Zinc(II)-catalyzed synthesis of propargylamines by coupling aldimines and ketimines with alkynes

Zinc(II)-catalyzed synthesis of propargyl amines by coupling of aldimines and ketimines with alkynes

Syeda Aaliya Shehzadi,[a] Aamer Saeed,[b] Filip Lemière,[c] Bert U. W. Maes,[a] and Kourosch Abbaspour Tehrani*[a]

Dedication ((optional))

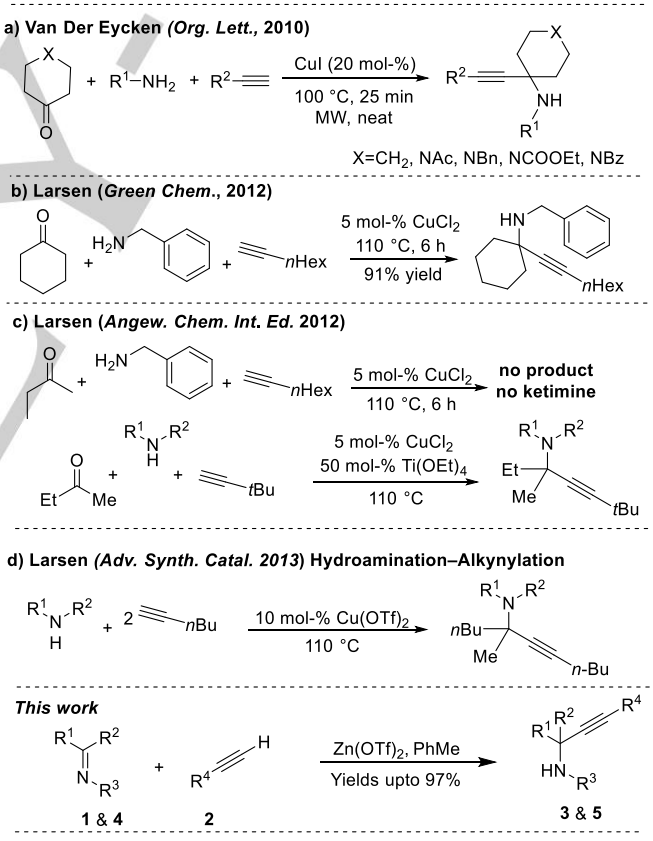
Abstract: A Zn(II) triflate-promoted reaction of aldimines or ketimines, derived from unactivated aldehydes or ketones and primary amines or α-amino acid esters, with terminal alkynes, leading to a rapid and efficient formation of tri- (from aldimines) and tetra- (from ketimines) substituted propargyl amines in good to excellent yields has been described. No additives or extra Lewis acid reagents are required for the ketimine-alkyne coupling.

Introduction

The synthesis of tri- and tetra- substituted propargyl amines has been widely investigated not only due to their intrinsic biological and pharmacological activities[1-4] but also due to their utility as chemical building blocks, in particular for the synthesis of nitrogen containing compounds such as allylamines, pyrrolidines, oxazoles and pyrroles.[5]

The most straightforward approach to synthesize propargyl amines is the condensation of Alkynes, Amines and Aldehydes (A^3) under catalytic conditions.[6] Other traditional methods involve the amination of propargylic triflates, propargylic phosphates, propargylic esters, oxyphosphonium salts and propargylic halides.[7] Still, convenient and more efficient methods to construct propargylic amines by direct coupling reactions, including acyclic aliphatic amines and alkynes, are extremely attractive. By extension, tetra-substituted propargyl amines can be derived from ketones, amines and alkynes under similar conditions as developed for aldehydes. Due to the lower reactivity of ketones (750 times less reactive then aldehydes)[8] the three-component coupling of Ketones, Amines and Alkynes (KA^2) has still been largely underdeveloped. Some special classes of more reactive ketones, like cyclohexanones can react under A^3-conditions and can be converted into the corresponding tetra-substituted propargyl amine.[9-11]

Ketimines are in general less reactive towards nucleophilic additions than aldimines owing to steric hindrance in the C-C bond-forming step, as well due to electronic effects. In order to circumvent this unreactivity in alkyne coupling reactions, some approaches, eventually enantioselective, make use of more reactive, ketiminium species by using secondary amines.[10, 12-13] Lewis acid activation of a *N*-thiophosphinoyl ketimine by Cu(I)[14] or Lewis acid activation of in situ generated imines by a $Ti(OEt)_4/CuCl_2$ couple also have been used (Scheme 1).[13,15] The introduction of electron withdrawing N-substituents such as thiophosphinoyl[14] and *p*-toluenesulfonyl[11] groups also enhance the reactivity of the corresponding ketimines towards catalytic alkyne addition.



Scheme 1. Previous approaches for tetra-substituted propargyl amines.

An alternative approach to tetrasubstituted propargyl amines involves $Cu(OTf)_2$[16a,b] or Zn(II)[16c] catalysed hydroamination of alkynes, leading to a ketiminium species, which finally undergoes alkynylation.[17] Recently, advances were made in the synthesis of propargyl amines using heterogeneous catalysts such as SiO_2@Cu monodispersed Cu-nanoparticles,[18]

[a] S. A. Shehzadi, B. U. W. Maes, K. Abbaspour Tehrani*
Organic Synthesis, Department of Chemistry, University of Antwerp, Groenenborgerlaan 171, B-2020, Antwerp, Belgium
E-mail: kourosch.abbaspourtehrani@uantwerpen.be
https://www.uantwerpen.be/en/rg/orsy/
[b] A. Saeed
Department of Chemistry, Quaid-I-Azam University, Islamabad 45320 Pakistan
[c] F. Lemière
Biomolecular & Analytical Mass Spectrometry and Center for Proteomics, Department of Chemistry, University of Antwerp, B-2020 Antwerp, Belgium

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

Cu(I)-N_2S_2-salen type complex covalently anchored onto MCM-41 silica, bis[2-(phenylthio)benzylidene]-1,2-ethylenediamine copper(I) complexes, $[Cu(N_2S_2)]X$-Y (X = CN, Cl, Br, I),[19] mesoporous two-dimensional copper silicate catalyst (CuSBA-15)[20] and $CuFe_2O_4$ nanoparticles.[21] The majority of these methods are limited to aromatic aldehydes and cyclic amines. Between this variety of metal acetylides, Cu-acetylide and Zn-acetylide are more nucleophilic.[22] Zinc acetylides have been found to be even more reactive then their Cu counterparts when reacted with nitrones as already investigated by Carreira.[23] Zinc triflate also has been applied in some special cases like for the addition of cyclopropylacetylene to reactive cyclic trifluoromethylated *N*-acyl imines.[24] Keeping in mind the lower reactivity of ketimines as compared to aldimines there is hence the need to increase the nucleophilicity of the attacking alkyne nucleophile. So far, to the best of our knowledge, no example of a Zn-catalyzed alkynylation of N-alkyl aldimines and ketimines has been reported. Therefore, important challenges remain and room for improvement exists. In the present study we focused on the reaction between *N*-alkyl aldimines and ketimines with alkynes in the presence of catalytic amounts of zinc salts.

Results and Discussion

As a starting point, the sterically hindered pivaldehyde, *n*-propylamine (an aliphatic primary amine) and phenylacetylene were reacted under one pot conditions in the presence of 10 mol-% of $Zn(OTf)_2$ and molecular sieves in toluene. Besides 10% conversion to the desired propargyl amine **3aa**, also traces of aldimine **1a** and propargylic alcohol, which has been reported by aldehyde-alkyne coupling in the presence of stoechiometric $Zn(OTf)_2$[25] were observed in the ^{1}H NMR. Problably the Zn salt is acting here as a Lewis acid catalysing the imine formation, hence rendering it unavailable for acetylide generation. Forced by this result further studies were continued using the preformed imine of pivaldehyde namely, 2,2-dimethyl-*N*-propylpropan-1-imine (**1a**). The reaction of **1a** with 1 equiv of phenylacetylene **2a** in the presence of 25 mol-% of $Zn(OTf)_2$ delivered the propargyl amine **3aa** in 72% yield (Table 1, entry 1). Other zinc salts, like $ZnCl_2$, $ZnBr_2$, ZnI_2 and $Zn(OAc)_2$ as catalyst all proved less active than $Zn(OTf)_2$ (Table 1, entries 2-6).

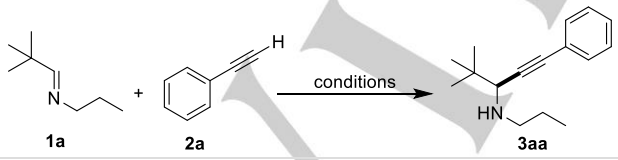


Table 1. Optimization of catalyst and reaction conditions for aldimine-alkyne coupling.

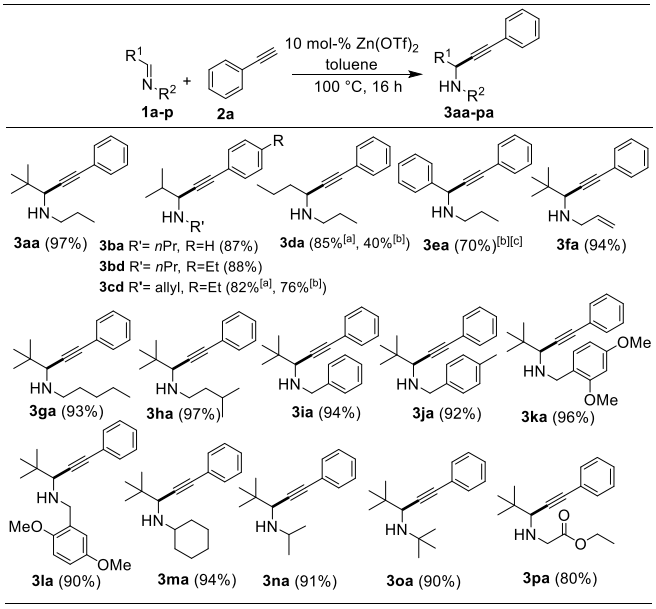
Entry[a]	Catalyst (mol-%)	*T*/*t* (°C/h)	Solvent	Yield of **3**[b] (%)
1	$Zn(OTf)_2$ (25)	100/10	PhMe	72
2	$ZnCl_2$ (25)	100/24	PhMe	78
3	$ZnCl_2$ (50)	50/24	CH_2Cl_2	55[f]
4	$ZnBr_2$ (25)	100/24	PhMe	51
5	ZnI_2 (25)	100/24	PhMe	43
6	$Zn(OAc)_2$ (25)	100/24	PhMe	NR[d]
7	$In(OTf)_3$ (25)	100/24	PhMe	77[f]
8	$In(OTf)_3$ (50)	50/24	CH_2Cl_2	64
9	$Zn(OTf)_2$ (50)	100/24	PhMe	96
10	$Zn(OTf)_2$ (50)	50/24	CH_2Cl_2	88
11	$Zn(OTf)_2$ (10)	100/16	PhMe	96
12	$CuBr_2$ (10) [c]	100/24	PhMe	92
13	$CuCl_2$ (10) [c]	100/24	PhMe	88
14	CuI_2 (10) [c]	100/10	PhMe	89
15	$Cu(OTf)_2$ (10)	100/24	PhMe	72[e]

[a] All reactions were carried out with 0.5 mmol of imine in 2 mL of solvent. [b] Isolated yields. [c] Under argon. [d] NR = no reaction. [e] Also diphenyl-1,3-butadiyne was formed. [f] 2 equiv of **2a** was used.

