Substituted and fused spiro[benzo-2-azepine-3,1´-cyclohexanes]

A. V. Varlamov, D. G. Grudinin, A. I. Chernyshev, A. N. Levov, I. Yu. Lobanov, R. S. Borisov, and F. I. Zubkov★

Peoples' Friendship University of Russia,
6 ul. Miklukho-Maklaya, 117198 Moscow, Russian Federation.
Fax: +7 (095) 955 0779. E-mail: fzubkov@sci.pfu.edu.ru

5-Methyl-4,5-dihydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane] *N*-oxide was rearranged into 5-methyl-1-oxo-1,2,4,5-tetrahydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane]. The latter was used for the synthesis of spiro{triazolo[3,4-*a*]- and -tetrazolo[5,1-*a*]benzo-2-azepinecyclohexanes}.

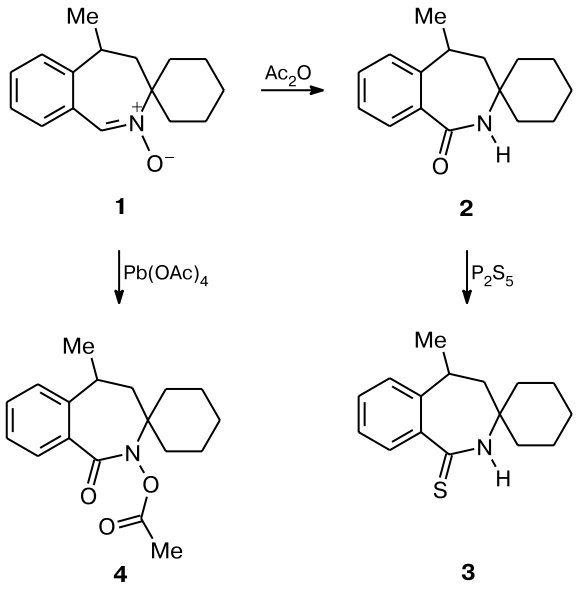
Key words: spiro[benzo-2-azepinecyclohexanes], spiro{azolo[5,1-*a*]benzo-2-azepinecyclohexanes}, rearrangements, cyclic nitrones, fused triazoles, fused tetrazoles.

Substituted benzoazepines possess a broad spectrum of biological activities. The benzoazepine ring is the major fragment of a series of alkaloids.[1] In galantamine, lycoramine, and narwedine, this fragment is spiro-fused to the cyclohexane ring. Earlier, a multistep preparative procedure has been developed for the synthesis of tetrahydrospiro[benzo-2-azepine-3,1´-cycloalkanes(piperidines)], which are structural analogs of the above-mentioned alkaloids, based on intramolecular cyclization of readily accessible homoallylamines.[2—4] This stimulated systematic studies of their reactivities.

In the present study, we summarized the results of the synthesis of substituted and fused derivatives of this heterocyclic system starting from 1-oxo(thioxo)tetrahydrospiro[benzo-2-azepine-3,1´-cyclohexanes].

The rearrangement of 5-methyl-4,5-dihydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane] *N*-oxide (**1**)[3] in refluxing acetic anhydride[5] afforded 1-oxospiro[benzo-2-azepine-3,1´-cyclohexane] **2** in quantitative yield. The reaction of phosphorus pentasulfide with lactam **2** produced thiolactam **3** (Scheme 1).

Scheme 1



Oxidation of *N*-oxide **1** with lead tetraacetate in benzene afforded the *O*-acetyl derivative of hydroxamic acid **4** of the benzo-2-azepine series in 90% yield. Manganese dioxide in benzene and potassium periodate in chloroform in the presence of a crown ether do not oxidize nitrone **1**.

