BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 794—798 (1971) [Vol. 44, No. 3

Derivatives of Ditriazinylamine

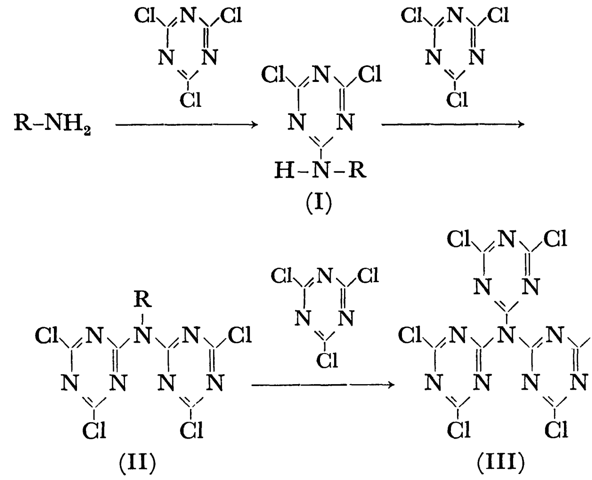
Yoshiaki Fukushima, Noboru Nohara, Yōji Hashida,
Shizen Sekiguchi, and Kohji Matsui

Department of Synthetic Chemistry, Faculty of Engineering, Gunma University, Tenjincho, Kiryu, Gunma

(Received August 10, 1970)

Various substituted ditriazinylamines were synthesized by the reaction of *N,N*-bis(4,6-dichloro-*s*-triazin-2-yl)-amine, *N,N*-bis(4-chloro-6-phenyl-*s*-triazin-2-yl)amine, or 2-chloro-4-phenyl-*s*-triazin-2-yl-2′,4′-dichloro-*s*-triazin-2′-ylamine with nucleophilic reagents. The reaction of *N,N,N*-tris(4,6-dichloro-*s*-triazin-2-yl)amine with sodium methoxide was also examined. In this case, various products were obtained, depending upon the amount of sodium methoxide used. A Hammett plot of the substituent constants($\sum \sigma_m$) *vs.* the pK_a' or the imino proton shifts of the above-mentioned ditriazinylamines gives a linear relationship.

In a previous paper[1] we reported that ammonia or amines react with cyanuric chloride to give *N,N*-bis(4,6-dichloro-*s*-triazin-2-yl)amines (II) or *N,N,N*-tris(4,6-dichloro-*s*-triazin-2-yl)amine (III).



R=H, Alkyl, Aryl

The active chlorine atoms of these polytriazinylamines were replaced by nucleophilic reagents much more readily than those of amino-chloro-*s*-triazines, such as I.

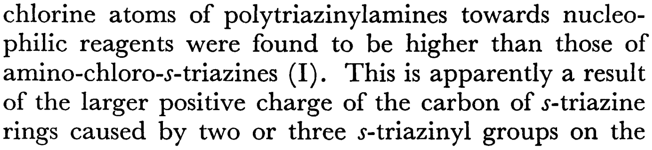
In addition, it was found that the *N,N*-bis(*s*-triazinyl)-amines which have been derived from I (R=H) with the replacement of the chlorine atoms behave as an acid in the presence of two triazinyl groups and that their acidities depend upon the natures of the substituents in the triazine rings.

The substituent effects in nitrogen heteroaromatic compounds have been extensively studied. For example, the Hammett equation is found to be applicable to the derivatives of the pyridine or pyrimidine series by using the substituent constants of benzene series.[2,3] However, the substituent constants applicable to triazine derivatives have not been studied systematically. Thus, with the derivatives of the *s*-triazine series substituent effects have been studied only qualitatively. Recently, the Hammett equation was observed to be applicable to the basicities of ring-nitrogen atoms of 6-substituted-2,4-diamino-*s*-triazines.[4,5] However, there have been no studies of the application of the Hammett equation to the reactions of side chains of triazine rings.

