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GUANAMINE HALOGEN DERIVATIVES WITH FLUOROALKYL GROUPS

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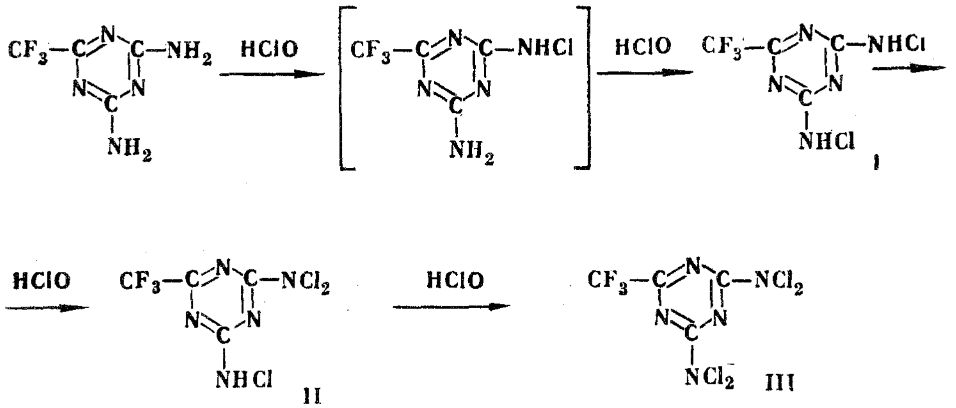
A study is made of chlorination and bromination of 4, 6-diamino-s-triazines, with the following fluoro groups at position 2: CF_3, CF_2H, CFH_2, CFClH, $CClF_2$, and $CFCl_2$. The reactions were carried out at 5-10° and with excess water (15-20 fold). A reaction mechanism is based on intermediate formation of hypochlorous and hypobromous acids, which then react with the amino group. It is shown that the hydrogen atoms are replaced stepwise. In all cases bromination is slower than chlorination, and the N-bromo-substituted compounds less stable than the corresponding chlorine ones. Free hydrogens in the fluoroalkyl radicals are substituted last of all.

The literature, which relates mainly to patents [1-5], gives details of methods of halogenation, as well as of properties of some halogen derivatives of amino-s-triazines, in particular of melamine or 2, 4, 6-triamino-s-triazine (chloro-, bromo-, iodomelamines) [6]. The chloromelamines, which are the most accessible, have been successfully used for preparing some individual chloro compounds, e.g., halogenoketones [1], and also for some reactions with unsaturated compounds to prepare various chlorohydrins. Halogen derivatives of melamine cyanurate, of cyanuric acid [7-10, 14], and other melamine derivatives [15] have been described.

In connection with the new method of preparing guanamines with electrophilic substituents CF_2H, CFClH, CFH_2 at position 2, discovered by the present authors, and also in connection with synthesizing other derivatives of this kind, it was appropriate to investigate their hitherto completely unknown halogen derivatives. There are indications of the use of halogenomelamines as oxidants and bleaches in the textile industry [17-20], for sterilizing water [16], as ion-exchange resins [11], as antiseptics and degassing agents [18-20]. In particular, they can find extensive application in treating wounds [21]. N-Chloromelamine is used in the food industry [12, 13] for preserving fruit and vegetables, and also in the rubber industry as a vulcanization accelerator. Interesting properties would be expected for the halogenoamines synthesized, especially since introduction of fluoroalkyl groups into the triazine ring should enhance the physiological action [22].

Investigation of the mechanism of the reaction taking place when the guanamines which have been synthesized, are chlorinated and brominated, showed that reaction proceeds as with other triazines, i.e., that it involves hypochlorous and hypobromous acids, according to the equation:

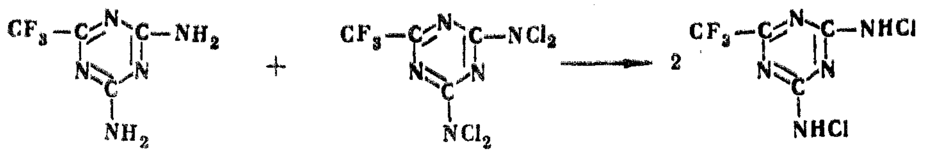


(1)

