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An α-Diaminoboryl Carbanion Assisted Stereoselective Single-Pot Preparation of α,β-Disubstituted Acrylonitriles

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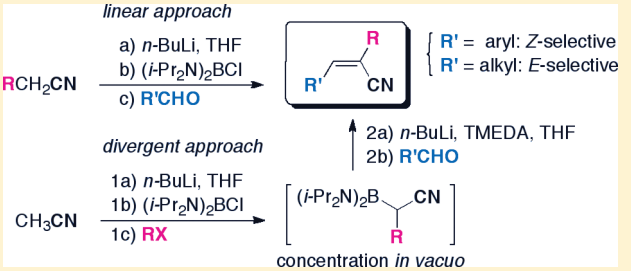
Supporting Information

ABSTRACT: An α-diaminoboryl carbanion-mediated one-pot olefination directly converts an acetonitrile or the homologous nitrile into a series of α,β-disubstituted acrylonitriles in a stereoselective manner. The protocol involves the formation of an α-substituted α-diaminoboryl acetonitrile and subsequent olefination with an aldehyde. The use of an aryl or conjugated aldehyde preferentially leads to a (Z)-acrylonitrile, while an aliphatic aldehyde gave an (E)-isomer as a major product. Two complementary approaches, a linear method and a divergent method, are developed.

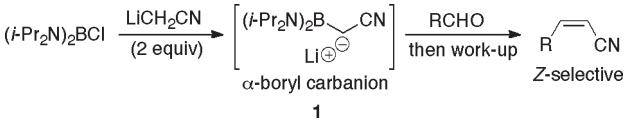


A one-pot or purification-free multistep transformation is an ideal, green synthetic approach for rapid access to a series of organic compounds. Such a protocol often simplifies the synthesis and improves the overall reaction efficiency. In addition, when a synthetic intermediate is an unstable species to isolate, a "single-pot" synthesis is particularly advantageous and practically superior to a conventional step-by-step approach. Therefore, exploring an operationally simple, multistep method without isolation/purification has been continuously of great importance in the synthetic community.[1]

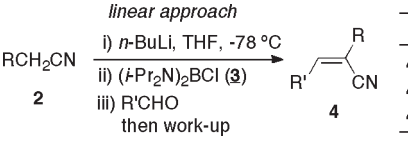
Our recent study[2] of α-boryl carbanion chemistry[3] successfully achieved a one-pot stereoselective synthesis of β-monosubstituted (Z)-acrylonitriles (Scheme 1). The use of a mildly Lewis acidic and sterically hindered diaminoboryl group prevented the formation of an undesired "ate" complex even in the presence of a nucleophilic base, $LiCH_2CN$. This unusual base compatibility of the boron eventually enabled a facile preparation of carbanion **1** and subsequent olefination with an aldehyde.

Acrylonitrile, namely α,β-unsaturated cyanide, represents a versatile intermediate in organic synthesis.[4] A variety of acrylonitiriles, in particular, β-monosubstituted and β,β-disubstituted acrylonitriles, are often directly prepared from an aldehyde or a ketone by means of a standard olefination, i.e., Wittig/Horner−Emmons[5] and Peterson[6] type reactions; however, those conditions are less commonly employed for the synthesis of α,β-disubstituted acrylonitriles, partly due to the need of prior modification and/or preparation of the reagents.[7] An alternative, multistep method via a Baylis−Hillman adduct is also available.[8] Since our α-diaminoboryl carbanion **1** revealed sufficient olefinating ability as well as good stereoselectivity to lead to a series of β-monosubstituted acrylonitriles, we anticipated that further modifications of this protocol may allow us to establish a more efficient path to access the titled compounds.

Scheme 1. One-Pot Synthesis of (Z)-Acrylonitrile



Scheme 2. One-Pot Synthesis of α,β-Disubstituted Acrylonitrile



	R	R'	Z:E	yield
4a	Me	Ph	70:30	94%
4b	Et	Ph	70:30	90%
4c	Bn	Ph	87:13	61%

As an initial investigation, the applicability of the one-pot olefination described in Scheme 1 to a substituted acetonitrile (RCH_2CN) was examined. Treatment of bis(diisopropylamino)chloroborane reagent **3**[9] with 2 equiv of a lithiated nitrile[10] of **2**, followed by the addition of benzaldehyde, smoothly gave the corresponding olefinic products **4a**−**c** in fair to good yield with (Z)-stereoselectivity (Scheme 2).

