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Enantioselective synthesis of monofluorinated allylic compounds: Pd-catalyzed asymmetric allylations of dimethyl 2-fluoromalonate using new *N*-sulfinyl-based ligands

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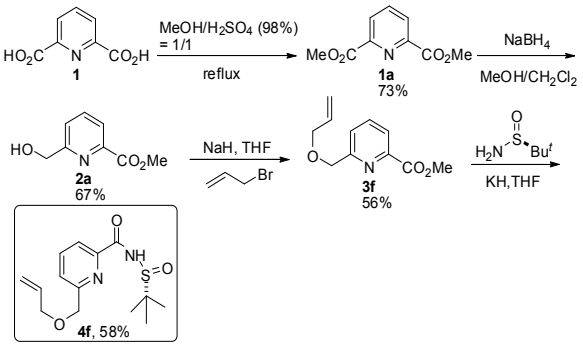
New chiral *S*,*N*- and *S*,*P*-ligands started from *tert*-butanesulfinamide were synthesized in four steps, applying for Pd-catalyzed asymmetric allylic substitutions of dimethyl 2-fluoromalonate. The induced effect of the Pd/*S*,*N*-ligand catalyst on the enantioselectivity depends on steric demand of the substituent at *o*-position of the pyridine ring. This method produced monofluorinated allylation products in up to high yield and high enantioselectivity.

Introduction

Optically active fluorinated compounds are of great importance to medicinal and materiel chemistry.[1] Especially, chiral fluorinated compounds such as *Pharmacia*, *Clofarabin*, and *Difluprednate* are popular drugs, which contain monofluorinated methylene group.[2] Palladium (Pd)-catalyze asymmetric allylic substitution has become a powerful method for a C-C bond formation.[3] To this context, a variety of carbon nucleophiles was explored during the past several decades;[3] however, fluorinated methane derivative as a prenucleophile has less been described.[4] Chiral ligands play a significant role in asymmetric catalysis for the synthesis of fluorinated compounds.[5] A very few ligands including PHOX[4a] and Feringa's ligand[4b] were effective for the synthesis of fluorinated allylic compounds by transition metal-catalyzed asymmetric allylic substitutions. Therefore, novel effective ligands still are highly desirable. Ligands based on phosphorus and/or nitrogen have been wildly utilized in asymmetric catalysis.[5] As known, chiral sulfoxide is an auxiliary for asymmetric synthesis[6] and coordination chemistry[7], consequently, the design of new sulphurous ligands for transition metal-catalyzed asymmetric reactions are rapidly increasing in recent years.[8] Ellman reported the asymmetric synthesis of amines by using enantiopure *tert*-butanesulfinamide.[9] In addition, *N*-sulfinyl urea and thiorea-based organocatalyst and *N*-sulfinyl prolinamide have been developed for a variety of nucleophilic additions to carbonyl, imine, and nitroolefin functionalities.[10] Recently, the use of *N*-sulfinyl ligands in both rhodium-catalyzed asymmetric conjugate additions and Pd-catalyzed asymmetric allylic substitution was well reviewed by Trost[11]. In this paper, we report the design and synthesis of chiral *S*,*N*-ligands, which are employed in Pd-catalyzed asymmetric allylic substitution of allylic acetates with dimethyl 2-fluoromalonate.



Scheme 1 The representative synthesis of the *S*,*N*-ligand **4f**.

Results and discussion

At the outset, we aimed at the design and synthesis of *N*-sulfinyl-based ligands. On the basis of *tert*-butanesulfinamide that was developed by Ellman,[9] the *S*,*N*-ligands **4a**–**j** were developed. A representative *N*-sulfinyl-based ligand **4f** was prepared according to the following sequence (Scheme 1). Di-esterification of 2,6-pyridinedicarboxylic acid (**1**) with methanol in the presence of sulfuric acid (H_2SO_4, 98%) provided dimethyl pyridine-2,6-dicarboxylate (**1a**) in a 73% yield.[12] A selective reduction of **1a** with sodium borohydride ($NaBH_4$) in methanol and dichloromethane (DCM) afforded methyl 6-(hydroxymethyl)picolinate (**2a**) in a 67% yield.[13] The treatment of **2a** with sodium hydride (NaH) in THF,

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following by reacting with allyl bromide produced methyl 6-(allyloxymethyl)picolinate (**3f**) in a 56% yield.[14] Finally, (*R*)-*tert*-butanesulfinamide was treated with potassium hydride (KH) in THF, following by reacting with methyl 6-(allyloxymethyl)picolinate (**3f**) to give an amidation product (**4f**) in a 58% yield.[15] The other *S*,*N*-ligands **4a**–**e**, **4g**–**h**, **4ia**–**4ib**, and **4j** were also synthesized according to the similar sequence (see: SI).

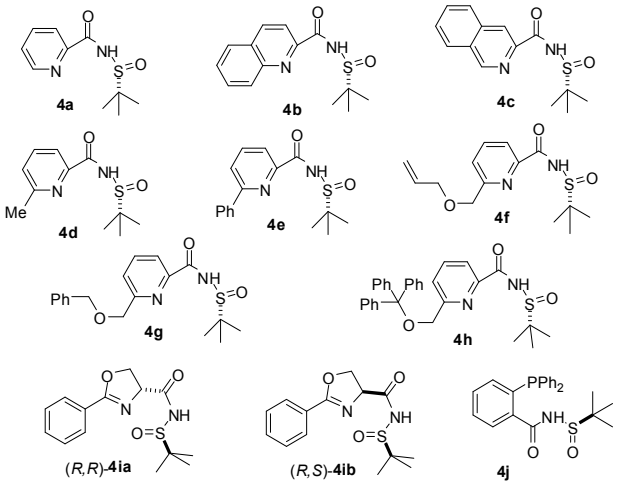
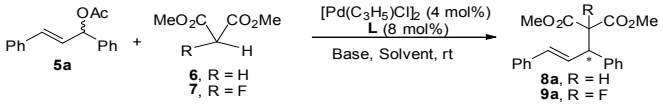


Figure 2 The *S*, *N*- and *S*,*P*-ligands **4a–j**.

