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Efficient catalytic asymmetric synthesis of α-substituted phenyloxyacetyloxy and aroyloxy phosphonates

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Abstract—Optically active α-substituted phenyloxyacetyloxy and aroyloxy phosphonates have been synthesized via catalytic asymmetric hydrogenation of the corresponding prochiral α,β-unsaturated phosphonates using Rh(I)/(*R*,*R*)-Me-DuPhos as the catalyst in methanol at 18 °C. The asymmetric hydrogenation reaction exhibits excellent enantioselectivity with enantiomeric excesses from 91 to 96%.

1. Introduction

The biological importance of phosphonates was recognized over 45 years ago.[1] Among them, α-substituted phosphonates are particularly important in connection with their remarkable biological activities. They have been widely used as enzyme inhibitors,[2] antibacterial agents,[3] anti-HIV agents,[4] botryticides,[5] and haptens for catalytic antibodies.[6] For these reasons, the synthesis of α-substituted phosphonates and their functionalized derivatives is an important objective.[7] The absolute configuration of α-substituted phosphonates can affect their biological activity,[8] thus stimulating interest in the asymmetric synthesis of these compounds. For example, intensive efforts have been made in the asymmetric synthesis of optically active α-amino and α-hydroxy phosphonates in recent years.[9] Enantioselective and catalytic processes are especially attractive. Elegant examples include enantioselective synthesis of α-hydroxy and/or α-amino phosphonates via asymmetric hydrogenation,[10] asymmetric borane reduction,[11] asymmetric dihydroxylation and aminohydroxylation,[12] and asymmetric hydrophosphonylation.[13]

Although numerous methods are available for the asymmetric synthesis of α-hydroxy and α-amino phosphonates, there are no reports concerning the straightforward route to asymmetric synthesis of α-substituted phenyloxyacetyloxy and aroyloxy phosphonates, two kinds of important derivatives of α-hydroxy phosphonates. Recently, we have synthesized a series of racemic α-substituted phosphonates and examined their biological activities.[14] It has been found that α-substituted phenyloxyacetyloxy and aroyloxy phosphonates, for example, dimethyl α-(2,4-dichlorophenoxyacetoxy) ethyl phosphonate, are good inhibitors of pyruvate dehydrogenases and exhibit potent herbicidal activities.[14] Considering the importance of chirality for biologically active molecules, synthesis of optically active α-substituted phenoxyacetyloxyl and aroyloxy phosphonates is of great interest. Based on the pioneering work of Burk and Imamoto,[10] we herein describe the catalytic asymmetric synthesis of α-substituted phenyloxyacetyloxy and aroyloxy phosphonates via asymmetric hydrogenation of the corresponding prochiral α,β-unsaturated phosphonates using Rh(I)/(*R*,*R*)-Me-DuPhos complex as the catalyst.

2. Results and discussion

The α-substituted α,β-unsaturated phosphonates are synthesized by a two-step procedure as shown in Scheme 1. The Arbuzov reaction of acyl chlorides **2** and trialkyl phosphates **1** gave α-keto phosphonates **3**, which were then treated with various aroyl chlorides or substituted phenoxyacetyl chlorides in the presence of Et_3N from 0 °C to room temperature to exclusively afford *E*-α-substituted α,β-unsaturated phosphonates **4a**–**4w** in 56–95% isolated yields.[15] To our knowledge, the α,β-unsaturated phosphonates **4a**–**4w** are novel and first synthesized.

Keywords: Asymmetric catalysis; Chirality; Phosphonate; Hydrogenation.
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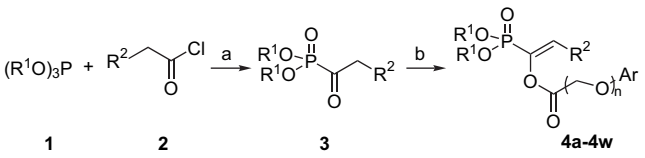


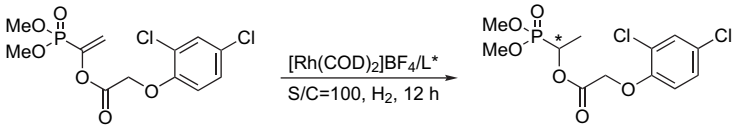
R^1=Me or Et; R^2=H or Me; Ar=phenyl, substituted phenyl, thiophenyl, or furfuryl; n=0 or 1.
(a) 0 °C-rt, 12 h. (b) Substituted aroyl or phenoxyacetyl chlorides, Et_3N, THF, 0 °C-rt, 3 h.

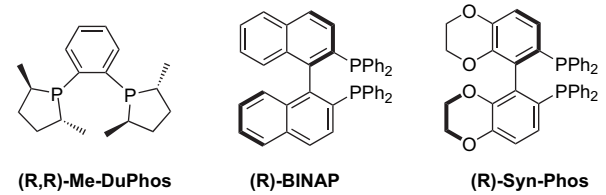
Scheme 1.

In the search for an efficient catalyst, a variety of chiral bisphosphine ligands and a monodentate phosphorus ligand have been screened by using $[Rh(COD)_2]BF_4$ as the catalyst precursor and the results are summarized in Table 1. With dimethyl α-(2,4-dichlorophenoxyacetoxy) vinyl phosphonate **4a** as a representative substrate, the asymmetric hydrogenation was initially effected in methanol with hydrogen pressure of 4 atm using the in situ generated chiral Rh(I)-complexes (Table 1, entries 1–5). The ligands employed played an important role in this transformation, with Me-DuPhos being an excellent ligand (Table 1, entry 1). Under these reaction conditions, the asymmetric hydrogenation could be completed within 12 h at 18 °C with excellent conversion (>95%) and enantiomeric excess (ee, 94%). Although (*R*)-*syn*-Phos and (4*S*,5*S*)-DIOP were also effective as added ligands for this rhodium(I)-catalyzed hydrogenation, the results were generally inferior to those of (*R*,*R*)-Me-DuPhos (Table 1, entries 1, 3, and 4). Compared to other bidentate phosphine, (*R*)-BINAP is almost ineffective (Table 1, entry 2), which is consistent with other asymmetric hydrogenations of enol derivatives.[16] Hydrogenation of **4a** with Rh-(*R*)-MA-Me catalyst under analogous reaction conditions resulted in only poor conversion (Table 1, entry 5). With dichloromethane as the solvent and under higher pressure of H_2, the chiral monodentate ligand, (*R*)-MA-Me, can be used for this reaction, but it is not as effective as (*R*,*R*)-Me-DuPhos in terms of either activity or stereoselectivity (Table 1, entry 6). The method to generate the chiral catalyst has no obvious effects on either reactivity or enantioselectivity, and the reaction gave almost identical results, irrespective of the use of the in situ generated catalyst or commercially available one (Table 1, entries 1 vs 7). Note that $[Rh(COD)_2]BF_4$/(*R*,*R*)-Me-DuPhos and [(COD)Rh-(*S*,*S*)-Me-DuPhos]OTf constitute the same stereochemical environment, although the respective absolute configurations are different (Table 1, entries 1 and 7).

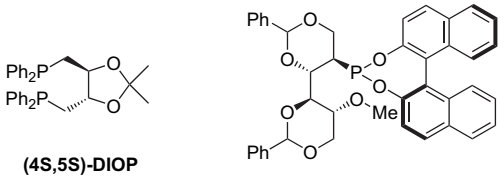
Table 2 summarizes some results of the effect of varying the reaction conditions. Using the $[Rh(COD)_2]BF_4$/(*R*,*R*)-Me-DuPhos catalyst system, we observed that the enantioselectivity of the reaction depended on the solvents employed (Table 2). Although the catalytic hydrogenation went to completion in both CH_2Cl_2 and THF, the reaction led to 78 and 88% ee, respectively (Table 2, entries 2 and 3). Almost no reaction was observed in toluene probably due to the little solubility of the catalyst in toluene (Table 2, entry 4).

Table 1. Ligands screening on the asymmetric hydrogenation





(R,R)-Me-DuPhos (R)-BINAP (R)-Syn-Phos

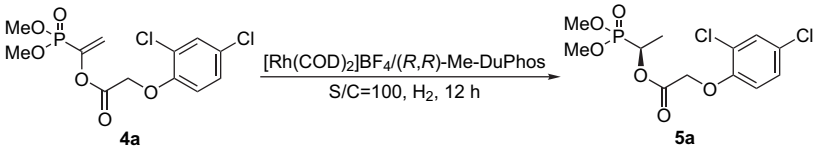


(4S,5S)-DIOP (R)-MA-Me

Entry	Pressure (atm)	Solvent	Ligand	Conv.[a] (%)	ee[b] (%)
1	4	MeOH	(*R*,*R*)-Me-DuPhos	>95	94
2	4	MeOH	(*R*)-BINAP	<5	nd
3	4	MeOH	(*R*)-*syn*-Phos	50	32
4	4	MeOH	(4*S*,5*S*)-DIOP	59	16
5	4	MeOH	(*R*)-MA-Me	<5	nd
6	10	CH_2Cl_2	(*R*)-MA-Me	64	36
7	4	MeOH	(*S*,*S*)-Me-DuPhos[c]	>95	−94

[a] Conversions were determined by ^1H NMR.
[b] Enantiomeric excesses were determined by chiral HPLC on a Daicel Chiralcel OJ-H column.
[c] Commercially available [(COD)Rh-(*S*,*S*)-Me-DuPhos]OTf as the catalyst.

