Synthesis of 4-amino-6-chloro-1,3,5-triazin-2(1*H*)-ones

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Conditions for selective substitution for one chlorine atom in 2-(R,R´-amino)-4,6-dichloro-1,3,5-triazines with a hydroxide ion were elaborated. Spectral and calculation methods showed that the products formed are in the lactam form, *i.e.*, have the structure of 4-chloro-6-(R,R´-amino)-1,3,5-triazin-2(1*H*)-ones.

Key words: 1,3,5-triazines, 1,3,5-triazinones, lactim-lactam tautomerism, nucleophilic substitution, hydrolysis, quantum chemical calculations.

1,3,5-Triazine derivatives are widely used as herbicides,[1—3] polymeric materials,[4—7] pharmaceuticals,[8—10] explosives,[11—15] dyes,[16,17] *etc*. A number of published reviews[18—25] summarize various aspects of chemistry and application of this very important class of heterocycles. Among them, chloro-1,3,5-triazine derivatives are studied the most, since they are widely used as intermediates in the synthesis of more complex molecules.[22—24]

However, among a vast amount of publications on 1,3,5-triazines we found no works purposefully devoted to the studies of preparation and structure of 2-amino-4-chloro-1,3,5-triazinones. Only several publications describe selected examples of this type of compounds,[10,17,26—30] whereas information on their structure is virtually absent. It should be noted that aminochloro-1,3,5-triazinones are one of possible metabolites in decomposition of the triazine herbicides,[2] that makes studies on their chemistry and structure very relevant.

The presence of a hydroxyl functional group on the 1,3,5-triazine ring suggests a possibility of the lactim-lactam tautomerism. For example, in the solid state such derivatives are known to normally exist as 1,3,5-triazinones, *i.e.*, in the lactam form (cyanuric acid, ammeline, ammelide, *etc*.).[18—24] At the same time, the calculations[31] in the gas phase for ammeline (4,6-diamino-1,3,5-triazin-2(1*H*)-one) showed that the lactim form (*i.e*. 4,6-diamino-2-hydroxy-1,3,5-triazine) is energetically more favorable. By now, 2-hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine bound to the complex with a 1,4-dioxane molecule is the only experimentally confirmed (X-ray diffraction data) hydroxy-1,3,5-triazine.[25,32]

2-Hydroxy derivatives of 4-(R^1R^2-amino)-6-chloro-1,3,5-triazines can exist in several tautomeric forms (Scheme 1) differing in placement of the hydrogen atom, *viz.*, a lactim (**A**), three lactam (**B**—**D**), and three zwitterionic structures (**E**—**G**).

The present work describes synthesis of a number of secondary and tertiary (chloro-1,3,5-triazine)amines containing a hydroxy(oxo) group as the third substituent on the triazine ring, their structure was studied by spectroscopic methods, as well as calculations performed enable evaluation of the most probable placement of the proton in the chain of tautomeric transformations given in Scheme 1.

Results and Discussion

Substitution for the chlorine atoms in 2,4,6-trichloro-1,3,5-triazine (**1**, cyanuric chloride) upon the action of amines proceeds stepwise. In this case, an important role in how many chlorine atoms undergo the nucleophilic attack is played by the reaction temperature, amine basicity, steric factors, and the type of solvent used.[18—20,33—37] The first chlorine atom is usually replaced at temperatures below 0 °C, the second at 10—50 °C, the third at 90—100 °C.[19,20] However, in the case when strongly basic amines are used, substitution for two chlorine atoms in cyanuric chloride **1** can take place already at 0 °C.[33—37] Acetone, dioxane, DMSO, as well as their aqueous solu-

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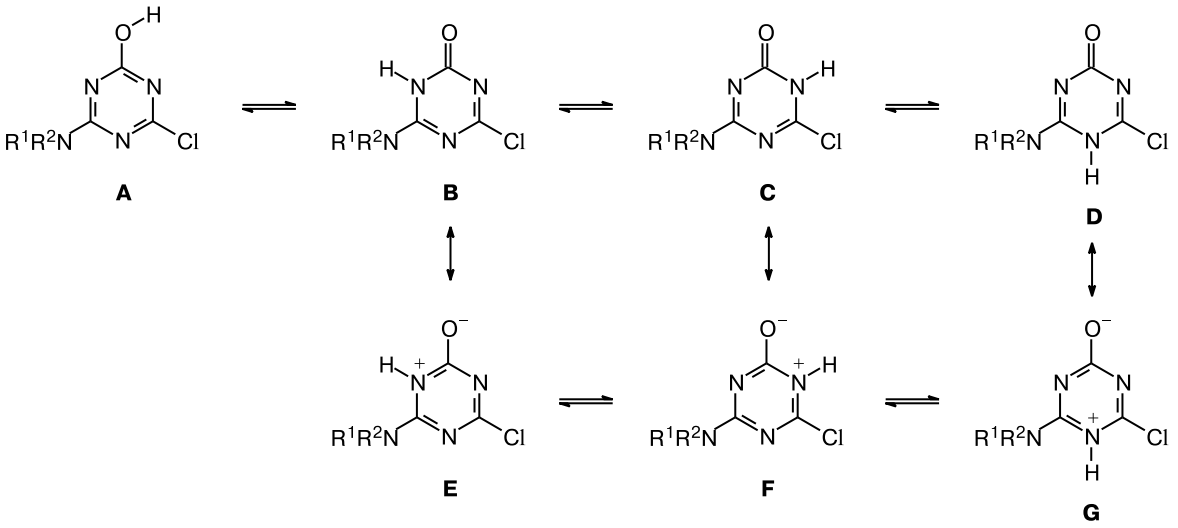
Scheme 1



tions, are usually used as solvents; benzene, diethyl ether, and some other solvents are used seldom. Excess amine or various bases (tertiary amines, sodium (potassium) carbonate or bicarbonate) are used as acceptors of hydrogen chloride formed in the reaction.[18—20,33—37]

In the present work, 2-amino-4,6-dichloro-1,3,5-triazines **2a**—**k** were synthesized from cyanuric chloride **1** in diethyl ether (Scheme 2). Use of 2—2.2 mol of amine per 1 mol of cyanuric chloride **1** and conducting the reaction at temperatures below −10 °C enabled us not only to selectively substitute for one chlorine atom, but also to increase the yields of dichloro derivatives **2a**—**k** by 10—20% as compared to those obtain earlier. The products isolated were of such a good quality (according to the TLC data and melting points, Table 1), that they did not require additional purification and could be used in subsequent reactions.

Hydrolysis of cyanuric chloride, mono- and disubstituted chloro-1,3,5-triazines is very important reaction. In some cases it is useful (for example, in deactivation of triazine herbicides), and in a number of cases it is undesirable, since leads to the side products, for example, in the synthesis of 1,3,5-triazine derivatives in aqueous solvents or even in the presence of atmospheric moisture. Hydrolysis of cyanuric chloride was studied the most thoroughly in the works,[44—46] the authors even succeeded in obtaining sodium salts of 4,6-dichloro-2-hydroxy-1,3,5-triazine and 4-chloro-2-hydroxy-1,3,5-triazin-6-one, however, failed in isolation of the hydroxy(oxo) derivatives themselves. It should be noted that hydrolysis of chloro-1,3,5-triazines is facilitated by both bases and acids. It is known that the reaction of cyanuric chloride and monosubstituted dichloro-1,3,5-triazines with water in the presence of acids proceeds nonselectively and results in the formation of cyanuric acid or monosubstituted 1,3,5-triazinediones, respectively.[19,20,46] There is the only example of selective hydrolysis of one chlorine atom in 2-anilino-4,6-dichloro-1,3,5-triazine in the presence of acetic acid.[47]

At the same time, diamino(dialkoxy)-substituted chloro-1,3,5-triazines are more resistant to hydrolysis. Thus, 2,4-diamino-6-chloro-1,3,5-triazine can be recrystallized from boiling water without noticeable decomposition.[19] Hydrolysis in the presence of bases is effected stepwise, however this stepwise character is less pronounced than in substitution with amines. In this case, depending on the base used, its amount, and temperature, hydrolysis proceeds in different ways. It is known[19] that action of 10% aqueous sodium hydroxide on cyanuric chloride **1** results

