Synthesis of *N*,*N*′-di(*tert*-butyl)bispidin-9-ones

A. I. Kuznetsov,[a]* *I. M. Senan,*[a]* *and T. M. Serova*[b]*

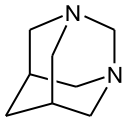
[a]*M. V. Lomonosov Moscow State University of Fine Chemical Technologies, 86 prosp. Vernadskogo, 119571 Moscow, Russian Federation. E-mail: tetraza@mail.ru*

[b]*Institute of Physiologically Active Compounds, Russian Academy of Sciences, Chernogolovka, Moscow Region, Russian Federation. E-mail: serova@ipac.ac.ru*

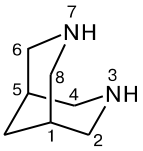
Condensation of 1,3,5-tri(*tert*-butyl)-1,3,5-triazacyclohexane with acetone gave 3,7-di(*tert*-butyl)-1,5-bis[(*tert*-butylamino)methyl]bispidin-9-one. Reactions with ethyl methyl ketone and other ketones of the formula RCH_2COCH_3 yielded 5-R-3,7-di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]bispidin-9-ones, while reactions with diethyl ketone and other symmetrical ketones of the formula RCH_2COCH_2R afforded 1,5-R-3,7-di(*tert*-butyl)bispidin-9-ones.

Key words: bispidine, 3,7-diazabicyclo[3.3.1]nonane, condensation, acetone, ethyl methyl ketone, diethyl ketone, 1,3,5-tri(*tert*-butyl)-1,3,5-triazacyclohexane, 3,7-di(*tert*-butyl)bispidin-9-one derivatives, 3,7-di(*tert*-butyl)-3,7-diazabicyclo[3.3.1]nonan-9-one derivatives.

In recent years, researchers dealing with azaadamantane chemistry[1] have experienced a renewal of interest in structurally related 1,3-diazaadamantane (1,3-diazatricyclo[3.3.1.1^{3,7}]decane) and bispidine (3,7-diazabicyclo[3.3.1]nonane).[2—4]



1,3-Diazaadamantane



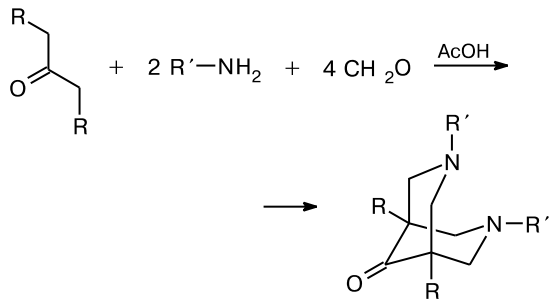
Bispidine

This is explained by their various physiological activity[5,6] and the tendency of bispidine derivatives to form complexes[7,8] with, *e.g.*, transition metal salts. The most accessible bispidine derivatives are bispidin-9-ones containing substituents at the bridgehead atoms 1 and 5, which can be prepared by condensation of ketones with formaldehyde and primary amines according to the Mannich reaction pattern (Scheme 1).

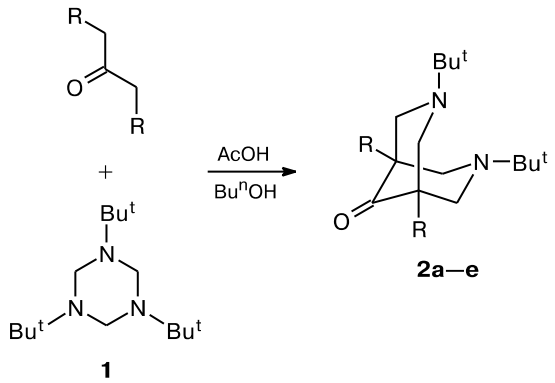
Here we present the data for the transformation of 1,3,5-tri(*tert*-butyl)-1,3,5-triazacyclohexane[9] (**1**) into 3,7-di(*tert*-butyl)-3,7-diazabicyclo[3.3.1]nonan-9-ones (*N*,*N*′-di(*tert*-butyl)bispidin-9-ones) **2**—**5** by condensation with acetone and other ketones. The *tert*-butyl groups were used as substituents at the N atoms because they can subsequently be removed.[10]

By condensation of triazacyclohexane **1** with ketones containing four acidic H atoms, we obtained 1,5-disubstituted *N*,*N*′-di(*tert*-butyl)bispidin-9-ones **2a**—**e** in 58—88% yields (Scheme 2).

