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Enantioselective Syntheses of 4*H*-3,1-Benzoxazines via Catalytic Asymmetric Chlorocyclization of *o*-Vinylanilides

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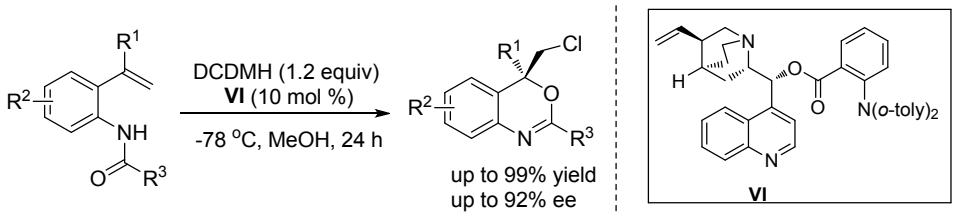


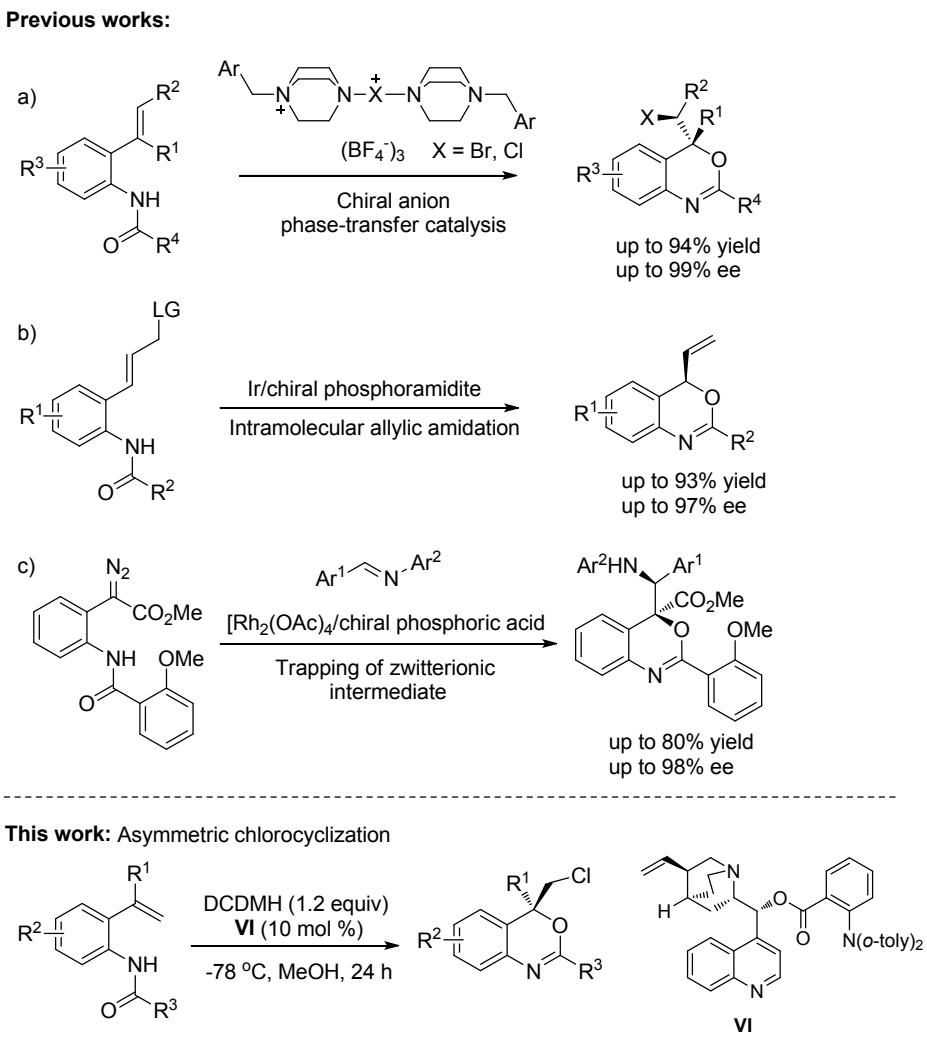
ABSTRACT: The catalytic asymmetric halocyclization of alkene is a powerful and straightforward strategy for the synthesis of chiral heterocyclic compounds. Herein, an effective approach to chiral benzoxazine derivatives through organocatalyzed chlorocyclization of *o*-vinylanilides was reported. This method provides facile access to a series of chiral benzoxazines in good to excellent yields (up to 99% yield) and with high level enantiocontrol (up to 92% ee).

INTRODUCTION

4*H*-3,1-benzoxazines are important heterocyclic compounds in medicinal chemistry due to their wide spectrum of biological activities.[1] Although substantial effort has been devoted to the synthesis of benzoxazine derivatives,[2] methods for enantioselective synthesis of 4*H*-3,1-benzoxazines are rare. To the best of our knowledge, only a few examples to prepare 4*H*-3,1-benzoxazine analogues stereoselectively have been reported.[3] Pioneering enantioselective synthesis of 4*H*-3,1-benzoxazines was reported by the group of Toste through treating *o*-vinylanilides with monoalkyl DABCO-derived (Bis)aminehalonium reagent via chiral anion phase-transfer catalysis (Scheme 1a).[3a] Afterwards, an asymmetric synthesis of 4H-3,1-benzoxazines via enantioselective iridium-catalysed intramolecular allylic amidation has been developed by Feringa's group (Scheme 1b).[3b] Very recently, Hu and coworkers reported an approach to benzoxazines involving rhodium-catalyzed electrophilic trapping of zwitterionic intermediates by imines (Scheme 1c).[3c] Despite these progresses, the novel approach to the enantioselective synthesis of 4*H*-3,1-benzoxazines allowing various substitution patterns is still highly desirable.

The catalytic asymmetric halogenation of alkene is one of the most promising research fields in recent years,[4] especially the intramolecular alkene halofunctionalization reactions have been successfully applied as powerful and straightforward strategies to construct the chiral cyclic compounds such as lactones,[5] cyclic ethers,[6] nitrogen heterocycles,[7] and related structures[8]. However, the improvement of these reactions scope to understand the reactivity of halonium ions and access valuable chiral heterocyclic products remain attractive. Consequently, inspired by the success of asymmetric chlorocyclization reactions for the synthesis of chiral oxazolines, dihydrooxazines and related compounds,[9] we wish to report here our efforts toward the novel synthesis of the chiral 4*H*-3,1-benzoxazines via the chlorocyclization of *o*-vinylanilides.

Scheme 1. The Approaches to Chiral 4*H*-3,1-Benzoxazines



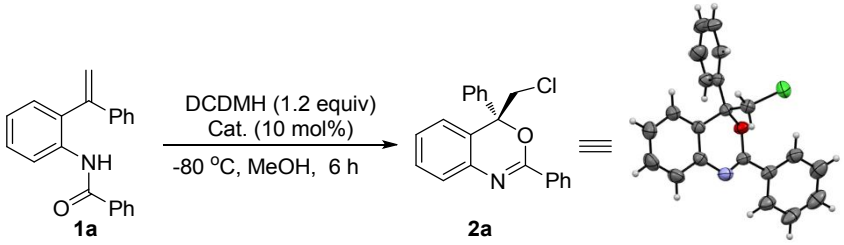
RESULTS AND DISCUSSION

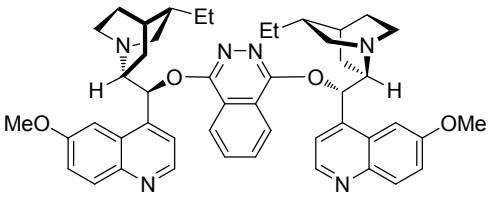
At the initial stage of our investigation, the easily synthesized *N*-(2-(1-phenylvinyl)phenyl)benzamide **1a** was selected as the model substrate for the evaluation of various chiral organocatalysts, and all reactions were carried out in MeOH at -80 °C for 6 h using DCDMH as the chlorenium source (Scheme 2). Firstly, when $(DHQD)_2PHAL$ was used as the catalyst, the desired product **2a** can be obtained in good enantioselectivity while the yield is poor. Disappointingly, the thiourea catalyst **II** and **III** also afforded **2a** with unacceptable yields (10% and 5%, respectively). Although above chiral privileged catalysts were not able to deliver the benzoxazine with excellent yield and enantioselectivity, we are very pleased to finally find that by using the **IV** as catalyst, the desired product **2a** was obtained in 78% yield and 46% ee. Encouraged by this result, a series of Cinchonidine-

derived chiral esters **V-VII** were examined, to our delight, the best yield and enantioselectivity could be achieved by using catalyst **VI** (84% yield and 92% ee), this catalyst has been successfully proved as an efficient catalyst in our previous work for asymmetric synthesis of 1,4-dihydro-2*H*-3,1-benzoxazin-2-one.[9i] Moreover, the structure and absolute configuration of the product **2a** were confirmed by X-ray crystallography.[10] Afterwards, the similar catalysts **VIII-X** derived from Cinchonine, Quinine and Quinidine were further investigated, however, none of them could provide favorable results.

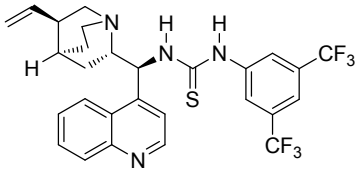
After identified the suitable catalyst, the solvents were then screened to determine the optimal reaction conditions, (Table 1, entries 1 to 6). The screening results of different solvents revealed that CH_2Cl_2, toluene, THF and the mixture of MeOH/CF_3CH_2OH resulted in the remarkable decrease of the enantioselectivies (Table 1, entries 2 to 6). The alcoholic solvents showed obvious advantage, methanol provided the best result in terms of the enantioselectivity and the yield. Ethanol was also found to be a suitable solvent but provided the product in lower enantioselectivity (80% ee, entry 2). Furthermore, the chlorenium source such as TCCA, NCS and DCDPH (Table 1, entries 7 to 10) showed great negligible impact on the reaction, led to significant decrease in the enantioselectivities or completely retarded the reaction. Unfortunately, this catalysis system was proved wholly ineffective in the bromocyclization and iodocyclization by using DBDMH, NBS, DIDMH and NIS as the halogen source, delivered the products with very low yields or enantioselectivities (Table 1, entries 11 to 14).

