JOC The Journal of Organic Chemistry

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Construction of 1,4-Benzodiazepine Skeleton from 2-(Arylamino)benzamides through PhI(OAc)$_2$-Mediated Oxidative C−N Bond Formation

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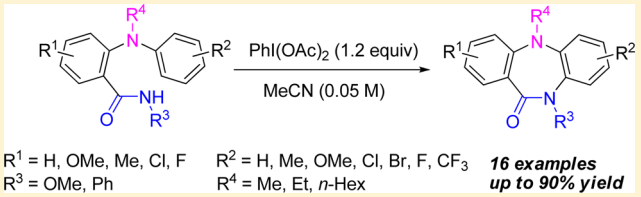
Supporting Information

ABSTRACT: New compounds involving the biologically important 1,4-benzodiazepine skeleton were conveniently constructed from 2-(arylamino)benzamides through PhI(OAc)$_2$-mediated oxidative C−N bond formation. The attractive features of this new synthetic strategy include mild reaction conditions, the heavy-metal-free characteristic of the oxidative coupling process, and the flexibility to tolerate a broad scope of substrates.



INTRODUCTION

To date, the development of novel methods for the synthesis of heterocycles has been and remains a hot topic in medicinal chemistry. The 1,4-benzodiazepine skeleton, one of the key heterocyclic structures, is widely adopted in many biologically important pharmaceutical agents. For example, both dibenzepin (**A**), a widely prescribed antidepressant drug,[1] and histone deacetylase (HDAC) inhibitors (**B**) possess the 1,4-benzodiazepine motif in their structures.[2] In addition, the 1,4-benzodiazepine-containing compounds have been used as building blocks for the synthesis of other agents with desirable biological activities. For example, compound **C**, a derivative of 1,4-benzodiazepine, was found to possess anti-inflammatory properties.[3] Clozapine (**D**), which comprises a 1,4-benzodiazepine skeleton and a methylpiperazine system, is an atypical antipsychotic medication used in the treatment of schizophrenia.[4] Furthermore, analogues of 1,4-benzodiazepine have also played important roles in the discovery of new drugs. For example, gastrozepin (**E**), with the replacement of one phenyl ring with a pyridinyl ring, is regarded as the first M1-selective muscarinic receptor antagonist that has been introduced into ulcer therapy (Figure 1).[5]

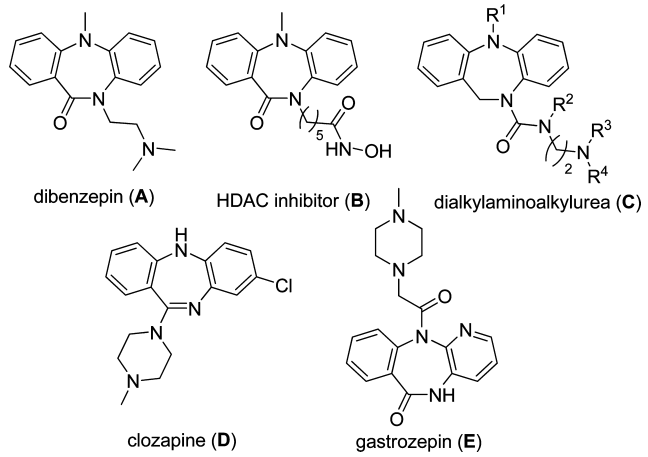


Figure 1. Representative biologically important 1,4-benzodiazepines, their derivatives, and analogues.

Because of the significant roles played by 1,4-benzodiazepine derivatives and their analogues in medicinal chemistry, many synthetic strategies have been developed for the construction of this class of privileged medicinal scaffolds. A literature survey indicates that existing strategies can be generally classified into the following six categories (Figure 2). In 1985, Giani and coworkers[6] reported a one-step approach involving the reaction between 2-chlorobenzoic acid and *o*-phenylendiamine by using powdered copper as catalyst and chlorobenzene as solvent (Figure 2, path a). Starting from 2-iodoaniline and substituted 1-fluoro-2-nitrobenzene, Lu and Alper[7] developed a palladium-mediated intramolecular carbonylation reaction to assemble the 1,4-benzodiazepine skeleton (Figure 2, path b). A cascade reduction/lactamization approach has also been applied by Bunce and Schammerhorn[8] to synthesize 1,4-benzodiazepine under dissolving-metal conditions using iron and acetic acid (Figure 2, path c). Mediated by $POCl_3$, substituted ethyl 2-(phenylamino)phenyl carbamate underwent intramolecular lactamization through the electrophilic aromatic substitution to give the corresponding 1,4-benzodiazepine compound (Figure 2, path d).[9] In 2011, Tsvelikhovsky and Buchwald[10] achieved a one-step synthesis of dibenzodiazepines and their

Received: October 29, 2013
Published: January 15, 2014

   dx.doi.org/10.1021/jo402413g | J. Org. Chem. 2014, 79, 955−962

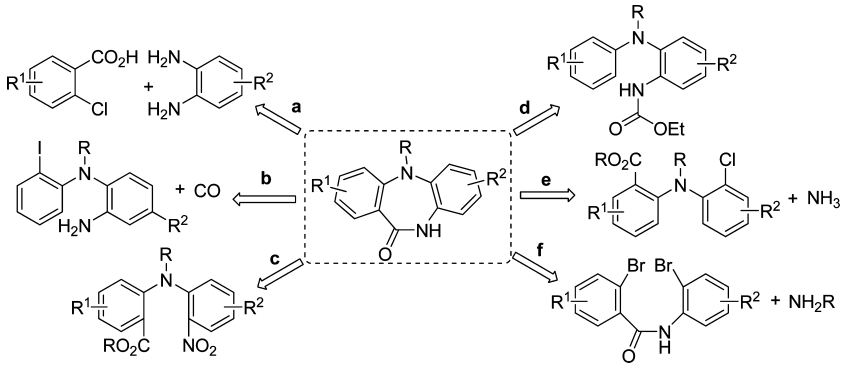
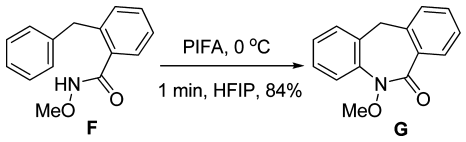


Figure 2. Common synthetic strategies for the construction of the 1,4-benzodiazepine skeleton.

structural analogues from a palladium-catalyzed reaction between alkyl 2-(2-chlorophenylamino)benzoate and ammonia (Figure 2, path e). In the same year, Ma and et al.[11] reported an efficient synthesis of 1,4-benzodiazepines through double amination of *ortho*-substituted aryl bromides (Figure 2, path f). Although existing methods have their own merits in the preparation of the corresponding 1,4-benzodiazepine compounds, the majority of them require, unfortunately, the involvement of a transition metal. Thus, developing alternative, heavy-metal-free strategies are still in demand. In this paper, we report the assemblage of a 1,4-benzodiazepine framework from the readily available substituted *N*-methoxy-2-(methylphenylamino)benzamide through an intramolecular oxidative C−N bond formation in the final step.

