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Graphical Abstract

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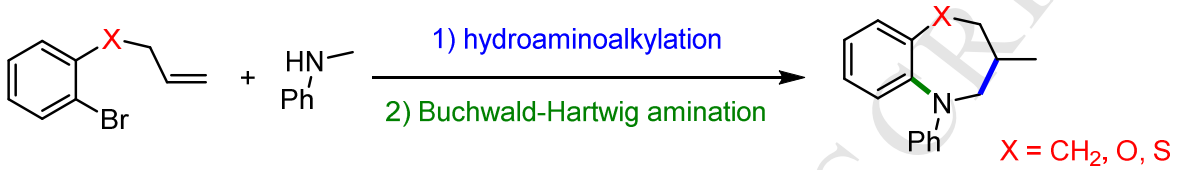
Tobias Kaper, Sven Doye*
Institut für Chemie, Universität Oldenburg, Carl-von-Ossietzky-Str. 9-11, 26129 Oldenburg, Germany



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ABSTRACT

Reaction sequences consisting of an initial intermolecular titanium-catalyzed hydroaminoalkylation of a suitably *ortho*-bromophenyl-substituted alkene and a subsequent intramolecular Buchwald-Hartwig amination are used for the synthesis of benzazepine, benzoxazepine, and benzothiazepine derivatives. While in the latter two cases, the hydroaminoalkylation products obtained from an allyl (2-bromophenyl) ether or an allyl (2-bromophenyl) thioether must be purified prior to the subsequent palladium-catalyzed amination step, both reactions can be combined to an efficient one-pot procedure for the synthesis of 2,3,4,5-tetrahydrobenzo[*b*]azepines when 4-(2-bromophenyl)-1-butene and various *N*-methylanilines are used as the starting materials.

1. Introduction

Benzo-annulated, nitrogen-containing, seven-membered heterocycles such as benzazepines [1], benzodiazepines [2], benzoxazepines [3], or benzothiazepines [4] represent an important class of compounds in medicinal chemistry with various pharmacological properties (Figure 1). For example, the ACE inhibitor benazepril (a benzazepine derivative) [5] and the calcium channel blocker diltiacem (a benzothiazepine derivative) [6] are used to treat high blood pressure, while many members of the benzodiazepine family (e.g. clobazam) are commonly known as psychoactive drugs.

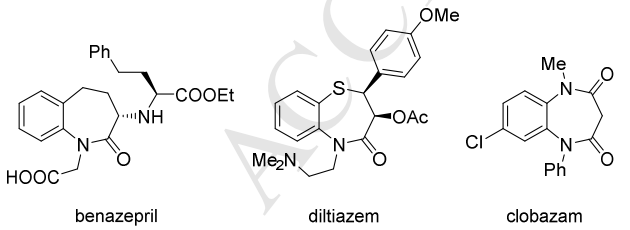


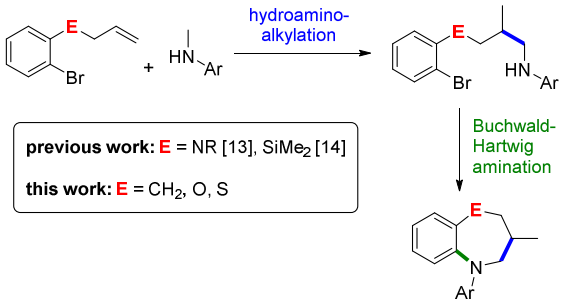
Figure 1. Pharmacologically relevant examples of benzo-annulated, nitrogen-containing, seven-membered heterocycles.

From a synthetic point of view, classical chemical transformations such as condensation reactions which form amide or imine moieties [7] or 1,4-addition reactions of hetero atom nucleophiles to α,β-unsaturated carbonyl compounds [8] have often been used as key steps to build up the seven-membered rings of the target compounds. However, on the other hand, even one of the earliest reports on the palladium-catalyzed amination of aryl halides [9] which is now known as the Buchwald-Hartwig amination [10] contains an example of the conversion of a suitable 4-(2-bromophenyl)butylamine into a 2,3,4,5-tetrahydrobenzo[*b*]azepine. Based on this result and our own achievements in the field of titanium-catalyzed alkene hydroaminoalkylation [11,12], we recently developed new one-pot procedures for the synthesis of 1,5-benzodiazepines [13] and 1,5-benzoazasilepines [14] which take place by an initial regioselective intermolecular hydroaminoalkylation reaction of an *N*-allyl-2-bromoaniline or an allyl(2-bromophenyl)silane and a subsequent intramolecular Buchwald-Hartwig amination (Scheme 1, E = NR, $SiMe_2$). In this context it is worth mentioning that closely related one-pot procedures that combine a titanium- or a tantalum-catalyzed alkene hydroaminoalkylation with a subsequent palladium-catalyzed Buchwald-Hartwig amination have also been developed for the synthesis of 1,4-benzoazasilines [15] or indolines [16] and in addition, a titanium-catalyzed alkyne hydroamination was used as the initial step of a corresponding one-pot indole synthesis [17]. On the other hand, to the best of our knowledge, corresponding reaction sequences for the synthesis of benzazepine, benzoxazepine, and benzothiazepine derivatives (Scheme 1, E = CH_2, O, S) have not been reported yet.

Although hydroaminoalkylation reactions of alkenes with secondary amines can be achieved in the presence of selected late transition metal catalysts [18], group 4 [11] and group 5 [19]

* Corresponding author. Fax: +49-441-798-3329; e-mail: doye@uni-oldenburg.de

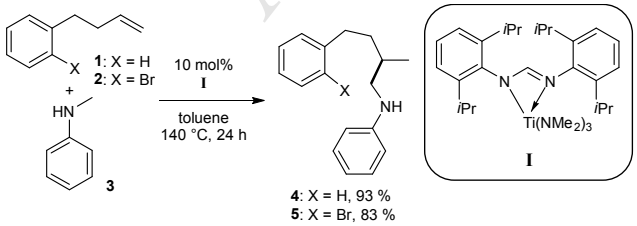
metal catalysts offer a number of significant advantages. For example, the latter catalysts do not require the presence of a directing or protecting group on the nitrogen of the amine substrate and in addition, terminal alkyl-substituted alkenes are usually converted into the branched hydroaminoalkylation products with good to excellent regioselectivities.



Scheme 1. Synthesis of benzo-annulated seven-membered nitrogen-containing heterocycles by alkene hydroaminoalkylation/Buchwald-Hartwig amination sequences.

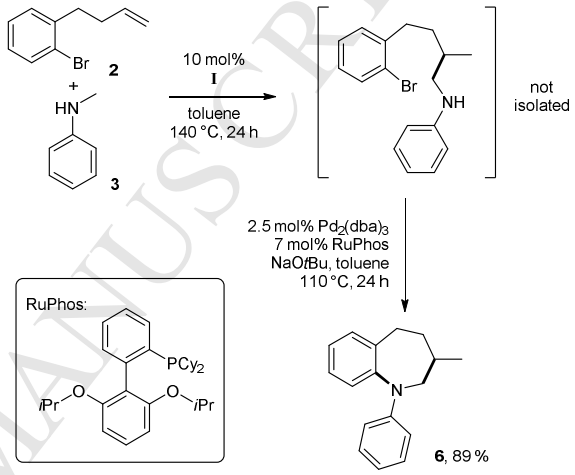
2. Results and discussion

Initial hydroaminoalkylation reactions of 4-phenyl-1-butene (**1**) and 4-(2-bromophenyl)-1-butene (**2**) with *N*-methylaniline (**3**, Scheme 2) were performed in the presence of the titanium formamidinate catalyst **I** that was originally used by Eisen et al. as a polymerization catalyst [20]. In this context, it is important to mention that catalysts **I** was also found to exhibit exceptionally high catalytic activity in hydroaminoalkylation reactions which for example, even allows the use of 1,2-disubstituted alkenes as starting materials [21]. Further advantages of catalyst **I** are the high regioselectivity in favor of the branched products observed in hydroaminoalkylation reactions of mono-substituted alkenes such as allylbenzene [21] and the fact that this catalyst has already been used successfully in one-pot hydroaminoalkylation/Buchwald-Hartwig amination sequences [13,14]. Our study started with an initial experiment in which the non-halogenated substrate 4-phenyl-1-butene (**1**) was reacted with *N*-methylaniline (**3**) in toluene at 140 °C for 24 h in the presence of 10 mol% of catalyst **I** (Scheme 2). After the corresponding branched hydroaminoalkylation product **4** had been obtained in excellent yield of 93 %, the halogenated substrate 4-(2-bromophenyl)-1-butene (**2**) was also reacted with **3** under identical conditions and as observed before [13], the presence of the *ortho*-bromo substituent in **2**, which is required for the planned subsequent intramolecular Buchwald-Hartwig amination, did not lead to a dramatically reduced yield. Even in this case, the branched hydroaminoalkylation product **5** could be isolated in 83 % yield. In this context, it should also be mentioned that in both experiments, formation of linear hydroaminoalkylation products was not observed by GC-analysis.



