Brominations of Some 1,2,4-Triazine 2-Oxides

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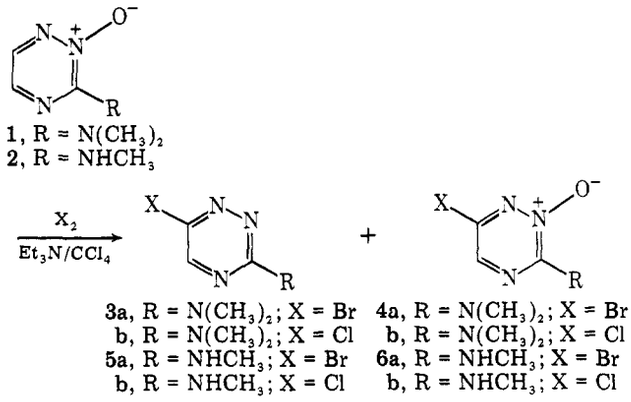
Some unique brominations of 1,2,4-triazine 2-oxides are described. It was found that 6-brominated, deoxygenated 6-brominated, and deoxygenated products are obtained, depending upon the reaction conditions. Mechanisms for these transformations are suggested, and supportive evidence for these is offered.

We have recently described the selective N-1 and N-2 oxidations of several 1,2,4-triazine derivatives[1] as well as some interesting transformations of these *N*-oxides.[2] As a continuation of our studies involving these systems, we now wish to report some unique brominations of some 1,2,4-triazine 2-oxides.

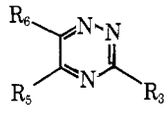
Treatment of 3-dimethylamino- (**1**) and 3-monomethylamino-1,2,4-triazine 2-oxides (**2**) with bromine and triethylamine gave, in each case, two products. In the former instance the minor component was found to be identical in all respects with the known[2] 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**). As added proof of identity, this compound was treated with sodium methoxide, and the product thus obtained was compared with and found to be identical with authentic 6-methoxy-3-dimethylamino-1,2,4-triazine (**7**).[2]

The mass spectra of the main components (**4a** and **6a**) of the bromination reactions indicated that the *N*-oxide moiety had been retained. Both ^1H and ^{13}C NMR spectroscopy proved to be inconclusive as to the position of bromination since only small chemical shift differences are involved between H-5 and H-6 as well as C-5 and C-6. An x-ray analysis of the monobromo-3-monomethylamino-1,2,4-triazine 2-oxide (**6a**) clearly indicates that the bromine is substituted at position 6 (see Figure 1 of supplementary material).



When this reaction was carried out on 3-amino-1,2,4-triazine 2-oxide (**8**), only one product, 6-bromo-3-amino-1,2,4-triazine 2-oxide (**9a**) (cf. Table I), was obtained.

Table I. Analytical Data for Some 6-Halo-1,2,4-triazines and Their 2-Oxides



Compd	Molecular formula	Substituents R_3	R_5	R_6	NMR shifts,[a] δ R_3	R_5	Mp,[b] °C	Analysis C Calcd (Found)	H Calcd (Found)	N Calcd (Found)
4a	$C_5H_7N_4OBr$	$N(CH_3)_2$	H	Br	3.26	7.82	131–132.5	27.42 (27.62)	3.22 (3.24)	25.88 (25.47)
6a	$C_4H_5N_4OBr$	$NHCH_3$	H	Br	3.15 (d)	7.80	146–147	23.43 (23.66)	2.63 (2.48)	27.33 (27.20)
4b	$C_5H_7N_4OCl$	$N(CH_3)_2$	H	Cl	3.28	7.87	93–96	34.39 (34.64)	4.04 (4.09)	32.10 (31.97)
6b	$C_4H_5N_4OCl$	$NHCH_3$	H	Cl	3.18 (d)	7.83	95–97	29.91 (30.21)	3.14 (3.19)	34.90 (35.03)
9a	$C_3H_3N_4OBr$	NH_2	H	Br	8.50	8.40	138–139	18.86 (19.12)	1.58 (1.63)	29.43 (29.16)
9b	$C_3H_3N_4OCl$	NH_2	H	Cl	8.54	8.36	147–148.5	24.59 (24.79)	2.06 (2.15)	38.24 (38.01)
5b	$C_4H_5N_4Cl$	$NHCH_3$	H	Cl	3.12 (d)	8.16	84–85	33.23 (33.09)	3.48 (3.64)	38.76 (38.57)
3b	$C_5H_7N_4Cl$	$N(CH_3)_2$	H	Cl	3.28	8.12	55–57	37.86 (37.94)	4.44 (4.35)	35.33 (35.16)
14	$C_7H_9N_4ClO$	NC_4H_8O	H	Cl	3.88	8.18	68.5–70	41.90 (42.11)	4.52 (4.60)	27.93 (27.69)
15	$C_8H_{11}N_4Cl$	NC_5H_{10}	H	Cl	3.85 1.71	8.10	140	48.36 (48.10)	5.58 (5.61)	28.2 (27.9)
5a	$C_4H_5N_4Br$	$NHCH_3$	H	Br	3.10 (d)	8.28	70–72	25.41 (25.20)	2.66 (2.69)	29.64 (29.78)