This paper will report on the nucleophilic substitution reactions of II or III, and the substituent effect on the pK_a or chemical shift of the imino protons of *N,N*-bis(*s*-triazinyl)amines.

Results and Discussion

I. Reaction of N,N-*Bis(4,6-dichloro-*s*-triazin-2-yl)amines (II) or* N,N,N-*Tris(4,6-dichloro-*s*-triazin-2-yl)amine (III) with Nucleophilic Reagents.* The reactivities of active chlorine atoms of polytriazinylamines towards nucleophilic reagents were found to be higher than those of amino-chloro-*s*-triazines (I). This is apparently a result of the larger positive charge of the carbon of *s*-triazine rings caused by two or three *s*-triazinyl groups on the same nitrogen atom. Thus, with excess amines, alcohols, mercaptans or thiophenols, II or III reacted to give replaced products, which were derived with the replacement of all the active chlorine atoms in II or III, even at room temperature, while amino-dichloro-*s*-triazines (I) reacted to give only partially-replaced products. The reaction of *N,N*-bis(4,6-dichloro-*s*-triazin-2-yl)aniline (II, R=phenyl) with primary or secondary amines gave only replaced products, but in the reaction of II (R=phenyl) or III with sodium methoxide, various products were obtained, depending upon the amount of sodium methoxide used. With excess sodium methoxide not only were the active chlorine atoms replaced, but also the cleavage of the triazinyl group was observed, even at room temperature, however, the reaction of II (R=H) with excess sodium methoxide gave only the replaced product IV.



II (R=H) IV

This is probably due to the fact that IV reacts with sodium methoxide to give an anion in which the elec-

---

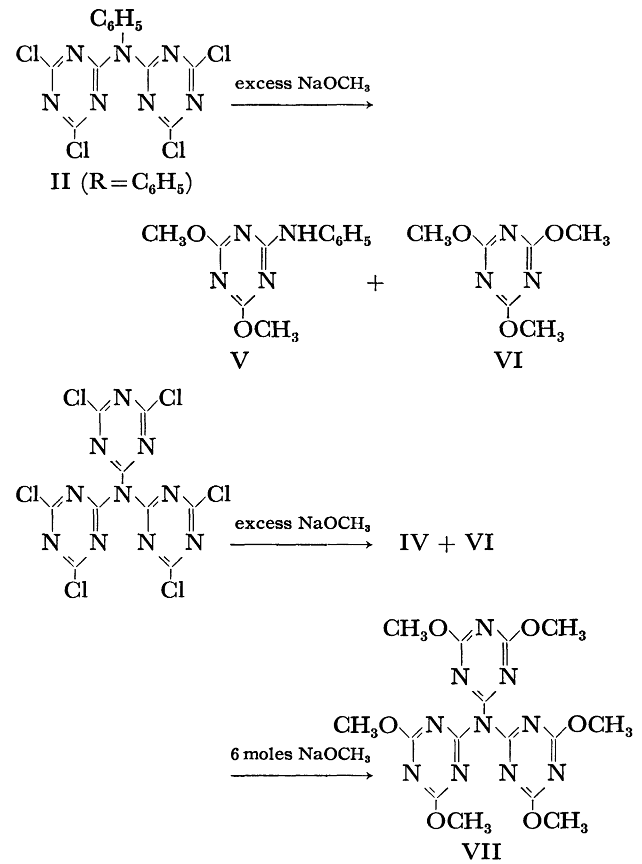
[1] N. Nohara, S. Sekiguchi, and K. Matsui, *J. Heterocycl. Chem.*, **7**, 519 (1970).

[2] For example, Y. Ohtsuji and E. Imoto, *Nippon Kagaku Zasshi*, **80**, 1293 (1959); H. H. Jaffé, *J. Org. Chem.*, **23**, 1790 (1958); R. Joeckle, E. D. Schmidt, and R. Meck, *Z. Naturforsch.*, **21**, 1906 (1966).

