1 Heck–Suzuki Tandem Reaction for the Synthesis of 3-Benzazepines

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ABSTRACT: A novel procedure for the Heck–Suzuki tandem reaction suitable for the construction of nitrogen-containing medium rings was developed to provide access toward the 3-benzazepine framework.

10 ■ INTRODUCTION

11 The 3-benzazepine core is present in a large variety of natural
12 products and important pharmaceuticals and might be rightfully
13 regarded as a *privileged structure*.¹ Therefore, it has served as a
14 target motif for a large number of synthetic studies. Successful
15 examples include various types of ring-expansion reactions,²
16 insertion of allenes into the Pd–C bond of *ortho*-palladated
17 phenethylamines,³ and heterocyclizations involving either intra-
18 molecular reductive amination⁴ or transition-metal-catalyzed
19 triple-bond hydroamination.⁵ Radical,⁶ Friedel–Crafts,⁷ and
20 Heck-type⁸ carbocyclizations are also among the most applied
21 methodologies for the 3-benzazepine assembly.

22 In 1994, Tietze and Schimpf described an efficient route
23 toward 3-benzazepines starting from propargylamides contain-
24 ing an aryl iodide moiety by applying an intramolecular
25 version of the reductive Heck reaction that is also referred to as
26 formal triple bond hydroarylation.^{9,10} Later on, our group
27 established a more general protocol that utilizes readily
28 accessible propargylamides derived from 3-substituted propiolic
29 acids and *o*-bromophenethylamines.¹¹ Subsequently, we have
30 expanded this approach to the use of Ugi reaction derived
31 propargylamides¹² and A³-coupling derived propargylamines¹³
32 aiming to introduce an additional diversity in the resulting
33 3-benzazepines.

34 These reductive Heck approaches operate through the cyclic
35 intermediate **A**, resulting from the oxidative addition of aryl
36 bromide to the Pd(0)-species and subsequent triple bond
37 insertion, which then undergoes the reduction with HCOONa
38 (sodium formate) into the 3-benzazepine of type **2**. Trapping
39 this intermediate with an organoboron reagent **3** should
40 hypothetically result in the formation of the 3-benzazepine of
41 type **4** (Scheme 1). Such Heck–Suzuki tandem reactions are
42 well-known in the literature and have been previously
43 demonstrated to be highly efficient for the assembly of five-
44 and six-membered hetero-¹⁴ and alicycles.¹⁵ Moreover, this

Scheme 1. Synthesis of the 3-Benzazepine Framework through Palladium-Catalyzed Carbocyclizations of Propargylic Precursors

Previous work

Current work

strategy proved to be useful for the synthesis of seven-
45 membered dibenzoxapine derivatives.¹⁶ However, to the best of
46 our knowledge, no general protocol allowing the application of
47 this process for the synthesis of nitrogen-containing medium-
48 rings is known in the literature. In order to fill this gap we
49 aimed to examine the Heck–Suzuki tandem reaction for the
50 synthesis and further diversification of the 3-benzazepine
51 scaffold. Herein we present the detailed studies on the scope
52 and limitations of the resulting procedure.

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Table 1. Screening of Parameters for the Model Reaction of **1a** and **3a**^a

entry	x	Pd cat.	base	conditions	solvent	yield ^b (%)	conversion ^b (%)
1	1.5	Pd(PPh ₃) ₄	K ₃ PO ₄	MW, 110 °C, 15 min	DMF	13	70
2	1.5	Pd(PPh ₃) ₄	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	31	100
3	1.2	Pd(PPh ₃) ₄	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	16	95
4	1.5	Pd(PPh ₃) ₄	KOAc	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	48	86
5	1.5	Pd(PPh ₃) ₄	Na ₂ CO ₃	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	30	100
6	1.5	Pd(PPh ₃) ₄	CS ₂ CO ₃	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	21	100
7	1.5	Pd(PPh ₃) ₄	<i>t</i> BuOK	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	16	100
8	1.5	Pd(PPh ₃) ₂ Cl ₂	KOAc	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	36	90
9	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	55	100
10	1.5	Pd(OAc) ₂ /PPh ₃	KOAc	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	41	88
11	1.8	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(3:1)	48	100
12	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(1:1)	17	100
13	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 110 °C, 15 min	DMA/H ₂ O(3:1)	50	100
14	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(4:1)	58 (51) ^c	100
15	1.5	Pd(OAc) ₂ /PPh ₃	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(4:1)	43	100
16	1.5	Pd ₂ dba ₃ /PPh ₃	K ₃ PO ₄	MW, 110 °C, 15 min	DMF/H ₂ O(4:1)	37	100
17	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 90 °C, 25 min	DMF/H ₂ O(4:1)	44	94
18	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	MW, 120 °C, 10 min	DMF/H ₂ O(4:1)	31	88
19	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	oil bath, 90 °C, 2 h	DMF/H ₂ O(4:1)	39	100
20	1.5	Pd(PPh ₃) ₂ Cl ₂	K ₃ PO ₄	oil bath, 110 °C, 1 h	DMF/water(4:1)	35	100

^aThe reactions were run on a 0.2 mmol scale in 2.25 mL of solvent. ^bYields and conversions were determined by ¹H NMR using 3,4,5-trimethoxybenzaldehyde as internal standard. ^cIsolated yield is given in parentheses.

Table 2. Comparison of the Reactivity of Different Organoboron Reagents **3**^a

Entry	Ph-[B] (3)	Yield ^b	Conversion ^b
1	PhB(OH) ₂ 3a	58 (51) ^c	100
2	PhBF ₃ K 3b	29	100
3	3c	52 (45) ^c	100
4	3d	14	34

^aThe reactions were run on a 0.2 mmol scale in 2.25 mL of solvent. ^bYields and conversions were determined by ¹H NMR using 3,4,5-trimethoxybenzaldehyde as internal standard. ^cIsolated yields are given in parentheses.

54 ■ RESULTS AND DISCUSSION

55 The reaction conditions for the Heck–Suzuki tandem process
 56 were adjusted using propargylamide **1a** and phenylboronic acid
 57 **3a** as model substrates (Table 1). Pd(PPh₃)₄-catalyzed reaction
 58 of **1a** with 1.5 equiv of **3a** and K₃PO₄ as a base conducted
 59 under microwave irradiation at 110 °C for 15 min in DMF
 60 resulted in 70% conversion of **1a** but gave only 13% yield of
 61 the desired 3-benzazepine **4a** as determined by ¹H NMR of the

crude material after workup (Table 1, entry 1). Switching to
 a DMF/water (3:1) mixture as solvent system led to full
 conversion of **1a** and an improved 31% yield for **4a** (Table 1,
 entry 2). An attempt to decrease the excess phenylboronic acid
3a resulted in incomplete conversion of **1a** (Table 1, entry 3).
 Next, we screened various bases in combination with different
 Pd catalysts (Table 1, entries 4–10). The Pd(PPh₃)₂Cl₂/K₃PO₄
 combination was found to be the best, delivering target **4a** in a 69

Table 3. Scope and Limitations of the Heck–Suzuki Tandem Reaction Procedure for the Synthesis of 3-Benzazepine and 3-Benzazocine Frameworks^a

Entry	y	Conditions	Propargylamine or propargylamine 1	Organoboron reagent 3	Product 4	Yield ^b	
						4	5
1	3	110°C, 15 min				51	nd ^c
2	3	110°C, 15 min	1a			35	nd ^c
3	3	110°C, 15 min	1a			47	nd ^c
4	3	110°C, 15 min	1a			34	nd ^c
5	3	110°C, 15 min	1a			52	nd ^c
6	3	110°C, 15 min	1a			48	nd ^c
7	3	110°C, 25 min	1a			42	16
8	3	110°C, 15 min	1a			53	nd ^c
9	3	110°C, 15 min	1a			60	nd ^c

