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Asymmetric cyanosilylation of ketones catalyzed by recyclable polymer-supported copper(II) salen complexes

Gurusamy Rajagopal *, Shanmugam Selvaraj, Karuthamohamed Dhahagani

Department of Chemistry, Government Arts College, Melur 625 106, Madurai, India

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ABSTRACT

Various ketones have undergone asymmetric trimethylsilylcyanation at room temperature with $(CH_3)_3SiCN$ (TMSCN) in the presence of a chiral-supported Cu(salen) complex and Ph_3PO as the catalyst. Aromatic, aliphatic, and heterocyclic ketones have been converted into the corresponding cyanohydrin trimethylsilyl ethers in 83–96% yields with 52–84% ee. Several factors concerning the reactivity and enantioselectivity have been discussed. A double activation where Cu(salen) plays the role of Lewis acid and Ph_3PO acts as a Lewis base is reported. Poly(ethylene glycol) monomethyl ether (MeO-PEG) has been used as a soluble support while JandaJel (JJ) and Merrifield (MF) resins served as insoluble supports. Each polymer is linked to the salen catalyst through a glutarate spacer. The soluble catalysts were recovered by precipitation with a suitable solvent while the insoluble catalysts were simply filtered from the reaction mixture. The JandaJel-attached Cu(salen) catalyst could be used for five cycles with the retention of efficiency and the Merrifield-bound Cu(salen) catalyst was found to loose activity with each use.

1. Introduction

Chiral cyanohydrins are useful intermediates because their two functional groups can be easily transformed into various homochiral ones, including α-hydroxy acids,[1,2] α-hydroxy aldehydes,[3] α-hydroxy ketones,[3] β-hydroxy amines,[2,3] and α-amino acid derivatives.[4] A number of catalysts for the asymmetric addition of cyanide to carbonyl compounds[5] are known, including synthetic peptides and chiral transition metal complexes. Significant advances have been made in developing efficient catalysts for the synthesis of chiral cyanohydrins[6–9] using Snapper and Hoveyda's peptide-Al catalysts,[10] Jacobsen's thiourea catalysts,[11] Feng's double-activation,[12–20] an amino acid salt,[21] and Deng's chiral Lewis base.[22,23] In search for new methodologies, Belokon and North have reported a bimetallic Ti(IV) salen complex[24] while Shibasaki et al. have used bifunctional catalysts with Ti(IV),[25,26] $Gd(OiPr)_3$,[27] and $Sm(OiPr)_3$[28] for the enantioselective cyanosilylation of ketones. Kim et al. have reported Al and Mn monomeric salen complexes for the cyanosilylation of ketones with triphenylphosphine oxide as an additive at room temperature.[29,30] Recently Khan et al. reported[31–33,1b,34] the use of polymeric metal vanadium and manganese complexes as enantioselective catalysts for the cyanosilylation of various carbonyl compounds.

Supported metal complexes have continuously attracted increasing interest because of the advantages that they offer with respect to their soluble counterparts.[35] Some of these advantages are their robustness, the increased air and moisture stability, ease of separation, and the potential recyclability, when used as heterogeneous catalysts. The supports on which the metal complexes are immobilized are inorganic or organic polymers. Typical inorganic supports are oxides bearing surface hydroxyl groups, acting as[36,37] (or being precursors of) ligands for suitable metal-containing moieties.[38–41] Using organic co-polymers as supports for transition metal complexes allows us to conjugate the controllable flexibility of the matrix with the possibility of fine tuning the physical properties (polarity, swellability, morphology, etc.) of the material with a suitable combination of co-monomers and crosslinkers.

Chiral Cu complex catalysts for asymmetric reactions such as aziridination,[42] Diels–Alder reaction,[43] cyclopropanation,[44] and carbenoid insertion of diazoacetates into the Si–H bond of silanes[45,46] have been studied and recently the complexes of Cu(II) with chiral bidentate ligands of bisoxazolines for the asymmetric Henry reaction have shown promising results.[47] Although several salen-based metal complexes have already been used for the cyanosilylation of ketones, no work has been reported for copper salen complexes.

