was neutralized with 25% NH_4OH without permitting the mixture to heat up. The precipitates were filtered off, washed with ice water, and dried in air. The products were crystallized from ethanol (VIII), n-propanol (IX), and acetone (X).

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BROMINATION OF 8R-4-PHENYL-2,3-DIHYDRO-1H-1,5-BENZODIAZEPINONES-2

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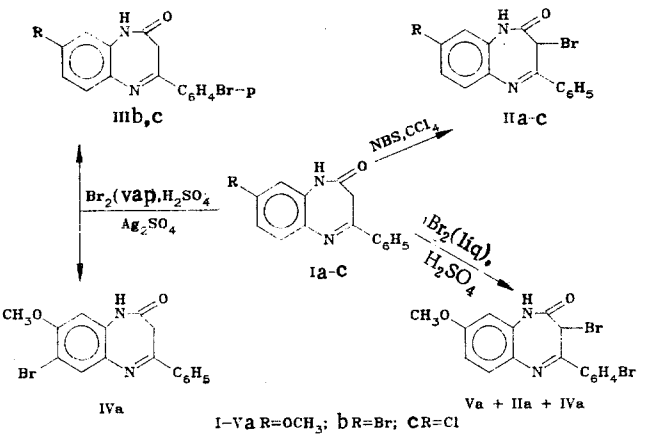
UDC 547.892:542.944.1

The influence of the nature of the substituents and the brominating agent on the direction of the bromination of 8R-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepinones-2 containing various substituents in the annelated benzene ring.

Protonation of the heterocycle deactivates the annelated benzene ring of 4-phenyl-2,3-dihydro-1H-1,5-benzodiazepinone-2 and promotes the incorporation of bromine into the phenyl radical [1]. This communication is devoted to a study of the bromination of 8R-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepinones-2 (Ia-c), containing substituents of different types in the benzene ring of the heterocycle:



I-V a R=OCH_3; b R=Br; c R=Cl

Bromination of compounds Ia-c by N-bromosuccinimide in CCl_4 solution with heating for 6 h leads to 3-bromo-4-phenyl-8R-2,3-dihydro-1H-1,5-benzodiazepinones-2 (IIa-c). The PMR spectra of compounds IIa-c contain a singlet of the methine proton at 6.02-6.04 ppm. The product of acid hydrolysis [2] of compounds IIa-c is α-bromoacetophenone, which confirms the indicated reaction pathway.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1133-1135, August, 1984. Original article submitted April 21, 1983; revision submitted January 28, 1984.

0009-3122/84/2008-0927$08.50

TABLE 1. Bromoderivatives of 4-Phenyl-8R-2,3-dihydro-1H-1,5-benzodiazepinones-2

Compound	mp, °C	IR spectrum, cm^{-1}			Found, %				Empirical formula	Calculated, %				Yield, %
		C=O	C=N	NH	C	H	N	Br		C	H	N	Br	
IIa	201—202	1680	1620	3350, 3200	55,6	3,7	8,1	23,0	$C_{16}H_{13}BrN_2O_2$	55,6	3,7	8,1	23,1	70
IIb	185—186	1675	1610	3340, 3210	45,5	2,5	7,2	40,5	$C_{15}H_{10}Br_2N_2O$	45,6	2,5	7,1	40,6	72
IIc	203—204	1676	1620	3330, 3260	51,4	2,8	8,1	—	$C_{15}H_{10}BrClN_2O$	51,5	2,8	8,0	—	64
IIIb	193—194	1675	1610	3335, 3270	46,0	2,5	7,8	41,0	$C_{15}H_{10}Br_2N_2O$	45,6	2,5	7,6	40,6	70
IIIc	249	1675	1610	3340, 3200	51,0	3,0	8,1	—	$C_{15}H_{10}BrClN_2O$	51,5	2,8	8,0	—	62
IVa	228—230	1676	1615	3200	55,5	3,6	8,1	32,1	$C_{16}H_{13}BrN_2O_2$	55,5	3,7	8,1	23,1	52
Va	180—181	1675	1615	3330, 3200	45,3	2,7	6,7	37,7	$C_{16}H_{12}BrN_2O_2$	45,2	2,8	6,6	37,7	25

