SYNTHESIS AND STUDY OF SOME TRIAZOLOQUINAZOLINES

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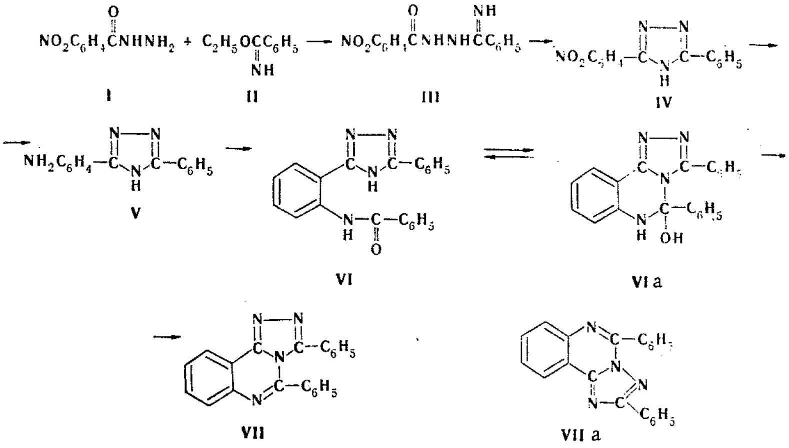
The cyclodehydration of 2-acylaminophenyl-1,2,4-triazoles has given a series of mono- and ditriazoloquinazolines. The dependence of the thermal characteristics of the compounds synthesized on their structure has been studied.

We have previously synthesized heat-stable polymers containing triazoloquinazoline rings – polytriazoloquinazolines [1]. For a more detailed study of the various characteristics of these polymers (spectral, thermal, etc.) and to determine the optimum conditions for their synthesis, and also in view of the fact that individual triazoloquinones [2] have been studied inadequately at the present time, in the present work we undertook the investigation of a series of mono- and ditriazoloquinazolines modeling the polytriazoloquinazolines.

As the general method for the synthesis of these compounds, we selected the cyclodehydration of aromatic 2-acylaminophenyl-1,2,4-triazoles (VI, IXa-h, XVIIa-c). 3,5-Diphenyl-1,2,4-triazolo[4,3-c]quinazoline (VII) was obtained by the following route:



The structures of 2-nitrobenzoylbenzamidrazone (III), 5-(2-nitrophenyl)-3-phenyl-1,2,4-triazole (IV), 5-(2-aminophenyl)-3-phenyl-1,2,4-triazole (V), 5-(2-benzamidophenyl)-3-phenyl-1,2,4-triazole (VI), and (VII) were confirmed by elementary and spectral analysis [1]. The cyclization of (VI) into (VII), probably taking place in a similar manner to the formation of tetrazolo[1,5-c]quinazoline [3] through the corresponding hydroxy dihydro compound (VIa) was accompanied by the disappearance in the IR spectrum of absorption bands in the 1610-1670- and 2800-3200-cm^{-1} regions that are characteristic of amide bonds and of the NH group of a triazole ring and by the appearance of absorption bands in the 1380-cm^{-1} region which are characteristic for a tertiary nitrogen atom.

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TABLE 1. Conditions for the Synthesis and Purification and Some Properties of the Compounds Obtained

