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SYNTHESIS OF Z-β-SILOXYACRYLONITRILES AND STUDY OF THEIR DIENOPHILIC PROPERTIES

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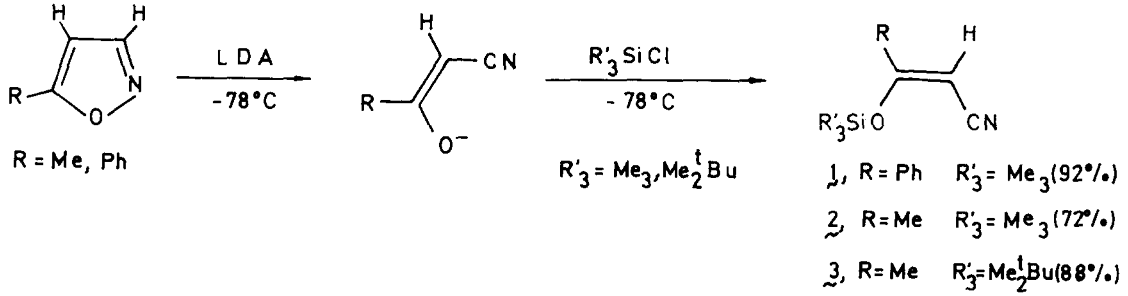
Abstract. A general method for the synthesis of Z-β-siloxyacrylonitriles from isoxazoles is reported. Their dienophilic activity is also described.

Although the preparation of silyl enol ethers by capture of enolate anions with silylating agents has been studied extensively[1,2] there have not been reports of the application of this method to β-ketonitriles. On the other hand, because of the low stability and easy autopolymerisation of ketonitriles, they are not suitable compounds as starting materials for the synthesis of β-siloxyacrylonitriles. However, it is known that 3-unsubstituted isoxazoles undergo ring cleavage by attack of bases to give β-ketonitrile enolates "in situ".[3]

In this paper we wish to describe an easy and apparently general method for the stereoselective synthesis of Z-β-siloxyacrylonitriles from isoxazole precursors. We also decided to examine the dienophilic properties of these substrates.

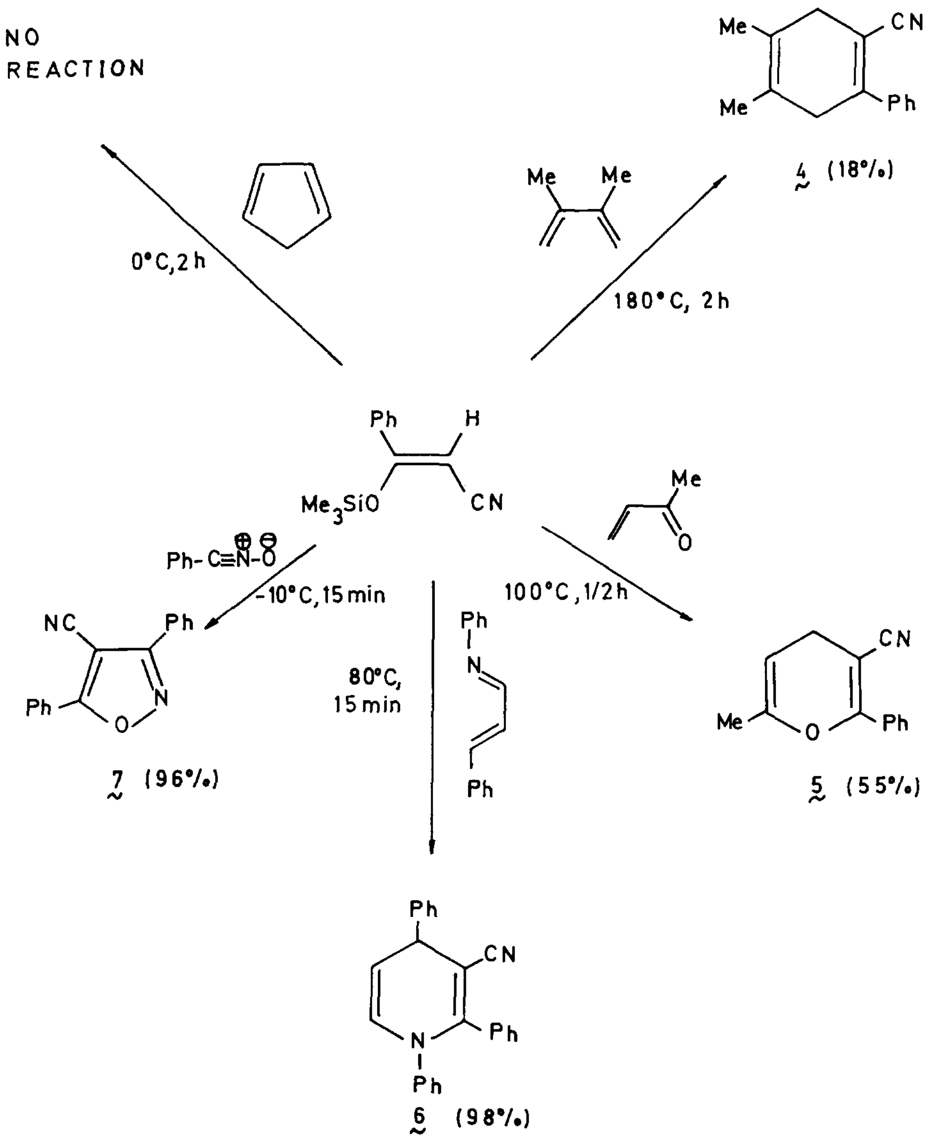
To our knowledge, there have not appeared reports on the synthesis of β-siloxyacrylonitriles except for the hydrosilation of benzoylacetonitrile with triethylsilane under catalysis by $(Ph_3)_3RhCl$ and a small amount of phenylthioethylsilane.[4]

