Indium(III)-Catalyzed One-Pot Synthesis of Alkyl Cyanides from Carboxylic Acids

Toshimitsu Moriya, Kohei Shoji, Shinichiro Yoneda, Reiko Ikeda, Takeo Konakahara, Norio Sakai*

Department of Pure and Applied Chemistry, Faculty of Science and Technology, Tokyo University of Science (RIKADAI), Noda, Chiba 278-8510, Japan
Fax +81(4)71239890; E-mail: sakachem@rs.noda.tus.ac.jp

Received: 10.08.2013; Accepted after revision: 12.09.2013

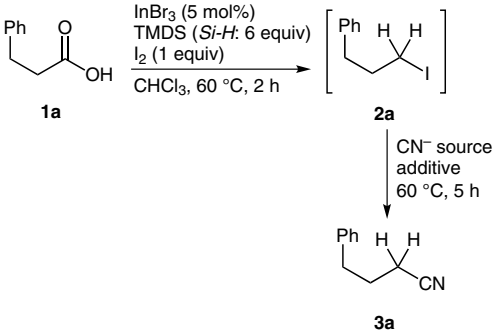
Abstract: The one-pot preparation of alkyl cyanides from carboxylic acids via alkyl iodides or alkyl bromides, which were in situ generated either by indium(III)-catalyzed reductive iodination or bromination of carboxylic acids, is described.

Key words: indium, deoxygenation, halogenation, carboxylic acids, nitriles

Cyanides behave as a central building block or precursor for an easy preparation of ketones, aldehydes, primary amines, and carboxylic acids in organic synthesis and pharmaceutical chemistry.[1] For example, cyanides are easily converted to primary amines by hydrogenation, or can be transformed to a carboxylic acid and its derivative by hydrolysis under basic conditions.[2] Also, the conventional method for the preparation of cyanides has been an S_N2 reaction of alkyl halides with metal cyanides, such as potassium cyanide and sodium cyanide.[3] Metal cyanides generally have high toxicity, which has led to an avoidance of their use even in laboratory-scale synthesis. To overcome these problems, in the past two decades, trimethylsilyl cyanide (Me_3SiCN), which has low toxicity but less reactivity than metal cyanides, has been used as a nitrile surrogate.[4] Thus far, various functional group conversions by the combination of an indium(III) compound and Me_3SiCN have been achieved. For instance, the Indium(III)-catalyzed direct conversion of α-aryl alcohols into α-aryl cyanides, and the 1,2- or 1,4-addition of Me_3SiCN to enones have been disclosed.[5,6] To the best of our knowledge, however, there has been no report on the reductive one-pot conversion of carboxylic acids to nitriles. Therefore, we developed the chemoselective reduction of a carbonyl group of esters, amides, and carboxylic acids by indium tribromide ($InBr_3$) and triethylsilane.[7] Along with the reducing system, we also developed a chemoselective reduction of carboxylic acids and a facile preparation of alkyl bromides.[8] During these ongoing studies, we noticed that the utility of this reducing system could be applied to a one-pot synthesis of alkyl cyanides from carboxylic acids by the addition of a cyanide ion source to an in situ generated alkyl halide intermediate. Herein, we report the first example of a one-pot synthesis of alkyl cyanides via the $InBr_3$-catalyzed reductive bromination/iodination of carboxylic acids.

When 3-phenylpropionic acid (**1a**) was initially treated with $InBr_3$ (5 mol%), tetramethyldisiloxane (TMDS) (Si–H: 6 equiv), and I_2 (1 equiv) at 60 °C in chloroform for 1 hour, the corresponding iodide **2a** was formed in quantitative yield. Then, to directly transform the alkyl iodide into the nitrile in the same pot, tetrabutylammonium cyanide (TBACN) (2 equiv) was added to the reaction mixture, which led to a conversion to the desired 1-cyano-3-phenylpropane (**3a**) in a 60% yield (Table 1, entry 1). Instead of TBACN, which has high toxicity and hygroscopicity, Me_3SiCN was then used as a cyanide ion source not to produce the expected alkyl cyanide **3a**, but to recover the alkyl iodide **2a** in quantitative yield (entry 2). This result showed that cleavage of the Si–C bond of Me_3SiCN did not occur under the conditions. Thus, to generate the free cyanide, a mixture of potassium fluoride (2 equiv) and 18-crown-6-ether (2 equiv), which captures the potassium