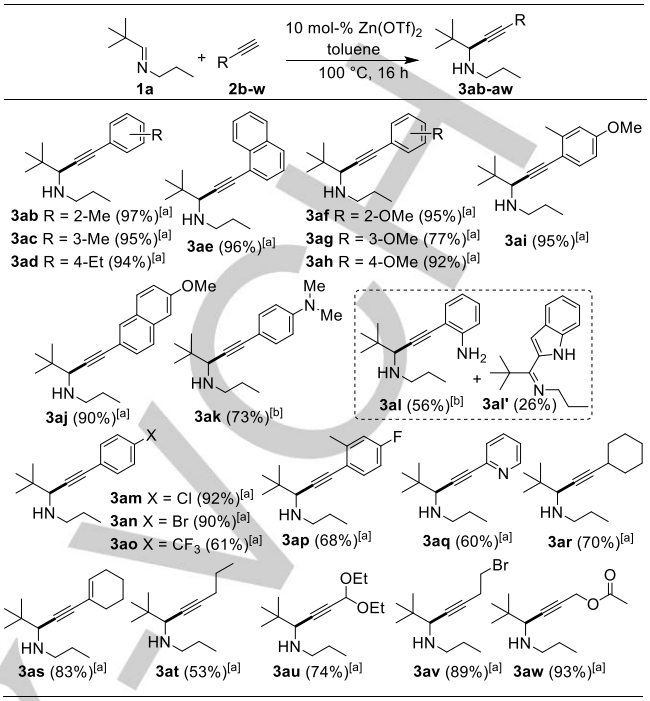
Since $In(OTf)_3$ in CH_2Cl_2 was identified previously by our group as a good catalyst for alkyne coupling of α,α-dichloroaldimines[26], imine **1a** was also reacted with phenylacetylene and 25 mol-% of $In(OTf)_3$ in toluene (Table 1, entry 7). Interestingly this electron rich aldimine gave rise to an isolated yield of 77% of the corresponding propargyl amine. In almost all cases toluene gave superior yields compared to CH_2Cl_2. By increasing the $Zn(OTf)_2$ catalyst amount until 50 mol-% and the reaction time to 24 h at 100 °C, 96% yield of product **3aa** was obtained (Table 1, entry 9). By decreasing the $Zn(OTf)_2$ catalyst to 10 mol-% and using toluene as solvent at 100 °C, no appreciable decrease in yield was noticed (Table 1, entry 11). Below 10 mol-% of $Zn(OTf)_2$ the product yield dropped dramatically (see Table S1). By replacing the air by argon, as required when using copper catalysts (Table 1, entries 12-15), no significant improvement in the yield of **3aa** was observed. In view of the results in Table 1 an optimum yield of 96% of **3aa** was obtained when aldimine **1a** was reacted with **2a** in the presence of 10 mol-% $Zn(OTf)_2$ as catalyst and toluene as solvent at 100 °C for 16 h in a sealed vial. These conditions were applied for further reactions.

With these optimized conditions in hand, the scope of the reaction was explored using a broad range of imines, prepared by condensing aldehydes and primary amines in the presence of anhydrous magnesium sulfate as a drying agent. The imines derived from pivaldehyde, the enolisable isobutyraldehyde and butyraldehyde (Scheme 2, **3ba-3da**) were well tolerated under the developed conditions. In case of benzaldimine some undefined side reactions were observed at 100 °C, while by lowering the temperature to 50 °C for 16 h, starting material was still present. By increasing the reaction temperature to 70 °C for 24 h, using 1.5 equiv of phenylacetylene with 15 mol-% of $Zn(OTf)_2$ catalyst, the desired 1,3-diphenyl-*N*-propylprop-2-yn-1-amine (**3ea**) was obtained in 70% yield.

Further, it was observed that a number of nitrogen substituents on the imine, including propyl, allyl, *n*-pentyl, *iso*-amyl, benzyl and methoxy substituted benzylamines as well as more sterically hindered groups like *iso*-propyl, cyclohexyl, *tert*-butyl and alkoxycarbonylmethyl all gave excellent yields of the secondary propargyl amines **3** (Scheme 2, **3fa-3pa**).



Scheme 2. Scope of the evaluated A^3 reaction: variation of the aldehyde and amine component. [a] Yield after basic work up. [b] Yield after column chromatography on silica gel. [c] 15 mol-% $Zn(OTf)_2$, 1.5 equiv phenylacetylene, 70 °C, 24 h.

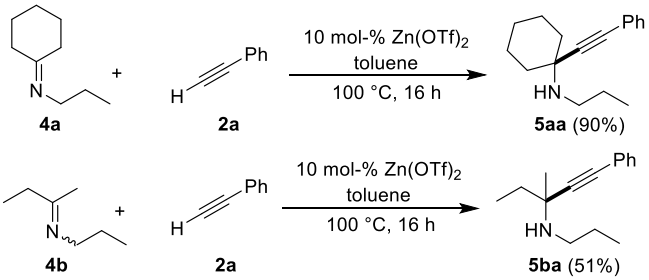


Scheme 3. Scope of the evaluated A^3 reaction: variation of the alkyne component. [a] Yield after basic work up. [b] Yield after column chromatography.

While exploring the substrate scope of alkyne substituents, it was revealed that both aryl and alkyl acetylenes could be used. Aromatic alkynes with a variety of electron-withdrawing and electron-donating substituents were successfully coupled with pivaldimines (Scheme 3). A wide variety of aliphatic alkynes with functional groups, like *tertiary* amines, acetal, ester, halide or even a hetarene in the alkyne moiety were tolerated. Only the reaction of 3- and 4-aminophenylacetylene furnished complex mixtures, while 2-aminophenylacetylene gave propargylamine **3al** in 56% yield together with 26% of an intramolecular hydroamination-oxidation side product **3al'**[27] (Scheme 3).

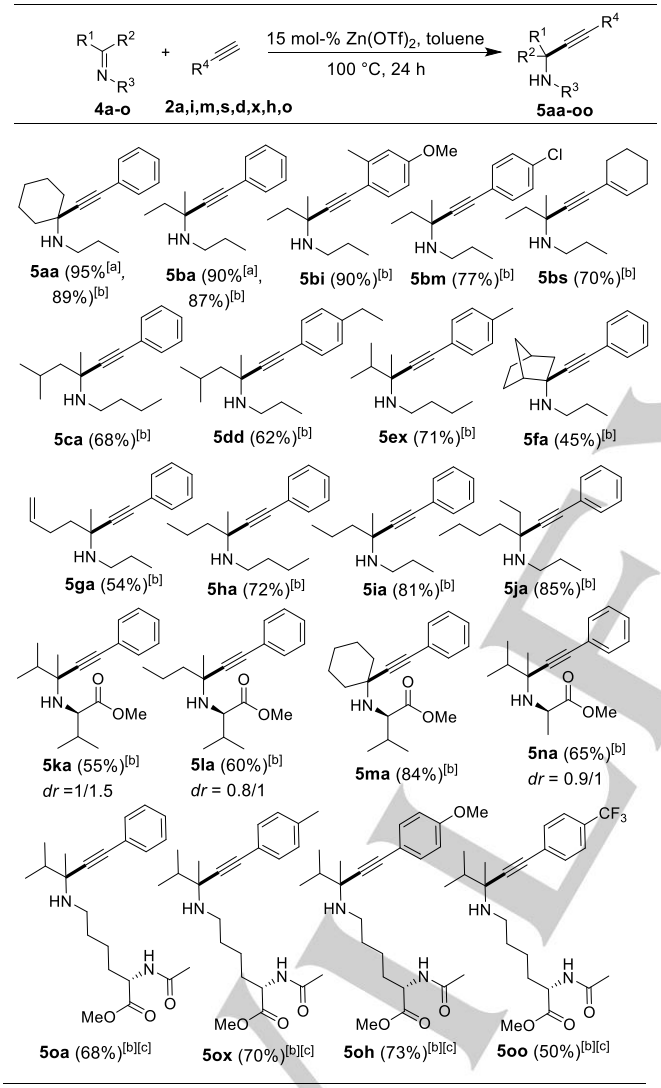
Encouraged by the generality of these results, we turned our efforts towards the more challenging coupling of alkynes with ketimines. As a preliminary experiment, butanone, butylamine and phenylacetylene were reacted in the presence of 50 mol-% $Ti(OEt_4)$ and 5 mol % $CuCl_2$ in toluene at 110 °C for 24 h, according to the recent literature.[15] Since no reaction was observed, the catalytic system was changed to 15 mol-% $Zn(OTf)_2$, which besides some traces of imine and some traces of the corresponding tertiairy propargylic alcohol[28] afforded no product at all. When benzyl amine was reacted with butanone and phenylacetylene in 20 mol-% $Zn(OTf)_2$ in the presence of 4Å MS or $Ti(OiPr)_4$ as drying agent, we were gratified to observe 15-20% conversion to the corresponding propargylic amine. Since imine formation is crucial in this conversion, further optimization was focused on using the ketimines. Ketimines were prepared from ketones and the appropriate primary amine using either activated molecular sieves,[29] concd HCl[30] or $Ti(OiPr)_4$ [31] as water scavengers.

In a first attempt, *N*-propylcyclohexanimine (**4a**) was reacted under the conditions for aldimine coupling. Interestingly, this conversion went smoothly and furnished the corresponding tetrasubstituted propargylamine **5aa** in 90% yield (Scheme 4). Next, the generality of this method was verified by reacting the less reactive *N*-propylbutan-2-imine (**4b**) with **2a** and 10 mol-% of $Zn(OTf)_2$ as a catalyst. Because of the rather low yield of tetrasubstituted propargyl amine **5ba** (51%), (Scheme 4) more catalyst (15 mol-%) and a longer reaction time (24 h) was applied, leading to a 90% yield of **5ba**. The addition of more $Zn(OTf)_2$ or an extra equivalent of alkyne had no noticeable effect on the yield. Finally, the application of 15 mol-% catalyst in toluene at 100 °C for 24 h was selected as the standard condition for the coupling of alkynes with ketimines (**4a-o**) (Scheme 5).



Scheme 4. Cyclic and acyclic ketimine-alkyne coupling.

The substrate scope was then explored, especially focusing on enolizable ketones and primary acyclic amines, those classes being the more difficult and less explored coupling partners. A number of ketones with different chain lengths and functionalized alkynes reacted very well under the developed conditions to deliver propargyl amines with α-amino tertiary carbon in good yields (Scheme 4, **5aa-5ja**). Imines derived from hetarene containing ketones like phenyl(pyridin-2-yl)-methanone (**4q**)[32] and phenyl(pyridin-4-yl)methanone (**4r**)[32] did not react with phenylacetylene, even not when adding 0.5 equiv of $Zn(OTf)_2$.



Scheme 5. $Zn(OTf)_2$-catalyzed reaction between ketimines and alkynes. All reactions were carried out at 0.5 mmol scale of ketimine **4** in a sealed vial for 24 h. [a] Yields after basic workup. [b] Yields after column chromatography on silica gel. [c] *dr* not determined.

Very few examples of coupling reactions of α-amino ester with ketones and alkynes have been reported. The existing method is limited to cyclohexanone and acetone using 20 mol-% of CuBr to deliver trisubstituted propargylamines in moderate to low yield.[33] Since α-amino ester side chains are present in various important drugs and allow to functionalize peptide chains with a range of different functional groups,[34] several ketimines (**4k-o**) derived from natural α-amino acids such as L-valine methyl ester, L-alanine methyl ester and L-lysine methyl ester were prepared (see SI). The reaction of these functionalized ketimines with various alkynes in the presence of 15 mol-% of $Zn(OTf)_2$ all proved feasible, leading to diastereomeric mixtures of secondary propargylic amines bearing a α-tetrasubstituted carbon center (Scheme 5, **5ka-5oo**).

Conclusions

In conclusion, a convenient and operationally simple Zn(II)-catalyzed synthesis of secondary propargyl amines, bearing tri- and tetrasubstituted α-carbons starting from imines and alkynes is demonstrated. A broad range of functional groups (aliphatic and aromatic halides, amines, ester, acetal, MeO, CF_3, alkyl) were well tolerated on the alkyne moiety. Also enolizable and sterically hindered aldimines, enolizable acyclic and cyclic ketimines and ketimines derived from α-amino esters, which traditionally are very difficult reaction partners, were coupled in good to excellent yields.

Experimental Section

General experimental procedure for the aldimine-alkyne coupling
In an oven dried 10 mL vial containing 1 mL of toluene and a stirring bar, the aldimines **1a-p** (0.5 mmol), the acetylene (0.5 mmol, 1 equiv) and $Zn(OTf)_2$ (0.018 g, 0.05 mmol) were added successively and the vial was sealed under air. The reaction mixture was stirred at 100ºC for 16 h. Afterwards the reaction mixture was diluted with CH_2Cl_2 (10 mL) washed and extracted with 0.5 N NaOH (10 mL). The organic phase was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure to get pure product. In almost all cases pure products were obtained unless otherwise stated.

4,4-Dimethyl-1-phenyl-*N*-propylpent-1-yn-3-amine (3aa): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 - 7.40 (m, 2H, $CH_{arom,\ ortho}$), 7.28 - 7.26 (m, 3H, $CH_{arom,\ meta}$ and $CH_{arom,\ para}$), 3.15 (s, 1H, CH), 2.96 - 2.90 (m, 1H, NC(H)H), 2.62 - 2.55 (m, 1H, NC(H)H), 1.59 - 1.45 (m, 2H, NCH_2CH_2), 1.05 (s, 9H, $C(CH_3)_3$), 0.95 (t, J = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6 ($C_{arom,\ ortho}$), 128.2 ($C_{arom,\ meta}$), 127.7 ($C_{arom,\ para}$), 123.8 ($C_{arom,\ quat}$), 91.0 and 84.1 (C≡C), 61.1 (NCH), 50.8 (NCH_2), 35.1 ($C(CH_3)_3$), 26.6 ($C(CH_3)_3$), 23.2 (CH_2CH_3), 11.8 (CH_2CH_3) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{23}N+H]^+$: 230.1903; found 230.1899.

