s-TRIAZINES

VI. Synthesis of N-Monoalkyl-Substituted Guanamines, Containing Fluoroalkyl Radicals, and Some of Their Reactions*

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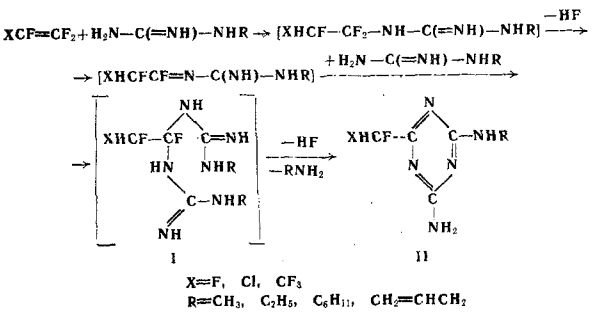
The reaction of tetrafluoroethylene, trifluorochloroethylene, and perfluoropropene with methyl-, ethyl-, cyclo- hexyl- and allylguanidines in dimethylformamide is investigated, and is shown to give N-monoalkyl-substituted guanamines containing CF_2H, CFClH, and CF_3CFH radicals, and hydrofluorides of alkylguanidines and alkylamines. A mechanism for the reaction is proposed. To confirm the structures of the guanamines, IR spectra of the most important compounds are given. Cyanoethylation and chlorination of some guanamines are investigated.

2-Alkyl(aryl)-4-amino-6-alkylamino-s-triazines are used as corrosion inhibitors, physiologically active compounds, and polymers. Most of the derivatives of this type are synthesized by the reaction between alkyl(aryl)guanidines and carboxylic acids [2], their anhydrides [3], acid chlorides [4–6], and esters [7–9], as well as by reaction of alkylcyanoguanidines with various nitriles [10]. The literature also describes a method based on fusing 2-alkyl-4, 6-diamino-s-triazine with amine hydrochlorides [11].

N-Substituted guanamines containing fluoroalkyl groups are of considerable interest, since the strongly electrophilic radical in the molecule considerably modifies the nature of the two amino groups, which can be turned to account in synthetic work. Known compounds of this type synthesized by the Rackman method [12] are 2-fluoroalkyl-4-amino-6-alkyl(aryl) amino-s-triazines [13,14], as well as 6-cyclohexyl-amino- and 6-piperidino-2-trifluoromethyl-4-amino-s-triazines [15].

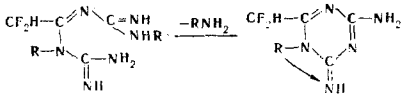
*For Part V see [1]

By analogy with a previously described method [16], we have developed a simple synthesis of N-mono-substituted guanimines containing fluoroalkyl groups from monoalkyl-substituted guanidines and φ-olefins. Monoalkylguanidines are bases as strong as guanidine itself [17], consequently φ-olefins react with them to give derivatives of the s-triazine series (II), hydrofluorides of monoalkylguanidine, and an alkylamine.



X=F, Cl, CF_3
R=CH_3, C_2H_5, C_6H_{11}, CH_2=$CHCH_2$

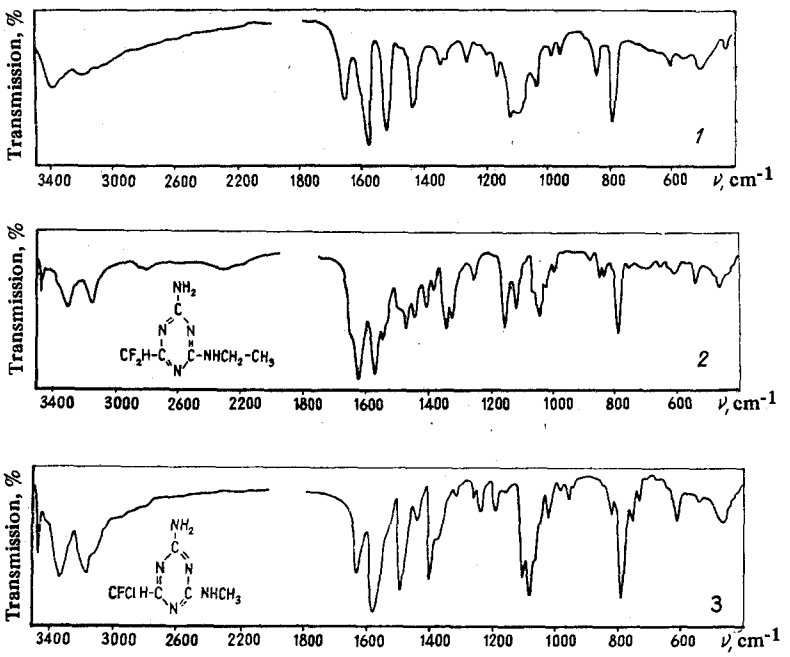
Formation of II via I is demonstrated in the work of Knunyants and coworkers [18]. The structure of II clearly shows that free amino groups participate in the particular reaction. If an alkylamino group participated in the reaction, migration of the alkyl group on the ring nitrogen would be hindered.



