Mild and Efficient Silylcyanation of Aldehydes Catalyzed by Zirconium Complex

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An efficient method of addition of trimethylsilyl cyanide to aldehydes by employing a zirconium complex as the catalyst has been described. A variety of aromatic, aliphatic, cyclic and heterocyclic aldehydes has been converted into corresponding trimethylsilyl ethers in excellent yield within short reaction time.

**Key Words :** Zirconium complex, Aldehydes, TMSCN, Silylcyanation

Introduction

Cyanohydrins[1] occupy very important role in organic synthesis due to their synthetic versatility that can easily be converted into various polyfunctionalized building blocks, including α-hydroxy compounds and β-amino alcohols. Diorganotin dichloride[2] catalyzes the addition of trimethyl-silyl cyanide (TMSCN) to various ketones and aldehydes. A very similar addition to the carbonyl compounds[3] was also found to be catalyzed by copper(II) triflate. Silylcyanation of aromatic ketones[4] is strongly promoted in organic solutions of lithium perchlorate and lithium tetrafluoroborate. Layered zirconium hydrogen phosphate exchanged with potassium ion[5] was found to be an efficient catalyst for silylcyanation of carbonyl compounds. Indium tribromide ($InBr_3$)[6] is a very effective catalyst for the addition of TMSCN to function-alized ketones. Silylcyanation of ketones[7] were also achiev-ed by salen/Ti(iPro)$_4$/N-oxides as the catalysts. Recently we[8] have employed KF, CsF and *N*-methylmorpholine *N*-oxide (NMO) for the silylcyanation of the aldehydes and ketones. We have developed a new ligand which is complexed with $Zr(OPr^i)_4$ for the catalyst of Silylcyanation.

Results and Discussion

Representative examples of the synthesis of various silylethers from aromatic, vinylic, cyclic and heterocyclic aldehydes are compared with the previous ones in Table 1. Unsubstituted and substituted benzaldehydes (entries 1-6) undergo very smooth silylcyanation (reaction time: 1 1/2~2 1/2 hr) with over 93% yield. This indicates that the electronic effect of substituent hardly plays role for the silylcyanation of various benzaldehydes. Vinylic aldehydes (entries 7 and 8) show very facile reactivities towards trimethylsilyl cyanide with excellent outcome. Cyclic (entry 9) and heterocyclic (entry 10) aldehydes were also easily converted into the silylethers for the excellent result in terms of yield and reaction period.

The mechanism of silylcyanation may occur in the following manner.[9,10] The zirconium catalyst **1** may react with $(CH_3)_3$Si-CN to generate CN and $(CH_3)_3$ Si·**1**. The anion CN adds to aldehyde for the formation of **2**. $(CH_3)_3$Si moiety of $(CH_3)_3$ Si·**1** is transferred to **2** to give the product **3** and **1**.

$$(CH_3)_3Si-CN + \mathbf{1} \longrightarrow CN^- + (CH_3)_3Si \bullet \mathbf{1} \qquad (1)$$

$$(2)$$

$$(3)$$
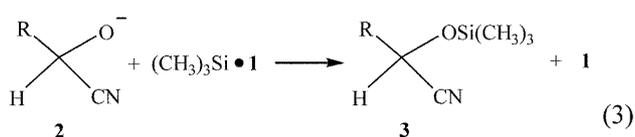
A very effective catalytic system for silylcyanation of various kinds of aldehydes has been developed. The mild conditions, short reaction time, novel catalyst and the wide range of substrate applicability represent the notable features of the procedure.

Experimental Section

Silylcyanation of the Aldehydes. Aldehyde (1 mmol), TMSCN (1.2 equiv.) and Zr-complex (2 mol %) were dissolved in 5 mL of CH_2Cl_2 and reacted for 2-3 hour. The reaction mixture was dried to dryness with rotary evaporator. To this dried mixture 25 mL of H_2O was added and the product was extracted with 60 mL of CH_2Cl_2 four times. CH_2Cl_2 solution was dried on $MgSO_4$ and distilled on vacuum. This was purified on Silica gel chromatography (hexane : ethyl acetate = 9 : 1) to give the pure sample. ^{1}H and ^{13}C NMR and HRMS were taken for the purified samples.

Synthesis of 2-N-(2-Hydroxy-2-Methylethylimino)-4-Pentanone (HMEIP). 2,4-pentanedione (0.15 mol) and 1-amino-2-propanol (0.1 mol) were dissolved in 100 mL of CH_2Cl_2 and stirred for 1 day. The solvent was evaporated
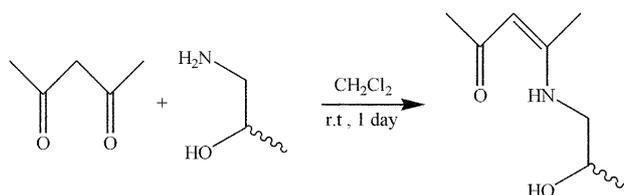
Table 1. Trimethylsilylcyanation of Aldehydes by Zirconium Complex