Table 1 Examination of Cyanide Anion Source

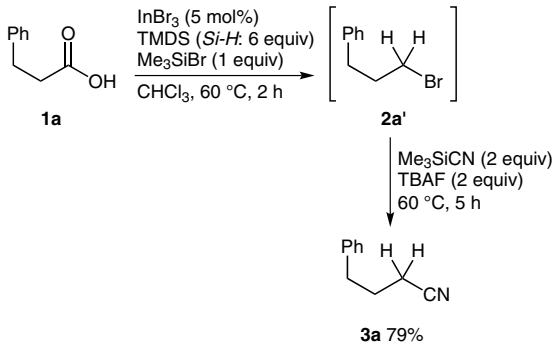


Entry	CN^- source (equiv)	Additive (equiv)	Yield (%)[a]	
			2a	**3a**
1	TBACN (2)	none	ND[b]	60
2	Me_3SiCN (2)	none	99	ND[b]
3	Me_3SiCN (2)	KF (2) 18-crown-6-ether (2)	ND[b]	93
4	Me_3SiCN (2)	TBAF (2)	ND[b]	95[c]
5	Me_3SiCN (2)	TBAF (1)	trace	51

[a] GC yield.
[b] ND: Not detected.
[c] Isolated yield.

SYNTHESIS 2013, 45, 3233–3238
Advanced online publication: 27.09.2013
DOI: 10.1055/s-0033-1339903; Art ID: SS-2013-F0561-OP

cation, were added to the resultant solution, and, as expected, the yield of the alkyl cyanide **3a** was improved to 93% (entry 3). Similarly, the use of tetrabutylammonium fluoride (TBAF) also had the predictive effect of producing alkyl cyanide **3a** in quantitative yield (entry 4). These results showed that a hypervalent cyanosilicate,[9] which functioned as a nucleophilic cyanide source, was in situ generated from TBAF and Me_3SiCN. However, in the case of using one equivalent of TBAF, the yield of the alkyl cyanide declined to a moderate amount, possibly because the remaining silane deactivated the TBAF (entry 5). Hence, the fluoride anion source required 2 equivalents to complete the cyanation. Instead, when a trimethylsilyl bromide (Me_3SiBr) was used, as the bromide source, the same alkyl cyanide **3a** was obtained in a good yield through the alkyl bromide intermediate **2a′** (Scheme 1).

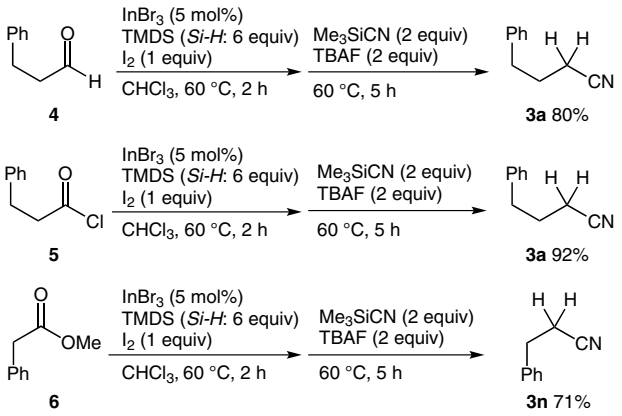


Scheme 1 One-pot synthesis of the cyanide via the alkyl bromide

To generalize this reaction, a one-pot synthesis of various alkyl cyanides from carboxylic acids was carried out under optimal conditions (Table 2). The reaction was carried out by two methods, either through alkyl iodides (method A) or alkyl bromides (method B).[10] When the reaction was conducted with an aliphatic carboxylic acid **1b**, the corresponding cyanide **3b** was obtained in a 76% yield via the alkyl bromide (method B) (Table 2, entry 2). However, a similar reaction via an alkyl iodide (method A) did not form the desired product **3b**, but instead the intramolecular Friedel–Crafts product, 1,2,3,4-tetrahydronaphthalene (**3b′**), was formed in quantitative yield. Carboxylic acids bearing a fluorenyl or a naphthyl group were transformed into the expected cyanides **3c** and **3d** in high yields via method B (entries 2 and 3). Functional groups, such as methyl, halogens, and hydroxy group, tolerated the reducing conditions (entries 4–8). The use of benzoic acid (**1j**) did not produce the expected cyanide **3j** (entry 9). In this case, it seemed that the corresponding intermediate, such as benzyl iodide or benzyl bromide, was formed in situ during the reaction. However, these intermediates might decompose under this reducing conditions.[11] Benzoic acids bearing an electron-withdrawing group, such as a trifluoromethyl group, underwent cyanation to produce the expected cyanide **3k** in practical yields (entry 10). The cyanation of dicarboxylic acid, **1l**, was effectively achieved by double doses of the reagents (entry 11). Although the yield of the cyanide **3m** was low, the synthesis of the cyanide with a thioether moiety was also successful (entry 12).[12]

