Study of alkaloids from plants of Siberia and Altai
4.* *N*-Deethylation of diterpene alkaloids of the aconitane type

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A method for *N*-deethylation of diterpene alkaloids of the aconitane type by the Cope reaction was developed using conversions of lappaconitine and elatine as examples. The previously unknown nitrones of *N*-deethylated lappaconitine, elatine, and elatidine were prepared.

Key words: diterpene alkaloids, *N*-deethylation, lappaconitine, elatine, nitrones, *Aconitum septentrionale* K., *Delphinium elatum* L.

Diterpene alkaloids of the aconitane series are very promising natural compounds due to their biological activity and the possibility of their isolation from widespread plants of Siberia and Altai.[1—5] One of the lines of investigation of these alkaloids deals with transformations of their molecules with the aim of preparing new structural types of active agents. In the present work, we report the previously unknown conversions of alkaloids of the aconitane type directed to changing the structure of one of the key centers, *viz.*, of the heterocyclic fragment of the molecules. We chose lappaconitine (**1**) and elatine (**2**), which were isolated from roots of northern wolfsbane *Aconitum septentrionale* K. and candle larkspur *Delphinium elatum* L., respectively, as objects of studies.

Previously,[6] we have studied thermal decomposition of *N*-oxides of compounds **1** and **2** according to the Cope reaction** (Scheme 1). The previously unknown elatine *N*-oxide (**6**) was prepared as a solvate with $CHCl_3$ by oxidation of elatine **2** with perbenzoic acid. The structure of compound **6** was confirmed by the NMR spectral data. As expected,[8] the ^{13}C signals for the atoms directly bound to the nitrogen atom (C(17), C(19), and $\underline{C}H_2CH_3$) are shifted downfield by 15—20 ppm, whereas the signal for the carbon atom of the methyl group of the N—Et fragment is shifted upfield by 5.3 ppm compared to the corresponding signals in the ^{13}C NMR spectrum of elatine.[9] Note also the downfield shift of the ^1H signal of the methyl group of the NEt fragment ($\Delta\delta \approx 0.25$) compared to that in the ^1H NMR spectrum of elatine **2**.

Thermolysis of *N*-oxides **3** and **6** *in vacuo* afforded hydroxylamine derivatives, *viz.*, *N*-deethyl-*N*-hydroxylappaconitine (**4**) and *N*-deethyl-*N*-hydroxyelatine (**7**), respectively. Treatment of hydroxylamine **7** with acetic anhydride gave the individual *N*-deethyl-*N*-acetoxyelatine (**8**) in quantitative yield. In the ^{13}C NMR spectra of compounds **4** and **7**, as in the spectra of *N*-oxides **3** and **6**, the signals for the carbon atoms directly bound to the nitrogen atom are shifted downfield by 4—6 ppm compared to the corresponding signals of lappaconitine **1** and elatine **2**, respectively.

Under the action of $K_3Fe(CN)_6/NaHCO_3$,[10] compounds **4** and **7** formed nitrones of *N*-deethyllappaconitine (**5**) and *N*-deethylelatine (**9**). Nitrone **5** was also prepared[7] by oxidation of hydroxylamine **4** with MnO_2. The ^1H NMR spectra of nitrones **5** and **9** have signals for the H(19) protons at δ 7.23 and 6.88, respectively. The ^{13}C NMR spectra of these compounds have doublet signals for the sp^2-hybridized carbon atoms at δ 133.2 and 134.8. The above-mentioned chemical shifts agree with the data for compounds containing structurally similar fragments of nitrones (see Refs. 11 and 12).

It should be noted that the preparation of nitrone of *N*-deethylelatidine (**11**) from elatidine (**12**) through formation of *N*-oxide is complicated by the formation of a number of by-products. We synthesized this nitrone according to an alternative procedure. Hydrolysis of compound **7** with an alcoholic solution of NaOH afforded a mixture of *N*-deethyl-*N*-hydroxyelatidine (**10**) and the structurally related nitrone **11** (the **10** : **11** ratio was ≈ 3 : 1). Apparently, the latter was formed due to autooxidation of hydroxylamine **10** in an alkaline medium (*cf.* Ref. 13). We found that compound **10** was completely oxidized to form nitrone **11** under the action of $K_3Fe(CN)_6/NaHCO_3$. Nitrone **11**, in turn, gave compound **10** in 87% yield upon reduction with sodium borohydride. The chemical shifts of the corresponding carbon atoms in the ^{13}C NMR spectra of hydroxylamines **7** and **10** as well as of nitrones **9** and **11** are very similar (Table 1). The above-considered regularities of the changes

* For Part 3, see Ref. 1.