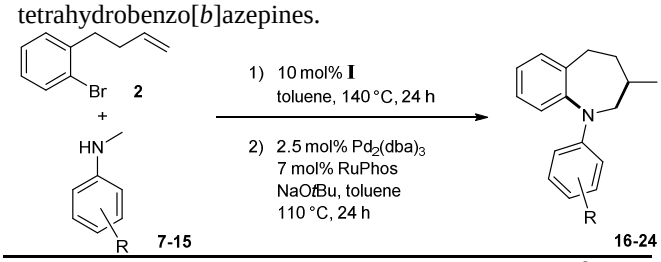
Scheme 2. Hydroaminoalkylation of 4-phenyl-1-butene (**1**) and 4-(2-bromophenyl)-1-butene (**2**) with *N*-methylaniline (**3**) in the presence of catalyst **I**.

With these results in hand, we then directly attempted to perform the hydroaminoalkylation of **2** with **3** and a subsequent Buchwald-Hartwig amination following a one-pot protocol (Scheme 3). For that purpose, we first repeated the reaction between **2** and **3** under the reaction conditions described above. Then 2.5 mol% $Pd_2(dba)_3$, 7 mol% RuPhos, NaO*t*Bu and additional toluene were directly added to the obtained crude hydroaminoalkylation reaction mixture and the resulting mixture was heated to 110 °C for 24 h. Finally, the crude product was purified by flash column chromatography to give to the desired 2,3,4,5-tetrahydrobenzo[*b*]azepine **6** in 89 % yield. Interestingly, the two-step one-pot procedure from **2** to **6** gave a better isolated yield than the initial hydroaminoalkylation reaction from which product **5** could only be isolated in 83 % yield. A plausible explanation for this observation is the decreased polarity of the tertiary amine **6** compared to the secondary amine **5** which facilitates the final chromatographic purification.



Scheme 3. One-pot hydroaminoalkylation/Buchwald-Hartwig amination sequence for the synthesis of 2,3,4,5-tetrahydro-benzo[*b*]azepine **6**.

Table 1. One-pot procedure for the synthesis of 2,3,4,5-tetrahydrobenzo[*b*]azepines.



Entry	R	Yield (%)[a]
1	*p*-Me (**7**)	88 (**16**)
2	*p*-OMe (**8**)	70 (**17**)
3	*p*-F (**9**)	85 (**18**)
4	*p*-OCF_3 (**10**)	80 (**19**)
5	*m*-Me (**11**)	77 (**20**)
6	*p*-*i*Pr (**12**)	59 (**21**)
7	*p*-Cl (**13**)	71 (**22**)
8	*p*-SMe (**14**)	79 (**23**)
9	*m*-F (**15**)	62 (**24**)

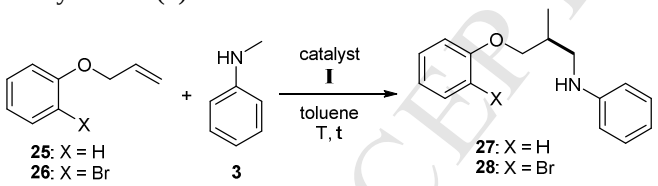
[a] Reaction conditions: 1) 4-(2-bromophenyl)-1-butene (**2**, 464 mg, 2.2 mmol), aniline (2.0 mmol), **I** (109 mg, 0.2 mmol, 10 mol%), toluene (1 mL), 140 °C, 24 h; 2) $Pd_2(dba)_3$

(46 mg, 0.05 mmol, 2.5 mol%), RuPhos (65 mg, 0.14 mmol, 7.0 mol%), NaO*t*Bu (261 mg, 2.7 mmol), toluene (5 mL), 110 °C, 24 h. Isolated yield.

To investigate the scope of the new one-pot procedure for the synthesis of 2,3,4,5-tetrahydrobenzo[*b*]azepines, we then reacted **2** with the *para*- and *meta*-substituted *N*-methylanilines **7**-**15** (Table 1). In this context, it should be mentioned that we did not use any *ortho*-substituted *N*-methylanilines because these substrates are known to react sluggishly in titanium-catalyzed hydroaminoalkylation reactions [12e,13,21]. As can be seen from Table 1, **2** reacts smoothly with **7**-**15** to give the desired 2,3,4,5-tetrahydrobenzo[*b*]azepines **16**-**24** in good to very good yields of 59-88 %. Overall, it turned out that the one-pot procedure not only tolerates alkyl and ether substitution but also the presence of pharmacologically relevant fluoro and thioether substituents. In addition, the chloro substituent present in product **22** offers various possibilities for further functionalization.

In comparison with 4-phenyl-1-butene (**1**), the corresponding allyl ether **25** (Table 2) was then found to be significantly less reactive in hydroaminoalkylation reactions with *N*-methylaniline (**3**). While under the reaction conditions described above (10 mol% **I**, 140 °C, 24 h) **1** had been converted into the hydroaminoalkylation product **4** in 93 % yield (Scheme 2), the allyl ether **25** delivered the desired product **27** in only 47 % yield (Table 2, entry 1). However, the yield could easily be improved to acceptable 70 % by extending the reaction time to 48 h (Table 2, entry 2). On the other hand, hydroaminoalkylation reactions of allyl (2-bromophenyl) ether (**26**) turned out to be even more challenging. In the presence of 10 mol% of catalyst **I**, reactions performed at 140 or 160 °C for 24 or 48 h (Table 2, entries 3-5) gave the corresponding product **28** only in disappointing yields between 7 and 15 %. Fortunately, it finally turned out that the yield of the hydroaminoalkylation reaction could be improved to 60 % with a catalyst loading of 20 mol% and a reaction time of 48 h at 160 °C (Table 2, entry 7).

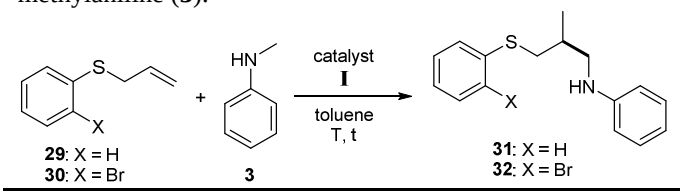
Table 2. Hydroaminoalkylation of allylethers with *N*-methylaniline (**3**).



Entry	X	Catalyst (mol%)	T (°C)	t (h)	Yield (%)[a]
1	H	10	140	24	47 (**27**)
2	H	10	140	48	70 (**27**)
3	Br	10	140	24	15 (**28**)
4	Br	10	140	48	13 (**28**)
5	Br	10	160	24	7 (**28**)
6	Br	20	160	24	55 (**28**)
7	Br	20	160	48	60 (**28**)

[a] Reaction conditions: allyl ether (2.2 mmol), *N*-methylaniline (**3**, 214 mg, 2.0 mmol), **I** (10 or 20 mol%), toluene (1 mL), 140 or 160 °C, 24 or 48 h. Isolated yield.