Scheme 2

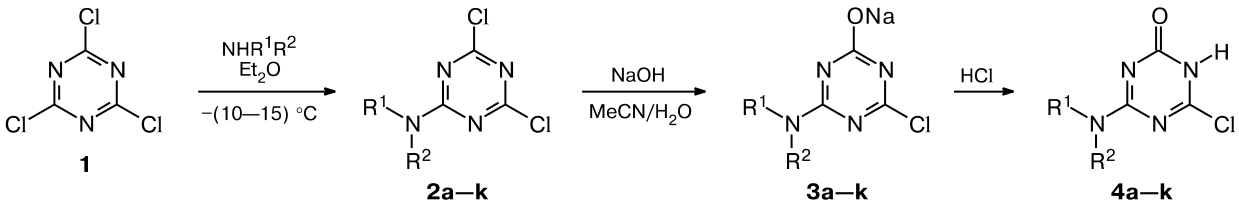
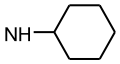
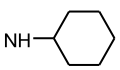


Table 1. Yields and physicochemical characteristics of compounds **2a—k**, **4a—k**, and **13a—i**

Compound	NR^1R^2	Yield (%)	M.p.*/°C	R_f (eluent)**	Molecular formula	Found / Calculated (%)			Molecular weight
						C	H	N	
2a	NH_2	79	240 (with decomp.) (235—236)[38]	0.22 (DCE)	$C_3H_2Cl_2N_4$	21.79 / 21.84	1.18 / 1.22	34.03 / 33.96	164.98
2b	NMe_2	85	121—122 (123—124)[28]	0.55 (DCE)	$C_5H_6Cl_2N_4$	31.20 / 31.11	3.20 / 3.13	29.05 / 29.02	193.04
2c	NHPr	90	67—69 (70—71)[39]	0.61 (DCE)	$C_6H_8Cl_2N_4$	34.72 / 34.80	3.95 / 3.89	27.12 / 27.06	
2d	$NHPr^i$	80	38—40 (37—40)[39]	0.53 (DCE)	$C_6H_8Cl_2N_4$	34.85 / 34.80	3.96 / 3.89	27.00 / 27.06	207.06
2e		81	Colorless oil (oil)[36]	0.52 (DCE)	$C_9H_{12}Cl_2N_4$	43.68 / 43.74	4.96 / 4.89	22.74 / 22.67	247.13
2f	PhNH	87	132—134 (134—135)[40]	0.47 (DCE)	$C_9H_6Cl_2N_4$	44.91 / 44.84	2.58 / 2.51	23.15 / 23.24	241.08
2g	$4\text{-}MeC_6H_4NH$	94	127—129 (129—131)[40]	0.51 (DCE)	$C_{10}H_8Cl_2N_4$	47.02 / 47.08	3.24 / 3.16	21.98 / 21.96	255.11
2h		77	93—95	0.64 (DCE)	$C_7H_8Cl_2N_4$	38.43 / 38.38	3.77 / 3.68	25.59 / 25.57	219.07
2i		87	72—74 (72—74)[41]	0.59 (DCE)	$C_8H_{10}Cl_2N_4$	41.16 / 41.22	4.34 / 4.32	23.96 / 24.04	233.10
2j		88	152—153 (154—156)[42]	0.46 (DCE)	$C_7H_8Cl_2N_4O$	35.72 / 35.77	3.49 / 3.43	23.81 / 23.83	235.07
2k	AdNH	65	135—137 (136—137)[43]	0.52 (DCE)	$C_{13}H_{16}Cl_2N_4$	52.21 / 52.19	5.47 / 5.39	18.80 / 18.73	299.21
4a	NH_2	82	>350	0.21 (DCE—MeOH (2 : 1))	$C_3H_3ClN_4O$	24.50 / 24.59	2.13 / 2.06	38.14 / 38.23	146.54
4b	NMe_2	66	196—198 (with decomp.) (198)[28]	0.50 (DCE—MeOH (2 : 1))	$C_5H_7ClN_4O$	34.48 / 34.40	4.10 / 4.04	32.01 / 32.09	174.59
4c	NHPr	87	181—182	0.37 (DCE—MeOH (4 : 1))	$C_6H_9ClN_4O$	38.16 / 38.21	4.94 / 4.81	29.62 / 29.70	188.62
4d	$NHPr^i$	61	169—170	0.44 (DCE—MeOH (4 : 1))	$C_6H_9ClN_4O$	38.29 / 38.21	4.78 / 4.81	29.77 / 29.70	188.62
4e		77	270—273 (with decomp.)	0.38 (DCE—MeOH (4 : 1))	$C_9H_{13}ClN_4O$	47.22 / 47.27	5.63 / 5.73	24.52 / 24.50	228.68
4f	PhNH	93	292—293 (with decomp.)	0.53 (DCE—MeOH (2 : 1))	$C_9H_7ClN_4O$	48.65 / 48.55	3.11 / 3.17	25.24 / 25.17	222.64
4g	$4\text{-}MeC_6H_4NH$	90	>350	0.54 (DCE—MeOH (2 : 1))	$C_{10}H_9ClN_4O$	50.72 / 50.75	3.83 / 3.75	23.76 / 23.67	236.66
4h		56	245—246 (with decomp.)	0.62 (DCE—MeOH (2 : 1))	$C_7H_9ClN_4O$	41.88 / 41.91	4.45 / 4.52	28.01 / 27.93	200.63

(*to be continued*)

Table 1 (*continued*)

Compound	NR^1R^2	Yield (%)	M.p.*/°C	R_f (eluent)**	Molecular formula	Found / Calculated (%)			Molecular weight
						C	H	N	
4i		65	170—172 (with decomp.)	0.57 (DCE—MeOH (2 : 1))	$C_8H_{11}ClN_4O$	44.66 / 44.76	5.23 / 5.17	26.03 / 26.10	214.66
4j		68	265—267 (with decomp.)	0.26 (DCE—MeOH (4 : 1))	$C_7H_9ClN_4O_2$	38.73 / 38.81	4.14 / 4.19	25.89 / 25.86	216.63
4k	AdNH	86	>350	0.37 (DCE—MeOH (4 : 1))	$C_{13}H_{17}ClN_4O$	55.56 / 55.62	6.06 / 6.10	20.05 / 19.96	280.76
13a	NMe_2 (R^3 = Me)	92	307—309	0.63 (DCE—MeOH (2 : 1))	$C_6H_{10}N_4O_2 \cdot HCl$	34.96 / 34.88	5.40 / 5.37	27.02 / 27.11	206.63
13b	NMe_2 (R^3 = Et)	85	305—307	0.61 (DCE—MeOH (2 : 1))	$C_7H_{12}N_4O_2 \cdot HCl$	38.21 / 38.10	5.99 / 5.94	25.40 / 25.39	220.66
13c	NMe_2 (R^3 = Pr)	83	312—314	0.65 (DCE—MeOH (2 : 1))	$C_8H_{14}N_4O_2 \cdot HCl$	41.03 / 40.94	6.37 / 6.44	23.92 / 23.87	234.69
13d	NHPr (R^3 = Me)	90	281—283	0.43 (DCE—MeOH (2 : 1))	$C_7H_{12}N_4O_2 \cdot HCl$	38.16 / 38.10	5.84 / 5.94	25.53 / 25.39	220.66
13e	NHPr (R^3 = Et)	82	302—304	0.39 (DCE—MeOH (2 : 1))	$C_8H_{14}N_4O_2 \cdot HCl$	40.83 / 40.94	6.39 / 6.44	23.80 / 23.87	234.69
13f	NHPr (R^3 = Pr)	84	300—303	0.43 (DCE—MeOH (2 : 1))	$C_9H_{16}N_4O_2 \cdot HCl$	43.54 / 43.46	6.95 / 6.89	22.46 / 22.53	248.71
13g	 (R^3 = Me)	85	310—312	0.58 (DCE—MeOH (2 : 1))	$C_8H_{12}N_4O_3 \cdot HCl$	38.55 / 38.64	5.19 / 5.27	22.58 / 22.53	248.67
13h	 (R^3 = Et)	80	314—316	0.53 (DCE—MeOH (2 : 1))	$C_9H_{14}N_4O_3 \cdot HCl$	41.21 / 41.15	5.69 / 5.76	21.48 / 21.33	262.70
13i	 (R^3 = Pr)	82	301—304	0.59 (DCE—MeOH (2 : 1))	$C_{10}H_{16}N_4O_3 \cdot HCl$	43.31 / 43.40	6.26 / 6.19	20.34 / 20.25	276.72

