SYNTHESIS AND TRANSFORMATIONS OF POLYHEDRAL COMPOUNDS.

14*. OPENING OF HEXAHYDROPYRIMIDINE RING OF 2-SUBSTITUTED 1,3-DIAZAADAMANTANES BY ELECTROPHILIC REAGENTS

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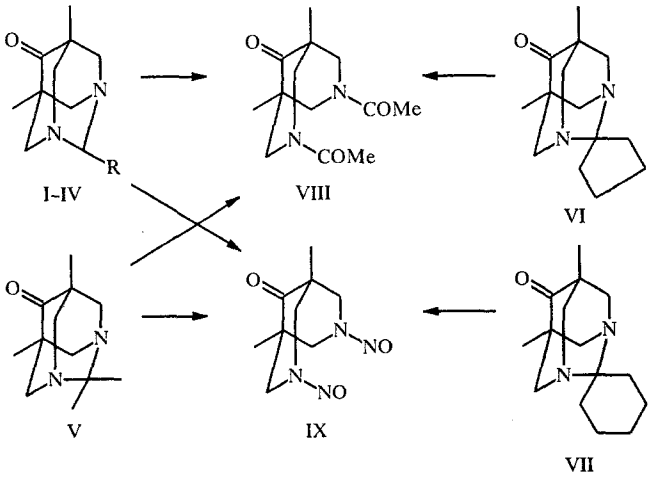
It was found that a cleavage of the N–C bonds of C-mono- and C,C-disubstituted methylenediamino groups of 1,3-diazaadamantanes takes place by the action of electrophilic reagents.

Data are given in the literature on the cleavage of N–C bonds of the methylenediamino group of 1,3-diazaadamantane by the action of various electrophilic reagents, resulting in the opening of the hexahydropyrimidine ring of 1,3-diazaadamantane and the formation of the corresponding derivatives of 3,7-diazabicyclo[3.3.1]nonane [2]. However, no data whatsoever are available on the reaction of 2-substituted and 2,2-disubstituted 1,3-diazaadamantanes with electrophilic reagents, and hence, on the cleavage of the N–C bonds of C-mono- and C,C-disubstituted methylenediamino groups of 1,3-diazaadamantanes by the action of electrophilic reagents.

In the present work we studied the reaction of 1,3-diazaadamantanes containing C-mono- or C,C-disubstituted methylenediamino groups with a series of electrophilic reagents of various classes, in particular, with acetic anhydride, benzoyl chloride, nitrous acid, and benzyl chloride.

We found that in the reaction of 5,7-dimethyl-6-oxo-1,3-diazaadamantanes, both those not containing a substituent (I), and those containing an ethyl (II), phenyl (III), 3′-pyridyl (IV) group, or two methyl groups at the 2-position (V) [3], with



I R=H; II R=Et; III R=Ph; IV R=pyrid-3-yl.

*For Communication 13, see [1].

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TABLE 1. Reaction of 2-Substituted 1,3-Diazaadamantanes II-VI with Acetic Anhydride at 15-18°C

1,3-Diazaadamantane	Time of reaction, h	Yield of VIII*, %
II	4	80
III	48	80
IV	300	
IV	2**	90
V	2	92
VI	2	88

*mp 264-265°C, R_f(A) 0.55.
**At 70°C.

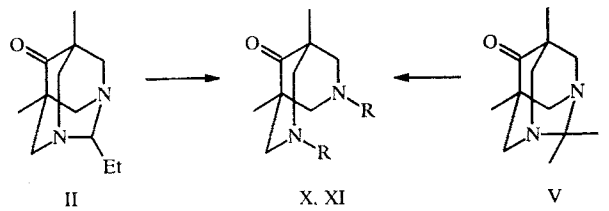
TABLE 2. Reaction of 2-Substituted 1,3-Diazaadamantanes II-V, VII with Nitrous Acid

1,3-Diazaadamantane	Diazaadamantane g/HCl, ml	Yield of IX,* g (%)
II	0,52/5	0,5 (83)
III	0,59/10	0,5 (91)
IV	0,75/5	0,5 (90)
V	0,52/7	0,5 (84)
VII	0,62/7	0,4 (71)

*mp 228-229°C; R_f(A) 0.77.

acetic anhydride and nitrous acid, and also of 5,7-dimethyl-6-oxospiro[1,3-diazaadamantane-2-cyclopentane] (VI) [3] with acetic anhydride and 5,7-dimethyl-6-oxospiro[1,3-diazaadamantane-2-cyclohexane] (VII) [3] with nitrous acid, 3,7-diacetyl- (VIII), and 3,7-dinitroso-9-oxo-3,7-diazabicyclo[3.3.1]nonanes (IX), respectively are formed.