2. Results and discussion

Acetophenone was chosen as a test substrate to determine the best conditions for the cyanosilylation. The reactivity and enantioselectivity of the cyanation reaction are strongly dependent upon the nature of the solvent used.[48] Therefore, catalytic enantioselective

* Corresponding author. Tel.: +91 452 2416002; fax: +91 452 2415467.
E-mail address: rajagopal@yahoo.com (G. Rajagopal).

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cyanation reactions were conducted in different solvents, such as 1,2-dichloroethane, CH_3CN, toluene, and THF with catalyst **6** under identical reaction conditions. From Table 1, it can be seen that CH_2Cl_2 was the most appropriate solvent (entries 1–6). Solvent CH_3CN was also a suitable solvent for this system with a slightly longer reaction time (entry 7). The use of toluene and THF afforded a low yield of nitriles with longer reaction times (entries 8 and 9).

The catalyst loading and reaction temperature were also found to be an essential factor for the enantioselective cyanation reaction. To determine the effect of the catalytic loading in improving the yield, we performed the reaction with 1–15 mol % of catalyst **6** in CH_2Cl_2. For 10–15 mol % catalytic loading, the reactions took place with less reaction time and with high yields (entries 1 and 2). Further reduction in the amount of catalyst from 10 to 5 mol % gave 94% yield in 11 h (entry 3). We found that the reaction proceeds even with 3 mol % of catalyst providing 94% yield of nitriles within 10 h (entry 4). For 1–2 mol % of catalytic loading, longer reaction time was required (entries 5 and 6). Lowering the temperature from room temperature to −40 °C greatly increased the reaction time with a slight increase in ee (entries 10–14). Neither the copper complex nor the Ph_3PO induced any enantioselectivity. The reaction appears to be catalyzed by a double activation process that occurs through the catalysis of both chiral Lewis acid and achiral Lewis base. The Cu(salen) complex functions as a weak Lewis acid to activate the ketone oxygen and Ph_3PO acts as a strong Lewis base for the activation of TMSCN (Fig. 1). Based on above observations, the reaction conditions of entry 4 were chosen for the present asymmetric cyanosilylation of ketones at room temperature because of the shorter reaction times and good ee.

To determine the efficiency of supported copper salen complexes, we carried out the cyanosilylation of acetophenone in the presence of Ph_3PO as an additive under identical reaction conditions and the results are summarized in Table 2. The soluble PEG and insoluble Merrifield resin-based copper complexes have less activity compared to an insoluble JandaJel-based copper complex (Fig. 2). This may be due to the fact that the JandaJels contain flexible tetrahydrofuran-derived crosslinkers and exhibit superior swelling in common organic solvents. This increase in swelling capacity implies a better contact between the reagents and substrates linked to the resin. Furthermore, the increased swelling of JandaJel would result in a better solvation of the reaction complex and would therefore minimize any loss of enantioselectivity resulting from heterogenization of the catalyst.

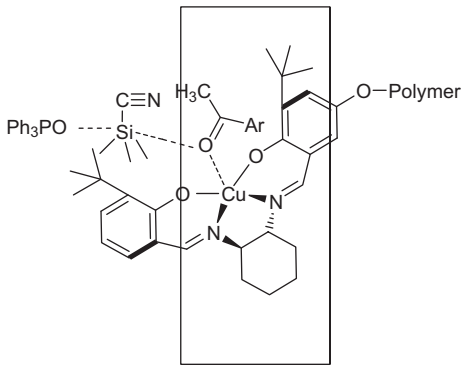


Figure 1. Transition state involved in the enantioselective cyanosilylation of ketones by double-activation catalysis.

