Highly Efficient Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Enones with Water as the Additive

Jingya Yang,[a,b] Yongbin Shen,[a] Fu-Xue Chen*[a]

[a] Department of Applied Chemistry, School of Chemical Engineering & the Environment, Beijing Institute of Technology, 5 South Zhongguancun Street, Haidian District, Beijing 100081, P. R. of China

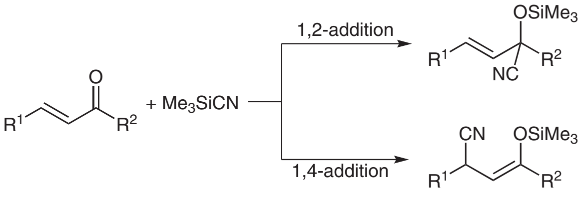
[b] College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, P. R. of China
Fax +86(10)68918296; E-mail: fuxue.chen@bit.edu.cn

Received 25 November 2009; revised 15 December 2009

Abstract: A facile and efficient 1,4-addition of Me_3SiCN to enones has been achieved with perfect regioselectivity using Cs_2CO_3 as catalyst. Thus, with 0.5 mol% of Cs_2CO_3 and 4 equivalents of H_2O as the additive excellent yields (81–99%) of β-cyanoketones are obtained within one to five hours. Both aromatic and aliphatic enones are found suitable substrates for this protocol.

Key words: 1,4-addition, catalysis, enones, nitriles, regioselectivity

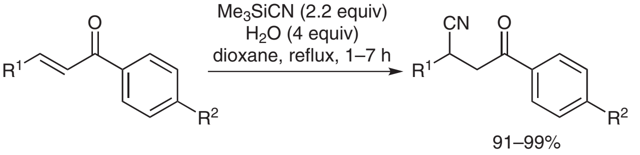
As one of the most general and versatile methods for C–C bond formation, the conjugate addition to α,β-unsaturated carbonyl compounds has received much attention.[1] In this context, the transition-metal-catalyzed 1,4-additions of aryl[2] and alkyl reagents have been well developed,[3] yet the 1,4-addition of weak nucleophile cyanide to α,β-unsaturated carbonyl compounds with high regioselectivity remains challenging (Scheme 1).



Scheme 1 Additions of Me_3SiCN to enones

On the other hand, 1,4-addition of cyanide to enones has been extensively utilized in syntheses of biologically active molecules[4] and complex natural products.[5] In the literature, frequently employed methods involve Me_3SiCN[6] and Et_2AlCN[7] as the cyanide sources and Et_3Al[6,8a] and $Pd(OAc)_2$[9] as Lewis acid catalysts.[8] Ionic liquid and microwave also have been applied to this transformation in line with the concept of green chemistry.[10,11] Recently, Shibasaki and co-workers reported an entirely distinct nickel(0)–cyclooctadiene (COD) complex toward the elegant synthesis of Tamiflu,[12] an important anti-influenza drug, and subsequent Ni(0) and $Gd(OTf)_3$ cooperative catalyst in the 1,4-addition of Me_3SiCN to a wide variety of aliphatic enones.[13] The first example of catalytic enantioselective conjugate addition of cyanide to enones is also disclosed by Shibasaki.[14] Though these significant achievements have been made, 1,4-additon of Me_3SiCN to a broad scope of enones is still demanding.[15]

Previously, we presented a CsF-catalyzed 1,4-addition of Me_3SiCN to aromatic enones with excellent yield and regioselectivity (Scheme 2).[16] Unfortunately, aliphatic enones are not suitable substrates. Although CsF has good solubility in dioxane and catalytic activity, it is relatively expensive and much hygroscopic. Moreover, fluoride ion is harmful to the environment. Compared to CsF, Cs_2CO_3 is inexpensive and stable to moisture, which is widely used as catalyst or base in organic synthesis,[17] but only in few examples of conjugate addition reactions.[18] To the best our knowledge, Cs_2CO_3 is scarcely applied to the 1,4-addition of cyanide to α,β-unsaturated carbonyl compounds. Herein, we report an efficient Cs_2CO_3-catalyzed 1,4-addition of Me_3SiCN to both aromatic and aliphatic enones.



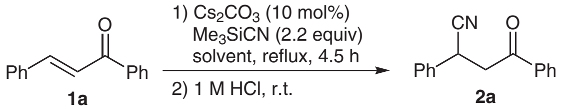
Scheme 2 CsF-catalyzed 1,4-addition of Me_3SiCN to aromatic enones

Model reaction is conducted with chalcone (**1a**) and Me_3SiCN. Initially, the effect of solvent is evaluated with Cs_2CO_3 (10 mol%) as the catalyst at different reflux temperature (Table 1). The yields of the 1,4-addition product **2a** differ significantly based on the solvent used. When CH_2Cl_2 is used as the solvent, no conversion occurs (Table 1, entry 1). However, poor yield is obtained in THF (Table 1, entry 2) as well as trace product in toluene (Table 1, entry 3). Although with similar boiling point to toluene, dioxane gives excellent yield of 92% (Table 1, entry 4). However, when more polar solvents such as DMF and DMSO with higher boiling point are used, the isolated yields decrease sharply (Table 1, entries 5, 6).

With dioxane as the solvent, the effects of reaction temperature and time on the model reaction are investigated (Table 2). When increasing the temperature from 40 °C to

SYNTHESIS 2010, No. 8, pp 1325–1333
Advanced online publication: 29.01.2010
DOI: 10.1055/s-0029-1218653; Art ID: F22209SS

Table 1 Effect of Solvent on the Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Chalcone (**1a**)[a]

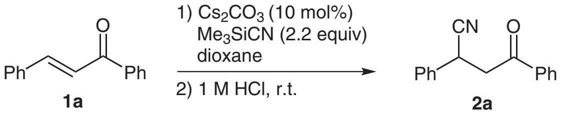


Entry	Solvent[b]	Yield (%)[c]
1	CH_2Cl_2	0
2	THF	10
3	toluene	trace
4	dioxane	92
5	DMF	34
6	DMSO	27

[a] Reaction conditions: chalcone (**1a**; 0.15 mmol), Me_3SiCN (0.33 mmol, 2.2 equiv), Cs_2CO_3 (10 mol%), solvent (1.5 mL), reflux, 4.5 h.
[b] Anhydrous solvent.
[c] Isolated yield.

reflux temperature, the yield increases stepwise (Table 2, entries 1–3). However, overheated dioxane is unfavorable to the yield (Table 2, entry 4). A reaction time of 4.5 hours is necessary for good conversion; otherwise gradually decreased yield is obtained with relatively shorter reaction time (Table 2, entries 5, 6).

