Chemistry of Natural Compounds, Vol. 40, No. 6, 2004

ALKALOIDS OF *Delphinium corymbosum*

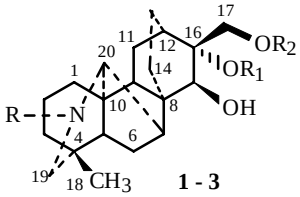
B. T. Salimov

UDC 547.944/945

The structure of the C_{20}-diterpenoid alkaloid cordizine, which was isolated previously from Delphinium corymbosum, *was discussed in detail. A scheme for the possible biosynthetic pathway of the lycoctonine precursor of C_{19}-norditerpenoid bases was proposed based on the simultaneous occurrence in the plant of denudatine and lycoctonine.*

Key words: *Delphinium corymbosum*, diterpenoid alkaloids cordizine, N-ethyl-de-N-methyldictysine, corumdizine, corumdizinine, possible biosynthetic pathway.

Isolation from the aerial part of *Delphinium corymbosum* Rgl. of the diterpenoid alkaloids N-ethyl-de-N-methyldictysine (**1**), corumdizine (**2**), corumdizinine (**3**), cordizine (**4**), and delcorinine (**5**) has been reported [1]. The spectra of the acetonides of dictysine (**6**) and N-ethyl-de-N-methyldictysine (**7**) show that **1** differs from dictysine (**8**) by the presence of an N-ethyl instead of an N-methyl [2, 3].



1 - 3

1: R = C_2H_5, $R_1 = R_2 = H$
2: R = C_2H_5, $R_1 + R_2 = CH_2$
3: R = CH_3, $R_1 + R_2 = CH_2$

The similarity observed in the PMR and mass spectra of **2** and **7** [3, 4] led to the conclusion that **2**, in contrast with **1**, contains a C(16),C(17)-methylenedioxy group instead of C(16),C(17)-dihydroxyls.

Spectra of **3** [4] showed that it differs from **2** by the presence of an N-methyl instead of an N-ethyl and has structure **3**.

The structure of the new C_{19}-norditerpenoid alkaloid **5** was discussed previously [5]. In this article, we describe in more detail the structure of the new C_{20}-diterpenoid alkaloid **4**.

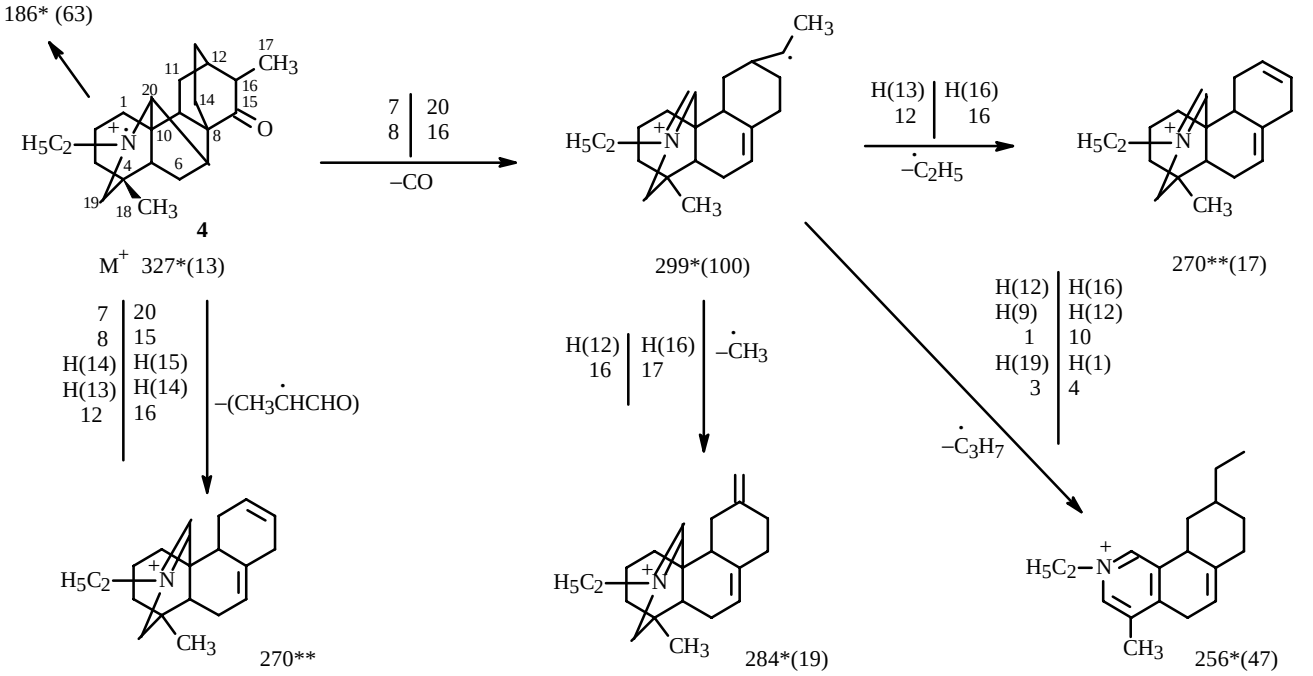
The composition of **4** is $C_{22}H_{33}NO$, found 327.2561 (HRMS), calc. 327.2562. According to the PMR spectrum [4], **4** contains an N-ethyl and secondary and tertiary methyls. The IR spectrum of **4** [4] has a strong absorption band at 1719 cm^{-1} that is consistent with a carbonyl in a six-membered ring.

