The Direct Synthesis of Unsymmetrical Vicinal Diamines from Terminal Alkynes: A Tandem Sequential Approach for the Synthesis of Imidazolidinones

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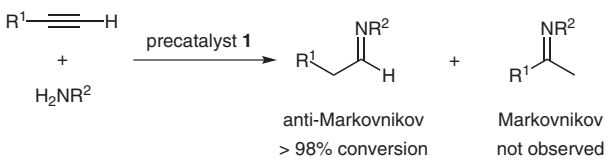
Abstract: The combination of titanium-catalyzed anti-Markovnikov hydroamination of terminal alkynes with the Strecker reaction is used in the synthesis of unsymmetrical vicinal diamines via the one-pot synthesis of α-cyanoamines. This methodology is further applied to the efficient synthesis of imidazolidinones. An easy-to-use bis(amidate)titanium precatalyst permits efficient approaches to heterocyclic chemistry from terminal alkynes.

Key words: hydroamination, titanium, amines, heterocycles, tandem reactions

The synthesis of functionalized nitrogen-containing molecules is of ongoing interest in organic chemistry, as these molecules have found widespread applications in areas such as pharmaceuticals,[1–3] detergents, and dyes.[4–7] Furthermore, the development of new methodologies to synthesize nitrogen-containing molecules from alternative starting materials is of great importance, as this allows the chemist enhanced flexibility in synthetic design. Unsymmetrically substituted vicinal diamines belong to an important class of nitrogen-containing molecules[8–13] whose synthesis is particularly challenging.[12,14,15] Herein we describe a tandem C–N- and C–C-bond-forming reaction sequence resulting from the one-pot combination of catalytic hydroamination and the Strecker reaction and its applications in the efficient synthesis of unsymmetrical vicinal diamines directly from terminal alkynes.

Hydroamination is the addition of nitrogen and hydrogen atoms across a carbon–carbon multiple bond that can be efficiently mediated by a range of metal-based catalysts.[16–65] In the hydroamination of terminal alkynes (Equation 1), we have reported bis(amidate)bis(amido)titanium precatalyst **1** (Figure 1) as an active and very regioselective catalytic complex for the formation of the anti-Markovnikov imine in the catalytic hydroamination of terminal alkynes with primary amines.[66,67]



Equation 1

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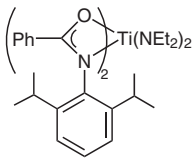


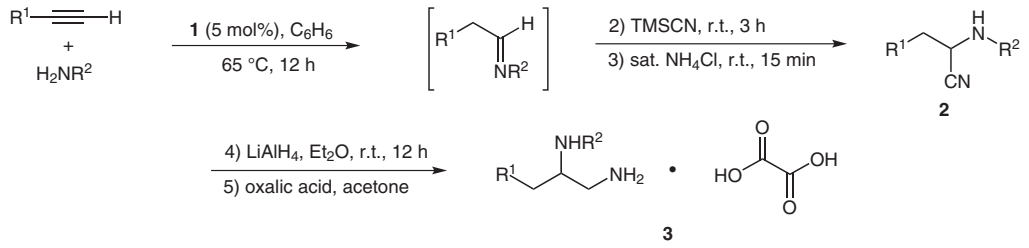
1

Figure 1

Furthermore, complex **1** (Figure 1) is very tolerant of many different functional groups, such as protected alcohols and amines, esters, and amides.[15] This functional-group tolerance and high regioselectivity, combined with the fact that there are no byproducts formed during the hydroamination reaction results in the facile synthesis of a wide variety of aldimines that do not require isolation or purification before use in further synthetic steps.

The Strecker reaction uses imines as intermediates in the synthesis of α-cyanoamines and α-amino acid derivatives. Typically the imines are derived from aldehydes and are isolated and purified before use. Because the aldimine functionality is easily hydrolyzed, this isolation step can lead to reduced substrate scope and low yields, especially for alkylimines. However, catalytic hydroamination generates a broad range of aldimines quantitatively, with 100% atom economy, and do not require isolation. Therefore, the combination of catalytic hydroamination with the Strecker reaction leads to the one-pot synthesis of α-cyanoamines from terminal alkynes (Scheme 1).[68] The good functional-group tolerance of hydroamination precatalyst **1** results in the potential incorporation of different functionalities into the final α-cyanoamine products. Furthermore, these α-cyanoamines have the potential to be used as intermediates in the synthesis of other important classes of organic molecules, including α-amino acid derivatives and β-amino alcohols.

In particular, this contribution demonstrates that the α-cyanoamines formed through the tandem sequential reaction using terminal alkyne substrates would be ideal precursors in the synthesis of unsymmetrical vicinal diamines (Scheme 1). Along with an unsymmetrical substitution pattern, diamines formed through this route would contain both a primary and a secondary amine in the same molecule. Furthermore, these diamines can be used as precursors for heterocycles such as piperazines,[69] *N*,*N*′-substituted carbenes,[70] imidazolidines,[71] and imidazolidinones.

