Efficient Synthesis of Imidazole-Fused Benzodiazepines Using Palladium-Catalyzed Intramolecular C–N Bond Formation Reaction

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Abstract: An efficient three-step synthetic route to imidazole-fused benzodiazepines from imidazole-2-carbaldehyde is described. Application of intramolecular Buchwald–Hartwig cycloamination reaction in the final step is shown to be a convenient method for the synthesis of fused seven-membered diazacycles. The reactions proceeded smoothly with both aliphatic and aromatic amines.

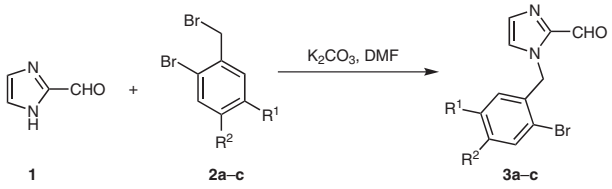
Key words: palladium, catalysis, amination, cyclization, benzodiazepine

There is a growing interest over the past few years in the synthesis of nitrogen containing heterocycle-fused benzazepines and benzodiazepines due to their crucial role as main structural motif in many pharmacologically active molecules. The clinical importance and commercial success associated with the benzodiazepine class of central nervous system (CNS)-active agents and the utility of 1,4-diazepines as peptidomimetic scaffolds have led the medicinal chemists to recognize them as privileged structures. Particularly, imidazobenzodiazepines[1] and related ligands interact selectively for a neuro-inhibitory, postsynaptic $GABA_A$ receptor[1f,g] with high affinity. Accordingly, they may act as agonists, partial agonists,[1b] and antagonists. The therapeutic applications of benzodiazepines include anxiolytics,[2] antiarrhythmics,[3] vasopressin antagonists,[4] and cholecystokinin antagonists.[5] Some of the benzodiazepines such as arfendazam, lofendazam,[6] triflubazam,[7] and clobazam exhibit a wide range of biological activities while others like telenzepine act as antisecretory agents.[8] Recently, several compounds have been formally licensed for clinical use (e.g., Nevirapine) and others are at the preclinical and/or clinical development stage (e.g., Tivirapine and UK-129 485[9]). Tetrahydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-2(1*H*)-thione, assigned the acronym TIBO,[1d,e] is the first member of a series of potent selective and noncompetitive inhibitors of HIV-l reverse transcriptase.

Despite the immense importance of imidazobenzodiazepines, only a few groups[1] have reported their synthesis. These methods either require lengthy sequence of reactions or harsh reaction conditions. For quite some time, we have been engaged in the synthesis of several benzannulated and dibenzannulated medium ring heterocycles employing palladium-catalyzed intramolecular C–N bond forming cyclization reaction.[10–12] The copper- or palladium-catalyzed intramolecular Buchwald–Hartwig aryl amination reaction[13] appeared particularly suitable for this purpose. In continuation of these efforts, we became interested in applying this method in the synthesis of imidazole-fused benzodiazepines. To the best of our knowledge no other group has reported the synthesis of this important synthetic target using this method.

The requisite starting materials **3a**–**c** were prepared in good to excellent yields by reaction between imidazole-2-carbaldehyde (**1**) and either 2-bromobenzyl bromide (**2a**) or substituted 2-bromobenzyl bromides **2b**,**c** in the presence of anhydrous potassium carbonate in anhydrous DMF at room temperature (Table 1).

Table 1 Synthesis of N-Benzylated Imidazo-2-carbaldehydes[a]



1 2a–c 3a–c

Entry	R^1	R^2	Benzyl bromide	Product	Time (h)	Yield (%)[b]
1	H	H	**2a**	**3a**	16	95
2	OCH_2O		**2b**	**3b**	17	92
3	OMe	H	**2c**	**3c**	16	94

[a] Reaction conditions: imidazole-2-carbaldehyde (1 equiv), 2-bromobenzyl bromide (1.2 equiv), K_2CO_3 (2 equiv), anhyd DMF (5 mL/mmol), r.t., 16–17 h.
[b] Isolated yield.

Imine formation with aliphatic and aromatic amines and subsequent $NaBH_4$ reduction in ethanol afforded the desired amine precursors **4a–l** in good yields (Table 2).

The amine precursor **4a** was then used as model substrate for the optimization of intramolecular cycloamination reaction. Initially with the conditions used by Buchwald[13a] (Table 3, entry 1) no desired product was obtained and the starting material **4a** was recovered. Changing the catalyst to $Pd_2(dba)_3$ or $Pd(OAc)_2$ also failed to afford the desired

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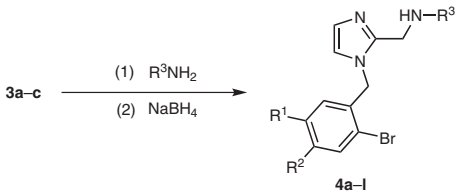
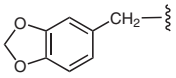
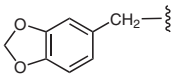
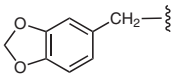
Table 2 Synthesis of Imidazo N-Alkylated Amines **4a–l**[a]



Entry	R^1	R^2	R^3	Product	Yield (%)[b]
1	H	H	Ph	**4a**	72
2	H	H	*i*-Pr	**4b**	70
3	H	H		**4c**	73
4	OMe	H	*i*-Pr	**4d**	77
5	OMe	H	Ph	**4e**	75
6	OMe	H	Bn	**4f**	74
7	OMe	H		**4g**	71
8	OCH_2O		*i*-Pr	**4h**	69
9	OCH_2O		Bn	**4i**	68
10	OCH_2O		Ph	**4j**	71
11	OCH_2O		4-$MeOC_6H_4$	**4k**	75
12	OCH_2O			**4l**	73

[a] Reaction conditions: 1) N-benzylated imidazole-2-carbaldehyde (1 equiv), amines (1.5 equiv), EtOH (10 mL/mmol), r.t., 12 h. 2) $NaBH_4$ (2.5 equiv), EtOH (20 mL/mmol), 0 °C, 2–3 h.
[b] Isolated yield.