Scheme 1



Scheme 2



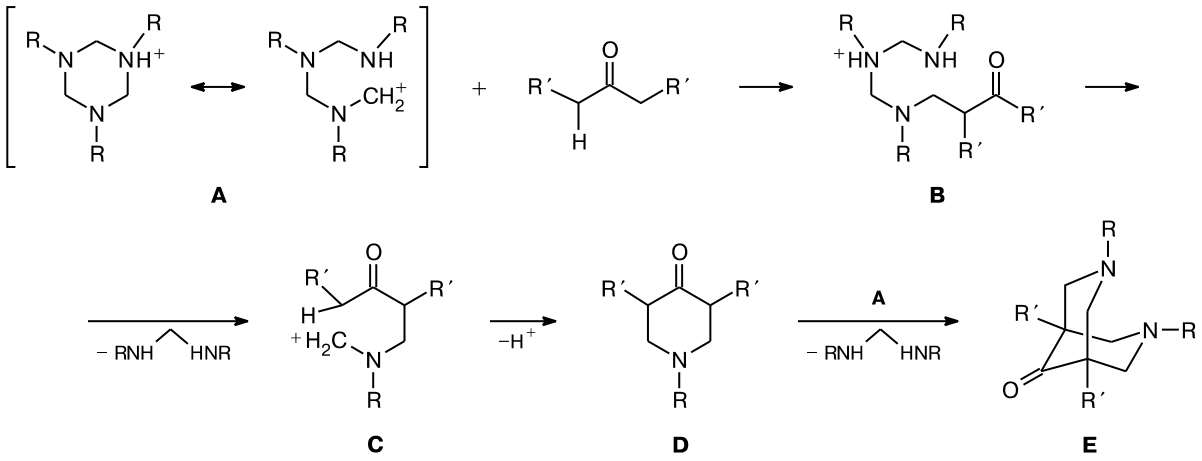
2: R = Me (**a**), Et (**b**), Pr (**c**), Bn (**d**), Ph (**e**)

The yield of dimethylbispidinone **2a** was 72%; earlier,[11] this compound has been obtained by condensation of

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 307—311, February, 2012.

1066-5285/12/6102-308

Scheme 3



diethyl ketone with *tert*-butylamine and formaldehyde in 30% yield (see Scheme 1).

A possible mechanism of the reaction of 1,3,5-triazacyclohexanes with ketones is shown in Scheme 3.

In a first step, AcOH protonates triazacyclohexane to give carbenium immonium cation **A**, which further reacts with the starting ketone. The resulting adduct **B** eliminates methylenediamine molecule $RHN—CH_2—NHR$ and is transformed through intermediate **C** into piperidone **D**. Piperidone **D** reacts in a similar way with a second triazacyclohexane molecule to give bispidinone **E** as a final product. Scheme 3 displays only some of the possible intermediates. The possibility of the intermediate formation of piperidone **D** was experimentally confirmed with 1-*tert*-butyl-3-[(*tert*-butylamino)methyl]-5-(phenylthio)-piperidin-4-one (**3**) as an example (Scheme 4).

We carried out the synthesis of bispidinones under different reaction conditions. *n*-Butanol was used as a solvent for compounds **2a**—**e**. The highest yield of bispidinones was achieved when the molar ratio of ketone : triazacyclohexane : AcOH was 1 : 1.3 : 2.8. Bispidinones **4a**—**d** and **5** were obtained in EtOH.

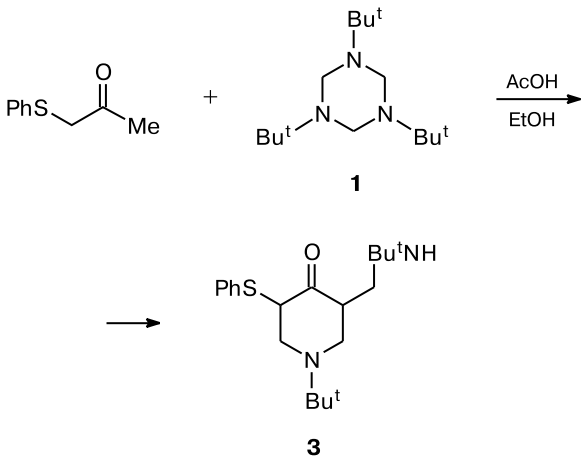
Condensation of triazacyclohexane **1** with ketones containing five acidic H atoms (RCH_2COCH_3), gave earlier unknown 5-substituted *N*,*N*′-di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]bispidin-9-ones **4a**—**d** in 50—70% yields (Scheme 5).