With the *S*,*N*- and *S*,*P*-ligands **4a**–**j** in hand, we turned our attention to examine those *S*,*N*-ligands for a model reaction between (*E*)-1,3-diphenylprop-2-en-1-yl acetate (**5a**) and sodium dimethyl malonate (**6a**) under palladium catalyst. Interestingly, the formation of **8a** was observed in a 48% yield with 10% enantiomeric excess (ee) when the reaction was performed in the presence of sodium hydride (NaH) and THF with the assistance of a catalyst made from $[Pd(C_3H_5)Cl]_2$ and **4a** at room temperature (Table 1). A diversity of *S*,*N*-ligands such as **4a**–**j** was examined. We found that the induced effect of the Pd/*S*,*N*-lignad on the enantioselectivity strongly depends upon the position of substituent at the pyridine ring (Table 1, entries 2–5). For example, substituent at *o*-position gave the superior ee value (entry 2 vs. entry 3). Steric demand of the substituent on the pyridine ring also plays a significant role (Table, entries 4–8). **4f** led to a superior result, 80% yield and 82% ee (Table 1, entry 6).[16] Either **4g** or **4h** gave fair yields and good ee values although they are structurally similar to **4f** (Table 1, entries 7–8). Either (*R*,*R*)-**4ia**[17] or (*R*,*S*)-**4ib** that contains two chiral centers[18] gave rise to the poor results (Table 1, entries 9–10) and no matched-mismatched effect was observed in these cases.[2a] The *S*,*P*-ligand **4j** resulted in a good yield with moderate ee in short period of reaction time (Table 1, entry 11). The examination of the bases revealed that Cs_2CO_3 is the optimum base (Table 1, entries 6, 12–13). More significantly, dimethyl 2-fluoromalonate (**7**)[4d] instead of **6** was explored and it gave the corresponding fluorinated **9a** in a 70% yield and 90% ee (Table 1, entry 14). These results encouraged us to further examine the allylation of dimethyl 2-fluoromalonate (**7**) under Pd catalysis because of the importance of fluorinated compounds in pharmaceutical industry.[1,2] Consequently, the solvent survey indicated that DCM resulted in the best result, a 94% yield and 90% ee (Table 1, entries 14–16). In contrast, the commercial available ligands such as (*R*,*R*)-Trost[19], (*R*)-BINAP[20], Josiphos[21], and **4j** were respectively tested under the optimized conditions; Trost ligand gave 73% yield and 55% ee; (*R*)-BINAP ligand led to 92% yield and 87% ee; and Josiphos ligand gave the allylic product **9a** with 65% yield but in racemic form; *S*,*P*-ligand **4j** gave a 79% yield and 74% ee.

Table 1 Optimizing conditions for a Pd-catalyzed allylation by using the new ligands.[a]



Entry	L	Solvent	Base	Time (h)	Yield [b] (%)	*ee* [d] (%)
1	**4a**	THF	NaH	12	**8a**, 48	10
2	**4b**	THF	NaH	40	**8a**, 62	70
3	**4c**	THF	NaH	48	**8a**, 36	53
4	**4d**	THF	NaH	48	**8a**, 55	74
5	**4e**	THF	NaH	48	**8a**, 41	71
6	**4f**	THF	NaH	48	**8a**, 80	82
7	**4g**	THF	NaH	48	**8a**, 58	80
8	**4h**	THF	NaH	48	**8a**, 52	77
9	**4ia**	THF	NaH	48	**8a**, 30	30
10	**4ib**	THF	NaH	48	**8a**, 22	47
11	**4j**	THF	NaH	24	**8a**, 82	74
12	**4f**	THF	Cs_2CO_3	48	**8a**, 90	93
13[c]	**4f**	THF	BSA/KOAc	48	**8a**, 14	80
14	**4f**	THF	Cs_2CO_3	48	**9a**, 70	90
15	**4f**	Toluene	Cs_2CO_3	48	**9a**, 35	42
16	**4f**	DCM	Cs_2CO_3	16	**9a**, 94	90

[a] The reactions were carried out in various solvent (2.5 mL) with 4.0 mol % of $[Pd(C_3H_5)Cl]_2$, 8.0 mol % of ligand, 1.0 equiv of (*E*)-1,3-diphenylprop-2-en-1-yl acetate **5a** (0.2 mmol), 3.0 equiv of dimethyl malonate **6** or **7** (1.5 mmol) and 3.0 equiv of base at room temperature. [b] Isolated yield. [c] 3.0 equiv of BSA (*N*,*O*-bis(trimethylsilyl)acetamide, 0.6 mmol) and 4 mol% of KOAc. [d] Determined by chiral HPLC.

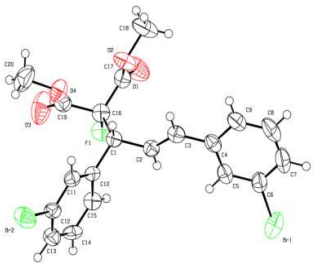
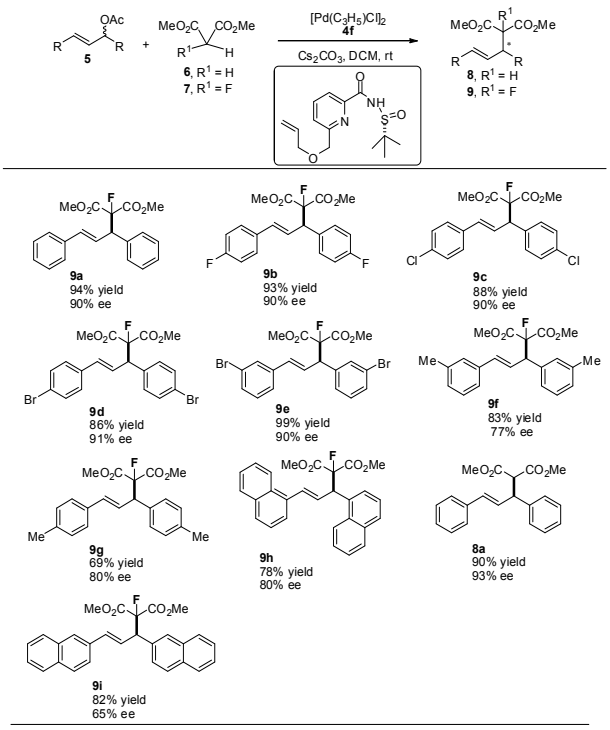


Figure 3 The X-ray structure of (*R*)-**9e**.

Using this method, the generality and scope of allylic acetates **5** and nucleophiles were examined under the optimized conditions (Table 2). Upon using dimethyl 2-fluoromalonate (**7**), (*E*)-1,3-diphenylprop-2-en-1-yl acetate (**5a**) and aryl-sbustituted allylic acetates **5b**–**e** with electron-withdrawing group on the phenyl ring (e.g., 4-F, 4-Cl, 4-Br and 3-Br) produced the allylic products **9a**–**e** in high yields with high enantioselectivities (Table 2). In contrast, aryl-substituted allylic acetates **5f**–**g** with electron-donating group on the phenyl ring (e.g., 4-Me and 3-Me) gave the allylic products **9f**–**g** in good yields with high enantioselectivities (Table 2).

