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Synthesis of Symmetric 1,4-Diamino-2-Butynes via a Cu(I)-Catalyzed One-Pot A^3-Coupling/Decarboxylative Coupling of a Propiolic Acid, an Aldehyde, and an Amine

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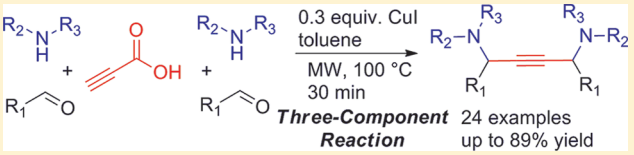
Supporting Information

ABSTRACT: A novel microwave-assisted approach for the one-pot Cu(I)-catalyzed A^3-coupling/decarboxylative coupling (PA^2-coupling) of a propiolic acid, an aldehyde, and an amine, resulting in the formation of diversely substituted 1,4-diamino-2-butynes, is described. It is noteworthy that this new multicomponent coupling provides an efficient access to introduce alkyl and aryl group at the 1,4-position of the 1,4-diamino-2-butynes.



1,4-Diamino-2-butynes, containing the propargylamine structural motif, are effective antioxidants and valuable intermediates for the preparation of many biologically active compounds and natural products.[1] Conventionally, 1,4-diamino-2-butynes are synthesized by nucleophilic substitution reaction of 2-butyne 1,4-dihalides with amines.[2] Recently, Knochel reported a copper-catalyzed addition of trimethylsilylacetylene to enamines (Scheme 1, a),[3] and Vogel described a $(t\text{-BuO})_2$ oxidative C−C cross-coupling of tertiary amines with triethylsilylacetylene catalyzed by $FeCl_2$ (Scheme 1, b),[4] but only one example is provided in each case. Then Nakamura discovered an alternative approach to symmetric 1,4-diamino-2-butynes involving deacetylenative self-coupling of propargylamines (Scheme 1, c).[5] Although these approaches disclose elegant progresses to 1,4-diamino-2-butynes, they are still accessed in multiple steps requiring relatively long synthetic procedures. Thus, there is a need for the development of an environmentally friendly, economical and diverse method having a high functional group tolerance.

Over the past decade, transition-metal-catalyzed decarboxylative coupling reactions have gained particular interest because of their inherent advantage that the in situ generated organometallic species from simple carboxylic acids are applied to replace relatively expensive, toxic, or highly sensitive organometallic reagents to undergo cross-coupling reaction.[6] Such reactions typically involve the formation of carbon−carbon bonds[7−9] and carbon−heteroatom bonds[10] for the synthesis of pharmaceuticals and biologically active natural products. Sequential decarboxylative coupling reactions of propiolic acid have recently been achieved for the synthesis of diarylalkynes[11] and 1,4-diaryl-substituted 1,3-diynes.[12] However, to the best of our knowledge, the application of propiolic acid in a decarboxylative process to access 1,4-diamino-2-butynes has not yet been performed.

In our previous investigations, we have successfully applied multicomponent decarboxylative coupling reactions for the generation of propargylamines and oxazolidinones.[13] Herein, we report a novel Cu(I)-catalyzed one-pot decarboxylative coupling of propiolic acid, an aldehyde, and an amine (PA^2 coupling) under microwave irradiation which provides a broad spectrum of functional groups at 1,4-position of the 1,4-diamino-2-butynes that can be introduced (Scheme 1, d).

As depicted in Table 1, the investigations were initiated with 3-methylbutanal (**1a**), *N*-methylbenzylamine (**2a**), and propiolic acid (**3**) as model substrates to find the optimal conditions. Our first attempts were focused on the evaluation of the efficiency of various solvents under microwave irradiation in the presence of 20 mol % of CuI (Table 1, entries 1−5). Gratifyingly, 61% yield of the desired product **4a** was obtained when toluene was employed at 100 °C (Table 1, entry 1). Encouraged by this result, we subsequently examined various catalysts. Among the copper salts tested, CuI seemed to be the most active catalyst for this decarboxylative coupling reaction (Table 1, entries 1 and 6−11). The use of other catalysts, such as CuBr, CuOTf, and $Cu(OTf)_2$ led to a lower yield of the desired 1,4-diamino-2-butyne (Table 1, entries 6, 8, and 10). Varying the concentration of CuI resulted in changes in both the yield of **4a**, and the amount of propargylamine and unknown byproduct (Table 1, entries 1 and 12−14). We found that 30% CuI gave a higher yield compared to the use of 10% CuI, 20% CuI, or 40% CuI. Further screening revealed that a lower or higher reaction temperature proved to be inferior in conversions to the desired 1,4-diamino-2-butynes (Table 1, entries 15 and 16), while increasing the irradiation time to