With acetone as the starting ketone, the condensation involves all the six H atoms to form *N*,*N*′-di(*tert*-butyl)-1,5-bis[(*tert*-butylamino)methyl]bispidin-9-one (**5**) in 40% yield (Scheme 6).

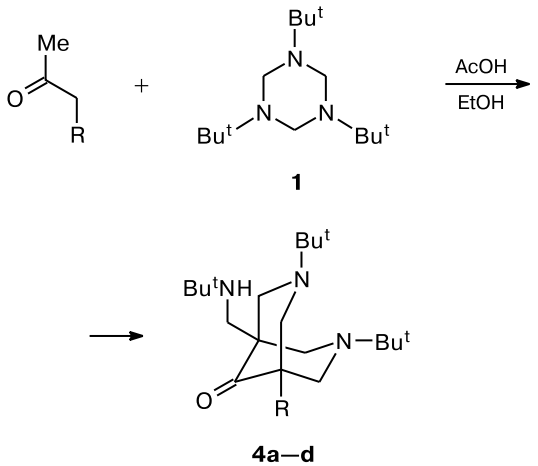
The structures of compounds **2**—**5** were confirmed by elemental analysis data and NMR and mass spectra.

To sum up, we developed an efficient method for the synthesis of 1,5-disubstituted 3,7-di(*tert*-butyl)-3,7-diazabicyclo[3.3.1]nonan-9-ones (*N*,*N*′-di(*tert*-butyl)bispidin-9-ones). The method involves condensation of acetone

Scheme 4

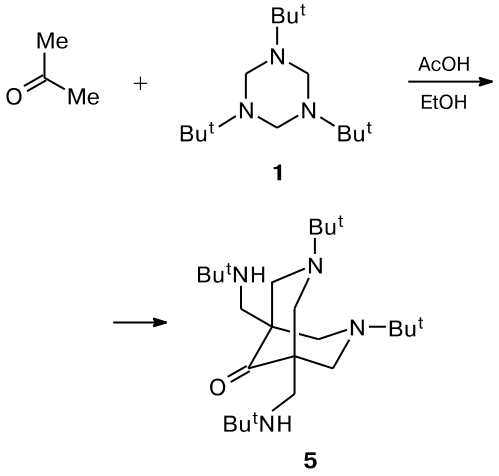


Scheme 5



4: R = Me (**a**), Bn (**b**), PhS (**c**), $Me_2C=CHCH_2$ (**d**)

Scheme 6



and some other ketones with 1,3,5-tri(*tert*-butyl)-1,3,5-triazacyclohexane **1**.

Experimental

Domestic solvents and reagents (reagent grade) were used. 1-(Phenylthio)propan-2-one was prepared as described earlier.[12] IR spectra were recorded on a Bruker IFSv spectrophotometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 (^{1}H) and 75.47 MHz (^{13}C)) in $CDCl_3$ with $SiMe_4$ as the internal standard. Mass spectra (EI) were measured on an MS-30 Kratos instrument (direct inlet probe, ionization voltage 70 eV, ion source temperature 200 °C). High-resolution mass spectra (ESI)[13] were recorded on a Bruker micrOTOF II instrument in the positive (capillary voltage 4500 V) or negative ion mode (capillary voltage 3200 V). The *m*/*z* scan range was 50—3000 Da; the instrument was calibrated externally or internally (Electrospray Calibrant Solution, Fluka). Solutions in acetonitrile, methanol, or water were syringed at a rate of 3 μL min^{-1}. Nitrogen was used as a spraying gas (4 L min^{-1}); the interface temperature was 180 °C. Melting points were determined on a PTP-M instrument.

1,5-Disubstituted 3,7-di(*tert*-butyl)-3,7-diazabicyclo[3.3.1]nonan-9-ones 2a—d (general procedure). A solution of the ketone RCH_2COCH_2R (50 mmol), triazacyclohexane **1** (16.60 g, 65 mmol), and AcOH (8.41 g, 140 mmol) in Bu^{n}OH (25 mL) was gently refluxed for 2 h. The reaction mixture was concentrated and alkalified with K_2CO_3 to pH 10. The product was extracted with boiling toluene (3Ч20 mL), the extract was concentrated, and the residue was recrystallized from toluene.