4-Methyl-1-phenyl-*N*-propylpent-1-yn-3-amine (3ba): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.41 (m, 2H, aromatic), 7.30 – 7.26 (m, 3H, aromatic), 3.40 (d, J = 5.3 Hz, 1H, NCH), 2.91 – 2.85 (m, 1H, NC(H)H), 2.65 – 2.59 (m, 1H, NC(H)H), 1.98 - 1.90 (m, 1H, $(CH_3)_2CH$), 1.59 – 1.49 (m, 2H, NCH_2CH_2), 1.06 and 1.05 (2 × d, J = 6.7 Hz, 2 x 3H, $CH(CH_3)_2$), 0.95 (t, J = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.7, 128.2, 127.8, 123.7, 90.1, 84.3, 57.1, 50.0, 32.9, 23.3,

19.9, 17.9, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{21}N+H]^+$: 216.1747; found 216.1743.

1-(4-Ethylphenyl)-4-methyl-*N*-propylpent-1-yn-3-amine (3bd): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.1 Hz, 2H, aromatic), 7.12 (d, *J* = 8.1 Hz, 2H, aromatic), 3.39 (d, *J* = 5.3 Hz, 1H, NCH), 2.89 – 2.84 (m, 1H, NC(H)H)), 2.63 (q, *J* = 7.6 Hz, 2H CH_3CH_2Ph), 2.66 – 2.58 (m, 1H, overlapped signal, NC(H)H)), 1.95 - 1.90 (m, 1H, $(CH_3)_2CH$), 1.60 – 1.48 (m, 2H, NCH_2CH_2), 1.22 (t, *J* = 7.6 Hz, 3H, CH_3CH_2Ph), 1.05 and 1.04 (2 × d, *J* = 6.7 Hz, 2 × 3H, $CH(CH_3)_2$), 0.95 (t, *J* = 7.4 Hz, 3H, $NCH_2CH_2CH_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.2, 131.7, 127.8, 120.8, 89.2, 84.4, 57.1, 50.0, 32.9, 28.8, 23.2, 19.9, 17.8, 15.4, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}N+H]^+$: 244.2060; found 244.2055.

***N*-Allyl-1-(4-ethylphenyl)-4-methylpent-1-yn-3-amine (3cd):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.0 Hz, 2H, aromatic), 7.12 (d, *J* = 8.0 Hz, 2H, aromatic), 5.94 (ddt, *J* = 16.4, 10.3, 6.0 Hz, 1H, CH═CH_2), 5.24 (dd, *J* = 17.2, 1.4 Hz, 1H, CH═C(H)H), 5.11 (d, *J* = 10.2 Hz, 1H, CH═C(H)H), 3.55 (dd, *J* = 13.8, 5.7 Hz, 1H, NC(H)H), 3.42 (d, *J* = 5.3 Hz, 1H, NCH), 3.33 (dd, *J* = 13.8, 6.4 Hz, 1H, N-C(H)H), 2.63 (q, *J* = 7.6 Hz, 2H, CH_2CH_3), 1.96 – 1.89 (m, 1H, $(CH_3)_2CH$)), 1.22 (t, *J* = 7.6 Hz, 3H, CH_2CH_3), 1.06 and 1.05 (2 × d, *J* = 6.7 Hz, 2 × 3H, $(CH_3)_2CH$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.2, 136.8, 131.7, 127.8, 120.8, 116.1, 88.8, 84.7, 56.4, 50.5, 33.0, 28.8, 19.9, 17.9, 15.4 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{23}N+H]^+$: 242.1903; found 242.1900.

1-Phenyl-*N*-propylhex-1-yn-3-amine (3da): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.40 (m, 2H, aromatic), 7.28 – 7.26 (m, 3H, aromatic), 3.58 (dd, *J* = 5.9, 7.7 Hz, 1H, NCH), 2.88 (ddd, *J* = 11.2, 8.3, 6.5 Hz, 1H, NC(H)H), 2.63 (ddd, *J* = 11.2, 8.4, 6.0 Hz, 1H, NC(H)H), 1.70 – 1.64 (m, 2H), 1.57 – 1.50 (m, 4H), 1.26 (br s, 1H, NH), 0.97 (t, *J* = 7.2 Hz, 3H, CH_3), 0.95 (t, *J* = 7.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.7, 128.2, 127.8, 123.6, 91.5, 83.5, 50.6, 49.6, 38.4, 23.3, 19.5, 13.9, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{21}N+H]^+$: 216.1747; found 216.1750.

1,3-Diphenyl-*N*-propylprop-2-yn-1-amine (3ea): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 – 7.57 (m, 2H, aromatic), 7.47 – 7.44 (m, 2H, aromatic), 7.37 – 7.33 (m, 3H, aromatic), 7.29 – 7.25 (m, 3H, aromatic), 4.79 (s, 1H, NCH), 2.80 (ddd, *J* = 11.2, 7.7, 7.2 Hz, 1H, NC(H)H), 2.68 (ddd, *J* = 11.2, 7.8, 6.5 Hz, 1H, NC(H)H), 1.58 – 1.51 (m, 2H, NCH_2CH_2), 0.93 (t, *J* = 7.4 Hz, 3H, CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.7, 131.7, 128.5, 128.2, 128.1, 127.7, 127.6, 123.2, 89.7, 85.3, 54.7, 49.3, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{19}N+H]^+$: 250.1590; found 250.1586.

***N*-Allyl-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3fa):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 - 7.40 (m, 2H, aromatic), 7.28 - 7.26 (m, 3H, aromatic), 5.93 (m, 1H, HC=CH_2), 5.25 (ddd, *J* = 17.2, 3.3, 1.5 Hz, 1H, HC=C(H)H), 5.10 (ddd, *J* = 10.2, 3.0, 1.5 Hz, 1H, HC=C(H)H), 3.59 (ddt, *J* = 14.0, 5.4, 1.5 Hz, 1H, NC(H)H), 3.31 (ddt, *J* = 14.0, 6.5, 1.2 Hz, 1H, NC(H)H), 3.19 (s, 1H, NCH), 1.15 (br s, 1H, NH), 1.06 (s, 9H, $C(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.1, 131.7, 131.6, 128.2, 127.7, 123.7, 116.0, 90.4, 84.5, 60.3, 51.1, 35.0, 26.6 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{21}N+H]^+$: 228.1747; found 228.1746.

4,4-Dimethyl-*N*-pentyl-1-phenylpent-1-yn-3-amine (3ga): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 - 7.40 (m, 2H, aromatic), 7.29 - 7.25 (m, 3H, aromatic), 3.15 (s, 1H, NCH), 2.96 (ddd, *J* = 11.3, 8.2, 6.4 Hz, 1H, NC(H)H), 2.60 (ddd, *J* = 11.3, 8.2, 6.0 Hz, 1H, NCHH), 1.58 – 1.44 (m, 2H, NCH_2CH_2), 1.35 – 1.33 (m, 4H, $CH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.90 (t, *J* = 7.0 Hz, 3H, CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6, 128.2, 127.7, 123.9, 90.9, 84.1, 61.2, 48.9, 35.1, 29.8, 29.6, 26.6, 22.7, 14.1 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{27}N+H]^+$: 258.2216; found 258.2221.

***N*-Isopentyl-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3ha):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.39 (m, 2H, aromatic), 7.26 – 7.25 (m, 3H, aromatic), 3.14 (s, 1H, NCH), 3.00 (ddd, *J* = 11.3, 8.6, 6.2 Hz, 1H, NC(H)H), 2.68 (ddd, *J* = 11.3, 8.6, 6.2 Hz, 1H, NC(H)H), 1.73 – 1.63 (m, 1H, $CH(CH_3)_2$), 1.41 – 1.36 (m, 2H, NCH_2CH_2), 1.05 (s, 9H, $C(CH_3)_3$), 0.92 (d, *J* = 6.7 Hz, 6H, $CH(CH_3)_2$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6, 128.2, 127.6, 123.9, 90.9, 84.2, 61.3, 47.0, 39.2, 35.1, 26.6, 26.2, 22.8, 22.6 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{27}N+H]^+$: 258.2216; found 258.2212.

***N*-Benzyl-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3ia):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.40 (m, 4H, aromatic), 7.34 – 7.23 (m, 6H, aromatic), 4.15 (d, *J* = 13.3 Hz, 1H, NC(H)H), 3.87 (d, *J* = 13.3 Hz, 1H NC(H)H), 3.16 (s, 1H, NCH), 1.33 (broad s, 1H, NH), 1.06 (s, 9H, $C(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.6, 131.7, 128.4, 128.3, 128.3, 127.8, 126.9, 123.8, 90.4, 84.5, 60.2, 52.4, 35.1, 26.6 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{20}H_{23}N+H]^+$: 278.1903; found 278.1909.

4,4-Dimethyl-*N*-(4-methylbenzyl)-1-phenylpent-1-yn-3-amine (3ja): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.41 (m, 2H, Ph), 7.28 (m, 3H + 2H, Ph and *p*-MePh), 7.12 (d, *J* = 7.8 Hz, 2H,), 4.10 (d, *J* = 13.1 Hz, 1H, NC(H)H), 3.82 (d, *J* = 13.1 Hz, 1H, NC(H)H), 3.15 (s, 1H, NCH), 2.32 (s, 3H, $PhCH_3$), 1.29 (br s, 1H, NH), 1.05 (s, 9H, $C(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 136.4, 131.6, 128.9, 128.3, 128.2, 127.7, 123.8, 90.5, 84.5, 60.1, 52.1, 35.1, 26.6, 21.1 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{20}H_{23}N+H]^+$: 292.2060; found 292.2054.

***N*-(2,4-Dimethoxybenzyl)-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3ka):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.41 (m, 2H, aromatic), 7.26 – 7.23 (m, 4H, aromatic) 6.44 – 6.42 (m, 2H, aromatic), 4.10 (d, *J* = 13.4 Hz, 1H, NC(H)H), 3.78 (d, *J* = 13.4 Hz, 1H, NC(H)H), 3.78 and 3.77 (2 × s, 2 × 3H, 2 × OCH_3), 3.15 (s, 1H, NCH), 1.64 (broad s, 1H, NH), 1.04 (s, 9H, $C(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 158.8, 131.6, 130.5, 128.2, 127.6, 124.0, 121.0, 103.8, 98.6, 90.6, 84.3, 60.3, 55.3 (2 carbon), 47.7, 35.0, 26.6 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{22}H_{27}NO_2+H]^+$: 338.2115; found 338.2114.

***N*-(2,5-Dimethoxybenzyl)-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3la):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 – 7.41 (m, 2H, Ph), 7.28 – 7.24 (m, 3H, Ph), 7.01 (d, *J* = 2.8 Hz, 1H, diOMePh), 6.76 (d, *J* = 8.8 Hz, 1H, diOMePh), 6.72 (dd *J* = 8.8, 2.8 Hz, 1H, diOMePh), 4.14 (d, *J* = 13.9 Hz, 1H, NC(H)H), 3.84 (d, *J* = 13.9 Hz, 1H, NC(H)H), 3.76 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.18 (s, 1H, NCH), 1.70 (broad s, 1H, NH), 1.06 (s, 9H, $C(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 152.0, 131.6, 129.9, 128.2, 127.7, 123.9, 116.0, 112.1, 111.4, 90.4, 84.5, 60.5, 56.0, 55.6, 47.9, 35.1, 26.6 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{22}H_{27}NO_2+H]^+$: 338.2115; found 338.2107.

***N*-(4,4-Dimethyl-1-phenylpent-1-yn-3-yl)cyclohexanamine (3ma) :** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 - 7.39 (m, 2H, aromatic), 7.28 - 7.26 (m, 3H, aromatic), 3.23 (s, 1H, C≡CCH), 2.75 (tt, *J* = 9.8, 3.7 Hz, 1H, CH-*Cy*), 1.77 – 1.58 (m, 6H, *Cy*), 1.35 – 1.18 (m, 4H, *Cy*), 1.04 (s, 9H, $C(CH_3)_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6, 128.2, 127.6, 124.0, 91.6, 83.5, 57.9, 55.0, 35.0, 34.7, 32.5, 26.6, 26.3, 25.1, 24.6 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{19}H_{27}N+H]^+$: 270.2216; found 270.2235.

