SYNTHESIS AND PROPERTIES OF sym-TRIAZINE DERIVATIVES.

6.* SYNTHESIS OF 2-AMINO- AND 2,4-DIAMINO-sym-TRIAZINES CONTAINING STERICALLY HINDERED PHENOL SEGMENTS

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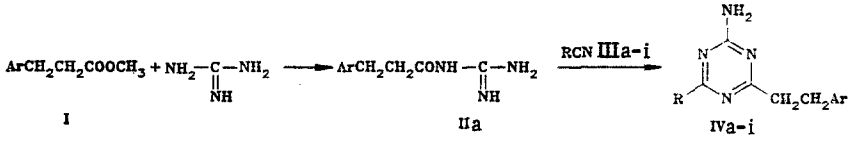
UDC 547.551.43'569.5'491.8.07: 543.422

2-Amino-4,6-disubstituted-sym-triazines containing sterically hindered phenol segments were synthesized by cyclocondensation of N-acrylguanidines with nitriles or thiocyanates. The same compounds can be obtained by condensation of N-acylguanidine with iminoester hydrochlorides. The reaction of methyl β-(4-hydroxy-3,5-di-tert-butylphenyl)propionate with biguanides gives N-substituted 2,4-diamino-6-R-sym-triazines that contain a shielded phenol residue.

In order to obtain antioxidants of increased thermal stability and in continuation of previous work [2, 3] on the synthesis of sym-triazines containing shielded phenol residues, we undertook the synthesis of their 2-amino- and 2,4-diamino derivatives. In the present work the key compound for the synthesis of such sym-triazine derivatives was methyl β-(4-hydroxy-3,5-di-tert-butylphenyl)propionate (I).

For the synthesis of 2-amino-sym-triazines containing sterically hindered phenol segments we chose cyclocondensation of N-acylguanidines with acid nitriles [4]. The initial N-[β-(4-hydroxy-3,5-di-tert-butylphenyl)propionyl]guanidine (IIa) forms in good yield when ester I and guanidine base are heated in alcohol.

The cyclocondensation of N-acylguanidine IIa with various acid nitriles and with thiocyanates forms 2-amino-4-R-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazines (IVa-i, method A).



I IIa IVa-i

Ar = 4-hydroxy-3,5-di-tert-butylphenyl; III, IVa R=CH_3, b R=C_5H_{11}, c R=CCl_3, d R=C_6H_5, e R=$C_6H_5CH_2$, f R=$ArCH_2CH_2$, g R=$ArSCH_2CH_2$, h R=CH_3S, i R=ArS

In each case the duration of the reaction was determined by the nature and reactivity of the nitrile. The reaction of IIa with caproic, benzoic, and phenylacetic nitriles was carried out at 160-170°C for 10-12 h; the nitrile was added in some excess and functioned simultaneously as solvent. When acetonitrile and trichloroacetonitrile are used, the respective 2-amino-sym-triazines IVa, c form in good yield (Table 1) after prolonged boiling (18-20 h) of initial IIa in excess nitrile. Compound IIa underwent cyclocondensation with nitriles IVf, g by boiling equimolar amounts of the reagents in DMFA for 12-15 h.

The reaction of compound IIa with thiocyanates IIIh, i forms the thio derivatives of 2-amino-sym-triazine IVh, i in high yield. In this case the reaction goes under milder conditions – the reagents, in 1:1 molar ratio, are boiled in alcohol for 5-6 h.

The 2-amino-sym-triazines IVc, d were also synthesized by an alternative method, viz., cyclocondensation of β-(4-hydroxy-3,5-di-tert-butylphenyl)propionitrile (IIIf) with the respective N-acylguanidines IIb, c (method B). However, in this case the yield of IVc, d did not exceed 45-50%.

*For Communication 5, see [1].

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1392-1397, October, 1987. Original article submitted June 25, 1986.

