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Synthesis of 4-Methyl-6-*N*-(4-R-phenyl)-1-azabicyclo-[3.2.1]octane-3-enes

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Abstract—1-Azabicyclo[3.2.1]oct-3-ene were synthesized by the intramolecular carbocationic cyclization of 1-[2-hydroxy-2-(4-R-phenyl)ethyl]-1,2,3,6-tetrahydropyridines in a trifluoromethanesulfonic acid medium

Keywords: 1-azabicyclo[3.2.1]oct-3-ene, 1,2,3,6-tetrahydropyridine, trifluoromethanesulfonic acid, intramolecular cyclization, carbocation

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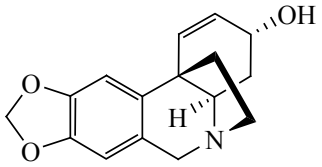
INTRODUCTION

The 1-azabicyclo[3.2.1]octane fragment is found in alkaloids isolated from some plants of the *Amaryllidaceae* family. These substances are known to exhibit a wide range of biological activities. For example, the alkaloids crinine and montanine (Fig. 1), as well as their derivatives, show antimalarial, antifungal, antitumor, antiviral, antibacterial, antihistamine, and cholinomimetic activity and some types of psychopharmacological activity [1–8].

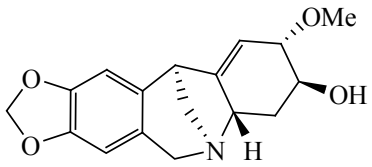
The synthesis of 1-azabicyclo[3.2.1]octane derivatives is much less documented than the synthesis of related bicyclic structures with the nitrogen atom in the bridging positions. The reported methods for constructing the 1-azabicyclo[3.2.1]octane core usually produce mixtures of products and involve a few stages, including intramolecular cyclizations initiated by radical or nucleophilic agents [9–17].

Taking into account that the generation and transformation of superelectrophilic intermediates is a dynamically developing area of organic chemistry [18], we consider 1,2,3,6-tetrahydropyridine systems containing at least two reaction centers as very promising objects for research in terms of the synthesis of new bi- and polycyclic compounds structurally similar to natural alkaloids and potentially having biological activity.

As known, treatment of 1-alkyl-1,2,3,6-tetrahydropyridines with TfOH gives a dicationic intermediate [19, 20], which enters inter- and intramolecular Friedel–Crafts reactions as an alkylating agent [21–23]. Furthermore, we showed that 1-[2-(adamantan-1-yl)-2-hydroxyethyl]-1,2,3,6-tetrahydropyridines undergo an intramolecular skeletal Wagner–Meerwein rearrangement under the action of TfOH, resulting in the formation of substituted 1-azabicyclo[3.3.1]non-3-enes annulated with the homoadamantane core [24]. Thus, depending on the nature of the substituent at the nitrogen atom of 1,2,3,6-tetrahydropyridine, the multiple bond can function either as a nucleophilic center or as a precursor of an electrophilic center in reactions in acidic media.



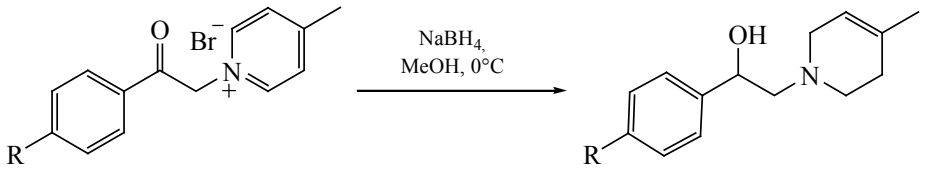
Crinine



Montanine

Fig. 1. Structure of alkaloids.

Scheme 1.



1a–1f **2a–2f**

2a, 90% **2d**, 90%
2b, 79% **2e**, 82%
2c, 88% **2f**, 98%

R = H (**a**), CH_3 (**b**), OCH_3 (**c**), F (**d**), Cl (**e**), NO_2 (**f**).