** The thermolysis of lappaconitine *N*-oxide **3** has been reported previously.[7]

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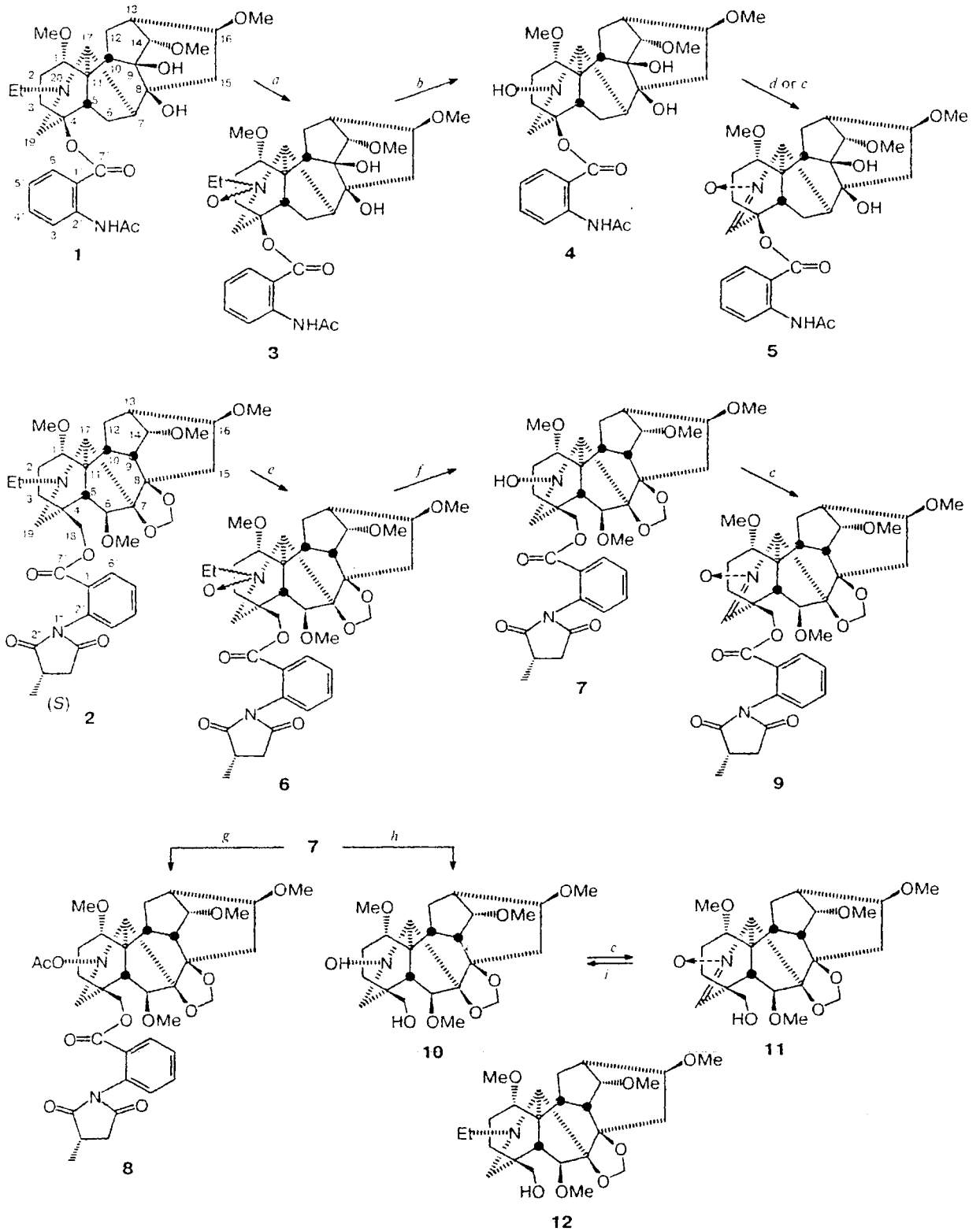
Scheme 1



Reagents and conditions: *a*) *m*-CPBA, $CHCl_3$, 20 °C, 4 h; *b*) 100—140 °C, 5 Torr, 2 h; *c*) $K_3Fe(CN)_6/NaHCO_3$, $CHCl_3$, 20 °C, 3 h; *d*) MnO_2, $CHCl_3$, 20 °C, 9.5 h; *e*) $PhCO_3H$, 20 °C, 16 h; *f*) 95 °C, 3 Torr, 1 h; *g*) Ac_2O, 95 °C, 15 min; *h*) NaOH/EtOH, ~80 °C, 0.5 h; *i*) $NaBH_4$/MeOH, 0.5 h.

Table 1. Chemical shifts and the assignment of the signals in the ^{13}C NMR spectra of compounds **4**—**7** and **9**—**12** (δ)

