Microwave-Assisted Catalytic Intermolecular Hydroamination of Alkynes

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Irradiation of reaction mixtures containing an alkyne, an amine, and a catalytic amount of Cp_2TiMe_2 in toluene with microwaves at a frequency of 2.45 GHz and a power output of 180–300 W results in fast reactions to give the corresponding hydroamination products. The initially formed imines can easily be reduced to secondary amines by use of H_2/Pd, $LiAlH_4$, or $NaCNBH_3$/*p*-TsOH. The microwave-assisted hydroamination reactions go to completion within one tenth (or less) of the time required for reactions run conventionally in an oil bath at 105 °C. By using the microwave technology, it is possible to achieve turnover frequencies TOF > 10 h^{-1}. Furthermore, when Cp_2TiMe_2 is used as the catalyst, hydroamination products of terminal alkynes can be isolated in reasonable yields for the first time. The addition of amines to terminal alkynes gives access to both the Markovnikov and the anti-Markovnikov products. Observed regioselectivities are different for terminal aryl- and alkylalkynes.

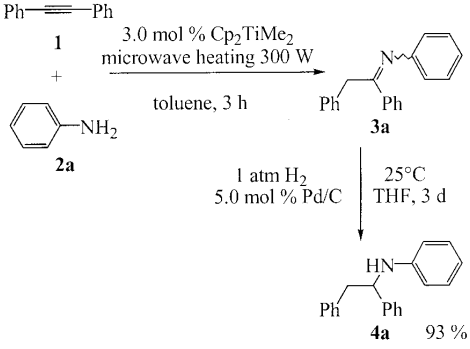
Introduction

Nitrogen-containing molecules are among the most important classes of chemical substances. They play outstanding roles as biologically active compounds and as industrial chemicals. In the past, these facts lay behind the development of a large number of methods for the synthesis of amines, imines, and enamines. Among these methods, the direct addition of ammonia or amines to alkenes and alkynes − the so-called hydroamination of alkenes and alkynes − represents the most attractive approach, because the desired higher substituted nitrogen-containing products are formed in a single reaction step from inexpensive starting materials without production of waste. At present, however, no general hydroamination procedure for a wide variety of substrates is known.[1−3]

We have recently shown that dimethyltitanocene, Cp_2TiMe_2,[4] represents an excellent catalyst for intermolecular hydroamination of alkynes.[5] The procedure developed with this catalyst enables primary arylamines, as well as primary *tert*- and *sec*-alkylamines, to be coupled with several disubstituted alkynes in good to moderate yields, although primary *n*-alkylamines and terminal alkynes can only be coupled in poor yields. Unfortunately, elevated temperatures (100−120 °C) and long reaction times (up to 72 h) are usually required for the reaction to proceed.

Results and Discussion

During a study directed toward optimizing and generalizing our recently developed hydroamination methodology for alkynes, we discovered that the reaction times could be dramatically shortened under conditions that employed microwave heating instead of conventional heating.[6] In an initial experiment, a typical reaction mixture containing 1.0 equiv. of diphenylacetylene (**1**), 1.0 equiv. of aniline (**2a**), and 3.0 mol % of Cp_2TiMe_2 in toluene was irradiated at a frequency of 2.45 GHz using a Prolabo Synthewave 402 microwave reactor with a power output of 300 W for 3 h. After that time, TLC analysis showed that the starting materials had been completely consumed.[7] In a control experiment, no conversion was observed in the absence of Cp_2TiMe_2. Subsequent hydrogenation of the initially formed imine **3a** with H_2 and 5 mol % of Pd/C gave access to amine **4a** in 93% yield (Scheme 1).



Scheme 1. Microwave-assisted hydroamination of diphenylacetylene (**1**) with aniline (**2a**) and subsequent reduction of the initially formed imine **3a**

In comparison, a control experiment performed in an oil bath at 105 °C showed that a reaction time of 30 h was necessary to obtain 100% conversion for the same reaction. This observation shows that application of microwave heating can reduce the required reaction time by a factor of 10. The corresponding turnover frequency for this first example is at least 10 h^{-1}, which is high for a catalytic intermolecular hydroamination process. With this initial result in mind, we conjectured that the reaction times for the dimethyltitanocene-catalyzed hydroamination of alkynes might generally

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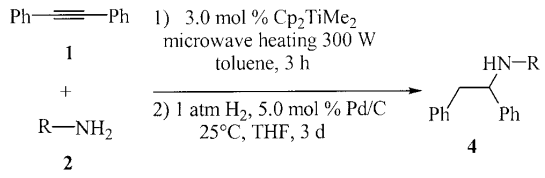
be minimized by use of microwave irradiation. We further assumed that short reaction times might increase the yield of reactions when terminal alkynes were employed, because side reactions (such as aldol-type reaction of initially formed imines), would have only a short time to occur.

In order to investigate the scope and limitations of the new procedure, we first examined reactions of diphenylacetylene (**1**) with a wide variety of amines under microwave irradiation conditions. Scheme 2 and Table 1 summarize the obtained results. Unless otherwise noted, the reactions were carried out with microwave irradiation at a frequency of 2.45 GHz at a power output of 300 W for 3 h, with a catalyst loading of 3.0 mol % of Cp_2TiMe_2. The solvent was always toluene and the reaction mixtures usually contained alkyne and amine in a 1:1 ratio. Reduction of the initially formed imine was typically performed with 1 atm of H_2, and 5.0 mol % of Pd/C as the catalyst.

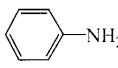
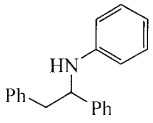
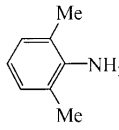
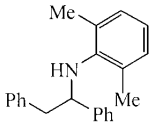
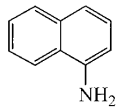
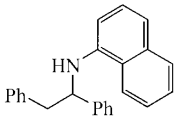
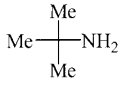
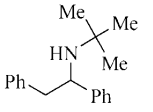
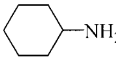
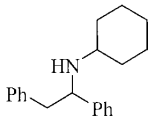
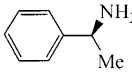
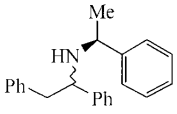
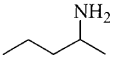
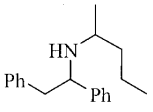
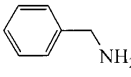
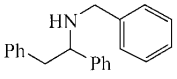


Scheme 2. Microwave-assisted hydroamination of diphenylacetylene (**1**) with various amines and subsequent reduction

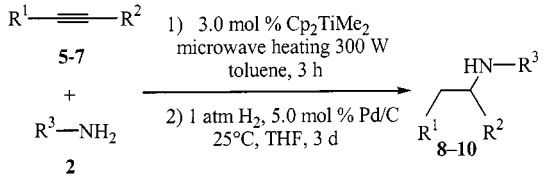
As can be seen from Table 1, arylamines (Entries 1−3), as well as *tert*- and *sec*-alkylamines (Entries 4−7), can successfully be induced to react with diphenylacetylene (**1**) under microwave conditions. All hydroamination reactions (Entries 1−7) went to completion within 3 h. After reduction of the initially formed imines, the corresponding secondary amines **4a**−**g** could be isolated in good yields. However, the imine formed from **1** and the sterically demanding 2,6-dimethylaniline (**2b**) (Entry 2) could not successfully be hydrogenated. Only reduction using the strongly nucleophilic reducing agent $LiAlH_4$ gave access to the desired product **4b**, in 82% yield. Particularly interesting is the reaction between **1** and the enantiomerically pure amine (*S*)-1-phenylethylamine (**2f**) (*ee* = 99%) (Entry 6). After reduction with $NaCNBH_3$/*p*-TsOH, two diastereomers of the resulting product **4f** were obtained in a 5:2 ratio. GC analysis performed by König et al. showed that the *ee* values for the two diastereomers of **4f** were only 87%. In an additional hydroamination experiment between **1** and **2f**, the amine **2f** could be reisolated after hydrolysis (SiO_2) of the initially formed imine. GC analysis of reisolated **2f** showed that the *ee* value had decreased to 86%. It is therefore clear that the hydroamination step occurs with partial racemization at the α-carbon atom of the employed amine. Unfortunately, the usage of benzylamine **2h** (Entry 8), which was a poor substrate in our initial studies,[5a] gave access only to very small amounts (2% yield) of the desired product **4h**.

