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Heteroadamantanes and Their Derivatives: XXV.* Synthesis of 3,6-Diazahomoadamantane-9-spirothiiranes

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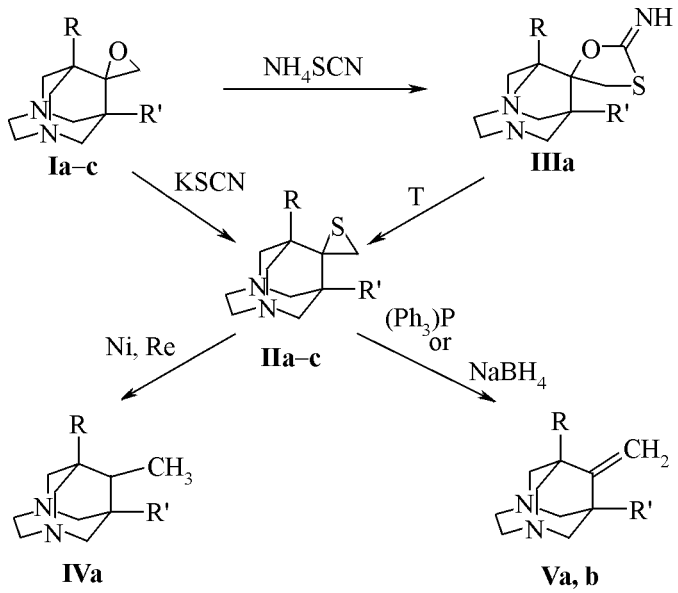
Abstract—By treating 3,6-diazahomoadamantane-9-spirooxiranes with potassium thiocyanate 3,6-diazahomoadamantane-9-spirothiiranes were obtained which further by reductive desulfuration were converted into 3-methyl- and 9-methylene-3,6-diazahomoadamantanes.

We formerly carried out a reaction of 3,6-diazahomoadamantan-9-ones [2, 3] with trimethylsulfoxonium iodide and solid alkali in *tert*-butanol to obtain 3,6-diazahomoadamantane-9-spirooxiranes (**I**). Here we report on synthesis from oxiranes **I** of 3,6-diazahomoadamantane-9-spirothiiranes (**II**).



R = H, R' = C_6H_5 (**a**); R = H, R' = CH_3 (**b**); R = R' = CH_3 (**c**).

To convert 3,6-diazahomoadamantane-9-spirooxiranes (**I**) into the respective spirothiiranes **II** we reacted the oxiranes **I** with potassium thiocyanate [5–8]. This reaction is known to proceed via formation of iminooxathiolanes [9]. This assumption was confirmed by reaction of oxirane **Ia** with ammonium thiocyanate in acetic acid at 50–60°C that afforded 3,6-diazahomoadamantane-9-spiro-5'-(2'-imino-1',3'-oxathiolane) (**IIIa**) which on heating was converted into thiirane **IIa**.

The desulfuration of spirothiirane **IIa** on Raney nickel in 2-propanol resulted in formation of 1-phenyl-3,6-diazahomoadamantane (**IVa**) with a methyl group attached to the bridging (C^9) carbon atom. By reaction of 1-phenyl-3,6-diazahomoadamantane-9-spirothiirane (**IIa**) with sodium borohydride we were first to synthesize 3,6-diazahomoadamantane **Va** with a

* For communication XXIV see [1].

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methylene group attached to the bridging (C^9) carbon. Compounds **Va, b** were also obtained by reductive desulfuration of 3,6-diazahomoadamantane-9-spirothiiranes (**IIa, b**) with triphenylphosphine.

The structure of compounds **II–V** was confirmed by IR, mass spectra. and also by ^{1}H NMR spectra.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer Bruker IFSv from samples pelletized with KBr. ^{1}H NMR spectra of compounds synthesized were registered on spectrometer WM Bruker at operating frequency 250.13 MHz from solutions in $CDCl_3$, internal reference TMS. Mass spectra were measured on Finnigan MAT 90 instrument with direct sample admission into the ion source, accelerating voltage 5 kV, emission current 100 μA, ionizing electrons energy 70eV, ionizing chamber temperature 200°C. Perfluorokerosene was used as standard. Resolution M/ΔM attained 10000.

