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Synthesis of Substituted Bridged Carboxylic Acids of the Adamantane Series

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Abstract—A number of new 1,3,6- and 1,4,4-tri- and 1,3,6,6-tetrasubstituted polyfunctional derivatives were synthesized starting from bridged carboxylic acids of the adamantane series. The reactions were carried out in acidic media. A number of new amino acids were synthesized from 1-acetylamino- and 1,3-diacetylamino derivatives. The synthesized compounds can be considered as a molecular platform for the synthesis of new polymeric materials.

Keywords: 2-substituted adamantanes, oxidation, adamantane, carboxylic acids, amino acids, sulfiric acid–nitric acid mixture

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The unique geometry of the practically spherical adamantane core, along with the tripoid (C_{3v} symmetry group) or tetragonal (T_d symmetry group) configuration of its 1,3,5-tri- or 1,3,5,7-tetrasubstituted derivatives, creates the prerequisites for the design of polymer molecules with a fixed arrangement of fragments responsible for the functional properties of materials. At present this direction is intensively developing, and 1,3,5-tri- or 1,3,5,7-tetrasubstituted adamantane derivatives have already been used to create materials with valuable properties [1–20]. At the same time, the development of new synthetic approaches to polyfunctional 1,3,5-tri- or 1,3,5,7-tetrasubstituted adamantanes continues to attract researchers' effort [21–23].

At the same time, the use of 1,3,6- and 1,4,4-trisubstituted and 1,3,6,6-tetrasubstituted adamantane derivatives as the synthetic platform for previously unknown tri- and tetrapoid systems have never been reported, probably, because such substrates are not very much available. The introduction of several functional groups simultaneously in the bridgehead and bridge positions changes the configuration of such structures (Fig. 1, C_s and C_{2v} symmetry groups), and this can impart new properties to macromolecules obtained on the basis of such polyfunctional derivatives. Therefore, further research into the synthesis of difficulty available 1,3,6-, 1,4,4-, and 1,3,6,6-polysubstituted adamantane derivatives is a relevant task.

At the same time, the methods of synthesis of 1,3,6-trisubstituted adamantane derivatives are poorly documented. Most the reported procedures make use of 1,3,6-tribromoadamantane [24] as the starting compound for the synthesis of adamantane-1,3,6-triol [25] and 1,3,6-triphenyladamantane and 6-bromo-1,3-dichloroadamantane [26]. The synthesis of trisubstituted functionalized adamantanes, 5,7-diphenyladamantane-2-carboxylic acid [27] and 6-aminoadamantane-1,3-diol [28], from respectively adamantane-2-carboxylic acid and adamantane-2-amine via the stage of bromination was reported.

2,2-Disubstituted derivatives were used as the starting materials for the synthesis 1,4,4-trisubstituted and 1,3,6,6-tetrasubstituted adamantanes. For example, 1,4,4-trinitroadamantane, 1,3,6,6-tetranitroadamantane, and 3,6,6-trinitroadamantane-1-diol were prepared starting from 2,2-dinitroadamantane [29]. 1,4,4-Trifluoroadamantane and 1-(trifluoromethyl)-3,6,6-trifluroadamantane were prepared from 2-hydroxyadamantane-2-carboxylic acid under the action of SF_4 in HF in different conditions [30]. A single example of the synthesis of a potential anticancer drug from 4,4-dimethyladamantan-1-ol, which was obtained by oxidation of 2,2-dimethyladamantane [31]. The reaction of bridged halo-substituted adamanatanes with nitric acid in the presence of acetic anhydride leads to the introduction of a nitroxy group into the

