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SYNTHESIS AND PROPERTIES OF DERIVATIVES OF *sym*-TRIAZINE. 15.* SYNTHESIS OF AMINE DERIVATIVES OF *sym*-TRIAZINE THAT CONTAIN INDOLE GROUPS

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By the cyclocondensation of imino esters of acids of the indole series with N-acylguanidines, 2-amino-4,6-disubstituted sym*-triazine are obtained that contain indole groups. The reaction of N-(indolyl-3-imidolyl)-guanidine with esters of carboxylic acids leads to 2-amino-4-(3-indolyl)-6-substituted* sym*-triazines. Indolyl-containing N-substituted 2,4-diamino-*sym*-triazines are synthesized by the reaction of imino esters of indole acids with biguanides. Similar products are also formed when 2-amino-4-trichloromethyl-*sym*-triazines that contain indole substituents react with dimethylamine, morpholine, or furfurylamine.*

In a continuation of our investigations of the synthesis of heteryl substituted *sym*-triazines by cyclocondensation reactions involving functional derivatives of carboxylic acids [2-5], we report here on the preparation of 2-amino- and N-substituted 2,4-diamino-*sym*-triazines containing indole groups.

Information on the preparation and properties of amino derivatives of this type of *sym*-triazine is extremely limited [6-8], despite the fact that these compounds are of interest as potentially biologically active materials or intermediates for their preparation.

To synthesize these compounds we have used the condensation of ethylimino esters — derivatives of indole-3-carboxylic (Ia), 1-methylindole-3-carboxylic (Ib), and indole-3-acetic (Ic) acid with N-acylguanidines (IIa-d) [2, 3, 9] and N,N-disubstituted biguanides (IIIa-c). It has been established that when equimolar quantities of imino esters Ia-c and N-acylguanidines IIa-d are boiled in absolute ethanol (2-3 h), 2-amino-4,6-disubstituted *sym*-triazines IVa-l containing indole groups are formed in 83-91% yield (Table 1, method A). Note that nitriles and amides of the corresponding acid of the indole series are found as by-products in the reaction mixtures by means of TLC.

It is known [2, 3, 9, 10] that 2-amino-*sym*-triazines can be prepared by the condensation of N-imidoylguanidines with esters of carboxylic acids. In the present work, we decided to use this method for the synthesis of indolyl-containing 2-amino-*sym*-triazines. Thus, when equimolar quantities of N-(indolyl-3-imidoyl)guanidine (V) and the ethyl esters of various acids react in absolute ethanol (boiling, 1.5-2 h), 2-amino-4-(3-indolyl)-6-substituted *sym*-triazines (IVa-d, m-o) are formed in high yields (Table 1, method B).

The most widespread method of preparing N-substituted 2,4-diamino-6-alkyl(aryl, heteryl)-*sym*-triazines (guanamines) is the cyclocondensation of N-substituted biguanides with esters of carboxylic acids [2, 3, 8, 11, 12]. However, when used in reactions with N-substituted biguanides IIIa-c, the esters of indole 3-carboxylic, 1-methylindole-3-carboxylic, and indolyl-3-acetic acid form the corresponding indolyl-containing N-substituted 2,4-diamino-*sym*-triazines (VIa-i) in low yields (23-35%) along with unidentified, high-melting (T_{mp} > 350°C) by-products that are poorly soluble in most organic solvents. In order to synthesize these *sym*-triazine derivatives, we have studied the cyclocondensation of imino esters Ia-c with N-substituted biguanides IIIa-c. It has been established that desired products VIa-i are formed in 67-85% yield when equimolar amounts of

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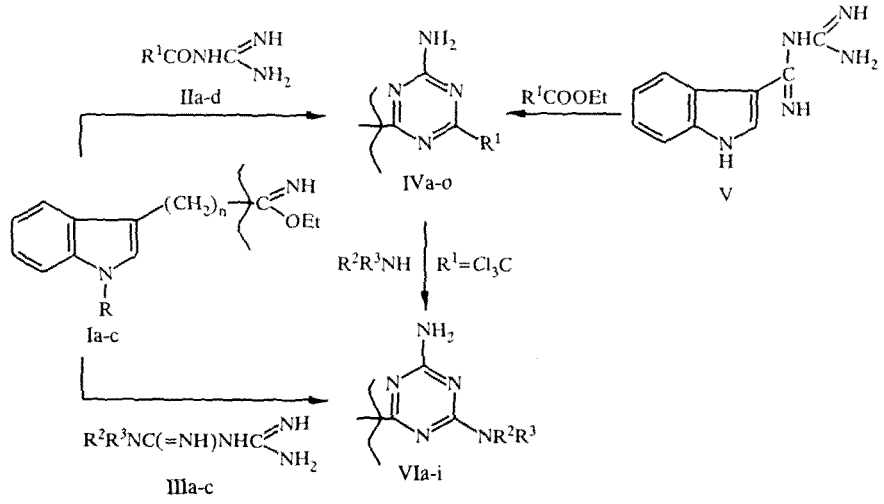
TABLE 1. Characteristics of the Synthesized Compounds