Compound	Conditions of synthesis, °C (h)	Solvent for crystallization	mp, °C	Decomp. pt., °C			Empirical formula	Found, %			Calc., %			Yield, %
				start of dec. I	max. dec. I	max. dec. II		C	H	N	C	H	N	
IXa		DMFA*+water(2 : 1)	328—330				$C_{36}H_{26}N_8O_2$	71,3	4,4	18,1	71,6	4,3	18,6	86
IXb		DMFA+water(2 : 1)	380—382				$C_{36}H_{26}N_8O_2$	72,2	4,3	18,3	71,6	4,3	18,6	83
IXc		DMFA	355—358				$C_{42}H_{30}N_8O_2$	74,0	4,5	15,9	74,3	4,4	16,4	80
IXd		DMFA	391—394				$C_{40}H_{28}N_8O_2$	73,7	4,0	17,0	73,6	4,3	17,2	78
IXe		DMFA+water(1 : 2)	330				$C_{35}H_{25}N_9O_2$	69,3	4,1	20,6	69,6	4.1	20,9	81
IXf		DMFA+water(1 : 1)	320				$C_{42}H_{30}N_8O_3$	71,9	4,2	16,0	72,0	4,3	16,2	75
IXg		DMFA	315				$C_{43}H_{30}N_8O_3$	72,8	4,2	15,9	73,1	4,2	15,9	78
IXh		DMFA+water(1 : 1)	308—310				$C_{42}H_{30}N_8O_4S$	67,6	4,2	15,9	67,9	4,0	16,0	84
Xa	375—385 (4)	DMFA	333—335	440	490	560	$C_{36}H_{22}N_8$	75,9	3,8	19,5	76,3	3,9	19,8	75
Xb	375—385 (4)	DMAA*	368—370	440	500	580	$C_{36}H_{22}N_8$	76,0	3,8	19,6	76,3	3,9	19,8	76
Xc	360—375 (4)	DMFA + EtOH (1 : 1)	356—358	460	505	590	$C_{42}H_{26}N_8$	77,3	4,1	17,3	78,5	4,0	17,4	80
Xd	390—395 (4)	DMAA	397—400	460	505	590	$C_{40}H_{24}N_8$	77,5	3,4	17,7	77,9	3,9	18,2	75
Xe	400 (4)	DMFA	366—367	450	500	580	$C_{35}H_{21}N_9$	73,4	4,0	22,2	74,0	3,7	22,2	82
Xf	300—320 (4)	DMAA + EtOH (1 : 1)	310	430	510	600	$C_{42}H_{26}N_8O$	72,1	4,1	16,6	73,6	3,9	17,0	80
Xg	400 (4)	DMFA	330—331	500	520	580	$C_{43}H_{26}N_8O$	76,6	3,8	16,8	77,0	3,9	16,7	85
Xh	330—335 (4)	DMAA	345—348	460	515	580	$C_{42}H_{26}N_8O_2S$	70,9	3,5	15,8	71,1	3,7	15,9	80
XIa		Ether	71				$C_{12}H_{16}N_2O_2$	65,1	7,3	12,7	65,4	7.3	12,8	75
XIb		Acetone	102—103				$C_{12}H_{16}N_2O_2$	65,4	7,1	12,6	65,4	7,3	12,8	73
XIc		Ether	67—68				$C_{11}H_{15}N_3O_2$	59,9	6,8	18,8	59,8	6,8	19,0	70
XIIIa		Pyridine	—				$C_8H_{12}N_6$	49,6	6,0	43,8	50,0	6,2	43,7	85
XIIIb		Pyridine	—				$C_8H_{12}N_6$	49,8	6,1	43,9	50,0	6,2	43,7	85
XIIIc		Water	230—231				$C_7H_{11}N_7$	43,8	5,6	50,6	43,5	5,7	50,8	88
XIVa		DMFA	230 (dec.)				$C_{22}H_{18}N_8O_6$	53,6	3,6	22,5	53,9	3,7	22,8	90
XIVb		DMFA + water(1 : 1)	245 (dec.)				$C_{22}H_{18}N_8O_6$	53,7	3,6	22,5	53,9	3,7	22,8	92
XIVc		EtOH	199—200 (dec.)				$C_{21}H_{17}N_9O_6$	51,0	3,4	25,6	51,4	3,5	25,7	88
XVa	260 (3)	EtOH + water (1 : 1)	246—247				$C_{22}H_{14}N_8O_4$	59,3	2,8	24,3	58,1	3,1	24,7	78
XVb	260 (3)	Acetone + H_2O (1 : 2)	313—315				$C_{22}H_{14}N_8O_4$	57,7	2,9	24,6	58,1	3,1	24,7	80
XVc	210 (4)	Acetone + H_2O (1 : 4)	315				$C_{21}H_{13}N_9O_4$	55,1	2,4	27,3	55,4	2,4	27,7	90
XVIa		Dioxane + H_2O (1 : 1)	318—320				$C_{22}H_{18}N_8$	66,0	4,9	27,9	66,6	4,6	28,3	70
XVIb		DMFA + water (1 : 2)	330—331				$C_{22}H_{18}N_8$	66,8	4,5	28,0	66,6	4,6	28,3	75
XVIc		EtOH	342—344				$C_{21}H_{17}N_9$	63,4	3,9	31,6	63,8	4,0	31,9	70
XVIIa		EtOH	310				$C_{36}H_{26}N_8O_2$	69,8	4,5	18,7	71,6	4,3	18,7	85
XVIIb		DMFA	382—383				$C_{36}H_{26}N_8O_2$	71,1	4,4	18,3	71,6	4,3	18,7	80
XVIIc			220				$C_{35}H_{25}N_9O_2$	70,5	4,2	21,1	70,8	4,9	21,3	75
XVIIIa	325—330 (3)	Acetone	315	420	490	570	$C_{36}H_{22}N_8$	76,8	3,9	19,2	76,1	3,9	19,8	76
XVIIIb	370 (4)	DMFA + water(1 : 1)	340—343	430	495	570	$C_{36}H_{22}N_8$	76,7	3,4	19,7	76,1	3,9	19,8	65
XVIIIc	350 (4)		330—332	410	485	550	$C_{35}H_{21}N_9$	73,9	3,5	21,2	74,1	3,7	22,2	65

