The Reaction of Azidotriazines with Pyridines and Triphenylphosphine

Kenji FUJINUMA, Yoji HASHIDA, and Kohji MATSUI*

Department of Synthetic Chemistry, Faculty of Engineering, Gunma University, Kiryu, Gunma 376

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2-Azido-4,6-dimethoxy-1,3,5-triazine (**1a**) gave an adduct with pyridine in a molar ratio of 1: 1. On the contrary, 2-azido-4,6-bis(dimethylamino)-1,3,5-triazine (**1b**) did not react with pyridine. Similarly, **1a** gave an adduct with 3-methylpyridine, whereas in the reactions of **1a** with 2-methyl-, 4-methyl-, and 2,6-dimethylpyridines, 2-amino-4,6-dimethoxy-1,3,5-triazine was obtained instead of the adduct. On the other hand, **1a** and **1b** gave the corresponding triazinyliminophosphoranes with triphenylphosphine.

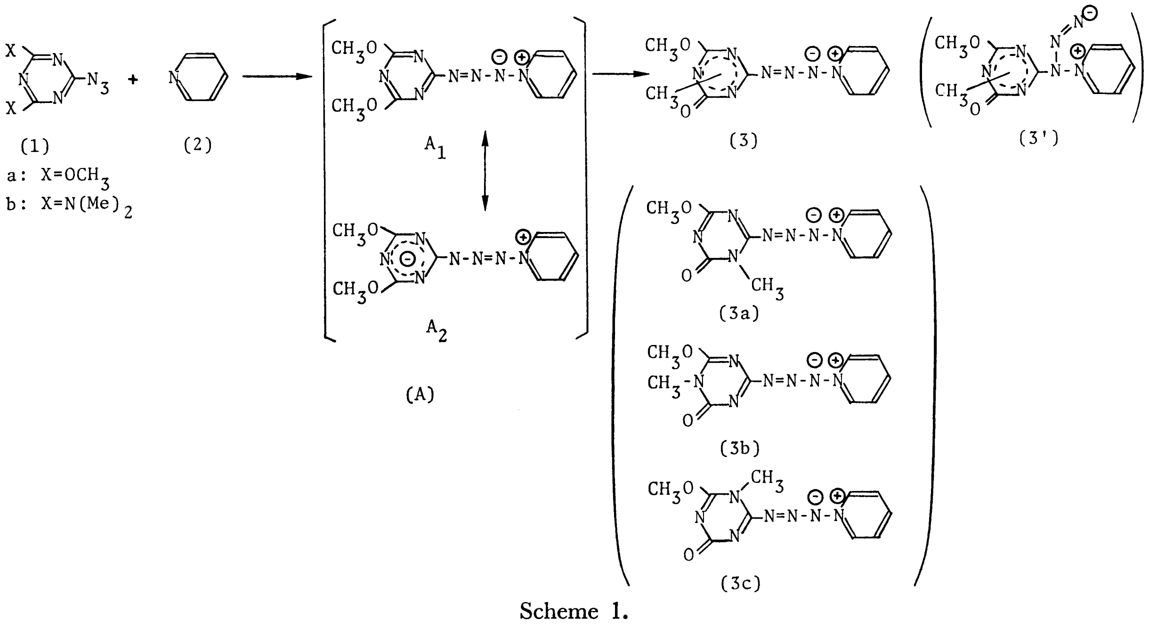
Organic azides are well known to react with organic bases to yield the corresponding ylides.1) During the course of our study of the reactions of azido-1,3,5-triazines, it has become apparent that azido-1,3,5-triazines have unique properties situated between those of ordinary aryl and acyl azides.2) Thus, triazinyl ylides, if prepared, are expected to have different characters from those of ordinary acyl and aryl ylides. On the other hand, even though the reaction of azidotriazine with an organic base can be expected to be one of the general routes for the preparation of triazinyl ylides, this reaction has not yet been investigated. This paper will report the thermal reactions of azidotriazines with several pyridine derivatives and triphenylphosphine.

