the internal standard (δ = 76.9 ppm). The spectra were recorded at a sample temperature of 50°C with complete suppression of the spin—spin coupling with the protons.

3-(p-Chlorophenyl)iminoquinuclidine (IV). A mixture of 12.5 g (0.1 mole) of 3-quinuclidone, 12.75 g (0.1 mole) of 4-chloroaniline, and 150 ml of toluene was heated in the presence of a catalytic amount of p-toluenesulfonic acid in a Dean—Stark apparatus until the liberation of water ceased (10-12 h). The reaction mixture was then treated with charcoal, and the toluene was removed by distillation. The residue was fractionated in vacuo at 2 mm. Two fractions were collected: the first fraction had bp 84-132°C (1.8 g), and the second fraction had bp 162-163°C (16.65 g). The second fraction was identified as IV. Redistillation of the first fraction gave 0.8 g of a product with bp 118-119°C (25 mm), which was identified as an azeotropic mixture of the starting components in an equimolar ratio. Found: C 61.9; H 6.7; Cl 14.3; N 11.1%. $C_7H_{11}NO + C_6H_6ClN$. Calculated: C 61.8; H 6.7; Cl 14.1; N 11.1%.

An azeotropic mixture of the above composition was also obtained by distillation of equimolar amounts of 3-quinuclidone and 4-chloroaniline.

The formation of azeotropic mixtures was also observed in the preparation of azomethines I and VI-VIII. Compounds I-III and VI-XI were synthesized by the method used to prepare IV (see Table 5).

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REACTION OF 2,3-DIOXO-4-(N,N-DIMETHYLAMINOMETHYLENE)HEXAHYDROAZEPINE WITH HYDRAZINE AND ITS DERIVATIVES*

R. G. Glushkov, T. V. Stezhko, T. F. Vlasova, and O. S. Anisimova

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8-Oxo-8H-4,5,6,7-tetrahydropyrazolo[5,4-c]azepine and a mixture of 2-phenyl-8-oxo-8H-4,5,6,7-tetrahydro[3,4-c]azepine and 2,3-dioxo-4-formylhexahydroazepine 4-phenylhydrazone were obtained in the reactions of 2,3-dioxo-4-(N,N-dimethylaminomethylene)-hexahydroazepine with hydrazine and phenylhydrazine, respectively. Cyclization of 2,3-dioxo-4-formylhexahydroazepine 4-phenylhydrazone gave 1-phenyl-8-oxo-8H-4,5,6,7-tetrahydropyrazolo[5,4-c]azepine. The reaction of 2,3-dioxo-4-(N,N-dimethylaminomethylene)hexahydroazepine with semicarbazide and thiosemicarbazide gives 2,3-dioxo-4-formylhexahydroazepine 4-semicarbazone and 4-thiosemicarbazone.

In order to synthesize some condensed heterocyclic compounds, in the present research we studied the reactions of 2,3-dioxo-4-(N,N-dimethylaminomethylene)hexahydroazepine (I) [2] with hydrazine and its derivatives — phenylhydrazine, thiosemicarbazide, and semicarbazide.

The reaction of enamino ketone I with hydrazine leads to the formation of pyrazole II in close to quantitative yield. The reaction of enamino ketone I with phenylhydrazine proceeds

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S. Ordzhonikidze All Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow 119021.

