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One-Pot Procedure for the Synthesis of *N*-Substituted 2-(Arylmethyl)pyrrolidines from 1-Aryl-2-cyclopropylalkynes and Primary Amines by a Hydroamination/Cyclopropylimine Rearrangement/Reduction Sequence

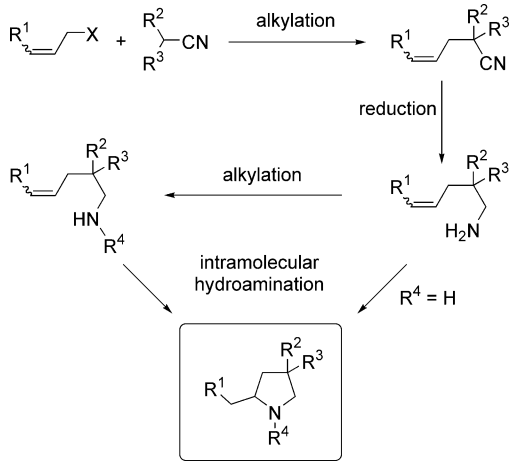
Kerstin Gräbe,[a] Björn Zwafelink,[a] and Sven Doye*[a]

Keywords: Alkynes / Amines / Reduction / Hydroamination / Titanium / Rearrangement

A one-pot procedure for the synthesis of *N*-substituted 2-(arylmethyl)pyrrolidines from 1-aryl-2-cyclopropylalkynes and primary amines is presented. The procedure proceeded first through an $[Ind_2TiMe_2]$-catalyzed regioselective hydroamination of a 1-aryl-2-cyclopropylalkyne with a primary amine. The resulting cyclopropylimine, which was not isolated, was then forced to undergo a cyclopropylimine rearrangement in the presence of catalytic amounts of NH_4Cl at 145 °C to deliver the corresponding 2-pyrroline. A subsequent reduction performed with $NaBH_3CN$ and $ZnCl_2$ finally gave the desired *N*-substituted 2-(arylmethyl)pyrrolidine.

Introduction

The hydroamination of alkenes[1] is regarded as an environmentally friendly and ecologically desirable process. Consequently, much effort has been spent on the identification of catalysts that allow the addition of N–H across carbon–carbon double bonds.[1,2] Despite the great progress achieved during the last few years, it should be noted that most of the existing catalytic systems are only suitable for intramolecular reactions of aminoalkenes. The majority of published examples of hydroamination reactions describe cyclization reactions of 1-amino-4-pentene derivatives that give access to the corresponding 2-substituted pyrrolidines (Scheme 1). However, from a synthetic point of view, this hydroamination approach towards the synthesis of pyrrolidines is not particularly elegant because the method generally used for the synthesis of the starting materials, the 1-amino-4-pentene derivatives,[3] is not very flexible. Usually, the first step is an alkylation of a suitable nitrile with an allylic halide. The resulting 4-pentenenitrile is then reduced in a second step to give the corresponding 1-amino-4-pentene. A final intramolecular hydroamination yields a 2-substituted and *N*-unsubstituted pyrrolidine. To obtain the corresponding *N*-substituted products, a further alkylation (or arylation) is required. Alternatively, the 1-amino-4-pentene can be converted into a secondary amine, which is then used as the substrate in an intramolecular hydroamination reaction. However, in most cases the hydroamination approach is used to obtain 2-methylpyrrolidines (R^1 = H) with additional substituents in the 4-position (R^2, $R^3 \neq$ H). The Thorpe–Ingold effect is responsible for the fact that with many hydroamination catalysts only geminally disubstituted 1-amino-4-pentenes (R^2, $R^3 \neq$ H) undergo successful cyclization reactions. Furthermore, it has been found for many catalysts that only monosubstituted (R^1 = H) or phenyl-substituted alkene moieties (R^1 = Ph) are tolerated. With these limitations in mind we started a project to develop an alternative hydroamination approach towards the synthesis of 2-substituted pyrrolidines.



Scheme 1. Synthesis of 2-substituted pyrrolidines from 1-amino-4-pentenes by intramolecular hydroamination.

[a] Institut für Reine und Angewandte Chemie,
Universität Oldenburg,
Carl-von-Ossietzky-Str. 9–11, 26111 Oldenburg, Germany
Fax: +49-441-798-3329
E-mail: doye@uni-oldenburg.de

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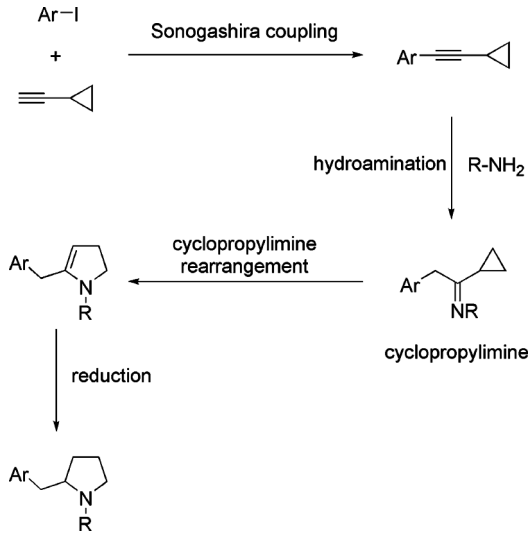
In contrast to the intermolecular hydroamination of alkenes, the corresponding protocols for the intermolecular addition of amines to alkynes are well established.[4] In particular, Ti complexes have been shown to catalyze the hydroamination of all classes of alkynes with primary amines.[5] Particularly interesting is the fact that the corresponding reactions of unsymmetrically substituted 1-alkyl-2-arylalkynes take place with high anti-Markovnikov selectivity. Correspondingly, 1-aryl-2-cyclopropylalkynes undergo hydroamination reactions with primary amines to give cyclopropylimine derivatives (Scheme 2). However, at elevated temperatures, cyclopropylimines are known to undergo an acid-catalyzed rearrangement to give 2-pyrrolines,[6] which can be further reduced to the desired pyrrolidines. Obvious advantages of the envisioned strategy are the commercial availability of many primary amines and the easy accessibility of 1-aryl-2-cyclopropylalkynes from common aryl halides and cyclopropylacetylene by Sonogashira coupling. Additionally, it should be noted that the cyclopropylimine rearrangement does not require the presence of any additional substituents in the cyclopropyl ring. Consequently, the new approach should offer a simple way to synthesize 2-substituted pyrrolidines that do not possess any further substituents in the carbon chain of the heterocyclic ring.

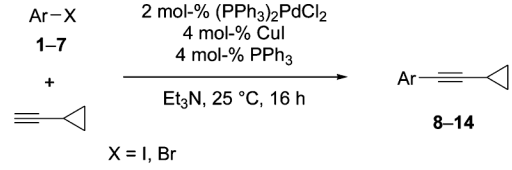


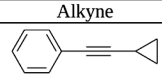
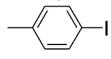
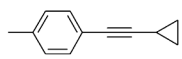
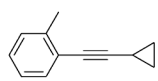
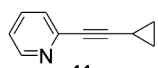
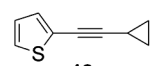
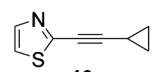
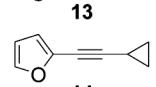
Scheme 2. Synthesis of 2-(arylmethyl)pyrrolidines from aryl halides, cyclopropylacetylene, and primary amines.

Results and Discussion

Initial Sonogashira coupling reactions performed with the commercially available aryl halides **1**–**6** (Table 1) or 2-iodofuran (**7**) and cyclopropylacetylene[7] gave the desired 1-aryl-2-cyclopropylalkynes **8**–**14** in moderate to excellent yields (58–96%). The coupling reactions were usually performed under standard Sonogashira conditions in the presence of 2 mol-% $[(PPh_3)_2PdCl_2]$, 4 mol-% PPh_3, and 4 mol-% CuI. Because coupling reactions employing 2-bromothiazole (**6**) do not give satisfactory yields under these conditions,[8] a catalyst system consisting of 5 mol-% $[(PhCN)_2PdCl_2]$, 10 mol-% PPh_3, and 5 mol-% $Cu(OAc)_2{\cdot}H_2O$ was used for this substrate.[8,9]

Table 1. Synthesis of 1-aryl-2-cyclopropylalkynes by Sonogashira coupling.



Entry	Aryl halide	Alkyne	Yield [%][a]
1	 **1**	 **8**	91
2	 **2**	 **9**	96
3	 **3**	 **10**	70
4	 **4**	 **11**	91
5	 **5**	 **12**	85
6	 **6**	 **13**	68[b]
7	 **7**	 **14**	58

[a] Reaction conditions: aryl halide (10.0 mmol), cyclopropylacetylene (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-%), NEt_3 (30 mL), 25 °C, 16 h. The yields refer to isolated pure compounds. [b] Different reaction conditions were used for the coupling reaction of 2-bromo-1,3-thiazole (**6**): aryl halide (10.0 mmol), alkyne (10.0 mmol), $[(PhCN)_2PdCl_2]$ (0.5 mmol, 5.0 mol-%), PPh_3 (1.0 mmol, 10.0 mol-%), $Cu(OAc)_2{\cdot}H_2O$ (0.5 mmol, 5.0 mol-%), diisopropylamine (20 mL), 45 °C, 12 h.

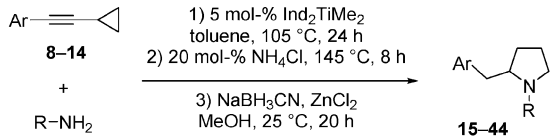
With the 1-aryl-2-cyclopropylalkynes **8**–**14** in hand we turned our attention towards the envisioned hydroamination/cyclopropylimine rearrangement/reduction sequence (Scheme 2, Table 2). Thus, we performed an initial hydroamination reaction between 1-phenyl-2-cyclopropylacetylene (**8**) and *p*-toluidine in the presence of 5 mol-% $[Ind_2TiMe_2]$ (Ind = η^5-indenyl) in toluene at 105 °C. After 24 h, a sample of the reaction mixture was transferred into an NMR tube and diluted with $CDCl_3$. NMR analysis of this sample showed that the alkyne **8** was completely transformed into the corresponding (*p*-tolylmethyl)cyclopropylimine. The regioselectivity of the addition was determined to be >98:2. The subsequent cyclopropylimine rearrangement was then achieved by the direct addition of 20 mol-% NH_4Cl and heating of the reaction mixture at 145 °C for 8 h. After that time, the formation of the expected 2-pyrroline was confirmed by ^1H NMR spectroscopy. For the final reduction,

$NaBH_3CN$, $ZnCl_2$, and methanol were added to the reaction mixture, which was stirred at room temperature for 20 h. It was possible to isolate the desired pyrrolidine **15** in 90% yield (Table 2, Entry 1). Surprisingly, the obtained pure product **15** turned out to be relatively unstable, and complete decomposition of **15** took place within 1 h.

