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THE STRUCTURES OF ANHWEIDELPHININE, BULLEYANITINES A–C, PUBERACONITINE, AND PUBERACONITIDINE

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ABSTRACT.—The structures of the six norditerpenoid alkaloids listed in the title have been reported to contain a β-methoxyl group at C-1. However, the ^{13}C-nmr spectral evidence for all these alkaloids and chemical correlation studies of puberaconitine and puberaconitidine clearly indicate a C-1 α-methoxyl group. In contrast to mass spectral evidence, ^{13}C-nmr shift data can be reliably used as a diagnostic tool for the assignment of configuration of the oxygen function at C-1 in this family of alkaloids.

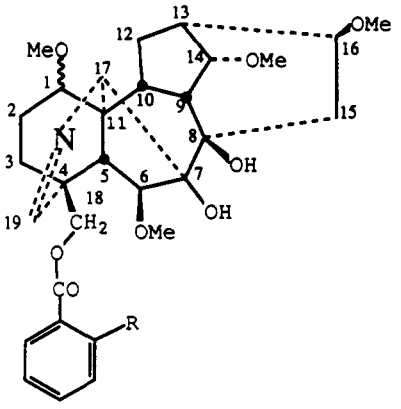
Recent publications assigning incorrect structures to anhweidelphinine [**1**] (1–4), bulleyanitine A [**2**], bulleyanitine B [**3**], and bulleyanitine C [**4**] (5,6) prompt us to correct the structures assigned to these norditerpenoid alkaloids.

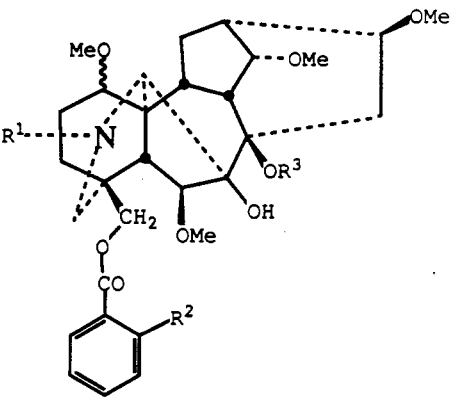
To date, more than 300 norditerpenoid alkaloids have been isolated from various *Aconitum, Consolida,* and *Delphinium* species, and their structures have been determined. With few exceptions, most of these alkaloids contain an oxygen function at the C-1 position, which exists as an OH or OMe group or forms an either linkage with C-19. Only two naturally occurring alkaloids, namely delphirine (1-*epi*-neoline) (7,8) and talatizidine (9,10), have been shown to possess a β-hydroxyl group at C-1.

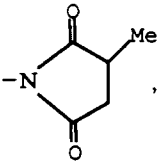
Prior to 1981, a number of lycoctonine-type alkaloids were mistakenly assigned a β-methoxyl group at C-1, partly due to an error in the X-ray structure determination of a lycoctonine derivative, which was subsequently corrected (11). At the same time, on the basis of chemical correlation studies, the structures of 37 lycoctonine-type alkaloids were revised and all were shown to have a C-1 α-methoxyl group (12). Early mass-spectral studies on some lycoctonine-type alkaloids with an assumed C-1 β-methoxyl group attempted to generalize the fragmentation pattern of C-1α and C-1β methoxylated alkaloids (13,14). Because the configuration of the methoxyl group at C-1 in all these alkaloids has been since revised to α, the earlier mass-spectral evidence for assigning the configuration of newly isolated alkaloids will naturally lead to erroneous conclusions.

The Chinese workers invoke the mass spectral fragmentation evidence (1–6) for assigning the C-1 β-methoxyl group to their alkaloids **1–4**. Similarly in 1983, in a study of the alkaloids of *Aconitum barbatum*, Yu and Das (15) assigned a C-1 β-methoxyl configuration for puberaconitine [**5**] and puberaconitidine [**6**] on the basis of mass-spectral fragmentation pattern. These authors methylated puberaconitine and puberaconidine to give the corresponding methyl esters, septentriodine and septentrionine, respectively. Because the structures of the latter two alkaloids have been revised to C-1 α-methoxyl compounds (12), the alkaloids puberaconitine and puberaconidine must also bear C-1 α-methoxyl groups. The structures of puberaconitine and puberaconitidine therefore need to be corrected to **7** and **8**, respectively. This conclusion is also supported by the ^{13}C-nmr spectrum of puberaconitine, which shows a signal for C-1 at 83.8 ppm (vide infra).

