SYNTHESIS AND STUDY OF THE CYCLIZATION PATHWAYS AND REACTIVITIES OF α-DIAZOIMIDOLATES

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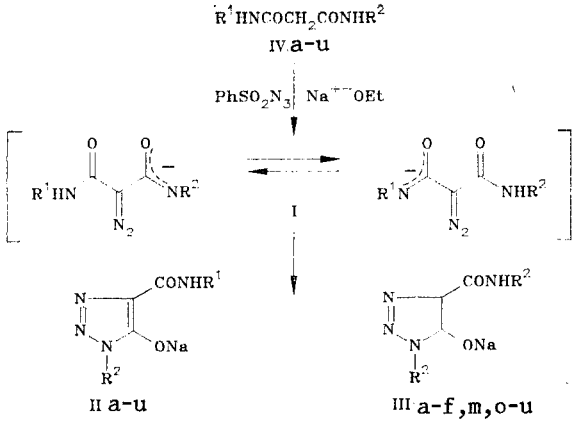
The reaction of unsymmetrical N,N'-disubstituted malonamides with benzenesulfonyl azide in the presence of sodium ethoxide gives individual sodium 1,2,3-triazol-5-olates or mixtures of their isomers, from the relative amounts of which the effect of substituents in the amido groups on the cyclization pathways and reactivities of α-diazoimidolates was ascertained.

The reactions of 2-diazo-2-cyanoacetic acid amides with bases [1], malonic acid amides with benzenesulfonyl azide in the presence of sodium ethoxide [2], and methyl 2-diazomalonate with aliphatic amines [3] are known methods for obtaining 1,2,3-triazol-5-olates — intermediates in the synthesis of 2-aza analogs of the antitumorigenic antibiotic bredenine [4]. These transformations proceed through intermediate α-diazoimidolates I, which are highly reactive and unstable compounds. Experimental studies of the monomolecular transformations of I have not been previously carried out. In particular, their reactivities in heterocyclization reactions have not been studied, and this sort of study is necessary to predict the structures of the final products. The determination of characteristics of this sort is fraught with considerable difficulties, since α-diazoimidolates undergo cyclization to 1,2,3-triazol-5-olates under the conditions used to synthesize them.

To study the reactivities of α-diazoimidolates we accomplished the synthesis and carried out an investigation of the pathways of cyclization of 2-diazomalonimidolates I to isomeric 1,2,3-triazol-5-olates II and III. In our research we used a way to study the reactivities of unstable compounds based on the method of competitive reactions that we previously used for investigating the reactivities of α-diazoimines [5]. Since the cyclization of I to triazoles II and III proceeds irreversibly, the ratio of the isomeric triazoles formed in the reaction characterizes the relative reactivities of the two imidoyl groups and, consequently, the change in the rate of cyclization of α-diazoimidolates when substituent R^1 is replaced by R^2.

Monosubstituted malonodiamides IVa-f, m, which have alkyl groupings as substituents, react with benzenesulfonyl azide in the presence of sodium ethoxide to give mixtures of two isomers IIa-f, m and IIIa-f, m. In contrast to IVa-f, m, 2-carbamoylacetic acid anilides IVg-*l*, n undergo diazo transfer to give only 1-aryl-substituted 1,2,3-triazol-5-olates IIg-*l*, n.

In the diazo transfer reaction malonodiarylamides VIa-f, m should be known to form mixtures of triazoles IIo-u and IIIo-u; the ratio of the isomers in each case will depend on the electronic properties of the substituent in the para position of the benzene ring. In this connection, as the internal standard that makes it possible to determine the ratio of isomers from the integral value in the PMR spectrum (in d_6-DMSO) we selected the methoxy group, the signal of which is located in a region that is free of signals of other groups (3.7-3.8 ppm).



