羟基取代乙二胺衍生物与醛反应化学选择性合成取代苯并噁嗪和咪唑啉

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摘要 在 $\text{La}(\text{OTf})_3$ 的催化作用下, 羟基取代乙二胺衍生物与醛通过环化反应, 高化学选择性、高效地合成多官能团取代的 1,3-咪唑啉和 3,1-苯并噁嗪类化合物。脂肪醛和芳香醛都适用于该反应体系。探索了可能的反应机理, O 原子和 N 原子的亲核性对反应的化学选择性起着非常重要的作用。该方法的优点是只需调节羟基取代乙二胺分子中亚甲基的位置, 就可以高化学选择性地合成 1,3-咪唑啉或 3,1-苯并噁嗪类化合物。

关键词 羟基取代乙二胺; 1,3-咪唑啉; 3,1-苯并噁嗪; 化学选择性; 合成

Chemoselective Synthesis of Substituted Benzoxazines and Imidazolidines by Reactions of Hydroxyl Substituted Ethylenediamine Derivatives with Aldehydes

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Abstract Lewis acid $\text{La}(\text{OTf})_3$ -catalyzed chemoselective cyclization of hydroxyl substituted ethylenediamine derivatives with aldehydes has been described for the first time, which provides efficient access to diversely functionalized 1,3-imidazolidines and 3,1-benzoxazines in generally good yields only by adjusting the position of the methylene group within hydroxyl substituted ethylenediamines. The reaction is suitable to aromatic aldehydes and aliphatic ones. Plausible mechanisms are also proposed to explain the observed reaction modes, wherein the nucleophilicity of nitrogen and oxygen atoms plays an important role in controlling the chemoselectivity.

Keywords hydroxyl substituted ethylenediamine; 1,3-imidazolidine; 3,1-benzoxazine; chemoselectivity; synthesis

1 Introduction

It is well known that reactions of 2-aminomethyl phenol with aldehydes or ketones generate 1,3-benzoxazines.^[1~4] It has been a more frequently used and important method to access these chemicals although many other ways have been reported in the past few decades.^[5~9] The importance

of the synthesis of 1,3-benzoxazine derivatives attributes to their broad biological activities.^[2,10~18] Similarly, condensation reactions of 2-aminobenzyl alcohol with aldehydes or ketones give 3,1-benzoxazine derivatives.^[19,20] These compounds also possess many biological activities like herbicidal,^[21] fungicidal,^[22] anticancer,^[23] anti-proliferative activity,^[24] potent progesterone receptor (PR) agonists,^[19]

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DNA-binding antitumor agents^[25] and α -chymotrypsin inhibitors.^[26] On the other hand, reactions of 1,2-ethylenediamine or its derivatives with aldehydes produce 1,3-imidazolidines,^[27–30] and provide a useful route to these biologically important compounds.^[31,32] However, there is few reports^[33] about the reactions of aldehydes with 2-((aminoethyl)aminomethyl)phenols or 2-((aminoethyl)amino)benzyl alcohols, which are also named as hydroxyl substituted ethylenediamines. Hence, we were interested in studying the reaction of aldehydes with 2-((aminoethyl)aminomethyl)phenol (**1**) derived from 2-aminomethyl-phenol, or with 2-((aminoethyl)amino)benzyl alcohol (**2**) derived from 2-aminobenzyl alcohol. In theory, the reaction should give two products of benzoxazine and imidazolidine. But, interestingly, it was found that the reactions of **1** with aldehydes proceeded through a formal [4 + 1] cyclization manner,^[34,35] giving 1,3-imidazolidines instead (Scheme 1). It demonstrated that the hydroxyl group did not take part in the reaction, since no benzoxazine was detected. Recently, Kim and Chin *et al.*^[33] reported that 1,2-bis(2-hydroxyphenyl)-1,2-diaminoethane could react with aldehydes to furnish imidazolidines.

Scheme 1 Preparation of substrates **1** and reactions of **1** with aldehydes **4**

In contrast, when we used similar type of compound, 2-((aminoethyl)amino)benzyl alcohol (**2**), to react with aldehydes, the reactions proceeded via a formal [5 + 1] annulation fashion to give 3,1-benzoxazines rather than 1,3-imidazolidines with excellent chemoselectivity under identical conditions. Notably, to our best knowledge, this work represents the first example of preparation of 3,1-benzoxazines and 1,3-imidazolidines that can be controlled by adjusting the position of the methylene group within hydroxyl substituted ethylenediamine derivatives. Herein, we wish to report these interesting findings in detail.

2 Results and discussion

Initially, we carried out the reaction of 2-((4-methoxyphenyl)aminoethyl)aminomethylphenol (**1a**)^[36] and 4-nitrobenzaldehydes (**4a**). Surprisingly, the reaction gave 1,3-imidazolidine **5aa** in 18% yield at 80 °C in chloroform/cyclohexane (*V* : *V* = 1 : 4) without catalyst, and no

1,3-benzoxazine **6aa** was observed (Entry 1, Table 1). Fortunately, the yield was enhanced to 54% when using TsOH (10 mol%) as the catalyst (Entry 2, Table 1). Encouraged by this result, we also tried TMSCl, BF₃·OEt₂, SnCl₄, and La(OTf)₃ as catalyst, and found that La(OTf)₃ was the best one, increasing the yield to 60% (Entry 6). Variation of the catalyst loading diminished the reaction yield (Entries 7 and 8). The yield was further raised to 76% by shortening the reaction time from 4 h to 3 h when the reaction was performed at 80 °C (Entry 12). A brief screen of solvents demonstrated that a mixture of chloroform/cyclohexane (*V* : *V* = 1 : 4) is suitable for the reaction, and other solvents such as toluene, chloroform, THF or Et₂O resulted in obvious decrease of the yield.

Table 1 Optimization of the reaction conditions for cyclization of **1a** and **4a**^a

Entry	Conditions	<i>n</i> (1a)/ <i>n</i> (4a)	Yield ^b /%
1	No catalyst, 80 °C, 5 h	1/1.4	18
2	TsOH (10 mol%), 80 °C, 5 h	1/1.4	54
3	TMSCl (10 mol%), 80 °C, 5 h	1/1.4	57
4	BF ₃ ·OEt ₂ (10 mol%), 80 °C, 5 h	1/1.4	56
5	SnCl ₄ (10 mol%), 80 °C, 5 h	1/1.4	58
6	La(OTf) ₃ (10 mol%), 80 °C, 5 h	1/1.4	60
7	La(OTf) ₃ (15 mol%), 80 °C, 5 h	1/1.4	51
8	La(OTf) ₃ (5 mol%), 80 °C, 5 h	1/1.4	44
9	La(OTf) ₃ (10 mol%), 90 °C, 5 h	1/1.4	39
10	La(OTf) ₃ (10 mol%), 70 °C, 5 h	1/1.4	47
11	La(OTf) ₃ (10 mol%), 80 °C, 4 h	1/1.4	67
12	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.4	76
13	La(OTf) ₃ (10 mol%), 80 °C, 1.5 h	1/1.4	46
14	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.2	41
15	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.3	64
16	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.5	43
17 ^c	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.4	66
18 ^d	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.4	60
19 ^e	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.4	59
20 ^f	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.4	34
21 ^g	La(OTf) ₃ (10 mol%), 80 °C, 3 h	1/1.4	52

^a Unless otherwise mentioned, solvent: chloroform/cyclohexane (*V* : *V* = 1 : 4). Catalyst load based on **1a**. ^b Isolated yield. ^c Solvent: chloroform/cyclohexane (*V* : *V* = 1 : 2). ^d Solvent: CHCl₃. ^e Solvent: toluene. ^f Solvent: THF. ^g Solvent: Et₂O.

Under the above optimized reaction conditions, compound **1a** also reacted with 3- and 2-nitrobenzaldehydes giving 1,3-imidazolidines **5ab** and **5ac** in moderate yields (Entries 2, 3, Table 2). Then, we continued investigation into the substrate scope of 2-((arylaminoethyl)aminomethyl)phenol (**1**).

thyl)phenols (**1**) by the reactions with nitrobenzaldehyde, and the substrate scope of aldehydes **4** by the reactions with compound **1b** ($R=4\text{-CH}_3$). As shown in Entries 4~12, the catalytic system was applicable to a wide range of compounds **1** bearing different R substituents, affording 1,3-imidazolidines **5** in moderate to good yields. It seems that the electronic nature and the position of the R substituent exhibit no apparent effect on the yields. Also, the results indicated that the reaction was suitable for aromatic and aliphatic aldehydes, and the reaction of aromatic aldehydes gave higher yields than those of aliphatic aldehydes. It should be noted that all reactions only gave rise to 1,3-imidazolidines **5**, and no 1,3-benzoxazines **6** was detected, providing efficient access to 1,2,3-trisubstituted 1,3-imidazolidines.

