SYNTHESIS AND THERMAL DECOMPOSITION OF HALOALKOXY-sym-TRIAZINES

I. SYNTHESIS OF CHLOROETHOXY-sym-TRIAZINES AND THEIR CONVERSION TO DIHYDROIMIDAZO-sym-TRIAZINES

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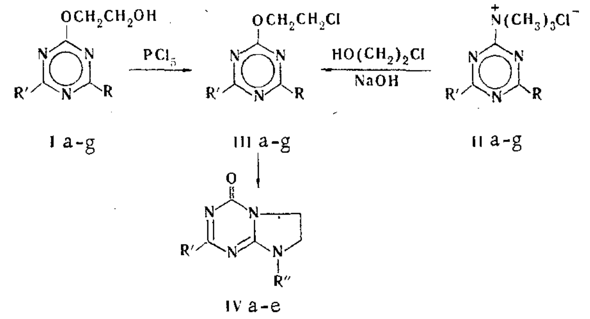
The reaction of 4,6-bis[alkyl(dialkyl)amino]- or (4-alkylamino-6-dialkylamino-sym-triazin-2-yl)trimethylammonium chlorides with ethylene chlorohydrin and the action of phosphorus pentachloride on 2-β-hydroxyethoxy-sym-triazines give 2-β-chloroethoxy derivatives of sym-triazine, which on heating are converted to imidazo[1,2-a]-sym-triazine derivatives.

Like 2-(β-hydroxyethoxy)- and 2-(β-hydroxyethylthio)-4,6-bis[alkyl(dialkyl)amino]-sym-triazines [1]. 2-(β-chloroethoxy)-4,6-bis[alkyl(dialkyl)amino]- or 4-alkyl-6-dialkylamino-sym-triazines (III) could be of interest as physiologically active compounds.

We obtained these compounds by the action of phosphorus pentachloride on the appropriate alcohols (I) and also by reaction of quaternary ammonium salts II with ethylene chlorohydrin:



I—III a $R=R'=NHCH_3$; b $R=R'=NHC_2H_5$; c $R=R'=NHC_3H_7\text{-}i$; d $R=NHCH_3$, $R'=N(CH_3)_2$; e $R=NHC_2H_5$, $R'=N(C_2H_5)_2$; f $R=R'=N(CH_3)_2$; g $R=R'=N(C_2H_5)_2$; IV a $R'=NHCH_3$, $R''=CH_3$; b $R'=NHC_2H_5$, $R''=C_2H_5$; c $R'=NHC_3H_7\text{-}i$, $R''=C_3H_7\text{-}i$; d $R'=N(CH_3)_2$, $R''=CH_3$; e $R'=N(C_2H_5)_2$, $R''=C_2H_5$

We were unable to replace the hydroxyl group of alcohols I by means of thionyl chloride, since IIIa-g proved to be unstable at moderate temperatures. Compounds IV, which differ sharply from the starting chloro derivatives, are formed when they are heated in benzene and toluene. Under similar conditions 2-alkoxy-4,6-bisalkylamino-sym-triazines do not undergo any changes whatsoever. Isomerization of alkoxy-sym-triazines to N-alkyl derivatives usually occurs at higher temperatures and upon longer heating [2].

Considering the fact that 2-hydroxyethoxy-sym-triazines I, in contrast to 2-chloroethoxy derivatives III, remain unchanged when they are heated, it might be assumed that the formation of intramolecular quaternary salts V, which are cleaved by the action of the chloride ion to give N-β-chloroethyl-sym-triazines VI, precedes the formation of IV. Triazines VI undergo intramolecular quaternization to give salts VII, which, in the case of IIIf, g, are unstable under the reaction conditions and are converted, with splitting out of alkyl chlorides, to final products IVd, e. In the case of IIIa-e, however, the dehydrochlorination of intermediately

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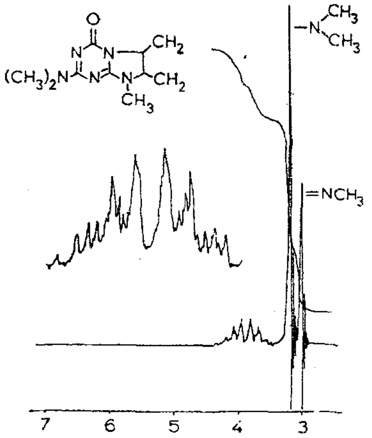


Fig. 1. PMR spectrum of IVd.

