Aluminium Phthalocyanine: An Active and Simple Catalyst for Cyanosilylation of Ketones

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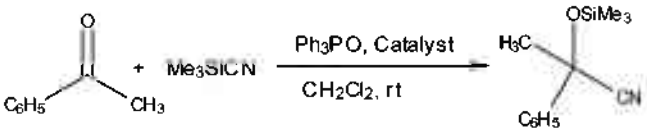
Cyanohydrin trimethylsilyl ethers are versatile intermediates in the synthesis of α-hydroxy acids and α-amino alcohols.[3] Transfer of a cyano group from TMSCN to carbonyl compounds can be catalyzed by varuiys reagents[4,5] including Lewis acids, Lewis bases, metal alkoxides, bifunctional catalysts, and inorganic salts. Many metal complexes including Zn(II), Ti(IV), Cu(II), Ce(IV), Al(III), In(III), La(III), VO(IV), Gd(III) and Sm(III) have been successfully employed as Lewis acids for the addition of HCN or TMSCN to aldehydes and ketones.[6] Also, organic amines, such as thiourea[7] and tetramethylguanidine,[8] and P(RN-CH_2CH_2)N, non-ionic strong base[9] were utilized as effective catalysts for cyanosilylation of aldehyde and ketones. Lithium chloride[10] and BINOL-based aluminium complexes[11,12] were employed as active and simple catalysts for the reaction as well. Very recently, the facile cyanosilylation of carbonyl compounds by the activation of TMSCN with *N*-heterocyclic carbenes have been reported.[13,14] Metal phthalocyanines (Mpc) are easily accessible, stable and a cost effective catalysts for variety of organic reactions.[15]

In the continuation of our work on cyanosilylation,[16] we are interested in exposing the example of usability of AlPc for cyanosilylation of ketones.

We have recently reported asymmetric cyanosilylation of aldehydes[17] and ketones[18] using Al(salen)/Ph_3PO catalytic system as double activation method. Adopting this methodology, we first carried out the cyanosilylation of ketone using different type of metal phthalocyanines containing manganese (Mn), iron (Fe) and aluminum (Al) as catalysts and Ph_3PO as an additive. Thus, acetophenone was treated with 1.2 equivalent of TMSCN in one portion at rt in dichloromethane in the presence of 5 mol% of each of the catalyst and 10 mol % of Ph_3PO. As shown in Table 1, the reaction with Al phthalocyanine smoothly proceeded to give the product in 90% yield. However, when manganese phthalocyanine (MnPc) and the iron phthalocyanine (FePc) were employed as catalysts, no reactions were observed (entries 1-3). This may be due to the difference in the Lewis acidic properties of metals. Next, we examined solvent effects for this reaction by using several solvents including CH_3CN, CH_2Cl_2 and THF. CH_2Cl_2 provided the best result (entries 3-5). In this reaction, the use of 5 mole% of Ph_3PO gave somewhat lower yield (entry 6). The increase of quantity of AlPc from 5 to 10 mol% does not change the reaction time and yield (entry 7). No reaction took place without Ph_3PO (entry 8). This indicates a double activation process occurring through the catalysis of both Lewis acid and Lewis base. The aluminium phthalocyanine functions as a Lewis acid to activate the ketone while Ph_3PO acts as a Lewis base for the activation of TMSCN.

Table 1. Cyanosilylation of acetophenone under various conditions



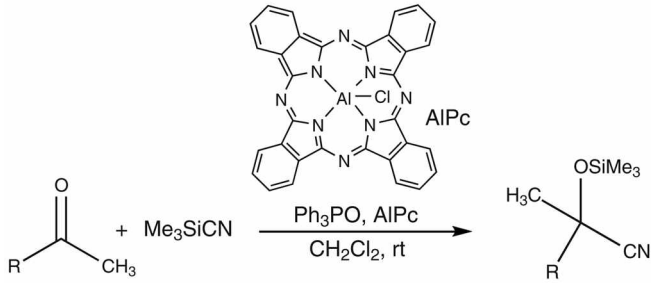
Entry	Catalyst	Catalyst (%)	Ph_3PO	Solvent	Time (h)	Yield[a] (%)
1	MnPc	5	10	CH_2Cl_2	6	Trace
2	FePc	5	10	CH_2Cl_2	6	Trace
3	AlPc	5	10	CH_2Cl_2	3	90
4	AlPc	5	10	CH_3CN	3	85
5	AlPc	5	10	THF	3	78
6	AlPc	5	5	CH_2Cl_2	4	82
7	AlPc	10	10	CH_2Cl_2	3	90
8	AlPc	5	–	CH_2Cl_2	6	–

