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PAPER

Construction of functionalized 2,3-dihydro-1,4-benzoxazines *via* [5 + 1] annulations of 2-halo-1,3-dicarbonyl compounds with imines†

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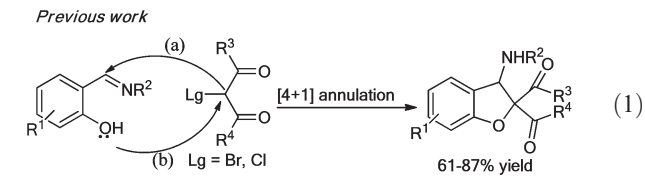
A series of functionalized 2,3-dihydro-1,4-benzoxazines were obtained in moderate to excellent yields *via* domino [5 + 1] annulations of 2-halo-1,3-dicarbonyl compounds **2** with imines **1** under mild conditions and the application of this method in the synthesis of bioactive analogues, such as functionalized tetracyclic-1,4-benzoxazines which contain two new heterocyclic rings and one quaternary carbon center has also been developed.

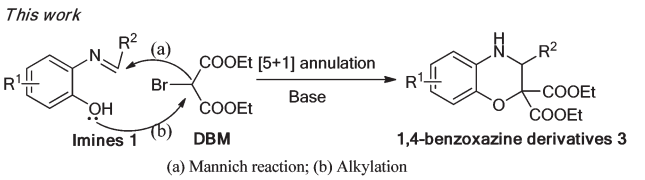
Introduction

2,3-Dihydro-1,4-benzoxazines are an important class of heterocyclic molecules, principally because this heterocyclic ring is an important recognition element in many natural products,[1] biologically active and medicinally significant compounds.[2] Natural products and pharmaceuticals possessing the 1,4-benzoxazine skeleton exhibit a wide range of biological activities.[3–11] For example, 1,4-benzoxazine derivatives are potential drugs for treating infections,[3] heart disease,[4] diabetes,[5] neurodegenerative,[7,8] inflammatory,[7,8] autoimmune[7,8] and cardiovascular disorders.[7,8] Some additional biologically active 1,4-benzoxazines have also been described in a broader-context review.[11] Due to the importance of 1,4-benzoxazines, different approaches towards the synthesis of 2-amino-2-chromene derivatives have been reported over the past few decades, and 1,4-benzoxazin derivatives are often achieved from substituted 2-aminophenols or substituted 2-nitrophenols.[12,13] However, most of the reported methods have one or more of the following drawbacks: such as low yields owing to the somewhat lengthy, toxic catalysts used, complicated reaction assembly, and tedious workup *etc.* As part of our medicinal chemistry research program, we required a robust facile synthesis of 1,4-benzoxazine derivatives wherein we could vary the different substitutions. Herein we report an efficient, mild, and convenient method for the preparation of these derivatives *via* [5 + 1] annulation (Mannich–alkylation). Notably, we also present the first asymmetric [5 + 1] annulation (Mannich–alkylation) of diethyl α-bromomalonate (DBM) with imines **1** with moderate to good enantioselectivities catalyzed by readily available chiral phase-transfer catalysts (PTC).

In the course of our investigation on the use of 2-halo-1,3-dicarbonyl compounds (*e.g.* diethyl α-bromomalonate and diethyl α-chloromalonate) in organic synthesis, the 2-halo-1,3-dicarbonyl compounds turned out to be highly reactive and versatile. Especially, the bromo or chloro group could behave as a better leaving group in the reaction. Recently, a series of functionalized 2,3-dihydrobenzofurans were easily obtained in moderate to excellent yields under mild conditions from 2-halo-1,3-dicarbonyl compounds in our group (eqn (1)).[14] Encouraged by the successful results mentioned above, we conceived that 1,4-benzoxazine derivatives **3** could be synthesized *via* the [5 + 1] annulations of diethyl α-bromomalonate (DBM) with imines **1** (eqn (2)).



(1)



(2)

Results and discussion

The initial investigation started with the reaction of (*E*)-2-(benzylideneamino)phenol **1a** with diethyl α-bromomalonate (DBM)

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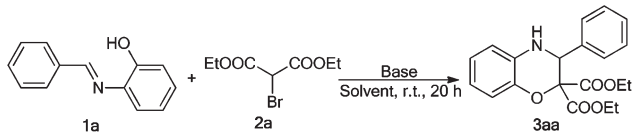
Table 1 Reaction of (*E*)-2-(benzylideneamino)phenol **1a** and diethyl α-bromomalonate **2a** under different conditions[a]



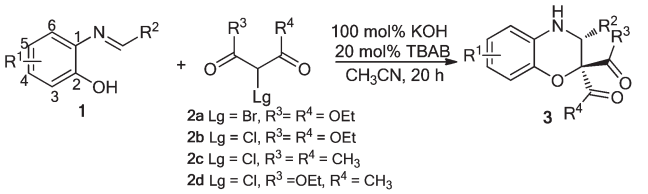
Entry	Base	Solvent	Yield[b] (%)
1	DBU	CH_3CN	83
2	DABCO	CH_3CN	0
3[c]	KOAc	CH_3CN	63
4[c]	K_2CO_3	CH_3CN	78
5[c]	**KOH**	**CH_3CN**	**87**
6[c]	KOH	Toluene	65
7[c]	KOH	DCM	74
8[c]	KOH	DMSO	21
9[c]	KOH	Ethanol	3
10[c]	KOH	H_2O	0

[a] Otherwise noted, the reactions performed with 0.10 mmol of **1a**, 0.20 mmol of **2a**, 100 mol% of base in 1 mL solvent at room temperature. [b] Isolated yield. [c] 20 mol% of TBAB was used.

2a. As could have been expected, the domino reaction proceeded to provide desired product **3aa** in good yield when the reaction was carried out in the presence of DBU (1,8-diazabicyclo[5,4,0]-undec-7-ene) in CH_3CN at room temperature for 20 h (83% yield, Table 1, entry 1). Other bases such as KOAc and K_2CO_3, were also screened and moderate yields were obtained (entries 3–4). Weaker base DABCO (1,4-diazabicyclo[2.2.2]octane) was inert in this reaction (entry 2). On the contrary, the best result was obtained when the reaction was catalyzed with stronger base KOH (87% yield, entry 5). Subsequently, we investigated the effects of solvent on the reactivity. Low yields were obtained, when other solvents, such as toluene and DCM, were used (entries 6–7). When the reaction was carried out in strong polar solvents, poor results were achieved due to decomposition of imine **1a** (entries 8–10). Based on the above screening, the optimal reaction conditions (1.0 equiv **1a** and 2.0 equiv **2a** in CH_3CN with 1 equiv KOH and 0.2 equiv TBAB, room temperature) were established.

