Electronic Supplementary Information

Enantioselective Aza-Friedel–Crafts Reaction of Furan with α-Ketimino Esters Induced by a Conjugated Double Hydrogen Bond Network of Chiral Bis(phosphoric Acid) Catalysts

Manabu Hatano, Haruka Okamoto, Taro Kawakami, Kohei Toh, Hidefumi Nakatsuji, Akira Sakakura* and Kazuaki Ishihara*

Table of Contents:
1. General methods. S2
2. Preparation of chiral C₂-symmetric bis(phosphoric acid)s (R)-5 (Method 1). S3
3. Preparation of chiral C₂-symmetric bis(phosphoric acid)s (R)-5 (Method 2). S6
4. X-ray analysis of (R)-5c•(pyridine)₂ (Fig. 2). S9
5. Preparation of chiral C₁-symmetric bis(phosphoric acid)s (R)-9. S11
6. Preparation of chiral C₁-symmetric bis(phosphoric acid)s (R)-10. S15
7. Preparation of α-ketimino esters 1. S19
8. Representative procedures for the enantioselective aza-Friedel–Crafts reaction of 2 with 1 (Table1 and Eq. 1). S20
9. Screening of achiral catalysts in the probe reaction of 2 with 1a. S22
10. Screening of chiral catalysts in the probe reaction of 2 with 1a. S23
11. Screening of chiral catalysts in the probe reaction of 2 with 1b. S24
12. Calculation of the electrostatic potential of phosphoric acids. S25
13. Optimization of the concentration, drying agents, solvents, and substrates in the reaction of 2 with 1. S31
14. Preparation of (R)-6 (Scheme 1). S33
15. Non-linear effect in the reaction of 2 with 1a (Fig. 3). S35
16. ESI-MS analysis of catalysts. S37
17. Preparation of α-ketimino esters 7. S41
18. Representative procedures for the enantioselective aza-Friedel–Crafts reaction of 2 with 7 (Table 2 and Scheme 2). S46
19. Optimization of catalysts, protecting groups on substrates, and reaction temperature in the reaction of 2 with 7a. S53
20. Preparation of (R)-S32 and the control experiments. S57
21. Transformation of 3b to 12–14 by selective reduction (Scheme 3a). S59
22. Transformation of 14 to γ-butenolide 16 (Scheme 3a). S61
23. Transformation of 11 to 17 (Scheme 3b). S62
24. Transformation of 11 to 18 (Scheme 3c). S63
25. Transformation of 18a to 19 (Scheme 3d). S66
26. Gram-scale reaction and transformation to amino acid 21 (Scheme 4). S69
27. Theoretical study on the E/Z-geometry of substrates 1b and 7a. S71
28. Possible transition states for the reactions. S72
29. References. S73

Appendix A: ¹H and ¹³C spectra. S-A1 to S-A67
Appendix B: HPLC spectra. S-B1 to S-B16
1. General methods.

$^1$H NMR spectra were measured on a JEOL ECS400 (400 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration, and assignment. $^{13}$C NMR spectra were measured on a JEOL ECS400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.10 ppm). $^{19}$F NMR spectra were measured on a JEOL ECS-400 (376 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the external standard (CFCl₃ at 0 ppm). $^{31}$P NMR spectra were measured on a JEOL ECS-400 (161 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the external standard (H₃PO₄ at 0 ppm). High resolution mass spectral analyses were performed at Chemical Instrument Center, Nagoya University (JEOL JMS-700 (FAB), Bruker Daltonics micrOTOF-QII (ESI)). Infrared (IR) spectra were recorded on a JASCO FT/IR 460 plus spectrometer. In situ-IR analysis was performed by Mettler-Toledo ReactIR 15. High performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-M20A and chiral column of Daicel CHIRALCEL, CHIRALPAK; AD-H, AS-H, OD-H, OD-3, IA-3, IC-3. Optical rotations were measured on Rudolph Autopol IV digital polarimeter. DFT calculation was performed by Spartan’10 for Macintosh from Wavefunction, Inc. X-ray analysis was performed by Rigaku PILATUS-200K. The products were purified by column chromatography on silica gel (E. Merck Art. 9385; Kanto Chemical Co., Inc. 37560). For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), anisaldehyde, KMnO₄, and phosphomolybdic acid. In experiments that required dry solvents such as chloroform, dichloromethane, methanol, acetonitrile, etc. were distilled in prior to use. 2-Methoxyfuran is commercially available, and 2-ethoxyfuran was prepared according to the literature procedure.¹
2. Preparation of chiral $C_2$-symmetric bis(phosphoric acid)s ($R$)-5 (Method 1).

Preparation of ($R$)-$S_2$: A solution of ($R$)-$S_1$ (4.05 g, 5.45 mmol) and sodium hydride (ca. 60\% w/w oil dispersion, 480 mg, 12 mmol) in THF (55 mL) was stirred at 0 °C for 30 min under a nitrogen atmosphere. Diallyl chlorophosphate $^2$ (3.55 mL, 21.7 mmol) was slowly added at 0 °C, and the mixture was stirred at room temperature for 4 h. The resulting mixture was then cooled in ice bath, and diluted with ethyl acetate (40 mL) and water (20 mL). The product was extracted with ethyl acetate (20 mL $\times$ 2) and washed with brine (20 mL). The combined extracts were dried over Na$_2$SO$_4$. The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: $n$-hexane:EtOAc = 5:1 to 3:1) to give the product ($R$)-$S_2$ as colorless solid (4.05 g, 70\% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.17-3.24 (m, 2H), 3.49-3.60 (m, 4H), 3.73-3.81 (m, 2H), 4.75-4.84 (m, 8H), 5.15-5.25 (m, 2H), 5.26-5.38 (m, 2H), 7.32-7.42 (m, 8H), 7.44-7.50 (m, 10H), 7.73 (d, $J = 7.3$ Hz, 8H), 7.84 (t, $J = 1.4$ Hz, 2H), 7.90 (d, $J = 8.2$ Hz, 2H), 7.92 (d, $J = 1.4$ Hz, 4H), 8.06 (s, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) Many peaks overlapped. $\delta$ 67.4, 67.7, 124.7, 125.3, 126.1, 126.9, 127.3, 127.5, 127.6, 127.7, 128.9, 131.3, 131.6, 132.0, 132.3, 133.7, 134.7, 139.3, 141.1, 145.4. $^{31}$P NMR (160 MHz, CDCl$_3$) $\delta$ -5.8. HRMS (FAB+) calcd for C$_{68}$H$_{57}$O$_8$P$_2$ [M+H]$^+$ 1063.3529, found 1063.3527.

Preparation of ($R$)-3,3'-di(3,5-terphenyl)-1,1'-binaphthyl-2,2'-bis(phosphoric acid) (($R$)-5a): Pyrrolidine (690 µL, 8.4 mmol) and tetrakis(triphenylphosphine)palladium (0) (1.76 g, 1.52 mmol) was added to a solution of ($R$)-$S_2$ (4.05 g, 3.80 mmol) in N,N-dimethylformamide (38 mL) at 0 °C. The reaction mixture was stirred at room temperature for 4 h. The solution was put onto a column with the anion exchange resin (DOWEX Cl$^-$ form), which was prepared in advance. The sample-mounted resin was washed with THF (300 mL). Then THF and 12 M HCl aqueous solution (v/v = 10/1, 500 mL) was passed through the resin, and the filtrate was collected. The
acidic layer was concentrated under reduced pressure, and extracted with dichloromethane (20 mL × 2) and washed with 1 M HCl aqueous solution (10 mL). The resulting organic layer was concentrated under reduced pressure. The obtained product was dissolved in toluene (20 mL), and the volatiles were thoroughly removed under reduce pressure. The product was dissolved in dichloromethane (10 mL), and the excess amount of n-hexane was added to give of (R)-5a as a white-yellow powder (3.02 g, 88% yield). A trace amount of Et₂O remained. ¹H NMR (400 MHz, THF-d₈) δ 3.50-5.00 (br, 4H), 7.30-7.37 (m, 4H), 7.38-7.51 (m, 12H), 7.57 (d, J = 8.2 Hz, 2H), 7.81 (d, J = 7.6 Hz, 8H), 7.88 (s, 2H), 8.00-8.04 (m, 6H), 8.23 (s, 2H). ¹³C NMR (100 MHz, THF-d₈) δ 125.7 (2C), 126.1 (2C), 126.5 (2C), 126.7 (2C), 127.6 (2C), 128.0 (4C), 128.2 (8C), 129.0 (6C), 129.5 (8C), 132.4 (2C), 132.7 (2C), 133.6 (2C), 136.4 (2C), 140.4 (2C), 142.3 (4C), 142.4 (4C), 147.4 (2C) [Contamination of a trace amount of acetone (δ 30.2) through the ¹³C NMR analysis.]. ³¹P NMR (160 MHz, THF-d₈) δ –0.13. IR (KBr) 3448, 3052, 2890, 1496, 1423, 1359, 1246, 1194, O P O P OH OH (R)-3,3’-Diphenyl-1,1’-binaphthyl-2,2’-bis(phosphoric acid) ((R)-S3): Prepared by Method 1. 83% yield for the first step and 97% yield for the second step. A trace amount of n-hexane remained. White-yellow soild. ¹H NMR (400 MHz, THF-d₈) δ 7.31 (t, J = 7.3 Hz, 2H), 7.37-7.41 (m, 6H), 7.47 (t, J = 6.9 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 6.9 Hz, 4H), 7.97 (d, J = 8.2 Hz, 2H), 8.02 (s, 2H) (Four P-OH moieties were not clearly observed.). ¹³C NMR (100 MHz, THF-d₈) δ 125.5 (2C), 125.9 (2C), 126.2 (2C), 126.9 (2C), 126.2 (2C), 126.9 (2C), 127.5 (2C), 128.1 (4C), 128.6 (2C), 130.6 (4C), 131.6 (2C), 132.2 (2C), 133.0 (2C), 136.3 (2C), 139.1 (2C), 146.9 (2C). ³¹P NMR (160 MHz, THF-d₈) δ –0.2. IR (KBr) 3448, 3052, 2890, 1496, 1423, 1359, 1246, 1194, 1034, 1002 cm⁻¹. [α]D²⁷ = +178.8 (c 1.00, THF). M.p. 218 °C (decomposition). HRMS (FAB–) calcd for C₅₆H₃₉O₈P₂ [M–H]– 901.2120, found 901.2138.

Preparation of anion exchange resin: Commercially available DOWEX Cl⁻ form ion-exchange resin (ca. 100 mL) in a column was washed with 1 M HCl aqueous solution (200 mL) until the yellow eluate would be colorless. The resin was washed with water (200 mL) until the acidic eluate would be neutral by monitoring with pH test paper. The resin was washed with 1 M NaOH aqueous solution (200 mL) and then water (500 mL) until the basic eluate would be neutral by monitoring with pH test paper. 

![Diagram of (R)-3,3'-Diphenyl-1,1'-binaphthyl-2,2'-bis(phosphoric acid) ((R)-S3)](image-url)
1149, 1033 cm$^{-1}$. M.p. 171 °C (decomposition). $[\alpha]_D^{27} = +174.7$ (c 1.00, THF). HRMS (FAB–) calcd for C$_{32}$H$_{23}$O$_8$P$_2$ [M–H]$^-$ 597.0874, found 597.0891.

(R)-3,3’-Di(4-biphenyl)-1,1’-binaphthyl-2,2’-bis(phosphoric acid) ((R)-S4): Prepared by Method 1. 35% yield for the first step and 83% yield for the second step. A trace amount of DMF remained. White-yellow powder. $^1$H NMR (400 MHz, THF-d$_8$) $\delta$ 4.50-5.02 (br, 4H), 7.31 (t, $J = 7.3$ Hz, 2H), 7.39-7.46 (m, 6H), 7.48 (t, $J = 6.9$ Hz, 2H), 7.58 (d, $J = 8.2$ Hz, 2H), 7.66-7.76 (m, 8H), 7.82 (d, $J = 8.2$ Hz, 4H), 8.00 (d, $J = 8.2$ Hz, 2H), 8.10 (s, 2H). $^{13}$C NMR (100 MHz, THF-d$_8$) $\delta$ 125.9 (2C), 126.3 (2C), 126.6 (2C), 127.0 (4C), 127.3 (2C), 127.6 (4C), 127.9 (2C), 128.9 (2C), 129.4 (4C), 131.4 (4C), 132.0 (2C), 132.6 (2C), 133.3 (2C), 136.2 (2C), 138.5 (2C), 140.6 (2C), 141.7 (2C), 147.2 (2C). $^{31}$P NMR (160 MHz, THF-d$_8$) $\delta$ 0.1. IR (KBr) 3411, 3029, 1489, 1194, 1034 cm$^{-1}$. M.p. 206 °C (decomposition). $[\alpha]_D^{27} = +177.1$ (c 1.00, THF). HRMS (FAB–) calcd for C$_{44}$H$_{31}$O$_8$P$_2$ [M–H]$^-$ 749.1494, found 749.1488.
3. Preparation of chiral \( C_2 \)-symmetric bis(phosphoric acid)s \((R)-5\) (Method 2).

Preparation of \((R)-6\):
A solution of \((R)-5\) (2.27 g, 3.02 mmol) and sodium hydride (ca. 60\% w/w oil dispersion, 266 mg, 6.65 mmol) in THF (30 mL) was stirred at 0 °C for 30 min under a nitrogen atmosphere. Diallyl chlorophosphate (1.97 mL, 12.0 mmol) was slowly added at 0 °C, and the mixture was stirred at room temperature for 4 h. The resulting mixture was then cooled in ice bath, and diluted with ethyl acetate (40 mL) and water (20 mL). The product was extracted with ethyl acetate (20 mL \( \times \) 2) and washed with brine (20 mL). The product was extracted with ethyl acetate (20 mL \( \times \) 2) and washed with brine (20 mL). The combined extracts were dried over Na\(_2\)SO\(_4\). The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: \( n \)-hexane:EtOAc = 20:1 to 10:1) to give the product \((R)-6\) as colorless solid (2.39 g, 87\% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.62-1.92 (m, 8H), 2.09-2.23 (m, 2H), 2.51-2.66 (m, 2H), 2.73-2.95 (m, 4H), 3.50-3.59 (m, 1H), 3.64-3.73 (m, 1H), 3.74-3.87 (m, 2H), 4.83-4.90 (m, 2H), 4.99-5.07 (m, 2H), 5.27-5.39 (m, 1H), 5.48-5.59 (m, 1H), 6.61 (s, 1H), 7.22-7.26 (m, 2H), 7.32-7.47 (m, 2H), 7.65-7.72 (m, 8H), 7.72-7.77 (m, 4H), 7.82-7.85 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) Many peaks overlapped. \( \delta \) 22.7, 23.0, 23.2, 23.4, 27.1, 27.4, 29.6, 29.8, 67.5 (d, \( J_{C-P} = 5.7 \) Hz), 68.2 (d, \( J_{C-P} = 5.7 \) Hz), 117.5, 117.6, 124.7, 125.2, 127.2, 127.4, 127.5, 127.6, 127.7, 128.7, 128.9, 129.8, 130.4, 130.8, 131.0, 131.6, 131.8, 131.9 (d, \( J_{C-P} = 7.6 \) Hz), 132.3 (d, \( J_{C-P} = 8.6 \) Hz), 135.7, 136.0, 138.0,
Preparation of (R)-S7: To a solution of (R)-S6 (2.20 g, 2.41 mmol) and triethylamine (1.34 mL, 9.6 mmol) in THF (6 mL) was added phosphorus trichloride (255 µL, 2.92 mmol) at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 30 min, and then allyl alcohol (670 µL, 9.85 mmol) was slowly added at 0 °C. The mixture was stirred at room temperature for 1 h. The resulting mixture was diluted with ethyl acetate (40 mL) and water (20 mL). The product was extracted with ethyl acetate (20 mL × 2) and washed with brine (20 mL). The combined extracts were dried over Na2SO4. The organic phase was concentrated under reduced pressure to give a colorless solid mixture of products (R)-S7 and its partially air-oxidized compound (i.e., (R)-S8), which were used for the next step without the further purification.

Preparation of (R)-S8: A solution of the obtained (R)-S7 (and (R)-S8) (2.41 mmol based on (R)-S6) in dichloromethane (24 mL) was added tert-butyl hydroperoxide (TBHP, ca. 5.5 M in nonane solution, 870 µL, 4.79 mmol) at 0 °C. The mixture was stirred at room temperature for 30 min. The resulting mixture was diluted with ethyl acetate (40 mL) and saturated Na2S2O3 aqueous solution (10 mL). The product was extracted with ethyl acetate (20 mL × 2) and washed by brine (20 mL). The combined extracts were dried over Na2SO4. The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1 to 2:1) to give the desired product (R)-S8 as colorless solid (1.41 g, 55% yield based on 2.41 mmol of (R)-S6). 1H NMR (400 MHz, CDCl3) δ 1.71-1.86 (m, 8H), 2.31-2.45 (m, 2H), 2.70-2.91 (m, 6H), 3.52-3.61 (m, 2H), 3.70-3.88 (m, 6H), 4.83-4.91 (m, 4H), 4.95-5.07 (m, 4H), 5.34-5.45 (m, 2H), 5.48-5.59 (m, 2H), 7.16 (s, 2H), 7.37 (t, J = 7.3 Hz, 8H), 7.69 (d, J = 7.3 Hz, 8H), 7.72-7.78 (m, 6H). 13C NMR (100 MHz, CDCl3) δ 22.8 (2C), 23.0 (2C), 27.6 (2C), 29.6 (2C), 67.4 (d, J_C-P = 5.7 Hz, 2C), 67.5 (d, J_C-P = 5.7 Hz, 2C), 117.2 (2C), 117.5 (2C), 125.0 (2C), 127.4 (8C), 127.5 (4C), 128.0 (4C), 128.9 (8C), 129.1 (2C), 131.9 (2C), 132.1 (2C), 132.4 (d, J_C-P = 7.6 Hz, 2C), 132.6 (d, J_C-P = 8.5 Hz, 2C), 134.9 (2C), 138.5 (2C), 139.5 (2C), 141.1 (4C), 141.6 (4C), 144.1 (d, J_C-P = 7.6 Hz, 2C). 31P NMR (160 MHz, CDCl3) δ −6.12. IR (KBr) 3448, 3059, 3033, 2935, 2860, 1734, 1594, 1492, 1452, 1423, 1409, 1278, 1196, 1031 cm⁻¹. M.p. 238-240 °C. [α]D = −87.2 (c 1.00, CHCl3). HRMS (ESI+) calcd for C62H56O8P2 [M+H]+ 1071.4148, found 1071.4138.
Preparation of (R)-3,3’-di(3,5-terphenyl)-1,1’-(5,5’,6,6’,7,7’,8,8’-octahydro-binaphthyl)-2,2’-bis(phosphoric acid) ((R)-5c): (R)-S8 was used for the next step with the same procedure described above, and (R)-5c was obtained as a white-yellow powder (0.937 g, 78% yield). A small amount (4%) of inseparable n-hexane remained, and the purity of (R)-5c was 95% (i.e., 74% yield equivalent). \(^1\)H NMR (400 MHz, THF-\(d_8\)) \(\delta\) 1.60-1.91 (m, 8H), 2.10-2.20 (m, 2H), 2.75-2.98 (m, 6H), 7.27 (t, \(J = 7.3\) Hz, 4H), 7.32 (t, \(J = 7.3\) Hz, 8H), 7.44 (t, \(J = 7.3\) Hz, 8H), 7.74-7.85 (m, 14H), 9.01 (br, 4H). \(^{13}\)C NMR (100 MHz, THF-\(d_8\)) \(\delta\) 23.8 (2C), 24.1 (2C), 28.1 (2C), 30.4 (2C), 125.2 (2C), 127.9 (4C), 128.1 (8C), 128.8 (4C), 129.4 (8C), 130.8 (2C), 132.7 (2C), 133.9 (2C), 135.1 (2C), 137.1 (2C), 140.9 (2C), 142.0 (4C), 142.5 (4C), 146.2 (2C). \(^{31}\)P NMR (160 MHz, THF-\(d_8\)) \(\delta\) 0.32. IR (KBr) 3621, 3419, 2928, 2857, 1594, 1497, 1449, 1409, 1035 cm\(^{-1}\). M.p. 194 °C (decomposition). \([\alpha]_D^{23} = -99.2\) (c 1.00, THF). HRMS (FAB–) calcd for C\(_{56}\)H\(_{47}\)O\(_8\)P\(_2\) [M–H]\(^–\) 909.2746, found 909.2729.

(R)-3,3’-Di(3,5-di(\(o\)-tolyl)phenyl)-1,1’-binaphthyl-2,2’-bis(phosphoric acid) ((R)-5b): Prepared by Method 2. A trace amount of \(n\)-hexane, DMF, and EtOAc remained. A white-yellow powder. \(^1\)H NMR (400 MHz, THF-\(d_8\)) \(\delta\) 2.39 (s, 12H), 7.18-7.64 (m, 26H), 7.56 (d, \(J = 8.7\) Hz, 2H), 7.62 (d, \(J = 1.8\) Hz, 4H), 7.98 (d, \(J = 8.2\) Hz, 2H), 8.14 (s, 2H). \(^{13}\)C NMR (100 MHz, THF-\(d_8\)) \(\delta\) 20.9 (4C), 125.8 (2C), 126.4 (6C), 126.6 (2C), 127.5 (2C), 127.9 (4C), 128.9 (2C), 129.7 (2C), 130.6 (8C), 131.0 (4C), 132.0 (2C), 132.6 (2C), 133.5 (2C), 136.4 (4C), 136.8 (2C), 139.3 (2C), 142.2 (4C), 143.0 (4C), 147.4 (2C). \(^{31}\)P NMR (160 MHz, THF-\(d_8\)) \(\delta\) –0.08. IR (KBr) 3057, 2923, 2237, 1594, 1493, 1451, 1399, 1239, 1189, 1151, 1097, 1042 cm\(^{-1}\). M.p. 223 °C (decomposition). \([\alpha]_D^{28} = +242.3\) (c 1.00, CHCl\(_3\)). HRMS (ESI–) calcd for C\(_{60}\)H\(_{47}\)O\(_8\)P\(_2\) [M–H]\(^–\) 957.2752, found 952.2756.
4. X-ray analysis of \((R)-5c\cdot(pyridine)_{2}\) (Fig. 2).