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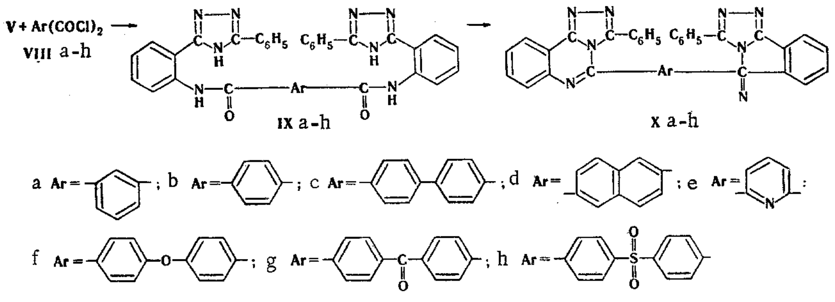
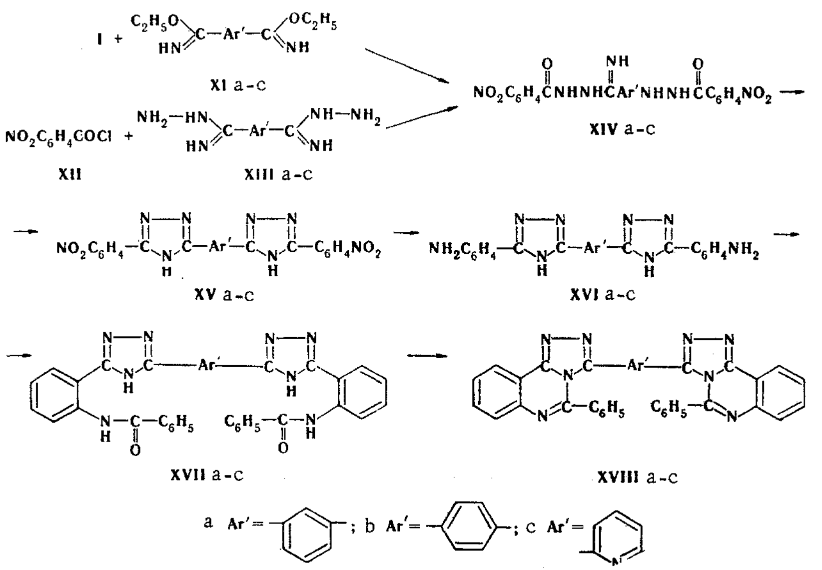
*DMFA – dimethylformamide; DMAA – dimethylacetamide.

The cyclodehydration of (VI) may lead either to compound (VII) or to a product isomeric with it – 2,5-diphenyl[1,2,4]triazolo[1,5-c]quinazoline (VIIa). However, we succeeded in isolating only one product. The structure of the compound obtained is being investigated at the present time; the triazoloquinazolines described in the present paper are provisionally considered to be the 1,2,4-triazolo[4,3-c]quinazolines.