With the optimal reaction conditions in hand, the scope of the domino [5 + 1] annulation of 2-halo-1,3-dicarbonyl compounds **2** with imines **1** was explored (Table 2). To assess the impact of the structural and functional motifs on the reaction, we tested a range of imines **1**. For all cases, 2-halo-1,3-dicarbonyl compounds **2** reacted with imines **1** led to the corresponding substituted 2,3-dihydro-1,4-benzoxazines **3** in moderate to good yields. High yields were obtained in [5 + 1] annulation of diethyl α-bromomalonate (DBM) **2a** with electron-withdrawing substituents on the aryl ring of imines **1** (Table 2, entries 6–12 and 15–16). On the contrary, electron-donating substituents on the aryl ring of imines **1** tended to decrease the reactivity and yields (entries 2–5 and 13–14). Imines **1** with electron-withdrawing substituents or electron-donating substituents on the *ortho*, *meta* or *para* positions (R^2) afforded 2,3-dihydro-1,4-benzoxazines **3** with slightly inferior yields (entries 3–5 and 6–8). The reaction with aliphatic imine **1q** gave desired product **3qa** in moderate yield (entry 17). To extend the scope of the domino

Table 2 Synthesis of different substituted 2,3-dihydro-1,4-benzoxazines[a]



Entry	R^1	R^2 (**1**)	**2**	Yield[b] (%) (**3**)
1	H	Ph (**1a**)	**2a**	87 (**3aa**)
2	H	*p*-$CH_3C_6H_4$ (**1b**)	**2a**	72 (**3ba**)
3	H	*p*-$CH_3OC_6H_4$ (**1c**)	**2a**	71 (**3ca**)
4	H	*o*-$CH_3OC_6H_4$ (**1d**)	**2a**	69 (**3da**)
5	H	*m*-$CH_3OC_6H_4$(**1e**)	**2a**	67 (**3ea**)
6	H	*p*-ClC_6H_4(**1f**)	**2a**	83 (**3fa**)
7	H	*m*-ClC_6H_4 (**1g**)	**2a**	81 (**3ga**)
8	H	*o*-ClC_6H_4 (**1h**)	**2a**	81 (**3ha**)
9	H	*p*-BrC_6H_4 (**1i**)	**2a**	86 (**3ia**)
10	H	*o*-BrC_6H_4 (**1j**)	**2a**	79 (**3ja**)
11	H	*p*-$NO_2C_6H_4$ (**1k**)	**2a**	81 (**3ka**)
12	H	*o*-$NO_2C_6H_4$ (**1l**)	**2a**	75 (**3la**)
13	4-Me	Ph (**1m**)	**2a**	76 (**3ma**)
14	5-Me	Ph (**1n**)	**2a**	73 (**3na**)
15	4-Cl	Ph (**1o**)	**2a**	82 (**3oa**)
16	5-Cl	Ph (**1p**)	**2a**	85 (**3pa**)
17[c]	H	C_2H_5 (**1q**)	**2a**	51 (**3qa**)
18	H	Ph (**1a**)	**2b**	83 (**3ab**)
19	H	Ph (**1a**)	**2c**	56 (**3ac**)
20	H	Ph (**1a**)	**2d**	53 (dr 66 : 34)[d] (**3ad**)

[a] Otherwise noted, the reactions performed with 0.10 mmol of **1**, 0.20 mmol of **2**, 20 mol% of TBAB, 100 mol% of KOH in 1 mL of CH_3CN at room temperature. [b] Isolated yield. [c] 0.10 mmol of propanal, 0.10 mmol of 2-aminophenol and 4 Å MS (10.0 mg) were stirred in 1 mL of CH_2Cl_2 under N_2 for 1 h, then 0.10 mmol of **2a**, 20 mol% of TBAB, 100 mol% of KOH were added. [d] Determined by ^1H NMR.

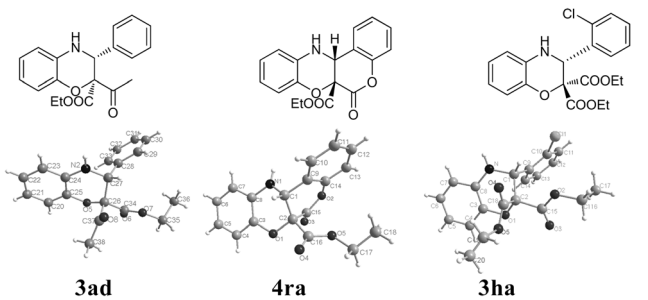
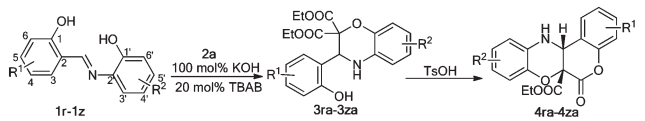


Fig. 1 X-ray crystal structures of **3ad**, **4ra** and enantiopure **3ha**.

reaction further, other 2-halo-1,3-dicarbonyl compounds **2b–2d** which also contain a good leaving group (Cl), were utilized as nucleophiles in the [5 + 1] annulation under the same conditions (entries 18–20). A good yield was obtained when the domino reaction of imine **1a** with diethyl α-chloromalonate **2b** (entry 18), while 2-halo-1,3-dicarbonyl compounds **2c–2d** afforded 2,3-dihydro-1,4-benzoxazines **3ac–3ad** in moderate yields (entries 19–20). The relative stereochemistry of products **3aa–3ad** was established by a single crystal X-ray diffraction study of compound **3ad** (Fig. 1).

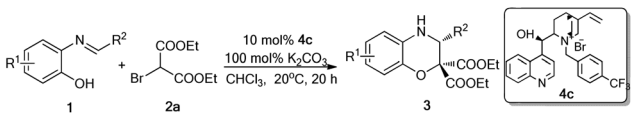
Table 3 Synthesis of different tetracyclic 2,3-dihydro-1,4-benzoxazines[a]



Entry	R^1	R^2	(1)	Product 4	Yield[b] (%)	dr[c]
1	H	H	(**1r**)	(**4ra**)	61	>99 : 1
2	H	4′-Me	(**1s**)	(**4sa**)	63	>99 : 1
3	H	5′-Me	(**1t**)	(**4ta**)	46	>99 : 1
4	H	4′-Cl	(**1u**)	(**4ua**)	56	>99 : 1
5	H	5′-Cl	(**1v**)	(**4va**)	45	60 : 40
6	5-OMe	H	(**1w**)	(**4wa**)	66	>99 : 1
7	4-Me	H	(**1x**)	(**4xa**)	74	>99 : 1
8	4-Cl	H	(**1y**)	(**4ya**)	48	>99 : 1
9	4-Br	H	(**1z**)	(**4za**)	47	>99 : 1

[a] Otherwise noted, the reactions performed with 0.10 mmol of **1**, 0.20 mmol of **2a**, 20 mol% of TBAB, 100 mol% of KOH in 1 mL of CH_3CN at room temperature to afford **3**. Then 0.10 mmol of **3** and 10 mol% of *p*-toluenesulfonic acid were refluxed in toluene for 2 h to generate **4**. [b] Isolated yield for two steps. [c] Determined by ^1H NMR.