Having identified a suitable experimental protocol for the envisioned synthetic strategy we performed a number of reactions under identical conditions with various alkynes and amines (Table 2). First, it was recognized that comparably high yields (86 and 70%) of the stable pyrrolidines **16** and **17** (Table 2, Entries 2 and 3) were obtained when the alkylamines cyclopentylamine or *tert*-butylamine were used with alkyne **8**. In contrast, the reaction with benzylamine gave the desired pyrrolidine **18** with a significantly decreased yield of only 23%. A simple explanation for this observation could be the decreased reactivity of high-boiling and sterically less hindered amines in the [Ind_2TiMe_2]-catalyzed hydroamination reactions of alkynes.[5m] Because it has previously been found[5m] that much higher yields from [Ind_2TiMe_2]-catalyzed hydroamination reactions are obtained when amines like benzylamine are added slowly to the reaction mixture, an additional reaction with a correspondingly changed experimental protocol in which benzylamine was added slowly to the reaction mixture over a period of 4 h at 105 °C was performed. In this experiment, the desired pyrrolidine **18** was formed in 63% yield (Table 2, Entry 4). Correspondingly, all other reaction sequences involving the use of benzylamine were performed under these conditions. Although the corresponding reactions performed with 1-cyclopropyl-2-(*p*-tolyl)acetylene (**9**) and one of the four amines (*p*-toluidine, cyclopentylamine, *tert*-butylamine, benzylamine) gave results (Table 2, Entries 5–8) that are almost identical to those obtained with 1-cyclopropyl-2-phenylacetylene (**8**), the reaction sequence performed with the *ortho*-substituted alkyne **10** and *tert*-butylamine only led to trace amounts of pyrrolidine **25**. Because 70% of the alkyne **10** could be recovered from the reaction mixture, it can be assumed that this poor result is mainly caused by steric repulsion between the bulky amine and the *ortho* substituent of the alkyne during the hydroamination step. The improved results obtained with the sterically less demanding amines *p*-toluidine, cyclopentylamine, and benzylamine (Table 2, Entries 9, 10, 12) are in good agreement with this explanation. However, **25** could be isolated with a slightly better yield of 22% (Table 2, Entry 11, footnote [c]) when the cyclopropylimine rearrangement was performed in the presence of stoichiometric amounts of NH_4Cl (1 equiv.). This result suggests that the sterically demanding *tert*-butyl substituent at the nitrogen atom of the initially formed imine in combination with a bulky aryl system also leads to a less efficient rearrangement reaction.

In contrast to the phenyl-substituted alkynes **8**–**10**, the pyridine-containing alkyne **11** turned out to be a poor substrate (Table 2, Entries 13–17). Employing this alkyne in combination with *p*-toluidine, cyclopentylamine, *tert*-butylamine, or benzylamine led to the isolation of only one of the desired pyrrolidines (**27**, Table 2, Entry 13) in poor

Table 2. One-pot synthesis of 2-(arylmethyl)pyrrolidines from 1-aryl-2-cyclopropylalkynes by a hydroamination/cyclopropylimine rearrangement/reduction sequence.



Entry	Alkyne	R	Product	Yield [%][a]
1	**8**	*p*-Tol	**15**	90
2	**8**	cyclopentyl	**16**	86
3	**8**	*t*Bu	**17**	70
4	**8**	Bn	**18**	63[b]
5	**9**	*p*-Tol	**19**	95
6	**9**	cyclopentyl	**20**	84
7	**9**	*t*Bu	**21**	77
8	**9**	Bn	**22**	75
9	**10**	*p*-Tol	**23**	93
10	**10**	cyclopentyl	**24**	81
11	**10**	*t*Bu	**25**	< 5[c,d]

Table 2. *(Continued)*

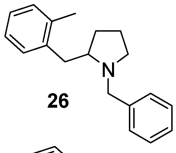
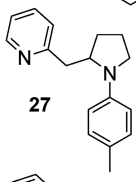
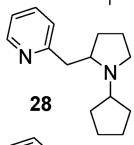
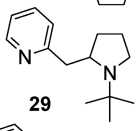
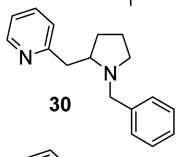
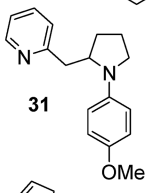
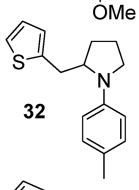
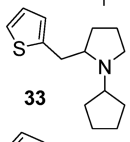
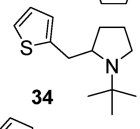
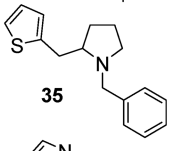
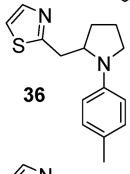
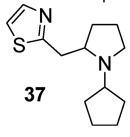
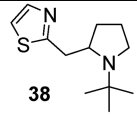
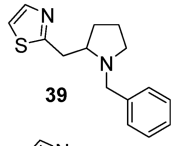
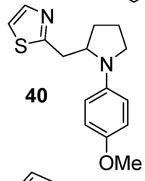
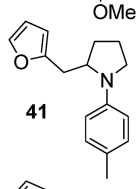
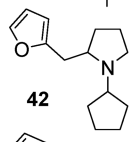
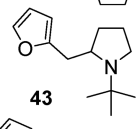
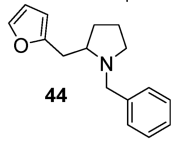
Entry	Alkyne	R	Product	Yield [%][a]
12	**10**	Bn	 **26**	48[b]
13	**11**	*p*-Tol	 **27**	15
14	**11**	cyclopentyl	 **28**	< 5[d]
15	**11**	*t*Bu	 **29**	< 5[d]
16	**11**	Bn	 **30**	< 5[d]
17	**11**	4-MeOC$_6$H$_4$	 **31**	18
18	**12**	*p*-Tol	 **32**	72
19	**12**	cyclopentyl	 **33**	87
20	**12**	*t*Bu	 **34**	71
21	**12**	Bn	 **35**	57[b]
22	**13**	*p*-Tol	 **36**	86
23	**13**	cyclopentyl	 **37**	< 5[d]

Table 2. *(Continued)*

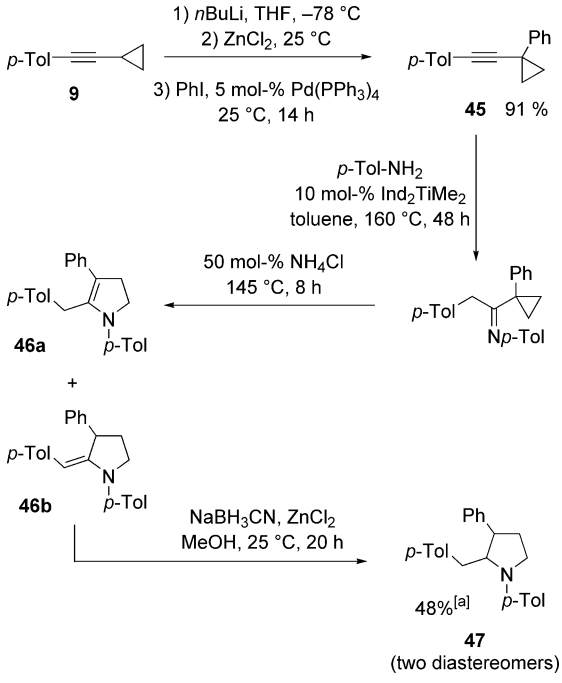
Entry	Alkyne	R	Product	Yield [%][a]
24	**13**	*t*Bu	 **38**	< 5[d]
25	**13**	Bn	 **39**	< 5[d]
26	**13**	4-MeOC$_6$H$_4$	 **40**	35
27	**14**	*p*-Tol	 **41**	< 5[d]
28	**14**	cyclopentyl	 **42**	< 5[d]
29	**14**	*t*Bu	 **43**	< 5[d]
30	**14**	Bn	 **44**	< 5[d]

[a] Reaction conditions: (a) alkyne (2.40 mmol), amine (2.64 mmol), [Ind_2TiMe_2] (0.12 mmol, 5.0 mol-%), 105 °C, 24 h; (b) NH_4Cl (0.48 mmol, 20 mol-%), 145 °C, 5–7 h; (c) $NaBH_3CN$ (4.80 mmol), $ZnCl_2$ (2.40 mmol), MeOH, 25 °C, 20 h. [b] The amine was added slowly to the reaction mixture over a period of 4 h. [c] A yield of 22% was obtained when the cyclopropylimine rearrangement step was performed with 2.40 mmol of NH_4Cl (100 mol-%). [d] Estimated by NMR spectroscopy.

yield (15%) along with a large amount of decomposition products. All the other reactions performed with **11** led to the complete consumption of the alkyne and the formation of a number of unidentified compounds. Owing to the fact that the only successful reaction was achieved with the arylamine *p*-toluidine we also performed the reaction with 4-methoxyaniline (Table 2, Entry 17), which gave the desired pyrrolidine in 18% yield. This result suggests that this one-pot procedure with alkyne **11** can only be successfully performed with arylamines. Fortunately, not all heteroaromatic systems cause comparable problems. By using *p*-toluidine, cyclopentylamine, or *tert*-butylamine, it was possible to convert the thiophene-containing alkyne **12** (Table 2, Entries 18–20) into the corresponding pyrrolidines **32**, **33**, and **34** in 72, 87, and 71% yields, respectively. In addition, the corresponding *N*-benzyl-substituted product **35** was iso-

lated in an acceptable yield of 57% from a reaction in which the amine was added slowly to the reaction mixture (Table 2, Entry 21). Further reactions performed with the thiazolyl-substituted alkyne **13** (Table 2, Entries 22–26) gave results similar to those obtained with the pyridine-containing alkyne **11**. Although the reaction sequence performed with *p*-toluidine gave the pyrrolidine **36** in a very good yield (86%), it was not possible to isolate the desired products from the reactions performed with cyclopentylamine, *tert*-butylamine, or benzylamine. In all these cases, a number of unidentified compounds were formed. However, an additional experiment with 4-methoxyaniline gave the corresponding product in 35% yield (Table 2, Entry 26). This result suggests that the thiazole-containing alkyne **13** is another example of a substrate that can only be used in combination with an aromatic amine. Finally, reactions with the furan-containing alkyne **14** turned out to be unsuccessful with all the amines employed. In this context, it should be noted that although the desired products **41**–**44** could not be isolated, in situ ^{1}H NMR studies undoubtedly proved the formation of pyrrolidine derivatives during the reaction performed with **14** and *p*-toluidine. Unfortunately, this reaction seems to take place along with a decomposition of the acid-sensitive furan ring.

