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Preparation and Reactions of Di-1,3,5-triazinyl Ethers. I. Preparation of Di-1,3,5-triazinyl Ethers

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Synopsis. Di-1,3,5-triazinyl ethers have been prepared by the condensation of 2-chloro-1,3,5-triazines with potassium 1,3,5-triazin-2-olate in acetonitrile in the presence of a small amount of cyclic polyether. Di-1,3,5-triazinyl ether was also prepared by the reaction of 2-chloro-1,3,5-triazine with potassium nitrite.

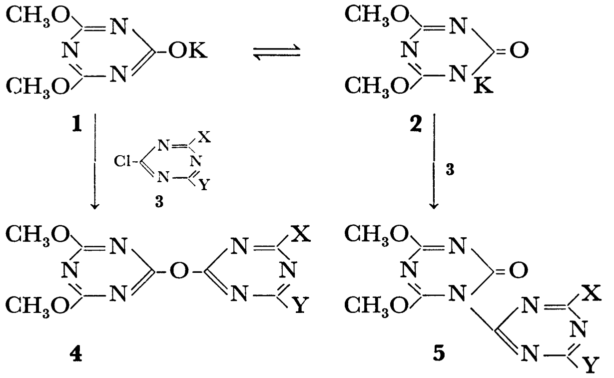
A number of derivatives of 1,3,5-triazine have been prepared by the condensation of 2-chloro-1,3,5-triazines with various nucleophiles.[1] Among the compounds investigated amines[2] and sulfides[3,4] containing two or three triazine nuclei on the same N or S atom are of particular interest because of their unique chemical behavior. This paper reports two preparative methods for di-1,3,5-triazinyl ethers.

Results and Discussion

Reaction of 2-Chloro-1,3,5-triazines with 1,3,5-Triazin-2-ol. The Williamson synthesis which involves the reaction of sodium alkoxide with an alkyl halide was considered applicable to the synthesis of di-1,3,5-triazinyl ethers. 1,3,5-Triazine nuclei are electron-withdrawing, and therefore the di-1,3,5-triazinyl ethers would be expected to have properties similar to those of acid anhydrides. Consequently a proper choice of solvent is important in the preparation of di-1,3,5-triazinyl ethers, because a solvent of high nucleophilicity will react with the di-1,3,5-triazinyl ethers formed to afford derivatives of the mono triazine nucleus.

Among the solvents investigated acetonitrile was found to be the most suitable. In acetonitrile, reaction took place very slowly when potassium 4,6-dimethoxy-1,3,5-triazin-2-olate (**1**, Scheme 1) was heated with an equimolecular amount of 2-chloro-4,6-dimethoxy-1,3,5-triazine (**3c**); after heating for 48 h, di-1,3,5-triazinyl ether (**4c**) was obtained (yield 44%; No. 4, Table 1). The addition of a small amount of 18-crown-6 accelerated the reaction; chlorotriazine (**3c**) disappeared within 30 min to give di-1,3,5-triazinyl ether (**4c**) (yield 58%; No. 5). From the mechanism[5] generally accepted, the catalytic effect of the cyclic polyether can be explained in terms of the presence of a "bared" triazinolate anion which attacks chlorotriazine much more readily.

The product (**4c**) had a parent mass peak of 296 and a PMR signal for the methyl protons was observed as a sharp singlet at δ 4.09. In addition, the IR spectrum of **4c** did not show the presence of $C{=}O$ group. 1,3,5-Triazin-2-ol is known to exist as a tautomeric mixture of (**1**) and (**2**); thus, there is a possible isomer (**5**) as shown in Scheme 1. However, from the evidence the indication is that the product has the structure (**4**). The yield of di-1,3,5-triazinyl ether was found to be sensitive to the amount of cyclic polyether employed, *e.g.*, when dibenzo-18-crown-6 was used, yield of di-1,3,5-triazinyl ether (**4c**) increased to 65% (No. 6).



a: $X=Y=Cl$
b: $X=Cl$, $Y=OCH_3$
c: $X=Y=OCH_3$
d: $X=OCH_3$, $Y=NEt_2$
e: $X=Y=NEt_2$

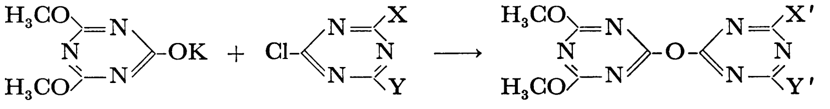
Scheme 1.

The condensation of triazinol with chlorotriazine is affected by the substituents in the triazine nucleus. In the reaction with **1**. chlorotriazines having electron-withdrawing substituents such as Cl– (**3a**, **3b**) and/or CH_3O– (**3c**) afforded the di-1,3,5-triazinyl ether (**4a**—**c**). However, chlorotriazines (**4d**, **4e**) containing electron-donating substituents such as dialkylamino groups gave only the starting materials, and no desired di-1,3,5-triazinyl ether (No. 7, 8). When chlorotriazine possessed more than one active halogen atom, ditriazinyl ethers involving more than one ether oxygen atom were obtained. For example, in the reaction of potassium 4,6-dimethoxy-1,3,5-triazin-2-olate (**1**) with cyanuric chloride (**4a**) in a molar ratio of 2:1, 2-chloro-4,6-bis(4,6-dimethoxy-2-triazinyloxy)-1,3,5-triazine was obtained (No. 1). When the reaction was carried out in a molar ratio of 3:1, all active chlorine atoms were replaced by dimethoxytriazinyloxy groups (No. 2).