Atom	**4**	**5**	**6**	**7**	**9**	**10**	**11**	**12**
C(1)	83.2	81.6	84.3	82.9	82.7	83.0	82.7	83.2
C(2)	26.0	21.6	23.3	26.4	23.7	26.7	23.6	26.1
C(3)	30.9	29.5	30.9	30.5	28.8	30.1	28.9	31.0
C(4)	84.9	84.6	39.0	38.8	42.8	40.0	44.2	37.8
C(5)	47.2*	41.7	50.9	51.4	48.9	50.9	48.6	51.8
C(6)	23.9	24.0	87.8	88.8	89.5	88.7	88.9	89.0
C(7)	47.1*	47.0	88.2	90.8	89.0	91.0	89.3	91.9
C(8)	75.4	74.3	83.8	83.7	83.0	83.8	82.9	83.0
C(9)	78.6	76.2	39.0	39.7	39.3	39.9	39.2	39.7
C(10)	49.9	52.7	50.6	47.8	46.8	48.0	46.6	48.3
C(11)	50.4	52.8	49.6	50.3	50.6	50.4	50.8	49.7
C(12)	26.8	26.9	28.2	27.5	28.3	27.6	27.6	27.6
C(13)	36.6	36.4	36.0	38.5	38.3	38.5	38.0	38.2
C(14)	89.9	89.1	80.7	80.2	78.5	80.7	78.9	81.4
C(15)	44.3	43.5	33.6	34.2	33.8	34.4	34.0	34.5
C(16)	82.7	80.0	81.9	81.0	80.7	81.2	80.7	81.3
C(17)	66.4	75.4	79.4	67.8	77.3	68.0	76.5	64.0
C(18)	—	—	69.8	68.7	66.2	67.3	64.5	67.8
C(19)	60.0	133.2	72.9	58.7	134.8	59.3	139.5	52.9
N—$\underline{C}H_2CH_3$	—	—	69.8	—	—	—	—	50.1
N—$CH_2\underline{C}H_3$	—	—	8.5	—	—	—	—	13.5
1-OCH_3	56.5	56.6	56.0	55.2	55.6	55.3	55.6	54.7
6-OCH_3	—	—	57.5	57.5	57.7	57.5	57.7	57.4
14-OCH_3	57.8	57.7	59.0	58.9	59.4	58.7	58.8	58.3
16-OCH_3	56.0	56.7	56.2	55.9	56.3	56.0	56.2	55.7
C(1′)	115.4	114.5	126.0	126.6	126.3	—	—	—
C(2′)	141.6	141.7	132.6	132.7	132.9	—	—	—
C(3′)	120.2	120.2	129.0	129.0	129.3	—	—	—
C(4′)	134.4	134.8	133.5	133.3	133.8	—	—	—
C(5′)	122.2	122.2	130.7	130.8	130.9	—	—	—
C(6′)	130.9	130.6	129.6	129.6	129.9	—	—	—
C(7′)	167.1	166.0	163.5	163.7	163.7	—	—	—
C(2″)	—	—	175.3	175.4	175.7	—	—	—
C(3″)	—	—	34.8	34.9	35.2	—	—	—
C(4″)	—	—	36.5	36.7	36.9	—	—	—
C(5″)	—	—	179.3	179.4	179.6	—	—	—
OCH_2O	—	—	93.4	93.9	94.3	94.0	94.1	93.1
$CH_3\underline{C}O$	168.8	168.0	—	—	—	—	—	
$\underline{C}H_3CO$	25.4	25.2	—	—	—	—	—	—
C(3″)H_3	—	—	15.9	16.1	16.3	—	—	—

* The assignments might be reversed.

in the chemical shifts on going from the initial alkaloids to their *N*-deethylhydroxylamino derivatives are also observed in the ^{13}C NMR spectra of elatidine **12** and *N*-deethyl-*N*-hydroxyelatidine **10** (see Table 1).

To summarize, we developed a method for *N*-deethylation of diterpene alkaloids of the aconitane type according to the Cope reaction and propose a convenient procedure for the preparation of nitrones of *N*-deethylated lappaconitine (**1**), elatine (**2**), and elatidine (**12**).

Experimental

We used freshly distilled solvents, reagents of chemically pure grade, and MnO_2 of "catalysis" grade (TU 6-09-5192-84, Reakhim). Analytical TLC of lappaconitine **1** and its derivatives **3**—**5** was performed using Alufol neutral (Type E) plates (Merck) with a $CHCl_3$—MeCN—propan-2-ol mixture (6 : 4 : 1 by volume) as the eluent. Analytical and preparative TLC of elatine **2** and its derivatives **6**—**12** were carried out using glass plates with a layer of sorbent (0.04 g cm^{-2}; 5/40 μm neutral Al_2O_3 (Chemapol, Czech Republic) containing 1 wt.% of the luminophore K-35 (TU 6-09-1458-76, Russia) and 3% of Na_2CO_3), which were prepared according to a procedure described previously.[2] Prior to chromatography, the plates were activated by heating at 70 °C for 30 min. The spots of alkaloids in dried plates were visualized with UV light. In the case of the analytical chromatograms, the spots were also visualized with iodine vapor.

The IR spectra were recorded on a Vector 22 spectrometer. The UV spectra were measured on a Specord UV VIS spectrophotometer. The molecular weights and the elemental compositions of the new compounds were determined on a high-resolution Finnigan MAT 8200 mass spectrometer. The melting points were determined on a Kofler stage.

