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Enantioselective Synthesis of Chiral Phosphonates via Rh/f-spiroPhos Catalyzed Asymmetric Hydrogenation of β,β-Disubstituted Unsaturated Phosphonates

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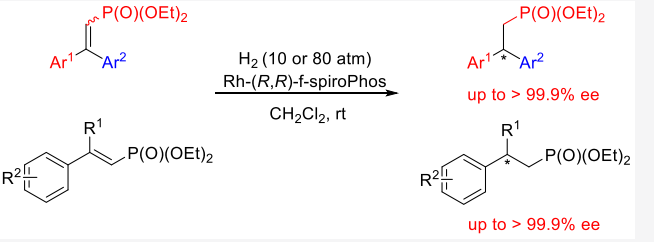
ABSTRACT: The first asymmetric hydrogenation of β,β-diaryl unsaturated phosphonates has been realized for synthesis of β,β-diaryl chiral phosphonates with excellent enantioselectivities (up to 99.9% ee) catalyzed by the Rh-(*R*,*R*)-f-spiroPhos complex. Furthermore, this catalyst also exhibits comparably excellent performance for β-aryl-β-alkyl unsaturated phosphonates providing the corresponding chiral phosphonates with up to 99.9% ee values. This methodology provides a straightforward access to asymmetric synthesis of chiral phosphonates.



INTRODUCTION

Chiral phosphonates are important in organic chemistry and medicinal chemistry and widely exist in natural products, pharmaceuticals, pesticides, and biologically active compounds. For example, chiral phosphonates can be used as antibacterial agents,[1] enzyme inhibitors,[2] and intermediates in biosynthetic processes[3] (Figure 1). More significantly, chiral ligands and catalysts containing phosphorus, such as chiral phosphorus acids, play a crucial role in the field of asymmetric catalysis.[4]

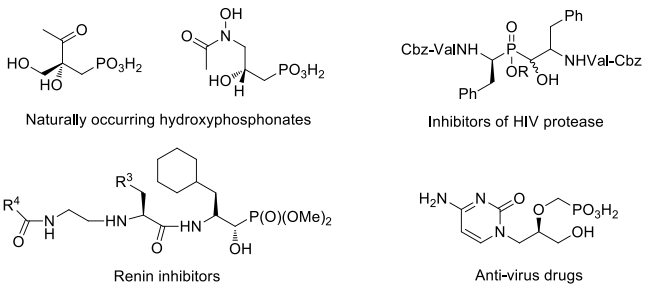


Figure 1. Selected examples of natural and biologically active phosphonates.

As a result, the synthesis of chiral phosphonates has attracted increased attention due to its importance in pharmaceutical and chemical synthesis and the catalysis field. Asymmetric catalytic hydrogenation of α,β-unsaturated phosphonates provides a convenient and efficient approach to the synthesis of chiral phosphonates. To date, transition metal or biocatalytic asymmetric hydrogenation of various α,β-unsaturated phosphonates including α- or β-acylamino-, α- or β-acyloxy-, β-aryl-β-alkyl, or β-dialkyl unsaturated phosphonates, and α,β-unsaturated γ-ketophosphonates has been reported with satisfactory enantioselectivities by Hu et al., Zheng et al., Andersson et al., and other groups.[5−9] Surprisingly, there has been no example on the asymmetric hydrogenation of β-diaryl unsaturated phosphonates explored so far. It can be presumably attributed to the bigger aromatic conjugated system and the much bulkier steric hindrance of this class of substrates, which perhaps makes them more stable and prevents the effective coordination of many catalysts with the substrates resulting in relatively lower activity or enantioselectivity.[10]

Recently, a chiral ferrocenyl diphosphine ligand containing the privileged spirobiindane skeleton,[11] f-spiroPhos, was developed by our group. It exhibited high efficiency and enantioselectivity in the transition metal catalyzed asymmetric hydrogenation of various prochiral substrates including α,β-unsaturated nitriles, sulfones, and imines. All these substrates were able to be successfully hydrogenated to produce the desired chiral products in high yields with excellent enantioselectivities achieved.[12] Encouraged by these promising results, we herein wish to tackle the unexplored β,β-diaryl unsaturated phosphonate substrates in asymmetric hydrogenation and report the first asymmetric hydrogenation of β,β-

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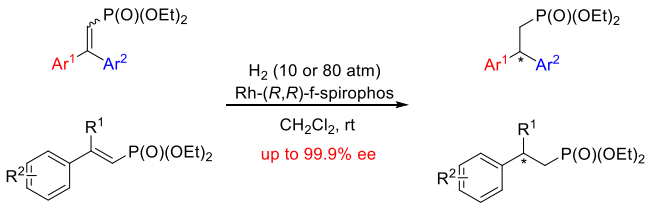
J. Org. Chem. XXXX, XXX, XXX−XXX

diaryl unsaturated phosphonates to provide chiral diaryl phosphonates with excellent enantioselectivities of up to 99.9% ee, which affords a highly enantioselective and straightforward approach to synthesis of both chiral diaryl and β-aryl-β-alkyl phosphonates (Scheme 1).

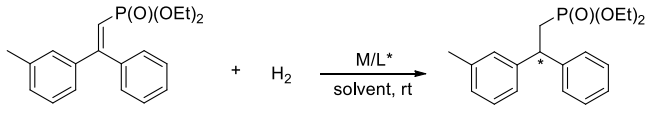
Scheme 1. Rh-Catalyzed Asymmetric Hydrogenation of α,β-Unsaturated Phosphonates



RESULTS AND DISCUSSION

The investigation initially began with the hydrogenation of diethyl (*E*)-(2-phenyl-2-(*m*-tolyl)vinyl)phosphonate **1a** as the model substrate under 80 atm of H_2 in CH_2Cl_2 at room temperature for 24 h using the complex generated *in situ* of $[Rh(COD)Cl]_2$ and (*R*,*R*)-f-spiroPhos. To our disappointment, only trace product was afforded (Table 1, entry 1).

Table 1. Asymmetric Hydrogenation of Diethyl (*E*)-(2-Phenyl-2-(*m*-tolyl)vinyl)phosphonate 1a, Optimizing Reaction Conditions[a]



1a **2a**

entry	precursor	L	solvent	conv. (%)[b]	ee (%)[c]
1	$[Rh(COD)Cl]_2$	L1	CH_2Cl_2	trace	ND
2	$[Rh(COD)_2]BF_4$	L1	CH_2Cl_2	59	94
3	$[Rh(COD)_2]OTf$	L1	CH_2Cl_2	18	89
4	**$[Rh(COD)_2]PF_6$**	**L1**	**CH_2Cl_2**	**>99**	**94**
5	$[Rh(COD)_2]PF_6$	L2	CH_2Cl_2	>99	14
6	$[Rh(COD)_2]PF_6$	L3	CH_2Cl_2	98	7
7	$[Rh(COD)_2]PF_6$	L4	CH_2Cl_2	63	66
8	$[Rh(COD)_2]PF_6$	L5	CH_2Cl_2	83	85
9	$[Rh(COD)_2]PF_6$	L6	CH_2Cl_2	>99	56
10	$[Rh(COD)_2]PF_6$	L1	toluene	18	69
11	$[Rh(COD)_2]PF_6$	L1	THF	13	86
12	$[Rh(COD)_2]PF_6$	L1	Et_2O	trace	ND
13	$[Rh(COD)_2]PF_6$	L1	CH_3OH	5	ND
14	$[Rh(COD)_2]PF_6$	L1	1,4-dioxane	4	ND

[a]Unless otherwise mentioned, all reactions were carried out for 24 h with a Rh/ligand/substrate **1a** ratio of 1:1.1:100 under 80 atm of H_2. [b]Determined by GC analysis. [c]Determined by chiral supercritical fluid chromatography (SFC).

However, when the metal precursor was replaced with cationic $[Rh(COD)_2]BF_4$, the desired product **2a** was afforded with pretty high enantioselectivity (94% ee) albeit in a moderate conversion (Table 1, entry 2). Inspired by the result, other rhodium precursors with various counterions were evaluated. Gratifyingly, the precursor $[Rh(COD)_2]PF_6$ could achieve not only comparably high enantioselectivity (95% ee) but complete conversion (Table 1, entry 4). As illustrated in Table 1, a significant counterion effect was observed in this hydrogenation. The counterion structure, perhaps bulkier steric hindrance, had an obvious influence on the catalyst efficiency, which revealed the different interaction of counterions with the metal center.[13,14] Subsequently, a variety of chiral electron-rich diphosphine ligands including JosiPhos, DuanPhos, Ph-BPE, and f-Binaphane were applied to the hydrogenation in order to reach higher activity and enantioselectivity (Figure 2). Although most of them could give good to high conversions, the relatively lower enantioselectivities were achieved with 85% ee at most (Table 1, entries 5−9). Finally, this transformation was also evaluated in other solvents. It was revealed that the hydrogenation was sensitive to the solvent effect. Most of the solvents, such as toluene, THF, Et_2O, CH_3OH, and 1,4-dioxane, only provided very poor conversions (Table 1, entries 10−14).

Encouraged by the promising result obtained in the hydrogenation of diethyl (*E*)-(2-phenyl-2-(m-tolyl)vinyl)-phosphonate **1a**, we then prepared a variety of β,β-diaryl unsaturated phosphonates **1** and applied them to the asymmetric hydrogenation under the optimal reaction conditions (Table 2). It was found that all of the substrates examined (**1a−1l**) could be successfully hydrogenated to produce the corresponding chiral phosphonates in high yields with excellent enantioselectivities, 90−99.9% ee. As the results revealed in Table 2, the electronic properties of the substituent at the meta- or para- position of the aromatic ring had no obvious influence on the enantioselectivity and reactivity. For example, regardless of the electron-donating substituents (Me, **1a−1b** and **1e**) or electron-withdrawing substituents (F or Cl, **1c** and **1f−1g**), the substrates could be smoothly hydrogenated to provide the corresponding products with full conversions and high enantioselectivities, 91−94% ee. Notably, the substrates with a Cl (**1j**) or F group (**1k**) at the ortho-position as well as the 1-naphthyl substrate **1l** could achieve extremely high enantioselecitivities, up to 99.9% ee, albeit with slightly lower conversions. The steric hindrance at the ortho-position presumably could make it easier to distinguish the relatively increased difference between two aryl groups for the catalyst, which had a positive influence on much higher enantioselectivity but with a negative effect on the reactivity. Remarkably, this catalyst could also exhibit comparable enantioselectivity in the hydrogenation of the corresponding (*Z*)-isomers to afford the products with an opposite absolute configuration in contrast to that obtained from (*E*)-isomers. The substrates (*Z*)-**1d** and (*Z*)-**1h** were hydrogenated providing the desired products **2d** and **2h** with 90% and 97% ee, respectively.

