RADICAL CARBAMOYLATION OF 1,2,3-TRIAZINIUM 2-DICYANOMETHYLIDES

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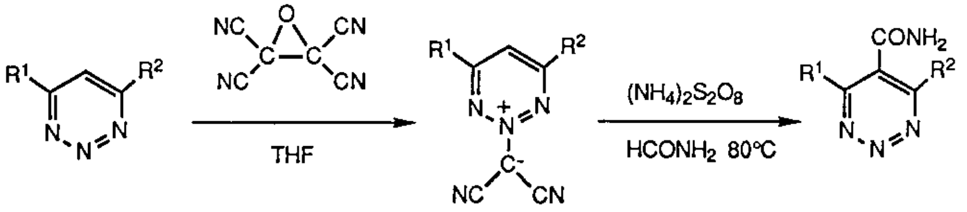
Abstract — The nucleophilic radical carbamoylation of 4,6-disubstituted 1,2,3-triazinium 2-dicyanomethylides occurred at their 5-positions followed by the elimination of dicyanomethylene to form 5-substituted 1,2,3-triazines. The reaction did not proceed when parent triazines were adopted as the substrates.

Monocyclic 1,2,3-triazines[1] are highly π-deficient heteroaromatics, so that they readily reacted with nucleophiles. The introduction of some substituents into 1,2,3-triazine rings has been attempted employing anionic nucleophiles, such as alkoxy anion and organo metallic reagents.[2] However, the usual methods of nucleophilic substitution (addition of nucleophile followed by oxidation)[3] could not be available for triazine ring systems, because ring opening reaction with the evolution of nitrogen occurred simultaneously with the attack of nucleophiles at 4-position of 1,2,3-triazines.[4] Thus, in order to synthesize substituted 1,2,3-triazines, we investigated the radical reaction of 1,2,3-triazine derivatives. In this paper we wish to report the introduction of carbamoyl group into 1,2,3-triazine ring system by the use of radical substitution reaction.

Minisci *et al.* have reported[5] the substitution of protonated heteroaromatic bases by nucleophilic radicals. The method, however, did not give good results for 1,2,3-triazines which were unstable in a protic medium.[6] We hence investigated the radical substitution reaction in whch no adding process of acid was included, and it was revealed that 1,2,3-triazinium dicyanomethylides reacted with carbamoyl radical to afford 5-carbamoyltriazines in moderate to good yields.



1 2 3

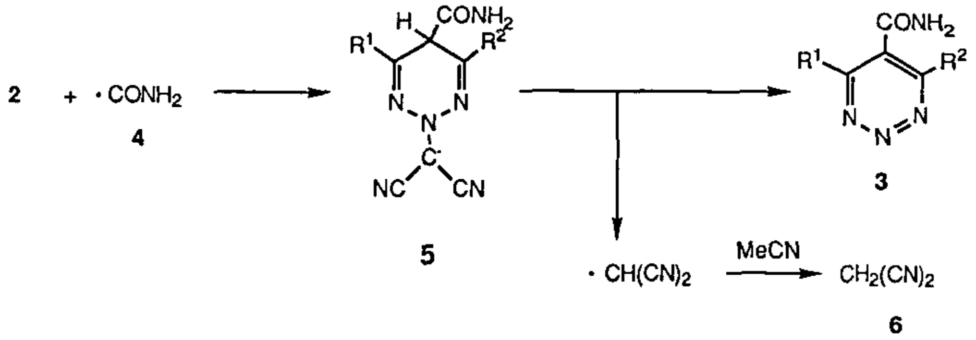
Scheme 1

1,2,3-Triazinium 2-dicyanomethylides[7] were readily prepared allowing 1,2,3-triazines to react with tetracyanoethylene oxide(TCNEO) in THF. TCNEO[8] was synthesized by the reaction of tetracyanoethylene with 30% aq. H_2O_2 in acetonitrile and used without purification. Triazinium dicyanomethylides (0.2 mmol) thus obtained and $(NH_4)_2S_2O_8$ (0.5 mmol) were dissolved in $HCONH_2$ (3 ml) and heated at 80° C for 2 h. The solution exhibited red color at first, and gradually turned to pale yellow with the progress of the reaction. Then the reaction mixture, being slightly acidic, was neutralized with aqueous sodium carbonate and the solvent was removed under reduced pressure. The residue was chromatographed on alumina to give 5-carbamoyl-1,2,3-triazines (3) (Scheme 1 and Table) as colorless solids.

Table Isolated Yields of (2) and Corresponding Carbamoyltriazines (3)

	R^1	R^2	Yield of **2** (mp)	Yield of **3** (mp)
1a[1]	Me	Me	86 % (194 °C)	69 % (210 °C)
1b	Me	Ph	80 % (201 °C)	71 % (192 °C)
1c	Ph	Ph	82 % (296 °C)	68 % (230 °C)
1d	Et	Et	97 % (142 °C)	61 % (174 °C)
1e	Me	Et	82 % (138 °C)	46 % (167 °C)

Thus, the direct introduction of substituent into 1,2,3-triazine ring system was achieved by way of 1,2,3-triazinium 2-dicyanomethylide. The reason for bringing about smooth substitution could be considered that dicyanomethylene group caused 1,2,3-triazine ring to be more π-deficient and their reactivity with nucleophilic radicals was increased, and that dicyanomethylene group acted as a good leaving group after addition of carbamoyl radical at triazine ring. The reaction mechanism is shown in Scheme 2. Carbamoyl radical (4) was generated according to Minisci's method,[9] using ammonium persulfate as a radical source. The radical (4) was suggested to be a nucleophilic one, thus (4) easily reacted with triazinium dicyanomethylide (2) whose electron deficiency was increased enough by the introduction of dicyanomethylene group. Moreover, the intermediate (5) was supposed to be stable because of the existence of two cyano groups adjacent to the radical center. Thereafter, dicyanomethyl radical was released to give carbamoyltriazine (3). Dicyanomethyl radical was thought to abstract hydrogen from the solvent to afford malononitrile (6). The presence of 6 in the reaction mixture was confirmed by comparison of retention time and mass fragmentaion with those of the authentic sample on gc-ms.



Scheme 2

Our method of the radical substitution reaction of a triazine ring system, in which the property of the 1,2,3-triazinium 2-dicyanomethylide is well utilized, was proved to be synthetically available in addition to be taken interest in the reaction mechanism. The reaction might be particularly useful when the parent substrate is unstable under acidic conditions. Application of the present method to the introduction of alkyl species or other functional groups is now under progress.

REFERENCES AND NOTES

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4. For example, unsubstituted 1,2,3-triazine decomposed accompanied by nitrogen evolution even when it was dissolved in methanol.
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6. When **1a** was allowed to react with $(NH_4)_2S_2O_8$ in conc.H_2SO_4/$HCONH_2$ (1/10) at 80 °C, only trace amount of **3a** was obtained.
7. Triazine and tetracyanoethylene oxide (1.2 eq.) were allowed to react in THF at room temperature for 1-2 days. Triazinium dicyanomethylides were obtained as yellow crystals. The detailed results will be reported in succeeding papers.
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