EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201402464

Synthesis of *N*,*N*-Disubstituted 3-Amino-1,4-diynes and 3-Amino-1-ynes by Addition of Alkynyldimethylaluminum Reagents to *N*,*N*-Disubstituted Formamides and N,O-Acetals

Balaji L. Korbad[a] and Sang-Hyeup Lee*[a]

Keywords: Synthetic methods / Nucleophilic addition / Aluminum / Alkynes / Amides

A wide range of alkynyldimethylaluminum reagents, which were derived from terminal alkynes and trimethylaluminum, underwent a double addition to *N*,*N*-disubstituted formamides and their acetals to provide the corresponding *N*,*N*-disubstituted 3-amino-1,4-diynes in moderate to excellent yields. Also, these reagents smoothly underwent the addition to N,O-acetals to give the corresponding *N*,*N*-disubstituted 3-amino-1-ynes in excellent yields.

Introduction

Organoaluminum reagents have received considerable attention because of their low cost and high selectivity, and they are frequently used to develop new synthetic methods in organic chemistry.[1] They presently have a wide range of applications as reagents in transition-metal-catalyzed coupling[2] and addition reactions[3] and as the catalyst in polymerization reactions.[4] The high Lewis acidity of organoaluminum reagents provides an efficient method for the hydro- and carboalumination of alkynes.[5,6] Recently, Micouin et al. developed an alkynyldimethylaluminum reagent that was formed from the reaction of terminal alkynes and trimethylaluminum by using a catalytic amount of Et_3N.[6b,6c] This reagent has also been utilized in a wide range of organic transformations such as the ring-opening alkynylation of activated epoxides[7] and oxazolidines[8] as well as addition reactions with acid chloride and *N*-*p*-tolylsulfinylimines to form α,β-alkynyl ketones and chiral propargylamines, respectively.[9] In addition, this reagent has been employed in the synthesis of leustroducsin B,[10] aluminoisoxazoles, pyrazoles,[11] and 1,4,5-trisubstituted triazoles.[12]

Propargylamine is a key structural unit in natural products[13] and pharmaceutical agents[14] and also one of the synthons for the synthesis of nitrogen-containing heterocycles such as pyrroles, pyrrolidines, oxazolidinones, and imidazoles.[15] Several methods have been reported for the preparation of propargylamines. They can be accessed by the addition of a metal acetylide to *N*,*N*-dialkylformamide dimethyl acetals, imines, and thioformamides.[16] Alternative approaches involve the Cu-catalyzed coupling of terminal alkynes with *N*,*N*-dialkylformamide dialkyl acetals, but *N*,*N*-dialkylformamides cannot be directly coupled by this method.[17] Multicomponent coupling reactions between amines, aldehydes, and terminal alkynes have also been reported.[18] Many disadvantages are associated with these aforementioned methods. For example, expensive metals and ligands are required in many of the reported cases. With traditional methods, the employment of strong bases (e.g., butyllithium, lithium diisopropylamide, and organomagnesium reagents) limits the functional group tolerance. Although the reaction of 1-(α-aminoalkyl)benzotriazoles with sodium dialkynyldiethylaluminates was reported by Ahn et al.,[19] these precursors are difficult to prepare. So far there has been no precedent for the direct use of *N*,*N*-dialkylformamides as substrates.

As part of our ongoing program on the development of new synthetic methods that utilize organoaluminum reagents,[20] we recently reported the syntheses of α,β-alkynyl ketones and N–H ketimines by the reactions of nitriles with alkynyldimethylaluminum reagents that are derived from terminal alkynes.[20a] As a continuation of our interest in the use of these reagents, we herein report the addition of these reagents to *N*,*N*-disubstituted formamides and N,O-acetals to yield *N*,*N*-disubstituted 3-amino-1,4-diynes and 3-amino-1-ynes, respectively.

Results and Discussion

Initially, we attempted the formylation of alkynyldimethylaluminum reagent **1a** by using *N*,*N*-dimethylformamide (DMF, **2a**, 1.2 equiv.) as the source of the formyl group.[21] Although the reaction failed to afford the initially desired 3-phenylpropiolaldehyde, we surprisingly found that

[a] Department of Life Chemistry, Catholic University of Daegu, Gyeongsan-si, Gyeongbuk 712-702, Korea
E-mail: leeshh@cu.ac.kr
http://dept.cu.ac.kr/user/chem/index.html

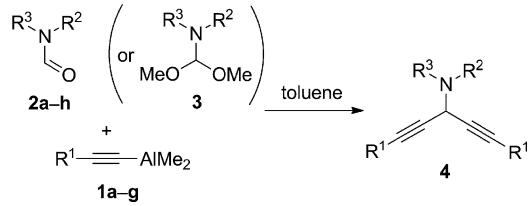
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402464.

N,*N*-disubstituted 3-amino-1,4-diyne **4a** was obtained as the main product (40% yield), as confirmed by ^{1}H NMR analysis and HRMS. To the best of our knowledge, this is the first report of a double addition of an alkynyldimethylaluminum reagent to a formyl group of an *N*,*N*-disubstituted formamide. Encouraged by this, DMF (**2a**, 1 equiv.) was then set as the limiting reagent and treated with the alkynyldimethylaluminum reagent **1a** (2.5 equiv.) in toluene at room temperature to give **4a** in 90% yield after 16 h of reaction time.

The molar ratio of the reagents [i.e., **1a**/DMF (**2a**)], the reaction temperature, and the solvent were then examined. The use of an excess amount of **1a** (5.0 equiv.) did not significantly improve the yield. To accelerate the reaction, it was performed at a higher temperature. Indeed, in this case, the reaction was completed within 3 h at 40–60 °C to give **4a** in a comparable yield (92% yield) to that performed at room temperature reaction (see Table 1, Entry 1). The employment of a higher temperature (>60 °C) could accelerate the rate of reaction more significantly, however, this resulted in a lowered yield and the formation of colored impurities. Of the solvents tested, dichloroethane gave a comparable good yield, whereas that with tetrahydrofuran (THF) gave a somewhat lowered yield.