The absolute configuration of the hydrogenation product **2h** was determined and assigned to be the (*R*) configuration by X-ray crystallographic analysis (Scheme 2). The absolute configuration of product **2g** could also be assigned to be (*S*) by comparison with optical rotation data of the product **2h**. On the basis of the result, the enantio-determining transition model for Rh-catalyzed asymmetric hydrogenation of β,β-diaryl α,β-unsaturated phosphonates was proposed.

In addition, the asymmetric hydrogenation of β-aryl-β-alkyl α,β-unsaturated phosphonates was also investigated using this catalyst system. The diethyl (*E*)-(2-phenylprop-1-en-1-yl)-phosphonate **3a** was initially hydrogenated under the optimal reaction conditions using 1.0 mol % catalyst loading. Likewise, both full conversion and excellent enantioselectivity (94% ee) were achieved. It was noteworthy that the substrate **3a** could

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J. Org. Chem. XXXX, XXX, XXX−XXX

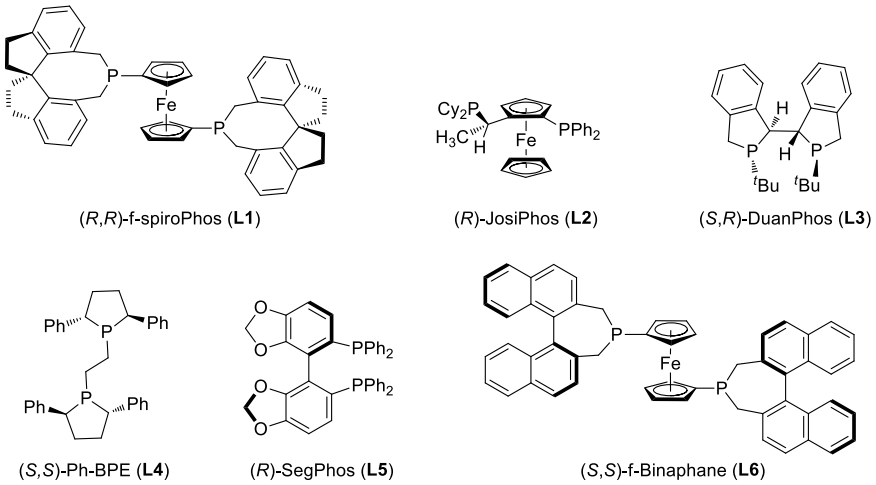
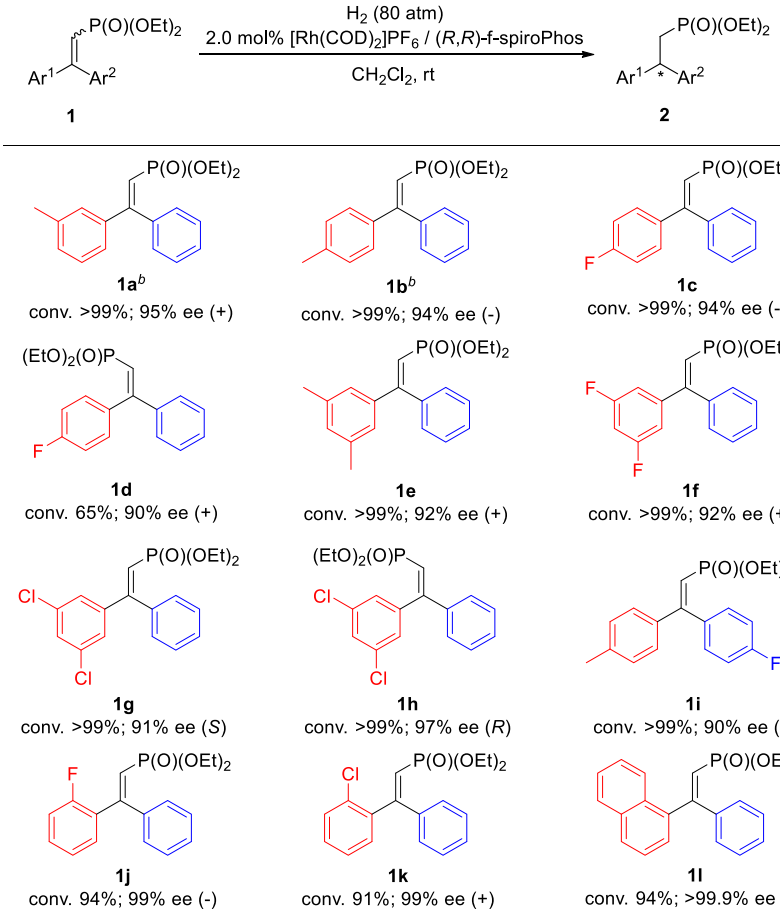


Figure 2. Structures of the phosphine ligands screened for hydrogenation of **1a**.

Table 2. Rh-Catalyzed Asymmetric Hydrogenation of *β,β*-Diaryl *α,β*-Unsaturated Phosphonates 1[a]



[a]Unless otherwise mentioned, all reactions were carried out with a $[Rh(COD)_2]PF_6$/(*R,R*)-f-spiroPhos/substrate ratio of 2.0:2.2:100, CH_2Cl_2, 80 atm H_2, rt, 24 h. The conversion was determined by ^1H NMR spectroscopy or GC analysis; the enantioselectivity was determined by SFC or HPLC analysis using a chiral stationary phase. [b]1.0 mol % $[Rh(COD)_2]PF_6$.

be completely hydrogenated in an hour under 1.0 atm hydrogen pressure to produce the desired **4a** with remained enantioselectivity, 94% ee. Moreover, besides the precursor $[Rh(COD)_2]PF_6$, $[Rh(COD)_2]BF_4$ was also proven as an efficient alternative precursor for this hydrogenation, and comparably excellent enantioselectivity with complete conversion was achieved. Subsequently, a series of (*E*)-*β*-aryl-*β*-alkyl *α,β*-unsaturated phosphonates **3a−k** were prepared and successfully hydrogenated to afford the desired products **4a−k** with full conversion and excellent enantioselectivities, 92−99.9% ee (Table 3). The electron property and position of the substituents at the phenyl ring of the substrates had no obvious influence on both the reactivity and the enantioselectivity. Generally, the substrates with electron-withdrawing substitu-

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J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 2. X-ray Crystal Structure of the Product (*R*)-2h, and the Proposed Enantio-Determining Transition Model for Rh-Catalyzed Asymmetric Hydrogenation of *β*,*β*-Diaryl *α*,*β*-Unsaturated Phosphonates

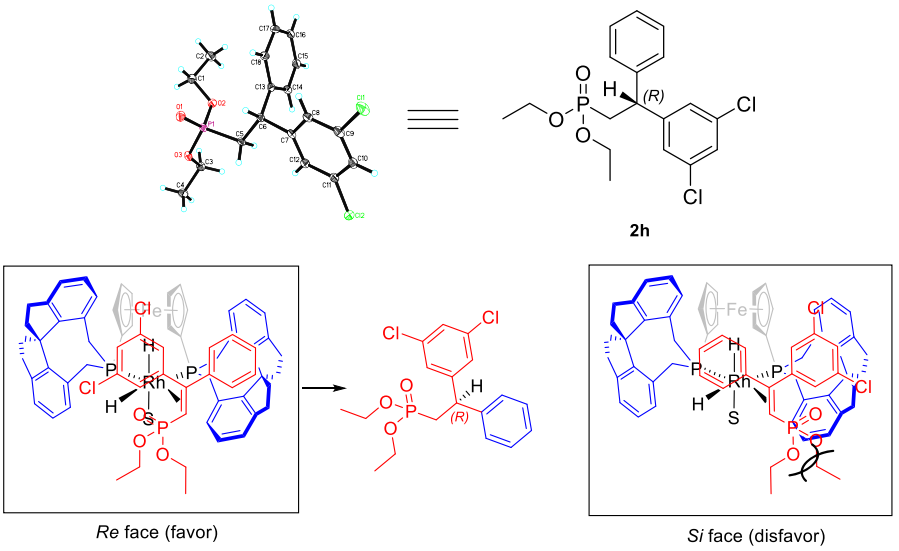
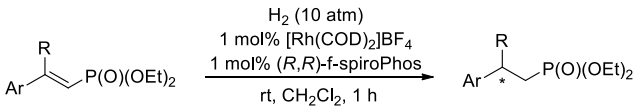
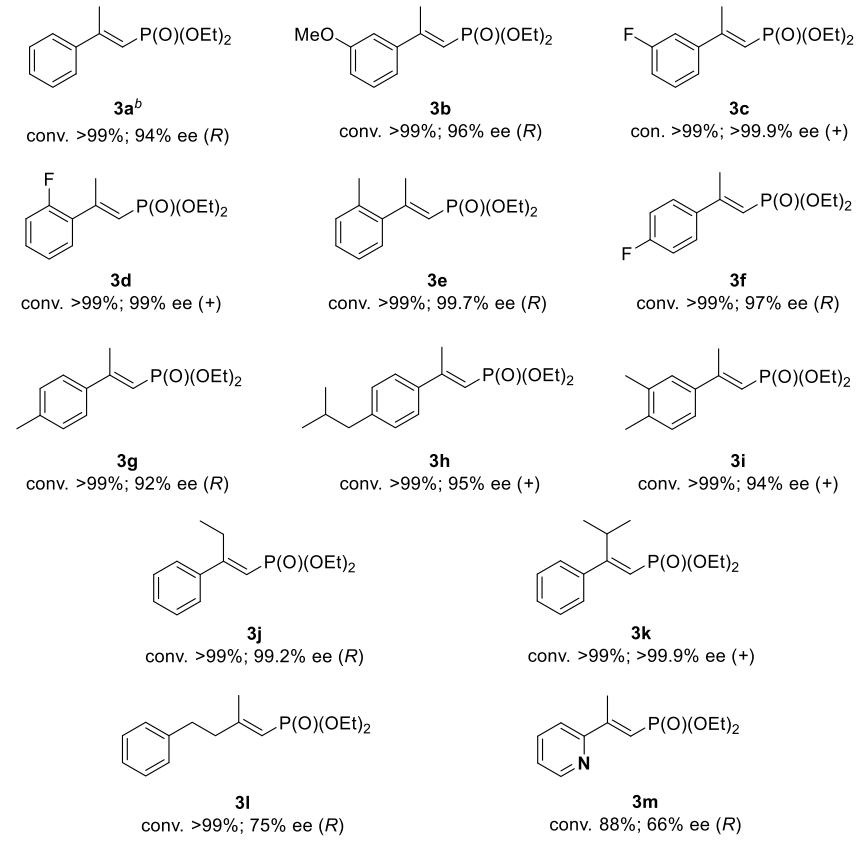


