DOI 10.5012/bkcs.2011.32.5.1575

Efficient, Rapid and Solvent-free Cyanosilylation of Aldehydes and Ketones Catalyzed by $SbCl_3$

S. A. Pourmousavi* and H. Salahshornia

*School of Chemistry, Damghan University, Damghan 36715364 Iran. *E-mail: pourmousavi@du.ac.ir*
Received February 22, 2011, Accepted March 21, 2011

Antimony trichloride ($SbCl_3$) was demonstrated to be an effective catalyst for the cyanosilylation of a wide variety of carbonyl compounds under solvent-free conditions. The reactions proceeded smoothly at room temperature to afford the corresponding cyanosilylethers in good to excellent yields.

Key Words : $SbCl_3$, Trimethylsilyl cyanide, Trimethylsilylethers, Solvent free conditions, TMSCN, Carbonyl compounds

Introduction

Cyanosilylation of carbonyl compounds is an efficient procedure for the synthesis of silylated cyanohydrins, which are readily converted to several significant building blocks such as α-hydroxy acids, α-hydroxy aldehydes, 1, 2 diols, α-amino alcohols etc.[1] In view of the importance of cyanohydrins, much attention has been focused on the development of practical methods for the synthesis of cyanohydrins. Among them, the cyanosilylation of carbonyl compounds using trimethylsilyl cyanide (TMSCN) is widely utilized for the synthesis of cyanohydrins. Several reagents including Lewis acids, Lewis bases, metal alkoxides, bifunctional catalysts, iodine and inorganic salts have been found to effectively transfer the cyano group from TMSCN to carbonyl compounds.[2] Various types of Lewis acids such as $AlCl_3$,[3] $BiBr_3$,[4] BF_3,[5] InX_3 (X = Br,[6] F,[7] $LnCl_3$ (Ln = La, Ce, Sm),[8] $MgBr_2$,[5] $SnCl_4$,[5] R_2SnCl_2 (R= *n*-C_4H_9, C_6H_5),[9] $TiCl_4$,[5] ZnI_2,[10] LiCl,[11] and $NbCl_5$[12] have been reported for cyanosilylation of aldehydes. In many of the reported results presence of solvent are essential for the cyanosilylation reactions.

Recently, antimony trichloride ($SbCl_3$) has been used as an efficient Lewis acid catalyst in promoting various organic transformations such as Friedel-Crafts alkylation of nitrogen heterocycles,[13] reductions with $NaBH_4$,[14,15] cleavage of trityl ethers,[16] and in the synthesis of some heterocycles.[17] $SbCl_3$ is commercially available, inexpensive and easier to handle than other metal halides such as $InCl_3$, $GdCl_3$ and $TiCl_4$.[18] To the best of our knowledge, there is no report of the use of $SbCl_3$ as a mild catalyst for cyanosilylation reactions. In continuation of our program to develop environmentally benign methods under solvent free conditions,[19] we wish to herein report an efficient and facile procedure for cyanosilylation of aldehydes and ketones catalyzed by $SbCl_3$ at room temperature under solvent-free conditions.

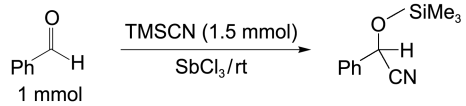
Results and Discussion

We started to study the cyanosilylation by examining the conditions required for the reaction involving benzaldehyde (1 mmol) and TMSCN (1.5 mmol) to give the corresponding cyanosilylether in the presences of various solvent and also under solvent free conditions. The results are summarized in Table 1.

The optimum amount of catalyst (17 mol %) was determined from experiments corresponding to entries 1-4. Entry 5 shows that no reaction was observed in the absence of catalyst even after a long reaction time (24 h). Entries 6-11 show the effect of various solvents on the time of the reaction and yield of the product. The best reaction conditions require the presence of small amounts of $SbCl_3$ (17 mol %) and 1.5 mmol of TMSCN with respect to the benzaldehyde (1 mmol) at room temperature under solvent-free conditions (Entry 5).

In order to understand the scope and limitations of $SbCl_3$ catalyzed procedure for the cyanosilylation reaction, various aldehydes were treated with TMSCN under solvent free conditions. The results are shown in Table 2.

