

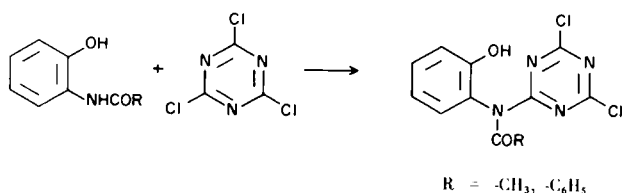
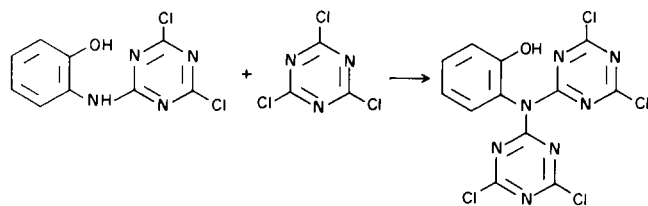
Smiles Rearrangement on *s*-Triazine Derivatives

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1. Introduction.

In the previous paper (1), we reported that *N*-(*s*-triazinyl)- or *N*-acyl-2-aminophenol reacts with chloro-*s*-triazine to give *N,N*-bis(*s*-triazinyl)- or *N*-acyl-*N*-(*s*-triazin-2-yl)-2-aminophenol.



Two possible paths for this reaction may be considered, direct displacement of the halogen by the amide nitrogen and Smiles rearrangement of preformed *O*-(*s*-triazinyl)-2-aminophenol.

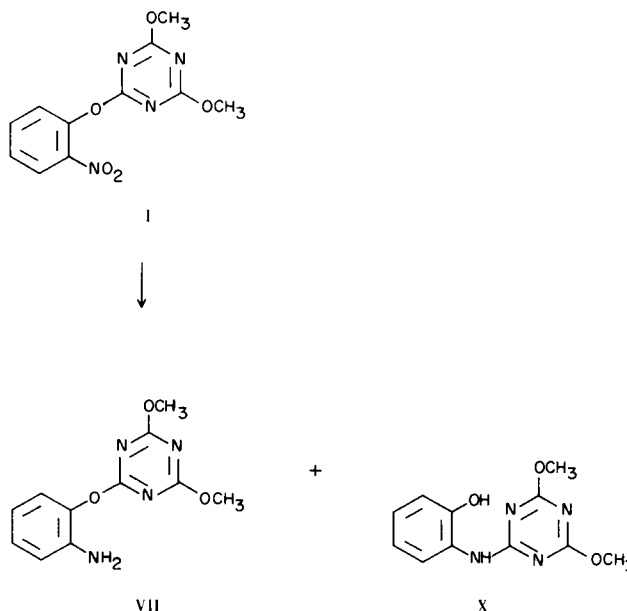
In order to determine the reaction path, the Smiles rearrangement on *s*-triazine derivatives has been studied, and this paper reports the rearrangement of *O*-(*s*-triazinyl)-2-aminophenols.

2. Results and Discussion.

2-1. Rearrangement of *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-aminophenol (VII) in the Catalytic Hydrogenation of *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-nitrophenol (I).

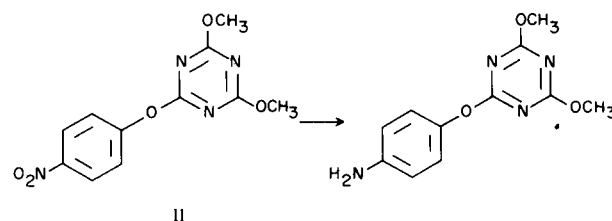
To obtain *O*-(*s*-triazinyl)-2-aminophenol, two processes can be considered, condensation of *o*-aminophenol with chloro-*s*-triazine and hydrogenation of *O*-(*s*-triazinyl)-2-nitrophenol.

Catalytic hydrogenation of derivatives of *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-nitrophenol (I) in dioxane using Raney Nickel as a catalyst gave two products.



One product was found to be the normal hydrogenation product with the *s*-triazine ring bonded to the oxygen of *o*-aminophenol, while the other was found to be *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (X) apparently formed by the migration of the *s*-triazinyl group from oxygen to nitrogen.

The 4-nitrophenol derivatives, on the other hand—for example, *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-4-nitrophenol (II)—gave only the normal hydrogenation products under similar conditions



Therefore, the migration of the triazinyl group described above is thought to proceed *via* the Smiles rearrangement.

