ISSN 1070-4280, Russian Journal of Organic Chemistry, 2009, Vol. 45, No. 7, pp. 1018–1023. © Pleiades Publishing, Ltd., 2009.
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Reactions of N-Substituted 3-Azabicyclo[3.3.1]nonan-9-ones with N,N-, N,S-, and N,O-Binucleophiles

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Received July 16, 2008

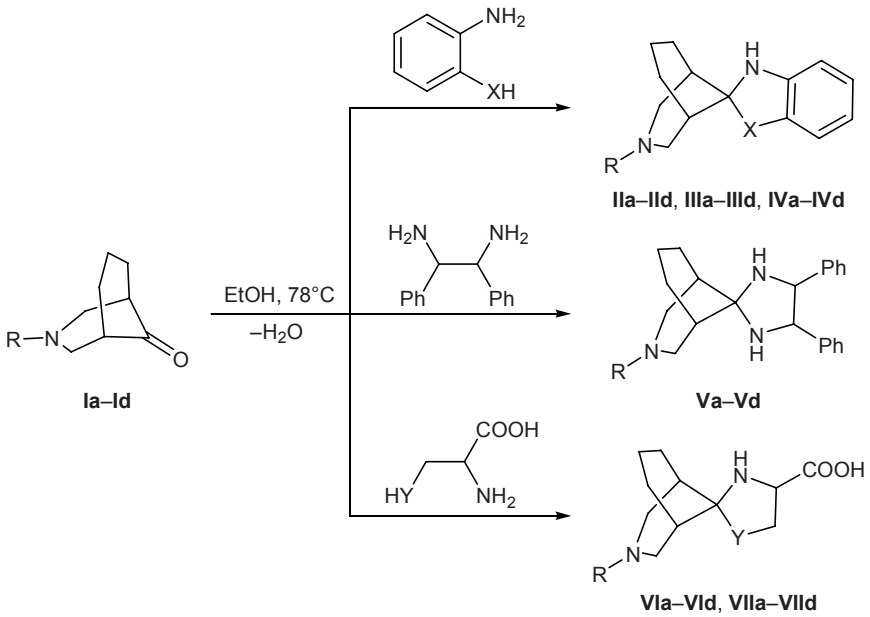
Abstract—Condensation of N-substituted 3-azabicyclo[3.3.1]nonan-9-ones with difunctional N,N-, N,S-, and N,O-centered nucleophiles (*o*-phenylenediamine, 1,2-diphenylethane-1,2-diamine, 2-aminobenzenethiol, cysteine, 2-aminophenol, serine) gave the corresponding spiro heterocyclic compounds fused at the C^9 atom. Treatment of *N*-*tert*-butoxycarbonyl-substituted spiro compounds with anhydrous hydrogen chloride resulted in elimination of the *tert*-butoxycarbonyl group with formation of spiro[3-azabicyclo[3.3.1]nonane-9,2′-azole] hydrochlorides.

DOI: 10.1134/S1070428009070069

Interest of researchers [1–5] in compounds containing azabicyclic fragments originates from high and versatile biological activity found for some their representatives, in particular spasmolytic, psychotropic, analgesic, antiarrythmic, etc., which is analogous to the activity typical of diterpene alkaloids [1].

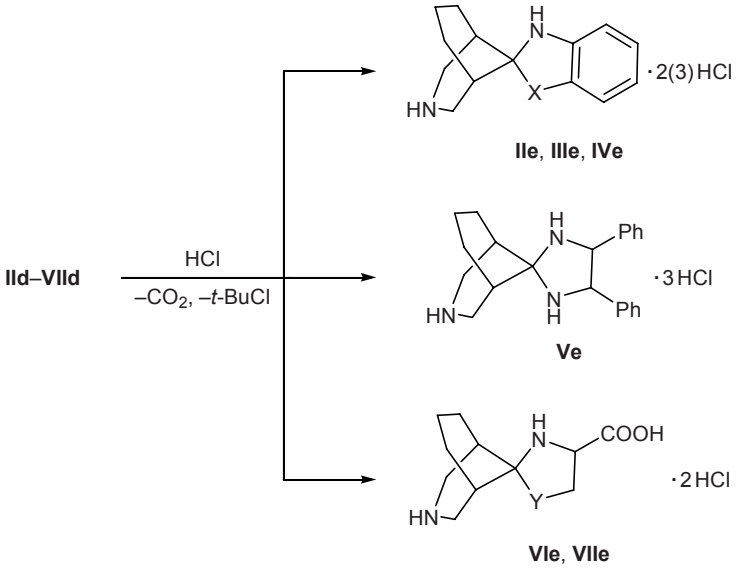
In the present work we examined reactions of previously synthesized [7] N-substituted 3-azabicyclo-[3.3.1]nonan-9-ones **Ia**–**Id** with difunctional N,N-, N,S-, and N,O-centered nucleophiles. As nucleophiles we used *o*-phenylenediamine and 1,2-diphenylethane-1,2-diamine (N,N), 2-aminobenzenethiol and cysteine (N,S), and 2-aminophenol and serine (N,O). These nucleophiles fairly smoothly reacted with compounds **Ia**–**Id** at the carbonyl group on heating equimolar amounts of the reactants in ethanol or aqueous ethanol (in reactions with amino acids) in the presence of a catalytic amount of trifluoroacetic acid. As a result,