The optical rotation was measured on a Polamat A polarimeter. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 instrument (operating at 200.13 and 50.32 MHz for ^1H and ^{13}C, respectively) at 25 °C with resonance stabilization using the signal of deuterium of the solvent ($CDCl_3$). The chemical shifts were measured relative to the signal of the solvent ($CHCl_3$): δ(H) 7.24 and δ(C) 76.90. The multiplicities of the signals in the ^{13}C NMR spectra were determined according to standard procedures in the *J*-modulation mode (JMOD) and using the off-resonance irradiation of protons. The assignment of the signals in the NMR spectra of compounds **5**, **11**, and **12** was made with the use of different types of proton-proton and carbon-proton correlations. The 2D $^1H-^1H$ (COSY) and $^{13}C-^1H$ (COSY 125 Hz, COLOC 7 Hz) NMR spectra were measured on a Bruker DRX 500 instrument operating at 500.13 and 125.76 MHz for ^1H and ^{13}C, respectively, with the use of standard programs (Bruker). The data of ^{13}C NMR spectroscopy of compounds **4**—**7** and **9**—**12** are given in Table 1.

Lappaconitine 1 was isolated from air-dried roots of northern wolfsbane *Aconitum septentrionale* K., which were collected in the Novosibirsk region in August 1997. The yield was 0.5% with respect to the weight of the dry raw material, m.p. 220—221 °C (Me_2CO), $[\alpha]^{20}_{578}$ +29.4° (*c* 1.7, $CHCl_3$) (lit. data[14]: isolated from *A. orientale Mill.*, m.p. 217—218 °C (Me_2CO), $[\alpha]_D$ +25.8° (*c* 9.0, $CHCl_3$); lit. data[15]: isolated from *A. septentrionale* K., m.p. 227 °C (Et_2O), $[\alpha]^{25}_D$ +28.2° (*c* 2.1, $CHCl_3$)). The results of ^1H and ^{13}C NMR spectroscopy are in complete agreement with the published data.[8,16]

Elatine **2** was isolated according to a known procedure[1] from air-dried roots of candle larkspur (*Delphinium elatum* L.), which were collected in the Maiminskii district (Altai) in August 1998. The yield was 0.74% with respect to the weight of the dry raw material, M.p. 222—225 °C (EtOH), $[\alpha]^{20}_{578}$ +3.7° (*c* 3.0, $CHCl_3$) (lit. data[17]: m.p. 222—225 °C (EtOH), $[\alpha]_D$ +3.4° (*c* 3.5, $CHCl_3$)). The data of ^1H and ^{13}C NMR spectroscopy are identical to those for synthetic elatine prepared by methylenation of methyllycaconitine.[9]

Elatidine 12 was prepared by alkaline hydrolysis of elatine **2** according to a procedure reported previously,[17] m.p. 172—174 °C (Me_2CO), $[\alpha]^{20}_{578}$ −4.0° (*c* 10.6, $CHCl_3$) (lit. data[17]: m.p. 172—174 °C (Me_2CO)). ^1H NMR, δ: 0.95 (t, 3 H, $NCH_2C\underline{H}_3$, J = 7 Hz); 1.27—1.35 (m, 2 H, $H_aC(3)$ and HC(5)); 1.57—1.66 (m, 2 H, $H_bC(3)$ and $H_aC(12)$); 1.75 (dd, 1 H, $H_aC(15)$, J = 16 Hz and J = 7.5 Hz); 1.96—2.06 (m, 3 H, $H_2C(2)$ and HC(10)); 2.12 (d, 1 H, $H_aC(19)$, J = 12 Hz); 2.22 (t, 1 H, HC(13), J = 5 Hz); 2.32 (dd, 1 H, $H_bC(15)$, J = 16 Hz and J = 8.5 Hz); 2.35 (br.s, 1 H, OH); 2.46 (dd, 1 H, $H_bC(12)$, J = 14 Hz and J = 3.5 Hz); 2.52—2.59 (m, 2 H, $H_bC(19)$ and H_a of the $C\underline{H}_2CH_3$ group); 2.72 (dq, 1 H, H_b of the $C\underline{H}_2CH_3$ group, J = 13 Hz and J = 7 Hz); 2.89 (t, 1 H, HC(14), J = 8.5 Hz); 3.03 (s, 1 H, HC(17)); 3.15 (m, 1 H, HC(16)); 3.16 (s, 3 H, $O(1)CH_3$); 3.23 (s, 3 H, $O(16)CH_3$); 3.25 (d, 1 H, $H_aC(18)$, J = 10.5 Hz); 3.26 (s, 3 H, $O(14)CH_3$); 3.32 (s, 3 H, $O(6)CH_3$); 3.39 (d, 1 H, $H_bC(18)$, J = 10.5 Hz); 3.52 (br.s, 2 H, HC(1) and HC(6)); 3.58 (t, 1 H, HC(9), J = 6.5 Hz); 4.94 (s, 2 H, OCH_2O).

