ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 10, pp. 1527–1533. © Pleiades Publishing, Ltd., 2010.
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3-Substituted 3-Azabicyclo[3.3.1]nonan-9-ols and Their Transformations Involving the Hydroxy Group

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Received November 16, 2009

Abstract—The reduction of 3-benzyl- and 3-*tert*-butoxycarbonyl-3-azabicyclo[3.3.1]nonan-9-ones with sodium tetrahydridoborate gave the corresponding alcohols as mixtures of α- and β-epimers at a ratio of 2:3. The resulting alcohols reacted with acetyl chloride and methanesulfonyl chloride at the hydroxy group to form *O*-acetyl and *O*-methylsulfonyl derivatives. Reactions of the latter with potassium iodide and sodium azide afforded 3-substituted 9-iodo(azido)-3-azabicyclo[3.3.1]nonanes. 9-Iodo derivatives were treated with triphenylphosphine to obtain triphenylphosphonium salts which were converted into the corresponding phosphonium ylides by the action of sodium methoxide in methanol, and the ylides readily reacted with benzaldehyde according to Wittig.

DOI: 10.1134/S1070428010100143

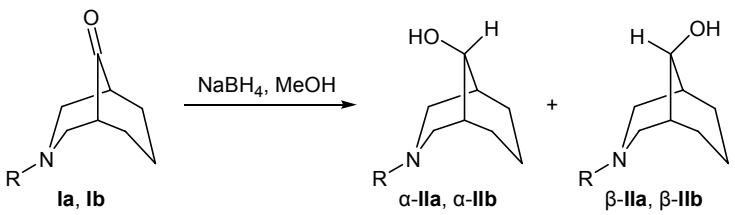
We previously developed [1] a convenient procedure for the synthesis of 3-substituted 3-azabicyclo-[3.3.1]nonan-9-ones that are promising as synthons due to the presence of functional groups in their molecules. Interest in compounds possessing a 3-azabicyclo-[3.3.1]nonane system is determined by their structural similarity to terpene alkaloids [2] which exhibit high biological activity.

By reduction of ketones **Ia** and **Ib** with sodium tetrahydridoborate in methanol we obtained a mixture of α- and β-epimeric alcohols **IIa** and **IIb** in almost quantitative yield (Scheme 1). In both cases, the ratios of α- and β-epimers were fairly similar (~2:3); the epimer ratio was determined from the intensities of two doublets belonging to the 9-H proton in the ^{1}H NMR spectra. According to published data [3–5], the 9-H proton in the major β-epimer resonates in a stronger field, at δ 3.67–3.71 ppm, and the corresponding signal of the α-epimer is observed at δ 3.95–3.98 ppm. We failed to separate epimer mixtures into individual compounds, so that further chemical transformations were performed with mixtures α-**IIa**/β-**IIa** and α-**IIb**/β-**IIb**, and epimeric composition of the products was determined on the basis of their ^{1}H NMR spectra (see Experimental).

Alcohols **IIa** and **IIb** reacted with acetyl chloride and methanesulfonyl chloride in the presence of pyridine to give the corresponding 9-*O*-acetyl- and 9-*O*-methylsulfonyl derivatives **III** and **IV** (Scheme 2) which were subjected to further chemical transformations. By heating compounds **IVa** and **IVb** with potassium iodide in acetone or with sodium azide in dimethyl sulfoxide (DMSO) we obtained iodides **Va** and **Vb** and azides **VIa** and **VIb** as a result of nucleophilic replacement of the methylsulfonyl group.

The ^{1}H NMR spectra of compounds **III** and **IV** contained singlets from methyl protons in the acetyl and methylsulfonyl groups. The ratio of α- and

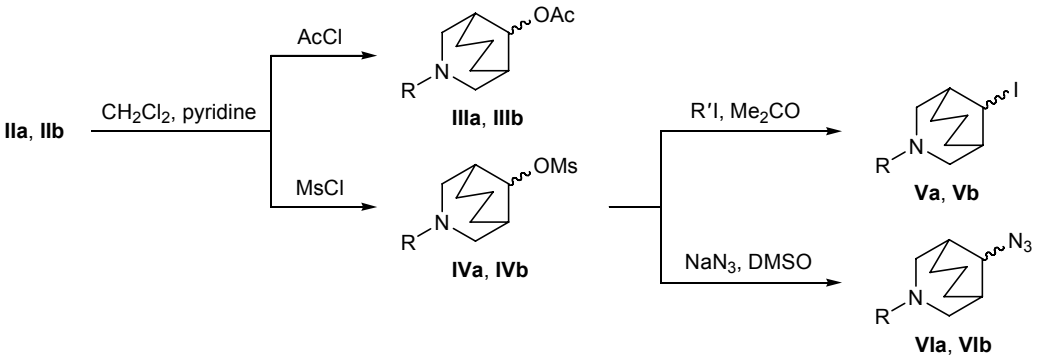
Scheme 1.



Ia, **Ib** α-**IIa**, α-**IIb** β-**IIa**, β-**IIb**

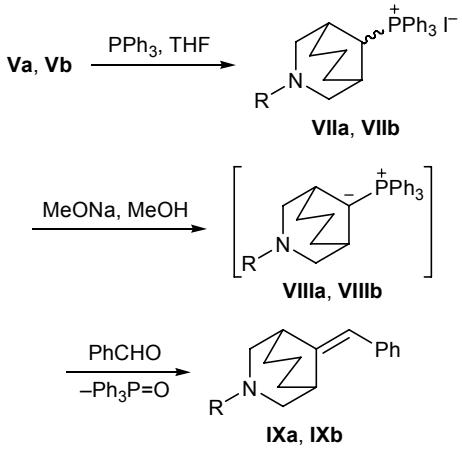
R = $PhCH_2$ (**a**), $Me_3COC(O)$ (**b**).

