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sym-TRIAZINE DERIVATIVES.

9.* REACTION OF sym-TRIAZINES CONTAINING TRICHLOROMETHYL AND ETHOXYCARBONYL GROUPS WITH PHENYLHYDRAZINE

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Using the example of the reaction of 1,3,5-triazines simultaneously containing trichloromethyl and ethoxycarbonyl substituents with phenylhydrazine, it was shown that the presence of even one ester group leads to ring transformation. Depending on the number of the ester groups in the initial 1,3,5-triazine, the reaction products are either 1,2,4-triazole or 1,2,4-triazine derivatives.

It was previously shown that in the reaction of 2,4,6-triethoxycarbonyl-1,3,5-triazine (I) with phenylhydrazine (II) the product is 5-amino-6-oxo-1-phenyl-3-ethoxycarbonyl-1,6-dihydro-1,2,4-triazine (III, Scheme 1 on page 1376) [1].

It was of interest to study the reaction of hydrazine II with 1,3,5-triazines also containing other substituents besides the ethoxycarbonyl groups. The most easily accessible were 2,4,6-tris(trichloromethyl)-, 2,4-bis(trichloromethyl)-6-ethoxycarbonyl- and 2-trichloromethyl-4,6-bis(ethoxycarbonyl)-1,3,5-triazines (IV, V, and VI) which were obtained by joint trimerization of trichloroacetonitrile and ethyl cyanoformate by a method described in [2].

*For Communication 8, see [1].

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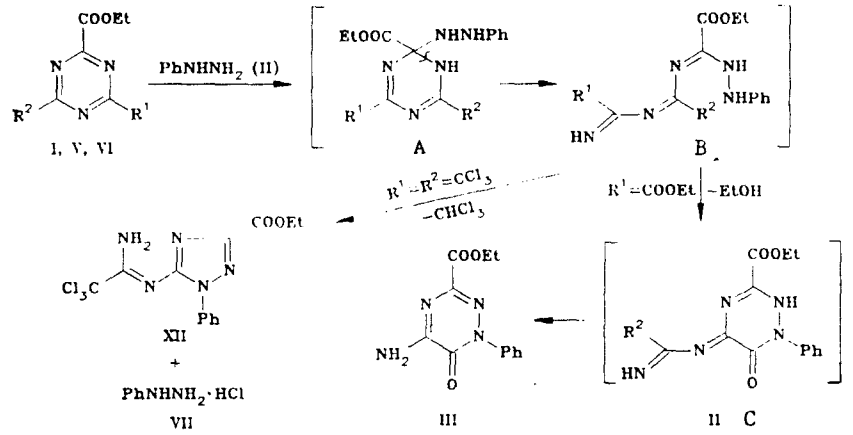
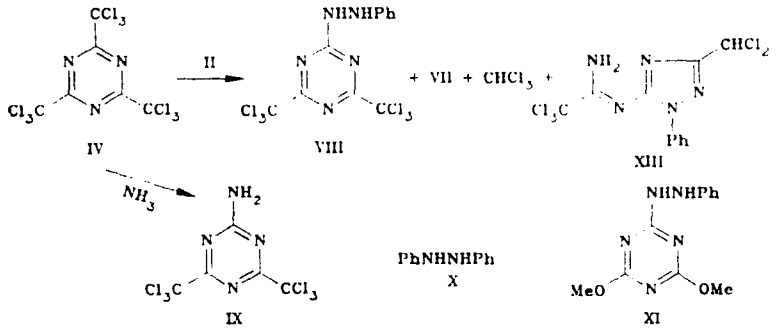
Scheme 1



I $R^1=R^2=COOEt$; V $R^1=R^2=CCl_3$; VI $R^1=COOEt$, $R^2=CCl_3$

According to literature data [3], the trichloromethyl group in compounds of the type under consideration behaves as a pseudohalogen and is readily substituted by the action of nucleophilic reagents with splitting off of chloroform.

In the reaction of compounds II and IV, phenylhydrazine hydrochloride (VII) was reported as the only isolated product [4]; its formation can be explained by the ability of the halogen atoms in the trichloromethyl group to react with phenylhydrazine II with the evolution of hydrogen chloride [5], which when in excess forms phenylhydrazine hydrochloride VII.