It has been well-known that reactions of hypervalent iodine reagents with *N*-alkoxyamide compounds afford a stabilized nitrenium ion as intermediate, which undergo intramolecular aromatic electrophilic cyclization to give various *N*-containing heterocycles.[12] For example, in 2003, Kikugawa reported that 2-benzyl-*N*-methoxybenzamide **F** underwent PIFA-mediated oxidative C−N bond formation to give 5-methoxy-5*H*-dibenzo[*b*,*e*]azepin-6(11*H*)-one **G** in good yield (Scheme 1).[12d] In this regard, we envisaged that the same strategy should be applicable to the construction of the seven-membered lactam ring of 1,4-benodiazepine, **2**, an analogous substrate of 5-methoxy-5*H*-dibenzo[*b*,*e*]azepin-6(11*H*)-one **G** differing by a functional "linker" between two phenyl rings. Figure 3 describes the retrosynthesis of **2**, where **2** is formed through the ring-closure reaction of **1**, which can be prepared by the amidation of carboxylic acid **3**.[13] Compound **3** can in turn be easily tracked back to ester **4** and 2-(phenylamino)benzoic acid **5**.[14,15] The synthesis of **5** can be readily realized through the CuI-catalyzed cross-coupling reaction between various anilines **6** and 2-bromobenzoic acids **7**.[16]

Scheme 1. Previous PIFA-Mediated Oxidative C−N Bond Formation



RESULTS AND DISCUSSION

After the simplest 2-(arylamino)benzamide **1a** was prepared by a series of reactions proposed in the retrosynthetic analysis, we proceeded to test the feasibility of the very last step, namely, the ring-closure step to convert **1a** to 1,4-benzodiazepine **2a** using the proposed protocol of oxidative C−N bond formation. Initially, the reaction was carried out at room temperature by using 1.2 equivalents of PIFA as oxidant and DCM as solvent. To our delight, the reaction did undergo the expected C−N bond formation and gave the desired cyclized product, albeit in a low yield of 27% (Table 1, entry 1). Other hypervalent iodine reagents including PhIO, IBX, and DMP were also tested, but none of them was effective for the reaction (Table 1, entries 2−4). Further optimization study found that the use of PIDA, on the other hand, significantly improved the yield to 56% (Table 1, entry 5). Solvent-screening studies revealed that acetonitrile offered the best result, affording **2a** in 69% yield (Table 1, entries 5−10). Further investigations led us find that decreasing the concentration of the substrate in MeCN to 0.05 M

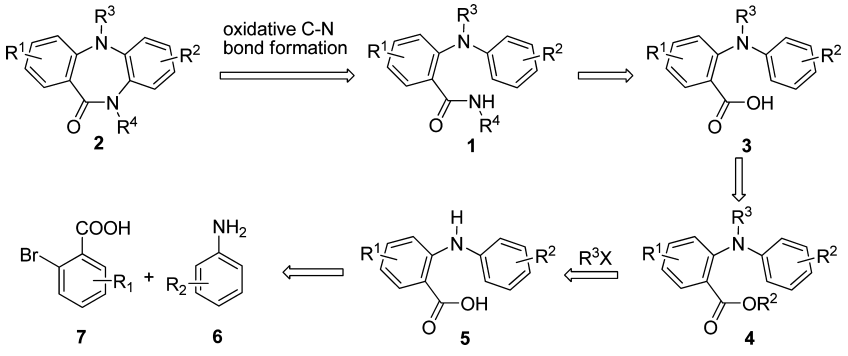
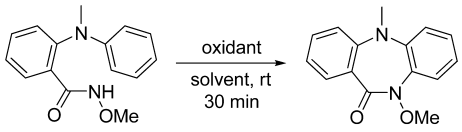


Figure 3. Retrosynthetic analysis of 1,4-benzodiazepine.

dx.doi.org/10.1021/jo402413g | *J. Org. Chem.* 2014, 79, 955−962

Table 1. Optimization of Reaction Conditions[a]



1a 2a

entry	oxidant	additive	solvent	conc (M)	yield[b] (%)
1	PIFA	none	DCM	0.1	27
2	PhIO	none	DCM	0.1	trace
3	IBX	none	DCM	0.1	ND
4	DMP	none	DCM	0.1	ND
5	PIDA	none	DCM	0.1	56
6	PIDA	none	toluene	0.1	33
7	PIDA	none	acetone	0.1	27
8	PIDA	none	THF	0.1	trace
9	PIDA	none	TFEA	0.1	26
10	PIDA	none	MeCN	0.1	69
11	PIDA	none	MeCN	0.2	51
12	PIDA	none	MeCN	0.05	82
13	PIDA	$BF_3 \cdot Et_2O$[c]	MeCN	0.05	trace
14	PIDA	TFA[c]	MeCN	0.05	41

[a]Reaction conditions: **1a** and oxidant in solvent, at rt in 30 min. [b]Isolated yields. [c]0.1 equiv of additive was added. Under the optimal conditions (Table 1, entry 12), the generality of the method was investigated.

maximized the yield to a satisfactory 82% yield (Table 1, entry 12).

Additional attempts to further improve the yield such as by introducing a catalytic amount of additive of $BF_3 \cdot Et_2O$ or TFA in the temperature range of −20−0 °C gave less satisfactory results (Table 1, entries 13−15).[17]

Under the optimal conditions, a variety of 2-(arylamino)-benzamides prepared via the retrosynthesis layout described above were examined to probe the generality as well as limitation of the ring-closure method. The results are summarized in Table 2. It was found that the presence of a methoxy group at the *para* position of phenyl ring B slightly improved the yield of the desired cyclized product **2b** to an excellent 90% yield (Table 2, entry 2). With the methoxy group substituted at the *meta* position in ring B as in **1c,d**, the reaction afforded only one regioisomer of **2c,d**, respectively, in slightly lowered yields (Table 1, entries 3 and 4). For substrates bearing two methoxy groups on ring B, the reaction afforded the cyclized product **2e,f** as the single regioisomer, in even lower yields, due to the formation of more unidentified byproducts (Table 2, entries 5 and 6). Other than fluoro as a substituent on ring A, the method also worked well for substrates with R^1 being methyl, chloro, and bromo, seemingly insensitive to the electronic nature of the subsituents in ring B (Table 2, entries 7−11). However, in cases where the substrates bear a bromo or CF_3 substituent at the *meta* position of ring B, the reaction produced a separable mixture of two regioisomers, with the more favored one resulting from the *para*-attack (Table 2, entries 12 and 13). The method was also applicable to the substrates in which the methyl group on the N-atom was changed into an ethyl or long-chained *n*-hexyl group (Table 2, entries 14 and 15). However, when the methoxy group was replaced by a phenyl group, the reaction afforded the desired cyclized product **1p** in a much lower yield (Table 2, entry 16). This result indicates that under the described conditions *N*-phenyl-2-(methylphenylamino)benzamide may also generate a nitrenium ion, which can trigger the subsequent electrophilic cyclization. It is worth noting that no desired cyclized product was observed from the reaction when the methoxy group in **1a** was replaced with a methyl group, supported by both the TLC and ^{1}H NMR experiments (not shown).

