Ind_2TiMe_2-Catalyzed Addition of Methyl- and Ethylamine to Alkynes

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Keywords: Alkynes / Amines / Homogeneous catalysis / Hydroamination / Titanium

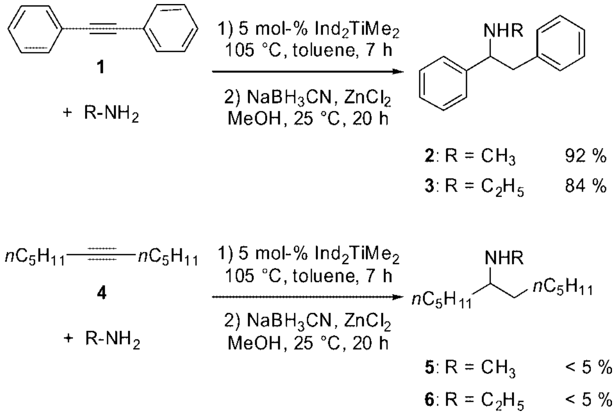
We describe a very simple hydrogenation-like experimental protocol for the addition of gaseous methyl- and ethylamine to alkynes in the presence of Ind_2TiMe_2 as the catalyst. For efficient hydroamination reactions it is sufficient to stir a mixture of the alkyne and the catalyst in toluene at temperatures between 80 °C (terminal alkynes) and 105 °C (internal alkynes) under a constant pressure of 1 atm of the corresponding amine. After subsequent reduction of the initially formed imines, methyl- and ethylamine derivatives are the final products of the described one-pot reaction sequences. In the case of 2-alkyl-1-phenylalkynes as starting materials, biologically interesting 2-phenylethylamine derivatives possessing a small methyl or ethyl substituent at the N atom are easily accessible by the new reaction protocol.

Introduction

During the last few years, Ti-catalyzed hydroaminations of alkynes have attracted much attention.[1] While most Ti complexes efficiently catalyze the addition of less basic arylamines to alkynes, corresponding reactions employing basic alkylamines are more challenging. Among the class of alkylamines, sterically less hindered *n*-alkyl- and benzylamines usually show the lowest reactivity.[2] However, from a biological point of view the generation of methylamino groups is highly desirable since many biologically active compounds possess this sub-structure. As a consequence, we investigated the addition of gaseous methylamine (and ethylamine) to alkynes.[3] Subsequent reductions of the expected *N*-methyl imine products should give access to the desired methylamine derivatives.

Results and Discussion

Based on mechanistic investigations of the Ind_2TiMe_2-catalyzed hydroamination of alkynes, which suggest that the addition of sterically less hindered amines to alkynes is inverse first order in the concentration of the amine,[4] we simply stirred solutions of diphenylacetylene (**1**) in toluene in the presence of 5 mol-% Ind_2TiMe_2 (Ind = indenyl) at 105 °C in 100-mL Schlenk tubes (Ø 30 mm) under methylamine (1 atm, b. p. –6 °C). For that purpose, we used a regular Schlenk vacuum line filled with methylamine (instead of argon). We assumed that this simple hydrogenation-like set-up of the experiments automatically results in low concentrations of gaseous methylamine in the liquid phase and in fast reactions. After some optimization studies, which were mainly focused on the size of the magnetic stirring bar (optimum: 15 × 4.5 mm) used for the reactions, we were delighted to see that the addition of methylamine to diphenylacetylene (**1**) goes to completion within less than 7 h at 105 °C in the presence of 5 mol-% of Ind_2TiMe_2 (91% conversion after 5 h). After subsequent reduction of the initially formed imine with $NaBH_3CN/ZnCl_2$ in methanol (one-pot procedure), the desired methylamine derivative **2** was isolated in 92% yield (Scheme 1).



Scheme 1. Ind_2TiMe_2-catalyzed hydroamination of symmetrically substituted internal alkynes with methyl- and ethylamine and subsequent reduction.

An additional experiment, employing gaseous ethylamine (b. p. 17 °C) also gave the expected product **3** in very good yield (84%). However, corresponding reactions of the dialkylalkyne 6-dodecyne (**4**) were less successful. In both hydroamination/reduction experiments performed with methyl- and ethylamine only trace amounts of the desired products **5** and **6** were formed.

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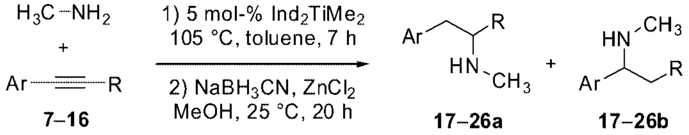
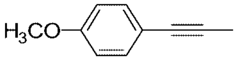
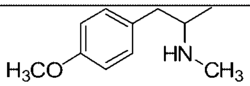
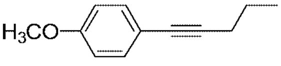
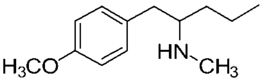
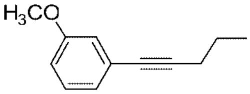
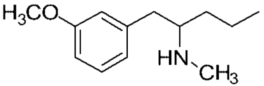
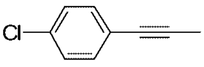
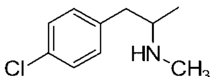
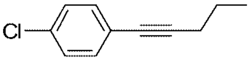
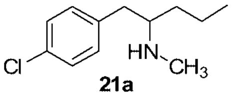
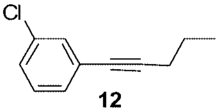
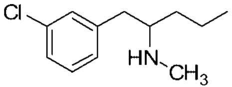
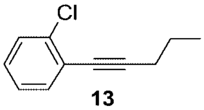
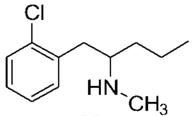
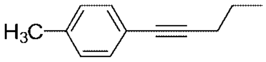
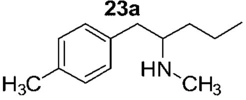
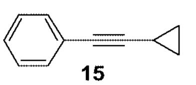
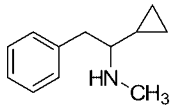
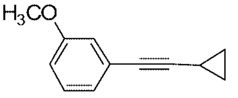
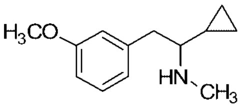
Since dialkylalkynes had turned out to be poor substrates for Ind_2TiMe_2-catalyzed addition reactions of methyl- and ethylamine, we focused on reaction sequences of unsymmetrically substituted 2-alkyl-1-phenylalkynes (Table 1). Under the reaction conditions described above, methylamine smoothly reacted with the alkynes **7**–**16**. As the result of the good regioselectivity generally observed for Ind_2TiMe_2-catalyzed hydroamination reactions,[4,5] 2-phenylethylamine derivatives **17**–**26a** possessing a biologically interesting methylamino group were obtained after subsequent reduction as the major products. Except in the case of *ortho*-substituted **23a**, the products were obtained in good yields. However, the poor yield of **23a** mainly reflects the decreased rate of the hydroamination of the sterically more demanding *ortho*-substituted alkyne substrate **13**. In this context, it is worth to mention that, in order to compare the various experiments, all hydroamination reactions were stopped after 7 h. The results shown in Table 1 further

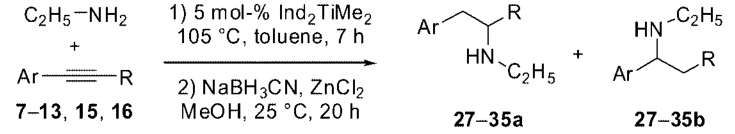
Table 1. Ind_2TiMe_2-catalyzed hydroamination of 2-alkyl-1-phenylalkynes with methylamine and subsequent reduction.

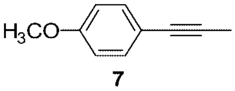
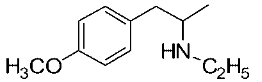
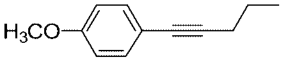
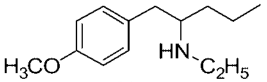
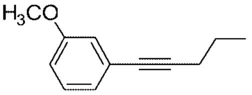
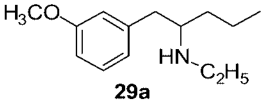
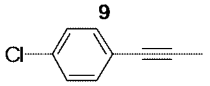
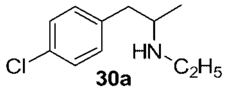
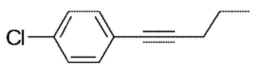
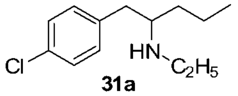
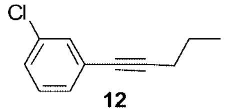
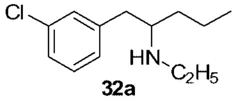
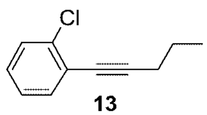
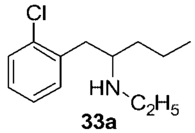
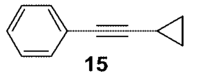
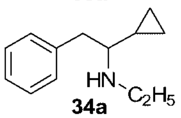
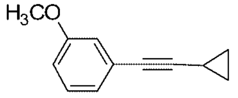
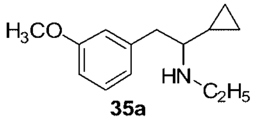


Entry	Alkyne	Yield (**a**+**b**) [%][a]	Ratio (**a**/**b**)[b]	Product	Yield (**a**) [%][c]
1	 **7**	88	92:8	 **17a**	80
2	 **8**	68	91:9	 **18a**	58
3	 **9**	75	96:4	 **19a**	59
4	 **10**	87	93:7	 **20a**	77
5	 **11**	76	92:8	 **21a**	71
6	 **12**	71	96:4	 **22a**	62
7	 **13**	39	91:9	 **23a**	27
8	 **14**	77	97:3	 **24a**	70
9	 **15**	65	3:1	 **25a**	48
10	 **16**	68	5:1	 **26a**	57

[a] Reaction conditions: 1) alkyne (4.0 mmol), Ind_2TiMe_2 (0.2 mmol, 5.0 mol-%), methylamine (1 atm), toluene, 105 °C, 7 h; 2) $NaBH_3CN$ (8.0 mmol), $ZnCl_2$ (4.0 mmol), MeOH, 25 °C, 20 h. [b] Determined by GC/MS analyses prior to chromatography. [c] Obtained after one chromatography. A complete separation of the regioisomers can be achieved by two subsequent chromatographies.

