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碱性调控的选择性: 通过 *N*-烷基-*N*-(2-(吡啶-2-基氨基)苯基)甲酰胺合成苯并咪唑酮和苯二氮䓬类化合物

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摘要 发展了一种碱控制选择性合成苯并咪唑酮和吡啶并苯二氮䓬衍生物的方法. 该方法以 *N*-烷基-*N*-(2-(吡啶-2-基氨基)苯基)甲酰胺类化合物为原料, 以 $K_2S_2O_8$ 为氧化剂, 当选用 NaOAc 为碱时, 高选择性地得到了一系列苯并咪唑酮衍生物; 当选用 $NaHCO_3$ 为碱时, 得到了一系列吡啶并苯二氮䓬衍生物. 通过自由基捕捉实验的研究, 提出了相应可能的反应机理. 苯二氮䓬的克级放大实验和官能化衍生化实验说明该方法具有一定应用前景.

关键词 苯并咪唑酮; 苯二氮䓬; 氧化剂诱导; 无金属

Basicity-Tuned Selectivity: Synthesis of Benzimidazolone and Benzodiazepine from *N*-Alkyl-*N*-(2-(pyridin-2-ylamino)-phenyl)formamides

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Abstract A base-controlled strategy for the selective preparation of benzimidazolone and pyrido-benzodiazepine derivatives was developed. The *N*-alkyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamides underwent selective coupling to synthesize a series of benzimidazolones when NaOAc was used as bases and employed $K_2S_2O_8$ as oxidants. By changing bases to $NaHCO_3$, a series of benzodiazepines was obtained. The possible reaction mechanism was proposed based on the radical-trapping experiments. The applicability of this protocol is demonstrated by scale-up experiments and the functionalization of benzodiazepine products.

Keywords benzimidazolone; benzodiazepine; oxidant-induced; metal-free

1 Introduction

Benzimidazolone and pyrido-benzodiazepine derivatives are important heterocycle scaffolds that have significant roles in the synthesis of pharmaceuticals and natural products.[1] The benzimidazolone derivatives are critical urea compounds with the biological and pharmacological activities, such as potassium channel activators[2] and virus fusion inhibitors (Figure 1a).[3]

The synthetic methods that have been developed to con-

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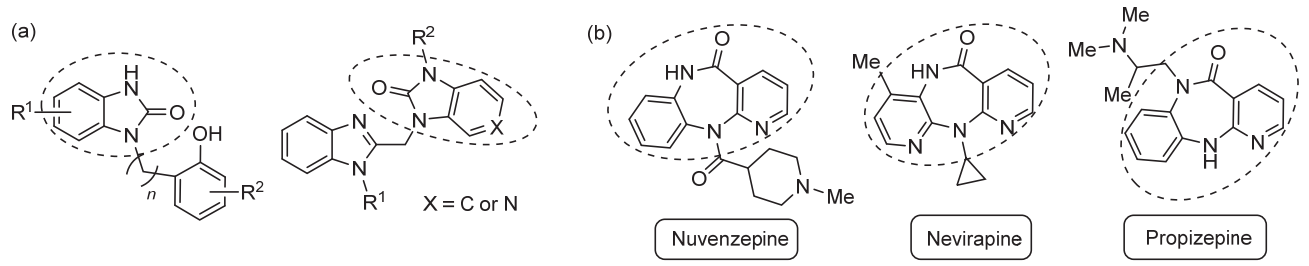
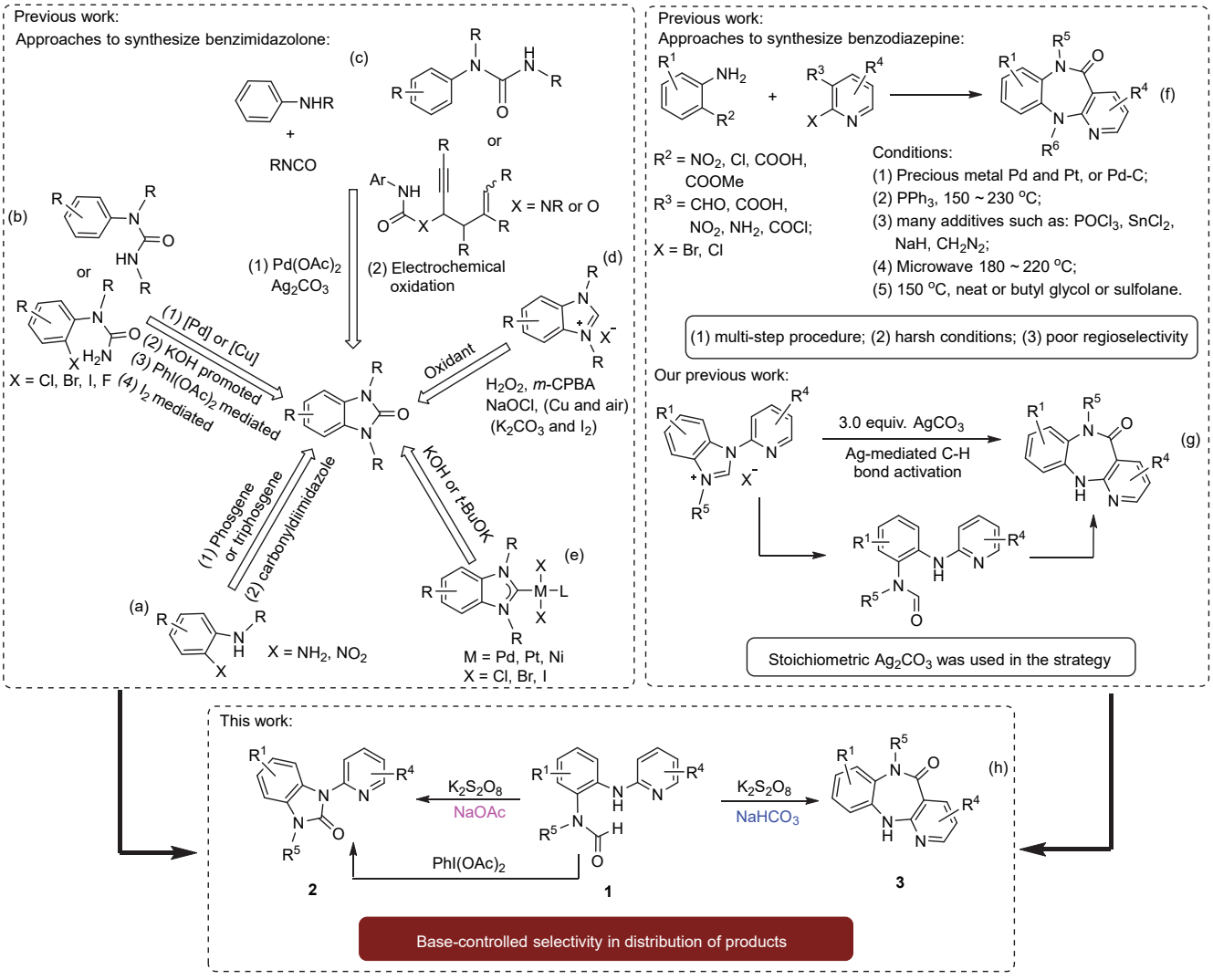


Figure 1 Structures of biologically active benzimidazolone and pyrido-benzodiazepine derivatives

struct benzimidazolone compounds are shown in Schemes 1. Early synthetic methods used benzene-1,2-diamines or nitroanilines with phosgene,[4] triphosgene,[5] or carbonyldiimidazole[6] as starting materials (Scheme 1a). The alternative strategy was developed by Cu-[7] or Pd-catalyzed,[8] KOH-promoted,[9] or oxidant-mediated intramolecular cyclization (Scheme 1b).[10]

In 2016, Youn *et al.*[11] reported a one-pot method for the synthesis of benzimidazolone from (hetero)aromatic amines and isocyanates catalyzed by Pd(II)/Ag(I) system (Scheme 1c). Xu's group[12] and Liu's group,[13] independently, have reported electrochemical intramolecular dehydrogenative reaction (Scheme 1c).

The oxidants promoted protocols for the synthesis of benzimidazolones, in which the use of benzimidazolium salts as raw materials, were developed (Scheme 1d).[14] The *in situ* catalytic system in combination with Cu powder and *N*-heterocyclic carbene (NHC) was also developed to prepare benzimidazolones (Scheme 1d).[15] A series of Pt-, (Scheme 1e).[16] The diphosphino-functionalized 1,3-



Scheme 1 Previous approaches to synthesize benzimidazolone and pyrido-benzodiazepine

dialkylimidazolium salts were used as starting materials to Pd-, and Ni-NHC complexes were successfully converted into benzimidazolones using base anions as oxygen source prepare 2-imidazolones through intramolecular dehydrogenative C—N coupling.[17]

Pyrido-benzodiazepine derivatives have attracted some interest owing to their unique biological activities,[18] *e.g.* nuvenzepine,[19] nevirapine[20] and propizepine[21] (Figure 1b). Hence, the development of a simple and sustainable synthetic method for pyrido-benzodiazepine derivatives has been a longstanding goal.[22] Most of the previously synthetic approaches for benzodiazepines focus on *ortho*-phenyldiamine as starting materials (Scheme 1f).[23] It is difficult to control selectivity of two NH_2 groups bearing benzene ring.[23b,24] To overcome the drawback, *ortho*-phenyldiamine has been replaced by starting materials with two different substituents, such as *ortho*-nitroaniline,[24] 2-aminobenzoate,[25] and 2-halonitrobenzenes[26] (Scheme 1f). Direct C—H bond functionalization has advantages in control of selectivity and atom economy for the modification of molecules.[27] Recently, our group developed a method for the synthesis of pyrido-benzodiazepines through continuous ring opening/ring closure of benzimidazolium salts (Scheme 1g).[28] However, this protocol still required stoichiometric amounts of Ag_2CO_3 (3.0 equiv.). The transition-metal catalyzed oxidative reactions have emerged as a powerful method to form C—C and C—heteroatom bonds, in which oxidant plays a critical role in catalyst regeneration.[29] $K_2S_2O_8$ is an inexpensive oxidant that has been used widely in palladium and silver-catalyzed C—H bond activation reactions.[30] A series of $K_2S_2O_8$ promoted transformations under metal-free condition were described.[31] Inspired by these research on formation C—C bond induced by oxidant,[32] we envisioned that synthesis of pyrido-benzodiazepines could be realized through oxidant-induced strategy.

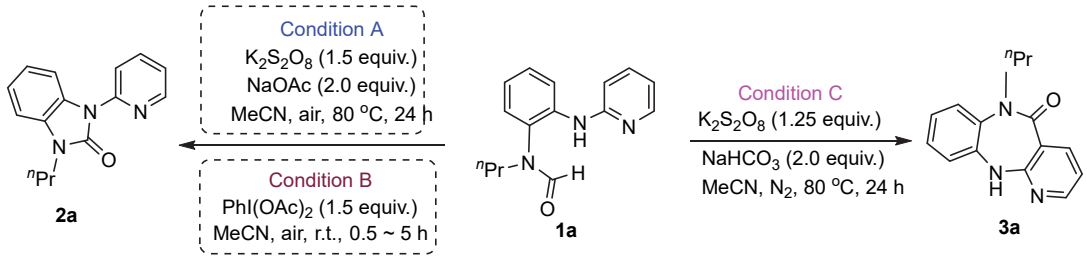
Previous studies[33] have discovered that imidazolium salts or benzimidazolium salts were hydrolyzed to form ring opened products in the presence of water under basic condition. We have sought to use ring opened products, such as *N*-alkyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamides, as starting materials to prepare pyridobenzodiazepines. In this work, we report a base-controlled strategy for selective synthesis of benzimidazolones and pyrido-benzodiazepines from *N*-alkyl-*N*-(2-(pyridin-2-ylamino)phenyl)-formamides under metal-free condition (Scheme 1h).

