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Synthesis of (3-Hydroxyadamantan-1-yl)methanols

E. A. Ivleva[a],* A. V. Pogulyaiko[a], and Yu. N. Klimochkin[a]

[a] *Samara State Technical University, ul. Molodogvardeiskaya 244, Samara, 443100 Russia*
**e-mail: elena.a.ivleva@yandex.com*

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Abstract—A convenient procedure has been developed for the synthesis of (3-hydroxyadamantan-1-yl)-methanols on the basis of nitroxylation of adamantan-1-ylmethanols with fuming nitring acid and subsequent reduction of intermediate nitric acid esters with hydrazine hydrate. The title diols have also been obtained by the reduction of 1-nitroxy-3-(nitroxymethyl)adamantanes. The nitroxylation process is accompanied by oxidation with the formation of substituted adamantane-1-carboxylic acids.

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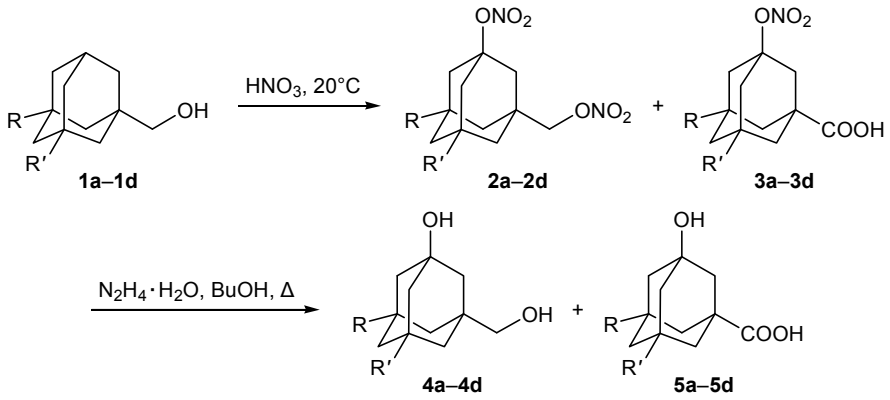
In recent time, new methods of synthesis of polysubstituted adamantanes have been extensively developed, and the scope of their application has been extended [1–13]. The unique geometry of almost spherical adamantane core in combination with the tripod and quadripod configurations of 1,3,5-tri- and 1,3,5,7-tetrasubstituted derivatives makes it possible to build up molecular assemblies with fixed orientation of substituents responsible for functional properties of materials based thereon [14–28]. However, there are a few published data on methods of synthesis of polyfunctionalized adamantane derivatives in which, on the one hand, the position of substituents is firmly fixed and, on the other hand, their conformational mobility is restricted due to the presence of spacers, e.g., one or several methylene units [29–34]. The use of such compounds as starting materials in the synthesis of molecular assemblies is predetermined by a set of properties which could be imparted to the final products; e.g., the latter could be used as photosensors, systems for targeted drug delivery to damaged cells, and materials for medical diagnostics [35–39].

Development of new synthetic approaches to polyhydric alcohols with restricted conformational mobility is important for functionalization of cage structures, which is especially significant taking into account prospects of using adamantane polyesters as main components of oils for high-temperature gas turbine engines [40–43]. Therefore, the goal of the present work was to develop a preparative procedure for the synthesis of difficultly accessible (3-hydroxyadamantan-1-yl)methanols.

The known methods of synthesis of (3-hydroxyadamantan-1-yl)methanol include reduction of 3-hydroxyadamantane-1-carboxylic acid [44–47], hydrolysis of 1-bromo-3-(hydroxymethyl)adamantane [48], and hydroxymethylation of 1-hydroxy-3-iodoadamantane [49]. The synthesis of (3-hydroxyadamantan-1-yl)methanol by reduction of 3-(nitroxymethyl)adamantan-1-ol has also been reported [50].

