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CONDENSATION OF 4-AMINO-3-HYDRAZINO-1,2,4-TRIAZOLINE-5-THIONE WITH α- and β-DICARBONYL COMPOUNDS

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sym-Triazolo[3,4-b][1,2,4,5]tetraazepines were obtained by condensation of 4-amino-3-hydrazino-1,2,4-triazoline-5-thione with α-dicarbonyl compounds, and 1-[4-amino-1,2,4-triazol-3-yl]-3,5-dialkylpyrazoles were obtained by condensation of the same thione with β-dicarbonyl compounds.

In the present research we investigated the reaction of 4-amino-3-hydrazino-1,2,4-triazoline-5-thione (I) with α- and β-dicarbonyl compounds. This thione contains three vicinal functional groups, and this makes it possible to obtain unusual heterocyclic compounds from it. Thus sym-triazolo[3,4-b]tetraazepines (II, III) were obtained when I was heated with α-dicarbonyl compounds (benzil and phenylglyoxal) in acidic media. It is interesting to note that only monohydrazones are formed in the reaction of 4-amino-3-hydrazino-1,2,4-triazole (which differs from I with respect to the absence of a thioamide group) with benzil and diacetyl in acidic media [1].

The reaction of hydrazine I with α-dicarbonyl compounds was investigated in the case of acetylacetone and some unsymmetrical polyfluorinated β-diketones [2]. The ability of β-diketones to undergo keto–enol tautomerism made it possible to expect the formation of condensed triazolotriazepines or compounds with a triazolopyrazole structure (IV) and, considering the data on the condensation of I with α-dicarbonyl compounds, compounds of the II type in the case of condensation with I.

Monotypic IV-IX, the individuality and purity of which were confirmed by thin-layer chromatography (TLC), were obtained in the condensation of I with β-diketones in alcohol containing hydrochloric acid. Their structures were studied in the case of IV. This compound reacts with p-nitrobenzaldehyde to give azomethine X, which makes it possible to exclude structures of the II type from consideration. The presence of a free amino group in IV was also confirmed by the fact that its methylthio derivative (XI) is readily deaminated to give XII. In addition, IV undergoes condensation with such difunctional compounds as α-chloropropionitrile and ω-bromoacetophenone to give s-triazolothiadiazepine XIII and sym-triazolothiadiazine XIV, respectively. The IR spectra of IV-IX contain absorption bands at 1600, 3220, and 3305 cm^{-1}, which are characteristic for the amino group and can be ascribed to deformation vibrations and symmetrical and asymmetrical stretching vibrations, respectively [3]. One absorption band is observed in the UV spectra of each of these compounds.

The selection of structure IV was made on the basis of the mass spectra of II, IV, VI, and VIII. The steric hindrance in structure IV makes the system deviate from the coplanar state, and this is responsible for cleavage of the interannular bond and the recording of peaks of ions corresponding in mass to one (IV) or both (VI and VIII) hetaryl fragments in

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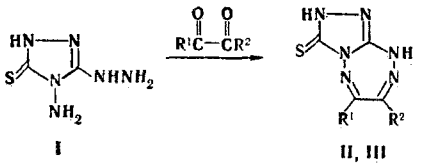
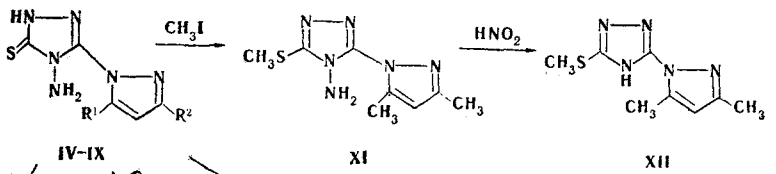
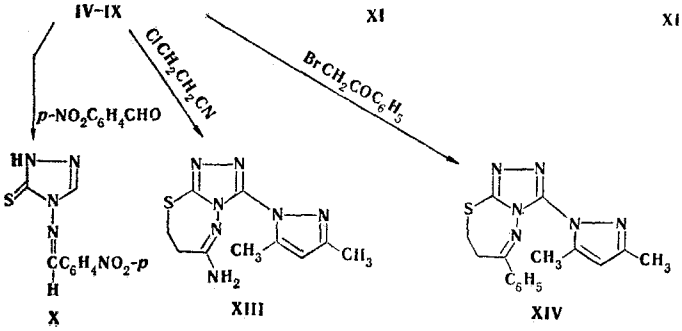
the mass spectra. Migration of a labile hydrogen atom from one of the rings of the system to the site of cleavage is possible in this case [5]. The ion peaks with m/e 96, 97, 132, 133, and 183 in the spectra of samples of IV, VI, and VIII, respectively, correspond to the structures of 5-substituted methylpyrazoles and their hydrogenated analogs (in the case of migration of two hydrogen atoms from the triazoline ring). The occurrence of rearrangements of this type is evidently associated with the possibility of the formation of a more stable six-membered ring by expansion of the triazoline ring. This fragmentation pathway for the molecular ions (MI) is characteristic for structure IV. The presence of pseudomolecular ions with the structure of 5-substituted 3-methylpyrazoles is proved by the subsequent trend of the fragmentation. The interpretation of the fragment ions of, for example, IV with m/e 96, 95, 81, 68, 67, and 55 therefore does not present any difficulties.



