

Reactions of Chloro-*s*-triazines with Aminophenol

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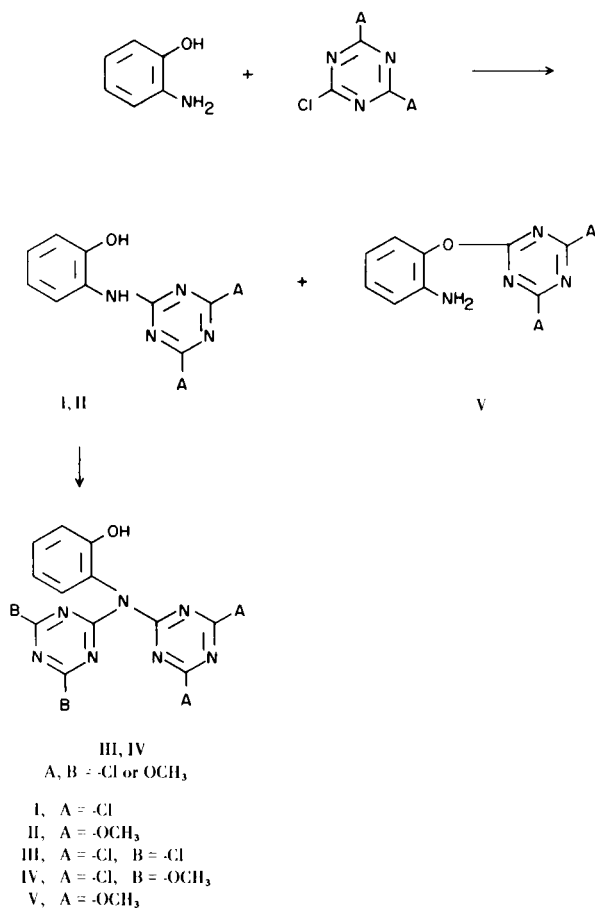
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A number of derivatives of *s*-triazine have been prepared by the condensation of cyanuric chloride and other chloro-*s*-triazines with nucleophilic reagents (I), but reactions of chloro-*s*-triazines with polyfunctional nucleophilic reagents have not been studied systematically.

Therefore, it was of interest to investigate reactions of chloro-*s*-triazines with polyfunctional nucleophilic reagents. This paper reports the reactions of chloro-*s*-triazines with *o*-aminophenol and *N*-substituted *o*-aminophenols.

A. Reaction of Chloro-*s*-triazines with *o*-Aminophenol.

The condensation of *o*-aminophenol with cyanuric chloride or 2-chloro-4,6-dimethoxy-*s*-triazine (CDMT) in the presence of alkali gave various reaction products depending upon the reaction conditions. For example, the reaction of *o*-aminophenol with CDMT in molar ratio



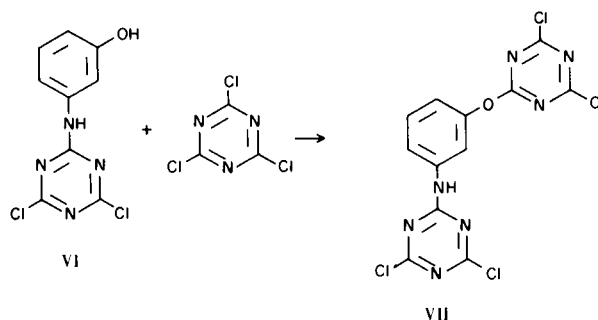
1:1 under neutral or mild alkaline conditions gave *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (II) as the major product, while under strongly alkaline condition with sodium hydroxide, *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (V) was obtained as the major product. This difference in the products formed may be attributed to the fact that the relative nucleophilic reactivity of the amino and hydroxyl groups varies with the basicity of the reaction medium.

*N*-(*s*-triazinyl)-2-aminophenols were found to condense with cyanuric chloride in the presence of alkali to give secondary condensation products. These secondary condensation products have two triazinyl groups on the amino nitrogen atom based upon nmr and infrared spectra, elemental analyses and solubility in alkaline solution. Thus, the condensation reaction takes place on the *s*-triazinylamino group in preference to the hydroxyl group which functions as a phenoxide anion in the presence of sodium hydroxide.