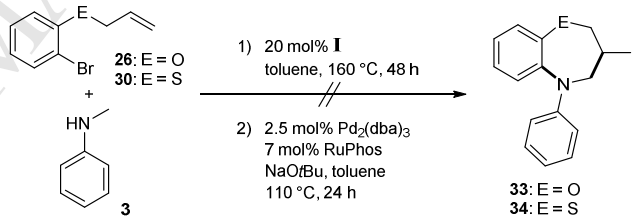
Table 3. Hydroaminoalkylation of allyl thioethers with *N*-methylaniline (**3**).



Entry	X	Catalyst (mol%)	T (°C)	t (h)	Yield (%)[a]
1	H	10	140	24	45 (**31**)
2	H	10	140	48	55 (**31**)
3	Br	10	140	24	14 (**32**)
4	Br	20	160	24	55 (**32**)
5	Br	20	160	48	71 (**32**)

[a] Reaction conditions: allyl thioether (2.2 mmol), *N*-methylaniline (**3**, 214 mg, 2.0 mmol), **I** (10 or 20 mol%), toluene (1 mL), 140 or 160 °C, 24 or 48 h. Isolated yield.

Additional hydroaminoalkylation reactions performed with the allyl thioethers **29** and **30** (Table 3) and *N*-methylaniline (**3**) then revealed a comparably reduced reactivity of the sulfur derivatives and as a result, it was again necessary to heat the reaction mixture to 160 °C for 48 h in the presence of 20 mol% of **I** to convert the allyl (2-bromophenyl) thioether **30** into the corresponding hydroaminoalkylation product **32** in 71 % yield (Table 3, entry 5).

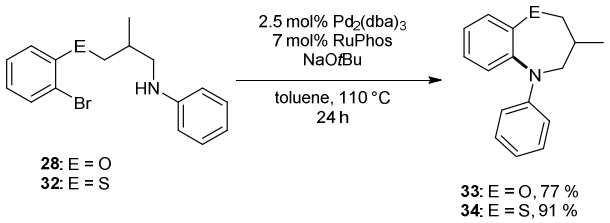


Scheme 4. Attempted one-pot procedure for the synthesis of benzoxazepine and benzothiazepine derivatives.

After suitable reaction conditions for the hydroaminoalkylation of the *ortho*-bromo substituted allyl ether **26** and the allyl thioether **30** had been identified, we used these conditions for one-pot hydroaminoalkylation/Buchwald-Hartwig amination sequences which were expected to directly give access to the benzoxazepine derivative **33** and the benzothiazepine derivative **34** (Scheme 4). However, although for the second reaction, the conditions that had already been used successfully for the one-pot synthesis of the 2,3,4,5-tetrahydrobenzo[*b*]azepines (Scheme 3, Table 1) were applied, these experiments failed. In both cases, complex reaction mixtures were formed during the one-pot experiments and it was not possible to isolate the expected products **33** and **34** in pure form. GC-analysis of the crude reaction mixtures showed that both steps, the initial hydroaminoalkylation and the subsequent cyclization reaction, did not go to completion and in addition, the obtained product mixtures were contaminated with relatively large amounts of further impurities like the formamidine which is formed by decomposition of catalyst **I** during the workup procedure. In this context, it must be regarded as a severe drawback that a catalyst loading of 20 mol% of **I** had to be applied for the initial hydroaminoalkylation reactions of the

substrates **26** and **30**. Additional attempts to achieve the one-pot reaction sequences by the use of a pre-formed palladium catalyst generated in situ by heating a toluene mixture of $Pd_2(dba)_3$ and RuPhos did not lead to improved results.

To circumvent the problems that are caused by an incomplete hydroaminoalkylation reaction and the formamidine contamination of the product which increases with an increasing catalyst loading in the hydroaminoalkylation step, we finally decided to perform the palladium-catalyzed cyclization reactions with the purified hydroaminoalkylation products **28** and **32** (Scheme 5). Fortunately, in these cases, the intramolecular Buchwald-Hartwig amination reactions took place smoothly to give the desired benzoxazepine derivative **33** and the benzothiazepine derivative **34** in good yields of 77 % and 91 %, respectively (Scheme 5).



Scheme 5. Synthesis of benzoxazepine and benzothiazepine derivatives.

3. Conclusion

In summary, it was shown that reaction sequences consisting of an initial intermolecular titanium-catalyzed hydroaminoalkylation of a suitably *ortho*-bromophenyl-substituted alkene and a subsequent intramolecular Buchwald-Hartwig amination can be used for the synthesis of benzazepine, benzoxazepine, and benzothiazepine derivatives. While in the latter two cases, the hydroaminoalkylation products obtained from an allyl (2-bromophenyl) ether or an allyl (2-bromophenyl) thioether must be purified prior to the subsequent palladium-catalyzed amination step, both reactions can be combined to an efficient one-pot procedure for the synthesis of benzazepine derivatives when 4-(2-bromophenyl)-1-butene and various *N*-methylanilines are used as the starting materials.

4. Experimental section

Unless otherwise noted, all reactions were performed under an inert atmosphere of nitrogen in oven-dried Schlenk tubes (Duran glassware, 100 mL, ø = 30 mm) equipped with Teflon® stopcocks and magnetic stirring bars (15 × 4.5 mm). Toluene was purified by distillation from sodium wire and degassed. Catalyst **I** [20] and the alkenes [22-24] were synthesized according to literature procedures. Prior to use, all substrates were distilled and degassed. Catalyst **I**, the alkenes, the *N*-methylanilines, and toluene were stored in a nitrogen-filled glove box (M. Braun, Unilab). All other chemicals were purchased from commercial sources and were used without further purification. For flash chromatography, silica gel from GRACE Davison (particle size 0.037-0.063 mm) was used. Light petroleum ether (b.p. 40-60 °C, PE), *tert*-butyl methyl ether (MTBE), CH_2Cl_2 and EtOAc used for flash chromatography were distilled prior to use. For thin layer chromatography, silica on TLC aluminium foils with fluorescent indicator 254 nm from Fluka was used. The substances were detected with UV light and iodine. All products that have already been reported in the literature were identified by comparison of the obtained ^{1}H NMR and ^{13}C NMR spectra with those reported in the literature. New compounds were additionally characterized by infrared (IR) spectroscopy, GC-MS and high resolution mass spectrometry (HRMS). NMR spectra were recorded on the following spectrometers: Bruker Fourier 300, Bruker Avance DRX 500 or Bruker Avance III, 500 MHz. All ^{1}H NMR spectra are reported in δ units (ppm) relative to the signal of TMS at 0.00 ppm or relative to the signal of $CDCl_3$ at 7.26 ppm. *J* values are given in Hz. All ^{13}C NMR spectra are reported in δ units (ppm) relative to the central line of the triplet for $CDCl_3$ at 77.0 ppm. Infrared spectra were recorded on a Bruker Vector 22 spectrometer or a Bruker Tensor 27 spectrometer (ATR). MS analyses were performed on a Thermo Scientific DFS (CI or EI) or a Waters Q-TOF Premier (ESI+, TOF) spectrometer. High resolution mass spectra (HRMS) were recorded on a Waters Q-TOF Premier spectrometer in EI or ESI mode (ESI+, TOF). GC-MS analyses were performed on a Thermo Finnigan Focus gas chromatograph (column: Agilent DB- 5, length = 30 m, inner diameter = 0.32 mm, film thickness = 0.25 µm, (94 %-methyl)-(5 %-phenyl)-(1 %-vinyl)polysiloxane) equipped with a DSQ mass detector (EI). GC analyses were performed on a Shimadzu GC-2010 gas chromatograph equipped with a flame ionization detector.

