REACTION OF HALO-sym-TRIAZINES WITH N-ALKYLHYDROXYLAMINES

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The reaction of 2-chloro-4-methoxy-(benzyloxy, methylthio)-6-alkylamino-sym-triazines with N-alkylhydroxylamine to give the corresponding N-alkylhydroxylamino derivatives of sym-triazine has been examined. The IR spectra of the compounds prepared are discussed.

We have previously noted [1,2] the increased reactivity of N-methyl, N-phenyl, and unsubstituted hydroxylamines in their reactions with cyanuric chloride and 2,4-dichloro-6-(di)alkylamino-sym-triazines The extreme lability of the main products of these reactions [2-chloro-4-(di)alkylamino-6-aryl(alkyl)hydroxylamino-sym-triazines] was demonstrated, and some reactions characterizing these compounds as N-hydroxylamino derivatives were carried out.

In this paper, the reaction of 2-chloro-4-R'-6-alkylamino-sym-triazines ($R^1 = OCH_3$, $OCH_2C_6H_5$, or SCH_3) with hydroxylamines ($R^2 = CH_3$, C_2H_5, or $i\text{-}C_3H_7$) is considered. This reaction proceeds under somewhat milder conditions than those described for the replacement of the third chlorine atom in sym-triazines by the more basic alkylamine residues. The reaction was carried out in aqueous dioxane at pH ~ 7-8 in a stream of nitrogen at 50-80° C for 2-3 hr to give the N-alkylhydroxylamino-sym-triazines in quite good yields, in some instances exceeding 80% despite the difficulties in purification from partially resinified products.

All the compounds prepared (see Table 1) have the same properties as those recorded for 2-chloro-4-dialkylamino-6-N-arylhydroxylamino-sym-triazines [2]. They dissolve readily in dilute alkalis and are reprecipitated unchanged on acidification to pH 7, they give intense blue-violet colors with $FeCl_3$, and on thin layer chromatograms are readily visualized as blue spots without the use of a developing agent. The main difference between the 2-alkylthio derivatives and the corresponding 2-chloro analogs lies in their thermal stability, especially toward distillation in a high vacuum. Thus, in every case which we have examined, the N-triazinyl derivatives of the N-alkylhydroxylamines obtained were in agreement with the results obtained in an investigation of the reaction of N-substituted hydroxylamines with other acylating agents [3,4].

The structure of the 2-R-4-alkylamino-6-N-alkylhydroxylamino-sym-triazines has been confirmed by their IR spectra (Fig. 1). We see from the spectra of 2-alkoxy-4-alkylamino-6-N-methylhydroxylamino-sym-triazines (II and III) that bands due to the stretching vibrations of the free OH group, as in N-phenylhydroxylamine derivatives of sym-triazines (I) [2], appear indirectly. At the same time, the spectra of II and III in the 3000-3500-cm^{-1} region are more complex than that of I due to the presence of the additional NH group in the 4-position. Comparison of these spectra with those of the model isomeric compounds IV and V [5], however, shows the presence of a hydroxyl group in the molecules of these compounds.

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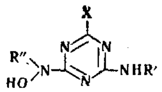
TABLE 1