A number of di{3-phenyl[1,2,4]triazolo[4,3-c]quinazolin-5-yl} arenes (Xa-h; Table 1) were obtained by the reaction of (V) with the dichlorides of aromatic dicarboxylic acids (VIIIa-h) followed by the thermal cyclodehydration of the resulting di[2-(3-phenyl-1,2,4-triazol-5-yl)phenylcarbamoyl]arenes (IXa-h).



The synthesis of the di{5-phenyl[1,2,4]triazolo[4,3-c]quinazolin-3-yl} arenes (XVIIIa-c) began with aromatic diamines containing 1,2,4-triazole rings in the ortho positions to the amino groups. The diamines were obtained by a method analogous to that used for the synthesis of (V) [1] involving the reaction of diesters of bicarbimidic acids (XIa-c) with (I) or of diamidrazones of aromatic dicarboxylic acids (XIIIa-c) with 2-nitrobenzoyl chloride (XII), the cyclization of the resulting di(2-nitrobenzoylamidrazones) (XIVa-c) to the di[5-(2-nitrophenyl)triazol-3-yl]arenes (XVa-c), and the reduction of the latter to the di[5-(2-aminophenyl)-1,2,4-triazol-3-yl]arenes (XVIa-c). The benzoylation of the diamines (XVIa-c) gave the di[5-(2-benzamidophenyl)-1,2,4-triazol-3-yl]arenes (XVIIa-c), the cyclodehydration of which yielded the di{5-phenyl-1,2,4-triazolo[4,3-c]quinazolin-3-yl} arenes (XVIIIa-c).



The study of the thermal stability of the model compounds synthesized by differential thermal analysis and dynamic thermogravimetry in air has shown that all the ditriazoloquinazolines undergo degradation in two stages.

EXPERIMENTAL

2-Nitrobenzoic hydrazide (I) was synthesized as described previously [1]. mp 123°C (from water). According to the literature [4], mp 123°C.

Benzimidic ester (II) was obtained by Pinner's method [5] and purified by distillation at 104-105°C (2 mm). According to Pinner [5], bp 101-102°C (5mm).

2-Nitrobenzoylbenzamidrazone (III). A mixture of 0.01 mole of (I) and 0.01 mole of (II) in 30 ml of ethanol was boiled for 2 h. The yellow product that separated out was filtered off. Yield 83%, mp 185°C (decomp., from ethanol).

5-(2-Nitrophenyl)-3-phenyl-1,2,4-triazole (IV) was obtained by heating (III) in vacuum (pressure of 1 mm) at 200-210°C for 3 h. Yield 77%. mp 185-186°C [from a mixture of ethanol and water (1 : 4)].

5-(2-Aminophenyl)-3-phenyl-1,2,4-triazole (V). A mixture of 0.01 mole of (IV) and 0.25 mole of hydrazine hydrate was heated with Raney nickel in 50 ml of ethanol at 60°C for 3-4 h. The (V) was isolated by pouring the reaction mixture into water. Yield 85%. mp 190°C [from a mixture of ethanol and water (1 : 1)].

5-(2-Benzamidophenyl)-3-phenyl-1,2,4-triazole (VI). A mixture of 0.01 mole of (V), 0.01 mole of benzoyl chloride, and 30 ml of dimethylacetamide was kept at 0°C for 3 h and was then poured into cold water, and the (VI) that separated out was filtered off. Yield 79%. mp 256°C (decomp., from ethanol).

3,5-Diphenyl-1,2,4-triazolo[4,3-c]quinazoline (VII) was obtained by the heat treatment of (VI) in vacuum at 260-270°C for 3-4 h [1]. Yield 80%; mp 175°C (from ethanol) [1].

The dichlorides of aromatic dicarboxylic acids (VIIIa-h) were obtained by treating the appropriate acids with thionyl chloride in the presence of catalytic amounts of pyridine. After the removal of the excess of thionyl chloride by distillation, the dichlorides were purified by crystallization from anhydrous inert solvents or by distillation. The di(acid chloride)s obtained had the melting points given in the literature [6-13].