[3] For example, S. Mizukami and E. Hirai, *J. Org. Chem.*, **31**, 1199 (1966).

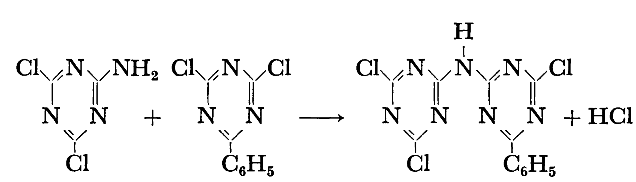
[4] G. Morimoto, *Nippon Kagaku Zasshi*, **87**, 790 (1966).

[5] T. Tashiro and M. Yasuda, *Kobunshi Kagaku*, **26**, 853 (1969).

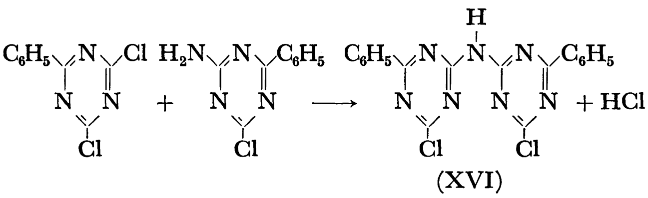


tron densities of the 2,2′-carbons of triazinyl groups are too high for them to be attacked by a methoxide anion.

II. Substituent Effects on the pK$_a$′ Values of Ditriazinylamines. Most of the ditriazinylamines with the general formula shown in Table 1 were synthesized from I by the nucleophilic substitution described in the preceding paragraph. The ditriazinylamine (VIII) was obtained by the condensation between 2,4-dichloro-6-phenyl-*s*-triazine and 2-amino-4,6-dichloro-*s*-triazine, the compound IX, by the nucleophilic substitution of the active chlorine atoms of VIII, and the compound XVI by the condensation between 2,4-dichloro-6-phenyl-*s*-triazine and 2-amino-4-chloro-6-phenyl-*s*-triazine.



(VIII)



(XVI)

Most of these triazinyl derivatives were found to dissolve in a sodium hydroxide solution, with the simultaneous formation of the corresponding anions which have absorption bands in the region with wavelength longer than those of the original compounds. Thus, the pK$_a$′ values of these compounds can be measured spectrophotometrically. As the measurement is carried out in a mixed solvent of water and methyl cellosolve, we will describe pK$_a$′ instead of pK$_a$.[6]

However, in the cases of derivatives (VIII, XI, and XVI), the spectrophotometrical measurement of the pK$_a$′ values was found to be impossible because of their non-solubilities in a sodium hydroxide solution or because of the ready hydrolyses of their active chlorine atoms in an aqueous solution. Table 2 lists the pK$_a$′ values measured in a mixed solvent of methyl cellosolve and water (70/30) at 25°C. As the pK$_a$′ values thus obtained resulted from the summation of the four substituent effects ($\sum\sigma_m$), and as the positions of the substituents correspond to the meta position of benzene derivatives, Table 2 also lists the summation of σ_m.

From these results, it is apparent that the more electron-attractive the substituent becomes, the more the acidity increases. A Hammett plot of pK$_a$′ against $\sum\sigma_m$ is shown in Fig. 1. The ρ value calculated by the method of least squares is −4.12, with a correlation coefficient of 0.956.