Scheme 2.



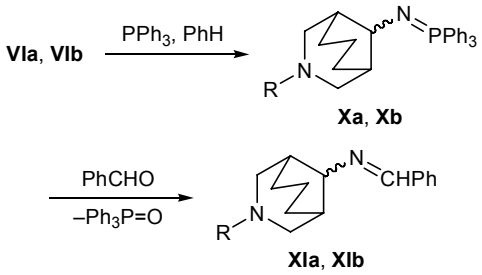
β-epimers for compounds **III**–**VI** was the same as for the initial alcohols. In the IR spectra of **III**–**VI** we observed absorption bands typical of vibrations of bonds in the acetyl, methylsulfonyl, and azido groups (see Experimental). The structure of compounds **V** and **VI** was confirmed by their chemical transformations. In particular, by heating iodides **Va** and **Vb** with triphenylphosphine in tetrahydrofuran (THF) under pressure we synthesized triphenylphosphonium salts **VIIa** and **VIIb**. Treatment of the latter with sodium methoxide in methanol readily produced unstable phosphonium ylides **VIIIa** and **VIIIb** which reacted *in situ* with benzaldehyde according to Wittig. As a result, unsaturated 9-benzylidene derivatives **IXa** and **IXb** were formed in high yield (Scheme 3).

Scheme 3.

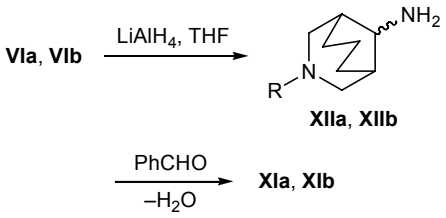


Azides **VIa** and **VIb** also reacted with triphenylphosphine, but under milder conditions, on heating in boiling benzene. The reaction was accompanied by evolution of nitrogen (Staudinger reaction), and the products were phosphazo compounds **Xa** and **Xb** whose reaction with benzaldehyde (aza-Wittig) afforded bicyclic Schiff bases **XIa** and **XIb** and triphenylphosphine oxide (Scheme 4). Schiff bases **XIa** and **XIb** were also obtained by reduction of azides **VIa** and **VIb** with lithium tetrahydridoaluminate in anhydrous THF at room temperature, followed by reaction of primary amines **XIIa** and **XIIb** with benzaldehyde (Scheme 5).

Scheme 4.

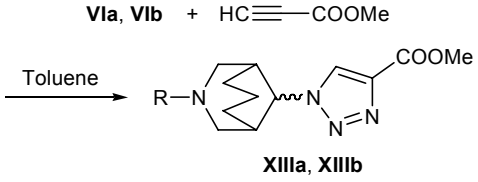


Scheme 5.



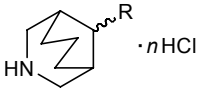
Azides **VIa** and **VIb** reacted with methyl prop-2-ynoate in boiling toluene to give 1,2,3-triazoles **XIIIa** and **XIIIb** (Scheme 6). In the ^{1}H NMR spectra of compounds **XI**–**XIII**, the 9-H signal is doubled, indicating that these compounds are mixtures of α- and β-epimers

Scheme 6.



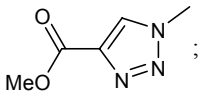
whose ratio was determined from the signal intensities (see Experimental).

Compounds **IIb**–**VIIb**, **XIIb**, and **XIIIb** having a *tert*-butoxycarbonyl group (Boc) on the nitrogen readily lost that group on treatment with a saturated solution of hydrogen chloride in anhydrous dioxane, and the corresponding NH derivatives were formed in high yield as hydrochlorides **IIc**–**VIIc**, **XIIc**, and **XIIIc**. Analogous *N*-benzyl derivatives under similar conditions were converted into water-soluble hydrochlorides without elimination of the substituent at the nitrogen atom.



IIc–**VIIc**, **XIIc**, **XIIIc**

II, R = HO; **III**, R = AcO; **IV**, R = $MeSO_2$; **V**, R = I; **VI**, R = N_3;

VII, R = $I^-Ph_3P^+$; **XII**, R = H_3N^+; **XIII**, R =  ;

II–**V**, **VII**, *n* = 1; **VI**, **XII**, **XIII**, *n* = 2.

Apart from IR and ^{1}H NMR spectra, the structure of the newly synthesized compounds was confirmed by elemental analyses and mass spectra (electrospray ionization).

EXPERIMENTAL

The IR spectra were recorded in KBr on a Specord 75IR spectrometer. The ^{1}H NMR spectra were measured on a Bruker DPX-400 instrument (400 MHz) from solutions in $CDCl_3$ (**II**–**VI**, **IX**–**XIII**) or DMSO-d_6 (**VIIa**, **VIIb**, **IIc**–**VIIc**, **IXc**–**XIIIc**) using hexamethyldisiloxane as internal reference. The mass spectra (atmospheric pressure chemical ionization) were obtained on a Thermo Finnigan Surveyor MSQ mass spectrometer. The purity of the products was checked by TLC on Silufol UV-254 plates using hexane–ethyl acetate (2:1) as eluent.

