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HETEROADAMANTANES AND THEIR DERIVATIVES. 23.* REDUCTION OF NITROARYL DERIVATIVES OF 3,6-DIAZAHOMOADAMANTANE

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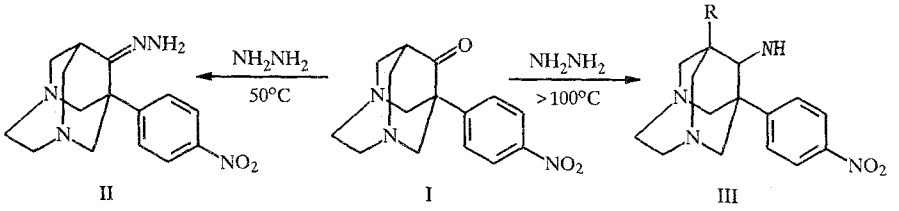
It has been found that nitroaryl derivatives of diazahomoadamantane can be reduced selectively by hydrazine. New data are presented on the noncatalytic reduction of p-nitrophenyldiazahomoadamantane by hydrazine hydrate.

The work reported here is a continuation of studies of the reduction of nitrophenyl derivatives of diazahomoadamantane. It had been shown previously that when derivatives of p-nitrophenyldiazahomoadamantane are heated for a prolonged time with excess hydrazine hydrate without catalyst, the nitro group is reduced to an amino group [2]. It is known that aromatic nitro compounds can be reduced to the corresponding amines by various reagents, including hydrazine in the presence of catalysts [3]. Data have also been reported on the reduction of aromatic nitro compounds to the corresponding amines by hydrazine upon heating in a sealed ampul [4].

In this article we are presenting new information on the reduction of nitrophenyl derivaties of diazahomoadamantane. As the starting material we used 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (I), which was obtained by nitration of phenyldiazahomoadamantane [2].



We have investigated the reduction of p-nitrophenyldiazahomoadamantone (I) by hydrazine hydrate. We established that this reaction can be performed selectively. Thus, when the ketone I is refluxed with excess hydrazine hydrate for 4 h, the hydrazone of aminophenyldiazahomoadamantane is formed with an 83% yield [2]. If the reaction is performed at a temperature no higher than 50°C, the hydrazone of 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (II) can be obtained as the main product, with a 95% yield. The IR spectrum of II exhibits intense absorption bands of stretching vibrations of the nitro group at 1523 and 1350 cm^{-1}, and also of the C=N and NH groups at 1652 and 3340 cm^{-1}, respectively.

It should be noted that the hydrazones II and III can form the corresponding azines IV and V, but at a higher temperature (200°C) than for mono- and disubstituted diazahomoadamantanes [5]. The azine V can also be obtained with a 79% yield by reduction of the azine IV with hydrazine hydrate.

*For Communication 22 see [1].

