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Ethynylation of Lappaconitine as a Route to Modification of Alkaloids

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Abstract

Methods of the synthesis of a new group of acetylenic derivatives of lappaconitine were developed using Sonogashira reaction, starting from 5′-iodolappaconitine and terminal acetylenes in the system $Pd(PPh_3)_2Cl_2$–CuI–Et_3N. Terminal 1,3-butadiyne was introduced into lappaconitine molecule for the first time.

Key words: Sonogashira reaction, new groups of acetylenic derivatives of lappaconitine, terminal 1,3-butadiyne

INTRODUCTION

Due to the synthesis transformations of the metabolites of plant and microbial origin, allowing the introduction of highly efficient medical preparations into practical medicine, this direction of organic synthesis has become one of the most important areas of modern medical chemistry [1–3]. Studying the structures of natural metabolites one cannot but notice that more and more frequently the compounds are revealed the molecules of which contain two or more structural fragments of different types [4–6]. This defines the urgent character of the area involving metabolite transformation, which combines design and synthesis of conjugates containing the blocks of different nature.

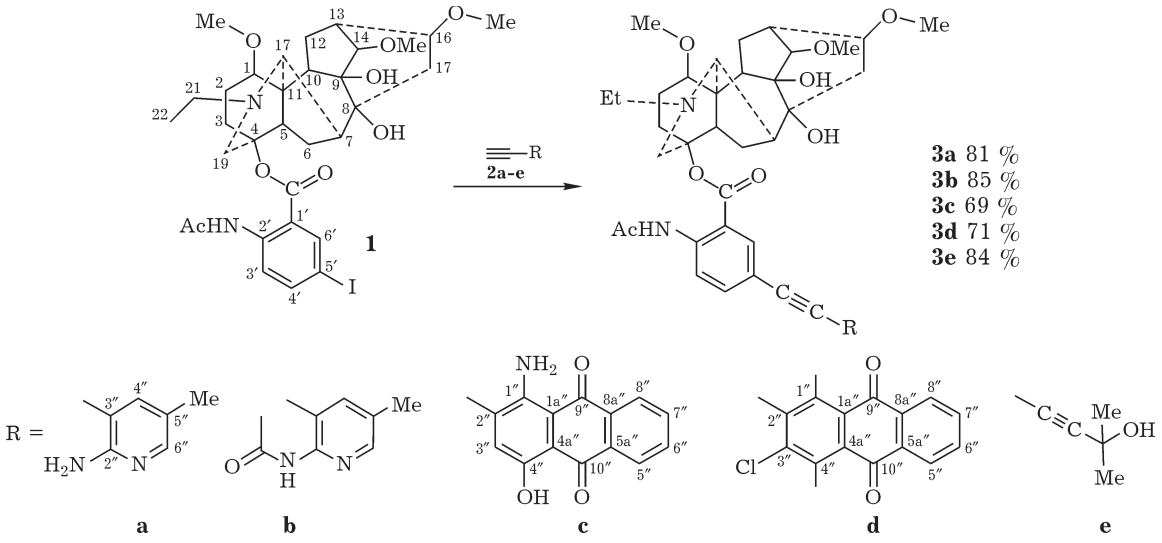
For example, the following hybrids have been described: steroid – antibiotic [7], steroid – nucleoside [8], triterpenoid – peptide, triterpenoid – phenol acids [9].

RESULTS AND DISCUSSION

The subject under investigation was the transformations of diterpenoid alkaloid lappaconitine which is formed in the plants of *Aconitum* genus, widespread in the regions of Siberia, the Altay and the Urals. According to the data reported in [10], at the territory of the southern Urals and Bashkortostan alone, the roots of *A. septentrionale* Koelle may be harvested in the amount sufficient for the establishment of large-scale production of lappaconitine, without detriment to ecology. It is known [11] that antiarrythmic preparation allapinine was developed on the basis of the hydrobromide of an alkaloid. However, it is quite possible that the pharmacological potential of lappaconitine is not limited to this kind of activity. Modification of its structure can reveal new properties. We have extended the approach to lappaconitine modification based on the synthesis of acetylene-containing derivatives [11, 12] to the introduction of the fragments of pyridine and 9,10-anthraquinone types.

In this connection, we carried out the synthesis of a new series of alkynyl-substituted lappaconitines by means of the cross-coupling of 5′-iodolappaconitine **1** with corresponding terminal acetylenes **2a–e** (Scheme 1).

