Two New N-Acetylated Spermidine Alkaloids from Capparis decidua

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TWO NEW *N*-ACETYLATED SPERMIDINE ALKALOIDS FROM *CAPPARIS DECIDUA*

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ABSTRACT.—Two new spermidine alkaloids, 14-*N*-acetylisocodonocarpine [**1**] and 15-*N*-acetylcapparisine [**2**], have been isolated from the root bark of *Capparis decidua*, and their structures have been determined based on the spectral and chemical data including 2D nmr.

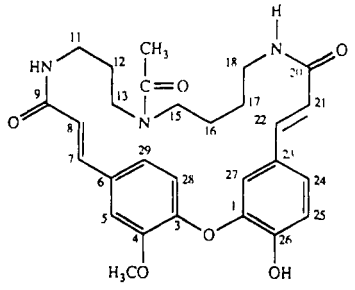
Capparis decidua (Forssk.) Edgew. syn. *Capparis aphylla* Roth. (Capparidaceae) is one of the common shrubs of the arid plains of Pakistan (1). The medicinal importance and the compounds isolated from this genus have been described in our previous communications (1,2).

The present communication reports the isolation and structural elucidation of two new naturally occurring acetates from *C. decidua*. One of them is 14-*N*-acetylisocodonocarpine [**1**], while the other is 15-*N*-acetylcapparisine [**2**]. The exact attachment of the spermidine moiety in the skeleton of both the compounds was proven with the help of mass fragmentation.

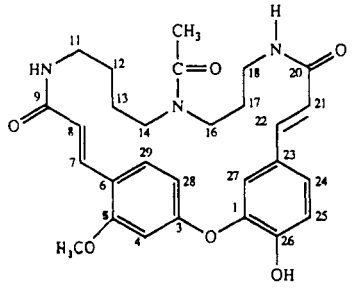
The uv spectrum of both compounds displayed similar maxima (see Experimental), i.e., at 218 nm (log ϵ 3.12), 286 nm (log ϵ 2.84), and a shoulder at 310 nm. These values are very close to those of isocodonocarpine (1), capparisine (2), cadabicine (3), and codonocarpine (4).

The hreims of **1** and **2** showed molecular ion peaks at *m/z* 507.2375 corresponding to the molecular formula $C_{28}H_{33}N_3O_6$ (calcd 507.2369). The ir spectra of both compounds exhibited bands at 3300–3200 (br OH and NH), 1660 (α,β-unsaturated amide), and 1600 cm^{-1} (aromatic ring). In addition to these bands there was a band at 1740 cm^{-1} indicating the presence of an acetyl group in the alkaloids. This band was not present in the alkaloids so far isolated from this source.

The ^{1}H-nmr and ^{13}C-nmr spectra of **1** as well as **2** showed doubling of several signals which was due to slowly interconverting *E* and *Z* conformers with regard to the amide bond (5,6). The spectral data of compound **1** showed many similarities with isocodonocarpine (1), and compound **2** was likewise similar to capparisine (2). The 3H singlets at δ 1.89 and 2.06 were attributed to *N*-acetates. The upfield position of the singlets and the presence of two singlets (due to isomers) with a total integration of 3H



1
11 26-OAc



2
12 26-OAc

in both the compounds showed the occurrence of *N*-acetates rather then phenolic acetates.

The ^{1}H-nmr assignments (see Experimental) for **1** have been confirmed by 2D correlation of proton shifts through a COSY-45° and 2D-*J*-resolved experiments. The coupling interactions were established by COSY-45° experiment. Two doublets at δ 5.65 (H-21) and 7.25 (H-22) were coupled with each other, whereas doublets of H-7 at δ 7.48 and H-8 at δ 6.38 are coupled with each other. The double doublet due to H-24 at δ 7.18 had cross peaks with H-25 (δ 7.05) and H-27 (δ 6.53), Similarly a double doublet of H-29 at 7.55 had cross peaks with H-5 (δ 7.89) and H-28 (δ 6.78).

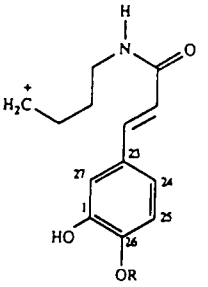
The positions of the OMe group in **1** and **2** were decided on the basis of ^{1}H- and ^{13}C-nmr spectral data. In the case of **2**, C-3 and C-5 bear oxygen functions; therefore the signal of H-4 is shifted upfield, i.e., at δ 7.10, and shows meta coupling of $J = 3.3$ Hz. In **1**, on the other hand, the signal of this proton is a doublet at δ 7.89 ($J = 2.0$ Hz) and is assigned to H-5.