Compound	Molecular formula	T_{mp}, °C*	R_f (solvent system)	Yield, %
IVa	$C_{12}H_8Cl_3N_5$	194...195 (decomp.)	0,70 (a)	84 (A), 88 (B)
IVb	$C_{17}H_{13}N_5$	251...253 (decomp.)	0,41 (a)	89 (A), 76 (B)
IVc	$C_{15}H_{11}N_5O$	287...288	0,56 (b)	86 (A), 83 (B)
IVd	$C_{16}H_{12}N_6$	239...240	0,24 (b)	89 (A), 81 (B)
IVe	$C_{13}H_{10}Cl_3N_5$	148...149,5 (decomp.)	0,83 (c)	83 (A)
IVf	$C_{18}H_{15}N_5$	210...212	0,54 (c)	88 (A)
IVg	$C_{16}H_{13}N_5O$	237...239 (decomp.)	0,75 (b)	87 (A)
IVh	$C_{17}H_{14}N_6$	202...203	0,53 (a)	91 (A)
IVi	$C_{13}H_{10}Cl_3N_5$	157...158 (decomp.)	0,62 (c)	86 (A)
IVj	$C_{18}H_{15}N_5$	173...174	0,40 (c)	83 (A)
IVk	$C_{16}H_{13}N_5O$	202...204	0,51 (c)	85 (A)
IV*l*	$C_{17}H_{14}N_6$	188...189,5	0,35 (c)	88 (A)
IVm	$C_{16}H_{19}N_5$	141...143	0,52 (a)	79 (B)
IVn	$C_{15}H_{10}N_6O_3$	235...236 (decomp.)	0,45 (b)	87 (B)
IVo	$C_{17}H_{13}N_5O$	228...229	0,50 (a)	81 (B)
VIa	$C_{13}H_{14}N_6$	142...143,5	0,39 (b)	85 (C), 70 (D)
VIb	$C_{15}H_{16}N_6O$	135...136	0,53 (a)	80 (C), 65 (D)
VIc	$C_{16}H_{14}N_6O$	158...160	0,47 (c)	74 (C), 67 (D)
VI*d*	$C_{14}H_{16}N_6$	oil	0,50 (b)	75 (C), 74 (D)
VIe	$C_{16}H_{18}N_6O$	66...67,5	0,53 (c)	82 (C), 80 (D)
VIf	$C_{17}H_{16}N_6O$	100...102	0,63 (b)	67 (C), 72 (D)
VIg	$C_{14}H_{16}N_6$	57...58	0,70 (b)	81 (C), 72 (D)
VIh	$C_{16}H_{18}N_6O$	oil	0,34 (c)	69 (C), 64 (D)
VIi	$C_{17}H_{16}N_6O$	118...120	0,59 (a)	77 (C), 68 (D)

*Compounds were recrystallized from aqueous dioxane (IVa, e, VIf), aqueous DMF (IVb-d, n, o, VIc), aqueous ethanol (IVf, h-k, VIa, b, i), a 5:1 cyclohexane–methanol mixture (IVg, VIe, g), or butanol (IVi, m).



Ia, IVa-d, i-o, VIa-c R = H, n = 0; Ib, IVe-h, VId-f R = Me, n = 0; Ic, IVi-*l*, VIg-i R = H, n = 1; IIa, IVa, e, i $R^1 = Cl_3C$; IIb, IVb, f, j R^1 = Ph; IIc, IVc, g, k R^1 = 2-furyl; IId, IVd, h, R^1 = 3-pyridyl; IVm $R^1 = C_5H_{11}$; IVn R^1 = 5-nitrofuryl-2; IVo R^1 = (E)-β-(2-furyl)-vinyl; IIIa, VIa, d, g $R^2 = R^3$ = Me; IIIb, VIb, e, h $R^2 + R^3 = (CH_2)_2O(CH_2)_2$; IIIc, VIc, f, R^2 = furfuryl, R^3 = H

TABLE 2. PMR Spectral Data for the Amine Derivatives of *sym*-Triazines IV and VI