It should be stressed that the realization of cross-coupling under the conditions of Pd–Cu catalyzed reaction was not evident in view of the polyfunctional character of the initial molecule and the presence of a voluminous alicy-



Scheme 1.

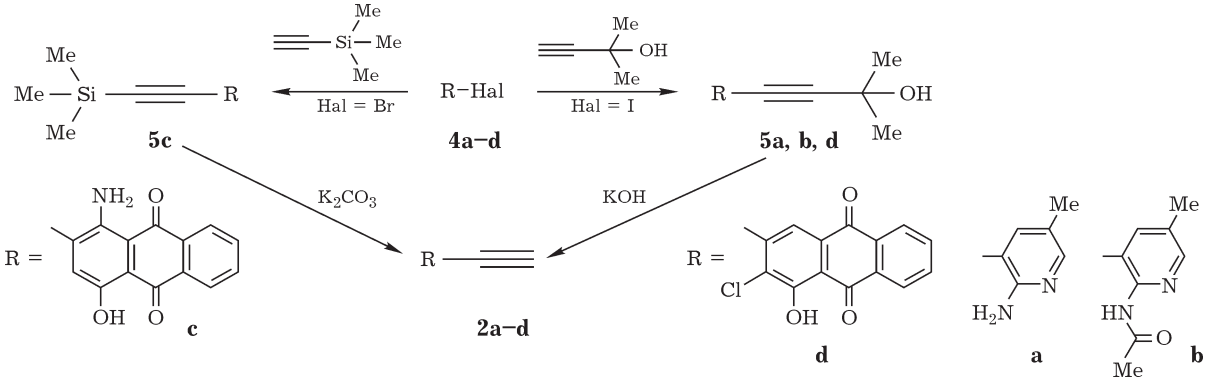
clic group overhanging above the aromatic residue. Nevertheless, the target twice-substituted acetylenes **3a–e** were obtained under the standard conditions of Sonogashira reaction in the system $Pd(PPh_3)_2Cl_2$–CuI–Et_3N in toluene [13, 14] with a high yield (70–85 %). The structure of terminal acetylenes **2a–e** weakly affects the duration of reaction which lasts for 1–2 h.

It was reported previously that high anticancer activity was discovered in natural and synthetic diacetylenic derivatives [15, 16]. Among them, important place is occupied by conjugated butadiynyl carbinols [17]. In this connection, we introduced a diacetylenic fragment into the molecule, with the yield of compound **3e** equal to 84 %.

It must be noted that the direct introduction of 1,3-butadiynyl group into the aromatic nucleus according to Sonogashira reaction is a non-trivial problem due to the instability of the molecules of terminal diacetylenes [18].

For the synthesis of terminal 1,3-butadiyn-1-hydroxy-2-methylhexa-3,5-diyne **2e**, we used the procedure previously improved by us. It involves cleavage of diacetylenic alcohol [19]. The use of high-boiling (non-volatile) *m*-pentaphenyl ether as a solvent minimizes tarring of labile diacetylene and increases the yield of the target 1,3-diyne **2e** up to 93 %. The previous procedure (without the use of the solvent) allowed one to obtain the product with the yield 56 % [20].

Initial terminal acetylenes were synthesized from the corresponding bromo- and iodoarenes **4a–d** by cross-coupling with dimethylethynylcarbinol followed by decomposition of the formed tertiary acetylenic alcohols **5a**,**b**,**d** according to the back Favorsky reaction [21] (Scheme 2).



Scheme 2.

However, in the case of 1-amino-2-ethynyl-4-hydroxyanthraquinone, at the final stage strong tarring occurred instead of the expected formation of the product of elimination of acetylenic alcohol. The use of trimethylsilyl derivative **5c** allowed us to obtain the target terminal acetylene **2c** (99 %). The latter was introduced into the reaction of cross-coupling with iodide **I**.

The structure of the compounds was proved on the basis of the data of elemental analysis, IR, ^{1}H, ^{13}C NMR and high-resolution mass spectra.

