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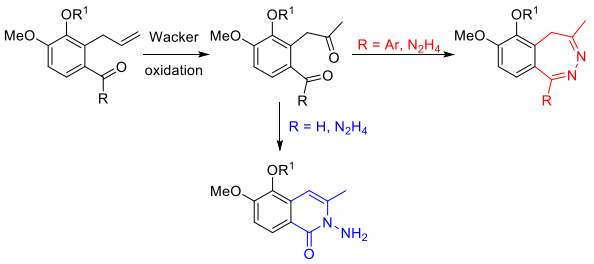


ABSTRACT

A new, four-step synthetic route for substituted 2,3-benzodiazepines **1**, starting from aldehyde **4**, was developed with excellent overall yields. This route was carried out by the 1,2-addition of **4** with various aromatic Grignard reagents, PCC-oxidation, and aerobic Wacker-type oxidation of the olefinic group of **6**, followed by condensation of the resulting 1,5-dicarbonyl **7** with N_2H_4. Isoquinolones **9** were obtained when an aldehyde group was used instead of a ketone. The key structures were confirmed by X-ray single crystal diffraction analysis.

INTRODUCTION

The benzodiazepine moiety is considered a prominent skeleton in medicinal chemistry, and many biologically active compounds, such as those with anti-inflammatory, anticonvulsant, antianxiety, antidepressive, sedative, psychoactive and hypnotic activities, possess this important core.[1] Among them, substituted 2,3-benzodiazepines **1** act as tranquilizing agents and constitute the partial molecules of meaningful scaffolds known as noncompetitive 2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl)propionic acid (AMPA) receptor antagonists, which exert anticonvulsant and neuroprotective activities.[2] Further, tofisopam, which is the most activated derivative, was found to be a highly active nonsedative, anxiolytic in humans.[3] Other representative 2,3-benzodiazepines, such as girisopam and nerisopam, are biologically active (Figure 1). Some synthetic routes for the synthesis of the 2,3-benzodiazepine skeleton, such as the four-step formation starting from arylethanols or arylacetones,[4] base-mediated reaction of arynes with β-diketones[5] and acid-promoted transformation from 2-benzopyrylium salts[6] have been reported. Herein, a facile synthetic route starting from commercially available materials with higher isolated yields is reported.

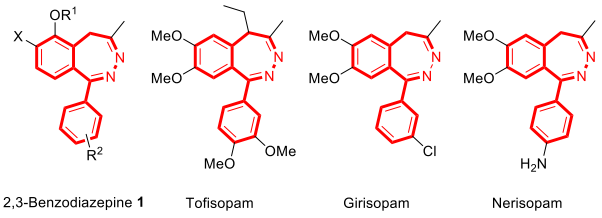


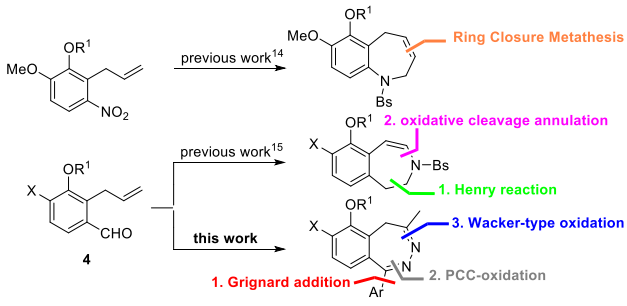
Figure 1. Bioactive 2,3-benzodiazepines

RESULTS AND DISCUSSION

Recently, we developed a series of synthetic routes toward benzofused compounds, such as 1-azahomoisotwistanes,[7] benzodioxepanes,[8] benzo[*g*]indazoles,[9] benzo[*g*]chrysenes,[10] 2-naphthols,[11] isochromenes[12] and isoquinolines,[13] by using commercially available isovanillin (**2a**) as a starting

material. All of the compounds were derived from the versatile 2-allylbenzaldehyde (**4**), which was easily prepared via a three-step synthesis with moderate overall yields by a reaction procedure of *O*-allylation and Claisen rearrangement followed by *O*-alkylation. We established the synthetic procedures for substituted benzazepines, including dihydro-1-benzazepines[14] and tetrahydro-3-benzazepines via the facile, efficient and high-yields synthetic routes.[15] Based on these results, the synthesis of dinitrogen-containing, heterocyclic 2,3-benzodiazepines **1**, skeletons from 2-allylbenzaldehyde **2** was our goal (Scheme1).

Allylbenzenes are well-known molecules with naturally occurring scaffolds that are mainly isolated from plants.[16] Among them, generalized allylbenzenes, such as 2-propenylbenzenes and 1-propenylbenzenes, are widely used in the pharmaceutical, materials chemistry, fragrance, and cosmetic industries and are also important intermediates for the construction of complicated compounds in organic chemistry.[17]

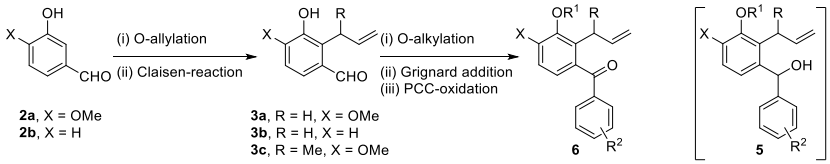


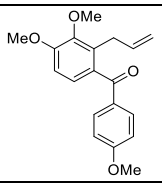
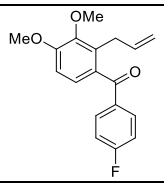
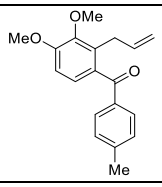
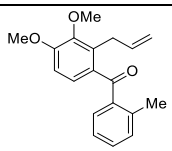
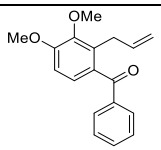
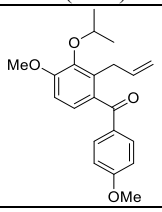
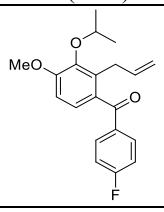
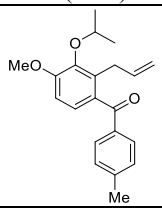
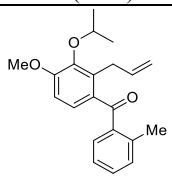
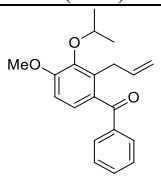
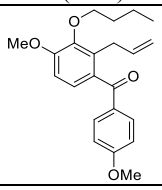
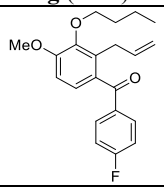
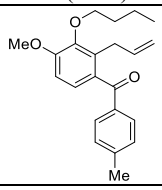
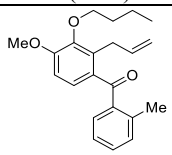
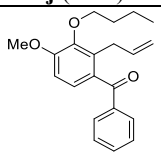
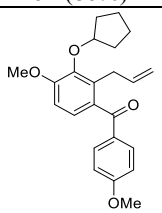
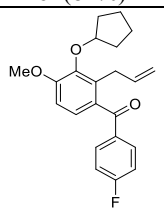
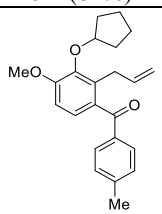
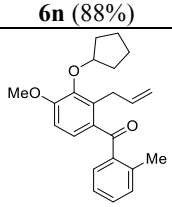
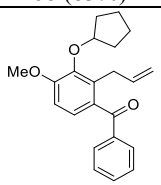
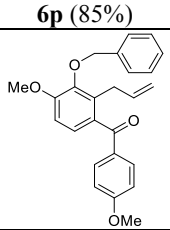
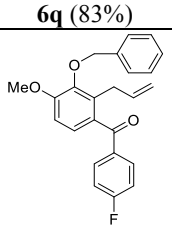
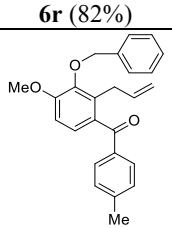
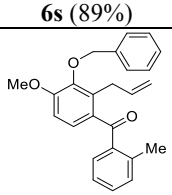
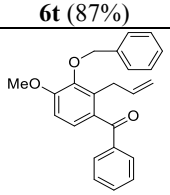
Scheme 1. Synthesis of benzofused nitrogen-containing compounds

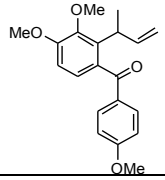
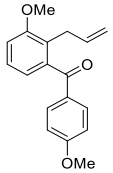
On the basis of our successful experiments, including Grignard addition of aldehydes, PCC-oxidation of secondary alcohols and aerobic Wacker-type oxidation of the resulting terminal olefins,[11] we believed that it may be possible to develop a synthetic route for the 1,5-dicarbonyl skeleton **7**, which can condense with N_2H_4 to afford 2,3-benzodiazepines. As shown in Table 1, an efficient five-step synthetic route was employed to build **6** from isovanillin (**2a**) and 2-hydroxybenzaldehyde (**2b**)

via (i) *O*-allylation with allyl or *trans*-crotyl bromide (R = H or Me), (ii) Claisen rearrangement with decalin, (iii) *O*-alkylation or *O*-benzylation of **3** with alkyl or benzyl bromide, (iv) Grignard 1,2-addition with arylmagnesium bromide (R_2 = 4-$OMeC_6H_4$, 4-FC_6H_4, 4-MeC_6H_4, 2-MeC_6H_4 and C_6H_5) and (v) oxidation with pyridinium chlorochromate (PCC).

Table 1. Five-step synthesis of **6**[a, b]



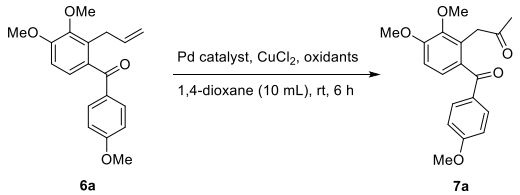
				
6a (90%)	**6b** (83%)	**6c** (85%)	**6d** (86%)	**6e** (88%)
				
6f (86%)	**6g** (87%)	**6h** (84%)	**6i** (89%)	**6j** (87%)
				
6k (86%)	**6l** (84%)	**6m** (81%)	**6n** (88%)	**6o** (83%)
				
6p (85%)	**6q** (83%)	**6r** (82%)	**6s** (89%)	**6t** (87%)
				
6u (85%)	**6v** (83%)	**6w** (81%)	**6x** (90%)	**6y** (86%)

	
6z (84%)	**6aa** (78%)

[a] The reactions were conducted on a 1.0 mmol scale with **2**. [b] The isolated products **6a**-**6aa** were >95% pure as determined by ^{1}H NMR analysis.