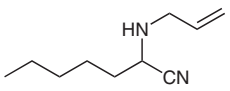
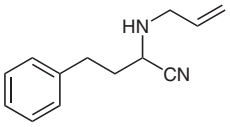
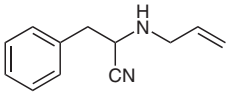
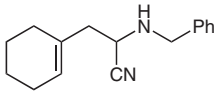
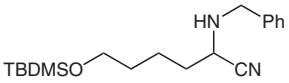
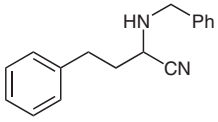
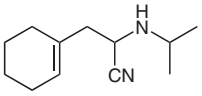
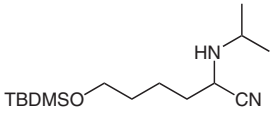
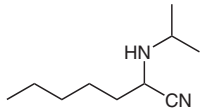


Scheme 1

The combination of a terminal alkyne, a primary amine, and precatalyst **1** (5 mol%) in benzene at 65 °C leads to the exclusive formation of the anti-Markovnikov imine in quantitative conversion. Trimethylsilyl cyanide is then added to the reaction mixture via syringe at room temperature, and the resultant TMS-protected α-cyanoamines are quenched with saturated ammonium chloride to form the α-cyanoamine products **2** in one pot (Scheme 1). A range of alkyl-substituted α-cyanoamines **2a–m**, incorporating various functional groups, have been synthesized by this tandem sequential reaction (Table 1).

All the α-cyanoamines are formed quantitatively from the terminal alkyne starting material (Scheme 1, Table 1). While the purification of these molecules is not trivial,[3] spectroscopic experiments show that only the amide proligand (resulting from the decomposition of **1** upon work-up) is present in the crude reaction mixture. Because

Table 1 Quantitative Formation of α-Cyanoamines **2a–i** Synthesized Directly from Terminal Alkynes and Primary Amines[a]

Entry	R^1 (from alkyne)	R^2 (from amine)	α-Cyanoamine[b] **2**	
1	Bu	Allyl		**2a**
2	Bn	Allyl		**2b**
3	Ph	Allyl		**2c**
4	cyclohex-1-enyl	Bn		**2d**
5	$(CH_2)_3$OTBDMS	Bn		**2e**
6	Bn	Bn		**2f**
7	cyclohex-1-enyl	*i*-Pr		**2g**
8	$(CH_2)_3$OTBDMS	*i*-Pr		**2h**
9	Bu	*i*-Pr		**2i**

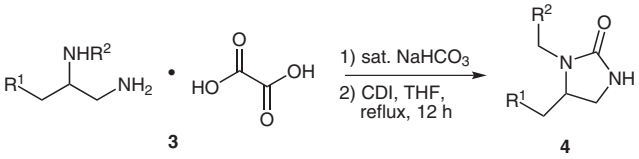
[a] See Scheme 1.
[b] All unpurified α-cyanoamines were characterized in the presence of the amide proligand.

α-cyanoamines are used as intermediates in the formation of other functionalized small molecules, it is critical that the amide proligand does not interfere with further reactivity,[68] and thus purification at this stage is unnecessary. Allylamine can be used successfully as a substrate in this reaction (Table 1, entries 1–3). Allylamine can be used as a protecting group for a primary amine and has an additional functionality available for further reactions. It should also be noted that, to the best of our knowledge, **1** is the only reported group 4 hydroamination precatalyst that can be used with the allylamine substrate. Benzylamine can also be used in this sequence with alkynes that contain alkyl or aryl groups, as well as protected alcohols (Table 1, entries 4–6). Benzylamine is an important substrate, as the amine can be deprotected at a later step to give the primary amine. Finally, more steric bulk can also be incorporated into the amine substrate (see Table 1, entries 7–9) along with alkynes possessing various functional groups.

The synthesis of unsymmetrical vicinal diamines **3a–h** is accomplished through the reduction of the corresponding α-cyanoamines **2** with lithium aluminum hydride (Scheme 1, Table 2). Following reduction, the free diamines obtained are susceptible to decomposition, and consequently these highly functionalized compounds are separated from the proligand by acid–base extraction and subsequent precipitation of their corresponding oxalate salts (Scheme 1). These materials may be stored indefinitely. Representative examples of unsymmetrical diamines **3** that have been synthesized from terminal alkynes by this methodology in good isolated yields over five synthetic steps are shown in Table 2.

The synthesized diamines **3a–h** (Table 2) contain various functionalities in the backbone including long alkyl chains, aryl substituents, and cyclic alkyl substituents. The nitrogen substituents include the bulky isopropyl group, a benzyl functionality that can be removed, and an allyl group that could lead to further functionalization or undergo deprotection to give the amine. While these straightforward compounds may be anticipated to have been previously reported, it should be noted that six of the eight diamines presented in Table 2 (exceptions being **3d** and **3e**) are new compounds, and, as such, their full characterization data are included in the experimental section.