Table 3. Rh-Catalyzed Asymmetric Hydrogenation of *β*-Aryl-*β*-alkyl *α*,*β*-Unsaturated Phosphonates 3[a]





[a]Unless otherwise mentioned, all reactions were carried out with a $[Rh(COD)_2]BF_4$/(*R*,*R*)-f-spiroPhos/substrate ratio of 1.0:1.1:100, CH_2Cl_2, 10 atm H_2, rt, 1.0 h. The conversion was determined by ^1H NMR spectroscopy or GC analysis; the enantioselectivity was determined by SFC or HPLC analysis using a chiral stationary phase. [b]1.0 atm H_2, 1.0 h.

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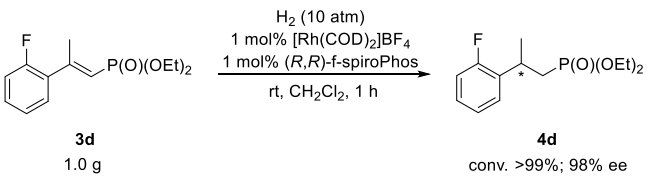
J. Org. Chem. XXXX, XXX, XXX−XXX

ents on the phenyl ring gave higher enantioselectivities than those with electron-donating substituents. For example, substrates **3b** and **3g** with a *meta*-methoxy or a *para*-methyl substituent gave 96% ee and 92% ee, while substrates **3c** and **3f** bearing a fluoro substituent at meta- or para- position of the phenyl ring provided enantioselectivities as high as 99.9% and 97% ee, respectively. Significantly, the catalyst could still maintain excellent activity and enantioselectivity for the subtrates with steric hindrance. The ortho-substituted substrates **3d** and **3e** exhibited similar reactivity and were also completely hydrogenated under low hydrogen pressure in an hour with comparable enantioselectivities of up to 99.7% ee. When the R group was changed to bulkier ethyl or isopropyl (**3j** and **3k**), both the reactivity and the enantioselectivity were not decreased. The desired products **4j** and **4k** were obtained with full conversion and excellent enantioselectivities, 99.2% and 99.9% ee, respectively. However, the dialkyl substrate **3l** only achieved 75% ee albeit with a full conversion, which could perhaps be attributed to the flexibility of the alkyl group. When the phenyl was replaced with a 2-pyridyl group (**3m**), both the reactivity and the enantioselectivity were decreased.

Finally, the hydrogenation on a gram-scale was evaluated using one of the substrates. The full conversion was still achieved in an hour providing the desired product **4d** with excellent enantioselectivity of 98% ee (Scheme 3).

Scheme 3. Asymmetric Hydrogenation of *β,β*-Disubstituted Unsaturated Phosphonate 3d on Gram Scale



CONCLUSIONS

In summary, we have developed a highly efficient method for enantioselective synthesis of various chiral phosphonates. By employing a Rh-(*R,R*)-f-spiroPhos complex, a wide range of *α,β*-unsaturated phosphonates including the (*E*)- and (*Z*)-isomers of *β,β*-diaryl and *β*-aryl-*β*-alkyl *α,β*-unsaturated phosphonates were smoothly transformed into chiral phosphonates in high yields and excellent enantioselectivities of up to 99.9% ee. This methodology provides a straightforward access to asymmetric synthesis of chiral phosphonates.

EXPERIMENTAL SECTION

General Information. All the air- or moisture-sensitive reactions and manipulations were performed by using standard Schlenk techniques and in a nitrogen-filled glovebox. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV (400 MHz) spectrometers and JEOL JNM-ECX600P and JNM-ECS600 (400 or 600 MHz) spectrometers. ($CDCl_3$ was the solvent used for the NMR analysis, with TMS as the internal standard.) Optical rotation was determined using an Autopol III Automatic polarimeter (Rudolph research Analyical). HPLC analysis was conducted on an Agilent 1260 series instrument. SFC analysis was conducted on an Agilent 1260 series instrument. HRMS were recorded on a Waters LCT Premier XE mass spectrometer with TOF.

General Procedures for the Synthesis of Substrates 1 and 3. *General Procedure A.* NaH (1.3 equiv, 13.0 mmol, 60% in oil) was placed in an oven-dried 250 mL, three-neck round-bottom flask. THF (1.8 mL/mmol) was added under nitrogen. The reaction mixture was cooled and a solution of tetraethyl methylenedisphosphonate (1.2 equiv, 12.0 mmol) in THF (0.4 mL/mmol) was slowly added, and the resulting mixture was stirred at room temperature for 30 min. A solution of ketone (1.0 equiv, 10.0 mmol) in THF (1.42 mL/mmol) was then added to the reaction. The solution was stirred at room temperature until no starting material was detected by TLC. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and distilled to dryness in vacuo. The residue was purified by chromatography giving **1** and **3**.[8b]

General Procedure B. The dialkyl phosphite (1.4 equiv, 14.0 mmol) was added to a brown suspension of Cu_2O (0.14 equiv, 1.4 mmol) in acetonitrile (28.6 mL/mmol). Then, the corresponding alkyne (1.0 equiv, 10.0 mmol) was added, and the reaction mixture was warmed to 70 °C and stirred overnight under air. The reaction mixture turned a pale-green clear solution. The solvent was evaporated in vacuo, and the crude product was purified by flash column chromatography (silica gel, EtOAc/PE) to give diethyl (phenylethynyl)phosphonate.[12d,15]

CuBr (1.28 equiv, 12.8 mmol) was added to an oven-dried 250 mL three-neck round-bottom flask under nitrogen, THF (4.0 mL/mmol) was added, and the reaction mixture was cooled to −20 °C. Then, LiBr (1.3 equiv, 13.0 mmol) in THF (0.8 mL/mmol) was added, followed by stirring for 10 min. The RMgBr (1.3 equiv, 13.0 mmol) was added dropwise at −20 °C, followed by stirring for 15 min. After that, the solution was cooled to −78 °C, and a solution of the diethyl (phenylethynyl)phosphonate (1.0 equiv, 10.0 mmol) in THF (4.0 mL/mmol) was added dropwise and stirred at −78 °C for 1 h. The reaction was quenched with MeOH, and the reaction mixture was washed with saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2. The combined organic extracts were washed with water and brine and then dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by chromatography giving **1b**, **1e**, **1f**, **1g**, and **1h**.[2a,b]

*(E)-Diethyl-(2-phenyl-2-(m-tolyl)vinyl)phosphonate (**1a**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 2.50 g, yield: 42%. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.36 (s, 5H), 7.25−7.14 (m, 2 H), 7.09 (s, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.14 (d, *J* = 15.7 Hz, 1H), 3.95−3.75 (m, 4H), 2.30 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): *δ* (ppm) 160.4 (d, *J* = 5.9 Hz), 141.7 (d, *J* = 22.4 Hz), 139.1 (d, *J* = 7.4 Hz), 138.1, 130.3, 129.8, 128.9, 128.7, 128.3, 127.9, 125.6, 114.7 (d, *J* = 192.9 Hz), 61.6 (d, *J* = 6.1 Hz), 21.5, 16.2 (d, *J* = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* (ppm) 17.4; TOF-HRMS Calculated for $C_{19}H_{24}O_3P$ ($[M + H]^+$): 331.1457, found 331.1460.

*(E)-Diethyl-(2-phenyl-2-(p-tolyl)vinyl)phosphonate (**1b**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.50 g, yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.36 (s, 5H), 7.25−7.10 (m, 4H), 6.14 (d, *J* = 15.6 Hz, 1H), 3.94−3.74 (m, 4H), 2.34 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): *δ* (ppm) 160.1 (d, *J* = 6.1 Hz), 139.7, 139.2 (d, *J* = 7.5 Hz), 138.8 (d, *J* = 22.3 Hz), 130.2−129.5 (m), 129.1, 128.6, 128.2, 127.9, 113.8 (d, *J* = 193.6 Hz), 61.6 (d, *J* = 6.0 Hz), 21.3, 16.2 (d, *J* = 6.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) *δ* (ppm) 17.6; TOF-HRMS Calculated for $C_{19}H_{24}O_3P$ ($[M + H]^+$): 331.1457, found 331.1460.

*(E)-Diethyl-(2-(4-fluorophenyl)-2-phenylvinyl)phosphonate (**1c**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow solid; 0.60 g, yield: 25%; MP: 48−50 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.37−7.28 (m, 5H), 7.25−7.23 (m, 2H), 7.05 (t, *J* = 8.2 Hz, 2H), 6.14 (d, *J* = 15.2 Hz, 1H), 3.95−3.80 (m, 4H), 1.16−1.12 (m, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): *δ* (ppm) 163.1 (d, *J* = 248.4 Hz), 159.2 (d, *J* = 5.8 Hz), 141.5 (d, *J* = 22.1 Hz), 135.1−134.9 (m), 131.8 (d, *J* = 8.1 Hz), 123.0−129.2 (m), 128.5, 128.3, 115.2 (d, *J* = 192.91), 114.9 (d, *J* = 21.5 Hz), 61.7 (d, *J* = 6.1 Hz), 16.3 (d, *J* = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): *δ* (ppm) 17.0; TOF-HRMS Calculated for $C_{18}H_{21}O_3FP$ ($[M + H]^+$): 335.1206, found 335.1205.

