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SYNTHESIS AND STUDY OF ANTIOXIDANT ACTIVITY OF 5,7-DIALKYLDIAZAADAMANTANES CONTAINING CARBOXYLIC ACID FRAGMENTS

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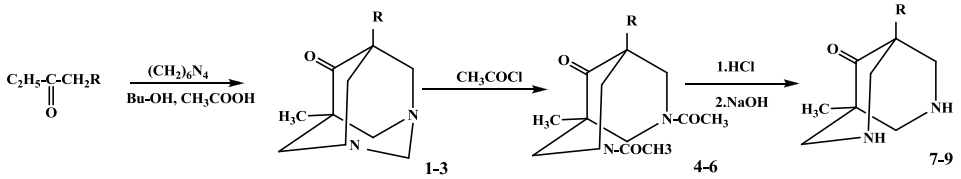
For the first time, 9-oxo-1-methyl-5-ethyl-(5-propyl-, 5-butyl)-3,7-diazabicyclo/3.3.1/-nonanes were synthesized. By condensation of the latter and 9-hydroxy-1,5-(dimethyl-, diethyl-, dipropopyl-, dibutyl)-3,7-diazabicyclo/3.3.1/nonanes with pyruvic or levulinic acid, new 2-substituted diazaadamantanes containing a carboxyl group were obtained. According to the results of biological tests, some compounds of this series have weak antioxidant activity.

References 7.

Our early works were devoted to the synthesis and study of the biological activity of some 2-substituted diazaadamantanes containing aromatic or aliphatic substituents at the 5th and 7th positions of the adamantane ring [1-4]. It was of interest to synthesize diazabicyclononanes with various radicals in these positions, such as methylethyl, methylpropyl and methylbutyl **7-9**. The synthesis was carried out according to Scheme 1.

Scheme 1



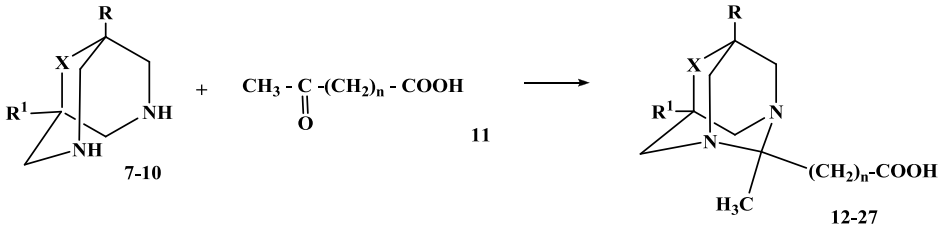
R = C_2H_5, C_3H_7, C_4H_9

Mannich reaction from ethylpropyl, ethylbutyl, ethylpentylketones, urotropine in butanol in the presence of acetic acid gave diazaadamantanes **1-3**, which were further converted by diacetyl chloride to diacetyl derivatives **4-6**. By acid hydrolysis and further alkaline treatment of **4-6,** 1-methyl-5-ethyl-, 1-

methyl-5-propyl-, 1-methyl-5-butyl-9-oxo-3,7-diazabicyclo/3.3.1/- nonanes **7-9** were synthesized**.**

The combination of compounds of the adamantane series with acid fragments is of great interest for the synthesis of new derivatives of various types. The antimicrobial and antibacterial activity of these compounds is known [5]. However, in the literature there are no data on diazadamantane acids. For the synthesis of such compounds, 5,7-dialkyl-substituted diazabicyclononanes **7-10** (compound **10** was obtained by reducing the keto group in the corresponding bicyclononanes with sodium borohydride) were condensed with pyruvic or levulinic acid. As a result, compounds **12-27** containing an acid fragment in the second position of the diazaadamantane ring were obtained (Scheme 2).

Scheme 2



X = O, R = R^1 = CH_3, n = 0 (12); R = R^1 = CH_3, n = 2 (13); R = R^1 = C_2H_5, n = 0 (14); R = R^1 =C_2H_5, n = 2 (15); R = CH_3, R^1 = C_2H_5, n = 2 (16); R = CH_3, R^1 = C_3H_7, n = 2 (17); R = R^1 = C_3H_7, n = 0 (18); R = R^1 = C_3H_7, n = 2 (19); R = CH_3, R^1 = C_4H_9, n = 2 (20); R = R^1 = C_4H_9, n = 2 (21); R = R^1 =iso-C_3H_7, n = 0 (22); X = OH, R = R^1 = CH_3, n = 2 (23); R = R^1 = C_2H_5, n = 0 (24); R = R^1 = C_2H_5, n = 2 (25); R = R^1 = C_3H_7, n = 2 (26); R = R^1 = C_6H_5, n = 2 (27).