With the optimized conditions in hand (i.e., *N*,*N*-dialkylformamides/alkynyldimethylaluminum reagent, 1:2.5, toluene, 40 °C), the scope and limitations of this reaction were examined by employing a wide range of terminal alkynes and *N*,*N*-disubstituted formamides or the corresponding acetal (see Table 1). The reactivity of the alkyne substrate was not significantly affected by the substitution pattern of the benzene ring in the acetylenes (see Table 1, Entries 1–3). Alkyl and heterocyclic substituted acetylenes underwent the reaction with **2a** to give the corresponding product in good to high yield (see Table 1, Entries 4–7). Then, we examined the scope of *N*,*N*-disubstituted formamides **2**. *N*,*N*-dialkylformamides that were derived from acyclic and cyclic dialkylamines (i.e., **2b**–**2e**) smoothly underwent the reaction with various aromatic, aliphatic, and heteroaromatic alkynyldimethylaluminum reagents to afford the corresponding products in high yields (see Table 1, Entries 8–21). *N*-alkyl-*N*-aryl and *N*,*N*-diarylformamides (i.e., **2f** and **2g**, respectively) also underwent the reaction with alkynyldimethylaluminum reagents at room temperature for 6 h to give the corresponding products in moderate yields (see Table 1, Entries 22–24). The primary amide (R^2 and R^3 = H, see Table 1, Entry 25) and secondary amides (R^2 = alkyl or aryl, R^3 = H, data not shown here) were consumed under the reaction conditions but gave complex mixtures of products, which were not further analyzed. We also found that 1,1-dimethoxy-*N*,*N*-dimethylmethanamine (**3**), a dimethylacetal of DMF, was a suitable substrate. Acetal **3** underwent the reaction with the alkynyldimethylaluminum reagents at 60 °C for 3 h to afford the desired products in good yields (see Table 1, Entries 26–28). It should be noted that the above results could be reproduced when the reaction was performed at room temperature for an extended period of time (16 h).

Table 1. Double addition of alkynyldimethylaluminum reagents to *N*,*N*-disubstituted formamides and their dialkyl acetals.[a]



Entry	**1** (R^1)	**2** (R^2,R^3)	Product	% Yield[b]
1	**1a** (Ph)	**2a** (Me, Me)	**4a**	92
2	**1b** (4-MeC_6H_4)	**2a**	**4b**	89
3	**1c** (4-ClC_6H_4)	**2a**	**4c**	82
4	**1d** [$CH_3(CH_2)_4$]	**2a**	**4d**	88
5	**1e** [Ph$(CH_2)_2$]	**2a**	**4e**	95
6	**1f** (cyclopropyl)	**2a**	**4f**	90
7	**1g** (thiophenyl)	**2a**	**4g**	80
8	**1a**	**2b** [–$(CH_2)_5$–]	**4h**	97
9	**1a**	**2c** (Et, Et)	**4i**	75
10	**1a**	**2d** [–$(CH_2)_2O(CH_2)_2$–]	**4j**	95
11	**1b**	**2b**	**4k**	93
12	**1c**	**2b**	**4l**	90
13	**1d**	**2b**	**4m**	95
14	**1d**	**2c**	**4n**	73
15	**1d**	**2d**	**4o**	88
16	**1e**	**2b**	**4p**	98
17	**1f**	**2b**	**4q**	85
18	**1f**	**2c**	**4r**	63
19	**1f**	**2e** [-$(CH_2)_4$-]	**4s**	89
20	**1f**	**2d**	**4t**	96
21	**1g**	**2b**	**4u**	82
22	**1d**	**2f** (Ph, Me)	**4v**	75
23	**1f**	**2f**	**4w**	70
24	**1d**	**2g** (Ph, Ph)	**4x**	70
25	**1a**	**2h** (H, H)	**4y**	–[c]
26	**1a**	**3** (Me, Me)	**4a**	95
27	**1d**	**3**	**4d**	92
28	**1f**	**3**	**4f**	85

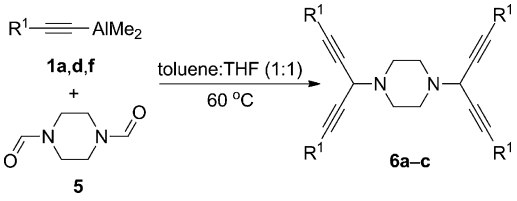
[a] Reagents and conditions: alkynyldimethylaluminum reagent **1**/formamide **2** (or acetal **3**), 2.5:1, toluene [4 mL mmol^{-1} of formamide **2** (or acetal **3**)], 0→40 °C for 3 h (Entries 1–7), 0→60 °C for 3 h (Entries 8–21 and 26–28), 0→r.t. for 6 h (Entries 22–25). [b] Isolated yield based on **2** or **3**. [c] Complex mixture.

Next, piperazine-1,4-dicarbaldehyde (**5**), a substrate that contains two formyl groups, was treated with an excess amount of the alkynyldimethylaluminum reagent. This reaction afforded the desired symmetrical product **6** in moderate yield (see Table 2, Entries 1–3).

We then tried to expand the scope of this protocol by employing different types of substrates, and we were pleased to find that N,O-acetals[22] **7** are also good substrates (see Table 3). When treated with alkynyldimethylaluminum reagents **1** (1.2 equiv.) at room temperature in toluene, the alkoxy group of the **7** was substituted by the alkynyl unit to afford within a short period of time (<30 min) the corresponding alkynylamines **8** in excellent yields (see Table 3, Entries 1–11).

To examine the functional group tolerance, **7a** was combined with an equimolar amount of either methyl benzoate, benzonitrile, nitrobenzene, or styrene oxide and then treated

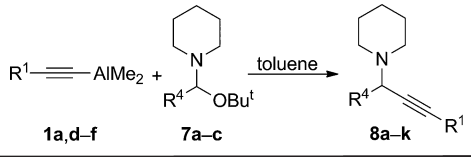
Table 2. Synthesis of symmetrical propargylamines.[a]



Entry	**1** (R^1)	Product	% Yield[b]
1	**1a** (Ph)	**6a**	68
2	**1d** [$CH_3(CH_2)_4$]	**6b**	65
3	**1f** (cyclopropyl)	**6c**	60

[a] Reagents and conditions: alkynyldimethylaluminum reagent **1**/1,4-dicarbaldehyde **5**, (5:1), toluene/tetrahydrofuran (1:1, 4 mL mmol^{-1} of **5**), 0→60 °C, 5 h. [b] Isolated yield based on **5**.

Table 3. Monoaddition of alkynyldimethylaluminum reagents to N,O-acetals.[a]

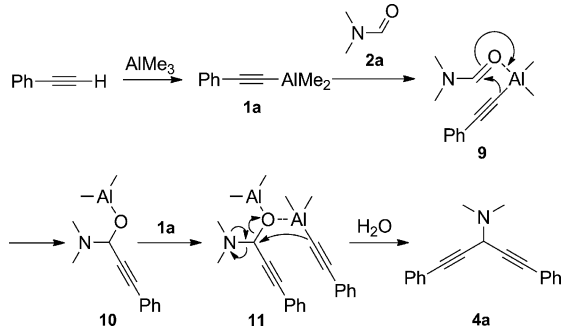


Entry	**1** (R^1)	**7** (R^4)	Product	% Yield[b]
1	**1a** (Ph)	**7a** (Ph)	**8a**	98
2	**1d** [$CH_3(CH_2)_4$]	**7a**	**8b**	94
3	**1e** [$Ph(CH_2)_2$]	**7a**	**8c**	98
4	**1f** (cyclopropyl)	**7a**	**8d**	90
5	**1a**	**7b** (4-ClC_6H_4)	**8e**	97
6	**1f**	**7b**	**8f**	92
7	**1a**	**7c** (H)	**8g**	98
8	**1c** (4-ClC_6H_4)	**7c**	**8h**	97
9	**1d**	**7c**	**8i**	97
10	**1e**	**7c**	**8j**	95
11	**1f**	**7c**	**8k**	96

[a] Reagents and conditions: alkynyldimethylaluminum reagent **1**/N,O-acetal **7** (1.2:1), toluene (4 mL mmol^{-1} of **7**), 0→r.t., 30 min. [b] Isolated yield based on **7**.

with **1a** (1.2 equiv.). We found that the ester, nitrile, and nitro groups were stable under the reaction conditions, and the desired product **8a** was obtained in >90% yield. On the other hand, the epoxide ring of styrene oxide was reactive, and the reaction afforded the ring-opened product as well as **8a** in 60% yield.