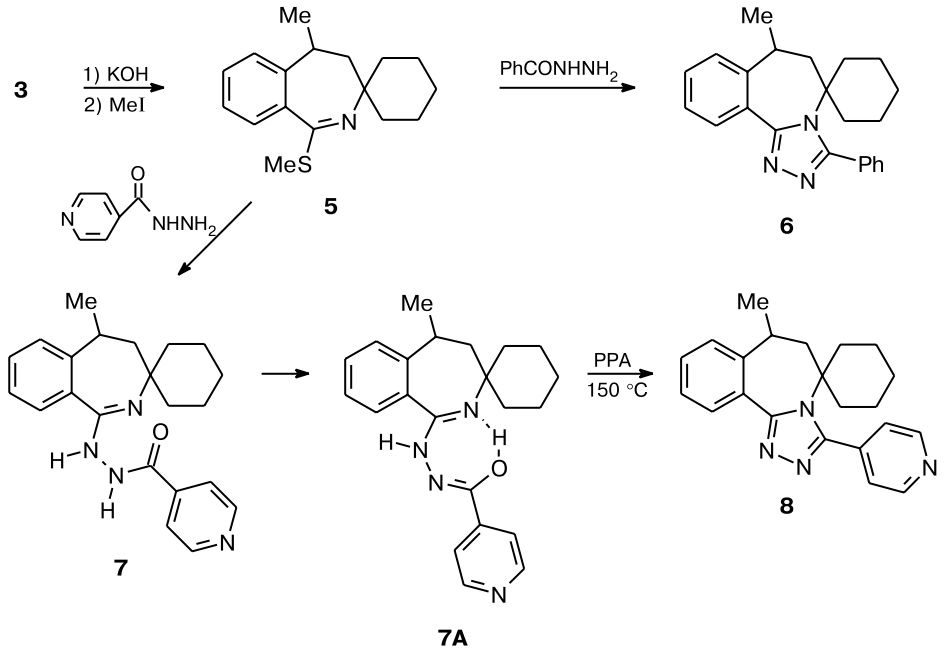
It is known[6] that *O*- and *S*-alkylated lactams and thiolactams are promising synthons for the introduction of various nucleophilic substituents and annelation of heterocyclic fragments at the C—N bond. Therefore, thiolactam **3** was transformed into 5-methyl-1-methylthio-4,5-dihydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane] (**5**) in high yield by the reaction with methyl iodide in DMSO. Condensation of compound **5** with benzohydrazide in refluxing butanol gave rise to spiro[triazolobenzo-2-azepinecyclohexane] **6** (Scheme 2).

Condensation of thioimidate **5** with isonicotinohydrazide under the same conditions afforded derivative **7**. According to the IR spectroscopic data (the absence of a CO stretching band at 1650—1720 cm^{-1}), the latter exists in an iminol form **7A** due apparently to strong intramolecular hydrogen bonding. Heating of compound **7A** in polyphosphoric acid at 150 °C gave 3-(4-pyridyl)spiro[triazolobenzo-2-azepinecyclohexane] **8** in 17% yield.

Attempts to *O*-alkylate lactam **2** with triethyloxonium tetrafluoroborate, dimethyl sulfate, or methyl chloroformate failed. In the latter case, *N*-methoxycarbonyl

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1647—1651, August, 2004.

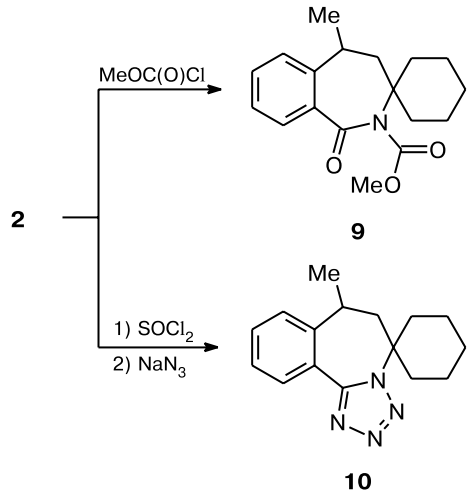
Scheme 2



PPA is polyphosphoric acid

lactam **9** was obtained in 73% yield (Scheme 3). Successive treatment of lactam **2** with thionyl chloride and sodium azide afforded spiro[tetrazolobenzo-2-azepinecyclohexane] **10**.

