HETEROADAMANTANES AND THEIR DERIVATIVES. 17.*
WOLFF–KISHNER REDUCTION OF 3,6-DIAZAHOMOADAMANTAN-9-ONES

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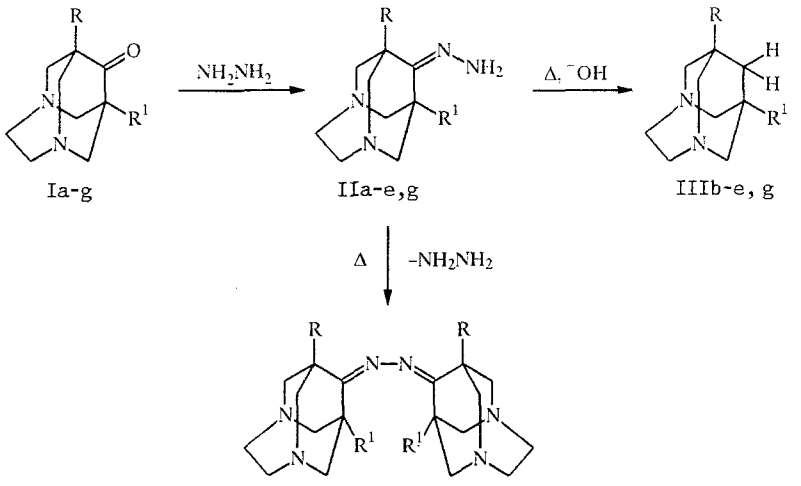
Wolff–Kishner reduction of the keto group of 3,6-diazahomoadamantan-9-ones to a methylene group was investigated. It was shown that diazahomoadamantanones yield hydrazones in the reaction with hydrazine hydrate, and they are converted into 3,6-diazahomoadamantane derivatives with one or two substituents in nodal positions when heated with a base. Unsubstituted 3,6-diazahomoadamantane is not formed in these conditions, since 3,6-diazahomoadamantan-9-one hydrazone is converted into azine when heated above 70°C. Other hydrazones are also converted into azines when heated, but at a higher temperature — above 150°C.

Condensation of ketones with 1,3,6,8-tetraazatricyclo[4.4.1.$1^{3,8}$]dodecane (tetramethylenediethylenetetramine) significantly facilitates obtaining 3,6-diazahomoadamantan-9-one (Ia) and its derivatives with one or two substituents in nodal positions. In addition to the previously described [2, 3] diazahomoadamantanones Ia-e, 1-(2-acetylhydroxyethyl)-3,6-diazahomoadamantan-9-one (If) was obtained from the available 5-acetylhydroxypentan-2-one for the first time. In addition, the method of preparation of unsubstituted diazahomoadamantanone Ia was improved and the yield was increased from 12 to 27%.



I—IV a R = R^1 = H; b R = R^1 = Me; c R = Me, R^1 = H; d R = Ph, R^1 = H; e R = Ph, R^1 = Me, f R = $MeCOOCH_2CH_2$, R^1 = H; g R = $HOCH_2CH_2$, R^1 = H

*See [1] for Communication 16.

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TABLE 1. Properties of the Prepared Compounds