Results and Discussion

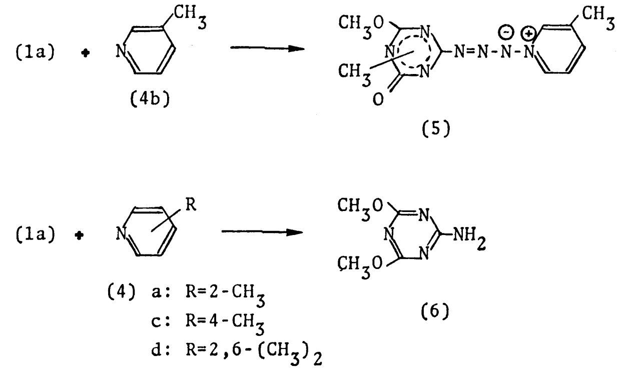
Reactions of Azido-1,3,5-triazines with Pyridine. When 2-azido-4,6-dimethoxy-1,3,5-triazine (**1a**) was heated in pyridine (**2**) under reflux, an 1: 1 adduct (**3**) was obtained in a quantitative yield (Scheme 1). On the basis of the spectral data, one of the methyl groups of the adduct was found to be located at the ring nitrogen atom. For the adduct, **3** and **3'** are suggested as possible; of the two, **3** may be more stable. Among three possible structures (**3a, 3b**, and **3c**), **3a** is most probable, because the highest stabilization by the delocalization of the negative charge can be expected in this case.3) **3** is considered to result from an intermediate (**A**) produced by the addition of azidotriazine to pyridine, followed by the O→N migration of one methyl group. The facile migration of the methyl group in the intermediate (**A**) is probably due to a decrease in the aromaticity of the triazine ring because of a large contribution of the $\mathbf{A}_2$ formula.

On the other hand, when 2-azido-4,6-bis(dimethylamino)-1,3,5-triazine (**1b**) was refluxed in pyridine, most of the starting material was recovered. The intertness of this azidotriazine is probably due to the weak electrophilic reactivity of the azido group in the presence of two electron-donating dimethylamino groups in the triazine nucleus.

Reaction of Azido-1,3,5-triazine (1a) with Methylpyridines. When 2-azido-4,6-dimethoxy-1,3,5-triazine (**1a**) was refluxed in methylpyridines, the reaction was found to occur in different manners depending upon the position of the methyl group in the pyridine nucleus (Scheme 2). In the reaction with 3-methylpyridine (**4b**), an similar (**5**)4) adduct to that found in the case of pyridine was formed. However, in the cases of 2-methyl- (**4a**), 4-methyl- (**4c**), and 2,6-dimethylpyridine (**4d**), **1a** gave 2-amino-4,6-



Scheme 1.



Scheme 2.

dimethoxy-1,3,5-triazine (**6**) as the major product. Aminotriazine (**6**) seems to be produced by the hydrogen abstraction of triazinylnitrene formed by the decomposition of azidotriazine (**1a**). However, monoazidotriazines are thermally stable and do not decompose up to 195 °C.[5] Therefore, a process involving triazinylnitrene as a reactive intermediate is improbable. Moreover, azidotriazine (**1a**) was found to decompose slowly in 2-methylpyridine, even at room temperature, to afford the same aminotriazine (**6**). This evidence suggests the existence of another intermediate which can give aminotriazine rather than triazinylnitrene. It would seem reasonable to consider that the adducts which are formed by the combination of azidotriazine with methylpyridine or dimethylpyridine decompose to give aminotriazine when the methyl group is attached at the 2- and/or 4-position (Scheme 3).

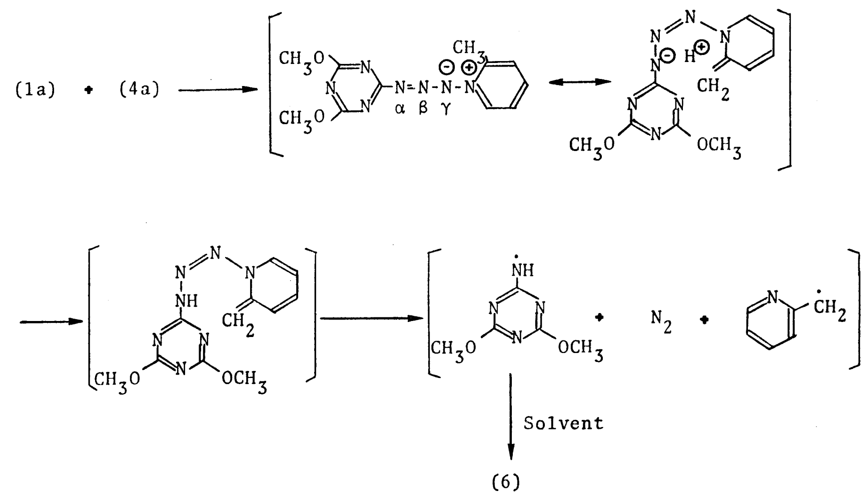
In the adducts to 2- and 4-methylpyridines, methyl hydrogen atoms are readily removable as protons because of the cationic character of the ring nitrogen of pyridine. Thus, in these cases, methyl hydrogen would be abstracted by the α-nitrogen of the adduct as a proton, intra- (in the cases of 2-methyl- and 2,6-dimethylpyridine) or intermolecularly (in the case of 4-methylpyridine), to give *N*-triazinyltriazenes. Ordinary 1,3-diaryltriazenes are known to be thermally not very stable and are known to decompose homolytically at about 140—150 °C, even in the absence of acid.[6] Therefore, if *N*-triazinyltriazene is produced, it can be expected to decompose, even at the boiling points of methylpyridines, to afford pyridylmethyl and triazinylamino radicals. The latter may react with the solvent to give aminotriazine (**6**).

