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SYNTHESIS AND CONVERSIONS OF POLYHEDRAL COMPOUNDS

18.* CONVERSION OF 1,3-DIAZA- AND 1,3,5-TRIAZA-ADAMANTANES INTO NEW NITROGEN-CONTAINING POLYHEDRAL COMPOUNDS UNDER THE INFLUENCE OF DIBASIC ACID DICHLORIDES

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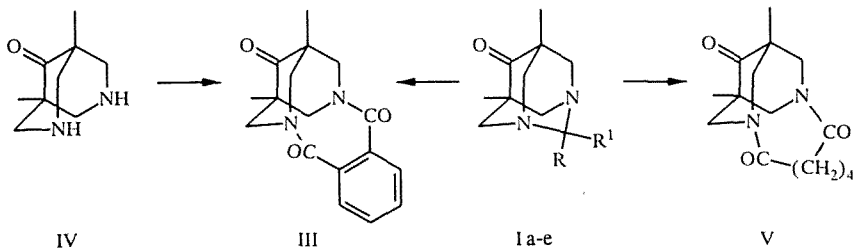
Derivatives of 1,3-diaza- and 1,3,5-triazaadamantanes react with dicarboxylic acid dichlorides, forming derivatives of new heteropolyhedral compounds containing a dicarboxylic acid residue in place of CH_2 or CRR^1 of the methylidenamino fragment of the azaadamantanes.

It was shown previously that the interaction of 1,3-diaza- and 1,3,5-triazaadamantanes with monocarboxylic acid chlorides yields the 3,7-diacyl derivatives of the corresponding azabicyclo[3.3.1]nonanes [2-5]. No information has been reported in the literature on the interactions of such azaadamantanes with dicarboxylic acid dichlorides. Owing to the bifunctionality of these compounds, we can expect different reactions, including the formation of new nitrogen-containing polyhedral compounds. We have investigated the reaction of 5,7-dimethyl-6-oxo-1,3-diazaadamantane (Ia), its 2-mono- and 2,2-disubstituted derivatives (Ib-e) [6], and 7-nitro-1,3,5-triazaadamantane (II) with the dichlorides of phthalic and adipic acids. Upon the interaction of the diazaadamantane Ia with phthalic acid dichloride in a 1:1 ratio in the presence of sodium bicarbonate in aqueous dioxane or in the presence of triethylamine in dioxane, a derivative of a previously unknown benzodiazatricyclotridecane III is formed, containing a phthalic acid residue in place of the CH_2 of the methylenediamino fragment of the diazaadamantane Ia. Compound III is also formed by the action of phthalic acid dichloride on 2-ethyl- (Ib), 2,2-dimethyl- (Ic), 2-spirocyclohexyl- (Id), or 2-phenyl-5,7-dimethyl-6,-oxo-1,3-diazaadamantane (Ie), and also on 1,5-dimethyl-9-oxo-3,7-diazabicylo[3.3.1]nonane (IV)



IV III Ia-e V

Ia,b,e R=H; Ia R^1=H; Ib R^1=C_2H_5; Ic R=R^1=CH_3; Id RR^1=*c*-C_6H_{11}; Ie R^1=C_6H_5

Analogously, in the interaction of the diazaadamantanes Ia-c with adipic acid dichloride in the presence of triethylamine in dioxane, a derivative of diazatricyclopentadecane V is formed, containing an adipic acid residue in place of the CH_2 or CRR^1 groups of the indicated diazaadamantanes.

*For Communication 17, see [1].