In the reaction of 5,7-dimethyl-6-oxo-1,3-diazaadamantanes containing an ethyl group or two methyl groups at the 2-position with benzoyl chloride or benzyl chloride, then similarly to compound I [4, 5], 3,7-dibenozyl (X) and 3,7-dibenzyl-3,7-diazabicyclo[3.3.1]nonanes (XI), respectively, are formed



II X, XI V

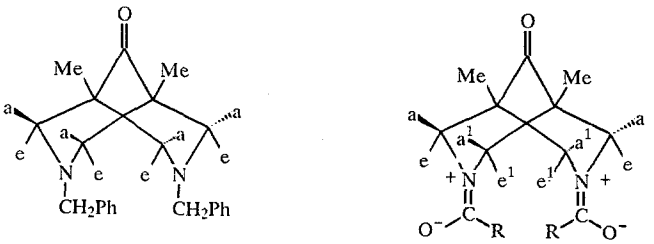
X R=COPh; XI R=CH_2Ph

Thus, we have found that the action of electrophilic reagents results in a cleavage of the N–C bond of the C-mono- and C,C-di-substituted methylenediamino groups of 1,3-diazaadamantanes, whereby the latter occurs irrespectively of the

character and number of substituents at the carbon atom of the methylenediamino group. The rate of cleavage of the N–C bonds of the methylenediamino group of 1,3-diazaadamantanes by the action of acetic anhydride changes depending on the character of the substituent at the 2-position: It is greater in the presence of alkyl substituents and less in the presence of aryl substituents (Table 1).

The structure of the synthesized compounds was verified by elemental analysis and also by the IR, UV, PMR, and mass spectra. Purity was monitored by TLC. 3,7-Dibenzoyl- (X) and 3,7-dibenzyl-1,5-dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]nonanes (XI) were identical with the compounds previously obtained in [4, 5].

In the PMR spectrum of 3,7-dibenzyl-1,5-dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]nonane (IX), the axial and equatorial protons of the diazabicyclononane skeleton, similarly as in [6], appear in the form of two doublets (the AB system). The inhibition of the rotation of the acyl groups around the amide bond in the diacyldiazabicyclononanes leads in the PMR spectra of 3,7-diacetyl- (VIII) and 3,7-dibenzoyl-1,5-dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]nonanes (X) to the disturbance of the equivalency of the axial and equatorial protons of the methylene groups because of the contribution of the $-O-C=N^+$ structure [7]. As a result, eight protons of the diazabicyclononane skeleton form four doublets (two AB systems). The spin–spin interaction between the H_e and $H_{e'}$ protons and also $H_{a'}$ leads to further splitting of each doublet as follows:



The PMR spectrum of 1,5-dimethyl-3,7-dinitroso-9-oxo-3,7-diazabicyclo[3.3.1]nonane (IX) is more complex, possibly because of the inhibition of rotation of the nitroso groups around the N–NO bond and the interpretation of its spectrum is difficult to make (see also [8]).

EXPERIMENTAL

The IR spectra were run in mineral oil on a UR-20 spectrophotometer. The PMR spectra were obtained on a Varian T-60 spectrometer using TMS as an internal standard. The molecular weights were determined mass-spectrometrically on an MX-1320 spectrometer with direct introduction of the sample into the ionic source. The energy of the ionizing electrons was 60 eV. The UV spectra were run on a Specord spectrophotometer. The course of the reactions and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 plates: in systems: A) n-propanol–water (7:3); B) benzene–ethanol (10:1); C) chloroform–methanol (1:1). The development was carried out by iodine vapors or ninhydrin.

The data of the elemental analysis for compounds VIII-XI for C, H, N, correspond to the calculated values.

3,7-Diacetyl-1,5-dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]nonane (VII), $C_{13}H_{20}N_2O_3$). A. A 25-ml portion of acetic anhydride was added to 5 g (28 mmoles) of diazaadamantanes I and the mixture was stirred for 8 h at 15-18°C or 30 min at 70°C. A 25 ml-portion of water was added and the stirring was continued for a further 30 min. The solvent was distilled off in vacuo and 15 ml of cold water was added to the residue. The precipitate was filtered off, washed with 25 ml of cold water, and recrystallized from water. Yield, 5.8 g (82%) and 4.6 g (64.8%) of VIII, respectively (depending on the above indicated temperature and time of reaction), mp 264-265°C (from water). R_f 0.55 (A). IR spectrum: 1650 (C=O amide), 1730 cm^{-1} (C=O) ketone). UV spectrum (in alcohol), λ_{max} (ε): 204 (6330), 231 nm (3160). PMR spectrum ($CDCl_3$): 0.93 (6H, s, $2CH_3$), 2.0 (6H, s, $2CH_3CO$), 2.67 (2H, d × d, J = 14 Hz, J = 3 Hz, 2.6–CH_a–N), 3.15 (2H, d × d, J = 13 Hz, J = 3 Hz, 4.8–CH_a–N), 4.0 (2H, d × d, J = 13 Hz, J = 3 Hz, 4.8-CH_e–N), 4.97 ppm (2H, d × d, J = 14 Hz, J = 3 Hz, 2.6–CH_e–N). M^+ 252.

