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AMIDES OF *N*-DEACETYLLAPPACONITINE AND AMINO ACIDS

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Amides were prepared from N*-deacetyllappaconitine and the amino acids glycine, taurine, and γ-aminobutyric acid.*

Keywords: diterpene alkaloids, *N*-deacetyllappaconitine, glycine, taurine, γ-aminobutyric acid.

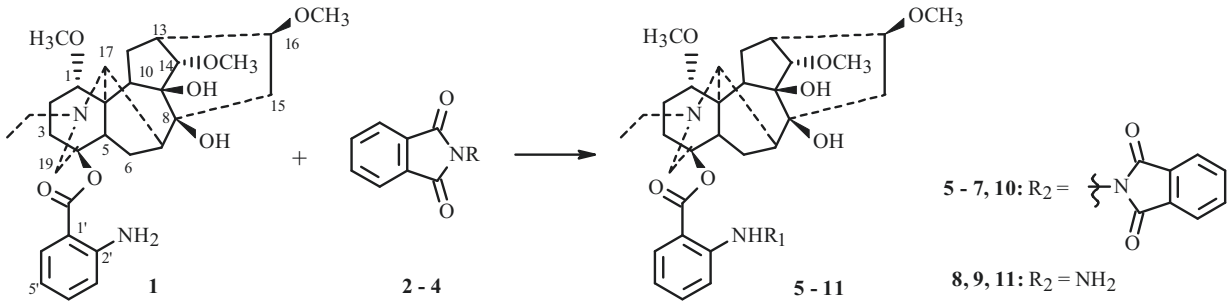
Several *N*-deacetyllappaconitines with various substituents on the aromatic N atom have been reported. In particular, the reaction of *N*-deacetyllappaconitine with benzoic, methacrylic, crotonic, cinnamic, chloroacetic, and methanesulfonic acids in anhydrous CH_2Cl_2 in the presence of Py produced the corresponding *N*-substituted deacetyllappaconitines in 72–86% yield. *N*-Chloroacetyl-*N*′-deacetyllappaconitine reacted with secondary amines (diethylamine, morpholine, *N*-methylpiperazine) to give the corresponding *N*-substituted glycyl amides [1].

Stressful situations are known to be one reason for the growth in the incidence of ischemic cardiac disease and the occurrence of myocardial infarct. Neutral amino acids γ-aminobutyric acid, glycine, β-alanine, and taurine are so-called inhibitory mediators that regulate excitation *in vivo*.

In continuation of studies of the modification of *N*-deacetyllappaconitine (**1**), several derivatives containing amino-acid residues were synthesized.

Amino acids were introduced into **1** by using known methods to synthesize *N*-phthalimidoacids of glycine, γ-aminobutyric acid [2], and taurine [3], which were converted to the corresponding acid chlorides **2** and **3** and sulfonyl chloride **4**. Compound **1** was acylated by heating in CH_2Cl_2 in the presence of Et_3N. Resulting derivatives **5**–**7** were purified by column chromatography (CC). The yields of acylated products were 79–89%.

The structures of **5**–**7** were confirmed by IR spectroscopy and mass spectrometry. A series of 2D NMR spectral experiments allowed complete assignment of resonances for C-atoms and H atoms bonded to them in PMR and ^{13}C NMR spectra. Table 1 confirmed that the synthesized compounds contained phthalimido groups with resonances for aromatic C atoms (δ_C 123–134 ppm) and additional resonances for three CO groups bonded to a N atom (δ_C 164–167 ppm).



R = CH_2COCl (**2**); $CH_2CH_2CH_2COCl$ (**3**); R = $CH_2CH_2SO_2Cl$ (**4**)
R_1 = $COCH_2R_2$ (**5,8**); R_1 = $COCH_2CH_2CH_2R_2$ (**6**); $SO_2CH_2CH_2R_2$ (**7,9**); $COCH_2NHSO_2CH_2CH_2R_2$ (**10,11**)

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TABLE 1. ^{13}C NMR Spectra of *N*-Acyl and *N*-Sulfonamide Derivatives of *N*-Deacetyllappaconitine (**1**) ($CDCl_3$, δ, ppm)

