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Enantioselective synthesis of optically active alkylphosphonates via Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates

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A B S T R A C T

The Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates using (S_c,S_p)-WalPhos as the chiral ligand is reported, in which a wide range of optically active β-substituted alkylphosphonates were obtained in good yields and with good to excellent enantioselectivities (86–98% ee). In contrast to the Rh/(R_c,S_a)-FAPhos system previously reported by us, the present catalytic system shows a wider substrate scope, and can perform the hydrogenation under milder reaction conditions.

1. Introduction

Optically active alkylphosphonic acid derivatives have recently received significant attention for their interesting biological properties as phosphorus analogues of carboxylic acids,[1] as well as their synthetic utilities as chiral building blocks.[2] Over the past decades, some stoichiometric and catalytic asymmetric syntheses have been developed for constructing chiral 1-arylethylphosphonates.[3] However, the enantioselective synthesis of chiral β-substituted alkylphosphonates by a catalytic method is still rarely explored.[4] In 1999, Hayashi et al. described the enantioselective synthesis of chiral β-aryl substituted alkylphosphonates via catalytic asymmetric 1,4-addition to 1-alkenylphosphonates using a chiral phosphine-Rh catalyst and arylboroxines as the arylating reagents.[5] Considering its inherent efficiency and atom economy, we surmised that the catalytic asymmetric hydrogenation should be a powerful tool for the synthesis of chiral phosphonate derivatives.[6] With this strategy, we have recently developed several new synthetic methods via the Rh-catalyzed asymmetric hydrogenation of the corresponding β-substituted α,β-unsaturated phosphonates[7] and β-substituted β,γ-unsaturated phosphonates.[8] Excellent enantioselectivities have been achieved in the Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates by employing a chiral ferrocenyl monophosphoramidite ligand, (R_c,S_a)-FAPhos (Fig. 1).[7] However, the hydrogenation conditions with the Rh/(R_c,S_a)-FAPhos system were harsh, normally requiring 40 atm of hydrogen pressure for complete conversion. Furthermore, the Rh/(R_c,S_a)-FAPhos catalytic system gave low conversions or low enantioselectivity in the hydrogenation of some substrates, such as (*E*)-diethyl 2-*o*-tolylprop-1-enylphosphonate, (*E*)-diethyl 2-phenylpent-1-enylphosphonate, and (*E*)-diethyl (2,3-dihydronaphthalen-4(1*H*)-ylidene)methylphosphonate even under an elevated hydrogenation temperature and pressure (Fig. 1).

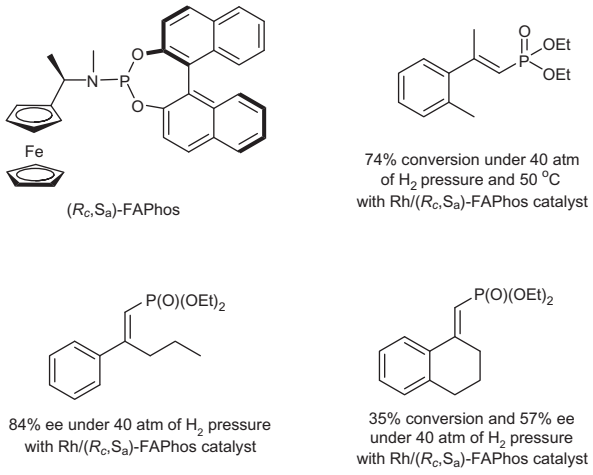

Figure 1. The structure of (R_c,S_a)-FAPhos and some challenging substrates with the Rh/FAPhos catalytic system.

The shortcomings of the Rh/(R_c,S_a)-FAPhos catalytic system prompted us to search for a more reactive and enantioselective catalyst for the Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates. As a result, we herein

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report that the commercially available bidentate phosphorus ligand, (S_c,S_p)-WalPhos, was identified as the optimal ligand for the Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates, providing various chiral β-substituted alkylphosphonates in good yields and with good to high enantioselectivities under mild hydrogenation condition.

2. Results and discussion

We have previously reported that some bidentate phosphorus ligands such as Me-Duphos, BINAP and Bophoz, give unsatisfactory results in the Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates.[7] In an attempt to search for a more effective ligand, we focused our studies on screening ferrocene-based bidentate ligands such as TaniaPhos[9] and WalPhos[10] (Fig. 2) because of their demonstrated track record at effecting Rh-catalyzed asymmetric hydrogenations. Initially, (*E*)-**1a** was selected as the model substrate, and the hydrogenation was performed under 10 atm of H_2 pressure in CH_2Cl_2 for 24 h. The results (Table 1) showed that the Rh/Taniaphos complex displayed high reactivity, but low enantioselectivity (entry 4). We found that (S_c,S_p)-WalPhos exhibited excellent results, in which full conversion and 93% ee were obtained (entry 5). Similar results were achieved when (R_c,S_p)-WalPhos was used (entry 6). These results showed that the central chirality in this ligand type was not so important in order to induce high enantioselectivity. The Rh/(S_c,S_p)-WalPhos proved to be highly efficient for this hydrogenation, in which full conversion and high enantioselectivity were obtained even at a catalyst loading as low as 0.1 mol % (entry 7). However, the corresponding (R_c,S_p)-WalPhos only provided 56% conversion even under a hydrogen pressure of 40 atm (entry 8). We therefore identified (S_c,S_p)-WalPhos as the optimal ligand for this hydrogenation. Solvent screening suggested that the nature of the solvent had some effect on the reactivity and enantioselectivity. However, no results surpassed those obtained in CH_2Cl_2. For example, although the reactions in MeOH, THF, and *i*-PrOH gave full conversion, ee-values were lower than those obtained in CH_2Cl_2 (entries 10–12). When the hydrogenation was performed in toluene, a decreased conversion of 89% was observed (entry 9).