In addition, we investigated the behavior of the dialkylalkyne 3-hexyne (**5**) and the alkyl(aryl)alkynes 1-phenylpropyne (**6**) and 1-phenylbutyne (**7**) in microwave-assisted hydroamination reactions. The results are summarized in Scheme 3 and Table 2. We found that, in the presence of 3.0 mol % of Cp_2TiMe_2, the employed alkynes smoothly reacted with various amines (**2a**, **2f**, **2i**, **2j**) within 3 h. After subsequent reduction, the corresponding secondary amines were obtained in good to moderate yields. As observed before,[5] the unsymmetrically substituted alkyl(aryl)alkynes **6** and **7** gave access to the anti-Markovnikov products exclusively (Entries 3−5). Furthermore, Table 2 shows that the amine 4-methoxyaniline (**2j**), which reacted with **6** in reasonable yield (Entry 4), is a particularly interesting substrate. Since the C−N bond in 4-methoxyaniline derivatives can easily be cleaved under oxidative conditions by ceric ammonium nitrate (CAN),[8] **2j** can be viewed as an ammonia equivalent. Again, partial racemization was observed during the hydroamination/reduction sequence with the enantiomerically pure substrate **2f** (Entry 5).

Table 1. Microwave-assisted hydroamination of diphenylacetylene (**1**) with various amines and subsequent reduction

entry	amine **2**	product **4**	yield (%)
1	 **2a**	 **4a**	93
2	 **2b**	 **4b**	82[a]
3	 **2c**	 **4c**	58[b]
4	 **2d**	 **4d**	72[c]
5	 **2e**	 **4e**	78
6	 **2f**	 **4f**	78[d] [e] [f]
7	 **2g**	 **4g**	67
8	 **2h**	 **4h**	2[g]

[a] Reduction: $LiAlH_4$, THF, 65 °C, 6 h. − [b] Microwave irradiation: 285 W, 2 h. − [c] Amine/alkyne, 3:1. − [d] Amine/alkyne, 2:1. − [e] Reduction: $NaCNBH_3$, *p*-TsOH, 25 °C, THF, 4 h. − [f] Two diastereomers with 87.2% and 86.6% *ee* were obtained. − [g] Microwave irradiation: 300 W, 6 h.



Scheme 3. Microwave-assisted hydroamination of dialkylalkynes and alkyl(aryl)alkynes with various amines and subsequent reduction

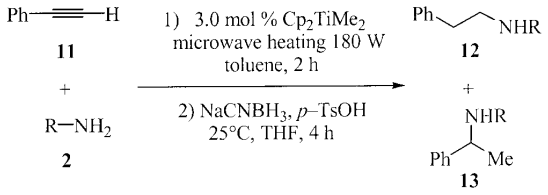
Table 2. Microwave-assisted hydroamination of dialkylalkynes and alkyl(aryl)alkynes with various amines and subsequent reduction

entry	alkyne **5–7**	amine **2**	product **8–10**	yield (%)
1	Et—≡—Et (**5**)	**2a**	**8a**	54[a]
2	Et—≡—Et (**5**)	**2i**	**8i**	59[b],[c]
3	Ph—≡—Me (**6**)	**2f**	**9f**	70[d]
4	Ph—≡—Me (**6**)	**2j**	**9j**	68[c],[e]
5	Ph—≡—Et (**7**)	**2f**	**10f**	59[c],[f]

[a] Microwave irradiation: 255 W, 3 h. – [b] Microwave irradiation: 210 W, 3 h. – [c] Reduction: $NaCNBH_3$, *p*-TsOH, 25 °C, THF, 4 h. – [d] The *ee* values of the two obtained diastereomers have not been determined. – [e] Microwave irradiation: 210 W, 2 h. – [f] Two diastereomers with 86.4% and 79.6% *ee* were obtained.

With these promising results in mind, we finally focused on the intermolecular hydroamination of terminal alkynes. As reported before, terminal alkynes are usually poor substrates for the Cp_2TiMe_2-catalyzed intermolecular hydroamination of alkynes. Prior to this publication, we had only been able to isolate hydroamination products from reactions between phenylacetylene (**11**) and either 1-naphthylamine[5a] or α-aminodiphenylmethane,[5b] in 23% and 41% yields. In both cases we had isolated the anti-Markovnikov product exclusively. We had previously speculated that fast aldol-type side reactions of the initially formed aldimines, which are more reactive than the usually obtained ketimines, may be responsible for these problems. We therefore conjectured that the short reaction times of the microwave irradiation technique should be suitable to expand the scope of Cp_2TiMe_2-catalyzed intermolecular hydroamination of alkynes to terminal alkynes.

We first found out that, under microwave conditions, Cp_2TiMe_2-catalyzed reactions between phenylacetylene (**11**) and amines are relatively fast. Even if the microwave irradiation was carried out at a power output of only 180 W, reactions between phenylacetylene (**11**) and amines such as **2a**, **2f**, and **2i** went to completion within 2 h (3.0 mol % of catalyst). The initially formed imines were reduced with $NaCNBH_3$/*p*-TsOH to yield the corresponding secondary amines. Surprisingly, mixtures of the two regioisomers **12** and **13** were isolated from these reactions in various ratios (Scheme 4, Table 3). Separation of the obtained isomers was only possible for **12f** and **13f** (Entry 2). However, **12a/13a** and **12i/13i** could be identified from the ^1H NMR spectra of the isolated mixtures.



Scheme 4. Microwave-assisted hydroamination of phenylacetylene (**11**) with various amines and subsequent reduction

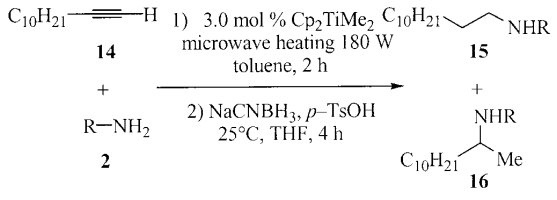
Table 3. Microwave-assisted hydroamination of phenylacetylene (**11**) with various amines and subsequent reduction

entry	amine **2**	products and ratio **12**:**13**	yield (%)
1	**2a**	**12a**, **13a** 3:1	67
2	**2f**	**12f**, **13f** 1:2.4	34[a]
3	**2i**	**12i**, **13i** 4:1	87[b]

[a] The *ee* values of **12f** and the two obtained diastereomers of **13f** have not been determined. – [b] Microwave irradiation: 210 W, 2 h.