Crystal data of \((R)-5c\cdot(pyridine)_{2}\) (Fig. S1): Compound \((R)-5c\cdot(pyridine)_{2}\) was recrystallized in benzene for X-ray analysis. Formula C_{67}H_{60}Cl_{2}N_{2}O_{8}P_{2}, colorless, crystal dimensions 0.20 × 0.20 × 0.20 mm^{3}, orthorhombic, space group \(P2_12_12_1\) (#19), \(a = 11.4778(15)\) Å, \(b = 13.6448(18)\) Å, \(c = 36.849(5)\) Å, \(\alpha = 90.00\) °, \(\beta = 90.00\) °, \(\gamma = 90.00\) °, \(V = 5771.0(13)\) Å^{3}, \(Z = 4\), \(\rho_{\text{calc}} = 1.328\) g cm^{-3}, \(F(000) = 2416\), \(\mu(\text{MoK}\alpha) = 0.228\) mm^{-1}, \(T = 123\) K. 39877 reflections collected, 12226 independent reflections with \(I > 2\sigma(I)\) (\(2\theta_{\text{max}} = 27.53\) °), and 746 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. Flack x = –0.001(17). \(R_1 = 0.0374\) and \(wR_2 = 0.0884\). GOF =1.017. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1520625. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Web page: http://www.ccdc.cam.ac.uk/].
Fig. S1  ORTEP drawing of (R)-5c•(pyridine)$_2$. (a) Side view. (b) Top view. Some hydrogen atoms were omitted for clarity.
5. Preparation of chiral $C_1$-symmetric bis(phosphoric acid)s ($R$)-9.

**Method A**

![Chemical structure of ($R$)-S9a](image1)

[Chemical structure of ($R$)-S10a](image2)

**Preparation of ($R$)-S10a: A solution of chiral diol ($R$)-S9a$^3$ (1.67 g, 3.25 mmol) and sodium hydride (ca. 60% w/w oil dispersion, 400 mg, 9.9 mmol) in THF (33 mL) was stirred at 0 °C for 3 h under a nitrogen atmosphere. Diallyl chlorophosphate$^2$ (1.30 mL, 7.9 mmol) was slowly added at 0 °C, and the mixture was stirred at room temperature for 9 h. The resulting mixture was then cooled in ice bath, and diluted with ethyl acetate (20 mL) and water (10 mL). The product was extracted with ethyl acetate (10 mL × 2) and washed with brine (10 mL). The combined extracts were dried over Na$_2$SO$_4$. The organic phase was concentrated under reduced pressure, and the crude was roughly purified by short silica gel column chromatography (eluent: n-hexane:EtoAc = 5:1). Impure ($R$)-S10a was obtained in ca. 75% yield (2.0 g).

**Preparation of ($R$)-9a: Pyrrolidine (430 µL, 5.3 mmol) and tetrakis(triphenylphosphine)palladium (0) (1.1 g, 0.96 mmol) was added to a solution of ($R$)-S10a (impure, 2.0 g, 2.4 mmol) in $N,N$-dimethylformamide (24 mL) at 0 °C. The reaction mixture was stirred at room temperature for 5 h. The solution was put onto a column with the anion exchange resin (DOWEX Cl$^-$ form. See below for the preparation of the resin), which was prepared in advance. The sample-mounted resin was washed with THF (300 mL). Then THF and 12 M HCl aqueous solution (v/v = 10/1, 500 mL) was passed through the resin, and the filtrate was collected. The acidic layer was concentrated under reduced pressure, and extracted with dichloromethane (20 mL × 2) and washed with 1 M HCl aqueous solution (10 mL). The resulting organic layer was concentrated under reduced pressure. The obtained product was dissolved in toluene (20 mL), and the volatiles were thoroughly removed under reduced pressure. The product was dissolved in dichloromethane (10 mL), and the excess amount of n-hexane was added to give pure ($R$)-9a as a white-yellow powder (0.924 g, 42% yield in two steps).
(R)-3-(3,5-Ter phenyl)-1,1'-binaphthyl-2,2'-bis(phosphoric acid) ((R)-9a): Light brown solid. 

$^1$H NMR (400 MHz, THF-$d_8$) δ 7.18 (d, $J = 8.7$ Hz, 1H), 7.23-7.50 (m, 11H), 7.59 (d, $J = 8.7$ Hz, 1H), 7.80 (d, $J = 7.3$ Hz, 4H), 7.87 (s, 1H), 7.94 (d, $J = 7.8$ Hz, 1H), 7.95-8.05 (m, 4H), 8.19 (s, 1H), 9.81 (brs, 4H). 

$^{13}$C NMR (100 MHz, THF-$d_8$) Peaks are overlapped. δ 122.4, 124.0 (d, $J_{C-P} = 5.7$ Hz), 125.6, 125.9, 126.4, 126.5, 127.4, 127.6, 128.0, 128.1, 128.9, 129.0, 129.5, 130.6, 132.2, 132.5, 133.9, 134.4, 136.2, 140.3, 142.2, 142.3, 147.2 (d, $J_{C-P} = 6.7$ Hz), 149.2 (d, $J_{C-P} = 5.7$ Hz). 

$^{31}$P NMR (160 MHz, THF-$d_8$) δ −2.07, 1.27. IR (KBr) 3058, 2923, 2851, 2240, 1595, 1404, 1237, 1032, 998 cm$^{-1}$. M.p. was not available due to decomposition. $[\alpha]_D^{27} = +186.8$ (c 1.00, CHCl$_3$).

HRMS (FAB+) calcd for C$_{38}$H$_{29}$O$_8$P$_2$ [M+H]$^+$ 675.1338, found 675.1326.

**Method B**

![Chemical structure](image)

Preparation of (R)-S11b, (R)-S11b', and (R)-S10b (or (R)-S11c, (R)-S11c', and (R)-S10c): A solution of chiral diol (R)-S9b (Ar = 2,4,6-iPr$_3$C$_6$H$_2$) (3.8 mmol) and sodium hydride (ca. 60% w/w oil dispersion, 440 mg, 11 mmol) in THF (38 mL) was stirred at 0 °C for 3 h under a nitrogen atmosphere. Diallyl chlorophosphate (1.8 mL, 9.1 mmol) was slowly added at 0 °C, and the mixture was stirred at room temperature for 7 h. The resulting mixture was then cooled in ice bath, and diluted with ethyl acetate (20 mL) and water (10 mL). The product was extracted with ethyl acetate (10 mL $\times$ 2) and washed with brine (10 mL). The combined extracts were dried over Na$_2$SO$_4$. The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1) to give the
mixture of (R)-S11b, (R)-S11b', and (R)-S10b (or (R)-S11c, (R)-S11c', and (R)-S10c) which was used for the next step without the further purification.

Preparation of (R)-S12b, (R)-S12b', and (R)-S10b (or (R)-S12c, (R)-S12c', and (R)-S10c): To a solution of the mixture of (R)-S11b, (R)-S11b', and (R)-S10b (or (R)-S11c, (R)-S11c', and (R)-S10c) (based on 3.8 mmol of starting (R)-S9b (or (R)-S9c)) and triethylamine (2.6 mL, 19 mmol) in THF (38 mL) was added phosphorus trichloride (460 µL, 5.3 mmol) at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 30 min, and then allyl alcohol (1.6 mL, 19 mmol) was slowly added at 0 °C. The mixture was stirred at room temperature for 1 h. The resulting mixture was diluted with ethyl acetate (40 mL) and water (20 mL). The product was extracted with ethyl acetate (20 mL × 2) and washed with brine (20 mL). The combined extracts were dried over Na2SO4. The organic phase was concentrated under reduced pressure, and the crude products (R)-S12b, (R)-S12b', and (R)-S10b (or (R)-S12c, (R)-S12c', and (R)-S10c) were used for the next step without the further purification.

Preparation of (R)-S10b or (R)-S10c: A solution of the obtained crude products S12b, S12b', and (R)-S10b (or (R)-S12c, (R)-S12c', and (R)-S10c) (based on 3.8 mmol of starting (R)-S9b (or (R)-S9c)) in dichloromethane (38 mL) was added tert-butyl hydroperoxide (TBHP, ca. 5.5 M in nonane solution, 3.5 mL, 19 mmol) at 0 °C. The mixture was stirred at room temperature for 30 min. The resulting mixture was diluted with ethyl acetate (40 mL) and saturated Na2S2O3 aqueous solution (10 mL). The product was extracted with ethyl acetate (20 mL × 2) and washed by brine (20 mL). The combined extracts were dried over Na2SO4. The organic phase was concentrated under reduced pressure, and the crude was roughly purified by short silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1) to give (R)-S10b (or (R)-S10c) (impure).

Preparation of (R)-9b or (R)-9c: (R)-9b and (R)-9c were prepared by the similar procedure for (R)-9a described above.

(R)-3-(2,4,6-Triisopropylphenyl)-1,1'-binaphthyl-2,2'-bis(phosphoric acid) ((R)-9b): Prepared by Method B (Typically 45–55% yield in four steps from (R)-S9b). Light brown solid. 1H NMR (400 MHz, THF-d8) δ 1.00 (d, J = 6.9 Hz, 3H), 1.23 (d, J = 6.9 Hz, 3H), 1.25 (d, J = 6.9 Hz, 3H), 1.27 (d, J = 6.9 Hz, 9H), 2.84 (septet, J = 6.9 Hz, 1H), 2.91 (septet, J = 6.9 Hz, 1H), 2.97 (septet, J = 6.9 Hz, 1H), 7.03 (d, J = 1.4 Hz, 1H), 7.13 (d, J = 1.4 Hz, 1H), 7.17 (d, J = 8.3 Hz, 1H), 7.20 (d, J = 8.7 Hz, 1H), 7.22-7.31 (m, 2H), 7.34-7.45 (m, 2H), 7.61 (d, J = 9.2 Hz, 1H), 7.80 (brs,
4H), 7.84-7.95 (m, 3H), 7.98 (d, $J = 9.2$ Hz, 1H). $^{13}$C NMR (100 MHz, THF-$d_8$) Peaks are overlapped. $\delta$ 23.6, 23.8, 24.5, 24.6, 25.5, 27.4, 31.9, 32.0, 35.4, 120.7, 121.7, 122.6, 123.7 (d, $J_{C-P} = 6.7$ Hz), 125.4 (d, $J_{C-P} = 3.8$ Hz), 125.7, 126.3, 126.7, 127.0, 128.7, 128.8, 130.4, 132.0, 132.2, 132.5, 133.1, 133.9, 134.5, 134.7, 148.2, 148.3 (d, $J_{C-P} = 6.7$ Hz), 148.9, 149.0, 149.3 (d, $J_{C-P} = 5.7$ Hz). $^{31}$P NMR (160 MHz, THF-$d_8$) $\delta$ –3.42, 0.78. IR (KBr) 3462, 2961, 2869, 1603, 1509, 1466, 1415, 1362, 1210, 1001 cm$^{-1}$. M.p. was not available due to decomposition. [$\alpha$]$^D_{24} = +257.2$ (c 1.00, CHCl$_3$). HRMS (FAB+) calcd for C$_{35}$H$_{39}$O$_8$P$_2$ [M+H]$^+$ 649.2120, found 649.2119.

(R)-3-(2,4,6-Tricyclohexylphenyl)-1,1’-binaphthyl-2,2’-bis(phosphoric acid) ((R)-9c):
Prepared by Method B (Typically 25–35% yield in four steps from (R)-S9c). Light brown solid. $^1$H NMR (400 MHz, THF-$d_8$) $\delta$ 1.01-2.00 (m, 28H), 2.11 (d, $J = 12.4$ Hz, 2H), 2.38-2.61 (m, 3H), 6.90 (br, 4H), 6.99 (s, 1H), 7.07 (s, 1H), 7.15 (d, $J = 8.2$ Hz, 1H), 7.21-7.34 (m, 3H), 7.36-7.48 (m, 2H), 7.57 (d, $J = 9.2$ Hz, 1H), 7.83 (s, 1H), 7.88 (d, $J = 8.2$ Hz, 1H), 7.93 (d, $J = 8.3$ Hz, 1H), 8.00 (d, $J = 9.2$ Hz, 1H). $^{13}$C NMR (100 MHz, THF-$d_8$) Peaks are overlapped. $\delta$ 27.2, 27.3, 27.5, 27.8, 28.0, 28.2, 33.4, 34.1, 35.5, 35.6, 36.5, 38.3, 42.7, 42.9, 45.9, 122.0, 122.8, 123.2, 124.0 (d, $J_{C-P} = 6.7$ Hz), 125.2 (d, $J_{C-P} = 4.8$ Hz), 125.8, 126.2, 126.5, 126.7, 127.0, 127.3, 128.7, 128.9, 130.3, 131.9, 132.2, 132.9, 133.5, 133.9, 134.5, 147.0, 147.7, 148.2, 148.3 (d, $J_{C-P} = 6.7$ Hz), 149.3 (d, $J_{C-P} = 6.7$ Hz). $^{31}$P NMR (160 MHz, THF-$d_8$) $\delta$ –2.83, 1.64. IR (KBr) 3457, 2925, 2850, 1602, 1448, 1228, 1148, 1035, 1001 cm$^{-1}$. M.p. was not available due to decomposition. [$\alpha$]$^D_{25} = +213.6$ (c 1.00, CHCl$_3$). HRMS (FAB+) calcd for C$_{44}$H$_{51}$O$_8$P$_2$ [M+H]$^+$ 769.3059, found 769.3081.
6. Preparation of chiral C₁-symmetric bis(phosphoric acid)s (R)-10.

To a solution of (R)-9 (0.030 mmol) in dichloromethane (2 mL), one drop of N,N-dimethylformamide was added at room temperature. Then oxalyl chloride (5.1 µL, 0.060 mmol) was added at room temperature, and the mixture was warmed to 40 °C. The mixture was stirred at 40 °C for 5 min. Toluene (2 mL) was then added to the resulting mixture, and the volatiles were removed in vacuo under heat conditions (ca. 40–50 °C). The obtained product (R)-S13 was used in the next step without further purification. Compound (R)-S13 was dissolved in 2-propanol (2 mL) and the solution was stirred at room temperature for 48 h. 2-Propanol was then removed in vacuo. (R)-10 was separated by silica gel column chromatography (eluent: CHCl₃:MeOH = 9:1 to 4:1). The isolated (R)-10 was dissolved in chloroform (10 mL), and washed with 1 M HCl aqueous solution (10 mL). The resulting organic layer was concentrated under reduced pressure. The obtained compound was dissolved in toluene (2 mL), and the volatiles were thoroughly removed under reduced pressure to give pure (R)-10 as light brown solid.

(1R)-3-((1,1’:3’,1’’-Terphenyl]-5’-yl)-2’-((hydroxy(isopropoxy)phosphoryl)oxy)-[1,1’-binaphthalen]-2-yl dihydrogen phosphate ((R)-10a): 17% yield in 2 steps. Light brown solid. 

\(^1\)H NMR (400 MHz, THF-d₈) δ 0.99 (d, J = 6.0 Hz, 3H), 1.13 (d, J = 6.4 Hz, 3H), 4.39 (m, 1H), 7.03 (br, 3H), 7.24 (d, J = 8.7 Hz, 1H), 7.27-7.37 (m, 4H), 7.38-7.49 (m, 7H), 7.72-7.83 (m, 5H), 7.85-7.91 (m, 1H), 7.85-8.06 (m, 5H), 8.19 (s, 1H). \(^13\)C NMR (100 MHz, THF-d₈) Peaks are overlapped. δ 23.5 (d, J₁C-P = 4.8 Hz), 23.7 (d, J₂C-P = 5.7 Hz), 73.6 (d, J₃C-P = 5.7 Hz), 121.4, 123.6 (d, J₄C-P = 7.6 Hz), 125.6, 125.8, 126.5, 126.6, 127.4, 127.5, 128.0, 128.1, 128.9, 129.5, 130.8,
132.2, 132.5, 133.9, 134.5, 136.0, 140.4, 142.3, 142.4, 146.9 (d, $J_{C-P} = 6.7$ Hz), 149.1 (d, $J_{C-P} = 5.7$ Hz). $^3$P NMR (160 MHz, THF-$d_8$) δ 3.37, −3.04. IR (KBr) 3450, 3059, 2925, 2853, 1595, 1498, 1467, 1405, 1237, 1149, 1001 cm$^{-1}$. M.p. was not available due to decomposition. $[\alpha]_D^{20} = +184.3$ (c 1.00, CHCl$_3$). HRMS (FAB+) calcd for C$_{41}$H$_{35}$O$_8$P$_2$ [M+H]$^+$ 717.1807, found 717.1789.

(R)-2’-(((Hydroxy(isopropoxy)phosphoryl)oxy)-3-(2,4,6-triisopropylphenyl)-[1,1’-binaphthalen]-2-yl dihydrogen phosphate ((R)-10b): 50% yield in 2 steps. Light brown solid. $^1$H NMR (400 MHz, THF-$d_8$) δ 0.70 (d, $J = 6.8$ Hz, 3H), 1.03 (d, $J = 6.9$ Hz, 3H), 1.08 (d, $J = 6.9$ Hz, 3H), 1.19-1.35 (m, 15H), 2.74-2.99 (m, 3H), 4.20 (m, 1H), 6.72 (br, 3H), 7.05 (d, $J = 1.4$ Hz, 1H), 7.12 (d, $J = 1.4$ Hz, 1H), 7.22-7.49 (m, 6H), 7.83-7.96 (m, 4H), 7.99 (d, $J = 9.2$ Hz, 1H). $^{13}$C NMR (100 MHz, THF-$d_8$) Peaks are overlapped. δ 23.1 (d, $J_{C-P} = 4.8$ Hz), 23.6, 23.8, 24.5, 27.0, 31.9, 32.0, 35.3, 72.8 (d, $J_{C-P} = 6.7$ Hz), 120.7, 121.2, 121.6, 122.9 (d, $J_{C-P} = 8.6$ Hz), 125.3, 125.6, 126.3, 126.4, 126.8, 127.1, 127.2, 128.7, 128.8, 130.7, 132.1, 132.2, 132.3, 133.2, 133.4, 134.4, 147.9 (d, $J_{C-P} = 7.6$ Hz), 148.1, 148.8, 148.9, 149.1 (d, $J_{C-P} = 5.7$ Hz). $^3$P NMR (160 MHz, THF-$d_8$) δ −4.96, −4.88. IR (KBr) 3451, 2959, 2927, 2869, 1626, 1467, 1415, 1362, 1230, 1033, 999 cm$^{-1}$. M.p. was not available due to decomposition. $[\alpha]_D^{28} = +254.3$ (c 1.00, CHCl$_3$). HRMS (FAB+) calcd for C$_{38}$H$_{45}$O$_8$P$_2$ [M+H]$^+$ 691.2590, found 691.2599.

(R)-2’-(((Hydroxy(isopropoxy)phosphoryl)oxy)-3-(2,4,6-tricyclohexylphenyl)-[1,1’-binaphthalen]-2-yl dihydrogen phosphate ((R)-10c): 58% yield in 2 steps. Light brown solid. $^1$H NMR (400 MHz, THF-$d_8$) δ 0.97-1.80 (m, 23H), 1.03 (d, $J = 6.4$ Hz, 3H), 1.07 (d, $J = 6.4$ Hz, 3H), 1.80-1.96 (m, 5H), 1.98-2.13 (m, 2H), 2.39-2.57 (m, 3H), 4.41 (m, 1H), 7.00 (d, $J = 1.4$ Hz, 1H), 7.08 (d, $J = 1.4$ Hz, 1H), 7.22 (d, $J = 8.2$ Hz, 1H), 7.24-7.35 (m, 3H), 7.35-7.45 (m, 2H), 7.82 (d, $J = 9.2$ Hz, 1H), 7.83 (s, 1H), 7.88 (d, $J = 8.3$ Hz, 1H), 7.94 (d, $J = 8.2$ Hz, 1H), 8.01 (d, $J = 9.2$ Hz, 1H), 9.54 (br, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) Peaks are overlapped. δ 23.5 (d, $J_{C-P} = 4.8$ Hz), 23.7 (d, $J_{C-P} = 4.8$ Hz), 27.1, 27.2, 27.4, 27.8, 28.0, 28.1, 33.7, 33.9, 35.5, 35.6, 36.3, 38.2, 42.7, 45.9, 73.4 (d, $J_{C-P} = 5.7$ Hz), 121.7, 122.0, 123.1, 123.3 (d, $J_{C-P} = 6.7$ Hz), 125.1 (d, $J_{C-P} = 6.7$ Hz), 146.9 (d, $J_{C-P} = 6.7$ Hz), 149.1 (d, $J_{C-P} = 5.7$ Hz).
3.8 Hz), 125.7, 126.3, 126.6, 127.2, 127.3, 128.7, 129.0, 130.6, 132.0, 132.2, 132.7, 133.5, 133.9, 134.3, 134.6, 147.0, 147.8, 147.9 (d, J_{C-P} = 6.7 Hz), 148.1, 149.2 (d, J_{C-P} = 5.7 Hz).  

$^{31}$P NMR (160 MHz, DMSO-$d_6$) $\delta$ –4.04, –2.88.  IR (KBr) 3448, 2925, 2850, 1626, 1448, 1231, 1147, 1033, 999 cm$^{-1}$.  M.p. was not available due to decomposition.  $[\alpha]_D^{26} = 193.6$ (c 1.00, CHCl$_3$).  

HRMS (FAB+) calcd for C$_{47}$H$_{57}$O$_8$P$_2$ [M+H]$^+$ 811.3529, found 811.3523.

We tried to crystallize (R)-10c, but we could not obtain a suitable crystal for X-ray analysis.  Instead, we obtained a suitable crystal of racemic-10c.  By X-ray analysis, we unambiguously confirmed the structure of 10c (Fig. S3), in particular, the position of the $i$-Pr moiety.  The other possible isomer (R)-10c’ was not obtained in our preparation, probably due to steric constraints of the bulky aryl moiety at the 3-position of the binaphthyl of (R)-S13c (Fig. S2).  

