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Cyanosilylation of carbonyl compounds catalyzed by sodium L-histidine

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An efficient protocol for the addition of trimethyl silanecarbonitrile to carbonyl compounds by employing 1 mol% of L-histidine sodium salt alone as the catalyst is presented. A variety of aromatic, aliphatic and cyclic carbonyl compounds have been converted into the corresponding trimethylethers in excellent yield (up to 99%) under mild conditions. Copyright © 2007 John Wiley & Sons, Ltd.

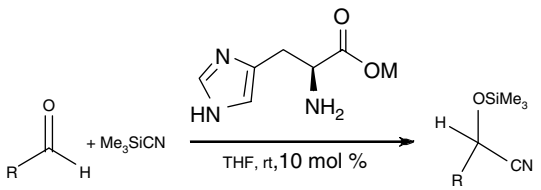
KEYWORDS: cyanosilylation; aldehydes; ketones; sodium L-histidine; cyanohydrins

INTRODUCTION

Silylcyanation reaction of carbonyl compounds is one of the simplest strategies to synthesize polyfunctionlized organic molecules. Cyanohydrins are highly versatile synthetic blocks in organic synthesis as they may be easily converted into functional groups such as α-hydroxy acids, α-hydroxy aldehydes, 1, 2 diols, α-amino alcohols, etc.

Great efforts have been devoted to the development of catalytic systems for the silylcyanation of aldehydes and ketones during the past few decades.[1–4] Trimethylsilylcyanide has most effectively been used as the source of cyanide ion. Several reagents including Lewis acids, Lewis bases, metal alkoxides, bifunctional catalysts, iodine and inorganic salts have been found effectively to transfer the cyano group from trimethyl silanecarbonitrile (TMSCN) to carbonyl compounds.[5–9] However, in many of the catalyzed reactions the presence of additives is essential to activate the catalyst for cyanosilylation.[10–16] A metal-free, organic molecule catalyzed reaction is more attractive because of the mildness of the reaction conditions and the potential for further conversion. However it is only very recent years that such examples have begun to appear in the literature.[17–21] We have developed several catalytic systems for the synthesis of chiral[22–26] and achiral[27–31] cyanosilylether.

During our research for new type of organocatalysts, we have decided to investigate the possibility of using L-histidine to catalyze the cyanosilylation of carbonyl compounds with TMSCN. There are very few reports available in the literature regarding the use of amino acids for organic reactions. L-Proline has been used as an organocatalyst in several reactions.[32–34] Quite recently Feng and co-workers reported that the sodium salt of *N*-phenyl glycine is an effective catalyst for the enantioselective cyanosilylation of ketones.[35] L-histidine is very rarely used as a catalyst in organic reactions.[36,37] We intend to search the catalytic potentialities of L-histidine in cyanosilylation reactions. Our initial catalyst screening revealed that L-histidine sodium salt is an effective catalyst that leads to the product in the formation of 92% yield at room temperature without any additive. Pure L-histidine (loading, 10 mol%; yield, 50%; time, 40 h), lithium salt of L-histidine (loading, 10 mol%; yield, 84%; time, 70 min) and potassium salt of L-histidine (loading, 10 mol%; yield, 88%; time, 60 min) are less effective than the sodium salt of L-histidine (loading, 10 mol%; yield, 92%; time, 25 min; Scheme 1).



Scheme 1. **1a**, M = H; **1b**, M = Li; **1c**, M = K; **1d**, M = Na.

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EXPERIMENTAL

Materials and instruments

In all cases the ^{1}H NMR (200 MHz) spectra were recorded with Varian Gemini 2000 spectrophotometer. Chemical shifts are reported in ppm in $CDCl_3$ with tetramethylsilane as internal standard. ^{13}C NMR data were collected on a Varian Gemini 2000 spectrophotometer (400 MHz). Enantionmer ratios were determined by HPLC analysis on Chiracel OD (H), AS and OB (H) columns in comparisons with authentic racemates. Tetrahydrofuran (THF) supplied by J.T. Baker U.S.A. (HPLC grade, H_2O by KF, coulometric 0.003%) was used as the solvent for the reaction. L-histidine was supplied by Sigma Aldrich with >99% purity. TMSCN, aldehydes and ketones were purchased from Aldrich.