Each of the above listed procedures utilizes disubstituted adamantanes as starting compounds. In this work we selected adamantan-1-ylmethanols **1a**–**1d** as initial substrates for the synthesis of (3-hydroxyadamantan-1-yl)methanols **4a**–**4d**. The structure of the target compounds suggested that oxidation of commercially available adamantan-1-ylmethanols **1a**–**1d** could be appropriate since such methods ensured good results in the synthesis of a wide series of polyfunctional adamantane derivatives [30, 31, 51–55]. However, our attempts to oxidize adamantan-1-ylmethanol (**1a**) with a mixture of nitric and sulfuric acids were unsuccessful; when 2.2 equiv of fuming nitric acid was used, we isolated only 3-(nitroxymethyl)adamantane [56]. Increase of the amount of fuming nitric acid to 6 equiv and reaction time led to the formation of a complex mixture of compounds containing mainly products of oxidation of the hydroxymethyl group (adamantane-1-carboxylic acid, 3-hydroxyadamantane-1-carboxylic acid, and 3-nitroxyadamantane-1-carboxylic acid). No homoadamantane derivatives were detected since the initial compound was added to a preliminarily prepared mixture of sulfuric and nitric acids.

Scheme 1.



R = R′ = H (**a**); R = Me, R′ = H (**b**); R = Et, R′ = H (**c**); R = R′ = Me (**d**).

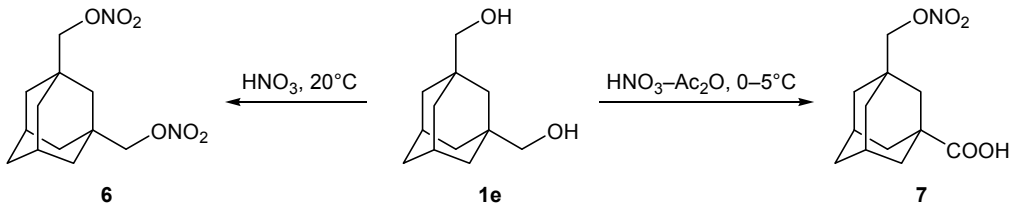
Mono- and dinitroxy derivatives of adamantane were used as starting compounds in the synthesis of a wide series of polyfunctional adamantane derivatives [57–62], including alcohols [63–67]. Nitroxy derivatives in which the ONO_2 group is separated from the adamantane skeleton by a methylene unit are exceptionally hydrolytically stable neopentyl type structures [50]. We have developed a procedure for the preparation of (3-hydroxyadamantan-1-yl)methanols **4a**–**4d** via initial nitroxylation of adamantan-1-ylmethanols **1a**–**1d** to the corresponding 3-(nitroxymethyl)adamantan-1-yl nitrates **2a**–**2d** and subsequent reduction of the latter (without preliminary isolation) with hydrazine hydrate (Scheme 1).

Alcohols **1a**–**1d** were subjected to nitroxylation with 40–70 equiv of fuming nitric acid at room temperature. Dinitroxy derivatives **2a**–**2d** thus formed were extracted into butan-1-ol, hydrazine hydrate was added to the extract, and the mixture was refluxed for 3 h. The yields of diols **4a**–**4d** were 67–75%. The OH protons of **4a**–**4d** resonated in the ^{1}H NMR spectra at δ 4.18–4.32 ppm. In the ^{13}C NMR spectra of **4a**–**4d**, the signal of the quaternary carbon atom linked to the hydroxy group was located at δ_C 68–69 ppm, and the CH_2OH signal was observed at δ_C 70–71 ppm. In addition, we isolated 3-hydroxyadamantane-1-carboxylic acids **5a**–**5d** as by-products (8–15%) formed as a result of oxidation of the hydroxymethyl group.