Primary condensation products from cyanuric chloride or CDMT and *o*-aminophenol, gave the desired *N,N*-bis-*s*-triazinyl compounds (III) (IV), while most of the primary condensation products from CDMT and arylamines with no *ortho* hydroxyl group failed to give the desired *N,N*-bis-*s*-triazinyl compounds.

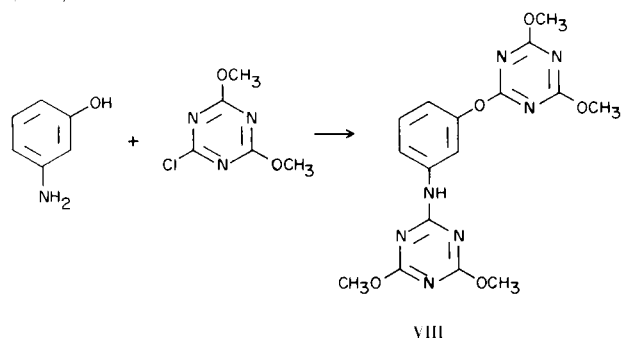
*N,N*-Bis-*s*-triazinyl compounds of similar structure have recently been proposed as unstable intermediates in the base-catalyzed reaction of *N,O*-bis-*s*-triazinyl-8-amino-1-naphthol-3,6-disulfonic acid by Budziarek (2), but these intermediates were not isolated and their chemical properties are still unknown.

Although *N,N*-bis-*s*-triazinyl compounds were obtained in the reaction of cyanuric chloride with primary condensation products formed from usual aromatic primary



amines and cyanuric chloride (3), *N*-(4,6-dichloro-*s*-triazin-2-yl)-3-aminophenol (VI), a primary condensation product formed from *m*-aminophenol and cyanuric chloride, gave the *N,O*-bis-*s*-triazinyl-3-aminophenol (VII) when reacted with cyanuric chloride under similar conditions.

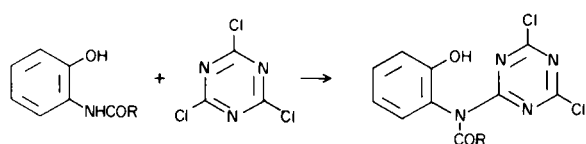
In addition, the 1:2 mixture of *m*-aminophenol and CDMT gave *N,O*-bis(4,6-dimethoxy-*s*-triazin-2-yl)-3-aminophenol (VIII).



Therefore, it seems reasonable to assume that the abnormal course taken with *o*-aminophenol may be attributed to the presence of the *ortho* hydroxyl group.

#### B. Reaction of Chloro-*s*-triazines with *N*-Acyl-2-aminophenols.

Since the chemical properties of an amino group attached to the triazine nucleus are similar to those of an amide, the abnormal course observed in the reaction of *N*-(*s*-triazinyl)-2-aminophenol with chloro-*s*-triazines would also be expected in the reaction of *N*-acyl-2-aminophenols with chloro-*s*-triazines giving *N*-acyl-*N*-(*s*-triazinyl)-2-aminophenols as major products. Compounds of this type have been recently reported as unstable intermediates in the reaction of *O*-(*s*-triazinyl)-*N*-acyl-8-amino-1-naphthol-3,6-disulfonic acid with alkali (2). The reaction of *N*-acyl-2-aminophenol, for example, *N*-acetyl- or *N*-benzoyl-2-aminophenol, with cyanuric chloride or other chloro-*s*-triazines in the presence of sodium hydroxide gave *N*-acyl-*N*-(*s*-triazinyl)-2-aminophenols (IX), (X) in good yields. Thus, as with *N*-(*s*-triazinyl)-2-aminophenol, the reaction was found to take place on the acylamino group and the phenolic hydroxyl group remained unaffected.