Since most of the Smiles rearrangements take place in

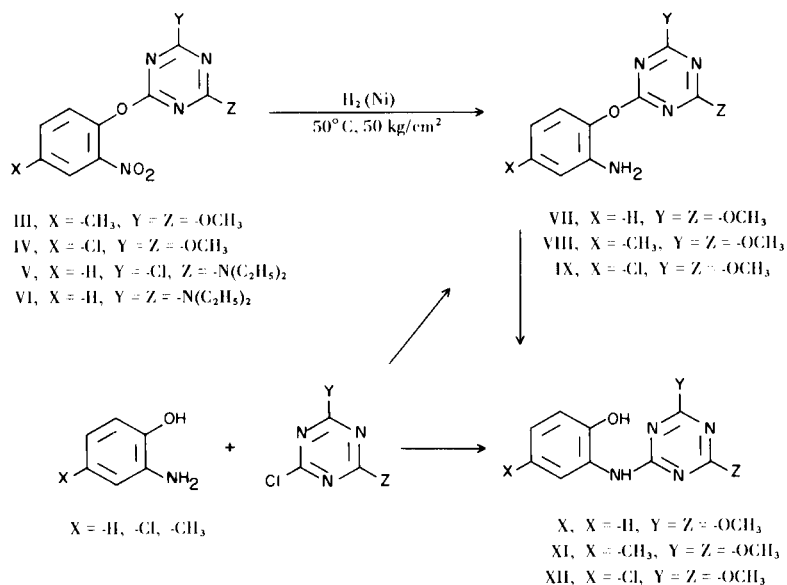
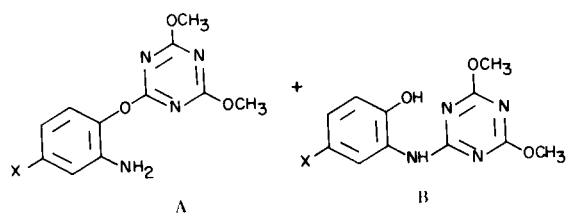
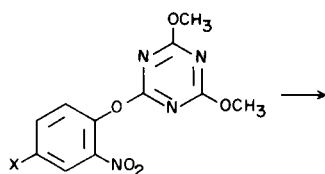


TABLE I

Ratio of Rearranged and Unrearranged Product
 in the Catalytic Hydrogenation of 4-Substituted
O-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-nitrophenols

H ₂	50 kg./cm ²
Reaction Temp.	50° C
Reaction Time	2 hours



X	Yield (A + B) %	Product Ratio	
		A	B
-H (I)	98	5	95
-CH ₃ (III)	95	89	11
-Cl (IV)	81	94	6

alkaline medium, the hydrogenation of *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-nitrophenol (I) was carried out using Raney Nickel pretreated with dilute acetic acid followed by water in order to prevent the catalytic effect by alkali in the catalyst. Despite this precaution, however, the rearrangement still took place.

2-2. Effect of Substituents on the Smiles Rearrangement.

Substituents in *O*-(*s*-triazinyl)-2-aminophenol were found to affect the progress of the Smiles rearrangement to a great extent, but the effect of substituents differs according to the nature and the position of substituents.

In Table I are listed the substituent effects on the total yields and the ratios of unrearranged to rearranged product in the catalytic hydrogenation of 4-substituted derivatives of *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-nitrophenol.

It can be seen from Table I that the introduction of a methyl group or a chlorine atom into the 4-position of *o*-nitrophenol lowers the yield of the rearranged product considerably.

The effect of a substituent in the aminophenol moiety may be considered from two aspects. One is the influence of the substituent upon the nucleophilic reactivity of the attacking amino group and the other is the influence upon the stability of the leaving phenoxide anion. In the former, an electron releasing effect of a substituent favors the rearrangement, while an electron attracting effect favors the latter.

In the cases studied, the position of the substituent was *meta* to the amino and *para* to the hydroxyl group; therefore it is assumed that the more the σ_m value of a substituent becomes negative and the more the σ_p value becomes positive, the more readily the rearrangement occurs. In

these cases the substituent effect upon the rearrangement may be evaluated by the value $-\sigma_m + \sigma_p$ of the substituent. For the methyl group, this value is -0.101 , and that of the chlorine atom is -0.146 (2). From these figures, it is apparent that the facility of the rearrangement varies according to the following order,



and this order is consistent with the results in Table I.