Catalyst preparation

Method 1

L-Histidine (1 mol%) was stirred with NaOH (1 mol%) in dry THF (0.5 ml) at room temperature for 0.5 h under nitrogen atmosphere. The catalyst prepared was immediately used for the reaction.

Method 2

The salt of L-histidine was prepared by adding 1 equivalent of alkali metal hydroxide to 1 equivalent L-histidine in methanol at 0 °C and stirring at room temperature for 3 h. After the solvent was evaporated, the salts were dried at 25 °C in a vacuum.

Preparation of cyanohydrin trimethylsilylether

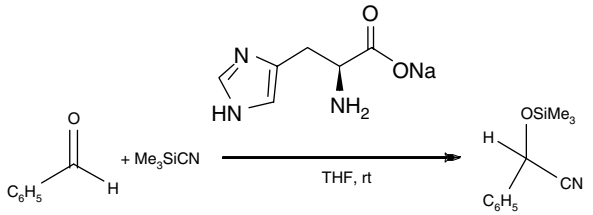
To 1 mol% of the sodium salt of L-histidine prepared by method 1, TMSCN (2.4 equiv.) and THF (0.5 ml) were added and stirred at room temperature in a 10 ml round-bottom flask. To this mixture aldehyde or ketone (1 mmol) was added drop-wise using a syringe pump. The reaction mixture was stirred continuously under the conditions mentioned in Table 1 and the progress of the reaction was followed by TLC. The reaction mixture was purified by silica gel flash chromatography by using EtOAc–hexane (1 : 9) mixture as eluent. The silylethers thus obtained were identified by ^{1}H and ^{13}C NMR data, which are consistent with the structure. Caution: TMSCN is moisture-sensitive and highly toxic and it must be used in well-ventilated hood.

Spectral data of all the compounds

2-Phenyl-2-(trimethylsilyloxy)acetonitrile (Table 2, entry 1)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.257$ (s, 9H), 5.52 (s, 1H), 7.42–7.47 (m, 5H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.32$, 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, HPLC (Daicel Chiralcel OD-H, ^{i}PrOH–hexane = 0.25 : 99.75, flow = 0.25 ml min^{-1}) 17.88 and 18.32 min.

Table 1. Cyanosilylation of benzaldehyde under various conditions[a]



Entry	Catalyst	Time (min)	Temperature	Yield (%)[b,c]	ee%[d]
1	30	35	r.t.	82	—
2	20	30	r.t.	80	13
3	10	25	r.t.	92	9
4	5	22	r.t.	93	5
5	3	15	r.t.	99	—
6	1	13	r.t.	96	9
7	0.5	90	r.t.	70	5
8	0.1	120	r.t.	50	13
9	1	1320	−10 °C	99	1
10	5	120	−10 °C	99	3
11	5	390	−80 °C	100	3
12[e]	1	15	r.t.	96	rac
13[f]	—	30 h	r.t.	83	rac

[a] 1 mmol of the benzaldehyde, 2.4 equiv. TMSCN and 0.5 ml of solvent were added to 1 mol % of freshly prepared catalyst by method 1. [b] Conversion was 100% (from ^{1}H NMR analysis). [c] Isolated yield. [d] ee determined from Chiracel OD-H column. [e] Reaction conducted in the presence of 0.05 mmol 2,6-di-tert-butyl pyridine. [f] Reaction conducted in the presence of 3 mol% of 4-methyl imidazole as catalyst.
r.t., room temperature.