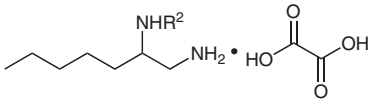
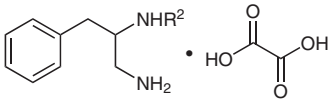
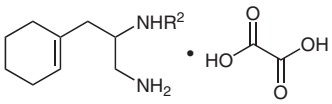
As mentioned earlier, diamines are useful starting materials for the synthesis of various heterocycles including imidazolidinones. The imidazolidinone functionality has been investigated in a number of compounds for pharmaceutical applications.[72–76] Furthermore, imidazolidinones have been used as both ligands[77] and chiral auxiliaries.[78] Here, the synthesis of three novel imidazolidinones **4a–c** from the corresponding diamines **3** is presented (Equation 2, Table 3). This is accomplished with the reaction of the appropriate diamine oxalates **3** with a base to obtain the free diamines, followed by reaction with *N*,*N*-carbonyldiimidazole (CDI) in refluxing tetrahydrofuran (Equation 2). This leads to the formation of the corresponding imidazolidinones **4** in high yields after column chromatography (Table 3).



Equation 2

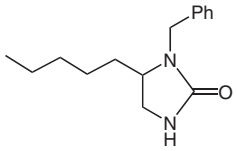
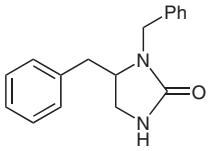
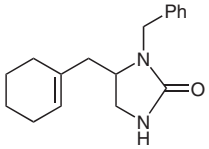
The synthesis of these molecules is very efficient and notably requires only one purification step by column chromatography. The intermediate compounds, namely the α-cyanoamines **2** and the vicinal diamines **3**, can both be used without purification towards the synthesis of the imidazolidinones **4**. Furthermore, while both the vicinal diamines **3** and the imidazolidinones **4** are synthesized in a

Table 2 Diamines **3** Synthesized by a Tandem Reaction Sequence

Entry	Diamine product	R^2	**3**	Yield[a] (%)
1		Bn	**3a**	65
2		*i*-Pr	**3b**	69
3		Allyl	**3c**	59
4		Bn	**3d**	55
5		*i*-Pr	**3e**	54
6		Allyl	**3f**	60
7		Bn	**3g**	56
8		Allyl	**3h**	50

[a] Overall isolated yield calculated from terminal alkyne.

Table 3 Imidazolidinones **4** Synthesized from Diamines **3**

Entry	Imidazolidinone	4	Yield[a] (%)
1		**4a**	82 (53)[b]
2		**4b**	75 (41)[b]
4		**4c**	85 (48)[b]

[a] Isolated yield of **4** from diamine **3**, after column chromatography.
[b] Overall yield of **4** calculated from the corresponding terminal alkyne.

racemic fashion here, there are established methodologies for their resolution through diastereomer formation.[79–82]

In conclusion, we have described a tandem C–N- and C–C-bond-forming reaction sequence that uses a titanium-catalyzed anti-Markovnikov hydroamination as a key step for generating imines in situ for application in the Strecker reaction. This methodology has been used to synthesize a number of important classes of organic molecules such as α-cyanoamines, unsymmetrical vicinal diamines, and imidazolidinones from terminal alkynes. In particular, the atom-economical, catalytic formation of the aldimines, along with the one-pot formation of α-cyanoamines represent an efficient methodology that is environmentally friendly by reducing solvent volumes typically required for multiple isolation and purification steps. Ongoing efforts focus on asymmetric versions of this reaction to prepare enantiomerically enriched unsymmetrical vicinal diamines as important compounds in heterocycle synthesis.

Except where otherwise noted, all reactions and manipulations were carried out at r.t. without precautions to exclude atmospheric moisture. All solvents for workup procedures were used as received from Aldrich or Sigma. Anhydrous benzene and Et_2O were purified on an alumina column and stored under a N_2 atmosphere. $Ti(NMe_2)_4$ was purchased and used as received. Hex-1-yne, phenylacetylene, and 1-ethynylcyclohexene were purchased from Aldrich. All alkynes were dried over 4 Å MS for 12 h before they were distilled, and degassed. The alkynes were then transferred into a N_2-filled glovebox and further dried over 4 Å MS for an additional 12 h before use. All primary amines were purchased from Aldrich and dried over CaH_2 for 12 h before they were distilled and degassed. The amines were then stored in the N_2-filled glovebox and further dried over 4 Å MS for an additional 12 h before use. All other chemicals were reagent grade and used as received from commercial suppliers. All NMR spectra were acquired from samples in deuterated solvents (purchased from Cambridge Isotope Labs) at r.t. in the UBC Chemistry NMR facility on a Bruker Avance 300 spectrometer [300 MHz (^{1}H) and 75 MHz (^{13}C)], a Bruker Avance 400 spectrometer [400 MHz (^{1}H) and 100 MHz (^{13}C)] or a Bruker Avance 600 spectrometer [600 MHz (^{1}H) and 150 MHz (^{13}C)], and chemical shifts are given relative to residual solvent. IR spectra were recorded on a Nicolet 4700 FT-IR spectrophotometer in transmission mode as KBr discs between 400 and 4000 cm^{-1} at a resolution of ±4 cm^{-1}. LR-MS were obtained using ESI-MS and APCI-MS (atmospheric pressure chemical ionization mass spectrometry) in the UBC Chemistry Mass Spectrometry facility on the open-access MS. EI-MS, HRMS, and elemental analysis were performed by the UBC Chemistry Mass Spectrometry facility. Plates used for TLC (0.2-mm silica gel 60 F_{254} on alumina) and silica gel used for column chromatography (70–230 and 230–400 mesh) were purchased from Silicycle (Montreal, QC, Canada). TLC spots were visualized under a UVG-54 Mineralight® short-wave UV lamp (λ = 254 nm). The following compounds were synthesized according to literature procedures: *N*-(2,6-diisopropylphenyl)benzamide,[66] bis[*N*-(2,6-diisopropylphenyl)benzamidato]bis(diethylamido)titanium (**1**),[66] 3-phenylprop-1-yne,[83] and 1-(*tert*-butyldimethylsiloxy)pent-4-yne.[84]