Next, for the aerobic Wacker reaction of **6** with a terminal olefin moiety, **6a** was selected as the model substrate in a Pd^{II}/Cu^{II} system catalyzed oxidation. Then, the condensation reaction of in situ generated **7** with N_2H_4 took place. As shown in Table 2, after screening different Wacker-type oxidative conditions and our previous work,[11,18] we still believed that the $PdCl_2/CuCl_2$ system-mediated Wacker-type oxidation by O_2 was better than other oxidants such as CAN, DDQ, IBX, Oxone, *t*-BuO_2H and TBHP, which all gave lower yields (entries 1-6). When molecular oxygen was used as the oxidant, the isolated yield increased to 91% (entry 7). No apparent yield was isolated when the amounts of $PdCl_2$ and $CuCl_2$ were increased (entries 8-10). Changing the Pd(II) catalyst from $PdCl_2$ to $Pd(OAc)_2$, $PdBr_2$, $PdCl_2(MeCN)_2$, $PdCl_2(PPh_3)_2$ or $Pd_2(dba)_3$ gave a similar yield of the desired 1,5-dicarbonyl **7a** as shown in entries 11-15. Without molecular oxygen, **7a** was only isolated in a 15% yield, with **6a** recovered in a yield of 80% (entry 16).

Table 2. Reaction conditions of **6a**[a,b]



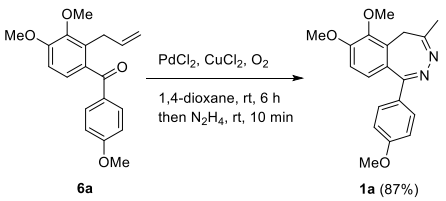
6a **7a**

entry	Pd^{II} (mol %)	$CuCl_2$ (eq.)	oxidants (eq.)	yield (%)[b]
1	$PdCl_2$ (5.8)	1.5	CAN (1.0)	20[c]

2	$PdCl_2$ (5.8)	1.5	DDQ (1.0)	18[c]
3	$PdCl_2$ (5.8)	1.5	IBX (1.0)	15[c]
4	$PdCl_2$ (5.8)	1.5	Oxone (1.0)	16[c]
5	$PdCl_2$ (5.8)	1.5	*t*-BuO_2H (1.0)	19[c]
6	$PdCl_2$ (5.8)	1.5	TBHP (1.0)	14[c]
7	**$PdCl_2$ (5.8)**	1.5	**O_2**	**91[d]**
8	$PdCl_2$ (11.6)	1.5	O_2	85[d]
9	$PdCl_2$ (5.8)	3.0	O_2	83[d]
10	$PdCl_2$ (11.6)	3.0	O_2	84[d]
11	$Pd(OAc)_2$ (5.8)	1.5	O_2	85[d]
12	$PdBr_2$ (5.8)	1.5	O_2	86[d]
13	$PdCl_2(ACN)_2$ (5.8)	1.5	O_2	85[d]
14	$PdCl_2(PPh_3)_2$ (5.8)	1.5	O_2	83[d]
15	$Pd_2(dba)_3$ (5.8)	1.5	O_2	83[d]
16	$PdCl_2$ (5.8)	1.5	air	15[e]

[a] The reactions were conducted on a 1.0 mmol scale with **6a**. [b] **7a** was >95% pure as determined by ^1H NMR analysis. [c] Unknown products were obtained (entry1, 5%; entry 2, 6%; entry 3, 6%; entry 4, 5%; entry 5, 7%; entry 6, 5%). [d] Trace amounts (< 5%) of unknown products were obtained. [e] The starting material **6a** was recovered in 80% yield.

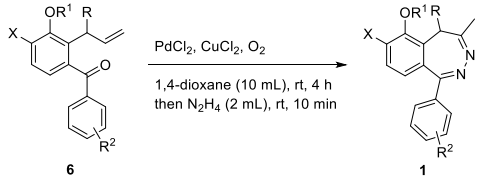
The above results show that **7a** was isolated in high yield (Table 2, entry 7). An efficient synthetic route for substituted 2,3-benzodiazepines **1** from **6** was created. Based on the results, **6a** was selected as the model substrate to test the feasibility of a one-pot method with N_2H_4. Accordingly, the desired product **1a** was obtained in good yield, and the overall two-step yield was 87% (Scheme 2).

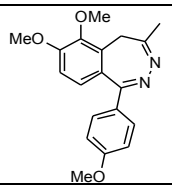
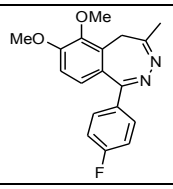
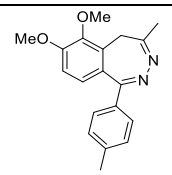
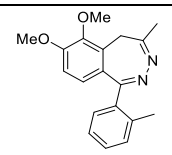
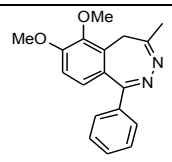
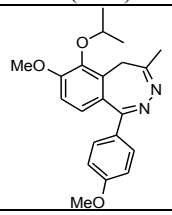
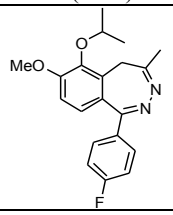
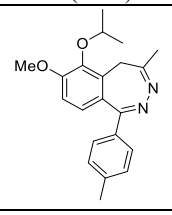
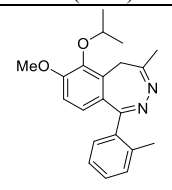
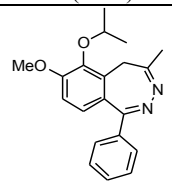
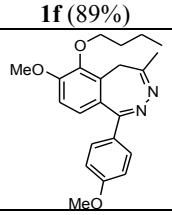
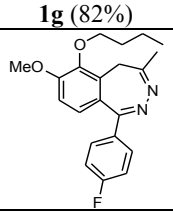
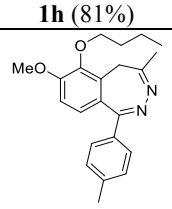
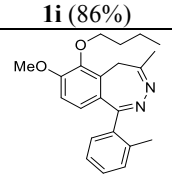
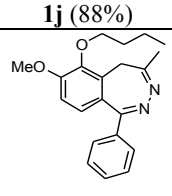


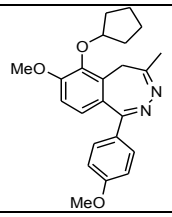
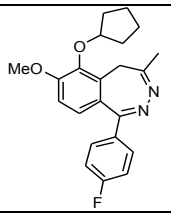
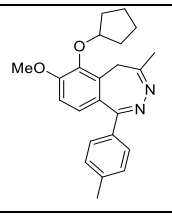
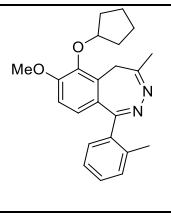
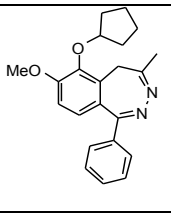
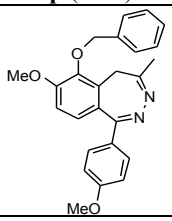
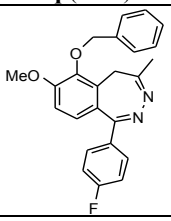
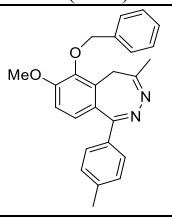
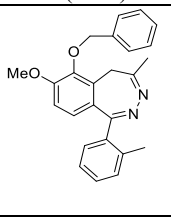
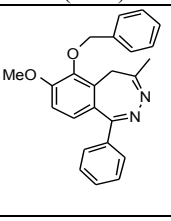
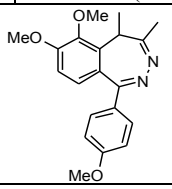
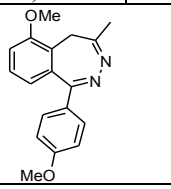
Scheme 2. One-pot synthetic route for **1a** from **6a**

Based on the optimal conditions (Scheme 2), we further examined the substrate scope and generality of the reaction. The electron-donating group (R^2 = 4-OMe) and various aryl substituents on **6**, including an electron-withdrawing group (R^2 = 4-F) and electron-neutral groups (R^2 = 4-Me, 2-Me or H), were all also suitable for the synthesis of **1b**-**1e**. Changing the R^1 substituents of **6** to isopropyl, *n*-butyl, cyclopentyl and benzyl groups was well tolerated, providing the desired **1f-1y** products. Accordingly, **1z** (X = OMe, R = Me) and **1aa** (X = H, R = H) were also synthesized in this transformation. Consequently, **6a**-**6aa** were synthesized in this successive procedure, which included a Wacker-type oxidation and condensation with N_2H_4 to synthesize 2,3-benzodiazepines **1a**-**1aa** in high yields ranging from 79% to 90%. All of the compound structures and corresponding isolated yields for **1a**-**1aa** are shown in Table 3. The structures of **1a**, **1c**, **1p** and **7y** were determined by single-crystal X-ray crystallography.[19]

Table 3. Synthesis of **1**[a]

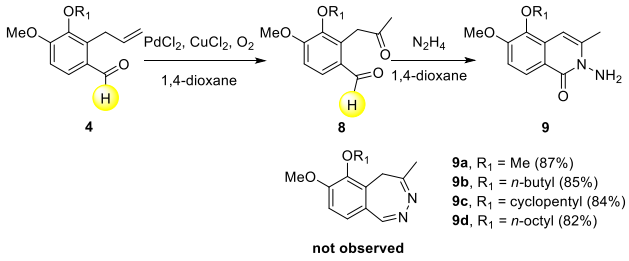


				
1a (87%)	**1b** (88%)	**1c** (83%)	**1d** (86%)	**1e** (90%)
				
1f (89%)	**1g** (82%)	**1h** (81%)	**1i** (86%)	**1j** (88%)
				