Table 3 Optimization of the Cycloamination Reaction of **4a**

Entry	Reaction conditions	Pd (mol%)[a]	Yield (%)[b]
1	$Pd(PPh_3)_4$, K_2CO_3, toluene, reflux, 16 h	10	–[c]
2	$Pd_2(dba)_3$, K_2CO_3, DMF, 120 °C, 17 h	10	–[c]
3	$Pd(OAc)_2$, K_2CO_3, DMF, 120 °C, 16 h	10	–[c]
4	$Pd(OAc)_2$, (*o*-tol)$_3$P, *t*-BuOK, toluene, reflux, 18 h	10	20
5	$Pd(OAc)_2$, DPPF, K_2CO_3, toluene, reflux, 17 h	10	22
6	$Pd(OAc)_2$, DPPF, *t*-BuOK, toluene, reflux, 18 h	10	30
7	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, toluene, reflux, 16 h	10	58
8	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, toluene, reflux, 17 h	6	43
9	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, toluene, reflux, 16 h	20	73[d]
10	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, toluene, reflux, 17 h	30	70
11	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, toluene, reflux, 17 h	40	67
12	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, DME, reflux, 17 h	20	35
13	$Pd_2(dba)_3$, (±)-BINAP, *t*-BuOK, 1,4-dioxane, reflux, 17 h	20	43
14	$Pd_2(dba)_3$, (±)-BINAP, Cs_2CO_3, toluene, reflux, 17 h	20	35
15	$Pd_2(dba)_3$, (*o*-tol)$_3$P, *t*-BuOK, toluene, reflux, 18 h	20	30
16	$Pd_2(dba)_3$, DPPF, *t*-BuOK, toluene, reflux, 18 h	20	56

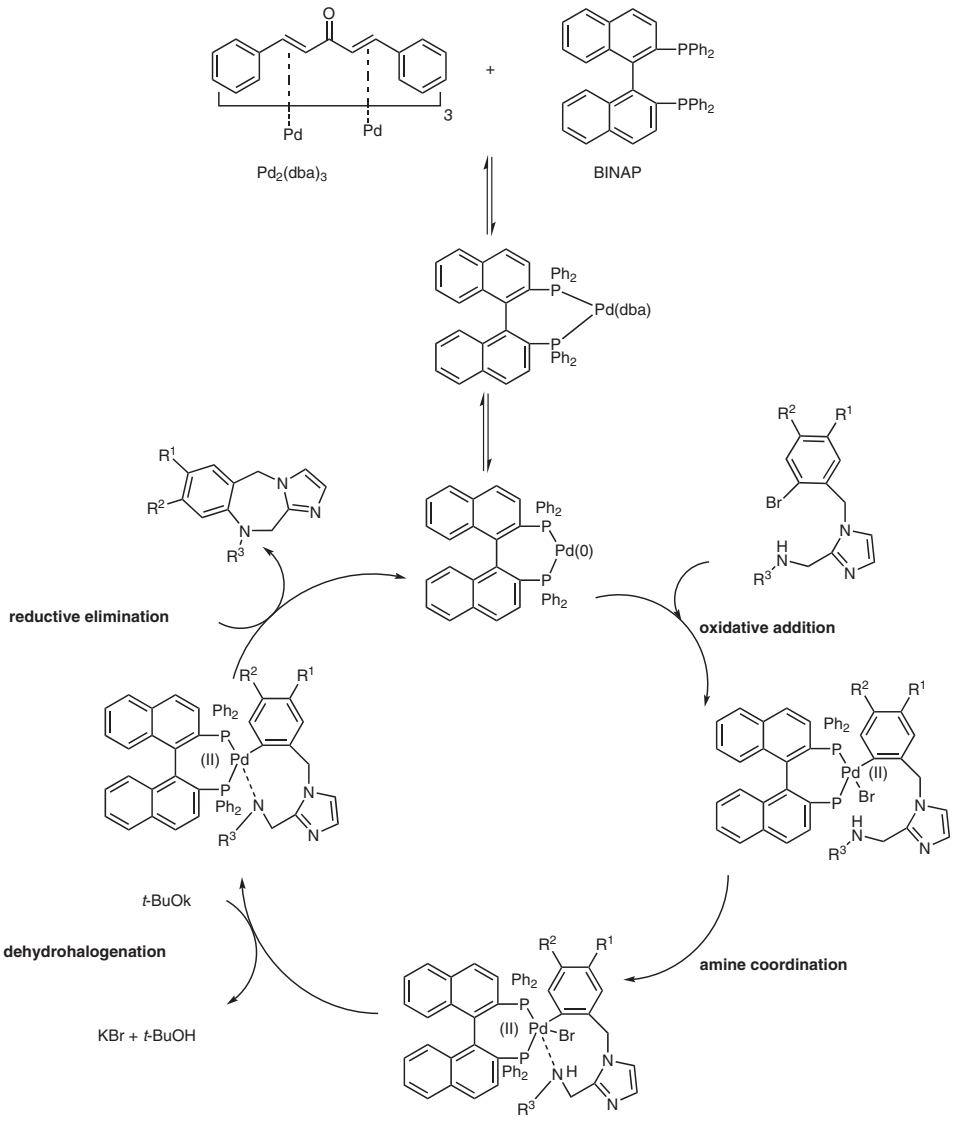
[a] Pd (10 mol%) refers to $Pd_2(dba)_3$ (5 mol%), $Pd(OAc)_2$ (10 mol%), and $Pd(PPh_3)_4$ (10 mol%).
[b] Isolated yield.
[c] No desired product was isolated.
[d] Optimized reaction conditions: **4a** (1 equiv), $Pd_2(dba)_3$ (10 mol%; 20 mol% in Pd), (±)-BINAP (10 mol%), *t*-BuOK (2 equiv), toluene (10 mL/mmol), reflux.

product in the absence of a ligand (entries 2, 3). The reaction did take place in the presence of a ligand, with $Pd_2(dba)_3$ proving superior to $Pd(OAc)_2$ at equivalent (10 mol% Pd) catalyst loading (entries 4–7), but the yield was still low (58%). Then, the Pd loading was varied from 6 to 40 mol% using $Pd_2(dba)_3$ as Pd source, which improved the yield to 73% at 20% Pd loading (entry 9). Changing the base to Cs_2CO_3, using other monodentate (tri-*o*-tolylphosphine) or bidentate (DPPF) ligands and employing different solvents (DME or 1,4-dioxane) proved less satisfactory (entries 12–16).

Use of copper catalyst (CuI, 5 mol%) and *t*-BuOK (2 equiv) with different ligands [1,10-phenanthroline or (±)-*trans*-1,2-cyclohexanediamine or *N*,*N*′-dimethylethylenediamine, 10 mol%] and solvents like DMF (at 120 °C) or toluene (reflux) also did not lead to the desired cyclic product.

The optimized protocol for the palladium-catalyzed intramolecular aryl amination of **4a** thus employs $Pd_2(dba)_3$ (10 mol%) as catalyst, (±)-BINAP (10 mol%) as ligand, *t*-BuOK (2 equiv) as base, and toluene as solvent at reflux to furnish **5a**. Employing these conditions, other substrates **4b–l** were treated to afford **5b–l** in 63–76% yield (Table 4). A probable mechanism[13b,c,14] of intramolecular aryl amination for the synthesis of benzodiazepines is outlined in Scheme 1.