In every case reaction of monalkylguanidines with φ-olefins is accompanied by great evolution of heat.

Chlorination Products from Guanamines

Compound	Mp, °C	Formula	Found, %				Calculated, %			
			Cl	Cl (act)	F	N	Cl	Cl (act)	F	N
2-Difluoromethyl-4-dichloroamino-6-chloromethylamino-s-triazine	67—68	$C_5H_4Cl_3F_2N_5$	37.5	74.7	13.7	25.3	38.1	76.2	13.6	25.2
2-Difluoromethyl-4-dichloroamino-6-chloroethylamino-s-triazine	30—31	$C_6H_6Cl_3F_2N_5$	36.0	71.1	12.8	24.2	36.4	72.8	13.0	24.0
2-Fluorochloromethyl-4-dichloroamino-6-chloromethylamino-s-triazine	73.5—74.5	$C_5H_4Cl_4FN_5$	47.4	70.3	6.3	23.6	48.2	72.0	6.4	23.7
2-Difluoromethyl-4-dichloroamino-6-cyclohexylamino-s-triazine	75—76	$C_{10}H_{13}Cl_2F_2N_5$	23.3	44.3	11.8	22.1	22.7	45.4	12.2	22.5



IR spectra:
1) 2-Difluoromethyl-4-amino-6-methylamino-s-triazine (III); 2) 2-difluoromethyl-4-amino-6-ethylamino-s-triazine (IV); 3) 2-fluorochloromethyl-4-amino-6-methylamino-s-triazine (V).

If monoalkylguanidines react with tetrafluoroethylene to give quantitative yields of s-triazines, with trifluorochloroethylene and in particular perfluoropropene, reaction is considerably complicated by extensive resinification, lowering the yields of the end products. The structures of the s-triazines synthesized are also shown by the IR spectra.* Thus with the IR spectra of compounds III, IV and V (figure) bands at 790 and 1500 cm^{-1} are assigned to the triazine ring, and the occurrence of bands in the 1620–1660 and 3200–3400 cm^{-1} regions clearly show the presence of an amino group. Bands at 1140–1200 cm^{-1} can be assigned to =NH groups. Absorption bands at about 1350 cm^{-1} correspond to methyl groups.

It was previously shown that guanamines containing CF_3, CF_2H, and CF_2Cl radicals are readily cyanoethylated to give quantitative yields of tetracyanoethyl derivatives [19]. It was of interest to show how the presence of alkyl groups at the amino group is reflected in the reaction of cyanoethylation of 2-polyfluoroalkyl-4-amino-6-alkyamino-s-triazines. Cyanoethylation was studied with 2-difluoromethyl-4-amino-6-methyl(ethyl, allyl)amino-s-triazines. It was shown that the first two of those compounds are rapidly and quantitatively cyanoethylated even at room temperature, and that increasing the temperature, or decreasing the amount of catalyst leads to resinification and decrease in yield. Introduction of a methyl or ethyl group greatly accelerates cyanoethylation, but on passing to the guanamine with an allyl group, cyanoethylation could not in general be effected.

A study was also made of the halogenation of N-monoalkylguanamines containing fluoroalkyl radicals. Their chlorination in aqueous solution in the presence of sodium bicarbonate takes two hours at 2–10°, to give a high yield of N^4,N^4, N^6-trichloro-substitution product, while the 2-difluoromethyl-4-amino-6-cyclohexylamino-s-triazine gives N^4, N^4-dichloro-substitution product.