Table 2. Investigation of reaction conditions on the asymmetric hydrogenation



Entry	Pressure (atm)	Temp (°C)	Solvent	Conv.[a] (%)	ee[b] (%)
1	4	18	MeOH	>95	94
2	4	18	CH_2Cl_2	>95	78
3	4	18	THF	>95	88
4	4	18	Toluene	<5	nd
5	4	50	MeOH	>95	94
6	1.3	18	MeOH	>95	94
7	10	18	MeOH	>95	94
8[c]	4	18	MeOH	15	93

[a] Conversions were determined by ^{1}H NMR.
[b] Enantiomeric excesses were determined by chiral HPLC on a Daicel Chiralcel OJ-H column.
[c] S/C=500:1.

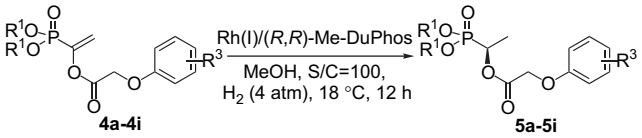
Changing the hydrogen pressure to 1.3 or 10 atm resulted in identical results (Table 2, entries 6 and 7 vs 1). Increasing the reaction temperature from 18 to 50 °C did not affect the reaction (Table 2, entries 1 and 5). Reducing the catalyst loading to S/C=500:1 resulted in much lower conversion, only 15%. However, it did not decrease the ee value very much (Table 2, entry 8).

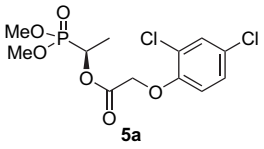
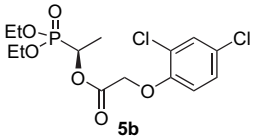
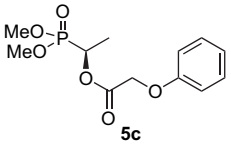
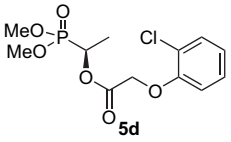
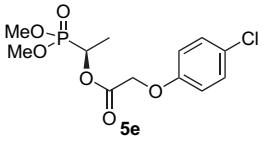
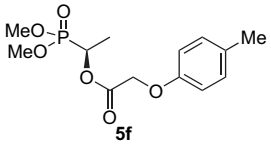
The asymmetric hydrogenation of a series of substituted α,β-unsaturated phosphonates was then performed using 1 mol % of in situ generated Rh(I)-catalyst in MeOH at 4 atm of H_2 for 12 h at 18 °C and the results are summarized in Tables 3 and 4. This rhodium-catalyzed hydrogenation exhibits broad substrate scope and excellent levels of enantioselectivity from 91 to 96% ee.

Our main objective was to develop a practical route to a diverse range of optically active α-substituted ethyl phosphonates **5a**–**5u**. Table 3 shows the results of the synthesis of chiral aroyloxyacetyloxylethyl phosphonates via asymmetric hydrogenation. Substrates with *O*,*O*-dimethyl or *O*,*O*-diethyl were hydrogenated with excellent enantiomeric excesses ranging from 91 to 96% ee. The hydrogenation reaction took place very well regardless of various electron-withdrawing or electron-donating substituent on the different positions of the aromatic ring. The biological study showed that the hydrogenation product, for example, (*S*)-diethyl α-(2,4-dichlorophenoxyacetoxy) ethyl phosphonate **5b** exhibited potent herbicidal activity.

Burk and co-workers have demonstrated that the Me-DuPhos-Rh is capable of hydrogenating enolbenzoates with some examples.[10c] In order to examine the diversity of the substrates, we have synthesized a variety of α,α-disubstituted- and α,α,β-trisubstituted vinyl phosphonates with different substituents on the benzene ring as well as some substrates with *O*- or *S*-heterocycles and subjected them to our standard reaction conditions. It was found that the substituted benzoxyl alkyl phosphonates **5j**–**5p** with electron-donating or electron-withdrawing group on the aromatic ring were also obtained with excellent ee values (Table 4, entries 1–7). The asymmetric hydrogenation of heterocyclic substrates went smoothly to afford the expected

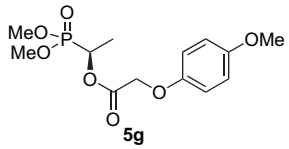
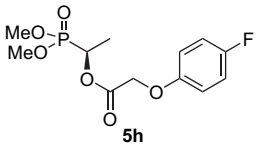
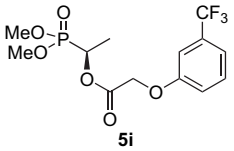
Table 3. Results of the catalytic asymmetric hydrogenation of various α-substituted phenyloxyacetyloxy-α,β-unsaturated phosphonates



Entry	Product	Conv.[a] (%)	ee[b] (%)	Config.[c]
1	 **5a**	>95	94	*S*-(+)
2	 **5b**	>95	96	(*S*)-(+)
3	 **5c**	>95	93	(*S*)-(+)
4	 **5d**	>95	93	(*S*)-(+)
5	 **5e**	>95	95	(*S*)-(+)
6	 **5f**	>95	91	(*S*)-(+)

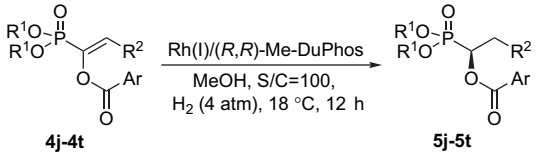
(*continued*)

Table 3. (*continued*)

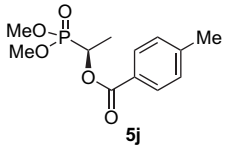
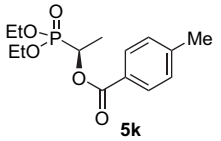
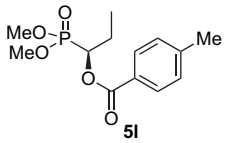
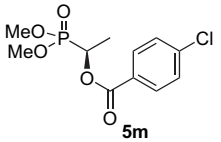
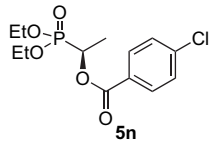
Entry	Product	Conv.[a] (%)	ee[b] (%)	Config.[c]
7	 **5g**	91	95	(*S*)-(+)
8	 **5h**	>95	94	(*S*)-(+)
9	 **5i**	>95	92	(*S*)-(+)

[a] Conversions were determined by ^{1}H NMR.
[b] Enantiomeric excesses were determined by chiral HPLC on a Daicel Chiralcel OJ-H or AS-H column.
[c] Configurations were assigned on the basis of correlation between HPLC elution order, optical rotation, and catalyst configuration relative to the known compound **6a**.

