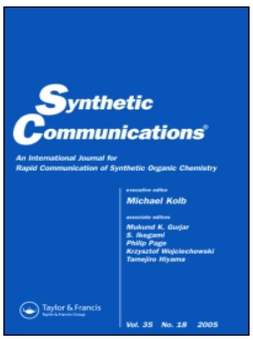

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TBD-catalyzed cyanosilylation of aldehydes and ketones

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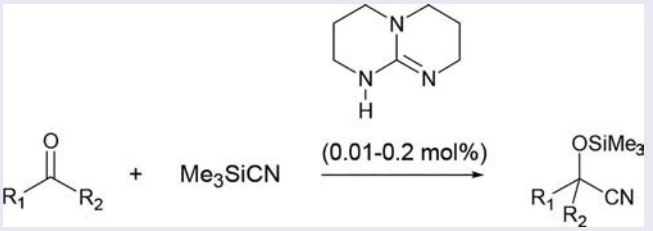
ABSTRACT

This study examines the catalytic efficacy of 1,5,7-triazabicyclo[4,4,0]dec-5-ene (TBD) in the cyanosilylation of aldehydes and ketones. In an aldehyde reaction, the corresponding products were obtained at high yield using minimal TBD (0.01 mol%). TBD was similarly effective in various ketone reactions.

GRAPHICAL ABSTRACT



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KEYWORDS
Base catalyst; cyanosilylation; guanidine; organocatalyst

Introduction

The addition of trimethylsilyl cyanide (TMSCN) to carbonyl compounds (cyanosilylation) is among the most fundamental carbon–carbon bond-formation reactions in modern organic chemistry.[1] The resultant cyanohydrins are easily converted into important molecules including α-hydroxyl carbonyl compounds and β-amino alcohols. The efficiency of this transformation is enhanced by catalytic systems such as Lewis acids, organocatalysts, metal salts, and inorganic solid acids and bases.[2] Base catalysts, such as phosphines,[3] phosphonium salts,[4] amines,[5] ammonium salts,[6] *N*-oxides,[7] guanidine,[8] and *N*-heterocyclic carbine,[9] have also been studied and achieved high efficiency. In this study, we explore a new catalyst, 1,5,7-triazabicyclo[4,4,0]dec-5-ene (TBD), for the cyanosilylation reaction.

It is well known that TBD is a strong Lewis base owing to its distorted ring structures. Consequently, TBD is employed as an organobase catalyst in multiple unique reactions such as the Henry reaction,[11] the Michael reaction,[13] intramolecular aldol reaction,[17] ring-opening polymerization,[14] the Wittig and Horner–Wadsworth–Emmons reaction,[12] conjugate addition to activated alkenes,[15] ester aminolysis,[16] pyrazoline synthesis,[18] and others.[19] Although TBD usually behaves as a base, it also contains an acidic N–H

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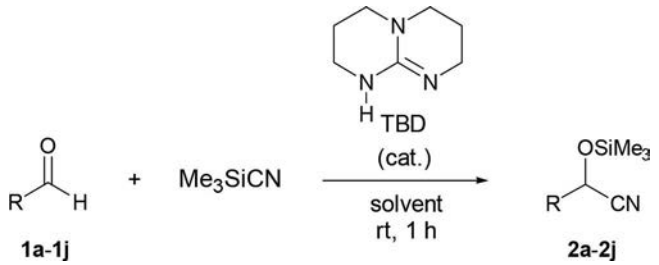
Supplemental data (experimental details and copies of ^{1}H and ^{13}C NMR spectra of products **2a–2j** and **4a–4j**) can be accessed on the publisher's website.

group; therefore, TBD may act as a bifunctional acid–base catalyst.[20] Recently, we also employed TBD as the catalyst in aldehyde trifluoromethylation[21] and organocatalyst in the ring opening of aziridines.[22] Herein, we report the efficient catalytic activity of TBD in the cyanosilylation of aldehydes and ketones.