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Scheme 1. Approaches for the Synthesis of 1,4-Diamino-2-butynes

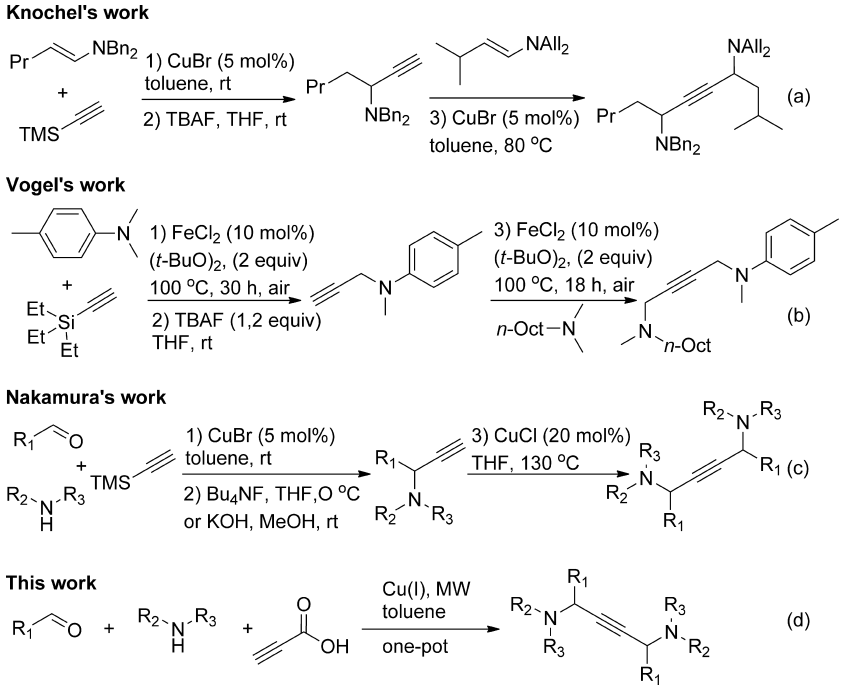
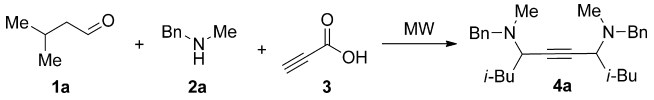


Table 1. Optimization of the Reaction Conditions[a]



entry	Cu catalyst (equiv)	solvent	temp (°C)	time	yield[b] (%)
1	CuI (0.2)	toluene	100	30 min	61
2	CuI (0.2)	dioxane	100	30 min	35
3	CuI (0.2)	THF	100	30 min	55
4	CuI (0.2)	ethanol	100	30 min	42
5	CuI (0.2)	DCE	100	30 min	38
6	CuBr (0.2)	toluene	100	30 min	47
7	CuCl (0.2)	toluene	100	30 min	49
8	CuOTf (0.2)	toluene	100	30 min	18
9	$Cu(MeCN)_4PF_6$ (0.2)	toluene	100	30 min	25
10	$Cu(OTf)_2$ (0.2)	toluene	100	30 min	13
11	$CuCl_2$ (0.2)	toluene	100	30 min	52
12	CuI (0.4)	toluene	100	30 min	74
13	**CuI (0.3)**	**toluene**	**100**	**30 min**	**82**
14	CuI (0.1)	toluene	100	30 min	43
15	CuI (0.3)	toluene	90	30 min	59
16	CuI (0.3)	toluene	115	30 min	78
17	CuI (0.3)	toluene	100	45 min	77
18	CuI (0.3)	toluene	100	21 h	81[c]

[a]Reactions were performed using 3-methylbutanal (2.2 mmol), *N*-methylbenzylamine (2.5 mmol), propiolic acid (1.0 mmol), and solvent (1 mL) under microwave irradiation at 100 °C and 80 W maximum power. [b]Isolated yields based on propiolic acid. [c]Conventional heating.

45 min also resulted in a decreased yield of 77% (Table 1, entry 17). A control experiment showed that the desired product **4a** was obtained in a yield of 83% after an extended reaction time of 21 h under conventional heating condition (Table 1, entry 18).

With the optimized reaction conditions established (Table 1, entry 13), we next evaluated the substrate scope of the aldehydes and the amines (Table 2). In general, good yields were obtained when using aliphatic aldehydes (Table 2, entries 1−8). However, benzaldehyde afforded the desired compound in only 28% yield (Table 2, entry 9). Reactions with secondary amines, such as *N*-substituted benzylamines, seemed to be working quite well (Table 2, entries 10−12). Furthermore, dienyne-based compounds, which are very useful substrates for the construction of double-ringed systems,[14] were successfully formed employing this protocol (Table 2, entries 13−15). The reaction also worked efficiently with cyclic (Table 2, entry 16) and aliphatic amines (Table 2, entries 17 and 18), affording the desired compounds in 74−89% yield. On the contrary, the use of primary amine resulted in only trace amount of **4t** together with several unidentified byproducts (Table 2, entry 20). To expand the scope of this approach, various combinations of aldehydes and amines were evaluated. All reactions provided good yields (Table 2, entries 20−24). The final products appear as a mixture of two diastereomers, which are inseparable by chromatography and spectroscopically.