2-(4-Methylphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 2)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.142$ (s, 9H), 2.29 (s, 3H), 5.49 (s, 1H), 7.18 (d, 2H) 7.25 (d, 2H) ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.28$, 55.78, 63.87, 114.66, 119.47, 127.58, 128.78, 160.23. HRMS (EI): m/z calcd for $C_{12}H_{17}NOSi(M^+)$: 219.1079; found: 219.1069, HPLC (Daicel Chiralcel AS, ^{i}PrOH–hexane = 1 : 99, flow = 0.25 ml min^{-1}) 15.54 and 16.66 min.

m-Tolyl-2-(trimethylsilyloxy)acetonitrile (entry 3)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.232$ (s, 9H), 5.45 (s, 1H), 2.38–2.42 (m, 3H) 7.26–7.28 (m, 4H) ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.123$, 21.46, 63.72, 119.21, 123.41, 126.93, 128.74, 130.02, 136.07, 138.74. HRMS (EI): m/z calcd for $C_{12}H_{17}NOSi$ (M^+): 219.1079; found: 219.1072, HPLC (Daicel Chiralcel AS, ^{i}PrOH–hexane = 1 : 99, flow = 0.25 ml min^{-1}) 14.79 and 15.82 min.

2-(4-Methoxyphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 4)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.38$ (s, 9H), 3.83 (s, 3H), 5.44 (s, 1H), 6.96 (d, 2H), 7.42 (d, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz):

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$\delta = -0.26$, 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: 235.1026, HPLC (Daicel Chiralcel AS, ^{i}PrOH–hexane = 0.25 : 99.75, flow = 0.25 ml min^{-1}) 15.94 and16.99 min.

2-(4-tert-butylphenyl)-2-(trimethylsilyloxy) acetonitrile(entry 5)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.23$ (s, 9H), 1.32 (s, 9H), 5.38 (s, 1H), 7.09–7.21 (m, 5H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.39$, 31.12, 34.52, 63.33, 119.28, 125.73, 126.04, 133.19, 152.47. HRMS (EI): m/z calcd for $C_{15}H_{23}NOSi$ (M^+): 261.1549; found: 261.1552.

2-(3-Phenoxyphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 6)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.218$ (s, 9H), 5.42 (s, 1H), 7.01–7.20 (m, 5H), 7.34–7.38 (m, 4H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.16$, 63.28, 116.37, 118.85, 119.17, 119.30, 120.64, 123.75, 129.81, 130.22, 138.08, 156.39, 157.88. HRMS (EI): m/z calcd for $C_{17}H_{19}NO_2Si$ (M^+): 297.1185; found: 297.1182, HPLC (Daicel Chiralcel AS, ^{i}PrOH–hexane = 1 : 99, flow = 0.25 ml min^{-1}) 16.21 and 16.89 min.

2-(4-Nitrophenyl)-2-(trimethylsilyloxy) acetonitrile (entry 7)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.286$ (s, 9H), 5.62 (s, 1H), 7.78 (d, 2H), 8.32 (d, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.28$, 65.02, 118.35, 124.25, 139.54, 147.12. HPLC (Daicel Chiralcel AS, ^{i}PrOH–hexane = 1 : 99, flow = 0.25 ml min^{-1}) 14.21 and 15.49 min.

2-(Naphthalene-1-yl)-2-(trimethylsilyloxy)acetonitrile (entry 8)

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.226$ (s, 9H), 6.05 (s, 1H), 7.45–7.7 (m, 3H) 7.85–7.95 (m, 3H), 8.23 (d, 1H) ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.285$, 63.4, 118.45, 122.37, 125.62, 125.01, 126.3, 128.3, 131.01, 133.45, 136.12.

2-Furanyl (trimethylsilyloxy)acetonitrile (entry 9)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.21$ (s, 9H), 5.58 (s, 1H), 6.41–6.43 (m, 1H), 6.57–6.6 (m, 1H), 7.4–7.52 (m, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\dot{\delta}$ −0.42, 57.42, 109.71, 110.76, 117.12, 143.87, 148.23. HRMS (EI): m/z calcd. for $C_9H_{13}NO_2Si$ (M^+): 195.0715; found: 195.0712.