Table 2 Effects of Temperature and Time on the Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Chalcone (**1a**)[a]

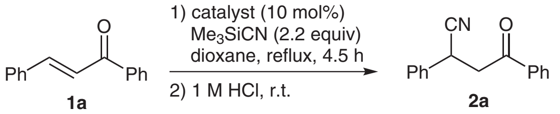


Entry	Temp (°C)	Time (h)	Yield (%)[b]
1	40	4.5	trace
2	80	4.5	31
3	reflux	4.5	92
4[c]	120	4.5	76
5	reflux	2.5	61
6	reflux	1	33

[a] Reaction conditions: chalcone (**1a**; 0.15 mmol), Me_3SiCN (0.33 mmol, 2.2 equiv), Cs_2CO_3 (10 mol%), dioxane (1.5 mL).
[b] Isolated yield.
[c] In a sealed tube.

On the basis of above results, various catalysts are screened in the model reaction in dioxane at reflux temperature (Table 3). A yield of 24% is obtained with 10 mol% of Na_2CO_3 (Table 3, entry 1). K_2CO_3 gives yet unsatisfactory 40% yield (Table 3, entry 2). Delightedly, Cs_2CO_3 makes the reaction proceed smoothly to afford the product **2a** in 92% yield (Table 3, entry 3). Comparing the results of Na_2CO_3, K_2CO_3, and Cs_2CO_3, the possible 'cesium effect' can not be ruled out.[19] Nevertheless, control experiment using more basic CsOH gives inferior result (Table 3, entry 4). CsCl yields the product in only 10% (Table 3, entry 5). At present reaction conditions, CsF gives less amount of **2a** (Table 3, entry 6). Hence, Cs_2CO_3 shows the best catalytic activity.

Table 3 Catalyst Screening in the Model Reaction[a]



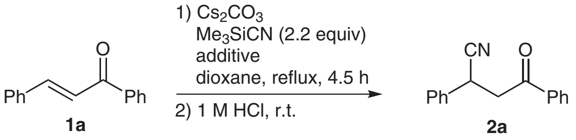
Entry	Catalyst	Yield (%)[b]
1	Na_2CO_3	24
2	K_2CO_3	40
3	Cs_2CO_3	92
4	CsOH	77
5	CsCl	10
6	CsF	72

[a] Reaction conditions: chalcone (**1a**; 0.15 mmol), Me_3SiCN (0.33 mmol, 2.2 equiv), catalyst (10 mol%), dioxane (1.5 mL), reflux, 4.5 h.
[b] Isolated yield.

Subsequently, effects of catalyst loading and additives are investigated with results listed in Table 4. Reasonably, as reducing the catalyst loading from 10 mol% to 1 mol% the yield of product **2a** decreases gradually from 92% to 64% (Table 4, entries 1–3). Considering that proton is needed to complete the reaction sequence and the significant improvement by protic additives in the conjugate addition of Me_3SiCN to α,β-unsaturated carbonyl compounds in recent years,[14,15] the effect of protonic additive is studied with 1 mol% of Cs_2CO_3 (Table 4, entries 4–9). Thus, alcohol and phenol (2,6-dimethylphenol, DMP) are introduced into the reaction mixture giving moderate increase of the yield of **2a** (Table 4, entries 4 and 5 vs. entry 3). An encouraging result is obtained when H_2O is added (Table 4, entries 6–8). The reaction proceeds cleanly and gives the highest yield with 4 equivalents of water (Table 4, entry 8). However, much excessive amount of H_2O reduces the yield of **2a** (Table 4, entry 9). In addition, as an adequate amount of water has been introduced into the reaction resulting in no formation of *O*-trimethylsilyl 1,4-adduct enolate in the reaction mixture, the subsequent quenching with 1 M HCl is not needed anymore (Table 4, entry 8).

Water is frequently used in modern organic synthesis and has been comprehensively reviewed.[20] From the results in Table 4, it implies that H_2O is not only used to provide proton (Table 4, entry 7 vs. entries 4 and 5). In this case, H_2O probably facilitates the reversion of possible 1,2-addition followed by a fast irreversible 1,4-addition.[14] Side evidence comes from the fact that neither 1,4-adduct silyl

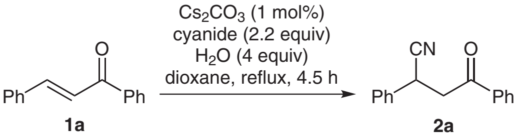
Table 4 Effects of Catalyst Loading and Additive on the Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Chalcone (**1a**)[a]



Entry	Cs_2CO_3 (mol%)	Additive (equiv)[b]	Yield (%)[c]
1	10	–	92
2	5	–	71
3	1	–	64
4	1	*i*-PrOH (1)	79
5	1	DMP (1)	75
6	1	H_2O (0.3)	84
7	1	H_2O (1)	87
8[d]	1	H_2O (4)	92
9	1	H_2O (1:5)[e]	29

[a] Reaction conditions: chalcone (**1a**; 0.15 mmol), Me_3SiCN (0.33 mmol, 2.2 equiv), dioxane (1.5 mL), reflux, 4.5 h.
[b] Relative to **1a**.
[c] Isolated yield.
[d] Comparable yield is obtained without quencher (1 M HCl).
[e] Volume ratio of H_2O to dioxane. DMP = 2,6-dimethylphenol.

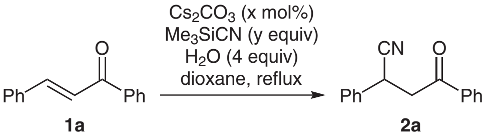
Table 5 Effect of Cyanide Source on the Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Chalcone (**1a**)[a]



Entry	Cyanide source	Yield (%)[b]
1	Me_3SiCN	92
2	*t*-Bu(Me)$_2$SiCN	66
3	$K_3Fe(CN)_6$	0
4	CuCN	0

[a] Reaction conditions: chalcone (**1a**; 0.15 mmol), cyanide (0.33 mmol, 2.2 equiv), catalyst (1 mol%), dioxane (1.5 mL), reflux, 4.5 h.
[b] Isolated yield.