On the basis of the results described above, a plausible mechanism for the product formation is depicted in Scheme 1 with **1a** and **2a** as the model substrates. Phenylacetylene undergoes a reaction with trimethylaluminum to afford alkynyldimethylaluminum reagent **1a**, as evidenced by the evolution of methane gas. Then, reagent **1a** coordinates to **2a** to activate the carbonyl group and form Lewis acid-base complex **9**. The addition of the acetylide to the carbonyl group through a four-membered cyclic transition state affords aluminated N,O-acetal intermediate **10**. Then, the second molecule of **1a** coordinates to the oxygen atom of **10** to give complex **11**. Iminium formation and concomitant attack of the acetylide moiety followed by treatment with H_2O/tetrahydrofuran (1:1) affords product **4a**.



Scheme 1. Plausible mechanism.

Conclusions

In summary, we have demonstrated that alkynyldimethylaluminum reagents efficiently undergo reaction with a variety of *N*,*N*-disubstituted formamides and their acetals under mild reaction conditions to produce the corresponding *N*,*N*-disubstituted 3-amino-1,4-diynes in moderate to excellent yields. Moreover, when these reagents are treated with N,O-acetals, the corresponding *N*,*N*-disubstituted 3-amino-1-ynes are produced in excellent yields. Cyano, ester, and nitro functional groups were tolerated under the optimized reaction conditions. This is a simple and effective method for the preparation of a variety of propargylamines.

Experimental Section

General Methods: Unless otherwise noted, commercially available chemicals were obtained from a commercial supplier and used without further purification. 1-[*tert*-Butoxy(phenyl)methyl]piperidine (**7a**),[22a] 1-[*tert*-butoxy(4-chlorophenyl)methyl]piperidine (**7b**),[22a] and 1-(*tert*-butoxymethyl)piperidine (**7c**)[22b] were prepared according to their respective literature procedures. Thin layer chromatography was carried out with Merck 60 F254 plates with a 0.25 mm thickness. Flash chromatography was carried out with Merck silica gel 60 (230–400 mesh), and a mixture of ethyl acetate/hexanes was employed as the eluent. The NMR spectroscopic data were recorded with an Agilent V NMR (at 600 MHz for ^{1}H and at 150 MHz for ^{13}C) or a Varian INOVA-399 (at 400 MHz for ^{1}H and at 100 MHz for ^{13}C). Chemical shifts (δ) are reported in ppm relative to tetramethylsilane as an internal reference. High resolution mass spectrometry data were obtained from Korea Basic Science Institute (Daegu) with a Jeol JMS 700 high resolution mass spectrometer. The mass spectrometer operated in the EI and FAB mode at 70 eV, and the MS spectra were recorded in the range of mass-to-charge ratios from 50 to 650.

General Procedure for the Double Addition of Alkynyldimethylaluminum Reagents 1 to *N*,*N*-Dialkylformamides 2 [or 1,1-Dimethoxy-*N*,*N*-dimethylmethanamine (3)] – *N*,*N*-Dimethyl-1,5-diphenylpenta-1,4-diyn-3-amine (4a): (see Table 1, Entry 1). A solution of alkynyldimethylaluminum **1a** was prepared according to the described procedure.[6b] The solution of alkynyldimethylaluminum **1a** (1.4 M in toluene, 1.8 mL, 2.5 mmol) was added dropwise to a

solution of *N*,*N*-dimethylformamide **2a** (0.073 g, 1.0 mmol) in toluene (4 mL) under argon. The resulting mixture was stirred at 40 °C, and the progress of the reaction was monitored by TLC. Upon completion (3 h), the mixture was diluted with THF (5 mL). The reaction mixture was then quenched by the dropwise addition of THF/water (1:1, 2 mL). The resulting mixture was stirred for 20 min and then filtered through Celite®, which was rinsed with THF (5 mL). The combined filtrates were evaporated to dryness to provide the crude product, which was purified by chromatography on a silica gel column (ethyl acetate/hexanes, 2:8) to provide propargylamine **4a** (0.238 g, 0.92 mmol, 92%) as a light yellow oil.

The procedures for those compounds in Table 1, Entries 2–7 were performed under the same reaction conditions (40 °C for 3 h). Those for Table 1, Entries 8–21 and 26–28 were carried out at 60 °C for 3 h. Those for Table 1, Entries 22–25 were performed at room temperature for 6 h and then purified by column chromatography (toluene/hexanes, 2:8).

***N*,*N*-Dimethyl-1,5-diphenylpenta-1,4-diyn-3-amine (4a):**[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.48 (s, 6 H), 4.78 (s, 1 H), 7.27–7.33 (m, 6 H), 7.46–7.53 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 41.3, 50.0, 83.5, 84.4, 122.5, 128.2, 128.3, 131.8 ppm. HRMS (EI+): calcd. for $C_{19}H_{17}N$ $[M]^+$ 259.1361; found 259.1359.

***N*,*N*-Dimethyl-1,5-di-*p*-tolylpenta-1,4-diyn-3-amine (4b):**[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.33 (s, 6 H), 2.47 (s, 6 H), 4.75 (s, 1 H), 7.10 (d, J = 8.4 Hz, 4 H), 7.38 (d, J = 8.4 Hz, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.4, 41.3, 50.1, 82.9, 84.5, 119.5, 128.9, 131.7, 138.4 ppm. HRMS (EI+): calcd. for $C_{21}H_{21}N$ $[M]^+$ 287.1674; found 287.1670.

1,5-Bis(4-chlorophenyl)-*N*,*N*-dimethylpenta-1,4-diyn-3-amine (4c):[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.46 (s, 6 H), 4.75 (s, 1 H), 7.25–7.32 (m, 4 H), 7.38–7.44 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 41.4, 50.0, 83.5, 84.3, 121.0, 128.6, 133.1, 134.5 ppm. HRMS (EI+): calcd. for $C_{19}H_{15}Cl_2N$ $[M]^+$ 327.0582; found 327.0579.