Scheme 1.



R = $PhCH_2$ (**a**), 4-$MeC_6H_4CH_2$ (**b**), 4-$FC_6H_4CH_2$ (**c**), *t*-BuOC(O) (**d**); **II**, X = NH; **III**, X = S; **IV**, X = O; **VI**, Y = S; **VII**, Y = O.

Scheme 2.



we isolated spiro[3-azabicyclo[3.3.1]nonane-9,2′-azole] derivatives **II**–**VII** in 65–85% yield (Scheme 1).

Compounds **II**–**VII** are colorless or light yellow crystalline substances which are readily soluble in polar organic solvents but insoluble in water. Their structure was confirmed by elemental analyses and IR, ^{1}H NMR, and mass (electrospray ionization) spectra. The IR spectra of **II**–**VII** contained absorption bands at 3320–3410 cm^{-1} due to stretching vibrations of N–H bonds; in the IR spectra of carboxylic acids **VIa**–**VId** and **VIIa**–**VIId** absorption bands belonging to stretching vibrations of O–H (3125–3280 cm^{-1}) and C=O bonds (1680–1690 cm^{-1}) in the carboxy groups were present. In the ^{1}H NMR spectra of the products we observed signals from protons in the 3-azabicyclo-[3.3.1]nonane system [7], multiplet signals from protons in other (aromatic) fragments, and a broadened singlet from the carboxylic OH proton.

Treatment of *N*-*tert*-butoxycarbonyl derivatives **IId**–**VIId** with a saturated solution of hydrogen chloride in anhydrous dioxane resulted in facile elimination of the *tert*-butoxycarbonyl group to produce the corresponding hydrochlorides **IIe**–**VIIe** in almost quantitative yield. Under analogous conditions, other N-substituted compounds **II**–**VII** (**a**–**c**) were converted into water-soluble hydrochlorides without loss of substituent on the nitrogen.

Thus the reaction of N-substituted 3-azabicyclo-[3.3.1]nonan-9-ones with difunctional nucleophiles ensures preparation of spiro-fused heterocyclic compounds containing an azabicyclic fragment. The products may be promising as substrates for further transformations, as well as potential biologically active substances.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Specord 75 IR spectrometer. The ^{1}H NMR spectra were measured from solutions in DMSO-d_6 on a Bruker DPX-400 instrument (400 MHz) using hexamethyldisiloxane as internal reference. The mass spectra (atmospheric pressure chemical ionization) were obtained on a Thermo Finnigan Surveyor MSQ GC–MS system (USA). The progress of reactions was monitored by TLC on Silufol UV-254 plates using hexane–ethyl acetate (5:1) as eluent.

3-Benzyl-1′,3′-dihydrospiro[3-azabicyclo[3.3.1]-nonane-9,2′-benzimidazole] (IIa). Compound **Ia** [7], 0.458 g (2 mmol), was dissolved in 10 ml of ethanol, 0.216 g (2 mmol) of *o*-phenylenediamine and 0.1 ml of trifluoroacetic acid were added, and the mixture was stirred for 6 h on heating under reflux until the initial compound disappeared completely according to the TLC data. The solvent was distilled off under reduced pressure, and the residue was recrystallized from aqueous ethanol. Yield 0.46 g (72%), mp 136–137°C. IR spectrum, ν, cm^{-1}: 3405, 3328 (NH). ^{1}H NMR spectrum, δ, ppm: 1.42–2.08 m (6H, CH_2), 2.24–2.32 m (2H, CH), 2.84 d (2H, NCH_2), 2.95 d (2H, NCH_2), 3.42 s (2H, PhC**H**$_2$N), 3.85 br.s (2H, NH), 6.97–7.41 m (9H, H_{arom}). Mass spectrum: *m*/*z* 320 $[M + H]^+$. Found,

%: C 78.85; H 7.86; N 13.22. $C_{21}H_{25}N_3$. Calculated, %: C 79.01; H 7.83; N 13.16.