Table 4 Asymmetric synthesis of differently substituted 2,3-dihydro-1,4-benzoxazines[a]



Entry	R^1	R^2	(1)	Product 3	Yield[b] (%)	ee[c] (%)
1	H	Ph	(**1a**)	**3aa**	66	81
2	H	*p*-$CH_3C_6H_4$	(**1b**)	**3ba**	51	60
3	H	*p*-$CH_3OC_6H_4$	(**1c**)	**3ca**	48	61
4	H	*p*-ClC_6H_4	(**1f**)	**3fa**	62	30
5	H	*o*-ClC_6H_4	(**1h**)	**3ha**	70	63
6	H	*o*-BrC_6H_4	(**1j**)	**3ja**	65	44
7	4-Me	Ph	(**1m**)	**3ma**	63	62
8	5-Me	Ph	(**1n**)	**3na**	57	60
9	5-Cl	Ph	(**1p**)	**3pa**	61	54

[a] Otherwise noted, the reactions performed with 0.10 mmol of **1**, 0.20 mmol of **2a**, 10 mol% of **4c**, 100 mol% of K_2CO_3 in 1 mL of CH_3Cl at 20 °C. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Development of novel synthetic methods for the construction of new analogues of bioactive heterocyclic compounds represents a major challenge in synthetic organic and medicinal chemistry. Having succeeded in synthesizing 2,3-dihydro-1,4-benzoxazines, we considered that 1,4-benzoxazines fused to coumarins provide new analogues of bioactive heterocyclic compounds that might have important biological and pharmaceutical activities. Thus, we turned our attention to the possible synthesis of tetracyclic 2,3-dihydro-1,4-benzoxazines **4ra–4za** from functionalized imines **1r–1z**. However, no tetracyclic 2,3-dihydro-1,4-benzoxazine **4ra** but 2,3-dihydro-1,4-benzoxazine **3ra** was isolated under the above optimal reaction conditions. Fortunately, tetracyclic 2,3-dihydro-1,4-benzoxazine **4ra** was obtained in good yield when 2,3-dihydro-1,4-benzoxazine **3ra** was treated with *p*-toluenesulfonic acid in toluene. Then the scope of the [5 + 1] annulation was extended to various imines **1** and diethyl α-bromomalonate **2a**. The reaction scopes proved to be broad with respect to imines and the novel transformations were highly diastereoselective. It appeared that substituents' electronics have a minimal impact on efficiencies of the [5 + 1] annulation. Good yields were obtained in the [5 + 1] annulation of diethyl α-bromomalonate **2a** with electron-donating substituent on the aryl ring of imines **1** (Table 3, entries 2, 6, 7). This method features the creation of two new heterocyclic rings and one quaternary carbon center in a simple procedure. The relative stereochemistry of products was also established by a single crystal X-ray diffraction study of compound **4ra** (Fig. 1).

Catalytic asymmetric construction of 1,4-benzoxazines is somewhat difficult, and optically active 1,4-benzoxazines are mostly constructed by the asymmetric reduction of imines in the literature.[15] Therefore, there is an eager desire for a new synthetic method that allows the easy preparation of chiral 1,4-benzoxazines with good feasibility to assemble various substitution patterns. Herein we present a new organocatalytic enantioselective [5 + 1] annulation of diethyl α-bromomalonate with imines **1** to afford chiral 1,4-benzoxazines. After a series of organic solvents, bases and chiral PTC were screened for the [5 + 1] annulation of diethyl α-bromomalonate with imine **1a** (see Table S1 in the ESI†), the optimal reaction conditions (1.0 equiv **1**, 2.0 equiv **2a** and 1.0 equiv K_2CO_3 in $CHCl_3$ with 10 mol% **4c** at 20 °C) were established. Subsequently, the scope of the present organocatalytic asymmetric [5 + 1] annulation using catalyst **4c** was extended to various imines **1** and diethyl α-bromomalonate **2a**. As illustrated in Table 4, for the reactions of DBM, moderate to good results were achieved with various imines **1** bearing various substitutions (Table 4, entries 1–9). The good enantioselectivity was obtained with moderate yield for the model reaction (entry 1). It appeared that substituents' electronics have a minimal impact on enantioselectivities of the [5 + 1] annulation. Moderate enantioselectivities were obtained in the [5 + 1] annulation of DBM with electron-donating substituent (R^2) on aryl ring of imines **1** (entries 2 and 3). On the contrary, an electron-withdrawing substituent (R^2) on aryl ring of imines **1** tended to decrease the enantioselectivity (entry 4). Imine **1h** with electron-withdrawing substituent on the *ortho* position (R^2) afford 1,4-benzoxazines with moderate enantioselectivity (entry 5). In addition, imines **1** with electron-withdrawing substituents or electron-donating substituents on the aromatic ring (R^1) afford 1,4-benzoxazines with slightly inferior enantioselectivities (entries 7–9). The absolute configuration of the substituted 1,4-benzoxazines was confirmed by a single-crystal X-ray analysis of representative enantiopure **3ha** that bears a chlorine atom. As shown in Fig. 1, it composes of (*C1R*) configuration.

Conclusions

In summary, an efficient, mild, and convenient domino reaction for preparing differently substituted 1,4-benzoxazines from readily available starting materials was developed. In this transformation, a broad substrate scope has been demonstrated. This

methodology provides facile access to various new analogues of bioactive heterocyclic compounds – tetracyclic-1,4-benzoxazines which contain two new heterocyclic rings and one quaternary carbon center. In addition, we also have successfully demonstrated the first asymmetric [5 + 1] annulation of α-bromomalonate (DBM) **2a** to imines **1** with fair to good enantioselectivities, employing readily available chiral quaternary ammonium salts as organocatalysts. Application of this method in the synthesis of other pharmaceutically intriguing compounds is being actively pursued, and the results will be disclosed in due course.

Experimental section

General methods

NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (160–200 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz (Bruker Avance). Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) for ^{13}C NMR spectroscopy. Coupling constants (J) are given in Hz. ESI-HRMS spectrometer was measured with a Finnigan LCQ^{DECA} ion trap mass spectrometer. Optical rotations were measured at 589 nm at 20 °C. Enantiomeric excess was determined by HPLC analysis on Chiralpak AS, IC and OD columns.