Results and discussion

First, *p*-anisaldehyde was reacted with trimethylsilyl cyanide in the presence of 1 mol% TBD in CH_3CN at room temperature. The reaction proceeded smoothly and the product was obtained in high yield. Next, we reduced the catalyst quantity to 0.1 mol% and achieved the same smooth reaction. Finally, we found that a product was obtained in 91% even at 0.01 mol% of TBD. The product was obtained in lower yield when 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,1,3,3-tetramethylguanidine (TMG), and 7-methyl-TBD (MTBD) were used instead of TBD (Table 1, entries 1 vs. 4–6). These reactive differences suggest that TBD has a role of both bicyclic strong Lewis base and acid–base bifunctional catalyst in the cyanosilylation catalysis. We performed a reference

Table 1. Cyanosilylation of various aldehydes.[a]



Entry	Cat. (mol%)	Aldehyde	Time	Product	Yield (%)
1	1	4-$CH_3OC_6H_4CHO$	1 h	**2a**	98
2	0.1				92
3	0.01				93
4			12 h		32[b]
5			12 h		40[c]
6			12 h		36[d]
7			1 h		85[e]
8			12 h		55[f]
9			12 h		45[g]
10		C_6H_5CHO	0.5 h	**2b**	83
11		4-ClC_6H_4CHO	0.5 h	**2c**	95
12		4-$NO_2C_6H_4CHO$	2 h	**2d**	65
13		α-Naphthaldehyde	2 h	**2e**	91
14		β-Naphthaldehyde	1 h	**2f**	90
15		$C_6H_5CH_2CH_2CHO$	4 h	**2g**	85
16		$C_8H_{17}CHO$	2 h	**2h**	79
17		c-$C_6H_{11}CHO$	2 h	**2i**	81
18		2-Furaldehyde	0.5 h	**2j**	92

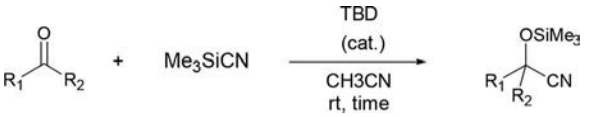
[a]Isolated yield.
[b]MTBD was used instead of TBD.
[c]TMG was used instead of TBD.
[d]DBU was used instead of TBD.
[e]In DMF.
[f]In THF.
[g]In CH_2Cl_2.

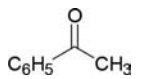
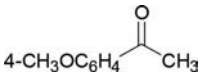
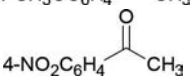
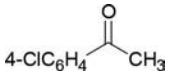
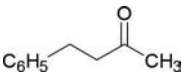
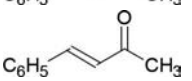
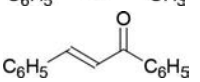
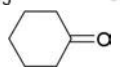
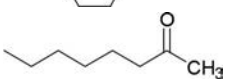
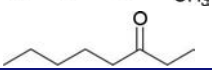
study of the solvent. Among several candidate solvents (CH_3CN, tetrahydrofuran [THF], dimethylformamide [DMF], and CH_2Cl_2), CH_3CN proved to be the most suitable for this reaction. To clarify the scope of the reaction, we subjected several aldehydes to 0.01 mol% TBD in CH_3CN (Table 2). Both aromatic and aliphatic aldehydes reacted smoothly and delivered the products in good to high yields. In the case of 4-nitrobenzaldehyde, the starting material was rapidly consumed; however, the product yield was not good. In this case, it is likely that attack at the NO_2 group occurred.

Moreover, we investigated the scope of TBD-catalyzed ketone reactions (Table 2). The ketone reactions required slightly larger catalyst quantities (0.1–0.2 mol%) than the aldehyde reactions. In this condition, aromatic, aliphatic, acyclic, and cyclic ketones all delivered good results. Slightly longer reaction times were needed in the reaction of aromatic aldehydes bearing electron-donating groups on the aromatic ring. Only 1,2-addition products were observed for benzalacetone and chalcone.