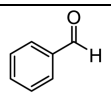
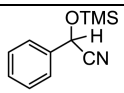
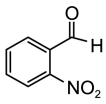
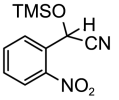
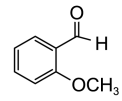
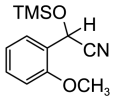
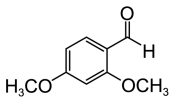
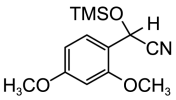
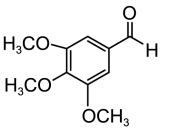
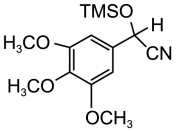
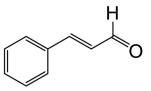
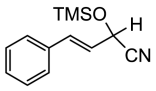
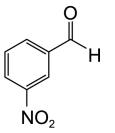
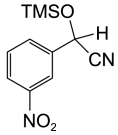
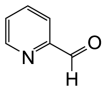
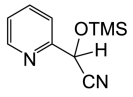
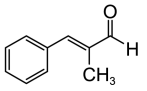
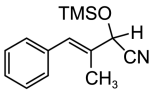
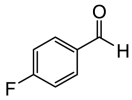
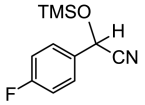
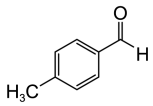
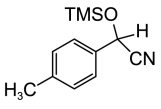
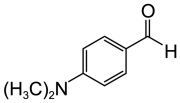
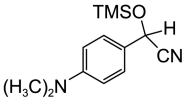
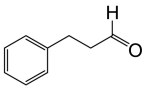
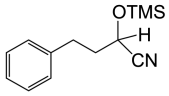
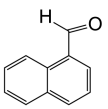
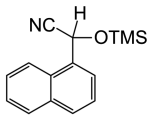
Table 1. Cyanosilylation of benzaldehyde under various conditions at rt



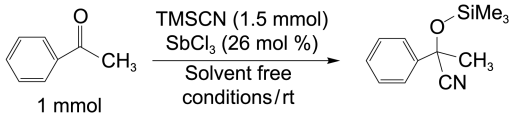
Entry	Solvent	Amounts of catalyst (mol %)	Time (min)	Yield[a]
1	-	4.4	240	30
2	-	13	60	80
3	-	17	30	90
4	-	26	30	90
5		-	24h	0
6	THF	17	300	40
7	Ethyl acetate	17	15	0
8	Ethanol	17	60	20
9	Acetonitrile	17	30	20
10	Dichloromethane	17	240	50
11	*n*-Hexane	17	60	40

[a]The yields refer to isolated pure products.

Table 2. Cyanosilylation of aldehydes (1 mmol) in the presences of TMSCN (1.5 mmol) at rt by catalytic amounts of $SbCl_3$ (0.17 mmol) under solvent free conditions

Entry	Substrate	product	Time (min)	Yield[a]
1			30	90
2			15	90
3			5	98
4			15	93
5			15	70
6			15	95
7			90	60
8			5	97
9			10	90
10			60	70
11			45	90
12			60	88
13			15	80
14			10	90

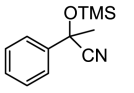
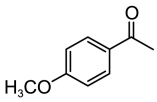
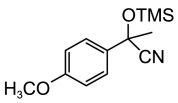
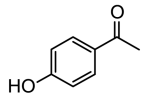
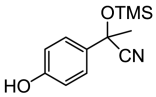
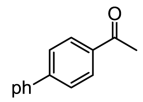
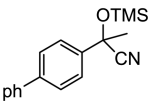
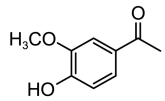
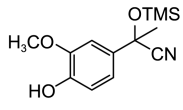
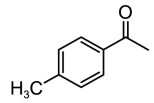
[a]Confirmed by comparison with authentic samples (IR, TLC and ^{1}H-NMR). [b]Yield of isolated pure product after purification.



Scheme 1

As shown in Table 2, aromatic and aliphatic aldehydes were converted into the corresponding cyanohydrin trimethylsilylether for relatively short reaction time in good to excellent yields at room temperature. It should be noted that α,β-unsaturated carbonyl such as cinnamaldehyde and α-methyl-cinnamaldehyde were predominantly converted to

Table 3. Cyanosilylation of ketones (1 mmol) in the presences of TMSCN (1.5 mmol) at rt by catalytic amounts of $SbCl_3$ (0.26 mmol) under solvent free conditions

Entry	substrate	product	Time (min)	Yield[a]
1			15	98
2			10	98
3			150	50
4			45	80
5			60	70
6			30	90
7			120	98
8			240	95
9			15	95
10			60	50
11			90	80
12			10	98

[a]Confirmed by comparison with authentic samples (IR, TLC and ^{1}H-NMR). [b]Yield of isolated pure product after purification.