Scheme 2. The Catalyst Evaluation of Asymmetric Chlorocyclization [a, b, c]

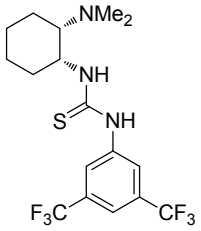




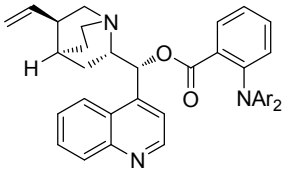
I: 5% yield, -69% ee



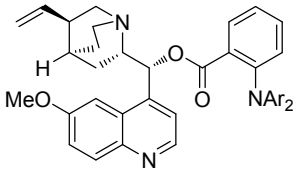
II: 10% yield, -3% ee



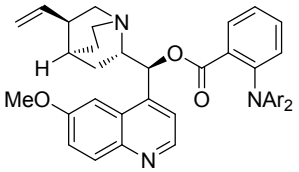
III: 5% yield, -89% ee



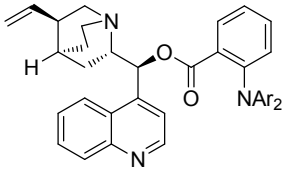
IV: Ar = Ph, 78% yield, 46% ee
V: Ar = *p*-toly, 82% yield, 51% ee
VI: Ar = *o*-toly, 84% yield, 92% ee
VII: Ar = *o*-isopropylphenyl, 69% yield, 37% ee



VIII: Ar = *o*-toly, 88% yield, 35% ee



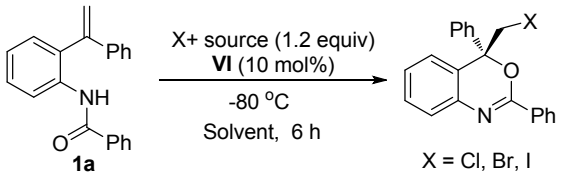
IX: Ar = *o*-toly, 47% yield, -45% ee



X: Ar = *o*-toly, 75% yield, -54% ee

[a] The reaction was carried out with **1a** (0.10 mmol), DCDMH (0.12 mmol) and chiral catalyst (0.01 mmol) in MeOH (2.0 mL) at -80 °C; DCDMH = 1,3-Dichloro-5,5-dimethylhydantoin; [b] yield of isolated; [c] ee was determined by HPLC analysis on a chiral stationary phase.

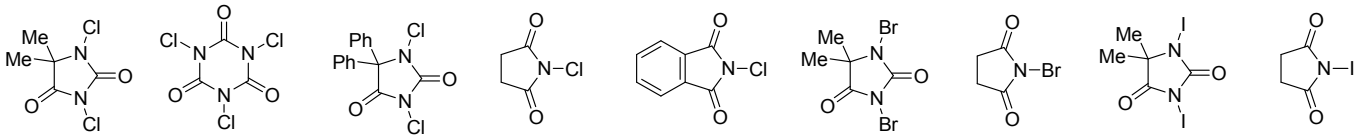
Table 1. Effects of Solvent and Halogenium Source[a]



Entry	Halogenium Source	Solvent	Yield (%)[b]	Ee (%)[c]
1	DCDMH	MeOH	84	92
2	DCDMH	EtOH	83	80

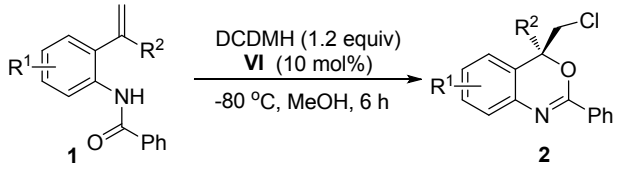
3	DCDMH	CH_2Cl_2	23	47
4[d]	DCDMH	toluene	N.D.	---
5	DCDMH	THF	41	15
6	DCDMH	MeOH/CF_3CH_2OH	98	57
7	TCCA	MeOH	83	55
8	DCDPH	MeOH	95	79
9[d]	NCS	MeOH	ND	---
10[d]	NCP	MeOH	ND	---
11	DBDMH	MeOH	93	11
12	NBS	MeOH	8	18
13	DIDMH	MeOH	31	1
14	NIS	MeOH	2	37

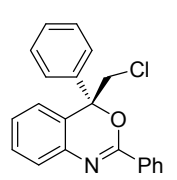
[a] The reaction was carried out with **1a** (0.10 mmol), X^+ (0.12 mmol) and chiral catalyst **VI** (0.01 mmol) in solvent (2.0 mL) at -80 °C. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase. [d] not detected.



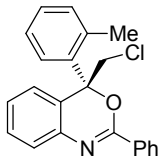
Having established the optimized reaction conditions, the scope and limitations of the substrates have been investigated. The substrates bearing various substituents on the phenyl ring at the alkene moiety were firstly explored. Most electron-donating groups including methyl and methoxy and electron-withdrawing groups such as trifluoromethyl were perfectly compatible with the reaction conditions, and the corresponding products were obtained in 65-92% yield with 16-92% ee (Scheme 3, **2a** to **2h**). To our surprise, there is a sharp loss of ee value when *o*-methyl group substituted (Scheme 3, entry **2b**), which could be possibly ascribed to the enhanced steric hindrance. 2-Naphthyl substituted substrate provided the corresponding product **2h** in moderate yield and good ee. It is noteworthy that aliphatic substrates also could deliver the products **2i** and **2j** in excellent yields with slightly low enantioselectivities. The substrates of various substituted aniline derivatives were further examined (Scheme 3, **2k** to **2p**). However, the reaction exhibited poor tolerance to substituents of the aniline no matter is the electron-donating or electron-withdrawing group, only the 5-fluoro substituted aniline derived *o*-vinylanilide could provide the best result, 56% yield and 91% ee were obtained (Scheme 3, entry **2o**). In addition, to demonstrate the potential synthetic utility of this new method, a 1.0 mmol scale reaction of **1a** was carried out and the chiral 4*H*-3,1-benzoxazine product **2a** was isolated in 80% yield and 91% ee.

Scheme 3. Scope of Substrates[a]

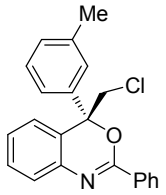




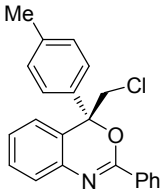
2a: 84%, 92% ee
80%, 91% ee[b]



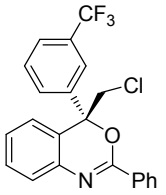
2b: 65%, 16% ee



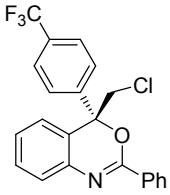
2c: 77%, 89% ee



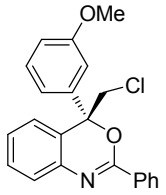
2d: 92%, 82% ee



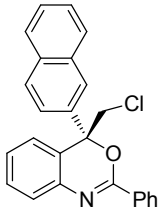
2e: 88%, 87% ee



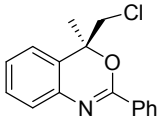
2f: 88%, 87% ee



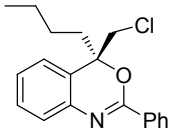
2g: 93%, 90% ee



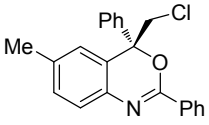
2h: 66%, 84% ee



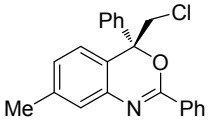
2i: 90%, 64% ee



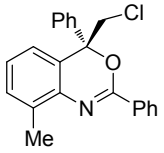
2j: 96%, 49% ee



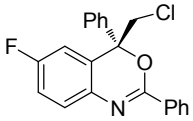
2k: 86%, 60% ee



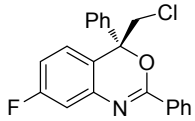
2l: 92%, 76% ee



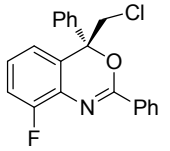
2m: 92%, 80% ee



2n: 20%, 75% ee



2o: 56%, 91% ee



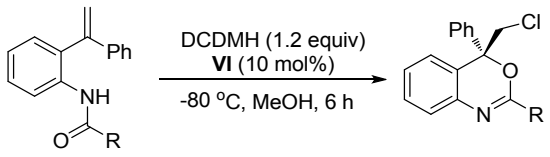
2p: 56%, 70% ee

[a] Reaction conditions: **1** (0.10 mmol), DCDMH (0.12 mmol) and chiral catalyst **VI** (0.01 mmol) in MeOH (2.0 mL) at -80 °C, isolated yields; [b] 1.0 mmol scale reaction.

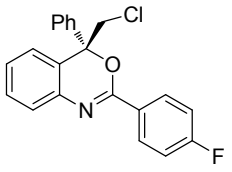
To further explore the scope compatibility of the reaction, a series of amides were then investigated (Scheme 4). The electronic nature of substituent to the aromatic ring of amide had no obvious impact on the enantioselectivity. Both electron-donating groups such as methoxy and electron-withdrawing groups including fluoro, chloro, and bromo even the *para*-NO_2 were perfectly compatible with the reaction conditions, and the corresponding products were obtained in 62-99% yield with 80-89% ee (Scheme 4, **4a** to **4j**). Additionally, the positions of the substituent on the phenyl ring didn't dramatically affect the chemical yield and stereoselectivity of the reaction. For substrates bearing halogen or methoxy group to

the aromatic ring moiety on different positions, good yields and high ees were generally obtained (Scheme 4, entries **4a**, **4d** to **4i**). Gratifyingly, the aliphatic amides were well compatible with the present conditions, leading to the desired products in good yields and high enantioselectivies (Scheme 4, entries **4k** to **4m**), and the structure and absolute configuration of the product **4k** were further confirmed by X-ray crystallography.[10] Nonetheless, heteroarylamide also reacted smoothly to give the 4*H*-3,1-benzoxazine product with 96% yield and 70% ee (Scheme 4, entry **4n**).