Table 3. continued

Entry	y	Conditions	Propargylamide or propargylamine 1	Organoboron reagent 3	Product 4	Yield ^b	
						4	5
10	3	110°C, 15 min	1a	3m	4j	37	27
11	3	110°C, 15 min	1a	3n	4k	52	nd ^c
12	3	110°C, 15 min	1a	3p	4l	40 (50) ^d	nd ^c
13	4	115°C, 30 min	1a			67 (90) ^d	nd ^c
14	3+2	115°C, 20+15 min	1a			72 (100) ^d	nd ^c
15	4	110°C, 25 min	1b	3a	4m	49	nd ^c
16	3+2	115°C, 20+15 min	1b	3p	4n	80	nd ^c
17	3	110°C, 15 min	1c	3a	4o	15	6
18	3+2	115°C, 20+15 min	1c	3p	4p	18	nd ^c
19	3	110°C, 15 min	1d	3a	4q	69	nd ^c
20	3+2	115°C, 20+15 min	1d	3p	4r	83	nd ^c
21	3	110°C, 15 min	1e	3a	4s	45	nd ^c
22	3+2	115°C, 20+15 min	1e	3p	4t	79	nd ^c

Table 3. continued

Entry	y	Conditions	Propargylamide or propargylamine 1	Organoboron reagent 3	Product 4	Yield ^b	
						4	5
23	3	110°C, 15 min		3a		13	34
24	3+2	115°C, 20+15 min	1f	3p		59	nd ^c
25	3+2	110°C, 25+15 min		3a		27	35 ^e
26	3+3	115°C, 25+15 min	1g	3p		55	nd ^c

^aThe reactions were run on a 0.2 mmol scale in 2.25 mL of solvent. ^bIsolated yields. ^cnd = not detected or difficult to determine clearly. ^dConversions are given in parentheses. ^eYield was determined by ¹H NMR using 3,4,5-trimethoxybenzaldehyde as internal standard.

70 good NMR yield of 55% (Table 1, entry 9). Interestingly,
71 increasing the excess phenylboronic acid **3a** up to 1.8 equiv did
72 not provide a better yield of **4a** (Table 1, entry 11). Changing
73 the DMF–water ratio to 1:1 led to a significant drop in the
74 yield of **4a** (Table 1, entry 12). The reaction in a DMA/water
75 (3:1) mixture gave a slightly decreased yield of **4a** compared to
76 the analogous reaction in DMF/water (3:1) (Table 1, entry 13
77 versus entry 9). Finally, reaction in DMF/water (4:1) delivered
78 3-benzazepine **4a** in a best observed NMR yield of 58%, which
79 corresponds to 51% isolated yield after column chromatography
80 and recrystallization from diethyl ether (Table 1, entry 14).
81 Further attempts to increase the yield of **4a** by tuning the
82 catalytic system were unproductive (Table 1, entries 15 and 16).
83 In addition, no further improvement was achieved by changing
84 the reaction temperature as well as by applying conventional oil
85 bath heating (Table 1, entries 17–20).

86 We then decided to compare the reactivity of several common
87 phenylorganoboron reagents **3a–d** in the model reaction with
88 **1a** (Table 2). Phenylboronic acid **3a** was found to be the most
89 efficient coupling partner (Table 2, entry 1). Nonetheless, the
90 use of potassium phenyltrifluoroborate **3b** and phenylboronic
91 acid pinacol ester **3c** also resulted in a full conversion of **1a**,
92 although the yields for the desired 3-benzazepine **4a** were
93 lower in these cases (Table 2, entries 2 and 3 versus entry 1).
94 The application of phenylboronic acid MIDA ester **3d** gave a
95 very low conversion of **1a** and as a result a poor yield for target
96 compound **4a** (Table 2, entry 4).

97 Having these results in hand, we decided to evaluate the
98 scope and limitations of our procedure (Table 3). First we have
99 screened a number of aromatic **3a,e–k** and heteroaromatic
100 **3l,m** boronic acids in combination with propargylamide **1a**. All
101 reactions were successful, delivering the desired 3-benzazepines
102 **4a–j** in up to 60% yield (Table 3, entries 1–10). The reaction
103 of **1a** with penten-1-ylboronic acid **3n** also resulted in a good
104 52% yield of 3-benzazepine **4k** (Table 3, entry 11). At the
105 same time, the application of vinylpotassium trifluoroborate **3p**

required some adjustments of the reaction conditions in
order to reach a full conversion of **1a** but finally allowed to
obtain 3-benzazepine **4l** in a very good yield of 72% (Table 3,
entries 12–14). Next, we have screened the reactivity of various
propargylamides **1b–e** in combination with phenylboronic
acid **3a** and with vinylpotassium trifluoroborate **3p** (Table 3,
entries 15–22). Gratifyingly, the isolated yields of the desired
3-benzazepines in several cases have reached 80% yield.
However, in the reactions with propargylamide **1c** derived
from phenylpropionic acid, only very poor yields were obtained
(Table 3, entries 17 and 18). In the case of reactions with
propargylamide **1f**, an expanded eight-membered ring could be
constructed although the yields for the resulting 3-benzazocines
4u and **4v** are significantly lower than for analogues
3-benzazepines **4a** and **4l** (Table 3, entries 23 and 24 versus
entries 1 and 14). Importantly, A³-coupling derived propargyl-
amine **1g** was also found to be applicable in this process
(Table 3, entries 25 and 26).

The reactions with vinylpotassium trifluoroborate **3p** in all
cases led to higher yields of the desired benzazepine and
benzazocine products compared to the analogues reactions with
phenylboronic acid **3a** (Table 3, entries 14, 16, 18, 20, 22, 24,
and 26 versus entries 1, 15, 17, 19, 21, 23, and 25). This result
could be attributed to the smaller size of the introduced vinyl
fragment compared to the phenyl one.

In some cases, in addition to the desired Heck–Suzuki
product **4** the formation of byproduct **5** that results from the
direct Suzuki coupling of the aryl bromide moiety of **1** with
organoboron reagent **3** could be observed. In several instances,
such products **5** could be isolated and characterized (Table 3,
entries 7, 10, 17, 23, and 25).

Finally, we investigated the reactions of propargylamides **1a**
and **1d** with 2-phenyl-1-ethynylboronic acid pinacol ester **3o**
(Table 4). Interestingly, in this case, in addition to the standard
product **4** another unexpected 3-benzazepine product **6** was
formed resulting from the double incorporation of organoboron

Table 4. Heck–Suzuki Tandem Reaction with 2-Phenyl-1-ethynylboronic Acid Pinacol Ester 3o^a

Entry	Propargylamide 1	x	Product 4	Yield of 4 ^b	Product 6	Yield of 6 ^b
1	1a	1.5		24		10
2		1.5		19		13
3	1d	1.2		23		9
4		2.5		20 ^c		14 ^c

^aThe reactions were run on a 0.2 mmol scale in 2.25 mL of solvent. ^bIsolated yields. ^cYields were determined by ¹H NMR using 3,4,5-trimethoxybenzaldehyde as internal standard.

reagent **3o**. We attempted to tune the **4** to **6** ratio by changing the amounts of **3o** added to the reaction; however, no significant effect was achieved.

The structures of all prepared 3-benzazepines **4a–t,w–z** and **6** and 3-benzazocines **4u,v** were confirmed by ¹H and ¹³C NMR spectroscopy and HRMS. In addition, the structures of four representative products **4m,t,z** and **6b** were assured by X-ray crystallographic analysis.¹⁷

CONCLUSION

In summary, we have developed a novel protocol for the tandem Heck–Suzuki reaction showing that it can be successfully applied for the construction of nitrogen-containing medium rings. Importantly, our methodology employs propargylamides/amines comprising an aryl bromide functionality, while most of the known procedures leading to nitrogen-containing five- and six-membered heterocycles^{14a–c} generally rely on more reactive aryl iodides. The adaptability of the developed procedure toward the various organoboron sources has also been evaluated.