With these encouraging results in the hydrogenation of (*E*)-**1a**, we proceeded to investigate the scope of this transformation on various β-substituted α,β-unsaturated phosphonates **1a–s**, using (S_c,S_p)-WalPhos as the ligand and CH_2Cl_2 as the solvent under a hydrogen pressure of 10 atm at room temperature for 24 h. As shown in Table 2, a wide range of β-aryl-α,β-unsaturated phosphonates (*E*)-**1a**–**1l** were hydrogenated to provide the corresponding 2-arylpropylphosphonates with good yields and high enantioselectivities (up to 94% ee). The results indicated that the present catalytic system has a high tolerance with regard to the electronic properties of the substituent on the phenyl ring in terms of reactivity and enantioselectivity. However, the substitution pattern of the substituent on the phenyl ring had some effect on the enantioselectivity; the *ortho*-substituted substrates tended to give lower enantioselectivities than their *meta*- and *para*-analogues. Thus,

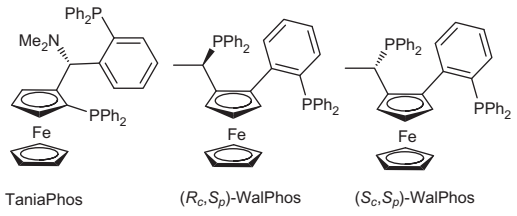
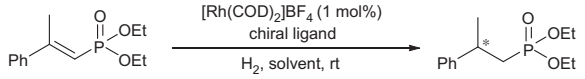


Figure 2. Ligands for the asymmetric hydrogenation.

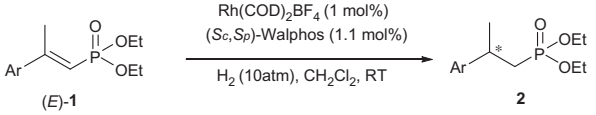
Table 1
Asymmetric hydrogenation of diethyl (*E*)-(2-phenyl-1-propenyl)phosphonate **1a**[a]



Entry	Ligand	Solvent	Conv.[b] (%)	ee[c] (%)
1	(*R*,*R*)-Me-DuPhos	CH_2Cl_2	—	—[d]
2	(*S*)-BINAP	CH_2Cl_2	84	30 (*S*)
3	(S_c,R_p)-Me-BoPhoz	CH_2Cl_2	100	75 (*R*)
4	(S_c,S_p)-TaniaPhos	CH_2Cl_2	100	54 (*R*)
5	(S_c,S_p)-WalPhos	CH_2Cl_2	100	93 (*R*)
6	(R_c,S_p)-WalPhos	CH_2Cl_2	100	94 (*R*)
7[e]	(S_c,S_p)-WalPhos	CH_2Cl_2	100	93 (*R*)
8[f]	(R_c,S_p)-WalPhos	CH_2Cl_2	56	92 (*R*)
9	(S_c,S_p)-WalPhos	Toluene	89	82 (*R*)
10	(S_c,S_p)-WalPhos	*i*-PrOH	100	86 (*R*)
11	(S_c,S_p)-WalPhos	MeOH	100	88 (*R*)
12	(S_c,S_p)-WalPhos	THF	100	87 (*R*)

[a] The reactions were carried out with 0.25 mmol of substrate at room temperature under an H_2 pressure of 10 atm in 2 mL of the indicated solvent for 24 h.
[b] Degrees of conversion were determined by GC.
[c] The ee values were determined by HPLC on a chiral column.
[d] Not determined because of low conversion.
[e] The reaction was performed at 20 atm hydrogen pressure and 0.1% catalyst loading.
[f] The reaction was performed at 40 atm hydrogen pressure and 0.1% catalyst loading.

Table 2
Asymmetric hydrogenation of diethyl (*E*)-(2-aryl-1-propenyl)phosphonates **1a–n**[a]



Entry	Substrate	Ar	Yield[b] (%)	ee[c] (%)
1	**1a**	Ph	98	93 (*R*)
2	**1b**	2-$MeOC_6H_4$	93	87 (+)
3	**1c**	3-$MeOC_6H_4$	96	94 (+)
4	**1d**	4-$MeOC_6H_4$	98	94 (+)
5	**1e**	2-MeC_6H_4	95	86 (+)
6	**1f**	3-MeC_6H_4	98	94 (+)
7	**1g**	4-MeC_6H_4	96	94 (+)
8	**1h**	3-$CF_3C_6H_4$	98	92 (+)
9	**1i**	4-$CF_3C_6H_4$	98	93 (+)
10	**1j**	4-FC_6H_4	97	94 (+)
11	**1k**	4-ClC_6H_4	98	94 (+)
12	**1l**	4-BrC_6H_4	94	95 (+)
13	**1m**	2-Naphthyl	98	91 (+)
14	**1n**	2-Thiophenyl	98	98 (+)

[a] All reactions were carried out with 0.25 mmol of substrate at room temperature under a H_2 pressure of 10 atm in 2 mL of CH_2Cl_2 for 24 h. Substrate/$Rh(COD)_2BF_4$/ligand = 1/0.01/0.011.
[b] Isolated yields.
[c] The ee values were determined by HPLC on a chiral column (Chiralpak AD-H or OJ-H). The absolute configuration was determined by comparing the specific rotation with the reported data.

the hydrogenation of 3- and 4-methoxy substituted substrates gave ee-values of 94% ee (entries 3 and 4), while the hydrogenation of the corresponding 2-methoxy substituted one only provided 87% ee (entry 2). The reason for this is presumably due to the steric hindrance of the *ortho*-substituent. Although relatively low enantioselectivities were obtained for *ortho*-substituted substrates, it should be noted that these results represented progress in contrast to that reported recently with an Rh/(R_c,S_a)-FAPhos catalyst. With the Rh/(R_c,S_a)-FAPhos catalyst, incomplete conversion was achieved even at higher hydrogenation temperatures (50 °C) and higher hydrogenation pressure (40 atm).[7] Diethyl (*E*)-[2-(2-naph-

thyl)-1-propenyl]phosphonate **1m** was a suitable substrate, giving the hydrogenation product **2m** in 98% yield and 91% ee (entry 13). (*S*)-Heteroaromatic substrate **1n** was also a good substrate for this hydrogenation, affording the hydrogenation product in with 98% yields and 98% ee (entry 14). These results demonstrated the efficiency of the present catalytic system in the hydrogenation of β-aryl substituted α,β-unsaturated phosphonates.

To further illustrate the synthetic interest in this highly enantioselective procedure, a series of structurally diverse α,β-unsaturated phosphonates (Fig. 3), including those that were less efficient substrates with the Rh/(R_c,S_a)-FAPhos catalyst, were submitted to this hydrogenation under the optimized hydrogenation conditions, and the results are summarized in Table 3.