EXPERIMENTAL

Monoalkylguanidines containing methyl, ethyl, and allyl radicals were prepared as described in the literature [20].

Cyclohexylguanidine. A mixture of 1.2 mole cyclohexylamine hydrochloride and 1 mole cyanoguanidine was heated at 150°, until it became molten (30 min), then held at 180° for 3–3.5 hr. Then it was taken up in a small amount of EtOH, and filtered, the filtrate cooled, and excess ether used to effect preciptation. The operation was repeated 2–3 times, to give a 40% yield of pure cyclohexylguanidine hydrochloride.

2-Difluoromethyl-4-amino-6-methylamino-s-triazine. 36.5 g (0.5 mole) Methylguanidine and 100 ml dimethylformamide were put in a four-necked 150 ml flask, fitted with stirrer, thermometer, and gas inlet and outlet tubes, heated to 70°, and dry tetrafluoroethylene bubbled in with vigorous stirring. The supply of tetrafluoroethylene was controlled so that the temperature stayed at 70–80°, and it was stopped when the temperature fell to 50°. The precipitate (20.9 g) of mixed hydrofluorides of methylguanidine and methylamine was filtered off, the filtrate left for 24 hr, then the solvent distilled off under vacuum. 50 ml Water was added to the pasty residue, and the crystals that precipitated were filtered off, washed with water and recrystallized twice from water, yield 16 g (55%), white crystals, readily soluble in boiling water, dimethylformamide, MeOH, acetonitrile, and aqueous acids, mp 172–173° (ex water). Found: C 34.05; H 4.10; F 21.30; N 40.50%, calculated for $C_5H_7F_2N_5$: C 34.28; H 4.00; F 21.71; N 40.00%.

2-Difluoromethyl-4-amino-6-ethylamino-s-triazine. The same flask was filled with 43.5 g (0.5 mole) ethylguanidine and 100 ml dimethylformamide, and the tetrafluoroethylene bubbled in at 100°. The precipitate of hydrofluorides of ethylamine and ethylguanidine (28 g) was filtered off, and white crystals separated from the filtrate. They were purified by dissolving in 10% HCl, boiling with decolorizing carbon, and making slightly alkaline with 10% NaOH. The crystals precipitated were filtered off, yield 15 g (51%), mp 119.5–120.5° (ex water). Found: C 38.40; H 5.00; F 20.25; N 36.70%, calculated for $C_6H_9F_2N_5$: C 38.10; H 4.76; F 20.01; N 37.10%.

2-Difluoromethyl-4-amino-6-cyclohexylamino-s-triazine. The same flask was filled with 22 g (0.155 mole)cyclohexylguanidine and 40 ml dimethylformamide, and tetrafluoroethylene bubbled in at 80–90°, 100 ml water added, and the whole left for 24 hr. The crystals that precipitated were filtered off, yield 5.6 g (45%), mp 147–148° (ex aqueous EtOH). Found: F 15.59; N 29.15%, calculated for $C_{10}H_{15}F_2N_5$: F 15.63; N 28.30%.

2-Difluoromethyl-4-amino-6-allylamino-s-triazine. The same flask was filled with 45.5 g (0.46 mole) allylguanidine and 100 ml dimethylformamide, and the tetrafluoroethylene introduced into the mixture at 50°. Immediately after completion of the reaction, the products were poured into 200 ml water and the whole left for 24 hr. The crystals that came out were filtered off, and recrystallized twice from a mixture of 50 ml MeOH and 200 ml water, yield 14.4 g (47%), mp 137–138°. Found: F 18.97; N 34.83%, calculated for $C_7H_9F_2N_5$: F 18.93; N 34.32%.

2-Fluorochloromethyl-4-amino-6-methylamino-s-triazine. The same flask was filled with 36.5 g (0.5 mole) methylguanidine and 150 ml dimethylformamide. Trifluorochloroethylene diluted with an equal amount of nitrogen was passed into the mixture at 30–40°, when marked resinification occurred. The crystals of hydrofluorides were filtered off, and solvent vacuum distilled off from the filtrate at a temperature not over 45°. 100 ml water was added to the oil residue and the whole kept for 48 hr at 0°. The crystals were then filtered off and dissolved in a minimum amount of 10% HCl, and the solution was boiled with decolorizing carbon and neutralized with 10% NaOH. The white crystals were separated off and carefully washed with water to remove NaCl, yield 6.5 g (21%) mp 143.5–144.5°. Found: 31.22; Cl 17.80; F 9.60; N 36.12%, calculated for $C_5H_7ClFN_5$: C 31.34; Cl 18.52; F 9.92; N 36.52%.

