A Flexible Synthesis of Indoline, Indolizidine, and Pyrrolizidine Derivatives

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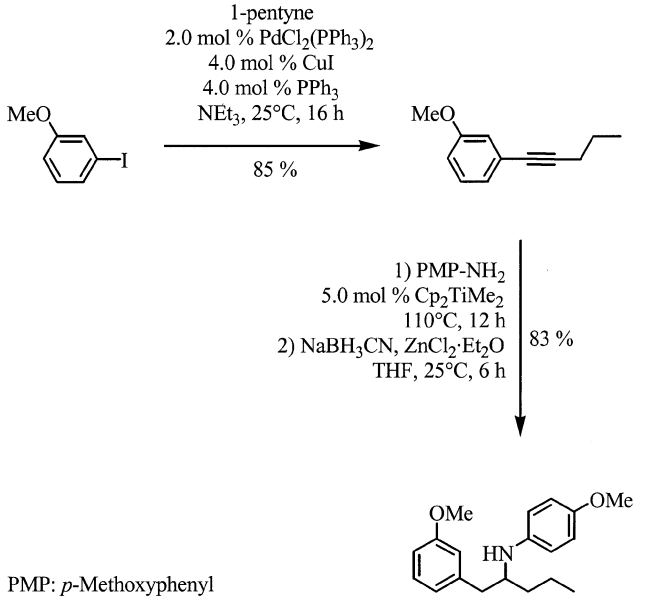
New and flexible procedures for the synthesis of indoline, indolizidine, and pyrrolizidine derivatives are described. By these new procedures, the target compounds can be synthesized with high diversity from three building blocks (*ortho*-bromo- or *ortho*-chloro-iodobenzenes, terminal alkynes, and primary amines). The synthetic strategies presented include Sonogashira couplings, Cp_2TiMe_2-catalyzed hydroaminations of alkynes, and Pd-catalyzed aminations of aryl halides as key steps. Since many of the employed starting materials are commercially available or easily accessible, a huge number of indoline, indolizidine, and pyrrolizidine derivatives is theoretically obtainable by the standard reaction sequences developed. Since the experimental procedures are simple and mostly catalytic, applications of the described methods for automated synthesis are also imaginable.

Introduction

During the last few years, catalytic hydroamination reactions of alkenes and alkynes have been investigated extensively.[1] While the hydroamination of alkenes is still limited to more or less activated alkenes, great progress has been achieved in the case of alkynes over the last four years.[2] Among the various catalysts identified for hydroamination reactions of alkynes, group-IV metal complexes play an outstanding role because they offer the possibility to convert both terminal and internal alkynes into the corresponding imines.[3] Furthermore, good regioselectivities of amine additions are observed in reactions of unsymmetrically substituted 2-alkyl-1-arylalkynes in the presence of titanium complexes such as $[Cp_2TiMe_2]$,[4] giving access to the corresponding anti-Markovnikov products.[5] These advantages, combined with the fact that 2-alkyl-1-arylalkynes can easily be obtained by Sonogashira coupling reactions,[6] have already been utilized for a flexible, three-step synthesis of biologically interesting 2-arylethylamine derivatives employing aryl halides, terminal alkynes, and primary amines as building blocks.[7] A representative example of the strategy, including a final reduction of the initially formed hydroamination product (imine), is given in Scheme 1. In this context, it is worth to mention that the hydroamination step and the final reduction are performed as a one-pot operation.



Scheme 1. Representative example for the flexible synthesis of 2-arylethylamine derivatives from aryl halides, terminal alkynes, and primary amines

Furthermore, it has been shown that titanium complexes also catalyze intramolecular hydroamination reactions.[8] By a corresponding approach, γ- and δ-aminoalkynes can be converted into cyclic amines by $[Cp_2TiMe_2]$-catalyzed cyclization and subsequent reduction with $NaBH_3CN$ in the presence of $ZnCl_2{\cdot}Et_2O$.[8d] Interestingly, aminoalkynes with a phenyl substituent directly bound to the alkyne sp center give access to products also possessing the biologically attractive 2-arylethylamine substructure (Scheme 2).

Being aware of the importance of indoline, indolizidine, and pyrrolizidine derivatives with regard to biological activity and organic synthesis,[9] we recently decided to combine and extend both strategies to develop a new and flexible synthetic pathway to molecules containing the corresponding substructures as well as a 2-phenylethyl-

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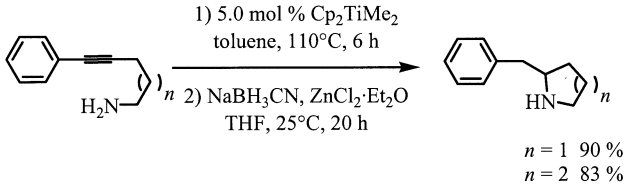
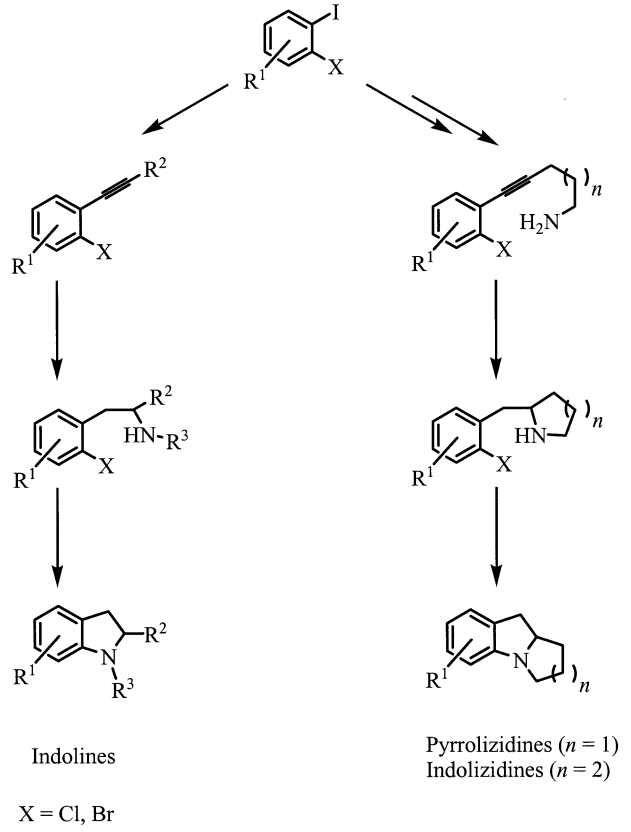


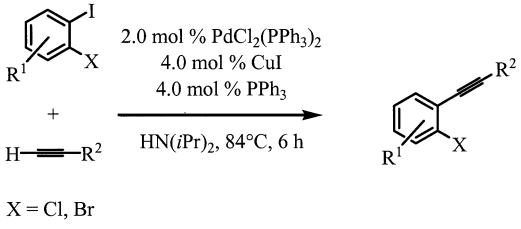
Scheme 2. Representative examples of the synthesis of 2-phenylethylamine derivatives from aminoalkyl(phenyl)alkynes

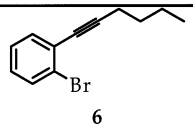
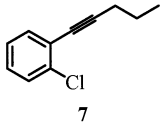
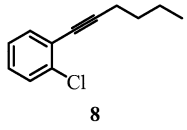
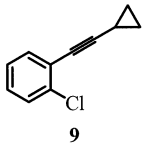
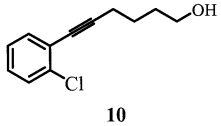
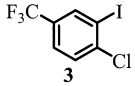
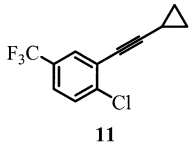
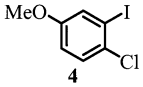
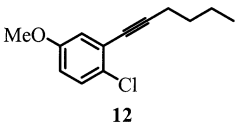
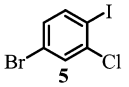
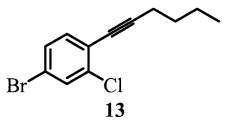
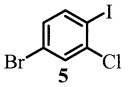
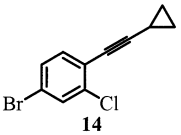
amine moiety (Scheme 3). For that purpose, we planned to use *ortho*-bromo- or *ortho*-chloro-functionalized 2-alkyl-1-phenylalkynes and aminoalkyl(phenyl)alkynes in place of simple 2-alkyl-1-phenylalkynes and aminoalkyl(phenyl)-alkynes as starting materials for the one-pot hydroamination reduction sequence. In this case, the reduced hydroamination products should be suitable substrates for a final palladium-catalyzed intramolecular amination reaction (Buchwald−Hartwig reaction),[10] giving access to the desired target molecules. Since the slightly modified starting materials should still be obtainable in a straightforward manner from simple, and in most cases commercially available, building blocks (e.g., 1-bromo- or 1-chloro-2-iodobenzenes and terminal alkynes) the desired strategy should offer high synthetic flexibility. For that reason, a corresponding approach (Scheme 3) should be suitable for the fast generation of many indoline, indolizidine, and pyrroliz-



Scheme 3. A flexible approach towards the synthesis of indoline, indolizidine, and pyrrolizidine derivatives containing a 2-phenylethylamine substructure from 1-bromo- or 1-chloro-2-iodobenzenes, terminal alkynes, and primary amines

Table 1. Synthesis of *ortho*-bromo- and *ortho*-chloro-substituted 2-alkyl-1-phenylalkynes by Sonogashira coupling



entry	aryl halide	product	yield [%][a]
1	 **1**	 **6**	78
2	 **2**	 **7**	99
3	 **2**	 **8**	98
4	 **2**	 **9**	99
5	 **2**	 **10**	99
6	 **3**	 **11**	97
7	 **4**	 **12**	95
8	 **5**	 **13**	94
9	 **5**	 **14**	97

[a] Reaction conditions: aryl halide (10.0 mmol), alkyne (10.0 mmol), $[PdCl_2(PPh_3)_2]$ (0.2 mmol, 2.0 mol %), CuI (0.4 mmol, 4.0 mol %), PPh_3 (0.4 mmol, 4.0 mol %), $HN(iPr)_2$, 84 °C, 6 h; yields represent isolated yields of pure compounds.

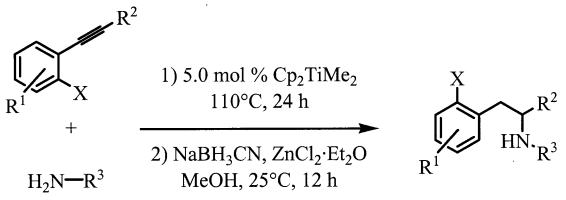
idine derivatives containing a 2-phenylethylamine substructure (a library), that could be used for further applications in organic synthesis as well as for biological tests.

Results and Discussion

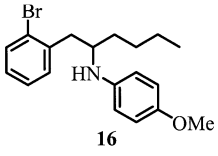
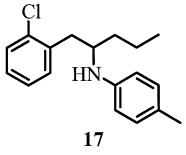
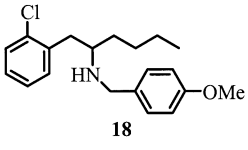
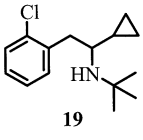
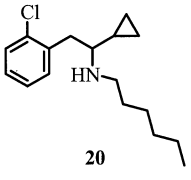
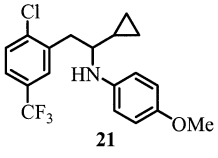
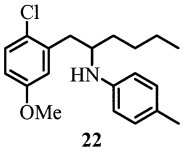
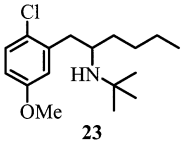
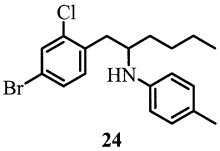
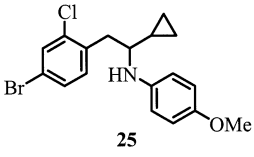
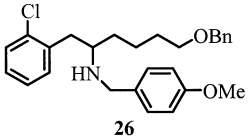
Starting from readily available and more or less highly functionalized 1-bromo- or 1-chloro-2-iodobenzenes **1**–**5** and terminal alkynes we first synthesized a number of *ortho*-bromo- and *ortho*-chloro-substituted 2-alkyl-1-phenylalkynes by Sonogashira coupling reactions. The reactions were usually performed under standard Sonogashira conditions, giving access to the corresponding alkynes **6**–**14** in high yields (Table 1). As expected, reactions took place exclusively at the more reactive iodo-substituted carbon centers of the aromatic bis- or tris-halides.

Since the side chain-functionalized compound **10** possesses a hydroxy group, which is not tolerated under the

Table 2. Synthesis of *ortho*-bromo- and *ortho*-chloro-substituted 2-phenylethylamine derivatives by regioselective hydroamination and subsequent in situ reduction

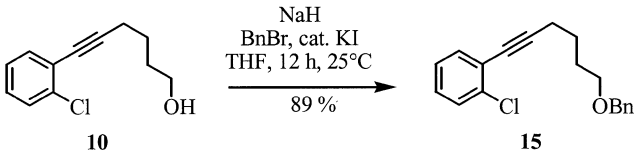


X = Cl, Br

entry	alkyne	product	yield [%][a]
1	**6**	 **16**	74[b]
2	**7**	 **17**	83
3	**8**	 **18**	58[c] [d]
4	**9**	 **19**	63
5	**9**	 **20**	66[c] [e]
6	**11**	 **21**	73
7	**12**	 **22**	94
8	**12**	 **23**	71
9	**13**	 **24**	73
10	**14**	 **25**	79
11	**15**	 **26**	48[c] [f]

[a] Reaction conditions: a) alkyne (4.0 mmol), amine (4.0 mmol), [Cp_2TiMe_2] (c = 0.48 mol/L in toluene, 0.2 mmol, 5.0 mol %), 110 °C, 24 h; b) $NaBH_3CN$ (8.0 mmol), $ZnCl_2{\cdot}Et_2O$ (c = 1.0 mol/L in Et_2O, 4.0 mmol), MeOH, 25 °C, 12 h. Yields represent isolated yields of pure compounds. [b] 10.0 mol % [Cp_2TiMe_2] was used for the hydroamination step. [c] [$Cp^*_2TiMe_2$] (c = 0.50 mol/L in toluene, 0.4 mmol, 10.0 mol %) was used as catalyst for the hydroamination step. [d] 30% of the Markovnikov regioisomer was obtained. [e] 29% of the Markovnikov regioisomer was obtained. [f] 39% of the Markovnikov regioisomer was obtained.

conditions of $[Cp_2TiMe_2]$-catalyzed hydroamination reactions, this substrate was converted into the corresponding benzyl ether **15** under standard conditions prior to further transformations (Scheme 4).