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J. Org. Chem. XXXX, XXX, XXX−XXX

*(Z)-Diethyl (2-(4-fluorophenyl)-2-phenylvinyl)phosphonate (**1d**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.85 g, yield: 36%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.38−7.24 (m, 7H), 7.07 (t, J = 8.7 Hz, 2H), 6.16 (d, J = 15.2 Hz, 1H), 3.97−3.83 (m, 4H), 1.16 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 163.6 (d, J = 250.2 Hz), 159.2 (d, J = 7.3 Hz), 138.9, 138.4−137.37 (m), 135.9 (d, J = 7.9 Hz), 130.2 (d, J = 9.0 Hz), 129.8, 128.7, 115.3 (d, J = 22.0 Hz), 114.4 (d, J = 192.4 Hz), 61.6 (d, J = 6.7 Hz), 16.2 (d, J = 7.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 17.0; TOF-HRMS Calculated for $C_{18}H_{21}O_3FP$ ([M + H]$^+$): 335.1206, found 335.1205.

*(E)-Diethyl-(2-(3,5-dimethylphenyl)-2-phenylvinyl)phosphonate (**1e**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow solid; 1.20 g, yield: 93%; MP: 60−62 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36 (s, 5H), 6.98 (s, 1H), 6.87 (s, 2H), 6.12 (d, J = 15.8 Hz, 1H), 4.03−3.41 (m, 4H), 2.26 (s, 6H), 1.11 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 160.57 (d, J = 5.8 Hz), 141.75 (d, J = 22.1 Hz), 139.23, 137.92, 129.90 (d, J = 254.9 Hz), 129.84, 127.02 (d, J = 164.3 Hz), 114.50 (d, J = 192.5 Hz), 61.55 (d, J = 6.0 Hz), 21.32, 16.23 (d, J = 6.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 17.5; TOF-HRMS Calculated for $C_{20}H_{26}O_3P$ ([M + H]$^+$): 345.1614, found 345.1610.

*(E)-Diethyl (2-(3,5-difluorophenyl)-2-phenylvinyl)phosphonate (**1f**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.70 g, yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37−7.29 (m, 3H), 7.23 (d, J = 1.9 Hz, 2H), 6.91−6.80 (m, 3H), 6.22 (d, J = 14.5 Hz, 1H), 4.00−3.88 (m, 4H), 1.19 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 163.8 (d, J = 12.6 Hz), 161.3 (d, J = 12.8 Hz), 157.5 (dd, J = 4.8, 2.1 Hz), 143.0−141.5 (m), 140.2 (d, J = 21.7 Hz), 129.9, 128.3 (d, J = 64.0 Hz), 116.5 (d, J = 192.6 Hz), 113.0 (d, J = 25.9 Hz), 104.0 (t, J = 25.2 Hz), 61.8 (d, J = 6.0 Hz), 16.3 (d, J = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 16.0; TOF-HRMS Calculated for $C_{18}H_{20}O_3F_2P$ ([M + H]$^+$): 353.1112, found 353.1110.

*(E)-Diethyl (2-(3,5-dichlorophenyl)-2-phenylvinyl)phosphonate (**1g**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.66 g, yield: 41%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39−7.31 (m, 3H), 7.25−7.23 (m, 5H), 6.24 (d, J = 14.6 Hz, 1H), 4.03−3.87 (m, 4H), 1.20 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 157.1 (d, J = 5.9 Hz), 141.8 (d, J = 8.2 Hz), 140.1 (d, J = 21.6 Hz), 134.6, 130.0, 128.7, 128.6, 128.2, 128.1, 116.9 (d, J = 193.1 Hz), 61.9 (d, J = 6.9 Hz), 16.3 (d, J = 7.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 15.9; TOF-HRMS Calculated for $C_{18}H_{20}O_3PCl_2$ ([M + H]$^+$): 385.0521, found 385.0520.

*(Z)-Diethyl (2-(3,5-dichlorophenyl)-2-phenylvinyl)phosphonate (**1h**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as white solid; 1.00 g, yield: 53%; MP: 68−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39 (dt, J = 3.8, 2.7 Hz, 3H), 7.35−7.32 (m, 3H), 7.13 (d, J = 1.9 Hz, 2H), 6.15 (d, J = 14.2 Hz, 1H), 3.93−3.77 (m, 4H), 1.12 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 157.2 (d, J = 7.8 Hz), 144.7 (d, J = 23.4 Hz), 137.7 (d, J = 8.3 Hz), 135.2, 129.7, 129.3, 129.2, 128.3, 126.7, 117.7 (d, J = 193.4 Hz), 61.8 (d, J = 6.7 Hz), 16.2 (d, J = 7.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 15.7; TOF-HRMS Calculated for $C_{18}H_{20}O_3PCl_2$ ([M + H]$^+$): 385.0521, found 385.0520.

*(Z)-Diethyl (2-(4-fluorophenyl)-2-(p-tolyl)vinyl)phosphonate (**1i**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as white solid; 1.20 g, yield: 30%; MP: 94−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.35 (dd, J = 8.0, 5.5 Hz, 2H), 7.15−7.10 (m, 4H), 7.06 (t, J = 8.3 Hz, 2H), 6.13 (d, J = 15.3 Hz, 1H), 3.97−3.80 (m, 4H), 2.35 (s, 3H), 1.15 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 163.3−157.6 (m), 139.9, 138.8, 138.6, 135.1 (dd, J = 7.8, 2.7 Hz), 131.8 (d, J = 8.0 Hz), 129.2, 128.2, 114.9 (d, J = 21.5 Hz), 114.2 (d, J = 188.6), 61.6 (d, J = 6.0 Hz), 21.3, 16.3 (d, J = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 17.4; TOF-HRMS Calculated for $C_{19}H_{23}O_3FP$ ([M + H]$^+$): 349.1363, found 349.1360.

*(E)-Diethyl (2-(2-fluorophenyl)-2-phenylvinyl)phosphonate (**1j**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as a white solid; 0.90 g, yield: 20%; MP: 52−54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41−7.39 (m, 2H), 7.34−7.32 (m, 3H), 7.29−7.27 (m, 1H), 7.13−7.00 (m, 3H), 6.12 (d, J = 15.4 Hz, 1H), 3.93−3.83 (m, 4H), 1.11 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 160.0 (d, J = 250.9 Hz), 154.7 (d, J = 6.3 Hz), 139.1 (d, J = 7.5 Hz), 131.3 (d, J = 2.5 Hz), 130.7 (d, J = 8.5 Hz), 130.1 (dd, J = 22.7, 12.1 Hz), 129.3, 128.9, 127.9, 124.1 (d, J = 3.8 Hz), 119.2 (dd, J = 189.3, 4.3 Hz), 116.3 (d, J = 22.4 Hz), 61.8 (d, J = 6.1 Hz), 16.2 (d, J = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 15.1; TOF-HRMS Calculated for $C_{18}H_{21}O_3FP$ ([M + H]$^+$): 335.1206, found 335.1205.

*(E)-Diethyl (2-(2-chlorophenyl)-2-phenylvinyl)phosphonate (**1k**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 1.20 g, yield: 42%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.46−7.43 (m, 2H), 7.38−7.35 (m, 1H), 7.31 (dt, J = 3.5, 1.4 Hz, 3H), 7.28−7.22 (m, 3H), 5.92 (d, J = 15.3 Hz, 1H), 3.99−3.86 (m, 4H), 1.12 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 158.07 (d, J = 5.9 Hz), 141.78 (d, J = 22.8 Hz), 138.53 (d, J = 7.1 Hz), 132.48, 130.89, 130.21, 129.63, 129.45, 129.02, 127.86, 126.74, 61.85 (d, J = 6.0 Hz), 16.18 (d, J = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 17.4; TOF-HRMS Calculated for $C_{18}H_{21}O_3PCl$ ([M + H]$^+$): 351.0911, found 351.0908.

*(E)-Diethyl (2-(naphthalen-1-yl)-2-phenylvinyl)phosphonate (**1l**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.75 g, yield: 32%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.86−7.81 (m, 3H), 7.54 (dd, J = 6.6, 3.0 Hz, 2H), 7.46−7.36 (m, 4H), 7.31−7.25 (m, 3H), 6.04 (d, J = 16.3 Hz, 1H), 4.03−3.91 (m, 4H), 1.15 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 160.1 (d, J = 5.2 Hz), 141.0, 140.8, 139.8 (d, J = 7.2 Hz), 133.9, 131.0, 129.3, 129.1 (d, J = 3.1 Hz), 128.4, 128.1, 127.1, 126.6, 126.0, 125.9, 125.1, 118.8 (d, J = 186.3 Hz), 61.9 (d, J = 6.0 Hz), 16.2 (d, J = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 16.5; TOF-HRMS Calculated for $C_{22}H_{24}O_3P$ ([M + H]$^+$): 367.1457, found 367.1460.