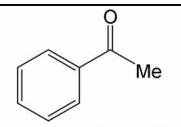
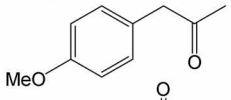
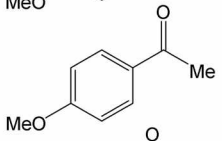
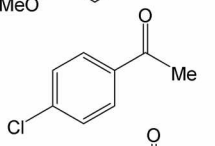
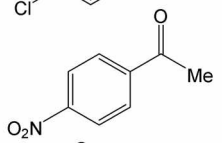
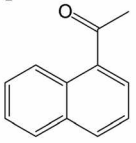
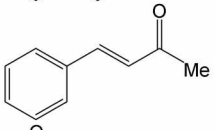
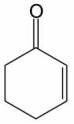
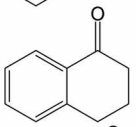
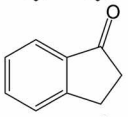
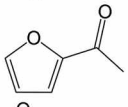
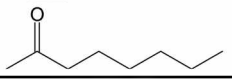
[a]Isolated yield

Based on the results in Table 1, we examined catalytic cyanosilylation of various ketones using the same methodology. As shown in Table 2, several aromatic ketones undergo very smooth cyanosilylation with around 90% yield (entries 1-5). The substituents on the phenyl group have little effect on reaction time and yield. 1-Acetonaphthone gave desired silylether in excellent yield (entry 6). Both aromatic (entry 7) and aliphatic (entry 8) α,β-unsaturated ketones undergo silylcyanation in excellent yields. It should be noted that α-tetralone and 1-indanone were also proved good substrates for silylcyanation reaction (entries 9-10). 2-Acetyl furan, a heterocyclic ketone (entry 11) gives corresponding silylether in good yield (85%). This result indicates that AlPc can selectively activate the carbonyl function of the ketone, keeping the furan ring intact. Open chain aliphatic ketone, 2-octanone, was smoothly undergoing the reaction (entry 12).

AlPc/Ph_3PO system is superior in activity to TMSCN when compared with other systems reported for the silylcyanation of carbonyl compounds.[4d,21,22] The present system indicates that greater yield with quite short reaction time. This method is effective, particularly, for the cyanation of aliphatic and aromatic ketones in low catalytic loading and

Table 2. Trimethylsilylcyanation of ketones using AlPc/Ph_3PO as catalysts[a]



Entry	Substrate	Time (h)	Yield (%)[b]
1		3 20 12 68	90 85[c] 28[d] 80[e]
2		2.45	92
3		2.45	90
4		2.45	90
5		3.30 80	85 76[e]
6		3	92
7		3	90
8		3	88
9		3.15 50	85 80[c]
10		3.15	90
11		3.0	85
12		2.45	90

[a]5 mol % of AlPc and 10 mol % of Ph_3PO in 2 mL of CH_2Cl_2. [b]Isolated yield. [c]Ref. 4d. [d]Ref. 21. [e]Ref. 22.

mild conditions.

In summary, we have identified a new class of readily available organometallic catalyst that efficiently promoted the cyanosilylation of ketones under mild conditions. This could be the first example of phthalocyanine based catalyst used for cyanosilylation reactions. The studies about mechanistic details and recovery of the catalyst are currently under investigation.

Experimental Section

Silylcyanation of Acetophenone; 2-Trimethylsilyloxy-2-phenylpropanenitrile (Table 2; Entry 1) Acetophenone (120 mg, 1 mmol) was added to a stirred CH_2Cl_2 (2 mL) solution of the catalyst [5 mol-% Aluminium phthalocyanine and 10 mol-% Ph_3PO] and the mixture stirred for 10 min at RT. TMSCN (1.5 equiv) was then added with a syringepump and the mixture was stirred continuously and progress of the reaction was followed by TLC. After 3 h the reaction mixture was purified by Silica gel flash chromatography by using EtOAc-hexane (1 : 9) mixture as eluent. 2-Trimethylsilyloxy-2-phenylpropanenitrile was obtained as colourless oil (Yield: 90%). The other substrates (entries 2-12 in Table 2) were also silylcyanated by using the same procedure. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.16 (s, 9H), 1.84 (s, 3H), 7.36-7.55 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 0.89, 33.41, 71.46, 121.45, 124.46, 128.48, 141.87.