C atom	**5**	**6**	**7**	**8**	**9**	**10**	**11**
1	84.2	84.2	84.0	84.2	84.0	84.1	84.1
2	26.7	26.8	26.7	26.8	26.7	26.7	26.7
3	31.4	31.8	31.7	31.8	31.8	31.8	31.8
4	84.7	84.6	85.2	84.4	85.3	85.1	85.1
5	48.7	48.6	48.5	48.6	48.3	48.5	48.4
6	24.0	24.1	24.1	24.2	24.1	24.1	24.2
7	47.5	47.6	47.6	47.5	47.6	47.5	47.6
8	75.6	75.6	75.6	75.6	75.6	75.6	75.6
9	78.5	78.6	78.6	78.6	78.6	78.6	78.6
10	49.7	49.8	49.8	49.8	49.9	49.8	49.9
11	50.8	50.9	50.9	50.9	51.0	50.9	50.9
12	26.2	26.2	26.2	26.2	26.2	26.2	26.2
13	36.2	36.3	36.3	36.2	36.2	36.2	36.2
14	90.1	90.1	90.1	90.2	90.1	90.1	90.1
15	44.8	44.8	44.8	44.8	44.7	44.8	44.8
16	82.9	82.9	82.8	82.9	82.8	82.8	82.8
17	61.5	61.5	61.5	61.5	61.5	61.5	61.5
19	55.1	55.4	55.3	55.5	55.4	55.4	55.5
$N\underline{C}H_2CH_3$	48.9	49.0	48.9	49.0	49.0	49.0	49.0
$NCH_2\underline{C}H_3$	13.7	13.6	13.5	13.6	13.5	13.5	13.5
1-OCH_3	56.7	56.6	56.5	56.6	56.6	56.6	56.5
14-OCH_3	57.9	57.9	57.9	57.9	57.9	57.9	57.9
16-OCH_3	56.1	56.1	56.1	56.2	56.2	56.1	56.1
OCO	167.6	167.3	167.1	166.9	167.2	167.4	167.4
1′	115.8	115.8	116.4	116.8	116.4	116.2	116.4
2′	140.8	141.5	140.3	140.7	140.6	140.6	140.5
3′	120.0	120.2	117.7	120.5	118.0	120.3	120.4
4′	134.6	134.3	134.6	134.2	134.7	134.4	134.4
5′	122.9	122.3	122.8	122.6	122.8	123.1	123.2
6′	130.9	131.0	131.7	131.2	131.8	131.2	131.2
$CO\underline{C}H_2$	41.7			46.4		46.8	46.5
$CO\underline{C}H_2CH_2CH_2$		35.6					
$COCH_2\underline{C}H_2CH_2$		24.2					
$COCH_2CH_2\underline{C}H_2$		37.4					
NHCO	164.8	170.7		172.3		167.1	167.2
$N(CO)_2$	167.6	168.4	167.4			168.4	
1″, 6″	132.3	132.1	132.0			131.9	
2″, 5″	134.1	133.9	134.6			134.2	
3″, 4″	123.6	123.2	123.4			123.5	
$SO_2\underline{C}H_2CH_2$			49.2		54.7	50.5	54.6
$SO_2CH_2\underline{C}H_2$			32.4		36.8	32.8	36.9

The protection in **5** and **7** was removed by refluxing in EtOH with 85% hydrazine hydrate without purifying the amides obtained beforehand from the acylation step. The standard work up and purification by CC over SiO_2 produced **8** and **9** and 67 and 71% yields (total for two steps). The protection could not be removed from **6** because it hydrolyzed to *N*-deacetyllappaconitine and lappaconine.

Repeated acylation of **8** by phthalimidoethanesulfonyl chloride (**4**) analogously as above produced **10** and **11** after removal of the protection in 70% yield (total for two steps).

Based on 1D and 2D NMR experiments (DEPT, COSY, HSQC, and HMBC), resonances in PMR and ^{13}C NMR spectra of the synthesized compounds were fully assigned (Table 1).

EXPERIMENTAL

General comments were published [4].