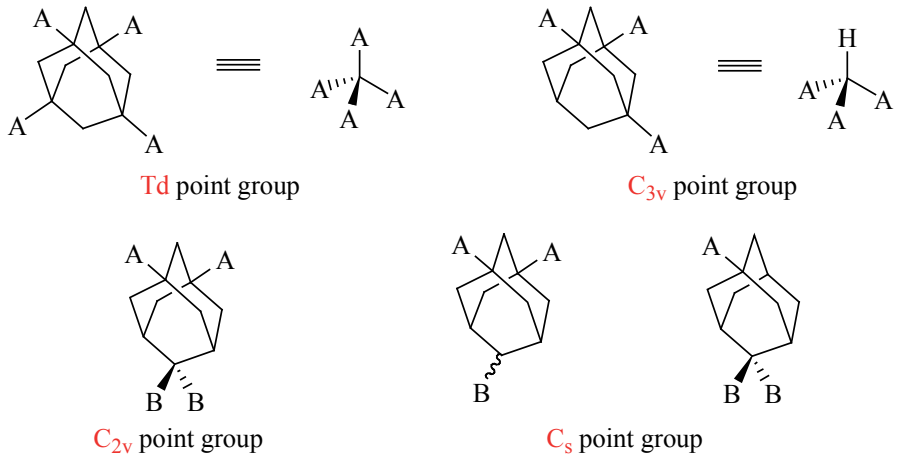


Fig. 1. Symmetry groups of tri- and tetrasubstituted adamantanes.

bridgehead position of the adamantane core and formation of 1,4,4-trisubstituted derivatives [32].

At present no methods of synthesis of polyfunctional 1,3,6- and 1,4,4-trisubstituted and 1,3,6,6-tetrasubstituted adamantane derivatives, which would allow introduction of other functional groups into the adamantane core. This task can be solved through the functionalization of 2-substituted and 2,2-disubstituted adamantanes by nucleophilic substitution in acid media.

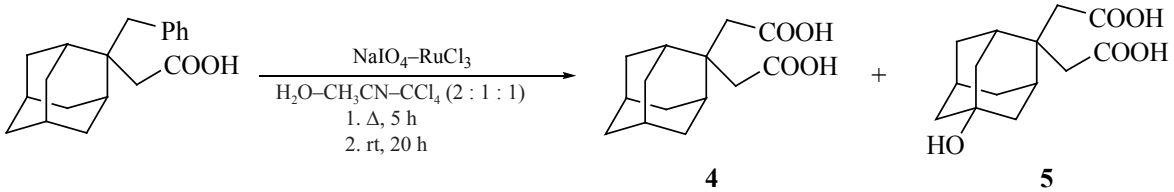
As starting compounds we used 2-(adamantan-2-yl)-acetic acid (**1**), adamantane-2-carboxylic acid (**2**), *N*-(2 adamantan-2-yl)acetamide (**3**), and 2,2'-(adamantane-2,2-diyl)diacetic acid (**4**). Acid **1** was prepared by known procedures [33–35]. Acid **2** was obtained by the oxidative cleavage of spiro(adamantane-2,2'-oxirane) in fuming nitric acid [36], and 2-(acetylamino)adamantane (**3**), by a modified procedure from adamantan-2-ol. 2,2'-(Adamantane-2,2-diyl)diacetic acid (**4**) was prepared by the oxidative cleavage of the aromatic fragment in 2-(2-benzyladamantan-2-yl)acetic acid in the $NaIO_4$–$RuCl_3$ system [37] (Scheme 1).

The yield of acid **4** after recrystallization from water was 30%. Apparently, the reaction involves more profound oxidative processes that destroy the adamantane core. The carboxyl proton signals in the ^{1}H NMR spectrum appear as a singlet at 11.88 ppm, and the proton signals of the methylene groups linked to carboxyls, as a singlet at 2.69 ppm. The ^{13}C NMR signals of the quaternary carboxyl carbons are observed at 173.9 ppm, and the signal of the quaternary carbon of the adamantane core appears at 40.5 ppm.