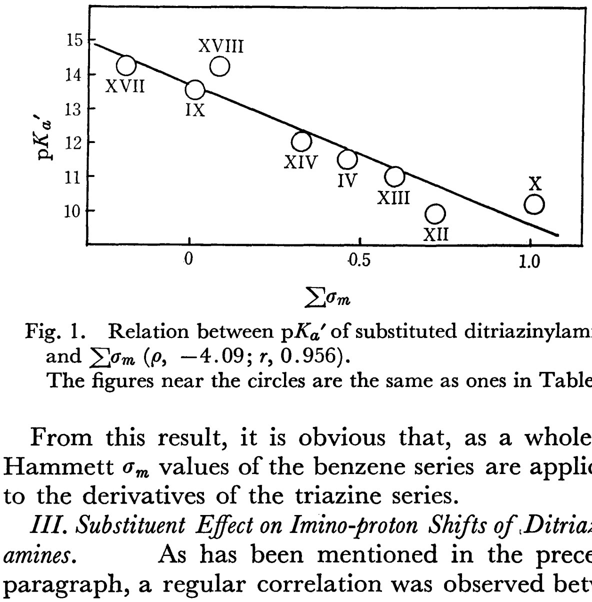


Fig. 1. Relation between pK$_a$′ of substituted ditriazinylamines and $\sum\sigma_m$ (ρ, −4.09; r, 0.956).
The figures near the circles are the same as ones in Table 2.

From this result, it is obvious that, as a whole, the Hammett σ_m values of the benzene series are applicable to the derivatives of the triazine series.

III. Substituent Effect on Imino-proton Shifts of Ditriazinylamines. As has been mentioned in the preceding paragraph, a regular correlation was observed between pK$_a$′ and σ_m for the dissociation of the derivatives of ditriazinylamine.

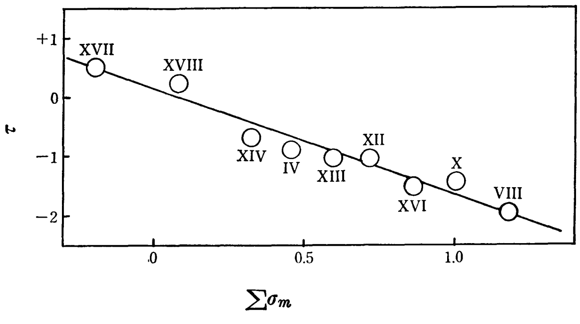


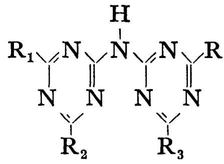
Fig. 2. Relation between imino-proton shifts of substituted ditriazinylamines and $\sum\sigma_m$ (ρ, −1.76; r, 0.977).
The figures near the circles are the same as ones in Table 3.

---

[6] M. Syz and H. Zollinger, *Helv. Chim. Acta*, **48**, 383 (1965).

[7] R. J. Ouellette, *Can. J. Chem.*, **43**, 707 (1965).

TABLE 1. STRUCTURES OF VARIOUS DITRIAZINYLAMINES



Compound No.	R_1	R_2	R_3	Yield %	Mp (°C)	Solvent for recrystallization	Anal. Found C	H	Cl
IV	CH_3O	CH_3O	CH_3O	60	185.5—186.5	Benzene	40.69	4.60	—
VIII	Cl	Cl	C_6H_5	17	204.5—206	(Sublimation)	40.63	1.83	—
IX	$(CH_3)_2N$	Cl	C_6H_5	95	202.5—204.5	Benzene-Ligroin	52.15	4.89	9.5
X	C_6H_5O	C_6H_5O	C_6H_5O	51	163—164	Methanol	66.16	3.86	—
XI	C_6H_5NH	C_6H_5NH	C_6H_5NH	57	338.5—340.5	Pyridine	66.81	4.58	—
XII	C_6H_5S	C_6H_5S	C_6H_5S	38	129.5—132	Methanol	59.52	3.38	—
XIII	CH_3S	CH_3S	CH_3S	70	183—184	Benzene	32.83	3.89	—
XIV	$(CH_3)_2N$	Cl	Cl	82	247—248.5	(Sublimation)	36.51	4.07	—
XV	$(C_2H_5)_2N$	Cl	Cl	61	112—113	Petroleum ether	43.15	5.48	—
XVI	C_6H_5	Cl	Cl	43	219.5—221	Benzene	54.95	2.99	—
XVII	$(CH_3)_2N$	CH_3O	CH_3O	81	191.5—192.5	Methanol	45.30	6.20	—
XVIII	$(CH_3)_2N$	C_6H_5O	C_6H_5O	75	190—190.5	Methanol	59.36	5.26	—