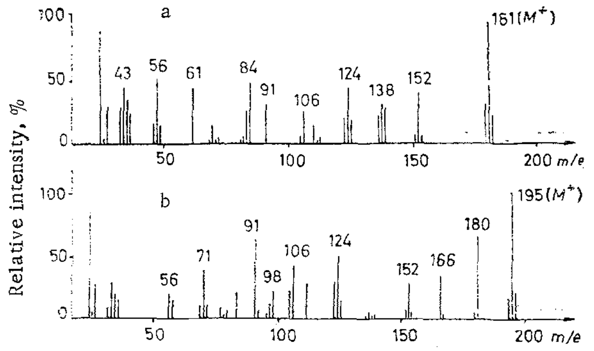
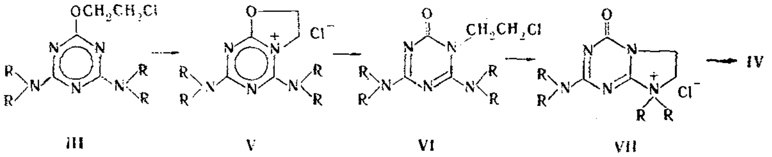


Fig. 2. Mass spectra: a) IVa; b) IVd.

formed salts VII occurs when they are treated with a solution of alkali. The structures of IVa-e as imidazo-sym-triazine derivatives are confirmed by the results of elementary analysis and IR and PMR spectroscopic data.

The IR spectrum of IIIb contains absorption bands of NH groups at 3320 and 3390 cm^{-1} and of a C−O−C group at 1065, 1080, 1160, and 1185 cm^{-1}; ring vibrations are observed at 1540, 1560, and 1600 cm^{-1}. The absorption band of the NH group in the spectrum of IVb appears at 3325 cm^{-1}, the band of the C=O group (conjugated) appears at 1685 cm^{-1}, and the band of ring vibrations shows up at 1560, 1585, and 1615 cm^{-1}. The absorption bands of a C−O−C group also vanish in the IR spectrum of IVd, obtained from IIId and IIIf, an absorption band of a C=O group appears at 1695 cm^{-1}, and ring vibrations show up at 1530, 1570, and 1630 cm^{-1}.



The PMR spectrum of IVd, in which the two triplets characteristic for the OCH_2CH_2Cl fragment of IIId (an A_2B_2 spin system) are converted to the symmetrical multiplet centered at 3.9 ppm characteristic for an AA'BB' system, is presented in Fig. 1. This sort of conversion constitutes evidence that the CH_2CH_2 group in IVd constitutes part of a fixed, i.e., cyclic system. Data from the mass spectra of IVa and IVd (Fig. 2, spectra a and b) also speak in favor of an imidazotriazine structure.

The pathways for the formation of a series of characteristic fragments that prove the proposed structures of the compounds are presented below on the basis of the metastable transitions and shifts of the corresponding peaks in the spectra of IVa, d:

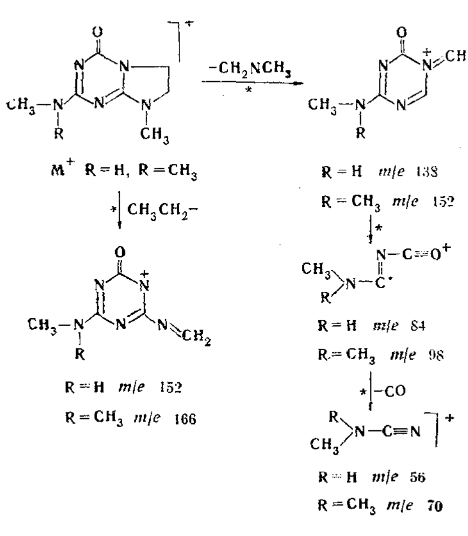


TABLE 1. 2-(β-Chloroethoxy)-4,6-bis[alkyl(dialkyl)amino]- and 4-Alkylamino-6-dialkylamino-sym-triazines

