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ALKALOIDS OF *Arundo donax*. XII. STRUCTURE OF THE NEW DIMERIC INDOLE ALKALOID ARUNDACINE

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The new dimeric indole alkaloid arundacine is isolated from the polar fraction of the total alkaloids from Arundo donax *L. roots. The structure 3-N,N-dimethylaminoethyl-5-hydroxy-4-(3′-N′-acetyl-N′-methylaminoethylindol-1′-yl)indole is established using spectral data (IR, UV, mass, one-dimensional ^1H and ^{13}C NMR, various two-dimensional spectra).*

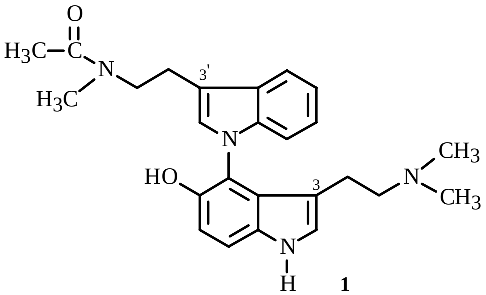
Key words: *Arundo donax* L., alkaloids, arundacine, two-dimensional NMR spectroscopies (COSY, NOESY, HSQC, HMBC).

In continuation of the study of alkaloids from *Arundo donax* L. [1], we isolated the new alkaloid arundacine from the polar fraction of the total alkaloids by column chromatography and rechromatography.

Arundacine (**1**) is a white crystalline base, mp 192-193°C (acetone). It is freely soluble in CH_3OH and $CHCl_3$; difficultly, in acetone; and insoluble in ether, hexane, and benzene.

The UV spectrum contains maxima at 223 and 284 nm (log ε 4.55 and 3.95, respectively) that are characteristic of the indole chromophore. The IR spectrum has absorption bands of active H (3400-3175 cm^{-1}, NH, OH), amide carbonyl (1630 cm^{-1}), aromatic ring (1600, 1509 cm^{-1}), and stretching and deformation vibrations of CH_2– and CH_3– groups. The mass spectrum has a strong peak for the molecular ion with *m/z* 418 that confirms the composition $C_{25}H_{31}N_4O_3$. The base peak is the ion with *m/z* 417 $[M - H]^+$.

These spectral properties and the molecular weight of **1** indicate that arundacine is a dimer. The presence in the mass spectrum of **1** of the diagnostic peak with *m/z* 130 [2] indicates that the structure is based on the indole system; the peak with *m/z* 204, the presence of the bufotenine fragment in **1** [3].



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The mass spectrum contains a peak for the ion with *m/z* 332 that is formed via loss of a fragment of mass 86 amu. This corresponds to loss of C_4H_8O from the molecular ion, i.e., the $CH_2–N(CH_3)COCH_3$ group.

Therefore, the structure of arundacine contains two indole fragments, one of which is bufotenine; the other, an indole nucleus with the $CH_2–N(CH_3)COCH_3$ side chain.

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TABLE 1. Chemical Shifts for Two Conformers of Arundacine in Py-d$_5$

C Atom	^{1}H		^{13}C	
	c-conformer	*t*-conformer	*c*-conformer	*t*-conformer
1	11.928*	11.901*		
2	7.36	7.36	125.41	125.30
3			112.28	112.28
3a			117.08*	116.98*
4			128.79*	128.40*
5			149.05	149.05
6	7.37	7.37	113.11	113.11
7	7.645* d 7.9	7.629* d 7.7	113.11*	113.00*
7a			126.81	126.81
8	2.26, 2.38	2.26, 2.38	23.79*	23.68*
9	2.15, 2.28	2.15, 2.28	61.22	61.22
10	1.902*	1.890*	45.07*	45.05*
OH	~9.77	~9.77		
2′	7.40	7.35	129.19*	129.00*
3′			113.26	113.26
3′a			133.16	133.16
4′	7.910 d 8.6	7.759 d 7.0	111.87*	111.67*
5′	7.20	7.25	119.39*	118.94*
6′	7.32	7.21	122.28*	122.13*
7′	7.37	7.37	119.61*	119.44*
7′a			139.64	139.64
8′	3.09, 3.15	3.01, 3.04	23.84	24.72
9′	3.81, 3.85	3.56, 3.59	48.80	51.57
10′	2.845	3.060	36.35	33.13
Ac	2.043	2.131	21.94	21.40
C=O			169.93	169.93

A comparison of the mass spectrum of **1** and that of arundamine [4] showed that their molecular ions differ by 42 amu. This leads to the conclusion that arundacine is evidently an N-acyl derivative of arundamine [5].

We confirmed this hypothesis by studying the structure of arundacine using various types of two-dimensional (2D) NMR techniques.