The structure of the synthesized compounds was confirmed by elemental analysis, IR, ^1H and ^{13}C NMR spectra.

The antioxidant activity of the synthesized compounds was studied in rat brain tissue homogenates in experiments *in vitro* according to the method [6,7]. Lipid peroxidation was evaluated in a non-enzymatic lipid peroxidation system by the yield of one of the final products of malondialdehyde (MDA), which was determined by the ratio of the density of the studied substances to the control, expressed as a percentage. A sample with induced lipid peroxidation was used as a control.

Studies showed that the studied compounds did not exhibit a noticeable antioxidant effect. The highest activity was detected in compound **27** at a concentration of 10^{-3} M. The degree of influence of the latter led to inhibition of the lipid oxidation process in the form of a decrease in MDA by 28% ($P < 0.05$) compared to the control. A similar, but less pronounced effect was found in compounds **24** and **25** by 14, 18.5%, respectively, at the same concentration. The remaining compounds did not have a significant antioxidant effect. The data obtained indicate that among the studied compounds, only compounds having a

hydroxyl group in the diazaadamantane fragment exhibit a weak antioxidant effect.

Experimental part

IR spectra were recorded on a "Nicolet Avatar 330 FT-IR" spectrometer from samples dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian "Mercury-300VX" instrument at 303 *K* with a frequency of 300.078 and 75.46 *MHz*, respectively. In the assignment of signals, the methods of double resonance, DEPT and HMQC were used. Chemical shifts are given in ppm relative to the internal TMS for DMSO-d_6/CCl_4 1/3 solutions. The course of the reactions and the purity of the substances were controlled using thin-layer chromatography on "Silufol UV-254" plates using propanol-water (7:3) as eluent, spots were visualized by treatment with iodine vapor.

General procedure for the preparation of 5-methyl-7-ethyl, 5-methyl-7-propyl, 5-methyl-7-butyl-6-oxo-1,3-diazaadamantane (1-3). A mixture of 10 *mmol* of the corresponding ketone, 7.6 *mmol* of urotropine, 30 *ml* of n-butanol and 10 *ml* of acetic acid is boiled for 3 *h*. Butanol is then distilled off, the residue is recrystallized from hexane.

5-Methyl-7-ethyl-6-oxo-1,3-diazaadamantane (1). Yield 1.6 *g* (81%), R_f 0.42, mp 70-71°C. IR-spectrum, ν, cm^{-1}: 1710 (C = O). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.78-0.88 m (6H, 2×CH_3); 1.28 dd (2H, J = 5.8, 5.9 CH_2CH_3); 2.88 dd (4H, J = 7.0, 1.4, 2×NCH_2); 3.21 dd (4H, J = 13.8, 1.2, 2×NCH_2); 3.98 s (2H, NCH_2). Found, %: C 68.15; H 9.35; N 14.28. $C_{11}H_{18}N_2O$. Calculated, %: C 68.05; H 9.27; N 14.43.

5-Methyl-7-propyl-6-oxo-1,3-diazaadamantane (2). Yield 1.6 *g* (78%), R_f 0.41, mp 74-75°C. IR-spectrum, ν, cm^{-1}: 1710 (C=O). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.76-0.87 m (6H, 2×CH_3); 1.26 dd (4H, J = 5.9, 7.1 $CH_2CH_2CH_3$); 2.86 dd (4H, J = 7.1, 4.2, 2×NCH_2); 3.25 dd (4H, J = 13.8, 1.2, 2×NCH_2); 4.01 s (2H, NCH_2). Found, %: C 70.98; H 9.16; N 12.61. $C_{12}H_{20}N_2O$. Calculated, %: C 70.90; H 9.09; N 12.72.

5-Methyl-7-butyl-6-oxo-1,3-diazaadamantane (3). Yield 1.6 *g* (80%), R_f 0.47, mp 61°C. IR-spectrum, ν, cm^{-1}: 1708 (C = O). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.80-0.91 m (6H, 2×CH_3); 1.32 dd (6H, J = 7.1, 2.4, 3×CH_2); 2.84 dd (4H, J = 8.1, 2.4, 2×NCH_2); 3.26 dd (4H, J = 12.5, 2.4, 2×NCH_2); 4.01 s (2H, NCH_2). Found, %: C 70.80; H 9.17; N 12.63. $C_{13}H_{22}N_2O$. Calculated, %: C 70.91; H 9.10; N 12.73.