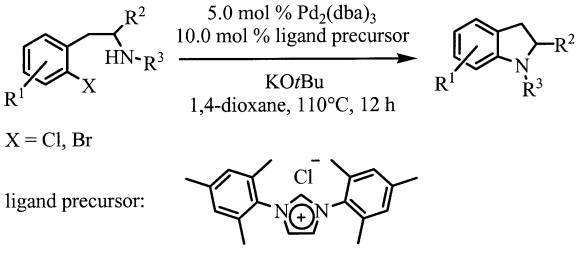


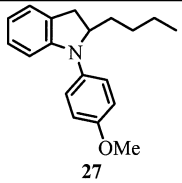
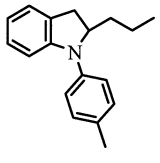
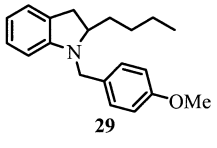
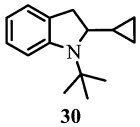
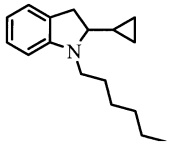
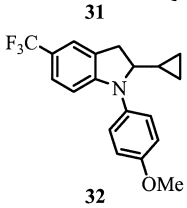
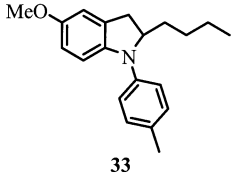
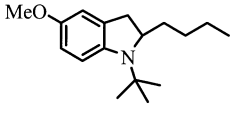
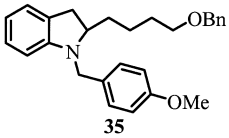
10 **15**

Scheme 4. Protection of the hydroxy group of **10** as a benzyl ether

Subsequently, the obtained alkynes **6**−**9** and **11**−**15** were regioselectively hydroaminated in the presence of catalytic amounts (5.0 mol %) of $[Cp_2TiMe_2]$ at 110 °C in the presence of various amines. The initially formed imine products were not isolated but were directly reduced to yield the stable *ortho*-bromo- and *ortho*-chloro-functionalized 2-phenylethylamine derivatives **16**−**26** (Table 2). Particularly interesting are reactions employing *para*-methoxyaniline (PMP-NH_2, Entries 1, 6, 10) and *para*-methoxybenzylamine (PMB-NH_2, Entries 3, 11) because these amines represent potential ammonia equivalents. However, for reactions involving sterically less demanding amines such as *para*-methoxybenzylamine (Entries 3, 11) and *n*-hexylamine (Entry 5) it was necessary to use $[Cp^*_2TiMe_2]$ as catalyst for a successful hydroamination step.[11] As observed before, the obtained regioselectivities of the hydroamination reactions are poor in these cases. In all corresponding reactions, large amounts (29−39%) of the corresponding Markovnikov re-

Table 3. Palladium-catalyzed cyclization to indoline derivatives



entry	amine	product	yield [%][a]
1	**16**	 **27**	97[b]
2	**17**	 **28**	99
3	**18**	 **29**	98
4	**19**	 **30**	99
5	**20**		97
6	**21**	 **31**	95
7	**22**	 **33**	89
8	**23**	 **34**	86
9	**26**	 **35**	92

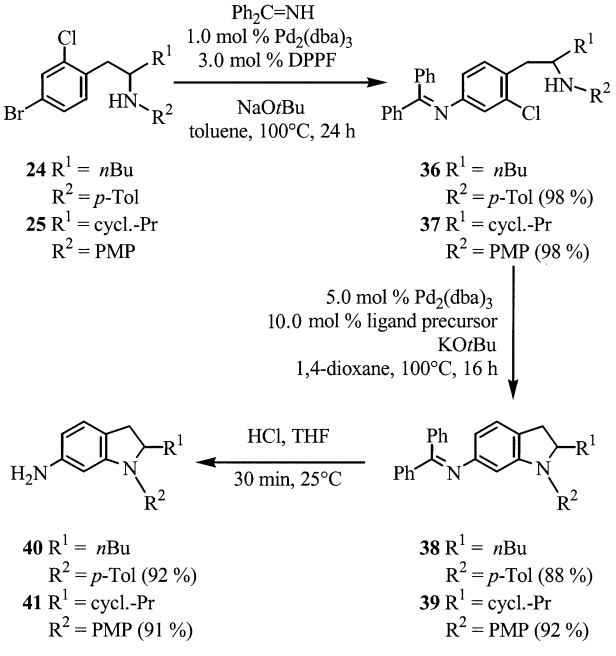
[a] Reaction conditions: amine (2.0 mmol), $[Pd_2(dba)_3]$ (0.1 mmol, 5.0 mol %), ligand precursor (0.2 mmol, 10.0 mol %), KO*t*Bu (3.0 mmol), 1,4-dioxane, 110 °C, 12 h. Yields represent isolated yields of pure compounds. [b] Reaction conditions: amine (2.0 mmol), $[Pd(PPh_3)_4]$ (0.1 mmol, 5.0 mol %), K_2CO_3 (4.0 mmol), NaO*t*Bu (4.0 mmol), toluene, 110 °C, 5 h.

gioisomers were isolated along with the desired products (48−58%).

Finally, the *ortho*-bromo- and *ortho*-chloro-substituted 2-phenylethylamines **16**−**23** and **26** were converted into indoline derivatives **27**−**35** in the presence of a palladium catalyst. Depending on the nature of the halide (Br or Cl), different catalyst systems were used. The bromo derivative **16** was treated with NaO*t*Bu and [$Pd(PPh_3)_4$], while the chloro derivatives required the presence of KO*t*Bu, [$Pd_2(dba)_3$], and a carbene ligand (Table 3). Product **35** is especially interesting, because the protected oxygen functionality in the side chain offers the possibility for further transformations (e.g. cyclizations). Furthermore, the N-protected indolines **27**, **29**, **32**, and **35** can be seen as precursors for the corresponding unprotected derivatives.

This flexible synthetic strategy is characterized by the fact that the indoline target compounds can be synthesized from three building blocks in only four steps. Since many of these building blocks are commercially available, a huge number of indoline derivatives is theoretically accessible by following the developed standard reaction sequence. Since the experimental procedures are simple and mostly catalytic, application of the method to automated synthesis is also imaginable.

As can be seen from Table 1 and 2, it was also possible to perform the first three steps of the reaction sequence starting from 1-bromo-3-chloro-4-iodobenzene (**5**). In this case, the presence of the additional bromo substituent in the 2-phenylethylamine products **24** and **25** (Table 2) offers the possibility to introduce further functionalities. For that purpose, we chose a Pd-catalyzed intermolecular amination reaction employing benzophenone imine which took place at the bromo-substituted centers in **24** and **25** and established a nitrogen functionality at the aromatic systems

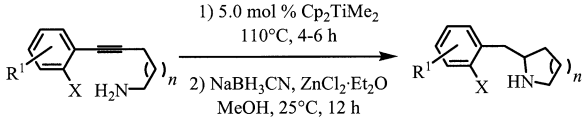


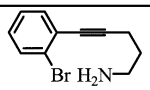
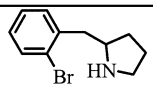
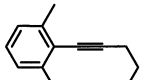
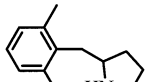
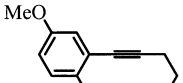
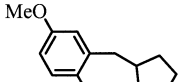
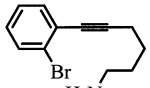
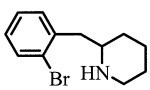
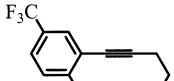
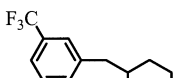
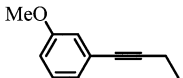
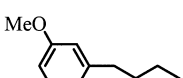
Scheme 5. Synthesis of NH_2-substituted indoline derivatives

(Scheme 5).[12] The obtained imine products **36** and **37** could then be converted into nitrogen-functionalized indoline derivatives **38** and **39** by a second Pd-catalyzed intramolecular amination reaction. A final cleavage of the C−N double bonds gave access to the corresponding derivatives **40** and **41** containing unprotected NH_2 groups (Scheme 5).

Indolizidine and pyrrolizidine derivatives were found to be accessible in a related manner from *ortho*-bromo- and *ortho*-chloro-functionalized aminoalkyl(phenyl)alkynes **42**−**47**, which could be synthesized in a flexible manner from 1-bromo- or 1-chloro-2-iodobenzenes by literature procedures, with a Sonogashira reaction as the key step.[8d,13] Again, a one-pot hydroamination reduction se-

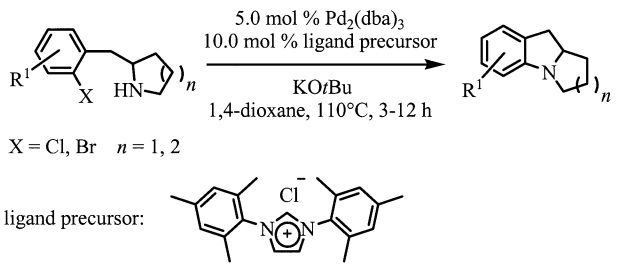
Table 4. Synthesis of pyrrolidine and piperidine derivatives from *ortho*-bromo- and *ortho*-chloro-substituted aminoalkyl(phenyl)alkynes by hydroamination and subsequent in situ reduction

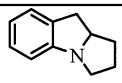
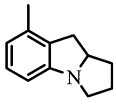
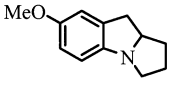
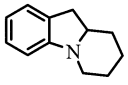
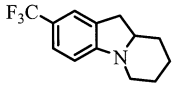
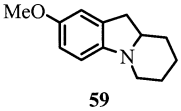


entry	aminoalkyne	product	yield [%][a]
1	 **42**	 **48**	88
2	 **43**	 **49**	62
3	 **44**	 **50**	97
4	 **45**	 **51**	67
5	 **46**	 **52**	94
6	 **47**	 **53**	97

[a] Reaction conditions: a) aminoalkyne (4.0 mmol), [Cp_2TiMe_2] (c = 0.48 mol/L in toluene, 0.2 mmol, 5.0 mol %), 110 °C, 4−6 h; b) $NaBH_3CN$ (8.0 mmol), $ZnCl_2$·Et_2O (c = 1.0 mol/L in Et_2O, 4.0 mmol), MeOH, 25 °C, 12 h. Yields represent isolated yields of pure compounds.

Table 5. Palladium-catalyzed cyclization to indolizidine and pyrrolizidine derivatives



entry	amine	product	yield [%][a]
1	**48**	 **54**	71[b]
2	**49**	 **55**	99
3	**50**	 **56**	-
4	**51**	 **57**	64[b]
5	**52**	 **58**	97
6	**53**	 **59**	79

[a] Reaction conditions: amine (1.0 mmol), [$Pd_2(dba)_3$] (0.05 mmol, 5.0 mol %), ligand precursor (0.1 mmol, 10.0 mol %), KO*t*Bu (1.5 mmol), 1,4-dioxane, 110 °C, 3−12 h. Yields represent isolated yields of pure compounds. [b] Reaction conditions: amine (1.0 mmol), [$Pd(PPh_3)_4$] (0.05 mmol, 5.0 mol %), K_2CO_3 (2.0 mmol), NaO*t*Bu (2.0 mmol), toluene, 110 °C, 6 h.

quence was used to produce the corresponding *ortho*-bromo- and *ortho*-chloro-substituted 2-phenylethylamine derivatives containing pyrrolidine and piperidine substructures (**48**−**53**) in good yields (Table 4).

Palladium-catalyzed cyclization reactions employing the piperidine derivatives **51**−**53** smoothly gave the desired indolizidines **57**−**59** in good yields, while the pyrrolidine derivative **50** did not react successfully (Table 5). An explanation for this lack of reactivity may be seen in the combination of two factors: (i) the presence of an electron-rich and therefore less reactive aromatic system, and (ii) the greater ring strain in this substrate than in the corresponding piperidine derivative **53**. However, the other molecules containing a five-membered cyclic amine structure (**48**, **49**) did undergo successful cyclization. Interestingly, under optimized conditions, better yields were obtained from chlorobenzenes (Table 5, Entries 2, 5, 6) than from bromobenzenes (Table 5, Entries 1, 4).

Conclusion

In summary, the procedures developed for the synthesis of indoline, indolizidine, and pyrrolizidine derivatives again show that clever combinations of recently developed, modern catalytic organic transformations offer flexible and efficient synthetic pathways to biologically interesting classes of molecules. The major advantage of the described (and related) synthetic strategies is the fact that thousands of products are theoretically accessible from a relative small number of readily available building blocks by a standard procedure. Interestingly, the [Cp_2TiMe_2]-catalyzed hydroamination of alkynes demonstrates once more that it does not represent just another curiosity from organometallic laboratories but should be regarded as a new and powerful tool for organic synthesis. In our opinion, this judgment is underlined by the fact that all yields reported in this publication are isolated yields.

Experimental Section

General Remarks: All reactions were performed under argon in flame-dried Duran glassware (e.g., Schlenk tubes fitted with Teflon stopcocks). Toluene was distilled from molten sodium under argon. Methanol was dried with molecular sieves (3 Å). [Cp_2TiMe_2] was synthesized according to ref.[4a] 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride according to ref.[14] aminoalkynes **42**−**47** according to ref.[8d,13] and compound **4** according to ref.[15] All other reagents were purchased from commercial sources and were used without further purification. Unless otherwise noted, yields refer to isolated yields of pure compounds as gauged by TLC and ^1H and ^{13}C NMR spectroscopy. All products were characterized by ^1H NMR, ^{13}C NMR, and infrared (IR) spectroscopy, and mass spectrometry (MS). New compounds were further characterized by high-resolution mass spectrometry (HRMS) or CHN elemental analysis. NMR spectra were recorded with a Bruker Avance 400 MHz spectrometer. All ^1H NMR spectra are reported in δ units ppm downfield from tetramethylsilane internal 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 ppm. Infrared spectra were recorded with a Bruker Vector 22 spectrometer by 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 or a Micromass LCT (ESI). Elemental analysis were carried out on an Elementar Vario EL machine. PE: light petroleum ether, b.p. 40−60 °C.

Sonogashira Coupling. General Procedure A: CuI (77 mg, 0.4 mmol, 4.0 mol %), [$(PPh_3)_2PdCl_2$] (141 mg, 0.2 mmol, 2.0 mol %), PPh_3 (105 mg, 0.4 mmol, 4.0 mol %), and HN(*i*Pr)$_2$ (30 mL) were placed in a round-bottomed flask containing a magnetic stirring bar. After addition of the aryl halide (10.0 mmol), the mixture was stirred for 30 min at 25 °C, and the alkyne (10.0 mmol) was then added. After this had been stirred at 84 °C for a further 6 h, saturated NH_4Cl solution was added. The mixture was extracted with *tert*-butyl methyl ether (3 ×). The combined organic layers were dried with

$MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Alkyne 6: General Procedure A was used to synthesize alkyne **6** from 1-bromo-2-iodobenzene (**1**) and 1-hexyne. After purification by flash chromatography (PE), compound **6** (1.85 g, 7.80 mmol, 78%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.3 Hz, 3 H), 1.48−1.67 (m, 4 H), 2.47 (t, *J* = 7.0 Hz, 2 H), 7.10 (td, *J* = 7.7, 1.7 Hz, 1 H), 7.21 (td, *J* = 7.6, 1.6 Hz, 1 H), 7.42 (dd, *J* = 7.7, 1.6 Hz, 1 H), 7.55 (dd, *J* = 8.0, 1.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.6 (CH_3), 19.2 (CH_2), 22.0 (CH_2), 30.6 (CH_2), 79.3 (C), 95.6 (C), 125.4 (C), 126.1 (C), 126.8 (CH), 128.6 (CH), 132.2 (CH), 133.3 (CH) ppm. IR: $\tilde{\nu}$ = 3061, 2957, 2931, 2871, 2234, 1588, 1558, 1468, 1433, 1026, 749 cm^{-1}. MS (25 °C): *m*/*z* (%) = 238 (74) [M^+(^{81}Br)], 236, (77) [M^+(^{79}Br)], 223 (36), 221 (39), 195 (50), 193 (51), 182 (26), 180 (23), 142 (100), 128 (71), 115 (65), 91 (24). HRMS: calcd. ($C_{12}H_{13}Br$) 236.0201; found 236.0195.