For our purposes we used 5-methyl- and 5-phenylisoxazole as starting compounds and trimethylchlorosilane and t-butyldimethylchlorosilane as silylating agents. Isoxazoles were obtained by standard means.[5,6] Reaction occurs at low temperature and the Z-stereochemistry of the β-siloxyacrylonitrile is controlled by the initial geometry of isoxazole nucleus and the kinetic conditions of the reaction. If the reaction is carried out above -30°C, mixtures of Z and E stereoisomers (ratio 1:1) are obtained.



Yields refer to isolated homogeneous products. A typical experimental procedure is provided.

We have extended the work to the study of the dienophilic activity of **1**. For this purpose, we studied the reaction of a series of representative homo- and heterodienes (see below) with **1**. The 1,3-dipolar addition of benzonitrile oxide to **1** was also examined. The initial adducts were not isolated. The crude products were chromatographed on silica-gel to afford the desilylated adducts **4** - **7**.



The dienophilic activity of 1 toward homodienes was proved to be only fair. While cyclopentadiene fails to add to 1, 2,3-dimethylbutadiene gives modest yields after heating at 180°C. On the contrary, the reaction of heterodienes and benzonitrile oxide with 1 afforded the adducts 5 - 7 in excellent yields. These results are not surprising if we take into account that the essential feature in a Diels-Alder reaction is that the two components should have complementary electronic character.[7] Thus, the reaction takes place between an electron-rich dienophile (1) and electron-poor dienes (heterodienes). It should be noted that the reaction is highly regioselective. A general experimental procedure is indicated.

Although the reaction seems to proceed via desilylation of the initial Diels-Alder adduct, followed by dehydration, we defer any definitive statements regarding mechanism. However we note that the reaction reported here should prove of some consequence to the field of heterocyclic synthesis.

β-Siloxyacrylonitriles. General Procedure.

To a cooled (-78°C) solution of lithium diisopropylamide (20 mmol) in tetrahydrofuran (50 ml), stirred under nitrogen, is slowly added by syringe 5-methyl- or 5-phenylisoxazole (20 mmol). The resulting solution is stirred for 1 h at -78°C, then quenched with trimethylchlorosilane or dimethyl-t-butylchlorosilane (22 mmol) and allowed to warm to room temperature. The lithium salts were filtered. Rotoevaporation of the solvent and distillation gave 1 - 3 which were homogeneous by g.l.c. and exhibited physical and spectral properties which are indicated.[8]

Reaction of 1 with Homo- and Heterodienes. General Procedure.