*(E)-Diethyl (2-phenylprop-1-en-1-yl)phosphonate (**3a**).* Purification by column chromatography (silica gel, PE:EA = 1:1) afforded the product as yellow oil; 0.50 g, yield: 64%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.47−7.45 (m, 2H), 7.36−7.34 (m, 3H), 5.89 (d, J = 16.5 Hz, 1H), 4.11 (dtd, J = 8.1, 7.1, 1.0 Hz, 4H), 2.49 (d, J = 3.3 Hz, 3H), 1.34 (t, J = 7.0 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-(3-methoxyphenyl)prop-1-en-1-yl)phosphonate (**3b**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 1.50 g, yield: 58%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.24−7.20 (m, 1H), 6.99 (d, J = 7.4 Hz, 1H), 6.93−6.92 (m, 1H), 6.85−6.83 (m, 1H), 6.01−5.50 (m, 1H), 4.07 (dd, J = 8.5, 6.4 Hz, 4H), 3.76 (s, 3H), 2.43 (d, J = 2.0 Hz, 3H), 1.30 (t, J = 7.1 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-(3-fluorophenyl)prop-1-en-1-yl)phosphonate (**3c**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.75 g, yield: 59%; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.30 (td, J = 8.0, 6.0 Hz, 1H), 7.21 (d, J = 7.9 Hz, 1H), 7.12 (dt, J = 10.2, 2.1 Hz, 1H), 7.01 (td, J = 8.2, 2.2 Hz, 1H), 5.88 (d, J = 15.9 Hz, 1H), 4.10 (m, 4H), 2.45 (d, J = 3.2 Hz, 3H), 1.32 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 162.9 (d, J = 246.3 Hz), 156.6 (d, J = 8.4 Hz), 144.1 (d, J = 23.7 Hz), 130.1 (d, J = 8.3 Hz), 121.7 (d, J = 2.9 Hz), 116.0 (d, J = 21.3 Hz), 114.9 (d, J = 190.3 Hz), 113.2 (d, J = 22.3 Hz), 61.7 (d, J = 5.7 Hz), 19.3 (d, J = 7.1 Hz), 16.5 (d, J = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 17.1; TOF-HRMS Calculated for $C_{13}H_{19}O_3FP$ ([M + H]$^+$): 273.1050, found 273.1048.

*(E)-Diethyl (2-(2-fluorophenyl)prop-1-en-1-yl)phosphonate (**3d**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.50 g, yield: 46%; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.29−7.25 (m, 2H), 7.11 (t, J = 7.5 Hz, 1H), 7.05 (dd, J = 10.9, 8.3 Hz, 1H), 5.77 (d, J = 17.0 Hz, 1H), 4.14−4.10 (m, 4H), 2.46−2.45 (m, 3H), 1.35 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR

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J. Org. Chem. XXXX, XXX, XXX−XXX

(151 MHz, $CDCl_3$): δ (ppm) 159.3 (d, J = 249.3 Hz), 154.8 (d, J = 10.2 Hz), 130.9 (dd, J = 24.8, 13.4 Hz), 130.2 (d, J = 9.1 Hz), 126.6 (dd, J = 720.0, 4.1 Hz), 120.9−116.8 (m), 116.1 (d, J = 23.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 17.4; TOF-HRMS Calculated for $C_{13}H_{19}O_3FP$ ($[M + H]^+$): 273.1050, found 373.1048.

*(E)-Diethyl (2-(o-tolyl)prop-1-en-1-yl)phosphonate (**3e**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.60 g, yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.19−7.05 (m, 3H), 7.05 (d, J = 6.9 Hz, 1H), 5.49 (dd, J = 18.7, 1.3 Hz, 1H), 4.12 (p, J = 7.1 Hz, 4H), 2.37 (dd, J = 3.4, 1.2 Hz, 3H), 2.28 (s, 3H), 1.35 (t, J = 7.1 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-(4-fluorophenyl)prop-1-en-1-yl)phosphonate (**3f**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.75 g, yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40−7.37 (m, 2H), 7.34−7.30 (m, 2H), 5.87 (dd, J = 15.9, 1.0 Hz, 1H), 4.11 (dd, J = 7.9, 7.1 Hz, 4H), 2.46 (dd, J = 3.3, 1.1 Hz, 3H), 1.34 (t, J = 7.1 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-(p-tolyl)prop-1-en-1-yl)phosphonate (**3g**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.80 g, yield: 60%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 5.87 (dd, J = 16.6, 1.0 Hz, 1H), 4.15−4.07 (m, 4H), 2.47 (dd, J = 3.3, 1.0 Hz, 3H), 2.35 (s, 3H), 1.34 (t, J = 7.1 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-(4-isobutylphenyl)prop-1-en-1-yl)phosphonate (**3h**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.90 g, yield: 46%; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.39 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 5.89 (dt, J = 16.6, 1.0 Hz, 1H), 4.11 (p, J = 7.1 Hz, 4H), 2.49−2.46 (m, 5H), 1.85 (dt, J = 13.5, 6.8 Hz, 1H), 1.34 (t, J = 7.1 Hz, 6H), 0.89 (d, J = 6.6 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$) δ (ppm) 158.1 (d, J = 9.3 Hz), 143.2, 139.1 (d, J = 24.0 Hz), 129.3, 125.9, 112.5 (d, J = 190.7 Hz), 61.5 (d, J = 6.1 Hz), 45.1, 30.2, 22.4, 19.2 (d, J = 7.5 Hz), 16.5 (d, J = 7.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 19.3; TOF-HRMS Calculated for $C_{17}H_{28}O_3P$ ($[M + H]^+$): 311.1770, found 311.1773.

*(E)-Diethyl (2-(3,4-dimethylphenyl)prop-1-en-1-yl)phosphonate (**3i**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.50 g, yield: 42%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.23 (s, 1H), 7.20 (dd, J = 7.9, 1.9 Hz, 1H), 7.10 (d, J = 7.9 Hz, 1H), 5.89−5.84 (m, 1H), 4.14−4.07 (m, 4H), 2.46 (dd, J = 3.2, 0.8 Hz, 3H), 2.26 (d, J = 3.5 Hz, 6H), 1.33 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 158.3 (d, J = 8.0 Hz), 139.4 (d, J = 23.5 Hz), 138.1, 136.7, 129.8, 127.3, 123.5, 112.3 (d, J = 190.5 Hz), 61.5 (d, J = 5.6 Hz), 19.9, 19.6, 19.3 (d, J = 7.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 19.3; TOF-HRMS Calculated for $C_{15}H_{24}O_3P$ ($[M + H]^+$): 283.1457, found 283.1460.

*(E)-Diethyl (2-phenylbut-1-en-1-yl)phosphonate (**3j**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.50 g, yield: 30%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) δ 7.41−7.39 (m, 2H), 7.36−7.33 (m, 3H), 5.74 (d, J = 17.2 Hz, 1H), 4.11 (m, 4H), 2.99 (qd, J = 7.5, 2.3 Hz, 2H), 1.34 (t, J = 7.1 Hz, 6H), 1.02 (t, J = 7.5 Hz, 3H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (3-methyl-2-phenylbut-1-en-1-yl)phosphonate (**3k**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 0.65 g, yield: 25%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 (dd, J = 5.1, 1.8 Hz, 3H), 7.16−7.15 (m, 2H), 5.42 (d, J = 18.8 Hz, 1H), 4.11 (m, 4H), 3.73 (m, 1H), 1.34 (t, J = 7.0 Hz, 6H), 1.07 (d, J = 6.9 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-methyl-4-phenylbut-1-en-1-yl)phosphonate (**3l**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as a colorless oil; 1.44 g, yield: 51%. ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.27−7.25 (m, 2H), 7.15−7.20 (m, 3H), 5.37 (d, 1H, J = 18.2 Hz, 1H), 3.95−4.02 (m, 4H), 2.77−2.81 (m, 2H), 2.45−2.49 (m, 2H), 2.11 (s, 3H), 1.28 (t, J = 7.0 Hz, 6H). ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 141.0, 128.6, 128.1, 126.8, 126.0 (d, J = 23.0 Hz), 61.8, 34.6, 30.9, 30.1, 25.0, 16.5. The analytical data are consistent with the literature.[8b]

*(E)-Diethyl (2-(pyridin-2-yl)prop-1-en-1-yl)phosphonate (**3m**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil; 1.45 g, yield: 58%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.59 (d, J = 4.7 Hz, 1H), 7.71−7.63 (t, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.24−7.20 (m, 1H), 6.56 (d, J = 15.0 Hz, 1H), 4.14−4.06 (q, J = 8.8 Hz 4H), 2.52 (d, J = 1.9 Hz, 3H), 1.31 (t, J = 7.1 Hz, 6H). ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 157.1 (d, J = 98.4 Hz), 155.7 (d, J = 33.6 Hz), 149.2, 136.8, 123.7, 120.6, 115.9 (d, J = 756.0 Hz), 61.6 (d, J = 19.8 Hz), 17.6 (d, J = 28.2 Hz), 16.4 (d, J = 28.8 Hz) The analytical data are consistent with the literature.[8b]

*General Procedure for Asymmetric Hydrogenation of Compound **1**.* A stock solution was made by mixing $[Rh(COD)_2]PF_6$ with (*R*,*R*)-f-spiroPhos in a 1:1.1 molar ratio in solvent (CH_2Cl_2) at room temperature for 20 min in a nitrogen-filled glovebox. An aliquot of the catalyst solution (1.0 mL, 0.02 equiv, 0.0025 mmol) was transferred by syringe into the vials charged with different substrates **1** (1.0 equiv, 0.125 mmol for each) in anhydrous solvent (CH_2Cl_2) (2.0 mL). The vials were subsequently transferred into an autoclave and then hydrogen gas was charged. The reaction was then stirred under H_2 (80 atm) at r.t. for 24 h. The hydrogen gas was released slowly and carefully. The solution was passed through a short column of silica gel to remove the metal complex. The conversion of products was determined by GC or ^{1}H NMR analysis. The crude products were concentrated and purified by column chromatography, and the ee values were determined by HPLC or SFC analysis on a chiral stationary phase.[12d]

*General Procedure for Asymmetric Hydrogenation of Compound **3**.* A stock solution was made by mixing $[Rh(COD)_2]BF_4$ with (*R*,*R*)-f-spiroPhos in a 1:1.1 molar ratio in solvent (CH_2Cl_2) at room temperature for 20 min in a nitrogen-filled glovebox. An aliquot of the catalyst solution (1.0 mL, 0.01 equiv, 0.00125 mmol) was transferred by syringe into the vials charged with different substrates **3** (1.0 equiv, 0.125 mmol for each) in anhydrous solvent (CH_2Cl_2) (2.0 mL). The vials were subsequently transferred into an autoclave and then hydrogen gas was charged. The reaction was then stirred under H_2 (10 atm) at r.t. for 1 h. The hydrogen gas was released slowly and carefully. The solution was passed through a short column of silica gel to remove the metal complex. The conversion of products was determined by GC or ^{1}H NMR analysis. The crude products were concentrated and purified by column chromatography and the ee values were determined by HPLC or SFC analysis on a chiral stationary phase.[12d]

*(+)-Diethyl (2-phenyl-2-(m-tolyl)ethyl)phosphonate (**2a**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 40.7 mg, yield: 98%; 95% ee; $[\alpha]_D^{20}$ = +0.8 (c = 0.6, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 210 nm) t_R = 2.9 min (major), t_R = 2.5 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.27−7.24 (m, 4H), 7.18−7.13 (m, 2H), 7.07 (d, J = 7.9 Hz, 2H), 6.97 (d, J = 7.7 Hz, 1H), 4.39 (dt, J = 11.7, 7.5 Hz, 1H), 3.90−3.67 (m, 4H), 2.55 (dd, J = 18.2, 7.6 Hz, 2H), 2.29 (s, 3H), 1.09 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 144.3, 144.2, 144.1, 138.1, 128.6, 128.5, 127.8, 127.4, 126.6, 124.7, 61.4 (d, J = 6.5 Hz), 45.8−21.1 (m), 32.5 (d, J = 140.6 Hz), 29.8, 16.3 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 30.0; TOF-HRMS Calculated for $C_{19}H_{26}O_3P$ ($[M + H]^+$): 333.1614, found 333.1611.

