HALOGENATION OF HETEROCYCLIC ACETYLENIC MONO- AND DIAMINES

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Cyclic acetylenic monoamines, synthesized by the decomposition of the corresponding acetylenic aminoalcohols, and diamines, obtained by the Mannich reaction, give the products of the monoaddition of the halogens at the triple bond in aqueous solutions of acids.

The majority of the acetylenic nitrogen-containing compounds possesses physiological activity [1, 2]. We previously described [3, 4] the isolation of unsaturated halogen-containing amino-compounds from acetylenic aminoalcohols. In the given work, the results of the synthesis of previously unknown halogen-containing compounds from heterocyclic acetylenic mono- and diamines are presented. The acetylenic amines may be synthesized by the condensation of secondary amines with acetylene in the presence of paraformaldehyde [5, 6]. Under normal reaction conditions, it is impossible to stop at the stage of monoamine formation, and therefore the acetylenic diamines are the main product. Under laboratory conditions, it is more convenient to synthesize the monoamines using the reverse Favorskii reaction, i.e., by the cleaving of the corresponding acetylenic amino-alcohols (I)-(IV) [7] in the presence of KOH or $Ba(OH)_2$. The decomposition of the compounds (II) and (IV) thereby requires more drastic conditions (KOH, 160°C) than those for the decomposition of (I) and (III) [$Ba(OH)_2$, 140°C]; the increase in the temperature of the pyrolysis in the presence of KOH favors the prototropic isomerization and leads to a decrease in the yield of the main product. The structure of the heterocyclic acetylenic monoamines (V)-(VIII) obtained is confirmed by their condensation with acetone or methyl ethyl ketone to the same acetylenic aminoalcohols (I)-(IV) (Table 1).

$$R^1R^2C(OH)C{\equiv}CCH_2NR_2$$

I-IV

I NR_2= piperidyl $R^1=R^2=CH_3$; II NR_2= piperidyl $R^1=CH_3$, $R^2=C_2H_5$; III NR_2= morpholyl,, $R^1=R^2=CH_3$; IV NR_2=morpholyl, $R^1=CH_3$, $R^2=C_2H_5$

At the present time, there is a very small amount of data [10, 11] on the addition of halogens to the acetylenic mono- and diamines. We found that the chlorination and bromination of the compounds (V)-(VIII) proceeds without complications and leads to the formation, in good yields, of the dihalides in accord with the data of [12] (Table 2).

TABLE 1. Physicochemical Constants of the Acetylenic Amines and Aminoalcohols (I)-(VIII)

Compound	bp, °C (mm of Hg stem)	n_D^{20}	d_4^{20}	Yield, %	Hydrochloride/dihydrochloride, mp, °C	Methiodide/dimethiodide, mp, °C
I	113 (3)	1,4905	0,9836	85	—	—
II	124 (3)	1,4921	0,9548	76	—	—
III	120 (3)	1,4918	0,9801	72	—	—
IV	130 (3)	1,4923	0.9651	68	—	—
V	72 (35) [8]	1,4706	1.0046	78	178...179	138...139
VI	68 (10) [8]	1,4738	1.0018	63	166...167	132...133
VII	149 (3) [9]	1,4954	1.0561	55	280...281	218...220
VIII	151 (3) (mp 75°C)	1,4931	1.0656	63	252...253	215...217

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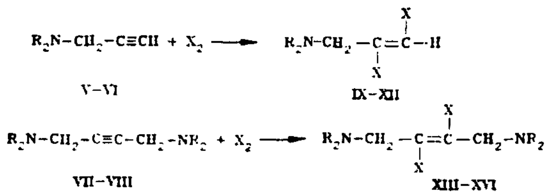
TABLE 2. Characteristics of the Halogenated Acetylenic Amines (IX)-(XVI)

Compound	mp, °C	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	N	halogen		C	H	N	halogen	
IX	93...94	49.5	6.6	7.2	36.5	$C_8H_{13}Cl_2N$	49.5	6.7	7.2	36.6	80
X	102...103	33.9	4.4	9.8	56.5	$C_8H_{13}Br_2N$	33.9	4.6	9.9	56.5	93
XI	89...90	42.8	5.6	7.1	36.1	$C_7H_{11}Cl_2NO$	42.8	5.6	7.1	36.2	76
XII	101...102	29.2	3.8	4.7	56.1	$C_7H_{11}Br_2NO$	29.5	3.8	4.9	56.1	79
XIII	158...159	57.7	8.2	9.6	24.4	$C_{14}H_{24}Cl_2N_2$	57.7	8.2	9.6	24.4	82
XIV	166...167	44.2	6.3	7.3	42.0	$C_{14}H_{24}Br_2N_2$	44.2	6.3	7.4	42.1	85
XV	140...141	48.7	6.7	9.4	24.0	$C_{12}H_{20}Cl_2N_2O_2$	48.8	6.8	9.5	24.1	84
XVI	156...157	37.5	5.2	7.2	41.4	$C_{12}H_{20}Br_2N_2O_2$	37.5	5.2	7.3	41.7	86

