REACTION OF 2,4,6-TRICHLORO-1,3,5-TRIAZINE WITH NUCLEOPHILIC REAGENTS IN THE PRESENCE OF TERTIARY AMINES

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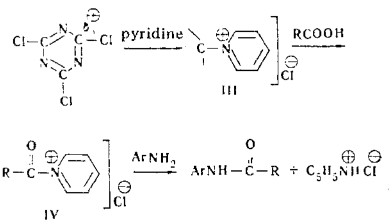
A mechanism for the nucleophilic substitution of halogen in cyanuric chloride in the presence of tertiary amines is proposed. When carboxylic acids react with cyanuric chloride in the presence of tertiary amines, quaternary acylammonium salts are formed which can be used as acylating agents.

Nucleophilic replacement of the chlorine atoms in 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride) is of great practical importance. It is known that the process is catalyzed by carboxylic acids [1] and tertiary amines [2], in particular pyridine. According to the literature [2], in the reaction of cyanuric chloride with primary amines the addition product I is formed in the first stage of the reaction, its subsequent transformation being accelerated both by acids and by pyridine and being completed by the formation of the amino-substituted cyanuric chloride II.

If the reaction of cyanuric chloride with primary amines actually takes place through a stage of the formation of the intermediate product I, the combined action of this product of a carboxylic acid and pyridine should also lead to the substituted product II (provided that the primary amine and the carboxylic acid do not react with one another). However, experiments that we have carried out on the reaction of cyanuric chloride with primary amines (and also with other nucleophilic reagents) in the presence of equimolar amounts of pyridine and carboxylic acid led to acyl derivatives of the amines and also to hydroxy and mercapto compounds. It is obvious that this result is not in harmony with the mechanism of the nucleophilic substitution of the chlorine in cyanuric chloride discussed above. On the contrary, the direction of the reaction that we have observed can be explained by the fact that the rate of rereaction of the pyridine with the cyanuric chloride is greater than the rate of reaction of the latter with the primary amines, i.e., by the formation in the first stage of the process of the quaternary cyanurylammonium salt III.

The quaternary cyanurylammonium salts are unstable reactive compounds that are the intermediate products of a whole series of reactions of cyanuric chloride in the presence of tertiary amines [3–5], and they have been isolated repeatedly [6]. On reacting with a carboxylic acid, cyanurylammonium salts form acylammonium salts [7], which, as is well known, are strong acylating agents. In the light of what has been said, the scheme of the reaction can be shown in the following way:



To confirm the proposed scheme, the primary amine was omitted from the reaction. Cyanuric chloride, m-nitrobenzoic acid, and pyridine in a molar ratio of 1 : 2 : 2 were heated in chlorobenzene to 60° C and left for 12 hr. Under these conditions, in addition to the acylpyridinium salt, the anhydride and chloride of the carboxylic acid were isolated from the reaction mixture with yields of 27 and 6%, respectively, which, as is well known, are the same as those given by acylpyridinium salts.

The reaction considered is similar to the acylation of carboxylic acids in the presence of halogenocyclo-

Preparation of Acyl Derivatives

Nucleophilic reactant	Carboxylic acid*	Tertiary amine	Solvent	Acyl derivative	
				Mp, °C	yield, %
4-Aminoazobenzene	Acetic	Pyridine	Pyridine	151—152[12]	91.0
” ”	” ”	” ”	Acetic acid	” ”	89.0
” ”	” ”	” ”	Chlorobenzene	150—151	86.5
” ”	” ”	Quinoline	Acetic acid	” ”	85.0
Naphth-2-ylamine	Isovaleric	Pyridine	Pyridine	138[13]	83.0
Naphth-2-ol	Acetic	” ”	” ”	69[14]	82.0
Thionaphth-2-ol	” ”	” ”	” ”	52—53[15]	77.0

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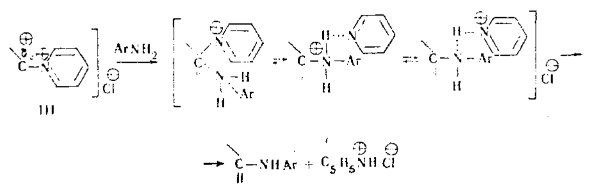
*The molar ratio of cyanuric chloride to nuncleophilic reactant to carboxylic acid, in those cases where the latter was not the solvent, was 1 : 3 : 3.

phosphazenes and tertiary amines [8] and agrees completely with the nature of cyanuric chloride as an acid chloride [9,10]. It is obvious that the highly reactive cyanurylpyridinium salt III can also react with the primary amine, as well as the acylpyridinium salts IV. In actual fact, in a number of experiments substituted cyanuric chlorides were isolated in low yield from the products of the reaction of cyanuric chloride, amines, and carboxylic acids in the presence of pyridine. However, the rate of the reaction of a cyanurylpyridinium salt with carboxylic acids is apparently so great that the formation of the products of the replacement of the chlorine in cyanuric chloride scarcely takes place in the presence of acids. Acyl derivatives of amines and of hydroxy and mercapto compounds were obtained with any order of addition of the reactants. The maximum yield of acyl derivatives was found when the cyanuric chloride was added last and when the pyridine or the acid was used as solvent or in an amount somewhat greater than that necessary for the reaction.

Where there was no acid in the reaction mixture, the ordinary nucleophilic replacement of the chlorine atom in the acid chloride (cyanuric chloride) in the presence of a tertiary amine (pyridine) acting as catalyst, took place.



It is obvious that in compound III the partial positive charge on the carbon atom of the triazine ring considerably exeeds that in cyanuric chloride because of the greater electrophilicity of the pyridinium residue as compared with the electrophilicity of the chlorine atom. The nucleophilic attack of the chlorine atoms of the triazine ring is facilitated by the formation of the intermediate compound.

EXPERIMENTAL

4-Phenylazoanilide of propionic acid. A solution of 3.42 g (~0.016 mole) of 4-aminoazobenzene in 10 ml of pyridine was treated with 1.4 g (~0.016 mole) of propionic acid, and the mixture was heated to 95° C. Then 1.8 g (0.01 mole) of cyanuric chloride was added, and the mixture was stirred at the same temperature for 20 min, after which it was passed through a column of alumina, giving 3.8 g (86.7%) of reaction product with mp 169–170° C; according to the literature [11], mp 170° C.

Naphth-2-yl propionate. A mixture of 4.3 g (0.03 mole) of naphth-2-ol, 3 ml of propionic acid, and 11 ml of pyridine was heated to 95° C, and 2 g (~0.011 mole) of cyanuric chloride was added. The mixture was stirred at 95° C for 20 min and was then poured into water. The product obtained, with an unpleasant aniseed smell, was crystallized from acetone, giving 4.4 g of naphth-2-yl propionate (yield 74%) with mp 49–50° C. According to the literature [7], mp 51° C.

The acyl derivatives of the compounds given in the table were obtained under similar conditions.

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