To extend the method to the synthesis of more substituted pyrrolidines, we synthesized alkyne **45** (Scheme 3), which contains a 1,1-disubstituted cyclopropyl ring. To this end, the propargylic position of alkyne **9** was first lithiated. Subsequent transmetalation with $ZnCl_2$ and Negishi coupling with iodobenzene (**1**) gave the desired alkyne **45** in 91% yield.[11] Fortunately, the hydroamination/cyclopropylimine rearrangement/reduction sequence performed with



Scheme 3. Synthesis of the 1,2,3-trisubstituted pyrrolidine **47**. [a] 43% of unconsumed starting material (**45**) was recovered.

p-toluidine resulted in the formation of a diastereomeric mixture of the desired pyrrolidine **47**. However, it was found that the initial hydroamination reaction is slow, which can probably be explained by the steric hindrance caused by the bulky 1-phenylcyclopropyl substituent of the alkyne **45**. After some optimization, we performed the initial hydroamination in the presence of 10 mol-% [Ind_2TiMe_2] at 160 °C for 48 h and the subsequent cyclopropylimine rearrangement with 50 mol-% NH_4Cl at 145 °C for 8 h. After subsequent reduction of the formed enamines **46a** and **46b**, the desired pyrrolidine **47** was obtained as a 54:46 mixture of two diastereomers in 48% yield. Owing to the slow hydroamination step, 43% of the starting material **45** was also recovered.

Conclusions

We have developed a new one-pot procedure for the synthesis of *N*-substituted 2-(arylmethyl)pyrrolidines from 1-aryl-2-cyclopropylalkynes and primary amines. The procedure proceeds first by a regioselective hydroamination of a 1-aryl-2-cyclopropylalkyne with a primary amine performed in the presence of 5 mol-% [Ind_2TiMe_2]. The resulting cyclopropylimine, which is not isolated, is then forced to undergo a cyclopropylimine rearrangement in the presence of substoichiometric amounts of NH_4Cl at 145 °C to give the corresponding 2-pyrroline. Subsequent reduction using $NaBH_3CN$ and $ZnCl_2$ finally gives the desired *N*-substituted 2-(arylmethyl)pyrrolidine. Obvious advantages of the new protocol are the commercial availability of many primary amines and the easy accessibility of 1-aryl-2-cyclopropylalkynes from common aryl halides and cyclopropylacetylene by Sonogashira coupling. As a consequence, structural variations of the aromatic substituent as well as changes of the substituent at the nitrogen atom of the pyrrolidine product can easily be achieved. Further studies extending the method to more substituted alkyne substrates are presently underway in our laboratories.

Experimental Section

General: All reactions were performed under argon or nitrogen in oven-dried Duran glassware using standard Schlenk-line and glovebox techniques. [Ind_2TiMe_2] was synthesized according to a literature procedure.[10] Toluene (toluene extra dry with molecular sieves, 99.85%, water < 50 ppm) and methanol (methanol extra dry, 99.9%, water < 50 ppm) were purchased from Acros Organics. Cyclopropylacetylene was either purchased from Acros Organics or synthesized according to a literature procedure.[7] *p*-Toluidine was purified by Kugelrohr distillation. 2-Iodofuran (**7**) was synthesized according to a literature procedure.[12] Cyclopentylamine, benzylamine, triethylamine, and *tert*-butylamine were purified and dried by distillation (20 cm Vigreux column) from CaH_2 on molecular sieves at ambient pressure under an inert gas. All other reagents were purchased from commercial sources and were used without further purification. All alkynes, amines and [Ind_2TiMe_2] were stored in a nitrogen-filled glove box (M. Braun, Unilab). [Ind_2TiMe_2] was cooled to –30 °C. Unless otherwise noted, yields

refer to isolated yields of pure compounds as gauged by thin-layer chromatography (TLC) and ^{1}H and ^{13}C NMR spectroscopy. All products were characterized by ^{1}H and ^{13}C NMR, and IR spectroscopy and mass spectrometry (MS). Additional characterization data were obtained by high-resolution mass spectrometry (HRMS). NMR spectra were recorded with the following spectrometers: Bruker Avance DPX 300, Bruker Avance DRX 500, and Bruker Avance III 500. All ^{1}H NMR spectra are reported in δ units (ppm) relative to the signal for $CDCl_3$ at δ = 7.26 ppm. All ^{13}C NMR spectra are reported in δ units (ppm) relative to the central line of the triplet for $CDCl_3$ at δ = 77.0 ppm. IR spectra were recorded with a Bruker Tensor 27 spectrometer using an attenuated total reflection (ATR) method. Mass spectra were recorded with a Finnigan MAT 95 spectrometer (EI with an ionization potential of 70 eV or CI with isobutane as ionization gas). GC analyses were performed with a Shimadzu GC-2010 gas chromatograph equipped with a flame-ionization detector. GC–MS analyses were performed with a Thermo Finnigan Focus gas chromatograph equipped with a DSQ mass detector. TLC analyses were performed with Polygram® SIL G/UV254 plates from Macherey–Nagel. Compounds were detected by using UV light or iodine. Silica gel 60 from Fluka (230–400 mesh, particle size 40–63 μm) was used for flash chromatography (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 NEt_3 (30 mL) were placed in a round-bottomed flask equipped with a magnetic stirring bar. After addition of the aryl halide (10.0 mmol), the mixture was stirred at 25 °C for 30 min, and cyclopropylacetylene (661 mg, 10.0 mmol) was then added. After this had been stirred at 25 °C for 16 h, saturated NH_4Cl solution was added. The mixture was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by Kugelrohr distillation and subsequent flash chromatography (SiO_2).

Alkyne 8: General procedure A was used to synthesize alkyne **8** from iodobenzene (**1**) and cyclopropylacetylene. After purification by Kugelrohr distillation (130 °C, 0.56 mbar) and subsequent flash chromatography (PE), compound **8** (1.29 g, 9.13 mmol, 91%) was isolated as a light-yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.78–0.82 (m, 2 H, 8-H), 0.83–0.89 (m, 2 H, 8-H), 1.41–1.48 (m, 1 H, 7-H), 7.23–7.28 (m, 3 H, Ar-H), 7.35–7.39 (m, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.1 (CH), 8.6 (CH_2), 75.8 (C), 93.4 (C), 123.9 (C), 127.4 (CH), 128.2 (CH), 131.6 (CH) ppm. IR (neat): $\tilde{\nu}$ = 3083, 3057, 3015, 2235, 1599, 1494, 1030, 955, 834, 813, 755, 692 cm^{-1}. MS (EI): *m*/*z* (%) = 142 (95) $[M]^+$, 141 (100) $[M - H]^+$, 115 (32) $[M - C_2H_2]^+$, 43 (38) $[C_3H_7]^+$. HRMS (EI): calcd. for $C_{11}H_{10}$ 142.0783; found 142.0786.

Alkyne 9: General procedure A was used to synthesize alkyne **9** from 4-iodotoluene (**2**) and cyclopropylacetylene. After purification by Kugelrohr distillation (80 °C, 0.30 mbar) and subsequent flash chromatography (PE), compound **9** (1.50 g, 9.60 mmol, 96%) was isolated as a light-yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.79–0.84 (m, 2 H, 8-H), 0.84–0.90 (m, 2 H, 8-H), 1.43–1.49 (m, 1 H, 7-H), 2.34 (s, 3 H, 9-H), 7.09 (d, $^3J_{H,H}$ = 8.1 Hz, Ar-H), 7.29 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.1 (CH), 8.5 (CH_2), 21.3 (CH_3), 75.8 (C), 92.5 (C), 120.8 (C), 128.9 (CH), 131.4 (CH), 137.3 (C) ppm. IR (neat): $\tilde{\nu}$ = 3081, 3011, 2921, 2864, 2234, 1510, 1052, 1028, 954, 839, 814 cm^{-1}. MS (CI): *m*/*z* (%) = 157 (100) $[M + H]^+$, 156 (97) $[M]^+$, 141 (22) $[M - CH_3]^+$, 105 (12) $[M - C_4H_3]^+$. HRMS (CI): calcd. for $C_{12}H_{12}$ + H 157.1017; found 157.1019.

Alkyne 10: General procedure A was used to synthesize alkyne **10** from 2-iodotoluene (**3**) and cyclopropylacetylene. After purification by Kugelrohr distillation (90 °C, 0.56 mbar) and subsequent flash chromatography (PE), compound **10** (1.10 g, 7.04 mmol, 70%) was isolated as a light-yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.77–0.84 (m, 2 H, 10-H), 0.86–0.92 (m, 2 H, 10-H), 1.46–1.53 (m, 1 H, 9-H), 2.39 (s, 3 H, 11-H), 7.06–7.12 (m, 1 H, Ar-H), 7.13–7.18 (m, 2 H, Ar-H), 7.35 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.3 (CH), 8.8 (CH_2), 20.6 (CH_3), 74.5 (C), 97.5 (C), 123.7 (C), 125.4 (CH), 127.4 (CH), 129.2 (CH), 131.8 (CH), 140.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 3095, 3015, 2922, 2231, 1602, 1488, 1457, 1030, 956, 755, 718 cm^{-1}. MS (EI): *m*/*z* (%) = 156 (100) $[M]^+$, 141 (57) $[M - CH_3]^+$, 128 (45) $[M - C_2H_4]^+$, 115 (62) $[M - C_3H_5]^+$. HRMS (EI): calcd. for $C_{12}H_{12}$ 156.0939; found 156.0936.

Alkyne 11: General procedure A was used to synthesize alkyne **11** from 2-iodopyridine (**4**) and cyclopropylacetylene. After purification by Kugelrohr distillation (125 °C, 0.56 mbar) and subsequent flash chromatography (PE/EtOAc, 5:1), compound **11** (1.29 g, 9.13 mmol, 91%) was isolated as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.82–0.87 (m, 4 H, 10-H), 1.39–1.47 (m, 1 H, 9-H), 7.10 (ddd, $^3J_{H,H}$ = 7.7, 5.0, $^4J_{H,H}$ = 0.8 Hz, 1 H, Ar-H), 7.30 (br. d, $^3J_{H,H}$ = 7.9 Hz, 1 H, Ar-H), 7.58 (td, $^3J_{H,H}$ = 7.6, $^4J_{H,H}$ = 1.7 Hz, 1 H, Ar-H), 8.46 (br. d, $^3J_{H,H}$ = 4.4 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.0 (CH), 8.7 (CH_2), 75.5 (C), 94.1 (C), 122.0 (CH), 126.6 (CH), 135.9 (CH), 143.8 (C), 149.7 (CH) ppm. IR (neat): $\tilde{\nu}$ = 3047, 3007, 2237, 2221, 1580, 1466, 1429, 1061, 961, 782, 747 cm^{-1}. MS (EI): *m*/*z* (%) = 143 (100) $[M]^+$, 142 (70) $[M - H]^+$, 117 (98) $[M - C_2H_2]^+$, 115 (35) $[M - C_2H_4]^+$. HRMS (EI): calcd. for $C_{10}H_9N$ 143.0735; found 143.0734.