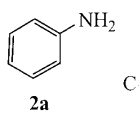
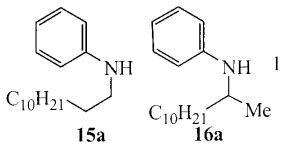
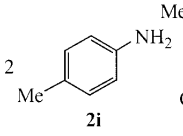
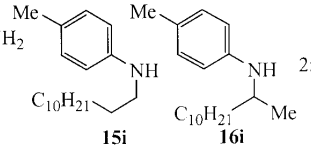
The obtained yields (**12** + **13**) for reactions between phenylacetylene (**11**) and either aniline (**2a**) or 4-methylaniline (**2i**) were 67% and 87%, respectively (Entries 1 and 3). Formation of the anti-Markovnikov product (**12a**, **12i**) was favored in both reactions. However, if the alkylamine **2f** was employed, the yield dropped to 34% and the selectivity was reversed (Entry 2). In this case, the Markovnikov product **13f** became the major amination product. Furthermore, a large quantity of nonpolar side products, which could not be separated further, was isolated. The structures of these products has not yet been determined, but data from MS analysis suggest that di- or trimerization products of phenylacetylene (**11**) are present in the obtained mixture.

Inspired by these results, we investigated further reactions between the unactivated alkyne 1-dodecyne (**14**) and the arylamines **2a** and **2i**. The hydroamination reactions were carried out at a power output of 180 or 210 W for 2 h in the presence of 3.0 mol % of Cp_2TiMe_2, the initially formed imines being reduced with $NaCNBH_3$/*p*-TsOH. The desired secondary amines were isolated as mixtures of regioisomers, in 49% and 80% yields (Scheme 5, Table 4). Again, the regioisomers could not be separated. Determination of the structures of the isomers was carried out by GC/MS and ^{1}H NMR analysis. Surprisingly, the Markovnikov products **16a** and **16i** were the major products, in contrast to the behavior of phenylacetylene (**11**). At present, it is not clear what factors are responsible for this switch in regioselectivity. Attempts to hydroaminate silylated alkynes have not yet been successful.



Scheme 5. Microwave-assisted hydroamination of 1-dodecyne (**14**) with various amines and subsequent reduction

Table 4. Microwave-assisted hydroamination of 1-dodecyne (**14**) with various amines and subsequent reduction

entry	amine **2**	products and ratio **15**:**16**	yield (%)
1	 **2a**	 **15a** **16a**	1:7	49
2	 **2i**	 **15i** **16i**	2:5	80[a]

[a] Microwave irradiation: 210 W, 2 h.

There has previously been much speculation regarding the reasons for the observed rate enhancements of organic reactions performed under microwave irradiation conditions.[6] One simple and reasonable explanation is that reaction mixtures under microwave conditions are just heated to higher temperatures than in conventionally heated reactions. Because we were not able to determine the temperature inside the reaction mixtures during microwave irradiation, we are unable to rule out this explanation. As a control experiment, we performed a comparable reaction between diphenylacetylene (**1**) and aniline (**2a**) in the presence of 3.0 mol % of Cp_2TiMe_2 in toluene at 190 °C in an oil bath. This experiment showed that the reaction at 190 °C also reached 100% conversion within 3 h. This result undoubtedly shows that the rates observed for reactions performed under microwave irradiation conditions are comparable to those observed at 190 °C. However, from a practical point of view the microwave heating technique is a viable option for performing Cp_2TiMe_2-catalyzed hydroamination reactions conveniently and safely in a short time.

Conclusion

In summary, we have shown that reaction times for the dimethyltitanocene-catalyzed intermolecular hydroamination of alkynes can be significantly shortened by performing the experiments in a microwave reactor. The microwave-assisted reactions go to completion within one tenth (or less) of the time required for reactions run conventionally in an oil bath at 105 °C. With the microwave technique, it was possible to achieve turnover frequencies TOF > 10 h^{-1}. Furthermore, hydroamination products of terminal alkynes could be isolated in reasonable yields for the first time when Cp_2TiMe_2 was used as the catalyst. Surprisingly, we found that addition of amines to terminal alkynes gave access to both the Markovnikov- and the anti-Markovnikov products. The observed regioselectivities were different for terminal aryl- and alkylalkynes.

Experimental Section

General Remarks: All reactions were performed under argon in flame-dried Duran glassware (Schlenk tubes equipped with Teflon stopcocks). Toluene was distilled from molten sodium under argon. Dimethyltitanocene was synthesized according to ref.[4a] Unless otherwise noted, all reagents were purchased from commercial sources and were used without further purification. Microwave irradiation was carried out at a frequency of 2.45 GHz, using a Prolabo Synthewave 402 microwave reactor with a maximum power output of 300 W (power is controllable between 0 and 100%). Yields refer to isolated yields of 95% or higher purity, as determined by GC, ^{1}H NMR, and elemental analysis for new compounds. All products were characterized by ^{1}H NMR, ^{13}C NMR, and infrared (IR) spectroscopy, and mass spectrometry (MS). New compounds were further characterized by CHN elemental analysis. Unless otherwise noted, NMR spectra were recorded in $CDCl_3$ with a Bruker Avance 400 MHz spectrometer. All ^{1}H NMR spectra are reported in δ units ppm downfield from tetramethylsilane in-

ternal standard. All ^{13}C NMR spectra are reported in δ units ppm relative to the central line of the triplet for $CDCl_3$ at δ = 77.0. Infrared spectra were recorded with a Bruker Vector 22 spectrometer, using an attenuated total reflection (ATR) method. Mass spectra were recorded with a Finnigan MAT 312 or a VG Autospec (EI) with an ionization potential of 70 eV. Elemental analyses were carried out with an Elementar Vario EL machine. Gas chromatography analyses were performed with a Hewlett−Packard HP 6890 series gas chromatograph. GC/MS analyses were performed with a Shimadzu GC-17A gas chromatograph equipped with a Shimadzu QP-5000 mass spectrometer. The *ee* values for compounds **4f** and **10f** were determined by gas-chromatographic separation with modified cyclodextrins in Professor W. A. König's group. PE: light petroleum ether, b.p. 40−60 °C.

Hydroamination. − General Procedure A: The amine (2.4 mmol), the alkyne (2.4 mmol), toluene (1.0 mL), and a solution of Cp_2TiMe_2 (0.126 mL, 0.57 mol/L in toluene, 0.072 mmol, 3.0 mol %) were placed in a Schlenk tube. The Schlenk tube was then sealed with a Teflon stopcock and transferred to the microwave reactor. The mixture was irradiated at 100% power output (300 W) for 3 h. After cooling to room temperature, the volatile components were removed under vacuum.

Reduction. − General Procedure B (H_2, Pd/C): Pd/C (255 mg, 5% Pd, 0.12 mmol Pd, 5.0 mol %) was stirred in THF (3.0 mL) at 25 °C under 1 atm of H_2 for 30 min. A solution of the crude hydroamination product in THF (3.0 mL) was then added. The resulting mixture was stirred under 1 atm H_2 at 25 °C for 72 h. Filtration, concentration, and purification by flash chromatography on silica gel afforded the analytically pure product.

Reduction. − General Procedure C ($LiAlH_4$): A solution of the crude hydroamination product in THF (2.0 mL) was added to a suspension of $LiAlH_4$ (182 mg, 4.8 mmol) in THF (5.0 mL) at room temperature. The mixture was then heated to 65 °C for 6 h. After cooling to room temperature, the mixture was slowly poured into ice-cold water (20 mL). CH_2Cl_2 (20 mL) and 2 M KOH (3.0 mL) were added and the resulting mixture was stirred for 30 min. The organic layer was separated and the water layer was extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. Purification by flash chromatography on silica gel afforded the analytically pure product.

Reduction. − General Procedure D ($NaCNBH_3$): The crude hydroamination product was dissolved in THF (2.0 mL). $NaCNBH_3$ (302 mg, 4.8 mmol) and *p*-toluenesulfonic acid monohydrate (46 mg, 0.24 mmol) were added and the mixture was stirred at room temperature. After 4 h, diethyl ether (5.0 mL) and 2 N HCl (5.0 mL) were added. The mixture was stirred for 1 h at room temperature. The organic layer was separated and saturated $NaHCO_3$ solution was added to the water layer until pH = 7 was reached. The water layer was extracted with diethyl ether (2 ×). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. Purification by flash chromatography on silica gel afforded the analytically pure product.