With respect to substituents in the *s*-triazine ring, it was found that the yields of rearranged products also depended upon the nature of substituents in the *s*-triazine nucleus. These substituents affect the electron density of the *s*-triazine carbon, and the reactivity of the *s*-triazine carbon toward nucleophilic attack by the amino group varies with the electron density of the *s*-triazine carbon. Therefore, it can be assumed that in *O*-(*s*-triazinyl)-2-aminophenol the more positive the *s*-triazine carbon becomes the more readily the rearrangement occurs and electron attracting substituents facilitate the rearrangement by decreasing the electron density of the *s*-triazine carbon. This accounts for the fact that the yield of rearranged product of the 4-chloro-6-diethylamino derivative is much higher than that of the bis(diethylamino)derivative as shown in Table II.

In Table II are listed the yields of rearranged products in the catalytic hydrogenation of *O*-(4-chloro-6-diethylamino-*s*-triazin-2-yl)-2-nitrophenol (I), *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-nitrophenol (II) and *O*-[4,6-bis(diethylamino)-*s*-triazin-2-yl]-2-nitrophenol (VI).

2-3. Effect of Reaction Conditions on the Smiles Rearrangement.

It was found that the degree of rearrangement of derivatives of *O*-(*s*-triazinyl)-2-aminophenol also depends upon reaction conditions, rearrangement being especially favored in the presence of acid. That is, derivatives of *O*-(*s*-triazinyl)-2-aminophenol were found to dissolve readily in dilute hydrochloric acid, and after a few minutes, rearranged products separated from the solution in almost quantitative yields in all cases. Moreover, *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (VII) was found to rearrange even on standing in a solid state at room temperature in a slightly acidic atmosphere.

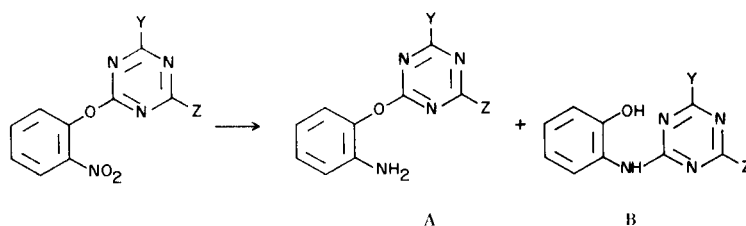
Catalytic effects of acid on the Smiles rearrangement have been already studied in the case of pyridine derivatives, where the rearrangement reactions were carried out by heating in the presence of acid (3). Based upon our data and the results of the literature, it is apparent that the acid-catalysed rearrangement of *s*-triazine derivatives occur much more readily than that of pyridine derivatives.

It is thought that the acid-catalysed Smiles rearrangement of *s*-triazine derivatives proceeds by a mechanism similar to that of the pyridine derivatives (3), but the greater speed of rearrangement of the *s*-triazine derivatives may be attributed to the high positive character of the *s*-triazine carbon due to the presence of the three ring-nitrogen atoms.

The ready base-catalysed Smiles rearrangement at room temperature on *s*-triazine derivatives has also been observed

TABLE II

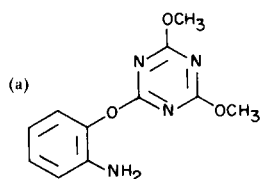
Ratio of Rearranged and Unrearranged Product in the Catalytic Hydrogenation of Derivatives of *O*-(*s*-Triazin-2-yl)-2-nitrophenol



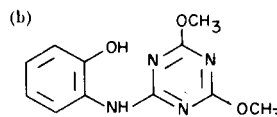
Y	Z	Reaction Temp. °C	Reaction Time hours	H ₂ press kg./cm ²	Solvent	Yield % (A + B)	Product Ratio	
							A	B
-OCH ₃	-OCH ₃ (I)	50	2	50	Dioxane	98	5	95
-Cl	-N(C ₂ H ₅) ₂ (V)	20	5	50	Dioxane	92	----	100
-N(C ₂ H ₅) ₂	-N(C ₂ H ₅) ₂ (VI)	20	5	50	Dioxane	95	100	----
		50	2	50	Methanol	95	100	----

TABLE III
Ratio of Rearranged and Unrearranged Product in the
Catalytic Hydrogenation of *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-nitrophenol

Reaction Temp. °C	Reaction Time hours	Total Yield %	Product Ratio	
			<i>O</i> -(<i>s</i> -triazin-2-yl) derivative (a)	<i>N</i> -(<i>s</i> -triazin-2-yl) derivative (b)
50 (Commercial Raney Ni)	2	98	5	95
50 (Raney Ni pretreated with AcOH and H ₂ O)	2	95	16	84
20 (Raney Ni pretreated with AcOH and H ₂ O)	5	78	80	20



VII



X

recently with *O,N*-bis(*s*-triazin-2-yl)- or *O*-(*s*-triazin-2-yl)-*N*-acyl derivatives of 8-amino-1-naphthol-3,6-disulfonic acid (4).