Compound	Chemical shift, δ, ppm*							SSCC (J), Hz
	Indole group protons					NH_2 (2H, ex.b.s.)	Other protons	
	2-H (1H)	4-H (1H, d)	5-H, 6-H (2H, m)	7-H (1H, d)	N—R			
1	2	3	4	5	6	7	8	9
IV a	7,58 d	7,64	7,07...7,18	7,40	8,12 (1H, s)	5,92	–	J_{12} = 2,5, J_{45} = J_{67} = 7,3
IV b	7,74 d	7,60	*2	7,32	8,24 (1H, b.s.)	5,83	6,89...7,23 (7H, m, H_{Ph})*2	J_{12} = 2,7, J_{45} = J_{67} = 7,5
IV c	7,68 d	7,60	7,12...7,23	7,35	8,30 (1H, b.s.)	6,08	6,24 (1H, d.d., 3-H_{fur}), 6,79 (1H, d.d., 4-H_{fur}), 7,45 (1H, d.d., 5-H_{fur})	J_{12} = 3,0, J_{45} = J_{67} = 7,2, $J_{3S fur}$ = =0,7, $J_{34 fur}$ = 3,6, $J_{45 fur}$ = 1,8
IV d	7,72 d	7,63	7,10...7,25	7,45	8,18 (1H, b.s.)	6,15	7,82...8,03 (4H, m, H_{pyrid}),	J_{12} = 3,3, J_{45} = J_{67} = 7,1
IV e	7,55 s	7,70	7,15...7,27	7,36	3,38 (3H, s)	5,76	–	J_{45} = J_{67} = 7,6
IV f	7,64 s	7,72	*2	7,44	3,30 (3H, s)	6,05	6,95...7,30 (7H, m, H_{Ph})	J_{45} = J_{67} = 7,3
IV g	7,76 s	7,63	7,08...7,23	7,48	3,27 (3H, s)	5,85	6,33 (1H, d.d., 3-H), 6,80 (1H, d.d., 4-H), 7,32 (1H, d.d., 5-H)	J_{45} = J_{67} = 8,0, $J_{3S fur}$ = 0,8, $J_{34 fur}$ = 3,5, $J_{45 fur}$ = 1,7
IV h	7,50 s	7,65	7,02...7,16	7,37	3,35 (3H, s)	6,36	7,76...7,94 (4H, m, H_{pyrid}),	J_{45} = J_{67} = 7,2
IV i	7,56 d	7,70	6,92...7,12	7,30	8,27 (1H, b.s.)	6,17	3,92 (2H, s, CH_2)	J_{12} = 3,4, J_{45} = J_{67} = 8,2
IV j	7,60 d	7,94	*2	7,43	8,10 (1H, b.s.)	5,94	4,14 (2H, s, CH_2), 6,90...7,27 (7H, m, H_{Ph})	J_{12} = 2,7, J_{45} = J_{67} = 7,6
IV k	7,53 d	7,68	6,95...7,08	7,38	8,32 (1H, b.s.)	5,84	3,96 (2H, s, CH_2), 6,27 (1H, d.d., 3-H_{fur}), 6,76 (1H, d.d., 4-H_{fur}), 7,20 (1H, d.d., 5-H_{fur})	J_{12} = 2,3, J_{45} = J_{67} = 7,8, $J_{3S fur}$ = =0,9, $J_{34 fur}$ = 3,5, $J_{45 fur}$ = 1,9
IV *l*	7,57 d	7,71	7,13...7,26	7,38	8,34 (1H, b.s.)	6,08	4,07 (2H, s, CH_2), 7,75...8,05 (4H, m, H_{pyrid}),	J_{12} = 2,8, J_{45} = J_{67} = 7,4
IV m	7,72 d	7,62	7,10...7,27	7,45	8,15 (1H, b.s.)	6,22	1,14 (3H, t, Me), 1,30...1,56 (6H, m, CH_2), 3,05 (2H, t, CH_2)	J_{12} = 2,9, J_{45} = J_{67} = 8,1

TABLE 2 (continued)