Table 2 Substrate scope for the preparation of compounds **5**^a

Entry	R (1)	R ¹ (4)	5	Yield ^b /%
1	4-CH ₃ O (1a)	4-O ₂ NC ₆ H ₄ (4a)	5aa	76
2	4-CH ₃ O (1a)	3-O ₂ NC ₆ H ₄ (4b)	5ab	50
3	4-CH ₃ O (1a)	2-O ₂ NC ₆ H ₄ (4c)	5ac	69
4	4-CH ₃ (1b)	4-O ₂ NC ₆ H ₄ (4a)	5ba	78
5	4-CH ₃ (1b)	3-O ₂ NC ₆ H ₄ (4b)	5bb	65
6	4-CH ₃ (1b)	2-O ₂ NC ₆ H ₄ (4c)	5bc	72
7	3-CH ₃ (1c)	4-O ₂ NC ₆ H ₄ (4a)	5ca	80
8	3-CH ₃ (1c)	3-O ₂ NC ₆ H ₄ (4b)	5cb	85
9	3-CH ₃ (1c)	2-O ₂ NC ₆ H ₄ (4c)	5cc	69
10	4-Cl (1d)	4-O ₂ NC ₆ H ₄ (4a)	5da	81
11	4-Cl (1d)	3-O ₂ NC ₆ H ₄ (4b)	5db	71
12	4-Cl (1d)	2-O ₂ NC ₆ H ₄ (4c)	5dc	88
13	4-CH ₃ (1b)	H (4d)	5bd	63
14 ^c	4-CH ₃ (1b)	CH ₃ (4e)	5be	58
15	4-CH ₃ (1b)	CH ₃ CH ₂ (4f)	5bf	55
16	4-CH ₃ (1b)	2-Furyl (4g)	5bg	68

^a Reaction conditions: The molar ratio of **1** to **4** is 1 : 1.4 for all reactions. La(OTf)₃: 10 mol% based on 2-((arylaminoethyl)aminomethyl)phenol (**1**). Solvent: chloroform/cyclohexane ($V : V = 1 : 4$). Reaction time: 3 h. Temperature: 80 °C. ^b Isolated yield. ^c Temperature: 25 °C, solvent: CHCl₃.

The structures of 1,3-imidazolidines **5** were all fully characterized by IR, ¹H NMR, ¹³C NMR and HRMS. This can be illustrated with compound **5ba**. In ¹H NMR spectrum, a typical singlet at δ 5.17 corresponds to the proton of NCHN moiety incorporated within the imidazolidine ring.^[33] A singlet peak at δ 2.22 corresponds to the proton of CH₃. In ¹³C NMR, the carbon of NCHN shows signal at δ 80.9, and signal at δ 20.4 for CH₃. The structure of **5ba** was further confirmed by X-ray diffraction analysis (Figure 1).^[37]

We considered that the formation of 1,3-imidazolidines **5** was probably due to the stronger nucleophilicity of the nitrogen atom compared with the oxygen atom in compound **1**. To verify this, reactions of 2-((N -substituted car-

Figure 1 Crystal structure of compound **5ba**

bamoylmethylamino)methyl)phenols **3a**~**3c** with 4-nitrobenzaldehyde (**4a**) were performed in the presence of La(OTf)₃ under 80 °C in chloroform/cyclohexane ($V : V = 1 : 4$). As expected, the reaction indeed worked smoothly to give 1,3-benzoxazines **7aa**~**7ca** in 57%~71% yields (Scheme 2). The results showed that the nitrogen atom of the amide did not take part in the cyclization reaction because of its weaker nucleophilicity, which is reduced by the strong electronegativity of the acyl group.

Reaction conditions: La(OTf)₃ (5 mol%), $n(\mathbf{3})/n(\mathbf{4}) = 1 : 1.1$, solvent: chloroform/cyclohexane ($V : V = 1 : 4$), 80 °C, 3 h.

Scheme 2 Reaction of **3** with **4** to synthesize 1,3-benzoxazine **7**

However, in sharp contrast to the reaction as shown in Scheme 1, it was found that the reaction of 2-(((2-methylphenyl)aminoethyl)amino)benzyl alcohol (**2a**)^[36] with 4-nitrobenzaldehyde **4a** gave no 1,3-imidazolidines **8aa** but 3,1-benzoxazine **9aa** in 46% yield in the presence of TMSCl (20 mol%) (Entry 2, Table 3). Though Lewis acids BF₃•OEt₂ and SnCl₄ could also catalyze the reaction to afford **9aa** in good yields, La(OTf)₃ gave the highest yield of 82% under the same reaction conditions (Entry 5). The yield was further improved to 87% with decreasing the amount of La(OTf)₃ to 10 mol%, but diminished to 85% when the catalyst loading was reduced to 5 mol% (Entry 8). Modification of the molar ratio of compound **2a** and **4a** to 1 : 1.4 gave 92% yield (Entry 10). Prolonging the reaction time did not improve the yield (Entry 13). It should be pointed out that the reaction did not work without any catalyst (Entry 1).

With the optimized reaction conditions in hand, we then explored the substrate scope of compounds **2** and aldehydes

Table 3 Optimization of the conditions for cyclization of **2a** and **4a**^a

Entry	Conditions	<i>n</i> (2a)/ <i>n</i> (4a)	Yield/% of 9aa
1	No catalyst	1/1.2	0
2	TMSCl (20 mol%)	1/1.2	46
3	BF ₃ •OEt ₂ (20 mol%)	1/1.2	51
4	SnCl ₄ (20 mol%)	1/1.2	73
5	La(OTf) ₃ (20 mol%)	1/1.2	82
6	La(OTf) ₃ (15 mol%)	1/1.2	83
7	La(OTf) ₃ (10 mol%)	1/1.2	87
8	La(OTf) ₃ (5 mol%)	1/1.2	85
9	La(OTf) ₃ (10 mol%)	1/1.3	88
10	La(OTf)₃ (10 mol%)	1/1.4	92
11	La(OTf) ₃ (10 mol%)	1/1.5	88
12 ^b	La(OTf) ₃ (10 mol%)	1/1.4	89
13 ^c	La(OTf) ₃ (10 mol%)	1/1.4	88

^a Solvent: chloroform/cyclohexane (*V* : *V* = 1 : 4), 65 °C, [38] 5 h. ^b 3 h. ^c 7 h.

4. As shown in Table 4, the catalytic system is applicable to a wide range of R substituent and various aldehydes. It is noteworthy that in all cases 1,3-imidazolidines **8** were not observed, even when R is higher electron-releasing groups of 4-methylbenzyl and 2-methoxybenzyl. Moreover, the reactions of nitrobenzaldehydes gave higher yields than aliphatic aldehydes. The position of the nitro group affected the yields in the order of *para* > *meta* > *ortho* probably due to the steric hindrance. These results clearly indicated that the reaction of 2-((aminoethyl)amino)benzyl alcohol (**2**) with aldehydes gave 3,1-benzoxazines with high chemoselectivity. This is also the first example of using La(OTf)₃ as catalyst to prepare 3,1-benzoxazines.

The structures of 3,1-benzoxazines **9** were also characterized by IR, ¹H NMR, ¹³C NMR and HRMS. As illustrated with compound **9aa** in ¹H NMR spectrum, a characteristic singlet at δ 5.83 corresponds to the proton of OCHN moiety incorporated within the benzoxazine ring. Particularly, the OCH₂Ph proton absorbs as two doublets at δ 4.79 and 4.53 instead of a singlet peak. These signals are the characteristic indicator of the formation of benzoxazine ring.^[2] In ¹³C NMR, the carbon of OCHN shows signal at δ 87.2, and signal at δ 63.1 for OCH₂Ph.

Based on the above results, we proposed a plausible

Table 4 Substrate scope for the preparation of compounds **9**^a

Entry	R (2)	R ¹ (4)	9	Yield ^b /%
1	2-CH ₃ C ₆ H ₄ (2a)	4-NO ₂ C ₆ H ₄ (4a)	9aa	92
2	2-CH ₃ C ₆ H ₄ (2a)	3-NO ₂ C ₆ H ₄ (4b)	9ab	81
3	2-CH ₃ C ₆ H ₄ (2a)	2-NO ₂ C ₆ H ₄ (4c)	9ac	77
4	4-CH ₃ C ₆ H ₄ (2b)	4-NO ₂ C ₆ H ₄ (4a)	9ba	82
5	4-CH ₃ C ₆ H ₄ (2b)	3-NO ₂ C ₆ H ₄ (4b)	9bb	72
6	4-CH ₃ C ₆ H ₄ (2b)	2-NO ₂ C ₆ H ₄ (4c)	9bc	71
7	4-ClC ₆ H ₄ (2c)	4-NO ₂ C ₆ H ₄ (4a)	9ca	90
8	4-ClC ₆ H ₄ (2c)	3-NO ₂ C ₆ H ₄ (4b)	9cb	86
9	4-ClC ₆ H ₄ (2c)	2-NO ₂ C ₆ H ₄ (4c)	9cc	66
10	C ₆ H ₅ (2d)	4-NO ₂ C ₆ H ₄ (4a)	9da	86
11	C ₆ H ₅ (2d)	3-NO ₂ C ₆ H ₄ (4b)	9db	85
12	C ₆ H ₅ (2d)	2-NO ₂ C ₆ H ₄ (4c)	9dc	68
13 ^c	2-CH ₃ C ₆ H ₄ (2a)	H (4d)	9ad	60
14	2-CH ₃ C ₆ H ₄ (2a)	CH ₃ (4e)	9ae	56
15	2-CH ₃ C ₆ H ₄ (2a)	CH ₃ CH ₂ (4f)	9af	58
16	2-CH ₃ C ₆ H ₄ (2a)	2-furyl (4g)	9ag	79
17	4-CH ₃ C ₆ H ₄ CH ₂ (2e)	H (4d)	9ed	48
18	2-CH ₃ OC ₆ H ₄ CH ₂ (2f)	H (4d)	9fd	45

