Solvent-free Cyanosilylation of Carboxyl Compounds Catalyzed by NbCl₅

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A simple and convenient method for the addition of TMSCN to carbonyl compounds is described. NbCl₅ is found to possess a strong Lewis acid property to transform carbonyl compounds smoothly to the corresponding cyanosilyl ether in high yields (up to 99%) in solvent-free conditions.

Key Words: Cyanohydrins, Aldehydes, Ketones, Solvent-free, NbCl₅

Introduction

Cyanosilylation of carbonyl compounds is one of the most efficient methods for the synthesis of silylated cyanohydrins. It is well known that cyanohydrins are important intermediates for the synthesis of α-hydroxy aldehydes, α-hydroxyacids, β-aminoalcohols, α-cyano ketones, etc. Several reagents including Lewis acids, Lewis bases, metal alkoxides, bifunctional catalysts, iodine, inorganic salts have been found to effectively transfer the cyano group from TMSCN to carbonyl compounds. But in many of the reported results presence of solvent and additives are essential for the cyanosilylation reactions. We wish to herein report a simple and efficient method for the synthesis of silyl cyanohydrins in presence of catalytic amount of NbCl₅ at rt in solvent-free conditions.

Results and Discussion

The catalytic activity of NbCl₅ has been tested for the cyanosilylation reaction of benzaldehyde and TMSCN at rt. As shown in Table 1, NbCl₅ exhibits excellent catalytic activity under solvent-free conditions. 0.5 mol% of NbCl₅ gives silyl ether for relatively short reaction time in good to excellent isolated yields (entries 1-14) at rt. Benzaldehyde completed the reaction within 10 minutes but the yield is reduced to 94%. Consequently 1 mol% catalytic loading is considered optimal for present reactions. A series of carbonyl compounds react with TMSCN in the presence of NbCl₅ under solvent-free conditions.

Table 1. Cyanosilylation of benzaldehyde under various conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1</td>
<td>50h</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>30</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>15</td>
<td>99</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>7</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>40</td>
<td>94</td>
</tr>
</tbody>
</table>

- NbCl₅ is added to a mixture of 1 mmole of the benzaldehyde and 1.2 equiv. TMSCN. *isolated yield. In presence of CH₂Cl₂.

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reactions in terms of reaction time and yield.

We have also examined the catalytic activity of NbCl₅ for several ketones (entries 15, 16 & 17). The 2-cyclohexen-1-one completed the reaction within 15 minutes but the yield is 83% (entry 15). 2-Octanone completed the reaction with 380 minutes with yield of 97%. The aromatic acetophenone took nearly 46 hours to complete the reaction with yield of 90%. The reactions with the aldehydes may be facile than with ketones due to the steric reason. The mechanism of cyano-silylation of carbonyl compounds catalyzed by NbCl₅ is proposed as follows. NbCl₅ can acts as a source of nucleophilic Cl⁻. When NbCl₅ acts a nucleophilic chloride ion, a pentavalent silicon compound is formed (1), which is the reactive species. The hypervalent silicon compound reacts with carbonyl compound so as to give rise to the cyano-silylether (2) (Scheme 1). There are various reports available regarding the formation of hypervalent silicate ions due to the presence of nucleophiles. The ¹H NMR and ¹³C NMR spectrum of TMSCN and a mixture of TMSCN and NbCl₅ are monitored. The CH₃ peak of TMSCN observed at 0.354 ppm was found to be shifted to 0.185 ppm in the ¹H NMR spectrum of mixture of TMSCN and NbCl₅. The ¹³C spectrum of TMSCN is also shifted from 1.98 ppm to 2.90 ppm. The shift of TMSCN peak in both ¹H NMR and ¹³C NMR spectra may be due to the formation of pentavalent silicon compound as suggested in mechanism (Scheme 1).

In conclusion, we have developed a new, mild and efficient catalyst for cyanosilylation of various carbonyl compounds. The reported procedure clearly demonstrated that NbCl₅ is an excellent catalyst for the preparation of racemic silylethers in relatively short reaction time with low catalyst loading under solvent-free conditions. The important features of our method are: mild reaction conditions, simple work up, solvent-free condition, inexpensive and readily available catalyst. The studies are in progress to confirm the mechanistic pathway as well as the reusability of the catalyst NbCl₅.

**Experimental Section**

Silylcyanation of benzaldehyde: 2-phenyl-2-(trimethyl-silyloxy)acetonitrile (Table 2, entry 1) A mixture of benzaldehyde (1mmole), dispersed NbCl₅ (1 mol%) and TMSCN (1.2 equiv.) were stirred for 15 min at rt in a 10 mL round bottom flask. Then 0.5 mL of CH₂Cl₂ was added to the mixture and stirred for 10 min. The reaction mixture was
purified by silica gel flash chromatography by using EtOAc-hexane (1:9) mixture as eluent. The desired 2-phenyl-2-(trimethylsilyloxy)acetonitrile was obtained as colourless oil (yield 99%). The yield determined by 1H NMR was 100%. 1H NMR (CDCl3, 200 MHz): δ = 0.257 (s, 9H), 5.52 (s, 1H), 7.42-7.47 (m, 5H). 13C NMR (CDCl3, 100 MHz): δ = −0.32, 63.59, 119.12, 126.29, 128.87, 129.27, 136.18. HRMS (EI): m/z calcd. for C13H15NOSi (M+): 205.0923; found: 205.0912.

