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Diversity-Oriented Microwave-Assisted Synthesis of the 3-Benzazepine Framework

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An efficient diversity-oriented procedure for the two-step synthesis of 3-benzazepines is described. The Cu^I-catalyzed three-component coupling of an aldehyde, an alkyne and an amine (A^3-coupling) provides the required propargylamines and assures the generation of diversity. The Pd-catalyzed intramolecular acetylene hydroarylation reaction selectively creates the seven-membered 3-benzazepine framework with full control over the ring size and the geometry around the double bond. Microwave irradiation is demonstrated to be highly efficient in promoting both steps.

Introduction

The 3-benzazepine framework is widespread among biologically active and natural compounds. Several efforts have been made towards the synthesis of alkaloids such as aphanorphine,[1] lennoxamine,[2] and cephalotaxine[3] (Figure 1) due to their challenging chemical structures and interesting biological activities. Dizocilpine, also known as MK-801, represents a noncompetitive *N*-methyl-D-aspartate (NMDA) receptor antagonist and has been extensively studied for treatment of neurodegenerative diseases such as Huntington's, Alzheimer's, and amyotrophic lateral sclerosis.[4] Variously substituted at position 1, different 3-benzazepines have been synthesized and studied for the use as potent NMDA receptor antagonists (Figure 1).[5]

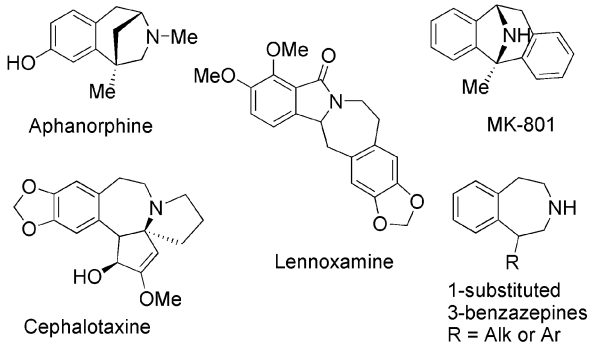

Figure 1. Alkaloids and NMDA receptor antagonist containing the 3-benzazepine framework.

The seven-membered ring of the 3-benzazepine scaffold has been constructed through various methods including intramolecular Friedel–Crafts alkylation,[1b–1d,6] intramolecular radical cyclization[1a,1e] and C–N bond formation via intramolecular reductive amination.[5] Transition-metal-catalyzed reactions were also used for generating the 3-benzazepine framework.[3a,3b,7] Recently, we have reported a novel approach towards the selective and facile formation of 1-substituted 3-benzazepinones through the microwave-assisted Pd-catalyzed intramolecular acetylene hydroarylation[8–9] reaction, which occurs with full regio- and stereoselectivity.[10]

Results and Discussion

Herein we wish to report a new and efficient two-step protocol for the diversity-oriented synthesis of 3-benzazepines **3**, applying a microwave-assisted Cu^I-catalyzed three-component coupling of an aldehyde, an alkyne and an amine (well established multicomponent reaction commonly called A^3-coupling)[11–12] providing the required propargylamines **2**, followed by a regio- and stereoselective Pd-catalyzed intramolecular acetylene hydroarylation (Scheme 1).

The reaction conditions for the A^3-coupling were optimized applying the 2-phenylethylamine **1a**,[13] isovaleraldehyde and phenylacetylene in a ratio (1:1.1:2).[14] The reaction was performed with 10 mol-% CuI as the catalyst under solventless conditions. Gratifyingly upon microwave irradiation at a ceiling temperature of 90 °C and a maximum power of 50 W for 30 min the desired propargylamine **2a** was formed in 79% yield (Table 1, entry 1). Increasing the amount of catalyst to 15 mol-% resulted in an excellent

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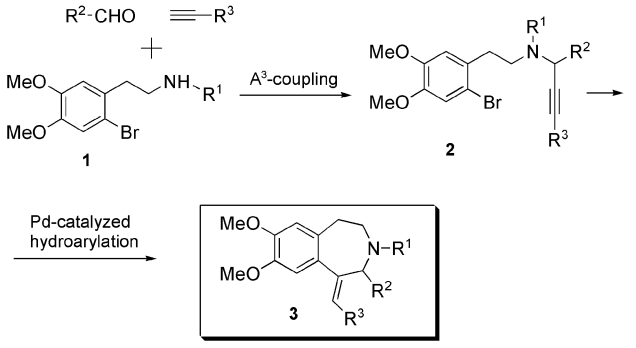
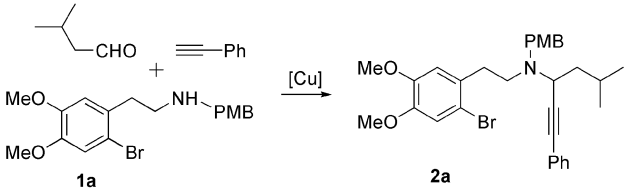


Scheme 1. Retrosynthesis for the construction of the 3-benzazepine framework.

yield of 92% (Table 1, entry 2). The application of CuBr instead of CuI delivered compound **2a** in a comparable yield of 86% (Table 1, entry 3). However, when the reaction was conducted at a lower temperature of 70 °C the propargylamine **2a** was obtained in a moderate yield of 68% (Table 1, entry 4). Also a shorter irradiation time of 20 min resulted in a lower yield (Table 1, entry 5). Solventless conditions seemed to be appropriate as the use of toluene resulted in a comparable yield of 89% (Table 1, entry 6). When the reaction was conducted under conventional heating at 90 °C for 3 h the desired propargylamine **2a** was also obtained in a high yield of 90% (Table 1, entry 7). However, our attempt to perform the reaction at 25 °C met with failure (Table 1, entry 8).

Table 1. Optimization of the A^3-coupling conditions.[a]

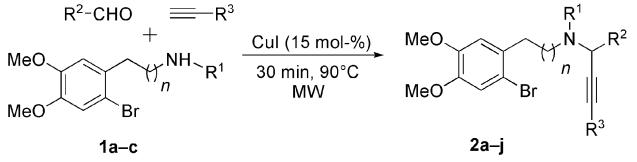


Entry	Temp. [°C]	Catalyst (mol-%)	Time [min]	Condition[b]	Yield[c]
1	90	CuI (10)	30	neat, MW	79
2	90	CuI (15)	30	neat, MW	92
3	90	CuBr (15)	30	neat, MW	86
4	70	CuI (15)	30	neat, MW	68
5	90	CuI (15)	20	neat, MW	76
6	90	CuI (15)	30	toluene, MW	89
7	90	CuI (15)	3 h	toluene, conventional	90
8	25	CuI (5)	24 h	toluene, conventional	–[d]

[a] The reactions were performed with the amine **1a** (0.5 mmol), isovaleraldehyde (0.55 mmol) and phenylacetylene (1 mmol). [b] When the reaction was run under microwave irradiation a maximum power of 50 W was used. [c] Isolated yields are reported. [d] 2-Phenylethylamine **1a** was recovered.