Compound	Chemical shift, δ, ppm*							SSCC (J), Hz
	Indole group protons					NH_2 (2H, ex.b.s.)	Other protons	
	2-H (1H)	4-H (1H, d)	5-H, 6-H (2H, m)	7-H (1H, d)	N—R			
1	2	3	4	5	6	7	8	9
IV n	7,65 d	7,77	6,93...7,16	7,31	8,26 (1H, b.s.)	5,90	6,68 (1H, d, 3-H_{fur}), 7,47 (1H, d, 4-H_{fur}),	J_{12} = 3,2, J_{45} = J_{67} = 7,5, $J_{34\,fur}$ = = 3,9
IV o	7,82 d	7,66	6,90...7,18	7,46	8,17 (1H, b.s.)	6,10	6,34 (1H, d.d., 3-H_{fur}), 6,62 (1H, d.d., 4-H_{fur}), 6,84 (1H, d, α-CH=), 7,32 (1H, d.d., 5-H_{fur}), 7,55 (1H, d, β-CH=)	J_{12} = 2,6, J_{45} = J_{67} = 8,2, $J_{35\,fur}$ = = 0,7, J_{34fur} = 3,4, J_{45fur} = 1,8, $J\alpha\beta$ = 14,5
VI a	7,68 d	7,58	7,03...7,25	7,37	8,20 (1H, b.s.)	6,28	3,26 (6H, ex.b.s., Me_2N)	J_{12} = 2,8, J_{45} = J_{67} = 7,3
VI b	7,53 d	7,65	7,12...7,31	7,41	8,24 (1H, b.s.)	6,08	2,50...2,66 (4H, m, NCH_2), 3,46...3,57 (4H, m, OCH_2)	J_{12} = 2,5, J_{45} = J_{67} = 7,3
VI c	7,75 d	7,62	7,05...7,24	7,48	8,13 (1H, b.s.)	6,17	3,28 (2H, d, CH_2), 5,68 (1H, b.s.) NH), 6,30 (1H, d.d., 3-H_{fur}), 6,65 (1H, d.d., 4-H_{fur}), 7,33 (1H, d.d., 5-H_{fur}),	J_{12} = 3,0, J_{45} = J_{67} = 7,4, $J_{35\,fur}$ = =0,9, J_{34fur} = 3,5, J_{45fur} = 1,8
VI d	7,62 s	7,73	6,93...7,15	7,36	3,24 (3H, s)	6,23	3,48 (6H, ex.b.s., Me_2N)	J_{45} = J_{67} = 8,1
VI e	7,55 s	7,67	7,08...7,27	7,43	3,37 (3H, s)	5,91	2,41...2,54 (4H, m, NCH_2), 3,56...3,68 (4H, m, OCH_2)	J_{45} = J_{67} = 7,8
VI f	7,60 c	7,71	6,94...7,08	7,40	3,30 (3H, s)	6,07	3,12 (2H, d, CH_2), 5,52 (1H, b.s. NH), 6,25 (1H, d.d., 3-H_{fur}), 6,78 (1H, d.d., 4-H_{fur}), 7,22 (1H, d.d., 5-H_{fur}),	J_{45} = J_{67} = 7,3, $J_{35\,fur}$ = 0,8, J_{34fur} = 3,6, J_{45fur} = 1,7
VI g	7,56 d	7,68	7,09...7,27	7,35	8,05 (1H, b.s.)	5,85	3,37 (6H, ex.b.s., Me_2N), 4,22 (2H, s, CH_2)	J_{12} = 2,7, J_{45} = J_{67} = 7,4
VI h	7,50 d	7,62	6,96...7,12	7,43	8,16 (1H, b.s.)	6,17	2,45...2,63 (4H, m, NCH_2), 3,40...3,62 (4H, m, OCH_2), 4,20 (2H, c, CH_2)	J_{12} = 3,1, J_{45} = J_{67} = 7,5
VI i	7,77 d	7,65	7,02...7,14	7,45	8,27 (1H, b.s.)	6,27	3,26 (2H, d, CH_2), 4,12 (2H, s, CH_2), 5,67 (1H, b.s.) NH), 6,24 (1H, d.d., 3-H_{fur}), 6,71 (1H, d.d., 4-H_{fur}), 7,32 (1H, d.d., 5-H_{fur}),	J_{12} = 2,9, J_{45} = J_{67} = 8,2, $J_{35\,fur}$ = = 0,9, J_{34} = 3,4, $J_{45\,fur}$ = 1,9

*The spectra of compounds IVa, e-i and VIb, d-h were recorded in CD_3OD; of the remaining compounds, in DMSO-D_6.

*2The signals from protons 5-H, 6-H, and the phenyl groups overlapped, forming multiplets with the intensity of 7 H.