4.1. General procedures

General procedure A for the hydroaminoalkylation of alkenes with *N*-methylaniline: An oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was transferred into a nitrogen-filled glovebox and charged with catalyst **I** (0.2 mmol, 10 mol% or 0.4 mmol, 20 mol%) and toluene (0.5 mL). Afterwards *N*-methylaniline (214 mg, 2.0 mmol), the alkene (2.2 mmol) and toluene (0.5 mL) were added. After heating the mixture to 140 or 160 °C for 24 or 48 hours, the crude product was purified by flash chromatography (SiO_2).

General procedure B for the one-pot synthesis of 2,3,4,5-tetrahydrobenzo[*b*]azepines: An oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was transferred into a nitrogen-filled glovebox and charged with catalyst **I** (109 mg, 0.2 mmol, 10 mol%) and toluene (0.5 mL). Afterwards the *N*-methylaniline (2.0 mmol), 4-(2-bromophenyl)-1-butene (464 mg, 2.2 mmol) and toluene (0.5 mL) were added. After the mixture had been heated to 140 °C for 24 hours, the Schlenk tube was cooled to room temperature and transferred back into a nitrogen-filled glovebox. Then $Pd_2(dba)_3$ (46 mg, 0.05 mmol, 2.5 mol%), RuPhos (65 mg, 0.14 mmol, 7 mol%), NaO*t*Bu (261 mg, 2.7 mmol) and toluene (5 mL) were added. After heating the mixture to 110 °C for additional 24 hours, the crude product was purified by flash chromatography (SiO_2).

General procedure C for the intramolecular Buchwald-Hartwig amination: An oven-dried Schlenk tube equipped with a Teflon stopcock and a magnetic stirring bar was transferred into a nitrogen-filled glovebox and charged with the respective starting material [**28** (1.66 mmol) or **32** (1.39 mmol)], toluene (1 mL), $Pd_2(dba)_3$ (2.5 mol%), RuPhos (7 mol%), NaO*t*Bu (1.3 equiv), and toluene (4 mL). After heating the mixture to 110 °C for 24 hours, the crude product was purified by flash chromatography (SiO_2).

*4.2. Synthesis of N-(2-methyl-4-phenylbutyl)aniline (**4**)*

General procedure A (10 mol% **I**, 140 °C, 24 h) was used to synthesize compound **4**. After purification by flash chromatography (PE/MTBE, 40:1), **4** (445 mg, 1.86 mmol, 93 %) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42-7.39 (m, 2 H, Ar-*H*), 7.32-7.26 (m, 5 H, Ar-*H*), 6.83-6.80 (m, 1 H, Ar-*H*), 6.71-6.69 (m, 2 H, Ar-*H*), 3.77 (s, 1 H, N*H*),

3.19 (dd, *J* = 12.3, 5.6 Hz, 1 H, CH_2), 3.04 (dd, *J* = 12.3, 6.9 Hz, 1 H, CH_2), 2.88-2.82 (m, 1 H, CH_2), 2.76-2.70 (m, 1 H, CH_2), 1.95-1.88 (m, 2 H, CH_2, C*H*), 1.67-1.60 (m, 1 H, CH_2), 1.16 (d, *J* = 6.5 Hz, 3 H, CH_3) ppm. ^{13}C{^{1}H} NMR (125 MHz, JMOD, $CDCl_3$): δ = 148.4 (C), 142.4 (C), 129.1 (CH), 128.3 (CH), 128.3 (CH), 125.7 (CH), 117.0 (CH), 112.7 (CH), 50.1 (CH_2), 36.5 (CH_2), 33.2 (CH_2), 32.5 (CH), 17.9 (CH_3) ppm. GC-MS: *m/z* (%) = 239 (50) $[M]^+$, 106 (100), 91 (10), 77 (14) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{17}H_{21}N^+$: 239.1669, found: 239.1667. IR (ATR, neat): 1/λ = 3419, 3053, 3024, 2925, 2856, 1601, 1505, 1472, 1454, 1430, 1379, 1319, 1256, 1179, 1153, 1117, 1068, 1030, 991, 904, 866, 745, 691, 619 cm^{-1}.

*4.3. Synthesis of N-(4-(2-bromophenyl)-2-methylbutyl)aniline (**5**)*

General procedure A (10 mol% **I**, 140 °C, 24 h) was used to synthesize compound **5**. After purification by flash chromatography (PE/MTBE, 40:1), **5** (512 mg, 1.66 mmol, 83 %) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76-7.74 (m, 1 H, Ar-*H*), 7.43-7.39 (m, 4 H, Ar-*H*), 7.28-7.25 (m, 1 H, Ar-*H*), 6.94-6.91 (m, 1 H, Ar-*H*), 6.84-6.82 (m, 2 H, Ar-*H*), 3.93 (br. s, 1 H, N*H*), 3.33 (dd, *J* = 12.3, 6.0 Hz, 1 H, CH_2), 3.19 (dd, *J* = 12.1, 7.2 Hz, 1 H, CH_2), 3.09-3.03 (m, 1 H, CH_2), 2.98-2.92 (m, 1 H, CH_2), 2.09-2.04 (m, 1 H, C*H*), 2.02-1.95 (m, 1 H, CH_2), 1.77-1.69 (m, 1 H, CH_2), 1.31 (d, *J* = 6.6 Hz, CH_3) ppm. ^{13}C{^{1}H} NMR (125 MHz, DEPT, $CDCl_3$): δ = 148.4 (C), 141.7 (C), 132.7 (CH), 130.1 (CH), 129.1 (CH), 127.5 (CH), 127.4 (CH), 124.3 (C), 117.0 (CH), 112.6 (CH), 50.0 (CH_2), 34.9 (CH_2), 33.6 (CH_2), 32.8 (CH), 17.9 (CH_3) ppm. GC-MS: *m/z* (%) = 317 (19) $[M]^+$, 106 (100), 77 (11) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{17}H_{20}{}^{79}BrN^+$: 317.0774, found: 317.0762. IR (ATR, neat): 1/λ =3079, 3049, 3021, 2914, 1601, 1505, 1470, 1437, 1379, 1319, 1258, 1179, 1153, 1075, 1022, 991, 866, 744, 691, 658, 628, 592, 575 cm^{-1}.

*4.4. Synthesis of 3-methyl-1-phenyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**6**)*

General procedure B was used to synthesize compound **6**. After purification by flash chromatography (PE/MTBE, 40:1), **6** (422 mg, 1.78 mmol, 89 %) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28-7.26 (m, 1 H, Ar-*H*), 7.24-7.13 (m, 5 H, Ar-*H*), 6.67 (m, 1 H, Ar-*H*), 6.60-6.59 (m, 2 H, Ar-*H*), 4.04 (d, *J* = 14.5 Hz, CH_2), 2.82-2.77 (m, 1 H, CH_2), 2.69,-2.61 (m, 2 H, C*H*, CH_2), 2.16-2.09 (m, 1 H, CH_2), 1.91-1.87 (m, 1 H, CH_2), 1.22-1.14 (m, 1 H, CH_2), 0.93 (d, *J* = 6.8 Hz, CH_2) ppm. ^{13}C{^{1}H} NMR (125 MHz, DEPT, $CDCl_3$): δ = 147.6 (C), 146.0 (C), 141.5 (C), 130.5 (CH), 129.1 (CH), 128.7 (CH), 127.2 (CH), 126.4 (CH), 116.3 (CH), 112.4 (CH), 55.5 (CH_2), 35.1 (CH_2), 32.8 (CH_2), 31.8 (CH), 19.4 (CH_3) ppm. GC-MS: *m/z* (%) = 237 (100) $[M]^+$, 194 (100), 91 (37), 77 (24) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{17}H_{19}N^+$: 237.1512, found: 237.1510. IR (ATR, neat): 1/λ = 3060, 3022, 2948, 2923, 2869, 2846, 1593, 1496, 1456, 1370, 1352, 1340, 1316, 1298, 1257, 1219, 1190, 1175, 1156, 1118, 1095, 1065, 1039, 990, 994, 895, 865, 841, 768, 743, 689, 629, 599, 582 cm^{-1}.