General Method for Preparing Phthalimidoacids. A mixture of amino acid (0.01 mol) and thoroughly ground phthalic anhydride (0.01 mol) was heated for 30 min at 145–150°C on an oil bath [2] and cooled. The solid reaction product was dissolved in hot MeOH (10 mL), filtered, and diluted with H_2O (10 mL). The phthalimidoacids precipitated during slow cooling.

Phthalimidoacetic Acid. $C_{10}H_7O_4N$. Yield 86%, mp 191–192°C. High-resolution mass spectrum, *m/z* 204.1701 $[M - H]^-$. Calcd 204.1707.

γ-Phthalimidobutyric Acid. Yield 90%, mp 108–111°C. ^1H NMR spectrum (500 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.76–1.90 (2H, m), 2.29 (2H, t, J = 7.2), 3.62 (2H, t, J = 6.8), 7.75–7.92 (4H, m, Ar), 12.10 (1H, s). ^{13}C NMR spectrum (125 MHz, DMSO-d_6, δ, ppm): 173.8, 167.9, 134.2, 137.6, 122.9, 36.8, 30.9, 23.3.

General Method for Preparing Phthalimidoacid Chlorides. A mixture of amino-acid phthalyl derivative (0.001 mol) and thionylchloride (6 mL) was refluxed for 3 h at 50°C. The excess of thionylchloride was vacuum distilled. Anhydrous toluene was added to the reaction flask and distilled off *in vacuo* three times for complete removal of thionylchloride. Then, obtained chlorides **2** and **3** were used for acylation.

Phthalimidoethanesulfonyl Chloride (4). According to the literature method [3], phthalic anhydride (0.072 mol) was treated with a suspension of taurine (0.068 mol) and KOAc (0.072 mol) in glacial AcOH (24 mL), refluxed for 2 h until completely dissolved, cooled to 5°C, and filtered to remove the precipitate of potassium 2-phthalimidoethanesulfonate, which was rinsed with AcOH and MeOH and dried in air and *in vacuo*. Yield 76%, mp >300°C. PMR spectrum (500 MHz, D_2O, δ, ppm, J/Hz): 7.85 (4H, m), 4.05 (3H, t, J = 8), 3.25 (2H, t, J = 8).

The obtained salt (0.017 mol) in C_6H_6 (50 mL) was treated with PCl_5 (0.012 mol), refluxed for 1 h, treated again with PCl_5 (0.012 mol), refluxed for 1.5 h, and evaporated. The residue was mixed with powdered ice (30 g). Solid **4** was filtered off, rinsed with ice water, and dried in air. Yield 61%, mp 158–159°C.

General Method for Acylating *N*-deacetyllappaconitine with Phthalimidoacid Chlorides. The obtained phthalimidoacid chloride was treated with a solution of **1** (1.1 mmol) in CH_2Cl_2 (15 mL) and Et_3N (0.45 mL). The mixture was stirred at 40°C for 4 h, made basic with soda to pH 9, and extracted with $CHCl_3$ (3 × 15 mL). The extract was dried over anhydrous Na_2SO_4. The solvent was distilled off. The product was either used without isolation for removal of the phthalimide protection or purified by CC over SiO_2 using $CHCl_3$–MeOH (99:1).