Table 6 Effects of Catalyst Loading and Concentration of Chalcone (**1a**) on the Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN[a]



Entry	Cs_2CO_3 (mol%)[b]	Me_3SiCN (equiv)[b]	Concn (M)[c]	Time (h)	Yield (%)[d]
1	1	2.2	0.05	4.5	59
2	1	2.2	0.1	4.5	92
3	1	2.2	0.3	3	99
4	1	2.2	0.6	3	99
5	1	2.2	1	4.5	95
6	1	1.5	0.3	3	97
7	1	1.2	0.3	3	88
8	0.5	2.2	0.3	3.5	99
9	0.5	2.2	0.6	3	99
10	0.5	1.5	0.6	3	99
11	0.3	1.5	1	5.5	95
12	0.1	2.2	1	7	36
13[e]	0.5	1.5	0.6	4.5	93

[a] Reaction conditions: dioxane, reflux.
[b] Relative to **1a**.
[c] Concentration of **1a**.
[d] Isolated yield.
[e] Performed on gram scale, see experimental section.

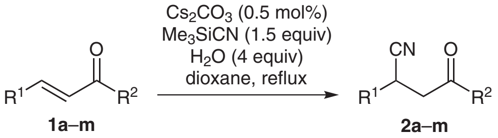
enolate nor 1,2-adduct silyl ether is detected by TLC monitoring during the course of the reaction in the presence of water (Table 4, entries 7 and 8), though alkali carbonate has been used to catalyze the 1,2-addition of Me_3SiCN to ketones in the literature.[21]

Further, several cyanide sources involving inorganic cyanides are examined referring to the above conditions (Table 5). Compared to Me_3SiCN, *tert*-butyldimethylsilyl cyanide (TBSCN) gives inferior yield (entry 2 vs. 1), which is not in line with Shibasaki's observation.[14] With inorganic cyanides such as $K_3Fe(CN)_6$ and CuCN, no reaction takes place at all (entries 3 and 4).

To obtain the best catalyst efficiency, subsequent optimization focusing on concentration of chalcone (**1a**) and equivalent of Me_3SiCN is carried out (Table 6). First, concentration of chalcone is changed from 0.05 M to 1 M stepwise with 1 mol% of Cs_2CO_3 and 2.2 equivalents of Me_3SiCN in the presence of 4 equivalents of H_2O (Table 6, entries 1–5). Reaction at low concentration leads to a slow reaction rate and thus a low yield (Table 6, entry 1). As increasing the concentration, the reactions afford almost stoichiometric product **2a** at 0.3 M and 0.6 M within a shorter reaction time (Table 6, entries 3 and 4 vs. entry 2). However, at much higher concentration (1 M) the model reaction produces lower yield even with a longer reaction time (Table 6, entry 5). Second, lowering the equivalent of Me_3SiCN shows that 1.5 equivalents of Me_3SiCN are enough for a comparative yield at 0.3 M (Table 6, entry 6 vs. entries 5 and 7). Encouraged by these results, further decrease of the catalyst loading to 0.5 mol% is performed at 0.3 M and 0.6 M also giving excellent yields (Table 6, entries 8–10). Furthermore, the satisfactory result is retained even with much low catalyst loading at 0.3 mol% of Cs_2CO_3 and 1.5 equivalents of Me_3SiCN at much concentrated of chalcone (**1a**) (Table 6, entry 11). However, further decrease of catalyst loading to 0.1 mol% results in either longer reaction time or low yield (Table 6, entry 12). For considerable reaction rate, the catalyst loading is determined to be 0.5 mol% at 0.6 M of chalcone (**1a**) (Table 6, entry 10). This protocol is such practical that it can be easily scaled up to gram scale in 93% isolated yield of **2a** (Table 6, entry 13).

With the optimal reaction conditions at hand – enones (0.3 mol, 0.6 M), Me_3SiCN (1.5 equiv), Cs_2CO_3 (0.5 mol%), H_2O (4 equiv to enones) in dioxane (0.5 mL) at reflux temperature – the substrate generality is evaluated (Table 7). In general, the chalcone derivatives give excellent yields (90–99%) at varying reaction rate (Table 7, entries 1–9). With electron-donating substituents the reactions proceed slowly than chalcone (Table 7, entries 2–5 vs. entry 1). On the other hand, electron-deficient α,β-unsaturated enones are converted into β-cyanoketones much quickly (Table 7, entries 6–9). β-Alkyl substituted enone **1j** also gives excellent yield under these conditions (Table 7, entry 10). Most excitingly, the present protocol can be applied to aliphatic enones with excellent yields (Table 7, entries 11–13).

Table 7 Substrate Generality of Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Enones[a]



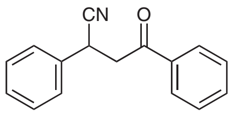
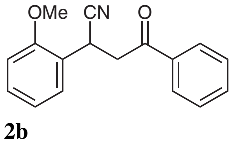
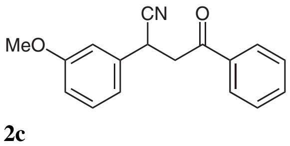
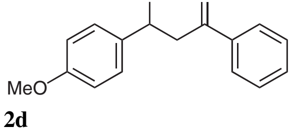
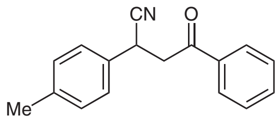
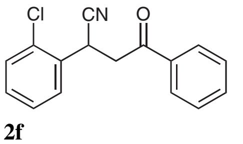
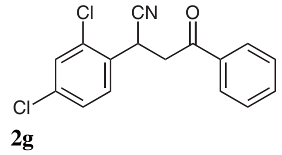
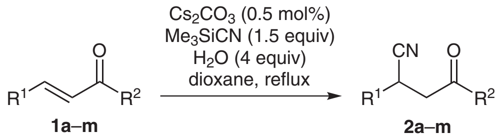
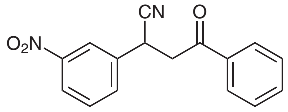
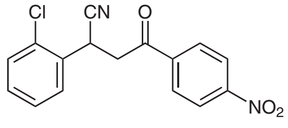
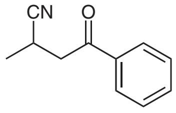
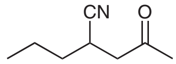
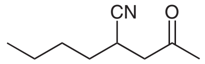
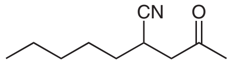
Entry	Product	Time (h)	Yield (%)[b]
1	 **2a**	3	99[c]
2	 **2b**	5	97
3	 **2c**	4	99
4	 **2d**	5	98
5	 **2e**	5	99
6	 **2f**	1	99
7	 **2g**	1	98

Table 7 Substrate Generality of Cs_2CO_3-Catalyzed 1,4-Addition of Me_3SiCN to Enones[a] (continued)



Entry	Product	Time (h)	Yield (%)[b]
8	 **2h**	1	90
9	 **2i**	1	94
10	 **2j**	1	99
11	 **2k**	3	81
12	 **2l**	3	98
13	 **2m**	3	99

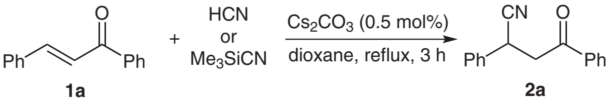
[a] Reaction conditions: enones (0.3 mmol, 0.6 M), Me_3SiCN (0.45 mmol, 1.5 equiv), Cs_2CO_3 (0.5 mol%), H_2O (4 equiv), dioxane (0.5 mL), reflux for indicated reaction times.