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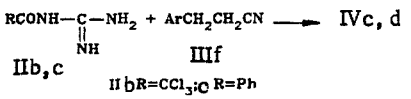
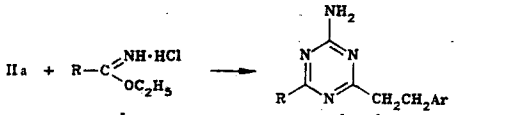


IIb, c IIIf IVc, d

IIb R=CCl_3; c R=Ph

It is known [5] that 2-amino-4,6-disubstituted-sym-triazines with two identical ring substituents are usually obtained by cyclocondensation of nitriles with guanidine. However, the reaction of nitrile IIIf with guanidine (at 2:1 molar ratio) is accompanied by significant resinification of the reaction mixture, from which 2-amino-sym-triazine IVf could be isolated in only 35% yield,

In the reaction with N-acylguanidines it was promising to use, instead of nitriles, their more reactive derivatives, the iminoester hydrochlorides Va-d (method C). In this case the respective 2-amino-sym-triazines (IVa, d, e, j) form in high yield (88-92%) when equimolar amounts of the reagents are boiled in alcohol for a short time (2-3 h).

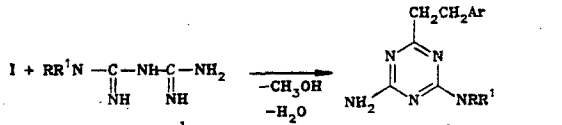


va-d IVa,d,e,j

IVa Va R=CH_3; IVd Vb R=C_6H_5; IVe Vc R=$C_6H_5CH_2$; IVj, Vd R=Ar

It should be noted that compound IVj could not be synthesized from 4-hydroxy-3,5-di-tert-butylbenzonitrile, which has low reactivity [6]. After prolonged (96 h) boiling of the reagents in DMFA we isolated the starting nitrile in almost quantitative yield.

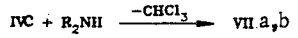
It is known [7, 8] that the reaction of esters with biguanides forms 2,4-diamino-6-R-sym-triazines (guanamines). In the present work we studied the use of the reaction of ester I with N-substituted biguanides (VIa-d) to synthesize 2,4-diamino-sym-triazines containing sterically hindered phenol segments.



VIa-d VIIa-d

VI, VIIa R=R'=CH_3; b R=R'=C_2H_5; c R=CH_3, R'=$C_{18}H_{37}$; d R=H, R'=C_6H_5

We find that the N-substituted 2,4-diamino-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)-ethyl]-sym-triazines (VIIa-d) are formed in 75-82% yield after prolonged boiling (14-18 h) of equimolar amounts of the reagents in alcohol in the presence of sodium ethylate (method D). Compounds VIIa, b were also obtained by countersynthesis, by replacing the Cl_3C group in the respective 2-amino-sym-triazine IVc (method E). It is known [9] that a trichloromethyl group attached to a sym-triazine ring can be split off by reaction with a nucleophilic reagent as an anion that adds a proton to form chloroform. The Cl_3C in compound IVc can be replaced by dimethylamino or diethylamino by heating with excess amine in nonaqueous medium.



VIIa R=CH_3; VIIb R=C_2H_5

The composition and structure of the synthesized amino- and diamino-sym-triazines (IVa-j, VIIa-d) are in good agreement with elemental composition and IR and PMR spectral data.

The IR spectra of these sym-triazines show the characteristic absorption band in the 3650-3645 cm^{-1} region that corresponds to the shielded phenolic hydroxyl [10]. In the 1265-1210 cm^{-1} range there are two bands characteristic of Ar—O—H bond vibrations, and in the 885-880 and 825-815 range those of the 4-substituted benzene ring [11]. There are also absorption maxima of various intensities in the 1570-1560, 1412-1405, 1115-1100, 1010-995, 812-805, and 710-705 regions that belong to valence, extraplanar, and planar deformation vibrations of the sym-triazine ring [12-14]. In the region of NH valence vibrations the spectra of amino- and diamino-sym-triazines show two broad bands; one is in the 3460-3335 cm^{-1} region (ν_{as} NH), the other in the 3185-3150 cm^{-1} range (ν_s NH). The location and shape of the NH valence vibration doublet is evidence that a strong hydrogen bond is present in these compounds in the crystalline state [12, 15]. The intense maxima in the 1675-1665 cm^{-1}