EXPERIMENTAL

The IR spectra of the compounds were recorded on a Bruker Vector 22 spectrometer in KBr tablets. NMR spectra were measured on a Bruker AV-400 spectrometer (400.13 MHz) in $CDCl_3$ or in DMSO-D_6. Mass spectra were recorded on a Thermo Scientific DFS (Double Focusing Sector Mass Spectrometer) of Thermo Electron Corporation by means of the direct injection (temperature of ionization in chamber: 220–270 °C, ionization voltage 70 eV). Chromatographic examination was made using Merck 60 silica gel (0.063–0.2 mm) and Al_2O_3 (0.05–0.15 mm, TU 6-09-3916–75, Russia) of the II degree of activity according to Brockman, the TLC control was performed with Silufol 60 F254 plates.

In connection with the complicacy of assignment of the signals from hydrogen atoms of the polycyclic frame of lappaconitine molecule, only characteristic signals are indicated in ^{1}H NMR spectra of compounds **3a–e.**

1-Amino-2-(trimethylsilyl)ethynyl-4-hydroxy-9,10-anthraquinone (5c). To the solution of 2.47 g (7.76 mmol) of 1-amino-2-bromo-4-hydroxy-9,10-anthraquinone **4c** in 100 mL of benzene in argon flow, we add sequentially 20 mg of CuI, 20 mg of $Pd(PPh_3)_2Cl_2$, 6 mL of Et_3N and 1.7 mL (9.73 mmol) of trimethylsilylacetylene. Then the mixture is heated to 42 °C and mixed for 6 h. The reaction mixture without cooling is filtered through the layer of Al_2O_3 (2.5 × 0.5 cm), the column is washed with benzene. The solvent is removed in vacuum. The precipitate is filtered through the layer of Al_2O_3 (2.5 × 6 cm), layer of SiO_2 (2.5 × 2 cm) and activated carbon (2.5 × 3 cm), elutriated with toluene. The solvent is removed in vacuum. The product is 2.06 g (79 %) of compound **5c**, m. p. 143–146 °C. ^{1}H NMR spectrum (δ, ppm; *J*, Hz): 0.34 (t, 9H, $(CH_3)_3$); 7.32 (s, 1H, 3-H); 7.75–7.80 (m, 2H, 5-, 8-H); 8.30–8.35 (m, 2H, 6-, 7-H); 13.33 (s, 1H, OH). IR spectrum (KBr), ν, cm^{-1}: 1629 (C=O), 1249 (C≡C), 2954 (CH_3), 3433 and 3468 (NH_2).

1-Amino-2-ethynyl-4-hydroxy-9,10-anthraquinone (2c). To the solution of 2.06 g (6.13 mmol) of 1-amino-2-(trimethylsilyl)ethynyl-4-hydroxy-9,10-anthraquinone **5c** in 16 mL of methanol, we add 0.09 g (0.65 mmol) of potash and mix for 2 h at room temperature. Then 30 mL of water is added to the reaction mixture, and the formed precipitate is filtered through Schott filter. The humid precipitate is dried at a temperature of 49 °C for 24 h to the constant mass. The product is 1.59 g (99 %) of compound **2c**, m. p. 212–214 °C. Mass spectrum, found: *m/z* 263.0578 $[M]^+$. $C_{16}H_9N_1O_3$. Calculated: 263.0577. ^{1}H NMR spectrum (δ, ppm; *J*, Hz): 7.81 (m, 2H, 5-, 8-H); 8.05 (s, 1H, 3-H); 8.24 (m, 2H, 6-, 7-H); 12.90 (br. s, 1H, OH). IR spectrum (KBr), ν, cm^{-1}: 1626 (C=O), 2104 (C≡C), 3278 (≡C–H), 3406 (NH_2).

2-Chloro-3-(3-hydroxy-3-methylbut-1-ynyl)-9,10-anthraquinone (5d). To the solution of 4.04 g (10.96 mmol) of 2-iodo-3-chloro-9,10-anthraquinone **4d** in 50 mL of benzene in argon flow, we add sequentially 20 mg of CuI, 20 mg of $Pd(PPh_3)_2Cl_2$, 3 mL of Et_3N and 1.2 mL (12.4 mmol) of dimethylethynylcarbinol. Then the mixture is heated to boiling and mixed for 11 h. The reaction mixture without cooling is filtered through the layer of Al_2O_3 (2.5×0.5 cm), elution with ethyl acetate is carried out. The solvent is removed in vacuum. The precipitate is recrystallized from benzene. The product is 3.19 g (90 %) of compound **5d**, m. p. 172–173 °C. Mass spectrum, found: *m/z* 324.05676 $[M]^+$. $C_{19}H_{13}ClO_3$. Calculated: 324.05532. ^{1}H NMR spectrum (δ, ppm; *J*, Hz): 1.66 (s, 6H, $(CH_3)_2$); 2.12 (s, 1H, OH); 7.80 (m, 2H, 5-, 8-H); 8.2–8.3 (m, 2H, 6-, 7-H); 8.27 (d, 1H, 1-H, J = 0.4) and 8.33 (d, 1H, 4-H, J = 0.4). IR spectrum (KBr), ν, cm^{-1}: 1660 and 1675 (C=O), 2212 (C≡C), 2983 (CH_3) and 3492 (OH).

