HETEROADAMANTANES AND THEIR DERIVATIVES

18.* SYNTHESIS OF DERIVATIVES OF 1-PHENYL-3,6-DIAZAHOMOADAMANTANE WITH NITRO AND AMINO GROUPS AT THE BENZENE RING AND FUNCTIONAL GROUPS AT THE BACKBONE $C_{(9)}$ ATOM

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1-p-nitrophenyl-3,6-diazahomoadamantane and 1-p-nitrophenyl-3,6-diazahomoadamantan-9-one were obtained by nitration of 1-phenyl-3,6-diazahomoadamantane and 1-phenyl-3,6-diazahomoadamantan-9-one with a mixture of potassium nitrate and sulfuric acid; 1-p-nitrophenyl-3,6-diazahomoadamantan-9-one was reduced with sodium borohydride to 1-p-nitrophenyl-3,6-diazahomoadamantan-9-ol. It was found that the nitro groups of these nitrophenyldiazahomoadamantanes were reduced to amino groups by heating with hydrazine hydrate without a catalyst. 1-p-Aminophenyl-3,6-diazahomoadamantan-9-one was obtained by reduction of nitrophenylazahomoadamantanone with tin in sulfuric acid, and 9-amino-1-p-aminophenyl-3,6-diazahomo-adamantane was obtained by reduction of its oxime with a nickel—aluminum alloy in water—base medium.

1-Phenyl-3,6-diazahomoadamantan-9-one I, synthesized by condensation of methyl benzyl ketone with tetramethylenediethylenetetramine [2], and the 1-phenyl-3,6-diazahomoadamantane II obtained from it in the Wolff—Kishner reaction are convenient intermediate products for obtaining phenyldiazahomoadamantane derivatives with functional groups at the benzene ring and backbone of the $C_{(9)}$ atom. 1-*p*-nitrophenyl-3,6-diazahomoadamantane III and 1-*p*-nitrophenyl-3,6-diazahomoadamantan-9-one IV were prepared by nitration of compounds I and II with a mixture of potassium nitrate and sulfuric acid [3]. The IR spectra of these compounds contain absorption bands from nitro group stretching vibrations in the region of 1505, 1340 and 1510, 1340 cm^{-1}, respectively. The spectrum of nitroketone IV also contains an absorption band of carbonyl group stretching vibrations in the 1698 cm^{-1} region. For the starting phenyldiazahomoadamantanone I, this band appears in the 1710 cm^{-1} region, i.e., incorporation of a nitro group in the phenyl ring significantly shifts the absorption band of the carbonyl group to the lower frequency region. The preservation of the backbone was confirmed by the PMR spectra, which have groups of characteristic signals, and the *p*-orientation of the nitro groups was confirmed by the fact that aromatic protons form characteristic AA'BB' systems in them. (See scheme at the top of the next page.)

Wanting to obtain nitrophenyldiazahomoadamantane III from nitrophenyldiazahomoadamantanone IV by the Wolff—Kishner reaction and compare the efficiency of the schemes of preparing it via compound II or IV, the last compound was heated with hydrazine hydrate in conditions of preparation of diazahomoadamantanone hydrazones [2]. It was found that in prolonged heating of nitrophenyldiazahomoadamantanone IV with an excess of hydrazine hydrate, its nitro group is reduced to an amino group and 1-*p*-aminophenyl-3,6-diazahomoadamantan-9-one V hydrazone is formed as a result. There are no absorption bands of nitro group stretching vibrations in its IR spectrum and there is an absorption band of a C=N azomethine group in the 1630 cm^{-1} region. NH_2 groups absorb in the 3346 and 3100 cm^{-1} region.

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*See [1] for 17.