I II, III

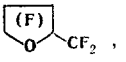


IV–IX XI XII

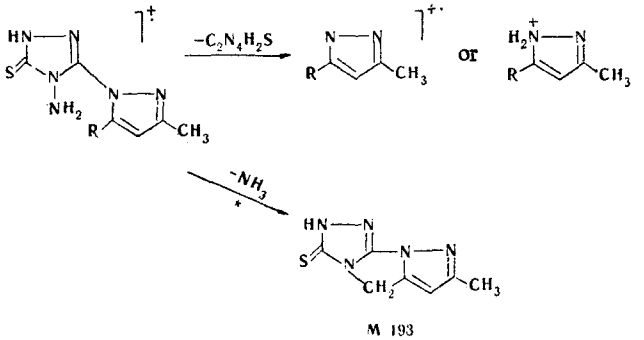


X XIII XIV

II $R^1=C_6H_5$, $R^2=C_6H_5$; III $R^1=C_6H_5$, $R^2=H$; IV $R^1=CH_3$, $R^2=CH_3$; V $R^1=H(CF_2)_4$, $R^2=CH_3$; VI $R'=H(CF_2)_2$, $R^2=CH_3$; VII $R'=H(CF_2)_2$, $R^2=C_2H_5$; VIII $R'=HCF_2$, $R^2=CH_3$;

IX $R'=$  , $R^2=CH_3$

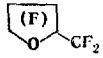
It is known [6] that under the influence of electron impact methyl-substituted pyrazoles lose H or CH_3 and are converted to the corresponding pyridazinium cation, from which N_2 and HCN particles are subsequently detached. The presence of fluorinated substituents for VI and VIII leads to additional variants of fragmentation that are characteristic for organofluorine compounds (for example, to detachment of HF, CF_2, and other particles). In addition, the existence of the $(M - NH_3)^+$ process for IV, which is associated with transfer of a hydrogen atom because of the "peri effect," is of interest; this may be characteric only for an MI with structure IV.



M 193

The structure was proved more rigorously by measurement of the metastable ions that are formed as a result of dissociative ionization of the MI by means of the DADi technique [7].

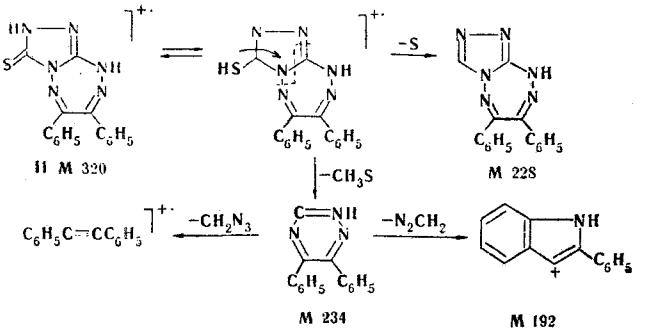
TABLE 1. Products of the Condensation of 4-Amino-3-hydrazino-1,2,4-triazoline-5-thione with α- and β-Dicarbonyl Compounds