The bromination of benzodiazepinones Ia-c by bromine vapor in concentrated sulfuric acid in the presence of silver sulfate proceeds differently. Thus, compounds Ib, c, containing electron acceptor substituents, like the unsubstituted diazepinone [1], form 4-(p-bromophenyl)-8R-2,3-dihydro-1H-1,5-benzodiazepinone-2 (IIIb, c). In the PMR spectra of these compounds, signals of the protons of the methylene groups (3.43-3.55 ppm) and the singlet of NH (9.12-10.60 ppm) are observed. Acid cleavage of substances IIIb, c leads to p-bromoacetophenone.

The increase in the activity of the annelated benzene ring (compound Ia) after bromination under the same conditions leads to 7-bromo-8-methoxy-2,3-dihydro-1H-1,5-benzodiazepinone-2 (IVa), the PMR spectrum of which contains the singlet of the methylene protons at 4.06 ppm. In acid cleavage of substance IVa, 4-methoxy-5-bromo-o-phenylenediamine was isolated. The structure of compound IVa was confirmed by the identity of its UV spectrum with the spectra of 7-bromosubstituted diazepinones [1].

In the bromination of the diazepinone Ia with liquid bromine in sulfuric acid, a mixture of three substances is formed and can be separated by the method of column chromatography. According to the data of the IR spectra, melting point, and R_f, two of the compounds obtained are identical with the bromoderivatives IIa and IVa. Elementary analysis of the third substance showed the presence of two bromine atoms, while the absence of an intense band at 240-260 nm in the UV spectrum and the hypsochromic effect of the long-wave band are characteristic of compounds with bromine in the 3-position [1, 3]. The PMR spectrum, which does not contain the signals of the methylene protons and has a singlet of the protons of the methine group at 6.03 ppm, agrees with the structure Va. The production of p-bromophenacyl bromide in acid hydrolysis confirms this conclusion.

EXPERIMENTAL

The course of the reactions and the purity of the compounds obtained was monitored by thin-layer chromatography on Silufol UV-254. The UV spectra were recorded on a Specord UV-vis spectrophotometer in ethanol. The IR spectra were obtained on a UR-20 instrument in KBr tablets. The PMR spectra were recorded on a Tesla BS-487C spectrometer (70 MHz) in trifluoroacetic acid, internal standard HMDS.

Bromination of 8R-4-Phenyl-2,3-dihydro-1H-1,5-benzodiazepinone-2. A. To a solution of 10 mmoles of the benzodiazepinone-2 Ia-c in 40 ml of CCl_4 we added 1.93 g (10 mmoles) of N-bromosuccinimide. The mixture was boiled with mixing for 6-8 h, the succinimide that precipitated was filtered off, the filtrate was evaporated, and the residue was recrystallized. The yields and constants are cited in Table 1.

B. Bromine vapors (0.384 g, 2.4 mmoles) were bubbled into a mixture consisting of 2 mmoles of the diazepinone Ia in 15 ml conc. H_2SO_4 and 0.624 g (2 mmoles) of silver sulfate in an atmosphere of nitrogen. The precipitate formed was removed, the filtrate neutralized to pH 5-6 with a solution of potassium hydroxide, and the newly formed precipitate added to the first and recrystallized from ethanol.

C. To 0.53 g (2 mmoles) of the benzodiazepinone Ia in 15 ml of conc. H_2SO_4, 0.352 g (2.2 mmoles) of bromine in 5 ml of glacial acetic acid was added dropwise with mixing over a period of 1 h, and the mixture was exposed for 5 h. The reaction mass was poured out onto ice, the crystals removed, the filtrate neutralized to pH 5-6 with a potassium hydroxide solution, and the precipitate formed was filtered off and added to the first. The mixture of IIa, IVa, and Va obtained was separated by column chromatography on silica gel, eluent: benzene–ethyl acetate, 7:3. Yield of Va 25%, R_f 0.74.

