HETEROADAMANTANES AND THEIR DERIVATIVES.
21.* SYNTHESIS OF THIOUREAS OF THE 3,6-DIAZAHOMOADAMANTANE SERIES

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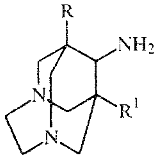
Unsubstituted and phenyl-substituted thioureas were obtained by the action of benzoyl isothiocyanate and phenyl isothiocyanate on amino-substituted diazahomoadamantanes.

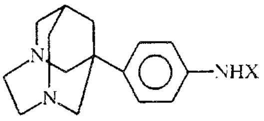
Thiourea derivatives find extensive application in practice. Respiratory stimulators, diuretics, analgesics, and other pharmacological agents have been found among representatives of this class of compounds. Many substituted thioureas exhibit herbicidal, fungicidal, and nematocidal activity and are used in combatting pests of agricultural crops. In addition, they find application as vulcanization accelerators, corrosion inhibitors, antioxidants, etc.

A study of adamantane derivatives in order to search for compounds that have useful properties in a practical respect demonstrated the promising character of the utilization of di- and triazaadamantylthioureas as antifogging agents in the development of photographic materials [2, 3]. In our paper we therefore describe the synthesis of thioureido derivatives of 3,6-diazahomoadamantane in order to find the areas of their practical application.

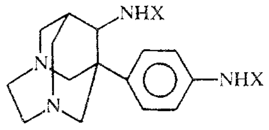
To synthesize thioureas of the 3,6-diazahomoadamantane series we used, as starting compounds, amines Ia-e, as well as amine If and diamine Ig, which we previously obtained either by reduction of oximes with an Ni–Al alloy (50:50) [4] or by reduction of nitro derivatives with hydrazine hydrate without a catalyst [5].



Ia-e



Ia-f IIIf



Ig-IIIg

Ia-e a R = H, R^1 = Me; b R = H, R^1 = Ph; c R = H, R^1 = CH_2CH_2OH; d R = H, R^1 = p-$CH_2C_6H_4OH$;
f R = R^1 = Me; If,g X = H; IIf,g X = $CSNH_2$; IIIf,g X = CSNHPh

The investigated transformations of the indicated amines are presented in the diagram in the case of Ia-e. (See scheme at the middle of the next page.)

Benzoylthioureas are obtained by the action on amines Ia, b, e-g of benzoyl isothiocyanate [6] formed *in situ* from benzoyl chloride and ammonium thiocyanate in acetone [7]. The benzoylthioureas are treated, without isolation, with an aqueous alkali solution with slight heating, and unsubstituted thioureas IIa, b, e-g of the 3,6-diazahomoadamantane series.

The reaction of equimolar amounts of phenyl isothiocyanate with solutions of amines Ia-g in toluene leads to phenyl-substituted thioureas IIIa-g.

The properties and yields of products II and III are presented in Table 1. High and, in a number of cases, maximum intensities of the M^+ ion peaks are characteristic for their mass spectra (see Table 2). The fragmentation of the M^+ ions of IIa, b, e and IIIa-c leads to the development of both ions that are usually observed for 3,6-diazahomoadamantane derivatives and ions that are formed as a result of cleavage of the functional substituent.

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*For Communication 20 see [1].

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TABLE 1. Characteristics of the 3,6-Diazahomoadamantylthioureas

Compound	Empirical formula	mp, °C	IR spectrum, ν, cm^{-1}	Yield, %
II a	$C_{11}H_{20}N_4S$	213...214	3440, 3350, 3250 (NH), 1635 (NCSN)	85
II b	$C_{16}H_{22}N_4S$	202...203	3360, 3280, 3180 (NH), 1595 arom. 1620 (NCSN)	75
II e	$C_{11}H_{22}N_4S$	207...208	3400, 3240, 3060 (NH), 1635 (NCSN)	54
IIf	$C_{16}H_{22}N_4S$	217...219	3366 (NH), 1592 arom. 1552 (NCSN)	68
IIg	$C_{17}H_{24}N_6S_2$	160...162	3420, 3310 (NH), 1605 arom. 1652 (NCSN)	58
IIIa	$C_{17}H_{24}N_4S$	143...145	3390, 3150 (NH), 1580 arom., 1520 (NCSN)	71
IIIb	$C_{22}H_{26}N_4S$	169...170	3380, 3130 (NH), 1600 arom. 1535 (NCSN)	86
IIIc	$C_{17}H_{26}N_4OS$	94...95	3278 (OH, NH), 1600 arom. 1539 (NCSN)	63
IIId	$C_{23}H_{28}N_4OS$	159...160	1590 arom., 1510 (NCSN)	85
IIIe	$C_{18}H_{26}N_4S$	154...155	1580 arom., 1520 (NCSN)	87
IIIf	$C_{22}H_{26}N_4S$	177...178	3366 (NH), 1591 arom. 1521 (NCSN)	79
III g	$C_{29}H_{32}N_6S_2$	165...167	3385, 3190 (NH), 1595 arom. 1535 (NCSN)	77