A plausible reaction mechanism is proposed in Scheme 2. The reaction is initiated by cation exchange between propiolic acid **3** and the copper salt affording copper species **A**. Subsequently, the process would involve two possible pathways. The first pathway is Cu(I)-catalyzed decarboxylation of **A** to alkynylcopper **B** followed by coupling reaction with in situ formed iminium salt **C** affording propargylamine copper complex **E** (path a). Another pathway involves Cu(I)-catalyzed coupling of **A** and **C** resulting in the formation of intermediate **D**, followed by decarboxylation to provide **E** (path b). This common intermediate **E** undergoes further coupling yielding the desired 1,4-diamino-2-butyne **4** with the concomitant regeneration of the Cu(I) catalyst.

In summary, we have developed the first Cu(I)-catalyzed A^3-coupling/decarboxylative coupling protocol applying propiolic

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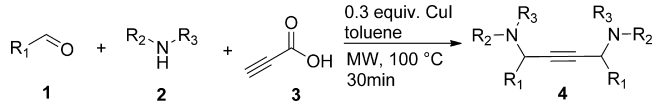
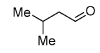
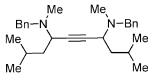
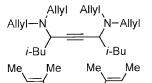
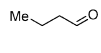
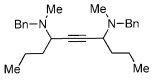
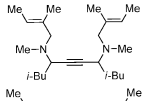
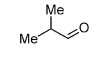
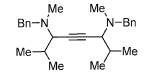
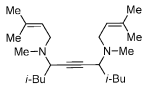
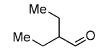
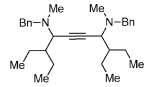
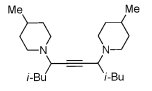
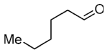
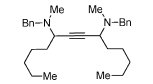
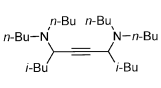
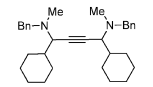
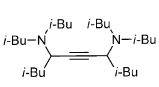
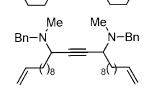
Table 2. Scope and Limitations of the Protocol[a]



entry	aldehyde **1**	amine **2**	product **4**		yield[b] (%)	entry	aldehyde **1**	amine **2**	product **4**		yield[b] (%)
1				**4a**	82	13				**4m**	58
2				**4b**	64	14				**4n**	84
3				**4c**	60	15				**4o**	53
4				**4d**	43	16				**4p**	74
5				**4e**	51	17				**4q**	89
6				**4f**	77	18				**4r**	80
7				**4g**	80	19				**4s**	trace
8				**4h**	70	20				**4t**	82
9				**4i**	28	21				**4u**	74
10				**4j**	71	22				**4v**	72
11				**4k**	83						
12				**4l**	89						

[a]A mixture of aldehyde 1 (2.2 mmol), amine 2 (2.5 mmol), propiolic acid 3 (1.0 mmol), CuI (0.3 equiv) and toluene (1 mL) was irradiated at a ceiling temperature of 100 °C and a maximum power of 80 W for 30 min. [b]Isolated yields.

Scheme 2. Proposed Reaction Pathways

acid, an aldehyde, and an amine (PA^2-coupling) for the construction of symmetric 1,4-diamino-2-butynes in high yields. This efficient, fast, and economical one-pot approach is applicable to a broad scope of aldehydes and amines under microwave irradiation.

EXPERIMENTAL SECTION

General Information. All solvents and reagents were purchased from commercial sources and were used without prior purification. All microwave irradiation experiments were carried out in a dedicated CEM-Discover monomode microwave apparatus, operating at a frequency of 2.45 GHz with continuous irradiation power from 0 to 300 W. The reactions were carried out in 10 mL glass tubes, sealed with Teflon septum and placed in the microwave cavity. The reaction mixture was irradiated at a required ceiling temperature using maximum power for the stipulated time, and the reaction mixture temperatures were measured by the external IR sensor. The reaction tube was cooled to ambient temperature with air jet cooling. TLC analysis was performed on aluminum backed plates SIL G/UV254. The products were purified by silica gel (200−300 mesh) column chromatography. ^{1}H NMR spectra were recorded at 300 MHz, ^{13}C NMR spectra at 75 MHz correspondingly with tetramethylsilane or solvent ($CDCl_3$) as internal standard. Chemical shifts are reported in values δ (ppm) and coupling constants given in hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet) and m (multiplet). High-resolution mass spectra were recorded by using ion source temperature 150−250 °C as required and the double-focusing

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magnetic sector analyzer. High-resolution EI-mass spectra were performed with a resolution of 10000.