TABLE 1. Properties of Synthesized Compounds

Compound	T_{mp}, °C	Rf (solvent system)	Found, %			Empirical formula	Calculated, %			Yield, % (method of synthesis)
			C	H	N		C	H	N	
IVa	110—112	0,71 (A)	70,1	8,9	16,2	$C_{20}H_{30}N_4O$	70,2	8,8	16,4	76 (A), 92 (C),
IVb	198—200	0,62 (B)	72,2	9,6	13,9	$C_{24}H_{38}N_4O$	72,4	9,5	14,1	71 (A),
IVc	278—280**	0,68 (A)	54,0	6,0	12,4	$C_{20}H_{27}Cl_3N_4O$	53,9	6,1	12,6	67 (A), 45 (B),
IVd	180—182	0,54 (B)	74,2	8,0	14,1	$C_{25}H_{32}N_4O$	74,3	7,9	13,9	75 (A), 50 (B) 90 (C)
IVe	178—179	0,26 (C)	74,7	8,1	13,3	$C_{26}H_{34}N_4O$	74,6	8,1	13,4	82 (A), 91 (C)
IVf	250—251,5	0,74 (B)	74,9	9,2	10,2	$C_{35}H_{52}N_4O_2$	75,0	9,3	10,0	68 (A)
IVg	Oil ***	0,38 (C)	71,0	8,7	9,7	$C_{35}H_{52}N_4O_2S$	70,9	8,8	9,5	62 (A)
IVh	195—197**	0,66 (A)	64,1	7,9	15,1	$C_{20}H_{30}N_4OS$	64,2	8,0	15,0	87 (A)
IVi	88—90***	0,43 (B)	70,1	8,4	10,1	$C_{33}H_{48}N_4O_2S$	70,2	8,5	9,9	85 (A)
IVj	350	0,39 (B)	74,5	8,9	10,3	$C_{33}H_{48}N_4O_2$	74,4	9,0	10,5	88 (C)
VIIa	160—161,5	0,83 (A)	67,8	9,0	18,7	$C_{21}H_{33}N_5O$	67,9	8,9	18,9	82 (D), 75 (E)
VIIb	145—147	0,74 (A)	69,3	9,2	17,6	$C_{23}H_{37}N_5O$	69,2	9,3	17,5	76 (D), 85 (E)
VIIc	Oil ***	0,52 (C)	—	—	11,7	$C_{38}H_{67}N_5O$	—	—	11,5	75 (D)
VIId	234—235	0,35 (B)	71,5	8,0	16,6	$C_{25}H_{33}N_5O$	71,6	7,9	16,7	78 (D)

*Compounds IVa and VIIa were recrystallized from 3:1 hexane—alcohol; IVb, f, VIIb, from aqueous alcohol; IVd from aqueous DMFA; IVe from 4:1 hexane—acetone; IVj from aqueous ethylene glycol; VIId from n-butyl alcohol.

**Purified by reprecipitation by dry ether from absolute alcohol.

***Purified by chromatography on Al_2O_3 column. IVg picrate, mp 305-306°C (from alcohol, with dec.). VIIc picrate, mp 54-55°C (from aqueous acetone). Found, %: C 63.1; H 8.2; N 13.2. $C_{38}H_{67}N_5O \cdot C_6H_3N_3O_7$. Calculated, %: C 63.0; H 8.3; N 13.4.

region belong to the scissors vibrations of NH bonds in primary amines, which are typical of amino derivatives of sym-triazine [15]. Corresponding to C—N valence vibrations are a series of medium-intensity bands in the 1380-1000 cm^{-1} region. The absorption maxima in the 1380-1345 cm^{-1} range in the spectra of all our sym-triazines should, according to [16], be assigned to N—ring bond valence vibrations, while the frequencies at 1240-1230, 1185-1175, 1135-1130, and 1060-1050 cm^{-1} in the spectra of compounds VIIa-d belong to the N—alkyl(phenyl) bond vibrations.

The PMR spectra of the amino- and diamino-sym-triazines (IVa-j, VIIa-d) also confirm the proposed structure. The hydroxyl proton signals appear as singlets in the 4.80-5.12 ppm region, which is typical of sterically hindered phenols [10]. The tert-butyl radical proton signals appear as broadened singlets in the 1.64-1.80 ppm range. The aromatic protons of the hydroxyaryl segments are represented by singlet signals at 7.12-7.35 ppm [17]. The complex multiplets in the 4.35-4.70 ppm ranging by their intensity into four proton units should be assigned to the protons of the ethylene radical. All the amino proton signals are present as broadened singlets in the 6.84-7.05 ppm range.