General procedure for the preparation of 1-methyl-5-ethyl (propyl, butyl)-9-oxo-3,7-diacetyldiazabicyclo/3.3.1/nonanes (4-6). To a solution of 9 *mmol* of the correspondingadamantane 1-3 in a mixture of 50 *ml* of benzene and 20 *ml* of water with stirring, 25 *mmol* of acetyl chloride is added dropwise at room temperature. The benzene layer is separated, washed with water, dried over $MgSO_4$ and distilled off. The residue is recrystallized from acetone.

1-Methyl-5-ethyl-9-oxo-3,7-diacetyldiazabicyclo/3.3.1/nonane (4). Yield 1.8 *g* (68%), R_f 0.61, mp 161°C. IR-spectrum, ν, cm^{-1}: 1637 (N-C = O). 1715 (C

= O). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.98 dd (6H, J = 6.9, 2.4 2×CH_3); 1.52 q (2H, CH_2); 2.05 s (6H, 2×$COCH_3$); 2.66 br.d (2H, J = 12.5, NCH_2); 3.34 ddd (2H, J = 5.8, 2.4, 1.2, NCH_2); 4.05 dd (2H, J = 5.9, 2.4, NCH_2); 4.96 ddd (2H, J = 5.8, 2.4, 1.2, NCH_2). ^{13}C NMR spectrum, ppm: 7.3 (2×CH_3); 15.9 (CH_2); 20.9 (CH_2); 23.2 (CH_2); 45.2 (CH_2); 47.3 (CH_2); 50.3 (C*); 52.3 (C*); 54.9 (C*); 56.8 (C*); 168.3 (C); 168.4 (C*); 210.7 (C*). Found, %: C 63.27; H 8.41; N 10.38. $C_{14}H_{22}N_3O_3$. Calculated, %: C 63.15; H 8.31; N 10.50.

1-Methyl-5-propyl-9-oxo-3,7-diacetyldiazabicyclo/3.3.1/nonane (5). Yield 2.1 *g* (77.7%), R_f 0.62, mp 168°C. IR-spectrum, ν, cm^{-1}: 1637 (N-C = O). 1715 (C = O). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.88-096 m (6H, 2×CH_3); 1.54 dd (4H, J = 5.8, 5.9, 2×CH_2); 2.1 s (6H, 2×$COCH_3$); 2.64 d (2H, J = 12.8, NCH_2); 3.32 ddd (2H, J = 5.8, 2.4, 1.2, NCH_2); 4.1 ddd (2H, J = 5.8, 5.9, 1.4, NCH_2); 4.98 ddd (2H, J = 5.8, 2.4, 1.2, 2×NCH_2). Found, %: C 67.72; H 9.20; N 9.68. $C_{16}H_{24}N_2O_3$. Calculated, %: C 67.6; H 9.11; N 9.80.

1-Methyl-5-butyl-9-oxo-3,7-diacetyldiazabicyclo/3.3.1/nonane (6). Yield 2.0 *g* (70.4%), R_f 0.63, mp 168°C (acetone). IR-spectrum, ν, cm^{-1}: 1637 (N-C = O). 1715 (C = O). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.86-094 m (6H, 2×CH_3); 1.58 dd (6H, J = 5.8, 5.9, 3×CH_2); 2.24 s (6H, 2×$COCH_3$); 2.68 br.d (2H, J = 12.9, NCH_2); 3.31 ddd (2H, J = 5.8, 2.4, 1.2, NCH_2); 4.2 ddd (2H, J = 5.8, 5.9, 1.4, NCH_2); 4.96 ddd (2H, J = 5.8, 2.4, 1.2, NCH_2). Found, %: C 65.42; H 8.96; N 9.38. $C_{16}H_{26}N_3O_3$. Calculated, %: C 65.3; H 8.80; N 9.5.

General procedure for the preparation of 1-methyl-5-(ethyl, propyl, butyl)-9-oxo-3,7-diazabicyclo/ 3.3.1 /nonane (7-9). 5 *mmol* of diacetyl **(4-6)** and 25 *ml* of 4N HCL are boiled for 5 *h*. After cooling, the precipitated crystals are filtered off, dissolved in a small amount of ice water, and neutralized with NaOH to pH 9, after cooling, the precipitate is filtered, washed with a small amount of ice water and recrystallized from ethyl acetate. 1,5-Dimethyl-(dipropyl-, diethyl-, -diphenyl)-9-hydroxy-3,7-diazabicyclo /3.3.1/nonanes **10** were obtained according to the procedure [3].