Although the results further proved the synthetic utility of this α-diaminoboryl carbanion species, the reaction efficiency of the method, now called a "linear approach", seemed to be slightly substrate-dependent because different lithiated nitriles vary in reactivity. In fact, 3-phenylpropionitrile afforded **4** (**4c**) in much lower yield (61%) than propionitrile and butyronitrile (Scheme 2). In addition, since this linear approach theoretically

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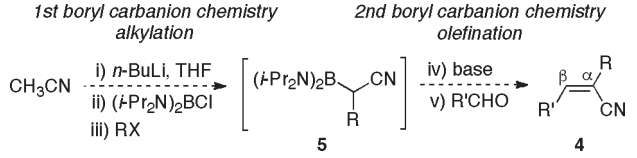
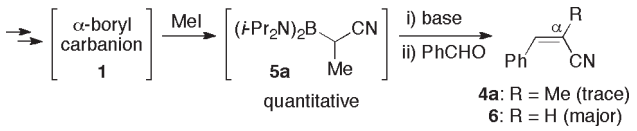
Scheme 3. Proposed Divergent Approach



Scheme 4. Initial One-Pot Attempt



requires 2 equiv of nitrile **2**,[11] the use of an expensive and/or not readily available precious nitrile under such conditions is not desirable. In order to avoid such practical limitations, an alternative but more general approach as illustrated in Scheme 3 by taking advantage of the nature of an α-boryl carbanion was therefore proposed. Reaction of carbanion **1** with alkyl halide (RX) is supposed to form an alkylated intermediate **5** which is presumably the same species as the one directly prepared from **2** (RCH_2CN) by the linear approach. Treatment of **5** with a base followed by the addition of an aldehyde ought to provide product **4**. This new procedure, now called a "divergent approach", starting from simple acetonitrile (CH_3CN) seemed to be more flexible and versatile to access various acrylonitriles of **4**.

The alkylation of **1** with methyl iodide quantitatively afforded **5a**, which was confirmed by the crude ^{1}H NMR analysis (Scheme 4). Subsequently, the in situ generated intermediate **5a** was directly treated with a base (e.g., *n*-BuLi, LiHMDS, or LiTMP) to generate the corresponding α-diaminoboryl carbanion for the next olefination step; however, the major product observed under the conditions was not the desired olefin **4a** but was consistently β-monosubstituted acrylonitrile **6** without the initial methyl group on the α carbon.

Assumedly, since the initial boryl carbanion species **1** was generated from chlorodiaminoborane **3** by treatment with 2 equiv of $LiCH_2CN$;[11] after the formation of **5a**, 1 equiv of acetonitrile should exist in the reaction system. In the next step, as the acetonitrile is more rapidly deprotonated by a base than the sterically congested boryl acetonitrile **5a**, the regenerated $LiCH_2CN$ then reacts with an aldehyde to form an oxyanion intermediate which likely undergoes β-elimination with the assistance of **5a** to provide the undesired β-monosubstituted acrylonitrile **6**.

On the basis of these assumptions, following the alkylation step, the reaction mixture **5a** was simply concentrated under reduced pressure to get rid of the remaining CH_3CN (Scheme 5) and then used for the next olefination without further purification. Excitedly, this modified procedure effectively afforded the corresponding acrylonitrile **4a** in good yield (83%). The stereoselectivity of **4a** from this divergent approach was identical to that of **4a** prepared from the linear approach. This implies that both approaches, as expected, involve the same carbanion intermediate for the olefination. For the effective deprotonation of **5a** by *n*-BuLi, the presence of TMEDA was highly essential. Without TMEDA, the yield of **4a** dropped to 20−30%.

Scheme 5. Synthesis of 4a via Divergent Approach

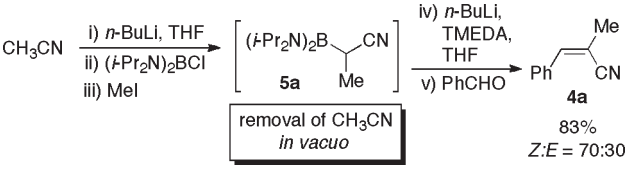
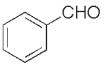
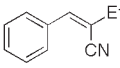
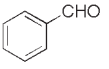
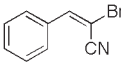
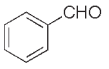
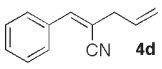
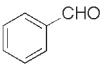
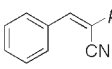
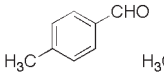
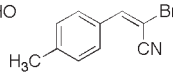
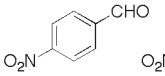
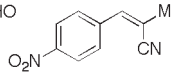
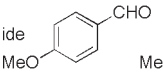
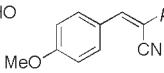
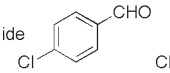
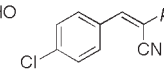
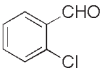
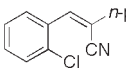