2 Results and discussion

The reaction condition for the synthesis of benzimidazolone and pyrido-benzodiazepine derivatives were first optimized by using *N*-propyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamide (**1a**) (which was prepared as procedure in experimental part) as model substrate (Table 1). The reactions were performed by using $K_2S_2O_8$ as an oxidant in MeCN at 80 ℃ for 24 h in the presence of a base. The corresponding benzimidazolone (**2a**) and pyrido-benzodiazepine **3a** were obtained using NaOAc and $NaHCO_3$ as bases, respectively, affording 80% (**2a**) and 68% (**3a**) yields, and yields of byproducts **3a** and **2a** under two conditions were 0 and trace (Table 1, Entry 1). An interesting result was that **1a** also converted to **2a** with a yield of 82% in the presence of 1.5 equiv. of $PhI(OAc)_2$ for 0.5 h at room temperature (Table 1, Entry 1). The reaction was difficult to complete in the absence of $K_2S_2O_8$ or $PhI(OAc)_2$ or bases (Table 1, Entry 2), which indicated that both oxidant and base played critical roles in two transformations. Subsequently, base screening showed that *t*-BuOLi, Na_2CO_3, $KHCO_3$ and K_2CO_3 did not promote two transformations (Table 1, Entry 3). Several solvents, including MeCN, dichloroethane (DCE), dimethyl sulfoxide (DMSO), and 1,4-dioxane, were screened, and MeCN was found to be the most effective solvent (Table 1, Entry 4). Mixed solvents of MeCN/H_2O were tested to increase the solubility of $K_2S_2O_8$, but yields of two products were not improved (Table 1, Entry 4). Both $Na_2S_2O_8$ and $(NH_4)_2S_2O_8$ showed lower performance than $K_2S_2O_8$ under conditions A and C, and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and *t*-butyl hydroperoxide (TBHP) had no promoting effect in two transformations (Table 1, Entry 5). The concentration of oxidant and base was investigated. Note that increasing amount of oxidant did not improve the yield of **2a**, but it reduced yield of **3a** (Table 1, Entry 6). A 2.0 equiv. of base was found to be suitable for two reactions (Table 1, Entry 7). Decreasing temperature to 50 ℃ or increasing temperature to 100 ℃ did not improve yield of **2a** and **3a** under conditions A and C (Table 1, Entry 8). Increasing temperature from room temerature to 50 ℃ did not improve yield of **2a** in conditions B (Table 1, Entry 8). Replacing nitrogen atmosphere by an air atmosphere slightly reduced yield of **3a** (Table 1, Entry 9). Finally, reaction time was investigated under different conditions. Prolonging reaction time from 0.5 h to 5.0 h had not an evident change in yield of **2a** under condition B (Table 1, Entry 10). Prolonging reaction time to 48 h did not improve yield of **2a** and **3a** under conditions A and C (Table 1, Entry 10).

The scope of benzimidazolone under optimized reaction condition is shown in Table 2. First, a series of *N*-substituted functionalities bearing substrates were well tolerated and the corresponding benzimidazolone products were obtained in yields of 25%～82% (**2a**～**2g**), but substrates with bromopropyl and benzhydryl groups showed low reactivity under both condition A and condition B (**2h** and **2i**). Next, we explored reactivity of substrates with halogen atoms on pyridine ring, which afforded corresponding products in moderate yield (**2j**～**2o**). Similarly, substrates on pyridine ring bearing electron-donating groups smoothly preceeded and affording desired products **2p**～**2s** in 21%～71% yields. Note that substrates bearing strong electron-withdrawing groups on the pyridine ring showed low reactivity. For

Table 1 Optimization of conditions



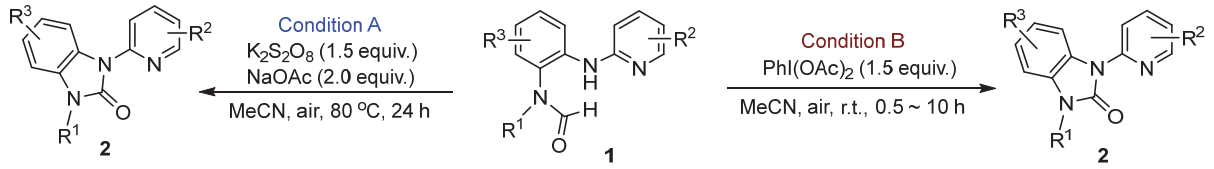
Entry	**2a**, Condition A[a]	**2a**, Condition B[b]	**3a**, Condition C[c]
1	**2a**, 80%; (**3a**, 0)	**2a**, 82%	**3a**, 68%; (**2a**, trace)
2	No $K_2S_2O_8$, **2a**, 0 No base, **2a**, 8%	No PhI(OAc)$_2$, **2a**, 0	No $K_2S_2O_8$, **3a**, 0 No base, **3a**, trace
3	LiO*t*-Bu instead of NaOAc, **2a**, 12% Na_2CO_3 instead of NaOAc, **2a**, 10% $KHCO_3$ instead of NaOAc, **2a**, trace K_2CO_3 instead of NaOAc, **2a**, 11%	—	LiO*t*-Bu instead of $NaHCO_3$, **3a**, 26% Na_2CO_3 instead of $NaHCO_3$, **3a**, 29% $KHCO_3$ instead of $NaHCO_3$, **3a**, 10% K_2CO_3 instead of $NaHCO_3$, **3a**, 22%
4	DCE instead of MeCN, **2a**, 30% DMSO instead of MeCN, **2a**, 26% 1,4-Dioxane instead of MeCN, **2a**, 35% MeCN/H_2O (V∶V=1∶1), **2a**, 36%	DCE instead of MeCN, **2a**, 69% DMSO instead of MeCN, **2a**, 80% 1,4-Dioxane instead of MeCN, **2a**, 77% MeCN/H_2O (V∶V=1∶1), **2a**, 40%	DCE instead of MeCN, **3a**, 40% DMSO instead of MeCN, **3a**, 15% 1,4-Dioxane instead of MeCN, **3a**, 10% MeCN/H_2O (V∶V=1∶1), **3a**, 26%
5	$Na_2S_2O_8$ instead of $K_2S_2O_8$, **2a**, 39% $(NH_4)_2S_2O_8$ instead of $K_2S_2O_8$, **2a**, 45% DDQ instead of $K_2S_2O_8$, **2a**, 0 TBHP instead of $K_2S_2O_8$, **2a**, 0	$Na_2S_2O_8$ instead of PhI(OAc)$_2$, **2a**, 0 $(NH_4)_2S_2O_8$ instead of PhI(OAc)$_2$, **2a**, 0 DDQ instead of PhI(OAc)$_2$, **2a**, 0 TBHP instead of PhI(OAc)$_2$, **2a**, 0	$Na_2S_2O_8$ instead of $K_2S_2O_8$, **3a**, 38% $(NH_4)_2S_2O_8$ instead of $K_2S_2O_8$, **3a**, 32% DDQ instead of $K_2S_2O_8$, **3a**, 0 TBHP instead of $K_2S_2O_8$, **3a**, trace
6	$K_2S_2O_8$ (1.0 equiv.), **2a**, 65% $K_2S_2O_8$ (1.5 equiv.), **2a**, 80% $K_2S_2O_8$ (2.0 equiv.), **2a**, 79%	PhI(OAc)$_2$ (1.0 equiv.), **2a**, 47% PhI(OAc)$_2$ (1.5 equiv.), **2a**, 82% PhI(OAc)$_2$ (2.0 equiv.), **2a**, 84%	$K_2S_2O_8$ (1.0 equiv.), **3a**, 36% $K_2S_2O_8$ (1.5 equiv.), **3a**, 61% $K_2S_2O_8$ (2.0 equiv.), **3a**, 23%
7	NaOAc (1.5 equiv.), **2a**, 69% NaOAc (2.0 equiv.), **2a**, 80% NaOAc (3.0 equiv.), **2a**, 78%	—	$NaHCO_3$ (1.5 equiv.), **3a**, 61% $NaHCO_3$ (2.0 equiv.), **3a**, 69% $NaHCO_3$ (3.0 equiv.), **3a**, 67%
8	100 ℃ instead of 80 ℃, **2a**, 80% 50 ℃ instead of 80 ℃, **2a**, 58%	50 ℃ instead of r.t., **2a**, 85%	100 ℃ instead of 80 ℃, **3a**, 65% 50 ℃ instead of 80 ℃, **3a**, 47%
9	—	—	Air, **3a**, 59%
10	48 h, **2a**, 80%	5 h, **2a**, 80%	48 h, **3a**, 65%

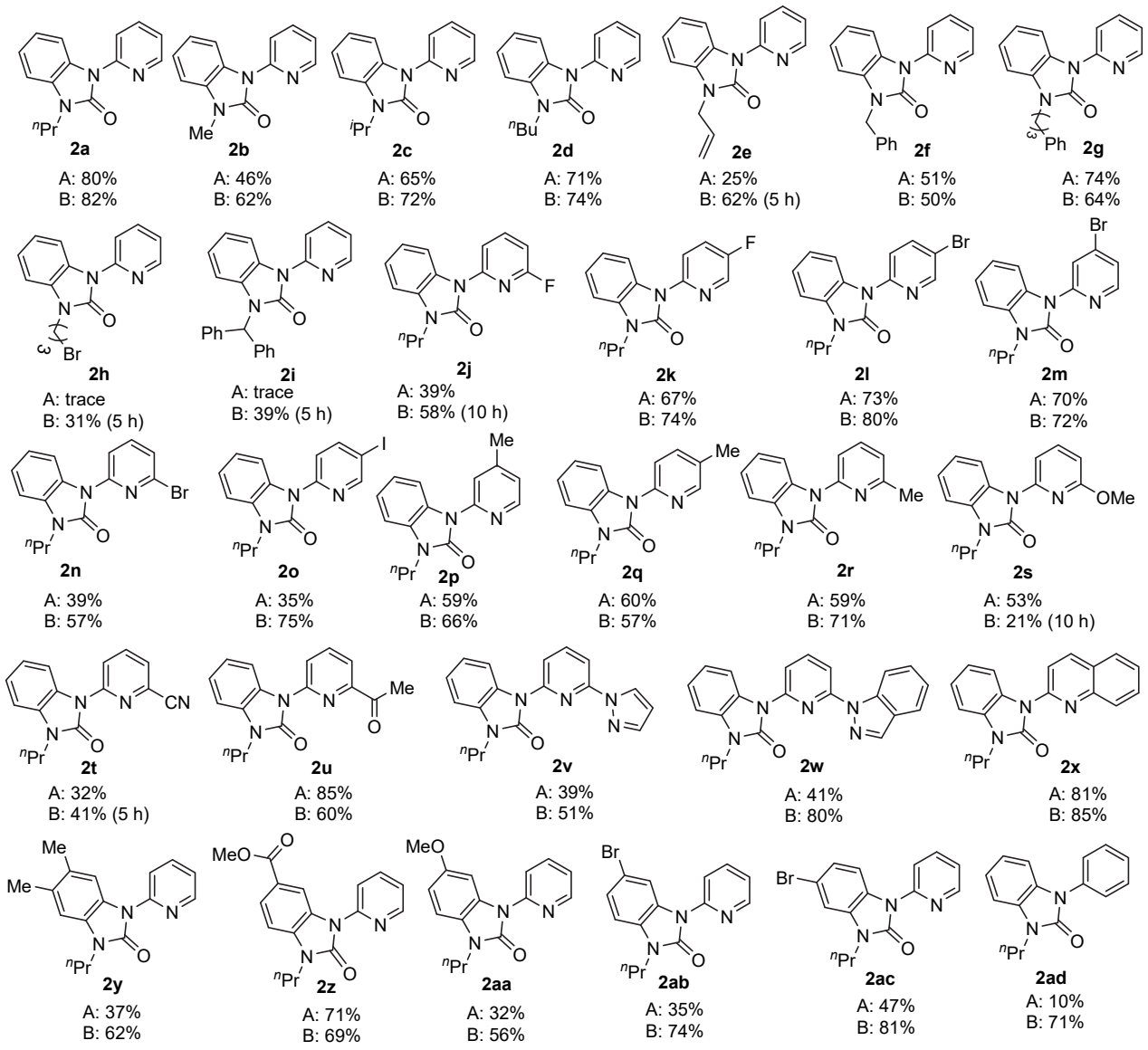
[a] Condition A: **1a** (0.2 mmol), $K_2S_2O_8$ (0.3 mmol, 1.5 equiv.), NaOAc (0.4 mmol, 2.0 equiv.), MeCN (2 mL), air, 80 ℃, 24 h; isolated yields. [b] Condition B: **1a** (0.2 mmol), PhI(OAc)$_2$ (0.3 mmol, 1.5 equiv.), MeCN (2 mL), air, room temperature, 0.5 h; isolated yields. [c] Condition C: **1a** (0.2 mmol), $K_2S_2O_8$ (0.25 mmol, 1.25 equiv.), $NaHCO_3$ (0.4 mmol, 2.0 equiv.), MeCN (2 mL), N_2, 80 ℃, 24 h; isolated yields.

example, 6-cyano substrate gave lower product yields both under conditions A and B (**2t**, 32% and 41%, respectively). A wide range of functional groups on pyridine ring, including acetyl groups and pyrazolyl, indazolyl, and quinoline groups, were also suitable for this transformation, and resulted in products **2u**～**2x** in 41%～85% yields. The effect of substituents on the benzimidazole ring on this transformation was next explored. Fortunately, various substrates bearing functional groups were converted into corresponding products in yields of 32%～81% (**2y**～**2ac**). Notably, replacing the pyridine ring by a benzene ring significantly inhibited reactivity of substrates under condition A (**2ad**, 10%), whereas good yield of **2ad** under condition B was achieved (**2ad**, 71%).

