6α/6β-HYDROXY-3-O-METHYLEPIMARITIDINE, TWO NEW ALKALOIDS FROM NARCISSUS TAZETTA L. VAR. CHINENSIS ROEM[1]

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Abstract—Two new alkaloids, 6α/6β-hydroxy-3-O-methylepimaritidine (3-epipapyramine) (4 and 5) were isolated from the bulbs of Narcissus tazetta L. var. chinensis Roem. together with four known alkaloids, maritidine, 3-O-methylmaritidine, epigalanthamine and lycoramine. The structures of 4 and 5 were determined on the basis of their IR, UV, CD, ^{1}H-NMR and MS fragments.

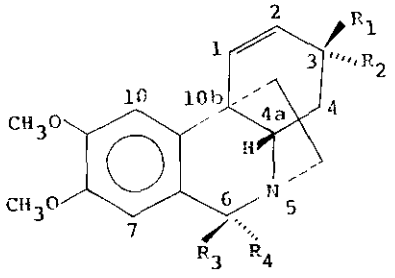
Narcissus tazetta L. var. chinensis Roem. (Amaryllidaceae) is cultivated in China as a decorative plant, the bulbs of this plant were also used for treatment of tumor in folk medicine. In continuation of our studies on the alkaloids of this plant we have reported the isolation of 9 alkaloids: lycorine, tazettine, pluviine, pseudolycorine, pretazettine, galanthamine, lycorenine, homolycorine and haemanthidine[2,3]. Pretazettine was proved to be one of the antitumor active components.[4] We reported here the isolation and structure elucidation of two new alkaloids of 6-hydroxy-5,10b-ethanophenanthridine type: 6α/6β-hydroxy-3-O-methylepimaritidine (4 and 5) a pair of C-3-epimer of papyramine (6 and 7). These two new alkaloids were isolated together as an inseparable mixture from the weak basic fraction along with two known alkaloids, maritidine (1) and 3-O-methyl-maritidine (3) by repeated chromatography over alumina column, eluted with chloroform and purified by preparative thin layer chromatography on silica gel plates eluted with chloroform-methanol (4:1, V/V). Additionally, two other known alkaloids, epigalanthamine (8) and lycoramine (9) have also been isolated from the mother liquor of pretazettine. The identification of 1, 3, 8 and 9 was carried out by comparison of their melting points and spectral data with those of the authentic samples. There was a first report of isolation of 1, 3, 8 and 9 from this plant.

6α/6β-Hydroxy-3-O-methylepimaritidine (4 and 5): pale yellow crystals, R_f 0.60

silica gel 60 F_{254} plate, chloroform-methanol (8:2, V/V), $[\alpha]_D^{20}$-10.2° (c=0.45, chloroform). The UV spectrum λ_{max}^{MeOH} nm(logε): 232(3.86), 283(3.42) and the IR spectrum (3400, 1600, 1505 cm^{-1}) showed the characteristic absorption of a hydroxy group and an aromatic ring containing methoxy groups.