As has been described before, in the case of 3-methylpyridine, the reaction stopped at the stage of adduct formation, because the proton transfer from the methyl group to the α-nitrogen was difficult because of the weak acidity of the methyl hydrogen atoms. In other words, in the reactions of azidotriazines with pyridine derivatives, the initial product was the 1 : 1 adduct in every case. However, a difference was observed in the subsequent process of the reaction depending upon the stability of the adduct. In the cases of pyridine and 3-methylpyridine, the adducts underwent the O→N migration of the methyl group to afford the rearranged product, while in the cases of 2-methyl-, 4-methyl-, and 2,6-dimethylpyridine, the adducts decomposed to give aminotriazine as the final product.

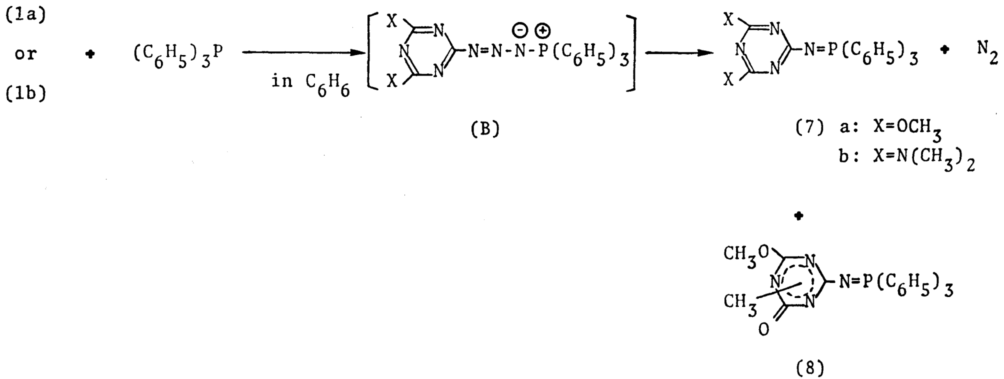
Although various adducts of organic azides to bases have been known, no adducts resulting from organic azides and amines have yet been reported. Thus, it may be said that the **3** and **5** adducts are novel examples of isolable adduct of azide and amine.

The adducts from pyridine and 3-methylpyridine were thermally stable; they did not decompose upon heating at the boiling point of pyridine or methylpyridine. By means of differential thermal analysis, no decomposition was observed below 190 °C; above this temperature, the adducts showed a slight weight loss. The TG curve of the adducts showed a weight loss corresponding to the loss of the pyridine component when they were heated at 220 °C. However, when the adducts were heated at 200—230 °C for 1 h, the resulting products were dark polymeric substances which were insoluble in most of organic solvent; from the reaction mixture *N*-(1-pyridinio)triazinylaminide could not be isolated.

Reaction of Azido-1,3,5-triazines with Triphenylphosphine. The reaction of organic azides with tertiary phosphines



Scheme 3.



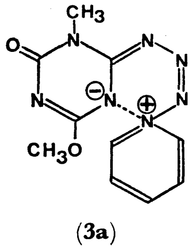
Scheme 4.

is known to be the oldest method for the preparation of iminophosphoranes; in some cases, the 1: 1 adduct of azide with phosphine is isolated as an intermediate.[7–9] However, these adducts are thermally not very stable and afford iminophosphoranes, with the loss of nitrogen, upon heating.