3-Benzyl-3-azabicyclo[3.3.1]nonan-9-ol (IIa). Compound **Ia**, 22.9 g (0.1 mol), was dissolved in 180 ml of anhydrous methanol, 11.3 g (0.3 mol) of sodium tetrahydridoborate was added under stirring over a period of 50 min, and the mixture was stirred for 3 h (until the initial ketone disappeared according to the TLC data). The mixture was diluted with 300 ml of water, 200 ml of methylene chloride was added, the organic phase was separated, and the aqueous phase was extracted with methylene chloride (2×100 ml). The extracts were combined with the organic phase, washed with water, and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to isolate compound **IIa** as a mixture of α- and β-epimers, which was crystallized from hexane on cooling to –20°C. Yield 23 g (100%), α/β ratio 2:3. IR spectrum: ν 3428 cm^{-1} (OH). ^{1}H NMR spectrum, δ, ppm: 1.41–2.08 m (6H, CH_2), 2.28–2.32 m (2H, CH), 2.83 d (2H, NCH_2), 2.95 d (2H, NCH_2), 3.40 s (2H, Ph**C**H_2), 3.67 d (9-H, β), 3.95 d (9-H, α), 7.21–7.38 m (5H, C_6H_5). Mass spectrum: *m*/*z* 232 $[M + H]^+$. Found, %: C 77.83; H 9.01; N 6.28. $C_{15}H_{21}NO$. Calculated, %: C 77.92; H 9.09; N 6.06.

***tert*-Butyl 9-hydroxy-3-azabicyclo[3.3.1]nonane-3-carboxylate (IIb)** was synthesized in a similar way. Yield 99%, α/β ratio 38:62. IR spectrum, ν, cm^{-1}: 3431 (OH), 1681 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.30 s (9H, *t*-Bu), 1.46–2.07 m (6H, CH_2), 2.36–2.42 m (2H, CH), 3.40 d (2H, NCH_2), 3.62 d (2H, NCH_2), 3.71 d (9-H, β), 3.98 d (9-H, α). Mass spectrum, *m*/*z*: 242 $[M + H]^+$, 185 $[M - 57 + H]^+$, 141 $[M - 101 + H]^+$. Found, %: C 64.68; H 9.47; N 5.63. $C_{13}H_{23}NO_3$. Calculated, %: C 64.73; H 9.54; N 5.81.

3-Benzyl-3-azabicyclo[3.3.1]non-9-yl acetate (IIIa). A solution of 0.24 g (3 mmol) of acetyl chloride in 3 ml of methylene chloride was added under stirring at 0–5°C to a mixture of 0.46 g (2 mmol) of alcohol **IIa** and 0.2 g (2.5 mmol) of anhydrous pyridine in 5 ml of anhydrous methylene chloride. The mixture was allowed to warm up to room temperature and was stirred for 2 h until the initial alcohol disappeared completely (TLC). The mixture was poured into 20 ml of water, the organic phase was separated, and the aqueous phase was extracted with methylene chloride (2×10 ml). The extracts were combined with the organic phase and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to isolate 0.42 g (77%) of compound **IIIa** as a mixture of α- and β-epimers at a ratio of 2:3. IR spectrum: ν 1692 cm^{-1} (C=O). ^{1}H NMR spectrum, δ, ppm: 1.42–1.82 m (6H, CH_2), 2.01 s (3H, CH_3), 2.29–2.34 m (2H, CH), 2.85 d (2H, NCH_2), 2.94 d (2H, NCH_2), 3.42 s (2H, Ph**C**H_2), 3.72 s (9-H, β), 4.05 s (9-H, α), 7.24–7.43 m (5H, C_6H_5). Mass spectrum: *m*/*z* 274 $[M + H]^+$. Found, %: C 74.82; H 8.51; N 5.06. $C_{17}H_{23}NO_2$. Calculated, %: C 74.72; H 8.42; N 5.13.

***tert*-Butyl 9-acetoxy-3-azabicyclo[3.3.1]nonane-3-carboxylate (IIIb)** was synthesized in a similar way. Yield 82%, α/β ratio 41:59. IR spectrum, ν, cm^{-1}: 1695, 1682 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.32 s

(9H, *t*-Bu), 1.48–2.10 m (9H, CH_2, CH_3CO), 2.38–2.47 m (2H, CH), 3.42 d (2H, NCH_2), 3.65 d (2H, NCH_2), 3.82 d (9-H, β), 4.08 d (9-H, α). Mass spectrum, *m/z:* 284 $[M + H]^+$, 227 $[M - 57 + H]^+$, 183 $[M - 101 + H]^+$. Found, %: C 63.48; H 8.76; N 4.85. $C_{15}H_{25}NO_4$. Calculated, %: C 63.60; H 8.83; N 4.95.

3-Benzyl-3-azabicyclo[3.3.1]non-9-yl methanesulfonate (IVa). A solution of 2.9 g (25 mmol) of methanesulfonyl chloride in 10 ml of methylene chloride was added under stirring at 15–20°C to a mixture of 4.6 g (20 mmol) of alcohol **IIa** and 2 g (25 mmol) of anhydrous pyridine in 30 ml of anhydrous methylene chloride. The mixture was stirred for 12 h until the initial alcohol disappeared completely (TLC) and poured into 300 ml of water, the organic phase was separated, and the aqueous phase was extracted with methylene chloride (2×50 ml). The extracts were combined with the organic phase, washed with water, and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave 4.92 g (80%) of compound **IVa** as a mixture of α- and β-epimers at a ratio of 35:65. IR spectrum, ν, cm^{-1}: 1358, 1172 (SO_2). ^1H NMR spectrum, δ, ppm: 1.39–2.08 m (6H, CH_2), 2.27–2.39 m (2H, CH), 2.94 s (3H, H_3CSO_2), 2.98 d (2H, NCH_2), 3.08 d (2H, NCH_2), 3.43 s (2H, PhC**H**$_2$), 3.78 s (9-H, β), 4.07 s (9-H, α), 7.25–7.42 m (5H, C_6H_5). Mass spectrum: *m/z* 310 $[M + H]^+$. Found, %: C 62.24; H 7.32; N 4.61. $C_{16}H_{23}NO_3S$. Calculated, %: C 62.14; H 7.44; N 4.53.

