Chemistry of Heterocyclic Compounds, Vol. 30, No. 3, 1994

SYNTHESIS AND CONVERSIONS OF POLYHEDRAL COMPOUNDS

19.* OPENING OF RING OF 1,3,6-TRIAZOHOMOADAMANTANE BY ELECTROPHILIC REAGENTS

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A new method has been developed for obtaining 8-nitro-1,3,6-triazahomoadamantane. By the action of electrophilic reagents on this compound, N–C bonds of the methylenediamino fragment are ruptured, forming derivatives of 1,4,8-triazabicyclo[4.3.1]decane. Depending on the conditions in reactions of 8-nitro-1,3,6-triazohomoadamantane with benzoyl chloride and nitrous acid, derivatives of either 1,4,8-triazabicyclo[4.3.1]decane or hexahydro-1,4-diazepine may be obtained. The formation of the latter proceeds through the above-mentioned derivatives of 1,4,8-triazabicyclo[4.3.1]decane.

We have developed a new method for obtaining 8-nitro-1,3,6-triazahomoadamantane (I) in high yields by the interaction of nitromethane with ethylenediamine and urotropin in a 1:1:1 ratio in dilute acetic acid (see [2, 3] regarding the preparation of the triazahomoadamantane I by other methods). It was established that in the absence of acetic acid or water, the triazahomoadamantane I is not formed. The best yields of the triazahomoadamantane I are obtained when using 50% acetic acid in a fourfold excess.

Nothing is reported on the literature on the interaction of 1,3,6-triazahomoadamantane with any sort of electrophilic reagent, or on rupture of the N–C bonds of the methylenediamino fragment. With the aim of investigating the possibility of opening a ring of 1,3,6-triazahomoadamantane, and also studying the properties of the resulting products, 8-nitro-1,3,6-triazahomoadamantane I was subjected to the action of a number of electrophilic reagents of different classes, in particular acetic anhydride, acetyl chloride, benzoyl chloride, p-toluenesulfonyl chloride, and nitrous acid.

Upon heating the triazahomoadamantane I in acetic anhydride, 4,8-diacetyl-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (II) is formed; i.e., the action of acetic anhydride results in rupture of N–C bonds of one methylenediamino fragment of the triazahomoadamantane ring, forming the diacetyl derivative of the previously unknown 1,4,8-triazabicyclo[4.3.1]decane. Interaction of the triazahomoadamantane I with acetyl chloride or p-toluenesulfonyl chloride in a ratio from 1:2.5 to 1:3 in a mixture of water with an organic solvent, in the presence of bases, leads to the formation of (respectively) 4,8-diacetyl- (II) and 4,8-ditosyl-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (III). At the same time, upon interaction of the triazahomoadamantane I with benzoyl chloride in the presence of bases, the product obtained, depending on the reaction conditions and the reactant ratio, may be either 4,8-dibenzoyl-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (IV) or 6-benzoylaminomethyl-6-nitro-1,4-dibenzoylhexahydro-1,4-diazepine (V).

Thus, when the reaction is carried out in a mixture of water with ether (reactant ratio 1:2.2, 1.5 h), the dibenzoyltriazabicyclodecane IV precipitates from the reaction mixture. In contrast, when the same reaction is carried out at a mixture of water with ethyl acetate (reactant ratio 1:3.5, 3 h), the dibenzoyldiazepine V is recovered from the ethyl acetate solution.

Analogously, upon interaction of the triazahomoadamantane I with nitrous acid, depending on the reaction conditions, either of two different substances may be formed. When the reaction is carried out in acetic acid, 4,8-dinitroso-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (VI) is formed, and in sulfuric acid, 6-nitro-6-chloromethyl-1,4-dinitrosohexahydro-1,4-diazepine (VII).

*For Communication 18, see [1].

