CONAMBINE, A NEW NORDITERPENOID ALKALOID FROM *CONSOLIDA AMBIGUA* SEEDS

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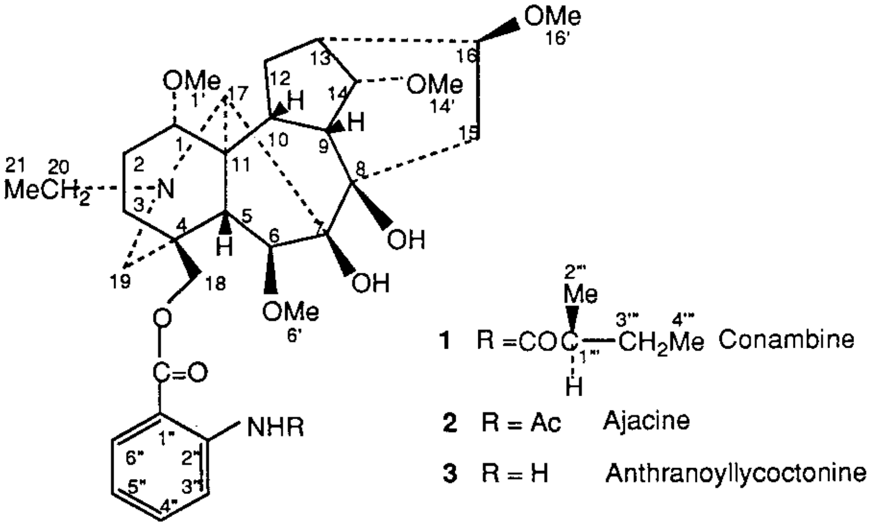
Abstract – A new norditerpenoiod alkaloid, "conambine" (**1**) has been isolated from the seeds of *Consolida ambigua* L. Its structure has been established on the basis of its spectroscopic data and chemical correlation with anthranoyllycoctonine (**3**).

Earlier communications[1-9] from our laboratory reported thirty-three norditerpenoid alkaloids and three diterpenoid alkaloids from the aerial parts and seeds of *Consolida ambigua* L., P. W. Ball and V. H. Heywood.[10] A novel alkaloid, ajabicine, isolated from the leaves, is an interesting diterpenoid alkaloid of twenty carbon atoms, but possessing the bicyclo[3.2.1]octane ring system found in all the norditerpenoid alkaloids.[11]

In this communication we report the isolation and determination of structure of a new norditerpenoid alkaloid, conambine (**1**), on the basis of its spectroscopic data (HRMS, IR, ^1H, ^{13}C, DEPT NMR) and chemical correlation with anthranoyllycoctonine (**3**).

In one of our previous papers[3] we reported isolation of 7.25 g of a mixture of alkaloids (fraction E-2) as described in the Scheme.[3] The mother liquor (E-2 ml) left after isolating ajacine and methyllycaconitine was subjected to column chromatography when fractions 48-101 gave alkaloids ajacine, ajadine, delsimine and ajacusine as described.[3] A portion of these fractions (48-101) was divided into fractions A, B, and C by preparatory TLC. Fraction A gave more of ajacine and its mother liquor showed a mixture of alkaloids. This mL on further investigation by preparative TLC and crystallization of the fractions gave an alkaloid (7.1 mg) which melted at 127-129° C. Examination of its NMR spectra (^1H and ^{13}C) indicated them to be different from those of all the alkaloids isolated from this plant as well as different from all known norditerpenoid alkaloids. On the basis of the following physical and spectroscopic data and chemical correlation the alkaloid was assigned structure **1**.

