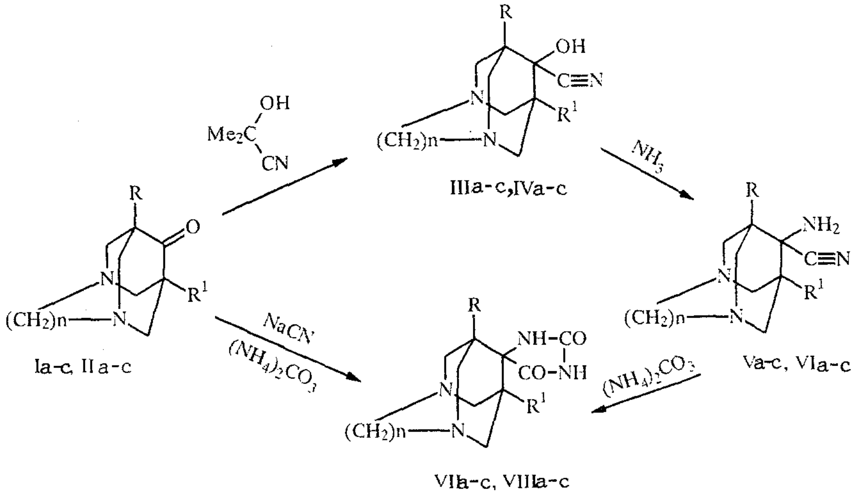
HETEROADAMANTANES AND THEIR DERIVATIVES.
16.* SYNTHESIS OF SPIROIMIDAZOLIDINE-2,4-DIONES OF THE DIAZA- AND DIAZAHOMOADAMANTANE SERIES

A. I. Kuznetsov, T. D. Sokolova,
I. A. Vladimirova, T. M. Serova,
M. Yu. D'yakov, L. A. Shundrin,
A. S. Moskovkin, and B. V. Unkovskii

6-Cyano-1,3-diazaadamantan-6-ols and 9-cyano-3,6-diazahomoadamantan-9-ols, whose reaction with ammonia forms the corresponding 6-cyano-6-amino-1,3-diaza- and 9-cyano-9-amino-3,6-diazahomoadamantanes, were prepared by the exchange reaction of 1,3-diazaadamantan-6-ones and 3,6-diazahomoadamantan-9-ones with acetone cyanohydrin. When heated with ammonium carbonate, spirohydantoins were directly obtained from the former compounds and from the initial ketones by Bucherer—Bergs synthesis.

We previously [2] reported synthesis of 6-cyano-5,7-dimethyl-1,3-diazaadamantan-6-ol (IIIc) by the exchange reaction of 5,7-dimethyl-1,3-diazaadamantan-6-one (Ic) with acetone cyanohydrin. 6-Cyano-5-methyl- and 6-cyano-5-phenyl-1,3-diazaadamantan-6-ols (IIIa, b) were prepared by the same method from 5-methyl- and 5-phenyl-1,3-diazaadamantan-6-ones (Ia, b) [3] and 9-cyano-1-methyl-, 9-cyano-1-phenyl-, and 9-cyano-1,8-dimethyl-3,6-diazahomoadamantan-9-oles (IVa-c) were prepared from 1-methyl-, 1-phenyl, and 1,8-dimethyl-3,6-diazahomoadamantan-9-ones (IIa-c) [4, 5].



I, III, V, VII n=1; III, IV, VI, VIII n=2;a R=Me, R^1=H; b R=Ph, R^1=H, c R=R^1=Me

---

*See [1] for Communication 15.

M. V. Lomonosov Institute of Precision Chemical Technology, Moscow 119831. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 648-652, May, 1992. Original article submitted March 25, 1991.