Most norditerpenoid alkaloids that bear an α-methoxyl group at C-1 show in the ^{13}C-nmr spectrum a chemical shift range of 83.0–85.5 ppm (16). A hydroxyl substitution at C-3, C-5, or C-10 is expected to exhibit an upfield shift of about 2–6 ppm (γ effect) on carbon C-1. Thus, in all the aconitine-type al-



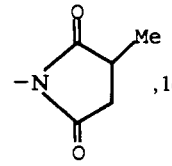


1 R=  , 1β-OMe

2 R=$NHCOCH_2CH(Me)CONH_2$, 1β-OMe

3 $R^1=R^3=H$, $R^2=NHCOCH(Me)CH_2CONH_2$, 1β-OMe

4 $R^1=R^3=H$, $R^2=NHCOCH_2CH(Me)CONH_2$, 1β-OMe

11 R=  ,1α-OMe

5 $R^1=Et$, $R^2=NHCO(CH_2)_2CO_2H$, $R^3=H$, 1β-OMe

6 $R^1=Et$, $R^2=NHCO(CH_2)CO_2H$, $R^3=Me$, 1β-OMe

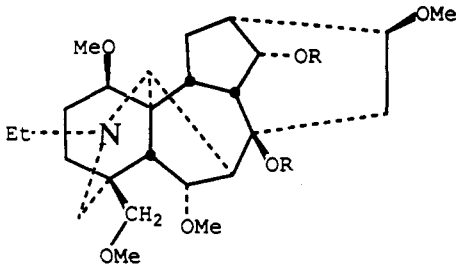
12 R=$NHCOCH_2CH(Me)CONH_2$, 1α-OMe

7 $R^1=Et$, $R^2=NHCO(CH_2)_2CO_2H$, $R^3=H$, 1α-OMe

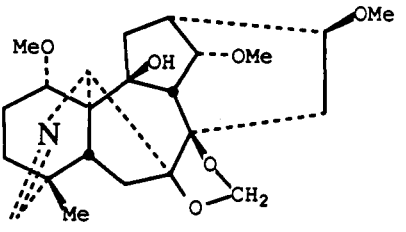
8 $R^1=Et$, $R^2=NHCO(CH_2)_2CO_2H$, $R^3=Me$, 1α-OMe

13 $R^1=R^3=H$, $R^2=NHCOCH(Me)CH_2CONH_2$, 1α-OMe

14 $R^1=R^3=H$, $R^2=NHCOCH_2CH(Me)CONH_2$, 1α-OMe



9 R=Ac
10 R=H



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kaloids bearing a hydroxyl group at C-3 (equatorial hydroxyl), C-1 bearing an α-methoxyl group appears in the range 82.5–83.5 ppm. In the few examples (bonvalol, bonvalatine) of alkaloids bearing an axial hydroxyl group at C-5, C-1 appears around 76.5 ppm (17). Most of the diterpenoid alkaloids bear-