Table 1. Divergent Approach with Aromatic Aldehyde

entry	RX	R'CHO	product (**4**)	*Z*:*E* [a]	yield (%)[b]
1	EtI		 **4b**	70:30	71
2	BnBr		 **4c**	86:14	84
3			 **4d**	70:30	83
4	*p*-xylyl bromide		 **4e**	88:12	89
5	BnBr		 **4f**	88:12	96
6	MeI		 **4g**	81:19	80
7	*p*-xylyl bromide		 **4h**	n.d.[c]	72[d]
8	*p*-xylyl bromide		 **4i**	86:14	90
9	*n*-pentyl iodide		 **4j**	85:15	72

[a] Determined by ^{1}H NMR of the crude reaction mixture. [b] Combined isolated yield of *Z* and *E* isomers. [c] Not determined. [d] Isolated yield of Z isomer.

Table 1 illustrates different combination patterns between an alkyl halide and an aromatic aldehyde tested. Like methyl iodide, the other alkyl halides such as ethyl iodide, benzyl bromide, allyl bromide, and *p*-xylyl bromide cleanly underwent alkylation with carbanion **1** as well as subsequent olefination with benzaldehyde (entries 1−4). Functionalized aromatic aldehydes with a methyl, nitro, methoxy, or chloro group were also examined (entries 5−8). Both electron-rich and electron-deficient aldehydes were efficiently converted into the corresponding products **4f**−**i** in good yields (72−96%). Similarly, an ortho-substituted benzaldehyde (entry 9) provided the desired acrylonitrile **4j** in 72% yield. All of the entries were consistently *Z*-stereoselective. The *E*/*Z* isomers shown in Table 1 as well as Table 2 are separable by silica gel column chromatography using toluene as eluent.

Subsequently, aliphatic aldehydes were investigated (Table 2). Interestingly, unlike "aromatic" aldehydes, all primary and secondary "aliphatic" aldehydes examined led to *E* olefinic isomers as a major product (entries 1−4). A tertiary aliphatic aldehyde

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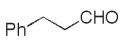
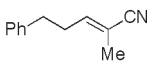
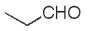
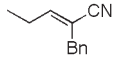
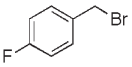
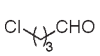
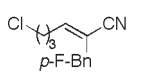
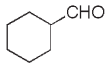
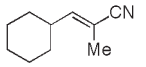
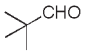
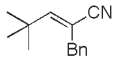
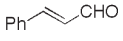
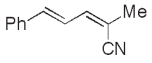
Table 2. Divergent Approach with Aliphatic Aldehyde

entry	RX	R'CHO	product (**4**)		*Z*:*E* [a]	yield (%)[b]
1	MeI			**4k**	11:89 (12:88)	87 (73)[c]
2	BnBr			**4l**	16:84	99
3				**4m**	12:88	76
4	MeI			**4n**	24:76 (23:77)	84 (83)[c]
5	BnBr			**4o**	–	0 (0)[c]
6	MeI			**4p**	69:31	82

[a] Determined by ^{1}H NMR of the crude reaction mixture. [b] Combined isolated yield of *Z* and *E* isomers. [c] By linear approach.

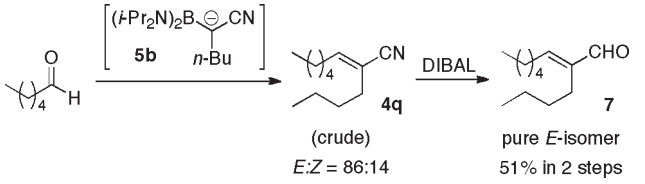
(entry 5) did not give any desired product, presumably due to the steric interference. A conjugated aldehyde, *trans*-cinnamaldehyde, underwent *Z*-olefination (entry 6). The mechanistic rationale for these reversed selectivities between "aromatic" and "aliphatic" aldehydes is still inconclusive and under investigation. Even though our previous report[2] took advantage of a common steric approach model (the Bassindale–Taylor model)[12] to explain the *Z*-stereoselectivity of a β-monosubstitued acrylonitrile in Scheme 1, the approach model does not fit well to account for the current system. Lastly, this divergent approach was employed in the synthesis of (*E*)-2-butyl-2-octenal **7** (Scheme 6), which is known as an alarm pheromone of the African weaver ant, *Oecophylla longinoda*.[13] Treatment of *n*-hexanal with carbanion **5b**, followed by DIBAL reduction of crude **4q** (*E*/*Z* = 86:14), readily provided the target compound **7** in 51% yield over two steps.

In summary, an α-diaminoboryl carbanion-mediated single-pot approach to an α,β-disubstituted acrylonitrile has been successfully established. Two alternative but complementary approaches efficiently provided the titled acrylonitrile in good yield with decent stereoselectivity. An aryl aldehyde preferentially led to a (*Z*)-isomer. In contrast, an aliphatic aldehyde gave an (*E*)-isomer as a major product. Mechanistic details on the stereoinduction and further synthetic applications of an α-diaminoboryl carbanion will be reported in due course.