Table 4. Results of the catalytic asymmetric hydrogenation of various α-substituted aroyloxy-α,β-unsaturated phosphonates

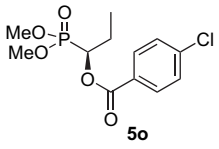
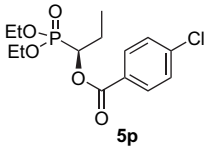
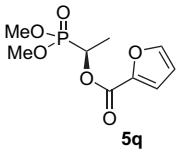
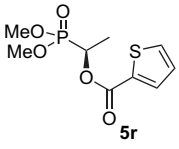
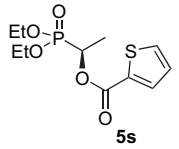
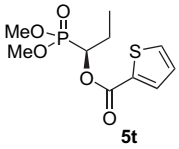


4j-4t **5j-5t**

Entry	Product	Conv.[a] (%)	ee[b] (%)	Config.[c]
1	 **5j**	>95	95	(*S*)-(−)
2	 **5k**	>95	95	(*S*)-(−)
3	 **5l**	>95	94	(*S*)-(+)
4	 **5m**	>95	95	(*S*)-(−)
5	 **5n**	>95	96	(*S*)-(−)

(*continued*)

Table 4. (*continued*)

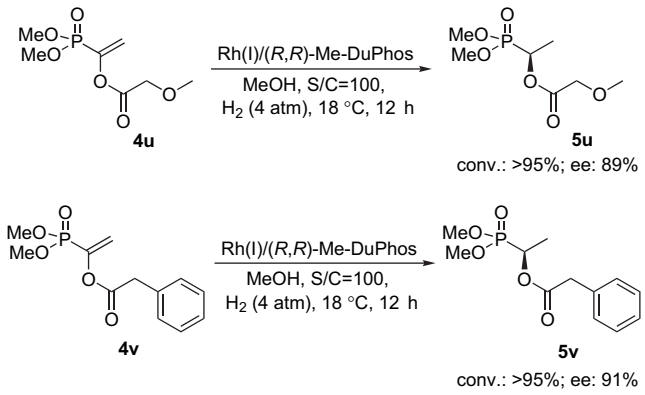
Entry	Product	Conv.[a] (%)	ee[b] (%)	Config.[c]
6	 **5o**	>95	91	(*S*)-(+)
7	 **5p**	>95	92	(*S*)-(+)
8	 **5q**	>95	96	(*S*)-(−)
9	 **5r**	>95	95	(*S*)-(−)
10	 **5s**	>95	95	(*S*)-(−)
11[d]	 **5t**	>95	94	(*S*)-(+)

[a] Conversions were determined by ^{1}H NMR.
[b] Enantiomeric excesses were determined by chiral HPLC on a Daicel Chiralcel OJ-H column.
[c] Configurations were assigned on the basis of correlation between HPLC elution order, optical rotation, and catalyst configuration relative to the known compound **6a**.
[d] Under 10 atm H_2 pressure.

products **5q**–**5t** in great conversions with excellent enantioselectivities (Table 4, entries 8–11). Although the strong thiophilicity of transition metals might make the catalytic reaction ineffective,[17] the catalytic hydrogenation of **4r**, **4s**, and **4t** was carried out in more than 95% conversions under mild conditions, respectively. α,α,β-Trisubstituted-α,β-unsaturated phosphonates **4t** were only partially hydrogenated under the optimized reaction conditions after 12 h, and this is perhaps due to a combination of steric or electronic effect.[10a] However, with higher H_2 pressure (10 atm), **4t** goes to completion smoothly (Table 4, entry 11).

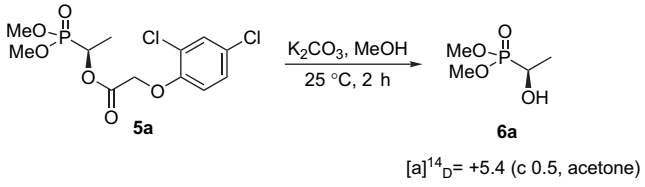
In the case of **4u** and **4v**, the reaction gave similarly high conversion but a slightly low enantioselectivity (89 and 91% ee, respectively, Scheme 2).

The α-substituted phenyloxyacetyloxy and aroyloxy phosphonates **5** can be simply deprotected using K_2CO_3 in MeOH at room temperature for 2 h to afford the corresponding



Scheme 2.

α-hydroxy phosphonates **6**. In order to determine the absolute configuration of the hydrogenation products, **5a** was converted to the previously reported compound **6a**, as shown in Scheme 3. The $[\alpha]_D$ value of **6a** is the same as the one reported in the literature,[17] which indicates that the absolute configuration of the hydrogenation products is *S* configuration.



Scheme 3.

3. Conclusion

In summary, we have synthesized a series of optically active phenoxyacetyloxyl and aroyloxy phosphonates in high enantiomeric purity via catalytic asymmetric hydrogenation using Rh(I)/(*R*,*R*)-Me-DuPhos as the catalytic system in methanol and most of the target compounds including their precursors are novel. The methodology described herein represents one of the most straightforward routes to these compounds.

4. Experimental

4.1. General procedure for the preparation of α,β-unsaturated phosphonates (the preparation of 4a is representative)

Acetyl chloride (2.5 mL, 35 mmol) was cooled to 0 °C in an oven-dried flask fitted with an addition funnel. Trimethyl phosphite (5 mL, 42 mmol) was added dropwise. A balloon was used to compensate for the released methyl chloride. When the addition was complete, the reaction was warmed to room temperature and stirred overnight. The mixture was concentrated under vacuum to remove volatile impurities and then the crude material was taken directly to next step. THF (40 mL) and 2,4-dichlorophenoxy acetyl chloride (5 mL, 28.2 mmol) were added to the crude product, and the system was chilled to 0 °C. Et_3N (4.5 mL) was dissolved in 20 mL of THF, and this solution was then added slowly to the reaction mixtures. After stirred for 45 min, the reaction mixture was warmed up to room temperature and stirred for another 3 h. The reaction mixture was diluted with EtOAc (200 mL), which was washed with saturated $NaHCO_3$ (100 mL×3), brine (75 mL), and then dried with $MgSO_4$. The solvent was removed in vacuo to give yellow oil, which was purified on silica gel (EtOAc:petroleum ether=1:1) to give 5.93 g of **4a** as white solid in 59% isolated yield.

4.1.1. *O*,*O*-Dimethyl α-(2,4-dichlorophenoxyacetoxy) vinyl phosphonate (4a). White solid; yield 59%; mp 78–80 °C; IR (KBr) 1799, 1636, 1587, 1487, 1252, 1144, 1024, 814, 800 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, 1H, *J*=2.4 Hz), 7.20 (dd, 1H, *J*=8.8 and 2.4 Hz), 6.86 (d, 1H, *J*=8.8 Hz), 6.11 (dd, 1H, *J*=6.8 and 2.4 Hz), 5.86 (dd, 1H, *J*=34.4 and 2.4 Hz), 4.86 (s, 2H), 3.76 (d, 6H, *J*=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.2, 53.3, 65.9, 114.3, 114.9, 122.2, 122.5, 124.3, 127.5, 127.7, 130.5, 143.3, 145.6, 152.2, 166.0, 166.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.70; MS (EI) *m*/*z* 354 (M^+-1), 355 (M^+), 357 (M^++2). Anal. Calcd for $C_{12}H_{13}Cl_2O_6P$: C, 40.59; H, 3.69. Found: C, 40.38; H, 3.76.

4.1.2. Diethyl α-(2,4-dichlorophenoxyacetoxy) vinyl phosphonate (4b). Pale yellow liquid; yield 75%; IR (KBr) 2984, 1784, 1630, 1585, 1480, 1263, 1161, 1022, 801 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, 1H, *J*=2.4 Hz), 7.19 (dd, 1H, *J*=8.8 and 2.4 Hz), 6.86 (d, 1H, *J*=8.8 Hz), 6.10 (dd, 1H, *J*=6.8 and 2.4 Hz), 5.81 (dd, 1H, *J*=34.4 and 2.4 Hz), 4.85 (s, 2H), 4.17–4.09 (m, 4H), 1.33 (t, 6H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 16.1, 57.7, 66.0, 115.0, 121.4, 121.6, 124.4, 127.5, 127.7, 130.5, 144.6, 146.8, 152.3, 166.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.75; MS (EI) *m*/*z* 382 (M^+-1), 383 (M^+), 385 (M^++2). Anal. Calcd for $C_{14}H_{17}Cl_2O_6P$: C, 43.88; H, 4.47. Found: C, 43.48; H, 4.76.

4.1.3. Dimethyl α-phenoxyacetoxy vinyl phosphonate (4c). Little yellow solid; yield 68%; mp 57–59 °C; IR (KBr) 2969, 1778, 1630, 1599, 1589, 1492, 1445, 1378, 1260, 1161, 1017, 946, 840, 797, 755, 695, 586, 532 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, 2H, *J*=7.8 Hz), 7.02 (t, 1H, *J*=7.2 Hz), 6.94 (d, 2H, *J*=8.0 Hz), 6.13 (dd, 1H, *J*=10.8 and 2.2 Hz), 5.85 (dd, 1H, *J*=34.6 and 2.2 Hz), 4.80 (s, 2H), 3.76 (d, 6H, *J*=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.45, 53.51, 65.1, 114.8, 122.2, 122.4, 122.6, 129.8, 145.6, 157.6, 166.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.16; MS (EI) *m*/*z* 286 (M^+), 287 (M^++1). Anal. Calcd for $C_{12}H_{15}O_6P$: C, 50.36; H, 5.28. Found: C, 50.12; H, 5.35.