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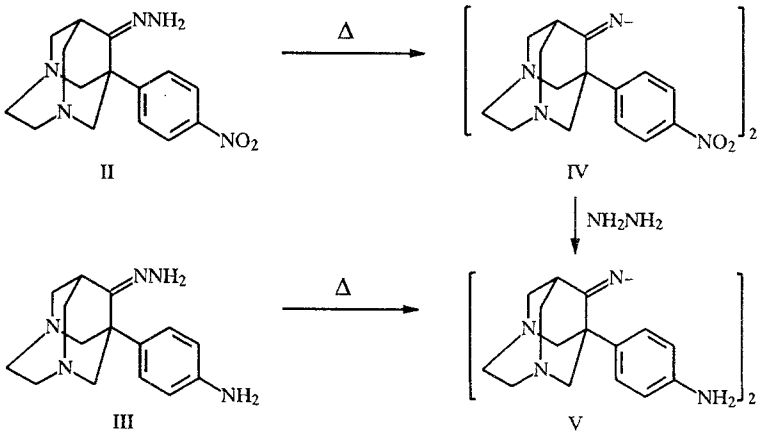
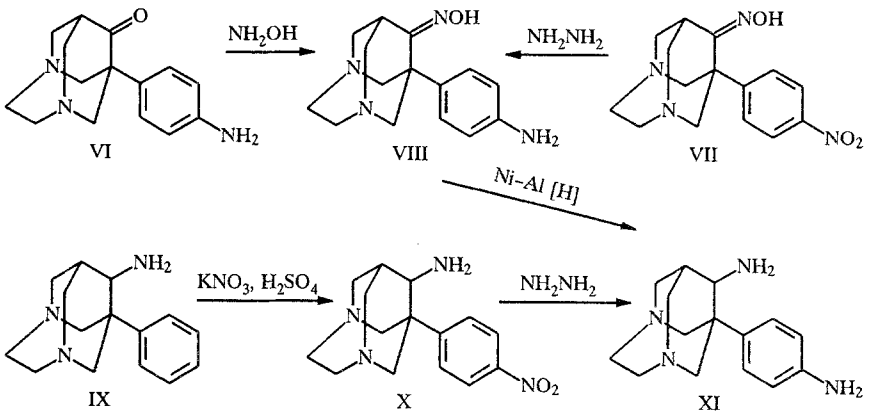


The structure of compounds IV and V was confirmed by a combination of IR and mass spectrometric data (Tables 1 and 2). In the mass spectra of compounds II, IV, and V, peaks of the respective molecular ions (M^+) are observed. Fragmentation of the M^+ of these compounds leads to the formation of the nitrogen-containing ions $[C_4H_{10}N]^+$ (m/z 72) and $[C_3H_8N]^+$ (m/z 58), which are characteristic for decomposition of the 3,6-diazahomoadamantane skeleton. Decomposition of the M^+ ion of the hydrazone II or the azines IV and V proceeds with rupture of the N–N bond, forming ions $[M - NH_2]^+$ and $[M - N - Ad]^+$, with subsequent detachment of nitrogen-containing molecules $C_nH_{2n+1}N$ (n = 1-3), with the most intense ion peaks corresponding to elimination of C_2H_5N molecules.



In [2] we reported the synthesis of the diamine (XI) with a 59% yield, based on 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (I). We developed other schemes for obtaining the diamine XI, using as the initial compounds 1-(4-aminophenyl)-3,6-diazahomoadamantan-9-one (VI) [2], the oxime of 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (VII) [2], and 9-amino-1-phenyl-3,6-diazahomoadamantane (IX) [6]. The diamine XI was obtained with a 63% yield by reduction of the oxime VIII with Ni–Al alloy (50:50); the oxime was synthesized either by the action of hydroxylamine on the ketone VI or the action of hydrazine hydrate on the oxime VII. Heating of 9-amino-1-(4-nitrophenyl)-3,6-diazahomoadamantane (X) with excess hydrazine hydrate also leads to the diamine XI (89% yield). Compound X was obtained by nitration of the amine IX. The latter scheme is the more convenient for preparative purposes. The structures of compounds VI-XI were confirmed by IR and mass spectrometric data.

EXPERIMENTAL

The IR spectra of the compounds were recorded in a Bruker IFS-113v spectrometer in KBr tablets. The mass spectra were obtained in a Finnigan MRT-90 instrument with direct introduction of the sample into the ion source, with an electron

TABLE 1. Characteristics of Synthesized Compounds

Compound	Empirical formula	mp, °C	IR spectrum, ν, cm^{-1}	Yield, % (and method)
II	$C_{15}H_{19}N_5O_2$	159...161	3340 (NH); 1652 (C=N); 1523, 1350 (NO_2)	95
IV	$C_{30}H_{134}N_8O_4$	188...190	1631 (C=N); 1525, 1346 (NO_2)	74
V	$C_{30}H_{38}N_8$	178...180	3340, 3320 (NH); 1647 (C=N)	69 (A) 79 (B)
VIII	$C_{15}H_{20}N_4O$	251...253	3220, 3338, 3368 (NH, OH); 1650 (C=N)	68 (A) 97 (B)
X	$C_{15}H_{19}N_4O_2$	55...56	3374 (NH); 1525, 1348 (NO_2)	70
XI	$C_{15}H_{32}N_4$	170...172	3425, 3338 (NH)	89 (A) 63 (B)