In addition, this cyanation was extended to a large-scale synthesis (10.0 mmol, 1.50 g) of 3-phenylpropionic acid (**1a**) as under method A. The reaction proceeded smoothly, and 3-phenylpropyl cyanide (**3a**) was obtained in 85% yield (1.23 g).

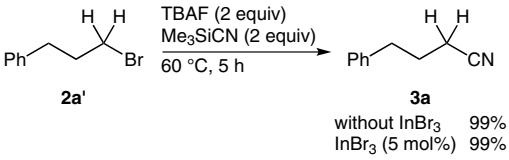
To expand the range of applicable substrates, various carbonyl compounds, such as an aldehyde, an acyl halide, and an ester were applied to this reaction system (Scheme 2). For instance, 3-phenylpropanal (**4**) was treated with $InBr_3$ (5 mol%), TMDS (Si–H: 6 equiv), and I_2 (1 equiv) in chloroform at 60 °C for two hours in situ to form the corresponding alkyl iodide. The successive addition of TBAF (2 equiv) and Me_3SiCN (2 equiv) to the iodide and stirring at 60 °C for five hours gave the expected alkyl cyanide **3a** in an 80% yield.



Scheme 2 One-pot synthesis of cyanides from various carbonyl compounds

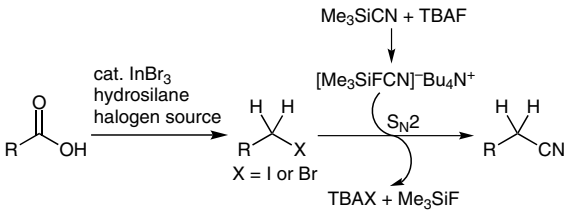
By using the same treatment, the acyl chloride **5** and the ester **6** also produced the corresponding alkyl cyanides **3a** and **3n** in good to high yields.

To demonstrate the role of $InBr_3$ in the nucleophilic cyanation series, 1-bromo-3-phenylpropane (**2a′**), TBAF (2 equiv), and Me_3SiCN (2 equiv) reacted either with $InBr_3$ or without the catalyst (Scheme 3). Without reference to the addition of $InBr_3$, because cyanation also proceeded to produce cyanide **3a** in quantitative yield, these results showed that $InBr_3$ did not participate in the cyanation step.



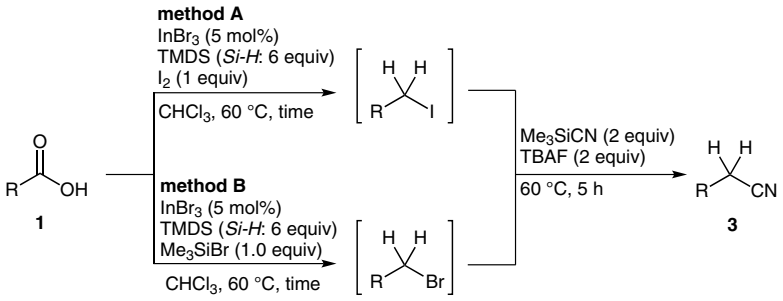
Scheme 3 Control experiments for the cyanation of alkyl bromide