Alkyne 7: General Procedure A was used to synthesize alkyne **7** from 1-chloro-2-iodobenzene (**2**) and 1-pentyne. After purification by flash chromatography (PE), compound **7** (1.76 g, 9.85 mmol, 99%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.3 Hz, 3 H), 1.66 (sept, *J* = 7.2 Hz, 2 H), 2.45 (t, *J* = 7.0 Hz, 2 H), 7.14−7.20 (m, 2 H), 7.34−7.38 (m, 1 H), 7.40−7.45 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.5 (CH_3), 21.8 (CH_2), 22.1 (CH_2), 77.7 (C), 96.0 (C), 126.3 (CH), 128.4 (CH), 129.1 (CH), 133.3 (CH), 135.7 (C), 140.2 (C) ppm. IR: $\tilde{\nu}$ = 3069, 2963, 2933, 2233, 1473, 1065, 1033, 749 cm^{-1}. MS (25 °C): *m*/*z* (%) = 180 (77) [M^+(^{37}Cl)], 178 (97) [M^+(^{35}Cl)], 163 (52), 149 (100) [$M^+ - C_2H_5$], 143 (79) [$M^+ - Cl$], 136 (60), 128 (80), 115 (57), 111 (23), 101 (18), 87 (17), 75 (30). HRMS: calcd. ($C_{11}H_{11}Cl$) 178.0549; found 178.0555.

Alkyne 8: General Procedure A was used to synthesize alkyne **8** from 1-chloro-2-iodobenzene (**2**) and 1-hexyne. After purification by flash chromatography (PE), compound **8** (1.89 g, 9.82 mmol, 98%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.3 Hz, 3 H), 1.47−1.66 (m, 4 H), 2.47 (t, *J* = 7.0 Hz, 2 H), 7.15−7.20 (m, 2 H), 7.35−7.37 (m, 1 H), 7.43−7.44 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.6 (CH_3), 19.3 (CH_2), 21.9 (CH_2), 30.7 (CH_2), 77.5 (C), 96.1 (C), 123.9 (C), 126.3 (CH), 128.4 (CH), 129.1 (CH), 133.3 (CH), 135.7 (C) ppm. IR: $\tilde{\nu}$ = 3068, 2958, 2931, 2872, 2234, 1591, 1562, 1473, 1428, 1065, 1033, 750 cm^{-1}. MS (25 °C): *m*/*z* (%) = 192 (58) [M^+], 177 (65), 163 (35), 149 (100), 142 (53), 129 (67), 115 (56), 91 (16), 77 (14). HRMS: calcd. ($C_{12}H_{13}Cl$) 192.0697; found 192.0706.

Alkyne 9: General Procedure A was used to synthesize alkyne **9** from 1-chloro-2-iodobenzene (**2**) and cyclopropylacetylene (*c* = 70% in toluene). After purification by flash chromatography (PE), compound **9** (1.75 g, 9.91 mmol, 99%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83−0.93 (m, 4 H), 1.47−1.55 (m, 1 H), 7.12−7.19 (m, 2 H), 7.77−7.36 (m, 1 H), 7.38−7.41 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.4 (CH), 8.9 (CH_2), 72.6 (C), 99.2 (C), 123.7 (C), 126.2 (CH), 128.3 (CH), 129.0 (CH), 133.2 (CH), 135.7 (C) ppm. IR: $\tilde{\nu}$ = 3013, 2230, 1474, 1436, 1055, 749 cm^{-1}. MS (25 °C): *m*/*z* (%) = 176 (92) [M^+], 141 (100) [$M^+ - Cl$], 139 (67), 115 (67), 87 (22), 79 (19). HRMS: calcd. ($C_{11}H_9Cl$) 176.0393; found 176.0383. $C_{11}H_9Cl$ (176.6): calcd. C 74.79, H 5.14; found C 74.50, H 5.09.

Alkyne 10: General Procedure A was used to synthesize alkyne **10** from 1-chloro-2-iodobenzene (**2**) and 5-hexynol. After purification by flash chromatography (PE/EtOAc, 10:1), compound **10** (2.08 g, 9.97 mmol, 99%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.67−1.82 (m, 4 H), 2.51 (t, *J* = 6.7 Hz, 2 H), 3.70 (t, *J* = 6.0 Hz, 2 H), 7.14−7.21 (m, 2 H), 7.35−7.37 (m, 1 H), 7.41−7.43 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 19.3 (CH_2), 24.8 (CH_2), 31.7 (CH_2), 62.3 (CH_2), 77.8 (C), 95.6 (C), 123.6 (C), 126.3 (CH), 128.5 (CH), 129.0 (CH), 133.2 (CH), 135.6 (C) ppm. IR: $\tilde{\nu}$ = 3307, 2937, 2935, 2233, 1561, 1473, 1429, 1062, 1032, 750 cm^{-1}. MS (60 °C): *m*/*z* (%) = 210 (27) [M^+(^{37}Cl)], 208 (26) [M^+(^{35}Cl)], 190 (10), 173 (72), 164 (78), 149 (80), 141 (47), 129 (100), 114 (59), 99 (17), 91 (15), 75 (21). HRMS: calcd. ($C_{12}H_{13}ClO$) 208.0655; found 208.0653.

Alkyne 11: General Procedure A was used to synthesize alkyne **11** from 1-chloro-2-iodo-4-trifluoromethylbenzene (**3**) and cyclopropylacetylene (*c* = 70% in toluene). After purification by flash chromatography (PE), compound **11** (2.37 g, 9.69 mmol, 97%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86−0.97 (m, 4 H), 1.48−1.55 (m, 1 H), 7.40 (dd, *J* = 8.4, 1.8 Hz, 1 H), 7.47 (d, *J* = 8.4 Hz, 1 H), 7.66 (d, *J* = 2.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.3 (CH), 9.0 (CH_2), 71.6 (C), 101.3 (C), 123.4 (CF_3, q, *J* = 272 Hz), 124.7 (C), 124.8 (CH, q, *J* = 3 Hz), 129.1 (C, q, *J* = 33 Hz), 129.6 (CH), 130.1 (CH, q, *J* = 4 Hz), 139.4 (C, q, *J* = 1 Hz) ppm. IR: $\tilde{\nu}$ = 3098, 3016, 2235, 1607, 1327, 1126, 1078, 825 cm^{-1}. MS (25 °C): *m*/*z* (%) = 244 (100) [M^+], 209 (93) [$M^+ - Cl$], 175 (57) [$M^+ - CF_3$], 139 (50), 99 (13), 87 (12), 74 (11). HRMS: calcd. ($C_{12}H_8ClF_3$) 244.0267; found 244.0268.

Alkyne 12: General Procedure A was used to synthesize alkyne **12** from 1-chloro-2-iodo-4-methoxybenzene (**4**) and 1-hexyne. After purification by flash chromatography (PE/EtOAc, 20:1), compound **12** (2.11 g, 9.47 mmol, 95%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.3 Hz, 3 H), 1.46−1.56 (m, 2 H), 1.58−1.65 (m, 2 H), 2.46 (t, *J* = 6.9 Hz, 2 H), 3.76 (s, 3 H), 6.75 (dd, *J* = 8.9, 3.1 Hz, 1 H), 6.95 (d, *J* = 3.0 Hz, 1 H), 7.24 (d, *J* = 8.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.6 (CH_3), 19.2 (CH_2), 21.9 (CH_2), 30.6 (CH_2), 55.5 (CH_3), 77.6 (C), 95.9 (C), 115.3 (CH), 117.6 (CH), 124.3 (C), 127.3 (C), 129.7 (CH), 157.7 (C) ppm. IR: $\tilde{\nu}$ = 2957, 2933, 2872, 2232, 1593, 1567, 1468, 1398, 1290, 1209, 1172, 1028, 804 cm^{-1}. MS (60 °C): *m*/*z* (%) = 223 (100), 207 (47), 194 (18), 187 (42), 179 (99), 172 (92), 166 (20), 158 (50), 145 (29), 128 (25), 115 (41), 101 (19). HRMS: calcd. ($C_{13}H_{15}ClO$) 222.0811; found 222.0811. $C_{13}H_{15}ClO$ (222.7): calcd. C 70.11, H 6.79; found C 70.17, H 6.62.

Alkyne 13: General Procedure A was used to synthesize alkyne **13** from 1-bromo-3-chloro-4-iodobenzene (**5**) and 1-hexyne. After purification by flash chromatography (PE), compound **13** (2.55 g, 9.39 mmol, 94%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.3 Hz, 3 H), 1.45−1.55 (m, 2 H), 1.58−1.65 (m, 2 H), 2.45 (t, *J* = 7.0 Hz, 2 H), 7.27 (d, *J* = 8.5 Hz, 1 H), 7.30 (dd, *J* = 8.3, 1.8 Hz, 1 H), 7.54 (d, *J* = 1.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.6 (CH_3), 19.3 (CH_2), 21.9 (CH_2), 30.5 (CH_2), 76.7 (C), 97.4 (C), 121.3 (C), 123.0 (C), 129.6 (CH), 131.8 (CH), 134.0 (CH), 136.6 (C) ppm. IR: $\tilde{\nu}$ = 2957, 2951, 2234, 1579, 1542, 1420, 1082, 1065, 816 cm^{-1}. MS (25 °C): *m*/*z* (%) = 272 (100) [M^+(^{81}Br)], 270 (99) [M^+(^{79}Br)], 257 (99), 255 (83), 229 (99), 227 (93), 216 (63), 214 (43), 193 (20), 191 (19), 176 (99), 162 (88), 156 (92), 150 (60), 141 (58), 131 (68), 87 (21), 75 (23). HRMS: calcd. ($C_{12}H_{12}BrCl$) 269.9811; found 269.9812. $C_{12}H_{12}BrCl$ (271.6): calcd. C 53.07, H 4.45; found C 52.70, H 4.45.

Alkyne 14: General Procedure A was used to synthesize alkyne **14** from 1-bromo-3-chloro-4-iodobenzene (**5**) and cyclopropylacetylene (*c* = 70% in toluene). After purification by flash chromatogra-

phy (PE), compound **14** (2.48 g, 9.70 mmol, 97%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83−0.94 (m, 4 H), 1.45−1.52 (m, 1 H), 7.24 (d, *J* = 8.4 Hz, 1 H), 7.29 (dd, *J* = 8.3, 1.9 Hz, 1 H), 7.51 (d, *J* = 1.9 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.4 (CH), 8.9 (CH_2), 71.8 (C), 100.5 (C), 121.2 (C), 122.8 (C), 129.6 (CH), 131.8 (CH), 134.0 (CH), 136.6 (C) ppm. IR: ṽ = 3091, 3011, 2236, 1578, 1540, 1471, 1082, 1054, 1028, 814 cm^{-1}. MS (25 °C): *m*/*z* (%) = 256 (100) [M^+(^{81}Br)], 254 (93) [M^+(^{79}Br)], 221 (69), 219 (72), 175 (79), 139 (86), 118 (76). HRMS: calcd. ($C_{11}H_8BrCl$) 253.9498; found 253.9499. $C_{11}H_8BrCl$ (255.5): calcd. C 51.70, H 3.16; found C 51.57, H 3.18.

Alkyne 15: Sodium hydride (288 mg, *c* = 60% in oil, 7.8 mmol) and THF (5.0 mL) were placed in a round-bottomed flask containing a magnetic stirring bar. After addition of a solution of alkyne **10** (1.25 g, 6.0 mmol) in THF (5.0 mL), the mixture was stirred at 25 °C for 30 min, and benzyl bromide (927 μL, 7.2 mmol) and a catalytic amount of potassium iodide were then added. After this had been stirred at 25 °C for 12 h, water was added. The mixture was extracted with *tert*-butyl methyl ether (3 ×). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. After purification by flash chromatography (PE/EtOAc, 20:1) on SiO_2, compound **15** (1.60 g, 5.35 mmol, 89%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70−1.87 (m, 4 H), 2.49 (t, *J* = 6.8 Hz, 2 H), 3.53 (t, *J* = 6.2 Hz, 2 H), 4.51 (s, 2 H), 7.12−7.19 (m, 2 H), 7.23−7.36 (m, 6 H), 7.40−7.42 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 19.4 (CH_2), 25.3 (CH_2), 28.8 (CH_2), 69.8 (CH_2), 72.8 (CH_2), 77.8 (C), 95.7 (C), 123.8 (C), 126.3 (CH), 127.5 (CH), 127.6 (CH), 128.3 (CH), 128.5 (CH), 129.1 (CH), 133.2 (CH), 135.7 (C), 138.6 (C) ppm. IR: ṽ = 3063, 3030, 2936, 2859, 2234, 1495, 1473, 1453, 1429, 1104, 1065, 751, 734, 696 cm^{-1}. MS (70 °C): *m*/*z* (%) = 298 (11) [M^+], 207 (21), 191 (11), 163 (4), 149 (27), 139 (17), 125 (60), 115 (18), 105 (19), 91 (100), 77 (8). HRMS: calcd. ($C_{19}H_{19}ClO$) 298.1124; found 298.1126.

Hydroamination/Reduction. General Procedure B: A Schlenk tube fitted with a Teflon stopcock and containing a magnetic stirring bar was charged with amine (4.0 mmol), alkyne (4.0 mmol), and a solution of [Cp_2TiMe_2] (0.41 mL, *c* = 0.48 mol/L in toluene, 0.2 mmol, 5.0 mol %). The mixture was heated to 110 °C for 24 h (TLC monitoring). Then, a mixture of $NaBH_3CN$ (503 mg, 8.0 mmol) and $ZnCl_2$·Et_2O (4.0 mL, *c* = 1.0 mol/L in Et_2O, 4.0 mmol) in MeOH (10 mL) was added. After this had been stirred at 25 °C for 12 h, HCl (2 N) and CH_2Cl_2 were added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 ×). KOH (2 N) was added to the aqueous layer until pH = 12 was reached. The basic aqueous layer was extracted with CH_2Cl_2 (2 ×). The combined organic layers were extracted with KOH (2 N) and brine. After drying with Na_2SO_4 and concentration under vacuum, the residue was purified by flash chromatography (SiO_2).

Amine 16: General Procedure B was used to synthesize amine **16** from 4-methoxyaniline and alkyne **6**. [Cp_2TiMe_2] (10.0 mol %) was used for the hydroamination step. After purification by flash chromatography (PE/EtOAc, 10:1), compound **16** (1.07 g, 2.95 mmol, 74%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.2 Hz, 3 H), 1.24−1.57 (m, 6 H), 2.88 (dd, *J* = 13.8, 6.4 Hz, 1 H), 2.97 (dd, *J* = 13.7, 7.1 Hz, 1 H), 3.25 (br. s, 1 H), 3.63−3.67 (m, 1 H), 3.72 (s, 3 H), 6.53 (d, *J* = 9.0 Hz, 2 H), 6.73 (d, *J* = 8.9 Hz, 2 H), 7.01−7.05 (m, 1 H), 7.16−7.21 (m, 2 H), 7.51 (d, *J* = 7.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 22.8 (CH_2), 28.2 (CH_2), 34.6 (CH_2), 41.6 (CH_2), 54.4 (CH), 55.8 (CH_3), 114.5 (CH), 114.9 (CH), 124.9 (C), 127.2 (CH), 127.8 (CH), 131.5 (CH), 132.8 (CH), 138.9 (C), 142.0 (C), 151.8 (C) ppm. MS (70 °C): *m*/*z* (%) = 363 (22) [M^+(^{81}Br)], 361 (23) [M^+(^{79}Br)], 306 (8), 304 (7), 272 (32), 192 (100), 175 (20), 171 (14), 169 (14), 149 (23), 136 (17), 134 (18), 85 (50). HRMS: calcd. ($C_{19}H_{24}BrNO$) 361.1041; found 361.1042.