Compound	R^1	R^2	mp, °C *	Found, %			Empirical formula	Calc., %			ν_{NH_2}, cm^{-1}	λ_{max}, nm (lg ε)	R_f	Yield, %
				C	H	N		C	H	N				
II	C_6H_5	C_6H_5	245—247	59,5	3,8	—	$C_{16}H_{12}N_6S$	59,9	3,8	—	—	—	—	91
III	C_6H_5	H	240—242	50,4	3,4	—	$C_{10}H_8N_6S$	49,9	3,3	—	—	—	—	60
IV	CH_3	CH_3	186—187	39,9	4,9	39,7	$C_7H_{10}N_6S$	39,9	4,8	39,9	1600, 3220	256 (4,28)	0,54	64
V	$H(CF_2)_4$	CH_3	136—137	29,7	2,3	21,1	$C_{10}H_8N_6SF_8$	29,9	2,2	20,9	1610, 3280, 3335	256 (4,36)	0,75	59
VI	$H(CF_2)_2$	CH_3	112—113	32,7	2,9	28,5	$C_8H_8N_6SF_4$	32,5	2,7	28,4	1610, 3265, 3310	256 (4,35)	0,76	79
VII	$H(CF_2)_2$	C_2H_5	122—123	34,7	3,5	26,9	$C_9H_{11}N_6SF_4$	34,8	3,5	27,1	1600, 3300 (br)	256 (4,30)	0,74	70
VIII	HCF_2	CH_3	178—179	33,9	3,4	34,2	$C_7H_6N_6SF_9$	34,1	3,3	34,1	1625, 3270, 2340	256 (4,41)	0,73	72
IX		CH_3	150—152	28,9	1,5	18,6	$C_{11}H_6N_6SF_9$	28,6	1,5	18,4	1605, 3270 (br)	256 (4,28)	0,60	65

*Crystallization solvents: butanol for II and III, and 50% ethanol for IV, V, VI-VIII, and IX.

It was shown that the fragmentation of the MI is accompanied by independent processes involving the elimination of HNCS—NNH, $C_2N_4H_2S$, and C_2N_4HS particles; the presence of $(M - NH_3)^+$ (for IV) and $(M - HNCS - NNH)^+$ and $(M - C_2N_4H_2S)^+$ ions, which are formed by direct fragmentation of the MI, constitutes evidence in favor of only one form of MI — structure IV [8].

The structures of the tetraazepines were also confirmed by mass spectrometry (in the case of II). The absence in the spectrum of intense fragment ions generated by cleavage of the interannular bond provides evidence for condensation of the rings. It is known [9] that azepine structures are distinguished by appreciable stability with respect to electron impact and have a tendency to undergo ring contraction during fragmentation. The character of the fragmentation of the MI or II confirms this.



Thus the condensation of I with dicarbonyl compounds evidently commences with attack at the β-nitrogen atom of the hydrazine group; this is in agreement with the data in [10]. However, the direction of subsequent cyclization is determined by the nature of the dicarbonyl compound. The α-dicarbonyl compounds used in this research exist only in the ketone form, and cyclization takes place at the primary amino group. In the case of β-diketones, which are 80-100% enolized, condensation at the α-nitrogen atom becomes possible. In addition, the formation of a strained four-membered ring in the reaction with α-dicarbonyl compounds is unfavorable, and a seven-membered azepine ring is formed. From the data in [11] on the relative activities of the carbonyl groups in unsymmetrical β-diketones it may be assumed that the carbonyl group bonded to the nonfluorinated substituent primarily undergoes attack.

EXPERIMENTAL

The mass spectra were obtained with a Varian Mat-311 spectrometer. The samples were introduced directly into the ion source at 100-150°C, an ionizing voltage of 70 eV, a cathode emission current of 1 mA, and an accelerating voltage of 3 kV. Peaks with intensities ≥5% are presented. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of 10^{-3} M solutions of the compounds in ethanol were obtained with a Specord UV-vis spectrophotometer. Thin-layer chromatography was carried out on silufol UV-254 plates in an ethyl acetate—chloroform—methanol system (3:6:1).

4-Amino-3-hydrazino-1,2-triazoline-5-thione (I) was obtained by the method in [1].

[4,2,1]Triazolo[3,4-b][1,2,4,5]tetraazepines (II and III). A 0.5-g (3.4 mmole) sample of I was dissolved in 20 ml of 50% alcohol containing 1 ml of concentrated HCl, 0.75 g (3.6 mmole) of the corresponding α-diketone was added, and the mixture was heated. It was then cooled, and the orange precipitate was removed by filtration and recrystallized.