Having the optimized microwave-assisted protocol at hand, we generated a small library of propargylamines **2a**–**j** (Table 2). An array of aromatic and aliphatic alkynes and aldehydes were successfully explored as partners in the A^3-coupling reaction with various amines **1a**–**c**.[13] All reactions proceeded smoothly delivering the corresponding propargylamines **2a**–**j** in 73–95% yield (Table 2, entries 1–10). To circumvent problems associated with the handling of gaseous formaldehyde, 1,3,5-trioxane was successfully used (Table 2, entry 6). In one case the use of toluene was required to prevent the formation of a side-product due to double addition of alkyne to amine (vide infra) (Table 2, entry 5).[15]

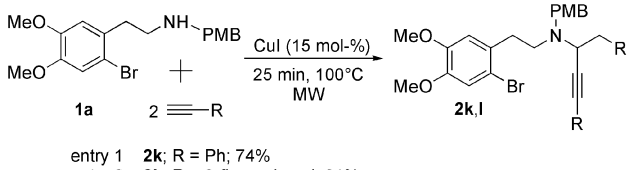
Table 2. Generation of propargylamines applying the optimized A^3-coupling protocol.[a]



Entry (product)	R^1, *n*	R^2	R^3	Yield[b]
1 (**2a**)	PMB, 1	*i*Bu	Ph	92
2 (**2b**)	PMB, 1	*i*Bu	4-fluorophenyl	87
3 (**2c**)	PMB, 1	Pr	Ph	95
4 (**2d**)	PMB, 1	Ph	Pr	73
5 (**2e**)	PMB, 1	Ph	4-methoxyphenyl	81[c]
6 (**2f**)	PMB, 1	H[d]	Ph	80
7 (**2g**)	*i*Pr, 1	*i*Bu	Ph	86
8 (**2h**)	*i*Pr, 1	*i*Bu	thiophene-3-yl	81
9 (**2i**)	PMB, 2	*i*Bu	Ph	82
10 (**2j**)	PMB, 2	Pr	4-methoxyphenyl	91

[a] The reactions were carried out with the amine **1** (0.5 mmol), an aldehyde (0.55 mmol) and an alkyne (1 mmol) in the presence of CuI (15 mol-%), neat, under microwave irradiation at a ceiling temperature of 90 °C and a maximum power of 50 W for 30 min. [b] Isolated yields are reported. [c] The reaction was performed in toluene (2 mL). [d] The reaction was performed with 1,3,5-trioxane (0.2 mmol).

We have also examined the Cu^I-catalyzed tandem *anti*-Markovnikov hydroamination and alkyne addition reaction recently reported by Li for the synthesis of propargylamines[15] (Scheme 2). Gratifyingly propargylamines **2k**,**l** resulted from the reaction of alkyne and amine **1a** in a ratio (1.5:0.5), using similar microwave-assisted conditions as for our A^3-coupling protocol, at a slightly increased ceiling temperature of 100 °C (Scheme 2).

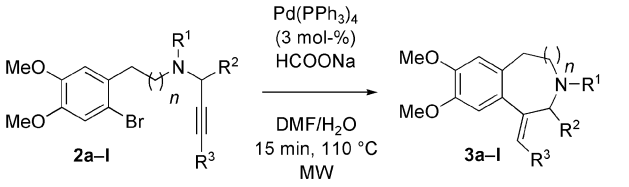


Scheme 2. Generation of propargylamines **2k**,**l** via a Cu^I-catalyzed tandem *anti*-Markovnikov hydroamination, alkyne addition reaction.

We then investigated the cyclization of the generated propargylamines **2a**–**h**,**k**,**l** applying our previously reported Pd-catalyzed intramolecular acetylene hydroarylation protocol that was developed for propargylic amides.[10] Carrying out the reactions under microwave irradiation at a ceiling tem-

perature of 110 °C and a maximum power of 100 W for 15 min in the presence of 3 mol-% of $Pd(PPh_3)_4$ as the catalyst and sodium formate as the reducing agent, the desired 3-benzazepines **3a**–**h**,**k**,**l** were obtained in yields of 63–91% (Table 3, entries 1–8, 11–12). To explore the general applicability of our strategy for the synthesis of medium-sized rings, we also evaluated the protocol for the generation of benzo-azocines. Reacting the propargylamines **2i**,**j** we were able to achieve the expanded 8-membered rings **3i**,**j** in 40% and 32%, respectively (Table 3, entries 9 and 10). The lower yields could probably be ascribed to the higher conformational freedom of the starting propargylamines **2i**,**j**. As a result the formation of considerable amount of debrominated by-product **4** was observed (see Scheme 3).

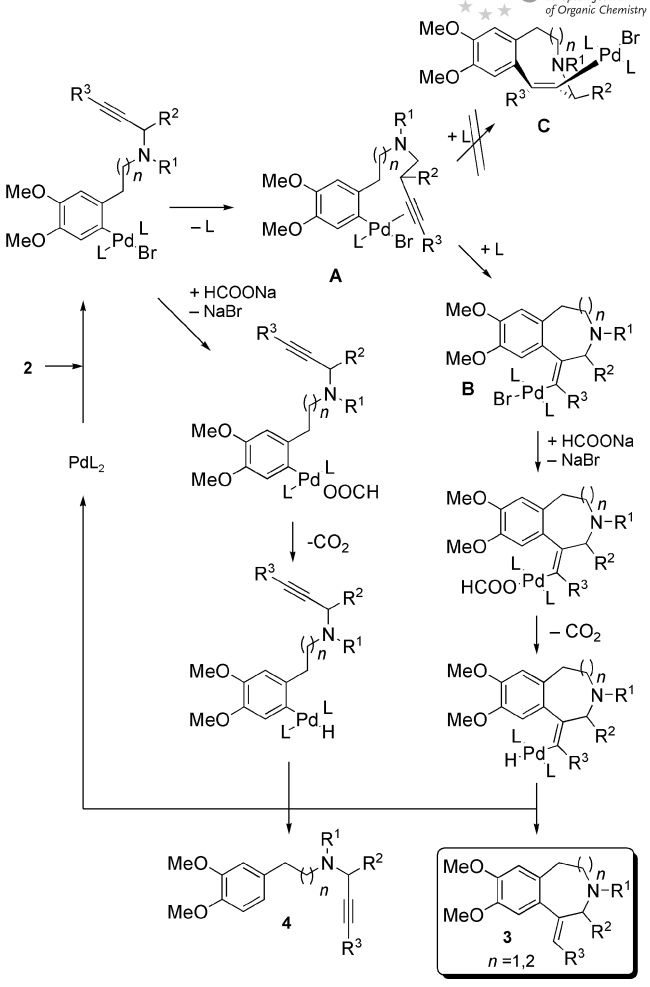
Table 3. Scope and limitations of the process.[a]