Amine 17: General Procedure B was used to synthesize amine **17** from 4-methylaniline and alkyne **7**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **17** (955 mg, 3.32 mmol, 83%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.33−1.57 (m, 4 H), 2.21 (s, 3 H), 2.86 (dd, *J* = 13.7, 6.6 Hz, 1 H), 3.00 (dd, *J* = 13.7, 6.7 Hz, 1 H), 3.38 (br. s, 1 H), 3.70 (m, 1 H), 6.51 (d, *J* = 8.0 Hz, 2 H), 6.94 (d, *J* = 8.0 Hz, 2 H), 7.09−7.16 (m, 2 H), 7.19−7.23 (m, 1 H), 7.32−7.34 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 19.2 (CH_2), 20.3 (CH_3), 37.0 (CH_2), 38.9 (CH_2), 53.3 (CH), 113.1 (CH), 126.0 (C), 126.6 (CH), 127.5 (CH), 129.5 (CH), 129.7 (CH), 131.5 (CH), 134.3 (C), 137.1 (C), 145.4 (C) ppm. IR: ṽ = 3407, 3016, 2956, 2929, 2869, 1617, 1517, 1474, 1442, 1036, 805, 748 cm^{-1}. MS (70 °C): *m*/*z* (%) = 287 (30) [M^+], 244 (30) [$M^+ - C_3H_7$], 209 (19), 162 (100), 132 (19), 125 (19), 120 (24), 106 (13), 91 (24). HRMS: calcd. ($C_{18}H_{22}ClN$) 287.1441; found 287.1441. $C_{18}H_{22}ClN$ (287.8): calcd. C 75.11, H 7.70, N 4.87; found C 75.00, H 7.71, N 5.02.

Amine 18: General Procedure B was used to synthesize amine **18** from 4-methoxybenzylamine and alkyne **8**. [$Cp^*_2TiMe_2$] (*c* = 0.50 mol/L in toluene, 0.4 mmol, 10.0 mol %) was used as catalyst for the hydroamination step. After purification by flash chromatography (PE/EtOAc, 3:1), compound **18** (770 mg, 2.32 mmol, 58%) and its Markovnikov regioisomer (396 mg, 1.19 mmol, 30%) were isolated as colorless oils. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.23−1.47 (m, 6 H), 2.78−2.91 (m, 3 H), 3.66 (d, *J* = 12.8 Hz, 1 H), 3.72 (d, *J* = 12.9 Hz, 1 H), 3.77 (s, 3 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 7.12 (d, *J* = 8.7 Hz, 2 H), 7.12−7.21 (m, 3 H), 7.33 (dd, *J* = 7.0, 2.1 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 22.9 (CH_2), 27.9 (CH_2), 33.9 (CH_2), 39.0 (CH_2), 50.7 (CH_2), 55.2 (CH_3), 56.7 (CH), 113.7 (CH), 126.5 (CH), 127.5 (CH), 129.1 (CH), 129.5 (CH), 131.6 (CH), 133.0 (C), 134.3 (C), 137.7 (C), 158.4 (C) ppm. IR: ṽ = 3338, 2953, 2928, 2857, 2834, 1611, 1585, 1510, 1464, 1243, 1172, 1035, 822, 748 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{20}H_{26}ClNO$+H) 332.1781; found 332.1796. $C_{20}H_{26}ClNO$ (331.9): calcd. C 72.38, H 7.90, N 4.22; found C 72.39, H 7.79, N 4.16. Characterization of the Markovnikov regioisomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.8 Hz, 3 H), 1.22−1.36 (m, 6 H), 1.65 (q, *J* = 7.5 Hz, 2 H), 3.47 (d, *J* = 12.7 Hz, 1 H), 3.54 (d, *J* = 12.8 Hz, 1 H), 3.79 (s, 3 H), 4.20 (t, *J* = 6.6 Hz, 1 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 7.17 (td, *J* = 7.6, 1.5 Hz, 1 H), 7.19 (d, *J* = 8.5 Hz, 2 H), 7.28 (td, *J* = 7.5, 1.2 Hz, 1 H) 7.34 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.54 (dd, *J* = 7.8, 1.5 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 22.5 (CH_2), 25.7 (CH_2), 31.8 (CH_2), 37.1 (CH_2), 51.0 (CH_2), 55.2 (CH_3), 58.3 (CH), 113.7 (CH), 127.0 (CH), 127.7 (CH), 128.1 (CH), 129.3 (CH), 129.5 (CH), 132.8 (C), 133.9 (C), 141.8 (C), 158.6 (C) ppm. IR: ṽ = 3338, 2953, 2929, 2856, 1611, 1585, 1510, 1463, 1440, 1244, 1173, 1034, 821, 752 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{20}H_{26}ClNO$+H) 332.1781; found 332.1780. $C_{20}H_{26}ClNO$ (331.9): calcd. C 72.38, H 7.90, N 4.22; found C 72.71, H 7.58, N 4.89.

Amine 19: General Procedure B was used to synthesize amine **19** from *tert*-butylamine and alkyne **9**. After purification by flash chromatography (PE/EtOAc, 1:1), compound **19** (635 mg, 2.52 mmol, 63%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$):

δ = −0.15 to −0.09 (m, 1 H), 0.06−0.12 (m, 1 H), 0.25−0.31 (m, 1 H), 0.34−0.41 (m, 1 H), 0.71−0.81 (m, 1 H), 1.05 (s, 9 H), 2.35 (q, *J* = 8.2 Hz, 1 H), 2.89 (dd, *J* = 13.0, 7.8 Hz, 1 H), 3.04 (dd, *J* = 13.2, 6.2 Hz, 1 H), 7.10−7.17 (m, 2 H), 7.24−7.27 (m, 1 H), 7.30−7.32 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 3.6 (CH_2), 4.8 (CH_2), 18.4 (CH), 30.2 (CH_3), 43.0 (CH_2), 50.3 (C), 56.2 (CH), 126.2 (CH), 127.3 (CH), 129.2 (CH), 132.3 (CH), 134.2 (C), 137.9 (C) ppm. IR: ṽ = 3074, 2963, 1474, 1441, 1388, 1361, 1051, 747 cm^{-1}. MS (25 °C): *m*/*z* (%) = 237 (14) [M^+ + H − CH_3], 154 (15), 126 (84), 91 (11), 77 (4), 70 (100). HRMS: calcd. ($C_{14}H_{20}ClN$) 237.1284; found 237.1236. $C_{15}H_{22}ClN$ (251.8): calcd. C 71.55, H 8.81, N 5.56; found C 71.10, H 8.79, N 5.35.

Amine 20: General Procedure B was used to synthesize amine **20** from 1-hexylamine and alkyne **9**. [$Cp^*_2TiMe_2$] (*c* = 0.50 mol/L in toluene, 0.4 mmol, 10.0 mol %) was used as catalyst for the hydroamination step. After purification by flash chromatography (PE/EtOAc, 7:1 → 1:1), compound **20** (738 mg, 2.64 mmol, 66%) and its Markovnikov regioisomer (323 mg, 1.15 mmol, 29%) were isolated as bright yellow oils. ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.15 to −0.10 (m, 1 H), 0.13−0.19 (m, 1 H), 0.30−0.36 (m, 1 H), 0.46−0.53 (m, 1 H), 0.73−0.81 (m, 1 H), 0.87 (t, *J* = 6.7 Hz, 3 H), 1.24−1.45 (m, 8 H), 2.05 (td, *J* = 9.1, 6.7 Hz, 1 H), 2.53−2.60 (m, 1 H), 2.73−2.80 (m, 1 H), 2.98 (d, *J* = 6.8 Hz, 2 H), 7.12−7.19 (m, 2 H), 7.25−7.27 (m, 1 H), 7.33−7.34 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 2.4 (CH_2), 4.0 (CH_2), 14.0 (CH_3), 16.3 (CH), 22.6 (CH_2), 26.9 (CH_2), 30.2 (CH_2), 31.7 (CH_2), 40.0 (CH_2), 47.8 (CH_2), 63.1 (CH), 126.4 (CH), 127.5 (CH), 129.4 (CH), 131.9 (CH), 134.2 (C), 137.5 (C) ppm. IR: ṽ = 3668, 3074, 3000, 2924, 2854, 1571, 1473, 1442, 1121, 1051, 1019, 747, 681 cm^{-1}. MS (25 °C): *m*/*z* (%) = 279 (3) [M^+], 238 (7), 208 (6), 154 (100), 125 (32), 91 (16), 70 (32). HRMS (ESI, CH_3CN): calcd. ($C_{17}H_{26}ClN$+H) 280.1832; found 280.1824. $C_{17}H_{26}ClN$ (279.9): calcd. C 72.96, H 9.36, N 5.01; found C 72.60, H 9.00, N 4.69. Because of the presence of impurities in the obtained Markovnikov regioisomer, this product was not fully characterized.

Amine 21: General Procedure B was used to synthesize amine **21** from 4-methoxyaniline and alkyne **11**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **21** (1.08 g, 2.92 mmol, 73%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78−0.87 (m, 1 H), 2.97 (dd, *J* = 12.9, 7.0 Hz, 1 H), 3.01−3.07 (m, 1 H), 3.25 (dd, *J* = 12.7, 5.6 Hz, 1 H), 3.42 (br. s, 1 H), 3.72 (s, 3 H), 6.56 (d, *J* = 8.9 Hz, 2 H), 6.74 (d, *J* = 8.9 Hz, 2 H), 7.37 (dd, *J* = 8.4, 1.9 Hz, 1 H), 7.43 (d, *J* = 8.4 Hz, 1 H), 7.50 (d, *J* = 1.6 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 2.7 (CH_2), 4.0 (CH_2), 16.4 (CH), 36.6 (CH_2), 55.7 (CH_3), 58.5 (CH), 114.9 (CH), 115.0 (CH), 123.8 (CF_3, q, *J* = 272 Hz), 124.3 (CH, q, *J* = 4 Hz), 128.9 (CH, q, *J* = 4 Hz), 128.9 (C, q, *J* = 33 Hz), 129.8 (CH), 138.0 (C), 138.0 (C), 141.6 (C), 152.2 (C) ppm. IR: ṽ = 3401, 3081, 3000, 2932, 2832, 1611, 1582, 1509, 1328, 1275, 1232, 1167, 1122, 818 cm^{-1}. MS (70 °C): *m*/*z* (%) = 369 (59) [M^+], 328 (4), 193 (13), 176 (100), 158 (60), 143 (82), 115 (12), 81 (15), 77 (9). HRMS: calcd. ($C_{19}H_{19}ClF_3NO$) 369.1107; found 369.1107. $C_{19}H_{19}ClF_3NO$ (369.8): calcd. C 61.71, H 5.18, N 3.79; found C 61.66, H 5.29, N 4.09.

Amine 22: General Procedure B was used to synthesize amine **22** from 4-methylaniline and alkyne **12**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **22** (1.25 g, 3.77 mmol, 94%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.1 Hz, 3 H), 1.26−1.60 (m, 6 H), 2.21 (s, 3 H), 2.82 (dd, *J* = 13.7, 6.5 Hz, 1 H), 2.96 (dd, *J* = 13.7, 6.5 Hz, 1 H), 3.39 (br. s, 1 H), 3.66−3.69 (m, 1 H), 3.71 (s, 3 H), 6.51 (d, *J* = 8.4 Hz, 2 H), 6.66 (dd, *J* = 8.7, 3.0 Hz, 1 H), 6.73 (d, *J* = 3.0 Hz, 1 H), 6.94 (d, *J* = 8.2 Hz, 2 H), 7.22 (d, *J* = 8.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 20.3 (CH_3), 22.7 (CH_2), 28.2 (CH_2), 34.5 (CH_2), 39.0 (CH_2), 53.5 (CH), 55.4 (CH_3), 113.0 (CH), 113.2 (CH), 117.1 (CH), 125.8 (C), 126.0 (C), 129.7 (CH), 130.0 (CH), 138.0 (C), 145.4 (C), 158.1 (C) ppm. IR: ṽ = 3401, 2954, 2930, 2858, 1617, 1518, 1476, 1298, 1240, 1063, 1026, 803 cm^{-1}. MS (70 °C): *m*/*z* (%) = 333 (7) [M^+(^{37}Cl)], 331 (6) [M^+(^{35}Cl)], 274 (5), 223 (47), 207 (14), 176 (100), 172 (17), 155 (10), 134 (27), 120 (32), 86 (10). HRMS (ESI, CH_3CN): calcd. ($C_{20}H_{26}ClNO$+H) 332.1781; found 332.1765. $C_{20}H_{26}ClNO$ (331.9): calcd. C 72.38, H 7.90, N 4.22; found C 72.49, H 7.74, N 4.14.

Amine 23: General Procedure B was used to synthesize amine **23** from *tert*-butylamine and alkyne **12**. After purification by flash chromatography (PE/EtOAc, 1:1), compound **23** (843 mg, 2.83 mmol, 71%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 0.95 (s, 9 H), 1.29−1.39 (m, 6 H), 2.60 (dd, *J* = 13.2, 7.7 Hz, 1 H), 2.85 (dd, *J* = 13.2, 6.0 Hz, 1 H), 2.89−2.94 (m, 1 H), 3.78 (s, 3 H), 6.69 (dd, *J* = 8.7, 3.1 Hz, 1 H), 6.76 (d, *J* = 3.0 Hz, 1 H), 7.23 (d, *J* = 8.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 22.9 (CH_2), 28.4 (CH_2), 29.9 (CH_3), 37.6 (CH_2), 41.6 (CH_2), 50.7 (C), 51.8 (CH), 55.4 (CH_3), 112.8 (CH), 117.5 (CH), 125.7 (C), 130.0 (CH), 139.1 (C), 157.9 (C) ppm. IR: ṽ = 2955, 2932, 2859, 1597, 1574, 1476, 1465, 1387, 1361, 1240, 1161, 1027, 800 cm^{-1}. MS (60 °C): *m*/*z* (%) = 297 (1) [M^+], 282 (16), 241 (21), 184 (32), 155 (22), 142 (61), 86 (100). HRMS (ESI, CH_3CN): calcd. ($C_{17}H_{28}ClNO$+H) 298.1938; found 298.1936. $C_{17}H_{28}ClNO$ (297.9): calcd. C 68.55, H 9.47, N 4.70; found C 68.58, H 9.34, N 4.50.

Amine 24: General Procedure B was used to synthesize amine **24** from 4-methylaniline and alkyne **13**. After purification by flash chromatography (PE/EtOAc, 20:1), compound **24** (1.11 g, 2.92 mmol, 73%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.2 Hz, 3 H), 1.25−1.58 (m, 6 H), 2.21 (s, 3 H), 2.82 (dd, *J* = 13.7, 6.2 Hz, 1 H), 2.92 (dd, *J* = 13.8, 6.8 Hz, 1 H), 3.32 (br. s, 1 H), 3.64 (m, 1 H), 6.48 (d, *J* = 8.5 Hz, 2 H), 6.94 (d, *J* = 8.2 Hz, 2 H), 7.06 (d, *J* = 8.3 Hz, 1 H), 7.26 (dd, *J* = 8.2, 2.0 Hz, 1 H), 7.49 (d, *J* = 2.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 20.3 (CH_3), 22.7 (CH_2), 28.2 (CH_2), 34.5 (CH_2), 38.4 (CH_2), 53.4 (CH), 113.2 (CH), 120.1 (C), 126.2 (C), 129.8 (CH), 131.9 (CH), 132.6 (CH), 135.2 (C), 136.2 (C), 145.2 (C) ppm. MS (60 °C): *m*/*z* (%) = 381 (24) [M^+(^{81}Br)], 379 (19) [M^+(^{79}Br)], 324 (10), 322 (8), 269 (29), 226 (40), 205 (13), 203 (10), 176 (100), 120 (32), 91 (28), 77 (9). HRMS: calcd. ($C_{19}H_{23}BrClN$) 379.0702; found 379.0703. $C_{19}H_{23}BrClN$ (380.8): calcd. C 59.94, H 6.09, N 3.68; found C 59.97, H 5.72, N 3.66.