*(−)-Diethyl (2-phenyl-2-(p-tolyl)ethyl)phosphonate (**2b**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 40.3 mg, yield: 97%; 94% ee; $[\alpha]_D^{20}$ = −2.2 (c = 0.6, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 5/95, flow rate = 3.0 mL/min, l = 210 nm) t_R = 6.5 min (major), t_R = 6.1 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.27−7.25 (m, 4H), 7.16 (d, J = 8.0 Hz, 3H), 7.07 (d, J = 7.9 Hz, 2H), 4.40 (dt, J = 11.6, 7.5 Hz, 1H), 3.89−3.68 (m, 4H), 2.55 (ddd, J = 18.4, 7.5, 1.1 Hz, 2H), 2.27 (s, 3H), 1.09 (td, J = 7.1, 2.4 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 144.4 (d, J = 9.7 Hz), 141.3 (d, J = 10.9 Hz), 136.1, 129.3, 128.6, 127.7, 127.5, 126.5, 61.4 (d, J = 6.5 Hz),

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J. Org. Chem. XXXX, XXX, XXX−XXX

45.1, 32.5 (d, J = 140.1 Hz), 21.0, 16.3 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 30.1; TOF-HRMS Calculated for $C_{19}H_{26}O_3P$ ($[M + H]^+$): 333.1614, found 333.1611.

*(−)-Diethyl (2-(4-fluorophenyl)-2-phenylethyl)phosphonate (**2c**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 40.3 mg, yield: 96%; 94% ee; $[\alpha]_D^{20}$ = −1.4 (c = 0.4, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 230 nm) t_R = 2.4 min (major), t_R = 2.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.27−7.17 (m, 7H), 6.95 (t, J = 8.7 Hz, 2H), 4.43 (dt, J = 11.5, 7.6 Hz, 1H), 3.90−3.72 (m, 4H), 2.56−2.49 (m, 2H), 1.10 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 161.6 (d, J = 244.8 Hz), 144.1 (d, J = 10.8 Hz), 139.9 (d, J = 10.1 Hz), 129.3 (d, J = 8.0 Hz), 128.7, 127.6, 126.8, 115.4 (d, J = 21.3 Hz), 61.4 (d, J = 5.6 Hz), 44.8 (d, J = 2.7 Hz), 32.6 (d, J = 140.8 Hz), 16.3 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 29.6; TOF-HRMS Calculated for $C_{18}H_{23}O_3FP$ ($[M + H]^+$): 337.1363, found 337.1360.

*(+)-Diethyl (2-(4-fluorophenyl)-2-phenylethyl)phosphonate (**2d**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 26.1 mg, yield: 62%; 90% ee; $[\alpha]_D^{20}$ = +0.1 (c = 3.8, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 210 nm) t_R = 2.6 min (major), t_R = 2.4 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.27−7.17 (m, 7H), 6.95 (t, J = 8.7 Hz, 2H), 4.43 (dt, J = 11.5, 7.6 Hz, 1H), 3.90−3.72 (m, 4H), 2.56−2.49 (m, 2H), 1.10 (t, J = 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 161.62 (d, J = 244.8 Hz), 144.05 (d, J = 10.8 Hz), 139.89 (d, J = 10.1 Hz), 129.26 (d, J = 8.0 Hz), 128.71, 127.59, 126.76, 115.35 (d, J = 21.3 Hz), 61.43 (d, J = 5.6 Hz), 44.82 (d, J = 2.7 Hz), 32.58 (d, J = 140.8 Hz), 16.28 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 29.6; TOF-HRMS Calculated for $C_{18}H_{23}O_3FP$ ($[M + H]^+$): 337.1363, found 337.1360.

*(+)-Diethyl (2-(3,5-dimethylphenyl)-2-phenylethyl)phosphonate (**2e**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 41.1 mg, yield: 95%; 92% ee; $[\alpha]_D^{20}$ = +0.8 (c = 0.6, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 15/85, flow rate = 3.0 mL/min, l = 230 nm) t_R = 2.0 min (major), t_R = 1.7 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30−7.24 (m, 5H), 7.17−7.13 (m, 1H), 6.88 (s, 2H), 6.80 (s, 1H), 4.36 (dt, J = 11.8, 7.5 Hz, 1H), 3.91−3.68 (m, 4H), 2.55 (ddd, J = 18.4, 7.5, 2.8 Hz, 2H), 2.25 (s, 6H), 1.09 (td, J = 7.1, 2.0 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 144.3 (d, J = 9.4 Hz), 144.1 (d, J = 11.0 Hz), 138.0, 128.6, 128.3, 127.8, 126.5, 125.5, 61.4 (d, J = 6.4 Hz), 45.4 (d, J = 2.6 Hz), 32.5 (d, J = 140.3 Hz), 21.4, 16.3 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 30.2; TOF-HRMS Calculated for $C_{20}H_{28}O_3P$ ($[M + H]^+$): 347.177, found 347.1775.

*(+)-Diethyl (2-(3,5-difluorophenyl)-2-phenylethyl)phosphonate (**2f**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as white solid, 41.6 mg, yield: 94%; MP: 62−64 °C; 92% ee; $[\alpha]_D^{20}$ = +4.5 (c = 0.2, CH_2Cl_2); HPLC (Lux 5u Amylose-1, isopropanol/hexane = 20/80, flow rate = 1.0 mL/min, l = 254 nm) t_R = 5.6 min (major), t_R = 6.4 min (minor); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.29−7.28 (m, 2H), 7.25−7.23 (m, 3H), 6.80−6.78 (m, 2H), 6.61−6.59 (m, 1H), 4.40 (dt, J = 11.4, 7.5 Hz, 1H), 3.93−3.72 (m, 4H), 2.50 (ddd, J = 18.5, 7.5, 2.5 Hz, 2H), 1.14−1.09 (m, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 163.9 (d, J = 13.5 Hz), 162.2 (d, J = 13.6 Hz), 148.2 (d, J = 10.5 Hz), 142.8 (d, J = 10.8 Hz), 128.3 (d, J = 186.4 Hz), 127.2, 111.2−109.1 (m), 102.1 (t, J = 25.7 Hz), 61.6 (dd, J = 15.0, 7.0 Hz), 45.3, 32.1 (d, J = 141.8 Hz), 16.3 (d, J = 6.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 28.88; TOF-HRMS Calculated for $C_{18}H_{22}O_3F_2P$ ($[M + H]^+$): 355.1269, found 355.1270.

*(−)-Diethyl (2-(3,5-dichlorophenyl)-2-phenylethyl)phosphonate (**2g**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow solid, 45.8 mg, yield: 95%; MP: 88−90 °C; 91% ee; $[\alpha]_D^{20}$ = −9.3 (c = 1.0, CH_2Cl_2); SFC (Lux 5u Amylose-2, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 230 nm) t_R = 3.1 min (major), t_R = 4.2 min (minor); ^{1}H NMR: (600 MHz, $CDCl_3$): δ (ppm) 7.30−7.29 (m, 2H), 7.25−7.22 (m, 3H), 7.17 (d, J = 1.9 Hz, 1H), 7.15 (d, J = 1.8 Hz, 2H), 4.38 (dt, J = 11.4, 7.5 Hz, 1H), 4.07−3.76 (m, 4H), 2.49 (ddd, J = 18.4, 7.5, 1.9 Hz, 2H), 1.13 (dt, J = 15.4, 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 147.5 (d, J = 9.7 Hz), 142.7 (d, J = 11.0 Hz), 135.0, 128.9, 127.6, 127.2, 126.9, 126.5, 62.8−58.5 (m), 39.0 (d, J = 1243.5 Hz), 30.6 (d, J = 163.3 Hz), 16.3 (d, J = 6.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 28.7; TOF-HRMS Calculated for $C_{18}H_{21}O_3NaPCl_2$ ($[M + Na]^+$): 409.0497, found 409.0501.

*(+)-Diethyl (2-(3,5-dichlorophenyl)-2-phenylethyl)phosphonate (**2h**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow solid, 44.4 mg, yield: 92%; MP: 88−90 °C; 97% ee; $[\alpha]_D^{20}$ = +10.1 (c = 0.7, CH_2Cl_2); SFC (Lux 5u Amylose-2, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 230 nm) t_R = 3.9 min (major), t_R = 3.0 min (minor); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.30−7.29 (m, 2H), 7.25−7.22 (m, 3H), 7.17 (d, J = 1.9 Hz, 1H), 7.15 (d, J = 1.8 Hz, 2H), 4.38 (dt, J = 11.4, 7.5 Hz, 1H), 4.07−3.76 (m, 4H), 2.49 (ddd, J = 18.4, 7.5, 1.9 Hz, 2H), 1.13 (dt, J = 15.4, 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 147.5 (d, J = 9.7 Hz), 142.7 (d, J = 11.0 Hz), 135.0, 128.9, 127.6, 127.2, 126.9, 126.5, 62.8−58.5 (m), 39.0 (d, J = 1243.5 Hz), 30.6 (d, J = 163.3 Hz), 16.3 (d, J = 6.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 28.7; TOF-HRMS Calculated for $C_{18}H_{21}O_3NaPCl_2$ ($[M + Na]^+$): 409.0497, found 409.0501.