Synthesis of different substituted 2,3-dihydro-1,4-benzoxazines. *General procedure*: **1a** (19.7 mg, 0.10 mmol), **2a** (47.4 mg, 0.20 mmol), TBAB (6.44 mg, 0.02 mmol) and KOH (5.6 mg, 0.10 mmol) were stirred in CH_3CN (1 mL) at room temperature for 20 h. Then flash chromatography on silica gel (10% ethylacetate/petroleum ether) gave product **3aa** as a white solid (30.8 mg, 87% yield).

Synthesis of different tetracyclic 2,3-dihydro-1,4-benzoxazines. *General procedure*: **1r** (21.3 mg, 0.10 mmol), **2a** (47.4 mg, 0.20 mmol), TBAB (6.44 mg, 0.02 mmol) and KOH (5.6 mg, 0.10 mmol) were stirred in CH_3CN (1 mL) at room temperature for 20 h. Then flash chromatography on silica gel (10% ethylacetate/petroleum ether) gave product **3ra** as a white solid (24.1 mg, 65% yield); **3ra** (37.1 mg, 0.10 mmol) and *p*-toluenesulfonic acid (1.72 mg, 0.01 mmol) were refluxed in toluene for 2 h. Then flash chromatography on silica gel (20% ethylacetate/petroleum ether) gave product **4ra** as a white solid (30.5 mg, 94% yield).

Asymmetric synthesis of differently substituted 2,3-dihydro-1,4-benzoxazines. *General procedure*: **1a** (19.7 mg, 0.10 mmol), **2a** (47.4 mg, 0.20 mmol), K_2CO_3 (13.8 mg, 0.10 mmol) and **4c** (5.32 mg, 0.01 mol) were stirred in $CHCl_3$ (1 mL) at 20 °C for 20 h. Then flash chromatography on silica gel (10% ethyl acetate/petroleum ether) gave product **3aa** as a white solid (23.4 mg, 66% yield).

Diethyl 3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3aa). White solid, mp: 127–128 °C; 30.8 mg, yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 3.5 Hz, 5H), 7.12 (dd, J = 8.0, 1.3 Hz, 1H), 6.87 (td, J = 7.7, 1.4 Hz, 1H), 6.74 (td, J = 8.0, 1.5 Hz, 1H), 6.62 (dd, J = 7.9, 1.4 Hz, 1H), 5.30 (d, J = 3.9 Hz, 1H), 4.38 (s, 1H), 4.27–4.13 (m, 2H), 4.12–4.10 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.9, 140.9, 139.2, 131.5, 128.4, 128.2, 127.8, 123.1, 118.8, 117.8, 115.2, 82.6, 62.6, 62.4, 56.9, 13.8, 13.7; IR (KBr) cm^{-1} 3384, 2986, 1756, 1611, 1499, 1450, 1272, 1214, 1152, 748, 704; ESI-HRMS: calcd for $C_{20}H_{21}NO_5$ + H 356.1492, found 356.1495.

(*R*)-Diethyl 3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylatediethyl (3aa). 23.4 mg, yield 66%; $[\alpha]_D^{20}$ = −18 (c 0.67, $CHCl_3$), ee = 81.0%; The enantiomeric ratio was determined by HPLC on Chiralpak IC column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 10.42 min, t_{minor} = 7.63 min.

Diethyl 3-*p*-tolyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ba). White solid, mp: 114–115 °C; 26.5 mg, yield 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (t, J = 9.8 Hz, 3H), 7.04 (d, J = 7.9 Hz, 2H), 6.85 (t, J = 7.6 Hz, 1H), 6.72 (t, J = 7.7 Hz, 1H), 6.60 (d, J = 7.8 Hz, 1H), 5.25 (s, 1H), 4.36 (s, 1H), 4.27–4.12 (m, 2H), 4.11–4.00 (m, 2H), 2.27 (s, 3H), 1.10 (t, J = 6.1 Hz, 3H), 1.07 (t, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.9, 141.0, 137.9, 136.2, 131.6, 129.1, 127.7, 123.0, 118.7, 117.7, 115.1, 82.7, 62.5, 62.3, 56.6, 21.0, 13.8, 13.7; IR (KBr) cm^{-1} 3401, 2981, 1749, 1612, 1501, 1455, 1249, 1212, 1181, 831, 743; ESI-HRMS: calcd for $C_{21}H_{23}NO_5$ + H 370.1649, found 370.1644.

(*R*)-Diethyl 3-*p*-tolyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ba). 18.8 mg, yield 51%; $[\alpha]_D^{20}$ = −38.9 (c 0.57, $CHCl_3$), ee = 60.0%; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 14.27 min, t_{minor} = 7.08 min.

Diethyl 3-(4-methoxyphenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ca). White solid, mp: 94–95 °C; 27.3 mg, yield 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.16 (m, 2H), 7.12 (dd, J = 8.0, 1.4 Hz, 1H), 6.86 (td, J = 7.6, 1.4 Hz, 1H), 6.80–6.70 (m, 3H), 6.61 (dd, J = 7.9, 1.5 Hz, 1H), 5.25 (s, 1H), 4.37 (s, 1H), 4.28–4.14 (m, 2H), 4.14–4.01 (m, 2H), 3.74 (s, 3H), 1.12 (t, J = 4.5 Hz, 3H), 1.09 (t, J = 4.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 165.0, 159.4, 140.9, 131.5, 131.4, 129.0, 123.0, 118.7, 117.7, 115.2, 113.7, 82.8, 62.6, 62.3, 56.2, 55.2, 13.8; IR (KBr) cm^{-1} 3407, 2977, 1747, 1612, 1508, 1458, 1251, 1212, 1179, 834, 747; ESI-HRMS: calcd for $C_{21}H_{23}NO_6$ + H 386.1598, found 386.1597.

(*R*)-Diethyl 3-(4-methoxyphenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ca). 18.4 mg, yield 48%; $[\alpha]_D^{20}$ = −64.5 (*c* = 1.10, $CHCl_3$), ee = 61.0%; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 23.09 min, t_{minor} = 10.51 min.

Diethyl 3-(2-methoxyphenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3da). White solid, mp: 81–83 °C; 26.5 mg, yield 69%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 7.7 Hz, 1H), 7.18 (dd, J = 11.2, 4.5 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 6.87–6.75 (m, 3H), 6.74–6.66 (m, 1H), 6.53 (dd, J = 7.7, 1.3 Hz, 1H), 5.80 (d, J = 3.5 Hz, 1H), 4.41 (d, J = 3.0 Hz, 1H),

4.31–4.16 (m, 2H), 4.16–4.06 (m, 2H), 3.87 (s, 3H), 1.15 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 165.1, 156.6, 141.2, 131.2, 128.8, 127.7, 122.6, 120.8, 118.9, 117.3, 115.6, 110.0, 82.8, 62.6, 62.3, 55.4, 48.8, 13.8, 13.6; IR (KBr) cm^{-1} 3399, 2972, 1745, 1612, 1504, 1453, 1250, 1212, 1170, 841, 739; ESI-HRMS: calcd for $C_{21}H_{23}NO_6$ + H 386.1598, found 386.1617.