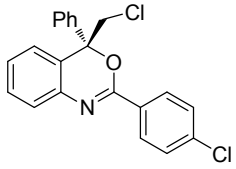
Scheme 4. Scope of Amides[a]



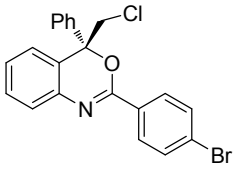
3 **4**



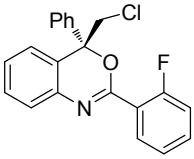
4a: 88%, 89% ee



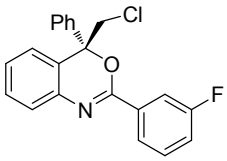
4b: 99%, 87% ee



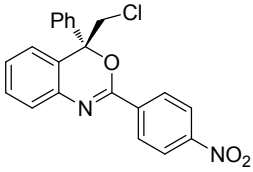
4c: 62%, 88% ee



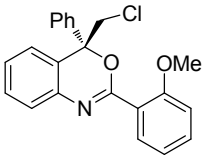
4d: 99%, 80% ee



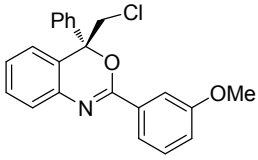
4e: 99%, 86% ee



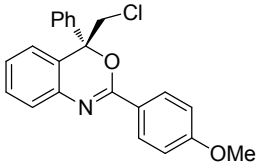
4f: 65%, 87% ee



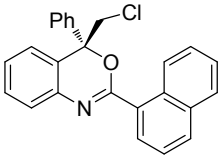
4g: 65%, 83% ee



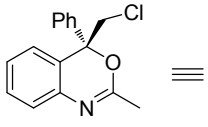
4h: 90%, 85% ee



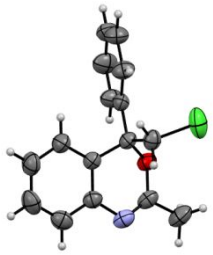
4i: 90%, 86% ee

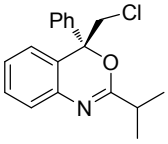


4j: 85%, 86% ee

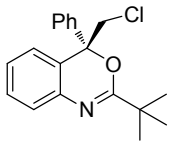


4k: 89%, 91% ee

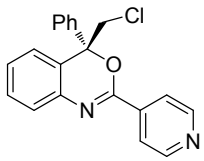




4l: 90%, 92% ee



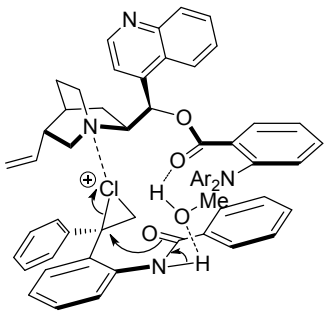
4m: 99%, 74% ee



4n: 96%, 70% ee

[a] Reaction conditions: **1** (0.10 mmol), DCDMH (0.12 mmol) and catalyst **VI** (0.01 mmol) in MeOH (2.0 mL) at -80 °C, isolated yields.

Scheme 5. Proposed Working Model



According to the above results and previous studies,[9a, d, h] a plausible working model was proposed in Scheme 5 (the hydantoin ion was omitted). On the one hand, the tertiary amine in the cinchonidine moiety may activate the chloronium specie to provide a chiral environment; on the other hand, H-bond formed between the benzamide NH in the substrate and the catalyst possibly mediated by MeOH increases the nucleophilicity of the amide group, meanwhile, the formed spatial configuration maybe is another factor for the high level enantiocontrol of the reaction.

CONCLUSIONS

In conclusion, an efficient protocol for the rapid synthesis of chiral 4*H*-3,1-benzoxazines by catalytic asymmetric chlorocyclization of *o*-vinylanilides has been described. Notably, a broad range of valuable chiral 4*H*-3,1-benzoxazines were synthesized in good yields with high enantioselectivities by means of this newly developed method. The biological evaluation of these optically active 4*H*-3,1-benzoxazines is currently ongoing in our laboratory.

EXPERIMENTAL SECTION

General Methods. Unless otherwise mentioned, all commercially available reagents were used without further purification. Chromatographic separations were performed using silica gel 200–300 mesh. The NMR spectra reagents were recorded in $CDCl_3$ on 400 or 600 MHz instrument with TMS as the internal standard. Chemical–shift values are given in ppm and referenced to the internal standard, TMS (tetramethylsilane). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q,

quadruplet; m, multiplet; dd, doublet of doublets, and br s, broad singlet. The coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined using a micromelting point apparatus without corrections. High–resolution mass spectra (HRMS) were recorded on a BioTOFQ mass spectrometer with an ESI source. X-ray crystallography analysis of the single crystal was performed on an Agilent SuperNova-CCD X-ray diffractometer. Optical rotation was obtained from Rudolph Research Analytical Autopol VI automatic polarimeter. Enantiomeric excesses were determined by HPLC using Daicel® Chiralcel OJ–H, OD–H or Daicel® Chiralpak AD–H, IF, IA column using *n*–hexane/*i*–PrOH as a mobile phase and detected by UV at 254 nm. Melting points were measured using a SGWX-4A microscopy melting point meter and are uncorrected.

Compounds **1a-1j**,[2l, 2p, 11] **1k–1p**,[13] **3a-3m**,[2l, 2p, 11] **3n**[12] were prepared according to the literature methods. **1a**,[2p] **1i**,[3a] **1j**,[14] **1k**,[2p] **1m-1n**,[2p] **3d**,[2o] **3k**,[15] **3l-3m**[16] are known compounds and their analysis data were identical with the reported data.

*N–(2–(1–(o–tolyl)vinyl)phenyl)benzamide (**1b**):* 217 mg, 88% yield, white solid, mp: 46 – 48 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.2 Hz, 1H), 8.03 (s, 1H), 7.48 – 7.45 (m, 1H), 7.37 – 7.26 (m, 7H), 7.22 – 7.14 (m, 3H), 5.60 (d, J = 27.9 Hz, 2H), 2.07 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 165.2, 147.6, 140.4, 136.1, 135.1, 134.8, 132.6, 131.7, 131.5, 130.2, 129.7, 128.8, 128.6, 128.5, 126.9, 126.8, 124.6, 121.7, 121.3, 20.9; IR (KBr, cm^{-1}) 3406, 1678, 1579, 1520, 1446, 1299, 1250, 918, 758, 707, 587.

*N–(2–(1–(m–tolyl)vinyl)phenyl)benzamide (**1c**):* 173 mg, 98% yield, white solid, mp: 72 – 76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.2 Hz, 1H), 7.71 (s, 1H), 7.35 – 7.28 (m, 2H), 7.25 – 7.21 (m, 1H), 7.21 – 7.01 (m, 9H), 5.74 (s, 1H), 5.28 (s, 1H), 2.21 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 165.0, 146.6, 139.1, 138.9, 135.5, 134.9, 131.8, 131.6, 130.6, 129.6, 129.1, 129.0, 128.5, 127.5, 126.8, 124.3, 124.1, 121.0, 117.8, 21.5; IR (KBr, cm^{-1}) 3405, 1678, 1579, 1520, 1446, 1299, 1250, 918, 758, 707, 587.

*N–(2–(1–(p–tolyl)vinyl)phenyl)benzamide (**1d**):* 254 mg, 98% yield, white solid, mp: 91 – 95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.2 Hz, 1H), 7.88 (s, 1H), 7.48 – 7.41 (m, 2H), 7.37 – 7.28 (m,

7H), 7.26 – 7.16 (m, 3H), 5.90 – 5.85 (m, 1H), 5.41 – 5.36 (m, 1H), 2.37 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 165.0, 146.2, 138.9, 136.1, 135.5, 134.9, 131.8, 131.6, 130.6, 129.8, 128.9, 128.5, 126.8, 124.3, 120.9, 116.9, 21.2; IR (KBr, cm^{-1}) 2924, 1787, 1721, 1680, 1604, 1580, 1522, 1448, 1304, 1251, 1215, 1019, 828, 760, 708.

*N–(2–(1–(3–(trifluoromethyl)phenyl)vinyl)phenyl)benzamide (**1e**):* 257 mg, 70% yield, white solid, mp: 118 – 122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.2 Hz, 1H), 7.70 (s, 1H), 7.61 (s, 1H), 7.49 (d, J = 7.0 Hz, 1H), 7.43 – 7.28 (m, 4H), 7.27 – 7.22 (m, 4H), 7.20 – 7.10 (m, 1H), 5.91 (s, 1H), 5.47 (s, 1H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 165.2, 145.4, 140.2, 135.4, 134.7, 131.9, 131.5 (q, $J_{C\text{-}F}$ =32.4 Hz), 131.2, 130.7, 130.4, 129.7, 129.5, 128.8, 126.6, 125.4 (q, $J_{C\text{-}F}$ = 3.2Hz), 124.8, 124.0 (q, $J_{C\text{-}F}$ = 271.0 Hz), 123.1 (q, $J_{C\text{-}F}$ = 3.5 Hz), 121.8, 119.4; IR (KBr, cm^{-1}) 3666, 3222, 1821, 1636, 1579, 1521, 1488, 1443, 1339, 1304, 1172, 1131, 1073, 913, 812, 772, 755, 710, 644.

*N–(2–(1–(4–(trifluoromethyl)phenyl)vinyl)phenyl)benzamide (**1f**):* 419 mg, 87% yield, white solid, mp: 136 – 143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.2 Hz, 1H), 7.67 – 7.56 (m, 3H), 7.52 – 7.41 (m, 4H), 7.36 – 7.19 (m, 6H), 6.00 (s, 1H), 5.57 (s, 1H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 165.3, 145.5, 142.8, 135.3, 134.8, 131.9, 131.3, 131.2, 130.9 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.7, 130.6, 129.5, 128.8, 127.2, 126.7, 126.0 (q, $J_{C\text{-}F}$ = 3.5Hz), 124.8, 124.1 (q, $J_{C\text{-}F}$ = 272.0 Hz), 121.9, 119.8; IR (KBr, cm^{-1}) 3240, 1647, 1524, 1485, 1326, 1157, 1120, 1068, 850, 749, 714, 690.

*N–(2–(1–(3–methoxyphenyl)vinyl)phenyl)benzamide (**1g**):* 247 mg, 75% yield, white solid, mp: 76 – 80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 8.1 Hz, 1H), 7.82 (s, 1H), 7.48 – 7.30 (m, 7H), 7.27 – 7.14 (m, 2H), 7.11 (d, J = 1.4 Hz, 1H), 7.02 – 6.95 (m, 1H), 6.64 (d, J = 7.5 Hz, 1H), 5.96 – 5.90 (m, 1H), 5.43 (s, 1H), 3.78 (s, 3H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 165.0, 159.9, 146.4, 138.9, 136.4, 135.5, 131.8, 130.7, 129.6, 129.2, 129.1, 128.9, 126.8, 124.4, 121.1, 118.3, 118.1, 117.8, 112.2, 55.5; IR (KBr, cm^{-1}) 3417, 1678, 1579, 1522, 1489, 1449, 1306, 1247, 1042, 912, 760, 707.

*N–(2–(1–(naphthalen–2–yl)vinyl)phenyl)benzamide (**1h**):* 420 mg, 86% yield, white solid, mp: 109 – 111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, d, J = 8.2 Hz), 7.85 (3H, q, J = 8.3 Hz), 7.80 – 7.75 (2H, m), 7.56 (1H, d, J = 8.5 Hz), 7.52 – 7.45 (3H, m), 7.30 (1H, t, J = 7.4 Hz), 7.26 – 7.22 (1H, m),

7.12 (2H, d, J = 7.7 Hz), 7.06 (2H, t, J = 7.6 Hz), 6.03 (1H, s), 5.52 (1H, s); $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$) δ 165.2, 146.5, 136.6, 135.7, 134.8, 133.6, 133.4, 131.7, 131.6, 130.7, 129.2, 129.0, 128.5, 127.7, 126.8, 126.7, 126.5, 124.5, 124.4, 121.1, 118.4; IR (KBr, cm^{-1}) 3416, 3058, 1678, 1580, 1521, 1447, 1304, 1252, 900, 823, 755, 708, 584, 476.