Exceptionally, with substrate **1q** (R^2 = *p*-nitro), the homocoupling product **2q** was observed, instead of the cyclization product (Scheme 2). This result indicates that the presence of a strong electron-withdrawing group in the phenyl ring to which the N-atom is to attach prevents the electrophilic cyclization from occurring but allows for the intermolecular N−N bond formation through the electrophilic attack of the generated nitrenium ion onto the nuclophilic N-center of the amide.[18]

Another noticeable property of **2a** is its potential as a building block for the synthesis of valuable pharmaceutical agents with biological activities. Illustrated in Scheme 3, the methoxy group in **2a** can be deported to afford **3a** through a known procedure in which Pd/C (10%) was utilized as a catalyst and HOAc as solvent under an atmosphere of hydrogen.[19] The obtained **3a**, which contains a free NH moiety, could then be used for synthesizing antidepressant dibenzepine **A**[20] and HDAC inhibitor **B**.[2]

CONCLUSION

In summary, we have developed an alternative useful strategy for construction of the 1,4-benzodiazepine skeleton. The appealing features of the present approach are its generality in terms of substrate scope, the mild reaction conditions, and most of all, the heavy-metal-free characteristic of the key oxidative coupling process. The *N*-methoxy group in the final products can be readily removed and thus allows for further derivatization of the amide moiety.

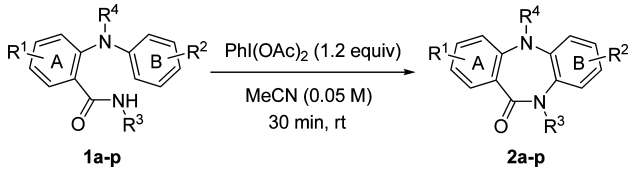
EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR spectra were recorded on a 600 or 500 MHz instrument (150 or 125 MHz for ^{13}C NMR) at 25 °C. Chemical shift values are given in ppm and refer to the internal standard TMS set as 0.00 ppm. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quadruplet; qui, quintuplet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The coupling constants, *J*, are reported in hertz (Hz). Low-resolution mass spectrometry (ESI) was performed on an ion-trap spectrometer. High-resolution mass spectra (HRMS) were obtained on a Q-TOF microspectrometer. Melting points were determined with a national micromelting point apparatus without corrections. Flash chromatography was performed on silica gel 200−300 mesh, and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE). Thin-layer chromatography (TLC) was performed on glass-backed plates precoated with silica 60 GF254, which were developed using standard visualizing agents. All air- or moisture-sensitive reactions were conducted under a positive pressure of nitrogen. Different substituted phenylanthranilic acids[16] and methyl 2-(methyl(phenyl)amino)-benzoate[14] were synthesized according to the literature procedures. Dioxane, THF, and acetonitrile were dried by CaH_2 before use. Other reagents and solvents were purchased as reagent grade and used without further purification.

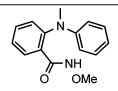
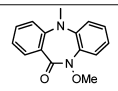
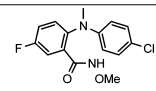
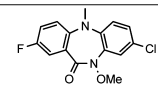
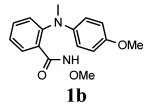
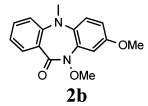
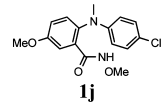
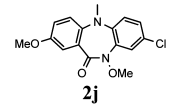
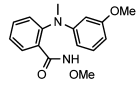
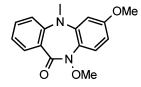
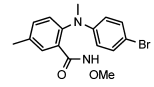
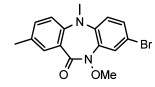
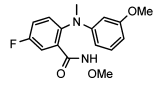
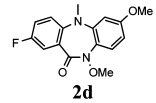
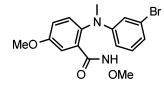
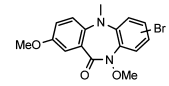
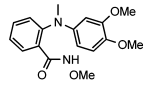
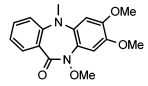
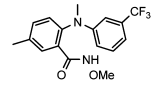
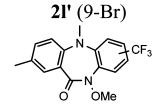
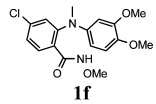
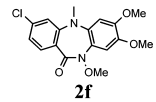
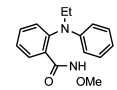
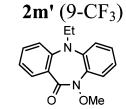
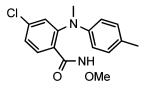
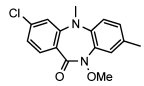
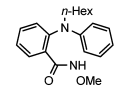
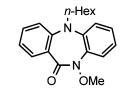
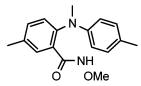
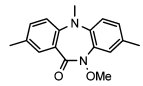
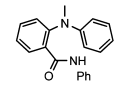
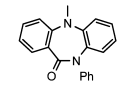
General Procedures for the Preparation of Substrates 1a−q.[13−16] Substituted 2-bromobenzoic acid (10 mmol), substituted aniline (10 mmol), *N*-methylmorpholine (1.7 mL, 15 mmol), and Cu(I) oxide (0.72 g, 5 mmol) were heated to reflux in dioxane (30 mL) under nitrogen for 16 h. The resulting dark reaction mixture was allowed to cool slowly to room temperature before HCl (4 M, 20 mL) was added. The precipitate was filtrated, washed with water (10 mL × 2), and then taken up by DMF (20 mL). To the solution was added NaH (1.20 g, 30 mmol) portionwise under an ice bath. The mixture

dx.doi.org/10.1021/jo402413g | J. Org. Chem. 2014, 79, 955−962

Table 2. PIDA-Mediated Synthesis of 1,4-Benzodiazepine Derivatives[a]

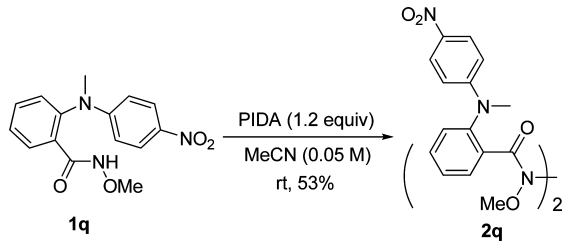


1a-p 2a-p

entry	substrate 1	product 2	yield (%)[b]	entry	substrate 1	product 2	yield (%)[b]
1	 1a	 2a	82	9	 1i	 2i	83
2	 1b	 2b	90	10	 1j	 2j	78
3	 1c	 2c	76	11	 1k	 2k	71
4	 1d	 2d	73	12	 1l	 2l (7-Br) 2l' (9-Br)	79[c]
5	 1e	 2e	60	13[c]	 1m	 2m (7-CF_3) 2m' (9-CF_3)	67[d]
6	 1f	 2f	72	14	 1n	 2n	83
7	 1g	 2g	81	15	 1o	 2o	77
8	 1h	 2h	84	16	 1p	 2p	30

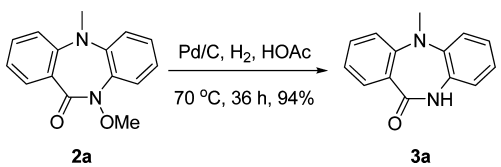
[a]General conditions: **1** (1.0 equiv), PIDA (1.2 equiv) in MeCN (0.05 M), stirred at rt for 30 min. [b]Isolated yields. [c]The two regioisomers were separable, **2l**/**2l′** = 1.8:1. [d]The two regioisomers were separable, **2m**/**2m′** = 2.0:1.