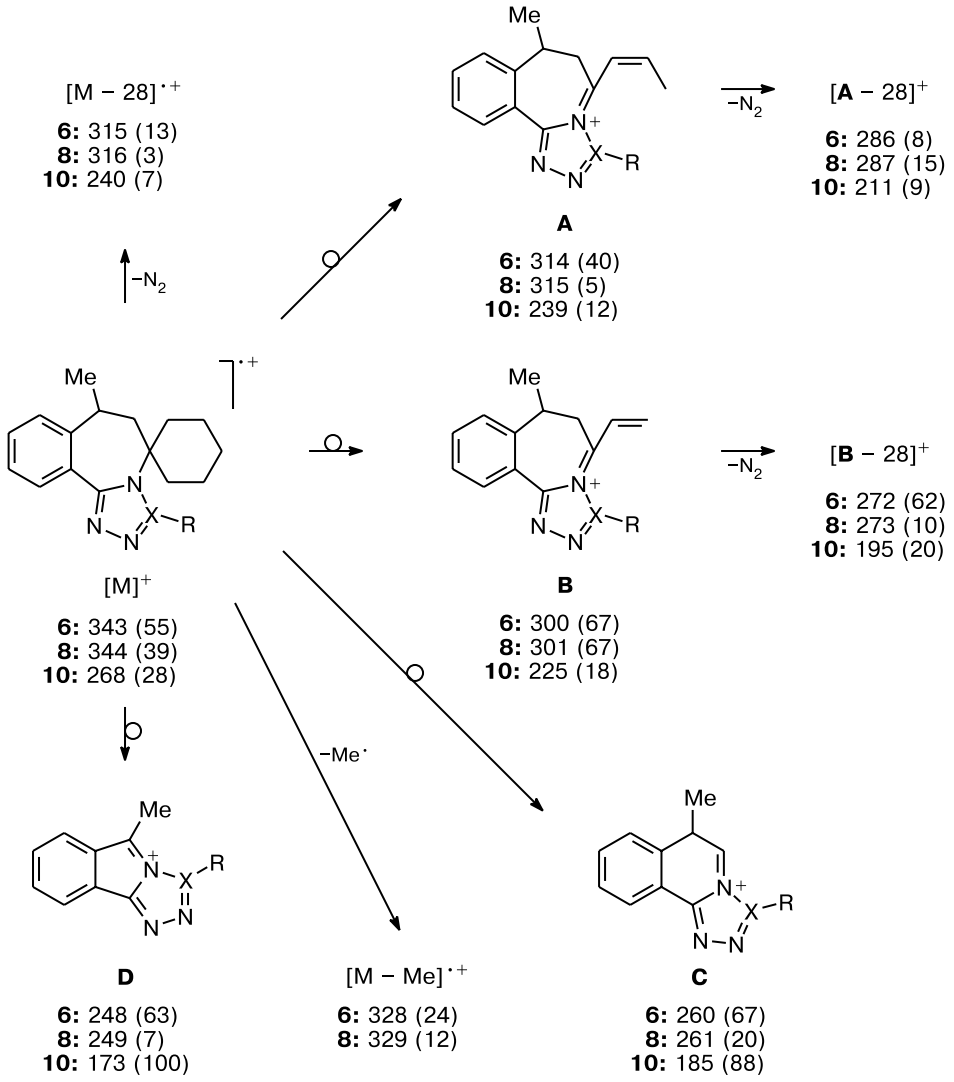
Scheme 3



Compounds **6**, **8**, and **10** were characterized by EI mass spectrometry. It was found that these compounds are rather poorly resistant to EI and form a substantial amount of fragmentation ions (Scheme 4). By analogy with fragmentation of 3*H*-spiro[benzo-2-azepine-3,1′-cycloalkanes] described earlier,[7] we suggested that the fragmentation of the molecular ions of compounds **6**, **8**, and **10** is accompanied by the retro-Diels—Alder reaction resulting in cleavage of the alicyclic ring and elimination of the alkyl fragment to form stable conjugated systems with localization of a charge on the N atom (**A** and **B**). We related the formation of the $[M - 28]^{\bullet +}$, $[\mathbf{A} - 28]^{+}$, and $[\mathbf{B} - 28]^{+}$ ions to elimination of a nitrogen molecule taking into account that this process has been observed earlier for substituted tri- and tetrazoles.[8—11] We also hypothesized that decomposition of the azepine fragment of the molecule affords the ion **C**. The presence of the latter in structurally analogous compounds, *viz.*, 3*H*-spiro[benzo-2-azepine-3,1′-cycloalkanes], has been confirmed earlier by high-resolution mass spectrometry (unpublished data). By analogy with 3*H*-spiro[benzo-2-azepine-3,1′-cycloalkanes], the structure of fused isoindole was assigned to the ion **D**. For 3*H*-spiro[benzo-2-azepine-3,1′-cycloalkanes], it was established that an analogous ion is derived directly from the molecular ion (data were obtained with the use of metastable ions). The high-resolution mass spectra confirmed the assumed structure. Another fragmentation path of the molecular ion involves elimination of the methyl fragment from the benzylic position of the azepine ring ($[M - 15]^{\bullet +}$).