The assigned structures of **5b–l** were determined on the basis of their IR, ^{1}H NMR, ^{13}C NMR, mass spectra, and elemental analysis. The ^{1}H NMR spectrum of **5a** consisted of two singlets at δ = 4.95 and 4.86 for the benzylic methylene protons and methylene protons attached to ni-



Scheme 1 Proposed mechanism for the synthesis of imidazobenzodiazepine

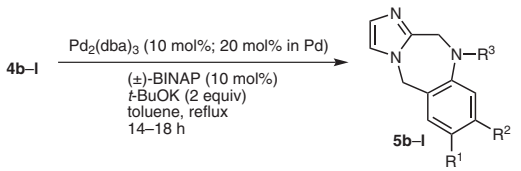
trogen of the aniline moiety, along with signals for eleven aromatic protons (δ = 6.77–7.42). The ^{13}C NMR spectrum showed signals assignable to 17 carbons in agreement with the structure. The mass spectrum displayed a peak at *m*/*z* 262 for the $[M + H]^+$ ion. The features of the ^{1}H and ^{13}C NMR spectra of compounds **5b**–**l** were broadly similar to those of **5a**, except for the signals for the aromatic moieties and the alkyl/aryl groups, which exhibited the expected changes in signal patterns.

The present strategy thus establishes transition-metal-catalyzed cycloamination as a suitable synthetic tool for the preparation of imidazole-fused benzodiazepine. But it could not be extended to the synthesis of pyrrole-fused benzodiazepines.

In summary, we have established a straightforward efficient three-step synthetic route to imidazole-fused seven-membered diazacycles from imidazole-2-carbaldehyde using palladium-catalyzed intramolecular cycloamination reaction as the key step. Development of new analogues of benzodiazepines is highly desirable as this may lead to a promising antidepressant drug. This finding opens up the possibility of obtaining synthetically challenging imidazole-fused seven-membered benzoheterocycles.

Reactions at r.t. imply a temperature of 25 °C. Required reagents were obtained from commercial sources and used without purification. The solvents used were of technical grade, and freshly distilled prior to use. All melting points were obtained on a laboratory melting point bath and are uncorrected. ^{1}H (300 MHz, 600 MHz) and ^{13}C (75 MHz, 150 MHz) NMR spectra were recorded using $CDCl_3$ as solvent and TMS as internal standard on Bruker DPX 300 MHz and Bruker DRX 600 MHz NMR instruments. Chemical shifts are stated in parts per million in δ scales. IR spectra were recorded on a Jasco-FTIR Model-410 using KBr pellets or in neat condition. Mass spectra were measured in ESIMS (+) or EIMS mode. DI-EIMS were recorded on a Shimadzu GCMS (model no QP5050A) and ESIMS were done on a Waters Micromass Q-TOF micro™ mass spectrometer. TLC was performed on precoated plates (0.25 nm, silica gel 60 F_{254}). Petroleum ether (PE) used refers to the fraction boiling in the 60–80 °C range.

Table 4 Synthesis of Imidazobenzodiazepines **5b–l**[a]



Entry	Substrate	Product	Time (h)	Yield (%)[a]
1	**4b**	**5b**	18	68
2	**4c**	**5c**	17	65
3	**4d**	**5d**	16	71
4	**4e**	**5e**	18	68
5	**4f**	**5f**	15	76
6	**4g**	**5g**	14	72
7	**4h**	**5h**	16	70
8	**4i**	**5i**	18	75
9	**4j**	**5j**	15	74
10	**4k**	**5k**	17	67
11	**4l**	**5l**	16	63

[a] Isolated yield.

1-(2-Bromobenzyl)-1*H*-imidazole-2-carbaldehydes 3a–c; General Procedure

To a stirred solution of imidazole-2-carbaldehyde (**1**; 0.5 g, 5.2 mmol) in anhyd DMF (20 mL) was added K_2CO_3 (1.4 g, 10.41 mmol) and the mixture was stirred at r.t. for 30 min. Thereafter, the appropriate 2-bromobenzyl bromide **2** (6.25 mmol, 1.2 equiv) was added and the stirring was continued for about 16–17 h at r.t. On completion of the reaction as monitored by TLC (eluent: PE–EtOAc, 1:1), the solution was poured into H_2O (70 mL), and extracted with EtOAc (4 × 30 mL). The combined organic layers were washed with H_2O (40 mL), followed by brine (30 mL), dried (Na_2SO_4), filtered, and the solvent was evaporated in vacuo. The crude product was purified via column chromatography over neutral alumina (EtOAc–PE, 1:9) to give **3a–c**.

1-(2-Bromobenzyl)-1*H*-imidazole-2-carbaldehyde (3a)

Yield: 1.30 g (95%); yellow solid; mp 80–82 °C; R_f = 0.55 (PE–EtOAc, 3:2).

IR (KBr): 2846, 1678, 1465, 1411, 1337, 1294, 1244, 1155, 1024, 774, 664 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.73 (s, 2 H), 6.91 (d, *J* = 6.9 Hz, 1 H), 7.15 (s, 1 H), 7.18–7.30 (m, 2 H), 7.32 (s, 1 H), 7.61 (d, *J* = 7.5 Hz, 1 H), 9.87 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 50.8 (CH_2), 123.2 (C), 126.2 (CH), 128.0 (CH), 129.1 (CH), 129.9 (CH), 131.9 (CH), 133.1 (CH), 135.2 (C), 143.4 (C), 182.1 (CHO).

MS (ESI): *m*/*z* = 265, 267 ([M + H$^+$] for ^{79}Br and ^{81}Br), 287, 289 ([M + Na$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{11}H_9BrN_2O$: C, 49.84; H, 3.42; N, 10.57. Found: C, 49.64; H, 3.47; N, 10.67.

1-(2-Bromo-4,5-methylenedioxybenzyl)-1*H*-imidazole-2-carbaldehyde (3b)

Yield: 1.47 g (92%); white solid; mp 84–86 °C; R_f = 0.65 (PE–EtOAc, 3:7).

IR (KBr): 2908, 2842, 1681, 1626, 1478, 1412, 1249, 1110, 1036, 929, 858, 763, 681, 521 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64 (s, 2 H), 5.99 (s, 2 H), 6.54 (s, 1 H), 7.05 (s, 1 H), 7.20 (s, 1 H), 7.31 (s, 1 H), 9.87 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 50.4 (CH_2), 102.0 (CH_2), 109.3 (CH), 112.9 (CH), 114.1 (C), 125.9 (CH), 128.1 (C), 131.9 (CH), 143.1 (C), 147.9 (C), 148.5 (C), 182.2 (CH).

MS (ESI): *m*/*z* = 309, 311 ([M + H$^+$] for ^{79}Br and ^{81}Br), 331, 333 ([M + Na$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{12}H_9BrN_2O_3$: C, 46.63; H, 2.93; N, 9.06. Found: C, 46.85; H, 2.88; N, 9.18.