Lappaconitine *N*-oxide (3). A solution of lappaconitine **1** (1.40 g, 2.39 mmol) in $CHCl_3$ (12 mL) was added with stirring to a solution of MCPBA (1.20 g, 6.94 mmol) in $CHCl_3$ (13 mL). The reaction mixture was kept at ~20 °C for 4 h. Then the organic acids were removed by shaking with a saturated $NaHCO_3$ solution. The chloroform layer was dried with $MgSO_4$, the solvent was removed, and product **3** was obtained in a yield of 1.32 g (92%), m.p. 161—162 °C (with decomp., needles from $CHCl_3-Me_2CO$), $[\alpha]^{20}_{578}$ +23.5° (*c* 0.17, $CHCl_3$). The product was identified based on the ^1H and ^{13}C NMR spectral data.[8]

***N*-Deethyl-*N*-hydroxylappaconitine, {4-[(2-acetylamino)-benzoyloxy]-1α,14α,16β-trimethoxyaconitane-8,9,20-triol} (4).** Lappaconitine *N*-oxide **3** (0.231 g) was heated at 100—140 °C (5 Torr) for 2 h. Compound **4** was obtained in a yield of 0.205 g (94%), m.p. 135—139 °C (with decomp., from a Me_2CO—pentane mixture), $[\alpha]^{20}_{578}$ +15.8° (*c* 0.25, $CHCl_3$). High-resolution MS, *m/z*: 572.2733 $[M]^+$. $C_{30}H_{40}N_2O_9$. Calculated: M 572.2734. MS, *m/z* (I_{rel} (%)): $[M]^+$ 572 (2), $[M - 2H]^+$ 570 (21), 526 (21), 393 (78), 377 (100), 376 (91), 162 (90), and 120 (49). ^1H NMR, δ: 2.17 (s, 3 H, H_3CCO); 3.25, 3.28, and 3.67 (all s, 3 H each, 1-OMe, 16-OMe, and 14-OMe, respectively); 3.06 (d) and 3.89 (d) (AB system, 1 H each, $H_2C(19)$, J = 11 Hz); 6.98 (ddd, 1 H, HC(5′), J = 8.0 Hz, J = 7.5 Hz, and J < 1.0 Hz); 7.45 (ddd, 1 H, HC(4′), J = 8.0 Hz, J = 8.0 Hz, and J = 1.5 Hz); 7.87 (dd, 1 H, HC(6′), J = 7.5 Hz and J = 1.5 Hz); 8.62 (dd, 1 H, HC(3′), J = 8.0 Hz and J < 1.0 Hz); 10.94 (s, 1 H, NH). IR (KBr), ν/cm^{-1}: 750, 1185, 1260, 1290, 1310, 1360, 1440, 1520, 1575, 1600, 1675, 1690, 2810, 2920, 3400. IR (CCl_4), ν/cm^{-1}: 3300 (NH), 3540 (OH, free and associated), 3575 (N—OH).

Nitrone of *N*-deethyllappaconitine, {4-[(2-acetylamino)-benzoyloxy]-1α,14α,16β-trimethoxyaconit-19-ene-8,9-diol 20-oxide} (5). MnO_2 (0.174 g, 2.0 mmol) was added portionwise with stirring to a solution of compound **4** (0.288 g, 0.5 mmol) in $CHCl_3$ (4 mL). The mixture was stirred at ~20 °C until the initial compound was consumed (9.5 h, TLC control). The precipitate was separated, and the filtrate was concentrated and dried *in vacuo*. Nitrone **5** was obtained as an amorphous powder in a yield of 0.221 g (77%). $[\alpha]^{20}_{578}$ −9.7° (*c* 2.47, $CHCl_3$). High-resolution MS, *m/z*: 570.2595 $[M]^+$. $C_{30}H_{48}N_2O_9$. Calculated: M 570.2577. ^1H NMR, δ: 1.40 (m, 1 H, HC(12)); 1.73 (m, 1 H, HC(15)); 1.81 (m, 1 H, HC(6)); 1.96 (m, 1 H, HC(15)); 2.08 (m, 3 H, HC(2), HC(3), HC(12)); 2.15 (m, 1 H, HC(7)); 2.19 (s, 3 H, H_3CCO); 2.40 (m, 1 H, HC(13)); 2.42 (d, 1 H, HC(10), J = 4.0 Hz); 2.47 (m, 1 H, HC(3)); 2.61 (m, 2 H, HC(2), HC(6)); 2.72 (d, 1 H, HC(5), J = 3.1 Hz); 3.25, 3.26, and 3.36 (all s, 3 H each, 1-OMe, 16-OMe, and 14-OMe, respectively); 3.32 (m, 1 H, HC(1)); 3.37 (m, 1 H, HC(16)); 3.41 (m, 1 H, HC(14)); 3.70 (s, 1 H, HC(17)); 6.99 (ddd, 1 H, HC(5′), J = 7.5 Hz, J = 7.5 Hz, and J = 1.0 Hz); 7.23 (s, 1 H, HC(19)); 7.49 (ddd, 1 H, HC(4′), J = 8.0 Hz, J = 7.5 Hz, and J = 1.5 Hz); 7.86 (dd, 1 H, HC(6′), J = 7.5 Hz and J = 1.5 Hz); 8.66 (dd, 1 H, HC(3′), J = 8.0 Hz and J = 1.0 Hz); 10.81 (s, 1 H, NH). IR (KBr), ν/cm^{-1}: 750, 1080, 1110, 1260, 1290, 1360, 1440, 1520, 1575, 1600, 1675, 2825, 2880, 2950, 3400. UV (MeOH), λ_{max}/nm (lg ε): 224 (4.32), 253 (4.17), 312 (3.56).