[b] Isolated yield.

[c] Performed on gram scale, 93% yield (see experimental section).

To shed light on the possible origin of the remarkable performance of the 1,4-addition reaction catalyzed by Cs_2CO_3 with H_2O as additive, several control experiments are performed (Table 8). Considering possible generation of HCN in situ from Me_3SiCN and H_2O to participate in the reaction, HCN is investigated as another cyanide source. As expected, the yield is considerably lower either with or without H_2O (Table 8, entries 1 and 2). However, excellent yield can be obtained when Me_3SiCN is employed (Table 8, entry 3). These phenomena indicate that HCN generated in situ from Me_3SiCN and H_2O does not account for the perfect 1,4-addition efficiency while Me_3SiCN is likely to be the real cyanating reagent,[22] or at least that HCN as the only cyanide source makes the reaction inferior to the combined use of Me_3SiCN and H_2O.[15f] In our opinion, as shown in Scheme 3, water here is mainly used to fasten the catalytic cycle by protonation of the *O*-trimethylsilyl 1,4-adduct enolate affording the β-cyanoketone and in part to suppress the possible 1,2-addition as well.[21a,b]

Table 8 Control Experiments[a]



Entry	Cyanide source	H_2O (equiv)[b]	Yield (%)[c]
1	HCN[d]	–	52
2	HCN[d]	4	61
3	Me_3SiCN	4	99

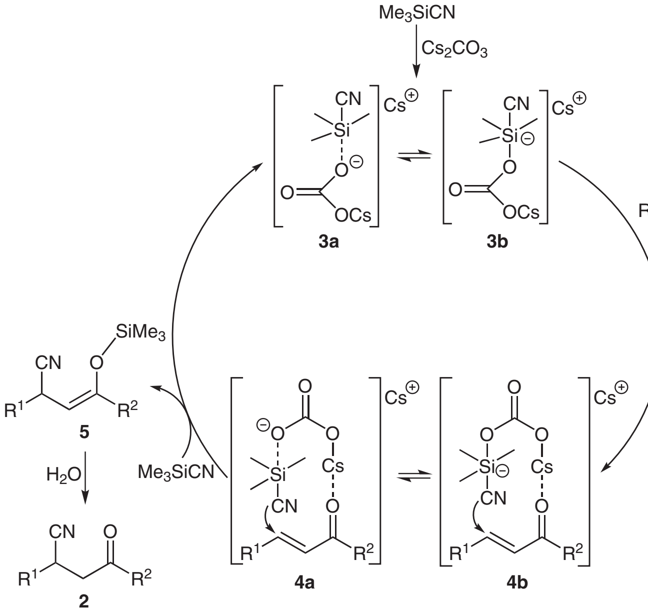
[a] Reaction conditions: chalcone (**1a**; 0.3 mmol, 0.6 M), cyanide source (0.45 mmol, 1.5 equiv), Cs_2CO_3 (0.5 mol%), dioxane (0.5 mL), reflux for 3 h.

[b] Relative to **1a**.

[c] Isolated yield.

[d] HCN solution was generated prior to use from equal molar ratio of Me_3SiCN and MeOH.

Hypervalent silicon species must be involved in the transition state (Scheme 3). It is a general known chemistry



Scheme 3 Proposed catalytic cycle

that the reactions of silicon reagents usually involve hypervalent silicon through nucleophilic activation.[21a,23] In the present less strong dipolar dioxane, we proposed pentacoordinated silicate **3a**,**b** as the real cyanide reagent formed by the interaction between Me_3SiCN and the partially dissociated carbonate anion of Cs_2CO_3.[19,21a] Subsequently, the silicate species **3** undergoes conjugate addition through a dual activation transition state **4**[24] affording silyl enolate **5** and regeneration of **3a**,**b**, in which **5** is immediately hydrolyzed by water into **2**.

In conclusion, a successful Cs_2CO_3-catalyzed 1,4-addition of Me_3SiCN to both aromatic and aliphatic enones has been achieved. The 1,4-adducts are obtained in excellent yields with 0.5 mol% of Cs_2CO_3 and 4 equivalents of H_2O as the additive within one to five hours. The facile availability of the catalyst and high regioselectivity of the reaction make it much more practical. It can be easily scaled up to gram scale with excellent yield. Further mechanistic elucidation and extension to asymmetric version of this protocol are under way in our group.[25]

NMR spectra were recorded on a Bruker AVIII 400 spectrometer, operating at 400 MHz for ^1H NMR, and 100 MHz for ^{13}C NMR. Chemical shifts for ^1H NMR and ^{13}C NMR spectra are reported as δ in units of parts per million (ppm) downfield from Me_4Si and relative to the signal of $CDCl_3$. The IR spectra were recorded on a Perkin-Elmer Spectrum One with KBr pellets for solids and as films for liquids. The elemental analyses were performed on an Elementar Vario MICRO CUBE instrument. All melting points were determined on a XT4A melting point apparatus and uncorrected. Analytical TLC was performed using F254 precoated silica gel plate. Column chromatography was performed with silica gel (200–300 mesh). Petroleum ether (PE) used had a boiling point range of 60–90 °C.

All reactions were carried out under argon atmosphere using typical vacuum-line techniques unless otherwise noted. Me_3SiCN and Cs_2CO_3 were purchased from Alfa Aesar and used directly. All solvents were dried under argon prior to use. Enones **1a–j** were synthesized according to reported procedure.[26] Enones **1k–m** were purchased from Alfa Aesar and used directly.