3,7-Di(*tert*-butyl)-1,5-dimethyl-3,7-diazabicyclo[3.3.1]nonan-9-one (2a). Yield 10.10 g (72%), white crystals, m.p. 124—126 °C (from toluene) (*cf.* Ref. 11: m.p. 128—130 °C). Found (%): C, 72.70; H, 11.38; N, 10.11. $C_{17}H_{32}N_2O$. Calculated (%): C, 72.81; H, 11.50; N, 9.99. IR, ν/cm^{-1}: 1720 (C=O). ^{1}H NMR, δ: 0.92 (s, 6 H, 2 Me); 1.01 (s, 18 H, 2 Me_3C); 2.42 (d, 4 H, 2 NCH_2C, J = 10.0 Hz); 3.00 (d, 4 H, 2 NCH_2C, J = 10.0 Hz). ^{13}C NMR, δ: 216.20 (CO(9)), 58.41 (C(2), C(4), C(6), C(8)), 52.72 (3,7-CN), 46.24 (C(1), C(5)), 26.23 (2 C($\underline{C}H_3)_3$), 20.22 (1,5-Me). MS, *m*/*z* (I_{rel} (%)): 280 [M]$^+$ (49), 223 (48), 194 (65), 180 (82), 124 (100), 100 (89), 86 (74), 84 (45), 70 (85), 57 (81), 43 (37).

3,7-Di(*tert*-butyl)-1,5-diethyl-3,7-diazabicyclo-[3.3.1]nonan-9-one (2b). Yield 9.00 g (58%), white crystals, m.p. 56—58 °C (from toluene). Found (%): C, 74.32; H, 11.96; N, 8.75. $C_{19}H_{36}N_2O$. Calculated (%): C, 73.97; H, 11.76; N, 9.08. IR, ν/cm^{-1}: 1720 (C=O). ^{1}H NMR, δ: 0.88 (t, 6 H, 2 $CH_2C\underline{H}_3$, J = 7.3 Hz); 1.05 (s, 18 H, 2 Me_3C); 1.42 (q, 4 H, 2 $C\underline{H}_2Me$, J = 8.1 Hz); 2.50 (d, 4 H, 2 NCH_2C, J = 10.3 Hz); 3.00 (d, 4 H, 2 NCH_2C, J = 10.3 Hz). ^{13}C NMR, δ: 217.18 (CO(9)), 56.35 (C(2), C(4), C(6), C(8)), 53.52 (3,7-CN), 49.68 (C(1), C(5)), 26.65 (2 C($\underline{C}H_3)_3$), 26.59 (1,5-$\underline{C}H_2$Me), 7.84 (1,5-$CH_2\underline{C}H_3$). MS, *m*/*z* (I_{rel} (%)): 308 [M]$^+$ (22), 223 (71), 209 (34), 152 (100), 100 (77), 84 (19), 70 (18), 57 (83), 43 (77).

3,7-Di(*tert*-butyl)-1,5-dipropyl-3,7-diazabicyclo[3.3.1]nonan-9-one (2c). Yield 11.80 g (69%), white crystals, m.p. 86—88 °C (from toluene). Found (%): C, 75.46; H, 12.04; N, 8.14. $C_{21}H_{40}N_2O$. Calculated (%): C, 74.94; H, 11.98; N, 8.32. IR, ν/cm^{-1}: 1710 (C=O). ^{1}H NMR, δ: 0.90 (s, 6 H, 2 $CH_2C\underline{H}_3$); 1.05 (s, 18 H, 2 Me_3C); 1.35 (s, 8 H, 2 $CC\underline{H}_2C\underline{H}_2$Me); 2.50 (d, 4 H, 2 NCH_2C, J = 10.3 Hz); 3.00 (d, 4 H, 2 NCH_2C, J = 10.3 Hz). ^{13}C NMR, δ: 217.22 (CO(9)), 56.77 (C(2), C(4), C(6), C(8)), 53.49 (3,7-CN), 49.71 (C(1), C(5)), 36.68 (1,5-$\underline{C}H_2$Et), 26.60 (2 C($\underline{C}H_3)_3$), 16.66 (1,5-$CH_2\underline{C}H_2$Me), 15.22 (1,5-$(CH_2)_2\underline{C}H_3$). MS, *m*/*z* (I_{rel} (%)): 336 [M]$^+$ (25), 279 (22), 250 (54), 236 (83), 180 (94), 100 (100), 86 (24), 70 (23), 57 (46), 45 (53).