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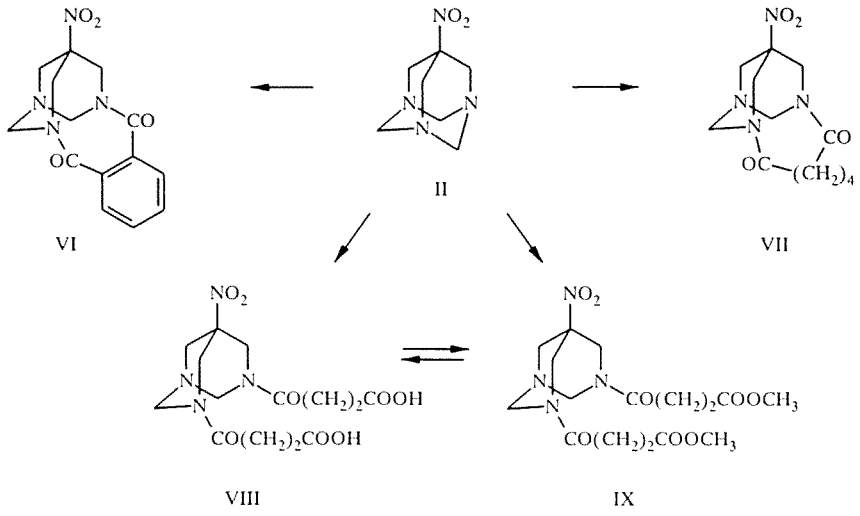
These results indicate that, regardless of the presence or absence of substituents in the methylenediamino fragment of the diazaadamantane, the action of phthalic or adipic acid dichloride results in rupture of N–C bonds in this group, forming derivatives of benzodiazatricyclotridecane III and diazatricyclopentadecane V, respectively.

Interaction of 7-nitro-1,3,5-triazaadamantane (II) with phthalic or adipic acid dichloride under the above-indicated conditions results in the formation of derivatives of new heteropolyhedral compounds — benzotriazatricyclotridecane VI and triazatricyclopentadecane VII, respectively. In this case as well, the CH_2 of the methylenediamino group of the triazaadamantane II is replaced by a phthalic or adipic acid residue.



It was established that the best yield of compound VII is obtained by using a large volume of dioxane (THF or ethyl acetate may be used in place of the dioxane), and by dropwise addition of equimolar quantities of the adipic acid dichloride and the triazaadamantane II.

In contrast, in the interaction of the triazaadamantane II with succinic acid dichloride under the conditions used in the reaction of the triazaadamantane II with monocarboxylic acid chlorides [4], we did not recover the corresponding heteropolyhedral compound from the reaction medium, but only 3,7-bis(β-carboxypropionyl)-1,3,7-triazabicyclo[3.3.1]nonane (VIII), with a yield of only 16%. The compound VIII, by reaction with diazaomethane, is converted to the corresponding dimethyl ester IX, which is also obtained by interaction of the triazaadamantane II with the acid chloride of monomethyl succinate under the conditions described in [4]. Hydrolysis of the ester groups of the dimethyl ester IX leads to the triazabicyclononane VIII.

In the IR spectra of compounds III and V-VII there are bands corresponding to absorption by C=O of the amide group in the 1640-1670 cm^{-1} region. The molecular weights of III, V, and VI (determined by mass spectrometry) and the molecular weight of VII (determined cryoscopically in camphor) matched the calculated values. Of the PMR spectra of the heteropolyhedral compounds, we were able to decipher only the spectrum of compound III. In this compound, the four axial protons of the methylene groups of the diazabicyclononane framework are manifested in the form of two doublets, and the four equatorial protons in the form of a single doublet, whereas in the spectra of 3,7-diacyl derivatives of 3,7-diazabicyclo[3.3.1]nonane, these protons are represented in the form of two doublets [5].

EXPERIMENTAL

The IR spectra were taken in white mineral oil on UR-20 and Specord IR spectrometers. The PMR spectra were obtained in a Varian T-60 instrument in $CDCl_3$, internal standard TMS. The molecular weights were determined by mass spectrometry in an MKh-1320 instrument with direct introduction of the sample into the ion source. The ionizing electron energy was 60 eV. The course of the reaction and the purity of the substances were monitored by TLC on Silufol UV-254

plates in the following systems: n-butanol–acetic acid–water, 3:1:1 (A); n-propanol–water, 7:3 (B) and 1:1 (C). Development by ninhydrin.

The elemental analyses of compounds III and V-IX for C, H, and N matched the calculated values.