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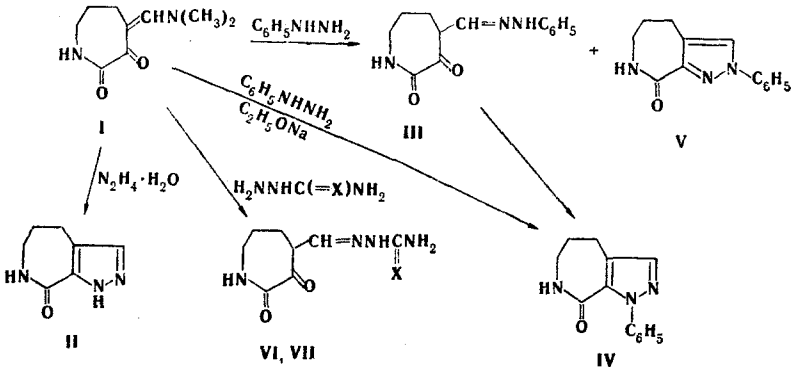
ambiguously. Two substances were isolated in alcohol. One of the compounds which precipitated when the reaction mixture was cooled was found to be phenylhydrazone III. Its PMR spectrum contains signals of a methylidyne proton and protons of the hexahydroazepine ring. The other compound, which was isolated from the mother liquor is, according to the mass-spectral data and the results of elementary analysis, the product of dehydration of phenylhydrazone III. Considering the mild reaction conditions under which this substance is formed and which exclude opening of the lactam ring and recyclization of the resulting amino acid, we assumed that it is one of the two isomeric pyrazoloazepines IV or V. In order to establish its structure we studied the cyclization of phenylhydrazone III to pyrazoloazepine IV. Attempts to achieve cyclization by prolonged heating in alcohol were unsuccessful; however, pyrazolo[5,4-c]azepine (IV), which was also synthesized directly from enamino ketone I by heating it with phenylhydrazine in alcohol in the presence of sodium ethoxide, was obtained by heating phenylhydrazone III in acetic acid or in alcohol in the presence of sodium ethoxide, as well as in diphenyl ether at ∿ 200°C. In connection with the fact that pyrazoloazepine IV differs from the compound mentioned above, the pyrazolo[3,4-c]azepine (V) structure was proposed for the latter.



VI X=S; VII X=O

The chemical shifts of the signals of the protons of the hexahydroazepine ring in the PMR spectra of IV and V are virtually identical. However, the signal of the methylidyne proton in the 3 position of pyrazoloazepine V is shifted ∿ 0.8 ppm to weak field as compared with the spectrum of IV due to the anisotropic effect of the phenyl ring. The absorption band of the C=O group is found at 1670 cm^{-1} in the IR spectrum of IV, whereas this band is found at 1655 cm^{-1} in the spectrum of V. An examination of the molecular models of IV and V shows that the difference can be explained by steric hindrance due to the protons of the phenyl fragment and the oxygen atom of the C=O group in IV, as a result of which the carbonyl group is partially removed from conjugation with the pyrazole ring. The structures of isomeric pyrazoloazepines IV and V are also confirmed by the mass spectra, in which intense molecular ion peaks (m/e 227) are observed. The spectra are characterized by fragments from the stepwise cleavage of the bonds in the lactam ring: m/e 198 $(M - NHCH_2)^{+\cdot}$, 184 $(M - NHCO)^{+\cdot}$, 170 $(M - NHCH_2 - CO)^{+\cdot}$, 169 $(M - CONH - CH_3)^{+}$, 157 $(M - CONH - C_2H_3)^{+}$, 156 $(M - CONH - C_2H_4)^{+\cdot}$, 155 $(M - CONH - C_2H_5)^{+}$, 143 $(M - CONH - C_3H_5)^{+}$, however, the spectra differ with respect to the relative intensities of the enumerated peaks. In addition, a feature of the spectrum of V that confirms the presence of a phenyl group attached to the N_2 atom is the presence of an intense peak with m/e 104, which evidently belongs to the $C_6H_5\overset{+}{N}{\equiv}CH$ ion. With respect to the character of the fragmentation the mass spectrum of pyrazoloazepine II is similar to the spectra of IV and V. It is interesting to note than an $(M - OH)^{+}$ ion peak, which corresponds to fragmentation of the lactim forms of these compounds, is observed in the spectra of all pyrazoloazepines II, IV, and V.