1-Phenyl-3,6-diazahomoadamantane-9-spirothiirane (IIa). (a) To a solution of 0.20 g (0.78 mmol) of 1-phenyl-3,6-diazahomoadamantane-9-spirooxirane (**Ia**) in 10 ml of 2-propanol was added a solution of 0.68 g (7.00 mmol) of potassium thiocyanate in 4 ml of water. The mixture was boiled for 20 h, the solvent was removed in a vacuum. The dry residue was treated with hot heptane (5 × 15 ml), and heptane was distilled off. The residue was recrystallized from heptane. We obtained 0.19 g (91%) of compound **IIa**, mp 137–138°C. IR spectrum, ν, cm^{-1}: 3051, 1251 (C–S); 1595, 1498 (arom). ^{1}H NMR spectrum, δ, ppm: 3.17 m (4H, NCH_2CH_2N); 3.88 d, 3.87 d, 3.61 d, 3.46 d, 3.10–2.90 m (8H, $4NCH_2C$, ^2J 14.0 Hz); 7.10–7.50 m (5H, arom); 2.24 br.s, 2.13 br.s (2H, CH_2). Mass spectrum, *m/z* (I_{rel}, %): 272 $[M]^+$ (100), 240 (43), 239 (93), 197 (80), 196 (35), 184 (31), 182 (54), 58 (34), 57 (47), 43 (33), 42 (35).

(b) A solution of 0.2 g (0.67 mmol) of 1-phenyl-3,6-diazahomoadamantane-9-spiro-5'-(2'-imino-1',3'-oxathiolane) (**IIIa**) was heated in 2-propanol for 1 h, the solvent was removed in a vacuum, the solid residue was treated with hot heptane. On recrystallization from heptane 0.14 g (82%) of compound **IIa** was obtained.

1-Methyl-3,6-diazahomoadamantane-9-spirothiirane (IIb) was prepared in the same way as compound **IIa** from 1.0 g (5 mmol) of 1-methyl-3,6-diazahomoadamantane-9-spirooxirane (**Ib**) and 4.5 g of potassium thiocyanate in 15 ml of water. Yield of compound **IIb** 0.83 g (77%), mp 62–61°C. IR spectrum, ν, cm^{-1}: 3047, 1250 (C–S). ^{1}H NMR spectrum, δ, ppm: 3.18 m (4H, NCH_2CH_2N); 3.33 d, 3.18 d, 2.98 d, 2.74 d, 3.12–2.28 m (8H, $4NCH_2C$, ^2J 14.0 Hz); 1.35 br.s (1H, CH); 0.79 s (3H, CH_3); 2.12 br.s, 2.24 br.s (2H, CH_2). Mass spectrum, *m/z* (I_{rel}, %): 210 $[M]^+$ (100), 178 (45), 177 (86), 161 (21), 146 (16), 115 (14), 103 (27), 58 (64), 57 (32), 43 (68), 41 (29).

1,8-Dimethyl-3,6-diazahomoadamantane-9-spirothiirane (IIc) was prepared in the same way as compound **IIa** from 0.20 g (0.96 mmol) of 1,8-dimethyl-3,6-diazahomoadamantane-9-spirooxirane (**Ic**) and 0.93 g of potassium thiocyanate in 10 ml of water. Yield of compound **IIc** 0.17 g (77%), mp 108–109°C. ^{1}H NMR spectrum, δ, ppm: 3.15 m (4H, NCH_2CH_2N); 3.08 d, 2.93 d, 2.88 d, 2.65 d (8H, $4NCH_2C$, ^2J 14.0 Hz); 2.39 s (2H, CH_2); 0.58 s (6H, $2CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 224 $[M]^+$ (100), 240 (43), 239 (93), 149 (94), 135 (28), 134 (56), 121 (24), 120 (21), 72 (45), 58 (41), 42 (18).

1-Phenyl-3,6-diazahomoadamantane-9-spiro-5'-(2'-imino-1',3'-oxathiolane) (IIIa). To a solution of 1.45 g (19 mmol) of ammonium thiocyanate in 25 ml of acetic acid at 50–60°C while stirring was added by small portions 1.00 g (3.90 mmol) of 1-phenyl-3,6-diazahomoadamantane-9-spirooxirane (**Ia**). The mixture was kept for 1.5 h, and then a saturated solution of potassium carbonate was added to pH 9. The reaction product was extracted into ether (6 × 5 ml). The extracts were dried with potassium hydroxide, ether was distilled off. We obtained 0.62 g (50%) of compound **IIIa**, mp 164–165°C. IR spectrum, ν, cm^{-1}: 3284 (NH); 1645 (C=N); 1496 (arom). Mass spectrum, *m/z* (I_{rel}, %): 315 $[M]^+$ (11), 272 (95), 240 (51), 239 (100), 197 (89), 196 (44), 182 (66), 72 (41), 58 (45), 43 (40), 42 (47).