***N*-Isopropyl-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3na):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.39 (m, 2H, aromatic), 7.28 – 7.26 (m, 3H, aromatic), 3.19 (s, 1H, C≡CCH), 3.13 (septet, *J* = 6.20 Hz, 1H, $CH(CH_3)_2$), 1.12 (d, *J* = 6.3 Hz, 3H, $CH(CH_3)CH_3$), 1.04 (s, 9H, $C(CH_3)_3$), 1.01 (d, *J* =

6.1 Hz, 3H, $CH(CH_3)CH_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6, 128.2, 127.6, 123.9, 91.3, 83.7, 58.4, 46.9, 34.9, 26.6, 24.4, 21.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{23}N+H]^+$: 230.1903; found 230.1904.

***N*-(*tert*-Butyl)-4,4-dimethyl-1-phenylpent-1-yn-3-amine (3oa):** ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38 – 7.36 (m, 2H, aromatic), 7.27 – 7.24 (m, 3H, aromatic), 3.13 (s, 1H, C≡CCH), 1.16 (s, 9H, $C(CH_3)_3$), 1.02 (s, 9H, $C(CH_3)_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.1, 128.0, 127.3, 124.0, 94.0, 83.0, 54.0, 50.7, 35.3, 29.8, 26.2 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}N+H]^+$: 244.2060; found 244.2071.

Ethyl (4,4-dimethyl-1-phenylpent-1-yn-3-yl)glycinate (3pa): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34 – 7.31 (m, 2H, aromatic), 7.20 – 7.18 (m, 3H, aromatic), 4.09 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 3.59 (d, *J* = 17.2 Hz, 1H, $NCHHCO_2$), 3.48 (d, *J* = 17.2 Hz, 1H, $NCHHCO_2$), 3.23 (s, 1H, $CH(CH_3)_3$), 1.70 (br s, 1H, NH), 1.17 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 1.01 (s, 9H, $CH(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4 (C=O), 130.6, 127.2, 126.9, 122.4, 88.0 (C≡C), 84.1 (C≡C), 59.8, 59.6, 48.6, 34.1, 25.5, 13.2 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{23}NO_2+H]^+$: 274.1802; found 274.1815.

4,4-Dimethyl-*N*-propyl-1-(*o*-tolyl)pent-1-yn-3-amine (3ab): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 7.4 Hz, 1H, aromatic), 7.17 – 7.07 (m, 3H, aromatic), 3.19 (s, 1H, NCH), 2.95 (ddd, *J* = 11.3, 7.9, 6.6, 1H, NC(H)H), 2.61 (ddd, *J* = 11.3, 8.0, 6.0, 1H, NC(H)H), 2.43 (s, 3H, $PhCH_3$), 1.61 – 1.45 (m, 2H, NCH_2CH_2), 1.07 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.8, 132.0, 129.3, 127.7, 125.5, 123.7, 94.9, 83.0, 61.3, 50.8, 35.0, 26.6, 23.2, 20.9, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}N+H]^+$: 244.2060; found 244.2059.

4,4-Dimethyl-*N*-propyl-1-(*m*-tolyl)pent-1-yn-3-amine (3ac): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24 - 7.20 (m, 2H, aromatic), 7.15 (t, *J* = 7.5 Hz, 1H, aromatic), 7.06 (d, *J* = 7.6 Hz, 1H, aromatic), 3.13 (s, 1H, NCH), 2.93 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.58 (ddd, *J* = 11.3, 8.0, 6.1 Hz, 1H, NC(H)H), 2.30 (s, 3H, $PhCH_3$), 1.60 – 1.44 (m, 2H, $NCH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 132.2, 128.7, 128.5, 128.1, 123.7, 90.5, 84.2, 61.1, 50.8, 35.1, 26.6, 23.2, 21.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}N+H]^+$: 244.2060; found 244.2061.

1-(4-Ethylphenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3ad): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.1 Hz, 2H, aromatic), 7.11 (d, *J* = 8.1 Hz, 2H, aromatic), 3.14 (s, 1H, NCH), 2.93 (ddd, *J* = 11.3, 8.0, 6.6, 1H, NC(H)H), 2.61 – 2.55 (m, 1H, NC(H)H), 2.62 (q overlapping, *J* = 7.4 Hz, $PhCH_2CH_3$), 1.60 – 1.44 (m, 2H, $NCH_2CH_2CH_3$), 1.21 (t, *J* = 7.6 Hz, 3H, $NCH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.94 (t, *J* = 7.4 Hz, 3H, $PhCH_2CH_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.0, 131.6, 127.8, 121.1, 90.1, 84.2, 61.1, 50.8, 35.1, 28.8, 26.6, 23.2, 15.4, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{27}N+H]^+$: 258.2276; found 258.2222.

4,4-Dimethyl-1-(naphthalen-1-yl)-*N*-propylpent-1-yn-3-amine (3ae): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 8.3 Hz, 1H, aromatic), 7.79 (d, *J* = 8.0 Hz, 1H, aromatic), 7.73 (d, *J* = 7.3 Hz, 1H, aromatic), 7.64 (d, *J* = 7.0 Hz, 1H, aromatic), 7.53 (dt, *J* = 7.0 Hz, 1.3 Hz, 1H, aromatic), 7.46 (dt, *J* = 7.3 Hz, 1.3 Hz, 1H, aromatic), 7.36 (t, *J* = 7.1 Hz, 1H, aromatic), 3.30 (s, 1H, C≡CCH), 3.07 – 3.03 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.68 (ddd, *J* = 11.3, 8.0, 6.0 Hz, 1H, NC(H)H), 1.64 – 1.49 (m, 2H, $NCH_2CH_2CH_3$), 1.14 (s, 9H, $C(CH_3)_3$), 0.97 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.4, 133.2, 130.3, 128.2, 128.1, 126.5, 126.2, 125.2, 121.5, 96.0, 82.2, 61.4, 50.8, 35.2, 26.7, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{20}H_{25}N+H]^+$: 280.2060; found 280.2066.

1-(2-Methoxyphenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3af): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37 (dd, *J* = 7.4 Hz, 1.5 Hz, 1H, aromatic), 7.22 (dt, *J* = 8.0 Hz, 1.6 Hz, 1H, aromatic), 6.88 – 6.82 (m, 2H, aromatic), 3.83 (s, 3H, OCH_3), 3.19 (s, 1H, C≡CCH), 2.97 (ddd, *J* = 11.3, 8.1, 6.5 Hz, 1H, NC(H)H), 2.61 (ddd, *J* = 11.3, 8.2, 6.0 Hz, 1H, NC(H)H), 1.61 – 1.45 (m, 2H, $NCH_2CH_2CH_3$), 1.07 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 133.3, 129.0, 120.3, 113.2, 110.8, 95.2, 80.2, 61.3, 55.7, 50.7, 35.1, 26.6, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}NO+H]^+$: 260.2009; found 260.2004.

1-(3-Methoxyphenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3ag): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (t, *J* = 7.9 Hz, 1H, aromatic), 7.01 (d, *J* = 7.6 Hz, 1H, aromatic), 6.94 (t, *J* = 2.3 Hz, 1H, aromatic), 6.82 (dd, *J* = 8.3 Hz, 2.6 Hz, 1H, aromatic), 3.77 (s, 3H, OCH_3), 3.14 (s, 1H, C≡CCH), 2.93 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.58 (ddd, *J* = 11.3, 8.0, 6.1 Hz, 1H, NC(H)H), 1.60 – 1.45 (m, 2H, $NCH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 129.2, 124.9, 124.2, 116.7, 114.1, 90.8, 84.0, 61.1, 55.2, 50.8, 35.1, 26.6, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}NO+H]^+$: 260.2009; found 260.2002.

1-(4-Methoxyphenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3ah): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.8 Hz, 2H, aromatic), 6.81 (d, *J* = 8.8 Hz, 2H, aromatic), 3.77 (s, 3H, OCH_3), 3.13 (s, 1H, C≡CCH), 2.92 (ddd, *J* = 11.3, 8.0, 6.5 Hz, 1H, NC(H)H), 2.57 (ddd, *J* = 11.3, 8.1, 6.0 Hz, 1H, NC(H)H), 1.58 – 1.46 (m, 2H, $NCH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.94 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 132.9, 116.0, 113.9, 89.3, 83.8, 61.1, 55.2, 50.8, 35.1, 26.6, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}NO+H]^+$: 260.2009; found 260.2006.

1-(4-Methoxy-2-methylphenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3ai): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 8.5 Hz, 1H, aromatic), 6.72 (d, *J* = 2.5 Hz, 1H, aromatic), 6.65 (dd, *J* = 8.5 Hz, *J* = 2.5 Hz, 1H, aromatic), 3.76 (s, 3H, OCH_3), 3.17 (s, 1H, C≡CCH), 2.94 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.60 (ddd, *J* = 11.4, 8.1, 6.0 Hz, 1H, NC(H)H), 2.41 (s, 3H, $PhCH_3$), 1.60 – 1.45 (m, 2H, $NCH_2CH_2CH_3$), 1.06 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 141.5, 133.2, 116.0, 115.0, 111.1, 93.2, 82.8, 61.3, 55.2, 50.8, 35.0, 26.6, 23.2, 21.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{28}NO+H]^+$: 275.2244; found 275.2240.

1-(6-Methoxynaphthalen-2-yl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3aj): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (s, 1H, aromatic), 7.62 (t, *J* = 9.4 Hz, 2H, aromatic), 7.43 (dd, *J* = 8.4 Hz, 1.4 Hz, 1H, aromatic), 7.11 (dd, *J* = 8.9 Hz, 2.5 Hz, 1H, aromatic), 7.04 (d, *J* = 2.4 Hz, 1H, aromatic), 3.85 (s, 3H, OCH_3), 3.18 (s, 1H, C≡CCH), 2.97 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.61 (ddd, *J* = 11.4, 8.0, 6.1 Hz,, 1H, NC(H)H), 1.60 – 1.48 (m, 2H, $NCH_2CH_2CH_3$), 1.09 (s, 9H, $C(CH_3)_3$), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 133.8, 130.9, 129.3, 129.1, 128.5, 126.6, 119.2, 118.7, 105.8, 90.5, 84.5, 61.2, 55.2, 50.8, 35.1, 26.6, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{21}H_{27}NO+H]^+$: 310.2171; found 310.2168.

4-(4,4-Dimethyl-3-(propylamino)pent-1-yn-1-yl)-*N*,*N*-dimethylaniline (3ak): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.9 Hz, 2H, aromatic), 6.61 (d, *J* = 8.9 Hz, 2H, aromatic), 3.13 (s, 1H, C≡CCH), 2.96 – 2.90 (m overlap, 1H, NC(H)H), 2.93 (s overlap, 6H, $N(CH_3)_2$), 2.58 (ddd, *J* = 11.4, 8.2, 6.0 Hz, 1H, NC(H)H), 1.58 – 1.46 (m, 2H, $NCH_2CH_2CH_3$), 1.04 (s, 9H,

$C(CH_3)_3$), 0.94 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 149.8, 132.6, 112.0, 111.0, 88.2, 84.7, 61.2, 50.8, 40.3, 35.1, 26.6, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{28}N_2+H]^+$: 273.2325; found 273.2320.

2-(4,4-Dimethyl-3-(propylamino)pent-1-yn-1-yl)aniline (3al): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.26 (dd, *J* = 7.7, 1.2 Hz, 1H, aromatic), 7.09 (dt, *J* = 7.7 Hz, 1.5 Hz, 1H, aromatic), 6.70 – 6.65 (m, 2H, aromatic), 4.16 (broad s, 2H, NH_2), 3.21 (s, 1H, C≡CCH), 2.93 (ddd, *J* = 11.3, 8.0, 6.6 Hz, 1H, NC(H)H), 2.60 (ddd, *J* = 11.3, 8.0, 6.0 Hz, 1H, NC(H)H), 1.60 – 1.48 (m, 2H, $NCH_2CH_2CH_3$), 1.07 (s, 9H, $C(CH_3)_3$), 0.94 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 147.6, 132.2, 129.1, 117.9, 114.2, 108.7, 96.1, 80.7, 61.4, 50.8, 35.0, 26.7, 23.1, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{24}N_2+H]^+$: 245.2012; found 245.2018.

1-(1*H*-Indol-2-yl)-2,2-dimethyl-*N*-propylpropan-1-imine (3al'): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.96 (d, *J* = 9.0 Hz, 1H, CH-4), 7.66 (d, *J* = 8.5Hz, 1H, CH-7), 7.57 (t, *J* = 7.2 Hz, 1H, CH-6), 7.35 (t, *J* = 8.1 Hz, 1H, CH-5), 6.55 (s, 1H, CH-3), 4.82 (broad s, 1H, NH), 3.32 – 3.27 (m, 2H, NCH_2), 1.85 – 1.75 (m, 2H, NCH_2CH_2), 1.45 (s, 9H, $C(CH_3)_3$), 1.09 (t, *J* = 7.4 Hz, 3H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 170.0 (C=N), 149.6 (C-2), 147.9 (C-7a), 128.6 (CH-4 and CH-6), 123.9 (CH-5), 118.8 (CH-7), 117.4 (C-3a), 95.4 (CH-3), 45.0 (NCH_2), 38.0 ($C(CH_3)_3$), 30.3 ($C(CH_3)_3$), 22.4 (CH_2CH_3), 11.9 (CH_3) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{22}N_2+H]^+$: 243.1861; found 243.1862.