The mass spectrum and its fragmentation pattern of 4 and 5 were very similar to those of 6 and 7 isolated from Narcissus papyraceus Ker-Gawl.[5] The high resolution mass spectrum showed that the epimers 4 and 5 have a MW of 317.1602 consistent with molecular formula of $C_{18}H_{23}NO_4$ calcd. m/z 317.1627, which was identical with that of papyramine (6 and 7). The fragmentation pattern of 4 and 5 is very similar to those of 6 and 7. The base peak at m/z 262 ($M^{+\cdot}$-C_3H_5N) is characteristic for the alkaloids in the crinine series with a double bond between C-1 and C-2 and no hydroxy substituent at C-11. The mass spectrum also confirmed the existence of both an aliphatic OMe and OH groups in the epimers. There were peaks at m/z 286 ($M^{+\cdot}$-OMe), 300($M^{+\cdot}$-OH) and at m/z 268 ($M^{+\cdot}$-CH_5O_2), which must be formed by elimination of both OMe and OH groups in addition to H· from $M^{+\cdot}$. Both the resemblance of the fragmentation of 4 and 5 with that of papyramine (6 and 7) at the ready expulsion of the OH group were compatible with location of OMe group at C-3 and the OH group at the benzylic C-6 which has been deduced from the ^{1}H-NMR spectrum (see Fig. 1).[5,6,9,12] Comparison of the proton magnetic resonance spectra of 4 and 5 with those of 6 and 7 also showed their close relationship. The ^{1}H-NMR spectrum (90 MHz in $CDCl_3$) of 4 and 5 showed the important signals: 7.05, 6.90, 6.83 and 6.80 (2H, s, two aromatic protons), 6.60 (1H, dd, J=10Hz, 3.5Hz, H-1), 5.75-6.10(2H, m, H-2 and C-6-OH), 6.13 and 5.38 (1H, s, H-6), 3.39 and 3.37 (3H, s, C-3-OMe), 3.89 (6H, s, two aromatic methoxy protons).

The ^{1}H-NMR spectrum indicated that these were two C-6 epimers in the solution and that the 4 and 5 were C-3 epimers of 6 and 7. The evidence of this is that the signals of H-1 were appeared at 6.60, as a double of doublet with coupling



1. R_1=OH, R_2=R_3=R_4=H
2. R_1=R_3=R_4=H, R_2=OH
3. R_1=OCH_3, R_2=R_3=R_4=H
4. R_1=R_3=H, R_2=OCH_3, R_4=OH
5. R_1=R_4=H, R_2=OCH_3, R_3=OH
6. R_1=OCH_3, R_2=R_3=H, R_4=OH
7. R_1=OCH_3, R_2=R_4=H, R_3=OH

constant $J_{1,2}$=10 Hz and $J_{1,3}$=3.5 Hz, which were similar to those of epimaritidine (2), but not to those of papyramine (6 and 7). (see Table 1)[5,7,10]

Table 1. Comparison of ^{1}H-NMR spectral Data [a)]

	1	2	3	4,5	6,7
H-1	6.66d	6.49dd	6.55d	6.60dd	6.66d
H-2	5.95dd	5.82d	6.11dd	5.90m	6.00dd
H-3	4.3m	4.4m	4.3m	4.1m	4.0m
$J_{1,2}$	10	10	10	10	10
$J_{2,3}$	5	0	5	1.5	5
$J_{1,3}$	0	2	0	3.5	0