Amine 4a: General procedures A and B were used to convert diphenylacetylene (**1**) and aniline (**2a**) into the title product. Purification by flash chromatography (PE/EtOAc, 15:1) afforded **4a** (610 mg, 93%) as a bright yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.60 (br. s, 1 H), 3.03 (dd, *J* = 13.9, 8.1 Hz, 1 H), 3.14 (dd, *J* = 13.9, 5.8 Hz, 1 H), 4.57 (dd, *J* = 8.2, 5.8 Hz, 1 H), 6.47 (d, *J* = 8.0 Hz, 2 H), 6.63 (t, *J* = 7.4 Hz, 1 H), 7.04 (t, *J* = 7.5 Hz, 2 H), 7.11 (d, *J* = 6.8 Hz, 2 H), 7.15−7.35 (m, 8 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 45.0 (CH_2), 59.5 (CH), 113.9 (CH), 117.8 (CH), 126.5 (CH), 126.7 (CH), 127.1 (CH), 128.5 (CH), 128.5 (CH), 129.0 (CH), 129.2 (CH), 137.6 (C), 143.1 (C), 146.9 (C); IR: $\tilde{\nu}$ = 3422, 3085, 3063, 2999, 2926, 2855, 1673, 1601, 1504, 1453, 1428, 1355, 1317, 1263, 1178, 993, 912, 872, 829 cm^{-1}; MS (70 °C): *m*/*z* (%) = 274 (1) [M^+ + 1], 196 (5), 182 (79), 120 (16), 105 (100), 91 (45), 77 (36), 65 (6); $C_{20}H_{19}N$ (273.4): calcd. C 87.87, H 7.00, N 5.12; found C 87.84, H 7.17, N 4.93.

Amine 4b: General procedures A and C were used to convert diphenylacetylene (**1**) and 2,6-dimethylaniline (**2b**) into the title product. Purification by flash chromatography (PE/EtOAc, 12:1) afforded **4b** (594 mg, 82%) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.05 (s, 6 H), 3.12 (dd, *J* = 12.0, 8.0 Hz, 1 H), 3.24 (dd, *J* = 12.0, 8.0 Hz, 1 H), 4.39 (t, *J* = 8.0 Hz, 1 H), 6.74 (t, *J* = 7.4 Hz, 1 H), 6.88 (d, *J* = 7.4 Hz, 2 H), 7.01−7.23 (m, 10 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 18.9 (CH_3), 43.4 (CH_2), 63.3 (CH), 121.5 (CH), 126.1 (CH), 126.8 (CH), 127.1 (CH), 128.1 (CH), 128.3 (CH), 128.8 (CH), 129.2 (C), 129.4 (CH), 138.7 (C), 143.3 (C), 144.4 (C); IR: $\tilde{\nu}$ = 3401, 3061, 3027, 2945, 2855, 1595, 1494, 1474, 1453, 1257, 1216, 1098, 1029, 915, 763, 740, 698 cm^{-1}; MS (25 °C): *m*/*z* (%) = 300 (14) [M^+ − 1], 208 (100), 105 (31), 91 (21), 77 (10); $C_{22}H_{23}N$ (301.4): calcd. C 87.66, H 7.69, N 4.65; found C 87.36, H 7.60, N 4.51.

Amine 4c: General procedures A and B were used to convert diphenylacetylene (**1**) and 1-naphthylamine (**2c**) into the title product. The microwave irradiation was carried out at a power output of 95% (285 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 18:1) afforded **4c** (450 mg, 58%) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.15 (dd, *J* = 13.9, 5.5 Hz, 1 H), 3.28 (dd, *J* = 13.9, 8.3 Hz, 1 H), 4.75 (dd, *J* = 8.3, 5.5 Hz, 1 H), 4.85 (br. s, 1 H), 6.34 (d, *J* = 6.4 Hz, 1 H), 7.10−7.33 (m, 10 H), 7.35−7.44 (m, 4 H), 7.71−7.77 (m, 2 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 45.3 (CH_2), 59.2 (CH), 106.5 (CH), 117.5 (CH), 119.7 (CH), 123.6 (CH), 124.7 (CH), 125.6 (CH), 126.4 (CH), 126.9 (CH), 127.1 (CH), 128.6 (CH), 128.7 (CH), 128.7 (CH), 129.2 (CH), 134.1 (C), 137.6 (C), 142.0 (C), 143.0 (C); IR: $\tilde{\nu}$ = 3427, 3064, 2999, 2925, 2854, 1581, 1525, 1495, 1479, 1454, 1408, 1345, 1279, 1253, 1115, 899, 844 cm^{-1}; MS (70 °C): *m*/*z* (%) = 323 (2) [M^+], 232 (8), 196 (3), 182 (25), 128 (3), 105 (19), 91 (100), 77 (5), 65 (10); $C_{24}H_{21}N$ (323.4): calcd. C 89.13, H 6.54, N 4.33; found C 88.94, H 6.52, N 4.12.

Amine 4d: General procedures A and B were used to convert diphenylacetylene (**1**) and *tert*-butylamine (**2d**) into the title product. Because of the low boiling point of *tert*-butylamine, an excess of amine (7.2 mmol) was used in the hydroamination step. Purification by flash chromatography (PE/EtOAc, 10:1) afforded **4d** (438 mg, 72%) as a bright yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.84 (s, 9 H), 2.72 (dd, *J* = 12.0, 9.0 Hz, 1 H), 2.92 (dd, *J* = 12.0, 5.6 Hz, 1 H), 3.98 (dd, *J* = 9.0, 5.6 Hz, 1 H), 7.12 (d, *J* = 7.0 Hz, 2 H), 7.15−7.30 (m, 6 H), 7.38 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 29.8 (CH_3), 47.1 (CH_2), 51.2 (C), 59.3 (CH), 126.3 (CH), 126.4 (CH), 127.1 (CH), 128.1 (CH), 128.3 (CH), 129.3 (CH), 139.2 (C), 147.4 (C); IR: $\tilde{\nu}$ = 3085, 3064, 2999, 2963, 2861, 1601, 1494, 1454, 1390, 1365, 1251, 1230, 1096, 1069, 1029, 910, 570, 555, 520 cm^{-1}; MS (25 °C): *m*/*z* (%) = 238 (1) [M^+ − CH_3], 181 (11), 162 (72), 106 (100), 91 (9), 77 (6); purity by GC: > 99%. **4d** has already been described in ref.[9]

Amine 4e: General procedures A and B were used to convert diphenylacetylene (**1**) and cyclohexylamine (**2e**) into the title product. Purification by flash chromatography (PE/EtOAc, 12:1) afforded **4e** (521 mg, 78%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$):

δ = 0.72−0.89 (m, 1 H), 0.95−1.16 (m, 4 H), 1.20−1.75 (m, 5 H), 1.85 (br. d, *J* = 12.4 Hz, 1 H), 2.21 (m, 1 H), 2.84 (dd, *J* = 13.4, 8.0 Hz, 1 H), 2.91 (dd, *J* = 13.4, 6.0 Hz, 1 H), 4.05 (dd, *J* = 6.1, 8.0 Hz, 1 H), 7.10 (d, *J* = 6.9 Hz, 2 H), 7.13−7.35 (m, 8 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.7 (CH_2), 25.1 (CH_2), 26.0 (CH_2), 32.6 (CH_2), 34.7 (CH_2), 45.6 (CH_2), 53.4 (CH), 61.1 (CH), 126.2 (CH), 126.8 (CH), 127.2 (CH), 128.2 (CH), 128.2 (CH), 129.2 (CH), 139.0 (C), 144.5 (C); IR: ṽ = 3322, 3084, 3064, 2999, 2932, 2854, 1602, 1494, 1453, 1346, 1261, 1144, 1071, 1029, 913, 891, 627, 569, 533 cm^{-1}; MS (60 °C): *m/z* (%) = 278 (1) [M^+ − 1], 188 (100), 165 (5), 106 (66), 91 (19), 77 (6); $C_{20}H_{25}N$ (279.4): calcd. C 85.97, H 9.02, N 5.01; found C 85.73, H 9.09, N 4.93.