II—IV a—l R^1=H, m,n R^1=Me, o-u R^1=C_6H_4OMe-4; a R^2=Me, b R^2=Et, c R^2=Pr-*i*, d R^2=Bu, e R^2=C_6H_{11}-*cyclo*, f R^2=Bz, g R^2=Ph, h R^2=C_6H_4Me-4, i R^2=C_6H_4OMe-4, j R^2=C_6H_4Br-4, k R^2=C_6H_4COOEt-4, l R^2=$C_6H_4NO_2$-4; m R^2=Bz; n R^2=C_6H_4Me-4; o R^2=Ph, p R^2=C_6H_4Me-4, q R^2=$C_6H_4NHCOMe$-4, r R^2=C_6H_4Cl-4, s R^2=C_6H_4Br-4, t R^2=C_6H_4COMe-4, u R^2=C_6H_4COOEt-4

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TABLE 1. Percentages of Isomeric Sodium 1,2,3-Triazol-5-olates II and III and Competition Constants (K_c)

R^1	R^2	Compound	Fraction, %	Compound	Fraction, %	K_c
H	Me	IIa	57,8	IIIa	42,2	1,37
H	Et	IIb	48,3	IIIb	51,7	0,93
H	Pr-*i*	IIc	62,0	IIIc	38,0	1,63
H	Bu	IId	60,0	IIId	40,0	1,50
H	C_6H_{11}-*cyclo*	IIe	73,0	IIIe	27,0	2,70
H	Bz	IIf	86,8	IIIf	13,2	6,58
H	Ar	IIg-ℓ	100	IIIg-ℓ	0,0	
Me	Bz	IIm	83,0	IIIm	17,0	4,88
Me	C_6H_4Me-4	IIn	100	IIIn	0,0	
C_6H_4OMe-4	Ph	IIo	51,8	IIIo	48,2	1,07
C_6H_4OMe-4	C_6H_4Me-4	IIp	49,1	IIIp	50,8	0,97
C_6H_4OMe-4	$C_6H_4NHCOMe$-4	IIq	58,6	IIIq	41,4	1,42
C_6H_4OMe-4	C_6H_4Cl-4	IIr	72,5	IIIr	27,5	2,64
C_6H_4OMe-4	C_6H_6Br-4	IIs	74,3	IIIs	25,7	2,89
C_6H_4OMe-4	C_6H_4COMe-4	IIt	78,7	IIIt	21,3	3,69
C_6H_4OMe-4	C_6H_4COOEt-4	IIu	80,1	IIIu	19,8	4,05

TABLE 2. ^{13}C NMR Spectra of Sodium 1,2,3-Triazol-5-olates IIa, g, h, k, n, VII, and VIII

Compound	R^1	COR^2, CN	Chemical shifts, δ, ppm			
			$C_{CN,CO}$	$C_{(5)}$	$C_{(4)}$	$C_{CH_2,Me}$
IIa	Me	$CONH_2$	165,94	159,40	118,62	29,32 (R^1)
IIg	Ph	$CONH_2$	165,45	159,27	119,71	20,48 (R^1)
IIh	C_6H_4Me-4	$CONH_2$	165,45	159,15	119,71	
IIk	$C_6H_4CO_2Et$-4	$CONH_2$	165,33 (R^2); 165,09 (R^1)	159,57	119,89	14,11 (CH_3); 60,46 (CH_2)
IIn	C_6H_4Me-4	CONHMe	164,34	158,91	119,93	20,51 (R^1); 24,72 (R^2)
VII	Me	CONHMe	164,67	158,97	118,80	29,32 (R^1); 24,72 (R^2)
VIII	Me	C≡N	97,72	161,70	118,59	29,41 (R^1)

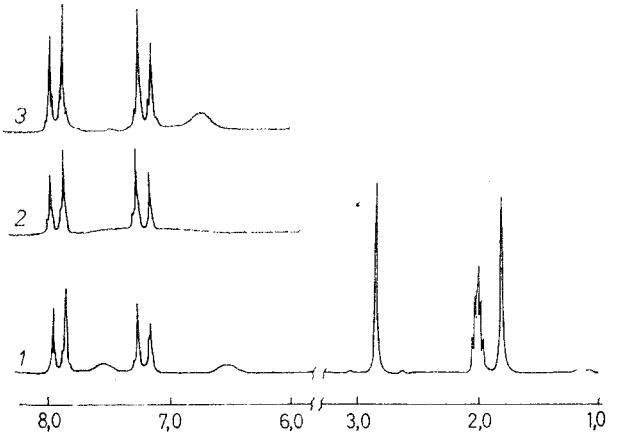


Fig. 1. Temperature dependence of the PMR spectrum of IIi at: 1) 20°C; 2) 60°C; 3) 100°C.

In fact, in all cases in the diazo transfer to VIa-f, m we isolated mixtures of 1,2,3-triazol-5-olates IIo-u and IIIo-u, the ratios of which were determined from PMR spectral data (Table 1).