a) 90 MHz, (ppm) downfield from TMS in $CDCl_3$

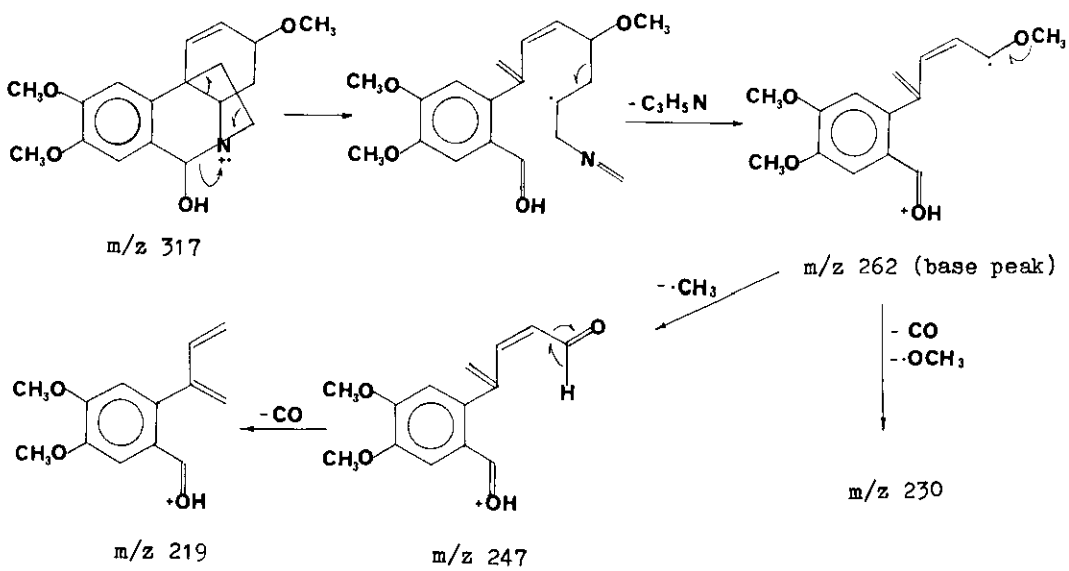


Figure 1. Mass Spectral Fragments of 4,5 and 6,7

The CD spectrum of 4 and 5 were also similar to those of papyramine (6 and 7). On the basis of these spectral data structures of 4 and 5 were assigned to be 6α/6β-hydroxy-3-O-methylepimaritidine a pair of C-3 epimers of papyramine (6 and 7), corresponding to 6-hydroxy-5,10b-ethanophenanthridine alkaloids of haemanthidine-type.[11,13]

REFERENCES AND NOTES

1. Part IX in the series "Studies on the Alkaloids of Amaryllidaceae" presented at the International Symposium on Organic Chemistry of Medicinal Natural Products (IUPAC), Shanghai, China, Nov. 1985, and at the 24th Annual Meeting of American Society of Pharmacognosy, the University of Mississippi, U.S.A., July. 1983. For part VIII see ref 3.
2. S.H.Hung and C.C.Tsai, Acta Pharmaceutica Sinica, 1962, 9, 548.
3. G.E.Ma, R.J.Tang, C.E.Lu and S.H.Hung, Yaoxue Tongbao, 1979, 14, 204.
4. G.E.Ma, S.H.Hung, S.Y.Chang, C.L.Yang, F.L.Lu, J.X.Han, and B.Shu, Zhongliu Fangzhi Yanjiu, 1979, (6), 1.
5. S.H.Hung, G.E.Ma, and G.Q.Sun, Acta Chemica Sinica, 1981, 39, 529.
6. P.Longevialle, D.H.Smith, A.L.Burlingame, H.M.Fales, and R.J.Highet, Organic Mass Spectrometry, 1973, 7, 401.
7. S.Tani, N.Kobayashi, H.Fujiwara, T.Shingu, and A.Kato, Chem. Pharm. Bull., 1981, 29, 3381.
8. R.D.Haugwitz, P.W.Jeffes, and E.Wenkert, J. Chem. Soc., 1965, 2001.
9. A.A.Ali, H.Kating, and A.W.Frahm, Phytochemistry, 1981, 20, 1173.
10. S.Ghosal, Ashutosh, and S.Razdan, Phytochemistry, 1985, 24, 635.
11. G.G.Deangelis and W.C.Wildman, Tetrahedron Lett., 1969, 729.
12. The mass spectrum of 3 and 4: m/z 317($M^{+\cdot}$, 26%), 302($M^{+\cdot}$-15, 4), 300($M^{+\cdot}$-17, 4), 286($M^{+\cdot}$-31, 11), 274(6), 273(61), 268(11), 263(15), 262(100), 261(8), 260(15), 259(7), 258(7), 256(12), 247(48), 233(25), 229(26), 219(20), 204(33), 203(58), 201(24), 188(22), 115(61). The mass spectra were obtained with a M-80 mass spectrometer (HRMS) and a Finnigan-3200 GC/MS/DS instrument.
13. The CD spectrum of 3 and 4 (c=0.064, methanol), 24°C, $(\theta)^{246}$ 0, $(\theta)^{286}$ +6439, $(\theta)^{308}$ 0.

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