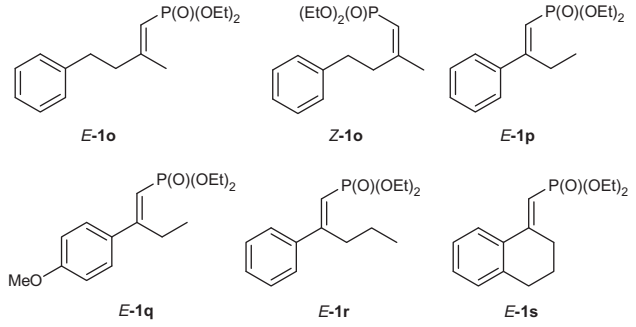
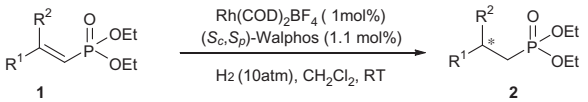


Figure 3. Substrates for the asymmetric hydrogenation.

The results indicated that the Rh/(S_c,S_p)-WalPhos complex was also highly efficient for the hydrogenation of β-alkyl substituted α,β-unsaturated phosphonates such as (*E*)-**1o**, providing the hydrogenation product in good yields and with excellent enantioselectivity of 96% ee (entry 1). For the hydrogenation of the corresponding (*Z*)-substrate [(*Z*)-**1o**], similar results were achieved with the absolute configuration of the hydrogenation product opposite to that obtained in the hydrogenation of its (*E*)-isomer (entry 2). The hydrogenation of (*E*)-**1p**, (*E*)-**1q,** and (*E*)-**1r** proved to be as efficient as in the hydrogenation of their 1-ethenylphosphonate analogues, giving the hydrogenation products in good yields with ee-values of 93%, 94% and 93%, respectively (entries 3–5). The hydrogenation of (*E*)-diethyl (2,3-dihydronaphthalen-4(1*H*)-ylidene)methylphos-phonate also gave the good yield and 93% ee (entry 6). Only 57% ee and 35% conversion were achieved for the hydrogenation of **1s**, while 84% ee and full conversion for the hydrogenation of **1r** when (R_c,S_a)-FAPhos was used, even under a hydrogen pressure of 40 atm.

Table 3
Asymmetric hydrogenation of α,β-unsaturated phosphonates **1o–s**[a]



Entry	Substrate	Yield[b] (%)	ee[c] (%)
1	(*E*)-**1o**	98	96 (+)
2	(*Z*)-**1o**	98	97 (−)
3	(*E*)-**1p**	99	93 (+)
4	(*E*)-**1q**	98	94 (+)
5	(*E*)-**1r**	99	93 (+)
6	(*E*)-**1s**	99	93 (−)

[a] All reactions were carried out with 0.25 mmol of substrate at room temperature under an H_2 pressure of 10 atm in 2 mL of CH_2Cl_2 for 24 h. Substrate/$Rh(COD)_2BF_4$/ligand = 1/0.01/0.011.
[b] Isolated yields.
[c] The ee values were determined by HPLC on a chiral column (Chiralpak AD-H or OJ-H).

3. Conclusion

In conclusion, we have identified that (S_c,S_p)-WalPhos is a suitable ligand for the Rh-catalyzed asymmetric hydrogenation of β-substituted α,β-unsaturated phosphonates, in which good yields and up to 98% ee were obtained for a wide range of substrates under mild hydrogenation conditions. This catalytic system is potentially practical for the synthesis of optically active β-substituted alkylphosphonates. The development of new catalytic methods to synthesize chiral alkylphosphonates is still in progress.

4. Experimental

4.1. General methods

All reactions and manipulations were performed in a nitrogen-filled glove-box or under nitrogen using Schlenk techniques unless otherwise noted. All solvents were distilled under argon in the presence of the following desiccants: sodium-benzophenone-ketyl for diethyl ether (Et_2O), tetrahydrofuran (THF), CaH_2 for dichloromethane (CH_2Cl_2). NMR spectra were obtained on Bruker DRX 400 spectrometers. ^{31}P NMR shifts were referenced to external 85% H_3PO_4, while ^{13}C and ^{1}H NMR shifts were referenced to the residual signals of deuterated solvents.

4.2. General procedure for the preparation of β-substituted α,β-unsaturated phosphonates

A solution of $(EtO)_2P(O)CH_2P(O)(OEt)_2$ (1.44 g, 5 mmol) in THF (2 mL) was slowly added at 0 °C to a slurry of NaH (0.19 g, 5.5 mmol, 70% in oil) in THF (10 mL). After the addition, the mixture was stirred at room temperature for 0.5 h. To the mixture, a solution of ketone (4.25 mmol) in THF (3 mL) was added. The reaction mixture was stirred at room temperature until the ketone disappeared when monitored by TLC. The mixture was then diluted with ether and washed with an aqueous solution of saturated NH_4Cl (25 mL × 1) and brine (25 mL × 1). The organic layer was separated, and dried over anhydrous $NaSO_4$. After removal of the volatiles, the residue was purified by column chromatography (silica gel, AcOEt/hexane 1:1).

4.2.1. (*E*)-Diethyl 2-phenylprop-1-enylphosphonate 1a[7]

Colorless oil, yield: 60%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.0 Hz, 6H), 2.51 (d, J = 2.9 Hz, 3H), 4.09–4.17 (m, 4H), 5.90 (d, J = 16.6 Hz, 1H), 7.35–7.38 (m, 3H), 7.46–7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 19.2 (d, J = 7.0 Hz), 61.4, 61.5, 113.4 (d, J = 189.0 Hz), 126.0, 128.5, 129.2, 141.8 (d, J = 23.0 Hz), 158.2 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.6.

4.2.2. (*E*)-Diethyl 2-(2-methoxyphenyl)prop-1-enylphosphonate 1b[4]

Colorless oil, yield: 52%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.1 Hz, 6H), 2.44 (d, J = 3.1 Hz, 3H), 3.80 (d, J = 6.2 Hz, 3H), 4.10–4.17 (m, 4H), 5.66 (d, J = 18.7 Hz, 1H), 6.88–6.94 (m, 2H), 7.14–7.16 (m, 1H), 7.26–7.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 20.9 (d, J = 7.0 Hz), 55.4, 61.3, 61.4, 111.0, 115.9 (d, J = 183.0 Hz), 120.5, 128.6, 129.5, 133.1 (d, J = 24.0 Hz), 156.0, 159.4 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.0.