Amine 4f: General procedures A and D were used to convert diphenylacetylene (**1**) and (*S*)-1-phenylethylamine (**2f**) into the title product. An excess of amine (4.8 mmol) was used in the hydroamination step. Purification by flash chromatography (PE/EtOAc, 3:1) afforded **4f** (562 mg, 78%) as a bright yellow oil. The two obtained diastereomers (ratio 5:2; *ee*: 87.2% and 86.6%) could not be separated by flash chromatography. The ^{1}H and ^{13}C NMR spectroscopic data refer to the major diastereomer. The other characterization data refer to the diastereomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (d, *J* = 6.8 Hz, 3 H), 1.74 (br. s, 1 H), 2.78 (dd, *J* = 13.6, 9.3 Hz, 1 H), 2.87 (dd, *J* = 13.6, 5.1 Hz, 1 H), 3.45 (q, *J* = 6.8 Hz, 1 H), 3.55 (dd, *J* = 9.3, 5.1 Hz, 1 H), 6.77−6.84 (m, 2 H), 7.01−7.06 (m, 2 H), 7.13−7.34 (m, 11 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.8 (CH_3), 45.3 (CH_2), 54.8 (CH), 61.0 (CH), 126.3 (CH), 126.3 (CH), 126.6 (CH), 126.9 (CH), 127.3 (CH), 128.2 (CH), 128.2 (CH), 128.3 (CH), 129.3 (CH), 138.7 (C), 144.1 (C), 145.3 (C); IR: ṽ = 3319, 3082, 3061, 3026, 2960, 2922, 2850, 1602, 1493, 1466, 1453, 1369, 1201, 1131, 1110, 1070, 1028, 910, 758, 698 cm^{-1}; MS (25 °C): *m/z* (%) = 210 (94) [M^+ − C_7H_7], 181 (8), 105 (100), 91 (16), 77 (21); $C_{22}H_{23}N$ (301.4): calcd. C 87.66, H 7.69, N 4.64; found C 87.27, H 7.72, N 4.56.

Amine 4g: General procedures A and B were used to convert diphenylacetylene (**1**) and 2-aminopentane (**2g**) into the title product. Purification by flash chromatography (PE/EtOAc, 10:1) afforded **4g** (432 mg, 67%) as a bright yellow oil. The two obtained diastereomers (ratio 10:1) could not be separated by flash chromatography. The ^{1}H and ^{13}C NMR spectroscopic data refer to the major diastereomer. The other characterization data refer to the diastereomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78 (t, *J* = 7.0 Hz, 3 H), 0.86 (d, *J* = 6.1 Hz, 3 H), 1.10−1.34 (m, 4 H), 2.37 (m, 1 H), 2.90 (m, 2 H), 4.00 (t, *J* = 7.0 Hz, 1 H), 7.07 (d, *J* = 6.9 Hz, 2 H), 7.13−7.33 (m, 8 H) ppm; ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 19.2 (CH_2), 19.6 (CH_3), 40.5 (CH_2), 45.6 (CH_2), 49.4 (CH), 61.4 (CH), 126.2 (CH), 126.8 (CH), 127.3 (CH), 128.1 (CH), 128.2 (CH), 129.2 (CH), 139.0 (C), 144.0 (C) ppm; IR: ṽ = 3062, 3026, 2956, 2925, 2870, 1602, 1494, 1453, 1372, 1157, 1069, 1028, 912, 757, 697 cm^{-1}; MS (25 °C): *m/z* (%) = 266 (16) [M^+ − 1], 252 (19), 224 (100), 202 (10); $C_{19}H_{25}N$ (267.4): calcd. C 85.34, H 9.42, N 5.23; found C 84.86, H 9.34, N 4.70.

Amine 4h: General procedures A and B were used to convert diphenylacetylene (**1**) and benzylamine (**2h**) into the title product. The microwave irradiation was carried out at a power output of 100% (300 W) for 6 h. Purification by flash chromatography (PE/EtOAc, 10:1) afforded **4h** (14 mg, 2%) as a colorless solid. Because of the small amount of isolated product, identification of **4h** was carried out only by its ^{1}H NMR spectrum. Compound **4h** has already been described in reference.[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.92 (s, 1 H), 2.97 (m, 2 H), 3.47 (d, *J* = 13.5 Hz, 1 H), 3.67 (d, *J* = 13.5 Hz, 1 H), 3.89 (t, *J* = 7.0 Hz, 1 H), 7.05−7.40 (m, 15 H).

Amine 8a: General procedures A and B were used to convert 3-hexyne (**5**) and aniline (**2a**) into the title product. Because of the low boiling point of 3-hexyne, an excess of alkyne (4.8 mmol) was used in the hydroamination step. For procedure A, only 0.5 mL toluene was used. The microwave irradiation was carried out at a power output of 85% (255 W) for 3 h. Purification by flash chromatography (PE/EtOAc, 15:1) afforded **8a** (230 mg, 54%) as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.2 Hz, 3 H), 0.91 (t, *J* = 7.4 Hz, 3 H), 1.30−1.65 (m, 6 H), 3.29 (quint, *J* = 5.8 Hz, 1 H), 3.35−3.75 (br. s, 1 H), 6.56 (d, *J* = 7.8 Hz, 2 H), 6.64 (t, *J* = 7.3 Hz, 1 H), 7.14 (dd, *J* = 8.4, 7.4 Hz, 2 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 10.0 (CH_3), 14.2 (CH_3), 19.1 (CH_2), 27.2 (CH_2), 36.6 (CH_2), 53.9 (CH), 112.9 (CH), 116.5 (CH), 129.2 (CH), 148.0 (C); IR: ṽ = 3399, 3052, 3018, 2958, 2930, 2872, 1601, 1504, 1461, 1429, 1379, 1319, 1274, 1179, 1153, 1076, 1032, 992, 893, 865, 745, 691 cm^{-1}; MS (25 °C): *m/z* (%) = 177 (31) [M^+], 148 (90), 134 (100), 118 (10), 106 (15), 91 (3), 77 (8), 65 (3); Purity by GC 97.4%. Compound **8a** has already been described in ref.[11]

Amine 8i: General procedures A and D were used to convert 3-hexyne (**5**) and 4-methylaniline (**2i**) into the title product. Because of the low boiling point of 3-hexyne, an excess of alkyne (4.8 mmol) was used in the hydroamination step. For procedure A, only 0.5 mL toluene was used. The microwave irradiation was carried out at a power output of 70% (210 W) for 3 h. Purification by flash chromatography (PE/EtOAc, 15:1) afforded **8i** (271 mg, 59%) as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 3 H), 0.91 (t, *J* = 7.4 Hz, 3 H), 1.20−1.65 (m, 6 H), 2.23 (s, 3 H), 3.25 (quint, *J* = 5.8 Hz, 1 H), 6.51 (d, *J* = 8.2 Hz, 2 H), 6.96 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 9.9 (CH_3), 14.2 (CH_3), 19.2 (CH_3), 20.3 (CH_2), 27.2 (CH_2), 36.6 (CH_2), 54.3 (CH), 113.3 (CH), 125.9 (C), 129.7 (CH), 145.7 (C); IR: ṽ = 3401, 3015, 2958, 2927, 2871, 1618, 1518, 1460, 1405, 1379, 1318, 1300, 1271, 1181, 1152, 1119, 804 cm^{-1}; MS (25 °C): *m/z* (%) = 191 (36) [M^+], 162 (94), 148 (100), 134 (5), 120 (9), 106 (9), 91 (7), 77 (3), 65 (3); purity by GC: 96.1%. **8i** has already been described in ref.[11]