We carried out the reaction of hydrazine II with sym-triazine IV at a 4:1 ratio of the reagents at 20°C for 24 h. The yield of product VII was 46%. A substitution product of the trichloromethyl group – 2-(β-phenylhydrazino)-2,4-bis(trichloromethyl)-1,3,5-triazine (VIII) was also isolated in 44% yield by means of column chromatography on silica gel. Chloroform was detected in the reaction mixture by means of GLC. At 1:1 molar ratios of compounds II and IV, about 50% of triazine IV is recovered unchanged and the yield of hydrochloride VII decreases by a factor of 3 and that of triazine VIII by a factor of 2.

The structure of compound VIII was proved by spectral methods. The chemical shifts of the carbons of the triazine ring and the trichloromethyl substituents in the ^{13}C NMR spectrum (Table 1) differ little from the corresponding values for 1,3,5-triazines IV and V and are particularly close for the model compound 2-amino-4,6-bis(trichloromethyl)-1,3,5-triazine (IX). It should be noted that, in the case of compound IX, the chemical shifts of the triazine carbon atoms in the ^{13}C NMR spectra and the chemical shift of the mobile NH-protons in the ^1H NMR spectra indicate the predominance of the aminic tautomeric form.

The presence of a phenylhydrazine residue in compound VIII is indicated by the similarity of the values of the chemical shifts of the carbon atoms and the phenyl ring protons in the NMR spectra of triazine VIII and the model compound – hydrazobenzene (X, Table 2).

The existence of compound VIII in the tautomeric form shown in the above scheme is confirmed by spin–spin interaction between two vicinal protons of the hydrazine residue (J_{NHNH} = 4 Hz).

In contrast to triazines IV, V, IX, in the ^{13}C NMR spectrum of triazine VIII a nonequivalency of carbon atoms is observed in the 4- and 6-positions of the triazine ring and of substituents in these positions. This is clearly due to inhibited rotation of the phenylhydrazine residue with respect to the $C_{(2)}$-NHNHPh bond and is also characteristic for the model compound 4,6-dimethoxy-2-(β-phenylhydrazino)-1,3,5-triazine (XI), in the ^1H NMR spectrum of which the signals of the methoxy

groups – broad singlets at room temperature – coalesce on heating. This effect may be due to the partial double-bond character of the $C_{(2)}$–N bond and indicates interaction of π-electrons of the 1,3,5-triazine ring with the p-electrons of the nitrogen atom of the phenylhydrazine residue.

The presence of a phenylhydrazine residue causes compounds VIII and XI to be unstable in the presence of atmospheric oxygen (solutions change color on silica gel). The structural similarity of compounds VIII and XI is also indicated by the similarity of their UV spectra: for compound VIII, λ_{max}, nm (log ε) is equal to 241 (4.3) and 283 (3.7) and for compound XI – 234 (4.2) and 280 (3.4).

A group of low-intensity peaks of the molecular ion (M^+ 419*) is observed in the mass spectrum of triazine VIII. The ratio of the peak intensities in this group indicates the presence of six chlorine atoms in the molecule, i.e., the retention of two trichloromethyl groups. There were no peaks corresponding to the elimination of the trichloromethyl group from the molecular ion. The most intense peaks in the spectrum of compound VIII (Table 3) belong to the PhN_2^+ (105) and Ph^+ (77) ions and to the products of their further decomposition. The absence of other decomposition paths makes it impossible to draw conclusions from mass spectrum data on the structure of compound VIII.

In the mass spectrum of compound XI an intense peak of a molecular ion (247), and peaks of Ph^+ (77), $PhNH^+$ (92), $PhNH_2^+$ (105), $[M\text{-}PhNH_2]^+$ (142), and $[M\text{–}PhN\text{–}OMe]^+$ (126) ions are observed.

Thus, the action of phenylhydrazine on triazine IV leads to substitution of the trichloromethyl group by a phenylhydrazine residue with retention of the 1,3,5-triazine ring.

The reaction of hydrazine II with triazine V containing two trichloromethyl and one ethoxycarbonyl groups proceeds in a different way. In the reaction of these compounds (molar ratios 1:1.5) at 20°C, instead of the expected product of a nucleophilic substitution of one of the trichloromethyl groups by a phenylhydrazine residue, (1-phenyl-3-ethoxycarbonyl-1H-1,2,4-triazolyl-5)-N-trichloroacetamidine was obtained in an 81% yield (XII, Scheme 1). The yield of product XII remained practically unchanged when the amount of hydrazine II was increased to 2 moles per mole of triazine V.