2-Trimethylsilyloxy-3-(4'-methoxyphenyl)-2-methylphenylpropanenitrile (Entry 2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.14 (s, 9H), 1.50 (s, 3H), 2.91 (d, 2H, J = 3.4 Hz), 3.80 (s, 3H), 6.88 (d, 2H, J = 8.8 Hz), 7.22 (d, 2H, J = 8.4 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.06, 28.64, 48.21, 55.21, 69.98, 113.57, 121.76, 126.76, 131.66, 158.98.

2-Trimethylsilyloxy-2-(4'-methoxyphenyl)phenylpropanenitrile (Entry 3). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.16 (s, 9H), 1.85 (s, 3H), 3.83 (s, 3H), 6.95 (d, 2H, J = 8.8 Hz), 7.50 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 0.98, 33.31, 55.21, 71.18, 113.80, 121.70, 125.96, 133.95, 159.72. HRMS (EI): *m/z* calcd for $C_{13}H_{19}NO_2Si$ (M^+): 249.1185; found: 249.1183.

2-Trimethylsilyloxy-2-(4'-cholorophenyl)phenylpropanenitrile (Entry 4). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.22 (s, 9H), 1.86 (s, 3H), 7.41-7.47 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.00, 33.44, 71.02, 121.17, 126.05, 128.78, 134.56, 140.68.

2-Trimethylsilyloxy-2-(4'-nitrophenyl)phenylpropanenitrile (Entry 5). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.24 (s, 9H), 1.89 (s, 3H), 7.76 (d, 2H, J = 9.2 Hz), 8.31 (d, 2H, J = 9.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.09, 29.21, 76.42, 120.98, 124.03, 127.15, 129.88, 142.53.

2-(1-Naphthalen-1-yl)-2-(trimethylsilyloxy) propanenitrile (Entry 6). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.13 (s, 9H), 2.19 (s, 3H), 7.45-7.57 (m, 3H), 7.85-7.93 (m, 3H), 8.56 (dd, 1H) ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.05, 31.66, 73.12, 121.75, 124.59, 125.49, 125.74, 125.99, 129.07, 129.32, 130.10.

2-Trimethylsilyloxy-2-methyl-4-phenyl-3-butenenitrile (Entry 7). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.24 (s, 9H), 1.74 (s, 3H), 6.16 (d, 1H, J = 15.83 Hz), 6.92 (d, 1H, J = 15.8 Hz), 7.31-7.41 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.30, 30.79, 69.89, 120.60, 126.82, 128.53, 128.70, 129.47, 130.89, 135.06.

1-Trimethylsilyloxy-2-cyclohexenecarbonitrile (Entry 8). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.24 (s, 9H), 1.77-1.87 (m, 2H), 1.94-2.11 (m, 4H), 5.77 (m, 1H), 5.94-5.99 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 1.40, 18.26, 24.20, 36.86, 66.71, 121.75, 127.53, 132.49. HRMS (EI): *m/z* calcd for $C_{10}H_{17}NOSi$ (M^+): 195.1079; found: 195.1073.

1-Trimethylsilyloxy-1,2,3,4-tetrahydronaphthalene-1-carbonitrile (Entry 9). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.23 (s, 9H), 1.83-2.41 (m, 4H), 2.81 (t, 2H, 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.

Trimethylsilyloxy-1-indancarbonitrile (entry 10). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.12 (s, 9H), 2.29-2.42 (m, 1H), 2.57-2.70 (m, 1H), 2.82-3.08 (m, 2 H), 7.24-7.55 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 1.12, 29.37, 42.79, 76.46, 121.04, 124.08, 125.44, 127.71, 129.94, 142.08.

2-Trimethylsilyloxy-2-furan-2-yl-propanenitrile (Entry 11). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.09 (s, 9H), 1.92 (s, 3H), 6.35-6.40 (m, 1H), 6.47-6.50 (m, 1H), 7.41-7.43 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 0.49, 28.37, 65.89, 108.14, 110.68, 120.23, 143.09, 151.63.

2-Trimethylsilyloxy-2-methyloctanenitrile (entry 12). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.22 (s, 9H), 0.91 (t, 3H, 6.60 Hz), 1.31-1.74 (m, 8H), 1.57 (s, 3H), 1.68-1.74 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 1:15, 13.88, 22.38, 24.09, 28.76, 28.84, 31.47, 43.25, 69.56, 121.91.

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