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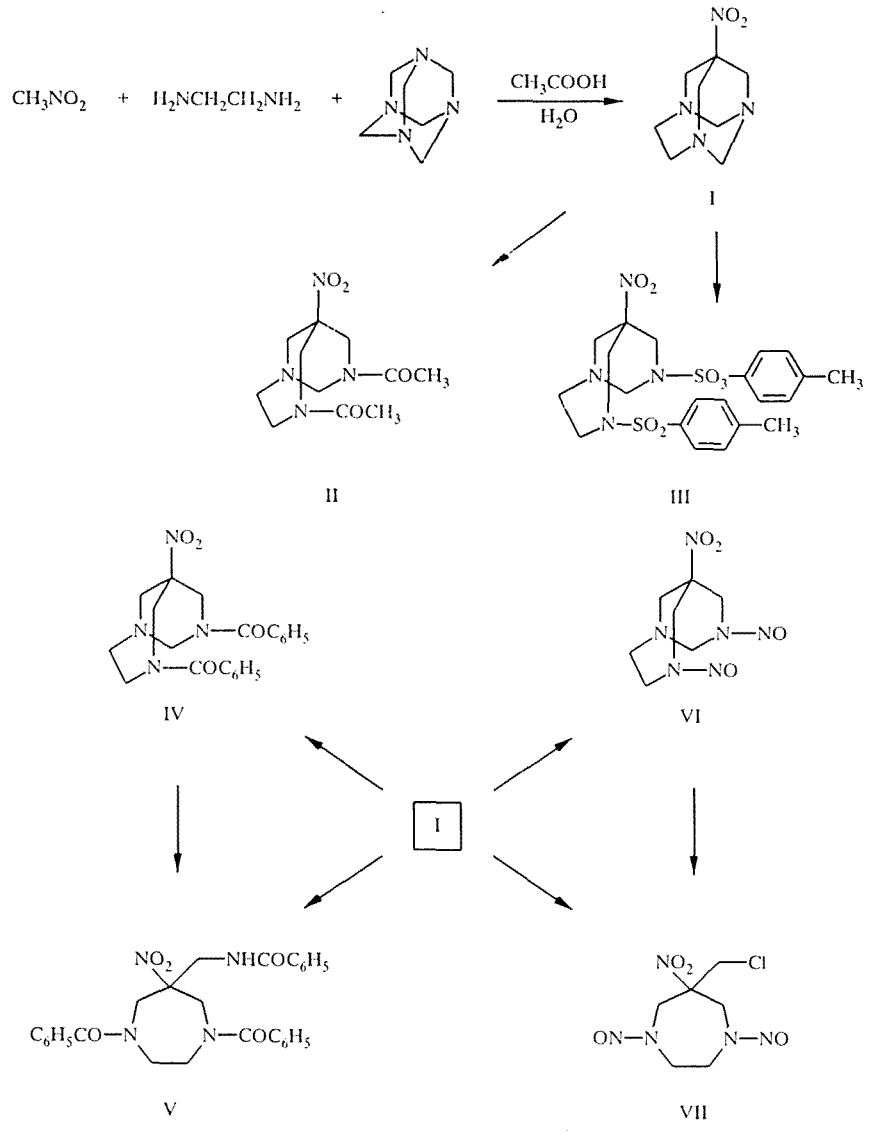

It was established by means of TLC that the hexahydrodiazepines V and VII are obtained through the intermediate formation of the corresponding triazabicyclodecanes IV and VI. This conclusion was further supported by the fact that, under the conditions that we found for the formation of diazepines, compounds IV and VI, when subjected to the action of benzoyl chloride and nitrous acid are converted to the respective hexahydrodiazepines V and VII.