3,4-Benzo-8,10-dimethyl-2,5,9-trioxo-1,6-diazatricyclo[6.3.1.1^{6,10}]tridecane (III, $C_{17}H_{18}N_2O_3$). ***A.*** To a mixture of 0.9 g (5 mmoles) of the diazaadamantane Ia and 1.05 g (12.5 mmoles) of $NaHCO_3$ in 5 ml of water and 150 ml of dioxane, 1 g (5 mmoles) of phthalic acid dichloride was added over the course of 3 h. The reaction mixture was stirred at 2 h at room temperature and then filtered. The filtrate was vacuum-distilled, 15 ml of water was added to the residue, and the resulting crystals were filtered off, washed with water and $NaHCO_3$ solution and then again with water, vacuum-dried over KOH, and recrystallized from ethanol: mp 293-294°C (from ethanol), R_f 0.62 (A). IR spectrum, cm^{-1}: 1600 (C=C arom.), 1640 (C=O amide), 1700 (C=O ketone). PMR spectrum, cm^{-1} (J in Hz): 0.9 (3H, s, CH_3); 1.02 (3H, s, CH_3); 2.85 (2H, d, J = 14, $2CH_a$–N); 3.0 (2H, d, J = 14, $2CH_a$–N); 4.03 (4H, d, J = 14, $4CH_e$–N); 7.5-8.0 (4H, m, arom. protons). M^+ 298. Yield 1.1 g (70%).

B. To a solution of 0.9 g (5 mmoles) of the diazaadamantane Ia in 150 ml of dioxane, a solution of 1.2 g (12 mmoles) of triethylamine in 10 ml of dioxane and 1.0 g (5 mmoles) of phthalic acid dichloride in 10 ml of dioxane was added over the course of 4 h. The mixture was stirred for an additional 2 h and then processed as in method A. Product mp 293-294°C (from ethanol), R_f 0.62 (A). Yield 0.4 g (34%).

C. Reactions with the diazaadamantanes Ib-e were performed by analogy with method A. In the case of Ie, the dropwise addition was continued for 7 h with a 1/2 reactant ratio; mp 293-294°C, R_f 0.62 (A). Yields of compound III from diazaadamantanes Ib-e were 50, 61, 58, and 31%, respectively.

D. To a mixture of 100 ml of dioxane and 3 ml of water, while stirring, there was added, over a 4-h period, 0.4 g (2.3 mmoles) of the diazabicyclononane IV, 0.5 g (2.5 mmoles) of phthalic acid dichloride, and 0.4 g (5 mmoles) of $NaHCO_3$. The mixture was stirred an additional 2 h and then processed by method A; mp 293-294°C, R_f 0.62 (A). Yield 0.1 g (14%).

10,12-Dimethyl-2,7,11-trioxo-1,8-diazatricyclo[8.3.1.1^{8,12}]pentadecane (V, $C_{15}H_{22}N_2O_3$). ***A.*** To 50 ml of dioxane, there was added, over a 4-h period, 1.8 g (10 mmoles) of the diazaadamantane Ia in 25 ml of dioxane, 2 g (11 moles) of adipic acid dichloride in 25 ml of dioxane, and 2.5 g (25 mmoles) of triethylamine. The reaction mixture was filtered, the solvent was removed under vacuum, and the residue was crystallized from hexane and washed with successively with water, 10% NaOH solution, and water, and then dried. Product mp 276-278°C (from dichloromethane), R_f 0.65 (B). IR spectrum, cm^{-1}: 1650 (C=O amide), 1710 (C=O ketone). M^+ 278. Yield 1.8 g (65%).

B. Reactions with the diazaadamantanes Ib,c were performed by analogy with method A; product mp 276-278°C (from dichloromethane), R_f 0.65 (B). The yield of compound V from the diazaadamantanes Ib,c was 53 and 58%, respectively.

5,6-Benzo-4,7-dioxo-10-nitro-1,3,8-triazatricyclo[6.3.1.1^{3,10}]tridecane (VI, $C_{14}H_{14}N_4O_4$). To a solution of 1.84 g (0.01 mole) of the triazaadamantane II and 3.4 g (0.04 mole) of $NaHCO_3$ in 60 ml of ethyl acetate and 20 ml of water, 2.54 g (0.012 mole) of phthalic acid dichloride was added with mixing over the course of 2 h. The ethyl acetate layer was separated, washed with water, and evaporated under vacuum; the residue was processed by analogy with compound III; mp 151-152°C (from ethanol), R_f 0.65 (B). IR spectrum, cm^{-1}: 1540 (C–NO_2), 1600 (C=C arom.), 1650, 1670 cm^{-1} (C=O amide). M^+ 302. Yield 1 g (33%).