^a Reaction conditions: The molar ratio of *n*(**2**) : *n*(**4**) = 1 : 1.4 for all reactions. La(OTf)₃: 10 mol% based on 2-((aminoethyl)amino) benzyl alcohol **2**. Solvent: chloroform/cyclohexane (*V* : *V* = 1 : 4). Reaction time: 5 h. Temperature: 65 °C. ^b Isolated yield. ^c Formaldehyde used. Temperature: 90 °C.

mechanism for the formation of 1,3-imidazolidine and 3,1-benzoxazine (Scheme 3). Compound **1** react with the catalyzed-activated aldehyde, followed by an elimination to give imine **A**. Because of relatively higher nucleophilicity of the nitrogen atom than oxygen, an intramolecular addition of the nitrogen to the activated N=C double bond delivers compound **B**. Finally, 1,3-imidazolidine **5** is produced by deprotonation. Similarly, imine **C** is generated from the reaction of compounds **2** with activated aldehyde after by elimination (path a). In compound **C**, the nucleophilicity of the oxygen is probably higher than N-2 due to the electron-releasing nature of the methylene group. So, the oxygen attacks the activated N=C bond leading to compound **D**. At last, elimination of a proton affords 3,1-benzoxazine **9**. Alternatively, because the nucleophilicity of the oxygen atom is close to that of N-1, the oxygen can also attack the aldehyde to form active intermediate **E** (path b). Then, nucleophilic attack by N-1 atom gives compound **F**, which undergoes deprotonation to deliver 3,1-benzoxazine **9**.

Scheme 3 Plausible mechanisms of the formation of imidazolidines and benzoxazines

3 Conclusions

In summary, we have developed Lewis acid $\text{La}(\text{OTf})_3$ -catalyzed chemoselective cyclizations of hydroxyl substituted ethylenediamine derivatives with aldehydes for the first time. This protocol shows broad substrate scope and high functional group tolerance with respect to both reaction partners, providing efficient access to diversely functionalized 1,3-imidazolidines and 3,1-benzoxazines in generally good yields. Plausible mechanisms for the formation of 1,3-imidazolidine and 3,1-benzoxazine derivatives were also proposed, and the high chemoselectivity of the reactions could be attributed to the different nucleophilicity of nitrogen and oxygen atoms in the substrates. This is also the first example of application of $\text{La}(\text{OTf})_3$ as a catalyst towards preparation of substituted 1,3-imidazolidine and 3,1-benzoxazine derivatives.

4 Experimental section

4.1 General information

Infrared spectra were recorded on a Nicolet-6700 FT-IR. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance-500 MHz spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C), using TMS as an internal standard. HRMS were recorded on a Waters UPLC/XEVOQ-TOF LC/MS instrument. Melting points were determined on a WRS-1B digital melting point instrument and were uncorrected. All solvents were dried by standard procedure. Commercially available reagents were used as received without further purification. Compounds **1** and **2** were prepared according to the Ref. [36].

4.2 General procedure for the synthesis of 1,2,3-trisubstituted imidazolidines **5**

Under nitrogen atmosphere, into a 50 mL three-necked

round bottom flask equipped with a condenser, 2-(((4-methoxyphenyl)aminoethyl)aminomethyl)phenol (**1a**) (0.27 g, 1.0 mmol), 4-nitrobenzaldehyde (0.211 g, 1.4 mmol), $\text{La}(\text{OTf})_3$ (0.059 g, 0.1 mmol), chloroform/cyclohexane (20 mL, $V:V=1:4$) were added with stirring bar. The solution was heated at 80 °C for 3 h (checked by TLC). Then, the solvent was evaporated under reduced pressure. Ethyl acetate (30 mL) was added to the residue, and the solution washed sequentially with saturated NaHSO_3 (20 mL $\times$ 3), water (30 mL $\times$ 3) and saturated brine (30 mL $\times$ 3). The organic phase was dried over Na_2SO_4 , and filtered. The filtrate was evaporated under reduced pressure, and the obtained residue was purified by silica gel flash chromatography (ethyl acetate/petroleum ether as eluents) to give red viscous oily product **5aa**.

1-(2-Hydroxybenzyl)-2-(4-nitrophenyl)-3-(4-methoxyphenyl)-1,3-imidazolidine (**5aa**): 310 mg, yield 76%. Red viscous oil; ^1H NMR (500 MHz, CDCl_3) δ : 9.63 (s, 1H), 8.19 (d, $J=8.7$ Hz, 2H), 7.50 (d, $J=8.6$ Hz, 2H), 7.20~7.23 (m, 1H), 6.95 (d, $J=7.3$ Hz, 1H), 6.85 (d, $J=8.1$ Hz, 1H), 6.81 (t, $J=7.4$ Hz, 1H), 6.77 (d, $J=9.0$ Hz, 2H), 6.40 (d, $J=8.9$ Hz, 2H), 5.12 (s, 1H), 4.00 (d, $J=13.5$ Hz, 1H), 3.82~3.83 (m, 1H), 3.77 (d, $J=13.5$ Hz, 1H), 3.69~3.73 (m, 4H), 3.28~3.33 (m, 1H), 3.05~3.09 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 152.2, 148.21, 147.4, 139.9, 129.7, 128.9, 128.6 (2C), 124.1 (2C), 121.4, 119.8, 116.6, 115.1 (2C), 113.5 (2C), 81.3, 56.9, 55.8, 50.2, 47.0; IR (KBr) ν : 3453, 3086, 1617, 1514, 1486, 1457, 1349, 1243, 1179, 813, 757 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 406.1767, found 406.1764.

1-(2-Hydroxybenzyl)-2-(3-nitrophenyl)-3-(4-methoxyphenyl)-1,3-imidazolidine (**5ab**): 200 mg, yield 50%. Red solid, m.p. 135.7~135.9 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.63 (s, 1H), 8.18~8.18 (m, 2H), 7.67 (d, $J=7.7$ Hz, 1H), 7.51~7.55 (m, 1H), 7.19~7.22 (m, 1H), 6.95 (d, $J=$

6.6 Hz, 1H), 6.79~6.84 (m, 2H), 6.75~6.77 (m, 2H), 6.39~6.42 (m, 2H), 5.09 (s, 1H), 4.00 (d, $J=13.5$ Hz, 1H), 3.86~3.89 (m, 1H), 3.76 (d, $J=13.5$ Hz, 1H), 3.67~3.71 (m, 4H), 3.31~3.34 (m, 1H), 3.04~3.08 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 152.2, 148.6, 142.5, 139.9, 133.6, 130.0, 129.6, 128.9, 123.9, 122.7, 121.3, 119.8, 116.6, 115.0 (2C), 113.6 (2C), 81.5, 56.8, 55.8, 50.2, 47.3; IR (KBr) ν : 3451, 3089, 1619, 1530, 1458, 1400, 1348, 1244, 1116, 815, 796 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 406.1767, found 406.1762.

1-(2-Hydroxybenzyl)-2-(2-nitrophenyl)-3-(4-methoxyphenyl)-1,3-imidazolidine (**5ac**): 280 mg, yield 69%. Red solid, m.p. 143.1~143.3 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.30 (s, 1H), 8.01 (d, $J=7.9$ Hz, 1H), 7.47~7.54 (m, 3H), 7.17 (t, $J=7.5$ Hz, 1H), 6.97 (d, $J=7.2$ Hz, 1H), 6.78~6.82 (m, 4H), 6.47 (d, $J=8.6$ Hz, 2H), 5.98 (s, 1H), 4.36 (d, $J=13.4$ Hz, 1H), 3.71~3.75 (m, 6H), 3.07~3.12 (m, 1H), 3.01 (d, $J=4.8$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.3, 152.1, 149.3, 139.9, 135.2, 133.6, 129.7, 129.4, 129.2, 129.1, 125.6, 121.4, 119.5, 116.5, 115.2 (2C), 113.2 (2C), 79.2, 57.5, 55.9, 47.8, 45.9; IR (KBr) ν : 3449, 3011, 1617, 1587, 1587, 1462, 1441, 1351, 1281, 1185, 810, 792 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 406.1767, found 406.1771.

1-(2-Hydroxybenzyl)-2-(4-nitrophenyl)-3-(4-methylphenyl)-1,3-imidazolidine (**5ba**): 300 mg, yield 78%. Red solid, m.p. 124.0~124.5 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.65 (s, 1H), 8.20 (d, $J=8.7$ Hz, 2H), 7.48 (d, $J=8.7$ Hz, 2H), 7.21~7.23 (m, 1H), 6.99 (d, $J=8.4$ Hz, 2H), 6.95 (d, $J=7.4$ Hz, 1H), 6.86 (d, $J=8.1$ Hz, 1H), 6.82 (t, $J=7.4$ Hz, 1H), 6.36 (d, $J=8.4$ Hz, 2H), 5.17 (s, 1H), 4.01 (d, $J=13.5$ Hz, 1H), 3.74~3.81 (m, 3H), 3.29~3.31 (m, 1H), 3.09~3.10 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 148.1, 147.2, 143.2, 129.9 (2C), 129.7, 129.0, 128.5 (2C), 127.1, 124.1 (2C), 121.4, 119.8, 116.7, 112.5 (2C), 80.9, 57.1, 50.0, 46.5, 20.4; IR (KBr) ν : 3450, 3077, 1617, 1520, 1484, 1345, 1272, 1249, 1177, 833, 761 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1815.