EXPERIMENTAL SECTION

General Information. ¹H and ¹³C NMR spectra were recorded at 300 and 75 MHz, respectively. The ¹H and ¹³C chemical shifts are reported in parts per million relative to tetramethylsilane using the residual solvent signal as the internal reference. High-resolution EI mass spectra were recorded with a resolution of 10000. The ion source temperature was 150–250 °C, as required. High-resolution ESI mass spectra were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer. Samples were infused at 3 μL/min, and spectra were obtained in positive-ionization mode with a resolution of 15000 (fwhm) using leucine enkephalin as lock mass. Reversed-phase HPLC separation was performed using a C18 (5 μm × 150 nm × 22 mm) preparative column.

The microwave reactions were carried out in 10 mL glass tubes and sealed with a Teflon septum using a dedicated CEM-Discover mono-mode microwave apparatus, operating with a frequency of 2.45 GHz.

The temperature of microwave reactions was measured by an inbuilt infrared temperature probe.

Synthesis of the Starting Materials. The preparation procedures and analytical data for compounds **1a,c–f**^{11a} and **1g**¹³ have been described by us previously.

Synthesis of N-(2-Bromo-4,5-dimethoxyphenethyl)-N-(4-methoxybenzyl)pent-2-ynamide (1b). 2-(2-Bromo-4,5-dimethoxyphenyl)-N-(4-methoxybenzyl)ethanamine (496 mg, 1.3 mmol) was added in one portion to a mixture of pent-2-ynoic acid (134 mg, 1.37 mmol) and DCC (283 mg, 1.37 mmol) in dry DCM (6 mL). The reaction mixture was stirred overnight at rt. The subsequently formed precipitate of N,N'-dicyclohexylurea was filtered off and washed with DCM. The combined organic layers were concentrated and subjected to column chromatography on silica gel with EtOAc/heptane (3:7) as eluent to deliver pure **1b** as a 2:3 mixture of rotamers. Yield: 382 mg, 64%. Pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.26–7.14 (m, 2H), 6.99 (s, 0.4H), 6.97 (s, 0.6H), 6.90–6.81 (m, 2H), 6.74 (s, 0.6H), 6.56 (s, 0.4H), 4.53 (s, 2H), 3.87–3.76 (m, 9H), 3.70–3.62 (m, 0.8H), 3.50–3.41 (m, 1.2H), 2.97–2.85 (m, 2H), 2.43–2.30 (m, 2H), 1.24–1.15 (m, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 159.3, 159.1, 154.9, 154.7, 148.52, 148.49, 148.4, 148.2, 130.1, 129.8, 129.6, 129.1, 128.9, 128.5, 115.5, 115.3, 114.3, 114.04, 113.96, 113.6, 113.5, 94.2, 93.9, 73.8, 73.4, 56.2, 56.11, 56.09, 55.3, 55.2, 52.8, 47.8, 47.2, 44.0, 35.0, 33.1, 12.93, 12.86, 12.8, 12.7. HRMS (EI): m/z [M]⁺ calcd for C₂₃H₂₆BrNO₄ 459.1045, found 459.1059.

General Procedure for the Heck–Suzuki Tandem Reaction for the Synthesis of 3-Benzazepines 4a–k,m,o,q,s,y,z and 6a,b and benzazocine 4u. Pd(PPh₃)₂Cl₂ (4.2 mg, 3 mol %), organoboron reagent **3** (0.3 mmol), and propargylamide **1** (0.2 mmol) were loaded into a microwave instrument vial and dissolved in DMF (1.8 mL). Then K₃PO₄ (85 mg, 0.4 mmol) was added followed by distilled water (0.45 mL). The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at a set temperature of 110 °C for 15 min utilizing a maximum power of 100 W. Upon completion of the reaction, the vial was cooled with a stream of air. The reaction mixture was diluted with EtOAc (50 mL), washed with water (2 × 50 mL), dried over MgSO₄, and concentrated under reduced pressure. The resulting crude material was subjected to the appropriate purification procedure.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(1-phenylethylidene)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4a**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4a**. Yield: 45 mg, 51%. White amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.31–7.22 (m, 2H), 7.20–7.05 (m, 5H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.45 (s, 1H), 6.18 (s, 1H), 5.02 (d, *J* = 14.8 Hz, 1H), 4.39–4.17 (m, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 3.39–3.25 (m, 4H), 2.98–2.88 (m, 2H), 2.33 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 159.1, 147.9, 146.5, 141.9, 137.5, 134.6, 129.7, 129.4, 128.6, 128.1, 127.7, 126.7, 125.5, 115.4, 114.1, 111.9, 55.7, 55.32, 55.30, 47.5, 44.5, 31.8, 22.1. HRMS (EI): *m/z* [M]⁺ calcd for C₂₈H₂₉NO₄ 443.2097, found 443.2096.

(*E*)-1-(1-(4-Ethoxyphenyl)ethylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4b**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4b**. Yield: 34 mg, 35%. White solid. Mp: 174–176 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.25 (d, *J* = 7.8 Hz, 2H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.68 (d, *J* = 8.3 Hz, 2H), 6.45 (s, 1H), 6.23 (s, 1H), 5.01 (d, *J* = 14.6 Hz, 1H), 4.37–4.16 (m, 2H), 4.01–3.89 (m, 2H), 3.81 (s, 3H), 3.79 (m, 3H), 3.38–3.26 (m, 4H), 2.97–2.87 (m, 2H), 2.40 (s, 3H), 1.36 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 171.8, 159.0, 157.7, 147.9, 146.6, 137.0, 133.9, 133.7, 129.8, 129.7, 129.4, 127.6, 125.8, 115.4, 114.1, 114.0, 111.9, 63.3, 55.7, 55.4, 55.3, 47.5, 44.5, 31.8, 22.0, 14.8; HRMS (EI): *m/z* [M]⁺ calcd for C₃₀H₃₃NO₅ 487.2359, found 487.2354.

(*E*)-7,8-dimethoxy-3-(4-methoxybenzyl)-1-(1-(naphthalen-2-yl)ethylidene)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4c**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4c**. Yield: 46 mg, 47%. Beige solid. Mp: 243–246 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.74–7.62 (m, 3H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.44–7.36 (m, 2H), 7.28 (d, *J* = 8.6 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.46 (s, 1H), 6.22 (s, 1H), 5.04 (d, *J* = 14.7 Hz, 1H), 4.43–4.25 (m, 2H), 3.81 (s, 3H), 3.76 (s, 3H), 3.43–3.32 (m, 1H), 3.07 (s, 3H), 3.01–2.92 (m, 2H), 2.42 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 159.1, 148.0, 146.5, 139.5, 137.3, 135.0, 133.2, 132.1, 129.7, 129.4, 127.8, 127.7, 127.5, 127.34, 127.30, 127.0, 126.1, 125.9, 125.4, 115.5, 114.1, 112.0, 55.6, 55.3, 55.2, 47.5, 44.6, 31.9, 22.3; HRMS (EI): *m/z* [M]⁺ calcd for C₃₂H₃₁NO₄ 493.2253, found 493.2269.

(*E*)-methyl 3-(1-(7,8-dimethoxy-3-(4-methoxybenzyl)-2-oxo-2,3,4,5-tetrahydro-1*H*-benz[diazepin-1-ylidene)ethyl)benzoate (**4d**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4d**. Yield: 34 mg, 34%. Beige solid. Mp: 132–135 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.87–7.76 (m, 2H), 7.31–7.16 (m, 4H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.46 (s, 1H), 6.15 (s, 1H), 4.99 (d, *J* = 14.7 Hz, 1H), 4.41–4.18 (m, 2H), 3.87 (s, 3H), 3.81 (s, 3H), 3.78 (s, 3H), 3.42–3.22 (m, 4H), 3.01–2.84 (m, 2H), 2.34 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.3, 166.7, 159.1, 148.1, 146.6, 142.3, 136.3, 135.6, 133.3, 130.1, 129.7, 129.6, 129.4, 128.1, 128.0, 127.9, 124.9, 115.2, 114.1, 112.1, 55.7, 55.4, 55.3, 52.1, 47.5, 44.6, 31.8, 22.0. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₃₀H₃₂NO₆ 502.2224, found 502.2218.