4.2.3. (*E*)-Diethyl 2-(3-methoxyphenyl)prop-1-enylphosphonate 1c[4]

Colorless oil, yield: 58%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.1 Hz, 6H), 2.49 (d, J = 3.2 Hz, 3H), 3.82 (s, 3H), 4.10–4.17 (m, 4H), 5.90 (d, J = 16.6 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 6.99 (s, 1H), 7.07 (d, J = 7.7 Hz, 1H), 7.26–7.30 (m, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 16.4, 16.5, 19.4 (d, J = 6.0 Hz), 55.3, 61.5, 61.5, 111.9, 113.7 (d, J = 189.0 Hz), 114.4, 118.5, 129.5, 143.3 (d, J = 24.0 Hz), 158.1 (d, J = 6.0 Hz), 159.6; ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.5.

4.2.4. (*E*)-Diethyl 2-(4-methoxyphenyl)prop-1-enylphosphonate 1d[7]

Colorless oil, yield: 63%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 7.0 Hz, 6H), 2.48 (d, J = 3.1 Hz, 3H), 3.82 (s, 3H), 4.09–4.16 (m, 4H), 5.85 (d, J = 16.5 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.4, 19.1 (d, J = 7.0 Hz), 55.3, 61.4, 61.5, 111.1 (d, J = 191.0 Hz), 113.8, 127.4, 133.8 (d, J = 24.0 Hz), 157.4 (d, J = 8.0 Hz), 160.5; ^{31}P NMR (162 MHz, $CDCl_3$): δ 19.3.

4.2.5. (*E*)-Diethyl 2-*o*-tolylprop-1-enylphosphonate 1e[4]

Colorless oil, yield: 45%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.0 Hz, 6H), 2.29 (s, 3H), 2.38 (d, J = 3.2 Hz, 3H), 4.10–4.18 (m, 4H), 5.51 (d, J = 18.7 Hz, 1H), 7.06–7.08 (m, 1H), 7.14–7.19 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.5, 19.6, 21.9 (d, J = 6.0 Hz), 61.4, 61.5, 116.3 (d, J = 183.0 Hz), 125.8, 126.7, 127.7, 130.4, 133.3, 144.1 (d, J = 23.0 Hz), 161.2 (d, J = 6.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 17.4.

4.2.6. (*E*)-Diethyl 2-*m*-tolylprop-1-enylphosphonate 1f[7]

Colorless oil, yield: 48%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 7.0 Hz, 6H), 2.36 (s, 3H), 2.50 (d, J = 3.2 Hz, 3H), 4.09–4.17 (m, 4H), 5.89 (d, J = 16.7 Hz, 1H), 7.15–7.17 (m, 1H), 7.22–7.27 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 19.3 (d, J = 7.0 Hz), 21.4, 61.4, 61.4, 113.2 (d, J = 189.0 Hz), 123.1, 126.6, 128.4, 129.9, 138.0, 141.8 (d, J = 24.0 Hz), 158.3 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.6.

4.2.7. (*E*)-Diethyl 2-*p*-tolylprop-1-enylphosphonate 1g[7]

Colorless oil, yield: 61%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 7.0 Hz, 6H), 2.35 (s, 3H), 2.48 (d, J = 2.7 Hz, 3H), 4.09–4.16 (m, 4H), 5.89 (d, J = 16.6 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 19.1 (d, J = 7.0 Hz), 21.1, 61.4, 61.5, 112.3 (d, J = 189.0 Hz), 125.9, 129.2, 138.7 (d, J = 23.0 Hz), 139.3, 158.0 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.9.

4.2.8. (*E*)-Diethyl 2-[3-(trifluoromethyl)phenyl]prop-1-enylphosphonate 1h[7]

Colorless oil, yield: 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, J = 7.1 Hz, 6H), 2.53 (d, J = 3.1 Hz, 3H), 4.11–4.18 (m, 4H), 5.94 (d, J = 15.6 Hz, 1H), 7.48–7.52 (m, 1H), 7.61–7.66 (m, 2H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 19.2, 61.6, 115.6 (d, J = 190.0 Hz), 122.5, 122.8, 125.3, 125.6, 129.1, 129.3, 142.7 (d, J = 24.0 Hz), 156.3; ^{31}P NMR (162 MHz, $CDCl_3$): δ 17.3.

4.2.9. (*E*)-Diethyl 2-(4-(trifluoromethyl)phenyl)prop-1-enylphosphonate 1i[7]

Colorless oil, yield: 75%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, J = 7.1 Hz, 6H), 2.52 (d, J = 3.1 Hz, 3H), 4.11–4.18 (m, 4H), 5.94 (d, J = 15.7 Hz, 1H), 7.56 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 19.2, 61.6, 116.0 (d, J = 189.0 Hz), 125.3, 125.4, 126.4, 145.4 (d, J = 24.0 Hz), 156.5 (d, J = 7.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 17.3.

4.2.10. (*E*)-Diethyl 2-(4-fluorophenyl)prop-1-enylphosphonate 1j[7]

Colorless oil, yield: 68%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.1 Hz, 6H), 2.49 (d, J = 3.0 Hz, 3H), 4.10–4.17 (m, 4H), 5.87 (d, J = 16.1 Hz, 1H), 7.02–7.07 (m, 2H), 7.44–7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.4, 19.3 (d, J = 7.0 Hz), 61.5, 61.5, 113.5 (d, J = 190.0 Hz), 115.4 (d, J = 22.0 Hz), 127.8 (d, J = 8.0 Hz), 137.7 (d, J = 24.0 Hz), 156.8 (d, J = 8.0 Hz), 162.0, 164.5; ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.3.

4.2.11. (*E*)-Diethyl 2-(4-chlorophenyl)prop-1-enylphosphonate 1k[7]

Colorless oil, yield: 65%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.0 Hz, 6H), 2.48 (d, J = 2.4 Hz, 3H), 4.10–4.17 (m, 4H), 5.89 (d, J = 16.0 Hz, 1H), 7.31–7.34 (m, 2H), 7.40–7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.4, 19.2 (d, J = 7.0 Hz), 61.5, 61.6, 114.1 (d, J = 189.0 Hz), 127.3, 128.7, 135.1, 140.1 (d, J = 24.0 Hz), 156.6 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.1.

4.2.12. (*E*)-Diethyl 2-(4-bromophenyl)prop-1-enylphosphonate 1l[7]

Colorless oil, yield: 66%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H), 2.48 (d, J = 3.0 Hz, 3H), 4.10–4.17 (m, 4H), 5.89 (d, J = 16.0 Hz, 1H), 7.32–7.34 (m, 2H), 7.47–7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.4, 19.1 (d, J = 7.0 Hz), 61.6, 61.6, 114.2 (d, J = 190.0 Hz), 123.4, 127.6, 131.6, 140.6 (d, J = 24.0 Hz), 156.7 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.0.