1-Methyl-5-ethyl-9-oxo-3,7-diazabicyclo/3.3.1/nonane (7). Yield 1.2 *g* (82%), R_f 0.32, mp 40-41°C. IR-spectrum, ν, cm^{-1}: 1715 (C = O), 3354 (NH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.78 s (3H, CH_3); 0.82 t (3H, J = 7.1, CH_2CH_3); 1.31 q (2H, CH_2CH_3, J = 8.1, NCH_2); 2.78 br.d (4H, J = 12.5, 2×NCH_2); 3.01 br.s (2H, NH); 3.35 ddd (2H, J = 5.8, 5.9, 1.4, 2×NCH_2). Found, %: C 66.05; H 9.70; N 15.30. $C_{10}H_{18}N_2O$. Calculated, %: C 65.93; H 9.80; N 15.38.

1-Methyl-5-propyl-9-oxo-3,7-diazabicyclo/3.3.1/nonane (8). Yield 1.5 *g* (76.3%), R_f 0.33, mp 71-72°C. IR-spectrum, ν, cm^{-1}: 1697 (C = O), 3354 (NH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.74 s (3H, CH_3); 0.88 s (3H, CH_3); 1.22 br.s (4H, 2×CH_3); 2.76 dd (4H, J = 5.9, 2.4, 2×NCH_2); 2.90 br.s (2H, 2×NH); 3.28 br.d (2H, J = 12.5, NCH_2). ^{13}C NMR spectrum, ppm: 14.8 (2×CH_3); 16.0 (CH_2); 17.0 (CH_2); 33.9 (2×C*); 48.8 (CH_2); 51.1 (CH_2); 59.1 (CH_2); 61.2 (CH_2); 213.7 (C*). Found, %: C 67.50; H 10.28; N 14.35. $C_{11}H_{20}N_2O$. Calculated, %: C 67.34; H 10.20; N 14.43.

1-Methyl-5-butyl-9-oxo-3,7-diazabicyclo/3.3.1/nonane (9). Yield 1.4 *g* (67.3%), R_f 0.35, mp 56-58°C. IR-spectrum, ν, cm^{-1}: 1696 (C = O), 3352 (NH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.76 s (3H, CH_3); 0.91 s (3H, J = 7.0, CH_3); 1.11-1.36 m (6H, 3×CH_2); 2.77 br.d (2H, J = 12.5, NCH_2); 2.78 br.d (2H, J = 12.5, NCH_2); 2.90 br.s (2H, 2×NH); 3.20 br.d (2H, J = 12.8, NCH_2). 3.28 br.d (2H, J = 12.5, NCH_2). ^{13}C NMR spectrum, ppm: 13.6 (CH_3); 17.0 (CH_2); 23.2 (CH_2); 25.0 (CH_2); 31.3 (C*); 48.8 (2×CH_2); 50.9 (C*); 59.1 (2×CH_2); 61.3 (2×CH_2); 213.8 (C*). Found, %: C 69.31; H 10.64; N 13.40. $C_{14}H_{22}N_2O$. Calculated, %: C 69.23; H 10.57; N 13.46.

General production procedure (12-29). To a water-alcohol solution (1:1) of 5 *mmol* of the corresponding diazabicyclo/3.3.1/nonane **7-9**, a solution of 5 *mmol* of levulinic or pyruvic acid in 10 *ml* of water is added. The mixture is stirred for 1 *h* and left overnight. The solution is evaporated in vacuo, the remaining mass is triturated with ethyl acetate and recrystallized from a mixture of isopropanol:benzene 1:1.

2-Carboxy-2,5,7-trimethyl-6-oxo-1,3-diazaadamanane (12). Yield 1.8 *g* (75.8%), R_f 0.38, mp 232-233°C (isopropanol:benzene 1:1). IR-spectrum, ν, cm^{-1}: 1704 (C = O); 1983 (C = Acid); 3490 (OH Acid). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.78-1.02 m (6H, 2×CH_3); 1.32 d (2H, J = 5.9, NCH_2); 1.86-2.06 m (2H, NCH_2); 2.68-2.82 m (4H, 2×NCH_2); 3.21-3.48 m (3H, CH_3); 5.62 br.s (1H, COOH). Found, %: C 60.60; H 7.58; N 11.65. $C_{12}H_{18}N_2O_3$. Calculated, %: C 60.50; H 7.50; N 11.76.

2-Carboxyethyl-2,5,7-trimethyl-6-oxo-1,3-diazaadamanane (13). Yield 1.8 *g* (67.7%), R_f 0.41, mp 231-232°C (ethyl acetate). IR-spectrum, ν, cm^{-1}: 1708 (C = O); 1985 (C = Acid); 2490 (OH Acid). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.82 s (3H, CH_3); 0.83 s (3H, CH_3); 1.47 s (3H, CH_3); 2.16-2.31 m (4H, 2×CH_2); 2.63-2.71 m (4H, NCH_2); 3.59-3.67 m (4H, NCH_2); 11.63 br.s (1H, COOH). Found, %: C 63.26; H, 8.39; N 10.38. $C_{14}H_{22}N_2O_3$. Calculated, %: C 63.15; H 8.27; N 10.52.