TABLE 1. Cyanohydrins, Aminonitriles, and Spirohydantoins III-VIII

Compound	Empirical formula	Mp, °C	IR spectrum, cm^{-1}	Yield, % %
IIIa	$C_{10}H_{15}N_3O$	137...138	2220 (C≡N), 3040 (OH)	53
IIIb	$C_{15}H_{17}N_3O$	169...170	2225 (C≡N), 3040 (OH)	89
IVa	$C_{11}H_{17}N_3O$	167...168	2200 (C≡N), 3050 (OH)	77
IVb	$C_{16}H_{19}N_3O$	128...129	2220 (C≡N), 3040 (OH)	87
IVc	$C_{12}H_{19}N_3O$	173...174	2200 (C≡N), 3050 (OH)	91
Va	$C_{10}H_{16}N_4$	182...183	2220 (C≡N), 3250, 3190 (NH)	97
Vb	$C_{15}H_{18}N_4$	174...175	2215 (C≡N), 3385, 3305 (NH)	90
Vc	$C_{11}H_{18}N_4$	184...185	2200 (C≡N), 3340, 3250, 3185 (NH)	96
VIa	$C_{11}H_{18}N_4$	117...119	2207 (C≡N), 3350, 3310, 3150 (NH)	86
VIb	$C_{16}H_{20}N_4$	164...165	2215 (C≡N), 3380, 3310 (NH)	79
VIIa	$C_{11}H_{16}N_4O_2$ (Monohydrate)	334...336	1750, 1710 (C=O), 3450, 3260, 3150 (NH)	A. 56 B. 81
VIIb	$C_{16}H_{18}N_4O_2$ (Monohydrate)	335...337 (decomp.)	1755, 1700 (C=O), 3440, 3310 (NH)	A. 79 B. 83
VIIc	$C_{12}H_{18}N_4O_2$	348...351 (decomp.)	1750, 1710 (C=O), 3190, 3100 (NH)	A. 67 B. 69
VIIIa	$C_{12}H_{18}N_4O_2$	279...280	1760, 1690 (C=O), 3600, 3180 (NH)	A. 90 B. 92
VIIIb	$C_{17}H_{20}N_4O_2$	263...264	1760, 1710 (C=O), 3520, 3220 (NH)	F. 96 B. 97
VIIIc	$C_{13}H_{20}N_4O_2$	283...284	1790, 1760 (C=O), 3290, 3190 (NH)	B. 89

The corresponding aminonitriles Va-c and VIa, b were obtained in the reaction of cyanohydrins IIIa-c and IVa, b with ammonia and methanol at room temperature. Spirohydantoins VIIa-c and VIIIa, b were prepared by heating aminonitriles Va-c and VIa, b with ammonium carbonate in ethanol. The same compounds and compound VIIIc were also directly obtained from starting ketones Ia-c and IIa-c by Bucherer—Bergs synthesis by heating them with a mixture of sodium cyanide and ammonium carbonate.

The structure of the compounds was confirmed by the spectral data. There were no absorption bands of carbonyl groups, while absorption bands of stretching vibrations of a nitrile group in the 2225-2200 cm^{-1} region and a hydroxyl group in the 3050-3040 cm^{-1} were present in the IR spectra of cyanohydrins III and IV (Table 1). The absorption bands of the nitrile group in the 2200-2220 cm^{-1} region persisted in the spectra of aminonitriles V and VI, while absorption bands of an amino group in the 3150-3385 cm^{-1} region were observed instead of hydroxyl group absorption bands.

The IR spectra of hydantoins VII and VIII did not contain the absorption bands of the nitrile group, but absorption bands of stretching vibrations of carbonyl groups were observed in the 1790-1750 (ureide) and 1690-1760 cm^{-1} region (amide).

The ESR spectra of compounds III-VIII (Table 2) have groups of signals characteristic of 1,3-diaza- and 3,6-diazahomoadamantane backbones and signals of protons of substituents in nodal positions of the corresponding multiplet.

The structure of these compounds was also confirmed by the mass spectra (Table 3). Cleavage of a molecule of HCN is the basic direction of decomposition of the molecular ions (M^+) of cyanohydrins and aminonitriles III-VI, and the peak of the $[M-HCN]^+$ ion formed has the maximum intensity in compounds Va, c. Further decomposition of the $[M-HCN]^+$ ions in the spectra of these compounds is similar to decomposition of M^+ ions of the previously investigated, corresponding diazaadamantanones Ia-c and diazahomoadamantanones IIa-c [5, 6], respectively. Further fragmentation of the $[M-HCN]^+$ ion with cleavage of the C_2H_4N molecule is characteristic of cyanohydrins and aminonitriles in the 1,3-diazaadamantane series [3, 5], and the corresponding peaks have the highest intensity in the spectra of cyanohydrins III. Cleavage of a nitrogen-containing ion with *m/z* 58 from this ion is more probable for cyanohydrins and aminonitriles in the 3,6-diazahomoadamantane series [4, 5].

