Phosphomolybdic Acid Supported on Silica Gel as an Efficient and Reusable Catalyst for Cyanosilylation of Aldehydes

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Phosphomolybdic acid supported on silica gel (PMA-SiO_2) is an efficient catalyst for the activation of TMSCN for the facile cyanosilylation of various aldehydes. Cyano transfer from TMSCN to aldehyde proceeds smoothly at rt in presence of 0.8 mol % of PMA-SiO_2 leading to a range of cyanosilylether in excellent yield (mostly over 93%) within short reaction time (30 min). The catalyst can be recovered and reused several times without loss of activity.

Key Words : PMA-SiO_2, Heterogeneous catalysis, Cyanosilylation, Aldehydes

Introduction

Cyanosilylation of carbonyl compound is an efficient procedure for synthesis of silylated cyanohydrins. Cyanohydrins represents one of the most valuable synthon that can be elaborated into a variety of useful synthetic building blocks, such as α-hydroxy acids, α-hydroxy aldehyde, 1,2-diols, α-amino alcohol.[1-5] Because of their importance in organic synthesis and life science, a large body of work has been devoted to the development of synthesis of cyanohydrin. One of the most common methods to prepare cyanohydrin involves the cyanosilylation of carbonyl compound using TMSCN (trimethylsilyl cyanide). Transfer of cyano group from TMSCN to carbonyl compound can be catalyzed by plethora of reagents,[6-15] including Lewis acids, Lewis base, metal alkoxide, bifunctional catalyst and inorganic salts. Our group has developed numerous chiral and achiral catalytic systems for the cyanosilylation of carbonyl compound.[16-27] Phosphomolybdic acid belongs to the class of heteropolyacids (HPA). HPA are several times stronger than H_2SO_4, TsOH, $BF_3 \cdot Et_2O$ and $ZnCl_2$.[28] This makes it possible to carry out reaction in low concentration and lower temperature. Synthetically a variety of method has been developed and commercialized using HPA as catalys. For example oxidation of alcohol,[29] Fries rearrangement of phenyl acetate,[30] regioselective ring opening of aziridines,[31] chemoselective deprotection of isopropylidene acetals[32] and hydrolysis of *tert*-butyldimethylsilyl ether[33] have been reported with HPA.

Results and Discussion

In continuation of our efforts to explore the synthetic utility of phosphomolybdic acid,[34] we report herein cyanosilylation of aldehydes with TMSCN using 0.8 mol% of phosphomolybdic acid supported on silica gel. Anisaldehyde (1 mmol) reacts with TMSCN (1.2 mmol) at rt in presence of 0.8 mol % of PMA-SiO_2 [45] to give 97% yield within 10 min. Accordingly we further examine the structurally diverse aldehydes like aliphatic, aromatic and heterocyclic aldehydes. Aromatic aldehydes with electron-donating groups such as anisaldehyde, *p*-tolualdehyde and 2-hydroxy-4-methoxy benzaldehyde produce 97, 91 and 94% yield, respectively (entries 1, 2 and 3). Naphthaldehyde gave the corresponding silylether in excellent yield (entry 6). The effect of substituent on aromatic ring plays very important role in cyanosilylation. Even unsubstituted benzaldehyde gives no

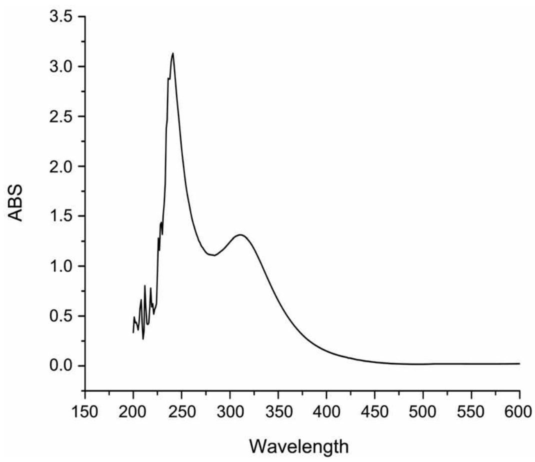


Figure 1. UV-Visible Spectrum of PMA + THF.