In the ^1H and ^{13}C NMR spectra of compound XII (Table 4), the values of the chemical shifts of the phenyl substituent nuclei are characteristic and sharply differ from the corresponding values for compounds VIII, X, and XI, in which the phenylhydrazine residue is present in the NHNHPh form. Using [1] as a basis, it can be asserted that these differences in the chemical shifts in the NMR spectra of compound XII are due to the inclusion of the phenylhydrazine residue in the cyclic system of 1,2,4-triazole. This is also supported by the values of the chemical shifts of the carbon atoms at the 3 and 5 positions of the triazole ring.

*Here and below, for chlorine-containing molecules, the mass numbers of ions containing ^{35}Cl are given (the m/z values are given in brackets).

TABLE 1. ^{13}C NMR Spectra of Compounds IV, V, VIII-X

Compound	Chemical shifts, δ, ppm (SSCC, J_{CH}, Hz)			
	2-C	4,6-C	2-R	4,6-R
IV	176,6	176,6	93,6 (CCl_3)	93,6 (CCl_3)
V	167,4	176,3	160,7 (CO, t J=3,3); 64,0 (CH_2, t J=149,5; q J=4,5); 14,0 (CH_3, q J=128; t, J=2,5)	93,8 (CCl_3)
IX	167,9	175,0		94,7 (CCl_3)
VIII	168,6 (d J=8,5)	175,5, 174,8	146,4** (t, J=8,5); 114,7 (d, J=159,5; t, J=6,5); 129,3 (d, J=160,8; J=8); 122,5 (d J=162,7; t, J=7,6)	94,69 (CCl_3); 94,64 (CCl_3)
XI	170,1 (d, J=8,0)	172,4; 172,8 br. s	148,1** (t J=8,8); 113,5 (d, J=160); 129,1 (d J=161, d J=8); 120,9 (d J=162,7; t, J=7,4)	54,8 (OCH_3, J=147,5)
X			148,7; 112,2; 129,2; 119,7	

*For compounds IV, V, IX-XI, the solvent was $CDCl_3$, whose signal was taken as a standard (δ = 77.0 ppm). The solvent for compound VIII was $CDCl_3$, with TMS used as internal standard, δ_{CDCl_3} = 76.99 ppm.

**The chemical shifts of the carbon atoms of the phenyl substituents given in the sequence $C_{1'}$, $C_{2'(6')}$, $C_{3'(5')}$, $C_{4'}$.

TABLE 2. ^{1}H NMR Spectra of Compounds V, VIII, IX-XI

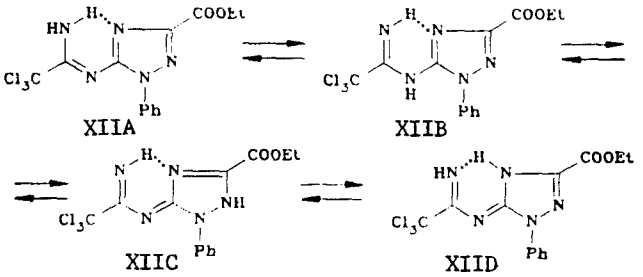
Compound*	Substituent	Chemical shifts, δ, ppm (J_{NHNH}, Hz)
V	2-$COOC_2H_5$	1,39 (t, CH_3); 4,52 (q CH_2)
IX	2-NH_2	6,49 (br.s NH_2)
VIII	2-NHNH—C_6H_5	6,25 (d); 8,02 (d NHNH, J=4,1); 6,94 (d 2′,6′-H); 7,27 (t 3′,5′-H); 6,98 (t, 4′-H)
XI	2-NHNH—C_6H_5	6,13 (d); 7,24 (d NHNH, J=3,6); 6,88 (d 2′,6′-H); 7,23 (t 3′,5′-H); 6,90 (t 4′-H)
	4,6-OCH_3	3,94 (br.s OCH_3); 3,88 (br.s OCH_3)
X	—	5,62 (br.s, NH); 6,86 (d, 2,6-H); 7,22 (t, 3,5-H); 6,84 (t, 4-H)

*Solvent for compound V was DMSO-D_6, for VIII-XI, $CDCl_3$; internal standard TMS.