1k (89%)	**1l** (85%)	**1m** (82%)	**1n** (86%)	**1o** (88%)

				
1p (90%)	**1q** (85%)	**1r** (84%)	**1s** (84%)	**1t** (85%)
				
1u (89%)	**1v** (83%)	**1w** (81%)	**1x** (85%)	**1y** (84%)
				
1z (85%)		**1aa** (79%)		

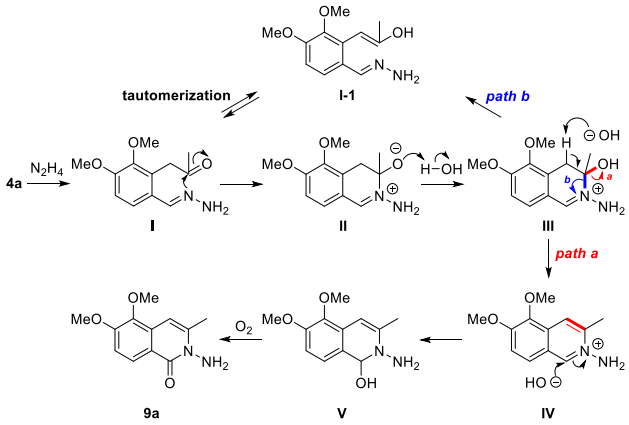
[a] Optimal reaction conditions: (i) compound **6** (1.0 mmol), $PdCl_2$ (10 mg, 5.8 mol %), $CuCl_2$ (200 mg, 1.5 mmol), O_2 (bubbled), dioxane (10 mL), rt, 10 h, (ii) N_2H_4 (2 mL), rt, 10 min. [b] The isolated products **1a**-**1aa** were >95% pure as determined by ^1H NMR analysis.

Isoquinolone is an important molecular framework in alkaloidal natural products, and compounds that contain this skeleton show distinct bioactivities.[20] Due to their chemical stability, isoquinolones are frequently used as building blocks.[21] Among them, functionalized isoquinolin-1(2*H*)-ones appear in numerous natural products and drugs.[22] Although a number of methods for the synthesis of isoquinolin-1(2*H*)-ones and their derivatives are available, the development of efficient approaches for the synthesis of the isoquinolin-1(2*H*)-one skeleton is of interest.[23] Starting material **6** when changed to **4**, which has an H atom instead of the Ar substituent group (ketone→aldehyde), and a Wacker-type oxidation afforded compound **8**. Then, **8** reacted with N_2H_4 under optimized conditions. Intriguingly, the desired 2,3-benzodiazepine was not observed, but the substituted isoquinolones **9a**-**9d** were isolated in good yields (Scheme 3). The structure of **9a** was confirmed by single-crystal X-ray crystallography (see Supporting Information).[19]



Scheme 3. Synthesis of **1** and **9**

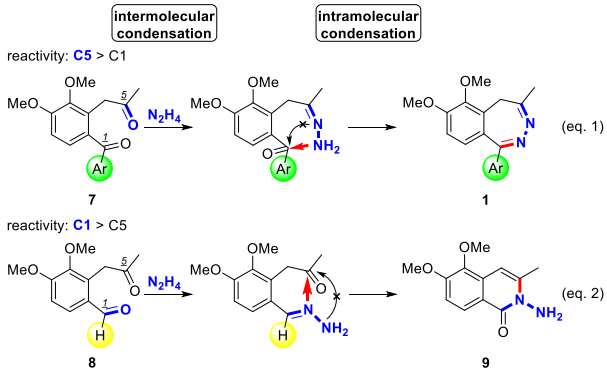
The possible mechanism for the synthesis of **9a** is shown in Scheme 4. First, the pathway intermediate **I** should form via the condensation of **4a** with N_2H_4. With an intramolecular aldol-type condensation of **I**, **IV** was formed from the hydrated reaction of **II** and dehydration of **III** (path a). In another route (path b), the deprotonative elimination of hydroxyl anion from **III** to install the alkene is likely to compete with the cleavage of the C-N bond leading to formation of an enol **I-1**, which will reverse to **I** by tautomerization. Then, in situ hydration generated **IV** to achieve **V**. Finally, the oxygen-catalyzed oxidation of **V** was conducted to formed **9a**.



Scheme 4. Possible mechanism

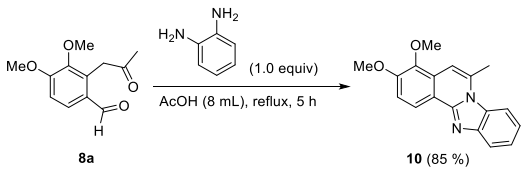
The differential behavior of **7** and **8** with N_2H_4 was discussed in Scheme 5. For the construction of 2,3-benzodiazepines **1**, we think that N_2H_4 first preferred to treat with C5 position of **7** via

intermolecular condensation (carbonyl reactivity: C5 > C1). Subsequently, the formal (5+2) annulation was achieved by intramolecular condensation between primary amine and benzylic ketone (eq. 1). Compared with the formation of isoquinolin-1(2*H*)-ones **9**, the formyl group (C1) of aldehydes **8** favored to react with N_2H_4 than C5 carbonyl position by intermolecular condensation. In the following intramolecular process, the formal (5+1) annulation of tertiary amine with ketone was conducted due to the tendency of the ring closure (six-membered > seven-membered), as shown in equation 2. Therefore, N_2H_4 played as a key condensation role for the construction of bicycles **1** and **9** via the intermolecular and intramolecular routes.



Scheme 5. Differential behavior of **7** and **8** with N_2H_4

On the basis of our successful experiments for the synthesis of substituted quinoxalines,[24] we changed the di-nitrogen source from N_2H_4 (H_2N-NH_2) to 1,2-diaminobenzene (H_2N-C-C-NH_2). **8a** was transformed into benzimidazo[2,1-*a*]isoquinoline **10** in high yield (Scheme 6).



Scheme 6. Synthesis of **10**

In summary, we have presented a facile synthetic route for the synthesis of substituted 2,3-benzodiazepines via Grignard addition, PCC-oxidation, aerobic Wacker-type oxidation and the condensation with N_2H_4 in high yields. Changing the functional group from allylketone to allylaldehyde, one-pot procedure of Wacker-type oxidation/N_2H_4 or 1,2-diaminobenzene condensation provided the functionalized isoquinolin-1(2*H*)-ones and benzimidazo[2,1-*a*]isoquinoline in good to excellent yields under the optimal conditions. This protocol started from simple starting materials and reagents, provided a new synthetic route toward the skeleton of 2,3-benzodiazepines. The structural frameworks of key products were confirmed by X-Ray single crystal diffraction analysis. Further investigation regarding synthetic applications of 2-allylbenzaldehyde and bioactive applications of and 2,3-benzodiazepines will be conducted and published in due course.

EXPERIMENT SECTION

General

All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Purity was determined by NMR and melting point. Melting points were determined with a SMP3 melting apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Varian spectrometer operating at 400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (*J*) are given in Hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer microTOF-Q by ESI using a hybrid ion-trap. X-ray crystal structures were obtained with an diffractometer (CAD4, Kappa CCD).

General synthetic procedure for synthesis of 6a-6aa is as follows

A solution of a Grignard reagent (1.0 M in THF, 1.5 mL, 1.5 mmol) was added to a stirred solution of skeleton **4** (1.0 mmol) in THF (10 mL) at ice bath. The reaction mixture was stirred at rt for 5 h. Water (5 mL) was added to the reaction mixture and the mixture was filtered through a short plug of Celite. The filtrate was concentrated under reduced pressure. The residue was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford different crude product under reduced pressure. Without further purification, a solution of the resulting secondary alcohol **5** in DCM (10 mL) was added to a mixture of pyridinium chlorochromate (430 mg, 2.0 mmol) and Celite (500 mg) in DCM (20 mL). After being stirred at rt for 3 h, the mixture was filtered through a short silica gel column. The filtrate was dried, filtered, and evaporated to yield crude compound. Purification on silica gel (hexanes/EtOAc = 6/1~3/1) afforded **6a-6aa**.

(2-Allyl-3,4-dimethoxyphenyl)(4-methoxyphenyl)methanone (6a).[13a]

Yield = 90% (281 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.89-5.79 (m, 1H), 4.86-4.79 (m, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.51 (dt, *J* = 1.2, 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 163.1, 154.0, 147.3, 136.9, 133.3, 132.2 (2x), 132.0, 130.7, 125.1, 115.0, 113.2 (2x), 108.7, 60.4, 55.4, 55.1, 30.4; HRMS (ESI, M^++Na) calcd for $C_{19}H_{20}O_4Na$ 335.1259, found 335.1252.

(2-Allyl-3,4-dimethoxyphenyl)(4-fluorophenyl)methanone (6b).[13a]

Yield = 83% (249 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.77 (m, 2H), 7.13-7.07 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 5.93-5.83 (m, 1H), 4.90-4.84 (m, 2H), 3.92 (s, 3H), 3.85 (s, 3H), 3.58 (dt, *J* = 1.6, 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.9, 165.5 (d, *J* = 253.2 Hz), 154.7, 147.8, 137.1, 134.7 (d, *J* = 3.1 Hz,), 134.1, 132.8 (d, *J* = 9.1 Hz, 2x), 131.6, 125.9, 115.4, 115.3 (d, *J* = 21.9 Hz, 2x), 108.9, 60.9, 55.7, 30.5; HRMS (ESI, M^++H) calcd for $C_{18}H_{18}FO_3$ 301.1240, found 301.1244.

(2-Allyl-3,4-dimethoxyphenyl)(*p*-tolyl)methanone (6c).

Yield = 85% (252 mg); Colorless solid; mp = 59-60 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.94-5.84 (m, 1H), 4.91-4.85 (m, 2H), 3.91 (s, 3H), 3.85 (s, 3H), 3.58 (dt, *J* = 1.6, 6.0 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 154.5, 147.7, 143.6, 137.2, 135.8, 134.0, 132.2, 130.4 (2x), 128.9 (2x), 125.9, 115.3, 108.9, 60.8, 55.7, 30.6, 21.6; HRMS (ESI, M^++H) calcd for $C_{19}H_{21}O_3$ 297.1491, found 297.1493.