We realized the conversion of 1-[2-hydroxy-2-(4-R-phenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridines **2a–2f** into 1-azabicyclo[3.2.1]oct-3-enes **3a–3f** in a trifluoromethanesulfonic acid medium.

RESULTS AND DISCUSSION

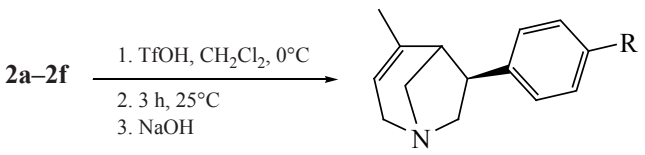
The starting 1-[2-hydroxy-2-(4-R-phenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridines **2a–2f** were prepared by the reduction of quaternary salts **1a–1f** with sodium borohydride in methanol (Scheme 1) by the procedure described in [25, 26]. 4-Methylpyridinum salts **1a–1f** were synthesized by the standard quaternization of 4-picoline with 4-R-phenacyl bromides [27–31].

The ^{1}H NMR spectra of compounds **2a–2f** display the methylene proton signals of the 1,2,3,6-tetrahydropyridine and 2-hydroxyethyl fragments at 2.08–3.30 ppm and the OH proton signal as a broadened singlet at 4.05–4.23 ppm. The pyrimidine double bond proton signals are observed at 5.34–5.37 ppm, and the aromatic protons give signals at 6.80–8.20 ppm. The ^{13}C NMR spectra of compounds **2a–2f** all contain a signal of the tertiary carbon atom of the 2-hydroxyethyl group at 68.2–69.1 ppm and pyrimidine C^4=C^5 carbon signals at 118.0–118.8 and 132.9–137.8 ppm, respectively. The signals of the carbon atoms of the aromatic system are observed at 115.2–161.1 ppm. In the case of fluorine derivative **2d**, the signals of aromatic carbons are split due to coupling with the ^{19}F nuclei.

4-Methyl-1,2,3,6-tetrahydropyridines **2a–2f** were then treated with TfOH to obtain cyclic intramolecular cationic cyclization products 1-azabicyclo[3.2.1]oct-3-enes **3a–3f** in yields of 52–94% (Scheme 2). The reaction was carried out in an excess of TfOH at room temperature for 24 h (TLC monitoring, eluent *i*-PrOH). The products were isolated by column chromatography (eluent CH_2Cl_2–*i*-PrOH, 1 : 1). It is worth noting that the reactions with electron-acceptor-substituted tetrahydropyridines **2d–2f** provide cyclization products in noticeably lower yields. Attempted cyclization in concentrated sulfuric acid was unsuccessful.

The ^{1}H NMR spectra of compounds **3a–3f**, the signals of the protons of the bicyclic core are observed at 2.45–4.60 ppm, the signals of the double bond protons appear at 5.26–6.00 ppm, and aromatic protons give signals at 6.98–7.25 ppm. The presence in the ^{13}C NMR spectra of products **3a–3f** of two tertiary carbon signals in the range of 33.0–51.0 ppm provide evidence for the occurrence of intramolecular cyclization; the signals of the double bond C^5 and C^4 atoms of the bicycle appear at 111.5–114.8 and 138.0–147.5 ppm, respectively. The signals of the carbon atoms of the aromatic system are

Scheme 2.



3a–3f

3a, 83% **3d**, 65%
3b, 94% **3e**, 83%
3c, 93% **3f**, 52%

R = H (**a**), CH_3 (**b**), OCH_3 (**c**), F (**d**), Cl (**e**), NO_2 (**f**).

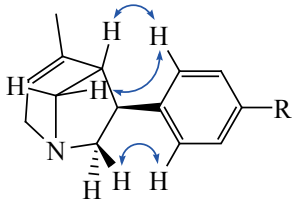
observed at 114.2–162.1 ppm. In the case of fluorine derivative **3d**, the aromatic carbon signals are split due to coupling with the ^{19}F nuclei.