(*E*)-1-(1-(3-Fluorophenyl)ethylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4e**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4e**. Yield: 48 mg, 52%. White solid. Mp: 163–165 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.25 (d, *J* = 8.0 Hz, 2H), 7.13 (q, *J* = 7.2 Hz, 1H), 6.92–6.76 (m, 5H), 6.46 (s, 1H), 6.20 (s, 1H), 4.99 (d, *J* = 14.7 Hz, 1H), 4.34 (d, *J* = 14.7 Hz, 1H), 4.26–4.13 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.39–3.29 (m, 4H), 2.97–2.89 (m, 2H), 2.30 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.3, 162.5 (d, *J* = 245.9 Hz), 159.1, 148.2,

146.6, 144.3 (d, *J* = 7.5 Hz), 136.1 (d, *J* = 1.9 Hz), 135.5, 129.59, 129.55 (d, *J* = 7.3 Hz), 129.4, 127.8, 125.0, 124.4 (d, *J* = 2.8 Hz), 115.6 (d, *J* = 21.6 Hz), 115.1, 114.1, 113.7 (d, *J* = 21.1 Hz), 112.1, 55.7, 55.4, 55.3, 47.5, 44.5, 31.8, 21.9. HRMS (EI): *m/z* [M]⁺ calcd for C₂₈H₂₈FNO₄ 461.2002, found 461.2025.

(*E*)-1-(1-(3-Chlorophenyl)ethylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4f**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4f**. Yield: 46 mg, 48%. White solid. Mp: 161–163 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.25 (d, *J* = 8.6 Hz, 2H), 7.15–7.03 (m, 3H), 6.98–6.92 (m, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.46 (s, 1H), 6.19 (s, 1H), 4.99 (d, *J* = 14.7 Hz, 1H), 4.34 (d, *J* = 14.7 Hz, 1H), 4.26–4.12 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.39–3.29 (m, 4H), 2.97–2.87 (m, 2H), 2.29 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.2, 159.1, 148.2, 146.6, 143.9, 136.0, 135.7, 133.9, 129.6, 129.4, 129.3, 128.6, 127.8, 126.89, 126.86, 124.9, 115.2, 114.1, 112.1, 55.7, 55.4, 55.3, 47.5, 44.5, 31.8, 22.0. HRMS (EI): *m/z* [M]⁺ calcd for C₂₈H₂₈ClNO₄ 477.1707, found 477.1720.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(1-(3-(trifluoromethyl)phenyl)ethylidene)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4g**). The reaction time was 25 min. The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization from diethyl ether to deliver pure **4g**. The mother liquor was evaporated and subjected to reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–70–70–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver a second portion of pure **4g** (*t_R* = 42 min). Combined yield: 43 mg, 42%. White solid. Mp: 142–144 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.45–7.36 (m, 2H), 7.31–7.19 (m, 4H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.46 (s, 1H), 6.11 (s, 1H), 5.00 (d, *J* = 14.7 Hz, 1H), 4.35 (d, *J* = 14.7 Hz, 1H), 2.30–2.15 (m, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.42–3.26 (m, 4H), 2.98–2.88 (m, 2H), 2.34 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.1, 159.1, 148.3, 146.7, 142.9, 136.2, 135.9, 132.0, 130.6 (q, *J* = 32.1 Hz), 129.6, 129.4, 128.6, 128.0, 125.4 (q, *J* = 3.6 Hz), 123.9 (d, *J* = 272.2 Hz), 124.7, 123.4 (q, *J* = 4.1 Hz), 115.1, 114.1, 112.2, 55.8, 55.3, 47.6, 44.6, 31.8, 21.8. HRMS (EI): *m/z* [M]⁺ calcd for C₂₉H₂₈F₃NO₄ 511.1970, found 511.1975. Further elution provided *N*-(2-(4,5-dimethoxy-3'-(trifluoromethyl)biphenyl-2-yl)ethyl)-*N*-(4-methoxybenzyl)but-2-ynamide (**5g**) as a 3:2 mixture of rotamers (*t_R* = 45 min). Yield: 16 mg, 16%. Pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.70–7.40 (m, 4H), 6.95–6.85 (m, 2H), 6.84–6.72 (m, 2.6H), 6.72–6.68 (m, 0.8H), 6.67 (s, 0.6H), 4.31 (s, 1.2H), 4.17 (s, 0.8H), 3.92 (s, 1.8H), 3.91 (s, 1.2H), 3.87 (s, 1.2H), 3.86 (s, 1.8H), 3.79 (s, 1.8H), 3.77 (s, 1.2H), 3.48–3.36 (m, 0.8H), 3.30–3.17 (m, 1.2H), 2.85–2.65 (m, 2H), 1.97 (s, 1.8H), 1.92 (s, 3.33 1.2H). ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 159.0, 154.64, 154.56, 148.84, 148.77, 147.65, 147.4, 142.14, 142.08, 133.1, 132.9, 132.6, 130.7 (m), 129.5, 128.9, 128.7, 128.6, 128.52, 128.45, 128.2, 128.0, 126.1 (m), 123.7 (m), 114.0, 113.9, 113.2, 113.0, 112.9, 112.8, 89.0, 88.6, 73.5, 73.4, 56.09, 56.05, 56.02, 55.3, 55.2, 52.3, 48.9, 46.6, 45.1, 31.6, 30.0, 4.0, 3.9. HRMS (EI): *m/z* [M]⁺ calcd for C₂₉H₂₈F₃NO₄ 511.1970, found 511.1987.

(*E*)-1-(1-(4-Acetylphenyl)ethylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1*H*-benz[diazepin-2(3*H*)-one (**4h**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–70–70–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4h** (*t_R* = 31 min). Yield: 51.5 mg, 53%. Yellow amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.47 (s, 1H), 6.15 (s, 1H), 5.00 (d, *J* = 14.7 Hz, 1H), 4.35 (d, *J* = 14.7 Hz, 1H), 4.30–4.16 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.41–3.32 (m, 1H), 3.28 (s, 3H), 2.98–2.90 (m, 2H), 2.53 (s, 3H), 2.33 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 197.4, 171.1, 159.1, 148.3, 147.2, 146.6, 136.3, 136.1, 135.3, 129.6, 129.4, 128.9, 128.1, 127.9, 125.0, 115.2, 114.1, 355