After purification, we isolated the oxidation by-product 2,2'-(5-hydroxyadamantane-2,2-diyl)diacetic acid (**5**). The formation of hydroxy acid **5** is associated with the increased reaction temperature. McNeill and Du Bois reported the oxidation of a tertiary C–H bond in adamantane substrates in the $KBrO_3$–$RuCl_3$ system [38]. It should be noted that hydroxy acid **5** did not form, when the reaction was performed at room temperature. The ^{1}H NMR spectrum displays a carboxyl proton signal as a broadened singlet at 12.20 ppm and a hydroxyl proton signals as a singlet at 4.28 ppm. In the ^{13}C NMR spectrum, the quaternary carbon atoms of the COOH groups appear at 173.8 and 174.0 ppm, and the signal of the quaternary carbon atom linked to the OH group is observed at 66.3 ppm.

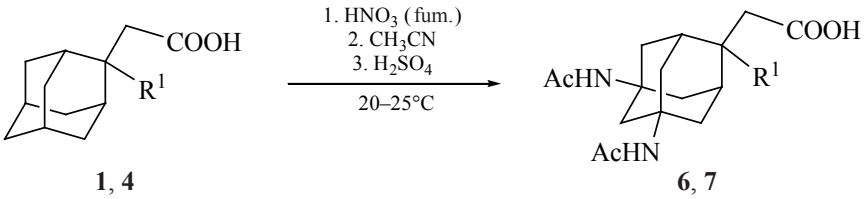
From acids **1** and **4**, by the one-pot synthesis by the procedure in [21], we obtained the corresponding 1,3,6- and 1,3,6,6-substituted adamantanes: 2-(5,7-diacetami-

Scheme 1.



4 **5**

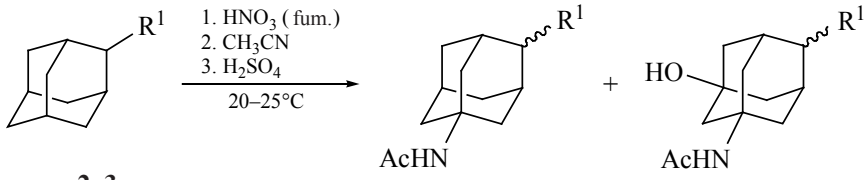
Scheme 2.



1, **4** **6**, **7**

R^1 = H (**1**, **6**), CH_2COOH (**4**, **7**).

Scheme 3.



2, **3**

R^1 = COOH (**2**), NHAc (**3**).

doadamantan-2-yl)acetic acid (**6**) and 2,2'-(5,7-diacetamidoadamantane-2,2-diyl)diacetic acid (**7**) (Scheme 2).

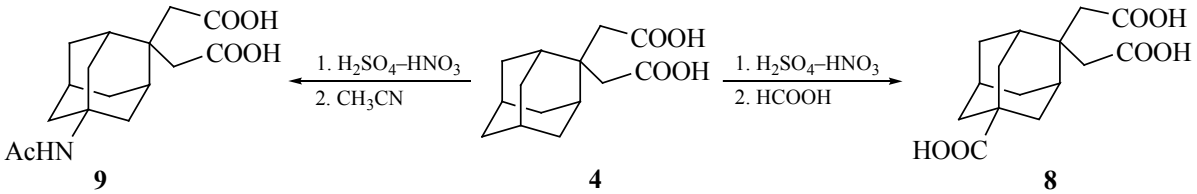
The synthesis protocol involved consecutive nitroxylation of the starting frame substrates **1** and **4** in fuming nitric acid, Ritter reaction with acetonitrile, and transformation of monoacetamides formed in situ into (diacetylamino)adamantanes **6** and **7** under the action of H_2SO_4. The reactions were performed with 20 equiv of fuming nitric acid and an excess of 98% H_2SO_4 in the case of substrate **1** and with 100% H_2SO_4 in the case of substrate **4**. The yields of products **6** and **7** were 53 and 32%, respectively. The NH proton signals of compounds **6** and **7** appear as singlets at 7.25–7.36 ppm. In the ^{13}C NMR spectra, the signals of the quaternary carbon atoms linked to the amide fragments appear at 52.1–52.2 ppm, and the signals of the quaternary carbon atoms of the acetamide fragment, at 169.1–169.3 ppm.