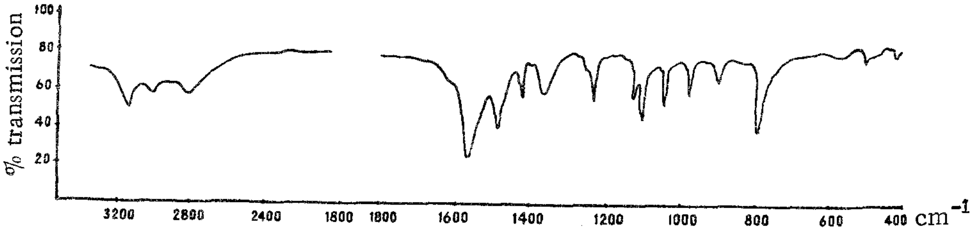
In accordance with this reaction mechanism, the conditions chosen for carrying out reaction were such that the quantities of hypochlorous and hypobromous acid necessary for halogenation would be formed more rapidly and more completely. It was found experimentally that the reaction must be carried out in the presence of excess water. 70-90 ml water was taken for 5 g compound, and the reaction run with stirring and cooling, keeping the temperature at 5-10°. Two to four hours were taken for the reaction, using energetic stirring and uniform halogen delivery. When guanamines with incompletely fluorinated groups, e.g., CF_2H, CFH_2, were exhaustively chlorinated, chlorine replaced the hydrogen in such a group, but only after all the hydrogens in the amino group had been replaced by chlorine. This made it possible to synthesize tetra-substituted guanamines by chlorinating a guanamine with the CF_2Cl group, as well as by exhaustively chlorinating a guanamine with the CF_2H group, and to establish their identities. When the 4, 6-bis(dichloroamino)-s-triazines synthesized were heated with free guanamine in aqueous acetic acid, they reacted thus:

Halogen Derivatives of Guanamines

Compound no.	Compound name	Mp, °C	Formula	Found, %		Calculated, %		Yield, %
				Cl(Br)	N	Cl(Br)	N	
I	2-Trifluoromethyl-4, 6-bis(chloroamino)-s-triazine	180—181	$C_4H_2Cl_2F_3N_5$	28.2	28.4	28.6	28.2	19
II	2-Trifluoromethyl-4-dichloroamino-6-chloroamino-s-triazine	105—106	$C_4HCl_3F_3N_5$	36.8	24.6	37.7	24.8	25
III	2-Trifluoromethyl-4, 6-bis(dichloroamino-s-triazine	124—125	$C_4Cl_4F_3N_5$	45.3	21.9	44.9	22.0	47
IV	2-Trifluoromethyl-4, 6-bis(bromoamino)-s-triazine	160—163	$C_4H_2Br_2F_3N_5$	Br−46.4	21.2	Br−47.5	20.8	24
V	2-Trifluoromethyl-4-dibromoamino-6-bromoamino-s-triazine	143.5—144.5	$C_4HBr_3F_3N_5$	Br−57.4	16.3	Br−57.7	16.8	6
VI	2-Difluoromethyl-4, 6-bis(chloroamino)-s-triazine	167—169	$C_4H_3Cl_2F_2N_5$	29.8	29.8	30.9	30.4	15
VII	2-Difluoromethyl-4, 6-bis(dichloroamino)-s-triazine	52	$C_4HCl_4F_2N_5$	46.8	22.8	47.5	23.4	74
VIII	2-Difluorochloromethyl-4, 6-bis(dichloroamino)-s-triazine	67—68	$C_4Cl_5F_2N_5$	52.6	20.9	53.1	21.1	65
IX	2-Difluorochloromethyl-4, 6-bis(bromoamino)-s-triazine	201—203	$C_4H_3Br_2F_2N_5$	Br — 49.2	21.8	Br−50.1	22.2	33
X	2-Fluorochloromethyl-4, 6-bis(chloroamino)-s-triazine	184.5—186	$C_4H_3Cl_3FN_5$	43.5	28.0	43.2	28.4	21
XI	2-Fluorochloromethyl -4-dichloroamino-6-chloroamino-s-triazine	83—86	$C_4H_2Cl_4FN_5$	51.0	24.6	50.3	24.8	35
XII	2-Fluorochloromethyl-4, 6-bis(bromoamino)-s-triazine	202—204	$C_4H_3Br_2ClFN_5$	Cl+Br−58.2	20.5	Cl+Br−58.3	20.9	27
XIII	2-Difluorochloromethyl-4-dichloroamino-6-chloroamino-s-triazine	100—101	$C_4HCl_4F_2N_5$	47.8	23.0	47.5	23.4	69
XIV	2-Fluorodichloromethyl-4-dichloroamino-6-chloroamino-s-triazine	100—103	$C_4HCl_5FN_5$	56.2	22.0	56.2	22.2	75
XV	2-Fluoromethyl-4, 6-bis(chloroamino)-s-triazine	195—196	$C_4H_4Cl_2FN_5$	33.4	35.1	33.0	33.5	38
XVI	2-Fluoromethyl-4, 6-bis(dichloroamino)-s-triazine	103—105	$C_4H_2Cl_4FN_5$	49.4	24.5	50.6	24.9	51



The disproportionation reaction described by Arsem [1] for the reaction between hexachloromelamine and melamine, obtained here. Bromotriazines disproportionate more readily than chlorotriazines.