α-Cyanoamines 2; General Procedure

An oven-dried 110-mL Schlenk tube was brought into the glovebox and charged with alkyne (1.7 mmol), primary amine (3.4 mmol), **1** (0.06 g, 0.09 mmol), and benzene (2 mL). The Schlenk flask was sealed with a greased glass stopper and sidearm stopcock, and removed from the glovebox. The soln was stirred at 65 °C for 12 h before it was cooled to r.t. The soln was then frozen using liquid N_2, and the headspace of the flask was evacuated under vacuum. The flask was warmed to r.t., and then taped with electrical tape before it was brought back into the glovebox where TMSCN (0.23 mL, 1.7 mmol) was added by syringe. The flask was again sealed and removed from the glovebox, and then stirred for 3 h within a fume hood. The soln was then opened to the atmosphere, diluted with CH_2Cl_2 (20 mL), and quenched with sat. NH_4Cl (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with brine (1 × 20 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the α-cyanoamine **2** as a pale yellow oily compound. All characterizations of the crude products were performed in the presence of the amide proligand from the hydroamination precatalyst, which was present in the samples as 9–13% of the reaction mixture. The signals in the NMR spectra from the proligand[66] are not listed. All crude products were isolated in quantitative yield.

2-(Allylamino)heptanenitrile (2a)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, ^3J = 6.8 Hz, 3 H, CH_3), 1.32–1.42 [m, 4 H, (CH_2)$_2$], 1.50–1.52 (m, 2 H, CH_2), 1.70–1.77 (m, 2 H, CH_2), 3.30–3.32 (m, 1 H, NCH_2), 3.50–3.56 (m, 3 H, NCH_2, NC*H*), 5.17 (d, ^3J = 10 Hz, ^2J = 0.6 Hz, 1 H, HCCH_2), 5.28 (d, ^3J = 17 Hz, ^2J = 1.4 Hz, 1 H, NCCH_2), 5.82–5.89 (m, 1 H, *H*CCH$_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4, 22.5, 25.4, 31.3, 33.6, 49.9, 50.3, 117.6, 120.4, 135.2.

MS (CI): *m*/*z* (%) = 167.3 (100) [M + H].

HRMS (CI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{19}N_2$: 167.1548; found: 167.1542.

2-(Allylamino)-4-phenylbutanenitrile (2b)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (br s, 1 H, N*H*), 2.07–2.17 (m, 2 H, CH_2), 2.79–2.93 (m, 2 H, CH_2), 3.25–3.31 (m, 1 H, NCH_2), 3.48–3.55 (m, 2 H, NCH_2, NC*H*), 5.16 (d, ^3J = 10 Hz, 1 H, HCCH_2), 5.27 (d, ^3J = 16 Hz, 1 H, HCCH_2), 5.81–5.91 (m, 1 H, *H*CCH$_2$), 7.08–7.37 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.8, 35.1, 49.1, 50.2, 117.5, 120.2, 126.5, 128.5, 128.7, 135.0, 140.0.

MS (CI): *m/z* (%) = 201.3 (100) [M + H], 174.3 (100) [M – CN].

HRMS (CI): *m/z* [M + H]$^+$ calcd for $C_{13}H_{17}N_2$: 201.1392; found: 201.1388.

2-(Allylamino)-3-phenylpropanenitrile (2c)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (br s, 1 H, N*H*), 3.00–3.20 (m, 2 H, PhCH_2), 3.29 (dd, ^2J = 12 Hz, ^3J = 6.4 Hz, 1 H, NHCH_2), 3.52 (dd, ^2J = 13 Hz, ^3J = 5 Hz, 1 H, NHCH_2), 3.80 (t, ^3J = 6.6 Hz, 1 H, PhCH_2C*H*), 5.17 (d, ^3J = 10 Hz, ^2J = 0.8 Hz, 1 H, HCCH_2), 5.26 (d, ^3J = 16 Hz, ^2J = 1.2 Hz, 1 H, HCCH_2), 5.78–5.88 (m, 1 H, *H*CCH$_2$), 7.20–7.42 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.6, 50.3, 51.0, 117.8, 119.7, 127.7, 128.9, 129.7, 135.0, 146.6.

MS (CI): *m/z* (%) = 187.3 (100) [M + H].