Table 2
Cyanosilylation of acetophenone with various supported Cu(salen) complexes

Catalyst	Mol %	Time (h)	Yield (%)	ee (%)
PEG-Cu(salen)	3	22	85	67
JJ-Cu(salen)	3	10	94	84
Merrifield-Cu(salen)	3	20	86	60

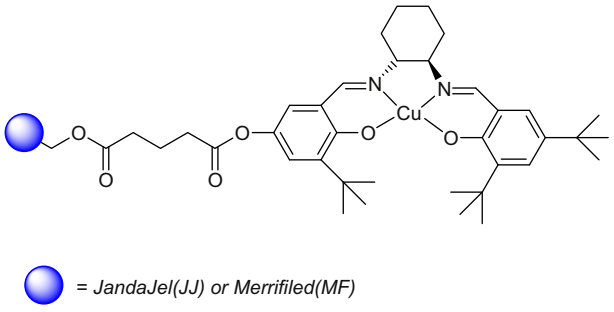
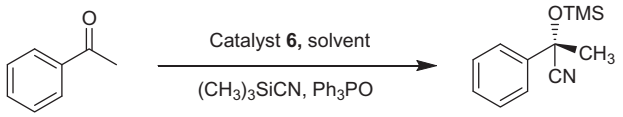


Figure 2. Structure of polymer supported copper complexes.

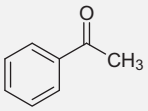
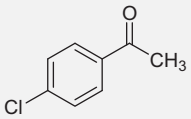
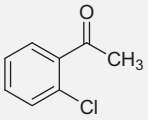
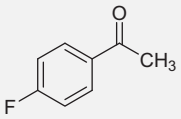
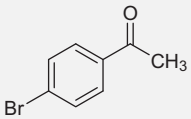
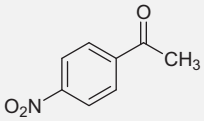
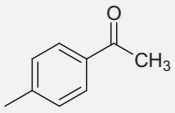
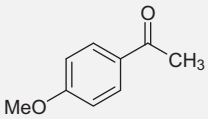
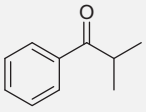
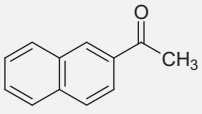
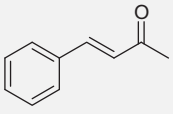
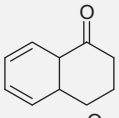
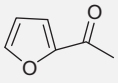
Table 1
Cyanosilylation of acetophenone under various reaction conditions[a]



Entry	Catalyst loading (mol %)	Additive	Solvent	Temp (°C)	Time (h)	Yield[b] (%)	ee (%)
1	15	Ph_3PO	CH_2Cl_2	rt	8	96	78
2	10	Ph_3PO	CH_2Cl_2	rt	9	94	80
3	5	Ph_3PO	CH_2Cl_2	rt	11	94	83
4	3	Ph_3PO	CH_2Cl_2	rt	10	94	84
5	2	Ph_3PO	CH_2Cl_2	rt	15	95	77
6	1	Ph_3PO	CH_2Cl_2	rt	20	90	70
7	3	Ph_3PO	CH_3CN	rt	15	90	65
8	3	Ph_3PO	Toluene	rt	40	70	51
9	3	Ph_3PO	THF	rt	40	80	40
10	3	Ph_3PO	CH_2Cl_2	0	25	95	85
11	3	Ph_3PO	CH_2Cl_2	−10	36	94	86
12	3	Ph_3PO	CH_2Cl_2	−20	45	93	86
13	3	Ph_3PO	CH_2Cl_2	−30	60	93	86
14	3	Ph_3PO	CH_2Cl_2	−40	72	94	84

[a] Reagent and condition: 1.0 mmol of acetophenone; 1.0 mmol of TMSCN.
[b] Isolated yield.

Table 3
Addition of TMSCN to ketones catalyzed by supported JJ-Cu(salen) complex

Entry	Substrate	Time (h)	Yield[a] (%)	ee (%)
1		10	94	84
2		12	90	67
3		16	91	60
4		9	90	70
5		9	89	71
6		18	90	61
7		14	92	65
8		15	90	82
9		12	88	63
10		10	93	75
11		18	85	52
12		18	83	63
13		15	90	61

[a] Isolated yield.

Under the optimized reaction conditions as described earlier (Table 1, entry 3), we extended this protocol of cyanosilylation reaction to a variety of aromatic and aliphatic ketones using complex **2** as catalyst. The data in Table 3 are indicative of the applicability of this protocol over a range of substrates where good to excellent isolated yield (83–94%) and ee (52–84%) for the products were achieved in 9–18 h (entries 1–13).