It should be noted that the reactions of adamantane-2-carboxylic acid (**2**) or 2-(acetylamino)adamantane (**3**) in the presence of 20% oleum gave no corresponding acetylamino derivatives. Instead, mixtures comprising monoacetylamino derivatives (*Z*/*E*-mixtures) and oxidation products, as evidenced by the presence of the quaternary carbon atoms at 66.0–68.0 ppm in the ^{13}C NMR spectra (Scheme 3). Apparently, the hydroxy derivative does not further undergo nucleophilic substitution because the acetylamino and carboxy groups have a stronger deactivating effect than the carboxymethyl group. Evidence for this suggestion comes from the results of kinetic studies on the nitroxylation [39–41] and oxidation of frame substrates in a sulfuric–nitric acid mixture [42].

From acid **4** we prepared novel 1,4,4-trisubstituted derivatives: 2,2'-(5-carboxyadamantane-2,2-diyl)diacetic acid (**8**) and 2,2'-(5-acetamidoadamantane-2,2-diyl)diacetic acid (**9**) (Scheme 4). Functionalization was performed in a sulfuric–nitric acid mixture (3 equiv of fuming nitric acid and 96% of sulfuric acid). The yields of compounds **8** and **9** were 27 and 30%, respectively.

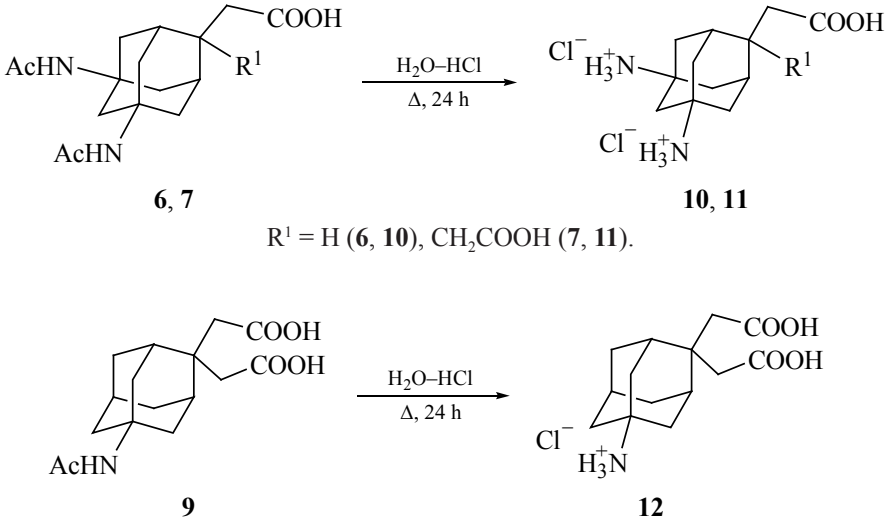
In the ^{13}C NMR of compound **8**, the signals of the quaternary carboxyl carbon atoms are observed at 178.7, 173.8, and 173.7 ppm. In the ^1H NMR spectrum of compound **9**, the acetamide proton signal appears as a singlet at 7.32 ppm. In the ^{13}C NMR spectrum of compound **9**, the signal of the quaternary carbon atom of the acetamide fragment is observed at 161.1 ppm and the signal of the

Scheme 4.



9 **4** **8**

Scheme 5.



quaternary carbon atom linked to the nitrogen atom, at 51.1 ppm.

Compounds **6**, **7**, and **9** were converted into corresponding amino acids **10–12** by 24-h heating in 2% HCl (Scheme 5). Amino acids **10–12** were obtained as hydrochlorides with quantitative yields.