The hreims of **1** clearly shows that the $(CH_2)_3$ unit of the spermidine moiety is on the "left" and the $(CH_2)_4$ moiety is on "right" side of the molecule. The situation is just the reverse in the case of **2**. The peaks at *m/z* 234 and 276 of compound **1** and its diacetates correspond to ions **3** and **4** show that the hydroxyl group is attached to the phenyl ring having butyl unit, otherwise there should be a peak at *m/z* 248, which was not observed, in the ms of **1**. The peaks at *m/z* 292 and 334 correspond to ions **5** and **6**, respectively. The peaks at these positions are not observed in the ms of 15-*N*-acetylcapparisine [**2**].

The peaks at *m/z* 220 and 262 of its diacetate in the eims of compound **2** correspond to ions **7** and **8** and show that the OH group is attached to the phenyl ring bearing the $(CH_2)_3$ unit; otherwise there should be peaks at *m/z* 234 and 276, which were observed in the eims of **1** but not in **2**. Similarly the peaks at *m/z* 277 and 319, corresponding to ions **9** and **10**, proved the same situation.

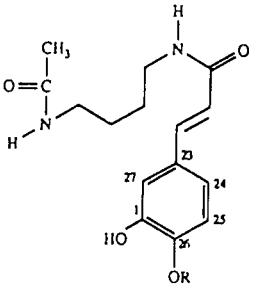
The ms fragmentation proposed for cadabicine (3) and isocodonocarpine (1) was found to be same as that of compound **1**.

All of the above arguments suggest that the structure of 14-*N*-acetylisocodonocarpine [**1**] resembles that of isocodonocarpine. It also shows similarities with codonocarpine (4) with the presence of an OMe group at C-4, but with a different attachment of the spermidine moiety. Compound **2** is suggested to be the 15-*N*-acetyl of capparisine.



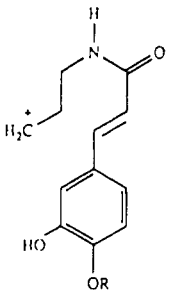
3 R=H *m/z* 234.1137
(calcd 234.1130 for $C_{13}H_{16}NO_3$)

4 R=Ac *m/z* 276.1249
(calcd 276.1235 for $C_{15}H_{18}NO_4$)



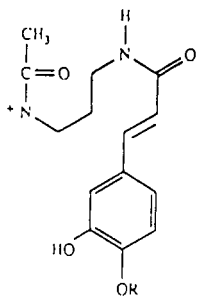
5 R=H *m/z* 292.1426
(calcd 292.1423 for $C_{15}H_{20}N_2O_4$)

6 R=Ac *m/z* 334.1531
(calcd 334.1528 for $C_{17}H_{22}N_2O_5$)



7 R=H *m/z* 220.0979
(calcd 220.0973 for $C_{12}H_{14}NO_3$)

8 R=Ac *m/z* 262.1172
(calcd 262.1079 for $C_{14}H_{16}NO_4$)



9 R=H *m/z* 277.1181
(calcd 277.1188 for $C_{14}H_{17}N_2O_4$)

10 R=Ac *m/z* 319.1291
(calcd 319.1293 for $C_{16}H_{19}N_2O_5$)

TABLE 1. ^{13}C-nmr Spectra of **1** and **2** ($CDCl_3 + CD_3OD$, 75.43 MHz).

Carbon	Compound	
	1	**2**
C-1	151.90	147.30
C-3	152.42	153.31
C-4	147.73	127.19
C-5	140.24	142.10
C-6	134.05	133.75
C-7	139.98[b]	140.19[a]
C-8	125.53/126.09[a,d]	126.09/126.74[b,d]
C-9	166.45[c]	167.77
C-11	45.14/45.34[d]	46.54
C-12	22.28—22.84[d]	27.24
C-13	38.83/39.20[d]	39.68
C-14	—	36.81/37.37[d]
C-15	37.62/37.82[d]	—
C-16	28.63/28.90[d]	28.25/28.61[d]
C-17	26.45/26.84[d]	26.86/26.98[d]
C-18	42.14	44.07
C-20	166.83[c]	169.00
C-21	124.24[a]	126.50[b]
C-22	139.78/139.92[b,d]	140.23[a]
C-23	132.85	132.55
C-24	123.06	123.70
C-25	112.99	109.80
C-26	147.44	142.52
C-27	121.12	122.01
C-28	117.86	124.86
C-29	122.07	129.94
NC*O*Me	168.10	171.90
NCO*Me*	20.88/21.81[d]	21.11/21.17[d]
OMe	55.95	56.49

[a,b,c]Assignments may be interchangeable.
[d]Observed doubling of signals due to conformers with regard to the amide bond.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—General procedures were as previously described (1).