The other substances mentioned in Table 2 were also silylated by using the same procedure.

2-(4-Methylphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 2). 1H NMR (CDCl3, 200 MHz): δ = 0.142 (s, 9H), 2.29 (s, 3H), 5.49 (s, 1H), 7.18 (d, 2H) 7.25 (d, 2H) 13C NMR (CDCl3, 100 MHz): δ = 12.03, 21.46, 63.72, 119.21, 123.41, 126.93, 128.74, 130.42, 130.07, 137.74.

2-(Methoxyphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 3). 1H NMR (CDCl3, 200 MHz): δ = 0.232 (s, 9H), 5.45 (s, 1H), 2.38-2.42 (m, 3H) 7.26-7.28 (m, 4H). 13C NMR (CDCl3, 100 MHz): δ = 0.123, 31.12, 34.52, 63.33, 119.28, 125.73, 126.04, 133.19, 152.47. HRMS (EI): m/z calcd. for C13H15NOSi (M+): 235.1029; found: 235.1032.

2-(3-Ter-butylphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 5). 1H NMR (CDCl3, 200 MHz): δ = 0.23 (s, 9H), 1.32 (s, 9H), 5.38 (s, 1H), 7.09-7.21 (m, 5H). 13C NMR (CDCl3, 100 MHz): δ = −0.39, 31.12, 34.52, 63.33, 119.28, 125.73, 126.04, 133.19, 152.47. HRMS (EI): m/z calcd. for C13H15NOSi (M+): 261.1549; found: 261.1552.

2-(2-Chlorophenyl)-2-(trimethylsilyloxy)acetonitrile (entry 6). 1H NMR (CDCl3, 200 MHz): δ = 0.252 (s, 9H), 5.81 (s, 1H) 7.32-7.4 (m, 3H), 7.72 (d, 1H) 13C NMR (CDCl3, 100 MHz): δ = 0.206, 60.75, 126.76, 129.64, 130.51.

2-(3-Chlorophenyl)-2-(trimethylsilyloxy)acetonitrile (entry 7). 1H NMR (CDCl3, 200 MHz): δ = 0.25 (s, 9H), 5.42 (s, 1H) 7.35-7.37 (m, 3H), 7.47 (s, 1H) 13C NMR (CDCl3, 100 MHz): δ = −0.176, 62.93, 124.256, 126.39, 129.45, 130.14.

2-(4-Chlorophenyl)-2-(trimethylsilyloxy)acetonitrile (entry 8). 1H NMR (CDCl3, 200 MHz): δ = 0.25 (s, 9H), 5.42 (s, 1H) 7.01-7.20 (m, 5H), 7.34-7.38 (m, 4H). 13C NMR (CDCl3, 100 MHz): δ = −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.

2-(Phenoxophenyl)-2-(trimethylsilyloxy)acetonitrile (entry 9). 1H NMR (CDCl3, 200 MHz): δ = 0.218 (s, 9H), 5.42 (s, 1H), 7.01-7.20 (m, 5H), 7.34-7.38 (m, 4H). 13C NMR (CDCl3, 100 MHz): δ = −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.

2-Furanyl (trimethylsilyloxy)acetonitrile (entry 10). 1H NMR (CDCl3, 200 MHz): δ = 0.21 (s, 9H), 5.58 (s, 1H), 6.41-6.43 (m, 1H), 6.57-6.66 (m, 1H), 7.4-7.52 (m, 1H). 13C NMR (CDCl3, 100 MHz): −0.42, 5.72, 109.71, 110.76, 117.12, 143.87, 148.23. HRMS (EI): m/z calcd. for C13H14NOSi (M+): 219.0715; found: 219.0712.

1-(Trimethylsilyloxy)-2-cyclohexene carboxonitrile (entry 15). 1H NMR (CDCl3, 200 MHz): δ = 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) 9.57-9.59 (d, 1H). 13C NMR (CDCl3, 100 MHz): δ = 1.62, 18.45, 24.39, 37.00, 66.50, 121.80, 127.5, and 132.5. HRMS (EI): m/z calcd. for C13H17NO2Si (M+): 213.1079; found: 213.1082.

2-Trifluoromethyl-2-(trimethylsilyloxy)acetonitrile (entry 17). 1H NMR (CDCl3, 200 MHz): δ = 0.16 (s, 9H), 1.84 (s, 3H), 7.36-7.55 (m, 5H). 13C NMR (CDCl3, 100 MHz): δ = 0.89, 33.42, 71.46, 121.45, 124.46, 128.48, 141.87. HRMS (EI): m/z calcd. for C13H13NO2Si (M+): 219.0799; found: 219.0792.

Trifluoromethylsilanecarbonitrile (TMSCN). 1H NMR (CDCl3, 200 MHz): δ = 0.354. 13C NMR (CDCl3, 100 MHz): δ = 1.98, 126.97.

A mixture of Trimethylsilanecarbonitrile and NbCl5.

1H NMR (CDCl3, 200 MHz): δ = 0.185. 13C NMR (CDCl3, 100 MHz): δ = 2.90, 127.23.

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References


