JOC The Journal of Organic Chemistry

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Microwave-Assisted Decarboxylative Three-Component Coupling of a 2-Oxoacetic Acid, an Amine, and an Alkyne

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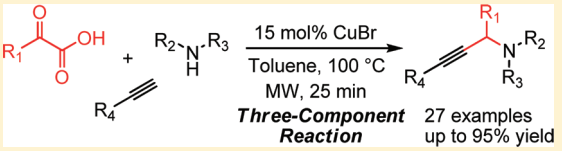
Supporting Information

ABSTRACT: A novel and efficient microwave-assisted decarboxylative three-component coupling of a 2-oxoacetic acid, an amine, and an alkyne (OA^2-coulpling) has been developed. This new multicomponent coupling constitutes an efficient approach for the synthesis of polysubstituted propargylamines in the presence of a catalytic amount of copper(I) catalyst.



Propargylamines are abundantly occurring components and valuable intermediates for the preparation of many nitrogen-containing biologically active compounds and natural products.[1] The traditional syntheses of propargylamines use strong bases such as butyllithium, organomagnesium reagents, or lithium diisopropylamide, exploiting the relatively high acidity of the terminal acetylene to form alkynyl metal compounds. The stoichiometric quantities of the reagents required, as well as their high sensitivity to moisture, render these processes fairly unattractive.[2]

During recent years, significant efforts have been made in order to develop useful approaches for the synthesis of propargylamines, especially employing multicomponent reactions (MCRs).[3] The three-component coupling of an aldehyde, an alkyne, and an amine, commonly referred to as A^3-coupling, has received much attention.[4] This excellent type of multicomponent reaction provides with its synthetic efficiency, intrinsic atom economy, and procedural simplicity an elegant entry to propargylamines.[5] Recently, substantial progress has been achieved for their synthesis. Urriolabeitia[6] and Zhang[7] discovered a new approach to propargylamines involving C−C and C−N bond formation through C−Cl bond activation of dichloromethane. Li reported a copper-catalyzed alkynylation of sp^3-C−H adjacent to nitrogen,[8] and Seidel and Li described a decarboxylative coupling of α-amino acids[9] with terminal alkynes. In our previous studies, we demonstrated that the aldehyde could be efficiently replaced by a ketone (KA^2-coupling),[10] and we also successfully applied primary amines, which are known to be difficult reaction partners, for the generation of secondary alkylpropargylamines in high yields.[11]

The decarboxylative coupling reactions have recently gained particular interest due to the inherent advantage that simple carboxylic acids represent a powerful alternative for C−C bond formation under relatively neutral conditions compared to preformed organometallic reagents.[12] The decarboxylative coupling of 2-oxoacetic acids has been widely used as a valuable synthetic strategy for the synthesis of ketones[13] and azomethines.[14] However, to the best of our knowledge, there are no literature examples describing the application of 2-oxoacetic acids in a decarboxylative process to access propargylamines. Herein, we report an unprecedented Cu(I)-catalyzed new three-component coupling of a 2-oxoacetic acid, an amine, and an alkyne under microwave irradiation.

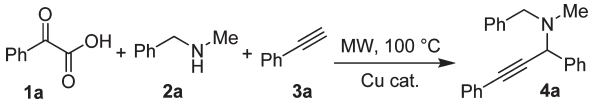
Our initial investigations employing phenylglyoxylic acid **1a**, *N*-methylbenzylamine **2a**, and phenylacetylene **3a** as model substrates in combination with 20% CuI as a catalyst focused on the evaluation of the efficiency of various solvents under microwave irradiation (Table 1, entries 1−5). Among the solvents tested, toluene seemed to be the most effective for this decarboxylative coupling reaction (Table 1, entry 5). A slightly lower yield was obtained when using acetonitrile as a solvent. Encouraged by this result, we subsequently examined various catalysts and reaction times. This led to the discovery that CuBr and CuCl were superior catalysts compared to CuI (Table 1, entries 5−7). Regarding the concentrations of the catalysts, we found that 15% CuBr resulted in a high yield, contrary to the use of 10% CuBr or 15% CuCl (Table 1, entries 12−14). A lower reaction temperature of 80 °C reduced the yield of the propargylamine **4a** to 70% (Table 1, entry 15), while reducing the irradiation time to 15 min also resulted in a decreased yield of 87% (Table 1, entry 16). In comparison, when the reaction was conducted under conventional heating using the same conditions, the desired propargylamine **4a** was obtained in a yield of 86% after an extended reaction time of 20 h (Table 1, entry 17).

