A Simple, Safe, and Inexpensive Preparation of Trimethylsilyl Cyanide

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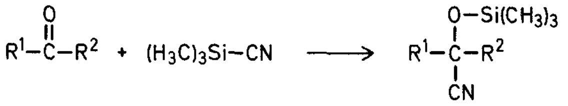
In recent years, trimethylsilyl cyanide (**2**) has been shown to be an excellent reagent for the direct conversion of aldehydes and ketones **1** into silylated cyanohydrins **3**[1-5]. The excellent yields, exclusive 1,2-additions to α,β-unsaturated carbonyl compounds, and ease of adduct formation even with ketones that are normally resistant to cyanohydrin formation make this reaction one of the few truly general transformations in synthetic organic chemistry.



$$R^1-\overset{\overset{\displaystyle O}{\|}}{C}-R^2 + (H_3C)_3Si-CN \longrightarrow R^1-\overset{\overset{\displaystyle O-Si(CH_3)_3}{|}}{\underset{\underset{\displaystyle CN}{|}}{C}}-R^2$$

1 **2** **3**

Silylated cyanohydrins have found considerable synthetic utility in the regioselective protection of *p*-quinones[6], as precursors to acyl anion equivalents[7,8,9], as intermediates for the preparation of β-aminomethyl alcohols[3], and as precursors to certain cyanohydrins themselves[10]. In addition, α-amino amides and α-amino acids have been prepared via addition of **2** to Schiff bases and oximes[11,12].

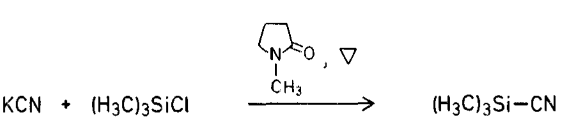
To date, numerous preparations of **2** have been described, the majority of which have basically utilized one of two approaches: (1) use of the very expensive reagent silver cyanide or (2) procedures requiring the handling of extremely toxic hydrogen cyanide[13]. Two recent, improved preparations[14,15] are merely modifications of these two approaches and, although they offer some advantages, are still only marginal improvements.

We recently reported[16] that aldehydes and ketones can be cyanosilylated by heating with a mixture of potassium

0039-7881/79/0732-0523 $ 03.00

cyanide and trimethylsilyl chloride in an appropriate solvent such as acetonitrile or dimethylformamide. At that time we postulated that **2** might be formed *in situ* as an intermediate in the reaction. Due to our inability to extend this *in situ* cyanosilylation procedure to the imine system[17], and the general utility of **2**, we decided to investigate the possibility of preparing **2** directly from potassium cyanide and trimethylsilyl chloride.

We have now found that potassium cyanide can quite efficiently be utilized for the synthesis of **2** and, contrary to previous belief[15], without the need for crown ether catalysis. Simply heating a mixture of trimethylsilyl chloride and potassium cyanide in a dipolar aprotic solvent produces **2** in good yield and purity. For convenience, *N*-methylpyrrolidinone was chosen as the solvent. The choice of a high boiling solvent (b.p. 202°) allows for easy monitoring of the reaction (one simply follows the reflux temperature as it changes from 57°, the b.p. of trimethylsilyl chloride, to that of **2**). Then **2** is readily distilled directly from the pot.



4 **5** **2**

Utilizing this procedure, **2** was obtained in 71% yield; the yield should not be considered optimum since scrupulous drying of the glassware and solvent was not performed.

The simplicity of this procedure suggests its modification for the preparation of a number of other useful organosilanes such as trimethylsilyl azide, trimethylsilyl isocyanate, and trimethylsilyl iodide.

Trimethylsilyl Cyanide (2):

Dry potassium cyanide (65 g, 1 mol), trimethylsilyl chloride (43.4 g, 0.4 mol) and *N*-methylpyrrolidinone (100 ml) are placed in a 1000 ml flask. The contents are then stirred mechanically and heated overnight (16 h), by which time the reflux temperature had reached ~105°. A distillation head and short column (15 cm) are attached and, after collecting a small forerun containing a mixture of hexamethyldisiloxane and **2**, the pure product is collected; yield: 28.0 g (71%); b.p. 115–118° (Lit.[3] b.p. 114–117°, 117–118°); n_D^{20}: 1.3897; purity by G.L.C. ≥98%.

Received: February 20, 1978

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