[a] NMR spectra were taken in $CDCl_3$. [b] Melting points were taken on a Thomas-Hoover melting point apparatus.

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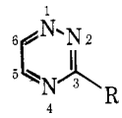
Table II. Product Distribution in the Bromination of Some 1,2,4-Triazine 2-Oxides[a]



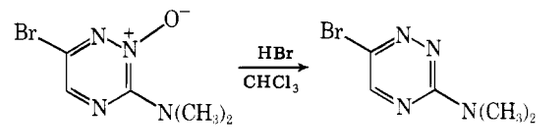
Compd	Substituent	Reactant	Yield, % (6-halotriazine)	Yield, % (6-halo 2-oxide)
1	$N(CH_3)_2$	$Et_3N/Br_2/CCl_4$	28 (**3a**)	65 (**4a**)
		$K_2CO_3/Br_2/CCl_4$	7 (**3a**)	70 (**4a**)
		NBS/CH_2Cl_2	13 (**3a**)	67 (**4a**)
		$Et_3N/Cl_2/CCl_4$	5 (**3b**)	40 (**4b**)
2	$NHCH_3$	$Et_3N/Br_2/CCl_4$	5 (**5a**)	75 (**6a**)
		$K_2CO_3/Br_2/CCl_4$	5 (**5a**)	80 (**6a**)
		NBS/CH_2Cl_2		70 (**6a**)
		$Et_3N/Cl_2/CCl_4$	6 (**5b**)	78 (**6b**)
8	NH_2	$K_2CO_3/Br_2/CH_2Cl_2/CH_3CN$		50 (**9a**)
		$K_2CO_3/Br_2/CH_2Cl_2/CH_3CN$		72 (**9b**)
11	OCH_3	$Et_3N/Br_2/CHCl_3$		
10	SCH_3	$Et_3N/Br_2/CHCl_3$		

[a] Registry no.: **1**, 61178-04-9; **2**, 63197-00-2; **3a**, 63197-14-8; **3b**, 65914-96-7; **4a**, 65914-99-0; **4b**, 65915-00-6; **5a**, 65914-97-8; **5b**, 65914-98-9; **6a**, 65915-01-7; **6b**, 65915-02-8; **8**, 61177-95-5; **9a**, 65915-03-9; **9b**, 65915-04-0; **10**, 63197-03-5; **11**, 61178-03-8.

These halogenations were also carried out with chlorine and other halogenating agents. The conditions and yields of products are given in Table II. Under these same conditions, 3-methylthio- (**10**) and 3-methoxy-1,2,4-triazine 2-oxides (**11**) do not react.