The protonated amino groups of compounds **10–12** give singlets at 8.1–8.5 ppm in the ^{1}H NMR spectra, and the quaternary carbon atoms of the adamantane core, linked to the amino groups, resonate at 52.0–53.0 ppm.

EXPERIMENTAL

The IR spectra were measured on a Shimadzu IR Affinity-1 spectrometer with an ATR attachment. The ^{1}H and ^{13}C NMR spectra were obtained on a JEOL NMR-ECX400 spectrometer at 400 and 100 MHz, respectively, internal reference TMS. The melting points were measured in capillaries on an SRS OptiMelt MPA 100 and are uncorrected. The elemental analyses were obtained on an EuroVector 3000 EA analyzer using L-cystine as standard. The starting compounds were prepared by known procedures {spiro(adamantane-2,2'-oxirane) [43], 2-(2-benzyladamantan-2-yl)acetic acid [44, 45]}, or taken from the collection of reagents, Chair of Organic Chemistry, Samara State University; purity ≥ 95.0%.

2-(Adamantan-2-yl)acetic acid (1) was prepared according to [33–35].

Adamantane-2-carboxylic acid (2). Fuming nitric acid, 26.7 mL (0.644 mol), was added dropwise to a cold (–15 to –10°C) solution of 8.9 g (0.053 mol) of spiro(adamantane-2,2'-oxirane) in 106.8 mL of CCl_4. The reaction mixture was kept for 2–3 h under cooling and then allowed to warm to room temperature and washed with water. The organic layer was separated and treated with aquoues KOH. The aqueous layer was brought to pH 1 with HCl, and the precipitate was filtered off, washed with water, and dried to obtain 5.9 g (66%) of acid **2**, colorless crystals, mp 139–142°C (145.5–145.8°C [36]).

***N*-(Adamantan-2-yl)acetamide (3).** Adamantan-2-ol, 10 g (0.07 mol), was added to a mixture of 60 mL 94% of H_2SO_4 and 20 mL (0.38 mol) of acetonitrile at a temperature not higher than 20°C. After 15-min stirring at room temperature, the reaction mixture was poured onto ice. The precipitate was filtered off, washed with water, dried, and recrystallized from petroleum ether to obtain 12.06 g (95%) of compound **3**, colorless crystals, mp 194–195°C (190°C [46]).

2,2'-(Adamantane-2,2-diyl)diacetic acid (4). Sodium periodate, 75 g (0.350 mol), and 0.365 g (0.002 mol) of $RuCl_3$ were added in succession to a vigorously stirred solution of 5 g (0.018 mol) of 2-(2-benzyladamantan-2-yl)acetic acid in a mixture of 170 mL of H_2O, 85 mL of CH_3CN, and 85 mL of CCl_4. The reaction mixture was heated under reflux for 5 h and then stirred for an additional 20 h at room temperature and filtered through Celite. The aqueous phase was extracted with ethyl acetate (5 × 10 mL). The organic fractions were combined, dried over Na_2SO_4, and evaporated in a vacuum. The oily residue was poured with 150 mL of acetone, undissolved inorganic salts were filtered off, and the mother liquor was evaporated in a vacuum. The residue was

mixed with 50 mL of dioxane and 50 mL of acetone, the precipitate of **2,2'-(5-hydroxyadamantane-2,2-diyl)-diacetic acid (5)** was filtered off , the mother liquor was evaporated, and the oily residue was recrystallized from water to obtain 1.33 g (30%) of acid **4**, colorless crystals, mp 191–194°C. IR spectrum, ν, cm^{-1}: 2906, 2881, 2862 (CH_{Ad}), 1739 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.48–1.51 m (4H, CH_{Ad}), 1.62 s (2H, CH_{Ad}), 1.76–1.82 m (4H, CH_{Ad}), 1.99–2.03 m (4H, CH_{Ad}), 2.69 s (4H, $2CH_2$), 11.88 s (2H, COOH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 27.4 (CH), 32.8 (CH_2), 33.4 (CH), 38.0 (CH_2), 39.6 (CH_2), 40.5, 173.9. Found, %: C 66.70; H 8.06. $C_{14}H_{20}O_4$. Calculated, %: C 66.65; H 7.99.

