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Reaction of Cyanotrimethylsilane with Oxiranes. Effects of Catalysts or Mediators on Regioselectivity and Ambident Character

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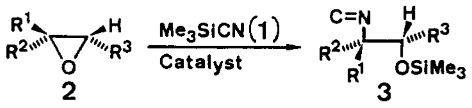
Reaction of cyanotrimethylsilane with oxiranes under the catalytic action of Lewis acids $Pd(CN)_2$, $SnCl_2$, or Me_3Ga affords 2-trimethylsiloxy isocyanides by regio- and stereoselective attack of isocyanide on the more substituted carbon. The reaction mediated by aluminium alkoxides gives predominantly 3-trimethylsiloxy nitriles by the selective attack of cyanide on the less substituted carbon.

Cyanotrimethylsilane (1) has attracted considerable attention as a versatile reagent for the synthesis of nitriles by highly selective cyanosilylation of various carbonyl compounds.[1-4] On the other hand, ambident nucleophilicity of 1 has been reported in the substitution reactions with tertiary alkyl chlorides.[5-7] Although recent communications on addition reaction of 1 to oxiranes have suggested the selective utilization of the ambident reactivity of 1 in the opening of oxiranes,[8-13] relations between the ambident reactivity and reaction conditions, solvents, and catalysts have not been clarified. This paper describes controlled utilization of ambident reactivity of 1 to effect either isocyanosilylation or cyanosilylation of oxiranes 2. Reaction of oxirane **2a** with 1 under catalytic action of $Pd(CN)_2$ afforded 2-(trimethylsiloxy)ethyl isocyanide (**3a**) quantitatively. Likewise, cyclohexene oxide (**2e**) afforded *trans*-2-(trimethylsiloxy)cyclohexyl isocyanide (**3e**) exclusively by $Pd(CN)_2$-catalyzed reaction with 1. In place of $Pd(CN)_2$, $SnCl_2$[14] and Me_3Ga[15] were also effective catalysts (Table I, entries 11–13). Although the formation of isocyanide **3e** from **2e** has been reported under the catalytic action of $ZnCl_2$ or ZnI_2,[8] the $Pd(CN)_2$- or Me_3Ga-catalyzed reactions proceeded under milder conditions to give **3e** in better yields. The regio- and stereoselective reactions of 1 with various oxiranes 2 under catalytic action of $Pd(CN)_2$, $SnCl_2$, or Me_3Ga (Scheme I) are summarized in Table I. Nitriles could not be detected in any of the reaction mixtures.

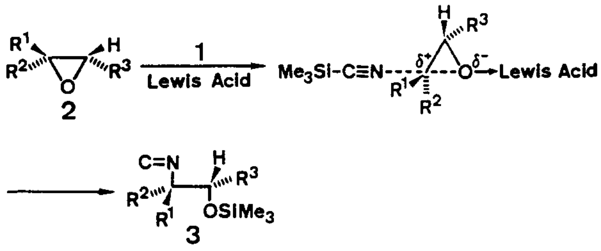
Except for methyloxirane (**2b**), 2-trimethylsiloxy isocyanides 3 are prepared from various oxiranes 2 by regioselective attack of isocyanide on the more substituted carbon with inversion of configuration. Reaction at tertiary carbon atoms also proceeded stereospecifically (entry 14, 17, and 18).

Scheme I

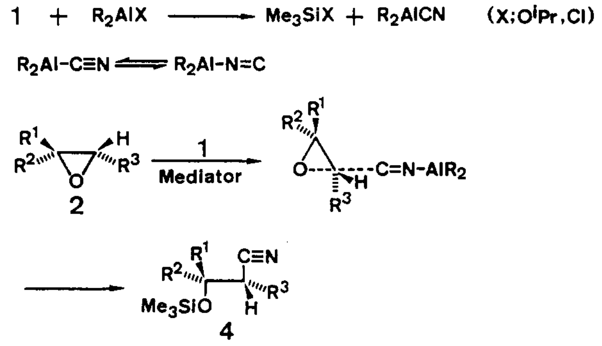


Catalyst; $Pd(CN)_2$, $SnCl_2$, Me_3Ga

Scheme II



Scheme III



Mediator; $Al(O^iPr)_3$, $^iBu_2Al(O^iPr)$, Et_2AlCl

The following observations do not give any information about the formation of an active isocyanide species by the reaction of 1 with $Pd(CN)_2$, $SnCl_2$, or Me_3Ga: (1) treatment of oxiranes 2 with $Pd(CN)_2$ in refluxing dichloromethane did not give any product, (2) treatment of 1 with oxiranes 2 without any catalyst resulted in the recovery of starting materials, and (3) Sn–CN species could not be detected by ^{119}Sn and ^{13}C NMR measurements in a mixture of $SnCl_2$ and 1.