Table 4. Comparison of cyanosilylation of acetophenone with TMSCN in the presence of $SbCl_3$ with some of those reported catalyst in literature

Entry	Catalyst (mol %)	Solvent	Time	Yield[Ref.]
1	$SbCl_3$ (26)	-	15	98
2	$Fe(Cp)_2PF_6$ (2.5)	-	10	93[20]
3	$InBr_3$ (1)	CH_2Cl_2	180	90[6]
4	$Cu(OTf)_2$ (5)	CH_2Cl_2	1200	85[21]
5	R_2SnCl_2 (10)	-	2700	93[9]
6	$LiClO_4$ (100)	-	180	86[22]
7	CsF (10)	CH_3CN	60	95[23]
8	*N*-methylmorpholine *N*-oxide (30)	-	480	98[24]
9	$(CH_3CH_2)_3N$ (20)	-	120	90[25]
10	$AuCl_3$(1)	CH_2Cl_2	30	94[26]

the 1,2-adducts, leaving the olefinic function intact (Table 2 entries 6, 9). No conjugated addition product was observed. In addition, pyridyl 2-carbaldehyde as a heteroaromatic aldehyde has undergone the reaction within 5 minutes with 97% yield.

Although $SbCl_3$ was optimized for the reaction of aldehydes, it was also found to be an efficient catalyst for the cyanosilylation of ketones. Thus, acetophenone underwent cyanosilylation with $SbCl_3$ (26 mol %) within 15 min in 98% yield (Scheme 1).

The catalytic system was applicable for a wide range of ketones with excellent yield. The results are summarized in Table 3. According to the result in Table 3 various ketones were converted to the corresponding cyanosilylether in the presences of TMSCN (1.5 mmol) by a catalytic amount of $SbCl_3$ (26 mol %) at room temperature under solvent free conditions in good to excellent yields.

The data illustrated in Table 3 demonstrates that a variety of aryl and alkyl ketones may be employed in the $SbCl_3$ catalyzed process and give the corresponding trimethylsilyl ethers in 50-98% yields.

To illustrate the efficiency of the proposed method, Table 4 compares the cyanosilylation of acetophenone by $SbCl_3$ with some of those reported in the literature.

As shown in Table 4 although some improvements like using smaller amount of catalyst have been observed in some of the reported method but there are still some limitations such as longer reaction time (Table 4 Entry 3-10) and using CH_2Cl_2 and CH_3CN as toxic and volatile organic solvents (Table 4 Entry 3, 4, 7 and 10). On the other hand in the case of $Fe(Cp)_2PF_6$ (Table 4 Entry 2) although the reaction time is smaller than the present method under solvent free condition but this catalyst is very expensive, so our method will be superior to these reported methods.

Conclusion

In summary, antimony trichloride was identified as a highly effective Lewis acid to promote the cyanosilylation of a wide variety of unconjugated and conjugated aldehydes and ketones. The relatively short reaction times, good to high yields of the products, the simple and clean work-up, and the mild reaction conditions make this method a useful addition to the present methodologies for the cyanosilylation of carbonyl compounds. On the other hand this method may contribute to the development of green chemistry because of its possible application under solvent-free condition.

Experimental

General. Yields refer to isolated pure products. The products were characterized by their spectral (^{1}H-NMR, IR). All ^{1}H-NMR spectra were recorded at Bruker avance 500 MHz NMR in $CDCl_3$ relative to TMS (0.00 ppm). IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. TLC was performed on Silica-gel polygram SIL G/UV 254 plates.

Cyanosilylation of Carbonyl Compound. To a stirred mixture of aldehyde (1 mmol) and TMSCN (1.5 mmol) was added $SbCl_3$ (17 mol % for aldehydes and 26 mol % for ketones) at room temperature in a 10 mL round bottom flask. The reaction mixture was stirred continuously and progress of the reaction was followed by TLC using Cyclohexane/Ethylacetate (9:1) as eluent. After completion of the reaction, the mixture was washed with *n*-hexane (3 × 5 mL) and filtered off. The combined organic layers were washed with distillated water (3 × 5 mL) and then dried over $MgSO_4$ and evaporated under vacuum to give almost pure cyanosilylether. Further purification, if necessary, was preceded using preparative TLC by an appropriate solvent.

Caution. TMSCN must be used in a well ventilated hood due to its high toxicity and moisture sensitive nature.

Spectral Data of Some Selected Compounds.

2-Trimethylsilyloxy-2-phenylacetonitrile (Table 2, Entry 1):[12] FTIR (KBr, neat): ν 2229 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.29 (s, 9H), 5.55 (s, 1H), 7.43-7.53 (m, 5H), ppm.

2-Trimethylsilyloxy-2-phenylpropanenitrile (Table 3, Entry 1):[26] FTIR (KBr, neat): ν 2229 cm^{-1}, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.22 (s, 9H), 1.91 (s, 3H), 7.36-7.60 (m, 5H), ppm.

2-Trimethylsilyloxy-2-(4-methoxyphenyl)propanenitrile (Table 3, Entry 2):[26] FTIR (KBr, neat): ν 2228 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.21 (s, 9H), 1.89 (s, 3H), 3.85 (s, 3H), 6.94-6.96 (m, 2H), 7.50-7.52 (m, 2H) ppm.

