CIMICIDUPHYTINE - A NEW DIMERIC INDOLE ALKALOID FROM HAPLOPHYTON CIMICIDUM (APOCYNACEAE)

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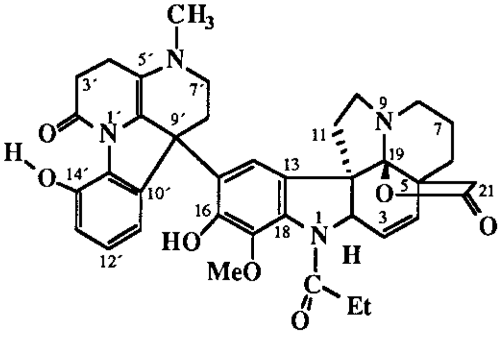
Abstract - Cimiciduphytine, a new dimeric indole alkaloid from Haplophyton cimicidum (Apocynaceae) has been assigned the aspidosperma-canthinone bisindole structure (1).

Several monomeric and dimeric indole alkaloids have been isolated from Haplophyton cimicidum (Apocynaceae).[1-6] In continuation of our study[1-6] of alkaloids from H. cimicidum, we have isolated and determined the structure of a new dimeric indole alkaloid cimiciduphytine. Cimiciduphytine was one of the minor alkaloids that were isolated when the alkali-soluble base residues from the isolation of haplophytine,[2] the major alkaloid of H. cimicidum were subjected to pH-gradient counter-`current distribution.[4-6] Cimiciduphytine (1), $C_{38}H_{40}N_4O_7$ (by high resolution mass spectrometry), crystallized from ethanol as small plates, mp 287-290°C (decomp.). Its mass spectrum indicated a molecular ion (68%) at m/z 664. Other significant ions in the mass spectrum were at m/z 605(25), 563(6), 412(12), 411(23), 410(17), 255(23), 172(24), 170(30) and 159(25). The nmr spectrum of cimiciduphytine ($CDCl_3$) indicated the presence of one C-methyl of an N-propionyl function at δ 1.23 (t, J = 7 Hz, 3H) coupled to a two proton quartet at 2.64. It also exhibited signals for an aliphatic N-methyl at δ 2.45 (s, 3H), an aromatic methoxyl at 3.68 (s, 3H), two vinyl protons at 5.55 (dd, J=10, 2 Hz, 1H), 5.73 (dd, J=10, 2 Hz, 1H) and four aromatic protons at 6.24 (dd, J=8, 1 Hz, 1H), 6.83 (dd, J=8, 1 Hz, 1H), 6.95 (t, J=8 Hz, 1H) and 7.54 (s, 1H). There were also two D_2O exchangeable protons at δ 7.20 and 11.33. The KBr infrared spectrum of cimiciduphytine showed hydroxyl absorption at 3430 cm^{-1} and carbonyl absorptions at 1745 (lactone CO) and 1625 cm^{-1} (amide CO). The uv spectrum (ethanol) exhibited maxima at 223 (ε 42,000), 260 (ε 16,000), 290 nm (ε 3,000) indicative of the presence of a dihydroindole system.[7]

The assignment of structure (1) to cimiciduphytine was based on its spectral data. The presence of a strong band in its ir spectrum at 1745 cm^{-1} suggested that cimiciduphytine is a γ-lactonic alkaloid like its companion γ-lactonic alkaloids of the aspidoalbine skeletal type.[2-6] This was supported by its mass spectrum which exhibited a fragmentation pattern characteristic of lactonic alkaloids of the aspidoalbine skeletal type.[8] The high resolution mass spectrum of (1) was very informative. Ions at m/z 605 (M^+ -CO_2, CH_3), 563 (M^+ -CO_2, CH_3CH_2CO) were indicative of the presence of lactonic and propionyl functions in cimiciduphytine. The significant ion at m/z 255 ($C_{15}H_{15}N_2O_2$) represented the canthinone portion of (1). The same ion (same composition) was also prominent in the mass spectra of cimilophytine (2),[5] cimiciphytine and norcimiciphytine,[4] three lactonic alkaloids that had previously been isolated from H. cimicidum. The ion at m/z 411 ($C_{23}H_{27}N_2O_5$) was derived from the aspidosperma portion of (1) analogous to the situation with cimilophytine (2).[5] The nmr spectrum of (1) which exhibited important similarities to that of 2 was also very informative. It clearly indicated that the location and pattern of the four aromatic protons in cimiciduphytine (1) were similar to those of cimilophytine (2). These consisted of the single aromatic proton on the aspidosperma portion of (1) and the three adjacent aromatic protons on the canthinone portion. The strongly hydrogen-bonded hydroxyl at δ 11.33 was similar to that exhibited by cimilophytine (δ 11.49) and was assigned to the proton of the phenol hydrogen-bonded to the δ-lactam carbonyl[4] of the canthinone portion of (1). The second hydroxyl group (at δ 7.20) was placed at C-16 and the methoxyl (δ 3.68) at C-17 because the hydroxyl group was not hydrogen-bonded to the carbonyl of the N-propionyl group. Moreover a C-16 methoxyl would have been shielded similar to those exhibited in the nmr spectra of cimilophytine (2),[5] cimiciphytine[4] and haplophytine.[2] In contrast with the situation in cimilophytine,[5] both the nmr and mass spectra of (1) indicated the absence of a tertiary C-16' hydroxyl group in the compound. The presence in nmr of (1) of two vicinal vinyl protons coupled with each other and one other proton indicated the presence of a 3,4-double bond in cimiciduphytine, analogous to those exhibited in the spectra of haplophytine,[2] cimiciphytine and norcimiciphytine.[4] Cimiciduphytine is thus a new bisindole alkaloid derived by the coupling of an unrearranged canthiphytine unit with a dehydroisocimicidine unit.



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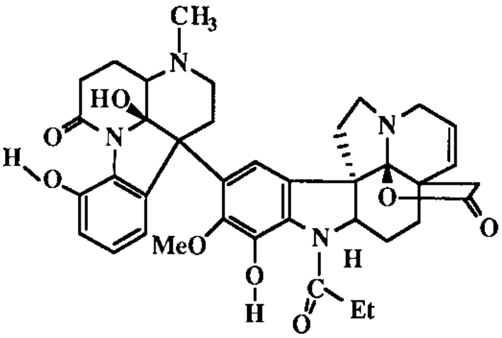

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