Compounds **IIb**–**IId**, **IIIa**–**IIId**, **IVa**–**IVd**, and **Va**–**Vd** were synthesized in a similar way.

3-(4-Methylbenzyl)-1′,3′-dihydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-benzimidazole] (IIb). Yield 85%, mp 142–143°C. IR spectrum, ν, cm^{-1}: 3410, 3325 (NH). ^1H NMR spectrum, δ, ppm: 1.45–2.09 m (6H, CH_2), 2.23 s (3H, CH_3), 2.31–2.38 m (2H, CH), 2.86 d (2H, NCH_2), 2.96 d (2H, NCH_2), 3.44 s (2H, 3-CH_2), 3.82 br.s (2H, NH), 7.11 d (2H, C_6H_4, J = 8.0 Hz), 7.24 d (2H, C_6H_4, J = 8.0 Hz). Mass spectrum: m/z 334 $[M + H]^+$. Found, %: C 79.18; H 8.01; N 12.48. $C_{22}H_{27}N_3$. Calculated, %: C 79.29; H 8.10; N 12.60.

3-(4-Fluorobenzyl)-1′,3′-dihydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-benzimidazole] (IIc). Yield 65%, mp 139–140°C. IR spectrum, ν, cm^{-1}: 3412, 3328 (NH). ^1H NMR spectrum, δ, ppm: 1.41–2.10 m (6H, CH_2), 2.23–2.34 m (2H, CH), 2.87 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.46 s (2H, 3-CH_2), 3.87 br.s (2H, NH), 7.01–7.43 m (8H, H_{arom}). Mass spectrum: m/z 338 $[M + H]^+$. Found, %: C 74.63; H 7.05; N 12.28. $C_{21}G_{24}FN_3$. Calculated, %: C 74.79; H 7.12; N 12.46.

***tert*-Butyl 1′,3′-dihydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-benzimidazole]-3-carboxylate (IId).** Yield 78%, mp 152–153°C. IR spectrum, ν, cm^{-1}: 3409, 3338 (NH); 1683 (C=O). ^1H NMR spectrum, δ, ppm: 1.32 s (9H, *t*-Bu), 1.43–2.12 m (6H, CH_2), 2.23–2.34 m (2H, CH), 2.85 d (2H, NCH_2), 2.96 d (2H, NCH_2), 3.92 br.s (2H, NH), 6.98–7.32 m (4H, H_{arom}). Mass spectrum, m/z: 330 $[M + H]^+$, 273 $[M - 57 + H]^+$, 229 $[M - 101 + H]^+$. Found, %: C 69.18; H 8.31; N 12.63. $C_{19}H_{27}N_3O_2$. Calculated, %: C 69.32; H 8.20; N 12.76.

3-Benzyl-3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzothiazole] (IIIa). Yield 73%, mp 124–125°C. IR spectrum, ν, cm^{-1}: 3396, 3340 (NH). ^1H NMR spectrum, δ, ppm: 1.43–2.08 m (6H, CH_2), 2.25–2.34 m (2H, CH), 2.86 d (2H, NCH_2), 2.96 d (2H, NCH_2), 3.42 s (2H, 3-CH_2), 3.84 br.s (1H, NH), 7.08–7.48 m (9H, H_{arom}). Mass spectrum: m/z: 337 $[M + H]^+$. Found, %: C 74.91; H 7.04; N 8.26. $C_{21}H_{24}N_2S$. Calculated, %: C 75.02; H 7.14; N 8.33.

3-(4-Methylbenzyl)-3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzothiazole] (IIIb). Yield 83%, mp 130–131°C. IR spectrum, ν, cm^{-1}: 3395, 3341 (NH). ^1H NMR spectrum, δ, ppm: 1.45–2.10 m (6H, CH_2), 2.23 s (3H, CH_3), 2.30–2.37 m (2H, CH), 2.86 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.45 s (2H, 3-CH_2), 3.86 br.s (1H, NH), 7.12 d (2H, C_6H_4, J = 7.8 Hz), 7.26 d (2H, C_6H_4, J = 7.8 Hz). Mass spectrum: m/z 351 $[M + H]^+$. Found, %: C 75.35; H 7.48; N 7.83. $C_{22}H_{26}N_2S$. Calculated, %: C 75.44; H 7.42; N 7.99.