Diethyl 3-(3-methoxyphenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ea). White solid, mp: 91–92 °C; 25.8 mg, yield 67%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.07 (m, 2H), 6.90–6.69 (m, 5H), 6.62 (dd, J = 7.8, 1.4 Hz, 1H), 5.27 (s, 1H), 4.37 (s, 1H), 4.28–4.14 (m, 2H), 4.14–4.02 (m, 2H), 3.69 (s, 3H), 1.11 (t, J = 5.1 Hz, 3H), 1.08 (t, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.9, 159.4, 140.9, 140.6, 131.4, 129.5, 123.1, 120.1, 118.8, 117.8, 115.2, 113.7, 113.4, 82.6, 62.7, 62.4, 56.7, 55.1, 13.9, 13.8; IR (KBr) cm^{-1} 3407, 2974, 1749, 1611, 1500, 1456, 1253, 1215, 1180, 827, 738; ESI-HRMS: calcd for $C_{21}H_{23}NO_6$ + H 386.1598, found 386.1617.

Diethyl 3-(4-chlorophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3fa). White solid, mp: 109–110 °C; 32.3 mg, yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.14 (m, 4H), 7.11 (d, J = 8.0 Hz, 1H), 6.87 (t, J = 7.2 Hz, 1H), 6.75 (t, J = 7.7 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 5.29 (s, 1H), 4.39 (s, 1H), 4.27–4.13 (m, 2H), 4.13–4.00 (m, 2H), 1.15–1.10 (m, 3H), 1.10–1.03 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 164.8, 140.8, 137.7, 134.1, 131.1, 129.2, 128.6, 123.2, 119.0, 117.9, 115.3, 82.4, 62.7, 62.5, 56.3, 13.8; IR (KBr) cm^{-1} 3400, 2983, 1758, 1727, 1612, 1500, 1298, 1213, 1141, 866, 743; ESI-HRMS: calcd for $C_{20}H_{20}ClNO_5$ + H 390.1103, found 390.1140.

(*R*)-Diethyl 3-(4-chlorophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3fa). 24.1 mg, yield 62%; $[\alpha]_D^{20}$ = −40.0 (c 0.50, $CHCl_3$), ee = 30.0%; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 16.47 min, t_{minor} = 8.13 min.

Diethyl 3-(3-chlorophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ga). White solid, mp: 130–131 °C; 31.5 mg, yield 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 2H), 7.14 (dd, J = 19.5, 8.3 Hz, 3H), 6.88 (t, J = 7.3 Hz, 1H), 6.75 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 5.28 (d, J = 3.7 Hz, 1H), 4.42 (s, 1H), 4.27–4.14 (m, 2H), 4.13–4.05 (m, 2H), 1.16–1.10 (m, 3H), 1.10–1.04 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 164.8, 141.2, 140.8, 134.1, 131.1, 129.8, 128.3, 128.1, 125.9, 123.3, 119.0, 118.0, 115.2, 82.3, 62.7, 62.6, 56.6, 13.8, 13.7; IR (KBr) cm^{-1} 3398, 2979, 1752, 1721, 1612, 1500, 1291, 1213, 1143, 857, 751; ESI-HRMS: calcd for $C_{20}H_{20}ClNO_5$ + H 390.1103, found 390.1140.

Diethyl 3-(2-chlorophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ha). White solid, mp: 120–122 °C; 31.5 mg, yield 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, J = 7.4, 2.0 Hz, 1H), 7.35 (dd, J = 7.7, 1.5 Hz, 1H), 7.20–7.10 (m, 3H), 6.83 (dd, J = 10.8, 4.4 Hz, 1H), 6.79–6.70 (m, 1H), 6.57 (dd, J = 7.8, 1.3 Hz, 1H), 5.94 (d, J = 4.7 Hz, 1H), 4.46 (d, J = 4.6 Hz, 1H), 4.35–4.18 (m, 2H), 4.17–4.05 (m, 2H), 1.16 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 164.2, 140.8, 136.6, 133.4, 130.4, 129.4, 129.1, 128.7, 127.5, 123.0, 119.1, 117.7, 115.5, 82.2, 62.8, 62.5, 51.6, 13.8, 13.5; IR (KBr) cm^{-1} 3400, 2978, 1752, 1728, 1613, 1500, 1295, 1211, 1146, 868, 743; ESI-HRMS: calcd for $C_{20}H_{20}ClNO_5$ + H 390.1103, found 390.1091.

(*R*)-Diethyl 3-(2-chlorophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ha). 27.2 mg, yield 70%; $[\alpha]_D^{20}$ = −15.4 (c = 1.17, $CHCl_3$), ee = 63.0%; The enantiomeric ratio was determined by HPLC on Chiralpak OD column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 6.72 min, t_{minor} = 5.85 min.

Diethyl 3-(4-bromophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ia). White solid, mp: 118–119 °C; 38.0 mg, yield 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.3 Hz, 2H), 7.24–6.96 (m, 3H), 6.88 (t, J = 7.3 Hz, 1H), 6.75 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.4 Hz, 1H), 5.27 (s, 1H), 4.37 (s, 1H), 4.25–4.14 (m, 2H), 4.13–4.04 (m, 2H), 1.11 (d, J = 6.3 Hz, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 164.8, 140.8, 138.2, 131.5, 131.1, 129.5, 123.2, 122.3, 119.1, 117.9, 115.3, 82.3, 62.7, 62.5, 56.4, 13.8; IR (KBr) cm^{-1} 3402, 2980, 1750, 1724, 1611, 1500, 1297, 1214, 1138, 860, 748; ESI-HRMS: calcd for $C_{20}H_{20}BrNO_5$ + H 434.0598, found 434.0602.

Diethyl 3-(2-bromophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ja). White solid, mp: 129–130 °C; 34.9 mg, yield 79%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 7.7 Hz, 1H), 7.17 (dd, J = 13.4, 7.3 Hz, 2H), 7.09 (t, J = 7.2 Hz, 1H), 6.83 (t, J = 7.4 Hz, 1H), 6.75 (t, J = 7.4 Hz, 1H), 6.56 (d, J = 7.7 Hz, 1H), 5.91 (d, J = 4.4 Hz, 1H), 4.50 (d, J = 3.7 Hz, 1H), 4.28–4.18 (m, 2H), 4.17–4.05 (m, 2H), 1.16 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 164.6, 140.7, 138.1, 132.8, 130.3, 129.4, 128.8, 128.2, 124.1, 123.0, 119.1, 117.6, 115.5, 82.3, 62.8, 62.5, 54.2, 13.8, 13.6; IR (KBr) cm^{-1} 3398, 2976, 1753, 1728, 1611, 1502, 1290, 1214, 1146, 857, 744; ESI-HRMS: calcd for $C_{20}H_{20}BrNO_5$ + H 434.0598, found 434.0586.