Regio- and stereoselective isocyanosilylation with 1 can be explained: (1) coordination of Lewis acids to oxygen activate oxiranes 2 by stretching the bond between oxygen and more substituted carbon and (2) weakly nucleophilic 1 attacks the more electrophilic site of the activated oxiranes (Scheme II).

When reaction of 1 with 2 was carried out in the presence of aluminum chloride or aluminum alkoxide, 3-trimethylsiloxy nitriles 4 were obtained exclusively. Among the aluminium compounds examined, $Al(OPr\text{-}i)_3$ and (i-

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Table I. Formation of Isonitriles 3 from Oxiranes 2

entry	oxirane	R^1	R^2	R^3	condtn[a]	product (yield, %)
1	**2a**	H	H	H	A	**3a** (99)
2	**2b**	CH_3	H	H	A	**3b** (49), **3k**[b] (49)
3	**2b**	CH_3	H	H	B	**3b** (41), **3k** (41)
4	**2b**	CH_3	H	H	C	**3b** (49), **3k** (49)
5	**2c**	CH_3	CH_3	H	A	**3c** (99)
6	**2c**	CH_3	CH_3	H	B	**3c** (99)
7	**2c**	CH_3	CH_3	H	C	**3c** (90)
8	**2d**	$H_2C{=}CH$	H	H	A	**3d** (89)
9	**2d**	$H_2C{=}CH$	H	H	B	**3d** (81)
10	**2d**	$H_2C{=}CH$	H	H	C	**3d** (88)
11	**2e**	H	$-(CH_2)_4-$		A	**3d** (99)
12	**2e**	H	$-(CH_2)_4-$		B	**3e** (90)
13	**2e**	H	$-(CH_2)_4-$		C	**3e** (100)
14	**2f**	CH_3	$-(CH_2)_4-$		A	**3f** (99)
15	**2g**	H	Et	Et	A	**3g**[c] (84)
16	**2h**	Et	H	Et	A	**3h**[c] (82)
17	**2i**	Et	Me	Me	A	**3i**[c] (90)
18	**2j**	Me	Et	Me	A	**3j**[c] (95)

[a] Conditions: A, $Pd(CN)_2$ (0.05 equiv); B, $SnCl_2$ (0.05 equiv); C, Me_3Ga (0.05 equiv). [b] Attack of isocyanide on less substituted carbon gave $C{=}NCH_2CHMeOSiMe_3$ (**3k**). [c] Homogeneity was determined by GLC as well as NMR.

Table II. Formation of Nitriles 4 from Oxiranes 2

entry	oxirane	R^1	R^2	R^3	condtn[a]	product[b] (yield, %)
1	2a	H	H	H	D	**4a** (80)
2	2a	H	H	H	E or F	**4a** (100)
3	2b	CH_3	H	H	D	**4b** (82)
4	2b	CH_3	H	H	E or F	**4b** (100)
5	2c	CH_3	CH_3	H	D	**4c** (13), **3c** (21), **6**[c] (11)
6	2c	CH_3	CH_3	H	E	**4c** (44), **3c** (41)
7	2c	CH_3	CH_3	H	F	**4c** (51), **3c** (6)
8	2c	CH_3	CH_3	H	G	**4c** (90)
9	2c	CH_3	CH_3	H	H	**4c** (8), **5c**[d] (71) [79][e]
10	2e	H	$-(CH_2)_4-$		D	**4e** (79), **3e** (trace)
11	2e	H	$-(CH_2)_4-$		E	**4e** (90), **3e** (3)
12	2e	H	$-(CH_2)_4-$		F	**4e** (90), **3e** (trace)
13	2e	H	$-(CH_2)_4-$		G	**4e** (80)
14	2f	CH_3	$-(CH_2)_4-$		G	**4f** (34), **4l**[f] (31)
15	2f	CH_3	$-(CH_2)_4-$		H	**4f** (60), **5f** (7) [67], **4l** (15), **5l** (3) [18]
16	2g	H	Et	Et	G	**4g** (89)
17	2g	H	Et	Et	H	**4g** (10), **5g** (90) [100]
18	2h	Et	H	Et	G	**4h** (87)
19	2h	Et	H	Et	H	**4h** (10), **5h** (90) [100]
20	2i	Et	Me	Me	H	**4i** (20), **5i** (41) [61], **4m**[g] (20), **5m** (7) [20]

[a] Conditions: D, Et_2AlCl (0.04 equiv); E, i-Bu_2AlO-i-Pr (0.2 equiv); F, $Al(OPr$-$i)_3$ (0.1 equiv); G, $(i$-$Bu)_2AlOPr$-i (1.5 equiv); H, $Al(OPr$-$i)_3$ (1.5 equiv). [b] Stereochemistry was determined by NMR. [c] 2-(Trimethylsiloxy)butanenitrile (**5**) was produced as byproduct. [d] Compound **5** is protodesilylated product of 4. [e] The figures in square brackets indicate the combined yields of 4 and the corresponding **5**. [f] Attack of cyanide on more substituted carbon gave *threo*-1-methyl-2-(trimethylsiloxy)-1-cyclohexanecarbonitrile (**4l**). [g] Attack of cyanide on the more substituted carbon afforded *erythro*-2-ethyl-2-methyl-3-(trimethylsiloxy)butanenitrile (**4m**).