Amine 9f: General procedures A and B were used to convert 1-phenylpropyne (**6**) and (*S*)-1-phenylethylamine (**2f**) into the title product. For procedure A, only 0.5 mL toluene was used. Purification by flash chromatography (PE/EtOAc, 10:1) afforded **9f** (401 mg, 70%) as a colorless oil. The two obtained diastereomers (ratio 7:1) could not be separated by flash chromatography. The ^{1}H and ^{13}C NMR spectroscopic data refer to the major diastereomer. The other characterization data refer to the diastereomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.4 Hz, 3 H), 1.30 (d, *J* = 6.7 Hz, 3 H), 1.86 (br. s, 1 H), 2.49 (dd *J* = 13.0, 7.5 Hz, 1 H), 2.76 (m, 1 H), 2.88 (dd, *J* = 13.0, 5.0 Hz, 1 H), 3.93 (q, *J* = 6.7 Hz, 1 H), 7.07 (d, *J* = 6.9 Hz, 2 H), 7.15−7.40 (m, 8 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.0 (CH_3), 24.4 (CH_3), 42.5 (CH_2), 51.9 (CH), 55.3 (CH), 125.9 (CH), 126.5 (CH), 126.8 (CH), 128.2 (CH), 128.4 (CH), 129.3 (CH), 139.5 (C), 145.7 (C); IR: ṽ = 3061, 3025, 2961, 2923, 2865, 1602, 1493, 1452, 1370, 1272, 1200, 1127, 1086, 1029, 965, 909, 848, 761, 744, 699 cm^{-1}; MS (25 °C): *m/z* (%) = 224 (2) [M^+ − CH_3], 210 (5), 148 (57), 105 (100), 91 (15), 77 (9), 65 (3); purity by GC: 95.8%. Compound **9f** has already been described in reference.[12]

Amine 9j: General procedures A and D were used to convert 1-phenylpropyne (**6**) and 4-methoxyaniline (**2j**) into the title product. The scale of the reaction was only 0.8 mmol. The microwave irradiation was carried out at a power output of 70% (210 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 10:1) afforded **9j** (131 mg, 68%) as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$):

δ = 1.13 (d, *J* = 6.3 Hz, 3 H), 2.67 (dd, *J* = 13.3, 7.4 Hz, 1 H), 2.94 (dd, *J* = 13.3, 4.6 Hz, 1 H), 3.20 (br. s, 1 H), 3.68 (m, 1 H), 3.75 (s, 3 H), 6.62 (d, *J* = 8.8 Hz, 2 H), 6.79 (d, *J* = 8.8 Hz, 2 H), 7.10−7.35 (m, 5 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 20.1 (CH_3), 42.2 (CH_2), 50.7 (CH), 55.8 (CH_3), 115.0 (CH), 115.3 (CH), 126.2 (CH), 128.3 (CH), 129.5 (CH), 138.6 (C), 141.0 (C), 152.2 (C); IR: ṽ = 3391, 3026, 2928, 2831, 1508, 1453, 1407, 1375, 1281, 1231, 1178, 1149, 1109, 1092, 1035, 817, 796, 743, 699 cm^{-1}; MS (25 °C): *m*/*z* (%) = 241 (17) [M$^+$], 212 (3), 191 (3), 150 (100), 135 (3), 122 (2), 107 (5), 91 (6), 77 (2); $C_{16}H_{19}NO$ (241.3): calcd. C 79.63, H 7.94, N 5.80; found C 79.60, H 8.09, N 5.72.

Amine 10f: General procedures A and D were used to convert 1-phenylbutyne (**7**) and (*S*)-1-phenylethylamine (**2f**) into the title product. For procedure A, only 0.5 mL of toluene was used. Purification by flash chromatography (PE/EtOAc, 10:1) afforded **10f** (356 mg, 59%) as a colorless oil. The two obtained diastereomers (ratio 5:3; *ee*: 79.6% and 86.4%) could not be separated by flash chromatography. For further purification the obtained amine was converted into the hydrochloride salt. It was therefore dissolved in MeOH (2.0 mL), and HCl (5.0 mL, 1.0 mol/L in Et_2O) was added at room temperature. The mixture was stirred for 20 h at room temperature. Filtration afforded **10f·HCl** (376 mg, 54%) as a colorless solid. The characterization data refer to the diastereomeric mixture of amine hydrochloride salts. ^{1}H NMR (400 MHz, D_2O): δ = 0.88 (t, *J* = 7.2 Hz, 3 H), 0.99 (t, *J* = 7.2 Hz, 3 H), 1.42−1.92 (m, 10 H), 2.77−3.37 (m, 6 H), 4.42−4.62 (m, 2 H), 7.02−7.62 m (20 H); ^{13}C NMR (100.6 MHz, DEPT, D_2O): δ = 10.7 (CH_3), 11.2 (CH_3), 21.8 (CH_3), 22.0 (CH_3), 25.2 (CH_2), 26.1 (CH_2), 37.8 (CH_2), 39.0 (CH_2), 59.3 (CH), 59.6 (CH), 61.5 (CH), 61.7 (CH), 129.4 (CH), 130.2 (CH), 130.3 (CH), 130.3 (CH), 131.9 (CH), 131.9 (CH), 132.0 (CH), 132.1 (CH), 132.3 (CH), 132.4 (CH), 132.5 (CH), 132.6 (CH), 138.5 (C), 138.6 (C), 138.6 (C), 139.2 (C); IR: ṽ = 2973, 2748, 2706, 2667, 2467, 1582, 1497, 1455, 1382, 1313, 1280, 1213, 1157, 1077, 1032, 968, 924, 765, 742, 699 cm^{-1}; MS (25 °C): *m*/*z* (%) = 224 (2), 162 (93), 120 (9), 105 (100), 92 (14), 79 (6), 77 (7); purity by GC (amine): > 99%. Compound **10f** has already been described in ref.[12]

Amines 12a/13a: General procedures A and D were used to convert phenylacetylene (**11**) and aniline (**2a**) into the title products. The scale of the reaction was only 1.8 mmol. For procedure A, only 0.5 mL of toluene was used. The microwave irradiation was carried out at a power output of 60% (180 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 8:1) afforded a mixture of the regioisomers **12a** and **13a** (239 mg, 67%) in a ratio **12a/13a** = 3:1 as a bright yellow oil. The two obtained isomers could not be separated by flash chromatography. The ^{1}H and ^{13}C NMR spectroscopic data refer to the major isomer **12a**. The other characterization data refer to the mixture of isomers. The minor isomer **13a** was identified by its ^{1}H NMR signals at δ = 1.48 (d, *J* = 6.8 Hz, 3 H) and 4.45 (q, *J* = 6.8 Hz, 1 H). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.88 (t, *J* = 7.1 Hz, 2 H), 3.36 (t, *J* = 7.1 Hz, 2 H), 3.75 (br. s, 1 H), 6.50−7.40 (m, 10 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 35.4 (CH_2), 45.0 (CH_2), 113.0 (CH), 117.5 (CH), 126.4 (CH), 128.5 (CH), 128.7 (CH), 129.2 (CH), 139.2 (C), 147.9 (C); IR: ṽ = 3407, 3052, 3024, 2922, 1599, 1504, 1452, 1430, 1371, 1316, 1257, 1179, 1154, 1114, 1073, 1029, 991, 869, 745, 690 cm^{-1}; MS (25 °C): *m*/*z* (%) = 197 (45) [M$^+$], 182 (25), 120 (4), 106 (100), 93 (12), 91 (7), 76 (16), 65 (1); purity by GC (**12a** + **13a**): > 99%. **12a** and **13a** have already been described.[13,14]