***N*,*N*-Dimethylpentadeca-6,9-diyn-8-amine (4d):**[17] ^{1}H NMR (600 MHz, $CDCl_3$); δ = 0.90 (t, J = 7.2 Hz, 6 H), 1.27–1.43 (m, 8 H), 1.53 (quint, J = 7.4 Hz, 4 H), 2.22 (dt, J = 2.2, 7.4 Hz, 4 H), 2.31 (s, 6 H), 4.28 (t, J = 2.1 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.8, 18.5, 22.0, 28.3, 30.9, 40.9, 48.9, 74.8, 84.3 ppm. HRMS (FAB+): calcd. for $C_{17}H_{28}N$ [M – 1] 246.2216; found 246.2225.

***N*,*N*-Dimethyl-1,9-diphenylnona-3,6-diyn-5-amine (4e):** ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.22 (s, 6 H), 2.51 (dt, J = 2.4, 7.5 Hz, 4 H), 2.83 (t, J = 7.5 Hz, 4 H), 4.25 (t, J = 2.1 Hz, 1 H), 7.17–7.22 (m, 6 H), 7.27–7.80 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.8, 35.0, 40.9, 48.9, 75.4, 83.6, 126.1, 128.2, 128.3, 140.5 ppm. HRMS (FAB+): calcd. for $C_{23}H_{24}N$ [M – 1] 314.1903; found 314.1913.

1,5-Dicyclopropyl-*N*,*N*-dimethylpenta-1,4-diyn-3-amine (4f):[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.65–0.81 (m, 8 H), 1.20–1.30 (m, 2 H), 2.27 (s, 6 H), 4.21 (t, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 0.0, 8.7, 41.5, 49.6, 70.5, 88.1 ppm. HRMS (EI+): calcd. for $C_{13}H_{17}N$ $[M]^+$ 187.1361; found 187.1357.

***N*,*N*-Dimethyl-1,5-di(thiophen-2-yl)penta-1,4-diyn-3-amine (4g):**[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.45 (s, 6 H), 4.79 (s, 1 H), 6.94–6.98 (m, 2 H), 7.22–7.26 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 41.2, 50.2, 77.8, 86.9, 122.1, 126.6, 127.0, 132.2 ppm. HRMS (EI+): calcd. for $C_{15}H_{13}NS_2$ $[M]^+$ 271.0489; found 271.0486.

1-(1,5-Diphenylpenta-1,4-diyn-3-yl)piperidine (4h):[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.38 (br. s, 2 H), 1.60 (quint, J = 5.7 Hz, 4 H), 2.68 (br. s, 4 H), 4.68 (s, 1 H), 7.16–7.23 (m, 6 H), 7.34–7.43 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.1, 25.9, 50.2, 50.4, 83.9, 84.3, 122.6, 128.1, 128.2, 131.8 ppm. HRMS (EI+): calcd. for $C_{22}H_{21}N$ $[M]^+$ 299.1674; found 299.1672.

***N*,*N*-Diethyl-1,5-diphenylpenta-1,4-diyn-3-amine (4i):**[17] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.19 (t, J = 6.9 Hz, 6 H), 2.80 (q, J = 7.2 Hz, 4 H), 4.98 (s, 1 H), 7.20–7.35 (m, 6 H), 7.40–7.51 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.4, 45.1, 45.8, 83.8, 84.7, 122.8, 128.16, 128.24, 131.8 ppm. HRMS (EI+): calcd. for $C_{21}H_{21}N$ $[M]^+$ 287.1674; found 287.1671.

1-(1,5-Diphenylpenta-1,4-diyn-3-yl)morpholine (4j):[16d] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.84 (t, J = 4.8 Hz, 4 H), 3.82 (t, J = 4.8 Hz, 4 H), 4.77 (s, 1 H), 7.25–7.35 (m, 6 H), 7.40–7.52 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 49.5, 49.8, 66.8, 83.1, 84.9, 122.3, 128.2, 128.5, 131.8 ppm. HRMS (EI+): calcd. for $C_{21}H_{19}NO$ $[M]^+$ 301.1467; found 301.1466.

1-(1,5-Di-*p*-tolylpenta-1,4-diyn-3-yl)piperidine (4k): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.49 (br. s, 2 H), 1.71 (quint, J = 5.7 Hz, 4 H), 2.34 (s, 6 H), 2.78 (br. s, 4 H), 4.77 (s, 1 H), 7.11 (d, J = 8.4 Hz, 4 H), 7.40 (d, J = 7.8 Hz, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.1, 23.9, 25.7, 50.0, 50.2, 83.1, 84.2, 119.4, 128.6, 131.5, 138.0 ppm. HRMS (EI+): calcd. for $C_{24}H_{25}N$ $[M]^+$ 327.1987; found 327.1985.

1-[1,5-Bis(4-chlorophenyl)penta-1,4-diyn-3-yl]piperidine (4l): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.48 (br. s, 2 H), 1.69 (quint, J = 5.6 Hz, 4 H), 2.74 (br. s, 4 H), 4.75 (s, 1 H), 7.27–7.35 (m, 4 H), 7.35–7.42 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.1, 25.9, 50.2, 50.5, 83.4, 84.8, 121.1, 128.5, 133.1, 134.4 ppm. HRMS (EI+): calcd. for $C_{22}H_{19}Cl_2N$ $[M]^+$ 367.0895; found 367.0891.

1-(Pentadeca-6,9-diyn-8-yl)piperidine (4m): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.2 Hz, 6 H), 1.28–1.48 (m, 10 H), 1.52 (quint, J = 7.3 Hz, 4 H), 1.64 (quint, J = 5.6 Hz, 4 H), 2.21 (dt, J = 2.2, 7.2 Hz, 4 H), 2.59 (br. s, 4 H), 4.27 (t, J = 2.0 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.8, 18.5, 22.0, 24.2, 25.8, 28.2, 30.9, 49.1, 49.9, 75.1, 84.2 ppm. HRMS (EI+): calcd. for $C_{20}H_{33}N$ $[M]^+$ 287.2613; found 287.2610.

***N*,*N*-Diethylpentadeca-6,9-diyn-8-amine (4n):** ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.2 Hz, 6 H), 1.10 (t, J = 6.9 Hz, 6 H), 1.28–1.42 (m, 8 H), 1.52 (quint, J = 7.4 Hz, 4 H), 2.20 (dt, J = 1.8, 6.9 Hz, 4 H), 2.62 (q, J = 7.4 Hz, 4 H), 4.49 (t, J = 2.1 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.3, 13.9, 18.6, 22.1, 28.3, 31.0, 44.60, 44.64, 75.8, 83.7 ppm. HRMS (EI+): calcd. for $C_{19}H_{33}N$ $[M]^+$ 275.2613; found 275.2610.