Entry (product)	R^1, *n*	R^2	R^3	Yield[b]
1 (**3a**)	PMB, 1	*i*Bu	Ph	80
2 (**3b**)	PMB, 1	*i*Bu	4-fluorophenyl	84
3 (**3c**)	PMB, 1	Pr	Ph	91
4 (**3d**)	PMB, 1	Ph	Pr	77
5 (**3e**)	PMB, 1	Ph	4-methoxyphenyl	70
6 (**3f**)	PMB, 1	H	Ph	70
7 (**3g**)	*i*Pr, 1	*i*Bu	Ph	72
8 (**3h**)	*i*Pr, 1	*i*Bu	thiophene-3-yl	73
9 (**3i**)	PMB, 2	*i*Bu	Ph	40
10 (**3j**)	PMB, 2	Pr	4-methoxyphenyl	32
11 (**3k**)	PMB, 1	Bn	Ph	71
12 (**3l**)	PMB, 1		3-fluorophenyl	63

[a] The reactions were carried out with propargylamines **2a**–**l** (0.4 mmol) in the presence of HCOONa (0.6 mmol) and $Pd(PPh_3)_4$ (3 mol-%) in DMF/H_2O (3:1) (6 mL), under microwave irradiation at a ceiling temperature of 110 °C and a maximum power of 100 W for 15 min. [b] Isolated yields are reported.

A possible pathway of the Pd-catalyzed intramolecular acetylene hydroarylation is presented in Scheme 3. Due to the *syn*-addition to the triple bond, our strategy exclusively provides compounds **3** possessing the *Z*-configuration of the exocyclic double bond. Moreover, the regioselectivity of the hydroarylation reaction and, as a result, the ring size of the generated medium-sized ring, is also governed by the mode of reaction. As the initially generated arylpalladium π-complex **A** is transformed into a σ-vinyl palladium complex **B** via simultaneous *syn*-addition to the triple bond, endocyclization via a hypothetical intermediate **C** is fairly unlikely due to the high strain exerted by the *trans*-geometry around the double bond in the medium-sized ring. As a result only 7- or eight-membered rings are formed (*n* = 1 or 2). An alternative pathway resulting in the formation of the debrominated by-product **4** is also presented (Scheme 3).



Scheme 3. Proposed pathway of the Pd-catalyzed intramolecular acetylene hydroarylation reaction.

Conclusions

In summary, we have developed a new and efficient two-step protocol for the diversity-oriented synthesis of 3-benzazepines. The first step is a Cu^I-catalyzed three-component coupling of an aldehyde, an alkyne and an amine (A^3-coupling) leading to propargylamines, that are the key intermediates for the regio- and stereoselective Pd-catalyzed intramolecular acetylene hydroarylation that generates the 3-benzazepine skeleton. Microwave irradiation is demonstrated to be highly effecient in promoting both steps. The applicability of this strategy for the synthesis of some benzazepine alkaloids and analogues is under current investigation.

Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 instrument. The ^1H and ^{13}C chemical shifts were reported

in parts per million (ppm) relative to tetramethylsilane using the residual solvent signal as the internal reference. Mass spectra were run using a Micromass Quattro II apparatus (ESI) with MASSLYNX data system or a Thermo Finnigan LCQ Advantage apparatus (ESI). High-resolution mass spectra were recorded on a Kratos MS50TC system. The ion source temperature was 150–250 °C, as required. High-resolution EI-mass spectra were recorded with a resolution of 10000.