***N*-[2-(1,3-Dioxoisoindolin-2-yl)acetyl]-*N*-deacetyllappaconitine (5).** Yield 81%. High-resolution mass spectrum, *m/z* 728.3173 $[M - H]^-$, calcd 728.3178. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 728 $((M - 1)^+$, 0.5), 714 $((M - 15)^+$, 0.8), 698 $((M - 31)^+$, 5). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1777 (O–CO), 1715 (N–CO), 1680 (NHCO), 1130–1080 (C–O). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.07 (3H, t, J = 7.1, $C\underline{H}_3CH_2N$), 1.50 (1H, m, H_a-6), 1.55 (1H, m, H_a-3), 1.97 (1H, m, H_a-12), 2.00 (1H, m, H_a-15), 2.02 (1H, m, H_a-2), 2.04 (1H, m, H-10), 2.05 (1H, m, H_b-2), 2.10 (1H, m, H-7), 2.19 (1H, m, H-5), 2.24 (1H, m, H_b-3), 2.32 (1H, d, J = 11.8, H_a-19), 2.34 (1H, m, H-13), 2.35 (1H, m, H_b-15), 2.40 (1H, m, $CH_3C\underline{H}_aN$), 2.48 (1H, m, H_b-12), 2.52 (1H, m, $CH_3C\underline{H}_bN$), 2.68 (1H, dd, J = 15.1, 7.4, H_b-6), 2.94 (1H, s, H-17), 3.10 (1H, m, H-1), 3.11 (1H, d, J = 11.8, H_b-19), 3.28 (1H, m, H-16), 3.29 (3H, s, 1-OCH_3), 3.30 (3H, s, 16-OCH_3), 3.39 (3H, s, 14-OCH_3), 3.43 (1H, d, J = 4.8, H-14), 4.51 (1H, d, J = 16.9, $COCH_a$), 4.60 (1H, d, J = 16.9, $COCH_b$), 7.03 (1H, t, J = 7.7, H-5′), 7.48 (1H, t, J = 7.5, 8.2, H-4′), 7.77 (2H, m, H-2″, 5″), 7.84 (1H, d, J = 8.0, H-6′), 7.92 (2H, m, H-3″, 4″), 8.62 (1H, d, J = 8.4, H-3′), 11.65 (1H, s, NH).

***N*-[4-(1,3-Dioxoisoindolin-2-yl)butanoyl]-*N*-deacetyllappaconitine (6).** Yield 89%. High-resolution mass spectrum, *m/z* 756.3497 $[M - H]^-$, calcd 756.3491. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 756 $((M - 1)^+$, 0.1), 742 $((M - 15)^+$, 0.2), 726 $((M - 31)^+$, 0.9). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1772 (O–CO), 1710 (N–CO), 1673 (NHCO), 1130–1080 (C–O). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.11 (3H, t, J = 7.2, $C\underline{H}_3CH_2N$), 1.58 (1H, dd, J = 15.0, 8.3, H_a-6), 1.78 (1H, m, H_a-3), 1.97 (1H, m, H_a-12), 2.01 (1H, dd, J = 14.8, 7.6, H_a-15), 2.07 (1H, m, H-10), 2.12 (2H, m, $COCH_2C\underline{H}_2CH_2$), 2.14 (1H, m, H-7), 2.17 (1H, m, H_a-2), 2.27 (1H, m, H_b-2), 2.36 (2H, m, H-5, 13), 2.39 (1H, m, H_b-15), 2.49 (1H, m, H_b-12; 2H, m, $COC\underline{H}_2CH_2CH_2$), 2.50 (1H, m, $CH_3C\underline{H}_aN$), 2.54 (1H, d, J = 11.4, H_a-19), 2.55 (1H, m, $CH_3C\underline{H}_вN$), 2.66 (1H, m, H_b-3), 2.68 (1H, m, H_b-6), 3.00 (1H, s, H-17), 3.18 (1H, m, H-1), 3.29 (3H, s, 1-OCH_3), 3.30 (3H, s, 16-OCH_3; 1H, m, H-16), 3.39 (3H, s, 14-OCH_3), 3.43 (1H, d, J = 4.6, H-14), 3.58 (1H, d, J = 11.4, H_b-19), 3.80 (2H, t, J = 6.8, $COCH_2CH_2C\underline{H}_2$), 6.98 (1H, t, J = 7.6, H-5′), 7.42 (1H, t, J = 7.9, H-4′), 7.66 (2H, m, H-2″, 5″), 7.79 (2H, m, H-3″, 4″), 7.89 (1H, d, J = 8.0, H-6′), 8.57 (1H, d, J = 8.2, H-3′), 11.03 (1H, s, NH).