The IR spectra of lactams **2**, **4**, and **9** show a stretching band of the cyclic C=O group in the region of 1641—1654 cm^{-1}; the stretching band of the exocyclic C=O group in compounds **4** and **9** is observed at 1754 cm^{-1}. In the IR spectrum of compound **3**, the bands at 1221 and 1241 cm^{-1} are assigned to C=S stretching

Scheme 4



X = C, R = Ph (**6**); X = C, R = 4-pyridyl (**8**); X = N (**10**)

vibrations. In the spectrum of compound **5**, the band at 1641 cm^{-1} is assigned to C=N stretching vibrations.

The ^1H NMR spectra of compounds **2**, **3**, **5**, and **10** (Table 1) have signals for all groups of protons present in the molecules with the chemical shifts and coupling constants corresponding to their positions in the molecules. The protons of the CH_2 groups of the azepine fragment appear as two doublets of doublets at δ 1.65—2.15 and 2.05—2.53 for the pseudoaxial and pseudoequatorial protons, respectively. The large coupling constant between the proton of C<u>H</u>—Me and one of the CH_2 protons (J = 9.8—11.9 Hz) is unambiguously indicative of the pseudoaxial orientation of the former proton. Hence, the methyl group in the azepine ring is in a pseudoequatorial orientation in all the compounds under consideration. This fact is consistent with the X-ray diffraction data for the nitro derivative of spirobenzoazepinecyclohexane.[7] Annelation of the azole ring in compounds **6**, **8**, and **10** is responsible for a downfield shift of the aromatic proton H(11) due to the influence of the lone electron pair of the N atom in the *peri* position.

Experimental

The IR spectra were recorded on a Specord UR-75 spectrometer in KBr pellets. The mass spectra were obtained on a Finnigan MAT Incos 50 instrument with direct inlet of the sample into the ion source; the ionizing energy was 70 eV. The ^1H NMR spectra were recorded on a Bruker WP-200 instrument (200 MHz) in $CDCl_3$ with Me_4Si as the internal standard. The TLC analysis was performed on Silufol UV 254 plates (visualization with iodine vapor). Column chromatography was car-

Table 1. ^{1}H NMR spectra of spiro[benzo-2-azepinecyclohexanes] **2—10**

Compound	δ (*J*/Hz)						
	benzo-2-azepine fragment					H of cyclohexane (m)	other protons
	H(4a) (H(6a))	H(4e) (H(6e))	H(5) (H(7))	5-Me (7-Me)	H arom. (m)		
2	1.65 (dd, *J* = 11.6, *J* = 13.7)	2.05 (dd, *J* = 5.8, *J* = 13.7)	3.32 (qdd, *J* = 7.0, *J* = 5.8, *J* = 11.6)	1.36 (d, *J* = 7.0)	7.24—7.67	0.80—1.65	5.95 (br.s, NH)
3	1.73 (dd, *J* = 11.9, *J* = 13.7)	2.12 (dd, *J* = 5.8, *J* = 13.7)	2.97 (qdd, *J* = 6.7, *J* = 5.8, *J* = 11.9)	1.37 (d, *J* = 6.7)	7.18—7.88	0.70—1.80	8.23 (br.s, NH)
4	1.64 (m)	2.22 (m)	3.81 (m)	1.38 (d, *J* = 6.8)	7.20—7.70	0.85—1.95	—
5	1.74 (dd, *J* = 11.9, *J* = 13.7)	2.15 (dd, *J* = 5.5, *J* = 13.7)	2.93 (qdd, *J* = 6.7, *J* = 5.5, *J* = 11.9)	1.27 (d, *J* = 6.7)	7.15—7.40	0.65—2.00	2.45 (s, MeS)
6	2.12 (dd, *J* = 11.3, *J* = 14.0)	2.28 (dd, *J* = 5.5, *J* = 14.0)	3.11 (qdd, *J* = 7.0, *J* = 5.5, *J* = 11.3)	1.40 (d, *J* = 7.0)	7.25—7.60; 7.95 (1 H)	0.80—1.80	—
7	1.80 (dd, *J* = 11.9, *J* = 13.7)	2.19 (dd, *J* = 5.5, *J* = 13.7)	3.10 (qdd, *J* = 6.7, *J* = 5.5, *J* = 11.9)	1.39 (d, *J* = 6.7)	7.35—7.65	1.10—1.80	7.96 (BB´, 3-pyridyl); 8.66 (AA´, 2-pyridyl)
8	2.15 (dd, *J* = 11.3, *J* = 14.2)	2.35 (dd, *J* = 5.4, *J* = 14.2)	3.10 (qdd, *J* = 7.0, *J* = 5.4, *J* = 11.3)	1.42 (d, *J* = 7.0)	7.25—7.60; 8.10 (1 H)	0.50—1.80	7.90 (BB´, 3-pyridyl); 8.63 (AA´, 2-pyridyl)
9	1.86 (dd, *J* = 11.6, *J* = 13.7)	2.15 (dd, *J* = 5.5, *J* = 13.7)	3.38 (qdd, *J* = 6.7, *J* = 5.5, *J* = 11.6)	1.39 (d, *J* = 6.7)	7.23—7.64	1.00—1.80	3.96 (s, MeO)
10	1.98 (dd, *J* = 9.8, *J* = 14.7)	2.53 (dd, *J* = 3.1, *J* = 14.7)	2.96 (qdd, *J* = 7.0; *J* = 3.1; *J* = 9.8)	1.44 (d, *J* = 7.0)	7.30—7.55; 8.12 (1 H)	1.80—2.20; 2.63	2.28 (s, MeCO)