Elatine *N*-oxide, {4*S*-4-[2-(3*S*-3-methyl-2,5-dioxo-1-pyrrolidinyl)benzoyloxymethyl]-20-ethyl-1α,6β,14α,16β-tetramethoxy-7,8-[methylenebis(oxy)]aconitane 20-oxide} (6), a solvate with chloroform. A solution of $PhCO_3H$ (1.03 g, 7.46 mmol) in $CHCl_3$ (13 mL) cooled to 5 °C was added dropwise with stirring to a solution of elatine **2** (1.03 g, 1.48 mmol) in $CHCl_3$ (13 mL). The resulting solution was kept at 20 °C for 16 h, the organic acids were removed by shaking with a saturated $NaHCO_3$ solution (4×14 mL), and the reaction solution was filtered. Chloroform was distilled off *in vacuo*. The residue was dissolved in propan-2-ol and subjected to preparative TLC using a $PrⁱOH-Et_2O$ mixture (1 : 4 by volume) as the eluent. The product was eluted (with MeOH) from the UV-absorbing band of the sorbent (R_f 0.48), the solvent was removed, the residue was dissolved in $CHCl_3$, and the solution was filtered. After removal of $CHCl_3$, the residue was dried (20—25 °C, 20 Torr). An amorphous powder of the

solvate of elatine *N*-oxide **6** with chloroform was obtained in a yield of 1.01 g (82%), $[\alpha]^{20}_{578}$ −6.8° (*c* 4.4, $CHCl_3$). According to the data of analytical TLC (under conditions of preparative TLC), the product did not contain admixtures visualized with iodine vapor (R_f 0.48 and 0.93 for *N*-oxide **6** and elatine **2** as the reference, respectively). For the solvate of compound **6**, found (%): C, 55.79, 55.88; H, 6.20, 6.11; Cl, 12.10, 12.40; N, 3.38, 3.41. $C_{38}H_{50}N_2O_{11}\cdot CHCl_3$ ($C_{39}H_{51}Cl_3N_2O_{11}$). Calculated (%): C, 56.41; H, 6.20; Cl, 12.81; N, 3.37. ^{1}H NMR, δ: 1.30—1.40 (m, 6 H, $H_3CC(3'')$ and $C\underline{H}_3CH_2$); 3.18 (6 H), 3.24 (3 H), and 3.30 (3 H) (all s, 1-OMe, 6-OMe, 14-OMe, and 16-OMe); 5.00 (s, 2 H, OCH_2O); 7.15 (dd, 1 H, HC(3′), J = 8 Hz and J = 2 Hz); 7.24 (s, $CHCl_3$); 7.44 (td, 1 H, HC(5′), J = 8 Hz and J = 2 Hz); 7.53 (td, 1 H, HC(4′), J = 8 Hz and J = 2 Hz); 7.90 (dd, 1 H, HC(6′), J = 8 Hz and J = 2 Hz). IR (KBr), ν/cm^{-1}: 1090, 1124, 1187, 1262, 1295, 1371, 1454, 1494, 1715 (C=O), 2754, 2823, 2886, 2937. UV (EtOH), λ_{max}/nm (lg ε): 233 (3.79) and 278 (2.83).

***N*-Deethyl-*N*-hydroxyelatine, {4*S*-4-[2-(3*S*-3-methyl-2,5-dioxo-1-pyrrolidinyl)benzoyloxymethyl]-1α,6β,14α,16β-tetramethoxy-7,8-[methylenebis(oxy)]aconitan-20-ol} (7).** The chloroform solvate of elatine *N*-oxide **6** (0.830 g) was heated to 95 °C with continuous evacuation (3 Torr) and kept under these conditions for 1 h. The thermolysate was dissolved in $CHCl_3$ and chromatographed under the conditions used for purification of *N*-oxide **6** (see above). The sorbent of the UV-absorbing band with R_f 0.67 was collected, the product was eluted with MeOH, the solvent was removed *in vacuo*, the residue was dissolved in $CHCl_3$, and the solution was filtered. Chloroform was removed *in vacuo*, and the residue was dried at 20 Torr and recrystallized from boiling Pr^{i}OH. Compound **7** was obtained in a yield of 0.519 g (76%), m.p. 228—230 °C, $[\alpha]^{20}_{578}$ −1.7 ° (*c* 4.7, $CHCl_3$). Found (%): C, 63.49, 63.38; H, 7.11, 6.97; N, 4.04, 4.17. $C_{36}H_{46}N_2O_{11}$. Calculated (%): C, 63.32; H, 6.80; N, 4.10. ^{1}H NMR, δ: 1.40 (br.d, 3 H, $CH_3C(3'')$, J = 7 Hz); 3.23, 3.25, 3.28, and 3.36 (all s, 3 H each, 1-OMe, 6-OMe, 14-OMe, and 16-OMe); 5.07 (s, 2 H, OCH_2O); 6.09 (s, 1 H, OH); 7.20 (dd, 1 H, HC(3′), J = 8 Hz and J = 2 Hz); 7.46 (td, 1 H, HC(5′), J = 8 Hz and J = 2 Hz); 7.61 (td, 1 H, HC(4′), J = 8 Hz and J = 2 Hz), 7.97 (dd, 1 H, HC(6′), J = 8 Hz and J = 2 Hz). IR (KBr), ν/cm^{-1}: 1089, 1135, 1186, 1258, 1296, 1393, 1454, 1492, 1716 (C=O), 2823, 2880, 2937, 2968. UV (EtOH), λ_{max}/nm (lg ε): 230 (3.60), 275 (2.73).