Amine 25: General Procedure B was used to synthesize amine **25** from 4-methoxyaniline and alkyne **14**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **25** (1.20 g, 3.15 mmol, 79%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.02−0.06 (m, 1 H), 0.20−0.26 (m, 1 H), 0.36−0.46 (m, 2 H), 2.90 (dd, *J* = 13.1, 6.6 Hz, 1 H), 3.01 (dd, *J* = 13.7, 6.7 Hz, 1 H), 3.12 (dd, *J* = 13.1, 5.9 Hz, 1 H), 3.73 (s, 3 H), 6.55 (d, *J* = 8.9 Hz, 2 H), 6.74 (d, *J* = 8.9 Hz, 2 H), 7.11 (d, *J* = 8.2 Hz, 1 H), 7.26 (dd, *J* = 8.2, 2.0 Hz, 1 H), 7.50 (d, *J* = 2.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 2.6 (CH_2), 4.0 (CH_2), 16.3 (CH), 38.9 (CH_2), 55.7 (CH_3), 58.5 (CH), 114.8 (CH), 120.1 (C), 129.6 (CH), 131.8 (CH), 133.0 (CH), 135.2 (C), 136.0 (C), 141.7 (C), 152.0 (C) ppm. IR: ṽ = 3394, 2998, 2930, 2830, 1583, 1508, 1469, 1231, 1036, 815 cm^{-1}. MS (100 °C): *m*/*z* (%) = 382 (11) [M^+(^{81}Br)], 379 (17) [M^+(^{79}Br)], 205 (10), 203 (12), 176 (100), 160 (23), 146 (10), 144 (10), 134 (17), 130 (10), 86 (13).

HRMS (ESI, CH_3CN): calcd. ($C_{18}H_{19}BrClNO+H$) 380.0417; found 380.0431. $C_{18}H_{19}BrClNO$ (380.7): calcd. C 56.79, H 5.03, N 3.68; found C 57.23, H 4.71, N 3.59.

Amine 26: General Procedure B was used to synthesize amine **26** from 4-methoxybenzylamine and alkyne **15**. [$Cp^*_2TiMe_2$] (c = 0.50 mol/L in toluene, 0.4 mmol, 10.0 mol %) was used as catalyst for the hydroamination step. After purification by flash chromatography (PE/EtOAc, 1:1), compound **26** (845 mg, 1.93 mmol, 48%) and its Markovnikov regioisomer (682 mg, 1.56 mmol, 39%) were obtained as colorless oils. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (br. s, 1 H), 1.38−1.60 (m, 6 H), 2.77−2.91 (m, 3 H), 3.44 (t, J = 6.4 Hz, 2 H), 3.66 (d, J = 12.9 Hz, 1 H), 3.71 (d, J = 12.9 Hz, 1 H), 3.77 (s, 3 H), 4.48 (s, 2 H), 6.79 (d, J = 8.7 Hz, 2 H), 7.11 (d, J = 8.7 Hz, 2 H), 7.13−7.20 (m, 3 H), 7.24−7.34 (m, 6 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 22.3 (CH_2), 29.8 (CH_2), 33.9 (CH_2), 39.0 (CH_2), 50.6 (CH_2), 55.2 (CH_3), 56.6 (CH), 70.2 (CH_2), 72.8 (CH_2), 113.7 (CH), 126.5 (CH), 127.4 (CH), 127.5 (CH), 127.6 (CH), 128.3 (CH), 129.1 (CH), 129.5 (CH), 131.6 (CH), 132.9 (C), 134.3 (C), 137.6 (C), 138.6 (C), 158.5 (C) ppm. IR: $\tilde{\nu}$ = 3338, 3062, 3029, 2932, 2855, 1611, 1585, 1530, 1454, 1441, 1244, 1101, 1034, 802, 748, 734, 696 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{27}H_{32}ClNO_2+H$) 438.2200; found 438.2205. $C_{27}H_{32}ClNO_2$ (438.0): calcd. C 74.04, H 7.36, N 3.20; found C 74.12, H 7.37, N 3.59. Characterization of the Markovnikov regioisomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22−1.40 (m, 4 H), 1.53−1.69 (m, 4 H), 3.41 (t, J = 6.6 Hz, 2 H), 3.46 (d, J = 12.8 Hz, 1 H), 3.53 (d, J = 12.8 Hz, 1 H), 3.78 (s, 3 H), 4.19 (t, J = 6.7 Hz, 1 H), 4.46 (s, 2 H), 6.83 (d, J = 8.7 Hz, 2 H), 7.18 (d, J = 8.5 Hz, 2 H), 7.14−7.19 (m, 1 H), 7.24−7.35 (m, 7 H), 7.52 (dd, J = 7.7, 1.4 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 25.9 (CH_2), 26.1 (CH_2), 29.6 (CH_2), 37.0 (CH_2), 51.0 (CH_2), 55.2 (CH_3), 58.2 (CH), 70.3 (CH_2), 72.8 (CH_2), 113.7 (CH), 127.0 (CH), 127.4 (CH), 127.5 (CH), 127.7 (CH), 128.1 (CH), 128.3 (CH), 129.3 (CH), 129.5 (CH), 132.8 (C), 133.8 (C), 138.7 (C), 141.6 (C), 158.6 (C) ppm. IR: $\tilde{\nu}$ = 3062, 3030, 2932, 2855, 1611, 1585, 1510, 1454, 1244, 1100, 1032, 821, 752, 734, 696 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{27}H_{32}ClNO_2+H$) 438.2200; found 438.2216. $C_{27}H_{32}ClNO_2$ (438.0): calcd. C 74.04, H 7.36, N 3.20; found C 74.06, H 7.31, N 3.64.

Indoline 27: A Schlenk tube fitted with a Teflon stopcock and containing a magnetic stirring bar was charged with amine **16** (725 mg, 2.0 mmol), [$Pd(PPh_3)_4$] (116 mg, 0.1 mmol, 5.0 mol %), K_2CO_3 (553 mg, 4.0 mmol), NaOtBu (384 mg, 4.0 mmol), and toluene (5.0 mL). The mixture was heated to 110 °C for 5 h (TLC monitoring). The reaction mixture was filtered through SiO_2. After the SiO_2 had been washed with CH_2Cl_2, the organic layer was concentrated under vacuum. Purification by flash chromatography on SiO_2 (PE/EtOAc, 5:1) gave compound **27** (546 mg, 1.94 mmol, 97%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, J = 6.9 Hz, 3 H), 1.20−1.38 (m, 4 H), 1.47−1.55 (m, 1 H), 1.69−1.76 (m, 1 H), 2.81 (dd, J = 15.4, 9.4 Hz, 1 H), 3.22 (dd, J = 15.4, 8.8 Hz, 1 H), 3.81 (s, 3 H), 4.08 (qd, J = 9.2, 3.2 Hz, 1 H), 6.46 (d, J = 7.9 Hz, 1 H), 6.66 (td, J = 7.3, 0.8 Hz, 1 H), 6.92 (d, J = 8.9 Hz, 2 H), 6.96 (t, J = 7.7 Hz, 1 H), 7.09 (d, J = 7.2 Hz, 1 H), 7.16 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 22.8 (CH_2), 27.7 (CH_2), 34.9 (CH_2), 55.4 (CH_2), 65.7 (CH), 107.3 (CH), 114.6 (CH), 117.9 (CH), 124.5 (CH), 125.9 (CH), 127.1 (CH), 129.0 (C), 137.0 (C), 151.3 (C), 156.5 (C) ppm. IR: $\tilde{\nu}$ = 3098, 3046, 2929, 2857, 1602, 1507, 1480, 1458, 1439, 1241, 1036, 831, 742 cm^{-1}. MS (25 °C): m/z (%) = 281 (59) [M^+], 224 (100), 131 (10), 91 (8). HRMS: calcd. ($C_{19}H_{23}NO$) 281.1780; found 281.1779. $C_{19}H_{23}NO$ (281.4): calcd. C 81.10, H 8.24, N 4.98; found C 80.80, H 8.30, N 4.81.

Synthesis of Indolines. General Procedure C: A Schlenk tube fitted with a Teflon stopcock and containing a magnetic stirring bar was charged with amine (2.0 mmol), [$Pd_2(dba)_3$] (92 mg, 0.1 mmol, 5.0 mol %), 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (68 mg, 0.2 mmol, 10.0 mol %), KOtBu (337 mg, 3.0 mmol), and 1,4-dioxane (5.0 mL). The mixture was heated to 110 °C for 12 h (TLC monitoring). The reaction mixture was filtered through SiO_2. After the SiO_2 had been washed with CH_2Cl_2, the organic layer was concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Indoline 28: General Procedure C was used to synthesize indoline **28** from amine **17**. After purification by flash chromatography (PE/EtOAc, 20:1), compound **28** (501 mg, 1.99 mmol, 99%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.3 Hz, 3 H), 1.25−1.56 (m, 3 H), 1.71−1.78 (m, 1 H), 2.34 (s, 3 H), 2.81 (dd, J = 15.4, 8.5 Hz, 1 H), 3.24 (dd, J = 15.5, 9.0 Hz, 1 H), 4.19 (ddd, J = 17.8, 8.9, 3.1 Hz, 1 H), 6.63−6.69 (m, 2 H), 6.97 (m, 1 H), 7.08−7.18 (m, 5 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.2 (CH_3), 18.7 (CH_2), 20.9 (CH_3), 34.8 (CH_2), 36.0 (CH_2), 64.6 (CH), 107.7 (CH), 118.1 (CH), 123.0 (CH), 124.6 (CH), 127.1 (CH), 129.3 (C), 129.8 (CH), 133.0 (C), 141.2 (C), 150.7 (C) ppm. IR: $\tilde{\nu}$ = 3026, 2955, 2927, 2862, 1601, 1511, 1479, 1459, 1291, 812, 740 cm^{-1}. MS (25 °C): m/z (%) = 251 (60) [M^+], 208 (100), 193 (26), 116 (11), 91 (33), 77 (5). HRMS: calcd. ($C_{18}H_{21}N$) 251.1674; found 251.1673. $C_{18}H_{21}N$ (251.4): calcd. C 86.01, H 8.42, N 5.57; found C 85.73, H 8.31, N 5.71.

Indoline 29: General Procedure C was used to synthesize indoline **29** from amine **18**. After purification by flash chromatography (PE/EtOAc, 20:1), compound **29** (580 mg, 1.96 mmol, 98%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 3 H), 1.20−1.37 (m, 4 H), 1.46−1.56 (m, 1 H), 1.77−1.83 (m, 1 H), 2.70 (dd, J = 15.6, 9.9 Hz, 1 H), 3.12 (dd, J = 15.5, 9.9 Hz, 1 H), 3.57 (qd, J = 9.5, 3.1 Hz, 1 H), 3.78 (s, 3 H), 4.11 (d, J = 15.9 Hz, 1 H), 4.32 (d, J = 15.9 Hz, 1 H), 6.32 (d, J = 7.8 Hz, 1 H), 6.61 (td, J = 7.3, 0.6 Hz, 1 H), 6.84 (d, J = 8.7 Hz, 2 H), 6.97 (t, J = 7.7 Hz, 1 H), 7.03 (d, J = 7.2 Hz, 1 H), 7.25 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 22.9 (CH_2), 27.8 (CH_2), 33.7 (CH_2), 35.1 (CH_2), 50.8 (CH_2), 55.2 (CH_3), 65.0 (CH), 106.8 (CH), 113.8 (CH), 117.2 (CH), 124.1 (CH), 127.3 (CH), 128.4 (CH), 128.8 (C), 131.2 (C), 152.9 (C), 158.5 (C) ppm. IR: $\tilde{\nu}$ = 3026, 2953, 2927, 2856, 1606, 1510, 1483, 1461, 1241, 1171, 1035, 820, 741 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{20}H_{25}NO+H$) 296.2014; found 296.2010. $C_{20}H_{25}NO$ (295.4): calcd. C 81.31, H 8.53, N 4.74; found C 81.39, H 8.50, N 5.31.

Indoline 30: General Procedure C was used to synthesize indoline **30** from amine **19**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **30** (425 mg, 1.97 mmol, 99%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.13−0.19 (m, 1 H), 0.31−0.42 (m, 2 H), 0.50−0.57 (m, 1 H), 0.91−0.99 (m, 1 H), 1.37 (s, 9 H), 2.65 (d, J = 14.6 Hz, 1 H), 3.11−3.22 (m, 2 H), 6.67 (td, J = 7.3, 0.6 Hz, 1 H), 6.82 (d, J = 7.8 Hz, 1 H), 7.00 (t, J = 7.7 Hz, 1 H), 7.07 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 2.4 (CH_2), 6.1 (CH_2), 17.3 (CH), 28.8 (CH_3), 36.4 (CH_2), 54.3 (C), 64.3 (CH), 113.7 (CH), 117.9 (CH), 124.3 (CH), 126.3 (CH), 132.5 (C), 149.2 (C) ppm. IR: $\tilde{\nu}$ = 3072, 2972, 1606, 1475, 1392, 1362, 1019, 736 cm^{-1}. MS (25 °C): m/z (%) = 215 (72) [M^+], 200 (79), 174 (19), 159 (66), 118 (100), 77 (9), 91 (26). HRMS: calcd. ($C_{15}H_{21}N$) 215.1674; found 215.1663. $C_{15}H_{21}N$ (215.3): calcd. C 83.67, H 9.83, N 6.50; found C 83.32, H 9.17, N 6.13.

Indoline 31: General Procedure C was used to synthesize indoline **31** from amine **20**. After purification by flash chromatography (PE), compound **31** (471 mg, 1.94 mmol, 97%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08−0.14 (m, 1 H), 0.32−0.38 (m, 1 H), 0.45−0.52 (m, 1 H), 0.63−0.69 (m, 1 H), 0.89 (t, *J* = 6.7 Hz, 1 H), 0.93−0.98 (m, 1 H), 1.26−1.38 (m, 6 H), 2.79−2.88 (m, 2 H), 3.03−3.30 (m, 3 H), 6.36 (d, *J* = 7.8 Hz, 1 H), 6.57 (td, *J* = 7.3, 0.7 Hz, 1 H), 7.00 (d, *J* = 7.3 Hz, 1 H), 7.03 (t, *J* = 7.7 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.2 (CH_2), 5.1 (CH_2), 14.0 (CH_3), 14.8 (CH), 22.7 (CH_2), 26.5 (CH_2), 27.1 (CH_2), 31.7 (CH_2), 35.7 (CH_2), 46.4 (CH_2), 69.7 (CH), 105.6 (CH), 116.4 (CH), 124.0 (CH), 127.3 (CH), 128.5 (C), 152.4 (C) ppm. IR: ṽ = 3076, 3001, 2926, 2854, 1606, 1483, 1461, 1260, 1020, 740, 714 cm^{-1}. MS (25 °C): *m*/*z* (%) = 243 (60) [M$^+$], 202 (46), 172 (71), 130 (50), 118 (40), 91 (28). HRMS (ESI, CH_3CN): calcd. ($C_{17}H_{25}N$+H) 244.2065; found 244.2061. $C_{17}H_{25}N$ (243.4): calcd. C 83.39, H 10.35, N 5.75; found C 83.42, H 10.53, N 5.50.