Next, the scope of substrates for the synthesis of pyridobenzodiazepine derivatives was invetigated (Table 3). Under standard condition C, *N*-alkyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamides bearing various *N*-substituted groups afforded desired products in moderate yields (**3a**～**3g**). The substrates bearing electron-donating groups on pyridine ring, such as 4-methyl, 5-methyl, and 6-methyl groups, were converted into corresponding products in good yields (**3h**～**3j**). However, it was difficult to obtain 6-methoxy product (**3k**). The influence of the different halogen atoms bearing pyridine ring on reactivity was investigated. The reaction proceeded smoothly for

Table 2 Synthesis of benzimidazolone[a]

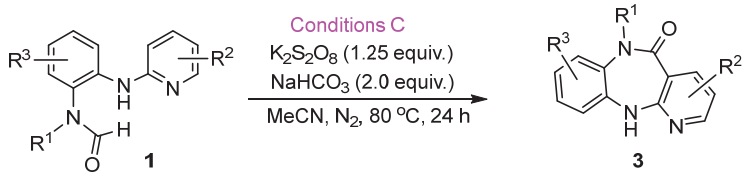


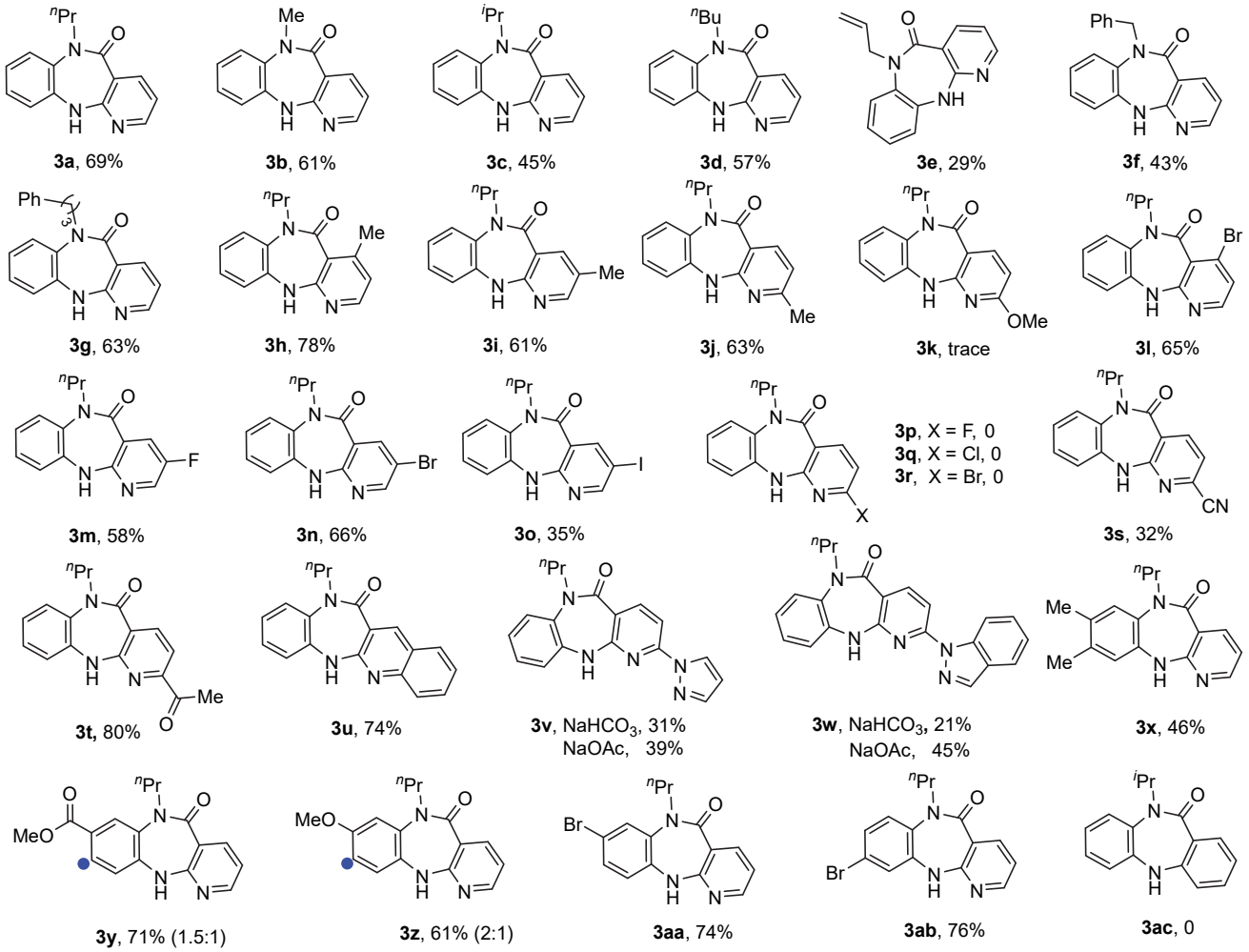


[a] Reaction conditions: condition A: **1** (0.2 mmol), $K_2S_2O_8$ (0.3 mmol, 1.5 equiv.), NaOAc (0.4 mmol, 2.0 equiv.), MeCN (2 mL), air, 80 ℃, 24 h; isolated yields; condition B: **1** (0.2 mmol), $PhI(OAc)_2$ (0.3 mmol, 1.5 equiv.), MeCN (2 mL), air, room temperature, 0.5 h; isolated yields.

substrates with chloro, bromo, and iodine atoms at 4- or 5-position on pyridine ring to afford desired products in 35%～66% yields (**3l**～**3o**). Unfortunately, no products were isolated under condition C using substrates with fluorine, chlorine, and bromine atoms at 6-position on pyridine ring (**3p**～**3r**). The substrate with cyano group at the 6-position on pyridine ring gave a lower yield (**3s**, 32%). The substrates with 6-acetyl groups and quinoline showed high reactivity and afforded good yields of **3t** and **3u**. The substrates containing pyrazolyl and indazolyl groups afforded low yields with both NaOAc and $NaHCO_3$, where NaOAc outperformed $NaHCO_3$ (**3v**～**3w**). Futhurmore, the influence of substituents on benzene ring on reactivity was investigated. As shown in Table 3, a wide range of substituted substrates on benzene ring were well tolerated and converted to the desired products in moderate to good yields (**3x**～**3ab**). However, a mixture of products was obtained when methoxy- or carboxylate-substituted substrates were employed (**3y** and **3z**). No product was detected when pyridine ring was replaced with a benzene ring (**3ac**); therefore, only starting materials containing a pyridine ring were investigated in trans-

Table 3 Synthesis of pyrido-benzodiazepine[a]



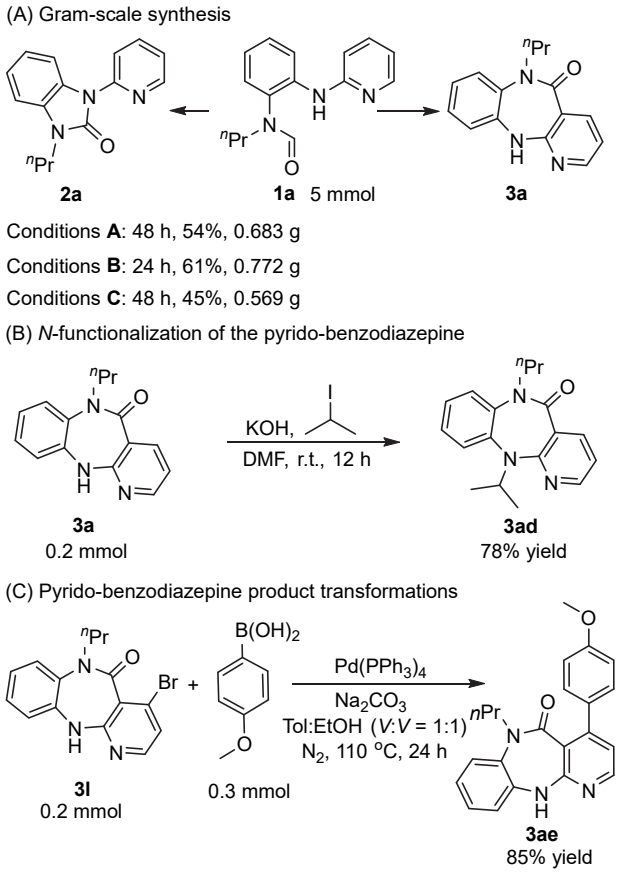


[a] Reaction conditions: condition C: **1** (0.2 mmol), $K_2S_2O_8$ (0.25 mmol, 1.25 equiv.), $NaHCO_3$ (0.4 mmol, 2.0 equiv.), MeCN (2 mL), N_2, 80 ℃, 24 h; isolated yields.

formation.

To evaluate the practicality and scalability of the developed methods for the synthesis of benzimidazolone and pyrido-benzodiazepine, the reaction was performed on a 5 mmol scale under standard conditions A, B and C, respectively (Scheme 2A). **2a** was obtained in yields of 54% and 61% under conditions A and B when prolonging reaction time to 48 and 24 h, respectively (Scheme 2A). **3a** was also isolated in a yield of 45% under condition C when reaction time was prolonged to 48 h (Scheme 2A). To demonstrate the application of the pyrido-benzodiazepine, *N*-alkylation reaction of **3a** was performed, and affording **3ad** in 78% yield (Scheme 2B). **3l** reacted with (4-methoxyphenyl)-boronic acid to give corresponding product **3ae** through a Suzuki coupling reaction (Scheme 2C).

To elucidate a plausible reaction mechanism for selective synthesis of benzimidazolones and pyrido-benzodiazepines, a range of radical-trapping experiments were performed using 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) as radical scavengers (Scheme 3). The addition of TEMPO (2.0 equiv.) under condition A resulted in 30% yield of **2a**. It is inferred that TEMPO has played a role in an oxidant, so that reaction was not completely suppressed under condition A. To prove results above, BHT was used as a radical scavenger. In the presence of BHT (2.0 equiv.), only a 12% yield of **2a** was isolated (Scheme 3). The results suggested that a radical mechanism may have been involved under condition A. Radical-trapping experiments were conducted under condition B. However, the radical inhibi-



Scheme 2 Gram-scale synthesis and product transformations

tor did not significantly reduce yield of **2a** under condition B (Scheme 3), which demonstrated that a radical process was not involved under condition B. In contrast, reaction for the synthesis of product **3a** was completely inhibited under condition C, and the radical trapping product **3AA** was obtained in 15% yield (Scheme 3).