1-(2-Bromo-5-methoxybenzyl)-1*H*-imidazole-2-carbaldehyde (3c)

Yield: 1.48 g (94%); white solid; mp 78–80 °C; R_f = 0.65 (PE–EtOAc, 2:3).

IR (KBr): 2863, 1683, 1569, 1476, 1412, 1339, 1259, 1159, 1044, 1018, 919, 879, 805, 745, 598 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 3 H), 5.67 (s, 2 H), 6.48 (d, *J* = 3.0 Hz, 1 H), 6.73 (dd, *J* = 3.0 Hz, 8.7 Hz, 1 H), 7.17 (s, 1 H), 7.30 (s, 1 H), 7.47 (d, *J* = 8.7 Hz, 1 H), 9.85 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 50.7 (CH_2), 55.4 (OCH_3), 113.4 (C), 115.2 (2 CH), 126.2 (CH), 131.9 (CH), 133.7 (CH), 136.1 (C), 143.3 (C), 159.4 (C), 182.1 (CHO).

MS (ESI): *m*/*z* = 295, 297 ([M + H$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{12}H_{11}BrN_2O_2$: C, 48.84; H, 3.76; N, 9.49. Found: C, 48.64; H, 3.80; N, 9.59.

1-(2-Bromobenzyl)-2-(phenylaminomethyl)-1*H*-imidazoles 4a–l; General Procedure

To an ethanolic solution (20 mL) of **3a–c** (0.85–1.89 mmol, 1 equiv) was added the respective alkyl/aryl amine (1.27–2.83 mmol, 1.5 equiv) and the reaction mixture was stirred at r.t. for 12 h. After cooling to 0 °C, $NaBH_4$ (2.12–4.72 mmol, 2.5 equiv) was added portionwise and the mixture was stirred for 2–3 h. On completion of the reaction as monitored by TLC (eluent: EtOAc), the solvent was removed under vacuum. The mixture was extracted with EtOAc (2 × 20 mL), and the combined organic extracts were washed with sat. aq $NaHCO_3$ (25 mL) and H_2O (2 × 20 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by column chromatography over neutral alumina (EtOAc–PE, 3:1) to afford the compounds **4a–l**.

1-(2-Bromobenzyl)-2-(phenylaminomethyl)-1*H*-imidazole (4a)

Yield: 0.22 g (72%); brownish sticky mass; R_f = 0.38 (PE–EtOAc, 1:1).

IR (neat): 2923, 1685, 1601, 1501, 1436, 1315, 1262, 1216, 1105, 1026, 752 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.30 (s, 2 H), 5.24 (s, 2 H), 6.64–6.76 (m, 4 H), 6.89 (s, 1 H), 7.08 (s, 1 H), 7.14–7.26 (m, 4 H), 7.60 (d, *J* = 6.0 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.1 (CH_2), 49.7 (CH_2), 113.2 (2 CH), 118.2 (CH), 121.0 (CH), 122.5 (C), 127.7 (CH), 128.0 (CH), 128.1 (CH), 129.2 (2 CH), 129.7 (CH) 133.1 (CH), 135.3 (C), 145.4 (C), 147.4 (C).

MS (ESI): *m*/*z* = 342, 344 ([M + H$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{17}H_{16}BrN_3$: C, 59.66; H, 4.71; N, 12.28. Found: C, 59.86; H, 4.75; N, 12.18.

1-(2-Bromobenzyl)-2-(isopropylaminomethyl)-1*H*-imidazole (4b)
Yield: 0.35 g (70%); yellowish sticky mass; R_f = 0.27 (PE–EtOAc, 3:7).

IR (neat): 2964, 2866, 1685, 1643, 1469, 1441, 1346, 1279, 1165, 1117, 1027, 747, 665 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 6.3 Hz, 6 H), 2.76–2.84 (m, 1 H), 3.78 (s, 2 H), 5.30 (s, 2 H), 6.68 (d, *J* = 6.9 Hz, 1 H), 6.86 (s, 1 H), 7.02 (s, 1 H), 7.09–7.33 (m, 2 H), 7.59 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6 (2 CH_3), 43.3 (CH_2), 48.4 (CH), 49.6 (CH_2), 120.6 (CH), 122.3 (C), 127.5 (CH), 127.9 (2 CH), 129.4 (CH) 132.8 (CH), 136.0 (C), 146.8 (C).

MS (ESI): *m*/*z* = 308, 310 ([M + H^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{14}H_{18}BrN_3$: C, 54.56; H, 5.89; N, 13.63. Found: C, 54.77; H, 5.86; N, 13.73.

1-(2-Bromobenzyl)-2-(3,4- methylenedioxybenzylaminomethyl)-1*H*-imidazole (4c)
Yield: 0.25 g (73%); yellowish sticky mass; R_f = 0.30 (PE–EtOAc, 3:7).

IR (neat): 2956, 2860, 1409, 1305, 1161, 1011, 846, 510 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 2 H), 3.80 (s, 2 H), 5.92 (s, 2 H), 6.64–6.75 (m, 4 H), 6.86 (s, 1 H), 7.03 (s, 2 H), 7.14–7.23 (m, 3 H), 7.60 (dd, *J* = 1.2, 6.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.0 (CH_2), 49.6 (CH_2), 53.2 (CH_2), 100.8 (CH_2), 108.0 (CH), 108.6 (CH), 120.6 (CH), 121.2 (CH), 122.3 (C), 127.7 (CH), 127.9 (2 CH), 129.3 (CH), 132.8 (CH), 133.6 (C), 136.1 (C), 146.5 (C), 146.6 (C), 147.6 (C).

MS (ESI): *m*/*z* = 400, 402 ([M + H^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{19}H_{18}BrN_3O_2$: C, 57.01; H, 4.53; N, 10.50. Found: C, 57.22; H, 4.58; N, 10.50.

1-(2-Bromo-5-methoxybenzyl)-2-(isopropylaminomethyl)-1*H*-imidazole (4d)
Yield: 0.24 g (77%); yellowish sticky mass; R_f = 0.35 (EtOAc).

IR (neat): 2962, 1593, 1470, 1375, 1288, 1238, 1164, 1118, 1056, 1018, 925, 856, 809, 734 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.03 (d, *J* = 6.0 Hz, 6 H), 2.77–2.83 (m, 1 H), 3.67 (s, 3 H), 3.78 (s, 2 H), 5.25 (s, 2 H), 6.25 (s, 1 H), 6.70–6.73 (dd, *J* = 2.4, 8.7 Hz, 1 H), 6.87 (s, 1 H), 7.02 (s, 1 H), 7.47 (d, *J* = 8.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6 (2 CH_3), 43.5 (CH_2), 48.5 (CH), 49.5 (CH_2), 55.3 (OCH_3), 112.4 (C), 113.9 (CH), 114.6 (CH), 120.5 (CH), 127.6 (CH), 133.4 (CH) 137.1 (C), 146.9 (C), 159.4 (C).