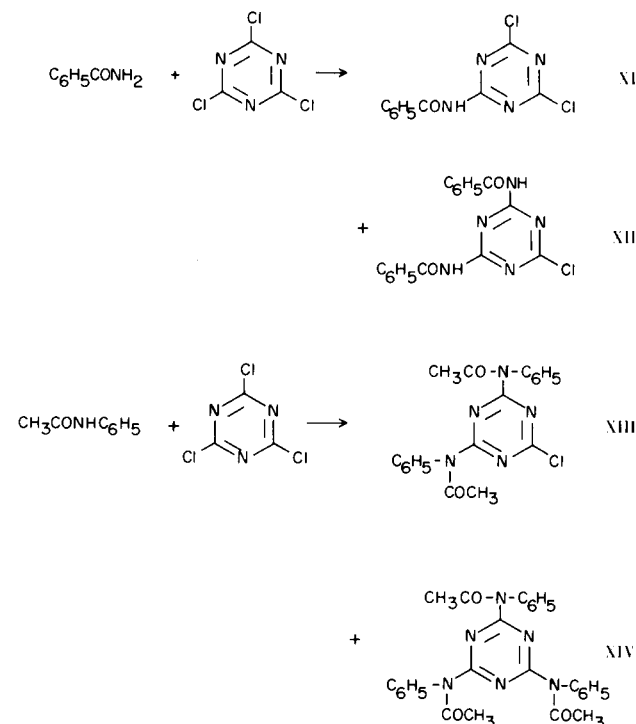
IX. R -CH<sub>3</sub>  
X. R -C<sub>6</sub>H<sub>5</sub>

However, in the case of *N,O*-dibenzoyl-2-aminophenol and *N*-acetyl-*o*-anisidine, no derivatives of the *N*-acyl-*N*-triazine type were obtained under similar conditions.

Furthermore, the fact that no reaction occurred when *N*-acylarylamines without an *o*-hydroxyl group were treated with chloro-*s*-triazines in alkaline solution also indicates that an *ortho* hydroxyl group capable of interacting with alkali is necessary for this reaction to occur.

Also in the case of *N*-acetylthranilic acid and *N*-acetylorthanilic acid the desired *N*-acetyl-*N*-*s*-triazinyl compounds were not obtained. Thus, it is clear that the *o*-carboxyl or *o*-sulfonate group has no appreciable effect upon the reactivity of an amide group.

These results prompted reactions of chloro-*s*-triazines with sodium salts of *N*-acylarylamines which contain no *ortho* hydroxyl group. Dioxane was found to be the most suitable solvent. The condensation products formed from the sodium salt of benzamide or acetanilide and cyanuric chloride gave XI, XII, XIII and XIV.

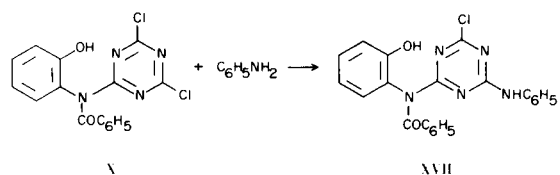
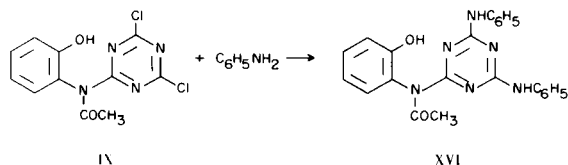
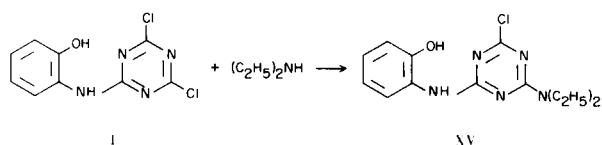


Similar participation of the neighbouring hydroxyl group has been reported in the reaction of cyanuric chloride with such *o*-hydroxyarylamides as *o*-hydroxybenzanilide or 3-hydroxy-2-naphthanilide to give the corresponding *N*-chloro-*s*-triazinylanilides (4). In these cases, it is assumed that the reaction proceeds by the direct replacement of a halogen by an amide nitrogen, involving intramolecular nucleophilic catalysis by a phenoxide anion.

However the possibility of the Smiles rearrangement can not be completely excluded.

C. Reaction of *N,N*-Bis(4,6-dichloro-*s*-triazin-2-yl)- (III) or *N*-Acyl-*N*-(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (IX, X) with Sodium Methoxide.

