsecurinine are at 2.9-3.4 (m), 6.50 (d), and 6.75 ppm (dd), respectively and those in viroallosecurinine are at 3.65 (dd), 6.66 (d), and 6.83 (dd)[9]. In these reorts the configuration of H2 was concluded as β. The chemical shift patterns of H2, H14 and H15 for these two compounds however indicated that the configuration of H2 should be α based on the reasons mentioned earlier. In this report we therefore wish to revise the earlier claimed norsecurinine[10] and viroallosecurinine[9] as *epi*-norsecurinine and virosecurinine, respectively.

The ^{13}C NMR spectrum of NA1 showed 12 peaks and the assignment of which was made on the basis of the ^{13}C NMR spectra for *ent*-norsecurinine[4], securinine and allosecurinine[5]. It is also interesting to note that ^{13}C NMR spectra of allosecurinine[6] and virosecurinine[11] appeared to be similar. The ^{1}H and ^{13}C NMR spectra as well as TLC of NA2 were identical with those of virosecurinine **3**.

Experimental Section

Extraction. The fresh leaves (4.5 kg) of *B. coronata* were repeatedly extracted with fresh methanol until the final extract (four times) gave a negative Meyers test for alkaloids. The methanol extracts were combined and evaporated under vacuum to give 300 g of a dark brown viscous residue which was dissolved in $CHCl_3$ and extracted with pet. ether. The $CHCl_3$ layer was extracted with 1% H_2SO_4. The acidic layer was basified with Na_2CO_3 to *p*H 8 and extracted with $CHCl_3$. The chloroform extract was then evaporated to dryness under vacuum to give 6 g of a crude solid. The aqueous layer was further basified to *p*H 12 using ammonia and extracted with BuOH which on evaporation *in vacuo* gave 25 g of another solid.

Isolation of alkaloids. The chloroform extract revealed 3 spots on TLC which gave positive test for alkaloids. It was then subjected to column chromatography over silica gel (mesh 70-230). From the elution with $CHCl_3$-CH_3OH a set of 17 fractions (each nearly 50 ml) was collected; the major constituents were found to be present in fractions 2 and 3. Fraction 3 was further fractionated by column chromatography and the fractions containing major alkaloids were combined and subjected to preparative TLC giving three compounds designated as NA1, NA2 and NA3. Compound NA1 was a light brown oil and identified as *ent*-norsecurinine **2**. Compound NA2 was further purified by recrystallization from ethyl acetate to give 75 mg of virosecurinine **3**, as colourless prisms (m.p. 125-27°) while NA3 was recrystallized from $CHCl_3$ to give 50 mg of securinine **1** as a crystalline solid (m.p. 140-42°). Fraction 2 was subjected to preparative TLC which furnished pure virosecurinine and securinine.

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