VICARIOUS NUCLEOPHILIC SUBSTITUTION OF 1,2,3-TRIAZINES#

Takashi Itoh, Kazuhiro Nagata, Mamiko Okada, and Akio Ohsawa*

School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai,
Shinagawa-ku, Tokyo 142, Japan

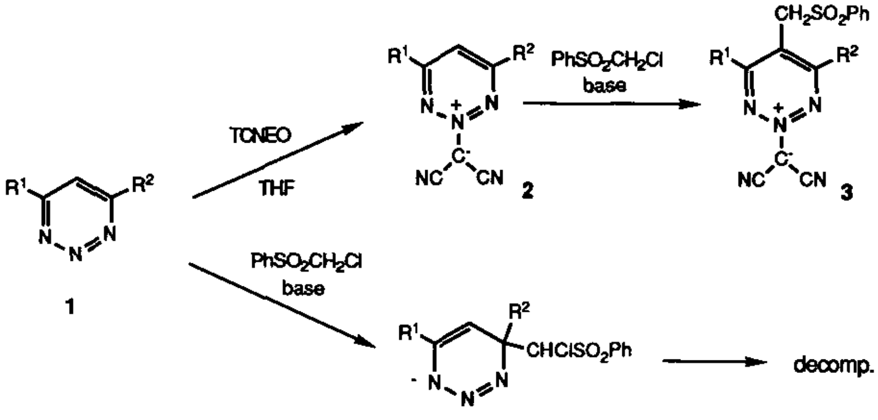
Abstract - Vicarious nucleophilic substitution of 1,2,3-triazinium 2-dicyanomethylides with 1-chloromethyl phenyl sulfone proceeded to give corresponding 5-substituted derivatives. Dicyanomethylene group was readily eliminated by radical reaction to afford 5-phenylsulfonylmethyl-1,2,3-triazines.

1,2,3-Triazines[1] are among the polyazaheteroaromatics which have fully aromatic nature,[2] although the ring system is considerably unstable because of the tendency of N_2 elimination.[3] While several attempts were carried out to synthesize substituted triazines *via* nucleophilic reaction,[4] attack at C-4 position proceeded predominantly to result in ring-opening accompanied by elimination of N_2.[5] Thus the general method for the nucleophilic substitution of electron-deficient heteroaromatics (nucleophilic addition followed by oxidation)[6] cannot be available for 1,2,3-triazine ring.

Vicarious nucleophilic substitution (VNS), which has been developed by Makosza *et al.*,[7] has been proved to be useful for the substitution of nitroarenes which have no leaving groups. The reaction was applied to a few of electron-deficient heteroaromatics without nitro group.[8] Thus, VNS was expected to be effective for 1,2,3-triazines. In this paper, we describe VNS reaction of 1,2,3-triazine derivatives.

Since the attempts of direct VNS to 1,2,3-triazine (**1**) resulted in the decomposition of the substrate probably because of ring-opening caused by the attack at C-4 position (Scheme 1), other triazine derivatives were investigated. 1,2,3-Triazinium 2-dicyanomethylides (**2**), which were prepared by the reaction of **1** with tetracyanoethylene oxide (TCNEO),[9] were suggested to have the tendency to react with nucleophilic radical at their C-5 position.[10] Hence, the reaction was carried out using **2** as substrate, and it was revealed that phenyl sulfonylmethyl group was introduced at C-5 position (Scheme 1 and Table).

This paper is dedicated to Professor E. C. Taylor on the occasion of his 70th birthday.



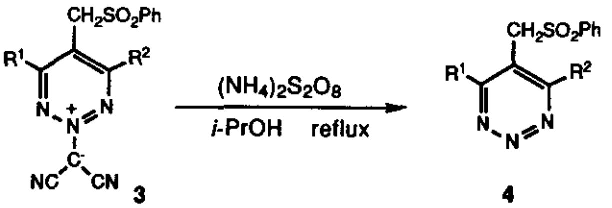
Scheme 1

Table Yields of 5-Phenylsulfonylmethyltriazinium Dicyanomethylides (3)

entry	substrate	R^1	R^2	yield of 2[10]	conditions	yield of 3
1	a	Me	Me	86%	t-BuOK-DMSO	65%
2	b	Me	Et	82%	t-BuOK-DMSO	57%
3	c	Me	Ph	80%	NaH-THF/DMSO	54%
4	d	Et	Et	97%	t-BuOK-DMSO	55%
5	e	Ph	Ph	82%	NaH-THF/DMSO	84%

The compounds (3) thus obtained were transformed to corresponding 5-phenylsulfonylmethyl-1,2,3-triazines (4) under reflux of isopropanol in the presence of ammonium persulfate[11] (Scheme 2).

In the typical experiment, 1-chloromethyl phenyl sulfone (2 mmol) and a base (potassium *t*-butoxide or sodium hydride) (2.2 mmol) were allowed to react in dimethyl sulfoxide (DMSO) or tetrahydrofuran (THF) (3 ml) for 30 min at room temperature. Then the solution was added to the DMSO solution (3 ml) of 2 (1 mmol) at room temperature and allowed to stand for 10 min. The reaction was stopped by the addition of 10% HCl (10 ml), and the mixture was extracted with ethyl acetate. The extract was dried over MgSO$_4$, and the solvent was evaporated off to leave the residue, which was chromatographed on alumina to afford **3**.



a	70%
b	79%
c	67%
d	76%
e	76%

Scheme 2

The compound (**3**) and ammonium persulfate (5 eq.) were suspended in isopropanol and the reaction mixture was refluxed for 30 min. Thereafter, water was added and the mixture was neutralized with sodium carbonate, extracted with methylene chloride, which was dried over $MgSO_4$ and evaporated to give almost pure **4**.

In this paper, we described the VNS reaction of 1,2,3-triazines *via* their dicyanomethylide derivatives. It was shown that dicyanomethylene group changed the reaction site from 4- to 5-positions, and was readily removed by the radical reaction to afford 5-substituted triazines. The introduction of phenylsulfonylmethyl group might be of use because it is easily transformed to the other substituents.[12] The reaction mechanism and the application will be reported elsewhere.[13]

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