Chemistry of Natural Compounds, Vol. 45, No. 6, 2009

OXIDATION OF ACONITINE BY POTASSIUM PERMANGANATE. A NEW *N*-DE-ETHYL-7,17-SECOIMINO DERIVATIVE

M. N. Sultankhodzhaev

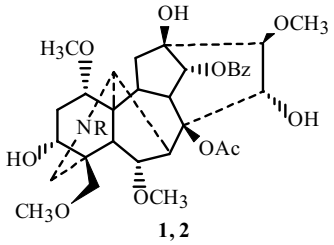
UDC 547.944/945

The alkaloid aconitine was oxidized by potassium permanganate in aqueous acetone. It was shown that the oxidation formed three products including the previously described N-*de-ethylaconitine,* N-*de-ethyl-19-oxoaconitine, and a new* N-*de-ethyl-7,17-secoimino derivative. The structure of the new product was proposed based on spectral data (IR, mass, PMR and* ^{13}*C NMR spectra).*

Key words: diterpenoid alkaloid, aconitine, $KMnO_4$ oxidation, new *N*-de-ethyl-7,17-secoimino derivative.

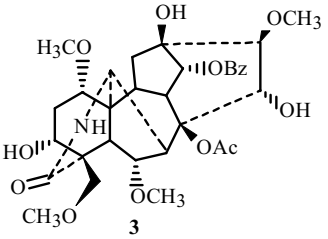
Oxidation of diterpenoid alkaloids by $KMnO_4$ is one method for removing an alkyl substituent from the N atom [1]. The course of the reaction depends on the stereochemistry of the C-6 methoxy group, which sterically shields the more reactive C-19 ring methylene in the case of its α-orientation, as occurs in aconitine (**1**), so that the permanganate ion attacks primarily the *N*-ethyl group. It has been reported that oxidation of **1** by $KMnO_4$ in acetone:water (50%) for 20 min produced *N*-de-ethyl-19-aconitine (**2**, 30%), *N*-de-ethyloxoaconitine (**3**, 31%), and starting material (**1**, 27%) [1].

In order to prepare **2**, we oxidized aconitine under analogous conditions and produced the desired product (28%), *N*-de-ethyl-19-oxoaconitine (**3**, 32%), and a new crystalline *N*-de-ethyl-7,17-secoimino derivative (**4**, 30%). The product had formula $C_{30}H_{39}NO_9$ (HRMS). The IR spectrum contained absorption bands for hydroxyls (3376 cm^{-1}), ester carbonyl (1728), and ether (1107). Table 1 lists the PMR and ^{13}C NMR data. Resonances were assigned by comparison with spectra of secojesaconitine [2] and other related alkaloids [3, 4]. According to the PMR spectrum, the product contained four methoxyls and C-14 benzoyl aromatic protons. However, resonances for *N*-ethyl and acetoxy were missing from the spectrum. The PMR spectrum of **4** showed resonances for two olefinic protons. The resonance of the C-7 olefinic proton was observed at 5.62 ppm as a broad doublet of doublets (J_1 = 2.7 Hz, J_2 = 3.9 Hz) and the C-17 proton at 7.83 ppm as a doublet (J = 1.7 Hz). Resonances of olefinic C atoms at 137.8 (C-7), 137.7 (C-8), and 165.1 (C-17) in the ^{13}C NMR spectrum confirmed that there were C-7–C-8 and N–C-17 double bonds. The lack of acetoxyl and *N*-ethyl groups in the oxidation product indicated that the C-7–C-17 bond had cleaved with loss of acetyl and *N*-ethyl groups and formation of C-7–C-8 and N–C-17 double bonds.

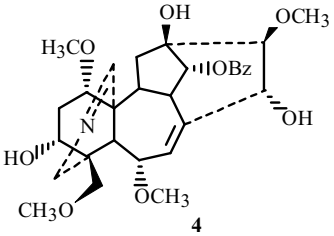


1, 2

1: R = C_2H_5; **2:** R = H



3



4

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: niruno@mail.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 708–709, November–December, 2009. Original article submitted April 20, 2009.