* Literature data are given in parentheses.
** DCE stands for dichloroethane.

in substitution for only two chlorine atoms to give 2-chloro-1,3,5-triazin-4,6-dione, whereas the third chlorine atom is substituted for only at 120 °C. Hydrolysis of compound **1** in water in the presence of excess sodium bicarbonate gives, judging from the amount of consumed base, sodium salt of 4,6-dichloro-2-hydroxy-1,3,5-triazine, however, only cyanuric acid is formed upon acidification of the aqueous solution.[19] Kinetics of hydrolysis of the chlorine atom in 2-(R^1R^2-amino)-4,6-dichloro-1,3,5-triazines were also studied;[46,48—51] To reach homogeneity of the medium (*i.e.*, to increase the solubility of the starting dichloro derivatives), we added solvents well miscible with water (dioxane, acetone, DMSO). According to the data in the work,[50] use of alcohols as the cosolvents leads to the substitution for the chlorine atom with the alkoxy group and complete suppression of its substitution by a hydroxy group. In addition, the hydrolysis product exhibits acidic properties (pK_a for 4-chloro-6-ethylamino-1,3,5-triazin-2(3*H*)-one is 6.70, for 4-chloro-6-diethylamino-1,3,5-triazin-2(3*H*)-one it is 6.68),[50] that requires two equivalents of an alkali. The reaction is slow in the absence of cosolvents. Thus, in the reaction of sodium hydroxide (1.1 mol) with 2-amino-4,6-dichloro-1,3,5-triazine (1 mol) in water at 20—25 °C, ~30% of the starting dichloro derivative remain still unreacted after 15 h.[27]

To sum up, for the selective substitution for one chlorine atom in 2-(R^1R^2-amino)-4,6-dichloro-1,3,5-triazines **2a**—**k** to occur, it is necessary to apply conditions providing a complete conversion of the starting compounds **2a**—**k**, but which do not lead to substitution for the third chlorine atom.

Taking into account the data on the selective substitution for one chlorine atom in molecules **2a**—**k** given above, we have chosen the water—acetonitrile system. Substitution for the chlorine in **2a**—**k** (see Scheme 2) was effected by the action of 10% aqueous sodium hydroxide at 20—25 °C with the molar ratio sodium hydroxide : **2a**—**k** equal to (2—2.4) : 1. When the base is added gradually, the reaction course is more even. Introduction of 20 vol.% of acetonitrile from the total amount of the sodium hydroxide solution provided a required homogeneity of the reaction mixture for all the dichloro-1,3,5-triazines **2a**—**k**. Completion of the reaction was detected by TLC.

The time (*t*, the complete conversion) required for hydrolysis of 2-(R^1R^2-amino)-4,6-dichloro-1,3,5-triazines **2a**—**k** with various substituents NHR^1R^2 is given below.

NHR^1R^2	*t*/h	NHR^1R^2	*t*/h
NH_2	28	NHC_6H_4Me-*p*	24
NMe_2	10	$N(CH_2)_4$	20
NHPr	22	$N(CH_2)_5$	20
$NHPr^i$	22	$N(CH_2CH_2)_2O$	20
NHC_6H_{10}-*cyclo*	22	NHAd	24
NHPh	24		

It is seen that the time necessary for the reaction to reach completion virtually does not depend on the structure of amine fragment in the triazine ring and only in the case of dimethylamine substituent the reaction is somewhat faster than in other cases. To isolate the target 4-amino-6-chloro-1,3,5-triazin-2(3*H*)-ones **4a**—**k**, the homogeneous reaction mixture containing salt **3a**—**k** was acidified with dilute hydrochloric acid to pH 3—4. Triazin-2(1*H*)-ones **4a**—**k** are obtained in good yields (see Table 1) and are contaminated with neither the starting compounds, nor the products of further hydrolysis.

To sum up, we found conditions for selective hydrolysis of one chlorine atom in molecules of 2-(R^1R^2-amino)-4,6-dichloro-1,3,5-triazines **2a**—**k** containing structurally different amino substituents.

For clarification of specific structural characteristics of obtained 1,3,5-triazinones **4a**—**k** having three different substituents, we performed detailed spectral analysis taking into account the literature data on 1,3,5-triazines with substituents of similar type. The major issue which requires clarification is position of the proton, whose migration is responsible for the possibility of the lactim-lactam tautomerism (see Scheme 1).

In the IR spectra of compounds **4a**—**k** (Tables 2 and 3), a strong absorption band is present in the region 1686—1707 cm^{-1} characteristic of the amide-type C=O group, that corresponds more to tautomer **B**, **C**, or **D**, rather than **A**.

According to the literature data (see Table 3), in 1,3,5-triazinones **5a—f**, **6a—c**, **7**, and **9a,b** an absorption band of the carbonyl group is in the region 1665—1695 cm^{-1}. Position of the C=O band in the synthesized compounds **4a—k** is the closest to that in compounds **7**, **9b**, and **10b—c**, which is apparently due to a similar electron effect of the third substituent. Note that the absence of a proton on the nitrogen atoms of the 1,3,5-triazinone ring adjacent to the carbonyl group (*i.e.*, for the fragment —CO—NR—) leads to the shift of absorption bands of the carbonyl group to 1710—1740 cm^{-1}, that is also observed in the spectra of 5-aryl-4,6-dichloro-1,3,5-triazin-2(5*H*)-ones **8a—c**.[55] The presence in compounds **10a** and **10c** of the lactam fragment —CO—NH— was unambiguously confirmed by the X-ray diffraction data.[58]

In the IR spectrum of 4,6-di(pyridinium-1-yl)-1,3,5-triazin-2-olate chloride **12** (see Ref. 59), no absorption band is found in the region 1650—1750 cm^{-1}, that most likely allows us to rule out consideration of zwitterionic structures of the type **E**, **F**, **G** for compounds **4a—k** (see Scheme 1).

Absorption of the N—H bonds in compounds **4a—k** are found in the regions 3300—3420 and 3190—3060 cm^{-1} as broad bands of medium intensity, which are due to the presence of the exocyclic NH group and the ring NH fragment (see Table 2). For compounds **4b**,**h—j**, which have no NH fragment in the amino substituent, absorption is observed in the region 3090—3150 cm^{-1}, that can be assigned to the absorption of the cyclic NH. These data are in good agreement with the range (3100—3200 cm^{-1}) given in the work[54] for the structures containing a lactam fragment —CO—NH—.