Entry	Substrate	Time (h)	Yield (%)
1	CHO	1.5	97%
		0.3[3]	81%[3]
		2[4]	95%[4]
		2[4]	100%[4]
		0.3[5]	98%[5]
		3[6b]	90%[6b]
2	MeO—CHO	2	95%
		0.2[5]	96%[5]
3	tBu—CHO	2.5	93%
4	Me—CHO	2	96%
		9[7b]	99%[7b]
5	Cl—CHO	2	94%
		3[3]	75%[3]
6	Ph—O—C6H4—CHO	2.5	96%
7	(geranial) CHO	2	96%
8	CH3CH=CH—CHO	3	91%
9	cyclohexyl—CHO	3	95%
10	furfural CHO	2	95%
		3[3]	75[3]

and the remaining solid was recrystallized from CH_2Cl_2 (10 mL) and ethyl ether (140 mL) to give 95% yield of HMEIP. mp = 76 °C. ^{1}H-NMR (CDCl3, 200 MHz) 10.91 (br s, 1H, C(O)CH=C(NH)), 4.95 (s, 1H, C(O)CHC(NH)), 3.93 (m, 1H, NCH2CH(Me)OH), 3.47 (br s, 1H, NCH2CH(Me)OH), 3.24 (q, 2H, HNCH2C), 1.96 (s, 3H, CH=C(NH)CH3), 1.92 (s, 3H, CH3C(O)CH),1.22 (d, 3H,HNCH2C(CH3)OH). ^{13}C-NMR (CDCl3, 50 MHz) 194.82 (CH3C(O)CH), 163.95 (CH=C(NH)CH3), 95.70 (C(O)CH=C(NH)), 66.69 (NCH2CH(Me)OH), 50.61 (NCH2C), 28.68 (CH3C(O)CH), 20.82 (NCH2C(CH3)OH), 19.28 (CH=C(NH)CH3). EIMS

(70 eV): M/Z=157 (M[+]).

Synthesis of Zirconium Complex. In the glove box,
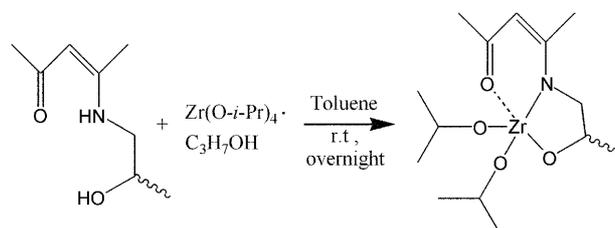
zirconium(III)-isopropoxide-isopropanol complex (7.0 mmol) was dissolved in 50 mL of toluene, and a toluene solution of HMEIP (6.4 mmol) added under N_2 atmosphere and refluxed overnight. Solvent was evaporated and the remaining residue was washed with n-hexane to give the pure monomeric zirconium complex (yield: 90%). mp = 270 °C. ^{1}H-NMR (CDCl3, 200 MHz) 4.99 (s, 1H, C(O)CHC(NH)), 4.84 (br m, 2H, OCH(Me)2), 4.02 (m, 1H, OCHMeCH2), 3.55 (m, 2H NCH2CH(Me)O), 1.87 (br, 12H,OCH(CH3)2), 1.22 (s, 3H, CH=C(NH)CH3), 1.19 (s, 3H, CH3C(O)CH), 0.88 (m, 3H, NCH2CH(CH3)O). ^{13}C-NMR (CDCl3, 50 MHz) 173.78 (CH3C(O)CH), 165.72 (CH=C(NH)CH3), 100.37 (C(O)CH=C(NH)), 69.20 (NCH2CH(Me)O), 58.84 (NCH2-CH(Me)O), 29.42 (CH3C(O)CH), 26.34 (ZrOCH(CH3)2), 25.08 (ZrOCH(CH3)2), 22.38 (NCH2C(CH3)O, CH=C(NH)-CH3), 19.28 (CH=C(NH)CH3). Anal. Calc. for $C_{13}H_{25}$-NO4Zr: C, 44.54; H, 7.19; N, 4.00. Found: C, 44.09; H, 7.38; N, 3.84%.

2-Phenyl-2-(trimethylsilyloxy)acetonitrile (Entry 1). ^{1}H NMR (CDCl3, 200 MHz): δ 0.25 (s, 9H), 5.52 (s, 1H), 7.41-7.47 (m, 5H). ^{13}C NMR (CDCl3, 50 MHz): δ −0.33, 63.59, 119.12, 126.29, 128.87, 129.27, 136.18. HRMS (EI): *m/z* calcd for $C_{11}H_{15}NOSi$ (M[+]): 205.0923; found: 205.0912.