Table 2. Ind_2TiMe_2-catalyzed hydroamination of 2-alkyl-1-phenylalkynes with ethylamine and subsequent reduction.



Entry	Alkyne	Yield (**a**+**b**) [%][a]	Ratio (**a**/**b**)[b]	Product	Yield (**a**) [%][c]
1	 **7**	81	92:8	 **27a**	77
2	 **8**	73	94:6	 **28a**	65
3	 **9**	69	96:4	 **29a**	50
4	 **10**	86	91:9	 **30a**	72
5	 **11**	74	94:6	 **31a**	70
6	 **12**	76	93:7	 **32a**	68
7	 **13**	45	93:7	 **33a**	33
8	 **15**	58	3:1	 **34a**	44
9	 **16**	57	5:1	 **35a**	47

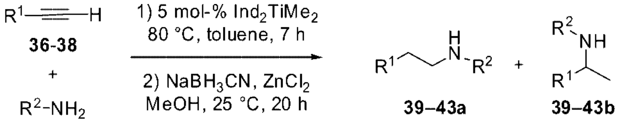
[a] Reaction conditions: 1) alkyne (4.0 mmol), Ind_2TiMe_2 (0.2 mmol, 5.0 mol-%), ethylamine (1 atm), toluene, 105 °C, 7 h; 2) $NaBH_3CN$ (8.0 mmol), $ZnCl_2$ (4.0 mmol), MeOH, 25 °C, 20 h. [b] Determined by GC/MS analyses prior to chromatography. [c] Obtained after one chromatography. A complete separation of the regioisomers can be achieved by two subsequent chromatographies.

prove that chloro and methoxy substituents in the phenyl ring do not significantly influence the efficiency of the reaction sequences. As observed before,[4] the regioselectivities of the hydroamination reactions decrease with increasing size of the alkyl substituents of the 2-alkyl-1-phenylalkyne substrates (compare entries 3 and 10).

Table 2 summarizes corresponding hydroamination/reduction one-pot experiments employing ethylamine. However, with regard to yields and regioselectivities, the results are comparable to those obtained with methylamine.

Finally, we focused on additions of methyl- and ethylamine to terminal alkynes (Table 3). In this case, it was found that better yields were obtained when the hydroamination reactions were performed at 80 °C (105 °C, yields <15%). An explanation for this result is the well known fact that terminal alkynes, especially arylalkynes tend to undergo oligomerization reactions at elevated temperatures in the presence of many Ti complexes.[4,6] However, compared to the results obtained with most of the internal alkynes, the yields shown in Table 3 are only moderate. Since it is well established that the regioselectivity of hydroaminations of terminal alkynes decreases with decreasing size of the amine,[4,7] it is not surprising that the additions of methyl- and ethylamine to alkynes **36–38** take place without any regioselectivity.

Table 3. Ind_2TiMe_2-catalyzed hydroamination of terminal alkynes with methyl- and ethylamine and subsequent reduction.



Entry	Alkyne	R^1	R^2	Yield (**a**+**b**) [%][a]	Ratio (**a**/**b**)[b]
1	**36**	4-H_3CO-C_6H_4	C_2H_5	43 (**39a/b**)	1:1
2	**37**	4-Cl-C_6H_4		42 (**40a/b**)	1:1
3	**38**	*n*$C_{10}H_{21}$		62 (**41a/b**)	1:1
4	**36**	4-H_3CO-C_6H_4	CH_3	39 (**42a/b**)	1:1
5	**38**	*n*$C_{10}H_{21}$		61 (**43a/b**)	1:1

[a] Reaction conditions: 1) alkyne (4.0 mmol), Ind_2TiMe_2 (0.2 mmol, 5.0 mol-%), amine (1 atm), toluene, 80 °C, 7 h; 2) $NaBH_3CN$ (8.0 mmol), $ZnCl_2$ (4.0 mmol), MeOH, 25 °C, 20 h. [b] Determined by GC/MS analyses prior to chromatography.

Conclusions

In summary, we have presented a very simple hydrogenation-like experimental protocol for the addition of gaseous methyl- and ethylamine to alkynes in the presence of Ind_2TiMe_2 as the catalyst. For efficient hydroamination reactions it is sufficient to stir a mixture of the alkyne and the catalyst in toluene at temperatures between 80 °C (terminal alkynes) and 105 °C (internal alkynes) under a constant pressure of 1 atm of the corresponding amine. After subsequent reduction of the initially formed imines, methyl- and ethylamine derivatives are the final products of the described one-pot reaction sequences. While the yields of the products obtained from terminal alkynes are only moderate, good results are observed when diphenyl- and 2-alkyl-1-phenylalkynes are employed as starting materials. In the case of 2-alkyl-1-phenylalkynes, the hydroamination reactions take place with good regioselectivities (*anti*-Markovnikov). Correspondingly, biologically interesting 2-phenylethylamine derivatives possessing a methyl or ethyl substituent at the N atom are easily accessible by the new reaction protocol.

Experimental Section

General Remarks: All reactions were performed in flame-dried Schlenk tubes (Duran glassware, 100 mL, Ø 30 mm) equipped with Teflon stopcocks and magnetic stirring bars (15 × 4.5 mm). Toluene was distilled from molten sodium under argon. Ind_2TiMe_2 was synthesized according to ref.[8] or purchased from MCAT.[9] Diphenylacetylene (**1**) was dissolved in CH_2Cl_2, dried with Na_2SO_4, and recovered by evaporation of the solvent. Alkynes **4**, **7**–**16**, and **36**–**38** were purified by distillation. Methyl- and ethylamine were received from BASF AG (Ludwigshafen). All other reagents were received from commercial sources and were used without further purification. Unless otherwise noted, yields refer to isolated yields of pure compounds as gauged by thin-layer chromatography (TLC), ^1H and ^{13}C NMR spectroscopy. All products were characterized by ^1H NMR, ^{13}C NMR, infrared (IR) spectroscopy, and mass spectrometry (MS). Additional characterization data were obtained by CHN elemental analysis and/or high-resolution mass spectrometry (HRMS). NMR spectra were recorded with the following spectrometers: Bruker Avance ARX 250, Bruker Avance DRX 300, Bruker AC 300, Bruker Avance DRX 400, Bruker Avance DRX 500. All ^1H NMR spectra are reported in δ units ppm relative to the signal for $CDCl_3$ at $\delta = 7.26$ ppm. All ^{13}C NMR spectra are reported in δ units ppm relative to the central line of the triplet for $CDCl_3$ at $\delta = 77.0$ ppm. Infrared spectra were recorded with a Bruker Vector 22 spectrometer using an attenuated total reflection (ATR) method. Mass spectra were recorded with a JEOL JMS-700 or a Finnigan TSQ 700 (EI) spectrometer with an ionization potential of 70 eV. Elemental analyses were carried out with an Elementar Vario EL machine. GC/MS analyses were performed with a Hewlett–Packard HP 5890 Series II gas chromatograph equipped with a Hewlett–Packard HP 5972 Series I Mass Selective Detector. PE: light petroleum ether, b. p. 40–60 °C.

Addition of Methyl- or Ethylamine to Internal Alkynes. General Procedure A: Under Ar, the alkyne (4.0 mmol) and Ind_2TiMe_2 (62 mg, 0.20 mmol, 5.0 mol-%) were placed in a Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar. The Schlenk tube was then connected to a vacuum line operated with gaseous methyl- or ethylamine (instead of argon or nitrogen). After evacuation, the Schlenk tube was flushed with the gaseous amine (1 atm, 3 ×). Then, toluene (2.0 mL) was added and the resulting mixture was stirred under a constant pressure of 1 atm of methyl- or ethylamine at 105 °C for 7 h. The resulting dark brown solution was cooled to room temperature and a mixture of $NaBH_3CN$ (503 mg, 8.0 mmol) and $ZnCl_2$ (543 mg, 4.0 mmol) in methanol (20 mL) was added. After this had been stirred at 25 °C for 16 h, CH_2Cl_2 (50 mL) and saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (50 mL). After extraction, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 × 50 mL) and the combined organic layers were dried with $MgSO_4$. After concentration under vacuum, the crude mixture of regioisomers was analyzed by GC/MS (if applicable) and purified by flash chromatography (SiO_2).

Addition of Methyl- or Ethylamine to Terminal Alkynes. General Procedure B: Under Ar, the alkyne (4.0 mmol) and Ind_2TiMe_2 (62 mg, 0.20 mmol, 5.0 mol-%) were placed in a Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar. The Schlenk tube was then connected to a vacuum line operated with gaseous methyl- or ethylamine (instead of argon or nitrogen). After evacuation, the Schlenk tube was flushed with the gaseous amine (1 atm, 3 ×). Then, toluene (2.0 mL) was added and the resulting mixture was stirred under a constant pressure of 1 atm of methyl- or ethylamine at 80 °C for 7 h. The resulting dark brown solution was cooled to room temperature and a mixture of $NaBH_3CN$ (503 mg, 8.0 mmol) and $ZnCl_2$ (543 mg, 4.0 mmol) in methanol (20 mL) was added. After this had been stirred at 25 °C for 16 h, CH_2Cl_2 (50 mL) and saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (50 mL). After extraction, the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 × 50 mL) and the combined organic layers were dried with $MgSO_4$. After concentration under vacuum, the crude mixture of regioisomers was analyzed by GC/MS and purified by flash chromatography (SiO_2).

Amine 2: General procedure A was used to synthesize amine **2** from diphenylacetylene (**1**) and methylamine. After purification by flash chromatography (PE/EtOAc, 1:1), amine **2** (777 mg, 3.68 mmol, 92 %) was isolated as a colorless oil. ^1H NMR (250 MHz, $CDCl_3$):

δ = 1.49 (br. s, 1 H), 2.21 (s, 3 H), 2.88 (dd, J = 13.2, 8.0 Hz, 1 H), 2.96 (dd, J = 13.2, 5.6 Hz, 1 H), 3.72 (dd, J = 8.3, 5.8 Hz, 1 H), 7.13–7.31 (m, 10 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 34.7 (CH$_3$), 45.2 (CH$_2$), 66.9 (CH), 126.4 (CH), 127.1 (CH), 127.3 (CH), 128.3 (CH), 128.4 (CH), 129.3 (CH), 138.9 (C), 143.5 (C) ppm. IR: $\tilde{\nu}$ = 3084, 3061, 3027, 2972, 2936, 2846, 2789, 1602, 1494, 1474, 1453, 1443, 1353, 1133, 1070, 1029, 758, 700 cm^{-1}. MS (25 °C): m/z (%) = 212 (19) [MH$^+$], 120 (100) [M$^+$ – C$_7$H$_7$], 91 (27) [C$_7$H$_7$$^+$], 77 (8). C$_{15}H_{17}$N (211.3): calcd. C 85.26, H 8.11, N 6.63; found C 85.31, H 8.12, N 6.92.