X	R¹	R²	mp, °C, or bp, °C (nm)	Molecular formula	Found, %			Calculated, %			Purification method	Yield, %
					C	H	N	C	H	N		
OCH_3	C_2H_5	CH_3	100—101	$C_7H_{13}N_5O_2$	42.2	7.0	35.1	42.2	6.6	35.2	Washed free from impurities with cold ether	60
OCH_3	n-C_3H_7	CH_3	55—56 148—149 (0.08)	$C_8H_{15}N_5O_2$	45.3	7.5	32.5	45.0	7.1	32.8	Distillation in vacuo (the residue partly resinified)	64
OCH_3	i-C_3H_7	CH_3	75—76 129—130 (0.05)	$C_8H_{15}N_5O_2$	45.0	7.2	32.5	45.0	7.1	32.8	Precipitated from ether with n-pentane	58
SCH_3	i-C_3H_7	CH_3	90—91	$C_8H_{15}N_5OS$	42.1	6.9	30.4	41.9	6.6	30.6	Precipitated from a 2-N alkaline solution with acetic acid	71
SCH_3	n-C_3H_7	CH_3	54—56	$C_8H_{15}N_5OS$	42.3	6.4	S13.6	41.9	6.6	S14.0	Distillation in vacuo	62
OCH_3	C_2H_5	C_2H_5	75—77 138—139 (0.1)	$C_8H_{15}N_5O_2$	45.0	7.0	32.4	45.0	7.1	32.8	Distillation in vacuo	80,3
OCH_3	i-C_3H_7	C_2H_5	98—100 138—140 (0.04)	$C_9H_{17}N_5O_2$	47.6	7.8	30.8	47.6	7.5	30.8	„ „	70,5
OCH_3	C_2H_5	i-C_3H_7	136—137 (0.03)	$C_9H_{17}N_5O_2$	47.9	8.2	30.9	47.6	7.5	30.8	„ „	85
OCH_3	i-C_3H_7	i-C_3H_7	145—147 (0.17)	$C_{10}H_{19}N_5O_2$	50.2	8.0	29.2	49.8	7.9	29.0	„ „	80
$OCH_2C_6H_5$	i-C_3H_7	CH_3	57—59	$C_{14}H_{19}N_5O_2$	58.7	7.0	24.5	58.1	6.6	24.2	„ „†	50

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* Yield calculated on purified product.

† The compound resinified on distillation in high vacuum. It was purified as follows: 2 g of the crude product was dissolved in 8 ml of warm ethanol and the solution cooled to ~ 20° C. Water (20 ml) was added, then 10% aqueous NaOH until the precipitate dissolved. Acetic acid was then added to pH 7, and the slightly bluish crystals were filtered off, washed with water, and dried in the vacuum desiccator over P_2O_5, then over NaOH, to give 1 g of product.

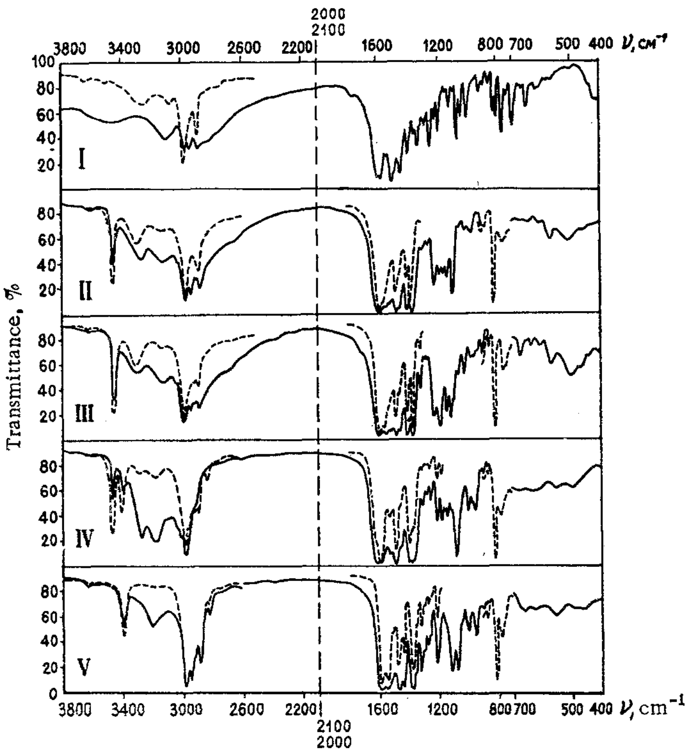

Fig. 1. IR Absorption spectra of hydroxylamino-sym-triazines: I) 2-chloro-4-di-n-propylamino-6-N-phenylhydroxylamino-sym-triazine, II) 2-methoxy-4-n-propylamino-6-N-methylhydroxylamino-sym-triazine, III) 2-methoxy-4-isopropylamino-6-N-methylhydroxylamino-sym-triazine, IV) 2-methoxy-4-n-propylamino-6-methoxyamino-sym-triazine, and V) 2-methoxy-4-di-n-propylamino-6-methoxyamino-sym-triazine.

