SHORT PAPER

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A practical and improved method for the preparation of trimethylsilyl cyanide catalysed by PEG400 and zinc iodide[†]

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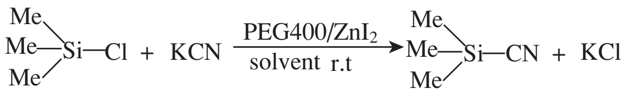
The useful synthetic reagent trimethylsilyl cyanide was readily prepared in high yield by the cyanation of trimethylchlorosilane with potassium cyanide in the presence of PEG400 and zinc iodide under stirring at room temperature or ultrasonic radiation.

Keywords: trimethylsilyl cyanide, trimethylchlorosilane, PEG400, zinc iodide, ultrasonic radiation

To date, trimethylsilyl cyanide (TMSCN) has been utilised successfully in achieving a multitude of organic transformations in high yields and under mild conditions.[1] It is a useful and effective reagent for the preparation of β-amino alcohols, α-aminonitriles and α-trimethylsiloxyacrylonitriles from the corresponding ketone, imines and ketenes.[2] It can also react rapidly with the carbonyl group of aldehydes to give silylated cyanohydrins, which have found to be useful as acyl anion equivalents in many synthetic reactions,[3] or react selectively with α,β-unsaturated ketones and aldehydes to afford the corresponding 1,2-adducts without the formation of 1,4-adducts.[4] In recent years, more and more investigations have been carried out on the asymmetric addition of TMSCN to ketones and aldehydes in the presence of chiral catalysis.[5-6] In addition, an asymmetric Strecker synthesis of α-aminonitriles using TMSCN as cyanating agent has been extensively as well as intensively studied.[7]

Literature surveys indicate that TMSCN was first prepared in modest yield by the action of hexamethyldisilane on hydrogen cyanide.[8] Although numerous methods have been described for the preparation of this excellent cyanating agent few of them can be regarded as completely satisfactory. The majority of these methods have basically utilised the approaches as follows: (1) use of expensive metal cyanides, such as AgCN,[9] TlCN,[10] and LiCN[2] as cyanide source; (2) requiring the participation of the extremely toxic hydrogen cyanide;[11] (3) application of dipolar aprotic solvents with a high boiling point, such as DMF[12] and N-methylpyrrolidinone[13] to carry out the experiment at a reflux temperature; and (4) promoting the reaction by the phase transfer catalyst (PTC). However, the application of 18-crown-6 as PTC affords a yield of only 45%[14] and the use of the quarternary ammonium salt Adogen 464 in N-methylpyrrolidinone only gives a medium yield.[15] Other improved preparations are merely modifications of these approaches that lead to only a small improvement in yield or work-up simplicity. A recent preparation of TMSCN by the reaction of trimethylchlorosilane (TMSCl) with NaCN supported on Amberlite XAD-4 in N-methylpyrrolidinone,[16] although giving an excellent yield, inevitably suffers from the cost of the expensive polymer and solvent. It is obvious, therefore, that the application of cheaper cyanide source such as potassium cyanide or sodium cyanide and readily available common solvents for the preparation of TMSCN is economic and preferable.

In continuation of our investigation on the application of PEG400 to replace the expensive and toxic crown-ether as a phase transfer catalyst,[17] we herein report an alternative and convenient method for the preparation of TMSCN by the cyanaion of TMSCl with the readily available potassium cyanide catalysed by PEG400 and zinc iodide. Both acetonitrile and dichloromethane were used as solvent and several metal iodides were tried in our experiment. The experimental results are listed in Table 1.



$$\mathrm{Me_3Si{-}Cl} + \mathrm{KCN} \xrightarrow[\text{solvent r.t}]{\text{PEG400/ZnI}_2} \mathrm{Me_3Si{-}CN} + \mathrm{KCl}$$

Scheme 1

Because TMSCl would react with the two terminal hydroxyl groups of PEG400 to give PEG400-silyated ether, a two-fold excess of TMSCl over PEG400 was used. We also found that the overdosing of PEG400 elongated the time for the filtration in the solid–liquid separation procedure, presumably because that the inorganic solid "glued" by the viscous PEG400-silyated ether made it difficult for the liquid to penetrate through. While lower dosage of PEG400 will not catalyse the reaction effectively, nevertheless an appropriate amount of PEG400 (5%mol) should be necessary for ensuring a better catalytic ability. An excess (20%) of potassium cyanide is used for ensuring complete conversion of the substrate within an appropriate period of time.