2-Carboxy-2-methyl-5,7-diethyl-6-oxo-1,3-diazaadamanane (14). Yield 1.9 *g* (71.4%), R_f 0.43, mp 240-241°C (ethyl acetate). IR-spectrum, ν, cm^{-1}: 1718 (C = O); 3365 (OH acid). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.82-0.96 m (6H, 2×CH_3); 1.22-1.38 m (4H, 2×NCH_2); 1.62 s (3H, CH_3); 2.78-2.87 m (4H, 2×NCH_2); 3.42 br.d (2H, J = 12.6, NCH_2); 3.58 br.s.d (2H, J = 13.3, NCH_2); 4.46 br.s (1H, COOH). Found, %: C 63.27; H 8.15; N 10.40. $C_{14}H_{22}N_2O_3$. Calculated, %: C 63.15; H 8.2; N 10.51.

2-Carboxyethyl-2-methyl-5,7-diethyl-6-oxo-1,3-diazaadamanane (15). Yield 2.1 *g* (71.5%), R_f 0.43, mp 187-188°C (isopropanol:methanol 1:1). IR-spectrum, ν, cm^{-1}: 1704 (C = O); 2490 (COOH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.84 d (6H, J = 7.0, 2×CH_3); 1.22-1.38 m (4H, 2×NCH_2); 1.42 s (3H, CH_3); 2.20 dd (2H, J = 13.9, 2.4, CH_2); 2.28 dd (2H, J = 13.3, 2.4, CH_2); 2.66 dd (4H, J = 8.0, 7.1, NCH_2); 3.62 d (4H, J = 5.9, 2×CH_2); 11.61 br.s (1H, COOH). Found, %: C 65.43; H 8.95; N 9.40. $C_{16}H_{26}N_2O_3$. Calculated, %: C 65.31; H 8.84; N 9.52.

2-Carboxyethyl-2,5-dimethyl-7-ethyl-6-oxo-1,3-diazaadamanane (16). Yield 2 *g* (72.1%), R_f 0.33, mp 188-189°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, *cm* $^{-1}$: 1710 (C = O); 3595 (OH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.84-0.98 m (6H, 2×CH_3); 1.32 d (2H, CH_2CH_3); 1.41 s (3H, CH_3); 2.32 dd (4H, J = 13.9, 15.9, 2×CH_2); 2.70 dd (4H, J = 13.8, 12.9, 2×NCH_2); 3.62 dd (4H, J = 12.4, 12.5, 2×NCH_2); 4.36 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 7.2 (CH_3); 15.6 (CH_3); 21.6 (CH_3); 23.1 (C*); 28.3 (CH_2); 30.7 (C*); 44.4 (CH_2); 45.5 (CH_2); 45.7 (CH_2); 46.6 (CH_2); 56.8 (CH_2); 57.5 and 58.9 (CH_2); 72.2 (C*); 174.2 (COOH); 209.1 (C*). Found, %: C 80.47; H 8.65; N 10.11. $C_{15}H_{24}N_2O_3$. Calculated, %: C 80.35; H 8.57; N 10.0.

2-Carboxyethyl-2,5-dimethyl-6-oxo-7-propyl-1,3-diazaadamanane (17). Yield 2 *g* (68%), R_f 0.38, mp 192-193°C (isopropanol:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 1704, 1983 (C = O); 2490 (OH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.82 m (3H, CH_3); 0.91 s (3H, CH_3); 1.36 br.s (4H, 2×CH_2); 1.41 s (3H, CH_3); 2.18-2.31 m (4H, 2×CH_2); 2.61-2.74 m (4H, 2×NCH_2); 5.59-5.67 m (4H, 2×NCH_2); 11.62 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 14.61 (CH_3); 15.6 (CH_3); 15.7 (CH_3); 21.5 (CH_2); 21.6 (CH_2); 28.3 (C*); 30.6 (C*); 43.7 (CH_2); 44.4 (CH_2); 45.8 (CH_2); 46.7 (CH_2); 57.2 (CH_2); 59.7 (CH_2); 72.1 (C*); 174.5 (COOH); 208.9 (C*). Found, %: C 65.46; H 8.97; N 9.41. $C_{16}H_{26}N_2O_3$. Calculated, %: C 65.32; H 8.84; N 9.52.