***N*-Deethyl-*N*-acetoxyelatine, {20-acetoxy-4*S*-4-[2-(3*S*-3-methyl-2,5-dioxo-1-pyrrolidinyl)benzoyloxymethyl]-1α,6β,14α,16β-tetramethoxy-7,8-[methylenebis(oxy)]aconitane} (8).** Compound **7** (0.113 g, 0.168 mmol) was dissolved in Ac_2O (0.556 g, 5.45 mmol) upon heating on a bath (95 °C). The solution was kept at this temperature for 15 min, the solvent was removed *in vacuo*, and the residue was dried (95 °C, 3 Torr). Crystalline acetate **8** was obtained in a yield of 0.120 g (100%), m.p. 222—224 °C, $[\alpha]^{20}_{578}$ −8.8° (*c* 2.5, $CHCl_3$). According to the data of analytical TLC, a only spot with R_f 0.80 was observed (a Pr^{i}OH—Et_2O mixture (1 : 4 by volume) as the eluent; compound **7** with R_f 0.67 was used as the reference). Found (%): C, 63.19, 63.43; H, 7.12, 7.22; N, 3.77, 3.80. $C_{38}H_{48}N_2O_{12}$. Calculated (%): C, 62.96; H, 6.69; N, 3.87. ^{1}H NMR, δ: 1.43 (d, 3 H, $CH_3C(3'')$, J = 7 Hz); 2.07 (s, 3 H, H_3CCO); 3.27, 3.32, 3.33, and 3.41 (all s, 3 H each, 1-OMe, 6-OMe, 14-OMe, and 16-OMe); 5.11 (s, 1 H) and 5.12 (s, 1 H) (OCH_2O); 7.24 (dd, 1 H, HC(3′), J = 8 Hz and J = 2 Hz); 7.50 (td, 1 H, HC(5′), J = 8 Hz and J = 2 Hz); 7.65 (td, 1 H, HC(4′), J = 8 Hz and J = 2 Hz); 7.98 (dd, 1 H, HC(6′), J = 8 Hz and J = 2 Hz). IR (KBr), ν/cm^{-1}: 967, 1012, 1090, 1108, 1130, 1204, 1265, 1295, 1366, 1396, 1459, 1497, 1604, 1721 (C=O), 1773 (C=O), 2819, 2886, 2934, 2968, 3089. UV (EtOH), λ_{max}/nm (lg ε): 230 (3.78), 278 (2.88).

Nitrone of *N*-deethylelatine, {4*R*-4-[2-(3*S*-3-methyl-2,5-dioxo-1-pyrrolidinyl)benzoyloxymethyl]-1α,6β,14α,16β-tetramethoxy-7,8-[methylenebis(oxy)]aconit-19-ene 20-oxide} (9). A solution of compound **7** (0.300 g, 0.446 mmol) in $CHCl_3$ (12 mL) was vigorously stirred with a solution of $K_3Fe(CN)_6$ (3.30 g, 10 mmol) and $NaHCO_3$ (0.84 g, 10 mmol) in water (18 mL) until the initial compound completely disappeared in the chloroform layer (3 h, TLC control, a Pr^{i}OH—Et_2O mixture (1 : 4 by volume) as the eluent; R_f 0.67 and R_f 0.30 for compounds **7** and **9**, respectively). The organic layer was separated and dried with $MgSO_4$. After removal of the solvent, nitrone **9** was obtained as an amorphous powder in a yield of 0.272 g (91%), $[\alpha]^{20}_{578}$ −11.1° (*c* 1.8, $CHCl_3$). High-resolution MS, *m/z*: 680.2949 $[M]^+$. $C_{36}H_{44}N_2O_{11}$. Calculated: M 680.2945. ^{1}H NMR, δ: 1.43 (d, 3 H, $H_3CC(3'')$, J = 7 Hz); 3.24, 3.31, 3.33, and 3.42 (all s, 3 H each, 1-OMe, 6-OMe, 14-OMe, and 16-OMe); 4.28 and 4.32 (both d, AB system, 1 H each, $H_2C(18)$, J = 10 Hz); 5.14 and 5.18 (both s, 1 H each, OCH_2O); 6.88 (s, 1 H, HC(19)); 7.26 (dd, 1 H, HC(3′), J = 8 Hz and J = 2 Hz); 7.51 (td, 1 H, HC(5′), J = 8 Hz and J = 2 Hz); 7.68 (td, 1 H, HC(4′), J = 8 Hz and J = 2 Hz); 8.01 (dd, 1 H, HC(6′), J = 8 Hz and J = 2 Hz). IR (KBr), ν/cm^{-1}: 715, 747, 910, 1048, 1089, 1119, 1189, 1234, 1261, 1295, 1371, 1391, 1454, 1494, 1715 (C=O), 1773 (C=O), 2824, 2891, 2938. UV (EtOH), λ_{max}/nm (lg ε): 240 (3.62).