ried out using Woelm 32/63 silica gel and aluminum oxide (Brockmann activity I). The melting points were determined in glass capillaries and are uncorrected.

5-Methyl-1-oxo-1,2,4,5-tetrahydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane] (2). Nitrone **1** (3.00 g, 12.3 mmol) was refluxed in Ac_2O (20 mL) for 1 h. After completion of the reaction, volatile products were distilled off *in vacuo* and the residue was alkalified with aqueous ammonia to pH 9—9.5. The precipitate that formed was filtered off, washed with water, dried, and recrystallized from a 1 : 10 AcOEt—hexane mixture. Compound **2** was obtained in a yield of 2.45 g (82%) as white crystals, m.p. 150—152 °C, R_f 0.26 (AcOEt—hexane, 1 : 1). Found (%): C, 79.25; H, 9.00; N, 5.46. $C_{16}H_{21}NO$. Calculated (%): C, 79.01; H, 8.64; N, 5.76. IR, ν/cm^{-1}: 3270, 3185 (NH); 1641 (C=O), 1394 (NH). MS, *m/z* (I_{rel} (%)): 243 $[M]^+$ (61), 228 (18), 226 (1), 214 (7), 201 (12), 200 (100), 187 (10), 186 (8), 172 (22), 160 (8), 159 (17), 158 (9), 147 (74), 145 (13), 132 (10), 131 (57), 128 (13), 117 (15), 116 (8), 115 (20), 103 (44), 98 (27), 91 (20), 77 (43), 65 (10), 54 (19), 41 (53), 39 (30).

5-Methyl-1-thioxo-1,2,4,5-tetrahydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane] (3). A solution of lactam **2** (2 g, 8.2 mmol) and P_2S_5 (0.37 g, 1.64 mmol) was refluxed in anhydrous *o*-xylene (20 mL) for 1.5 h (TLC control). The solution was decanted and the resinous residue was treated with refluxing *o*-xylene (20 mL). The solutions were combined, and the solvent was removed *in vacuo*. The residue was crystallized from a 1 : 10 AcOEt—hexane mixture. Compound **3** was obtained in a yield of 1.67 g (79%) as pale-yellow crystals, m.p. 165—168.5 °C, R_f 0.68 (AcOEt—hexane, 1 : 1). Found (%): C, 74.00; H, 7.88; N, 5.53. $C_{16}H_{21}NS$. Calculated (%): C, 74.13; H, 8.11; N, 5.41. IR, ν/cm^{-1}: 3174 (NH); 1221, 1241 (C=S). MS, *m/z* (I_{rel} (%)): 259 $[M]^+$ (100), 258 (13), 244 (4), 230 (13), 227 (12), 226 (70), 217 (29), 216 (30), 202 (6), 188 (6), 184 (5), 176 (27), 174 (12), 170 (12), 164 (28), 163 (85), 162 (38), 161 (12), 149 (18), 148 (20), 147 (42), 145 (27), 132 (10), 131 (26), 130 (57), 117 (9), 116 (14), 115 (30), 103 (23), 98 (75), 95 (9), 91 (15), 81 (12), 77 (28), 67 (14), 55 (21), 44 (35), 41 (42).