2-Carboxy-2-methyl-5,7-dipropyl-6-oxo-1,3-diazaadamanane (18). Yield 2.1 *g* (68.2%), R_f 0.35, mp 202-203°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 1644, 1718 (C = O); 3365 (OH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.81-1.08 m (6H, 2×CH_3); 1.1-1.42 m (9H, 3×CH_2, CH_3); 1.62 s (0.6H) and 1.85 s (1.4H, CH_2); 2.78-2.86 m (4H, 2×NCH_2); 3.25-3.58 m (4H, 2×NCH_2); 6.5 br.s (1H, COOH). Found, %: C 65.50; H 8.98; N 9.43. $C_{16}H_{26}N_2O_3$. Calculated, %: C 65.35; H 8.85; N 9.52.

2-Carboxyethyl-2-methyl-6-oxo-5,7-dipropyl-1,3-diazaadamanane (19). Yield 2.2 *g* (68.3%), R_f 0.34, mp 219-220°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 1697.1980 (C = O); 3365 (OH acid). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.96 s (6H, 2×CH_3); 1.18-1.38 m (8H, 4×CH_2); 1.41 s (3H, CH_3); 2.18 dd (2H, J = 13.9, 2.4, CH_2); 2.28 dd (2H, J = 13.3, 2.4, CH_2); 2.66 dd (4H, J = 5.8.5.9, 2×NCH_2); 3.62 d (4H, J = 5.9, 2×NCH_2); 11.62 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 14.6 (CH_3); 15.6 (CH_3); 15.7 (CH_3); 21.6 (CH_2); 28.2 (C*); 30.6 (C*); 32.9 (CH_2); 38.9 (CH_2); 39.5 (CH_2); 39.9 (CH_2); 40.0 (CH_2); 45.9 (CH_2); 46.8 (CH_2); 57.2 (CH_2); 57.8 (CH_2); 72.3 (C*); 174.1 (COOH); 208.8 (C*). Found, %: C 67.20; H 9.42; N 8.58. $C_{18}H_{30}N_2O_3$. Calculated, %: C 67.08; H 9.31; N 8.69.

2-Carboxyethyl-2,7-dimethyl-5-butyl-6-oxo-1,3-diazaadamanane (20). Yield 2.1 *g* (69.8%), R_f 0.42, m.p. 189-190°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 1645, 1710 (C = O); 3365 (OH acid). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.81 s (1.5H) and 0.82 s (1.5H, CH_3); 0.92 t (3H, J = 6.8, CH_3-Bu); 1.21-1.37 m (6H, 3×CH_2-Bu); 1.45 s (1.5H) and 1.46 s (1.5H, CH_3); 2.13-2.31 m (4H, CH_2CH_2); 2.61-2.72 m (4H, 2×NCH_2); 3.58-3.68 m (4H, 2×NCH_2);

11.78 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 13.6 (CH_3); 15.6 (CH_3); 21.5 (CH_2); 23.0 (CH_2); 24.4 (CH_2); 24.5 (CH_2); 28.2 (CH_2); 28.5 (C*); 30.3 (C*); 30.6 (C*); 44.4 (2×CH_2); 45.6 (CH_2); 57.8 (2×CH_2); 59.8 (2×CH_2); 72.1 (C*); 174.1 (COOH); 208.9 (C*). Found, %: C 69.07; H 9.30; N 7.95. $C_{17}H_{28}N_2O_3$. Calculated, %: C 68.96; H 9.19; N 8.04.

2-Carboxyethyl-2-methyl-6-oxo-5,7-dibutyl-1,3-diazaadamanane (21). Yield 2.4 *g* (69%), R_f 0.40, mp 193-194°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 1698.1980 (C = O); 3365 (OH acid). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.88 s (6H, 2×CH_3); 1.18-1.38 m (12H, 6×CH_2); 1.44 s (3H, CH_3); 2.20 dd (2H, J = 13.3, 2.4, CH_2); 2.28 dd (2H, J = 12.6, 2.4, NCH_2); 2.68 dd (4H, J = 5.8.5.9, 2×NCH_2); 3.61 d (4H, J = 5.9, 2×NCH_2); 11.62 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 13.5 (CH_3); 21.6 (CH_3); 23.0 (CH_3); 24.5 (CH_2); 24.6 (CH_2); 28.2 (CH_2); 30.3 (C*); 30.6 (C*); 38.9 (CH_2); 39.2 (CH_2); 40.05 (CH_2); 45.7 (CH_2); 46.6 (CH_2); 57.3 (CH_2); 57.9 (CH_2); 72.3 (CH_2); 95.5 (CH_2); 95.6 (CH_2); 174.1 (COOH); 208.8 (C*). Found, %: C 73.60; H 7.22; N 7.02. $C_{20}H_{34}N_2O_3$. Calculated, %: C 73.47; H 7.14; N 7.14.