112.1, 55.7, 55.4, 55.3, 47.5, 44.5, 31.8, 26.5, 21.8. HRMS (EI): m/z [M]⁺ calcd for C₃₀H₃₁NO₅ 485.2202, found 485.2207.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(1-(pyridin-4-yl)-ethylidene)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4i**). The material after workup was subjected to column chromatography on silica gel with EtOAc as eluent followed by reversed-phase preparative HPLC using gradient pump mode and MeCN/H₂O (20–30–30–40–100%, 10 min intervals) as eluent with a flow rate of 10 mL/min to deliver pure **4i** (t_R = 37 min). Yield: 53 mg, 60%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 8.42 (bs, 2H), 7.25 (d, J = 8.3 Hz, 2H), 7.08–7.00 (m, 2H), 6.88 (d, J = 8.3 Hz, 2H), 6.49 (s, 1H), 6.14 (s, 1H), 4.97 (d, J = 14.7 Hz, 1H), 4.36 (d, J = 14.7 Hz, 1H), 4.26–4.12 (m, 1H), 3.84–3.76 (m, 6H), 3.42–3.30 (m, 4H), 2.98–2.89 (m, 2H), 2.31 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 170.8, 159.2, 150.5, 149.1, 148.6, 146.8, 137.2, 134.4, 129.5, 129.4, 128.0, 124.3, 123.7, 114.9, 114.1, 112.3, 55.7, 55.5, 55.3, 47.6, 44.5, 31.8, 21.3. HRMS (EI): m/z [M]⁺ calcd for C₂₇H₂₈N₂O₄ 444.2049, found 444.2065.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(1-(thiophene-3-yl)-ethylidene)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4j**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–60–70–70–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4j** (t_R = 35 min). Yield: 33 mg, 37%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.24 (d, J = 8.3 Hz, 2H), 7.08–7.01 (m, 2H), 6.87 (d, J = 8.3 Hz, 2H), 6.66–6.60 (m, 1H), 6.49 (s, 1H), 6.36 (s, 1H), 4.98 (d, J = 14.7 Hz, 1H), 4.34 (d, J = 14.7 Hz, 1H), 4.25–4.10 (m, 1H), 3.86–3.75 (m, 6H), 3.43 (s, 3H), 3.36–3.25 (m, 1H), 2.96–2.86 (m, 2H), 2.32 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 159.0, 148.4, 146.8, 141.9, 134.1, 131.7, 129.7, 129.4, 128.3, 127.5, 125.7, 124.3, 123.7, 114.8, 114.0, 112.1, 55.7, 55.5, 55.3, 47.5, 44.5, 31.7, 21.6. HRMS (EI): m/z [M]⁺ calcd for C₂₆H₂₇NO₄S 449.1661, found 449.1648. Further elution provided *N*-(4,5-dimethoxy-2-(thiophene-3-yl)phenethyl)-*N*-(4-methoxybenzyl)but-2-ynamide (**5j**) as a ~3:2 mixture of rotamers (t_R = 39 min). Yield: 24 mg, 27%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.44–7.34 (m, 2H), 7.17–7.10 (m, 1H), 7.10–7.04 (m, 1H), 7.03–6.94 (m, 2H), 6.87–6.73 (m, 3.6H), 6.67 (s, 0.4H), 4.39 (s, 1.2H), 4.25 (s, 0.8H), 3.90 (s, 1.8H), 3.89 (s, 1.2H), 3.86 (s, 1.2H), 3.85 (s, 1.8H), 3.80 (s, 1.8H), 3.78 (s, 1.2H), 3.52–3.41 (m, 0.8H), 3.35–3.23 (m, 1.2H), 2.91–2.73 (m, 2H), 1.98 (s, 1.8H), 1.96 (s, 1.2H). ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 159.0, 154.7, 154.6, 148.5, 148.4, 147.5, 147.2, 141.55, 141.54, 129.6, 129.3, 129.14, 129.10, 128.9, 128.80, 128.77, 128.73, 128.5, 128.4, 125.5, 125.3, 122.6, 122.5, 114.0, 113.9, 113.5, 113.3, 112.9, 112.8, 88.9, 88.6, 73.6, 73.5, 56.1, 56.00, 55.98, 55.95, 55.30, 55.26, 52.2, 49.1, 46.5, 45.2, 31.9, 30.3, 4.06, 4.05. HRMS (EI): m/z [M]⁺ calcd for C₂₆H₂₇NO₄S 449.1661, found 449.1670.

(*E*)-1-((*E*)-Hept-3-en-2-ylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4k**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (4:1 → 7:3) as eluent to deliver pure **4k**. Last fractions containing **4k** overlapping with other impurities were concentrated separately and resubjected to column chromatography to deliver a second portion of pure **4k**. Combined yield: 45 mg, 52%. Pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.21 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.74 (s, 1H), 6.53 (s, 1H), 6.36 (dt, J = 15.6, 1.2 Hz, 1H), 5.92 (dt, J = 15.6, 7.0 Hz, 1H), 4.93 (d, J = 14.7 Hz, 1H), 4.29 (d, J = 14.7 Hz, 1H), 4.05–3.92 (m, 1H), 3.88–3.75 (m, 9H), 3.26–3.13 (m, 1H), 2.89–2.75 (m, 2H), 2.14–1.96 (m, 5H), 1.46–1.31 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 172.1, 159.0, 148.4, 146.5, 134.0, 133.9, 133.2, 129.8, 129.34, 129.28, 128.0, 125.1, 115.4, 114.0, 112.5, 55.9, 55.8, 55.3, 47.4, 44.4, 35.3, 31.7, 22.5, 16.3, 13.7. HRMS (EI): m/z [M]⁺ calcd for C₂₇H₃₃NO₄ 435.2410, found 435.2415.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(1-phenylpropylidene)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4m**). An increased Pd(PPh₃)₂Cl₂ (5.6 mg, 4 mol %) loading and extended reaction time of 25 min were used. The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by reversed-phase preparative HPLC

with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–60–70–70–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4m** (t_R = 39 min). Yield: 45 mg, 49%. White solid. Mp: 191–193 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.30–7.04 (m, 8H), 6.88 (d, J = 8.3 Hz, 2H), 6.43 (s, 1H), 6.18 (s, 1H), 5.05 (d, J = 14.7 Hz, 1H), 4.37–4.18 (m, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.39–3.25 (m, 4H), 3.14–3.01 (m, 1H), 2.97–2.87 (m, 2H), 2.68–2.53 (m, 1H), 1.60 (s, 2H), 0.92 (t, J = 7.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 159.0, 147.8, 146.4, 143.7, 140.3, 134.3, 129.7, 129.4, 129.2, 128.0, 127.6, 126.7, 125.6, 115.3, 114.0, 111.9, 55.6, 55.32, 55.30, 47.5, 44.6, 31.8, 28.2, 12.4. HRMS (EI): m/z [M]⁺ calcd for C₂₉H₃₁NO₄ 457.2253, found 457.2251.

1-(Diphenylmethylene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4o**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (50–60–70–80–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min (8 mL/min for two first intervals) to deliver pure **4o** (t_R = 24 min). Yield: 15 mg, 15%. White amorphous solid; ¹H NMR (300 MHz, CDCl₃): δ 7.57–7.46 (m, 2H), 7.42–7.32 (m, 3H), 7.16–7.00 (m, 5H), 6.69–6.59 (m, 4H), 6.53 (s, 1H), 6.37 (s, 1H), 5.05 (d, J = 14.9 Hz, 1H), 4.32–4.17 (m, 1H), 3.87 (d, J = 14.9 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 3.41 (s, 3H), 3.25–3.96 (m, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 158.7, 148.3, 146.9, 140.71, 140.66, 140.63, 136.4, 130.1, 129.7, 129.3, 128.8, 127.93, 127.85, 127.8, 127.3, 126.8, 125.5, 114.3, 113.8, 112.2, 55.7, 55.5, 55.2, 46.9, 44.4, 31.8; HRMS (ESI): m/z [M + H]⁺ calcd for C₃₃H₃₂NO₄ 506.2326, found 506.2318. Further elution provided *N*-(2-(4,5-dimethoxybiphenyl-2-yl)ethyl)-*N*-(4-methoxybenzyl)-3-phenylpropionamide (**5o**) as a ~1:1 mixture of rotamers (t_R = 31 min). Yield: 6 mg, 6%. Pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.54–7.24 (m, 10H), 7.01–6.89 (m, 2H), 6.85–6.74 (m, 2.5H), 6.72 (s, 0.5H), 6.71 (s, 0.5H), 6.67 (s, 0.5H), 4.39 (s, 1H), 4.24 (s, 1H), 3.92 (s, 1.5H), 3.85 (s, 1.5H), 3.83 (s, 1.5H), 2 × 3.79 (s, 1.5H), 3.63 (s, 1.5H), 3.56–3.44 (m, 1H), 3.37–3.25 (m, 1H), 2.95–2.74 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 159.0, 154.5, 154.4, 148.33, 148.30, 147.4, 147.2, 141.4, 141.3, 134.6, 134.3, 132.4, 132.2, 130.04, 130.01, 129.8, 129.5, 129.4, 128.9, 128.7, 128.6, 128.5, 128.4, 128.31, 128.27, 128.24, 127.6, 127.1, 126.9, 120.6, 120.5, 114.0, 113.9, 113.4, 113.3, 112.8, 112.6, 90.0, 89.7, 81.9, 81.8, 56.1, 55.9, 55.7, 55.29, 55.27, 52.3, 49.3, 46.8, 45.4, 32.0, 30.1. HRMS (EI): m/z [M]⁺ calcd for C₃₃H₃₁NO₄ 505.2253, found 505.2283.