To determine the structures of 1,2,3-triazol-5-olates IIa-u and IIIa-f, m, o-u we used IR, PMR, and ^{13}C NMR spectroscopy, which make it possible to establish the structures of these compounds from a large number of characteristics. Two absorption bands (II, IIIa, f, m) or the superimposition of two bands (II, IIIb-e), which belong to stretching vibrations of carbonyl groups of two isomers, are observed in the IR spectra of II and IIIa-f, m at 1615-1640 cm^{-1}. In the PMR spectra of mixtures of isomers II and IIIa-f, m the signals of the protons of the substituents

TABLE 3. Characteristics of Sodium 1,2,3-Triazol-5-olates IIa-u and IIIa-f, m, o-u

Compound	Empirical formula	PMR spectrum, δ, ppm (SSCC, J, Hz)	Yield, %
IIa, IIIa	$C_4H_5N_4O_2 \cdot Na$	3,30 (3H, s, Me); 2,74 (3H, d, J=5,5, Me); 2,75 (3H, s, Me)	62
IIb IIIb	$C_5H_7N_4O_2 \cdot Na$	3,77 (2H, q, J=7,2, CH_2); 3,22 (2H, q, J=7,2, CH_2); 1,21 (3H, t, J=7,2, Me); 1,06 (3H, t, J=7,2 Hz, Me)	66
IIc, IIIc	$C_6H_9N_4O_2 \cdot Na$	4,66...4,54 (1H, m, CH); 3,86...3,74 (1H, m, CH); 1,42 (6H, d, J=6,4, 2Me); 1,05 (6H, d, J=6,4, 2Me)	67
IId, IIId	$C_7H_{11}N_4O_2 \cdot Na$	3,74 (2H, t, J=7,2, CH_2); 3,33 (2H, d, J=9,2, CH_2); 1,66...1,20 (4H, m, CH_2CH_2); 0,89 (3H, t, J=7,2, Me); 0,88 (3H, t, J=7,2, Me)	65
IIe, IIIe	$C_9H_{13}N_4O_2 \cdot Na$	4,00...3,90 (1H, m, CH); 3,58...3,45 (1H, m, CH); 1,80...1,00 (10H, m, C_5H_{10})	61
IIf, IIIf	$C_{10}H_9N_4O_2 \cdot Na$	7,37...7,20 (5H, m, Ph); 4,97 (2H, s, CH_2); 4,37 (2H, s, d, J=7,2 CH_2)	58
IIg	$C_9H_7N_4O_2 \cdot Na$	8,20...7,05 (6H, m, Ph, NH*); 6,68 (1H, s, NH*)	67
IIh	$C_{10}H_9N_4O_2 \cdot Na$	8,01...7,14 (4H, m, C_6H_4); 7,54 (1H, s, NH*); 6,63 (1H, s, NH*); 2,31 (3H, s, Me)	72
IIi	$C_{10}H_9N_4O_2 \cdot Na$	7,97...6,86 (4H, m, C_6H_4); 7,50 (1H, s, NH*); 6,60 (1H, s, NH*); 3,76 (3H, s, OMe)	70
IIj	$C_9H_6BrN_4O_2 \cdot Na$	8,15...7,44 (4H, m, C_6H_4); 7,50 (1H, s, NH*); 6,55 (1H, s, NH*)	71
IIk	$C_{12}H_{11}N_4O_4 \cdot Na$	8,40...7,90 (4H, m, C_6H_4); 7,54 (1H, s, NH*); 6,66 (1H, s, NH*); 4,32 (2H, q, J=7,2, CH_2); 1,34 (3H, t, J=7,2, Me)	80
IIl	$C_9H_6N_5O_4 \cdot Na$	8,70...8,05 (4H, m, C_6H_4); 7,53 (1H, s, NH*); 6,58 (1H, s, NH*)	83
IIm, IIIm	$C_{11}H_{11}N_4O_2 \cdot Na$	7,37...7,20 (5H, m, Ph); 5,05 (2H, s, CH_2); 4,32 (2H, s, d, J=7,2, CH_2); 3,35 (3H, s, Me); 2,75 (3H, s, d, J=5,5 Me)	44
IIn	$C_{11}H_{11}N_4O_2 \cdot Na$	8,03...7,14 (5H, m, C_6H_4, NH); 2,74 (3H, s, d, J=5,5, Me); 2,32 (3H, s, Me)	75
IIo, IIIo	$C_{16}H_{13}N_4O_3 \cdot Na$	10,61 (1H, s, NH); 10,41 (1H, s, NH); 8,10...6,84 (9H, m, Ph, C_6H_4); 3,79 (3H, s, OMe); 3,72 (3H, s, OMe)	91
IIp, IIIp	$C_{17}H_{15}N_4O_3 \cdot Na$	10,58 (1H, s, NH); 10,49 (1H, s, NH); 8,00...6,84 (8H, m, $2C_6H_4$); 3,78 (3H, s, OMe); 3,72 (3H, s, OMe); 2,32 (3H, s, Me); 3,25 (3H, s, Me)	92
IIq IIIc	$C_{18}H_{16}N_5O_4 \cdot Na$	10,59 (1H, s, NH); 10,49 (1H, s, NH); 10,00 (1H, s, NH); 9,82 (1H, s, NH); 8,00...6,83 (8H, m, $2C_6H_4$); 3,78 (3H, s, OMe); 3,72 (3H, s, OMe); 2,05 (3H, s, C(O)Me); 2,01 (3H, s, C(O)Me)	87
IIr, IIIr	$C_{16}H_{12}ClN_4O_3 \cdot Na$	10,80 (1H, s, NH); 10,41 (1H, s, NH); 8,17...6,35 (8H, m, $2C_6H_4$); 3,78 (3H, s, OMe); 3,72 (3H, s, OMe)	93
IIs, IIIs	$C_{16}H_{12}BrN_4O_3 \cdot Na$	10,80 (1H, s, NH); 10,37 (1H, s, NH); 8,13...6,84 (8H, m, $2C_6H_4$); 3,78 (3H, s, OMe); 3,72 (3H, s, OMe)	93
IIt, IIIt	$C_{18}H_{15}N_4O_4 \cdot Na$	11,05 (1H, s, NH); 10,35 (1H, s, NH); 8,35...6,85 (8H, m, $2C_6H_4$); 3,79 (3H, s, OMe); 3,73 (3H, s, OMe); 2,59 (3H, s, C(O)Me); 2,51 (3H, s, C(O)Me)	90
IIu, IIIu	$C_{19}H_{17}N_4O_5 \cdot Na$	11,04 (1H, s, NH); 10,36 (1H, s, NH); 8,33...6,85 (8H, m, $2C_6H_4$); 4,33 (2H, q, J=7,2, CH_2); 4,29 (2H, q, J=7,2, CH_2); 3,79 (3H, s, OMe); 3,73 (3H, s, OMe); 1,34 (3H, t, J=7,2, Me); 1,32 (3H, t, J=7,2, Me)	87