4.2.13. (*E*)-Diethyl 2-(naphthalen-2-yl)prop-1-enylphosphonate 1m[7]

Colorless oil, yield: 49%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, J = 7.1 Hz, 6H), 2.62 (d, J = 3.1 Hz, 3H), 4.12–4.19 (m, 4H), 6.06 (d, J = 16.3 Hz, 1H), 7.46–7.48 (m, 2H), 7.56–7.59 (m, 1H), 7.78–7.84 (m, 3H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.5, 19.3 (d, J = 7.0 Hz), 61.5, 61.6, 113.9 (d, J = 189.0 Hz), 123.6, 125.6, 126.6, 126.8, 127.6, 128.2, 128.5, 133.0, 133.5, 138.8 (d, J = 24.0 Hz), 157.8 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.6.

4.2.14. (*E*)-Diethyl 2-(thiophen-2-yl)prop-1-enylphosphonate 1n[7]

Straw yellow oil, yield: 41%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, J = 7.1 Hz, 6H), 2.51 (d, J = 3.0 Hz, 3H), 4.08–4.15 (m, 4H), 5.95 (d, J = 14.3 Hz, 1H), 7.01–7.03 (m, 1H), 7.24–7.26 (m, 1H), 7.30–7.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 18.8 (d, J = 6.0 Hz), 61.4, 61.5, 110.5 (d, J = 193.0 Hz), 126.4, 127.2, 127.9, 145.4 (d, J = 27.0 Hz), 150.1 (d, J = 9.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.3.

4.2.15. (*E*)-Diethyl 2-methyl-4-phenylbut-1-enylphosphonate (*E*)-1o[11]

Colorless oil, yield: 53%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, J = 7.0 Hz, 6H), 2.12 (s, 3H), 2.45–2.49 (m, 2H), 2.77–2.81 (m, 2H), 3.95–4.02 (m, 4H), 5.37 (d, J = 18.3 Hz, 1H), 7.15–7.20 (m, 3H), 7.25–7.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 20.1 (d, J = 6.0 Hz), 33.6, 43.1 (d, J = 23.0 Hz), 61.2, 61.2, 112.2 (d, J = 187.0 Hz), 126.1, 128.3, 128.5, 140.8, 161.9 (d, J = 5.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.5.

4.2.16. (*Z*)-Diethyl 2-methyl-4-phenylbut-1-enylphosphonate (*Z*)-1o[11]

Colorless oil, yield: 14%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, J = 7.0 Hz, 6H), 1.94 (s, 3H), 2.77–2.85 (m, 4H), 3.99–4.06 (m, 4H), 5.41 (d, J = 18.3 Hz, 1H), 7.16–7.19 (m, 1H), 7.26–7.27 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.5, 26.0 (d, J = 24.0 Hz), 34.7, 36.9 (d, J = 6.0 Hz), 61.2, 61.2, 113.1 (d, J = 188.0 Hz), 126.0, 128.4, 128.5, 141.4, 162.5 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 17.8.

4.2.17. (*E*)-Diethyl 2-phenylbut-1-enylphosphonate (*E*)-1p[7]

Colorless oil, yield: 30%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03 (t, J = 7.2 Hz, 3H), 1.36 (t, J = 7.2 Hz, 6H), 2.98–3.04 (m, 2H), 4.09–

4.16 (m, 4H), 5.75 (d, J = 17.6 Hz, 1H), 7.35–7.38 (m, 3H), 7.40–7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5, 16.4, 16.5, 25.9 (d, J = 7.0 Hz), 61.5, 61.6, 113.3 (d, J = 189.0 Hz), 126.5, 128.5, 129.0, 140.7 (d, J = 24.0 Hz), 166.0 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.3.

4.2.18. (*E*)-Diethyl 2-(4-methoxyphenyl)but-1-enylphosphonate (*E*)-1q

Colorless oil, yield: 56%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (t, J = 7.2 Hz, 3H), 1.35 (t, J = 7.2 Hz, 6H), 2.95–3.00 (m, 2H), 3.83 (s, 1H), 4.09–4.16 (m, 4H), 5.71 (d, J = 16.8 Hz, 1H), 6.88–6.90 (m, 2H), 7.38–7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 16.4, 16.5, 25.6 (d, J = 7.0 Hz), 55.3, 61.5, 61.6, 111.1 (d, J = 190.0 Hz), 113.9, 127.9, 132.6 (d, J = 23.0 Hz), 160.4, 164.1 (d, J = 9.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 19.0.

4.2.19. (*E*)-Diethyl 2-phenylpent-1-enylphosphonate (*E*)-1r[12]

Colorless oil, yield: 30%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, J = 7.4 Hz, 3H), 1.36 (t, J = 7.0 Hz, 6H), 1.39–1.45 (m, 2H), 2.95–2.99 (m, 2H), 4.09–4.17 (m, 4H), 5.76 (d, J = 17.1 Hz, 1H), 7.34–7.36 (m, 3H), 7.39–7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 16.4, 16.5, 22.0, 34.4 (d, J = 7.0 Hz), 61.4, 61.5, 114.1 (d, J = 189.0 Hz), 126.5, 128.5, 128.9, 141.2 (d, J = 24.0 Hz), 163.6 (d, J = 9.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.3.

4.2.20. (*E*)-Diethyl (2,3-dihydronaphthalen-4(1*H*)-ylid-ene) methylphosphonate (*E*)-1s

Colorless oil, yield: 22%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, J = 7.4 Hz, 6H), 1.93–1.99 (m, 2H), 2.58–2.61 (m, 2H), 2.83–2.86 (m, 2H), 3.92–3.99 (m, 4H), 5.56 (d, J = 14.4 Hz, 1H), 7.10–7.12 (m, 1H), 7.18–7.22 (m, 1H), 7.26–7.29 (m, 1H), 8.04–8.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0, 16.1, 23.6, 29.3, 36.8 (d, J = 22.0 Hz), 61.4, 61.5, 110.2 (d, J = 188.0 Hz), 125.3, 128.1, 129.6 (d, J = 15.0 Hz), 133.5 (d, J = 6.0 Hz), 138.9, 158.6; ^{31}P NMR (162 MHz, $CDCl_3$): δ 17.9.