The abovementioned results indicated that a radical process was probably involved under conditions A and C. Thus, plausible mechanisms for oxidant-induced pathway to synthesize two heterocycle scaffolds under conditions A, B and C were proposed (Scheme 4). The mechanism for the synthesis of **2a** under condition A is shown in Scheme 4. **1a** is first deprotonated by NaOAc to generate nitrogen anion **4**. Then, **4** is oxidized by a sulfate radical anion to produce nitrogen radical species **5**, which subsequently undergoes an intramolecular radical addition to produce alkoxy radical **6**. The product is obtained after the loss of a hydrogen radical. The mechanism under condition B is consistent with previous report.[34] Compound **1a** reacts with $PhI(OAc)_2$ to produce intermediate **7**, which undergoes an intramolecular nucleophilic addition to afford intermediate **8** and further deprotonation to produce **9**. Finally, **2a** is formed by removal of PhI and HOAc. A possible mechanism for the synthesis of pyrido-benzodiazepine **3a** is shown on the bottom of Scheme 4. Similarly, HCO_3^- deprotonates amino group of **1a** and generates nitrogen anion **4**, which is then oxidized by sulfate radical anion to afford corresponding nitrogen radical species **5**. 1,5-HAT take places from **5** to give acyl radical species **10**. The acyl radical species **10** reacts with pyridine ring via radical addition to form intermediate **11**, which is further oxidized by the sulfate radical anion and undergoes deprotonation to furnish benzodiazepine **3a**.

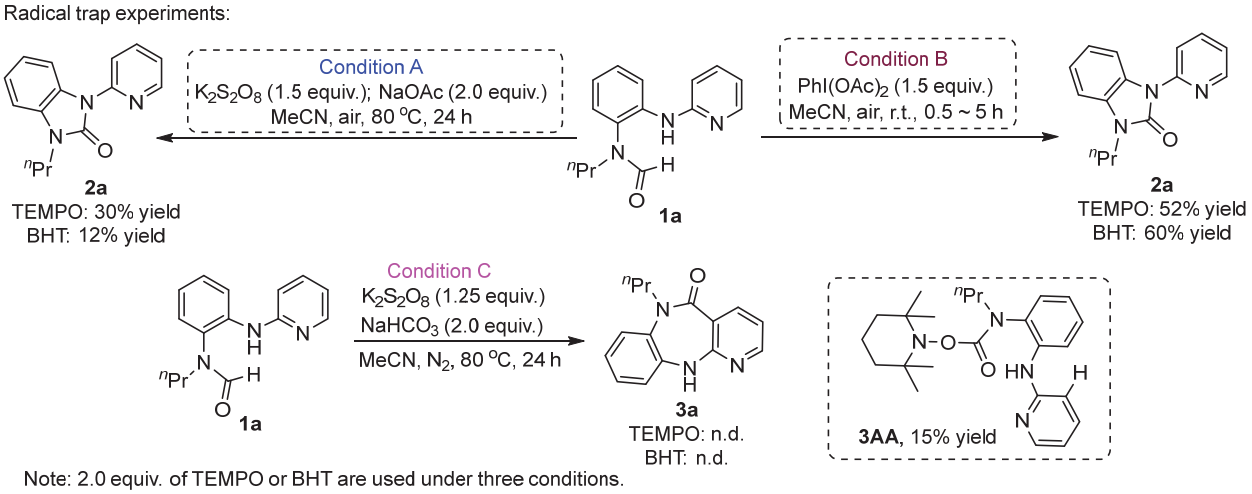
3 Conclusions

In summary, we have developed a route to construct benzimidazolone and pyrido-benzodiazepine derivatives via a base-controlled strategy. The method has advantage of the use of inexpensive oxidants under metal-free condition. However, the substrates scope limits to pyridine ring in the synthesis of benzodiazepines. Further transformations of *N*-alkyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamides are underway in the future work.

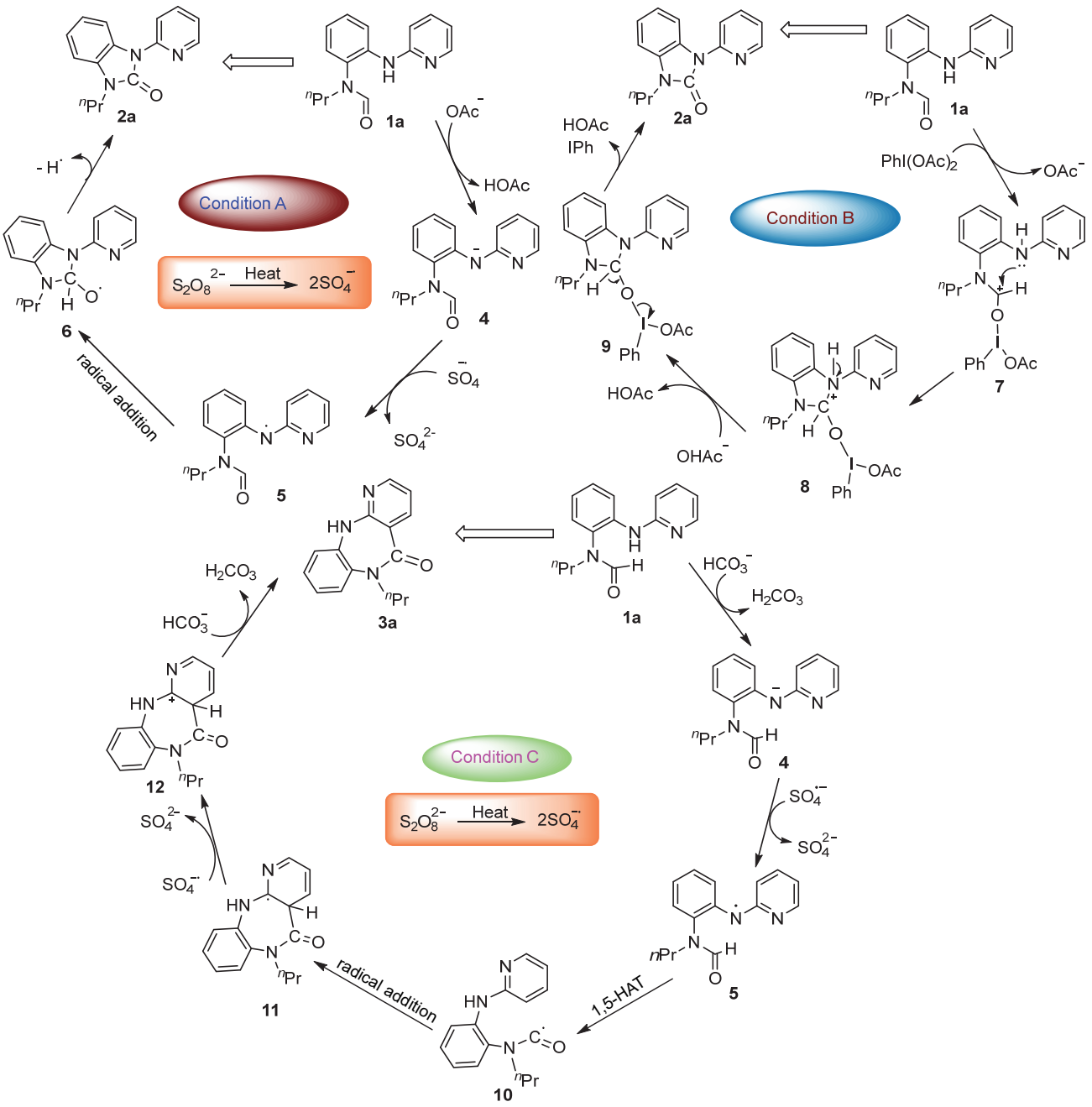
4 Experimental section

4.1 General information

Unless otherwise stated, all solvents, oxidants, and bases



Scheme 3 Radical trap experiments for conditions A～C



Scheme 4 Plausible mechanism for the synthesis of benzimidazolones and pyrido-benzodiazepines

were purchased from commercial suppliers and used without further purification. The benzimidazolium salts, which were used as starting materials to prepare *N*-alkyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamides, were synthesized based on methods we have previously reported.[35]

4.2 Analytical methods

NMR spectra were recorded using a Bruker Avance III HD 400 spectrometer using TMS as an internal standard (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). High-resolution mass spectrometry (HRMS) data were collected on a Bruker ultrafleXtreme MALDI TOF/TOF mass spectrometer.

4.3 General experimental procedure for the synthesis of *N*-propyl-*N*-(2-(pyridin-2-ylamino)phenyl)-formamide derivatives (**1a**)

3-Propyl-1-(pyridin-2-yl)-1*H*-benzo[*d*]imidazol-3-ium iodide (365 mg, 1.0 mmol) and KO*t*-Bu (134 mg, 1.2 mmol) were placed in a 50 mL reaction tube with a stir bar. The reaction mixture was stirred with 8 mL of water for 2 h at room temperature. Then pour brine (30 mL) into the tube and extracted three times with dichloromethane (15 mL×3). The desired *N*-propyl-*N*-(2-(pyridin-2-ylamino)-phenyl)formamide (**1a**)[36] was isolated by flash chromatography in 99% yield.

4.4 General experimental procedure for the synthesis of the benzimidazolones **2**

Condition A: *N*-Propyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamide **1** (0.2 mmol), NaOAc (32.8 mg, 0.4 mmol), and $K_2S_2O_8$ (81.0 mg, 0.3 mmol) were placed in a 25 mL reaction tube with a stir bar, and acetonitrile (2 mL) was added to reaction tube. The mixture was stirred at 80 ℃ for 24 h. Then the mixture was concentrated under vacuum and benzimidazolones **2** were obtained by column chromatography (petroleum ether/ethyl acetate).

Condition B: *N*-Propyl-*N*-(2-(pyridin-2-ylamino)-phenyl) formamide **1** (0.2 mmol), and $PhI(OAc)_2$ (96.6 mg, 0.3 mmol) were placed in a 25 mL reaction tube with a stir bar, and acetonitrile (2 mL) was added. The mixture was stirred at room temperature for 0.5～5.0 h in air. Then the mixture was concentrated under vacuum and benzimidazolones **2** were obtained by column chromatography (petroleum ether/ethyl acetate).

4.5 General experimental procedure for the synthesis of the benzodiazepines **3**

Condition C: *N*-Propyl-*N*-(2-(pyridin-2-ylamino)phenyl)formamide **1** (0.2 mmol), $NaHCO_3$ (33.6 mg, 0.4 mmol), and $K_2S_2O_8$ (67.5 mg, 0.25 mmol) were placed in a 25 mL reaction tube with a stir bar. The reaction tube was vacuumed and then filled with nitrogen thrice. Subsequently, acetonitrile (2 mL) was added to the reaction tube. The mixture was stirred at 80 ℃ for 24 h. Then the mixture was concentrated under vacuum and the benzodiazepines **3** were obtained by column chromatography (petroleum ether/ethyl acetate).

1-Propyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2a**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, *V*∶*V*=20∶1), a pale yellow oil (A: 80% yield, 40.5 mg; B: 82% yield, 41.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (ddd, *J*=0.4, 1.6, 8.0 Hz, 1H), 8.14 (dt, *J*=8.0, 1.2 Hz, 1H), 8.09～8.07 (m, 1H), 7.84 (ddd, *J*=1.6, 7.2, 9.6 Hz, 1H), 7.23～7.11 (m, 3H), 7.05～7.03 (m, 1H), 3.93～3.90 (m, 2H), 1.88～1.79 (m, 2H), 1.01 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.0, 150.5, 148.0, 138.2, 129.7, 127.7, 122.6, 121.7, 121.0, 117.7, 113.1, 107.6, 42.7, 21.6, 11.4. HRMS (MALDI-TOF) calcd for $C_{15}H_{15}N_3OH$ $[M+H]^+$ 254.1288, found 254.1285.

1-Methyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2b**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, *V*∶*V*=30∶1), a white solid (A: 46% yield, 20.7 mg; B: 62% yield, 27.9 mg); m.p. 86.5～87.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57～8.55 (m, 1H), 8.14 (d, *J*=8.4 Hz, 1H), 8.09～8.06 (m, 1H), 7.87～7.82 (m, 1H), 7.23～7.14 (m, 3H), 7.02 (dd, *J*=7.6, 1.2 Hz, 1H), 3.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.2, 150.4, 148.0, 138.2, 130.2, 127.7, 122.7, 121.9, 121.1, 117.6, 113.1, 107.4, 27.1. HRMS (MALDI-TOF) calcd for $C_{13}H_{11}N_3OH$ $[M+H]^+$ 226.0975, found 226.0971.