5,7-Diisopropyl-2-carboxy-2-methyl-6-oxo-1,3-diazaadamantane (22). Yield 1.2 *g* (82%), R_f 0.31, mp > 300°C (DMF). IR-spectrum, ν, *cm*$^{-1}$: 1670, 1714 (C = O); 2600 (OH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.84 d (6H, J = 7.0, 2×CH3-isopropyl); 0.91 d (6H, J = 7.0, 2×CH_3-isopropyl); 1.63 cc (3H, CH_3); 1.85 s (1H, J = 7.0, CH-isopropyl); 1.90 s (1H, J = 7.0, CH-isopropyl); 2.84 br.s (2H, J = 13.8, NCH_2); 2.90 br.d (2H, J = 13.6, NCH_2); 3.51-3.70 m (4H, 2×NCH_2); 4.25 br.s (1H, COOH). Found, %: C 65.50; H 9.00; N 9.36. $C_{16}H_{26}N_2O_3$. Calculated, %: C 65.35; H 8.86; N 9.52.

2-Carboxyethyl-6-hydroxy-2,5,7-trimethyl-1,3-diazaadamantane (23). Yield 1.7 *g* (75%), R_f 0.31, mp 286-287°C (isopropanol:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 2600 (OH); 3246 (COOH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.64 s (6H, 2×CH_3); 1.31 s (3H, CH_3); 1.98-2.18 m (4H, 2×CH_2); 2.51 s (2H, NCH_2); 2.82-3.02 m (6H, 3×NCH_2); 3.33 t (2H, J = 12.8, CHOH); 8.76 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 19.87 (2×CH_3); 21.57 (CH_3); 29.08 (C*); 29.45 (CH_2); 30.4 (C*); 31.04 (CH_2); 51.09 (CH_2); 51.12 (CH_2); 57.06 (CH_2); 57.67 (CH_2); 79.3 (C*); 78.63 (CH); 175.20 (C*). Found, %: C 62.58; H 8.83; N 10.34. $C_{14}H_{24}N_2O_3$. Calculated, %: C 62.69; H 8.95; N 10.44.

2-Carboxy-2-methyl-5,7-diethyl-6-hydroxy-1,3-diazaadamantane (24). Yield 1.8 *g* (67.4%), R_f 0.31, mp 280-282°C (isopropanol:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 2600 (OH); 3246 (COOH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.77-0.88 m (6H, 2×CH_3); 1.08-1.22 m (4H, 2×CH_2); 1.32 s (3H, CH_3); 1.96 dd (2H, J = 13.3, 2.4, NCH_2); 2.21 dd (2H, J = 13.3, 2.4, NCH_2); 2.78-3.02 m (4H, 2×NCH_2); 3.22-3.36 m (2H, CHOH); 4.46 br.s (1H, COOH). Found, %: C 72.08; H 7.78; N 11.33. $C_{14}H_{24}N_2O_3$. Calculated, %: C 71.96; H 7.91; N 11.44.

2-Carboxyethyl-2-methyl-5,7-diethyl-6-hydroxy-1,3-diazaadamantane (25). Yield 2.1 *g* (71.4%), R_f 0.41, mp 269-270°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, *cm*$^{-1}$: 2600 (OH); 3245 (COOH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 0.66-0.78 m (6H, 2×CH_3); 0.91-1.10 m (3H, CH_3); 1.13-1.28 m (4H,

2×CH_2); 2.01-2.38 m (6H, 3×CH_2); 2.8-3.06 m (5H, 2×CH_2, CH); 3.18-3.22 m (2H, NCH_2); 3.32 s (1H, OH); 4.8 br.s (1H, COOH). ^{13}C NMR spectrum, ppm: 5.93 (CH_3) and 5.96 (CH_3); 21.71 (CH_3); 25.2 (C*); 25.3, 29.26 (CH_2); 30.37 (C*); 31.08 (CH_2); 50.50 (CH_2); 51.13 (CH_2); 51.16 (CH_2); 53.93 (CH_2); 53.97 (CH_2); 54.59 (CH2); 72.79 (C*); 73.19 (CH); 95.4 (C*); 174.98 (COOH). Found, %: C 64.98; H 9.59; N 10.32. $C_{16}H_{28}N_2O_3$. Calculated, %: C 64.85; H 9.48; N 10.43.