3-(4-Fluorobenzyl)-3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzothiazole] (IIIc). Yield 68%, mp 132–133°C. IR spectrum, ν, cm^{-1}: 3398, 3343 (NH). ^1H NMR spectrum, δ, ppm: 1.42–2.09 m (6H, CH_2), 2.23–2.34 m (2H, CH), 2.88 d (2H, NCH_2), 2.98 d (2H, NCH_2), 3.45 s (2H, 3-CH_2), 3.87 br.s (1H, NH), 7.12–7.50 m (8H, H_{arom}). Mass spectrum: m/z 355 $[M + H]^+$. Found, %: C 71.12; H 6.57; N 7.83. $C_{21}H_{23}F\,N_2S$. Calculated, %: C 71.20; H 6.49; N 7.90.

***tert*-Butyl 3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzothiazole]-3-carboxylate (IIId).** Yield 75%, mp 162–163°C. IR spectrum, ν, cm^{-1}: 3394, 3342 (NH); 1683 (C=O). ^1H NMR spectrum, δ, ppm: 1.32 s (9H, *t*-Bu), 1.45–2.09 m (6H, CH_2), 2.26–2.38 m (2H, CH), 2.88 d (2H, NCH_2), 2.98 d (2H, NCH_2), 3.86 br.s (1H, NH), 7.10–7.43 m (4H, H_{arom}). Mass spectrum, m/z: 347 $[M + H]^+$, 290 $[M - 57 + H]^+$, 246 $[M - 101 + H]^+$. Found, %: C 65.87; H 7.38; N 8.13. $C_{19}H_{26}N_2O_2S$. Calculated, %: C 65.92; H 7.51; N 8.09.

3-Benzyl-3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzoxazole] (IVa). Yield 68%, mp 141–142°C. IR spectrum, ν, cm^{-1}: 3395, 3342 (NH). ^1H NMR spectrum, δ, ppm: 1.45–2.10 m (6H, CH_2), 2.25–2.36 m (2H, CH), 2.88 d (2H, NCH_2), 2.96 d (2H, NCH_2), 3.44 s (2H, Ph**C**H_2), 3.84 br.s (1H, NH), 7.12–7.61 m (9H, H_{arom}). Mass spectrum: m/z: 321 $[M + H]^+$. Found, %: C 78.85; H 7.36; N 8.67. $C_{21}H_{24}N_2O$. Calculated, %: C 78.76; H 7.50; N 8.74.

3-(4-Methylbenzyl)-3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzoxazole] (IVb). Yield 82%, mp 153–154°C. IR spectrum, ν, cm^{-1}: 3398, 3345 (NH). ^1H NMR spectrum, δ, ppm: 1.46–2.11 m (6H, CH_2), 2.24 s (3H, CH_3), 2.30–2.38 m (2H, CH), 2.88 d (2H, NCH_2), 2.98 d (2H, NCH_2), 3.45 s (2H, 3-CH_2), 3.86 br.s (1H, NH), 7.14 d (2H, C_6H_4, J = 7.8 Hz), 7.25 d (2H, C_6H_4, J = 7.8 Hz). Mass spectrum, m/z: 335 $[M + H]^+$. Found, %: C 78.91; H 7.63; N 8.27. $C_{22}H_{26}N_2O$. Calculated, %: C 79.06; H 7.78; N 8.38.

3-(4-Fluorobenzyl)-3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzoxazole] (IVc). Yield 69%, mp 149–150°C. IR spectrum, ν, cm^{-1}: 3398, 3345 (NH). ^1H NMR spectrum, δ, ppm: 1.46–2.12 m (6H, CH_2), 2.25–2.38 m (2H, CH), 2.92 d (2H, NCH_2), 2.99 d (2H, NCH_2), 3.47 s (2H, 3-CH_2), 3.91 br.s (1H, NH), 7.15–7.64 m (8H, H_{arom}). Mass spectrum:

m/*z* 339 $[M + H]^+$. Found, %: C 74.43; H 6.76; N 8.17. $C_{21}H_{23}FN_2O$. Calculated, %: C 74.57; H 6.80; N 8.28.

***tert*-Butyl 3′*H*-spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]benzoxazole]-3-carboxylate (IVd).** Yield 74%, mp 168–169°C. IR spectrum, ν, cm^{-1}: 3397, 3348 (NH); 1684 (C=O). ^1H NMR spectrum, δ, ppm: 1.31 s (9H, *t*-Bu), 1.4–2.14 m (6H, CH_2), 2.26–2.35 m (2H, CH), 2.89 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.88 br.s (1H, NH), 7.15–7.62 m (4H, H_{arom}). Mass spectrum, *m*/*z*: 331 $[M + H]^+$, 274 $[M - 57 + H]^+$, 230 $[M - 101 + H]^+$. Found, %: C 69.18; H 7.64; N 8.32. $C_{19}H_{26}N_2O_3$. Calculated, %: C 69.11; H 7.87; N 8.48.