Indoline 32: General Procedure C was used to synthesize indoline **32** from amine **21**. After purification by flash chromatography (PE), compound **32** (634 mg, 1.90 mmol, 95%) was isolated as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.12 to −0.06 (m, 1 H), 0.07−0.13 (m, 1 H), 0.45−0.46 (m, 2 H), 0.98−1.07 (m, 1 H), 2.98 (dd, *J* = 15.9, 8.4 Hz, 1 H), 3.28 (dd, *J* = 15.9, 9.1 Hz, 1 H), 3.43 (q, *J* = 8.7 Hz, 1 H), 3.83 (s, 3 H), 6.32 (d, *J* = 8.3 Hz, 1 H), 6.93 (d, *J* = 8.9 Hz, 2 H), 7.20 (d, *J* = 8.9 Hz, 3 H), 7.28 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.6 (CH_2), 5.2 (CH_2), 15.3 (CH), 34.9 (CH_2), 55.4 (CH_3), 72.1 (CH), 106.2 (CH), 114.7 (CH), 119.2 (C, q, *J* = 32 Hz), 121.4 (CH, q, *J* = 4 Hz), 125.2 (CF_3, q, *J* = 270 Hz), 125.3 (CH, q, *J* = 4 Hz), 127.8 (CH), 129.0 (C), 136.0 (C), 154.2 (C), 157.7 (C) ppm. IR: ṽ = 3079, 3013, 2960, 2902, 1621, 1513, 1456, 1328, 1276, 1247, 1217, 1091, 1028, 820, 816 cm^{-1}. MS (80 °C): *m*/*z* (%) = 333 (100) [M$^+$], 318 (27), 314 (28), 305 (29), 292 (81), 278 (25), 261 (25), 248 (28), 235 (20), 224 (21), 198 (28), 159 (25), 146 (18). HRMS: calcd. ($C_{19}H_{18}F_3NO$) 333.1340; found 333.1341. $C_{19}H_{18}F_3NO$ (333.4): calcd. C 68.46, H 5.44, N 4.20; found C 68.66, H 5.40, N 4.06.

Indoline 33: General Procedure C was used to synthesize indoline **33** from amine **22**. After purification by flash chromatography (PE), compound **33** (528 mg, 1.79 mmol, 89%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.8 Hz, 3 H), 1.26−1.31 (m, 4 H), 1.49−1.57 (m, 1 H), 1.74−1.80 (m, 1 H), 2.32 (s, 3 H), 2.76 (dd, *J* = 15.6, 8.0 Hz, 1 H), 3.21 (dd, *J* = 15.6, 8.7 Hz, 1 H), 3.74 (s, 3 H), 4.11 (qd, *J* = 8.7, 3.1 Hz, 1 H), 6.55 (dd, *J* = 8.5, 2.5 Hz, 1 H), 6.62 (d, *J* = 8.5 Hz, 1 H), 6.75 (d, *J* = 2.5 Hz, 1 H), 7.10 (d, *J* = 8.5 Hz, 2 H), 7.15 (d, *J* = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 20.8 (CH_3), 22.8 (CH_2), 27.6 (CH_2), 33.5 (CH_2), 35.1 (CH_2), 56.0 (CH_3), 65.2 (CH), 108.5 (CH), 111.5 (CH), 112.0 (CH), 121.8 (CH), 129.8 (CH), 131.0 (C), 132.1 (C), 142.2 (C), 144.0 (C), 153.1 (C) ppm. IR: ṽ = 2928, 2859, 1614, 1596, 1512, 1484, 1373, 1246, 1035, 797 cm^{-1}. MS (90 °C): *m*/*z* (%) = 295 (77) [M$^+$], 238 (100), 207 (11). HRMS (ESI, CH_3CN): calcd. ($C_{20}H_{25}NO$+H) 296.2014; found 296.2003. $C_{20}H_{25}NO$ (295.4): calcd. C 81.31, H 8.53, N 4.74; found C 81.14, H 8.17, N 4.53.

Indoline 34: General Procedure C was used to synthesize indoline **34** from amine **23**. After purification by flash chromatography (PE/EtOAc, 20:1), compound **34** (451 mg, 1.72 mmol, 86%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.26 (s, 9 H), 1.27−1.45 (m, 6 H), 2.43 (d, *J* = 15.7 Hz, 1 H), 3.14 (dd, *J* = 15.7, 8.7 Hz, 1 H), 3.62−3.67 (m, 1 H), 3.73 (s, 3 H), 6.56 (dd, *J* = 8.6, 2.6 Hz, 1 H), 6.69 (d, *J* = 2.6 Hz, 1 H), 6.78 (d, *J* = 8.5 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 22.8 (CH_2), 28.0 (CH_3), 28.8 (CH_3), 35.5 (CH_2), 36.7 (CH_2), 55.6 (CH_3), 55.7 (C), 60.3 (CH), 111.0 (CH), 111.1 (CH), 116.8 (CH), 135.4 (C), 143.4 (C), 153.8 (C) ppm. IR: ṽ = 2955, 2932, 2871, 1577, 1522, 1483, 1466, 1390, 1362, 1257, 1213, 1190, 1179, 1038, 802 cm^{-1}. MS (25 °C): *m*/*z* (%) = 261 (78) [M$^+$], 246 (76), 206 (85), 190 (13), 174 (13), 160 (32), 148 (100), 133 (47), 117 (26). HRMS (ESI, CH_3CN): calcd. ($C_{17}H_{27}NO$+H) 262.2171; found 262.2182. $C_{17}H_{27}NO$ (261.4): calcd. C 78.11, H 10.41, N 5.36; found C 77.83, H 10.14, N 4.97.

Indoline 35: General Procedure C was used to synthesize indoline **35** from amine **26**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **35** (742 mg, 1.84 mmol, 92%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31−1.66 (m, 5 H), 1.76−1.85 (m, 1 H), 2.70 (dd, *J* = 15.6, 9.8 Hz, 1 H), 3.12 (dd, *J* = 15.6, 8.7 Hz, 1 H), 3.44 (t, *J* = 6.5 Hz, 2 H), 3.57 (qd, *J* = 9.2, 3.1 Hz, 1 H), 3.77 (s, 3 H), 4.10 (d, *J* = 15.9 Hz, 1 H), 4.30 (d, *J* = 15.9 Hz, 1 H), 4.48 (s, 2 H), 6.32 (d, *J* = 7.8 Hz, 1 H), 6.61 (td, *J* = 7.4, 0.5 Hz, 1 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 6.97 (t, *J* = 8.7 Hz, 1 H), 7.03 (d, *J* = 7.2 Hz, 1 H), 7.23 (d, *J* = 8.7 Hz, 2 H), 7.24−7.35 (m, 5 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 22.3 (CH_2), 29.9 (CH_2), 33.7 (CH_2), 35.0 (CH_2), 50.8 (CH_2), 55.2 (CH_3), 64.9 (CH), 70.2 (CH_2), 72.9 (CH_2), 106.8 (CH), 113.8 (CH), 117.2 (CH), 124.1 (CH), 127.3 (CH), 127.5 (CH), 127.6 (CH), 128.3 (CH), 128.4 (CH), 128.7 (C), 131.1 (C), 138.6 (C), 152.9 (C), 158.5 (C) ppm. IR: ṽ = 3029, 3002, 2923, 2839, 1608, 1512, 1488, 1453, 1350, 1247, 1107, 1035, 827, 811, 747, 736, 716, 696 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{27}H_{31}NO_2$+H) 402.2433; found 402.2424. $C_{27}H_{31}NO_2$ (401.54): calcd. C 80.76, H 7.78, N 3.49; found C 80.41, H 7.47, N 3.35.

Synthesis of Benzophenone Imine Compounds. General Procedure D: A Schlenk tube fitted with a Teflon stopcock and containing a magnetic stirring bar was charged with amine (2.5 mmol), benzophenone imine (544 mg, 3.0 mmol), [$Pd_2(dba)_3$] (27 mg, 0.03 mmol, 1.0 mol %), 1,1′-bis(diphenylphosphanyl)ferrocene (DPPF, 44 mg, 0.08 mmol, 3.0 mol %), NaO*t*Bu (336 mg, 3.5 mmol), and toluene (5.0 mL). The mixture was heated to 100 °C for 24 h (TLC monitoring). The reaction mixture was filtered through SiO_2. After the SiO_2 had been washed with CH_2Cl_2, the organic layer was concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Amine 36: General Procedure D was used to synthesize amine **36** from amine **24**. After purification by flash chromatography (PE/EtOAc, 20:1), compound **36** (1.18 g, 2.45 mmol, 98%) was isolated as a bright yellow oil, contaminated with benzophenone imine impurities. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.9 Hz, 3 H), 1.25−1.48 (m, 6 H), 2.21 (s, 3 H), 2.69 (dd, *J* = 13.7, 7.0 Hz, 1 H), 2.91 (dd, *J* = 13.7, 6.3 Hz, 1 H), 3.32 (br. s, 1 H), 3.56−3.59 (m, 1 H), 6.47 (dd, *J* = 8.1, 2.1 Hz, 1 H), 6.49 (d, *J* = 8.4 Hz, 2 H), 6.78 (d, *J* = 2.1 Hz, 1 H), 6.93 (dd, *J* = 8.2, 3.1 Hz, 3 H), 7.07 (dd, *J* = 8.0, 1.4 Hz, 2 H), 7.19−7.28 (m, 3 H), 7.37−7.40 (m, 2 H), 7.44−7.49 (m, 1 H), 7.71−7.73 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 20.3 (CH_3), 22.6 (CH_2), 28.1 (CH_2), 34.2 (CH_2), 38.2 (CH_2), 53.6 (CH), 113.1 (CH), 119.4 (CH), 122.0 (CH), 125.9 (C), 127.9 (CH), 128.2 (CH), 128.7 (CH), 129.3 (CH), 129.7 (CH), 130.9 (CH), 131.2 (CH), 131.5 (C), 134.0 (C), 135.8 (C), 139.3 (C), 145.5 (C), 150.5 (C), 169.0 (C) ppm. IR: ṽ = 3402, 3022, 2924, 2852, 1660, 1616, 1594, 1518, 1482, 1445, 1317, 1291, 960, 805, 693 cm^{-1}. MS (150 °C): *m*/*z* (%) = 480 (7) [M$^+$], 444 (4), 305 (83), 182 (27), 176 (100), 120 (23), 105 (49), 84 (43), 77 (53). HRMS (ESI, CH_3CN): calcd. ($C_{32}H_{33}ClN_2$+H) 481.2411; found 481.2402.

Amine 37: General Procedure D was used to synthesize amine **37** from amine **25**. After purification by flash chromatography (PE/EtOAc, 5:1), compound **37** (1.18 g, 2.45 mmol, 98%) was isolated as a bright yellow oil, contaminated with benzophenone imine impurities. ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.31 to −0.15 (m, 1 H), 0.11−0.17 (m, 1 H), 0.20−0.26 (m, 1 H), 0.32−0.40 (m, 1 H), 0.73−0.81 (m, 1 H), 2.74 (dd, *J* = 13.3, 7.8 Hz, 1 H), 2.85−2.91 (m, 1 H), 3.13 (dd, *J* = 13.3, 5.5 Hz, 1 H), 3.73 (s, 3 H), 6.49 (dd, *J* = 8.0, 2.1 Hz, 1 H), 6.57 (d, *J* = 8.9 Hz, 2 H), 6.74 (d, *J* = 9.0 Hz, 2 H), 6.78 (d, *J* = 2.0 Hz, 1 H), 6.99 (d, *J* = 8.2 Hz, 1 H), 7.08−7.11 (m, 2 H), 7.22−7.29 (m, 3 H), 7.38−7.41 (m, 2 H), 7.45−7.49 (m, 1 H), 7.72−7.74 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 2.4 (CH_2), 4.1 (CH_2), 16.3 (CH), 39.0 (CH_2), 55.8 (CH_3), 59.0 (CH), 114.8 (CH), 114.9 (CH), 119.2 (CH), 121.8 (CH), 128.0 (CH), 128.2 (CH), 128.7 (CH), 129.3 (CH), 129.3 (CH), 130.9 (CH), 131.4 (CH), 131.6 (CH), 133.9 (C), 135.8 (C), 139.2 (C), 142.0 (C), 150.6 (C), 152.0 (C), 169.1 (C) ppm. IR: ṽ = 3075, 3000, 2925, 2854, 1571, 1473, 1442, 1121, 1051, 1019, 823, 747, 681 cm^{-1}. MS (160 °C): *m/z* (%) = 480 (4) [M$^+$], 307 (41), 305 (100), 176 (74), 160 (11), 134 (6), 105 (7). HRMS (ESI, CH_3CN): calcd. ($C_{31}H_{29}ClN_2O$+H) 481.2047; found 481.2037.

Indoline 38: General Procedure C was used to synthesize indoline **38** from amine **36**. The mixture was heated to 100 °C for 16 h. After purification by flash chromatography (PE/EtOAc, 50:1), compound **38** (782 mg, 1.76 mmol, 88%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.7 Hz, 3 H), 1.24−1.26 (m, 4 H), 1.42−1.51 (m, 1 H), 1.68−1.72 (m, 1 H), 2.29 (s, 3 H), 2.68 (dd, *J* = 15.4, 7.6 Hz, 1 H), 3.13 (dd, *J* = 15.4, 8.9 Hz, 1 H), 4.08 (qd, *J* = 8.9, 3.0 Hz, 1 H), 6.04 (d, *J* = 1.6 Hz, 1 H), 6.18 (dd, *J* = 7.7, 1.8 Hz, 1 H), 6.78 (d, *J* = 8.3 Hz, 2 H), 6.89 (d, *J* = 7.7 Hz, 1 H), 7.03 (d, *J* = 8.2 Hz, 2 H), 7.13−7.15 (m, 2 H), 7.27−7.48 (m, 6 H), 7.79 (dd, *J* = 7.0, 1.4 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.1 (CH_3), 20.8 (CH_3), 22.7 (CH_2), 27.4 (CH_2), 33.4 (CH_2), 34.3 (CH_2), 65.0 (CH), 101.9 (CH), 111.7 (CH), 122.1 (CH), 124.2 (CH), 124.6 (C), 127.8 (CH), 128.0 (CH), 128.3 (CH), 129.2 (CH), 129.5 (CH), 129.6 (CH), 130.3 (CH), 132.2 (C), 136.7 (C), 140.1 (C), 141.0 (C), 149.7 (C), 150.4 (C), 167.4 (C) ppm. IR: ṽ = 3058, 3025, 2954, 2928, 2858, 1661, 1597, 1511, 1480, 1276, 809, 695 cm^{-1}. MS (80 °C): *m/z* (%) = 445 (2) [M$^+$ + H], 388 (2), 280 (6), 182 (100), 131 (24), 105 (97), 77 (77). HRMS (ESI, CH_3CN): calcd. ($C_{32}H_{32}N_2$+H) 445.2644; found 445.2652.