a) Measured in methanol

TABLE 2. pK_a' VALUES OF DERIVATIVES OF DITRIAZINYLAMINES

Compound No.	$\sum\sigma_m$	pK_a'
IV	0.460[a]	11.51
IX	0.011[a,b]	13.59
X	1.008[a]	10.22
XII	0.72[c]	9.95
XIII	0.60[a]	11.01
XIV	0.324[a,b]	12.06
XV	—	12.43
XVII	−0.192[a,b]	14.25
XVIII	0.082[a,b]	14.26

a) D.H. McDaniel and H.C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

b) H.H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

c) S. Oae, "Yuki Ioukagobutsu no Kagaku," Vol. 1, Tokyo Kagaku Dojin Co., Tokyo (1960), p. 117.

TABLE 3. CHEMICAL SHIFT OF IMINOPROTONS OF SUBSTITUTED DITRIAZINYLAMINES

Compound No.	$\sum\sigma_m$	τ
IV	0.460[a]	−0.89
VIII	1.179[a]	−1.93
X	1.008[a]	−1.45
XI	—	+0.40
XII	0.72[c]	−1.06
XIII	0.60[a]	−1.04
XIV	0.324[a,b]	−0.68
XVI	0.866[a]	−1.54
XVII	−0.192[a,b]	+0.49
XVIII	0.082[a,b]	+0.23

The references a, b, and c are the same as ones in the footnote of Table 2.

In recent papers,[7,8] correlations have been noted between Hammett's σ constants and the chemical shifts of hydroxyl protons in *m*- and *p*-substituted phenols and amino protons in *m*- and *p*-substituted anilines. Consequently, a similar relation might also be expected between the chemical shifts of the imino protons of ditriazinylamines and the σ constants of substituents in the triazine rings.

Table 3 lists the imino-proton shifts of substituted ditriazinylamines, using DMSO-d_6 as a solvent at 25°C. In this solvent the positions of these signals do not shift with any variation in the concentration. A Hammett plot of imino proton shifts against $\sum \sigma_m$ is shown in Fig. 2. The ρ value was found to be 1.76, with a correlation coefficient of 0.977. From these results, it is apparent that, in the triazine derivatives, the electronic effects of the substituents are transmitted to the reaction site effectively and that, as a whole, Hammett's σ_m is also applicable to these polytriazinylamines.

Experimental

The infrared spectra were measured in potassium bromide discs on a Jasco D-301 spectrophotometer. The ultraviolet spectra were recorded on a Hitachi-124 UV-VIS spectrophotometer. The NMR spectra were recorded on a Varian A-60D spectrometer. The elemental analyses were performed in the Micro-analytical Center of the University of Gunma. All the K_a' values were determined spectrophotometrically in a mixed solvent of methyl cellosolve and water (70/30), (volume ratio), according to the method of Albert and serjeant.[9]

N,N-*Bis(4,6-dichloro-*s*-triazin-2-yl)amine (II, R=H).* The compound II (R=H) was prepared by the method

---

[8] T. Yamamoto, W. F. Reynolds, and H. M. Hutton, *Can. J. Chem.*, **43**, 2668 (1965).

[9] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., Ltd., New York (1962).

(%) Calcd C	H	Cl	Infrared spectra (cm^{-1}) NH	triazine	UV spectra[a)] λ_{max} (mμ)
40.69	4.44	—	3340	810	253
40.65	1.71	—	3240	853	—
51.68	4.88	9.5	3300	820	—
66.29	3.90	—	—	817	257
66.78	4.67	—	3400	815	—
59.28	3.48	—	3330	840	—
33.41	3.64	—	3315	850	263
36.38	4.00	—	3400	830	256
43.62	5.49	—	3260	800	—
54.56	2.80	—	3200	830	—
44.86	5.96	—	3420	810	244
59.32	5.20	—	3400	790	—

described in a previous paper.[1)]

N,N-*Bis(4,6-dimethoxy-*s*-triazin-2-yl)amine (IV).* A solution of 2.3 g (0.1 mol) of sodium in 50 m*l* of methanol was added, at room temperature, to a soltion of 6.3 g (0.02 mol) of II (R=H) in 250 m*l* of methanol. After refluxing for 6 hr, the mixture was poured into 500 m*l* of ice-water neutralized with hydrochloric acid, filtered, and dried.