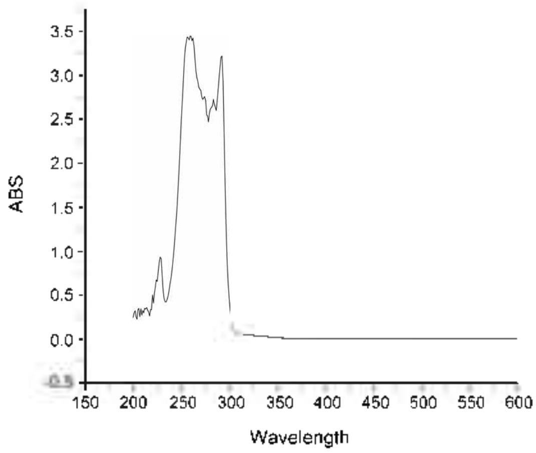
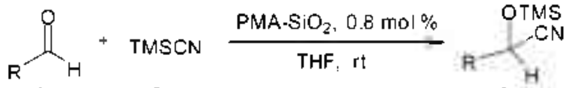


Figure 2. UV-Visible Spectrum of Reaction Mixture.

Table 1. Cyanosilylation of various aldehydes with TMSCN catalyzed by PMA-SiO_2[a]



1 2 3a-p

Entry	Substrate	Product (3)[b]	Time (min)	Yield (%)[c]
1	4-Meo-C_6H_4CHO	**3a**	10	97
			24h	87[35]
			12h	60[36]
			0.5h	69[37]
			10	91[38]
2	4-Me-C_6H_4CHO	**3b**	12	91
			24h	92[35]
			12h	80[36]
3	4-Meo-2-OHC6H3CHO	**3c**	10	94
4	3-OPh-C_6H_4CHO	**3d**	18	88
5	2-Cl-C_6H_4CHO	**3e**	35	64
6	$C_{10}H_7$CHO	**3f**	8	97
			5h	90[39]
			0.5h	94[37]
			0.5h	99[40]
			10	85[38]
7	C_6H_5CH=CHCHO	**3g**	15	97
			24h	94[35]
			12h	63[36]
			3h	75[42]
			1h	81[41]
			0.5h	75[37]
8	$C_6H_5CH_2$CHO	**3h**	5	98
9	$(Me)_2$-CHCHO	**3i**	23	77
10	$(Me)_2CHCHCH_2$CH(Me)-CH_2CHO	**3j**	28	82
11	Me(CH2)2CHO	**3k**	8	95
12	$Me(CH_2)_4$CHO	**3l**	16	90
13	C_6H_9CHO	**3m**	20	93
14	C_6H_{11}CHO	**3n**	12	93
			2h	99[40]
			0.5h	94[44]
15	3-CNC_6H_4CHO	**3o**	3h	58[d]
16	C_4H_3OCHO	**3p**	12h	NR

[a]60 mg of PMA-SiO_2 (0.008 mmol) was added to a mixture of 1.0 mmol of benzaldehyde and 1.2 mmol of TMSCN in THF. [b]All products were characterized and compared by ^{1}H, ^{13}C NMR with literature [16-21]. [c]Isolated yield. [d]1.8 mol % catalyst used.

product. Trifluro-*p*-tolualdehyde, 3- and 4-chlorobenzaldehyde are also unable to yield corresponding cyanosilylether even after overnight reaction. Among all the electron-withdrawing chlorine substituent only 2-chlorobenzaldehyde produces 64% yield within 35 min (entry 5). Unsaturated branched citral is smoothly converted to cyanosilylether in 82% yield in 28 min (entry 10). Cinnamaldehyde gives 97% yield within 15 min (entry 7). Aliphatic and branched aliphatic aldehydes were silylated in good to high yield. Butyraldehyde and hexanal gives 95 and 90% of yield in 8 and 16 min, respectively (entries 11 and 12). But isobutyraldehyde requires longer reaction time (23 min) with less