Amine 3: General procedure A was used to synthesize amine **3** from diphenylacetylene (**1**) and ethylamine. After purification by flash chromatography (PE/EtOAc, 3:1), amine **3** (757 mg, 3.36 mmol, 84%) was isolated as a colorless oil. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.95 (t, J = 7.2 Hz, 3 H), 1.36 (br. s, 1 H), 2.34–2.45 (m, 2 H), 2.87–2.93 (m, 2 H), 3.83 (t, J = 6.6 Hz, 1 H), 7.08–7.28 (m, 10 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 15.3 (CH$_3$), 42.0 (CH$_2$), 45.3 (CH$_2$), 64.9 (CH), 126.3 (CH), 127.0 (CH), 127.3 (CH), 128.3 (CH), 128.4 (CH), 129.3 (CH), 139.0 (C), 144.0 (C) ppm. IR: $\tilde{\nu}$ = 3061, 3026, 2965, 2920, 2868, 2815, 1602, 1494, 1463, 1453, 1143, 1070, 1030, 790, 699 cm^{-1}. MS (25 °C): m/z (%) = 226 (27) [MH$^+$], 134 (100) [M$^+$ – C$_7$H$_8$], 91 (50) [C$_7$H$_7$$^+$], 79 (27), 77 (21). C$_{16}H_{19}$N (225.3): calcd. C 85.29, H 8.50, N 6.22; found C 85.00, H 8.56, N 6.29.

Amine 17a: General procedure A was used to synthesize amine **17a** from 1-(4-methoxyphenyl)-1-propyne (**7**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **17a** (573 mg, 3.20 mmol, 80%) and a mixture of regioisomers **17a** and **17b** (57 mg, 0.32 mmol, 8%) were obtained as colorless oils. **17a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.04 (d, J = 5.9 Hz, 3 H), 1.38 (s, 1 H), 2.39 (s, 3 H), 2.53–2.77 (m, 3 H), 3.79 (s, 3 H), 6.84 (d, J = 8.4 Hz, 2 H), 7.10 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 19.7 (CH$_3$), 34.0 (CH$_3$), 42.6 (CH$_2$), 55.2 (CH), 56.5 (CH$_3$), 113.8 (CH), 130.2 (CH), 131.5 (C), 158.1 (C) ppm. IR: $\tilde{\nu}$ = 3031, 2971, 2834, 2789, 1612, 1513, 1441, 1251, 1178, 1037, 806, 754 cm^{-1}. HRMS (%) calcd. [C$_{11}$H$_{17}$NO$^+$] 179.1310, found 179.1300 (4); calcd. [C$_{11}$H$_{16}$NO$^+$] 178.1232, found 178.1222 (6); calcd. [C$_{10}$H$_{14}$NO$^+$] 164.1075, found 164.1067 (10); calcd. [C$_8$H$_9$O$^+$] 121.0653, found 121.0648 (40); calcd. [C$_6$H$_6$$^+$] 78.0470, found 78.0461 (13); calcd. [C$_3$H$_8$N$^+$] 58.0657, found 58.0643 (100); calcd. [C$_3$H$_7$$^+$] 43.0548, found 43.0557 (23). C$_{11}$H$_{17}$NO (179.3): calcd. C 73.70, H 9.56, N 7.81; found C 73.21, H 9.56, N 7.94.

Amine 18a: General procedure A was used to synthesize amine **18a** from 1-(4-methoxyphenyl)-1-pentyne (**8**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **18a** (480 mg, 2.32 mmol, 58%) and a mixture of regioisomers **18a** and **18b** (84 mg, 0.41 mmol, 10%) were obtained as colorless oils. **18a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.91 (t, J = 6.6 Hz, 3 H), 1.36–1.40 (m, 4 H), 2.37 (s, 3 H), 2.57–2.69 (m, 3 H), 3.79 (s, 3 H), 6.82 (d, J = 8.4 Hz, 2 H), 7.08 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.9 (CH$_3$), 19.5 (CH$_2$), 34.3 (CH$_3$), 36.1 (CH$_2$), 39.9 (CH$_2$), 55.8 (CH$_3$), 61.3 (CH), 114.4 (CH), 130.7 (CH), 132.3 (C), 158.6 (C) ppm. IR: $\tilde{\nu}$ = 3336, 2956, 2931, 2871, 2789, 1612, 1513, 1465, 1352, 1301, 1248, 1038, 834 cm^{-1}. HRMS (%) calcd. [C$_{13}$H$_{21}$NO$^+$] 207.1623, found 207.1591 (1); calcd. [C$_{13}$H$_{20}$NO$^+$] 206.1545, found 206.1521 (4); calcd. [C$_{10}$H$_{14}$NO$^+$] 164.1075, found 164.1079 (33); calcd. [C$_9$H$_{12}$NO$^+$] 150.0919, found 150.0944 (89); calcd. [C$_8$H$_9$O$^+$] 121.0653, found 121.0660 (52); calcd. [C$_5$H$_{12}$N$^+$] 86.0970, found 86.0988 (100). C$_{13}$H$_{21}$NO (207.3): calcd. C 75.31, H 10.21, N 6.76; found C 75.03, H 10.31, N 6.62.

Amine 19a: General procedure A was used to synthesize amine **19a** from 1-(3-methoxyphenyl)-1-pentyne (**9**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 10:1), amine **19a** (489 mg, 2.36 mmol, 59%) and a mixture of regioisomers **19a** and **19b** (130 mg, 0.63 mmol, 16%) were obtained as colorless oils. **19a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.97 (t, J = 7.0 Hz, 3 H), 1.38–1.51 (m, 4 H), 2.42 (s, 3 H), 2.66–2.77 (m, 3 H), 3.85 (s, 3 H), 6.79–6.84 (m, 3 H), 7.17–7.25 (dd, J = 7.7, 7.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.9 (CH$_3$), 19.5 (CH$_2$), 34.3 (CH$_3$), 36.2 (CH$_2$), 41.0 (CH$_2$), 55.7 (CH$_3$), 61.1 (CH), 111.9 (CH), 115.6 (CH), 122.3 (CH), 129.9 (CH), 142.0 (C), 160.2 (C) ppm. IR: $\tilde{\nu}$ = 2956, 2932, 2871, 2835, 2791, 1601, 1584, 1489, 1455, 1261, 1153, 1049, 778, 696 cm^{-1}. HRMS (%) calcd. [C$_{13}$H$_{21}$NO$^+$] 207.1623, found 207.1595 (2); calcd. [C$_{10}$H$_{14}$NO$^+$] 164.1075, found 164.1074 (96); calcd. [C$_8$H$_9$O$^+$] 121.0653, found 121.0662 (45); calcd. [C$_5$H$_{12}$N$^+$] 86.0970, found 86.0980 (100). C$_{13}$H$_{21}$NO (207.3): calcd. C 75.31, H 10.21, N 6.76, O 7.72; found C 75.34, H 10.41, N 6.55.

Amine 20a: General procedure A was used to synthesize amine **20a** from 1-(4-chlorophenyl)-1-propyne (**10**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **20a** (563 mg, 3.06 mmol, 77%) and a mixture of regioisomers **20a** and **20b** (75 mg, 0.41 mmol, 10%) were obtained as colorless oils. **20a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.04 (d, J = 6.3 Hz, 3 H), 1.39 (br. s, 1 H), 2.41 (s, 3 H), 2.55–2.61 (dd, J = 7.0, 6.3 Hz, 1 H), 2.68–2.81 (m, 2 H), 7.11 (d, J = 8.5 Hz, 2 H), 7.27 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 19.5 (CH$_3$), 33.9 (CH$_3$), 42.6 (CH$_2$), 56.2 (CH), 128.5 (CH), 130.6 (CH), 132.0 (C), 137.9 (C) ppm. IR: $\tilde{\nu}$ = 3026, 2967, 2932, 2849, 2790, 1492, 1446, 1407, 1372, 1090, 1016, 800, 666 cm^{-1}. HRMS (%) calcd. [C$_{10}$H$_{14}$N^{35}Cl$^+$] 183.0815, found 183.0737 (11); calcd. [C$_{10}$H$_{13}$N^{37}Cl$^+$] 184.0707, found 184.0714 (66); calcd. [C$_{10}$H$_{13}$N^{35}Cl$^+$] 182.0737, found 182.0714 (22); calcd. [C$_9$H$_{11}$N^{37}Cl$^+$] 170.0551, found 170.0574 (15); calcd. [C$_9$H$_{11}$N^{35}Cl$^+$] 168.0580, found 168.0570 (45); calcd. [C$_7$H$_6$N^{37}Cl$^+$] 127.0129, found 127.0128 (32); calcd. [C$_7$H$_6$N^{35}Cl$^+$] 125.0158, found 125.0128 (95). C$_{10}$H$_{14}$ClN (183.7): C 65.39, H 7.68, N 7.63; found C 65.11, H 7.56, N 7.73.

Amine 21a: General procedure A was used to synthesize amine **21a** from 1-(4-chlorophenyl)-1-pentyne (**11**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **21a** (601 mg, 2.84 mmol, 71%) and a mixture of regioisomers **21a** and **21b** (42 mg, 0.20 mmol, 5%) were obtained as colorless oils. **21a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.89 (t, J = 7.0 Hz, 3 H), 1.15 (br. s, 1 H), 1.34–1.37 (m, 4 H), 2.37 (s, 3 H), 2.60–2.64 (m, 3 H), 7.10 (d, J = 8.1 Hz, 2 H), 7.24 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.3 (CH$_3$), 18.9 (CH$_2$), 33.7 (CH$_3$), 35.5 (CH$_2$), 39.6 (CH$_2$), 60.5 (CH), 128.5 (CH), 130.6 (CH), 131.8 (C), 138.2 (C) ppm. IR: $\tilde{\nu}$ = 3026, 2957, 2931, 2871, 2791, 1492, 1090, 1016, 799 cm^{-1}. HRMS (%) calcd. [C$_{12}$H$_{18}$N^{37}Cl$^+$] 213.1098, found 213.1077 (1); calcd. [C$_{12}$H$_{17}$N^{37}Cl$^+$] 212.1020, found 212.1024 (2); calcd. [C$_{12}$H$_{18}$N^{35}Cl$^+$] 211.1128, found 211.1174 (1); calcd. [C$_{12}$H$_{17}$N^{35}Cl$^+$] 210.1050, found 210.1026 (5); calcd. [C$_9$H$_{11}$N^{37}Cl$^+$] 170.0551, found 170.0536 (39); calcd. [C$_9$H$_{11}$N^{35}Cl$^+$] 168.0580, found 168.0566 (100); calcd. [C$_9$H$_{11}$N$^+$] 133.0891, found 133.0887 (24); calcd. [C$_7$H$_6$N^{37}Cl$^+$] 127.0129, found 127.0145 (24); calcd. [C$_7$H$_6$N^{35}Cl$^+$] 125.0158, found 125.0152 (72); calcd. [C$_5$H$_{12}$N$^+$] 86.0970, found 86.0977 (100). C$_{12}$H$_{18}$ClN (211.7): calcd. C 68.07, H 8.57, N 6.62; found C 67.78, H 8.56, N 6.64.