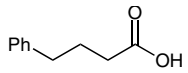
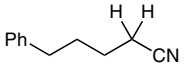
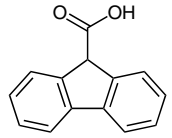
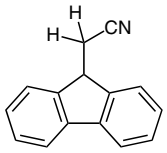
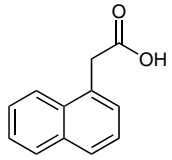
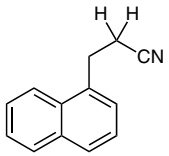
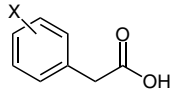
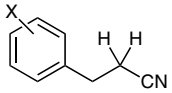
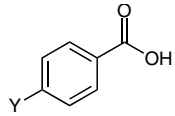
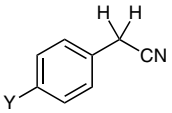
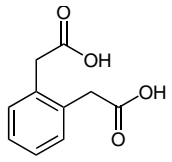
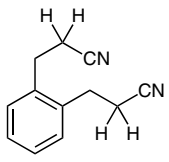
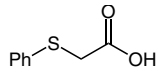
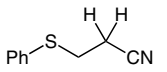
Based on these control experiments, a reaction pathway for the one-pot synthesis of alkyl cyanides from carboxylic acids is shown in Scheme 4. First, the $InBr_3$-catalyzed reductive bromination or iodination of carboxylic acids occurred to form the corresponding alkyl bromides or iodides.[8] Then, nucleophilic substitution with $[Me_3SiFCN]^-Bu_4N^+$, which was generated in situ from Me_3SiCN and TBAF,[9] produced the desired alkyl cyanides.



Scheme 4 Plausible reaction pathway

Table 2 One-Pot Synthesis of Alkyl Cyanides from Carboxylic Acids



Entry	Substrate			Method	Time (h)	Product			Yield (%)[a]
1			**1b**	A B	0.5 4			**3b**	ND[b] 76
2			**1c**	B	1			**3c**	87
3			**1d**	B	1			**3d**	96
4		X = 2-Me	**1e**	B	1		X = 2-Me	**3e**	96
5		X = 4-Cl	**1f**	A	3		X = 4-Cl	**3f**	81
6		X = 4-Br	**1g**	A	2		X = 4-Br	**3g**	83
7		X = 2-I	**1h**	B	1		X = 2-I	**3h**	72
8		X = 4-OH	**1i**	B	1		X = 4-OH	**3i**	91
9		Y = H	**1j**	A B	1 2		Y = H	**3j**	ND[b] ND[b]
10		Y = CF_3	**1k**	B	2		Y = CF_3	**3k**	79
11[c]			**1l**	B	1			**3l**	66
12			**1m**	A B	0.5 0.5			**3m**	34 31

[a] Isolated yield.
[b] ND: Not detected.
[c] Double doses of catalyst and reagent were used.

In summary, we have demonstrated the one-pot synthesis of alkyl cyanides from carboxylic acids via alkyl bromides or iodides by $InBr_3$-catalyzed reductive bromination or iodination. The procedure could also apply to the transformation of other carbonyl compounds, such as aldehydes, acyl chlorides, and esters. The investigation on the transformation of carboxylic acids to other functional groups is ongoing in our laboratory.

NMR spectra were recorded on JMN-EPC-500 (JEOL) or JMN-AL-300 (JEOL) spectrometers. ^{1}H NMR spectra were recorded at 500 (or 300) MHz using TMS as an internal standard. ^{13}C NMR spectra were recorded at 125 (or 75) MHz using the residual solvent resonances, respectively. High-resolution mass spectra (EI) were recorded on GC-Mate (JEOL) spectrometer. IR spectra were recorded on a Nicolet Continuum (Thermo) spectrometer. TLC was carried out on silica gel 60 F_{254}. Column chromatography was performed by silica gel 60 F_{254}. Experimental manipulations were carried out under an N_2 atmosphere, unless otherwise noted. $CHCl_3$ was distilled from P_2O_5 and then redistilled again from K_2CO_3, and was kept over molecular sieves (4 Å). $InBr_3$, I_2, Me_3SiBr, tetramethyldisiloxane, Bu_4NF (1 M THF solution), Me_3SiCN, and carboxylic acids **1** were commercially available, and were used without further purification.