In considering the possible schemes for the conversion of enamino ketone I to pyrazoloazepine V, one should take into account the fact that the reactivity of the C=O group in enamino ketones with respect to nucleophilic agents is reduced to the electron-donor effect of the dimethylamino group, and it is therefore difficult to assume that the conversion of enamino ketone I to V proceeds through the intermediate 2,3-dioxo-4-(N,N-dimethylaminomethylene)hexahydroazepine 3-phenylhydrazone. One cannot exclude the possibility that V is formed from phenylhydrazone III by the action on it of excess phenylhydrazine through 2,3-dioxo-4-formylhexahydroazepine 3,4-bis(phenylhydrazone). However, attempts to synthesize pyrazoloazepine V by heating phenylhydrazone III with phenylhydrazine under various conditions were

TABLE 1. Properties of II-VII

Compound	mp, °C (solvent)	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
II	222—224 (2-propanol)	55,7	6,0	27,7	$C_7H_9N_3O$	55,6	6,0	27,8	96
III	144—147 (2-propanol)	63,7	6,3	17,0	$C_{13}H_{15}N_3O_2$	63,7	6,2	17,1	58
IV	160—163(ethyl acetate)	68,8	5,8	18,5	$C_{13}H_{13}N_3O$	68,7	5,8	18,5	Quant.[a]
V	189—192 (ethyl acetate)	68,5	5,9	18,5	$C_{13}H_{13}N_3O$	68,7	5,8	18,5	13
VI[b]	169—170 (dec., MeOH)	42,1	5,0	24,5	$C_8H_{12}N_4O_2S$	42,1	5,3	24,5	87
VII	215—217 (dec., water)	45,0	5,9	26,4	$C_8H_{12}N_4O_3$	45,3	5,7	26,4	50

[a]Method A. [b]Found: S 14.1%. Calculated: S 14.1%.

unsuccessful. The conversion of enamino ketone I to pyrazoloazepine V evidently proceeds through a cyclic transition state, which arises as a result of attack by the secondary NH group of phenylhydrazine on the enamine fragment of I and by the NH_2 group of phenylhydrazine on the C=O group of enamino ketone I.

The reaction of enamino ketone I with thiosemicarbazide and semicarbazide proceeds in the same manner as in the case of transamination of enamino lactams [3] to give thiosemicarbazone VI and semicarbazone VII. The structure of these substances as 4-formyl-2,3-dioxohexahydroazepine derivatives rather than the corresponding hydroxy methylene compounds was confirmed in the case of semicarbazone VII by the PMR spectrum, in which, in addition to multiplet signals of the protons in the 4-7 positions of the hexahydroazepine ring, a doublet signal of the CH=N proton of the semicarbazone fragment is observed at 6.99 ppm (J = 1.5 Hz). The shift of the signals of the protons of the CH_2 group in the 5 position to stronger field (1.85 ppm) as compared with starting enamino ketone I (2.51 ppm) [2] also constitutes evidence in favor of the semicarbazone structure of VII.

EXPERIMENTAL

The UV spectra of the compounds were recorded with an EPS-3 spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were recorded with Perkin—Elmer 457 and UR-10 spectrometers. The PMR spectra of solutions of the compounds in $CDCl_3$ (III) and $(CD_3)_2SO-CCl_4$ (IV, V, VI, and VII) were recorded with a JMH-4H-100 spectrometer with tetramethylsilane as the internal standard. The mass spectra were recorded with an MAT-112 spectrometer at an ionizing voltage of 50 eV and an ionization chamber temperature of 140°C. The melting points of the compounds were determined with an MP-1 apparatus (Gamato Scientific Co., Ltd.). The purity of the substances was monitored by chromatography on Silufol UV-254 plates.

8-Oxo-8H-4,5,6,7-tetrahydropyrazolo[5,4-c]azepine (II). A 0.55 g (11 mmole) sample of hydrazine hydrate was added dropwise to a suspension of 1.8 g (10 mmole) of enamino ketone I in 20 ml of absolute alcohol, and the mixture was stirred at 20°C for 2 h. It was then cooled in ice, and the precipitate was removed by filtration, washed with alcohol, and dried. Evaporation of the mother liquor and treatment of the residue with ether gave an additional amount of pyrazoloazepine II (Tables 1 and 3).

2,3-Dioxo-4-formylhexahydroazepine 4-Phenylhydrazone (III) and 2-Phenyl-8-oxo-8H-4,5,6,7-tetrahydropyrazolo[3,4-c]azepine (V). A 4.85 g (33 mmole) sample of freshly distilled phenylhydrazine was added dropwise to a suspension of 5.45 g (30 mmole) of I in 60 ml of absolute alcohol, and the mixture was stirred at 20°C for 4 h. It was then cooled, and phenylhydrazone III was removed by filtration (Tables 1 and 2). The mother liquor was evaporated in vacuo, and the residue was triturated successively with absolute ether and ethyl acetate and removed by filtration to give pyrazoloazepine V (Tables 1 and 3).