Some adamantane derivatives containing a nitroxymethyl group in the bridgehead position were reported to exhibit neuroprotective and vasodilator activities [68]. Therefore, we isolated dinitroxy derivatives **2a**–**2d** with a view to studying their biological activity. The yields of **2a**–**2d** were 63–70%, and 3-(nitroxymethyl)adamantane-1-carboxylic acids **3a**–**3d** were isolated as by-products in 7–14% yield. The ^{1}H NMR spectra of **2a**–**2d** displayed a singlet at δ 4.15–4.20 ppm due to protons of the CH_2ONO_2 group. The quaternary carbon atom linked to the ONO_2 group resonated in the ^{13}C NMR spectra at δ_C 89–91 ppm, and the CH_2ONO_2 carbon signal was located at δ_C 80–81 ppm. The ^{1}H NMR spectra of acids **3a**–**3d** contained a downfield singlet at δ 12.00 ppm due to OH proton of the carboxy group, and the carbonyl carbon signal was observed at δ_C 181 ppm. The isolated dinitroxy derivatives **2a**–**2d** were reduced to diols **4a**–**4d** in 88–93% yield.

The nitroxylation of adamantane-1,3-diyldimethanol (**1e**) with fuming nitric acid at 20°C afforded 1,3-bis(nitroxymethyl)adamantane (**6**) as the only isolated product. When the reaction was carried out in a mixture of nitric acid with acetic anhydride, the product was 3-(nitroxymethyl)adamantane-1-carboxylic acid (**7**) (Scheme 2). The reaction was not accompanied by oxidation of the unsubstituted bridgehead carbon atom, presumably due to acceptor effect of two

Scheme 2.



nitroxymethyl groups. The ^{13}C NMR spectrum of **7** showed a signal at δ_C 178 ppm due to carbonyl carbon atom and CH_2ONO_2 signal at δ_C 82 ppm, whereas no signal assignable to quaternary carbon atom linked to the ONO_2 group was present (δ_C ~90 ppm).

In summary, we have developed a simple procedure for the synthesis of (3-hydroxyadamantan-1-yl)-methanols **4a**–**4d** in high yields from commercially available starting compounds. The isolated compounds can be used in the synthesis of new materials with valuable properties, as well as substrates for studying biological activity.

EXPERIMENTAL

The mass spectra were recorded on a Thermo Finnigan DSQ GC/MS instrument [ZB5MS quartz capillary column, 30×0.32 mm, film thickness 0.25 μm; carrier gas helium, flow rate 1.5 mL/min; oven temperature programming from 80°C (1 min) to 340°C at a rate of 20 deg/min; injector temperature 300°C; electron impact, 70 eV). The ^1H and ^{13}C NMR spectra were measured on a Jeol JNM ECX-400 spectrometer at 400 MHz for ^1H using DMSO-d_6 as solvent. The IR spectra were recorded on a Shimadzu IR Affinity-1 spectrometer equipped with an ATR accessory. The elemental analyses were obtained on a Euro Vector 3000 EA analyzer using L-cystine as calibration standard.

Dinitroxy derivatives 2a–2d and acids 3a–3d (*general procedure*). Adamantan-1-ylmethanol **1a**–**1d**, 2 g, was added in portions over 5–10 min with vigorous stirring to fuming nitric acid at 15–20°C. The resulting solution was vigorously stirred for 1 h at 20°C and poured onto 500 g of crushed ice. The product was extracted into methylene chloride (3× 10 mL), the extract was washed with 5% aqueous potassium hydroxide (4×10 mL) and then with water until neutral washings. The organic phase was dried and evaporated to dryness, and the residue was recrystallized from aqueous methanol. The alkaline washings were acidified with hydrochloric acid, and the precipitate of 3-nitroxyadamantane-1-carboxylic acid **3a**–**3d** was filtered off.

3-(Nitroxymethyl)adamantan-1-yl nitrate (2a) was synthesized from 2 g (0.0012 mol) of **1a** and 20 mL of fuming nitric acid. Yield 2.3 g (70%), mp 62–64°C; published data [50]: mp 63–64°C.