Having optimized the conditions in hand (Table 1, entry 13), we next evaluated the scope of the procedure by varying the 2-oxoacetic acid, the amine, and the alkyne (Table 2). Both secondary and primary amines were explored as reaction partners (Table 2, entries 1−10), and good yields were obtained using

Received: July 4, 2011
Published: August 08, 2011

dx.doi.org/10.1021/jo2013725 | *J. Org. Chem.* 2011, 76, 7608–7613

Table 1. Optimization of the Conditions[a]



entry	Cu catalyst (mol %)	solvent	time (min)	yield[b] (%)
1	CuI (20)	EtOH	25	61
2	CuI (20)	THF	25	39
3	CuI (20)	MeCN	25	83
4	CuI (20)	DCE	25	75
5	CuI (20)	toluene	25	85
6	CuBr (20)	toluene	25	96
7	CuCl (20)	toluene	25	94
8	CuOTf (20)	toluene	25	76
9	$Cu(OTf)_2$ (20)	toluene	25	63
10	$Cu(OAc)_2$ (20)	toluene	25	40
11	Cu_2O (20)	toluene	25	15
12	CuCl (15)	toluene	25	78
13	CuBr (15)	toluene	25	95
14	CuBr (10)	toluene	25	73
15	CuBr (15)	toluene	25	70[c]
16	CuBr (15)	toluene	15	87
17	CuBr (15)	toluene	20 h	86[d]

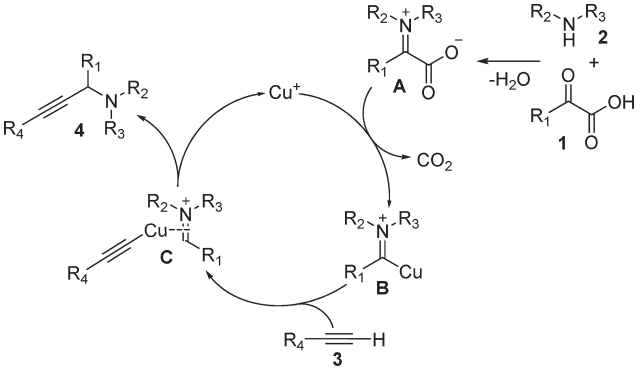
[a] Reactions were performed using phenylglyoxylic acid (1.1 mmol), *N*-methylbenzylamine (1.0 mmol), phenylacetylene (1.5 mmol), and solvent (1 mL) under microwave irradiation at 100 °C and 80 W maximum power. [b] Isolated yields based on *N*-methylbenzylamine. [c] Reaction carried out at 80 °C. [d] Conventional heating.

secondary amines, except in the case of dibutylamine (Table 2, entry 5). However, similar to A^3-coupling,[15] primary amines provided the desired compounds only in low to moderate yields (Table 2, entries 9 and 10). All reactions seemed to be working excellently when various alkynes were used. Both electron-rich (Table 2, entries 11−15) and electron-poor aryl-substituted alkynes (Table 2, entry 16) were effective, although a slightly lower yield was obtained with a *para*-butoxy substituent (Table 2, entry 15). The reaction also worked well with thiophen-2-alkyne (Table 2, entry 17) and aliphatic alkynes (Table 2, entries 18−21), yielding the desired compounds in 82−87% yield. To expand the scope of the protocol, a variety of 2-oxoacetic acids were also evaluated. Aliphatic and heterocyclic 2-oxoacetic acids gave good results (Table 2, entries 22−27).

A tentative mechanism for this decarboxylative three-component coupling is proposed in Scheme 1. The in situ formed iminium salt **A** undergoes a Cu(I)-catalyzed decarboxylation to afford the iminium−copper species **B**.[14] The latter undergoes reaction with the alkyne **3**, resulting in the formation of the intermediate copper complex **C**. Further conversion results in the generation of the desired propargylamine **4** with concomitant regeneration of the Cu(I) catalyst.[16]

In conclusion, we have successfully developed a novel microwave-assisted decarboxylative three-component coupling of a 2-oxoacetic acid, an amine, and an alkyne (OA^2-coupling), providing an efficient approach for the synthesis of polysubstituted propargylamines in the presence of a catalytic amount of copper(I) catalyst. Interestingly, the reactions were also applicable to sterically hindered and primary amines as well as to various aliphatic alkynes. Therefore, this new decarboxylative

Scheme 1. Proposed Mechanism for the OA^2-Coupling



OA^2-coupling can be regarded as a welcomed additional method for the generally applied A^3-coupling reaction.