$Bu)_2AlOPr$-i afforded satisfactory results, but Et_2AlCl[12] gave mixture with polysubstituted oxiranes. Oxirane **2a** gave nitrile **4a** in quantitative yield, and methyloxirane (**2b**) afforded **4b** exclusively by regioselective attack of cyanide on the less substituted carbon of oxirane (Scheme III). Results of the formation of nitriles 4 from various oxiranes 2 are summarized in Table II.

The Et_2AlCl-mediated reaction of 2,2-dimethyloxirane (**2c**) with **1** gave a complex mixture which contained 3-trimethylsiloxy nitrile **4c**, isocyanide **3c**, and 2-trimethylsiloxy nitrile **6** (entry 5). The formation of **6** can be explained by the isomerization of **2c** to 2-methylpropanal, which reacts with **1** to give **6**. Whereas minor amounts of all three aluminum compounds produced some isocyanide **3** as a byproduct in the formation of nitrile **4c** from **2c** (Table II, entries 5–7), use of 1.5 equiv of $(i$-$Bu)_2AlOPr$-i suppressed the formation of isonitrile **3c**, and nitrile **4c** was obtained regio- and stereoselectively (entry 8). Use of 1.5 equiv of $Al(OPr$-$i)_3$ gave mixtures of **4** with the protodesilylated product **5**, the latter sometimes being the predominant product (Table II, entries 9, 15, 17, and 20).

In contrast to the formation of isocyanides **3** under the catalytic action of soft Lewis acids $Pd(CN)_2$, $SnCl_2$, and Me_3Ga, the formation of nitriles **4** can be explained by the reaction of oxirane with Al–CN species to give cyanoaluminated product[12,16] that undergoes transmetalation with **1** to give a 3-trimethylsiloxy nitrile with regeneration of Al–CN species. The isolation of trimethylsilyl isopropoxide from the reaction mixture of **1** with aluminium isopropoxide suggests the formation of Al–CN species.

Diethylaluminium cyanide seems to be produced by the reaction of **1** with diethylaluminium chloride. When cyanotrimethylsilane was treated with diethylaluminium chloride in heptane at 25 °C for 3 h and the reaction mixture than distilled under reduced pressure, a viscous oil was obtained whose ^{13}C NMR spectrum is identical with that of authentic diethylaluminum cyanide.[17] Addition of **2b** to this oil afforded 3-hydroxybutanenitrile in 56%

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[16] Nagata, W.; Yoshioka, M.; Okumura, T. *Tetrahedron Lett.* **1966**, 847.

[17] ^{13}C NMR showed only one sharp signal at 143.10 ($C{\equiv}N$) ppm except for alkyl carbons. ^{14}N and ^{27}Al NMR did not give any information.

yield after hydrolytic workup. When chlorotrimethylsilane was added to the reaction mixture before hydrolytic workup, 3-(trimethylsiloxy)butanenitrile (**4b**) was obtained in 55% yield.

Diethylaluminium cyanide was reported to exist as a polymer or a tetramer[18,19] and NMR measurements support a polymeric structure.[17,20] A polymeric structure would allow isomerization of Al–CN to Al–NC,[20] and a strongly nucleophilic Al–NC species showed attack on the less substituted carbon of oxirane by an S_N2-type reaction.

Reaction of **2f** and **2i** with **1** gave a mixture of two cyanides **4** (Table II, entries 15, 20).

Since optically active oxiranes can be prepared easily, the above described regio- and stereoselective procedures should be useful for the production of optically active isocyanides **3** as well as nitriles **4**.

Experimental Section

Cyanotrimethylsilane (1) was prepared by the reaction of chlorotrimethylsilane with KCN under the catalytic action of 18-crowh-6[21] under vigorous stirring. Oxiranes were prepared via reported procedures.[22]

All reactions were carried out under argon atmosphere.

Proton and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, on a Varian XL-200 spectrometer using $CDCl_3$ as solvent, and chemical shifts are recorded as δ vs. Me_4Si.[23] High resolution mass spectra were measured on a Hitachi M-80 mass spectrometer using PFK as internal standard. IR spectra were recorded on a JASCO IR-810 spectrometer and are reported in a wavenumbers (cm^{-1}).