1-(4-Chlorophenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3am): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.33 (d, *J* = 8.5 Hz, 2H, aromatic), 7.24 (d, *J* = 8.5 Hz, 2H, aromatic), 3.13 (s, 1H, C≡CCH), 2.91 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.57 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 1.58 – 1.44 (m, 2H, $NCH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 133.6, 132.8, 128.5, 122.3, 92.0, 83.1, 61.1, 50.8, 35.1, 26.6, 23.2, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{22}NCl+H]^+$: 264.1514; found 264.1517.

1-(4-Bromophenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3an): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.40 (d, *J* = 8.5 Hz, 2H, aromatic), 7.26 (d, *J* = 8.5 Hz, 2H, aromatic), 3.13 (s, 1H, C≡CCH), 2.91 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.56 (ddd, *J* = 11.3, 8.0, 6.1 Hz, 1H, NC(H)H), 1.59 – 1.44 (m, 2H, $NCH_2CH_2CH_3$), 1.04 (s, 9H, $C(CH_3)_3$), 0.94 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 133.5, 133.1, 131.4, 121.8, 92.2, 83.1, 61.1, 50.7, 35.1, 26.6, 23.1, 11.8. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{22}NBr+H]^+$: 308.1008; found 308.1006.

4,4-Dimethyl-*N*-propyl-1-(4-(trifluoromethyl)phenyl)pent-1-yn-3-amine (3ao): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.54 (d, *J* = 8.5 Hz, 2H, aromatic), 7.50 (d, *J* = 8.5 Hz, 2H, aromatic), 3.17 (s, 1H, C≡CCH), 2.93 (ddd, *J* = 11.3, 7.8, 6.7 Hz, 1H, NC(H)H), 2.59 (ddd, *J* = 11.4, 7.9, 6.1 Hz, 1H, N-CHH), 1.59 – 1.48 (m, 2H, $NCH_2CH_2CH_3$), 1.06 (s, 9H, $C(CH_3)_3$), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 131.9, 129.6 (q, *J* = 32.6 Hz), 127.7 (q, *J* = 1.2 Hz), 125.2 (q, *J* = 3.8 Hz), 124.1 (q, $^1J_{C\text{-}F}$ = 272.0 Hz, CF_3), 93.9, 83.1, 61.2, 50.9, 35.2, 26.6, 23.2, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{22}NF_3+H]^+$: 298.1766; found 298.1776.

1-(4-Fluoro-3-methylphenyl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3ap): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.24 (d, *J* = 7.3 Hz, 1H, aromatic), 7.22– 7.17 (m, 1H, aromatic), 6.90 (t, 1H, *J* = 8.9 Hz, aromatic), 3.12 (s, 1H, C≡CCH), 2.92 (ddd, *J* = 11.3, 7.9, 6.6 Hz, 1H, NC(H)H), 2.57 (ddd, *J* = 11.4, 8.0, 6.1 Hz, 1H, NC(H)H), 2.23 (d, *J* = 1.7 Hz, 3H, $PhCH_3$), 1.58 – 1.46 (m, 2H, $NCH_2CH_2CH_3$), 1.05 (s, 9H, $C(CH_3)_3$), 0.95 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 160.9 (d, $^1J_{C\text{-}F}$ = 247.2 Hz, CF), 134.7 (d, *J* = 5.3 Hz), 130.7 (d, *J* = 8.2 Hz), 125.0 (d, *J* = 18.0 Hz), 119.5 (d, *J* = 3.8 Hz) , 115.0 (d, *J* = 23.0 Hz), 90.1 (d, *J* = 1.2 Hz), 83.3, 61.1, 50.8, 35.1, 26.6, 23.2, 14.3 (d, *J* = 3.5 Hz), 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{24}NF+H]^+$: 262.1966; found 262.1986.

4,4-Dimethyl-*N*-propyl-1-(pyridin-2-yl)pent-1-yn-3-amine (3aq): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 8.56 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H, aromatic), 7.61 (dt, *J* = 7.7 Hz, 1.8 Hz, 1H, aromatic), 7.40 (td, *J* = 7.8 Hz, 0.9 Hz, 1H, aromatic), 7.19 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H, aromatic), 3.18 (s, 1H, C≡CCH), 2.96 (ddd, *J* = 11.4, 8.0, 6.5 Hz, 1H, NC(H)H), 2.58 (ddd, *J* = 11.4, 8.1, 6.1 Hz, 1H, NC(H)H), 1.54 – 1.45 (m, 2H, $NCH_2CH_2CH_3$), 1.38 (br s, 1H, NH), 1.07 (s, 9H, $C(CH_3)_3$), 0.94 (t, *J* = 7.4 Hz, 3H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 149.9, 143.8, 136.0, 127.1, 122.4, 91.4, 83.9, 61.0, 50.8, 35.2, 26.6, 23.2, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{22}N_2+H]^+$: 231.1856; found 231.1852.

1-Cyclohexyl-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3ar): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 2.91 (d, *J* = 1.8 Hz, 1H, NCH), 2.84 (ddd, *J* = 11.3, 8.1, 6.6 Hz, 1H, NC(H)H), 2.50 (ddd, *J* = 11.3, 8.1, 6.0 Hz, 1H, NC(H)H), 2.43 – 2.39 (m, 1H, $CHCH_2$), 1.79 – 1.67 (m, 4H, *Cy*), 1.52 – 1.42 (m, 6H, *Cy*), 1.44 – 1.28 (m, 2H, $NCH_2CH_2CH_3$), 0.97 (s, 9H, $C(CH_3)_3$), 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 88.2, 80.8, 60.6, 50.7, 34.8, 33.13, 33.09, 29.1, 26.5, 26.1, 24.8, 23.1, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{29}N+H]^+$: 236.2373; found 236.2370.

1-(Cyclohex-1-en-1-yl)-4,4-dimethyl-*N*-propylpent-1-yn-3-amine (3as): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 6.05 – 6.03 (m, 1H ,C=CH), 3.03 (s, 1H, C≡CCH), 2.85 (ddd, *J* = 11.3, 8.0, 6.6 Hz, 1H, NC(H)H), 2.51 (ddd, *J* = 11.3, 8.1, 6.0 Hz, 1H, NC(H)H), 2.13 – 2.08 (m, 4H), 1.67 – 1.42 (m, 6H), 0.99 (s, 9H, $C(CH_3)_3$), 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 133.3, 121.0, 87.9, 85.9, 61.0, 50.7, 35.0, 29.7, 26.6, 25.6, 23.2, 22.4, 21.7, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{27}N+H]^+$: 234.2216; found 234.2210.

2,2-Dimethyl-*N*-propyloct-4-yn-3-amine (3at): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 2.91 (t, *J* = 2.0 Hz, 1H, NCH), 2.85 (ddd, *J* = 11.3, 8.1, 6.5 Hz, 1H, NC(H)H), 2.50 (ddd, *J* = 11.3, 8.2, 6.0 Hz, 1H, NC(H)H), 2.18 (td, *J* = 6.9, 2.0 Hz, 2H, $CH_2C{\equiv}C$), 1.57 – 1.44 (m, 4H, overlapped signal), 0.99 (t, *J* = 7.3 Hz, 3H, CH_2CH_3), 0.98 (s, 9H, $C(CH_3)_3$) 0.93 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm.^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 83.8, 81.0, 60.7, 50.7, 34.8, 26.5, 23.1, 22.6, 20.8, 13.5, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{13}H_{25}N+H]^+$: 196.2060; found 196.2067.

6,6-Diethoxy-2,2-dimethyl-*N*-propylhex-4-yn-3-amine (3au): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 5.31 (d, *J* = 0.9 Hz, 1H, $CH(OEt)_2$), 3.74 (dq, *J* = 9.2, 7.1 Hz, 2H, $CH(OCH_2CH_3)OCH_2CH_3$), 3.60 (dq, *J* = 9.2, 7.1 Hz, 2H, $CH(OCH_2CH_3)OCH_2CH_3$), 2.99 (d, *J* = 1.1 Hz, 1H, NCH), 2.85 (ddd, *J* = 11.3, 8.0, 6.6 Hz, 1H, NC(H)H), 2.50 (ddd, *J* = 11.3, 8.0, 6.1 Hz, 1H, NC(H)H), 1.55 – 1.39 (m, 2H, NCH_2CH_2), 1.23 (t, *J* = 7.1 Hz, 6H, $(OCH_2CH_3)_2$), 0.99 (s, 9H, $C(CH_3)_3$), 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 91.6, 86.7, 79.6, 60.7, 60.7, 60.5, 50.6, 34.8, 26.5, 23.1, 15.1, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{29}NO_2+H]^+$: 256.2271; found 256.2277.

7-Bromo-2,2-dimethyl-*N*-propylhept-4-yn-3-amine (3av): ^1H NMR (400 MHz, $CDCl_3$): *δ* = 3.43 (t, *J* = 7.2 Hz, 2H, CH_2Br), 2.91 (t, *J* = 1.9 Hz, 1H, NCH), 2.84 (ddd, *J* = 11.3, 8.0, 6.6 Hz, 1H, NC(H)H), 2.77 (td, *J* = 7.2, 1.9 Hz, 2H, CH_2CH_2Br), 2.49 (ddd, *J* = 11.3, 8.1, 6.1 Hz, 1H, NC(H)H), 1.46 – 1.42 (m, 2H, $NCH_2CH_2CH_3$), 0.98 (s, 9H, $C(CH_3)_3$), 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* =

83.4, 80.5, 60.6, 50.7, 34.8, 30.3, 26.5, 23.4, 23.1, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{12}H_{22}NBr+H]^+$: 260.1008; found 260.1010.

5,5-Dimethyl-4-(propylamino)hex-2-yn-1-yl acetate (3aw): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.71 (d, *J* = 1.8 Hz, 2H, CH_2O), 2.96 (t, *J* = 1.8 Hz, 1H, NCH), 2.83 (ddd, *J* = 11.3, 8.0, 6.6 Hz, 1H, NC(H)H), 2.48 (ddd, *J* = 11.3, 8.0, 6.1 Hz, 1H, NC(H)H), 2.08 (s, 3H, $COCH_3$), 1.54 – 1.42 (m, 2H, N-$CH_2CH_2CH_3$), 0.98 (s, 9H, $C(CH_3)_3$), 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3, 88.1, 77.7, 60.6, 52.7, 50.6, 34.8, 26.5, 23.1, 20.8, 11.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{13}H_{23}NO_2+H]^+$: 226.1802; found 226.1809.

General experimental procedure for the synthesis of ketimine-alkyne coupling

In an oven dried 10 mL vial containing 1 mL of toluene and a stirring bar, the ketimines **4a-o** (0.5 mmol), the acetylenes (0.5 mmol, 1 equiv) and $Zn(OTf)_2$ (0.027 g, 0.75 mmol) were added successively and the vial was sealed under air. The reaction mixture was stirred at 100 ºC for 24 h. Afterwards the reaction mixture was diluted with CH_2Cl_2 (10 mL) washed and extracted with 0.5 N NaOH (10 mL). The organic phase was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Crude reaction mixture was purified by silica gel column chromatography using EtOAc/*n*-Heptane (10:90) as solvent system to get the final product.

1-(Phenylethynyl)-*N*-propylcyclohexan-1-amine (5aa): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.40 (m, 2H, aromatic), 7.31 – 7.24 (m, 3H, aromatic), 2.77 (t, *J* = 7.3 Hz, 2H, NCH_2), 1.97-1.90 (m, 2H, *c*Hex), 1.72 – 1.39 (m, 8H, overlapped signal *c*Hex), 1.30-1.19 and 0.84-0.91 (2 × m, 2 × 1H, *c*Hex), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$, referenced to solvent δ_C 77.00): δ = 131.6, 128.1, 127.6, 123.8, 93.7, 84.4, 54.9, 45.2, 38.2, 25.9, 23.8, 23.0, 11.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{23}N+H]^+$: 242.1903; found 242.1904.