1,5-Dibenzyl-3,7-di(*tert*-butyl)-3,7-diazabicyclo[3.3.1]nonan-9-one (2d). Yield 16.24 g (75%), white crystals, m.p. 184—185 °C (from toluene). Found (%): C, 80.67; H, 9.27; N, 6.63. $C_{29}H_{40}N_2O$. Calculated (%): C, 80.51; H, 9.32; N, 6.47. IR, ν/cm^{-1}: 1715 (C=O), 1598 (Ar). ^{1}H NMR, δ: 0.96 (s, 18 H, 2 Me_3C); 2.76 (d, 4 H, 2 NCH_2C, J = 10.0 Hz); 2.98 (d, 4 H, 2 NCH_2C, J = 10.0 Hz); 2.90 (s, 4 H, 2 CCH_2, Ar); 7.18—7.45 (m, 10 H, 2 Ar). MS, *m*/*z* (I_{rel} (%)): 432 [M]$^+$ (25), 375 (22), 332 (54), 248 (83), 100 (100), 91 (30), 77 (23), 57 (46), 43 (53).

3,7-Di(*tert*-butyl)-1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonan-9-one (2e). A solution of 1,3-diphenylpropan-2-one (10.51 g, 50 mmol), triazacyclohexane **1** (16.60 g, 65 mmol), and AcOH (8.41 g, 140 mmol) in Bu^{n}OH (20 mL) was gently refluxed for 2 h. The precipitate that formed was filtered off, washed with Pr^{i}OH (10 mL), and recrystallized from EtOH. The yield of compound **2e** was 17.71 g (88%), white crystals, m.p. 210—211 °C (from EtOH). Found (%): C, 79.99; H, 9.04; N, 7.16. $C_{27}H_{36}N_2O$. Calculated (%): C, 80.15; H, 8.97; N, 6.92. IR, ν/cm^{-1}: 1715 (C=O), 1595 (Ar). ^{1}H NMR, δ: 1.14 (s, 18 H, 2 Me_3C); 3.10 (d, 4 H, 2 NCH_2C, J = 10.2 Hz); 3.59 (d, 4 H, 2 NCH_2C, J = 10.2 Hz); 7.04—7.30 (m, 10 H, 2 Ar). ^{13}C NMR, δ: 211.36 (CO(9)), 143.83, 129.12, 127.45, 126.10 (2 Ph), 58.14 (C(2), C(4), C(6), C(8)), 54.71 (C(1), C(5)), 53.72 (3,7-CN), 26.43 (2 C($\underline{C}H_3)_3$). MS, *m*/*z* (I_{rel} (%)): 404 [M]$^+$ (18), 347 (17), 318 (69), 304 (53), 248 (57), 132 (32), 100 (100), 91 (46), 77 (30), 57 (46), 43 (58).

1-*tert*-Butyl-3-[(*tert*-butylamino)methyl]-5-(phenylthio)-piperidin-4-one (3). A solution of 1-(phenylthio)propan-2-one (1.66 g, 10 mmol), triazacyclohexane **1** (2.55 g, 10 mmol), and AcOH (0.72 g, 12 mmol) in EtOH (20 mL) was refluxed for 6 h. The reaction mixture was concentrated and alkalified with K_2CO_3 to pH 10. The product was extracted with boiling toluene

(3×10 mL). The extract was concentrated and the residue was recrystallized from EtOH. The yield of compound **3** was 2.50 g (72%), white crystals, m.p. 85—87 °C (from EtOH). Found (%): C, 68.97; H, 9.67; N, 8.10. $C_{20}H_{32}N_2OS$. Calculated (%): C, 68.92; H, 9.25; N, 8.04. IR, ν/cm^{-1}: 3327 (NH), 1715 (C=O), 580 (C—S). ^{1}H NMR, δ: 1.05 (s, 18 H, 2 Me_3CN); 1.92 (s, 1 H, NH); 2.29 (s, 2 H, C$\underline{H}_2$NH); 2.31 (d, 2 H, NCH$_2$, J = 9.5 Hz); 2.78 (d, 1 H, CH, J = 8.8 Hz); 3.40 (d, 2 H, NCH$_2$C, J = 11.7 Hz); 4.00 (d, 1 H, CHS, J = 8.8 Hz); 7.27—7.41 (m, 5 H, Ar). ^{13}C NMR, δ: 202.84 (CO), 136.92, 129.53, 129.11, 128.76 (SPh), 64.55 (2 CN), 57.67 (CHS), 53.89 (2 CH_2N), 52.74 (CH_2NH), 26.38 (2 C($\underline{C}H_3$)$_3$), 25.54 (CH). MS, *m/z*: found 349.2310 [M + H]$^+$; $C_{20}H_{32}N_2OS$; calculated M = 348.2235.