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 and ^{13}C NMR spectra were recorded on 300 or 600 MHz NMR instrument. The ^{1}H chemical shifts are reported in parts per million relative to tetramethylsilane. High-resolution mass spectra were recorded by using ion source temperature of 150−250 °C as required. High-resolution EI mass spectra were performed with a resolution of 10 000.

General Procedure for the Synthesis of Propagylamines 4. 2-Oxoacetic acid **1** (1.1 mmol) was dissolved in toluene (1 mL), applying a microwave vial along with a stirring bar, and then amine **2** (1.0 mmol), acetylene **3** (1.5 mmol), and copper bromide (0.15 mmol) were added. The reaction vessel was sealed and irradiated in a CEM-Discover for 25 min at a ceiling temperature of 100 °C. The resulting reaction mixture was loaded on a column and flashed on silica gel (8−10% EtOAc/heptane) to afford the desired product **4**.

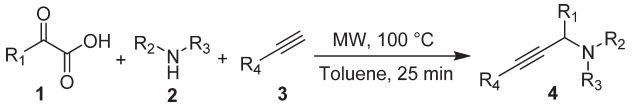
***N*-Benzyl-*N*-methyl-1,3-diphenylprop-2-yn-1-amine (Table 2, entry 1):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.61−3.75 (m, 2H), 4.92 (s, 1H), 7.23−7.42 (m, 1H), 7.54−7.57 (m, 2H), 7.68 (d, J = 7.45 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.2, 59.1, 59.7, 84.9, 88.8, 123.5, 127.2, 127.7, 128.3, 128.5, 128.6, 129.2, 132.0, 132.6, 139.2, 139.4; HRMS (EI) m/z calcd for $C_{23}H_{21}N$ [M + H] 311.1674, found 311.1694.

4-(1,3-Diphenylprop-2-ynyl)morpholine (Table 2, entry 2): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.61 (s, 4H), 3.75 (s, 4H), 4.77 (s, 1H), 7.28−7.37 (m, 6H), 7.49−7.52 (m, 2H), 7.63 (d, J = 7.45 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 49.9, 62.1, 67.2, 85.2, 88.6, 123.1, 127.9, 128.3, 128.4, 128.7, 131.9, 137.9; HRMS (EI) m/z calcd for $C_{19}H_{19}ON$ [M + H] 277.1467, found 277.1462.

***N*-(1,3-Diphenylprop-2-ynyl)-*N*-methylprop-2-en-1-amine (Table 2, entry 3):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.22

dx.doi.org/10.1021/jo2013725 |J. Org. Chem. 2011, 76, 7608–7613

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



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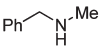
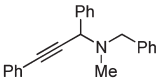
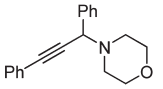
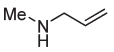
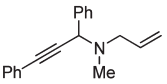
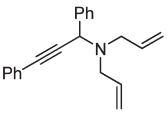
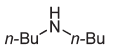
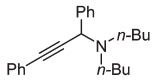
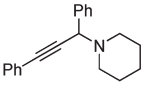
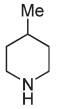
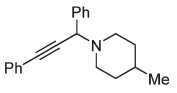
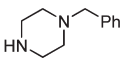
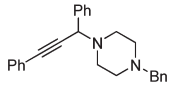
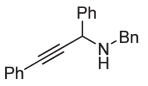
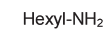
1					95
2					87
3					80
4					83
5					61
6					92
7					85
8					89
9					26
10					55
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dx.doi.org/10.1021/jo2013725 |J. Org. Chem. 2011, 76, 7608–7613