*4.5. Synthesis of 3-methyl-1-(p-tolyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**16**)*

General procedure B was used to synthesize compound **16**. After purification by flash chromatography (PE/MTBE, 40:1), **16** (442 mg, 1.76 mmol, 88 %) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27-7.26 (m, 1 H, Ar-*H*), 7.24-7.20 (m, 1 H, Ar-*H*), 7.18-7.14 (m, 2 H, Ar-*H*), 6.98-6.96 (m, 2 H, Ar-*H*), 6.54-6.53 (m, 2 H, Ar-*H*), 4.02 (d, *J* = 14.4 Hz, CH_2), 2.82-2.77 (m, 1 H, CH_2), 2.70-2.63 (m, 2 H, C*H*, CH_2), 2.24 (s, 3 H, CH_3), 2.14-2.06 (m, 1 H, CH_2), 1.91-1.86 (m, 1 H, CH_2), 1.22-1.15 (m, 1 H, CH_2), 0.93 (d, *J* = 6.8 Hz, CH_3) ppm. ^{13}C{^{1}H} NMR (125 MHz, DEPT, $CDCl_3$): δ = 146.4 (C), 145.6 (C), 141.4 (C), 130.5 (CH), 129.6 (CH), 128.6 (CH), 127.2 (CH), 126.1 (CH), 125.5 (C), 112.8 (CH), 55.7 (CH_2), 35.0 (CH_2), 32.9 (CH_2), 31.9 (CH), 20.2 (CH_3), 19.4 (CH_3) ppm. GC-MS: *m/z* (%) = 251 (100) $[M]^+$, 208 (47), 194 (10), 174 (6). HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{18}H_{21}N^+$: 251.1669, found: 251.1663 $[M]^+$. IR (ATR, neat): 1/λ = 3023, 2918, 1616, 1598, 1569, 1513, 1489, 1454, 1436, 1369, 1350, 1315, 1284, 1257, 1206, 1189, 1175, 1132, 1115, 1086, 1053, 1010, 944, 895, 844, 801, 776, 758, 742, 703, 645, 624 cm^{-1}.

*4.6. Synthesis of 1-(4-methoxyphenyl)-3-methyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**17**)*

General procedure B was used to synthesize compound **17**. After purification by flash chromatography (PE/MTBE, 40:1), **17** (374 mg, 1.40 mmol, 70 %) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27-7.26 (m, 1 H, Ar-*H*), 7.23-7.19 (m, 1 H, Ar-*H*), 7.16-7.12 (m, 2 H, Ar-*H*), 6.80-6.77 (m, 2 H, Ar-*H*), 6.64-6.61 (m, 2 H, Ar-*H*), 3.98 (d, *J* = 14.2 Hz, CH_2), 3.77 (s, 3 H, CH_3), 2.84 (dd, *J* = 14.2, 11.2 Hz, 1 H, CH_2), 2.74-2.67 (m, 2 H, C*H*, CH_2), 2.15-2.05 (m, 1 H, CH_2), 1.94-1.88 (m, 1 H, CH_2), 1.25-1.18 (m, 1 H, CH_2), 0.95 (d, *J* = 6.8 Hz, CH_3) ppm. ^{13}C{^{1}H} NMR (125 MHz, DEPT, $CDCl_3$): δ = 151.5 (C), 147.12 (C), 142.5 (C), 140.8 (C), 130.4 (CH), 128.0 (CH), 127.1 (CH), 125.5 (C), 114.8 (CH), 114.7 (CH), 56.3 (CH_2), 55.7 (CH_3), 34.8 (CH_2), 32.9 (CH_2), 32.1 (CH), 19.4 (CH_3) ppm. GC-MS: *m/z* (%) = 267 (100) $[M]^+$, 252 (28), 224 (12), 210 (19). HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{18}H_{21}ON^+$: 267.1618, found: 267.1615. IR (ATR, neat): 1/λ = 2994, 2925, 2831, 1617, 1576, 1506, 1489, 1453, 1349, 1289, 1238, 1176, 1126, 1085, 1065, 1038, 944, 895, 814, 797, 757, 643, 621 cm^{-1}.

*4.7. Synthesis of 1-(4-fluorophenyl)-3-methyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**18**)*

General procedure B was used to synthesize compound **18**. After purification by flash chromatography (PE/MTBE, 40:1), **18** (434 mg, 1.70 mmol, 85 %) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27-7.26 (m, 1 H, Ar-*H*), 7.24-7.20 (m, 1 H, Ar-*H*), 7.18-7.13 (m, 2 H, Ar-*H*), 6.87-6.83 (m, 2 H, Ar-*H*), 6.54-6.52 (m, 2 H, Ar-*H*), 3.97 (d, *J* = 14.4 Hz, 1 H, CH_2), 2.83 (dd, *J* = 14.2, 11.3 Hz, 1 H, CH_2), 2.71-2.62 (m, 2 H, CH_2, C*H*), 2.14-2.05 (m, 1 H, CH_2), 1.93-1.87 (m, 1 H, CH_2), 1.24-1.16 (m, 1 H, CH_2), 0.93 (d, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C{^{1}H} NMR (125 MHz, DEPT, $CDCl_3$): δ = 154.3 (d, $^1J_{C,F}$ = 235 Hz, C), 146.4 (C), 144.4 (C), 141.3 (C), 130.6 (CH), 128.4 (CH), 127.3 (CH), 126.2 (CH), 115.4 (d, $^2J_{C,F}$ = 22 Hz, CH), 113.7 (d, $^3J_{C,F}$ = 7 Hz, CH), 56.1 (CH_2), 34.9 (CH_2), 32.8 (CH_2), 31.9 (CH), 19.3 (CH_3) ppm. GC-MS: *m/z* (%) = 255 (100) $[M]^+$, 212 (85), 198 (13), 91 (20), 77 (6) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{17}H_{18}FN^+$: 255.1418, found: 255.1416. IR (ATR, neat): 1/λ = 3053, 3022, 2949, 2926, 2870, 2847, 1503, 1490, 1455, 1370, 1370, 1352, 1304, 1285, 1250, 1223, 1193, 1176, 1159, 1120, 1084, 1065, 1040, 945, 895, 813, 778, 758, 745, 691, 642, 621, 572 cm^{-1}.

*4.8. Synthesis of 3-methyl-1-(4-(trifluoromethoxy)phenyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**19**)*

General procedure B was used to synthesize compound **19**. After purification by flash chromatography (PE/MTBE, 40:1), **19** (514 mg, 1.60 mmol, 80 %) was isolated as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28-7.26 (m, 1 H, Ar-*H*), 7.25-7.21 (m, 1 H, Ar-*H*), 7.20-7.15 (m, 2 H, Ar-*H*), 6.98-6.96 (m, 2 H, Ar-*H*), 6.53-6.49 (m, 2 H, Ar-*H*), 3.97 (d, *J* = 14.6 Hz, 1 H, CH_2), 2.82 (dd, *J* = 14.2, 11.5 Hz, 1 H, CH_2), 2.66-2.58 (m, 2 H, CH_2, C*H*),

2.14-2.05 (m, 1 H, CH_2), 1.92-1.82 (m, 1 H, CH_2), 1.22-1.14 (m, 1 H, CH_2), 0.92 (d, J = 6.8 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, DEPT, $CDCl_3$): δ = 146.5 (C), 145.6 (C), 141.5 (C), 139.8 (C), 130.7 (CH), 128.6 (CH), 127.5 (CH), 126.8 (CH), 122.1 (CH), 120.8 (q, $^1J_{C,F}$ = 255 Hz, C), 112.7 (CH), 55.8 (CH_2), 35.1 (CH_2), 32.8 (CH_2), 31.8 (CH), 19.3 (CH_3) ppm. MS (ESI, +): *m/z* (%) = 322 (45) $[M+H]^+$, 220 (75), 176 (100), 162 (60). HRMS (ESI, +): $[M+H]^+$ calculated for $C_{18}H_{19}F_3N^+$: 322.1409, found: 322.1419. IR (ATR, neat): 1/λ = 3058, 3024, 2951, 2928, 2872, 2849, 1492, 1455, 1376, 1355, 1248, 1220, 1204, 1154, 1124, 1085, 1065, 1040, 1008, 945, 917, 896, 828, 804, 778, 765, 748, 724, 700, 668, 650, 626, 614, 582, 559 cm^{-1}.