Electronic and steric factors for different substituents on the aromatic ring have little effect on the yield and ee. *o*-Chlorophenylmethyl ketone appeared to be more susceptible to the steric effect compared to *p*-chloromethyl ketone resulting in a much longer reaction time and high %ee (Table 3, entries 2 and3). *p*-Fluoro and bromo derivatives gave good enantioselectivity (Table 3, entries 4 and 5). Electron-withdrawing substituents (Table 3, entries 6–8) had a favorable influence on the cyanosilylation in terms of reaction yield and gave moderate ee. Cyanosilylation of isobutylphenone (entry 9) and naphthyl ketone gave good ee (Table 3, entries 9 and 10). Moderate conversions (85–90%) and ee's (52–63%) were obtained when the cyanosilylation reaction was carried out with 4-phenyl-3-buten-2-one (Table 3, entry 11) and aliphatic ketones (Table 3, entries 12 and 13).

To access the recyclability of the polymer-bound Cu(salen) catalyst, the catalytic runs were carried out for the cyanosilylation of 4-methoxy acetophenone which was taken as a representative substrate by adding fresh reactants. After one catalytic cycle, by adding hexane-cold ether mixture the PEG-bounded Cu(salen) catalyst was precipitated out due to its high molecular weight and lower solubility in the reaction medium. From the data in Table 4 it is evident that the PEG-based catalyst worked well for up to three cycles with a small decrease in reactivity and enantioselectivity. With limited success in recycling the soluble polymer-bound catalysts, we hoped that the insoluble supports would provide a more robust environment for the salen framework. Recovery of both the JandaJel and the Merrifield resin-bound catalysts was easily accomplished by filtration of the reaction mixture. The JandaJel-derived catalyst could be used five times without a significant drop in selectivity. The Merrifield-bound catalyst lost activity with each use and was essentially ineffective by the third recycle. It is not entirely clear why the JandaJel-bound catalyst was slightly more robust than Merrifield-bound catalyst but this may be a consequence of microenvironment effects caused by the resin.

Table 4
Studies on the recyclability of the polymer-bound catalysts at rt

Catalyst	Run	Time (h)	Yield[a] (%)	ee (%)
PEG-Cu(salen)	1	22	90	65
	2	23	88	62
	3	25	85	60
	4	30	70	50
JJ-Cu(salen)	1	15	90	80
	2	15	88	78
	3	16	85	75
	4	18	80	70
	5	18	75	65
MF-Cu(salen)	1	20	80	60
	2	24	70	51
	3	30	68	42
	4	35	65	41
	5	40	50	40

[a] Isolated yields.

3. Conclusions

We have described the evaluation of soluble and insoluble polymer-supported Cu(salen) complexes for use in asymmetric cyanosilylation reactions. A highly efficient double activation catalysis by supported Cu(salen)/Ph_3PO has been developed for the enantioselective cyanosilylation of various ketones. The cyanosilylation takes place under comparatively mild conditions in terms of temperature and reaction time. The JandaJel polymeric catalyst performed well in terms of reactivity and enantioselectivity with the

added advantage of recyclability for five times. Further investigations to clarify the reaction mechanism and efforts to extend the use of the present catalytic system to other organic transformations are currently in progress.

4. Experimental

4.1. General

All ketones and polymers were purchased from Sigma–Aldrich. ^{1}H and ^{13}C NMR were taken utilizing a Varian Jemini 2000 (300 MHz) or a Varian Unity Inova 400 (400 MHz) or a Bruker Avance 400 NMR spectrometer. The ee% was determined by chiral HPLC column (DAICEL CHIRALCEL OJ-H, DAICEL CHIRALCEL OD-H and DAICEL CHIRALCEL OB-H). Analytical high performance liquid chromatography (HPLC) was performed on Gilson 305 series HPLC using the indicated chiral column. All data was in accordance with literature values. Absolute configurations were determined by the specific rotation.[49]