5-Substituted 3,7-di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]-3,7-diazabicyclo[3.3.1]nonan-9-ones 4a—d (general procedure). A solution of the ketone RCH_2COCH_3 (10 mmol), triazacyclohexane **1** (5.11 g, 20 mmol), and AcOH (2.64 g, 44 mmol) in EtOH (25 mL) was refluxed for 6 h. The reaction mixture was concentrated and alkalified with K_2CO_3 to pH 10. The product was extracted with boiling toluene (3Ч15 mL). The extract was concentrated and the residue was recrystallized from EtOH.

3,7-Di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]-5-methyl-3,7-diazabicyclo[3.3.1]nonan-9-one (4a). Yield 2.50 g (71%), white crystals, m.p. 88—90 °C (from EtOH). Found (%): C, 71.54; H, 11.63; N, 12.03. $C_{21}H_{41}N_3O$. Calculated (%): C, 71.74; H, 11.75; N, 11.95. IR, ν/cm^{-1}: 3405, 3318 (NH), 1711 (C=O). ^{1}H NMR, δ: 0.92 (s, 3 H, Me); 1.00 (s, 9 H, (C$\underline{H}_3$)$_3$CNH); 1.01 (s, 18 H, 2 Me_3CN); 1.02 (s, 1 H, NH); 2.45 (s, 2 H, CC$\underline{H}_2$NH); 2.42 (d, 2 H, NCH$_2$C, J = 10.3 Hz); 2.94 (d, 2 H, NCH$_2$C, J = 10.3 Hz); 2.72 (d, 2 H, NCH$_2$C, J = 10.1 Hz); 3.02 (d, 2 H, NCH$_2$C, J = 10.1 Hz). ^{13}C NMR, δ: 217.99 (CO(9)), 58.80 (C(4), C(6)), 55.52 (C(2), C(8)), 53.37 (3,7-CN), 50.49 (CNH), 49.98 (CH_2NH), 46.82 (C(5)), 46.04 (C(1)), 29.17 (NHC($\underline{C}H_3$)$_3$), 26.69 (2 C($\underline{C}H_3$)$_3$), 20.67 (5-Me). MS, *m/z*: found 352.3318 [M + H]$^+$; $C_{21}H_{41}N_3O$; calculated M = 351.3450.

5-Benzyl-3,7-di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (4b). Yield 3.20 g (75%), white crystals, m.p. 107—109 °C (from EtOH). Found (%): C, 75.80; H, 10.57; N, 9.36. $C_{27}H_{45}N_3O$. Calculated (%): C, 75.83; H, 10.61; N, 9.83. IR, ν/cm^{-1}: 3333 (NH), 1711 (C=O). ^{1}H NMR, δ: 0.95 (s, 18 H, 2 Me_3CN); 1.02 (s, 9 H, (C$\underline{H}_3$)$_3$CNH); 1.13 (s, 1 H, NH); 2.50 (s, 2 H, CC$\underline{H}_2$NH); 2.64 (d, 2 H, NCH$_2$C, J = 9.0 Hz); 2.90 (d, 2 H, NCH$_2$C, J = 9.0 Hz); 2.76 (s, 2 H, CCH$_2$Ar); 2.74 (d, 2 H, NCH$_2$C, J = 8.7 Hz); 2.93 (d, 2 H, NCH$_2$C, J = 8.7 Hz); 7.09—7.24 (m, 5 H, Ar). ^{13}C NMR, δ: 217.45 (CO(9)), 138.43, 130.89, 128.11, 126.14 (Ph), 56.03 (C(4), C(6)), 55.62 (C(2), C(8)), 53.63 (3,7-CN), 50.77 (CNH), 50.41 (CH_2NH), 46.22 (C(5)), 46.04 (C(1)), 38.96 (1-$\underline{C}H_2$Ph), 29.23 (NHC($\underline{C}H_3$)$_3$), 26.69 (2 C($\underline{C}H_3$)$_3$). MS, *m/z*: found 428.3614 [M + H]$^+$; $C_{27}H_{45}N_3O$; calculated M = 427.3562.