Mass spectrum of II, m/e:

41 (14,0), 42 (8,0), 43 (14,0), 44 (10,6), 45 (5,7), 50 (11,0), 51 (31,6), 52 (6,0), 56 (15,0), 63 (13,2), 75 (8,0), 76 (25,6), 77 (45,7), 78 (5,3), 88 (7,7), 89 (44,0), 102 (7,4), 103 (62,1), 104 (35,0), 105 (55,0), 115 (8,7), 126 (12,3), 129 (10,5), 139 (11,0), 142 (13,8), 150 (8,4), 151 (18,5), 152 (19,4), 163 (6,5), 164 (5,9), 165 (40,0), 166 (8,7), 175 (5,3), 176 (30,8), 177 (19,4), 178 (100,0), 179 (17,6), 189 (5,5), 190 (16,3), 191 (8,4), 192 (85,4), 193 (40,6), 194 (5,6), 234 (53,0), 235 (9,6), 248 (17,1), 262 (6,4), 288 (15,3), 320 (53,0), 321 (12,3).

1-(4-Amino-5-thioxo-1,2,4-triazol-3-yl)-3,5-dimethylpyrazole (IV). A 1-g (6.8 mmole) sample of I was dissolved by heating in 20 ml of water and 2 ml of concentrated HCl, 1 ml (10 mmole) of acetylacetone was added, and the mixture was refluxed for 1.5 h. It was then

cooled, and the precipitated crystals were removed by filtration and recrystallized. Compounds V-IX were similarly obtained. Mass spectra, m/e:

32 (56,7), 34 (9,1), 39 (34,3), 40 (13,1), 41 (26,5), 42 (39,6), 43 (10,6), 44 (11,1), 45 (6,2), 51 (6,1), 51 (6,0), 53 (12,3), 54 (18,0), 55 (11,9), 56 (9,8), 57 (10,0), 59 (10,7), 60 (9,8), 65 (8,6), 66 (15,6), 67 (27,4), 68 (6,6), 69 (5,5), 77 (6,8), 80 (7,6), 81 (15,2), 82 (7,1), 83 (6,4), 85 (5,4), 91 (6,1), 93 (5,6), 95 (35,9), 96 (18,6), 97 (33,1), 107 (15,9), 108 (5,1), 121 (21,1), 124 (7,8), 136 (10,1), 149 (6,3), 152 (6,8), 165 (8,3), 193 (11,5), 209 (5,8), 210 (100,0), 211 (11,5), 212 (6,4); VII 40 (7,9), 41 (13,0), 42 (37,3), 43 (26,9), 44 (9,7), 45 (14,6), 46 (6,2), 47 (5,7), 51 (52,8), 52 (14,3), 53 (10,5), 54 (12,4), 55 (7,8), 56 (77,0), 57 (24,5), 58 (8,1), 59 (51,4), 60 (51,2), 61 (5,2), 64 (5,0), 65 (7,0), 66 (19,9), 67 (14,6), 70 (15,6), 74 (7,3), 75 (31,1), 76 (5,2), 77 (8,9), 80 (6,5), 81 (8,7), 82 (5,2), 83 (7,8), 85 (13,1), 89 (5,5), 90 (5,8), 91 (6,5), 92 (6,3), 101 (31,8), 102 (8,1), 106 (6,3), 108 (17,0), 109 (5,7), 113 (21,4), 114 (31,4), 115 (5,7), 116 (6,2), 131 (28,5), 138 (13,0), 142 (6,2), 156 (10,4), 157 (7,0), 159 (6,0), 163 (15,6), 181 (5,3), 183 (100,0), 184 (7,1), 208 (21,4), 296 (80,9), 297 (9,7); VIII 40 (11,8), 41 (17,4), 42 (25,2), 43 (28,7), 44 (9,2), 45 (12,4), 50 (6,7), 51 (25,5), 52 (15,3), 53 (9,2), 54 (11,8), 55 (10,9), 56 (27,0), 57 (23,5), 58 (8,0), 59 (28,7), 60 (42,0), 64 (6,1), 65 (6,5), 66 (30,2), 67 (24,8), 68 (6,2), 69 (7,6), 70 (11,5), 71 (6,5), 73 (6,5), 74 (6,5), 75 (6,5), 77 (6,9), 78 (5,5), 81 (11,3), 83 (13,0), 84 (6,5), 85 (14,9), 91 (6,7), 92 (5,0), 93 (5,0), 101 (5,0), 108 (9,9), 113 (52,2), 114 (13,4), 131 (16,6), 132 (7,6), 133 (67,2), 138 (44,0), 139 (5,7), 140 (7,3), 143 (5,7), 158 (20,2), 182 (9,2), 246 (100,0), 247 (9,9), 248 (5,6).