1,4-Addition of Me_3SiCN to Enones 1a–m; General Procedure

After Cs_2CO_3 (0.5 mg, 0.0015 mmol, 0.5 mol%), enone **1** (0.3 mmol), and dioxane (0.5 mL) were charged into a dry Schlenk tube equipped with cold finger under argon, Me_3SiCN (57 μL, 0.45 mmol, 1.5 equiv) and H_2O (22 μL, 1.2 mmol, 4 equiv) were added. The reaction mixture was stirred at reflux temperature until the reaction was complete (monitored by TLC). Then, H_2O (2 mL) was added at r.t. and the resulting mixture was extracted with EtOAc (5 mL) (***Caution!*** HCN generated in the reaction mixture is highly toxic. Those operations should be conducted in a well-ventilated hood). The extract was washed with H_2O (2 mL), brine (3 mL), dried (Na_2SO_4), and concentrated. The crude product was purified by flash column chromatography on silica gel (PE–EtOAc, 20:1, unless otherwise noted) to afford pure products **2** (Table 7).

1,4-Addition of Me_3SiCN to Chalcone (1a) on Gram Scale; 4-Oxo-2,4-diphenylbutanenitrile (2a)

To a suspension of Cs_2CO_3 (7.8 mg, 0.024 mmol, 0.5 mol%) and chalcone (**1a**; 1 g, 4.8 mmol) in anhyd dioxane (8.0 mL) in a 50 mL Schlenk tube equipped with cold finger under argon were added Me_3SiCN (0.91 mL, 7.2 mmol, 1.5 equiv) and H_2O (0.34 mL, 19.2 mmol, 4 equiv) sequentially. The reaction mixture was stirred at reflux temperature for 4.5 h. Upon completion of the reaction as noted by TLC monitoring, H_2O (5 mL) was added to quench the reaction at r.t. The resulting mixture was extracted with EtOAc (20 mL) (***Caution!*** HCN generated in the reaction mixture is highly toxic. Those operations should be conducted in a well-ventilated hood). The extract was washed with H_2O (3 × 4 mL), brine (5 mL), dried (Na_2SO_4), and concentrated. The crude solid was washed with hot PE–EtOAc (20:1, 2 × 5 mL) to afford pure **2a** (1054 mg, 93%) as a yellowish brown solid.

When performed on 0.3 mmol scale (optimized general procedure), yield: 99%; white solid; mp 120–122 °C (Lit.[11] mp 122–125 °C).

IR (KBr): 1681, 2236 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.52 (dd, J = 6.0, 18.0 Hz, 1 H, $NCCHCH_AH_BCO$), 3.74 (dd, J = 8.0, 18.0 Hz, 1 H, $NCCHCH_AH_B$-

CO), 4.57 (dd, *J* = 6.0, 8.0 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.34–7.49 (m, 7 H, ArH), 7.58–7.62 (m, 1 H, ArH), 7.92–7.94 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.9, 44.5, 120.6, 127.5, 128.1, 128.4, 128.8, 129.3, 133.9, 135.3, 135.8, 194.6.

2-(2-Methoxyphenyl)-4-oxo-4-phenylbutanenitrile (2b)
Yield: 97%; white solid; mp 84–86 °C.

IR (KBr): 1685, 2245 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50 (dd, *J* = 4.8, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.65 (dd, *J* = 8.8, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 3.87 (s, 3 H, OCH_3), 4.78 (dd, *J* = 4.8, 8.8 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 6.91–7.02 (m, 2 H, ArH), 7.31–7.35 (m, 1 H, ArH), 7.45–7.51 (m, 3 H, ArH), 7.56–7.61 (m, 1 H, ArH), 7.93–7.95 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.5, 42.2, 55.6, 111.0, 120.5, 121.1, 123.2, 128.1, 128.7, 129.0, 129.8, 133.6, 136.0, 156.3, 195.3.

2-(3-Methoxyphenyl)-4-oxo-4-phenylbutanenitrile (2c)
Yield: 99%; white solid; mp 106–108 °C.

IR (KBr): 1678, 2236 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50 (dd, *J* = 6.0, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.72 (dd, *J* = 8.0, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 3.82 (s, 3 H, OCH_3), 4.55 (dd, *J* = 6.0, 8.0 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 6.86–6.88 (m, 1 H, ArH), 6.96–7.02 (m, 2 H, ArH), 7.28–7.32 (m, 1 H, ArH), 7.45–7.49 (m, 2 H, ArH), 7.58–7.62 (m, 1 H, ArH), 7.92–7.94 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.9, 44.5, 55.4, 113.3, 113.8, 119.6, 120.5, 128.1, 128.8, 130.4, 133.9, 135.8, 136.7, 160.2, 194.6.

2-(4-Methoxyphenyl)-4-oxo-4-phenylbutanenitrile (2d)
Yield: 98%; white solid; mp 111–113 °C (Lit.[11] mp 113–114 °C).

IR (KBr): 1677, 2234 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.49 (dd, *J* = 6.4, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.73 (dd, *J* = 7.6, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 3.80 (s, 3 H, OCH_3), 4.53 (dd, *J* = 6.4, 7.6 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 6.89–6.92 (m, 2 H, ArH), 7.33–7.36 (m, 2 H, ArH), 7.45–7.49 (m, 2 H, ArH), 7.57–7.61 (m, 1 H, ArH), 7.91–7.93 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.2, 44.6, 55.4, 114.6, 120.9, 127.2, 128.1, 128.7, 128.8, 133.8, 135.8, 159.6, 194.7.

4-Oxo-4-phenyl-2-*p*-tolylbutanenitrile (2e)
Yield: 99%; white solid; mp 129–131 °C (Lit.[11] 135–137 °C).

IR (KBr): 1674, 2239 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 3.49 (dd, *J* = 6.4, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.70 (dd, *J* = 8.0, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 4.53 (dd, *J* = 6.4, 8.0 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.19 (d, *J* = 8.0 Hz, 2 H, ArH), 7.31 (d, *J* = 8.0 Hz, 2 H, ArH), 7.45–7.48 (m, 2 H, ArH), 7.57–7.61 (m, 1 H, ArH), 7.91–7.93 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 31.5, 44.6, 120.8, 127.4, 128.1, 128.8, 129.9, 132.3, 133.8, 135.8, 138.3, 194.7.

2-(2-Chlorophenyl)-4-oxo-4-phenylbutanenitrile (2f)
Yield: 99%; white solid; mp 100–102 °C (Lit.[27] mp 106–108 °C).