Alkyne 12: General procedure A was used to synthesize alkyne **12** from 2-iodothiophene (**5**) and cyclopropylacetylene. After purification by Kugelrohr distillation (70 °C, 0.50 mbar) and subsequent flash chromatography (PE), compound **12** (1.26 g, 8.50 mmol, 85%) was isolated as light-brown liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.79–0.84 (m, 2 H, 9-H), 0.84–0.91 (m, 2 H, 9-H), 1.43–1.50 (m, 1 H, 8-H), 6.91 (dd, $^3J_{H,H}$ = 5.1, 3.7 Hz, 1 H, Ar-H), 7.10 (d, $^3J_{H,H}$ = 3.5 Hz, 1 H, Ar-H), 7.15 (d, $^3J_{H,H}$ = 5.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.3 (CH), 8.7 (CH_2), 68.8 (C), 97.4 (C), 124.2 (C), 125.9 (CH), 126.7 (CH), 131.2 (CH) ppm. IR (neat): $\tilde{\nu}$ = 3093, 3012, 2222, 1519, 1428, 1243, 1204, 1173, 1028, 931, 850, 828, 810, 693 cm^{-1}. MS (EI): *m*/*z* (%) = 148 (100) $[M]^+$, 147 (95) $[M - H]^+$, 115 (30) $[M - HS]^+$, 43 (22) $[C_3H_7]^+$. HRMS (EI): calcd. for C_9H_8S 148.0348; found 148.0347.

Alkyne 13: $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1.0 mmol, 10.0 mol-%), $[(PhCN)_2PdCl_2]$ (193 mg, 0.5 mmol, 5.0 mol-%), PPh_3 (262 mg, 1.0 mmol, 10.0 mol-%), and diisopropylamine (30 mL) were placed in a round-bottomed flask equipped with a magnetic stirring bar. After the addition of 2-bromo-1,3-thiazole (**6**; 1.64 g, 10.0 mmol), the mixture was stirred at 25 °C for 30 min, and cyclopropylacetylene (661 mg, 10.0 mmol) was then added. After this mixture had been stirred at 25 °C for 16 h, a saturated NH_4Cl solution was added. The mixture was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. After purification by Kugelrohr distillation (140 °C, 1.3 mbar) and subsequent flash chromatography (PE/EtOAc, 5:1), compound **13** (1.01 g, 6.80 mmol, 68%) was isolated as a yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.85–1.03 (m, 4 H, 9-H), 1.41–1.56 (m, 1 H, 8-H), 7.25 (d, $^3J_{H,H}$ = 3.3 Hz, 1 H, Ar-H), 7.74 (d, $^3J_{H,H}$ = 3.2 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.2 (CH), 8.9 (CH_2), 69.2

(C), 99.4 (C), 119.7 (CH), 143.0 (CH), 149.5 (C) ppm. IR (neat): $\tilde{\nu}$ = 3114, 3082, 3011, 2221, 1480, 1225, 1138, 1084, 1053, 936, 873, 814, 721, 619 cm^{-1}. MS (EI): *m*/*z* (%) = 149 (56) $[M]^+$, 58 (58) $[C_2H_2S]^+$, 43 (100) $[C_3H_7]^+$. HRMS (EI): calcd. for C_8H_7NS 149.0299; found 149.0298.

Alkyne 14: General procedure A was used to synthesize alkyne **14** from 2-iodofuran (**7**) and cyclopropylacetylene. After purification by flash chromatography (PE/EtOAc, 40:1), compound **14** (772 mg, 5.84 mmol, 58%) was isolated as a light-yellow liquid. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.82–0.85 (m, 2 H, 9-H), 0.86–0.92 (m, 2 H, 9-H), 1.43–1.51 (m, 1 H, 8-H), 6.33 (dd, $^3J_{H,H}$ = 3.2, 2.0 Hz, 1 H, Ar-H), 6.46 (d, $^3J_{H,H}$ = 3.4 Hz, 1 H, Ar-H), 7.31 (d, $^3J_{H,H}$ = 1.6 Hz, Ar-H) ppm. ^{13}C NMR (126 MHz, DEPT, $CDCl_3$): δ = 0.0 (CH), 8.7 (CH_2), 65.9 (C), 97.8 (C), 110.6 (CH), 114.0 (CH), 137.6 (C), 142.7 (CH) ppm. IR (neat): $\tilde{\nu}$ = 3120, 3097, 3015, 2235, 1576, 1491, 1213, 1183, 1156, 1016, 965, 908, 812, 738 cm^{-1}. MS (EI): *m*/*z* (%) = 132 (100) $[M]^+$, 131 (23) $[M - H]^+$, 103 (66) $[M - C_2H_4]^+$, 78 (41) $[M - C_4H_6]^+$, 77 (38) $[M - C_3H_3O]^+$, 76 (22) $[M - C_3H_4O]^+$, 50 (21) $[C_4H_2]^+$. HRMS (EI): calcd. for C_9H_8O 132.0575; found 132.0577.

Hydroamination/Cyclopropylimine Rearrangement/Reduction Sequence. General Procedure B: A Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with the alkyne (2.40 mmol), the amine (2.64 mmol), $[Ind_2TiMe_2]$ (37 mg, 0.12 mmol, 5.0 mol-%), and toluene (1.0 mL). The resulting mixture was heated at 105 °C for 24 h. After cooling to room temperature, NH_4Cl (26 mg, 0.49 mmol, 20 mol-%) was added, and the mixture was heated at 145 °C for 8 h. Then the mixture was cooled to room temperature, and a mixture of $NaBH_3CN$ (302 mg, 4.80 mmol) and $ZnCl_2$ (326 mg, 2.40 mmol) in MeOH (10 mL) was added. After this mixture had been stirred at 25 °C for 20 h, CH_2Cl_2 (50 mL) and a saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered, and the solid residue was washed with CH_2Cl_2 (50 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (6 × 50 mL). The combined organic layers were dried with Mg_2SO_4. After concentration under vacuum the residue was purified by flash chromatography (SiO_2).

2-Benzyl-1-(*p*-tolyl)pyrrolidine (15): General procedure B was used to synthesize pyrrolidine **15** from alkyne **8** and *p*-toluidine. After purification by flash chromatography (PE/EtOAc, 40:1), compound **15** (543 mg, 2.16 mmol, 90%) was isolated as a yellow liquid. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.80 (br. s, 4 H, 3-H, 4-H), 2.29 (s, 3 H, 15-H), 2.54 (dd, $^2J_{H,H}$ = 13.0, $^3J_{H,H}$ = 9.6 Hz, 1 H, 6-H), 3.04 (d, $^2J_{H,H}$ = 13.6 Hz, 1 H, 6-H), 3.10 (dt, $J_{H,H}$ = 7.8, 7.5 Hz, 1 H, CHN), 3.35 (br. s, 1 H, CHN), 3.92 (br. s, 1 H, CHN), 6.63 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, *p*Tol-H), 7.10 (d, $^3J_{H,H}$ = 7.6 Hz, 2 H, *p*Tol-H), 7.15–7.22 (m, 3 H, Ar-H), 7.27 (m, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2 (CH_3), 22.9 (CH_2), 29.4 (CH_2), 38.5 (CH_2), 48.4 (CH_2), 59.7 (CH), 111.8 (CH), 124.2 (C), 125.9 (CH), 128.2 (CH), 129.2 (CH), 129.7 (CH), 139.4 (C), 144.8 (C) ppm. IR (neat): $\tilde{\nu}$ = 3062, 3025, 2965, 2922, 2859, 1619, 1518, 1452, 1361, 1165, 978, 798, 738, 698 cm^{-1}.

2-Benzyl-1-cyclopentylpyrrolidine (16): General procedure B was used to synthesize pyrrolidine **16** from alkyne **8** and cyclopentylamine. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc), compound **16** (473 mg, 2.06 mmol, 86%) was isolated as a brown liquid. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.48–1.86 (m, 11 H), 1.91–2.00 (m, 1 H), 2.44 (dd, $^2J_{H,H}$ = 13.0, $^3J_{H,H}$ = 10.6 Hz, 1 H, 6-H), 2.55 (dt, $J_{H,H}$ = 7.1, 8.9 Hz, 1 H, CHN), 2.93–3.01 (m, 1 H, CHN), 3.02–3.12 (m, 3 H, CHN, 6-H), 7.15–7.21 (m, 3 H, Ar-H), 7.24–7.30 (m, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.7 (CH_2), 23.7 (CH_2), 24.0 (CH_2), 29.0 (CH_2), 29.8 (CH_2), 32.1 (CH_2), 40.8 (CH_2), 51.3 (CH_2), 64.1 (CH), 64.4 (CH), 125.8 (CH), 128.2 (CH), 129.1 (CH), 140.4 (C) ppm. IR (neat): $\tilde{\nu}$ = 3027, 2954, 2869, 2789, 1605, 1496, 1454, 1344, 1215, 1134, 742, 700 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 230 (100) $[M + H]^+$, 138 (45) $[M - C_7H_7]^+$. HRMS (CI): calcd. for $C_{16}H_{23}N$ + H 230.1909; found 230.1911.

2-Benzyl-1-*tert*-butylpyrrolidine (17): General procedure B was used to synthesize pyrrolidine **17** from alkyne **8** and *tert*-butylamine. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc + 3% 7 M NH_3 in MeOH), compound **17** (366 mg, 1.68 mmol, 70%) was isolated as an orange liquid. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.17 (s, 9 H, *t*Bu), 1.37–1.46 (m, 1 H), 1.63 (dd, $J_{H,H}$ = 12.3, 6.0 Hz, 1 H), 1.68–1.77 (m, 1 H), 1.78–1.91 (m, 1 H), 2.52 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 11.0 Hz, 1 H, 6-H), 2.65 (ddd, $J_{H,H}$ = 11.2, 9.0, 5.8 Hz, 1 H, CHN), 2.86 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 2.8 Hz, 1 H, 6-H), 3.03 (t, *J* = 7.8 Hz, 1 H, CHN), 3.20 (td, *J* = 9.7, 2.8 Hz, 1 H, CHN), 7.15–7.21 (m, 3 H, Ar-H), 7.24–7.30 (m, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.3 (CH_2), 26.8 (CH_3), 29.8 (CH_2), 45.7 (CH_2), 48.6 (CH_2), 54.4 (C), 59.6 (CH), 125.9 (CH), 128.3 (CH), 129.2 (CH), 140.8 (C) ppm. IR (neat): $\tilde{\nu}$ = 3025, 2995, 2906, 2868, 2820, 1603, 1452, 1494, 1364, 1228, 1124, 1016, 739, 698 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 218 (100) $[M + H]^+$, 126 (35) $[M - C_7H_8]^+$. HRMS (CI): calcd. for $C_{15}H_{23}N$ + H 218.1909; found 218.1908.