(*R*)-Diethyl 3-(2-bromophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ja). 28.1 mg, yield 65%; $[\alpha]_D^{20}$ = −24.2 (*c* = 0.87, $CHCl_3$), ee = 44.0%; The enantiomeric ratio was determined by HPLC on Chiralpak OD column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 6.75 min, t_{minor} = 5.90 min.

Diethyl 3-(4-nitrophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ka). Yellow solid, mp: 136–137 °C; 32.4 mg, yield 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.14 (d, J = 8.0 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.80 (t, J = 7.7 Hz, 1H), 6.70–6.64 (m, 1H), 5.44 (d, J = 5.1 Hz, 1H), 4.46 (d, J = 5.0 Hz, 1H), 4.29–4.15 (m, 2H), 4.14–4.03 (m, 2H), 1.16–1.11 (m, 3H), 1.11–1.05 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 164.6, 147.6, 146.3, 140.7, 130.6, 128.9, 123.6, 123.5, 119.5, 118.1, 115.5, 81.8, 62.9, 62.7, 56.5, 13.8, 13.7; IR (KBr) cm^{-1} 3408, 2969, 1750, 1733, 1611, 1505, 1288, 1211, 1175, 869, 735; ESI-HRMS: calcd for $C_{20}H_{20}N_2O_7$ + H 401.1343, found 401.1343.

Diethyl 3-(2-nitrophenyl)-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3la). Yellow solid, mp: 153–155 °C;

30.0 mg, yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 6.86 (t, J = 7.4 Hz, 1H), 6.77 (t, J = 7.3 Hz, 1H), 6.59 (d, J = 7.8 Hz, 1H), 5.81 (d, J = 4.3 Hz, 1H), 4.75 (d, J = 3.8 Hz, 1H), 4.30–4.13 (m, 2H), 4.08–4.03 (m, 2H), 1.15 (t, J = 7.1 Hz, 3H), 0.98 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 164.4, 149.8, 140.4, 133.6, 133.5, 130.1, 128.9, 128.6, 124.4, 123.2, 119.2, 117.6, 115.4, 82.4, 63.0, 62.7, 49.9, 13.8, 13.5; IR (KBr) cm^{-1} 3393, 2979, 1759, 1726, 1615, 1507, 1293, 1210, 1177, 855, 748; ESI-HRMS: calcd for $C_{20}H_{20}N_2O_7$ + H 401.1343, found 401.1350.

Diethyl 6-methyl-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ma). White solid, mp: 125–127 °C; 28.1 mg, yield 76%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (s, 5H), 7.00 (d, J = 8.2 Hz, 1H), 6.54 (dd, J = 8.1, 1.3 Hz, 1H), 6.43 (d, J = 0.9 Hz, 1H), 5.28 (s, 1H), 4.36 (s, 1H), 4.26–4.13 (m, 2H), 4.12–3.99 (m, 2H), 2.22 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 165.1, 139.3, 138.7, 132.6, 131.1, 128.4, 128.2, 127.8, 119.4, 117.5, 115.6, 82.6, 62.6, 62.4, 56.8, 20.9, 13.9, 13.7; IR (KBr) cm^{-1} 3376, 2982, 1763, 1741, 1615, 1500, 1450, 1295, 1216, 1151, 854, 793, 701; ESI-HRMS: calcd for $C_{21}H_{23}NO_5$ + H 370.1649, found 370.1647.

(*R*)-Diethyl 6-methyl-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ma). 18.8 mg, yield 63%; $[\alpha]_D^{20}$ = −49.2 (c = 2.03, $CHCl_3$), ee = 62.0%; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 13.79 min, t_{minor} = 7.35 min.

Diethyl 7-methyl-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3na). White solid, mp: 94–95 °C; 26.9 mg, yield 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (s, 5H), 6.96 (s, 1H), 6.68 (dd, J = 8.0, 1.1 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 5.26 (s, 1H), 4.29 (s, 1H), 4.25–4.15 (m,2H), 4.12–4.01 (m,2H), 2.27 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 165.1, 141.0, 139.3, 128.8, 128.6, 128.4, 128.1, 127.8, 123.6, 118.2, 115.4, 82.6, 62.6, 62.3, 56.9, 20.6, 13.8, 13.7; IR (KBr) cm^{-1} 3371, 2974, 1761, 1749, 1613, 1500, 1450, 1290, 1213, 1163, 859, 787, 703; ESI-HRMS: calcd for $C_{21}H_{23}NO_5$ + H 370.1649, found 370.1647.

(*R*)-Diethyl 7-methyl-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3na). 21.0 mg, yield 57%; $[\alpha]_D^{20}$ = −21.9 (c = 0.87, $CHCl_3$), ee = 60.0%; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 12.41 min, t_{minor} = 7.02 min.

Diethyl 6-chloro-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3oa). White solid, mp: 134–135 °C; 31.9 mg, yield 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.18 (m, 5H), 7.03 (d, J = 8.6 Hz, 1H), 6.68 (dd, J = 8.6, 2.4 Hz, 1H), 6.60 (d, J = 2.3 Hz, 1H), 5.29 (d, J = 4.3 Hz, 1H), 4.53 (d, J = 4.2 Hz, 1H), 4.28–4.13 (m, 2H), 4.11–3.99 (m, 2H), 1.13 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 164.6, 139.3, 138.7, 132.5, 128.5, 128.4, 127.9, 127.8, 118.8, 118.3, 114.4, 82.6, 62.8, 62.6, 56.5, 13.9, 13.7; IR (KBr) cm^{-1} 3367, 2988, 1764, 1741, 1608, 1501, 1289, 1216, 1151, 847, 790, 702; ESI-HRMS: calcd for $C_{20}H_{20}ClNO_5$ + H 390.1103, found 390.1138.

Diethyl 7-chloro-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3pa). White solid, mp: 110–111 °C; 33.1 mg, yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.20 (m, 5H), 7.14 (d, J = 2.3 Hz, 1H), 6.84 (dd, J = 8.5, 2.3 Hz, 1H), 6.54 (d, J = 8.5 Hz, 1H), 5.28 (s, 1H), 4.43 (s, 1H), 4.28–4.14 (m, 2H), 4.12–3.99 (m, 2H), 1.14 (t, J = 7.1 Hz, 3H), 1.04 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.5, 141.2, 138.8, 130.2, 128.5, 128.4, 127.8, 123.1, 123.0, 117.9, 115.7, 82.6, 62.8, 62.5, 56.6, 13.8, 13.7; IR (KBr) cm^{-1} 3364, 2991, 1762, 1743, 1600, 1500, 1284, 1213, 1157, 854, 788, 707; ESI-HRMS: calcd for $C_{20}H_{20}ClNO_5$ + H 390.1103, found 390.1075.