***tert*-Butyl 9-methylsulfonyloxy-3-azabicyclo-[3.3.1]nonane-3-carboxylate (IVb)** was synthesized in a similar way. Yield 83%, α/β ratio 38:62. IR spectrum, ν, cm^{-1}: 1683 (C=O); 1360, 1173 (SO_2). ^1H NMR spectrum, δ, ppm: 1.34 s (9H, *t*-Bu), 1.42–2.12 m (6H, CH_2), 2.38–2.42 m (2H, CH), 2.95 s (3H, H_3CSO_2), 2.99 d (2H, NCH_2), 3.08 d (2H, NCH_2), 3.81 d (9-H, β), 4.10 d (9-H, α). Mass spectrum, *m/z*: 320 $[M + H]^+$, 263 $[M - 57 + H]^+$, 219 $[M - 101 + H]^+$. Found, %: C 52.71; H 7.58; N 4.32. $C_{14}H_{25}NO_5S$. Calculated, %: C 52.66; H 7.84; N 4.39.

3-Benzyl-9-iodo-3-azabicyclo[3.3.1]nonane (Va). A mixture of 4.63 g (15 mmol) of compound **IVa** and 7.47 g (45 mmol) of anhydrous potassium iodide in 50 ml of anhydrous acetone was heated for 12 h under reflux with stirring (until the initial compound disappeared completely according to the TLC data). The mixture was cooled, diluted with 200 ml of water, and extracted with methylene chloride (3×80 ml). The extracts were combined, washed with water, and dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure to isolate compound **Va** as a mixture of α- and β-epimers at a ratio of 42:58. Yield 4.62 g (90%). ^1H NMR spectrum, δ, ppm: 1.41–2.08 m (6H, CH_2), 2.17–2.21 m (2H, CH), 2.85 d (2H, NCH_2), 2.98 d (2H, NCH_2), 3.40 s (2H, PhC**H**$_2$), 3.65 s (9-H, β), 3.97 s (9-H, α), 7.26–7.43 m (5H, C_6H_5). Mass spectrum: *m/z* 342 $[M + H]^+$. Found, %: C 52.65; H 5.78; N 3.86. $C_{15}H_{20}IN$. Calculated, %: C 52.79; H 5.87; N 4.11.

***tert*-Butyl 9-iodo-3-azabicyclo[3.3.1]nonane-3-carboxylate (Vb)** was synthesized in a similar way. Yield 90%, α/β ratio 2:3. IR spectrum: ν 1681 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 1.32 s (9H, *t*-Bu), 1.47–2.10 m (6H, CH_2), 2.38–2.45 m (2H, CH), 3.42 d (2H, NCH_2), 3.64 d (2H, NCH_2), 3.68 s (9-H, β), 3.98 s (9-H, α). Mass spectrum, *m/z*: 352 $[M + H]^+$, 295 $[M - 57 + H]^+$, 251 $[M - 101 + H]^+$. Found, %: C 44.28; H 6.17; N 4.05. $C_{13}H_{22}INO_2$. Calculated, %: C 44.44; H 6.27; N 3.99.

9-Azido-3-benzyl-3-azabicyclo[3.3.1]nonane (VIa). A mixture of 4.63 g (15 mmol) of compound **IVa** and 2.93 g (45 mmol) of sodium azide in 12 ml of DMSO was stirred for 6 h at 100°C (until the initial compound disappeared completely according to the TLC data). The mixture was cooled, diluted with 150 ml of water, and extracted with methylene chloride (2×50 ml). The extracts were combined, washed with three portions of water, and dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure to isolate 3.41 g (89%) of compound **VIa** as a mixture of α- and β-epimers at a ratio of 2:3. IR spectrum: ν 2108 cm^{-1} (N_3). ^1H NMR spectrum, δ, ppm: 1.39–2.03 m (6H, CH_2), 2.16–2.21 m (2H, CH), 2.82 d (2H, NCH_2), 2.96 d (2H, NCH_2), 3.42 s (2H, PhC**H**$_2$), 3.58 s (9-H, β), 3.81 s (9-H, α), 7.24–7.36 m (5H, C_6H_5). Mass spectrum: *m/z* 257 $[M + H]^+$. Found, %: C 70.24; H 7.93; N 21.47. $C_{15}H_{20}N_4$. Calculated, %: C 70.31; H 7.81; N 21.88.

***tert*-Butyl 9-azido-3-azabicyclo[3.3.1]nonane-3-carboxylate (VIb)** was synthesized in a similar way. Yield 87%, α/β ratio 2:3. IR spectrum, ν, cm^{-1}: 2106 (N_3), 1682 (C=O). ^1H NMR spectrum, δ, ppm: 1.30 s (9H, *t*-Bu), 1.47–2.09 m (6H, CH_2), 2.37–2.42 m (2H, CH), 3.41 d (2H, NCH_2), 3.62 d (2H, NCH_2), 3.72 d (9-H, β), 3.97 d (9-H, α). Mass spectrum, *m/z*: 267 $[M + H]^+$, 210 $[M - 57 + H]^+$, 166 $[M - 101 + H]^+$. Found, %: C 58.43; H 8.16; N 20.85. $C_{13}H_{22}N_4O_2$. Calculated, %: C 58.65; H 8.27; N 21.05.