The formation of the deoxygenated products in these bromination reactions along with our previous report on the deoxygenative alkoxylation of these *N*-oxides[2] led us to examine their reactivity toward the halogen acids in aprotic solvents. Upon treatment of 3-dimethylamino- (**1**), 3-monomethylamino- (**2**), 3-morpholino- (**12**), or 3-piperidino-1,2,4-triazine 2-oxides (**13**) with dry HCl gas in chloroform (cf. Scheme I), only one major product was obtained in each case. The mass spectra of these compounds showed that the products had lost the *N*-oxide function, while the ^1H NMR spectra clearly indicate that we are dealing with 6-chloro-3-substituted-1,2,4-triazines (**3b, 5b, 14,** and **15**). The reaction was also attempted with 3-amino- (**8**), 3-methoxy- (**11**) 3-chloro- (**16**), and 3-methylthio-1,2,4-triazine 2-oxides (**10**) under similar conditions. The starting materials were recovered in all of these instances.

In order to determine if the deoxygenated products observed in the bromination reaction arise from the presence of hydrobromic acid in the reaction mixture, 6-bromo-3-dimethylamino-1,2,4-triazine 2-oxide (**4a**) was treated with HBr in chloroform. The product obtained proved to be 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**), identical with an authentic sample.



4a **3a**

When 3-dimethylamino- (**1**) and 3-monomethylamino-1,2,4-triazine 2-oxides (**2**) were treated with gaseous HBr in chloroform (cf. Scheme I), two products were obtained in each case. Comparison of their ^1H NMR spectra clearly shows them to be 3-dimethylamino- (**18**) and 6-bromo-3-dimethylamino-1,2,4-triazines (**3a**) and 3-monomethylamino- (**19**) and 6-bromo-3-monomethylamino-1,2,4-triazines (**5a**), respectively.

As in the reactions with HCl, 3-amino- (**8**), 3-methoxy- (**11**), 3-methylthio- (**10**), and 3-bromo-1,2,4-triazine 2-oxides (**20**) do not react under similar conditions.

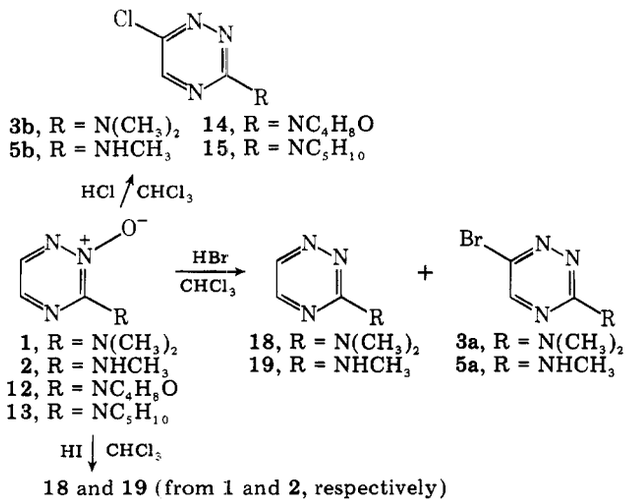
Treatment of 3-dimethylamino- (**1**) and 3-monomethylamino-1,2,4-triazine 2-oxides (**2**) with hydrogen iodide gives good yields of 3-dimethylamino- (**18**) and 3-monomethylamino-1,2,4-triazines (**19**) (cf. Scheme I).

In order to determine if it is necessary to have the halogen present as an acid, and not simply as an anion, 3-dimethylamino-1,2,4-triazine 2-oxide (**1**) was treated with potassium bromide in the presence of 18-crown-6. The starting material was recovered quantitatively.

In previous work we reported the bromination of some 1,2,4-triazine 1-oxide derivatives. In these reactions, no deoxygenated products were obtained. When 3-methoxy- (**21**), 3-monomethylamino- (**22**), and 3-dimethylamino-1,2,4-triazine 1-oxides (**23**) are treated with hydrochloric or hydrobromic acid in chloroform, no brominated or deoxygenated products are observed.