The spirohydantoin ring present in the molecules of compounds VII and VIII significantly increases their resistance to electron impact, and the M^+ ion peaks in the spectra of these compounds have the maximum intensity. Both directions of decomposition of M^+ common for 1,3-diazaadamantane [6] and 3,6-diazahomoadamantane [5] derivatives and the directions typical of substituted hydantoins [7, 8] are characteristic of the mass spectral behavior of these compounds. Fragmentation

TABLE 2. ESR spectra of Cyanohydrins, Aminonitriles, and Spirohydantoins

Compound	Chemical shift, δ, ppm			
	$N(CH_2)_nN$	NCH_2C	R, R^1	other
IIIa	4,83, 3,96 d	3,50...2,75 m	1,67 sH, 0,88 s CH_3	6,10 s OH
IIIb	4,19, 4,05 d	3,59...3,12 m	1,87 s H, 7,38 m C_6H_5	
IVa	2,94 m	3,04, 2,80 d; 2,77, 2,70 d; 2,60, 2,57 d	1,97 s H, 0,30 s CH_3	
Va	4,16, 3,95 d	3,64...2,76 m	1,53 s H, 0,86 s CH_3	1,83 br.s NH_2
Vb	4,38, 4,21 d	4,12...3,72 m, 3,54...3,04 m	1,62 s H, 7,42 m C_6H_5	1,97 br.s NH_2
Vc	3,95 s	3,51...2,76 m	0,85 s CH_3	1,72 br.s NH_2
VIa	3,05 m	3,74 m; 3,53, 2,84 d; 3,27, 2,25 d; 2,51 m	1,83 s H, 0,88 s CH_3	1,74 br.s NH_2
VIb	3,12 m	4,38, 2,84 d; 4,10, 2,94 d; 3,92, 2,58 m	1,90 s H, 7,6...7,3 m C_6H_5	1,63 br.s NH_2
VIIIa	3,34 m	3,93, 3,67 d; 3,42, 3,13 d; 3,10, 2,99 d; 2,94 d	2,14 sH, 0,42 s CH_3	
VIIIb	3,02 m	4,21 m; 3,77 m; 3,59 m; 2,67 m	1,82 s H, 7,8...7,2 m	8,74 s NH

of the M^+ ions of hydantoins VII and VIII in this case is due to successive cleavage of molecules of CO and HNCO from the hydantoin ring.

EXPERIMENTAL

The IR spectra were recorded on a Specord 71-1P spectrometer (in petrolatum), the ESR spectra were made on a Bruker M-250 (in $CDCl_3$) with TMS as the internal standard, and the mass spectra were made on a Kratos MS-80 with direct introduction of the sample into the ion source, ionizing electron energy of 70 eV, and ionization temperature of 150°C.

The properties of compounds III-VIII are reported in Tables 1-3.

The data from elemental analysis for C, H, and N corresponded to the calculations.

6-Cyano-5-methyl-1,3-diazaadamantan-6-ol (IIIa). A mixture of 0.29 g (1.8 mmole) of methyldiazaadamantanone Ia and 0.75 g (8.8 mmole) of acetone cyanohydrin in 5 ml of isopropyl alcohol was heated for 6 h at 45-50°C, evaporated, and the residue was crystallized from heptane—ethyl acetate mixture, 2:1, yielding 0.18 g of cyanohydrin IIIa.

6-Cyano-5-phenyl-1,3-diazaadamantan-6-ol (IIIb). Here 1.98 g of cyanohydrin IIIb was obtained similarly from 2.0 g (8.8 mmole) of phenyldiazaadamantanone Ib and 3.73 g (44 mmole) of acetocyanohydrin in 5 ml of isopropyl alcohol.

9-Cyano-1-methyl-3,6-diazahomoadamantan-9-ol (IVa). Similarly, 1.59 g of cyanohydrin IVa was obtained from 1.8 g (10 mmole) of methyldiazahomoadamantanone IIa and 3 g (35 mmole) of acetone cyanohydrin in 30 ml of isopropyl alcohol.

9-Cyano-1-phenyl-3,6-diazahomoadamantan-9-ol (IVb). Here 1.17 g of cyanohydrin IVb was obtained analogously from 1.21 g (5 mmole) of phenyldiazahomoadamantanone IIb and 1.5 g (18 mmole) of acetone cyanohydrin in 15 ml of methanol. (In contrast to the preceding experiments, the reaction mixture was only evaporated to 1/2 of the initial volume, and the precipitated crystals were filtered off and crystallized from ethyl acetate.)

9-Cyano-1,8-dimethyl-3,6-diazahomoadamantan-9-ol (IVc). Here 1.0 g of cyanohydrin IVc was obtained analogously from 0.97 g (5 mmole) of dimethyldiazahomoadamantanone IIc and 0.9 g (10 mmole) of acetone cyanohydrin in 15 ml of isopropyl alcohol.

6-Cyano-6-amino-5-methyl-1,3-diazaadamantane (Va). A solution of 2.0 g (14 mmole) of cyanohydrin IIIa in 12 ml of methanol was saturated with gaseous ammonia for 1 h with external cooling, left at ambient temperature for 5 days, evaporated, and crystallized from hexane—acetone mixture, 1:1, producing 1.92 g of aminonitrile Va.