3-Benzyl-4′,5′-diphenyl-1′,3′,4′,5′-tetrahydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-imidazole] (Va). Yield 83%, mp 106–107°C. IR spectrum, ν, cm^{-1}: 3402, 3386, 3320 (NH). ^1H NMR spectrum, δ, ppm: 1.42–2.07 m (6H, CH_2), 2.24–2.34 m (2H, CH), 2.87–3.11 m (6H, NCH_2, NCH), 3.43 s (2H, PhC**H**$_2$), 3.85 br.s (2H, NH), 7.21–7.48 m (15H, C_6H_5). Mass spectrum: *m*/*z* 424 $[M + H]^+$. Found, %: C 82.19; H 7.73; N 10.05. $C_{29}H_{33}N_3$. Calculated, %: C 82.28; H 7.80; N 9.92.

3-(4-Methylbenzyl)-4′,5′-diphenyl-1′,3′,4′,5′-tetrahydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-imidazole] (Vb). Yield 82%, mp 120–121°C. IR spectrum, ν, cm^{-1}: 3405, 3391, 3325 (NH). ^1H NMR spectrum, δ, ppm: 1.43–2.05 m (6H, CH_2), 2.23–2.36 m (5H, CH_3, CH), 2.89–3.12 m (6H, NCH_2, NCH), 3.44 s (2H, 3-CH_2), 3.62 br.s (1H, NH), 3.89 br.s (1H, NH), 7.11 d (2H, C_6H_4, J = 8.1 Hz), 7.24 d (2H, C_6H_4, J = 8.1 Hz). Mass spectrum: *m*/*z* 438 $[M + H]^+$. Found, %: C 82.26; H 7.93; N 9.54. $C_{30}H_{35}N_3$. Calculated, %: C 82.39; H 8.00; N 9.60.

3-(4-Fluorobenzyl)-4′,5′-diphenyl-1′,3′,4′,5′-tetrahydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-imidazole] (Vc). Yield 72%, mp 114–115°C. IR spectrum, ν, cm^{-1}: 3405, 3387, 3321 (NH). ^1H NMR spectrum, δ, ppm: 1.45–2.11 m (6H, CH_2), 2.25–2.32 m (2H, CH), 2.91–3.15 m (6H, NCH_2, NCH), 3.48 s (2H, 3-CH_2), 3.92 br.s (2H, NH), 7.23–7.64 m (14H, H_{arom}). Mass spectrum: *m*/*z* 442 $[M + H]^+$. Found, %: C 78.74; H 9.27; N 9.48. $C_{29}H_{32}FN_3$. Calculated, %: C 78.93; H 9.19; N 9.52.

***tert*-Butyl 4′,5′-diphenyl-1′,3′,4′,5′-tetrahydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-imidazole]-3-carboxylate (Vd).** Yield 84%, mp 138–139°C. IR spectrum, ν, cm^{-1}: 3408, 3392, 3328 (NH); 1685 (C=O). ^1H NMR spectrum, δ, ppm: 1.31 s (9H, *t*-Bu), 1.43–2.06 m (6H, CH_2), 2.25–2.36 m (2H, CH), 2.89–3.15 m (6H, NCH_2, NCH), 3.86 br.s (2H, NH), 7.18–7.46 m (10H, C_6H_5). Mass spectrum: *m*/*z* 425 $[M + H]^+$, 368 $[M - 57 + H]^+$, 324 $[M - 101 + H]^+$. Found, %: C 76.28; H 6.03; N 9.81. $C_{27}H_{26}N_3O_2$. Calculated, %: C 76.43; H 6.13; N 9.90.