1,2-Dibenzylpyrrolidine (18): General procedure B was used to synthesize pyrrolidine **18** from alkyne **8** and benzylamine. However, in contrast to general procedure B, the amine was added slowly to the reaction mixture over a period of 4 h. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc), compound **18** (379 mg, 1.51 mmol, 63%) was isolated as an orange liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.54–1.65 (m, 2 H), 1.65–1.79 (m, 2 H), 2.18 (td, $J_{H,H}$ = 9.1, 7.9 Hz, 1 H), 2.54 (dd, $^2J_{H,H}$ = 13.1, $^3J_{H,H}$ = 9.4 Hz, 1 H, 6-H), 2.63–2.71 (m, 1 H), 2.95 (td, $J_{H,H}$ = 5.9, 2.7 Hz, 1 H), 3.07 (dd, $^2J_{H,H}$ = 13.1, $^3J_{H,H}$ = 4.0 Hz, 1 H, 6-H), 3.30 (d, $^2J_{H,H}$ = 12.9 Hz, 1 H, NCH_2Ph), 4.11 (d, $^2J_{H,H}$ = 12.9 Hz, 1 H, NCH_2Ph), 7.15–7.39 (m, 10 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.9 (CH_2), 30.4 (CH_2), 40.9 (CH_2), 54.2 (CH_2), 58.8 (CH_2), 65.8 (CH), 125.9 (CH), 126.8 (CH), 128.2 (CH), 128.2 (CH), 129.0 (CH), 129.2 (CH), 139.4 (C), 140.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 3028, 2923, 2790, 1604, 1496, 1455, 1359, 1123, 1075, 1030, 917, 736, 698 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 252 (100) $[M + H]^+$, 160 (10) $[M - C_7H_7]^+$. HRMS (CI): calcd. for $C_{18}H_{21}N$ + H 252.1752; found 252.1755.

2-(4-Methylbenzyl)-1-(*p*-tolyl)pyrrolidine (19): General procedure B was used to synthesize pyrrolidine **19** from alkyne **9** and *p*-toluidine. After purification by flash chromatography (PE/EtOAc, 100:1), compound **19** (605 mg, 2.28 mmol, 95%) was isolated as an orange oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.79–1.96 (m, 4 H), 2.29 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3), 2.52 (dd, $^2J_{H,H}$ = 13.7, $^3J_{H,H}$ = 9.6 Hz, 1 H, 6-H), 3.03 (dd, $^2J_{H,H}$ = 13.7, $^3J_{H,H}$ = 3.0 Hz, 1 H, 6-H), 3.12–3.20 (m, 1 H, CHN), 3.36–3.46 (m, 1 H, CHN), 3.88–3.96 (m, 1 H, CHN), 6.64 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, Ar-H), 7.10 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, Ar-H), 7.12–7.35 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2 (CH_3), 21.0 (CH_3), 23.1 (CH_2), 29.5 (CH_2), 38.3 (CH_2), 48.6 (CH_2), 60.0 (CH), 111.9 (CH), 124.5 (C), 129.1 (CH), 129.2 (CH), 129.8 (CH), 135.6 (C), 136.6 (C), 145.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 3013, 2966, 2920, 2860, 1619, 1518, 1362, 1344, 1329, 1165, 797, 731 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 266 (68) $[M + H]^+$, 265 (55) $[M]^+$, 161 (11) $[M - C_8H_8]^+$, 160 (100) $[M - C_8H_9]^+$. HRMS (CI): calcd. for $C_{19}H_{23}N$ + H 266.1909; found 266.1912.

1-Cyclopentyl-2-(4-methylbenzyl)pyrrolidine (20): General procedure B was used to synthesize pyrrolidine **20** from alkyne **9** and cyclopentylamine. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc + 3% 7 M NH_3 in MeOH), compound **20** (492 mg, 2.02 mmol, 84%) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48–1.86 (m, 11 H), 1.89–1.99 (m, 1 H), 2.32 (s, 3 H, CH_3), 2.37 (dd, $^2J_{H,H}$ = 13.1, $^3J_{H,H}$ = 10.6 Hz, 1 H, 6-H), 2.50–2.58 (m, 1 H, CHN), 2.87–2.95 (m, 1 H, CHN), 2.97–3.10 (m, 3 H, CHN, 6-H), 7.05–7.10 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.0 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.1 (CH_2), 29.1 (CH_2), 29.9 (CH_2), 32.3 (CH_2), 40.6 (CH_2), 51.4 (CH_2), 64.1 (CH), 64.5 (CH), 128.9 (CH), 129.0 (CH), 135.3 (C), 137.5 (C) ppm. IR (neat): $\tilde{\nu}$ = 2951, 2866, 2787, 2731, 1892, 1514, 1447, 1342, 1212, 1131, 910, 793 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 244 (38) $[M + H]^+$, 138 (100) $[M - C_8H_{10}]^+$. HRMS (CI): calcd. for $C_{17}H_{25}N$ + H 244.2065; found 244.2068.

1-*tert*-Butyl-2-(4-methylbenzyl)pyrrolidine (21): General procedure B was used to synthesize pyrrolidine **21** from alkyne **9** and *tert*-butylamine. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc + 3% 7 M NH_3 in MeOH), compound **21** (428 mg, 1.85 mmol, 77%) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 9 H, *t*Bu), 1.34–1.46 (m, 1 H), 1.61 (dd, $J_{H,H}$ = 12.3, 6.0 Hz, 1 H), 1.66–1.76 (m, 1 H), 1.76–1.90 (m, 1 H), 2.32 (s, 3 H, CH_3), 2.46 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 10.9 Hz, 1 H, 6-H), 2.65 (ddd, $J_{H,H}$ = 11.2, 9.0, 5.9 Hz, 1 H, CHN), 2.79 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 3.0 Hz, 1 H, 6-H), 2.99 (t, $J_{H,H}$ = 7.8 Hz, 1 H, CHN), 3.15 (td, $J_{H,H}$ = 9.6, 2.5 Hz, 1 H, CHN), 7.05–7.11 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz): δ = 21.0 (CH_3), 24.3 (CH_2), 26.9 (CH_3), 29.8 (CH_2), 45.5 (CH_2), 48.6 (CH_2), 54.1 (C), 59.5 (CH), 128.9 (CH), 129.1 (CH), 135.3 (C), 137.9 (C) ppm. IR (neat): $\tilde{\nu}$ = 2965, 2906, 2868, 2820, 1515, 1364, 1255, 1229, 1123, 1017, 794 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 232 (45) $[M + H]^+$, 126 (100) $[M - C_8H_9]^+$, 89 (18) $[C_7H_5]^+$, 70 (19) $[C_5H_{10}]^+$. HRMS (CI): calcd. for $C_{16}H_{25}N$ + H 232.2065; found 232.2061.

1-Benzyl-2-(4-methylbenzyl)pyrrolidine (22): General procedure B was used to synthesize pyrrolidine **22** from alkyne **9** and benzylamine. However, in contrast to general procedure B, the amine was added slowly to the reaction mixture over a period of 4 h. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc), compound **22** (478 mg, 1.80 mmol, 75%) was isolated as a dark-orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.51–1.79 (m, 4 H), 2.18 (q, $J_{H,H}$ = 8.8 Hz, 1 H, CHN), 2.31 (s, 3 H, CH_3), 2.52 (dd, $^2J_{H,H}$ = 13.1, $^3J_{H,H}$ = 9.3 Hz, 1 H, 6-H), 2.59–2.68 (m, 1 H, CHN), 2.95 (br. t, $J_{H,H}$ = 7.3 Hz, 1 H, CHN), 3.04 (dd, $^2J_{H,H}$ = 13.1, $^3J_{H,H}$ = 3.9 Hz, 1 H, 6-H), 3.29 (d, ^2J = 12.8 Hz, 1 H, NCH_2Ph), 4.12 (d, ^2J = 12.9 Hz, 1 H, NCH_2Ph), 7.06–7.12 (m, 4 H, Ar-H), 7.22–7.27 (m, 1 H, Ar-H), 7.29–7.38 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.0 (CH_3), 21.9 (CH_2), 30.4 (CH_2), 40.4 (CH_2), 54.3 (CH_2), 58.9 (CH_2), 65.8 (CH), 126.9 (CH), 128.2 (CH), 128.9 (CH), 129.0 (CH), 129.1 (CH), 135.3 (C), 136.9 (C) ppm. IR (neat): $\tilde{\nu}$ = 3025, 2920, 2871, 2787, 1514, 1494, 1453, 1357, 1121, 1028, 799, 734, 697 cm^{-1}. GC–MS (CI, 25 °C): *m*/*z* (%) = 265 (2) $[M]^+$, 175 (12) $[M - C_7H_6]^+$, 133 (61) $[M - C_{10}H_{12}]^+$, 132 (100) $[C_{10}H_{12}]^+$, 105 (19) $[C_8H_9]^+$. HRMS (EI): calcd. for $C_{19}H_{23}N$ 265.1831; found 265.1835.

2-(2-Methylbenzyl)-1-(*p*-tolyl)pyrrolidine (23): General procedure B was used to synthesize pyrrolidine **23** from alkyne **10** and *p*-toluidine. After purification by flash chromatography (PE/EtOAc, 100:1), compound **23** (591 mg, 2.23 mmol, 93%) was isolated as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.76–1.87 (m, 2 H), 1.91–2.03 (m, 2 H), 2.26 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.56 (dd, $^2J_{H,H}$ = 14.2, $^3J_{H,H}$ = 9.9 Hz, 1 H, 6-H), 3.08 (dd, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 3.7 Hz, 1 H, 6-H), 3.17 (td, $J_{H,H}$ = 8.8, 7.7 Hz, 1 H, CHN), 3.45 (td, $J_{H,H}$ = 8.3, 2.8 Hz, 1 H, CHN), 4.02–4.09 (m, 1 H, CHN), 6.61 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, *p*Tol-H), 7.06 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, *p*Tol-H), 7.10–7.23 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.1 (CH_3), 20.2 (CH_3), 23.3 (CH_2), 29.5 (CH_2), 35.3 (CH_2), 48.5 (CH_2), 58.8 (CH), 111.8 (CH), 124.5 (C), 125.9 (CH), 126.1 (CH), 129.8 (CH), 130.3 (CH), 136.5 (C), 138.0 (C), 145.1 (C) ppm. IR (neat): $\tilde{\nu}$ = 3013, 2965, 1619, 1518, 1459, 1360, 1344, 1152, 975, 909, 798, 739 cm^{-1}. MS (EI, 25 °C): *m*/*z* (%) = 265 (5) $[M]^+$, 161 (18) $[M - C_8H_8]^+$, 160 (100) $[M - C_8H_9]^+$, 91 (10) $[C_7H_7]^+$. HRMS (EI): calcd. for $C_{19}H_{23}N$ 265.1830; found 265.1829.