In the ^1H NMR spectra of compounds **4a—k**, the signal for the acidic proton is found in the region δ 10.8—11.8 as a broad singlet. Such a position of the proton signal corresponds to the fragment N—H and agrees with the shifts observed in the spectra of compounds **7**, **9a—b**, and **10b**. In the complex of 2-hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine with dioxane, the signal for the proton of the hydroxyl group appears in the region δ 12 as a broad singlet ($CDCl_3$).[32]

The ^{13}C NMR spectrum of compound **4b** completely agrees with that published earlier.[28] In the ^{13}C NMR spectrum of compound **11**, only two signals for the quaternary carbon atoms are found at δ 158.2 and 158.7, which the authors of the work[29] interpret as an overlap of the signals for two carbon atoms of the 1,3,5-triazine ring. The ^{13}C NMR spectra of compounds **4a—k** exhibit a high-field shift of the signals for all the ring carbon atoms: thus, for the carbon atom bonded to the chlorine atom, by 18—20 ppm with respect to the signal for the carbon atom in cyanuric chloride (δ 172.5);[28] for the signal of the carbon atom bonded to the amino group, by 10—15 ppm with respect to the signal for the carbon atom in 2,4,6-tris-(dimethylamino)-1,3,5-triazine (δ 165.9).[28] The signal for the carbon atom of the carbonyl group in compounds **4a—k** is close to the signal for the carbon atom in cyanuric acid (δ 149.8).[28] Similar pattern in the ^{13}C NMR spectra is observed for the series of disubstituted 1,3,5-triazinones

Table 2. Spectral characteristics of 6-amino-4-chloro-1,3,5-triazin-2(1*H*)-ones **4a—k** and 4-alkoxy-6-amino-1,3,5-triazin-2(1*H*)-one hydrochlorides **13a—i**

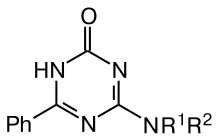
Compound	IR, ν/cm^{-1}	^1H NMR (DMSO-d_6), δ	^{13}C NMR (DMSO-d_6), δ			
			C(2)	C(4)	C(6)	Other
4a	3192, 3038, 2777, 1707 (C=O), 1674, 1551, 1477, 1396, 1342, 1300, 1188, 1134, 997, 862, 793, 712, 638	8.90 (br.s, 2 H, NH_2); 11.77 (br.s, 1 H, NH)	148.06	154.04	149.89	—
4b	3095, 3012, 2984, 2957, 2887, 2820, 1701 (C=O), 1624, 1524, 1499, 1468, 1445, 1418, 1389, 1306, 1213, 993, 847, 787, 735	3.10, 3.12 (both s, 6 H, NMe, Δν = 6 Hz); 11.34 (br.s, 1 H, NH)	150.84	153.55	150.84	38.90, 39.10 (NMe_2)
4c	3068, 2964, 2943, 2926, 2750, 2714, 1701 (C=O), 1637, 1512, 1466, 1377, 1352, 1294, 1265, 1001, 852, 785	0.88 (t, 3 H, Me, *J* = 7 Hz); 1.51 (m, 2 H, CH_2); 3.27 t, 2 H, (NCH_2, *J* = 6.7 Hz); 9.00 (br.s, 1 H, NH); 11.41 (br.s, 1 H, NH)	148.34	153.39	151.02	10.98 (Me); 21.73 (CH_2); 42.76 (NCH_2)
4d	3176, 3068, 2974, 2931, 2735, 1707 (C=O), 1630, 1514, 1460, 1446, 1371, 1338, 1311, 1265, 1003, 849, 785	1.16 (d, 6 H, Me, *J* = 6.5 Hz); 4.02 (m, 1 H, CH); 9.13 (br.s, 1 H, NH); 11.47 (br.s, 1 H, NH)	148.17	152.22	150.80	22.03 (Me); 43.91 (NCH)
4e	3169, 3066, 2931, 2858, 2731, 1703 (C=O), 1632, 1578, 1512, 1456, 1362, 1306, 1275, 1259, 1030, 1001, 835, 785	1.26 m, 1.52 d, 1.67 s, 1.80 d (10 H, *cyclo*-C_6H_{10}); 3.71 (m, 1 H, CH); 8.52 (br.s, 1 H, NH); 11.13 (br.s, 1 H, NH)	148.96	153.06	152.02	23.76, 24.74, 31.71, 49.45, 49.55 (*cyclo*-C_6H_{11})
4f	3051, 2982, 2930, 2903, 2729, 2631, 1701 (C=O), 1618, 1585, 1518, 1499, 1464, 1439, 1369, 1259, 997, 854, 781, 752, 729, 667	7.15 t, 7.37 t, 7.54 d (5 H, Ph); 9.60 (br.s, 1 H, NH); 10.95 (br.s, 1 H, NH)	154.07	154.07	154.07	121.78, 124.81, 129.02, 136.76 (Ph)
4g	3338, 3091, 3003, 1701 (C=O), 1612, 1578, 1487, 1385, 1315, 1286, 1246, 999, 928, 816, 779, 752, 735, 625	2.28 (s, 3H, Me); 7.18, 7.39 (both d, 4 H, *p*-C_6H_4, *J* = 8 Hz); 9.12 (br.s, 1 H, NH); 11.03 (br.s, 1 H, NH)	153.87	153.87	153.87	20.58 (Me), 122.30, 129.54, 133.71, 134.53 (*p*-C_6H_4)
4h	3117, 2982, 2930, 2891, 2795, 1691 (C=O), 1624, 1608, 1522, 1491, 1458, 1419, 1362, 1279, 1186, 1140, 993, 787	1.92 (d, 4 H, CH_2, *J* = 6.3 Hz); 3.50 (s, 4 H, CH_2NCH_2); 11.48 (br.s, 1 H, NH)	150.03	150.03	150.03	24.57 (CH_2), 48.62 (NCH_2)
4i	3118, 3043, 2943, 2858, 2806, 1686 (C=O), 1610, 1529, 1491, 1450, 1416, 1292, 1271, 1209, 1111, 1009, 978, 852, 785	1.54, 1.59 (both d, 6 H, CH_2, *J* = 4 Hz); 3.64 (t, 4 H, CH_2NCH_2, *J* = 4 Hz); 11.30 (br.s, 1 H, NH)	150.64	151.61	150.64	22.76 (CH_2), 24.65 (CH_2), 46.44 (NCH_2)
4j	3151, 3115, 3032, 2968, 2933, 2858, 2804, 1686 (C=O), 1605, 1541, 1493, 1419, 1369, 1296, 1256, 1157, 1109, 1018, 980, 928, 839, 783	3.63 (d, 8 H, NCH_2CH_2O, *J* = 6.8 Hz); 11.05 (br.s, 1 H, NH)	152.15	153.98 154.05	153.51	44.89, 44.95 (NCH_2); 65.46, 65.57 (OCH_2)
4k	3421, 3276, 3077, 3025, 2908, 2850, 2780, 1720 (C=O), 1618, 1591, 1513, 1457, 1405, 1363, 1309, 1295, 1249, 1232, 1159, 1132, 1097, 1004, 977, 842, 815, 794	1.57 s, 1.60 s, 1.62 s, 1.98 s, 2.02 s (15 H, Ad); 7.83 (br.s, 1 H, NH); 10.81 (br.s, 1 H, NH)	154.59	154.59	154.59	29.13, 36.06, 41.08, 53.12 (Ad)
13a	3344, 2956, 2879, 2840, 2763, 2692, 2622, 1747, 1660, 1606, 1537, 1486, 1402, 1322, 1224, 1089, 927, 883, 838, 765	3.17, 3.21 (both s, 6 H, NMe, Δν = 16 Hz); 3.97 (s, 3 H, OMe); 10.72 (br.s, 0.6 H, NH)	150.73	162.52	157.72	38.15, 38.34 (NMe_2); 57.02 (OMe)

(*to be continued)*)

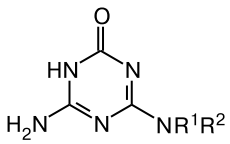
Table 2 (*continued*)