1-[4-(p-Nitrobenzylideneamino)-5-thioxo-1,2,4-triazolin-3-yl]-3,5-dimethylpyrazole (X). A 0.5-g (2.38 mmole) sample of IV was dissolved in 10 ml of ethanol, a few drops of concentrated HCl and 0.36 g (2.38 mmole) of p-nitrobenzaldehyde were added, and the mixture was refluxed for 15-20 min. It was then cooled, and the precipitated crystals were removed by filtration to give 0.6 g (80%) of azomethine with mp 193-194°C (from 50% ethanol). Found: C 48.6; H 3.9; S 9.1%. $C_{14}H_{13}N_7O_2S$. Calculated: C 48.9; H 3.8; S 9.3%.

1-(4-Amino-5-methylthio-1,2,4-triazol-3-yl)-3,5-dimethylpyrazole (XI). A 1-g (4.8 mmole) sample of IV was dissolved in 9 ml of 2 N NaOH, and a solution of 0.68 ml (4.8 mmole) of methyl iodide in 12 ml of alcohol was added. After 1 h, the mixture was neutralized to pH 7 with acetic acid and allowed to stand for 10 h. The solution was then evaporated to dryness on a water bath, and the residue was recrystallized from water to give 0.9 g (85%) of XI with mp 122-123°C (from water). Found: C 42.7; H 5.3; S 14.3%. $C_8H_{12}N_6S$. Calculated: C 42.8; H 5.4; S 14.4%.

1-(5-Methylthio-1,2,4-triazol-3-yl)-3,5-dimethylpyrazole (XII). A 0.5-g (2.2 mmole) sample of XI was dissolved by heating in 15 ml of 1 N HCl, the solution was cooled, and 0.3 g (4.3 mmole) of $NaNO_2$ was added in small portions. The mixture was then neutralized to pH 7 with 1 N NaOH, and the precipitate was removed by filtration to give 0.35 g (74%) of XII with mp 115-116°C (from water). Found: C 45.6; H 5.0; S 15.3%. $C_8H_{11}N_5S$. Calculated: C 45.8; H 5.3; S 15.3%.

3-(3,5-Dimethylpyrazolyl)[4,2,1]tetrazolo[4,3-b][1,3,4,7]aminothiadiazepine (XIII). A 0.5-g (2.38 mmole) sample of IV was dissolved in 15 ml of ethanol containing 0.2 g of NaOH, 0.4 ml (4.4 mmole) of α-chloropropionitrile was added, and the mixture was heated on a water bath for 1 h. The precipitated NaCl was removed by filtration of the hot mixture, the mother liquor was cooled, and the colorless precipitate was removed by filtration to give 0.46 g (78%) of a product with mp 114-115°C (from water). Found: C 43.3; H 5.2; S 12.8%. $C_9H_{13}N_7S$. Calculated: C 43.0; H 5.2; S 12.7%.

3-(3,5-Dimethylpyrazolyl)[4,2,1]triazolo[4,3-b][1,3,4]thiadiazine (XIV). A mixture of 0.5 g (2.38 mmole) of IV, 0.5 g (2.5 mmole) of bromoacetophenone, and 15 ml of alcohol was heated on a water bath for 2 h, after which the resulting solution was evaporated to dryness on a water bath, and the residue was treated with 25 ml of 1 N HCl at 40°C. The mixture was filtered, and the solid was treated with 2 N NaOH to give 0.52 g (70%) of a product with mp 165-166°C (from ethanol). Found: C 58.3; H 4.7; S 9.9%. $C_{15}H_{14}N_6S$. Calculated: C 58.4; H 4.5; S 10.0%.

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