2,2'-(5-Hydroxyadamantane-2,2-diyl)diacetic acid (5). Yield 0.15 g (3.4%), colorless crystals, mp 186–190°C. IR spectrum, cm^{-1}: 3435 (OH), 2929, 2882, 2870 (CH_{Ad}), 1693 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.25–1.35 m (3H, CH_{Ad}), 1.43–1.49 m (2H, CH_{Ad}), 1.79–2.01 m (8H, CH_{Ad}), 2.62 s (4H, $2CH_2$), 4.29 s (1H, OH), 12.20 br.s (2H, COOH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 29.6 (CH), 31.6 (CH_2), 35.9 (CH), 37.7 (CH_2), 38.4 (CH_2), 38.8 (C), 40.9 (CH_2), 47.3 (CH_2), 66.3, 173.8, 174.0. Found, %: C 62.73; H 7.57. $C_{14}H_{20}O_5$. Calculated, %: C 62.67; H 7.51.

Synthesis of 1,3,6- and 1,4,4-trisubstituted and 1,3,6,6-tetrasubstituted adamantane derivatives.

2-(5,7-Acetamidoadamantan-2-yl)acetic acid (6). Acid **1**, 2 g (0.0103 mol), was added under stirring in portions at a temperature not higher than 20°C to 8.7 mL (0.206 mol) of fuming nitric acid. The resulting solution was stirred at 20–25°C for 2 h, after which 8 mL (0.152 mol) of acetonitrile was added dropwise. The mixture was stirred for 1 h at 20°C and, after the addition of 34.8 mL (0.653 mol) of 98% H_2SO_4, stirred for an additional 17 h at 20–25°C, poured onto 500 g of crushed ice and brought to pH 5 with $NaHCO_3$ under stirring. The product was extracted with butanol (10 × 10 mL), and the alcohol was dried by azeotropic distillation of water and evaporated in a vacuum. The residue was poured 30 mL with ethyl acetate, and the precipitate that formed was filtered off and dried to obtain 1.68 g (53%) of compound **6**, colorless crystals, mp 237–239°C. IR spectrum, ν, cm^{-1}: 3342 (NH), 2970, 2924, 2873 (CH_{Ad}), 1732, 1697 (C=O). ^1H NMR spectrum, δ, ppm: 1.52–1.54 m (2H, CH_{Ad}), 1.69 s (6H, CH_3), 1.70–1.78 m (2H, CH_{Ad}), 1.84–1.90 m (5H, CH_{Ad}), 1.95–1.99 m (2H, CH_{Ad}), 2.05 s (2H, CH_{Ad}), 2.25 d (2H, CH_2COOH, *J* 7.3 Hz), 7.34 s (1H, NH), 7.35 s (1H, NH), 11.83 br.s (1 H, COOH). ^{13}C NMR spectrum, δ, ppm: 24.2 (CH_3), 33.2 (CH), 34.6 (CH_2), 37.3 (CH_2), 39.1 (CH), 41.7 (CH_2), 45.8 (CH_2), 52.1, 52.2, 169.2, 169.3, 174.5. Found, %: C 62.37; H 7.90; N 9.14. $C_{16}H_{24}N_2O_4$. Calculated, %: C 62.32; H 7.84; N 9.08.