TABLE 3. Mass Spectra of Amine Derivatives of *sym*-Triazine*

Compound	m/z (I_{rel}, %)
IV a	327*2 (12, $M^{+\cdot}$), 292*2 (36), 257*2 (100), 222 (18), 143 (25), 142 (52), 117*2 (15), 116 (31), 108*2 (38), 88 (16), 63 (24)
IV b	287 (100, $M^{+\cdot}$), 286 (44), 143 (34), 142 (56), 116 (17), 115 (10), 104 (13), 103 (26), 89 (31), 77 (20), 63 (14)
IV c	277 (33, $M^{+\cdot}$), 276 (15), 248 (13), 142 (51), 116 (18), 94 (41), 93 (100), 89 (17), 64 (44), 37 (22)
IV d	288 (100, $M^{+\cdot}$), 287 (54), 143 (13), 142 (24), 116 (21), 105 (17), 104 (62), 89 (14), 78 (24), 51 (12), 37 (46)
IV e	341*2 (7,5, $M^{+\cdot}$), 306*2 (25), 271*2 (100), 157 (18), 156 (60), 130 (52), 117*2 (11), 108*2 (43), 103 (17), 77 (33)
IV f	301 (100, $M^{+\cdot}$), 300 (40), 157 (12), 156 (35), 130 (72), 115 (15), 104 (21), 103 (52), 89 (16), 77 (38), 57 (28)
IV g	291 (16, $M^{+\cdot}$), 262 (32), 252 (14), 157 (16), 156 (54), 130 (19), 94 (35), 93 (100), 103 (24), 64 (22), 37 (12)
IV h	302 (100, $M^{+\cdot}$), 301 (37), 157 (13), 156 (50), 130 (27), 115 (17), 105 (18), 104 (63), 103 (24), 51 (21), 38 (16)
IV i	341*2 (12, $M^{+\cdot}$), 306*2 (25), 271*2 (100), 157 (15), 156 (35), 130 (57), 129 (15), 117*2 (20), 108*2 (47), 103 (18), 77 (45)
IV j	301 (27, $M^{+\cdot}$), 300 (13), 157 (21), 156 (57), 130 (100), 104 (21), 103 (72), 102 (19), 77 (52), 57 (10), 37 (24)
IV k	291 (11, $M^{+\cdot}$), 262 (38), 252 (17), 157 (14), 156 (32), 130 (100), 103 (51), 94 (22), 93 (64), 77 (20), 64 (35)
IV *l*	302 (48, $M^{+\cdot}$), 301 (21), 156 (25), 130 (100), 105 (34), 104 (15), 103 (21), 102 (13), 78 (17), 77 (62), 51 (14)
IV m	281 (16, $M^{+\cdot}$), 238 (34), 255 (100, M-C_4H_8), 143 (12), 142 (17), 116 (31), 115 (18), 90 (12), 89 (16), 88 (43), 63 (34)
IV n	322 (8, $M^{+\cdot}$), 292 (19, M-NO), 276 (15), 248 (37), 143 (23), 142 (100), 138 (27), 116 (39), 88 (42), 84 (17), 64 (21)
IV o	303 (13, $M^{+\cdot}$), 274 (17), 264 (43), 143 (17), 142 (45), 120 (23), 119 (100), 116 (37), 115 (18), 93 (35), 88 (26)
VI a	254 (100, $M^{+\cdot}$), 253 (51), 239 (15), 225 (11), 143 (21), 142 (58), 116 (19), 89 (31), 88 (14), 70 (17), 63 (39)
VI c	306 (47, $M^{+\cdot}$), 305 (20), 239 (16), 212 (100), 143 (21), 142 (64), 116 (22), 95 (13), 89 (27), 88 (12), 63 (47)
VI d	268 (100, $M^{+\cdot}$), 267 (43), 253 (15), 239 (26), 157 (22), 156 (67), 130 (15), 129 (13), 115 (37), 89 (17), 77 (39)
VI f	320 (24, $M^{+\cdot}$), 319 (16), 253 (15), 226 (100), 157 (19), 156 (43), 130 (21), 129 (11), 115 (25), 103 (19), 77 (47)
VI g	268 (36, $M^{+\cdot}$), 267 (14), 253 (16), 239 (20), 224 (13), 157 (12), 156 (24), 130 (100), 103 (16), 102 (21), 77 (31)
VI i	320 (15, $M^{+\cdot}$), 253 (16), 226 (74), 157 (13), 156 (42), 122 (12), 103 (27), 102 (14), 95 (16), 77 (24), 67 (17)

*The molecular ion and the 10 most intense peaks are shown.

*2Ions containing the lightest chlorine isotope.

the reactants are boiled (4-5 h) in absolute ethanol (Table 1, method C). Note that the replacement of ethanol by higher-boiling solvents (dioxane, 1-butanol, DMF) did not lead to a noticeable increase in the yields of these compounds.

Previously [13, 14] it was shown that the reactions of 2-amino-4-trichloromethyl-6-substituted *sym*-triazines with aliphatic amines give N-substituted 2,4-diamino-*sym*-triazines as a result of the nucleophilic substitution of the Cl_3C group. We used this method also to prepare *sym*-triazines VIa-i. Better yields of 2-amino-4-dimethylamino-*sym*-triazines VIa, d, g (70-74%) are achieved by passing gaseous dimethylamine into solutions of 2-amino-4-trichloromethyl-*sym*-triazines IVa, e, i in DMF at 150-155°C, and of 2-amino-4-morpholino- (VIb, e, h) and 2-amino-4-furfurylamino-*sym*-triazines (VIc, f, i) (60-72%) by heating (120-130°C) compounds IVa, e, i with excess morphine or furfurylamine in dioxane under pressure (method D).