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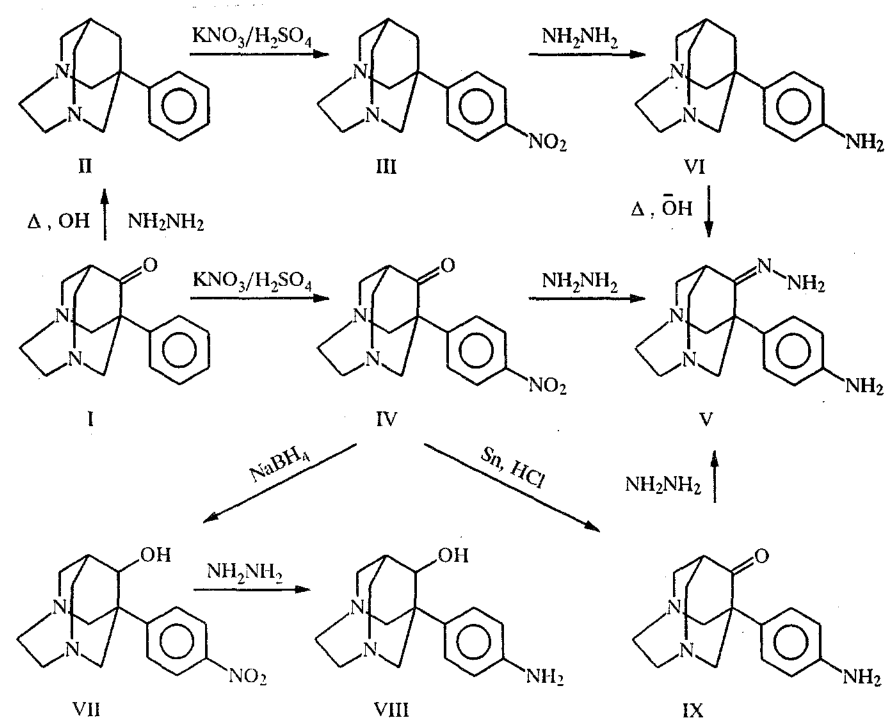
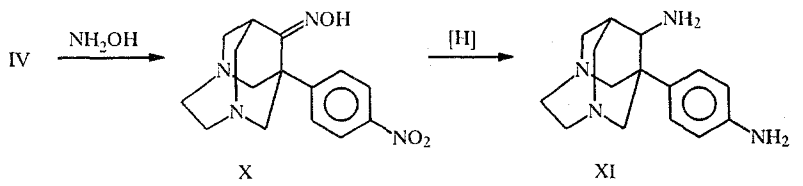


When hydrazone V is melted with a base, 1-*p*-aminophenyl-3,6-diazahomoadamantane VI is formed, and its amino group absorbs in the 3450, 3380, and 3180 cm^{-1} region of the IR spectrum. Its mass spectrum has a molecular ion peak with *m/z* 243. Aminophenyldiazahomoadamantane VI is also formed when nitrophenyldiazahomoadamantane III is heated with an excess of hydrazine hydrate with no catalyst.

Reduction of 1-*p*-nitrophenyl-3,6-diazahomoadamantan-9-ol VII, prepared in turn by reduction of nitrophenyldiazahomoadamantanone IV with sodium borohydride, into 1-*p*-aminophenyl-3,6-diazahomoadamantan-9-ol VIII by heating with hydrazine hydrate, is a third example of noncatalytic reduction of the nitro group of ntirophenyldiazahomoadamantanes into an amino group. There are no absorption bands of the nitro group in the 1520 and 1350 cm^{-1} region for starting nitro alcohol VII in the IR spectrum of aminophenyldiazahomoadamantanol VIII. The hydroxyl and amino groups absorb in compound VIII in the region of 3338 and 3205 cm^{-1}.

Reduction was conducted with tin in hydrochloric acid to reduce the nitro group of nitrophenyldiazahomoadamantanone IV without affecting the carbonyl group, and 1-*p*-aminophenyl-3,6-diazahomoadamantan-9-one IX was obtained as a result. Its IR spectrum has an absorption band of carbonyl group stretching vibrations in the 1705 cm^{-1} region and no absorption bands of the nitro group in the starting IV. The amino group absorbs in the 3450, 3380, and 3180 cm^{-1} region. Aminophenyldiazahomoadamantanone V hydrazone, totally identical to the compound obtained from nitrophenyldiazahomoadamantanone IV, was obtained by heating this aminoketone with hydrazine hydrate.

9-Amino-1-*p*-aminophenyl-3,6-diazahomoadamantane XI was obtained by reduction of 1-*p*-nitrophenyl-3,6-diazahomoadamantan-9-one oxime X, prepared by reaction hydroxylamine with ketone IV in water—alcohol medium, with nickel—aluminum alloy (50:50) in water—base medium.



Its IR spectrum contains no absorption band of the C=N azomethine group in the initial oxime in the 1630 cm^{-1} region and nitro group in the 1520 and 1350 cm^{-1} region, but has amino group absorption bands in the 3430, 3310, and 3200 cm^{-1} region.