3-Methyl-1-phenyl-*N*-propylpent-1-yn-3-amine (5ba): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.40 (m, 2H, aromatic), 7.28 – 7.27 (m, 3H, aromatic), 2.81 – 2.66 (m, 2H, NCH_2), 1.77 – 1.60 (m, 2H, CH_3CH_2), 1.58 – 1.49 (m, 2H, $CH_3CH_2CH_2$), 1.38 (s, 3H, C_qCH_3), 1.05 (t, *J* = 7.5 Hz, 3H, CH_3CH_2), 0.97 (t, *J* = 7.4 Hz, 3H, $CH_3CH_2CH_2$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6 (CH_{meta}), 128.2 (CH_{ortho}), 127.7 (CH_{para}), 123.7 ($C_{q\ arom}$), 94.0 ($MeC_qC{\equiv}C$), 83.1 ($C{\equiv}CC_{q\ arom}$), 54.3 (C_qCH_3), 46.0 (NCH_2), 34.9 (CH_3CH_2), 26.5 (C_qCH_3), 23.8 ($CH_3CH_2CH_2$), 12.0 ($CH_3CH_2CH_2$), 8.9 (CH_3CH_2) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{21}N+H]^+$: 216.1747; found 216.1740.

1-(4-Methoxy-2-methylphenyl)-3-methyl-*N*-propylpent-1-yn-3-amine (5bi): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.5 Hz, 1H, aromatic), 6.63 (d, *J* = 2.2 Hz, 1H, aromatic), 6.56 (dd, *J* = 8.5, 2.2 Hz, 1H, aromatic), 3.67 (s, 3H, OCH_3), 2.72 – 2.60 (m, 2H, NCH_2), 2.31 (s, 3H, $PhCH_3$), 1.68 – 1.52 (m, 2H, CH_2CH_3), 1.50 – 1.39 (m, 2H, CH_2CH_3), 1.29 (s, 3H, C_qCH_3), 0.98 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 0.87 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$ referenced to solvent δ_C 77.00): δ = 159.0, 141.3, 132.9, 115.6, 114.8, 111.0, 96.1, 81.5, 55.0, 54.3, 45.9, 34.8, 26.5, 23.7, 20.9, 11.8, 8.8 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}NO+H]^+$: 260.2009; found 260.2014.

1-(4-Chlorophenyl)-3-methyl-N-propylpent-1-yn-3-amine (5bm): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.5 Hz, 2H, aromatic), 7.25 (d, *J* = 8.5 Hz, 2H, aromatic), 2.79 – 2.64 (m, 2H, NCH_2), 1.74 – 1.56 (m, 2H, CH_2CH_3), 1.56 – 1.48 (m, 2H, CH_2CH_3), 1.36 (s, 3H, C_qCH_3), 1.04 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.7, 132.9, 128.5, 122.2, 95.0 (C≡C), 82.0 (C≡C), 54.3, 46.0, 34.8, 26.4, 23.8, 12.0, 9.0 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{20}NCl+H]^+$: 250.1357; found 250.1362.

1-(Cyclohex-1-en-1-yl)-3-methyl-*N*-propylpent-1-yn-3-amine (5bs): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.08 – 5.97 (m, 1H, C=CH), 2.68 – 2.62 (m, 2H, NCH_2), 2.10 – 2.07 (m, 4H), 1.66 – 1.54 (m, 6H), 1.54 – 1.46 (m, 2H), 1.23 (s, 3H, C_qCH_3), 0.99 (t, 3H, *J* = 7.4 Hz, CH_3), 0.95 (t, 3H, *J* = 7.4 Hz, CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.5, 120.8, 91.0, 84.8, 54.1, 45.9, 34.9, 29.7, 26.6, 25.6, 23.8, 22.4, 21.6, 12.0, 8.9 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{15}H_{25}N+H]^+$: 220.2060; found 220.2050.

***N*-Butyl-3,5-dimethyl-1-phenylhex-1-yn-3-amine (5ca):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 - 7.37 (m, 2H, aromatic), 7.28 - 7.26 (m, 3H, aromatic), 2.82 – 2.72 (m, 2H, NCH_2), 1.99 – 1.89 (m, 1H, $CH(CH_3)_2$), 1.63 (dd, *J* = 13.7, 6.0 Hz, 1H, C(H)HCH), 1.55 (dd, *J* = 13.8, 5.7 Hz, 1H, C(H)HCH), 1.52 – 1.46 and 1.44 – 1.34 (2×m, 2×2H, $CH_2CH_2CH_3$), 1.40 (s overlap, 3H, C_qCH_3), 1.05 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$), 1.03 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)CH_3$), 0.94 (t, *J* = 7.2 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.5, 128.2, 127.7, 123.8, 94.6, 83.2, 53.5, 50.9, 43.5, 32.8, 27.6, 24.9, 24.7, 24.5, 20.6, 14.0 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{27}N+H]^+$: 258.2216; found 258.2210.

3,5-Dimethyl-1-phenyl-*N*-propylhex-1-yn-3-amine (5dd): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 8.1 Hz, 2H, aromatic), 7.11 (d, *J* = 8.1 Hz, 2H, aromatic), 2.77 (ddd, *J* = 10.5, 7.8, 7.0 Hz, 1H, NC(H)H), 2.69 (ddd, *J* = 10.6, 8.1, 6.5 Hz, 1H, NC(H)H), 2.80 – 2.66 (m, 2H), 2.62 (q, *J* = 7.6 Hz, 2H, $PhCH_2CH_3$), 2.00 – 1.87 (m, 1H, $CH(CH_3)_2$), 1.62 (dd, *J* = 13.7, 6.0 Hz, 1H, C(H)HCH), 1.57 – 1.46 (m, 3H, C(H)HCH and CH_2CH_3), 1.39 (s, 3H, C_qCH_3), 1.21 (t, *J* = 7.6 Hz, 3H, $PhCH_2CH_3$), 1.05 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)CH_3$), 1.03 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)CH_3$), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.0, 131.5, 127.8, 121.0, 93.7, 83.3, 53.5, 51.0, 45.8, 28.8, 27.7, 24.9, 24.7, 24.5, 23.8, 15.4, 12.0 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}N+H]^+$: 272.2373; found 272.2370.

***N*-Butyl-3,4-dimethyl-1-(*p*-tolyl)pent-1-yn-3-amine (5ex):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.1 Hz, 2H, aromatic), 7.08 (d, *J* = 7.9 Hz, 2H, aromatic), 2.81 – 2.68 (m, 2H, NCH_2), 2.33 (s, 3H, $PhCH_3$), 1.87 (septet, *J* = 6.7 Hz, 1H, $CH(CH_3)_2$), 1.51 – 1.37 (m, 4H), 1.30 (s, 3H, C_qCH_3), 1.07 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$), 1.02 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$), 0.93 (t, *J* = 7.2 Hz, 3H, CH_2CH_3), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.6, 131.5, 129.0, 120.8, 93.1, 83.5, 57.6, 43.5, 36.7, 32.9, 23.2, 21.4, 20.7, 18.1, 17.2, 14.1 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{27}N+H]^+$: 258.2216; found 258.2210.

2-(Phenylethynyl)-*N*-propylbicyclo[2.2.1]heptan-2-amine (5fa): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 - 7.38 (m, 2H, aromatic), 7.30 - 7.24 (m, 3H, aromatic), 2.80 (ddd, *J* = 10.9, 7.6, 6.7 Hz, 1H, NC(H)H), 2.50 (ddd, *J* = 10.9, 7.8, 6.6 Hz, 1H, NC(H)H), 2.42 (broad d, *J* = 3.5 Hz, 1H), 2.24 (broad t, J = 4.0 Hz, 1H), 2.13 (ddd, *J* = 12.2, 4.7, 3.0 Hz, 1H), 1.94 (broad d, *J* = 9.9 Hz, 1H), 1.87 – 1.82 (m, 1H), 1.57 - 1.47 (m, 2H), 1.39 – 1.25 (m, 4H), 1.20 (dd, *J* = 12.3, 2.9 Hz, 1H), 0.96 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), NH overlapping ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.5, 128.2, 127.5, 124.1, 96.4, 82.3, 60.3, 47.8, 47.5, 46.8, 38.6, 36.5, 29.3, 23.8, 21.6, 12.1 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{23}N+H]^+$: 254.1903; found 254.1913.

***N*-Benzyl-3-methyl-1-phenylhept-6-en-1-yn-3-amine (5ga):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 – 7.39 (m, 2H, aromatic), 7.30 - 7.25 (m, 3H, aromatic), 5.88 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H, $CH{=}CH_2$), 5.07 (ddd, *J* = 17.1, 3.4, 1.6 Hz, 1H, CH=C(H)H), 4.97 (dd, *J* = 10.2, 1.8 Hz, 1H, CH=C(H)H), 2.78 – 2.68 (m, 2H, NCH_2), 2.33 – 2.26 (m, 2H), 1.82 – 1.68

(m, 2H), 1.56 – 1.50 (m, 2H), 1.40 (s, 3H, C_qCH_3), 1.28 (broad s, 1H, NH), 0.97 (t, *J* = 7.4 Hz, 3H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 138.6, 131.6, 128.2, 127.8, 123.6, 114.5, 93.8, 83.3, 53.7, 45.9, 41.2, 29.1, 27.1, 23.8, 12.0 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{23}N+H]^+$: 242.1903; found 242.1900.

***N*-Butyl-3-methyl-1-phenylhex-1-yn-3-amine (5ha):** ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.41 – 7.38 (m, 2H, aromatic), 7.29 – 7.25 (m, 3H, aromatic), 2.83 – 2.71 (m, 2H, NCH_2), 1.67 – 1.48 (m, 6H), 1.42 – 1.41 (m, 1H), 1.38 (s, 3H, C_qCH_3), 1.22 (broad s, 1H, NH), 0.97 (t, *J* = 7.0 Hz, 3H, CH_3), 0.94 (t, *J* = 7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 131.6, 128.2, 127.7, 123.7, 94.2, 83.0, 53.8, 44.6, 43.7, 32.8, 27.1, 20.6, 17.9, 14.5, 14.0 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{25}N+H]^+$: 244.2060; found 244.2050.

3-Methyl-1-phenyl-*N*-propylhex-1-yn-3-amine (5ia): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.41 - 7.39 (m, 2H, aromatic), 7.29 - 7.25 (m, 3H, aromatic), 2.79 - 2.69 (m, 2H, NCH_2), 1.67-1.50 (m, 6H), 1.38 (s, 3H, C_qCH_3), 1.25 (broad s, 1H, NH), 0.99 (t, 3H, *J* = 7.1 Hz, CH_3), 0.98 (t, 3H, *J* = 7.4 Hz, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 131.6, 128.2, 127.7, 123.7, 94.2, 83.0, 53.8, 46.0, 44.6, 27.1, 23.8, 17.9, 14.5, 12.0 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{16}H_{23}N+H]^+$: 230.1903; found 230.1916.

3-Ethyl-1-phenyl-*N*-propylhept-1-yn-3-amine (5ja): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = *δ* = 7.41 – 7.39 (m, 2H, aromatic), 7.28 – 7.26 (m, 3H, aromatic), 2.67 (t, *J* = 7.2 Hz, 2H, NCH_2), 1.70 – 1.61 (m, 4H), 1.52 (q, *J* = 7.2 Hz, 2H, $C_qCH_2CH_3$), 1.44 – 1.35 (m, 4H), 1.00 (t, 3H, *J* = 7.4 Hz, CH_3), 0.97 (t, 3H, *J* = 7.4 Hz, CH_3), 0.94 (t, 3H, *J* = 7.1 Hz, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 131.6, 128.2, 127.6, 123.9, 93.9, 83.7, 57.3, 45.5, 38.0, 31.3, 26.1, 23.9, 23.1, 14.1, 12.0, 8.4 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{18}H_{27}N+H]^+$: 258.2216; found 258.2220.

Methyl (3,4-dimethyl-1-phenylpent-1-yn-3-yl)-D-valinate (5ka): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.39 – 7.34 (m, 2H, minor & major, aromatic), 7.26 – 7.23 (m, 3H, minor & major, aromatic), 3.58 (s, 3H, OCH_3 minor), 3.51 (s, 3H, OCH_3 major), 3.40 (d, *J* = 5.6 Hz, 1H, NCH minor), 3.27 (d, *J* = 5.6 Hz, 1H, NCH major), 2.01 (broad s, 1H, NH minor & major), 1.88 – 1.78 (m, 3H, $CH(CH_3)_2$ minor & major), 1.26 (s, 3H, C_qCH_3 minor & major), 1.10 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$ major), 1.09 (d, *J* = 6.6 Hz, 3H, $CH(CH_3)CH_3$ minor), 1.06 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$ major), 1.09 (d, *J* = 6.6 Hz, 3H, $CH(CH_3)CH_3$ minor), 0.96 (d, *J* = 7.6 Hz, 3H, $CH(CH_3)CH_3$ minor), 0.94 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)CH_3$ minor & major), 0.92 (d, *J* = 7.0 Hz, 3H, $CH(CH_3)CH_3$ major) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 177.1 (C=O, minor), 176.8 (C=O, major), 131.6 (minor & major), 128.2 (minor), 128.1 (minor), 127.72 (minor), 127.66 (major), 123.6 ($C_{q\ arom}$ minor & major), 93.3 (C≡C, minor), 93.2 (C≡C, major), 84.3 (C≡C, major), 84.2 (C≡C, minor), 62.4 (NCH, minor), 61.9 (NCH, major), 57.4 (C_qMe, minor), 56.8 (C_qMe, major), 51.5 (OCH_3, minor), 51.4 (OCH_3, major), 38.2 (major), 36.7 (minor), 32.8 (minor), 32.7 (major), 24.1, 24.0 (minor), 19.6 (minor), 19.5, 18.5 (minor), 18.4, 18.3 (minor), 17.9, 17.6, 17.2 (minor) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{19}H_{27}NO_2+H]^+$: 302.2115; found 302.2120.