EXPERIMENTAL SECTION

Materials and Methods. All experiments were performed in flame-dried glassware fitted with rubber septa under argon atmosphere. Tetrahydrofuran (THF) was distilled over sodium/benzophenone ketyl. Tetramethylethylenediamine (TMEDA) was distilled over calcium hydride. Bis(diisopropylamino)chloroborane **3**[9] and 4-chlorobutanal[14] (Table 2, entry 3) were prepared in accordance with literature procedure. Unless otherwise noted, all other reagents were obtained from commercial sources and used as received. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded at 300 or 500 MHz. Data are presented as follows:

Scheme 6. Short-Step Synthesis of (*E*)-2-Butyl-2-octenal



chemical shift (in ppm on the δ scale relative to δH 7.26 for the residual protons in $CDCl_3$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (*J*/Hz), integration. Coupling constants were taken directly from the spectra and are uncorrected. ^{13}C NMR spectra were recorded at 75 or 125 MHz, and all chemical shift values are reported in ppm on the δ scale, with an internal reference of δC 77.0 for $CDCl_3$. Analytical TLC was performed on silica gel plates using UV light and/or potassium permanganate stain followed by heating. Flash column chromatography was performed on silica gel 60A (32–63D).

General Procedure for Linear Approach. Into a flame-dried round-bottomed flask was added dry THF (8.0 mL) under an argon atmosphere. After the mixture was cooled to −78 °C (acetone/dry ice bath), *n*-BuLi (880 μL, 2.5 M in hexane, 2.2 mmol) and a nitrile (3.3 mmol) were added dropwise, respectively. After the mixture was stirred for 5 min, $(i\text{-Pr}_2\text{N})_2\text{BCl}$ (300 μL, 1.1 mmol) was then slowly added. After another 1 h of stirring, an aldehyde (1.0 mmol) was added. The reaction mixture was stirred for an additional 1 h at −78 °C and quenched with half-saturated NH_4Cl (5 mL) (−78 °C to rt over 30 min). After the phase separation, the aqueous layer was extracted with Et_2O (×2). The combined organics were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by SiO_2 column chromatography (hexane/EtOAc eluent system) to afford the corresponding acrylonitrile as a mixture of *E*/*Z* isomers. (Note: *E*/*Z* ratio was determined by ^{1}H NMR of the crude reaction mixture.)

General Procedure for Divergent Approach. Into a flame-dried round-bottomed flask was added dry THF (8.0 mL) under an argon atmosphere. After the mixture was cooled to −78 °C (acetone/dry ice bath), *n*-BuLi (1.0 mL, 2.5 M in hexane, 2.5 mmol) and dry CH_3CN (195 μL, 3.75 mmol) were added dropwise, respectively. After the mixture was stirred for 20 min, $(i\text{-Pr}_2\text{N})_2\text{BCl}$ (342 μL, 1.25 mmol) was then slowly added. After another 1 h of stirring, alkyl halide (1.25 mmol) was added. The reaction mixture was stirred for an additional 1 h at 0 °C and then concentrated under reduced pressure. Subsequently, dry THF (6.0 mL) was add into the crude mixture under an argon atmosphere. After the mixture was cooled to −78 °C (acetone/dry ice bath), tetramethylethylenediamine (188 μL, 1.25 mmol) and *n*-BuLi (500 μL, 2.5 M in hexane, 1.25 mmol) were added dropwise. After the mixture was stirred for 1 h, an aldehyde (1.0 mmol) was slowly added, and the resulting mixture was stirred for 1.5 h at the same temperature. The reaction mixture was then quenched with half-saturated NH_4Cl (6 mL) (−78 °C to rt over 30 min). After the phase separation, the aqueous layer was extracted with Et_2O (×2). The combined organics were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by SiO_2 column chromatography (hexane/EtOAc eluent system) to afford the corresponding acrylonitrile as a mixture of *E*/*Z* isomers. (Note: *E*/*Z* ratio was determined by ^{1}H NMR of the crude reaction mixture.) The *E*/*Z* mixture was subsequently separated for characterization purpose. The use of toluene as an eluent for SiO_2 column chromatography allowed for isolation of each isomer. The *E*/*Z* configurations were determined, based on the fact that, in ^{13}C NMR spectrum, the allylic carbon (on the α-carbon) of an α,β-disubstituted (*E*)-acrylonitrile appears upper field than the same carbon of the (*Z*)-isomer,[8l] and in

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^{1}H NMR spectrum, the vinylic proton on the β-carbon of (*Z*)-isomer appears upper field than the same proton of the *E*-isomer.[8a]