Table 2. Continued

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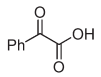
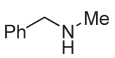
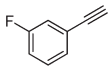
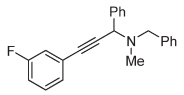
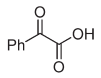
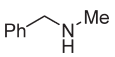
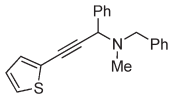
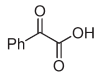
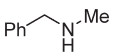
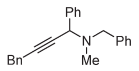
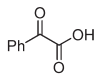
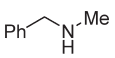
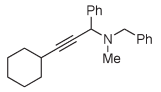
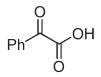
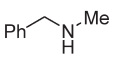
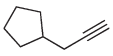
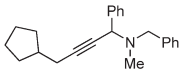
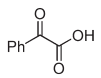
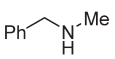
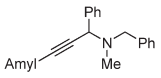
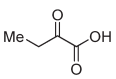
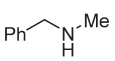
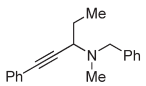
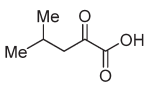
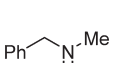
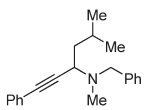
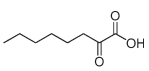
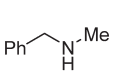
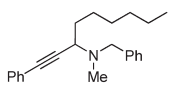
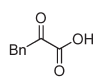
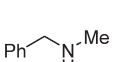
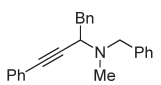
16					95
17					90
18					84
19					82
20					87
21					86
22					71
23					94
24					92
25					84
26					88
27					90

[a] A mixture of 2-oxoacetic acid **1** (1.1 mmol), amine **2** (1.0 mmol), alkyne **3** (1.5 mmol), CuBr (15 mol %), and solvent (1 mL) was irradiated at a ceiling temperature of 100 °C and a maximum power of 80 W for 25 min. [b] Isolated yields are reported.

(s, 3H), 3.18 (d, J = 6.18 Hz, 2H), 4.97 (s, 1H), 5.16 (d, J = 9.89 Hz, 1H), 5.28 (d, J = 16.69, 1H), 5.85−5.98 (m, 1H), 7.25−7.38 (m, 6H), 7.52 (d, J = 3.57 Hz, 2H), 7.64 (d, J = 7.34 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 37.8, 57.9, 59.7, 84.9, 88.4, 117.7, 123.2, 127.5, 128.1, 128.3, 128.4, 131.8, 136.1, 138.9; HRMS (EI) m/z calcd for $C_{19}H_{19}N$ [M + H] 261.1517, found 261.1502.

***N*-Allyl-*N*-(1,3-diphenylprop-2-ynyl)prop-2-en-1-amine (Table 2, entry 4):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.02−3.09 (m, 2H), 3.25−3.31 (m, 2H), 5.12 (d, J = 11.00 Hz, 3H), 5.27 (d, J = 17.12 Hz, 2H), 5.79−5.92 (m, 2H), 7.23−7.36 (m, 6H), 7. 53 (t, J = 7.34 Hz, 2H), 7.69 (d, J = 7.57, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 53.5, 56.5, 85.3, 87.9, 117.3, 123.3, 127.4, 128.1, 128.2, 128.3, 131.8, 136.5, 139.3; HRMS (EI) m/z calcd for $C_{21}H_{21}N$ [M + H] 287.1674, found 287.1669.

***N*-Butyl-*N*-(1,3-diphenylprop-2-ynyl)butan-1-amine (Table 2, entry 5):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, J = 14.12 Hz, 6H), 1.22−1.47 (m, 8H), 2.50 (t, J = 13.60 Hz, 4H), 5.02 (s, 1H), 7.21−7.35 (m, 6H), 7. 50 (d, J = 4.19 Hz, 2H), 7.68 (d, J = 7.84 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0, 20.5, 30.5, 50.6, 57.4, 86.1, 87.6, 117.3, 123.5, 127.2, 127.9, 128.3, 128.4, 131.8, 139.9; HRMS (EI) m/z calcd for $C_{23}H_{29}N$ [M + H] 319.2300, found 319.2315.

dx.doi.org/10.1021/jo2013725 |*J. Org. Chem.* 2011, 76, 7608–7613

1-(1,3-Diphenylprop-2-ynyl)piperidine (Table 2, entry 6): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39−1.45 (m, 2H), 1.54−1.62 (m, 4H), 2.55 (d, J = 9.66 Hz, 4H), 4.78, (s, 1H), 7.22−7.35 (m, 6H), 7. 48−7.51 (m, 2H), 7.63 (d, J = 7.39 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 24.4, 26.2, 50.6, 62.3, 86.0, 87.9, 117.3, 123.3, 127.4, 128.0, 128.2, 128.4, 131.8, 138.6; HRMS (EI) m/z calcd for $C_{20}H_{21}N$ [M + H] 275.1674, found 275.1681.