Racemic-10c does not have a conjugated intramolecular double hydrogen bond network as seen for (R)-5c•(pyridine) in Fig. S1.  Indeed, racemic-10c formed a dimer due to an intermolecular hydrogen bond network as shown in Fig. S4.  The dimer structure is symmetric: one is (R)-10c and the other is (S)-10c.  Intramolecular hydrogen bonds are not observed among dimers.  (R)-10c and (S)-10c have one intramolecular hydrogen bond (1.696 Å), respectively, and four hydrogen bonds (1.576–1.848 Å) are observed between (R)-10c and (S)-10c.  This dimerization of racemic-10c might disturb the formation of a conjugated intramolecular double hydrogen bond network.  To date, it is still unclear whether or not optically pure (R)-10c would form a dimer.  However, by the ESI-MS analysis of (R)-10c (Fig. S7f), (R)-10c might be a monomer as a major species.

\[ \text{(R)-10c} \quad \text{(R)-10c'} \quad \text{(Not obtained)} \]

\[ \text{Fig. S2} \quad \text{(R)-10c and a possible isomer (R)-10c'.} \quad \text{(R)-10c'} \text{ was not obtained in our preparation.} \]

Crystal data of racemic-10c (Figs. S3 and S4):  Racemic-10c was recrystallized in chloroform–n-hexane for X-ray analysis.  Formula C$_{47}$H$_{56}$O$_8$P$_2$, colorless, crystal dimensions 0.15 × 0.13 × 0.12 mm$^3$, monoclinic, space group $P$–$I$ (#2), $a = 12.7831$ (18) Å, $b = 14.6459$ (16) Å, $c = 14.800$ (2) Å, $\alpha = 116.231$ (11) °, $\beta = 101.896$ (13) °, $\gamma = 102.26$ (2) °, $V = 2282.1$ (6) Å$^3$, $Z = 2$, $\rho_{\text{calc}} = 1.180$ g cm$^{-3}$, $F(000) = 864$, $\mu$(MoK$\alpha$) = 0.145 mm$^{-1}$, $T = 93$ K.  19527 reflections collected, 9800 independent reflections with $I > 2\sigma(I)$ ($2\theta_{\text{max}} = 27.55$ °), and 532 parameters were used for the solution of the structure.  The non-hydrogen atoms were refined anisotropically.  $R_I = 0.0477$ and $wR_2 = 0.1472$.  GOF = 1.091.  Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1834632.
Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Web page: http://www.ccdc.cam.ac.uk/].

**Fig. S3** ORTEP drawing of *racemic-10c*.

**Fig. S4** Dimer structure of *racemic-10c* (*R/S*-pair).
7. Preparation of $\alpha$-ketimino esters 1.

![Chemical structure](image)

$\beta,\gamma$-Alkynyl-$\alpha$-imino esters 1: Ketoesters $\text{S14}$ were prepared based on the reported procedures.$^{4-6}$ Compounds 1 were prepared on the basis of a literature procedure.$^7$ To a well-dried round bottom two necks flask (50 mL) with ketoester $\text{S14}$ (5.0 mmol) and $N$-Cbz-triphenyliminophosphorane$^8$ (2.06 g, 5.0 mmol) was added toluene (10 mL). The mixture was heated to 120 °C and stirred for 6 h. After cooling to room temperature, volatiles were removed under reduced pressure. The resultant residue was purified by MPLC (eluent: $n$-hexane:EtOAc = typically 100:0 to 80:20) to give the desired product 1.

**Ethyl 2-(((benzyloxy)carbonyl)imino)-4-phenylbut-3-ynoate (1a):** 37% yield. Yellow-orange oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.41 (t, $J = 6.9$ Hz, 3H), 4.42 (q, $J = 6.9$ Hz, 2H), 5.35 (s, 2H), 7.27-7.50 (m, 10H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 14.0, 63.4, 68.8, 81.0, 102.5, 119.4, 128.5 (7C) 131.1, 132.9 (2C), 134.9, 146.0, 160.7, 161.1. IR (neat) 3456, 2983, 2198, 1733, 1615, 1490, 1444, 1373, 1216, 1101, 1021 cm$^{-1}$. HRMS (FAB+) calcd for C$_{20}$H$_{18}$NO$_4$ [M+H]$^+$ 336.1236, found 336.1241.

**Ethyl 2-(((benzyloxy)carbonyl)imino)-4-(triisopropylsilyl)but-3-ynoate (1b):** 78% yield. Light yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.04-1.15 (m, 21H), 1.37 (t, $J = 6.9$ Hz, 3H), 4.37 (q, $J = 6.9$ Hz, 2H), 5.27 (s, 2H), 7.33-7.42 (m, 5H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 10.8 (3C), 13.8, 18.3 (6C), 63.1, 68.8, 96.5, 108.5, 128.3 (2C), 128.4 (3C), 134.5, 145.4, 160.1, 160.7. IR (neat) 3461, 2944, 2866, 2152, 1748, 1618, 1462, 1370, 1220, 1132, 1021 cm$^{-1}$. HRMS (FAB+) calcd for C$_{23}$H$_{34}$NO$_4$Si [M+H]$^+$ 416.2257, found 416.2265.
8. Representative procedures for the enantioselective aza-Friedel–Crafts reaction of 2 with 1 (Table 1 and Eq. 1).

**Standard conditions (0.20 mmol scale):** To a well-dried pyrex Schlenk tube charged with activated MS 5Å (50 mg) under a nitrogen atmosphere were added catalyst (R)-5b (9.6 mg, 0.010 mmol) in dichloromethane (1.0 mL) and α-ketimino ester 1b (83 mg, 0.20 mmol). The mixture was diluted with dichloromethane (1.0 mL) and cooled to –78 °C. 2-Methoxyfuran 2 (37 µL, 0.40 mmol) was added and the mixture was stirred at –78 °C for 24 h. To quench the reaction, silica gel (4 mL) was added to the mixture at –78 °C. The resultant silica gel was thoroughly washed with **n**-hexane and ethyl acetate (3:1, 200 mL) at room temperature. The filtrate was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: **n**-hexane:EtOAc = 5:1 to 3:1) to give the product 3b (85.3 mg, 83%, 91% ee). The catalyst could be recovered as some metal (Li, Na, K, Ca, etc.) salts of (R)-5b through the same silica gel column chromatography (eluent: CHCl₃:MeOH = 3:1) quantitatively. When the catalyst would be reused for the catalysis, the further purification with washing by 1 M HCl aqueous solution is necessary (>99% recovery). The enantiomeric purity of 3b was determined by chiral HPLC analysis (91% ee).

**Gram-scale synthesis:** To a well-dried pyrex Schlenk tube charged with activated MS 5Å (50 mg) under a nitrogen atmosphere were added catalyst (R)-5b (230 mg, 0.24 mmol) in dichloromethane (14 mL) and α-ketimino ester 1b (2.00 g, 4.8 mmol). The mixture was diluted with dichloromethane (34 mL) and cooled to –78 °C. 2-Methoxyfuran 2 (880 µL, 9.6 mmol) was added and the mixture was stirred at –78 °C for 36 h. To quench the reaction, silica gel (100 mL) was added to the mixture at –78 °C. The resultant silica gel was thoroughly washed with
$n$-hexane and ethyl acetate (3:1, 400 mL) at room temperature. The filtrate was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: $n$-hexane:EtOAc = 5:1 to 3:1) to give the product 3b (1.89 g, 77% yield). The catalyst could be recovered as some metal salts of ($R$)-5b through the same silica gel column chromatography (eluent: CHCl₃:MeOH = 3:1) quantitatively. When the catalyst would be reused for the catalysis, the further purification with washing by 1 M HCl aqueous solution is necessary (>99% recovery). The enantiomeric purity of 3b was determined by chiral HPLC analysis (91% ee).

**Ethyl ($S$)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl)-4-phenylbut-3-ynoate (3a):** 88% yield, 76% ee. Colorless oil. $^1$H NMR (400 MHz, CDCl₃) δ 1.26 (t, $J = 6.8$ Hz, 3H), 3.82 (s, 3H), 4.22-4.38 (m, 2H), 5.09 (d, $J = 12.1$ Hz, 1H), 5.14 (d, $J = 12.1$ Hz, 1H), 5.15 (d, $J = 3.6$ Hz, 1H), 6.21 (br, 1H), 6.60 (br, 1H), 7.28-7.39 (m, 8H), 7.46 (br, 2H). IR (neat) 3409, 2979, 2936, 2906, 1734, 1615, 1576, 1490, 1369, 1260, 1022 cm⁻¹. [α]D₂⁶ = −2.8 (c 1.00, CHCl₃, 76% ee (S)). HPLC analysis; AD-H, n-hexane/i-PrOH = 1/1, 254 nm, 1.0 mL/min, $t_R = 15.9$ min (major, $S$), 32.4 min (minor, $R$). HRMS (FAB+) calcd for C₂₅H₂₃NNaO₆ [M+Na]⁺ 456.1423, found 456.1418.

**Ethyl ($S$)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl)-4-(triisopropylsilyl)but-3-ynoate (3b):** 83% yield, 91% ee. Pale yellow oil. $^1$H NMR (400 MHz, CDCl₃) δ 1.23 (t, $J = 6.9$ Hz, 3H), 3.80 (s, 3H), 4.15 (br, 1H), 4.31 (br, 1H), 5.09 (d, $J = 12.4$ Hz, 1H), 5.12 (d, $J = 2.8$ Hz, 1H), 5.14 (d, $J = 12.4$ Hz, 1H), 6.11 (br, 1H), 6.54 (br, 1H), 7.25-7.38 (m, 5H). IR (neat) 3418, 2943, 2176, 1746, 1614, 1574, 1470, 1369, 1257, 1019 cm⁻¹. [α]D₂⁴ = −2.8 (c 1.00, CHCl₃, 91% ee (S)). HPLC analysis; AD-H, n-hexane/i-PrOH = 9/1, 254 nm, 0.6 mL/min, $t_R = 10.3$ min (major, $S$), 12.0 min (minor, $R$). HRMS (FAB+) calcd for C₂₈H₃₉NNaO₆Si [M+Na]⁺ 536.2444, found 536.2437.
9. Screening of achiral catalysts in the probe reaction of 2 with 1a.

The screening of achiral catalysts in the probe reaction of 2 with 1a is summarized in Table S1. The pK_a values of the acid compounds used here are generally available in the literature. The desired product 3a was obtained in better yield and chemoselectivity by catalysts, particularly some carboxylic acids such as CHF_2CO_2H and CCl_3CO_2H (entries 3 and 4), with pK_a values of 2.5–6.5 in DMSO and 0.65–1.24 in H_2O. The pK_a range was comparable to the pK_a values of phosphoric acids (entries 10 and 11).

Table S1  Screening of the achiral catalysts in the probe reaction of 2 with 1a.

| Entry | Catalyst       | pK_a (calcd)^a | pK_a in H_2O^b | pK_a in DMSO | Reaction time (h) | Conversion (%) | Yield (%) |
|-------|----------------|----------------|----------------|-------------|------------------|----------------|-----------|
| 1     | CH_3CO_2H      | 4.79           | 4.76           | 12.3^c      | 24               | 0              | 0         |
| 2     | CH_2BrCO_2H    | 2.73           | 2.86           | –           | 24               | 13             | 13        |
| 3     | CHF_2CO_2H     | 1.32           | 1.24           | 6.45^d      | 24               | 56             | 52        |
| 4     | CCl_3CO_2H     | 0.09           | 0.65           | 2.5^e        | 24               | >99            | 59        |
| 5     | CF_3CO_2H      | 0.05           | 0.26           | 3.5^e        | 12               | >99            | 53        |
| 6     | HCl^f          | –              | –8.00          | 1.8^f        | 3                | >99            | 59        |
| 7     | p-CH_2C_6H_4SO_3H | –0.43         | –1.34          | 0.9^g        | 12               | >99            | 34        |
| 8     | CF_3SO_3H      | –3.91          | –13.0          | 0.3^i        | 6                | >99            | 0         |
| 9     | (CF_3SO_2)_2NH | –10.42         | –              | 2.4^b        | 3                | >99            | 0         |
| 10    | PhOP(=O)(OH)_2 | 1.25           | 1.42^f         | –           | 24               | 51             | 49        |
| 11    | (PhO)_2P(=O)OH | 1.12           | 0.26^f         | 3.7^b        | 24               | 60             | 60        |

^a Data in SciFinder. Calculated using ACD/Labs Software V11.02. ^b D. Gryko, M. Zimnicka and R. Lipiński, J. Org. Chem., 2007, 72, 964. ^c F. G. Bordwell, Acc. Chem. Res., 1988, 21, 456. ^d C. D. Ritchie and S. Lu, J. Am. Chem. Soc., 1990, 112, 7748. ^e H.-s. Kim, T. D. Chung and H. Kim, J. Electroanal. Chem., 2001, 498, 209. ^f 1 M HCl in diethyl ether was used as HCl source. ^g H. Kim, J. Gao and D. Burgessa, J. Int. J. Pharm., 2009, 377, 105. ^h C. Yang, X.-S. Xue, X. Li and J.-P. Cheng, J. Org. Chem., 2014, 79, 4340. ^i D. Shamir, I. Zilbermann, E. Maimon, A. I. Shames, H. Cohen and D. Meyerstein, Inorg. Chim. Acta, 2010, 363, 2819. ^j F. Krašovec and J. Jan, Croat. Chem. Acta, 1963, 35, 183. ^k P. Christ, A. G. Lindsay, S. S. Vormittag, J.-M. Neudröffl, A. Berkessel and A. M. C. O’Donoghue, Chem. Eur. J., 2011, 17, 8524.
10. Screening of chiral catalysts in the probe reaction of 2 with 1a.

Screening of chiral catalysts in the probe reaction of 2 with 1a is summarized in Scheme S1. The catalytic activities of conventional chiral phosphoric acids, such as (R)-S15,9 (R)-4a,10 and (R)-4b,11 and (R)-4c12 were moderate, but the enatio-induction were low. In contrast, bis(phosphoric acid)s (R)-5a and (R)-5b showed higher catalytic reactivities with high enantioselectivities, although sterically less hindered (R)-S3 and (R)-S4 showed low catalytic activities due to their low solubility. Less acidic (R)-5c did not provide better reactivity than (R)-5a or (R)-5b. Highly acidic chiral 3,3’-Ar₂-BINSA (R)-S1613 gave a poor result, since significant amounts of byproducts were obtained due to the strong acidity of (R)-S16.

Scheme S1  Screening of the catalysts in the probe reaction of 2 with 1a.
11. Screening of chiral catalysts in the probe reaction of 2 with 1b.

Substrate 1b was much less reactive than 1a. Therefore, the screening of chiral catalysts in the probe reaction of 2 with 1b was examined again (Scheme S2). As a result, the catalytic activities of conventional chiral phosphoric acids (R)-4a and (R)-4b were low. An increase in the amount of (R)-4b from 5 mol% to 10 mol% slightly improved both the yield and the enantioselectivity. Moreover, chiral BINOL-derived phosphoric acids (R)-4c (i.e., TRIP) and (R)-S17 were also quite inactive (<10% conversion). Chiral VAPOL-derived phosphoric acid (R)-S18 moderately promoted the reaction but with low enantioselectivity. Chiral phosphoramide (R)-S19 was also ineffective. Byproducts were obtained in the catalysis of (R)-S18 (ca. 15% based on 1b) and (R)-S19 (ca. 20% based on 1b). In contrast, bis(phosphoric acid)s (R)-5a and (R)-5b showed high yields with high enantioselectivities (up to 91% ee). In this reaction, less acidic (R)-5c gave a much lower yield and lower enantioselectivity (76% ee) than (R)-5a or (R)-5b. Based on these results, we selected (R)-5b as an optimized catalyst for this reaction.

Scheme S2  Screening of the catalysts in the probe reaction of 2 with 1b.
12. Calculation of the electrostatic potential of phosphoric acids.

An effective approach to estimating molecular $pK_a$ values from simple density functional calculations has been developed by Liu.$^{14}$ Various compounds show a strong correlation between experimental $pK_a$ values and molecular electrostatic potential (MEP). As a result of their research, a linear relationship between the MEP and experimental $pK_a$ values has been established. Therefore, we performed preliminary theoretical calculations using Spartan’10 for Macintosh from Wavefunction, Inc. (Fig. S5 and Table S2). The geometries of $S20–S26$ were optimized with gradient-corrected density functional theory (DFT) calculations with B3LYP using the 6-31+G* basis set, after MMFF (molecular mechanics) and HF/3-21G ($ab$ $initio$ molecular orbital method) calculations. We first investigated the MEP values of simple compounds $S20$ and $S21$, which have known $pK_a$ values ($pK_a = 0.26^{15}$ for $S20$ and $1.42^{16}$ for $S21$). As a result, a higher MEP value was observed in $S20$ than in $S21$, and our preliminary calculations for these model compounds may support a relationship between $pK_a$ and MEP values.

![Fig. S5](image_url) Calculation of electrostatic potential (kcal/mol).

| $pK_a$ values in $H_2O$ |  |
|------------------------|---|
| S20 | S21 |
| $pK_a 0.26^{15}$ | $pK_a 1.42^{16}$ |
First, we investigated the effect of external hydrogen bonding in S22 and S23, which involves one hydrogen bonding between two molecules of S20 and two hydrogen bondings between two molecules of S21, respectively. Also, we observed a higher value of MEP (75.2 kcal/mol) for S23 than for S21 (69.0 kcal/mol). These results should clearly support the idea that appropriate hydrogen bonding between two molecules of phosphoric acids would increase the Brønsted acidity.

Next, we investigated the effect of two internal hydrogen bondings in S24 as a simple model of (R)-5. As a result, we observed a higher value of MEP (78.0 kcal/mol) for cyclic S24 than for acyclic S23 (75.2 kcal/mol), although S23 and S24 have different ester moieties. Moreover, the MEP value for S25 (75.9 kcal/mol) as a model of (R)-10 was lower than that for S24. Moreover, the MEP value for S26 (76.5 kcal/mol) as a model of (R)-4 was lower than that for S24 (78.0 kcal/mol). Accordingly, (R)-5 might be expected to be more acidic than (R)-4, and (R)-10 might be expected to be less acidic than (R)-4 as shown in Fig. S6. It should be noted that the estimated order in Fig. S6 does not involve steric factors of the catalysts (also see Fig. S9).

**Fig. S6** Possible order of the strength of Brønsted acidity of (R)-5, (R)-4, and (R)-10.

**Table S2** Summary of DFT calculation of S20–S26 by using B3LYP/6-31+G*.

| Number | Atom | Charge | X(A)     | Y(A)     | Z(A)     |
|--------|------|--------|----------|----------|----------|
| 1      | P    | 0      | -0.1230  | -1.9290  | 0.0840   |
| 2      | O    | 0      | -1.0150  | -2.7570  | 0.9210   |
| 3      | O    | 0      | 0.7820   | -2.7490  | -0.9730  |
| 4      | H    | 0      | 0.4900   | -3.6740  | -1.0280  |
| 5      | O    | 0      | -0.8030  | -0.8630  | -0.9230  |
|   |   |   |   |
|---|---|---|---|
| 6 | O | 0 | 0.9300 | -1.0820 | 0.9590 |
| 7 | C | 0 | -1.6920 | 0.1460 | -0.5180 |
| 8 | C | 0 | -3.4510 | 2.2030 | 0.1120 |
| 9 | C | 0 | -2.7580 | -0.1150 | 0.3430 |
|10 | C | 0 | -1.4910 | 1.4090 | -1.0730 |
|11 | C | 0 | -2.3790 | 2.4380 | -0.7550 |
|12 | C | 0 | -3.6340 | 0.9290 | 0.6570 |
|13 | H | 0 | -2.8950 | -1.1080 | 0.7590 |
|14 | H | 0 | -0.6490 | 1.5710 | -1.7390 |
|15 | H | 0 | -2.2290 | 3.4250 | -1.1840 |
|16 | H | 0 | -4.4660 | 0.7380 | 1.3290 |
|17 | H | 0 | -4.1390 | 3.0070 | 0.3590 |
|18 | C | 0 | 1.7690 | -0.0460 | 0.5320 |
|19 | C | 0 | 3.4810 | 2.0440 | -0.1290 |
|20 | C | 0 | 1.9280 | 1.0150 | 1.4220 |
|21 | C | 0 | 2.4550 | -0.0880 | -0.6820 |
|22 | C | 0 | 3.3100 | 0.9700 | -1.0060 |
|23 | C | 0 | 2.7890 | 2.0610 | 1.0860 |
|24 | H | 0 | 1.3790 | 1.0090 | 2.3590 |
|25 | H | 0 | 2.3310 | -0.9280 | -1.3560 |
|26 | H | 0 | 3.8470 | 0.9450 | -1.9510 |
|27 | H | 0 | 2.9160 | 2.8910 | 1.7760 |
|28 | H | 0 | 4.1510 | 2.8600 | -0.3880 |

**S21**

Job type: Single point.
Method: RB3LYP
Basis set: 6-31+G*
Number of shells: 65
Number of basis functions: 208
Multiplicity: 1
Parallel Job: 4 threads
SCF model:
A restricted hybrid HF-DFT SCF calculation will be performed using Pulay DIIS + Geometric Direct Minimization
SCF total energy: \(-799.9624168\) hartrees

|   |   |   |   |
|---|---|---|---|
| 1 | H | 0 | 2.9260 | -2.1460 | 0.0000 |
| 2 | C | 0 | 1.0520 | 1.2170 | 0.0000 |
| 3 | C | 0 | 3.1100 | -0.0130 | 0.0000 |
| 4 | C | 0 | 2.4390 | 1.3960 | 0.0000 |
| 5 | C | 0 | 0.3400 | 0.0250 | 0.0000 |
| 6 | H | 0 | 4.1860 | -0.0300 | 0.0000 |
| 7 | H | 0 | 2.9890 | 2.1200 | 0.0000 |
| 8 | H | 0 | 0.5220 | 2.1520 | 0.0000 |
| 9 | P | 0 | -1.4480 | 0.1060 | 0.0000 |
| 10 | O | 0 | -2.0390 | 1.4380 | 0.0000 |
| 11 | O | 0 | -1.8790 | -0.7790 | -1.2560 |
| 12 | H | 0 | -2.5920 | -0.3810 | -1.7420 |
| 13 | O | 0 | -1.8790 | -0.7790 | 1.2560 |
| 14 | O | 0 | -2.0390 | 1.4380 | 0.0000 |