3-Nitroxyadamantane-1-carboxylic acid (3a). Yield 0.2 g (7%), mp 144–145°C; published data [50]: mp 145–147°C.

5-Methyl-3-(nitroxymethyl)adamantan-1-yl nitrate (2b) was synthesized from 2 g (0.011 mol) of **1b** and 24 mL of fuming nitric acid. Yield 2.0 g (63%), mp 35–37°C. IR spectrum, ν, cm^{-1}: 2952, 2912, 2852 (C–H_{Ad}), 1612 (ONO_2), 1274 (ONO_2). ^1H NMR spectrum, δ, ppm: 0.94 s (3H, CH_3); 1.31–1.39 m (4H), 1.42–1.47 m (2H), 1.79–1.81 m (2H), 1.90–1.93 m (2H), and 2.00–2.02 m (2H) (CH_2, Ad); 2.35–2.39 m (1H, CH, Ad), 4.15 s (2H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 29.6 (CH_3), 30.4 (CH), 34.0, 37.0 (CH_2), 37.8 (CH_2), 38.2 (CH_2), 40.5 (CH_2), 42.1 (CH_2), 44.6 (CH_2), 45.5, 80.2 (CH_2), 89.8. Found, %: C 50.42; H 6.40; N 9.84. $C_{12}H_{18}N_2O_6$. Calculated, %: C 50.35; H 6.34; N 9.79.

5-Methyl-3-nitroxyadamantane-1-carboxylic acid (3b). Yield 0.28 g (10%), mp 85–86°C. IR spectrum, ν, cm^{-1}: 2945, 2914, 2864 (C–H_{Ad}), 1691 (C=O), 1612 (ONO_2), 1274 (ONO_2). ^1H NMR spectrum, δ, ppm: 0.97 s (3H, CH_3); 1.43–1.45 m (2H), 1.63 s (2H), 1.80 s (2H), 1.83 s (2H), 1.98–2.08 m (2H), and 2.18–2.26 m (2H) (CH_2, Ad); 2.39–2.43 m (1H, CH, Ad), 11.19 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 29.7 (CH_3), 30.5 (CH), 34.0, 36.7 (CH_2), 38.1 (CH_2), 39.7 (CH_2), 41.9 (CH_2), 44.2 (CH_2), 44.2, 45.4 (CH_2), 89.7, 182.1. Found, %: C 56.53; H 6.78; N 5.54. $C_{12}H_{17}NO_5$. Calculated, %: C 56.46; H 6.71; N 5.49.

3-Ethyl-5-(nitroxymethyl)adamantan-1-yl nitrate (2c) was synthesized from 2 g (0.01 mol) of **1c** and 20 mL of fuming nitric acid. Yield 2.1 g (67%), n_D^{20} = 1.4982. IR spectrum, ν, cm^{-1}: 2962, 2912, 2852 (C–H_{Ad}), 1612 (ONO_2), 1274 (ONO_2). ^1H NMR spectrum, δ, ppm: 0.82 t (3H, CH_3, J = 7.56 Hz), 1.23–1.28 m (2H, $CH_3C\mathbf{H}_2$); 1.41–1.49 m (2H), 1.53–1.61 m (2H), 1.79 s (4H), and 1.90–2.05 m (4H) (CH_2, Ad); 2.39–2.42 m (1H, CH, Ad), 4.17 s (2H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 7.2 (CH_3), 30.3 (CH), 35.2 (CH_2), 36.7, 37.4 (CH_2), 38.6 (CH_2), 39.6 (CH_2), 40.8 (CH_2), 42.3 (CH_2), 43.2 (CH_2), 44.1, 80.3 (CH_2), 90.1. Found, %: C 52.06; H 6.78; N 9.40. $C_{13}H_{20}N_2O_6$. Calculated, %: C 51.99; H 6.71; N 9.33.