1-Isopropyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2c**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, *V*∶*V*=20∶1), a colorless oil (A: 65% yield, 32.9 mg; B: 72% yield, 36.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (ddd, *J*=0.8, 2.0, 5.2 Hz, 1H), 8.08 (dt, *J*=8.0, 1.2 Hz, 1H), 8.03～8.01 (m, 1H), 7.85 (ddd, *J*=2.0, 7.2, 9.2 Hz, 1H), 7.23～7.09 (m, 4H), 4.85～4.74 (m, 1H), 1.60 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.4, 150.3, 148.1, 138.1, 128.5, 127.9, 122.3, 121.3, 121.2, 118.2, 112.8, 108.9, 45.2, 20.1. HRMS (MALDI-TOF) calcd for $C_{15}H_{15}N_3OH$ $[M+H]^+$ 254.1288, found 254.1282.

1-Butyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2d**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, *V*∶*V*=20∶1), a colorless oil (A: 71% yield, 37.9 mg; B: 74% yield, 39.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (ddd, *J*=0.8, 2.0, 4.8 Hz, 1H), 8.15 (dt, *J*=8.4, 0.8 Hz, 1H), 8.09～8.07 (m, 1H), 7.84 (ddd, *J*=2.0, 7.2, 9.2 Hz, 1H), 7.23～7.11 (m, 3H), 7.05～7.03 (m, 1H), 3.95 (t, *J*=7.2 Hz, 2H), 1.82～1.74 (m, 2H), 1.49～1.39 (m, 2H), 0.97 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.9, 150.5, 148.0, 138.1, 129.65, 127.7, 122.6, 121.7, 121.0, 117.7, 113.1, 107.6, 40.9, 30.3, 20.1, 13.8. HRMS (MALDI-TOF) calcd for $C_{16}H_{17}N_3OH$ $[M+H]^+$ 268.1444, found 268.1449.

1-Allyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2e**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, *V*∶*V*=15∶1), a colorless oil (A: 25% yield, 12.5 mg; B: 62% yield, 31.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (ddd, *J*=0.8, 2.0, 5.4 Hz, 1H), 8.15 (d, *J*=8.0 Hz, 1H), 8.12～8.06 (m, 1H), 7.85 (ddd, *J*=2.0, 7.2, 9.2 Hz, 1H), 7.22 (ddd, *J*=0.8, 4.8, 7.2 Hz, 1H), 7.18～7.11 (m, 2H), 7.05～7.02 (m, 1H), 5.99～5.90 (m, 1H), 5.31～5.25 (m, 2H), 4.58 (dt, *J*=5.6, 1.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.8, 150.4, 148.0, 138.2, 131.7, 129.4, 127.7, 122.7, 121.9, 121.1, 117.8, 117.7, 113.1, 108.2, 43.5. HRMS (MALDI-TOF) calcd for $C_{15}H_{13}N_3OH$ $[M+H]^+$ 252.1131, found 252.1130.

1-Benzyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2f**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, *V*∶*V*=15∶1), a colorless oil (A: 51% yield, 30.7 mg; B: 50% yield, 30.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (dd, *J*=6.0, 1.2 Hz, 1H), 8.11 (d, *J*=8.0 Hz, 1H), 8.02～8.00 (m, 1H), 7.81～7.77 (m, 1H), 7.31～7.14 (m, 6H), 7.07～7.00 (m, 2H), 6.89～6.86 (m, 1H), 5.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.2, 150.4, 148.1, 138.2, 135.9, 129.4, 128.8, 127.8, 127.5, 122.7, 122.0, 121.2, 117.7, 113.1, 108.2, 44.9. HRMS (MALDI-TOF) calcd for $C_{19}H_{15}N_3OH$ $[M+H]^+$ 302.1288, found 302.1284.

1-Benzyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2g**): Following the general conditions A and B, purification by flash chromatography (petroleum/

EtOAc, V∶V=20∶1), a light red oil (A: 74% yield, 48.7 mg; B: 64% yield, 42.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57～8.55 (m, 1H), 8.14 (d, J=8.4 Hz, 1H), 8.08～8.06 (m, 1H), 7.87～7.83 (m, 1H), 7.30～7.10 (m, 8H), 6.96～6.94 (m, 1H), 3.98 (t, J=7.6 Hz, 2H), 2.77～2.73 (m, 2H), 2.19～2.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.9, 150.4, 148.0, 141.0, 138.2, 129.5, 128.5, 128.4, 127.8, 126.1, 122.6, 121.8, 121.1, 117.7, 113.1, 107.6, 40.7, 33.1, 29.6. HRMS (MALDI-TOF) calcd for $C_{21}H_{19}N_3ONa$ $[M+Na]^+$ 352.1420, found 352.1439.

1-(Bromomethyl)-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2h**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=15∶1), a colorless oil (A: trace; B: 31% yield, 20.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57～8.56 (m, 1H), 8.11 (d, J=8.0 Hz, 1H), 8.08～8.06 (m, 1H), 7.85 (ddd, J=2.0, 7.2, 9.2 Hz, 1H), 7.24～7.13 (m, 4H), 4.11 (t, J=6.4 Hz, 2H), 3.48 (t, J=6.4 Hz, 2H), 2.41～2.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.9, 150.2, 148.1, 138.2, 129.5, 127.7, 122.8, 122.0, 121.2, 117.7, 113.2, 107.5, 39.6, 31.4, 30.4. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}BrN_3OH$ $[M+H]^+$ 332.0393, found 332.0396.

1-Benzhydryl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo-[*d*]imidazol-2-one (**2i**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=10∶1), a white solid (A: trace; B: 39% yield, 29.4 mg); m.p. 102.1～102.6 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (ddd, J=0.8, 2.0, 5.2 Hz, 1H), 8.15 (dt, J=8.4, 0.8 Hz, 1H), 8.06 (dd, J=8.0, 0.8 Hz, 1H), 7.86 (ddd, J=2.0, 7.2, 8.0 Hz, 1H), 7.38～7.30 (m, 10H), 7.24 (ddd, J=0.8, 4.8, 7.2 Hz, 1H), 7.11 (s, 1H), 7.07 (td, J=8.0, 1.2 Hz, 1H), 6.91 (td, J=8.0, 1.2 Hz, 1H), 6.56 (dd, J=8.0, 0.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.2, 150.3, 148.0, 138.2, 137.9, 128.9, 128.6, 128.6, 127.9, 127.9, 122.4, 121.7, 121.3, 118.1, 112.9, 110.7, 59.8. HRMS (MALDI-TOF) calcd for $C_{25}H_{19}N_3OH$ $[M+H]^+$ 378.1601, found 378.1609.

1-(6-Fluoropyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2j**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 39% yield, 21.1 mg; B: 58% yield, 31.4 mg); m.p. 89.2～90.1 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.26～8.24 (m, 1H), 8.20～8.18 (m, 1H), 7.93 (q, J=8.0 Hz, 1H), 7.23～7.14 (m, 2H), 7.05～7.03 (m, 1H), 6.84～6.81 (m, 1H), 3.93～3.89 (m, 2H), 1.88～1.79 (m, 2H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9, 160.6, 152.8, 148.9, 148.7, 142.9, 142.8, 129.6, 127.1, 123.0, 121.9, 113.9, 113.5, 113.4, 107.7, 105.6, 105.3, 42.8, 21.5, 11.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −67.857. HRMS (ESI-TOF) calcd for $C_{15}H_{14}FN_3OH$ $[M+H]^+$ 272.1194, found 272.1197.

1-(5-Fluoropyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2k**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a white solid (A: 67% yield, 36.3 mg; B: 74% yield, 40.1 mg); m.p. 82.0～84.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40 (d, J=1.6 Hz, 1H), 8.18 (dd, J=9.2, 4.0 Hz, 1H), 8.00 (dd, J=7.6, 0.8 Hz, 1H), 7.61～7.56 (m, 1H), 7.21～7.11 (m, 2H), 7.05 (dd, J=7.6, 1.2 Hz, 1H), 3.93～3.90 (m, 2H), 1.88～1.79 (m, 2H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.5, 155.9, 152.9, 146.4, 135.7, 135.4, 129.6, 127.6, 125.4, 125.2, 122.7, 121.7, 118.8, 118.7, 112.7, 107.7, 42.8, 21.5, 11.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −130.45. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}FN_3OH$ $[M+H]^+$ 272.1194, found 272.1198.

1-(5-Bromopyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2l**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a light yellow solid (A: 73% yield, 48.3 mg; B: 80% yield, 52.9 mg); m.p. 93.2～94.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.59 (dd, J=2.4, 0.4 Hz, 1H), 8.17 (dd, J=8.8, 0.4 Hz, 1H), 8.11～8.09 (m, 1H), 7.94 (dd, J=8.8, 2.8 Hz, 1H), 7.21～7.12 (m, 2H), 7.06～7.04 (m, 1H), 3.92～3.89 (m, 2H), 1.88～1.79 (m, 2H), 1.01 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 151.8, 148.2, 147.7, 139.6, 128.6, 126.3, 121.8, 120.8, 117.5, 115.5, 112.4, 106.7, 41.7, 20.5, 10.4. HRMS (ESI-TOF) calcd for $C_{15}H_{14}BrN_3OH$ $[M+H]^+$ 332.0393, found 332.0399.

1-(4-Bromopyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2m**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a white solid (A: 70% yield, 46.3 mg; B: 72% yield, 47.6 mg); m.p. 68.0～70.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44～8.43 (m, 1H), 7.30～8.28 (m, 1H), 8.10～8.09 (m, 1H), 7.30～7.29 (m, 1H), 7.21～6.98 (m, 3H), 3.86～3.84 (m, 2H), 1.77～1.76 (m, 2H), 0.96～0.93 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.8, 151.4, 148.3, 134.1, 129.7, 127., 124.20, 123.0, 121.8, 120.2, 113.7, 107.7, 42.8, 21.5, 11.4. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}BrN_3OH$ $[M+H]^+$ 332.0393, found 332.0398.

1-(6-Bromopyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2n**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a light yellow solid (A: 39% yield, 25.8 mg; B: 57% yield, 37.7 mg); m.p. 87.3～88.5 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28 (dd, J=8.4, 0.8 Hz, 1H), 8.22～8.19 (m, 1H), 7.68 (t, J=7.6 Hz, 1H), 7.37 (dd, J=7.6, 0.4 Hz, 1H), 7.23～7.15 (m, 2H), 7.06～7.02 (m, 1H), 3.92～3.88 (m, 2H), 1.87～1.78 (m, 2H), 1.00 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7, 150.3, 140.3, 139.1, 129.7, 127.1, 124.6, 123.1, 122.0, 115.1, 113.8, 107.7, 42.7, 21.5, 11.4. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}BrN_3ONa$ $[M+Na]^+$ 354.0212, found 354.0220.

1-(5-Iodopyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo-[*d*]imidazol-2-one (**2o**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 35% yield, 26.5 mg; B: 75% yield, 56.8 mg); m.p. 87.3～88.5 ℃. ^{1}H

NMR (400 MHz, $CDCl_3$) δ: 8.73 (dd, J=2.0, 1.2 Hz, 1H), 8.12～8.06 (m, 3H), 7.20～7.11 (m, 2H), 7.04 (dd, J=7.6, 1.2 Hz, 1H), 3.92～3.88 (m, 2H), 1.87～1.78 (m, 2H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.8, 152.8, 149.8, 146.1, 129.7, 127.2, 122.9, 121.8, 118.9, 113.6, 107.7, 88.1, 42.8, 21.5, 11.4. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}IN_3OH$ $[M+H]^+$ 380.0254, found 380.0258.