Table 2 Pd-catalyzed allylic substitutions of allylic acetates **5** with 2-fluoromalonate (**7**). [a,b,c,d]



a

The reactions were carried out in DCM (2.5 mL) with 4.0 mol % $[Pd(C_3H_5)Cl]_2$, 8.0 mol % of **4f**, 1.0 equiv of racemic allylic acetates (**5**, 0.2 mmol), 3.0 equiv of 2-fluoromalonate (**7**, 1.5 mmol) and 3.0 equiv of Cs_2CO_3 at room temperature. *b* Isolated yield. *c* Determined by chiral HPLC. *d* THF was used for **8a**.

(*E*)-1,3-Di(naphthalen-1-yl)allyl acetate **5h** afforded the corresponding **9h** in a good yield and enantioselectivity (Table 2). (*E*)-1,3-Di(naphthalen-2-yl)allyl acetate **5i** gave rise to **9i** in a better yield and lower enantioselectivity then that of **9h** (Table 2). Using sodium dimethyl malonate (**6a**), the allylic substrate **5a** gave rise to the corresponding **8a** in an excellent yield and high enantioselectivity (Table 2).

The X-ray crystal structure analysis of **9e** revealed its absolute configuration as *R* (Figure 3).[22]

Conclusions

In summary, we developed a practical method for the synthesis of new *S*,*N*- and *S*,*P*-ligands made from *tert*-butanesulfinamide. Those *S*,*N*- and *S*,*P*-ligands were utilized in Pd-catalyzed asymmetric allylic substitutions of dimethyl 2-fluoromalonate, in which allyl group at *o*-position of the pyridine ring plays a crucial role for the enantioselectivity. This method allows for the synthesis of monofluorinated allylic products in good to high yields with good to high enantioselectivities.

Experimental

General

Progress of the reactions was monitored by thin-layer chromatography using silica plates and the spots were visualized under UV-light and/or after charring with potassium permanganate. Column chromatography was performed over silica gel (300–400 mesh) eluted with gradients of petroleum ether and ethyl acetate. Column fractions were concentrated under reduced pressure at temperatures not more than 45 °C. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent with TMS as an internal reference on a 400 MHz NMR spectrometer. Chemical shifts δ were denoted with reference to TMS or solvent residual ($CDCl_3$: δ 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C) peak given in ppm (parts per million) and coupling constants *J* are measured in Hz (hertz). FT-IR spectra were recorded on a KBr thin film. Mass spectra were recorded on HP5973N.

General procedure for the synthesis of the ligand 4f.

A reaction mixture of 2,6-pyridinedicarboxylic acid **1** (4.00 g, 24.0 mmol) in methanol (10 mL) and concentrated sulfuric acid (10 mL) was refluxed for 4h. After that, the reaction mixture was added into water (30 mL), and the aqueous solution was neutralized with sodium carbonate. The reaction mixture was extracted with chloroform (4 x 25 mL). The combined extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated to produce dimethyl pyridine-2,6-dicarboxylate (**1a**) as a white solid (3.40 g, 73% yield).

$NaBH_4$ (0.82 g, 21.5 mmol) was slowly added into a solution of dimethyl pyridine-2,6-dicarboxylate (**1a**, 3.72 g, 19.1 mmol) in a mixture of MeOH/CH_2Cl_2 (5/2, 70 mL) at 0 °C. The reaction mixture was stirred for 3h at room temperature and then quenched with an aqueous saturated NH_4Cl solution. After extraction with CH_2Cl_2 (3 x 50 mL), the combined organic layers were dried with Na_2SO_4, and the solvent was removed under reduced pressure. The resulting crude residue was purified by column chromatography (methylene chloride/MeOH = 10/1), giving methyl 6-(hydroxymethyl)picolinate **2a** (2.13 g, 67%) as a white solid.

A flame dried round bottom flask was charged with sodium hydride (NaH, 60% w/w in oil, 0.43 g, 10.8 mmol) and 20 mL of THF under argon. To this stirring suspension at room temperature was slowly

added 6-(hydroxymethyl)picolinate **2a** (1.03 g, 6.2 mmol) over 5 minutes. The reaction was stirred for 30 minutes and then cooled to 0 °C. Allyl bromide (1.0 mL, 11.6 mmol) was slowly added dropwise and the reaction was stirred at 0 °C for 20 minutes. The reaction was warmed to room temperature and stirred for 16 hours under argon. The mixture was filtered through a pad of silica gel and the solvent was evaporated under reduced pressure. The crude residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to give the desired products **3f** as a yellow oil (0.71g, 56%).

To a suspension of KH (0.11 g, 2.7 mmol) in THF (10 mL) was added a solution of (*R*)-*tert*-butanesulfinamide (0.33 g, 2.7 mmol) in THF (5 mL) under argon. The mixture was stirred at room temperature for 1 hour. A solution of **3f** (0.58 g, 2.7 mmol) in THF (5 mL) was then added dropwise via syringe. After stirring for 1 hour, the reaction mixture was filtered through a pad of silica gel and the solvent was evaporated under reduced pressure. The crude residue was purified by flash column chromatography (petroleum ether/ ethyl acetate = 3/2) to give **4f** as a thick oil (0.47g, 58%).

Compounds **4a**, **4b**, **4c**, **4d**, **4e**, **4g**, **4h** and **4j** were synthesized according to the similar procedure.

The procedure for the synthesis of 3h.

Dissolved methyl 6-(hydroxylmethyl) picolinate **2a** (1.06 g, 6.6 mmol), triphenylbromomethane (2.54 g, 7.8 mmol), triethylamine (2.0 mL, 14.4 mmol) and 4-dimethylaminopyridine (0.065 g, 0.53 mmol) to 20 mL of methylene chloride and the reaction mixture was refluxed for 2 hours. And then the reaction mixture was filtered through a pad of silica gel. After that, evaporating the solvent under reduced pressure and purifying by flash column chromatography (petroleum ether/ ethyl acetate = 3/1) gave **3h** as a white solid (2.04 g, 78%).