TABLE 3. Electron Impact Mass Spectra of Compounds VIII, XI-XVI*

Compound	m/z (I_{rel}, %)
VIII	*419* (5), 386 (5), 108 (5), 105 (60), 92 (5), 91 (5), 78 (8), 77 (100), 65 (15), 51 (15)
XI	247 (100), 142 (29), 126 (20), 105 (16), 101 (7), 99 (8), 92 (16), 91 (15), 83 (7), 77 (57), 72 (40), 70 (23), 69 (21), 65 (30), 58 (35), 51 (12), 41 (21)
XIII	*350* (9), *270* (100), *232* (19), 102 (10), 91 (30), 77 (23), 64 (10)
XII	*375* (5), 258 (100), 230 (5), 212 (77), 144 (8), 119 (7), 118 (9), 117 (16), 91 (30), 77 (43), 65 (13), 64 (15), 51 (17)
XIV	233 (9), 232 (55), 187 (30), 160 (67), 133 (6), 119 (78), 118 (18), 117 (13), 92 (10), 91 (100), 78 (10), 77 (53), 65 (20), 64 (20), 51 (22), 43 (14)
XV	204 (52), 133 (44), 119 (9), 118 (13), 92 (13), 91 (100), 90 (5), 77 (34), 65 (16), 64 (31), 63 (12), 51 (29), 50 (6), 43 (25), 41 (6)
XVI	161 (11), 160 (91), 133 (11), 118 (26), 92 (7), 91 (100), 77 (25), 65 (10), 64 (27), 63 (12), 51 (20), 43 (15), 41 (5)

*The mass numbers of ions are given having $J_{rel} \geq 5\%$. The m/z values for chlorine containing ions, calculated for the ^{35}Cl isotope, are shown in italics.



The ^{1}H and ^{13}C NMR spectra confirm the presence in compound XII of the proposed substituents at the $C_{(3)}$ and $C_{(5)}$ atoms, whereby in the ^{1}H NMR spectra two signals correspond to two mobile protons. The signal of one of the protons is shifted by 2.5 ppm to a weak field when the $CDCl_3$ solvent is replaced by DMSO-D_6, clearly because of the formation of an intermolecular hydrogen bond with the solvent. The signal of the other proton remains in the strong field, both in DMSO-D_6 and in $CDCl_3$, which is probably due to its participation in an intramolecular hydrogen bond, according to the proposed structure for triazole XII. Compound XII may theoretically exist in several tautomeric forms A-D. However, an appreciable contribution of forms C and D with a proton at one of the cyclic nitrogen atoms does not appears to be very probable, since for these forms the NH-group protons are observed in a considerably weaker field ($\delta_{NH} \geq 13$ ppm) [6, 7].

TABLE 4. NMR Spectra of Compounds XII-XVI

Compound	Solvent*	Chemical shifts, δ, ppm (J_{CH}, Hz)**							
		3-C	5-C	1′	2′, 6′	3′, 5′	4′	3-R_1	5-R_2
					^{1}H NMR spectrum***				
XII	$CDCl_3$				8,07	7,48	7,38	4,52 (q, CH_2); 1,46 (t, CH_3)	6,77; 9,78 (br.s, NH_2)
XII	DMSO-D_6				7,99	7,57	7,45	4,40 (q, CH_2); 1,35 (t, CH_3)	9,26; 9,53 (br.s, NH_2)
XIII	$CDCl_3$				8,02	7,47	7,35	6,80 (s, $CHCl_2$)	6,74; 9,76 (br.s, NH_2)
XIV	$CDCl_3$				7,52	7,56	7,43	4,40 (q, CH_2); 1,39 (t, CH_3)	6,37 (br.s, NH_2)
XIV	DMSO-D_6				7,57	7,57	7,48	4,29 (q, CH_2); 1,29 (t, CH_3)	6,70 (br.s, NH_2)
XV	DMSO-D_6				7,56	7,56	7,47		6,64 (br.s, NH_2)
XVI	$CDCl_3$				7,53	7,53	7,45		5,92 (br.s, NH_2)
					^{13}C NMR spectrum				
XII	$CDCl_3$	150,7	155,1	137,0 (t, J=10; t, J=3)	123,3 (d, J=164)	128,7 (d, J=161,5; J=8)	127,6 (d J=161,8; t, J=7,5)	160,1 (t, CO, J=3,5); 62 (t, CH_2, J=148,4; q, J=4,4)	14,3 (q, CH_3, J=127,4; t, J=2,5); 158,4 (C=N); 94,2 (d, CCl_3, J=12,5)
XIV	$CDCl_3$	151,6	155,5	136,1 (t, J=7)	123,9 (d, J=164; t, J=6)	129,8 (d J=162,8; d J=7)	128,9 (d, J=163; t, J=7)	160,3 (t, CO, J=3,5); 61,7 (t, CH_2, J=148,3; q, J=4,5)	14,3 (q, CH_3, J=127,3; t, J=2,5)
XV	DMSO-D_6	152,1	155,3	136,5 (t, J=7)	123,2 (d, J=164,7)	129,4 (d, J=162,6; d J=5,5)	127,8 (d J=161,5; d J=6,5)	161,3	
XVI	$CDCl_3$	149,5 (d J=205,5)	153,4	136,8 —	123,3 (d, J=165)	129,8 (d J=162,6; d J=6)	128,2 (d J=162,5)		

*Internal standard TMS.