3-Methyl-2-trimethylsilyloxybutanenitrile(entry 10)

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.2$ (s, 9H), 0.88–1.05 (m, 6H), 1.94–1.96 (m, 1H), 4.16 (d, 1H) ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.335$, 17.68, 33.921, 67.28, 119.94.

2-(Trimethylsilyloxy) pent-3-enenitrile (entry 11)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.24$ (s, 9H), 1.74 (d, 3H), 4.90 (d, 1H), 5.51–5.62 (m, 1H), 5.93–6.04 (m, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.40$, 17.17, 61.92, 118.45, 126.06, 130.88. HRMS (EI): m/z calcd for $C_8H_{15}NOSi$ (M^+): 169.0922; found: 169.0917.

Cyclohexyl (trimethylsilyloxy) acetonitrile (entry 12)

^{1}H NMR ($CDCl_3$, 200 MHz,): $\delta = 0.26$ (s, 9H), 1.18–1.29 (m, 5H), 1.68–1.88 (m, 6H), 4.15 (d, 1H) ^{13}C NMR ($CDCl_3$, 400 MHz,): $\delta = -0.335$, 25.47, 26.09, 28.15, 28.21, 42.98, 66.55, 119.39. HPLC (Daicel Chiralcel OD, ^{i}PrOH–hexane = 0.25 : 99.75, flow = 0.75 ml min^{-1}) 30.187 and 32.82 min.

4,8-Dimethyl-2-(trimethylsilyloxy)nona-3, 7-dienenitrile (entry 13)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.197$ (s, 9H), 1.59 (s, 3H), 1.68–1.78 (m, 6H), 2.10–2.12 (m, 4H), 5.12–5.19 (m, 2H), 5.38–5.41 (m, 1 H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = -0.14, 16.75, 17.66, 23.18, 25.83, 39.13, 58.42, 119.50, 120.59,$ 123.14, 133.04, 142.83. HRMS (EI): m/z calcd for $C_{14}H_{25}NOSi$ (M^+): 251.1705; found: 251.1707. HPLC (Daicel Chiralcel OD ^{i}PrOH–hexane = 0.25 : 99.75, flow = 0.75 ml min^{-1}) 12.12 and 13.34 min.

2-Trimethylsilyloxy-2-phenylpropanenitrile (entry 14)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.16$ (s, 9H), 1.84 (s, 3H), 7.36–7.55 (m, 5H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 0.89$, 33.42, 71.46, 121.45, 124.46, 128.48, 141.87. HRMS (EI): m/z calcd for $C_{12}H_{17}NOSi$ (M^+): 219.1079; found: 219.1069, HPLC (Daicel Chiralcel OB-H, ^{i}PrOH–hexane = 0.5 : 99.5, flow = 0.25 ml min^{-1}) 15.15 and 15.78 min.

1-(Trimethylsilyloxy)-2-cyclohexenecarbonitrile (entry 15)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.24$ (s, 9H), 1.74–1.86 (m, 2H), 1.91–1.98 (m, 2H), 2.04–2.18 (m, 2H), 5.72–5.8 (m, 1H), 5.97–5.99 (d, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 1.62, 18.45,$ 24.39, 37.00, 66.50, 121.80, 127.5, and 132.5. HRMS (EI): m/z calcd for $C_{10}H_{17}NOSi$ (M^+): 195.1079; found: 195.1072.

2-(Trimethylsilyloxy)-2-methyloctanenitrile (entry 16)

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.22$ (s, 9H), 0.87–0.91 (t, 3H), 1.29–1.32 (m, 8H), 1.56 (s, 3H), 1.68–1.71 (m, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 1.42$, 14.12, 22.62, 24.32, 28.98, 29.05, 31.69, 43.44, 69.70 and 122.16. HRMS (EI): m/z calcd for $C_{12}H_{25}NOSi$ (M^+): 227.1705; found: 227.1710.

Trimethyl silanecarbonitrile

^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.354$. ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 1.98$, 126.97.