The IR spectra of *sym*-triazine amine derivatives IVa-o and VIa-i contain absorption maxim characteristic of stretching (1570-1555, 1530-1520, 1425-1415), "breathing" (1120-1105, 1010-995), out-of-plane (820-805), and in-plane (715-695 cm^{-1}) ring deformation vibrations of *sym*-triazines [2-5, 9, 14-16]. In the spectra of compounds IVa, e, i, which contain trichloromethyl groups, these bands are shifted to lower frequencies compared to the bands of other amino- and diamino-*sym*-

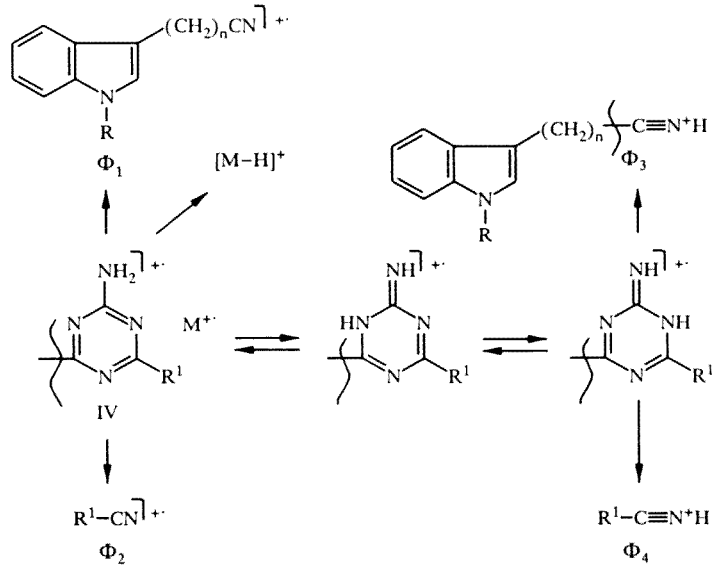
triazines. In addition to these vibrations, absorptions are also found characteristic of 3-substituted indoles [16, 17] at 1625-1615, 1595-1580, 1510-1495 (ν ring), 950-930, and 805-785 cm^{-1} (γ CH).

The NH stretches appear in the spectra of compounds IVa-d, i-o and VIa-c, g-i as two broad absorption bands at 3470-3375 and 3190-3120 (ν_{as} and ν_s NH in the NH_2 groups) [2, 9, 15], and also as an intense band at 3280-3200 cm^{-1} (ν NH of the indole group [16, 17]). In the spectra of 2-amino-4-furfurylamino-*sym*-triazines VIc, f, i, the stretching vibrations of the NH and NH_2 groups overlap and appear as a broad band at 3415-3170 cm^{-1} with an extremely poor separation of the maxima. Intense absorption maxima at 1685-1645 cm^{-1} are found in the spectra of all of the synthesized compounds. These belong to the N–H scissoring vibration in primary amine groups and are characteristic of associated amino derivatives of *sym*-triazine [9, 18].

In the PMR spectra of *sym*-triazines IVa-o and VIa-i (Table 2), the signals of the primary amine group protons appear as broad singlets of two proton units of intensity at 5.76-6.36 ppm. Signals are also found that are characteristic of 3-substituted indoles [16, 17, 19]: the 4-H proton doublet is shifted to a lower field (7.58-7.74 ppm), and the multiplet from the 5-H and 6-H protons is shifted still lower (6.90-7.31 ppm). The signal from the 2-H proton of the indole ring appears as a doublet with SSCC J_{12} = 2.3-3.4 Hz (compounds IVa-d, i-o; VIa-c, g-i) or as a singlet (compound IVe-h, VId-f) at 7.50-7.82 ppm; i.e., in comparison with unsubstituted indole and 3-phenylindole (6.68 and 7.03 ppm, respectively [19]), it is shifted to a lower field. The furan ring protons in the spectra of *sym*-triazines IVc, g, k, o and VIc, f, give three groups of signals (doublet of doublets) at 6.24-6.33 ppm, which is characteristic of 2-substituted furans [20].

The mass spectra of the synthesized amine derivatives of *sym*-triazine, IV and VI, also support the proposed structure. The molecular masses found correspond to the calculated, and the nature of the further fragmentations agree with the structures presented. Peaks of the molecular ions, $M^{+\bullet}$ (7.5-100%), are present in the mass spectra of all of the *sym*-triazines studied (Table 3). The stability of these ions depends on the susceptibility of the substituents to fragmentation under electron impact. Peaks of $[M-H]^+$ ions are found in the spectra of all of the compounds investigated. The intensity of these peaks is about one-half that of the corresponding M^+, which is characteristic of amine derivatives of *sym*-triazines [9, 21].

The basic fragmentation paths of the molecular ions of 2-amino-*sym*-triazines IVb-d, f-h, j-o and the 2,4-diamino-*sym*-triazines are connected with the destruction of the triazine ring, which leads to odd-electron fragments Φ_1 and Φ_2 and even-electron fragments Φ_3 and Φ_4, which is typical for aryl- and heteryl-substituted *sym*-triazines [21, 22]. The formation of ions of protonated nitriles Φ_3 and Φ_4, the intensity of whose peaks is one-half to one-third that of the corresponding peaks of Φ_1 and Φ_2, obviously occurs as a result of a prior rearrangement of $M^{+\bullet}$ — a transfer of a hydrogen atom from an amine group to an endocyclic nitrogen atom [21].



