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STUDIES ON THE ALKALOIDS OF *RHAZYA STRICTA*

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Continuing our investigations (1-7) on *Rhazya stricta* Decsne. (Apocynaceae) (8), we describe here the isolation from the roots and identification of a dimeric indole alkaloid, didemethoxycarbonyltetrahydrosecamine (DDCTHS). Condylocarpine was also isolated from the leaves. DDCTHS was obtained as a colorless, amorphous material that gave a light yellow color with $CeSO_4$ solution. The uv spectrum was characteristic for the indole chromophore, and its ir spectrum did not show any peak in the carbonyl region. Accurate mass measurements afforded the exact mass to be 564.4141, corresponding to the molecular formula $C_{38}H_{52}N_4$. The ^{1}H-nmr spectrum was identical to that reported for DDCTHS (9-12). The alkaloid probably arises in the plant by hydrolysis and decarboxylation of tetrahydrosecamine (THS), and it has been previously prepared synthetically from THS and demethoxycarbonyltetrahydrosecamine (DCTHS) by this procedure (9-11).

Condylocarpine was isolated as an amorphous material which gave a blue color with $CeSO_4$ solution. The uv spectrum was characteristic for the anilinoacrylate chromophore. The ir spectrum showed the presence of an α,β-unsaturated ester. The molecular formula was established by hrms to be $C_{20}H_{22}N_2O_2$ (calcd. 322.1681; obsd. 322.1671). On the basis of comparison of nmr and other spectral data with the earlier reported values (13,14), the alkaloid isolated was identified as condylocarpine. Condylocarpine has been reported earlier from *Diplorrhynchus condylocarpon* (15) but has not been isolated from *R. stricta*.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURE.—The uv spectra were recorded on a Shimadzu UV-240 spectrophotometer; ir spectra were recorded on a JASCO A-302 IR spectrophotometer; mass spectra were recorded on Finnigan MAT 312 and Finnigan MAT 112 mass spectrometers connected to a PDP 11/34 (DEC) computer system; the ^{1}H-nmr spectra were recorded in $CDCl_3$ on a Bruker AM-300 nmr spectrometer. The optical rotation was determined with a Polaratronic D instrument.

PLANT MATERIAL.—The plant material was collected in November 1984, from a village near Karachi, and was identified by the Botany Department of Karachi University where a voucher specimen is deposited.

ISOLATION OF DIDEMETHOXYCARBONYLTETRAHYDROSECAMINE.—The crude alkaloids obtained from the ethanolic extracts of the roots of the plant were extracted with $CHCl_3$ at different pH values according to their differential basicities. The fraction obtained at pH 8 was subjected to column chromatography on a silica gel column with Me_2CO as eluent. Preparative tlc on a fraction using silica gel GF-254 precoated plates (E. Merck) with light petroleum (40-60°)-Me_2CO (7:3) as a solvent system afforded a new alkaloid, DDCTHS as a colorless, amorphous material (5.0 mg, 6.66×10^{-6}% yield), which gave an orange color with Dragendorff's reagent and light yellow color with $CeSO_4$ solution; $[\alpha]^{20}D+30°$ $CHCl_3$; uv λ max (MeOH) 224, 284, 290 nm (sh) and λ min (MeOH) 255 nm; ir ν max ($CHCl_3$) 3500, 2880, 1360, 1140, 1015 cm^{-1}; ms *m/z* 564 (0.43%), 451 (0.54%), 438 (0.33%), 295 (3.65%), 283 (1.12%), 126 (100%), 112 (0.87%); ^{1}H nmr (300 MHz, $CDCl_3$) δ (ppm) 0.69 (6H, t, J=7.3 Hz, C-18, C-18′ H), 1.16 (4H, m, C-19, C-19′ H) (9-12).

ISOLATION OF CONDYLOCARPINE.—The EtOH extract of the fresh leaves of *R. stricta* was concentrated, acidified with 5% HCl, filtered, and basified with NH_3 to pH 9 which resulted in some precipitation. The precipitate was subjected to column chromatography on a silica gel column. The fraction obtained on elution with light petroleum (40-60°) -Me_2CO (7:3) afforded a mixture of alkaloids. This mixture was subjected to preparative tlc using silica gel GF-254 precoated plates (E. Merck) with light petroleum (40-60°)-Me_2CO-diethylamine (7.9:2.0:0.1) as a solvent system, and an alkaloid (condylocarpine) was separated as an amorphous material (2.5 mg, 3.73×10^{-5}% yield), which gave an orange color with Dragendorff's reagent and a blue color with $CeSO_4$ solution; $[\alpha]^{20}D+909°$ $CHCl_3$; uv λ max (MeOH) 223, 290, 328 nm, λ min (MeOH) 265 and 307 nm; ir ν max ($CHCl_3$) 3650, 1688, and 1607 cm^{-1}; ms *m/z* 322 (100%), 307 (34%), 279 (39%), 267 (15%), 252 (73%), 235 (91%), 121 (77%). ^{1}H nmr (300 MHz, $CDCl_3$) δ (ppm) 1.60 (3H, d, $J_{18,19}$=7.38 Hz, C-18H), 3.79 (3H, s, $COOCH_3$), 3.90 (1H, m, C-15H), 4.10 (1H, s, C-3H), 5.32 (1H, q, $J_{19,18}$=7.38 Hz, C-19H), 6.78 (1H, d, $J_{12,11}$=7.70 Hz, C-12H), 6.92 (1H, dd, $J_{10,9}$=7.70 Hz, $J_{10,11}$=7.48 Hz, C-10H), 7.14 (1H, dd, $J_{11,10}$=7.48 Hz, $J_{11,12}$=7.70 Hz, C-11H), 7.33 (1H, d, $J_{9,10}$=7.70 Hz, C-9H), 8.63 (1H, s, N-H).

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FURANOCOUMARINS OF *HERACLEUM BRUNONIS*

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In a program (1) to screen high altitude (above 3200 m) plants of Himalayan glacier areas for active medicinal compounds and to investigate such plants chemically, *Heracleum brunonis* Benth. (Umbelliferae) was collected and found to be rich in furanocoumarins. Four known furanocoumarins have been isolated and identified.

EXPERIMENTAL

PLANT MATERIAL.—The roots of *H. brunonis* were collected in September 1984, at an altitude of 4,000 m from the Pindari glacier area in Kumanon Himalaya, U.P., India. Reference plant material is available in the Herbarium of the Forest Research Institute, Dehradun, No. FRI Dehradun (DD) Lace 1673.

EXTRACTION AND ISOLATION OF FURANOCOUMARINS.—The dried roots of the plant were pulverized, extracted with 80% MeOH, concentrated under vacuum, and partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was subjected to silica gel G tlc and observed under long wavelength uv light (365 nm). Six spots showed intense blue to yellow fluorescence and showed color changes characteristic of coumarins when sprayed with alcoholic KOH and alkaline hydroxylamine followed by $FeCl_3$.

On subjecting the $CHCl_3$ extract to silica gel G column chromatography and eluting with different proportions of combinations of petroleum ether/C_6H_6 and C_6H_6/EtOAc, six fractions were collected. The purity of of each fraction was further ascertained by using a Waters Associates hplc fitted with a RCSS-Z module system and refractive index and variable wavelength (190-750 nm) uv detectors.

Out of the six fractions, four known coumarins, (+)-columbianetin, imperatorin, (+)-heraclenol and bergapten, were identified (2-6) by means of mp, mmp, co-hplc, uv, ir, ^{1}H-nmr, and ms methods as well as by comparisons with authentic samples.

Full details of the isolation and identification are available on request to the senior author.