*Compounds II and IV were recrystallized from isopropyl alcohol, compounds V, VIII, and X from toluene.

TABLE 2. Mass Spectra of Synthesized Compounds

Compound	Values of m/z (and relative intensity, %)
II	301 (25), 285 (2), 242 (2), 115 (6), 102 (1), 83 (4), 72 (85), 58 (100), 56 (10), 44 (12), 42 (12)
IV	570 (0,6), 285 (3), 185 (1), 115 (1), 106 (2), 97 (2), 83 (10), 72 (100), 58 (36), 44 (68), 42 (17)
V	510 (1), 255 (4), 201 (6), 250 (15), 184 (20), 140 (65), 116 (75), 92 (70), 77 (69), 72 (100), 58 (86)
VIII	272 (71), 255 (60), 226 (10), 212 (25), 198 (5), 183 (9), 159 (4), 144 (5), 117 (5), 72 (80), 58 (100)
X	288 (72), 271 (10), 216 (19), 199 (13), 115 (10), 85 (19), 72 (42), 58 (75), 56 (86), 44 (100), 42 (65)
XI	258 (100), 241 (4), 229 (34), 185 (37), 171 (40), 144 (18), 132 (18), 106 (13), 85 (28), 72 (58), 58 (43)

ionizing energy 70 eV, ionization chamber temperature 200°C, and perfluorokerosine standard. The resolution $M/\Delta M$ = 10,000. The characteristics of the compounds are listed in Tables 1 and 2.

The elemental analyses matched the calculated values. Certain syntheses were described previously in [2, 6]: 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (I); hydrazone of 1-(4-aminophenyl)-3,6-diazahomoadamantan-9-one (III); 1-(4-aminophenyl)-3,6-diazahomoadamantan-9-one (VI); oxime of 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (VII); and 9-amino-1-phenyl-3,6-diazahomoadamantane.

Hydrazone of 1-(4-Nitrophenyl)-3,6-diazahomoadamantan-9-one (II). A mixture of 0.10 g (0.35 mmoles) of 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (I) and 1.5 ml of hydrazine hydrate (80%) was heated at 50-60°C for 4 h. The precipitate that formed upon cooling was filtered off and purified by recrystallization from isopropyl alcohol. Obtained 0.10 g (95.3%) of compound II.

1,2-Bis-[1-(4-nitrophenyl)-3,6-diazahomoadamantylidene-9]hydrazine (IV). Heated 0.10 g (1.32 mmoles) of the hydrazone of 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (II) at 200-220°C for 4 h. The solid residue was extracted with isopropyl alcohol. After recrystallization from isopropyl alcohol, obtained 0.07 g (73.9%) of compound IV.

1,2-Bis-[1-(4-aminophenyl)-3,6-diazahomoadamantylidene-9]hydrazine (V). *A.* By analogy with the preparation of IV, from 0.20 g (0.74 mmoles) of the hydrazone of 1-(4-aminophenyl)-3,6-diazahomoadamantan-9-one (III), upon heating, obtained 0.13 g (69.1%) of compound V.

B. By analogy with the preparation of II, from 0.10 g (0.17 mmoles) of 1,2-bis-[1-(4-nitrophenyl)-3,6-diazahomoadamantylidene-9]hydrazine (IV) and 1.5 ml of hydrazine hydrate (80%), obtained 0.07 g (78.7%) of compound V, which was completely identical to the compound obtained by method A with respect to melting point and IR and mass spectra.