Thus, interaction of the triazahomoadamantane I with carboxylic and arylsulfonic acid chlorides, and also with nitrous acid, leads to rupture of N–C bonds of one methylenediamino fragment of the 1,3,6-triazahomoadamantane, forming the corresponding 4,8-disubstituted 1,4,8-triazabicyclo[4.3.1]decane. (See [4-6] regarding the rupture of N–C bonds of one methylenediamino fragment of 7-nitro-1,3,5-triazaadamantane under the action of these electrophilic reagents, forming the corresponding 3,7-disubstituted 1,3,7-triazabicyclo[3.3.1]nonane.) On the other hand, the action of benzoyl chloride or nitrous acid may also lead to rupture of N–C bonds of the NCH_2NCOR and NCH_2NNO fragments in compounds IV and VI, forming derivatives of hexahydro-1,4-diazepine. (See [7] regarding rupture of N–C bonds of these fragments in derivatives of 1,3,7-triazabicyclo[3.3.1]nonane to form derivatives of hexahydropyrimidine.) The molecular weights of the synthesized compounds, as determined by mass spectrometry, matched the calculated values. In the IR spectra of compounds II, IV, and V, bands are observed corresponding to absorption by the CO of the amide group in the 1630-1650 cm^{-1} region; for compound III, absorption of the N–SO_2 group is observed at 1170-1180 cm^{-1}; for compounds VI and VII, absorption of the N–NO group is observed in the 1460-1480 cm^{-1} region. The PMR spectra of the triazahomoadamantanes II, IV, and VI and the dinitrosohexahydrodiazepine VII are complex and difficult to interpret.

EXPERIMENTAL

IR spectra were taken in Specord and UR-20 spectrometers in white mineral oil. PMR spectra were taken in a Varian T-60 instrument, internal standard TMS. Mass spectra were taken in an MKh-1320 spectrometer. The course of the reaction and the purity of the substances were monitored by TLC on Silufol UV-254 plates in the following systems: (A) n-propanol–water, 7:3; (B) acetone–hexane, 1:1; (C) acetone–hexane, 2:3.

Elemental analyses of compounds I-VII for C, H, N, S, and Cl matched the calculated values.

8-Nitro-1,3,6-triazahomoadamantane(I, $C_8H_{14}N_4N_2$). A. A mixture of 14 g (0.1 mole) of urotropin in 24 ml of water was heated until the urotropin was completely dissolved; then, 6.1 g (0.1 mole) of nitromethane, 6 g (0.1 mole) of ethylenediamine, and 24 g (0.4 mole) of acetic acid were added. A violent reaction, accompanied by a rise of temperature and the development of color in the mixture, continued for 1 h. After cooling, the mixture was extracted with benzene (5 × 150 ml). The benzene solution was washed with water, dried with magnesium sulfate, and evaporated. The remaining yellow crystals were recrystallized from acetone. Obtained 12 g (66%) of compound I, mp 190-191°C, R_f 0.42 (A). IR spectrum, cm^{-1}: 1350, 1550 (C–NO_2). M^+ 198. PMR spectrum ($CDCl_3$), ppm (J in Hz): 3.13 (4H, s, 4.5-CH_2); 3.3-3.65 (6H, m, 7, 9, 11-CH_2); 3.47 (2H, d, J = 14 Hz, 2, 10-CH_a); 4.01 ppm (2H, d, J = 14 Hz, 2, 10-CH_e).

B. The reaction was performed in the same manner as in method A, but with slight changes in conditions: a) In the absence of acetic acid and water, no triazaadamantane was formed; b) when using 12 g (0.2 mole) or 6 g (0.1 mole) of acetic acid, the respective yields of I were 54% and 51%; compare with method A; c) when using half the quantity of water (12 ml instead of 24 ml in method A), the yield of compound I was 23%.

4,8-Diacetyl-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (II, $C_{11}H_{18}N_4O_4$). A. A solution of 4.95 g (0.025 mole) of the triazahomoadamantane I in 16.6 ml of acetic anhydride was heated on a water bath for 35 min. Then 160 ml of water was added, and the mixture was evaporated to dryness under vacuum. The residue was dissolved in 150 ml of ethyl acetate; the ethyl acetate solution was washed with a 10% sodium carbonate solution and then with water, dried over magnesium sulfate, and evaporated. The residue was crystallized from hexane and recrystallized from acetone. Obtained 4.5 g (66.7%) of II, mp 127-128°C, R_f 0.37 (A). IR spectrum, cm^{-1}: 1350, 1360, 1370 (C–NO_2), 1650 (C=O amide). M^+ 270.