2-Methyl-3-phenylacrylonitrile (4a). Column chromatography (Hex/EtOAc = 99/1) yielded **4a** (118 mg, 83%, *Z*/*E* = 70:30). ***Z*-Isomer** (major): R_f 0.81 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72−7.68 (m, 2H), 7.44−7.36 (m, 3H), 6.94 (apparent s, 1H), 2.16 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 133.8, 129.8, 128.8, 128.4, 119.2, 106.1, 22.2. This product spectroscopically matched that of the known compound.[8i] ***E*-Isomer** (minor): R_f 0.76 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.31 (m, 5H), 7.21 (apparent s, 1H), 2.15 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 134.0, 129.27, 129.24, 128.6, 121.2, 109.6, 16.7. This product spectroscopically matched that of the known compound.[15]

2-Benzylidenebutanenitrile (4b). Column chromatography (Hex/EtOAc = 99/1) yielded **4b** (111 mg, 71%, *Z*/*E* = 70:30). ***Z*-Isomer** (major): R_f 0.86 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74−7.70 (m, 2H), 7.45−7.36 (m, 3H), 6.94 (apparent s, 1H), 2.44 (qd, *J* = 7.5, 1.2 Hz, 2H), 1.26 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 133.8, 129.8, 128.7, 128.5, 118.7, 112.9, 29.6, 13.0; HRMS (TOF MS ES$^+$) calcd for $C_{11}H_{11}NNa$ 180.0789 [M + Na]$^+$, found 180.0818. ***E*-Isomer** (minor): R_f 0.83 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.20 (m, 6H), 2.54−2.47 (m, 2H), 1.26 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 134.1, 129.2, 129.1, 128.7, 120.2, 117.2, 22.9, 12.8; HRMS (TOF MS ES$^+$) calcd for $C_{11}H_{11}NNa$ 180.0789 [M + Na]$^+$, found 180.0787.

2-Benzyl-3-phenylacrylonitrile (4c). Column chromatography (Hex/EtOAc = 99/1) yielded **4c** (185 mg, 84%, *Z*/*E* = 86:14). ***Z*-Isomer** (major): R_f 0.92 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75−7.73 (m, 2H), 7.42−7.29 (m, 8H), 6.98 (s, 1H), 3.72 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 136.4, 133.5, 130.1, 128.89, 128.87, 128.8, 128.7, 127.3, 118.7, 110.8, 42.2. This product spectroscopically matched that of the known compound.[8d] ***E*-Isomer** (minor): R_f 0.86 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.24 (m, 11H), 3.82 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 136.4, 133.7, 129.5, 129.0, 128.9, 128.8, 128.3, 127.2, 120.2, 114.1, 35.5; HRMS (TOF MS ES$^+$) calcd for $C_{16}H_{13}NNa$ 242.0946 [M + Na]$^+$, found 242.0941.

2-Benzylidenepent-4-enenitrile (4d). Column chromatography (Hex/EtOAc = 99/1) yielded **4d** (140 mg, 83%, *Z*/*E* = 70:30). ***Z*-Isomer** (major): R_f 0.88 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (apparent d, *J* = 7.0 Hz, 2H), 7.42−7.40 (m, 3H), 6.96 (s, 1H), 5.93−5.87 (m, 1H), 5.29−5.25 (m, 2H), 3.14 (d, *J* = 6.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 133.6, 132.8, 130.1, 128.8, 128.6, 118.8, 118.6, 109.5, 40.0. This product spectroscopically matched that of the known compound.[16] ***E*-Isomer** (minor): R_f 0.84 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.30 (m, 6H), 5.97−5.90 (m, 1H), 5.30−5.26 (m, 2H), 3.21 (d, *J* = 5.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.1, 133.7 132.4, 129.5, 129.0, 128.7, 120.2, 118.2, 113.0, 33.9; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{11}NNa$ 192.0789 [M + Na]$^+$, found 192.0786.

2-(4-Methylbenzyl)-3-phenylacrylonitrile (4e). Column chromatography (Hex/EtOAc = 99/1) yielded **4e** (208 mg, 89%, *Z*/*E* = 88:12). ***Z*-Isomer** (major): R_f 0.90 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (apparent d, *J* = 6.0 Hz, 2H), 7.41−7.39 (m, 3H), 7.18 (s, 4H), 6.95 (s, 1H), 3.67 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 137.0, 133.6, 133.3, 130.0, 129.6, 128.80, 128.77, 128.65, 118.7, 111.1, 41.8, 21.1. This product spectroscopically matched that of the known compound.[8f] ***E*-Isomer** (minor): R_f 0.85 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.36 (m, 6H), 7.15 (s, 4H), 3.78 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 136.9, 133.8, 133.3, 129.6, 129.5, 129.0, 128.8, 128.2, 120.3, 114.3, 35.1, 21.1; HRMS (TOF MS ES$^+$) calcd for $C_{17}H_{15}NNa$ 256.1102 [M + Na]$^+$, found 256.1097.