The procedure for the synthesis of 4ia and 4ib.[23]

L-Serine methyl ester hydrochloride (1.36 g, 8.7 mmol) was suspended in methylene chloride (20 mL), and then triethylamine (1.8 mL, 1.31 g, 12.9 mmol) was slowly added into the reaction mixture. When the dissolution of the amine hydrochloride was complete, benzimino ethyl ether hydrochloride (1.62 g, 8.7 mmol) was added as one portion. The reaction mixture was refluxed for 4 hours under argon. The pink reaction mixture was washed twice with saturated sodium bicarbonate, and the combined aqueous extracts were extracted with methylene chloride (2 x 20 mL). The combined methylene chloride extracts were washed with brine, dried over magnesium sulfate, and filtered. The solvent was removed at reduced pressure. The crude residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to provide the oxazoline methyl ester (*S*)-**3i** in 54% yield (0.97 g, 4.7 mmol).

To a suspension of KH (0.11 g, 2.7 mmol) in THF (10 mL) was added a solution of (*R*)-*tert*-butanesulfinamide (0.32 g, 2.7 mmol) in THF (5 mL). The mixture was stirred at room temperature for 1 hour. A solution of (*S*)-**3i** (0.58 g, 2.8 mmol) in THF (5 mL) was then added dropwise *via* syringe. After stirring for 1 hour, the reaction mixture was filtered through a pad of silica gel and the solvent was evaporated under reduced pressure. The crude residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 3/2) to give **4ia** (0.25 g, 30%) and **4ib** (0.18 g, 21%) as white solid.

General procedure for Pd-catalysed allylic alkylation of dimethyl malonate.

$[Pd(C_3H_5)Cl]_2$ (2.9 mg, 0.008 mmol) and ligand **4f** (0.017 mmol) were dissolved in THF (1.0 mL) in a dry Schlenk tube filled with argon. The reaction mixture was stirred at room temperature for 30 minutes, and then racemic 1,3-diphenylprop-1-en-3-ylacetate **5a** (50.6 mg, 0.2 mmol) was added to the reaction system *via* a syringe and stirred at room temperature for another 10 minutes. After that, a freshly prepared solution of dimethyl 2-sodiomalonate, which was prepared by suspending sodium hydride (60%w/w in oil, 24.7 mg, 0.6 mmol) in THF (1.5 mL) and dimethyl malonate **6** (95.3 mg, 0.72 mmol), was added dropwise. After 48 hours, the reaction mixture was filtered through celite. The solvent was evaporated under reduced pressure. The crude residue was purified by flash chromatography (petroleum ether/ethyl acetate = 9/1) to yield **8a** as a colorless thick oil (56.0 mg, 80% yield).

General procedure for Pd-catalysed allylic alkylation of dimethyl 2-fluoromalonate 7.

$[Pd(C_3H_5)Cl]_2$ (2.9 mg, 0.008 mmol) and ligand **4f** (5.0 mg, 0.017 mmol**)** were dissolved in THF (2.5 mL) in a dry Schlenk tube filled with argon. The reaction mixture stirred at room temperature for 30 minutes. Allylic acetates **5** (0.2 mmol) was added to the reaction system and the reaction mixture was stirred at room temperature for another 10 min. After that, dimethyl 2-fluoromalonate **7** (108.7 mg, 0.6 mmol) and Cs_2CO_3 (197.9 mg, 0.6 mmol) were added into the reaction mixture. The reaction mixture was stirred at room temperature overnight and then filtered through celite. The solvent was evaporated under reduced pressure. The crude residue was purified by flash column chromatography (petroleum ether/methylene chloride = 1/1) to give the desired products **9** as a white solid.

Dimethyl pyridine-2,6-dicarboxylate (1a)[23]: 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34-8.31 (d, *J* = 7.6 Hz,2H), 8.06-8.02 (dd, *J* = 8.0, 7.6Hz, 1H), 4.04 (s, 6H).

Methyl 6-(hydroxymethyl)picolinate (2a)[23]: 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (d, *J* = 7.6 Hz,1H), 7.85 (dd, *J* = 8.0, 7.6Hz, 1H), 7.57 (d, *J* = 7.6Hz, 1H), 4.87(s, 2H), 4.20-4.05 (m, 2H), 3.98 (s, 3H).

Methyl 6-(allyloxymethyl)picolinate (3f): 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 (d, *J* = 7.6 Hz,1H), 7.87 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 5.98 (ddd, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.35 (d, *J* = 17.2 Hz, 1H), 5.24 (d, *J* =10.0 Hz, 1H), 4.76 (s, 2H), 4.14 (d, *J* =5.2 Hz, 1H), 4.00(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =165.6, 159.4, 147.1, 137.4, 134.1, 124.3, 123.6, 117.3, 72.6, 71.8, 52.7. HRMS (ESI) calcd for $C_{11}H_{13}NNaO_3$ ($[M+Na]^+$): 230.0793, Found: 230.0788. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3801, 3741, 3628, 2951, 2916, 2848, 2359, 1456, 1437, 1314, 1292, 1227, 1138, 1081, 992, 927, 761.

Methyl 6-(benzyloxymethyl)picolinate (3g)[23]: 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (d, *J* = 7.6 Hz,1H), 7.84 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.27-7.40 (m, 5H), 4.79 (s, 2H), 4.66 (s, 2H), 3.99 (s, 3H).

Methyl 6-(trityloxymethyl)picolinate (3h): White solid; 78% yield; mp: 100.4–101.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05-7.99 (m, 2H), 7.91-7.85 (m, 1H), 7.51-7.48 (m, 6H), 7.32-7.20 (m, 9H), 4.51 (s, 2H), 3.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =165.6, 160.1, 146.9, 143.6, 137.5, 128.5, 127.9, 127.1, 123.8, 124.4, 87.4, 66.8, 52.8. HRMS (EI) calcd for $C_{27}H_{23}NNaO_3$ ($[M+Na]^+$): 432.1576, Found: 432.1570. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3837, 3801, 3744, 3675, 3649, 3058, 3031, 2949, 1743, 1724, 1683, 1652, 1591, 1575, 1506, 1409, 1447, 1384, 1359, 1313, 1292, 1225, 1193, 1151, 1137, 1095, 1076, 1032, 991, 899, 763, 746, 649, 632.

(*S*)-Methyl 2-phenyl-4,5-dihydrooxazole-4-carboxylate (3i)[23]: 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99-7.96 (m, 2H), 7.51-7.46 (m, 1H), 7.42-7.38 (m, 2H), 4.97-4.92 (m, 1H), 4.71-4.66 (m, 1H), 4.60-4.55 (m, 1H) 3.80 (s, 3H).