B. To a solution of 1.98 g (0.01 mole) of the triazahomoadamantane I in 70 ml of ethyl acetate and 30 ml of water, 4.2 g (0.05 mole) of sodium bicarbonate was added. Then, 2 g (0.025 mole) of acetyl chloride was added dropwise over the course of 30 min at room temperature, while stirring. The ethyl acetate layer was washed with water, dried with magnesium sulfate, and evaporated; the residual oil was triturated with ether (3 × 50 ml). The resulting crystals were filtered off, washed with ether, and recrystallized from acetone. Yield 1.35 g (50%) of II, mp 127-128°C, R_f 0.37 (A).

4,8-Ditosyl-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (III, $C_{21}H_{26}N_4O_6S_2$). To a mixture of 5.94 g (0.03 mole) of the triazahomoadamantane I in 210 ml of dioxane, 70 ml of water, 5 g of sodium chloride, and 16 g (0.15 mole) of sodium carbonate, a 14.3-g quantity (0.075 mole) of p-toluenesulfonyl chloride was added in parts over the course of 6 h. The mixture was stirred for another 30 min, and the dioxane layer was decanted. The dioxane was evaporated under vacuum, and the residue was triturated with 100 ml of a 5% sodium bicarbonate solution. The resulting crystals were filtered off and washed first with water to neutral reaction, then with 50 ml of ethanol. Obtained 14 g (94.5%) of III, mp 200-201°C, R_f 0.34 (B). IR spectrum, cm^{-1}: 1180 (N–SO_2), 1350, 1550 (C–NO_2), 1600 (C=C arom.). M^+ 494.

4,8-Dibenzoyl-6-nitro-1,4,8-triazatricyclo[4.3.1]decane (IV, $C_{21}H_{22}N_4O_4$). To a solution of 4.95 g (0.025 mole) of the triazahomoadamantane I in 100 ml of water and 300 ml of ether, 7 g (0.13 mole) of potassium hydroxide was added; then 7.73 g (0.055 mole) of benzoyl chloride was added dropwise over the course of 1 h. The mixture was stirred for an additional 30 min and then filtered. The precipitate was washed with water to neutral reaction, dried, and recrystallized from methanol. Obtained 5.5 g (55.8%) of IV mp 184-185°C, R_f 0.45 (C). IR spectrum, cm^{-1}: 1340, 1540 (C–NO_2), 1580, 1600 (C=C arom.), 1620-1630 (C=O amide). M^+ 394.

1,4-Dibenzoyl-6-(benzoylaminomethyl)-6-nitrohexahydro-1,4-diazepine (V, $C_{27}H_{26}N_4O_5$). A. To a solution of 3.96 g (0.02 mole) of the triazahomoadamantane I in 50 ml of water and 100 ml of ethyl acetate, 6 g (0.07 mole) of sodium bicarbonate was added, and then 10 g (0.07 mole) of benzoyl chloride was added dropwise over the course of 3 h. The ethyl acetate layer was washed with water, dried with sodium sulfate, and evaporated under vacuum. The residue was crystallized from ether and recrystallized from ethanol, obtaining 8.5 g (86%) of V, mp 140-141°C, R_f 0.27 (C). IR spectrum, cm^{-1}: 1350, 1390 (C–NO_2), 1580, 1600 (C=C arom.), 1660-1680 (C=O amide), 3300-3380 (NH amide). M^+ 486. PMR spectrum (acetone-d_6), ppm: 3.60 (1H, s, NH); 3.63 (4H, s, 2,3-CH_2); 4.0-4.6 (6H, m, 5,7-CH_2, $\underline{CH_2}$NH); 7.28-8.6 ppm (15H, m, CH arom. protons).

