A NEW SPREMIDINE ALKALOID FROM *CAPPARIS DECIDUA*

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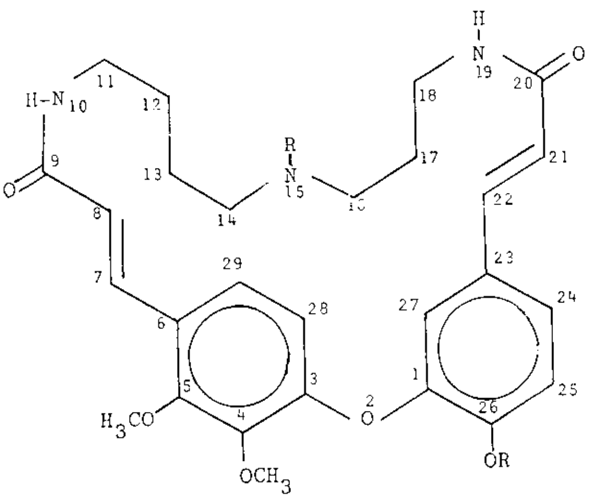
Abstract - A new spermidine alkaloid, named capparidisine, has been isolated from the root bark of Capparis decidua and its structure was eluciated by spectral studies.

Cappris decidua (Forssk.) Edgew (Capparidaceae) is one of the common shrubs of the arid plains of Pakistan[1]. Its roots have long been known in the oriental medicine[2]. The crude drug has been used as a laxative, antidote of poison, anthelmintic and is the treatment of cardiac troubles, boils and toothache. The bark is reported to the used as cure for asthma, inflammation and gout[3,4]. Some species of Capparis have been investigated chemically and the isolation of stachydrine, β-carotene, β-sitosterol, rutin, isothiocyanate glucosides, hydrocarbons and fatty acids has been reported[5-10]. The present communication reports the isolation and structure elucidation of a new spermidine alkaloid, named as capparidisine, from the root bark of Capparis decidua.

Repeated silica gel column chromatography of the alkaloidal material from the dried root bark led to the isolation of pure crystalline capparidisine (I), mp 180-181°C. It gave a positive test for phenol with ferric chloride reagent. According to the high resolution mass spectrum, which showed molecular ion peak at m/z 495.2369, this compound as a molecular formula $C_{27}H_{33}N_3O_6$. The uv spectrum showed maxima at 220 (log ε 2.69), 283 (log ε 2.75) and a shoulder at 310 nm, which are similar to codonocarpine[11]. The ir spectrum exhibits bands at 3400 (br, OH, NH), 1660 (α β -unsat. amide) and 1610 cm^{-1} (aromatic ring, C=C).



I, R = H
II, R = $COCH_3$

Acetylation of capparidisine yielded a crystalline diacetate (II), mp 290°C, which showed molecular ion peak at m/z (579.2589) corresponding to the formula $C_{31}H_{37}N_3O_8$ (Calc. 579.2580). Its ir spectrum revealed bands at 1765 (phenolic acetate) and 1660 cm^{-1} (amide). The ^{1}H-nmr (300 MHz) and ^{13}C-nmr (25.1 MHz) spectra of capparidisine diacetate in DMSO-d_6 showed doubling of several signals which is due to the slowly interconverting E and Z isomers with regards to amide bond. This phenomenon has been reported earlier in amides[12,13] and also observed by us in cadabicine, another spermidine alkaloid isolated from Cadaba forinosa[14]. Thus the ^{1}H-nmr spectrum of II showed two singlets at δ1.69 and 1.98, together integrating for 3H, due to the N-COCH_3 group. A singlet at δ2.50 (3H) is attributed to the phenolic acetate protons. The multiplets appearing between δ1.23-1.69 (6H) and δ3.13-3.60 (8H) are assigned to three methylene group adjacent to other methylenes and four mehtylens groups adjacent to nitrogen atoms respectively. The presence of two methoxy groups in the alkaloid is revealed by two singlets at δ3.77 (3H) and 3.80 (3H). Four doublets at δ5.84, 6.60, 7.18 and 7.50 (1H each, J = 15.5Hz) indicate the presence of four olefinic protons of two trans cinnamic acid moieties. A doublet at δ6.35 (J = 2.8Hz) arises from H-27 with meta coupling only. In addition, there are three doublets at δ 7.19, 7.24 and 7.97 (each 1H, J = 8.5Hz) exhibiting only ortho coupling. They are assigned to H-25, H-28 and H-29 respectively. The H-24 gives rise to a double doublet at δ7.38 with an ortho (J = 8.5Hz) and a meta coupling (J = 2.8 Hz). These signals show that the two methoxy groups are attached in ortho position at C-4 and C-5. The assignments have been confirmed with the 2D correlation of proton shifts through a COSY-45 experiment as well as as through a two dimensional J resolved pmr spectrum. The ^{13}C-nmr (table 1) and the mass spectrum (Figure 1) also support the proposed structure I for capparidisine. The presence of the spermidine moiety in capparidisine is indicated by the ^{1}H-nmr and ^{13}C-nmr spectra which clearly show the presence of seven methylene groups four of which are adjacent to nitrogen. The chemical shifts of the methylene protons and carbons are very near those observed in cadabicine, the structure of which has been proved through x-ray crystallographic studies[14]. The mass spectral fragmentation pattern also supports the presence of spermidine moiety in capparidisine. The occurrence of spermidine alkaloid in capparis decidua is interesting from the chemotaxonomical point of view also because this class of alkaloids have already been isolated from cadaba[14], a genus belonging to the same family (capparidaceae) as well as in Codonocarpus, a genus belonging to a taxonomically closely related family(Cruciferae). The mass spectrum fragmentation shows that the spermidine moiety is joined with the rest of the molecule in the manner shown in structure I. The alternative structure with opposite attachment of the spermidine can therefore be ruled out.