3,7-Di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]-5-phenylthio-3,7-diazabicyclo[3.3.1]nonan-9-one (4c). Yield 3.00 g (67%), white crystals, m.p. 128—130 °C (from EtOH). Found (%): C, 69.97; H, 10.20; N, 9.14. $C_{26}H_{43}N_3OS$. Calculated (%): C, 70.06; H, 9.72; N, 9.43. IR, ν/cm^{-1}: 3327 (NH), 1715 (C=O), 580 (C—S). ^{1}H NMR, δ: 1.00 (s, 18 H, 2 Me_3CN); 1.05 (s, 9 H, (C$\underline{H}_3$)$_3$CNH); 1.13 (s, 1 H, NH); 2.56 (s, 2 H, CC$\underline{H}_2$NH); 2.82 (d, 2 H, NCH$_2$C, J = 10.3 Hz); 2.96 (t, 4 H, 2 NCH$_2$C, J = 8.8 Hz); 3.25 (d, 2 H, NCH$_2$C, J = 11.0 Hz); 7.27—7.52 (m, 5 H, Ar). ^{13}C NMR, δ: 211.51 (CO(9)), 135.73, 131.94, 128.58, 128.01 (SPh), 61.71 (C(5)), 57.96 (C(4), C(6)), 55.24 (C(2), C(8)), 53.73 (3,7-CN), 51.23 (CNH), 49.92 (CH_2NH), 46.08 (C(1)), 29.08 (NHC($\underline{C}H_3$)$_3$), 26.58 (2 C($\underline{C}H_3$)$_3$). MS, *m/z*: found 446.3156 [M + H]$^+$; $C_{26}H_{43}N_3OS$; calculated M = 445.3127.

3,7-Di(*tert*-butyl)-1-[(*tert*-butylamino)methyl]-5-(3-methylbut-2-enyl)-3,7-diazabicyclo[3.3.1]nonan-9-one (4d). Yield 2.80 g (69%), white crystals, m.p. 122—123 °C (from EtOH). Found (%): C, 73.76; H, 11.35; N, 10.25. $C_{25}H_{47}N_3O$. Calculated (%): C, 74.02; H, 11.68; N, 10.36. IR, ν/cm^{-1}: 3330 (NH), 1711 (C=O), 1656 (C=C). ^{1}H NMR, δ: 1.06 (s, 27 H, 3 Me_3CN); 1.26 (s, 1 H, NH); 1.61, 1.71 (both s, 3 H each, (C$\underline{H}_3$)$_2$C=CH); 2.12 (d, 2 H, C$\underline{H}_2$CH=C, J = 7.5 Hz); 2.52 (s, 2 H, CC$\underline{H}_2$NH); 2.54, 3.02 (both d, 4 H each, 2 NCH$_2$C, J = 11.0 Hz); 2.77 (d, 2 H, NCH$_2$C, J = 10.3 Hz); 2.99 (d, 2 H, NCH$_2$C, J = 10.3 Hz); 5.17 (t, 1 H, CH=C, J = 6.0 Hz). ^{13}C NMR, δ: 217.81 (CO(9)), 133.62 (C=), 120.22 (CH=), 56.32 (C(4), C(6)), 55.62 (C(2), C(8)), 53.50 (3,7-CN), 50.49 (CNH), 50.19 (CH_2NH), 49.99 (C(1)), 46.16 (C(5)), 32.09 (5-$\underline{C}H_2$C=), 29.15 (NHC($\underline{C}H_3$)$_3$), 26.67 (2 C($\underline{C}H_3$)$_3$), 26.04, 17.95 (=C($\underline{C}H_3$)$_2$). MS, *m/z*: found 406.3798 [M + H]$^+$; $C_{25}H_{47}N_3O$; calculated M = 405.3719.