The ^{1}H and ^{13}C NMR signals of compounds **3a–3f** were assigned on the basis of the DEPT-135 ^{13}C NMR spectra ands and 2D HMBC ^{1}H–^{13}C and HETCOR ^{1}H–^{13}C experiments. The orientation of the aromatic substituent in compounds **3a–3f** was determined using the 2D NOESY NMR experiment. The spectra of compounds **3a–3f** contain cross-peaks indicative of the through-space interaction of the *ortho* protons of the benzene ring with the proton at C^5, *exo*-oriented proton at C^7, and *anti*-oriented proton at C^8 (Fig. 2). This finding points to an *exo* orientation of the 4-R-phenyl substituent.

Let us consider the plausible reaction route, using the example of tetrahydropyridine **2a** (Scheme 3). The initial protonation of both the tetrahydropyridine nitrogen atom and the hydroxyl group, followed by dehydration of the oxonium ion leads to the formation of dication **A** containing a benzyl-type cationic center, which further attacks the multiple bond of the tetrahydropyridine moiety. As a result, dication **B** is formed, whose subsequent deprotonation leads to 1-azabicyclo[3.2.1]-oct-3-ene **3a**. The fact that compound **4a** formed by the Friedel–Crafts intramolecular alkylation involving the *ortho* positions of the phenyl ring was not detected can be explained by a hindered reaction of the aromatic system with the cationic center at the C^4 atom of intermediate **B** because of the rigidly fixed configuration of the forming bicyclic core.

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu IR Affinity-1 spectrometer in KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded on a JEOL NMR-ECX400 spectrometer at 400 and 100 MHz, respectively, using TMS as an internal standard. The melting points were determined by the capillary method on an SRS OptiMelt MPA 100 apparatus and are uncorrected. Thin-layer chromatography was performed on Sorbfil PSTH-AF-A-UV plates [layer 90–120 μm, UV indicator (254 nm)], spot visualization by exposure to iodine vapor. The elemental analyses were obtained on a EuroVector 3000 EA elemental analyzer using L-cystine as a standard.



3a–3f

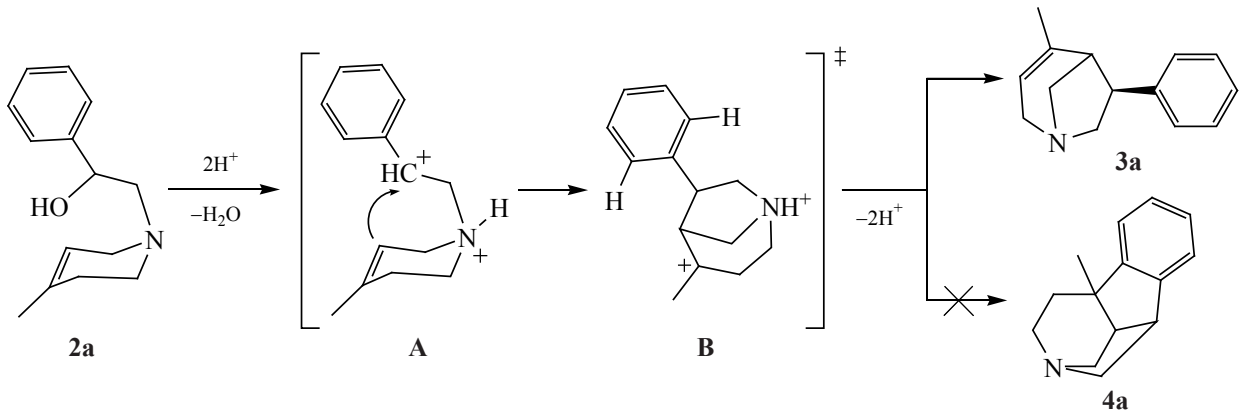
R = H (**a**), CH_3 (**b**), OCH_3 (**c**), F (**d**), Cl (**e**), NO_2 (**f**).

Fig. 2. Through-space interactions of hydrogen atoms in compounds **3a–3f**, detected by NOESY NMR analysis.

Quaternary salts **1a–1f** were prepared by a known procedure, and the melting points of the products are consistent with those reported in [27–31].

