SYNTHESIS AND SOME CHEMICAL TRANSFORMATIONS OF N-(2,4-DICHLORO-s-TRIAZIN-6-YL)-N-ALKYL-N'-ALKYLCHLOROFORMAMIDINES

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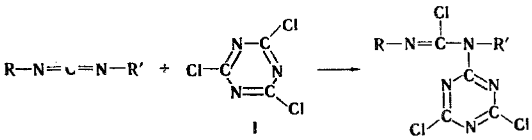
The reaction of cyanuric acid chloride (2,4,6-trichloro-1,3,5-triazine) with a number of dialkylcarbodiimides was investigated. It is shown that the corresponding N-(2,4-dichloro-s-triazin-6-yl)-N-alkyl-N'-alkylchloroformamidines are formed as a result of the reaction. The reaction of the synthesized chloroformamidines with primary and secondary amines was investigated. It is shown that the reaction takes place with substitution of the chlorine atom in the triazine ring.

A number of melamine derivatives display bactericidal and insecticidal activity and are antibiotics. From this point of view the preparation of new derivatives of cyanuric acid chloride (2,4,6-trichloro-1,3,5-triazine) and a study of their properties are of interest. We studied the reaction of cyanuric acid chloride (I) with a number of carbodiimides and the reaction of the resulting chloroformamidines with nucleophilic reagents. At the start of our research it was known [1] that dicyclohexylcarbodiimide reacts with I to give a product of addition to one C═N bond of the carbodiimide.

In a study of the effect of solvents on the course of the reaction between carbodiimides that contain alkyl and cycloalkyl substituents we found that the reaction does not take place in solvents such as diethyl ether, n-heptane, benzene, and acetonitrile. On the other hand, the reaction takes place quite smoothly in methylene chloride at 20°C and is complete in 30 min to 7 h [as monitored by thin-layer chromatography (TLC)]. The corresponding addition products, viz., N-(2,4-dichloro-s-triazin-6-yl)-N-alkyl-N'-alkylchloroformamidines (IIa-e), were isolated in 50-85% yields (see Table 1).



I

II a-e

II a $R=R'=-CH(CH_3)_2$; b $R=R'=\text{cyclo-}C_6H_{11}$; c $R=R'=-C(CH_3)_3$; d $R=-C(CH_3)_3$, $R'=\text{cyclo-}C_6H_{11}$; e $R=-C(CH_3)_3$, $R'=-CH(CH_3)_2$

The yields of reaction products decreased somewhat when the reaction was carried out in chloroform. An increase in the reaction temperature also leads to a decrease in the yields of the desired products, probably as a consequence of an increase in the rate of polymerization of the carbodiimide under the influence of traces of HCl contained in I. The steric effects of the substituents in the carbodiimide molecule have a great influence on the course of the addition reaction. We were unable to obtain products of addition of I to the readily polymerized N-methyl-N'-n-propyl- and N-allyl-N'-n-propylcarbodiimides. The reaction is complete in 30-45 min with dicyclohexylcarbodiimide, as compared with 5-7 h in the case of carbodiimides that contain mixed cycloalkyl, n-alkyl, and isoalkyl substituents. In the case of N,N'-di-tert-butylcarbodiimide an addition product was obtained in satisfactory yield (50%) only after refluxing in methylene chloride for 7 h. We also established that replacement of one chlorine atom in the I molecule by an aminoaryl or aminoalkyl substituent leads to the loss of the ability of the triazine to undergo the addition reaction under the investigated conditions.

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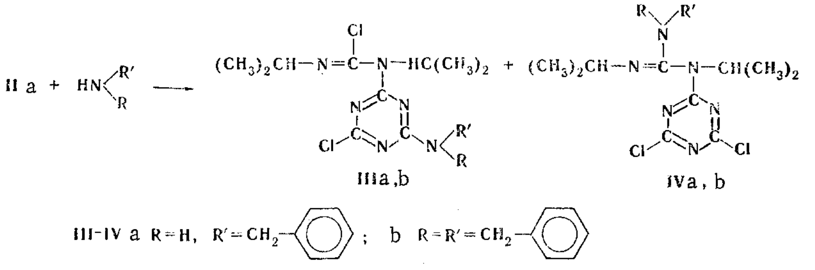
The compositions and structures of the compounds obtained were confirmed by the results of elementary analysis and by the IR and PMR spectra.

An analysis of the PMR spectra made it possible to conclude that only one of the possible isomers is formed in the case of unsymmetrically constructed carbodiimides and that the triazine grouping is attached to the nitrogen atom that is bonded to the least sterically hindered substituent.

It is known that exchange of the chlorine atoms is, as a rule, a stepwise process in the reaction of I with nucleophiles; as the chlorine atoms are replaced, their reactivities decrease [2]. In this connection it was of interest to compare the relative reactivities of the chlorine atoms in the triazine ring and in the open chain.

A study of the reaction of IIa with benzyl- and dibenzylamine showed that when the reaction is carried out in the presence of sodium bicarbonate, it leads to compounds that are contaminated with hydrolysis products. The reaction was therefore carried out by the method in [3] with a twofold excess of the amine. The IR spectra of the compounds obtained contain a band at 1680 cm^{-1}, which was also present in the spectra of chloroformamidines IIa-e and was assigned to the $\mathrm{Cl{-}\overset{|}{C}{=}N}$ bond. This fact made it possible to assume that the reaction proceeds with replacement of the chlorine atom in the triazine ring to give structure III, since otherwise one obviously might have expected a shift of this band to the longer-wave region.