(3-Benzyl-3-azabicyclo[3.3.1]non-9-yl)triphenylphosphonium iodide (VIIa). A mixture of 3.41 g

(10 mmol) of compound **Va** and 2.62 g (10 mmol) of triphenylphosphine in 15 ml of anhydrous THF was heated for 10 h at 120°C in a sealed ampule. The ampule was cooled and opened, the mixture was diluted with 100 ml of anhydrous diethyl ether and left to stand for 15 h, and the precipitate was filtered off, washed with 50 ml of diethyl ether, and dried. Yield 4.25 g (71%), mixture of α- and β-epimers at a ratio of 46:54, mp 172–176°C. ^{1}H NMR spectrum, δ, ppm: 1.45–2.14 m (6H, CH_2), 2.37–2.45 m (2H, CH), 2.91 d (2H, NCH_2), 3.06 d (2H, NCH_2), 3.42 s (2H, PhC**H**$_2$), 3.84 m (9-H, β), 4.12 m (9-H, α), 7.32–7.54 m (5H, C_6H_5), 7.92–8.63 m (15H, $^+PPh_3$). Mass spectrum: *m*/*z* 477 $[M + H]^+$. Found, %: C 65.31; H 5.68; N 2.36. $C_{33}H_{35}INP$. Calculated, %: C 65.67; H 5.80; N 2.32.

(3-*tert*-Butoxycarbonyl-3-azabicyclo[3.3.1]non-9-yl)triphenylphosphonium iodide (VIIb) was synthesized in a similar way. Yield 66%, α/β ratio 42:58. IR spectrum: ν 1681 cm^{-1} (C=O). ^{1}H NMR spectrum, δ, ppm: 1.38 s (9H, *t*-Bu), 1.52–2.21 m (6H, CH_2), 2.45–2.51 m (2H, CH), 3.54 d (2H, NCH_2), 3.68 d (2H, NCH_2), 3.88 m (9-H, β), 4.15 m (9-H, α), 8.02–8.76 m (15H, Ph). Mass spectrum, *m*/*z*: 487 $[M + H]^+$, 430 $[M - 57 + H]^+$, 386 $[M - 101 + H]^+$. Found, %: C 60.31; H 5.93; N 2.19. $C_{31}H_{37}INO_2P$. Calculated, %: C 60.68; H 6.04; N 2.28.

3-Benzyl-9-benzylidene-3-azabicyclo[3.3.1]-nonane (IXa). Phosphonium salt **VIIa**, 2.38 g (5 mmol), was dissolved in 20 ml of anhydrous methanol, a solution of 5.5 mmol of sodium methoxide in 10 ml of anhydrous methanol was added under argon, and the mixture was stirred for 3 h. Benzaldehyde, 0.53 g (5 mmol), was added to the resulting orange solution of ylide **VIIIa**, the mixture was heated for 6 h under reflux, the solvent was removed under reduced pressure, and the residue was dissolved in ethyl acetate and subjected to chromatography on silica gel using ethyl acetate–hexane (1:3) as eluent. Yield 1.12 g (74%), mp 98–100°C (from hexane). IR spectrum: ν 1618 cm^{-1} (C=C). ^{1}H NMR spectrum, δ, ppm: 1.38–2.05 m (6H, CH_2), 2.16–2.25 m (2H, CH), 2.79 d (2H, NCH_2), 2.87 d (2H, NCH_2), 3.38 s (2H, PhC**H**$_2$), 6.62 s (1H, =CH), 6.98–7.42 m (10H, C_6H_5). Mass spectrum: *m*/*z* 304 $[M + H]^+$. Found, %: C 86.93; H 8.16; N 4.45. $C_{22}H_{25}N$. Calculated, %: C 87.13; H 8.25; N 4.62.

***tert*-Butyl 9-benzylidene-3-azabicyclo[3.3.1]-nonane-3-carboxylate (IXb)** was synthesized in a similar way. Yield 72%, mp 133–135°C (from hexane). IR spectrum, ν, cm^{-1}: 1682 (C=O), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.31 s (9H, *t*-Bu), 1.45–2.08 m (6H, CH_2), 2.37–2.44 m (2H, CH), 3.41 d (2H, NCH_2), 3.60 d (2H, NCH_2), 6.65 s (1H, =CH), 7.01–7.12 m (5H, C_6H_5). Mass spectrum, *m*/*z*: 314 $[M + H]^+$, 257 $[M - 57 + H]^+$, 213 $[M - 101 + H]^+$. Found, %: C 76.51; H 8.46; N 4.38. $C_{20}H_{27}NO_2$. Calculated, %: C 76.43; H 8.63; N 4.47.