***N*-[2-(1,3-Dioxoisoindolin-2-yl)ethanesulfonyl]-*N*-deacetyllappaconitine (7).** A solution of **1** (0.2 mmol) in CH_2Cl_2 (4 mL) was treated with 2-phthalimidoethanesulfonyl chloride (**4**, 0.3 mmol) and Et_3N (0.1 mL). The mixture was stirred at room temperature for 4 h. The product was purified by CC over SiO_2 using $CHCl_3$–MeOH (98.5:1.5). Yield 79%. High-resolution mass spectrum, *m/z* 779.3086 $[M]^+$, calcd 779.3082. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 779 (M^+, 0.5), 764 ($(M - 15)^+$, 0.5), 748 ($(M - 31)^+$, 5). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1682 (NHSO), 1130–1080 (C–O). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.14 (3H, t, J = 7.1, $C\underline{H}_3CH_2N$), 1.59 (1H, m, J = 15.1, 8.2, H_a-6), 1.78 (1H, m, H_a-3), 2.00 (1H, m, H_a-12), 2.03 (1H, m, H_a-15), 2.11 (1H, m, H-10), 2.15 (1H, m, H-7), 2.17 (1H, m, H_a-2), 2.31 (1H, m, H_b-2), 2.37 (1H, m, H-5), 2.38 (2H, m, H-13, H_b-15); 2.50 (1H, m, H_b-12); 2.51 (1H, m, $CH_3C\underline{H}_aN$); 2.55 (1H, d, J = 11.5, H_a-19); 2.57 (1H, m, $CH_3C\underline{H}_bN$); 2.70 (1H, m, H_b-3; 1H, dd, H_b-6), 3.01 (1H, s, H-17), 3.19 (1H, m, H-1), 3.30 (3H, s, 1-OCH_3), 3.31 (1H, m, H-16), 3.32 (3H, s, 16-OCH_3), 3.41 (3H, s, 14-OCH_3), 3.44 (1H, d, J = 4.6, H-14), 3.57 (2H, m, J = 13.9, 7.1, $SO_2C\underline{H}_2CH_2$), 3.62 (1H, d, J = 11.5, H_b-19), 4.14 (2H, m, J = 13.8, 6.9, $SO_2CH_2C\underline{H}_2$), 7.02 (1H, t, J = 8.1, H-5′), 7.47 (1H, t, J = 15.9, 7.0, H-4′), 7.62 (1H, d, J = 8.3, H-3′), 7.70 (2H, m, H-2″, 5″), 7.80 (2H, m, H-3″, 4″), 7.88 (1H, d, J = 8.0, H-6′), 10.67 (1H, s, NH).

General Method for Removing Phthalyl Protection. A solution of amide **5**, **7**, or **10** in EtOH (4 mL) was treated with hydrazine hydrate (85%, 0.4 mL), refluxed for 1 h, and evaporated. The residue was treated with water and acidified with HCl solution (1 N). The phthalyl hydrazide was filtered off. The eluate was evaporated to dryness. The products were purified by CC over SiO_2 using $CHCl_3$–MeOH (99:1).

***N*-Glycyl-*N*-deacetyllappaconitine (8).** Yield 69%. High-resolution mass spectrum, *m/z* 598.3127 $[M - H]^-$, calcd 598.3123. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 598 ($(M - 1)^+$, 0.8), 584 ($(M - 15)^+$, 0.6), 568 ($(M - 31)^+$, 4.5). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1740 (O–CO), 1673 (NHCO), 1130–1080 (C–O). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.11 (3H, t, J = 7.1, $C\underline{H}_3CH_2N$), 1.60 (1H, m, J = 15.0, 8.2, H_a-6), 1.80 (1H, m, H_a-3), 1.96 (1H, m, H_a-12), 2.01 (1H, m, H_a-15), 2.08 (1H, m, H-10), 2.15 (2H, m, H_a-2, H-7), 2.28 (1H, m, H_b-2), 2.36 (1H, m, H-13), 2.39 (1H, m, H_b-15), 2.41 (1H, m, H-5), 2.49 (1H, m, $CH_3C\underline{H}_aN$), 2.50 (1H, m, H_b-12), 2.54 (1H, m, $CH_3C\underline{H}_bN$), 2.55 (1H, d, J = 11.3, H_a-19), 2.67 (1H, m, H_b-3), 2.68 (1H, dd, J = 15.0, 7.4, H_b-6), 2.99 (1H, s, H-17), 3.18 (1H, m, H-1), 3.28 (3H, s, 1-OCH_3), 3.30 (1H, m, H-16; 3H, s, 16-OCH_3), 3.40 (3H, s, 14-OCH_3), 3.43 (1H, d, J = 4.5, H-14), 3.54 (2H, s, $COCH_2$), 3.60 (1H, d, J = 11.3, H_b-19), 7.04 (1H, t, J = 7.6, H-5′), 7.49 (1H, t, J = 7.5, 15.1, H-4′), 7.92 (1H, d, J = 7.7, H-6′), 8.71 (1H, d, J = 8.4, H-3′), 11.75 (1H, s, NH).