1-(4-Methylpyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2p**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a pale yellow oil (A: 59% yield, 31.5 mg; B: 66% yield, 35.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, J=4.8 Hz, 1H), 8.02 (dd, J=7.6, 0.8 Hz, 1H), 7.94 (s, 1H), 7.18～7.09 (m, 2H), 7.05～7.02 (m, 2H), 3.93～3.89 (m, 2H), 2.44 (s, 3H), 1.88～1.79 (m, 2H), 1.01 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.1, 150.4, 149.6, 147.7, 129.6, 127.9, 122.4, 122.4, 121.7, 118.4, 112.9, 107.6, 42.7, 21.6, 21.3, 11.4. HRMS (MALDI-TOF) calcd for $C_{16}H_{17}N_3OH$ $[M+H]^+$ 268.1444, found 268.1449.

1-(5-Methylpyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2q**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a light red solid (A: 60% yield, 32.0 mg; B: 57% yield, 30.4 mg); m.p. 75.4～76.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.31～8.30 (m, 1H), 7.91～7.88 (m, 2H), 7.60～7.57 (m, 1H), 7.11～7.02 (m, 2H), 6.98～6.96 (m, 1H), 3.86～3.82 (m, 2H), 2.31 (s, 3H), 1.81～1.72 (m, 2H), 0.94 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.1, 148.1, 148.0, 138.8, 130., 129.65, 127.9, 122.4, 121.6, 117.4, 112.6, 107.6, 77.4, 77.0, 76.7, 42.7, 21.6, 18.0, 11.4. HRMS (MALDI-TOF) calcd for $C_{16}H_{17}N_3OH$ $[M+H]^+$ 268.1444, found 268.1441.

1-(6-Methylpyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2r**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a pale yellow oil (A: 59% yield, 310.5 mg; B: 71% yield, 38.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08～8.06 (m, 1H), 7.92 (d, J=8.0 Hz, 1H), 7.73 (t, J=7.6 Hz, 1H), 7.18～7.10 (m, 2H), 7.08～7.02 (m, 2H), 3.93～3.89 (m, 2H), 2.61 (s, 3H), 1.87～1.78 (m, 2H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.2, 153.0, 149.7, 138.5, 129.7, 127.9, 122.5, 121.6, 120.6, 114.6, 113.0, 107.6, 42.7, 24.2, 21.6, 11.4. HRMS (MALDI-TOF) calcd for $C_{16}H_{17}N_3OH$ $[M+H]^+$ 268.1444, found 268.1450.

1-(6-Methoxypyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2s**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a colorless oil (A: 53% yield, 30.0 mg; B: 21% yield, 11.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (dd, J=7.6, 0.8 Hz, 1H), 7.74～7.72 (m, 2H), 7.20～7.10 (m, 2H), 7.05 (dd, J=8.0, 1.2 Hz, 1H), 6.70～6.65 (m, 1H), 4.00 (s, 3H), 3.93～3.89 (m, 2H), 1.88～1.79 (m, 2H), 1.02 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.0, 152.9, 147.9, 140.5, 129.6, 127.8, 122.4, 121.4, 113.1, 109.4, 107.6, 107.5, 53.9, 42.8, 21.6, 11.4. HRMS (MALDI-TOF) calcd for $C_{16}H_{17}N_3O_2H$ $[M+H]^+$ 284.1394, found 284.1399.

6-(2-*Oxo*-3-propyl-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)picolinonitrile (**2t**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a white solid (A: 32% yield, 17.7 mg; B: 41% yield, 22.7 mg); m.p. 117.8～118.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.68 (dd, J=8.8, 0.8 Hz, 1H), 8.31～8.29 (m, 1H), 7.96 (dd, J=8.8, 7.6 Hz, 1H), 7.59 (dd, J=7.2, 0.8 Hz, 1H), 7.25～7.17 (m, 2H), 7.07～7.05 (m, 1H), 3.93～3.89 (m, 2H), 1.88～1.79 (m, 2H), 1.02 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.8, 151.9, 139.1, 131.3, 129.7, 126.8, 125.2, 123.6, 122.2, 120.2, 116.9, 114.5, 107.8, 42.8, 21.4, 11.4. HRMS (MALDI-TOF) calcd for $C_{16}H_{14}N_4ONa$ $[M+Na]^+$ 301.1060, found 301.1076.

1-(6-Acetylpyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2u**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 85% yield, 50.1 mg; B: 60% yield, 35.4 mg); m.p. 87.4～87.8 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.46 (dd, J=8.0, 1.2 Hz, 1H), 8.21～8.19 (m, 1H), 8.02～7.95 (m, 2H), 7.25～7.08 (m, 2H), 7.10～7.08 (m, 1H), 3.95～3.92 (m, 2H), 2.78 (s, 3H), 1.90～1.81 (m, 2H), 1.03 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 199.3, 153.0, 151.7, 149.8, 139.1, 129.8, 127.4, 122.9, 121.8, 120.9, 118.7, 113.2, 107.9, 42.8, 26.3, 21.5, 11.4. HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_3O_2H$ $[M+H]^+$ 296.1394, found 296.1397.

1-(6-(1H-pyrazol-1-yl)pyridin-2-yl)-3-propyl-1,3-dihydro-2H-benzo[*d*]imidazol-2-one (**2v**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=10∶1), a white solid (A: 39% yield, 24.8 mg; B: 51% yield, 32.5 mg); m.p. 145.6～1468.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.53 (d, J=2.4 Hz, 1H), 8.08 (t, J=7.2 Hz, 2H), 7.98 (t, J=8.0 Hz, 1H), 7.89 (d, J=8.0 Hz, 1H), 7.78 (d, J=1.6 Hz, 1H), 7.24-7.15 (m, 2H), 7.10～7.08 (m, 1H), 6.51 (t, J=2.0 Hz, 1H), 3.95～3.92 (m, 2H), 1.90～1.81 (m, 2H), 1.03 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.9, 150.0, 148.7, 142.3, 140.9, 129.8, 127.5, 127.1, 122.9, 121.7, 114.6, 112.9, 109.0, 108.1, 107.9, 42.8, 21.5, 11.4. HRMS (MALDI-TOF) calcd for $C_{18}H_{17}N_5ONa$ $[M+Na]^+$ 342.1325, found 342.1342.

1-(6-(1*H*-indazol-1-yl)pyridin-2-yl)-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2w**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=15∶1), a white solid (A: 41% yield, 30.2 mg; B: 80% yield, 59.0 mg); m.p. 90.3～91.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.69 (dd, J=8.4, 0.8 Hz, 1H), 8.14 (d, J=0.8 Hz, 1H), 8.03～7.99 (m, 3H), 7.93～7.88 (m, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.87 (s, 1H), 7.43～7.39 (m, 1H), 7.29～7.19 (m, 2H), 7.12～7.07 (m, 2H), 3.98～3.95 (m, 2H), 1.94～1.85 (m,

2H), 1.06 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.9, 152.7, 147.9, 140.5, 138.7, 137.2, 129.8, 128.1, 127., 126.14, 122.7, 122.7, 121.6, 120.8, 115.4, 113.8, 113.1, 110.6, 107.8, 42.9, 21.6, 11.5. HRMS (MALDI-TOF) calcd for $C_{22}H_{19}N_5ONa$ $[M+Na]^+$ 392.1482, found 392.1499.

1-Propyl-3-(quinolin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]-imidazol-2-one (**2x**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 81% yield, 49.0 mg; B: 85% yield, 51.5 mg); m.p. 82.0～84.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.45～8.39 (m, 2H), 8.29 (d, J=8.8 Hz, 1H), 7.09 (d, J=8.8 Hz, 1H), 7.86 (dd, J=8.0, 1.2 Hz, 1H), 7.76～7.72 (m, 1H), 7.56～7.52 (m, 1H), 7.24～7.12 (m, 2H), 7.08～7.06 (m, 1H), 3.96～3.93 (m, 2H), 1.91～1.82 (m, 2H), 1.03 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.3, 149.9, 146.6, 138.2, 129.9, 129.9, 128.4, 127.8, 127.5, 126.5, 126.1, 122.9, 121.8, 116.4, 113.9, 107.7, 42.8, 21.5, 11.4. HRMS (ESI-TOF) calcd for $C_{19}H_{17}N_3OH$ $[M+H]^+$ 304.1444, found 304.1447.

5,6-Dimethyl-1-propyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2y**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 37% yield, 20.8 mg; B: 62% yield, 34.8 mg); m.p. 132.6～132.8 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (ddd, J=0.8, 2.0, 4.8 Hz, 1H), 8.14 (dt, J=8.4, 0.8 Hz, 1H), 7.87 (s, 1H), 7.83 (ddd, J=2.0, 7.6, 9.6 Hz, 1H), 7.19 (ddd, J=0.8, 4.8, 7.2 Hz, 1H), 6.82 (s, 1H), 3.89～3.85 (m, 2H), 2.32 (d, J=3.6 Hz, 6H), 1.87～1.78 (m, 2H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.1, 150.7, 147.9, 138.1, 130.8, 129.8, 127.7, 125.7, 120.7, 117.5, 114.1, 108.7, 42.7, 21.6, 20.1, 20.0, 11.4. HRMS (ESI-TOF) calcd for $C_{17}H_{19}N_3OH$ $[M+H]^+$ 282.1601, found 282.1595.

Methyl 2-*oxo*-1-propyl-3-(pyridin-2-yl)-2,3-dihydro-1*H*-benzo[*d*]imidazole-5-carboxylate (**2z**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 71% yield, 44.1 mg; B: 69% yield, 42.9 mg); m.p. 132.6～132.8 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.58 (ddd, J=0.8, 2.0, 4.8 Hz, 1H), 8.14～8.09 (m, 2H), 7.90～7.86 (m, 2H), 7.73 (d, J=1.2 Hz, 1H), 7.28～7.25 (m, 1H), 3.97～3.94 (m, 5H), 1.91～1.82 (m, 2H), 1.03 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.1, 153.1, 149.9, 148.1, 138.4, 131.4, 129.6, 124.5, 124.1, 121.6, 117.7, 112.5, 108.8, 52.2, 42.9, 21.5, 11.3. HRMS (MALDI-TOF) calcd for $C_{17}H_{17}N_3O_3Na$ $[M+Na]^+$ 334.1162, found 334.1178.

5-Methoxy-1-propyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2aa**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a white solid (A: 32% yield, 18.1 mg; B: 56% yield, 31.7 mg); m.p. 132.6～132.8 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.55 (ddd, J=0.8, 1.6, 4.8 Hz, 1H), 8.15 (dt, J=8.4, 0.8 Hz, 1H), 7.84 (ddd, J=2.0, 7.6, 9.6 Hz, 1H), 7.76 (d, J=2.8 Hz, 1H), 7.21 (ddd, J=1.2, 4.8, 7.6 Hz, 1H), 6.92 (d, J=8.4 Hz, 1H), 6.75 (dd, J=8.8, 2.8 Hz, 1H), 3.90～3.86 (m, 2H), 3.83 (s, 3H), 1.86～1.77 (m, 2H), 1.00 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.5, 153.3, 150.5, 147.9, 138.2, 128.4, 123.8, 121.0, 117.7, 108.4, 107.8, 100.3, 56.1, 42.7, 21.6, 11.4. HRMS (ESI-TOF) calcd for $C_{16}H_{17}N_3O_2H$ $[M+H]^+$ 284.1394, found 284.1395.

5-Bromo-1-propyl-3-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2ab**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 35% yield, 23.1 mg; B: 74% yield, 48.9 mg); m.p. 66.4～66.8 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.54 (ddd, J=0.8, 1.6, 4.8 Hz, 1H), 8.17～8.15 (m, 1H), 8.01 (d, J=8.0, 1.2 Hz, 1H), 7.85 (ddd, J=2.0, 7.2, 9.6 Hz, 1H), 7.25～7.02 (m, 2H), 7.16 (d, J=1.6 Hz, 1H), 3.89～3.85 (m, 2H), 1.87～1.77 (m, 2H), 1.01 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7, 150.2, 147.9, 138.3, 130.9, 126.7, 124.4, 121.2, 117.4, 115.3, 114.7, 110.7, 42.9, 21.4, 11.3. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}BrN_3OH$ $[M+H]^+$ 332.0393, found 332.0398.