*4.9. Synthesis of 3-methyl-1-(m-tolyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**20**)*

General procedure B was used to synthesize compound **20**. After purification by flash chromatography (PE/MTBE, 40:1), **20** (397 mg, 1.55 mmol, 77 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.27-7.16 (m, 4 H, Ar-*H*), 7.05-7.02 (m, 1 H, Ar-*H*), 6.50-6.49 (m, 1 H, Ar-*H*), 6.41-6.36 (m, 2 H, Ar-*H*), 4.02 (d, J = 14.3 Hz, 1 H, CH_2), 2.80-2.75 (m, 2 H, CH_2), 2.69-2.61 (m, 2 H, CH_2, C*H*), 2.23 (s, 3 H, CH_3), 2.14-2.07 (m, 1 H, CH_2), 1.90-1.86 (m, 1 H, CH_2), 1.20-1.13 (m, 1 H, CH_2), 0.93 (d, J = 6.7 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, DEPT, $CDCl_3$): δ = 147.6 (C), 146.1 (C), 141.5 (C), 138.8 (C), 130.5 (CH), 130.0 (CH), 128.7 (CH), 127.2 (CH), 126.3 (CH), 117.4 (CH), 113.2 (CH), 109.8 (CH), 55.6 (CH_2), 35.1 (CH_2), 32.9 (CH_2), 31.9 (CH), 21.9 (CH_3), 19.4 (CH_3) ppm. MS (ESI, +): *m/z* (%) = 252 (43) $[M+H]^+$, 196 (100), 181 (63), 108 (16), 91 (30) $[C_7H_7]^+$. HRMS (ESI, +): $[M+H]^+$ calculated for $C_{18}H_{22}N^+$: 252.1742, found: 252.1752. IR (ATR, neat): 1/λ = 3024, 2948, 2922, 2867, 1604, 1596, 1577, 1522, 1490, 1454, 1366, 1350, 1327, 1293, 1254, 1224, 1170, 1132, 1100, 1041, 1022, 991, 931, 905, 879, 857, 841, 813, 757, 742, 690, 659, 630, 605, 583 cm^{-1}.

*4.10. Synthesis of 1-(4-isopropylphenyl)-3-methyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**21**)*

General procedure B was used to synthesize compound **21**. After purification by flash chromatography (PE/MTBE, 40:1), **21** (514 mg, 1.18 mmol, 59 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.28-7.27 (m, 1 H, Ar-*H*), 7.24-7.14 (m, 3 H, Ar-*H*), 7.05-7.01 (m, 2 H, Ar-*H*), 6.57-6.56 (m, 2 H, Ar-*H*), 4.02 (d, J = 14.4 Hz, 1 H, CH_2), 2.85-2.77 (m, 2 H, CH_2, C*H*), 2.72-2.63 (m, 2 H, CH_2, C*H*), 2.17-2.06 (m, 1 H, CH_2), 1.92-1.86 (m, 1 H, CH_2), 1.23 (d, J = 6.9 Hz, 3 H, CH_3), 1.22 (d, J = 6.8 Hz, 3 H, CH_3), 1.21-1.17 (m, 1 H, CH_2), 0.93 (d, J = 6.8 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, JMOD, $CDCl_3$): δ = 146.4 (C), 145.8 (C), 141.4 (C), 136.7 (C), 130.4 (CH), 128.6 (CH), 127.1 (CH), 126.9 (CH), 126.1 (CH), 112.6 (CH), 55.7 (CH_2), 35.9 (CH_2), 32.9 (CH), 32.9 (CH_2), 32.0 (CH), 24.2 (CH_3), 24.2 (CH_3), 19.4 (CH_3) ppm. MS (ESI, +): *m/z* (%) = 280 (32) $[M+H]^+$, 238 (11), 182 (100), 134 (3). HRMS (ESI, +): $[M+H]^+$ calculated for $C_{20}H_{26}N^+$: 280.2063, found: 280.2065. IR (ATR, neat): 1/λ = 3062, 3023, 2954, 2925, 2868, 1614, 1598,1567, 1512, 1490, 1454, 1370, 1351, 1304, 1281, 1255, 1219, 1191, 1176, 1147, 1124, 1085, 1052, 1040, 1022, 944, 895, 865, 843, 817, 782, 752, 699, 644, 624, 579 cm^{-1}.

*4.11. Synthesis of 1-(4-chlorophenyl)-3-methyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**22**)*

General procedure B was used to synthesize compound **22**. After purification by flash chromatography (PE/MTBE, 40:1), **22** (386 mg, 1.42 mmol, 71 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.28-7.14 (m, 4 H, Ar-*H*), 7.08-7.04 (m, 2 H, Ar-*H*), 6.49-6.47 (m, 2 H, Ar-*H*), 3.96 (d, J = 14.6 Hz, 1 H, CH_2), 2.82-2.77 (m, 1 H, CH_2), 2.66-2.58 (m, 2 H, CH_2, C*H*), 2.12-2.04 (m, 1 H, CH_2), 1.90-1.87 (m, 1 H, CH_2), 1.21-1.13 (m, 1 H, CH_2), 0.92 (d, J = 6.8 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, JMOD, $CDCl_3$): δ = 146.3 (C), 145.6 (C), 141.5 (C), 130.6 (CH), 128.9 (CH), 128.6 (CH), 127.4 (CH), 126.7 (CH), 121.0 (C), 113.5 (CH), 55.7 (CH_2), 35.0 (CH_2), 32.8 (CH_2), 31.8 (CH), 19.3 (CH_3) ppm. MS (ESI, +): *m/z* (%) = 272 (8) $[M+H]^+$, 237 (8), 216 (13), 181 (100). HRMS (ESI, +): $[M+H]^+$ calculated for $C_{17}H_{19}ClN^+$: 272.1202, found: 272.1206. IR (ATR, neat): 1/λ = 3063, 3038, 2949, 2925, 2870, 2847, 1592, 1489, 1454, 1439, 1371, 1352, 1308, 1283, 1259, 1250, 1219, 1176, 1127, 1097, 1085, 1064, 1040, 1022, 999, 944, 925, 895, 842, 811, 772, 750, 725, 699, 650, 637, 622, 583, 559 cm^{-1}.

*4.12. Synthesis of 3-methyl-1-(4-(methylthio)phenyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**23**)*

General procedure B was used to synthesize compound **23**. After purification by flash chromatography (PE/MTBE, 40:1), **23** (447 mg, 1.58 mmol, 79 %) was isolated as a brown oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.28-7.26 (m, 1 H, Ar-*H*), 7.24-7.21 (m, 1 H, Ar-*H*), 7.19-7.16 (m, 4 H, Ar-*H*), 6.54-6.52 (m, 2 H, Ar-*H*), 3.99 (d, J = 14.5 Hz, 1 H, CH_2), 2.82-2.77 (m, 1 H, CH_2), 2.65-2.62 (m, 2 H, CH_2, C*H*), 2.39 (s, 3 H, CH_3), 2.15-2.06 (m, 1 H, CH_2), 1.91-1.86 (m, 1 H, CH_2), 1.21-1.14 (m, 1 H, CH_2), 0.93 (d, J = 6.8 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, JMOD, $CDCl_3$): δ = 146.6 (C), 145.7 (C), 141.4 (C), 131.4 (CH), 130.5 (CH), 128.6 (CH), 127.3 (CH), 126.6 (CH), 123.0 (C), 113.0 (CH), 55.6 (CH_2), 35.0 (CH_2), 32.8 (CH_2), 31.9 (CH), 19.3 (CH_3), 19.1 (CH_3) ppm. MS (ESI, +): *m/z* (%) = 284 (51) $[M+H]^+$, 237 (40), 181 (100), 138 (18). HRMS (ESI, +): $[M+H]^+$ calculated for $C_{18}H_{22}NS^+$: 284.1470, found: 284.1473. IR (ATR, neat): 1/λ = 3063, 3028, 2947, 2916, 2868, 2845, 1589, 1553, 1491, 1454, 1437, 1371, 1351, 1306**,** 1280, 1280, 1258, 1249, 1219, 1191, 1175, 1132**,** 1105, 1084, 1063, 1039, 966, 945, 895, 866, 842, 812, 778, 750, 647, 623, 583, 559 cm^{-1}.