MS (ESI): *m*/*z* = 338, 340 ([M + H^+] for ^{79}Br and ^{81}Br), 360, 362 ([M + Na^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{15}H_{20}BrN_3O$: C, 53.26; H, 5.96; N, 12.42. Found: C, 53.48; H, 5.92; N, 12.56.

1-(2-Bromo-5-methoxybenzyl)-2-(phenylaminomethyl)-1*H*-imidazole (4e)
Yield: 0.33 g (75%); white solid; R_f = 0.58 (PE–EtOAc, 2:3).

IR (KBr): 2927, 2845, 1688, 1600, 1471, 1286, 1160, 1056, 1019, 924, 865, 810, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.59 (s, 3 H), 4.23 (s, 2 H), 5.19 (s, 2 H), 6.19 (d, *J* = 3.0 Hz, 1 H), 6.64–6.78 (m, 4 H), 6.90 (s, 1 H), 7.08–7.18 (m, 3 H), 7.45 (d, *J* = 8.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.2 (CH_2), 49.7 (CH_2), 55.3 (OCH_3), 112.4 (C), 113.2 (2 CH), 113.9 (CH), 115.0 (CH), 118.1 (CH), 121.0 (CH), 128.0 (CH), 129.2 (2 CH), 133.6 (CH), 136.4 (C), 145.4 (C), 147.5 (C), 159.5 (C).

MS (ESI): *m*/*z* = 372, 374 ([M + H^+] for ^{79}Br and ^{81}Br), 394, 396 ([M + Na^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{18}H_{18}BrN_3O$: C, 58.08; H, 4.87; N, 11.29. Found: C, 58.28; H, 4.90; N, 11.40.

1-(2-Bromo-5-methoxybenzyl)-2-(benzylaminomethyl)-1*H*-imidazole (4f)
Yield: 0.36 g (74%); yellowish sticky mass; R_f = 0.4 (EtOAc).

IR (neat): 2934, 2838, 1645, 1594, 1469, 1350, 1288, 1239, 1161, 1020, 738, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.63 (s, 3 H), 3.79 (s, 2 H), 3.81 (s, 2 H), 5.23 (s, 2 H), 6.24 (d, *J* = 3.0 Hz, 1 H), 6.69 (dd, *J* = 3.0, 8.7 Hz, 1 H), 6.86 (d, *J* = 1.2 Hz, 1 H), 7.02 (d, *J* = 1.2 Hz, 1 H), 7.22–7.26 (m, 5 H), 7.46 (d, *J* = 9.0 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.9 (CH_2), 49.4 (CH_2), 53.1 (CH_2), 55.1 (OCH_3), 112.2 (C), 113.8 (CH), 114.3 (CH), 120.4 (CH), 126.7 (CH), 127.4 (CH), 128.0 (2 CH), 128.1 (2 CH), 133.2 (CH), 136.9 (C), 139.4 (C), 146.3 (C), 159.2 (C).

MS (ESI): *m*/*z* = 386, 388 ([M + H^+] for ^{79}Br and ^{81}Br), 408, 410 ([M + Na^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{19}H_{20}BrN_3O$: C, 59.08; H, 5.22; N, 10.88. Found: C, 59.28; H, 5.19; N, 10.98.

1-(2-Bromo-5-methoxybenzyl)-2-(3,4-methylenedioxybenzylaminomethyl)-1*H*-imidazole (4g)
Yield: 0.32 g (71%); pale brownish sticky mass; R_f = 0.26 (EtOAc).

IR (neat): 2928, 1720, 1597, 1480, 1245, 1121, 1040, 930, 809, 739 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.65 (s, 3 H), 3.70 (s, 2 H), 3.80 (s, 2 H), 5.22 (s, 2 H), 5.92 (s, 2 H), 6.23 (d, *J* = 3.0 Hz, 1 H), 6.69–6.73 (m, 3 H), 6.79 (s, 1 H), 6.87 (d, *J* = 0.9 Hz, 1 H), 7.03 (d, *J* = 0.9 Hz, 1 H), 7.46 (d, *J* = 8.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.0 (CH_2), 49.6 (CH_2), 53.2 (CH_2), 55.3 (CH_3), 100.8 (CH_2), 108.0 (CH), 108.6 (CH), 112.4 (C), 114.0 (CH), 114.5 (CH), 120.6 (CH), 121.2 (CH), 127.7 (CH), 133.4 (CH), 133.6 (C), 137.1 (C), 146.5 (C), 146.6 (C), 147.6 (C), 159.4 (C).

MS (ESI): *m*/*z* = 430, 432 ([M + H^+] for ^{79}Br and ^{81}Br), 452, 454 ([M + Na^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{20}H_{20}BrN_3O_3$: C, 55.83; H, 4.68; N, 9.77. Found: C, 54.63; H, 4.64; N, 9.90.

1-(2-Bromo-4,5-methylenedioxybenzyl)-2-(isopropylaminomethyl)-1*H*-imidazole (4h)
Yield: 0.46 g (69%); pale yellowish sticky mass; R_f = 0.28 (PE–EtOAc, 3:7).

IR (neat): 3263, 2963, 2909, 1683, 1488, 1374, 1243, 1162, 1109, 1034, 929, 847, 733, 509 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 6.3 Hz, 6 H), 2.79–2.87 (m, 1 H), 3.80 (s, 2 H), 5.19 (s, 2 H), 5.96 (s, 2 H), 6.30 (s, 1 H), 6.85 (s, 1 H), 7.00 (d, *J* = 11.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7 (2 CH_3), 43.6 (CH_2), 48.5 (CH), 49.3 (CH_2), 101.9 (CH_2), 108.3 (CH), 112.8 (CH), 112.9 (C), 120.3 (CH), 127.6 (CH), 129.2 (C) 146.8 (C), 147.9 (C), 148.0 (C).

MS (ESI): *m*/*z* = 352, 354 ([M + H^+] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{15}H_{18}BrN_3O_2$: C, 51.15; H, 5.15; N, 11.93. Found: C, 51.35; H, 5.10; N, 11.81.

1-(2-Bromo-4,5-methylenedioxybenzyl)-2-(benzylaminomethyl)-1*H*-imidazole (4i)
Yield: 0.41 g (68%); yellowish sticky mass; R_f = 0.35 (PE–EtOAc, 3:7).