The molecular formula of the new alkaloid, $C_{37}H_{54}N_2O_9$ was established by FAB-HRMS which showed a $[M+H]^+$ at *m/z* 671.3907; calculated for $C_{37}H_{55}N_2O_9$, $[M+H]^+$, *m/z* 671.3907. ESIMS also gave a molecular ion peak at *m/z* 671.4 $[M+H]^+$; $[\alpha]_D$ +47.3° (c=0.32, $CHCl_3$); IR ν_{max} 3565, 3451, 3298, 1720, 1690, 1350, 1271, 1101 and 751 cm.$^{-1}$ A completely decoupled ^{13}C NMR spectrum showed 36 signals for the 37 carbon atoms of the molecule. A signal at δ 83.9 represented two carbons on the basis of its intensity. The DEPT spectra showed eight signals for quaternary carbons at δ 175.8, 168.1, 142.1, 114.5, 88.5, 77.2, 49.1, 37.5; thirteen signals for fourteen methines at δ 135.0, 130.3, 122.4, 120.6, 90.8, 83.9 (2 C), 82.4, 64.5, 50.2, 46.0, 45.0, 43.1, 38.0; eight signals for methylenes at δ 69.6, 52.3, 51.0, 33.6, 32.1, 28.6, 27.3, 26.1, and seven signals for methyl carbons at δ 58.0, 57.9, 56.3, 55.9, 17.3, 14.0, 11.8 (see Table 1). The ^{1}H NMR spectrum showed presence of four methoxyl groups at δ 3.26, 3.35, 3.38, and 3.41 (each 3H, s), an *N*-Et group at δ 1.07 (3H, t, *J* =7.3 Hz, Me of *N* Et), a methyl of an ethyl group at δ 0.97 (3H, t, *J* =7.1 Hz, Me of Et). The signal at δ 1.29 (3H, d, *J* =7.9 Hz) indicated the presence of a methyl group in –CH-Me system. The signals at δ 8.78 (1H, dd, *J* =8.5 and 1.5 Hz), 7.97 (1H, dd, *J* = 7.6 and 1.6 Hz), 7.58 (1H, t, *J* =7.4 Hz) and 7.12 (1H, t, *J* =7.2 Hz) suggest a disubstituted aromatic system in the molecule. A signal at δ 11.05 (1H, brs) suggests the presence of a -*N*H proton attached to the aromatic system as in ajacine, ajadine[12] and ajadinine.[7] These signals along with carbon-13 signals at δ 168.1 s, 114.5 s, 142.1 s, 120.6 d, 135.0 d, 122.4 d, and 130.3 d indicate the presence of an anthranoyl ester group in the molecule. A carbonyl carbon at δ 175.8 along with two methyls at δ 17.3, 11.8 and a methine at δ 46.0 suggests the presence of a 2-methylbutyryl group in the molecule as in glaucedine, glaucenine,[13] and elanine.[14] The ^{13}C NMR chemical shifts of the *(S)*-(+)-2-methylbutyryl group in all of these alkaloids [δ 176.9 (C=O), 41.2 d, 16.2 q (-CH-CH_3), 26.3 t (-CH_2)and 11.2 q (CH_3)] are identical, but in conambine (**1**) they are some what different (see Table), suggesting that the *(S)*- (+)-2-methylbutyryl group in **1** is in a different environment than in glaucedine, glaucenine and elanine. The presence of methoxyls, *N* -Et groups and biogenetic considerations suggest that conambine is a lycoctonine-type norditerpenoid alkaloid. Most of the ^{13}C NMR chemical shifts in **1** are identical with those reported for ajacine[7] (see Table).



1 R =COC—CH$_2$Me Conambine

2 R = Ac Ajacine

3 R = H Anthranoyllycoctonine

Acidic hydrolysis of **1** furnished anthranoyllycoctonine (**3**) having identical TLC, IR and ^1H NMR spectra with those of an authentic sample.

Table. ^{13}C NMR Chemical Shifts [a] and Assignments [b] for conambine (**1**) and its comparison with published shifts of ajacine (**2**).[7]

Carbon	1	2	Carbon	1	2
1	83.9 (CH)	83.7	20	51.0 (CH_2)	50.8
2	26.1 (CH_2)	25.8	21	14.0 (CH_3)	13.8
3	32.1 (CH_2)	31.8	1'	55.9 (CH_3)	55.6
4	37.5 (C)	37.3	6'	57.9 (CH_3)	57.9
5	50.2 (CH)	50.0	14'	58.0 (CH_3)	57.6
6	90.8 (CH)	90.7	16'	56.3 (CH_3)	56.1
7	88.5 (C)	88.2	Anth.C=O	168.1 (C)	176.8
8	77.2 (C)	77.3	1"	114.5 (C)	114.3
9	43.1 (CH)	43.0	2"	142.1 (C)	141.6
10	45.0 (CH)	45.8	3"	120.6 (CH)	120.3
11	49.1 (C)	48.1	4"	135.0 (CH)	134.7
12	28.6 (CH_2)	28.5	5"	122.4 (CH)	122.3
13	38.0 (CH)	37.8	6"	130.3 (CH)	130.1
14	83.9 (CH)	83.6	C=O	175.8 (C)	-
15	33.6 (CH_2)	33.4	1'''	46.0 (CH)	-
16	82.4 (CH)	82.3	2'''	17.3 (CH_3)	-
17	64.5 (CH)	64.3	3'''	27.3 (CH_2)	-
18	69.6 (CH_2)	69.5	4'''	11.8 (CH_3)	-
19	52.3 (CH_2)	52.2	*N*-H Ac C=O	-	168.9
			CH_3	-	25.3