(2-Allyl-3,4-dimethoxyphenyl)(*o*-tolyl)methanone (6d).[13a]

Yield = 86% (255 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.15 (m, 4H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.05-5.95 (m, 1H), 5.00-4.94 (m, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.77 (dt, *J* = 1.6, 6.4 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 155.4, 147.7, 139.7, 137.6, 137.3, 135.1, 132.0, 131.0, 130.5, 129.8, 128.4, 125.1, 115.1, 108.7, 60.8, 55.6, 30.3, 20.3; HRMS (ESI, M^++H) calcd for $C_{19}H_{21}O_3$ 297.1491, found 297.1496.

(2-Allyl-3,4-dimethoxyphenyl)(phenyl)methanone (6e).[13a]

Yield = 88% (248 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.75 (m, 2H), 7.57-7.52 (m, 1H), 7.44-7.40 (m, 2H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.95-5.86 (m, 1H), 4.92-4.89 (m, 1H), 4.88-4.86 (m, 1H), 3.91 (s, 3H), 3.85 (s, 3H), 3.60 (dt, *J* = 1.6, 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 154.6, 147.7, 138.4, 137.1, 134.2, 132.6, 131.7, 130.1 (2x), 128.1 (2x), 126.2, 115.3, 108.8, 60.8, 55.7, 30.5; HRMS (ESI, M^++Na) calcd for $C_{18}H_{18}O_3Na$ 305.1154, found 305.1146.

(2-Allyl-3-isopropoxy-4-methoxyphenyl)(4-methoxyphenyl)methanone (6f).

Yield = 86% (293 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 1H), 5.84-5.74 (m, 1H), 4.83-4.78 (m, 2H), 4.58-4.51 (m, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.59 (dt, *J* = 1.6, 6.4 Hz, 2H), 1.29 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.3, 163.2, 154.2, 145.1, 136.6, 133.8, 132.9, 132.4 (2x), 131.1, 124.8, 115.2, 113.3 (2x), 108.6, 74.7, 55.5, 55.3, 30.8, 22.5 (2x); HRMS (ESI, M^++Na) calcd for $C_{21}H_{24}O_4Na$ 363.1572, found 363.1566.

(2-Allyl-3-isopropoxy-4-methoxyphenyl)(4-fluorophenyl)methanone (6g).

Yield = 87% (285 mg); Colorless solid; mp = 46-47 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.8 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.07-7.02 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 5.83-5.73 (m, 1H), 4.81-4.76 (m, 2H), 4.57-4.51 (m, 1H), 3.83 (s, 3H), 3.61 (dt, *J* = 1.6, 6.0 Hz, 2H), 1.27 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.9, 165.3 (d, *J* = 252.5 Hz), 154.6, 145.2, 136.6, 134.6 (d, *J* = 3.0 Hz), 134.2, 132.5 (d, *J* = 9.1 Hz, 2x), 131.5, 125.2, 115.3, 115.1 (d, *J* = 21.2 Hz, 2x), 108.6, 74.7, 55.4, 30.5, 22.4 (2x); HRMS (ESI, M^++Na) calcd for $C_{20}H_{21}FO_3Na$ 351.1372, found 351.1366.

(2-Allyl-3-isopropoxy-4-methoxyphenyl)(*p*-tolyl)methanone (6h).

Yield = 84% (272 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.86-5.76 (m, 1H), 4.85-4.80 (m, 2H), 4.58-4.52 (m, 1H), 3.88 (s, 3H), 3.62 (dt, *J* = 1.6, 6.4 Hz, 2H), 2.41 (s, 3H), 1.31 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 154.5, 145.2, 143.4, 136.8, 135.9, 134.3, 132.3, 130.3 (2x), 128.9 (2x), 125.4, 115.4, 108.6, 74.9, 55.6, 30.8, 22.6 (2x), 21.6; HRMS (ESI, M^++H) calcd for $C_{21}H_{25}O_3Na$ 325.1804, found 325.1809.

(2-Allyl-3-isopropoxy-4-methoxyphenyl)(*o*-tolyl)methanone (6i).

Yield = 89% (289 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.32 (m, 1H), 7.28-7.23 (m, 2H), 7.19-7.15 (m, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 5.96-5.86 (m, 1H), 4.95-4.90 (m, 2H), 4.58-4.52 (m, 1H), 3.86 (s, 3H), 3.79 (dt, *J* = 1.6, 6.4 Hz, 2H), 2.39 (s, 3H), 1.31 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 155.4, 145.3, 139.7, 137.8, 137.0, 135.5, 132.3, 131.1, 130.5, 129.9, 127.8, 125.1, 115.2, 108.5, 74.8, 55.5, 30.5, 22.5 (2x), 20.4; HRMS (ESI, M^++Na) calcd for $C_{21}H_{24}O_3Na$ 347.1623, found 347.1617.

(2-Allyl-3-isopropoxy-4-methoxyphenyl)(phenyl)methanone (6j).

Yield = 87% (270 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77-7.74 (m, 2H), 7.57-7.53 (m, 1H), 7.45-7.41 (m, 2H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.87-5.77 (m, 1H), 4.86-4.83 (m, 1H), 4.82-4.80 (m, 1H), 4.59-4.53 (m, 1H), 3.88 (s, 3H), 3.64 (dt, *J* = 1.6, 6.4 Hz, 2H), 1.31 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.7, 154.8, 145.3, 138.5, 136.8, 134.6, 132.6, 130.5, 130.2 (2x), 128.2 (2x), 125.8, 115.4, 108.6, 74.9, 55.6, 30.7, 22.6 (2x); HRMS (ESI, M^++Na) calcd for $C_{20}H_{22}O_3Na$ 333.1467, found 333.1460.

(2-Allyl-3-butoxy-4-methoxyphenyl)(4-methoxyphenyl)methanone (6k).

Yield = 86% (305 mg); Colorless solid; mp = 59-60 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.91-5.81 (m, 1H), 4.86-4.82 (m, 2H), 3.96 (t, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.56 (d, *J* = 1.6, 6.0 Hz, 2H), 1.81-1.74 (m, 2H), 1.55-1.46 (m, 2H), 0.97 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 163.3, 154.3, 146.8, 137.1, 133.6, 132.5 (2x), 132.3, 131.1, 125.2, 115.1, 113.3 (2x), 108.8, 72.9, 55.6, 55.3, 32.3, 30.6, 19.1, 13.8; HRMS (ESI, M^++Na) calcd for $C_{22}H_{26}O_4Na$ 377.1729, found 377.1722.

(2-Allyl-3-butoxy-4-methoxyphenyl)(4-fluorophenyl)methanone (6l).

Yield = 84% (287 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.10-7.04 (m, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.91-5.81 (m, 1H), 4.85-4.80 (m, 2H), 3.96 (t, *J* = 6.4 Hz, 2H), 3.87 (s, 3H), 3.58 (dt, *J* = 1.6, 6.0 Hz, 2H), 1.80-1.73 (m, 2H), 1.55-1.46 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 165.4 (d, *J* = 253.2 Hz), 154.7, 146.9, 137.0, 134.7 (d, *J* = 3.0 Hz), 134.1, 132.6 (d, *J* = 9.1 Hz, 2x), 131.4, 125.7, 115.2 (d, *J* = 22.0 Hz, 2x), 115.2, 108.8, 72.9, 55.6, 32.3, 30.4, 19.1, 13.8; HRMS (ESI, M^++Na) calcd for $C_{21}H_{23}FO_3Na$ 365.1529, found 365.1525.

(2-Allyl-3-butoxy-4-methoxyphenyl)(*p*-tolyl)methanone (6m).

Yield = 81% (274 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 5.93-5.83 (m, 1H), 4.89-4.83 (m, 2H), 3.97 (t, *J* = 6.4 Hz, 2H), 3.89 (s, 3H), 3.59 (dt, *J* = 1.6, 6.4 Hz, 2H), 2.41 (s, 3H), 1.82-1.75 (m, 2H), 1.57-1.47 (m, 2H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3, 154.6, 146.9, 143.5, 137.2, 135.8, 134.1, 132.1, 130.4 (2x), 128.9 (2x), 125.7, 115.2, 108.8, 73.0, 55.7, 32.3, 30.6, 21.6, 19.2, 13.9; HRMS (ESI, M^++H) calcd for $C_{22}H_{27}O_3$ 339.1960, found 339.1965.

(2-Allyl-3-butoxy-4-methoxyphenyl)(*o*-tolyl)methanone (6n).

Yield = 88% (342 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.33 (m, 1H), 7.27-7.23 (m, 2H), 7.20-7.16 (m, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.03-5.93 (m, 1H), 4.98-4.92 (m, 2H), 3.96 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.77 (dt, *J* = 1.6, 6.0 Hz, 2H), 2.38 (s, 3H), 1.83-1.76 (m, 2H), 1.57-1.48 (m, 2H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 155.5, 147.0, 139.8, 137.7, 137.4, 135.3, 132.1, 131.1, 130.5, 129.9, 128.3, 125.2, 115.1, 108.7, 73.1, 55.6, 32.3, 30.4, 20.4, 19.2, 13.9; HRMS (ESI, M^++Na) calcd for $C_{22}H_{26}O_3Na$ 361.1780, found 361.1775.

(2-Allyl-3-butoxy-4-methoxyphenyl)(phenyl)methanone (6o).

Yield = 83% (269 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77-7.74 (m, 2H), 7.55-7.50 (m, 1H), 7.42-7.39 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.94-5.84 (m, 1H), 4.90-4.84 (m, 2H), 3.98 (t, *J* = 6.4 Hz, 2H), 3.87 (s, 3H), 3.63 (dt, *J* = 1.6, 6.4 Hz, 2H), 1.82-1.75 (m, 2H), 1.57-1.47 (m, 2H), 0.98 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 154.7, 146.9, 138.4, 137.1, 134.2, 132.5, 131.6, 130.1 (2x), 128.1 (2x), 126.0, 115.1, 108.7, 72.9, 55.6, 32.3, 30.5, 19.1, 13.8; HRMS (ESI, M^++Na) calcd for $C_{21}H_{24}O_3Na$ 347.1623, found 347.1619.

(2-Allyl-3-(cyclopentyloxy)-4-methoxyphenyl)(4-methoxyphenyl)methanone (6p).