TABLE 1. Parameters of the PMR and IR Spectra of 1-Phenyl-3,6-diazahomoadamantane Derivatives

Compound	Proton chemical shifts, δ, ppm					IR spectrum, cm^{-1}
	NCH_2CH_2N, m	NCH_2C, b	H, c	C_6H_4, m	C_6H_4Y, $C_{(9)}X$	
III	3,09	3,29, 3,18, 3,24, 2,84	2,05	7,65...7,40; 8,25...8,05	2,14 s H_2	1505, 1340 (NO_2)
IV	3,27	3,67, 3,42, 3,60, 3,24	2,75	7,65...7,50; 8,20...8,08		1510, 1340 (NO_2), 1698 (CO)
V	3,22	3,65, 3,17, 3,42, 3,05	3,73	7,30...7,01; 6,71...6,50	1,73 s $C_6H_4NH_2$; 5,0 s NH_2	1630 (C=N), 3230, 3120 (NH_2)
VI	3,06	3,27, 3,19, 3,10, 2,82	2,00	6,72...6,52; 7,27...7,08	1,73 s $C_6H_4NH_2$; 2,08 s H_2	3450, 3350, 3180 (NH_2)
VII	3,14	3,83, 2,97, 3,68, 2,80, 3,42, 3,20, 3,09, 2,58	1,77	7,73...7,48: 8,27...8,08	2,01 s H; 4,34 s OH	1520, 1350 (NO_2), 3100 (OH)
X	3,22	3,68, 3,16, 3,40, 3,02	1,61	7,67...7,41; 8,22...8,06	7,60 s OH	3220, 3110 (NH_2), 1630 (C=N), 1520, 1350 (NO_2)
XI	3,13	2,79, 3,60, 3,42, 2,96, 3,16, 2,74, 3,11, 2,58	3,43	6,71...6,52; 7,30...7,01	1,18 s $C_6H_4NH_2$; 3,68 s NH_2; 1,82 s H	3430, 3310, 3200 (NH_2)

TABLE 2. Mass Spectra of Compounds III-X

Compound	m/z Relative intensity, %
III	273 (100), 229 (37), 215 (34), 213 (29), 201 (21), 200 (31), 115 (29), 58 (58), 55 (46), 55 (25), 42 (24)
IV	287 (100), 286 (94), 115 (69), 102 (58), 84 (63), 82 (50), 58(98), 57 (92), 56 (65), 55 (92), 54 (56)
V	271 (18), 255 (46), 212 (27), 185 (18), 117 (17), 72 (72), 58 (100), 57 (16), 44 (18), 42 (56), 41 (19)
VI	243 (100), 242 (20), 199 (29), 185 (37), 171 (22), 170 (21), 58 (56), 57 (17), 44 (17), 42 (37)
VII	289 (50), 111 (17), 84 (14), 74 (25), 72 (31), 58 (100), 57 (37), 44 (36), 43 (19), 42 (60), 41 (24)
X	302 (26), 286 (14), 285 (100), 284 (19), 256 (14), 242 (21), 58 (39), 57 (12), 43 (15), 42 (42), 41 (19)

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*The M+ ion peaks and 10 most intense ion peaks in the mass spectra are reported.

EXPERIMENTAL

The IR spectra were recorded on a Specord 71-IR spectrometer (in Vaseline oil), the PMR spectra were made on a Bruker M-250 (in $CDCl_3$), TMS internal standard, and the mass spectra were obtained on a Kratos MS-80 with direct introduction of the sample in the ion source, 70 eV electron ionization energy, 150°C ionization chamber temperature, and perfluorokerosine standard. Resolution of $M/\Delta M = 10{,}000$.

The characteristics of compounds III-XI are reported in Tables 1 and 2.

The data from elemental analysis for C, H, N, and the molecular masses based on mass spectroscopic data are in agreement with the calculated values.

1-*p*-Nitrophenyl-3,6-diazahomoadamantane (III, $C_{15}H_{19}N_3O_2$). While stirring, 2.00 g (8.7 mmole) of 1-phenyl-3,6-diazahomoadamantane II was added by small portions over 15 min to a solution of 0.88 g (8.7 mmole) of potassium nitrate in 18 ml of conc. sulfuric acid, cooled to 0-5°C; it was then stirred without cooling for 1.5 h, poured in 100 ml of water, neutralized with potash to pH 8-9, and the sediment formed was filtered off, dried in a vacuum desiccator, and extracted with toluene (3 × 15 ml). The extract was filtered and evaporated, and the sediment was crystallized from toluene, yielding 2.07 g (91%) of nitrophenyldiazahomoadamantane III, mp = 97-98°C.

1-*p*-Nitrophenyl-3,6-diazahomoadamantan-9-one (IV, $C_{15}H_{17}N_3O_3$). Similarly, 7.7 g (65%) of nitrophenyldiazahomoadamantanone IV, mp = 163-165°C, was obtained from 10.0 g (40 mmole) of 1-phenyl-3,6-diazahomoadamantan-9-one I in nitration with a mixture of 4.0 g (40 mmole) of potassium nitrite and 50 ml of conc. sulfuric acid.

1-*p*-Aminophenyl-3,6-diazahomoadamantan-9-one hydrazone (V, $C_{15}H_{21}N_5$). A. A solution of 0.71 g (2.5 mmole) of nitrophenyldiazahomoadamantanone IV in 10 ml of 80% hydrazine hydrate was heated for 3 h, evaporated dry, and sediment was crystallized from toluene, yielding 0.95 g (91%) aminophenyldiazahomoadamantanone hydrazone V, mp = 226-227°C.