**S22**

Job type: Single point.
Method: RB3LYP
Basis set: 6-31+G*
Number of shells: 216
Number of basis functions: 698
Multiplicity: 1
Parallel Job: 4 threads
SCF model:
A restricted hybrid HF-DFT SCF calculation will be performed using Pulay DIIS + Geometric Direct Minimization
SCF total energy: \(-2212.5169304\) hartrees

|   |   |   |   |
|---|---|---|---|
| 1 | P | 0 | 2.6350 | 1.0200 | 0.1910 |
| 2 | O | 0 | 1.2380 | 0.9950 | -0.1950 |
| 3 | O | 0 | 3.5540 | 0.7700 | -1.0590 |
S23
Job type: Single point.
Method: R3LYP
Basis set: 6-31+G*
Number of shells: 140
Number of basis functions: 454
Multiplicity: 1
Parallel Job: 4 threads
SCF model:
A restricted hybrid HF-DFT SCF calculation will be performed using Pulay DIIS + Geometric Direct Minimization
SCF total energy: -1750.4488325 hartrees

----------------------------------------

4  O  0  3.0820  0.0130  1.3200
5  C  0  4.9370  0.7760  -1.0970
6  C  0  7.6870  0.7430  -1.2990
7  C  0  5.6210  1.9700  -1.0960
8  C  0  5.5960  -0.4310  -1.2100
9  C  0  6.9800  -0.4420  -1.3100
10 C  0  7.0050  1.9450  -1.1940
11 H  0  5.0790  2.8930  -1.0250
12 H  0  5.0300  -1.3390  -1.2280
13 H  0  7.5010  -1.3770  -1.4010
14 H  0  7.5470  2.8690  -1.1930
15 H  0  8.7600  0.7310  -1.3770
16 C  0  2.8490  -4.0830  1.5970
17 C  0  2.4940  -4.1680  2.0110
18 C  0  3.1360  2.3680  0.8330
19 H  0  3.4640  2.2820  1.7290
20 P  0  -2.1720  -0.2450  -0.3530
21 O  0  -2.7930  0.6400  0.8100
22 O  0  -3.3570  -0.4720  -1.3760
23 O  0  -2.7790  -1.1550  -0.9570
24 C  0  -2.4800  -3.5980  -0.7420
25 C  0  -3.4230  1.8580  0.7920
26 C  0  -4.7220  4.2930  0.9770
27 C  0  -3.8920  2.2970  2.0220
28 C  0  -3.5950  2.6230  -0.3510
29 C  0  -4.2480  3.8400  -0.2440
30 C  0  -4.5380  3.5130  2.1110
31 H  0  -3.7410  1.6780  2.8880
32 H  0  -3.2230  2.2910  -1.3010
33 H  0  -4.3800  4.4360  -1.1300
34 C  0  -4.8990  3.8510  3.0680
35 C  0  -5.2250  5.2400  1.0460
36 H  0  -1.2800  0.7000  -1.2110
37 H  0  -0.3690  0.7970  -0.9080
----------------------------------------
| Number | Atom | Charge | X(A)  | Y(A)  | Z(A)   |
|--------|------|--------|-------|-------|--------|
|  1     | C    | 0      | 2.5410| 0.5420| -0.2660|
|  2     | C    | 0      | 3.1880| 2.5380| 1.0700 |
|  3     | C    | 0      | 1.8620| 1.3210| 0.6670 |
|  4     | C    | 0      | 3.8890| 0.7390| -0.5500|
|  5     | C    | 0      | 4.5770| 1.7470| 0.1280 |
|  6     | C    | 0      | 2.5640| 2.3230| 1.3370 |
|  7     | C    | 0      | 4.3780| 0.1120| -1.2870|
|  8     | H    | 0      | 0.8100| 1.1370| 0.8580 |
|  9     | H    | 0      | 3.9180| 2.5380| 1.0700 |
| 10     | H    | 0      | 1.8620| 1.3210| 0.6670 |
| 11     | H    | 0      | 3.8890| 0.7390| -0.5500|
| 12     | H    | 0      | 4.5770| 1.7470| 0.1280 |
| 13     | H    | 0      | 2.5640| 2.3230| 1.3370 |
| 14     | H    | 0      | 4.3780| 0.1120| -1.2870|

S24
Job type: Single point.
Method: RB3LYP
Basis set: 6-31+G*
Number of shells: 88
Number of basis functions: 290
Multiplicity: 1
Parallel Job: 4 threads
SCF model:
A restricted hybrid HF-DFT SCF calculation will be performed using Pulay DIIS + Geometric Direct Minimization
SCF total energy:   -1441.9200909 hartrees

S25
Job type: Single point.
Method: RB3LYP
Basis set: 6-31+G*
Number of shells: 97
Number of basis functions: 313
### SCF model:
A restricted hybrid HF-DFT SCF calculation will be performed using Pulay DIIS + Geometric Direct Minimization

### SCF total energy:
-1481.2250368 hartrees

| Number | Atom | Charge | X(A)  | Y(A)  | Z(A)  |
|--------|------|--------|-------|-------|-------|
| 1      | C    | 0      | -0.2400 | 2.9900 | 0.4210 |
| 2      | H    | 0      | -0.1970 | 3.8860 | 1.0390 |
| 3      | C    | 0      | -1.4760 | 2.7510 | -0.3360 |
| 4      | H    | 0      | -1.9010 | 3.5910 | -0.8840 |
| 5      | C    | 0      | 0.8700  | 2.2430 | 0.3970  |
| 6      | H    | 0      | 1.7550  | 2.4700 | 0.9840  |
| 7      | C    | 0      | -2.1880 | 1.6190 | -0.3600 |
| 8      | H    | 0      | -3.1030 | 1.4990 | -0.9320 |
| 9      | O    | 0      | 1.0000  | 1.1770 | -0.4760 |
| 10     | O    | 0      | -1.8500 | 0.5440 | 0.4450  |
| 11     | P    | 0      | 1.6700  | -0.2480 | -0.1260 |
| 12     | O    | 0      | 1.2040  | -0.8530 | 1.1630  |
| 13     | P    | 0      | -1.9250 | -1.0170 | 0.0580  |
| 14     | O    | 0      | -1.2860 | -1.3760 | -1.2480 |
| 15     | O    | 0      | -3.5000 | -1.3450 | 0.0880  |
| 16     | H    | 0      | -3.7390 | -2.0100 | -0.5800 |
| 17     | O    | 0      | -1.3420 | -1.6860 | 1.3620  |
| 18     | H    | 0      | -0.3650 | -1.4740 | 1.4510  |
| 19     | O    | 0      | 1.3850  | -1.0810 | -1.4430 |
| 20     | H    | 0      | 0.4100  | -1.2960 | -1.5260 |
| 21     | O    | 0      | 3.2340  | 0.0700  | -0.1680 |
| 22     | C    | 0      | 4.1870  | -0.9160 | 0.2930  |
| 23     | H    | 0      | 3.9330  | -1.2420 | 1.3060  |
| 24     | H    | 0      | 5.1550  | -0.4160 | 0.2840  |
| 25     | H    | 0      | 4.2000  | -1.7690 | -0.3910 |

---

### Job type: Single point.
Method: RB3LYP
Basis set: 6-31+G*
Number of shells: 56
Number of basis functions: 185
Multiplicity: 1

### SCF total energy:
-797.7340994 hartrees

| Number | Atom | Charge | X(A)  | Y(A)  | Z(A)  |
|--------|------|--------|-------|-------|-------|
| 1      | C    | 0      | -2.1770 | 0.7520 | -0.1110 |
| 2      | H    | 0      | -3.0770 | 1.2520 | -0.4610 |
| 3      | C    | 0      | -2.2210 | -0.6930 | 0.0810 |
| 4      | H    | 0      | -3.1650 | -1.1450 | 0.3760 |
| 5      | C    | 0      | -1.1090 | 1.5270 | 0.1290 |
| 6      | H    | 0      | -1.0900 | 2.6000 | -0.0280 |
| 7      | C    | 0      | -1.1820 | -1.5220 | -0.0980 |
| 8      | H    | 0      | -1.2240 | -2.5950 | 0.0550 |
| 9      | O    | 0      | 0.0570  | 1.0620 | 0.7170  |
| 10     | O    | 0      | 0.0360  | -1.1110 | -0.6160 |
| 11     | P    | 0      | 1.0430  | -0.0640 | 0.0970  |
| 12     | O    | 0      | 2.0100  | -0.5680 | 1.0890  |
| 13     | O    | 0      | 1.6950  | 0.5900  | -1.2250 |
| 14     | H    | 0      | 2.6560  | 0.6850  | -1.1160 |

---
13. Optimization of the concentration, drying agents, solvents, and substrates in the reaction of 2 with 1.

The effects of the concentration of substrate 1b and drying agents were examined (Table S3). As a result, 0.1 M (based on 1b) conditions showed better enantioselectivity than 0.05 M and 0.2 M (entries 1–3). The drying agent used did not significantly affect the enantioselectivity, but did affect the reactivity (i.e., the reaction time for full conversion) and chemoselectivity for unknown byproducts, which might be triggered by the reaction of water with 1b and/or 2 (entries 4–7). As a result, MS 5Å was better than MS 3Å, MS 4Å, and MgSO4. Next, the general solvent effect was examined (Table S4). As a result, polar solvents were not suitable at all, and dichloromethane was much better than the other solvents tested. The reaction temperature was also examined (entries 7–9), and a lower temperature gave higher enantioselectivity (92–94% ee), although the yields were decreased (46–52%).

**Table S3** Effect of molecular sieves and concentration of substrate 1b.

| Entry | Drying agent | Concentration (M) based on 1b | Reaction time (h) | Yield (%) | ee (%) |
|-------|--------------|------------------------------|------------------|-----------|--------|
| 1     | –            | 0.05                         | 12               | 87        | 84     |
| 2     | –            | 0.1                          | 17               | 72        | 90     |
| 3     | –            | 0.2                          | 12               | 68        | 88     |
| 4     | MS 3Å        | 0.1                          | 48               | 85        | 89     |
| 5     | MS 4Å        | 0.1                          | 24               | 74        | 89     |
| 6     | **MS 5Å**    | **0.1**                      | 24               | **83**    | **91** |
| 7     | MgSO4        | 0.1                          | 24               | 59        | 89     |

**Table S4** Effect of solvents and temperature.

| Entry | Solvent | Temperature (°C) | Reaction time (h) | Yield (%) | ee (%) |
|-------|---------|------------------|------------------|-----------|--------|
| 1     | Et2O    | –78              | 24               | 0         | –      |
| 2     | EtOAc   | –78              | 24               | 0         | –      |
| 3     | EtNO2   | –78              | 24               | 0         | –      |
| 4     | EtCN    | –78              | 24               | 0         | –      |
| 5     | toluene | –78              | 24               | 35        | 9      |
| 6     | **CH2Cl2** | **–78**        | 24               | **83**    | **91** |
| 7     | CH2Cl2  | –60              | 14               | 78        | 76     |
| 8     | CH2Cl2  | –90              | 48               | 52        | 92     |
| 9     | CH2Cl2  | –95              | 48               | 46        | 94     |
Next, β,γ-alkynyl-α-imino esters 1 were optimized with the use of (R)-5b (Table S5). To avoid the effect of adventitious water, which might react with 1 and 2 to give undesired products, powdered MS 5Å was used as a drying agent. As a result, the reaction of 2 with 1a (R\textsuperscript{1} = Ph, CO\textsubscript{2}R\textsuperscript{2} = CO\textsubscript{2}Et, CO\textsubscript{2}R\textsuperscript{3} = Cbz) proceeded smoothly, and a slightly better result (88% yield and 76% ee) was observed (entry 1). Next, we changed the terminal R\textsuperscript{1} group of the acetylene from a Ph group to sterically hindered silyl groups (entries 2–6). As a result, the enantioselectivity of the corresponding product 3 was improved according to the bulkiness of the silyl group (also see a possible transition state on page S72). Ultimately, when we used 1b (R\textsuperscript{1} = i-Pr\textsubscript{3}Si, CO\textsubscript{2}R\textsuperscript{2} = CO\textsubscript{2}Et, CO\textsubscript{2}R\textsuperscript{3} = Cbz) with a bulky i-Pr\textsubscript{3}Si group, 3b was obtained in 83% yield with 91% ee (entry 6). The ester groups CO\textsubscript{2}R\textsuperscript{2} and C\textsubscript{=N}CO\textsubscript{2}R\textsuperscript{3} in 1 were also optimized. However, we did not find better ester groups to replace CO\textsubscript{2}Et for CO\textsubscript{2}R\textsuperscript{2} and Cbz for CO\textsubscript{2}R\textsuperscript{3} (entries 7–10). Based on these results, we selected 1b (R\textsuperscript{1} = i-Pr\textsubscript{3}Si, CO\textsubscript{2}R\textsuperscript{2} = CO\textsubscript{2}Et, CO\textsubscript{2}R\textsuperscript{3} = Cbz) as an optimized catalyst for this reaction.

**Table S5** Screening of substrates.\(^a\)

| Entry | R\textsuperscript{1} | CO\textsubscript{2}R\textsuperscript{2} | CO\textsubscript{2}R\textsuperscript{3} | Yield (%) | ee (%) |
|-------|----------------------|-----------------------------|-----------------------------|-----------|-------|
| 1\(^b\) | Ph | CO\textsubscript{2}Et | CO\textsubscript{2}Bn (Cbz) | 88 | 76 |
| 2 | Et\textsubscript{3}Si | CO\textsubscript{2}Et | Cbz | 82 | 85 |
| 3 | Ph\textsubscript{3}Si | CO\textsubscript{2}Et | Cbz | 89 | 79 |
| 4 | t-BuMe\textsubscript{2}Si | CO\textsubscript{2}Et | Cbz | 88 | 82 |
| 5 | t-BuPh\textsubscript{2}Si | CO\textsubscript{2}Et | Cbz | 76 | 88 |
| 6\(^c\) | i-Pr\textsubscript{3}Si | CO\textsubscript{2}Et | Cbz | \textbf{83} | \textbf{91} |
| 7 | i-Pr\textsubscript{3}Si | CO\textsubscript{2}Et | CO\textsubscript{2}Me | 39 | 88 |
| 8 | i-Pr\textsubscript{3}Si | CO\textsubscript{2}Et | CO\textsubscript{2}t-Bu (Boc) | 33 | 57 |
| 9 | i-Pr\textsubscript{3}Si | CO\textsubscript{2}Me | Cbz | 80 | 83 |
| 10 | i-Pr\textsubscript{3}Si | Cbz | Cbz | 91 | 86 |

\(^a\) The reaction was carried out with (R)-5b (5 mol%), 1 (1 equiv), and 2 (2 equiv) in dichloromethane (0.1 M based on 1) at −78 °C for 24 h. \(^b\) 1a:3a system. Reaction time was 6 h. \(^c\) 1b:3b system. Reaction time was 6 h
14. Preparation of (R)-6 (Scheme 1).

To a solution of (R)-5b (9.6 mg, 0.010 mmol) in dichloromethane (0.2 mL), one drop of N,N-dimethylformamide was added at room temperature. Then oxalyl chloride (3.0 µL, 0.035 mmol) was added at room temperature, and the mixture was warmed to 40 °C. The mixture was stirred at 40 °C for 5 min. Volatiles were removed in vacuo under heat conditions (ca. 40–50 °C). The obtained product (R)-S27 would be used in the next step without further purification.

(R)-S27 was dissolved in methanol (2 mL) and the solution was stirred at room temperature for 4 h. Excess methanol was then removed in vacuo. The obtained product was dissolved in toluene (2 mL), and the volatiles were thoroughly removed under reduced pressure to give pure (R)-6a as white-yellow solid (>99%, 9.7 mg). A trace amount of DMF remained.

**Methyl ester (R)-6a:**

$^1$H NMR (400 MHz, THF-$d_8$) 2.38 (s, 6H), 2.39 (s, 6H), 3.15 (d, J= 11.5 Hz, 3H), 4.84 (br, 3H), 7.16-7.40 (m, 20H), 7.43-7.49 (m, 2H), 7.54 (t, J= 8.7 Hz, 2H), 7.60 (t, J= 2.3 Hz, 4H), 7.98 (d, J= 8.2 Hz, 2H), 8.13 (s, 1H), 8.15 (s, 1H). $^{13}$C NMR (100 MHz, THF-$d_8$) δ 20.8 (2C), 20.9 (2C), 54.2 (d, J_{C-P} = 5.7 Hz), 125.4, 125.9, 126.5-126.8 (m, 8C), 127.6 (2C), 127.9 (2C), 128.1 (2C), 129.0 (2C), 129.8, 129.9, 130.6 (8C), 131.0 (2C), 131.1 (2C), 132.3, 132.4, 132.7 (2C), 133.4, 133.6, 136.2 (2C), 136.4 (3C), 136.5, 139.3 (2C), 142.2 (2C), 142.4 (2C), 142.6 (2C), 143.0 (2C), 146.7 (d, J_{C-P} = 7.6 Hz), 147.2 (d, J_{C-P} = 5.7 Hz) [Contamination of a trace amount of acetone (δ 30.2)] through the $^{13}$C NMR analysis. $^{31}$P NMR (160 MHz, THF-$d_8$) δ –0.27, 0.75. IR (KBr) 3448, 2924, 2854, 1593, 1492, 1450, 1398, 1239, 1188, 1058 cm$^{-1}$. M.p. 142 °C (decomposition). $[\alpha]_{D}^{23} = +189.6$ (c 1.00, CHCl$_3$). HRMS (ESI–) calcd for C$_{61}$H$_{49}$O$_8$P$_2$ [M–H]$^-$ 971.2908, found 971.2911.

To a solution of (R)-6a (97.3 mg, 0.10 mmol) in dichloromethane (2 mL), three drops of N,N-dimethylformamide was added at room temperature. Then oxalyl chloride (15 µL, 0.175 mmol) was added at room temperature, and the mixture was warmed to 40 °C. The mixture was
stirred at 40 °C for 5 min. Then oxalyl chloride (15 µL, 0.175 mmol) was added at room temperature, and the mixture was warmed to 40 °C. The mixture was stirred at 40 °C for 5 min. Volatiles were removed in vacuo under heat conditions (ca. 40–50 °C). The obtained product \((\text{R})-\text{S28}\) would be used in the next step without further purification. \((\text{R})-\text{S28}\) was dissolved in mixed solvent of dichloromethane (2 mL) and methanol (4 ml) the solution was stirred at room temperature for 2 h. The solution was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: CHCl₃:MeOH = 8:1 to 1:1) to give \((\text{R})-\text{6b}\), which would be contaminated with alkali and alkali earth metal ions. The obtained \((\text{R})-\text{6b}\) was dissolved in dichloromethane, and throughly washed with 1 M HCl aqueous solution, and the organic phase was separated. After the removal of volatiles under reduced pressure, the residue was dissolved in toluene, and the volatiles were thoroughly removed under reduced pressure to give pure \((\text{R})-\text{6b}\) as white-yellow solid (87%, 86.1 mg).

**Dimethyl ester \((\text{R})-\text{6b}\):**  
\(^1\)H NMR (400 MHz, THF-\(d_8\)) \(\delta\) 2.40 (s, 12H), 3.10 (d, \(J = 11.5\) Hz, 6H), 4.19 (br, 2H), 7.19-7.30 (m, 12H), 7.32-7.43 (m, 8H), 7.47 (t, \(J = 7.8\) Hz, 2H), 7.57 (d, \(J = 8.7\) Hz, 2H), 7.61 (s, 4H), 7.98 (d, \(J = 7.8\) Hz, 2H), 8.15 (s, 2H).  
\(^{13}\)C NMR (100 MHz, THF-\(d_8\)) \(\delta\) 20.9 (4C), 54.3 (d, \(J_{C-P} = 4.8\) Hz, 2C), 125.6 (2C), 126.6 (4C), 126.7 (2C), 126.9 (2C), 127.7 (2C), 128.1 (4C), 129.0 (2C), 130.0 (2C), 130.5 (4C), 130.6 (4C), 131.1 (4C), 132.6 (2C), 132.7 (2C), 133.5 (2C), 136.2 (6C), 139.3 (2C), 142.4 (4C), 142.7 (4C), 146.5 (d, \(J_{C-P} = 6.7\) Hz, 2C) [Contamination of a trace amount of acetone (\(\delta 30.2\)) through the \(^{13}\)C NMR analysis.]. \(^{31}\)P NMR (160 MHz, THF-\(d_8\)) \(\delta\) –1.4. IR (KBr) 3433, 2953, 2927, 2853, 1593, 1492, 1450, 1400, 1241, 1187, 1151, 1060 cm⁻¹. M.p. 140 °C (decomposition). \([\alpha]_D^{22} = +212.4\) (c 1.00, CHCl₃). HRMS (ESI–) calcd for C₆₂H₅₁O₈P₂ [M–H]– 985.3065, found 985.3065.

Summary of the reaction with the use of \((\text{R})-\text{5b}\), \((\text{R})-\text{6a}\), and \((\text{R})-\text{6b}\) is shown in Scheme S3.

\[\text{Ar} = 3,5-(\text{o-Tol})₂\text{C}_₆\text{H}_₃\]

**Scheme S3** Role of Brønsted acid in the catalysts.
15. Non-linear effect in the reaction of 2 with 1a (Fig. 3).

The presence of a non-linear effect was examined in the reaction of 2-methoxyfuran 2 (0.80 mmol) with α-ketimino ester 1a (0.40 mmol) in the presence of (R)-5b (5 mol%, 0% ee to 100% ee) in dichloromethane (0.1 M based on 1a) at –78 °C for 6 h. As shown in Scheme S4, a non-linear effect was not observed. Moreover, the yields of (S)-3a were independent of the enantiopurity of (R)-5b, and (S)-3a was obtained in a consistent yield of 71–75%. Therefore, a possible active species might be the monomeric structure of (R)-5b.

We also examined the reaction of 2 with 1a in the presence of (R)-4a or (R)-4b (5 mol%, 0% ee to 100% ee) in dichloromethane (0.1 M based on 1a) at –78 °C (Schemes S5 and S6). The reaction time was 12 h for (R)-4a catalysis, and 6 h for (R)-4b catalysis. As shown in Scheme S5, a positive non-linear effect was observed for (R)-4a-catalysis. This result strongly suggests that (R)-4a-catalysis might involve the dimeric structure of (R)-4a. In contrast, as shown in Scheme S6, a non-linear effect was not observed for (R)-4b-catalysis. This result strongly suggests again that a possible active species might be the monomeric structure of (R)-4b. The P=O moiety of (R)-4b is much less basic than (R)-4a, and therefore, the dimeric structure might not be involved in (R)-4b catalysis.
**Scheme S5**  Plot of the yield (%) and ee of (S)-3a vs. ee of (R)-4a.