Mechanistic Considerations. In proposing a mechanism for both electrophilic and deoxygenative bromination of the 1,2,4-triazine 2-oxides, several factors need to be considered. The first of these is the electron-donating ability, as exemplified by Hammet substituent constants, of the 3 substituent. Table III lists the various 3 substituents, their Hammet substituent constants,[3] and whether or not they undergo elec-

Scheme I



18 and **19** (from **1** and **2**, respectively)

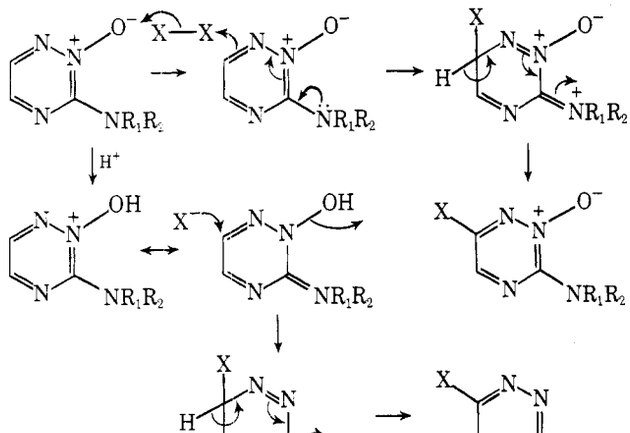
Table III. Hammet Substituent Constants

Substituent	σ_{para}[a]	Electrophilic bromination	Deoxygenative bromination
$N(CH_3)_2$	−0 600	Reacts	Reacts
$NHCH_3$	−0.592	Reacts	Reacts
NH_2	−0.660	Reacts	No reaction
SCH_3	−0.047	No reaction	No reaction
Cl	+0.227	No reaction	No reaction
Br	+0.232	No reaction	No reaction

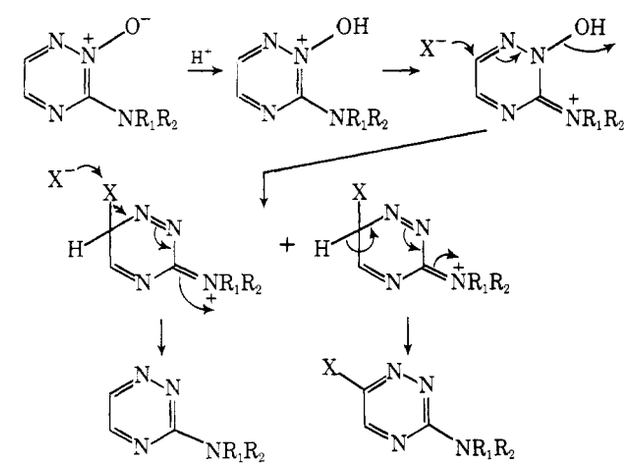
[a] Taken from ref 3.

trophilic or deoxygenative bromination. Except for the 3-amino derivative 8, only those groups that donate their electrons very efficiently (high negative σ_{para}'s) react under the conditions used in these brominations. Secondly, treatment of 6-bromo-3-dimethylamino-1,2,4-triazine 2-oxide (**4a**) with hydrobromic acid gave only the deoxygenated derivative. Thirdly, treatment of 3-dimethylamino-1,2,4-triazine 2-oxide (**1**) with Br^- gave no brominated or deoxygenated products. Fourthly, when the reactions were run with hydroiodic acid under a nitrogen atmosphere, the presence of iodine was indicated (starch–iodine tests). Finally, none of the 1,2,4-triazine 1-oxides give deoxygenated products.

On the basis of this evidence, the following two mechanistic pathways can be suggested. (1) For the products arising from electrophilic bromination conditions, the mechanism is straightforward. As the reaction proceeds, small amounts of



hydrobromic acid are built up, and the possibility of protonation of the *N*-oxide becomes feasible. This allows the molecule to be attacked by bromide, with subsequent loss of the elements of water. The small amounts of deoxygenated product formed can be attributed to the hydrobromic acid formed under the reaction conditions.



(2) For the deoxygenative bromination of the 1,2,4-triazine 2-oxides, a similar mechanism may be suggested. One would expect that the attack of halogen anion on the ring substituted halogen would be dependent upon the polarizability of the halogen. This is, in fact, born out since chloride anion does not react in this manner while bromide anion gives both products and iodide anion gives exclusively the product arising via this path.

In summary, the 1,2,4-triazine 2-oxides undergo some rather unique transformations. They are subject to electrophilic bromination, deoxygenation bromination, and deoxygenation. These transformations provide synthetic routes to many substituted 1,2,4-triazines and their 2-oxides. Further studies of the synthetic utility of these reactions in this and related ring systems are in progress.