IR (neat): 3261, 2904, 2788, 1489, 1242, 1106, 1034, 925, 851, 751, 698, 493 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 2 H), 3.84 (s, 2 H), 5.17 (s, 2 H), 5.94 (s, 2 H), 6.26 (s, 1 H), 6.85 (s, 1 H), 7.02 (d, *J* = 5.1 Hz, 2 H), 7.27 (d, *J* = 5.7 Hz, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.3 (CH_2), 49.4 (CH_2), 53.4 (CH_2), 101.9 (CH_2), 108.2 (CH), 112.8 (CH), 112.9 (C), 120.5 (C), 127.0 (2 CH), 127.7 (CH), 128.1 (2 CH), 128.4 (2 CH), 129.2 (C), 139.7 (C), 146.5 (C), 148.0 (C).

MS (ESI): *m*/*z* = 400, 402 ([M + H$^+$] for ^{79}Br and ^{81}Br), 422, 424 ([M + Na$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{19}H_{18}BrN_3O_2$: C, 57.01; H, 4.53; N, 10.50. Found: C, 57.21; H, 4.50; N, 10.40.

1-(2-Bromo-4,5-methylenedioxybenzyl)-2-(phenylaminomethyl)-1*H*-imidazole (4j)

Yield: 0.26 g (71%); white solid; mp 136–138 °C; R_f = 0.75 (PE–EtOAc, 3:7).

IR (KBr): 1605, 1504, 1473, 1414, 1321, 1234, 1107, 1031, 926, 850, 751, 697, 515 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.30 (s, 2 H), 5.13 (s, 2 H), 5.95 (s, 2 H), 6.20 (s, 1 H), 6.67 (d, *J* = 7.8 Hz, 2 H), 6.74 (t, *J* = 6.9 Hz, 1 H), 6.88 (s, 1 H), 7.05 (d, *J* = 8.7 Hz, 2 H), 7.18 (t, *J* = 7.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.1 (CH_2), 49.5 (CH_2), 101.9 (CH_2), 108.0 (CH), 112.8 (CH), 112.9 (C), 113.1 (2 CH), 118.0 (CH), 120.8 (CH), 127.8 (CH), 128.4 (C), 129.1 (2 CH), 145.1 (C), 147.4 (C), 147.9 (C), 148.1 (C).

MS (ESI): *m*/*z* = 386, 388 ([M + H$^+$] for ^{79}Br and ^{81}Br), 408, 410 ([M + Na$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{18}H_{16}BrN_3O_2$: C, 55.97; H, 4.18; N, 10.88. Found: C, 55.77; H, 4.13; N, 10.98.

1-(2-Bromo-4,5-methylenedioxybenzyl)-2-(4-methoxyphenylaminomethyl)-1*H*-imidazole (4k)

Yield: 0.27 g (75%); brownish sticky mass; R_f = 0.61 (PE–EtOAc, 3:7).

IR (neat): 2919, 2842, 1622, 1510, 1480, 1240, 1115, 1037, 930, 825, 754 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.74 (s, 3 H), 4.29 (s, 2 H), 5.15 (s, 2 H), 5.96 (s, 2 H), 6.19 (s, 1 H), 6.63 (d, *J* = 9.0 Hz, 2 H), 6.76 (d, *J* = 9.0 Hz, 2 H), 6.87 (s, 1 H), 7.05 (d, *J* = 9.0 Hz, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 42.1 (CH_2), 49.6 (CH_2), 55.7 (OCH_3), 102.0 (CH_2), 108.2 (CH), 112.8 (CH), 112.9 (C), 114.7 (4 CH), 120.7 (CH), 127.6 (CH), 128.4 (C) 141.6 (C), 145.5 (C), 148.0 (C), 148.2 (C), 152.6 (C).

MS (ESI): *m*/*z* = 416, 417 ([M + H$^+$] for ^{79}Br and ^{81}Br), 438, 440 ([M + Na$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{19}H_{18}BrN_3O_3$: C, 54.82; H, 4.36; N, 10.09. Found: C, 54.72; H, 4.40; N, 10.19.

1-(2-Bromo-4,5-methylenedioxybenzyl)-2-(3,4-methylenedioxybenzylaminomethyl)-1*H*-imidazole (4l)

Yield: 0.28 g (73%); light brown solid; mp 138–140 °C; R_f = 0.30 (PE–EtOAc, 3:7).

IR (KBr): 3250, 2960, 2899, 1680, 1500, 1340, 920, 840 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 2 H), 3.80 (s, 2 H), 5.15 (s, 2 H), 5.92 (s, 2 H), 5.95 (s, 2 H), 6.24 (s, 1 H), 6.72–6.85 (m, 4 H), 7.01 (d like, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.0 (CH_2), 49.4 (CH_2), 53.2 (CH_2), 100.8 (CH_2), 101.9 (CH_2), 107.9 (CH), 108.1 (CH), 108.6 (CH), 112.7 (CH), 112.8 (C), 120.5 (CH), 121.2 (CH), 127.7 (CH), 129.2 (C), 129.9 (C), 133.6 (C), 146.5 (C), 147.6 (C), 147.9 (C), 148.0 (C).

MS (ESI): *m*/*z* = 444, 446 ([M + H$^+$] for ^{79}Br and ^{81}Br).

Anal. Calcd for $C_{20}H_{18}BrN_3O_4$: C, 54.07; H, 4.08; N, 9.46. Found: C, 54.29; H, 4.03; N, 9.56.

4,10-Dihydro-5*H*-imidazo[2,1-*c*][1,4]benzodiazepines 5a–l; General Procedure

To a stirred solution of **4a–l** (0.92–1.63 mmol, 1 equiv) in anhyd toluene (15 mL) were added *t*-BuOK (1.84–3.26 mmol, 2 equiv), (±)-BINAP (10 mol%), and $Pd_2(dba)_3$ (10 mol%, Pd: 20 mol%). The reaction mixture was refluxed for 14–18 h under N_2 atmosphere. After completion of the reaction (monitored by TLC, eluent: EtOAc), toluene was evaporated under vacuum, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H_2O (3 × 20 mL), followed by brine (30 mL), dried (Na_2SO_4), filtered, and the solvent was evaporated under vacuum. The crude mass was purified by column chromatography over neutral alumina to afford the desired compounds **5a–l**.

4,10-Dihydro-5*H*-phenylimidazo[2,1-*c*][1,4]benzodiazepine (5a)

Yield: 0.21 g (73%); brownish sticky mass; R_f = 0.51 (PE–EtOAc, 3:7).

IR (neat): 1664, 1596, 1494, 1453, 1304, 1248, 1158, 1123, 1076, 748, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.87 (s, 2 H), 4.95 (s, 2 H), 6.77 (d, *J* = 8.1 Hz, 2 H), 6.81–6.86 (m, 2 H), 6.95 (d, *J* = 0.9 Hz, 1 H), 7.16–7.22 (m, 2 H), 7.25–7.32 (m, 2 H), 7.35–7.42 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.4 (CH_2), 49.5 (CH_2), 115.0 (2 CH), 119.5 (CH), 120.0 (CH), 127.0 (CH), 127.1 (CH), 129.0 (CH), 129.2 (2 CH), 129.5 (CH), 130.5 (CH), 135.1 (C), 144.2 (C), 147.1 (C), 147.8 (C).