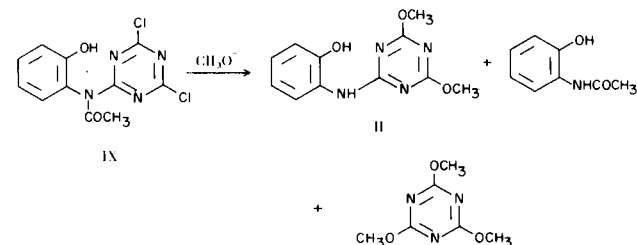
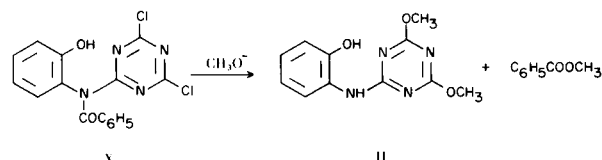
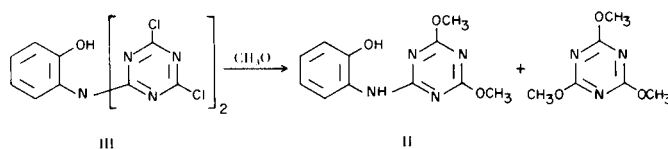
The reaction of I or IX and X with primary or secondary amines gave substitution products, but in the reactions of these derivatives of *o*-aminophenol with excess



sodium methoxide not only were the active chlorine atoms replaced but also cleavage of the *s*-triazinyl or acyl group was observed even at room temperature. For instance, *N,N*-bis(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (III) reacted with sodium methoxide to give *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (II) and trimethyl cyanurate, but the reaction of *N*-(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (I) with sodium methoxide gave the substitution product only. This easy cleavage of one of two *s*-triazinyl groups on the amino nitrogen atom may be attributed to the larger positive charge of the carbon of the *s*-triazine nucleus caused by two *s*-triazinyl groups on the same nitrogen atom.

While *N*-benzoyl-*N*-(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (X) gave *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (II) and benzoic acid which is probably produced by the decomposition of preformed methyl benzoate, *N*-Acetyl-*N*-(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (IX) yielded three products, trimethyl cyanurate, *N*-acetyl-2-aminophenol and *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (II), by the nucleophilic attack by methoxide anion

on the carbon of the *s*-triazine nucleus or the carbonyl carbon of the acyl group.



## EXPERIMENTAL

Infrared spectra were measured in potassium bromide discs on a Jasco D-301 spectrophotometer.

Elemental analyses were performed in the Micro Analytical Center of the University of Gunma.

### *N*-(4,6-Dichloro-*s*-triazin-2-yl)-2-aminophenol (I).

To a solution of 80 ml. of acetone containing 18.5 g. (0.1 mole) of cyanuric chloride was added dropwise with stirring at 0 to 5° 10.9 g. (0.1 mole) of *o*-aminophenol in 90 ml. of acetone. The mixture was neutralized with 2 *N* sodium carbonate and poured into 500 ml. of ice-water. The precipitate was collected by filtration and dried to give 23.1 g. (90%) of crude I. Recrystallization from benzene gave an analytical sample of I, m.p. 187-188° dec.; infrared  $\text{cm}^{-1}$ , (NH) 3500; (OH) 3275 (broad); (triazine) 780.

*Anal.* Calcd. for  $\text{C}_9\text{H}_6\text{Cl}_2\text{N}_4\text{O}$ : C, 42.04; H, 2.35. Found: C, 42.56; H, 2.44.

### *N*-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-aminophenol (II).

A solution of 5.4 g. (0.05 mole) of *o*-aminophenol in 40 ml. of acetone was added dropwise with stirring at room temperature to a solution of 8.8 g. (0.05 mole) of 2-chloro-4,6-dimethoxy-*s*-triazine (CDMT). After the addition the temperature was raised to ca. 35° and the mixture was stirred for 3-4 hours, while being neutralized with the 2 *N* sodium carbonate during the reaction. The mixture was processed according to the procedure for I to give 10.1 g. (81%) of crude II. Recrystallization from benzene gave an analytical sample of II, m.p. 172-172.5°; infrared  $\text{cm}^{-1}$ , (NH) 3520; (OH) 3050 (broad); (triazine) 810.

*Anal.* Calcd. for  $C_{11}H_{12}N_4O_3$ : C, 53.22; H, 4.87. Found: C, 53.09; H, 4.98.

*N,N*-Bis(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (III) and *N*-(4,6-Dichloro-*s*-triazin-2-yl)-*N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (IV).

To a solution of 20 ml. of acetone containing 5.1 g. (0.02 mole) of cyanuric chloride was added dropwise with stirring at 0 to 5°, 3.7 g. (0.02 mole) of I in 25 ml. of acetone. The mixture was neutralized with 10% sodium hydroxide and processed according to the procedure for I to give 7.3 g. (91%) of crude III. An analytical sample was obtained upon recrystallization from benzene, m.p. 209-210°; infrared  $cm^{-1}$ , (OH) 3360; (triazine) 800.