4-(Pentadeca-6,9-diyn-8-yl)morpholine (4o): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.2 Hz, 6 H), 1.27–1.42 (m, 8 H), 1.53 (quint, J = 7.2 Hz, 4 H), 2.2 (dt, J = 2.0, 7.4 Hz, 4 H), 2.67 (t, J = 4.0 Hz, 4 H), 3.77 (t, J = 4.0 Hz, 4 H), 4.28 (t, J = 2.1 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9, 18.6, 22.1, 28.3, 31.0, 48.9, 49.2, 66.9, 74.4, 85.1 ppm. HRMS (EI+): calcd. for $C_{19}H_{31}NO$ $[M]^+$ 289.2406; found 289.2404.

1-(1,9-Diphenylnona-3,6-diyn-5-yl)piperidine (4p): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.39 (br. s, 2 H), 1.58 (t, J = 4.5 Hz, 4 H), 2.30–2.60 (m, 8 H), 2.83 (dt, J = 2.4, 7.2 Hz, 4 H), 4.24 (q, J = 2.2 Hz, 1 H), 7.16–7.23 (m, 6 H), 7.25–7.30 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.8, 24.0, 25.8, 34.9, 49.1, 49.9, 75.8, 83.5, 126.1, 128.2, 128.4, 140.5 ppm. HRMS (EI+): calcd. for $C_{26}H_{29}N$ $[M]^+$ 355.2300; found 355.2296.

1-(1,5-Dicyclopropylpenta-1,4-diyn-3-yl)piperidine (4q): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.66–0.78 (m, 8 H), 1.20–1.30 (m, 2 H), 1.43 (br. s, 2 H), 1.62 (quint, J = 5.7 Hz, 4 H), 2.53 (br. s, 4 H),

4.21 (t, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.6, 24.7, 26.4, 49.7, 50.5, 70.8, 87.8 ppm. HRMS (EI+): calcd. for $C_{16}H_{21}N$ $[M]^+$ 227.1674; found 227.1671.

1,5-Dicyclopropyl-*N*,*N*-diethylpenta-1,4-diyn-3-amine (4r): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.66–0.79 (m, 8 H), 1.07 (t, J = 6.9 Hz, 6 H), 1.20–1.29 (m, 2 H), 2.58 (q, J = 7.2 Hz, 4 H), 4.42 (t, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.6, 13.8, 45.1, 45.2, 71.4, 87.2 ppm. HRMS (EI+): calcd. for $C_{15}H_{21}N$ $[M]^+$ 215.1674; found 215.1674.

1-(1,5-Dicyclopropylpenta-1,4-diyn-3-yl)pyrrolidine (4s): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.62–0.78 (m, 8 H), 1.18–1.29 (m, 2 H), 1.79 (quint, J = 3.3 Hz, 4 H), 2.61–2.72 (m, 4 H), 4.40 (t, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.7, 24.1, 45.3, 49.8, 71.2, 87.4 ppm. HRMS (EI+): calcd. for $C_{15}H_{19}N$ $[M]^+$ 213.1517; found 213.1516.

1-(1,5-Dicyclopropylpenta-1,4-diyn-3-yl)morpholine (4t): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.65–0.80 (m, 8 H), 1.15–1.30 (m, 2 H), 2.62 (t, J = 4.8 Hz, 4 H), 3.75 (t, J = 4.8 Hz, 4 H), 4.21 (t, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.8, 49.4, 49.7, 67.4, 70.1, 88.6 ppm. HRMS (EI+): calcd. for $C_{15}H_{19}NO$ $[M]^+$ 229.1467; found 229.1464.

1-[1,5-Di(thiophen-2-yl)penta-1,4-diyn-3-yl]piperidine (4u): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.47 (br. s, 2 H), 1.68 (quint, J = 5.7 Hz, 4 H), 2.73 (br. s, 4 H), 4.79 (s, 1 H), 6.90–6.97 (m, 2 H), 7.20–7.27 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.0, 25.9, 50.5, 50.6, 77.9, 87.5, 122.5, 126.8, 127.1, 132.4 ppm. HRMS (EI+): calcd. for $C_{18}H_{17}NS_2$ $[M]^+$ 311.0802; found 311.0805.

***N*-Methyl-*N*-(pentadeca-6,9-diyn-8-yl)aniline (4v):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.2 Hz, 6 H), 1.20–1.38 (m, 8 H), 1.47 (quint, J = 7.1 Hz, 4 H), 2.19 (dt, J = 2.0, 7.2 Hz, 4 H), 2.97 (s, 3 H), 5.28 (t, J = 2.0 Hz, 1 H), 6.84 (t, J = 7.4 Hz, 1 H), 6.92–7.00 (m, 2 H), 7.18–7.30 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 18.9, 22.4, 28.5, 31.2, 34.8, 45.5, 75.8, 84.3, 116.7, 119.7, 129.1, 149.4 ppm. HRMS (EI+): calcd. for $C_{22}H_{31}N$ $[M]^+$ 309.2457; found 309.2455.

***N*-(1,5-Dicyclopropylpenta-1,4-diyn-3-yl)-*N*-methylaniline (4w):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.56–0.82 (m, 8 H), 1.17–1.28 (m, 2 H), 2.92 (s, 3 H), 5.20 (s, 1 H), 6.83 (t, J = 7.2 Hz, 1 H), 6.90 (d, J = 8.0 Hz, 2 H), 7.18–7.29 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –0.3, 8.37, 8.39, 34.7, 45.5, 70.8, 87.2, 116.6, 119.6, 129.0, 149.3 ppm. HRMS (EI+): calcd. for $C_{18}H_{19}N$ $[M]^+$ 249.1517; found 249.1514.

***N*-(Pentadeca-6,9-diyn-8-yl)-*N*-phenylaniline (4x):** ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.1 Hz, 6 H), 1.27–1.33 (m, 8 H), 1.46 (quint, J = 7.1 Hz, 4 H), 2.18 (dt, J = 2.2, 7.1 Hz, 4 H), 5.56 (t, J = 2.2 Hz, 1 H), 7.03–7.08 (m, 2 H), 7.12–7.18 (m, 4 H), 7.26–7.31 (m, 4 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.0, 18.7, 22.2, 28.1, 30.9, 44.7, 76.1, 85.0, 122.6, 123.3, 128.8, 146.9 ppm. HRMS (EI+): calcd. for $C_{27}H_{33}N$ $[M]^+$ 371.2613; found 371.2614.