EXPERIMENTAL

IR spectra were obtained with a UR-20 instrument in KBr tablets or in mineral oil suspension. PMR spectra were obtained with a Tesla BS-487C spectrometer (80 MHz) in CCl_4 or in DMSO-D_6 with HMDS as internal standard. Composition of reaction mixtures and purity of compounds obtained was monitored by TLC on Al_2O_3 standard activity II, in 10:1 benzene—alcohol (A); 20:1 benzene—alcohol (B); and 20:1 hexane—alcohol (C); development with iodine vapor. The properties of the synthesized compounds are shown in Table 1.

N-Trichloroacetyl- and N-benzoylguanidine (IIb, c) were obtained by the method of [18]; ethyl iminoester hydrochloride of 4-hydroxy-3,5-di-tert-butylbenzoic acid (Vd) was synthesized according to [6].

N-[β-4-Hydroxy-3,5-di-tert-butylphenyl)propionyl]guanidine (IIa). To a stirred solution of sodium ethylate, prepared from 0.71 g (0.031 mole) of sodium in 100 ml of absolute alcohol, was added 2.94 g (0.031 mole) of guanidine hydrochloride portionwise. The reaction mixture was boiled for 1 h 30 min and then cooled to 0°C, and the precipitate of NaCl was filtered off. To the stirred filtrate was added 9.0 g (0.031 mole) of ester I, the mixture was boiled 10 h, and the solvent was distilled off in vacuum. The residue was washed with hexane (3 × 30 ml) and chromatographed on an Al_2O_3 column (h = 90, d = 3.5 cm). Elution with benzene removed a small amount of initial ester I from the column, R_f 0.84 (benzene); then elution with 5:1 benzene–acetone removed N-acylguanidine IIa. Yield 8.7 g (88%), mp 190-191.5°C, R_f 0.21 (system A). IR spectrum: 3650 (ν_{OH}), 3380-3290 (ν_{NH}), 2960, 2920, 2865 (ν_{C-H}), 1695 ($\nu_{C=O}$), 1675 (ν_{NH}), 1640 ($\nu_{C=N}$), 1560 (ν_{NH}), 1295, 1200, 1170 (ν_{C-N}), 930, 880, 740 cm^{-1}. Found, %: C 67.9; H 9.0; N 13.3. $C_{18}H_{29}N_3O_2$. Calculated, %: C 67.7; H 9.1; N 13.2.

2-Amino-4-trichloromethyl-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (IVc). A. A mixture of 5.0 g (0.016 mole) of compound IIa and 28.9 g (0.2 mole) of IIIc was boiled with stirring for 18-20 h until the starting IIa had disappeared from the reaction mixture (monitored by TLC). The mixture was evaporated in vacuum. The residue was washed with hot hexane (3 × 15 ml), chromatographed on an Al_2O_3 column (h = 50, d = 3.5 cm), and eluted with 5:1 benzene–methanol. PMR spectrum of compound IVa (1:1 CCl_4–DMSO-D_6): 1.66 (18H, s, tert-C_4H_9); 4.50-4.58 (4H, m, $-CH_2-CH_2-$); 5.05 (1H, s, OH); 7.05 (2H, br, NH_2); 7.24 ppm (2H, s, arom.). Compound IVa was synthesized analogously from IIa and nitrile IIIa. PMR spectrum (1:2 CCl_4–DMSO-D_6): 1.70 (18H, s, tert-C_4H_9); 2.38 (3H, s, CH_3); 4.58-4.64 (4H, m, CH_2-CH_2); 4.88 (1H, s, OH); 6.92 (2H, br, NH_2); 7.18 ppm (2H, s, arom.).