Synthesis of *N*-(2-Bromobenzyl)butan-1-amine 2l. A solution of 2-bromobenzaldehyde (10 mmol) and butan-1-amine (10 mmol) in toluene (50 mL) was refluxed in a Dean−Stark apparatus for 3 h. After removal of toluene in vacuo, the corresponding imine derivative was used directly in the next step without further purification. $NaBH_4$ (20 mmol) was added portionwise to a solution of the previously obtained imine in MeOH (60 mL) at room temperature. The mixture was stirred for 2 h, and then saturated aqueous NH_4Cl solution (20 mL) was added. After the mixture was stirred for 30 min, the solvent was removed under vacuum. The crude mixture was dissolved in CH_2Cl_2 (40 mL) and washed with water (20 mL) and brine (30 mL). The organic solution was dried (Na_2SO_4), filtered, and concentrated in vacuum. The crude oily amines were purified by flash column chromatography with ethyl acetate−heptanes (80:20) as eluent.[15]

Synthesis of *N*-Benzyl-2,3-dimethylbut-2-en-1-amine (2m). A solution of *N*-benzyl-2,2,2-trifluoroacetamide (47.12 mmol, 9.37 g) in dry THF (50 mL) was added dropwise to a mixture of NaH (60 wt % disp) (1.5 equiv, 2.83 g) and NaI (10 mol %) in THF (50 mL) at rt under argon. Upon completion of addition, the mixture was allowed to stir for 1 h. Then 2-(bromomethyl)-3-methylbut-2-ene[16] (1.2 equiv, 9.22 g) was added dropwise, and the mixture was brought to reflux. After overnight reflux, the reaction was cooled to rt, quenched with H_2O, and extracted with Et_2O. The organic layer was concentrated under reduced pressure. The residue was dissolved in a mixture of MeOH (50 mL), H_2O (30 mL), and KOH (4.67 g). The resulting solution was refluxed for 2 h, concentrated under reduced pressure down to 20−30 mL, and extracted with Et_2O. The organic layer was washed with brine and dried (Na_2SO_4). Distillation under reduced pressure from CaH_2 afforded pure **2m**.[17]

(*E*)-*N*,2-Dimethylbut-2-en-1-amine (20) was prepared according to ref 18.

***N*,3-Dimethylbut-2-en-1-amine (2p)** was prepared according to ref 19.

General Procedure for the Synthesis of Propagylamines 4. A mixture of aldehyde **1** (2.2 mmol), amine **2** (2.5 mmol), and propiolic acid **3** (1.0 mmol) was dissolved in toluene (1.0 mL) applying a microwave vial along with a magnetic stir bar, and then copper bromide (0.3 mmol) was added. The reaction vessel was sealed and irradiated in the cavity of CEM-Discover microwave reactor at a ceiling temperature of 100 °C and a maximum power of 80 W for 30 min. The resulting reaction mixture was loaded on a silica gel column and flashed with 6−10% EtOAc in heptanes to afford the desired product **4** as light yellow oil.

***N*⁴,*N*⁷-Dibenzyl-*N*⁴,*N*⁷,2,9-tetramethyldec-5-yne-4,7-diamine (4a):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, J = 6.60 Hz, 12H), 1.51−1.65 (m, 4H), 1.86−1.95 (m, 2H), 2.23 (s, 6H), 3.50 (d, J = 13.02 Hz, 2H), 3.54 (t, J = 7.44 Hz, 2H), 3.70 (d, J = 13.02 Hz, 2H), 7.21 (t, J = 7.07 Hz, 2H), 7.27−7.37 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.7, 25.2, 37.9, 43.5, 43.5, 53.8, 59.5, 82.8, 127.1, 128.3, 129.1, 139.6; HRMS (EI) m/z calcd for $C_{28}H_{40}N_2$ $[M]^+$ 404.3191, found 404.3195.

***N*⁴,*N*⁷-Dibenzyl-*N*⁴,*N*⁷-dimethyldec-5-yne-4,7-diamine (4b):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 7.26 Hz, 6H), 1.45−1.56 (m, 4H), 1.64−1.68 (m, 4H), 2.24 (s, 6H), 3.47 (t, J = 7.53 Hz, 2H), 3.51 (d, J = 13.17 Hz, 2H), 3.70 (d, J = 13.17 Hz, 2H), 7.22 (t, J = 6.96 Hz, 2H), 7.28−7.37 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 13.9, 19.9, 36.6, 37.8, 55.3, 59.3, 82.7, 126.9, 128.2, 129.0, 139.5; HRMS (EI) m/z calcd for $C_{26}H_{36}N_2$ $[M]^+$ 376.2878, found 376.2865.