2,2'-(5,7-Diacetamidoadamantane-2,2-diyl)diacetic acid (7) was prepared in a similar way from 1.0 g (0.004 mol) of acid **4**, 3.3 mL (0.08 mol) of fuming nitric acid, 2.5 mL (0.05 mol) of acetonitrile, and 23.3 mL (0.44 mol) of 100% H_2SO_4. Yield 0.46 g (32%), colorless crystals, mp 260–262°C. ^1H NMR spectrum, δ, ppm: 1.50–1.53 m (4H, CH_{Ad}), 1.69 s (6H, CH_3), 1.74 s (2H, CH_{Ad}), 1.80–1.84 m (2H, CH_{Ad}), 1.90–2.06 m (4H, CH_{Ad}), 2.40 s (4H, CH_2), 7.25 s (2H, NH). ^{13}C NMR spectrum, δ, ppm: 24.3 (CH_3), 36.1 (CH), 36.8 (CH_2), 40.7, 42.8 (CH_2), 44.0 (CH_2), 52.1, 169.1, 175.1. Found, %: C 59.05; H 7.20; N 7.70. $C_{18}H_{26}N_2O_6$. Calculated, %: C 59.00; H 7.15; N 7.65.

2,2'-(5-Carboxyadamantane-2,2-diyl)diacetic acid (8). Fuming nitric acid, 0.4 mL (0.010 mol), was added dropwise to a solution of 0.8 g (0.003 mol) of acid **4** in 10 mL of 96% H_2SO_4 at a temperature not higher than 20–25°C. The mixture was kept at a given temperature for 2 h, after which 2 mL (0.053 mol) of 100% formic acid was added dropwise. The reaction mixture was stirred for 48 h and then poured onto ice. The precipitate that formed was filtered off, washed with water, suspended in ethyl acetate, filtered off, and dried to obtain 0.25 g (27%) of acid **8**, colorless crystals, mp 170–173°C. IR spectrum, ν, cm^{-1}: 2916, 2873, 2854 (CH_{Ad}), 1720, 1683 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.42–1.45 m (2H, CH_{Ad}), 1.56–1.70 m (4H, CH_{Ad}), 1.87–1.99 m (5H, CH_{Ad}), 2.07–2.10 m (2H, CH_{Ad}), 2.64–2.69 m (4H, CH_2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 27.2 (CH), 31.8 (CH_2), 33.2 (CH), 34.4 (CH_2), 35.8, 38.9, 40.8 (CH_2), 40.9 (CH_2), 173.7, 173.8, 178.7. Found, %: C 60.84; H 6.85. $C_{15}H_{20}O_6$. Calculated, %: C 60.80; H 6.80.

2,2'-(5-Acetamidoadamantane-2,2-diyl)diacetic acid (9). Fuming nitric acid, 0.3 mL (0.007 mol), was added dropwise to a solution of 0.54 g (0.002 mol of acid **4** in 6 mL of 96% H_2SO_4 at a temperature not higher than 20–25°C. The mixture was kept at a given temperature for 2 h, after which 1 mL (0.019 mol) of acetonitrile was added dropwise. The reaction mixture was stirred for 3 h and poured onto 15 g of crushed ice and brought to pH 5 with $NaHCO_3$ under stirring. The product was

extracted with butanol (10 × 5 mL), and the alcohol was dried by azeotropic distillation of water and evaporated in a vacuum. The residue was poured with 30 mL of ethyl acetate, and the precipitate that formed was filtered off and dried to obtain 0.21 g (32%) of compound **9**, colorless crystals, mp 220–222°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.32–1.35 m (2H, CH_{Ad}), 1.51–1.54 m (4H, CH_{Ad}), 1.69–1.74 m (8H, CH_3, CH_{Ad}), 1.90–2.05 m (2H, CH_{Ad}), 2.35–2.42 m (4H, CH_2), 7.32 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 24.3 (CH_3), 28.8 (CH), 32.1 (CH_2), 36.1 (CH), 36.8 (CH_2), 39.4, 42.8 (CH_2), 43.6 (CH_2), 44.0 (CH_2), 51.1, 169.1, 175.1, 175.2. Found, %: C 62.17; H 7.54; N 4.58. $C_{16}H_{23}NO_5$. Calculated, %: C 62.12; H 7.49; N 4.53.