N,N,N-*Tris(4,6-dimethoxy-*s*-triazin-2-yl)amine (VII).* To a stirred solution of 1.0 g (0.0022 mol) of III, which is the condensation product between II (R=H) and cyanuric chloride,[1)] in 30 m*l* of methanol, we added drop by drop and at room temperature, a solution of 0.3 g (0.013 mol) of sodium in 20 m*l* of methanol. After an additional 4 hr's stirring at 35—40°C, the methanol was distilled off under reduced pressure. The recrystallization of the residue from benzene yielded 0.70 g (74%) of VII; mp 206—206.5°C.

Found: C, 41.49; H, 4.14%. Calcd for $C_{15}H_{18}N_{10}O_6$; C, 41.48; H, 4.18%.

*4-Chloro-6-phenyl-*s*-triazin-2-yl-4′,6′-dichloro-*s*-triazin-2′-ylamine (VIII).* To a stirred solution of 1.7 g (0.01 mol) of 2-amino-4,6-dichloro-*s*-triazine and 2.3 g (0.01 mol) of 2,4-dichloro-6-phenyl-*s*-triazine in 150 m*l* of acetone, we added, drop by drop and below 5°C, a solution of 0.4 g (0.01 mol) of sodium hydroxide in 4 m*l* of water. After an additional one hr's stirring, the mixture was poured into 500 m*l* of ice water and filtered. The filtrate was acidified with hydrochloric acid. The precipitate thus formed was filtered and dried.

*4-Dimethylamino-6-phenyl-*s*-triazin-2-yl-4′-chloro-6′-dimethylamino-*s*-triazin-2′-ylamine (IX).* Into a solution of 3.6 g (0.01 mol) of VIII in 150 m*l* of acetone, we stirred drop by drop and below 10°C, 4.6 m*l* (0.04 mol) of a 40% aqueous dimethylamine solution. After an additional 3 hr's stirring, the mixture was poured into 500 m*l* of ice water, the precipitate thus formed was filtered and dried.

In the reaction of VIII with dimethylamine, it is expected from a comparison of the σ_m values for the phenyl, chlorine, and dimethylamino substituents that, first, one of the chlorine atoms of the dichloro-*s*-triazinyl group of VIII and then chlorine atom of the chlorophenyl-*s*-triazinyl group, may be replaced by dimethylamino groups. Therefore, the main product of the above-mentioned reaction was assumed to be 4-dimethylamino-6-phenyl-*s*-triazin-2-yl-4′-chloro-6′-dimethylamino-*s*-triazin-2′-ylamine (IX).

N,N-*Bis(4,6-diphenoxy-*s*-triazin-2-yl)amine (X).* A solution of 4.0 g (0.1 mol) of sodium hydroxide in 40 m*l* of water was added, at room temperature, to a solution of 6.3 g (0.02 mol) of II (R=H) and 9.4 g (0.1 mol) of phenol in 200 m*l* of benzene. After 3 hr's stirring, the mixture was refluxed for 3 hr. The benzene layer was separated and dried over calcium chloride. Then, the benzene was distilled off under reduced pressure, and the residue was collected.

The compound XI, XII and XIII were prepared in a similar manner by the reaction of II (R=H) with aniline thiophenol, and methyl mercaptan respectively.