5-Bromo-3-propyl-1-(pyridin-2-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2ac**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=20∶1), a white solid (A: 47% yield, 31.1 mg; B: 81% yield, 53.6 mg); m.p. 101.7～101.9 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (ddd, J=0.8, 2.0, 4.8 Hz, 1H), 8.31 (d, J=2.0 Hz, 1H), 8.15 (dt, J=2.0, 1.2 Hz, 1H), 7.85 (ddd, J=2.0, 7.2, 9.6 Hz, 1H), 7.30 (dd, J=8.4, 2.0 Hz, 1H), 7.24 (ddd, J=0.8, 4.8, 7.2 Hz, 1H), 6.9 (d, J=8.4 Hz, 1H), 3.91～3.87 (m, 2H), 1.86～1.77 (m, 2H), 1.00 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7, 150.1, 148.1, 138.3, 128.8, 128.6, 125.4, 121.3, 117.4, 116.4, 114.3, 108.7, 42.8, 21.5, 11.4, 42.9, 21.5, 11.3. HRMS (MALDI-TOF) calcd for $C_{15}H_{14}BrN_3OH$ $[M+H]^+$ 332.0393, found 332.0390.

1-Phenyl-3-propyl-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2ad**): Following the general conditions A and B, purification by flash chromatography (petroleum/EtOAc, V∶V=15∶1), a colorless oil (A: 10% yield, 5.04 mg; B: 71% yield, 35.7 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57～7.50 (m, 4H), 7.41～7.37 (m, 1H), 7.16～7.03 (m, 4H), 3.94～3.91 (m, 2H), 1.90～1.81 (m, 2H), 1.03 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.4, 134.8, 129.7, 129.5, 127.5, 125.9, 121.8, 121.2, 108.7, 107.9, 42.9, 21.7, 11.4. HRMS (MALDI-TOF) calcd for $C_{16}H_{16}N_2OH$ $[M+H]^+$ 253.1335, found 253.1338.

6-Propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]-diazepin-5-one (**3a**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=20∶1): a white solid (69% yield, 34.9 mg), m.p. 117～118 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (dd, J=4.8, 1.6 Hz, 1H), 8.18 (dd, J=7.6, 2.0 Hz, 1H), 7.24 (dd, J=8.0, J=4.0 Hz, 1H), 7.13～7.06 (m, 2H), 7.00～6.96 (m, 2H), 6.41 (s, 1H), 4.05 (t, J=7.2 Hz, 2H), 1.66～1.61 (m, 2H), 0.91 (t, J=7.2 Hz, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ: 167.4, 160.5, 150.6, 142.2, 141.7, 133.1, 126.3, 124.6, 124.4, 121.1, 119.2, 118.4, 51.3, 21.1, 11.1.

6-Methyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]-diazepin-5-one (**3b**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=20∶1): a white solid (61% yield, 27.4 mg), m.p. 166～167 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23～8.21 (m, 2H), 7.18 (dd, *J*=7.6, 1.6 Hz, 1H), 7.15～7.07 (m, 2H), 6.99～6.95 (m, 2H), 6.87 (s, 1H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 160.3, 150.9, 142.3, 139.9, 134.5, 126.1, 124.6, 123.2, 120.8, 118.3, 38.1.

6-Isopropyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3c**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=20∶1): a white solid (45% yield, 22.7 mg), m.p. 179～180 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (d, *J*=4.0 Hz, 1H), 8.15 (d, *J*=8.0 Hz, 1H), 7.35～7.30 (m, 1H), 7.13～7.11 (m, 2H), 7.02～6.96 (m, 2H), 6.40 (s, 1H), 4.62～4.59 (m, 1H), 1.47 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.8, 160.8, 150.3, 142.8, 142.1, 132.5, 126.7, 125.3, 124.1, 121.1, 119.8, 118.4, 54.0, 21.8.

6-Butyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]-diazepin-5-one (**3d**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=15∶1): a white solid (57% yield, 30.4 mg), m.p. 116～117 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21～8.20 (m, 1H),8.17 (d, *J*=8.0 Hz, 1H), 7.24 (s, 1H), 7.14～7.08 (m, 2H), 7.00～6.95 (m, 2H), 6.60 (s, 1H), 4.07 (t, *J*=7.2 Hz, 2H), 1.64～1.56 (m, 2H), 1.38～1.32 (m, 2H), 0.84 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.4, 160.9, 150.5, 142.2, 141.9, 133.2, 126.3, 124.5, 124.3, 121.2, 119.3, 118.2, 49.4, 29.9, 19.8, 13.7.

6-Allyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]-diazepin-5-one (**3e**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=15∶1): a white solid (29% yield, 14.5 mg), m.p. 102～103 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23～8.17 (m, 2H), 7.35～7.32 (m, 1H), 7.10～7.08 (m, 2H), 6.99～6.96 (m, 2H), 6.65 (s, 1H), 6.07～5.97 (m, 1H), 5.33 (d, *J*=20.0 Hz, 1H), 5.23 (d, *J*=8.0 Hz, 1H), 4.63～4.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.1, 160.3, 150.9, 142.2, 140.6, 133.8, 133.6, 126.4, 124.5, 123.8, 120.9, 118.8, 118.5, 116.9, 53.3.

6-Benzyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]-diazepin-5-one (**3f**):[28] Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=5∶1): a white solid (43% yield, 25.8 mg), m.p. 144～145 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.25 (d, *J*=5.6 Hz, 2H), 7.35 (d, *J*=7.6 Hz, 2H), 7.31～7.26 (m, 2H), 7.23～7.19 (m, 2H), 7.16～6.96 (m, 5H), 5.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.6, 160.7, 150.9, 142.4, 141.1, 137.3, 133.4, 128.6, 127.1, 127.0, 126.5, 124.5, 124.0, 121.1, 118.8, 118.4, 53.9.

6-(3-Phenylpropyl)-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3g**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=15∶1): a white solid (63% yield, 41.4 mg), m.p. 142～143 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23～8.18 (m, 2H), 7.26～7.04 (m, 10H), 6.5 (s, 1H), 4.13～4.09 (m, 2H), 2.67～2.63 (m, 2H), 1.99～1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.6, 160.9, 150.6, 142.3, 142.1, 141.5, 133.1, 128.5, 128.4, 126.5, 125.9, 124.6, 124.5, 121.2, 119.3, 118.4, 49.1, 32.8, 29.5.

4-Methyl-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3h**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=20∶1): a white solid (78% yield, 41.6 mg), m.p. 171～172 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, *J*=4.0 Hz, 1H), 7.30～7.28 (m, 1H), 7.14～7.07 (m, 2H), 7.00～6.98 (m, 1H), 6.81 (d, *J*=4.0 Hz, 1H), 4.13 (s, 2H), 2.46 (s, 3H), 1.67 (s, 2H), 0.93 (t, *J*=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.6, 161.9, 152.8, 148.1, 143.4, 133.5, 126.2, 124.4, 124.3, 121.9, 121.1, 119.7, 51.7, 21.4, 20.6, 11.2.

3-Methyl-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3i**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=15∶1): a white solid (61% yield, 32.5 mg), m.p. 186～187 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, *J*=2.4 Hz, 2H), 7.24～7.22 (m, 1H), 7.19～7.10 (m, 2H), 6.99～6.96 (m, 1H), 6.28 (s, 1H), 4.06～4.03 (m, 2H), 2.25 (s, 3H), 1.68～1.59 (m, 2H), 0.91 (t, *J*=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 158.4, 150.9, 142.1, 133.0, 127.9, 126.3, 124.4, 124.4, 121.0, 118.7, 51.3, 21.1, 17.4, 11.1.

2-Methyl-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3j**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=15∶1): a white solid (63% yield, 33.6 mg), m.p. 119～120 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, *J*=8.0 Hz, 1H), 7.23～7.21 (m, 1H), 7.10～7.06 (m, 2H), 6.99～6.97 (m, 1H), 6.81 (d, *J*=8.0 Hz, 1H), 6.50 (s, 1H), 4.05 (m, 2H), 2.42 (s, 3H), 1.65～1.58 (m, 2H), 0.90 (t, *J*=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.6, 160.7, 159.8, 142.4, 141.7, 133.1, 126.1, 124.4, 124.4, 121.0, 118.1, 116.1, 51.1, 24.0, 21.1, 11.1.

4-Bromo-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3l**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, *V*∶*V*=20∶1): a white solid (65% yield, 43.0 mg), m.p. 164～165 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J*=5.2 Hz, 1H), 7.33 (d, *J*=8.0, 1H), 7.21～7.10 (m, 3H), 7.01～6.99 (m, 1H), 6.34 (s, 1H), 4.32～3.72 (m, 2H), 1.65 (s, 2H), 0.92 (t, *J*=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.6, 162.5, 148.7, 142.4, 136.2, 133.2, 126.4, 125.1, 124.7, 124.7, 121.3, 120.6, 51.9, 21.2, 11.2.

3-Fluoro-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3m**)[28]: Following the general condition C, purification by flash chromatography (petroleum

ether/EtOAc, V∶V=30∶1): a white solid (58% yield, 31.4 mg), m.p. 157～158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, J=4.0 Hz, 1H), 7.91 (dd, J=8.4, 2.8 Hz, 1H), 7.25～7.24 (m, 1H), 7.16～7.10 (m, 2H), 7.00～6.98 (m, 1H), 6.33 (s, 1H), 4.05 (t, J=8.0 Hz, 2H), 1.68～1.59 (m, 2H), 0.91 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1, 157.4, 156.7, 154.9, 141.7, 138.6, 138.3, 132.9, 128.4, 128.2, 126.5, 124.8, 124.6, 121.1, 120.0, 51.4, 21.0, 11.1.

3-Bromo-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3n**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=20∶1): a white solid (66% yield, 43.7 mg), m.p. 176～177 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.25 (d, J=4.0 Hz, 2H), 7.25～7.23 (m, 1H), 7.17～7.10 (m, 2H), 6.99～6.97 (m, 1H), 6.43 (s, 1H), 4.04 (t, J=8.0 Hz, 2H), 1.65～1.60 (m, 2H), 0.90 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1, 159.0, 151.3, 144.0, 141.1, 132.8, 126.5, 124.9, 124.6, 121.2, 120.4, 113.2, 51.4, 21.0, 11.1.

3-Iodo-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3o**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=20∶1): a white solid (35% yield, 26.5 mg), m.p. 149～150 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40～8.37 (m, 2H), 7.25～7.22 (m, 1H), 7.14～7.12 (m, 2H), 6.98～6.96 (m, 1H), 6.32 (s, 1H), 4.03 (t, J=8.0 Hz, 2H), 1.65～1.50 (m, 2H), 0.90 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ166.0, 159.4, 156.0, 149.3, 140.9, 132.7, 126.4, 124.8, 124.4, 121.1, 120.8, 83.2, 51.3, 20.9, 11.0.

5-*Oxo*-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]diazepine-2-carbonitrile (**3s**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=15∶1): a white solid (32% yield, 17.8 mg), m.p. 181～182 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28 (d, J=8.0 Hz, 1H), 7.34 (d, J=8.0 Hz, 1H), 7.28～7.25 (m, 1H), 7.21～7.14 (m, 2H), 7.03～7.01 (m, 1H), 6.50 (s, 1H), 4.05 (t, J=8.0 Hz, 2H), 1.66～1.61 (m, 2H), 0.90 (t, J=7.6 Hz, 3H); 13C NMR (100 MHz, $CDCl_3$): δ165.8, 160.8, 143.5, 140.1, 133.6, 132.7, 126.9, 125.5, 124.8, 122.9, 121.6, 116.6, 51.7, 21.1, 11.2.

2-Acetyl-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3t**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=15∶1): a white solid (80% yield, 47.2 mg), m.p. 138～139 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.27 (d, J=8.0 Hz, 1H), 7.65 (d, J=8.0 Hz, 1H), 7.28～7.26 (m, 1H), 7.17～7.14 (m, 2H), 7.05～7.03 (m, 1H), 6.39 (s, 1H), 4.06 (t, J=8.0 Hz, 2H), 2.65 (s, 3H), 1.68～1.62 (m, 2H), 0.91 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.9, 166.6, 159.6, 153.4, 143.1, 141.0, 132.8, 126.5, 124.9, 124.6, 122.1, 121.2, 116.2, 51.4, 25.9, 21.0, 11.1.

