NEW ALKALOIDS FROM *DELPHINIUM ANDERSONII* GRAY

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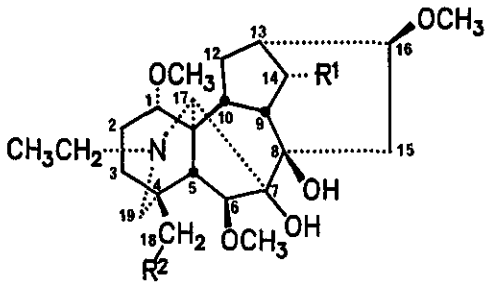
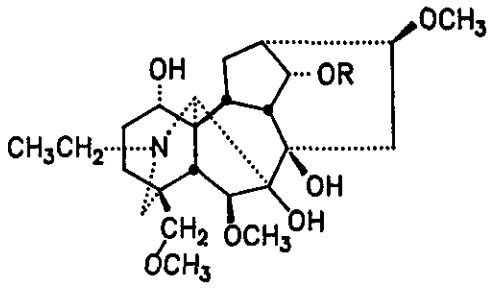
Abstract - Investigation of Delphinium andersonii Gray afforded, in addition to ten known diterpenoid alkaloids, two new alkaloids, andersonidine (10) and 14-acetylnudicaulidine (11). Structures were deduced on the basis of spectroscopic evidence.

Earlier[1], we reported the isolation of andersonine and 14-deacetylnudicauline (**4**) and six known diterpenoid alkaloids (delavaine, delectinine, lycoctonine, methyllycaconitine, nudicauline, and takaosamine) from the aerial parts of *Delphinium andersonii* Gray. In continuation of our work on the minor constituents of *D. andersonii* we report here the isolation of two new and ten known alkaloids. Of the ten known alkaloids six of them have not been reported previously from *D. andersonii.*

Extraction of the aerial parts of *D. andersonii* with 95% EtOH gave an extract.[1] A portion of this extract was treated with $CHCl_3$ and the $CHCl_3$-soluble portion was subjected to gradient pH fractionation[2] to yield 9.85 g of an alkaloid mixture. Vacuum liquid chromatography (vlc)[3] and centrifugally accelerated, radial, thin-layer chromatography[4,5] *in succession afforded* 14-acetylbrowniine (**1**)[6,7], 14-acetyldelcosine (**2**)[6,8], browniine (**3**)[9,10], 14-deacetylnudicauline (**4**)[1], delcosine (**5**)[6,8] deltaline (**6**)[11,12], dictyocarpine (**7**)[7], methyllycaconitine (**8**)[7], nudicauline (**9**)[13] and two new alkaloids, andersonidine (**10**) and 14-acetylnudicaulidine (**11**). The plant material left after extraction with 95% EtOH was further extracted with 75% EtOH. Investigation of this extract as indicated above gave *lycoctonine* (**12**)[8,14] as well as **5, 6, 10** and **11.** Of the known alkaloids, 14-acetylbrowniine, 14-acetyldelcosine, browniine, delcosine, deltaline, and dictyocarpine have not previously been reported from *D. andersonii.* The identity of known alkaloids was established spectroscopically and by direct comparison with authentic samples.

Andersonidine (**10**), mp 127-130°C cor. and $[\alpha]_D^{27}$ +39.1° (c 0.565, $CHCl_3$), has the molecular formula $C_{33}H_{46}N_2O_9$ (eims: M^+, 614). Its infrared spectrum (nujol) indicated the presence of hydroxyl (3500 and 3450 cm^{-1}), amine (3320 cm^{-1}) and ester (1740 and 1685 cm^{-1}) functionalities. The existence of an anthranoyl ester moiety was readily inferred by the presence of aromatic protons at δ 7.79 (dd, J = 8,1, 1.2 Hz), 7.29 (dt, J = 1.2, 8.1 Hz), 6.68 (tbr, J = 7.8 Hz) and 6.67 (dbr, J = 7.8 Hz) and amino protons at δ 5.77 (2H, br) in the ^1H nmr spectrum. The ^{13}C nmr data (Table 1) as well as the mass spectrum (base peak at m/z 120) supported this assignment. Further analysis of the ^1H nmr spectrum indicated the presence of a downfield proton (δ4.77, t, J = 4.8 Hz) and an AB



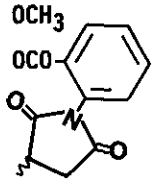


1 R^1 = $OCOCH_3$; R^2 = OCH_3

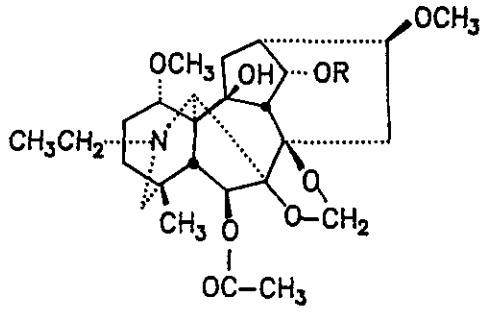
2 R = $COCH_3$

3 R^1 = OH; R^2 = OCH_3

4 R^1 = OH; R^2 = OCO-



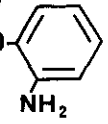
5 R = H



8 R^1 = OCH_3; R^2 = AS IN 4

9 R^1 = OH; R^2 = AS IN 4

10 R^1 = $OCOCH_3$; R^2 = OCO-



11 R^1 = $OCOCH_3$; R^2 = H

12 R^1 = OCH_3; R^2 = OH

13 R^1 = OH; R^2 = H

6 R = CH_3

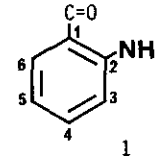
7 R = H

system of two protons (δ4.14 and 4.09, J = 11.5 Hz) with ester functions, three methoxyls (δ3.36, 3.32 and 3.25), an acetate (δ2.06) and an *N*-ethyl group (δ1.06, t, J = 7 Hz). The above data indicate that C-14 and C-18 bear the ester functions. *The assignment of the acetate at C-14 and* the anthranoyl ester at C-18 as shown in **10** was based on the chemical shift (δ4.77) of H-14 (H-14 resonates near δ5.00 in the presence of an aroyl ester[15]), and by the fact that all the naturally-occurring lycoctonine-type alkaloids known to date possess anthranoyl and its analogous ester groups only at C-18.[15] Confirmatory evidence for structure **10** was provided by the comparison of the ^{13}C nmr resonances of **1** with those of nudicauline (**9**)[13], an alkaloid which differs in the nature of the C-18 ester moiety.