A mixture of 1 (11 mmol) and the corresponding homo- or heterodiene (10 mmol) is heated in a sealed tube at a temperature and for a period which is indicated above (see scheme). The crude product is chromatographed on silica-gel with dichloromethane as solvent to give adducts 4 - 7. Physical and spectral characteristics of these adducts are indicated.[8] Reaction of 1 with benzonitrile oxide is carried out by adding 1 (10 mmol) to a ethereal solution (30 ml) of the nitrile oxide (11 mmol) at -10°C. After 15 min the bath is removed and the precipitate filtered. Rotoevaporation gave a solid residue 7.[8]

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8. Physical and spectral characteristics of **1**: B.p. 84-88°C / 2 mm Hg. Calc., C, 66.31; H, 6.95; N, 6.44; found: C, 66.50; H, 6.87; N, 6.49. IR (film): 2200, 1610, 1600, 1580, 840, 740 cm^{-1}. ^{1}H-NMR (60 MHz, Cl_4C) δ 7.3-7.5 (m, 5H), 5.1 (s, 1H), 0.3 (s, 9H).
2: B.p. 60-65° C / 3 mm Hg. Calc.: C, 54.15; H, 8.44; N, 9.02; found: C, 53.97; H, 8.49; N, 8.97. IR (film): 2210, 1630, 820 cm^{-1}. ^{1}H-NMR (60 MHz, Cl_4C) δ 4.6 (s, 1H), 2.2 (s, 3H), 0.5 (s, 9H).
3: B.p. 92-97°/3 mm Hg. Calc.: C, 60.86; H, 9.70; N, 7.10; found: C, 60.68; H, 9.77; N, 7.23. IR (film): 2210, 1630, 820 cm^{-1}. ^{1}H-NMR (60 MHz, Cl_4C) δ 4.5 (s, 1H), 2.0 (s, 3H), 1.1 (s, 9H), 0.3 (s, 6H).
4: Viscous oil. Calc.: C, 86.08; H, 7.22; N, 6.69; found: C, 86.22; H, 7.31; N, 6.73. IR (film): 2200, 1650, 1600, 1580, 1500, 770, 700 cm^{-1}. ^{1}H-NMR (60 MHz, Cl_4C) δ 7.6-7.4 (m, 5H) , 2.5 (m, 2H), 2.2 (m, 2H), 1.6 (s, 6H).
5: Viscous oil. Calc.: C, 79.16; H, 5.62; N, 7.10; found: C, 78.99; H, 5.77; N, 7.23. IR(film): 2210, 1620, 1600, 1580, 760, 700 cm^{-1}. ^{1}H-NMR (60 MHz, Cl_4C) δ 7.4-8.3 (m, 5H), 4.6 (dd, J=6 Hz, 9 Hz, 1H), 2.9 (d, J=9 Hz, 1H), 2.8 (d, J=6 Hz, 1H), 2.2 (s, 3H).
6: M.p. 135°C (ethanol). Calc.: 86.20; H, 5.42; N, 8.38; found: C, 86.37; H, 5.36; N, 8.25. IR (Nujol): 2220, 1600, 1580, 1500, 930, 760, 700 cm^{-1}. ^{1}H-NMR (60 MHz, $(CD_3)_2CO$) δ 6.7-8.0 (m, 15 H), 5.5 (dd, J=5.5 Hz, 3 Hz, 1H), 4.0 (dd, J=5.5 Hz, 5 Hz, 1H), 4.7 (dd, J=5 Hz, 3 Hz, 1H).
7: M.p. 131°C (ethanol). Calc.: 78.03; H, 4.09; N, 11.37; found: C, 77.88; H, 4.25; N, 11.50. IR (Nujol): 2240, 1600, 1570, 790 cm^{-1}. ^{1}H-NMR (60 MHz, Cl_4C) δ 7.4-8.3 (m, 10 H).

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