Scheme 2. PIDA-Mediated Homocoupling of Substrate 1q



1q 2q

Scheme 3. Removal of Methoxy Group in 2a



2a 3a

was stirred at room temperature for 15 min, and then methyl iodide (3.1 mL, 0.1 mol) was added dropwise at 0 °C. For substrate **1n** and **1o**, the same molar of the corresponding alkyl bromide was used. The mixture was stirred at room temperature until the substrate disappeared as determined by TLC. Then water (20 mL) was added slowly at 0 °C. The mixture was extracted with EtOAc (50 mL × 3). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and then evaporated to remove the solvent under vacuum to give crude substituted methyl 2-(methyl(phenyl)amino)-benzoate, which was used direclty for the next step.

To a solution of substituted methyl 2-(methyl(phenyl)amino)-benzoate in EtOH/H_2O (20 mL, 1:2 (v/v)) was added potassium hydroxide (1.68 g, 30 mmol). The resulting mixture was heated at reflux until TLC indicated total consumption of the substrate. The solvent was removed under vacuum, and the residue was dissolved into water (20 mL) and diluted with HCl (1 M) until no more precipitate was formed. The mixture was extracted with EtOAc (50 mL × 3), and the combined organic layer was dried with anhydrous Na_2SO_4. The solvent was removed via evaporation, and the resulting solid was dissolved in THF (20 mL). To the solution was then added 1,1′-carbonyldiimidazole (2.43 g, 15 mmol) in one portion under an atmosphere of nitrogen with stirring for 30 min. Then methoxylamine

dx.doi.org/10.1021/jo402413g | J. Org. Chem. 2014, 79, 955−962

hydrochloride (1.00 g, 12 mmol) and triethylamine (1.7 mL, 12 mmol) were added, and the reaction mixture was stirred at room temperature until TLC indicated completion of the reaction. Saturated aqueous $NaHCO_3$ (10 mL) was then added to the reaction mixture. The mixture was extracted with EtOAc (50 mL × 3), and the combined organic layer was dried with anhydrous Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by silica gel column chromatography using EA/PE as eluent to give the final substrate **1a−q**. Compound **1p** was prepared by similar procedures except aniline was used instead of methoxylamine hydrochloride as the starting material.

*N-Methoxy-2-(methyl(phenyl)amino)benzamide (**1a**):* yield for four steps 64%, 1.64 g; white solid; mp 83−87 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.64 (s, 1H), 8.13 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.23 (t, J = 7.8 Hz, 2H), 7.11 (d, J = 7.8 Hz 1H), 6.90 (t, J = 7.2 Hz, 1H), 6.77 (d, J = 8.4 Hz, 2H), 3.67 (s, 3H), 3.20 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.5, 149.0, 148.0, 133.2, 131.4, 129.7, 129.3, 127.7, 126.8, 120.5, 116.3, 64.1, 41.0; HRMS (ESI) calcd for $C_{15}H_{16}N_2NaO_2^+$ [M + Na^+] 279.1104, found 279.1098.

*N-Methoxy-2-((4-methoxyphenyl)(methyl)amino)benzamide (**1b**):* yield for four steps 49%, 1.40 g; light yellow solid; mp 64−66 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.06 (s, 1H), 8.16 (d, J = 7.2 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.82 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 3.76 (s, 3H), 3.74 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.7, 154.5, 149.1, 143.0, 133.1, 131.4, 128.8, 126.7, 126.3, 118.7, 114.7, 64.2, 55.6, 41.7; HRMS (ESI) calcd for $C_{16}H_{18}N_2NaO_3^+$ [M + Na^+] 309.1210, found 309.1207.

*N-Methoxy-2-((3-methoxyphenyl)(methyl)amino)benzamide (**1c**):* yield for four steps 49%, 1.40 g; light yellow solid; mp 74−76 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.16 (d, J = 5.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 6.47 (d, J = 7.8 Hz, 1H), 6.34 (d, J = 8.4 Hz, 1H), 6.31 (s, 1H), 3.74 (d, J = 1.8 Hz, 3H), 3.72 (d, J = 3.6 Hz, 3H), 3.18 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.5, 160.7, 150.3, 147.7, 133.2, 131.5, 130.1, 129.4, 127.9, 127.1, 109.0, 105.1, 102.8, 64.2, 55.2, 40.9; HRMS (ESI) calcd for $C_{16}H_{18}N_2NaO_3^+$ [M + Na^+] 309.1210, found 309.1211.

*5-Fluoro-N-methoxy-2-((3-methoxyphenyl)(methyl)amino)-benzamide (**1d**):* yield for four steps 50%, 1.52 g; yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.65 (br s, 1H), 7.90 (d, J = 9.0 Hz, 1H), 7.15−7.19 (m, 2H), 7.09 (dd, J = 9.0, 4.8 Hz, 1H), 6.49 (d, J = 7.8 Hz, 1H), 6.32 (d, J = 7.8 Hz, 1H), 6.29 (t, J = 8.4 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.9, 161.0 (d, J_{C-F} = 248.4 Hz), 161.8, 150.2, 143.7 (d, J_{C-F} = 3.3 Hz), 131.8, 130.2, 130.0 (d, J_{C-F} = 8.2 Hz), 120.4 (d, J_{C-F} = 22.8 Hz), 117.9 (d, J_{C-F} = 24.6 Hz), 109.0, 105.3, 102.9, 64.3, 55.3, 41.0; HRMS (ESI) calcd for $C_{16}H_{17}{}^{19}FN_2NaO_3^+$ [M + Na^+] 327.1115, found 327.1116.

*2-((3,4-Dimethoxyphenyl)(methyl)amino)-N-methoxybenzamide (**1e**):* yield for four steps 57%, 1.80 g; yellow solid; mp 71−74 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.99 (s, 1H), 8.19 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 7.08 (d, J = 7.8 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.40 (d, J = 8.4 Hz, 1H), 6.33 (s, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 3.74 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 149.7, 148.8, 144.2, 143.4, 133.1, 131.4, 128.9, 126.9, 126.5, 112.2, 108.5, 102.9, 64.2, 56.3, 56.0, 41.7; HRMS (ESI) calcd for $C_{17}H_{20}N_2NaO_4^+$ [M + Na^+] 339.1315, found 339.1317.

