SYNTHESIS AND REACTIONS OF SOME SUBSTITUTED 1, 3, 5-TRIAZINES*

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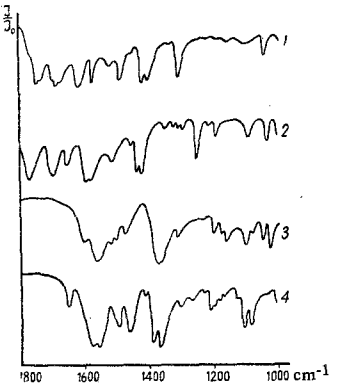
The reactions of 2-substituted 4, 6-dihydroxytriazines with PCl_5 and $SOCl_2$ are investigated. It is shown that conversion of 2-(aryl- and substituted styryl)-4, 6-dihydroxy-1, 3, 5-triazine to the corresponding 4, 6-dichloro compounds is accompanied by ring opening and, in the case of styryl derivatives, by chlorination of the ethylene group. Analysis of the IR spectra of 4, 6-dihydroxytriazines establishes that under ordinary conditions they are 4, 6-dihydroxytetrahydrotriazines. Shift of the lactim-lactam equilibrium towards the oxo form is considered to be the reason why these compounds react with difficulty with $SOCl_2$. A mechanism for the reaction of triazine hydroxy derivatives with PCl_5 is put forward. New substituted triazines and intermediates are synthesized.

We have found that reaction of 2-methyl-4, 6-dihydroxytriazine with PCl_5 in $POCl_3$ at the boiling point of the reactants is accompanied by opening of the triazine ring, and gives a low yield of 2-trichloromethyl-4, 6-dichlorotriazine [1]. The action of the same reagent on 2-benzyl-4, 6-dihydroxytriazine under similar conditions gives 2-(α, α-dichlorobenzyl)-4, 6-dichlorotriazine; in this case reaction is considerably faster, and is not accompanied by appreciable splitting of the triazine ring [2]. The reaction of 2-aryl-4, 6-dihydroxytriazines with PCl_5 gives 2-aryl-4, 6-dichlorotriazines [3–8], and in several cases the yields are high [5, 7, 8], and no triazine ring-opening was found.

Repetition of the synthesis of aryldichlorotriazines by the above method showed reaction to be accompanied by triazine ring opening, though the extent was small. The presence of carbon dioxide in the gases evolved indicates this. Phosgene is not formed, unlike what happens with methyltriazine.

It was of interest to follow the reaction of PCl_5 with the derivative 2-styryl-4, 6-dihydroxytriazine. For that purpose the isomeric 2-nitrostyryl-4, 6-dihydroxytriazine (I) and 2-(p-methoxystyryl)-4, 6-dihydroxytriazine (II) were synthesized. The first was obtained by a route similar to that previously followed [6] in synthesizing aryldihydroxytriazines. II was synthesized by condensing 2-methyl-4, 6-dihydroxytriazine with anisaldehyde.

Reaction of the derivatives of 4, 6-dihydroxytriazine derivatives prepared with PCl_5 showed that there the desired reaction, formation of substituted 2-styryl-4, 6-dichlorotriazine, is accompanied not only by ring opening, but also by chlorination of the aliphatic group to 2-(chlorostyryl)-4, 6-dichlorotriazines. Obviously, addition of chlorine to the double bond, such as occurs when PCl_5 acts on olefins, among them stilbene [9], does not occur here. As in the case of the methyl derivative [1], opening of the triazine ring is accompanied by formation of phosgene, ammonia, and evidently chloramine.



IR Spectra: 1) 2-phenyl-4, 6-"dihydroxytriazine"; 2) 2-styrl-4, 6-"dihydroxytriazine"; 3) 2-phenyl-4, 6-dimethoxytriazine; 4) 2-styrl-4, 6-dimethoxytriazine.

The resultant mixture of 2-styryl- and -(chlorostyryl)-4, 6-dichlorotriazines is difficult to separate. To identify the dichlorides, they were converted to the corresponding, more easily separated, 4, 6-dimethoxytriazines. In the case of the nitro compounds, chlorination of the ethylene group proceeds to a lesser extent than with the methoxystyryl derivatives.