A mixture of trimethyl silanecarbonitrile and sodium salt of L-histidine

^{1}H NMR ($CDCl_{3+}$ DMSO, 200 MHz): $\delta = 0.269$ (s, 9H), 1.72–1.77 (m, 2H), 3.59–3.63 (m, 1H), 6.61–6.78 (m, 1H) 7.41–7.5 (m, 1H), 7.96–8.00 (m, 1H), 13.01 (m, 1H). ^{13}C NMR ($CDCl_{3+}$ DMSO, 400 MHz): 1.174, 24.764, 66.812, 118.563, 125.863, 145.81, 147.535, 174.47.

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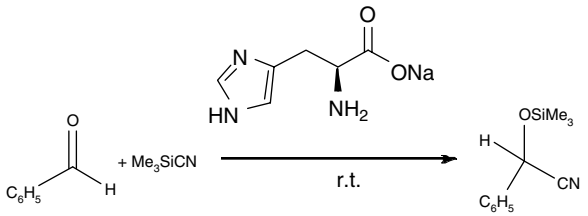
RESULTS AND DISCUSSION

Optimization of other reaction parameters led to further improvements in yield. Benzaldehyde is taken as the substrate for optimization. Initially the effect of loading of catalyst on the cyanosilylation of benzaldehyde was examined (entries 1–8, Table 1). The loading was varied from 0.1 to 30 mol%. When the loading was decreased from 30 to 3 mol%, the yield of the product was increased from 82 to 99% (entries 1–5). With 1 mol% of the catalyst, the yield was 96% (entry 6). On further reduction of catalyst loading to 0.5 and 0.1 mol%, the reaction took longer time for the completion and the yield was very much reduced (entries 7 and 8). At −10 °C, the yield of the product is enhanced to 99% with 1 mol % of the catalyst with reaction time of 1320 min. The reaction time could be reduced from 1320 to 120 min by increasing the catalyst amount to 5 mol%. We have found that at −80 °C the yield of the product was 100% by using 5 mol% of catalyst with

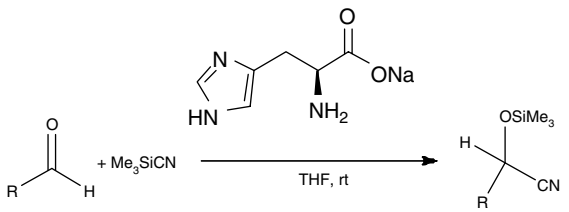
Table 2. Influence of solvent on cyanosilylation of benzaldehyde[a]

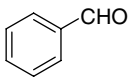
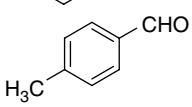
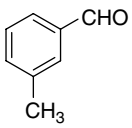
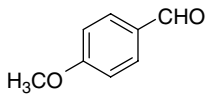
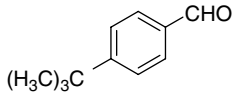
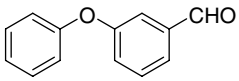
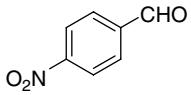
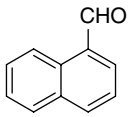
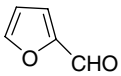
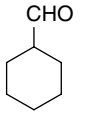
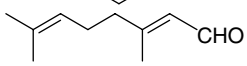
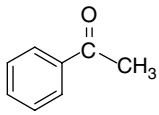
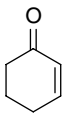
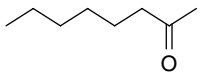


Entry	Solvent (0.5 ml)	Time (min)	Yield (%)
1	THF	25	96
2	CH_2Cl_2	1140	80
3	$CHCl_3$	120	88
4	CH_3CN	720	85
5	$(C_2H_5)_2O$	90	90

[a] 1 mmol of the benzaldehyde, 2.4 equiv. TMSCN were added to 1 mol% of the catalyst prepared by method 2.