(*R*)-*N*-(*tert*-Butylsulfinyl)picolinamide (4a): White solid; 90% yield; mp: 68.4–70.5 °C; $[\alpha]_D^{20}$ = -28.3° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.62-9.54(m, 1H), 8.64 (d, *J* = 4.0 Hz,1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.96 (dd, *J* = 7.6, 7.6Hz, 1H), 7.59 (dd, *J* = 7.2, 6.4 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.2, 148.1, 147.4, 137.4, 127.2, 122.3, 56.3, 21.6. HRMS (ESI) calcd for $C_{10}H_{14}N_2NaO_2S$ ($[M+Na]^+$): 249.0647, Found: 249.0598. IR (KBr): ν_{max} (cm^{-1}) = 3676, 3413, 3304, 3058, 2967, 2869, 1703, 1638, 1590, 1449, 1389, 1292, 1269, 1185, 1106, 1080, 1040, 998, 871, 818, 788, 737, 697, 620.

(*R*)-*N*-(*tert*-Butylsulfinyl)quinoline-2-carboxamide (4b): White solid; 58% yield; mp: 155.7–156.2 °C; $[\alpha]_D^{20}$ = -56.4° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.76-9.70 (m, 1H), 8.35 (d, *J* = 8.4 Hz,1H), 8.27 (d, *J* = 8.4 Hz, 1H), 8.11(d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.81 (dd, *J* = 7.6, 7.6Hz, 1H), 7.59 (dd, *J* = 7.6, 7.2 Hz, 1H), 7.67 (dd, *J* = 7.6, 7.2 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =164.8, 147.6, 146.2, 137.9, 130.5, 129.8, 129.6, 128.7, 127.7, 118.6, 57.1, 22.0. HRMS (ESI) calcd for $C_{14}H_{16}N_2NaO_2S$ ($[M+Na]^+$): 299.0830, Found: 299.0769. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 2962, 1844, 1700, 1651, 1558, 1540, 1488, 1396, 1362, 1340, 1262, 1099, 1075, 1013, 903, 847, 763.

(*R*)-*N*-(*tert*-Butylsulfinyl)isoquinoline-1-carboxamide (4c): White solid; 43% yield; mp: 61.4–64.6 °C; $[\alpha]_D^{20}$ = -312.0° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.00-9.95 (m, 1H), 9.54 (d, *J* = 8.0 Hz, 1H), 8.50 (d, *J* = 5.2 Hz, 1H), 7.90-7.87 (m, 2H), 7.78-7.69 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =166.0, 145.2, 140.1, 137.4, 130.7, 129.4, 127.1, 127.0, 126.9, 125.8, 56.8, 22.1. HRMS (ESI) calcd for $C_{14}H_{16}N_2NaO_2S$ ($[M+Na]^+$): 299.0830, Found: 299.0824. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3801, 3747, 3710, 3649, 3056, 2963, 2922, 1698, 1370, 1330, 1083, 847, 749.

(*R*)-*N*-(*tert*-Butylsulfinyl)-6-methylpicolinamide (4d): White solid; 18% yield; mp: 127.8–128.7 °C; $[\alpha]_D^{20}$ = -133.3° (c 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.62-9.52 (m, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.78 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.37 ((d, *J* = 7.2 Hz, 1H), 2.59 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =164.9, 157.7, 147.4, 137.8, 127.2, 120.0, 57.0, 24.2, 22.1. HRMS (ESI) calcd for $C_{11}H_{16}N_2NaO_2S$ ($[M+Na]^+$): 263.0830, Found: 263.0825. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3801, 3747, 3710, 3649, 2923, 1734, 1701, 1651, 1595, 1558, 1540, 1393, 1362, 1259, 1186, 1091, 1072, 994, 848, 826, 753, 601.

(*R*)-*N*-(*tert*-Butylsulfinyl)-6-phenylpicolinamide (4e): White solid; 67% yield; mp: 130.8–131.9 °C; $[\alpha]_D^{20}$ = -282.0° (c 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.71-9.62 (m, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 8.00-7.96 (m, 4H), 7.55-7.48 ((m, 3H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =164.7, 156.4, 147.8, 138.6, 137.7, 129.8, 129.0, 126.8, 124.3, 121.3, 57.0, 22.1. HRMS (ESI) calcd for $C_{11}H_{16}N_2NaO_3S$ ($[M+Na]^+$): 325.0987, Found: 325.0981. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3629, 3063, 2963, 1702, 1460, 1389, 1185, 1085, 848, 814, 751, 604.

(*R*)-6-(Allyloxymethyl)-*N*-(*tert*-butylsulfinyl)picolinamide (4f): thick yellow oil; 58% yield; $[\alpha]_D^{20}$ = -52.9° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.52-9.44 (m, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.94 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 5.98 (ddd, *J* = 19.4, 10.8, 5.6 Hz, 1H), 5.37 (d, *J* = 17.2 Hz, 1H), 5.26 (d, *J* =10.4 Hz, 1H), 4.68 (s, 2H), 4.15 (d, *J* =5.6 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =164.3, 157.9, 146.9, 138.2, 133.9, 125.0, 121.3, 117.3, 72.0, 71.7, 56.8, 21.8. HRMS (ESI) calcd for $C_{14}H_{20}N_2NaO_3S$ ($[M+Na]^+$): 319.1092, Found: 319.1084. IR (KBr): ν_{max} (cm^{-1}) = 3901, 3853, 3801, 3747, 3649, 1734, 1700, 1685, 1651, 1472, 1395, 1361, 1261, 1072, 829, 752, 595.

(*R*)-6-(Benzyloxymethyl)-*N*-(*tert*-butylsulfinyl)picolinamide (4g): White solid; 39% yield; mp: 86.5–87.8 °C; $[\alpha]_D^{20}$ = -289.6° (c 0.7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.46-9.38 (m, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.92 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.41-7.32 (m, 5H), 4.70 (s, 2H), 4.68 (s, 2H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.5, 158.0, 147.2, 138.3, 137.5, 128.5, 127.9, 127.7, 125.2, 121.6, 73.0, 72.3, 57.0, 22.0. HRMS (ESI) calcd for $C_{18}H_{22}N_2NaO_3S$ ($[M+Na]^+$): 369.1249, Found: 369.1244. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3649, 3064, 2286, 1734, 1700, 1651, 1558, 1540, 1393, 1361, 1261, 1071, 995, 848, 824, 751, 602.