1-(2-Hydroxybenzyl)-2-(3-nitrophenyl)-3-(4-methylphenyl)-1,3-imidazolidine (**5bb**): 250 mg, yield 65%. Red viscous oil; ^1H NMR (500 MHz, CDCl_3) δ : 9.65 (s, 1H), 8.17 (d, $J=7.3$ Hz, 2H), 7.67 (d, $J=7.3$ Hz, 1H), 7.52~7.55 (m, $J=11.9$, 4.5 Hz, 1H), 7.22 (t, $J=7.7$ Hz, 1H), 6.96~7.00 (m, 3H), 6.80~6.86 (m, 2H), 6.39 (d, $J=8.3$ Hz, 2H), 5.17 (s, 1H), 4.01 (d, $J=13.5$ Hz, 1H), 3.81~3.90 (m, 1H), 3.74~3.78 (m, 2H), 3.31~3.36 (m, 1H), 3.06~3.10 (m, 1H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.1, 148.5, 143.2, 142.3, 133.5, 129.9, 129.9 (2C), 129.6, 128.9, 127.0, 123.8, 122.6, 121.3, 119.8, 116.6, 112.6 (2C), 81.1, 56.8, 50.0, 46.8, 20.3; IR (KBr) ν : 3419, 3084, 2925, 1614, 1528, 1487, 1274, 1094, 893, 763 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1813.

1-(2-Hydroxybenzyl)-2-(2-nitrophenyl)-3-(4-methylphenyl)-1,3-imidazolidine (**5bc**): 280 mg, yield 72%. Orange solid, m.p. 169.5~170.0 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.33 (s, 1H), 8.04 (d, $J=8.0$ Hz, 1H), 7.55 (t, $J=7.5$ Hz,

1H), 7.49 (t, $J=8.0$ Hz, 2H), 7.18 (t, $J=7.7$ Hz, 1H), 7.05 (d, $J=8.1$ Hz, 2H), 6.97 (d, $J=7.4$ Hz, 1H), 6.80 (dd, $J=17.4$, 8.2 Hz, 2H), 6.46 (d, $J=8.1$ Hz, 2H), 6.07 (s, 1H), 4.39 (d, $J=13.5$ Hz, 1H), 3.74~3.76 (m, 2H), 3.63~3.65 (m, 1H), 3.02~3.06 (m, 2H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.3, 149.1, 143.2, 135.1, 133.6, 130.1 (2C), 129.7, 129.4, 129.1, 129.1, 126.9, 125.7, 121.4, 119.5, 116.5, 112.3 (2C), 79.1, 57.6, 47.4, 45.5, 20.4; IR (KBr) ν : 3142, 3014, 1617, 1589, 1483, 1353, 1255, 1127, 837, 798 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1822.

1-(2-Hydroxybenzyl)-2-(4-nitrophenyl)-3-(3-methylphenyl)-1,3-imidazolidine (**5ca**): 310 mg, yield 80%. Orange solid, m.p. 162.5~163.5 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.65 (s, 1H), 8.20 (d, $J=8.7$ Hz, 2H), 7.47 (d, $J=8.7$ Hz, 2H), 7.21~7.24 (m, 1H), 7.05 (t, $J=7.8$ Hz, 1H), 6.96 (d, $J=7.4$ Hz, 1H), 6.87 (d, $J=8.1$ Hz, 1H), 6.82 (t, $J=7.4$ Hz, 1H), 6.58 (d, $J=7.4$ Hz, 1H), 6.28 (s, 1H), 6.22 (d, $J=8.2$ Hz, 1H), 5.22 (s, 1H), 4.00 (d, $J=13.5$ Hz, 1H), 3.77~3.81 (m, 3H), 3.27~3.30 (m, 1H), 3.08~3.11 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 148.2, 147.1, 145.4, 139.4, 129.7, 129.4, 129.1, 128.4 (2C), 124.2 (2C), 121.4, 119.9, 118.8, 116.7, 113.3, 109.7, 80.7, 57.2, 49.9, 46.3, 21.9; IR (KBr) ν : 3136, 3098, 1603, 1514, 1450, 1346, 1253, 1187, 852, 766 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1821.

1-(2-Hydroxybenzyl)-2-(3-nitrophenyl)-3-(3-methylphenyl)-1,3-imidazolidine (**5cb**): 330 mg, yield 85%. Yellow solid, m.p. 112.3~113.8 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.64 (s, 1H), 8.16~8.19 (m, 2H), 7.66 (d, $J=7.6$ Hz, 1H), 7.54 (t, $J=7.8$ Hz, 1H), 7.23 (t, $J=7.7$ Hz, 1H), 7.06 (t, $J=7.8$ Hz, 1H), 6.96 (d, $J=7.4$ Hz, 1H), 6.87 (d, $J=8.1$ Hz, 1H), 6.82 (t, $J=7.3$ Hz, 1H), 6.59 (d, $J=7.4$ Hz, 1H), 6.32 (s, 1H), 6.25 (d, $J=8.1$ Hz, 1H), 5.21 (s, 1H), 4.01 (d, $J=13.5$ Hz, 1H), 3.85~3.87 (m, 1H), 3.75~3.81 (m, 2H), 3.31~3.33 (m, 1H), 3.08~3.10 (m, 1H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 148.6, 145.4, 142.3, 139.3, 133.5, 130.0, 129.7, 129.3, 129.0, 123.9, 122.5, 121.3, 119.8, 118.9, 116.7, 113.4, 109.8, 80.9, 56.9, 49.9, 46.6, 21.9; IR (KBr) ν : 3451, 1604, 1524, 1489, 1359, 1206, 1191, 873, 771 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1814.

1-(2-Hydroxybenzyl)-2-(2-nitrophenyl)-3-(3-methylphenyl)-1,3-imidazolidine (**5cc**): 270 mg, yield 69%. Red viscous oil; ^1H NMR (500 MHz, CDCl_3) δ : 9.29 (s, 1H), 8.05~8.07 (m, 1H), 7.54~7.56 (m, 1H), 7.50~7.52 (m, 1H), 7.46 (d, $J=7.6$ Hz, 1H), 7.18 (t, $J=7.2$ Hz, 1H), 7.11 (t, $J=7.8$ Hz, 1H), 6.97 (d, $J=7.3$ Hz, 1H), 6.82 (d, $J=8.1$ Hz, 1H), 6.79 (t, $J=7.4$ Hz, 1H), 6.61 (d, $J=7.4$ Hz, 1H), 6.37 (s, 1H), 6.34 (d, $J=8.1$ Hz, 1H), 6.12 (s, 1H), 4.40 (d, $J=13.5$ Hz, 1H), 3.74~3.80 (m, 2H), 3.63~3.66 (m, 1H), 3.02~3.06 (m, 2H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 149.0, 145.3, 139.4, 134.9, 133.5, 129.6, 129.4, 129.3, 129.1, 128.9, 125.6, 121.3, 119.4, 118.7, 116.5, 112.9, 109.5, 78.9, 57.58, 47.2, 45.2, 21.8; IR (KBr) ν : 3447, 3110, 1604, 1560, 1457, 1400, 1356, 1249, 1185, 854, 755 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+$

$\text{H}]^+$ 390.1818, found 390.1815.

1-(2-Hydroxybenzyl)-2-(4-nitrophenyl)-3-(4-chlorophenyl)-1,3-imidazolidine (**5da**): 330 mg, yield 81%. Yellow solid, m.p. 126.1~126.7 °C; ^1H NMR (500 MHz, CDCl_3) δ : 8.20 (d, $J=8.6$ Hz, 2H), 7.44 (d, $J=8.6$ Hz, 2H), 7.23 (t, $J=7.2$ Hz, 1H), 7.10 (d, $J=8.9$ Hz, 2H), 6.95 (d, $J=7.4$ Hz, 1H), 6.86 (d, $J=8.0$ Hz, 1H), 6.82 (t, $J=7.4$ Hz, 1H), 6.34 (d, $J=8.9$ Hz, 2H), 5.17 (s, 1H), 3.98 (d, $J=13.4$ Hz, 1H), 3.78~3.81 (m, 2H), 3.73~3.76 (m, 1H), 3.28~3.33 (m, 1H), 3.09~3.14 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.1, 148.3, 146.5, 143.8, 129.8, 129.3 (2C), 129.1, 128.4 (2C), 124.2 (2C), 122.9, 121.2, 119.9, 116.7, 113.6 (2C), 80.8, 56.9, 49.9, 46.5; IR (KBr) ν : 3448, 3101, 1599, 1466, 1347, 1269, 1187, 832, 761 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 410.1271, found 410.1268.