Compound	IR, ν/cm^{-1}	^1H NMR (DMSO-d_6), δ	^{13}C NMR (DMSO-d_6), δ			
			C(2)	C(4)	C(6)	Other
13b	3548, 3392, 3261, 2908, 2875, 2765, 2726, 2707, 2676, 2628, 1749, 1660, 1608, 1540, 1492, 1415, 1396, 1373, 1319, 1220, 1091, 1000, 891, 864, 827, 763	1.30 (t, 3 H, Me, J = 8.0 Hz); 3.16, 3.20 (both s, 6 H, NMe, Δν = 16 Hz); 4.46 (q, 2 H, OCH_2, J = 8.0 Hz)	150.19	161.67	157.31	14.36 (Me); 38.44, 38.94 (NMe_2); 66.86 (OCH_2)
13c	3157, 3031, 2979, 2879, 2817, 2780, 1726, 1673, 1585, 1525, 1427, 1398, 1375, 1288, 1238, 1062, 1051, 885, 837, 761	0.91 (t, 3 H, Me, J = 7.8 Hz); 1.68 (sextet, 2 H, CH_2, J = 7.8 Hz); 3.09, 3.14 (both s, 6 H, NMe, Δν = 20 Hz); 4.32 (t, 2 H, OCH_2, J = 7.8 Hz); 10.50 (br.s, 1 H, NH)	153.82	162.50	156.18	10.60 (Me); 21.78 (CH_2); 37.78 (NMe_2); 70.81 (OCH_2)
13d	3267, 2966, 2877, 2804, 2686, 2622, 1753, 1650, 1589, 1558, 1527, 1432, 1328, 1307, 1195, 1155, 1083, 1037, 927, 837, 771	0.88 (t, 3 H, Me, J = 8.0 Hz); 1.53 (m, 2 H, CH_2); 3.38 (m, 2 H, CH_2); 4.00 (s, 3 H, OMe); 9.54 (br.s, 0.5 H, NH); 11.05 (br.s, 0.2 H, NH)	148.39	163.97	158.27	11.47, 11.59 (Me); 22.11, 22.31 (CH_2); 43.15, 43.27, 43.45 (NCH_2); 57.45 (OMe)
13e	3149, 3066, 2962, 2931, 2871, 2797, 2771, 2774, 2682 1739, 1660, 1585, 1533, 1438, 1371, 1319, 1180, 1151, 1101, 958, 865, 759	0.88 (t, 3 H, Me, J = 7.8 Hz); 1.30 (t, 3 H, Me, J = 7.6 Hz); 1.53 (m, 2 H, CH_2); 3.39 (m, 2 H, CH_2); 4.48 (q, 2 H, OCH_2, J = 7.6 Hz); 9.53 (br.s, 0.8 H, NH); 11.15 (br.s, 0.3 H, NH)	148.18	163.18	158.26	11.47, 11.56, 11.67 (Me); 14.35, 14.47 (CH_2); 22.11, 22.35 (CH_2); 42.98, 43.27 (NCH_2); 67.31 (OCH_2)
13f	3131, 3066, 2964, 2937, 2873, 2798, 2761, 2624, 1741, 1658, 1585, 1537, 1438, 1332, 1317, 1089, 941, 760	0.89, 0.92 (m, 6 H, Me); 1.50 (m, 2 H, CH_2); 1.71 (m, 2 H, CH_2); 3.35 (t, 2 H, CH_2, J = 7.6 Hz); 4.36 (t, 2 H, OCH_2, J = 7.6 Hz); 9.42 (br.s, 1 H, NH); 10.92 (br.s, 0.8 H, NH)	148.46	163.48	158.27	10.51 (Me); 11.61, 11.66 (Me); 21.79 (CH_2); 22.12, 22.34 (CH_2); 42.75, 43.27, 43.42 (NCH_2); 72.27 (OCH_2)
13g	3099, 3006, 2929, 2860, 2814, 2746, 1741, 1606, 1542, 1488, 1442, 1419, 1326, 1307, 1274, 1110, 1066, 1008, 931, 916, 875, 767	3.64, 3.81 (m, 8 H, NCH_2CH_2O); 3.96 (s, 3 H, OMe); 10.72 (br.s, 0.7 H, NH)	151.62	163.08	157.99	45.40, 46.06 (NCH_2); 56.92 (OMe); 65.99 (OCH_2)
13h	3162, 3054, 2993, 2941, 2798, 1741, 1668, 1585, 1468, 1442, 1403, 1378, 1344, 1270, 1180, 1114, 1056, 1010, 883, 827, 765	1.28 (t, 3 H, Me, J = 7.8 Hz); 3.67, 3.82 (m, 8 H, NCH_2CH_2O); 4.66 (q, 2 H, OCH_2, J = 7.8 Hz); 10.70 (br.s, 0.3 H, NH)	151.26	162.36	157.73	14.40 (Me); 45.41, 46.12 (NCH_2); 65.98, 66.13 (OCH_2); 66.62 (OCH_2)
13i	3342, 3023, 2975, 2860, 2809, 2684, 1754, 1625, 1602, 1542, 1490, 1444, 1390, 1378, 1317, 1272, 1112, 1064, 1012, 896, 858, 771	0.90 (t, 3 H, Me, J = 7.6 Hz); 1.67 (q, 2 H, CH_2, J = 7.6 Hz); 3.65, 3.81 (m, 8 H, NCH_2CH_2O); 4.36 (t, 2 H, OCH_2, J = 7.6 Hz);	151.05	162.47	157.52	10.54 (Me); 21.81 (CH_2); 45.49, 46.15 (NCH_2); 65.75, 65.99 (OCH_2); 71.79 (OCH_2)

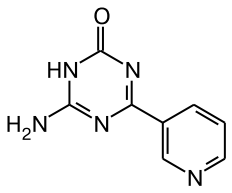
Note. Position of the proton in the molecule of **11** was not determined, judging by the name of the compound in the Results and Discussion and Experimental sections.[29]



5a—f



6a—c



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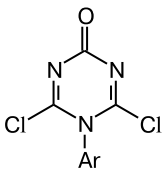
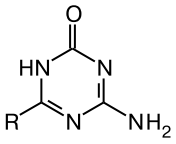
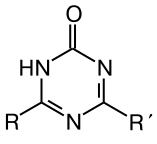


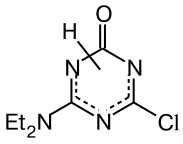
8a—c



9a,b



10a—c



11

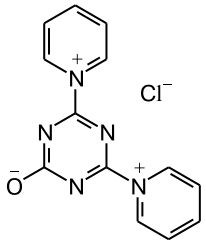


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Table 3. Spectral characteristics of substituted 1,3,5-triazinones

Compound	$\nu_{C=O}$ (KBr)/cm^{-1}	δ (NH of 1,3,5-triazine ring) (DMSO-d_6)
4a—k	1686—1707	10.81—11.77
5a ($NR^1R^2 = NMe_2$)	1675 (see Ref. 52)	—
5b ($NR^1R^2 = N(CH_2)_5$)	1680 (see Ref. 52)	—
5c ($NR^1R^2 = N(CH_2CH_2)_2O$)	1670 (see Ref. 52)	—
5d (NR^1R^2 = NBu)	—	11.80 (see Ref. 53)
5e ($NR^1R^2 = NCH_2Ph$)	1670 (see Ref. 53)	—
5f (NR^1R^2 = NHPh)	1665 (see Ref. 53)	10.05—10.25 (see Ref. 53)
6a ($NR^1R^2 = N(CH_2CH_2)_2O$)	1690 (see Ref. 54)	10.21 (see Ref. 54)
6b ($NR^1R^2 = N(CH_2)_5$)	1680 (see Ref. 54)	9.78 (see Ref. 54)
6c (NR^1R^2 = N(Me)Ph)	1660 (see Ref. 54)	10.20 (see Ref. 54)
7	1698 (see Ref. 54)	11.47 (see Ref. 54)
8a (R = Ph)	1710 (see Ref. 55)	—
8b (R = 2,6-(MeC_6H_3)$_2$)	1730 (see Ref. 55)	—
8c (R = 4-Br-2,6-(MeC_6H_2)$_2$)	1720, 1740 (see Ref. 55)	—
9a (R = Ph)	—	11.60 (see Ref. 56)
9b (R = β-D-ribofuranosyl)	1693 (see Ref. 57)	11.24 (see Ref. 57)
10a (R = R′ = $N(CH_2CH_2)_2O$)	—	10.52 (see Ref. 58)
10b (R = R′ = $N(CH_2)_5$)	1670 (see Ref. 58)	11.45 (see Ref. 58)
10c (R = OMe, R′ = $N(CH_2CH_2)_2O$)	1690 (see Ref. 58)	12.30 (see Ref. 58)
11	—	11.13, 11.54 (see Ref. 29)