 0009-3130/09/4506-0844

TABLE 1. PMR (400 MHz, $CDCl_3$, ppm) and ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) Spectra of *N*-De-ethyl-7,17-secoimino Derivative **4**

C atom	δ_C	δ_H	C atom	δ_C	δ_H
1	79.5	1.10 (dd, J = 10.0, 5.00)	16	79.2	3.33 (d, J = 5.2)
2	33.0		17	92.1	7.83 (d, J = 1.7)
3	71.0	3.82 (dd, J = 10.0, 5.00)	18	76.5	3.71, 3.74 (d, J = 9.01)
4	47.9		19	51.5	2.13, 3.29 (d, J = 11.2)
5	43.6		1-OCH_3	56.8	3.20
6	87.0	4.48 (dtd, J = 2.2, 2.3, 2.2)	6-OCH_3	57.9	3.22
7	137.8	5.62 (br.dd, J = 2.7, 3.9)	16-OCH_3	61.6	3.76
8	137.7		18-OCH_3	59.0	3.31
9	42.7		Ar-CO	166.3	
10	41.5		Ar-C-1′	133.2	
11	51.5		Ar-C-2′	131.0	8.03 (d, J = 8.1)
12	38.6		Ar-C-3′	129.9	7.43 (t, J = 7.7)
13	73.9		Ar-C-4′	128.5	7.56 (t, J = 7.4)
14	79.5	5.09 (d, J = 4.2)	Ar-C-5′	129.9	7.43 (t, J = 7.7)
15	79.2	4.82 (dd, J = 2.6, 2.7)	Ar-C-6′	131.0	8.03 (d, J = 8.1)

EXPERIMENTAL

IR spectra in KBr disks were recorded on a Vector 22 spectrometer; mass spectra, in a JMS 600 H instrument using electron impact. PMR and ^{13}C NMR spectra in $CDCl_3$ were taken from a Bruker instrument at operating frequencies 400 and 100.6 MHz, respectively, with TMS internal standard. TLC used KSK silica gel and solvent systems $CHCl_3$:CH_3OH (10:1, 50:1, 100:1) and C_6H_6:CH_3OH (4:1).

Oxidation of Aconitine (1) by $KMnO_4$. A solution of aconitine (1 g) in purified acetone (100 mL) was treated at room temperature with $KMnO_4$ (1 g) dissolved in acetone:water (200 mL, 50%) and shaken for 20 min. The excess of $KMnO_4$ was decomposed by sodium sulfite. The resulting precipitate of MnO_2 was filtered off. Acetone was distilled from the mother liquor. The cooled aqueous solution was acidified with H_2SO_4 (2%) until the solution was acidic. The acidic solution was washed with benzene (4×). Solvent was distilled to afford crystalline *N*-de-ethyl-19-oxoaconitine (**3**, 0.32 g), mp 265–267°C (acetone). Then the acidic solution was made basic with Na_2CO_3 and extracted with $CHCl_3$. The extract was dried over Na_2SO_4. Solvent was removed. The solid was chromatographed over a column of deactivated Al_2O_3 with elution by benzene with gradual addition of MeOH. The benzene and benzene:MeOH (50:1) effluents afforded with the use of acetone crystalline *N*-de-ethyl 7,17-secoimino derivative **4** (0.3 g). Elution by benzene:MeOH (25:1, 10:1, 1:1) afforded amorphous **2** (0.28 g).

***N*-De-ethyl-7,17-secoaconitine (4).** $C_{30}H_{39}NO_9$ (HRMS 557.26859, calcd 557.27503), mp 232–234°C (acetone).

IR spectrum (ν_{max}, cm^{-1}): 3376, 2932, 2885, 2832, 1728, 1637, 1600, 1493, 1465, 1451, 1415, 1379, 1352, 1318, 1285, 1264, 1225, 1198, 1183, 1107, 1080, 1076, 1048, 987, 964, 933, 915, 873, 715, 669, 642, 612, 595.

Mass spectrum (*m*/*z*, %): 557 (1.8) $[M]^+$, 542 (3.1), 526 (20.3), 104 (100), 59 (5.0).

Table 1 lists the PMR and ^{13}C NMR spectra.

ACKNOWLEDGMENT

The work was supported financially by the Academy of Sciences of the Republic of Uzbekistan (Grant FA-F3-T.147).

REFERENCES

1. O. Achmatowicz, Jr., Y. Tsuda, and L. Marion, *Can. J. Chem.*, **43**, 2336 (1965).
2. H. Bando, K. Wada, T. Amija, Y. Fujimoto, and K. Kobayashi, *Chem. Pharm. Bull.*, **36**, 1604 (1988).
3. T. Zhapova, L. D. Modonova, and A. A. Semenov, *Chem. Nat. Comp.*, **21**, 717 (1985).
4. G.-Y. Hang, P. Cai, J.-Z. Wang, and K. Snyder, *J. Nat. Prod.*, **51**, 364 (1988).