**Scheme S6**  Plot of the yield (%) and ee of (S)-3a vs. ee of (R)-4b.
16. ESI-MS analysis of catalysts.

[Preparation of the samples for S20 (Fig. S7a), (R)-S15 (Fig. S7b), and (R)-S3 (Fig. S7c)] Acid (0.01 mmol) was dissolved in dichloromethane (200 µL) in a test tube at room temperature. After 30 min, 20 µL of the resulting solution was diluted with mixed solvent of dichloromethane (80 µL), methanol (50 µL) and acetonitrile (50 µL) in a test tube (final concentration: 5.0 mM), and passed through a membrane filter (200 mm mesh) just before injection. The spectra are shown in Figs. S5a–c.

[Preparation of the samples for (R)-S3 (Fig. S7d), (R)-5b (Fig. S7e), (R)-10c (Fig. S7f)] Acid (0.01 mmol) was dissolved in dichloromethane (200 µL) in a test tube at room temperature. After 30 min, 20 µL of the resulting solution was diluted with dichloromethane (180 µL) in a test tube (final concentration: 5.0 mM), and passed through a membrane filter (200 mm mesh) just before injection. The spectra are shown in Figs. S5d–f.

Since S20 and (R)-S15 could not be detected in less polar solvents such as dichloromethane probably due to the inherent ionization problem with S20 and (R)-S15, we first used polar solvents. As a result, the ESI-MS (negative) analysis of S20 in CH2Cl2/MeOH/CH3CN = 2/1/1, as shown in Fig. S7a, clearly suggests that S20 would not be a monomer. Instead, a dimer, trimer, tetramer, 5-mer, and 6-mer were observed under polar solvent conditions. (R)-S15 as shown in Figs. S5b would be a monomer, but a dimer, trimer, and tetramer were also observed as major species. In sharp contrast, the population of dimer, trimer, and tetramer of (R)-S3 in CH2Cl2/MeOH/CH3CN = 2/1/1 was reduced, as shown in Fig. S7c. Next, we used CH2Cl2 alone for highly soluble (R)-S3, as shown in Fig. S7d. As a result, a trimer and tetramer were not observed and the population of dimer was greatly decreased. Less polar solvents might be favored for hydrogen bonding, and the intramolecular double hydrogen bond network might be maintained under CH2Cl2 solvent conditions. Moreover, much more sterically hindered (R)-5b and (R)-10c in CH2Cl2 gave spectra (Figs. S5e and S5f) that were quite similar to that in Fig. S7d. Overall, this ESI-MS analysis suggests that bis(phosphoric acid)s, such as (R)-S3, (R)-5b, (R)-10c, would remain mostly as a monomer, whereas phosphoric acids, such as S20 and (R)-S15, would easily exhibit dimer, trimer, and tetramer forms. Overall, Fig. S8 summarizes the possible aggregation of the catalysts S20, (R)-S15, (R)-5b, and (R)-10c.

The correlation between the possible acidity (see Table S1, and Figs. S5 and S6), aggregation (see Figs. S7 and S8), and catalytic activity (see Table S1 and Scheme S1) of the catalysts is shown in Fig. S9. Catalyst (R)-5b might have much better Bronsted acidity than the others, and might avoid aggregation due to neutralization of the highly Bronsted basic P=O moiety through the conjugated double hydrogen bond network. As a result, catalyst (R)-5b would show better results than the others.
Fig. S7  ESI-MS (negative) spectrum of catalysts. (a) S20 in CH$_2$Cl$_2$/MeOH/CH$_3$CN.  (b) (R)-S15 in CH$_2$Cl$_2$/MeOH/CH$_3$CN.  (c) (R)-S3 in CH$_2$Cl$_2$/MeOH/CH$_3$CN.  (d) (R)-S3 in CH$_2$Cl$_2$.  (e) (R)-5b in CH$_2$Cl$_2$.  (f) (R)-10c in CH$_2$Cl$_2$.  

Chemical Formula: C$_{32}$H$_{32}$O$_{4}$P
Exact Mass: 500.1177
Fig. S7 (continued)
**Fig. S8** Possible equilibriums among monomer, dimer, and trimer of catalysts.

| Catalyst | Even polar solvent conditions | Polor and less-polar solvent conditions |
|----------|-------------------------------|----------------------------------------|
| (R)-S15  | Dimer of (R)-S15              | (Dimer)                                |
| (R)-S3   |                               | (Dimer)                                |
| (R)-5b   |                               |                                        |
| (R)-10c  |                               |                                        |

Brønsted acidity: + + +++ ++ – –
Aggregation: +++ ++ – –
Catalytic activity: + ++ +++ ++

**Fig. S9** Correlations among the possible acidity, aggregation, and catalytic activity of the catalysts.
17. Preparation of α-ketimino esters 7.

α-Ketimino esters 7 were prepared based on the literature procedure. A suspension of rhodium(II) acetate dimer (Rh₂(OAc)₄, 6.6 mg, 0.5 mol%), methyl carbamate (225 mg, 3.0 mmol), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 817 mg, 3.6 mmol), and well-dried MS 4Å (2 g) in dichloromethane (15 mL) was stirred at room temperature. Then the diazo compound S29 (3.3 mmol) in dichloromethane (10 mL) was added to the suspension over 1 h via a syringe pump. After completion of the addition, the reaction mixture was stirred for another 0.5 h. The resulting mixture was filtered through a pad of Celite, and the filtrate was condensed under reduced pressure. The residue was purified by silica gel column chromatography (eluent: dichloromethane) to give the desired product 7.

**Benzyl 2-((methoxycarbonyl)imino)-2-phenylacetate (7a):** Light yellow oil. $^1$H NMR (400 MHz, CDCl₃) δ 3.65 (s, 3H), 5.37 (s, 2H), 7.36-7.46 (m, 7H), 7.56 (t, $J$ = 7.3 Hz, 1H), 7.86 (d, $J$ = 7.8 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl₃) δ 53.7, 68.4, 128.7 (2C), 128.8 (2C), 128.9, 129.0 (2C), 129.4 (2C), 132.0, 133.3, 134.2, 162.1, 162.4, 162.9. IR (neat) 2953, 1739, 1635, 1450, 1316, 1232, 1004 cm⁻¹. HRMS (FAB+) calcd for C₁₇H₁₆NO₄ [M+H]+ 298.1079, found 298.1069.

**Benzyl 2-(4-fluorophenyl)-2-((methoxycarbonyl)imino)acetate (7b):** Light yellow oil. $^1$H NMR (400 MHz, CDCl₃) δ 3.64 (s, 3H), 5.36 (s, 2H), 7.08-7.15 (m, 2H), 7.35-7.45 (m, 5H), 7.86-7.95 (m, 2H). $^{13}$C NMR (100 MHz, CDCl₃) δ 53.7, 68.5, 116.1 (d, $J_{C-F}$ = 21.9 Hz, 2C), 128.2 (d, $J_{C-F}$ = 2.9 Hz), 128.8 (2C), 129.0 (3C), 131.9 (d, $J_{C-F}$ = 8.6 Hz, 2C), 134.0, 161.4, 161.9, 162.1, 165.8 (d, $J_{C-F}$ = 254.6 Hz). $^{19}$F NMR (376 MHz, CDCl₃) δ –104.2. IR (neat) 2954, 2846, 1739, 1636, 1593, 1509, 1437, 1415, 1324, 1229, 1158, 1037, 1002 cm⁻¹. HRMS (FAB+) calcd for C₁₇H₁₅FNO₄ [M+H]+ 316.0985, found 316.0994.
Benzyl 2-(2-fluorophenyl)-2-((methoxycarbonyl)imino)acetate (7c): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$, 50 °C) δ 3.70 (s, 3H), 5.31 (s, 2H), 7.08 (t, $J = 8.7$ Hz, 1H), 7.20 (t, $J = 7.3$ Hz, 1H), 7.30-7.40 (m, 5H), 7.49 (q, $J = 6.9$ Hz, 1H), 7.75 (br, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, 50 °C) δ 53.7, 68.6, 116.2 (d, $J_{C-F} = 21.0$ Hz), 121.9 (d, $J_{C-F} = 10.5$ Hz), 124.7 (d, $J_{C-F} = 2.9$ Hz), 128.7 (2C), 128.8 (3C), 130.5, 134.4, 134.5 (d, $J_{C-F} = 8.6$ Hz), 158.9, 161.5, 161.6, 161.7 (d, $J_{C-F} = 253.6$ Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ −111.5. IR (neat) 3035, 2955, 1745, 1639, 1613, 1486, 1457, 1266, 1229, 1000 cm$^{-1}$. HRMS (ESI+) calcd for C$_{17}$H$_{15}$FNO$_4$ [M+H]$^+$ 316.0980, found 316.0986.

Benzyl 2-(4-chlorophenyl)-2-((methoxycarbonyl)imino)acetate (7d): Light yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.64 (s, 3H), 5.36 (s, 2H), 7.35-7.44 (m, 7H), 7.82 (d, $J = 8.2$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 53.8, 68.6, 128.8 (2C), 129.1 (5C), 130.5, 130.7 (2C), 134.0, 139.8, 161.4, 161.9 (2C). IR (neat) 2953, 1739, 1633, 1592, 1568, 1492, 1436, 1405, 1377, 1321, 1284, 1232, 1176, 1092, 1037, 1002 cm$^{-1}$. HRMS (FAB+) calcd for C$_{17}$H$_{15}$ClNO$_4$ [M+H]$^+$ 332.0690, found 332.0681.

Benzyl 2-(3-bromophenyl)-2-((methoxycarbonyl)imino)acetate (7e): Light yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.64 (s, 3H), 5.36 (s, 2H), 7.30 (t, $J = 7.8$ Hz, 1H), 7.35-7.45 (m, 5H), 7.67 (dm, $J = 7.8$ Hz, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 8.03 (s, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 53.8, 68.7, 122.9, 128.0, 128.9 (2C), 129.1 (3C), 130.2, 132.2, 134.0 (2C), 136.1, 160.9, 161.6, 161.7. IR (neat) 2953, 1739, 1638, 1231, 1198 cm$^{-1}$. HRMS (FAB+) calcd for C$_{17}$H$_{15}$BrNO$_4$ [M+H]$^+$ 376.0184, found 376.0174.
Benzyl 2-((methoxycarbonyl)imino)-2-(4-(trifluoromethyl)phenyl)acetate (7f): Light yellow oil.  

$^1$H NMR (400 MHz, CDCl$_3$) δ 3.65 (s, 3H), 5.37 (s, 2H), 7.37-7.45 (m, 5H), 7.69 (d, $J = 8.7$ Hz, 2H), 7.98 (d, $J = 7.8$ Hz, 2H).  

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 53.9, 68.8, 123.6 (q, $J_{C-F} = 271.3$ Hz), 125.7 (q, $J_{C-F} = 3.8$ Hz, 2C), 128.9 (2C), 129.2 (3C), 129.8 (2C), 133.9, 134.4 (q, $J_{C-F} = 32.4$ Hz), 135.4, 160.6, 161.3, 161.6.  

$^{19}$F NMR (376 MHz, CDCl$_3$) δ –63.1.  

IR (neat) 2956, 1740, 1643, 1438, 1413, 1328, 1233, 1129, 1068, 1001 cm$^{-1}$.  

HRMS (FAB+) calcd for C$_{18}$H$_{15}$F$_3$NO$_4$ [M+H]$^+$ 366.0953, found 366.0957.

Benzyl 2-((methoxycarbonyl)imino)-2-(4-nitrophenyl)acetate (7g): Yellow powder.  

$^1$H NMR (400 MHz, CDCl$_3$) δ 3.65 (s, 3H), 5.38 (s, 2H), 7.39-7.44 (m, 5H), 8.05 (d, $J = 8.3$ Hz, 2H), 8.27 (d, $J = 8.7$ Hz, 2H).  

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 53.9, 69.1, 123.7 (2C), 128.9 (2C), 129.2 (2C), 129.3, 130.5 (2C), 133.7, 137.7, 150.2, 159.4, 160.7, 161.3.  

IR (KBr) 3115, 2962, 2953, 1742, 1724, 1644, 1522, 1350, 1318, 1246, 1199, 1004 cm$^{-1}$.  

M.p. 72-74 °C (decomposition).  

HRMS (FAB+) calcd for C$_{17}$H$_{15}$N$_2$O$_6$ [M+H]$^+$ 343.0930, found 343.0932.

Benzyl 2-((methoxycarbonyl)imino)-2-(4-methoxyphenyl)acetate (7h): Light yellow oil.  

$^1$H NMR (400 MHz, CDCl$_3$) δ 3.65 (s, 3H), 3.87 (s, 3H), 5.36 (s, 2H), 6.92 (d, $J = 8.7$ Hz, 2H), 7.34-7.47 (m, 5H), 7.85 (d, $J = 8.2$ Hz, 2H).  

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 53.7, 55.6, 68.2, 114.3 (2C), 124.5, 128.8 (2C), 128.9, 129.0 (2C), 131.7 (2C), 134.4, 162.4, 163.1, 163.2, 164.0.  

IR (neat) 2953, 1739, 1598, 1571, 1514, 1310, 1228, 1168 cm$^{-1}$.  

HRMS (FAB+) calcd for C$_{18}$H$_{17}$NNaO$_5$ [M+Na]$^+$ 350.1004, found 350.1016.
Benzyl 2-((methoxycarbonyl)imino)-2-(p-tolyl)acetate (7i): Light yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.41 (s, 3H), 3.65 (s, 3H), 5.36 (s, 2H), 7.23 (d, $J = 8.2$ Hz, 2H), 7.33-7.49 (m, 5H), 7.76 (d, $J = 8.2$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.8, 53.7, 68.3, 128.8 (2C), 128.9, 129.0 (2C), 129.3, 129.5 (2C), 129.6 (2C), 134.3, 144.5, 162.3, 162.8, 163.2. IR (neat) 3033, 2953, 1740, 1633, 1605, 1436, 1323, 1228, 1177, 1038, 1003 cm$^{-1}$. HRMS (FAB+) calcd for C$_{18}$H$_{17}$NNaO$_4$ [M+Na]$^+$ 334.1055, found 334.1047.

Benzyl 2-((methoxycarbonyl)imino)-2-(m-tolyl)acetate (7j): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.36 (s, 3H), 3.66 (s, 3H), 5.37 (s, 2H), 7.30-7.44 (m, 7H), 7.65 (s, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.4, 53.8, 68.3, 126.7, 128.7, 128.8 (2C), 129.0, 129.1 (2C), 129.8, 132.0, 134.30, 134.34, 138.7, 162.2, 162.7, 163.5. IR (neat) 3034, 2953, 1740, 1634, 1436, 1323, 1229, 1163, 1025 cm$^{-1}$. HRMS (ESI+) calcd for C$_{18}$H$_{18}$NO$_4$ [M+H]$^+$ 312.1230, found 312.1237.

Benzyl 2-((methoxycarbonyl)imino)-2-(m-tolyl)acetate (7k): Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.32 (br, 3H), 3.68 (s, 3H), 5.31 (s, 2H), 7.23 (t, $J = 7.8$ Hz, 3H), 7.34-7.42 (m, 6H). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 19.8, 53.6, 68.4, 126.1, 128.6 (3C), 128.8 (2C), 129.9, 131.3, 131.6, 132.4, 134.4, 137.4, 161.0, 161.4, 162.4. IR (neat) 3065, 3033, 2954, 1740, 1643, 1456, 1436, 1379, 1320, 1213, 1029, 1000 cm$^{-1}$. HRMS (FAB+) calcd for C$_{18}$H$_{17}$NNaO$_4$ [M+Na]$^+$ 334.1055, found 334.1062.

Benzyl 2-((methoxycarbonyl)imino)-2-(naphthalen-2-yl)acetate (7l): Light yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.69 (s, 3H), 5.43 (s, 2H), 7.38-7.50 (m, 5H), 7.52 (d, $J = 6.9$ Hz, 1H),
7.60 (d, J = 6.9 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 8.7 Hz, 1H), 8.01 (d, J = 8.7 Hz, 1H), 8.25 (s, 1H). 13C NMR (100 MHz, CDCl3) δ 53.8, 68.4, 124.1, 127.0, 127.9, 128.8 (3C), 128.9, 129.0, 129.2 (2C), 129.4, 129.5, 132.3, 132.5, 134.3, 135.7, 162.2, 162.7, 163.3. IR (neat) 3065, 3031, 2957, 2894, 2838, 1739, 1638, 1562, 1435, 1010 cm⁻¹. HRMS (FAB+) calcd for C21H18NO4 [M+H]+ 348.1236, found 348.1243.

Benzyl 2-((methoxycarbonyl)imino)-2-(naphthalen-1-yl)acetate (7m): Light yellow oil. 1H NMR (400 MHz, CDCl3, 50 °C) δ 3.68 (s, 3H), 5.28 (s, 2H), 7.20-7.32 (m, 5H), 7.40-7.41 (m, 3H), 7.61 (d, J = 6.4 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 8.11 (br, 1H). 13C NMR (100 MHz, CDCl3, 60 °C) δ 53.6, 68.5, 124.7, 124.9, 126.6, 127.6, 128.66 (6C), 128.71, 128.76, 130.7, 132.1, 133.7, 134.5, 161.6, 162.5, 163.1. IR (neat) 3035, 2953, 1738, 1642, 1436, 1313, 1227, 1177, 1101, 1026 cm⁻¹. HRMS (ESI+) calcd for C21H18NO4 [M+H]+ 348.1230, found 348.1230.

Benzyl 2-((methoxycarbonyl)imino)-2-(thiophen-3-yl)acetate (7n): Light yellow oil. 1H NMR (400 MHz, CDCl3) δ 3.62 (s, 3H), 5.35 (s, 2H), 7.34 (dd, J = 5.3, 3.0 Hz, 1H), 7.35-7.46 (m, 5H), 7.60 (d, J = 4.6 Hz, 1H), 8.12 (d, J = 1.8 Hz, 1H). 13C NMR (100 MHz, CDCl3) δ 53.6, 68.6, 126.7, 127.3, 128.8 (2C), 129.0 (3C), 134.1, 134.3, 135.4, 155.8, 161.5, 162.1. IR (neat) 3112, 2952, 1739, 1628, 1517, 1434, 1304, 1227, 1177, 1080, 1018 cm⁻¹. HRMS (FAB+) calcd for C15H13NNaO4S [M+H]+ 326.0463, found 326.0470.

Benzyl 2-((methoxycarbonyl)amino)-3-methylbut-2-enoate (7o): Light yellow solid. 1H NMR (400 MHz, CDCl3) δ 1.89 (s, 3H), 2.17 (s, 3H), 3.48-3.85 (br, 3H), 5.19 (s, 2H), 5.62-6.00 (br, 1H), 7.29-7.39 (m, 5H). 13C NMR (100 MHz, CDCl3) δ 21.5, 22.6, 52.6, 66.7, 121.1, 128.2 (3C), 128.6 (2C), 135.9, 147.0, 155.4, 164.8. IR (KBr) 3297, 3035, 2954, 1719, 1697, 1517, 1380, 1304, 1271, 1225, 1094, 1068 cm⁻¹. M.p. 54 °C. HRMS (FAB+) calcd for C14H17NNaO4 [M+Na]+ 286.1055, found 286.1053.
18. Representative procedures for the enantioselective aza-Friedel–Crafts reaction of 2 with 7 (Table 2 and Scheme 2).

To a well-dried pyrex Schlenk tube charged with activated MS 5 Å (50 mg) under a nitrogen atmosphere were added (R)-10c (8.1 mg, 0.010 mmol) in dichloromethane (1 mL) at –78 °C. After 5 min, α-ketimino ester 7 (0.20 mmol) in dichloromethane (1 mL), and 2-methoxyfuran 2 (37 µL, 0.40 mmol) were added at –78 °C. The reaction mixture was allowed to warm to –60 °C and was then stirred at that temperature for 3 h. To quench the reaction, triethylamine (0.1 mL) was added to the mixture at –60 °C, and the mixture was concentrated under reduced pressure at room temperature. The residue was purified by the silica gel column chromatography (eluent: n-hexane/EtOAc = 3/1 to 1/1) to give the desired product 8. The enantiomeric purity was determined by chiral HPLC analysis.

Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-phenylacetate (8a): –60 °C, 3 h, 93% yield, 95% ee. Coloreless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.60 (s, 3H), 3.78 (s, 3H), 5.12 (d, $J$ = 3.2 Hz, 1H), 5.16 (d, $J$ = 12.4 Hz, 1H), 5.21 (d, $J$ = 12.4 Hz, 1H), 6.22 (s, 1H), 6.38 (s, 1H), 7.12-7.18 (m, 2H), 7.24-7.29 (3H), 7.29-7.35 (m, 3H), 7.44-7.50 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 52.1, 57.6, 65.3, 68.0, 80.2, 112.4, 127.3 (2C), 127.8 (2C), 128.2, 128.3 (2C), 128.41 (2C), 128.43, 135.1, 137.2, 140.6, 154.8, 161.1, 169.3. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ –113.8. IR (neat) 3399, 2952, 1731, 1574, 1495, 1450. 1367, 1262, 1024 cm$^{-1}$. [$\alpha$]$^D_{27}$ = –2.4 (c 1.00, CHCl$_3$, 95% ee). HPLC analysis; AD-H, n-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, $t_R$ = 13.6 min (minor, S), 17.5 min (major, R). HRMS (FAB+) calcd for C$_{22}$H$_{21}$NNaO$_6$ [M+Na]$^+$ 418.1267, found 418.1252.
Benzyl \((R)-2-(4-fluorophenyl)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)acetate\) (8b): –60 °C, 3 h, 96% yield, 96% ee. Coloreless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 3.60\) (s, 3H), \(3.80\) (s, 3H), \(5.12\) (d, \(J = 3.2\) Hz, 1H), \(5.17\) (d, \(J = 12.4\) Hz, 1H), \(5.21\) (d, \(J = 12.4\) Hz, 1H), \(6.24\) (s, 1H), \(6.32\) (d, \(J = 3.2\) Hz, 1H), \(6.96-7.03\) (m, 2H), \(7.13-7.19\) (m, 2H), \(7.26-7.31\) (m, 3H), \(7.43-7.49\) (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 52.2, 57.7, 64.8, 68.2, 80.2, 112.5, 115.1\) (d, \(J_{C-F} = 21.9\) Hz, 2C), \(127.9\) (2C), \(128.3, 128.5\) (2C), \(129.3\) (d, \(J_{C-F} = 7.6\) Hz, 2C), \(132.9, 134.9, 140.4, 154.8, 161.2, 162.6\) (d, \(J_{C-F} = 246.9\) Hz), 169.2. \(^{19}\)F NMR (367 MHz, CDCl\(_3\)) \(\delta -113.8\). IR (neat) 3409, 2952, 1734, 1615, 1576, 1507, 1456, 1367, 1262, 1024 cm\(^{-1}\). \([\alpha]_D^{26} = -8.4\) (c 1.00, CHCl\(_3\), 96% ee). HPLC analysis; AD-H, \(n\)-hexane/i-PrOH = 1/1, 240 nm, 0.6 mL/min, \(t_R = 12.6\) min (minor, \(S\)), 15.5 min (major, \(R\)). HRMS (FAB+) calcd for C\(_{22}\)H\(_{21}\)FNO\(_6\) \([\text{M+H}]^+\) 414.1353, found 414.1364.