3,7-Di(*tert*-butyl)-1,5-bis[(*tert*-butyl)aminomethyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (5). A solution of acetone (2.90 g, 50 mmol), triazacyclohexane **1** (25.53 g, 100 mmol), and AcOH (13.21 g, 120 mmol) in EtOH (100 mL) was refluxed for 6 h. The reaction mixture was concentrated and alkalified with K_2CO_3 to pH 10, and stirred. The product was extracted with boiling toluene (3×20 mL). The extract was concentrated and the residue was recrystallized from EtOH. The yield of compound **5** was 8.50 g (40%), white crystals, m.p. 128—130 °C (from EtOH). Found (%): C, 71.16; H, 11.85; N, 12.98. $C_{25}H_{50}N_4O$. Calculated (%): C, 71.04; H, 11.92; N, 13.25. IR, ν/cm^{-1}: 3323 (NH), 1706 (C=O). ^{1}H NMR, δ: 0.97 (s, 18 H, 6 MeCN); 0.98 (s, 2 H, 2 NH); 0.99 (s, 18 H, 6 C$\underline{H}_3$CNH); 2.42 (s, 4 H, 2 CC$\underline{H}_2$NH); 2.90 (d, 4 H, 2 NCH$_2$C, J = 10.3 Hz); 2.67 (d, 4 H, 2 NCH$_2$C, J = 10.3 Hz). ^{13}C NMR, δ: 218.79 (CO(9)), 55.62 (C(2), C(4), C(6), C(8)), 53.61 (3,7-CN), 50.61 (2 CNH), 50.05 (2 CH_2NH), 46.04 (C(1), C(5)), 29.21 (2 NHC($\underline{C}H_3$)$_3$), 26.78 (2 N—C($\underline{C}H_3$)$_3$). MS, *m/z*: found 423.4048 [M + H]$^+$; $C_{25}H_{50}N_4O$; calculated M = 422.3985.

References

1. A. I. Kuznetsov, *Azaadamantany. Uspekhi khimii adamantana* [*Azaadamantanes. Achievements in Adamantane Chemistry*], Khimiya, Moscow, 2007, 194 pp. (in Russian).
2. S. Z. Vatsadze, V. S. Tyurin, A. I. Zatsman, M. A. Manaenkova, V. S. Semashko, D. P. Kut´ko, N. V. Zyk, A. V. Churakov, L. G. Kuz´mina, *Zh. Org. Khim.*, 2006, **42**, 1244 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2006, **42**, 1225].
3. Sh. Levinger, Y. Scharabi-Romen, A. Mainfeld, A. Albeck, *J. Org. Chem.*, 2008, **73**, 7793.
4. A. V. Ivachtchenko, A. Khvat, S. E. Tkachenko, Yu. B. Sandulenko, V. Y. Vvedensky, *Tetrahedron Lett.*, 2004, **45**, 6733.
5. T. Siener, A. Cambareri, U. Kuhl, W. Englberger, M. Haurand, B. Kögel, U. Holzgrabe, *J. Med. Chem.*, 2000, **43**, 3746.
6. G. L. Garrison, K. D. Berlin, B. J. Scherlag, R. Lazzara, E. Patterson, T. Fazekas, S. Sangiah, C. Chen, F. D. Schubot, D. Helm, *J. Med. Chem.*, 1996, **39**, 2559.

7. A. Gogoil, H. Grennberg, A. Axen, *Organometallics*, 1997, **16**, 1167.
8. K. J. Haack, R. Goddard, K. R. Pörschke, *J. Am. Chem. Soc.*, 1997, **119**, 7992.
9. L. M. R. Martinez-Aguilera, G. Cadenas-Pliego, R. Contreras, A. Flores-Parra, *Tetrahedron: Asymmetry*, 1995, **6**, 1585.
10. A. I. Kuznetsov, K. I. Romanova, E. B. Basargin, A. S. Moskovkin, B. V. Unkovskii, *Khim. Geterotsikl. Soedin.*, 1990, **4**, 535 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1990, **4**].
11. K. A. Potekhin, O. I. Levina, Yu. T. Struchkov, A. M. Svetlanova, R. S. Idrisova, V. A. Palyulin, N. S. Zefirov, *Zh. Vses. Khim. O-va im. D.I. Mendeleeva*, 1991, **1**, 87 [*Mendeleev Chem. J.*, 1991, **1**, 87].
12. H. L. Holland, F. M. Broun, F. Barrett, J. French, D. V. Johnson, *J. Ind. Microbiol. Biotechnol.*, 2003, **30**, 292.
13. P. A. Belyakov, V. I. Kadentsev, A. O. Chizhov, N. J. Kolotyrkina, A. S. Shashkov, V. P. Ananikov, *Mendeleev Commun.*, 2010, **20**, 125.

Received September 21, 2011;
in revised form December 7, 2011