Hydrolysis of Bromoderivatives IIa-c, IIIb, c, and Va. We boiled 1 mmole of the corresponding bromoderivatives of benzodiazepinone in 10 ml of 2 N H_2SO_4. The course of the reaction was followed chromatographically. The bromoderivatives of acetophenone isolated (IIIb, c, and Va) were identified according to the physicochemical constants; the acetophenone (IIa-c) was identified in the form of the semicarbazone.

Hydrolysis of 8-Methoxy-7-bromo-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepinone-2 (IVa). We heated 0.77 g (2 mmoles) of compound IVa in a solution consisting of 10 ml of ethanol and 10 ml of 5 N HCl, for 3 h. The cooled solution was neutralized to pH 6-7 with a solution of ammonia, and 4-methoxy-5-bromo-o-phenylenediamine with mp 81-82°C (from ethanol) was isolated.

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A NEW DERIVATIVE OF 1,5-DIHYDROPYRAZOLO[4,3-c][1,2,5]BENZOTRIAZEPINE

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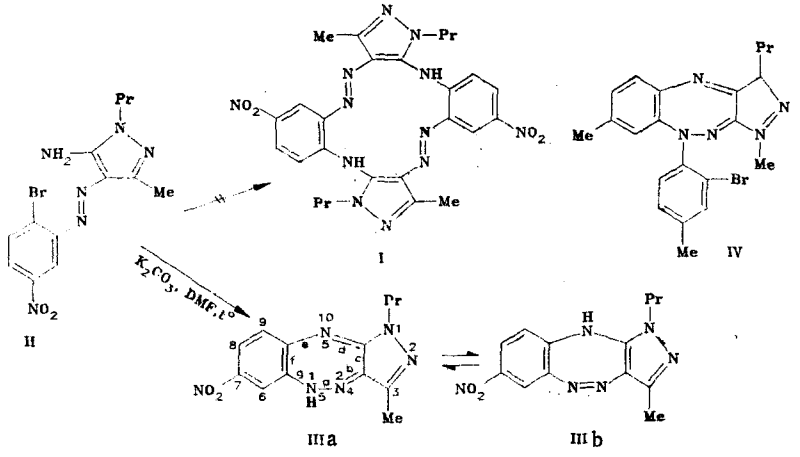
UDC 547.778'892:542.953.5:543.51'422.25'4

A new compound, 1,5-dihydro-3-methyl-7-nitro-propylpyrazolo[4,3-c][1,2,5]benzotriazepine, was synthesized by intramolecular cyclization of 5-amino-4-[(2-bromo-5-nitrophenyl)azo]-3-methyl-1-isopropylpyrazole, and it was established on the basis of the spectral data that the triazepine ring in the synthesized compound exists in two tautomeric forms — amino-azo- and hydrazone. The structure of the compound synthesized was confirmed by the data of the PMR, IR, electronic, and mass spectra.

In an attempt to produce the macrocyclic ligand I by nontemplate bimolecular autocyclization of compound II, 1,5-dihydro-3-methyl-7-nitro-1-propylpyrazolo[4,3-c][1,2,5]benzotriazepine (III), a product of intramolecular cyclization, was isolated.



The formation of the derivative 1,5-dihydropyrazolo[4,3-c][1,2,5]-benzotriazepine IV as a side product was previously observed in the intermolecular autocyclization of 5-amino-4-[(2-bromo-4-methylphenyl)-azo]-3-methyl-1-propylpyrazole [1, 2]. The new triazepine derivative III does not contain substituents at the nitrogen atom in the hydrazone group.

The pathways of decomposition of the molecular ions of triazepines III and IV are analogous. In the mass spectrum of compound III a peak of the molecular ion with m/z 286* is observed (100%). The seven-membered triazepine ring is stable; therefore at the first stage of the decomposition the pyrazole ring begins to break down, forming fragments characteristic of triazepine systems:

*Here and henceforth, the numbers characterizing an ion define the value of m/z.

All-Union Scientific-Research Institute of Chemical Reagents and Ultrapure Chemical Substances, Moscow 107258. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1136-1139, August, 1984. Original article submitted December 21, 1983.

 0009-3122/84/2008-0930$08.50