1-[2-Hydroxy-2-(4-R-phenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridines 2a–2f (*general procedure*). Sodium borohydride (0.2 g, 5.2 mmol) was added in portions with stirring to a cold (0°C) solution of 3.5 mmol of salt **1a–1f** in 15 mL of MeOH over the course of 1 h. Then cooling was removed, and the reaction mixture was stirred for another 2 h, diluted with water (60 mL), and the product was extracte Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified by recrystallization from ethanol.

Scheme 3.



1-(2-Hydroxy-2-phenylethyl)-4-methyl-1,2,3,6-tetrahydropyridine (2a). Yield 0.68 g (90%), brick red powder, mp 74–75°C. IR spectrum, ν, cm^{-1}: 3417, 2924, 2900, 2823, 2762, 1620, 1442, 1095, 1026, 702. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.68 s (3H, CH_3), 2.08 br.s (2H), 2.50–2.58 m (3H), 2.83 quintet (1H, ^4J 5.7 Hz), 2.94 d (1H, ^3J 15.6 Hz), 3.18 d (1H, ^3J 15.6 Hz), 4.12 br.s (1H, CHOH), 4.75 d.d (1H, ^4J 4.1, ^3J 9.6 Hz), 5.34–5.35 m (1H, CH^5), 7.21–7.26 m (1H), 7.29–7.37 m (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 23.0 (CH_3), 30.7 (CH_2), 50.2 (CH_2), 52.6 (CH_2), 66.0 (CH_2), 69.1 (CHOH), 118.8 (CH), 125.9 (CH_{Ph}), 127.5 (CH_{Ph}), 128.4 (CH_{Ph}), 132.9 (C_{quat}), 142.4 (C_{Ph}). Found, %: C 77.44; H 8.86; N 6.38. $C_{14}H_{19}NO$. Calculated, %: C 77.38; H 8.81; N 6.45.

1-[2-Hydroxy-2-(4-methylphenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridine (2b). Yield 0.63 g (79%), brown powder, mp 67–70°C. IR spectrum, ν, cm^{-1}: 3410, 2903, 2829, 1685, 1091, 1020, 708. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.71 s (3H, CH_3), 2.16 br.s (2H), 2.33 s (3H, CH_3), 2.62–2.71 m (3H), 2.91–2.94 m (1H), 3.07 d (1H, ^3J 8.0 Hz), 3.29 d (1H, ^3J 8.0 Hz), 4.12 br.s (1H, CHOH), 4.84 t (1H, CHOH, ^3J 8.0 Hz), 5.36 s (1H), 7.14 d (2H, ^3J 8.0 Hz), 7.26 d (2H, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.2 (CH_3), 22.9 (CH_3), 30.0 (CH_2), 50.2 (CH_2), 52.4 (CH_2), 65.7 (CH_2), 68.8 (CHOH), 118.0 (CH), 125.9 (CH_{Tol}), 129.1 (CH_{Tol}), 133.1 (C_{quat}), 137.3 (C_{Tol}), 138.9 (C_{Tol}). Found, %: C 77.96; H 9.20; N 6.13. $C_{15}H_{21}NO$. Calculated, %: C 77.88; H 9.15; N 6.05.

1-[2-Hydroxy-2-(4-methoxyphenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridine (2c). Yield 0.76 g (88%), brown powder, mp 70–72°C. IR spectrum, ν, cm^{-1}: 3390, 2900, 2825, 1670, 1250, 1014. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.69 s (3H, CH_3), 2.09 br.s (2H), 2.51–2.59 m (3H), 2.81–2.87 m (1H), 2.95 d (1H, ^3J 16.0 Hz), 3.18 d (1H, ^3J 16.0 Hz), 3.78 s (3H, OCH_3), 4.23 br.s (1H, CHOH), 4.72 t (1H, CHOH, ^3J 8.0 Hz), 5.36 s (1H, CH), 6.87 d (2H, ^3J 8.0 Hz), 7.29 d (2H, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 23.0 (CH_3), 30.7 (CH_2), 50.2 (CH_2), 52.6 (CH_2), 55.3 (OCH_3), 66.1 (CH_2), 68.7 (CHOH), 113.8 (CH_{arom}), 118.9 (CH), 127.2 (CH_{arom}), 132.9 (C_{arom}–CH–OCH_3), 134.4 (C_{quat}), 159.1 (C_{arom}–O). Found, %: C 72.77; H 5.54; N 5.73. $C_{15}H_{21}NO_2$. Calculated, %: C 72.84; H 5.56; N 5.66.