B. To a mixture of 9.85 g (0.025 mole) of the dibenzoyltriazabicyclodecane IV in 125 ml of water and 50 ml of ethyl acetate, 10 g (0.07 mole) of benzoyl chloride was added dropwise over the course of 2 h. The ethyl acetate layer was washed with water, dried with sodium sulfate, and evaporated. The residue was crystallized from ether and recrystallized from ethanol, obtaining 0.6 g (49%) of V, mp 140-141°C, R_f 0.27 (C). IR spectrum, cm^{-1}: 1350, 1390 (C–NO_2), 1580, 1600 (C=C arom.), 1660-1680 (C=O amide), 3300-3380 (NM amide). M^+ 486.

4,8-Dinitroso-6-nitro-1,4,8-triazabicyclo[4.3.1]decane (VI, $C_7H_2N_6O_4$). To a solution of 2.97 g (0.015 mole) of the triazaadamantane I in 100 ml of water, there was added 40 ml of acetic acid and 6 g (0.09 mole) of sodium nitrite dissolved in 6 ml of water. The mixture was allowed to stand for 25 min. The resulting precipitate was filtered off, washed with water to neutral reaction, dried, and recrystallized from methanol, obtaining 3 g (81.9%) of VI, mp 146-147°C, R_f 0.36 (B). IR spectrum, cm^{-1}: 1340, 1360, 1550 (C–NO_2), 1460-1480 (N–N=O). M^+ 244.

1,4-Dinitroso-6-nitro-6-chloromethylhexahydro-1,4-diazepine (VII, $C_6H_{10}N_5O_4Cl$). **A**. To a solution of 1.98 g (0.01 mole) of the triazahomoadamantane I in 20 ml of water and 4 ml of hydrochloric acid, a solution of 2.8 g (0.04 mole) of sodium nitrite in 6 ml of water was added dropwise, while holding the temperature at 0° to +5°C. The resulting precipitate was filtered off, washed with water, dried, and recrystallized from ethanol, obtaining 1.3 g (52%) of VII, mp 121-123°C, R_f 0.35 (B). IR spectrum, cm^{-1}: 1350, 1380, 1570 (C–NO_2), 1470-1480 (N–N=O). M^+ 251.

B. To a solution of 1.2 g (5 mmoles) of the dinitrosotriazabicyclodecane VI in 30 ml of water and 2 ml of hydrochloric acid, a solution of 1.4 g (0.02 mole) of sodium nitrite in 5 ml of water was added dropwise over the course of 2-3 min. The mixture was stirred an additional 3-5 min, after which the precipitate was filtered off, washed with water, dried, and recrystallized from ethanol, obtaining 0.9 g (72%) of VII, mp 121-123°C, R_f 0.35 (B).

REFERENCES

1. Ts. E. Agadzhanyan, G. L. Arutyunyan, and G. G. Adamyan, Khim. Geterotsikl. Soedin., No. 3, 393 (1994).
2. A. I. Kuznetsov, V. A. Kosmakov, and A. S. Moskovkin, Khim. Geterotsikl. Soedin., No. 5, 681 (1990).
3. Ts. E. Agadzhanyan, A. D. Arutyunyan, and G. S. Saakyan, Khim. Geterotsikl. Soedin., No. 8, 1098 (1992).
4. A. F. Farminer and G. A. Webb, J. Chem. Soc., Perkin Trans. I, No. 9, 940 (1976).
5. E. B. Hodge, J. Org. Chem., **37**, 320 (1972).
6. Ts. E. Agadzhanyan and R. A. Movsesyan, USSR Inventor's Certificate 937,457, Byull. Izobret., No. 23, 109 (1982).
7. Ts. E. Agadzhanyan and R. A. Movsesyan, Arm. Khim. Zh., **36**, 678 (1983).