4.1.1. Synthesis of unsymmetrical salen ligand 1

4.1.1.1. 2-*tert*-Butyl-6-({2-[(3,5,di-*tert*-butyl-2-hydroxy-benzylidene)-amino]-cyclohexylimino}-methyl)-benzene-1,4-diol. To a solution of 3,5-di-*tert*-butylsalicylaldehyde (1.72 g, 7.53 mmol) and 3-*tert*-butyl-2,5-dihydroxybenzaldehyde (0.48 g, 2.45 mmol) in CH_2Cl_2 (15 mL) was added (1*R*,2*R*)-diaminocyclohexane (0.56 g, 4.89 mmol). The reaction mixture was allowed to stir at 25 °C for 15 h, after which it was concentrated in vacuo to give a yellow foam solid. This crude product (mixture of salen ligands) was purified by column chromatography on silica gel (gradient elution: 1:20–1:1, diethyl ether/hexanes) to give **1** (0.68 g, 55% yield) as a yellow foam. IR (KBr pellet): 3350 (br), 2933, 2860, 1632, 1595 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.20 (s, 1H), 8.10 (s, 1H), 6.85 (d, J = 2.4 Hz, 1H), 6.79 (d, J = 2.4 Hz, 1H), 6.44 (d, J = 3.2 Hz, 1H), 6.41 (d, J = 3.2 Hz, 1H), 3.25–3.19 (m, 2H), 2.0–1.95 (m, 8H), 1.31 (s, 18H), 1.19 (s, 9H). Anal. Calcd for $C_{32}H_{46}N_2O_3$: C, 75.85; H, 9.15; N, 5.53. Found: C, 75.50; H, 9.45; N, 5.30.

4.1.2. Synthesis salen glutarate (mono-ester) 2

Into a 50 mL two-necked round-bottomed flask, fitted with a nitrogen inlet, were placed a stirrer bar, glutaric anhydride (164 mg, 1.44 mmol), the unsymmetrical salen **1** (608 mg, 1.20 mmol), DMAP (176 mg, 1.44 mmol), and anhydrous CH_2Cl_2 (6 mL). The mixture was left to stir, under a nitrogen atmosphere, for 15 h at 25 °C after which it was concentrated in vacuo. The crude yellow oil was purified by flash column chromatography on silica gel (1:19, methanol/CH_2Cl_2). The title compound was obtained as a foam yellow solid (446 mg, 60% yield). IR (KBr pellet) 2940 (br), 1758, 1712, 1630, 1439 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.30 (s, 1H), 8.23 (s, 1H), 7.31 (d, J = 2.5 Hz, 1H), 7.10 (d, J = 2.5 Hz, 1H), 6.77–6.98 (m, 2H) 6.77–6.98 (m, 5H) 3.34 (m, 2H), 2.60 (t, J = 7.4 Hz, 2H), 2.50 (t, J = 7.2 Hz, 2H), 2.05 (q, J = 7.4 Hz, 2H), 1.98–1.5 (m, 8H), 1.42 (s, 9H), 1.28 (s, 18H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 178.7, 171.8, 165.8, 158.2, 157.9, 141.3, 139.9, 138.8, 136.3, 126.9, 125.9, 122.7, 121.3, 118.2, 117.7, 72.4, 72.2, 53.4, 34.9, 33.9, 33.2, 32.9, 31.6, 31.4, 29.4, 29.1, 24.2, 22.7, 22.6, 19.7, 14.1. Anal. Calcd for $C_{37}H_{52}N_2O_6$: C, 71.58; H, 8.44; N, 4.51. Found: C, 71.81; H, 8.55; N, 4.33.