(*E*)-3-Methyl-1-(1-phenylethylidene)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4q**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (50–60–70–80–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min (8 mL/min for two first intervals) to deliver pure **4q** (t_R = 14 min). Yield: 38 mg, 69%. White amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.21–6.97 (m, 7H), 6.82–6.68 (m, 2H), 4.55–4.39 (m, 1H), 3.40–3.06 (m, 6H), 2.27 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 141.5, 137.8, 135.3, 134.9, 133.7, 132.6, 129.9, 128.8, 127.9, 127.0, 126.8, 125.8, 47.7, 32.8, 31.5, 22.1. HRMS (ESI⁺): m/z [M + H]⁺ calcd for C₁₉H₂₀NO⁺ 278.1539, found 278.1534.

(*E*)-3-Isopropyl-1-(1-phenylethylidene)-4,5-dihydro-1H-benz[d]azepin-2(3H)-one (**4s**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (7:3) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–60–70–70–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4s** (t_R = 33 min). Yield: 27.5 mg, 45%. White amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.19–6.96 (m, 7H), 6.82–6.67 (m, 2H), 4.92 (sept, J = 6.8 Hz, 1H), 4.24–4.08 (m, 1H), 3.58–3.45 (m, 1H), 3.29–2.98 (m, 2H), 2.23 (s, 3H), 1.23 (d, J = 6.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 171.3, 141.6, 137.3, 135.7, 135.2, 133.9, 132.3, 129.8, 128.8, 127.9, 127.0, 126.7, 125.7, 43.6, 39.1, 34.5, 21.9, 20.8, 20.6. HRMS (EI): m/z [M]⁺ calcd for C₂₁H₂₃NO 305.1780, found 305.1773.

(*E*)-8,9-Dimethoxy-3-(4-methoxybenzyl)-1-(1-phenylethylidene)-3,4,5,6-tetrahydrobenzo[d]azepin-2(1*H*)-one (**4u**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (7:3 → 1:1) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–70–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4u** (*t_R* = 36 min). Yield: 12 mg, 13%. White amorphous solid; ¹H NMR (300 MHz, CDCl₃): δ 7.23–7.10 (m, 6H), 6.88–6.80 (m, 3H), 6.47 (s, 3H), 4.49 (bs, 2H), 3.84–3.74 (m, 8H), 3.58–3.49 (m, 2H), 2.67–2.57 (m, 2H), 2.24–2.14 (m, 3H), 1.76–1.57 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ 172.6, 159.0, 147.9, 147.0, 140.6, 134.9, 133.4, 131.9, 129.72, 129.69, 129.6, 127.9, 127.6, 126.9, 114.2, 113.9, 112.8, 55.9, 55.7, 55.3, 49.5, 49.1, 36.0, 28.9, 21.2; HRMS (EI): *m/z* [M]⁺ calcd for C₂₉H₃₁NO₄ 457.2253, found 457.2251. Further elution provided *N*-(3-(4,5-dimethoxybiphenyl-2-yl)propyl)-*N*-(4-methoxybenzyl)but-2-ynamide (**5u**) as a ~1:1 mixture of rotamers (*t_R* = 43 min). Yield: 31 mg, 34%. Colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.46–7.30 (m, 3H), 7.30–7.21 (m, 2H), 7.10–7.00 (m, 2H), 6.88–6.77 (m, 2H), 6.74 (s, 0.5H), 6.73 (s, 0.5H), 6.71 (s, 0.5H), 6.67 (s, 0.5H), 4.46 (s, 1H), 4.32 (s, 1H), 2 × 3.90 (s, 1.5H), 2 × 3.85 (s, 1.5H), 3.80 (s, 1.5H), 3.78 (s, 1.5H), 3.34–3.24 (m, 1H), 3.18–3.07 (m, 1H), 2.56–2.39 (m, 2H), 2.00 (s, 1.5H), 1.89 (s, 1.5H), 1.70–1.52 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 159.0, 154.8, 154.6, 148.1, 146.9, 146.8, 141.7, 141.6, 134.2, 133.9, 131.1, 130.8, 129.5, 129.41, 129.38, 128.9, 128.4, 128.23, 128.17, 126.9, 126.7, 114.0, 113.9, 113.4, 113.3, 112.20, 112.17, 89.0, 88.9, 73.7, 73.4, 56.05, 56.02, 55.96, 55.95, 55.3, 55.2, 51.6, 47.3, 46.2, 43.1, 30.03, 29.97, 29.8, 28.4, 4.1, 3.9. HRMS (EI): *m/z* [M]⁺ calcd for C₂₉H₃₁NO₄ 457.2253, found 457.2276.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(4-phenylbut-3-yn-2-ylidene)-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**4y**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (7:3 → 3:2) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–70–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4y** (*t_R* = 42 min). Yield: 22.4 mg, 24%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.34–7.19 (m, 8H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.53 (s, 1H), 4.95 (d, *J* = 14.7 Hz, 1H), 4.32 (d, *J* = 14.7 Hz, 1H), 4.07–3.94 (m, 1H), 3.86 (s, 3H), 3.81 (s, 6H), 3.32–3.20 (m, 1H), 2.97–2.80 (m, 2H), 2.22 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 159.1, 148.8, 146.4, 142.6, 131.4, 129.5, 128.4, 128.0, 125.2, 123.1, 119.2, 114.3, 114.1, 112.1, 94.2, 90.3, 55.84, 55.80, 55.3, 47.6, 44.5, 31.9, 21.0. HRMS (EI): *m/z* [M]⁺ calcd for C₃₀H₂₉NO₄ 467.2097, found 467.2075. Further elution provided (*E*)-1-((*Z*)-4,6-diphenylhex-3-en-5-yn-2-ylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**6a**) (*t_R* = 63 min). Yield: 11.4 mg, 10%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.62–7.48 (m, 4H), 7.43–7.18 (m, 8H), 7.07 (s, 1H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.82 (s, 1H), 6.55 (s, 1H), 4.99 (d, *J* = 14.7 Hz, 1H), 4.31 (d, *J* = 14.7 Hz, 1H), 4.12–3.97 (m, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.74 (s, 3H), 3.30–3.20 (m, 1H), 2.98–2.78 (m, 2H), 2.61 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.5, 159.1, 148.8, 146.6, 139.6, 139.5, 134.7, 134.1, 131.2, 129.6, 129.4, 128.6, 128.48, 128.45, 128.3, 127.9, 126.2, 125.0, 123.4, 123.2, 115.7, 114.1, 112.6, 98.7, 88.8, 55.9, 55.8, 55.3, 47.4, 44.3, 31.8, 19.3. HRMS (EI): *m/z* [M]⁺ calcd for C₃₈H₃₅NO₄ 569.2566, found 569.2596.