The Di[2-(3-phenyl-1,2,4-triazol-5-yl)phenylcarbamoyl]arenes (IXa-h). With stirring, 0.01 mole of an aromatic dicarboxylic acid dichloride was added to a solution of 0.02 mole of (V) in 50 ml of dimethylacetamide. The reaction mixture was stirred for 2-3 h and was poured into water. The white substance that separated out was filtered off and crystallized (Table 1).

The di{ 3-phenyl-1,2,4-triazolo[4,3-c]quinazol-5-yl} arenes (Xa-h) were obtained by the thermal dehydration of (IXa-h) in vacuum (pressure of 1 mm) at temperatures above their melting points. The conditions for the synthesis and purification of the compounds obtained, and also their main characteristics are given in Table 1.

Isophthalimidic ester (XIa) was obtained by the method of Toshiyuki et al. [14]; mp 71°C (from ether). According to the literature [14], mp 71°C.

Terephthalimidic ester (XIb) was obtained by the method of Zaitseva et al. [15]. mp 102-103°C (from acetone). According to the literature [15], 102.5-103.5°C.

Pyridine-2,6-dicarbimidic Ester (XIc). A mixture of 18.9 g (0.01 mole) of pyridine-2,6-dicarbonitrile [16], 250 ml of dioxane, and 15 ml of absolute ether was saturated with dry HCl at 0°C for 4 h. Then it was kept for five days and the precipitate that had formed was filtered off, washed with ether, and dried. The melting point of the pyridine-2,6-dicarbimidic ester dihydrochloride that was obtained was 110°C; treatment with 30% K_2CO_3 solution then gave the free pyridine-2,6-dicarbimidic ester with a yield of 70%; mp 67°C (from ether).

Diamidrazone of Isophthalic Acid (XIIIa). To a solution of 4.4 g (0.02 mole) of diethyl isophthalimidate in 40 ml of absolute ethanol was added 2.2 g (0.044 mole) of hydrazine hydrate, and the mixture was filtered and was then boiled for 15 min. After cooling to 0°C, yellow crystals deposited. The product was filtered off, washed with ether, dried, and recrystallized from pyridine. At 150°C, the product was orange, and at 280°C it became colorless.

The diamidrazone of terephthalic acid (XIIIb) was obtained by the method of Ried and Schomann [17]. The product had no melting point but lost its color at 180°C, in agreement with the literature [17].

The diamidrazone of pyridine-2,6-dicarboxylic acid was obtained by Hergenrother's method [18]. mp 231°C; according to the literature [18], mp 231°C.

The Di(2-nitrobenzoylamidrazones) (XIVa-c). a) A mixture of 1 mole of an ethyl dicarbimidate (XIa-c) and 2 moles of (I) in ethanol was boiled, and the yellow substance that separated out was filtered off and crystallized.

b) At 0°C, 0.02 mole of (XII) was added by drops to a stirred mixture of 0.01 mole of a diamidrazone of a dicarboxylic acid, 30 ml of dimethylacetamide, and 2.12 g (0.02 mole) of Na_2CO_3. The reaction mixture was stirred for 3 h and was poured into ice water, whereupon a yellow product separated out (Table 1).

The di[5-(2-nitrophenyl)-1,2,4-triazol-3-yl]arenes (XVa-c) were obtained by the heat treatment of (XIVa-c) above their melting points. The conditions for the synthesis and the main properties of (XVa-c) are given in Table 1.

The di[5-(2-aminophenyl)-1,2,4-triazol-3-yl]arenes (XVIa-c) were obtained by the reduction of compounds (XVa-c) with hydrazine hydrate over Raney nickel in boiling ethanol (Table 1).

The di[5-(2-benzamidophenyl)-1,2,4-triazol-3-yl]arenes (XVIIa-c) were obtained by standard procedures: with stirring, 0.02 mole of benzoyl chloride was added to a solution of 0.01 mole of one of the diamines (XVIa-c) in 40 ml of dimethylacetamide. The reaction mixture was stirred for 2-3 h and was poured into water. The precipitate that deposited was filtered off and crystallized.

The di{5-phenyl[1,2,4]triazolo[4,3-c]quinazolin-3-yl}arenes (XVIIIa-c) were obtained by the thermal cyclodehydration of (XVIIa-c) at 325-370°C for 3-4 h (pressure 1 mm) (Table 1).

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