4.1.4. Dimethyl α-(2-chlorophenoxyacetoxy) vinyl phosphonate (4d). Colorless liquid; yield 64%; IR (KBr) 2958, 1785, 1589, 1485, 1449, 1258, 1197, 1084, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, 1H, *J*=8.0 and 1.6 Hz), 7.23 (t, 1H, *J*=1.2 Hz), 6.98 (t, 1H, *J*=1.6 Hz), 6.91 (dd, 1H, *J*=4.0 and 1.2 Hz), 6.12 (dd, 1H, *J*=11.0 and 2.4 Hz), 5.86 (dd, 1H, *J*=34.8 and 2.4 Hz), 4.88 (s, 2H), 3.77–3.72 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.50, 53.51, 65.9, 114.1, 112.4, 122.6, 123.1, 123.5, 127.9, 130.8, 143.4, 145.6, 153.3, 166.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.08; MS (EI) *m*/*z* 320 (M^+-1), 321

(M^+), 322 (M^++1). Anal. Calcd for $C_{12}H_{14}ClO_6P$: C, 44.95; H, 4.40. Found: C, 44.75; H, 4.40.

4.1.5. Dimethyl α-(4-chlorophenoxyacetoxy) vinyl phosphonate (4e). Little yellow solid; yield 80%; mp 32–34 °C; IR (KBr) 2957, 1784, 1596, 1493, 1446, 1266, 1151, 1027, 834, 801, 640, 509 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, 2H, J=11.2 Hz), 6.87 (d, 2H, J=11.2 Hz), 6.11 (dd, 1H, J=10.6 and 2.4 Hz), 5.85 (dd, 1H, J=34.6 and 2.4 Hz), 4.77 (s, 2H), 3.77 (d, 6H, J=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.3, 53.4, 65.0, 115.99, 122.2, 122.4, 126.9, 129.3, 129.4, 143.0, 156.0, 166.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.12; MS (EI) m/z 320 (M^+). Anal. Calcd for $C_{12}H_{14}ClO_6P$: C, 44.95; H, 4.40. Found: C, 44.60; H, 4.74.

4.1.6. Dimethyl α-(4-methylphenoxyacetoxy) vinyl phosphonate (4f). Little yellow liquid; yield 87%; IR (KBr) 2958, 1786, 1613, 1512, 1445, 1250, 1149, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, 2H, J=8.4 Hz), 6.83 (d, 2H, J=8.4 Hz), 6.12 (dd, 1H, J=11.0 and 2.2 Hz), 5.85 (dd, 1H, J=36.6 and 2.2 Hz), 4.76 (s, 2H,), 3.78–3.75 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 53.37, 53.43, 65.2, 114.4, 114.6, 122.3, 122.6, 130.1, 131.4, 143.3, 145.6, 145.6, 155.5, 166.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.19; MS (EI) m/z 300 (M^+), 301 (M^++1). Anal. Calcd for $C_{13}H_{17}O_6P$: C, 52.00; H, 5.71. Found: C, 52.44; H, 5.48.

4.1.7. Dimethyl α-(4-methoxyphenoxyacetoxy) vinyl phosphonate (4g). Yellow liquid; yield 75%; IR (KBr) 2958, 1762, 1507, 1458, 1202, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.90–6.83 (m, 4H), 6.12 (dd, 1H, J=10.8 and 2.4 Hz), 5.84 (dd, 1H, J=34.6 and 2.2 Hz), 4.74 (s, 2H), 3.80–3.74 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.2, 53.3, 53.6, 65.8, 114.6, 115.8, 122.1, 122.4, 143.2, 145.4, 151.6, 154.6, 166.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.16; MS (EI) m/z 316 (M^+). Anal. Calcd for $C_{13}H_{17}O_7P$: C, 49.37; H, 5.42. Found: C, 49.02; H, 5.47.

4.1.8. Dimethyl α-(4-fluorophenoxyacetoxy) vinyl phosphonate (4h). Yellow liquid; yield 79%; IR (KBr) 2960, 1785, 1507, 1443, 1204, 1033, 831 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.00 (t, 2H, J=7.6 Hz), 6.91–6.88 (m, 2H), 6.11 (dd, 1H, J=10.6 and 2.4 Hz), 5.85 (dd, 1H, J=34.4 and 2.4 Hz), 4.76 (s, 2H), 3.77 (d, 6H, J=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.4, 53.5, 65.7, 116.0, 116.1, 116.3, 122.3, 122.5, 143.4, 145.6, 153.8, 156.9, 159.3, 166.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.14; MS (EI) m/z 304 (M^+), 305 (M^++1). Anal. Calcd for $C_{12}H_{14}FO_6P$: C, 47.38; H, 4.64. Found: C, 47.49; H, 4.60.

4.1.9. Dimethyl α-(3-trifluoromethylphenoxyacetoxy) vinyl phosphonate (4i). Little yellow liquid; yield 62%; IR (KBr) 2962, 2859, 1757, 1594, 1494, 1457, 1331, 1170, 1127, 1066 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, 1H, J=8.0 Hz), 7.30–7.28 (m, 1H), 7.16–7.12 (m, 2H), 6.13 (dd, 1H, J=11.2 and 2.4 Hz), 5.85 (dd, 1H, J=34.4 and 2.4 Hz), 4.84 (s, 2H), 3.76 (d, 6H, J=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.4, 53.5, 65.1, 111.69, 116.72, 118.3, 118.91, 118.95, 119.8, 122.4, 122.5, 122.7, 125.2, 130.4, 132.0, 132.3, 143.4, 145.6, 157.7, 166.28, 166.30; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.04; MS (EI) m/z 354 (M^+), 355 (M^++1). Anal. Calcd for $C_{13}H_{14}F_3O_6P$: C, 44.08; H, 3.98. Found: C, 44.19; H, 4.05.

4.1.10. Dimethyl α-(4-methylbenzoxy) vinyl phosphonate (4j). Pale yellow liquid; yield 87%; IR (KBr) 2956, 2854, 1739, 1612, 1578, 1457, 1265, 1176, 1025, 836, 801, 748, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 2H, J=8.4 Hz), 7.28 (d, 2H, J=8.0 Hz), 6.18 (dd, 1H, J=10.8 and 2.2 Hz), 5.92 (dd, 1H, J=34.2 and 2.2 Hz), 3.82 (d, 6H, J=11.2 Hz), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 53.18, 53.23, 121.9, 122.2, 126.0, 129.4, 130.3, 144.0, 144.9, 146.3, 164.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.33; MS (EI) m/z 270 (M^+). Anal. Calcd for $C_{12}H_{15}O_5P$: C, 53.34; H, 5.60. Found: C, 53.49; H, 5.44.

4.1.11. Diethyl α-(4-methylbenzoxy) vinyl phosphonate (4k). Pale yellow liquid; yield 78%; IR (KBr) 2984, 1740, 1611, 1577, 1478, 1393, 1267, 1198, 1019, 975, 798, 748, 687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 2H, J=8.4 Hz), 7.28 (d, 2H, J=8.4 Hz), 6.17 (dd, 1H, J=11.2 and 2.0 Hz), 5.90 (dd, 1H, J=35.2 and 2.0 Hz), 4.22–4.16 (m, 4H), 2.44 (s, 3H), 1.34 (t, 6H, J=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.36, 16.42, 21.90, 63.1, 63.2, 121.4, 121.7, 126.1, 129.5, 130.3, 144.9, 147.2, 164.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 7.46; MS (EI) m/z 299 (M^++1). Anal. Calcd for $C_{14}H_{19}ClO_5P$: C, 56.37; H, 6.42. Found: C, 56.56; H, 6.15.

4.1.12. (*E*)-Dimethyl α-(4-methylbenzoxy) propenyl phosphonate (4l). White solid; yield 88%; mp 36–39 °C; IR (KBr) 2960, 2856, 1737, 1662, 1612, 1446, 1262, 1179, 1017, 806, 752, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, 2H, J=8.0 Hz), 7.29 (d, 2H, J=8.4 Hz), 6.71–6.63 (m, 1H), 3.78 (d, 6H, J=11.2 Hz), 2.44 (s, 3H), 1.74 (dd, 3H, J=6.8 and 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 12.3, 21.8, 53.15, 53.20, 125.8, 129.4, 130.3, 135.1, 135.4, 139.2, 141.8, 144.8, 163.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 11.72; MS (EI) m/z 284 (M^+). Anal. Calcd for $C_{13}H_{17}O_5P$: C, 54.93; H, 6.03. Found: C, 54.84; H, 5.84.