Since 2-substituted 4, 6-dichlorotriazines, like cyanuric chloride, are of potential interest for synthesizing many substances required in various branches of the national economy, it was expedient to try to prepare them by treating dihydroxytriazines with reagents other than PCl_5.

The literature contains only one report regarding the possibility of converting 2-substituted 4, 6-dihydroxytriazines to the corresponding dichlorides by methods other than those given above [3–8]. Thus, a known method of converting 2-methyl-4, 6-dihydroxytriazine to 2-methyl-4, 6-dichlorotriazine is treatment with $POCl_3$ in the presence of a basic catalyst e.g., tertiary amines [11]. It is reported [12] that 2-aryl-4, 6-dichlorotriazines can be synthesized from the corresponding dihydroxy compounds and thionyl chloride in the presence of catalytic amounts of PCl_5.

We tried to prepare dichlorotriazines by treating 2-methyl-, phenyl, or styryl-4, 6-dihyroxytriazines, or their Na or K salts, with thionyl chloride under various conditions, particularly conditions similar to those used to prepare chlorides of carboxylic acids and sulfonyl chlorides [13–15], but the experiments

*As the paper deals only with 1, 3, 5-triazine derivatives, 1, 3, 5-triazine will simply be referred to as triazine.

Table 1

Vibration Frequencies of C=O, C=N, C=C Groups in Triazine Derivatives

Compound	C=O valence vibrations				C=O deformation vibrations				C=N valence vibrations		C=C valence vibrations	
	Antisymmetric		Symmetric		Planar		Out-of-plane					
	ν, cm^{-1}	I*	ν, cm^{-1}	I	ν, cm^{-1}	I	ν, cm^{-1}	I	ν, cm^{-1}	I	ν, cm^{-1}	I
Cyanuric acid	1710	very strong	1800	medium	545 535	very strong	765	weak	—		—	
2-Methyl-4, 6-dioxotetrahydrotriazine	1698	very strong	1767	very strong	546 534	medium	767	medium	1596	very strong	—	
2-Phenyl-4, 6-dioxotetrahydrotriazine	1682 1677 weak	very strong	1739 1730	strong	542	medium	768	medium	1610	very strong	—	
2-o-Methoxyphenyl-4, 6-dioxotetrahydrotriazine	1677	very strong	1735	very strong	546 527	medium	762	strong	1591	very strong	—	
2-Styryl-4, 6-dioxotetrahydrotriazine	1690	very strong	1760	very strong	551	medium	758	medium	1580	very strong	1652	very strong
2-p-Methoxystyryl-4, 6-dioxotetrahydrotriazine	1678	strong	1738	very strong	548	medium	—		1573	very strong	1648	very strong
2-p-Nitrostyryl-4, 6-dioxotetrahydrotriazine	1695	very strong	1765	very strong	550	medium	766	weak	1584	very strong	1637	strong
2-m-Nitrostyryl-4, 6-dioxotetrahydrotriazine	1700	very strong	1740	very strong	552	medium	740	medium	1593	very strong	1648	strong
2-o-Nitrostyryl-4, 6-dioxotetrahydrotriazine	1700	very strong	1795 1780	very strong	555 545	weak	760	medium	1594	very strong	1651	strong

*I = Intensity. The spectra were determined on solids tableted with KBr, concentration 0.4–0.5%. UR-10 spectrometer.