(*R*)-*N*-(*tert*-Butylsulfinyl)-6-(trityloxymethyl)picolinamide (4h): White solid; 54% yield; mp: 62.0–64.7 °C; $[\alpha]_D^{20}$ = -342.7° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.46-9.38 (m, 1H), 8.13 (d, *J* =

8.4 Hz,1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.87-7.79 (m, 1H), 7.67 (d, *J* = 7.6 Hz, 1H) 7.56-7.42 (m, 4H), 5.13-5.06 (m, 2H), 4.73 (s, 2H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =164.6, 158.5, 147.0, 143.5, 138.2, 128.6, 128.0, 127.3, 125.0, 121.3, 87.5, 66.4, 57.0, 22.0. HRMS (ESI) calcd for $C_{30}H_{30}N_2NaO_3S$ ($[M+Na]^+$): 521.1875, Found: 521.1870. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3649, 3566, 3478, 3058, 2924, 1734, 1700, 1651, 1594, 1558, 1394, 1362, 1262, 1216, 1069, 992, 899, 848, 825, 751, 705, 632, 604.

(*R*)-*N*-((*R*)-*tert*-Butylsulfinyl)-2-phenyl-4,5-dihydrooxazole-4-carboxamide (4ia): White solid; 30% yield; mp: 140.5–141.4 °C; $[\alpha]_D^{20}$ = -155.7° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21-8.15 (m, 1H), 7.96-7.94 (m, 2H), 7.56-7.52 (m, 1H), 7.46-7.42 (m, 2H), 4.92 (dd, *J* = 9.6, 9.6 Hz, 1H) 4.74-4.67 (m, 2H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =172.3, 166.4, 132.2, 128.5, 128.3, 126.4, 69.7, 69.5, 56.8, 21.9. HRMS (ESI) calcd for $C_{14}H_{18}N_2NaO_3S$ ($[M+Na]^+$): 317.0936, Found: 317.0926. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3837, 3747, 3673, 3648, 3474, 3065, 2962, 2922, 2851, 1701, 1639, 1577, 1558, 1393, 1362, 1293, 1172, 1088, 1069, 1026, 963, 893, 847, 784, 694, 605.

(*S*)-*N*-((*R*)-*tert*-**Butylsulfinyl)-2-phenyl-4,5-dihydrooxazole-4-carboxamide (4ib)**: White solid; 21% yield; mp: 152.7–154.1 °C; $[\alpha]_D^{20}$ = -247.5° (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.31-8.20 (m, 1H), 7.98-7.96 (m, 2H), 7.57-7.53 (m, 1H), 7.48-7.43 (m, 2H), 4.97 (dd, *J* = 10.4, 10.0 Hz, 1H) 4.71-4.66 (m, 2H), 1.24 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =172.6, 167.2, 132.3, 128.5, 126.4, 69.7, 69.1, 56.9, 22.0. HRMS (ESI) calcd for $C_{14}H_{18}N_2NaO_3S$ ($[M+Na]^+$): 317.0936, Found: 317.0923. IR (KBr): ν_{max} (cm^{-1}) = 3547, 3476, 3413, 3118, 2963, 2919, 2850, 1711, 1640, 1358, 1296, 1258, 1239, 1155, 1086, 1063, 1027, 971, 953, 895, 817, 786, 751, 699, 609.

(*R*)-*N*-(*tert*-**Butylsulfinyl)-2-(diphenylphosphino)benzamide** (**4j**): White solid; 42% yield; mp: 165.2–167.2 °C; $[\alpha]_D^{20}$ = -141.2° (c 2.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.40-8.28 (m, 1H), 7.79-7.76 (m, 1H), 7.43-7.31(m, 8H), 7.26-7.20 (m, 4H) 7.01-6.98 (m, 1H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =169.2, 138.7 (d, J_{C-P} = 25.5 Hz), 136.1 (ddd, J_{C-P} = 21.2, 11.7, 9.5 Hz), 134.4, 133.8 (d, J_{C-P} = 19.7 Hz), 133.6 (d, J_{C-P} = 19.6 Hz), 131.2, 130.0, 128.9, 128.8 (d, J_{C-P} = 5.1 Hz), 128.6 (dd, J_{C-P} = 7.3, 6.6 Hz), 57.3, 22.0. ^{31}P NMR (162 MHz, $CDCl_3$) δ = -10.40. HRMS (ESI) calcd for $C_{23}H_{24}NNaO_2PS$ ($[M+Na]^+$): 432.1163, Found: 432.1152. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3649, 3476, 3054, 1734, 1682, 1559, 1387, 1264, 1237, 1182, 1067, 870, 848, 748, 695, 608.

(*S*,*E*)-**Dimethyl 2-(1,3-diphenylallyl)malonate** (**8a**)[24]: 90% yield; $[\alpha]_D^{20}$ = -106.1° (c 1.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 12.47 min (minor); 17.47 min (major) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 0.8 mL/min] to be 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33-7.16 (m, 10H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.33 (dd, *J* = 15.6, 8.8 Hz, 1H), 4.27 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.96 (d, *J* = 10.8 Hz, 1H), 3.68 (s, 3H), 3.50 (s, 3H).

(*E*)-**Dimethyl 2-(1,3-diphenylallyl)-2-fluoromalonate** (**9a**)[25]: 94% yield; $[\alpha]_D^{20}$ = +26.9° (c 1.5, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 11.89 min (major); 14.23 min (minor) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 1.0 mL/min] to be 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40-7.21 (m, 10H), 6.59 (d, *J* = 15.6 Hz, 1H), 6.47 (dd, *J* = 15.6, 8.8 Hz, 1H), 4.54 (dd, *J* = 31.6, 9.2 Hz, 1H), 3.81 (s, 3H), 3.59 (s, 3H); ^{19}F NMR (100 MHz, $CDCl_3$) δ = -175.79.

(*E*)-**Diethyl 2-(1,3-bis(4-fluorophenyl)allyl)-2-fluoromalonate** (**9b**): White solid; 93% yield; mp: 90.7–92.1 °C; $[\alpha]_D^{20}$ = +63.5° (c 2.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 13.83 min (major); 15.31 min (minor) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 1.0 mL/min] to be 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38-7.29 (m, 4H), 7.04-6.95 (m, 4H), 6.52 (d, *J* = 15.6 Hz, 1H), 6.34 (dd, *J* = 15.6, 9.2 Hz, 1H), 4.52 (dd, *J* = 31.2, 9.2 Hz, 1H), 3.82 (s, 3H), 3.62 (s, 3H). ^{19}F NMR (100 MHz, $CDCl_3$) δ = -176.00, -114.17, -113.65. ^{13}C NMR (126 MHz, $CDCl_3$) δ =165.5 (d, J_{C-F} = 25.7 Hz), 165.0 (d, J_{C-F} = 25.7 Hz), 162.5 (d, J_{C-F} = 248.0 Hz), 162.3 (d, J_{C-F} = 247.8 Hz), 133.2, 132.4 (dd, J_{C-F} = 7.4, 3.8 Hz), 130.7 (dd, J_{C-F} = 8.3, 2.8 Hz), 128.1, 128.0, 127.2, 115.5 (d, J_{C-F} = 21.2 Hz), 115.4 (d, J_{C-F} = 22.0 Hz), 97.4 (d, J_{C-F} = 210.3 Hz), 53.5, 53.2, 52.9 (d, J_{C-F} = 18.3 Hz). HRMS (ESI) calcd for $C_{20}H_{17}F_3NaO_4$ ($[M+Na]^+$): 230.0793, Found: 230.0788. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3629, 3043, 1759, 1716, 1699, 1651, 1601, 1558, 1508, 1229, 1160, 1041, 970, 848, 827, 790, 750, 606.