3-Benzyl-9-(triphenyl-λ^5-phosphanylidene-amino)-3-azabicyclo[3.3.1]nonane (Xa). A mixture of 2.56 g (10 mmol) of azide **VIa** and 2.62 g (10 mmol) of triphenylphosphine in 30 ml of benzene was heated for 10 h under reflux (until the initial compounds disappeared according to the TLC data). The solvent was distilled off under reduced pressure, and the residue was crystallized from ethyl acetate–hexane (1:5). Compound **Xa** was isolated as a mixture of α- and β-epimers at a ratio of 41:59. Yield 3.68 g (75%), mp 125–128°C. ^{1}H NMR spectrum, δ, ppm: 1.38–2.04 m (6H, CH_2), 2.16–2.23 m (2H, CH), 2.83 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.43 s (2H, PhC**H**$_2$), 3.61 s (9-H, β), 3.84 s (9-H, α), 7.23–8.02 m (20H, C_6H_5). Mass spectrum: *m*/*z* 491 $[M + H]^+$. Found, %: C 80.73; H 7.04; N 5.62. $C_{33}H_{35}N_2P$. Calculated, %: C 80.82; H 7.14; N 5.71.

***tert*-Butyl 9-(triphenyl-λ^5-phosphanylidene-amino)-3-azabicyclo[3.3.1]nonane-3-carboxylate (Xb)** was synthesized in a similar way. Yield 78%, α/β ratio 45:55. IR spectrum: ν 1681 cm^{-1} (C=O). ^{1}H NMR spectrum, δ, ppm: 1.32 s (9H, *t*-Bu), 1.48–2.08 m (6H, CH_2), 2.35–2.44 m (2H, CH), 3.41 d (2H, NCH_2), 3.58 d (2H, NCH_2), 3.74 s (9-H, β), 3.98 s (9-H, α), 7.32–8.04 m (15H, C_6H_5). Mass spectrum, *m*/*z*: 501 $[M + H]^+$, 444 $[M - 57 + H]^+$, 400 $[M - 101 + H]^+$. Found, %: C 74.24; H 7.32; N 5.46. $C_{31}H_{37}N_2O_2P$. Calculated, %: C 74.40; H 7.40; N 5.60.

3-Benzyl-*N*-benzylidene-3-azabicyclo[3.3.1]-nonan-9-amine (XIa). A mixture of 0.98 g (2 mmol) of compound **Xa** and 0.21 g (2 mmol) of benzaldehyde in 10 ml of toluene was heated for 6 h under reflux (until the initial compounds disappeared according to the TLC data), the solvent was distilled off under reduced pressure, and the residue was dissolved in ethyl acetate and purified by chromatography on silica gel using ethyl acetate–hexane (1:2) as eluent. Compound **XIa** was isolated as a mixture of α- and β-epimers at a ratio of 38:62. Yield 0.53 g (83%). IR spectrum: ν 1608 cm^{-1} (C=N). ^{1}H NMR spectrum, δ, ppm: 1.39–2.08 m (6H, CH_2), 2.18–2.28 m (2H, CH), 2.82 d (2H, NCH_2), 2.93 d (2H, NCH_2), 3.40 s (2H, PhC**H**$_2$), 3.81 s (9-H, β), 4.02 s (9-H, α), 6.78 s (1H, =CH), 6.99–7.43 m (10H, C_6H_5). Mass spectrum:

m/*z* 319 $[M + H]^+$. Found, %: C 82.87; H 8.05; N 8.67. $C_{22}H_{26}N_2$. Calculated, %: C 83.02; H 8.18; N 8.81.

***tert*-Butyl 9-benzylideneamino-3-azabicyclo-[3.3.1]nonane-3-carboxylate (XIb)** was synthesized in a similar way. Yield 79%, α/β ratio 43:57. IR spectrum, ν, cm^{-1}: 1684 (C=O), 1608 (C=N). ^1H NMR spectrum, δ, ppm: 1.30 s (9H, *t*-Bu), 1.46–2.10 m (6H, CH_2), 2.38–2.42 m (2H, CH), 3.42 d (2H, NCH_2), 3.62 d (2H, NCH_2), 3.92 s (9-H, β), 4.05 s (9-H, α), 6.81 s (1H, =CH), 7.01–7.18 m (5H, C_6H_5). Mass spectrum, *m*/*z*: 329 $[M + H]^+$, 272 $[M - 57 + H]^+$, 228 $[M - 101 + H]^+$. Found, %: C 73.31; H 8.45; N 8.37. $C_{20}H_{28}N_2O_2$. Calculated, %: C 73.17; H 8.54; N 8.54.

3-Benzyl-3-azabicyclo[3.3.1]nonan-9-amine (XIIa). A solution of 2.56 g (10 mmol) of azide **VIa** in 20 ml of THF was added under argon to a suspension of 0.2 g (5.2 mmol) of lithium tetrahydridoaluminate in 10 ml of anhydrous THF, and the mixture was stirred for 5 h at room temperature (until the initial compounds disappeared according to the TLC data). The mixture was then treated with 30 ml of 10% aqueous ammonium chloride, stirred for 1 h, and filtered, and the filtrate was extracted with ethyl acetate (2×50 ml). The extracts were combined, washed with water, and dried over anhydrous sodium sulfate, the solvent was distilled off under reduced pressure, and the residue was crystallized from hexane on cooling to –20°C. Compound **XIIa** was isolated as a mixture of α- and β-epimers at a ratio of 35:65. Yield 1.48 g (64%), mp 65–68°C. IR spectrum, ν, cm^{-1}: 3367, 3358 (NH_2). ^1H NMR spectrum, δ, ppm: 1.36–2.04 m (6H, CH_2), 2.12–2.21 m (2H, CH), 2.78 d (2H, NCH_2), 2.85 d (2H, NCH_2), 3.36 s (2H, PhC**H**$_2$), 3.62 m (9-H, β), 3.86 m (9-H, α), 4.22 br.s (2H, NH_2), 7.02–7.17 m (5H, C_6H_5). Mass spectrum: *m*/*z* 231 $[M + H]^+$. Found, %: C 78.41; H 9.36; N 12.08. $C_{15}H_{22}N_2$. Calculated, %: C 78.26; H 9.57; N 12.17.