The PMR spectrum of arundacine has principal groups of signals and positions that are very similar to those of arundamine. The aromatic protons form a group of overlapping signals at 7.2-7.9 ppm. The protons of one substituent (C8′–C9′–N10′) appear as several multiplets in the range 2.8-3.9 ppm; the other substituent (C8–C9–N10), as a separate group of signals at 1.9-2.4 ppm.

The most important feature of the PMR spectrum of arundacine, in contrast with that of arundamine, is the appearance of a new signal for the NAc group, which replaces the NH10′ proton, and a doubling of practically all signals owing to two conformers of the NCH$_3$10′–COCH$_3$ group *cis* (*c*) and *trans* (*t*) to the methyls. The greatest splitting of the signals for the *c*- and *t*-isomers occurs for methylene H9′ (0.27 ppm), NMe10′ (0.215 ppm), and aromatic H4′ (0.15 ppm). The *c*- and *t*-splitting of the Ac protons is 0.09 ppm.

The fact that *c*- and *t*-splitting is observed for the NH1 proton, aromatic H7, and NMe10 is remarkable. The large splitting of the signal for aromatic H4′, which is comparable with that of the NMe10′ group, suggests that the *c*- and *t*-conformers of **1** differ not only in the orientation of the Ac group on N10′ but also in the positions of the whole C8′–C9′–N10′ side chain. These differences can be analyzed using the shape of the signals for H8′ and H9′ and 2D NMR spectra. The NOESY spectrum is most informative for separating the NMR signals of the *c*- and *t*-conformers and assigning the appropriate protons to them (Fig. 1).

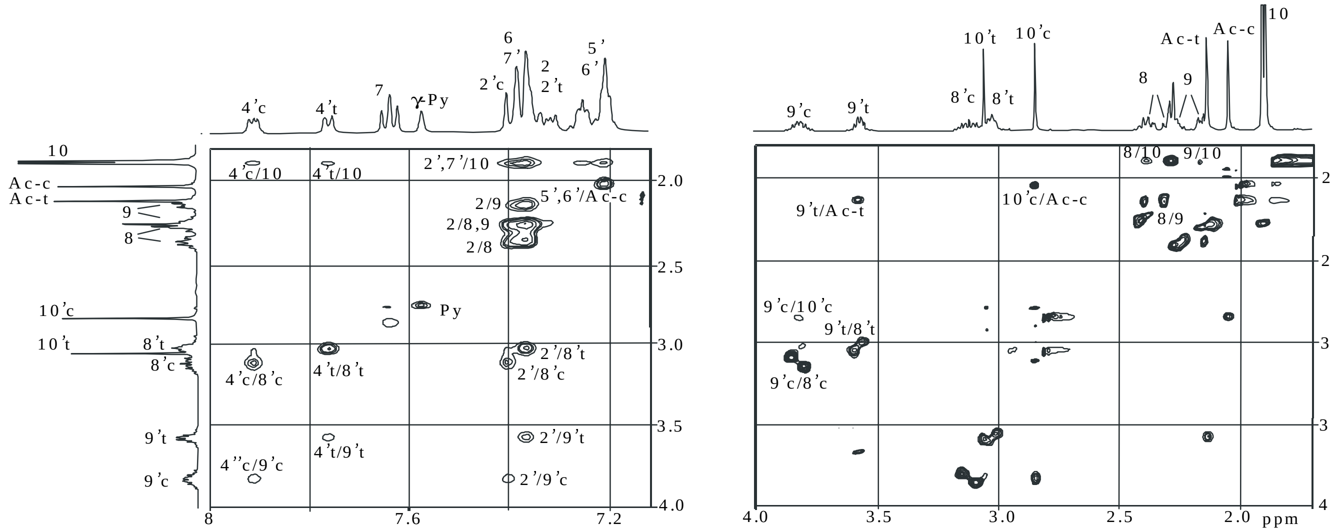

Fig. 1. NOESY spectrum of arundacine.

Two distinct singlets of the Ac group at 2.04 and 2.13 ppm in the NOESY spectrum that are not observed in the NMR spectra of arundamine have different correlations to their partners via through-space coupling. The signal at 2.04 ppm correlates with the NMe10′ group at 2.84 ppm. Obviously these are signals of the *c*-conformer. The signal at 2.13 ppm correlates with one of the methylene multiplets at 3.58 ppm. Obviously this multiplet belongs to H9′ protons; the corresponding signals, to the *t*-conformation of **1**. Cross-peaks between four methylene multiplets of H8′ and H9′ are found at 3.03, 3.12, 3.58, and 3.83 ppm. Two NOE correlations are clearly seen in the shape of the 2D signals in each of these couplings: 3.83/3.12 and 3.58/3.03 ppm. Therefore, each of these multiplets is formed by two signals with slightly differing chemical shifts.