1-[2-Hydroxy-2-(4-fluorophenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridine (2d). Yield 0.74 g (90%), brown powder, mp 101–103°C. IR spectrum, ν, cm^{-1}: 3385, 2903, 2829, 1665, 1230, 1091. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.70 s (3H, CH_3), 2.14 br.s (2H), 2.54–2.70 m (2H), 2.88–2.94 m (1H), 3.05 d (1H, ^3J 16.0 Hz), 3.27 d (1H, ^3J 16.0 Hz), 3.67–3.72 m (1H), 4.25 br.s (1H, CHOH), 4.81–4.84 m (1H, CHOH), 5.36 br.s (1H, CH^5), 6.99–7.03 m (2H), 7.25–7.36 m (2H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 22.9 (CH_3), 30.1 (CH_2), 50.2 (CH_2), 52.4 (CH_2), 65.6 (CH_2), 68.4 (CHOH), 115.2 d (CH_{arom}, $^2J_{CF}$ 21.0 Hz), 118.0 (CH), 127.6 d (CH_{arom}, $^3J_{CF}$ 7.0 Hz), 133.1 (C_{arom}), 137.8 (C_{quat}), 162.3 d (C_{arom}–F, $^1J_{CF}$ 244.0 Hz). Found, %: C 71.38; H 7.74; N 6.02. $C_{14}H_{18}FNO$. Calculated, %: C 71.46; H 7.71; N 5.95.

1-[2-Hydroxy-2-(4-chlorophenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridine (2e). Yield 0.72 g (82%), light-brown powder, mp 80–83°C. IR spectrum, ν, cm^{-1}: 3315, 3015, 2902, 1260, 1020, 830. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.69 s (3H, CH_3), 2.10 br.s (2H), 2.44–2.48 m (1H), 2.53–2.57 m (2H), 2.82–2.85 m (1H), 2.95 d (1H, ^3J 16.0 Hz), 3.15 d (1H, ^3J 16.0 Hz), 4.05 br.s (1H, CHOH), 4.71–4.75 m (1H, CHOH), 5.36 s (1H, CH^5), 7.30 s (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 22.9 (CH_3), 30.6 (CH_2), 50.2 (CH_2), 52.6 (CH_2), 65.8 (CH_2), 68.4 (CHOH), 118.7 (CH), 127.3 (CH_{arom}), 128.5 (CH_{arom}), 132.9 (C_{quat}), 133.1 (C_{arom}–Cl), 140.9 (C_{arom}). Found, %: C 66.73; H 7.24; N 5.63. $C_{14}H_{18}ClNO$. Calculated, %: C 66.79; H 7.21; N 5.56.

1-[2-Hydroxy-2-(4-nirophenyl)ethyl]-4-methyl-1,2,3,6-tetrahydropyridine (2f). Yield 0.90 g (98%), red-brown powder, mp 94–97°C. IR spectrum, ν, cm^{-1}: 3410, 2903, 2829, 1685, 1510, 1350, 1310, 1111, 760. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.71 s (3H, CH_3), 2.16 br.s (2H), 2.52–2.60 m (1H), 2.69–2.73 m (2H), 2.91–2.97 m (1H), 3.07 d (1H, ^3J 16.0 Hz), 3.29 d (1H, ^3J 16.0 Hz), 4.94–4.97 m (1H, CHOH), 5.37 s (1H, CH^5), 7.25 s (1H, CHOH), 7.56 d (2H, ^3J 8.0 Hz), 8.20 d (2H, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 22.9 (CH_3), 30.0 (CH_2), 50.2 (CH_2), 52.3 (CH_2), 65.1 (CH_2), 68.2 (CHOH), 117.8 (CH), 123.7 (CH_{arom}), 126.6 (CH_{arom}), 133.2 (C_{quat}), 147.4 (C_{arom}), 149.7 (C_{arom}–NO_2). Found, %: C 64.20; H 6.96; N 10.61. $C_{14}H_{18}N_2O_3$. Calculated, %: C 64.11; H 6.92; N 10.68.