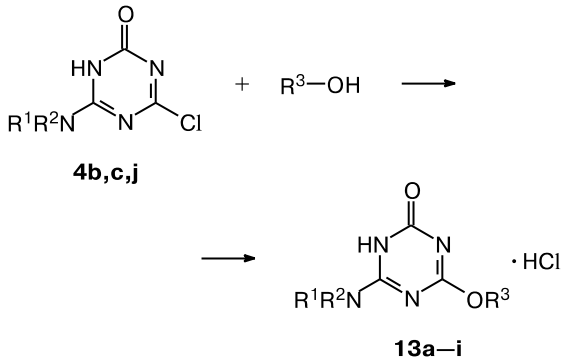
and monosubstituted 1,3,5-triazinediones.[23,28,60—62] The high- field shift of the signals for the carbon atoms is, in our opinion, caused by redistribution of electron density between 1,3,5-triazine ring and substituents. It is known[19] that the nitrogen atoms in the 1,3,5-triazine heteroaromatic ring carry partial negative charge due to their electron-withdrawing character, while the carbon atoms carry partial positive charge. Such a distribution of electron density is responsible for the position of signals for the carbon atoms in the ^{13}C NMR spectrum (δ 163—175),[23] as well as for the tendency of 1,3,5-triazine derivatives to nucleophilic substitution reactions. In the ^{13}C NMR spectrum of the complex of 2-hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine with dioxane, the signal for the carbon atom bonded to the hydroxyl group is found at δ 171 ($CDCl_3$).[32] In the ^{13}C NMR spectrum of *tert*-butylaminium salt of 2-hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine, the signal for the carbon atom bonded to the negatively charged oxygen is found at δ 165 (acetone-d_6).[63] Disruption of heteroaromatic character in compounds **4a—k** results in the fact that the ring nitrogen atom bearing a proton becomes an electron-donating substituent with respect to the rest of the conjugated system, which includes the carbonyl group and two C=N bonds of the ring. Displacement of the lone pair on the nitrogen atom toward the conjugated system leads to an increase in electron density on the carbon atoms of the 1,3,5-triazine ring and, as a consequence, to the high-field shift of the signals for the

carbon atoms in the 1,3,5-triazine ring (δ 148—154). To sum up, position of signals in the ^{13}C NMR spectra of compounds **4a**—**k** evidences also in favor of structures **B**, **C**, **D** and allows us to rule out structures **A**, **E**, **F**, **G**.

In order to determine the structure of 1,3,5-triazinones **4a**—**k**, we attempted to grow single crystals suitable for X-ray diffraction studies. Compounds **4a**—**k** have proved insoluble in nonpolar and weakly polar solvents, therefore, we used DMF, DMSO, acetone, acetonitrile, methanol, ethanol, and their mixtures to grow the crystals. However, no acceptable single crystal was obtained.

Moreover, use of alcohols or their mixtures with other solvents results in the reaction, leading to substitution for the chlorine in compounds **4** by an alkoxy group (Scheme 3). Thus, when compounds **4b**,**c**,**j** were dissolved in methanol, ethanol, or *n*-propanol at room temperature in the absence of bases, substitution for the chlorine is completed already within 24—96 h (see Experimental), in which case the corresponding 4-alkoxy-6-amino-1,3,5-triazin-2(1*H*)-one hydrochlorides **13a**—**i** are obtained in high yields.

Scheme 3



13: $NR^1R^2 = NMe_2$, R^3 = Me (**a**), Et (**b**), Pr (**c**);
NR^1R^2 = NHPr, R^3 = Me (**d**), Et (**e**), Pr (**f**)
$NR^1R^2 = N(CH_2CH_2)O$, R^3 = Me (**g**), Et (**h**), Pr (**i**)

The readiness of substitution for the chlorine atom in compounds **4b**,**c** is apparently accounted for by the fact that the guanidine fragment in the starting molecule plays the role of a base, whereas formation of the salt-like product is a driving force for the process.

Since the spectral characteristics do not allow us to unambiguously chose between possible tautomers (see Scheme 1), we performed quantum chemical calculations.

The calculations were performed in terms of the density functional theory using the GAUSSIAN program[64] and the M052X functional with the aug-cc-pvdz basis for tautomers **A**, **B**, **C**, **D** of the molecule **4b** with correction for the zero-point vibrations (ZPE). This approximation has been successfully used earlier[65,66] for analysis of geometry, energy, and intermolecular interactions. The choice between neutral (**B**, **C**, **D**) and zwitterionic (**E**, **F**, **G**) forms was made based on the distribution of bond distances in the triazine ring and the C—O bond distance. The values of atomic charges in this case are less indicative, since the signs "+" and "—" commonly shown in schemes, first, are very arbitrary, and a charge assigned to an atom is in reality spread between this atom and its neighbors. Second, the neutral and the zwitterionic forms are only two boundary cases (two canonical structures, see in Scheme 1), whereas a true electron structure of the molecule (mol) is their hybrid ($\psi_{mol} = a\psi_n + b\psi_i$, where ψ is the wave function, and the structure is assigned for either neutral (n), or zwitterionic (i) form depending on coefficients *a* and *b*). This is clearly illustrated by Table 4, in which the charge distributions (estimated in terms of the natural analysis of populations, included into the GAUSSIAN program) are given together with geometric characteristics.

As it is seen from the data given in Table 4, zwitterionic forms are less stable than their neutral counterparts **B**, **C**, **D**, obtained by optimization. This follows, first, from the C—O bond distance, which corresponds to that of a double bond, and, second, from the ring geometry, corresponding to the lactam structure.

Calculation of relative energies (Table 5) show that in the isolated state, *i.e.*, in the gas phase, the first tautomer out of **A**, **B**, **C**, and **D** is the most stable, that agrees with the data in the work.[31] Tautomer **D** has proved the most energetically unfavorable, being inferior to the iso-

Table 4. Bond distances and charge distributions in tautomers **A**—**D** of molecule **4b** in the isolated state (calculation in the M052X/aug-cc-pvdz approximation)

Tautomer	Bond distance*/Å							Charge/*e*			
	C(1)—O(1)	C(1)—N(1)	N(1)—C(2)	C(2)—N(2)	N(2)—C(3)	C(3)—N(3)	N(3)—C(1)	$-q_{O(1)}$	$-q_{N(1)}$	$-q_{N(2)}$	$-q_{N(3)}$
A	1.334	1.341	1.323	1.310	1.358	1.349	1.315	0.69	0.67	0.63	0.64
B	1.210	1.373	1.299	1.339	1.328	1.356	1.419	0.64	0.63	0.67	0.70
C	1.212	1.433	1.337	1.281	1.390	1.323	1.355	0.65	0.69	0.63	0.69
D	1.206	1.438	1.259	1.369	1.387	1.297	1.390	0.60	0.57	0.69	0.67
B**	1.222	1.370	1.308	1.323	1.343	1.361	1.400	0.71	0.68	0.67	0.68

* Numeration of atoms is shown in Figure 1.