***N*³,*N* ⁶-Dibenzyl-*N* ³,*N* ⁶,2,7-tetramethyloct-4-yne-3,6-diamine (4c):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, J = 6.42 Hz, 6H), 1.08 (d, J = 4.71 Hz, 6H), 1.81−1.90 (m, 2H), 2.22 (s, 6H), 2.98 (d, J = 9.96 Hz, 2H), 3.55 (d, J = 13.35 Hz, 2H), 3.71 (d, J = 13.38 Hz, 2H), 7.22 (t, J = 6.96 Hz, 2H), 7.30 (t, J = 7.25 Hz, 4H), 7.37 (d, J = 7.17 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.9, 19.9, 21.1, 21.2, 31.3, 31.4, 37.9, 37.9, 59.7, 63.0, 82.7, 126.9, 128.3, 129.0, 139.9; HRMS (EI) m/z calcd for $C_{26}H_{36}N_2$ $[M]^+$ 376.2878, found 376.2875.

***N*⁴,*N*⁷-Dibenzyl-3,8-diethyl-*N*⁴,*N*⁷-dimethyldec-5-yne-4,7-diamine (4d):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, J = 7.25 Hz, 6H), 0.89 (t, J = 7.34 Hz, 6H), 1.40−1.51 (m, 4H), 1.53−1.64 (m, 2H), 1.66−1.80 (m, 4H), 2.20 (s, 6H), 3.25 (d, J = 10.17 Hz, 2H), 3.53 (d, J = 13.38 Hz, 2H), 3.70 (d, J = 13.17 Hz, 2H), 7.23 (t, J = 6.98 Hz, 2H), 7.28−7.37 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 9.6, 10.6, 20.4, 22.3, 37.7, 37.8, 42.3, 42.4, 58.9, 59.8, 82.7, 126.8, 128.2, 128.9, 139.8; HRMS (EI) m/z calcd for $C_{30}H_{44}N_2$ $[M]^+$ 432.3504, found 432.3488.

***N*⁶,*N* ⁹-Dibenzyl-*N* ⁶,*N* ⁹-dimethyltetradec-7-yne-6,9-diamine (4e):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.90 (t, J = 6.68 Hz, 6H), 1.29−1.34 (m, 8H), 1.44−1.53 (m, 4H), 1.64−1.72 (m, 4H), 2.25 (s, 6H), 3.45 (t, J = 7.44 Hz, 2H), 3.51 (d, J = 13.20 Hz, 2H), 3.70 (d, J = 13.02 Hz, 2H), 7.23 (t, J = 6.98 Hz, 2H), 7.29−7.37 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1, 22.7, 26.4, 31.6, 34.4, 34.5, 37.9, 55.6, 59.3, 82.7, 126.8, 128.2, 129.0, 139.5; HRMS (EI) m/z calcd for $C_{30}H_{44}N_2$ $[M]^+$ 432.3504, found 432.3495.

***N*¹,*N*⁴-Dibenzyl-1,4-dicyclohexyl-*N*¹,*N*⁴-dimethylbut-2-yne-1,4-diamine (4f):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85−1.00 (m, 4H), 1.12−1.30 (m, 6H), 1.52−1.57 (m, 2H), 1.64−1.76 (m, 6H), 2.09−2.16 (m, 4H), 2.21 (s, 6H), 3.10 (d, J = 9.96 Hz, 2H), 3.52 (d, J = 13.38 Hz, 2H), 3.69 (d, J = 13.35 Hz, 2H), 7.22 (t, J = 6.87 Hz, 2H), 7.27−7.37 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 26.0, 26.2, 26.8, 30.3, 31.5, 37.8, 40.3, 40.4, 59.5, 61.5, 82.5, 126.8, 128.2, 128.8, 139.8; HRMS (EI) m/z calcd for $C_{32}H_{44}N_2$ $[M]^+$ 456.3504, found 456.3502.