*N–(5–methyl–2–(1–phenylvinyl)phenyl)benzamide (**1l**):* 133 mg, 88% yield, white solid, mp: 92 – 94 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.77 (s, 1H), 7.48 – 7.34 (m, 6H), 7.27 (m, 5H), 7.02 (d, J = 7.6 Hz, 1H), 5.88 (s, 1H), 5.42 (s, 1H), 2.45 (s, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 165.1, 146.5, 139.3, 139.2, 135.3, 135.0, 131.6, 130.5, 129.1, 129.0, 128.8, 128.6, 126.9, 126.8, 125.2, 121.7, 117.6, 21.7; IR (KBr, cm^{-1}) 3420, 3059, 1679, 1609, 1573, 1529, 1466, 1418, 1296, 1253, 1027, 908, 821, 783, 704, 595.

*N–(5–fluoro–2–(1–phenylvinyl)phenyl)benzamide (**1o**):* 350 mg, 99% yield, white solid, mp: 72 – 80 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 8.2 Hz, 1H), 8.06 (s, 1H), 7.54 – 7.28 (m, 11H), 6.95 (t, J = 8.5 Hz, 1H), 6.21 (s, 1H), 5.50 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 165.3, 160.1 (d, $J_{C\text{-}F}$ = 243.4 Hz), 139.2, 138.1, 137.3 (d, $J_{C\text{-}F}$ = 4.9 Hz), 134.8, 132.0, 129.8 (d, $J_{C\text{-}F}$ = 9.4 Hz), 129.1, 129.0, 128.8, 126.9, 126.3, 119.6, 119.2 (d, $J_{C\text{-}F}$ = 19.5 Hz), 116.1 (d, $J_{C\text{-}F}$ = 3.0 Hz), 111.2 (d, $J_{C\text{-}F}$ = 22.3 Hz); IR (KBr, cm^{-1}) 3418, 3061, 1684, 1583, 1523, 1492, 1461, 1308, 1251, 1119, 1028, 982, 919, 787, 747, 707, 660, 583, 531.

*N–(2–fluoro–6–(1–phenylvinyl)phenyl)benzamide (**1p**):* 190 mg, 98% yield, white solid, mp: 114 – 116 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 1H), 7.39 (d, J = 7.3 Hz, 2H), 7.29 (q, J = 8.9, 8.1 Hz, 8H), 7.22 (d, J = 13.7 Hz, 2H), 7.03 (s, 1H), 5.72 (s, 1H), 5.43 (s, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 165.3, 158.04 (d, $J_{C\text{-}F}$ = 249.1 Hz), 146.5, 140.5, 140.0, 133.7, 131.8, 128.9, 128.4, 128.3, 128.1 (d, $J_{C\text{-}F}$ = 8.5Hz), 127.2, 126.6, 126.1 (d, $J_{C\text{-}F}$ = 2.8 Hz), 122.7 (d, $J_{C\text{-}F}$ = 13.2 Hz), 117.5, 116.0 (d, $J_{C\text{-}F}$ = 20.6Hz); IR (KBr, cm^{-1}) 3285, 3060, 1660, 1606, 1578, 1514, 1491, 1466, 1294, 1263, 1026, 959, 909, 782, 707.

*4–Fluoro–N–(2–(1–phenylvinyl)phenyl)benzamide (**3a**):* 163 mg, 92% yield, white solid, mp: 108 – 112 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 8.2 Hz, 1H), 7.71 (s, 1H), 7.53 – 7.35 (m, 7H), 7.31 –

7.18 (m, 3H), 6.99 (t, J = 8.5 Hz, 2H), 5.93 (s, 1H), 5.47 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 164.8 (d, $J_{C\text{-}F}$ = 251.0 Hz), 164.0, 146.4, 139.0, 135.4, 131.7, 131.1 (d, $J_{C\text{-}F}$ = 3.0 Hz), 130.8, 129.2, 129.2 (d, $J_{C\text{-}F}$ = 3.3 Hz), 129.1, 128.9, 126.9, 124.6, 121.2, 118.1, 115.6 (d, $J_{C\text{-}F}$ = 21.9 Hz); IR (KBr, cm^{-1}) 3225, 1644, 1602, 1530, 1500, 1446, 1315, 1231, 909, 847, 765, 678, 576.

*4–Chloro–N–(2–(1–phenylvinyl)phenyl)benzamide (**3b**):* 171 mg, 95% yield, white solid, mp: 118 – 121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.2 Hz, 1H), 7.60 (s, 1H), 7.39 – 7.24 (m, 7H), 7.15 (dd, J = 13.5, 8.0 Hz, 3H), 7.05 (d, J = 8.4 Hz, 2H), 5.81 (s, 1H), 5.34 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 164.0, 146.3, 139.0, 137.9, 135.2, 133.3, 131.8, 130.8, 129.3, 129.2, 129.0, 128.8, 128.2, 126.9, 124.7, 121.1, 118.2; IR (KBr, cm^{-1}) 3224, 1680, 1638, 1593, 1524, 1488, 1447, 1308, 1091, 911, 843, 760, 706.

*4–Bromo–N–(2–(1–phenylvinyl)phenyl)benzamide (**3c**):* 167 mg, 86% yield, white solid, mp: 128 – 131 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.2 Hz, 1H), 7.60 (s, 1H), 7.31 (m, 8H), 7.14 (q, J = 8.1, 7.5 Hz, 1H), 6.98 (d, J = 8.4 Hz, 2H), 5.81 (s, 1H), 5.35 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 164.1, 146.3, 139.0, 135.2, 133.8, 131.8, 130.8, 129.3, 129.2, 129.0, 128.4, 126.9, 126.4, 124.7, 121.1, 118.2; IR (KBr, cm^{-1}) 3419, 1680, 1585, 1522, 1487, 1447, 1307, 1251, 1072, 1010, 910, 841, 757, 706, 582, 517.

*3–Fluoro–N–(2–(1–phenylvinyl)phenyl)benzamide (**3e**):* 408 mg, 64% yield, white solid, mp: 105 – 107 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 8.2 Hz, 1H), 7.70 (s, 1H), 7.50 – 7.30 (m, 7H), 7.24 (dq, J = 14.7, 7.7 Hz, 2H), 7.12 (t, J = 7.7 Hz, 1H), 6.97 (d, J = 7.9 Hz, 2H), 5.90 (s, 1H), 5.44 (s, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 163.8 (d, $J_{C\text{-}F}$ = 2.1Hz), 162.8 (d, $J_{C\text{-}F}$ = 246.8 Hz), 146.4, 139.0, 137.2 (d, $J_{C\text{-}F}$ = 6.5 Hz), 135.2, 131.9, 130.8, 130.3 (d, $J_{C\text{-}F}$ = 7.8 Hz), 129.3, 129.2, 129.1, 126.9, 124.7, 122.3 (d, $J_{C\text{-}F}$ = 2.8 Hz), 121.3, 118.7 (d, $J_{C\text{-}F}$ = 21.2 Hz), 118.1, 114.2 (d, $J_{C\text{-}F}$ = 22.9 Hz); IR (KBr, cm^{-1}) 3418, 1680, 1584, 1523, 1489, 1447, 1306, 1265, 1194, 755, 708.

*4–Nitro–N–(2–(1–phenylvinyl)phenyl)benzamide (**3f**):* 177 mg, 83% yield, white solid, mp: 149 – 158 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.2 Hz, 1H), 8.07 (d, J = 8.6 Hz, 2H), 7.67 (s, 1H), 7.44 – 7.30 (m, 7H), 7.27 (d, J = 8.8 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H), 5.86 (s, 1H), 5.40 (s, 1H);

$^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 162.9, 149.6, 146.1, 140.4, 138.9, 134.8, 132.0, 130.9, 129.4, 129.3, 129.1, 127.9, 126.9, 125.3, 123.8, 121.3, 118.5; IR (KBr, cm^{-1}) 1681, 1603, 1525, 1448, 1347, 1304, 1253, 851, 764, 712, 580.

*2–Methoxy–N–(2–(1–phenylvinyl)phenyl)benzamide (**3g**):* 247 mg, 75% yield, white soild, mp: 89 – 93 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.57 (d, J = 8.3 Hz, 1H), 8.18 (d, J = 6.7 Hz, 1H), 7.35 (dd, J = 17.3, 7.2 Hz, 4H), 7.22 (dq, J = 13.8, 6.8 Hz, 3H), 7.12 (dt, J = 14.6, 6.7 Hz, 2H), 7.01 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.00 (s, 1H), 5.34 (s, 1H), 3.51 (s, 3H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 163.4, 157.2, 146.0, 139.0, 136.5, 133.1, 132.5, 132.3, 130.0, 128.6, 128.3, 126.4, 123.9, 121.8, 121.3, 116.3, 111.3, 55.5; IR (KBr, cm^{-1}) 3337, 1667, 1583, 1532, 1449, 1309, 1236, 1021, 757, 711.

*3–Methoxy–N–(2–(1–phenylvinyl)phenyl)benzamide (**3h**):* 169 mg, 79% yield, white solid, mp: 117 – 120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 8.2 Hz, 1H), 7.81 (s, 1H), 7.49 – 7.30 (m, 7H), 7.19 (dt, J = 12.7, 7.8 Hz, 2H), 7.11 (s, 1H), 6.98 (d, J = 8.1 Hz, 1H), 6.63 (d, J = 7.5 Hz, 1H), 5.93 (s, 1H), 5.43 (s, 1H), 3.78 (s, 3H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 165.0, 159.9, 146.3, 138.9, 136.4, 135.5, 131.8, 130.7, 129.6, 129.2, 129.1, 128.9, 124.4, 121.1, 118.3, 118.1, 117.8, 112.2, 55.5; IR (KBr, cm^{-1}) 1678, 1581, 1520, 1489, 1446, 1305, 1270, 1041, 911, 757, 709, 595.

*4–Mthoxy–N–(2–(prop–1–en–2–yl)phenyl)benzamide (**3i**):* 230 mg, 71% yield, white soild, mp: 110 – 113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 8.2 Hz, 1H), 7.72 (s, 1H), 7.38 (tt, J = 18.9, 7.7 Hz, 7H), 7.21 (dd, J = 18.4, 8.0 Hz, 3H), 6.78 (d, J = 8.4 Hz, 2H), 5.90 (s, 1H), 5.42 (s, 1H), 3.80 (s, 3H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 164.6, 162.3, 146.5, 139.1, 135.7, 131.5, 130.7, 129.2, 129.1, 128.9, 128.7, 127.2, 126.9, 124.1, 121.0, 117.9, 113.8, 55.5; IR (KBr, cm^{-1}) 3422, 1674, 1606, 1579, 1505, 1446, 1305, 1249, 1176, 1112, 1029, 909, 842, 762, 704, 576.