Table 3. Cyanosilylation of various aldehydes and ketones with sodium L-histidine[a]



Entry	Substrate	Time (min)	Yield (%)[b,c]	ee(%)[d]
1		13	96	9
2		60	96	3
3		150	95	1
4		210	90	1
5		225	95	—
6		30	91	12
7		50	80	24
		20[e]	90[e]	
8		30	91	—
9		10	93	—
10	$(CH_3)_2CHCHO$	10	93	—
11	$CH_3CH{=}CHCHO$	10	92	—
12		10	92	25[f]
13		30	93	22[f]
14		80 h	95	9[g]
15		50 h	96	—
16		30 h	99	—

[a] 1 mmol of the benzaldehyde, 2.4 equiv. TMSCN and 0.5 ml of solvent were added to 1 mol% of the freshly prepared catalyst by method 1; [b] isolated yield (100% conversion as ^{1}HNMR analysis); [c] reproducibility was good; [d] ee determined from chiralcel AS column; [e] 3 mol% of the catalyst was used; [f] ee determined from chiralcel OD column; [g] ee determined from chiralcel OB (H) column.

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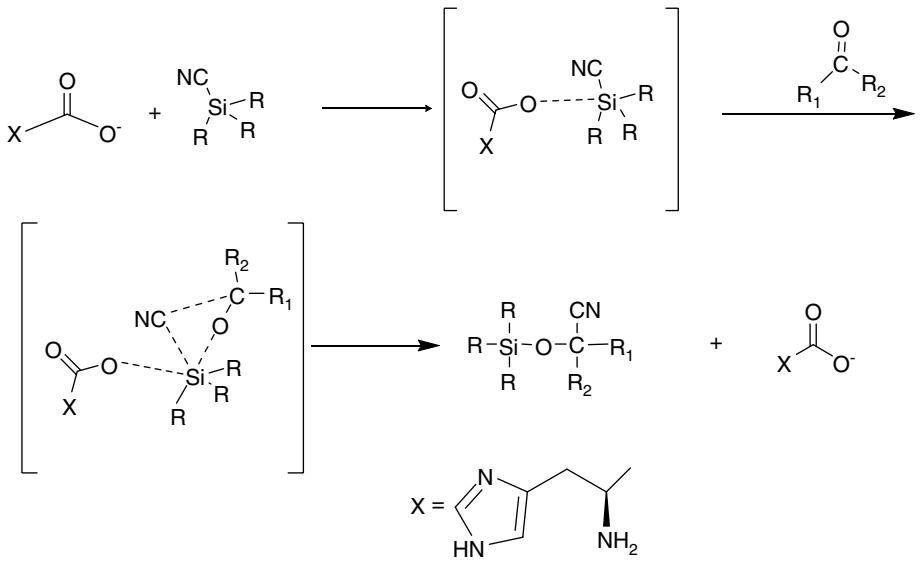
reaction time of 390 min. The ee of the product was very low in all cases. Among these studies (entries 1–11) the product with 96% yield (entry 6) is taken as the optimal. Accordingly we proceeded further studies with 1 mol% of the catalyst. Table 2 exhibits the effect of solvent on cyanosilylation of benzaldehyde. In addition to THF, CH_2Cl_2, $CHCl_3$, CH_3CN and $(C_2H_5)_2O$ were tested. Among these solvents the best result was obtained with THF (entry 1, Table 2).

L-Histidine sodium salt-catalyzed cyanosilylations were explored for a variety of aldehydes and ketones utilizing the conditions of entry 6 of Table 1. Table 3 summarizes the results obtained under the optimized conditions. The aromatic and aliphatic aldehydes were converted into the corresponding cyanohydrin trimethylsilylether in excellent isolated yields (entries 1–13) at room temperature. The experimental results indicated that para substitutions on the aromatic ring (entries 2, 4, 5 and 7) did not reveal unambiguous electronic effects. Electron donating groups such as *p*-methoxy and *p*-tert-butyl showed longer reaction times (210 and 225 min). *p*-Nitrobenzaldehyde took 50 min for 85% yield with 1 mol% of sodium L-histidine. Unsubstituted benzaldehyde took 13 min (entry 1) for the cyanosilylation, which is shorter than either of the foregoing results. The *m*-methyl group (150 min, entry 3) took longer than the *p*-methyl group (60 min, entry 2). *m*-Phenoxybenzaldehyde took 30 min to obtain 91% yield (entry 6). Acid-sensitive 2-fulfuraldehyde gave the product with 93% yield at 10 min (entry 9). This may indicate that the catalytic system selectively activated the carbonyl function and kept the furan ring intact. Various aliphatic aldehydes react much faster (from 10 to 30 min) than the aromatic counterparts for steric reasons. The yield of both aromatic and aliphatic aldehydes appeared comparable (>90%). The ee of various products was found to be very low in all cases. We also examined the catalytic activity of L-histidine sodium salt for several ketones (entries 14–16). The yields were excellent (>95%) but the reaction time was much longer (80, 50 and 30 h) because of increased steric hindrance. The reactions with the aldehydes took minutes, while hours were required for the cyanosilylation of ketones.