Methyl (3-methyl-1-phenylhex-1-yn-3-yl)-D-valinate (5la): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.36 – 7.34 (m, 2H, aromatic), 7.27 – 7.24 (m, 3H, aromatic), 3.57 (s, 3H, OCH_3 minor), 3.53 (s, 3H, OCH_3 major), 3.36 (d, *J* = 5.6 Hz, 1H, NCH minor), 3.28 (d, *J* = 5.6 Hz, 1H, NCH major), 2.03 (broad s, 1H, NH minor & major), 1.85 – 1.80 (m, 1H, $CH(CH_3)_2$ minor & major), 1.60 – 1.55 (m, 4H, $CH_2CH_2CH_3$ minor & major), 1.36 (s, 3H, CH_3C_q minor), 1.32 (s, 3H, CH_3C_q major), 1.00 – 0.87 (m, 9H, minor & major) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 176.9 (C=O minor), 176.8 (C=O major), 131.6 (minor & major), 128.14 (minor), 128.11 (major), 127.75 (minor), 127.72 (major), 123.5 (minor & major), 93.7 (C≡C, minor), 93.6 (C≡C, major), 83.7 (C≡C, major), 83.4 (C≡C, minor), 62.2 (minor), 62.0 (major), 53.5 (minor), 53.2 (major), 51.5 (minor), 51.4 (major), 45.5 (major), 44.3 (minor), 32.6 , 28.0 (minor), 27.5 (major), 19.5 (minor & major), 18.4 (minor), 18.4 (major), 17.94 (major), 17.89 (minor), 14.5 (minor), 14.4 (major) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{19}H_{27}NO_2+H]^+$: 302.2115; found 302.2115.

Methyl (1-(phenylethynyl)cyclohexyl)-D-valinate (5ma): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.39 – 7.37 (m, 2H, aromatic), 7.27 – 7.24 (m, 3H, aromatic), 3.55 (s, 3H, OCH_3), 3.35 (d, *J* = 5.6 Hz, 1H, NHCH), 1.99 (s, 1H, NH), 1.95 – 1.82 (m, 3H, *Cy*), 1.68 – 1.46 (m, 6H, Cy), 1.38 (dt, *J* = 12.1, 3.4 Hz, 1H), 1.27 – 1.18 (m, 1H), 0.95 (d, *J* = 7.1 Hz, 3H, $CH(CH_3)CH_3$), 0.93 (d, *J* = 7.1 Hz, 3H, $CH(CH_3)CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 176.9, 131.6, 128.1, 127.7, 123.6, 93.3, 84.9, 61.5, 54.4, 51.4, 39.3, 38.1, 32.6, 25.8, 23.1, 22.8, 19.5, 18.4 ppm. HRMS (ESI) *m*/*z* calculated for $[C_{22}H_{27}NO_2+H]^+$: 314.2115; found 314.2117.

Methyl (3,4-dimethyl-1-phenylpent-1-yn-3-yl)-D-alaninate (5na): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.39 – 7.37 (m, 2H, aromatic), 7.28 – 7.26 (m, 3H, aromatic), 3.70 (q, *J* = 7.1 Hz, 1H, $NHCHCH_3$), 3.61 (s, 3H, OCH_3), 1.91 – 1.84 (m, 1H, $CH(CH_3)_2$), 1.56 (broad s, 1H, NH), 1.31 (d, *J* = 7.1 Hz, 3H, $NHCHCH_3$), 1.29 (s, 3H, CH_3C_q), 1.08 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$), 1.01 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 177.8 (C=O), 131.6, 128.2, 127.8, 123.5 (C_q arom), 93.1 and 84.1 (PhC≡C), 57.3 (C_qCH_3), 52.5 ($NHCHCH_3$), 51.9 (OCH_3), 36.9 ($CH(CH_3)_2$), 23.8 (CH_3C_q), 21.1 ($NHCHCH_3$), 18.3 ($CH(CH_3)CH_3$), 17.0 ($CH(CH_3)CH_3$) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{17}H_{23}NO_2+H]^+$: 274.1802; found 274.1811. **Methyl (3,4-dimethyl-1-phenylpent-1-yn-3-yl)-D-alaninate (5na'):** ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.38 – 7.35 (m, 2H, aromatic), 7.27 – 7.26 (m, 3H, aromatic), 3.65 (q, *J* = 7.1 Hz, 1H, $NHCHCH_3$), 3.56 (s, 3H, OCH_3), 1.84 – 1.77 (m, 1H, $CH(CH_3CH_3)$), 1.31 – 1.29 (m overlapped, 3H, $NHCHCH_3$), 1.31 (s overlapped, 3H, CH_3C_q), 1.11 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$), 1.05 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 177.6, 131.6, 128.1, 127.8, 123.5, 92.5, 84.5, 57.5, 52.1, 51.8, 37.8, 24.6, 21.7, 17.9, 17.7 ppm.

Methyl N^2-acetyl-N^6-(3,4-dimethyl-1-phenylpent-1-yn-3-yl)-L-lysinate (5oa): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.41 – 7.39 (m, 2H, aromatic), 7.33 – 7.23 (m, 3H, aromatic), 6.05 (d, *J* = 7.6 Hz, 1H, $NHCOCH_3$), 4.61 (dt, *J* = 7.5, 5.6 Hz, 1H, $CHCO_2Me$), 3.72 (s, 3H, OCH_3), 2.77 (td, *J* = 11.3, 6.8 Hz, m, 1H, NC(H)H), 2.70 (td, *J* = 10.8, 7.3 Hz, m, 1H, NC(H)H), 2.00 (s, 3H, $NHCOCH_3$), 1.91 – 1.84 (m, 2H, NCH_2CH_2), 1.76 – 1.63 (m, 1H, $CH(CH_3)_2$), 1.55 – 1.46 (m, 3H), 1.45 – 1.35 (m, 2H), 1.30 (s, 3H, CH_3C_q), 1.07 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$), 1.01 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$), NH not visible ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 173.2 (CO_2Me), 169.8 (CONH), 131.6 (CH_{arom}), 128.2 (CH_{arom}), 127.7 (CH_{arom}), 123.7 (C_{ipso}), 93.6 (C≡C), 83.5 (C≡C), 57.5 (CH_3C_q), 52.3 (OCH_3), 52.1 ($CHCO_2Me$), 43.4 (NCH_2), 36.64, 36.63, 32.4 (CH_2), 30.2 (CH_2), 23.17, 23.15 (CH_2), 23.0, 18.1 ($CH(CH_3)CH_3$), 17.14, 17.13 ($CH(CH_3)CH_3$) ppm. HRMS (ESI) *m*/*z* calculated for $[C_{22}H_{32}N_2O_3+H]^+$: 373.2486; found 373.2480.

Methyl N^2-acetyl-N^6-(3,4-dimethyl-1-(*p*-tolyl)pent-1-yn-3-yl)-L-lysinate (5ox): ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.29 (d, *J* = 7.8 Hz, 2H, aromatic), 7.09 (d, *J* = 7.9 Hz, 2H, aromatic), 6.16 (d, *J* = 7.7 Hz, 1H, $NHCOCH_3$), 4.60 (td, *J* = 5.6, 7.5 Hz, 1H, $CHCO_2Me$), 3.72 (s, 3H, OCH_3), 2.77 (td, *J* = 11.5, 7.3 Hz, 1H, NC(H)H), 2.70 (td, *J* = 10.8, 7.3 Hz, 1H, NC(H)H), 2.33 (s, 3H, CH_3Ph), 2.00 (s, 3H, $NHCOCH_3$), 1.90 – 1.82 (m, 2H, NCH_2CH_2), 1.75 – 1.65 (m, 2H), 1.54 – 1.35 (m, 3H), 1.29 (s, 3H, CH_3C_q), 1.07 (d, *J* = 6.7 Hz, 3H, 3H, $CH(CH_3)CH_3$), 1.01 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$), NH overlapping ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 173.2 (CO_2Me), 169.9 (CONH), 137.7 ($C_{q\ arom}CH_3$), 131.5 (CH_{ortho}), 129.0 (CH_{meta}), 120.6 (C_{ipso}), 92.6 (ArC≡C), 83.6 (ArC≡C), 57.6 (C_qMe), 52.3 (OCH_3), 52.2 ($CHCO_2Me$), 43.3 (NCH_2), 36.63 (CH), 36.62 ($CH(CH_3)_2$),

32.3 (CH_2), 30.1 (CH_2), 23.2 (CH_2), 23.1 (Me), 23.0 (CH_3CONH), 21.4 (CH_3Ph), 18.1 $CH(CH_3)CH_3$), 17.1 $CH(CH_3)CH_3$) ppm. HRMS (ESI) *m/z* calculated for $[C_{23}H_{34}N_2O_3+H]^+$: 387.2642; found 387.2643.

Methyl N^2-acetyl-N^6-(1-(4-methoxyphenyl)-3,4-dimethylpent-1-yn-3-yl)-L-lysinate (5oh): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.5 Hz, 2H, arom CH_{meta}), 6.82 (d, *J* = 8.5 Hz, 2H, arom CH_{ortho}), 6.09 (d, *J* = 6.8 Hz, 1H, $NHCOCH_3$), 4.60 (dt, *J* = 7.5, 5.4 Hz, 1H, $CHCO_2Me$), 3.80 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 2.78 (dt, *J* = 13.2, 6.9 Hz, 1H, NC(H)H), 2.71 (dt, *J* = 10.9, 7.3 Hz, 1H, NC(H)H), 2.01 (s, 3H, $NHCOCH_3$), 1.91 – 1.86 (m, 3H), 1.72 - 1.67 (m, 1H), 1.54 – 1.38 (m, 3H), 1.30 (s, 3H, CH_3C_q), 1.07 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$), 1.01 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2 ($COOCH_3$), 169.9 (CONH), 159.3 ($C_{q\ arom}OCH_3$), 133.0 (CH_{meta}), 115.8 (C_{ipso}), 113.9 (CH_{ortho}), 91.61 and 91.58 (ArC≡C), 83.49 and 83.47 (ArC≡C), 57.8 and 57.7 (C_qMe), 55.3 ($COOCH_3$), 52.3 ($CHCO_2Me$), 52.2 ($C_{q\ arom}OCH_3$), 43.3 (NCH_2), 36.61 and 36.60 ($CH(CH_3)_2$), 32.4, 30.06 and 30.04 (CH_3C_q), 23.2, 23.0, 18.1 ($CH(CH_3)CH_3$), 17.2 ($CH(CH_3)CH_3$) ppm. HRMS (ESI) *m/z* calculated for $[C_{23}H_{34}N_2O_4+H]^+$: 403.2591; found 403.2598.