One-Pot Synthesis of Alkyl Cyanides from Carboxylic Acids; General Procedure

Method A: To a 5 mL screw-capped vial under a N_2 atmosphere containing freshly distilled $CHCl_3$ (0.6 mL) were successively added the respective carboxylic acid **1** (0.6 mmol), $InBr_3$ (10.6 mg, 0.0300 mmol), 1,1,3,3-tetramethyldisiloxane (318 μL, 1.80 mmol), and I_2 (152 mg, 0.0600 mmol). The resultant mixture was heated at 60 °C (bath temperature) and the consumption of the starting acid was monitored via GC analysis during the reaction time given in Table 2. After this process, to the resultant mixture was added a THF solution (1 mol/L) of Bu_4NF (1.2 mL, 1.2 mmol) and Me_3SiCN (1.20 mmol, 149 μL). The resultant mixture was further heated at 60 °C (bath temperature) for 5 h. The reaction was quenched with aq Na_2CO_3 (1 mL). The aqueous layer was extracted with EtOAc (3 × 5 mL), and the combined organic phases were dried (Na_2SO_4), then filtered, and evaporated under reduced pressure. The crude product was purified via silica gel chromatography (hexane–EtOAc, 99:1) to give the corresponding cyanide **3**.

Method B: To a 5 mL screw-capped vial under an N_2 atmosphere containing freshly distilled $CHCl_3$ (0.6 mL) were successively added the respective carboxylic acid **1** (0.6 mmol), $InBr_3$ (10.6 mg, 0.0300 mmol), 1,1,3,3-tetramethyldisiloxane (318 μL, 1.80 mmol), and Me_3SiBr (78.0 μL, 0.600 mmol). The resultant mixture was heated at 60 °C (bath temperature) and the consumption of the starting acid was monitored via GC analysis during the reaction time given in Table 2. After this process, to the resultant mixture was added a THF solution (1 mol/L) of Bu_4NF (1.2 mL, 1.2 mmol) and Me_3SiCN (1.20 mmol, 149 μL). The resultant mixture was further heated at 60 °C (bath temperature) for 5 h. The reaction was quenched with aq Na_2CO_3 (1 mL). The aqueous layer was extracted with EtOAc (3 × 5 mL), and the combined organic phases were dried (Na_2SO_4), then filtered, and evaporated under reduced pressure. The crude product was purified via silica gel chromatography (hexane–EtOAc, 99:1) to give the corresponding cyanide **3**.

Compounds **1a**–**m**, **4**, **5**, and **6** were commercially available. The compounds **3a**,[13] **3b**,[14] **3b′**,[15] **3d**,[16] **3f**,[17] **3i**,[18] **3k**,[19] **3m**,[20] and **3n**[21] shown in Table 2 and Scheme 2 were previously reported in the corresponding literature.

3-Phenylpropyl Cyanide (3a)[13]
Yield: 82.7 mg (95%); yellow oil.

IR (neat): 2247 cm^{-1} (CN).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.90 (quint, *J* = 7.5 Hz, 2 H), 2.30 (t, *J* = 7.5 Hz, 2 H), 2.77 (t, *J* = 7.5 Hz, 2 H), 7.18–7.21 (m, 3 H), 7.27–7.30 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.3, 26.8, 34.3, 119.4, 126.4, 128.4, 128.6, 139.6.

MS (EI): *m*/*z* = 145 (M^+, 100%).

4-Phenylbutyl Cyanide (3b)[14]
Yield: 72.5 mg (76%); yellow oil.

IR (neat): 2247 cm^{-1} (CN).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.56–1.72 (m, 2 H), 1.75–1.82 (m, 2 H), 2.34 (t, *J* = 7.5 Hz, 2 H), 2.66 (t, *J* = 7.5 Hz, 2 H), 7.16–7.20 (m, 3 H), 7.26–7.30 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.0, 24.8, 30.2, 35.0, 119.5, 126.1, 128.3, 128.4, 141.2.

MS (EI): *m*/*z* = 159 (M^+, 100%).

1,2,3,4-Tetrahydronaphthalene (3b′)[15]
Yield: 71.4 mg (90%); colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48–1.81 (m, 4 H), 2.74–2.76 (m, 4 H), 7.03–7.10 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.2, 29.4, 125.4, 129.1, 137.1.

MS (EI): *m*/*z* (%) = 132 (M^+, 75), 104 (M^+ – 18, 100).

9-(Cyanomethyl)fluorene (3c)
Yield: 107.1 mg (87%); yellow solid; mp 132–134 °C.