Compound	mp, °C	Found, %		Empirical formula	Calc., %		Yield, %	
		Cl	N		Cl	N	a	b
IIIa	122—123	16,7	32,4	$C_7H_{12}ClN_5O$	16,3	32,1	68	71
IIIb	84—85	14,6	28,2	$C_9H_{16}ClN_5O$	14,5	28,5	73	88
IIIc	113—115	13,2	25,8	$C_{11}H_{20}ClN_5O$	13,0	25,6	70	83
IIId	122—124	15,6	30,5	$C_8H_{14}ClN_5O$	15,3	30,2	87	97
IIIe	60—62	13,3	27,1	$C_{11}H_{20}ClN_5O$	13,0	27,0	83	97
IIIf	72—73	14,7	28,6	$C_9H_{16}ClN_5O$	14,5	28,5	81	88
IIIg	Oil	12,0	23,5	$C_{13}H_{24}ClN_5O$	11,8	23,2	80	83

TABLE 2. 2-Alkyl(dialkyl)amino-4-oxo-8-alkyl-6,7-dihydroimidazo-[1,2-a]-sym-triazines

Compound	mp, °C	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Cl	N		C	H	Cl	N	
IVa	232—233	46,6	6,4	—	38,9	$C_7H_{11}N_5O$	46,4	6,1	—	38,6	82
IVa · HCl	260—262	38,8	5,8	16,7	32,4	$C_7H_{11}N_5O \cdot HCl$	38,6	5,5	16,4	32,1	90
IVb	196—198	51,5	7,3	—	33,7	$C_9H_{15}N_5O$	51,7	7,1	—	33,4	89
IVb · HCl	233—235	44,2	6,7	14,6	28,8	$C_9H_{15}N_5O \cdot HCl$	43,9	6,5	14,5	28,5	99
IVc	207—209	55,8	8,3	—	29,7	$C_{11}H_{19}N_5O$	55,7	8,0	—	30,0	87
IVc · HCl	259—261	48,3	7,6	13,1	25,9	$C_{11}H_{19}N_5O \cdot HCl$	48,2	7,3	13,0	25,6	89
IVd	169—171	49,4	6,8	—	35,6	$C_8H_{13}N_5O$	49,2	6,7	—	35,9	91
IVd · HCl	203—204	41,7	6,3	15,5	30,4	$C_8H_{13}N_5O \cdot HCl$	41,5	6,0	15,3	30,2	98
IVe	94—95	55,4	8,3	—	30,2	$C_{11}H_{19}N_5O$	55,7	8,0	—	30,0	79
IVe · HCl	175—178	48,5	7,5	13,3	27,2	$C_{11}H_{19}N_5O \cdot HCl$	48,2	7,3	13,0	27,0	94

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer. The PMR spectra of $CDCl_3$ solutions of the compounds were recorded with a Varian T-60 spectrometer with tetramethylsilane as the internal standard. The individuality of the compounds was monitored by thin-layer chromatography (TLC) on activity II Al_2O_3 with elution by acetone–hexane (20 : 80 or 15 : 85) and development with 0.5% $AgNO_3$ solution and in UV light.

2-(β-Chloroethoxy)-4,6-bis[alkyl(dialkyl)amino]- or 4-Alkyl-6-dialkylamino-sym-triazines (IIIa-g, Table 1). A) A 0.1-mole sample of I was added with stirring and cooling (to −5°) to a suspension of 20.8 g (0.1 mole) of phosphorus pentachloride in 20 ml of absolute ether, after which the mixture was refluxed for 3 h. It was then allowed to stand overnight, after which it was diluted with ice water and neutralized with $NaHCO_3$. The precipitate was removed by filtration.

B) A total of 4.0 g (0.1 mole) of 10% NaOH solution was added slowly dropwise with stirring and cooling (to −5°) to a mixture of 0.1 mole of II and 32.3 g (0.4 mole) of ethylene chlorohydrin, after which the mixture was maintained under the same conditions for 1.5 h. It was then treated with 50 ml of water, and the resulting precipitate was removed by filtration.