Di-1,3,5-triazinyl ether was also prepared by treating chlorotriazine with potassium nitrite. In the attempt to prepare the nitrous acid ester of triazinol by treating chlorotriazine (**3c**) with potassium nitrite, instead of nitrous acid ester, di(triazinyl)ether (**4c**) was obtained. In this case, the presence of the cyclic polyether (18-crown-6) greatly accelerated the reaction (see, Experimental Section).

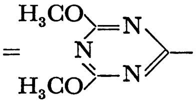
Although the mechanism of this reaction is not still clear, the reaction is assumed to proceed by the fol-

TABLE 1. REACTION OF POTASSIUM 4,6-DIMETHOXY-1,3,5-TRIAZIN-2-OLATE WITH 4,6-DISUBSTITUTED 2-CHLORO-1,3,5-TRIAZINES



No.	Substitnent		Product		Yield %	Mp °C	Recryst. solvent	Found (Calcd) %			
	X	Y	X'	Y'				C	H	N	Cl
1	Cl	Cl	OT	Cl	47[a]	162—163	Benzene	40.31	3.98	28.39	
								(40.54	4.08	28.37)	
2	Cl	Cl	OT	OT	57[a]	167—168	Benzene	36.88	2.91	29.46	8.10
								(36.67	2.84	29.61	8.33)
3	Cl	OCH_3	Cl	OCH_3	59[a]	128—129	Benzene	36.19	3.05	28.29	11.91
								(35.98	3.02	27.97	11.80)
4	OCH_3	OCH_3	OCH_3	OCH_3	44[b]	157—158	Benzene	39.93	3.50	31.03	
								(39.57	3.32	30.76)	
5	OCH_3	OCH_3	OCH_3	OCH_3	58[a]	—	—	—	—	—	—
6	OCH_3	OCH_3	OCH_3	OCH_3	65[c]	—	—	—	—	—	—
7	OCH_3	NEt_2	No ditriazinyl ether was formed.								
8	NEt_2	NEt_2									

T =



a) The reaction was carried out in the presence of 1/5 equimolar amount of 18-crown-6. b) The reaction was carried out in the absence of cyclic polyether. c) The reaction was carried out in the presence of 1/5 equimolar amount of dibenzo-18-crown-6.

lowing sequence (Scheme 2), analogous to the reaction of active chlororbenzene derivatives with potassium nitrite.[6] This reaction did not occur in the triazine derivatives bearing electron-donating substituents. For instance, in the reaction of 2-chloro-4,6-bis(diethylamino)-1,3,5-triazine (**3e**) with potassium nitrite in the presence of cyclic polyether, only the starting material was recovered even after long heating (120 h). This indicates that the first step in Scheme 2 did not occur.

$$\mathbf{3c} + 2KNO_2 \longrightarrow \mathbf{1} + N_2O_3 + KCl$$

$$\mathbf{1} + \mathbf{3c} \longrightarrow \mathbf{4c} + KCl$$

Scheme 2.

This method is limited to the preparation of the symmetric ditriazinyl ether, while the synthetic method by condensation of chlorotriazine with triazinol is applicable for the preparation of symmetric and unsymmetrical derivatives.

Experimental

All the melting points are uncorrected.

Preparation of Di-triazinyl Ethers by Condensation of Chlorotriazines with Triazinol. A example is shown of the reaction of 2-chloro-4,6-dimethoxy-1,3,5-triazine (**3c**) with potassium 4,6-dimethoxy-1,3,5-triazin-2-olate (**1**). A solution of **3c**(3.00 g, 17.1 mmol) in acetonitrile (50 ml) was added, drop by drop, into a solution of a mixture of **1** (3.37 g, 17.1 mmol) and 18-crown-6 (0.90 g, 3.41 mmol) in acetonitrile (50 ml) at room temperature. After stirring for 1 h under reflux, the solvent was removed *in vacuo*. The residue was chromatographed on a silica gel column with benzene–acetone (10:1, v/v) as eluent to give a crude product of di-1,3,5-triazinyl ether (**4c**). The recrystallization from benzene gave the pure material.

The reaction in the absence of cyclic polyether was carried out in a similar way as described above.

Reaction of 2-Chloro-4,6-dimethoxy-1,3,5-triazine (3c) with Pottassium Nitrite. To a solution containing potassium nitrite (2.01 g, 23.6 mmol) and 18-crown-6 (1.03 g, 3.88 mmol) in acetonitrile (50 ml) was added dropwise a solution of **3c** (2.50 g, 14.3 mmol) in acetonitrile (50 ml) and the mixture stirred for 3 h at room temperature. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene–acetone (10:1, v/v) as eluent to give di-1,3,5-triazinyl ether (**4c**); yield, 1.27 g (61%).

The reaction in the absence of cyclic polyether was carried out in a similar way in refluxing acetonitrile for 48 h to afford the same product (45%) and starting triazine derivative (18%).

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