(*R*)-Diethyl 7-chloro-3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3pa). 23.7 mg, yield 61%; $[\alpha]_D^{20}$ = −23.5 (c = 1.23, $CHCl_3$), ee = 54.0%; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10% 2-propanol/hexane, 1 mL min^{-1}), t_{major} = 15.55 min, t_{minor} = 8.14 min.

1,1′-(3-ethyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine-2,2-diyl)bis-(propan-1-one) (3qa). White solid, mp: 103–104 °C; 14.0 mg, yield 51%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 1H), 7.11 (t, J = 7.7 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.9 Hz, 1H), 4.93 (s, 1H), 4.50–4.43 (m, 2H), 4.41–4.29 (m, 2H), 3.72 (d, J = 6.8 Hz, 1H), 1.58 (s, 3H), 1.36–1.35 (m, 3H), 1.35–1.32 (m, 3H), 1.24 (t, J = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 155.5, 142.2, 130.2, 126.4, 125.7, 123.0, 116.1, 110.0, 88.9, 63.9, 63.0, 29.0, 22.6, 14.0, 13.9; IR (KBr) cm^{-1} 3380, 2979, 1756, 1612, 1501, 1450, 1212, 1152, 734, 704; ESI-HRMS: calcd for $C_{16}H_{21}NO_3$ + Na 298.1414, found 298.1361.

Diethyl 3-phenyl-3,4-dihydrobenzo[*b*][1,4]oxazine-2,2-dicarboxylate (3ab). White solid, mp: 127–128 °C; 29.4 mg, yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 5H), 7.12 (dd, J = 8.0, 1.3 Hz, 1H), 6.87 (td, J = 7.7, 1.4 Hz, 1H), 6.74 (td, J = 8.0, 1.5 Hz, 1H), 6.62 (dd, J = 7.9, 1.4 Hz, 1H), 5.30 (d, J = 3.9 Hz, 1H), 4.39 (s, 1H), 4.27–4.14 (m, 2H), 4.13–4.00 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.9, 140.9, 139.2, 131.5, 128.4, 128.2, 127.8, 123.1, 118.8, 117.8, 115.2, 82.6, 62.6, 62.4, 56.9, 13.8, 13.7; IR (KBr) cm^{-1} 3382, 2988, 1754, 1611, 1500, 1450, 1272, 1214, 1152, 748, 704; ESI-HRMS: calcd for $C_{20}H_{21}NO_5$ + H 356.1492, found 356.1502.

1,1′-(3-Phenyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine-2,2-diyl)-diethanone (3ac). White solid, mp: 143–144 °C; 16.5 mg, yield 56%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 3H), 7.15 (dd, J = 6.5, 2.8 Hz, 2H), 7.09 (dd, J = 8.0, 1.0 Hz, 1H), 6.93–6.86 (m, 1H), 6.81–6.74 (m, 1H), 6.63 (dd, J = 7.9, 1.2 Hz, 1H), 5.30 (s, 1H), 4.37 (s, 1H), 2.15 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 201.0, 140.6, 139.4, 132.3, 128.6, 128.0, 128.0, 123.4, 118.8, 117.4, 115.6, 93.0, 55.9, 26.8, 25.7; IR (KBr) cm^{-1} 3386, 2979, 1749, 1613, 1502, 1450, 1277, 1212, 1139, 733, 702; ESI-HRMS: calcd for $C_{18}H_{17}NO_3$ + H 296.1281, found 296.1279.

Ethyl 2-acetyl-3-phenyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine-2-carboxylate (3ad). White solid, mp: 127–130 °C; 17.2 mg, yield 53%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, J = 3.0 Hz, 3H), 7.19–7.15 (m, 2H), 7.07 (d, J = 8.0 Hz, 1H), 6.88 (dt, J = 13.4, 6.8 Hz, 1H), 6.77–6.73 (m, 1H), 6.64 (d, J = 7.9 Hz, 1H), 5.28 (s, 1H), 4.45 (s, 1H), 4.22–4.01 (m, 2H), 1.89 (s, 3H), 1.11–1.03 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 167.0, 139.3, 132.1, 128.5, 128.1, 127.8, 123.2, 118.6, 117.6, 115.2, 110.0, 87.4, 62.5, 56.8, 26.6, 13.8; IR (KBr) cm^{-1} 3389, 2984, 1757, 1612, 1503, 1450, 1277, 1211, 1147, 734, 700; ESI-HRMS: calcd for $C_{19}H_{19}NO_4$ + H 326.1387, found 326.1389.

Ethyl 6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*]-[1,4]oxazine-6a-carboxylate (4ra). White solid, mp: 167–169 °C; 30.2 mg, yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, J = 7.2 Hz, 1H), 7.36 (d, J = 7.4 Hz, 1H), 7.24–7.10 (m, 2H), 7.05 (d, J = 7.9 Hz, 1H), 6.87–6.78 (m, 2H), 6.63 (d, J = 7.7 Hz, 1H), 4.71 (s, 1H), 4.23–4.07 (m, 2H), 4.03 (s, 1H), 1.03 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 150.9, 141.4, 131.2, 129.7, 128.4, 125.1, 122.7, 121.0, 120.7, 117.1, 115.9, 63.1, 51.9, 13.6; ESI-HRMS: calcd for $C_{18}H_{15}NO_5$ + H 326.1023, found 326.1063.

Ethyl 10-methyl-6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6a-carboxylate (4sa). White solid, mp: 118–120 °C; 30.1 mg, yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, J = 7.8 Hz, 1H), 7.35 (d, J = 7.4 Hz, 1H), 7.17 (dd, J = 17.9, 7.9 Hz, 2H), 6.94 (d, J = 8.2 Hz, 1H), 6.44 (s, 1H), 4.70 (s, 1H), 4.23–4.07 (m, 2H), 3.95 (s, 1H), 2.21 (s, 3H), 1.03 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 150.9, 139.3, 132.3, 131.1, 129.2, 128.3, 125.1, 121.4, 121.1, 117.1, 116.8, 116.3, 63.1, 51.9, 20.7, 13.6; IR (KBr) cm^{-1} 3359, 2922, 1783, 1759, 1614, 1515, 1468, 1300, 1254, 1214, 1164, 803, 759; ESI-HRMS: calcd for $C_{19}H_{17}NO_5$ + H 340.1179, found 340.1191.