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[a] Chemical shifts in ppm down field from TMS.

[b] Multiplicities were determined by DEPT experiments.

Occurrence of the *S*-(+)-2-methylbutyryl ester group in norditerpenoid alkaloids was first reported from our laboratory;[13] the first alkaloids glaucedine and glaucenine isolated from *Delphinium glaucescens* were characterized by their partial synthesis.[13] By analogy the stereochemistry of 2-methylbutyryl group in **1** is shown to be *S*-(+)-2-methylbutyryl ester. However, there are several examples of the occurrence of 2-methylbutyryl ester in other alkaloids like valtropine, isolated from *Duboiseia leichhardtii*.[15] A number of veratrum alkaloids containing esters of *S*-(+)-2-methylbutric acid have been reported.[16]

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REFERENCES AND NOTES

1. S. W. Pelletier and R. S. Sawhney, *Heterocycles*, 1978, **9**, 463.
2. S. W. Pelletier and R. S. Sawhney, *Heterocycles*, 1978, **9**, 1241.
3. S. W. Pelletier, R. S. Sawhney, H. K. Desai, and N. V. Mody, *J. Nat. Prod.,* 1980, **43**, 395.
4. P. K. Kulanthaivel, H. K. Desai, and S. W. Pelletier, *J. Nat. Prod.*, 1989, **52**, 143.
5. X. Liang, S. A. Ross, Y. R. Sohni, H. M. Sayed, H. K. Desai, B. S. Joshi, and S. W. Pelletier, *J. Nat. Prod.*, 1991, **54**, 1283.
6. S. W. Pelletier, S. Bhandaru, H. K. Desai, S. A. Ross, and H. M. Sayed, *J. Nat. Prod.,* 1992, **55**, 736..
7. H. K. Desai, B. T. Cartwright, and S. W. Pelletier, *J. Nat. Prod.*, 1994, **57**, 677.
8. J. Lu, H. K. Desai, S. A. Ross, H. M. Sayed, and S. W. Pelletier, *J. Nat. Prod.,* 1993, **56**, 2098.
9. V. Venkateshwarlu, S. K. Srivastava, B. S. Joshi, H. K. Desai, and S. W. Pelletier, *J. Nat. Prod.*, 1995, **58**, 1527..
10. National List of Scientific Plant Names, Volumes 1 and 2, U. S. Department of Agriculture, Soil Conservation Service, (SCS-TP-159), Jan. 1982.
11. B. S. Joshi, M. S. Puar, H. K. Desai, S. A. Ross, J. Lu and S. W. Pelletier, *Tetrahedron Lett.,* 1993, **34**, 441.
12. S. W. Pelletier, N. V. Mody, B. S. Joshi, and L. C. Schramm, ^{13}C and ^{1}H NMR Assignments and Physical Constants of C_{19} Diterpenoid Alkaloids, in *Alkaloids, Chemical and Biological Perspectives,* Vol. 2, ed. by S. W. Pelletier, Wiley, N. Y. 1983, pp. 206-462.
13. S. W. Pelletier, O. D. Dailey, Jr., and N. V. Mody, *J. Org. Chem.,* 1981, **46**, 3284.
14. S. W. Pelletier, S. A. Ross, and H. K. Desai, *Phytochemistry*, 1990, **29**, 2381
15. E. I. Rosenblum, *Aust. J. Appl. Sci.*, 1954, **5**, 51 *(Chem. Abstr.*, 1954, **48**, 6648h).
16. S. M. Kupchan, and A. Afonso, *J. Am. Pharm. Assoc., Sci. Ed.,* 1959, **48**, 731 and references cited there in.

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