In the present work, rearranged products from *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-4-methyl-2-aminophenol (VIII) were obtained after heating in alkaline acetone under reflux for 5 hours and after stirring in acetone at room temperature for 40 hours.

In Table III are listed the ratio of the rearranged and the unrearranged products obtained in the catalytic hydrogenation of *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-nitrophenol (I) in the presence of Raney Nickel at various temperatures.

Table III shows that the higher the reaction temperature, the greater the yield of rearranged product.

However, when *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-4-methyl-2-aminophenol (VIII) was refluxed in acetone for 5 hours, only 2% of the rearranged product was obtained. Apparently the thermal rearrangement of this compound proceeds very slowly.

EXPERIMENTAL

O-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-nitrophenol (I) and *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-4-nitrophenol (II).

To a solution of 40 ml. of acetone containing 7 g. (0.05 mole) of *o*-nitrophenol (or *p*-nitrophenol) and 8.7 g. (0.05 mole) of 2-chloro-4,6-dimethoxy-*s*-triazine was added dropwise with stirring at 30 to 40° an equimolar amount of 10% sodium hydroxide solution. The mixture was further stirred for 10 hours and then

poured into 500 ml. of ice water. The resulting precipitate was collected by filtration and dried to give 12.3 g. (88%) of crude I or 12.9 g. (93%) of crude II. Recrystallization from benzene-ligroin gave analytical samples, m.p. 137.5-138.5° (I), 136-136.5° (II); infrared cm^{-1} , (triazine) 815 (in both cases).

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_5$: C, 47.48; H, 3.62. Found (I): C, 47.19; H, 3.73. Found (II): C, 47.81; H, 3.78.

O-(4,6-Dimethoxy-*s*-triazin-2-yl)-4-methyl-2-nitrophenol (III) and *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-4-chloro-2-nitrophenol (IV).

These compounds were prepared according to the procedure for I using the appropriate 4-substituted *o*-nitrophenol, yield 12.8 g. (88%) for crude III and 12.1 g. (77%) for crude IV. Recrystallization from benzene-ligroin gave analytical samples m.p. 113.5-114.5° (III), 119-120° (IV); infrared cm^{-1} , (triazine) 815 (III) and 820 (IV).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_5$ (III): C, 49.31; H, 4.14. Found: C, 49.70; H, 4.34.

Anal. Calcd. for $\text{C}_{11}\text{H}_9\text{ClN}_4\text{O}_5$ (IV): C, 42.25; H, 2.90. Found: C, 42.45; H, 2.98.

O-(4-Chloro-6-diethylamino-*s*-triazin-2-yl)-2-nitrophenol (V) and *O*-[4,6-Bis(diethylamino)-*s*-triazin-2-yl]-2-nitrophenol (VI).

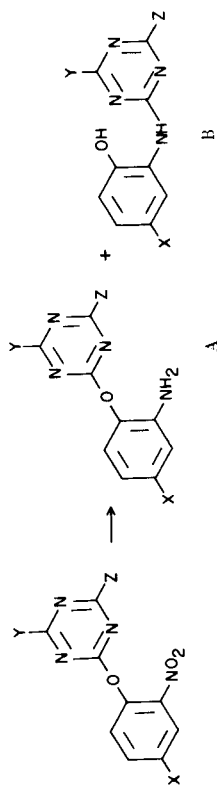
The compound V was prepared according to the procedure for I from 22.1 g. (0.1 mole) of 2,4-dichloro-6-diethylamino-*s*-triazine (5), yield 28.2 g. (87%) for crude V. Recrystallization from ligroin gave an analytical sample, m.p. 84-85°; infrared cm^{-1} , (triazine) 805.

Anal. Calcd. for $\text{C}_{13}\text{H}_{14}\text{ClN}_5\text{O}_3$: C, 48.23; H, 4.36; Cl, 11.0. Found: C, 48.70; H, 4.53; Cl, 11.1.