(*E*)-**Diethyl 2-(1,3-bis(4-chlorophenyl)allyl)-2-fluoromalonate** (**9c**): White solid; 88% yield; mp: 103.7–105.5 °C; $[\alpha]_D^{20}$ = +69.7° (c 2.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 18.06 min (major); 20.81 min (minor) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 1.0 mL/min] to be 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34-7.25 (m, 8H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.39 (dd, *J* = 15.6, 9.2 Hz, 1H), 4.52 (dd, *J* = 31.2, 8.8 Hz, 1H), 3.82 (s, 3H), 3.63 (s, 3H). ^{19}F NMR (100 MHz, $CDCl_3$) δ = -175.70. ^{13}C NMR (126 MHz, $CDCl_3$) δ =165.3 (d, J_{C-F} = 25.7 Hz), 164.9 (d, J_{C-F} = 25.7 Hz), 135.0, 134.7, 133.8, 133.7, 133.3, 130.4, 128.8, 128.7, 127.7, 124.8 (d, J_{C-F} = 3.6 Hz), 97.1 (d, J_{C-F} = 210.3 Hz), 53.5, 53.3, 53.0 (d, J_{C-F} = 18.2 Hz). HRMS (ESI) calcd for $C_{20}H_{17}Cl_2FNaO_4$ ($[M+Na]^+$): 433.0386, Found: 433.0380. IR (KBr): ν_{max} (cm^{-1}) = 3547, 3476, 3413, 2955, 1760, 1638, 1617, 1491, 1435, 1254, 1140, 1092, 1048, 1014, 970, 826, 803, 725, 625, 567.

(*E*)-**Dimethyl 2-(1,3-bis(4-bromophenyl)allyl)-2-fluoromalonate** (**9d**): White solid; 86% yield; mp: 71.0–72.6 °C; $[\alpha]_D^{20}$ = +30.9° (c 3.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 21.86 min (major); 26.72 min (minor) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 1.0 mL/min] to be 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46-7.44 (m, 2H), 7.41-7.38 (m, 2H), 7.27-7.25 (m, 2H), 7.20-7.18 (m, 2H), 6.49 (d, *J* = 15.6 Hz, 1H), 6.40 (dd, *J* = 15.6, 8.8 Hz, 1H), 4.50 (dd, *J* = 30.8, 8.4 Hz, 1H), 3.81 (s, 3H), 3.63 (s, 3H). ^{19}F NMR (100 MHz, $CDCl_3$) δ = -175.70. ^{13}C NMR (100 MHz, $CDCl_3$) δ

=165.2 (d, J_{C-F} = 25.6 Hz), 164.8 (d, J_{C-F} = 25.5 Hz), 135.4, 135.0, 133.4, 131.7, 131.6, 130.7, 130.0, 124.8, 122.0, 121.8, 97.0 (d, J_{C-F} = 208.7 Hz), 53.5, 53.3, 53.0 (d, J_{C-F} = 18.2 Hz). HRMS (ESI) calcd for $C_{20}H_{17}Br_2FNaO_4$ ([M+Na]$^+$): 520.9375, Found: 520.9375. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3477, 1759, 1716, 1699, 1650, 1617, 1558. 1541, 1487, 1254, 1140, 1072, 1010, 969, 848, 799, 766, 721, 612.

(*E*)-**Dimethyl 2-(1,3-bis(3-bromophenyl)allyl)-2-fluoromalonate** (**9e**): White solid; 99% yield; mp: 93.9–95.4 °C; $[\alpha]_D^{20}$ = +63.5° (c 2.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 12.93 min (minor); 13.94 min (major) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 0.8 mL/min] to be 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53-7.48 (m, 2H), 7.43-7.41 (m, 1H), 7.37-7.32 (m, 2H), 7.26-7.13 (m, 3H), 6.50 (d, *J* = 15.6 Hz, 1H), 6.41 (dd, *J* = 16.0, 8.8 Hz, 1H), 4.50 (dd, *J* = 30.8, 8.8 Hz, 1H), 3.83 (s, 3H), 3.65 (s, 3H). ^{19}F NMR (100 MHz, $CDCl_3$) δ = -175.46. ^{13}C NMR (100 MHz, $CDCl_3$) δ =165.2 (d, J_{C-F} = 25.5 Hz), 164.8 (d, J_{C-F} = 25.6 Hz), 138.6, 138.2, 133.3, 132.0, 131.0, 130.9, 130.2, 130.0, 129.3, 127.6, 125.4(d, J_{C-F} = 4.4 Hz), 125.2, 122.7, 122.6, 98.5 (d, J_{C-F} = 208.7 Hz), 53.7, 53.4, 53.1 (d, J_{C-F} = 18.3 Hz). HRMS (ESI) calcd for $C_{20}H_{17}Br_2FNaO_4$ ([M+Na]$^+$): 520.9375, Found: 520.9370. IR (KBr): ν_{max} (cm^{-1}) = 3901, 3747, 3648, 3549, 3479, 3414, 3236, 3060, 2954, 1759, 1716, 1699, 1636, 1617, 1559, 1540, 1473, 1457, 1434, 1260, 1141, 1072, 1048, 967, 767, 748, 606.