The composition and spectral properties of **4** are similar to those of **8** [3, 6] so that **4** can be assigned as a denudatine-type C_{20}-diterpenoid with the expanded formula $C_{18}H_{22}(N\text{-}C_2H_5)(CH_3)_2O$.

The elecron-impact mass spectrum of **4** contains peaks for ions with *m*/*z* 299, 284, 270, 256, and 186. The ion with *m*/*z* 299, of composition $C_{21}H_{33}N$ (HRMS), forms by loss of a carbonyl from the molecular ion. According to HRMS, the composition of the ion with *m*/*z* 270 is $C_{19}H_{18}N$; with *m*/*z* 186, $C_{13}H_{16}N$. Based on the shift to higher masses by 14 amu for the peaks of these ions relative to those of ions with *m*/*z* 256 and 172 that appear in the mass spectra of **8** [6], dehydrodictysine (**9**), and its diacetyl derivative **10** [2, 4] and on the presence in **4** of an N-ethyl instead of N-methyl, the conclusion can be drawn that **4** is based on the denudatine skeleton with a C-15 carbonyl and a C-16 secondary methyl.

S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (99871) 120 64 75, e-mail: root@icps.org.uz. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 476-478, November-December, 2004. Original article submitted June 7, 2004.

0009-3130/04/4006-0579



Scheme 1. Mass spectral fragmentation of **4** (fragment relative intensity in % is given in bracket; *, element compositions of the fragments were determined by HRMS; **, combined peaks.

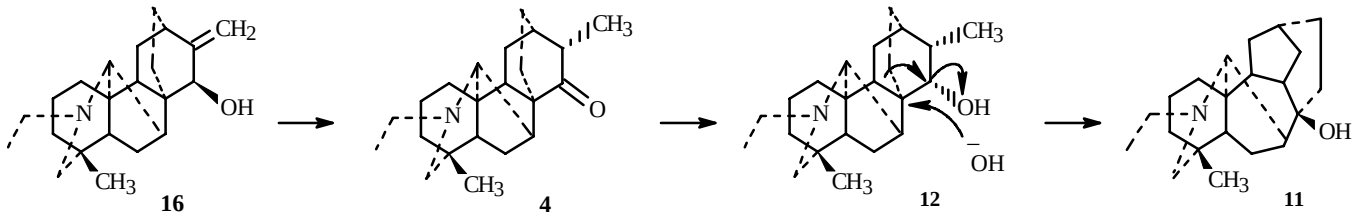
Scheme 1 shows the mass spectral fragmentation of **4**, which agrees with the above results.

A two-dimensional (2D) J-experiment and 2D heterocorrleation and homocorrelation NMR studies confirmed that **4** has the denudatine skeleton and established the α-configuration for the C(16)-CH_3 [7].

As noted earlier [5, 11], *D. corymbosum* contains **8** and ten lycoctonine-type diterpenoid alkaloids that, being tertiary bases, include the N-ethyl group. Starting with concepts of the biosynthesis of diterpenoid alkaloids [8-10], the simultaneous occurrence in *D. corymbosum* of **1**, **2**, **3**, and lycoctonine-type C_{19}-norditerpenoid bases provide a basis to propose that lycoctonine compounds form from **4** through the successive reactions: reduction of **4** and conversion of the reduction product into **11** (Scheme 2).

Considering that C-15 in atisine (**13**), atidine (**14**), and ajaconine (**15**) has a β-hydroxyl instead of an α-hydroxyl, which ensures that the C(8)–C(9) and C(15)–OH bonds are coplanar [coplanar C(13)–C(14) and C(8)–OH bonds according to the reference], it was proposed [9] that the atisine structure changes slightly during the transition atisine → lycoctonine. Therefore, it is interesting that **4** is apparently formed from denudatine precursor **16** (Scheme 2).

The possible biosynthetic pathway of the lycoctonine precursor of C_{19}-norditerpenoid bases, although it allows initial formation of a C(7)–C(17) bond [12], nevertheless includes removal of the exomethyl from the atisine compound, as noted previously [8].



Scheme 2. Possible biosynthetic pathway of the lycoctonine precursor of C_{19}-norditerpenoid alkaloids.