2-Benzyl-3-(*p*-tolyl)acrylonitrile (4f). Column chromatography (Hex/EtOAc = 99/1) yielded **4f** (224 mg, 96%, *Z*/*E* = 88:12). ***Z*-Isomer** (major): R_f 0.87 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.40−7.28 (m, 5H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.93 (s, 1H), 3.70 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 140.5, 136.6, 130.8, 129.5, 128.89, 128.85, 128.7, 127.3, 118.9, 109.4, 42.2, 21.4. This product spectroscopically matched that of the known compound.[8c] ***E*-Isomer** (minor): R_f 0.80 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.19 (m, 10H), 3.83 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 139.9, 136.5, 130.9, 129.5, 129.0, 128.9, 128.3, 127.2, 120.5, 112.9, 35.5, 21.4; HRMS (TOF MS ES$^+$) calcd for $C_{17}H_{15}NNa$ 256.1102 [M + Na]$^+$, found 256.1096.

2-Methyl-3-(4-nitrophenyl)acrylonitrile (4g). Column chromatography (Hex/EtOAc = 99/1) yielded **4g** (151 mg, 80%, *Z*/*E* = 81:19). ***Z*-Isomer** (major): R_f 0.79 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.01 (apparent s, 1H), 2.23 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 141.3, 139.7, 129.2, 124.0, 118.1, 111.1, 22.3. This product spectroscopically matched that of the known compound.[8i] ***E*-Isomer** (minor): R_f 0.75 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.26 (apparent s, 1H), 2.17 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 141.8, 140.0, 130.0, 123.9, 120.1, 113.7, 17.0; HRMS (TOF MS ES$^+$) calcd for $C_{10}H_8N_2O_2$Na 211.0483 [M + Na]$^+$, found 211.0476.

3-(4-Methoxyphenyl)-2-(4-methylbenzyl)acrylonitrile (4h). Column chromatography (toluene) yielded **4h** (190 mg, 72%, *Z*-isomer only). ***Z*-Isomer** (major): R_f 0.86 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.7 Hz, 2H), 7.18 (s, 4H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.89 (s, 1H), 3.84 (s, 3H), 3.64 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 143.3, 136.8, 133.7, 130.4, 129.5, 128.7, 126.3, 119.3, 114.1, 107.9, 55.3, 41.7, 21.1. This product spectroscopically matched that of the known compound.[8f]

3-(4-Chlorophenyl)-2-(4-methylbenzyl)acrylonitrile (4i). Column chromatography (Hex/EtOAc = 99/1) yielded **4i** (240 mg, 90%, *Z*/*E* = 86:14). ***Z*-Isomer** (major): R_f 0.94 (toluene); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.18 (s, 4H), 6.89 (s, 1H), 3.67 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 137.0, 135.8, 133.0, 132.0, 129.9, 129.6, 129.0, 128.8, 118.4, 111.7, 41.7, 21.0. This product spectroscopically matched that of the known compound.[8f] ***E*-Isomer** (minor): R_f 0.89 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.10 (m, 9H), 3.75 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 137.0, 135.6, 132.9, 132.1, 130.3, 129.7, 129.1, 128.1, 120.1, 114.9, 35.1, 21.1; HRMS (TOF MS ES$^+$) calcd for $C_{17}H_{14}ClNNa$ 290.0713 [M + Na]$^+$, found 290.0713.

2-(2-Chlorobenzylidene)hexanenitrile (4j). Column chromatography (Hex/EtOAc = 99/1) yielded **4j** (168 mg, 72%, *Z*/*E* = 85:15). ***Z*-Isomer** (major): R_f 0.93 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94−7.90 (m, 1H), 7.44−7.26 (m, 4H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.71−1.65 (m, 2H), 1.41−1.35 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 133.8, 132.3, 130.7, 129.6, 129.2, 127.1, 118.2, 115.1, 35.9, 30.8, 27.7, 22.3, 14.0. This product spectroscopically matched that of the known compound.[8g] ***E*-Isomer** (minor): R_f 0.91 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.21 (m, 5H), 2.35−2.30 (m, 2H), 1.65−1.60 (m, 2H), 1.29−1.26 (m, 4H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.2, 133.9, 132.5, 130.3, 130.0, 129.9, 126.6, 119.7, 118.1, 30.9, 29.3, 27.6, 22.2, 13.9; HRMS (TOF MS ES$^+$) calcd for $C_{14}H_{16}ClNNa$ 256.0869 [M + Na]$^+$, found 256.0864.