(*E*)-3-Methyl-1-(4-phenylbut-3-yn-2-ylidene)-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**4z**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (7:3) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–70–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4z** (*t_R* = 35 min). Yield: 11.5 mg, 19%. Yellow solid. Mp: 144–146 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.79–7.68 (m, 1H), 7.31–7.18 (m, 7H), 7.17–7.09 (m, 1H), 4.30–4.14 (m, 1H), 3.33–2.96 (m, 6H), 2.17 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 170.3, 142.8, 135.3, 133.2, 132.0, 131.5, 129.9, 128.3, 128.2, 128.1, 125.6, 123.1, 119.9, 93.6, 90.0, 47.6, 32.8, 31.6, 20.9. HRMS (EI): *m/z* [M]⁺ calcd for C₂₁H₁₉NO 301.1467,

found 301.1489. Further elution provided (*E*)-1-((*Z*)-4,6-diphenylhex-3-en-5-yn-2-ylidene)-3-methyl-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**6b**) (*t_R* = 55 min). Yield: 10.5 mg, 13%. Yellow solid. Mp: 180–183 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.60–7.46 (m, 4H), 7.41–7.12 (m, 10H), 7.00 (s, 1H), 4.35–4.20 (m, 1H), 3.32–2.95 (m, 6H), 2.56 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.4, 139.9, 139.6, 135.7, 134.6, 134.5, 133.2, 132.9, 131.2, 130.4, 128.5, 128.44, 128.38, 128.1, 127.8, 126.4, 125.8, 123.5, 123.4, 98.6, 88.9, 47.5, 32.6, 31.5, 19.2. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₉H₂₆NO 404.2009, found 404.2004.

General Procedure for the Heck–Suzuki Tandem Reaction for the Synthesis of 3-Benzazepines **4l,n,p,r,t** and Benzazocine **4v**.

Pd(PPh₃)₂Cl₂ (4.2 mg, 3 mol %), vinylpotassium trifluoroborate **3p** (40 mg, 0.3 mmol), and propargylamide **1** (0.2 mmol) were loaded into a microwave instrument vial and dissolved in DMF (1.8 mL). Then K₃PO₄ (85 mg, 0.4 mmol) was added followed by distilled water (0.45 mL). The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at the set temperature of 115 °C for 20 min utilizing a maximum power of 100 W. Upon completion of the irradiation time the vial was cooled with a stream of air, and then a fresh portion of Pd(PPh₃)₂Cl₂ (2.8 mg, 2 mol %) was added. The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at the set temperature of 115 °C for another 15 min. Upon completion of the reaction the vial was cooled with a stream of air. The reaction mixture was diluted with EtOAc (50 mL), washed with water (2 × 50 mL), dried over MgSO₄, and concentrated under reduced pressure. The resulting crude material was subjected to the appropriate purification procedure.

(*E*)-1-(But-3-en-2-ylidene)-7,8-dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**4l**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent to deliver pure **4l**. Yield: 57 mg, 72%. Beige amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.21 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.72 (s, 1H), 6.69 (dd, *J* = 17.4, 10.9 Hz, 1H), 6.53 (s, 1H), 5.44 (d, *J* = 17.4 Hz, 1H), 5.20 (d, *J* = 10.9 Hz, 1H), 4.92 (d, *J* = 14.7 Hz, 1H), 4.31 (d, *J* = 14.7 Hz, 1H), 4.04–3.91 (m, 1H), 3.87–3.77 (m, 9H), 3.27–3.15 (m, 1H), 2.89–2.77 (m, 2H), 2.08 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.7, 159.0, 148.6, 146.6, 136.6, 135.6, 133.1, 129.6, 129.3, 128.1, 124.6, 116.4, 115.3, 114.0, 112.6, 56.0, 55.9, 55.3, 47.4, 44.4, 31.7, 15.4. HRMS (EI): *m/z* [M]⁺ calcd for C₂₄H₂₇NO₄ 393.1940, found 393.1943.

(*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(pent-1-en-3-ylidene)-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**4n**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by recrystallization/washing with diethyl ether to deliver pure **4n**. Yield: 65 mg, 80%. Yellow solid. Mp: 164–166 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.70 (s, 1H), 6.61–6.47 (m, 2H), 5.46 (d, *J* = 17.5 Hz, 1H), 5.21 (d, *J* = 11.0 Hz, 1H), 4.94 (d, *J* = 14.7 Hz, 1H), 4.29 (d, *J* = 14.7 Hz, 1H), 4.05–3.74 (m, 11H), 3.27–3.15 (m, 1H), 2.90–2.66 (m, 3H), 2.55–2.40 (m, 1H), 1.14 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.7, 159.0, 148.6, 146.6, 138.8, 136.2, 133.9, 129.7, 129.4, 128.1, 124.8, 116.3, 115.3, 114.0, 112.6, 56.0, 55.8, 55.3, 47.3, 44.3, 31.7, 22.1, 13.5. HRMS (EI): *m/z* [M]⁺ calcd for C₂₅H₂₉NO₄ 407.2097, found 407.2097.

(*Z*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-1-(1-phenylallylidene)-4,5-dihydro-1*H*-benz[d]azepin-2(3*H*)-one (**4p**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (1:1) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O with 0.1% HCOOH (30–40–50–60–70–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4p** (*t_R* = 40 min). Yield: 16.4 mg, 18%. White amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.47–7.28 (m, 5H), 6.97–6.82 (m, 2H), 6.70 (s, 4H), 6.60 (s, 1H), 5.26 (d, *J* = 10.9 Hz, 1H), 4.95 (d, *J* = 15.8 Hz, 2H), 4.15–4.00 (m, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 3.84–3.73 (m, 4H), 3.21–3.10 (m, 1H), 3.04–2.86 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 170.5, 158.8, 148.9, 146.8, 138.8, 137.5, 137.3, 135.4, 129.7, 129.3, 129.2, 128.3, 127.9, 127.4, 124.2, 120.6, 114.8, 113.7, 112.8, 56.1, 55.9, 634

55.3, 46.7, 44.1, 31.6. HRMS (EI): m/z [M]⁺ calcd for C₂₉H₂₉NO₄ 455.2097, found 455.2086.

(*E*)-1-(*But-3-en-2-ylidene*)-3-methyl-4,5-dihydro-1*H*-benz[d]-azepin-2(3*H*)-one (**4r**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (3:2) as eluent to deliver pure **4r**. Yield: 37.7 mg, 83%. Yellow amorphous solid. ¹H NMR (300 MHz, CDCl₃): δ 7.27–7.08 (m, 4H), 6.64 (dd, *J* = 17.4, 10.9 Hz, 1H), 5.44 (d, *J* = 17.4 Hz, 1H), 5.19 (d, *J* = 10.9 Hz, 1H), 4.26–4.09 (m, 1H), 3.28–2.94 (m, 6H), 2.04 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 136.8, 135.7, 135.4, 133.6, 132.7, 132.6, 130.3, 127.8, 125.7, 116.7, 47.6, 32.6, 31.4, 15.4. HRMS (EI): m/z [M]⁺ calcd for C₁₅H₁₇NO 227.1310, found 227.1328.

(*E*)-1-(*But-3-en-2-ylidene*)-3-isopropyl-4,5-dihydro-1*H*-benz[d]-azepin-2(3*H*)-one (**4t**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (7:3 → 1:1) as eluent to deliver pure **4t**. Yield: 40.3 mg, 79%. Pale yellow solid. Mp: 136–138 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.24–7.08 (m, 4H), 6.63 (dd, *J* = 17.4, 10.9 Hz, 1H), 5.42 (dd, *J* = 17.4, 1.1 Hz, 1H), 5.17 (dd, *J* = 10.9, 1.1 Hz, 1H), 4.87 (sept, *J* = 6.8 Hz, 1H), 3.95–3.80 (m, 1H), 3.45–3.34 (m, 1H), 3.16–2.92 (m, 2H), 2.00 (s, 3H), 1.19 (d, *J* = 6.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 171.4, 137.6, 135.5, 133.1, 132.8, 132.5, 130.3, 127.7, 125.6, 116.4, 43.5, 38.9, 34.4, 20.7, 20.5, 15.1. HRMS (ESI): m/z [M + H]⁺ calcd for C₁₇H₂₂NO 256.1696, found 256.1697.