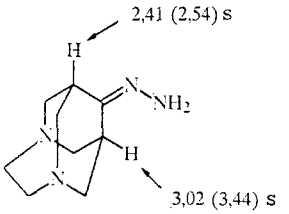
Compound	Empirical formula	Mpa, °C	IR spectrum, ν, cm^{-1}	ESR spectrum (in $CDCl_3$), δ, ppm				Yield, %
				$N-CH_2CH_2N$	$N-CH_2-C$, d	R, R'	other	
If	$C_{13}H_{20}N_2O_3$	74...75	1730 C=O ether., 1690 ketone	3,18 m	3,42, 3,14, 3,11, 3,04	2,03 s CH_3, 1,75t C—CH_2C, 4,14 tC—CH_2O, 2,58 s H	—	38
Ig	$C_{12}H_{18}N_2O_2$	68...69	1712, 1697, 1668 C=O, 3543, 3199 OH	3,19 m	3,43, 3,11, 3,22, 2,99	1,65 t C—CH_2—C, 3,68t C—CH_2—O, 2,62s H	—	97
IIa	$C_9H_{16}N_4$	129...131	1660 C=N, 3280, 3180 NH_2	3,15 s	3,34, 2,96, 3,28, 2,94	2,41 sH, 3,02s H	5,17 s NH_2	82
IIb	$C_{11}H_{20}N_4$	127...128	1635 C=N, 3320, 3160 NH_2	3,16 m	3,28, 2,80, 3,03, 2,60	0,90 sCH_3, 1,48 s 2H from CH_3, 3,22s 1H fromCH_3	5,38s NH_2	91
IIc	$C_{10}H_{18}N_4$	169...171	1635 C=N, 3200, 3100 NH_2	3,02 m	3,09, 2,99, 2,82, 2,61	0,73 s CH_3, 2,92 s H	4,85 s NH_2	88
IId	$C_{15}H_{20}N_4$	165...167	1640 C=N, 3160, 3040 NH_2	3,22 m	3,67, 3,13, 3,42, 3,04	7,41...7,19 m C_6H_5; 3,18s H	4,85 s NH_2	86
IIe	$C_{16}H_{22}N_4$	167...168	1640 C=N, 3240, 3160 NH_2	3,13 m	3,70, 2,95, 3,07, 2,77	7,36...7,14 m C_6H_4; 0,88 s CH_3	4,64 s NH_2	84
IIg	$C_{12}H_{20}N_4O$	132...133	1620 C=N, 3346, 3184 NH_2 and OH	3,15 m	3,27, 2,97, 3,14, 2,70	1,65 m C—CH_2—C, 3,54 mC—CH_2—O; 3,01 m.n.	5,00 s NH_2	91
IIIb	$C_{11}H_{20}N_2$	41...42*		3,06 s	2,74, 2,53	0,71 s CH_3	1,30 sC—CH_2—C	78
IIIc	$C_{10}H_{18}N_2$	53...54*		3,06 m	3,17, 2,83, 2,72, 2,52	0,66s CH3; 1,79 s H	1,56 sC—CH_2—C	72
IIId	$C_{15}H_{20}N_2$	119...120*	1605 arom.	3,17 m	3,23, 2,78, 3,06 m	7,4...7,1 m C_6H_5; 1,96 s H	2,10 sC—CH_2—C	79
IIIe	$C_{16}H_{22}N_2$	91...92*	1605 arom.	3,21 m	3,10, 3,00, 2,85, 2,66	7,4...7,2m C_6H_5; 1,86s CH_3	1,85 sC—CH_2—C	85
IIIg	$C_{12}H_{20}N_2O$	64...65	3492, 3373, 3244, 3078 OH	3,07 m	3,20, 2,73, 2,99, 2,66	1,55 t C—CH2—C; 1,93 s H	1,63 s	69
IVa	$C_{18}H_{28}N_6$	210...212*	1635 C=N	3,16 m	3,38, 3,03, 3,07, 2,95	3,44s H; 2,45 sH		79
IVb	$C_{22}H_{36}N_6$	175...176	1635 C=N	3,18 m	3,34, 3,20, 3,05, 2,86	0,99s CH3; 1,26 s 2Hfrom CH_3, 2,98 1H fromCH3		67
IVc	$C_{20}H_{32}N_6$	185...186*	1630 C=N	3,12 m	3,36, 2,88, 3,07, 2,96	0,82s CH3; 2,52 s H		74
IVd	$C_{30}H_{36}N_6$	246...247	1624 C=N	3,20 m	3,70, 3,35, 3,27, 2,97	7,50...7,10 m C_6H_5, 3,19 s H		73

Hydrazones IIa-e were prepared by heating diazahomoadamantanones Ia-f in an excess of hydrazine hydrate. The ester group of ketoester If undergoes hydrazinolysis in these conditions, and instead of hydrazone IIf, 1-(2-hydroxyethyl)-3,6-diazahomoadamantan-9-one (IIg) is formed, as indicated by the absence of an absorption band of stretching vibrations of the ester carbonyl in its IR spectrum. 1-(2-Hydroxyethyl)-3,6-diazahomoadamantan-9-one (Ig) itself is prepared by alkaline hydrolysis of ketoester If. Its IR spectrum does not contain the absorption band of ester carbonyl, while the absorption band of stretching vibrations of a ketone carbonyl group appears with two bands in the 1712 and 1697 cm^{-1} region. This type of absorption of the ketone group is probably due to the possibility of formation of a hydrogen bond with the hydroxyl group hydrogen.