IR (KBr): 2251 cm^{-1} (CN).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.82 (d, *J* = 7.5 Hz, 2 H), 4.18 (t, *J* = 7.5 Hz, 1 H), 7.33–7.37 (m, 2 H), 7.38–7.47 (m, 2 H), 7.67 (d, *J* = 7.2 Hz, 2 H), 7.78 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 42.9, 118.4, 120.3, 124.3, 127.6, 128.4, 140.8, 143.9.

MS (EI): *m*/*z* (%) = 205 (M^+, 70), 165 (M^+ – 40, 100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{11}N$: 205.0891; found: 205.0911.

1-(2-Cyanoethyl)naphthalene (3d)[16]
Yield: 104.4 mg (96%); dark red oil.

IR (neat): 2247 cm^{-1} (CN).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.77 (t, *J* = 7.5 Hz, 2 H), 3.45 (t, *J* = 7.5 Hz, 2 H), 7.39–7.47 (m, 2 H), 7.50–7.59 (m, 2 H), 7.79–7.81 (m, 1 H), 7.89–7.94 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.4, 28.7, 119.1, 122.6, 125.6, 125.9, 126.5, 128.1, 129.1, 131.0, 133.8, 133.9 (one signal was not observed due to overlapping).

MS (EI): *m*/*z* (%) = 181 (M^+, 50), 141 (M^+ – 40, 100).

2-Methylphenethyl Cyanide (3e)
Yield: 83.6 mg (96%); yellow oil.

IR (neat): 2247 cm^{-1} (CN).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.33 (s, 3 H), 2.58 (t, *J* = 7.5 Hz, 2 H), 2.98 (t, *J* = 7.5 Hz, 2 H), 7.16–7.19 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.0, 19.1, 28.9, 119.1, 126.5, 127.4, 128.7, 130.6, 135.8, 136.2.

MS (EI): *m*/*z* = 145 (M^+, 100%).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{10}H_{11}N$: 145.0891; found: 145.0908.

4-Chlorophenethyl Cyanide (3f)[17]
Yield: 80.5 mg (81%); yellow oil.

IR (neat): 2247 cm^{-1} (CN).

^1H NMR (500 MHz, $CDCl_3$): δ = 2.62 (t, *J* = 7.5 Hz, 2 H), 2.94 (t, *J* = 7.5 Hz, 2 H), 7.16–7.20 (m, 2 H), 7.30–7.34 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.3, 30.9, 118.7, 129.0, 129.6, 133.2, 136.4.

MS (EI): *m*/*z* (%) = 165 (M^+, 100), 166 (M^+ + 1, 10), 167 (M^+ + 2, 30), 168 (M^+ + 3, 5).

4-Bromophenethyl Cyanide (3g)
Yield: 104.6 mg (83%); yellow oil.

IR (neat): 2247 cm^{-1} (CN).

^1H NMR (500 MHz, $CDCl_3$): δ = 2.61 (t, *J* = 7.5 Hz, 2 H), 2.9 (t, *J* = 7.5 Hz, 2 H), 7.10–7.13 (m, 2 H), 7.45–7.48 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2, 30.9, 118.7, 121.2, 130.0, 132.0, 136.9.

MS (EI): *m*/*z* (%) = 209 (M^+, 70), 211 (M^+ + 2, 70), 169 (M^+ – 40, 100).

HRMS (EI): *m*/*z* calcd for C_9H_8BrN: 208.9840; found: 208.9830.

2-Iodophenethyl Cyanide (3h)
Yield: 111.1 mg (72%); yellow oil.

IR (neat): 2247 cm^{-1} (CN).

^1H NMR (500 MHz, $CDCl_3$): δ = 2.63–2.68 (m, 2 H), 3.05–3.09 (m, 2 H), 6.96–6.99 (m, 1 H), 7.30–7.36 (m, 2 H), 7.83–7.85 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.8, 36.5, 99.7, 118.6, 128.9, 129.2, 129.9, 139.8, 140.4.

MS (EI): *m*/*z* = 257 (M^+, 100%).

HRMS (EI): *m*/*z* calcd for C_9H_8IN: 256.9701; found: 256.9717.

4-Hydroxyphenethyl Cyanide (3i)[18]
Yield: 80.4 mg (91%); yellow oil.