IR (KBr): 1686, 2247 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.53 (dd, *J* = 4.8, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.68 (dd, *J* = 9.2, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 4.93 (dd, *J* = 4.8, 9.2 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.29–7.38 (m, 2 H, ArH), 7.42–7.50 (m, 3 H, ArH), 7.58–7.62 (m, 1 H, ArH), 7.67–7.69 (m, 1 H, ArH), 7.94–7.96 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.1, 42.4, 119.7, 127.8, 128.1, 128.8, 129.5, 129.9, 130.3, 132.7, 133.9, 135.6, 194.4.

2-(2,4-Dichlorophenyl)-4-oxo-4-phenylbutanenitrile (2g)
Yield: 98%; white solid; mp 90–91 °C.

IR (KBr): 1682, 2247 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.52 (dd, *J* = 4.8, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.67 (dd, *J* = 9.2, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 4.88 (dd, *J* = 4.8, 9.2 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.33–7.36 (m, 1 H, ArH), 7.45–7.50 (m, 3 H, ArH), 7.59–7.63 (m, 2 H, ArH), 7.93–7.95 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7, 42.2, 119.3, 128.08, 128.11, 128.9, 130.1, 130.5, 131.3, 133.5, 134.0, 135.3, 135.5, 194.1.

Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.18; H, 3.65; N, 4.60. Found: C, 63.06; H, 3.73; N, 4.65.

2-(3-Nitrophenyl)-4-oxo-4-phenylbutanenitrile (2h)
The purification of **2h** was performed by column chromatography with PE–EtOAc (10:1) as the eluent; yield: 90%; yellowish solid; mp 132–133 °C.

IR (KBr): 1680, 2245 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.61 (dd, *J* = 6.8, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.80 (dd, *J* = 6.8, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 4.72 (dd, *J* = 6.8, 6.8 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.47–7.51 (m, 2 H, ArH), 7.59–7.64 (m, 2 H, ArH), 7.83–7.85 (m, 1 H, ArH), 7.92–7.94 (m, 2 H, ArH), 8.20–8.23 (m, 1 H, ArH), 8.33–8.34 (m, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.6, 43.9, 119.5, 122.8, 123.6, 128.1, 129.0, 130.4, 133.9, 134.2, 135.3, 137.4, 148.7, 193.8.

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99. Found: C, 68.41; H, 4.45; N, 10.09.

2-(2-Chlorophenyl)-4-(4-nitrophenyl)-4-oxobutanenitrile (2i)
The purification of **2i** was performed by column chromatography with PE–EtOAc (10:1) as the eluent; yield: 94%; white solid; mp 126–127 °C.

IR (KBr): 1691, 2252 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.57 (dd, *J* = 4.4, 18.0 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.71 (dd, *J* = 9.6, 18.0 Hz, 1 H, NCCHCH$_\mathrm{A}$$H_B$CO), 4.93 (dd, *J* = 4.4, 9.6 Hz, 1 H, NCC*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.33–7.40 (m, 2 H, ArH), 7.44–7.46 (m, 1 H, ArH), 7.69–7.71 (m, 1 H, ArH), 8.10–8.13 (m, 2 H, ArH), 8.32–8.35 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.0, 42.9, 119.2, 124.1, 127.9, 129.2, 129.5, 130.2, 130.4, 132.1, 132.6, 139.9, 150.8, 193.1.

Anal. Calcd for $C_{16}H_{11}ClN_2O_3$: C, 61.06; H, 3.52; N, 8.90. Found: C, 61.88; H, 3.84; N, 8.87.

2-Methyl-4-oxo-4-phenylbutanenitrile (2j)
Yield: 99%; colorless oil.

IR (film): 1686, 2236 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (d, *J* = 6.8 Hz, 3 H, CH_3), 3.14 (dd, *J* = 6.4, 17.2 Hz, 1 H, NCCHCH_AH$_\mathrm{B}$CO), 3.27 (dd, *J* = 6.4, 13.2 Hz, 1 H, NC-CHCH$_\mathrm{A}$$H_B$CO), 3.24–3.37 (m, 1 H, NC-C*H*CH$_\mathrm{A}$H$_\mathrm{B}$CO), 7.40–7.44 (m, 2 H, ArH), 7.52–7.55 (m, 1 H, ArH), 7.87–7.89 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9, 20.5, 42.2, 122.6, 128.0, 128.8, 133.8, 135.9, 195.1.

4-Oxo-2-propylpentanenitrile (2k)
The purification of **2k** was performed by column chromatography with PE–EtOAc (10:1) as the eluent; yield: 81%; yellowish oil.

IR (film): 1721, 2241 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.0 Hz, 3 H, $\mathrm{C}H_3\mathrm{CH}_2$), 1.50–1.61 (m, 4 H, $\mathrm{CH_3}CH_2CH_2\mathrm{CHCN}$), 2.23 (s, 3 H, $\mathrm{COC}H_3$), 2.70 (dd, *J* = 6.5, 18.0 Hz, 1 H, $\mathrm{NCCHC}H_A\mathrm{H_BCO}$), 2.86 (dd, *J* = 7.0, 18.0 Hz, 1 H, $\mathrm{NCCHCH_A}H_B\mathrm{CO}$), 3.07–3.10 (m, 1 H, $\mathrm{NC}\text{-}\mathrm{C}H\mathrm{CH_AH_BCO}$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.5, 20.4, 25.8, 30.0, 33.8, 45.4, 121.6, 203.8.

2-(2-Oxopropyl)hexanenitrile (2l)

The purification of **2l** was performed by column chromatography with PE–EtOAc (10:1) as the eluent; yield: 98%; yellowish oil.

IR (film): 1721, 2241 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 3 H, $\mathrm{C}H_3\mathrm{CH}_2$), 1.22–1.61 (m, 6 H, $\mathrm{CH_3}CH_2CH_2\,CH_2\mathrm{CHCN}$), 2.20 (s, 3 H, $\mathrm{COC}H_3$), 2.67 (dd, *J* = 6.8, 18.0 Hz, 1 H, $\mathrm{NCCHC}H_A\mathrm{H_BCO}$), 2.87 (dd, *J* = 7.2, 18.0 Hz, 1 H, $\mathrm{NCCHCH_A}H_B\mathrm{CO}$), 3.03–3.07 (m, 1 H, $\mathrm{NC}\text{-}\mathrm{C}H\mathrm{CH_AH_BCO}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 22.1, 25.9, 29.1, 30.0, 31.5, 45.4, 121.6, 203.7.