Amine 22a: General procedure A was used to synthesize amine **22a** from 1-(3-chlorophenyl)-1-pentyne (**12**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **22a** (525 mg, 2.48 mmol, 62%) and a mixture of regioisomers **22a**

and **22b** (88 mg, 0.42 mmol, 9%) were obtained as colorless oils. **22a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.91 (t, J = 7.0 Hz, 3 H), 1.26–1.38 (m, 5 H), 2.38 (s, 3 H), 2.65 (m, 3 H), 7.06 (d, J = 6.6 Hz, 1 H), 7.17–7.19 (m, 3 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.0 (CH$_3$), 18.6 (CH$_2$), 33.5 (CH$_3$), 35.3 (CH$_2$), 39.8 (CH$_2$), 60.2 (CH), 126.0 (CH), 127.3 (CH), 129.1 (CH), 129.3 (CH), 133.9 (C), 141.7 (C) ppm. IR: $\tilde{\nu}$ = 3061, 2957, 2931, 2871, 2792, 1597, 1572, 1476, 1352, 1208, 1082, 883, 779, 700, 684 cm^{-1}. HRMS (%) calcd. $[C_{12}H_{18}N^{37}Cl^+]$ 213.1098, found 213.1046 (1); calcd. $[C_{12}H_{17}N^{37}Cl^+]$ 212.1020, found 212.0987 (2); calcd. $[C_{12}H_{18}N^{35}Cl^+]$ 211.1128, found 211.1063 (1); calcd. $[C_{12}H_{17}N^{35}Cl^+]$ 210.1050, found 210.1061 (7); calcd. $[C_9H_{11}N^{37}Cl^+]$ 170.0551, found 170.0561 (57); calcd. $[C_9H_{11}N^{35}Cl^+]$ 168.0580, found 168.0580 (100); calcd. $[C_7H_6N^{37}Cl^+]$ 127.0129, found 127.0124 (20); calcd. $[C_7H_6N^{35}Cl^+]$ 125.0158, found 125.0143 (64); calcd. $[C_5H_{12}N^+]$ 86.0970, found 86.0949 (100). $C_{12}H_{18}ClN$ (211.7): calcd. C 68.07, H 8.57, N 6.62; found C 67.78, H 8.55, N 6.49.

Amine 23a: General procedure A was used to synthesize amine **23a** from 1-(2-chlorophenyl)-1-pentyne (**13**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **23a** (228 mg, 1.08 mmol, 27%) and mixture of regioisomers **23a** and **23b** (102 mg, 0.48 mmol, 12%) were obtained as colorless oils. **23a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.90 (t, J = 7.0 Hz, 3 H), 1.31–1.46 (m, 5 H), 2.40 (s, 3 H), 2.76–2.90 (m, 3 H), 7.15–7.19 (m, 3 H), 7.30 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.3 (CH$_3$), 18.9 (CH$_2$), 33.7 (CH$_3$), 35.8 (CH$_2$), 38.4 (CH$_2$), 58.9 (CH), 126.6 (CH), 127.6 (CH), 129.6 (CH), 131.6 (CH), 134.3 (C), 137.7 (C) ppm. IR: $\tilde{\nu}$ = 3066, 2957, 2931, 2871, 2793, 1475, 1443, 1052, 750, 682 cm^{-1}. HRMS (%) calcd. $[C_{12}H_{17}N^{37}Cl^+]$ 212.1020. found 212.0992 (4); calcd. $[C_{12}H_{18}N^{35}Cl^+]$ 211.1128, found 211.1048 (2); calcd. $[C_{12}H_{17}N^{35}Cl^+]$ 210.1050, found 210.1040 (9); calcd. $[C_9H_{11}N^{37}Cl^+]$ 170.0551, found 170.0563 (66); calcd. $[C_9H_{11}N^{35}Cl^+]$ 168.0580, found 168.0583 (100); calcd. $[C_7H_6{}^{37}Cl^+]$ 127.0129, found 127.0123 (29); calcd. $[C_7H_6{}^{35}Cl^+]$ 125.0158, found 125.0146 (86); calcd. $[C_5H_{12}N^+]$ 86.0970, found 86.0990 (100). $C_{12}H_{18}ClN$ (211.7): calcd. C 68.07, H 8.57, N 6.62; found C 68.34, H 8.74, N 6.58.

Amine 24a: General procedure A was used to synthesize amine **24a** from 1-(4-methylphenyl)-1-pentyne (**14**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **24a** (536 mg, 2.80 mmol, 70%) and mixture of regioisomers **24a** and **24b** (53 mg, 0.28 mmol, 7%) were obtained as colorless oils. **24a:** ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.84 (t, J = 6.7 Hz, 3 H), 1.20–1.38 (m, 5 H), 2.24 (s, 3 H), 2.29 (s, 3 H), 2.45–2.70 (m, 3 H), 6.98 (d, J = 8.6 Hz, 2 H), 7.02 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, DEPT, CDCl$_3$): δ = 14.3 (CH$_3$), 18.8 (CH$_2$), 20.9 (CH$_3$), 33.7 (CH$_3$), 35.5 (CH$_2$), 39.8 (CH$_2$), 60.6 (CH), 129.0 (CH), 129.1 (CH), 135.4 (C), 136.5 (C) ppm. IR: $\tilde{\nu}$ = 3003, 2957, 2930, 2871, 2789, 1515, 1454, 1378, 1352, 1142, 1096, 823, 800 cm^{-1}. HRMS (%) calcd. $[C_{13}H_{21}N^+]$ 191.1674, found 191.1666 (1); calcd. $[C_{13}H_{20}N^+]$ 190.1596, found 190.1589 (5); calcd. $[C_{10}H_{14}N^+]$ 148.1126, found 148.1138 (76); calcd. $[C_9H_{11}N^+]$ 133.0891, found 133.0878 (12); calcd. $[C_8H_9{}^+]$ 105.0704, found 105.0686 (46); calcd. $[C_5H_{12}N^+]$ 86.0970, found 86.0974 (100); calcd. $[C_2H_6N^+]$ 44.0500, found 44.0511 (30). $C_{13}H_{21}N$ (191.3): calcd. C 81.61, H 11.06, N 7.32; found C 81.53, H 10.79, N 7.44.

Amines 25a/25b: General procedure A was used to synthesize amines **25a** and **25b** from 1-phenyl-2-cyclopropylethyne (**15**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **25a** (336 mg, 1.92 mmol, 48%) and amine **25b** (119 mg, 0.68 mmol, 17%) were obtained as colorless oils. **25a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = –0.06 to 0.02 (m, 1 H), 0.22–0.30 (m, 1 H), 0.37–0.46 (m, 1 H), 0.53–0.72 (m, 2 H), 1.36 (br. s, 1 H), 1.80–1.88 (dt, J = 8.8, 5.2 Hz, 1 H), 2.45 (s, 3 H), 2.75 (dd, J = 13.6, 8.1 Hz, 1 H), 2.91 (dd, J = 13.6, 5.2 Hz, 1 H), 7.19–7.31 (m, 5 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 1.7 (CH$_2$), 4.9 (CH$_2$), 15.7 (CH), 34.7 (CH$_3$), 41.8 (CH$_2$), 66.6 (CH), 126.1 (CH), 128.3 (CH), 129.4 (CH), 139.5 (C) ppm. IR: $\tilde{\nu}$ = 3076, 3026, 3000, 2939, 2849, 2787, 1603, 1494, 1453, 1140, 1073, 741, 699 cm^{-1}. HRMS (%) calcd. $[C_{12}H_{17}N^+]$ 175.1361, found 175.1323 (2); calcd. $[C_{12}H_{16}N^+]$ 174.1283, found 174.1299 (5); calcd. $[C_9H_{12}N^+]$ 134.0907, found 134.0975 (46); calcd. $[C_8H_{10}N^+]$ 120.0813, found 120.0801 (21); calcd. $[C_7H_7{}^+]$ 91.0548, found 91.0575 (100); calcd. $[C_5H_{10}N^+]$ 84.0813, found 84.0840 (100). **25b:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = –0.13 to –0.05 (m, 1 H), –0.01 to 0.07 (m, 1 H), 0.27–0.42 (m, 2 H), 0.46–0.54 (m, 1 H), 1.39–1.48 (m, 1 H), 1.61–1.69 (m, 1 H), 2.23 (s, 3 H), 3.54 (t, J = 6.6 Hz, 1 H), 7.18–7.28 (m, 5 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 4.1 (CH$_2$), 4.6 (CH$_2$), 8.2 (CH), 34.3 (CH$_3$), 43.0 (CH$_2$), 66.0 (CH), 127.0 (CH), 127.3 (CH), 128.3 (CH), 143.6 (C) ppm. IR: $\tilde{\nu}$ = 3076, 3000, 2924, 2850, 2789, 1602, 1475, 1136, 1017, 753, 701 cm^{-1}. HRMS (%) calcd. $[C_{12}H_{17}N^+]$ 175.1361, found 175.1360 (1); calcd. $[C_{10}H_{14}N^+]$ 148.1126, found 148.1138 (11); calcd. $[C_9H_{12}N^+]$ 134.0970, found 134.0964 (17); calcd. $[C_8H_{10}N^+]$ 120.0813, found 120.0815 (100); calcd. $[C_6H_{12}N^+]$ 98.0970, found 98.0963 (14); calcd. $[C_7H_7{}^+]$ 91.0548, found 91.0554 (18); calcd. $[C_5H_{10}N^+]$ 84.0813, found 84.0823 (13).