2-Alkyl(dialkyl)amino-4-oxo-8-alkyl-6,7-dihydroimidazo[1,2-a]-sym-triazines (IVa-e, Table 2). A suspension of 0.01 mole of IIIa-e in 10 ml of xylene was heated at 150° for 5 h, after which the hydrochlorides of IV were removed from the hot solution by filtration. A 0.4-g (0.01 mole) sample of 10% NaOH solution was added gradually to a solution of 0.01 mole of the hydrochloride in 5 ml of water, after which the mixture was evaporated to one-third of its original volume and extracted with chloroform. The extract was dried with $MgSO_4$, and the chloroform was removed by distillation to give IVa-e.

2-Dimethylamino-4-oxo-8-methyl-6,7-dihydroimidazo[1,2-a]-sym-triazine (IVd). A suspension of 2.45 g (0.01 mole) of IIIf in 10 ml of xylene was heated as described above, during which methyl chloride was evolved vigorously at 120-130°. The methyl chloride was trapped with an acetone solution of 0.76 g (0.01 mole) of thiourea. Compound IVd was isolated from the xylene solution, and 0.7 g (55%) of S-methylisouronium chloride, with mp 60-61° (mp 59-61° [4]), was removed from the acetone solution after 2 h by filtration. Found: Cl 28.7; S 25.6%. $C_2H_7ClN_2S$. Calculated: Cl 28.2; S 25.3%.

Imidazotriazine IVe was similarly obtained from IIIg.

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TETRAZOLE DERIVATIVES

XIII.* SYNTHESIS AND PROPERTIES OF 1-(1-METHYL-5-TETRAZOLYL)-3,5-DIPHENYLFORMAZAN, A TETRAZOLIUM SALT, AND THE VERDAZYL RADICAL

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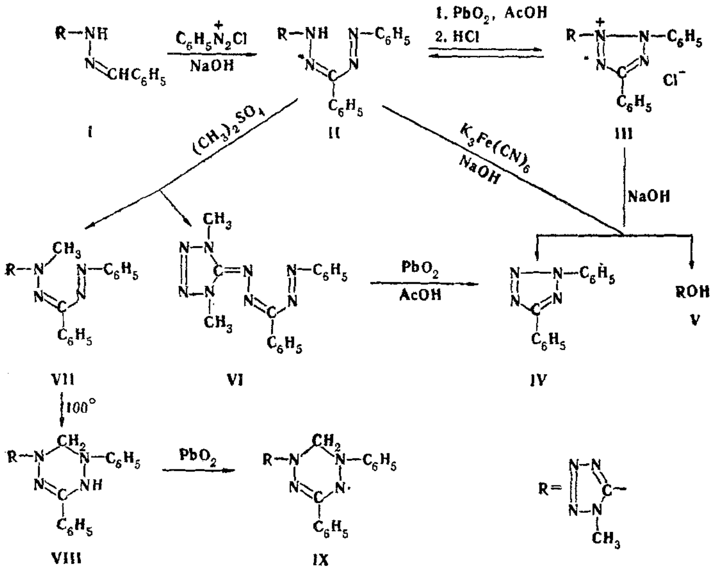
The formazan named in the title and its corresponding tetrazolium salt were synthesized. It is shown that both of these compounds are capable of cleavage to give two tetrazole fragments. Reaction products involving the ring and exocyclic nitrogen atoms are formed in the methylation of the formazan. The product from the exocyclic nitrogen atom on heating is converted to a leucoverdazyl radical, which is capable of undergoing oxidation to give the 1-(1-methyl-5-tetrasolyl)-3,5-diphenylverdazyl radical.

One of the characteristic peculiarities of formazans and verdazyl radicals containing a tetrazole residue attached to the $N_{(1)}$ atom is their ability to readily undergo oxidation to give the corresponding tetrazolium [2] and verdazylium [3] salts with betaine structures. In order to exclude the possibility of the formation of betaines, we attempted to obtain a formazan and a verdazyl radical containing a tetrazole residue with a methyl group in the 1 position.



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*See [1] for communication XII.

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