*N–(2–(1–phenylvinyl)phenyl)–1–naphthamide (**3j**):* 319 mg, 91% yield, white solid, mp: 86 – 89 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, J = 7.4 Hz, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.85 (dd, J = 18.4, 8.0 Hz, 2H), 7.64 (s, 1H), 7.55 – 7.45 (m, 3H), 7.36 (d, J = 7.5 Hz, 1H), 7.34 (s, 5H), 7.27 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 6.9 Hz, 1H), 5.84 (s, 1H), 5.40 (s, 1H); $^{13}C\{^{1}H\}$NMR (150 MHz, $CDCl_3$) δ 167.1,

146.2, 139.1, 135.7, 134.3, 133.8, 132.0, 131.0, 130.7, 130.2, 129.1, 129.0, 128.7, 128.3, 127.3, 126.8, 126.5, 125.5, 124.7, 124.6, 121.3, 117.7; IR (KBr, cm^{-1}) 1676, 1515, 1446, 1302, 1136, 906, 779, 707, 592, 503.

*N–(2–(1–phenylvinyl)phenyl)isonicotinamide (**3n**):* 414 mg, 69% yield, yellow solid, mp: 125 – 128 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 4.7 Hz, 2H), 8.40 (d, J = 8.1 Hz, 1H), 7.76 (s, 1H), 7.45 (t, J = 7.7 Hz, 1H), 7.38 (s, 6H), 7.29 – 7.21 (m, 1H), 7.05 (d, J = 5.0 Hz, 2H), 5.91 (s, 1H), 5.44 (s, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 163.0, 150.6, 146.1, 141.9, 138.9, 134.7, 132.0, 130.9, 129.3, 129.1, 126.8, 125.2, 121.4, 120.5, 118.5, 118.4, 118.3; IR (KBr, cm^{-1}) 3224, 1648, 1602, 1528, 1489, 1313, 905, 760, 682.

General Procedure for the Synthesis of 4*H*-3,1-benzoxazine.

To a solution of substrate (0.1 mmol, 1.0 equiv), **VI** (5.9 mg, 0.01 mmol, 0.1 equiv) in MeOH (4 mL) at -80 °C was added DCDMH (23.6 mg, 0.12 mmol, 1.2 equiv). The resulting mixture was stirred at -80 °C and monitored by TLC. Upon completion, the reaction was quenched by saturated aqueous solution of $Na_2S_2O_4$ at –80 °C, then warmed to room temperature. The aqueous phase was extracted with CH_2Cl_2, the combined organic phases were dried over anhydrous Na_2SO_4, filtered, and evaporated in *vacuo*. The residue was purified by flash column chromatography (PE/EA = 10:1) to afford the product.

*(S)–4–(Chloromethyl)–2,4–diphenyl–4H–benzo[d][1,3]oxazine (**2a**):* 28.1 mg, 84% yield, yellow solid, mp: 90 – 93 °C; $[\alpha]_D^{20}$ = 53.1 (*c* 0.10, $CDCl_3$, 92% ee); ^1H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.49 (dd, J = 18.6, 7.6 Hz, 4H), 7.42 (d, J = 6.9 Hz, 2H), 7.37 (tt, J = 14.2, 6.0 Hz, 3H), 7.28 (d, J = 5.0 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 4.34 – 4.25 (m, 2H). $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$) δ 156.2, 140.1, 139.7, 132.3, 131.8, 129.8, 128.8, 128.7, 128.5, 128.3, 126.7, 126.6, 125.8, 125.7, 125.1, 83.0, 48.6; IR (KBr, cm^{-1}) 2959, 2924, 2853, 1626, 1597, 1573, 1480, 1450, 1320, 1261, 1220, 1084,1026, 772, 731, 634; HRMS $(M + H)^+$ calcd for $C_{21}H_{17}ClNO$ 334.0993, found

334.0993; HPLC conditions: Daicel Chiralpak AD–H, *i*–PrOH/hexane = 0.5/99.5, 0.3 mL/min, 254 nm, t_1 = 36.3 min (major), t_2 = 40.5 min (minor).

*(S)–4–(Chloromethyl)–2–phenyl–4–(o–tolyl)–4H–benzo[d][1,3]oxazine (**2b**):* 22.5 mg, 65% yield, yellow solid, mp: 176–183 °C; $[\alpha]_D^{20}$ = 13.7 (*c* 0.10, $CHCl_3$, 16% ee); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.7 Hz, 2H), 7.68 – 7.61 (m, 1H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.41 – 7.29 (m, 4H), 7.25 – 7.18 (m, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 4.30 – 4.18 (m, 2H), 2.06 (s, 3H). ^{13}C{^{1}H}NMR (150 MHz, $CDCl_3$) δ 155.9, 139.3, 137.0, 133.4, 132.2, 131.8, 129.9, 129.2, 128.5, 128.4, 127.3, 126.9, 125.9, 125.4, 125.1, 83.0, 49.0, 21.7; IR (KBr, cm^{-1}) 2961, 2925, 2855, 1624, 1594, 1573, 1493, 1478, 1456, 1379,1322, 1300, 1261, 1176, 1084, 1070, 1026, 864, 799, 766, 724, 694, 633; HRMS (M + H)$^+$ calcd for $C_{22}H_{19}ClNO$ 348.1150, found 348.1142; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 9.7 min (major), t_2 = 11.4 min (minor).

*(S)–4–(Chloromethyl)–2–phenyl–4–(m–tolyl)–4H–benzo[d][1,3]oxazine (**2c**):* 26.0 mg, 77% yield, yellow oil; $[\alpha]_D^{20}$ = 48.8 (*c* 0.11, $CHCl_3$, 89% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.23 (m, 2H), 7.50 (dt, *J* = 14.5, 7.0 Hz, 3H), 7.44 – 7.36 (m, 2H), 7.31 – 7.20 (m, 4H), 7.12 (dd, *J* = 20.2, 5.7 Hz, 2H), 4.34 – 4.19 (m, 2H), 2.32 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 156.3, 140.0, 139.6, 138.4, 132.3, 131.8, 129.7, 129.6, 128.5, 128.4, 128.3, 127.3, 126.7, 125.7, 125.2, 123.6, 83.1, 48.6, 21.8; IR (KBr, cm^{-1}) 2956, 2925, 2854, 1627, 1597, 1574, 1492, 1480, 1456, 1319, 1261, 1243, 1085, 1070, 765, 738, 695; HRMS (M + H)$^+$ calcd for $C_{22}H_{19}ClNO$ 348.1150, found 348.1139; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 14.0 min (major), t_2 = 15.7 min (minor).

*(S)–4–(Chloromethyl)–2–phenyl–4–(p–tolyl)–4H–benzo[d][1,3]oxazine (**2d**):* 32.0 mg, 92% yield, yellow oil; $[\alpha]_D^{20}$ = 34.0 (*c* 0.10, $CHCl_3$, 82% ee); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.6 Hz, 2H), 7.55 – 7.49 (m, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.39 (d, *J* = 5.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 7.0 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 7.5 Hz, 1H), 4.30 – 4.20 (m, 2H), 2.32 (s, 3H); ^{13}C{^{1}H}NMR (150 MHz, $CDCl_3$) δ 156.4, 139.7, 138.7, 137.2, 132.3, 131.8, 129.7, 129.4, 128.5,

128.4, 126.7, 126.5, 125.8, 125.7, 125.1, 83.1, 48.6, 21.2; IR (KBr, cm^{-1}) 2957, 2954, 2854, 1626, 1597, 1573, 1511, 1492, 1480, 1455, 1320, 1260, 1244, 1176, 1085, 1070, 1026, 1000, 934, 816, 765, 742, 721; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO$ 348.1150, found 348.1134; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 11.1 min (major), t_2 = 13.4 min (minor).

(S)–4–(Chloromethyl)–2–phenyl–4–(3–(trifluoromethyl)phenyl)–4H–benzo[d][1,3]oxazine ***(2e)****:* 35.0 mg, 88% yield, colorless oil; $[\alpha]_D^{20}$ = 81.0 (*c* 0.10, $CHCl_3$, 87% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 – 8.21 (m, 2H), 7.74 (s, 1H), 7.64 (dd, *J* = 21.2, 7.8 Hz, 2H), 7.58 – 7.45 (m, 4H), 7.42 (d, *J* = 4.0 Hz, 2H), 7.27 – 7.21 (m, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 4.25 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 155.9, 141.0, 139.5, 132.0, 131.9, 131.1 (q, $J_{C\text{-}F}$ = 32.2 Hz), 130.2, 129.2, 128.6, 128.4 , 127.0, 126.0, 125.7 (q, $J_{C\text{-}F}$ = 3.3 Hz), 125.1, 124.9, 123.9 (q, $J_{C\text{-}F}$ = 271.0Hz), 123.6 (q, $J_{C\text{-}F}$ = 3.9 Hz), 82.5, 48.0; IR (KBr, cm^{-1}) 2959, 2928, 2856, 1727, 1627, 1597, 1574, 1493, 1480, 1450, 1330, 1288,1260, 1242, 1166, 1129, 1079, 1027, 907, 843, 804, 765, 745, 721; HRMS $(M + H)^+$ calcd for $C_{22}H_{16}ClF_3NO$ 402.0867, found 402.0848; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 11.1 min (major), t_2 = 13.0 min (minor).

(S)–4–(Chloromethyl)–2–phenyl–4–(4–(trifluoromethyl)phenyl)–4H–benzo[d][1,3]oxazine ***(2f)****:* 35.0 mg, 88% yield, colorless oil; $[\alpha]_D^{20}$ = 65.4 (*c* 0.09, $CHCl_3$, 87% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.23 (m, 2H), 7.62 (q, *J* = 8.5 Hz, 4H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 4.0 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 4.25 (s, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 155.9, 143.8, 139.5, 132.1, 131.9, 130.9 (q, $J_{C\text{-}F}$ = 32.4 Hz), 130.2, 128.6, 128.3, 127.2, 127.0, 126.0, 125.7 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125.1, 124.8, 124.1 (q, $J_{C\text{-}F}$ = 271.0 Hz), 82.6, 48.1; IR (KBr, cm^{-1}) 28, 2849, 1627, 1597, 1574, 1479, 1457, 1410, 1327, 1261, 1170, 1089, 1071, 1019, 801, 766, 749, 725, 695; HRMS $(M + H)^+$ calcd for $C_{22}H_{16}ClF_3NO$ 402.0867, found 402.0850; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 11.0 min (major), t_2 = 15.1 min (minor).