In the spectrum of V, bands are observed in the 3000-3500-cm^{-1} region with frequencies of 3392 and 3200 cm^{-1}, which are characteristic, respectively, of the stretching frequencies of the NH group in the free state, and when involved in intermolecular hydrogen bonding, since in dilute solutions the lower-frequency band almost disappears. By analogy with the spectrum of V, in the same region, the bands at 3175 and 3392 cm^{-1} in the spectrum of IV must be due to the stretching vibrations of the $NH(OCH_3)$group, and those band with frequencies 3454 and 3267 cm^{-1}, to the stretching vibrations of the NHC_3H_7-n group, both free and involved in hydrogen bonding. Comparison of the spectra of II and III with that of IV shows that the 3450 cm^{-1} band must be due to the stretching vibrations of the free NHC_3H_7-n group. In the spectra of these compounds, the bands at 3271 cm^{-1} (for II) and 3283 cm^{-1} (for III), by analogy with the spectrum of I [2], are assigned to intramolecular hydrogen bonding involving the OH group. This band is also present in the spectra of dilute solutions.

In the spectra of II and III, as well as in that of I, strong absorption occurs in the alkyl CH stretching region, but this band is absent in the spectra of dilute solutions of these same compounds and in the spectra recorded at 70° C (Fig. 2), and also in the corresponding isomers, for example, in the spectrum of IV. This absorption is explained by the formation of strong intermolecular hydrogen bonds with the participation of the OH group, as in compounds of type I.

The 3142-cm^{-1} band in II and III is assigned, by analogy with the spectrum of IV, to intermolecular hydrogen bonding involving the NHC_3H_7-ngroup. The intensity of this band is substantially reduced both in dilute solution, and in the spectra obtained at 70° C (Fig. 2).

The shift of the band for the stretching vibrations of NHC_3H_7-n under the influences of hydrogen bonding amounts to 312 cm^{-1} for II and III, while for the isomeric compounds with the NH(OAlk) group (IV), it

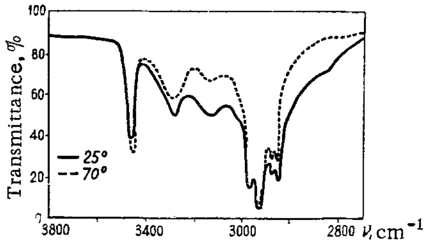

Fig. 2. IR absorption spectra of a solution of 2-methoxy-4-n-propylamino-6-N-methylhydroxylamino-sym-triazine (II) at 25.5° and 70° C.

is 187 cm^{-1}. The increase in the shift of the band for the NHC$_3$H$_7$-n stretching vibrations amounts to 1.7 times, and the presence of a strongly hydrogen bonded OH group also suggests the increase in acceptor properties of diamino-sym-triazines on replacement of the (RO)NH group by the isomeric (HO)(R)N group. Thus, the hydroxyl groups in II and III appear in the spectra as two bands, each corresponding to the type of hydrogen bonding (intra- and intermolecular) in which it participates. The presence of a free hydroxyl group in II and III is also shown by the independent synthesis of 2-methoxy-4-n-propylamino-6-N-methoxymethylamino-sym-triazine (VI) by methylation of the corresponding methoxyamino (IV) and N-methylhydroxylamino derivatives (II). Methylation of II proceeds in quantitative yield. Methylation of IV has been carried out previously [5]. The identity of VI as obtained by the two methods was established by their constants, elementary analyses, thin layer chromatography, and IR spectra.

EXPERIMENTAL

2-Chloro-4-R-6-alkylamino-sym-triazines (R=OCH$_3$, SCH$_3$) were obtained by the reaction between 2,4-dichloro-6-R-sym-triazines (R=OCH$_3$, SCH$_3$) [6] and the amines, by the method given in [7]. 2-Chloro-4-benzyloxy-6-alkylamino-sym-triazine obtained in a similar manner, yield 70%, mp 64-65° C. Found, %: C 56.7; H 5.6; Cl 12.8; N 20.1. Calculated for $C_{13}H_{15}ClN_4O$, %: C 56.0; H 5.4; Cl 12.7; N 20.1.