Experimental Section

Mass spectra were recorded with a Hitachi Perkin-Elmer RMU-6M instrument of all new compounds. Their molecular ions and fragmentation patterns are consistent with the indicated structures. A Varian HA-100 instrument was used to record ^1H NMR spectra. Melting points are corrected. Elemental analyses were performed by Atlantic Microlabs, Inc., Atlanta, Ga., and the Analytical Services Laboratory, Department of Chemistry, University of Alabama.

Reaction of 3-Dimethylamino-1,2,4-triazine 2-Oxide (1) and 3-Monomethylamino-1,2,4-triazine 2-Oxide (2). (a) In the Presence of Et_3N: To a solution of 140 mg (1 mmol) of 3-dimethylamino-1,2,4-triazine 2-oxide (1) dissolved in 30 mL of CCl_4 was added 320 mg (2 mmol) of Br_2. The solution was stirred at room temperature for 5 min, and 151 mg (1.5 mmol) of Et_3N was added. Stirring was continued for 2 h, after which time TLC showed no starting material. The solvent was removed in vacuo. The residue was chromatographed on silica gel (grade III) with $CHCl_3$ as eluent. The resulting component mixture was separated by thick-layer chromatography with 50:50 $CHCl_3/C_6H_6$ as eluent to give 142 mg (65%) of 6-bromo-3-dimethylamino-1,2,4-triazine 2-oxide (**4a**) and 28 mg (14%) of 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**), which was compared with an authentic sample.

In the case of 3-monomethylamino-1,2,4-triazine 2-oxide (**2**), 153 mg (75%) of 6-bromo-3-monomethylamino-1,2,4-triazine 2-oxide (**6a**) and 10 mg (5%) of 6-bromo-3-monomethylamino-1,2,4-triazine (**5a**) were obtained.

(b) In the Presence of K_2CO_3: To a solution of 500 mg (3.6 mmol) of 3-dimethylamino-1,2,4-triazine 2-oxide (1) in 75 mL of dry CCl_4 was added 1.14 g (7.1 mmol) of Br_2 and 1 g (7.1 mmol) of K_2CO_3. The resulting suspension was stirred for 2 h and the solvent removed in vacuo. The reside was passed through 25 g of alumina (grade III) with $CHCl_3$. The main yellow component was further separated as above to give 511 mg (70%) of 6-bromo-3-dimethylamino-1,2,4-triazine 2-oxide (**4a**) and 51 mg (7%) of 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**).

In the case of 3-monomethylamino-1,2,4-triazine 2-oxide (**2**), 590 mg (80%) of 6-bromo-3-monomethylamino-1,2,4-triazine 2-oxide (**6a**) and 34 mg (5%) of 6-bromo-3-monomethylamino-1,2,4-triazine (**5a**) were obtained.

(c) Thru the Action of NBS: To a solution of 100 mg (0.7 mmol) of 3-dimethylamino-1,2,4-triazine 2-oxide (1) in 40 mL of CH_2Cl_2 was added 248 mg (1.4 mmol) of NBS. The solution was stirred for 48 h, after which time the solvent was removed in vacuo. The residue was passed through 25 g of alumina (grade III) with $CHCl_3$. The yellow material was further purified as above, yielding 102 mg of (67%) 6-bromo-3-dimethylamino-1,2,4-triazine 2-oxide (**4a**) and 18 mg (13%) of 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**).

In the case of 3-monomethylamino-1,2,4-triazine 2-oxide (**2**), 153 mg (70%) of 6-bromo-3-monomethylamino-1,2,4-triazine 2-oxide (**6a**) was obtained only.