2-(2-Oxopropyl)heptanenitrile (2m)

The purification of **2m** was performed by column chromatography with PE–EtOAc (10:1) as the eluent; yield: 99%; yellowish oil.

IR (film): 1721, 2241 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.2 Hz, 3 H, $\mathrm{C}H_3\mathrm{CH}_2$), 1.25–1.36 (m, 4 H, $\mathrm{CH_3}CH_2CH_2$), 1.41–1.62 (m, 4 H, $CH_2CH_2\mathrm{CHCN}$), 2.19 (s, 3 H, $\mathrm{COC}H_3$), 2.66 (dd, *J* = 6.8, 18.0 Hz, 1 H, $\mathrm{NCCHC}H_A\mathrm{H_BCO}$), 2.86 (dd, *J* = 7.2, 18.0 Hz, 1 H, $\mathrm{NCCHCH_A}H_B\mathrm{CO}$), 3.00–3.06 (m, 1 H, $\mathrm{NCC}H\mathrm{CH_AH_BCO}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.4, 26.0, 26.7, 30.0, 31.1, 31.8, 45.4, 121.7, 203.7.

Acknowledgment

The authors thank Beijing Institute of Technology and NSFC (20972016) for financial support.

References

(1) (a) Shintani, R.; Hayashi, T. In *New Frontiers in Asymmetric Catalysis*; Mikami, K.; Lautens, M., Eds.; Wiley: New Jersey, **2007**, 59–100. (b) Carruthers, W.; Coldham, I. *Modern Methods of Organic Synthesis*, 4th ed.; Cambridge University Press: Cambridge, **2004**, 1–158.

(2) (a) Shintani, R.; Hayashi, T. *Aldrichimica Acta* **2009**, *42*, 31. (b) Brock, S.; Hose, D. R. J.; Moseley, J. D.; Parker, A. J.; Patel, I.; Williams, A. J. *Org. Process Res. Dev.* **2008**, *12*, 496. (c) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829.

(3) (a) Harutyunyan, S. R.; Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824. (b) López, F.; Minnaard, A. J.; Feringa, B. L. *Acc. Chem. Res.* **2007**, *40*, 179. (c) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346.

(4) For recent examples involving conjugate hydrocyanation of enones in the syntheses of active molecules, see:
(a) Nicolaou, K. C.; Stepan, A. F.; Lister, T.; Li, A.; Montero, A.; Tria, G. S.; Turner, C. I.; Tang, Y.; Wang, J.; Denton, R. M.; Edmonds, D. J. *J. Am. Chem. Soc.* **2008**, *130*, 13110. (b) Vázquez-Romero, A.; Rodríguez, J.; Lledó, A.; Verdaguer, X.; Riera, A. *Org. Lett.* **2008**, *10*, 4509.
(c) Winkler, M.; Knall, A. C.; Kulterer, M. R.; Klempier, N. *J. Org. Chem.* **2007**, *72*, 7423. (d) Hegedus, L. S.; Cross, J. *J. Org. Chem.* **2004**, *69*, 8492.

(5) For recent examples involving conjugate hydrocyanation of enones in the syntheses of natural products, see:
(a) Siwicka, A.; Cuperly, D.; Tedeschi, L.; Le Vézouët, R.; White, A. J. P.; Barrett, A. G. M. *Tetrahedron* **2007**, *63*, 5903. (b) Muratake, H.; Natsume, M. *Tetrahedron* **2006**, *62*, 7071. (c) Mander, L. N.; Thomson, R. J. *J. Org. Chem.* **2005**, *70*, 1654. (d) Rahman, S. M. A.; Ohno, H.; Yoshino, H.; Satoh, N.; Tsukaguchi, M.; Murakami, K.; Iwata, C.; Maezaki, N.; Tanaka, T. *Tetrahedron* **2001**, *57*, 127.
(e) Rahman, S. M. A.; Ohno, H.; Maezaki, N.; Iwata, C.; Tanaka, T. *Org. Lett.* **2000**, *2*, 2893.

(6) Utimoto, K.; Obayashi, M.; Shishiyama, Y.; Inoue, M.; Nozaki, H. *Tetrahedron Lett.* **1980**, *21*, 3389.

(7) Nagata, W.; Yoshioka, M. *Org. React.* **1977**, *25*, 255; and references cited therein.

(8) (a) Utimoto, K.; Wakabayashi, Y.; Horiie, T.; Inoue, M.; Shishiyama, Y.; Obayashi, M.; Nozaki, H. *Tetrahedron* **1983**, *39*, 967. (b) Gerus, I. I.; Kruchok, I. S.; Kukhar, V. P. *Tetrahedron Lett.* **1999**, *40*, 5923.

(9) Hayashi, M.; Kawabata, H.; Shimono, S.; Kakehi, A. *Tetrahedron Lett.* **2000**, *41*, 2591.

(10) Yadav, L. D. S.; Awasthi, C.; Rai, A. *Tetrahedron Lett.* **2008**, *49*, 6360.

(11) Iida, H.; Moromizato, T.; Hamana, H.; Matsumoto, K. *Tetrahedron Lett.* **2007**, *48*, 2037.

(12) (a) Yamatsugu, K.; Kamijo, S.; Suto, Y.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2007**, *48*, 1403. (b) Fukuta, Y.; Mita, T.; Fukuda, N.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 6312.

(13) Tanaka, Y.; Kanai, M.; Shibasaki, M. *Synlett* **2008**, 2295.

(14) Tanaka, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2008**, *130*, 6072.

(15) For examples of asymmetric addition of Me_3SiCN to α,β-unsaturated imides, see: (a) Mazet, C.; Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2008**, *47*, 1762. (b) Madhavan, N.; Weck, M. *Adv. Synth. Catal.* **2008**, *350*, 419. (c) Fujimori, I.; Mita, T.; Maki, K.; Shiro, M.; Sato, A.; Furusho, S.; Kanai, M.; Shibasaki, M. *Tetrahedron* **2007**, *63*, 5820.
(d) Mita, T.; Sasaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 514. (e) Sammis, G. M.; Danjo, H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 9928.
(f) Sammis, G. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2003**, *125*, 4442.

(16) Yang, J.; Wang, Y.; Wu, S.; Chen, F.-X. *Synlett* **2009**, 3365.