3-Ethyl-5-nitroxyadamantane-1-carboxylic acid (3c). Yield 0.33 g (12%), mp 88–89°C. IR spectrum, ν, cm^{-1}: 2945, 2914, 2860 (C–H_{Ad}), 1691 (C=O), 1612 (ONO_2), 1274 (ONO_2). ^1H NMR spectrum, δ, ppm: 0.83 t (3H, CH_3, J = 7.36 Hz), 1.29 q (2H, $CH_3C\mathbf{H}_2$); 1.40–1.47 m (2H), 1.58–1.65 m (2H), 1.81 s (4H), 1.99–2.11 m (2H), and 2.19–2.29 m (2H) (CH_2, Ad); 2.40–2.45 m (1H, CHAd), 11.00 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 7.1 (CH_3), 30.4 (CH), 35.2 (CH_2), 36.8, 37.1 (CH_2), 38.4 (CH_2), 39.4 (CH_2), 40.1 (CH_2), 41.9 (CH_2), 43.1 (CH_2), 44.4, 90.0, 181.9.

Found, %: C 58.07; H 7.16; N 5.24. $C_{13}H_{19}NO_5$. Calculated, %: C 57.98; H 7.11; N 5.20.

5,7-Dimethyl-3-(nitroxymethyl)adamantan-1-yl nitrate (2d) was synthesized from 2 g (0.01 mol) of **1d** and 30 mL of fuming nitric acid. Yield 2.0 g (65%), mp 70–72°C. IR spectrum, ν, cm^{-1}: 2952, 2910, 2862 (C–H_{Ad}), 1612 (ONO_2), 1274 (ONO_2). ^1H NMR spectrum, δ, ppm: 0.96 s (6H, CH_3); 1.17–1.35 m (6H), 1.72–1.79 m (4H), and 1.87 s (2H) (CH_2, Ad); 4.20 s (2H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 29.4 (CH_3), 34.2, 38.2, 39.9 (CH_2), 44.1 (CH_2), 44.9 (CH_2), 49.5 (CH_2), 80.0 (CH_2), 90.4. Found, %: C 52.05; H 6.77; N 9.38. $C_{13}H_{20}N_2O_6$. Calculated, %: C 51.99; H 6.71; N 9.33.

5,7-Dimethyl-3-nitroxyadamantane-1-carboxylic acid (3d). Yield 0.39 g (14%), mp 99–100°C. IR spectrum, ν, cm^{-1}: 2951, 2900, 2862 (C–H_{Ad}), 1693 (C=O), 1618 (ONO_2), 1282 (ONO_2). ^1H NMR spectrum, δ, ppm: 0.89 s (6H, CH_3); 1.06–1.10 m (2H), 1.35 s (8H), and 1.65–1.71 m (2H) (CH_2, Ad); 12.18 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 29.5 (CH_3), 34.5, 39.4 (CH_2), 42.3 (CH_2), 44.4 (CH_2), 49.8 (CH_2), 92.3, 178.28. Found, %: C 58.05; H 7.17; N 5.26. $C_{13}H_{19}NO_5$. Calculated, %: C 57.98; H 7.11; N 5.20.

Diols 4a–4d and acids 5a–5d (*general procedure***).** Adamantan-1-ylmethanol **1a**–**1d** was added in portions over 5–10 min with vigorous stirring to fuming nitric acid at 15–20°C. The resulting solution was vigorously stirred for 1 h at 20°C and poured onto 500 g of crushed ice. The product was extracted into butan-1-ol (6 mL), the organic layer was separated, 20 mL of hydrazine hydrate was added, and the mixture was refluxed for 3 h. The mixture was cooled, diluted with 10 mL of butan-1-ol, and washed with water (2× 20 mL), 5% aqueous potassium hydroxide (3×15 mL), and water again (2×10 mL). The organic phase was dried and evaporated under reduced pressure, and the residue was recrystallized from toluene. The alkaline washings were acidified with aqueous HCl, and the precipitate of 3-hydroxyadamantane-1-carboxylic acid **5a**–**5d** was filtered off.