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{12}H_{14}N_2$: 186.11570; found: 186.11579.

2-(Benzylamino)-3-cyclohex-1-enylpropanenitrile (2d)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53–1.63 [m, 4 H, (CH_2)$_2$], 1.83–2.03 [m, 4 H, (CH_2)$_2$], 2.51–2.54 (m, 2 H, CH_2), 3.60 (t, ^3J = 7.2 Hz, 1 H, C*H*), 3.82 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 4.09 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 5.60–5.62 (m, 1 H, C*H*), 7.22–7.59 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.2, 22.9, 25.4, 28.4, 42.0, 43.4, 51.7, 120.4, 126.8, 127.7, 128.2, 129.0, 131.9, 138.6.

MS (CI): *m/z* (%) = 241.4 (70) [M + H], 214.4 (40) [M – CN].

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{16}H_{20}N_2$: 240.16265; found: 240.16152.

2-(Benzylamino)-6-(*tert*-butyldimethylsiloxy)hexanenitrile (2e)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06 [s, 6 H, Si(CH_3)$_2$], 0.91 [s, 9 H, SiC(CH_3)$_3$], 1.49–1.60 [m, 4 H, (CH_2)$_2$], 1.78–1.83 (m, 2 H, CH_2), 3.51 (t, ^3J = 6.8 Hz, 1 H, C*H*), 3.62 (t, ^3J = 5.6 Hz, 2 H, OCH_2), 3.84 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 4.08 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 7.24–7.36 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.2, 18.5, 22.4, 26.1, 32.3, 33.5, 50.0, 51.8, 62.8, 120.4, 127.7, 128.5, 128.7, 138.6.

MS (CI): *m/z* (%) = 333.3 (100) [M + H].

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{19}H_{32}N_2OSi$: 332.22839; found: 332.22828.

2-(Benzylamino)-4-phenylbutanenitrile (2f)

^{1}H NMR (300 MHz, benzene-d_6): δ = 0.64 (br s, 1 H, N*H*), 1.49–1.57 (m, 2 H, PhCH$_2$CH_2), 2.42 (t, ^3J = 7.5 Hz, 2 H, PhCH_2), 2.91 (t, ^3J = 7.7 Hz, 1 H, C*H*), 3.42 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 3.66 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 6.88–6.90 (m, 2 H, Ar *H*), 7.01–7.13 (m, 8 H, Ar *H*).

^{13}C NMR (75 MHz, benzene-d_6): δ = 31.8, 35.2, 48.8, 51.6, 119.8, 126.5, 127.7, 128.6, 128.6, 128.8, 131.5, 139.1, 140.5.

ESI-MS: *m/z* (%) = 251.3 (80) [M + H], 224.3 (30) [M – CN].

HRMS (CI): *m/z* [M + H]$^+$ calcd for $C_{17}H_{19}N_2$: 251.1548; found: 251.1544.

3-Cyclohex-1-enyl-2-(isopropylamino)propanenitrile (2g)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 [d, ^3J = 6.4 Hz, 3 H, CH(CH_3)$_2$], 1.12 [d, ^3J = 6.4 Hz, 3 H, CH(CH_3)$_2$], 1.53–1.73 [m, 4 H, (CH_2)$_2$], 1.97–2.04 [m, 4 H, (CH_2)$_2$], 2.23–2.43 (m, 2 H, CH_2), 3.11 [sept, ^3J = 6.0 Hz, 1 H, C*H*(CH$_3$)$_2$], 3.68 (t, ^3J = 6.4 Hz, 1 H, C*H*), 5.61–5.63 (m, 1 H, C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 22,2, 22.9, 23.9, 25.4, 28.5, 42.4, 47.1, 47.3, 120.7, 126.7, 131.9.

MS (CI): *m/z* (%) =193.4 (100) [M + H].

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{12}H_{20}N_2$: 192.16265; found: 192.16277.

6-(*tert*-Butyldimethylsiloxy)-2-(isopropylamino)hexanenitrile (2h)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, Si(CH_3)$_2$], 0.90 [s, 9 H, SiC(CH_3)$_3$], 1.03 [d, ^3J = 6.0 Hz, 3 H, CH(CH_3)$_2$], 1.12 [d, ^3J = 6.4 Hz, 3 H, CH(CH_3)$_2$], 1.52–1.56 [m, 4 H, (CH_2)$_2$], 1.76–1.80 (m, 2 H, CH_2), 3.10 [sept, ^3J = 6.0 Hz, 1 H, C*H*(CH$_3$)$_2$], 3.56 (t, ^3J = 6.8 Hz, 1 H, C*H*), 3.61–3.65 (m, 2 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.1, 18.5, 21.5, 22.3, 23.8, 25.8, 32.3, 34.0, 47.1, 48.3, 62.8, 120.7.

MS (CI): *m/z* (%) = 285.3 (70) [M + H], 258.4 (100) [M – CN].

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{15}H_{32}N_2OSi$: 284.22839; found: 284.22825.