***N*¹¹,*N*¹⁴-Dibenzyl-*N*¹¹,*N*¹⁴-dimethyltetracosa-1,23-dien-12-yne-11,14-diamine (4g):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29−1.39 (m, 24H), 1.64−1.69 (m, 4H), 1.97−2.06 (m, 4H), 2.24 (s, 6H), 3.44 (t, J = 7.44 Hz, 2H), 3.51 (d, J = 13.17 Hz, 2H), 3.70 (d, J = 12.99 Hz, 2H), 4.93 (d, J = 13.38 Hz, 2H), 4.97 (d, J = 13.38 Hz, 2H), 5.73−5.86 (m, 2H), 7.23 (t, J = 6.98 Hz, 2H), 7.28−7.37 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.0, 26.7, 28.9, 28.9, 29.0, 29.1, 29.3, 29.5, 29.6, 29.7, 33.8, 34.4, 34.4, 37.8, 43.9, 55.5, 59.3, 82.7, 114.1, 126.9, 128.2, 129.0, 139.1, 139.5; HRMS (EI) m/z calcd for $C_{40}H_{60}N_2$ $[M]^+$ 568.4756, found 568.4773.

***N*³,*N*⁶-Dibenzyl-*N*³,*N*⁶-dimethyl-1,8-diphenyloct-4-yne-3,6-diamine (4h):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.94−2.10 (m, 4H), 2.27 (s, 6H), 2.81 (t, J = 7.64 Hz, 4H), 3.51 (t, J = 7.34 Hz, 2H), 3.53 (d, J = 13.20 Hz, 2H), 3.73 (d, J = 13.20 Hz, 2H), 7.13−7.33 (m, 16H), 7.37 (d, J = 7.14 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 32.8, 36.2, 36.2, 37.8, 55.0, 59.3, 82.8, 125.8, 127.0, 128.2, 128.3, 128.5, 128.9, 139.3, 141.8; HRMS (EI) m/z calcd for $C_{36}H_{40}N_2$ $[M]^+$ 500.3191, found 500.3183.

***N*¹,*N*⁴-Dibenzyl-*N*¹,*N*⁴-dimethyl-1,4-diphenylbut-2-yne-1,4-diamine (4i):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (s, 6H), 3.71 (d, J = 12.99 Hz, 2H), 3.80 (d, J = 12.99 Hz, 2H), 4.94(s, 2H), 7.25−7.40 (m, 12H), 7.44 (d, J = 7.17 Hz, 4H), 7.72 (d, J = 7.35 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.1, 59.1, 59.3, 83.2, 127.1, 127.5, 128.1, 128.3, 128.9, 139.2, 139.3; HRMS (EI) m/z calcd for $C_{32}H_{32}N_2$ $[M]^+$ 444.2565, found 444.2572.

***N*⁴,*N*⁷-Bis(3,4-dimethoxybenzyl)-*N*⁴,*N*⁷,2,9-tetramethyldec-5-yne-4,7-diamine (4j):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89−0.92 (m, 12H), 1.53−1.60 (m, 4H), 1.85−1.94 (m, 2H), 2.26 (s, 6H), 3.47 (d, J = 12.96 Hz, 2H), 3.52 (t, J = 7.71 Hz, 2H), 3.65 (d, J = 12.96 Hz, 2H), 3.86 (s, 6H), 3.88 (s, 6H), 6.81 (d, J = 7.17 Hz, 2H), 6.88 (d, J = 8.28 Hz, 2H), 6.94 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.6, 25.0, 37.6, 43.3, 53.0, 55.7, 55.8, 59.2, 82.6, 110.7, 112.0, 121.0, 132.0, 148.0, 148.9; HRMS (EI) m/z calcd for $C_{32}H_{48}N_2O_4$ $[M]^+$ 524.3614, found 524.3620.

***N*⁴,*N*⁴,*N*⁷,*N*⁷-Tetrabenzyl-2,9-dimethyldec-5-yne-4,7-diamine (4k):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73−0.85 (m, 12H), 1.45−1.57 (m, 2H), 1.63−1.75 (m, 2H), 1.74−1.95 (m, 2H), 3.35−3.59 (m, 6H), 3.79−3.92 (m, 4H), 7.20−7.44 (m, 20H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.3, 23.1, 25.0, 43.6, 50.0, 55.3, 82.8, 127.1, 128.4, 129.1, 140.1; HRMS (EI) m/z calcd for $C_{40}H_{48}N_2$ $[M]^+$ 556.3817, found 556.3810.

***N*⁴,*N*⁷-Bis(2-bromobenzyl)-*N*⁴,*N*⁷-dibutyl-2,9-dimethyldec-5-yne-4,7-diamine (4l):** light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84−0.91 (m, 18H), 1.25−1.56 (m, 12H), 1.85−1.93 (m, 2H), 2.56 (t, J = 7.07 Hz, 4H), 3.57 (t, J = 7.34 Hz, 2H), 3.70−3.84 (m, 4H),

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7.05 (t, J = 7.55 Hz, 2H), 7.26 (t, J = 7.53 Hz, 2H), 7.50 (d, J = 7.92 Hz, 2H), 7.59 (d, J = 7.53 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1, 20.7, 22.6, 25.0, 30.5, 43.6, 51.3, 55.5, 82.8, 124.2, 127.0, 127.9, 130.5, 132.4, 139.6; HRMS (EI) m/z calcd for $C_{34}H_{50}Br_2N_2$ $[M]^+$ 644.2341, found 644.2336.