1-Cyclopentyl-2-(2-methylbenzyl)pyrrolidine (24): General procedure B was used to synthesize pyrrolidine **24** from alkyne **10** and cyclopentylamine. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc + 3% 7 M NH_3 in MeOH), compound **24** (472 mg, 1.94 mmol, 81%) was isolated as a dark-orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.50–1.62 (m, 5 H), 1.63–1.75 (m, 4 H), 1.76–1.86 (m, 2 H), 1.91–1.99 (m, 1 H), 2.33 (s, 3 H, CH_3), 2.48 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 10.8 Hz, 1 H, 6-H), 2.58 (q, $J_{H,H}$ = 8.4 Hz, 1 H, CHN), 2.95–3.08 (m, 3 H, CHN, 6-H), 3.13 (quint, $^3J_{H,H}$ = 8.0 Hz, 1 H, CHN), 7.02–7.21 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.8 (CH_3), 22.8 (CH_2), 24.0 (CH_2), 24.2 (CH_2), 28.6 (CH_2), 29.9 (CH_2), 32.1 (CH_2), 37.8 (CH_2), 50.8 (CH_2), 62.6 (CH), 63.6 (CH), 125.7 (CH), 125.9 (CH), 129.8 (CH), 130.1 (CH), 136.2 (C), 138.6 (C) ppm. IR (neat): $\tilde{\nu}$ = 3018, 2953, 2869, 2795, 1689, 1605, 1493, 1453, 1344, 1214, 1119, 911, 742 cm^{-1}. GC–MS (CI, 25 °C): *m*/*z* (%) = 244 (37) $[M + H]^+$, 242 (9) $[M - H]^+$, 139 (8) $[M - C_8H_{10}]^+$, 138 (100) $[M - C_8H_9]^+$, 70 (7) $[C_5H_{10}]^+$. HRMS (EI): calcd. for $C_{17}H_{25}N$ 243.1987; found 243.1985.

1-*tert*-Butyl-2-(2-methylbenzyl)pyrrolidine (25): General procedure B was used to synthesize pyrrolidine **25** from alkyne **10** and *tert*-butylamine. However, in contrast to general procedure B, 100 mol-% of NH_4Cl (128 mg, 2.40 mmol) was used. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc + 3% 7 M NH_3 in MeOH), compound **25** (122 mg, 0.53 mmol, 22%) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 9 H, *t*Bu), 1.36–1.46 (m, 1 H), 1.57 (dd, $J_{H,H}$ = 12.4, 6.3 Hz, 1 H), 1.70–1.80 (m, 1 H), 1.82–1.94 (m, 1 H), 2.33 (s, 3 H, CH_3), 2.64 (dd, $^3J_{H,H}$ = 13.9, 10.7 Hz, 1 H, 6-H), 2.69 (ddd, $J_{H,H}$ = 11.2, 9.1, 6.0 Hz, 1 H, CHN), 2.76 (dd, $^2J_{H,H}$ = 14.1, $^3J_{H,H}$ = 3.9 Hz, 1 H, 6-H), 3.04 (t, J = 7.9 Hz, 1 H, CHN), 3.31 (m, 1 H, CHN), 7.06–7.27 (m, 4 H, Ar-H) ppm. ^{13}C NMR (126 MHz): δ = 20.2 (CH_3), 24.5 (CH_2), 26.9 (CH_3), 29.7 (CH_2), 42.0 (CH_2), 48.6 (CH_2), 54.1 (C), 58.0 (CH), 125.7 (CH), 125.8 (CH), 129.7 (CH), 130.2 (CH), 136.4 (C), 139.2 (C) ppm. IR (neat): $\tilde{\nu}$ = 3014, 2965, 2907, 2868, 2822, 1491, 1458, 1363, 1228, 1120, 1015, 739 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 232 (40) $[M + H]^+$, 126 (100) $[M - C_8H_9]^+$, 70 (14) $[C_5H_{10}]^+$. HRMS (CI): calcd. for $C_{16}H_{25}N$ + H 232.2065; found 232.2067.

1-Benzyl-2-(2-methylbenzyl)pyrrolidine (26): General procedure B was used to synthesize pyrrolidine **26** from alkyne **10** and benzylamine. However, in contrast to general procedure B, the amine was added slowly to the reaction mixture over a period of 4 h. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc), compound **26** (306 mg, 1.15 mmol, 48%) was isolated as a dark-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.58–1.70 (m, 2 H), 1.72–1.84 (m, 2 H), 2.20–2.29 (m, 1 H), 2.32 (s, 3 H, CH_3), 2.55–2.67 (m, 1 H), 2.69–2.81 (m, 1 H), 2.98–3.08 (m, 1 H), 3.14 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 4.0 Hz, 1 H, 6-H), 3.35 (d, $^2J_{H,H}$ = 12.4 Hz, 1 H, NCH_2Ph), 4.14 (d, $^2J_{H,H}$ = 12.8 Hz, 1 H, NCH_2Ph), 7.09–

7.15 (m, 3 H, Ar-H), 7.15–7.19 (m, 1 H, Ar-H), 7.27 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, Ar-H), 7.32 (t, $^3J_{H,H}$ = 7.4 Hz, 2 H, Ar-H), 7.38 (d, $^2J_{H,H}$ = 7.4 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.7 (CH_3), 21.9 (CH_2), 30.5 (CH_2), 37.9 (CH_2), 54.2 (CH_2), 58.9 (CH_2), 64.6 (CH), 125.8 (CH), 126.1 (CH), 127.0 (CH), 128.3 (CH), 129.1 (CH), 129.9 (CH), 130.2 (CH), 136.1 (C), 138.1 (C) ppm. IR (neat): $\tilde{\nu}$ = 3061, 3025, 2925, 2870, 2788, 1660, 1493, 1453, 1357, 1124, 1029, 740, 698 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 266 (28) [M + H]$^+$, 161 (11) [M – C_8H_8]$^+$, 160 (100) [M – C_8H_9]$^+$, 91 (32) [C_7H_7]$^+$, 89 (23) [C_7H_5]$^+$. HRMS (CI): calcd. for $C_{19}H_{23}N$ + H 266.1909; found 266.1907.

2-[1-(*p*-Tolyl)pyrrolidin-2-ylmethyl]pyridine (27): General procedure B was used to synthesize pyrrolidine **27** from alkyne **11** and *p*-toluidine. To separate unconsumed *p*-toluidine from **27**, the crude product was cooled to 0 °C, and pyridine (15 mL) and *p*-toluenesulfonyl chloride (915 mg, 4.80 mmol) were added. The resulting mixture was stirred while warming to room temperature for 12 h. Then the solution was acidified with 2 N aqueous HCl and washed with EtOAc (3 × 50 mL) to remove *N*-(*p*-tolyl)-*p*-toluenesulfonamide. The aqueous layer was neutralized with 2 N NaOH and then extracted with EtOAc (3 × 50 mL). The combined organic layers were subsequently dried with $MgSO_4$. After concentration under vacuum, the product was isolated by flash chromatography (PE/EtOAc, 5:1). Compound **27** (91 mg, 0.36 mmol, 15%) was isolated as a red oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.82–2.00 (m, 4 H), 2.27 (s, 3 H, CH_3), 2.74 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 9.5 Hz, 1 H, 6-H), 3.17 (td, $J_{H,H}$ = 8.1, 7.8 Hz, 1 H, CHN), 3.25 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 3.3 Hz, 1 H, 6-H), 3.40–3.47 (m, 1 H, CHN), 4.15 (m, 1 H, CHN), 6.60 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, *p*Tol-H), 7.08 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, *p*Tol-H), 7.12–7.19 (m, 2 H, Ar-H), 7.60 (td, $^3J_{H,H}$ = 7.6, $^4J_{H,H}$ = 1.3 Hz, 1 H, Ar-H), 8.59 (d, $^3J_{H,H}$ = 4.7 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2 (CH_3), 23.1 (CH_2), 29.6 (CH_2), 40.9 (CH_2), 48.6 (CH_2), 59.0 (CH), 112.0 (CH), 121.3 (CH), 124.0 (CH), 124.7 (C), 129.8 (CH), 136.3 (CH), 144.8 (C), 149.1 (CH), 159.7 (C) ppm. IR (neat): $\tilde{\nu}$ = 3010, 2964, 2924, 2862, 1620, 1589, 1521, 1474, 1435, 1364, 1166, 801, 754 cm^{-1}. GC–MS (EI, 25 °C): *m*/*z* (%) = 252 (1) [M]$^+$, 161 (11) [M – C_7H_7]$^+$, 160 (100) [M – C_6H_6N]$^+$, 118 (6) [M – $C_9H_{10}N$]$^+$, 91 (10) [C_7H_7]$^+$, 43 (8) [C_2H_5N]$^+$. HRMS (EI): calcd. for $C_{17}H_{20}N_2$ 252.1626; found 252.1625.