Indoline 39: General Procedure C was used to synthesize indoline **39** from amine **37**. The mixture was heated to 100 °C for 16 h. After purification by flash chromatography (PE/EtOAc, 20:1), compound **39** (819 mg, 1.84 mmol, 92%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.17 to −0.11 (m, 1 H), 0.02−0.08 (m, 1 H), 0.30−0.41 (m, 2 H), 0.94−1.03 (m, 1 H), 2.83 (dd, *J* = 15.3, 8.2 Hz, 1 H), 3.12 (dd, *J* = 15.4, 8.8 Hz, 1 H), 3.23 (q, *J* = 8.5 Hz, 1 H), 3.79 (s, 3 H), 5.78 (d, *J* = 1.8 Hz, 1 H), 6.17 (dd, *J* = 7.7, 1.8 Hz, 1 H), 6.78 (d, *J* = 9.0 Hz, 2 H), 6.90 (d, *J* = 8.9 Hz, 1 H), 6.88−6.92 (m, 1 H), 7.10−7.13 (m, 2 H), 7.27−7.42 (m, 6 H), 7.64−7.66 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.7 (CH_2), 5.1 (CH_2), 15.2 (CH), 35.1 (CH_2), 55.4 (CH_3), 72.4 (CH), 102.0 (CH), 111.3 (CH), 114.2 (CH), 124.1 (CH), 124.1 (C), 126.6 (CH), 127.8 (CH), 128.0 (CH), 128.2 (CH), 129.2 (CH), 129.5 (CH), 130.3 (CH), 136.7 (C), 137.8 (C), 140.1 (C), 150.6 (C), 151.4 (C), 156.6 (C), 167.4 (C) ppm. IR: ṽ = 2999, 2931, 2834, 1595, 1506, 1484, 1441, 1287, 1240, 1031, 832, 693 cm^{-1}. MS (150 °C): *m/z* (%) = 444 (100) [M$^+$], 403 (28), 222 (6). HRMS (ESI, CH_3CN): calcd. ($C_{31}H_{28}N_2O$+H) 445.2280; found 445.2302.

Cleavage of the Benzophenone Imine. General Procedure E: A round-bottomed flask containing a magnetic stirring bar was charged with indoline (1.5 mmol), THF (5.0 mL), and HCl (2 N, 0.5 mL). After this had been stirred at 25 °C for 30 min (TLC monitoring), KOH (2 N) and *tert*-butyl methyl ether were added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Indoline 40: General Procedure E was used to synthesize indoline **40** from indoline **38**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **40** (388 mg, 1.38 mmol, 92%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.8 Hz, 3 H), 1.25−1.33 (m, 4 H), 1.45−1.51 (m, 1 H), 1.70−1.76 (m, 1 H), 2.33 (s, 3 H), 2.70 (dd, *J* = 14.9, 8.5 Hz, 1 H), 3.12 (dd, *J* = 15.0, 8.6 Hz, 1 H), 3.26 (br. s, 2 H), 4.15 (qd, *J* = 8.9, 3.1 Hz, 1 H), 6.00−6.02 (m, 2 H), 6.86 (d, *J* = 8.0 Hz, 1 H), 7.11 (d, *J* = 8.5 Hz, 2 H), 7.16 (d, *J* = 8.3 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 20.8 (CH_3), 22.7 (CH_2), 27.6 (CH_2), 33.4 (CH_2), 34.1 (CH_2), 65.2 (CH), 95.8 (CH), 104.8 (CH), 119.5 (C), 123.4 (CH), 124.9 (CH), 129.8 (CH), 133.0 (C), 141.1 (C), 146.0 (C), 151.2 (C) ppm. IR: ṽ = 3444, 3361, 3024, 2926, 2857, 1607, 1510, 1496, 1378, 1304, 1200, 813 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{19}H_{24}N_2$+H) 281.2018; found 281.2020. $C_{19}H_{24}N_2$ (280.4): calcd. C 81.33, H 8.63, N 9.99; found C 80.87, H 8.26, N 9.54.

Indoline 41: General Procedure E was used to synthesize indoline **41** from indoline **39**. After purification by flash chromatography (PE/EtOAc, 10:1), compound **41** (381 mg, 1.36 mmol, 91%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.14 to −0.09 (m, 1 H), 0.05−0.11 (m, 1 H), 0.31−0.42 (m, 2 H), 0.97−1.06 (m, 1 H), 2.84 (dd, *J* = 14.7, 8.4 Hz, 1 H), 3.13 (dd, *J* = 15.1, 8.8 Hz, 1 H), 3.32 (q, *J* = 8.7 Hz, 1 H), 3.82 (s, 3 H), 5.76 (d, *J* = 2.0 Hz, 1 H), 6.01 (dd, *J* = 7.7, 2.1 Hz, 1 H), 6.85 (d, *J* = 7.7 Hz, 1 H), 6.90 (d, *J* = 8.9 Hz, 2 H), 7.22 (d, *J* = 8.9 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 0.6 (CH_2), 5.0 (CH_2), 15.2 (CH), 34.7 (CH_2), 55.4 (CH_3), 72.4 (CH), 95.9 (CH), 104.5 (CH), 114.4 (CH), 119.1 (C), 124.7 (CH), 127.7 (CH), 137.7 (C), 146.1 (C), 152.8 (C), 157.0 (C) ppm. IR: ṽ = 3444, 3361, 3000, 2933, 2835, 1615, 1497, 1456, 1286, 1239, 1031, 826 cm^{-1}. HRMS (ESI, CH_3CN): calcd. ($C_{18}H_{20}N_2O$+H) 281.1654; found 281.1660.

Amine 48: General Procedure B was used to synthesize amine **48** from aminoalkyne **42**. The reaction time for the hydroamination step was 4 h. After purification by flash chromatography (MeOH/EtOAc, 1:1), compound **48** (845 mg, 3.52 mmol, 88%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65−1.74 (m, 1 H), 1.84−1.95 (m, 3 H), 2.86 (dd, *J* = 13.3, 10.0 Hz, 1 H), 2.92−3.03 (m, 1 H), 3.30−3.45 (m, 1 H), 3.45−3.60 (m, 2 H), 5.15 (br. s, 1 H), 7.09−7.15 (m, 1 H), 7.24−7.28 (m, 2 H), 7.56 (d, *J* = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 22.9 (CH_2), 30.2 (CH_2), 38.2 (CH_2), 53.7 (CH_2), 65.4 (CH), 124.6 (C), 127.8 (CH), 128.8 (CH), 131.3 (CH), 133.2 (CH), 136.6 (C) ppm. IR: ṽ = 3102, 2982, 2961, 2858, 2422, 2405, 2200, 1657, 1470, 1435, 1375, 1360, 1275, 1220, 1166, 1133, 1118, 1077, 1045, 1023, 969, 943, 907, 864, 745, 697, 659, 598 cm^{-1}. MS (25 °C): *m/z* (%) = 241 (1) [M$^+$(^{81}Br)], 239 (1) [M$^+$(^{79}Br)], 238 (4), 199 (39), 197 (31), 172 (52), 170 (38), 157 (27), 155 (26), 145 (12), 143 (13), 130 (18), 128 (23), 121 (32), 116 (27), 115 (32), 114 (43), 107 (27), 103 (13), 95 (25), 91 (53), 82 (100), 77 (21), 70 (52), 65 (25). HRMS: calcd. ($C_{11}H_{14}BrN$) 239.0309; found 239.0192.

Amine 49: General Procedure B was used to synthesize amine **49** from aminoalkyne **43**. The reaction time for the hydroamination

step was 4 h. After purification by flash chromatography (PE/EtOAc, 1:1), compound **49** (523 mg, 2.49 mmol, 62%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.20−0.80 (br. s, 1 H), 1.47 (d, *J* = 6.5 Hz, 2 H), 1.57 (d, *J* = 6.5 Hz, 2 H), 1.85−2.05 (m, 2 H), 2.43 (s, 3 H), 3.27−3.45 (m, 2 H), 3.75−3.95 (m, 1 H), 7.10−7.14 (m, 2 H), 7.20−7.24 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 15.9 (CH_2), 18.9 (CH_2), 21.1 (CH_3), 29.2 (CH_2), 31.2 (CH_2), 54.8 (CH), 127.7 (CH), 128.5 (CH), 129.8 (CH), 132.0 (C), 134.4 (C), 139.4 (C) ppm. IR: $\tilde{\nu}$ = 3513, 3455, 3079, 2983, 1612, 1567, 1454, 1400, 1287, 1117, 1015, 959, 863, 784, 723 cm^{-1}. MS (180 °C): *m*/*z* (%) = 209 (3) [M$^+$], 174 (5), 139 (17), 126 (29), 115 (5), 113 (13), 105 (6), 91 (10), 70 (34), 65 (3). HRMS: calcd. ($C_{12}H_{16}ClN$) 209.0971; found 209.0928.

Amine 50: General Procedure B was used to synthesize amine **50** from aminoalkyne **44**. The reaction time for the hydroamination step was 4 h. After purification by flash chromatography (EtOAc), compound **50** (878 mg, 3.89 mmol, 97%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65−1.81 (m, 1 H), 1.82−1.96 (m, 1 H), 1.97−2.12 (m, 2 H), 3.04−3.15 (m, 3 H), 3.25−3.40 (m, 1 H), 3.60−3.70 (m, 1 H), 3.79 (s, 3 H), 6.10 (br. s, 1 H), 6.75 (dd, *J* = 8.8, 2.9 Hz, 1 H), 6.91 (d, *J* = 3.0 Hz, 1 H), 7.24 (d, *J* = 8.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 23.6 (CH_2), 30.2 (CH_2), 36.6 (CH_2), 45.4 (CH_2), 55.7 (CH_3), 60.1 (CH), 114.6 (CH), 116.4 (CH), 125.1 (C), 130.5 (CH), 135.5 (C), 158.6 (C) ppm. IR: $\tilde{\nu}$ = 2962, 2836, 1596, 1575, 1477, 1417, 1382, 1293, 1241, 1211, 1191, 1163, 1123, 1062, 1024, 929, 872, 809 cm^{-1}. MS (80 °C): *m*/*z* (%) = 226 (3) [M$^+$], 190 (3), 174 (3), 155 (11), 125 (6), 112 (100), 91 (4), 84 (7), 70 (92). HRMS: calcd. ($C_{12}H_{16}ClNO$) 225.0920; found 225.0880.

Amine 51: General Procedure B was used to synthesize amine **51** from aminoalkyne **45**. The reaction time for the hydroamination step was 6 h. After purification by flash chromatography (MeOH/EtOAc, 1:1), compound **51** (682 mg, 2.68 mmol, 67%) was isolated as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17−1.38 (m, 2 H), 1.34−1.58 (m, 1 H), 1.58 (d, *J* = 13.2 Hz, 1 H), 1.68 (d, *J* = 11.2 Hz, 1 H), 1.78 (d, *J* = 12.2 Hz, 1 H), 2.55 (dt, *J* = 11.7, 2.8 Hz, 1 H), 2.70 (dd, *J* = 12.4, 7.3 Hz, 1 H), 2.76−2.90 (m, 2 H), 3.02 (d, *J* = 12.3 Hz, 1 H), 7.02−7.11 (m, 1 H), 7.15−7.25 (m, 2 H), 7.54 (d, *J* = 7.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.8 (CH_2), 26.2 (CH_2), 32.7 (CH_2), 43.9 (CH_2), 47.2 (CH_2), 56.3 (CH), 124.9 (C), 127.2 (CH), 127.9 (CH), 131.5 (CH), 132.9 (CH), 138.6 (C) ppm. IR: $\tilde{\nu}$ = 3055, 2927, 2852, 2798, 2736, 1566, 1470, 1439, 1379, 1331, 1320, 1267, 1150, 1118, 1077, 1051, 1022, 981, 944, 930, 887, 808, 747, 718, 701, 659 cm^{-1}. MS (25 °C): *m*/*z* (%) = 254 (14) [M$^+$(^{81}Br)], 252 (15) [M$^+$(^{79}Br)], 224 (3), 198 (3), 196 (2), 171 (28), 169 (28), 144 (10), 130 (21), 128 (11), 118 (27), 115 (27), 103 (13), 98 (8), 91 (32), 90 (28), 84 (100), 82 (27), 77 (16), 70 (7), 68 (12), 65 (17). HRMS: calcd. ($C_{12}H_{16}BrN$) 253.0466; found 253.0305.

Amine 52: General Procedure B was used to synthesize amine **52** from aminoalkyne **46**. The reaction time for the hydroamination step was 6 h. After purification by flash chromatography (MeOH/EtOAc, 1:8), compound **52** (1.04 g, 3.74 mmol, 94%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31−1.42 (m, 1 H), 1.66 (d, *J* = 13.7 Hz, 1 H), 1.76−1.96 (m, 3 H), 1.96−2.12 (m, 1 H), 2.95 (t, *J* = 12.8 Hz, 1 H), 3.28−3.38 (m, 2 H), 3.58 (d, *J* = 12.9 Hz, 1 H), 3.70 (d, *J* = 9.2 Hz, 1 H), 7.42−7.52 (m, 2 H), 7.60 (s, 1 H), 8.90−10.20 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 21.9 (CH_2), 22.2 (CH_2), 27.3 (CH_2), 36.9 (CH_2), 44.8 (CH_2), 56.3 (CH), 123.4 (CF_3, q, *J* = 272 Hz), 125.6 (CH, q, *J* = 4 Hz), 128.7 (CH, q, *J* = 4 Hz), 129.5 (C, q, *J* = 33 Hz), 130.3 (CH), 134.8 (C), 138.2 (C) ppm. IR: $\tilde{\nu}$ = 3117, 3044, 2955, 2929, 2817, 2791, 2762, 2714, 2678, 2559, 2500, 2449, 2360, 2323, 2051, 1983, 1712, 1613, 1587, 1468, 1443, 1415, 1385, 1332, 1275, 1200, 1176, 1122, 1078, 1030, 990, 959, 933, 895, 828, 752, 729, 656, 600, 566, 533, 517 cm^{-1}. MS (60 °C): *m*/*z* (%) = 277 (1) [M$^+$], 240 (3), 222 (12), 193 (11), 159 (6), 158 (4), 145 (2), 98 (2), 85 (17), 84 (100), 70 (2), 67 (3). HRMS: calcd. ($C_{13}H_{15}ClF_3N$) 277.0845; found 277.0794.

Amine 53: General Procedure B was used to synthesize amine **53** from aminoalkyne **47**. The reaction time for the hydroamination step was 6 h. After purification by flash chromatography (MeOH/EtOAc, 1:8), compound **53** (929 mg, 3.88 mmol, 97%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32−1.42 (m, 1 H), 1.70−1.88 (m, 4 H), 1.90−2.05 (m, 1 H), 3.03 (t, *J* = 10.2 Hz, 1 H), 3.18−3.25 (m, 1 H), 3.44 (d, *J* = 9.6 Hz, 2 H), 3.76 (s, 3 H), 3.74−3.78 (m, 1 H), 6.71 (dd, *J* = 8.8, 3.0 Hz, 1 H), 7.00 (d, *J* = 2.9 Hz, 1 H), 7.18 (d, *J* = 8.8 Hz, 1 H), 8.00−8.70 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 22.1 (CH_2), 22.2 (CH_2), 27.5 (CH_2), 37.3 (CH_2), 45.8 (CH_2), 55.8 (CH_3), 57.7 (CH), 115.0 (CH), 117.0 (CH), 125.4 (C), 130.2 (CH), 134.3 (C), 158.5 (C) ppm. IR: $\tilde{\nu}$ = 2944, 2837, 1596, 1480, 1283, 1242, 1211, 1191, 1165, 1123, 1063, 1022, 981, 924, 873, 810, 734, 700 cm^{-1}. MS (100 °C): *m*/*z* (%) = 239 (1) [M$^+$], 202 (2), 155 (10), 148 (7), 128 (9), 115 (8), 105 (4), 98 (6), 92 (32), 91 (50), 85 (28), 84 (100), 77 (4), 65 (3). HRMS: calcd. ($C_{13}H_{18}ClNO$) 239.1076; found 239.1078.