3-Benzylspiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]thiazolidine]-4′-carboxylic acid (VIa). Compound **Ia**, 0.458 g (2 mmol), was dissolved in 10 ml of a 3:2 (by volume) ethanol–water mixture, 0.242 g of D,L-cysteine and 0.1 ml of trifluoroacetic acid were added, and the mixture was stirred for 4 h on heating under reflux (until the initial compound disappeared completely according to the TLC data). The solvent was distilled off under reduced pressure, and the residue was recrystallized from aqueous ethanol. Yield 0.44 g (67%), mp 176–177°C. IR spectrum, ν, cm^{-1}: 3398 (NH), 3195 (OH), 1688 (C=O). ^1H NMR spectrum, δ, ppm: 1.46–2.10 m (8H, CH_2), 2.23–2.34 m (2H, CH), 2.86 d (2H, NCH_2), 2.98 d (2H, NCH_2), 3.42 s (2H, PhC**H**$_2$), 3.68 m (1H, NCH), 4.08 br.s (1H, NH), 7.22–7.48 m (5H, C_6H_5), 11.72 br.s (1H, OH). Mass spectrum: *m*/*z* 333 $[M + H]^+$. Found, %: C 64.87; H 7.15; N 8.36. $C_{18}H_{24}N_2O_2S$. Calculated, %: C 65.08; H 7.22; N 8.43.

Compounds **VIb**–**VId** and **VIIa**–**VIId** were synthesized in a similar way.

3-(4-Methylbenzyl)spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]thiazolidine]-4′-carboxylic acid (VIb). Yield 71%, mp 181–182°C. IR spectrum, ν, cm^{-1}: 3397 (NH), 3192 (OH), 1690 (C=O). ^1H NMR spectrum, δ, ppm: 1.45–2.12 m (8H, CH_2), 2.23–2.36 m (5H, CH_3, CH), 2.88 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.42 s (2H, 3-CH_2), 3.65 m (1H, NCH), 4.07 br.s (1H, NH), 7.15 d (2H, C_6H_4, J = 7.9 Hz), 7.27 d (2H, C_6H_4, J = 7.9 Hz), 11.96 br.s (1H, OH). Mass spectrum: *m*/*z* 347 $[M + H]^+$. Found, %: C 68.54; H 7.75; N 8.26. $C_{19}H_{26}N_2O_2S$. Calculated, %: C 68.69; H 7.83; N 8.43.

3-(4-Fluorobenzyl)spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]thiazolidine]-4′-carboxylic acid (VIc). Yield 67%, mp 183–184°C. IR spectrum, ν, cm^{-1}: 3402 (NH), 3198 (OH), 1689 (C=O). ^1H NMR spectrum, δ, ppm: 1.48–2.15 m (8H, CH_2), 2.25–2.38 m (2H, CH), 2.88 d (2H, NCH_2), 2.98 d (2H, NCH_2), 3.45 s (2H, CH_2N), 3.69 m (1H, NCH), 4.10 br.s (1H, NH), 7.23–7.52 m (4H, C_6H_4), 11.89 br.s (1H, OH). Mass spectrum, *m*/*z*: 351 $[M+H]^+$. Found, %: C 61.63; H 6.53; N 8.09. $C_{18}H_{23}FN_2O_2S$. Calculated, %: C 61.73; H 6.57; N 8.00.

3-*tert*-Butoxycarbonylspiro[3-azabicyclo[3.3.1]-nonane-9,2′-[1,3]thiazolidine]-4′-carboxylic acid (VId). Yield 74%, mp 193–194°C. IR spectrum, ν,

cm^{-1}: 3402 (NH); 3196 (OH); 1692, 1685 (C=O). ^1H NMR spectrum, δ, ppm: 1.32 s (9H, *t*-Bu), 1.45–2.11 m (8H, CH_2), 2.2–2.36 m (2H, CH), 2.88 d (2H, NCH_2), 2.99 d (2H, NCH_2), 3.69 m (1H, NCH), 4.10 br.s (1H, NH), 11.89 br.s (1H, OH). Mass spectrum, *m*/*z*: 343 $[M+H]^+$, 286 $[M - 57 + H]^+$, 242 $[M - 101 + H]^+$. Found, %: C 56.03; H 7.57; N 8.25. $C_{16}H_{26}N_2O_4S$. Calculated, %: C 56.16; H 7.60; N 8.18.

3-Benzylspiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]oxazolidine]-4′-carboxylic acid (VIIa). Yield 71%, mp 183–184°C. IR spectrum, ν, cm^{-1}: 3402 (NH), 3280 (OH), 1690 (C=O). ^1H NMR spectrum, δ, ppm: 1.45–2.12 m (6H, CH_2), 2.25–2.38 m (2H, CH), 2.87 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.46 s (2H, PhC**H**$_2$), 3.78 m (1H, NCH), 4.01 d (2H, OCH_2), 4.21 br.s (1H, NH), 7.24–7.50 m (5H, C_6H_5), 12.02 br.s (1H, OH). Mass spectrum: *m*/*z* 317 $[M + H]^+$. Found, %: C 68.41; H 7.44; N 8.73. $C_{18}H_{24}N_2O_3$. Calculated, %: C 68.37; H 7.59; N 8.86.