**1′; 2′, 6′; 3′, 5′, and 4′ refer to the 1-Ph group.

***Signals in the ^{1}H NMR spectra, whose multiplicity is not indicated, are multiplets

In the mass spectrum of compound XII there are three chlorine atoms according to the intensity ratio of the isotopic peaks in the molecular ion group (M^+ 375). The character of the fragmentation of compound XII differs in principle from the fragmentation of compounds VIII and XI, which indicates sharp differences in the structure of these compounds. Thus, PhN_2^+ and $PhNH^+$ ions, characteristic for the fragmentation of 1,3,5-triazine derivatives VIII and XI, are absent in the spectrum of triazole XII. The peaks of the $[M–CCl_3]^+$ (258) and $[M–CCl_3–EtOH]^+$ (212) ions have maximal intensity in the spectrum of triazole XII.

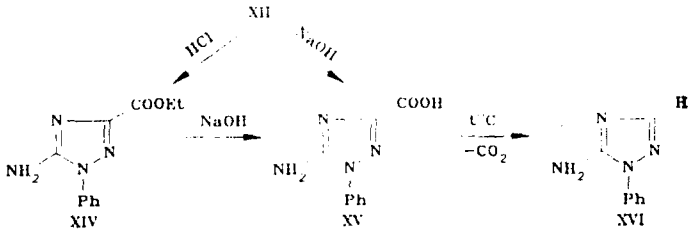
The ease of elimination of the trichloromethyl group from the molecular ion is explained by the facility of the delocalization of the charge in the triazolylamidyl cation, and proves that in triazole XII this group is not attached to the ring.

A structurally similar compound [(3-dichloromethyl-1-phenyl-1H-1,2,4-triazolyl-5)-N-trichloroacetamidine (XIII)] was isolated as a by-product (yield 2%) in the reaction of hydrazine II with triazine IV in a 10:1 ratio.

In the ^1H NMR spectrum of compound XIII, besides the proton signal of the dichloromethyl group, proton signals of the phenyl ring and two mobile NH protons are observed, which are completely identical to the corresponding signals for derivative XII.

In the mass spectrum of triazole XIII there is a group of peaks of the molecular ion (M^+ 385). The intensity ratio of the isotopic peaks indicates the presence of five chlorine atoms in the molecule. The character of the fragmentation is entirely different from that for compound VIII and similar to that for compound XII. The maximal intensity corresponds to the peak of the $[M–CCl_3]^+$ ion. In the spectrum peaks of the $[M–Cl]^+$ (350), $[M–CCl_3–HCl]^+$ (232), PhN^+ (91), Ph^+ (77) ions are also observed.

The 1,2,4-triazole structure of compound XII was confirmed by its chemical transformations



Hydrolysis of triazole XII in dilute alcoholic HCl proceeds with splitting of the C–N bond in the trichloroacetamidine fragment and formation of 5-amino-1-phenyl-3-ethoxycarbonyl-1-H-1,2,4-triazole (XIV).

In aqueous-alcoholic alkali, together with the splitting of the C–N bond in the trichloroacetamidine fragment, a saponification of the ester group also takes place. The 5-amino-1-phenyl-1-H-1,2,4-triazolyl-3-carboxylic acid (XV) formed* was also obtained during the alkaline hydrolysis of ester XIV (the identity of the compounds was also proved by the ^1H NMR method). Decarboxylation of acid XV leads to the formation of 5-amino-1-phenyl-1-H-1,2,4-triazole (XVI).

In the ^{13}C NMR spectra of compounds XIV-XVI, the chemical shifts of the triazole ring and phenyl substituent carbon atoms are similar to the corresponding values for triazole XII, which indicates the structural sameness of all the compounds of this series and supports the conclusion made on the preferential tautomeric forms of compound XII. In the spectrum of compound XVI, the value of the direct constant $^1J_{C_3H}$ = 205.5 Hz is characteristic for the –N–CH=N group in azines and azoles [9].