Microwave Irradiation Experiments: All microwave irradiation experiments were carried out in a dedicated CEM-Discover monomode microwave apparatus, operating at a frequency of 2.45 GHz with continuous irradiation power from 0–300 W. The reactions were carried out in 10 mL glass tubes, sealed with Teflon™ septum and placed in the microwave cavity. The reaction mixture was irradiated at the indicated ceiling temperature and maximum power for the stipulated time. Then it was cooled to ambient temperature with gas jet cooling.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-(4-methoxybenzyl)-5-methyl-1-phenylhex-1-yn-3-amine (2a):** General experimental procedure for A^3-coupling: Amine 1a (190 mg, 0.5 mmol), isovaleraldehyde (47 mg, 0.55 mmol), phenylacetylene (102 mg, 1 mmol) and CuI (14 mg, 15 mol-%) were loaded into the microwave instrument vial. The vial was evacuated and flushed with argon. The vial was sealed and irradiated with stirring at a ceiling temperature of 90 °C at 50 W maximum power level for 30 min. Upon completion of the reaction time the vial was cooled with a stream of air. The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine 2a as a yellow oil (256 mg, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.50–7.42 (m, 2 H), 7.36–7.25 (m, 5 H), 7.00 (s, 1 H), 6.86 (d, J = 8.6 Hz, 2 H), 6.68 (s, 1 H), 3.93 (d, J = 13.5 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 3.73 (t, J = 7.6 Hz, 1 H), 3.57 (d, J = 13.5 Hz, 1 H), 2.99–2.78 (m, 3 H), 2.75–2.62 (m, 1 H), 1.88–1.74 (m, 1 H), 1.70–1.47 (m, 2 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.81 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.57, 148.11, 147.85, 131.95, 131.78, 131.73, 130.05, 128.21, 127.77, 123.56, 115.40, 114.15, 113.67, 113.49, 88.79, 84.62, 56.12, 55.95, 55.23, 51.31, 50.87, 42.94, 35.12, 24.63, 22.78, 22.23 ppm. MS (ESI^+) calcd. for $C_{31}H_{36}BrNO_3$: 549.2; found: m/z 550.8 $[M + H]^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-1-(4-fluorophenyl)-*N*-(4-methoxybenzyl)-5-methylhex-1-yn-3-amine (2b):** Synthesized from isovaleraldehyde (47 mg, 0.55 mmol), 1-ethynyl-4-fluorobenzene (120 mg, 1 mmol) and amine **1a** (190 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2b** as a yellow oil (247 mg, 87%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.47–7.40 (m, 2 H), 7.30 (d, J = 8.6 Hz, 2 H), 7.0.5–6.97 (m, 3 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.68 (s, 1 H), 3.93 (d, J = 13.6 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 3.72 (t, J = 7.6 Hz, 1 H), 3.55 (d, J = 13.6 Hz, 1 H), 2.97–2.79 (m, 3 H), 2.72–2.62 (m, 1 H), 1.87–1.74 (m, 1 H), 1.69–1.60 (m, 1 H), 1.57–1.47 (m, 1 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.81 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 163.44, 160.97, 158.66, 148.23, 147.99, 133.59, 133.51, 132.00, 131.80, 130.04, 119.71, 119.67, 115.55, 115.54, 115.32, 114.21, 113.83, 113.56, 88.53, 88.52, 83.57, 56.17, 56.01, 55.48, 55.26, 51.37, 50.95, 43.01, 35.20, 24.68, 22.79, 22.23 ppm. MS (ESI^+) calcd. for $C_{31}H_{35}BrFNO_3$: 567.2; found: m/z 568.7 $[M + H]^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-(4-methoxybenzyl)-1-phenylhex-1-yn-3-amine (2c):** Synthesized from butyraldehyde (40 mg, 0.55 mmol), phenylacetylene (102 mg, 1 mmol) and amine **1a** (190 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2c** as a yellow oil (255 mg, 95%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.47–7.39 (m, 2 H), 7.34–7.20 (m, 5 H), 6.97 (s, 1 H), 6.83 (d, J = 8.6 Hz, 2 H), 6.65 (s, 1 H), 3.91 (d, J = 13.7 Hz, 1 H), 3.84 (s, 3 H), 3.82–3.78 (m, 6 H), 3.63 (t, J = 7.5 Hz, 1 H), 3.54 (d, J = 13.7 Hz, 1 H), 2.99–2.60 (m, 4 H), 1.71–1.58 (m, 2 H), 1.46–1.32 (m, 2 H), 0.85 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.55, 148.13, 147.85, 132.02, 131.91, 131.75, 129.94, 128.22, 127.77, 123.59, 115.41, 114.17, 113.68, 113.52, 88.75, 84.67, 56.14, 55.96, 55.31, 55.26, 53.09, 50.90, 36.23, 35.06, 19.73, 13.86 ppm. MS (ESI^+) calcd. for $C_{30}H_{34}BrNO_3$: 535.2; found: m/z 536.9 $[M + H]^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-(4-methoxybenzyl)-1-phenylhex-2-yn-1-amine (2d):** Synthesized from benzaldehyde (58 mg, 0.55 mmol), pent-1-yne (68 mg, 1 mmol) and amine **1a** (190 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2d** as a yellow oil (196 mg, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.55–7.48 (m, 2 H), 7.30–7.18 (m, 5 H), 6.91 (s, 1 H), 6.82 (d, J = 8.6 Hz, 2 H), 6.48 (s, 1 H), 4.73 (s, 1 H), 3.85–3.70 (m, 10 H), 3.49 (d, J = 13.4 Hz, 1 H), 2.82–2.58 (m, 4 H), 2.39–2.30 (m, 2 H), 1.72–1.58 (m, 2 H), 1.08 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.56, 147.99, 147.70, 139.93, 131.89, 131.77, 129.98, 128.27, 127.77, 127.02, 115.23, 114.18, 113.55, 113.40, 88.08, 75.37, 56.32, 56.11, 55.86, 55.24, 54.93, 50.26, 34.59, 22.66, 20.89, 13.69 ppm. MS (ESI^+) calcd. for $C_{30}H_{34}BrNO_3$: 535.2; found: m/z 536.8 $[M + H]^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-(4-methoxybenzyl)-3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-amine (2e):** Synthesized from benzaldehyde (58 mg, 0.55 mmol), 1-ethynyl-4-methoxybenzene (132 mg, 1 mmol) and amine **1a** (190 mg, 0.5 mmol). Reaction was carried out in 2 mL of toluene. The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2e** as a yellow oil (243 mg, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.61–7.54 (m, 2 H), 7.49 (d, J = 8.7 Hz, 2 H), 7.33–7.21 (m, 5 H), 6.93–6.79 (m, 5 H), 6.50 (s, 1 H), 4.95 (s, 1 H), 3.90 (d, J = 13.4 Hz, 1 H), 3.84 (s, 3 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 3.72 (s, 3 H), 3.59 (d, J = 13.4 Hz, 1 H), 2.87–2.68 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.47, 158.63, 148.02, 147.74, 139.46, 133.26, 131.78, 131.57, 130.03, 128.30, 127.90, 127.21, 115.40, 115.24, 114.19, 113.92, 113.60, 113.39, 87.88, 83.73, 56.81, 56.11, 55.85, 55.33, 55.24, 55.07, 50.40, 34.58 ppm. MS (ESI^+) calcd. for $C_{34}H_{34}BrNO_4$: 599.2; found: m/z 600.8 $[M + H]^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-(4-methoxybenzyl)-3-phenylprop-2-yn-1-amine (2f):** Synthesized from 1,3,5-trioxane (18 mg, 0.2 mmol), phenylacetylene (102 mg, 1 mmol) and amine **1a** (190 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2f** as a yellow oil (198 mg, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.50–7.40 (m, 2 H), 7.32–7.22 (m, 5 H), 6.98 (s, 1 H), 6.85 (d, J = 8.5 Hz, 2 H), 6.74 (s, 1 H), 3.83–3.75 (m, 9 H), 3.71 (s, 2 H), 3.60 (s, 2 H), 2.96–2.80 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.80, 148.30, 147.94, 131.76, 131.63, 130.58, 130.38, 128.32, 128.06, 123.35, 115.42, 114.23, 113.68, 113.36, 85.65, 84.58, 57.41, 56.15, 55.98, 55.28, 53.72, 42.28, 34.03 ppm. MS (ESI^+) calcd. for $C_{27}H_{28}BrNO_3$: 493.1; found: m/z 494.6 $[M + H]^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-isopropyl-5-methyl-1-phenylhex-1-yn-3-amine (2g):** Synthesized from isovaleraldehyde (47 mg, 0.55 mmol), phenylacetylene (102 mg, 1 mmol) and amine **1b** (151 mg, 0.5 mmol). The product was isolated by column

chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2g** as a brown oil (203 mg, 86%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.41–7.33 (m, 2 H), 7.30–7.22 (m, 3 H), 6.99 (s, 1 H), 6.72 (s, 1 H), 3.85–3.75 (m, 7 H), 3.25–3.07 (m, 1 H), 2.95–2.70 (m, 4 H); 1.90–1.72 (m, 1 H), 1.52 (t, J = 7.2 Hz, 2 H), 1.21–1.09 (m, 6 H), 0.95–0.85 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 148.13, 147.85, 132.26, 131.43, 128.18, 127.62, 123.81, 115.40, 114.14, 113.77, 91.64, 83.99, 56.13, 55.97, 50.82, 48.46, 47.28, 44.56, 36.94, 24.67, 22.62, 21.97, 18.28 ppm. MS (ESI$^+$) calcd. for $C_{26}H_{34}BrNO_2$: 471.2; found: m/z 472.8 [M + H]$^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-isopropyl-5-methyl-1-(thiophen-3-yl)hex-1-yn-3-amine (2h):** Synthesized from iso-valeraldehyde (47 mg, 0.55 mmol), 3-ethynylthiophene (108 mg, 1 mmol) and amine **1b** (151 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2h** as a brown oil (194 mg, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.28 (m, 1 H), 7.24–7.18 (m, 1 H), 7.07–7.01 (m, 1 H), 6.99 (s, 1 H), 6.72 (s, 1 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 3.76 (t, J = 7.6 Hz, 1 H), 3.22–3.06 (m, 1 H), 2.94–2.67 (m, 4 H); 1.90–1.70 (m, 1 H), 1.50 (t, J = 7.2 Hz, 2 H), 1.20–1.07 (m, 6 H), 0.95–0.83 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 148.12, 147.85, 132.26, 129.92, 127.54, 125.01, 122.78, 115.40, 114.14, 113.78, 91.17, 78.91, 56.13, 55.97, 50.74, 48.43, 47.27, 44.55, 36.99, 24.62, 22.63, 22.57, 22.01, 18.28 ppm. MS (ESI$^+$) calcd. for $C_{24}H_{32}BrNO_2S$: 477.1; found: m/z 478.7 [M + H]$^+$.

***N*-[3-(2-Bromo-4,5-dimethoxyphenyl)propyl]-*N*-(4-methoxybenzyl)-5-methyl-1-phenylhex-1-yn-3-amine (2i):** Synthesized from isovaleraldehyde (47 mg, 0.55 mmol), phenylacetylene (102 mg, 1 mmol) and amine **1c** (151 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2i** as a yellow oil (231 mg, 82%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.50–7.44 (m, 2 H), 7.37–7.31 (m, 5 H), 7.02 (s, 1 H), 6.88 (d, J = 8.6 Hz, 2 H), 6.69 (s, 1 H), 3.91–3.81 (m, 10 H), 3.75 (t, J = 7.6 Hz, 1 H), 3.46 (d, J = 13.6 Hz, 1 H), 2.86–2.67 (m, 2 H), 2.65–2.52 (m, 2 H), 2.00–1.88 (m, 1 H), 1.87–1.74 (m, 2 H), 1.71–1.54 (m, 2 H), 0.91 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.59, 148.39, 147.75, 133.99, 132.16, 131.76, 130.01, 128.25, 127.78, 123.69, 115.66, 114.04, 113.58, 112.93, 88.80, 84.77, 56.17, 56.05, 55.26, 51.34, 50.53, 43.16, 33.99, 28.88, 24.90, 22.76, 22.48 ppm. MS (ESI$^+$) calcd. for $C_{32}H_{38}BrNO_3$: 563.2; found: m/z 564.8 [M + H]$^+$.

***N*-[3-(2-Bromo-4,5-dimethoxyphenyl)propyl]-*N*-(4-methoxybenzyl)-1-(4-methoxyphenyl)hex-1-yn-3-amine (2j):** Synthesized from butyraldehyde (40 mg, 0.55 mmol), 1-ethynyl-4-methoxybenzene (132 mg, 1 mmol) and amine **1c** (151 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2j** as a yellow oil (264 mg, 91%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38 (d, J = 8.6 Hz, 2 H), 7.31 (d, J = 8.5 Hz, 2 H), 6.98 (s, 1 H), 6.88–6.80 (m, 2 H), 6.65 (s, 1 H), 3.89–3.76 (m, 13 H), 3.63 (t, J = 7.4 Hz, 1 H), 3.42 (d, J = 13.6 Hz, 1 H), 2.86–2.46 (m, 4 H), 1.87–1.60 (m, 4 H), 1.56–1.41 (m, 2 H), 0.89 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.19, 158.47, 148.28, 147.63, 134.00, 133.09, 132.28, 129.92, 115.77, 115.49, 113.94, 113.83, 113.51, 112.80, 86.98, 84.48, 56.13, 56.00, 55.30, 55.23, 55.05, 52.96, 50.45, 36.37, 33.96, 28.81, 19.88, 13.92 ppm. MS (ESI$^+$) calcd. for $C_{32}H_{38}BrNO_4$: 579.2; found: m/z 580.8 [M + H]$^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-*N*-(4-methoxybenzyl)-1,4-diphenylbut-3-yn-2-amine (2k):** General experimental procedure for Cu^I-catalyzed tandem anti-Markovnikov hydroamination and alkyne addition reaction: phenylacetylene (153 mg, 1.5 mmol), amine 1a (190 mg, 0.5 mmol) and CuI (14 mg, 15 mol-%) were loaded into the microwave instrument vial. The vial was evacuated and flushed with argon. The vial was sealed and irradiated with stirring at a ceiling temperature of 100 °C at 80 W maximum power level for 25 min. Upon completion of the reaction time the vial was cooled with a stream of air. The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2k** as yellow oil (216 mg, 74%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.45–7.36 (m, 2 H), 7.33–7.19 (m, 6 H), 7.16–7.07 (m, 4 H), 6.98 (s, 1 H), 6.76 (d, J = 8.6 Hz, 2 H), 6.60 (s, 1 H), 3.99–3.71 (m, 11 H), 3.58 (d, J = 13.8 Hz, 1 H), 3.06–2.64 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.50, 148.15, 147.90, 138.70, 131.82, 131.69, 131.43, 129.78, 129.51, 128.22, 128.01, 127.89, 126.20, 123.38, 115.34, 114.14, 113.72, 113.48, 87.86, 85.69, 56.12, 55.94, 55.43, 55.30, 55.24, 50.97, 40.49, 34.95 ppm. MS (ESI$^+$) calcd. for $C_{34}H_{34}BrNO_3$: 583.2; found: m/z 584.8 [M + H]$^+$.