4.3. General procedure for the asymmetric hydrogenation of α,β-unsaturated phosphonates

In a nitrogen-filled glovebox, $[Rh(COD)_2]BF_4$ (1.0 mg, 0.0025 mmol) and (S_c,S_p)-WalPhos (1.8 mg, 0.0028 mmol) were dissolved in degassed CH_2Cl_2 (1 mL) in a 5 mL vial. After stirring at room temperature for 15 min, a solution of α,β-unsaturated phosphonate **1** (0.25 mmol, S/C 100:1) in 1 mL of degassed CH_2Cl_2 was added. The resulting mixture was transferred to an autoclave, which was then charged with H_2 (10 atm). The hydrogenation was performed at room temperature for 24 h. After carefully releasing the hydrogen gas, the reaction was purified through a plug of silica gel (eluting with a mixture of hexanes/EtOAc) to afford **2**. The enantiomeric excess was determined by HPLC on a chiral column.

4.3.1. Diethyl 2-phenylpropylphosphonate 2a[5]

93.0% ee. $[\alpha]_D^{25} = +17.85$ (c 0.82, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 11.1 min; minor enantiomer: t_R = 12.2 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.39 (d, J = 7.0 Hz, 3H), 1.98–2.13 (m, 2H), 3.19–3.24 (m, 1H), 3.88–4.02 (m, 4H), 7.17–7.24 (m, 3H), 7.26–7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.3, 23.5 (d, J = 10.0 Hz), 34.6 (d, J = 13.0 Hz), 34.8 (d, J = 23.0 Hz), 61.2 (d, J = 6.0 Hz), 61.4 (d, J = 6.0 Hz), 126.4, 126.6, 128.5, 146.6 (d, J = 12.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.5.

4.3.2. Diethyl 2-(2-methoxyphenyl)propylphosphonate 2b

87% ee. $[\alpha]_D^{25} = +5.7$ (c 0.88, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 25.4 min; minor enantiomer: t_R = 29.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (t, J = 7.0 Hz, 6H), 1.38 (d, J = 7.0 Hz, 3H), 1.96–2.06 (m, 1H), 2.18–2.28 (m, 1H), 3.55 (q, J = 6.5 Hz, 1H), 3.82 (s, 3H), 3.96–4.05 (m, 4H), 6.84–6.86 (m, 1H), 6.89–6.93 (m, 1H), 7.16–7.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 21.2 (d, J = 7.0 Hz), 28.8, 32.4 (d, J = 137.0 Hz), 55.2, 61.2 (d, J = 7.0 Hz), 61.3 (d, J = 6.0 Hz), 110.6, 120.6, 127.3 (d, J = 9.0 Hz), 134.5 (d, J = 13.0 Hz), 156.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 31.6. HRMS calcd for $C_{14}H_{23}O_4P$: 286.1334, found 286.1335.

4.3.3. Diethyl 2-(3-methoxyphenyl)propylphosphonate 2c[5]

94% ee. $[\alpha]_D^{25} = +19.3$ (c 0.92, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 18.4 min; minor enantiomer: t_R = 20.4 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, J = 7.1 Hz, 3H), 1.26 (d, J = 7.1 Hz, 3H), 1.38 (d, J = 6.9 Hz, 3H), 2.00–2.12 (m, 2H), 3.18 (m, 1H), 3.79 (s, 3H), 3.92–4.05 (m, 4H), 6.73–6.77 (m, 2H), 6.82 (d, J = 7.7 Hz, 1H), 7.20–7.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 23.3 (d, J = 9.0 Hz), 33.5, 34.8 (d, J = 2.0 Hz), 55.2, 61.3 (d, J = 6.0 Hz), 61.5 (d, J = 6.0 Hz), 111.5, 112.6, 119.0, 129.5, 148.4 (d, J = 13.0 Hz), 159.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.5.

4.3.4. Diethyl 2-(4-methoxyphenyl)propylphosphonate 2d

94% ee. $[\alpha]_D^{25} = +21.7$ (c 0.84, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 18.1 min; minor enantiomer: t_R = 19.9 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.36 (d, J = 6.9 Hz, 3H), 1.99–2.09 (m, 2H), 3.15–3.20 (m, 1H), 3.78 (s, 3H), 3.90–4.04 (m, 4H), 6.84 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 23.7 (d, J = 10.0 Hz), 33.8, 35.1, 55.2, 61.2 (d, J = 7.0 Hz), 61.4 (d, J = 6.0 Hz), 113.8, 127.6, 138.8 (d, J = 12.0 Hz), 158.1; ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.7. HRMS calcd for $C_{14}H_{23}O_4P$: 286.1334, found 286.1338.

4.3.5. Diethyl 2-(2-methylphenyl)propylphosphonate 2e

86% ee. $[\alpha]_D^{25} = +11.9$ (c 0.76, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane /i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 9.2 min; minor enantiomer: t_R = 10.5 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.35 (d, J = 6.9 Hz, 3H), 2.00–2.06 (m, 2H), 2.38 (s, 3H), 3.17–3.20 (m, 1H), 3.90–4.01 (m, 4H), 7.08–7.11 (m, 2H), 7.17–7.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 19.4, 22.9 (d, J = 9.0 Hz), 29.5 (d, J = 29.0 Hz), 33.7 (d, J = 137.0 Hz), 61.2 (d, J = 7.0 Hz), 61.3 (d, J = 7.0 Hz), 125.1, 126.1, 126.3, 130.4, 135.0, 144.8 (d, J = 11.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.8. HRMS calcd for $C_{14}H_{23}O_3P$: 270.1385, found 270.1380.

4.3.6. Diethyl 2-(3-methylphenyl)propylphosphonate 2f

94% ee. $[\alpha]_D^{25} = +18.5$ (c 0.92, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 10.1 min; minor enantiomer: t_R = 11.0 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.39 (d, J = 6.9 Hz, 3H), 2.00–2.11 (m, 2H), 2.33 (s, 3H), 3.17–3.20 (m, 1H), 3.90–4.05 (m, 4H), 7.00–7.03 (m, 3H), 7.17–7.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 21.4, 23.5 (d, J = 6.0 Hz), 34.3 (d, J = 137.0 Hz), 34.6, 61.2 (d, J = 6.0 Hz), 61.4 (d, J = 6.0 Hz), 123.6, 127.1, 127.4, 128.4, 138.0, 146.7 (d, J = 12.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.7. HRMS calcd for $C_{14}H_{23}O_3P$: 270.1385, found 270.1384.