2-(Isopropylamino)heptanenitrile (2i)

^{1}H NMR (300 MHz, benzene-d_6): δ = 0.62 (br s, 1 H, N*H*), 0.77–0.83 [m, 9 H, CH(CH_3)$_2$, CH_3], 1.02–1.30 [m, 8 H, (CH_2)$_4$], 2.91 [sept, ^3J = 6.2 Hz, 1 H, C*H*(CH$_3$)$_2$], 3.09 (t, ^3J = 6.0 Hz, 1 H, C*H*).

^{13}C NMR (75 MHz, benzene-d_6): δ = 14.1, 21.4, 22.7, 23.7, 25.6, 31.5, 34.2, 46.9, 48.1, 120.5.

ESI-MS: *m/z* (%) = 169.2 (100) [M + H], 142.3 (90) [M – CN].

ESI-HRMS: *m/z* [M + H]$^+$ calcd for $C_{10}H_{21}N_2$: 169.1705; found: 169.1701.

Diamines 3; General Procedure

An oven-dried 110-mL Schlenk flask was charged with alkyne (4.9 mmol), primary amine (5.4 mmol), precatalyst **1** (0.18 g, 0.24 mmol), and benzene (6 mL). The Schlenk flask was sealed with a greased glass stopper and sidearm stopcock, and removed from the glovebox. The soln was stirred at 65 °C for 12 h before it was cooled to r.t. The soln was then frozen using liquid N_2, and the headspace of the flask was evacuated under vacuum. The flask was warmed to r.t., and taped with electrical tape before being brought back into the glovebox where TMSCN (0.65 mL, 4.9 mmol) was added by syringe. After the mixture had stirred for an additional 3 h, it was diluted with CH_2Cl_2 (30 mL), quenched with sat. NH_4Cl (30 mL), extracted with CH_2Cl_2 (3 × 30 mL), washed with brine (1 × 30 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the α-cyanoamine **2**.

Anhyd Et_2O (10 mL) was added to the α-cyanoamine and the soln was transferred to an oven-dried round-bottom flask that was charged with a Teflon-coated stirrer bar, and covered with a N_2 atmosphere. LAH (0.37 g, 9.8 mmol) was added to the soln in small portions over 20 min. The slurry was stirred at r.t. for 12 h. Subsequently, H_2O (0.37 mL) was added slowly to the soln, followed by 1 M NaOH (0.37 mL), and a further portion of H_2O (1.11 mL). The soln was stirred until a white precipitate had formed and there was no gray solid left in the reaction flask. It was then filtered into a separatory funnel and the white solid was washed with Et_2O (20 mL). The organic layer was extracted with 1 M HCl (3 × 30 mL). The combined aqueous layers were washed with CH_2Cl_2 (2 × 90 mL) and hexanes (1 × 90 mL). Then 5 M aq NaOH was added to the acidic aqueous layer until it was basic, as indicated by pH paper. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resultant oil was dissolved in a minimum amount of acetone and transferred to a small round-bottom flask. A soln of oxalic acid (0.44 g, 4.9 mmol) was prepared in a minimal amount of acetone and added dropwise to the soln containing the diamine in acetone. A white precipitate was immediately obvious. After complete addition of the oxalic acid, the precipitate was filtered, washed with Et_2O (30 mL), and dried under high vacuum. Generally, the recovered precipitate did not require any further purification, although re-

crystallization could be performed from mixtures of EtOH or MeOH and H_2O if necessary. The hygroscopic nature of these compounds along with the diprotic nature of the oxalic acid rendered elemental analysis unsuccessful as a characterization technique.

N^2-Benzylheptane-1,2-diamine·Oxalate (3a)
Yield: 65%.

^{1}H NMR (400 MHz, D_2O): δ = 0.86–0.88 (m, 3 H, CH_3), 1.31–1.40 [m, 6 H, (CH_2)$_3$], 1.84–1.90 (m, 2 H, CH_2), 3.42 (d, ^3J = 5.7 Hz, 2 H, CHCH_2NH$_2$), 3.61–3.65 (m, 1 H, C*H*), 4.32 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 4.38 (d, ^2J = 13 Hz, 1 H, NCH_2Ph), 7.49–7.51 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, D_2O): δ = 14.1, 22.6, 24.5, 28.6, 31.5, 40.0, 50.0, 56.6, 130.4, 130.7, 130.9, 131.1, 166.8.

ESI-MS: *m*/*z* (%) = 221.3 (100) [M + H].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{25}N_2$: 221.2018; found: 221.2017.

N^2-Isopropylheptane-1,2-diamine·Oxalate (3b)
Yield: 69%.

^{1}H NMR (300 MHz, D_2O): δ = 0.87–0.90 (m, 3 H, CH_3), 1.29–1.37 [m, 12 H, CH(CH_3)$_2$, (CH_2)$_3$], 1.76–1.81 (m, 2 H, CH_2), 3.37 (d, ^3J = 5.7 Hz, 2 H, CHCH_2NH$_2$), 3.58–3.65 [m, 2 H, C*H*(CH$_3$)$_2$, C*H*].

^{13}C NMR (75 MHz, D_2O): δ = 13.2, 18.0, 18.4, 21.8, 23.4, 27.8, 30.7, 39.0, 49.1, 52.8, 165.2.