TABLE 3. Chemical Shifts in the ^{1}H and ^{13}C NMR Spectra of the Monoamines, Diamines, and Their Halogen Derivatives, δ, ppm

Compound	Position of nuclei		^{1}H NMR spectra			^{13}C NMR spectra		
			V	IX	Δδ	V	IX	Δδ
V	Piperidine	2, 6	2.36	2.38	+0,02	52,7	54.3	+1.6
		3, 5	1.42	1.50	+0,08	26.2	26.7	+0.5
		4	1.42	1.50	+0.08	24.3	26.1	+0.8
IX		1	3.14	3,28	+0.14	47.4	62.4	+15.0
		2	—	—	—	78,9	124.2	+43.3
		3	2.53	6,68	+4,15	73.2	105.2	+32.0
			VI	XI		VI	XI	
VI	Morpholine	3, 5	2.40	2.39	−0,01	50.8	53.4	+2.6
		2, 6	3.56	3.56	0	66.1	66.9	+0.8
XI		1	3.18	3.30	+0.12	70.4	62.0	−8.6
		2	—	—	—	96.0	123.2	+27.2
		3	2,56	6,70	+4,14	52,3	106.3	+54
			VII	XIV		VII	XIV	
VII	Piperidine	2, 6	2.35	2.38	+0.03	53,0	54.0	+1,0
		3, 5	1,45	1.50	+0.05	26.4	26,4	0
XIV		4	1,45	1.50	+0.05	24.6	24.8	+0.2
		1, 4	3.13	3.38	+0.25	47,9	65.9	+18.0
		2, 3	—	—	—	79.7	121.7	+42.0
			VIII	XV		VIII	XV	
VIII	Morpholine	3, 5	2.46	2.48	+0,02	52,5	54.0	+1.5
		2, 6	3.64	3.24	−0.4	66,8	65.9	−0.7
XV		1, 4	3.64	3.66	+0.02	26,8	26.4	−0.4
		2, 3	—	—	—	54,2	103,8	+49,6



According to the data of the ^{1}H and ^{13}C NMR spectra, the majority of the signals undergoes a weak shift to low field with the introduction of the halogens (Table 3). The signals of the atoms of carbon and hydrogen in the β-position to the methyl-amino group undergo the largest shift. The steric proximity of the electronegative atoms allows the proposition of the trans-disposition of the halogens at the double bond. The absorption bands in the region of 3300 and 2140-2100 cm^{-1}, which are characteristic of the stretching vibrations of the acetylenic bonds C≡C and C–H, are absent from the IR spectra of the halogen derivatives of the mono- and diamines; this confirms the formation of the object products.

EXPERIMENTAL

The IR spectra of the synthesized compounds were taken on a UR-20 instrument using a thin layer. The ^1H and ^{13}C NMR spectra of the synthesized compounds were taken on a Varian XL-100 instrument. The initial acetylenic amines were taken in the pure form; the obtained halogen derivatives of the amines were taken in $CDCl_3$. The external standard was HMDS. The error of the measurement was δ ^{13}C ± 0.1 ppm.

We synthesized the acetylenic aminoalcohols (I)-(IV) according to the method of [13], and the heterocyclic acetylenic mono- (V), (VI) and diamines (VII), (VIII) according to the method of [7, 14].

1-Piperidino-2,3-dichloroprop-2-ene (IX). The solution of 10 g (0.08 mole) of 1-piperidinoprop-2-yne (V) in 50 ml of 34% hydrochloric acid is saturated with 18 g chlorine. The mixture is neutralized with a concentrated solution of potassium carbonate; the crystals which are formed are filtered off and washed several times with water. After drying them in air and recrystallization from ethanol, white crystals are obtained.

1-Piperidino-2,3-dibromoprop-2-ene (X). To the solution of 10 g (0.08 mole) of 1-piperidinoprop-2-yne (V) in 50 ml of 50% acetic acid are added 13.6 g (0.085 mole) of bromine with intense stirring and cooling with water. The mixture is left overnight prior to the neutralization with a concentrated solution of potassium carbonate; the crystals are filtered off, washed several times with water, and dried in air. After the recrystallization from ethanol, 36.6 g of the light yellow crystals are obtained.

Other dichlorine-containing (XI), (XIII), (XV) and dibromine-containing (XII), (IV), (XVI) heterocyclic mono- and diamines were also obtained by the methods described above.

When the heterocyclic acetylenic mono- and diamines (V)-(VIII) react with CH_3I and gaseous HCl, their methiodides and hydrochlorides are obtained (Table 1).

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