*Anal.* Calcd. for  $C_{12}H_5Cl_4N_7O$ : C, 35.58; H, 1.24. Found: C, 35.59; H, 1.11.

Crude IV was obtained from II (5.0 g., 0.02 mole) using the same procedure for the preparation of III from I, yield 6.5 g. (83%). Recrystallization from benzene gave an analytical sample of IV, m.p. 156.5-157°; infrared  $cm^{-1}$ , (OH) 3360; (triazine) 815.

*Anal.* Calcd. for  $C_{14}H_{11}Cl_2N_7O_3$ : C, 42.42; H, 2.76; Cl, 17.9. Found: C, 42.85; H, 2.76; Cl, 17.6.

#### *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-aminophenol (V).

To a stirred mixture of 20 ml. of water, 1 g. of sodium hydroxide and 2.8 g. (0.025 mole) of *o*-aminophenol was added at 5 to 10° 20 ml. of acetone. To this mixture was added dropwise with stirring at 5 to 10° a solution of 30 ml. of acetone containing 4.4 g. (0.025 mole) of CDMT. Stirring was continued for 3.5 hours until the mixture became neutral. The acetone was evaporated, the residue was extracted with benzene, and the benzene layer was washed with 5% sodium hydroxide followed by water. The benzene layer was dried and evaporated to give 3.6 g. (60%) of crude V. Recrystallization from petroleum ether gave an analytical sample of V, m.p. 89-90°.

*Anal.* Calcd. for  $C_{11}H_{12}N_4O_3$ : C, 53.22; H, 4.87. Found: C, 53.31; H, 5.00.

#### *N*-(4,6-Dichloro-*s*-triazin-2-yl)-3-aminophenol (VI).

A solution of 30 ml. of acetone containing 5.5 g. (0.05 mole) of *m*-aminophenol was added to a solution of 50 ml. of acetone containing 9.2 g. (0.05 mole) of cyanuric chloride. The mixture was neutralized with 2 *N* sodium carbonate, and stirring was further continued for 30 minutes. The mixture was then processed according to the procedure for I to give 11.8 g. (92%) of crude VI. Recrystallization from benzene gave an analytical sample of VI, m.p. 213-214° dec.; infrared  $cm^{-1}$ , (NH) 3530; (OH) 3460; (triazine) 780.

*Anal.* Calcd. for  $C_9H_6Cl_2N_4O$ : C, 42.04; H, 2.35; Cl, 27.5. Found: C, 41.95; H, 2.33; Cl, 27.0.

#### *N,O*-Bis(4,6-dichloro-*s*-triazin-2-yl)-3-aminophenol (VII).

Crude VII was obtained in the same manner as VI, using 5.0 g. (0.02 mole) of VI, yield 6.7 g. (83%). Recrystallization from benzene-ligroin gave an analytical sample of VII, m.p. 199-200°; infrared  $cm^{-1}$ , (NH) 3460; (triazine) 800.

*Anal.* Calcd. for  $C_{12}H_5Cl_4N_7O$ : C, 35.58; H, 1.24; Cl, 35.0. Found: C, 36.02; H, 1.25; Cl, 34.2.

#### *N,O*-Bis(4,6-dimethoxy-*s*-triazin-2-yl)-3-aminophenol (VIII).

To 20 ml. of water containing 3.3 g. (0.03 mole) of *m*-aminophenol and 2.4 g. (0.06 mole) of sodium hydroxide was added dropwise with stirring at 10 to 15° a solution of 50 ml. of acetone containing 10.5 g. (0.06 mole) of CDMT. Stirring was continued

for an additional 3 hours after which time the mixture was processed according to the procedure for I to give 3.2 g. (33%) of crude VIII. Recrystallization from dioxane gave an analytical sample of VIII, m.p. 189-190°; infrared  $cm^{-1}$ , (NH) 3500; (triazine) 800.

*Anal.* Calcd. for  $C_{16}H_{17}N_7O_5$ : C, 49.61; H, 4.39. Found: C, 49.50; H, 4.38.

The color test by potassium ferricyanide-ferric chloride or ammonium phosphomolybdate indicated that VII and VIII have no hydroxyl group.