4.3.7. Diethyl 2-(4-methylphenyl)propylphosphonate 2g[5]

94% ee. $[\alpha]_D^{25} = +22.15$ (c 0.74, $CHCl_3$). HPLC conditions: chiralpak AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 11.9 min; minor enantiomer: t_R = 13.3 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.1 Hz, 3H),

1.25 (t, J = 7.1 Hz, 3H), 1.37 (d, J = 7.0 Hz, 3H), 2.00–2.10 (m, 2H), 2.31 (s, 3H), 3.19 (m, 1H), 3.91–4.04 (m, 4H), 7.11–7.13 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 20.9, 23.5 (d, J = 9.0 Hz), 34.2 (d, J = 3.0 Hz), 35.4 (d, J = 137.0 Hz), 61.2 (d, J = 6.0 Hz), 61.4 (d, J = 6.0 Hz), 126.5, 129.1, 135.8, 143.7 (d, J = 12.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.7.

4.3.8. Diethyl 2-(3-(trifluoromethyl)phenyl)propylphos-phonate 2h

92% ee. $[\alpha]_D^{25} = +18.7$ (c 0.92, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 12.9 min; minor enantiomer: t_R = 14.1 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 1.41 (d, J = 7.0 Hz, 3H), 2.04–2.13 (m, 2H), 3.27–3.32 (m, 1H), 3.90–4.02 (m, 4H), 7.42–7.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2 (d, J = 4.0 Hz), 16.2 (d, J = 5.0 Hz), 23.5 (d, J = 10.0 Hz), 34.1 (d, J = 139.0 Hz), 34.7, 61.4 (d, J = 5.0 Hz), 61.4 (d, J = 6.0 Hz), 123.3 (d, J = 3.0 Hz), 123.5 (d, J = 3.0 Hz), 129.0, 130.3, 147.4 (d, J = 11.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.6. HRMS calcd for $C_{14}H_{20}F_3O_3P$: 324.1102, found 324.1110.

4.3.9. Diethyl 2-(4-(trifluoromethyl)phenyl)propylphos-phonate 2i[5]

93% ee. $[\alpha]_D^{25} = +18.2$ (c 0.92, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 17.3 min; minor enantiomer: t_R = 20.0 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.40 (d, J = 7.0 Hz, 3H), 2.04–2.12 (m, 2H), 3.27–3.31 (m, 1H), 3.90–4.04 (m, 4H), 7.36 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2 (d, J = 6.0 Hz), 16.3 (d, J = 5.0 Hz), 23.4 (d, J = 10.0 Hz), 34.0 (d, J = 139.0 Hz), 34.7, 61.4 (d, J = 7.0 Hz), 61.4 (d, J = 6.0 Hz), 122.8, 125.4 (d, J = 3.0 Hz), 127.2, 128.7 (q, J = 32.0 Hz), 150.5 (d, J = 10.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.7.

4.3.10. Diethyl 2-(4-fluorophenyl)propylphosphonate 2j

94% ee. $[\alpha]_D^{25} = +17.3$ (c 0.78, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 19.7 min; minor enantiomer: t_R = 21.1 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.36 (d, J = 7.0 Hz, 3H), 2.00–2.09 (m, 2H), 3.21–3.24 (m, 1H), 3.90–4.03 (m, 4H), 6.96–7.01 (m, 2H), 7.18–7.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.3, 23.7, 33.8, 35.1, 61.2, 61.4, 115.2, 128.2, 132.0, 142.3, 160.2, 162.6; ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.2. HRMS calcd for $C_{13}H_{20}FO_3P$: 274.1134, found 274.1133.

4.3.11. Diethyl 2-(4-chlorophenyl)propylphosphonate 2k

94% ee. $[\alpha]_D^{25} = +23.4$ (c 0.92, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 12.5 min; minor enantiomer: t_R = 13.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.36 (d, J = 6.9 Hz, 3H), 1.99–2.08 (m, 2H), 3.18–3.22 (m, 1H), 3.90–4.05 (m, 4H), 7.16–7.18 (m, 2H), 7.28–7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.4, 23.5 (d, J = 10.0 Hz), 34.2 (d, J = 138.0 Hz), 34.2, 61.3 (d, J = 6.0 Hz), 61.4 (d, J = 7.0 Hz), 128.1, 128.5, 132.0, 145.0 (d, J = 11.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.0. HRMS calcd for $C_{13}H_{20}ClO_3P$: 290.0839, found 290.0826.

4.3.12. Diethyl 2-(4-bromophenyl)propylphosphonate 2l

95% ee. $[\alpha]_D^{25} = +22.7$ (c 1.06, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 14.0 min; minor enantiomer: t_R = 15.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.36 (d, J = 6.9 Hz, 3H), 1.99–2.07 (m, 2H), 3.16–3.21 (m, 1H), 3.91–4.05 (m, 4H), 7.10–7.13 (m, 2H), 7.41–7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 23.5 (d, J = 10.0 Hz), 34.2 (d, J = 138.0 Hz), 34.3, 61.4 (d, J = 6.0 Hz), 61.5 (d, J = 7.0 Hz), 120.0, 128.5, 131.5, 145.6 (d, J = 11.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.0. HRMS calcd for $C_{13}H_{20}BrO_3P$: 334.0333, found 334.0344.

4.3.13. Diethyl 2-(naphthalen-2-yl)propylphosphonate 2m[5]

91% ee. $[\alpha]_D^{25} = +24.2$ (c 1.04, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 17.6 min; minor enantiomer: t_R = 23.0 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.47 (d, J = 6.9 Hz, 3H), 2.10–2.22 (m, 2H), 3.40 (m, 1H), 3.87–4.04 (m, 4H), 7.35–7.46 (m, 3H), 7.66 (s, 1H), 7.77–7.79 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.3 (d, J = 6.0 Hz), 23.4 (d, J = 9.0 Hz), 34.2 (d, J = 137.0 Hz), 34.8, 61.3 (d, J = 6.0 Hz), 61.5 (d, J = 6.0 Hz), 124.9, 125.2, 125.4, 126.0, 127.6, 127.6, 128.2, 132.3, 133.6, 144.10 (d, J = 11.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.5.