Treatment of 3-Dimethylamino-1,2,4-triazine 2-Oxide (1) with Cl_2 and Et_3N. To a solution of 199 mg (28 mmol) of Cl_2 in 150 mL of $CHCl_3$ was added 200 mg (1.4 mmol) of 3-dimethylamino-1,2,4-triazine 2-oxide along with 250 mg (2.5 mmol) of Et_3N. The mixture was stirred for 1 h and the solvent removed in vacuo. The residue was chromatographed by dry column chromatography on alumina (grade III) using 50:50 $CHCl_3/C_6H_6$ as eluent. The products were then sublimed at 0.05 Torr (45 °C) to yield 200 mg (40%) of 6-chloro-3-dimethylamino-1,2,4-triazine 2-oxide (**4b**) and 20 mg (4.5%) of 6-chloro-3-dimethylamino-1,2,4-triazone (**3b**).

In the case of 3-monomethylamino-1,2,4-triazine 2-oxide (**2**), 200 mg (78%) of 6-chloro-3-monomethylamino-1,2,4-triazine 2-oxide (**6b**)

and 15 mg (6%) of 6-chloro-3-monomethylamino-1,2,4-triazine (**5b**) were obtained.

Preparation of 6-Bromo-3-amino-1,2,4-triazine 2-Oxide (9a). To a solution of 222 mg (1.9 mmol) of 3-amino-1,2,4-triazine 2-oxide (**8**) dissolved in 100 mL of $CHCl_2$ and 40 mL of CH_3CN was added 704 mg (4.4 mmol) of Br_2, and the solution was stirred for 0.5 h. A 420-mg (4.9 mmol) amount of $NaHCO_3$ was then added, and stirring was continued for 1 h. The resulting mixture was filtered and the solvent evaporated. The residue was purified by thick-layer chromatography using silica (grade III) with CH_3CN as eluent to give 182 mg (50%) of 6-bromo-3-amino-1,2,4-triazine 2-oxide (**9a**).

The reaction was also carried out using Cl_2, and 200 mg (72%) of 6-chloro-3-amino-1,2,4-triazine 2-oxide (**9b**) was obtained.

Attempted Reaction of 3-Dimethylamino-1,2,4-triazine 2-Oxide (1) with KBr in the Presence of 18-Crown-6. To a dry 100-mL round-bottom flask containing 30 mL of dry benzene, 268 mg (1.4 mmol) of 18-crown-6, and 166 mg (1.4 mmol) of KBr was added 100 mg (0.7 mmol) of 3-dimethylamino-1,2,4-triazine 2-oxide (**1**) dissolved in 20 mL of benzene. The reaction mixture was refluxed for 4 days, after which time TLC showed only the presence of starting materials.

The above reaction was also attempted using 3-monomethylamino-1,2,4-triazine 2-oxide (**2**). Again, after 4 days at reflux, TLC showed no evidence of products.

Attempted Reaction of 3-Methylthio-1,2,4-triazine 2-Oxide (10) with Br_2 and Et_3N. To a solution of 100 mg (0.6 mmol) of 3-methylthio-1,2,4-triazine 2-oxide (**10**) in 20 mL of $CHCl_3$ was added 112 mg (0.6 mmol) of Br_2 in 5 mL of $CHCl_3$ and 60 mg (0.6 mmol) of Et_3N. The resulting solution was first stirred at room temperature for 24 h and then warmed gently for 16 h. The solution was evaporated and the residue chromatographed on alumina (grade III) with $CHCl_3$ as eluent to give 75 mg (75%) of 3-methylthio-1,2,4-triazine 2-oxide (**10**).

Attempted Reaction of 3-Methoxy-1,2,4-triazine 2-Oxide (11) with Br_2 and Et_3N. To a solution of 50 mg (0.39 mmol) of 3-methoxy-1,2,4-triazine 2-oxide (**11**) in 15 mL of $CHCl_3$ was added 112 mg (0.6 mmol) of Br_2 in 5 mL of $CHCl_3$ and 39 mg (0.39 mmol) of Et_3N. The resulting solution was stirred for 24 h and then warmed gently on a hot plate for 2 h. The solvent was evaporated and the residue purified by thick-layer chromatography on silica (grade III) with $CHCl_3$ as eluent to give 30 mg (60%) of 3-methoxy-1,2,4-triazine 2-oxide (**11**).