1-(2-Hydroxybenzyl)-2-(3-nitrophenyl)-3-(4-chlorophenyl)-1,3-imidazolidine (**5db**): 290 mg, yield 71%. Yellow solid, m.p. 111.1~112.0 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.47 (s, 1H), 8.16~8.19 (m, 1H), 8.12 (s, 1H), 7.62 (d, $J=7.7$ Hz, 1H), 7.54 (t, $J=7.9$ Hz, 1H), 7.22 (t, $J=7.8$ Hz, 1H), 7.10 (d, $J=8.8$ Hz, 2H), 6.95 (d, $J=7.3$ Hz, 1H), 6.85 (d, $J=8.1$ Hz, 1H), 6.82 (t, $J=7.4$ Hz, 1H), 6.36 (d, $J=8.9$ Hz, 2H), 5.15 (s, 1H), 3.99 (d, $J=13.5$ Hz, 1H), 3.83~3.88 (m, 1H), 3.79 (d, $J=13.5$ Hz, 1H), 3.73 (dd, $J=15.5$, 7.1 Hz, 1H), 3.31~3.36 (m, 1H), 3.08~3.12 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.1, 148.6, 143.9, 141.6, 133.5, 130.2, 129.8, 129.3 (2C), 129.0, 124.0, 122.9, 122.5, 121.2, 119.9, 116.7, 113.7 (2C), 80.9, 56.8, 50.0, 46.8; IR (KBr) ν : 3447, 3098, 1591, 1369, 1270, 1207, 1156, 1124, 892, 757 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 410.1271, found 410.1264.

1-(2-Hydroxybenzyl)-2-(2-nitrophenyl)-3-(4-chlorophenyl)-1,3-imidazolidine (**5dc**): 360 mg, yield 88%. Yellow solid, m.p. 152.2~152.7 °C; ^1H NMR (500 MHz, CDCl_3) δ : 9.14 (s, 1H), 8.04 (d, $J=7.7$ Hz, 1H), 7.56 (d, $J=7.2$ Hz, 1H), 7.52 (d, $J=7.5$ Hz, 1H), 7.40 (d, $J=7.0$ Hz, 1H), 7.15~7.18 (m, 3H), 6.98 (d, $J=6.3$ Hz, 1H), 6.81 (d, $J=6.8$ Hz, 2H), 6.44 (d, $J=7.6$ Hz, 2H), 6.05 (s, 1H), 4.37 (d, $J=13.1$ Hz, 1H), 3.74 (d, $J=12.5$ Hz, 2H), 3.64 (s, 1H), 3.06 (d, $J=8.8$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.2, 149.2, 143.8, 134.4, 133.6, 129.9, 129.5, 129.4 (2C), 129.2, 128.8, 125.8, 122.8, 121.2, 119.6, 116.6, 113.5 (2C), 78.9, 57.5, 47.5, 45.7; IR (KBr) ν : 3452, 3012, 1596, 1483, 1349, 1226, 1187, 884, 792 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 410.1271, found 410.1274.

1-(2-Hydroxybenzyl)-3-(4-methylphenyl)-1,3-imidazolidine (**5bd**): 170 mg, yield 63%. Yellow solid, m.p. 118.7~119.1 °C; ^1H NMR (500 MHz, CDCl_3) δ : 7.21 (td, $J=7.9$, 1.6 Hz, 1H), 7.00~7.05 (m, 3H), 6.87 (dd, $J=8.1$, 0.8 Hz, 1H), 6.81 (td, $J=7.4$, 1.1 Hz, 1H), 6.41~6.43 (m, 2H), 4.08 (s, 2H), 3.95 (s, 2H), 3.46 (t, $J=6.4$ Hz, 2H), 3.12 (t, $J=6.4$ Hz, 2H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.6, 144.1, 129.8 (2C), 129.2, 128.5, 126.2, 121.4, 119.3, 116.4, 111.9 (2C), 69.8, 57.7, 52.1, 46.1, 20.3; IR (KBr) ν : 3422, 3020, 1618, 1585, 1489, 1379, 1245, 1187, 893, 753 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 269.1654, found 269.1642.

1-(2-Hydroxybenzyl)-2-methyl-3-(4-methylphenyl)-1,3-imidazolidine (**5be**): 160 mg, yield 58%. Yellow viscous oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.20 (td, $J=7.9$, 1.6 Hz, 1H), 7.05 (d, $J=8.4$ Hz, 2H), 6.93 (dd, $J=7.4$, 1.1 Hz, 1H), 6.87 (dd, $J=8.1$, 1.0 Hz, 1H), 6.78 (td, $J=7.4$, 1.1 Hz, 1H), 6.45~6.47 (m, 2H), 4.47 (q, $J=5.7$ Hz, 1H), 3.99 (d, $J=13.7$ Hz, 1H), 3.78 (d, $J=13.7$ Hz, 1H), 3.44~3.46 (m, 2H), 3.34~3.38 (m, 1H), 2.99~3.02 (m, 1H), 2.26 (s, 3H), 1.34 (d, $J=5.8$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.8, 143.7, 129.8 (2C), 129.0, 128.6, 125.8, 121.6, 119.2, 116.4, 112.2 (2C), 74.9, 57.6, 49.4, 45.1, 20.2, 18.0; IR (KBr) ν : 3421, 3039, 2921, 1618, 1590, 1487, 1382, 1254, 1188, 870, 719 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 283.1810, found 283.1816.

1-(2-Hydroxybenzyl)-2-ethyl-3-(4-methylphenyl)-1,3-imidazolidine (**5bf**): 150 mg, yield 55%. Yellow viscous oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.20~7.24 (m, 1H), 7.08 (d, $J=8.3$ Hz, 2H), 6.91 (dd, $J=14.8$, 7.7 Hz, 2H), 6.79 (t, $J=7.4$ Hz, 1H), 6.49 (d, $J=8.5$ Hz, 2H), 4.28 (dd, $J=8.1$, 3.0 Hz, 1H), 3.97 (d, $J=13.6$ Hz, 1H), 3.73 (d, $J=13.6$ Hz, 1H), 3.45~3.48 (m, 1H), 3.37~3.39 (m, 1H), 3.31~3.35 (m, 1H), 3.01~3.03 (m, 1H), 2.28 (s, 3H), 1.74~1.80 (m, 1H), 1.65 (td, $J=14.8$, 7.4 Hz, 1H), 0.98 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.7, 143.9, 129.8 (2C), 129.1, 128.7, 125.6, 121.8, 119.2, 116.3, 111.9 (2C), 81.6, 59.0, 48.9, 44.5, 25.4, 20.2, 9.4; IR (KBr) ν : 3413, 3113, 2956, 1618, 1590, 1487, 1356, 1254, 1185, 895, 719 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 297.1967, found 297.1962.

1-(2-Hydroxybenzyl)-2-(furan-2-yl)-3-(4-methylphenyl)-1,3-imidazolidine (**5bg**): 230 mg, yield 68%. Yellow viscous oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.43 (s, 1H), 7.20 (t, $J=7.7$ Hz, 1H), 7.01 (d, $J=8.3$ Hz, 2H), 6.92 (d, $J=7.3$ Hz, 1H), 6.87 (d, $J=8.1$ Hz, 1H), 6.79 (t, $J=7.4$ Hz, 1H), 6.47 (d, $J=8.4$ Hz, 2H), 6.32~6.33 (m, 1H), 6.29 (d, $J=3.2$ Hz, 1H), 5.33 (s, 1H), 3.86 (d, $J=13.7$ Hz, 1H), 3.78 (d, $J=13.7$ Hz, 1H), 3.63~3.66 (m, 1H), 3.59 (dd, $J=15.2$, 8.1 Hz, 1H), 3.24~3.27 (m, 1H), 3.10~3.13 (m, 1H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.6, 151.9, 143.4, 142.9, 129.7 (2C), 129.1, 128.7, 126.4, 121.4, 119.3, 116.4, 112.1 (2C), 110.2, 109.6, 74.5, 55.6, 49.2, 45.7, 20.3; IR (KBr) ν : 3420, 3033, 2923, 1618, 1589, 1487, 1358, 1251, 1188, 874, 755 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 335.1760, found 335.1752.

4.3 Preparation of 2-aryl-3-(arylcabamoylmethyl)-1,3-benzoxazines 7

Under nitrogen atmosphere, into a 100 mL three-necked round bottom flask equipped with a condenser, 2-(((4-methylphenyl)carbamoylmethylamino)methyl)phenol (**3a**) (0.810 g, 3.0 mmol), 4-nitrobenzaldehyde (0.498 g, 3.3 mmol), $\text{La}(\text{OTf})_3$ (0.088 g, 0.15 mmol), chloroform/cyclohexane (30 mL, $V:V=1:4$) were added. The solution was heated at 80 °C for 3 h (checked by TLC). Then, the solvent was evaporated under reduced pressure. Ethyl acetate (50 mL) was added to the residue, and the solution washed sequentially with saturated NaHSO_3 (40 mL $\times$ 3),

water (40 mL×2) and saturated brine (40 mL×2). The organic phase was dried over Na₂SO₄, and filtered. The filtrate was evaporated under reduced pressure. The obtained residue was crystallized with ethyl acetate/petroleum ether to give yellow solid product **7aa**.

3-((4-Methylphenyl)carbamoylmethyl)-2-(4-nitrophenyl)-1,3-benzoxazine (**7aa**): 780 mg, yield 64%. Yellow solid, m.p. 126.1~127.2 °C; ¹H NMR (500 MHz, CDCl₃) δ: 8.55 (s, 1H), 8.24 (d, *J*=8.7 Hz, 2H), 7.66 (d, *J*=8.7 Hz, 2H), 7.33 (d, *J*=8.3 Hz, 2H), 7.23~7.25 (m, 1H), 7.12 (d, *J*=8.3 Hz, 2H), 6.95~6.97 (m, 3H), 5.87 (s, 1H), 5.02 (d, *J*=15.0 Hz, 1H), 4.77 (d, *J*=15.0 Hz, 1H), 4.05 (d, *J*=18.0 Hz, 1H), 3.87 (d, *J*=18.0 Hz, 1H), 2.32 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ: 167.4, 148.4, 144.0, 142.3, 134.5, 134.5, 129.6 (2C), 128.7 (2C), 128.6, 125.0, 124.1 (2C), 122.8, 121.3, 119.8 (2C), 115.8, 88.7, 64.9, 55.3, 20.9; IR (KBr) ν: 3406, 3021, 2922, 1667, 1609, 1521, 1459, 1346, 1254, 853, 787 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₂N₃O₄ [M+H]⁺ 404.1610, found 404.1613.