** Parameters of the tautomer **B** complex with DMSO are also given for comparison (see below).

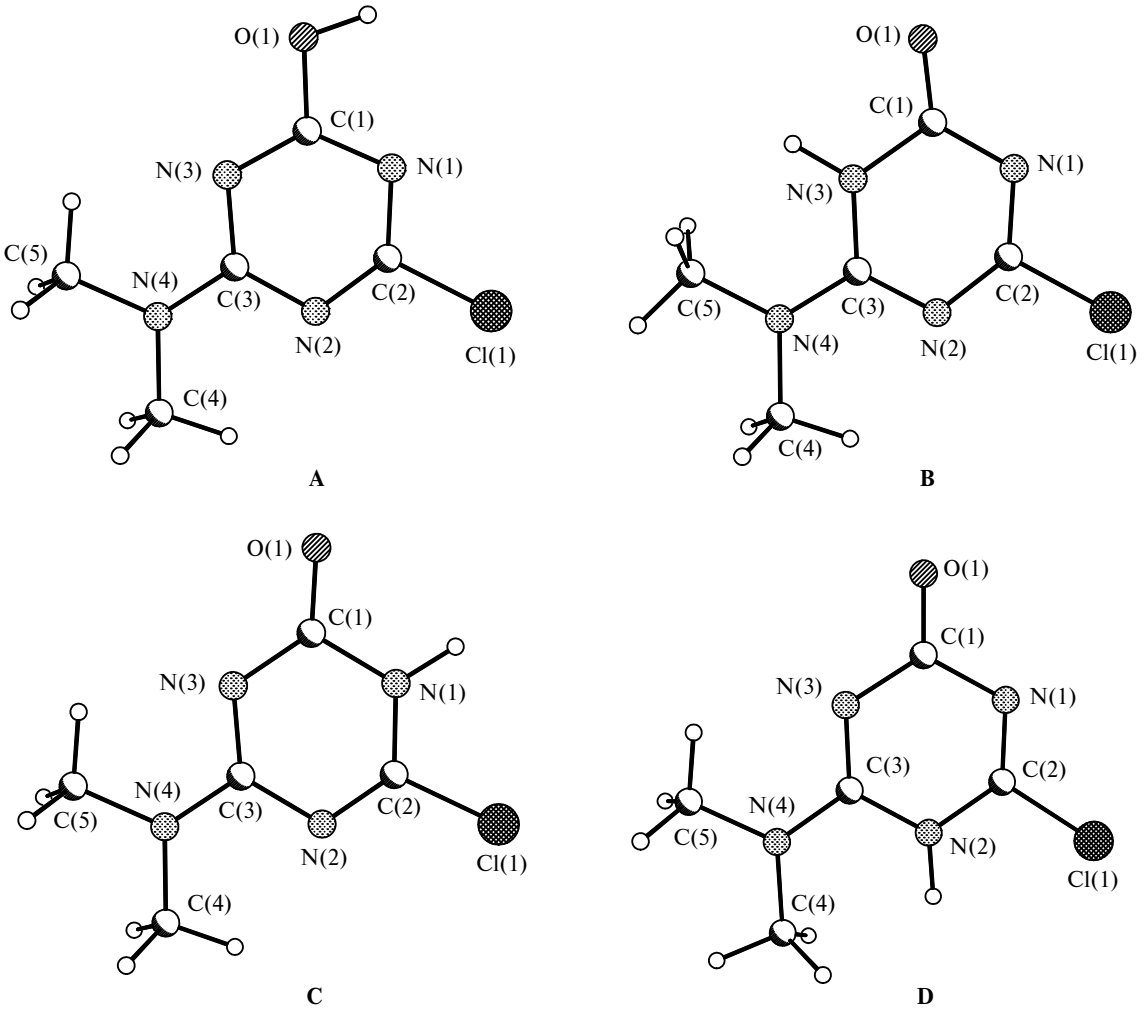


Fig. 1. General view of the optimized tautomers **A**—**D** of molecule **4b** with numeration of atoms.

mers placed under similar conditions by no less than 12—17 kcal mol^{-1}.

Usually reactions are carried out with compounds which are in the solid or liquid phases or in solution, *i.e.* in the condensed state, where there is a considerable influence of the surrounding, which can be arbitrary separated into two components: specific and nonspecific solvation. It is obvious that the calculation data for the isolated molecules are not informative enough about stabilization of different isomers and can be considered only as a "zero approximation".

Table 5. Relative energies* (E_{rel}) of tautomers **A**—**D** of molecule **4b** in the isolated state and in the 1,4-dioxane and DMSO fields (calculation in the M052X/aug-cc-pvdz approximation)

Tautomer	E_{rel}/kcal mol^{-1}		
	Isolated state	1,4-Dioxane	DMSO
A	0	0	2.6
B	5.3	2.0	0
C	3.0	1.5	2.1
D	18.0	13.8	19.5

* The energies should be compared within a column.

Taking this into account, we performed calculations for the isomers in solvents in terms of the model of self-consistent reaction field (SCRF, the model of the polarized continuum). Effect of specific solvation is not considered in the framework of this model. In order to make allowance, at least partially, for this effect, we have also analyzed H-bonded pairs including molecules of a compound and a solvent. Calculations were performed for both isolated pairs and pairs in the solvent field (simultaneous consideration of both polarization and specific solvation). This allows us to analyze both contributions into stabilization of each isomer. Calculation in terms of the SCRF model, simulating a solvent field, was performed in both a relatively weak field, mimicking influence of such sol-

Table 6. Relative energies (E_{rel}) of the H-bonded pairs of tautomer—solvent in the isolated state, in the 1,4-dioxane and DMSO fields (calculations in the M052X/aug-cc-pvdz approximation)

Pair	E_{rel}/kcal mol^{-1}			Pair	E_{rel}/kcal mol^{-1}		
	Isolated state	1,4-Dioxane	DMSO		Isolated state	1,4-Dioxane	DMSO
A...$MeNO_2$	0	0	2.6	**A**...DMSO	0	0	0
B...$MeNO_2$	1.6	0	0	**B**...DMSO	3.3	2.2	1.0
C...$MeNO_2$	1.8	1.4	2.8	**C**...DMSO	3.7	3.3	2.8
D...$MeNO_2$	18.2	13.7	9.6	**D**...DMSO	19.8	—	—

vent as 1,4-dioxane (ε = 2.2), and a strong field, corresponding to the action of DMSO (ε = 46.8). The data in Table 4 clearly demonstrate (for tautomer **B** as an example) that even for the highly polar solvent, optimization of geometry leads exactly to the neutral form (*i.e.*, the tautomer **B**, rather than **E**, that follows from the bond distance value for C=O, corresponding to that of a double bond). In this case, the solvent field shifts the equilibrium somewhat to the side of zwitterionic form (the C—O bond is elongated by 0.012 Å), and this was expected. However, this effect is very weak (see Table 4). Similar results were also obtained for tautomers **C** and **D** (are not included in Table 4). Therefore, the zwitterionic forms **E**, **F**, and **G** are excluded from our further consideration.

It is important that the relative stability of neutral tautomers **A**—**D** sharply changes in solvents, which is approximated in terms of the SCRF model. The most favorable in the isolated state tautomer **A** becomes third in stability in the DMSO field (see Table 5). Tautomer **A** is more favorable in the weak 1,4-dioxane field, though, the difference in relative energies decreases more than twofold as compared to the isolated state.

Calculation results for the H-bonded complexes of tautomers **A**—**D** with DMSO (strong H-bonding) and nitromethane (medium H-bonding) molecules, which were performed for these pairs in both the isolated state and the 1,4-dioxane and DMSO fields, are given in Table 6.

As it follows from Table 6, for the pair with nitromethane and in the isolated state, and in DMSO, as and in the case of the individual tautomers of compound **4b**, tautomer **A** is the most stable, in which case the gain in energy, as compared to tautomers **B** and **C**, is less than 2 kcal mol^{-1} for the pair with $MeNO_2$ and ~3.5 kcal mol^{-1} for the pair with the strong H-bond (in DMSO). Formation of H-bonds leads to the change in the relative stability of tautomers **B** and **C** (see Tables 5 and 6). Tautomer **D** remains the least stable form of compound **4b** in the case under consideration (*i.e.*, as a pair with the solvent), as well. This gives the reason to exclude it out of consideration.

Further, we have analyzed the nature of interactions of different forms of compound **4b** with $MeNO_2$ and DMSO in terms of the R. Bader topological theory "Atoms in molecules"[67,68] with subsequent application of the correlation between potential energy density in the critical point and the contact energy[69,70] to evaluate the bonding energy. The optimized structures of pairs (we were limited to the topological analysis of the isolated pairs tautomer—solvent, *i.e.*, without using the SCRF procedure) and the graph of their binding, plotted based on the search results for the critical points of the bond (3, −1), are given in Figure 2.