*(S)–4–(Chloromethyl)–4–(3–methoxyphenyl)–2–phenyl–4H–benzo[d][1,3]oxazine (**2g**):* 30.0 mg, 86% yield, colorless oil; $[\alpha]_D^{20}$ = 47.0 (*c* 0.09, $CHCl_3$, 90% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.2 Hz, 2H), 7.50 (dq, *J* = 14.6, 7.0 Hz, 3H), 7.39 (d, *J* = 4.7 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.04 – 6.95 (m, 2H), 6.85 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.25 (s, 2H), 3.71 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 159.8, 156.2, 141.7, 139.7, 132.3, 131.8, 129.8, 129.7, 128.5, 128.3, 126.7, 125.8, 125.6, 125.0, 118.8, 113.9, 112.9, 83.0, 55.3, 48.6; IR (KBr, cm^{-1}) 2956, 2925, 2854, 1672, 1626, 1598, 1575, 1523, 1482.1457, 1377, 1319, 1291, 1261, 1085, 1041; 766, 739, 694; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO_2$ 364.1099, found 364.1087; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 23.7min (major), t_2 = 26.1 min (minor).

*(S)–4–(Chloromethyl)–4–(naphthalen–2–yl)–2–phenyl–4H–benzo[d][1,3]oxazine (**2h**):* 25.3 mg, 66% yield, colorless oil; $[\alpha]_D^{20}$ =108.8 (*c* 0.10, $CHCl_3$, 84% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 6.9 Hz, 2H), 7.90 – 7.75 (m, 4H), 7.65 – 7.60 (m, 1H), 7.58 – 7.45 (m, 5H), 7.42 (d, *J* = 6.0 Hz, 2H), 7.27 – 7.22 (m, 1H), 4.45 – 4.30 (m, 2H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 156.2, 139.8, 137.4, 133.2, 132.8, 132.3, 131.8, 129.9, 128.7, 128.6, 128.5, 128.4, 127.7, 127.0, 126.7, 126.2, 125.9, 125.8, 125.3, 124.2, 83.2, 48.5; IR (KBr, cm^{-1}) 2956, 2925, 2854, 1626, 1597,1573, 1479, 1456, 1377, 1318, 1290, 1262, 1242, 1084, 1070, 1027, 931, 900, 856, 817, 765, 694, 477; HRMS $(M + H)^+$ calcd for $C_{25}H_{19}ClNO$ 384.1150, found 384.1134; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 27.4 min (major), t_2 = 30.8 min (minor).

*(S)–4–(Chloromethyl)–4–methyl–2–phenyl–4H–benzo[d][1,3]oxazine (**2i**):* 24.1 mg, 90% yield, yellow solid, mp: 56–59 °C; $[\alpha]_D^{20}$ = 8.1 (*c* 0.11, $CHCl_3$, 64% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.1 Hz, 2H), 7.48 (dt, *J* = 14.6, 7.0 Hz, 3H), 7.41 – 7.32 (m, 2H), 7.28 – 7.21 (m, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 3.76 (dd, *J* = 87.5, 11.9 Hz, 2H), 1.91 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 156.4, 139.3, 132.4, 131.7, 129.7, 128.4, 128.3, 127.0, 126.9, 125.6, 123.4, 79.0, 50.7, 24.0; IR (KBr, cm^{-1}) 2954, 2925, 2854, 1626, 1600, 1574, 1482, 1451, 1378, 1322, 1266, 1250, 1212, 1173, 1096, 1071, 1028, 942, 882, 864, 847, 163, 723, 695, 608, 527, 499; HRMS $(M + H)^+$ calcd for $C_{16}H_{15}ClNO$

272.0837, found 272.0833; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 13.1 min (major), t_2 = 15.5 min (minor).

*(S)-4-Butyl-4-(chloromethyl)-2-phenyl-4H-benzo[d][1,3]oxazine (**2j**):* 30 mg, 96% yield, colorless oil; $[\alpha]_D^{20}$ = 10.5 (*c* 0.20, $CHCl_3$, 49% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.1 Hz, 2H), 7.49 (m, 3H), 7.36 (d, *J* = 4.3 Hz, 2H), 7.24 (m, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 3.88 (d, *J* = 11.8 Hz, 1H), 3.75 (d, *J* = 11.8 Hz, 1H), 2.28 (m, 1H), 2.07 (m, 1H), 1.50 – 1.26 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 156.3, 139.9, 132.6, 131.6, 129.4, 128.4, 128.2, 126.7, 125.8, 125.0, 123.7, 82.1, 51.2, 37.0, 25.8, 22.9, 14.0. IR (KBr, cm^{-1}) 2959, 2926, 2858, 1628, 1600, 1574, 1485, 1455, 1321, 1261, 1088, 1024, 800, 764, 721; HRMS $(M + H)^+$ calcd for 314.1306, found 314.1303; HPLC conditions: Daicel Chiralcel OJ–H, *i*–PrOH/hexane = 10/90, 1.0 mL/min, 254 nm, t_1 = 5.3 min (major), t_2 = 6.5 min (minor).

*(S)–4–(Chloromethyl)–6–methyl–2,4–diphenyl–4H–benzo[d][1,3]oxazine (**2k**):* 30.0 mg, 86% yield, yellow solid, mp: 95–104 °C; $[\alpha]_D^{20}$ = 34.7 (*c* 0.12, $CHCl_3$, 60% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 7.2 Hz, 2H), 7.80 (dt, *J* = 17.4, 6.4 Hz, 5H), 7.65 (dt, *J* = 23.6, 7.3 Hz, 4H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.20 (s, 1H), 4.64 – 4.48 (m, 2H), 2.67 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 155.5, 140.2, 137.3, 136.6, 132.4, 131.6, 130.4, 128.7, 128.6, 128.4, 128.2, 126.6, 125.6, 125.5, 82.9, 48.6, 21.6; IR (KBr, cm^{-1}) 2960, 2924, 2854, 1628, 1602, 1577, 1493, 1449, 1318, 1260, 1248, 1176, 1086, 1070, 1026, 826, 798, 778, 757, 732, 694, 642, 566, 547, 508; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO$ 348.1150, found 348.1144; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 16.4 min (major), t_2 = 20.3 min (minor).

*(S)–4–(Chloromethyl)–7–methyl–2,4–diphenyl–4H–benzo[d][1,3]oxazine (**2l**):* 19.6 mg, 56% yield, colorless oil; $[\alpha]_D^{20}$ =61.1 (*c* 0.11, $CHCl_3$, 76% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 – 8.24 (m, 2H), 7.57 – 7.40 (m, 5H), 7.40 – 7.28 (m, 3H), 7.24 (s, 1H), 7.10 – 6.97 (m, 2H), 4.31 – 4.19 (m, 2H), 2.39 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 156.2, 140.4, 139.8, 139.5, 132.4, 131.7, 128.7, 128.6, 128.5, 128.3, 127.4, 126.5, 126.3, 124.9, 122.8, 83.0, 48.7, 21.3; IR (KBr, cm^{-1}) 2956, 2924, 2854, 1630, 1606, 1571, 1493, 1450, 1317, 1301, 1270, 1175, 1087, 1070, 1026, 1001, 884, 811, 778, 757,

732, 695, 631, 597, 582, 549; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO$ 348.1150, found 348.1142; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 15.8 min (major), t_2 = 17.6 min (minor).

*(S)–4–(Chloromethyl)–8–methyl–2,4–diphenyl–4H–benzo[d][1,3]oxazine (**2m**):* 32.3 mg, 92% yield, colorless oil; $[\alpha]_D^{20}$ = 66.3 (*c* 0.10, $CHCl_3$, 80% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.23 (m, 2H), 7.57 – 7.39 (m, 5H), 7.33 (q, *J* = 8.4, 7.4 Hz, 3H), 7.26 – 7.20 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 4.30 – 4.19 (m, 2H), 2.55 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 155.1, 140.3, 137.9, 134.4, 132.7, 131.6, 131.1, 128.7, 128.6, 128.4, 126.6, 126.0, 125.6, 122.7, 83.0, 48.5, 17.3; IR (KBr, cm^{-1}) 2956, 2924, 2853, 1626, 1589, 1576, 1493, 1462, 1450, 1377, 1317, 1302, 1255, 1228, 1176, 1094, 1070, 1026, 1000, 847, 803, 761, 732, 715, 694, 666, 646, 624, 563, 551; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO$ 348.1150, found 348.1144; HPLC conditions: Daicel Chiralcel OJ–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 32.4 min (major), t_2 = 40.1 min (minor).

*(S)–4–(Chloromethyl)–6–fluoro–2,4–diphenyl–4H-benzo[d][1,3]oxazine (**2n**):* 7.1mg, 20% yield, colorless oil; $[\alpha]_D^{20}$ = 64.9 (*c* 0.12, $CHCl_3$, 75% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.4 Hz, 2H), 7.57 – 7.41 (m, 5H), 7.41 – 7.29 (m, 4H), 7.09 (td, *J* = 8.5, 2.6 Hz, 1H), 6.83 (dd, *J* = 8.6, 2.6 Hz, 1H), 4.23 (q, *J* = 12.6 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 161.08 (d, $J_{C\text{-}F}$ = 245.0 Hz), 155.6, 139.5, 136.1 (d, $J_{C\text{-}F}$ = 2.7Hz), 132.0, 131.9, 129.0, 128.9, 128.5, 128.2, 127.4 (d, $J_{C\text{-}F}$ = 8.1 Hz), 127.2 (d, $J_{C\text{-}F}$ = 7.4 Hz), 126.4, 116.6 (d, $J_{C\text{-}F}$ = 22.1 Hz), 112.5 (d, $J_{C\text{-}F}$ = 75.5 Hz), 82.8, 48.3; IR (KBr, cm^{-1}) 2960, 2926, 2854, 1728, 1627, 1578, 1485, 1450, 1432, 1318, 1288, 1251, 1208, 1178, 1157, 1085, 1071, 1026, 956, 911, 864, 825, 800, 779, 755, 733, 694, 643, 569, 552, 512; HRMS $(M + H)^+$ calcd for $C_{21}H_{16}ClFNO$ 352.0899, found 352.0886; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 12.6 min (major), t_2 = 13.5 min (minor).

*(S)–4–(Chloromethyl)–7–fluoro–2,4–diphenyl–4H–benzo[d][1,3]oxazine (**2o**):* 20.1 mg, 56% yield, colorless oil; $[\alpha]_D^{20}$ = 63.4 (*c* 0.10, $CHCl_3$, 91% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.3 Hz, 2H), 7.58 – 7.40 (m, 5H), 7.35 (q, *J* = 5.8 Hz, 3H), 7.23 – 7.10 (m, 2H), 6.92 (d, *J* = 7.1 Hz, 1H), 4.33 – 4.20 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 156.7, 156.4 (d, $J_{C\text{-}F}$ = 252.4 Hz), 154.7 (d, $J_{C\text{-}F}$ = 26.6

Hz), 144.2, 139.8, 132.1, 131.9, 129.0, 128.5 (d, $J_{C\text{-}F}$ = 2.7 Hz), 128.8, 127.8, 126.8 (d, $J_{C\text{-}F}$ = 3.9 Hz), 126.4, 120.6 (d, $J_{C\text{-}F}$ = 3.7 Hz), 116.6 (d, $J_{C\text{-}F}$ = 19.7 Hz), 83.0, 48.6; IR (KBr, cm^{-1}) 2957, 2923, 2852, 1627, 1605, 1575, 1494, 1475, 1450, 1320, 1303, 1261, 1247, 1178, 1090, 1070, 1026, 1000, 896, 790, 777, 763, 748, 734, 713, 694, 668, 649, 630; HRMS $(M + H)^+$ calcd for $C_{21}H_{16}ClFNO$ 352.0899, found 352.0897; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 21.9 min (major), t_2 = 26.5 min (minor).