2-Methyl-5-phenylpent-2-enenitrile (4k). Column chromatography (Hex/EtOAc = 20/1) yielded **4k** (149 mg, 87%, *Z*/*E* = 11:89). ***E*-Isomer** (major): R_f 0.81 (toluene); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.12 (m, 5H), 6.32 (dt, *J* = 7.5, 0.8 Hz, 1H), 2.71 (t, *J* = 7.5 Hz, 2H), 2.45 (dt, *J* = 7.5, 7.5 Hz, 2H), 1.72 (d, 0.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 140.1, 128.4, 128.2, 126.2, 120.4, 109.8, 34.0, 30.1, 14.6; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{13}NNa$ 194.0946 [M + Na]$^+$, found 194.0940. ***Z*-Isomer** (minor): R_f 0.85 (toluene); ^{1}H NMR

(300 MHz, $CDCl_3$) δ 7.33−7.17 (m, 5H), 6.14 (t, J = 7.1 Hz, 1H), 2.75−2.65 (m, 4H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 140.2, 128.5, 128.3, 126.2, 117.9, 109.8, 34.7, 33.0, 20.0; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{13}NNa$ 194.0946 [M + Na]$^+$, found 194.0941.

2-Benzylpent-2-enenitrile (4l). Column chromatography (Hex/EtOAc = 98/2) yielded **4l** (169 mg, 99%, Z/E = 16:84). ***E*-Isomer** (major): R_f 0.82 (toluene); ^1H NMR (500 MHz, $CDCl_3$) δ 7.36−7.22 (m, 5H), 6.46 (t, J = 7.5 Hz, 1H), 3.56 (s, 2H), 2.33 (dq, J = 7.5, 7.5 Hz, 2H), 1.09 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.1, 136.7, 128.8, 128.3, 127.0, 119.9, 113.4, 34.6, 22.1, 12.9; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{13}NNa$ 194.0946 [M + Na]$^+$, found 194.0940. ***Z*-Isomer** (minor): R_f 0.86 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.19 (m, 5H), 6.18 (t, J = 7.5 Hz, 1H), 3.50 (s, 2H), 2.39 (dq, J = 7.5, 7.5 Hz, 2H), 1.06 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 136.6, 128.77, 128.73, 127.1, 117.4, 113.6, 40.2, 25.0, 13.1; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{13}NNa$ 194.0946 [M + Na]$^+$, found 194.0941.

6-Chloro-2-(4-fluorobenzyl)hex-2-enenitrile (4m). Column chromatography (Hex/EtOAc = 20/1) yielded **4m** (181 mg, 76%, Z/E = 12:88). ***E*-Isomer** (major): R_f 0.83 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 7.22−7.17 (m, 2H), 7.06−6.99 (m, 2H), 6.41 (t, J = 7.5 Hz, 1H), 3.59−3.55 (m, 4H), 2.50 (apparent q, J = 7.5 Hz, 2H), 1.99−1.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0 (d, $^1J_{CF}$ = 244.2 Hz), 146.5, 132.1 (d, $^4J_{CF}$ = 3.3 Hz), 130.0 (d, $^3J_{CF}$ = 8.0 Hz), 119.4, 115.8 (d, $^2J_{CF}$ = 21.5 Hz), 115.4, 43.8, 33.9, 30.8, 25.7; HRMS (TOF MS ES$^+$) calcd for $C_{14}H_{12}ClFNNa$ 260.0618 [M + Na]$^+$, found 260.0609. ***Z*-Isomer** (minor): R_f 0.88 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 7.19−7.14 (m, 2H), 7.06−7.00 (m, 2H), 6.18 (t, J = 7.5 Hz, 1H), 3.54 (t, 6.5, 2H), 3.50 (s, 2H), 2.55 (apparent q, 7.5 Hz, 2H) 1.93 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0 (d, $^1J_{CF}$ = 244.4 Hz), 146.4, 131.9 (d, $^4J_{CF}$ = 3.0 Hz), 130.2 (d, $^3J_{CF}$ = 8.0 Hz), 117.0, 115.7 (d, $^2J_{CF}$ = 21.3 Hz), 115.6, 43.8, 39.6, 31.3, 28.9; HRMS (TOF MS ES$^+$) calcd for $C_{14}H_{12}ClFNNa$ 260.0618 [M + Na]$^+$, found 260.0632.