Synthesis of compounds 3a–3f (*general procedure*). Trifluoromethanesulfonic acid, 4.4 mL (50 mmol), was added in portions over the course of 3 h to a solution

of 0.5 g of tetrahydropyridine **2a–2f** in 1.5 mL of anhydrous CH_2Cl_2, cooled to 0°C. Then cooling was removed, and the reaction mixture was stirred for 24 h, poured onto ice, adjusted to pH 12–13 with 20% NaOH solution, and the product was extracted with CH_2Cl_2 (3 × 20 mL). The extract was washed with saturated NaCl solution, and the combined organic extracts were dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was separated by column chromatography (eluent CH_2Cl_2–*i*-PrOH, 1 : 1).

4-Methyl-6-phenyl-1-azabicyclo[3.2.1]oct-3-ene (3a). Yield 0.38 g (83%), beige crystals, mp 93–95°C. IR spectrum, ν, cm^{-1}: 2989, 2935, 1604, 1504, 1454, 1384, 1056, 833, 771, 748, 698. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.38 s (3H, CH_3), 2.24 br.s (1H), 2.69–3.46 m (5H), 3.99–4.23 m (2H), 5.78–5.96 m (1H), 7.06–7.25 m (5H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 26.5 (CH_3), 44.7 (CH), 50.9 (CH), 59.7 (CH_2), 64.7 (CH_2), 69.7 (CH_2), 112.4 (CH), 123.0 (CH_{Ph}), 128.6 (CH_{Ph}), 129.0 (CH_{Ph}), 142.3 (C_{quat}), 147.4 (C_{Ph}). Found, %: C 84.43; H 8.62; N 6.95. $C_{14}H_{17}N$. Calculated, %: C 84.37; H 8.60; N 7.03.

4-Methyl-6-(*p*-tolyl)-1-azabicyclo[3.2.1]oct-3-ene (3b). Yield 0.43 g (94%), beige crystals, mp 91–92°C. IR spectrum, ν, cm^{-1}: 3076, 2979, 2930, 1614, 1050, 832. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 c (3H, CH_3), 2.27 c (3H, CH_3), 2.75–3.61 m (8H), 5.89–5.91 m (1H), 6.98–7.08 m (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.4 (CH_3), 26.4 (CH_3), 33.4 (CH), 44.3 (CH), 51.2 (CH_2), 58.3 (CH_2), 59.6 (CH_2), 113.5 (CH), 124.1 (CH_{Tol}), 129.5 (CH_{Tol}), 138.9 (C_{Tol}), 139.3 (C_{Tol}), 147.5 (C_{quat}). Found, %: C 84.37; H 8.97; N 6.66. $C_{15}H_{19}N$. Calculated, %: C 84.46; H 8.98; N 6.57.

6-(4-Methoxyphenyl)-4-methyl-1-azabicyclo-[3.2.1]oct-3-ene (3c). Yield 0.43 g (93%), beige crystals, mp 83–84°C. IR spectrum, ν, cm^{-1}: 3050, 2900, 2825, 1670, 1250, 1014. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.21 s (3H, CH_3), 2.46–3.69 m (8H), 3.76 s (3H, OCH_3), 5.34–5.40 m (1H), 7.17–7.25 m (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 18.4 (CH_3), 45.9 (CH), 50.3 (CH), 55.3 (CH_2), 58.3 (CH_3), 63.6 (CH_2), 68.8 (CH_2), 114.2 (CH_{arom}), 114.8 (CH), 128.8 (CH_{arom}), 139.0 (C_{arom}), 140.4 (C_{quat}), 159.3 ($\underline{C}OCH_3$). Found, %: C 78.63; H 8.41; N 6.90. $C_{15}H_{19}NO$. Calculated, %: C 78.56; H 8.35; N 6.98.