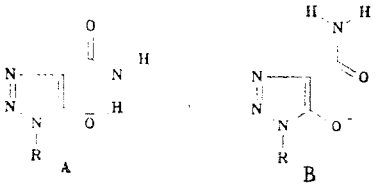
*Signals of nonequivalent protons of CONH groups.

bonded to the nitrogen atom in the 1 position of the triazole ring and to the amido grouping differ from one another with respect to their chemical shifts and multiplicities; this made it possible to determine the ratios of isomers II and III from the integral values of the signals of these protons (see Table 1).

Three absorption bands — the first at 3415-3460 cm^{-1}, the second at 3330-3390 cm^{-1}, and the third at 3295-3320 cm^{-1} — are observed in the IR spectra of 1,2,3-triazol-5-olates IIg-*l*, while two absorption bands at 3330 and 3240 cm^{-1} were observed in the IR spectrum of IIn; these bands were ascribed to stretching vibrations of the N—H bond in amido groups. The absorption of a carbonyl group in the IR spectra of these compounds shows up in the form of an intense band at 1620-1630 cm^{-1}.

Signals of protons of a methyl group at 2.75 ppm, which show up in the form of superimpositions of a doublet and a singlet, are observed in the PMR spectrum of IIn in d_6-DMSO. The partial transformation of the doublet to a singlet is associated with deuterium exchange of the protons of the NH group. The δ values and the multiplicity of the manifestation of the signals of the methyl group constitute evidence that it is located in the N-methylcarbamoyl grouping, which confirms the structure of IIn.