B. A solution of 0.2 g of diazaadamantane II-VI in 10 ml of acetic anhdride was stirred at room temperature or heated at 70°C to a complete disappearance of the starting material. A 15-ml portion of water was added, the mixture was allowed to stand for 2 h, the solvent was distilled off, and 10 ml of cold water was added to the residue, the precipitate was filtered off, washed with 15 ml of cold water, and recrystallized from water (see Table 1).

1,5-Dimethyl-3,7-dinitroso-9-oxo-3,7-diazabicyclo[3.3.1]nonane (IX, $C_9H_{14}N_4O_3$). **A.** Sodium nitrite (1.4 g, 20 mmoles) was added in small portions in the course of 30 min to a solution of 0.9 g (5 mmoles) of diazaadamantane I in 10 ml of 2 N hydrochloric acid. The precipitate formed was filtered off and recrystallized from ethanol, mp 228-229°C (from ethanol). R_f 0.77 (A). IR spectrum: 1460 (N–NO), 1710 cm^{-1} (C=O), M^+ 226. Yield, 1 g (88.5%).

B. Sodium nitrite (0.7 g, 10 mmoles) was added in small portions to a solution of 2.5 mmoles of diazaadamantane II-V, VII in 5-10 ml of 2 N hydrochloric acid. The precipitate obtained was filtered off, washed with water, and recrystallized from ethanol (Table 2).

3,7-Dibenzoyl-1,5-dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]nonane (X, $C_{23}H_{24}N_2O_3$). A 0.3-g portion (2.2 mmoles) of benzoyl chloride was added dropwise in the course of 10 min to a mixture of 0.2 g (1 mmole) of diazaadamantane II, V, 0.2 g (1 mmole) of sodium bicarbonate, and 10 ml of dioxane. The mixture was stirred for 1 h more, and the precipitate that separated out was filtered off. The filtrate was evaporated under vacuum, 50 ml of water was added to the residue, and the precipitate that formed was filtered off. The two precipitates were combined, washed with water, a 5% solution of sodium bicarbonate and water again, and recrystallized from ethanol. Yield, respectively, 0.34 g (90%) and 0.35 g of (92%) of X, mp 235-236°C (from ethanol). R_f 0.38 (B). IR spectrum, 1600 (C=C arom.), 1650-1690 (C=O amide), 1750 cm^{-1} (C=O ketone). PMR spectrum (DMSO-D_6): 0.67 (6H, s, $2CH_3$), 2.93 (2H, d, J = 14 Hz, 2.6–CH_a–N); 3.35 (2H, d, J = 13 Hz, 4.8–CH_a–N), 3.83 (2H, d, J = 13 Hz, 4.8–CH_e–N), 4.70 (2H, d, J = 14 Hz, 2.6–CH_e–N), 7.62 ppm (10H m, arom. protons).

3,7-Dibenzyl-1,5-dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]nonane (XI, $C_{23}H_{24}N_2O$). A 1.3-g portion (10 mmoles) of benzyl chloride was added at the boiling point to a solution of 1 g (5 mmoles) of diazaadamantane (II, V) in 40 ml of dioxane, and the mixture was neutralized with triethylamine (1.2 g, 2 mmoles). The mixture was boiled for 9 and 15 h, respectively, and then filtered. The filtrate was evaporated under vacuum, and the residue was dissolved in 50 ml of ethyl acetate. After drying over magnesium sulfate, the ethyl acetate solution was evaporated in vacuo to dryness, and the residue was crystallized from hexane. Yield, 1.2 g (69%) and 1.3 g (75%) of XI, respectively, mp 75-76°C (from an ethanol–water (1:2) mixture). R_f 0.50 (C). IR spectrum: 1610 (C=C arom.), 1750 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 0.94 (6H, s, $2CH_3$), 2.37 (4H, d, J = 11 Hz, $4CH_a$–N), 3.5 (4H, d, J = 11 Hz, $4CH_e$–N), 3.5 (4H, s, $2CH_2C_6H_5$), 7.3 ppm (10H, s, arom. protons).

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