The compound VI was prepared by the following method. To a solution of 40 ml. of acetone containing 19.4 g. (0.06 mole) of V was added 8.8 g. (0.12 mole) of diethylamine. The mixture was refluxed with stirring for 8 hours and then processed according to the procedure for I, yield 21.1 g. (98%) for crude VI. Recrystal-

TABLE IV

Ratio of Rearranged and Unrearranged Product in the Catalytic Hydrogenation of Derivatives of *O*-(*s*-Triazin-2-yl)-2-nitrophenol



X	Y	Z	Reaction Temp. °C	Reaction Time hours	Solvent	Yield (A + B) %	Product Ratio	Recrystallization Solvent	M.p. °C	Analyses %		
										C	H	Cl
-CH ₃	-OCH ₃	-OCH ₃ (III)	50	2	Dioxane	95	A 89 B 11	Benzene-ligroin Benzene	123-124 177.5-178	Calcd.: 54.95 Found: 54.95	5.38 5.44	
-Cl	-OCH ₃	-OCH ₃ (IV)	50	2	Dioxane	81	A 94 B 6	Benzene Monochlorobenzene	154-155 205 dec.	Calcd.: 46.73 Found: 47.31	3.92 3.95	12.5 12.8
-H	-Cl	-N(C ₂ H ₅) ₂ (V)	20	5	Methanol	92	A --- B 100	Benzene	169-169.5 (1)			
-H	-N(C ₂ H ₅) ₂	-N(C ₂ H ₅) ₂ (VI)	20	2	Dioxane	95	A 100 B ---	Petroleum ether	72.3-73	Calcd.: 61.59 Found: 61.79	8.18 7.93	
			50	2	Methanol	95	B ---					

lization from ligroin gave an analytical sample, m.p. 79.5-80.5°; infrared cm^{-1} , (triazine) 810.

Anal. Calcd. for $\text{C}_{17}\text{H}_{24}\text{N}_6\text{O}_3$: C, 56.65; H, 6.71. Found: C, 56.61; H, 6.71.

Hydrogenation of *O*-(*s*-Triazinyl)-2-nitrophenol and *O*-(*s*-Triazinyl)-4-nitrophenol.

The typical runs are shown in the case of I and II.

A mixture containing 100 ml. of dioxane, 5 g. (0.018 mole) of I and 3 g. of Raney Nickel (commercial grade) was stirred for 2 hours at 50° under a pressure of 50 kg./ cm^2 of hydrogen. After the catalyst was removed by filtration and the solvent was evaporated, crude *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (X) (1) and *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (VII) (1) were obtained separately by treating the residue with alkali. Total yield of crude products was 4.46 g. (98%). The product ratio X/VII was 95/5.

Similar treatment of II gave crude *O*-(4,6-dimethoxy-*s*-triazin-2-yl)-4-aminophenol quantitatively. Recrystallization from benzene-ligroin gave an analytical sample, m.p. 118-119°; infrared cm^{-1} , (NH_2) 3410; 3350; (triazine) 815.

Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}_3$: C, 53.22; H, 4.87. Found: C, 53.10; H, 4.61.

In Table IV are listed yields, melting points and elemental analyses of hydrogenation products from other derivatives of *O*-(*s*-triazinyl)-2-nitrophenol.

Base-catalyzed Smiles Rearrangement of *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-2-aminophenol (VII) and *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-4-methyl-2-aminophenol (VIII).

To a solution of 100 ml. of acetone containing 8.3 g. (0.033 mole) of VII (1) was added with stirring at 30° 35 ml. of 1 *N* sodium carbonate solution. The mixture was stirred for 40 hours, the acetone was removed by distillation and the residue was dis-

solved in 200 ml. of 3% sodium hydroxide solution. The solution was filtered and the filtrate was neutralized with dilute hydrochloric acid. The product which separated was collected by filtration and dried to give 7.1 g. (86%) of crude *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-2-aminophenol (X). Recrystallization from ethanol gave an analytical sample, m.p. 172-172.5° (1).

Similar treatment of VIII, except that it was refluxed in acetone for 5 hours, gave the crude rearranged product in 50% yield.

Thermal Smiles Rearrangement of *O*-(4,6-Dimethoxy-*s*-triazin-2-yl)-4-methyl-2-aminophenol (VIII).

After refluxing VIII in acetone for 5 hours, the mixture was processed according to the procedure for the base-catalyzed rearrangement of VIII to give crude rearranged product, *N*-(4,6-dimethoxy-*s*-triazin-2-yl)-4-methyl-2-aminophenol (XI) in 2% yield.

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