Methyl N^2-acetyl-N^6-(3,4-dimethyl-1-(4-(trifluoromethyl)phenyl)pent-1-yn-3-yl)-L-lysinate (5oo): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.3 Hz, 2H, aromatic), 7.50 (d, *J* = 8.2 Hz, 2H, aromatic), 6.05 (d, *J* = 7.4 Hz, 1H, $NHCOCH_3$), 4.62 (dt, *J* = 5.7, 7.6 Hz, 1H, $CHCO_2Me$), 3.73 (s, 3H, OCH_3), 2.80 – 2.68 (m, 2H, NCH_2), 2.01 (s, 3H, $NHCOCH_3$), 1.93 – 1.83 (m, 3H), 1.74 – 1.65 (m, 1H), 1.56 – 1.37 (m, 3H), 1.32 (s, 3H, CH_3C_q), 1.08 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)CH_3$), 1.02 (d, *J* = 6.8 Hz, 3H, $CH(CH_3)CH_3$), NH overlapping ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2 (CO_2Me), 169.85 and 169.84 (CONH), 131.9 ($CH_{meta}CCF_3$), 129.6 (q, $^2J_{C\text{-}F}$ = 32.6, $C_{ipso}CF_3$), 127.4 ($CH_{para}CCF_3$), 125.2 (q, $^3J_{C\text{-}F}$ = 3.7, $CH_{ortho}CCF_3$), 124.0 (q, , $^1J_{C\text{-}F}$ = 272.1, CF_3), 96.13 and 96.11 (ArC≡C), 82.6 (ArC≡C), 57.81 and 57.79 (C_q), 52.4 ($COOCH_3$), 52.1 ($CHCO_2Me$), 43.40 and 43.39 (NCH_2), 36.5 ($CH(CH_3)_2$), 32.5 (CH_3C_q), 30.1, 30.0, 23.2, 23.1, 22.8, 18.1 ($CH(CH_3)CH_3$), 17.1 ($CH(CH_3)CH_3$) ppm. HRMS (ESI) *m/z* calculated for $[C_{23}H_{31}N_2O_3F_3+H]^+$: 441.2360; found 441.2357.

Acknowledgments

This work was financed by Erasmus mundus, the FWO-Flanders, University of Antwerp (BOF), and the Hercules Foundation.

Keywords: A^3-coupling; KA^2-coupling; Alkyne; amines; Zinc

[1] For medicinal and pharmacological applications see: a) P. H. Yu, B. A. Davis, A. Boulton, *J. Med. Chem*. **1992**, *35*, 3705-3713; b) J. L. Wright, T. F. Gregory, S. R. Kesten, P. A. Boxer, K. A. Serpa, L. T. Meltzer, L. D. Wise, *J. Med. Chem*. **2000**, *43*, 3408-3419; c) M. Weinstock, C. Bejar, R. H. Wang, T. Poltyrev, A. Gross, J. P. M. Finberg, M. B. H. Youdim, *J. Neural. Transm. Suppl.* **2000**, *60*, 157-169; d) O. Weinreb, S. Mandel, O. Bar-Am, Y. Falach, M. Y. A. Tirosh, T. Amit, M. B. H. Youdim, *Neurotherapeutics* **2009**, *6,* 163-174; e) B. A. Orit, A. Tamar, W. Orly, Y. B. H. Moussa, M. Silvia, *J. Alzheimer's Dis.* **2010**, *21*, 361-371.

[2] A. H. V. Schapira, *Oxidative Stress and Neuroprotection. The use of rasagiline in Parkinson's disease. Vol. 71,* (Eds.: H. Parvez, P. Riederer), Vienna Springer, Austria, **2006**, pp. 157.

[3] a) A. Hoepping, K. M. J. George, J. F. Anderson, A. P. Kozikowski, *J. Med. Chem*. **2000**, *43*, 2064-2071; b) V. Bavetsias, J. H. Marriott, C. Melin, R. Kimbell, Z. S. Matusiak, F. T. Boyle, A. L. Jackman, *J. Med. Chem*. **2000**, *43*, 1910-1926; c) N. Miyachi, F. Kanda, M. Shibasaki, *J. Org. Chem*. **1989**, *54*, 3511-3511.

[4] a) Punja. N. Patent US4325966, **1982**; b) C. Swithenbank, P. J. McNulty, K. L. Viste*, J. Agric. Food Chem*. **1971**, *19*, 417-421.

[5] For chemical transformations see: a) M. A. Huffman, N. Yasuda, A. E. DeCamp, E. J. J. Grabowski, *J. Org. Chem*. **1995**, *60*, 1590-1594; b) M. Miura, M. Enna, K. Okuro, M. Nomura, *J. Org. Chem.* **1995**, *60*, 4999-5004; c) A. Jenmalm, W. Berts, Y. L. Li, K. Luthman, I. Csoregh, U. Hacksell, *J. Org. Chem.* **1994**, *59*, 1139-1148; d) R. Robles-Machin, J. Adrio, J. C. Carretero, *J. Org. Chem.* **2006**, *71*, 5023-5026; e) A. Ranjan, R. Yerande, P. B. Wakchaure, S. G. Yerande, D. H. Dethe, *Org. Lett*. **2014**, *16*, 5788-5791; f) Y. Yamamoto, H. Hayashi, T. Saigoku, H. Nishiyama, *J. Am. Chem. Soc*. **2005**, *127*, 10804-10805; g) A. Sinai, D. Vangel, T. Gati, P. Bombicz, Z. Nova, *Org. Lett.* **2015**, *17*, 4136-4139; h) A. S. K. Hashmi, A. M. Schuster, M. Schmuck, F. Rominger, *Eur. J. Org. Chem.* **2011**, 4595-4602; i) V. A. Peshkov, O. P. Pereshivko, P. A. Donets, V. P. Mehta, E. V. Van der Eycken, *Eur. J. Org. Chem.* **2010**, 4861-4867; j) E. Vessally, L. Edjlali, A. Hosseinian, A. Bekhradnia, M. D. Esrafili, *RSC Adv*. **2016**, *6*, 49730-49746; k) E. Vessally, *RSC Adv.* **2016**, *6*, 18619-18631; l) Y. Liu, *ARKIVOC*, **2013**, *2014*, 1-20.

[6] a) V. A. Peshkov, O. P. Pereshivko, E. V. Van der Eycken, *Chem. Soc. Rev*. **2012**, *41*, 3790-3807; b) A. Beillard, T.-X. Métro, X. Bantreil, J. Martinez, F. Lamaty, *Eur. J. Org. Chem.* **2017**, 4642-4647.

[7] a) Y. Imada, M. Yuasa, I. Nakamura, S.-I. Murahashi, *J. Org. Chem*. **1994**, *59*, 2282-2284; b) S. Czernecki, J.-M. Valéry, *J. Carbohydr. Chem*. **1990**, *9*, 767-770; c) B. Castro, C. Selve, *Bull. Soc. Chim. Fr.* **1971**, 4368; d) G. F. Hennion, R. S. Hanzel, *J. Am. Chem. Soc*. **1960**, *82*, 4908-4912; e) I. E. Kopka, A. Fataftah, M. W. Rathke, *J. Org. Chem*. **1980**, *45*, 4616-4622; f) P.-Q. Huang, W. Ou, F. Han, *Chem. Commun.* **2016**, *52*, 11967.

[8] J. P. Guthrie*, Can. J. Chem*. **1975**, *53*, 898-906.

[9] O. P. Pereshivko, V. A. Peshkov, E. V. Van der Eycken, *Org. Lett*. **2010**, *12*, 2638-2641.

[10] a) M. Cheng, Q. Zhang, X-Yu Hu, Bo-G. Li, Jian-Xin Ji, Albert S. C. Chan, *Adv. Synth. Catal*. **2011**, *353*, 1274-1278; b) N. Gommermann, C. Koradin, K. Polborn, P. Knochel*, Angew. Chem.* **2003**, *115*, 5941-5944; *Angew. Chem. Int. Ed*. **2003**, *42*, 5763-5766; c) N. Gommermann, P. Knochel, *Chem. Eur. J*. **2006**, *12*, 4380-4392.

[11] C. E. Meyet, C. J. Pierce, C. H. Larsen, *Org. Lett*. **2012**, *14*, 964-967.

[12] X. Tang, J. Kuanga, S. Ma, *Chem. Commun.* **2013**, *49*, 8976-8978.

[13] C. J. Pierce, C. H. Larsen, *Green Chem*. **2012**, *14*, 2672.

[14] L. Yin, Y. Otsuka, H. Takada, S. Mouri, R. Yazaki, N. Kumagai, M. Shibasaki, *Org. Lett*. **2013**, *15*, 698-701.

[15] C. J. Pierce, M. Nguyen, C. H. Larsen, *Angew. Chem.* **2012**, *124*, 12455-12458; *Angew. Chem. Int. Ed*. **2012**, *51*, 12289-12292.

[16] a) Z. L. Palchak, D. J. Lussier, C. J. Pierce, H. Yoo, C. H. Larsen. *Adv. Synth. Catal*. **2015**, *357*, 539-548; b) M. Periasamy, P. O. Reddy, I. Satyanarayana, L. Mohan, A. Edukondalu. *J. Org. Chem.* **2016**, *81*, 987-999; c) M. Biyikal, M. Porta, P. W. Roesky, S. Blechert, *Adv. Synth. Catal*. **2010**, *352*, 1870-1875.

[17] C. J. Pierce, H. Yoo, C. H. Larsen, *Adv. Synth. Catal*. **2013**, *355*, 3586-3590.

[18] H. Guo, X. Liu, Q. Xie, L. Wang, D. L. Peng, P. S. Branco, M. B. Gawande, *RSC Adv*. **2013**, *3*, 19812-19815.

[19] H. Naeimi, M. Moradian, *Appl. Organometal. Chem*. **2013**, *27*, 300-306.

[20] M. Srinivas, P. Srinivasu, S. K. Bhargava, M. L. Kantam, *Catalysis Today* **2013**, *208*, 66-71.

[21] R. Hudson, S. Ishikawa, C. J. Li, A. Moores, *Synlett* **2013**, *24*, 1637-1642.

[22] R. Fässler, C. S. Tomooka, D. E. Frantz, E. M. Carreira, *Proc. Nat. Acad. Sc.* **2004**, *101*, 5843-5845.

[23] D. E. Frantz, R. Fässler, E. M. Carreira, *J. Am. Chem. Soc*. **1999**, *121*, 11245-11246.

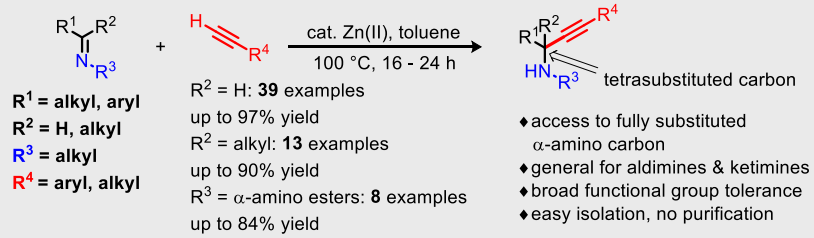
[24] B. Jiang, Y.-G. Si, *Angew. Chem*. **2004**, *116*, 218-220; *Angew. Chem. Int. Ed.* **2004**, *43*, 216-218.

[25] B. Jiang, Z. Chen, W. Xiong, *Chem. Commun*. **2002**, 1524-1525.

[26] C. C. Malakar, B. U. W. Maes, K. Abbaspour Tehrani, *Adv. Synth. Catal.* **2012**, *354*, 3461-3467.
[27] M. Zille, A. Stolle, A. Wild, U. S. Schubert, *RSC Adv.* **2014**, *4*, 13126-13133.
[28] W. J. Moran, A. Rodríguez, *Org. Biomol. Chem.* **2012**, *10*, 8590-8592.
[29] Y. Ma, E. Lobkovsky, D. B. Collum, *J. Org. Chem*. **2005**, *70*, 2335-2337.
[30] B. Miriyala, S. Bhattacharyyab, J. S. Williamson, Tetrahedron **2004**, *60*, 1463-1471.
[31] D. G. Korton, V. E. Haury, F. C. Davis, I. J. Mitchell, S. A. Ballard, *J. Org. Chem*. **1954**, *19*, 1054-1066.
[32] a) H. Sterckx, J. De Houwer, C. Mensch, I. Caretti, K. Abbaspour Tehrani, W. A. Herrebout, S. Van Doorslaer, B. U. W. Maes, *Chem. Sci.* **2016**, *7*, 346-357; b) H. Sterckx, J. De Houwer, C. Mensch, W. Herrebout, K. Abbaspour Tehrani, B. U. W. Maes, *Beilstein J. Org. Chem.* **2016**, *12,* 144-153.
[33] N. Sharma, U. K. Sharma, N. M. Mishra, E. V. Van der Eycken, *Adv. Synth. Catal.* **2014**, *356*, 1029-1037.
[34] L. Zhao, O. Basl, C.-J. Li, *Proc. Natl. Acad. Sci. USA*, **2009**, *106*, 4106-4111.

Entry for the Table of Contents (Please choose one layout)

FULL PAPER



Propargylamines

*Syeda Aaliya Shehzadi, Aamer Saeed, Filip Lemière, Bert U. W. Maes and Kourosch Abbaspour Tehrani**

Page No. – Page No.

Zinc(II)-catalyzed synthesis of propargyl amines by coupling of aldimines and ketimines with alkynes

Imines derived from unactivated aldehydes or ketones and primary amines or α-amino acid esters, react with a wide variety of terminal alkynes under Zn(II) triflate catalysis to give secondary propargyl amines bearing give tri- (from aldimines) and tetra- (from ketimines) substituted α-carbons.