Benzyl \((R)-2-(2-fluorophenyl)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)acetate\) (8c): –60 °C, 3 h, 90%, 97% ee. Colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 3.58\) (br, 3H), \(3.80\) (s, 3H), \(5.17\) (d, \(J = 3.2\) Hz, 1H), \(5.18\) (d, \(J = 12.4\) Hz, 1H), \(5.28\) (d, \(J = 12.4\) Hz, 1H), \(6.32\) (d, \(J = 3.2\) Hz, 1H), \(6.53\) (br, 1H), \(7.00\) (dd, \(J = 11.4, 8.3\) Hz, 1H), \(7.11\) (t, \(J = 7.3\) Hz, 1H), \(7.16-7.21\) (m, 2H), \(7.25-7.34\) (m, 4H), \(7.44\) (t, \(J = 7.8\) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 52.2, 57.9, 62.6, 68.5, 81.1, 112.3, 115.5\) (d, \(J_{C-F} = 21.9\) Hz), \(123.5\) (d, \(J_{C-F} = 3.8\) Hz), \(128.0\) (2C), \(128.4, 128.5\) (3C), \(130.4\) (d, \(J_{C-F} = 8.6\) Hz), \(131.7, 135.1, 138.1, 154.6, 160.2\) (d, \(J_{C-F} = 246.0\) Hz), 161.7, 169.3. \(^{19}\)F NMR (367 MHz, CDCl\(_3\)) \(\delta -114.1\). IR (neat) 3410, 2953, 1734, 1614, 1573, 1489, 1456, 1369, 1262, 1038 cm\(^{-1}\). \([\alpha]_D^{26} = -30.0\) (c 1.00, CHCl\(_3\), 97% ee). HPLC analysis; OD-3, \(n\)-hexane/i-PrOH = 1/1, 254 nm, 1.0 mL/min, \(t_R = 10.0\) min (major, \(R\)), 16.2 min (minor, \(S\)). HRMS (FAB+) calcd for C\(_{22}\)H\(_{20}\)NNaO\(_6\) \([\text{M+Na}]^+\) 436.1172, found 436.1185.

Benzyl \((R)-2-(4-chlorophenyl)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)acetate\) (8d): –60 °C, 3 h, 96% yield, 96% ee. Coloreless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 3.60\) (s, 3H), \(3.80\) (s, 3H), \(5.12\) (d, \(J = 3.7\) Hz, 1H), \(5.17\) (d, \(J = 12.4\) Hz, 1H), \(5.21\) (d, \(J = 12.4\) Hz, 1H), \(6.25\) (s, 1H), \(6.30\) (d, \(J = 3.2\) Hz, 1H), \(7.13-7.19\) (m, 2H), \(7.26-7.32\) (m, 5H), \(7.40-7.45\) (m, 2H).
\[ ^{13} \text{C NMR (100 MHz, CDCl}_3 \delta 52.2, 57.7, 64.9, 68.3, 80.3, 112.5, 127.9 (2C), 128.4 (3C), 128.5 (2C), 128.9 (2C), 134.4, 134.9, 135.7, 140.2, 154.8, 161.3, 169.0. IR (neat) 3407, 2952, 1733, 1615, 1577, 1492, 1367, 1262, 1024 \text{ cm}^{-1}. \]  
\[ [\alpha]_D^{27} = -8.8 \quad (c \quad 1.00, \text{ CHCl}_3 \quad 96\% \text{ ee}). \]  
HPLC analysis; AD-H, \( n\)-hexane/\( i\)-PrOH = 1/1, 254 nm, 0.6 mL/min, \( t_R = 13.2 \text{ min} \text{ (minor, S), 18.9 \text{ min} \text{ (major, R)} \). HRMS (FAB+) calcd for \( \text{C}_{22}\text{H}_{21}\text{ClNO}_6 [\text{M+H}]^+ 430.1057 \), found 430.1063.

**Benzyl \((R)\)-2-(3-bromophenyl)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)acetate (8e):**  
\[ -60 \, ^\circ \text{C, 3 h, 98\% yield, 97\% ee. Coloreless oil.} \]  
\[ ^1\text{H NMR (400 MHz, CDCl}_3 \delta 3.60 (s, 3H), 3.79 (s, 3H), 5.12 (d, \, \text{J} = 3.2 \text{ Hz, 1H}), 5.19 (s, 2H), 6.26 (br, 1H), 6.33 (br, 1H), 7.13-7.22 (m, 3H), 7.25-7.33 (m, 3H), 7.43 (t, \, \text{J} = 7.8 \text{ Hz, 2H}), 7.66 (t, \, \text{J} = 1.8 \text{ Hz, 1H}). \]  
\[ ^{13}\text{C NMR (100 MHz, CDCl}_3 \delta 52.3, 57.7, 64.9, 68.4, 80.3, 112.7, 122.4, 126.1, 127.9 (2C), 128.4, 128.5 (2C), 129.8, 130.6, 131.6, 134.8, 139.4, 140.0, 154.7, 161.3, 168.8. IR (neat) 3400, 2952, 2842, 1732, 1615, 1576, 1496, 1261, 1058, 1024 \text{ cm}^{-1}. \]  
\[ [\alpha]_D^{29} = -8.4 \quad (c \quad 1.00, \text{ CHCl}_3, 97\% \text{ ee}). \]  
HPLC analysis; AD-H, \( n\)-hexane/\( i\)-PrOH = 1/1, 254 nm, 0.6 mL/min, \( t_R = 10.6 \text{ min} \text{ (minor, S), 12.5 \text{ min} \text{ (major, R)} \). HRMS (FAB+) calcd for \( \text{C}_{22}\text{H}_{20}\text{BrNNaO}_6 [\text{M+Na}]^+ 496.0372 \), found 496.0382.

**Benzyl \((R)\)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(4-(trifluoromethyl)phenyl)acetate (8f):**  
\[ -60 \, ^\circ \text{C, 3 h, 92\% yield, 97\% ee. Colorless oil.} \]  
\[ ^1\text{H NMR (400 MHz, CDCl}_3 \delta 3.61 (s, 3H), 3.81 (s, 3H), 5.13 (d, \, \text{J} = 3.2 \text{ Hz, 1H}), 5.18 (d, \, \text{J} = 12.4 \text{ Hz, 1H}), 5.22 (d, \, \text{J} = 12.4 \text{ Hz, 1H}), 6.29 (d, \, \text{J} = 3.2 \text{ Hz, 1H}), 6.33 (s, 1H), 7.10-7.16 (m, 2H), 7.24-7.31 (m, 3H), 7.57 (d, \, \text{J} = 8.2 \text{ Hz, 2H}), 7.63 (d, \, \text{J} = 8.7 \text{ Hz, 2H}). \]  
\[ ^{13}\text{C NMR (100 MHz, CDCl}_3 \delta 52.3, 57.8, 65.2, 68.5, 80.4, 112.6, 124.0 (q, \, \text{J}_{\text{C-F}} = 270.8 \text{ Hz}), 125.2 (q, \, \text{J}_{\text{C-F}} = 2.9 \text{ Hz}, 2C), 127.9 (2C), 128.0 (2C), 128.5 (3C), 130.5 (q, \, \text{J}_{\text{C-F}} = 32.1 \text{ Hz}), 134.8, 140.0, 141.1 154.8, 161.4, 168.7. \]  
\[ ^{19}\text{F NMR (376 MHz, CDCl}_3 \delta -62.6. \]  
IR (neat) 3410, 2953, 1734, 1615, 1575, 1497, 1328, 1263, 1168, 1125, 1070, 1020 \text{ cm}^{-1}. \]  
\[ [\alpha]_D^{27} = -16.4 \quad (c \quad 1.00, \text{ CHCl}_3, 97\% \text{ ee}). \]  
HPLC analysis; IC-3, \( n\)-hexane/\( i\)-PrOH = 1/1, 254 nm, 1.0 mL/min, \( t_R = 18.1 \text{ min} \text{ (major, R), 29.5 \text{ min} \text{ (minor, S)} \). HRMS (FAB+) calcd for \( \text{C}_{23}\text{H}_{21}\text{F}_3\text{NO}_6 [\text{M+H}]^+ 464.1321 \), found 464.1319.
Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(4-nitrophenyl)acetate (8g): –60 °C, 3 h, 95% yield, 96% ee. Yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.61 (br, 3H), 3.81 (s, 3H), 5.14 (d, $J = 3.7$ Hz, 1H), 5.19 (d, $J = 12.4$ Hz, 1H), 5.23 (d, $J = 12.4$ Hz, 1H), 6.25 (d, $J = 3.2$ Hz, 1H), 6.37 (s, 1H), 7.13-7.21 (m, 2H), 7.27-7.32 (m, 3H), 7.69 (dt, $J = 9.6, 2.3$ Hz, 2H), 8.16 (dt, $J = 9.6, 2.3$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 52.4, 57.8, 65.1, 68.8, 80.5, 112.6, 123.2 (2C), 128.1 (2C), 128.5 (2C), 128.6, 128.8 (2C), 134.5, 139.4, 144.3, 147.6, 154.8, 161.5, 168.3. IR (neat) 3400, 3031, 2953, 2841, 1732, 1615, 1574, 1521, 1496, 1350, 1262, 1112, 1024 cm$^{-1}$. $[\alpha]_D^{27} = -22.0$ (c 1.00, CHCl$_3$, 96% ee). HPLC analysis; AD-H, $n$-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, $t_R = 16.7$ min (minor, S), 17.8 min (major, R). HRMS (FAB+) calcd for C$_{22}$H$_{20}$N$_2$NaO$_8$ [M+Na]$^+$ 463.1117, found 463.1120.

Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(4-methoxyphenyl)acetate (8h): –60 °C, 6 h, 83% yield, 82% ee. Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.60 (br, 3H), 3.79 (s, 6H), 5.12 (d, $J = 3.2$ Hz, 1H), 5.16 (d, $J = 12.4$ Hz, 1H), 5.21 (d, $J = 12.4$ Hz, 1H), 6.18 (br, 1H), 6.37 (d, $J = 3.2$ Hz, 1H), 6.83 (d, $J = 10.1$ Hz, 2H), 7.14-7.20 (m, 2H), 7.25-7.32 (m, 3H), 7.38 (d, $J = 10.1$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 52.1, 55.3, 57.6, 64.8, 68.0, 80.1, 112.3, 113.7 (2C), 127.8 (2C), 128.2, 128.4 (2C), 128.6 (2C), 129.2, 135.2, 140.8, 154.9, 159.6, 161.1, 169.5. IR (neat) 3398, 2953, 1733, 1614, 1576, 1509, 1457, 1367, 1258, 1181, 1026 cm$^{-1}$. $[\alpha]_D^{28} = -0.4$ (c 1.00, CHCl$_3$, 82% ee). HPLC analysis; AD-H, $n$-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, $t_R = 22.0$ min (minor, S), 34.1 min (major, R). HRMS (FAB+) calcd for C$_{23}$H$_{23}$NNaO$_7$ [M+Na]$^+$ 448.1372, found 448.1367.

Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(p-tolyl)acetate (8i): –60 °C, 6 h, 91% yield, 94% ee. Colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.33 (s, 3H), 3.60 (br, 3H), 3.79 (s, 3H), 5.11 (d, $J = 3.2$ Hz, 1H), 5.15 (d, $J = 12.4$ Hz, 1H), 5.22 (d, $J = 12.4$ Hz, 1H), 6.20 (br, 1H), 6.38 (d, $J = 2.8$ Hz, 1H), 7.12 (d, $J = 8.2$ Hz, 2H), 7.14-7.19 (m, 2H), 7.25-7.31 (m,
Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(m-tolyl)acetate (8j): –60 °C, 3 h, 94% yield, 95% ee. Coloreless oil. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.30 (s, 3H), 3.61 (br, 3H), 3.80 (s, 3H), 5.12 (d, \(J = 3.2\) Hz, 1H), 5.20 (s, 2H), 6.16 (br, 1H), 6.40 (d, \(J = 2.8\) Hz, 1H), 7.11 (d, \(J = 7.3\) Hz, 1H), 7.14-7.29 (m, 8H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.6, 52.2, 57.7, 65.2, 68.0, 80.1, 112.4, 124.4, 127.8, 129.9 (2C), 128.2, 128.3, 128.4 (2C), 129.3, 135.3, 137.2, 138.1, 140.7, 154.9, 161.1, 169.4. IR (neat) 3402, 2951, 1731, 1615, 1575, 1495, 1368, 1262, 1024 cm\(^{-1}\). \([\alpha]_D^{26} = -2.0\) (c 1.00, CHCl\(_3\), 95% ee). HPLC analysis; AD-H, \(n\)-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, \(t_R = 11.5\) min (minor, S), 15.5 min (major, R). HRMS (FAB+) calcd for C\(_{23}\)H\(_{23}\)NNaO\(_6\) [M+Na\(^+\)] 432.1423, found 432.1422.

Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(naphthalen-2-yl)acetate (8l): –60 °C, 12 h, 96% yield, 95% ee. Coloreless oil. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.61 (s, 3H), 3.79 (s, 3H), 5.15 (d, \(J = 3.2\) Hz, 1H), 5.17 (d, \(J = 12.4\) Hz, 1H), 5.22 (d, \(J = 12.4\) Hz, 1H), 6.33 (s, 1H), 6.42 (s, 1H), 7.12-7.17 (m, 2H), 7.19-7.27 (m, 3H), 7.43-7.51 (m, 2H), 7.58 (dd, \(J = 8.7, 2.3\) Hz, 1H), 7.73-7.83 (m, 3H), 7.92 (d, \(J = 1.4\) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 52.3, 57.7, 65.5, 68.2, 80.3, 112.6, 124.9, 126.3, 126.6, 126.8, 127.5, 127.9 (2C), 128.1, 128.3, 128.4 (2C), 128.6, 132.9, 133.1, 134.7, 135.1, 140.6, 155.0, 161.2, 169.3. IR (neat) 3406, 2952, 1731, 1614, 1575, 1496, 1368, 1262, 1024 cm\(^{-1}\). \([\alpha]_D^{25} = -1.6\) (c 1.00, CHCl\(_3\), 95% ee). HPLC analysis; AD-H, \(n\)-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, \(t_R = 18.4\) min (minor, S), 28.3 min (major, R). HRMS (FAB+) calcd for C\(_{26}\)H\(_{23}\)NNaO\(_6\) [M+Na\(^+\)] 468.1423, found 468.1429.
Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(naphthalen-1-yl)acetate (8m): \(-60 ^\circ C, 12\) h, 85\% yield, 90\% ee. White solid. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.52 (br, 3H), 3.81 (s, 3H), 5.13 (d, \(J = 12.4\) Hz, 1H), 5.19 (d, \(J = 12.4\) Hz, 1H), 5.20 (d, \(J = 3.2\) Hz, 1H), 6.36 (d, \(J = 3.2\) Hz, 1H), 6.42 (s, 1H), 6.96 (d, \(J = 7.4\) Hz, 2H), 7.15 (t, \(J = 7.3\) Hz, 2H), 7.21 (t, \(J = 7.3\) Hz, 1H), 7.30 (td, \(J = 7.8, 1.4\) Hz, 1H), 7.35-7.43 (m, 3H), 7.82 (d, \(J = 8.2\) Hz, 1H), 7.85 (d, \(J = 8.2\) Hz, 1H), 7.94 (d, \(J = 8.2\) Hz, 1H). \(^13C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 52.2, 57.8, 66.3, 68.4, 80.9, 112.2, 123.6, 124.9, 125.4, 126.5, 128.0 (2C), 128.2, 128.3 (2C), 128.4, 129.4, 129.7, 130.5, 133.8, 134.3, 134.7, 139.9, 154.7, 161.6, 170.5. IR (KBr) 3400, 2942, 1728, 1614, 1570, 1496, 1367, 1262, 1037 cm\(^{-1}\). M.p. 38-50 \(^\circ C\) (decomposition). \([\alpha]D^{25} = -50.0\) (c 1.00, CHCl\(_3\), 90\% ee). HPLC analysis; OD-3, \(n\)-hexane/i-PrOH = 1/1, 254 nm, 1.0 mL/min, \(t_R = 9.0\) min (major, R), 22.9 min (minor, S). HRMS (FAB+) calcd for C\(_{26}H_{23}NNaO\(_6\) [M+Na\(^+\)] 468.1423, found 468.1429.

Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(thiophen-3-yl)acetate (8n): \(-60 \)\(^\circ\) C, 3 h, 96\% yield, 87\% ee. Coloreless oil. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.61 (s, 3H), 3.80 (s, 3H), 5.11 (d, \(J = 3.2\) Hz, 1H), 5.20 (d, \(J = 12.8\) Hz, 1H), 5.24 (d, \(J = 12.4\) Hz, 1H), 6.26 (s, 1H), 6.29 (d, \(J = 3.2\) Hz, 1H), 7.14 (dd, \(J = 5.0, 1.4\) Hz, 1H), 7.17-7.21 (m, 2H), 7.25 (dd, \(J = 5.0, 3.2\) Hz, 1H), 7.27-7.32 (m, 3H), 7.36 (dd, \(J = 3.2, 1.4\) Hz, 1H). \(^13C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 52.2, 57.7, 62.7, 68.1, 80.3, 111.9, 124.3, 125.5, 127.3, 127.8 (2C), 128.3, 128.5 (2C), 135.1, 137.9, 140.6, 154.8, 161.1, 169.0. IR (neat) 3400, 2952, 2839, 1732, 1615, 1577, 1497, 1365, 1262, 1059, 1024 cm\(^{-1}\). \([\alpha]D^{27} = -7.6\) (c 1.00, CHCl\(_3\), 87\% ee). HPLC analysis; AD-H, \(n\)-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, \(t_R = 14.3\) min (minor, S), 16.2 min (major, R). HRMS (FAB+) calcd for C\(_{20}H_{19}NNaO\(_6\)S [M+Na\(^+\)] 424.0831, found 424.0828.

Benzyl (R)-2-((methoxycarbonyl)amino)-2-(5-ethoxyfuran-2-yl)-2-phenylacetate (8p): \(-60 \)\(^\circ\) C, 12 h, 94\% yield, 94\% ee. Colorless oil. \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.37 (t, \(J = 7.1\) Hz, 3H), 3.60 (br, 3H), 4.02 (q, \(J = 7.2\) Hz, 2H), 5.12 (d, \(J = 3.2\) Hz, 1H), 5.16 (d, \(J = 12.4\) Hz, 1H), 5.22 (d, \(J = 12.4\) Hz, 1H), 6.22 (s, 1H), 6.37 (d, \(J = 2.8\) Hz, 1H), 7.12-7.18 (m, 2H), 7.25-7.36 (m, 6H), 7.45-7.51 (m, 2H). \(^13C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.6, 52.2, 65.3, 66.8, 68.0, 81.1, 112.4, 127.3, 134.3, 134.7, 139.9, 154.7, 161.6, 170.5. IR (KBr) 3400, 2952, 2839, 1732, 1615, 1577, 1497, 1365, 1262, 1059, 1024 cm\(^{-1}\). \([\alpha]D^{27} = -7.6\) (c 1.00, CHCl\(_3\), 87\% ee). HPLC analysis; AD-H, \(n\)-hexane/i-PrOH = 1/1, 254 nm, 0.6 mL/min, \(t_R = 14.3\) min (minor, S), 16.2 min (major, R). HRMS (FAB+) calcd for C\(_{26}H_{23}NNaO\(_6\) [M+Na\(^+\)] 468.1423, found 468.1429.
(2C), 127.8 (2C), 128.2, 128.3 (2C), 128.4 (3C), 135.1, 137.2, 140.4, 154.8, 160.2, 169.4. IR (neat) 3140, 2982, 2953, 1734, 1612, 1572, 1496, 1450, 1261, 1026 cm\(^{-1}\). \([\alpha]_D^{26} = -7.6 \ (c \ 1.00, \text{CHCl}_3, 94\% \text{ ee})\). HPLC analysis; AD-H, \(n\)-hexane/i-PrOH = 1/1, 230 nm, 0.6 mL/min, \(t_R = 11.7 \ \text{min (minor, S)}, 12.8 \ \text{min (major, R)}\).

HRMS (FAB+) calced for C\(_{23}\)H\(_{23}\)NNaO\(_6\) [M+Na]\(^+\) 432.1423, found 432.1422.