***N*-Deethyl-*N*-hydroxyelatidine, {4*S*-4-hydroxymethyl-1α,6β,14α,16β-tetramethoxy-7,8-[methylenebis(oxy)]aconitan-20-ol} (10), and nitrone of *N*-deethylelatidine, {4*R*-4-hydroxymethyl-1α,6β,14α,16β-tetramethoxy-7,8-[methylenebis(oxy)]aconit-19-ene 20-oxide} (11).** An 8.3% NaOH solution (0.6 mL, contained 1.3 mmol of NaOH) was added to a solution of compound **7** (0.285 g, 0.423 mmol) in EtOH (5.7 mL). The resulting solution was refluxed for 0.5 h. Then the alcohol was distilled off *in vacuo* (the temperature of the bath was 80 °C) and the residue was treated with a mixture of water (1 mL) and $CHCl_3$ (5 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3×5 mL). The combined chloroform extracts were filtered and the solvent was removed *in vacuo*. The residue was obtained as a mixture of compounds **10** and **11** in a ratio of ~3 : 1 (according to the data of ^{1}H NMR spectroscopy) and a total yield of 0.158 g. Compounds **10** (weakly UV-absorbing band with R_f 0.64) and **11** (intensively absorbing band with R_f 0.49) were separated by preparative TLC (Pr^{i}OH as the eluent). The products were eluted with methanol and treated as in the case of isolation of *N*-oxide **6**. After removal of the chloroform, the residues were obtained as amorphous powders.

Compound 10, $[\alpha]^{20}_{578}$ −8.8° (*c* 2.5, $CHCl_3$). High-resolution MS, *m/z*: 449.2445 $[M - 18]^+$. For the $C_{24}H_{35}NO_7$ $[M - 18]^+$ ion, calculated: 449.2413. ^{1}H NMR, δ: 3.26, 3.29, 3.36, and 3.40 (all s, 3 H each, 1-OMe, 6-OMe, 14-OMe, and 16-OMe); 5.10 (s, 2 H, OCH_2O); 5.76 (br.s, 1 H, OH). IR (KBr), ν/cm^{-1}: 972, 1088, 1124, 1174, 1201, 1234, 1387, 1449, 1470, 1638, 2749, 2822, 2891, 2930.

Nitrone 11, $[\alpha]^{20}_{578}$ −0.8° (*c* 2.6, $CHCl_3$). High-resolution MS, *m/z*: 466.2427 $[M + 1]^+$. For the $C_{24}H_{36}NO_8$ $[M + 1]^+$ ion, calculated: 466.2441. ^{1}H NMR (500.13 MHz), δ: 1.53—1.61 (m, 2 H, $H_aC(3)$, $H_aC(12)$); 1.62 (s, 1 H, HC(5)); 1.72—1.97 (m, 5 H, $H_2C(2)$, $H_bC(3)$, HC(12), and $H_aC(15)$); 2.24 (m, 1 H, HC(10)); 2.35 (t, 1 H, HC(13), J = 4.5 Hz); 2.63 (dd, 1 H, $H_bC(15)$, J = 16 Hz and J = 8 Hz); 3.17 (t, 1 H, HC(16), J = 8 Hz); 3.31 (m, 1 H, HC(1)); 3.20, 3.27, 3.32, and 3.38 (all s, 3 H each, 1-OMe, 6-OMe, 14-OMe, and 16-OMe); 3.52 (t, 1 H, HC(9), J = 6 Hz); 3.59 (d) and 3.77

(d) (AB system, 1 H each, $H_2C(18)$, J = 10 Hz); 3.64 (t, 1 H, HC(14), J = 4.5 Hz); 3.67 (s, 1 H, HC(6)); 3.95 (s, 1 H, HC(17)); 4.72 (br.s, 1 H, OH); 5.05 and 5.11 (both s, 1 H each, OCH_2O); 7.04 (s, 1 H, HC(19)). IR (KBr), ν/cm^{-1}: 728, 916, 950, 1091, 1119, 1190, 1388, 1454, 2826, 2886, 2935. UV (EtOH), λ_{max}/nm (lg ε): 250 (3.46).

Reduction of nitrone 11. $NaBH_4$ (43 mg, 1.14 mmol) was added portionwise with stirring to a solution of nitrone **11** (24 mg, 0.052 mmol) in anhydrous MeOH (0.7 mL). After 0.5 h, water (1 mL) was added to the reaction mixture and the mixture was extracted with $CHCl_3$ (3×3 mL). The extract was filtered and concentrated *in vacuo*. Compound **10** was obtained in a yield of 21 mg (87%). This compound was virtually identical (according to the ^{1}H NMR spectral data) to the above-described sample.

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