2-Acetoxy-5-methyl-1-oxo-1,2,4,5-tetrahydro-3*H*-spiro[benzo-2-azepine-3,1´-cyclohexane] (4). A mixture of nitrone **1** (0.17 g, 0.7 mmol) and $Pb(OAc)_4$ (0.31 g, 0.7 mmol) in anhydrous benzene (20 mL) was stirred at 20 °C for 4 h (TLC control). The residue was filtered off and washed with anhydrous benzene. The solvent was distilled off and the residue was purified by column chromatography on Al_2O_3 (hexane—AcOEt, 1 : 1, as the eluent). Compound **4** was obtained in a yield of 0.19 g (90%) as white crystals, m.p. 88—90 °C (hexane), R_f 0.57

(AcOEt—hexane, 1 : 1). Found (%): C, 71.88; H, 7.53; N, 4.49. $C_{18}H_{23}NO_3$. Calculated (%): C, 71.76; H, 7.64; N, 4.65. IR, ν/cm^{-1}: 1754 (AcO), 1654 (N—C=O). MS, *m/z* (I_{rel} (%)): 301 $[M]^+$ (2), 260 (18), 259 (100), 243 (15), 242 (79), 241 (18), 228 (17), 227 (80), 226 (11), 216 (38), 200 (8), 186 (5), 176 (15), 171 (9), 160 (20), 148 (26), 147 (86), 146 (90), 145 (46), 144 (15), 133 (28), 132 (29), 131 (50), 130 (11), 129 (15), 128 (19), 117 (24), 116 (11), 115 (28), 114 (13), 105 (16), 104 (45), 103 (43), 98 (7), 91 (27), 81 (35), 77 (38), 67 (13), 55 (26), 43 [MeCO] (95), 42 [CH_2=C=O] (15), 41 (41).

5-Methyl-1-methylthio-4,5-dihydro-3*H*-spiro[benzo-2-azepine-3,1′-cyclohexane] (5). A solution of thiolactam **3** (0.5 g, 1.9 mmol) and KOH (0.21 g, 3.8 mmol) in anhydrous DMSO (15 mL) was stirred at 20 °C for 2 h. Then MeI (0.24 mL, 3.8 mmol) was added, the mixture was stirred at 20 °C for 4 h (TLC control), and DMSO was distilled off *in vacuo*. Water (50 mL) was added to the residue and the mixture was extracted with $CHCl_3$ (3×30 mL). The extract was dried with $MgSO_4$, $CHCl_3$ was distilled off, and the residue was chromatographed on a column with silica gel (AcOEt—hexane, 1 : 10, as the eluent). Compound **5** was isolated in a yield of 0.32 g (62%) as a pale-yellow oil, which crystallized on storage to give pale-yellow crystals, m.p. 50—52 °C, R_f 0.68 (AcOEt—hexane, 1 : 3). Found (%): C, 74.89; H, 8.32; N, 4.97. $C_{17}H_{23}NS$. Calculated (%): C, 74.73; H, 8.42; N, 5.13. IR, ν/cm^{-1}: 1621 (C=N). MS, *m/z* (I_{rel} (%)): 273 $[M]^+$ (21), 272 (13), 258 (12), 244 (4), 231 (8), 230 (7), 227 (17), 226 (100), 216 (6), 199 (5), 182 (5), 177 (8), 176 (5), 168 (6), 161 (6), 154 (4), 146 (8), 144 (24), 131 (18), 130 (87), 129 (24), 128 (24), 117 (7), 116 (20), 115 (21), 103 (25), 95 (7), 91 (9), 77 (20), 67 (15), 55 (26), 41 (43).

7-Methyl-3-phenyl-4,6,7,11b-tetrahydro-5*H*-spiro{1,2,4-triazolo[3,4-*a*]benzo-2-azepine-5,1′-cyclohexane} (6). A solution of thioimidate **5** (0.3 g, 1.1 mmol) and benzoylhydrazine (0.17 g, 1.3 mmol) in BuOH (10 mL) was refluxed for 31 h (TLC control). Then BuOH was distilled off and the residue was purified on a column with Al_2O_3 (AcOEt as the eluent). Compound **6** was obtained in a yield of 0.13 g (34%) as white crystals, m.p. 176—178 °C (AcOEt—hexane, 1 : 3), R_f 0.26 (AcOEt). Found (%): C, 80.65; H, 6.95; N, 12.02. $C_{23}H_{25}N_3$. Calculated (%): C, 80.47; H, 7.29; N, 12.24. MS, *m/z* (I_{rel} (%)): 343 $[M]^+$ (55), 342 (12), 328 (24), 315 (13), 314 (40), 302 (23), 301 (100), 300 (67), 286 (8), 273 (25), 272 (62), 262 (10), 261 (14), 260 (67), 250 (15), 249 (70), 248 (63), 247 (22), 246 (51), 235 (9), 234 (10), 232 (6), 226 (4), 211 (3), 197 (4), 184 (8), 165 (3), 155 (7), 144 (11), 143 (12), 142 (9), 141 (9), 131 (23), 130 (21), 129 (26), 128 (28), 117 (10), 116 (24), 115 (61), 104 (27), 103 (23), 91 (10), 81 (8), 77 (21), 55 (10), 41 (21), 39 (12).

