Brief Communications

Alkaloids of *Arundo donax* L. 13.* The structure of a new dimeric indole alkaloid, arundanine

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The structure of a new dimeric indole alkaloid, named arundanine, isolated from the roots of *Arundo donax L.* (*Poaceae*), was elucidated. Arundanine was identified as 3-(*N*,*N*-dimethylaminoethyl)-4-[3-(*N*,*N*-dimethylaminoethyl)indole-1-yl]-5-hydroxyindole on the basis of spectroscopic data and the transformation into the known alkaloid, arundamine.

The chemical investigation of plants as sources of alkaloids, structure elucidation of alkaloids, and identification of the most physiologically active compounds for medicine remain topical problems.

The plant *Arundo donax* L. (reed) (the Poaceae family, Gramineae) is a rich source of indole alkaloids possessing high biological activities.[2] The tincture from *A. donax* L. leaves has long been widely used in folk medicine.[2,3]

The alkaloids from the Central Asian *A. donax* L. species were intensely studied in 1975—77;[4,5] starting from 1994, these studies have been continued at the Institute of Chemistry of Plant Substances of the Uzbekistan Academy of Sciences.[6]

Study of the alkaloid composition of the roots of *A. donax* L. gathered in the Fergana region during the end of vegetation[7] resulted in the isolation of a number of new nitrogenous bases. The present work deals with structure elucidation for one of these compounds that we called arundanine (**1**). Arundanine (**1**) is readily soluble in methanol, ethanol, and a chloroform—methanol mixture and is poorly soluble in ethyl acetate and benzene.

The UV spectrum (EtOH) of arundanine (**1**) exhibits absorption maxima at λ 223 and 284 nm (log ε 4.65 and 4.07, respectively), indicating the presence of an indole chromophore.[8]

The mass spectrum of **1** contains a molecular ion peak with *m*/*z* 390, which differs from the corresponding peak of arundamine (**2**)[9,10] by 14 amu, and also ion peaks with *m*/*z* 204, 130 (32%), 115 (20%), 73, and 58 typical of

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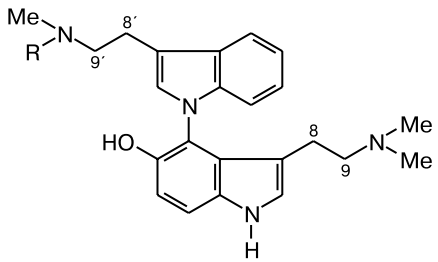
indole alkaloids,[11] for example, bufotenine (5-hydroxy-*N*,*N*-dimethyltryptamine).[12] The spectrum also exhibits a peak for an ion with *m/z* 188 (10%) with the elemental composition $C_{12}H_{16}N_2$, which corresponds to *N*,*N*-dimethyltryptamine.[13]

A comparison of the spectroscopic data for arundanine (**1**) (IR, UV, mass spectra) with those for arundamine (**2**) showed that these alkaloids are structurally related, and the difference between the masses of their molecular ions (14 amu) suggests that the former is the *N*-methyl derivative of the latter. This was confirmed by the synthesis of arundanine (**1**) from arundamine by the Hess methylation (formic acid, a 40% formaldehyde solution). The resulting product was identical to a natural arundanine specimen judging by TLC and the melting point of a mixed sample.

The ^{1}H NMR spectrum of arundanine (**1**) was interpreted in terms of the proposed structure considering the analogous spectrum of arundamine (**2**).[10] Like the spectrum of arundamine (**2**), the ^{1}H NMR spectrum of arundanine (**1**) recorded in $CDCl_3$ consists of characteristic groups of signals for aromatic protons at δ 6.95—7.70 and for aliphatic protons at δ 1.80—3.05. In particular, the H(2) and H(2′) protons of the five-membered rings in the indole nuclei resonate as two singlets at δ 6.97 and 7.08, respectively. The H(4′)—H(7′) four-spin system is represented by three signals, as in the ^{1}H NMR spectrum of arundamine (**2**). As in the case of arundamine (**2**), the broadened doublet (δ 7.68) corresponds to the H(4′) proton and the broader two-proton doublet at δ 7.15 (J = 6.0 Hz) is due to H(5′) and H(7′). The H(6′) proton in this four-spin system is responsible for a poorly resolved triplet at δ 6.99, which overlaps with the other two signals.