4.3.14. Diethyl 2-(thiophen-2-yl)propylphosphonate 2n

98% ee. $[\alpha]_D^{25} = +18.6$ (c 0.60, $CHCl_3$). HPLC conditions: chiralcel AD-H, 40 °C, n-hexane/i-propanol = 97/3, flow rate = 1.0 mL/min, major enantiomer: t_R = 12.0 min; minor enantiomer: t_R = 13.1 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, J = 7.1 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.48 (d, J = 6.9 Hz, 3H), 2.02–2.10 (m, 1H), 2.15–2.21 (m, 1H), 3.54 (m, 1H), 3.98–4.08 (m, 4H), 6.85–6.86 (m, 1H), 6.89–6.91 (m, 1H), 7.12–7.13 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.4, 24.2 (d, J = 7.0 Hz), 30.4 (d, J = 2.0 Hz), 35.7 (d, J = 138.0 Hz), 61.4 (d, J = 7.0 Hz), 61.5 (d, J = 6.0 Hz), 122.9, 123.0, 126.5, 150.9 (d, J = 15.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 29.5. HRMS calcd for $C_{11}H_{19}O_3PS$: 262.0793, found 262.0793.

4.3.15. Diethyl 2-methyl-4-phenylbutylphosphonate 2o[11]

96% ee. $[\alpha]_D^{25} = +12.3$ (c 0.86, $CHCl_3$). HPLC conditions: chiralcel OJ-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 12.4 min; minor enantiomer: t_R = 10.9 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (d, J = 6.6 Hz, 3H), 1.30 (t, J = 7.0 Hz, 6H), 1.56–1.67 (m, 2H), 1.76–1.79 (m, 2H), 1.83–1.84 (m, 1H), 2.58–2.66 (m, 2H), 4.02–4.09 (m, 4H), 7.14–7.18 (m, 3H), 7.24–7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.5, 20.8 (d, J = 7.0 Hz), 28.0 (d, J = 4.0 Hz), 32.8 (d, J = 138.0 Hz), 33.1, 40.0 (d, J = 4.0 Hz), 61.3 (d, J = 6.0 Hz), 61.3 (d, J = 5.0 Hz), 125.7, 128.3, 142.2; ^{31}P NMR (162 MHz, $CDCl_3$): δ 32.0.

4.3.16. Diethyl 2-phenylbutylphosphonate 2p

93% ee. $[\alpha]_D^{25} = +10.0$ (c 1.14, $CHCl_3$). HPLC conditions: chiralcel OJ-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 9.3 min; minor enantiomer: t_R = 7.8 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.75 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 1.60–1.66 (m, 1H), 1.82–1.87 (m, 1H), 2.06–2.14 (m, 2H), 2.91–2.92 (m, 1H), 3.76–3.96 (m, 4H), 7.17–7.21 (m, 3H), 7.27–7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 16.2, 16.3, 30.8 (d, J = 8.0 Hz), 32.8 (d, J = 139.0 Hz), 41.9 (d, J = 2.0 Hz), 61.2 (d, J = 7.0 Hz), 61.4 (d, J = 7.0 Hz), 126.4, 127.6, 128.3, 144.4 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.9. HRMS calcd for $C_{14}H_{23}O_3P$: 270.1385, found 270.1387.

4.3.17. Diethyl 2-(4-methoxyphenyl)butylphosphonate 2q

94% ee. $[\alpha]_D^{25} = +10.45$ (c 1.18, $CHCl_3$). HPLC conditions: chiralcel OJ-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 11.6 min; minor enantiomer: t_R = 10.4 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.75 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.58–1.60 (m, 1H), 1.81–1.85 (m, 1H), 2.02–2.11 (m, 2H), 2.91–2.92 (m, 1H), 3.78 (s,

3H), 3.80–3.98 (m, 4H), 6.82–6.85 (m, 2H), 7.09–7.12 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 16.2, 16.3, 30.8 (d, J = 13.0 Hz), 32.9 (d, J = 138.0 Hz), 41.0 (d, J = 3.0 Hz), 55.2, 61.1 (d, J = 7.0 Hz), 61.3 (d, J = 6.0 Hz), 113.7, 128.5, 136.4 (d, J = 8.0 Hz), 158.1; ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.9. HRMS calcd for $C_{15}H_{25}O_4P$: 300.1490, found 300.1491.

4.3.18. Diethyl 2-phenylpentylphosphonate 2r

93% ee. $[\alpha]_D^{25} = +7.9$ (c 1.22, $CHCl_3$). HPLC conditions: chiralcel OJ-H, 40 °C, n-hexane/i-propanol = 98/2, flow rate = 1.0 mL/min, major enantiomer: t_R = 7.4 min; minor enantiomer: t_R = 6.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (t, J = 7.2 Hz, 3H), 1.09–1.18 (m, 2H), 1.14 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 1.58–1.63 (m, 1H), 1.74–1.79 (m, 1H), 2.06–2.13 (m, 2H), 3.00–3.04 (m, 1H), 3.74–3.97 (m, 4H), 7.17–7.20 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 16.2, 16.3, 20.4, 33.1 (d, J = 139.0 Hz), 39.9 (d, J = 3.0 Hz), 40.1 (d, J = 13.0 Hz), 61.1 (d, J = 6.0 Hz), 61.3 (d, J = 6.0 Hz), 126.4, 127.5, 128.2 (d, J = 16.0 Hz), 144.6 (d, J = 8.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.9. HRMS calcd for $C_{15}H_{25}O_3P$: 284.1541, found 284.1536.

4.3.19. Diethyl (1,2,3,4-tetrahydronaphthalen-1-yl) methylphosphonate 2s

93% ee. $[\alpha]_D^{25} = -3.5$ (c 0.94, $CHCl_3$). HPLC conditions: chiralcel OD-H, 40 °C, n-hexane/i-propanol = 95/5, flow rate = 1.0 mL/min, major enantiomer: t_R = 6.8 min; minor enantiomer: t_R = 8.8 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (t, J = 7.2 Hz, 3H), 1.77–1.84 (m, 2H), 1.98–2.01 (m, 2H), 2.04–2.16 (m, 2H), 2.73–2.78 (m, 2H), 3.29 (m, 1H), 4.12–4.14 (m, 4H), 7.04–7.08 (m, 1H), 7.10–7.15 (m, 2H), 7.18–7.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 16.5, 19.2, 28.5, 29.4, 32.5, 33.4 (d, J = 136.0 Hz), 61.4 (d, J = 6.0 Hz), 61.6 (d, J = 6.0 Hz), 126.0 (d, J = 9.0 Hz), 128.6, 129.3, 136.9, 140.3 (d, J = 17.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 31.2. HRMS calcd for $C_{15}H_{23}O_3P$: 282.1385, found 282.1382.

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