When a solution of 2-azido-4,6-dimethoxy-1,3,5-triazine (**1a**) in benzene was added to a cold benzene solution of triphenylphosphine, the colorless solution soon became yellow. However, the color disappeared within a few minutes, with an evolution of nitrogen, and colorless crystals seperated out before long. The crystals, obtained in a good yield, were found to be *N*-(4,6-dimethoxy-1,3,5-triazin-2-yl)iminophosphorane (**7a**) (Scheme 4). Along with this major product, a product (**8**) resulting from an O→N migration of one of the methyl groups was also obtained. A similar reaction took place between 2-azido-4,6-bis(dimethylamino)-1,3,5-triazine (**1b**) and triphenylphosphine to give *N*-[4,6-bis(dimethylamino)-1,3,5-triazin-2-yl]iminophosphorane (**7b**) as the sole major product.

Even though attempts to isolate the initial adduct were unsuccessful, the progress of the reaction suggests that the reaction to give iminophosphorane proceeded *via* an 1: 1 adduct (**B**); since the monoazidotriazines do not decompose under the reaction conditions employed, it may be reasonable to assume that they are not monoazidotriazines, but 1: 1 adducts (**B**) that decomposed with an evolution of nitrogen.

In summary, it has been shown that the azidotriazine gave the stable 1: 1 adducts in reactions with pyridines (**2**, **4b**). On the other hand, azidotriazines gave iminophosphoranes with triphenylphosphine, in contrast to the behavior of common organic azides, which give isolable 1: 1 adducts with tertiary phosphine.[7–9] Although the reasons for the high stability of the **3** and **5** adducts are still ambiguous, one of the general factors may be given here. In the **3** and **5** adducts, the flow of the negative charge into a triazine ring is undoubtedly to be expected. Therefore, the adducts could be effectively stabilized by means of the electrostatic attraction between opposite charges, as is shown in the bottom of the left column.



(**3a**)

On the other hand, in the 1: 1 adducts (**B**) of azidotriazines with triphenylphosphine, the presence of three bulky phenyl groups at the phosphorus atom would hinder the approach of the phosphorus and ring nitrogen atoms; consequently, the stabilization by the attraction between the opposite charges would be weakened, and decomposition would take place much more easily.

Experimental

All the melting points are uncorrected.

Materials. The azidotriazines were prepared according to the procedures given in the previous paper.[5] The organic solvents were purified by the standard methods. Commercial pyridines were distilled before use. Triphenylphosphine of a reagent grade was used without purification.

Reaction of 2-Azido-4,6-dimethoxy-1,3,5-triazine (1a) with Pyridine. A solution of **1a** (17.1 g, 93.7 mmol) in pyridine (20 ml) was refluxed for 3 h. After cooling, the precipitate which resulted was collected by filtration. The recrystallization of the precipitate from EtOH and then from *i*-PrOH gave a pure adduct (**3**): mp 133—134 °C; yield, 17.9 g (73.0%); λ_{max} [EtOH], 242 nm; IR (KBr), 1700 cm^{-1} (C=O): PMR (DMSO-d_6), δ 3.88 (2H, s), 4.48 (3H, s), 8.00—9.30 (5H, m). Found: C, 45.94; H, 4.26; N, 37.52%. Calcd for $C_{10}H_{11}O_2N_7$: C, 45.97; H, 4.24; N, 37.42%.

Reaction of 2-Azido-4,6-dimethoxy-1,3,5-triazine (1a) with 3-Methylpyridine (4b). A solution of **1a** (1.50 g. 8.22 mmol) in 3-methylpyridine (10 ml) was refluxed for 3 h. After cooling, the resulting precipitate was collected by filtration. The recrystallization of the precipitate from *i*-PrOH gave a pure adduct (**5**): mp 161—162 °C; yield, 1.33 g (59%); PMR (DMSO-d_6), δ 2.52 (3H, s), 3.83 (3H, s), 4.37 (3H, s), 8.00—9.00 (4H, m). Found: C, 48.08; H, 4.82; N, 36.10%. Calcd for $C_{11}H_{13}N_7O_2$: C, 47.99; H, 4.76; N, 36.10%.