11-Propyl-6,11-dihydro-12*H*-benzo[2,3][1,4]diazepino-[5,6-*b*]quinolin-12-one (**3u**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=15∶1): a white solid (74% yield, 44.8 mg), m.p. 193～194 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.73 (s, 1H), 7.77 (t, J=8.0 Hz, 2H), 7.67～7.62 (m, 1H), 7.38～7.34 (m, 1H), 7.29 (d, J=8.0 Hz, 1H), 7.15～7.08 (m, 4H), 4.13 (t, J=7.6 Hz, 2H), 1.75～1.66 (m, 2H), 0.95 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.8, 158.9, 148.0, 144.2, 140.4, 133.2, 132.1, 129.0, 126.7, 126.6, 125.7, 125.0, 124.8, 124.4, 121.7, 120.8, 51.7, 21.3, 11.3.

6-Propyl-2-(1*H*-pyrazol-1-yl)-6,11-dihydro-5*H*-benzo-[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3v**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=20∶1): a white solid (31% yield, 19.7 mg; NaOAc instead of $NaHCO_3$: 39% yield, 24.8 mg), m.p. 167～168 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (d, J=4.0 Hz, 1H), 8.31 (d, J=8.0 Hz, 1H), 7.74 (s, 1H), 7.60 (d, J=8.0 Hz, 1H), 7.26～7.25 (m, 1H), 7.17～7.11 (m, 2H), 7.02～7.00 (m, 1H), 6.47 (s, 1H), 631 (s, 1H), 4.06 (t, J=8.0 Hz, 2H), 1.67～1.62 (m, 2H), 0.92 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.7, 159.0, 151.2, 144.8, 142.5, 140.6, 132.7, 127.1, 125.9, 124.5, 124.2, 120.7, 115.5, 108.0, 106.1, 50.9, 20.8, 10.8.

2-(1*H*-indazol-1-yl)-6-propyl-6,11-dihydro-5*H*-benzo-[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3w**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=30∶1): a white solid (21% yield, 15.4 mg; NaOAc instead of $NaHCO_3$: 45% yield, 33.2 mg), m.p. 220～221 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.77 (d, J=8.0 Hz, 1H), 8.32 (d, J=8.0 Hz, 1H), 8.21 (s, 1H), 7.78 (d, J=8.0 Hz, 1H), 7.70 (d, J=8.0 Hz, 1H), 7.56 (t, J=8.0 Hz, 1H), 7.34～7.28 (m, 2H), 7.16～7.12 (m, 2H), 7.08～7.05 (m, 1H), 6.36 (s, 1H), 4.08 (t, J=8.0 Hz, 2H), 1.69～1.64 (m, 2H), 0.93 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.8, 159.6, 154.9, 144.9, 141.6, 139.3, 138.4, 133.7, 128.6, 126.9, 126.7, 125.3, 125.0, 123.5, 121.6, 121.5, 115.9, 114.4, 108.2, 51.6, 21.6, 11.7.

8,9-Dimethyl-6-propyl-6,11-dihydro-5*H*-benzo[*b*]-pyrido[2,3-*e*][1,4]diazepin-5-one (**3x**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=15∶1): a white solid (46% yield, 25.8 mg), m.p. 167～168 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (d, J=8.0 Hz, 1H), 8.14 (d, J=8.0 Hz, 1H), 6.99 (s, 1H), 6.94 (dd, J=8.0 Hz, 4.8Hz, 1H), 6.76 (s, 1H), 6.29 (s, 1H), 4.03 (t, J=8.0 Hz, 2H), 2.21 (s, 3H), 2.19 (s, 3H), 1.66～1.61 (m, 2H), 0.91 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 160.8, 150.6, 142.0, 139.2, 134.9, 132.9, 130.4, 125.1, 122.0, 119.2, 118.3, 51.0, 21.1, 19.3, 19.1, 11.1.

Methyl 5-*oxo*-6-propyl-6,11-dihydro-5*H*-benzo[*b*]-pyrido[2,3-*e*][1,4]diazepine-8-carboxylate (**3y**)[28]: Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=30∶1): a white solid (71% yield, 44.1 mg), m.p. 135～136 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.25～8.24 (m, 1H), 8.21～8.17 (m, 1H), 7.94 (s, 0.65H), 7.79 (d, J=8.0 Hz, 1H),

7.70 (s, 0.43H), 7.29 (d, J=8.0 Hz, 0.41H), 7.04～6.99 (m, 1.6H), 6.63 (s, 0.63H), 6.50 (s, 0.41H), 4.10～4.05 (m, 2H), 3.91 (s, 3H), 1.68～1.63 (m, 2H), 0.91 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.0, 166.9, 166.0, 165.9, 159.9, 159.3, 151.1, 151.0, 145.9, 142.3, 142.2, 141.4, 137.2, 132.7, 127.9, 127.6, 126.5, 126.3, 125.7, 124.2, 122.4, 120.8, 119.0, 118.9, 118.8, 118.7, 52.3, 52.3, 51.6, 51.4, 21.0, 11.1.

8 and 9-Methoxy-6-propyl-6,11-dihydro-5*H*-benzo[*b*]-pyrido[2,3-*e*][1,4]diazepin-5-one (**3z**): Following the general condition C, purification by flash chromatography (petroleum ether∶EtOAc=5∶1, V∶V): a white solid (61% yield, 34.5 mg), m.p. 140～143 ℃; mixture of two isomers (2∶1, V∶V); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.22～8.15 (m, 2H), 7.13 (d, J=8.8 Hz, 0.7H), 6.99～6.91 (m, 1.3H), 6.78 (d, J=2.8 Hz, 0.3H), 6.68～6.66 (m, 0.7H), 6.65～6.64 (m, 1H), 6.55 (s, 0.3H), 6.52 (d, J=2.8 Hz, 0.7H), 4.06～3.99 (m, 2H), 3.77 (s, 1H), 3.75 (s, 2H), 1.69～1.58 (m, 2H), 0.94～0.86 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.4, 166.3, 159.9, 159.2, 156.7, 155.8, 149.7, 149.5, 141.9, 141.1, 141.0, 133.9, 133.0, 124.9, 124.3, 120.6, 118.4, 118.0, 117.6, 117.3, 110.3, 109.4, 109.2, 104.8, 54.7, 54.5, 50.1, 50.1, 20.1, 19.9, 13.1, 10.1. HRMS (ESI-TOF) calcd for $C_{16}H_{17}N_3O_2$ $[M+H]^+$ 284.1399, found 284.1398.

8-Bromo-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3aa**): Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=15∶1): a white solid (74% yield, 49.0 mg), m.p. 201～202 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (d, J=4.0 Hz, 1H), 8.17 (d, J=8.0 Hz, 1H), 7.36 (s, 1H), 7.20 (dd, J=8.0, 4.0 Hz, 1H), 7.00 (dd, J=7.6, 4.8 Hz, 1H), 6.87 (d, J=8.0 Hz, 1H), 6.40 (s, 1H), 4.02 (t, J=7.2 Hz, 2H), 1.68～1.61 (m, 2H), 0.92 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.0, 159.8, 151.0, 142.2, 140.7, 134.4, 129.1, 127.3, 122.3, 118.8, 116.8, 51.4, 21.0, 11.1; HRMS (ESI-TOF) calcd for $C_{15}H_{14}BrN_3O$ $[M+H]^+$ 332.0398, found 332.0403.

9-Bromo-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido-[2,3-*e*][1,4]diazepin-5-one (**3ab**): Following the general condition C, purification by flash chromatography (petroleum ether/EtOAc, V∶V=20∶1): a white solid (76% yield, 50.3 mg), m.p. 154～155 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.22 (dd, J=4.8, 1.6 Hz, 1H), 8.18 (dd, J=8.0, 2.0 Hz, 1H), 7.23 (dd, J=8.8, 2.4 Hz, 1H), 7.17 (d, J=2.4 Hz, 1H), 7.11 (d, J=8.4 Hz, 1H), 7.01 (dd, J=8.0, 4.8 Hz, 1H), 6.41 (s, 1H), 4.02 (t, J=7.2 Hz, 2H), 1.65～1.58 (m, 2H), 0.90 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.0, 159.7, 151.0, 142.9, 142.1, 132.2, 127.6, 125.8, 123.9, 119.0, 118.9, 51.3, 21.0, 11.1; HRMS (ESI-TOF) calcd for $C_{15}H_{14}BrN_3O$ $[M+H]^+$ 332.0398, found 332.0398.

11-Isopropyl-6-propyl-6,11-dihydro-5*H*-benzo[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3ad**): Purification by flash chromatography (petroleum/EtOAc, V∶V=30∶1), a white solid (78% yield, 46.0 mg). m.p. 133.0～133.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.32 (dd, J=4.8, 2.0 Hz, 1H), 7.97 (dd, J=7.6, 2.0 Hz, 1H), 7.27～7.24 (m, 2H), 7.17～7.09 (m, 2H), 6.98 (dd, J=7.6, 4.8 Hz, 1H), 4.66 (dt, J=13.6, 7.6 Hz, 1H), 4.59～4.50 (m, 1H), 3.62～3.59 (m, 1H), 1.71～1.54 (m, 3H), 1.34 (d, J=6.0 Hz, 3H), 1.26 (d, J=6.0 Hz, 3H), 0.96 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.8, 162.0, 149.9, 145.8, 139.9, 137.1, 125.8, 124.8, 124.6, 123.9, 123.9, 119.1, 49.8, 46.5, 22.5, 22.1, 21.2, 11.4. HRMS (MALDI-TOF) calcd for $C_{18}H_{21}N_3OH$ $[M+H]^+$ 296.1757, found 296.1751.

4-(4-Methoxyphenyl)-6-propyl-6,11-dihydro-5*H*-benzo-[*b*]pyrido[2,3-*e*][1,4]diazepin-5-one (**3ae**): Purification by flash chromatography (petroleum/EtOAc, V∶V=5∶1), a white solid (85% yield, 61.0 mg). m.p. 112.0～113.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J=5.2 Hz, 1H), 7.42 (dd, J=8.0, 1.6 Hz, 1H), 7.34～7.30 (m, 2H), 7.21～7.05 (m, 2H), 7.06 (dd, J=8.0, 1.6 Hz, 1H), 6.98 (d, J=5.2 Hz, 1H), 6.96～6.92 (m, 2H), 6.55 (s, 1H), 4.13 (s, 1H), 3.84 (s, 3H), 3.70 (s, 1H), 1.63 (s, 2H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 162.4, 160.2, 154.0, 148.8, 143.2, 134.0, 131.5, 129.4, 126.2, 124.7, 124.3, 121.3, 119.9, 118.1, 114.2, 55.3, 52.1, 21.2, 11.2. HRMS (ESI-TOF) calcd for $C_{22}H_{21}N_3O_2$ $[M+H]^+$ 360.1707, found 360.1706.

2,2,6,6-Tetramethylpiperidin-1-yl propyl(2-(pyridin-2-ylamino)phenyl)carbamate (**3AA**): Purification by flash chromatography (petroleum/EtOAc, V∶V=5∶1), a colorless oil (15% yield, 12.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.22～8.12 (m, 2H), 7.49 (t, J=6.8 Hz, 1H), 7.31～7.27 (m, 1H), 7.17 (d, J=7.6 Hz, 1H), 7.01 (t, J=7.2 Hz, 1H), 6.76～6.75 (m, 2H), 6.65 (s, 1H), 3.65～3.51 (m, 2H), 1.80 (s, 1H), 1.64～1.25 (m, 8H), 1.09 (s, 6H), 0.92～0.72 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.7, 148.2, 137.8, 137.6, 128.3, 115.5, 109.7, 60.4, 60.1, 51.7, 38.9, 32.1, 31.7, 21.6, 20.4, 16.9, 11.2. HRMS (ESI-TOF) calcd for $C_{24}H_{34}N_4O_2$ $[M+H]^+$ 411.2755, found 411.2746.

Supporting Information Experimental procedures for synthesis of *N*-propyl-*N*-(2-(pyridin-2-ylamino)phenyl)-formamide **1**, **3ad**, **3ae** and scale-up synthesis of **2a** and **3a**. The ^{1}H NMR and ^{13}C NMR spectra of products. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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