1-Phenyl-8-oxo-8H-4,5,6,7-tetrahydropyrazolo[5,4-c]azepine (IV). A) Thermal Cyclization of Phenylhydrazone III. A mixture of 3 g (12.2 mmole) of phenylhydrazone III and 2 ml of diphenyl ether was heated at 200°C for 2.5 h, after which it was cooled, and pyrazoloazepine IV was removed by filtration.

TABLE 2. Spectral Properties of 2,3-Dioxo-4-formylhexahydroazepine Derivatives (III, VI, and VII)

Compound	IR spectrum, cm^{-1}			PMR spectrum, ppm						
	C=O	C=N	NH, NH_2	4-CH	5-CH_2	6-CH_2	7-CH_2	$-CH=N$	arom. CH	NH, NH_2
III[a]	1660 (III)	1600	3350, 3320, 3250	3,46	2,12	1,59	2,81	5,90	6,77—7,30	
VI	1680, 1660	1600	3430, 3280—3100	—	—	—	—	—	—	
VII	1685, 1665, 1640	1600	3400, 3300—3200	3,18	1,85	1,53	2,93	6,99	—	5,93; 6,36; 8.00

[a] UV spectrum, λ_{max} (log ε): 238 (3.81) and 276 nm (4.11).

TABLE 3. Spectral Properties of Pyrazoloazepines (II, IV, and V)

Compound	IR spectrum, cm^{-1}		UV spectrum	PMR spectra, ppm					
	C=O	NH	λ_{max}, nm (lg ε)	3-CH	4-CH_2	5-CH_2	6-CH_2	NH	CH_{arom}
II	1640	3180	228 (4,09)	—	—	—	—	—	
IV	1670	3310, 3220	235 (4,03)	7,53	2,73	1,93	3,16	8,11	7,35
V	1655	3290, 3190	274 (4,19) 364 (2,56)	8,31	2,80	1,93	3,26	7,90—7,28	

B) Cyclization of Phenylhydrazone III in the Presence of Sodium Ethoxide. A 2.35 g (9.6 mmole) sample of phenylhydrazone III was added to a solution of sodium ethoxide (from 0.24 g of Na and 20 ml of absolute alcohol), and the mixture was refluxed for 5 h. It was then filtered, and the mother liquor was evaporated to dryness in vacuo. The residue was triturated with 10 ml of water to give pyrazoloazepine IV (Tables 1 and 3).

C) Reaction of Enamino Ketone I with Phenylhydrazine in Alcohol in the Presence of Sodium Ethoxide. A 7.3 g (0.04 mole) sample of I and 6.5 g (0.06 mole) of phenylhydrazine were added to a solution of sodium ethoxide (from 1 g of Na and 80 ml of absolute alcohol), and the mixture was refluxed for 4 h. It was then cooled, neutralized to pH 7 with 2 N H_2SO_4, and filtered. The mother liquor was evaporated to dryness in vacuo, and the residue was dissolved in chloroform. The solution was washed with water, dried with calcined sodium sulfate, and evaporated to dryness. The residue was triturated successively with petroleum ether and ethyl acetate to give pyrazoloazepine IV (Tables 1 and 3).

2,3-Dioxo-4-formylhexahydroazepine 4-Thiosemicarbazone (VI). A mixture of 7.3 g (40 mmole) of enamino ketone I and 5.6 g (44 mmole) of thiosemicarbazide hydrochloride was refluxed in 80 ml of absolute alcohol in the presence of 3 g (22 mmole) of potassium carbonate for 1 h, after which it was cooled, and the precipitate was removed by filtration, washed with water, and cooled (Tables 1 and 2).

2,3-Dioxo-4-formylhexahydroazepine 4-Semicarbazone (VII). This compound was similarly obtained from enamino ketone I and semicarbazide hydrochloride in alcohol in the presence of potassium hydroxide (Table 1 and 2).

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