The aliphatic region of the spectrum is represented by two singlets of methyl groups (δ 1.80 and 2.35) and four multiplets due to the methylene protons. As in the case of arundamine (**2**), the protons in the C(8)—C(9) side chain are shielded by the aromatic system of the second indole fragment of molecule **1**. The signals of the methylene protons of this side chain are shifted upfield and occur at δ 2.12 (H(8)) and 1.93 (H(9)). Since this assignment has not been confirmed by additional experiments, an alternative assignment is also possible. The signals of the H(8′) and H(9′) methylene protons are poorly resolved multiplets at δ 2.74 and 3.03, respectively.



1: R = Me
2: R = H

Thus, based on the UV, IR, and ^{1}H NMR spectroscopy, mass spectrometry, and the results of the Hess methylation, arundanine **1** was identified as 3-(*N*,*N*-dimethylaminoethyl)-4-[3-(*N*,*N*-dimethylaminoethyl)indol-1-yl]-5-hydroxyindole.

Experimental

UV spectra were recorded on a Perkin—Elmer L 416 FT spectrometer in ethanol, IR spectra were measured on a Perkin—Elmer 2000 instrument in KBr pellets, and mass spectra (EI, 70 eV) were run on an MKh-1310 spectrometer with direct sample inlet into the ion source; the ionization chamber temperature was 150 °C. ^{1}H NMR spectra were recorded on a Tesla BS-567 A/100 spectrometer in $CDCl_3$ at 30 °C using tetramethylsilane as the internal standard.

Column chromatography was carried out using 100/160 μm alumina (neutral), TLC was carried out on 5/40 μm Al_2O_3 plates in a 9 : 1 chloroform—methanol solvent mixture.

Isolation of arundanine. The sum of alkaloids from *A. donax* roots (45 g) gathered during rapid growth of the plant was applied onto a chromatographic column with Al_2O_3 and eluted with benzene and with chloroform—methanol mixtures with different compositions. Evaporation of the solvent from the fraction eluted with a 75 : 1 chloroform—methanol mixture resulted in precipitation of compound **1** (48 mg). The precipitate was separated and recrystallized twice from a 16 : 1 chloroform—hexane mixture.

Column chromatography on Al_2O_3 of 10.4 g of the sum of alkaloids from *A. donax* roots gathered at the end of vegetation, carried out by a similar procedure, gave 14 mg of arundanine (**1**).

Arundanine (1), m.p. 198—199 °C, R_f 0.93 (Al_2O_3, chloroform—methanol (9 : 1)). MS, *m/z* (I_{rel} (%)): 390 $[M]^+$, 375, 345, 332, 302, 273, 259, 204 (11), 188 (10), 146, 130 (32), 115 (20), 103, 73 (100), 58. $C_{24}H_{30}N_4O$. ^{1}H NMR ($CDCl_3$), δ: 1.80 (s, 6 H, NMe_2); 2.35 (s, 6 H, NMe_2); 1.93, 2.12 (both m, 4 H, H(9), H(8)); 2.74, 3.03 (both m, 4 H, H(8′), H(9′)); 6.97, 7.08 (both s, each 1 H, H(2), H(2′)); 7.34, 6.98 (both d, each 1 H, H(6), H(7), J = 8.7 Hz); 7.68 (d, 1 H, H(4′), J = 6.0 Hz); 7.15 (d, 2 H, H(5′), H(7′), J = 6.0 Hz); 6.99 (t, 1 H, H(6′)); 8.24 (NH).

Methylation of arundamine. A mixture of arundamine (0.21 g),[7] 85% formic acid (4 mL), and formalin (4 mL) was refluxed for 8 h. The reaction mixture was diluted with water and neutralized with a concentrated solution of ammonia, and the product was extracted with chloroform to give 0.12 g (55%) of a crystalline compound with m.p. 198—199 °C, identified as arundanine (**1**) based on TLC data, the undepressed melting point of a mixture with the specimen of **1** described above, and the mass spectrum.

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