Conversion of 6-Bromo-3-dimethylamino-1,2,4-triazine (3a) to 6-Methoxy-3-dimethylamino-1,2,4-triazine (7). To a solution of 600 mg (27 mmol) of 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**) in 20 mL of dry CH_3OH was added dropwise a solution of 136 mg (5.9 mmol) of Na in 10 mL of dry CH_3OH. The reaction mixture was refluxed for 4 h and then quenched with dry ice. The solvent was removed in vacuo and the residue chromatographed on alumina (grade III) to give 261 mg (70%) of 6-methoxy-3-dimethylamino-1,2,4-triazine (**7**).

Reaction of 6-Bromo-3-dimethylamino-1,2,4-triazine 2-Oxide (4a) with HBr. Into a solution of 100 mg (0.46 mmol) of 6-bromo-3-dimethylamino-1,2,4-triazine 2-oxide (**4a**) in 100 mL of $CHCl_3$ was bubbled dry HBr gas. The resulting solution was stirred overnight. Excess Na_2CO_3 was added, and stirring was continued for an additional hour. The mixture was then filtered and the solvent evaporated. The residue was purified by thick-layer chromatography on silica (grade III) using $CHCl_3$. The main component was sublimed at 0.05 Torr (60 °C) to give 66 mg (70%) of 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**).

Reaction of 3-Monomethylamino-1,2,4-triazine 2-Oxide (2) with HCl. Into a solution of 100 mg (0.79 mmol) of 3-monomethylamino-1,2,4-triazine 2-oxide (**2**) in 75 mL of $CHCl_3$ was bubbled dry HCl gas. The reaction mixture was stirred for 16 h, and excess Na_2CO_3 was added. The mixture was stirred for an additional 4 h and filtered, and the solvent was removed to give a yellow solid. This was sublimed at a 0.05 Torr (60 °C) to yield 97 mg (85%) of 6-chloro-3-monomethylamino-1,2,4-triazine (**5b**).

The reaction was also carried out using 3-dimethylamino-1,2,4-triazine 2-oxide (**1**), 3-morpholino-1,2,4-triazine 2-oxide (**12**), and 3-piperidino-1,2,4-triazine 2-oxide, giving 180 mg (64%) of 6-chloro-3-dimethylamino-1,2,4-triazine (**3b**), 80 mg (80%) of 6-chloro-3-morpholino-1,2,4-triazine (**14**), and 50 mg (50%) of 6-chloro-3-piperidino-1,2,4-triazine (**15**), respectively.

Reaction of 3-Monomethylamino-1,2,4-triazine 2-Oxide (2) with HBr. Into a solution of 140 mg (1.1 mmol) of **2** in 75 mL of $CHCl_3$ was bubbled dry HBr gas. The solution became cloudy, and stirring was continued overnight. Excess $NaHCO_3$ was added, the mixture was stirred for 3 h and filtered, and the solvent was evaporated. The residue was chromatographed on silica (grade III) with $CHCl_3$ as eluent to give 39 mg (25%) of 6-bromo-3-monomethylamino-1,2,4-triazine (**5a**) and 78 mg (64%) of 3-monomethylamino-1,2,4-triazine (**19**).

The reaction was also carried out using 3-dimethylamino-1,2,4-triazine 2-oxide (**1**), and 124 mg (41%) of 6-bromo-3-dimethylamino-1,2,4-triazine (**3a**) and 118 mg (50%) of 3-dimethylamino-1,2,4-triazine (**18**) were obtained.

Reaction of 3-Monomethylamino-1,2,4-triazine 2-Oxide (2) with HI. Into a solution of 250 mg (1.9 mmol) of 3-monomethylamino-1,2,4-triazine 2-oxide (**2**) in 75 mL of dry $CHCl_3$ was bubbled dry HI gas. The reaction mixture was kept under static dry oxygen-free N_2 gas and stirred overnight at room temperature. Excess Na_2CO_3 was added, and stirring was continued for an additional 4 h. The mixture was filtered and a portion of the filtrate tested with freshly prepared starch solution. The presence of I_2 was indicated by the blue color. The remainder of the filtrate was evaporated and the residue chromatographed on silica (grade III) with $CHCl_3$ as eluent to give 175 mg (79%) of 3-monomethylamino-1,2,4-triazine (**19**).