Ethyl 9-methyl-6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6a-carboxylate (4ta). White solid, mp: 206–208 °C; 27.4 mg, yield 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.34 (m, 2H), 7.16 (dd, J = 16.0, 8.1 Hz, 2H), 6.88 (s, 1H), 6.66 (d, J = 7.9 Hz, 1H), 6.54 (d, J = 7.9 Hz, 1H), 4.69 (s, 1H), 4.23–4.07 (m, 2H), 3.89 (s, 1H), 2.24 (s, 3H), 1.03 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 150.7, 141.0, 130.8, 129.7, 128.5, 127.7, 124.9, 123.1, 121.3, 117.0, 116.7, 115.8, 62.8, 51.7, 20.5, 13.5; IR (KBr) cm^{-1} 3361, 2925, 1780, 1751, 1613, 1509, 1463, 1300, 1252, 1214, 1166, 805, 751; ESI-HRMS: calcd for $C_{19}H_{17}NO_5$ + H 340.1179, found 340.1162.

Ethyl 10-chloro-6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6a-carboxylate (4ua). White solid, mp: 164–166 °C; 31.2 mg, yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (t, J = 7.8 Hz, 1H), 7.35 (d, J = 7.4 Hz, 1H), 7.22–7.15 (m, 2H), 6.97 (d, J = 8.6 Hz, 1H), 6.75 (d, J = 8.7 Hz, 1H), 6.62 (s, 1H), 4.72 (s, 1H), 4.26–4.14 (m, 2H), 4.11 (d, J = 7.8 Hz, 1H), 1.04 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 150.8, 139.8, 131.4, 130.5, 128.3, 127.5, 125.2, 120.5, 120.4, 118.2, 117.2, 115.4, 63.3, 51.6, 13.6; IR (KBr) cm^{-1} 3390, 2966, 1764, 1743, 1610, 1499, 1455, 1299, 1257, 1214, 1132, 803, 762; ESI-HRMS: calcd for $C_{18}H_{14}ClNO_5$ + H 360.0633, found 360.0687.

Ethyl 9-chloro-6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6a-carboxylate (4va). White solid, mp: 198–200 °C; 29.8 mg, yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.27 (m, 2H), 7.23–7.12 (m, 2H), 7.06 (s, 1H), 6.93 (s, 1H), 6.83 (d, J = 8.5 Hz, 1H), 6.56 (d, J = 8.5 Hz, 1H), 4.71 (s, 1H), 4.26–3.86 (m, 3H), 1.04 (t, J = 7.1 Hz, 2H), 0.85 (t, J = 7.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 150.3, 140.9, 130.6, 129.6, 128.5, 124.8, 122.9, 122.1, 120.9, 116.4, 116.2, 62.7, 51.0, 13.3; IR (KBr) cm^{-1} 3391, 2963, 1765, 1744, 1612, 1500, 1453, 1299, 1255, 1214, 1137, 806, 763; ESI-HRMS: calcd for $C_{18}H_{14}ClNO_5$ + H 360.0633, found 360.0645.

Ethyl 3-methoxy-6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6a-carboxylate (4wa). White solid, mp: 148–150 °C; 32.3 mg, yield 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 8.1 Hz, 1H), 7.06 (d, J = 7.9 Hz, 1H), 6.87–6.78 (m, 2H), 6.72–6.70 (m, 2H), 6.62 (dd, J = 7.6, 1.5 Hz, 1H), 4.64 (s, 1H), 4.24–4.09 (m, 2H), 3.94 (s, 1H), 3.82 (s, 3H), 1.07 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 152.0, 129.8, 129.2, 123.7, 122.7, 120.6, 117.1, 115.8, 115.0, 112.8, 110.8, 105.5, 102.8, 63.1, 55.7, 51.4, 13.7; IR (KBr) cm^{-1} 3351, 2969, 1791, 1726, 1615, 1499, 1433, 1271, 1207, 1169, 834, 744; ESI-HRMS: calcd for $C_{19}H_{17}NO_6$ + H 356.1129, found 356.1125.

Ethyl 2-methyl-6-oxo-6,6a,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6a-carboxylate (4xa). White solid, mp: 158–160 °C; 31.8 mg, yield 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.5 Hz, 1H), 7.16 (s, 1H), 7.05 (t, J = 9.0 Hz, 2H), 6.83 (dt, J = 22.0, 6.9 Hz, 2H), 6.63 (d, J = 7.7 Hz, 1H), 4.67 (s, 1H), 4.25–4.09 (m, 2H), 3.98 (s, 1H), 2.35 (s, 3H), 1.06 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 148.7, 141.4, 134.9, 131.6, 129.8, 128.8, 122.7, 120.6, 120.5, 117.1, 116.9, 115.8, 63.1, 51.9, 20.7, 13.6; IR (KBr) cm^{-1} 3348, 2966, 1790, 1725, 1615, 1499, 1436, 1270, 1204, 1175, 823, 743; ESI-HRMS: calcd for $C_{19}H_{17}NO_5$ + Na 362.0999, found 362.1013.

Ethyl 2-chloro-6-oxo-6,6*a*,12,12*a*-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6*a*-carboxylate (4ya). White solid, mp: 152–154 °C; 30.8 mg, yield 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.36 (m, 2H), 7.11–7.09 (m, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.87 (td, J = 7.5, 1.4 Hz, 1H), 6.81 (td, J = 7.7, 1.5 Hz, 1H), 6.67 (dd, J = 7.7, 1.4 Hz, 1H), 4.77 (s, 1H), 4.27–4.14 (m, 2H), 4.10 (s, 1H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 149.2, 141.3, 130.9, 130.2, 129.2, 128.1, 122.9, 121.0, 118.5, 117.2, 116.2, 63.3, 58.4, 51.5, 18.4, 13.7; IR (KBr) cm^{-1} 3344, 2969, 1793, 1720, 1611, 1501, 1428, 1273, 1201, 1181, 832, 737; ESI-HRMS: calcd for $C_{18}H_{14}ClNO_5$ + H 360.0633, found 360.0605.

Ethyl 2-bromo-6-oxo-6,6*a*,12,12a-tetrahydrobenzo[*b*]chromeno[4,3-*e*][1,4]oxazine-6*a*-carboxylate (4za). White solid, mp: 162–164 °C; 37.1 mg, yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.51 (m, 2H), 7.04 (dd, J = 7.6, 3.0 Hz, 2H), 6.85 (dt, J = 23.4, 7.5 Hz, 2H), 6.66 (d, J = 7.7 Hz, 1H), 4.77 (s, 1H), 4.28–4.12 (m, 2H), 4.05 (s, 1H), 1.12 (t, J = 7.1 Hz,

3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 149.8, 141.3, 133.9, 131.0, 129.2, 122.9, 121.0, 118.9, 117.6, 117.2, 116.2, 63.3, 51.4, 13.7; IR (KBr) cm^{-1} 3365, 2971, 1787, 1730, 1611, 1499, 1437, 1274, 1201, 1165, 845, 736; ESI-HRMS: calcd for $C_{18}H_{14}BrNO_5$ + H 404.0128, found 404.0136.

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