Two broad singlets related to signals of an unsubstituted amido group are observed in the PMR spectra of 1,2,3-triazol-5-olates IIg-m at weak field at 6.3-6.8 ppm and 7.2-7.7 ppm on the background of multiplets of aromatic protons (IIg-j) and at free field (IIk, l), but signals at weaker field at 9.0-11.5 ppm, which would correspond to the resonance of the proton of an aryl-substituted amido grouping, are not found. The nonequivalence of the protons of the amido group in the PMR spectra of IIg-m can be explained by the existence of retarded rotation of this group as a consequence of interaction of one of the protons with the olate function in the 5 position of the triazole ring (form **A**) or by the existence of IIg-m in the form of two conformers (**A** and **B**).



It is known [6] that when a compound is heated, the signals of the nonequivalent (because of retarded rotation) protons of an amino group become degenerate in the PMR spectra, and a signal of two protons oriented symmetrically relative to those that have vanished develops in place of them. An unsymmetrical orientation of this signal is usually associated with a change in the configuration of the molecule.

We investigated the temperature dependence at 20-100°C of the PMR spectrum of IIi and established that at 40-60°C the signals of the nonequivalent protons at 7.57 and 6.54 ppm become degenerate, while a signal of two equivalent protons of an amido group at 6.70 ppm, which is oriented asymmetrically relative to the vanished one-proton signals, develops at temperatures above 80°C (see Fig. 1). This constitutes evidence for a change in the configuration of the molecule that is probably associated with 180°C rotation of the carboxamide fragment about the $C_4—C_{CO}$ bond or with free rotation of the amido group about this bond. Free rotation of the amino group is also possible in both cases. Thus it was shown that IIh, i and, consequently, IIg, i-l exist in the form of conformer **A** at low temperatures and in the form of conformer **B** at high temperatures or that free rotation about the $C_4—C_{CO}$ and $C_{CO}—N_{NH_2}$ bonds exists.

To confirm the 1,2,3-triazol-5-olate IIh-m structure selected on the basis of the PMR spectra we studied the ^{13}C NMR spectra of IIg, h, k, n and model compounds, to serve as which we selected IIa and sodium 4-N-methylcarbamoyl-1-methyl-1,2,3-triazol-5-olate (VII) (see Table 2).

In the ^{13}C NMR spectra of IIg, h, k the signal of the ^{13}C atom of the carboxamido group is observed in the form of a singlet at 165.45 (IIg, h) and 165.33 ppm (IIk). When a methyl group is introduced into the carboxamido grouping, this signal in the ^{13}C NMR spectra of IVn and IIn shows up at stronger field at 164.67 and 164.34 ppm and is split by the protons of the methyl group into a quartet with a terminal spin-spin coupling constant (SSCC) of 3.7 and 3.1 Hz, respectively. The carbon atom in the 4 position of the triazole ring is observed in the ^{13}C NMR spectra of IIg, h, k in the form of a doublet with SSCC through three bonds of 3.7 and 3.6 Hz. In the ^{13}C NMR spectra of VII and IIn the signal of this atom shows up in the form of a singlet. The observed multiplicity is not in agreement with the rules of splitting of the signals of carbon atoms by hydrogen atoms, according to which the $C_{(4)}$ atom should be in the form of a triplet in the case of IIg, h, k, whereas it should be in the form of a doublet in the case of VII and IIn. The nonconformity of the multiplicity in this case, like the appearance of the hydrogen atoms of the amido group in the form of two broad singlets in the PMR spectra, can be explained by linking of one hydrogen atom of the amido group with the olate function in the 4 position of the triazole ring.

The assignment of the signals of the carbon atoms of the methyl groups of IIa, k and VII was made on the basis of the ^{13}C NMR spectrum for sodium 1-methyl-4-cyano-1,2,3-triazol-5-olate (VIII). It is apparent from the data in Table 2 that the signals at 29.32 and 29.41 ppm in the ^{13}C NMR spectra of IIa, VII, and VIII are related to

the carbon atoms of methyl groups in the 1 position of the triazole ring, while the signals at 24.72 ppm in the spectra of VII and IIn correspond to the carbon atoms of a methyl group in the amido grouping.

Thus an analysis of the spectral data confirmed the 1,2,3-triazole-5-olate IIg-n structure that we proposed.