Table 2

Constants of Compounds Prepared

Compound	Mp, °C	Formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
2-(m-Nitrophenyl)-4, 6-dichlorotriazine	147.5—149	$C_9H_4Cl_2N_4O_2$*	40.07	1.67	—	39.82	1.48	—	76
Nitrocinnamoyldicyanodiamide									
o-isomer	280 decomp.		—	—	26.51	—	—		50
m-isomer	280 decomp.	$C_{11}H_9N_5O_3$	—	—	26.83	—	—	27.03	64
p-isomer	256 decomp.		—	—	27.09	—	—		41
Nitrocinnamoylbiuret									
o-isomer	230 decomp.		47.45	3.59	19.34				60
m-isomer	198 decomp.	$C_{11}H_{10}N_4O_5$	47.16	4.04	19.55	47.52	3.63	20.15	61
p-isomer	246 decomp.		47.31	3.75	19.58				65
2-Nitrostyryl-4,6-dioxotetrahydrotriazine									
o-isomer	280 decomp.		50.84	3.08	21.38				63
m-isomer	285 decomp.	$C_{11}H_8N_4O_4$	50.40	3.20	20.85	50.80	3.08	21.55	57
p-isomer	280 decomp.		—	—	21.05				74
2-(p-Methoxystyryl)-4,6-dioxotetrahydrotriazine	285 decomp.	$C_{12}H_{11}N_3O_3$	58.46	4.57	17.29	58.78	4.49	17.13	70
2-(Nitrostyryl)-4,6-dimethoxytriazine									
o-isomer	163—164		—	—	19.51				—
m-isomer	169—170	$C_{13}H_{12}N_4O_4$	54.36	4.44	19.57	54.16	4.20	19.44	86
p-isomer	178.5—180		54.63	4.42	18.95				47
2-(p-Methoxystyryl)-4,6-dimethoxytriazine	78—80	$C_{14}H_{15}N_3O_3$	61.16	5.29	14.85	61.51	5.49	15.38	—
2-(p-Methoxychlorostyryl)-4,6-dimethoxytriazine	116—117.5	$C_{14}H_{14}ClN_3O_3$**	54.72	4.40	13.72	54.76	4.56	13.67	53

*Found: Cl 25.70%, calculated: Cl 26.20%.

**Found: Cl 10.91%, calculated: Cl 11.55%.

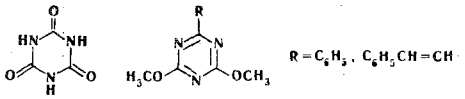
did not lead to the desired results, and after treatment the starting dihydroxy compounds were usually recovered in almost quantitative yield from the products. The dichloride could be obtained from phenyldihydroxytriazine in insignificant yield by using drastic conditions.

An explanation of the results obtained was sought in the data on the lactim-lactam equilibrium for the group of compounds considered, investigated by IR spectroscopy. It is known [16] that taking into account only the bond energies, the oxo (lactam) form is energetically preferred to the hydroxy (lactim) form, by 10 kcal/mole. Indeed, the IR spectra of a series of heterocyclic compound studied [17–19] show a decided predominance of the lactam form. However, this position is not invariable, since conjugation, substituents, or increasing the temperature can shift the equilibrium in favor of the hydroxy form. Thus it was recently shown [20] for α-pyridone, that the two forms are present in approximately equal amounts in the vapors. Obviously then the hydroxy form III is stabilized due to energy of conjugation.

III

The position of the lactim-lactam equilibrium in the case of the hydroxytriazine series has been investigated only for cyanuric acid. Both IR spectra [19, 21] and X-ray data [22] clearly show a symmetrical structure with three keto groups.

To determine the structures of the 4, 6-"dihydroxytriazines" was of interest to us, their IR spectra were investigated and compared with the spectra, under the same conditions, of the authentic trioxo derivative, cyanuric acid IV, and the corresponding dimethoxy derivatives V, with a ring of authentic aromatic nature.

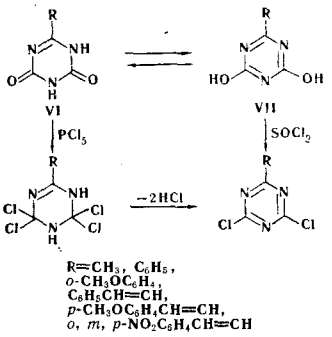


IV V

The figure shows IR spectra obtained for 2-phenyl- and 2-styryl-4, 6-dihydroxytriazines, and the corresponding 4, 6-dimethoxy derivatives. Consideration of the spectra of the dimethoxy derivatives shows that they are wholly similar to the spectra proper to triazine [23], a trichlorotriazine [24], and to the dichloro substitution products of triazine which we previously investigated, with an aromatic ring. The most characteristic feature of these spectra is the presence of two very intense aromatic ring vibration bands. The frequency of one of them, in the absence of a halogen substitutent, is 1360–1410 cm^{-1}, and ~1260 cm^{-1} when such a substituent is present, while the frequency of the second is 1500–1560 cm^{-1}.