4.1.3. Synthesis of PEG-supported salen ligand 3

To a solution of PEG_{5000} (2.60 g, 0.52 mmol), the unsymmetrical salen glutarate (mono-ester) (0.65 g, 1.04 mmol), and DMAP (0.03 g, 0.26 mmol) in CH_2Cl_2 (20 mL) was added DCC (0.23 g, 1.10 mmol). The reaction mixture was stirred at 25 °C for 24 h and the urea by-product was removed by filtering through a pad of Celite. The filtrate was then concentrated to 5 mL and then added dropwise into 200 mL of cold stirring diethyl ether. The yellow solid precipitate was filtered off, and dried under vacuum (2.25 g, 77% yield): IR (KBr pellet) 3330, 2890 (b), 1756, 1737, 1630, 1461, 1349 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.27 (s (br), 1H, –N=C–*H*), 8.20 (s (br), 1H), 7.31 (d, 1H), 6.95 (s (br), 1H), 6.88 (d, 1H), 6.73 (s (br), 1H,), 4.20 (m, 2H,), 3.34 (s, 3H), 2.54 (t, J = 7.3 Hz, 2H,), 2.42 (t, J = 7.3 Hz, 2H), 2.10–1.50 (m, 10H), 1.36 (s, 9H), 1.34 (s, 9H), 1.19 (s, 9H).

4.1.4. General procedure for the preparation of insoluble (salen) ligands: JJ-SALEN 4 and MF-SALEN 5

At first, DCC (2.1 equiv) was added to a solution of the insoluble resin (*J*anda*J*el or Merrifield) (1 equiv), salen glutarate (mono-ester) (1 equiv), and DMAP (0.5 equiv) in CH_2Cl_2 (15 mL/g of resin). The reaction mixture was vigorously stirred at room temperature for 24 h and filtered through a medium frit. The collected solid was washed sequentially with water, methanol, CH_2Cl_2, ether, and hexanes to give yellow beads. IR(KBr): JJ-SALEN: 3410, 1633, 1135, 1049, 988 cm^{-1}. MF-SALEN: 3390, 1607, 1389 cm^{-1}

4.1.5. General Procedure for the synthesis of copper complexes: JJ-SALEN-Cu 6 and MF-SALEN-Cu 7

A solution of polymer-supported 2-*tert*-butyl-6-({2-[(3,5-di-*tert*-butyl-2-hydroxy-benzylidene)-amino]-cyclohexylimino}-methyl)-benzene-1,4-diol (1 equiv) as prepared earlier was dissolved in mixed solvents of ethanol/CH_2Cl_2 (10:2, 15 ml) to which a methanolic solution of copper acetate tetrahydrate (1.25 equiv) was added dropwise under an inert atmosphere at room temperature. The resulting solution was refluxed for 24 h and then cooled to room temperature and was stirred for a further 12 h. The solution was filtered through a medium frit and the collected solid was washed with cold water, methanol, ether, and hexanes to give a dark brown powder. IR(KBr): JJ-SALEN-Cu: 1559, 1530, 1350, 1287, 484 cm^{-1}; MF-SALEN-Cu : 3415, 1595, 1338, 473 cm^{-1}

4.2. Procedure for supported Cu-salen-catalyzed asymmetric addition of trimethylsilyl cyanide to ketones

Supported Cu salen catalyst (3 mmol) was dissolved in dry CH_2Cl_2 (3 ml) and the solution was stirred at room temperature under a nitrogen atmosphere. To this solution, ketone (1 mmol) was added, followed by the dropwise addition of TMSCN (1 equiv). After the reaction was completed (as shown by TLC), the mixture was concentrated and the compound purified by flash column chromatography on silica gel (eluted with hexane/ethylacetate = 95:5). The silylethers thus obtained were identified by ^{1}H and ^{13}C NMR data, which are consistent with the structure.

4.2.1. 2-Trimethylsilyloxy-2-phenylpropanenitrile (Table 3, entry 1)

^{1}H NMR ($CDCl_3$) δ 0.17 (s, 9H), 1.85 (s, 3H), 7.36–7.558 (m, 5H, aromatic H); ^{13}C NMR ($CDCl_3$) δ 0.89, 33.4, 71.4, 121.4, 124.4, 128.6, 141.8; $[\alpha]_D^{24} = -15.1$ (c 1.18, $CHCl_3$) 84% ee; HRMS(MC) calcd for $C_{12}H_{17}NOSi$: 219.1079; found: 219.1082 HPLC (DAICEL CHIRALCEL OB-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 13.7 and 14.6 min.