N^4,N^4,N^7,N^7-Tetraallyl-2,9-dimethyldec-5-yne-4,7-diamine (4m): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 6.50 Hz, 12H), 1.49 (t, J = 7.25 Hz, 12H), 1.79−1.87 (m, 2H), 2.85−2.92 (m, 4H), 3.25−3.31 (m, 4H), 3.63 (t, J = 7.44 Hz, 2H), 5.11 (d, J = 9.90 Hz, 4H), 5.20 (d, J = 17.13 Hz, 4H), 5.77−5.90 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.4, 22.7, 25.1, 43.2, 43.3, 50.6, 54.1, 77.0, 82.7, 116.9, 136.8; HRMS (EI) m/z calcd for $C_{24}H_{40}N_2$ $[M]^+$ 356.3191, found 356.3181.

N^4,N^7,2,9-Tetramethyl-N^4,N^7-bis(2-methylbut-2-en-1-yl)dec-5-yne-4,7-diamine (4n): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89−0.92 (m, 12H), 1.47 (t, J = 7.25 Hz, 4H), 1.62 (s, 12H), 1.79−1.88 (m, 2H), 2.12 (s, 6H), 2.84 (d, J = 12.45 Hz, 2H), 2.95 (d, J = 12.42 Hz, 2H), 3.46 (t, J = 7.64 Hz, 2H), 5.39−5.43 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 13.3, 14.6, 22.5, 22.7, 25.1, 37.3, 53.2, 63.8, 82.5, 121.7, 133.9; HRMS (EI) m/z calcd for $C_{24}H_{44}N_2$ $[M]^+$ 360.3504, found 360.3490 .

N^4,N^7,2,9-Tetramethyl-N^4,N^7-bis(3-methylbut-2-en-1-yl)dec-5-yne-4,7-diamine (4o): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J = 6.50 Hz, 12H), 1.42−1.59 (m, 4H), 1.67 (s, 6H), 1.73 (s, 6H), 1.79−1.88 (m, 2H), 2.20 (s, 6H), 3.02 (d, J = 7.17 Hz, 4H), 3.54 (t, J = 7.53 Hz, 2H), 5.22 (t, J = 7.07 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.0, 22.1, 22.8, 25.2, 25.9, 37.4, 43.4, 52.6, 53.5, 82.7, 122.2, 135.0; HRMS (EI) m/z calcd for $C_{24}H_{44}N_2$ $[M]^+$ 360.3504, found 360.3512.

1,1′-(2,9-Dimethyldec-5-yne-4,7-diyl)bis(4-methylpiperidine) (4p): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90−0.95 (m, 18H), 1.16−1.47 (m, 8H), 1.53−1.67 (m, 6H), 1.79−1.87 (m, 2H), 2.17 (t, J = 10.31 Hz, 2H), 2.47 (t, J = 11.21 Hz, 2H), 2.66 (d, J = 11.31 Hz, 2H), 2.76 (d, J = 11.13 Hz, 2H), 3.41 (t, J = 7.53 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9, 23.3, 25.5, 31.0, 34.4, 34.7, 42.9, 43.0, 46.5, 53.1, 56.0, 83.1; HRMS (EI) m/z calcd for $C_{24}H_{44}N_2$ $[M]^+$ 360.3504, found 360.3508 .

N^4,N^4,N^7,N^7-Tetrabutyl-2,9-dimethyldec-5-yne-4,7-diamine (4q): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88−0.93 (m, 24H), 1.27−1.46 (m, 20H), 1.78−1.87 (m, 2H), 2.27−2.35 (m, 4H), 2.44−2.53 (m, 4H), 3.51 (t, J = 7.35 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1, 20.8, 22.4, 22.8, 30.9, 43.7, 51.5, 51.7, 82.9; HRMS (EI) m/z calcd for $C_{28}H_{56}N_2$ $[M]^+$ 420.4443, found 420.4446.

N^4,N^4,N^7,N^7-Tetraisobutyl-2,9-dimethyldec-5-yne-4,7-diamine (4r): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76−0.84 (m, 36H), 1.27−1.38 (m, 4H), 1.52−1.61 (m, 4H), 1.76−1.84 (m, 2H), 1.90−1.98 (m, 4H), 2.13−2.19 (m, 4H), 3.36 (t, J = 7.25 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.8, 21.1, 22.6, 22.7, 24.8, 26.6, 43.9, 51.5, 60.8, 82.4; HRMS (EI) m/z calcd for $C_{28}H_{56}N_2$ $[M]^+$ 420.4443, found 420.4449.