The structure of 14-acetylnudicaulidine (**11**), amorphous, $[\alpha]_D^{26}$ +18.9° (c 0.54, $CHCl_3$), was deduced on the basis of the following spectral data. Ir (nujol): ν_{max} 3460 (OH) and 1740 (ester) cm^{-1}; *eims:* *m/z* 479 (M^+, $C_{26}H_4NO_7$), 464 (M-15) and 448 (M-31); ^1H nmr ($CDCl_3$): δ 4.73 (t, J = 4.5 Hz, H-14β), 3.38, 3.30 and 3.22 (each s, OMe), 2.04 (s, OAc), 1.02 (t, J = 7 Hz, N-CH_2-CH_3) and 0.95 (s, CH_3-18). The alkaloid is unstable in $CDCl_3$ when kept overnight; hence its nmr data were determined in CD_3CN. ^1H Nmr (CD_3CN): δ 4.65 (H-14), 3.37, 3.22 and 3.19 (OMe), 1.91 (OAc), 0.98 (N-CH_2-CH_3) and 0.96 (CH_3-18). The above shifts were similar to those of nudicaulidine

(13)[9], except for the acetate signal and paramagnetic shift of H-14 ($\Delta\delta$0.77). The differences in their ^{13}C nmr shifts (Table 1), especially in the vicinity of C-14, also supported this assignment.

Table 1. ^{13}C nmr Spectral Data of Andersonidine (**10**) and 14-Acetylnudicaulidine (**11**).

Carbon*	10 ($CDCl_3$)	11 (CD_3CN)	Carbon	10	11
1	83.9	85.3	N-CH_2	51.0	51.6
2	26.1	27.5	CH_3	14.0	14.4
3	32.2	37.9	1'	55.7	55.9
4	37.6	34.8	6'	58.0	58.6
5	42.6	55.7	16'	56.2	56.1
6	90.7	92.2	C=O	171.8	171.9
7	88.3	89.4	CH_3	21.5	21.6
8	77.4	78.0	C=O	167.7	
9	50.1	46.4			
10	45.7	43.4			
11	49.0	50.0			
12	28.2	29.1	1	110.3	
13	38.2	38.7	2	150.7	
14	75.9	77.0	3	116.8	
15	33.7	34.8	4	134.3	
16	82.3	83.6	5	116.4	
17	64.5	65.4	6	130.7	
18	68.5	27.1			
19	52.4	57.4			

*Multiplicities were determined by a DEPT sequence.

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REFERENCES

1. A. M. Panu, P. Kulanthaivel, S. W. Pelletier, and J. D. Olsen, *Heterocycles*, in press.
2. S. W. Pelletier, B. S. Joshi, and H. K. Desai, "Techniques for Isolation of Alkaloids", in *Advances in Medicinal Plant Research*, editors: A. J. Vlietinck and R. A. Dommisse, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 1985, pp. 153-157.
3. S. W. Pelletier, H. P. Chokshi, and H. K. Desai, *J. Nat. Prod.*, 1986, **49**, 892.
4. H. K. Desai, B. S. Joshi, A. M. Panu, and S. W. Pelletier, *J. Chromatogr.*, 1985, **322**, 223.

5. H. K. Desai, E. R. Trumbull, and S. W. Pelletier, *J. Chromatogr.*, 1986, **366**, 439.
6. S. W. Pelletier, R. S. Sawhney, H. K. Desai, and N. V. Mody, *J. Nat. Prod.*, 1980, **43**, 395.
7. S. W. Pelletier, O. D. Dailey, Jr., N. V. Mody, and J. D. Olsen, *J. Org. Chem.*, 1981, **46**, 3284.
8. S. W. Pelletier, N. V. Mody, R. S. Sawhney, and J. Bhattacharrya, *Heterocycles*, 1977, **7**, 327.
9. M. H. Benn, M.A.M. Cameron, and O. E. Edwards, *Can. J. Chem.*, 1963, **41**, 477.
10. S. W. Pelletier and K. I. Varughese, *J. Nat. Prod.*, 1984, **47**, 643.
11. J. F. Couch, *J. Amer. Chem. Soc.*, 1936, **58**, 684.
12. S. W. Pelletier, N. V. Mody, K. I. Varughese, J. A. Maddry, and H. K. Desai, *J. Amer. Chem. Soc.*, 1981, **103**, 6536.
13. P. Kulanthaivel and M. H. Benn, *Heterocycles*, 1985, **23**, 2155.
14. S. Sakai, N. Shima, S. Hasegawa, and T. Okamoto, *J. Pharm. Soc. Japan*, 1978, **98**, 1376.
15. S. W. Pelletier, N. V. Mody, B. S. Joshi, and L. C. Schramm, in *Alkaloids: Chemical and Biological Perspectives*, Ed., S. W. Pelletier, Vol. 2, Chapter 5, pp. 205-462, John Wiley, New York, 1984.

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