IR (neat): 2253 cm^{-1} (CN).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.59 (t, *J* = 7.5 Hz, 2 H), 2.89 (t, *J* = 7.5 Hz, 2 H), 5.17 (s, 1 H), 6.77–6.81 (m, 2 H), 7.07–7.12 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7, 30.7, 115.7, 119.2, 129.5, 130.1, 154.8.

MS (EI): *m*/*z* (%) = 147 (M^+, 20), 107 (M^+ – 40, 100).

4-(Trifluoromethyl)benzyl Cyanide (3k)[19]
Yield: 87.8 mg (79%); yellow oil.

IR (neat): 2254 cm^{-1} (CN).

^1H NMR (500 MHz, $CDCl_3$): δ = 3.83 (s, 2 H), 7.47 (d, *J* = 8.0 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.6, 117.0, 123.9 (q, $J_{C,F}$ = 271.9 Hz), 126.2 (q, $J_{C,F}$ = 3.9 Hz), 128.4, 130.6 (q, $J_{C,F}$ = 32.6 Hz), 134.0.

MS (EI): *m*/*z* (%) = 185 (M^+, 70), 116 (M^+ – 69, 100).

1,2-Bis(2-cyanoethyl)benzene (3l)
Yield: 73.0 mg (66%); yellow oil.

IR (neat): 2256 cm^{-1} (CN).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.64 (t, *J* = 7.5 Hz, 4 H), 3.02 (t, *J* = 7.5 Hz, 4 H), 7.21–7.31 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.9, 27.9, 118.8, 128.0, 129.4, 135.8.

MS (EI): *m*/*z* (%) = 184 (M^+, 40), 144 (M^+ – 40, 100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{12}N_2$: 184.1000; found: 184.1022.

Phenylthioethyl Cyanide (3m)[20]
Yield: 33.3 mg (34%); yellow oil.

IR (neat): 2251 cm^{-1} (CN).

^1H NMR (500 MHz, $CDCl_3$): δ = 2.59 (t, *J* = 7.5 Hz, 2 H), 3.13 (t, *J* = 7.5 Hz, 2 H), 7.26–7.42 (m, 3 H), 7.42–7.44 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.2, 30.2, 117.9, 127.7, 129.3, 131.4, 133.1.

MS (EI): *m*/*z* (%) = 163 (M^+, 70), 123 (M^+ – 40, 100).

2-Phenylethyl Cyanide (3n)[21]
Yield: 55.9 mg (71%); yellow oil.

IR (neat): 2248 cm^{-1} (CN).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.62 (t, *J* = 7.5 Hz, 2 H), 2.96 (t, *J* = 7.5 Hz, 2 H), 7.22–7.37 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3, 31.5, 119.1, 127.2, 128.2, 128.9, 138.0.

MS (EI): *m*/*z* (%) = 131 (M^+, 90), 91 (M^+ – 40, 100).

Acknowledgment

This work was partially supported by a Grant-in-Aid for Scientific Research (C) (No. 25410120) supported by MEXT, and by a grant from the CCIS program supported by MEXT. The authors thank Shin-Etsu Chemical Co., Ltd., for a gift of the hydrosilanes.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