2-Ethynyl-3-chloro-9,10-anthraquinone (2d). To the solution of 1.41 g (4.35 mmol) of 2-chloro-3-(3-hydroxy-3-methylbut-1-ynyl)-9,10-an-

thraquinone **5d** in 15 mL of dry toluene, we add 0.32 g (5.70 mmol) of calcined KOH and heat to boiling mixing for 5 h. After the reaction is over, we add 10 mL of water to the mixture and perform extraction with 300 mL of toluene. The organic layer is dried above sodium sulphate, filtered and evaporated dry. The residue is sublimed at 190 °C, 2 mm Hg. The product is 0.86 g (74 %) of compound **2d**, m. p. 246–247 °C. Mass spectrum, found: m/z 266.0134 $[M]^+$. $C_{16}H_7ClO_2$. Calculated: 266.0135. ^{1}H NMR spectrum (δ, ppm; J, Hz): 3.64 (s, 1H, ≡CH); 7.79–7.84 (m, 2H, 5-, 8-H); 8.27–8.33 (m, 2H, 6- and 7-H); 8.31 (s, 1H, 4-H); 8.43 (d, 1H, 1-H, J = 3). IR spectrum (KBr), ν, cm^{-1}: 1680 (C=O), 2113 (C≡C) and 3273 (≡C–H).

4β-{2-Acetylamino-5-[(1-amino-4-hydroxy-9,10-anthranyl-2-yl)ethynyl]benzoyloxy}-1α,14α,16β -trimethoxy-20-ethylaconitane-8,9-diol (3c). To the solution of 1.07 g (1.5 mmol) of 5′-iodolappaconitine **1** in 30 mL of toluene in argon flow, we add sequentially 5 mg of CuI, 5 mg of $Pd(PPh_3)_2Cl_2$, 1 mL of Et_3N and 0.43 g (1.63 mmol) of 1-amino-2-ethynyl-4-hydroxy-9,10-anthraquinone **2c** and mix at 80 °C for 1.5 h. The hot reaction mixture is filtered through the layer of Al_2O_3 (1 × 0.5 cm), elution with toluene is carried out. The solvent is removed in vacuum. The oily residue is levigated with 20 mL of ether. The formed precipitate is filtered. The raw product, 1.27 g, is recrystallized from toluene with subsequent precipitation with light petroleum. Preparative TLC is applied to purify the product: the thickness of Al_2O_3 layer is 2 mm, the length of the start strip is 28 cm, eluting agent is ethyl acetate. The strip of the sorbent having a red-violet colour is collected. The product is elutriated from the sorbent with ethyl acetate. The solvent is removed in vacuum. The product is 0.88 g (69 %) of compound **3c**, m. p. 149–168 °C. Elemental analysis, calculated: C 68.15, H 6.08, N 4.97. Found, %: C 68.43, H 6.75, N 5.01. $C_{48}H_{51}N_3O_{11}$. ^{1}H NMR spectrum (δ, ppm; J, Hz): 1.15 (t, 3H, C(22)Me, J = 7); 2.27 (s, 3H, $COCH_3$); 3.0 (br.s, 1H, 17-H); 7.45 (s, 1H, 3″-H); 7.69 (dd, 1H, 4′-H, J = 9, J = 2); 7.7–7.8 (m, 2H, 6″- and 7″-H); 8.11 (d, 1H, 6′-H, J = 2); 8.3–8.4 (m, 2H, 5″- and 8″-H); 8.78 (d, 1H, 3′-H, J = 9); 11.21 (s, 1H, NH); 13,41 (s, 1H, OH). ^{13}C NMR spectrum (δ, ppm): 83.4 (C1), 26.5 (C2), 31.7 (C3), 85.4 (C4), 48.3 (C5), 24.1 (C6), 47.5 (C7), 75.4 (C8), 78.5 (C9), 49.7 (C10), 50.9 (C11), 26.1 (C12), 36.2 (C13), 90.0 (C14), 44.7 (C15), 82.7 (C16), 61.3 (C17), 55.3 (C19), 48.8 (C21), 13.4 (C22), 56.4 (1-OCH_3), 57.8 (14-OCH_3), 56.0 (16-OCH_3), 115.3 (C1′), 142.2 (C2′), 120.2 (C3′), 137.1 (C4′), 115.7 (C5′), 134.0 (C6′), 166.3 (COO), 25.4 ($\underline{C}H_3CO$), 169.0 ($CH_3\underline{C}O$), 83.4 and 99.3 (C=C), 182.8 and 186.9 (two C=O (9″ and 10"), 155.8 (C1″), 129.5 (C3″), 146.1 (C4″), 126.2 and 126.7 (C5″ and C8″), 134.0 and 132.7 (C6″ and C7″), 108.9, 113.7, 115.34, 121.3 and 134.6 (C1a″, C4a″, C5a″, C8a″ and C2″). IR spectrum (KBr), ν, cm^{-1}: 1588 and 1627 (C=O); 2104 (C≡C); 2921 (CH_3) and 3405 (NH).