B. Similarly, 0.07 g (83%) of aminophenyldiazahomoadamantanone hydrazone V, totally identical to the compound obtained with method A, was obtained from 0.08 g (0.03 mmole) of aminophenyldiazahomoadamantanone IX and 0.5 ml 80% hydrazine hydrate.

1-*p*-Aminophenyl-3,6-diazahomoadamantane (VI, $C_{15}H_{21}N_3$). A. A carefully stirred mixture of 0.15 g (0.5 mmole) of aminophenyldiazahomoadamantanone hydrazone V and 0.15 g of powdered potassium hydroxide was heated for 2 h at 220-240°C. The cooled melt was extracted with (3 × 5 ml) of ether, the solvent was distilled off, and the residue was sublimated in a water-jet pump vacuum, yielding 0.11 g (85%) of aminophenyldiazahomoadamantane VI, mp = 151-152°C.

B. A solution of 0.68 g (2.5 mmole) of nitrophenyldiazahomoadamantane III in 6 ml of 80% hydrazine hydrate was heated at boiling for 3.5 h, evaporated dry, and the residue was sublimated in a water-jet pump vacuum, yielding 0.51 g (86%) of aminophenyldiazahomoadamantane VI, totally identical to the compound obtained with method A.

1-*p*-Nitrophenyl-3,6-diazahomoadamantan-9-ol (VII, $C_{15}H_{21}N_3O$). While stirring, 0.56 g (15 mmole) of sodium borohydride was added to a solution of 3.0 g (10 mmole) of nitrophenyldiazahomoadamantanone IV in 60 ml of methanol and stirred for 4 h at ordinary temperature, then 5 ml of water was added, evaporated dry, and the residue was extracted with toluene (2 × 30 ml), the solvent was evaporated, and the sediment was crystallized from toluene, yielding 2.64 g (91%) of nitrophenyldiazahomoadamantanol VII, mp = 140-141°C.

1-p-Aminophenyl-3,6-diazahomoadamantan-9-ol (VIII, $C_{15}H_{21}N_3O$). A solution of 0.2 g (0.7 mmole) of nitrophenyldiazahomoadamantanol VII in 4 ml of 80% hydrazine hydrate was heated at boiling for 3.5 h, evaporated dry, and the residue was crystallized from toluene, yielding 0.15 g (84%) of aminophenyldiazahomoadamantanol VIII, mp = 97-98°C. IR spectrum: 3338, 3205 cm^{-1} (NH_2, OH).

1-p-Aminophenyl-3,6-diazahomoadamantan-9-one (IX, $C_{15}H_{19}N_3O$). A mixture of 5 m of conc. hydrochloric acid, 0.55 g (1.9 mmole) of nitrophenyldiazahomoadamantanone IV, and 0.5 g of finely granulated tin was heated for 1 h in a boiling water bath, dried with caustic soda, and evaporated, and the residue was crystallized from toluene, yielding 0.39 g (79%) of aminophenyldiazahomoadamantanone IX, mp = 172-174°C. IR spectrum: 1705 (CO), 3450, 3380, 3180 cm^{-1} (NH_2).

1-p-Nitrophenyl-3,6-diazahomoadamantan-9-one oxime (X, $C_{15}H_{18}N_4O_3$). While stirring, 5.3 g (50 mmole) of a solution of sodium carbonate in 20 ml of water was added by portions over 15 min to a solution of 5.74 g (20 mmole) of nitrophenyldiazahomoadamantanone IV and 3.47 g (50 mmole) of hydroxylamine hydrochloride in 20 ml of water at 60-70°C, and stirring at this temperature was continued for another 15 min. The precipitated sediment was filtered off, dried in a vacuum desiccator, and crystallized from toluene, yielding 4.05 g (67%) nitrophenyldiazahomoadamantanone oxime X, mp = 240-241°C.

9-Amino-1-p-aminophenyl-3,6-diazahomoadamantane (XI, $C_{15}H_{22}N_4$). A solution of 6.0 g of sodium hydroxide in 8 ml of water was added by drops over 1 h to a suspension of 1.0 g (3 mmole) of nitrophenyldiazahomoadamantanone oxime X and 6.0 g of nickel—aluminum alloy (50:50) in 11 ml of water while stirring energetically and not allowing the reaction mixture to heat above 50°C; stirring was continued for another 2 h, and the mixture was then cooled and extracted with ether (5 × 15 ml). The ether solution was dried with sodium hydroxide and evaporated, yielding 0.5 g (59%) of diamine XI, mp = 170-171°C.

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