*(−)-Diethyl (2-(4-fluorophenyl)-2-(p-tolyl)ethyl)phosphonate (**2i**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 40.7 mg, yield: 93%; 90% ee; $[\alpha]_D^{20}$ = −24.2 (c = 0.5, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 5/95, flow rate = 3.0 mL/min, l = 230 nm) t_R = 4.7 min (major), t_R = 5.2 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.24−7.20 (m, 2H), 7.13−7.06 (m, 4H), 6.96−6.92 (m, 2H), 4.39 (dt, J = 11.4, 7.6 Hz, 1H), 4.91−3.71 (m, 4H), 2.50 (dd, J = 18.4, 7.6 Hz, 2H), 2.27 (s, 3H), 1.11 (td, J = 7.1, 2.0 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 161.6 (d, J = 244.7 Hz), 141.1 (d, J = 11.4 Hz), 140.1 (dd, J = 9.4, 3.1 Hz), 136.3, 129.4, 129.2 (d, J = 7.9 Hz), 127.4, 115.3 (d, J = 21.2 Hz), 61.5, 44.4 (d, J = 2.6 Hz), 32.6 (d, J = 140.5 Hz), 21.0, 16.3 (d, J = 6.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 29.8; TOF-HRMS Calculated for $C_{19}H_{25}O_{3F}P$ ($[M + H]^+$): 351.1519, found 351.1521.

*(−)-Diethyl (2-(2-fluorophenyl)-2-phenylethyl)phosphonate (**2j**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 38.3 mg, yield: 91%; 99% ee; $[\alpha]_D^{20}$ = −4.4 (c = 0.5, CH_2Cl_2); SFC (Lux 5u Cellulose-4, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 210 nm) t_R = 3.3 min (major), t_R = 3.1 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31−7.24 (m, 5H), 7.19−7.05 (m, 2H), 7.07 (td, J = 7.5, 1.4 Hz, 1H), 6.97 (ddd, J = 10.7, 8.1, 1.3 Hz, 1H), 4.70 (dt, J = 11.7, 7.6 Hz, 1H), 3.93−3.74 (m, 4H), 2.69−2.51 (m, 2H), 1.13−1.09 (m, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ (ppm) 161.8, 143.0 (d, J = 10.9 Hz), 129.3, 129.1 (d, J = 4.3 Hz), 128.6, 128.3 (d, J = 8.4 Hz), 127.7, 126.8, 124.2, 115.8 (d, J = 22.5 Hz), 85.3−71.3 (m), 61.5 (dd, J = 9.3, 6.5 Hz), 39.3, 33.0−28.3 (m), 16.3 (d, J = 6.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 29.4; TOF-HRMS Calculated for $C_{18}H_{23}O_3FP$ ($[M + H]^+$): 337.1363, found 337.1360.

*(+)-Diethyl (2-(2-chlorophenyl)-2-phenylethyl)phosphonate (**2k**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 38.8 mg, yield: 88%; 99% ee; $[\alpha]_D^{20}$ = +19.0 (c = 0.4, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 210 nm) t_R = 3.3 min (major), t_R = 3.6 min (minor); ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm) 7.35−7.10 (m, 9H), 4.98 (dt, J = 11.7, 7.5 Hz, 1H), 3.95−3.76 (m, 4H), 2.56 (dd, J = 18.3, 7.5 Hz, 2H), 1.12 (ddd, J = 10.3, 7.5, 6.6 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 142.6 (d, J = 10.1 Hz), 141.4 (d, J = 10.4 Hz), 133.9, 130.0, 128.6, 128.5, 128.1, 127.8, 127.0, 126.8, 61.5 (t, J = 7.3 Hz), 41.4 (d, J = 2.4 Hz), 31.9 (d, J = 140.8 Hz), 16.3 (dd, J = 6.4, 2.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 29.0; TOF-HRMS Calculated for $C_{18}H_{23}O_3PCl$ ($[M + H]^+$): 353.1067, found 353.1066.

*(+)-Diethyl (2-(naphthalen-1-yl)-2-phenylethyl)phosphonate (**2l**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 41.4 mg, yield: 90%; >99.9%

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J. Org. Chem. XXXX, XXX, XXX−XXX

ee; $[\alpha]_D^{20}$ = +46.1 (*c* = 0.8, CH_2Cl_2); SFC (Lux 5u Amylose-2, MeOH/CO_2 = 3/97, flow rate = 3.0 mL/min, l = 230 nm) t_R = 27.8 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.23 (d, *J* = 8.0 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.72 (d, *J* = 9.4 Hz, 1H), 7.51−7.42 (m, 4H), 7.37−7.35 (m, 2H), 7.25 (d, *J* = 3.2 Hz, 2H), 7.18−7.11 (m, 1H), 5.29 (ddd, *J* = 12.2, 8.2, 6.5 Hz, 1H), 3.88−3.70 (m, 4H), 2.71−2.65 (m, 2H), 1.06 (dtd, *J* = 11.0, 7.1, 0.5 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 143.5 (d, *J* = 7.8 Hz), 140.0 (d, *J* = 11.9 Hz), 134.2, 131.3, 128.9, 128.5, 128.2, 127.5, 126.7, 126.3, 125.6, 125.3, 124.7, 123.8, 61.5 (d, *J* = 5.7 Hz), 40.7, 32.9 (d, *J* = 140.1 Hz), 16.2; ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 29.8; TOF-HRMS Calculated for $C_{22}H_{26}O_3P$ ([M + H]$^+$): 369.1614, found 369.1617.

*(R)-Diethyl (2-phenylpropyl)phosphonate (**4a**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 30.8 mg, yield: 97%; 94% ee; $[\alpha]_D^{20}$ = +18.6 (*c* = 0.5, CH_2Cl_2); HPLC (Lux 5u Amylose-1, isopropanol/hexane = 3/97, flow rate = 1.0 mL/min, l = 210 nm) t_R = 15.8 min (major), t_R = 17.1 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34−7.26 (m, 2H), 7.22−7.16 (m, 3H), 4.03−3.83 (m, 4H), 3.23−3.13 (m, 1H), 2.11−1.95 (m, 2H), 1.37 (d, *J* = 7.0 Hz, 3H), 1.26−1.17 (m, 6H); The analytical data are consistent with the literature.[8b]

*(R)-Diethyl (2-(3-methoxyphenyl)propyl)phosphonate (**4b**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 3.1 mg, yield: 96%; 96% ee; $[\alpha]_D^{20}$ = +22.6 (*c* = 0.7, CH_2Cl_2); SFC (Lux 5u Cellulose-2, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 230 nm) t_R = 2.4 min (major), t_R = 2.3 min (minor); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.20−7.17 (m, 1H), 6.81−6.70 (m, 3H), 4.01−3.89 (m, 4H), 3.78 (d, *J* = 10.9 Hz, 3H), 3.16 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.12−1.95 (m, 2H), 1.38−1.35 (m, 3H), 1.25−1.19 (m, 6H); The analytical data are consistent with the literature.[8c]

*(+)-Diethyl (2-(3-fluorophenyl)propyl)phosphonate (**4c**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 32.0 mg, yield: 94%; >99.9% ee; $[\alpha]_D^{20}$ = +26.5 (*c* = 0.4, CH_2Cl_2); SFC (Lux 5u Cellulose-2, MeOH/CO_2 = 2/98, flow rate = 2.0 mL/min, l = 254 nm) t_R = 13.6 min (major); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.25−7.22 (m, 1H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.92−6.86 (m, 2H), 4.02−3.89 (m, 4H), 3.23−3.18 (m, 1H), 2.10−1.96 (m, 2H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.22 (dt, *J* = 21.9, 7.0 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 163.0 (d, *J* = 245.3 Hz), 149.4 (dd, *J* = 12.7, 7.2 Hz), 130.1 (d, *J* = 8.9 Hz), 122.5 (d, *J* = 3.4 Hz), 113.7 (d, *J* = 21.7 Hz), 113.3 (d, *J* = 21.5 Hz), δ 61.5 (dd, *J* = 17.7, 7.2 Hz), 35.9−34.0 (m), 33.8, 23.5 (d, *J* = 10.4 Hz), 16.4 (t, *J* = 5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 30.3; TOF-HRMS Calculated for $C_{13}H_{21}O_3FP$ ([M + H]$^+$): 275.1206, found 275.1210.

*(+)-Diethyl (2-(2-fluorophenyl)propyl)phosphonate (**4d**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 33.0 mg, yield: 97%; 99% ee; $[\alpha]_D^{20}$ = +1.6 (*c* = 0.1, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 254 nm) t_R = 1.5 min (major), t_R = 1.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.23−7.12 (m, 2H), 7.08−7.03 (m, 1H), 7.00−6.95 (m, 1H), 4.01−3.90 (m, 4H), 3.45 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.23−1.98 (m, 1H), 1.40−1.37 (m, 3H), 1.23−1.19 (m, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 160.7 (d, *J* = 245.9 Hz), 133.1 (dd, *J* = 14.2, 11.3 Hz), 128.5 (d, *J* = 5.9 Hz), 128.0 (d, *J* = 9.0 Hz), 124.2 (d, *J* = 4.5 Hz), 115.6 (d, *J* = 22.8 Hz), 61.5 (dd, *J* = 11.9, 7.0 Hz), 32.8 (d, *J* = 139.4 Hz), 29.2, 22.1 (d, *J* = 10.5 Hz), 16.4 (d, *J* = 6.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 30.5; TOF-HRMS Calculated for $C_{13}H_{21}O_3FP$ ([M + H]$^+$): 275.1206, found 275.1210.

The gram scale hydrogenation of **3d** was performed according to the general procedure for asymmetric hydrogenation of **3** previously mentioned. The product **4d** was obtained as yellow oil in 97% yield, 0.98 g.