EXPERIMENTAL

The purity of the compounds was verified by TLC on KSK silica gel using $CHCl_3$:CH_3OH (9:1 and 20:1) and on Al_2O_3 (chromatography-grade) using $CHCl_3$, $CHCl_3$:CH_3OH (50:1), and ether:hexane (3:1). IR spectra were recorded on a UR-20 instrument in KBr disks; PMR spectra, on a JNM-4H-100/100 MHz spectrometer in $CDCl_3$ with HMDS internal standard; general and high-resolution mass spectra, in an MX-1310 instrument equipped with a direct probe into the ion source.

Isolation of 4. The remainder (1.32 g) of a stock solution of 6-deoxydelcorine perchlorate (1.49 g) [11] was chromatographed over a column of deactivated Al_2O_3 (1:70) [eluents hexane:ether 10:1 (fractions 1-21), 5:1 (22-60), 1:1 (61-68), 1:3 (69-80); fraction volume 10 mL]. Fractions 4-6 afforded **4** (0.037 g), mp 122-124°C (CH_3OH); fractions 69-77, 6-deoxydelcorine perchlorate (0.31 g) after acidification from $HClO_4$ (10%) in ethanol.

Isolation of N-Ethyl-de-N-methyldictysine (7), Corumdizine (2), and Corumdizinine (3) Acetonides. The remainder (5.3 g) of the stock solution after separation from fraction 4 of delcorine (1.1 g) and delphatine perchlorate (1.0 g) [11] was chromatographed over a column of Al_2O_3 (1:40) [eluent hexane:ether 10:1 (fractions 1-32) and 5:1 (33-45), fraction volume 100 mL]. Fractions 33-34 were rechromatographed over a column of deactivated Al_2O_3 to afford **2** (0.042 g). Fractions 37-42 were worked up with hexane to afford **3** (0.035 g), mp 104-105°C.

Fractions 5-8 (3.2 g) from chromatography of the remaining 5.3 g [11] were rechromatographed over a column of Al_2O_3 (1:70) [eluent hexane:ether 5:1 (fractions 1-10), fraction volume 100 mL]. Fractions 3-4 were worked up with acetone to isolate **7** acetonide (0.068 g), mp 87-89°C (acetone).

N-Ethyl-de-N-methyldictysine (1). A mixture of **7** (0.06 g) and H_2SO_4 (5.0 mL, 20%) was left at room temperature for 24 h, washed with ether, made basic with Na_2CO_3, and shaken with $CHCl_3$. The extract was dried and evaporated to afford **1** (0.052 g).

PMR spectrum (δ, J/Hz): 0.64 (3H, s, 4-CH_3), 0.95 (3H, t, J = 7.0, NCH_2CH_3), 3.25 (1H, br.s, H-20), 3.41, 4.09 (1H each, 2d, J = 12.0, H_2-16), 3.90 (1H, s, H-15α).

REFERENCES

1. B. T. Salimov, in: Proceedings of Second International Symposium on the Chemistry of Natural Compounds (SCNC), Eskisehir (1996), 56.
2. B. T. Salimov, B. Tashkhodzhaev, and M. S. Yunusov, *Khim. Prir. Soedin.*, 86 (1982).
3. R. Shakirov, M. V. Telezhenetskaya, I. A. Bessonova, S. F. Aripova, I. A. Israilov, M. N. Sultankhodzhaev, V. I. Vinogradova, V. I. Akhmedzhanova, T. S. Tulyaganov, B. T. Salimov, and V. A. Tel′nov, *Khim. Prir. Soedin.*, 957 (1996).
4. R. Shakirov, M. V. Telezhenetskaya, I. A. Bessonova, S. F. Aripova, I. A. Israilov, M. N. Sultankhodzhaev, V. I. Vinogradova, V. I. Akhmedzhanova, T. S. Tulyaganov, B. T. Salimov, and V. A. Tel′nov, *Khim. Prir. Soedin.*, 410 (1996).
5. B. T. Salimov, *Khim. Prir. Soedin.*, 231 (2001).
6. B. T. Salimov, M. S. Yunusov, Ya. V. Rashkes, and S. Yu. Yunuusov, *Khim. Prir. Soedin.*, 812 (1979).
7. Kh. M. Bobokulov, B. Salimov, M. G. Levkovich, and N. D. Abdullaev, in: *Nitrogen-Containing Heterocycles and Alkaloids*, V. G. Kartsev and G. A. Tolstikov, eds., Iridium Press, Moscow (2001), Vol. 2, p. 45.
8. Z. Valenta and K. Wiesner, *Chem. Ind.*, 354 (1956).
9. W. B. Whalley, *Tetrahedron*, **18**, 43 (1962).
10. M. N. Sultankhodzhaev and A. A. Nishanov, *Khim. Prir. Soedin.*, 337 (1995).
11. B. T. Salimov, M. S. Yunusov, N. D. Abdullaev, and Z. M. Vaisov, *Khim. Prir. Soedin.*, 95 (1985).
12. A. A. Nishanov, B. Tashkhodzhaev, M. N. Sultankhodzhaev, B. T. Ibragimov, and M. S. Yunusov, *Khim. Prir. Soedin.*, 39 (1989).