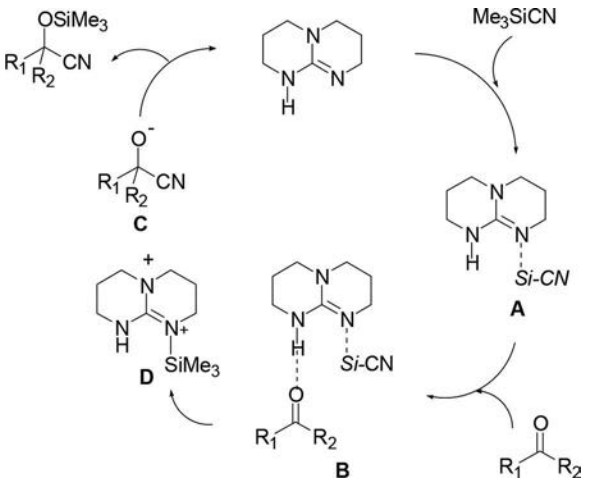
A possible mechanism is illustrated in Scheme 1. First, TBD coordinates the silicon atom of the TMSCN and the C-Si bond is activated (A). Next, hydrogen bond activates the carbonyl compound with the same molecule of TBD occurs (B). Both activated molecules can then readily react to produce the alkoxide anion of the cyanohydrin (C) and silylated

Table 2. TBD-catalyzed cyanosilylation of various ketones.[a]



Entry	Ketones	Cat. (mol%)	Time	Product	Yield (%)
1		0.1	2 h	**4a**	77
2			4 h	**4b**	88
3			2 h	**4c**	94
4			2 h	**4d**	87
5		0.2	1 h	**4e**	89
6		0.1	4 h	**4f**	85
7		0.2	4 h	**4g**	92
8		0.2	1 h	**4h**	83
9		0.1	4 h	**4i**	82
10		0.5	1 h	**4j**	94

[a]Isolated yield.



Scheme 1. Proposed mechanism.

TBD (D). Finally, silylation between the the alkoxide anion and silylated TBD occurs to give the silylated adduct with regeneration of TBD.

Conclusion

In conclusion, we demonstrated that TBD catalyzes the cyanosilylation of aldehydes and ketones. The corresponding products of a broad range of aldehydes were obtained at high yield under mild conditions using minimal TBD (0.01 mol%). TBD was similarly effective in the cyanosilylation of various ketones.

Experimental

Representative experimental procedures for TBD-catalyzed cyanosilylation of carbonyl compounds with TMSCN

A 1-mM solution of TBD/CH_3CN (10 μL, 0.01 μmol to 100 μL, 0.1 μmol) was added to a solution of carbonyl compounds (1.0 mmol) and TMSCN (1.1 mmol) in CH_3CN (1 mL) at room temperature. After the reaction was complete (as determined by thin-layer chromatography, TLC), the reaction mixture was quenched with water. The resultant mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with water and brine and dried with Na_2SO_4. After the filtration, the residue was concentrated in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/hexane = 1:10) to give the corresponding product as silylated form.

2-Phenyl-2-trimethylsilyloxyacetonitrile (2a)[5a]

The title compound was prepared according to the general procedure and the product was obtained as a colorless oil. Yield: 98% (0.231 g); ^{1}H NMR (500 Hz, $CDCl_3$) δ 0.22 (s, 9H),

5.49 (s, 1H), 7.36–7.43 (m, 3H), 7.46 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ-0.3, 63.7, 119.1, 126.3, 128.9, 129.3, 136.3.

2-Phenyl-2-trimethylsilyloxypropanenitrile (4a)[5a]

The title compound was prepared according to the general procedure and the product was obtained as a colorless oil. Yield: 77% (0.169 g); ^{1}H NMR (500 Hz, $CDCl_3$) δ 0.15 (s, 9H), 1.84 (s, 3H), 7.30–7.40 (m, 3H), 7.52 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 1.0, 35.6, 71.6, 121.7, 124.6, 128.6, 142.0.

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