***tert*-Butyl 9-amino-3-azabicyclo[3.3.1]nonane-3-carboxylate (XIIb)** was synthesized in a similar way. Yield 62%, mp 87–90°C, α/β ratio 48:52. IR spectrum, ν, cm^{-1}: 3364, 3351 (NH_2); 1684 (C=O). ^1H NMR spectrum, δ, ppm: 1.31 s (9H, *t*-Bu), 1.47–2.12 m (6H, CH_2), 2.36–2.41 m (2H, CH), 3.41 d (2H, NCH_2), 3.60 d (2H, NCH_2), 3.90 m (9-H, β), 4.06 m (9-H, α), 4.25 br.s (2H, NH_2). Mass spectrum, *m*/*z*: 241 $[M + H]^+$, 184 $[M - 57 + H]^+$, 140 $[M - 101 + H]^+$. Found, %: C 64.83; H 9.93; N 11.52. $C_{13}H_{24}N_2O_2$. Calculated, %: C 65.00; H 10.00; N 11.67.

Reaction of amines XIIa and XIIb with benzaldehyde. A mixture of 3 mmol of amine **Xa** or **Xb** and 3 mmol of freshly distilled benzaldehyde in 10 ml of toluene was heated under reflux over a period of 5 h. The solvent was slowly distilled off under atmospheric pressure, the residue was dissolved in ethyl acetate and subjected to chromatography on silica gel. Compound **XIa** or **XIb** was eluted with ethyl acetate–hexane (1:2); their yields were 78 and 83%, respectively.

Methyl 1-(3-benzyl-3-azabicyclo[3.3.1]non-9-yl)-1*H*-1,2,3-triazole-4-carboxylate (XIIIa). A mixture of 0.77 g (3 mmol) of azide **VIa** and 0.3 g (3.5 mmol) of methyl prop-2-ynoate in 5 ml of toluene was heated for 10 h under reflux (until the initial azide disappeared according to the TLC data). The solvent was distilled off under reduced pressure, and the residue was dissolved in ethyl acetate and purified by chromatography on silica gel. Compound **XIIIa** was isolated as a mixture of α- and β-epimers at a ratio of 45:55. Yield 0.52 g (51%), mp 148–152°C (from hexane). IR spectrum: ν 1698 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 1.38–2.08 m (6H, CH_2), 2.14–2.22 m (2H, CH), 2.79 d (2H, NCH_2), 2.86 d (2H, NCH_2), 3.38 s (2H, PhC**H**$_2$), 3.56 s (3H, OCH_3), 3.72 s (9-H, β), 3.92 s (9-H, α), 7.05–7.36 m (6H, 5-H, C_6H_5). Mass spectrum: *m*/*z* 341 $[M + H]^+$. Found, %: C 65.84; H 7.15; N 16.31. $C_{19}H_{24}N_4O_2$. Calculated, %: C 67.06; H 7.06; N 16.47.

Methyl 1-(3-*tert*-butoxycarbonyl-3-azabicyclo-[3.3.1]non-9-yl)-1*H*-1,2,3-triazole-4-carboxylate (XIIIb) was synthesized in a similar way. Yield 49%, α/β ratio 42:58. IR spectrum, ν, cm^{-1}: 1698, 1684 (C=O). ^1H NMR spectrum, δ, ppm: 1.32 s (9H, *t*-Bu), 1.48–2.15 m (6H, CH_2), 2.34–2.39 m (2H, CH), 3.42 d (2H, NCH_2), 3.58 d (2H, NCH_2), 3.68 s (3H, OCH_3), 3.91 s (9-H, β), 4.08 s (9-H, α), 7.11 s (1H, 5-H). Mass spectrum, *m*/*z*: 351 $[M + H]^+$, 294 $[M - 57 + H]^+$, 250 $[M - 101 + H]^+$. Found, %: C 58.12; H 7.27; N 15.86. $C_{17}H_{26}N_4O_4$. Calculated, %: C 58.29; H 7.43; N 16.00.

9-Hydroxy-3-azoniabicyclo[3.3.1]nonane chloride (IIc). Compound **IIb**, 1.16 g (5 mmol), was dissolved in 10 ml of anhydrous ethanol, 20 ml of a saturated solution (16%) of hydrogen chloride in anhydrous dioxane was added, and the mixture was stirred for 1 h and then heated for 1 h under reflux. The solvent was removed under reduced pressure, the residue was treated with 30 ml of anhydrous diethyl ether, and the mixture was left to stand for 20 h. The precipitate was filtered off, washed with 20 ml of diethyl ether, and dried under reduced pressure over P_2O_5. Yield 0.82 g (92%), decomposition point 178–183°C. IR spectrum, ν, cm^{-1}: 3431 (OH), 3382 ($^+NH_2$). ^1H NMR spectrum, δ, ppm: 1.51–2.24 m (6H, CH_2),

2.29–2.38 m (2H, CH), 3.41 d (2H, NCH_2), 3.62–3.96 m (3H, NCH_2, 9-H), 9.50 br.s (2H, $^+NH_2$) Mass spectrum: *m*/*z* 142 $[M + H]^+$. Found, %: C 53.67; H 8.83; N 7.76. $C_8H_{15}NO \cdot HCl$. Calculated, %: C 54.08; H 9.01; N 7.89.