To confirm the effect of substituents in the amido group on the rate of cyclization of diazoimidolates I we calculated the cyclization competition constants from the formula

$$K_c = K^1/K^2 = [II]/[III],$$

where K_c is the competition constant, K^1 is the rate constant for conversion of diazoimidolate I to triazole II, and K^2 is the rate constant for conversion of diazoimidolate I to triazole III.

The use of a large amount of sodium ethoxide (up to a twofold excess) and a change in the reaction temperature do not change the ratios of the isomeric 1,2,3-triazol-5-olates; this confirms that the reaction takes place through intermediate diazoimidolates I.

With respect to the degree of decrease in the rate of cyclization of diazoimidolates I the substituents can be arranged in the following order: Ar > > Bz > cyclo-C_6H_{11} > iso-Pr > Bu > Me > Et > H.

Analyses by means of the Hammett and Taft equation were carried out for the K_c constants for the cyclization of aryl derivatives I and alkyl derivatives I, respectively. For the reaction of diazomalonodiarylimidolates I the calculated ρ value is 0.9 ± 0.01 (correlation coefficient r = 0.98), as compared with $\rho = 1.8 \pm 0.01$ for alkyl derivatives I (with allowance for the steric constants, S = 0.8; r = 0.99).

These data constitute evidence for an increase in the rate of cyclization of diazoimidolates I when electron-acceptor substituents are introduced at the nitrogen atom of the imidoyl group. This effect is evidently associated with preferred reaction of the electrophilic diazo group with the nitrogen atom on which a higher negative charge is formed.

For the alkyl derivatives of diazoimidolates I the large steric and inductive effect of the substituents indicates the formation of imidolates as intermediates. On the other hand, a concerted mechanism is most likely for the aryl derivatives: localization of the partial negative charge on the nitrogen atom occurs simultaneously with cyclization.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Specord IR-75 spectrometer. The PMR spectra of solutions of IIa-n and IIIa-f were obtained with a Bruker WP-80 spectrometer (80.13 MHz); the resolution in recording of the PMR spectra was 0.15-0.30 Hz. The PMR spectra of solutions of 1,2,3-triazol-5-olates IIIo-u and IIo-u were recorded with a Varian VXR-400 spectrometer (400 MHz); the resolution in recording of the spectra was 0.03-0.05 Hz. The chemical shifts of the protons were measured with respect to the signal of the solvent (39.6 ppm for d_6-DMSO). The monitoring of the reactions and the determination of the compositions of the reaction mixtures were accomplished by means of TLC on Silufol UV-245 plates in various solvent systems; the chromatograms were developed in UV light and in iodine vapors.

Malonic acid diamides IVa-u were obtained by the methods described in [6].

The principal properties of 1,2,3-triazol-5-olates IIa-u and IIIa-f, m, o-u are presented in Table 3. The results of elementary analysis for C, H, N, and Hal for all of the synthesized compounds were in agreement with the calculated values.

Sodium 4-[N-R^2(R^1)-Carbamoyl]-1-R^1(R^2)-1,2,3-triazole-5-olates (IIa-u, IIIa-g, o-u). A 10-mmole sample of IVa-u was dissolved at 20-60°C in a solution of 10 mmole of sodium ethoxide in 10-15 ml of ethanol, 1.83 g (10 mmole) of benzenesulfonyl azide was added, and the reaction mixture was stirred at 24°C for 3 h and then allowed to stand for 24 h at this temperature. The precipitated IIe, m-u and IIIe, m, n-u were removed by filtration, washed with ether, and dried. In the case of IIa-d, f and IIIa-d, f the solvent was removed by distillation at reduced pressure, 15 ml of water was added, the undissolved benzenesulfonamide was removed by filtration, the filtrate was evaporated at reduced pressure, the residue was triturated in 30 ml of dry ether, and the precipitate was removed by filtration.