ISOLATION OF 14-*N*-ACETYLISOCODONOCARPINE [**1**] AND 15-*N*-ACETYLCAPPARISINE [**2**].—The crude alkaloidal mixture (45 g) isolated from the EtOH extract of the root bark was subjected to Si gel cc (70–230 mesh, E. Merck). Elution with $CHCl_3$-MeOH (94:6) led to the isolation of **1**. It was further purified by flash chromatography using Si gel 60 (230–400 mesh, E. Merck) and elution with $CHCl_3$-MeOH (90:10) to obtain **1**. Further impurities were removed through tlc Si gel 60 F_{254} (E. Merck) plates. The purity of **1** was checked by hptlc. Compound **2** was eluted by $CHCl_3$-MeOH (95:5). Further purifications were carried out on tlc using ($CHCl_3$-MeOH (8.5:1.5) and gave **2** (45 mg). Its purity was confirmed by hplc using RP-18 column in MeOH-H_2O (70:30). Both the compounds gave positive tests for phenols with aqueous $FeCl_3$ reagent.

14-N-*Acetylisocodonocarpine* [**1**].—Colorless amorphous powder: mp 234–236°; uv (MeOH) (log ε) λ max 218 (3.12), 286 (2.84), 310 nm (shoulder); ir ν max cm^{-1} ($CHCl_3$) 3300–3200, 1740, 1660, 1600; hreims *m/z* $[M]^+$ 507.2375 (calcd 507.2369 for $C_{28}H_{33}N_3O_6$); other peaks were found to be similar to those found previously (1); fdms $[M]^+$ 507; ^1H nmr ($CDCl_3/CD_3OD$) see discussion; ^{13}C nmr see Table 1.

15-N-*Acetylcapparisine* [**2**].—Amorphous powder: mp 178–180°; uv and ir were found to be almost similar to **1**; hreims *m/z* $[M]^+$ peaks were found to be same as for **1**, other important peaks (see Chart 1); fdms $[M]^+$ 507; ^1H nmr ($CDCl_3/CD_3OD$) δ 1.89 and 2.06 (s, 3H, NAc), 1.23–1.48 (m, 6H, 2 × H-12, 2 × H-13, 2 × H-17), 3.29–3.69 (m, 8H, 2 × H-11, 2 × H-14, 2 × H-16, 2 × H-18), 3.78 (s, 3H, OMe), 5.75, 6.56, 7.30, 7.55 (each d, 1H, J = 15.8 Hz, olefinic protons of *trans*-cinnamic acid), 6.35 (d, 1H, J = 3.5 Hz, H-27), 6.56 (dd, 1H, J = 8.5 Hz and 2.5 Hz, H-28), 6.82 (d, 1H, J = 9.5 Hz, H-25), 7.10 (d, 1H, J = 3.3 Hz, H-4), 7.17 (d, 1H, J = 9.8 Hz, H-29), 7.19 (dd, 1H, J = 9.0 Hz and 2.5 Hz, H-24); ^{13}C nmr see Table 1.

ACETYLATION OF **1**.—14-*N*-acetylisocodonocarpine (10 mg) was dissolved in Ac_2O (2 ml) with 0.5 ml of pyridine, warmed slightly, and kept overnight. The reaction mixture was worked up in the usual manner to yield amorphous 14-*N*-26-*O*-diacetylisocodonocarpine [**11**]. It gave a negative test for phenols with $FeCl_3$: mp 205–207° (crystallized from MeOH); uv λ max (MeOH) nm (log ε) 205 (3.33), 271 (3.36), 310 (shoulder); ir ($CHCl_3$) ν max cm^{-1}: 3400, 1760, 1745, 1655, 1600; hreims *m/z* $[M]^+$ 549.2485 (calcd 549.2475 for $C_{30}H_{35}N_3O_7$); ^1H nmr ($CDCl_3/CD_3OD$, 300 MHz) δ 1.73 and 2.21 (s, 3H, NAc), 2.45 (s, 3H, OAc). Other peaks were almost similar to those of compound **1**.

ACETYLATION OF **2**.—Acetylation of 15-*N*-acetylcapparisine (25 mg) was performed as described for **1**. Amorphous 15-*N*-26-*O*-diacetylcapparisine [**12**] was formed. It gave negative test for phenols with $FeCl_3$ reagent: mp 223–224°; uv and ir were found to be almost similar to those of **11**; hreims were found to be the same as those of **2**.

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