Amines 26a/26b: General procedure A was used to synthesize amines **26a** and **26b** from 1-(3-methoxyphenyl)-2-cyclopropylethyne (**16**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **26a** (465 mg, 2.26 mmol, 57%) and amine **26b** (93 mg, 0.45 mmol, 11%) were obtained as colorless oils. **26a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = –0.04 to 0.04 (m, 1 H), 0.23–0.31 (m, 1 H), 0.38–0.47 (m, 1 H), 0.54–0.74 (m, 2 H), 1.53 (br. s, 1 H), 1.84 (dd, J = 8.5, 3.7 Hz, 1 H), 2.44 (s, 3 H), 2.72 (dd, J = 13.2, 8.1 Hz, 1 H), 2.90 (dd, J = 13.6, 4.8 Hz, 1 H), 3.79 (s, 3 H), 6.74–6.80 (m, 3 H), 7.20 (dd, J = 8.8, 7.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 1.6 (CH$_2$), 5.1 (CH$_2$), 15.7 (CH), 34.6 (CH$_3$), 42.0 (CH$_2$), 55.1 (CH$_3$), 66.4 (CH), 111.4 (CH), 115.1 (CH), 121.8 (CH), 129.2 (CH), 141.1 (C), 159.6 (C) ppm. IR: $\tilde{\nu}$ = 3333, 3073, 2999, 2941, 2835, 2787, 1601, 1584, 1488, 1260, 1153, 1050, 697 cm^{-1}. HRMS (%) calcd. $[C_{13}H_{19}NO^+]$ 205.1467, found 205.1480 (1); calcd. $[C_{13}H_{18}NO^+]$ 204.1388, found 204.1397 (2); calcd. $[C_9H_{13}NO^+]$ 151.0997, found 151.0967 (62); calcd. $[C_9H_{12}NO^+]$ 150.0919, found 150.0929 (100); calcd. $[C_5H_{10}N^+]$ 84.0813, found 84.0830 (27). $C_{13}H_{19}NO$ (205.3): calcd. C 76.06, H 9.33, N 6.82; found C 75.54, H 9.42, N 6.88. **26b:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = –0.04 to –0.02 (m, 1 H), –0.01 to 0.02 (m, 1 H), 0.06–0.45 (m, 2 H), 0.55–0.60 (m, 1 H), 1.39–1.48 (m, 1 H), 1.62–1.71 (m, 2 H), 2.29 (s, 3 H), 3.55 (t, J = 6.6 Hz, 1 H), 3.81 (s, 3 H), 6.76–6.80 (m, 1 H), 6.87–6.90 (m, 2 H), 7.21 (d, J = 7.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 4.1 (CH$_2$), 4.7 (CH$_2$), 8.2 (CH), 34.6 (CH$_3$), 43.2 (CH$_2$), 55.2 (CH$_3$), 66.1 (CH), 112.2 (CH), 112.7 (CH), 119.7 (CH), 129.2 (CH), 146.0 (C), 159.7 (C) ppm. IR: $\tilde{\nu}$ = 3338, 3076, 2998, 2935, 2835, 2787, 1599, 1486, 1256, 1148, 1046, 783, 701 cm^{-1}. HRMS (%) calcd. $[C_{13}H_{19}NO^+]$ 205.1467, found 205.1435 (1); calcd. $[C_{13}H_{18}NO^+]$ 204.1388, found 204.1374 (3); calcd. $[C_9H_{13}NO^+]$ 151.0997, found 151.0961 (86); calcd. $[C_9H_{12}NO^+]$ 150.0919, found 150.0944 (100); calcd. $[C_8H_9NO^+]$ 135.0684, found 135.0659 (12); calcd. $[C_8H_9O^+]$ 121.0653, found 121.0650 (10); calcd. $[C_7H_9N^+]$ 107.0735, found 107.0738 (16).

Amine 27a: General procedure A was used to synthesize amine **27a** from 1-(4-methoxyphenyl)-1-propyne (**7**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 1:1), amine **27a**

(595 mg, 3.08 mmol, 77%) and a mixture of regioisomers **27a** and **27b** (33 mg, 0.17 mmol, 4%) were obtained as colorless oils. **27a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.01 (t, J = 6.2 Hz, 3 H), 1.04 (d, J = 7.1 Hz, 3 H), 2.54–2.58 (q, J = 6.1 Hz, 2 H), 2.61–2.66 (dd, J = 7.4, 7.0 Hz, 2 H), 2.81–2.89 (m, 1 H), 3.76 (s, 3 H), 6.80 (d, J = 8.6 Hz, 2 H), 7.06 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 15.4 (CH$_3$), 20.2 (CH$_3$), 41.5 (CH$_2$), 42.7 (CH$_3$), 54.6 (CH), 55.1 (CH$_3$), 113.7 (CH), 130.1 (CH), 131.5 (C), 158.0 (C) ppm. IR: $\tilde{\nu}$ = 2963, 2930, 2834, 1612, 1512, 1464, 1301, 1247, 1177, 1125, 1037, 808 cm^{-1}. MS (25 °C): m/z (%) = 194 (100) [MH$^+$], 164 (24) [M$^+$ – C$_2$H$_6$], 121 (18) [M$^+$ – C$_4$H$_{10}$N], 91 (4) [C$_7$H$_7$], 72 (69) [C$_4$H$_{10}$N]. C$_{12}$H$_{19}$NO (193.3): calcd. C 74.57, H 9.91, N 7.25; found C 74.09, H 10.08, N 7.25.

Amine 28a: General procedure A was used to synthesize amine **28a** from 1-(4-methoxyphenyl)-1-pentyne (**8**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 10:1), amine **28a** (575 mg, 2.60 mmol, 65%) and a mixture of regioisomers **28a** and **28b** (71 mg, 0.32 mmol, 8%) were obtained. **28a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.90 (t, J = 6.6 Hz, 3 H), 1.03 (t, J = 7.3 Hz, 3 H), 1.36–1.39 (m, 4 H), 2.53–2.71 (m, 5 H), 3.79 (s, 3 H), 6.81 (d, J = 8.5 Hz, 2 H), 7.08 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.3 (CH$_3$), 15.5 (CH$_3$), 19.0 (CH$_2$), 36.2 (CH$_2$), 39.9 (CH$_2$), 41.4 (CH$_2$), 55.2 (CH$_3$), 59.0 (CH), 113.8 (CH), 130.1 (CH), 131.8 (C), 157.9 (C) ppm. IR: $\tilde{\nu}$ = 3320, 2957, 2931, 2871, 2836, 1612, 1513, 1465, 1301, 1248, 1039, 834, 807 cm^{-1}. HRMS (%) calcd. [C$_{14}$H$_{23}$NO$^+$] 221.1780, found 221.1730 (2); calcd. [C$_{14}$H$_{22}$NO$^+$] 220.1701, found 220.1716 (7); calcd. [C$_{11}$H$_{16}$NO$^+$] 178.1232, found 178.1222 (57); calcd. [C$_{10}$H$_{14}$NO$^+$] 164.1075, found 164.1068 (40); calcd. [C$_8$H$_9$O$^+$] 121.0653, found 121.0649 (100); calcd. [C$_6$H$_{14}$N$^+$] 100.1126, found 100.1117 (100). C$_{14}$H$_{23}$ON (221.3): calcd. C 75.97, H 10.47, N 6.33; found C 76.08, H 10.76, N 6.48.

Amine 29a: General procedure A was used to synthesize amine **29a** from 1-(3-methoxyphenyl)-1-pentyne (**9**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 10:1), amine **29a** (442 mg, 2.00 mmol, 50%) and a mixture of regioisomers **29a** and **29b** (168 mg, 0.76 mmol, 19%) were obtained as colorless oils. **29a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.89 (t, J = 6.9 Hz, 3 H), 1.03 (t, J = 7.2 Hz, 3 H), 1.34–1.42 (m, 4 H), 2.51–2.75 (m, 5 H), 3.79 (s, 3 H), 6.73 (s, 1 H), 6.73–6.78 (m, 3 H), 7.17 (dd, J = 7.6, 7.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.1 (CH$_3$), 15.3 (CH$_3$), 18.8 (CH$_2$), 36.0 (CH$_2$), 40.7 (CH$_2$), 41.1 (CH$_2$), 54.9 (CH$_3$), 58.7 (CH), 111.1 (CH), 114.8 (CH), 121.5 (CH), 129.1 (CH) ppm. IR: $\tilde{\nu}$ = 2957, 2931, 2871, 2834, 1601, 1584, 1489, 1466, 1455, 1437, 1260, 1165, 1050, 778, 697 cm^{-1}. HRMS (%) calcd. [C$_{14}$H$_{23}$NO$^+$] 221.1780, found 221.1794 (2); calcd. [C$_{11}$H$_{16}$NO$^+$] 178.1232, found 178.1228 (100); calcd. [C$_8$H$_9$O$^+$] 121.0653, found 121.0662 (45); calcd. [C$_6$H$_{14}$N$^+$] 100.1126, found 100.1110 (100). C$_{14}$H$_{23}$NO (221.3): calcd. C 75.97, H 10.47, N 6.33; found C 75.60, H 10.49, N 6.58.