4β-{2-Acetylamino-5-[(2-amino-5-methylpyridyl-3-yl)ethynyl]benzoyloxy}-1α,14α,16β-trimethoxy-20-ethylaconitane-8,9-diol (3a) is synthesized similarly to **3c** (1 h, 80 °C). The yield is 0.58 g (81 %) of compound **3a**, m. p. 121–126 °C. Elemental analysis, calculated, %: C 67.21, H 7.05, N 7.84. Found, %: C 67.21, H 7.15, N 7.43. $C_{40}H_{50}N_4O_8$. Mass spectrum, found: m/z 714.3595 $[M]^+$. $C_{40}H_{50}N_4O_8$. Calculated: 714.3623. ^{1}H NMR spectrum (δ, ppm; J, Hz): 1.11 (t, 3H, C(22)Me, J = 7); 2.19 (s, 3H, $COCH_3$); 2.46 (s, 3H, C5"CH_3) 3.00 (s, 1H, 17-H)); 3.19 (dd, 1H, 1-H, J = 10, J = 7); 3.28, 3.30 and 3.40 (all the s, on 3H, 1-, 16-, and 14-OMe, respectively; 3.42 (d, 1H, 14-H, J = 4); 4.97 (s, 2H, NH_2); 7.49 (d, 1H, 4″-H, J = 1.5); 7.60 (dd, 1H, 4′-H, J = 9, J = 2); 7.87 (d, 1H, 6″-H, J = 1.5); 8.04 (d, 1H, 6′-H, J = 2); 8.72 (d, 1H, 3′-H, J = 9) and 11.16 (s, 1H, NH). ^{13}C NMR spectrum (δ, ppm): 84.2 (C1), 26.9 (C2), 31.9 (C3), 85.5 (C4), 48.7 (C5), 24.3 (C6), 47.8 (C7), 75.7 (C8), 78.8 (C9), 50.1 (C10), 51.2 (C11), 26.4 (C12), 36.5 (C13), 90.2 (C14), 44.8 (C15), 83.0 (C16), 61.6 (C17), 55.5 (C19), 49.1 (C21), 13.7 (C22), 56.7 (1-OCH_3), 58.1 (14-OCH_3), 56.3 (16-OCH_3), 116.0 (C1′), 142.2 (C2′), 120.5 (C3′), 137.2 (C4′), 116.6 (C5′), 134.5 (C6′), 166.8 (COO), 25.7 ($\underline{C}H_3CO$), 169.3 ($CH_3\underline{C}O$), 94.0 and 102.4 (C≡C), 149.4 C2″, 122.3 C3″, 140.6 C4″, 84.5 C5″, 147.9 C6″, 17.7 C5″$\underline{C}H_3$. IR spectrum (KBr), ν, cm^{-1}: 1684 and 1701 (C=O); 2207 (C≡C); 2818 (OCH_3), 2925; 3306 (CONH) and 3388 (NH).