Acknowledgments. We are thankful to the Damghan University for support of this work.

References

1. Gregory, R. J. H. *Chem. Rev.* **1999**, *99*, 3649.
2. Some of representative examples: (a) Bandini, M.; Cozzi, P. G.; Garelli, A.; Melchiorre, P.; Umani-Ronchi, A. *Eur. J. Org. Chem.* **2002**, 3243. (b) Cordoba, R.; Plumet, J. *Tetrahedron Lett.* **2003**, *44*, 6157. (c) Chen, F.-X.; Liu, X.; Qin, B.; Zhou, H.; Feng, X.; Zhang, G. *Synthesis* **2004**, *14*, 2266. (d) Aspinall, H. C.; Bickley, J. F.; Greeves, N.; Kelly, R. V.; Smith, P. M. *Organometallics* **2005**, *24*, 3458. (e) Liu, Y.; Liu, X.; Xin, J.; Feng, X. *Synlett* **2006**,

1085. (f) Kim, S. S.; Kim, D. W.; Rajagopal, G. *Synthesis* **2004**, 213.
3. Lidy, W.; Sundermeyer, W. *Chem. Ber*. **1973**, *106*, 587.
4. Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett*. **1997**, *38*, 7215.
5. Reetz, M. T.; Drewes, M. W.; Harms, K.; Reif, W. *Tetrahedron Lett*. **1988**, *29*, 3295.
6. Bandini, M.; Cozzi, P. G.; Garelli, A.; Melchiorre, P.; Unami-Ronchi, A. *Eur. J. Org. Chem*. **2002**, 3243.
7. Loh, T.-P.; Xu, K.-C.; Ho, D. S.-C.; Sim, K.-Y. *Synlett.* **1998**, 369.
8. Vougioukas, A. E.; Kagan, H. B. *Tetrahedron Lett*. **1987**, *28*, 5513.
9. Whitesell, J. K.; Apodaca, R. *Tetrahedron Lett*. **1996**, *37*, 2525.
10. Evans, D. A.; Truesdale, L. K.; Carroll, G. L. *J. Chem. Soc., Chem. Commun*. **1973**, 55.
11. Kurono, N.; Yamaguchi, M.; Suzuki, K.; Ohkuma, T. *J. Org. Chem.* **2005**, *70*, 6530.
12. Georgea, S. C.; Kim, S. S. *Bull. Korean Chem. Soc.* **2007**, *28*, 1170.
13. Liu,Y.-H.; Liu, Q.-S.; Zhang, Z.-H. *Tetrahedron Letters* **2009**, *50*, 916.
14. Sayama, S.; Inamura, Y. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 306.
15. Ren, P.; Pan, S.; Dong, T.; Wu, S. *Synth. Commun.* **1995**, *25*, 3799.
16. Wu, Q.; Wang, Y.; Chen, W.; Liu, H. *Synth. Commun.* **2006**, *36*, 1361.
17. Ganai, B. A.; Kumar, S.; Andotra, C. S.; Kapoor, K. K. *Synth. Commun.* **2006**, *36*, 803.
18. Darabi, H. R.; Aghapoor, K.; Mohsenzadeh, F.; Taala, F.; Asadollahnejad, N.; Badiei, A. *Catal. Lett.* **2009**, *133*, 84.
19. (a) Pourmousavi, S. A.; Salehi, P. *Bull. Korean Chem. Soc.* **2008**, *29*, 1332. (b) Pourmousavi, S. A.; Salehi, P. *Acta Chim. Slov.* **2009**, *56*, 734. (c) Pourmousavi, S. A.; Zinati, Z. *Turk. J. Chem.* **2009**, *33*, 385.
20. Khan, N.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Singh, S.; Jasra, R. V. *J. Organometal. Chem.* **2007**, *692*, 4361.
21. Saravanan, P.; Anand, R. V.; Singh, V. K. *Tetrahedron Lett*. **1998**, *39*, 3823.
22. Azizi, N.; Saidi, M. R. *J. Organometal. Chem.* **2003**, *688*, 283.
23. Kim, S. S.; Rajagopal, G.; Song, D. H. O. *J. Organomet. Chem*. **2004**, *689*, 1734.
24. Kim, S. S.; Kim, D. W.; Rajagopal, G. *Synthesis* **2004**, *2*, 213.
25. Baeza, A.; Najera, C.; Retamosa, M. G.; Sansano. J. M. *Synthesis* **2005**, *16*, 2787.
26. Cho, W. K.; Kang, S. M.; Medda, A. K.; Lee, J. K.; Choi, I. S.; Lee, H.-S. *Synthesis* **2008**, *4*, 507.