In the mass spectra of 2-amino-*sym*-triazines IVc, g, the intensity of the peaks of ion-radicals Φ_2 with m/z 93 is maximal. Further fragmentation of this ion in the spectra of compounds IVc, g, k occurs via a path typical of 2-furonitrile [22], with formation of ions with m/z 64 (22-44%), 39, and 37 (10-22%). In the spectra of these compounds and of *sym*-triazine IVo, processes are also observed that are due to the concurrent breakup of the furan ring, leading to the formation of fragment ions $[M-HCO]^+$ and $[M-C_3H_3]^+$ [22].

In the mass spectra of *sym*-triazines IVi-l and VIg-i, which contain the (3-indolyl)methyl group, the primary fragmentation of molecular ion M^+ involves, in addition to the above mentioned paths, the rupture of the bond between the aforementioned group and the triazine ring ("benzylic" rupture). As a result, a fragment ion is formed with m/z 130, having a quinoline ion structure [23], the intensity of whose peak is a maximum in the spectra of compounds IVj-i and VIg-i, its further disintegration leads to the appearance of three characteristic ions with m/z 103, 102, and 77.

A feature of the mass spectra of *sym*-triazines IVa, e, i under electron impact is the sequential ejection of three chlorine atoms from $M^{+\bullet}$ which occurs concurrently with the breakup of the *sym*-triazine ring. The peaks of the $[M-Cl_2]^{+\bullet}$ ion-radicals thus formed have the maximum intensity, and the $[M-Cl]^+$ an intensity 24-36% of the maximum. With the destruction of the triazine ring, fragment Φ_1 (52-60%) and Φ_3 (18-25%) are formed, as well as an ion with m/z 108 $[Cl_2CC\equiv N^+]$ (the result of splitting this ring into an $[M-Cl]^{+\bullet}$ ion). Appreciable peaks of ions with m/z 117 $[Cl_3C]^+$ are present in the spectra of these compounds.

The mass spectra of 2-amino-*sym*-triazines IVb, c, d, f, h and 2-amino-4-dimethylamino-*sym*-triazines VIa, d are characterized by the peaks of fragmentation involving the breakup of the triazine ring and formation of intense peaks of fragment ions $\Phi_1-\Phi_4$. Note that the further fragmentation of the Φ_1 ion with m/z 142 (from compounds IVa-d, i-o and VIa-c, where R = H, n = 0) takes place by a path typical of 3-cyanoindoles [22, 23] with formation of splinter ions with m/z 116 $[\Phi_1-CN]^+$, 115$[\Phi_1-HCN]^+$, 90, 89, 88, and 63. Analogous processes are also found in the fragmentation of the Φ_1 ion with m/z 156 (from compounds IVe-h and VId-f, where R = Me, n = 0), which leads to the appearance of several characteristic ions with m/z = 130 $[\Phi_1-CN]^+$, 129$[\Phi_1-HCN]^{+\bullet}$, 115$[\Phi_1$-$CN-CH_3]^+$, 102, 89, and 77.

In the spectra of pyridyl-substituted *sym*-triazines IVd, h, l there are rather intense peaks of splinter ions that arise from the destruction of the Φ_4 ion with m/z 105 by a path typical of cyanopyridines [22], with m/z 78 $[\Phi_4-HCN]^+$, 51 $[\Phi_4$-$HCN-HCN]^+$, 38, and 37.

In the mass spectra of 2-amino-4-dimethylamino-*sym*-triazines VIa, d, g there are peaks present of splinter ions $[M-Me]^+$ and $[M-Me_2N]^+$, the intensities of which are 6-18% that of the maximum. It is of definite interest that there are present in the spectra of these compounds peaks of $[M-29]^+$ ions, from the splitting off of CH_2NH particles, that are characteristics of dimethylamino derivatives of other heteroaromatic systems [24].

In the spectra of furfuryl-substituted *sym*-triazines VIc, f, i, one sees an appreciable elimination of the furyl radical from the molecular ion M^+ leading to the splinter ion $[M-C_4H_3O-HCN]^+$. Note that in contrast to the spectra of *sym*-triazines IVc, g, k, o, the spectra of these compounds do not show any concurrent disintegration of the furan ring.

EXPERIMENTAL

The IR spectra were taken on a Bruker IFS-48 instrument in KBr tables or mineral oil suspension. The PMR spectra were recorded on Bruker WP-100 SY (100 MHz) and Bruker WM-250 (250 MHz) instruments, TMS internal standard. The mass spectra were obtained on a Varian MAT-311 spectrometer, using direct introduction of the sample into the ion source (energy of the ionizing electrons, 70 eV; ion source temperature, 200°C, sample vaporization temperature, 120-140°C). The course of the reactions and the purity of the products obtained were monitored by means of TLC on Al_2O_3 (III degree Brockman activity) in solvent systems of 15:1 CCl_4/methanol (a), 10:1 CCl_4/methanol (b), and 20:1 benzene/methanol (c); developed with iodine vapor.