3-((4-Methoxyphenyl)carbamoylmethyl)-2-(4-nitrophenyl)-1,3-benzoxazine (**7ba**): 890 mg, yield 71%. Yellow solid, m.p. 118.2~119.4 °C; ¹H NMR (500 MHz, CDCl₃) δ: 8.49 (s, 1H), 8.23 (d, *J*=8.6 Hz, 2H), 7.64 (d, *J*=8.6 Hz, 2H), 7.33 (d, *J*=8.9 Hz, 2H), 7.24 (dd, *J*=8.4, 3.4 Hz, 1H), 6.93~6.95 (m, 3H), 6.84 (d, *J*=8.9 Hz, 2H), 5.85 (s, 1H), 4.99 (d, *J*=15.0 Hz, 1H), 4.74 (d, *J*=15.0 Hz, 1H), 4.04 (d, *J*=18.0 Hz, 1H), 3.85 (d, *J*=18.0 Hz, 1H), 3.78 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ: 167.2, 156.8, 148.4, 144.0, 142.3, 130.6, 130.2, 128.7 (2C), 125.1, 124.2 (2C), 122.7, 121.6 (2C), 121.2, 115.7, 114.3 (2C), 88.7, 64.9, 55.5, 55.3; IR (KBr) ν: 3353, 3037, 2964, 1664, 1603, 1527, 1487, 1460, 1350, 1225, 752 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₂N₃O₅ [M+H]⁺ 420.1559, found 420.1555.

3-(Phenylcarbamoylmethyl)-2-(4-nitrophenyl)-1,3-benzoxazine (**7ca**): 670 mg, yield 57%. Yellow solid, m.p. 124.6~125.3 °C; ¹H NMR (500 MHz, CDCl₃) δ: 8.67 (s, 1H), 8.23 (d, *J*=8.7 Hz, 2H), 7.65 (d, *J*=8.6 Hz, 2H), 7.46 (d, *J*=7.7 Hz, 2H), 7.32 (t, *J*=7.9 Hz, 2H), 7.23~7.25 (m, 1H), 7.13 (t, *J*=7.4 Hz, 1H), 6.93~6.97 (m, 3H), 5.88 (s, 1H), 5.01 (d, *J*=15.0 Hz, 1H), 4.76 (d, *J*=15.0 Hz, 1H), 4.06 (d, *J*=18.0 Hz, 1H), 3.88 (d, *J*=18.1 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ: 167.5, 148.4, 143.9, 142.3, 137.1, 129.2 (2C), 128.7, 128.7 (2C), 125.1, 124.8, 124.2 (2C), 122.8, 121.5, 119.8 (2C), 115.9, 88.7, 64.9, 55.5; IR (KBr) ν: 3365, 3053, 2922, 1666, 1600, 1519, 1466, 1350, 1263, 853, 747 cm⁻¹; HRMS (ESI) calcd for C₂₂H₂₀N₃O₄ [M+H]⁺ 390.1454, found 390.1450.

4.4 Preparation of 1-(arylaminoethyl)-2-aryl-3,1-benzoxazines 9

Under nitrogen atmosphere, into a 100 mL three-necked round bottom flask equipped with a condenser, 2-(((2-methylphenyl)aminoethyl)amino)benzyl alcohol (**2a**) (0.512 g, 2.0 mmol), 4-nitrobenzaldehyde (0.423 g, 2.8 mmol), La(OTf)₃ (0.117 g, 0.2 mmol), chloroform/cyclohexane (30 mL, *V*:*V*=1:4) were added with stirring bar. The solution was heated at 65 °C for 5 h (checked by TLC). Then,

the solvent was evaporated under reduced pressure. Ethyl acetate (50 mL) was added to the residue, and the solution washed sequentially with saturated NaHSO₃ (40 mL×3), water (40 mL×2) and saturated brine (40 mL×2). The organic phase was dried over Na₂SO₄, and filtered. The filtrate was evaporated under reduced pressure, and the obtained residue purified by silica gel flash chromatography (ethyl acetate/petroleum ether as eluents) to give yellow solid product **9aa**.

1-((2-Methylphenyl)aminoethyl)-2-(4-nitrophenyl)-3,1-benzoxazine (**9aa**): 720 mg, yield 92%. Yellow solid, m.p. 108.3~110.1 °C; ¹H NMR (500 MHz, CDCl₃) δ: 8.14 (d, *J*=8.7 Hz, 2H), 7.57 (d, *J*=8.6 Hz, 2H), 7.19~7.22 (m, 1H), 7.06 (dd, *J*=16.2, 8.1 Hz, 3H), 6.82~6.86 (m, 2H), 6.65 (t, *J*=7.3 Hz, 1H), 6.50 (d, *J*=8.0 Hz, 1H), 5.83 (s, 1H), 4.79 (d, *J*=14.9 Hz, 1H), 4.53 (d, *J*=14.9 Hz, 1H), 3.85 (dt, *J*=13.9, 3.7 Hz, 1H), 3.44~3.50 (m, 1H), 3.35~3.42 (m, 2H), 2.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ: 147.9, 145.7, 145.6, 141.9, 130.3, 128.8 (2C), 128.1, 127.2, 125.1, 123.8 (2C), 123.5, 122.4, 120.2, 117.3, 116.9, 109.6, 87.7, 63.1, 51.1, 41.7, 17.4; IR (KBr) ν: 3423, 3062, 2930, 1604, 1519, 1457, 1346, 1316, 1264, 1229, 1193, 1163, 853, 788 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₄N₃O₃ [M+H]⁺ 390.1818, found 390.1815.

1-((2-Methylphenyl)aminoethyl)-2-(3-nitrophenyl)-3,1-benzoxazine (**9ab**): 630 mg, yield 81%. Yellow oil; ¹H NMR (500 MHz, CDCl₃) δ: 8.29 (s, 1H), 8.14 (d, *J*=8.1 Hz, 1H), 7.76 (d, *J*=7.7 Hz, 1H), 7.49 (t, *J*=7.9 Hz, 1H), 7.21~7.24 (m, 1H), 7.08 (dt, *J*=12.1, 6.1 Hz, 3H), 6.84~6.86 (m, 2H), 6.67 (t, *J*=7.3 Hz, 1H), 6.52 (d, *J*=8.0 Hz, 1H), 5.85 (s, 1H), 4.82 (d, *J*=15.0 Hz, 1H), 4.58 (d, *J*=13.9 Hz, 1H), 3.88 (dt, *J*=13.4, 3.8 Hz, 1H), 3.48~3.54 (m, 1H), 3.37~3.44 (m, 2H), 2.11 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ: 148.6, 145.6, 141.9, 140.9, 133.9, 130.4, 129.7, 128.1, 127.1, 125.0, 123.5, 123.4, 122.9, 122.5, 120.3, 117.3, 117.3, 109.6, 87.5, 63.1, 51.2, 41.7, 17.4; IR (KBr) ν: 3407, 3063, 2921, 1608, 1521, 1459, 1346, 1317, 1255, 1191, 853, 747 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₄N₃O₃ [M+H]⁺ 390.1818, found 390.1813.

1-((2-Methylphenyl)aminoethyl)-2-(2-nitrophenyl)-3,1-benzoxazine (**9ac**): 600 mg, yield 77%. Yellow oil; ¹H NMR (500 MHz, CDCl₃) δ: 7.68~7.70 (m, 1H), 7.42~7.44 (m, 1H), 7.34~7.36 (m, 2H), 7.15 (t, *J*=9.0 Hz, 1H), 7.04 (t, *J*=7.7 Hz, 1H), 6.99 (t, *J*=7.0 Hz, 2H), 6.74~6.76 (m, 2H), 6.61 (t, *J*=7.3 Hz, 1H), 6.51 (d, *J*=8.0 Hz, 1H), 6.44 (s, 1H), 4.66 (d, *J*=15.0 Hz, 1H), 4.29 (d, *J*=15.0 Hz, 1H), 3.84 (dt, *J*=13.6, 5.0 Hz, 1H), 3.45~3.50 (m, 1H), 3.36~3.39 (m, 2H), 2.02 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ: 149.5, 145.6, 141.7, 132.1, 132.1, 130.4, 129.8, 129.6, 128.1, 127.1, 124.9, 124.6, 122.9, 122.7, 119.8, 117.3, 116.0, 109.6, 84.7, 63.1, 51.2, 41.7, 17.4; IR (KBr) ν: 3420, 3058, 2923, 1605, 1583, 1529, 1454, 1362, 1316, 1258, 1189, 1162, 785 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₄N₃O₃ [M+H]⁺ 390.1818, found 390.1822.