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SYNTHESIS AND STRUCTURES OF METHYL-SUBSTITUTED 1,2,4,5-TETRAHYDRO-3H-SPIRO(BENZ-2-AZEPINE-3,4′-PIPERIDINES)

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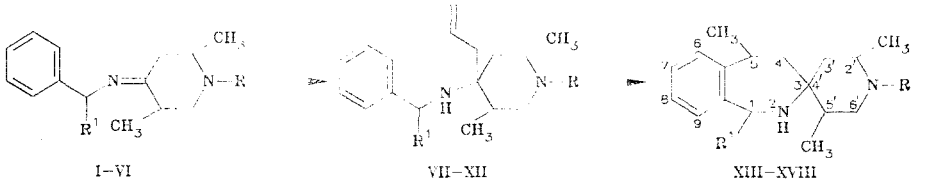
UDC 547.981.2+547.822.3+547.642

Methyl-substituted 1,2,4,5-tetrahydro-3H-spiro(benz-2-azepine-3,4′-piperidines) were obtained by the intramolecular cyclization of 4-allyl-4-N-benzyl(α-phenylethyl)aminopiperidines in an acidic medium. The individual isomers of 1′-benzyl-2′,5,5′-trimethyl-1,2,4,5-tetrahydro-3H-spiro(benz-2-azepine-3,4′-piperidine) were isolated, and their structures were established.

We have developed a preparative method for obtaining 1,2,3,4-tetrahydro-4-methylspiro(quinoline-2,1′-cycloalkanes) and -spiro(quinoline-2,4′-piperidines) by the intramolecular cyclization in an acidic medium of 1-N-arylaminocycloalkanes and 4-allyl-4-N-arylaminopiperidines, which were obtained from the corresponding Schiff bases and allylmagnesium bromide [1-3].

In the present research this method was used for the synthesis of compounds that are related to a new heterocyclic system — 1,2,4,5-tetrahydro-3H-spiro(benz-2-azepine-3,4′-piperidine).

The starting N-(1-methyl-, N-(1-n-propyl-, and N-(1-benzyl-2,5-dimethyl-4-piperidylidene)benzylamines (I, II, and III) and N-(1-methyl-, N-(1-n-propyl-, and N-(1-benzyl-2,5-dimethyl-4-piperidylidene)-α-phenylethylamines (IV, V, and VI) were obtained by condensation of the corresponding 4-piperidinones [4, 5] with benzyl- and α-phenylethylamines (see Table 1). Molecular-ion peaks corresponding to their empirical formulas are observed in the mass spectra of I-VI. The IR spectra contain an intense band of stretching vibrations of a C=N bond at 1669-1680 cm^{-1}.



I–VI VII–XII XIII–XVIII

I, IV, VII, X, XIII, XVI R=CH_3, II, V, VIII, XI, XIV, XVII R=$CH_2CH_2CH_3$, III, VI, IX, XII, XV, XVIII R=$CH_2C_6H_5$; I—III, VII—IX, XIII—XV R^1=H, IV—VI, X—XII, XVI—XVIII R^1=CH_3

1-Methyl-, 1-n-propyl-, and 1-benzyl-2,5-dimethyl-4-allyl-4-N-benzylaminopiperidines (VII, VIII, and IX) and 1-methyl-, 1-n-propyl-, and 1-benzyl-2,5-dimethyl-4-allyl-4-N-(α-phenylethyl)aminopiperidines (X, XI, and XII) were synthesized in 49-77% yields from Schiff bases I-VI and allylmagnesium bromide. Imine I and aminopiperidine VII were previously described in [2].

According to TLC data, aminopiperidines VII-XII are mixtures of stereoisomers. The molecular-ion peaks in the mass spectra of VII-XII correspond to their empirical formulas. The absorption bands in the IR spectra at 3310-3342 and 1620-1648 cm^{-1} confirm the presence of NH and CH=CH_2 groups.

1,2,4,5-Tetrahydro-1′,2′,5,5′-tetramethyl-, -2′,5,5′-trimethyl-1′-n-propyl-, -2′,5,5′-trimethyl-1′-benzyl-, -1,1′,2′,5,5′-pentamethyl-,-1,2′,5,5′-tetramethyl-1′-n-propyl-,and-1,2′,5,5′-tetramethyl-1′-benzyl-3H-spiro(benz-2-azepine-3,4′-piperidines) (XIII-XVIII), respectively, are formed in 29-52% yields from aminopiperidines VII-XII by the action of sulfuric acid as a result of intramolecular cyclization. Spiro compounds XIII-XVIII are complex mixtures of isomers. This is due to the fact that starting N-substituted allylaminopiperidines VII-XII are mixtures of isomers with respect to the location of the methyl groups in the $C_{(2')}$ and $C_{(5')}$ positions of the piperidine ring, as indicated by the presence of two signals from the protons of the N—CH_3 group in the PMR spectra of X, XIII,

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