The mechanism of cyanosilylation of carbonyl compounds with L-histidine salt may be proposed as follows. A hypervalent silicon intermediate is formed by the interaction between the carboxylate anion of L-histidine salt and TMSCN. It is an active cyanation intermediate since the nucelophility of the cyano group is enhanced by the electron donation from the hypervalent silicon. The silicon intermediate readily reacts with carbonyl compound followed by the immediate silylation to give the corresponding product. There are various reports available regarding the formation of hypervalent silicate ions due to the presence of nucleophiles.[35,38,39] The ^1H NMR and ^{13}C NMR spectra of both TMSCN and a mixture of TMSCN and sodium salt of L-histidine were monitored. The CH_3 peak of TMSCN observed at δ 0.354 ppm was found to be shifted to 0.269 ppm in the ^1H NMR spectrum of mixture of TMSCN and sodium salt of L-histidine. The ^{13}C spectrum of TMSCN was also shifted from 1.98 ppm at δ 1.174 ppm. The shift of TMSCN peak in both ^1H NMR and ^{13}C NMR spectra may be due to the formation of hypervalent silicon intermediate as suggested in mechanism (Scheme 2). In order to examine the possibility of hydrocynation and followed by *O*-silylation as a pathway to the cyanosilylation reactions, we conducted



Scheme 2. Mechanism of cyanosilylation of carbonyl compounds by sodium-L-histidine.

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the cyanosilylation of benzaldehyde in the presence of a non-nucleophilic base, 2,6-di-tert-butyl pyridine.[40] Spencer *et al*.[40] found that there was no reaction in the presence of 2,6-di-tert-butyl pyridine as it traps all the protons generated in the system. In contrast to this observation, we found that the reactions went on as usual as in the absence of base and produced about 96% yield within almost the same time (15 min; entries 6 and 12, Table 1). We also noticed that there was no peak corresponding to HCN in the ^{13}C spectrum of TMSCN and sodium L-histidine. This eliminates the possibility of two-step reaction, namely hydrocyantion followed by *O*-silylation. We also examined the role of imidazole moiety of L-histidine in the reaction mechanism by carrying out the reaction in the presence of 4-methyl imidazole (entry 13, Table 1) as did Cai and Roberts.[41] The reaction took 30 h to complete in the presence of 4-methyl imidazole and the product formed as racemic with yield of 83%. This indicates that the imidazole moiety of sodium L-histidine has no significant role in the reaction mechanism. Therefore the proposed mechanism in which the hypervalent silicon intermediate is formed by the interaction between the carboxylate anion of L-histidine salt and TMSCN is the most probable way in which the reaction proceeds.

CONCLUSION

We have developed a new, mild and highly efficient catalyst for cyanosilylation of various carbonyl compounds. The reported procedure clearly demonstrated that L-histidine sodium salt is a good catalyst for the preparation of racemic silylethers in a relatively short reaction time (in the case of aldehydes) with low catalyst loading under mild conditions. However there is very little chiral induction taking place. This could be the first example of an amino acid salt for the cyanosilylation of aldehydes. The important features of our method are: mild reaction conditions, simple work-up and wide substrate scope.

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