4.1.13. Dimethyl α-(4-chlorobenzoxy) vinyl phosphonate (4m). Colorless liquid; yield 95%; IR (KBr) 2959, 1735, 1633, 1595, 1402, 1263, 1191, 1013, 834, 751, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, 2H, J=6.8 and 2.0 Hz), 7.47 (dd, 2H, J=6.8 and 2.0 Hz), 6.18 (dd, 1H, J=10.8 and 2.0 Hz), 5.93 (dd, 1H, J=34.2 and 2.4 Hz), 3.82 (d, 6H, J=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.25, 53.30, 122.1, 122.3, 127.2, 128.8, 129.1, 131.5, 131.7, 140.6, 144.0, 146.2, 163.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.32; MS (EI) m/z 290 (M^+-1), 291 (M^+). Anal. Calcd for $C_{11}H_{12}ClO_5P$: C, 45.46; H, 4.16. Found: C, 45.48; H, 4.13.

4.1.14. Diethyl α-(4-chlorobenzoxy) vinyl phosphonate (4n). Colorless liquid; yield 82%; IR (KBr) 2984, 1743, 1633, 1593, 1488, 1401, 1264, 1195, 1016, 850, 754, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, 2H, J=8.8 Hz), 7.46 (d, 2H, J=8.4 Hz), 6.17 (dd, 1H, J=11.2 and 2.0 Hz), 5.90 (dd, 1H, J=34.8 and 2.0 Hz), 4.21–4.16 (m, 4H), 1.34 (t, 6H, J=6.8 Hz); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 16.06, 16.13, 62.98, 63.03, 121.3, 121.5, 127.4, 129.1, 131.6, 140.5, 145.0, 147.3, 163.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 7.36; MS (EI) *m/z* 319 (M^+). Anal. Calcd for $C_{13}H_{16}ClO_5P$: C, 48.99; H, 5.06. Found: C, 49.04; H, 4.97.

4.1.15. (*E*)-Dimethyl α-(4-chlorobenzoxy) propenyl phosphonate (4o). Colorless liquid; yield 86%; IR (KBr) 2956, 1740, 1660, 1593, 1488, 1402, 1260, 1174, 1023, 799, 754, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, 2H, *J*=6.8 and 2.0 Hz), 7.47 (dd, 2H, *J*=6.8 and 2.0 Hz), 6.71–6.61 (m, 1H), 3.80 (d, 6H, *J*=11.2 Hz), 1.75 (dd, 3H, *J*=6.8 and 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 12.0, 52.98, 53.03, 127.1, 129.1, 131.7, 135.1, 135.3, 137.1, 139.4, 140.5, 162.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 11.33; MS (EI) *m/z* 305 (M^+), 307 (M^++2). Anal. Calcd for $C_{12}H_{14}ClO_5P$: C, 47.31; H, 4.63. Found: C, 47.26; H, 4.73.

4.1.16. (*E*)-Diethyl α-(4-chlorobenzoxy) propenyl phosphonate (4p). White solid; yield 56%; mp 52–55 °C; IR (KBr) 2992, 1734, 1655, 1593, 1488, 1403, 1256, 1148, 1092, 1009, 976, 801, 751, 545 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, 2H, *J*=6.8 and 2.0 Hz), 7.47 (dd, 2H, *J*=6.8 and 2.0 Hz), 6.67–6.63 (m, 1H), 4.19–4.11 (m, 4H), 1.73 (dd, 3H, *J*=7.2 and 2.4 Hz), 1.32 (t, 6H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 12.3, 16.28, 16.34, 31.5, 62.7, 127.2, 129.0, 131.6, 134.3, 134.6, 140.3, 162.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 8.44; MS (EI) *m/z* 332 (M^+-1), 333 (M^+), 336 (M^++3). Anal. Calcd for $C_{14}H_{18}ClO_5P$: C, 50.54; H, 5.45. Found: C, 50.28; H, 5.59.

4.1.17. Dimethyl α-(2-furancarbonyl oxo) vinyl phosphonate (4q). Colorless liquid; yield 73%; IR (KBr) 2959, 2856, 1750, 1577, 1473, 1394, 1294, 1174, 1031, 884, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.32 (s, 1H), 6.58–6.57 (m, 1H), 6.19 (dd, 1H, *J*=11.0 and 2.0 Hz), 5.93 (dd, 1H, *J*=34.8 and 2.0 Hz), 3.82 (d, 6H, *J*=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.2, 53.3, 112.2, 119.9, 122.1, 122.3, 142.9, 143.1, 145.4, 147.4, 155.6, 154.6, 166.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.29; MS (EI) *m/z* 247 (M^++1), 248 (M^++2). Anal. Calcd for $C_9H_{11}O_6P$: C, 43.91; H, 4.50. Found: C, 43.73; H, 4.67.

4.1.18. Dimethyl α-(2-thiophenecarbonyl oxo) vinyl phosphonate (4r). Waxy solid; yield 85%; IR (KBr) 2957, 1732, 1630, 1522, 1462, 1415, 1267, 1197, 1027, 837, 793, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, 1H, *J*=3.2 Hz), 7.67 (d, 1H, *J*=4.4 Hz), 7.16 (t, 1H, *J*=4.4 Hz), 6.18 (dd, 1H, *J*=11.2 and 2.4 Hz), 5.94 (dd, 1H, *J*=34.4 and 2.4 Hz), 3.83 (d, 6H, *J*=11.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.28, 53.33, 121.8, 122.0, 128.0, 131.8, 133.9, 134.0, 134.97, 135.03, 143.7, 146.0, 159.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.74; MS (EI) *m/z* 262 (M^+), 263 (M^++1). Anal. Calcd for $C_9H_{11}O_5PS$: C, 41.22; H, 4.23. Found: C, 41.48; H, 4.26.

4.1.19. Diethyl α-(2-thiophenecarbonyl oxo) vinyl phosphonate (4s). Colorless liquid; yield 76%; IR (KBr) 2984, 1732, 1630, 1522, 1477, 1415, 1267, 1194, 1026, 851, 795, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, 1H, *J*=3.6 Hz), 7.66 (d, 1H, *J*=4.8 Hz), 7.16 (t, 1H, *J*=4.4 Hz), 6.18 (dd, 1H, *J*=10.8 and 2.0 Hz), 5.91 (dd, 1H, *J*=34.4 and 2.0 Hz), 4.19 (m, 4H), 1.35 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.06, 16.12, 121.5, 121.7, 128.2, 132.1, 134.0, 135.1, 144.8, 147.0, 159.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 7.25; MS (EI) *m/z* 290 (M^+), 291 (M^++1). Anal. Calcd for $C_{11}H_{15}O_5PS$: C, 45.52; H, 5.21. Found: C, 45.88; H, 5.16.

4.1.20. (*E*)-Dimethyl α-(2-thiophenecarbonyl oxo) propenyl phosphonate (4t). White solid; yield 92%; mp 84–85 °C; IR (KBr) 2954, 1737, 1664, 1523, 1414, 1259, 1149, 1011, 801, 752, 740, 541 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, 1H, *J*=3.6 and 0.8 Hz), 7.67 (dd, 1H, *J*=4.8 and 1.6 Hz), 7.17 (dd, 1H, *J*=4.8 and 4.0 Hz), 6.72–6.64 (m, 1H), 3.80 (d, 6H, *J*=11.2 Hz), 1.77 (dd, 3H, *J*=6.8 and 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 12.3, 53.29, 53.34, 128.5, 132.0, 134.2, 135.3, 135.7, 136.0, 137.1, 139.4, 159.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 11.38; MS (EI) *m/z* 276 (M^+), 277 (M^++1). Anal. Calcd for $C_{10}H_{13}O_5PS$: C, 43.48; H, 4.74. Found: C, 43.60; H, 4.81.

4.1.21. Dimethyl α-(methoxyacetoxy) vinyl phosphonate (4u). Colorless liquid; yield 80%; IR (KBr) 2959, 1775, 1630, 1456, 1376, 1263 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.11 (dd, 1H, *J*=10.4 and 2.3 Hz), 5.84 (dd, 1H, *J*=34.8 and 2.3 Hz), 4.2 (s, 2H), 3.79 (d, 6H, *J*=11.2 Hz), 3.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.4, 53.5, 59.6, 69.5, 122.2, 122.4, 143.4, 145.7, 168.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.11; MS (EI) *m/z* 224 (M^+), 225 (M^++1). Anal. Calcd for $C_7H_{13}O_6P$: C, 37.51; H, 5.85. Found: C, 37.32; H, 5.59.

4.1.22. Dimethyl α-(phenyl acetoxy) vinyl phosphonate (4v). Colorless liquid; yield 68%; IR (KBr) 3032, 2956, 1738, 1225, 1031, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.27 (m, 5H), 6.06 (dd, 1H, *J*=11.4 and 2.2 Hz), 5.77 (dd, 1H, *J*=35.2 and 2.4 Hz), 3.80–3.61 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.9, 53.1, 53.2, 121.7, 122.0, 127.4, 128.6, 129.2, 132.8, 143.6, 145.8, 168.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.59; MS (EI) *m/z* 270 (M^+). Anal. Calcd for $C_{12}H_{15}O_5P$: C, 53.34; H, 5.60. Found: C, 53.38; H, 5.66.