1-(1,3-Diphenylprop-2-ynyl)-4-methylpiperidine (Table 2, entry 7): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, J = 5.41 Hz, 3H), 1.10−1.34 (m, 3H), 1.53−1.68 (m, 2H), 2.15−2.22 (t, J = 21.09 Hz, 2H), 2.47−2.66 (m, 2H), 2.92 (d, J = 10.76 Hz, 1H) 4.81, (s, 1H), 7.24−7.37 (m, 6H), 7. 50 (d, J = 3.57 Hz, 2H), 7.62 (d, J = 7.32 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9, 30.8, 34.3, 34.7, 47.4, 52.7, 62.0, 86.1, 87.9, 123.3, 127.4, 128.0, 128.2, 128.5, 131.8, 138.7; HRMS (EI) m/z calcd for $C_{21}H_{23}N$ [M + H] 289.1817, found 289.1830.

1-Benzyl-4-(1,3-diphenylprop-2-ynyl)piperazine (Table 2, entry 8): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 4H), 2.63 (s, 4H), 3.46 (m, 2H), 4.77 (s, 1H), 7.17−7.33 (m, 11H), 7. 48 (t, J = 6.94 Hz, 2H), 7.61 (d, J = 7.48 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 53.5, 61.8, 63.3, 85.9, 88.4, 123.4, 127.2, 127.8, 128.4, 128.5, 128.7, 129.4, 132.0, 138.3, 138.5; HRMS (EI) m/z calcd for $C_{26}H_{26}N_2$ [M + H] 366.2096, found 366.2106.

***N*-Benzyl-1,3-diphenylprop-2-yn-1-amine (Table 2, entry 9):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.98 (s, 2H), 4.80 (s, 1H), 7.30−7.38 (m, 11H), 7. 48 (s, 2H), 7.61 (d, J = 6.76 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 51.1, 53.6, 85.7, 89.2, 123.1, 127.1, 127.6, 127.7, 128.1, 128.3, 128.4, 128.5, 131.7, 139.8, 140.3; HRMS (EI) m/z calcd for $C_{22}H_{19}N$ [M + H] 297.1517, found 297.1506.

***N*-(1,3-Diphenylprop-2-ynyl)hexan-1-amine (Table 2, entry 10):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (d, J = 6.42 Hz, 3H), 1.29 (s, 6H), 1.48 (d, J = 6.18 Hz, 2H), 2.66−2.74 (m, 1H), 2.79−2.88 (m, 1H), 4.78 (s, 1H), 7.26−7.37 (m, 6H), 7. 45 (d, J = 3.21 Hz, 2H), 7.58 (d, J = 7.32 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.2, 22.7, 27.2, 30.1, 31.9, 47.5, 54.8, 85.4, 89.6, 123.3, 127.6, 127.7, 128.2, 128.3, 128.6, 131.8, 140.8; HRMS (EI) m/z calcd for $C_{21}H_{25}N$ [M + H] 291.1987, found 291.1977.

***N*-Benzyl-3-(4-methoxyphenyl)-*N*-methyl-1-phenylprop-2-yn-1-amine (Table 2, entry 11):** ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.23 (s, 3H), 3.63 (d, J = 13.20 Hz, 1H), 3.70 (s, 3H), 3.71 (d, J = 13.20 Hz, 1H), 4.90 (s, 1H), 6.83 (d, J = 8.64 Hz, 2H), 7.19−7.34 (m, 6H), 7.40 (d, J = 7.56 Hz, 2H), 7.48 (d, J = 8.64 Hz, 2H), 7.68 (d, J = 7.92 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 38.2, 55.4, 59.1, 59.9, 83.4, 88.8, 114.2, 115.6, 127.3, 127.7, 128.3, 128.5, 128.6, 129.2, 133.5, 139.5, 139.6, 159.8; HRMS (EI) m/z calcd for $C_{24}H_{23}NO$ [M + H] 341.1780, found 341.1768.