ing a hydroxyl group at C-10 (axial) also show a γ effect, and C-1 appears in the range 77.0–80.0 ppm. Because there is only one naturally occurring norditerpenoid alkaloid having a C-1 β-methoxyl group [puberanine (15)], we had synthesized 1-*epi*-1-*O*-methyldelphisine [**9**] and 1-*epi*-1-*O*-methylneoline [**10**] (18). Both these compounds show a chemical shift for C-1 and ca. 78.5 ppm. Chasmanine, the C-1 epimer of **10** bearing a C-1 α-methoxyl group, exhibits a signal at 86.1 ppm indicating a downfield shift of about 7.5 ppm. On the other hand, alkaloids having an α-OH group at C-1 show a signal at about 69.5–72.5 ppm, and those with a β-OH group appear upfield around 68–69 ppm. The ^{13}C-nmr signals for C-1 in anhweidelphinine (84.5 ppm), bulleyanitine A (84.2 ppm), bulleyanitine B (83.7 ppm), and bulleyanitine C (83.7 ppm) clearly indicate that the C-1 methoxyl group in these alkaloids has an α configuration; therefore, these alkaloids should be assigned structures **11**, **12**, **13**, and **14**, respectively. Anhweidelphinine has also been isolated recently from *Delphinium nuttulianum* Pritz (19). Barbeline [**15**], an alkaloid having an azomethine function as in anhweidelphinine [**11**] and bulleyanitine A [**12**], shows the chemical shift for C-1 at 80.4 ppm (20). The upfield shift of ca. 4.0 ppm results from an OH group at C-10. The structure of barbeline [**15**] has been established by an X-ray structure determination. Apparently, the only naturally occurring norditerpenoid alkaloid having a β-methoxyl group at C-1 appears to be puberanine (1-*epi*-ranaconitine) which shows the chemical shift for C-1 at 81.4 ppm (15). ^{13}C-nmr shift data thus appear to be a reliable diagnostic method for assigning the configuration of the C-1 oxygen function in norditerpenoid alkaloids.

LITERATURE CITED

1. J.S. Jin and M.C. Zhong, in "Abstracts." International Symposium on Organic Chemistry of Medicinal Natural Products, IUPAC, Shanghai, China, Nov. 10–14, 1985, B-145.
2. J.S. Jin and M.C. Zhong, *Zhongchaoyao*, **17**, 1 (1986).
3. S.Y. Chen and Z.H. Jiang, *Acta Bot. Yunnanica*, **10**, 63 (1988).
4. J.S. Jin, *Zhongchaoyao*, **17**, 49 (1986).
5. S.Y. Chen, Z.H. Jiang, H. Wei, H.L. Liang, and J. Zhou, in "Abstracts." International Symposium on Plant Resources, Kunming, China, 1988, p. 49.
6. X. Wei, S.Y. Chen, B. Wei, and J. Zhou, *Acta Bot. Yunnanica*, **11**, 453 (1989).
7. S.W. Pelletier and J. Bhattacharyya, *Tetrahedron Lett.*, 4679 (1976).
8. S.W. Pelletier and Z. Djarmati, *J. Am. Chem. Soc.*, **98**, 2626 (1976).
9. S.W. Pelletier, L.H. Keith, and P.C. Parthasarathy, *J. Am. Chem. Soc.*, 4146 (1967).
10. V. Boido, O.E. Edwards, K.L. Handa, R.J. Kolt, and K.K. Purushothaman, *Can. J. Chem.*, **62**, 778 (1984).
11. M. Cygler, M. Przybylska, and O.E. Edwards, *Acta Crystallogr., Sect. B*, **38**(5), 1500 (1982).
12. S.W. Pelletier, N.V. Mody, K.I. Varughese, J.A. Maddry, and H.K. Desai, *J. Am. Chem. Soc.*, **103**, 6536 (1981).
13. M.S. Yunusov, Y.V. Rashkes, and S.Y. Yunusov, *Khim. Prir. Soedin.*, 85 (1972).
14. M.S. Yunusov, Y.V. Rashkes, V.A. Telnov, and S.Y. Yunusov, *Khim. Prir. Soedin.*, 515 (1969).
15. D. Yu and B.C. Das, *Planta Med.*, **49**, 85 (1983).
16. S.W. Pelletier, N.V. Mody, B.S. Joshi, and L.C. Schramm, in "Alkaloids: Chemical and Biological Perspectives." Ed. by S.W. Pelletier, John Wiley, New York, 1984, Vol. 2, pp. 205–462.
17. Q.P. Jiang and W.L. Sung, *Heterocycles*, **22**, 2429 (1984).
18. S.W. Pelletier and J.T. Etse, *J. Nat. Prod.*, **52**, 145 (1989).
19. Y. Bai, M. Benn, and W. Majak, *Heterocycles*, **29**, 1017 (1989).
20. B.S. Joshi, E.A. El-Kashoury, H.K. Desai, E.M. Holt, J.D. Olsen, and S.W. Pelletier, *Tetrahedron Lett.*, **29**, 2397 (1988).

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