B. A mixture of 3.27 g (0.015 mole) of IIb and 3.88 (0.015 mole) of IIIf was heated for 12 h at 170-175°C, cooled, and washed with hot benzene (3 × 15 ml). The residue was chromatographed on an Al_2O_3 column (h = 40, d = 3.5 cm), and eluted with 5:1 benzene–methanol. Analogously compound IVd was synthesized from N-acylguanidine IIc and nitrile IIIf. PMR spectrum of IVd (DMSO-D_6): 1.74 (18H, s, tert-C_4H_9); 4.40-4.48 (4H, m, $-CH_2-CH_2-$); 4.94 (1H, s, OH); 6.86 (2H, br, NH_2); 7.30-7.55 ppm (7H, m, arom.).

2-Amino-4-methyl-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (IVa). C. A mixture of 3.83 g (0.012 mole) of compound IIa and 1.48 g (0.012 mole) of iminoester hydrochloride Va in 20 ml of absolute alcohol was boiled with stirring for 2 h. The reaction mixture was concentrated to 6-8 ml, chromatographed on an Al_2O_3 column (h = 50, d = 3.5 cm), and eluted with 10:1 hexane–alcohol. Compounds IVd, e were synthesized analogously from IIa and iminoester hydrochlorides Vb, c.

2-Amino-4-pentyl-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (IVb). A. A mixture of 5.0 g (0.016 mole) of IIa and 15.5 g (0.16 mole) of IIIb was stirred for 10-12 h at 160-165°C until the starting IIa had disappeared from the reaction mixture (monitored by TLC). The reaction mixture was evaporated in vacuum, and the residue was washed with benzene (3 × 20 ml), and crystallized from an appropriate solvent with activated charcoal. Compounds IVd, e were synthesized analogously from IIa and nitriles IIId, e.

2-Amino-4,6-bis[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (IVf). A. A mixture of 3.2 g (0.01 mole) of IIa and 2.59 g (0.01 mole) of IIIf in 25 ml of DMFA was boiled with stirring for 15 h. The reaction mixture was cooled to 20°C and poured into 200 ml of cold water. The precipitate was filtered off, washed with cold acetone, and crystallized from an appropriate solvent. PMR spectrum (2:1 CCl_4–DMSO-D_6): 1.76 (36H, s, tert-C_4H_9); 4.35-4.45 (8H, m, CH_2-CH_2); 5.12 (2H, s, OH); 7.04 (2H, br, NH_2); 7.36 ppm (4H, s, arom.). Compound IVg was synthesized analogously from IIa and nitrile IIIg.

2-Amino-4-methylthio-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (IVh). A. A mixture of 3.2 g (0.01 mole) of IIa and 0.73 g (0.01 mole) of IIIh in 15 ml of alcohol ws boiled with stirring for 5 h. The reaction mixture was evaporated in vacuum. The residue was chromatographed on an Al_2O_3 column (h = 40, d = 3.5 cm) and eluted with 10:1 benzene–methanol. PMR spectrum (CCl_4): 1.78 (18H, s, tert-C_4H_9); 3.89 (3H, s, CH_3); 4.65-4.70 (4H, m, CH_2-CH_2); 4.98 (1H, s, OH); 6.95 (2H, s, NH_2); 7.22 ppm (2H, s, arom.). Compound IVi was synthesized analogously from IIa and thiocyanate IIIi.

2-Amino-4-(4-hydroxy-3,5-di-tert-butylphenyl)-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)-ethyl]-sym-triazine (IVj). C. A mixture of 3.19 g (0.01 mole) of IIa and 3.1 g (0.01 mole) of Vd in 30 ml of absolute alcohol was boiled with stirring for 3 h. The reaction mixture

was cooled to 20°C and poured into 150 ml of cold water. The precipitate was filtered off, washed with water and dried. PMR spectrum (DMSO-D_6): 1.72-1.76 (36H, br. s, tert-C_4H_9); 4.58-4.62 (4H, m, CH_2–CH_2); 4.92 (1H, s, OH); 5.08 (1H, s, OH); 7.08 (2H, br, NH_2); 7.24 (2H, s, arom.); 7.32 ppm (2H, s, arom.).