2-(4-Methoxyphenyl)-2-(trimethylsilyloxy) acetonitrile (Entry 2). ^{1}H NMR (CDCl3, 200 MHz): δ 0.24 (s, 9H), 3.84 (s, 3H), 5.45 (s, 1H), 6.96 (d, 2H, *J* = 8.8Hz), 7.38 (d, 2H, *J* = 8.8 Hz) ^{13}C NMR (CDCl3, 50 MHz): δ −0.23, 55.34, 63.34, 114.25, 119.32, 127.93, 128.46, 160.33. HRMS (EI): *m/z* calcd for $C_{12}H_{17}NO_2Si$ (M[+]): 235.1029; found: 235.1032.

2-(4-*tert*-Butylphenyl)-2-(trimethylsilyloxy) acetonitrile (Entry 3). ^{1}H NMR (CDCl3, 200 MHz): δ 0.25 (s, 9H), 1.34 (s, 9H), 5.49 (s, 1H), 7.43-7.44 (m, 5H). ^{13}C NMR (CDCl3, 50 MHz): δ −0.39, 31.10, 34.52, 63.32, 119.18, 125.73, 126.04, 133.19, 152.37. HRMS (EI): *m/z* calcd for $C_{15}H_{23}NOSi$ (M[+]): 261.1549; found: 261.1552.

2-(4-Methylphenyl)-2-(trimethylsilyloxy) acetonitrile (Entry 4). ^{1}H NMR (CDCl3, 200 MHz): δ 0.21 (s, 9H), 2.36 (s, 3H), 5.45 (s, 1H), 7.22 (d, 2H, *J* = 7.8 Hz), 7.37 (d, 2H, *J* = 7.8 Hz). ^{13}C NMR (CDCl3, 50 MHz): δ −0.25, 55.78, 63.87, 114.66, 119.47, 127.88, 128.77, 160.23. HRMS (EI): *m/z* calcd for $C_{12}H_{17}NOSi$ (M[+]): 219.1079; found: 219.1069

2-(4-Cholorophenyl)-2-(trimethylsilyloxy) acetonitrile (Entry 5). ^{1}H NMR (CDCl3, 200 MHz): δ 0.25 (s, 9H), 5.48 (s, 1H), 7.37-7.38 (m, 5H). ^{13}C NMR (CDCl3, 50 MHz): δ −0.33, 62.93, 118.76, 127.64, 129.12, 134.80, 135.28.

HRMS (EI): *m/z* calcd for $C_{11}H_{14}ClNOSi$ (M$^+$): 239.0533; found: 239.0589.

2-(4-Phenoxyphenyl)-2-(trimethylsilyloxy) acetonitrile (Entry 6). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.22 (s, 9H), 5.46 (s, 1H), 6.99-7.13 (m, 5H), 7.31-7.44 (m, 4H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ −0.26, 63.18, 117.50, 118.75, 119.48, 120.42, 124.04, 124.94, 128.02, 128.41, 129.92, 130.73, 131.98, 156.38, 158.84. HRMS (EI): *m/z* calcd for $C_{17}H_{19}NO_2Si$ (M$^+$): 297.1185; found: 297.1181.

4,8-Dimethyl-2-(trimethylsilyloxy)nona-3,7-dienenitrile (Entry 7). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.22 (s, 9H), 1.62 (s, 3H), 1.70-1.80 (m, 6H), 2.10-2.12 (m, 4H), 5.09-5.13 (m, 2H), 5.31-5.33 (m, 1 H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ −0.12, 16.76, 17.65, 23.18, 25.83, 39.13, 58.42, 119.50, 120.59, 123.14, 133.04, 142.82. HRMS (EI): *m/z* calcd for $C_{14}H_{25}NOSi$ (M$^+$): 251.1705; found: 251.1713.

2-(Trimethylsilyloxy)-pent-3-enenitrile (Entry 8). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.20 (s, 9H), 1.79 (dd, 3H, 2.4 Hz, 2.4 Hz), 4.90 (d, 1H, 8.4 Hz), 5.51-5.62 (m, 1H), 5.93-6.04 (m, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ −0.39, 17.16, 61.91, 118.55, 126.06, 130.98. HRMS (EI): *m/z* calcd for $C_8H_{15}NOSi$ (M$^+$): 169.0922; found: 169.0917.

Cyclohexyl (trimethylsilyloxy)acetonitrile (Entry 9). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.20 (s, 9H), 1.19-1.28 (m, 5H), 1.61-1.85 (m, 6H), 4.17 (d, 1H, 6.2 Hz). ^{13}C NMR (CDCl$_3$, 50 MHz): δ −0.59, 25.40, 25.92, 27.99, 42.82, 66.37, 119.28. HRMS (EI): *m/z* calcd for $C_{11}H_{21}NOSi$ (M$^+$): 211.1392; found: 211.1387.

2-Furanyl(trimethylsilyloxy)acetonitrile (Entry 10). ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.22 (s, 9H), 5.55 (s, 1H), 6.41-6.43 (m, 1H), 6.55-6.57 (m, 1H), 7.28-7.48 (m, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz): δ −0.43, 57.41, 109.70, 110.78, 117.11, 143.84, 148.20. HRMS (EI): *m/z* calcd for

$C_9H_{13}NO_2Si$ (M$^+$): 195.0715; found: 195.0712.

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