Evidence for the structures of the synthesized compounds was also obtained from the ^{13}C NMR spectra. In addition to signals that are characteristic for the carbon atoms of isopropyl groups, the ^{13}C NMR spectrum of IIa contains a signal at 128.03 ppm, which belongs to the carbon atom bonded to chlorine, as well as two signals with chemical shifts of 164.24 and 170.12 ppm, which are related to the carbon atoms of the triazine ring; the signal of the carbon atoms bonded to the chlorine atoms is found at weaker field. A new signal with a chemical shift of 153.41 ppm appears in the spectrum of IIIa, which confirms that the reaction takes place via the proposed scheme. It is evident that in the case of reaction via the alternative scheme (structure IVa) one must expect a shift to stronger field of the signal belonging to the carbon atom bonded to the chlorine atom in the linear chain.

Finally, in the PMR spectrum of the compound obtained from IIa and dibenzylamine two signals are observed for the CH_2 group. This fact may be the result of both retarded rotation of the dibenzylamino group in the molecule with structure IIIb and a similar effect in the molecule with structure IVb. The experimentally found free energy of the barrier to rotation (17.59 kcal/mole, determined by dynamic PMR) nevertheless constitutes evidence in favor of structure IIIb, since similar energies are known for triazine derivatives [4], whereas these values are lower for guanidine derivatives.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a BS-487C spectrometer (80 MHz) with hexamethyldisiloxane as the internal standard. The ^{13}C NMR spectra were measured with a Bruker Physic AG WH-90 spectrometer with an operating frequency of 22.63 MHz with respect to ^{13}C nuclei; the chemical shifts were determined relative to $CDCl_3$ (δ ^{13}C = 77.0 ppm).

N-(2,4-Dichloro-s-triazin-6-yl)-**N-Alyl-N'-alkylchloroformamidines** (IIa-d). A solution of 5 mmole of the corresponding carbodiimide in 2 ml of CH_2Cl_2 was added dropwise with vigorous stirring to a suspension of 5 mmole of I in 5 ml of absolute CH_2Cl_2, and the mixture was stirred at 20°C for the appropriate time (in the case of IIc the mixture was refluxed for 7 h).

TABLE 1. N-(2,4-Dichloro-s-triazin-6-yl)-N-alkyl-N'-alkylchloroformamidines (IIa-e)

Compound	mp,[a] °C (hexane)	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
IIa	36—37	39,5	5,0	21,6	$C_{10}H_{14}Cl_3N_5$	38,6	4,5	22,5	85
IIb	101—102[b]	49,6	6,1	18,2	$C_{16}H_{22}Cl_3N_5$	49,2	5,6	17,9	78
IIc	124—126	43,3	6,3	21,5	$C_{12}H_{18}Cl_3N_5$	42,5	5,3	20,7	52
IId	168—171	46,6	6,0	19,7	$C_{14}H_{20}Cl_3N_5$	46,1	5,5	19,2	80
IIe	75—77	41,3	4,4	22,4	$C_{11}H_{16}Cl_3N_5$	40,7	4,9	21,6	76

[a] The reaction was carried out in CH_2Cl_2 for 300-420 min (30 min in the case of IIb). [b] According to [1], this compound had mp 101°C.

The precipitate was removed by filtration, and the filtrate was concentrated and allowed to stand in the cold. The precipitated crystals were separated, washed with dry hexane, and dried.

N-(2-Chloro-4-benzylamino-s-triazin-6-yl)-N-isopropyl-N'-isopropylchloroformamidine (IIIa) and N-(2-Chloro-4-dibenzylamino-s-triazin-6-yl)-N-isopropyl-N'-isopropylchloroformamidine (IIIb). A 0.02-mole sample of the corresponding amine in ether was added at 3-5°C to a solution of 0.01 mole of IIa in absolute ether, and the mixture was stirred for 30 min. Cooling was discontinued, and the mixture was stirred at 20°C for another 30 min. The precipitated amine hydrochloride was removed by filtration, and the filtrate was concentrated and allowed to stand in the cold. The precipitated crystals were separated, washed with dry hexane, and dried. Compound IIIa, with mp 136-137°C (hexane), was obtained in 52% yield. Found: C 54.0; H 6.2; N 22.2%. $C_{17}H_{22}Cl_2N_6$. Calculated: C 53.5; H 5.8; N 22.0%. Compound IIIb, with mp 60-61°C (hexane), was obtained in 49% yield. Found: C 61.5; H 6.3; N 18.0%. $C_{24}H_{28}Cl_2N_6$. Calculated: C 61.2; H 5.9; N 17.8%. PMR spectrum: 1.12 (6H, J = 6.5 Hz, CH_3), 1.45 (6H, J = 7.25 Hz, CH_3), 3.90 (1H, m, CH), 5.10 (1H, m, CH), 4.83 (2H, CH_2), 4.72 (2H, CH_2), and 7.25 ppm (10H, C_6H_5).

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