Reaction of Epoxides with Cyanotrimethylsilane. Catalyzed by $Pd(CN)_2$ (Condition A). To a mixture of $Pd(CN)_2$ (0.04 g, 0.25 mmol, 0.05 equiv) and Me_3SiCN (1.0 mL, 7.5 mmol, 1.5 equiv) in 5 mL of CH_2Cl_2 was added an epoxide (5.0 mmol), and the mixture was heated at reflux under stirring for 2 h. Catalyst was removed from the reaction mixture by chromatography (short neutral alumina column, ether as eluent) and concentration of the eluate afforded the product.

Catalyzed by $SnCl_2$ (Condition B). To a ice-cooled mixture of $SnCl_2$ (0.05 g, 0.26 mmol, 0.05 equiv) and Me_3SiCN (1.0 mL, 7.5 mmol, 1.5 equiv) was added an epoxide (5.0 mmol), and the mixture was stirred at 0 °C for 15 min. The reaction mixture was worked up as described above.

Catalyzed by Me_3Ga (Condition C). To a mixture of a hexane solution of Me_3Ga (0.3 mL containing 0.24 mmol of Me_3Ga, 0.05 equiv) and **1** (1.0 mL, 7.5 mmol, 1.5 equiv) in 5 mL of CH_2Cl_2 was added an epoxide (5.0 mmol), and the mixture was stirred for 15 h at room temperature. The reaction mixture was worked up as described above.

Mediated by 0.04 Equivalent of Et_2AlCl (Condition D). A mixture of **1** (1.5 mL, 11.2 mmol, 1.1 equiv) and a heptane solution of Et_2AlCl (0.1 mL of 50% heptane solution, 0.4 mmol, 0.04 equiv) was stirred at room temperature for 15 min and an epoxide (10.0 mmol) was added dropwise during 30 min. An exothermic reaction was observed. The reaction mixture was poured onto a mixture of ice and 3 N NaOH and extracted with ether. The ethereal solution was washed with brine and dried over Na_2SO_4. Concentration of the filtrate afforded the product.

Mediated by 0.2 Equivalent of (*i*-Bu)$_2$AlOPr-*i* (Condition E). To an ice-cooled hexane solution of DIBAH (0.7 mL containing 1.05 mmol of DIBAH, 0.2 equiv) was added acetone (0.08 mL, 1.09 mmol), and the reaction mixture was stirred for 20 min at room temperature. Cyanotrimethylsilane (**1**, 1.0 mL, 7.5 mmol, 1.5 equiv) was added to the reaction mixture and the mixture was stirred for 2 h at room temperature. An epoxide (5.0 mmol) was added and the mixture was stirred for 15 h at room temperature. The reaction mixture was worked up as described above.

Mediated by 0.1 Equivalent of Al(OPr-*i*)$_3$ (Condition F). A mixture of Al(OPr-i)$_3$ (0.10 g, 0.49 mmol, 0.1 equiv) in Me_3SiCN (1.0 mL, 7.5 mmol, 1.5 equiv) was stirred for 2 h at room temperature. An epoxide (5.0 mmol) was added to the mixture and the whole was stirred for 15 h at room temperature. The reaction mixture was worked up as described above.

Mediated by 1.5 Equivalent of (*i*-Bu)$_2$AlOPr-*i* (Condition G). To an ice-cooled hexane solution of DIBAH (5.0 mL containing 7.5 mmol of DIBAH, 1.5 equiv) was added acetone (0.55 mL, 7.5 mmol), and the reaction mixture was stirred for 20 min at room temperature. Cyanotrimethylsilane (**1**, 1.0 mL, 7.5 mmol, 1.5 equiv) was added to the mixture and the whole was stirred for 2 h at room temperature. To the reaction mixture was added an epoxide (5.0 mmol), and the mixture was stirred for 15 h at room temperature. Then excess Me_3SiCl (2.0 mL, 16 mmol) was added and the mixture was stirred for 20 h at room temperature. The reaction mixture was worked up as described above.

Mediated by Stoichiometric Al(OPr-*i*)$_3$ (Condition H). A mixture of Al(OPr-*i*)$_3$ (1.53 g, 7.5 mmol, 1.5 equiv) and **1** (1.0 mL, 7.5 mmol, 1.5 equiv) in 5.0 mL of hexane was stirred for 2 h at room temperature. An epoxide (5.0 mmol) was added and the mixture was stirred at room temperature for 15 h. Then Me_3SiCl (5.0 mL, 39 mmol) was added and the mixture was stirred additionally for 20 h. The reaction mixture was worked up as described above.