9-Methyl-1-phenyl-3,6-diazahomoadamantane (IVa). To a solution of 0.27 g (1.00 mmol) of 1-phenyl-3,6-diazahomoadamantane-9-spirothiirane (**IIa**) in 15 ml of 2-propanol was added 2 g of freshly prepared Raney nickel, and the mixture was heated at reflux for 24 h with adding every 5 h (thrice) 2 g of fresh Raney nickel. The nickel was filtered off, washed with 2-propanol, the filtrate was evaporated in a vacuum. After recrystallization from heptane we obtained 0.17 g (71%) of compound **IVa**, mp 186–187°C. IR spectrum, ν, cm^{-1}: 1460 (arom). ^{1}H NMR spectrum, δ, ppm: 2.90 m (4H, NCH_2CH_2N); 3.88–2.22 m (8H, $4NCH_2C$); 6.95–7.27 m (5H, arom); 2.15 br.s (1H, $CHCH_3$); 0.75 d (3H, CH_3, ^3J 7.0 Hz). Mass spectrum, *m/z* (I_{rel}, %): 242 $[M]^+$ (57), 227 (38),

151 (41), 149 (63), 93 (25), 72 (86), 58 (100), 56 (76), 55 (87), 42 (43), 41 (22).

9-Methylene-1-phenyl-3,6-diazahomoadamantane (Va). (a) To a solution of 0.2 g (0.73 mmol) of 1-phenyl-3,6-diazahomoadamantane-9-spirothiirane (**IIa**) in 10 ml of 2-propanol was added 0.02 g of sodium borohydride, and the reaction mixture was heated at reflux for 10 h. The reaction mixture was evaporated in a vacuum, the solid residue was treated with minimum amount of water, water was distilled off, and the reaction product was extracted with hot heptane. We obtained 0.14 g (79%) of compound **Va**, mp 109–110°C. IR spectrum, ν, cm^{-1}: 1635 (C=C), 1500 (arom). ^{1}H NMR spectrum, δ, ppm: 3.19 m (4H, NCH_2CH_2N); 3.62 d, 3.40 d, 3.05 d, 2.98 d (8H, $4NCH_2C$, ^2J 14.0 Hz); 7.12–7.50 m (5H, arom); 4.83 d, 4.24 d (2H, CH_2, ^2J 1.5 Hz); 2.53 br.s (1H, CH). Mass spectrum, *m/z* (I_{rel}, %): 240 $[M]^+$ (60), 239 (39), 198 (14), 197 (100), 196 (20), 182 (11), 168 (9), 167 (11), 155 (8), 72 (9), 58 (15).

(b) A solution of 0.20 g (0.73 mmol) of 1-phenyl-3,6-diazahomoadamantane-9-spirothiirane (**IIa**) and 0.19 g (0.73 mmol) of triphenylphosphine in 19 ml of anhydrous ether was heated at weak boiling till precipitated colorless crystals. The crystals were separated. We obtained 0.16 g (76%) of $(C_6H_5)_3PS$, mp 151–152°C. The mother liquor was evaporated, the residue was subjected to TLC on glass plates (90 × 120) with unfixed layer of alumina, eluent chloroform. We obtained 0.12 g (67%) of compound **Va**.

9-Methylene-1-methyl-3,6-diazahomoadamantane (Vb) was obtained similarly to compound **Va** from 0.16 g (0.76 mmol) of 1-methyl-3,6-diazahomoadamantane-9-spirothiirane (**IIb**) and 0.02 g of sodium borohydride in 10 ml of 2-propanol within 10 h. Yield of compound **Vb** 0.12 g (75%), mp 94–95°C. IR spectrum, ν, cm^{-1}: 1641 (C=C). ^{1}H NMR spectrum, δ, ppm: 3.13 m (4H, NH_2CH_2N); 3.51 d, 3.38 d, 2.87 d, 2.72 d (8H, $4NCH_2C$, ^2J 14.0 Hz); 2.51 br.s (1H, CH); 4.76 d, 4.24 d (2H, CH_2, ^3J 1.5 Hz); 0.86 s (3H, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 178 $[M]^+$ (52), 162 (43), 153 (23), 152 (67), 121 (78), 72 (100), 71 (39), 57 (31), 56 (23), 42 (37), 41 (57).

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