6-Cyano-6-amino-5-phenyl-1,3-diazaadamantane (Vb). Similarly, 1.04 g of aminonitrile Vb was obtained from 1.53 g (6 mmole) of cyanohydrin IIIb after crystallization from hexane.

6-Cyano-6-amino-5,7-dimethyl-1,3-diazaadamantane (Vc). Similarly, 2.19 g of aminonitrile Vc was obtained from 2.3 g (11 mmole) of cyanohydrin IIIb.

TABLE 3. Mass Spectra of Compounds III-VIII

Compound	m/z (relative intensity, %)*
IIIa	193(1,4), 166(76), 124(100), 84(10), 70(11), 69(27), 68(17), 55(25), 43(12), 42(12), 41(39)
IIIb	255(15), 228(60), 186(100), 103(55), 77(37), 69(26), 68(22), 58(31), 43(30), 42(80), 41(29)
IIIc	207(22), 190(16), 180(41), 138(100), 110(18), 84(14), 82(20), 69(23), 55(19), 42(38), 41(30)
IVa	207(0,3), 180(71), 124(13), 84(19), 82(16), 68(10), 58(100), 57(29), 55(29), 42(41), 41(35)
IVb	269(2), 242(58), 241(19), 103(29), 84(22), 77(23), 72(27), 58(100), 57(46), 55(33), 42(32)
IVc	221(7), 194(27), 138(6), 96(10), 82(8), 69(9), 58(100), 57(11), 55(14), 42(22), 41(19)
Vb	254(18), 227(100), 226(33), 185(57), 184(65), 183(53), 170(79), 103(29), 70(61), 42(71), 41(36)
Vc	206(10), 179(100), 178(23), 137(64), 136(64), 136(38), 135(28), 122(52), 108(24), 68(22), 42(43), 41(37)
VIa	206(6), 179(100), 178(14), 137(15), 135(50), 122(13), 108(28), 96(10), 58(23), 42(21), 41(12)
VIb	268(72), 241(100), 240(36), 198(23), 197(48), 170(52), 115(19), 103(19), 58(26), 44(17), 42(25)
VIIa	236(100), 194(11), 139(16), 97(15), 96(17), 84(22), 82(16), 70(45), 68(27), 55(11), 42(20)
VIIb	298(100), 201(22), 158(17), 103(22), 70(73), 68(28), 55(19), 44(57), 43(57), 42(73), 41(39)
VIIc	250(100), 235(20), 139(26), 111(19), 96(17), 84(73), 82(33), 70(16), 68(19), 55(19), 42(21)
VIIIa	250(100), 179(20), 97(12), 96(19), 84(12), 82(33), 72(10), 68(13), 58(28), 57(11), 42(22)
VIIIb	312(100), 241(18), 240(15), 187(17), 159(16), 158(15), 115(11), 84(12), 82(11), 58(21), 42(16)

---

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

9-Cyano-9-amino-1-methyl-3,6-diazahomoadamantane (VIa). Here 0.43 g of aminonitrile VIa was obtained from 0.5 g (2.4 mmole) of cyanohydrin IVa in 3 ml of methanol after crystallization from ethyl acetate.

9-Cyano-9-amino-1-phenyl-3,6-diazahomoadamantane (VIb). Similarly, 0.71 g of aminonitrile VIb was obtained from 0.9 g (3.3 mmole) of cyanohydrin IVb in 6 ml of methanol. In contrast to the preceding experiment, aminonitrile VIb partially precipitated from the reaction mixture into the sediment. After it was separated, the mother liquor was evaporated to 1/2 of the initial volume, diluted with 5 ml of ether, filtered, and the residue was combined with the residue precipitated from the reaction mixture and crystallized from ethyl acetate.

5-Methyl-1,3-diazaadamantane-6-spiro-5′-imidazolidine-2,4-dione (VIIa). A. A mixture of 1.0 g (6.2 mmole) of methyldiazaadamantanone Ia, 0.44 g (9 mmole) of sodium cyanide, and 3.5 g (36 mmole) of ammonium carbonate in 7 ml of 50% ethanol was heated for 10 h at 55-65°C and for 1 h in a boiling water bath, evaporated to 1/2 of the initial volume, cooled, and the precipitated crystals were filtered off and crystallized from ethanol, producing 0.79 g of hydantoin VIIa.