4,9-Dioxo-12-nitro-1,3,10-triazatricyclo[8.3.1.1^{3,12}]pentadecane (VII, $C_{12}H_{18}N_4O_4$). To a mixture of 1.84 g (0.01 mole) of the triazaadamantane II in 300 ml of dioxane, at room temperature with mixing, 2 g (0.011 mole) of adipic acid dichloride in 35 ml of dioxane and 2.5 g (0.025 mole) of triethylamine were added over the course of 4 h. The precipitate was filtered off, washed successively with water, 10% NaOH solution, and water, and then dried; mp 288-290°C (from ethanol), R_f 0.70 (D). IR spectrum, cm^{-1}: 1550 (C–NO_2), 1650 (C=O amide). M 282±18. Yield 1.7 g (62%).

3,7-Bis(β-carboxypropionyl)-5-nitro-1,3,7-triazabicyclo[3.3.1]nonane (VIII, $C_{14}H_{20}N_4O_8$). ***A.*** To a solution of 1.84 g (0.01 mole) of the triazaadamantane II in 100 ml of ethyl acetate and 30 ml of saturated aqueous $NaHCO_3$ solution, 3.55 g (0.03 mole) of succinic acid dichloride was added dropwise with stirring. The aqueous layer was separated and neutralized with HCl; the resulting precipitate was filtered off, washed with 5 ml of water, vacuum-dried over KOH, and recrystallized from acetone and then from water. Product mp 210-212°C (decomp.), R_f 0.65 (B). IR spectrum, cm^{-1}: 1540 (C–NO_2), 1650 (C=O amide), 1725 (COOH), 3560 (OH). Yield 0.6 g (16%).

B. A solution of 4 g (0.01 mole of the triazabicyclononane IX and 2.52 g (0.03 mole) of $NaHCO_3$ was refluxed for 20 min, cooled, neutralized with HCl, extracted with ethyl acetate, and processed in the same manner as compound IX (method A). Product mp 210-212°C (decomp.) from acetone, water; R_f 0.65 (B). Yield 1 g (27%).

3,7-Bis(β-carbomethoxypropionyl)-5-nitro-1,3,7-triazabicyclo[3.3.1]nonane (IX, $C_{16}H_{24}N_4O_8$). ***A.*** To a solution of 1.84 g (0.01 mole) of the triazaadamantane II and 8.4 g (0.1 mole) of $NaHCO_3$ in 80 ml of THF and 20 ml of water, 3.5 g (0.023 mole) of β-carbomethoxypropionic acid chloride was added over the course of 20 min while mixing. The THF layer was separated and evaporated under vacuum. The residue was mixed with 30 ml of water and extracted with ethyl acetate (3 × 10 ml). The extract was washed with water, dried with $MgSO_4$, and evaporated under vacuum. The residue was recrystallized from ethyl acetate; mp 97-98°C, R_f 0.56 (B). IR spectrum, cm^{-1}: 1550 (C−NO_2), 1630, 1650, (C=O amide), 1730 (C=O ester). M^+ 400. Yield 3.8 g (95%).

B. To a solution of 0.5 g (1.3 mmoles) of the triazabicyclononane VIII in 50 ml of methanol and 5 ml of water, 50 ml of an ether solution of diazomethane was added while stirring. The mixture was evaporated under vacuum, and the residue was dissolved in ethyl acetate and processed by analogy with method A. Product mp 97-98°C (from ethyl acetate), R_f 0.56 (B). Yield 0.4 g (77%).

REFERENCES

1. Ts. E. Agadzhanyan, G. G. Minasyan, and G. G. Adamyan, Khim. Geterotsikl. Soedin., No. 1, 106 (1994).
2. Ts. E. Agadzhanyan and G. L. Arutyunyan, Arm. Khim. Zh., **34**, 963 (1981).
3. A. I. Kuznetsov and N. S. Zefirov, Usp. Khim., **8**, 1815 (1989).
4. Ts. E. Agadzhanyan and R. A. Movsesyan, USSR Inventor's Certificate 937,457, Byull. Izobret., No. 23, 109 (1992).
5. Ts. E. Agadzhanyan, A. D. Arutyunyan, and G. L. Arutyunyan, Khim. Geterotsikl. Soedin., No. 7, 9929 (1992).
6. G. S. Saakyan, G. L. Arutyunyan, Ts. E. Agadzhanyan, and R. V. Paronikyan, Arm. Khim. Zh., **39**, 242 (1986).