ESI-MS: *m*/*z* (%) = 173.3 (70) [M + H].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{25}N_2$: 173.2018; found: 173.2012.

N^2-Allylheptane-1,2-diamine·Oxalate (3c)
Yield: 59%.

^{1}H NMR (300 MHz, D_2O): δ = 0.87–0.91 (m, 3 H, CH_3), 1.32–1.45 [m, 6 H, (CH_2)$_3$], 1.80–1.86 (m, 2 H, CH_2), 3.40–3.43 (m, 2 H, CH_2NH$_2$), 3.59–3.65 (m, 1 H, CH$_2$C*H*), 3.77–3.82 (m, 2 H, NCH$_2$), 5.53–5.61 (m, 2 H, HCCH_2), 5.87–6.00 (m, 1 H, *H*CCH$_2$).

^{13}C NMR (100 MHz, D_2O): δ = 14.1, 22.6, 24.4, 28.6, 31.5, 39.7, 48.5, 56.1, 125.3, 127.8, 167.2.

ESI-MS: *m*/*z* (%) = 171.3 (100) [M + H].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{23}N_2$: 171.1861; found: 171.1863.

N^2-Benzyl-3-phenylpropane-1,2-diamine·Oxalate (3d)
Yield: 55%.

^{1}H NMR (300 MHz, D_2O): δ = 3.13–3.20 (m, 1 H, PhCH_2), 3.28–3.36 (m, 1 H, PhCH_2), 3.40–3.52 (m, 2 H, CH_2NH$_2$), 3.92–3.98 (m, 1 H, CH$_2$C*H*), 4.38 (s, 2 H, NCH_2Ph), 7.34–7.48 (m, 10 H, Ar *H*).

^{13}C NMR (100 MHz, D_2O): δ = 35.4, 40.3, 50.1, 57.5, 129.1, 130.2, 130.3, 130.4, 130.6, 130.8, 131.1, 134.9, 169.4.

ESI-MS: *m*/*z* (%) = 241.3 (100) [M + H].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{21}N_2$: 241.1705; found: 241.1700.

N^2-Isopropyl-3-phenylpropane-1,2-diamine·Oxalate (3e)
Yield: 54%.

^{1}H NMR (400 MHz, D_2O): δ = 1.34 [d, ^3J = 4.4 Hz, 6 H, CH(CH_3)$_2$], 3.11–3.16 (m, 1 H, PhCH_2), 3.24–3.29 (m, 1 H, PhCH_2), 3.35–3.46 (m, 2 H, CH_2NH$_2$), 3.59–3.65 [m, 1 H, C*H*(CH$_3$)$_2$], 3.95–3.98 (m, 1 H, CH$_2$C*H*), 7.39–7.50 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, D_2O): δ = 18.7, 19.4, 35.4, 40.4, 50.3, 54.9, 129.1, 130.3, 130.4, 134.8, 167.7.

ESI-MS: *m*/*z* (%) = 193.3 (100) [M + H].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{21}N_2$: 193.1705; found: 193.1710.

N^2-Allyl-3-phenylpropane-1,2-diamine·Oxalate (3f)
Yield: 60%.

^{1}H NMR (300 MHz, D_2O): δ = 3.09–3.14 (m, 1 H, PhCH_2), 3.24–3.29 (m, 1 H, PhCH_2), 3.34–3.39 (m, 1 H, CH_2NH$_2$), 3.44–3.50 (m, 1 H, CH_2NH$_2$), 3.73–3.83 (m, 2 H, NCH_2), 3.92–3.95 (m, 1 H, CH$_2$C*H*), 5.49–5.53 (m, 2 H, HCCH_2), 5.82–5.89 (m, 1 H, *H*CCH$_2$), 7.37–7.48 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, D_2O): δ = 35.3, 40.1, 48.6, 57.2, 125.4, 127.8, 129.1, 130.3, 130.4, 134.9, 168.8.

ESI-MS: *m*/*z* (%) = 191.3 (100) [M + H], 174.3 [M – NH$_2$].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{19}N_2$: 191.1548; found: 191.1544.

N^2-Benzyl-3-cyclohex-1-enylpropane-1,2-diamine·Oxalate (3g)
Yield: 56%.

^{1}H NMR (400 MHz, D_2O): δ = 1.51–1.69 [m, 4 H, (CH_2)$_2$], 1.83–2.03 [m, 4 H, (CH_2)$_2$], 2.46–2.58 (m, 2 H, CH_2CH), 3.33–3.51 (m, 2 H, CH_2NH$_2$), 3.68–3.71 (m, 1 H, CH$_2$C*H*), 4.37 (s, 2 H, NCH_2Ph), 5.75 (s, 1 H, C*H*), 7.47–7.50 (m, 5 H, Ar *H*).

^{13}C NMR (150 MHz, D_2O): δ = 20.8, 21.5, 24.3, 26.5, 36.9, 38.8, 48.4, 52.1, 128.3, 128.9, 129.3, 129.5, 130.1, 165.2.

ESI-MS: *m*/*z* (%) = 245.3 (100) [M + H].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{25}N_2$: 245.2018; found: 245.2020.