*4-Chloro-2-((3,4-dimethoxyphenyl)(methyl)amino)-N-methoxy-benzamide (**1f**):* yield for four steps 20%, 0.70 g; yellow solid; mp 89−93 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.80 (br s, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.30 (dd, J = 1.8, 8.4 Hz, 1H), 7.06 (d, J = 1.8 Hz, 1H), 6.81 (d, J = 9.0 Hz, 1H), 6.42 (dd, J = 2.4, 9.0 Hz, 1H), 6.36 (d, J = 2.4 Hz, 1H), 3.85 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.8, 150.0, 149.8, 144.7, 142.7, 138.6, 132.7, 127.0, 126.5, 112.1, 109.5, 103.4, 64.3, 56.3, 56.0, 41.9 (one carbon peak was missing due to overlapping); HRMS (ESI) calcd for $C_{17}H_{19}{}^{35}ClN_2NaO_4^+$ [M + Na^+] 373.0926, found 373.0926.

*4-Chloro-N-methoxy-2-(methyl(p-tolyl)amino)benzamide (**1g**):* yield for four steps 58%, 1.77 g; white solid; mp 122−124 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.70 (br s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.32 (dd, J = 2.4, 8.4 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 1.8 Hz, 1H), 6.72 (d, J = 8.4 Hz, 2H), 3.73 (s, 3H), 3.16 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 149.7, 146.2, 138.7, 132.8, 131.2, 130.0, 127.5, 127.2, 126.9, 117.4, 64.2, 41.4, 20.5; HRMS (ESI) calcd for $C_{16}H_{17}{}^{35}ClN_2NaO_2^+$ [M + Na^+] 327.0871, found 327.0871.

*N-Methoxy-5-methyl-2-(methyl(p-tolyl)amino)benzamide (**1h**):* yield for four steps 58%, 1.65 g; white solid; mp 100−103 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.96 (s, 1H), 8.02 (s, 1H), 7.25 (dd, J = 1.2, 7.8 Hz, 1H), 7.05 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 7.8 Hz, 1H), 6.69 (d, J = 8.4 Hz, 2H), 3.73 (s, 3H), 3.13 (s, 3H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 146.9, 146.0, 136.8, 134.0, 131.7, 130.0, 129.8, 128.8, 127.3, 116.6, 64.1, 41.1, 20.9, 20.4; HRMS (ESI) calcd for $C_{17}H_{20}N_2NaO_2^+$ [M + Na^+] 307.1417, found 307.1416.

*2-((4-Chlorophenyl)(methyl)amino)-5-fluoro-N-methoxybenzamide (**1i**):* yield for four steps 56%, 1.73 g; light yellow solid; mp 154−157 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.02 (s, 1H), 7.84 (d, J = 6.6 Hz, 1H), 7.18−7.20 (m, 3H), 7.08 (dd, J = 4.8, 9.0 Hz, 1H), 6.68 (d, J = 9.0 Hz, 2H), 3.72 (s, 3H), 3.17 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.9, 161.0 (d, J_{C-F} = 248.8 Hz), 147.5, 143.5, 131.8, 129.8 (d, J_{C-F} = 8.0 Hz), 129.3, 125.8, 120.4 (d, J_{C-F} = 23.1 Hz), 118.0 (d, J_{C-F} = 24.9 Hz), 117.2, 64.2, 41.2; HRMS (ESI) calcd for $C_{15}H_{14}{}^{35}Cl^{19}FN_2NaO_2^+$ [M + Na^+] 331.0620, found 331.0621.

*2-((4-Chlorophenyl)(methyl)amino)-N,5-dimethoxybenzamide (**1j**):* yield for four steps 37%, 1.19 g; light yellow solid; mp 141−146 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.59 (br s, 1H), 7.71 (d, J = 2.4 Hz, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.02 (dd, J = 3.0, 9.0 Hz, 1H), 6.98 (d, J = 9.0 Hz, 1H), 6.66 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H), 3.74 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.0, 158.4, 147.9, 140.1, 130.6, 129.2, 129.1, 125.3, 120.4, 116.9, 114.6, 64.3, 55.8, 41.1; HRMS (ESI) calcd for $C_{16}H_{17}{}^{35}ClN_2NaO_3^+$ [M + Na^+] 343.0820, found 343.0822.

*2-((4-Bromophenyl)(methyl)amino)-N-methoxy-5-methylbenzamide (**1k**):* yield for four steps 37%, 1.29 g; white solid; mp 160−162 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.33 (br s, 1H), 7.97 (s, 1H), 7.31−7.33 (m, 2H), 7.29 (dd, J = 1.8, 7.8 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.60−6.63 (m, 2H), 3.72 (s, 3H), 3.15 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 148.2, 144.7, 137.4, 134.1, 132.0, 131.8, 129.3, 127.6, 117.4, 112.5, 64.2, 40.9, 20.9; HRMS (ESI) calcd for $C_{16}H_{17}{}^{79}BrN_2NaO_2^+$ [M + Na^+] 371.0366, found 371.0368.

*2-((3-Bromophenyl)(methyl)amino)-N,5-dimethoxybenzamide (**1l**):* yield for four steps 54%, 1.97 g; light yellow solid; mp 101−104 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.33 (br s, 1H), 7.67 (d, J = 2.4 Hz, 1H), 7.07 (t, J = 7.8 Hz, 1H), 7.04 (dd, J = 3.0, 9.0 Hz, 1H), 6.99−7.00 (m, 2H), 6.88 (t, J = 2.4 Hz, 1H), 6.60 (dd, J = 1.8, 8.4 Hz, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 3.16 (s, 3H) ; ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.0, 158.5, 150.5, 139.5, 130.8, 130.5, 129.4, 123.4, 122.8, 120.3, 118.1, 114.7, 114.2, 64.2, 55.8, 40.9; HRMS (ESI) calcd for $C_{16}H_{17}{}^{79}BrN_2NaO_3^+$ [M + Na^+] 387.0315, found 387.0318.

*N-Methoxy-5-methyl-2-(methyl(3-(trifluoromethyl)phenyl)-amino)benzamide (**1m**):* yield for four steps 41%, 1.39 g; light yellow solid; mp 102−107 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.14 (s, 1H), 7.96 (s, 1H), 7.31−7.33 (m, 2H), 7.14 (d, J = 7.2 Hz, 1H), 6.99−7.00 (m, 2H), 6.84 (d, J = 8.4 Hz, 1H), 3.70 (s, 3H), 3.22 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.5, 149.4, 144.1, 137.6, 134.2, 131.7, 131.5, 129.7, 129.6, 127.8, 124.1 (d, J_{C-F} = 272.6 Hz), 118.8, 116.3, 111.4, 64.2, 40.9, 20.9; HRMS (ESI) calcd for $C_{17}H_{17}{}^{19}F_3N_2NaO_2^+$ [M + Na^+] 361.1134, found 361.1137.