2-(Trimethylsiloxy)ethyl isocyanide (3a): IR (neat) 2146, 1254; ^1H NMR 0.17 (9 H, s), 3.50 (2 H, m), 3.79 (2 H, m); ^{13}C NMR 156.9 (br s), 60.3, 44.0 (t, J = 7.0 Hz), –0.8; MS, calcd for $C_6H_{12}NOSi$ (M – H) 142.0686, found 142.0630; calcd for $C_5H_{10}NOSi$ (M – CH_3) 128.0531, found 128.0615. Anal. Calcd for $C_6H_{13}NOSi$: C, 50.30; H, 9.15; N, 9.78. Found: C, 50.01; H, 9.27; N, 9.96.

1-Methyl-2-(trimethylsiloxy)ethyl Isocyanide (3b) and 2-(Trimethylsiloxy)propyl Isocyanide (3k). A mixture of **3b** and **3k** was obtained but complete separation of each component in a pure state was unsuccessful. Elemental analysis of the mixture is shown below and the ratio of the two components was determined by ^1H NMR. Anal. Calcd for $C_7H_{15}NOSi$: C, 53.45; H, 9.61; N, 8.91. Found: C, 53.49; H, 9.72; N, 9.15. The ratio of two isomers was determined by ^1H NMR.

3b: IR (neat) 2146, 1253; ^1H NMR 0.17 (9 H, s), 1.3–1.4 (3 H, m), 3.5–3.75 (3 H, m); ^{13}C NMR 155.7 (t, J = 5.2 Hz), 65.1, 51.1 (t, J = 6.3 Hz), 20.5, –1.1; MS, calcd for $C_6H_{12}NOSi$ (M – CH_3) 142.0687, found 142.0781.

3k: ^1H NMR 0.16 (9 H, s), 1.23 (3 H, d, J = 6.1 Hz), 3.28–3.35 (2 H, m), 4.01 (1 H, m); ^{13}C NMR 157.2 (t, J = 5.1 Hz), 65.8, 48.6 (t, J = 6.9 Hz), 17.2, –0.5.

1,1-Dimethyl-2-(trimethylsiloxy)ethyl isocyanide (3c): IR (neat) 2132, 1253; ^1H NMR 0.16 (9 H, s), 1.38 (6 H, t, J = 2.0 Hz), 3.51 (2 H, t, J = 1.7 Hz); ^{13}C NMR 154.6 (br s), 69.2, 57.6 (t, J = 5.5 Hz), 25.0, –1.1; MS, calcd for $C_7H_{14}NOSi$ (M – CH_3) 156.0844, found 156.0818. Anal. Calcd for $C_8H_{17}NOsi$: C, 56.09; H, 10.00; N, 8.18. Found: C, 56.13; H, 10.14; N, 8.13.

1-[(Trimethylsiloxy)methyl]-2-propenyl isocyanide (3d): IR (neat) 2142, 1253; ^1H NMR 0.15 (9 H, s), 3.68 (2 H, br d, J = 6.4 Hz), 4.21 (1 H, m), 5.35 (1 H, ddd, J = 0.9, 1.5, 10.1 Hz), 5.50 (1 H, ddd, J = 0.9, 1.5, 16.9 Hz), 5.82 (1 H, m); ^{13}C NMR 157.9 (br s), 129.9, 117.4, 64.6, 58.3 (t, J = 6.8 Hz), –1.0; MS, calcd for $C_7H_{12}NOSi$ (M – CH_3) 154.0687, found 154.0508. Anal. Calcd for $C_8H_{15}NOSi$: C, 56.76; H, 8.93; N, 8.27. Found: C, 56.87; H, 9.93; N, 7.97.

***trans*-2-(Trimethylsiloxy)cyclohexyl isocyanide (3e)**: IR (neat) 2138, 1249; ^1H NMR, same as described in ref 6; ^{13}C NMR 155.3 (br s), 72.7, 58.4 (t, J = 6.5 Hz), 33.2, 31.0, 22.9, 22.8, 0.0; MS, calcd for $C_{10}H_{19}NOSi$ (M) 197.1235, found 197.1238; calcd for $C_9H_{16}NOSi$ (M – CH_3) 182.1000, found 182.0988. Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; N, 7.10. Found: C, 60.95, H, 9.93, N, 7.09.

Treatment of **3e** with KF in MeOH[8] afforded *trans*-2-isocyano-1-cyanohexanol whose stereochemistry was determined by the coupling constant (J = 8.4 Hz) of vicinal protons [–(CN)C-*HCH*(OH)-].

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[19] Coates, G. E.; Mukherjee, R. N. *J. Chem. Soc.* **1963**, 229.

[20] In a tetramer or a polymeric form, the CN moiety seems to bond with tetracoordinated Al on both C and N forming AlC≡NAl. A sharp single peak at 143.10, 8.20, –2.14 in ^{13}C NMR supports the structure.

[21] Zubrick, J. W. ; Dunbar, B. J.; Durst, H. D. *Tetrahedron Lett.* **1975**, 71.