*(R)-Diethyl (2-(o-tolyl)propyl)phosphonate (**4e**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 31.2 mg, yield: 93%; 99.7% ee; $[\alpha]_D^{20}$ = +13.8 (*c* = 0.6, CH_2Cl_2); SFC (Lux 5u Cellulose-2, MeOH/CO_2 = 5/95, flow rate = 3.0 mL/min, l = 210 nm) t_R = 3.8 min (major), t_R = 4.0 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.17−7.04 (m, 4H), 4.02−3.83 (m, 4H), 3.51−3.40 (m, 1H), 2.35 (d, *J* = 4.0 Hz, 3H), 2.09−1.94 (m, 2H), 1.35−1.31 (m, 3H), 1.20 (ddt, *J* = 11.3, 7.1, 3.5 Hz, 6H); The analytical data are consistent with the literature.[8b]

*(R)-Diethyl (2-(4-fluorophenyl)propyl)phosphonate (**4f**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 32.3 mg, yield: 95%; 97% ee; $[\alpha]_D^{20}$ = +5.2 (*c* = 6.6, CH_2Cl_2); HPLC (Lux 5u Cellulose-2, isopropanol/hexane = 5/95, flow rate = 1.0 mL/min, l = 254 nm) t_R = 12.4 min (major), t_R = 11.5 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29−7.16 (m, 4H), 3.95 (dq, *J* = 21.0, 7.1 Hz, 4H), 3.23−3.13 (m, 1H), 2.06 (ddd, *J* = 25.8, 17.4, 8.4 Hz, 1H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.26−1.17 (m, 6H); The analytical data are consistent with the literature.[8b]

*(R)-Diethyl (2-(p-tolyl)propyl)phosphonate (**4g**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 30.5 mg, yield: 91%; 92% ee; $[\alpha]_D^{20}$ = +0.5 (*c* = 1.2, CH_2Cl_2); SFC (Lux 5u Cellulose-2, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 210 nm) t_R = 3.7 min (major), t_R = 3.5 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.10 (s, 4H), 4.47−3.86 (m, 4H), 3.21−3.11 (m, 1H), 2.30 (s, 3H), 2.13−1.94 (m, 2H), 1.36 (dd, *J* = 6.9, 0.6 Hz, 3H), 1.27−1.19 (m, 6H).The analytical data are consistent with the literature.[8b]

*(+)-Diethyl (2-(4-isobutylphenyl)propyl)phosphonate (**4h**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 35.7 mg, yield: 92%; 95% ee; $[\alpha]_D^{20}$ = +21.8 (*c* = 1.0, CH_2Cl_2); SFC (Lux 5u Cellulose-2, MeOH/CO_2 = 5/95, flow rate = 3.0 mL/min, l = 230 nm) t_R = 4.0 min (major), t_R = 3.7 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.11 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 4.02−3.82 (m, 4H), 3.17 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.42 (d, *J* = 7.1 Hz, 1H), 2.14−1.97 (m, 2H), 1.82 (dt, *J* = 13.5, 6.7 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.21 (dt, *J* = 15.8, 7.0 Hz, 6H), 0.87 (dd, *J* = 6.6, 0.7 Hz, 6H); ^{13}C{^{1}H}NMR (151 MHz, $CDCl_3$): δ (ppm) 144.1 (d, *J* = 11.8 Hz), 139.8, 129.3, 126.5, 61.4 (dd, *J* = 29.9, 6.4 Hz), 45.1, 34.9, 34.7−33.6 (m), 30.3, 29.8, 23.7 (d, *J* = 9.4 Hz), 22.4, 16.4 (d, *J* = 6.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 31.0; TOF-HRMS Calculated for $C_{17}H_{30}O_3P$ ([M + H]$^+$): 313.1927, found 313.1925.

*(+)-Diethyl (2-(3,4-dimethylphenyl)propyl)phosphonate (**4i**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 33.9 mg, yield: 96%; 94% ee; $[\alpha]_D^{20}$ = +20.5 (*c* = 0.8, CH_2Cl_2); HPLC (Lux 5u Amylose-2, isopropanol/hexane = 5/95, flow rate = 1.0 mL/min, l = 230 nm) t_R = 8.5 min (major), t_R = 9.1 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.04 (d, *J* = 7.7 Hz, 1H), 6.95−6.92 (m, 2H), 4.04−3.89 (m, 4H), 3.19−3.07 (m, 1H), 2.21 (d, *J* = 8.2 Hz, 6H), 2.14−1.92 (m, 2H), 1.35 (d, *J* = 7.0 Hz, 3H), 1.23 (dt, *J* = 15.6, 7.1 Hz, 6H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$): δ (ppm) 144.4 (d, *J* = 13.1 Hz), 136.6, 134.6, 129.8, 128.1, 123.9, 61.4 (dd, *J* = 19.5, 6.5 Hz), 35.1, 34.3 (d, *J* = 3.5 Hz), 33.7, 23.5 (d, *J* = 8.4 Hz), 19.6 (d, *J* = 52.0 Hz), 16.4 (dd, *J* = 6.3, 2.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 31.2; TOF-HRMS Calculated for $C_{15}H_{26}O_3P$ ([M + H]$^+$): 285.1614, found 285.1612.

*(R)-Diethyl (2-phenylbutyl)phosphonate (**4j**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 31.5 mg, yield: 94%; 99.2% ee; $[\alpha]_D^{20}$ = +2.9 (*c* = 1.3, CH_2Cl_2); SFC (Lux 5u Cellulose-1, MeOH/CO_2 = 3/97, flow rate = 2.5 mL/min, l = 210 nm) t_R = 7.9 min (major), t_R = 8.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29−7.25 (m, 2H), 7.19−7.15 (m, 3H), 3.97−3.70 (m, 4H), 2.95−2.84 (m, 1H), 2.15−2.00 (m, 2H), 1.88−1.78 (m, 1H), 1.66−1.55 (m, 1H), 1.15 (dt, *J* = 25.1, 7.1 Hz, 6H), 0.73 (t, *J* = 7.3 Hz, 3H); The analytical data are consistent with the literature.[8b]

*(+)-Diethyl (3-methyl-2-phenylbutyl)phosphonate (**4k**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 33.2 mg, yield: 94%; >99.9% ee; $[\alpha]_D^{20}$ = +2.5 (*c* = 2.2, CH_2Cl_2); SFC (Lux 5u Cellulose-2, MeOH/CO_2 = 3/97, flow rate = 2.0 mL/min, l = 210 nm) t_R = 9.4 min (major), t_R = 10.2 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31−7.23 (m, 3H), 7.18−7.13 (m, 2H), 3.89−3.56 (m, 2H), 2.80 (dd, *J* = 11.6, 5.9

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J. Org. Chem. XXXX, XXX, XXX−XXX

Hz, 1H), 2.37−1.97 (m, 2H), 1.97−1.76 (m, 1H), 1.12 (t, J = 7.0 Hz, 3H), 1.03 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.9 Hz, 3H), 0.71 (d, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ (ppm) 142.76, 128.70, 128.02, 126.42, 61.24 (d, J = 29.4 Hz), 46.76, 34.31 (d, J = 15.7 Hz), 29.76 (d, J = 141.4 Hz), 20.77, 19.76, 16.27 (d, J = 6.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) 32.0; TOF-HRMS Calculated for $C_{15}H_{26}O_3P$ ($[M + H]^+$): 285.1614, found 285.1612.

*(R)-Diethyl (2-methyl-4-phenylbutyl)phosphonate (**4l**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as colorless oil; 35.5 mg, yield: 99%; 75% ee; $[\alpha]_D^{20}$ = +7.20 (c = 1.0, CH_2Cl_2); HPLC (Lux 5u Cellulose-3, isopropanol/hexane = 1/99, flow rate = 0.5 mL/min, l = 210 nm) t_R = 14.684 min (major), t_R = 14.122 min (minor); ^1H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.28−7.24 (m, 2H), 7.18−7.14 (m, 3H), 4.04−4.00 (m, 4H), 2.64−2.52 (m, 2H), 1.93−1.83 (m, 1H), 1.79−1.73 (m, 2H), 1.67−1.56 (m, 2H), 1.25 (t, J = 7.1 Hz, 6H), 1.08 (d, J = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 142.3, 128.4, 125.8, 61.4, 40.0 (d, J = 4.0 Hz), 33.3, 33.1, 32.4, 28.0, 20.8, 17.0. The analytical data are consistent with the literature.[8b]

*(R)-Diethyl (2-(pyridin-2-yl)propyl)phosphonate (**4m**).* Purification by column chromatography (silica gel, PE:EA = 2:1) afforded the product as yellow oil, 27.1 mg, yield: 85%; 66% ee; $[\alpha]_D^{20}$ = +18.4 (c = 1.0, CH_2Cl_2); SFC (Lux 5u Amylose-1, MeOH/CO_2 = 10/90, flow rate = 3.0 mL/min, l = 210 nm) t_R = 2.084 min (major), t_R = 2.734 min (minor); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.50 (d, J = 4.0 Hz, 1H), 7.56 (t, J = 8.0 Hz 1H), 7.15 (d, J = 7.8 Hz, 1H), 7.07 (t, J = 8.1 Hz, 1H), 3.91 (q, J = 14.4 Hz, 4H), 3.39−3.19 (m, 1H), 2.40 (dd, J = 25.2, 8.2 Hz, 1H), 2.01 (dd, J = 25.2, 8.2 Hz, 1H), 1.37 (d, J = 6.9 Hz, 3H), 1.14 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ (ppm) 164.9 (d, J = 96.0 Hz), 149.3, 136.5, 122.1, 121.6, 61.4, 36.6, 32.2 (d, J = 553.8 Hz), 22.7 (d, J = 38.4 Hz), 16.4 (d, J = 24.0 Hz). The analytical data are consistent with the literature.[8b]

Method for Crystal Growth of the Product 2h. The crystal of enantiomerically enriched **2h** was obtained by diffusion from the mixture solvent of CH_2Cl_2 and hexane. The product **2h** was dissolved in CH_2Cl_2 followed by an addition of 1.0 mL hexane, and then placed in the refrigerator (about −4 °C) carefully.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01397.

NMR, SFC, and HPLC spectra PDF)

Accession Codes

CCDC 2089539 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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