*2-(Ethyl(phenyl)amino)-N-methoxybenzamide (**1n**):* yield for four steps 38%, 1.03 g; light yellow solid; mp 107−110 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.51 (br s, 1H), 8.16 (d, J = 7.2 Hz, 1H), 7.48 (dt, J = 1.2, 8.4 Hz, 1H), 7.36−7.40 (m, 1H), 7.22−7.25 (m, 2H), 7.10 (d, J = 7.8 Hz, 1H), 6.89 (t, J = 7.2 Hz, 1H), 6.76 (d, J = 8.4 Hz, 2H), 3.71 (s, 3H), 3.64 (q, J = 7.2 Hz, 2H),1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.8, 148.1, 145.7, 132.9, 131.5, 130.8, 129.4, 129.2, 127.0, 120.2, 116.5, 64.2, 47.0, 12.0; HRMS (ESI) calcd for $C_{16}H_{18}N_2NaO_2^+$ [M + Na^+] 293.1260, found 293.1261.

dx.doi.org/10.1021/jo402413g | J. Org. Chem. 2014, 79, 955−962

*2-(Hexyl(phenyl)amino)-N-methoxybenzamide (**1o**):* yield for four steps 31%, 1.01 g; light yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.44 (br s, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.49 (dt, J = 1.8, 7.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 1H), 7.24 (t, J = 7.8 Hz, 2H), 7.12 (d, J = 7.8 Hz, 1H), 6.89 (t, J = 7.8 Hz, 1H), 6.74 (t, J = 8.4 Hz, 2H), 3.71 (s, 3H), 3.52 (t, J = 7.8 Hz, 2H), 1.59−1.64 (m, 2H), 1.27−1.31 (m, 6H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.8, 148.3, 146.0, 133.0, 131.6, 130.5, 129.5, 129.1, 127.0, 120.1, 116.3, 64.3, 53.1, 31.5, 26.8, 26.5, 22.6, 14.0; HRMS (ESI) calcd for $C_{20}H_{26}N_2NaO_2^+$ [M + Na$^+$] 349.1886, found 349.1889.

*2-(Methyl(phenyl)amino)-N-phenylbenzamide (**1p**):* yield for four steps 52%, 1.57 g; yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.65 (s, 1H), 8.38 (dd, J = 1.8, 7.8 Hz, 1H), 7.51 (dt, J = 1.8, 7.8 Hz, 1H), 7.42−7.45 (m, 3H), 7.26−7.30 (m, 4H), 7.16 (d, J = 7.8 Hz, 1H), 7.06 (t, J = 7.8 Hz, 1H), 6.95 (t, J = 7.8 Hz, 1H), 6.86 (d, J = 7.8 Hz, 2H), 3.26 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 148.9, 148.1, 138.3, 133.2, 131.9, 130.9, 129.5, 129.0, 128.1, 127.2, 124.1, 120.7, 120.1, 116.3, 41.0; HRMS (ESI) calcd for $C_{20}H_{18}N_2NaO^+$ [M + Na$^+$] 325.1311, found 325.1314.

*N-Methoxy-2-(methyl(4-nitrophenyl)amino)benzamide (**1q**):* yield for four steps 20%, 0.60 g; yellow solid; mp 117−123 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.15 (br s, 1H), 8.04 (d, J = 9.0 Hz, 2H), 7.77 (d, J = 7.2 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 6.58 (d, J = 9.0 Hz, 2H), 3.58 (s, 3H), 3.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.7, 153.7, 144.4, 138.7, 133.2, 131.6, 130.4, 129.1, 128.1, 125.8, 112.6, 64.1, 40.9; HRMS (ESI) calcd for $C_{15}H_{15}N_3NaO_4^+$ [M + Na$^+$] 324.0955, found 324.0957.

General Procedure for the Preparation of Product 2. To a solution of substrate **1** (1 mmol) in acetonitrile (20 mL) was added PIDA (386 mg, 1.2 mmol) portionwise under an ice bath within 15 min. Then the reaction mixture as stirred at room temperature for additional 30 min. The reaction mixture was treated with water (10 mL) and stirred for 5 min before saturated aqueous $NaHCO_3$ (10 mL) was added. The mixture was extracted with EtOAc (10 mL × 4). The combined organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography on silica gel using EA/PE as eluent to give the desired product.

*10-Methoxy-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11(10H)-one (**2a**):* yield 82%, 208 mg; yellow solid; mp 126−128 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (dd, J = 1.2, 7.8 Hz, 1H), 7.50 (dd, J = 1.8, 8.4 Hz, 1H), 7.41 (dt, J = 1.2, 7.8 Hz, 1H), 7.18 (dt, J = 1.8, 7.2 Hz, 1H), 7.12−7.15 (m, 2H), 7.07 (t, J = 8.4 Hz, 2H), 3.87 (s, 3H), 3.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.0, 153.0, 145.8, 133.8, 132.8, 132.1, 126.5, 125.6, 124.4, 123.1, 121.0, 118.5, 116.7, 62.3, 37.7; HRMS (ESI) calcd for $C_{15}H_{14}N_2NaO_2^+$ [M + Na$^+$] 277.0947, found 277.0949.

*8,10-Dimethoxy-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-(10H)-one (**2b**):* yield 90%, 256 mg; white solid; mp 125−127 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (dd, J = 1.2, 7.8 Hz, 1H), 7.40 (dt, J = 1.2, 7.8 Hz, 1H), 7.04−7.06 (m, 3H), 7.03 (s, 1H), 6.73 (dd, J = 2.4, 8.4 Hz, 1H), 3.89 (s, 3H), 3.77 (s, 3H), 3.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 156.6, 153.4, 138.8, 134.9, 132.8, 132.2, 125.4, 122.8, 119.2, 116.3, 112.2, 105.9, 100.0, 62.4, 55.7, 37.7; HRMS (ESI) calcd for $C_{16}H_{16}N_2NaO_3^+$ [M + Na$^+$] 307.1053, found 307.1054.

*7,10-Dimethoxy-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-(10H)-one (**2c**):* yield 76%, 216 mg; yellow solid; mp 125−130 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (dd, J = 1.8, 7.8 Hz, 1H), 7.38−7.40 (m, 2H), 7.07 (t, J = 7.8 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.66−6.69 (m, 2H), 3.83 (s, 3H), 3.79 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 158.4, 152.8, 147.7, 132.5, 131.9, 126.6, 126.0, 123.2, 122.3, 116.8, 109.0, 104.7, 62.0, 55.6, 37.5; HRMS (ESI) calcd for $C_{16}H_{16}N_2NaO_3^+$ [M + Na$^+$] 307.1053, found 307.1055.

