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AMINOMETHYLATION OF 1,2,4-TRIAZOLES AND TETRAZOLES

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UDC 547.792'796.1

Aminomethylation was accomplished in a series in which the starting amino compounds and the components of acidic character belong to the azole class. Two-ring Mannich bases are formed in the reaction of 4-amino-1,2,4-triazole or N-methyl-5-aminotetrazole in an aqueous medium with formaldehyde and NH-triazoles, the acidic properties of which are known.

Little study has been devoted to aminomethylation in the triazole and tetrazole series. The scanty data that are available relative to this problem pertain to the reaction of some CH acids of the nitroalkane series with formaldehyde and 4-amino-1,2,4-triazole [1] or 5-aminotetrazole [2]. We have for the first time accomplished aminomethylation in a series in which both the starting amino compounds and the components of acidic character belong to the azole class.

Two-ring Mannich bases — 4-aminomethylene(3-X-5-R-1,2,4-triazol-1-yl)triazoles (VIII-XIII) — are formed in the reaction of 4-amino-1,2,4-triazole with formaldehyde and NH triazoles I-VI.

Compounds of the same type, viz., 1-methyl-5-aminomethylene(3-X-5-R-1,2,4-triazol-1-yl)-tetrazoles (XIV, XV), are formed in the reaction of NH triazoles II and VII with 1-methyl-5-aminotetrazole.

An increase in the yields of the described Mannich bases is observed as the acidities of the starting NH-triazoles I-VII, the properties of which are known [3], increase. In the reaction scheme and in Table 1 VIII-XV are arranged in orders corresponding to the increase in the acidic properties of the starting compounds from pK_a 10.08 for 1,2,4-triazole (I) to pK_a 3.05 for 3-nitro-5-bromo-1,2,4-triazole (VII).

The position of the signals in the PMR spectra of the Mannich bases for the protons of the methylene groups, which link the nitrogen atom of the heteroring of the triazole (an acid) with the amino group, changes somewhat as a function of the electronic and magnetic effects of the substituents in the 3 and 5 positions of the triazole ring. The protons attached to the carbon atoms of the 4-amino-1,2,4-triazole heteroring in VIII-XIII are sterically equivalent and give a singlet at 8.1-8.4 ppm in the spectra of all of the compounds.

Siberian Technological Institute, Kransoyarsk 660049. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 549-551, April, 1982. Original article submitted May 20, 1981.

0009-3122/82/1804-0423$07.50

TABLE 1. Characteristics of the Synthesized Compounds

Compound	mp, * °C	PMR spectrum, δ, ppm				IR spectrum, cm^{-1}		Found, %			Empirical formula	Calc., %			Yield, %
		A ring, –CH	B ring, –CH	–CH$_2$	NH	ν_x	ν, A ring	C	H	N		C	H	N	
VIII	120—121	8,50s	8,10s	5,50	8,25	—	1520, 1490, 1300, 1140	36,2	4,5	59,0	$C_5H_7N_7$	36,4	4,2	59,4	55
IX	166—167	8,50 s	8,20s	5,40	8,00	2150 (N_3)	1510, 1430, 1350, 1130	29,2	2,9	68,0	$C_5H_6N_{10}$	29,1	2,9	68,0	60
X	151	8,70 s	8,40s	5,50	8,20	—	1510, 1400, 1290, 1140	30,1	3,1	49,6	$C_5H_6ClN_7$	30,1	3,0	49,1	62
XI	129—130	2,35 (CH_3)	8,45s	5,65	8,20	1560, 1320 (NO_2)	1520, 1430, 1300, 1130	31,6	3,6	49,7	$C_6H_8N_8O_2$	32,1	3,6	50,0	50
XII	159	8,85 s	8,30s	5,70	8,20	1560, 1320 (NO_2)	1515, 1430, 1300, 1120	28,3	3,4	52,4	$C_5H_6N_8O_2$	28,6	2,9	53,3	76
XIII	157	—	8,40 s	5,40	8,15	—	1490, 1440, 1290, 1130	25,1	2,2	42,1	$C_5H_5Cl_2N_7$	25,6	2,1	41,9	85
XIV	151—153	8,70s	3,80 (CH_3)	5,70	8,50	2150 (N_3)	1520, 1440, 1350, 1110	27,3	4,0	69,4	$C_5H_7N_{11}$	27,15	3,2	69,7	53
XV	190	—	3,90 (CH_3)	6,00	8,80	1560, 1320 (NO_2)	1500, 1440, 1290, 1130	19,7	1,9	41,6	$C_5H_6BrN_9O_2$†	19,74	2,0	41,4	65

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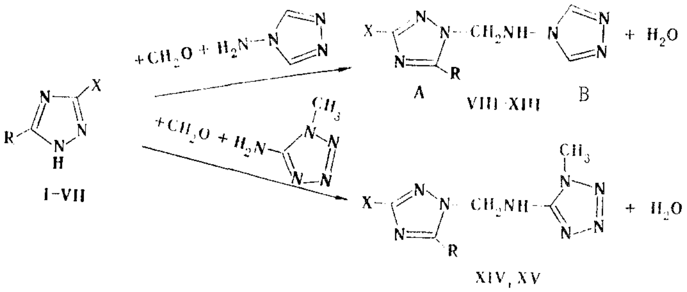
*The compounds were recrystallized: VIII-XI from ethanol, XII from water—ethanol, and XIII-XV from water.

†Found: Br 26.5%. Calculated: Br 26.3%.



I, VIII X=R=H; II, IX, XIV X=N_3, R=H; III, X X=Cl, R=H; IV, XI X=NO_2, R=CH_3;
V, XII X=NO_2, R=H; VI, XIII X=R=Cl; VII, XV X=NO_2, R=Br

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a Perkin–Elmer R-12 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of films of the compounds were recorded with a UR-20 spectrometer.

4-Aminomethylene(3-X-5-R-1,2,4-triazol-1-yl)-1,2,4-triazoles (VIII-XIII). A 1.9 ml (0.025 mole) sample of a 36% solution of formaldehyde was added at 40°C to a stirred suspension of 0.025 mole of 3-X-5-R-1,2,4-triazole I-VI and 2.3 g (0.025 mole) of 4-amino-1,2,4-triazole in 30 ml of water, and the mixture was heated at 60°C for 30 min. It was then cooled, and the precipitated crystals of IX, X, XII, or XIII were removed by filtration. In the preparation of VIII 0.1 g of NaOH was added to the reaction mixture. Crystalline VIII was isolated after completion of the reaction and maintenance of the reaction mixture at 3-5°C for 12 h. Compound XI was isolated by extraction of the cooled reaction solution with ethyl acetate. The compounds were purified by recrystallization from water, alcohol, or aqueous alcohol.

1-Methyl-5-aminomethylene(3-X-5-R-1,2,4-triazol-1-yl)tetrazoles (XIV, XV). These compounds were obtained from triazoles II and VII, respectively, formaldehyde, and 1-methyl-5-aminotetrazole by the method described for IX-XIII. In the preparation of XIV the time during which the reaction mixture was maintained at 60°C was increased to 1 h with subsequent evaporation to dryness. Compounds XIV and XV were recrystallized from water.

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