4.2. Typical procedure for the asymmetric hydrogenation (the preparation of 5a is representative)

In a glove box, the Rh/Me-DuPhos complex was made in situ by mixing $[Rh(COD)_2]BF_4$ (2.0 mg, 0.005 mmol) and (*R*,*R*)-Me-DuPhos (1.7 mg, 0.0055 mmol) in MeOH (2.0 mL). After the mixture was stirred at room temperature for 10 min, substrate **4a** (178 mg, 0.5 mmol) in MeOH (2.0 mL) was added by a syringe. The hydrogenation was performed at room temperature under 4 atm H_2 for 12 h. After carefully releasing the excess hydrogen, the conversion was determined by ^1H NMR analysis and it was found more than 95%. The reaction mixtures were concentrated and then passed through a silica gel plug using ethyl acetate and petroleum ether (3:1) as an eluant to give pure product **5a** (159 mg, 89% yield). The enantiomeric excess (ee value) was determined by comparison of the enantiomerically enriched sample to the racemate on chiral HPLC.

4.2.1. (*S*)-Dimethyl α-(2,4-dichlorophenoxyacetoxy) ethyl phosphonate (5a). Pale yellow liquid; 94% ee; $[\alpha]_D^{14}$ +15.2 (*c* 2.00, $CHCl_3$); IR (KBr) 2957, 1741, 1586, 1476, 1456,

1266, 1178, 1021, 836, 802 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, 1H, J=2.4 Hz), 7.16 (dd, 1H, J=8.8 and 2.4 Hz), 6.77 (d, 1H, J=8.8 Hz), 5.37 (p, 1H, J=7.2 Hz), 4.74 (s, 2H), 3.77 (t, 6H, J=10.4 Hz), 1.49 (dd, 3H, J=16.6 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 53.4, 64.4, 66.1, 114.8, 124.1, 127.2, 127.5, 130.3, 152.2, 167.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.46; MS (EI) m/z 356 (M^+-1), 357 (M^+), 358 (M^++1). Anal. Calcd for $C_{12}H_{15}Cl_2O_6P$: C, 40.36; H, 4.23. Found: C, 40.58; H, 4.34. Enantiomeric excess determination: HPLC, UV 202 nm, Chiralcel OJ-H, 1 mL/min, 10% 2-propanol/90% hexane, (*R*) t_1=48.57 min; (*S*) t_2=55.41 min.

4.2.2. (*S*)-Diethyl α-(2,4-dichlorophenoxyacetoxy) ethyl phosphonate (5b). Pale yellow liquid; 96% ee; $[\alpha]_D^{14}$ +15.1 (*c* 3.10, $CHCl_3$); IR (KBr) 2984, 1741, 1478, 1265, 1191, 1022, 801 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 1H, J=2.4 Hz), 7.17 (dd, 1H, J=8.8 and 2.4 Hz), 6.79 (d, 1H, J=8.8 Hz), 5.36 (p, 1H, J=7.2 Hz), 4.74 (s, 2H), 4.19–4.09 (m, 4H), 1.49 (dd, 3H, J=16.4 and 7.2 Hz), 1.31 (q, 6H, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 16.5, 63.0, 65.0, 66.3, 66.7, 114.9, 124.3, 127.7, 130.4, 152.3, 167.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.96; MS (EI) m/z 385 (M^+), 387 (M^++2), 388 (M^++3). Anal. Calcd for $C_{14}H_{19}Cl_2O_6P$: C, 43.66; H, 4.97. Found: C, 43.68; H, 4.77. HPLC, UV 293 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*R*) t_1=36.87 min; (*S*) t_2=43.63 min.

4.2.3. (*S*)-Dimethyl α-phenoxyacetoxy ethyl phosphonate (5c). Pale yellow liquid; 93% ee; $[\alpha]_D^{14}$ +12.9 (*c* 1.40, $CHCl_3$); IR (KBr) 2958, 1769, 1600, 1496, 1457, 1249, 1178, 1048, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H), 6.97 (t, 1H, J=7.4 Hz), 6.95–6.86 (m, 2H), 5.38 (p, 1H, J=7.2 Hz), 4.66 (s, 2H), 3.77–3.72 (m, 6H), 1.48 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 53.47, 53.53, 64.2, 65.2, 65.9, 114.7, 122.0, 129.7, 157.7, 168.0, 168.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.3; MS (EI) m/z 287 (M^+-1), 287 (M^+), 289 (M^++1). Anal. Calcd for $C_{12}H_{17}O_6P$: C, 50.00; H, 5.94. Found: C, 50.35; H, 5.87. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel OJ-H, 0.8 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=22.70 min; (*R*) t_2=26.16 min.

4.2.4. (*S*)-Dimethyl α-(2-chlorophenoxyacetoxy) ethyl phosphonate (5d). Yellow liquid; 93% ee; $[\alpha]_D^{14}$ +13.1 (*c* 1.20, $CHCl_3$); IR (KBr) 2958, 1769, 1589, 1485, 1449, 1378, 1246, 1189, 1407, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, 1H J=7.8 and 1.6 Hz), 7.21–7.19 (m, 1H), 6.98–6.94 (m, 1H), 6.86–6.84 (m, 1H), 5.44–5.37 (m, 1H), 4.78 (s, 2H), 3.80–3.73 (m, 6H), 1.51 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 53.6, 64.5, 65.2, 65.5, 66.1, 114.0, 114.7, 116.1, 122.9, 123.4, 127.8, 129.6, 129.7, 130.8, 153.4, 167.5, 167.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.09; MS (EI) m/z 322 (M^+-1), 323 (M^+), 324 (M^++1). Anal. Calcd for $C_{12}H_{16}ClO_6P$: C, 44.67; H, 5.00. Found: C, 44.54; H, 4.94. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel AS-H, 0.5 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=21.26 min; (*R*) t_2=23.20 min.

4.2.5. (*S*)-Dimethyl α-(4-chlorophenoxyacetoxy) ethyl phosphonate (5e). Yellow liquid; 95% ee; $[\alpha]_D^{14}$ +15.7 (*c* 1.30, $CHCl_3$); IR (KBr) 2958, 1768, 1493, 1247, 1188, 1049, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, 2H, J=7.0 and 2.0 Hz), 6.84 (dd, 2H, J=6.8 and 2.4 Hz), 5.40 (p, 1H, J=8.0 Hz), 4.67 (s, 2H), 3.81–3.76 (m, 6H), 1.51 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 53.4, 53.5, 53.6, 64.3, 65.4, 66.0, 116.1, 127.0, 129.6, 156.3, 167.65, 167.72; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.96; MS (EI) m/z 322 (M^+-1), 323 (M^+), 324 (M^++1). Anal. Calcd for $C_{12}H_{16}ClO_6P$: C, 44.67; H, 5.00. Found: C, 44.65; H, 4.95. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel AS-H, 0.5 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=20.93 min; (*R*) t_2=26.53 min.

4.2.6. (*S*)-Dimethyl α-(4-methylphenoxyacetoxy) ethyl phosphonate (5f). Colorless liquid; 91% ee; $[\alpha]_D^{14}$ +14.8 (*c* 1.38, $CHCl_3$); IR (KBr) 2957, 1769, 1512, 1447, 1291, 1248, 1178, 1048 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, 2H, J=8.0 Hz), 6.77 (d, 2H, J=8.0 Hz), 5.38 (p, 1H, J=7.2 Hz), 4.63 (s, 1H), 3.78–3.71 (m, 6H), 2.26 (s, 3H), 1.50 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 20.6, 64.1, 65.4, 65.8, 114.5, 130.1, 131.3, 155.6, 168.1, 168.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.40; MS (EI) m/z 322 (M^+-1), 302 (M^+), 303 (M^++1). Anal. Calcd for $C_{13}H_{19}O_6P$: C, 51.66; H, 6.34. Found: C, 51.58; H, 6.25. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel OJ-H, 0.8 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=21.60 min; (*R*) t_2=27.69 min.

4.2.7. (*S*)-Dimethyl α-(4-methoxyphenoxyacetoxy) ethyl phosphonate (5g). Pale yellow liquid; 95% ee; $[\alpha]_D^{14}$ +12.2 (*c* 0.74, $CHCl_3$); IR (KBr) 2958, 1769, 1059, 1446, 1244, 1183, 1032, 831 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.87–6.82 (m, 4H), 5.41 (p, 1H, J=7.2 Hz), 4.64 (s, 1H), 3.81–3.77 (m, 6H), 1.51 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 53.56, 53.62, 55.8, 64.2, 65.9, 66.2, 114.8, 116.0, 152.0, 154.8, 168.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.41; MS (EI) m/z 318 (M^+-1), 319 (M^+). Anal. Calcd for $C_{13}H_{19}O_7P$: C, 49.06; H, 6.02. Found: C, 48.66; H, 5.78. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel AS-H, 0.7 mL/min, 40% 2-propanol/60% hexane, (*S*) t_1=13.93 min; (*R*) t_2=20.14 min.