*2-Fluoro-7,10-dimethoxy-5-methyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2d**):* yield 73%, 220 mg; yellow solid; mp 154−158 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (dd, J = 3.0, 9.0 Hz, 1H), 7.40 (d, J = 9.0 Hz, 1H), 7.10 (dt, J = 3.0, 7.8 Hz, 1H), 7.01 (dd, J = 4.2, 7.8 Hz, 1H), 6.70 (dd, J = 2.4, 8.4 Hz, 1H), 6.66 (d, J = 1.8 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 158.6 (d, J_{C-F} = 243.1 Hz), 158.5, 148.9, 148.9, 147.8, 127.7, 126.2, 122.5, 119.3 (d, J_{C-F} = 22.7 Hz), 118.3 (d, J_{C-F} = 7.7 Hz), 118.0 (d, J_{C-F} = 24.3 Hz), 109.1, 104.6, 62.0, 55.6, 37.7; HRMS (ESI) calcd for $C_{16}H_{15}FN_2NaO_3^+$ [M + Na$^+$] 325.0959, found 325.0959.

*7,8,10-Trimethoxy-5-methyl-5H-dibenzo[b,e][1,4]diazepin-11-(10H)-one (**2e**):* yield 60%, 188 mg; yellow solid; decomposed when heated to 60 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (dd, J = 1.2, 7.8 Hz, 1H), 7.39 (dt, J = 1.2, 7.8 Hz, 1H), 7.02 (s, 1H), 7.04−7.08 (m, 2H), 6.65 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.0, 153.7, 147.6, 146.2, 139.1, 132.5, 132.1, 126.2, 125.9, 123.0, 116.4, 104.8, 102.2, 62.1, 56.3, 56.3, 37.5; HRMS (ESI) calcd for $C_{17}H_{18}N_2NaO_4^+$ [M + Na$^+$] 337.1159, found 337.1161.

*3-Chloro-7,8,10-trimethoxy-5-methyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2f**):* yield 72%, 251 mg; yellow solid; decomposed when heated to 80 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 1H), 7.03−7.04 (m, 2H), 7.01 (s, 1H), 6.65 (s, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.3, 154.4, 147.7, 146.5, 138.8, 138.0, 133.3, 126.2, 124.1, 123.1, 116.9, 104.6, 102.3, 62.2, 56.3, 56.3, 37.6; HRMS (ESI) calcd for $C_{17}H_{17}{}^{35}ClN_2NaO_4^+$ [M + Na$^+$] 371.0769, found 371.0773.

*3-Chloro-10-methoxy-5,8-dimethyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2g**):* yield 81%, 245 mg; white solid; mp 172−178 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, J = 9.0 Hz, 1H), 7.30 (s, 1H), 6.99−7.03 (m, 4H), 3.86 (s, 3H), 3.31 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.3, 154.0, 142.4, 138.9, 134.8, 133.5, 133.4, 127.3, 123.9, 123.1, 121.3, 118.4, 117.0, 62.4, 37.8, 20.8; HRMS (ESI) calcd for $C_{16}H_{15}{}^{35}ClN_2NaO_2^+$ [M + Na$^+$] 325.0714, found 325.0716.

*10-Methoxy-2,5,8-trimethyl-5H-dibenzo[b,e][1,4]diazepin-11-(10H)-one (**2h**):* yield 84%, 237 mg; white solid; mp 125−127 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, J = 1.8, 1H), 7.29 (s, 1H), 7.19 (dd, J = 1.8, 8.4 Hz, 1H), 6.96−7.00 (m, 2H), 6.93 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H), 3.29 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 151.0, 143.8, 134.0, 133.4, 132.5, 132.0, 127.1, 125.4, 121.4, 117.9, 116.3, 62.3, 37.5, 20.8, 20.4; HRMS (ESI) calcd for $C_{17}H_{18}N_2NaO_2^+$ [M + Na$^+$] 305.1260, found 305.1261.

*8-Chloro-2-fluoro-10-methoxy-5-methyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2i**):* yield 83%, 254 mg; yellow solid; mp 157−160 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, J = 8.4, 1H), 7.49 (s, 1H), 7.13−7.17 (m, 2H), 7.06 (d, J = 8.4, 1H), 7.02 (dd, J = 4.8, 8.4, 1H), 3.89 (s, 3H), 3.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.7, 158.5 (d, J_{C-F} = 243.6 Hz), 148.6, 144.1, 134.8, 129.9, 136.8, 126.5, 120.9, 119.8 (d, J_{C-F} = 22.7 Hz), 119.5, 118.2 (q, J_{C-F} = 8.2 Hz), 62.7, 38.0; HRMS (ESI) calcd for $C_{15}H_{12}{}^{35}Cl^{19}FN_2NaO_2^+$ [M + Na$^+$] 329.0464, found 329.0463.

*8-Chloro-2,10-dimethoxy-5-methyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2j**):* yield 78%, 248 mg; yellow solid; mp 117−123 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (d, J = 2.4, 1H), 7.39 (s, 1H), 7.13 (dd, J = 2.4, 9.0 Hz, 1H), 7.03 (d, J = 9.0 Hz, 1H), 6.99 (d, J = 1.2 Hz, 2H), 3.88 (s, 3H), 3.79 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 155.6, 146.0, 144.8, 134.9, 129.4, 126.3, 126.1, 120.9, 120.1, 119.1, 118.0, 115.0, 62.6, 55.7, 37.8; HRMS (ESI) calcd for $C_{16}H_{15}{}^{35}ClN_2NaO_3^+$ [M + Na$^+$] 341.0663, found 341.0662.

*8-Bromo-10-methoxy-2,5-dimethyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2k**):* yield 71%, 246 mg; white solid; mp 90−95 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (d, J = 1.8 Hz, 1H), 7.61 (d, J = 2.4 Hz, 1H), 7.27 (dd, J = 2.4, 9.0 Hz, 1H), 7.22 (dd, J = 1.8, 8.4 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 3.88 (s, 3H), 3.30 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.0, 150.2, 145.0, 135.2, 133.7, 133.0, 132.2, 129.1, 124.9, 123.7, 119.6, 116.8, 116.6, 62.6, 37.7, 20.4; HRMS (ESI) calcd for $C_{16}H_{15}{}^{79}BrN_2NaO_2^+$ [M + Na$^+$] 369.0209, found 369.0211.

*7-Bromo-2,10-dimethoxy-5-methyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2l**):* yield 51%, 185 mg; yellow solid; mp 133−135 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, J = 3.0 Hz, 1H), 7.34 (t, J = 4.8 Hz, 1H), 7.22−7.24 (m, 2H), 6.97−7.00 (m, 2H), 3.85 (s, 3H), 3.78 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 155.7, 147.5, 145.7, 132.9, 127.1, 126.3, 122.3, 121.4, 119.9,

dx.doi.org/10.1021/jo402413g | J. Org. Chem. 2014, 79, 955−962

119.6, 118.1, 115.0, 62.4, 55.7, 37.7; HRMS (ESI) calcd for $C_{16}H_{15}{}^{79}BrN_2NaO_3^+$ [M + Na^+] 385.0158, found 385.0158.