Table 1 Experimental results under the conditions of different solvents and catalysts

Entry	Solvent	PEG400/g	Catalyst	Reaction time/h	Yield/%
1	CH_2Cl_2	2	—	36	40
2	CH_2Cl_2	2	0.5gNaI	36	63
3	CH_2Cl_2	2	0.5gKI	36	58
4	CH_2Cl_2	—	0.5gZnI_2	36	5
5	CH_2Cl_2	1.5	0.5gZnI_2	24	75
6	CH_2Cl_2	2	0.5gZnI_2	20	86
7	CH_2Cl_2	3	0.5gZnI_2	18	78
8[a]	CH_2Cl_2	2	0.5gZnI_2	6	84
9	CH_3CN	2	0.5gZnI_2	2	92[b]

[a]The reaction was carried out under ultrasound radiation.
[b]Determined by GC.

It can be shown from Table 1 that the presence of a catalytic amount of metal iodide could obviously enhance the reaction rate as well as improve the overall yield. This can be explained by the fact that iodide anion, being a good nucleophilic ion as well as leaving group, always shows excellent catalytic effect in an SN2 reaction. However, the catalytic effect of the different metal iodide varies from each other under the same

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conditions. Among the three metal iodides, zinc iodide shows the best catalytic ability, while the reaction carried out in CH_2Cl_2 catalysed by KI and NaI only gave a medium yield. Little or no reaction was found to take place in the absence of PEG400 covering even longer periods of time. From this, we conclude that both PEG400 and metal iodide play important roles in the conversion of the reaction, while the importance of the former is primary.

In the case of entry 9 in Table 1, it can be seen that when acetonitrile was used as solvent, the reaction is complete within a very short period of time. However, we found that it was very difficult to separate the product from the solvent even when a 30cm Vigreux column was used. The distillate ranging from 70 to 72°C was collected, from which we proposed that an azeotropic mixture of TMSCN and acetonitrile might be formed, but further confirmation remained to be carried out. However, this method can be applied to a "one-pot" synthesis with TMSCN as a starting material and acetonitrile as a solvent. In our experiment, we found that ethyl ether is not a suitable solvent for the reaction in that it is not miscible with PEG400, which made it difficult for the cyanide anion to transport to the organic phase. CH_2Cl_2 is an ideal solvent for the reaction in that it is miscible with PEG400, recyclable, and has a boiling point much lower than that of the product, which can ensure an effective separation.

It was reported in earlier literature that ultrasonic radiation could promote the solvolytic dissociation of an inorganic salt by attacking its crystal lattice.[18] Based on this theory, we also carried out the experiment under ultrasonic radiation. As a result, the reaction rate was found greatly enhanced. However, although it is practical for a small-scale experimental preparation, it is not suitable for a large-scale industrial production.

In summary, we have found an excellent method for the preparation of TMSCN. Advantages of our method over these reported ones are lower reaction temperature, cheaper and more readily available reagents, recycling of the solvent and the simplicity of work-up.

Experimental

GC: GC-17A with 2m of column silicon-SE-30. A national ultrasound cleanser operating at 40MHz was used. The solvents were refined according to the literature. TMSCl was freshly distilled. Potassium cyanide was finely grounded and dried at 120°C under vacuum for 6 hours. PEG400 and zinc iodide are commercially available.

The general procedure for the preparation of TMSCN: A 100 ml three-necked, round-bottomed flask equipped with a magnetic bar and nitrogen inlet tube was charged successively with 0.5g of ZnI_2, 30ml of CH_2Cl_2, 2g (0.005mol) of PEG400, 7.8g (0.12mol) of potassium cyanide and 12g (0.11mol) of TMSCl. The mixture was stirred under nitrogen at room temperature (for the case in Entry 8, the flask containing the mixture was partly immersed into the ultrasonic cleanser thermostated at 20°C) for the period of time designated in Table 1. The process of the reaction was monitored by GC. After the completion of the reaction, the inorganic solids were filtered off and washed with small amount of dried CH_2Cl_2. After dichloromethane was distilled through a 5cm Vigreux column, 8.5g of TMSCN was collected at 115–117°C (lit.[9] b.p. 114–117°C), yield 86%; $n_D20=1.3891$ (lit.[3] $n_D20=1.3897$).

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