Communications to the Editor

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HALOGENATION OF 1,2,3-TRIAZINES

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4,6-Dimethyl-1,2,3-triazine was treated with bromine and chlorine under mild conditions to give the corresponding 5-halo derivatives. The electrophlic addition-elimination mechanism was suggested by the results of reactions using interhalogens such as BrCl, ICl, and IBr as the reagents.

KEYWORDS——1,2,3-triazine; 5-halo-1,2,3-triazine; interhalogen; adddition-elimination mechanism; halogenation

Monocyclic 1,2,3-triazines[1)] have such high π-deficiency that they are easily attacked by nucleophiles. For instance, in alkaline media, they were attacked at the 4-positions by hydroxide ions to give ring-opening products, and treating them with $NaBH_4$ in methanol resulted in the formation of 2,5-dihydro compounds (Chart 1).[2)]

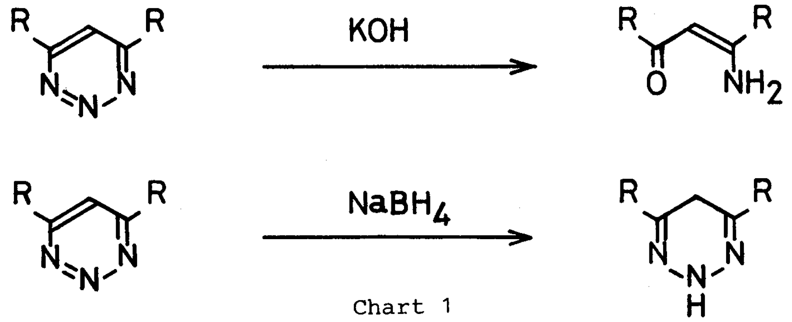
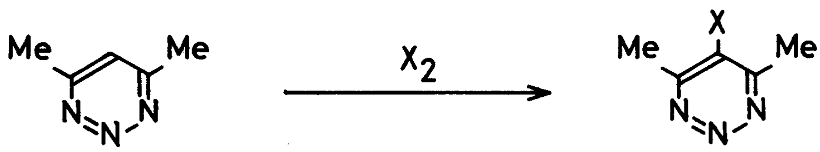


Chart 1

On the other hand, due to the high π-deficiency, 1,2,3-triazines are supposed to resist the attack of electrophiles. We report here the reaction of 4,6-dimethyl-1,2,3-triazine with halogens under mild conditions to form 5-halo compounds, and also the reaction mechanism.

4,6-Dimethyl-1,2,3-triazine (1) was treated with 1 mol eq of halogens in CCl_4 at 0°C for 0.5 h (Chart 2).



1 Chart 2 2

1 was treated with chlorine or bromine to give the 5-halo-4,6-dimethyl-1,2,3-triazines (2a: X=Cl, 2b: X=Br) in yields of 5% and 67%, respectively. With chlorination, prolonged reaction time (12 h) at room temperature led to a 31% increase in yield. The spectral data[3] of 2a and 2b corroborated the structure. Reaction with iodine failed to give the 5-iodo compound, the starting material being recovered completely. Considering the π-deficiency of 1 and the mild reaction conditions, the formation of 5-halo compounds (2) is rather unexpected. So to clarify the reaction mechanism, reactions were conducted with interhalogens such as BrCl, ICl, and IBr (Chart 3). The reaction of 1 with interhalogens gave 2, the yields of which are shown in the table.

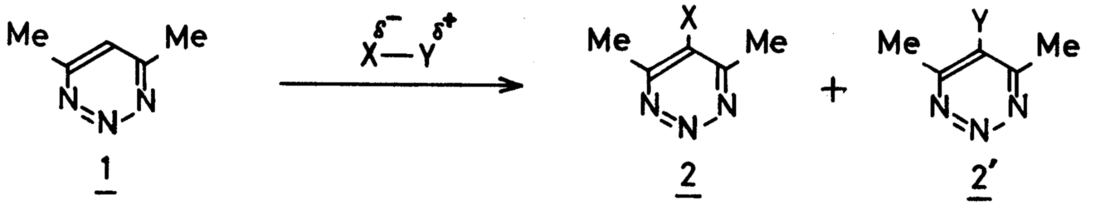


Chart 3

Table

Entry	Interhalogens	Yields	
		2	2'
1	BrCl(X=Cl, Y=Br)	41%	17%[4]
2	ICl(X=Cl, Y=I)	25%	0%
3	IBr(X=Br, Y=I)	Trace	0%

Because of the electronegativity of the constituent halogen atoms, interhalogen has a dipole and is known to add to olefins according to Markownikoff-type orientation.[5] The compound 2 thus obtained showed that a negatively charged halogen atom of an interhalogen molecule was introduced preferentially into the triazine. These facts doubtlessly indicate that the formation of 2 is not the result of an ordinary electrophilic substitution reaction. To explain this , the following electrophilic addition-elimination mechanism is proposed (Chart 4).