(*E*)-1-(*But-3-en-2-ylidene*)-8,9-dimethoxy-3-(4-methoxybenzyl)-3,4,5,6-tetrahydrobenzo[d]azocin-2(1*H*)-one (**4v**). The material obtained after workup was subjected to column chromatography on silica gel with heptane/EtOAc (4:1 → 3:1) as eluent to deliver pure **4v**. Last fractions containing **4v** overlapping with other impurities were concentrated separately and resubjected to column chromatography to deliver a second portion of pure **4v**. Combined yield: 48 mg, 59%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.15 (d, *J* = 8.5 Hz, 2H), 6.86–6.78 (m, 3H), 6.62 (s, 1H), 6.26 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.34 (d, *J* = 17.4, 0.8 Hz, 1H), 5.10 (d, *J* = 10.8, 0.8 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.79 (s, 3H), 3.45–3.30 (m, 2H), 2.71–2.59 (m, 2H), 1.95 (s, 3H), 1.74–1.56 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 172.3, 158.9, 148.2, 147.4, 136.9, 134.8, 132.3, 130.6, 129.7, 129.6, 129.2, 115.8, 113.9, 112.9, 112.8, 56.0, 55.9, 55.3, 49.8, 49.3, 36.2, 29.1, 14.6. HRMS (EI): m/z [M]⁺ calcd for C₂₅H₂₉NO₄ 407.2097, found 407.2078.

Synthesis of (*E*)-7,8-Dimethoxy-3-(4-methoxybenzyl)-2-phenyl-1-(1-phenylbutylidene)-2,3,4,5-tetrahydro-1*H*-benz[d]azepine (**4w**). Pd(PPh₃)₂Cl₂ (4.2 mg, 3 mol %), phenylboronic acid **3a** (36.6 mg, 0.3 mmol), and propargylamine **1g** (107 mg, 0.2 mmol) were loaded into a microwave instrument vial and dissolved in DMF (1.8 mL). Then K₃PO₄ (85 mg, 0.4 mmol) was added followed by distilled water (0.45 mL). The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at a set temperature of 110 °C for 25 min utilizing a maximum power of 100 W. Upon completion of the irradiation time, the vial was cooled with a stream of air, and then a fresh portion of Pd(PPh₃)₂Cl₂ (2.8 mg, 2 mol %) was added. The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at the set temperature of 110 °C for another 15 min. Upon completion of the reaction, the vial was cooled with a stream of air. The reaction mixture was diluted with EtOAc (50 mL), washed with water (2 × 50 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The resulting crude material was subjected to column chromatography on silica gel with heptane/EtOAc (23:2 → 17:3) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O (60–70–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min to deliver pure **4w** (*t*_R = 37 min). Yield: 29 mg, 27%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.30–7.10 (m, 7H), 7.06–6.92 (m, 3H), 6.91–6.78 (m, 4H), 6.47 (s, 1H), 5.66 (s, 1H), 4.94 (s, 1H), 3.82–3.71 (m, 7H), 3.40 (d, *J* = 13.7 Hz, 1H), 3.25 (s, 3H), 3.19–3.06 (m, 2H), 3.05–2.92 (m, 2H), 2.76–2.62 (m, 1H), 2.49–2.36 (m, 1H), 1.51–1.35 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 158.4, 146.9, 145.5, 143.4, 142.8, 141.3, 139.2, 132.4, 131.7, 131.0, 129.4, 129.0, 128.0, 127.8, 127.4, 126.5, 125.8, 117.2, 113.5, 111.1, 69.2, 57.9, 55.7, 55.5, 55.2, 47.2, 36.0, 35.2, 21.6, 14.4. HRMS (EI): m/z [M]⁺ calcd for

C₃₆H₃₉NO₃ 533.2930, found 533.2959. Further elution provided *N*-(2-(4,5-dimethoxybiphenyl-2-yl)ethyl)-*N*-(4-methoxybenzyl)-1-phenylhex-2-yn-1-amine (**5w**) contaminated with unknown impurities (*t*_R = 40 min). Amount of obtained material: 43 mg. NMR yield: 35%. ¹H NMR (300 MHz, CDCl₃): δ 7.53–7.44 (m, 2H), 7.35–7.00 (m, 10H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.66 (s, 1H), 6.58 (s, 1H), 4.61 (s, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 3.57 (d, *J* = 13.4 Hz, 1H), 3.32 (d, *J* = 13.4 Hz, 1H), 2.81–2.65 (m, 1H), 2.64–2.44 (m, 3H), 2.40–2.23 (m, 2H), 1.62 (q, *J* = 7.2 Hz, 2H), 1.06 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 158.5, 147.8, 146.7, 141.5, 140.0, 134.2, 131.9, 130.1, 129.9, 129.3, 128.2, 128.0, 127.8, 127.0, 126.6, 113.5, 113.1, 112.9, 88.0, 75.4, 56.2, 55.92, 55.87, 55.3, 54.5, 51.9, 31.5, 22.6, 20.9, 13.7. HRMS (EI): m/z [M]⁺ calcd for C₃₆H₃₉NO₃ 533.2930, found 533.2930.

Synthesis of (*E*)-1-(*Hex-1-en-3-ylidene*)-7,8-dimethoxy-3-(4-methoxybenzyl)-2-phenyl-2,3,4,5-tetrahydro-1*H*-benz[d]azepine (**4x**). Pd(PPh₃)₂Cl₂ (4.2 mg, 3 mol %), vinylpotassium trifluoroborate **3p** (40 mg, 0.3 mmol), and propargylamine **1g** (107 mg, 0.2 mmol) were loaded into a microwave instrument vial and dissolved in DMF (1.8 mL). Then K₃PO₄ (85 mg, 0.4 mmol) was added followed by distilled water (0.45 mL). The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at the set temperature of 115 °C for 25 min utilizing a maximum power of 100 W. Upon completion of the irradiation time, the vial was cooled with a stream of air, and then a fresh portion of Pd(PPh₃)₂Cl₂ (4.2 mg, 3 mol %) was added. The reaction vial was evacuated, flushed with argon, sealed, and irradiated under stirring at the set temperature of 115 °C for another 15 min. Upon completion of the reaction the vial was cooled with a stream of air. The reaction mixture was diluted with EtOAc (50 mL), washed with water (2 × 50 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The resulting crude material was subjected to column chromatography on silica gel with heptane/EtOAc (17:3) as eluent followed by reversed-phase preparative HPLC with gradient pump mode, MeCN/H₂O (50–60–70–80–80–90–100%, 10 min intervals) as eluent, and a flow rate of 10 mL/min (8 mL/min for two first intervals) to deliver pure **4x** (*t*_R = 51 min). Yield: 53 mg, 55%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.22–7.04 (m, 7H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.63 (s, 1H), 6.21 (dd, *J* = 17.5, 11.0 Hz, 1H), 6.08 (s, 1H), 5.17 (dd, *J* = 17.5, 1.1 Hz, 1H), 4.89 (dd, *J* = 11.0, 1.1 Hz, 1H), 4.79 (s, 1H), 3.90 (s, 3H), 3.78 (s, 3H), 3.70–3.58 (m, 4H), 3.27 (d, *J* = 13.8 Hz, 1H), 3.01–2.78 (m, 3H), 2.73–2.37 (m, 3H), 1.70–1.40 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 158.4, 147.7, 145.7, 142.4, 141.8, 137.0, 136.1, 132.2, 131.5, 129.9, 129.4, 128.2, 127.8, 126.7, 116.4, 113.5, 112.7, 111.7, 69.6, 57.8, 56.1, 55.8, 55.2, 47.2, 34.4, 29.8, 22.4, 14.8. HRMS (EI): m/z [M]⁺ calcd for C₃₂H₃₇NO₃ 483.2773, found 483.2787.

■ ASSOCIATED CONTENT

● Supporting Information

¹H and ¹³C NMR spectra for **1b**, **4a–z**, **5g,j,o,u,w**, and **6a,b**. X-ray crystallographic structures and CIF for **4m,t,z** and **6b**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00670.

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Notes

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