***N*-(2-Bromo-4,5-dimethoxyphenethyl)-1,4-bis(3-fluorophenyl)-*N*-(4-methoxybenzyl)but-3-yn-2-amine (2l):** Synthesized from 1-ethynyl-3-fluorobenzene (180 mg, 1.5 mmol) and amine **1a** (190 mg, 0.5 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **2l** as a yellow oil (251 mg, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.31–6.73 (m, 13 H), 6.60 (s, 1 H), 3.94 (d, J = 13.7 Hz, 1 H), 3.90–3.74 (m, 10 H), 3.55 (d, J = 13.7 Hz, 1 H), 3.06–2.64 3.90–3.74 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 164.25, 163.97, 161.00, 160.71, 158.66, 148.21, 148.02, 141.09, 141.00, 131.59, 131.05, 129.90, 129.82, 129.78, 129.44, 129.33, 127.62, 127.58, 125.17, 125.13, 125.08, 124.95, 118.67, 118.37, 116.39, 116.11, 115.52, 115.41, 115.24, 114.15, 113.70, 113.57, 113.29, 113.01, 88.55, 84.78, 84.73, 56.13, 55.96, 55.41, 55.28, 54.94, 50.88, 39.97, 34.97 ppm. MS (ESI$^+$) calcd. for $C_{34}H_{32}BrF_2NO_3$: 619.2; found: m/z 620.4 [M + H]$^+$.

(*Z*)-1-Benzylidene-2-isobutyl-7,8-dimethoxy-3-(4-methoxybenzyl)-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3a): General experimental procedure for Pd-catalyzed intramolecular acetylene hydroarylation: $Pd(PPh_3)_4$ (14 mg, 3 mol-%) and HCOONa (41 mg, 0.6 mmol) were loaded into the microwave instrument vial. The vial was evacuated and flushed with argon. Propargylamine **2a** (220 mg, 0.4 mmol) dissolved in DMF (4.5 mL) was added, followed by distilled water (1.5 mL). The vial was sealed and irradiated with stirring at a ceiling temperature of 110 °C at 100 W maximum power level for 15 min. Upon completion of the reaction time the vial was cooled with a stream of air. The reaction mixture was concentrated under reduced pressure. After dilution with DCM the organic phase was washed several times with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The products were isolated by column chromatography on silica gel yielding **3a** as a yellow oil (151 mg, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.33–7.19 (m, 5 H), 6.97 (d, J = 8.5 Hz, 2 H), 6.76–6.65 (m, 4 H), 6.60 (s, 1 H), 4.05 (t, J = 7.5 Hz, 1 H), 3.89 (s, 6 H), 3.77 (s, 3 H), 3.71 (d, J = 13.6 Hz, 1 H), 3.41 (d, J = 13.6 Hz, 1 H), 3.36–3.24 (m, 1 H), 3.14–3.01 (m, 1 H), 2.82–2.70 (m, 1 H), 2.31–2.18 (m, 1 H), 1.74–1.58 (m, 1 H), 1.56–1.43 (m, 1 H), 1.18–1.05 (m, 1 H), 0.75 (d, J = 6.6 Hz, 3 H), 0.67 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.23, 147.45, 146.87, 146.27, 137.92, 135.35, 132.07, 131.98, 131.05, 129.66, 129.01, 128.16, 126.59, 113.77, 113.26, 112.27, 57.09, 56.16, 56.01, 55.91, 55.22, 45.86, 38.60, 33.66, 24.51, 23.13, 22.46 ppm. HRMS (EI) for $C_{31}H_{37}NO_3$, calcd. 471.2773, found 471.2778.

(*Z*)-1-(4-Fluorobenzylidene)-2-isobutyl-7,8-dimethoxy-3-(4-methoxybenzyl)-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3b): Synthesized from **2b** (227 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3b** as a yellow oil (165 mg, 84%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.28–7.19 (m, 2 H), 7.01–6.91 (m, 4 H), 6.76–6.68 (m, 3 H), 6.61 (s, 1 H), 6.60 (s, 1 H), 3.98 (t, J = 7.5 Hz, 1 H), 3.89 (s, 6 H), 3.78 (s, 3 H), 3.70 (d, J = 13.6 Hz, 1 H), 3.45 (d, J = 13.6 Hz, 1 H), 3.35–3.22 (m, 1 H), 3.16–3.02 (m, 1 H), 2.84–2.72 (m, 1 H), 2.32–2.19 (m, 1 H), 1.72–1.56 (m, 1 H), 1.55–1.42 (m, 1 H), 1.16–1.03 (m, 1 H), 0.75 (d, J = 6.6 Hz, 3 H), 0.68 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 163.27, 160.02, 158.30, 147.52, 146.90, 146.52, 135.15, 133.88, 133.83, 131.95, 131.81, 130.61, 130.51, 129.91, 129.53, 115.15, 114.87, 113.69, 113.28, 112.30, 57.16, 56.18, 55.92, 55.60, 55.23, 46.18, 38.28, 33.82, 24.49, 23.07, 22.59 ppm. HRMS (EI) for $C_{31}H_{36}FNO_3$, calcd. 489.2679, found 489.2672.