2-[1-(*p*-Methoxyphenyl)pyrrolidin-2-ylmethyl]pyridine (31): General procedure B was used to synthesize pyrrolidine **31** from alkyne **11** and 4-methoxyaniline. After purification by flash chromatography (PE/EtOAc, 5:1), compound **31** (119 mg, 0.43 mmol, 18%) was isolated as a dark-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.88–2.02 (m, 4 H), 2.81 (m, 1 H), 3.16 (q, $J_{H,H}$ = 8.2 Hz, 1 H), 3.25 (dd, $^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 3.5 Hz, 1 H, 6-H), 3.46–3.53 (m, 1 H), 3.77 (s, 3 H, OCH_3), 4.10–4.18 (m, 1 H), 6.79 (d, $^3J_{H,H}$ = 8.3 Hz, 2 H, Ar-H), 6.88 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, Ar-H), 7.12–7.20 (m, 2 H), 7.60 (td, $^3J_{H,H}$ = 7.4, $^4J_{H,H}$ = 0.8 Hz, 1 H, Ar-H), 8.57 (d, $^3J_{H,H}$ = 4.6 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.1 (CH_2), 29.7 (CH_2), 40.6 (CH_2), 50.0 (CH_2), 55.9 (CH_3), 60.4 (CH), 113.9 (CH), 115.2 (CH), 121.4 (CH), 124.2 (CH), 126.8 (C), 136.6 (CH), 140.8 (C), 148.9 (CH), 159.3 (C) ppm. IR (neat): $\tilde{\nu}$ = 3043, 2958, 2830, 1588, 1510, 1471, 1434, 1364, 1238, 1179, 1038, 812, 755 cm^{-1}. GC–MS (EI, 25 °C): *m*/*z* (%) = 268 (8) [M]$^+$, 177 (16) [M – C_6H_5N]$^+$, 176 (100) [M – C_6H_6N]$^+$, 43 (18) [C_2H_5N]$^+$. HRMS (EI): calcd. for $C_{17}H_{20}N_2O$ 268.1576; found 268.1572.

2-(Thiophen-2-ylmethyl)-1-(*p*-tolyl)pyrrolidine (32): General Procedure B was used to synthesize pyrrolidine **32** from alkyne **12** and *p*-toluidine. After purification by flash chromatography (PE/EtOAc, 20:1), compound **32** (445 mg, 1.73 mmol, 72%) was isolated as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.88–1.99 (m, 4 H), 2.26 (s, 3 H, CH_3), 2.82 (dd, $^2J_{H,H}$ = 14.8, $^3J_{H,H}$ = 9.3 Hz, 1 H, 6-H), 3.12–3.18 (m, 1 H, CHN), 3.20 (dd, $^2J_{H,H}$ = 14.8, $^3J_{H,H}$ = 2.6 Hz, 6-H), 3.42–3.50 (m, 1 H, CHN), 3.91–3.98 (m, 1 H, CHN), 6.60 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, *p*Tol-H), 6.81–6.87 (m, 1 H, Ar-H), 6.98 (dd, $^3J_{H,H}$ = 5.1, 3.4 Hz, 1 H, Ar-H), 7.08 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, *p*Tol-H), 7.18 (dd, $^3J_{H,H}$ = 4.9, 1.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2 (CH_3), 23.1 (CH_2), 30.1 (CH_2), 33.3 (CH_2), 48.8 (CH_2), 60.0 (CH), 111.9 (CH), 123.8 (CH), 124.8 (C), 125.4 (CH), 126.8 (CH), 129.9 (CH), 141.6 (C), 144.9 (C) ppm. IR (neat): $\tilde{\nu}$ = 3009, 2965, 2917, 2871, 1619, 1518, 1361, 1342, 1326, 1173, 1159, 798, 691 cm^{-1}. MS (EI, 25 °C): *m*/*z* (%) = 257 (5) [M]$^+$, 160 (100) [$C_{12}H_{16}$]$^+$. HRMS: calcd. for $C_{16}H_{19}NS$ 257.1238; found 257.1237.

2-(Thiophen-2-ylmethyl)-1-cyclopentylpyrrolidine (33): General Procedure B was used to synthesize pyrrolidine **33** from alkyne **12** and cyclopentylamine. After purification by flash chromatography (EtOAc), compound **33** (493 mg, 2.09 mmol, 87%) was isolated as a brown liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.42–1.84 (m, 11 H), 1.86–1.98 (m, 1 H), 2.51 (td, $J_{H,H}$ = 9.0, 7.0 Hz, 1 H, CHN), 2.72 (dd, $^2J_{H,H}$ = 14.4, $^3J_{H,H}$ = 10.0 Hz, 1 H, 6-H), 2.90–3.07 (m, 3 H, CHN), 3.13 (dd, $^2J_{H,H}$ = 14.4, $^3J_{H,H}$ = 2.9 Hz, 1 H, 6-H), 6.80 (br. d, $^3J_{H,H}$ = 3.5 Hz, 1 H, Ar-H), 6.91 (dd, $^3J_{H,H}$ = 5.1, 3.4 Hz, 1 H, Ar-H), 7.12 (dd, $^3J_{H,H}$ = 5.4, $^4J_{H,H}$ = 0.9 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.1 (CH_2), 23.5 (CH_2), 24.0 (CH_2), 29.4 (CH_2), 30.3 (CH_2), 32.3 (CH_2), 35.8 (CH_2), 51.9 (CH_2), 64.3 (CH), 64.6 (CH), 123.4 (CH), 124.9 (CH), 126.5 (CH), 142.8 (C) ppm. IR (neat): $\tilde{\nu}$ = 2952, 2867, 2789, 1438, 1342, 1212, 1132, 1132, 850, 817, 688 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 236 (100) [M + H]$^+$, 138 [M – $C_7H_{10}S$]$^+$. HRMS (CI): calcd. for $C_{14}H_{21}NS$ + H 236.1473; found 236.1475.

1-*tert*-Butyl-2-(thiophen-2-ylmethyl)pyrrolidine (34): General Procedure B was used to synthesize pyrrolidine **34** from alkyne **12** and *tert*-butylamine. After purification by flash chromatography (PE/EtOAc, 10:1 → 1:1), compound **34** (381 mg, 1.70 mmol, 71%) was isolated as an orange liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 (s, 9 H, *t*Bu), 1.49–1.61 (m, 1 H), 1.66–1.83 (m, 3 H), 2.65 (td, $J_{H,H}$ = 9.4, 6.5 Hz, CHN), 2.81 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 10.9 Hz, 1 H, 6-H), 2.93 (br. d, $^2J_{H,H}$ = 14.4 Hz, 1 H, 6-H), 2.97–3.04 (m, 1 H, CHN), 3.21 (t, $J_{H,H}$ = 8.4 Hz, 1 H, CHN), 6.79 (d, $^3J_{H,H}$ = 3.1 Hz, 1 H, Ar-H), 6.92 (dd, $^3J_{H,H}$ = 5.0, 3.4 Hz, 1 H, Ar-H), 7.13 (dd, $^3J_{H,H}$ = 4.8, $^4J_{H,H}$ = 0.9 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.2 (CH_2), 26.7 (CH_3), 30.5 (CH_2), 39.8 (CH_2), 48.5 (CH_2), 54.0 (C), 59.4 (CH), 123.3 (CH), 124.8 (CH), 126.5 (CH), 143.1 (C) ppm. IR (neat): $\tilde{\nu}$ = 2965, 2869, 1438, 1388, 1364, 1254, 1228, 1180, 1125, 1017, 851, 812, 690 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 224 (100) [M + H]$^+$, 222 (75) [M – H]$^+$, 210 (10) [M – CH]$^+$, 127 (8) [M – C_5H_4S]$^+$, 126 (90) [M – C_5H_5S]$^+$, 89 (30) [C_4H_9S]. HRMS (CI): calcd. for $C_{13}H_{21}NS$ + H 224.1473; found 224.1470.

1-Benzyl-2-(thiophen-2-ylmethyl)pyrrolidine (35): General Procedure B was used to synthesize pyrrolidine **35** from alkyne **12** and benzylamine. However, in contrast to the general procedure B, the amine was added slowly to the reaction mixture over a period of 4 h. After purification by flash chromatography (PE/EtOAc, 10:1 → 1:1), compound **35** (307 mg, 1.37 mmol, 57%) was isolated as a yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.50–1.80 (m, 3 H), 1.82–1.93 (m, 1 H), 2.20 (td, $J_{H,H}$ = 9.1, 7.6 Hz, 1 H, CHN), 2.70–2.81 (m, 1 H, CHN), 2.87 (dd, $^2J_{H,H}$ = 14.4, $^3J_{H,H}$ = 8.4 Hz, 1 H, 6-H), 2.95 (td, $J_{H,H}$ = 8.2, 2.0 Hz, 1 H, CHN), 3.16 (dd, $^2J_{H,H}$ = 14.1, $^3J_{H,H}$ = 3.7 Hz, 1 H, 6-H), 3.33 (d, $^2J_{H,H}$ = 12.7 Hz, 1 H, NCH_2Ph), 4.09 (d, $^2J_{H,H}$ = 12.9 Hz, 1 H, NCH_2Ph), 6.83 (br. d,

$^3J_{H,H}$ = 2.8 Hz, 1 H, Ar-H), 6.92 (dd, $^3J_{H,H}$ = 5.2, 3.2 Hz, 1 H, Ar-H), 7.14 (dd, $^3J_{H,H}$ = 5.5, $^4J_{H,H}$ = 1.0 Hz, 1 H, Ar-H), 7.24 (t, $^3J_{H,H}$ = 7.3 Hz, 1 H, Ar-H), 7.32 (t, $^3J_{H,H}$ = 7.3 Hz, 2 H, Ar-H), 7.37 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.2 (CH_2), 30.3 (CH_2), 34.7 (CH_2), 54.3 (CH_2), 58.9 (CH_2), 65.1 (CH), 123.7 (CH), 125.3 (CH), 126.4 (CH), 126.9 (CH), 128.2 (CH), 129.0 (CH), 139.3 (C), 142.1 (C) ppm. IR (neat): $\tilde{\nu}$ = 3029, 2965, 2914, 2790, 1496, 1455, 1442, 1357, 1120, 1076, 1031, 851, 822, 737, 695 cm^{-1}. GC–MS (CI, 25 °C): *m*/*z* (%) = 258 (43) $[M + H]^+$, 256 (17) $[M - H]^+$, 161 (19) $[M - C_5H_5S]^+$, 160 (100) $[M - C_5H_6S]^+$, 91 (12) $[C_7H_7]^+$. HRMS (EI): calcd. for $C_{16}H_{19}NS$ 257.1238; found 257.1241.