Yield = 85% (311 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.85-5.75 (m, 1H), 4.91-4.86 (m, 1H), 4.83-4.77 (m, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.56 (dt, *J* = 1.6, 6.0 Hz, 2H), 1.93-1.71 (m, 6H), 1.61-1.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.4 163.3, 154.1, 145.5, 136.7, 133.8, 132.4 (2x), 132.4, 131.1, 124.7, 115.2, 113.3 (2x), 108.8, 84.6, 55.5, 55.4, 32.8 (2x), 30.7, 23.6 (2x); HRMS (ESI, M^++H) calcd for $C_{23}H_{27}O_4$ 367.1909, found 367.1904.

(2-Allyl-3-(cyclopentyloxy)-4-methoxyphenyl)(4-fluorophenyl)methanone (6q).

Yield = 83% (294 mg); Colorless solid; mp = 70-71 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.11-7.05 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.85-5.75 (m, 1H), 4.91-4.82 (m, 1H), 4.82-4.77 (m, 2H), 3.88 (s, 3H), 3.59 (dt, *J* = 1.6, 6.0 Hz, 2H), 1.93-1.70 (m, 6H), 1.62-1.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.1, 165.4 (d, *J* = 253.2 Hz), 154.5, 145.7, 136.7, 134.7 (d, *J* = 3.0 Hz), 134.2, 132.7 (d, *J* = 9.1 Hz, 2x), 131.6, 125.2, 115.3, 115.2 (d, *J* = 21.2 Hz, 2x), 108.8, 84.7, 55.6, 32.8 (2x), 30.6, 23.6 (2x);

HRMS (ESI, M^++Na) calcd for $C_{22}H_{23}FO_3Na$ 377.1529, found 377.1523.

(2-Allyl-3-(cyclopentyloxy)-4-methoxyphenyl)(*p*-tolyl)methanone (6r).

Yield = 82% (287 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 5.87-5.77 (m, 1H), 4.91-4.87 (m, 1H), 4.85-4.80 (m, 2H), 3.87 (s, 3H), 3.60 (dt, *J* = 1.6, 6.0 Hz, 2H), 2.40 (s, 3H), 1.94-1.72 (m, 6H), 1.62-1.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3, 154.3, 145.5, 143.4, 136.7, 135.8, 134.1, 132.1, 130.3 (2x), 128.8 (2x), 125.2, 115.2, 108.7, 84.6, 55.5, 32.8 (2x), 30.6, 23.6 (2x), 21.5; HRMS (ESI, M^++H) calcd for $C_{23}H_{27}O_3$ 351.1960, found 351.1965.

(2-Allyl-3-(cyclopentyloxy)-4-methoxyphenyl)(*o*-tolyl)methanone (6s).

Yield = 89% (312 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.33 (m, 1H), 7.28-7.23 (m, 2H), 7.19-7.15 (m, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 1H), 5.96-5.86 (m, 1H), 4.94-4.85 (m, 3H), 3.87 (s, 3H), 3.76 (dt, *J* = 1.6, 6.4 Hz, 2H), 2.39 (s, 3H), 1.94-1.81 (m, 4H), 1.79-1.72 (m, 2H), 1.64-1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 155.3, 145.7, 139.7, 137.8, 137.0, 135.3, 132.3, 131.1, 130.5, 129.9, 127.7, 125.1, 115.2, 108.7, 84.7, 55.6, 32.8 (2x), 30.4, 23.6 (2x), 20.4; HRMS (ESI, M^++Na) calcd for $C_{23}H_{26}O_3Na$ 373.1780, found 373.1773.

(2-Allyl-3-(cyclopentyloxy)-4-methoxyphenyl)(phenyl)methanone (6t).

Yield = 87% (292 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76-7.73 (m, 2H), 7.54-7.49 (m, 1H), 7.41-7.37 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 5.88-5.78 (m, 1H), 4.91-4.88 (m, 1H), 4.85-4.80 (m, 2H), 3.86 (s, 3H), 3.62 (dt, *J* = 1.6, 6.4 Hz, 2H), 1.94-1.70 (m, 6H), 1.64-1.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 154.4, 145.5, 138.4, 136.7, 134.2, 132.5, 131.7, 130.0 (2x), 128.0 (2x), 125.5, 115.2, 108.7, 84.5, 55.5, 32.7 (2x), 30.5, 23.5 (2x); HRMS (ESI, M^++Na) calcd for

$C_{22}H_{24}O_3Na$ 359.1623, found 359.1619.

(2-Allyl-3-(benzyloxy)-4-methoxyphenyl)(4-methoxyphenyl)methanone (6u).

Yield = 85% (330 mg); Colorless solid; mp = 65-66 ^oC (recrystallized from hexanes and EtOAc); ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.8 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.42-7.38 (m, 2H), 7.36-7.32 (m, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 5.93-5.83 (m, 1H), 5.07 (s, 2H), 4.88-4.83 (m, 2H), 3.93 (s, 3H), 3.85 (s, 3H), 3.57 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.1, 163.3, 154.3, 146.2, 137.6, 136.9, 133.8, 132.4 (2x), 132.4, 131.0, 128.2 (2x), 127.9 (2x), 127.8, 125.4, 115.3, 113.4 (2x), 109.0, 74.5, 55.6, 55.3, 30.8; HRMS (ESI, M^++Na) calcd for $C_{25}H_{24}O_4Na$ 411.1572, found 411.1567.

(2-Allyl-3-(benzyloxy)-4-methoxyphenyl)(4-fluorophenyl)methanone (6v).

Yield = 83% (312 mg); Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81-7.76 (m, 2H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.42-7.32 (m, 3H), 7.13-7.09 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 5.90-5.80 (m, 1H), 5.05 (s, 2H), 4.88-4.80 (m, 2H), 3.94 (s, 3H), 3.57 (dt, *J* = 1.6, 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 165.5 (d, *J* = 253.2 Hz), 154.8, 146.4, 137.6, 136.9, 134.7 (d, *J* = 3.1 Hz), 134.4, 132.7 (d, *J* = 9.1 Hz, 2x), 131.6, 128.4 (2x), 128.0 (2x), 127.9, 126.0, 115.4 (d, *J* = 22.0 Hz, 2x), 115.2, 109.0, 74.7, 55.7, 30.7; HRMS (ESI, M^++H) calcd for $C_{24}H_{22}FO_3$ 377.1553, found 377.1558.

(2-Allyl-3-(benzyloxy)-4-methoxyphenyl)(*p*-tolyl)methanone (6w).

Yield = 81% (301 mg); Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.43-7.39 (m, 2H), 7.37-7.33 (m, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 5.97-5.88 (m, 1H), 5.09 (s, 2H), 4.93-4.87 (m, 2H), 3.93 (s, 3H), 3.64 (dt, *J* = 1.6, 6.4 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 154.9, 146.7, 143.9, 138.0, 137.4,

136.1, 134.5, 132.5, 130.6 (2x), 129.2 (2x), 128.6 (2x), 128.3 (2x), 128.2, 126.4, 115.7, 109.3, 74.9, 56.0, 31.1, 21.9; HRMS (ESI, M^++H) calcd for $C_{25}H_{25}O_3$ 373.1804, found 373.1812.

(2-Allyl-3-(benzyloxy)-4-methoxyphenyl)(*o*-tolyl)methanone (6x).

Yield = 90% (335 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.2 Hz, 2H), 7.43-7.33 (m, 4H), 7.29-7.25 (m, 2H), 7.21-7.18 (m, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.03-5.94 (m, 1H), 5.05 (s, 2H), 4.97-4.92 (m, 2H), 3.93 (s, 3H), 3.77 (d, *J* = 6.0 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 155.5, 146.5, 139.7, 137.7, 137.6, 137.3, 135.4, 132.2, 131.1, 130.5, 129.8, 128.5, 128.3 (2x), 127.9 (2x), 127.9, 125.2, 115.2, 108.8, 74.7, 55.7, 30.5, 20.4; HRMS (ESI, M^++Na) calcd for $C_{25}H_{24}O_3$ 395.1623, found 395.1616.

(2-Allyl-3-(benzyloxy)-4-methoxyphenyl)(phenyl)methanone (6y).

Yield = 86% (308 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77-7.74 (m, 2H), 7.58-7.32 (m, 8H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 5.92-5.82 (m, 1H), 5.05 (s, 2H), 4.88-4.81 (m, 2H), 3.94 (s, 3H), 3.58 (dt, *J* = 1.6, 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 154.8, 146.4, 138.4, 137.7, 137.1, 134.5, 132.7, 130.2 (2x), 128.4 (2x), 128.2 (2x), 128.0 (2x), 127.9 (2x), 126.4, 115.4, 108.9, 74.7, 55.8, 30.8; HRMS (ESI, M^++Na) calcd for $C_{24}H_{22}O_3Na$ 381.1467, found 381.1460.

(2-(But-3-en-2-yl)-3,4-dimethoxyphenyl)(4-methoxyphenyl)methanone (6z).[13a]

Yield = 84% (274 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.8 Hz, 2H), 6.93-6.89 (m, 3H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.14 (ddd, *J* = 6.4, 10.8, 17.2 Hz, 1H), 4.90-4.85 (m, 2H), 3.90 (s, 3H), 3.87 (s, 6H), 3.69-3.62 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 163.6, 154.1, 148.0, 152.5, 138.2, 132.9, 132.6 (2x), 131.2, 123.7, 113.5 (2x), 113.4, 109.5, 60.6, 55.7, 55.5, 38.7, 19.6; HRMS (ESI, M^++H) calcd for $C_{20}H_{23}O_4$ 327.1596, found 327.1600.

(2-Allyl-3-methoxyphenyl)(4-methoxyphenyl)methanone (6aa).

Yield = 78% (220 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.8 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 9.2 Hz, 2H), 6.86 (d, *J* = 7.6 Hz, 1H), 5.91-5.81 (m, 1H), 4.86-4.80 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.39 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.8, 163.7, 157.8, 140.8, 136.4, 132.6 (2x), 130.5, 126.7, 126.6, 119.9, 115.0, 113.5 (2x), 111.7, 55.7, 55.4, 31.0; HRMS (ESI, M^++H) calcd for $C_{18}H_{19}O_3$ 283.1334, found 283.1337.