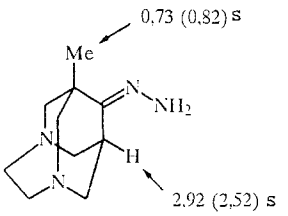
The number of carbon atoms separating functional groups in keto alcohol Ig favors the formation of a cyclic structure, but judging by the intensity of the carbonyl group absorption bands, it primarily remains in the chain form.

Wolff—Kishner melting of hydrazones IIb-e, g with a base causes the formation of 3,6-diazahomoadamantane derivatives with one IIIc-e, g or two IIIb substituents in nodal positions. Unsubstituted 3,6-diazahomoadamantane (IIIa) cannot be obtained with this method, since the unsubstituted diazahomoadamantanone hydrazone IIa is easily converted into azine IVa when heated above 70°C. For this reason, azine IVa is the basic product of the reaction of melting hydrazone IIa with a base. The other hydrazones IIb-d are also converted into the corresponding azines IVb-d when heated, but a higher temperature (above 150°C) is required for this.

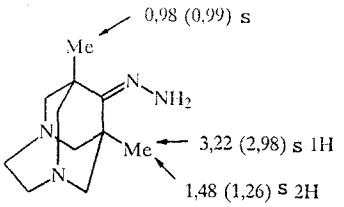
The formation of hydrazones IIa-e, g and azines IVa-d is confirmed by the IR spectra (Table 1), which exhibit characteristic absorption bands of stretching vibrations of an azomethine group in the 1660-1620 cm^{-1} region. The ESR spectra provide interesting information on the steric structure of these compounds (see Table 1). A comparison of the chemical shifts of the protons and methyl group protons in the nodal positions of the hydrazones, reported below, and in parentheses, azines, unsubstituted IIa and IVa, monomethyl IIc and IVc, and dimethyldiazahomoadamantanones IIb and IVb suggests that the methyl group in compounds IIc and IVc occupy the E-position with respect to the NH_2 group.



IIa (IVa)



IIc (IVc)



IIb (IVb)

There are intense, and in many cases maximum, molecular ion (M^+) peaks in the spectra of compounds II-IV (Table 2). Fragmentation of M^+ of compounds II-IV causes the formation of the nitrogen containing ions $[C_4H_{10}N]^+$ (*m/z* 72) and $[C_3H_8N]^+$ (*m/z* 58), characteristic of decomposition of the 3,6-diazahomoadamantane backbone [3].

Decomposition of the M^+ of hydrazones II and azines IV is similar to decomposition of the corresponding 1,3-diazaadamantane derivatives [4], i.e., it takes place with rupture of the N—N bond, formation of $[M\text{-}NH_2]^+$ and $[M\text{-}N\text{—}Ad]^+$ ions and subsequent cleavage of nitrogen-containing molecules $C_nH_{2n+1}N$ (n = 1-3). The most intense ion peaks corresponded to elimination of molecules of C_2H_5N.

EXPERIMENTAL

The IR spectra were recorded on a Specord 71-IR spectrometer (in petrolatum), the ESR spectra were recorded on a Bruker M-250 (in $CDCl_3$) with TMS as internal standard, and the mass spectra were obtained on a Kratos MS-80 with direct