(17) For reviews on Cs_2CO_3, see: (a) Lehmann, F. *Synlett* **2004**, 2447. (b) Flessner, T.; Doye, S. *J. Prakt. Chem.* **1999**, *341*, 186.

(18) (a) Ye, L.-W.; Wang, S.-B.; Wang, Q.-G.; Sun, X.-L.; Tang, Y.; Zhou, Y.-G. *Chem. Commun.* **2009**, 3092. (b) Enders, D.; Han, J.; Henseler, A. *Chem. Commun.* **2008**, 3989.
(c) Zare, A.; Hasaninejad, A.; Safinejad, R.; Moosavi-Zare, A. R.; Khalafi-Nezhad, A.; Beyzavi, M. H.; Miralai-Moredi, M.; Dehghani, E.; Kazerooni-Mojarrad, P. *ARKIVOC* **2008**, *(xvi)*, 61. (d) Ganguly, D.; Tang, H.; Rodriguez, M. J. *Synth. Commun.* **2007**, *37*, 4219. (e) Snider, B. B.; Wu, X.; Nakamura, S.; Hashimoto, S. *Org. Lett.* **2007**, *9*, 873.
(f) Lygo, B.; Allbutt, B.; Kirton, E. H. M. *Tetrahedron Lett.* **2005**, *46*, 4461. (g) Ooi, T.; Fujioka, S.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 11790. (h) Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2001**, *57*, 9827.
(i) Desmaële, D.; Louvet, J.-M. *Tetrahedron Lett.* **1994**, *35*, 2549. (j) Ouvrard, N.; Rodriguez, J.; Santelli, M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1651.

(19) For reviews on the 'cesium effect', see: (a) Ostrowicki, A.; Koepp, E.; Vögtle, F. In *Topics in Current Chemistry*, Vol.

161; Weber, E.; Vögtle, F., Eds.; Springer: Heidelberg, **1992**, 37–67. (b) Galli, C. *Org. Prep. Proced. Int.* **1992**, *24*, 285.

(20) For reviews on water in organic reactions, see: (a) Marcus, Y. *Chem. Rev.* **2009**, *109*, 1346. (b) Chanda, A.; Fokin, V. V. *Chem. Rev.* **2009**, *109*, 725. (c) Blackmond, D. G.; Armstrong, A.; Coombe, V.; Wells, A. *Angew. Chem. Int. Ed.* **2007**, *46*, 3798. (d) Garrett, B. C.; Dixon, D. A.; Camaioni, D. M.; Chipman, D. M.; Johnson, M. A.; Jonah, C. D.; Kimmel, G. A.; Miller, J. H.; Rescigno, T. N.; Rossky, P. J.; Xantheas, S. S.; Colson, S. D.; Laufer, A. H.; Ray, D.; Barbara, P. F.; Bartels, D. M.; Becker, K. H.; Bowen, K. H.; Bradforth, S. E.; Carmichael, I.; Coe, J. V.; Corrales, L. R.; Cowin, J. P.; Dupuis, M.; Eisenthal, K. B.; Franz, J. A.; Gutowski, M. S.; Jordan, K. D.; Kay, B. D.; LaVerne, J. A.; Lymar, S. V.; Madey, T. E.; McCurdy, C. W.; Meisel, D.; Mukamel, S.; Nilsson, A. R.; Orlando, T. M.; Petrik, N. G.; Pimblott, S. M.; Rustad, J. R.; Schenter, G. K.; Singer, S. J.; Tokmakoff, A.; Wang, L.-S.; Wittig, C.; Zwier, T. S. *Chem. Rev.* **2005**, *105*, 355.

(21) (a) Prakash, G. K. S.; Vaghoo, H.; Panja, C.; Surampudi, V.; Kultyshev, R.; Mathew, T.; Olah, G. A. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 3026. (b) He, B.; Li, Y.; Feng, X.; Zhang, G. *Synlett* **2004**, 1776. For examples of CsF-catalyzed silylcyanation of ketones, see: (c) Kim, S. S.; Rajagopal, G.; Song, D. H. *J. Organomet. Chem.* **2004**, *689*, 1734. (d) Kim, S. S.; Song, D. H. *Lett. Org. Chem.* **2004**, *1*, 264.

(22) Shen, K.; Liu, X.; Cai, Y.; Lin, L.; Feng, X. *Chem. Eur. J.* **2009**, *15*, 6008.

(23) For reviews on hypervalent silicon, see: (a) Denmark, S. E.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 1560. (b) Benaglia, M.; Guizzetti, S.; Pignataro, L. *Coord. Chem. Rev.* **2008**, *252*, 492. (c) Orito, Y.; Nakajima, M. *Synthesis* **2006**, 1391. (d) Rendler, S.; Oestreich, M. *Synthesis* **2005**, 1727. (e) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371. For early example of nucleophilic activation, see: (f) Holmes, I. P.; Kagan, H. B. *Tetrahedron Lett.* **2000**, *41*, 7453.

(24) For most recent reviews on dual activation, see: (a) Shibasaki, M.; Kanai, M.; Matsunaga, S.; Kumagai, N. *Acc. Chem. Res.* **2009**, *42*, 1117. (b) Liu, X.; Lin, L.; Feng, X. *Chem. Commun.* **2009**, 6145. (c) Bhadury, P. S.; Song, B. A.; Yang, S.; Hu, D. Y.; Xue, W. *Curr. Org. Synth.* **2009**, *6*, 380. (d) Paull, D. H.; Abraham, C. J.; Scerba, M. T.; Alden-Danforth, E.; Lectka, T. *Acc. Chem. Res.* **2008**, *41*, 655. (e) Motokura, K.; Tada, M.; Iwasawa, Y. *Chem. Asian J.* **2008**, *3*, 1230.

(25) Preliminary studies on asymmetric version of this protocol yielded racemic product using alkali metal salt of L-proline or chiral sodium phosphate as catalysts in the 1,4-addition of Me_3SiCN to chalcone (**1a**) in refluxing dioxane.

(26) (a) Moulton, B. E.; Duhme-Klair, A. K.; Fairlamb, I. J. S.; Lynam, J. M.; Whitwood, A. C. *Organometallics* **2007**, *26*, 6354. (b) Isleyen, A.; Dogan, Ö. *Tetrahedron: Asymmetry* **2007**, *18*, 679. (c) Ansari, F. L.; Nazir, S.; Noureen, H.; Mirza, B. *Chemistry & Biodiversity* **2005**, *2*, 1656.

(27) Davis, R. B. *J. Org. Chem.* **1959**, *24*, 879.