*(S)–4–(Chloromethyl)–8–fluoro–2,4–diphenyl–4H–benzo[d][1,3]oxazine (**2p**):* 13.7 mg, 38% yield, colorless oil; $[\alpha]_D^{20}$ = –92 (*c* 0.17, $CHCl_3$, 70% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.2 Hz, 2H), 7.57 – 7.37 (m, 5H), 7.37 (d, *J* = 8.1 Hz, 3H), 7.37 – 7.23 (m, 4H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.07 – 6.97 (m, 1H), 4.55 (d, *J* = 12.2 Hz, 1H), 4.35 (d, *J* = 13.8 Hz, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 158.2 (d, $J_{C\text{-}F}$ = 246.4 Hz), 156.5, 142.1 (d, $J_{C\text{-}F}$ = 2.9 Hz), 140.4, 132.0, 131.9, 130.6 (d, $J_{C\text{-}F}$ = 10.1 Hz), 129.2, 128.9, 128.5, 128.2, 125.8, 122.1 (d, $J_{C\text{-}F}$ = 2.4 Hz), 114.2 (d, $J_{C\text{-}F}$ = 23.5 Hz), 112.4 (d, $J_{C\text{-}F}$ = 12.8 Hz), 82.8, 77.5, 50.6; IR (KBr, cm^{-1}) 2957, 2925, 2855, 1745, 1610, 1577, 1461, 1377, 1261, 1095, 1020, 866, 799, 694; HRMS $(M + H)^+$ calcd for $C_{21}H_{16}ClFNO$ 352.0899, found 352.0895; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 12.3 min (major), t_2 = 14.7 min (minor).

*(S)–4–(Chloromethyl)–2–(4–fluorophenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4a**):* 29.0mg, 88% yield, colorless oil; $[\alpha]_D^{20}$ =45.8 (*c* 0.10, $CHCl_3$, 89% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.21 (m, 2H), 7.50 – 7.29 (m, 7H), 7.24 (dd, *J* = 10.6, 4.9 Hz, 1H), 7.19 – 7.06 (m, 3H), 4.32 – 4.20 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 165.2 (d, $J_{C\text{-}F}$ = 250.8 Hz), 155.3, 140.0, 139.6, 130.6 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.8, 128.9, 128.7, 128.5 (d, $J_{C\text{-}F}$ = 2.7 Hz), 126.7, 126.6, 125.7, 125.6, 125.1, 115.6 (d, $J_{C\text{-}F}$ = 21.8 Hz), 83.2, 48.5; IR (KBr, cm^{-1}) 2958, 2925, 2854,1679, 1658, 1627, 1598, 1577, 1554, 1508, 1478, 1461, 1378, 1316, 1292, 1261, 1236, 1153, 1083, 1015, 846, 807, 766, 734, 696, 677; HRMS $(M + H)^+$ calcd for $C_{21}H_{16}ClFNO$ 352.0899, found 352.0890; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 20.4 min (major), t_2 = 23.8 min (minor).

*(S)–4–(Chloromethyl)–2–(4–chlorophenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4b**):* 34.3 mg, 99% yield, white solid, mp: 42–48 °C; $[\alpha]_D^{20}$ =92.2 (*c* 0.09, $CHCl_3$, 87% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.2 Hz, 2H), 7.39 (ddt, *J* = 20.3, 14.4, 7.6 Hz, 9H), 7.26 – 7.21 (m, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 4.31 – 4.19 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 155.3, 140.0, 139.5, 138.0, 130.8, 129.9, 129.7, 128.9, 128.8, 128.8, 128.7, 126.9, 126.6, 125.8, 125.6, 125.2, 83.2, 48.5; IR (KBr, cm^{-1}) 2955, 2925, 2854, 1625, 1596, 1568, 1488, 1456, 1402, 1378, 1317, 1260, 1241, 1171, 1092, 1032, 1014, 839, 802, 766, 733, 696, 676, 669; HRMS $(M + H)^+$ calcd for $C_{21}H_{16}Cl_2NO$ 368.0604, found 368.0593; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 18.3 min (major), t_2 = 21.1 min (minor).

*(S)–2–(4–Bromophenyl)–4–(chloromethyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4c**):* 20.5 mg, 62% yield, yellow solid, mp: 85–91 °C; $[\alpha]_D^{20}$ =75.9 (*c* 0.11, $CHCl_3$, 88% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.38 (dt, *J* = 19.0, 7.3 Hz, 7H), 7.23 (d, *J* = 2.8 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 4.31 – 4.19 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 155.4, 140.0, 139.5, 131.8, 131.3, 129.9, 129.8, 128.9, 128.7, 126.9, 126.6, 126.5, 125.8, 125.6, 125.2, 83.2, 48.5; IR (KBr, cm^{-1}) 2957, 2925, 2854, 1624, 1591, 1565, 1524, 1485, 1457, 1397, 1378, 1318, 1261, 1173, 1084, 1011, 835, 801, 766, 732, 696, 670, 634, 590; HRMS $(M + H)^+$ calcd for $C_{21}H_{16}BrClFNO$ 412.0098, found 412.0079; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 19.8 min (major), t_2 = 23.8 min (minor).

*(S)–4–(Chloromethyl)–2–(2–fluorophenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4d**):* 35.0 mg, 99% yield, colorless oil; $[\alpha]_D^{20}$ = 30.8 (*c* 0.27, $CHCl_3$, 80% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.06 (m, 1H), 7.46 (dd, *J* = 12.9, 7.4 Hz, 3H), 7.42 – 7.32 (m, 5H), 7.31 – 7.21 (m, 2H), 7.18 (dd, *J* = 12.4, 3.8 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 4.34 – 4.23 (m, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 161.6 (d, $J_{C\text{-}F}$ = 257.1 Hz), 154.4 (d, $J_{C\text{-}F}$ = 4.4 Hz), 133.1 (d, $J_{C\text{-}F}$ = 8.8 Hz), 140.2, 139.5, 131.5, 129.8, 128.8 (d, $J_{C\text{-}F}$ = 26.8 Hz), 128.6, 127.1, 126.8, 126.0, 125.2, 125.0, 124.1 (d, $J_{C\text{-}F}$ = 3.6 Hz), 120.8 (d, $J_{C\text{-}F}$ = 9.0Hz), 117.1 (d, $J_{C\text{-}F}$ = 22.3 Hz) 83.6, 48.8; IR (KBr, cm^{-1}) 2960, 2925, 2855, 1626, 1597, 1574, 1490, 1454, 1325, 1273, 1259, 1223, 1158, 1114, 1074, 1032, 1001, 950, 860, 809, 763, 733, 697, 635, 584,

566, 548, 517, 497; HRMS (M + H)$^+$ calcd for $C_{21}H_{16}ClFNO$ 352.0899, found 352.0893; HPLC conditions: Daicel Chiralpak AD–H, *i*–PrOH/hexane = 1/99, 0.3 mL/min, 254 nm, t_1 = 38.8 min (major), t_2 = 42.0 min (minor).

*(S)–4–(Chloromethyl)–2–(3–fluorophenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4e**):* 35.0 mg, 99% yield, colorless oil; $[\alpha]_D^{20}$ = 67.7 (*c* 0.12, $CHCl_3$, 86% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.7 Hz, 1H), 7.95 (d, *J* = 9.7 Hz, 1H), 7.53 – 7.29 (m, 8H), 7.29 – 7.16 (m, 2H), 7.11 (d, *J* = 7.5 Hz, 1H), 4.33 – 4.15 (m, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 162.8 (d, $J_{C\text{-}F}$ = 244.7 Hz), 155.0, 140.0, 139.4, 134.6 (d, $J_{C\text{-}F}$ = 7.9 Hz), 130.0 (d, $J_{C\text{-}F}$ = 8.0 Hz), 129.9, 128.9, 128.7, 127.0, 126.5, 125.9, 125.6, 125.1, 124.0 (d, $J_{C\text{-}F}$ = 2.6 Hz), 118.7 (d, $J_{C\text{-}F}$ = 21.3 Hz), 115.2 (d, $J_{C\text{-}F}$ = 23.4 Hz), 83.3, 48.6; IR (KBr, cm^{-1}) 2960, 2926, 2853, 1627, 1586, 1485, 1447, 1322, 1269, 1243, 1193, 1154, 1083, 1069, 1034, 1001, 9445, 929, 874, 818, 796, 767, 733, 722, 697, 673, 635, 6002, 581, 549, 520, 494; HRMS (M + H)$^+$ calcd for $C_{21}H_{16}ClFNO$ 352.0899, found 352.0896; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 12.1 min (major), t_2 = 13.8 min (minor).

*(S)–4–(Chloromethyl)–2–(4–nitrophenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4f**):* 21.4 mg, 65% yield, yellow solid, mp: 133–137 °C; $[\alpha]_D^{20}$ =79.6 (*c* 0.10, $CHCl_3$, 87% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.6 Hz, 2H), 8.30 (d, *J* = 8.6 Hz, 2H), 7.46 – 7.33 (m, 7H), 7.33 – 7.28 (m, 1H), 7.26 (s, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 4.27 (q, *J* = 12.7 Hz, 2H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 154.1, 149.8, 139.8, 139.1, 138.2, 130.0, 129.1, 128.8, 127.8, 126.5, 126.3, 125.5, 125.3, 123.7, 83.7, 48.6; IR (KBr, cm^{-1}) 2956, 2925, 2854, 1627, 1595, 1522, 1482, 1457, 1409, 1347, 1318, 1261, 1243, 1085, 1014, 858, 845, 801, 771, 761, 733, 702, 635, 594; HRMS (M + H)$^+$ calcd for $C_{21}H_{16}ClN_2O_3$ 379.0844, found 379.0829; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 10/90, 1.0 mL/min, 254 nm, t_1 = 11.8 min (major), t_2 = 24.3 min (minor).

*(S)–4–(Chloromethyl)–2–(2–methoxyphenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4g**):* 21.5 mg, 65% yield, white solid, mp: 101–104 °C; $[\alpha]_D^{20}$ =42.1 (*c* 0.09, $CHCl_3$, 83% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.2 Hz, 1H), 7.58 – 7.30 (m, 8H), 7.24 (dd, *J* = 13.4, 5.5 Hz, 2H), 7.10 – 6.91 (m, 3H), 4.28 (s, 2H), 3.88 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 158.7, 157.0, 140.3, 139.4, 132.4, 131.3,

129.7, 128.8, 128.5, 127.1, 126.8, 125.8, 125.3, 124.9, 122.4, 120.6, 112.1, 83.6, 56.1, 48.8; IR (KBr, cm^{-1}) 2957, 2924, 2853, 1630, 1599, 1576, 1492, 1461, 1435, 1322, 1280, 1257, 1171, 1164, 1122, 1075, 1046, 1025, 1001, 794, 758, 733, 697, 634; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO_2$ 364.1099, found 364.1087; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 2/98, 0.5 mL/min, 254 nm, t_1 = 32.0 min (major), t_2 = 36.2 min (minor).