1-((4-Methylphenyl)aminoethyl)-2-(4-nitrophenyl)-3,1-benzoxazine (**9ba**): 640 mg, yield 82%. Yellow oil; ¹H NMR (500 MHz, CDCl₃) δ: 8.13 (d, *J*=8.7 Hz, 2H), 7.55

(d, $J=8.6$ Hz, 2H), 7.19 (dd, $J=8.4$, 3.4 Hz, 1H), 7.01 (d, $J=8.2$ Hz, 1H), 6.95 (d, $J=8.1$ Hz, 2H), 6.82 (d, $J=3.4$ Hz, 2H), 6.46 (d, $J=8.2$ Hz, 2H), 5.80 (s, 1H), 4.78 (d, $J=14.9$ Hz, 1H), 4.52 (d, $J=14.9$ Hz, 1H), 3.75 (dt, $J=13.9$, 3.8 Hz, 1H), 3.37~3.42 (m, 1H), 3.29~3.34 (m, 2H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 147.9, 145.8, 145.4, 141.9, 129.9 (2C), 128.8 (2C), 128.0, 127.1, 124.9, 123.8 (2C), 123.3, 120.0, 116.7, 113.2 (2C), 87.7, 63.1, 51.0, 42.2, 20.4; IR (KBr) ν : 3406, 3060, 2922, 1609, 1521, 1459, 1346, 1317, 1254, 1191, 853, 787 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1821.

1-((4-Methylphenyl)aminoethyl)-2-(3-nitrophenyl)-3,1-benzoxazine (**9bb**): 560 mg, yield 72%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 8.20~8.26 (m, 1H), 8.13 (d, $J=8.0$ Hz, 1H), 7.73 (d, $J=8.1$ Hz, 1H), 7.48 (t, $J=7.9$ Hz, 1H), 7.20 (dt, $J=8.5$, 3.3 Hz, 1H), 7.03 (d, $J=8.2$ Hz, 1H), 6.95 (d, $J=8.1$ Hz, 2H), 6.83 (d, $J=3.3$ Hz, 2H), 6.48 (d, $J=8.3$ Hz, 2H), 5.81 (s, 1H), 4.80 (d, $J=14.9$ Hz, 1H), 4.55 (d, $J=14.9$ Hz, 1H), 3.77 (dt, $J=13.3$, 3.8 Hz, 1H), 3.39~3.44 (m, 1H), 3.28~3.35 (m, 2H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 148.6, 145.3, 141.8, 140.9, 133.8, 129.9 (2C), 129.6, 128.0, 127.1, 124.9, 123.4, 123.2, 122.9, 120.0, 116.9, 113.2 (2C), 87.6, 63.1, 50.9, 42.1, 20.4; IR (KBr) ν : 3402, 3055, 2923, 1611, 1582, 1527, 1459, 1349, 1256, 1200, 807, 755 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1812.

1-((4-Methylphenyl)aminoethyl)-2-(2-nitrophenyl)-3,1-benzoxazine (**9bc**): 550 mg, yield 71%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.66 (dd, $J=8.4$, 3.3 Hz, 1H), 7.37~7.39 (m, 1H), 7.32~7.34 (m, 2H), 7.08~7.12 (m, 1H), 6.85~6.91 (m, 3H), 6.71 (t, $J=6.0$ Hz, 2H), 6.43 (d, $J=8.3$ Hz, 2H), 6.33 (s, 1H), 4.64 (d, $J=15.0$ Hz, 1H), 4.27 (d, $J=15.0$ Hz, 1H), 3.69 (dt, $J=13.5$, 5.1 Hz, 1H), 3.32~3.38 (m, 1H), 3.21~3.29 (m, 2H), 2.14 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 149.5, 145.4, 141.6, 132.2, 132.1, 129.7 (2C), 129.8, 129.5, 128.0, 127.0, 124.9, 124.5, 122.9, 119.7, 116.1, 113.4 (2C), 84.7, 63.2, 51.1, 42.2, 20.4; IR (KBr) ν : 3409, 3061, 2922, 1610, 1581, 1526, 1456, 1361, 1253, 1187, 787 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 390.1818, found 390.1823.

1-((4-Chlorophenyl)aminoethyl)-2-(4-nitrophenyl)-3,1-benzoxazine (**9ca**): 740 mg, yield 90%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 8.16 (d, $J=8.6$ Hz, 2H), 7.57 (d, $J=8.6$ Hz, 2H), 7.20 (t, $J=7.4$ Hz, 1H), 7.09 (d, $J=8.7$ Hz, 2H), 7.01 (d, $J=8.2$ Hz, 1H), 6.79~6.88 (m, 2H), 6.46 (d, $J=8.7$ Hz, 2H), 5.79 (s, 1H), 4.79 (d, $J=15.0$ Hz, 1H), 4.53 (d, $J=13.9$ Hz, 1H), 3.79 (dt, $J=13.2$, 3.7 Hz, 1H), 3.38~3.44 (m, 1H), 3.26~3.37 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 147.82, 146.14, 145.50, 141.55, 129.09 (2C), 128.6 (2C), 127.9, 124.9, 123.7 (2C), 123.4, 122.2, 120.2, 116.9, 113.9 (2C), 87.6, 62.9, 50.9, 41.8; IR (KBr) ν : 3421, 3055, 2925, 1600, 1520, 1498, 1460, 1346, 1316, 813, 749 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 410.1271, found 410.1267.

1-((4-Chlorophenyl)aminoethyl)-2-(3-nitrophenyl)-3,1-benzoxazine (**9cb**): 710 mg, yield 86%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 8.23 (s, 1H), 8.04 (d, $J=7.8$

Hz, 1H), 7.70 (d, $J=7.7$ Hz, 1H), 7.41 (t, $J=7.9$ Hz, 1H), 7.16 (dd, $J=8.3$, 3.3 Hz, 1H), 7.00 (t, $J=8.6$ Hz, 3H), 6.79 (d, $J=3.3$ Hz, 2H), 6.40 (d, $J=8.7$ Hz, 2H), 5.77 (s, 1H), 4.76 (d, $J=14.9$ Hz, 1H), 4.53 (d, $J=14.9$ Hz, 1H), 3.73 (dt, $J=13.1$, 3.8 Hz, 1H), 3.32~3.37 (m, 1H), 3.20~3.31 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 148.6, 146.4, 141.8, 140.9, 133.9, 129.8, 129.2 (2C), 128.1, 125.1, 123.5, 123.4, 122.9, 122.0, 120.3, 116.9, 114.1 (2C), 87.7, 63.2, 50.8, 41.9; IR (KBr) ν : 3416, 3056, 2933, 1601, 1529, 1499, 1460, 1396, 1348, 1254, 791 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 410.1271, found 410.1266.

1-((4-Chlorophenyl)aminoethyl)-2-(2-nitrophenyl)-3,1-benzoxazine (**9cc**): 540 mg, yield 66%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.69 (dd, $J=5.9$, 3.3 Hz, 1H), 7.43~7.45 (m, 1H), 7.38 (dd, $J=5.5$, 3.5 Hz, 2H), 7.16 (t, $J=7.0$ Hz, 1H), 7.05 (d, $J=8.7$ Hz, 2H), 6.96 (d, $J=8.2$ Hz, 1H), 6.74~6.83 (m, 2H), 6.45 (d, $J=8.7$ Hz, 2H), 6.38 (s, 1H), 4.69 (d, $J=15.0$ Hz, 1H), 4.35 (d, $J=15.0$ Hz, 1H), 3.74 (dt, $J=13.3$, 5.0 Hz, 1H), 3.35~3.39 (m, 1H), 3.23~3.32 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 149.4, 146.4, 141.6, 132.2, 131.9, 129.8, 129.6, 129.2 (2C), 128.1, 125.0, 123.5, 123.0, 122.1, 120.0, 116.3, 114.3 (2C), 84.8, 63.3, 50.8, 41.9; IR (KBr) ν : 3413, 3061, 2950, 1601, 1530, 1499, 1397, 1362, 1253, 1184, 817, 792 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 410.1271, found 410.1275.

1-(Phenylaminoethyl)-2-(4-nitrophenyl)-3,1-benzoxazine (**9da**): 580 mg, yield 86%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 8.10 (d, $J=8.8$ Hz, 2H), 7.52 (d, $J=8.5$ Hz, 2H), 7.17 (dt, $J=8.5$, 3.3 Hz, 1H), 7.11 (t, $J=7.9$ Hz, 2H), 6.98 (d, $J=8.2$ Hz, 1H), 6.80 (d, $J=6.0$ Hz, 2H), 6.66 (t, $J=7.3$ Hz, 1H), 6.50 (d, $J=7.8$ Hz, 2H), 5.78 (s, 1H), 4.76 (d, $J=14.9$ Hz, 1H), 4.50 (d, $J=14.9$ Hz, 1H), 3.73 (dt, $J=13.1$, 5.3 Hz, 1H), 3.36~3.41 (m, 1H), 3.26~3.34 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 147.9, 147.7, 145.8, 141.9, 129.4 (2C), 128.8 (2C), 128.0, 125.0, 123.8 (2C), 123.3, 120.1, 117.8, 116.8, 113.0 (2C), 87.7, 63.1, 50.9, 41.8; IR (KBr) ν : 3413, 3027, 1603, 1520, 1400, 1346, 1190, 794 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 376.1661, found 376.1656.