***N*-Tauryl-*N*-deacetyllappaconitine (9).** Yield 71%. High-resolution mass spectrum, *m/z* 648.2953 $[M - H]^-$, calcd 648.2949. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 648 ($(M - 1)^+$, 0.3), 634 ($(M - 15)^+$, 0.2), 618 ($(M - 31)^+$, 6). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1674 (NHSO), 1130–1080 (C–O). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.10 (3H, t, J = 7.2, $C\underline{H}_3CH_2N$), 1.56 (1H, m, J = 14.9, 8.3, H_a-6), 1.83 (1H, m, H_a-3), 1.97 (1H, m, H_a-12), 2.01 (1H, m, J = 15.0, 7.4, H_a-15), 2.10 (1H, m, J = 4.5, H-10), 2.16 (1H, m, H-7), 2.19 (1H, m, H_a-2), 2.28 (1H, m, H_b-2), 2.39 (1H, m, H-13), 2.39 (1H, m, H_b-15), 2.42 (1H, m, H-5), 2.50 (1H, m, H_b-12), 2.52 (1H, m, $CH_3C\underline{H}_aN$), 2.53 (1H, d, J = 11.3, H_a-19), 2.58 (1H, m, $CH_3C\underline{H}_bN$), 2.62 (1H, m, H_b-3), 2.68 (1H, dd, J = 14.9, 7.4, H_b-6), 3.00 (1H, s, H-17), 3.19 (1H, m, H-1), 3.21 (2H, m, $SO_2CH_2C\underline{H}_2$), 3.28 (3H, s, 1-OCH_3), 3.29 (2H, m, $SO_2C\underline{H}_2CH_2$), 3.30 (1H, m, H-16), 3.31 (3H, s, 16-OCH_3), 3.41 (3H, s, 14-OCH_3), 3.44 (1H, d, J = 4.5, H-14), 3.56 (1H, d, J = 11.3, H_b-19), 7.07 (1H, t, J = 7.4, H-5′), 7.50 (1H, t, J = 7.0, H-4′), 7.69 (1H, d, J = 8.3, H-3′), 7.93 (1H, d, J = 6.7, H-6′).

***N*-{2-[2-(1,3-Dioxoisoindolin-2-yl)ethylsulfamido]acetyl}-*N*-deacetyllappaconitine (10).** A solution of **8** (0.3 mmol) in CH_2Cl_2 (10 mL) was treated with 2-phthalylethanesulfonyl chloride (**4**, 0.3 mmol) and Et_3N (0.05 mL), stirred, and refluxed for 2 h. The product **10** was purified by CC over SiO_2 using $CHCl_3$–MeOH (99:1). Yield 65%. High-resolution mass spectrum, *m/z* 836.3223 $[M]^+$. Calcd 836.3226. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 836 (M^+, 0.1), 821 ($(M - 15)^+$, 0.1), 805 ($(M - 31)^+$, 0.2). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1684 (NHCO), 1130–1080 (C–O). ^1H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.12 (3H, t, J = 7.1, $C\underline{H}_3CH_2N$), 1.57 (1H, dd, J = 14.8, 8.3, H_a-6), 1.80 (1H, m, H_a-3), 2.00 (1H, m, H_a-12), 2.01 (1H, m, H_a-15), 2.09 (1H, m, H-10), 2.16 (1H, m, H-7), 2.18 (1H, m, H_a-2), 2.29 (1H, m, H_b-2), 2.37 (1H, m, H-13), 2.39 (2H, m, H-5, H_b-15), 2.50 (2H, m, H_b-12, $CH_3C\underline{H}_aN$), 2.56 (1H, m, $CH_3C\underline{H}_bN$), 2.59 (1H, d, J = 10.6, H_a-19), 2.64 (1H, m, H_b-3), 2.69 (1H, m, H_b-6), 3.00 (1H, s, H-17), 3.18 (1H, m, H-1), 3.29 (3H, s, 1-OCH_3), 3.31 (1H, m, H-16; 3H, s, 16-OCH_3), 3.40 (3H, s, 14-OCH_3), 3.43 (1H, d, J = 4.6, H-14), 3.50 (2H, m, $SO_2C\underline{H}_2CH_2$), 3.58 (1H, d, J = 10.6, H_b-19), 4.13 (2H, s, J = 3.1, $COCH_2$), 4.36 (2H, m, $SO_2CH_2C\underline{H}_2$), 7.03 (1H, t, J = 7.7, H-5′), 7.48 (1H, t, J = 7.8, H-4′), 7.63 (1H, d, J = 7.9, H-3′), 7.70 (2H, m, H-2″, 5″), 7.80 (2H, m, H-3″, 4″), 7.89 (1H, d, J = 8.0, H-6′), 10.67 (1H, s, NH).