TABLE 2. Mass Spectra of Compounds I-IV

Compound	m/z (relative intensity, %)*
Ig	210 (100), 180 (10), 179 (50), 137 (11), 136 (26), 72 (8), 58 (37), 57 (9), 55 (8), 42 (10), 41 (8)
IIa	180 (79), 121 (33), 95 (26), 82 (20), 72 (84), 69 (28), 58 (100), 57 (51), 56 (32), 55 (47), 42 (34)
IIc	194 (32), 136 (6), 124 (9), 109 (6), 82 (6), 72 (85), 69 (8), 58 (100), 57 (12), 56 (14), 55 (12)
IId	256 (100), 255 (71), 115 (61), 103 (50), 91 (48), 77 (47), 72 (99), 71 (53), 58 (84), 57 (56), 56 (55)
IIe	270 (37), 212 (10), 115 (6), 103 (6), 91 (7), 77 (6), 72 (100), 58 (48), 57 (7), 56 (9), 55 (6)
IIId	228 (42), 170 (20), 115 (22), 91 (38), 77 (25), 72 (17), 58 (100), 57 (24), 56 (19), 42 (49), 41 (28)
IIIe	242 (100), 241 (20), 198 (17), 184 (47), 170 (36), 169 (21), 91 (21), 58 (38), 57 (24), 45 (59), 42 (37)
IIIg	196 (100), 165 (57), 152 (25), 138 (30), 136 (22), 122 (46), 108 (24), 95 (33), 72 (22), 58 (42), 42 (22)
IVa	328 (47), 192 (18), 164 (41), 121 (25), 94 (16), 72 (100), 58 (31), 55 (14), 43 (18), 42 (51), 41 (31)
IVc	356 (27), 178 (27), 149 (23), 135 (36), 72 (100), 58 (31), 55 (24), 54 (24), 53 (26), 42 (37), 41 (24)

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

introduction of the sample in the ion source, ionizing electron energy of 70 eV, ionization temperature of 150°C, and perfluorokerosene as the standard. The resolution was $M/\Delta M = 10{,}000$.

The properties of compounds II-IV are reported in Tables 1 and 2.

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

3,6-diazahomoadamantan-9-one (Ia). A mixture of 1.68 g (10 mmole) of tetramethylenediethylenetetramine and 1.16 g (20 mmole) of glacial acetic acid in 5 ml of acetone was heated at 60-70°C for 5 min and stirred until the tetramethylenediethylenetetramine disappeared. The reaction mass was concentrated in a vacuum and extracted with hot heptane. The extract was passed through a layer of anhydrous Al_2O_3. The extracting agent was vacuum distilled and the dry residue was sublimated, yielding 0.45 g of diazahomoadamantanone Ia.

1-(2-Acetylhydroxyethyl)-3,6-diazahomoadamantan-9-one (If). A solution of 11.22 g (78 mmole) of 5-acetylhydroxy-2-pentanone, 12.76 g (78 mmole) of tetramethylenediethylenetetramine, and 14.42 g (240 mmole) of acetic acid in 40 ml of isopropyl alcohol was stirred for 2 h at room temperature, evaporated dry, the residue was extracted with hot heptane (5 × 100 ml), the extracting agent was distilled off, and the sediment was crystallized from heptane, yielding 7.30 g of acetylhydroxyethyldiazahomoadamantanone If.

2-(2-Hydroxyethyl)-3,6-diazahomoadamantan-9-one (Ig). A solution of 0.40 g (1.6 mmole) of acetylhydroxyethyldiazahomoadamantanone (If) and 0.06 g (1.6 mmole) of sodium hydroxide in 2 ml of 80% ethanol was stirred for 1.5 h, evaporated, the residue was extracted with toluene, the extracting agent was evaporated, and the sediment was crystallized from toluene, yielding 0.32 g of hydroxyethyldiazahomoadamantanone Ig.

3,6-Diazahomoadamantan-9-one hydrazone (IIa). While heating, 0.16 g (0.96 mmole) of diazahomoadamantanone (Ia) was dissolved in 2 ml of 80% hydrazine hydrate and left at ambient temperature for 3 days. The reaction mass was evaporated dry, and the residue was extracted with ether (5 × 6 ml), yielding 0.14 g of diazahomoadamantanone hydrazone IIa after evaporation of the extracting agent.

1,8-Dimethyl-3,6-diazahomoadamantan-9-one hydrazone (IIb). A solution of 0.97 g (5 mmole) of dimethyldiazahomoadamantanone (Ib) in 10 ml of an 80% solution of hydrazine hydrate was heated for 3 h while boiling, the reaction mixture was evaporated dry, and the residue was recrystallized from toluene, yielding 0.95 g of dimethyldiazahomoadamantanone hydrazone IIb.

1-Methyl-3,6-diazahomoadamantan-9-one hydrazone (IIc). Analogously, 0.85 g of methyldiazahomoadamantanone hydrazone IIc was obtained from 0.9 g (5 mmole) of methyldiazahomoadamantanone Ic.

1-Phenyl-3,6-diazahomoadamantan-9-one hydrazone (IId). Here 2.19 g of phenyldiazahomoadamantanone hydrazone IId was obtained from 2.42 g (10 mmole) of phenyldiazahomoadamantanone Id and 25 ml of 80% hydrazine hydrate after recrystallization from heptane.