6-(Carboxymethyl)adamantane-1,3-diaminium chloride (10). A mixture of 0.6 g of compound **6**, 28 mL of water, and 2 mL of 36% HCl was heated under reflux for 25 h and evaporated to dryness to obtain 0.58 g (100%) of compound **10**, colorless crystals, mp 330°C (decomp.). IR spectrum, ν, cm^{-1}: 3207 (NH), 2947, 2908, 2862 (CH_{Ad}), 1726 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.50–1.53 m (2H, CH_{Ad}), 1.76–1.83 m (4H, CH_{Ad}), 1.91–1.94 m (3H, CH_{Ad}), 2.01–2.04 m (4H, CH_{Ad}), 2.26 d (2H, CH_2COOH, J 7.3 Hz), 8.45 s (3H, NH_3^+), 8.49 s (3H, NH_3^+), 12.16 br.s (1H, COOH). ^{13}C NMR spectrum, δ, ppm: 32.3 (CH), 33.0 (CH_2), 36.5 (CH_2), 37.8 (CH), 39.8 (CH_2), 43.3 (CH_2), 52.0, 52.1, 173.9. Found, %: C 48.54; H 7.50; N 9.48. $C_{12}H_{22}Cl_2N_2O_2$. Calculated, %: C 48.49; H 7.46; N 9.43.

Compounds **11** and **12** were prepared in a similar way.

6,6-Bis(carboxymethyl)adamantane-1,3-diaminium chloride (11) was prepared from 0.185 g (0.5 mmol) of compound **7**. Yield 0.178 g (100%), colorless crystals, mp 330°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.52–1.57 m (4H, CH_{Ad}), 1.73 s (2H, CH_{Ad}), 1.79–1.84 m (2H, CH_{Ad}), 1.92–2.04 m (4H, CH_{Ad}), 2.36 s (4H, CH_2), 8.14 s (6H, NH_3^+), 12.02 br.s (2H, COOH). ^{13}C NMR spectrum, δ, ppm: 31.0 (CH_2), 34.3 (CH), 35.5 (CH_2), 39.6, 42.1 (CH_2), 51.2, 173.6. Found, %: C 47.38; H 6.86; N 7.94. $C_{14}H_{24}Cl_2N_2O_4$. Calculated, %: C 47.33; H 6.81; N 7.89.

4,4-Bis(carboxymethyl)adamantan-1-aminium chloride (12) was prepared from 0.150 g (0.48 mmol) of compound **9**. Yield 0.146 g (100%), colorless crystals, mp 290°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.33–1.36 m (2H, CH_{Ad}), 1.56–1.59 (2H, CH_{Ad}), 1.72 s (2H, CH_{Ad}), 1.93–1.97 m (3H, CH_{Ad}), 2.04–2.08 m (2H, CH_{Ad}), 2.18–2.21 m (2H, CH_{Ad}), 2.62–2.64 m (4H, CH_2), 8.14 s (3H, NH_3^+), 12.03 br.s (2H, COOH). ^{13}C NMR spectrum, δ, ppm: 28.1 (CH), 31.0 (CH_2), 34.3 (CH), 35.5 (CH_2), 37.4 (CH_2), 37.9 (CH_2), 38.5, 42.1 (CH_2), 51.2, 173.5, 173.6. Found, %: C 55.41; H 7.36; N 4.67. $C_{16}H_{23}NO_5$. Calculated, %: C 55.35; H 7.30; N 4.61.

CONCLUSIONS

A synthetic approach to novel tri- and tetrasubstituted adamantane derivatives containing substituents both in the bridgehead and bridge positions, which involves nucleophilic substitution in acid media, was developed. The synthesized 1,3,6- and 1,4,4-trisubstituted and 1,3,6,6-tetrasubstituted adamantane derivatives can be considered as structural blocks for the creation of next-generation functional materials.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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