***N*-Benzyl-3-(4-ethylphenyl)-*N*-methyl-1-phenylprop-2-yn-1-amine (Table 2, entry 12):** ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.20 (t, J = 15.42 Hz, 3H), 2.23 (s, 3H), 2.58−2.62 (m, 2H), 3.63 (d, J = 13.14 Hz, 1H), 3.71 (d, J = 13.14 Hz, 1H), 4.90 (s, 1H), 7.13(d, J = 7.92 Hz, 2H), 7.19−7.24 (m, 2H), 7.27−7.33 (m, 4H), 7. 40 (d, J = 7.33 Hz, 2H), 7.48 (d, J = 7.99 Hz, 2H), 7.68 (d, J = 7.99 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 15.8, 29.1, 38.3, 59.2, 59.9, 84.2, 89.1, 120.7, 127.3, 127.7, 128.2, 128.4, 128.5, 128.6, 129.3, 132.1, 139.5, 139.6, 144.8; HRMS (EI) m/z calcd for $C_{25}H_{25}N$ [M + H] 339.1987, found 339.1990.

***N*-Benzyl-*N*-methyl-1-phenyl-3-*p*-tolylprop-2-yn-1-amine (Table 2, entry 13):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.23 (s, 3H), 2.29 (s, 3H), 3.60−3.73 (m, 2H), 4.90 (s, 1H), 7.09 (d, J = 7.78 Hz, 2H), 7.19−7.46 (m, 10H), 7.68 (d, J = 7.32 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.7, 38.3, 59.2, 59.9, 84.2, 89.1, 120.5, 127.3, 127.7, 128.4, 128.5, 128.6, 129.3, 129.4, 132.0, 138.4, 139.4, 139.5, 139.6; HRMS (EI) m/z calcd for $C_{24}H_{23}N$ [M + H] 325.1830, found 325.1824.

***N*-Benzyl-3-(4-*tert*-butylphenyl)-*N*-methyl-1-phenylprop-2-yn-1-amine (Table 2, entry 14):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 9H), 2.23 (s, 3H), 3.61−3.74 (m, 2H), 4.91 (s, 1H), 7.21−7.42 (m, 10H), 7.51 (d, J = 7.87 Hz, 2H), 7.68 (d, J = 7.63 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 31.4, 34.9, 38.2, 59.1, 59.8, 84.2, 89.0, 120.5, 125.6, 127.3, 127.7, 128.3, 128.5, 128.6, 129.2, 131.9, 139.4, 139.5; HRMS (EI) m/z calcd for $C_{27}H_{29}N$ [M + H] 367.2300, found 367.2299.

***N*-Benzyl-3-(4-butoxyphenyl)-*N*-methyl-1-phenylprop-2-yn-1-amine (Table 2, entry 15):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J = 14.12 Hz, 3H), 1.44−1.51 (m, 2H), 1.70−1.77 (m, 2H), 2.23 (s, 3H), 3.60−3.73 (m, 2H), 3.93 (t, J = 12.63 Hz, 2H), 4.90 (s, 1H), 6.85 (d, J = 8.17 Hz, 2H), 7.22−7.50 (m, 10H), 7.67 (d, J = 7.43 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 13.8, 19.2, 31.2, 38.0, 58.9, 59.6, 67.7, 83.0, 88.6, 114.5, 115.1, 127.0, 127.4, 128.1, 128.2, 128.3, 129.0, 133.2, 139.3, 139.5; HRMS (EI) m/z calcd for $C_{27}H_{29}NO$ [M + H] 383.2249, found 383.2261.

***N*-Benzyl-3-(3-fluorophenyl)-*N*-methyl-1-phenylprop-2-yn-1-amine (Table 2, entry 16):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.23 (s, 3H), 3.59−3.74 (m, 2H), 4.90 (s, 1H), 6.99 (t, J = 17.26 Hz, 1H), 7.19−7.41 (m, 11H), 7.65 (d, J = 7.43 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.0, 58.9, 59.5, 85.9, 87.5, 115.4, 115.6, 118.5, 118.8, 125.0, 125.1, 127.1, 127.6, 127.7, 127.8, 128.2, 128.3, 128.9, 129.8, 129.9, 138.7, 139.1; HRMS (EI) m/z calcd for $C_{23}H_{20}NF$ [M + H] 329.1580, found 329.1570.