Amine 30a: General procedure A was used to synthesize amine **30a** from 1-(4-chlorophenyl)-1-propyne (**10**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 10:1), amine **30a** (569 mg, 2.88 mmol, 72%) and a mixture of regioisomers **30a** and **30b** (111 mg, 0.56 mmol, 14%) were obtained as colorless oils. **30a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.04–1.11 (m, 6 H), 1.50 (br. s, 1 H), 2.54–2.61 (q, J = 6.6 Hz, 2 H), 2.71–2.78 (dd, J = 13.2, 6.3 Hz, 2 H), 2.89–2.91 (m, 1 H), 7.11 (d, J = 8.1 Hz, 2 H), 7.28 (d, J = 8.1 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 15.4 (CH$_3$), 20.1 (CH$_3$), 41.5 (CH$_2$), 42.9 (CH$_2$), 54.5 (CH), 128.5 (CH), 130.6 (CH), 132.0 (C), 138.0 (C) ppm. IR: $\tilde{\nu}$ = 3297, 2966, 2926, 2869, 2816, 1492, 1455, 1407, 1374, 1134, 1090, 1016, 835, 731, 715, 665 cm^{-1}. HRMS (%) calcd. [C$_{11}$H$_{16}$N^{37}Cl$^+$] 199.0942, found 199.0935 (1); calcd. [C$_{11}$H$_{15}$N^{37}Cl$^+$] 198.0864, found 198.0873 (5); calcd. [C$_{11}$H$_{16}$N^{35}Cl$^+$] 197.0927, found 197.0916 (2); calcd. [C$_{11}$H$_{15}$N^{35}Cl$^+$] 196.0893, found 196.0873 (17); calcd. [C$_{10}$H$_{13}$N^{37}Cl$^+$] 184.0707, found 184.0714 (14); calcd. [C$_{10}$H$_{13}$N^{35}Cl$^+$] 182.0737, found 182.0736 (41); calcd. [C$_7$H$_6$N^{37}Cl$^+$] 127.0129, found 127.0119 (32); calcd. [C$_7$H$_6$N^{35}Cl$^+$] 125.0158, found 125.0140 (100); calcd. [C$_7$H$_7$$^+$] 91.0548, found 91.0561 (21); calcd. [C$_7$H$_5$$^+$] 89.0391, found 89.0400 (34); calcd. [C$_4$H$_{10}$N$^+$] 72.0813, found 72.0816 (100); calcd. [C$_2$H$_6$N$^+$] 44.0500, found 44.0519 (77). C$_{11}$H$_{16}$ClN (197.7): C 66.83, H 8.16, N 7.08; found C 66.57, H 8.35, N 7.30.

Amine 31a: General procedure A was used to synthesize amine **31a** from 1-(4-chlorophenyl)-1-pentyne (**11**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **31a** (632 mg, 2.80 mmol, 70%) and a mixture of regioisomers **31a** and **31b** (34 mg, 0.15 mmol, 4%) were obtained as colorless oils. **31a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.90 (t, J = 6.6 Hz, 3 H), 1.00 (t, J = 7.0 Hz, 3 H), 1.34–1.36 (m, 4 H), 2.57–2.72 (m, 5 H), 7.08 (d, J = 8.5 Hz, 2 H), 7.23 (d, J = 6.25 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.3 (CH$_3$), 15.5 (CH$_3$), 19.0 (CH$_2$), 36.2 (CH$_2$), 40.2 (CH$_2$), 41.4 (CH$_2$), 58.9 (CH), 128.4 (CH), 130.6 (CH), 131.8 (C), 138.3 (C) ppm. IR: $\tilde{\nu}$ = 2958, 2930, 2876, 1865, 1597, 1492, 1466, 1133, 1092, 1016, 833, 801, 745, 716, 665, 538 cm^{-1}. HRMS (%) calcd. [C$_{13}$H$_{20}$N^{37}Cl$^+$] 227.1255, found 227.1189 (1); calcd. [C$_{13}$H$_{19}$N^{37}Cl$^+$] 226.1177, found 226.1165 (2); calcd. [C$_{13}$H$_{20}$N^{35}Cl$^+$] 225.1284, found 225.1244 (1); calcd. [C$_{13}$H$_{19}$N^{35}Cl$^+$] 224.1206, found 224.1185 (8); calcd. [C$_{10}$H$_{13}$N^{37}Cl$^+$] 184.0707, found 184.0685 (41); calcd. [C$_{10}$H$_{13}$N^{35}Cl$^+$] 182.0737, found 182.0706 (100); calcd. [C$_7$H$_6$N^{37}Cl$^+$] 127.0129, found 127.0155 (32); calcd. [C$_7$H$_6$N^{35}Cl$^+$] 125.0158, found 125.0153 (94); calcd. [C$_6$H$_{14}$N$^+$] 100.1126, found 100.1129 (100). C$_{13}$H$_{20}$ClN (225.8): calcd. C 69.16, H 8.93, N 6.20; found C 68.97, H 8.98, N 6.40.

Amine 32a: General procedure A was used to synthesize amine **32a** from 1-(3-chlorophenyl)-1-pentyne (**12**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **32a** (611 mg, 2.71 mmol, 68%) and a mixture of regioisomers **32a** and **32b** (73 mg, 0.32 mmol, 8%) were obtained as colorless oils. **32a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.89 (t, J = 6.6 Hz, 3 H), 1.04 (t, J = 7.2 Hz, 3 H), 1.33–1.38 (m, 4 H), 2.58–2.74 (m, 5 H), 7.04 (d, J = 6.6 Hz, 1 H), 7.16–7.20 (m, 3 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.0 (CH$_3$), 15.3 (CH$_3$), 18.7 (CH$_2$), 35.9 (CH$_2$), 40.4 (CH$_2$), 41.1 (CH$_2$), 58.6 (CH), 126.0 (CH), 127.3 (CH), 129.1 (CH), 129.3 (CH), 133.9 (C), 141.8 (C) ppm. IR: $\tilde{\nu}$ = 2958, 2930, 2871, 1597, 1572, 1476, 1428, 1379, 1208, 1135, 1082, 999, 884, 780, 701, 684, 666 cm^{-1}. HRMS (%) calcd. [C$_{13}$H$_{20}$N^{37}Cl$^+$] 227.1284, found 227.1251 (1); calcd. [C$_{13}$H$_{19}$N^{37}Cl$^+$] 226.1177, found 226.1146 (2); calcd. [C$_{13}$H$_{20}$N^{35}Cl$^+$] 225.1284, found 225.1245 (1); calcd. [C$_{13}$H$_{19}$N^{35}Cl$^+$] 224.1206, found 224.1202 (5); calcd. [C$_{10}$H$_{13}$N^{37}Cl$^+$] 184.0707, found 184.0706 (34); calcd. [C$_{10}$H$_{13}$N^{35}Cl$^+$] 182.0737, found 182.0716 (100); calcd. [C$_7$H$_6$N^{37}Cl$^+$] 127.0129, found 127.0154 (15); calcd. [C$_7$H$_6$N^{35}Cl$^+$] 125.0158, found 125.0157 (52); calcd. [C$_6$H$_{14}$N$^+$] 100.1126, found 100.1121 (100). C$_{13}$H$_{20}$ClN (225.8): calcd. C 69.16, H 8.93, N 6.20; found C 69.16, H 8.99, N 6.30.

Amine 33a: General procedure A was used to synthesize amine **33a** from 1-(2-chlorophenyl)-1-pentyne (**13**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 10:1), amine **33a** (302 mg, 1.34 mmol, 33%) and a mixture of regioisomers **33a** and **33b** (103 mg, 0.46 mmol, 12%) were obtained as colorless oils. **33a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.90 (t, J = 7.0 Hz, 3 H), 1.04

(t, J = 7.0 Hz, 3 H), 1.29–1.49 (m, 4 H), 2.55–2.71 (m, 2 H), 2.76–2.90 (m, 3 H), 7.14–7.22 (m, 3 H), 7.32 (d, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 14.3 (CH_3), 15.6 (CH_3), 19.0 (CH_2), 36.5 (CH_2), 39.0 (CH_2), 41.4 (CH_2), 57.2 (CH), 126.6 (CH), 127.5 (CH), 129.6 (CH), 131.6 (CH), 134.3 (C), 137.7 (C) ppm. IR: $\tilde{\nu}$ = 3066, 2959, 2930, 2871, 1474, 1444, 1138, 1052, 1038, 750, 682 cm^{-1}. HRMS (%) calcd. [$C_{13}H_{19}N^{37}Cl^+$] 226.1177, found 226.1162 (2); calcd. [$C_{13}H_{19}N^{35}Cl^+$] 224.1206, found 224.1221 (5); calcd. [$C_{10}H_{13}N^{37}Cl^+$] 184.0707, found 184.0704 (31); calcd. [$C_{10}H_{13}N^{35}Cl^+$] 182.0737, found 182.0720 (98); calcd. [$C_7H_6{}^{37}Cl^+$] 127.0129, found 127.0145 (17); calcd. [$C_7H_6{}^{35}Cl^+$] 125.0158, found 125.0151 (50); calcd. [$C_6H_{14}N^+$] 100.1120, found 100.1123 (100). $C_{13}H_{20}ClN$ (225.13): calcd. C 69.16, H 8.93, N 6.20; found C 69.51, H 8.85, N 6.50.

Amines 34a/34b: General procedure A was used to synthesize amines **34a** and **34b** from 1-phenyl-2-cyclopropylethyne (**15**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **34a** (333 mg, 1.76 mmol, 44%) and amine **34b** (128 mg, 0.68 mmol, 14%) were obtained as colorless oils. **34a:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.08 to 0.00 (m, 1 H), 0.19–0.27 (m, 1 H), 0.36–0.45 (m, 1 H), 0.50–0.59 (m, 1 H), 0.67–0.78 (m, 1 H), 1.05 (t, J = 7.0 Hz, 3 H), 1.76 (br. s, 1 H), 1.94–2.01 (m, 1 H), 2.59 (dq, J = 11.4, 7.4 Hz, 1 H), 2.76–2.94 (m, 2 H), 7.19–7.31 (m, 5 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 2.2 (CH_2), 4.8 (CH_2), 15.4 (CH_3), 16.1 (CH), 42.0 (CH_2), 65.0 (CH), 126.1 (CH), 128.3 (CH), 129.4 (CH), 139.5 (C) ppm. IR: $\tilde{\nu}$ = 3076, 3063, 3026, 3000, 2967, 2922, 2869, 2848, 2805, 1603, 1494, 1453, 1141, 1031, 1019, 766, 699 cm^{-1}. HRMS (%) calcd. [$C_{13}H_{19}N^+$] 189.1517, found 189.1520 (1); calcd. [$C_{12}H_{16}N^+$] 174.1283, found 174.1296 (2); calcd. [$C_{11}H_{14}N^+$] 160.1126, found 160.1094 (3); calcd. [$C_{10}H_{14}N^+$] 148.1126, found 148.1133 (23); calcd. [$C_9H_{12}N^+$] 134.0970, found 134.0957 (57); calcd. [$C_6H_{12}N^+$] 98.0970, found 98.0988 (100); calcd. [$C_7H_7{}^+$] 91.0548, found 91.0540 (75). $C_{13}H_{19}N$ (189.3): calcd. C 82.48, H 10.12, N 7.40; found C 82.31, H 10.20, N 7.69. **34b:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.12 to –0.05 (m, 1 H), 0.00–0.07 (m, 1 H), 0.24–0.42 (m, 2 H), 0.45–0.55 (m, 1 H), 1.02 (t, J = 7.4 Hz, 3 H), 1.36–1.45 (m, 2 H), 1.60–1.68 (m, 1 H), 2.44 (dq, J = 8.9, 7.4 Hz, 2 H), 3.66 (t, J = 7.0 Hz, 1 H), 7.16–7.27 (m, 5 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 4.1 (CH_2), 4.6 (CH_2), 8.2 (CH), 15.4 (CH_3), 42.0 (CH_2), 43.4 (CH_2), 64.0 (CH), 126.8 (CH), 127.2 (CH), 128.2 (CH), 144.7 (C) ppm. IR: $\tilde{\nu}$ = 3076, 3024, 2966, 2920, 2840, 1602, 1492, 1453, 1133, 1016, 753, 701 cm^{-1}. HRMS (%) calcd. [$C_{13}H_{19}N^+$] 189.1517, found 189.1498 (1); calcd. [$C_9H_{13}N^+$] 135.1048, found 135.0999 (96); calcd. [$C_9H_{12}N^+$] 134.0970, found 134.0941 (100); calcd. [$C_7H_8N^+$] 106.0657, found 106.0639 (23); calcd. [$C_7H_6N^+$] 104.0500, found 104.0497 (19); calcd. [$C_7H_7{}^+$] 91.0548, found 91.0549 (47); calcd. [$C_6H_7{}^+$] 79.0548, found 79.0564 (36). $C_{13}H_{19}N$ (189.3): calcd. C 82.48, H 10.12, N 7.40; found C 82.05, H 9.90, N 7.70.