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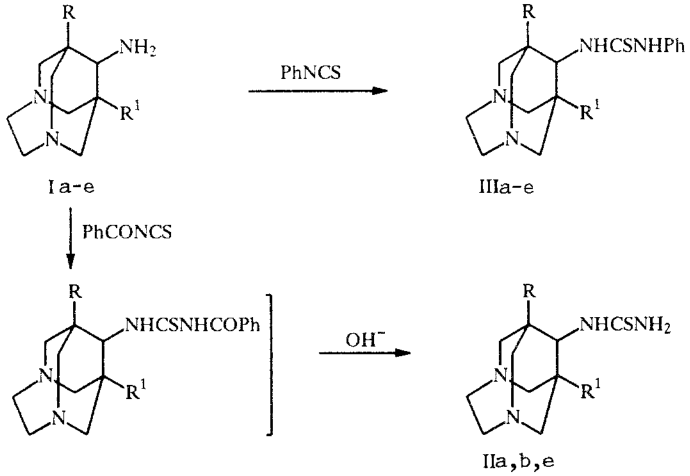
*Compound IIIa was recrystallized from THF, IIIb, c, e were recrystallized from toluene, and the remaining compounds were recrystallized from isopropyl alcohol.



Peaks of $[C_2H_4N]^+$ (m/z 42), $[C_3H_8N]^+$ (m/z 58), and $[C_4H_{10}N]^+$ (m/z 72) ions are typical for the mass spectra of all of the 3,6-diazahomoadamantane derivatives [8]. The peaks of the $[C_4H_{10}N]^+$ ions have the maximum intensity in the spectra of IIa, b, e. The processes involved in the formation of the $[M - C_3H_8N]^+$ and $[M - C_4H_{10}N]^+$ ions proved to be characteristic and had low intensities. Peaks of these ions are present only in the spectra of IIa, b, e. Detachment of the functional substituent to give the $[M - NHCSNH_2]^+$ ion is characteristic for thioureas IIa, b, e. The subsequent fragmentation of the latter ion proceeds with the elimination of nitrogen-containing C_nH_{2n+1} molecules (n = 2-4). In addition to these ions, peaks of ions that are due to cleavage of the functional substituent are present in the spectra of IIa, b, e: $[M - HS]^+$, $[M - H_2S]^+$, $[M - NH_3]^+$, and $[SCNH_2]^+$ (m/z 60) are present in the spectra of IIa, b, e.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Bruker IFS-113v spectrometer. The low- and high-resolution mass spectra were obtained with a Finnigan MRT-90 spectrometer with direct introduction of the samples into the ion source at an accelerating voltage of 5.0 eV, a cathode emission current of 100 μA, an ionizing-electron energy of 70

TABLE 2. Mass Spectra of II and III

Compound	m/z (ℓ_{rel}, %)
IIa	240 (100), 206 (8), 165 (10), 122 (10), 108 (15), 93 (8), 72 (47), 58 (12), 44 (18), 42 (20), 41 (9)
IIb	302 (100), 227 (8), 170 (13), 156 (7), 155 (11), 115 (7), 113 (10), 91 (15), 72 (28), 58 (7), 42 (11)
IIe	254 (100), 135 (10), 122 (15), 113 (14), 107 (12), 72 (51), 58 (10), 57 (10), 55 (13), 42 (16), 41 (12)
IIIa	316 (10), 258 (54), 229 (19), 198 (12), 184 (25), 171 (32), 159 (19), 149 (25), 135 (42), 72 (100)
IIIb	378 (2), 285 (24), 135 (13), 93 (75), 92 (9), 91 (11), 77 (16), 72 (100), 66 (23), 65 (15), 42 (21)
IIIc	346 (13), 312 (22), 263 (10), 253 (30), 195 (10), 138 (10), 93 (100), 72 (43), 66 (20), 42 (7)

eV, and an ionizing-chamber temperature of 200°C; perfluorinated kerosene was used as the standard, and resolution M/ΔM = 10,000.

The results of elementary analysis for C, H, N, and S were in agreement with the calculated values.

9-Thioureido-1-methyl-3,6-diazahomoadamantane (IIa). A 0.14-g (0.99 mmole) sample of benzoyl chloride was added to a solution of 0.09 g (1.18 mmole) of ammonium thiocyanate in 2 ml of acetone, and the resulting precipitate was removed by filtration. A solution of 0.15 g (0.83 mmole) of 9-amino-1-methyl-3,6-diazahomoadamantane Ia in 2 ml of acetone was added to the filtrate, and the mixture was heated on a water bath at 60-70°C for 15 min. A solution of 0.14 g (2.48 mmole) of KOH in 2 ml of water was then added with stirring, and the mixture was heated at 60-70°C for 30 min. The precipitated IIa was removed by filtration and recrystallized from isopropyl alcohol. The yield was 0.17 g.

Compounds IIb-g were similarly obtained. The solvents for recrystallization are indicated in Table 1.

1-Phenyl-3-(1-phenyl-3,6-diazahomo-9-adamantyl)thiourea (IIIb). A 0.67-g (5.00 mmole) sample of phenyl isothiocyanate in 5 ml of toluene was added with stirring at room temperature to a solution of 1.22 g (5.00 mmole) of 3-amino-1-phenyldiazahomoadamantane Ib in 30 ml of toluene, and the reaction mixture was allowed to stand at room temperature for 4 h. The precipitated IIIb was removed by filtration, washed with toluene (2 × 5 ml), and dried. The yield was 1.62 g.

Compounds IIIa, c-g were similarly obtained.

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