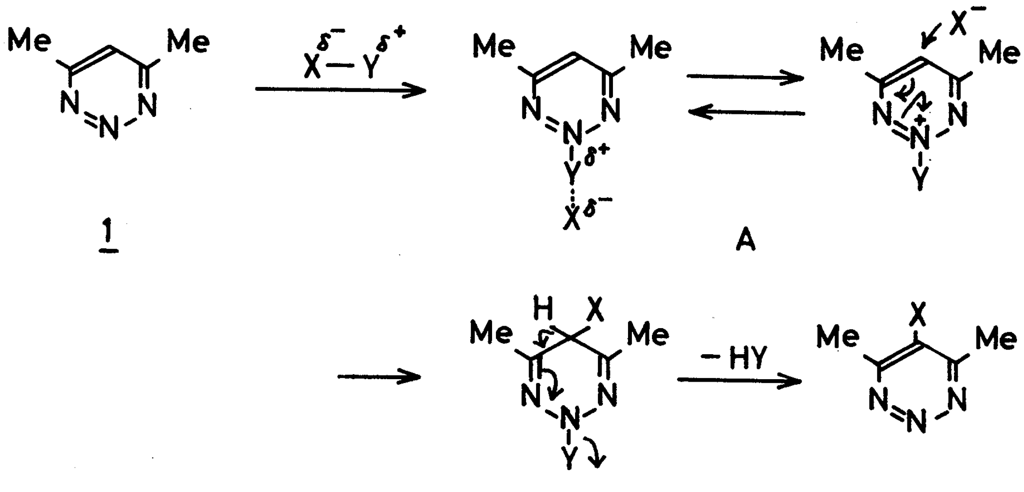


Chart 4 B 2

The positively charged halogen atom of the interhalogen molecule attacks the unshared electrons of the nitrogen in the 2-position, forming triazinium salt A. Ion X^-, then attacks the 5-position to form the intermediate 2,5-dihydro compound B.[6] Subsequent elimination of hydrogen halide from intermediate B reasonably gives 2. It is known that some azines form n-complexes with halogens.[7] 2-Methyl-1,2,3-triazinium salts are more reactive towards nucleophiles than 1,2,3-triazines.[2] 5-Halo compound (2) is considered to be formed by the attack of X^- on the electron-deficient position of n-complex A.

Although unsubstituted 1,2,3-triazine and 4-methyl-1,2,3-triazine also reacted with bromine under the described conditions to give 5-bromo compounds, their yields were very low and they were only detected and identified by the GC-MS of the reaction mixture.[8] Apparently, some decomposition reaction occurred to form unclarified products, due to the attack of halogen on the 4 (or 6) position.

REFERENCES AND NOTES

1) A. Ohsawa, H. Arai, H. Ohnishi, T. Itoh, T. Kaihoh, M. Okada, and H. Igeta, J. Org. Chem., 50, 5520, (1985).
2) A. Ohsawa, H. Arai, H. Ohnishi, T. Kaihoh, T. Itoh, K. Yamaguchi, H. Igeta, and Y. Iitaka, Yakugaku Zasshi, 105, 1122, (1985).
3) 2a; colorless needles, mp 89-90°(n-hexane). ^{1}H-NMR($CDCl_3$)δ:2.76(s). MS m/z: 145 (M^++2), 143 (M^+), 80[M^+-(N_2+Cl)], 76[M^++2-(N_2+CH_3CN)], 74[M^+-(N_2+CH_3CN)]. 2b; colorless needles, mp 104-105° (n-hexane). ^{1}H-NMR ($CDCl_3$)δ: 2.79(s). MS m/z: 189(M^++2), 187(M^+), 161(M^++2-N_2), 159(M^+-N_2),120[M^++2-(N_2+CH_3CN)],118[M^+-(N_2+CH_3CN)], 80[M^+-(N_2+Br)]. Compound 2b was identified by comparison with an authentic sample obtained by LTA oxidation of 1-amino-4-bromo-3,5-dimethylpyrazole, according to the method described in ref. 1.
4) 2b in Entry 1 may be due to the reaction of 1 with bromine formed from the partial dissociation of BrCl (A.I. Popov and J.J. Mannion, J. Am. Chem. Soc., 74, 222, (1952)).
5) a) P.B.D. de la Mare and S. Galandauer, J. Chem. Soc., 1958, 36; b) R.E. Buckles, J.L. Forrester, R.L. Burham, and T.W. Mcgee, J. Org. Chem., 25, 24, (1960); c) C.K. Ingold and H.G. Smith, J. Chem. Soc., 1931, 2742.
6) It is still uncertain whether the attack of nucleophile X^- proceeds through an intra- or an intermolecular mechanism.
7) For example, J.J. Eisch, "Advances in Heterocyclic Chemistry," Vol. 7, ed. by A.R. Katritzky and A.J. Boulton, Academic press,New York, 1966, p.1 and references cited therein.
8) 5-Bromo-1,2,3-triazine was authentically synthesized by oxidation of 1-amino-4-bromopyrazole using PbO_2-CF_3COOH; 5-bromo-4-methyl-1,2,3-triazine was also obtained by LTA oxidation of 1-amino-4-bromo-3(or 5)-methylpyrazole (see ref. 1).

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