3-(4-Methylbenzyl)spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]oxazolidine]-4′-carboxylate (VIIb). Yield 75%, mp 187–188°C. IR spectrum, ν, cm^{-1}: 3405 (NH), 3282 (OH), 1688 (C=O). ^1H NMR spectrum, δ, ppm: 1.47–2.10 m (6H, CH_2), 2.23–2.37 m (5H, CH_3, CH), 3.01 d (2H, NCH_2), 3.14 d (2H, NCH_2), 3.45 s (2H, 3-CH_2), 3.71 m (1H, NCH), 4.02 d (2H, OCH_2), 4.12 br.s (1H, NH), 7.18 d (2H, C_6H_4, J = 8.2 Hz), 7.32 d (2H, C_6H_4, J = 8.2 Hz), 12.05 br.s (1H, OH). Mass spectrum: *m*/*z* 331 $[M + H]^+$. Found, %: C 69.02; H 7.68; N 8.37. $C_{19}H_{26}N_2O_3$. Calculated, %: C 69.11; H 7.87; N 8.48.

3-(4-Fluorobenzyl)spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]oxazolidine]-4′-carboxylic acid (VIIc). Yield 73%, mp 190–191°C. IR spectrum, ν, cm^{-1}: 3405 (NH), 3282 (OH), 1692 (C=O). ^1H NMR spectrum, δ, ppm: 1.46–2.16 m (6H, CH_2), 2.28–2.41 m (2H, CH), 2.90 d (2H, NCH_2), 3.01 d (2H, NCH_2), 3.48 s (2H, 3-CH_2), 3.80 m (1H, NCH), 4.03 d (2H, OCH_2), 4.23 br.s (1H, NH), 7.28–7.63 m (4H, C_6H_4), 12.05 br.s (1H, OH). Mass spectrum: *m*/*z* 335 $[M + H]^+$. Found, %: C 64.75; H 6.72; N 8.26. $C_{18}H_{23}FN_2O_3$. Calculated, %: C 64.69; H 6.88; N 8.38.

3-*tert*-Butoxycarbonylspiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]oxazolidine]-4′-carboxylic acid (VIId). Yield 72%, mp 196–197°C. IR spectrum, ν, cm^{-1}: 3403 (NH); 3278 (OH); 1693, 1685 (C=O). ^1H NMR spectrum, δ, ppm: 1.31 s (9H, *t*-Bu), 1.45–2.14 m (6H, CH_2), 2.26–2.39 m (2H, CH), 2.89 d (2H, NCH_2), 2.97 d (2H, NCH_2), 3.79 m (1H, NCH), 4.02 d (2H, OCH_2), 4.22 br.s (1H, NH), 12.05 br.s (1H, OH). Mass spectrum, *m*/*z*: 327 $[M + H]^+$, 270 $[M - 57 + H]^+$, 226 $[M - 101 + H]^+$. Found, %: C 59.03; H 7.86; N 8.46. $C_{16}H_{26}N_2O_5$. Calculated, %: C 58.92; H 7.97; N 8.58.

1′,3′-Dihydrospiro[3-azabicyclo[3.3.1]nonane-9,2′-benzimidazole] trihydrochloride (IIe). Compound **IId**, 0.99 g (3 mmol), was dissolved in 10 ml of anhydrous ethanol, 15 ml of a saturated solution of hydrogen chloride (~15%) in anhydrous dioxane was added, and the mixture was stirred for 20 h and heated to the boiling point over a period of 5 min. 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 phosphoric anhydride. Yield 0.93 g (92%), mp 204–205°C. IR spectrum: ν 3428–3286 cm^{-1} (NH_2^+). ^1H NMR spectrum, δ, ppm: 1.56–2.28 m (6H, CH_2), 2.41–2.51 m (2H, CH), 3.68 m (2H, NCH_2), 3.79 m (2H, NCH_2), 7.32–8.02 m (4H, C_6H_4), 9.85 br.s (2H, NH_2^+), 10.08 br.s (4H, NH_2^+). Mass spectrum: *m*/*z* 230 $[M + H]^+$. Found, %: C 49.32; H 6.73; N 12.31. $C_{14}H_{19}N_3 \cdot 3HCl$. Calculated, %: C 49.65; H 6.50; N 12.40.

Hydrochlorides **IIIe**– **VIIe** were synthesized in a similar way.