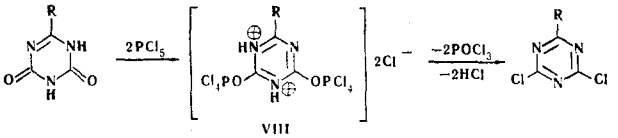
"Hydroxy derivatives" of triazine have a quite different character. On the one hand, most characteristic is the lack of intense bands which from their positions might be assigned to vibrations of the aromatic ring and, on the other hand, the presence of a series of bands undoubtedly due to the C=O group. As would be expected, the presence of two (and in cyanuric acid of three) carbonyl groups gives rise to splitting of the C=O group vibration frequencies found by us for "dihydroxytriazines" and cyanuric acid values [21]. Also given are C=N valence vibration frequencies, and for the styryl group, C=C vibration frequencies. The satisfactory constancy of frequencies and intensities confirms the interpretation of the spectra offered. Thus all the 4, 6-"dihydroxytriazine" derivatives that we have investigated, actually have a 4, 6-dioxotetrahydrotriazine structure (VI).

On the basis of what is stated above we postulate that oxo form VI of the triazine derivatives reacts with PCl_5, and that reaction involves replacement by chlorine, not of a hydroxyl group, but of a carbonyl oxygen, unlike what happens with carboxylic and sulfonic acids. The involvement of an oxo and not a hydroxy form of the "dihydroxytriazines" is evidently due to a side reaction triazine ring opening, for in this case the stable aromatic system of substituted sym-triazine is disrupted.



Higher temperature and possible solvents probably shift the tautomeric equilibrium towards the lactim form VII, and due to this there is partial reaction with thionyl chloride.

It is not excluded that the reaction of "dihydroxytriazines" with PCl_5 proceeds via the intermediate formation of the labile quaternary salt VIII, as occurs with anthrapyridone derivatives [25]. It has previously been postulated that triazinium ions of the ammonium ion type are formed when considering the mechanism of other reactions involving triazine derivatives [26, 27].



VIII

EXPERIMENTAL

Reaction of 2-aryl-4, 6-dihydroxytriazines with PCl_5. Reaction of 2-phenyl-4, 6-dihydroxytriazine, and of its isomeric nitro and methoxy substitution derivatives, with PCl_5 was carried out as described in [7]. The yields and constants of the 2-(Phenyl-, 2'- and 4'-methoxyphenyl- and 2'- and 4'-nitrophenyl)-4, 6-dichlorotriazines were those given in [6–8].

Table 2 gives yields, constants, and analytical data for 2-(3'-nitrophenyl)-4, 6-dichlorotriazine, and other compounds synthesized for the first time.

SUBSTITUTED 2-STYRYL-4, 6-DIHYDROXYTRIAZINES

Nitrocinnamoyldicyanodiamides. A solution or suspension was prepared of the K salt of dicyanodiamide, starting from 8.4 g (0.1 mole) of the latter, 47 ml acetone, and 10.5 g (0.19 mole) KOH in 35 ml water, stirred vigorously, and held at under 0° C, and a solution of 17 g (0.08 mole) cinnamyl chloride in 47 ml acetone was added dropwise over a period of 2 hr 30 min. Then 200–400 ml water was added to the suspension, the mixture filtered, and the filtrate acidified with dilute AcOH. The precipitate was washed with water, hot EtOH, and recrystallized from cellosolve.

Nitrocinnamoylbiurets. A suspension of 16 g (0.062 mole) nitrocinnamoyldicyanodiamine in 200 ml water was acidified with CHl, and stirred and heated on a steam bath for 7–9 hr, all the time being kept slightly acid to Congo Red. The precipitate was filtered off, washed twice with hot water, dried, and recrystallized from cellosolve. With the o-isomer there was marked frothing for the first two hours. When the m-isomer is hydrolyzed, the original suspension was first converted to a solution, from which a precipitate gradually came down. Evidently solution was due to intermediate formation of nitrocinnamoylguanylurea [28].

2-Nitrostyryl-4, 6-dioxoxtetrahydrotriazines. 10 g (0.038 mole) Nitrocinnamoylbiuret was treated with 3% KOH, the quantity of alkali taken being that required to dissolve the precipitate at 95° C. The solution was filtered to remove impurities, and acidified to pH 4.5 with dilute HCl. The precipitate was filtered off, washed with hot water, then with EtOH, and recrystallized from cellosolve.