The reaction was also carried out with 3-dimethylamino-1,2,4-triazine 2-oxide (**1**), and 175 mg (80%) of 3-dimethylamino-1,2,4-triazine (**18**) was obtained.

Attempted Reaction of 3-Chloro-1,2,4-triazine 2-Oxide (17) with HCl. Into a solution of 300 mg (2.5 mmol) of 3-chloro-1,2,4-triazine 2-oxide (**17**) in 30 mL of $CHCl_3$ was bubbled dry HCl gas. The resulting solution was stirred overnight. Excess Na_2CO_3 was added, and the mixture was stirred for an additional hour. The mixture was then filtered and the solvent evaporated to give 291 mg (97%) of 3-chloro-1,2,4-triazine 2-oxide (**17**).

Attempted Reaction of 3-Bromo-1,2,4-triazine 2-Oxide (20) with HBr. Into a solution of 300 mg (1.7 mmol) of 3-bromo-1,2,4-triazine 2-oxide (**20**) in 30 mL of $CHCl_3$ was bubbled dry HBr gas. The resulting solution was stirred overnight. Excess Na_2CO_3 was added, and the mixture was stirred for an additional hour. The mixture was filtered and the solvent evaporated to give 276 mg (92%) of 3-bromo-1,2,4-triazine 2-oxide (**20**).

Attempted Reaction of 3-Methylthio-1,2,4-triazine 2-Oxide (10) with HCl or HBr. Into a solution of 100 mg (0.6 mmol) of 3-methylthio-1,2,4-triazine 2-oxide (**10**) in 75 mL of $CHCl_3$ was bubbled dry HCl gas. The resulting solution was stirred overnight. Excess Na_2CO_3 was added, and stirring was continued for an additional 4 h. The mixture was filtered and the solvent removed to give 90 mg (90%) of 3-methylthio-1,2,4-triazine 2-oxide (**10**).

In the reaction with HBr, 95 mg (95%) of the starting material was recovered.

Attempted Reaction of 3-Methoxy-1,2,4-triazine 2-Oxide (11) with HCl for HBr. Into a solution of 100 mg (0.79 mmol) of 3-methoxy-1,2,4-triazine 2-oxide dissolved in 75 mL of $CHCl_3$ was bubbled dry HCl gas. The solution was stirred overnight. Excess Na_2CO_3 was added, and stirring was continued for an additional 4 h. The mixture was filtered and the solvent removed to give 75 mg (75%) of 3-methoxy-1,2,4-triazine 2-oxide (**11**).

The reaction was also carried out in the presence of HBr, and again, only starting material was recovered (92%).

Attempted Reaction of 3-Methoxy-1,2,4-triazine 1-Oxide (21) with HCl or HBr. Into a solution of 300 mg (2.4 mmol) of 3-methoxy-1,2,4-triazine 1-oxide (**21**) in 75 mL of $CHCl_3$ was bubbled dry HCl gas. The solution was stirred overnight and then extracted with 50 mL of saturated Na_2CO_3. The water layer was further extracted with $CHCl_3$ (2 × 100 mL), and the combined extracts were dried over Na_2CO_3. After filtration and evaporation of the solvent, 268 mg (89%) of 3-methoxy-1,2,4-triazine 1-oxide (**21**) was recovered.

The reaction was also carried out with 3-monomethylamino- (**22**) and 3-dimethylamino-1,2,4-triazine 1-oxides (**23**) with both HCl and HBr. In all cases, only starting material was recovered (81–93%).

Registry No.—**7,** 63197-02-4; **12,** 61178-05-0; **13,** 61178-06-1; **14,** 65915-05-1; **15,** 65915-06-2; **16,** 61178-03-8; **18,** 63197-03-5; **19,** 53300-17-7; **20,** 65915-07-3; **21,** 61178-02-7; **22,** 27531-67-5; **23,** 63197-06-8; **24,** 61178-07-2; **25,** 61202-85-5.

Supplementary Material Available: Tables I–III and Figure 1 of x-ray crystallographic data (4 pages). Ordering information is given on any current masthead page.

References and Notes

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