*4.13. Synthesis of 1-(3-fluorophenyl)-3-methyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (**24**)*

General procedure B was used to synthesize compound **24**. After purification by flash chromatography (PE/MTBE, 40:1), **24** (316 mg, 1.24 mmol, 62 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.28-7.25 (m, 1 H, Ar-*H*), 7.24-7.16 (m, 3 H, Ar-*H*), 7.07-7.02 (m, 1 H, Ar-*H*), 6.35-6.31 (m, 2 H, Ar-*H*), 6.27-6.24 (m, 1 H, Ar-*H*), 3.96 (d, J = 14.6 Hz, 1 H, CH_2), 2.80 (dd, J = 13.9, 11.8 Hz, 1 H, CH2), 2.66-2.60 (m, 2 H, CH_2, C*H*), 2.15-2.06 (m, 1 H, CH_2), 1.92-1.87 (m, 1 H, CH_2), 1.21-1.13 (m, 1 H, CH_2), 0.93 (d, J = 6.8 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, DEPT, $CDCl_3$): δ = 163.2 (d, $^1J_{C,F}$ = 242 Hz, C), 148.5 (d, $^3J_{C,F}$ = 11 Hz, C), 144.4 (C), 140.5 (C), 129.6 (CH), 129.1 (d, $^3J_{C,F}$ = 10 Hz, CH), 127.6 (CH), 126.4 (CH), 125.9 (CH), 106.9 (CH), 101.7 (d, $^2J_{C,F}$ = 22 Hz, CH), 98.3 (d, $^3J_{C,F}$ = 26 Hz, CH), 54.7 (CH_2), 34.1 (CH_2), 31.8 (CH_2), 30.9 (CH), 18.3 (CH_3) ppm. MS (ESI, +): *m/z* (%) = 256 (5) $[M+H]^+$, 200 (100), 180 (45). HRMS (ESI, +): $[M+H]^+$ calculated for $C_{17}H_{19}FN^+$: 256.1494, found: 256.1502. IR (ATR, neat): 1/λ = 3065, 3026, 2949, 2925, 2871, 2848, 1619, 1596, 1576, 1489, 1455, 1377, 1354, 1319, 1299, 1265, 1250, 1221, 1200, 1186, 1172, 1153, 1116, 1093, 997, 974, 933, 909, 884, 865, 821, 777, 754, 700, 680, 632, 602, 582 cm^{-1}.

*4.14. Synthesis of N-(2-methyl-3-phenoxypropyl)aniline (**27**)*

General procedure A (10 mol% **I**, 140 °C, 48 h) was used to synthesize compound **27**. After purification by flash chromatography (PE/MTBE, 40:1), **27** (338 mg, 1.40 mmol, 70 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ =

7.31-7.27 (m, 2 H, Ar-*H*), 7.19-7.16 (m, 2 H, Ar-*H*), 6.97-6.95 (m, 1 H, Ar-*H*), 6.97-6.91 (m, 2 H, Ar-*H*), 6.71-6.69 (m, 1 H, Ar-*H*), 6.71-6.64 (m, 2 H, Ar-*H*), 4.21 (br. s, N*H*), 3.96 (dd, *J* = 6.4, 9.1 Hz, 1 H, CH_2), 3.91 (dd, *J* = 6.4, 9.1 Hz, 1 H, CH_2), 3.30 (dd, *J* = 7.0, 12.7 Hz, 1 H, CH_2), 3.16 (dd, *J* = 6.1, 12.7 Hz, 1 H, CH_2), 2.33 (oct, *J* = 6.5 Hz, 1 H, C*H*), 1.13 (d, *J* = 6.9 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 158.9 (C), 148.2 (C), 129.4 (CH), 129.3 (CH), 120.8 (CH), 117.4 (CH), 114.5 (CH), 112.9 (CH), 71.3 (CH_2), 47.9 (CH_2), 33.2 (CH), 15.4 (CH_3) ppm. GC-MS (EI, 70 eV): *m/z* (%) = 241 (38) $[M]^+$, 106 (100) $[C_7H_8N]^+$, 94 (14) $[C_6H_5O]^+$, 77 (52) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{16}H_{19}NO^+$: 241.1467, found: 241.1460. IR (ATR, neat): 1/λ = 3417, 3056, 2958, 2923, 2874, 1599, 1586, 1496, 1467, 1433, 1392, 1320, 1300, 1241, 1173, 1153, 1078, 1053, 1001, 988, 881, 869, 812, 747, 690, 611, 601 cm^{-1}.

*4.15. Synthesis of N-(3-(2-bromophenoxy)-2-methylpropyl)-aniline (**28**)*

General procedure A (20 mol% **I**, 160 °C, 48 h) was used to synthesize compound **28**. After purification by flash chromatography (PE/MTBE, 40:1), **28** (384 mg, 1.20 mmol, 60 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.47 (dd, *J* = 7.9, 1.6 Hz, 1 H, Ar-*H*), 7.19-7.15 (m, 1 H, Ar-*H*), 7.12-7.08 (m, 2 H, Ar-*H*), 6.80-6.71 (m, 2 H, Ar-*H*), 6.66-6.55 (m, 3 H, Ar-*H*), 4.25 (br. s, N*H*), 3.98 (dd, *J* = 8.9, 4.4 Hz, 1 H, CH_2), 3.85 (dd, *J* = 8.9, 6.8 Hz, 1 H, CH_2), 3.26 (dd, *J* = 12.7, 7.4 Hz, 1 H, CH_2), 3.15 (dd, *J* = 12.7, 5.3 Hz, 1 H, CH_2), 2.35-2.29 (m, 1 H, C*H*), 1.08 (d, *J* = 7.0 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 155.1 (C), 148.3 (C), 133.3 (CH), 129.2 (CH), 128.5 (CH), 121.9 (CH), 117.1 (CH), 112.8 (CH), 112.7 (CH), 112.1(C), 72.8 (CH_2), 48.2 (CH_2), 33.1 (CH), 15.4 (CH_3) ppm. GC-MS (EI, 70 eV): *m/z* (%) = 319 (25) $[C_{16}H_{18}{}^{79}BrNO]^+$, 172 (6) $[C_6H_4{}^{79}BrO]^+$, 106 (100) $[C_7H_8N]^+$, 77 (39) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{16}H_{18}{}^{79}BrNO^+$: 319.0564, found: 319.0566. IR (ATR, neat): 1/λ = 3415, 3380, 3338, 3049, 3016, 2959, 2930, 2877, 1602, 1587, 1506, 1480, 1462, 1443, 1320, 1276, 1246, 1179, 1154, 1127, 1050, 1029, 990. 827, 744, 692, 665 cm^{-1}.