General Procedure for the Synthesis of Symmetrical Propargylamines 6 − 1,4-Bis(1,5-diphenylpenta-1,4-diyn-3-yl)piperazine (6a): (see Table 2, Entry 1). A solution of alkynyldimethylaluminum **1a** (1.4 M in toluene, 1.8 mL, 2.5 mmol) was added dropwise to a solution of piperazine-1,4-dicarbaldehyde (**5**, 0.071 g, 0.5 mmol) in toluene/THF (1:1, 4 mL) under argon. The resulting mixture was stirred at 60 °C, and the progress of the reaction was monitored by TLC. Upon completion (5 h), the mixture was diluted with THF (5 mL). Then, the reaction mixture was quenched by the dropwise addition of THF/water (2 mL, 1:1). The resulting mixture was stirred for 20 min and then filtered through Celite®, which was rinsed with THF (5 mL). The combined filtrates were evaporated to dryness to provide the crude product, which purified by chromatography on a silica gel column (ethyl acetate/hexanes, 2:8) to give 1,4-bis(1,5-diphenylpenta-1,4-diyn-3-yl)piperazine (**6a**, 0.175 g, 0.34 mmol, 68%) as a white solid.

The procedures for those compounds in Table 2, Entries 2 and 3 were performed under the same reaction conditions (60 °C for 5 h).

1,4-Bis(1,5-diphenylpenta-1,4-diyn-3-yl)piperazine (6a): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.01 (br. s, 8 H), 4.85 (s, 2 H), 7.27–7.33 (m, 12 H), 7.45–7.52 (m, 8 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 49.2, 49.5, 83.5, 84.9, 122.5, 128.2, 128.4, 131.9 ppm. HRMS (EI+): calcd. for $C_{38}H_{30}N_2$ $[M]^+$ 514.2409; found 514.2409.

1,4-Di(pentadeca-6,9-diyn-8-yl)piperazine (6b): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.89 (t, J = 6.9 Hz, 12 H), 1.26–1.40 (m, 16 H), 1.52 (quint, J = 7.2 Hz, 8 H), 2.16 (dt, J = 1.8, 6.9 Hz, 8 H), 2.76 (br. s, 8 H), 4.32 (t, J = 1.8 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9, 18.7, 22.1, 28.3, 31.1, 48.5, 48.7, 74.8, 84.8 ppm. HRMS (EI+): calcd. for $C_{34}H_{54}N_2$ $[M]^+$ 490.4287; found 490.4284.

1,4-Bis(1,5-dicyclopropylpenta-1,4-diyn-3-yl)piperazine (6c): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.65–0.79 (m, 16 H), 1.18–1.30 (m, 4 H), 2.71 (t, J = 1 Hz, 8 H), 4.26 (t, J = 1.7 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = –0.5, 8.2, 48.5, 48.7, 70.0, 87.8 ppm. HRMS (FAB+): calcd. for $C_{26}H_{31}N_2$ [M + 1] 371.2487; found 371.2488.

General Procedure for the Monoaddition of Alkynyldimethylaluminum Reagents to N,O-Acetals − 1-(1,3-Diphenylprop-2-yn-1-yl)piperidine (8a): (see Table 3, Entry 1). A solution of alkynyldimethylaluminum **1a** (1.4 M in toluene, approximately 0.86 mL, 1.2 mmol) was added dropwise to a solution of 1-[*tert*-butoxy(phenyl)methyl]piperidine (**7a**, 0.247 g, 1.0 mmol) in toluene (2 mL) at 0 °C. The resulting mixture was stirred at room temperature for 30 min, and the progress of the reaction was monitored by TLC. Then, the mixture was diluted with THF (5 mL), and the reaction mixture was quenched by the dropwise addition of THF/water (1:1, 1 mL). The resulting mixture was stirred for 20 min and then filtered through Celite®, which was rinsed with THF. The combined filtrates were evaporated to dryness to provide the crude product, which purified by chromatography on a silica gel column (ethyl acetate/hexanes, 1:10) to give 1-(1,3-diphenylprop-2-yn-1-yl)piperidine (**8a**, 0.269 g, 0.98 mmol, 98%) as a colorless oil.

The procedures for those compounds in Table 3, Entries 2–11 were performed under the same reaction conditions (room temperature for 30 min).

1-(1,3-Diphenylprop-2-yn-1-yl)piperidine (8a):[18a] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.38–1.48 (m, 2 H), 1.54–1.70 (m, 4 H), 2.60 (t, J = 5.1 Hz, 4 H), 4.86 (s, 1 H), 7.28–7.42 (m, 6 H), 7.49–7.59 (m, 2 H), 7.67 (d, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.2, 25.9, 50.4, 62.1, 85.8, 87.6, 123.1, 127.2, 127.75, 127.77, 128.0, 128.2, 131.5, 138.3 ppm. HRMS (EI+): calcd. for $C_{20}H_{21}N$ $[M]^+$ 275.1674; found 275.1676.

1-(1-Phenyloct-2-yn-1-yl)piperidine (8b): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.5 Hz, 3 H), 1.31–1.49 (m, 6 H), 1.52–1.66 (m, 6 H), 2.33 (dt, J = 2.0, 7.4 Hz, 2 H), 2.48 (br. s, 4 H), 4.56 (s, 1 H), 7.27 (t, J = 6.6 Hz, 1 H), 7.34 (t, J = 7.5 Hz, 2 H), 7.58 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.2, 19.0, 22.4, 24.7, 26.4, 28.9, 31.3, 50.7, 62.2, 76.4, 88.1, 127.3, 128.0, 128.7, 139.4 ppm. HRMS (EI+): calcd. for $C_{19}H_{27}N$ $[M]^+$ 269.2143; found 269.2145.

1-(1,5-Diphenylpent-2-yn-1-yl)piperidine (8c): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.40–1.49 (m, 2 H), 1.52–1.67 (m, 4 H), 2.46 (br. s, 4 H), 2.69 (dt, J = 1.1, 7.3 Hz, 2 H), 2.95 (t, J = 7.5 Hz, 2 H), 4.57 (s, 1 H), 7.25–7.38 (m, 8 H), 7.55 (d, J = 7.8 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.8, 24.3, 26.1, 35.3, 50.4, 61.9, 77.1, 86.9, 126.1, 127.1, 127.8, 128.2, 128.4, 128.5, 138.9, 140.6 ppm. HRMS (EI+): calcd. for $C_{22}H_{25}N$ $[M]^+$ 303.1987; found 303.1986.

1-(3-Cyclopropyl-1-phenylprop-2-yn-1-yl)piperidine (8d): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.65–0.82 (m, 4 H), 1.29–1.36 (m, 1 H), 1.37–1.45 (m, 2 H), 1.48–1.62 (m, 4 H), 2.35–2.52 (m, 4 H), 4.48 (s, 1 H), 7.20–7.30 (m, 1 H), 7.30 (t, J = 7.2 Hz, 2 H), 7.52 (d, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.8, 24.8, 26.5, 50.9, 62.3, 71.9, 91.4, 127.5, 128.2, 128.8, 139.5 ppm. HRMS (EI+): calcd. for $C_{17}H_{21}N$ $[M]^+$ 239.1674; found 239.1671.