2-Carboxyethyl-2-methyl-5,7-dipropyl-6-hydroxy-1,3-diazaadamantane (26). Yield 1.2 *g* (74%), R_f 0.3, mp 240-241°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, cm^{-1}: 2600 (OH); 3240 (COOH). 1H NMR spectrum, δ, ppm, *Hz*: 0.81-0.98 m (6H, 2×CH_3); 1.18 d (4H, J = 12.8, 2×CH_2); 1.22-1.36 m (3H, CH_3); 1.88-2.14 m (2H, CH_2); 2.21 dd (2H, J = 12.8, 1.4, CH_2); 2.80-2.96 m (4H, 2×CH_2); 3.31 ss (8H, J = 13.9, 4×NCH_2); 3.38 s (2H, CHOH); 4.42 br.s (1H, COOH). Found, %: C 66.80; H 10.00; N 8.52. $C_{18}H_{32}N_2O_3$. Calculated, %: C 66.67; H 9.87; N 8.64.

2-Carboxyethyl-2-methyl-5,7-diphenyl-6-hydroxy-1,3-diazaadamantane (27). Yield 2.7 *g* (68.9%), R_f 0.31, mp 239-240°C (ethyl acetate:methanol 1:1). IR-spectrum, ν, cm^{-1}: 1603 (arom); 2600 (OH); 3245 (COOH). ^{1}H NMR spectrum, δ, ppm, *Hz*: 1.42 s (3H, CH_3); 2.1-2.54 m (6H, 2×CH_2, NCH_2); 2.62 dd (1H, J = 5.8, 5.9, OH); 3.45-3.65 m (6H, 3×NCH_2); 4.05 dd (1H, CH); 4.46 br.s (COOH); 7.12-7.38 m (10H, H-arom). Found, %: C 73.60; H 7.22; N 7.02. $C_{24}H_{28}N_2O_3$. Calculated, %: C 73.47; H 7.14; N 7.14.

ԿԱՐԲՈՆԱԹԹՈՒՆԵՐԻ ՖՐԱԳՄԵՆՏ ՊԱՐՈՒՆԱԿՈՂ 5,7-ԴԻԱԼԿԻԼԴԻԱԶԱԱԴԱՄԱՆՏԱՆՆԵՐԻ ՍԻՆԹԵԶԸ ԵՎ ՆՐԱՆՑ ՀԱԿԱՕՔՍԻԴԱՆՏԱՅԻՆ ՀԱՏԿՈՒԹՅՈՒՆՆԵՐԻ ՈՒՍՈՒՄՆԱՍԻՐՈՒԹՅՈՒՆԸ

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Առաջին անգամ սինթեզվել են 3,7-դիազաբիցիկլո/3.3.1/նոնաններ, որոնք 1- և 5-դիրքերում ունեն տարբեր ալկիլ տեղակալիչներ՝ 1-մեթիլ-(5-էթիլ-, 5-պրոպիլ-, 5-բուտիլ): Սինթեզված դիազաբիցիկլոնոնանները կոնդենսվել են կետոթթուների՝ պիրոխաղողաթթվի կամ լևուլինաթթվի հետ: Արդյունքում ստացվել է դիազաադամանտանների նոր շարք, որտեղ 5- և 7-դիրքերում ալկիլ տեղակալիչներ են, 6-ում կետո, հիդրօքսիլ, իսկ 2-րդ դիրքում կարբոնաթթվային ֆրագմենտ:

Սինթեզված միացությունների կենսաբանական ուսումնասիրությունը ցույց է տվել, որ այս շարքի որոշ միացություններ ցուցաբերում են թույլ արտահայտված հակաօքսիդանտային ակտիվություն:

СИНТЕЗ И ИЗУЧЕНИЕ АНТИОКСИДАНТНОЙ АКТИВНОСТИ 5,7-ДИАЛКИЛДИАЗААДАМАНТАНОВ, СОДЕРЖАЩИХ ФРАГМЕНТЫ КАРБОНОВЫХ КИСЛОТ

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Реакцией Манниха впервые синтезированы смешанные 9-оксо-1-метил-(5-этил-, 5-пропил, 5-бутил-)-3,7-диазабицикло/3.3.1/нонаны. Конденсацией последних и 9-гидрокси--1,5-(диметил-, диэтил-, дипропил-, дибутил-)-3,7-диазабицикло/3.3.1/нонанов с пировиноградной или левулиновой кислотой синтезированы 16 новых 2-замещенных диазаадамантанов, содержащих фрагмент карбоновой кислоты.

Согласно результатам биологических испытаний, некоторые соединения этого ряда проявляют слабую антиоксидантную активность. Активны те соединения, в структуре которых находится гидроксильная группа в 6-ом положении адамантанового кольца.

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