[22] Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons, Inc.: New York, 1967; Vol. 1, p 135.

[23] ^{13}C NMR spectra were obtained by standard parameters sets of the instrument: flip angle 45° without pulse delay. Intensities of nitrile and isonitrile signals decreased by the pulse of flip angle 90° both with 1-s pulse delay and without delay.

trans-2-Isocyano-1-cyclohexanol: IR (Nujol) 3388, 2164; ^{13}C NMR, 153.2 (t, $J = 5.3$ Hz), 71.3, 58.4 (t, $J = 6.0$ Hz), 31.9, 30.8, 22.6.

threo-1-Methyl-2-(trimethylsiloxy)cyclohexyl isocyanide (3f): IR (neat) 2128, 1252; ^{1}H NMR 0.14 (9 H, s), 1.34 (3 H, t, $J = 2.0$ Hz), 1.40–1.70 (6 H, m), 1.70–1.95 (2 H, m), 3.72 (1 H, br dd, $J = 3.1, 5.3$ Hz); ^{13}C NMR 156.2 (t, $J = 4.5$ Hz), 73.0, 60.7 (t, $J = 5.4$ Hz), 34.1, 29.4, 23.8, 20.9, 19.7, –0.2; MS, calcd for $C_{10}H_{18}NOSi$ (M – CH_3) 196.1156, found 196.1203. Anal. Calcd for $C_{11}H_{21}NOSi$: C, 62.50; H, 10.01; N, 6.63. Found: C, 62.27; H, 10.26; N, 6.66.

threo-1-Ethyl-2-(trimethylsiloxy)butyl isocyanide (3g): IR (neat) 2136, 1251; ^{1}H NMR 0.15 (9 H, s), 0.92 (3 H, t, $J = 7.4$ Hz), 1.07 (3 H, t, $J = 7.3$ Hz), 1.43–1.80 (4 H, m), 3.40 (1 H, m), 3.59 (1 H, m); ^{13}C NMR 156.3 (br s), 73.9, 60.7 (t, $J = 5.8$ Hz), 26.1, 23.9, 10.4, 9.4, 0.1; MS, calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1156, found 184.1139. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.11; H, 10.80; N, 7.09.

erythro-1-Ethyl-2-(trimethylsiloxy)butyl isocyanide (3h): IR (neat) 2136, 1252; ^{1}H NMR 0.15 (9 H, s), 0.93 (3 H, t, $J = 7.4$ Hz), 1.07 (3 H, t, $J = 7.3$ Hz), 1.40–1.85 (4 H, m), 3.38 (1 H, m), 3.67 (1 H, br q, $J = 5.5$ Hz); ^{13}C NMR 156.6 (br s), 74.1, 60.7 (t, $J = 5.8$ Hz), 25.9, 23.3, 10.1, 9.0, 0.1; MS, calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1156, found 184.1224. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.07; H, 10.90, N, 7.02.

erythro-1-Ethyl-1-methyl-2-(trimethylsiloxy)propyl isocyanide (3i): IR (neat) 2128, 1252; ^{1}H NMR 0.14 (9 H, s), 1.03 (3 H, t, $J = 7.4$ Hz), 1.18 (3 H, d, $J = 6.2$ Hz), 1.27 (3 H, t, $J = 2.0$ Hz), 1.55–1.80 (2 H, m), 3.76 (1 H, tq, $J = 1.4, 6.2$ Hz); ^{13}C NMR, 154.6 (t, $J = 3.3$ Hz), 72.5, 65.2 (t, $J = 5.1$ Hz), 28.9, 21.3, 17.8, 7.7, 0.0; MS, calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1156, found 184.1289. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.24; H, 10.83; N, 6.73.

threo-1-Ethyl-1-methyl-2-(trimethylsiloxy)propyl isocyanide (3j): IR (neat) 2128, 1252; ^{1}H NMR 0.13 (9 H, s), 1.03 (3 H, t, $J = 7.4$ Hz), 1.23 (3 H, d, $J = 6.2$ Hz), 1.27 (3 H, t, $J = 2.0$ Hz), 1.60–1.85 (2 H, m), 3.78 (1 H, br q, $J = 6.2$ Hz); ^{13}C NMR 155.4 (t, $J = 3.4$ Hz), 71.9, 64.7 (t, $J = 5.3$ Hz), 29.8, 20.3, 17.9, 7.7, 0.0; MS, calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1157; found 184.1160. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.19; H, 10.87; N, 6.74.