2-(4'-Methoxystyryl)-4, 6-dioxoxtetrahydrotriazine. Similarly prepared [29]. A mixture of 10.8 g (0.08 mole) anisaldehyde, 13.1 g (0.08 mole) methyldihydroxytriazine hydrochloride [30], and 160 ml 5% HCl was heated and stirred for 1 hr at 100° C, cooled, the precipitate filtered off, washed with water, and vacuum dried at 60° C, then recrystallized from dimethylformamide.

Reaction of substituted 2-styryl-4, 6-dihydroxytriazines with PCl_5. A mixture of 0.01 mole substituted styryldihydroxytriazine, 4.4 g (0.021 mole) PCl_5, and 6 ml $POCl_3$ was refluxed until the suspension dissolved. With the o- and m-isomers of the nitro compounds, when the temperature reached 100°–105° C, the suspension became considerably more viscous, obviously because of formation of a labile intermediate compound, after which a solution was gradually formed. With the o- and p-isomers of the nitro compounds, reaction took 1.5–2.5 hr, with the m-isomer and methoxy substitution compound, 6–7 hr.

The chlorides of the triazines were isolated either by crystallizing by cooling to 0° C, or else by hydrolyzing the phosphorus chlorides with ice and water containing AcONa to keep the pH at 4–5. The compounds were purified by recrystallizing from petrol ether (bp 90°–100° C), or cyclohexane. The purified compounds gave a positive reaction for a double bond with $KMnO_4$, and did not contain P. The elementary analytical data corresponded to mixtures $C_{11}H_6O_2N_4Cl_2$ + + $C_{11}H_5O_2N_4Cl_3$, $C_{12}H_9Cl_2N_3O$ + $C_{12}H_8Cl_3N_3O$.

2-Nitrostyryl-4, 6-dimethoxytriazines. A suspension of 1.12 g (0.0037 mole) technical nitrostyryldichlorotriazine in 2 ml acetone was added to a solution of 0.32 g (0.008 mole) NaOH in 4 ml (0.1 mole) MeOH which was stirred and maintained at 22° C or less. The mixture was stirred for about 30 min at 20°–22° C and 30°–35° C, then for about 1 hr at 50° C. During reaction a few drops of methanolic NaOH were added the keep the reaction alkaline. A large excess of alkali was avoided. The precipitate was filtered off, extracted with 40–50 ml hot MeOH, and the dimethoxy derivative isolated from the extracts by first cooling and then evaporating. More compound was obtained by cooling the main filtrate. It was recrystallized from MeOH.

2-(4'-Methoxychlorostyryl)-4, 6-dimethoxytriazine. Prepared similarly to the above, keeping at 50° C for 3 hr. Isolated by cooling the main filtrate. Recrystallized from MeOH.

2-(4-Methoxystyryl)-4, 6-dimethoxytriazine. Isolated from the 3rd fraction by fractional evaporation of the MeOH extracts obtained in the above experiment, and recrystallized from MeOH.

The gases evolved during the reaction were washed in gas washers containing aniline water, barium hydroxide solution, dil HCl, NaOH solution, and water. HCl and CO_2 were found, and in the case of styryltriazines, $COCl_2$. Not found were $(CN)_2$, HCN, and NH_3. The phosgene was identified by formation of diphenylurea.

When the aqueous solution resulting from the hydrolysis of the phosphorus chlorides is treated with KI and starch, and acidified, a blue color is obtained, indicating the presence of an oxidizing agent, obviously chloramine. To detect ammonia, the hydrolysis products were made alkaline, and the readily volatile substances distilled off in steam and trapped in 2 N HCl. The acid solution was evaporated almost to dryness, the residue made alkaline with 20% NaOH and heated. Gases, which reacted alkaline and smelled of ammonia and amines were evolved.

Reaction of 2-phenyl-4, 6-dihydroxytriazine with thionyl chloride. A mixture of 5.6 g phenyldichlorotriazine, 7.8 ml $SOCl_2$, and 20 ml polychlorides (bp 170°–185° C) was heated and refluxed (130°–140° C) for 20 hr, $SOCl_2$ being added from time to time to keep the bp of the mixture at 140° C or less. The unreacted dihydroxy compound (mp 287°–288° C, decomp) was filtered off, the solvent taken off, and the residue vacuum sublimed, colorless crystals, mp 119°–120° C, undepressed mixed mp with phenyldichlorotriazine.

No reaction was found at lower temperature, and addition of chlorosulfonic acid, dimethylformamide, and pyridine [13–15] did not have any appreciable effect.

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