General synthetic procedure for synthesis of 1a-1aa and 9a-9d is as follows

A representative synthetic procedure of skeleton **1** or **9** is as follows: $PdCl_2$ (10 mg, 5.8 mol %) and $CuCl_2$ (200 mg, 1.5 mmol) were added to a solution of skeleton **6** or **4** (1.0 mmol) in dioxane (10 mL) at rt. Then oxygen was bubbled into the mixture for 2 h, and stirred at rt for 4 h. N_2H_4 (2 mL) was added to a reaction mixture at rt. The reaction mixturewas stirred at rt for 10 min. The residue was diluted with water (2 mL) and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 5/1~3/1) afforded skeleton **1a-1aa** and **9a-9d**.

6,7-Dimethoxy-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (1a).

Yield = 87% (282 mg); Colorless solid; mp = 196-197 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 3.91 (s, 3H), 3.90 (d, *J* = 12.0 Hz, 1H), 3.89 (s, 3H), 3.91 (s, 3H), 2.73 (d, *J* = 12.0 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 157.8, 155.6, 154.5, 144.0, 133.6, 131.5, 130.9 (2x), 126.5, 124.0, 113.4 (2x), 110.4, 61.3, 55.7, 55.2, 30.6, 23.3; HRMS (ESI, M^++H) calcd for $C_{19}H_{21}N_2O_3$ 325.1552, found 325.1546. Single-crystal X-ray diagram: crystal of **1a** was grown

by slow diffusion of EtOAc into a solution of **1a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/n, a = 8.1616(6) Å, b = 8.6757(7) Å, c = 22.6247(19) Å, V = 1601.9(2) Å^3, Z = 4, d_{calcd} = 1.345 g/cm^3, F(000) = 688, 2θ range 1.80-26.47^o, R indices (all data) $R1$ = 0.0418, w$R2$ = 0.1152.

1-(4-Fluorophenyl)-6,7-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine (1b).

Yield = 88% (275 mg); Colorless solid; mp = 150-151 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.8 Hz, 2H), 7.07 (t, J = 8.8 Hz, 2H), 7.00 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 3.95 (d, J = 12.0 Hz, 1H), 3.93 (s, 3H), 3.92 (s, 3H), 2.73 (d, J = 12.0 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9 (d, J = 248.7 Hz), 157.6, 156.0, 154.9, 144.3, 135.1 (d, J = 3.0 Hz), 133.7, 131.5 (d, J = 8.3 Hz, 2x), 126.4, 123.9, 115.1 (d, J = 22.0 Hz, 2x), 110.7, 61.4, 55.8, 30.7, 23.4; HRMS (ESI, M$^+$+H) calcd for $C_{18}H_{18}FN_2O_2$ 313.1352, found 313.1347.

6,7-Dimethoxy-4-methyl-1-*p*-tolyl-5H-benzo[d][1,2]diazepine (1c).

Yield = 83% (256 mg); Colorless solid; mp = 155-156 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.8 Hz, 1H), 6.86 (d, J = 8.8 Hz, 1H), 3.91 (d, J = 12.0 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.73 (d, J = 12.0 Hz, 1H), 2.37 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 155.5, 154.5, 144.0, 139.7, 136.2, 133.6, 129.4 (2x), 128.7 (2x), 126.4, 124.1, 110.4, 61.3, 55.7, 30.6, 23.3, 21.2; HRMS (ESI, M$^+$+H) calcd for $C_{19}H_{21}N_2O_2$ 309.1603, found 309.1596. Single-crystal X-ray diagram: crystal of **1c** was grown by slow diffusion of EtOAc into a solution of **1c** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, a = 7.1877(5) Å, b = 25.1688(16) Å, c = 9.8090(6) Å, V = 1664.46(19) Å^3, Z = 4, d_{calcd} = 1.231 g/cm^3, F(000) = 656, 2θ range 1.62-26.41^o, R indices (all data) $R1$ = 0.0649, w$R2$ = 0.1299.

6,7-Dimethoxy-4-methyl-1-*o*-tolyl-5H-benzo[d][1,2]diazepine (1d).

Yield = 86% (265 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.2 Hz, 1H), 7.32-7.22 (m, 2H), 7.18 (d, *J* = 7.2 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 4.01 (d, *J* = 12.0 Hz, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 2.80 (d, *J* = 12.0 Hz, 1H), 2.20 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 155.4, 154.7, 144.2, 139.3, 137.0, 132.6, 130.5, 130.4, 129.1, 125.9, 125.7, 125.6, 110.9, 61.5, 55.8, 30.6, 23.6, 20.2; HRMS (ESI, M^++H) calcd for $C_{19}H_{21}N_2O_2$ 309.1603, found 309.1599.

6,7-Dimethoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (1e).

Yield = 90% (265 mg); Colorless solid; mp = 131-132 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.37-7.32 (m, 3H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 3.91 (d, *J* = 12.0 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 2.71 (d, *J* = 12.0 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 155.4, 154.5, 143.9, 138.9, 133.5, 129.5, 129.4 (2x), 127.9 (2x), 126.3, 123.9, 110.5, 61.2, 55.6, 30.5, 23.2; HRMS (ESI, M^++H) calcd for $C_{18}H_{19}N_2O_2$ 295.1447, found 295.1441.

6-Isopropoxy-7-methoxy-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (1f).

Yield = 89% (313 mg); Colorless solid; mp = 158-159 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 4.54-4.48 (m, 1H), 3.95 (d, *J* = 12.0 Hz, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 2.74 (d, *J* = 12.0 Hz, 1H), 2.12 (s, 3H), 1.42 (d, *J* =6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 158.1, 156.1, 154.8, 141.9, 134.7, 131.7, 131.0 (2x), 126.1, 124.1, 113.4 (2x), 110.3, 75.4, 55.7, 55.3, 31.2, 23.4, 22.9, 22.1; HRMS (ESI, M^++H) calcd for $C_{21}H_{25}N_2O_3$ 353.1865, found

353.1860.

1-(4-Fluorophenyl)-6-isopropoxy-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (1g).

Yield = 82% (279 mg); Colorless solid; mp = 189-190 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 9.2 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.09-7.03 (m, 2H), 6.96 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 4.55-4.49 (m, 1H), 3.97 (d, *J* = 12.0 Hz, 1H), 3.88 (s, 3H), 2.72 (d, *J* = 12.0 Hz, 1H), 2.13 (s, 3H), 1.43 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (d, *J* = 247.9 Hz), 157.6, 156.0, 155.0, 142.0, 135.3 (d, *J* = 3.0 Hz), 134.7, 131.4 (d, *J* = 8.4 Hz, 2x), 125.9, 123.8, 115.0 (d, *J* = 21.2 Hz, 2x), 110.4, 75.4, 55.7, 31.2, 23.4, 22.9, 22.1; HRMS (ESI, M^{+}+H) calcd for $C_{20}H_{22}FN_2O_2$ 341.1665, found 341.1660.

6-Isopropoxy-7-methoxy-4-methyl-1-*p*-tolyl-5H-benzo[d][1,2]diazepine (1h).

Yield = 81% (272 mg); Colorless solid; mp = 115-116 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 4.54-4.48 (m, 1H), 3.95 (d, *J* = 12.0 Hz, 1H), 3.88 (s, 3H), 2.74 (d, *J* = 12.0 Hz, 1H), 2.38 (s, 3H), 2.13 (s, 3H), 1.43 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 156.1, 154.8, 141.9, 139.8, 136.3, 134.7, 129.5 (2x), 128.8 (2x), 126.1, 124.1, 110.3, 75.4, 55.7, 31.2, 23.4, 22.9, 22.1, 21.3; HRMS (ESI, M^{+}+H) calcd for $C_{21}H_{25}N_2O_2$ 337.1916, found 337.1909.

6-Isopropoxy-7-methoxy-4-methyl-1-*o*-tolyl-5H-benzo[d][1,2]diazepine (1i).

Yield = 86% (289 mg); Colorless solid; mp = 135-136 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 7.2 Hz, 1H), 7.30-7.22 (m, 2H), 7.15 (d, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 1H), 4.58-4.52 (m, 1H), 4.03 (d, *J* = 12.0 Hz, 1H), 3.84 (s, 3H),

2.79 (d, *J* = 12.0 Hz, 1H), 2.16 (s, 3H), 1.99 (s, 3H), 1.42 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 155.5, 154.8, 141.8, 139.5, 136.8, 133.8, 130.5, 130.2, 128.9, 125.8, 125.5, 125.2, 110.7, 75.0, 55.7, 31.0, 23.6, 22.8, 22.0, 20.0; HRMS (ESI, M^++H) calcd for $C_{21}H_{25}N_2O_2$ 337.1916, found 337.1911.

6-Isopropoxy-7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (1j).

Yield = 88% (284 mg); Colorless solid; mp = 133-134 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.39-7.37 (m, 3H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 4.55-4.48 (m, 1H), 3.96 (d, *J* = 12.0 Hz, 1H), 3.87 (s, 3H), 2.73 (d, *J* = 12.0 Hz, 1H), 2.13 (s, 3H), 1.42 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 155.9, 154.8, 141.8, 139.1, 134.7, 129.6, 129.5 (2x), 128.0 (2x), 126.0, 123.9, 110.3, 75.3, 55.7, 31.1, 23.4, 22.8, 22.1; HRMS (ESI, M^++H) calcd for $C_{20}H_{23}N_2O_2$ 323.1760, found 323.1755.

6-Butoxy-7-methoxy-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (1k).

Yield = 89% (326 mg); Colorless solid; mp = 166-167 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 1H), 4.07-3.98 (m, 2H), 3.92 (d, *J* = 11.6 Hz, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 2.74 (d, *J* = 11.6 Hz, 1H), 2.14 (s, 3H), 1.87-1.79 (m, 2H), 1.61-1.52 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 157.9, 155.7, 154.7, 143.4, 133.9, 131.7, 131.0 (2x), 126.3, 124.1, 113.4 (2x), 110.4, 73.7, 55.7, 55.3, 32.3, 30.8, 23.3, 19.2, 13.9; HRMS (ESI, M^++H) calcd for $C_{22}H_{27}N_2O_3$ 367.2022, found 367.2017.

6-Butoxy-1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (1l).