Hydrochlorides **IIIc**–**VIIc**, **XIIc**, and **XIIIc** were synthesized in a similar way.

9-Acetoxy-3-azoniabicyclo[3.3.1]nonane chloride (IIIc). Yield 96%, decomposition point 186–191°C. IR spectrum, ν, cm^{-1}: 3385 ($^+NH_2$), 1700 (C=O). ^1H NMR spectrum, δ, ppm: 1.52–2.25 m (9H, CH_2, CH_3), 2.30–2.39 m (2H, CH), 3.42 d (2H, NCH_2), 3.64–4.01 m (3H, NCH_2, 9-H), 9.56 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 184 $[M + H]^+$. Found, %: C 54.53; H 8.14; N 6.27. $C_{10}H_{17}NO_2 \cdot HCl$. Calculated, %: C 54.67; H 8.20; N 6.38.

9-Methylsulfonyloxy-3-azoniabicyclo[3.3.1]-nonane chloride (IVc). Yield 98%, decomposition point 175–178°C. IR spectrum, ν, cm^{-1}: 3388 ($^+NH_2$); 1361, 1178 (SO_2). ^1H NMR spectrum, δ, ppm: 1.52–2.26 m (6H, CH_2), 2.32–2.41 m (2H, CH), 2.98 s (3H, H_3CSO_2), 3.44 d (2H, NCH_2), 3.64–3.98 m (3H, NCH_2, 9-H), 9.52 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 220 $[M + H]^+$. Found, %: C 42.17; H 6.93; N 5.46. $C_9H_{17}NO_3S \cdot HCl$. Calculated, %: C 42.27; H 7.05; N 5.48.

9-Iodo-3-azoniabicyclo[3.3.1]nonane chloride (Vc). Yield 82%, decomposition point 168–172°C. IR spectrum: ν 3386 cm^{-1} ($^+NH_2$). ^1H NMR spectrum, δ, ppm: 1.50–2.25 m (6H, CH_2), 2.30–2.38 m (2H, CH), 3.42 d (2H, NCH_2), 3.62–3.95 m (3H, NCH_2, 9-H), 9.50 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 252 $[M + H]^+$. Found, %: C 33.43; H 4.68; N 4.75. $C_8H_{14}IN \cdot HCl$. Calculated, %: C 33.39; H 4.87; N 4.87.

9-Azido-3-azabicyclo[3.3.1]nonane dihydrochloride (VIc). Yield 94%, decomposition point 158–163°C. IR spectrum, ν, cm^{-1}: 3384 ($^+NH_2$), 2112 (N_3). ^1H NMR spectrum, δ, ppm: 1.51–2.24 m (6H, CH_2), 2.30–2.37 m (2H, CH), 3.44 d (2H, NCH_2), 3.66–4.01 m (3H, NCH_2, 9-H), 9.53 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 167 $[M + H]^+$. Found, %: C 39.72; H 5.68; N 23.34. $C_8H_{14}N_4 \cdot 2HCl$. Calculated, %: C 40.17; H 5.86; N 23.43.

(3-Azoniabicyclo[3.3.1]non-9-yl)triphenylphosphonium chloride iodide (VIIc). Yield 92%, decomposition point 204–208°C. IR spectrum: ν 3386 cm^{-1} ($^+NH_2$). ^1H NMR spectrum, δ, ppm: 1.52–2.24 m (6H, CH_2), 2.46–2.53 m (2H, CH), 3.68 d (2H, NCH_2), 3.74–4.05 m (3H, NCH_2, 9-H), 8.08–8.83 m (15H, Ph), 9.61 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 387 $[M + H]^+$. Found, %: C 56.60; H 5.34; N 2.47. $C_{26}H_{29}INP \cdot HCl$. Calculated, %: C 56.78; H 5.46; N 2.55.

3-Azoniabicyclo[3.3.1]non-9-ylammonium dichloride (XIIc). Yield 97%, decomposition point 208–211°C. IR spectrum, ν, cm^{-1}: 3398, 3387, 3378 ($^+NH_2$, $^+NH_3$). ^1H NMR spectrum, δ, ppm: 1.51–2.25 m (6H, CH_2), 2.48–2.56 m (2H, CH), 3.67 d (2H, NCH_2), 3.82–4.07 m (3H, NCH_2, 9-H), 8.93 br.s (3H, H_3N^+), 9.73 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 141 $[M + H]^+$. Found, %: C 44.83; H 8.26; N 13.08. $C_8H_{16}N_2 \cdot 2HCl$. Calculated, %: C 45.07; H 8.45; N 13.15.

1-(3-Azoniabicyclo[3.3.1]non-9-yl)-4-methoxycarbonyl-1*H*-1,2,3-triazolium dichloride (XIIIc). Yield 94%, decomposition point 218–221°C. IR spectrum, ν, cm^{-1}: 3396, 3382 ($^+NH_2$, ^+NH), 1705 (C=O). ^1H NMR spectrum, δ, ppm: 1.54–2.28 m (6H, CH_2), 2.47–2.55 m (2H, CH), 3.69 d (2H, NCH_2), 3.78 s (3H, OCH_3), 3.92–4.10 m (3H, NCH_2, 9-H), 7.68 s (1H, CH), 9.08 br.s (1H, NH^+), 9.64 br.s (2H, H_2N^+). Mass spectrum: *m*/*z* 251 $[M + H]^+$. Found, %: C 44.36; H 6.08; N 17.28. $C_{12}H_{18}N_4O_2 \cdot 2HCl$. Calculated, %: C 44.58; H 6.19; N 17.34.

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