2-R-4-Alkylamino-6-N-alkylhydroxylamino-sym-triazines (R=OCH$_3$, SCH$_3$, OCH$_2$C$_6$H$_5$). A 0.1-mole quantity of N-alkylhydroxylamine hydrochloride in 10 ml of water at a temperature of -10--5° C was neutralized with 0.1 mole of NaHCO$_3$ in 25 ml of water. To the resulting solution of the alkylhydroxylamine were added simultaneously at 5-10° C over 10 min 0.05 mole of 2-chloro-4-R-6-alkylamino-sym-triazine in 40 ml of dioxane and 0.2 mole of NaHCO$_3$ in 60 ml of water. The pH of the mixture after the addition was 8. The mixture was stirred for 2 hr at 55-60° C and 1 hr at 80° C (pH of mixture ~ 7). On heating, the initial suspension became greenish-violet in color. A stream of nitrogen was passed through the mixture during the entire reaction. The hot reaction mixture was cooled, half its volume of water was added, and acetic acid or dilute HCl was then added to pH 7. The mixture was cooled, saturated with sodium chloride, and extracted with benzene or ether (3 × 70 ml). The organic layer was dried over MgSO$_4$, the solvent removed, and the residue cooled to give 2-R-4-alkylamino-6-N-alkylhydroxylamino-sym-triazine, contaminated with an oily impurity which was removed by the method given in the Table 1.

2-Methoxy-4-n-propylamino-6-N-methoxymethylamino-sym-triazine (VI). To 3.8 g (0.0178 mole) of 2-methoxy-4-n-propylamino-6-N-methylhydroxylamino-sym-triazine (II) in 70 ml of dioxane was added 2.9 g (0.072 mole) of NaOH in 50 ml of water, followed by 4.52 g (0.036 mole) of dimethyl sulfate. The temperature of the mixture rose to 38° C. The mixture was heated at 45-50° C for 1 hr, and for 15 min at 70° C. Completion of the reaction was determined by chromatography. The starting material, when subjected to thin layer chromatography on silica gel with gypsum as the binder, using an acetone + n-hexane mixture (1 : 3) as the solvent, gave a blue spot with R_f 0.15 (before development), while VI was well visualized by development with Dragendorff's reagent as an orange spot, R_f 0.42. The mixture was cooled, acidified with acetic acid to pH 7, and extracted with ether. After drying the ether solution over MgSO$_4$, the solvent was removed to give 4 g (quantitative yield) of VI, bp 127-130° C (0.05 mm), n_D^{21} 1.5260, identical with the compound obtained previously [5] from the corresponding methoxyamino derivative. IR spectrum (in solution in CCl$_4$ and CH$_3$CN): 3454 and 3267 cm^{-1} (stretching frequencies of the free and bound NH groups in NHC$_3$H$_7$-n).

The IR spectra (Fig. 1) were taken on a UR-10 spectrophotometer in KBr disks and in solution in CCl$_4$ (700-400 and 3800-900-cm^{-1} regions), and in CH$_3$CN (900-700-cm^{-1} region). Constant thickness cells having KBr windows were used, the layer thickness being 0.1 and 0.4 mm, and also dismountable cells having quartz windows with layer thickness 20.1 mm for measuring the spectra of dilute solutions. Method of recording: slit program 4, recording speed 150 cm^{-1}/min, time for recording full diffraction 32 sec, recording rate 12 mm/100 cm^{-1}, recording carried out using a retarder. The following concentrations and layer thicknesses were used: I KBr disks, 0.0014 M in CCl$_4$, d 20.1 mm; II 0.1051 M in CCl$_4$, d 0.1 and 0.4 mm, 0.0021 M in CCl$_4$, d 20.1 mm, and 0.0165 M in CH$_3$CN, d 0.4 mm; III 0.1100 M in CCl$_4$, d 0.1 and

0.4 mm, 0.0022 M in CCl_4, d 20.1 mm, and 0.0163 M in CH_3CN, d 0.4 mm; IV 0.1040 M in CCl_4, d 0.1 and 0.4 mm, 0.0021 M , d 20.1 mm, and 0.0418 M, d 0.4 mm; V 0.0935 M, d 0.1 and 0.4 mm, 0.0019 M, d 20.1 mm, and 0.0134 M, d 0.4 mm.

The spectra in Fig. 2 were taken on an IKS-14 spectrophotometer in sealed quartz cells, layer thickness 0.1 mm, solution concentrations 0.0840 M in CCl_4. The cells were placed in a cylindrical oven, whose temperature was regulated and measured by means of an EPP-09 No. 2 potentiometer with a chromel dropping thermocouple.

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