References

(1) *The Chemistry of the Cyano Group*; Rappoport, Z., Ed.; Wiley-Interscience: London, **1970**.
(2) For some recent examples of functional transformations of cyanides, see: (a) Addis, D.; Enthaler, S.; Junge, K.; Wendt, B.; Beller, M. *Tetrahedron Lett.* **2009**, *50*, 3654. (b) Enthaler, S.; Addis, D.; Junge, K.; Erre, G.; Beller, M. *Chem. Eur. J.* **2008**, *14*, 9491. (c) Saavedra, J. Z.; Resemdez, A.; Rovira, A.; Eagon, S.; Haddenham, D.; Singaram, B. J. *J. Org. Chem.* **2012**, *77*, 221. (d) Lee, W.-C.; Sears, J. M.; Enow, R. A.; Eads, K.; Krogstad, D. A.; Frost, B. J. *Inorg. Chem.* **2013**, *52*, 1737.
(3) Furukawa, N.; Kishimoto, K.; Ogawa, S.; Kawai, T.; Fujihara, H.; Oae, S. *Tetrahedron Lett.* **1981**, *22*, 4409.
(4) For recent examples on the reactions using Me_3SiCN, see: Soleimani, E. *Synlett* **2007**, 1625; and references cited therein.
(5) Chen, G.; Wang, Z.; Wu, J.; Ding, K. *Org. Lett.* **2008**, *10*, 4573.
(6) Bandini, M.; Cozzi, G. P.; Giacomini, M.; Melchiorre, P.; Selva, S.; Umani-Ronchi, A. J. *J. Org. Chem.* **2002**, *67*, 3700.
(7) (a) Sakai, N.; Moriya, T.; Konakahara, T. *J. Org. Chem.* **2007**, *72*, 5920. (b) Sakai, N.; Fujii, K.; Konakahara, T. *Tetrahedron Lett.* **2008**, *49*, 6873. (c) Sakai, N.; Moriya, T.; Fujii, K.; Konakahara, T. *Synthesis* **2008**, 3533. (d) Sakai, N.; Nagasawa, K.; Ikeda, R.; Nakaike, Y.; Konakahara, T. *Tetrahedron Lett.* **2011**, *52*, 3133. (e) Sakai, N.; Usui, Y.; Ikeda, R.; Konakahara, T. *Adv. Synth. Catal.* **2011**, *353*, 3397. (f) Sakai, N.; Kawana, K.; Ikeda, R.; Nakaike, Y.; Konakahara, T. *Eur. J. Org. Chem.* **2011**, 3178. (g) Sakai, N.; Usui, Y.; Moriya, T.; Ikeda, R.; Konakahara, T. *Eur. J. Org. Chem.* **2012**, 4603.

(8) Bromination of carboxylic acids with this reducing system was already communicated, see: Moriya, T.; Yoneda, S.; Kawana, K.; Ikeda, R.; Konakahara, T.; Sakai, N. *Org. Lett.* **2012**, *14*, 4842.
(9) Hypervalent trimethylfluorocyanosilicate $[Me_3SiFCN]^-$ Bu_4N^+ was generated from Me_3SiCN (1 equiv) and TBAF (1 equiv) in situ and used without further purification. For the preparation of cyanosilicate, see: Soli, D. E.; Manoso, S. A.; Patterson, C. M.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 3171.
(10) The reactivity and handling of the cyanation by either method A or method B were almost equivalent. However, in several cases, method A produced unidentified by-products, which precluded isolating the desired alkyl cyanides.
(11) When benzyl bromide was treated with a mixture of TBAF and Me_3SiCN in the absence of both $InBr_3$ and TMDS, the corresponding cyanation product was obtained in good yield.
(12) It seemed that due to the decomposition of the phenylthio moiety, the yield of the product was low. Practically, the prolonged reaction time led to decomposition preventing the isolation of the product **3m**.
(13) Chiba, S.; Zhang, L.; Ang, Y. G.; Hui, W. B. *Org. Lett.* **2010**, *12*, 2052.
(14) Suzuki, Y.; Yoshino, T.; Moriyama, K.; Togo, H. *Tetrahedron* **2011**, *67*, 3809.
(15) Nador, F.; Moglie, Y.; Vitale, C.; Yus, M.; Alonso, F.; Radivoy, G. *Tetrahedron* **2010**, *66*, 4318.
(16) Gardner, R. A.; Delcros, J.-G.; Konate, F.; Breitbeil, F. III; Martin, B.; Sigman, M.; Huang, M.; Phanstiel, O. IV. *J. Med. Chem.* **2004**, *47*, 6055.
(17) Black, P. J.; Edwards, M. G.; Williams, M. J. *Eur. J. Org. Chem.* **2006**, 4367.
(18) Dong, C.-Z.; Ahamada-Himidi, A.; Plocki, S.; Aoun, D.; Touaibia, M.; Habich, M.-B.; Huet, J.; Redeuilh, C.; Ombeta, J. E.; Godfroid, J.-J.; Massicot, F.; Heymans, F. *Bioorg. Med. Chem.* **2005**, *13*, 1989.
(19) Velcicky, J.; Soicke, A.; Steiner, R.; Schmalz, H. G. *J. Am. Chem. Soc.* **2011**, *133*, 6948.
(20) Lenardao, E. J.; Trecha, D. O.; Ferreira, P. C.; Jacob, R. G.; Perin, G. *J. Braz. Chem. Soc.* **2009**, *20*, 93; *Chem. Abstr.* **2009**, *151*, 288540.
(21) Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **1980**, *45*, 114.