2-[1-(*p*-Tolyl)pyrrolidin-2-ylmethyl]thiazole (36): General procedure B was used to synthesize pyrrolidine **36** from alkyne **13** and *p*-toluidine. After purification by flash chromatography (PE/EtOAc, 40:1 → EtOAc), compound **36** (532 mg, 2.06 mmol, 86%) was isolated as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.87–2.04 (m, 4 H), 2.29 (s, 3 H, CH_3), 3.06 (dd, $^2J_{H,H}$ = 14.7, $^3J_{H,H}$ = 9.1 Hz, 1 H, 6-H), 3.14–3.22 (m, 1 H, CHN), 3.41 (dd, $^2J_{H,H}$ = 14.7, $^3J_{H,H}$ = 3.0 Hz, 1 H, 6-H), 3.44–3.52 (m, 1 H, CHN), 4.06–4.19 (m, 1 H, CHN), 6.64 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, *p*Tol-H), 7.10 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, *p*Tol-H), 7.24 (d, $^3J_{H,H}$ = 3.4 Hz, 1 H, Ar-H), 7.73 (d, $^3J_{H,H}$ = 3.3 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2 (CH_3), 23.0 (CH_2), 30.0 (CH_2), 36.3 (CH_2), 48.8 (CH_2), 58.7 (CH), 112.0 (CH), 118.7 (CH), 125.0 (C), 129.9 (CH), 142.4 (CH), 144.6 (C), 167.7 (C) ppm. IR (neat): $\tilde{\nu}$ = 3010, 2963, 2920, 2860, 2223, 1618, 1518, 1361, 1343, 1179, 1049, 938, 800, 721 cm^{-1}. MS (EI, 25 °C): *m*/*z* (%) = 258 (8) $[M]^+$, 161 (12) $[C_{12}H_{15}]^+$, 160 (100) $[C_{12}H_{16}]^+$, 91 (10) $[C_7H_7]^+$. HRMS (EI): calcd. for $C_{15}H_{18}N_2S$ 258.1191; found 258.1188.

2-[1-(*p*-Methoxyphenyl)pyrrolidin-2-ylmethyl]thiazole (40): General procedure B was used to synthesize pyrrolidine **40** from alkyne **13** and 4-methoxyaniline. After purification by flash chromatography (PE/EtOAc, 5:1), compound **40** (230 mg, 0.84 mmol, 35%) was isolated as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.84–2.03 (m, 4 H), 3.04 (dd, $^2J_{H,H}$ = 14.6, $^3J_{H,H}$ = 9.0 Hz, 1 H, 6-H), 3.11–3.29 (m, 1 H, CHN), 3.39 (dd, $^2J_{H,H}$ = 14.6, $^3J_{H,H}$ = 3.0 Hz, 1 H, 6-H), 3.43–3.49 (m, 1 H, CHN), 3.76 (s, 3 H, OCH_3), 4.07–4.25 (m, 1 H, CHN), 6.62–6.67 (m, 2 H, Ar-H), 6.86–6.90 (m, 2 H, Ar-H), 7.22 (d, $^3J_{H,H}$ = 3.3 Hz, 1 H, Ar-H), 7.73 (d, $^3J_{H,H}$ = 3.3 Hz, 1 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.2 (CH_2), 30.2 (CH_2), 36.5 (CH_2), 49.3 (CH_2), 56.0 (CH_3), 59.1 (CH), 112.9 (CH), 115.3 (CH), 118.7 (CH), 141.7 (C), 142.4 (CH), 151.2 (C), 167.7 (C) ppm. IR (neat): $\tilde{\nu}$ = 3076, 2949, 2830, 1735, 1618, 1509, 1461, 1363, 1238, 1178, 1037, 810, 723 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 275 (40) $[M + H]^+$, 274 (60) $[M]^+$, 176 (100) $[M - C_7H_{10}]^+$. HRMS (CI): calcd. for $C_{15}H_{18}N_2SO$ + H 275.1218; found 275.1220.

1-Phenyl-1-(*p*-tolylethynyl)cyclopropane (45): A 1.6 M solution of *n*BuLi in hexanes (0.90 mL, 1.41 mmol) was added to a solution of 1-cyclopropyl-2-(*p*-tolyl)acetylene (**9**; 182 mg, 1.17 mmol) in THF (3.0 mL) at –78 °C. After warming to room temperature and stirring for 1 h, a solution of dry $ZnCl_2$ (534 mg, 2.37 mmol) in THF (12 mL) was added. Then the mixture was stirred for 25 min, and $[Pd(PPh_3)_4]$ (45 mg, 0.039 mmol, 5 mol-%) and iodobenzene (**1**, 87 μL, 0.78 mmol) were added. After the mixture had been stirred at room temperature for an additional 14 h, a saturated aqueous NH_4Cl solution (3 mL) was added. The mixture was then extracted with Et_2O (6 × 2 mL), and the combined organic layers were dried with $MgSO_4$. After concentration under vacuum, the residue was purified by flash chromatography (SiO_2, PE) to give **45** (165 mg, 0.71 mmol, 91%) as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.32–1.36 (m, 2 H), 1.53–1.57 (m, 2 H), 2.35 (s, 3 H, CH_3), 7.11 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H, Ar-H), 7.21 (t, $^3J_{H,H}$ = 7.3 Hz, 1 H, Ar-H), 7.32 (t, $^3J_{H,H}$ = 7.9 Hz, 2 H, Ar-H), 7.34 (d, $^3J_{H,H}$ = 8.2 Hz, 2 H, Ar-H), 7.41 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.2 (C), 20.5 (CH_2), 21.4 (CH_3), 78.4 (C), 92.9 (C), 120.6 (C), 125.5 (CH), 126.0 (CH), 128.3 (CH), 128.9 (CH), 131.6 (CH), 137.7 (C), 142.0 (C) ppm. IR (neat): $\tilde{\nu}$ = 3086, 3027, 2920, 2236, 1905, 1602, 1509, 1496, 1097, 1028, 955, 815, 752, 695 cm^{-1}. MS (CI, 25 °C): *m*/*z* (%) = 233 (60) $[M + H]^+$, 232 (100) $[M]^+$, 231 (20) $[M - H]^+$, 217 (35) $[M - CH_3]^+$, 202 (13) $[M - C_2H_6]^+$, 105 (17) $[C_8H_9]^+$. HRMS (CI): calcd. for $C_{18}H_{16}$ + H 233.1330; found 233.1327.

2-(4-Methylbenzyl)-3-phenyl-1-(*p*-tolyl)pyrrolidine (47): A Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was charged with alkyne **45** (558 mg, 2.40 mmol), *p*-toluidine (282 mg, 2.64 mmol), $[Ind_2TiMe_2]$ (74 mg, 0.24 mmol, 10.0 mol-%), and toluene (1.0 mL). The resulting mixture was heated at 160 °C for 48 h. After cooling to room temperature, NH_4Cl (65 mg, 1.20 mmol, 50 mol-%) was added, and the mixture was heated at 145 °C for 8 h. Then the mixture was cooled to room temperature, and a mixture of $NaBH_3CN$ (302 mg, 4.80 mmol) and $ZnCl_2$ (326 mg, 2.40 mmol) in MeOH (10 mL) was added. After this mixture had been stirred at 25 °C for 20 h, CH_2Cl_2 (50 mL) and a saturated Na_2CO_3 solution (20 mL) were added. The resulting mixture was filtered, and the solid residue was washed with CH_2Cl_2 (50 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (6 × 50 mL) and the combined organic layers were dried with Na_2SO_4. After concentration under vacuum, the residue was purified by flash chromatography (SiO_2, PE/EtOAc, 40:1) to give **47** (387 mg, 1.15 mmol, 48%) as a mixture of two diastereomers. The diastereomeric ratio was determined by GC to be 54:46. In addition, it was possible to recover unconsumed alkyne **45** (240 mg, 1.03 mmol, 43%). ^{1}H NMR (500 MHz, $CDCl_3$, mixture of two diastereomers): δ = 1.85–1.94 (m, 1 H), 2.09–2.19 (m, 2 H), 2.22 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.26–2.34 (m, 2 H), 2.29 (s, 3 H, CH_3), 2.31 (s 3 H, CH_3), 2.55 (dd, $^2J_{H,H}$ = 14.0, $^3J_{H,H}$ = 3.0 Hz, 1 H), 2.72 (dd, $^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 5.6 Hz, 1 H), 2.76 (dd, $^2J_{H,H}$ = 13.8, $^3J_{H,H}$ = 9.0 Hz, 1 H), 3.05 (d, $^2J_{H,H}$ = 13.8 Hz, 1 H), 3.29 (q, $J_{H,H}$ = 8.7 Hz, 2 H), 3.35 (d, $J_{H,H}$ = 8.3 Hz, 1 H), 3.36–3.44 (m, 1 H), 3.50 (t, $J_{H,H}$ = 7.4 Hz, 1 H), 3.52–3.60 (m, 1 H), 4.11 (br. d, $^3J_{H,H}$ = 8.3 Hz, 1 H), 4.32 (m, 1 H), 6.50 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, Ar-H), 6.55 (d, $^3J_{H,H}$ = 7.6 Hz, 2 H, Ar-H), 6.66 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, Ar-H), 6.83 (d, $^3J_{H,H}$ = 7.7 Hz, 2 H, Ar-H), 6.96 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, Ar-H), 7.01 (d, $^3J_{H,H}$ = 8.0 Hz, 2 H, Ar-H), 7.05–7.14 (m, 6 H, Ar-H), 7.17 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, Ar-H), 7.20 (d, $^3J_{H,H}$ = 8.0 Hz, 2 H, Ar-H), 7.23 (t, $^3J_{H,H}$ = 8.5 Hz, 2 H, Ar-H), 7.30 (t, $^3J_{H,H}$ = 7.1 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$, mixture of two diastereomers): δ = 20.2 (CH_3), 20.3 (CH_3), 20.9 (CH_3), 21.0 (CH_3), 26.7 (CH_2), 31.2 (CH_2), 35.0 (CH_2), 37.8 (CH_2), 47.1 (CH_2), 47.4 (CH), 47.7 (CH_2), 47.7 (CH), 63.2 (CH), 65.9 (CH), 111.6 (CH), 112.1 (CH), 124.5 (C), 124.7 (C), 126.5 (CH), 126.8 (CH), 128.2 (CH), 128.4 (CH), 128.5 (CH), 128.7 (CH), 129.1 (CH), 129.4 (CH), 129.5 (CH), 129.7 (CH), 130.0 (CH), 134.9 (C), 135.7 (C), 135.8 (C), 136.3 (C), 139.2 (C), 144.2 (C), 145.3 (C), 145.4 (C) ppm. IR (neat, mixture of two diastereomers): $\tilde{\nu}$ = 3025, 2919, 2858, 1619, 1518, 1362, 1188, 1165, 907, 799, 729, 698 cm^{-1}. GC–MS (CI, 25 °C): First diastereomer: *m*/*z* (%) = 342 (44) $[M + H]^+$, 341 (37) $[M]^+$, 236 (100) $[M - C_8H_9]^+$, 89 (57) $[C_7H_5]^+$; second diastereomer: *m*/*z* (%) = 342 (46) $[M + H]^+$, 341 (41) $[M]^+$, 236 (100) $[M - C_8H_9]^+$, 89 (82) $[C_7H_5]^+$. HRMS (EI, mixture of two diastereomers): calcd. for $C_{25}H_{27}N$ 341.2143; found 341.2146.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra, including atom numbering of all synthesized compounds.

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