4.2.2. 2-Trimethylsilyloxy-2-(4′-chlorophenyl)propanenitrile (Table 3, entry 2)

^{1}H NMR ($CDCl_3$) δ 0.21 (s, 9H), 1.84 (s, 3H), 7.38 (m, 2H), 7.49 (m,2H); ^{13}C NMR ($CDCl_3$) δ 1.0, 33.4, 71.0, 121.1, 126.0, 128.7, 134.5, 140.6; $[\alpha]_D^{24} = -16.4$ (c 1.78, $CHCl_3$) 67% ee; HRMS (MC) calcd for $C_{12}H_{16}ClNOSi$: 253.0690; found: 253.0687 HPLC (DAICEL

CHIRALCEL OJ-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 19.8 and 20.6 min.

4.2.3. 2-Trimethylsilyloxy-2-(2′-chlorophenyl)propanenitrile (Table 3, entry 3)

^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 1.99 (s, 3H), 7.25–7.40 (m, 3H aromatic H), 7.68–7.71 (m, 1H aromatic H); ^{13}C NMR ($CDCl_3$) δ 1.0, 33.4, 70.9, 121.0, 122.7, 124.8, 128.8, 129.9, 134.6, 144.0; $[\alpha]_D^{24} = +11.4$ (*c* 1.20, $CHCl_3$) 60% ee; HRMS(MC) calcd for $C_{12}H_{16}ClNOSi$: 253.0691; found: 253.0687 HPLC (DAICEL CHIRALCEL OD-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 23.2 and 24.0 min.

4.2.4. 2-Trimethylsilyloxy-2-(4′-fluorophenyl)propanenitrile (Table 3, entry 4)

^{1}H NMR ($CDCl_3$) δ 0.18 (s, 9H), 1.84 (s, 3H), 7.08 (m, 2H), 7.52 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 1.0, 33.5, 71.0, 115.6, 121.4, 126.5, 138.0, 162.2; $[\alpha]_D^{24} = +16.4$ (*c* 1.3, $CHCl_3$) 70% ee; HRMS(MC) calcd for $C_{12}H_{16}FNOSi$: 237.0985; found: 237.0981 HPLC (DAICEL CHIRALCEL OB-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 16.4 and 18.5 min.

4.2.5. 2-Trimethylsilyloxy-2-(4′-bromophenyl)propanenitrile (Table 3, entry 5)

^{1}H NMR ($CDCl_3$) δ 0.19 (s, 9H), 1.83 (s, 3H), 7.40–7.4 (m, 2H), 7.51–7.55 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 1.0, 33.4, 71.0, 121.1, 122.7, 126.3, 131.7, 141.2; $[\alpha]_D^{22} = -14.8$ (*c* 1.50, $CHCl_3$) 71% ee; HRMS(MC) calcd for $C_{12}H_{16}BrNOSi$: 297.0185; found: 297.0181 HPLC (DAICEL CHIRALCEL OB-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 17.1 and 18.3 min.

4.2.6. 2-Trimethylsilyloxy-2-(4′-nitrophenyl)propanenitrile (Table 3, entry 6)

^{1}H NMR ($CDCl_3$) δ 0.25 (s, 9H), 1.87 (s, 3H), 7.75 (d, 2H), 8.30 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 1.0, 33.5, 71.0, 115.6, 121.4, 126.5, 138.0, 162.2; $[\alpha]_D^{22} = -14.4$ (*c* 1.60, $CHCl_3$) 61.2% ee) HRMS(MC) calcd for $C_{12}H_{16}N_2O_3Si$: 264.0930; found: 264.0933 HPLC (DAICEL CHIRALCEL OJ-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 20.3 and 21.2 min.

4.2.7. 2-Trimethylsilyloxy-2-(4′-methylphenyl)propanenitrile (Table 3, entry 7)

^{1}H NMR ($CDCl_3$) δ 0.16 (s, 9H), 1.84 (s, 3H), 2.36 (s, 3H), 7.21 (m, 2H), 7.43 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 1.1, 20.8, 33.5, 71.8, 121.9, 124.9, 128.3, 138.4, 139.8; $[\alpha]_D^{24} = -15.18$ (*c* 1.50, $CHCl_3$) 65% ee; HRMS(MC) calcd for $C_{13}H_{19}NOSi$: 233.1236; found: 233.1240 HPLC (DAICEL CHIRALCEL OJ-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 51.38 and 54.61 min.

