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# 1,3-DIPOLAR CYCLOADDITION OF BENZONITRILE OXIDE WITH VINYLSILANES

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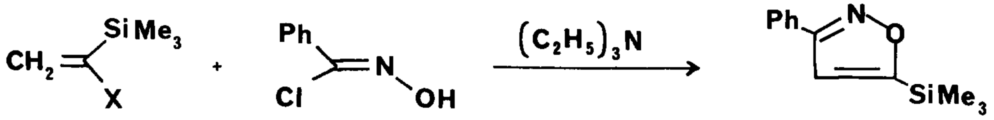
Abstract: The reaction of benzonitrile oxide with several vinylsilanes has been found to afford silylated isoxazoles. Relative rates for the cycloaddition reaction were determined.

The use of silicon based reagents to accomplish carbon-carbon bond forming reactions has attracted a great deal of attention in recent years.[1,2] In particular, vinylsilanes have been found to be versatile synthetic intermediates undergoing ready electrophilic desilylation with retention of stereochemistry.[3] Despite their extensive use in organic synthesis, vinylsilanes have been infrequently employed in [4+2]-cycloaddition reactions. Only occasional examples have been reported which make use of these substrates in Diels-Alder reactions.[4] Our interest in utilizing 1,3-dipolar cycloadditions of nitrilium betaines in organic synthesis[5] focused our attention on the reaction of benzonitrile oxide with vinylsilanes. In this communication we report the results of these studies.

Treatment of a carbon tetrachloride solution of either α-bromovinyltrimethylsilane[6] (1) or α-(2,4-dinitrophenylthio)vinyltrimethylsilane[7] (2) and benzohydroxamyl chloride with an excess of triethylamine gave rise to a high yield (*ca.* 65%) of 3-phenyl-5-trimethylsilylisoxazole (3). The structure of 3 was assigned on the basis of its spectral data as well as by its desilylation with cesium fluoride to give the known 3-phenylisoxazole.[8]



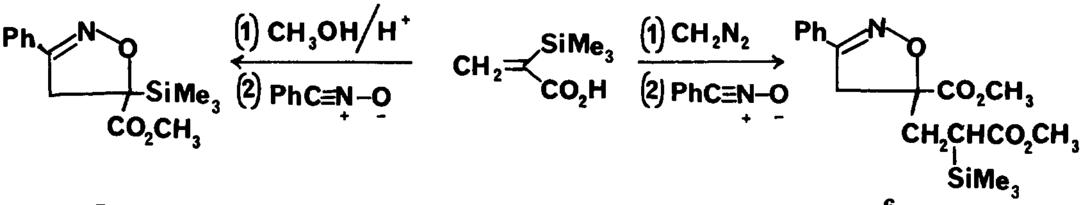
1 ; X = Br

2 ; $X = SC_6H_3(NO_2)_2$

3

The formation of 3 can be postulated to arise by an initial 1,3-dipolar cycloaddition of the transient nitrile oxide followed by elimination of the HX functionality.

Reaction of benzonitrile oxide with α-acetylvinyltrimethylsilane[9] under similar conditions gave 5-acetyl-4,5-dihydro-3-phenylisoxazole (4). The structure of this material was unambiguously confirmed by an independent synthesis which was accomplished by reacting benzonitrile oxide with methyl vinyl ketone. Treatment of this same 1,3-dipole with α-trimethylsilylmethyl acrylate gave the expected cycloadduct 5 which was easily characterized from its spectral and analytical data. Interestingly, it was found that treatment of 2-(trimethylsilyl) acrylic acid with an excess of diazomethane in ether at 0°C followed by reaction with benzonitrile oxide gave structure 6 as the major product. This material was assigned on the basis of its analytical (Anal. Calcd. $C_{18}H_{25}NO_5Si$) and