(3-Hydroxyadamantan-1-yl)methanol (4a) was synthesized from 2 g (0.012 mol) of **1a** and 20 mL of fuming nitric acid. Yield 1.6 g (75%), mp 140–142°C; published data [50]: mp 139–141°C.

3-Hydroxyadamantane-1-carboxylic acid (5a). Yield 0.18 g (8%), mp 203–205°C; published data [64]: mp 202–203°C.

(3-Hydroxy-5-methyladamantan-1-yl)methanol (4b) was synthesized from 2 g (0.011 mol) of **1b** and 24 mL of fuming nitric acid. Yield 1.45 g (67%), mp 126–128°C. IR spectrum, ν, cm^{-1}: 3317 (OH), 2962, 2912, 2850 (C–H_{Ad}). ^1H NMR spectrum, δ, ppm: 0.80 s (3H, CH_3); 0.90 s (2H), 1.49–1.59 m (4H), 1.65–1.77 m (4H), and 2.03 s (2H) (CH_2, Ad); 2.06 br.s (1H, CH, Ad), 2.96–2.97 m (2H, OCH_2), 4.20 s (1H, OH), 4.26 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 29.9 (CH), 30.3 (CH_3), 33.1, 42.7 (CH_2), 44.6 (CH_2), 46.2 (CH_2), 50.7 (CH_2), 51.6 (CH_2), 68.8, 71.0 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 196 (20) $[M]^+$, 165 (100), 121 (22), 109 (56), 107 (74), 91 (12). Found, %: C 73.48; H 10.33. $C_{12}H_{20}O_2$. Calculated, %: C 73.43; H 10.27.

3-Hydroxy-5-methyladamantane-1-carboxylic acid (5b). Yield 0.25 g (11%), mp 163–165°C; published data [64]: mp 163–164°C.

(3-Ethyl-3-hydroxyadamantan-1-yl)methanol (4c) was synthesized from 2 g (0.01 mol) of **1c** and 20 mL of fuming nitric acid. Yield 1.55 g (72%), mp 113–115°C. IR spectrum, ν, cm^{-1}: 3324 (OH), 2958, 2908, 2850 (C–H_{Ad}). ^1H NMR spectrum, δ, ppm: 0.70 t (3H, CH_3, J = 7.32 Hz), 1.09 q (2H, C**H**$_2$CH$_3$, J = 7.32 Hz); 1.18 s (2H), 1.45–1.53 m (4H), and 1.64–1.76 m (4H) (CH_2, Ad); 2.01–2.06 m (3H, CH_2, CH, Ad), 2.98–3.00 m (2H, OCH_2), 4.18 s (1H, OH), 4.24 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 7.6 (CH_3), 29.7 (CH), 35.2, 35.5 (CH_2), 42.7 (CH_2), 44.6 (CH_2), 46.2 (CH_2), 50.7 (CH_2), 51.6 (CH_2), 68.7, 70.9 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 210 (14) $[M]^+$, 179 (100), 121 (68), 95 (26), 79 (18). Found, %: C 74.31; H 10.60. $C_{13}H_{22}O_2$. Calculated, %: C 74.24; H 10.54.

5-Ethyl-3-hydroxyadamantane-1-carboxylic acid (5c). Yield 0.29 g (13%), mp 163–164°C [64].