2-Fluorochloromethyl-4-amino-6-ethylamino-s-triazine. The same flask was filled with 43.5 g (0.5 mole) ethylguanidine and 250 ml dimethylformamide. Trifluorochloroethylene diluted with nitrogen in the ratio 1 : 1 was bubbled into the solution at 20–30°. The crystals that precipitated (18.9 g) were filtered off, and the solvent vacuum distilled off from the filtrate at 45°. The dark oil that remained was dissolved in 10% HCl, and the solution was boiled with decolorizing carbon. Neutralization with 10% NaOH then precipitated an oil, which on standing crystallized to give white crystals. The operation was repeated 3 times mp 130.5–131.5. Found: Cl 17.00; F 9.15; N 33.75%, calculated for $C_6H_9ClFN_5$: Cl 17.25; F 9.25; N 34.08%.

2-Fluorochloromethyl-4-amino-6-cyclohexylamino-s-triazine. The same flask was filled with 19 g (0.135 mole) cyclohexylguanidine and 100 ml dimethylformamide, and trifluorochloroethylene was bubbled in at 30–40°. Then the crystals were filtered off, and solvent vacuum distilled off from the filtrate at 45°. The residual oil was dissolved in 10% HCl, boiled with decolorizing carbon, and neutralized with 40% KOH. On standing the oil that precipitated gave white crystals, recrystallized thrice from 50% aqueous MeOH, mp 136.5–138.5°. Found: Cl 13.15; F 7.52; N 27.25%, calculated for $C_{10}H_5ClFN_5$: Cl 13.70; F 7.35; N 27.00%.

2-(α-Hydroperfluoroethyl)-4-amino-6-ethylamino-s-triazine. The same flask was filled with 26.1 g (0.3 mole) ethylguanidine and

*The spectra were determined by E. N. Boitsov, with a UR-10 instrument, after tableting with KBr.

200 ml dimethylformamide, and perfluoropropene passed into the solution at 30-40°. The crystalline precipitate was filtered off, and solvent vacuum distilled off at 45°, after which vaccum distillation of the residual oil gave a cut with bp 134-140° (1 mm), from which white crystals separated out on standing, mp 114.5-115.5° (ex water). Found: C 35.45; H 4.42; F 31.26; N 29.52%, calculated for $C_7H_9F_4N_5$: C 35.14; H 3.76; F 31.80; N 29.29%.

Chlorination of guanamines. (table). A mixture of 0.025 mole of the desired guanamine, 5 g AcONa, and 70 ml water was vigorously stirred and cooled (5-10°) while chlorine was passed in for 2 hr. The next day the precipitate was filtered off, dried, and crystallized twice from dichloroethane. In a number of cases the chlorination products came down as an oil which crystallized on keeping.

Cyanoethylation of 2-difluoromethyl-4-amino-6-methylamino-s-triazine. 19 ml Acrylonitrile was added dropwise to a constantly stirred solution of 4 g (0.023 mole) 2-difluoromethyl-4-amino-6-methylamino-s-triazine in 50 ml dimethylformamide, and the product left for a few days at room temperature. The solvent was completely vacuum distilled off, and the residue treated with water, after which the crystals were separated off.

Cyanoethylation of 2-difluoro-4-N-methyl-β-cyanoethyl-6-N-di-β-cyanoethyl-s-triazine. Yield 5.5 g (76%), mp 93.5-94.5° (ex water). Found: C 50.8; H 5.0; F 11.9; N 31.1%, calculated for $C_{14}H_{15}F_2N_8$: C 50.3; H 4.8; F 11.4; N 33.6%.

2-Difluoromethyl-4-N-ethyl-β-cyanoethyl-6-N-di-β-cyanoethyl-s-triazine. This was synthesized similarly, mp 80-81° (ex water), yield 65%. Found: C 50.8; H 5.0; F 11.9; N 31.1%, calculated for $C_{15}H_{18}F_2N_8$: C 51.7; H 5.2; F 10.9; N 32.1%.

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