(*Z*)-1-Benzylidene-7,8-dimethoxy-3-(4-methoxybenzyl)-2-propyl-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3c): Synthesized from **2c** (215 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3c** as a yellow oil (167 mg, 91%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.33–7.18 (m, 5 H), 6.98 (d, J = 8.2 Hz, 2 H), 6.77–6.67 (m, 4 H), 6.60 (s, 1 H), 4.00–3.93 (m, 1 H), 3.89 (s, 6 H), 3.77 (s, 3 H), 3.71 (d, J = 13.7 Hz, 1 H), 3.42 (d, J = 13.7 Hz, 1 H), 3.36–3.23 (m, 1 H), 3.17–3.02 (m, 1 H), 2.83–2.70 (m, 1 H), 2.34–2.20 (m, 1 H), 1.61–1.47 (m, 1 H), 1.40–1.20 (m, 3 H), 0.80–0.72 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.24, 147.51, 146.92, 145.89, 137.92, 135.20, 132.07, 132.04, 131.46, 129.60, 129.08, 128.21, 126.59, 113.70, 113.32, 112.29, 57.93, 57.18, 56.21, 55.95, 55.25, 46.07, 33.74, 31.98, 19.59, 14.18 ppm. HRMS (EI) for $C_{30}H_{35}NO_3$, calcd. 457.2617, found 457.2591.

(*Z*)-1-Butylidene-7,8-dimethoxy-3-(4-methoxybenzyl)-2-phenyl-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3d): Synthesized from **2d** (215 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3d** as a yellow oil (141 mg, 77%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.26 (m, 4 H), 7.23–7.10 (m, 3 H), 6.84 (d, J = 8.6 Hz, 2 H), 6.51 (s, 1 H), 6.48 (s, 1 H), 5.64 (t, J = 7.2 Hz, 1 H), 4.88 (s, 1 H), 3.87–3.77 (m, 10 H), 3.59 (d, J = 13.7 Hz, 1 H), 3.14–2.83 (m, 3 H), 2.57–2.43 (m, 1 H), 2.37–2.22 (m, 1 H), 2.19–2.03 (m, 1 H), 1.56–1.41 (m, 2 H), 0.95 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.51, 147.52, 146.52, 142.46, 141.10, 134.12, 132.26, 131.25, 129.49, 127.97, 127.85, 126.31, 114.88, 113.57, 111.88, 65.56, 57.51, 56.21, 55.80, 55.26, 47.52, 34.17, 30.64, 23.17, 14.09 ppm. HRMS (EI) for $C_{30}H_{35}NO_3$, calcd. 457.2617, found 457.2623.

(*Z*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(4-methoxybenzylidene)-2-phenyl-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3e): Synthesized from **2e** (240 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3e** as a brownish solid (146 mg, 70%); m.p. 75–77 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.50–7.40 (m, 2 H), 7.26–7.18 (m, 2 H), 7.17–7.07 (m, 3 H), 6.95–6.88 (m, 3 H), 6.83 (s, 1 H), 6.76 (d, J = 8.6 Hz, 2 H), 6.61 (d, J = 8.6 Hz, 2 H), 6.48 (s, 1 H), 5.25 (s, 1 H), 3.87 (s, 3 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.73 (s, 3 H), 3.69 (d, J = 13.6 Hz, 1 H), 3.61 (d, J = 13.6 Hz, 1 H), 3.36–3.18 (m, 2 H), 3.07–2.95 (m, 1 H), 2.41–2.28 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.68, 158.17, 147.60, 146.80, 142.22, 141.78, 134.49, 134.06, 132.17, 131.57, 130.26, 129.86, 129.53, 128.19, 127.92, 126.28, 115.42, 113.77, 113.21, 112.22, 61.21, 56.67, 56.26, 55.81, 55.22, 55.13, 48.20, 33.34 ppm. HRMS (EI) for $C_{34}H_{35}NO_4$, calcd. 521.2566, found 521.2573.

(*Z*)-1-Benzylidene-7,8-dimethoxy-3-(4-methoxybenzyl)-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3f): Synthesized from **2f** (198 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3f** as a yellow oil (116 mg, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.53–7.42 (m, 2 H), 7.35–7.18 (m, 5 H), 6.89 (s, 1 H), 6.85 (d, J = 8.6 Hz, 2 H), 6.70 (s, 1 H), 6.64 (s, 1 H), 3.93 (s, 3 H), 3.88 (s, 3 H), 3.80 (s, 3 H), 3.59 (s, 2 H), 3.39 (br. s, 2 H), 2.96–2.72 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.71, 147.78, 147.13, 141.54, 137.46, 136.93, 131.87, 130.71, 130.62, 130.38, 129.23, 128.20, 126.76, 113.64, 112.53, 111.10, 61.76, 56.26, 56.19, 56.02, 55.29, 54.33, 34.32 ppm. HRMS (EI) for $C_{27}H_{29}NO_3$, calcd. 415.2147, found 415.2137.

(*Z*)-1-Benzylidene-2-isobutyl-3-isopropyl-7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3g): Synthesized from **2g** (189 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3g** as a yellow oil (113 mg, 72%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.40–7.29 (m, 4 H), 7.28–7.21 (m, 1 H), 6.72 (s, 1 H), 6.67 (s, 1 H), 6.59 (s, 1 H), 4.17 (t, J = 7.2 Hz, 1 H), 3.88 (s, 6 H), 3.22–2.81 (m, 4 H), 2.51–2.33 (m, 1 H), 1.68–1.51 (m, 1 H), 1.41–1.29 (m, 1 H), 1.28–1.17 (m, 1 H), 1.01 (d, J = 6.5 Hz, 3 H), 0.81–0.72 (m, 6 H), 0.67 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 147.60, 146.81, 146.62, 138.24, 134.64, 131.67, 131.17, 129.01, 128.11, 126.61, 113.71, 112.14, 56.20, 55.90, 55.16, 50.26, 42.33, 40.96, 35.52, 24.64, 23.05, 22.81, 21.79, 20.78 ppm. HRMS (EI) for $C_{26}H_{35}NO_2$, calcd. 393.2668, found 393.2657.

(*Z*)-2-Isobutyl-3-isopropyl-7,8-dimethoxy-1-(thiophen-3-ylmethylene)-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3h): Synthesized from **2h** (191 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3h** as a brown oil (117 mg, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.35–7.29 (m, 1 H), 7.20–7.14 (m, 1 H), 7.13–7.06 (m, 1 H), 6.69 (s, 1 H), 6.58 (s, 1 H), 6.53 (s, 1 H), 4.33–4.22 (m, 1 H), 3.88 (s, 3 H), 3.88 (s, 3 H), 3.19–2.91 (m, 4 H), 2.52–2.37 (m, 1 H), 1.68–1.53 (m, 1 H), 1.42–1.30 (m, 1 H), 1.29–1.18 (m, 1 H), 1.03 (d, J = 6.5 Hz, 3 H), 0.83–0.76 (m, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 147.63, 146.80, 138.80, 134.44, 131.50, 128.83, 125.60, 125.23, 122.57, 113.67, 112.11, 56.17, 55.89, 55.80, 50.63, 42.50, 41.21, 35.50, 24.74, 23.17, 22.89, 21.72, 20.71 ppm. HRMS (EI) for $C_{24}H_{33}O_2NS$, calcd. 399.2232, found 399.2193.