3-(Trimethylsiloxy)propanenitrile (4a): IR (neat) 2252, 1253; ^{1}H NMR 0.15 (9 H, s), 2.55 (2 H, t, $J = 6.4$ Hz), 3.81 (2 H, t, $J = 6.4$ Hz); ^{13}C NMR 117.8, 57.5, 21.3, –1.0; MS, calcd for $C_6H_{12}NOSi$ (M – H) 142.0687, found 142.0534; calcd for $C_5H_{10}NOSi$ (M – CH_3) 128.0530, found 128.0529. anal. Calcd for $C_6H_{13}NOSi$: C, 50.30; H, 9.15; N, 9.78. Found: C, 50.08; H, 9.30; N, 10.07.

3-(Trimethylsiloxy)butanenitrile (4b): IR (neat) 2248, 1252; ^{1}H NMR 0.16 (9 H, s), 1.29 (3 H, d, $J = 6.0$ Hz), 2.44 (2 H, d, $J = 6.0$ Hz), 4.12 (1 H, tq, $J = 6.0, 6.0$ Hz); ^{13}C NMR 117.4, 64.2, 27.6, 23.1, –0.4; MS, calcd for $C_6H_{12}NOSi$ (M – CH_3) 142.0687, found 142.0649. Anal. Calcd for C 53.45; H, 9.61; N, 8.91. Found: C, 53.57; H, 9.67; N, 9.01.

3-Methyl-3-(trimethylsiloxy)butanenitrile (4c): IR (neat) 2250, 1252; ^{1}H NMR 0.15 (9 H, s), 1.41 (6 H, s), 2.47 (2 H, s); ^{13}C NMR 117.7, 71.7, 33.8, 29.3, 2.1; MS, calcd for $C_7H_{14}NOSi$ (M – CH_3) 156.0843, found 156.0813. Anal. Calcd for $C_8H_{17}NOSi$: C, 56.09; H, 10.00; N, 8.18. Found: C, 56.03; H, 10.25; N, 7.93.

Al-Mediated Reaction of 2-Vinyloxirane (2d) with 1 under Condition F. The reaction gave a complex mixture which contained 3-(trimethylsiloxy)-4-pentenenitrile (**4d**) and isomers. Pure **4d** could not be obtained even by GLC, and **4d** was detected by ^{1}H NMR; in addition to vinyl protons and trimethylsilyl signals, 2.51 (d, $J = 6.1$ Hz), 4.4 (m) (intensity ratio of two signals, 2:1).

trans-2-(Trimethylsiloxy)-1-cyclohexanecarbonitrile (4e): IR (neat) 2240, 1252; ^{1}H NMR 0.17 (9 H, s), 1.15–1.40 (4 H, m), 1.50–1.85 (2 H, m), 1.90 (1 H, m), 2.10 (1 H, m), 2.41 (1H, ddd, $J = 3.9, 9.0, 11.3$ Hz), 3.68 (1 H, dt, $J = 4.1, 9.0$ Hz); ^{13}C NMR 120.9, 70.7, 37.2, 34.3, 27.7, 23.5, 22.8, –0.3; MS, calcd for $C_{10}H_{18}NOSi$ (M – H) 196.1156, found 196.1271; calcd for $C_9H_{16}NOSi$ (M – CH_3) 182.1000, found 182.0857. Anal. Calcd for $C_{10}H_{19}NOSi$: C, 60.86; H, 9.70; N, 7.10. Found: C, 60.69; H, 9.87; N, 7.16.

threo-2-Methyl-2-(trimethylsiloxy)-1-cyclohexanecarbonitrile (4f): IR (neat) 2238, 1251; ^{1}H NMR 0.14 (9 H, s), 1.35–1.80 (7 H, m), 1.43 (3 H, s), 2.01 (1 H, m), 2.61 (1 H, dd, $J = 3.8, 6.9$ Hz); ^{13}C NMR 121.4, 73.4, 41.5, 38.3, 26.7, 26.4, 23.0, 22.1, 2.7; MS, calcd for $C_{11}H_{21}NOSi$ (M) 211.1390, found 211.1327; calcd for $C_{10}H_{18}NOSi$ (M – CH_3) 196.1157, found 196.1341. Anal. Calcd for $C_{11}H_{21}NOSi$: C, 62.50; H, 10.01; N, 6.63. found: C, 62.67; H, 10.15; N, 6.61.

threo-1-Methyl-2-(trimethylsiloxy)-1-cyclohexanecarbonitrile (4l): IR (neat) 2236, 1252; ^{1}H NMR 0.13 (9 H, s), 1.27 (3 H, s), 1.35–1.90 (8 H, m), 3.84 (1 H, dd, $J = 2.5, 5.3$ Hz); ^{13}C NMR 124.8, 71.9, 32.3, 31.0, 26.7, 26.4, 22.2, 20.3, 0.5; MS, calcd for $C_{11}H_{21}NOSi$ (M) 211.1391, found 211.1310; calcd for $C_{10}H_{18}NOsi$ (M – CH_3) 196.1157, found 196.1184. Anal. Calcd for $C_{11}H_{21}NOSi$: C, 62.50; H, 10.01; N, 6.63. Found: C, 62.41; H, 10.22; N, 6.37.