#### *N*-Acetyl-*N*-(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (IX).

To a solution of 90 ml. of acetone containing 9 g. (0.05 mole) of cyanuric chloride was added dropwise with stirring at 0 to 5° 7.5 g. (0.05 mole) of *N*-acetyl-2-aminophenol in 20 ml. of 10% sodium hydroxide. The mixture was stirred for 10 minutes below 5° and then processed according to the procedure for I to give 13.5 g. (90%) of crude IX. Recrystallization from benzene-ligroin gave an analytical sample of IX, m.p. 169-170°; infrared  $cm^{-1}$ , (OH) 3480; (C=O) 1745; (triazine) 790.

*Anal.* Calcd. for  $C_{11}H_8Cl_2N_4O_2$ : C, 44.17; H, 2.70. Found: C, 44.59; H, 2.79.

#### *N*-Benzoyl-*N*-(4,6-dichloro-*s*-triazin-2-yl)-2-aminophenol (X).

Crude X was obtained in a similar manner as IX except for the use of 6.4 g. (0.03 mole) of *N*-benzoyl-2-aminophenol, yield 10.0 g. (93%). Recrystallization from benzene gave an analytical sample of X, m.p. 188-189°; infrared  $cm^{-1}$ , (OH) 3440; (C=O) 1735; (triazine) 790.

*Anal.* Calcd. for  $C_{16}H_{10}Cl_2N_4O_2$ : C, 53.20; H, 2.79; Cl, 19.6. Found: C, 53.31; H, 2.70; Cl, 19.0.

#### 2,4-Dichloro-6-benzamido-*s*-triazine (XI).

Into 9.7 g. (0.08 mole) of benzamide in 120 ml. of dioxane was added an equimolar amount of sodium and the mixture was refluxed for 5 hours. This mixture was then added in small portions with stirring at 10-15° to a solution of 40 ml. of dioxane containing 7.4 g. (0.04 mole) of cyanuric chloride and the temperature was raised to 40°. After stirring 3 hours, the mixture was concentrated to two-thirds of its original volume and poured into 500 ml. of ice-water. The filtrate was acidified with hydrochloric acid to yield 7.6 g. (71%) of crude crystalline XI. Recrystallization from benzene gave an analytical sample of XI, m.p. 183-184°.

*Anal.* Calcd. for  $C_{10}H_6Cl_2N_4O$ : C, 44.63; H, 2.25. Found: C, 44.81; H, 2.48.

#### 2-Chloro-4,6-dibenzamido-*s*-triazine (XII).

Crude XII was obtained in a similar manner as XI, using 9.7 g. (0.08 mole) of benzamide and 3.6 g. (0.02 mole) of cyanuric chloride, yield 5.7 g. (74%). An analytical sample was obtained upon recrystallization from benzene, m.p. 137-137.5°; infrared  $cm^{-1}$ , (NH) 3530; (C=O) 1710; (triazine) 810.

*Anal.* Calcd. for  $C_{17}H_{12}ClN_5O_2$ : C, 57.71; H, 3.42. Found: C, 58.06; H, 3.47.

#### 2-Chloro-4,6-diacetanilido-*s*-triazine (XIII).

To a solution of 100 ml. of dioxane containing 10.8 g. (0.08 mole) of acetanilide was added 1.8 g. (0.08 mole) of sodium. After refluxing for 5 hours the mixture was cooled and added with stirring at 15 to 20° to 7.4 g. (0.04 mole) of cyanuric chloride in 40 ml. of dioxane. The mixture was further stirred for 4 hours at 60°, concentrated to two-thirds of its original volume, and poured into 500 ml. of ice-water. The precipitate was collected by filtration and dried to give 13.2 g. (87%) of crude XIII. Recrystallization

from benzene gave an analytical sample of XIII, m.p. 203-204°; infrared  $\text{cm}^{-1}$ , (C=O) 1685; (triazine) 785.

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{16}\text{ClN}_5\text{O}_2$ : C, 59.76; H, 4.22. Found: C, 59.92; H, 4.37.

Tris(acetanilido)-s-triazine (XIV).

Crude XIV was obtained in a similar manner as XIII except for the use of 8.1 g. (0.06 mole) of acetanilide and 3.7 g. (0.02 mole) of cyanuric chloride, yield 7.1 g. (74%). Recrystallization from acetone gave an analytical sample of XIV, m.p. 223-224°; infrared  $\text{cm}^{-1}$ , (C=O) 1700; (triazine) 810.