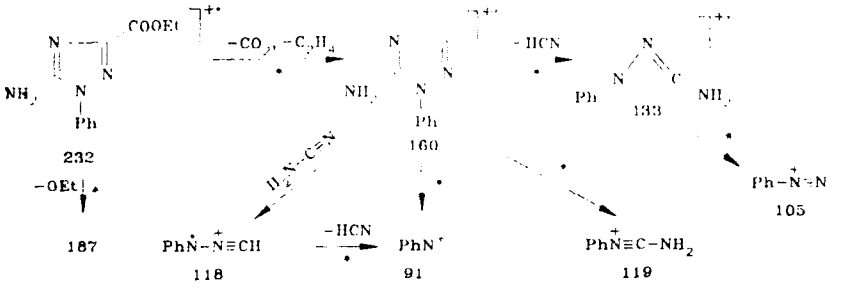
Compounds XIV-XVI exist in amino form, since in their ^1H NMR spectra, a signal was detected in a relatively strong field (6-7 ppm).

Comparison of the values of δ for the phenyl ring protons in compounds XII and XIV shows that splitting off of a part of a substituent at the $C_{(5)}$ atom of the triazole ring from triazole XII leads to leveling of these values. It is possible that the difference in the chemical shifts of the phenyl substituent protons in compound XII is caused by the strong anisotropic effect of the amidine residue, which is possible only when these two substituents are located close to one another. On transition from ester XIV to compounds XV and XVI, no noticeable changes are observed in the δ values for the phenyl ring protons. This indicates the distance of the phenyl substituent from the carboethoxyl group in the triazole XII and confirms the correctness of the proposed structures XII-XVI, as also indicated by the m/z values of the molecular ion peaks in the mass spectra of compounds XIV, XV, and XVI – 232, 204, and 160, respectively. The presence in the mass spectrum of compound XIV of

*The melting point of acid XV coincides with that described in [8] with an accuracy depending on the apparatus error; no other physicochemical data for acid XV are given in this paper.

intense peaks of the $[M–OEt]^+$ (187) and $[M–CO_2–C_2H_4]^+$ (160) ions indicates that the carbethoxy group is retained in this compound. In the mass spectrum of compound XIV intense peaks of ions with mass numbers 119 and 91 are also observed. Substitution of mobile hydrogen atoms in the molecule of XIV by deuterium upon heating the sample in deuteromethanol in a system of direct introduction to the mass spectrometer showed that ions M^+, 187, 160, 133, 119 contain two mobile protons; in the composition of ions 118 and 91, there are no mobile protons. These data, and also the results of the analysis of the PADI spectra, made it possible to propose the following scheme of fragmentation, which conforms with the structure of XIV.

Scheme 2



In the spectrum of acid XV, the same characteristic ions are observed as for compound XIV. According to the data of the PADI spectra and a spectrum of a sample in which the mobile protons are exchanged by deuterium, the sequence of formation of characteristic ions and their structure corresponds to Scheme 2. The main fragmentation of the molecular ion of triazole XVI according to the PADI spectra proceeds with the elimination of HCN (133) and $N{\equiv}C–NH_2$ (118) particles. Further fragmentation of these ions coincides with the fragmentation of similar ions in the spectra of compounds XIV and XV.

Triazole XVI that we obtained does not give a mixed melting point depression with an authentic sample synthesized according to [10]. The identity of the decarboxylation product XV and a compound obtained by a countersynthesis, was confirmed by the mass and ^1H NMR spectra.

In the reaction of phenylhydrazine with triazine VI taken in a 2:1 ratio, compound III was isolated in 17% yield, which, according to the IR spectrum and a mixed melting point, is identical with an authentic sample [1]. The starting compound VI was not detected in the reaction mixture by means of TLC. The process is accompanied by a considerable resinification. The hydrochloride VII was found in the reaction products mass-spectrometrically.

The above data allow us to draw conclusions on the patterns of the reaction of 1,3,5-triazines containing trichloromethyl and ethoxycarbonyl groups with phenylhydrazine II. In the presence of one ester group in sym-trihydrazine, the main reaction path is the substitution of the trichloromethyl group by a phenylhydrazine residue with the formation of triazine VIII. Replacement of even one trichloromethyl group in the 1,3,5-triazine derivative by an ester group (compound V, Scheme 1) results in recyclization becoming the main process. At the first stage, hydrazine II adds at the C=N bond of the triazine ring located adjacent with the ester group (intermediate A, Scheme 1). Then, the C–N bond in the 1,3,5-triazine ring is ruptured at the site of the addition of phenylhydrazine, and derivative B is formed. The cyclization paths of the latter depend on two other substituents R^1 and R^2 in the starting 1,3,5-triazine. If $R^1 = R^2 = CCl_3$, then the closing of a new ring proceeds through substitution of the trichloromethyl group by the phenylhydrazine nitrogen atom with the formation of 1,2,4-triazole XII and chloroform. A reaction of this type is also possible as a side reaction in the case of the 1,3,5-triazine derivative IV (formation of triazine XIII).