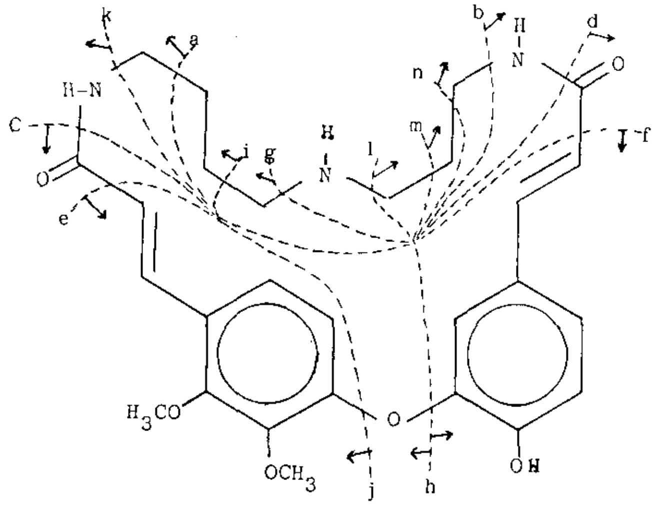
Table 1: ^{13}C-NMR chemical shift of II

Carbon No.	ppm	Carbon No.	ppm
1	151.80	20	164.86/164.78$^{+,c}$
3	155.72	21	124.67/124.80^{+}
4	148.69^{a}	22	138.00/138.16$^{+,b}$
5	148.71^{a}	23	132.99
6	134.56	24	123.79
7	137.81^{b}	25	110.52
8	125.22/125.45^{+}	26	143.36
9	164.67^{c}	27	122.13
11	47.79	28	123.60
12	27.01	29	129.30
13	38.33	O<u>C</u>OCH$_3$	168.53
14	37.98/38.27^{+}	OCO<u>C</u>H$_3$	21.15
16	27.69/27.77^{+}	N<u>C</u>OCH$_3$	169.13
17	26.11/26.52	NCO<u>C</u>H$_3$	21.25
18	42.49	OCH$_3$	56.79
		OCH$_3$	55.15

a,b,c = assignment may be reversed.

+ = doubling of peaks due to the presence of isomers.

Figure 1



	m/z	Mol.formula	Rel.Intens.
M^+	495	$[C_{27}H_{33}N_3O_6]$	3.0
M^+-OCH_3	465	$[C_{26}H_{31}N_3O_5]^+$	25.7
M^+-2OCH_3	435	$[C_{25}H_{29}N_3O_4]^+$	29.8
(a,b)	396	$[C_{21}H_{10}N_2O_6]^+$	12.3
(b,c)	367	$[C_{20}H_{17}NO_6]^+$	16.5
(c,d)	352	$[C_{20}H_{16}O_6]^+$	10.3
(e,f)	296	$[C_{18}H_{16}O_4]^+$	9.2
(g,h)	277	$[C_{15}H_{19}NO_4]^+$	75.4
(h,i)	263	$[C_{14}H_{17}NO_4]^+$	24.8
(j,k)	205	$[C_{11}H_{11}NO_3]^+$	4.1
(h,l)	203	$[C_{12}H_{13}NO_2]^+$	64.1
(c,j)	190	$[C_{11}H_{10}O_3]^+$	7.2
(h,m)	189	$[C_{11}H_{11}NO_2]^+$	6.1
(h,n)	175	$[C_{10}H_9NO_2]^+$	7.2
(e,j)	162	$[C_{10}H_{10}O_2]^+$	13.4
(b,h)	161	$[C_9H_7NO_2]^+$	100.0
(d,h)	146	$[C_9H_6O_2]^+$	53.6
(f,h)	118	$[C_8H_6O]^+$	45.3

EXPERIMENTAL

The uv spectra were measured in MeOH with a Shimadzu UC-240 Graphicord Spectrometer. The ir spectra were scanned in KBr disc on a Jasco-IRA-1 Spectrometer. The ^{1}H-nmr were recorded in DMSO-d_6 with a Bruker AM 300 Spectrometer using TMS as an internal standard, whereas the ^{13}C-nmr (broad band and gated spin echo) were recorded in DMSO-d_6 with a WM 100 Spectrometer at 25.1 MHz. The mass spectra were recorded on a Finnigan MAT 312 double focusing mas spectrometer coupled with PDP 11/34 computer system.