B. Here 1.22 g (6.4 mmole) of aminonitrile Va and 2.0 g (20 mmole) of ammonium carbonate in 6 ml of 50% ethanol were heated for 10 h at 55-60°C and 1 h in a boiling water bath, evaporated, and the sediment was crystallized from 80% ethanol, producing 1.2 g of hydantoin VIIa, totally identical to the compound obtained with method A.

5-Phenyl-1,3-diazaadamantane-6-spiro-5′-imidazolidine-2,4-dione (VIIb). A. Analogously, 0.98 g of hydantoin VIIb was obtained from 1.0 g (4.4 mmole) of phenyldiazaadamantane Ib, 0.32 g (6.5 mmole) of sodium cyanide, and 1.26 g (13 mmole) of ammonium carbonate.

B. Here 0.73 g of hydantoin VIIb was obtained analogously from 0.75 g (3 mmole) of aminonitrile Vb and 1.0 g (10 mmole) of ammonium carbonate.

5,7-Dimethyl-1,3-diazaadamantane-6-spiro-5′-imidazolidine-2,4-dione (VIIc). A. Herr 0.93 g of hydantoin VIIc was obtained analogously from 1.0 g (5.6 mmole) of dimethyldiazaadamantanone Ic, 0.4 g (8.2 mmole) of sodium cyanide, and 3.2 g (33 mmole) of ammonium carbonate.

B. Analogously, 1.09 g of hydantoin VIIc was obtained from 1.33 g (6.5 mmole) of aminonitrile Vc and 1.63 g (17 mmole) of ammonium carbonate.

1-Methyl-3,6-diazahomoadamantane-9-spiro-5′-imidazolidine-2,4-dione (VIIIa). A. Here 1.38 g of hydantoin VIIIa was obtained similarly from 1.08 g (6 mmole) of methyldiaza-homoadamantanone IIa, 0.44 g (9 mmole) of sodium cyanide, and 3.5 g (36 mmole) of ammonium carbonate.

B. Analogously 0.71 g of hydantoin VIIIa was obtained from 0.56 g (2.7 mmole) of aminonitrile VIa and 1.0 g (20 mmole) of ammonium carbonate.

1-Phenyl-3,6-diazahomoadamantane-9-spiro-5′-imidazolidine-2,4-dione (VIIIb). A. Here 1.8 g of hydantoin VIII b was obtained similarly from 1.45 g (6 mmole) of phenyldiazahomoadamantanone IIb, 0.44 g (9 mmole) of sodium cyanide, and 3.5 g (36 mmole) of ammonium carbonate in 7 ml of 50% ethanol. In contrast to the preceding experiments, VIIIb precipitated from the reaction mixture into the sediment.

B. Similarly, 0.81 g of hydantoin VIIIb was obtained from 0.73 g (2.7 mmole) of aminonitrile VIb and 1.0 g (10 mmole) of ammonium carbonate in 5 ml of 50% ethanol.

1,8-Dimethyl-3,6-diazahomoadamantane-9-spiro-5′-imidazolidine-2,4-dione (VIIIc). A. Here 0.71 g of hydantoin VIIIc was obtained from 0.58 g (3 mmole) of dimethyldiazahomoadamantanone IIc, 0.22 g (4.5 mmole) of sodium cyanide, and 1.75 g (18 mmole) of ammonium carbonate.

LITERATURE CITED

1. A. I. Kuznetsov, I. A. Vladimirova, T. M. Serova, and A. S. Moskovkin, Khim. Geterotsikl. Soedin., No. 5, 643 (1992).
2. A. I. Kuznetsov, E. B. Basargin, M. Kh. Ba, A. S. Moskovkin, I. I. Miroshnichenko, and M. Ya. Botnikov, Khim. Geterotsikl. Soedin., No. 5, 647 (1989).
3. A. I. Kuznetsov, E. B. Basargin, and M. Kh. Ba, Zh. Org. Khim., **21**, 2607 (1985).
4. A. I. Kuznetsov and I. A. Vladimirova, Khim. Geterotsikl. Soedin., No. 12, 1700 (1988).
5. A. I. Kuznetsov, I. A. Vladimirova, and E. B. Basargin, Khim. Geterotsikl. Soedin., No. 5, 675 (1990).
6. A. I. Kuznetsov, E. B. Basargin, A. S. Moskovkin, M. Kh. Ba, I. V. Miroshnichenko, M. Ya. Botnikov, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 12, 1679 (1985).
7. R. A. Corral, O. O. Drazi, A. M. Duffield, and C. Djerassi, Org. Mass Spectrom., **5**, 551 (1971).
8. J. Tamas, G. Czira, G. Simig, and K. Lempert, Org. Mass Spectrom., **10**, 390 (1975).