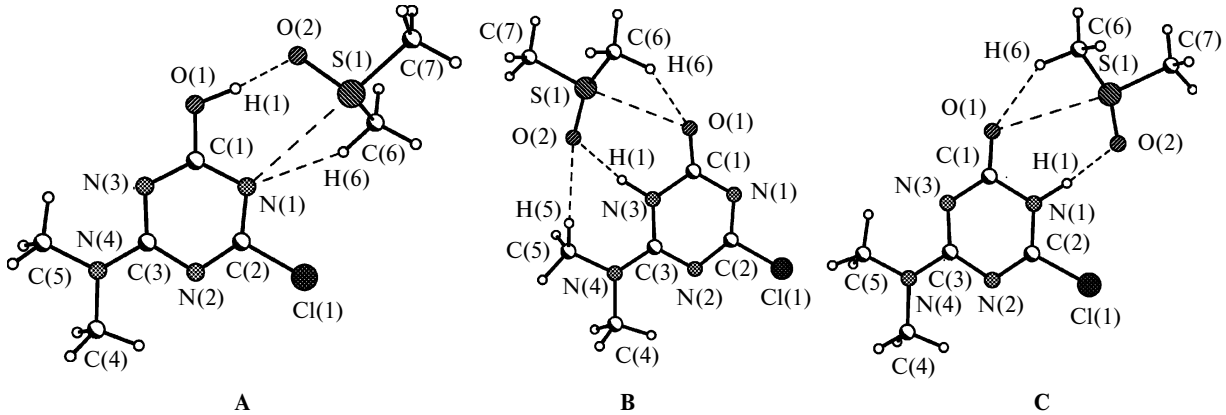


Fig. 2. The structure of the H-bonded pairs of tautomers **A**—**C** of molecule **4b** with the DMSO molecule (the pair with nitromethane molecule differs only in the absence of the S...O interaction and is not shown in Figure).

Energies of intermolecular binding for the pair tautomer—DMSO, evaluated as the sums of all the in-pair interactions, are −26.8, −18.3, and −20.0 kcal mol^{-1} for tautomers **A**, **B**, and **C**, respectively. For the pairs of tautomer—nitromethane, a relative difference in the binding energies is significantly lower, though, the sequence remains: −10.8, −10.1, and −10.3 kcal mol^{-1}, respectively.

It is logically to suppose that tautomer **A** H-bonded into the pair with the solvent should be energetically yet more favorable as compared to tautomers **B** and **C** than the individual tautomer **A**. However, the calculations performed (see Table 6) indicate that the converse is true. A relative gain in energy for the pair **A**—solvent is less than that for the individual tautomer (see Table 5, the first column). This, at first glance, contradiction can be explained if we take into account that, besides formation of H-bonds and shortened interactions in the pair tautomer—solvent, a DMSO or nitromethane molecule polarizes the molecule of **4b**. The polarization effect (nonspecific solvation), as shown above (see Table 6), leads to the decrease in stability of tautomer **A**, but increases that of tautomer **B**, whose interaction with the solvent molecule is the weakest.

If interaction of molecules in pair is strong enough, which is the case of DMSO, then the gain in energy due to the strong O—H...O bond is not swamped by the polarization effect, and tautomer **A** has proved the most favorable. If the proton is accepted by a weaker group, for example, a nitro group of nitromethane, the difference in the binding energy of tautomers with the solvent molecule decreases, and the influence of the strong solvent field becomes sufficient for stabilization of tautomer **B**. The results obtained explain, in particular, the formation of the lactim form in the H-bonded complex of 2-hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine with 1,4-dioxane,[56] whose lactim structure (*i.e.*, built similar to the type of tautomer **A**) of the triazine ring was confirmed by X-ray diffraction studies. Dioxane forms relatively strong H-bond, thereby stabilizing the lactim tautomer. In this case, the dioxane field, from which solution the crystals were obtained, is weak and, as a result, stabilization of the lactam structures due to the solvent field turned out to be smaller than stabilization of the lactim form due to the formation of H-bonding.

In conclusion, the calculations performed show that in the condensed state compound **4b**, depending on proportion of specific and nonspecific solvation effects, will exist as tautomer **A** or **B**, which are the most stable. Formation of tautomer **C** is improbable, whereas of tautomer **D**, virtually impossible.

On the whole, summarizing spectral and calculation data, we can say that in the solid state compounds **4a—k** exist as 6-amino-4-chloro-1,3,5-triazin-2(1*H*)-ones. In strongly polar solvents (of DMSO type), an equilibrium exists between tautomers **A** and **B**, whereas in weakly polar solvents, the equilibrium could have been (compounds **4a—k** do not dissolve in such solvents!) shifted to the side of tautomer **A**.

Experimental

Melting points were determined on a Gallenkamp melting point apparatus and were not corrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II spectrometer (^{1}H, 400.13; ^{13}C, 100.61 MHz). Chemical shifts in the ^{1}H and ^{13}C NMR spectra are given in the δ scale, using Me_4Si, as an internal standard. IR spectra were recorded on an Avatar 360 ESP spectrometer (KBr pellets). Elemental analysis was performed on a Eurovector EA 3000 instrument. Reaction course and purity of products were monitored by TLC on Silufol UV-254 plates.

2-Amino-4,6-dichloro-1,3,5-triazines 2a—k (general procedure). An amine (0.02 mol) (ammonia as a 25% aqueous solution, dimethylamine as a 33% aq. solution, other amines as a 10% solution in diethyl ether) was added dropwise to a vigorously stirred suspension of cyanuric chloride **1** (3.69 g, 0.02 mol) in diethyl ether (60 mL) at −(15—10) °C over 1 h. After addition of the amine, the reaction mixture was stirred for 30—45 min under the same conditions (TLC monitoring for cyanuric chloride, eluent DCE). Diethyl ether was evaporated to dryness, and the residue was treated with water (50 mL) using magnetic stirring. Insoluble white crystalline precipitate of **2a—d,f—k** was filtered off and dried. Compound **2e** was obtained by extraction with DCE (40 mL) of the residue after evaporation of diethyl ether. After the insoluble residue was separated, the DCE solution was dried with sodium sulfate and filtered, DCE was evaporated *in vacuo*, the residue was evacuated.

4-Amino-6-chloro-1,3,5-triazin-2(1*H*)-ones 4a—k (general procedure). 2-Amino-4,6-dichloro-1,3,5-triazine **2a—k** (0.002 mol) was added to a magnetically stirred mixture of 1.0 *M* aq. sodium hydroxide (4 mL) and acetonitrile (10 mL) at ~20 °C. The reaction mixture was stirred for 20 min under the same conditions, then 1.0 *M* aq. sodium hydroxide (4 mL) and 2-amino-4,6-dichloro-1,3,5-triazine **2a—k** (0.002 mol) were additionally added. After stirring for 20 min, this operation was repeated 3 more times. The completion of the reaction was monitored by TLC for the starting **2a—k** (eluent DCE). After it was over, the reaction mixture was filtered from a small amount of a precipitate, and the filtrate was acidified with a dilute hydrochloric acid to pH 2—3. Precipitates of compounds **4a—k** were filtered off, washed with water (2×30 mL), and dried. The yields and physicochemical properties of the products are given in Tables 1 and 2.

4-Alkoxy-6-amino-1,3,5-triazin-2(1*H*)-one hydrochlorides 13a—i (general procedure). 6-Amino-4-chloro-1,3,5-triazin-2(1*H*)-one **4b,c,j** (0.005 mol) was added to the corresponding alcohol (20 mL) at 20—25 °C with stirring. The reaction mixture was stirred under the same conditions (in methanol for 24 h, in ethanol for 72 h, in *n*-propanol for 96 h), monitoring the reaction progress by TLC for the starting **4b,c,j** (eluent methanol—DCE (4 : 1)). After completion of the reaction, the alcohol was evaporated to dryness, the residue was treated with water (20 mL) with magnetic stirring. An insoluble residue was filtered off, the filtrate was concentrated to dryness. The crystalline product obtained was suspended in diethyl ether, insoluble prod-

ucts **13a—i** were filtered off, dried at 100—110 °C. The yields and properties of the products are summarized in Tables 1 and 2.

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