*(S)–4–(Chloromethyl)–2–(3–methoxyphenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4h**):* 29.7 mg, 90% yield, colorless oil; $[\alpha]_D^{20}$ =84.2 (*c* 0.09, $CHCl_3$, 85% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.7 Hz, 1H), 7.83 (s, 1H), 7.45 (d, *J* = 7.0 Hz, 2H), 7.43 – 7.30 (m, 6H), 7.28 – 7.22 (m, 1H), 7.16 – 7.05 (m, 2H), 4.27 (q, *J* = 12.0 Hz, 2H), 3.89 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 159.7, 156.0, 140.0, 139.6, 133.7, 129.7, 129.5, 128.8, 128.7, 126.7, 126.5, 125.8, 125.7, 125.1, 120.8, 118.2, 113.0, 83.0, 55.5, 48.5; IR (KBr, cm^{-1}) 2959,2925, 2854, 1625, 1599, 1575, 1485, 1453, 1432, 1378, 1326, 1286, 1262, 1222, 1181, 1093, 1040, 870, 800, 768, 723, 697, 683, 669; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClFNO_2$ 364.1099, found 364.1087; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 10/90, 1.0 mL/min, 254 nm, t_1 = 6.7 min (minor), t_2 = 8.8 min (major).

*(S)–4–(Chloromethyl)–2–(4–methoxyphenyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4i**):* 29.7 mg, 90% yield, colorless oil; $[\alpha]_D^{20}$ =84.2 (*c* 0.09, $CHCl_3$, 86% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.9 Hz, 2H), 7.45 (d, *J* = 6.8 Hz, 2H), 7.42 – 7.27 (m, 5H), 7.22 (ddd, *J* = 8.5, 5.5, 3.2 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 2H), 4.25 (q, *J* = 12.0 Hz, 2H), 3.87 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 162.6, 156.1, 140.1, 140.0, 130.2, 129.7, 128.7, 128.6, 126.6, 126.2, 125.6, 125.4, 125.0, 124.7, 113.8, 82.8, 55.5, 48.4. IR (KBr, cm^{-1}) 2956, 2925, 2854, 1622, 1608, 1595, 1571, 1511, 1479, 1461, 1421, 1378, 1323, 1257, 1169, 1084, 1030, 840, 794, 767, 732, 697, 636, 574, 544; HRMS $(M + H)^+$ calcd for $C_{22}H_{19}ClNO_2$ 364.1099, found 364.1089; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 33.4 min (major), t_2 = 43.9 min (minor).

*(S)–4–(Chloromethyl)–2–(naphthalen–1–yl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4j**):* 27.0 mg, 71% yield, colorless oil; $[\alpha]_D^{20}$ =33.1 (*c* 0.11, $CHCl_3$, 86% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 8.6 Hz, 1H), 8.25 (d, *J* = 7.2 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.54 (m, 7H),

7.38 (q, J = 6.8 Hz, 3H), 7.31 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 4.34 (s, 2H).; $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 157.1, 140.3, 139.6, 134.1, 132.0, 131.2, 129.8, 129.7, 129.1, 128.9, 128.7, 128.6, 127.3, 127.1, 126.8, 126.5, 126.2, 126.0, 125.2, 125.1, 125.0, 83.5, 48.8; IR (KBr, cm^{-1}) 2956, 2925, 2855, 1629, 1589, 1575, 1509, 1456, 1378, 1307, 1261, 1239, 1189, 1116, 1078, 1009, 805, 777, 731, 696, 634, 583, 560; HRMS $(M + H)^+$ calcd for $C_{25}H_{19}ClNO$ 384.1150, found 384.1138; HPLC conditions: Daicel Chiralpak IF, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 18.0 min (major), t_2 = 19.3 min (minor).

*(S)–4–(Chloromethyl)–2–methyl–4–phenyl–4H–benzo[d][1,3]oxazine (**4k**):* 24.1 mg, 89% yield, white solid, mp: 135–138 °C; $[\alpha]_D^{20}$ = –128.4 (*c* 0.11, $CHCl_3$, 90% ee); ^1H NMR (600 MHz, $CDCl_3$) δ 7.34 (q, J = 7.5 Hz, 6H), 7.25 – 7.19 (m, 2H), 7.09 (d, J = 7.5 Hz, 1H), 4.14 (s, 2H), 2.24 (s, 3H); $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$) δ 159.8, 140.5, 139.1, 129.7, 128.9, 128.7, 126.4, 126.3, 125.1, 124.8, 124.5, 82.8, 48.9, 21.9; IR (KBr, cm^{-1}) 2957, 2925, 2855, 1739, 1647, 1604, 1581, 1481, 1459, 1376, 1259, 1223, 1182, 1164, 1024, 965, 801, 766, 732, 697, 637, 570, 516; HRMS $(M + H)^+$ calcd for $C_{16}H_{15}ClNO$ 272.0837, found 272.0831; HPLC conditions: Daicel Chiralpak IA, *i*–PrOH/hexane = 10/90, 1.0 mL/min, 254 nm, t_1 = 6.0 min (minor), t_2 = 8.9 min (major).

*(S)–4–(Chloromethyl)–2–isopropyl–4–phenyl–4H–benzo[d][1,3]oxazine (**4l**):* 27.0 mg, 90% yield, colorless oil; $[\alpha]_D^{20}$ = –43.3 (*c* 0.08, $CHCl_3$, -92% ee); ^1H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 6H), 7.25 (d, J = 7.3 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 7.7 Hz, 1H), 4.18 (d, J = 12.5 Hz, 1H), 4.13 (d, J = 12.5 Hz, 1H), 2.73 (p, J = 5.5 Hz, 1H), 1.29 (d, J = 2.4 Hz, 3H), 1.28 (d, J = 2.3 Hz, 3H); $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$) δ 165.7, 140.5, 139.2, 129.6, 128.7, 128.6, 126.7, 126.3, 125.2, 124.8, 82.3, 48.8, 34.6, 19.7, 19.6; IR (KBr, cm^{-1}) 2957, 2925, 2855, 1642, 1601, 1581, 1458, 1378, 1261, 1198, 1148, 1069, 1005, 803, 768, 733, 697, 634, 571; HRMS $(M + H)^+$ calcd for $C_{18}H_{19}ClNO$ 300.1150, found 300.1141; HPLC conditions: Daicel Chiralpak IA, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 12.3 min (minor), t_2 = 15.4 min (major).

*(S)–2–(tert–Butyl)–4–(chloromethyl)–4–phenyl–4H–benzo[d][1,3]oxazine (**4m**):* 37.0 mg, 99% yield, white solid, mp: 69–73 °C; $[\alpha]_D^{20}$ = 9.3 (*c* 0.11, $CHCl_3$, 74% ee); ^1H NMR (600 MHz, $CDCl_3$) δ 7.38 (d,

J = 4.2 Hz, 4H), 7.34 (q, J = 4.1 Hz, 1H), 7.31 (t, J = 7.9 Hz, 1H), 7.25 (s, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 7.7 Hz, 1H), 4.17 (d, J = 12.5 Hz, 1H), 4.10 (d, J = 12.5 Hz, 1H), 1.31 (s, 9H); $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$) δ 167.1, 140.6, 139.4, 129.6, 128.7, 128.5, 126.9, 126.3, 125.5, 125.2, 124.7, 82.2, 48.7, 37.7, 27.8; IR (KBr, cm^{-1}) 2959, 2928, 2868, 1688, 1634, 1600, 1580, 1482, 1456, 1433, 1393, 1364, 1305, 1267, 1219, 1170, 1143, 1117, 1057, 1031, 1003, 971, 942, 806, 769, 756, 735, 721, 697, 636, 596, 572, 540; HRMS $(M + H)^+$ calcd for $C_{19}H_{21}ClNO$ 314.1306, found 314.1301; HPLC conditions: Daicel Chiralcel OD–H, *i*–PrOH/hexane = 1/99, 0.5 mL/min, 254 nm, t_1 = 9.9 min (major), t_2 = 11.3 min (minor).

*(S)–4–(Chloromethyl)–4–phenyl–2–(pyridin–4–yl)–4H–benzo[d][1,3]oxazine (**4n**):* 32.1 mg, 96% yield, colorless oil; $[\alpha]_D^{20}$ = 52.2 (*c* 0.26, $CHCl_3$, 70% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 2H), 8.12 – 7.98 (m, 2H), 7.47 – 7.22 (m, 8H), 7.13 (d, J = 7.4 Hz, 1H), 4.26 (q, J = 12.6 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 154.2, 150.4, 139.9, 139.8, 139.0, 130.0, 129.1, 128.8, 127.7, 126.4, 126.3, 125.6, 125.2, 121.7, 83.5, 48.7; IR (KBr, cm^{-1}) 2956, 2925, 2855, 1629, 1598, 1554, 1479, 1457, 1409, 1378, 1328, 1313, 1264, 1223, 1158, 1094, 1063, 1033, 999, 834, 767, 731, 696, 683, 634, 579, 544; HRMS $(M + H)^+$ calcd for $C_{20}H_{16}ClN_2O$ 335.0946, found 335.0940; HPLC conditions: Daicel Chiralpak IF, *i*–PrOH/hexane = 5/95, 0.5 mL/min, 254 nm, t_1 = 28.6 min (major), t_2 = 30.6 min (minor).

The Procedure for 1 mmol Scale Preparation of 2a.

To a solution of **1a** (0.299 g, 1.0 mmol, 1 equiv), **VI** (59.4 mg, 0.10 mmol, 10 mol%) in MeOH (20 mL) at –80 °C was added DCDMH (236 mg, 1.2 mmol, 1.2 equiv). The resulting mixture was stirred at –80 °C and monitored by TLC. Upon completion, the reaction was quenched by saturated aqueous solution $Na_2S_2O_4$ at –80 °C then warmed to room temperature. The aqueous phase was extracted with CH_2Cl_2, the combined organic phases were dried over anhydrous Na_2SO_4, filtered, and evaporated in *vacuo*. The residue was purified by flash column chromatography (PE/EA = 10:1) to afford the product **2a** as yellow solid (267 mg, 80% yield, 91% ee).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Copies of NMR spectra and HPLC analysis (PDF)

X-ray crystallographic structure of **2a** (CIF)

X-ray crystallographic structure of **4k** (CIF)

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Notes

The authors declare no competing financial interest.

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