Synthesis of Pyrrolizidines and Indolizidines from Chloro Derivatives. General Procedure F: A Schlenk tube fitted with a Teflon stopcock and containing a magnetic stirring bar was charged with amine (1.0 mmol), [$Pd_2(dba)_3$] (46 mg, 0.05 mmol, 5.0 mol %), 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (34 mg, 0.1 mmol, 10.0 mol %), KO*t*Bu (168 mg, 1.5 mmol), and 1,4-dioxane (2.0 mL). After this had been stirred at 110 °C for 3−12 h (TLC monitoring), water and *tert*-butyl methyl ether were added. The organic layer was separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 ×). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Synthesis of Pyrrolizidines and Indolizidines from Bromo Derivatives. General Procedure G: A Schlenk tube fitted with a Teflon stopcock and containing a magnetic stirring bar was charged with amine (1.0 mmol), [$Pd(PPh_3)_4$] (58 mg, 0.05 mmol, 5.0 mol %), K_2CO_3 (276 mg, 2.0 mmol), NaO*t*Bu (192 mg, 2.0 mmol), and toluene (2.0 mL). After this had been stirred at 110 °C for 6 h (TLC monitoring), water and *tert*-butyl methyl ether were added. The organic layer was separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 ×). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography (SiO_2).

Pyrrolizidine 54: General Procedure G was used to synthesize pyrrolizidine **54** from amine **48**. After purification by flash chromatography (PE/EtOAc, 5:1), compound **54** (113 mg, 0.71 mmol, 71%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31−1.42 (m, 1 H), 1.82−1.90 (m, 3 H), 2.95 (dd, *J* = 16.1, 2.6 Hz, 1 H), 3.12−3.26 (m, 2 H), 3.45−3.55 (m, 1 H), 3.97−4.04 (m, 1 H), 6.67 (d, *J* = 7.8 Hz, 1 H), 6.81 (t, *J* = 7.2 Hz, 1 H), 7.07−7.15 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 25.7 (CH_2), 31.4 (CH_2), 34.0 (CH_2), 52.8 (CH_2), 65.4 (CH), 111.8 (CH), 120.3 (CH), 124.9 (CH), 127.7 (CH), 132.3 (C), 153.2 (C) ppm. IR: $\tilde{\nu}$ = 3069, 3046, 3022, 2957, 2926, 2872, 1603, 1475, 1456, 1434, 1358, 1313, 1263, 1224, 1180, 1152, 1114, 1089, 1070, 1021, 985, 957, 913, 867, 845, 744, 714, 695 cm^{-1}. MS (25 °C):

m/z (%) = 159 (100) [M^+], 144 (9), 131 (97), 117 (30), 103 (21), 91 (22), 89 (24), 77 (30), 65 (18).

Pyrrolizidine 55: General Procedure F was used to synthesize pyrrolizidine **55** from amine **49**. The reaction time was 12 h. After purification by flash chromatography (PE/EtOAc, 8:1), compound **55** (171 mg, 0.99 mmol, 99%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (quin, *J* = 9.9 Hz, 1 H), 1.78−1.94 (m, 3 H), 2.18 (s, 3 H), 2.87 (dd, *J* = 16.0, 3.2 Hz, 1 H), 3.02−3.19 (m, 2 H), 3.35−3.45 (m, 1 H), 3.85−3.95 (m, 1 H), 6.40 (d, *J* = 7.8 Hz, 1 H), 6.60 (d, *J* = 7.6 Hz, 1 H), 7.00 (t, *J* = 7.7 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 18.7 (CH_3), 25.8 (CH_2), 31.7 (CH_2), 32.9 (CH_2), 52.3 (CH_2), 65.0 (CH), 108.4 (CH), 120.4 (CH), 127.6 (CH), 128.6 (C), 134.2 (C), 154.4 (C) ppm. IR: ṽ = 3027, 2917, 1774, 1704, 1595, 1453, 1436, 1397, 1371, 1336, 1262, 1233, 1175, 1146, 1115, 1074, 1025, 959, 910, 882, 860, 767, 715 cm^{-1}. MS (25 °C): *m/z* (%) = 173 (100) [M^+], 158 (27), 144 (84), 130 (60), 115 (29), 103 (23), 91 (20), 87 (21), 77 (30), 65 (13). HRMS: calcd. ($C_{12}H_{15}N$) 173.1205; found 173.1204.

Indolizidine 57: General Procedure G was used to synthesize indolizidine **57** from amine **51**. After purification by flash chromatography (EtOAc), compound **57** (111 mg, 0.64 mmol, 64%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33−1.72 (m, 4 H), 1.76−1.92 (m, 2 H), 2.52−2.68 (m, 2 H), 2.94 (dd, *J* = 14.8, 7.5 Hz, 1 H), 3.15−3.26 (m, 1 H), 3.63 (dd, *J* = 12.0, 1.9 Hz, 1 H), 6.44 (d, *J* = 7.6 Hz, 1 H), 6.63 (t, *J* = 7.3 Hz, 1 H), 7.01−7.14 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.3 (CH_2), 24.6 (CH_2), 30.6 (CH_2), 35.5 (CH_2), 45.2 (CH_2), 65.2 (CH), 106.0 (CH), 119.5 (CH), 124.5 (CH), 127.2 (CH), 129.4 (C), 151.5 (C) ppm. IR: ṽ = 3048, 3025, 2930, 2850, 2789, 1608, 1480, 1456, 1441, 1384, 1360, 1337, 1316, 1299, 1283, 1250, 1210, 1178, 1151, 1134, 1117, 1089, 1056, 1020, 981, 972, 943, 915, 892, 860, 835, 821, 744, 729, 714 cm^{-1}. MS (25 °C): *m/z* (%) = 173 (100) [M^+], 158 (11), 144 (53), 132 (33), 130 (74), 117 (75), 103 (9), 91 (17), 89 (16), 77 (11), 65 (8).

Indolizidine 58: General Procedure F was used to synthesize indolizidine **58** from amine **52**. The reaction time was 3 h. After purification by flash chromatography (PE/EtOAc, 10:1), compound **58** (234 mg, 0.97 mmol, 97%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37−1.63 (m, 3 H), 1.70 (d, *J* = 12.8 Hz, 1 H), 1.86 (td, *J* = 13.4, 2.6 Hz, 2 H), 2.57 (dd, *J* = 15.2, 9.6 Hz, 1 H), 2.72 (td, *J* = 12.2, 3.0 Hz, 1 H), 3.01 (dd, *J* = 15.2, 7.8 Hz, 1 H), 3.37 (qd, *J* = 9.8, 2.8 Hz, 1 H), 3.63 (dd, *J* = 14.6, 4.4 Hz, 1 H), 6.35 (d, *J* = 8.2 Hz, 1 H), 7.23 (s, 1 H), 7.29 (d, *J* = 8.2 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.1 (CH_2), 24.5 (CH_2), 30.9 (CH_2), 35.0 (CH_2), 44.5 (CH_2), 64.4 (CH), 104.2 (CH), 118.5 (CH, q, *J* = 33 Hz), 121.3 (CH, q, *J* = 4 Hz), 125.2 (CF_3, q, *J* = 269 Hz), 125.3 (CH, q, *J* = 4 Hz), 129.3 (C), 154.0 (C) ppm. IR: ṽ = 2941, 2919, 2853, 2820, 1708, 1618, 1593, 1497, 1447, 1399, 1322, 1295, 1251, 1209, 1168, 1151, 1135, 1095, 1056, 1026, 975, 927, 890, 872, 853, 812, 758, 737, 699, 643, 626, 609, 580, 562, 530 cm^{-1}. MS (25 °C): *m/z* (%) = 241 (100) [M^+], 240 (100), 222 (13), 212 (19), 200 (12), 185 (22), 166 (5), 135 (3), 97 (4), 91 (3), 81 (4), 67 (3). HRMS: calcd. ($C_{13}H_{14}F_3N$) 241.1078; found 241.1078.

Indolizidine 59: General Procedure F was used to synthesize indolizidine **59** from amine **53**. The reaction time was 12 h. After purification by flash chromatography (PE/EtOAc, 20:1), compound **59** (130 mg, 0.79 mmol, 79%) was isolated as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (tq, *J* = 12.8, 3.4 Hz, 1 H), 1.73−1.45 (m, 3 H), 1.88−1.80 (m, 2 H), 2.54 (td, *J* = 12.0, 3.4 Hz, 2 H), 2.88 (dd, *J* = 14.8, 7.2 Hz, 1 H), 3.15−3.05 (m, 1 H), 3.57 (br. d, *J* = 12.7 Hz, 1 H), 3.73 (s, 3 H), 6.35 (d, *J* = 8.4 Hz, 1 H), 6.61 (dd, *J* = 8.4, 2.5 Hz, 1 H), 6.75 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 24.4 (CH_2), 24.6 (CH_2), 30.4 (CH_2), 35.8 (CH_2), 46.0 (CH_2), 56.0 (CH_3), 66.2 (CH), 106.0 (CH), 111.4 (CH), 112.4 (CH), 131.1 (C), 146.3 (C), 152.8 (C) ppm. IR: ṽ = 2932, 2853, 1666, 1595, 1485, 1452, 1382, 1283, 1245, 1206, 1155, 1134, 1061, 1033, 887, 855, 799, 761, 700 cm^{-1}. MS (25 °C): *m/z* (%) = 203 (97) [M^+], 202 (17), 189 (27), 188 (100), 185 (34), 174 (15), 160 (18), 157 (16), 147 (19), 142 (13), 133 (13), 117 (13), 104 (11), 91 (10), 77 (8), 65 (9). HRMS: calcd. ($C_{13}H_{17}NO$) 203.1310; found 203.1311.

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[1] For general reviews on hydroamination, see: [1a] I. A. Chekulaeva, L. V. Kondratjeva, *Russ. Chem. Rev.* **1965**, *34*, 669−680. [1b] D. Steinborn, R. Taube, *Z. Chem.* **1986**, *26*, 349−359. [1c] R. Taube, in *Applied Homogeneous Catalysis with Organometallic Compounds*, (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **1996**, p. 507−520. [1d] T. E. Müller, M. Beller, *Chem. Rev.* **1998**, *98*, 675−703. [1e] 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. [1f] E. Haak, S. Doye, *Chem. Unserer Zeit* **1999**, *33*, 296−303. [1g] M. Nobis, B. Drießen-Hölscher, *Angew. Chem.* **2001**, *113*, 4105−4108; *Angew. Chem. Int. Ed.* **2001**, *40*, 3983−3985. [1h] J. J. Brunet, D. Neibecker, in *Catalytic Heterofunctionalization*, (Eds.: A. Togni, H. Grützmacher), Wiley-VCH, Weinheim, **2001**, p. 91−141.

[2] For a review on hydroamination of alkynes, see: F. Pohlki, S. Doye, *Chem. Soc. Rev.* **2003**, *32*, 104−114.

[3] For a review on group-IV metal complexes as hydroamination catalysts, see: [3a] I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2003**, 935−946. For early studies on group-IV metal complexes as hydroamination catalysts, see: [3b] P. J. Walsh, A. M. Baranger, R. G. Bergman, *J. Am. Chem. Soc.* **1992**, *114*, 1708−1719. [3c] A. M. Baranger, P. J. Walsh, R. G. Bergman, *J. Am. Chem. Soc.* **1993**, *115*, 2753−2763. [3d] P. L. McGrane, M. Jensen, T. Livinghouse, *J. Am. Chem. Soc.* **1992**, *114*, 5459−5460. [3e] P. L. McGrane, T. Livinghouse, *J. Org. Chem.* **1992**, *57*, 1323−1324. [3f] P. L. McGrane, T. Livinghouse, *J. Am. Chem. Soc.* **1993**, *115*, 11485−11489.

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

[5] [5a] E. Haak, S. Doye, DE 199,13,522. [5b] E. Haak, I. Bytschkov, S. Doye, *Angew. Chem.* **1999**, *111*, 3584−3586; *Angew. Chem. Int. Ed.* **1999**, *38*, 3389−3391. [5c] E. Haak, H. Siebeneicher, S. Doye, *Org. Lett.* **2000**, *2*, 1935−1937. [5d] I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2001**, 4411−4418. [5e] F. Pohlki, S. Doye, *Angew. Chem.* **2001**, *113*, 2361−2364; *Angew. Chem. Int. Ed.* **2001**, *40*, 2305−2308. [5f] E. Haak, I. Bytschkov, S. Doye, *Eur. J. Org. Chem.* **2002**, 457−463.

[6] [6a] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467−4470. [6b] K. Sonogashira, in *Comprehensive Organic Synthesis*, (Eds.: B. M. Trost, I. A. Fleming), Pergamon Press, **1991**, vol. 3, p. 521−549.

[7] H. Siebeneicher, S. Doye, *Eur. J. Org. Chem.* **2002**, 1213−1220.

[8] [8a] P. L. McGrane, M. Jensen, T. Livinghouse, *J. Am. Chem.*

Soc. **1992**, *114*, 5459−5460. [8b] P. L. McGrane, T. Livinghouse, *J. Am. Chem. Soc.* **1993**, *115*, 11485−11489. [8c] P. L. McGrane, T. Livinghouse, *J. Org. Chem.* **1992**, *57*, 1323−1324. [8d] I. Bytschkov, S. Doye, *Tetrahedron Lett.* **2002**, *43*, 3715−3718. [8e] L. Ackermann, R. G. Bergman, *Org. Lett.* **2002**, *4*, 1475−1478.

[9] M. Hesse, *Alkaloide*, Verlag Helvetica Chimica Acta Zürich, Wiley-VCH, Weinheim, **2000**.

[10] For general reviews on Pd-catalyzed amination reactions of aryl halides, see: [10a] J. P. Wolfe, S. Wagaw, J.-F. Marcoux, S. L. Buchwald, *Acc. Chem. Res.* **1998**, *31*, 805−818. [10b] B. H. Yang, S. L. Buchwald, *J. Organomet. Chem.* **1999**, *576*, 125−146. [10c] A. R. Muci, S. L. Buchwald, *Top. Curr. Chem.* **2002**, *219*, 131−209. [10d] J. F. Hartwig, *Synlett* **1997**, 329−340. [10e] J. F. Hartwig, *Angew. Chem.* **1998**, *110*, 2154−2177; *Angew. Chem. Int. Ed.* **1998**, *37*, 2046−2067.

[11] A. Heutling, S. Doye, *J. Org. Chem.* **2002**, *67*, 1961−1964.

[12] The use of benzophenone imine as ammonia equivalent in Pd-catalyzed amination reactions was first reported by: J. P. Wolfe, J. Åhman, J. P. Sadighi, R. A. Singer, S. L. Buchwald, *Tetrahedron Lett.* **1997**, *38*, 6367−6370.

[13] [13a] M. R. Gagné, C. L. Stern, T. J. Marks, *J. Am. Chem. Soc.* **1992**, *114*, 275−294. [13b] I. Bytschkov, Ph.D. Dissertation, University of Hannover, **2002**.

[14] A. J. Arduengo, III, R. Krafczyk, R. Schmutzler, H. A. Craig, J. R. Goerlich, W. J. Marshall, M. Unverzagt, *Tetrahedron* **1999**, *55*, 14523−14534.

[15] N. Satyamurthy, J. R. Barrio, *J. Org. Chem.* **1983**, *48*, 4394−4396.

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