In the case of triazine VI, where R^1 = COOEt, $R^2 = CCl_3$, the phenylhydrazine nitrogen atom reacts with the ester group carbonyl. Thus, ethanol is split off, and the 1,2,4-triazine derivative C is formed, which by the action of another molecule of II converts into triazine III. In this case, during the cyclization of intermediate B, side processes related to the reactivity of the trichloromethyl group are possible, and the yield of 1,2,4-triazine III is low. When all three substituents in 1,3,5-triazine are ester groups (compound I), the recyclization proceeds unequivocally and the yield of compound III increases sharply.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were run on a Varian XL-200 spectrometer (200 MHz on ^1H nuclei and 50.3 MHz on ^{13}C nuclei). The UV spectra were recorded on a Perkin–Elmer 575 spectrophotometer in ethanol.* The electron impact and PADI

*The UV spectra were taken by T. Yu. Kurbatova.

mass spectra were obtained on a Varian MA-112 spectrometer at an energy of ionizing electrons of 70 eV and with direct introduction of the sample into the ionic source. The temperature of the ionization chamber was 180°C. The preparative chromatography was carried out on columns with Chemapol brand 40/100 μm silica gel using 50 g of silica gel per 1 g of the substance. The separation by the GLC method was carried out on a Chrom 5 apparatus (CSSR) with a heat conductivity detector, using helium as carrier gas, at a flow rate of 40 ml/min, sorbent polysorb 1, a 1000 × 3 mm column and at the temperature of 120-150°C.*

Reaction of 2,4,6-tris(Trichloromethyl)-1,3,5-triazine (IV) with Phenylhydrazine (II). A. A 2.16-g portion (5 mmoles) of triazine IV was dissolved in 25 ml of absolute ethanol, and 2.16 g (20 mmoles) of phenylhydrazine II was added. The mixture was allowed to stand for 24 h at 20°C and 1 g (46%) of hydrochloride VII was filtered off, which was identical with an authentic sample according to the IR spectrum and mixed melting point. After separation of hydrochloride VII, the alcoholic mother liquid was evaporated, deposited on a column with silica gel, eluted with heptane with increasing of the polarity of the eluent by addition of benzene. Using a heptane–benzene mixture (2:1), 0.93 g (yield 44%) of triazine VIII was eluted. Yellowish crystals, which are soluble in organic solvents; in chloroform on silica gel, the solutions of triazine VIII ($C_{11}H_7Cl_6N_5$) acquire a red color. Mp 163-164°C (from heptane). Chloroform was detected by the GLC method.

B. A similar reaction was carried out at a ratio of the reagents of 4.34 g of hydrazine IV to 10.8 g (100 mmoles) of hydrazine II in 60 ml of absolute ethanol. The yield of hydrochloride VII was 7.12 g (49%). By elution of the column with a heptane–benzene (3:1) mixture, 0.2 g (2%) of compound XIII ($C_{11}H_8N_5Cl_5$) was isolated. Colorless crystals, which are soluble in organic solvents, mp 128-129°C (from heptane). With further use of a heptane–benzene (2:1) mixture, 0.56 g (13%) of triazine VIII was eluted.

1-Phenyl-4-ethoxycarbonyltriazolyl-5-N-trichloroacetamidine (XII, $C_{13}H_{12}Cl_3N_5O_2$). A 1.26 g portion (12 mmoles) of hydrazine II was added to a suspension of 3.0 g (8 mmoles) of triazine V in 20 ml of absolute ethanol. The mixture was allowed to stand for 3 h at room temperature, and then 2.06 g of compound XII was filtered off. Colorless crystals, which are soluble in organic solvents, with heating soluble in alcohols, insoluble in heptane, water, mp 162-163°C (from ethanol). The alcoholic mother liquor after separation of triazole XII was evaporated, the residue was dissolved in chloroform, and 0.16 g of hydrochloride VII was filtered off. The chloroform mother liquor was deposited on a column with silica gel, and an additional 0.5 g of triazole XII was eluted with benzene. Overall yield 2.56 g (81%). Chloroform was detected by the GLC method.