threo-2-Ethyl-3-(trimethylsiloxy)pentanenitrile (4g): IR (neat) 2240, 1251; ^{1}H NMR 0.15 (9 H, s), 0.92 (3 H, t, $J = 7.5$ Hz), 1.10 (3 H, t, $J = 7.4$ Hz), 1.50–1.85 (4 H, m), 2.53 (1 H, ddd, $J = 4.4, 5.8, 9.4$ Hz), 3.67 (1 H, dt, $J = 4.4, 6.2$ Hz); ^{18C} NMR 119.8, 72.9, 40.0, 27.9, 21.9, 11.6, 9.3, –0.1; MS, calcd for $C_{10}H_{20}NOSi$ (M – H) 198.1313, found 198.1406; calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1156, found 184.1024. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.35; H, 10.64; N, 7.02.

erythro-2-Ethyl-3-(trimethylsiloxy)pentanenitrile (4h): IR (neat) 2238, 1252; ^{1}H NMR 0.15 (9 H, s), 0.94 (3 H, t, $J = 7.4$ Hz), 1.10 (3 H, t, $J = 7.3$ Hz), 1.45–1.85 (4 H, m), 2.54 (1 H, ddd, $J = 4.9, 6.4, 9.8$ Hz), 3.73 (1 H, dt, $J = 6.4, 5.6$ Hz); ^{13}C NMR, 120.2, 72.6, 40.0, 27.1, 21.0, 11.4, 8.9, –0.1; MS, calcd for $C_{10}H_{20}NOSi$ (M – H) 198.1313, found 198.1429; calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1156, found 184.1161. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.53; H, 10.90; N, 6.82.

erythro-2,3-Dimethyl-3-(trimethylsiloxy)pentanenitrile (4i): IR (neat) 2236, 1252; ^{1}H NMR 0.15 (9 H, s), 0.89 (3 H, t, $J = 7.5$ Hz), 1.24 (3 H, d, $J = 7.3$ Hz), 1.32 (3 H, s), 1.65 (2 H, dq, $J = 1.5, 7.5$ Hz), 2.72 (1 H, q, $J = 7.3$ Hz); ^{13}C NMR 123.0, 76.2, 32.7, 28.0, 19.0, 8.0, 2.3; MS, calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1157, found 184.1300. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.38; H, 10.80; N, 6.88.

erythro-2-Ethyl-2-methyl-3-(trimethylsiloxy)butanenitrile (4m): IR (neat) 2240, 1252; ^{1}H NMR 0.14 (9 H, s), 1.06 (3 H, t, $J = 7.4$ Hz), 1.22 (3 H, d, $J = 6.2$ Hz), 1.23 (3 H, s), 1.90 (2 H, dq, $J = 1.5, 7.4$ Hz), 3.76 (1 H, q, $J = 6.2$ Hz); ^{13}C MMR 121.6, 71.9, 36.8, 24.1, 18.7, 13.0, 0.2; MS, calcd for $C_9H_{18}NOSi$ (M – CH_3) 184.1156, found 184.1132. Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.25; H, 10.62; N, 7.03. Found: C, 60.13; H, 10.91; N, 6.85.

Reaction of Et_2AlCl with 1. Cyanotrimethylsilane (**1**, 2.0 mL, 15 mmol, 3.8 equiv) was added to a heptane solution of Et_2AlCl (1.0 mL of 50% solution, 4.0 mmol, 1.0 equiv), and the mixture was stirred for 3 h at 25 °C. Volatile materials were removed from the reaction mixture under reduced pressure (1 mmHg, 25 °C). Methyloxirane (**2b**, 0.23 g, 4.0 mmol) was added to the residue maintained at 0 °C. The reaction mixture was stirred for 15 min at room temperature. Hydrolytic workup of the reaction mixture afforded 3-hydroxybutanenitrile in 56% yield.

When chlorotrimethylsilane (1.0 mL, 7.9 mmol, 2.0 equiv) was added to the reaction mixture before the hydrolytic workup, workup with ice–3 N NaOH (as described above, condition D) gave 3-(trimethylsiloxy)butanenitrile (**4b**) in 55% yield.

Reaction of Al(OPr-_i_)$_3$ with 1. Cyanotrimethylsilane (**1**, 0.67 mL, 5.0 mmol) was added to Al(OPr-_i_)$_3$ (1.0 g, 4.9 mmol), and the mixture was stirred for 3 h at 25 °C. The reaction mixture was fractionally distilled under reduced pressure. NMR analysis of the low-boiling fraction (boiling points lower than 25 °C/1 mmHg) indicated the formation of trimethylisopropoxysilane.

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