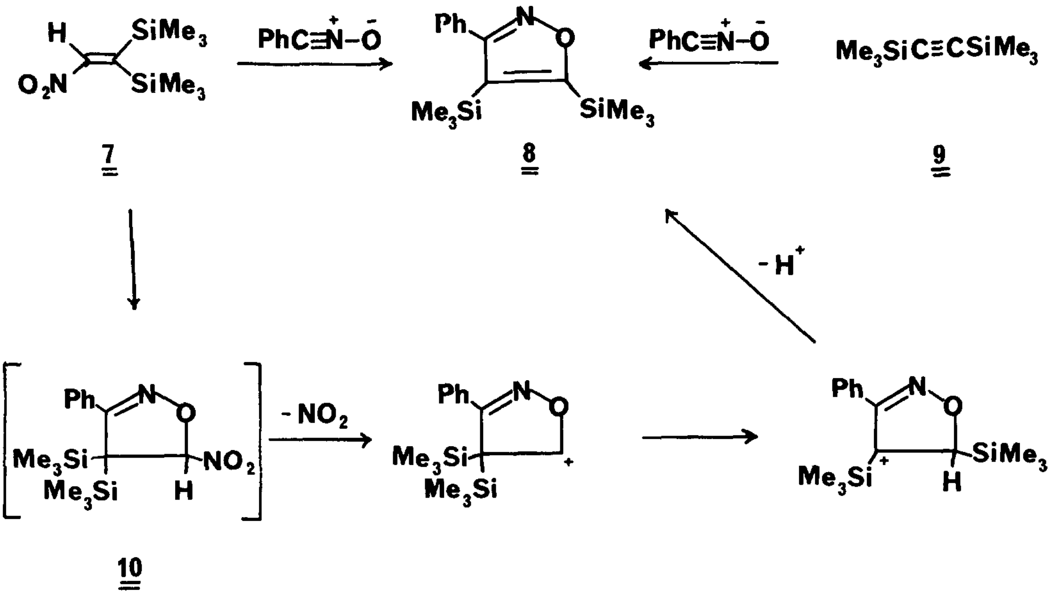
5

6

spectral data: NMR (90 MHz, benzene-$d_6$) δ 0.20 (9H, *s*), 2.32 (1H, *dd*, J=16.0 and 8.0 Hz), 2.72 (1H, *dd*, J=16.0 and 6.0 Hz), 3.10 (2H, *s*), 3.22 (3H, *s*), 3.39 (3H, *s*), 3.78 (1H, *dd*, J=8.0 and 6.0 Hz) and 7.1-7.8 (5H, *m*); m/e 363 ($M^+$), 291, 228, 200 and 146. The formation of 6 can be postulated to arise by an initial desilylation (possibly by the basic media present in the ethereal diazomethane) of the vinylsilane to give an allenic enolate which subsequently undergoes Michael addition to another molecule of starting material. In fact, treatment of the silylated carboxylic acid with just diazomethane afforded 2,5-dicarbomethoxy-4-trimethylsilyl-1-butene in high yield.

We also studied the cycloaddition of benzonitrile oxide with several nitrovinylsilanes. Treatment of 2-nitrovinyltrimethylsilane with benzonitrile oxide gave 3-phenylisoxazole. In contrast, however, the reaction of 1,1-bis(trimethylsilyl)-2-nitroethylene

(7) with the dipole produced 4,5-di(trimethylsilyl)-3-phenylisoxazole (8) in 70% yield. The structure of 8 was unambiguously established by comparison with an independently



synthesized sample prepared from bis(trimethylsilyl)acetylene (9). The formation of 8 can be postulated to arise by initial formation of cycloadduct 10 followed by loss of the nitro group,[10] 1,2-migration of a trimethylsilyl functionality and subsequent proton loss.

Numerous rate studies have been reported for the cycloaddition of 1,3-dipoles to alkenes and alkynes.[11] The "U-shaped" reactivity curve exhibited by benzonitrile oxide with various alkenes is evidence for a significant contribution from both the HOMO and LUMO of the nitrile oxide in the cycloaddition pathway.[12] Sustmann has classified such 1,3-dipoles as belonging to the type II category.[13] With the above vinyl substituted alkenes, benzonitrile oxide reacts with high regioselectivity to give 5-substituted isoxazoles. This orientation can be explained in terms of maximum orbital overlap of the nitrile oxide LUMO - vinylsilane HOMO.[14] Table I shows the order of reactivity of the various vinylsilanes employed in this study. It can be seen that the silylated alkene bearing the acetyl group is approximately nine times more reactive than the one bearing the carbomethoxy group. The silyl group also reduces the reactivity of the alkene towards the nitrile oxide and hence the non-silyl alkene is slightly more reactive in the cycloaddition reaction (see Table II).

TABLE I

| R | k |
|---|---|
| $CO_2CH_3$ | 1 |
| Br | 3 |
| SDNB | 7 |
| $COCH_3$ | 9 |

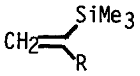


TABLE II

| R | $k_H/k_{SiMe_3}$ |
|---|---|
| $CO_2CH_3$ | 1.7 |
| SDNB | 1.5 |
| COME | 1.2 |
| Br | 1.0 |

Further 1,3-dipolar cycloaddition reactions of di and tri-substituted silylated alkenes with other dipoles is currently under investigation and will be reported at a later date.[15]

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## References and Notes

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