*4.16. Synthesis of N-(2-methyl-3-(phenylthio)propyl)aniline (**31**)*

General procedure A (10 mol% **I**, 140 °C, 48 h) was used to synthesize compound **31**. After purification by flash chromatography (PE/MTBE, 40:1), **31** (283 mg, 1.10 mmol, 55 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34-7.31 (m, 2 H, Ar-*H*), 7.28-7.24 (m, 2 H, Ar-*H*), 7.21-7.12 (m, 3 H, Ar-*H*), 6.69-6.64 (m, 1 H, Ar-*H*), 6.59-6.57 (m, 2 H, Ar-*H*), 3.90 (br. s, N*H*), 3.23 (dd, *J* = 12.9, 6.5 Hz, 1 H, CH_2), 3.05 (dd, *J* = 12.3, 6.0 Hz, 1 H, CH_2), 3.04 (dd, *J* = 13.0, 6.8 Hz, 1 H, CH_2), 2.86 (dd, *J* = 12.9, 6.8 Hz, 1 H, CH_2), 2.09 (oct, *J* = 6.6 Hz, 1 H, C*H*), 1.10 (d, *J* = 6.7 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 148.1 (C), 136.8 (C), 129.4 (CH), 129.1 (CH), 128.9 (CH), 125.9 (CH), 117.3 (CH), 112.8 (CH), 49.2 (CH_2), 38.8 (CH_2), 33.0 (CH), 17.9 (CH_3) ppm. GC-MS (EI, 70 eV): *m/z* (%) = 257 (39) $[M]^+$, 109 (11) $[C_6H_5S]^+$, 106 (100) $[C_7H_8N]^+$, 77 (45) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{16}H_{19}NS^+$: 257.1233, found: 257.1235. IR (ATR, neat): 1/λ = 3417, 3370, 3057, 3018, 2959, 2927, 2873, 1723, 1604, 1587, 1507, 1481, 1439, 1380, 1321, 1263, 1181, 1155, 1123, 1089, 1073, 1027, 993, 870, 741, 692, 622, 604 cm^{-1}.

*4.17. Synthesis of N-(3-((2-bromophenyl)thio)-2-methylpropyl)aniline (**32**)*

General procedure A (20 mol% **I**, 160 °C, 48 h) was used to synthesize compound **32**. After purification by flash chromatography (PE/MTBE, 40:1), **32** (478 mg, 1.42 mmol, 71 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.49 (dd, *J* = 7.9, 1.3 Hz, 1 H, Ar-*H*), 7.22-7.17 (m, 1 H, Ar-*H*), 7.17-7.09 (m, 3 H, Ar-*H*), 6.98-6.94 (m, 1 H, Ar-*H*), 6.67 (t, *J* = 7.3 Hz, 1 H, Ar-*H*), 6.58 (d, *J* = 7.7 Hz, 2 H, Ar-*H*), 3.21 (dd, *J* = 13.1, 6.8 Hz, 1 H, CH_2), 3.08 (dd, *J* = 13.1, 6.4 Hz, 1 H, CH_2), 3.05 (dd, *J* = 12.9, 6.0 Hz, 1 H, CH_2), 2.81 (dd, *J* = 12.6, 7.1 Hz, 1 H, CH_2), 2.12 (oct, *J* = 6.7 Hz, 1 H, C*H*), 1.11 (d, *J* = 6.7 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 147.9 (C), 138.1 (C), 133.0 (CH), 129.3 (CH), 128.1 (CH), 127.7 (CH), 126.5 (CH), 123.6 (C), 117.5 (CH), 112.9 (CH), 49.3 (CH_2), 38.0 (CH_2), 32.6 (CH), 18.0 (CH_3) ppm. GC-MS (EI, 70 eV): *m/z* (%) = 335 (26) $[C_{16}H_{18}{}^{79}BrNS]^+$, 132 (7), 106 (100) $[C_7H_8N]^+$, 77 (45) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{16}H_{18}{}^{79}BrNS^+$: 335.0338, found: 335.0338. IR (ATR, neat): 1/λ = 3416, 3364, 3052, 3021, 2957, 2927, 2868, 1601, 1558, 1505, 1448, 1427, 1379, 1320, 1255, 1179, 1154, 1107, 1070, 1040, 1019, 991, 868, 742, 714, 691 cm^{-1}.

*4.18. Synthesis of 3-methyl-5-phenyl-2,3,4,5-tetrahydrobenzo[b]-[1,4]oxazepine (**33**)*

General procedure C was used to synthesize compound **33** from **28** (532 mg, 1.66 mmol). After purification by flash chromatography (PE/MTBE, 40:1), **33** (304 mg, 1.27 mmol, 77 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.23-7.18 (m, 2 H, Ar-*H*), 7.12-7.10 (m, 1 H, Ar-*H*), 7.05-7.01 (m, 2 H, Ar-*H*), 6.95-6.90 (m, 3 H, Ar-*H*), 6.81-6.78 (m, 1 H, Ar-*H*), 4.20 (dd, *J* = 11.9, 4.1 Hz, 1 H, CH_2), 4.12 (dd, *J* = 14.8, 5.2 Hz, 1 H, CH_2), 3.75 (dd, *J* = 12.0, 4.9 Hz, 1 H, CH_2), 3.31 (dd, *J* = 14.7, 10.1 Hz, 1 H, CH_2), 2.34-2.43 (m, 1 H, C*H*), 1.00 (d, *J* = 6.9 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 155.1 (C), 148.3 (C), 136.9 (C), 129.2 (CH), 127.7 (CH), 125.3 (CH), 122.5 (CH), 121.5 (CH), 118.8 (CH), 116.1 (CH), 75.2 (CH_2), 54.3 (CH_2), 32.3 (CH), 15.2 (CH_3) ppm. GC-MS (EI, 70 eV): *m/z* (%) = 239 (54) $[M]^+$, 196 (100), 77 (12) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{16}H_{17}NO^+$: 239.1305, found: 239.1304. IR (ATR, neat): 1/λ = 3070, 3028, 2957, 1733, 1591, 1490, 1459, 1386, 1364, 1352, 1327, 1304, 1291, 1266, 1245, 1224, 1191, 1153, 1092, 1069, 1035, 1015, 985, 961, 940, 922, 850, 787, 744, 691, 627 cm^{-1}.

*4.19. Synthesis of 3-methyl-5-phenyl-2,3,4,5-tetrahydrobenzo[b]-[1,4]thiazepine (**34**)*

General procedure C was used to synthesize compound **34** from **32** (466 mg, 1.39 mmol). After purification by flash chromatography (PE/MTBE, 40:1), **34** (323 mg, 1.26 mmol, 91 %) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.7 Hz, 1 H, Ar-*H*), 7.20-7.16 (m, 4 H, Ar-*H*), 7.09-7.06 (m, 1 H, Ar-*H*), 6.79-6.69 (m, 3 H, Ar-*H*), 4.06 (dd, *J* = 15.2, 3.8 Hz, 1 H, CH_2), 3.27 (dd, *J* = 15.2, 10.7 Hz, 1 H, CH_2), 3.09 (dd, *J* = 13.9, 3.6 Hz, 1 H, CH_2), 2.52-2.47 (m, 1 H, C*H*), 2.43 (dd, *J* = 13.9, 6.7 Hz, 1 H, CH_2), 1.03 (d, *J* = 6.6 Hz, 3 H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 147.5 (C), 147.2 (C), 134.0 (C), 132.2 (CH), 129.1 (CH), 128.8 (CH), 127.5 (CH), 125.3 (CH), 117.8 (CH), 114.6 (CH), 54.5 (CH_2), 38.0 (CH_2), 31.9 (CH), 17.5 (CH_3) ppm. GC-MS (EI, 70 eV): *m/z* (%) = 255 (66) $[M]^+$, 212 (100), 108 (31), 77 (18) $[C_6H_5]^+$. HRMS (EI, 70 eV): $[M]^+$ calculated for $C_{16}H_{17}NS^+$: 255.1076, found: 255.1073. IR (ATR, neat): 1/λ = 3057, 2953, 2934, 2871, 1598, 1581, 1560, 1495, 1472, 1434, 1370, 1351, 1323, 1298, 1260, 1236, 1181, 1156, 1124, 1098, 1057, 1033, 991, 942, 879, 854, 825, 799, 741, 728, 691, 624 cm^{-1}.

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Supplementary Material

Supplementary data to this article (^{1}H NMR and ^{13}C NMR spectra) can be found online at https://doi.org/10.1016/_____.