Isolation

Dried and milled root bark of C.decidua was extracted with EtOH. The residue obtained on evaporation of alcoholic extract was partitioned into EtOAc and H_2O. The aqueous layer was basified with NH_3 (pH 9.0) and extracted with $CHCl_3$ repeatedly. The solvent from the $CHCl_3$ extract was evaporated under reduced pressure to yield a yellowish crude alkaloidal material. It was chromatographed on a column of silica gel. Elution with $CHCl_3$: MeOH: NH_3 (80 : 18 : 2) furnished capparidisine. Fractional crystallisation with methanol or with acetone-water mixture yielded pure alkaloid in the form of light cream coloured crystals, mp 180-181°C. The purity of the isolated capparidisine was checked on t.l.c. plate (silica gel, $CHCl_3$-MeOH-NH_3, 8:1.8:0.2) as well as reverse phase HPLC (RP-18 column) using MeOH-H_2O (7:3) as mobile phase.

Spectral Data of Capparidisine(I)

For uv and ir peaks see text. High resol. MS: m/z Found (calcd. for), 495.2369 ($C_{27}H_{33}N_3O_6$, 495.2355), 465.2234 ($C_{26}H_{31}N_3O_5$, 465.2263), 435.2127 ($C_{25}H_{29}N_3O_4$, 435.2157), 396.1362 ($C_{21}H_{20}N_2O_6$, 396.1321), 367.1065 ($C_{20}H_{17}NO_6$, 367.1055), 352.0961 ($C_{20}H_{16}O_6$, 352.0946), 296.1059 ($C_{18}H_{16}O_4$, 296.1048), 277.1324 ($C_{15}H_{19}NO_4$, 277.1313, 263.1175 ($C_{14}H_{17}NO_4$, 263.1157), 205.0734 ($C_{11}H_{11}NO_3$, 205.0738), 203.0948 ($C_{12}H_{13}NO_2$, 203.0946), 190.0689 ($C_{11}H_{10}O_3$, 190.0629), 189.0707 ($C_{11}H_{11}NO_2$, 189.0789), 175.0696 ($C_{10}H_9NO_2$, 175.0633), 162.0615 ($C_{10}H_{10}O_2$, 162.0680), 161.0491 ($C_9H_7NO_2$, 161.0476), 146.0361 ($C_9H_6O_2$, 146.0367), 118.0421 (C_8H_6O, 118.0418).

Capparidisine Diacetate (II)

Caparidisine (25 mg) was dissolved in Ac_2O - C_5H_5N (1.5:0.5 ml) with warming and then kept overnight at ambient temperature. On addition of water, the diacetate was obtained as an amorphous solid. It was recrystallised from methanol. The colourless crystals melted at 290°C. uv: λ_{max} 204 (log ε, 3.10), 275.9 (log ε, 3.25) and 310 (shoulder) nm. ir: ν_{max} 1765 (phenolic acetate), 1660 (amide). ^{1}H-nmr see text, ^{13}C-nmr see table 1. MS: m/z 579.2589 (M^+, calc. 579.2580), 537.2453 (M^+-CH_2=C=O, calc. 537.2486) 494.2275 (M^+-CH_2=C=O=CH_3CO, calc. 494.2275), 465.2251 ($C_{26}H_{31}N_3O_5$, calc. 465.2263), 435.2125 ($C_{25}H_{29}N_3O_4$, calc. 435.2157), 396.1343 ($C_{21}H_{20}N_2O_6$, calc. 396.1321), 367.1049 ($C_{20}H_{17}NO_6$, calc. 367.1055), 352.0954 ($C_{20}H_{16}O_6$, calc. 352.0946), 296.1057 ($C_{18}H_{16}O_4$, calc. 296.1048), 277.1317($C_{14}H_{19}NO_4$ calc. 277.1313) 263.1140 ($C_{14}H_{17}NO_4$, calc. 263.1157), 205.0744 ($C_{11}H_{11}NO_3$, calc. 205.0738), 203.0957 ($C_{12}H_{13}NO_2$, calc. 203.0946), 190.0656 ($C_{11}H_{10}O_3$, calc. 190.0629), 189.0758 ($C_{11}H_{11}NO_2$, calc. 189.0789), 175.0673 ($C_{10}H_9NO_2$, calc. 175.0633), 162.0660 ($C_{10}H_{10}O_2$, calc. 162.0680), 161.0494 ($C_9H_7NO_2$, calc. 161.0476), 146.0373 ($C_9H_6O_2$, calc. 146.0367), 118.0403 (C_8H_6O, calc. 118.0418).

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