4.2.8. 2-Trimethylsilyloxy-2-(4′-methoxylphenyl)propanenitrile (Table 3, entry 8)

^{1}H NMR ($CDCl_3$) δ 0.17 (s, 9H), 1.85 (s, 3H), 3.85 (s, 3H), 6.97 (m, 2H), 7.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 1.1, 33.41, 55.33, 71.28, 113.89, 121.81, 126.06, 134.04, 159.80; $[\alpha]_D^{24} = -18.1$ (*c* 1.65, $CHCl_3$) 82% ee; HRMS(MC) calcd for $C_{13}H_{19}NO_2Si$: 249.1185; found: 249.1182; HPLC (DAICEL CHIRALCEL OJ-H, *i*PrOH/hexane = 1/99, flow = 0.25 mL/min) 22.3 and 23.2 min.

4.2.9. 2-Trimethylsilyloxy-2-phenyl-3-methyl-butanenitrile (Table 3, entry 9)

^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H), 1.03 (q, *J* = 7.4 Hz, 6H), 1.97 (m, 1H), 7.38 (m, 3H), 7.50 (m, 2H); $[\alpha]_D^{24} = -46.0$ (*c* 4.1, $CHCl_3$) 92% ee; HRMS(MC) calcd for $C_{14}H_{21}NOSi$: 247.1392; found: 247.1395 HPLC (DAICEL CHIRALCEL OD, *i*PrOH/hexane = 1/99, flow = 0.5 mL/min) 6.36 and 6.84 min.

4.2.10. 2-(1-Naphthalen-1-yl)-2-(trimethylsilyloxy)propanenitrile (Table 3, entry 10)

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.23 (s, 9H), 2.2 (s, 3H), 7.41–7.65 (m, 3H), 7.85–7.95 (m, 3H), 8.60 (d, 2.4 Hz ,1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.0, 31.6, 73.1, 121.7, 123.5, 124.5, 125.4, 125.7, 125.9, 129.07, 129.32, 130.10, 134.5, 135.8.

4.2.11. 2-Trimethylsilyloxy-2-methyl-4-phenyl-3-butenenitrile (Table 3, entry 11)

^{1}H NMR ($CDCl_3$) δ 0.24 (s, 9H), 1.74 (s, 3H), 6.16 (d, 1H), 6.84 (d, 1H) 7.25–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 1.4, 30.8, 69.9, 120.6, 126.9, 128.6, 128.7, 129.5, 130.9, 135.1 $[\alpha]_D^{24} = -16.9$ (*c* 2.1, $CHCl_3$) 60% ee; HRMS(MC) calcd for $C_{14}H_{19}NOSi$: 245.1236; found: 245.1233 HPLC (DAICEL CHIRALCEL OJ-H, *i*PrOH/hexane = 1/99, flow = 0.5 mL/min) 11.36 and 14.02 min.

4.2.12. 1-Trimethylsilyloxy-1,2,3,4-tetrahydronaphthalene-1-carbonitrile (Table 3, entry 12)

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.21 (s, 9H), 1.83–2.41 (m, 4H), 2.81 (t, 2H, *J* = 7.00 Hz), 7.09–7.29 (m, 3H), 7.61–7.66 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.33, 18.69, 28.32, 37.73, 69.87, 122.11, 126.63, 128.02, 129.06, 129.26, 135.68, 136.11.

4.2.13. 2-Trimethylsilyloxy-2-furan-2-yl-propanenitrile (Table 3, entry 13)

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.22 (s, 9H), 1.88 (s, 3H), 6.35–6.40 (m, 1H), 6.47–6.50 (m, 1H), 7.41–7.43 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 0.49, 28.37, 65.89, 108.14, 110.68, 120.23, 143.09, 151.63.

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