Reaction of 2-Azido-4,6-dimethoxy-1,3,5-triazine (1a) with 2-Methylpyridine (4a), 4-Methylpyridine (4c), and 2,6-Dimethylpyridine (4d). A typical example is shown in the case of 2-methylpyridine. A solution of **1a** (2.00 g, 11.0 mmol) in 2-methylpyridine (10 ml) was refluxed for 6 h. After the removal of the solvent, the residue was extracted with hot MeOH. The extract was purified by column chromatography on alumina (eluent: MeOH) to give 2-amino-4,6-dimethoxy-1,3,5-triazine (**6**) (0.575 g, 33.5%, mp 221—222

°C), which was identified by a mixed-melting-point test with an authentic sample.[10]

When the reaction was performed for 10 days at room temperature, **6** was obtained in a yield of 37.5%.

Reaction of 2-Azido-4,6-dimethoxy-1,3,5-triazine (1a) with Triphenylphosphine. To a stirred solution of triphenylphosphine (2.88 g, 11.0 mmol) in benzene (30 ml) we added, drop by drop, a solution of **1a** (2.00 g, 11.0 mmol) in benzene (50 ml) at 5 °C. After stirring for 1 h at room temperature, the resulting colorless precipitate was collected by filtration and recrystallized from benzene to afford *N*-(4,6-dimethoxy-1,3,5-triazin-2-yl)iminophosphorane (**7a**); mp 184—185 °C; yield, 3.30 g (72%); MS *m/e* 416 (M^+): PMR (DMSO-d_6), δ 3.68 (6H, s), 7.25—8.07 (15H, m). Found: C, 66.33; H, 5.13; N, 13.39%. Clacd for $C_{23}H_{21}N_4O_2P$: C, 66.34; H, 5.08; N, 13.45%.

The filtrate was concentrated and chromatographed on a silica gel column (eluent; benzene: MeOH=10: 1, v/v) to give the crude product of **8**, which was then recrystallized from benzene to give an analytical sample: mp 182—184 °C; yield, 0.074 g (1.6%); MS *m/e* 416 (M^+); IR (KBr), 1694 cm^{-1} (C=O); PMR ($CDCl_3$), δ 3.57 (1H, s), 3.67 (1H, s), 7.28—8.05 (5H, m). Found: C, 66.96; H, 5.05; N, 13.81%. Calcd for $C_{23}H_{21}N_4O_2P$: C, 66.34; H, 5.08; N, 13.54%.

Reaction of 2-Azido-4,6-bis(dimethylamino)-1,3,5-triazine (1b) with Triphenylphosphine. The reaction of **1b** (1.00 g, 4.81 mmol) with triphenylphosphine (1.27 g, 4.81 mmol) was carried out in a similar way. After stirring for 1 h, the solvent was removed *in vacuo*. The residue was recrystallized from a mixture of benzene and ligroin to give *N*-bis(dimethylamino)-1,3,5-triazinyliminophosphorane (**7b**): mp 207—209 °C; yield, 0.888 g (41.7%); PMR (DMSO-d_6), δ 2.83 (12H, s), 7.46—7.97 (15H, m). Found: C, 67.68; H, 6.11; N, 19.00%. Calcd for $C_{25}H_{27}N_6P$: C, 67.85; H, 6.15; N, 18.99%.

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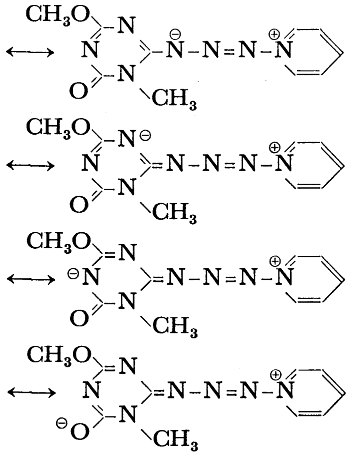
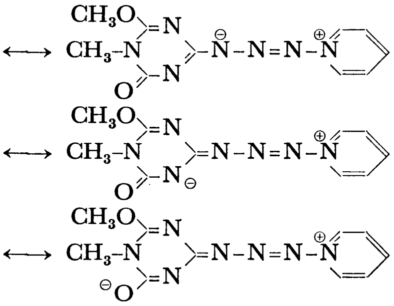
3) Structure **3a** can be written in terms of these five resonance structures:

(**3a**)



On the other hand, in the cases of the **3b** and **3c** structures, four resonance forms can be written respectively; *e.g.*, for **3b**:

(**3b**)



4) For the same reason as has been presented above, the **5** adduct is considered to have a sturcture like **3a**.

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