Yield = 85% (301 mg); Colorless solid; mp = 142-143 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H

NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.08-7.02 (m, 2H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 1H), 4.08-3.98 (m, 2H), 3.94 (d, *J* = 12.0 Hz, 1H), 3.89 (s, 3H), 2.71 (d, *J* = 12.0 Hz, 1H), 2.14 (s, 3H), 1.87-1.79 (m, 2H), 1.61-1.52 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (d, *J* = 247.9 Hz), 157.4, 155.7, 154.9, 143.5, 135.2 (d, *J* = 3.0 Hz), 133.9, 131.4 (d, *J* = 8.3 Hz, 2x), 126.1, 123.8, 115.0 (d, *J* = 21.2 Hz, 2x), 110.6, 73.7, 55.7, 32.3, 30.8, 23.4, 19.2, 13.9; HRMS (ESI, M^++H) calcd for $C_{21}H_{24}FN_2O_2$ 355.1822, found 355.1818.

6-Butoxy-7-methoxy-4-methyl-1-*p*-tolyl-5H-benzo[d][1,2]diazepine (1m).

Yield = 82% (287 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 4.09-3.98 (m, 2H), 3.94 (d, *J* = 12.0 Hz, 1H), 3.90 (s, 3H), 2.75 (d, *J* = 12.0 Hz, 1H), 2.39 (s, 3H), 2.16 (s, 3H), 1.88-1.80 (m, 2H), 1.63-1.51 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 156.0, 154.8, 143.4, 139.9, 136.3, 133.9, 129.6 (2x), 128.8 (2x), 126.4, 124.2, 110.5, 73.8, 55.8, 32.4, 30.9, 23.4, 21.3, 19.3, 13.9; HRMS (ESI, M^++H) calcd for $C_{22}H_{27}N_2O_2$ 351.2073, found 351.2066.

6-Butoxy-7-methoxy-4-methyl-1-*o*-tolyl-5H-benzo[d][1,2]diazepine (1n).

Yield = 86% (301 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.2 Hz, 1H), 7.31-7.22 (m, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 1H), 6.73 (d, *J* = 8.8 Hz, 1H), 4.06-4.01 (m, 2H), 4.01 (d, *J* = 12.0 Hz, 1H), 3.86 (s, 3H), 2.80 (d, *J* = 12.0 Hz, 1H), 2.19 (s, 3H), 2.02 (s, 3H), 1.88-1.80 (m, 2H), 1.63-1.53 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 155.2, 154.7, 143.4, 139.5, 136.9, 132.9, 130.5, 130.4, 129.0, 125.9, 125.6, 125.4, 110.8, 73.8, 55.7, 32.3, 30.7, 23.6, 20.1, 19.2, 13.9; HRMS (ESI, M^++H) calcd for $C_{22}H_{27}N_2O_2$ 351.2073, found 351.2065.

6-Butoxy-7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (1o).

Yield = 88% (296 mg); Colorless solid; mp = 89-90 °C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.39-7.33 (m, 3H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 4.08-3.98 (m, 2H), 3.94 (d, *J* = 12.0 Hz, 1H), 3.87 (s, 3H), 2.72 (d, *J* = 12.0 Hz, 1H), 2.14 (s, 3H), 1.87-1.79 (m, 2H), 1.59-1.53 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 155.5, 154.7, 143.3, 139.0, 133.8, 129.5, 129.5 (2x), 127.9 (2x), 126.2, 123.9, 110.4, 73.6, 55.6, 32.2, 30.7, 23.3, 19.1, 13.8; HRMS (ESI, M^++H) calcd for $C_{21}H_{25}N_2O_2$ 337.1916, found 337.1908.

6-(Cyclopentyloxy)-7-methoxy-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (1p).

Yield = 90% (340 mg); Colorless solid; mp = 156-157 °C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 9.2 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.88 (d, *J* = 9.2 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.87-4.83 (m, 1H), 3.87 (d, *J* = 11.6 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 2.72 (d, *J* = 11.6 Hz, 1H), 2.09 (s, 3H), 2.04-1.60 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 157.9, 155.8, 154.6, 142.0, 134.4, 131.6, 130.9 (2x), 125.8, 123.9, 113.3 (2x), 110.3, 85.0, 55.6, 55.1, 33.2, 32.1, 30.9, 23.6, 23.4, 23.2; HRMS (ESI, M^++H) calcd for $C_{23}H_{27}N_2O_3$ 379.2022, found 379.2018. Single-crystal X-ray diagram: crystal of **1p** was grown by slow diffusion of EtOAc into a solution of **1p** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group P -1, *a* = 8.4384(6) Å, *b* = 11.0458(8) Å, *c* = 12.1243(8) Å, *V* = 1041.25(13) Å^3, *Z* = 2, d_{calcd} = 1.207 g/cm^3, *F*(000) = 404, 2θ range 1.82-26.51°, *R* indices (all data) *R*1 = 0.0071, w*R*2 = 0.1461.

6-(Cyclopentyloxy)-1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (1q).

Yield = 85% (311 mg); Colorless solid; mp = 153-154 °C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.09-7.03 (m, 2H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 4.90-4.86 (m, 1H), 3.92 (d, *J* = 12.0 Hz, 1H), 3.88 (s, 3H),

3.72 (d, *J* = 12.0 Hz, 1H), 2.12 (s, 3H), 2.07-2.01 (m, 1H), 1.97-1.77 (m, 4H), 1.73-1.61 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (d, *J* = 248.6 Hz), 157.5, 155.9, 154.8, 142.3, 135.2 (d, *J* = 3.0 Hz), 134.5, 131.4 (d, *J* = 8.4 Hz, 2x), 125.7, 123.8, 115.0 (d, *J* = 21.2 Hz, 2x), 110.6, 85.2, 55.7, 33.4, 32.2, 31.1, 23.7, 23.5, 23.3; HRMS (ESI, M^++H) calcd for $C_{22}H_{24}FN_2O_2$ 367.1822, found 367.1817.

6-(Cyclopentyloxy)-7-methoxy-4-methyl-1-*p*-tolyl-5H-benzo[d][1,2]diazepine (1r).

Yield = 84% (304 mg); Colorless solid; mp = 156-157 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.89-4.85 (m, 1H), 3.90 (d, *J* = 11.6 Hz, 1H), 3.87 (s, 3H), 2.73 (d, *J* = 11.6 Hz, 1H), 2.37 (s, 3H), 2.11 (s, 3H), 2.07-2.01 (m, 1H), 1.96-1.77 (m, 4H), 1.70-1.61 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 155.8, 154.6, 142.1, 139.7, 136.3, 134.5, 129.5 (2x), 128.7 (2x), 125.9, 124.0, 110.4, 85.1, 55.6, 33.3, 32.1, 31.0, 23.6, 23.5, 23.3, 21.2; HRMS (ESI, M^++H) calcd for $C_{23}H_{27}N_2O_2$ 363.2073, found 363.2068.

6-(Cyclopentyloxy)-7-methoxy-4-methyl-1-*o*-tolyl-5H-benzo[d][1,2]diazepine (1s).

Yield = 84% (304 mg); Colorless solid; mp = 104-105 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 7.2 Hz, 1H), 7.31-7.22 (m, 2H), 7.16 (d, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 4.92-4.89 (m, 1H), 3.98 (d, *J* = 12.0 Hz, 1H), 3.85 (s, 3H), 2.80 (d, *J* = 12.0 Hz, 1H), 2.16 (s, 3H), 2.02 (s, 3H), 2.00-1.75 (m, 5H), 1.72-1.64 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 155.4, 154.6, 142.1, 139.5, 136.9, 133.7, 130.5, 130.3, 128.9, 125.9, 125.6, 125.1, 110.8, 84.9, 55.7, 33.3, 32.1, 30.9, 23.7, 23.6, 23.6, 20.1; HRMS (ESI, M^++H) calcd for $C_{23}H_{27}N_2O_2$ 363.2073, found 363.2067.

6-(Cyclopentyloxy)-7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (1t).

Yield = 85% (296 mg); Colorless solid; mp = 154-155 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.43-7.36 (m, 3H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 4.90-4.86 (m, 1H), 3.92 (d, *J* = 11.6 Hz, 1H), 3.89 (s, 3H), 2.74 (d, *J* = 11.6 Hz, 1H), 2.13 (s, 3H), 2.07-2.02 (m, 1H), 1.97-1.78 (m, 4H), 1.71-1.62 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 156.0, 154.8, 142.2, 139.1, 134.6, 129.65, 129.62 (2x), 128.0 (2x), 126.0, 124.1, 110.5, 85.2, 55.7, 33.4, 32.2, 31.1, 23.7, 23.5, 23.4; HRMS (ESI, M^++H) calcd for $C_{22}H_{25}N_2O_2$ 349.1916, found 349.1910.

6-(Benzyloxy)-7-methoxy-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (1u).

Yield = 89% (356 mg); Colorless solid; mp = 152-153 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.41-7.31 (m, 3H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.93-6.90 (m, 3H), 5.12 (d, *J* = 11.2 Hz, 1H), 5.08 (d, *J* = 11.2 Hz, 1H), 3.92 (s, 3H), 3.85 (d, *J* = 12.0 Hz, 1H), 3.82 (s, 3H), 2.61 (d, *J* = 12.0 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 157.8, 155.6, 154.5, 142.6, 137.1, 134.1, 131.5, 130.9 (2x), 128.3 (2x), 128.0, 127.9 (2x), 126.5, 124.0, 113.3 (2x), 110.4, 75.3, 55.7, 55.1, 30.7, 23.2; HRMS (ESI, M^++H) calcd for $C_{25}H_{25}N_2O_3$ 401.1865, found 401.1858.

6-(Benzyloxy)-1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (1v).

Yield = 83% (322 mg); Colorless solid; mp = 198-199 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.62 (m, 2H), 7.49-7.47 (m, 2H), 7.42-7.35 (m, 3H), 7.10-7.06 (m, 2H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 5.13 (d, *J* = 11.2 Hz, 1H), 5.09 (d, *J* = 11.2 Hz, 1H), 3.95 (s, 3H), 3.88 (d, *J* = 12.0 Hz, 1H), 2.59 (d, *J* = 12.0 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (d, *J* = 248.6 Hz), 157.4, 155.8, 154.8, 142.8, 137.1, 135.2 (d, *J* = 3.0 Hz), 134.2, 131.4 (d, *J* = 8.3 Hz, 2x), 128.4 (2x), 128.15, 128.05 (2x), 126.4, 123.8, 115.0 (d, *J* = 22.0 Hz, 2x), 110.6, 75.4, 55.8, 30.8, 23.3; HRMS (ESI, M^++H) calcd for $C_{24}H_{22}FN_2O_2$ 389.1665, found 389.1658.