1-(Phenylaminoethyl)-2-(3-nitrophenyl)-3,1-benzoxazine (**9db**): 570 mg, yield 85%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 8.26 (s, 1H), 8.11 (ddd, $J=8.1$, 5.6, 1.7 Hz, 1H), 7.72 (dd, $J=7.8$, 0.7 Hz, 1H), 7.46 (t, $J=7.9$ Hz, 1H), 7.19 (dt, $J=8.6$, 3.3 Hz, 1H), 7.11~7.14 (m, 2H), 7.02 (d, $J=8.2$ Hz, 1H), 6.82 (d, $J=3.2$ Hz, 2H), 6.68 (t, $J=7.3$ Hz, 1H), 6.52 (dd, $J=8.5$, 0.9 Hz, 2H), 5.80 (s, 1H), 4.79 (d, $J=14.9$ Hz, 1H), 4.55 (d, $J=14.9$ Hz, 1H), 3.76 (dt, $J=8.7$, 3.7 Hz, 1H), 3.38~3.42 (m, 1H), 3.29~3.36 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 148.6, 147.7, 141.9, 140.9, 133.9, 129.7, 129.4 (2C), 128.1, 125.0, 123.5, 123.3, 122.9, 120.1, 117.8, 116.9, 113.0 (2C), 87.6, 63.2, 50.9, 41.8; IR (KBr) ν : 3413, 3018, 1604, 1529, 1500, 1459, 1399, 1349, 1089, 790 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 376.1661, found 376.1657.

1-(Phenylaminoethyl)-2-(2-nitrophenyl)-3,1-benzoxazine (**9dc**): 460 mg, yield 68%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.72~7.74 (m, 1H), 7.45~7.47 (m, 1H), 7.39~

7.41 (m, 2H), 7.14~7.22 (m, 3H), 6.98 (d, $J=8.2$ Hz, 1H), 6.75~6.80 (m, 2H), 6.70 (t, $J=7.3$ Hz, 1H), 6.57 (d, $J=8.2$ Hz, 2H), 6.41 (s, 1H), 4.72 (d, $J=15.0$ Hz, 1H), 4.36 (d, $J=15.0$ Hz, 1H), 3.77 (dt, $J=13.3, 5.1$ Hz, 1H), 3.40~3.46 (m, 1H), 3.32~3.38 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 149.5, 147.7, 141.6, 132.1, 132.1, 129.8, 129.5, 129.4 (2C), 128.0, 124.9, 124.5, 122.9, 119.8, 117.8, 116.1, 113.2 (2C), 83.7, 63.3, 51.0, 41.8; IR (KBr) ν : 3414, 3014, 1617, 1529, 1501, 1400, 794 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 376.1661, found 376.1667.

1-((2-Methylphenyl)aminoethyl)-3,1-benzoxazine (**9ad**): 320 mg, yield 60%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.06 (dd, $J=13.7, 6.7$ Hz, 2H), 6.98 (d, $J=7.2$ Hz, 1H), 6.82 (d, $J=7.9$ Hz, 2H), 6.77 (t, $J=7.4$ Hz, 1H), 6.60 (t, $J=7.3$ Hz, 1H), 6.54 (d, $J=8.0$ Hz, 1H), 4.79 (s, 2H), 4.60 (s, 2H), 3.51 (t, $J=5.7$ Hz, 2H), 3.25 (t, $J=5.7$ Hz, 2H), 2.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 146.1, 143.9, 130.3, 127.6, 127.2, 125.3, 124.5, 122.7, 120.3, 117.5, 117.3, 109.9, 81.0, 67.9, 52.1, 41.9, 17.6; IR (KBr) ν : 3414, 3021, 1607, 1584, 1510, 1454, 1400, 1334, 1263, 794 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 269.1654, found 269.1651.

1-((2-Methylphenyl)aminoethyl)-2-methyl-3,1-benzoxazine (**9ae**): 320 mg, yield 56%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.08~7.13 (m, 2H), 7.02 (d, $J=7.2$ Hz, 1H), 6.89 (dd, $J=9.5, 4.1$ Hz, 1H), 6.80 (td, $J=7.5, 0.8$ Hz, 1H), 6.64 (td, $J=7.4, 0.7$ Hz, 1H), 6.57 (d, $J=8.0$ Hz, 1H), 4.85 (s, 2H), 4.80 (q, $J=6.0$ Hz, 1H), 3.62 (dt, $J=15.0, 5.9$ Hz, 1H), 3.53 (dt, $J=15.0, 6.1$ Hz, 1H), 3.29 (td, $J=6.0, 1.7$ Hz, 2H), 2.07 (s, 3H), 1.43 (d, $J=6.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 145.9, 143.1, 130.1, 127.4, 126.9, 124.7, 123.7, 122.4, 119.4, 116.9, 116.8, 109.5, 84.3, 64.5, 48.5, 41.7, 18.5, 17.4; IR (KBr) ν : 3419, 2928, 2850, 1605, 1584, 1499, 1457, 1402, 1368, 1322, 1261, 1230, 1176, 1135, 748 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 283.1810, found 283.1801.

1-((2-Methylphenyl)aminoethyl)-2-ethyl-3,1-benzoxazine (**9af**): 340 mg, yield 58%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.09~7.15 (m, 2H), 7.04 (d, $J=7.2$ Hz, 1H), 6.91~6.93 (m, 2H), 6.82 (t, $J=7.4$ Hz, 1H), 6.65 (t, $J=7.3$ Hz, 1H), 6.59 (d, $J=8.0$ Hz, 1H), 4.86 (dd, $J=35.7, 14.9$ Hz, 2H), 4.54 (t, $J=6.6$ Hz, 1H), 4.12 (s, 1H), 3.71 (dt, $J=14.7, 5.1$ Hz, 1H), 3.47~3.52 (m, 1H), 3.31 (d, $J=5.4$ Hz, 2H), 2.08 (s, 3H), 1.70~1.81 (m, 2H), 0.97 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 145.9, 142.7, 130.0, 127.3, 126.9, 124.7, 123.9, 122.4, 119.5, 117.5, 116.9, 109.6, 89.2, 63.2, 50.2, 41.6, 24.6, 17.3, 9.4; IR (KBr) ν : 3378, 2965, 1605, 1585, 1511, 1458, 1321, 1261, 1226, 749 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 297.1967, found 297.1960.

1-((2-Methylphenyl)aminoethyl)-2-(furan-2-yl)-3,1-benzoxazine (**9ag**): 530 mg, yield 79%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.34 (d, $J=1.0$ Hz, 1H), 7.06~7.11 (m, 2H), 7.01 (d, $J=7.2$ Hz, 1H), 6.88 (d, $J=8.1$ Hz, 1H), 6.75~6.79 (m, 2H), 6.63 (td, $J=7.4, 0.8$ Hz, 1H), 6.54 (d, $J=7.8$ Hz, 1H), 6.22 (dd, $J=3.2, 1.8$ Hz, 1H), 6.18 (d, $J=3.3$ Hz, 1H), 5.74 (s, 1H), 4.71 (d, $J=14.7$ Hz, 1H), 4.57 (d,

$J=14.7$ Hz, 1H), 3.71 (dt, $J=14.7, 5.0$ Hz, 1H), 3.42~3.45 (m, 1H), 3.30~3.33 (m, 2H), 2.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 150.9, 145.5, 142.9, 141.9, 130.0, 127.5, 126.9, 124.5, 122.5, 122.3, 118.9, 116.9, 115.0, 110.1, 109.9, 109.5, 83.0, 63.1, 50.3, 41.5, 17.2; IR (KBr) ν : 3419, 2926, 2852, 1605, 1585, 1503, 1456, 1365, 1322, 1261, 1227, 1143, 747 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 335.1760, found 335.1751.

1-((4-Methylbenzyl)aminoethyl)-3,1-benzoxazine (**9ed**): 270 mg, yield 48%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.22 (d, $J=7.8$ Hz, 2H), 7.11~7.17 (m, 3H), 6.90 (d, $J=7.5$ Hz, 1H), 6.79 (dd, $J=12.3, 7.8$ Hz, 2H), 4.87 (s, 2H), 4.72 (s, 2H), 3.53 (s, 2H), 3.45 (t, $J=7.1$ Hz, 2H), 2.64 (t, $J=7.1$ Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 143.8, 136.4, 135.6, 128.8 (2C), 128.8 (2C), 127.3, 124.7, 122.9, 118.7, 115.3, 80.8, 67.8, 55.4, 49.9, 42.5, 21.0; IR (KBr) ν : 3415, 1612, 1501, 1456, 1400, 794 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 283.1810, found 283.1818.

1-((2-Methoxybenzyl)aminoethyl)-3,1-benzoxazine (**9fd**): 270 mg, yield 45%. Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 7.30 (dd, $J=7.4, 1.5$ Hz, 1H), 7.20~7.23 (m, 1H), 7.09 (dd, $J=11.5, 3.9$ Hz, 1H), 6.84~6.92 (m, 3H), 6.76~6.80 (m, 2H), 4.84 (s, 2H), 4.70 (s, 2H), 3.80 (s, 3H), 3.56 (s, 2H), 3.46 (t, $J=7.1$ Hz, 2H), 2.65 (t, $J=7.1$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 157.6, 143.8, 130.5, 128.1, 127.3, 126.6, 124.8, 122.9, 120.1, 118.6, 115.3, 110.2, 80.9, 67.9, 55.8, 55.2, 49.9, 42.9; IR (KBr) ν : 3414, 3009, 1609, 1494, 1400, 1242, 1107, 753 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 299.1760, found 299.1751.

Supporting Information ^1H NMR and ^{13}C NMR spectra of compounds. The Supporting Information is available free of charge via the Internet at <http://sioc-journal.cn>.

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