1-(*N*′-Isonicotinoylhydrazino)-5-methyl-4,5-dihydro-3*H*-spiro[benzo-2-azepine-3,1′-cyclohexane] (7). Compound **7** was prepared according to the above-described procedure from thioimidate **5** (0.3 g, 1.1 mmol) and isonicotinohydrazide (0.3 g, 2.2 mmol) in BuOH (10 mL) in a yield of 0.1 g (26%) as pale-yellow crystals, m.p. 225—227 °C (AcOEt—hexane, 10 : 1), R_f 0.47 (AcOEt—EtOH, 1 : 1). Found (%): C, 72.78; H, 7.21; N, 15.29. $C_{22}H_{26}N_4O$. Calculated (%): C, 72.93; H, 7.18; N, 15.47. IR, ν/cm^{-1}: 3280 (NH), 3400 (OH), 1480 (C=N). MS, *m/z* (I_{rel} (%)): 362 $[M]^+$ (95), 319 (18), 266 (8), 241 (70), 226 (48), 199 (13), 144 (30), 137 (10), 130 (100), 115 (23), 106 (60), 98 (40), 78 (50), 51 (23), 41 (25).

7-Methyl-3-(4-pyridyl)-4,6,7,11b-tetrahydro-5*H*-spiro{1,2,4-triazolo[3,4-*a*]benzo-2-azepine-5,1′-cyclohexane} (8). A solution of compound **7** (0.3 g, 0.8 mmol) in polyphosphoric acid (3 mL) was heated at 150 °C for 2 h (TLC control), cooled, alkalified with aqueous ammonia, and extracted with $CHCl_3$ (3×50 mL). The extract was dried with $MgSO_4$, $CHCl_3$ was distilled off, and the residue was purified on a column with silica gel. Compound **8** was obtained in a yield of 50 mg (17%) as pale-yellow crystals, m.p. 180—181 °C (AcOEt—hexane, 1 : 3), R_f 0.43 (AcOEt). Found (%): C, 76.62; H, 6.73; N, 16.14. $C_{22}H_{24}N_4$. Calculated (%): C, 76.74; H, 6.98; N, 16.28. MS, *m/z* (I_{rel} (%)): 344 $[M]^+$ (49), 343 (10), 329 (12), 316 (3), 315 (5), 301 (67), 287 (15), 273 (10), 261 (20), 249 (7), 247 (20), 233 (4), 224 (10), 196 (12), 185 (15), 165 (13), 144 (12), 143 (17), 142 (12), 141 (10), 130 (13), 129 (13), 128 (20), 116 (13), 115 (21), 111 (29), 105 (17), 97 (46), 84 (27), 83 (50), 81 (29), 71 (61), 69 (56), 57 (100), 55 (68), 43 (70), 41 (46), 39 (10).

2-Methoxycarbonyl-5-methyl-1-oxo-1,2,4,5-tetrahydro-3*H*-spiro[benzo-2-azepine-3,1′-cyclohexane] (9). A solution of lactam **2** (0.5 g, 2 mmol) and methyl chloroformate (0.25 mL, 3 mmol) in anhydrous benzene (15 mL) was refluxed for 15 h (TLC control), the solvent was distilled off, and the residue was crystallized from hexane. Compound **9** was obtained in a yield of 0.44 g (73%) as white crystals, m.p. 99—101.5 °C, R_f 0.68 (AcOEt—hexane, 1 : 3). Found (%): C, 71.64; H, 7.67; N, 4.58. $C_{18}H_{23}NO_3$. Calculated (%): C, 71.76; H, 7.64; N, 4.65. IR, ν/cm^{-1}: 1750 (MeOC=O), 1641 (C=O). MS, *m/z* (I_{rel} (%)): 301 $[M]^+$ (4), 259 (12), 226 (8), 205 (11), 196 (11), 172 (10), 156 (100), 155 (22), 146 (17), 145 (26), 144 (11), 140 (37), 132 (37), 131 (88), 130 (17), 129 (21), 128 (22), 127 (24), 118 (12), 117 (38), 116 (17), 115 (48), 105 (17), 104 (31), 103 (74), 102 (14), 97 (12), 91 (39), 82 (11), 81 (28), 79 (18), 78 (28), 77 (64), 76 (31), 69 (11), 68 (56), 67 (16), 65 (12), 59 (71), 55 (51), 54 (14), 53 (18), 51 (15), 44 (17), 43 (14), 42 (24), 41 (63), 40 (15), 39 (32).