***N*-Benzyl-*N*-methyl-1-phenyl-3-(thiophen-2-yl)prop-2-yn-1-amine (Table 2, entry 17):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.22 (s, 3H), 3.58−3.72 (m, 2H), 4.89 (s, 1H), 7.17−7.45 (m, 11H), 7.66 (d, J = 7.53 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.3, 59.2, 60.0, 83.9, 84.6, 122.4, 125.6, 127.3, 127.8, 128.4, 128.6, 128.9, 129.2, 130.4, 139.2, 139.5; HRMS (EI) m/z calcd for $C_{21}H_{19}NS$ [M + H] = 317.1238, found 317.1244.

***N*-Benzyl-*N*-methyl-1,4-diphenylbut-2-yn-1-amine (Table 2, entry 18):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H), 3.54−3.75 (m, 2H), 3.75 (s, 2H), 4.75 (s, 1H), 7.18−7.42 (m, 13H), 7.64 (d, J = 7.53 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 25.6, 38.3, 59.2, 59.6, 77.8, 86.4, 126.9, 127.3, 127.7, 128.2, 128.4, 128.6, 128.8, 129.3, 137.4, 139.7; HRMS (EI) m/z calcd for $C_{24}H_{23}N$ [M + H] 325.1830, found 325.1834.

***N*-Benzyl-3-cyclohexyl-*N*-methyl-1-phenylprop-2-yn-1-amine (Table 2, entry 19):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35−1.60 (m, 6H), 1.78−1.89 (m, 4H), 2.13 (s, 3H), 2.58 (s, 1H), 3.51−3.64 (m, 2H), 4.68 (s, 1H), 7.21−7.39 (m, 8H), 7.61 (d, J = 7.85 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 24.8, 26.0, 29.2, 33.2, 37.8, 58.8, 59.1, 74.4, 93.2, 126.9, 127.2, 127.9, 128.2, 128.3, 129.0, 139.5, 139.7; HRMS (EI) m/z calcd for $C_{23}H_{27}N$ [M + H] 317.2143, found 317.2129.

***N*-Benzyl-4-cyclopentyl-*N*-methyl-1-phenylbut-2-yn-1-amine (Table 2, entry 20):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36−1.42 (m, 2H), 1.54−1.69 (m, 4H), 1.85 (d, J = 6.78 Hz, 2H), 2.09−2.14 (m, 4H), 2.36 (d, J = 6.70 Hz, 2H), 3.51−3.65 (m, 2H), 4.68 (s, 1H), 7.17−7.39 (m, 8H), 7.62 (d, J = 7.43 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 24.9, 25.7, 32.3, 38.1, 39.6, 59.0, 59.4, 75.0, 88.3, 127.1, 127.4, 128.1, 128.4, 128.5, 129.2, 139.7, 139.9; HRMS (EI) m/z calcd for $C_{23}H_{27}N$ [M + H] 317.2143, found 317.2134.

***N*-Benzyl-*N*-methyl-1-phenyloct-2-yn-1-amine (Table 2, entry 21):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 13.56 Hz, 3H), 1.31−1.52 (m, 4H), 1.57−1.64 (m, 2H), 2.14 (s, 3H), 2.35 (t, J = 13.56 Hz, 2H), 3.51−3.65 (m, 2H), 4.67 (s, 1H), 7.19−7.39 (m, 8H), 7.62 (d, J = 7.54 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.3, 19.0, 22.4, 29.1, 31.3, 38.0, 59.0, 59.4, 75.0, 89.0, 127.1, 127.4, 128.1, 128.4, 128.5, 129.1, 139.7, 139.9; HRMS (EI) m/z calcd for $C_{22}H_{27}N$ [M + H] 305.2143, found 305.2125.