3-Cyclohexyl-2-methylacrylonitirle (4n). Column chromatography (Hex/EtOAc = 20/1) yielded **4o** (125 mg, 84%, Z/E = 24:76). ***E*-Isomer** (major): R_f 0.77 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 6.17 (qd, J = 1.5, 9.6 Hz, 1H), 2.38−2.24 (m, 1H), 1.86 (d, J = 1.5 Hz, 1H), 1.76−1.59 (m, 5H), 1.36−1.06 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 120.9, 107.3, 37.6, 31.5, 25.6, 25.3, 14.8; HRMS (TOF MS ES$^+$) calcd for $C_{10}H_{15}NNa$ 172.1102 [M + Na]$^+$, found 172.1096. ***Z*-Isomer** (minor): R_f 0.85 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 5.96 (qd, J = 1.5, 9.9 Hz, 1H), 2.57−2.43 (m, 1H), 1.90 (d, J = 1.5 Hz, 3H), 1.76−1.62 (m, 5H), 1.41−1.02 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 118.3, 106.8, 40.8, 32.1, 25.6, 25.2, 20.1; HRMS (TOF MS ES$^+$) calcd for $C_{10}H_{15}NNa$ 172.1102 [M + Na]$^+$, found 172.1094.

2-Methyl-5-phenylpenta-2,4-dienenitrile (4p). Column chromatography (Hex/EtOAc = 25/1) yielded **4n** (139 mg, 82%, Z/E = 69:31). ***Z*-Isomer** (major): R_f 0.85 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (apparent d, J = 6.9 Hz, 2H), 7.40−7.30 (m, 3H), 7.14 (dd, J = 15.5, 11.3 Hz, 1H), 6.81−6.72 (m, 2H), 2.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 138.6, 135.8, 129.1, 128.8, 127.2, 124.6, 118.5, 107.8, 20.2; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{11}NNa$ 192.0789 [M + Na]$^+$, found 192.0767. ***E*-Isomer** (minor): R_f 0.79 (toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (apparent d, J = 6.6 Hz, 2H), 7.40−7.32 (m, 3H), 6.97 (dd, J = 14.7, 10.8 Hz, 1H), 6.91−6.79 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 139.8, 135.8, 129.3, 128.9, 127.2, 121.9, 107.4, 15.3; HRMS (TOF MS ES$^+$) calcd for $C_{12}H_{11}NNa$ 192.0789 [M + Na]$^+$, found 192.0785.

Synthesis of (*E*)-2-Butyl-2-octenal (7). Into a flame-dried round-bottomed flask was added dry THF (15 mL) under an argon atmosphere. After the mixture was cooled to −78 °C (acetone/dry ice bath), *n*-BuLi (2.0 mL, 2.5 M solution in hexanes, 5.0 mmol) and dry CH_3CN (390 μL, 7.5 mmol) were added dropwise, respectively. After the mixture was stirred for 20 min, $(i\text{-}Pr_2N)_2BCl$ (684 μL, 2.5 mmol) was then slowly added. After another 1 h of stirring, 1-iodobutane (285 μL, 2.5 mmol) was added. The reaction mixture was stirred for an additional 1 h at 0 °C and then concentrated under reduced pressure. Dry THF (15 mL) was subsequently added into the crude mixture under an argon atmosphere. After the mixture was cooled to −78 °C (acetone/dry ice bath), tetramethylethylenediamine (376 μL, 2.5 mmol) and *n*-BuLi (1.0 mL, 2.5 M solution in hexane, 2.5 mmol) were added dropwise. After the mixture was stirred for 1 h, hexanal (246 μL, 2.0 mmol) was slowly added, and the resulting mixture was stirred for 1.5 h at the same temperature. The reaction mixture was then quenched with half-saturated NH_4Cl (12 mL) (−78 °C to rt over 30 min). After the phase separation, the aqueous layer was extracted with Et_2O (×2), and the combined organics were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained crude product **4q** (E/Z = 86:14) was directly used for the next reaction. Into a solution of **4q** (236 mg, 1.31 mmol) in dry toluene (14 mL) under argon atmosphere was added DIBAL reagent (3.29 mL, 1.0 M solution in hexane, 3.29 mmol) slowly at −78 °C. After being stirred for 1.5 h at the same temperature, the reaction mixture was quenched with methanol (1.0 mL) and was then warmed to room temperature. The resulting mixture was diluted with CH_2Cl_2, filtered through a Celite pad, and concentrated under reduced pressure. The crude product was purified by SiO_2 column chromatography (toluene as eluent) to afford **7** (186 mg, 51% over two steps) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 9.36 (s, 1H), 6.44 (t, J = 7.5 Hz, 1H), 2.34−2.20 (m, 4H), 1.52−1.29 (m, 10H), 0.94−0.87 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 155.4, 143.8, 31.5, 30.9, 28.9, 28.4, 23.8, 22.8, 22.5, 14.0, 13.9. This product spectroscopically matched that of the known compound.[8g]

■ ASSOCIATED CONTENT

Supporting Information. ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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