(*E*)-**Dimethyl 2-(1,3-dim-tolylallyl)-2-fluoromalonate** (**9f**): White solid; 83% yield; mp: 97.7–99.4 °C; $[\alpha]_D^{20}$ = +45.0° (c 2.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 9.98 min (major); 11.28 min (minor) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 0.8 mL/min] to be 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.23-7.12 (m, 6H), 7.07-7.02 (m, 2H), 6.54 (d, *J* = 15.6 Hz, 1H), 6.44 (dd, *J* = 15.6, 9.2 Hz, 1H), 4.48 (dd, *J* = 31.2, 8.8 Hz, 1H), 3.80 (s, 3H), 3.61 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H). ^{19}F NMR (100 MHz, $CDCl_3$) δ = -175.76. ^{13}C NMR (126 MHz, $CDCl_3$) δ =165.6 (d, J_{C-F} = 25.7 Hz), 165.2 (d, J_{C-F} = 25.7 Hz), 138.1, 138.0, 136.7, 136.4, 134.2, 129.7, 128.6, 128.5, 128.4, 128.3, 127.1, 126.0, 124.5(d, *J* = 3.7 Hz), 123.7, 97.5 (d, J_{C-F} = 210.3 Hz), 53.8 (d, J_{C-F} = 18.3 Hz), 53.4, 53.0, 21.4, 21.2. HRMS (ESI) calcd for $C_{22}H_{23}FNaO_4$ ([M+Na]$^+$): 393.1478, Found: 393.1473. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3649, 3031, 2955, 1763, 1700, 1650, 1604, 1558, 1549, 1489, 1261, 1140, 1047, 967, 849, 777, 707, 607.

(*E*)-**Dimethyl 2-(1,3-dip-tolylallyl)-2-fluoromalonate** (**9g**): White solid; 69% yield; mp: 83.9–84.8 °C; $[\alpha]_D^{20}$ = +66.8° (c 1.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (254 nm, 25 °C) t_R = 14.63 min (major); 15.76 min (minor) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 0.8 mL/min] to be 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27-7.21 (m, 4H), 7.13-7.07 (m, 4H), 6.53 (d, *J* = 16.0 Hz, 1H), 6.40 (dd, *J* = 15.6, 8.8 Hz, 1H), 4.48 (dd, *J* = 31.6, 8.8 Hz, 1H), 3.80 (s, 3H), 3.61 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H), 2.30 (s, 3H). ^{19}F NMR (100 MHz, $CDCl_3$) δ = -176.00. ^{13}C NMR (100 MHz, $CDCl_3$) δ =165.7 (d, J_{C-F} = 25.5 Hz), 165.2 (d, J_{C-F} = 26.2 Hz), 137.6, 137.4, 133.9, 133.74, 133.69, 129.3, 129.1, 128.9, 126.4, 123.7 (d, J_{C-F} = 2.9 Hz), 97.6 (d, J_{C-F} = 208.0 Hz), 53.5 (d, J_{C-F} = 18.2 Hz), 53.4, 53.1, 21.1, 21.0. HRMS (ESI) calcd for $C_{22}H_{23}FNaO_4$ ([M+Na]$^+$): 393.1478, Found: 393.1477. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3648, 3027, 2954, 1762, 1650, 1616, 1558, 1512, 1257, 1139, 1045, 969, 848, 806, 586.

(*E*)-**Dimethyl 2-(1,3-di(naphthalen-1-yl)allyl)-2-fluoromalonate** (**9h**): White solid; 78% yield; mp: 106.3–108.2 °C; $[\alpha]_D^{20}$ = +63.6° (c 3.0, $CHCl_3$). The enantiomeric excess of the product was determined by HPLC analysis (214 nm, 25 °C) t_R = 9.80 min (minor); 23.02 min (major) [Diacel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol, 80/20, 0.8 mL/min] to be 80%. ^{1}H NMR (400 MHz, CDCl3) δ = 8.36 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.87-7.84 (m, 2H), 7.80-7.77 (m, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.62-7.58 (m, 1H), 7.51-7.33 (m, 7H), 6.51 (dd, *J* = 15.2, 8.4 Hz, 1H), 5.33 (dd, J = 9.6, 9.6 Hz, 1H), 5.69 (dd, *J* = 40.0, 9.2 Hz, 1H), 3.74 (s, 3H), 3.44 (s, 3H). ^{19}F NMR (100 MHz, CDCl3) δ = -174.10. ^{13}C NMR (126 MHz, $CDCl_3$) δ =166.1 (d, J_{C-F} = 25.7 Hz), 165.1 (d, J_{C-F} = 26.7 Hz), 134.3, 134.0, 133.4, 132.9, 131.9, 131.3, 131.0, 129.0, 128.45, 128.39, 128.2, 126.64, 126.60, 126.3, 126.0, 125.7, 125.6, 125.54, 125.48, 124.1, 123.6, 123.1, 97.9 (d, J_{C-F} = 210.3 Hz), 53.6, 53.0, 47.6 (d, J_{C-F} = 18.4 Hz). HRMS (ESI) calcd for $C_{28}H_{23}FNaO_4$ ([M+Na]$^+$): 465.1478, Found: 465.1482. IR (KBr): ν_{max} (cm^{-1}) = 3853, 3747, 3673, 3648, 3479, 3053, 2954, 2847, 1761, 1650, 1594, 1558, 1509, 1435, 1396, 1262, 1169, 1142, 1086, 1044, 969, 848, 797, 778, 736, 679, 602.

(*E*)-Dimethyl 2-(1, 3-bis(3-fluorophenyl)allyl)-2-fluoromalonate (**9i**): White solid; mp: 102.5–103.8 °C; 82% yield; $[\alpha]_D^{20}$ = +43.9° (c 0.4, $CHCl_3$). The *ee* of the product was determined by chiral HPLC [Daicel CHIRALCEL AD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10, flow rate = 1.0 mL/min; detection wavelength = 214 nm; t_R = 37.787 (major), 46.063 (minor) min] to be 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.90 (s, 1H), 7.86-7.74 (m, 6H), 7.69 (s, 1H), 7.59-7.55 (m, 2H), 7.48-7.46 (m, 2H), 7.44-7.41 (m, 2H), 6.77 (d, *J* = 15.6 Hz, 1H), 6.68 (dd, *J* = 16.0, 8.8 Hz, 1H), 4.78 (dd, *J* = 31.6, 8.8 Hz, 1H), 3.85 (s, 3H), 3.57 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -175.5. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.7 (d, *J* = 25.4 Hz), 165.2 (d, *J* = 25.7 Hz), 134.6, 134.2, 133.9, 133.4, 133.3, 133.1, 132.8, 128.4, 128.2, 128.0, 127.9, 127.6, 127.5, 126.9, 126.9, 126.6, 126.3, 126.1, 126.1, 126.0, 124.9 (d, *J* = 4.4 Hz), 123.5, 97.9 (d, *J* = 208.5 Hz), 54.0 (d, *J* = 18.3 Hz), 53.6, 53.3 (d, *J* = 18.5 Hz) ppm. IR(KBr): ν_{max} (cm^{-1}) = 3046, 2985, 2920, 2844, 1764, 1265, 1126, 1033, 970, 923, 830, 751. HRMS (ESI+) calcd for $C_{28}H_{23}FNaO_4$ [M+Na]$^+$: 465.1473, Found: 465.1476.

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