**Determination of absolute stereochemistry of 8e:**

To a solution of 8e (76.0 mg, 0.16 mmol, 97% ee) in diethyl ether (1.6 mL) was added methanol (13 \(\mu\)L, 0.32 mmol) followed by lithium borohydride (6.9 mg, 0.32 mmol) under nitrogen atmosphere at \(-78 \ ^{\circ}\C\). The mixture was stirred at 0 \(^{\circ}\C\) for 1 h. Saturated NH\(_4\)Cl aqueous solution (2 mL) was then added to the mixture. The mixture was extracted with diethyl ether (5 mL \(\times\) 2), and the combined organic layer was dried over Na\(_2\)SO\(_4\). The organic phase was concentrated under reduced pressure, and purified by silica gel column chromatography (eluent: \(n\)-hexane:EtOAc = 2:1 to 1:1), to give the desired product S30 in 83% yield (49.1 mg). White solid. 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.68 (s, 4H), 3.83 (s, 3H), 4.14 (m, 1H), 4.25 (dd, \(J = 12.1, 6.6 \ \text{Hz, 1H}\)) 5.12 (d, \(J = 3.2 \ \text{Hz, 1H}\)), 5.72 (s, 1H), 6.19 (d, \(J = 3.2 \ \text{Hz, 1H}\)), 7.18-7.28 (m, 2H), 7.41-7.47 (m, 2H). 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 52.6, 57.8, 63.3, 68.3, 80.0, 110.8, 122.6, 125.4, 129.8, 130.0, 131.1, 142.8 (2C), 156.5, 161.4. IR (KBr) 3232, 3073, 2953, 1690, 1615, 1567, 1439, 1370, 1283, 1261, 1098, 1047, 1021 cm\(^{-1}\). M.p. was not available due to decomposition. \([\alpha]_D^{27} = +4.0 \ (c \ 1.00, \text{CHCl}_3, 97\% \text{ ee})\). HRMS (FAB+) calced for C\(_{15}\)H\(_{16}\)BrNNaO\(_5\) [M+Na]\(^+\) 392.0110, found 392.0101.

**Crystal data of S30 (Fig. S10):** Compound S30 was recrystallized in diethyl ether for X-ray analysis. Formula C\(_{15}\)H\(_{16}\)BrNO\(_5\), colorless, crystal dimensions 0.35 \(\times\) 0.30 \(\times\) 0.25 mm\(^3\), monoclinic, space group P2\(_1\) \#4, a = 5.8577(16) Å, b = 14.389(4) Å, c = 9.621(3) Å, \(\alpha = 90.00 \ ^{\circ}\), \(\beta = 94.654(6) \ ^{\circ}\), \(\gamma = 90.00 \ ^{\circ}\), \(V = 808.2(4) \ \text{Å}^3\), \(Z = 2\), \(\rho_{\text{calc}} = 1.521 \ \text{g cm}^{-3}\), F(000) = 376, \(\mu(\text{MoK}\alpha) = 2.565 \ \text{mm}^{-1}\), \(T = 103 \ \text{K}\). 6877 reflections collected, 3178 independent reflections with \(I > 2\sigma(I)\) (\(2\theta_{\text{max}} = 27.492 \ ^{\circ}\)), and 217 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. Flack x = 0.002(5). \(R_1 = 0.0248\) and \(wR_2 = 0.0504\). GOF = 0.826. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1834631. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Web page: http://www.ccdc.cam.ac.uk/].
19. Optimization of catalysts, protecting groups on substrates, and reaction temperature in the reaction of 2 with 7a.

Screening of the chiral catalysts in the probe reaction of 2 with 7a is summarized in Scheme S7. The catalytic activities of chiral BINOL-derived phosphoric acids, such as (R)-4b and (R)-4c (i.e., TRIP), had no effect on either the yield or the enantioselectivity, and a prolonged reaction time (24 h) was needed. Chiral phosphoramidate (R)-S19 was also ineffective. Our chiral C$_2$-symmetric bis(phosphoric acid)s (R)-5a and (R)-5b showed better catalytic activities (12 h) than (R)-4b, (R)-4c, and (R)-S19, although the enantioselectivity was still low. Mono-methyl ester catalyst (R)-6a showed a similar result to (R)-5a and (R)-5b. In contrast, chiral C$_1$-symmetric bis(phosphoric acid)s (R)-10b and (R)-10c showed much better catalytic activity, and the reactions were finished within 3 h. In particular, 8a was obtained in 93% yield with 95% ee within 3 h when we used (R)-10c. Based on these results, we selected (R)-10c as an optimized catalyst for this reaction.
Scheme S7  Screening of the catalysts in the probe reaction of 2 with 7a.
Next, the protecting groups of the substrates 7 were optimized (Table S6). Here, we used unoptimized chiral bis(phosphoric acid) catalyst with \textit{n}-Pr protection. As a result, for \textit{N}-CO\textsubscript{2}Me-substrates, CO\textsubscript{2}Bn (Cbz) (entry 4) was much better than CO\textsubscript{2}Et (entry 1), CO\textsubscript{2}i-Pr (entry 2), and CO\textsubscript{2}t-Bu (Boc) (entry 3). Moreover, for Cbz-substrates, \textit{N}-CO\textsubscript{2}Me (entry 4) was much better than \textit{N}-Cbz (entry 5) and \textit{N}-Boc (entry 6).

\textit{Table S6} Optimization of the protecting groups of the substrates 7.

| Entry | CO\textsubscript{2}R\textsuperscript{1} | \textit{N}-CO\textsubscript{2}R\textsuperscript{2} | Yield (%) | ee (%) |
|-------|----------------|----------------|------------|--------|
| 1     | CO\textsubscript{2}Et | \textit{N}-CO\textsubscript{2}Me | 83         | 67     |
| 2     | CO\textsubscript{2}i-Pr | \textit{N}-CO\textsubscript{2}Me | 89         | 69     |
| 3     | CO\textsubscript{2}t-Bu (Boc) | \textit{N}-CO\textsubscript{2}Me | 78         | 72     |
| 4     | CO\textsubscript{2}Bn (Cbz) | \textit{N}-CO\textsubscript{2}Me | **89**     | **92** |
| 5     | Cbz           | \textit{N}-Cbz     | 76         | 19     |
| 6     | Cbz           | \textit{N}-Boc     | 83         | 0      |

Next, the ester moiety of the catalysts was optimized in a probe reaction of 2 with 7a (Table S7). Without protection, the enantioselectivity of 8a was low (entry 1). In contrast, either catalyst with Me (entry 2), \textit{n}-Pr (entry 3), or \textit{i}-Pr (entry 4) protection was effective, and 8a was obtained in high yields with high enantioselectivities (92–95\% ee). In particular, the catalyst with the \textit{i}-Pr moiety (i.e., (R)-10c, entry 4) slightly more effective (95\% ee) than the others.
Table S7  Optimization of the ester moiety of the catalysts.

| Entry | R           | Yield (%) | ee (%) |
|-------|-------------|-----------|--------|
| 1     | H [(R)-9c] | 82        | 18     |
| 2     | Me         | 92        | 92     |
| 3     | n-Pr       | 89        | 92     |
| 4     | i-Pr [(R)-10c] | 93   | 95     |

Next, the reaction temperature was examined in an unoptimized probe reaction (Table S8). At –78 °C, the reaction proceeded sluggishly, and the product was obtained in 79% yield with 70% ee (entry 1). At –40 °C, the reaction proceeded very smoothly, although the enantioselectivity was slightly reduced (64% ee) (entry 3). In contrast, at –60 °C, the reaction proceeded smoothly, and the product was obtained in 78% yield with 72% ee (entry 2). Based on these results, we set the temperature at –60 °C.

Table S8  Optimization of the reaction temperature.

| Entry | Temperature (°C) | Reaction time [h] | Yield (%) | ee (%) |
|-------|------------------|-------------------|-----------|--------|
| 1     | –78              | 24                | 79        | 70     |
| 2     | –60              | 12                | 78        | 72     |
| 3     | –40              | 1                 | 87        | 64     |
20. Preparation of (R)-S32 and the control experiments.

To a solution of (R)-10c (8.1 mg, 0.010 mmol) in dichloromethane (0.2 mL), one drop of N,N-dimethylformamide was added at room temperature. Then oxalyl chloride (3.0 µL, 0.035 mmol) was added at room temperature, and the mixture was warmed to 40 ºC. The mixture was stirred at 40 ºC for 5 min. Volatiles were removed in vacuo under heat conditions (ca. 40–50 ºC). The obtained (R)-S31 was used in the next step without further purification. (R)-S31 was dissolved in methanol (2 mL) and the solution was stirred at room temperature for 4 h. Excess methanol was then removed in vacuo. The obtained product was dissolved in toluene (2 mL), and the volatiles were thoroughly removed under reduced pressure to give (R)-S32 as light brown solid. (80% yield (ca. 90% purity, (R)-10c was involved), 6.8 mg).

Diisopropyl ((R)-3-(2,4,6-tricyclohexylphenyl)-[1,1’-binaphthalene]-2,2’-diyl) bis(hydrogen phosphate) ((R)-S32): ca. 90% purity (Impurity is inseparable (R)-10c, which might be generated by the reaction of (R)-S31 with adventitious water.). Light brown solid. $^1$H NMR (400 MHz, THF-$d_8$) $\delta$ 0.69 (d, $J$ = 6.4 Hz, 3H), 0.73 (d, $J$ = 6.4 Hz, 3H), 0.85-1.80 (m, 23H), 0.96 (d, $J$ = 6.0 Hz, 3H), 0.99 (d, $J$ = 6.0 Hz, 3H), 1.81-1.98 (m, 5H), 2.05-2.08 (m, 2H), 2.43-2.61 (m, 3H), 3.27 (m, 1H), 4.31 (m, 1H), 6.52 (br, 2H), 7.05 (s, 1H), 7.12 (s, 1H), 7.23-7.45 (m, 6H), 7.83 (s, 1H), 7.88 (d, $J$ = 8.2 Hz, 1H), 7.90-7.94 (m, 1H), 7.93 (d, $J$ = 8.2 Hz, 1H), 8.02 (d, $J$ = 9.2 Hz, 1H). $^{13}$C NMR (100 MHz, THF-$d_8$) Many peaks overlapped and are splited. $\delta$ 23.2, 23.3, 23.4, 23.5, 23.7, 23.8, 26.9, 27.0, 27.1, 27.6, 27.7, 27.8, 27.9, 30.5, 33.6, 35.4, 35.7, 35.5, 36.0, 37.8, 42.4, 42.6, 45.8, 72.3, 73.0, 73.1, 121.3, 122.3, 123.3, 125.1, 125.2, 125.5, 125.6, 126.3, 126.7, 127.1, 127.2, 128.5, 128.8, 130.6, 131.8, 132.0, 132.7, 133.7, 134.3, 146.7, 147.0, 147.1, 147.9, 148.0, 149.1, 149.2. $^{31}$P NMR (160 MHz, THF-$d_8$) $\delta$ -7.01, -4.83. IR (KBr) 3644, 3313, 2926, 2851, 1729, 1602, 1509, 1468, 1448, 1235, 1031, 997 cm$^{-1}$. M.p. 229-253 ºC (decomposition). $[\alpha]_D^{23}$ = +186.0 (c 1.00, CHCl$_3$). HRMS (FAB+) calcd for C$_{50}$H$_{63}$O$_8$P$_2$ [M+H]$^+$ 853.3998, found 853.4006.
Summary of the reaction with the use of (R)-9c, (R)-10c, and (R)-S32 is shown in Scheme S8.

**Scheme S8**  Role of Brønsted acid in the catalysts.
21. Transformation of 3b to 12–14 by selective reduction (Scheme 3a).

Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl)but-3-ynoate (11): THF (24 mL) was added to a two-necked round bottom flask with (S)-3b (1.04 g, 2.02 mmol, 91% ee), and the solution was stirred at room temperature. Tetrabuthylammonium fluoride (1.0 M in THF, 2.4 mL, 2.4 mmol) was added to the solution, and the mixture was stirred at room temperature for 5 min. The reaction mixture was passed through short silica gel with n-hexane and ethyl acetate (2:1). The filtrate was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1 to 2:1) to give the desired product 11 as yellow oil (724 mg, >99% yield). A trace amount of EtOAc and Et₂O remained. ¹H NMR (400 MHz, CDCl₃) δ 1.24 (t, J = 7.3 Hz, 3H), 2.62 (s, 1H), 3.82 (s, 3H), 4.29 (br, 2H), 5.09 (d, J = 12.4 Hz, 1H), 5.14 (d, J = 4.1 Hz, 1H), 5.15 (d, J = 12.4 Hz, 1H), 6.13 (br, 1H), 6.56 (br, 1H) 7.29-7.36 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 13.7, 55.8, 57.6, 63.5, 66.8, 73.1, 77.9, 80.7, 111.7, 128.0 (3C), 128.3 (2C), 135.9, 137.6, 153.8, 161.5, 166.3. IR (neat) 3413, 3292, 2979, 2124, 1758, 1614, 1574, 1020 cm⁻¹. [α]D²³ = +14.4 (c 1.00, CHCl₃, 91% ee). HRMS (FAB+) calcd for C₁₉H₁₉NNaO₆ [M+Na]⁺ 380.1110, found 380.1103.

Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl)butanoate (12): To a round bottom flask with 11 (129.7 mg, 0.363 mmol) and chlorotris(triphenylphosphine)rhodium(I) (Wilkinson’s catalyst) (37.0 mg, 0.040 mmol) was added benzene (10 mL) under a nitrogen atmosphere. The flask was purged with hydrogen with a balloon (1 atm). The mixture was stirred at 60 °C for 14 h. The reaction mixture was passed through short silica gel with n-hexane and ethyl acetate (3:1). The solution was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 9:1 to 3:1) to give the desired product 12 as colorless oil (131.1 mg, >99% yield). ¹H NMR (400 MHz, CDCl₃) δ 0.84 (t, J = 7.3 Hz, 3H), 1.21 (t, J = 7.3 Hz, 3H), 2.28 (m, 1H), 2.65 (br, 1H), 3.79 (s, 3H), 4.11-4.30 (m, 2H), 5.01 (d, J = 12.0 Hz, 1H), 5.08 (d, J = 12.0 Hz, 1H), 5.09 (d, J = 2.7 Hz, 1H), 6.18 (br, 1H), 6.25 (br, 1H), 7.27-7.38 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 7.8, 14.0, 25.5, 57.6, 62.3, 62.4, 66.4, 80.3, 108.9, 127.9 (2C), 128.0, 128.5 (2C), 136.5, 141.7, 153.9, 160.9, 170.6. IR (neat) 3420, 2978, 1726, 1578, 1496, 1369, 1304, 1251, 1069, 1022 cm⁻¹. [α]D²⁴ =
Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl)but-3-enoate (13): To a round bottom flask with 11 (79.8 mg, 0.223 mmol) and Lindlar’s catalyst (120 mg, 150 w/w%) was added ethanol (2 mL). The flask was purged with hydrogen with a balloon (1 atm). The mixture was stirred at 0 ºC for 30 min. The reaction mixture was passed through a pad of Celite with diethyl ether (20 mL). The solution was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 6:1 to 2:1) to give the desired product 13 as colorless oil (75.3 mg, 94% yield). ¹H NMR (400 MHz, CDCl₃) δ 1.21 (t, J = 6.9 Hz, 3H), 3.81 (s, 3H), 4.22 (br, 2H), 5.03 (d, J = 12.4 Hz, 1H), 5.10 (d, J = 2.7 Hz, 1H), 5.11 (d, J = 12.4 Hz, 1H), 5.38 (d, J = 10.5 Hz, 1H), 5.39 (d, J = 17.4 Hz, 1H), 6.14 (br, 1H), 6.26 (br, 1H), 6.40 (dd, J = 17.2, 10.5 Hz, 1H), 7.30-7.40 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 13.9, 57.7, 62.7, 62.9, 66.7, 80.4, 110.6, 117.1, 128.1 (3C), 128.5 (2C), 133.2, 136.4, 140.2, 154.0, 161.3, 169.2. IR (neat) 3414, 2940, 1731, 1614, 1576, 1496, 1386, 1259, 1023 cm –¹. [α]D²⁶ = +12.8 (c 1.00, CHCl₃, 91% ee). HRMS (FAB+) calcd for C₁₉H₂₃NNaO₆ [M+Na]+ 382.1267, found 382.1283.

Ethyl (S)-2-amino-2-(5-methoxyfuran-2-yl)butanoate (14): To a round bottom flask with 11 (198.9 mg, 0.557 mmol) and Lindlar’s catalyst (300 mg, 150 w/w%) was added ethanol (5.6 mL). The flask was purged with hydrogen with a balloon (1 atm). The mixture was stirred at room temperature for 2 h. The reaction mixture was passed through a pad of Celite with diethyl ether (80 mL). The solution was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 7:3 to 1:1) to give the desired product 14 as colorless oil (126.5 mg, >99% yield). ¹H NMR (400 MHz, CDCl₃) δ 0.92 (t, J = 7.3 Hz, 3H), 1.25 (t, J = 7.3 Hz, 3H), 1.89 (br, 2H), 1.96 (m, 1H), 2.11 (m, 1H), 3.81 (s, 3H), 4.12-4.26 (m, 2H), 5.07 (d, J = 3.2 Hz, 1H), 6.14 (d, J = 3.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 7.9, 14.1, 30.3, 57.6, 60.7, 61.5, 79.9, 106.9, 145.7, 160.9, 173.6. IR (neat) 3391, 2977, 2941, 1733, 1615, 1578, 1458, 1367, 1261, 1230, 1056, 1021 cm –¹. [α]D²⁷ = +29.2 (c 1.00, CHCl₃, 91% ee). HRMS (FAB+) calcd for C₁₀H₁₇NNaO₄ [M+Na]+ 250.1055, found 250.1061.
22. Transformation of 14 to γ-butenolide 16 (Scheme 3a).

Ethyl (S)-2-((tert-butoxycarbonyl)amino)-2-(5-methoxyfuran-2-yl)butanoate (S33): S33 was synthesized based on the literature procedure.\(^\text{20}\) THF (0.14 mL) was added to a pyrex Schlenk tube with 14 (61.1 mg, 0.268 mmol, 91% ee), and the solution was stirred at room temperature. Di-tert-butyl dicarbonate (61 µL, 0.282 mmol) was added to the solution, and the mixture was stirred at reflux temperature for 14 h. Volatiles were removed at room temperature under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 9:1 to 7:3) to give the desired product S33 as colorless oil (72.8 mg, 83% yield).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{): } \delta = 0.84 (t, J = 7.3 \text{ Hz}, 3\text{H}), 1.23 (t, J = 7.3 \text{ Hz}, 3\text{H}), 1.40 (s, 9\text{H}), 2.27 (m, 1\text{H}), 2.55 (br, 1\text{H}), 3.81 (s, 3\text{H}), 4.13-4.27 (m, 2\text{H}), 5.10 (d, J = 3.2 \text{ Hz}, 1\text{H}), 5.82 (br, 1\text{H}) 6.21 (d, J = 3.2 \text{ Hz}, 1\text{H}). \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{): } \delta = 7.9, 14.1, 25.8, 28.3 (3\text{C}), 57.7, 62.1 (2\text{C}), 79.4, 80.4, 142.1, 153.6, 160.8, 170.9. \]

IR (neat) 3429, 3134, 2978, 1724, 1615, 1578, 1487, 1367, 1307, 1261, 1168, 1135, 1068, 1022 cm\(^{-1}\). \[ [\alpha]_D^{22} = +42.0 (c 1.00, CHCl\text{3}, 91\% \text{ ee}). \]

HRMS (FAB+) calcd for C\(_{16}\)H\(_{25}\)NNaO\(_6\) [M+Na\(^+\)] 350.1580, found 350.1581.

6-Ethyl 1-methyl (S,Z)-5-((tert-butoxycarbonyl)amino)-5-ethyl-4-oxohex-2-enedioate (15): 15 was synthesized based on the literature procedure.\(^\text{21}\) Diethyl ether (3 mL) and saturated aqueous NaHCO\(_3\) (3 mL) were added to a round bottom flask with S33 (106.3 mg, 0.325 mmol, 91% ee), and the solution was stirred at 0 °C. N-bromosuccinimide (69.0 mg, 0.387 mmol) was added to the solution, and the mixture was stirred at 0 °C for 20 min. The resulting mixture was extracted with diethyl ether (10 mL × 3), and washed with brine (10 mL). The combined extracts were dried over Na\(_2\)SO\(_4\). The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 4:1 to 3:2) to give the desired product 15 as colorless oil (75.6 mg, 68% yield).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{): } \delta = 0.79 (t, J = 7.3 \text{ Hz}, 3\text{H}), 1.26 (t, J = 7.3 \text{ Hz}, 3\text{H}), 1.44 (s, 9\text{H}), 2.33 (m, 1\text{H}), 2.49 (m, 1\text{H}), 3.77 (s, 3\text{H}), 4.16-4.30 (m, 2\text{H}), 6.06 (s, 1\text{H}), 6.23 (d, J = 12.4 \text{ Hz}, 1\text{H}) 6.63 (d, J = 11.9 \text{ Hz}, 1\text{H}). \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{): } \delta = 7.5, 14.0, 25.5, 28.3 (3\text{C}), 52.3, 62.7, 72.3, 80.3, 131.3, 131.8, 154.1, 166.1, 168.3, 193.0. \]

IR (neat) 3423, 2979, 1717, 1486, 1368, 1247, 1168, 1054 cm\(^{-1}\). \[ [\alpha]_D^{23} = -20.8 (c 1.00, CHCl\text{3}, 91\% \text{ ee}). \]

HRMS (FAB+) calcd for C\(_{16}\)H\(_{25}\)NNaO\(_7\) [M+Na\(^+\)]
Ethyl (2S)-2-((tert-butoxycarbonyl)amino)-2-(5-oxo-2,5-dihydrofuran-2-yl)butanoate (16): 16 was synthesized based on the literature procedure. Methanol (4 mL) was added to a round bottom flask with 15 (75.6 mg, 0.220 mmol, 91% ee), and the solution was stirred at room temperature. Cerium(III) chloride heptahydrate (82.0 mg, 0.220 mmol) was added to the solution, and the mixture was stirred at room temperature for 10 min. The mixture was cooled to –78 °C, and sodium borohydride (8.3 mg, 0.219 mmol) was added. Then the mixture was warmed to room temperature and stirred at that temperature for 30 min. The resulting mixture was quenched with saturated aqueous NH₄Cl (5 mL), extracted with diethyl ether (10 mL × 3), and washed with brine (10 mL). The combined extracts were dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 4:1 to 3:2) to give the desired product 16 as colorless oil (57.9 mg, 84% yield, dr = 80:20). The absolute configuration has not been determined. Two diastereomers could not be separated from each other. IR (neat, mixture of isomer I and isomer II) 3422, 2979, 1762, 1497, 1369, 1315, 1252, 1164, 1092 cm⁻¹. HRMS (FAB+, mixture of I and II) calcd for C₁₅H₂₃NNaO₆ [M+Na]+ 336.1423, found 336.1425. Major isomer I: ¹H NMR (400 MHz, CDCl₃) δ 0.82 (t, J = 7.3 Hz, 3H), 1.31 (t, J = 7.3 Hz, 3H), 1.40 (s, 9H), 1.95 (m, 1H), 2.64 (m, 1H), 4.28 (q, J = 7.3 Hz, 2H), 5.53 (m, 2H), 6.09 (dd, J = 5.5, 1.8 Hz, 1H), 7.71 (d, J = 5.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 7.9, 14.1, 23.8, 28.2 (3C), 62.8, 65.6, 80.0, 85.3, 121.6, 153.7, 156.0, 170.4, 172.6. Minor isomer II: ¹H NMR (400 MHz, CDCl₃) δ 0.98 (t, J = 7.3 Hz, 3H), 1.28 (t, J = 7.3 Hz, 3H), 1.36 (s, 9H), 1.89-2.10 (m, 2H), 4.23 (q, J = 7.3 Hz, 2H), 4.84 (br, 1H), 5.57 (br, 1H), 5.99 (dd, J = 5.5, 1.8 Hz, 1H), 7.77 (d, J = 5.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 8.2, 14.2, 28.1 (3C), 29.0, 61.7, 63.9, 80.4, 82.9, 120.1, 154.1, 154.3, 169.8, 173.3.