Oxime of 1-(4-Aminophenyl)-3,6-diazahomoadamantan-9-one (VIII). *A.* To a solution of 0.50 g (1.94 mmoles) of 1-(4-aminophenyl)-3,6-diazahomoadamantan-9-one (VI) and 5 ml of water, at room temperature, 0.35 g (5.03 mmoles) of hydroxylamine hydrochloride and 5 ml of water were added. The mixture was heated to 60-70°C with stirring and dropwise

addition of a solution of 0.70 g (5.06 mmoles) of sodium carbonate in 8 ml of water. The reaction mixture was heated for 10 min. The precipitate obtained after cooling was filtered off and recrystallized from toluene. Obtained 0.36 g (68.0%) of compound VIII.

B. By analogy with the preparation of II, from 0.80 g (2.65 mmoles) of the oxime of 1-(4-nitrophenyl)-3,6-diazahomoadamantan-9-one (VII) and 8 ml of hydrazine hydrate (80%), obtained 0.70 g (97.1%) of compound VIII, which was completely identical to the substance obtained by method A with respect to melting point and IR and mass spectra.

9-Amino-1-(4-nitrophenyl)-3,6-diazahomoadamantane (X). To a mixture of 1.50 g (14.85 mmoles) of potassium nitrate and 20 ml of concentrated hydrochloric acid, at 0.5°C, 3.60 g (14.80 mmoles) of 9-amino-1-phenyl-3,6-diazahomoadamantane was added in portions while stirring vigorously. The reaction mixture was stirred at room temperature for 2 h. The product was then poured into water (60 ml) and neutralized with potassium carbonate (pH 8-9). The solid material was filtered off; the filtrate was evaporated down and extracted with toluene (4 × 20 ml). After recrystallization from heptane, obtained 3.00 g (70.3%) of compound X.

9-Amino-1-(4-aminophenyl)-3,6-diazahomoadamantane (XI). ***A.*** By analogy with the preparation of II, from 0.10 g (0.35 mmoles) of 9-amino-1-(4-nitrophenyl)-3,6-diazahomoadamantane (X) and 1.5 ml of hydrazine hydrate (80%), obtained 0.08 g (88.9%) of compound XI.

B. To a solution of 0.50 g (1.84 mmoles) of the oxime of 1-(4-aminophenyl)-3,6-diazahomoadamantan-9-one (VIII) in 20 ml of water, Ni–Al alloy (50:50) was added. Then, a solution of 2.0 g of sodium hydroxide in 5 ml of water was added dropwise with stirring. The mixture was stirred for 2 h and then extracted with ether (4 × 10 ml). The extract was dried over sodium hydroxide. Obtained 0.3 g (63.2%) of compound XI, completely identical with the product obtained by method A with respect to melting point and IR and mass spectra; the data also matched the results reported in [2].

REFERENCES

1. A. I. Kuznetsov, T. M. Serova, Ngu Chan, I. A. Vladimirova, and A. S. Moskovkin, Zh. Org. Khim. (1993) (in press).
2. A. I. Kuznetsov, U. Barri, G. Mazhed, and I. A. Vladimirova, Khim. Geterotsikl. Soedin., No. 9, 1262 (1992).
3. P. Sarmah and N. C. Barua, Tetrahedron Lett., **31**, 4065 (1990).
4. S. Abdel-Baky, M. Zhuang, and R. W. Giese, Synth. Commun., **21**, 161 (1991).
5. A. I. Kuznetsov, I. A. Vladimirova, T. M. Serova, and A. S. Moskovkin, Khim. Geterotsikl. Soedin., No. 5, 653 (1992).
6. A. I. Kuznetsov, I. A. Vladimirova, T. M. Serova, and A. S. Moskovkin, Khim. Geterotsikl. Soedin., No. 5, 643 (1992).