4β-{2-Acetylamino-5-[(2-aminoacetyl-5-methylpyridyl-3-yl)ethynyl]benzoyloxy}-1α,14α,16β-trimethoxy-20-ethylaconitane-8,9-diol (3b) is synthesized similarly to **3c** (2 h, 70 °C). The yield is 0.32 g (85 %) of compound

3b, m. p. 134–146 °C. Mass spectrum, found: *m/z* 756.3730 $[M]^+$. $C_{42}H_{52}N_4O_9$. Calculated: 756.3729. ^{1}H NMR spectrum (δ, ppm; *J*, Hz): 1.11 (t, 3H, C(22)Me, *J* = 7); 2.23 (s, 3H, $COCH_3$); 2.28 (s, 3H, $COCH_3$); 2.46 (s, 3H, CH_3); 3.00 (s, 1H, 17-H); 3.17 (dd, 1H, 1-H, *J* = 10, *J* = 7); 3.31, 3.33 and 3.43 (all the s, on 3H, 1-, 16-, and 14-OMe, respectively; 7.60 (dd, 1H, 4′-H, *J* = 8, *J* = 2); 7.67 (d, 1H, 6″-H, *J* = 2); 8.07 (d, 1H, 6′-H, *J* = 2); 8.17 (d, 1H, 4″-H, *J* = 2); 8.74 (d, 1H, 3′-H), *J* = 8); 11.19 (s, 1H, NH). ^{13}C NMR spectrum (δ, ppm): 84.2 (C1), 26.9 (C2), 31.9 (C3), 85.5 (C4), 48.7 (C5), 24.3 (C6), 47.8 (C7), 75.7 (C8), 78.8 (C9), 50.1 (C10), 51.2 (C11), 26.4 (C12), 36.5 (C13), 90.2 (C14), 44.8 (C15), 83.0 (C16), 61.6 (C17), 55.5 (C19), 49.1 (C21), 13.7 (C22), 56.7 (1-OCH_3), 58.1 (14-OCH_3), 56.3 (16-OCH_3), 116.0 (C1′), 142.2 (C2′), 120.5 (C3′), 137.2 (C4′), 116.1 (C5′), 134.5 (C6′), 166.8 (COO), 25.7 ($\underline{C}H_3CO$), 169.3 ($CH_3\underline{C}O$), 83.2 and 96.5 (C≡C), 149.4 (C2″), 128.6 (C3″), 141.2 (C4″), 116.1(C5″) 147.9 (C6″), 17.7 (C5″$\underline{C}H_3$). IR spectrum (KBr), ν, cm^{-1}: 1584, 1684, 1701 (C=O); 2207 (C≡C) and 2925 (CH_3).

4β-{2-Acetylamino-5-[(3-chloro-9,10-anthranyl-2-yl)ethynyl]benzoyloxy}-1α,14α,16β-trimethoxy-20-ethyl-aconitane-8,9-diol (3d) is synthesized similarly to **3c** (1 h, 80 °C). The yield is 0.3 g (71 %) of compound **3d**, m. p. 148–156 °C. Elemental analysis, calculated, %: C 67.88, H 5.81, N 3.30, Cl 4.17. Found, %: C 67.87, H 5.89, N 2.79, Cl 4.08. $C_{48}H_{49}ClN_2O_{10}$. ^{1}H NMR spectrum (δ, ppm; *J*, Hz): 1.12 (t, 3H, C(22)Me, *J* = 7); 2.23 (s, 3H, $COCH_3$); 3.02 (s, 1H, 17-H); 3.20 (dd, 1H, 1-H, *J* = 10, *J* = 7); 3.29, 3.30 and 3.40 (all the s, on 3H, 1-, 16-, and 14-OMe, respectively; 3.43 (d, lH, 14-H, *J* = 5); 7.69 (dd, 1H, 4′-H, *J* = 9, *J* = 2); 7.78–7.80 (m, 2H, 5″- and 8″-H); 8.12 (d, 1H, 6′-H, *J* = 2); 8.28–8.30 (m, 2H, 6"- and 7"-H); 8.32 and 8.45 (both s, on 1H, 1″- and 4″-H); 8.73 (d, 1H, 3′-H, *J* = 9) and 11.14 (s, 1H, NH). ^{13}C NMR spectrum (δ, ppm): 84.0 (C1), 26.7 (C2), 31.7 (C3), 85.4 (C4), 48.2 (C5), 24.1 (C6), 47.5 (C7), 75.5 (C8), 78.4 (C9), 49.7 (C10), 50.9 (C11), 26.1 (C12), 36.2 (C13), 90.0 (C14), 44.7 (C15), 82.8 (C16), 61.4 (C17), 55.4 (C19), 48.8 (C21), 13.4 (C22), 56.4 (1-OCH_3), 57.8 (14-OCH_3), 56.0 (16-OCH_3), 115.6 (C1′), 142.3 (C2′), 120.2 (C3′), 137.4 (C4′), 115.7 (C5′), 134.2 (C6′), 166.5 (COO), 25.4 ($\underline{C}H_3CO$), 169.0 ($CH_3\underline{C}O$), 94.0 and 102.4 (C≡C), 181.5 and 181.4 (two C=O (9″ and 10″), 128.8, 131.3, 132.7, 133.2 (8″a, 5″a, 4″a and 1″a), 127.2, 127.7, 128.1, 131.9, 134.2, 134.7 (1″, 4″, 5″, 6″, 7″ and 8″), 133.1 and 141.8 (2″ and 3″). IR spectrum (KBr), ν, cm^{-1}: 1679 and 1707 (C=O); 2211 (C≡C); 2817 (O–CH_3), 2923 (CH_3); 3473 (NH).