Amines 12f/13f: General procedures A and D were used to convert phenylacetylene (**11**) and (*S*)-1-phenylethylamine (**2f**) into the title products. The microwave irradiation was carried out at a power output of 60% (180 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 2:1) afforded **12f** (54 mg, 10%) as a colorless oil and the regioisomer **13f** (130 mg, 24%) as a bright yellow oil. The two diastereomers of **13f** (ratio 3:1) could not be separated by flash chromatography. The characterization data for **13f** refer to the mixture of diastereomers. **Compound 12f:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, *J* = 6.5 Hz, 3 H), 2.65−2.90 (m, 4 H), 3.80 (q, *J* = 6.5 Hz, 1 H), 7.10−7.40 (m, 10 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.3 (CH_3), 33.5 (CH_2), 47.7 (CH_2), 58.7 (CH), 126.7 (CH), 127.2 (CH), 128.6 (CH), 128.6 (CH), 129.1 (CH), 137.5 (C), 138.9 (C); IR: ṽ = 2983, 2818, 1733, 1646, 1551, 1496, 1455, 1374, 1243, 1118, 1044, 918, 863, 762, 699 cm^{-1}; MS (120 °C): *m*/*z* (%) = 225 (4) [M$^+$], 210 (60), 134 (40), 120 (10), 105 (100), 91 (8), 77 (15), 65 (2); purity by GC: 95.1%. Compound **12f** has already been described in reference.[10] **Compound 13f:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 and 1.35 (d, *J* = 6.5 Hz, 12 H), 3.52 and 3.77 (q, *J* = 6.5 Hz, 4 H), 7.10−7.40 (m, 20 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.0 (CH_3), 25.7 (CH_3), 55.8 (CH), 56.2 (CH), 126.6 (CH), 126.7 (CH), 126.8 (CH), 126.9 (CH), 128.4 (CH), 145.3 (C, br); IR: ṽ = 3061, 3025, 2961, 2924, 2862, 1601, 1582, 1492, 1450, 1368, 1202, 1124, 1070, 1023, 910, 760, 697 cm^{-1}; MS (25 °C): *m*/*z* (%) = 225 (4) [M$^+$], 210 (88), 148 (3), 120 (10), 105 (100), 91 (4), 77 (15), 65 (1); purity by GC: 99.0%. Compound **13f** has already been described in ref.[15]

Amines 12i/13i: General procedures A and D were used to convert phenylacetylene (**11**) and 4-methylaniline (**2i**) into the title products. The scale of the reaction was only 1.8 mmol. For procedure A, only 0.5 mL toluene was used. The microwave irradiation was carried out at a power output of 70% (210 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 10:1) afforded a mixture of the regioisomers **12i** and **13i** (331 mg, 87%) in a ratio **12i/13i** = 4:1 as a bright yellow oil. The two obtained isomers could not be separated by flash chromatography. The ^{1}H and ^{13}C NMR spectroscopic data refer to the major isomer **12i**. The other characterization data refer to the mixture of isomers. The minor isomer **13i** was identified by its ^{1}H NMR signals at δ = 1.47 (d, *J* = 6.8 Hz, 3 H) and 4.43 (q, *J* = 6.8 Hz, 1 H). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 3 H), 2.87 (t, *J* = 7.0 Hz, 2 H), 3.35 (t, *J* = 7.0 Hz, 2 H), 3.60 (br. s, 1 H), 6.53 (d, *J* = 8.3 Hz, 2 H), 6.99 (d, *J* = 8.3 Hz, 2 H), 7.10−7.40 (m, 5 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 20.5 (CH_3), 35.5 (CH_2), 45.4 (CH_2), 113.2 (CH), 126.3 (CH), 126.7 (C), 128.5 (CH), 128.7 (CH), 129.7 (CH), 139.3 (C), 145.6 (C); IR: ṽ = 3402, 3024, 2917, 2862, 1616, 1517, 1493, 1452, 1317, 1300, 1254, 1182, 1125, 1077, 1029, 965, 911, 806, 748, 697 cm^{-1}; MS (25 °C): *m*/*z* (%) = 211 (53) [M$^+$], 196 (30), 149 (7), 134 (21), 120 (100), 105 (16), 91 (15), 77 (7), 65 (5); purity by GC (**12i** + **13i**): 95.5%. **12i** and **13i** have already been described.[16,17]

Amines 15a/16a: General procedures A and D were used to convert 1-dodecyne (**14**) and aniline (**2a**) into the title products. For procedure A only 0.5 mL of toluene was used. The microwave irradiation was carried out at a power output of 60% (180 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 10:1) afforded a mixture of the regioisomers **15a** and **16a** (306 mg, 49%) in a ratio **15a/16a** = 1:7 as a bright yellow oil. The two obtained isomers could not be separated by flash chromatography. The ^{1}H and ^{13}C NMR spectroscopic data refer to the major isomer **16a**. The other characterization data refer to the mixture of isomers. The minor isomer **15a** was identified by GC/MS analysis. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.7 Hz, 3 H), 1.17 (d, *J* = 6.3 Hz, 3 H), 1.20−1.64 (m, 18 H), 3.38−3.48 (m, 1 H), 3.70 (br. s, 1 H), 6.59 (d, *J* = 7.8 Hz, 2 H), 6.67 (t, *J* = 7.3 Hz, 1 H), 7.16 (br. t, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 20.6 (CH_3),

22.7 (CH_2), 26.1 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 31.9 (CH_2), 37.1 (CH_2), 44.1 (CH_2), 48.8 (CH), 113.4 (CH), 117.1 (CH), 129.2 (CH),147.3 (C); IR: $\tilde{\nu}$ = 3403, 2955, 2922, 2852, 1601, 1503, 1464, 1427, 1376, 1317, 1255, 1178, 1153, 1075, 1031, 993, 865, 745, 721, 690 cm^{-1}; MS (25 °C): *m/z* (%) = 261 (100) [M^+], 246 (40), 121 (40), 106 (30), 91 (3), 77 (9), 65 (2); purity by GC (**15a** + **16a**): 98.6%. Compounds **15a** and **16a** have already been described.[18,19]

Amines 15i/16i: General procedures A and D were used to convert 1-dodecyne (**14**) and 4-methylaniline (**2i**) into the title products. For procedure A, only 0.5 mL of toluene was used. The microwave irradiation was carried out at a power output of 70% (210 W) for 2 h. Purification by flash chromatography (PE/EtOAc, 15:1) afforded a mixture of the regioisomers **15i** and **16i** (527 mg, 80%) in a ratio **15i/16i** = 2:5 as a bright yellow oil. The two obtained isomers could not be separated by flash chromatography. The ^1H and ^{13}C NMR spectroscopic data refer to the major isomer **16i**. The other characterization data refer to the mixture of isomers. The minor isomer **15i** was identified by GC/MS analysis. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.7 Hz, 3 H), 1.15 (d, *J* = 6.3 Hz, 3 H), 1.20−1.64 (m, 18 H), 2.23 (s, 3 H), 3.35−3.45 (m, 1 H), 6.54 (d, *J* = 8.1 Hz, 2 H), 6.97 (d, *J* = 8.1 Hz, 2 H); ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 18.4 (CH_2), 20.3 (CH_3), 20.6 (CH_3), 22.7 (CH_2), 26.1 (CH_2), 27.2 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 31.9 (CH_2), 37.1 (CH_2), 49.1 (CH), 113.7 (CH), 126.4 (C), 129.7 (CH), 146.1 (C); IR: $\tilde{\nu}$ = 3402, 2955, 2922, 2852, 1619, 1519, 1464, 1376, 1316, 1300, 1250, 1182, 1153, 1122, 1038, 965, 805, 721 cm^{-1}; MS (80 °C): *m/z* (%) = 275 (31) [M^+], 260 (10), 134 (100), 120 (8), 106 (5), 91 (5), 77 (2); purity by GC (**15i** + **16i**): > 99%. Compounds **15i** and **16i** have already been described in refs.[20,21]