6-(Benzyloxy)-7-methoxy-4-methyl-1-*p*-tolyl-5H-benzo[d][1,2]diazepine (1w).

Yield = 81% (311 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.42-7.33 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 5.13 (d, *J* = 11.2 Hz, 1H), 5.09 (d, *J* = 11.2 Hz, 1H), 3.95 (s, 3H), 3.86 (d, *J* = 12.0 Hz, 1H), 2.61 (d, *J* = 12.0 Hz, 1H), 2.40 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 155.8, 154.7, 142.8, 139.8, 137.2, 136.3, 134.3, 129.6 (2x), 128.8 (2x), 128.5 (2x), 128.2, 128.1 (2x), 126.7, 124.2, 110.5, 75.5, 55.8, 30.9, 23.3, 21.3; HRMS (ESI, M^++H) calcd for $C_{25}H_{25}N_2O_2$ 385.1916, found 385.1909.

6-(Benzyloxy)-7-methoxy-4-methyl-1-*o*-tolyl-5H-benzo[d][1,2]diazepine (1x).

Yield = 85% (327 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48-7.27 (m, 7H), 7.25-7.23 (m, 1H), 7.17-7.15 (m, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 5.14 (d, *J* = 11.2 Hz, 1H), 5.10 (d, *J* = 11.2 Hz, 1H), 3.92 (s, 3H), 3.86 (d, *J* = 12.0 Hz, 1H), 2.57 (d, *J* = 12.0 Hz, 1H), 2.11 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 155.5, 154.7, 142.4, 139.4, 136.9, 136.9, 133.4, 130.5, 130.3, 129.1, 128.4 (4x), 128.3, 125.8, 125.8, 125.6, 110.9, 75.3, 55.8, 30.8, 23.5, 20.2; HRMS (ESI, M^++H) calcd for $C_{25}H_{25}N_2O_2$ 385.1916, found 385.1909.

6-(Benzyloxy)-7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (1y).

Yield = 84% (311 mg); Colorless solid; mp = 157-158 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.41-7.32 (m, 6H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 5.13 (d, *J* = 11.2 Hz, 1H), 5.10 (d, *J* = 11.2 Hz, 1H), 3.92 (s, 3H), 3.88 (d, *J* = 11.6 Hz, 1H), 2.61 (d, *J* = 11.6 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 155.4, 154.5, 142.5, 138.9, 137.0, 134.0, 129.44, 129.36 (2x), 128.2 (2x), 127.9, 127.9 (2x), 127.8

(2x), 126.4, 123.8, 110.4, 75.2, 55.6, 30.6, 23.1; HRMS (ESI, M^++H) calcd for $C_{24}H_{23}N_2O_2$ 371.1760, found 371.1752.

6,7-Dimethoxy-1-(4-methoxyphenyl)-4,5-dimethyl-5H-benzo[d][1,2]diazepine (1z).

Yield = 85% (287 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 1H), 4.39 (q, *J* = 7.2 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.84 (s, 3H), 2.15 (s, 3H), 1.17 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 158.6, 157.0, 154.6, 144.3, 139.0, 132.4, 131.0, 130.9 (2x), 128.0, 122.9, 113.5 (2x), 110.6, 61.7, 55.8, 55.3, 35.9, 25.2; HRMS (ESI, M^++H) calcd for $C_{20}H_{23}N_2O_3$ 339.1709, found 339.1702.

6-Methoxy-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (1aa).

Yield = 79% (232 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 9.2 Hz, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.93-6.89 (m, 3H), 4.00 (d, *J* = 12.0 Hz, 1H), 3.91 (s, 3H), 3.83 (s, 3H), 2.62 (d, *J* = 12.0 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 158.4, 156.0, 155.0, 131.4, 131.3, 130.9 (2x), 128.3, 127.0, 122.1, 113.5 (2x), 112.1, 55.9, 55.3, 29.8, 23.4; HRMS (ESI, M^++H) calcd for $C_{18}H_{19}N_2O_2$ 295.1447, found 295.1439.

2-Amino-5,6-dimethoxy-3-methylisoquinolin-1(2*H*)-one (9a).

Yield = 87% (204 mg); Colorless solid; mp = 181-182 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 1H), 6.58 (s, 1H), 4.89 (br s, 2H), 3.95 (s, 3H), 3.87 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 154.3, 141.3, 140.9, 131.5, 124.4, 118.2, 111.6, 98.4, 61.0, 56.0, 19.8; HRMS (ESI, M^++Na) calcd for $C_{12}H_{14}N_2O_3Na$ 257.0902, found 257.0897.

2-Amino-5-butoxy-6-methoxy-3-methylisoquinolin-1(2*H*)-one (9b).

Yield = 85% (235 mg); Colorless gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 1H), 6.62 (s, 1H), 4.94 (br s, 2H), 4.01 (t, *J* = 6.8 Hz, 2H), 3.94 (s, 3H), 2.48 (s, 3H), 1.83-1.76 (m, 2H), 1.59-1.49 (m, 2H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 154.4, 140.7, 140.6, 131.9, 124.2, 118.2, 111.7, 98.8, 73.4, 56.0, 32.3, 19.9, 19.2, 13.9; HRMS (ESI, M^++H) calcd for $C_{15}H_{21}N_2O_3$ 277.1552, found 277.1548.

2-Amino-5-(cyclopentyloxy)-6-methoxy-3-methylisoquinolin-1(2*H*)-one (9c).

Yield = 84% (242 mg); Colorless solid; mp = 55-56 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 1H), 6.60 (s, 1H), 4.93-4.90 (m, 3H), 3.94 (s, 3H), 2.48 (s, 3H), 1.93-1.84 (m, 4H), 1.77-1.60 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 154.3, 140.3, 139.4, 132.6, 123.8, 118.2, 111.7, 99.2, 84.7, 56.0, 32.7 (2x), 23.7 (2x), 19.9; HRMS (ESI, M^++H) calcd for $C_{16}H_{21}N_2O_3$ 289.1552, found 289.1548.

2-Amino-6-methoxy-3-methyl-5-(octyloxy)isoquinolin-1(2*H*)-one (9d).

Yield = 82% (272 mg); Colorless solid; mp = 77-78 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 1H), 6.62 (s, 1H), 4.94 (br s, 2H), 4.00 (t, *J* = 6.8 Hz, 2H), 3.95 (s, 3H), 2.49 (s, 3H), 1.85-1.77 (m, 2H), 1.52-1.46 (m, 2H), 1.39-1.23 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 154.4, 140.7, 131.9, 124.2, 111.7, 98.8, 73.7, 56.0, 31.8, 30.2 (2x), 29.7, 29.4, 29.3, 26.0, 22.6, 19.9, 14.1; HRMS (ESI, M^++H) calcd for $C_{19}H_{29}N_2O_3$ 333.2178, found 333.2174.

General synthetic procedure for synthesis of 8a-b is as follows

A representative synthetic procedure of skeleton **8** is as follows: $PdCl_2$ (10 mg, 5.6 mol%) and $CuCl_2$ (200 mg, 1.5 mmol) were added to a solution of skeleton **4** (1.0 mmol) in the dioxane (10 mL) at rt. Then oxygen was bubbled into the mixture for 2 h, and stirred at rt for 13 h. The residue was diluted with water (2 mL) and the mixture was extracted with EtOAc (3x20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 10:1 to 6:1) afforded skeleton **8**.

3,4-Dimethoxy-2-(2-oxopropyl)benzaldehyde (8a).[11]

Yield = 90% (200 mg); Colorless solid; mp = 72-73 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.80 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 4.23 (s, 2H), 3.92 (s, 3H), 3.75 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.6, 191.9, 157.2, 148.0, 133.3, 130.3, 128.0, 110.1, 60.8, 55.8, 40.5, 30.0; HRMS (ESI, M^{+}+H) calcd for $C_{12}H_{15}O_4$ 223.0970, found 223.0977.

3-Butoxy-4-methoxy-2-(2-oxopropyl)benzaldehyde (8b).[11]

Yield = 86% (227 mg); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 4.25 (s, 2H), 3.92 (s, 3H), 3.87 (t, *J* = 6.8 Hz, 2H), 2.32 (s, 3H), 1.74-1.66 (m, 2H), 1.49-1.43 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.7, 192.0, 157.4, 147.4, 133.2, 130.3, 128.0, 110.0, 73.3, 55.8, 40.7, 32.2, 30.0 19.1, 13.8; HRMS (ESI, M^{+}+H) calcd for $C_{15}H_{21}O_4$ 265.1440, found 265.1446.

3,4-dimethoxy-6-methylbenzo[4,5]imidazo[2,1 *a*]isoquinoline (10).

1,2-diaminobenzene (108 mg, 1.0 mmol) was added to a solution of skeleton **8a** (1.0 mmol) in the AcOH (8 mL) at rt. The mixture was stirred at reflux for 5 h. The residue was diluted with aq $NaHCO_3$ (95%, 10 mL) and the mixture was extracted with EtOAc (3x20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 10:1 to 6:1) afforded compound **10**. Yield = 85% (248 mg); Colorless solid; mp = 141-142 ^{o}C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 8.8 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.49-7.45 (m, 1H), 7.34-7.30 (m, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.10 (s, 1H), 4.01 (s, 3H), 3.99 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 148.3, 144.0, 142.4, 135.1, 131.3, 127.1, 124.1, 121.6, 121.4, 119.4, 116.5, 113.8, 113.1, 104.9, 61.3, 56.1, 21.5; HRMS (ESI, M^++Na) calcd for $C_{18}H_{16}N_2O_2Na$ 315.1110, found 315.1114.

ASSOCIATED CONTENT

Supporting Information

Spectroscopic data for all compounds and X-ray analysis data of **1a**, **1c**, **1p**, **7y** and **9a**. This information is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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