IR spectrum of 2-difluoroamino-4, 6-bis(chloroamino)-s-triazine.

It was found that in all cases bromination is considerably slower than chlorination. So that complete substitution of the hydrogen atoms by bromine in the indicated triazines takes place with difficulty. Halogenation in weakly alkaline sodium acetate solutions is milder, and a mixture of halogen derivatives is usually formed. The indicated triazines are also satisfactorily halogenated in dilute acetic acid solution. The sequence of substitution of the hydrogens in the guanamine molecules is as shown in equation (1) above.

Introduction of two chlorine atoms leads to formation of 2-trifluoromethyl-4, 6-bis(chloroamino)-s-triazine. In connection with the reactivities of the first hydrogen atoms in the amino groups being higher, 2-trifluoromethyl-4-(N-dichloroamino)-6-amino-s-triazine is practically absent from the products. This is confirmed by the spectra of the dichloro-substituted triazines formed, and in particular, by the IR spectrum of 2-difluoromethyl-4, 6-bis(N-chloroamino-s-triazine (figure). In this latter no free amino group was detected.*

Fully chlorinated guanamines have much lower melting points than those containing less halogen, and they have higher solubilities in various chlorinated solvents. The bromo-derivatives are less stable, and, in particular, some tri- and tetrabromo-substituted ones gradually give off bromine on storage, and decompose with the evolution of bromine when their melting points are determined.

Experimental

Chlorination of 2-trifluoromethyl-4, 6-diamino-s-triazine. 5 g compound and 75 ml water were placed in a cylindrical reaction vessel, and 7.5 g NaOAc added. The mixture was vigorously stirred and cooled externally with ice, chlorine passed in for 3-4 hr, stirring and cooling continued for 2 hr more, and the reaction products then left overnight. Next day the precipitate was filtered off and dried. 7.5 g mixed chlorides was obtained; this was extracted with dichloroethane, and the insoluble material rejected. The solvent was evaporated off from the filtrate, and the residue fractionally crystallized from dichloroethane, to give three fractions: 2-trifluoromethyl-4, 6-bis(chloroamino)-s-triazine (I), 2-trifluoromethyl-4-dichloroamino-6-chloroamino-s-triazine (II), and 2-trifluoromethyl-4, 6-bis(dichloroamino)-s-triazine (III). The structure of compound I was also shown by a study of its IR spectrum. Absorption bands at 790 and 1560 cm^{-1} confirmed the presence of a triazine ring, and a band at 1100 cm^{-1} corresponded to the CF_2 group. The presence of a CH group was confirmed by absorption bands in the regions 1500 and 2800-3000 cm^{-1}. The absence of an absorption band at 1600 cm^{-1} showed the absence of the NH_2 group, indicating uniformity of distribution of chlorine over the two amino groups. The table gives all the melting points and analytical data for the compounds synthesized.

Chlorination of 2-difluoromethyl-4, 6-diamino-s-triazine. 5 g compound in 75 ml water was stirred vigorously, the temperature held at 0-10°, and chlorine passed in for 3 hr. Next day the precipitate was filtered off, and dried; the mixed chlorides weighed 8 g. Fractional crystallization from dichloroethane gave 2-difluoromethyl-4, 6-bis(chloroamino)-s-triazine (VI) and 2-difluoromethyl-4, 6-bis (dichloroamino)-s-triazine (VIII).

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*The spectrum of this compound was observed by E. N. Boitsovyi, in A. I. Finkel'shtein's laboratory, with a UR-10 spectrophotometer. The compound was tabletted with KBr.

The fully-substituted chlorination product 2-difluorochloromethyl-4, 6-bis(dichloroamino)-s-triazine (VIII) is obtained by exhaustive chlorination of 2-difluoromethyl-4, 6-diamino-s-triazine, and better by chlorinating 2-difluorochloromethyl-4, 6-diamino-s-triazine.

Bromination of 2-trifluoro-4, 6-diamino-s-triazine. 3.5 ml Br was slowly dropped into a well-stirred suspension comprising 5 g compound, 8.5 g KOAc, and 80 ml water, cooled with ice, and after the addition had ended, stirring and cooling were continued for 3 hr. Next day the crystalline product was centrifuged off and dried. Yield 7.3 g. After extracting with boiling dichloroethane, the residue weighed 1.4 g. After distilling off the dichloroethane, the residue was repeatedly recrystallized, when it gave 2-trifluoromethyl-4, 6-bis(bromoamino)-s-triazine (IV) and 2-trifluoromethyl-4-dibromoamino-6-bromoamino-s-triazine (V).

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