***N*-Benzyl-*N*-methyl-1-phenylpent-1-yn-3-amine (Table 2, entry 22):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (t, J = 14.88 Hz, 3H), 1.71−1.80 (m, 2H), 2.27 (s, 3H), 3.46−3.56 (m, 2H), 3.73 (d, J = 13.77 Hz, 1H), 7.22−7.38 (m, 8H), 7.45−7.48 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 11.3, 27.1, 37.8, 57.8, 59.2, 85.8, 87.4, 123.5, 126.9,

127.8, 128.2, 129.0, 131.8, 139.4; HRMS (EI) m/z calcd for $C_{19}H_{21}N$ [M + H] 263.1674, found 263.1671.

***N*-Benzyl-*N*,5-dimethyl-1-phenylhex-1-yn-3-amine (Table 2, entry 23):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88−0.92 (m, 6H), 1.50−1.71 (m, 2H), 1.85−1.98 (m, 1H), 2.26 (s, 3H), 3.53 (d, J = 12.98 Hz, 1H), 3.65−3.74 (m, 2H), 7.20−7.47 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.3, 19.0, 22.4, 29.1, 31.3, 38.0, 59.0, 59.4, 75.0, 89.0, 127.1, 127.4, 128.1, 128.4, 128.5, 129.1, 139.7, 139.9; HRMS (EI) m/z calcd for $C_{21}H_{25}N$ [M + H] 291.1987, found 291.1970.

***N*-Benzyl-*N*-methyl-1-phenylnon-1-yn-3-amine (Table 2, entry 24):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (s, 2H), 1.28 (s, 6H), 1.48 (s, 2H), 1.72 (s, 2H), 2.27 (s, 3H), 3.53 (d, J = 13.56 Hz, 1H), 3.56 (s, 1H), 3.72 (d, J = 13.56 Hz, 1H), 7.27−7.45 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.2, 22.8, 26.6, 29.1, 31.9, 34.1, 37.9, 56.1, 59.4, 85.9, 87.8, 123.7, 127.0, 127.9, 128.3, 129.1, 131.9, 139.6; HRMS (EI) m/z calcd for $C_{23}H_{29}N$ [M + H] 319.2300, found 319.2320.

***N*-Benzyl-*N*-methyl-1,4-diphenylbut-3-yn-2-amine (Table 2, entry 25):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.00−3.04 (m, 2H), 3.57 (d, J = 13.17 Hz, 1H), 3.73−3.86 (m, 2H), 7.21 (s, 13H), 7.41 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.1, 40.6, 58.1, 59.6, 87.0, 123.6, 126,6, 127.2, 128.2, 128.4, 128.5, 129.1, 129.7, 132.0, 138.9, 139.4; HRMS (EI) m/z calcd for $C_{24}H_{23}N$ [M + H] 325.1830, found 325.1820.

***N*-Benzyl-1-(furan-2-yl)-*N*-methyl-3-phenylprop-2-yn-1-amine (Table 2, entry 26):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.60 (d, J = 12.14 Hz, 1H), 3.73 (d, J = 12.14 Hz, 1H), 4.95 (s, 1H), 6.31 (s, 1H), 6.49 (s, 1H), 7.22−7.40 (m, 9H), 7.51 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.3, 54.1, 58.4, 83.1, 86.7, 109.2, 110.0, 122.8, 127.1, 128.3, 129.0, 131.9, 138.7, 142.6; HRMS (EI) m/z calcd for $C_{21}H_{19}NO$ [M + H] 301.1467, found 301.1461.

***N*-Benzyl-*N*-methyl-3-phenyl-1-(thiophen-2-yl)prop-2-yn-1-amine (Table 2, entry 27):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.57 (d, J = 13.17 Hz, 1H), 3.78 (d, J = 13.17 Hz, 1H), 5.06 (s, 1H), 6.93 (s, 1H), 7.25−7.53 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 38.6, 56.3, 58.4, 84.5, 87.6, 123.1, 125,7, 126.1, 126.4, 127.3, 128.5, 129.0, 132.1, 139.2, 144.6; HRMS (EI) m/z calcd for $C_{21}H_{19}NS$ [M + H] 317.1238, found 317.1242.

■ 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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■ ACKNOWLEDGMENT

The authors wish to thank the FWO (Fund for Scientific Research-Flanders (Belgium)) and the Research Fund of the University of Leuven for financial support to the laboratory. D.S.E. is grateful to the FWO for obtaining a postdoc fellowship. H.F. thanks the China Scholarship Council for financial support.

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