Thus, four protons have eight chemical shifts in the two conformations. The *t*-Ac signal exhibits an NOE correlation only with one multiplet at 3.58 ppm. Therefore, both signals of the *t*-H9′ geminal pair should belong to this multiplet. The two partners of through-space coupling with this geminal pair (*t*-H8′) resonate in the multiplet at 3.03 ppm. The assignment of the geminal pairs of H9′ protons to the multiplet at 3.83 ppm and *c*-H8′, at 3.12 ppm, becomes obvious. This is consistent with the weak NOE correlation between *c*-NMe10′ (2.84 ppm) and the multiplet for *c*-H9′ protons (3.83 ppm). The lack of good correlations between *c*-NMe10′ and the geminal pair *c*-H9′ indicates that they are oriented *trans* around the C9′–N10′ bond. The COSY spectrum confirms the assignment of the H8′ and H9′ protons. Only two cross-peaks are observed between these multiplets: *c*-H8′/*c*-H9′ (3.83/3.12 ppm) and *t*-H8′/*t*-H9′ (3.58/3.03 ppm). The HSQC 2D heterocorrelation spectrum confirms the formation of these multiplets by separate geminal pairs of protons. Signals of the corresponding CH$_2$ C atoms coalesce into a single correlation for these multiplets.

The second substituent of arundacine [C8–C9–N(Me)$_2$10] has signals at positions very similar to those for arundamine and is also identified using NOE correlations. The N(Me)$_2$10 group (1.89 and 1.90 ppm) forms a good correlation with the multiplet at 2.27 ppm and two weak correlations with multiplets at 2.16 and 2.38 ppm. Obviously this represents signals for methylene protons H8 and H9, like for arundamine. Their NOE correlations depicted in Fig. 1 as 8/9 confirms this. The COSY spectrum for these three multiplets shows that all signals correlate with each other. The HSQC spectrum reveals the formation scheme: 2.38 ppm, H8; 2.72 ppm, H8 + H9; 2.16 ppm, H9 protons. Therefore, the central multiplet has a doubled integral intensity. Signals of H8 and H9 could not be assigned to *c*- and *t*-conformers because they overlap, *c*-*t*-splitting for the signal of C9 is absent in the ^{13}C NMR spectrum, and the C8 signal has very small splitting (only 0.11 ppm).

The PMR spectrum of the aromatic parts of arundacine exhibits well resolved signals for H4′ and H7 and a complicated and unresolvable multiplet (7.20-7.40 ppm) for all remaining aromatic protons. Signals for *c*-H4′ and *t*-H4′ protons are easily identified by the NOE correlation to H8′ and H9′ protons. The two doublets for *c*-H7 and *t*-H7 could not be assigned. An alternate assignment is given in Table 1. Chemical shifts of the remaining aromatic protons were assigned based on 2D NOESY, HSQC, and HMBC spectra.

The correlations of N(Me)$_2$10 signals with all aromatic protons of the other half of the dimer and the correlation of the *c*-Ac methyl protons with aromatic H5′ and H6′ are important, like for arundamine. The lack of an analogous correlation for the *t*-Ac protons also indicates that the *c*-*t*-conformers differ not only in the *c*-*t*-orientations of the Ac group but also in the placement of the C8′–C9′–N10′ substituent.

The results indicate that arundacine has the structure 3-N,N-dimethylaminoethyl-5-hydroxy-4-(3′-N′-acetyl-N′-methylaminoethylindol-1′-yl)indole.

EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer model 2000 Fourier spectrometer in KBr pellets; UV spectra, on a Hitachi spectrophotometer in ethanol solution; mass spectra, in an MX 1310 spectrometer equipped with a direct probe into the ion chamber.

NMR spectra were recorded on a Bruker AM-500 spectrometer at working frequencies 500 MHz for protons and 125.8 MHz for ^{13}C.

We used aluminum oxide (neutral) 100/160 μm for column chromatography; aluminum oxide 5/40 μm plates and system 1 ($CHCl_3$—CH_3OH, 9:1) for TLC.

Arundacine (1). Isolation of Arundacine. Total alkaloids (10.4 g) from roots of *A. donax* L. collected at the end of growth were chromatographed over an aluminum-oxide column with elution by hexane, ether, benzene, $CHCl_3$, and $CHCl_3$—CH_3OH. Arundacine (12 mg), mp 192-193°C (acetone) was isolated from the $CHCl_3$—CH_3OH (50:1) fractions.

Total alkaloids (23 g) from *A. donax* L. roots collected during vigorous growth were chromatographed over an aluminum-oxide column using a method analogous to that above. Arundacine (50 mg) was isolated from the $CHCl_3$—CH_3OH (50:1) fractions.

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