*9-Bromo-2,10-dimethoxy-5-methyl-5H-dibenzo[b,e][1,4]-diazepin-11(10H)-one (**2l′**):* yield 28%, 102 mg; yellow solid; mp 200−204 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (dd, J = 1.8, 7.8 Hz, 1H), 7.30 (d, J = 3.0 Hz, 1H), 7.09−7.15 (m, 2H), 6.99 (d, J = 9.0 Hz, 1H), 6.93 (dd, J = 3.0, 9.0 Hz, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.7, 156.0, 153.0, 146.7, 130.9, 129.4, 128.6, 127.3, 120.0, 119.5, 118.2, 116.4, 114.3, 61.8, 55.7, 37.3; HRMS (ESI) calcd for $C_{16}H_{15}{}^{79}BrN_2NaO_3^+$ [M + Na^+] 385.0158, found 385.0160.

*10-Methoxy-2,5-dimethyl-7-(trifluoromethyl)-5H-dibenzo[b,e]-[1,4]diazepin-11(10H)-one (**2m**):* yield 43%, 144 mg; white solid; mp 121−122 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (d, J = 1.8 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.34 (s, 1H), 7.25−7.26 (m, 1H), 6.99 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.37 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.9, 149.9, 145.9, 137.1, 134.0, 133.3, 132.2, 128.3 (q, J_{C-F} = 32.9 Hz), 124.7, 121.2 (q, J_{C-F} = 3.8 Hz), 116.9, 115.5 (q, J_{C-F} = 3.6 Hz), 62.7, 37.7, 20.3; HRMS (ESI) calcd for $C_{17}H_{15}{}^{19}F_3N_2NaO_2^+$ [M + Na^+] 359.0978, found 359.0979.

*10-Methoxy-2,5-dimethyl-9-(trifluoromethyl)-5H-dibenzo[b,e]-[1,4]diazepin-11(10H)-one (**2m′**):* yield 22%, 74 mg; white solid; mp 201−203 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, J = 1.8 Hz, 1H), 7.46 (dd, J = 1.8, 7.8 Hz, 1H), 7.32−7.37 (m, 2H), 7.21 (dd, J = 1.8, 8.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 3.38 (s, 3H), 3.72 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 150.7 (d, J_{C-F} = 19.9 Hz), 133.7, 133.4, 131.6, 129.9, 127.4, 125.8, 125.6, 125.6, 124.0, 123.4 (q, J_{C-F} = 5.0 Hz), 122.2, 121.1, 117.0, 61.9, 61.8, 37.6, 20.3; HRMS (ESI) calcd for $C_{17}H_{15}{}^{19}F_3N_2NaO_2^+$ [M + Na^+] 359.0978, found 359.0980.

*5-Ethyl-10-methoxy-5H-dibenzo[b,e][1,4]diazepin-11(10H)-one (**2n**):* yield 83%, 222 mg; white solid; mp 142−145 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (dd, J = 1.2, 7.8 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 8.4 Hz, 2H), 7.04−7.07 (m, 2H), 3.86 (s, 3H), 3.71−3.84 (m, 2H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.0, 152.7, 144.8, 134.9, 132.6, 131.7, 127.0, 126.5, 124.4, 123.3, 121.5, 119.7, 118.0, 62.2, 43.2, 13.5; HRMS (ESI) calcd for $C_{16}H_{16}N_2NaO_2^+$ [M + Na^+] 291.1104, found 291.1104.

*5-Hexyl-10-methoxy-5H-dibenzo[b,e][1,4]diazepin-11(10H)-one (**2o**):* yield 77%, 249 mg; light yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 7.8 Hz, 2H), 7.03−7.07 (m, 2H), 3.86 (s, 3H), 3.67−3.79 (m, 2H), 1.57−1.64 (m, 2H), 1.38 (t, J = 6.0 Hz, 2H), 1.19−1.26 (m, 4H), 0.83 (t, J = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.1, 152.7, 144.8, 134.8, 132.6, 131.8, 126.8, 126.5, 124.4, 123.2, 121.3, 119.9, 118.1, 62.2, 48.6, 31.4, 27.3, 26.6, 22.7, 14.1; HRMS (ESI) calcd for $C_{20}H_{24}N_2NaO_2^+$ [M + Na^+] 347.1730, found 347.1733.

*5-Methyl-10-phenyl-5H-dibenzo[b,e][1,4]diazepin-11(10H)-one (**2p**):* yield 30%, 90 mg; yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, J = 1.2, 7.8 Hz, 1H), 7.37−7.43 (m, 5H), 7.30 (t, J = 7.2 Hz, 1H), 7.18 (dd, J = 1.2, 7.8 Hz, 1H), 7.06−7.09 (m, 3H), 6.88 (dt, J = 1.2, 7.8 Hz, 1H), 6.80 (dd, J = 1.2, 8.4 Hz, 1H), 3.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.5, 154.0, 148.5, 143.4, 137.0, 132.1, 132.1, 129.1, 128.8, 128.2, 127.1, 126.4, 125.7, 124.0, 123.2, 118.5, 116.0, 37.1; HRMS (ESI) calcd for $C_{20}H_{16}N_2NaO^+$ [M + Na^+] 323.1155, found 323.1154.

*Dimer of 1q (**2q**):* yield 67%, 200 mg; yellow solid; mp 70−74 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, J = 9.0 Hz, 2H), 7.57 (dt, J = 1.2, 7.8 Hz, 1H), 7.54 (d, J = 7.2 Hz, 1H), 7.40 (t, J = 7.8 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 6.50 (d, J = 9.6 Hz, 2H), 3.45 (s, 3H), 3.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 153.8, 144.3, 138.4, 132.8, 132.6, 129.1, 128.9, 127.3, 125.5, 112.4, 63.2, 40.9; HRMS (ESI) calcd for $C_{30}H_{28}N_6NaO_8^+$ [M + Na^+] 623.1861, found 623.1858.

General Procedures for the Preparation of 3a. A mixture of **2a** (1 mmol) and 10% Pd/C (20 mg) in acetic acid (5 mL), after being purged with hydrogen for 10 min, was heated to 70 °C under a positive pressure of hydrogen (hydrogen balloon). TLC was used to monitor the reaction process. When the reaction was completed, water (20 mL) was added, and the mixture was extracted with EtOAc (10 mL × 3). The combined organic layer was washed with 10% aqueous $NaHCO_3$ (20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum to afford the desired product **3a**.

*5,10-Dihydro-5-methyl-11H-dibenzo[b,e][1,4]diazepin-11-one (**3a**):*[7] yield 94%, 211 mg; yellow solid; mp 208−211 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.20 (s, 1H), 7.63 (dd, J = 1.5, 7.5 Hz, 1H), 7.48 (dt, J = 1.5, 7.8 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.03−7.12 (m, 4H), 3.26 (s, 3H); HRMS (ESI) m/z calcd for $C_{14}H_{12}N_2NaO^+$ [M + Na^+] 247.0842, found 247.0842.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectral data for all new compounds. The material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Y.D. acknowledges the National Natural Science Foundation of China (No. 21072148), Foundation (B) for Peiyang Scholar−Young Core Faculty of Tianjin University (No. 2013XR-0144), and the Innovation Foundation of Tianjin University (No. 2013XJ-0005) for financial support.

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