1-[1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-yl]piperidine (8e):[18e] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.38–1.47 (m, 2 H), 1.51–1.68 (m, 4 H), 2.54 (br. s, 4 H), 4.76 (s, 1 H), 7.29–7.36 (m, 5 H), 7.49–7.54 (m, 2 H), 7.58 (d, J = 7.8 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.3, 26.1, 50.6, 61.7, 85.3, 88.2, 123.1, 128.15, 128.16, 128.3, 129.8, 131.8, 133.2, 137.3 ppm. HRMS (EI+): calcd. for $C_{20}H_{20}ClN$ $[M]^+$ 309.1284; found 309.1288.

1-[1-(4-Chlorophenyl)-3-cyclopropylprop-2-yn-1-yl]piperidine (8f): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.69–0.75 (m, 2 H), 0.78–0.84 (m, 2 H), 1.30–1.37 (m, 1 H), 1.38–1.47 (m, 2 H), 1.48–1.63 (m, 4 H), 2.40 (br. s, 4 H), 4.46 (s, 1 H), 7.28 (d, J = 8.4 Hz, 2 H), 7.48 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.9, 24.8, 26.5, 50.9, 61.7, 71.3, 92.0, 128.4, 130.2, 133.3, 138.3 ppm. HRMS (EI+): calcd. for $C_{17}H_{20}ClN$ $[M]^+$ 273.1284; found 273.1286.

1-(3-Phenylprop-2-yn-1-yl)piperidine (8g):[18f] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.44 (br. s, 2 H), 1.64 (quint, J = 5.7 Hz, 4 H), 2.57 (br. s, 4 H), 3.47 (s, 2 H), 7.25–7.32 (m, 3 H), 7.38–7.45 (m, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 23.9, 25.9, 48.4, 53.4, 84.9, 85.0, 123.2, 127.8, 128.1, 131.6 ppm. HRMS (EI+): calcd. for $C_{14}H_{17}N$ $[M]^+$ 199.1361; found 199.1360.

1-[3-(4-Clorophenylprop-2-yn-1-yl)]piperidine (8h): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.44 (br. s, 2 H), 1.64 (quint, J = 5.6 Hz, 4 H), 2.55 (br. s, 4 H), 3.45 (s, 2 H), 7.25 (d, J = 8.5 Hz, 2 H), 7.35 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 23.8, 25.8, 48.3, 53.4, 83.7, 86.1, 121.7, 128.4, 132.8, 133.8 ppm. HRMS (EI+): calcd. for $C_{14}H_{16}ClN$ $[M]^+$ 233.0971; found 233.0967.

1-(Oct-2-yn-1-yl)piperidine (8i): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.2 Hz, 3 H), 1.28–1.46 (m, 6 H), 1.51 (quint, J = 7.4 Hz, 2 H), 1.61 (quint, J = 5.7 Hz, 4 H), 2.19 (tt, J = 2.4, 6.6 Hz, 2 H), 2.47 (br. s, 4 H), 3.21 (t, J = 2.4 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9, 18.6, 22.1, 24.0, 25.9, 28.5, 31.0, 48.0, 53.3, 75.2, 85.0 ppm. HRMS (EI+): calcd. for $C_{13}H_{23}N$ $[M]^+$ 193.1830; found 193.1828.

1-(5-Phenylpent-2-yn-1-yl)piperidine (8j): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.40 (br. s, 2 H), 1.58 (quint, J = 6.0 Hz, 4 H), 2.41 (br. s, 4 H), 2.49 (tt, J = 3.6, 7.8 Hz, 2 H), 2.82 (t, J = 7.5 Hz, 2 H), 3.18 (t, J = 2.1 Hz, 2 H), 7.14–7.22 (m, 3 H), 7.24–7.31 (m, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.8, 23.9, 25.8, 35.2, 48.0, 53.2, 76.1, 84.1, 126.1, 128.2, 128.3, 140.7 ppm. HRMS (EI+): calcd. for $C_{16}H_{21}N$ $[M]^+$ 227.1674; found 227.1671.

1-(3-Cyclopropylprop-2-yn-1-yl)piperidine (8k): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.62–0.75 (m, 4 H), 1.20–1.28 (m, 1 H), 1.34–1.48 (m, 2 H), 1.61 (quint, J = 5.7 Hz, 4 H), 2.45 (br. s, 4 H), 3.17 (d, J = 1.8 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 8.6, 24.5, 26.4, 48.6, 53.9, 71.2, 88.6 ppm. HRMS (EI+): calcd. for $C_{11}H_{17}N$ $[M]^+$ 163.1361; found 163.1359.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra for compounds **4a**–**4x**, **6a**–**6c**, and **8a**–**8k**.

Acknowledgments

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (grant number 2011-0007322).

[1] a) H. W. Roesky, *Inorg. Chem.* **2004**, *43*, 7284–7293; b) T. Mole, E. A. Jeffery, *Organoaluminum Compounds*, Elsevier, Amsterdam, **1972**; c) G. Bruno, *The Use of Aluminum Alkyls in Organic Synthesis* Ethyl Corporation, Baton Rouge, LA, USA, **1970**, **1973**, and **1980**; d) E.-I. Negishi, *Organometallics in Organic Synthesis* Wiley, New York, **1980**, vol. 1, p. 286.

[2] a) S. Baba, E.-I. Negishi, *J. Am. Chem. Soc.* **1976**, *98*, 6729–6731; b) E.-I. Negishi, S. Baba, *J. Chem. Soc., Chem. Commun.* **1976**, 596–597; c) S.-L. Ku, X.-P. Hui, C.-A. Chen, Y.-Y. Kuo, H.-M. Gau, *Chem. Commun.* **2007**, 3847–3849; d) W.-T. Shu, S. Zhou, H.-M. Gau, *Synthesis* **2009**, 4075–4081; e) T. Blumke, Y.-H. Chen, Z. Peng, P. Knochel, *Nature Chem.* **2010**, *2*, 313–318.

[3] a) M. Vuagnoux-d'Augustin, A. Allexakis, *Chem. Eur. J.* **2007**, *13*, 9647–9662; b) T. L. May, M. K. Brown, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2008**, *47*, 7358–7362; *Angew. Chem.* **2008**, *120*, 7468; c) P. Wipf, J. H. Simitrovich, C.-W. Moon, *J. Org. Chem.* **1992**, *57*, 3178–3186; d) G. Wilke, H. Muller, *Justus Liebigs Ann. Chem.* **1960**, *629*, 222–240; e) R. E. Ireland, P. Wipf, *J. Org. Chem.* **1990**, *55*, 1425–1426.

[4] a) B. Rajabalitabar, H. A. Nguyen, H. Cheradame, *Macromolecules* **1996**, *29*, 514–518; b) M. Bahadur, T. D. Shaffer, J. R. Ashbaugh, *Macromolecules* **2000**, *33*, 9548–9552; c) E. Y.-X. Chen, *Chem. Rev.* **2009**, *109*, 5157–5214; d) E. Y.-X. Chen, *Dalton Trans.* **2009**, 8784–8793; e) A. Fischbach, R. Anwander, *Adv. Polym. Sci.* **2006**, *204*, 155, and references cited therein.