N^2-Allyl-3-cyclohex-1-enylpropane-1,2-diamine·Oxalate (3h)
Yield: 50%.

^{1}H NMR (300 MHz, D_2O): δ = 1.46–1.56 [m, 4 H, (CH_2)$_2$], 1.86–1.94 [m, 4 H, (CH_2)$_2$], 2.35–2.42 (m, 2 H, CH_2CH), 3.27–3.33 (m, 2 H, CH_2NH$_2$), 3.62–3.73 (m, 3 H, CH$_2$C*H*), 5.43–5.46 (m, 2 H, HCCH_2), 5.49 (br s, 1 H, *H*CC), 5.71–5.90 (m, 1 H, *H*CCH$_2$).

^{13}C NMR (100 MHz, D_2O): δ = 22.4, 23.1, 25.8, 28.2, 38.2, 40.4, 48.4, 53.7, 125.5, 127.8, 129.6, 131.7, 169.0.

ESI-MS: *m*/*z* (%) = 195.3 (50) [M + H], 178.2 [M – NH$_2$].

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{23}N_2$: 195.1861; found: 195.1857.

Imidazolidinones; General Procedure
The diamine as the oxalate salt **3** (synthesized by the route described above; ca. 0.40 g) was dissolved in sat. NaHCO$_3$ (30 mL). The pH of the soln was determined to ensure that it was basic; if not, sat. NaHCO$_3$ was added 1 mL at a time until the soln was basic. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The diamine was then further dried on a high-vacuum line. To a flask containing free diamine (1.1 mmol, for example) was added anhyd THF (2 mL) and CDI (0.20 g, 1.2 mmol). The soln was then heated at reflux for 12 h and subsequently cooled to r.t. The solvent was removed under reduced pressure to yield the crude imidazolidinone **4**, which was purified by column chromatography (silica gel, MeOH–CH_2Cl_2 5:95). The yields given below are calculated from the diamine starting material **3**.

1-Benzyl-5-pentylimidazolidin-2-one (4a)
Yield: 82%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, ^3J = 6.8 Hz, 3 H, CH_3), 1.19–1.26 [m, 6 H, (CH_2)$_3$], 1.36–1.44 (m, 1 H, CHCH_2), 1.61–1.63 (m, 1 H, CHCH_2), 3.06–3.11 (m, 1 H, C*H*), 3.41–3.52 (m, 2 H,

NHCH_2), 4.03 (d, ^2J = 15 Hz, 1 H, PhCH_2), 4.75 (d, ^2J = 15 Hz, 1 H, PhCH_2), 5.31 (s, 1 H, N*H*), 7.21–7.35 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.7, 24.3, 31.8, 31.8, 45.6, 47.1, 51.8, 127.8, 128.2, 128.9, 136.7, 154.5.

ESI-MS: *m*/*z* (%) = 269.2 (100) [M + Na], 247.3 (10) [M + H].

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{22}N_2ONa$: 269.1630; found: 269.1624.

1,5-Dibenzylimidazolidin-2-one (4b)
Yield: 75%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.59–2.65 (m, 1 H, PhCH_2), 3.05–3.11 (m, 2 H, PhCH_2, NHCH_2), 3.22–3.26 (m, 1 H, NHCH_2), 3.69–3.75 (m, 1 H, CH_2C*H*), 4.07 (d, ^2J = 15 Hz, 1 H, NCH_2Ph), 4.69 (br s, 1 H, N*H*), 4.86 (d, ^2J = 15 Hz, 1 H, NCH_2Ph), 7.10–7.37 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.8, 43.8, 45.5, 56.3, 127.0, 127.7, 128.4, 128.8, 128.9, 129.3, 136.9, 137.2, 162.4.

ESI-MS: *m*/*z* (%) = 289.2 (100) [M + Na], 267.2 (30) [M + H].

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{18}N_2ONa$ 289.1317; found: 289.1308.

1-Benzyl-5-(cyclohex-1-enylmethyl)imidazolidin-2-one (4c)
Yield: 85%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50–1.52 (m, 4 H, CH_2), 1.71–1.73 (m, 2 H, CH_2), 1.94–1.99 (m, 3 H, CH_2, CCH_2), 2.38 (d, ^3J = 12 Hz, 1 H, CCH_2), 3.07 (t, ^3J = 7.8 Hz, 1 H, NHCH_2), 3.35 (t, ^3J = 8.6 Hz, 1 H, NHCH_2), 3.54–3.57 (m, 1 H, C*H*), 4.06 (d, ^2J = 15 Hz, 1 H, PhCH_2), 4.77 (d, ^2J = 15 Hz, 1 H, PhCH_2), 4.95 (s, 1 H, N*H*), 5.39 (s, 1 H, *H*CC), 7.25–7.42 (m, 5 H, Ar *H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.4, 22.9, 25.4, 28.7, 41.3, 44.1, 45.2, 53.5, 124.9, 127.5, 128.2, 128.7, 133.1, 137.6, 162.8.

ESI-MS: *m*/*z* (%) = 293.2 (100) [M + Na], 271.2 (60) [M + H].

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{22}N_2ONa$: 293.1630; found: 293.1625.

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