Table 2. Reusability of the Catalyst for Cyanosilylation of Anisaldehyde

No	Number of cycles	Time (min)	Yield (%)
1	1	10	95
2	2	24	94
3	3	45	94

yield compared to other aliphatic aldehydes (entry 9). Cyclic aliphatic aldehydes such as 1,2,3,6-tetrahydrobenzaldehyde and cyclohexane carboxaldehyde undergo cyanosilylation in 20 and 12 min both with 93% yield (entries 13 and 14). Acid sensitive 2-furaldehyde is heterocyclic compound which is unable to produce corresponding silylether under this reaction condition. 3-Cyanobenzaldehyde produces only 58% yield in quite long reaction time (entry 15).

PMA-SiO_2 can be reused three successive runs with slight decrease in yield and slight increase in reaction time (Table 2). The UV-visible spectrum of reaction mixture is recorded to identify the presence of PMA in solution. Figure 1 shows the characteristic absorption band of PMA (PMA + THF) at 310 nm[44] and Figure 2 is the for reaction mixture that shows the absence of PMA. This clearly indicates that there is no leaching of PMA from silica. PMA-SiO_2 is active and effective catalytic system considering the reaction time and yield comparing to literature catalytic systems[35-43] (Table 1).

Conclusion

We have described a simple, convenient and efficient protocol for the cyanosilylation of aldehydes using a phosphomolybdic acid supported on silica gel as reusable catalyst. The notable features of this method are mild reaction condition, simplicity in operation and environmentally friendly. Benzaldehyde containing electron-withdrawing groups and 2-furaldehyde are generally quite unreactive towards the cyanosilylation. The catalyst can be recovered by simple filtration and reused in subsequent runs.

Experimental

^{1}H NMR (200 MHz) spectra were recorded with Varian Gemini 2000 spectrometer. Chemical shifts are reported in $CDCl_3$ with tetramethylsilane as an internal standard. ^{13}C NMR data were collected on a Varian Gemini 400 spectrometer (100 MHz). Some compounds are also identified by HRMS (EI+) by Jeol DMX.

Spectroscopic data for selected compounds.

2-(4-Methoxyphenyl)-2-(trimethylsilyloxy)acetonitrile (entry 1): ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.204 (s, 9H), 3.82 (s, 3H), 5.43 (s, 1H), 6.90-6.93 (d, 2H), 7.37-7.39 (d, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = –0.10, 55.38, 63.38, 114.22, 119.32, 127.86, 128.46, 160.33. HRMS (EI): m/z $[M+H]^+$ calcd. for $C_{12}H_{17}NO_2Si$: 235.1029; found: 235.1026.

2-(2-Hydroxy-4-methoxyphenyl)-2-(trimethylsilyloxy) acetonitrile (entry 3): ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.199 (s, 9H), 3.78 (s, 3H), 5.78, (s, 1H), 7.26 (d, 2H) 7.29

(d, 1H), 9.24 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = −0.199, 55.33, 58.87, 104.90, 1.6.33, 119.49, 128.85, 153.084, 160.11.

(E)-4-Phenyl-2-(trimethylsilyloxy)but-3-enenitrile (entry 7): ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.25 (s, 9H), 5.10-5.12 (d, 1H), 6.19-6.2 (d, 1H), 6.79-6.8 (d, 1H) 7.35-7.39 (m, 5H) ^{13}C NMR (100 MHz, $CDCl_3$): δ = −0.02, 62.34, 118.48, 127.07, 128.45, 128.84, 128.89, 134.08, 135.16. HRMS (EI): m/z [M+H]$^+$ calcd. for $C_{13}H_{17}NOSi$: 231.1079; found: 231.1075.

2-(Cyclohex-3-enyl)-2-(trimethylsilyloxy)acetonitrle (entry 13): ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.21 (s, 9H), 1.60-2.12 (m, 7H), 4.23-4.27 (m, 1H), 5.70 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = −0.305, 23.93, 24.49, 26.80, 39.20, 65.84, 119.07, 124.89, 126.93. HRMS (EI): m/z [M+H]$^+$ calcd. for $C_{11}H_{19}NOSi$: 209.1236; found: 209.1236.

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