N-Substituted 2,4-Diamino-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazines (VIIa-d). D. To a stirred solution of sodium ethylate prepared from 1.20 g (0.055 mole) of sodium in 100 ml of absolute alcohol was added 0.05 mole of biguanide hydrochloride VIa-d at 0°C portion wise. The reaction mixture was stirred for 1 h, and the NaCl precipitate was filtered off. To the filtrate was added a solution of 14.6 g (0.05 mole) of compound I in 50 ml of absolute alcohol dropwise with stirring. The reaction mixture was boiled with stirring for 14-18 h, until the starting I disappeared (monitored by TLC), and evaporated in vacuum. The residue was washed with hot hexane (3 × 20 ml) and crystallized from an appropriate solvent. (In the synthesis of compound VIIc the residue was chromatographed on an Al_2O_3 column and eluted with 10:1 hexane–alcohol). PMR spectrum of VIIa (DMSO-D_6): 1.70 (18H, s, tert-C_4H_9); 3.08 (6H, d, CH_3); 4.35-4.40 (4H, m, CH_2–CH_2); 4.80 (1H, s, OH); 6.96 (2H, br, NH_2); 7.32 ppm (2H, s, arom.). PMR spectrum of VIIb (DMSO-D_6): 1.42 (6H, t, $CH_2\underline{CH_3}$); 1.68 (18H, s, tert-C_4H_9); 3.34 (4H, q, $\underline{CH_2}$–CH_3); 4.32-4.45 (4H, m, CH_2–CH_2); 4.88 (1H, s, OH); 6.98 (2H, br, NH_2); 7.26 ppm (2H, s, arom.).

2-Amino-4-dimethylamino-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (VIIa). E. Into a stirred solution of 4.45 g (0.01 mole) of compound IVc in 35 ml of dry DMFA was passed a stream of dry dimethylamine at 150°C for 2 h. The reaction mixture was cooled to 20°C and poured into 200 ml of cold water. The precipitate was filtered off, washed with water, and dried.

2-Amino-4-diethylamino-6-[β-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-sym-triazine (VIIb). E. A solution of 2.23 g (0.005 mole) of compound IVc and 3.65 g (0.05 mole) of diethylamine in 20 ml of dry dioxane was heated in a sealed ampul for 5 h at 135-140°C. The ampul was cooled to 20°C and the contents were poured into 150 ml of cold water, and the dark oil that separated was extracted with ether (3 × 40 ml). The extract was washed with water, dried over $CuSO_4$, and evaporated. The residue was chromatographed on an Al_2O_3 column (h = 45, d = 3.5 cm), and eluted with 20:1 benzene–methanol. After removal of solvent, sym-triazine VIIb was obtained as a viscous dark brown oil that crystallized after holding in the cold for 24 h.

LITERATURE CITED

1. V. I. Kelarev, M. Bellul', R. A. Karakhanov, Dibi Ammar, and A. F. Lunin, Khim. Geterotsikl. Soedin., No. 3, 356 (1987).
2. O. V. Malova, V. I. Kelarev, I. A. Golubeva, T. P. Vishnyakova, and A. F. Lunin, Zh. Vses. Khim. O., 29, No. 4, 462 (1984).
3. O. V. Malova, T. P. Vishnyakova, I. A. Golubeva, V. I. Kelarev, and A. F. Lunin, Khim. Geterotsikl. Soedin., No. 12, 1678 (1984).
4. P. B. Russell, G. H. Hitchings, B. H. Chase, and J. Walker, J. Am. Chem. Soc., 74, 5403 (1952).
5. H. Kabbe, K. Eiter, and E. Möller, Annalen, 704, 140 (1963).
6. V. I. Kelarev, S. G. Shvekhgeimer, V. N. Koshelev, A. F. Lunin, and G. A. Shvekhgeimer, Zh. Vses. Khim. O., No. 5, 582 (1982).
7. S. L. Shapiro, V. A. Parrino, K. Geiger, S. Kobrin, and L. Freedman, J. Am. Chem. Soc., 79, 5064 (1957).
8. E. M. Smolin and L. Rapoport, S-Triazine and Derivatives, Interscience, New York, London (1959), p. 224.
9. A. Kreutzberger, Adv. Chem. Soc., 34, 208 (1962).
10. V. V. Ershov, G. A. Nikiforov, and A. A. Volod'kin, Sterically Hindered Phenols [in Russian], Khimiya, Moscow (1972).
11. M. Avram and G. Hatteescu [sic], Infrared Spectroscopy, Wiley Interscience (1970), p. 527.
12. A. I. Finkel'shtein and E. N. Boitsov, Usp. Khim., 31, 1496 (1982).
13. A. R. Katritzky (ed.), Physical Methods in the Chemistry of Heterocyclic Compounds, Academic Press, New York (1963).
14. V. I. Kelarev, Dibi Ammar, A. F. Lunin, R. L. Ushakova, A. I. Mikaya, N. V. Petrova, and S. G. Shvekhgeimer, Zh. Org. Khim., 19, 2401 (1983).