1,4-Dicyclohexyl-N^1,N^4-dimethyl-N^1,N^4-bis(2-methylbut-2-en-1-yl)but-2-yne-1,4-diamine (4t): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79−0.99 (m, 4H), 1.15−1.28 (m, 6H), 1.38−1.50 (m, 2H), 1.61 (s, 12H), 1.66−1.76 (m, 6H), 2.08 (s, 10H), 2.84−2.91 (m, 4H), 2.95−3.02 (m, 2H), 5.32−5.45 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 13.3. 14.5, 26.1, 26.3, 26.9, 30.3, 31.5, 37.1, 40.2, 40.3, 61.0, 64.1, 82.4, 121.4, 121.7, 133.8, 134.2; HRMS (EI) m/z calcd for $C_{28}H_{48}N_2$ $[M]^+$ 412.3817, found 412.3813.

N^3,N^6-Dimethyl-N^3,N^6-bis((E)-2-methylbut-2-en-1-yl)-1,8-diphenyloct-4-yne-3,6-diamine (4u): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58−1.62 (m, 12H), 1.90−1.97 (m, 4H), 2.17 (s, 6H), 2.78 (t, J = 7.71 Hz, 4H), 2.87 (d, J = 12.42 Hz, 2H), 3.00 (d, J = 12.60 Hz, 2H), 3.41 (t, J = 7.44 Hz, 2H), 5.38−5.44 (m, 2H), 7.16−7.29 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.2, 20.8, 30.9, 33.1, 36.6, 51.5, 53.2, 83.0, 125.8, 128.3, 128.5, 142.2; HRMS (EI) m/z calcd for $C_{32}H_{44}N_2$ $[M]^+$ 456.3504, found 456.3510.

1,1′-(Tetracosa-1,23-dien-12-yne-11,14-diyl)bis(4-methylpiperidine) (4v): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 6H), 1.05−1.29 (m, 30H), 1.63 (s, 8H), 2.02−2.05 (m, 4H), 2.16 (t, J = 11.01 Hz, 2H), 2.45 (t, J = 10.83 Hz, 2H), 2.66 (d, J = 11.10 Hz, 2H), 2.78 (d, J = 10.92 Hz, 2H), 3.32 (s, 2H), 4.90−5.01(m, 4H), 5.38−5.44 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9, 27.0, 28.9, 29.1, 29.4, 29.5, 31.0, 33.8, 34.0, 34.1, 34.4, 34.6, 46.6, 53.0, 57.9, 83.2, 114.1, 139.1; HRMS (EI) m/z calcd for $C_{36}H_{64}N_2$ $[M]^+$ 524.5070, found 524.5057.

N^3,N^3,N^6,N^6-Tetrabutyl-1,8-diphenyloct-4-yne-3,6-diamine (4w): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.07 Hz, 12H), 1.26−1.41 (m, 16H), 1.88−1.95 (m, 4H), 2.31−2.40 (m, 4H), 2.49−2.58 (m, 4H), 2.77 (t, J = 7.82 Hz, 4H), 3.47 (t, J = 7.23 Hz, 2H), 7.13−7.29 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.2, 20.8, 30.9, 33.1, 36.6, 51.5, 53.2, 83.0, 125.8, 128.3, 128.5, 142.2; HRMS (EI) m/z calcd for $C_{36}H_{56}N_2$ $[M]^+$ 516.4443, found 516.4454.

N^{11},N^{14}-Bis(2-bromobenzyl)-N^{11},N^{14}-dibutyltetracosa-1,23-dien-12-yne-11,14-diamine (4x): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 7.16 Hz, 6H), 1.26−1.50 (m, 36H), 1.57−1.70 (m, 4H), 1.99−2.06 (m, 4H), 2.56 (t, J = 6.87 Hz, 4H), 3.47 (t, J = 7.25 Hz, 2H), 3.70−3.83 (m, 4H), 4.90−5.01 (m, 4H), 5.73−5.86 (m, 2H), 7.06 (t, J = 7.44 Hz, 2H), 7.26 (t, J = 7.44 Hz, 2H), 7.49 (d, J = 7.92 Hz, 2H), 7.60 (d, J = 7.53 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.2, 20.8, 26.8, 29.0, 29.2, 29.4, 29.5, 29.7, 30.6, 33.9, 34.6, 51.6, 53.4, 55.6, 83.0, 114.2, 124.3, 127.1, 128.0, 128.3, 129.1, 130.5, 132.5, 139.2, 139.8; HRMS (EI) m/z calcd for $C_{46}H_{70}Br_2N_2$ $[M]^+$ 808.3906, found 808.3898.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

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Notes

The authors declare no competing financial interest.

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