(*Z*)-1-Benzylidene-2-isobutyl-8,9-dimethoxy-3-(4-methoxybenzyl)-1,2,3,4,5,6-hexahydrobenzo[*d*]azocine (3i): Synthesized from **2i** (226 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3i** as a yellow oil (78 mg, 40%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.32–7.18 (m, 5 H), 6.99 (d, J = 8.5 Hz, 2 H), 6.73 (d, J = 8.5 Hz, 2 H), 6.66 (s, 1 H), 6.59 (s, 1 H), 6.43 (s, 1 H), 4.11 (t, J = 7.2 Hz, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.82–3.74 (m, 4 H), 3.71 (d, J = 13.7 Hz, 1 H), 2.98–2.81 (m, 1 H), 2.57–2.34 (m, 3 H), 1.94–1.76 (m, 1 H), 1.70–1.57 (m, 1 H), 1.39–1.17 (m, 3 H), 0.78–0.62 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.27, 148.03, 146.22, 145.66, 138.00, 134.67, 132.90, 132.06, 129.91, 129.67, 128.92, 128.11, 126.45, 113.60, 113.29, 111.40, 58.69, 56.35, 56.09, 55.88, 55.25, 41.60, 39.18, 32.53, 30.52, 24.66, 23.13, 22.69 ppm. HRMS (EI) for $C_{32}H_{39}NO_3$, calcd. 485.2930, found 485.2939.

(*Z*)-8,9-Dimethoxy-3-(4-methoxybenzyl)-1-(4-methoxybenzylidene)-2-propyl-1,2,3,4,5,6-hexahydrobenzo[*d*]azocine (3j): Synthesized from **2j** (232 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3j** as a slightly yellow oil (64 mg, 32%). ^{1}H

NMR ($CDCl_3$, 300 MHz): δ = 7.19 (d, J = 8.5 Hz, 2 H), 7.04 (d, J = 8.5 Hz, 2 H), 6.83 (d, J = 8.5 Hz, 2 H), 6.76 (d, J = 8.5 Hz, 2 H), 6.69 (s, 1 H), 6.63 (s, 1 H), 6.40 (s, 1 H), 4.12–4.05 (m, 1 H), 3.92 (s, 3 H), 3.90 (s, 3 H), 3.85–3.79 (m, 7 H), 3.49 (d, J = 13.8 Hz, 1 H), 2.99–2.85 (m, 1 H), 2.57–2.42 (m, 3 H), 1.95–1.81 (m, 1 H), 1.54–1.43 (m, 1 H), 1.42–1.28 (m, 4 H), 0.87–0.81 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.21, 158.20, 147.97, 146.22, 144.59, 134.88, 132.91, 132.09, 130.42, 130.04, 129.58, 129.51, 113.50, 113.22, 111.41, 60.17, 56.38, 56.09, 55.87, 55.21, 55.19, 41.82, 32.53, 32.33, 30.57, 19.94, 14.24 ppm. HRMS (EI) for $C_{32}H_{39}NO_4$, calcd. 501.2879, found 501.2878.

(*Z*)-2-Benzyl-1-benzylidene-7,8-dimethoxy-3-(4-methoxybenzyl)-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3k): Synthesized from **2k** (234 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3k** as a yellow oil (144 mg, 71%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.23–7.12 (m, 6 H), 6.98–6.82 (m, 6 H), 6.71–6.58 (m, 5 H), 4.28–4.18 (m, 1 H), 3.92 (s, 3 H), 3.87 (s, 3 H), 3.78 (s, 3 H), 3.72 (d, J = 13.6 Hz, 1 H), 3.42 (d, J = 13.6 Hz, 1 H), 3.37–3.14 (m, 2 H), 2.94–2.80 (m, 2 H), 2.78–2.66 (m, 1 H), 2.49–2.36 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.24, 147.64, 146.80, 144.05, 139.68, 137.63, 134.57, 132.24, 132.01, 131.54, 129.58, 129.53, 128.81, 128.01, 127.83, 126.55, 125.86, 114.28, 113.30, 112.27, 60.25, 57.62, 56.05, 55.97, 55.26, 46.84, 36.94, 34.07 ppm. HRMS (EI) for $C_{34}H_{35}NO_3$, calcd. 505.2617, found 505.2608.

(*Z*)-2-(3-Fluorobenzyl)-1-(3-fluorobenzylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-2,3,4,5-tetrahydro-1*H*-benzo[*d*]azepine (3l): Synthesized from **2l** (248 mg, 0.4 mmol). The product was isolated by column chromatography on silica gel (heptane/EtOAc/10–20%) yielding propargylamine **3l** as a yellow oil (137 mg, 63%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.22–7.08 (m, 2 H), 6.94- 6.83 (m, 4 H), 6.74–6.64 (m, 5 H), 6.63–6.54 (m, 4 H), 4.20–1.07 (m, 1 H), 3.92 (s, 3 H), 3.89 (s, 3 H), 3.79 (s, 3 H), 3.72 (d, J = 13.6 Hz, 1 H), 3.45 (d, J = 13.6 Hz, 1 H), 3.36–3.10 (m, 2 H), 2.95–2.80 (m, 2 H), 2.77–2.62 (m, 1 H), 2.53–2.37 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 164.20, 164.16, 160.96, 160.91, 158.41, 147.88, 146.94, 144.83, 142.17, 142.07, 139.70, 139.60, 133.84, 131.97, 131.18, 131.07, 129.53, 129.42, 129.38, 129.27, 125.11, 125.08, 124.49, 124.46, 116.49, 116.21, 115.75, 115.47, 114.05, 113.69, 113.38, 112.94, 112.66, 112.39, 60.15, 57.80, 56.01, 55.97, 55.28, 47.16, 36.47, 34.24 ppm. HRMS (EI) for $C_{34}H_{33}F_2NO_3$, calcd. 541.2429, found 541.2417.

Supporting Information (see also the footnote on the first page of this article): Complete experimental procedures, as well as ^1H NMR and ^{13}C NMR spectroscopic data for all new compounds.

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