MS (ESI): *m*/*z* = 262 [M + H]$^+$.

Anal. Calcd for $C_{17}H_{15}N_3$: C, 78.13; H, 5.79; N, 16.08. Found: C, 78.33; H, 5.75; N, 16.20.

4,10-Dihydro-5*H*-isopropylimidazo[2,1-*c*][1,4]benzodiazepine (5b)

Yield: 0.25 g (68%); brownish sticky mass; R_f = 0.32 (EtOAc).

IR (neat): 2969, 2928, 1675, 1598, 1491, 1456, 1375, 1315, 1275, 1170, 1122, 1051, 1010, 929, 742, 666 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.6 Hz, 6 H), 3.72–3.81 (m, 1 H), 4.33 (s, 2 H), 5.01 (s, 2 H), 6.84 (s, 1 H), 6.92 (s, 1 H), 7.00 (t, *J* = 6.6 Hz, 1 H), 7.22–7.36 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0 (2 CH_3), 47.2 (CH_2), 49.8 (CH_2), 52.2 (CH), 119.0 (CH), 121.2 (CH), 122.7 (CH), 126.5 (CH), 128.5 (CH), 129.6 (CH), 131.6 (C), 144.6 (C), 151.4 (C).

MS (ESI): *m*/*z* = 228 [M + H]$^+$.

Anal. Calcd for $C_{14}H_{17}N_3$: C, 73.98; H, 7.54; N, 18.49. Found: C, 73.76; H, 7.50; N, 18.60.

4,10-Dihydro-5*H*-(3,4-methylenedioxybenzyl)imidazo[2,1-*c*][1,4]benzodiazepine (5c)

Yield: 0.23 g (65%); pale yellowish sticky mass; R_f = 0.35 (EtOAc).

IR (neat): 1654, 1601, 1494, 1445,1247, 1124, 1038, 930, 46 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.25 (s, 2 H), 4.26 (s, 2 H), 5.14 (s, 2 H), 5.93 (s, 2 H), 6.75 (d, *J* = 7.8 Hz, 1 H), 6.87 (d, *J* = 14.7 Hz, 4 H), 7.05 (t, *J* = 7.3 Hz, 1 H), 7.21 (s, 1 H), 7.27 (s, 1 H), 7.36 (t, *J* = 7.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.5 (CH_2), 52.9 (CH_2), 58.3 (CH_2), 100.9 (CH_2), 108.1 (CH), 108.6 (CH), 119.2 (CH), 120.0 (CH), 121.8 (CH), 123.3 (CH), 126.9 (CH), 128.4 (CH), 129.8 (CH), 131.5 (C), 131.8 (C), 143.8 (C), 146.9 (C), 147.9 (C), 150.8 (C).

MS (ESI): *m*/*z* = 320 [M + H]$^+$, 342 [M + Na]$^+$.

Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.66; H, 5.41; N, 13.04.

4,10-Dihydro-5*H*-8-methoxy-5-isopropylimidazo[2,1-*c*][1,4]benzodiazepine (5d)
Yield: 0.27 g (71%); yellowish sticky mass; R_f = 0.27 (EtOAc).

IR (neat): 2966, 1644, 1607, 1499, 1428, 1267, 1166, 1043, 923, 817, 750 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, *J* = 6.3 Hz, 6 H), 3.63–3.67 (m, 1 H), 3.77 (s, 3 H), 4.28 (s, 2 H), 4.98 (s, 2 H), 6.79–6.82 (m, 2 H), 6.86 (dd, *J* = 3.0, 8.7 Hz, 1 H), 6.91 (s, 1 H), 7.20 (d, *J* = 8.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (2 CH_3), 48.5 (CH_2), 49.2 (CH_2), 52.1 (CH), 55.3 (OCH_3), 113.9 (CH), 114.1 (CH), 119.1 (CH), 122.9 (CH), 126.7 (CH), 133.9 (C), 144.3 (C), 144.8 (C), 155.2 (C).

MS (ESI): *m*/*z* = 258 $[M + H]^+$.

Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.01; H, 7.44; N, 16.33. Found: C, 69.81; H, 7.40; N, 16.45.

4,10-Dihydro-5*H*-8-methoxy-5-phenylimidazo[2,1-*c*][1,4]benzodiazepine (5e)
Yield: 0.22 g (68%); dark yellow solid; mp 98–100 °C; R_f = 0.35 (PE–EtOAc, 3:7).

IR (KBr): 1588, 1496, 1429, 1365, 1304, 1273, 1237, 1211, 1153, 1081, 1036, 882, 841, 748, 695, 566 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 4.77 (s, 2 H), 4.93 (s, 2 H), 6.72 (d, *J* = 8.1 Hz, 2 H), 6.79 (d, *J* = 9.6 Hz, 2 H), 6.94 (d, *J* = 8.4 Hz, 3 H), 7.17 (t, *J* = 7.6 Hz, 2 H), 7.28 (t like, *J* = 7.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.3 (CH_2), 49.6 (CH_2), 55.5 (OCH_3), 114.0 (2 CH), 114.9 (CH), 115.3 (CH), 118.8 (CH), 120.1 (CH), 127.1 (CH), 129.2 (CH), 130.4 (CH), 136.4 (C), 139.3 (C), 144.4 (C), 147.9 (C), 158.3 (C).

MS (EI): *m*/*z* = 291.

Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found: C, 74.40; H, 5.92; N, 14.32.

4,10-Dihydro-5*H*-8-methoxy-5-benzylimidazo[2,1-*c*][1,4]benzodiazepine (5f)
Yield: 0.31 g (76%); pale brown solid; mp 88–90 °C; R_f = 0.26 (EtOAc).

IR (KBr): 2922, 2808, 1501, 1450, 1375, 1255, 1206, 1149, 1046, 821, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 4.19 (s, 2 H), 4.31 (s, 2 H), 5.12 (s, 2 H), 6.86 (d like, 4 H), 7.17 (d, *J* = 8.7 Hz, 1 H), 7.23–7.33 (m, 3 H), 7.40 (d, *J* = 6.9 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.4 (CH_2), 53.7 (CH_2), 55.4 (OCH_3), 58.6 (CH_2), 114.1 (CH), 114.2 (CH), 119.2 (CH), 120.9 (CH), 126.8 (CH), 127.3 (CH), 128.3 (2 CH), 128.4 (2 CH), 133.3 (C), 138.0 (C), 143.8 (C), 143.9 (C), 155.5 (C).

MS (ESI): *m*/*z* = 306 $[M + H]^+$, 328 $[M + Na]^+$.

Anal. Calcd for $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76. Found: C, 74.53; H, 6.23; N, 13.86.