4-Methyl-6-(4-fluorophenyl)-1-azabicyclo[3.2.1]-oct-3-ene (3d). Yield 0.30 g (65%), white powder, mp 97–99°C. IR spectrum, ν, cm^{-1}: 3075, 2903, 2829, 1665, 1230, 1178, 1091. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.14 s (3H, CH_3), 1.20–1.32 m (1H), 2.52 s (1H), 3.25–3.28 m (1H), 3.59–3.76 m (3H), 4.08–4.21 m (2H), 5.26–5.34 m (1H), 7.02 d (2H, ^3J 8.0 Hz), 7.23 d (2H, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 22.0 (CH_3), 46.4 (CH), 50.6 (CH), 52.8 (CH_2), 55.7 (CH_2), 58.9 (CH_2), 111.5 (CH), 116.3 d (CH_{arom}, $^2J_{CF}$ 22.0 Hz), 128.4 d (CH_{arom}, $^3J_{CF}$ 8.0 Hz), 135.8 (C_{arom}–CH), 145.1 (C_{quat}), 162.1 d (C_{arom}–F, $^1J_{CF}$ 246.0 Hz). Found, %: C 77.31; H 7.39; N 6.54. $C_{14}H_{16}FN$. Calculated, %: C 77.39; H 7.42; N 6.45.

6-(4-Chlorophenyl)-4-methyl-1-azabicyclo[3.2.1]-oct-3-ene (3e). Yield 0.38 g (83%), gray powder, mp 91–94°C. IR spectrum, ν, cm^{-1}: 3080, 2979, 2930, 1504, 1020, 693. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.67 s (3H, CH_3), 3.76–3.85 m (2H), 4.20–4.34 m (5H), 4.49–4.53 m (1H), 5.95–6.00 m (1H), 7.04–7.15 m (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 22.8 (CH_3), 45.6 (CH), 50.1 (CH), 63.6 (CH_2), 64.7 (CH_2), 68.6 (CH_2), 113.4 (CH), 128.3 (CH_{arom}), 129.2 (CH_{arom}), 133.5 (C_{arom}–Cl), 138.0 (C_{arom}), 140.0 (C_{quat}). Found, %: C 71.99; H 6.97; N 5.92. $C_{14}H_{16}ClN$. Calculated, %: C 71.94; H 6.90; N 5.99.

3-Methyl-6-(4-nirophenyl)-1-azabicyclo[3.2.1]-oct-3-ene (3f). Yield 0.24 g (52%), yellow powder, mp 81–83°C. IR spectrum, ν, cm^{-1}: 3065, 2900, 2830, 1675, 1520, 1350, 1310, 1111, 760. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19 s (3H, CH_3), 2.98–4.69 m (8H), 5.38–5.46 m (1H), 7.78–7.55 m (2H), 8.12–8.17 m (2H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 22.9 (CH_3), 45.8 (CH), 50.7 (CH), 58.2 (CH_2), 63.5 (CH_2), 64.9 (CH_2), 113.9 (CH), 123.9 (CH_{arom}), 129.0 (CH_{arom}), 138.0 (C_{quat}), 142.4 (C_{arom}), 147.5 (C_{arom}). Found, %: C 68.90; H 6.64; N 11.40. $C_{14}H_{16}N_2O_2$. Calculated, %: C 68.83; H 6.60; N 11.47.

CONCLUSIONS

A series of novel 4-methyl-6-exo-(4-R-phenyl)-1-azabicyclo[3.2.1]oct-3-enes was synthesized by the one-step intramolecular carbocationic cyclization of 1-[2-hydroxy-2-(4-R-phenyl)ethyl]-1,2,3,6-tetrahydropyridines in trifluoromethanesulfonic acid. It was shown that the cyclization products of tetrahydropyridines **2d–2f** which contain electron-acceptor substituents in the benzene ring are formed in noticeably lower yields. The cyclization of 1,2,3,6-tetrahydropyridine **2a** in concentrated sulfuric acid did not occur. The

resulting data serve as a basis for further research on the stereochemical features of the reaction and the biological activity of the synthesized cyclic structures.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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