5-Amino-1-phenyl-3-ethoxycarbonyl-1-H-1,2,4-triazole (XIV, $C_{11}H_{22}N_4O_2$). A 0.6 g portion (1.6 mmoles) of triazole XII was dissolved with heating in 50 ml of ethanol, and 0.3 ml of concentrated HCl was added. The reaction mixture was allowed to stand at room temperature up to the disappearance of the starting compound XII as shown by TLC. The solvent was evaporated and the residue was deposited on a column with silica gel. The column was eluted first with chloroform with increasing of the polarity of the system by adding methanol. Elution with a chloroform–methanol (10:1) mixture gave 0.28 g (78%) of triazole XIV. Colorless crystals which are soluble in chloroform, acetone, methanol, and ethyl acetate, mp 131-132°C (benzene–heptane, 1:1).

5-Amino-1-phenyl-1-H-1,2,4-triazolyl-3-carboxylic Acid (XV, $C_9H_8N_4O_2$). A. A 0.3 g portion (7.5 mmoles) of sodium hydroxide in 5 ml of water was added to a solution of 0.6 g (1.6 mmoles) of triazole XII in 50 ml of alcohol. The mixture was allowed to stand at room temperature up to the disappearance of the starting compound XII according to TLC. The aqueous-alcoholic solution was acidified by HCl to pH ~4, the alcohol was evaporated, and the residue was crystallized from water. Yield 0.21 g (66%) of acid XV. Colorless crystals, which are soluble in DMSO, DMFA, and on heating in water and in alcohols, mp 208-210°C (from water).

B. The reaction mixture containing triazole XIV was made alkaline by a solution of sodium hydroxide to pH 9-10. After the disappearance of the starting compound XIV according to TLC, the solvent was evaporated, and the residue was crystallized from water. According to the ^1H NMR spectrum, the compound obtained was identical to acid XV.

5-Amino-1-phenyl-1-H-1,2,4-triazole (XVI). A 0.3 g portion (1.5 mmoles) of acid XV was heated for 5 min at 210°C at a water pump vacuum. After cooling, the residue (0.13 g) was transferred into a column of silica gel. Triazole XVI (0.5 g, 22%) was eluted with ethyl acetate. According to the mass and ^1H NMR spectra, the compound was identical to a sample obtained by a countersynthesis according to [10], and did not depress the melting point of a mixed sample.

*The GLC was carried out under the direction of V. A. Kuzovkin.

5-Amino-6-oxo-1-phenyl-3-ethoxycarbonyl-1,6-dihydro-1,2,4-triazine (III). A 0.88 g portion (8 mmoles) of hydrazine II was added to a suspension of 1.37 g (4 mmoles) of triazine VI in 20 ml of absolute ethanol. The reaction mixture was held while stirring for 3 h at 20°C, and 0.18 g (17%) of triazine III was filtered off, which according to the IR spectrum and the melting point of a mixed sample was identical to an authentic sample [1]. The alcoholic mother liquor was evaporated, and the residue was ground with ether. From ether, a precipitate was filtered off which, according to the mass spectral data, contained hydrochloride VII. Mass spectrum of a base of VII, m/z (I, %): 108 $[M_{base}]^+$ (100), 92 $[PhNH]^+$ (40), 91 $[PhH]^+$ (14), 77 $[Ph]^+$ (41).

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SYNTHESIS OF TRICYLIC SYSTEMS INCORPORATING THE AZEPINE RING

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Some tricyclic compounds (derivatives of pyrazino[2,1-a]benzazepine, diazepino[7,1-a]isoquinoline, and some pyrimido[6,1-a]isoquinolines) which are analogs of the anthelmintic praziquantel have been synthesized.

Tricyclic compounds incorporating the benzene ring and nonaromatic six- and seven-membered diazaheterocycles have received much less attention than the corresponding bicyclic heterocycles. Nevertheless, several of them have shown biological activity of various types [1-4]. The most important of these is the hexahydropyrazino[2,1-*a*]isoquinoline praziquantel (Ia), an anthelmintic with a wide spectrum of action [5]. It was therefore of interest to examine related systems.

The aim of the present investigation was to obtain analogs of praziquantel (Ia), namely the pyrazinobenzazepine (Ib), diazepinoisoquinolines (II) and (III), and pyrimidoisoquinolines (XVIa, b) and (XVII) (see scheme on page 1384).

The pyrazinobenzazepine (Ib) was obtained by cyclization of the ω-hydroxylatam, with the intermediate formation of the acylammonium cation [6]. The synthesis of (Ib) by cyclization of the hydroxypiperazinone (IV) to the pyrazinobenzazepine (V) followed by removal of the protection and acylation has been described [1]. This reaction requires the intermediate forma-

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