[5] a) J. J. Eisch, in: *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, New York, **1991**, vol. 8, p. 733–752; b) F. Gao, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 10961–10963; c) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207–2293; d) E.-I. Negishi, D. Y. Kondakov, *Chem. Soc. Rev.* **1996**, *25*, 417–426; e) A. G. Fallis, P. Forgione, *Tetrahedron* **2001**, *57*, 5899–5913.

[6] a) P. Binger, *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 686; *Angew. Chem.* **1963**, *75*, 918; b) B. Wang, M. Bonin, L. Micouin, *Org. Lett.* **2004**, *6*, 3481–3484; c) Y. Zhou, T. Lecourt, L. Micouin, *Adv. Synth. Catal.* **2009**, *351*, 2595–2598.

[7] M. Sasaki, M. Hatta, K. Tanino, M. Miyashita, *Tetrahedron Lett.* **2004**, *45*, 1911–1913.

[8] a) J. Blanchet, M. Bonin, A. Chiaroni, L. Micouin, C. Riche, H.-P. Husson, *Tetrahedron Lett.* **1999**, *40*, 2935–2938; b) C. Feuvrie, J. Blanchet, M. Bonin, L. Micouin, *Org. Lett.* **2004**, *6*, 2333–2336.

[9] a) B. Wang, M. Bonin, L. Micouin, *J. Org. Chem.* **2005**, *70*, 6126–6128; b) S. Turcaud, F. Berhal, J. Royer, *J. Org. Chem.* **2007**, *72*, 7893–7897.

[10] K. Miyashita, T. Tsunemi, T. Hosokawa, M. Ikejiri, T. Imanishi, *Tetrahedron Lett.* **2007**, *48*, 3829–3833.

[11] O. Jackowski, T. Lecourt, L. Micouin, *Org. Lett.* **2011**, *13*, 5664–5667.

[12] Y. Zhou, T. Lecourt, L. Micouin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2607–2610; *Angew. Chem.* **2010**, *122*, 2661.

[13] a) A. A. Boulton, *J. Med. Chem.* **1992**, *35*, 3705–3713; b) K. Kihara, T. Aoki, A. Moriguchi, H. Yamamoto, M. Maeda, N. Tojo, T. Yamanaka, M. Ohkubo, N. Matsuoka, J. Seki, S. Mu-

toh, *Drug Dev. Res.* **2004**, *61*, 233–241; c) K. Yamada, K. Tomioka, *Chem. Rev.* **2008**, *108*, 2874–2886.
[14] a) D. Cheng, F. Ling, Z. Li, W. Yao, C. Ma, *Org. Lett.* **2012**, *14*, 3146–3149; b) Z. Jiang, P. Lu, Y. Wang, *Org. Lett.* **2012**, *14*, 6266–6269; c) S. Hase, Y. Kayaki, T. Ikariya, *Organometallics* **2013**, *32*, 5285–5288; d) Y. Yamamoto, H. Hayashi, T. Saigoku, H. Nishiyama, *J. Am. Chem. Soc.* **2005**, *127*, 10804–10805.
[15] a) E. F. Kleinman, R. A. Volkmann, in: *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, New York, **1991**, vol. 2, p. 975; b) N. Gommermann, C. Koradin, P. Knochel, *Synthesis* **2002**, *14*, 2143–2149; c) J. Zhang, C. Wei, C.-J. Li, *Tetrahedron Lett.* **2002**, *43*, 5731–5733; d) C. Fischer, E. M. Carreira, *Org. Lett.* **2004**, *6*, 1497–1499.
[16] a) D. Mesnard, L. Miginiac, *J. Organomet. Chem.* **1989**, *373*, 1–10; b) T. Murai, Y. Mutoh, Y. Ohta, M. Murakami, *J. Am. Chem. Soc.* **2004**, *126*, 5968–5969; c) T. Murai, Y. Ohta, Y. Mutoh, *Tetrahedron Lett.* **2005**, *46*, 3637–3640; d) T. Murai, K. Ui, Narengerile, *J. Org. Chem.* **2009**, *74*, 5703–5706.
[17] B.-B. Yao, Y.-H. Zhang, Y. Li, *J. Org. Chem.* **2010**, *75*, 4554–4561.
[18] a) C. Wei, Z. Li, C.-J. Li, *Org. Lett.* **2003**, *5*, 4473–4475; b) X. Yao, C.-J. Li, *Org. Lett.* **2005**, *7*, 4395–4398; c) H. Feng, D. S. Ermolat'ev, G. Song, E. V. Van der Eycken, *J. Org. Chem.* **2011**, *76*, 7608–7613; d) C. E. Meyet, C. J. Pierce, C. H. Larsen, *Org. Lett.* **2012**, *14*, 964–967; e) A. Teimouri, A. N. Chermahini, M. Narimani, *Bull. Korean Chem. Soc.* **2012**, *33*, 1556–1560; f) K. Park, Y. Heo, S. Lee, *Org. Lett.* **2013**, *15*, 3322–3325.
[19] J.-H. Ahn, M.-J. Joung, N.-M. Yoon, *J. Org. Chem.* **1999**, *64*, 488–492.
[20] a) B. L. Korbad, S.-H. Lee, *Synlett* **2013**, *24*, 1953–1958; b) B. L. Korbad, S.-H. Lee, *Bull. Korean Chem. Soc.* **2013**, *34*, 1266–1268; c) S.-H. Lee, H. Matsushita, G. Koch, J. Zimmermann, B. Clapham, K. D. Janda, *J. Comb. Chem.* **2004**, *6*, 822–827; d) S.-H. Lee, H. Matsushita, B. Clapham, K. D. Janda, *Tetrahedron* **2004**, *60*, 3439–3443; e) H. Matsushita, S.-H. Lee, M. Joung, B. Clapham, K. D. Janda, *Tetrahedron Lett.* **2004**, *45*, 313–316.
[21] a) M. Journet, D. Cai, L. M. DiMichele, R. D. Larsen, *Tetrahedron Lett.* **1998**, *39*, 6427–6428; b) E. Campaigne, W. L. Archer, *J. Am. Chem. Soc.* **1953**, *75*, 989–991; c) R. M. Lanigan, P. Starkov, T. D. Sheppard, *J. Org. Chem.* **2013**, *78*, 4512–4523.
[22] a) A. T. Stewart, C. R. Hauser, *J. Am. Chem. Soc.* **1955**, *77*, 1098–1103; b) T. D. Stewart, W. E. Bradley, *J. Am. Chem. Soc.* **1932**, *54*, 4172–4183.

Received: April 22, 2014
Published Online: June 25, 2014