(3-Hydroxy-5,7-dimethyladamantan-1-yl)methanol (4d) was synthesized from 2 g (0.01 mol) of **1d** and 30 mL of fuming nitric acid. Yield 70%, mp 136–137°C. IR spectrum, ν, cm^{-1}: 3300 (OH), 2960, 2910, 2852 (C–H_{Ad}). ^1H NMR spectrum, δ, ppm: 0.79 s (3H, CH_3), 0.91–0.99 m and 1.14 s (6H each, CH_2, Ad), 2.99–3.00 m (2H, OCH_2), 4.27 s (1H, OH), 4.32 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 30.4 (CH_3), 33.7, 45.1 (CH_2), 46.2 (CH_2), 50.7 (CH_2), 51.7 (CH_2), 68.9, 71.1 (CH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 210 (5) $[M]^+$, 178 (100), 122 (40), 120 (84), 94 (10), 54 (10). Found, %: C 74.30; H 10.59. $C_{13}H_{22}O_2$. Calculated, %: C 74.24; H 10.54.

3-Hydroxy-5,7-dimethyladamantane-1-carboxylic acid (5d). Yield 0.33 g (15%), mp 228–230°C; published data [64]: mp 235–236°C.

(Adamantane-1,3-diyl)bis(methylene) dinitrate (6) was synthesized from 0.5 g (0.002 mol) of **1e** and 20 mL (0.2 mol) of fuming nitric acid. Yield 0.6 g (82%), mp 110–112°C. IR spectrum, ν, cm^{-1}: 2943, 2922, 2893 (C–H_{Ad}), 1618 (ONO_2), 1273 (ONO_2). ^1H NMR spectrum, δ, ppm: 1.15–1.23 m (10H) and 1.32 s (2H) (CH_2, Ad), 1.51–1.56 m (2H, CH, Ad), 4.12 s (4H, OCH_2). ^{13}C NMR spectrum, δ_C, ppm: 30.4 (CH), 31.3, 39.5 (CH_2), 44.6 (CH_2), 50.2 (CH_2), 81.1 (OCH_2), 90.4. Found, %: C 50.41; H 6.40; N 9.84. $C_{12}H_{18}N_2O_6$. Calculated, %: C 50.35; H 6.34; N 9.79.

3-(Nitroxymethyl)adamantane-1-carboxylic acid (7). A solution of 0.8 g (0.004 mol) of 1,3-bis(hydroxymethyl)adamantane (**1e**) in 7 mL (0.169 mol) of fuming nitric acid was cooled to 5°C, and 2 mL (0.018 mol) of acetic anhydride was added dropwise with vigorous stirring. The resulting solution was kept for 36 h at 0–2°C and was then poured onto ice. The precipitate was filtered off, washed with water, and dried. Yield 0.45 g (45%), mp 140–141°C. IR spectrum, ν, cm^{-1}: 2926, 2906, 2858 (C–H_{Ad}), 1689 (C=O), 1612 (ONO_2), 1271 (ONO_2). ^1H NMR spectrum, δ, ppm: 1.45–1.50 m (2H), 1.52–1.59 m (4H), and 1.64–1.79 m (6H) (CH_2, Ad); 2.01 br.s (2H, CH, Ad), 4.17 s (2H, OCH_2), 12.12 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 27.7 (CH), 33.7, 35.7 (CH_2), 37.9 (CH_2), 38.2 (CH_2), 38.3 (CH_2), 40.1 (CH_2), 82.0 (CH_2), 178.5 (C=O). Found, %: C 56.52; H 6.75; N 5.54. $C_{12}H_{17}NO_5$. Calculated, %: C 56.46; H 6.71; N 5.49.

Reduction of compounds 2a–2d (*general procedure***).** A mixture of 0.5 g of dinitrate **2a**–**2d**, 1 mL of butan-1-ol, and 3 mL of hydrazine hydrate was refluxed for 3 h. The resulting solution was cooled, diluted with 10 mL of water, and extracted with butan-1-ol (3 × 5 mL). The extract was washed with water and dried, the solvent was evaporated under reduced pressure, and the residue was recrystallized from toluene. Listed below are compound no., yield, and melting point: **4a**, 89%, 140–142°C; **4b**, 87%, 127–129°C; **4c**, 88%, 114–115°C; **4d**, 93%, 137–138°C.

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