4β-[2-Acetylamino-5-[(5-hydroxy-5-methylhexa-1,3-diynyl)benzoyloxy]-1α,14α,16β-trimethoxy-20-ethylaconitane-8,9-diol (3e) is synthesized similarly to **3c** (1.5 h, 45 °C). The yield is 1.17 g (84 %) of compound **3e**, m. p. 151–156 °C. Mass spectrum was recorded on a Bruker microTOF-Q 103, ES negative scan 100–2000 in MeOH. Found: *m/z* 689.3418 $[M-H^+]$. $C_{39}H_{50}N_2O_9$. Calculated: *M* = 690.3511. ^{1}H NMR spectrum (δ, ppm; *J*, Hz): 1.14 (t, 3H, C(22)Me, *J* = 7); 1.59 (s, 6H, $(CH_3)_2$), 2.23 (s, 3H, $COCH_3$); 3.02 (s, 1H, 17-H); 3.20 (dd, 1H, 1-H, *J* = 10, *J* = 7); 3.30, 3.32 *и* 3.42 (all the s, on 3H, 1-, 16-, and 14OMe, respectively; 3.46 (d, lH, 14-H, *J* = 5); 7.57 (dd, 1H, 4'-H, *J* = 9, *J* = 2); 8.01 (d, 1H, 6'-H, *J* = 2); 8.67 (d, 1H, 3'-H, *J* = 9) and 11.17 (s, 1H, NH). ^{13}C NMR spectrum (δ, ppm): 84.3 (C1), 27.0 (C2), 32.0 (C3), 85.6 (C4), 48.5 (C5), 24.3 (C6), 47.7 (C7), 75.8 (C8), 78.7 (C9), 50.0 (C10), 51.2 (C11), 26.4 (C12), 36.5 (C13), 90.3 (C14), 45.0 (C15), 83.1 (C16), 61.7 (C17), 55.6 (C19), 49.1 (C21), 13.7 (C22), 56.7 (1-OCH_3), 58.1 (14-OCH_3), 56.3 (16-OCH_3), 115.6 (C1′), 142.3 (C2′), 120.4 (C3′), 138.0 (C4′), 115.9 (C5′), 135.5 (C6′), 166.7 (COO), 25.7 ($\underline{C}H_3CO$), 169.3 ($CH_3\underline{C}O$), 65.7, 73.5, 77.8 and 87.3 (carbon atoms of 1,3-butadiynyl fragment), 67.1 $\underline{C}(CH_3)_2$, 31.3 $C(\underline{C}H_3)_2$. IR spectrum (KBr), ν, cm^{-1}: 1686 and 1702 (C=O); 2143 and 2234 (C≡C and C≡C); 2820 (OCH_3), 2927 (CH_3) and 3398 (NH).

CONCLUSION

Thus, in the present work we describe the synthesis of a new group of lappaconitine derivatives containing acetylenic, pyridine and 9,10-anthraquinone residues. On the one hand, this allows one to expand the range of compounds for the examination of basic antiarrythmic activity of this alkaloid; on the other hand, this allows us to study the possibility of broadening their pharmacological range.

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