N,N-*Bis(4-chloro-6-dimethylamino-*s*-triazin-2-yl)amine (XIV).* Into 200 m*l* of acetone containing 3.2 g (0.01 mol) of II (R=H), we stirred, drop by drop and below 5°C, 4.5 g (0.04 mol) of a 40% dimethylamine solution. After an additional 3 hr's stirring, the mixture was poured into 300 m*l* of ice-water, filtered, and dried. The compound XV was prepared in a similar manner by the reaction of II (R=H) with diethylamine.

N,N-*Bis(4-chloro-6-phenyl-*s*-triazin-2-yl)amine (XVI).* To a stirred solution of 150 m*l* of acetone containing 2.3 g (0.01 mol) of 2,4-dichloro-6-phenyl-*s*-triazine and 2.5 g (0.012 mol) of 2-amino-4-chloro-6-phenyl-*s*-triazine, we added drop by drop and below 5°C, a solution of 0.4 g (0.01 mol) of sodium hydroxide in 4 m*l* of water. After an additional 5 hr's stirring, the mixture was poured into 1 *l* of ice-water, made alkaline with sodium hydroxide, and filtered. The filtrate was acidified with hydrochloric acid. The precipitate thus obtained was filtered and dried.

N,N-*Bis(4-dimethylamino-6-methoxy-*s*-triazin-2-yl) amine (XVII).* To a solution of 3.8 g (0.01 mol) of XIV in 150 m*l* of methanol, we added, at room temperature, a solution of 0.7 g (0.03 mol) of sodium in 30 m*l* of methanol. After the mixture had been refluxed for 3 hr, the methanol was distilled off under reduced pressure and the resulting residue was collected.

N,N-*Bis(4-dimethylamino-6-phenoxy-*s*-triazin-2-yl) amine (XVIII).* Into a solution of 3.3 g (0.01 mol) of XIV and 1.9 g (0.02 mol) of phenol in 100 m*l* of dioxane, we stirred, at room temperature, 10 m*l* of an alkaline solution containing 1.0 g (0.025 mol) of sodium hydroxide. After heating at 70—80°C for 3 hr, the mixture was poured into 300 m*l* of ice-water, filtered, and dried.

Reaction of N,N-*Bis(4,6-dichloro-*s*-triazin-2-yl)aniline (II, R=Ph) with Excess Sodium Methoxide.* A solution of 1.8 g (0.08 mol) of sodium in 50 m*l* of methanol was added, at room temperature, to a solution of 3.8 g 0.01 mol) of II (R=Ph) in 50 m*l* of methanol. The mixture was stirred at 35°C for 6 hr. Then the mixture was poured into 1 *l* of ice-water, and neutralized with hydrochloric acid. The precipitate thus formed was separated by filtration and dried. Recrystallization from ligroin yielded 1.7 g (57%), mp 133—134°C, which was found to be identical with that of an authentic sample of V by a mixed-melting-point test. After the filtrate had been extracted with benzene, the benzene layer was dried over calcium chloride. The residue obtained after distilling off the benzene was recrystallized from ligroin to give 0.9 g (66 %) of a pure material; mp 133—134°C, which was found to be identical with that of an authentic sample of trimethyl cyanurate by a mixed-melting-point test.

Reaction of N,N,N-*Tris(4,6-dichloro-*s*-triazin-2-yl)amine (III) with Excess Sodium Methoxide.* A solution of 1.0 g (0.002 mol) of III and 0.35 g (0.015 mol) of sodium in 50 m*l* of methanol was stirred at 35—40°C for 4 hr. Then the mixture was poured into 200 m*l* of ice water. After this aqueous solution had been extracted with benzene and drying over calcium chloride, the benzene was distilled off. The residue was recrystallized from benzene. Yield, 0.4 g (68%); mp 185—186°C. By a mixed-melting-point test, this compound was proved to be IV. After the benzene had been distilled off from the filtrate, the residue was recrystallized from ligroin. Yield, 0.2 g (69%); mp 132—134°C. By a mixed-melting-point test, this compound was proved to be VI.