4.2.8. (*S*)-Dimethyl α-(4-fluorophenoxyacetoxy) ethyl phosphonate (5h). Pale yellow liquid; 94% ee; $[\alpha]_D^{14}$ +13.3 (*c* 1.24, $CHCl_3$); IR (KBr) 2959, 2856, 1769, 1507, 1447, 1249, 1186, 1031, 831 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.01–6.97 (m, 2H), 6.88–6.84 (m, 2H), 5.40 (p, 1H, J=7.2 Hz), 4.66 (s, 2H), 3.81–3.76 (m, 6H), 1.51 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 53.48, 53.54, 53.6, 64.3, 66.0, 116.0, 116.1, 116.3, 153.9, 156.8, 159.2, 167.9, 168.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.3; MS (EI) m/z 306 (M^+), 307 (M^++1). Anal. Calcd for $C_{12}H_{16}FO_6P$: C, 47.07; H, 5.27. Found: C, 46.80; H, 5.14. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel OJ-H, 0.8 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=20.76 min; (*R*) t_2=21.98 min.

4.2.9. (*S*)-Dimethyl α-(3-trifluoromethylphenoxyacetoxy) ethyl phosphonate (5i). Yellow liquid; 92% ee; $[\alpha]_D^{14}$ +10.3 (*c* 1.10, $CHCl_3$); IR (KBr) 2960, 2857, 1769, 1495, 1457,

1332, 1182, 1126, 1068, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (t, 1H, J=8.0 Hz), 7.28 (d, 1H, J=8.0 Hz), 7.12–7.08 (m, 2H, J=7.6 Hz), 5.41 (p, 1H, J=7.2 Hz), 4.74 (s, 1H), 3.81–3.76 (m, 6H), 1.51 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 53.4, 53.5, 53.57, 53.63, 64.4, 65.3, 66.1, 111.6, 111.7, 118.3, 118.7, 118.8, 122.6, 125.3, 130.4, 132.0, 132.3, 157.9, 167.47, 167.54; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.9; MS (EI) m/z 356 (M^+), 357 (M^++1). Anal. Calcd for $C_{13}H_{16}F_3O_6P$: C, 43.83; H, 4.53. Found: C, 43.92; H, 4.39. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel AS-H, 0.5 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=13.92 min; (*R*) t_2=15.20 min.

4.2.10. (*S*)-Dimethyl α-(4-methylbenzoxy) ethyl phosphonate (5j). Colorless liquid; 95% ee; $[\alpha]_D^{14}$ −19.61 (*c* 2.38, $CHCl_3$); IR (KBr) 2957, 2854, 1725, 1612, 1456, 1266, 1179, 1029, 832, 805, 753, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J=8.0 Hz), 7.21 (d, 2H, J=8.0 Hz), 5.51 (p, 1H, J=7.2 Hz), 3.82 (dd, 6H, J=10.4 and 4.4 Hz), 2.37 (s, 3H), 1.55 (dd, 3H, J=8.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 21.7, 53.3, 53.6, 63.5, 65.2, 126.6, 129.2, 129.9, 144.2, 165.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.86; MS (EI) m/z 271 (M^+-1), 272 (M^+), 273 (M^++1). Anal. Calcd for $C_{12}H_{17}O_5P$: C, 52.94; H, 6.29. Found: C, 53.15; H, 6.33. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=25.46 min; (*R*) t_2=28.38 min.

4.2.11. (*S*)-Diethyl α-(4-methylbenzoxy) ethyl phosphonate (5k). Pale yellow liquid; 95% ee; $[\alpha]_D^{14}$ −22.38 (*c* 1.82, $CHCl_3$); IR (KBr) 2985, 1724, 1613, 1266, 1023, 968, 799, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J=8.0 Hz), 7.22 (d, 2H, J=8.0 Hz), 5.49 (p, 1H, J=7.2 Hz), 4.19–4.12 (m, 4H), 2.38 (s, 3H), 1.55 (dd, 3H, J=16.8 and 7.2 Hz), 1.28 (t, 6H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 16.5, 21.7, 62.7, 63.0, 63.9, 65.6, 126.8, 129.2, 129.9, 144.2, 165.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.38; MS (EI) m/z 300 (M^+). Anal. Calcd for $C_{14}H_{21}ClO_5P$: C, 56.00; H, 7.05. Found: C, 56.24; H, 7.15. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=14.30 min; (*R*) t_2=16.40 min.

4.2.12. (*S*)-Dimethyl α-(4-methylbenzoxy) propanyl phosphonate (5l). Colorless liquid; 94% ee; $[\alpha]_D^{14}$ +8.63 (*c* 1.16, $CHCl_3$); IR (KBr) 2957, 2854, 1725, 1613, 1457, 1256, 1178, 1026, 835, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 2H, J=8.0 Hz), 7.26 (d, 2H, J=8.0 Hz), 5.48 (m, 1H), 3.79 (d, 6H, J=10.8 Hz), 2.42 (s, 3H), 2.06–1.99 (m, 2H), 1.03 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 21.8, 23.1, 53.3, 53.6, 68.3, 67.0, 126.6, 129.4, 130.1, 144.4, 165.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.15; MS (EI) m/z 286 (M^+). Anal. Calcd for $C_{13}H_{19}O_5P$: C, 54.54; H, 6.69. Found: C, 54.32; H, 6.81. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=21.95 min; (*R*) t_2=23.66 min.

4.2.13. (*S*)-Dimethyl α-(4-chlorobenzoxy) ethyl phosphonate (5m). Pale yellow liquid; 95% ee; $[\alpha]_D^{14}$ −19.6 (*c* 1.20, $CHCl_3$); IR (KBr) 2956, 1734, 1594, 1455, 1401, 1265, 1177, 1025, 832, 802, 759, 685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, 2H, J=8.4 Hz), 7.44 (d, 2H, J=8.4 Hz), 5.54 (p, 1H, J=7.6 Hz), 3.82 (dd, 6H, J=10.6 and 2.4 Hz), 1.60 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 53.3, 55.5, 63.9, 65.6, 127.7, 128.5, 128.8, 129.8, 131.2, 133,4, 139.9, 164.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.48; MS (EI) m/z 292 (M^+−1), 293 (M^+), 294 (M^++1), 295 (M^++2). Anal. Calcd for $C_{11}H_{14}ClO_5P$: C, 45.14; H, 4.82. Found: C, 45.46; H, 4.93. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=26.32 min; (*R*) t_2=28.40 min.

4.2.14. (*S*)-Diethyl α-(4-chlorobenzoxy) ethyl phosphonate (5n). Yellow liquid; 96% ee; $[\alpha]_D^{14}$ −14.49 (*c* 1.72, $CHCl_3$); IR (KBr) 2985, 1730, 1594, 1488, 1400, 1265, 1174, 1026, 795, 685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 2H, J=8.4 Hz), 7.40 (d, 2H, J=8.4 Hz), 5.48 (p, 1H, J=7.6 Hz), 4.20–4.13 (m, 4H), 1.56 (dd, 3H, J=16.8 and 7.2 Hz), 1.29 (t, 6H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 16.5, 62.9, 63.0, 64.4, 66.1, 128.0, 128.9, 131.3, 139.9, 164.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.02; MS (EI) m/z 321 (M^+). Anal. Calcd for $C_{13}H_{18}ClO_5P$: C, 48.69; H, 5.66. Found: C, 48.57; H, 5.95. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=14.79 min; (*R*) t_2=17.13 min.

4.2.15. (*S*)-Dimethyl α-(4-chlorobenzoxy) propanyl phosphonate (5o). Colorless liquid; 91% ee; $[\alpha]_D^{14}$ +7.14 (*c* 2.46, $CHCl_3$); IR (KBr) 2957, 1730, 1594, 1488, 1458, 1401, 1259, 1175, 1030, 833, 758, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, 2H, J=8.4 Hz), 7.40 (d, 2H, J=8.4 Hz), 5.45–5.40 (m, 1H), 3.76 (d, 6H, J=10.6 Hz), 2.04–1.93 (m, 2H), 1.00 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.2, 10.4, 23.0, 53.3, 53.4, 68.7, 70.3, 127.7, 128.9, 131.3, 140.0, 164.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.79; MS (EI) m/z 307 (M^+), 308 (M^++1), 309 (M^++2). Anal. Calcd for $C_{12}H_{16}ClO_5P$: C, 47.00; H, 5.26. Found: C, 47.24; H, 4.99. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=21.15 min; (*R*) t_2=23.25 min.