1-Phenyl-8-methyl-3,6-diazahomoadamantan-9-one hydrazone (IIe). Similarly, 1.13 g of phenylmethyldiazahomoadamantanone hydrazone IIe was obtained from 1.28 g (5 mmole) of phenylmethyldiazahomoadamantanone Ie and 15 ml of hydrazine hydrate after recrystallization from heptane while dissolving the initial ketone Ie in 5 m of isopropyl alcohol and heating for 36 h.

1-(2-Hydroxyethyl)-3,6-diazahomoadamantan-9-one (IIg). Here 0.50 g (2 mmole) of acetylhydroxyethyldiazahomoadamantanone IIf was dissolved in 5 ml of 80% hydrazine hydrate at 30-40°C and left for 7 days at ~20°C, evaporated dry in a vacuum at 30-40°C, and the residue was crystallized from toluene, yielding 0.40 g of hydroxyethyldiazahomoadamantanone hydrazone IIg.

1,8-Dimethyl-3,6-diazahomoadamantane (IIIb). A mixture of 0.21 g (1 mmole) of dimethyldiazahomoadamantanone hydrazone IIb and 0.3 g of powdered potassium hydroxide was heated at 220-240°C for 2 h. The cooled melt was extracted with ether (3 × 20 ml) and the solvent was distilled off. After purification by sublimation, 0.14 g of dimethyldiazahomoadamantane IIIb was obtained.

1-Methyl-3,6-diazahomoadamantane (IIIc). Similarly, 0.24 g of methyldiazahomoadamantane IIIc was obtained from 0.39 g (2 mmole) of methyldiazahomoadamantanone hydrazone IIc when melted with 0.59 g of powdered potassium hydroxide.

1-Phenyl-3,6-diazahomoadamantane (IIId). Here 0.3 g of phenyldiazahomoadamantane IIId was obtained from 0.44 g (1.8 mmole) of phenyldiazahomoadamantanone IId and 0.5 g of potassium hydroxide after sublimation.

1-Phenyl-8-methyl-3,6-diazahomoadamantane (IIIe). Here 0.16 g of phenylmethyldiazahomoadamantane IIIe was obtained after sublimation from 0.22 g (0.8 mmole) of phenylmethyldiazahomoadamantanone hydrazone IIe and 0.25 g of potassium hydroxide while heating for 3 h.

1-(2-Hydroxyethyl-3,6-diazahomoadamantane (IIIg). Here 0.18 g of hydroxyethyldiazahomoadamantane IIIg was obtained after recrystallization from ether from 0.30 g (1.3 mmole) of hydroxyethyldiazahomoadamantanone hydrazone IIg and 0.40 g of potassium hydroxide while heating to 220°C.

1,2-Bis-(3,6-diazahomoadamantalidene-9)hydrazine (IVa). A solution of 0.1 g (6.1 mmole) of diazahomomadamantanone Ia in 5 ml of 80% hydrazine hydrate was heated at boiling for 3 h, evaporated dry, and the residue was vacuum sublimated, yielding 0.78 g of diazahomoadamantanone azine IVa.

1,2-Bis-(1-methyl-3,6-diazahomoadamantalidene-9)hydrazone (IVc). Similarly, 0.66 g of methyldiazahomoadamantanone IVc was obtained from 0.9 g (5 mmole) of methyldiazahomoadamantanone Ic and 5 ml of 80% hydrazine hydrate.

1,2-Bis-(1,8-dimethyl-3,6-diazahomoadamantalidene-9)hydrazine (IVb). Here 0.2 g (0.96 mmole) of dimethyldiazahomoadamantanone hydrazone IIb was heated at 180°C for 30 min. The dry residue was extracted with toluene, and the extracting agent was distilled off. After recrystallization from heptane, 0.12 g of dimethyldiazahomoadamantanone azine IVb was obtained.

1,2-Bis-(1-phenyl-3,6-diazahomoadamantalidene-9)hydrazine (IVd). Here 0.07 g of phenyldiazahomoadamantanone IVd was obtained from 0.1 g (0.4 mmole) of phenyldiazahomoadamantanone hydrazone IId at 170°C.

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