***N*-[2-(2-Aminoethylsulfamido)acetyl]-*N*-deacetyllappaconitine (11).** Yield 70% (total for two steps). High-resolution mass spectrum, *m/z* 705.1184 $[M - H]^-$, calcd 705.1179. Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %):

705 ((M – 1)$^+$, 0.3), 691 ((M – 15)$^+$, 0.2), 675 ((M – 31)$^+$, 0.7). IR spectrum (KBr, ν, cm^{-1}): 3600–3200 (OH), 1684 (NHCO), 1130–1080 (C–O). ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.13 (3H, t, J = 7.1, $C\underline{H}_3CH_2N$), 1.57 (1H, dd, J = 14.9, 8.3, H_a-6), 1.85 (1H, m, H_a-3), 1.98 (1H, m, H_a-12), 2.04 (1H, m, H_a-15), 2.09 (1H, m, H-10), 2.17 (1H, m, H-7), 2.19 (1H, m, H_a-2), 2.28 (1H, m, H_b-2), 2.37 (1H, m, H-13), 2.40 (1H, m, H_b-15), 2.43 (1H, m, H-5), 2.50 (2H, m, H_b-12, $CH_3C\underline{H}_aN$), 2.56 (1H, m, $CH_3C\underline{H}_bN$), 2.57 (1H, d, J = 11.3, H_a-19), 2.62 (1H, m, H_b-3), 2.69 (1H, m, J = 14.9, 7.3, H_b-6), 3.01 (1H, s, H-17), 3.19 (1H, m, H-1), 3.30 (3H, s, 1-OCH_3), 3.32 (1H, m, H-16; 3H, s, 16-OCH_3; 2H each, m, $SO_2C\underline{H}_2CH_2$, $SO_2CH_2C\underline{H}_2$), 3.41 (3H, s, 14-OCH_3), 3.44 (1H, d, J = 4.6, H-14), 3.57 (1H, d, J = 11.3, H_b-19), 4.07 (2H, s, $COCH_2$), 7.10 (1H, t, J = 15.2, 7.6, H-5′), 7.51 (1H, t, J = 14.9, 7.4, H-4′), 7.69 (1H, d, J = 8.3, H-3′), 7.90 (1H, d, J = 7.6, H-6′), 11.43 (1H, s, NH).

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REFERENCES

1. V. E. Romanov, E. E. Shul′ts, M. M. Shakirov, and G. A. Tolstikov, *Chem. Nat. Compd.*, **44**, 346 (2008).
2. J. P. Greenstein and M. Winitz, *Chemistry of the Amino Acids*, 3 Vols., John Wiley & Sons, New York, 1961.
3. R. Winterbottom, J. W. Clapp, W. H. Miller, J. P. English, and R. O. Roblin, Jr., *J. Am. Chem. Soc.*, **69**, 1393 (1947).
4. T. M. Gabbasov, E. M. Tsyrlina, and S. G. Yunusova, *Chem. Nat. Compd.*, **54**, 947 (2018).