4.2.16. (*S*)-Diethyl α-(4-chlorobenzoxy) propanyl phosphonate (5p). Colorless liquid; 92% ee; $[\alpha]_D^{14}$ +6.55 (*c* 2.28, $CHCl_3$); IR (KBr) 2981, 1730, 1594, 1488, 1400, 1256, 1094, 1024, 971, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, 2H, J=8.4 Hz), 7.45 (d, 2H, J=8.4 Hz), 5.42 (m, 1H), 4.18–4.13 (m, 4H), 2.00 (m, 2H), 1.31 (q, 6H, J=7.2 Hz), 1.03 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.4, 10.5, 16.6, 23.0, 62.9, 69.1, 70.8, 127.9, 129.0, 131.3, 134.0, 165.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.26; MS (EI) m/z 333 (M^+−2), 335 (M^+), 337 (M^++2). Anal. Calcd for $C_{14}H_{20}ClO_5P$: C, 50.23; H, 6.02. Found: C, 50.49; H, 5.86. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=12.42 min; (*R*) t_2=13.35 min.

4.2.17. (*S*)-Dimethyl α-(2-furancarbonyl oxo) ethyl phosphonate (5q). Pale yellow liquid; 96% ee; $[\alpha]_D^{14}$ −18.6 (*c* 0.68, $CHCl_3$); IR (KBr) 2959, 2856, 1733, 1579, 1474, 1395, 1323, 1294, 1246, 1179, 1117, 1049, 939, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 1H, J=1.6 Hz), 7.26 (d, 1H, J=3.6 Hz), 6.54 (dd, 1H, J=3.6 and 1.6 Hz), 5.56–5.48 (m, 1H), 3.87–3.79 (m, 6H), 1.60 (dd, 3H, J=16.8 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3,

53.5, 53.6, 53.7, 53.8, 63.9, 65.6, 112.2, 119.1, 143.9, 147.1, 157.4, 157.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.71; MS (EI) m/z 248 (M^+-1), 249 (M^++1). Anal. Calcd for $C_9H_{13}O_6P$: C, 43.56; H, 5.28. Found: C, 43.81; H, 5.19. Enantiomeric excess determination: HPLC, UV 254 nm, Chiralcel OJ-H, 0.8 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=20.35 min; (*R*) t_2=25.83 min.

4.2.18. (*S*)-Dimethyl α-(2-thiophenecarbonyl oxo) ethyl phosphonate (5r). Colorless liquid; 95% ee; $[\alpha]_D^{14}$ −29.6 (*c* 3.64, $CHCl_3$); IR (KBr) 2957, 1720, 1524, 1456, 1417, 1260, 1180, 1029, 830, 795, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, 1H, *J*=3.6 Hz), 7.60 (d, 1H, *J*=4.8 Hz), 7.12 (t, 1H, *J*=4.4 Hz), 5.50 (p, 1H, *J*=7.6 Hz), 3.86–3.80 (M, 6H), 1.58 (dd, 3H, *J*=16.4 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 53.4, 53.7, 64.2, 65.9, 128.0, 132.8, 133.3, 143.3, 140.0, 161.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.21; MS (EI) m/z 263 (M^+-1), 264 (M^+), 265 (M^++1). Anal. Calcd for $C_9H_{13}O_5PS$: C, 40.91; H, 4.96. Found: C, 41.13; H, 4.61. HPLC, UV 246 nm, Chiralcel OJ-H, 0.5 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=53.43 min; (*R*) t_2=63.24 min.

4.2.19. (*S*)-Diethyl α-(2-thiophenecarbonyl oxo) ethyl phosphonate (5s). Yellow liquid; 95% ee; $[\alpha]_D^{14}$ −28.7 (*c* 1.12, $CHCl_3$); IR (KBr) 2985, 1717, 1524, 1417, 1362, 1257, 1094, 1046, 1024, 970 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.85 (m, 1H), 7.61 (dd, 1H, *J*=6.8 and 1.2 Hz), 7.14-7.11 (m, 1H), 5.48 (p, 1H, *J*=7.6 Hz), 4.25–4.17 (m, 4H), 1.59 (dd, 3H, *J*=16.4 and 7.2 Hz), 1.34 (t, 6H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 16.57, 16.63, 16.7, 62.9, 63.0, 63.2, 64.6, 66.3, 128.1, 133.0, 134.2, 161.0, 161.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.25; MS (EI) m/z 291 (M^+-1), 292 (M^+). Anal. Calcd for $C_{11}H_{17}O_5PS$: C, 45.20; H, 5.86. Found: C, 45.60; H, 5.59. Enantiomeric excess determination: HPLC, UV 254 nm, Chiralcel OJ-H, 0.8 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=8.98 min; (*R*) t_2=10.70 min.

4.2.20. (*S*)-Dimethyl α-(2-thiophenecarbonyl oxo) propanyl phosphonate (5t). Yellow liquid; 94% ee; $[\alpha]_D^{14}$ +2.79 (*c* 1.60, $CHCl_3$); IR (KBr) 2957, 2854, 1718, 1523, 1416, 1362, 1254, 1096, 1051 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, 1H, *J*=3.6 and 1.2 Hz), 7.62 (dd, 1H, *J*=4.8 and 1.2 Hz), 7.14 (dd, 1H, *J*=4.8 and 3.6 Hz), 5.45–5.39 (m, 1H), 3.84–3.79 (m, 6H), 2.06–1.95 (m, 2H), 1.05 (t, 3H, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 10.4, 23.1, 53.36, 53.42, 53.65, 53.72, 68.8, 70.5, 128.1, 132.7, 133.4, 134.4, 161.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.18; MS (EI) m/z 278 (M^+), 279 (M^++1). Anal. Calcd for $C_{10}H_{15}O_5PS$: C, 43.16; H, 5.43. Found: C, 43.00; H, 5.21. Enantiomeric excess determination: HPLC, UV 246 nm, Chiralcel OJ-H, 1 mL/min, 10% 2-propanol/90% hexane, (*S*) t_1=17.23 min; (*R*) t_2=21.65 min.

4.2.21. (*S*)-Dimethyl α-(methoxyacetoxy) ethyl phosphonate (5u). Pale yellow liquid; 89% ee; $[\alpha]_D^{14}$ +22.1 (*c* 0.88, $CHCl_3$); IR (KBr) 2959, 1764, 1455, 1247, 1186, 1128, 1049, 946, 834 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43–5.31 (m, 1H), 4.10 (s, 2H), 3.84–3.73 (m, 6H), 3.47 (s, 3H), 1.52 (dd, 3H, *J*=16.4 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 53.47, 53.53, 59.5, 63.7, 65.4, 69.7, 169.26, 169.33; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.71; MS (EI) m/z 226 (M^+), 227 (M^++1), 228 (M^++2). Anal. Calcd for $C_7H_{15}O_6P$: C, 37.17; H, 6.69. Found: C, 36.88; H, 6.49. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel AS-H, 0.5 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=15.44 min; (*R*) t_2=16.38 min.

4.2.22. (*S*)-Dimethyl α-(phenylacetoxy) ethyl phosphonate (5v). Colorless liquid; 91% ee; $[\alpha]_D^{14}$ +7.71 (*c* 0.74, $CHCl_3$); IR (KBr) 2957, 2854, 1745, 1455, 1247, 1148, 1049, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 5H), 5.30 (p, 1H, *J*=7.6 Hz), 3.72–3.68 (m, 8H), 1.47 (dd, 3H, *J*=16.4 and 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 41.4, 53.4, 53.5, 63.9, 65.6, 127.5, 128.8, 129.5, 133.6, 170.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.1; MS (EI) m/z 272 (M^+). Anal. Calcd for $C_{12}H_{17}O_5P$: C, 52.94; H, 6.29. Found: C, 52.89; H, 6.14. Enantiomeric excess determination: HPLC, UV 205 nm, Chiralcel AD-H, 0.5 mL/min, 20% 2-propanol/80% hexane, (*S*) t_1=10.09 min; (*R*) t_2=10.88 min.

4.2.23. (*S*)-Dimethyl (1-hydroxyethyl) phosphonate 6a. A purified sample of **5a** (530 mg, 1.5 mmol) was combined with anhydrous K_2CO_3 (620 mg, 3 equiv) in MeOH. The reaction mixture was stirred for 2 h at room temperature. MeOH was removed by evaporation and the residue was passed through a silica gel column using ethyl acetate as an eluant to give pure product **6a** (50 mg, 22% yield) as colorless oil. Spectral data matched with those reported in the literature.[18]

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Supplementary data

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