The elementary analysis for C, H, and N of the compounds synthesized agreed with the calculated values.

The starting ethylimino esters of indole-3-carboxylic (Ia) [25], 1-methylindole-3-carboxylic (Ib) [26], and indolyl-3-acetic (Ic) [25] acids, N-trichloroacetyl- (IIa) [27], N-benzoyl- (IIb) [27], N-(2-furoyl)- (IIc) [28], and N-pyridyl-3-carbonyl)guanidine (IId) [2], the hydrochlorides of N,N-dimethyl- (IIIa) [29], N,N-(3-oxapentamethylene)- (IIIb) [30], and N-furfurylbiguanide (IIIc) [30], as well as N-(indolyl-3-imidoyl)guanidine (V) [2] were prepared by methods given in the papers cited above.

2-Amino-4,6-disubstituted *sym*-Triazines (IVa-*l*). A. A mixture of 15 mmoles of ethylimino ester Ia-c and 15 mmoles of N-acylguanidine IIa-d in 50 ml absolute ethanol is boiled with stirring for 2-3 h. The reaction mass is cooled to 20°C and poured into 200 ml of cold water. The material precipitating is filtered off, washed on the filter with water dried, and crystallized from the appropriate solvent (see Table 1).

2-Amino-4-(3-indolyl)-6-substituted *sym*-Triazines (IVa-d, m-o). B. A mixture of 2.86 g (15 mmoles) of N-imidoylguanidine V and 15 mmoles of the ester of the appropriate acid in 50 ml of absolute ethanol is boiled when stirring for

1.5-2 h. The reaction mixture is cooled to 20°C and poured into 150 ml of cold water. The material precipitating is filtered off, dried, and crystallized from the appropriate solvent (see Table 1).

N-Substituted 2,4-Diamino-*sym*-triazines (VIa-m). C. Twelve mmoles of the hydrochloride of biguanide IIIa-c is added bit by bit with stirring at 0-5°C to a solution of sodium ethoxide, made from 0.27 g (12 mmoles) of sodium in 40 ml of absolute ethanol. The reaction mixture is stirred for 1 h at 20°C, cooled to −5°C, and the NaCl that precipitates is filtered off and washed on the filter with 10 ml of absolute ethanol. Twelve mmoles of ethylimino ester is added to the filtrate which is then boiled with stirring for 4-5 h. The reaction mixture is evaporated to dryness under reduced pressure, and the residue is either crystallized from the appropriate solvent (see Table 1) or (to prepare compounds VId, g, h) chromatographed on a column with Al_2O_3 (4.5 × 85 cm), eluting the mixture with 10:1 chloroform/acetone. After the solvent is removed, *sym*-triazines VId, h are obtained as viscous, dark yellow oils that cannot be crystallized. They are purified by a second chromatographing on Al_2O_3, with a 10:1 benzene/ethanol mixture as eluent.

2-Amino-4-dimethylamino-6-substituted *sym*-Triazines (VIa, d, g). D. Dry dimethylamine is passed into a stirred solution of 10 mmoles of 2-amino-4-trichloromethyl-*sym*-triazine IVa, e, i in 30 ml of anhydrous DMF at 150-155°C for 2 h. The reaction mixture is cooled to 20°C, the solvent removed under reduced pressure, and the residue washed with ether (2 × 15 ml) and crystallized from aqueous ethanol (to prepare *sym*-triazine VIa) or chromatographed on a column with Al_2O_3 (4.5 × 80 cm), with a 10:1 chloroform/acetone mixture as eluant.

2-Amino-4-morpholino-6-(3-indolyl)-*sym*-triazine (VIb). D. A mixture of 2.63 g (8 mmoles) of *sym*-triazine IVa and 4.8 g (56 mmoles) of morpholine in 35 ml of anhydrous dioxane is held for 5 h in 120-130°C in a sealed ampule. After having cooled to 20°C, the contents of the ampule are poured into 150 ml of cold water. The material precipitating is filtered off, washed on the filter with water, dried, and crystallized from aqueous ethanol.

In analogous fashion, 2-amino-4-morpholino-*sym*-triazines VIe, h and 2-amino-4-furfurylamino-*sym*-triazines VIc, f, i are synthesized from *sym*-triazines IVa, e, i and the corresponding substituted amines. Compound VIh separates as a dark oil which is extracted with methylene chloride (3 × 15 ml). The extract is washed with water, dried over Na_2SO_4, and evaporated to dryness. The residue is chromatographed on a column with Al_2O_3 (4.5 × 80 cm), with a 15:1 chloroform/acetone mixture as eluant.

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