4,10-Dihydro-5*H*-8-methoxy-5-(3,4-methylenedioxybenzyl)imidazo[2,1-*c*][1,4]benzodiazepine (5g)
Yield: 0.26 g (72%); pale yellow solid; mp 146–148 °C; R_f = 0.36 (EtOAc).

IR (KBr): 1496, 1439, 1375, 1245, 1201, 1125, 1033, 925, 866, 813, 732, 640, 540 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3 H), 4.16 (s, 2 H), 4.20 (s, 2 H), 5.10 (s, 2 H), 5.93 (s, 2 H), 6.74 (d, *J* = 7.8 Hz, 1 H), 6.84–6.90 (m, 6 H), 7.15 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.4 (CH_2), 53.5 (CH_2), 55.4 (OCH_3), 58.3 (CH_2), 100.8 (CH_2), 107.9 (CH), 108.5 (CH), 114.1 (CH), 114.2 (CH), 119.2 (CH), 120.9 (CH), 121.7 (CH), 126.8 (CH), 131.9 (C), 133.3 (C), 143.7 (C), 143.8 (C), 146.8 (C), 147.8 (C), 155.5 (C).

MS (ESI): *m*/*z* = 350 $[M + H]^+$, 372 $[M + Na]^+$.

Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.97; H, 5.52; N, 11.91.

4,10-Dihydro-5*H*-7,8-methylenedioxy-5-isopropylimidazo[2,1-*c*][1,4]benzodiazepine (5h)
Yield: 0.31 g (70%); yellowish sticky mass; R_f = 0.30 (EtOAc).

IR (neat): 2970, 2830, 1505, 1440, 1380, 1240, 1150, 1030, 940, 730 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.26 (d, *J* = 6.6 Hz, 6 H), 3.56–3.64 (m, 1 H), 4.27 (s, 2 H), 4.91 (s, 2 H), 5.93 (s, 2 H), 6.72 (s, 1 H), 6.82 (d, *J* = 9.0 Hz, 2 H), 6.91 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (2 CH_3), 48.6 (CH_2), 49.6 (CH_2), 52.3 (CH), 101.3 (CH_2), 103.7 (CH), 108.3 (CH), 119.1 (CH), 126.2 (C), 126.7 (CH), 143.2 (C), 144.6 (C), 145.8 (C), 148.3 (C).

MS (ESI): *m*/*z* = 272 $[M + H]^+$.

Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.18; H, 6.35; N, 15.60.

4,10-Dihydro-5*H*-7,8-methylenedioxy-5-benzylimidazo[2,1-*c*][1,4]benzodiazepine (5i)
Yield: 0.34 g (75%); yellowish sticky mass; R_f = 0.45 (EtOAc).

IR (neat): 1491, 1443, 1390, 1238, 1175, 1125, 1037, 932, 856, 750 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.19 (s, 2 H), 4.28 (s, 2 H), 5.05 (s, 2 H), 5.93 (s, 2 H), 6.75–6.88 (m, 4 H), 7.26–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.2 (CH_2), 53.7 (CH_2), 58.7 (CH_2), 101.4 (CH_2), 102.0 (CH), 108.3 (CH), 119.1 (CH), 125.5 (C), 126.6 (CH), 127.5 (CH), 128.4 (2 CH), 128.6 (2 CH), 137.8 (C), 143.3 (C), 143.7 (C), 145.2 (C), 148.4 (C).

MS (ESI): *m*/*z* = 320 $[M + H]^+$, 342 $[M + Na]^+$.

Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.66; H, 5.42; N, 13.06.

4,10-Dihydro-5*H*-7,8-methylenedioxy-5-phenylimidazo[2,1-*c*][1,4]benzodiazepine (5j)
Yield: 0.28 g (74%); pale yellow solid; mp 140–142 °C; R_f = 0.42 (PE–EtOAc, 3:7).

IR (KBr): 1597, 1492, 1382, 1299, 1227, 1192, 1120, 1038, 929, 864, 757, 691 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.72 (s, 2 H), 4.91 (s, 2 H), 6.02 (s, 2H), 6.74–6.84 (m, 5 H), 6.95 (s, 2 H), 7.19 (t, *J* = 7.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.1 (2 CH_2), 101.8 (CH_2), 109.1 (CH), 109.9 (CH), 114.2 (CH), 119.1 (CH), 119.9 (CH), 127.0 (CH), 128.7 (C), 129.2 (CH), 140.7 (C), 144.1 (C), 146.2 (C), 147.6 (C), 148.7 (C).

MS (ESI): *m*/*z* = 306 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.61; H, 4.90; N, 13.88.

4,10-Dihydro-5*H*-7,8-methylenedioxy-5-(4-methoxyphenyl)imidazo[2,1-*c*][1,4]benzodiazepine (5k)
Yield: 0.27 g (67%); yellowish sticky mass; R_f = 0.48 (EtOAc).

IR (neat): 1729, 1619, 1506, 1384, 1241, 1123, 1036, 931, 825, 755, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3 H), 4.80 (s, 2 H), 4.90 (s, 2 H), 5.98 (s, 2 H), 6.70–6.80 (m, 7 H), 6.97 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.3 (CH_2), 50.0 (CH_2), 55.6 (OCH_3), 101.7 (CH_2), 108.8 (CH), 109.2 (CH), 114.6 (2 CH), 117.2

(2 CH), 119.8 (CH), 126.5 (CH), 128.0 (C), 142.1 (C), 142.2 (C), 144.0 (C), 145.6 (C), 148.7 (C), 153.6 (C).

MS (ESI): m/z = 336 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.27; H, 5.08; N, 12.43.

4,10-Dihydro-5*H*-7,8-methylenedioxy-5-(3,4-methylenedioxybenzyl)imidazo[2,1-*c*][1,4]benzodiazepine (5l)

Yield: 0.21 g (63%); yellow solid; mp 182–184 °C; R_f = 0.31 (EtOAc).

IR (KBr): 2895, 2834, 1615, 1490, 1442, 1384, 1246, 1165, 1116, 1036, 930, 861, 729, 675 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.16 (s, 4 H), 5.03 (s, 2 H), 5.93 (s, 4 H), 6.75–6.88 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.1 (CH_2), 53.5 (CH_2), 58.4 (CH_2), 100.9 (CH_2), 101.3 (CH_2), 101.9 (CH), 108.0 (CH), 108.3 (CH), 108.6 (CH), 119.1 (CH), 121.8 (CH), 125.5 (C), 126.8 (CH), 131.6 (C), 143.3 (C), 143.6 (C), 145.2 (C), 146.9 (C), 147.9 (C), 148.3 (C).

MS (ESI): m/z = 364 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{15}N_3O_4$: C, 65.32; H, 4.33; N, 12.03. Found: C, 65.52; H, 4.30; N, 12.15.

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