*Anal.* Calcd. for  $\text{C}_{27}\text{H}_{24}\text{N}_6\text{O}_3$ : C, 67.48; H, 5.03. Found: C, 67.85; H, 5.07.

*N*-(4-Chloro-6-diethylamino-s-triazin-2-yl)-2-aminophenol (XV).

To a solution of 40 ml. of acetone containing 10.3 g. (0.04 mole) of I was added dropwise with stirring at room temperature 5.9 g. (0.08 mole) of diethylamine. The mixture was further refluxed for 5 hours, and then processed according to the procedure for I to give 10.4 g. (88%) of crude XV. Recrystallization from benzene gave an analytical sample of XV, m.p. 169-169.5°; infrared  $\text{cm}^{-1}$ , (NH) 3400; (OH) 3120 (triazine) 795.

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{16}\text{ClN}_5\text{O}$ : C, 53.15; H, 5.49; Cl, 12.1. Found: C, 53.32; H, 5.47; Cl, 12.2.

*N*-Acetyl-*N*-(4,6-dianilino-s-triazin-2-yl)-2-aminophenol (XVI).

To 6 g. (0.02 mole) of IX in 50 ml. of acetone was added dropwise with stirring at room temperature 7.4 g. (0.08 mole) of aniline in 20 ml. of acetone. Stirring was continued for 3 hours, poured into 500 ml. of ice-water, and acidified with hydrochloric acid. The precipitate was collected by filtration, washed with water and dried to give 7.6 g. (93%) of crude XVI. Recrystallization from benzene gave an analytical sample of XVI, m.p. 195-196°; infrared  $\text{cm}^{-1}$ , (NH) 3400; (OH) 3160; (C=O) 1755; (triazine) 805.

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{20}\text{N}_6\text{O}_2$ : C, 66.99; H, 4.85. Found: C, 66.99; H, 4.89.

*N*-Benzoyl-*N*-(4-chloro-6-anilino-s-triazin-2-yl)-2-aminophenol (XVII).

Crude XVII was obtained in a similar manner as XV except for the use of 7.2 g. (0.02 mole) of X and 3.7 g. (0.04 mole) of aniline, yield quantitative. Recrystallization from monochlorobenzene gave an analytical sample of XVII, m.p. 216-216.5°; infrared  $\text{cm}^{-1}$ , (NH) 3450; (OH) 3200 (broad); (C=O) 1735;

(triazine) 795.

*Anal.* Calcd. for  $\text{C}_{22}\text{H}_{16}\text{ClN}_5\text{O}_2$ : C, 63.23; H, 3.86; Cl, 8.5. Found: C, 63.57; H, 3.73; Cl, 8.5.

Reaction of *N*-(4,6-Dichloro-s-triazin-2-yl)-2-aminophenol (I) with Sodium Methoxide.

To a suspension of 5.1 g. (0.02 mole) of I in 30 ml. of methanol was added dropwise with stirring at 15° 1.9 g. (0.08 mole) of sodium dissolved in 20 ml. of methanol. The mixture was stirred for 24 hours, poured into 500 ml. of ice-water and acidified with hydrochloric acid. The precipitate was collected by filtration and dried to give 3.4 g. (69%) of crude II.

Reaction of *N,N*-Bis(4,6-dichloro-s-triazin-2-yl)-2-aminophenol (III) with Sodium Methoxide.

Treatment of 4 g. (0.01 mole) of III in a similar manner as in the reaction of I with sodium methoxide yielded 1.9 g. of II and 0.8 g. of trimethyl cyanurate.

Reaction of *N*-Acetyl-*N*-(4,6-dichloro-s-triazin-2-yl)-2-aminophenol (IX) with Sodium Methoxide.

Treatment of 9 g. (0.03 mole) of IX in a similar manner as in the reaction of I with sodium methoxide yielded 0.75 g. of *N*-acetyl-2-aminophenol, 5.3 g. of II and 0.85 g. of trimethyl cyanurate.

Reaction of *N*-Benzoyl-*N*-(4,6-dichloro-s-triazin-2-yl)-2-aminophenol (X) with Sodium Methoxide.

Treatment of 7.2 g. (0.02 mole) of X in a similar manner as in the reaction of I with sodium methoxide yielded 4.5 g. of II and 1.7 g. of benzoic acid.

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