15. A. I. Finkel'shtein, Opt. Spektrosk., 5, 264 (1958).
16. A. R. Katritzky and R. A. Jones, J. Chem. Soc., 3674 (1959).
17. T. N. Pliev, Zh. Prikl. Spektrosk., 13, 124 (1970).
18. W. Traube, Berichte, 43, 3580 (1910).

PURINES, PYRIMIDINES, AND CONDENSED SYSTEMS BASED ON THEM.

3.* 7,8-DIAMINOTHEOPHYLLINE

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UDC 547.857.4.04'873.542.951.1'958.3

By treating 8-aminotheophylline with hydroxylamine-O-sulfonic acid in aqueous alkali we have obtained 7,8-diaminotheophylline and studied its reactions with benzaldehyde, 1,2-dicarbonyl compounds, and acylating agents. We have established that in reactions with electrophiles, the N-amino group in 7,8-diaminotheophylline is more active than the amino group situated at the 8-position. An unexpected self-condensation of two molecules of 7,8-diaminotheophylline has been found in acid medium, leading to a purino[8,7-g]-7-azapteridine derivative.

In contrast to 8-aminotheophylline [2] there were no reports about 7-aminotheophyllines until recently. Only in 1981-83 was 7-aminotheophylline obtained by amination of theophylline with hydroxylamine-O-sulfonic acid [3, 4] or diphenylphosphinylhydroxylamine [5]. We set out to achieve the amination of 8-aminotheophylline in a similar manner and investigate the properties of the corresponding diamine, in particular, the possibility of building on condensed heterocycles to theophylline via the two amino groups.

When 8-aminotheophylline was treated with hydroxylamine-O-sulfonic acid in alkaline medium we obtained a diamine in 74% yield, to which we assigned the structure of 7,8-diaminotheophylline (I) by analogy with the results of [3-5]. The other possible isomer, 8,9-diaminotheophylline, was not detected in the reaction mixture, which is due no doubt to shielding of the $N_{(9)}$ by the methyl group at the 3-position.

Diamine I readily reacts with aromatic aldehydes such as benzaldehyde to give hydrazone II. It is confirmed that the reaction occurs on the N-amino group by the fact that 7-aminotheophylline undergoes a similar reaction while 8-aminotheophylline does not react with benzaldehyde under the same conditions. Even when diamine I is boiled with a large excess of benzaldehyde in acetic acid medium only the 7-amino group reacts. Our experiments carried out to cyclize hydrazone II to the corresponding triazoloxanthine III by heating it with oxidizing agents such as MnO_2 or nitrobenzene did not meet with success (a similar reaction in a series of ortho-arylenediamine monoanils occurs readily [6]). We found that in the reaction of 7,8-diaminotheophylline with glyoxal and 1,2-diketones (diacetyl, benzil, 4,5-acenaphthenequinone, and 9,10-phenanthrenequinone) both amino groups take part, with the result that the previously unknown triazino[3,2-f]xanthine derivatives IVa-e are formed. In addition to the data from elemental analysis and PMR spectra, the absence of an absorption band above 3100 cm^{-1} in the IR spectrum of the reaction products IVa-e is an indication of their structure. The yield of compounds IVa-e varies from 43 to 90%, while in the case of 1,2-diketones an acid catalyst is required to speed up the reaction. When irradiated with UV light compound IVc displays a bright yellow luminescence in its crystals, whereas in solution its luminescence is relatively weak. In the reaction of diamine I with glyoxal there is a by-product formed which is a bright yellow, high-melting, and difficultly soluble compound, to which was assigned the structure of azine V on the basis of the data from elemental analysis and IR spectroscopy.

*For Communication 2, see [1].

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0009-3122/87/2310-1123 $12.50