Amines 35a/35b: General procedure A was used to synthesize amines **35a** and **35b** from 1-(3-methoxyphenyl)-2-cyclopropylethyne (**16**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 10:1), amine **35a** (412 mg, 1.88 mmol, 47%) and amine **35b** (88 mg, 0.40 mmol, 10%) were obtained as colorless oils. **35a:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.05 to 0.03 (m, 1 H), 0.20–0.28 (m, 1 H), 0.37–0.46 (m, 1 H), 0.51–0.60 (m, 1 H), 0.66–0.77 (m, 1 H), 1.04 (t, J = 7.0 Hz, 3 H), 1.40 (br. s, 1 H), 1.91–1.99 (dd, J = 5.1 Hz, 3.6 Hz, 1 H), 2.53–2.59 (dd, J = 7.1 Hz, 4.1 Hz, 1 H), 2.70–2.86 (m, 3 H), 3.80 (s, 3 H), 6.75–6.76 (m, 3 H), 7.17–7.22 (m, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 2.2 (CH_2), 5.1 (CH_2), 15.7 (CH_3), 16.4 (CH), 42.3 (CH_2), 42.4 (CH_2), 55.3 (CH_3), 65.0 (CH), 111.6 (CH), 115.3 (CH), 122.0 (CH), 129.4 (CH), 141.3 (C), 159.8 (C) ppm. IR**:** $\tilde{\nu}$ = 2999, 2961, 2937, 2834, 1601, 1584, 1488, 1466, 1454, 1437, 11260, 1153, 1048, 1019, 783, 736, 696 cm^{-1}. HRMS (%) calcd. [$C_{14}H_{21}NO^+$] 219.1623, found 219.1544 (1); calcd. [$C_{11}H_{16}NO^+$] 178.1232, found 178.1222 (25); calcd. [$C_8H_9O^+$] 121.0653, found 121.0648 (71); calcd. [$C_6H_{12}N^+$] 98.0970, found 98.0948 (100); calcd. [$C_4H_{10}N^+$] 72.0813, found 72.0829 (66); calcd. [$C_4H_8N^+$] 70.0657, found 70.0680 (38). $C_{14}H_{21}NO$ (219.3): C 76.67, H 9.65, N 6.39; found C 76.41, H 9.58, N 6.59. **35b:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.07 to 0.01 (m, 1 H), 0.04–0.12 (m, 1 H), 0.30–0.47 (m, 2 H), 0.51–0.60 (m, 1 H), 1.07 (t, J = 7.2 Hz, 3 H), 1.38–1.48 (m, 1 H), 1.64–1.73 (m, 1 H), 2.49 (q, J = 7.1 Hz, 2 H), 3.67 (t, J = 6.9 Hz, 1 H), 3.80 (s, 3 H), 6.75 (d, J = 6.7 Hz, 1 H), 6.88 (s, 1 H), 6.90 (d, J = 6.8 Hz, 1 H), 7.19 (m, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 4.1 (CH_2), 4.6 (CH_2), 8.3 (CH), 15.4 (CH_3), 42.0 (CH_2), 43.3 (CH_2), 55.2 (CH_3), 64.0 (CH), 112.1 (CH), 112.7 (CH), 119.7 (CH), 129.1 (CH), 146.5 (C), 159.7 (C) ppm. IR: $\tilde{\nu}$ = 2999, 2962, 2919, 2834, 1599, 1486, 1465, 1260, 1047, 783, 701 cm^{-1}. HRMS (%) calcd. [$C_{14}H_{21}NO^+$] 219.1623, found 219.1601 (2); calcd. [$C_{14}H_{20}NO^+$] 218.1545, found 218.1559 (9); calcd. [$C_{10}H_{14}NO^+$] 164.1075, found 164.1090 (100); calcd. [$C_{10}H_{12}NO^+$] 162.0919, found 162.0923 (28); calcd. [$C_9H_{10}NO^+$] 148.0762, found 148.0790 (25); calcd. [$C_8H_9O^+$] 121.0653, found 121.0631 (63); calcd. [$C_7H_7{}^+$] 91.0548, found 91.0541 (29); calcd. [$C_6H_5{}^+$] 77.0391, found 77.0421 (31).

Amines 39a/39b: General procedure B was used to synthesize amines **39a** and **39b** from 4-methoxyphenylacetylene (**36**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **39a** (156 mg, 0.87 mmol, 22%) and amine **39b** (150 mg, 0.84 mmol, 21%) were obtained as colorless oils. **39a:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, J = 7.1 Hz, 3 H), 1.23 (br. s, 1 H), 2.66 (q, J = 7.1 Hz, 2 H), 2.75 (br. t, J = 7.1 Hz, 2 H), 2.85 (br. t, J = 6.5 Hz, 2 H), 3.78 (s, 3 H), 6.83 (d, J = 8.5 Hz, 2 H), 7.12 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 15.2 (CH_3), 35.5 (CH_2), 44.0 (CH_2), 51.2 (CH), 55.2 (CH_3), 113.9 (CH), 129.6 (CH), 132.2 (C), 158.0 (C) ppm. IR: $\tilde{\nu}$ = 2962, 2934, 2834, 1612, 1513, 1464, 1300, 1247, 1178, 1129, 1038, 822 cm^{-1}. HRMS (%) calcd. [$C_{11}H_{17}NO^+$] 179.1310, found 179.1314 (11); calcd. [$C_{10}H_{14}NO^+$] 164.1075, found 164.1080 (14); calcd. [$C_9H_{11}O^+$] 135.0810, found 135.0784 (19); [$C_8H_{10}O^+$] 122.0732, found 122.0743 (90); [$C_7H_7{}^+$] 91.0548, found 91.0563 (14); [$C_6H_6{}^+$] 78.0470, found 78.0477 (15); [$C_6H_5{}^+$] 77.0391, found 77.0397 (15). $C_{11}H_{17}NO$ (179.3): calcd. C 73.70, H 9.56, N 7.81; found C 73.28, H 9.28, N 7.88. **39b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.1 Hz, 3 H), 1.35 (d, J = 6.6 Hz, 3 H), 2.43–2.56 (m, 2 H), 3.73 (q, J = 6.5 Hz, 1 H), 3.80 (s, 3 H), 6.86 (d, J = 8.7 Hz, 2 H), 7.23 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 15.4 (CH_3), 24.2 (CH_3), 41.9 (CH_2), 55.2 (CH_3), 57.6 (CH), 113.7 (CH), 127.5 (CH), 137.9 (C), 158.5 (C) ppm. IR: $\tilde{\nu}$ = 2962, 2834, 1611, 1512, 1464, 1301, 1244, 1177, 1037, 832, 557 cm^{-1}. HRMS (%) calcd. [$C_{11}H_{17}NO^+$] 179.1310, found 179.1307 (4); calcd. [$C_{11}H_{16}NO^+$] 178.1232, found 178.1211 (3); calcd. [$C_{10}H_{14}NO^+$] 164.1075, found 164.1069 (100); calcd. [$C_9H_{11}O^+$] 135.0810, found 135.0793 (20). $C_{11}H_{17}NO$ (179.3): calcd. C 73.70, H 9.56, N 7.81; found C 74.11, H 9.92, N 7.33.

Amines 40a/40b: General procedure B was used to synthesize amines **40a** and **40b** from 4-chlorophenylacetylene (**37**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1), amine **40a** (120 mg, 0.65 mmol, 16%) and a mixture of regioisomers **40a** and **40b** (191 mg, 1.04 mmol, 26%) were obtained as colorless oils. **40a:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, J = 7.1 Hz, 3 H), 2.01 (br. s, 1 H), 2.69 (q, J = 7.2 Hz, 2 H), 2.77–2.92 (m, 4 H), 7.15 (d, J = 8.4 Hz, 2 H), 7.28 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 15.0 (CH_3), 35.6 (CH_2), 43.9 (CH_2), 50.72 (CH_2), 128.6 (CH), 130.0 (CH), 131.9 (C), 138.4 (C) ppm. IR: ṽ = 3025, 2967, 2926, 2816, 1492, 1092, 1015, 781 cm^{-1}. HRMS (%) calcd. [$C_{10}H_{14}N^{37}Cl^+$] 185.0785, found 185.0746 (2); calcd. [$C_{10}H_{13}N^{37}Cl^+$] 184.0707, found 184.0686 (5); calcd. [$C_{10}H_{14}N^{35}Cl^+$] 183.0815, found 183.0767 (5); calcd. [$C_{10}H_{13}N^{35}Cl^+$] 182.0737, found 182.0720 (15); calcd. [$C_8H_8{}^{37}Cl^+$] 141.0285, found 141.0299 (18); calcd. [$C_8H_8{}^{35}Cl^+$] 139.0315, found 139.0309 (54); calcd. [$C_7H_6{}^{37}Cl^+$] 127.0129, found 127.0143 (23); calcd. [$C_7H_6{}^{35}Cl^+$] 125.0158, found 125.0157 (72); calcd. [$C_8H_7{}^+$] 103.0548, found 103.0540 (63); calcd. [$C_7H_7{}^+$] 91.0548, found 91.0543 (23); calcd. [$C_7H_5{}^+$] 89.0391, found 89.0387 (46); calcd. [$C_3H_8N^+$] 58.0657, found 58.0659 (100); calcd. [CH_4N^+] 30.0344, found 30.0351 (100).