7-Methyl-4,6,7,11b-tetrahydro-5*H*-spiro{tetrazolo[5,1-*a*]benzo-2-azepine-5,1′-cyclohexane} (10). A solution of lactam **2** (0.3 g, 1.2 mmol) in $SOCl_2$ (0.23 mL, 3.6 mmol) was heated at 40—50 °C until the solid residue completely dissolved, $SOCl_2$ was distilled off, and the residue was dissolved in $CHCl_3$ (10 mL). The solution was slowly added dropwise to a solution of NaN_3 (0.16 g, 2.4 mmol) and Bu_4NI (0.04 g, 0.12 mmol) in water (10 mL). The mixture was stirred for 4 h (TLC control). The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$ (3×30 mL). The combined extracts were dried with $MgSO_4$, $CHCl_3$ was distilled off, and the residue was purified on a column with Al_2O_3 (AcOEt—hexane, 1 : 5, as the eluent). Compound **10** was obtained in a yield of 0.17 g (53%) as white crystals, m.p. 65—66 °C, R_f 0.64 (AcOEt—hexane, 1 : 1). Found (%): C, 71.80; H, 7.22; N, 20.53. $C_{16}H_{20}N_4$. Calculated (%): C, 71.64; H, 7.46; N, 20.90. MS, *m/z* (I_{rel} (%)): 268 $[M]^+$ (28), 240 (7), 239 (12), 226 (35), 225 (18), 198 (10), 197 (20), 187 (12), 185 (88), 173 (100), 172 (15), 155 (17), 146 (23), 145 (19), 144 (22), 143 (19), 142 (15), 141 (27), 131 (29), 130 (40), 129 (41), 128 (64), 117 (30), 116 (34), 115 (87), 111 (32), 110 (90), 103 (23), 95 (43), 94 (22), 91 (27), 77 (42), 67 (23), 56 (46), 55 (43), 43 (26), 41 (84), 39 (55).

References

1. V. Kouznetsov, A. Palma, and C. Ewert, *Curr. Org. Chem.*, 2001, **5**, 519.

2. V. V. Kuznetsov, S. V. Lantsetov, A. E. Aliev, A. V. Varlamov, and N. S. Prostakov, *Zh. Org. Khim.*, 1992, **28**, 74 [*Russ. J. Org. Chem.*, 1992, **28**, 61 (Engl. Transl.)].
3. V. V. Kouznetsov, A. R. Palma, S. Salas, L. Y. Vargas, F. I. Zubkov, A. V. Varlamov, and J. R. Martinez, *J. Heterocycl. Chem.*, 1997, **34**, 1591.
4. V. V. Kuznetsov, S. V. Lantsetov, A. E. Aliev, A. V. Varlamov, and N. S. Prostakov, *Khim. Geterotsikl. Soedin.*, 1991, 1528 [*Chem. Heterocycl. Compd.*, 1991, **27**, 1233 (Engl. Transl.)].
5. M. Lamchen, *Mechanisms of Molecular Migration*, Ed. B. S. Thyagarajan, Interscience, New York, 1968, **1**.
6. R. Madronero and S. Vega, *J. Heterocycl. Chem.*, 1978, **15**, 1127.
7. A. I. Mikaya, S. V. Lancetov, V. V. Kuznetsov, A. V. Varlamov, and N. S. Prostakov, *Org. Mass Spectrom.*, 1991, **26**, 763.
8. R. Lawrence and E. S. Waight, *Org. Mass Spectrom.*, 1970, **3**, 367.
9. K. T. Potts and E. Brugel, *Org. Mass Spectrom.*, 1971, **5**, 663.
10. D. M. Forkey and W. R. Carpenter, *Org. Mass Spectrom.*, 1969, **2**, 433.
11. K. T. Potts, T. Kevin, E. G. Brugel, and U. P. Singh, *Org. Mass Spectrom.*, 1971, **5**, 1.

Received December 2, 2003;
in revised form February 27, 2004