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[1] For general reviews, see: [1a] I. A. Chekulaeva, L. V. Kondratjeva, *Russ. Chem. Rev.* **1965**, *34*, 669−680; [1b] R. Taube in *Applied Homogeneous Catalysis with Organometallic Compounds* (Eds.: B. Cornils, W. A. Herrmann), VCH-Verlagsgesellschaft, Weinheim, **1996**, p. 507−520; [1c] T. E. Müller, M. Beller, *Chem. Rev.* **1998**, *98*, 675−703; [1d] T. E. Müller, M. Beller in *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, vol. 2, p. 316−330; [1e] E. Haak, S. Doye, *Chem. Unserer Zeit* **1999**, *33*, 296−303.

[2] For catalytic intramolecular hydroamination of aminoalkynes, see: [2a] K. Utimoto, *Pure Appl. Chem.* **1983**, *55*, 1845−1852; [2b] Y. Fukuda, K. Utimoto, H. Nozaki, *Heterocycles* **1987**, *25*, 297−300; [2c] P. L. McGrane, M. Jensen, T. Livinghouse, *J. Am. Chem. Soc.* **1992**, *114*, 5459−5460; [2d] P. L. McGrane, T. Livinghouse, *J. Org. Chem.* **1992**, *57*, 1323−1324; [2e] P. L. McGrane, T. Livinghouse, *J. Am. Chem. Soc.* **1993**, *115*, 11485−11489; [2f] D. Fairfax, M. Stein, T. Livinghouse, M. Jensen, *Organometallics* **1997**, *16*, 1523−1525; [2g] Y. Li, P.-F. Fu, T. J. Marks, *Organometallics* **1994**, *13*, 439−440; [2h] Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **1996**, *118*, 9295−9306; [2i] Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **1998**, *120*, 1757−1771; [2j] E. M. Campi, W. R. Jackson, *J. Organomet. Chem.* **1996**, *523*, 205−209; [2k] M. R. Bürgstein, H. Berberich, P. W. Roesky, *Organometallics* **1998**, *17*, 1452−1454; [2l] T. E. Müller, *Tetrahedron Lett.* **1998**, *39*, 5961−5962; [2m] T. E. Müller, M. Grosche, E. Herdtweck, A.-K. Pleier, E. Walter, Y.-K. Yan, *Organometallics* **2000**, *19*, 170−183; [2n] S. Burling, L. D. Fields, B. A. Messerle, *Organometallics* **2000**, *19*, 87−90; [2o] Y. K. Kim, T. Livinghouse, J. E. Bercaw, *Tetrahedron Lett.* **2001**, *42*, 2933−2935; [2p] T. Kondo, T. Okada, T. Suzuki, T.-a. Mitsudo, *J. Organomet. Chem.* **2001**, *622*, 149−154.

[3] For catalytic intermolecular hydroamination of alkynes, see: [3a] J. Barluenga, F. Aznar, *Synthesis* **1977**, 195−198; [3b] J. Barluenga, F. Aznar, R. Liz, R. Rodes, *J. Chem. Soc., Perkin Trans. 1* **1980**, 2732−2737; [3c] P. J. Walsh, A. M. Baranger, R. G. Bergman, *J. Am. Chem. Soc.* **1992**, *114*, 1708−1719; [3d] A. M. Baranger, P. J. Walsh, R. G. Bergman, *J. Am. Chem. Soc.* **1993**, *115*, 2753−2763; [3e] Y. Li, T. J. Marks, *Organometallics* **1996**, *15*, 3770−3772; [3f] A. Haskel, T. Straub, M. S. Eisen, *Organometallics* **1996**, *15*, 3773−3775; [3g] M. Tokunaga, M. Eckert, Y. Wakatsuki, *Angew. Chem.* **1999**, *111*, 3416−3419; *Angew. Chem. Int. Ed.* **1999**, *38*, 3222−3225; [3h] D. Tzalis, C. Koradin, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 6193−6195; [3i] See also refs.[2g,5]

[4] [4a] N. A. Petasis in *Encyclopedia of Reagents for Organic Synthesis* (Ed.: L. A. Paquette), John Wiley & Sons, **1995**, vol. 1, p. 470−473, and references therein; [4b] H. Siebeneicher, S. Doye, *J. Prakt. Chem.* **2000**, *342*, 102−106.

[5] [5a] E. Haak, I. Bytschkov, S. Doye, *Angew. Chem.* **1999**, *111*, 3584−3586; *Angew. Chem. Int. Ed.* **1999**, *38*, 3389−3391; [5b] E. Haak, H. Siebeneicher, S. Doye, *Org. Lett.* **2000**, *2*, 1935−1937; [5c] F. Pohlki, S. Doye, *Angew. Chem.* **2001**, *113*, 2361−2364; *Angew. Chem. Int. Ed.* **2001**, *40*, 2305−2308.

[6] For a critical review of the application of microwaves in organic chemistry, see: J. Herwig, R. Trainor in *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, vol. 2, p. 436−441, and references therein.

[7] Since all reactions were performed in sealed Schlenk tubes, it was not possible to determine the temperature inside the reaction mixtures during the microwave experiments.

[8] For example, see: P. Bravo, M. Guidetti, F. Viani, M. Zanda, A. L. Markovsky, A. E. Sorochinsky, I. V. Soloshonok, V. A. Soloshonok, *Tetrahedron* **1998**, *54*, 12789−12806.

[9] T. Ikariya, Y. Ishikawa, K. Hirai, S. Yoshikawa, *J. Organomet. Chem.* **1985**, *288*, 311−315.

[10] K. Mori, H. Sugiyama, M. Sekiya, *Chem. Pharm. Bull.* **1971**, *19*, 1722−1727.

[11] M. Montagne, G. Rousseau, *C. R. Hebd. Seances Acad. Sci.* **1933**, *196*, 1165−1167.

[12] U. B. Paulsen-Sörman, K.-H. Jönsson, B. G. A. Lindeke, *J. Med. Chem.* **1984**, *27*, 342−346.

[13] R. W. Franck, Sr., J. M. Gilligan, *J. Org. Chem.* **1971**, *36*, 222−224.

[14] R. S. Varma, R. Dahiya, *Tetrahedron* **1998**, *54*, 6293−6298.

[15] J. A. Marshall, J. Lebreton, *J. Am. Chem. Soc.* **1988**, *110*, 2925−2931.

[16] M. Takamatsu, M. Sekiya, *Chem. Pharm. Bull.* **1981**, *29*, 616−622.

[17] I. Lee, W. H. Lee, H. W. Lee, T. W. Bentley, *J. Chem. Soc., Perkin Trans. 2* **1993**, 141−146.

[18] T. V. Stupnikova, A. I. Serdyuk, V. N. Kalafat, R. S. Sagitullin, V. P. Marshtupa, *Chem. Heterocycl. Compd. (Engl. Transl.)* **1981**, 367−369.

[19] M. B. Gasc, J. Perie, A. Lattes, *Tetrahedron* **1978**, *34*, 1943−1950.

[20] E. B. Glebova, T. N. Wischnjakova, *Neftekhimia* **1976**, *16*, 614−618.

[21] F. Tanaka, *J. Pharm. Soc. Jpn.* **1943**, *63*, 343−353.

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