Amines 41a/41b: General procedure B was used to synthesize amines **41a** and **41b** from 1-dodecyne (**38**) and ethylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1, 5 vol-% NH$_3$), amine **41a** (261 mg, 1.22 mmol, 31%) and amine **41b** (258 mg, 1.21 mmol, 30%) were obtained as colorless oils. **41a**: ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.88 (t, J = 6.3 Hz, 3 H), 1.10 (t, J = 7.2 Hz, 3 H), 1.20–1.35 (m, 18 H), 1.40–1.55 (m, 2 H), 2.57–2.68 (m, 4 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.1 (CH$_3$), 15.4 (CH$_3$), 22.7 (CH$_2$), 27.5 (CH$_2$), 29.3 (CH$_2$), 29.6 (CH$_2$), 29.7 (CH$_2$), 30.3 (CH$_2$), 31.9 (CH$_2$), 44.2 (CH$_2$), 50.0 (CH$_2$) ppm. IR: ṽ = 2958, 2923, 2853, 2811, 1466, 1376, 1133, 722 cm^{-1}. HRMS (%) calcd. [$C_{14}H_{31}N^+$] 213.2457, found 213.2448 (7); calcd. [$C_{13}H_{28}N^+$] 198.2222, found 198.2231 (5); calcd. [$C_4H_{10}N^+$] 72.0813, found 72.0826 (14). $C_{14}H_{31}N$ (213.4): calcd. C 78.79, H 14.64, N 6.56; found C 78.34, H 14.77, N 6.62. **41b:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.87 (t, J = 6.2 Hz, 3 H), 1.03 (d, J = 6.3 Hz, 3 H), 1.11 (t, J = 7.2 Hz, 3 H), 1.20–1.40 (m, 18 H), 1.44 (br. s, 1 H), 2.54–2.75 (m, 3 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.1 (CH$_3$), 15.6 (CH$_3$), 20.4 (CH$_3$), 22.7 (CH$_2$), 26.1 (CH$_2$), 29.3 (CH$_2$), 29.6 (CH$_2$), 29.9 (CH$_2$), 31.9 (CH$_2$), 37.3 (CH$_2$), 41.5 (CH$_2$), 53.2 (CH) ppm. IR: ṽ = 2959, 2923, 2854, 1466, 1375, 1153, 1119, 721 cm^{-1}. HRMS (%) calcd. [$C_{14}H_{31}N^+$] 213.2457, found 213.2451 (2); calcd. [$C_{14}H_{30}N^+$] 212.2378, found 212.2389 (2), [$C_{13}H_{28}N^+$] 198.2222, found 198.2242 (19); calcd. [$C_4H_{10}N^+$] 72.0813, found 72.0821 (100). $C_{14}H_{31}N$ (213.4): calcd. C 78.79, H 14.64, N 6.56; found C 78.62, H 14.89, N 6.69.

Amines 42a/42b: General procedure B was used to synthesize amines **42a** and **42b** from 4-methoxyphenylacetylene (**36**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1, 5 vol.-% NH$_3$), amine **42a** (130 mg, 0.77 mmol, 20%) and amine **42b** (127 mg, 0.77 mmol, 19%) were obtained as colorless oils. **42a:** ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.52 (br. s, 1 H), 2.43 (s, 3 H), 2.70–2.83 (m, 4 H), 3.78 (s, 3 H), 6.84 (d, J = 8.6 Hz, 2 H), 7.12 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 35.0 (CH$_2$), 36.1 (CH$_3$), 53.2 (CH$_2$), 55.2 (CH$_3$), 113.9 (CH), 129.6 (CH), 131.9 (C), 158.0 (C) ppm. IR: ṽ = 3313, 2934, 2835, 2456, 2793, 1607, 1511, 1458, 1295, 1247, 1176, 1036, 821 cm^{-1}. HRMS (%) calcd. [$C_{10}H_{15}NO^+$] 165.1154, found 165.1131 (3); calcd. [$C_9H_{10}O^+$] 134.0732, found 134.0745 (100); calcd. [$C_8H_{10}O^+$] 122.0732, found 122.0723 (40); calcd. [$C_8H_9O^+$] 121.0653, found 121.0657 (72). **42b:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.35 (d, J = 6.6 Hz, 3 H), 2.29 (s, 3 H), 2.61 (br. s, 1 H), 3.62 (q, J = 6.6 Hz, 1 H), 3.79 (s, 3 H), 6.87 (d, J = 8.7 Hz, 2 H), 7.23 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 23.4 (CH$_3$), 34.0 (CH$_3$), 55.1 (CH$_3$), 59.4 (CH), 113.7 (CH), 127.6 (CH), 136.7 (C), 158.6 (C) ppm. IR: ṽ = 3330, 2957, 2835, 2788, 1611, 1512, 1463, 1246, 1178, 1036, 832 cm^{-1}. HRMS (%) calcd. [$C_{10}H_{15}NO^+$] 165.1154, found 165.1143 (6); calcd. [$C_{10}H_{14}NO^+$] 164.1075, found 164.1077 (9); calcd. [$C_9H_{12}NO^+$] 150.0919, found 150.0924 (100); calcd. [$C_9H_{11}O^+$] 135.0810, found 135.0784 (23). $C_{10}H_{15}NO$ (165.2): calcd. C 72.69, H 9.15, N 8.48; found C 72.87, H 9.24, N 7.62.

Amines 43a/43b: General procedure B was used to synthesize amines **43a** and **43b** from 1-dodecyne (**38**) and methylamine. After purification by flash chromatography (EtOAc/MeOH, 2:1, 5 vol.-% NH$_3$), amine **43a** (245 mg, 1.22 mmol, 31%) and amine **43b** (258 mg, 1.21 mmol, 30%) were obtained as colorless oils. **43a:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.88 (t, J = 6.3 Hz, 3 H), 1.20–1.38 (m, 18 H), 1.40–1.55 (m, 2 H), 2.01 (br. s, 1 H), 2.43 (s, 3 H), 2.56 (t, J = 7.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.1 (CH$_3$), 22.7 (CH$_2$), 27.3 (CH$_2$), 29.3 (CH$_2$), 29.6 (CH$_2$), 29.6 (CH$_2$), 29.7 (CH$_2$), 29.8 (CH$_2$), 31.9 (CH$_2$), 36.4 (CH$_3$), 52.1 (CH$_2$) ppm. IR: ṽ = 2924, 2854, 2790, 1558, 1467, 1380, 1310, 1068, 722 cm^{-1}. HRMS (%) calcd. [$C_{13}H_{29}N^+$] 199.2300, found 199.2292 (100); calcd. [$C_{13}H_{28}N^+$] 198.2222, found 198.2208 (25); calcd. [$C_{12}H_{26}N^+$] 184.2065, found 184.2054 (15); calcd. [$C_8H_{18}N^+$] 128.1439, found 128.1449 (8), calcd. [$C_6H_{14}N^+$] 100.1126, found 100.1134 (17). **43b:** ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.87 (t, J = 6.3 Hz, 3 H), 1.01 (d, J = 6.3 Hz, 3 H), 1.20–1.37 (m, 16 H), 1.38–1.50 (m, 2 H), 2.39 (s, 3 H), 2.45–2.55 (m, 1 H) ppm. ^{13}C NMR (75 MHz, DEPT, CDCl$_3$): δ = 14.1 (CH$_3$), 19.8 (CH$_3$), 22.7 (CH$_2$), 26.0 (CH$_2$), 29.3 (CH$_2$), 29.6 (CH$_2$), 29.6 (CH$_2$), 29.9 (CH$_2$), 31.9 (CH$_2$), 33.9 (CH$_3$), 36.9 (CH$_2$), 55.0 (CH) ppm. IR: ṽ = 2958, 2925, 2854, 2786, 1575, 1465, 1374, 1341, 1155, 722 cm^{-1}. HRMS (%) calcd. [$C_{13}H_{29}N^+$] 199.2300, found 199.2299 (6); calcd. [$C_{13}H_{28}N^+$] 198.2222, found 198.2226 (13); calcd. [$C_{12}H_{26}N^+$] 184.2065, found 184.2080 (75). $C_{13}H_{29}N$ (199.2): calcd. C 78.31, H 14.66, N 7.03; found C 77.99, H 15.07, N 7.12.

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[1] For reviews, see: a) I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2003**, 935–946; b) S. Doye, *Synlett* **2004**, 1653–1672; c) A. Odom, *Dalton. Trans.* **2005**, 225–233.

[2] a) E. Haak, I. Bytschkov, S. Doye, *Angew. Chem.* **1999**, *111*, 3584–3586; *Angew. Chem. Int. Ed.* **1999**, *38*, 3389–3391; b) A. Heutling, S. Doye, *J. Org. Chem.* **2002**, *67*, 1961–1964.

[3] For U- and Th-catalyzed additions of methyl- and ethylamine to alkynes, see: T. Straub, A. Haskel, T. G. Neyroud, M. Kapon, M. Botoshansky, M. S. Eisen, *Organometallics* **2001**, *20*, 5017–5035, and references cited therein.

[4] A. Heutling, F. Pohlki, S. Doye, *Chem. Eur. J.* **2004**, *10*, 3059–3071.

[5] For an explanation of the regioselectivity observed in group-IV metal catalyzed hydroaminations of alkynes, see: A. M. Baranger, P. J. Walsh, R. G. Bergman, *J. Am. Chem. Soc.* **1993**, *115*, 2753–2763.

[6] Y. Shi, J. T. Ciszewski, A. L. Odom, *Organometallics* **2001**, *20*, 3967–3969.

[7] a) A. Tillack, I. Garcia Castro, C. G. Hartung, M. Beller, *Angew. Chem.* **2002**, *114*, 2646–2648; *Angew. Chem. Int. Ed.* **2002**, *41*, 2541–2543; b) A. Tillack, H. Jiao, I. Garcia Castro, C. G. Hartung, M. Beller, *Chem. Eur. J.* **2004**, *10*, 2409–2420; c) A. Tillack, V. Khedkar, M. Beller, *Tetrahedron Lett.* **2004**, *45*, 8875–8878.

[8] A. Heutling, R. Severin, S. Doye, *Synthesis* **2005**, 1200–1204.

[9] www.mcat.de.

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