3′*H*-Spiro(3-azabicyclo[3.3.1]nonane-9,2′-[1,3]-benzothiazole] dihydrochloride (IIIe). Yield 96%, mp 221–222°C. IR spectrum: ν 3456–3295 cm^{-1} (NH_2^+). ^1H NMR spectrum, δ, ppm: 1.58–2.31 m (6H, CH_2), 2.42–2.50 m (2H, CH), 3.71 m (2H, NCH_2), 3.82 m (2H, NCH_2), 7.36–8.04 m (4H, C_6H_4), 9.73 br.s (2H, NH_2^+), 10.12 br.s (2H, NH_2^+). Mass spectrum: *m*/*z* 247 $[M + H]^+$. Found, %: C 52.73; H 6.32; N 8.81. $C_{14}H_{18}N_2S \cdot 2HCl$. Calculated, %: C 52.69; H 6.27; N 8.77.

3′*H*-Spiro(3-azabicyclo[3.3.1]nonane-9,2′-[1,3]-benzoxazole] dihydrochloride (IVe). Yield 97%, mp 228–230°C. IR spectrum: ν 3458–3286 cm^{-1} (NH_2^+). ^1H NMR spectrum, δ, ppm: 1.57–2.25 m (6H, CH_2), 2.41–2.49 m (2H, CH), 3.72 m (2H, NCH_2), 3.85 m (2H, NCH_2), 7.32–8.05 m (4H, C_6H_4), 9.75 br.s (2H, NH_2^+), 10.08 br.s (2H, NH_2^+). Mass spectrum: *m*/*z* 231 $[M + H]^+$. Found, %: C 55.38; H 6.75; N 9.18. $C_{14}H_{18}N_2O \cdot 2HCl$. Calculated, %: C 55.47; H 6.60; N 9.24.

4′,5′-Diphenylspiro[3-azabicyclo[3.3.1]nonane-9,2′-imidazolidine] trihydrochloride (Ve). Yield 94%, mp 252–254°C. IR spectrum: ν 3458–3264 cm^{-1} (NH_2^+). ^1H NMR spectrum, δ, ppm: 1.57–2.28 m (6H,

CH_2), 2.40–2.52 m (2H, CH), 3.67 m (2H, NCH_2), 3.80 m (2H, NCH_2), 4.08 m (2H, 4′-H, 5′-H), 7.28–7.63 m (10H, C_6H_5), 9.81 br.s (2H, NH_2^+), 10.12 br.s (4H, NH_2^+). Mass spectrum: *m*/*z* 334 $[M + H]^+$. Found, %: C 59.73; H 6.49; N 9.64. $C_{22}H_{27}N_3 \cdot 3HCl$. Calculated, %: C 59.68; H 6.78; N 9.49.

Spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]thiazolidine]-4′-carboxylic acid dihydrochloride (VIe). Yield 94%, mp 287–289°C. IR spectrum, ν, cm^{-1}: 3485–3304 (NH_2^+), 3258 (OH), 1692 (C=O). ^1H NMR spectrum, δ, ppm: 1.56–2.23 m (8H, CH_2), 2.36–2.48 m (2H, CH), 3.78 m (2H, NCH_2), 3.96 m (2H, NCH_2), 4.56 m (1H, NCH), 9.81 br.s (2H, NH_2^+), 10.22 br.s (2H, NH_2^+), 12.08 br.s (1H, OH). Mass spectrum: *m*/*z* 243 $[M + H]^+$. Found, %: C 41.74; H 6.21; N 8.56. $C_{11}H_{18}N_2O_2S \cdot 2HCl$. Calculated, %: C 41.93; H 6.35; N 8.89.

Spiro[3-azabicyclo[3.3.1]nonane-9,2′-[1,3]oxazolidine]-4′-carboxylic acid dihydrochloride (VIIe). Yield 95%, mp 291–293°C. IR spectrum, ν, cm^{-1}: 3502–3296 (NH_2^+), 3262 (OH), 1693 (C=O). ^1H NMR spectrum, δ, ppm: 1.57–2.26 m (6H, CH_2), 2.32–2.48 m (2H, CH), 3.82 m (2H, NCH_2), 3.95 m (2H, NCH_2), 4.12 d (2H, OCH_2), 4.58 m (1H, 4′-H), 9.83 br.s (2H, NH_2^+), 10.28 br.s (2H, NH_2^+), 12.15 br.s (1H, OH). Mass spectrum: *m*/*z* 227 $[M + H]^+$. Found, %: C 44.28; H 6.51; N 9.47. $C_{11}H_{18}N_2O_3 \cdot 2HCl$. Calculated, %: C 44.17; H 6.69; N 9.36.

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