23. Transformation of 11 to 17 (Scheme 3b).

Ethyl (S)-2-(benzofuran-2-yl)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl) acetate (17): 17 was synthesized based on the literature procedure. To a two-necked round bottom flask with 11 (233 mg, 0.651 mmol, 91% ee), 2-iodophenol (404 mg, 1.83 mmol), tetrakis(triphenylphosphine) palladium(0) (80 mg, 0.069 mmol), and copper(I) iodide (27 mg, 0.14 mmol) were added THF (3 mL) under a nitrogen atmosphere. Triethylamine (7 mL) was added to the solution at 0 °C, and the mixture was stirred at 70 °C for 6 h. The resulting mixture was then
cooled in ice bath, and diluted with diethyl ether (20 mL) and 1 M HCl aqueous solution (10 mL). The mixture was extracted with diethyl ether (20 mL × 2) and washed with brine (10 mL). The combined extracts were dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1 to 3:2) to give the product 17 as orange oil (104 mg, 36% yield). ¹H NMR (400 MHz, CDCl₃) δ 1.19 (t, J = 6.9 Hz, 3H), 3.83 (s, 3H), 4.26 (q, J = 6.9 Hz, 2H), 5.05 (s, 2H), 5.17 (d, J = 3.2 Hz, 1H), 6.44 (br, 1H), 6.49 (br, 1H), 6.94 (br, 1H), 7.20-7.40 (m, 7H), 7.44 (d, J = 8.2 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H) ¹³C NMR (100 MHz, CDCl₃) δ 13.9, 57.8, 61.5, 63.4, 66.9, 80.8, 107.0, 111.4, 111.9, 121.5, 123.0, 124.6, 128.0 (4C), 128.4 (2C), 136.2, 138.3, 152.0, 154.0, 154.7, 161.4, 167.5. IR (neat) 3412, 2975, 2938, 1734, 1615, 1574, 1496, 1454, 1369, 1256, 1121, 1024 cm⁻¹. [α]D²⁹ = +4.4 (c 1.00, CHCl₃, 91% ee). HRMS (FAB+) calcd for C₂₅H₂₃NNaO₇ [M+Na]+ 472.1372, found 472.1382.

24. Transformation of 11 to 18 (Scheme 3c).

**Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-2-(5-methoxyfuran-2-yl)-2-(1-tosyl-1H-indol-2-yl) acetate (18a):** 18a was synthesized based on the literature procedure.²² To a two-necked round bottom flask with 11 (154 mg, 0.432 mmol, 91% ee), N-(2-iodophenyl)-4-toluenesulfonamide (323 mg, 0.865 mmol), tetrakis(triphenylphosphine) palladium(0) (104 mg, 0.090 mmol), and copper(I) iodide (34 mg, 0.18 mmol) was added THF (1 mL) under a nitrogen atmosphere. Triethylamine (1 mL, 7.2 mmol) was added to the solution at 0 °C, and the mixture was stirred at 70 °C for 5 h. The resulting mixture was then cooled in ice bath, and diluted with diethyl ether (5 mL) and 1 M HCl aqueous solution (10 mL). The mixture was extracted with diethyl ether (20 mL × 2) and washed with brine (10 mL). The combined extracts were dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1 to 3:1) to give the product 18a as orange oil (257 mg, 99% yield). A trace amount of Et₂O and EtOAc remained. ¹H NMR (400 MHz, CDCl₃) δ 1.28 (t, J = 7.3 Hz, 3H), 2.25 (s, 3H), 3.82 (s, 3H), 4.32 (q, J = 7.3 Hz, 2H), 4.70 (d, J = 12.4 Hz, 1H), 4.99 (d, J = 12.4 Hz, 1H), 5.19 (d, J = 3.2 Hz, 1H), 6.32 (br, 1H), 6.62 (br, 1H), 6.82 (br, 1H), 7.02 (d, J = 7.8 Hz, 2H), 7.17-7.37 (m, 7H), 7.48 (d, J = 6.4 Hz, 1H), 7.57 (d, J = 7.3 Hz, 2H), 7.88 (d, J = 7.3 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 13.2, 22.2, 57.5, 62.2, 63.1, 66.1, 80.9, 111.7, 114.3, 116.7, 121.5, 123.2, 124.9, 126.3 (2C), 127.5 (2C), 127.8, 127.9, 128.3 (2C), 129.4 (2C), 136.1, 136.2, 136.8, 137.2, 138.8, 144.3, 153.5, 161.1, 167.6. IR (neat) 3415, 2978,
1736, 1613, 1572, 1495, 1452, 1366, 1250, 1175, 1036 cm⁻¹. \([\alpha]D^{26} = -79.2 (c 1.00, CHCl₃, 91\% ee)\). HRMS (FAB+) calcd for C₃₂H₃₀N₂NaO₈S [M+Na]^+ 625.1621, found 625.1635.

**Ethyl (S)-2-(((benzylloxy)carbonyl)amino)-2-(5-chloro-1-tosyl-1H-indol-2-yl)-2-(5-methoxyfuran-2-yl)acetate (18b):** A trace amount of Et₂O remained. Orange oil. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta 1.28 (t, J = 7.3 Hz, 3H)\), 2.27 (s, 3H), 3.82 (s, 3H), 4.32 (q, \(J = 7.3 Hz, 2H\)), 4.69 (d, \(J = 12.4 Hz, 1H\)), 4.99 (d, \(J = 12.4 Hz, 1H\)), 5.19 (d, \(J = 3.7 Hz, 1H\)), 6.30 (d, \(J = 3.2 Hz, 1H\)), 6.60 (br, 1H), 6.74 (br, 1H), 7.04 (d, \(J = 7.3 Hz, 2H\)), 7.20 (d, \(J = 9.2 Hz, 1H\)), 7.26-7.37 (m, 5H), 7.45 (s, 1H), 7.56 (d, \(J = 7.3 Hz, 2H\)), 7.81 (d, \(J = 8.2 Hz, 1H\)). \(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta 13.9, 21.5, 57.8, 62.3, 63.5, 66.4, 81.3, 112.0, 115.7, 116.1, 121.2, 125.3, 126.6 (2C), 127.9 (2C), 128.1, 128.6 (2C), 129.1, 129.4, 129.7 (2C), 135.8, 136.3 (2C), 138.6, 138.8, 144.7, 153.7, 161.3, 167.6. IR (neat) 3411, 2926, 1738, 1613, 1496, 1448, 1368, 1248, 1172, 1036 cm⁻¹. \([\alpha]D^{25} = -111.6 (c 1.00, \text{CHCl}_3, 91\% ee)\). HRMS (FAB+) calcd for C₃₂H₃₀ClN₂NaO₈S [M+Na]^+ 659.1231, found 659.1231.

**Ethyl (S)-2-(((benzylloxy)carbonyl)amino)-2-(5-methoxy-1-tosyl-1H-indol-2-yl)-2-(5-methoxyfuran-2-yl)acetate (18c):** Orange oil. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta 1.27 (t, J = 7.3 Hz, 3H)\), 2.24 (s, 3H), 3.78 (s, 3H), 3.81 (s, 3H), 4.32 (q, \(J = 7.3 Hz, 2H\)), 4.69 (d, \(J = 12.4 Hz, 1H\)), 4.99 (d, \(J = 12.8 Hz, 1H\)), 5.18 (d, \(J = 3.2 Hz, 1H\)), 6.30 (d, \(J = 2.8 Hz, 1H\)), 6.62 (s, 1H), 6.76 (s, 1H), 6.86 (d, \(J = 8.7 Hz, 1H\)), 6.92 (s, 1H), 7.01 (d, \(J = 7.8 Hz, 2H\)), 7.25-7.39 (m, 5H), 7.54 (d, \(J = 7.3 Hz, 2H\)), 7.78 (d, \(J = 8.7 Hz, 1H\)). \(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta 13.8, 21.3, 55.4, 57.6, 62.2, 63.1, 66.1, 81.0, 103.5, 111.7, 114.2, 115.3, 117.0, 126.3 (2C), 127.6 (2C), 127.9, 128.3 (2C), 128.9, 129.4 (2C), 131.9, 136.2, 136.3, 137.4, 138.9, 144.2, 153.5, 156.2, 161.1, 167.7. IR (neat) 3414, 2983, 1737, 1613, 1495, 1472, 1365, 1258, 1213, 1174, 1035 cm⁻¹. \([\alpha]D^{25} = -124.8 (c 1.00, \text{CHCl}_3, 91\% ee)\). HRMS (FAB+) calcd for C₃₃H₃₂ClN₂NaO₉S [M+Na]^+ 655.1726, found 655.1730.
Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-2-(6-chloro-1-tosyl-1H-indol-2-yl)-2-(5-methoxyfuran-2-yl)acetate (18d): A trace amount of Et₂O remained. Orange oil. ¹H NMR (400 MHz, CDCl₃) δ 1.28 (t, J = 7.3 Hz, 3H), 2.27 (s, 3H), 3.82 (s, 3H), 4.32 (q, J = 7.3 Hz, 2H), 4.67 (d, J = 12.4 Hz, 1H), 4.98 (d, J = 11.9 Hz, 1H), 5.18 (d, J = 3.2 Hz, 1H), 6.29 (d, J = 3.2 Hz, 1H), 6.58 (br, 1H), 6.76 (br, 1H), 7.06 (d, J = 7.8 Hz, 2H), 7.18 (dd, J = 8.2, 1.8 Hz, 1H), 7.25-7.42 (m, 6H), 7.58 (d, J = 7.8 Hz, 2H), 7.93 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 13.9, 21.5, 57.7, 62.3, 63.4, 66.3, 81.2, 111.9, 114.7, 116.3, 122.4, 124.1, 126.5 (2C), 126.6, 127.7 (2C), 128.1, 128.5 (2C), 129.7 (2C), 131.0, 136.2 (2C), 137.8 (2C), 138.9, 144.7, 153.7, 161.3, 167.6. IR (neat) 3411, 2936, 1737, 1613, 1495, 1448, 1368, 1250, 1174, 1035 cm⁻¹. [α]D²⁶ = –173.2 (c 1.00, CHCl₃, 91% ee). HRMS (FAB+) calcd for C₃₂H₂₉ClMN₂NaO₈S [M+Na]⁺ 659.1231, found 659.1209.

Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-4-(4-methoxy-2-((4-methylphenyl)sulfonamido)phenyl)-2-(5-methoxyfuran-2-yl)but-3-ynoate (S₃₄): S₃₄ was synthesized based on the literature procedure.²³ To a two-necked roundbottom flask with 11 (261 mg, 0.730 mmol, 91% ee), N-(2-iodophenyl)-4-toluenesulfonamide (590 mg, 1.46 mmol), tetrakis(triphenylphosphine)palladium(0) (42 mg, 0.0363 mmol), and copper(I) iodide (14 mg, 0.0735 mmol) was added THF (6 mL) under a nitrogen atmosphere. Triethylamine (2 mL, 14.3 mmol) was added to the solution at 0 °C, and the mixture was stirred at room temperature for 4 h. The resulting mixture was then cooled in ice bath, and diluted with diethyl ether (5 mL) and 1 M HCl aqueous solution (10 mL). The mixture was then washed with diethyl ether (20 mL × 2) and washed with brine (10 mL). The combined extracts were dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluents: n-hexane:EtOAc = 4:1 to 3:2) to give the product S₃₄ as orange oil (442.9 mg, 96% yield). ¹H NMR (400 MHz, CDCl₃) δ 1.28 (t, J = 7.3 Hz, 3H), 2.35 (s, 3H), 3.80 (s, 3H), 3.84 (s, 3H), 4.35 (q, J = 7.3 Hz, 2H), 5.15 (d, J = 3.2 Hz, 1H), 5.20 (d, J = 11.9 Hz, 1H), 5.29 (d, J = 11.9 Hz, 1H), 6.25 (d, J = 11.9 Hz, 1H), 6.58 (br, 1H), 6.76 (br, 1H), 7.06 (d, J = 7.8 Hz, 2H), 7.18 (dd, J = 8.2, 1.8 Hz, 1H), 7.25-7.42 (m, 6H), 7.58 (d, J = 7.8 Hz, 2H), 7.93 (s, 1H).
Ethyl (S)-2-(((benzyloxy)carbonyl)amino)-2-(6-methoxy-1-tosyl-1H-indol-2-yl)-2-(5-methoxyfuran-2-yl)acetate (18e): 18e was synthesized based on the literature procedure. Toluene (7 mL) was added to a round bottom flask with S34 (443 mg, 0.70 mmol), and the solution was stirred at room temperature. Silver(I) acetate (23.0 mg, 0.138 mmol) was added to the solution, and the mixture was stirred at 100 °C for 1 h. The reaction mixture was passed through short silica gel (eluent: n-hexane:EtOAc = 2:1). The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 4:1 to 3:2) to give the desired product 18e as orange oil (390 mg, 88% yield).

25. Transformation of 18a to 19 (Scheme 3d).
Ethyl (2S)-2-(((Benzyloxy)carbonyl)amino)-2-(4-methoxy-1,4-epoxynaphthalen-1(4H)-yl)-2-(1-tosyl-1H-indol-2-yl)acetate (S35): S35 was synthesized based on the literature procedure.25 To a well-dried pyrex Schlenk tube with cesium fluoride (261 mg, 1.72 mmol) in THF (4 mL) was added 18-crown-6 (680 mg, 2.58 mmol) in THF (4 mL). 2-(Trimethylsilyl)phenyl trifluoromethanesulfonate (210 µL, 0.86 mmol) was added, and the mixture was stirred at room temperature for 30 min. The mixture was cooled to –78 °C, and 18a (257 mg, 0.426 mmol) in THF (2 mL) was added. Then the mixture was warmed to room temperature and stirred at that temperature for 2 h. The resulting mixture was diluted with water (5 mL), extracted with diethyl ether (20 mL × 2), and washed with brine (10 mL). The combined extracts were dried over Na2SO4. The organic phase was concentrated under reduced pressure, and the resultant residue was roughly purified by short silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1 to 3:1) to give the product S35 as light blue oil (294 mg, >99% yield, dr = ca. 1:1), which was used in the next step as soon as possible. 

1H NMR (400 MHz, CDCl3) Many peaks of the diastereomers (dr = ca. 1:1) overlapped. δ 1.27 (t, J = 7.3 Hz, 6H), 2.29 (s, 6H), 3.65 (s, 6H), 4.19-4.43 (m, 4H), 4.79 (d, J = 11.9 Hz, 2H), 5.12 (d, J = 10.5 Hz, 2H), 6.66-8.87 (m, 38H), 8.15 (d, J = 7.4 Hz, 2H), 8.28 (br, 2H). 13C NMR (100 MHz, CDCl3) Many peaks of the diastereomers (dr = ca. 1:1) overlapped. δ 13.8, 14.0, 15.1, 21.6, 29.8, 55.4, 59.1, 63.1, 64.2, 65.6, 66.5, 66.8, 83.5, 102.5, 114.5, 114.7, 119.5, 121.4, 121.9, 122.2, 123.2, 123.5, 123.6, 125.0, 125.6, 126.1, 126.4, 126.7, 126.9, 127.4, 127.8, 127.9, 128.1, 128.3, 128.5, 129.7, 136.3, 137.7, 144.4, 144.7, 149.3, 153.8, 166.9, 169.7. HRMS (FAB+) calcd for C38H34N2NaO8S [M+Na]+ 701.1934, found 701.1909.

Ethyl (R)-6-methoxy-2-oxo-4-(1-tosyl-1H-indol-2-yl)-3,4-dihydro-2H-naphtho[2,1-e][1,3] oxazine-4-carboxylate (19a): To a two-necked round bottom flask with S35 (294 mg, 0.43 mmol) were added acetic acid (9 mL) and 12 M HCl aqueous solution (1 mL). The solution was stirred at 80 °C for 3 h. Then the resulting mixture was diluted with diethyl ether (20 mL) and NaHCO3 aqueous solution (200 mL). The mixture was extracted with diethyl ether (20 mL × 2) and washed with brine (10 mL). The combined extracts were dried over Na2SO4. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 5:1 to 3:1) to give the product 19a as colorless solid (241 mg, 98% yield). The enantiomeric purity of 19a was determined by chiral HPLC analysis (91% ee). 1H NMR (400 MHz, CDCl3) δ 1.33 (t, J = 6.9 Hz, 3H), 2.37 (s, 3H), 3.69 (s, 3H), 4.31 (m, 1H), 4.44 (m, 1H), 6.09 (s, 1H), 6.81 (s, 1H), 7.13 (t, J = 8.0 Hz, 1H), 7.20 (t, J = 8.2 Hz, 1H), 7.24-7.34 (m, 4H), 7.61-7.70 (m, 3H), 7.80 (d, J = 8.2 Hz, 2H), 8.31 (d, J = 9.1 Hz, 1H), 8.37 (d, J = 8.7 Hz, 1H). 13C NMR (100 MHz, CDCl3) δ 14.1, 21.7, 56.0, 63.5, 64.5, 99.4, 111.5, 114.2, 114.7, 121.7, 121.9, 122.1, 123.8, 124.3, 125.8, 126.4, 127.2 (2C), 127.6 (2C), 127.9, 130.2 (2C), 135.3, 136.8, 139.8, 140.9, 145.5, 149.0, 152.3, 168.9. IR (KBr) 3359, 2925, 1731, 1593, 1460, 1354, 1243, 1170, 1106, 1089, 1057 cm–1. M.p. 142 °C (decomposition). [α]D30 = −204.3 (c 1.00, CHCl3, 91% ee). HRMS (FAB+) calcd for C31H26N2NaO8S [M+Na]+ 701.1934, found 701.1909.
593.1340. HPLC analysis; OD-3 × 2, n-hexane/i-PrOH = 4/1, 254 nm, 0.6 mL/min, \( t_R = 25.2 \) min (major, \( R \)), 29.9 min (minor, \( S \)).

**Crystal data of 19a (Fig. S11):** Compound 19a was recrystallized in benzene for X-ray analysis. Formula \( \text{C}_{32}\text{H}_{27}\text{Cl}_{3}\text{N}_{2}\text{O}_{7}\text{S} \), colorless, crystal dimensions \( 0.75 \times 0.12 \times 0.10 \) mm\(^3\), monoclinic, space group \( \text{P2}_1 \) (#4), \( a = 10.664(3) \) Å, \( b = 10.372(2) \) Å, \( c = 14.789(4) \) Å, \( \alpha = 90.00^\circ \), \( \beta = 104.778(6)^\circ \), \( \gamma = 90.00^\circ \), \( V = 1581.7(7) \) Å\(^3\), \( Z = 2 \), \( \rho_{\text{calc}} = 1.449 \) g cm\(^{-3}\), \( F(000) = 712 \), \( \mu(\text{MoKc}) = 0.407 \) mm\(^{-1}\), \( T = 123 \) K. 13598 reflections collected, 6894 independent reflections with \( I > 2\sigma(I) \) (\( 2\theta_{\text{max}} = 27.48^\circ \)), and 469 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. Flack \( x = 0.009(16) \). \( R_1 = 0.0318 \) and \( wR_2 = 0.0794 \). GOF = 1.041. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1520624. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Web page: http://www.ccdc.cam.ac.uk/].

![ORTEP drawing of 19a](Fig. S11)

**Ethyl (R)-6-methoxy-2-oxo-4-(1-tosyl-1H-indol-2-yl)-3,4-dihydro-2H-anthra[2,1-e][1,3]oxazine-4-carboxylate (19b):** 3-(Trimethylsilyl)-2-naphthyl trifluoromethanesulfonate was used
in place of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate in the procedure above. A trace amount of Et₂O remained. Yellow viscous oil. ¹H NMR (400 MHz, CDCl₃) δ 1.34 (t, J = 6.9 Hz, 3H), 2.38 (s, 3H), 4.03 (s, 3H), 4.33 (m, 1H), 4.45 (m, 1H), 6.19 (s, 1H), 6.69 (s, 1H), 7.13 (t, J = 7.3 Hz, 1H), 7.21 (t, J = 7.3 Hz, 1H), 7.29-7.31 (m, 3H), 7.36 (s, 1H), 7.56-7.59 (m, 2H), 7.64 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 8.2 Hz, 2H), 8.06-8.13 (m, 2H), 8.87 (s, 1H), 8.96 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 14.2, 21.7, 56.0, 63.5, 64.6, 97.1, 109.7, 114.3, 114.7, 121.5, 121.6, 121.7, 122.7, 123.8, 125.1, 125.8, 126.8 (2C), 127.3 (2C), 127.7, 128.7, 128.8, 130.2 (2C), 132.4, 132.5, 135.4, 136.9, 139.9, 140.8, 145.5, 149.0, 152.5, 169.0. IR (neat) 3416, 2975, 2927, 1741, 1459, 1358, 1308, 1089, 1041 cm⁻¹. [α]D³¹ = –92.0 (c 1.00, CHCl₃, 91% ee). HRMS (FAB+) calcd for C₃₅H₂₈N₂NaO₇S [M+Na]⁺ 643.1515, found 643.1504.

26. Gram-scale reaction and transformation to amino acid 21 (Scheme 4).

5 mmol scale reaction of 7e: To a well-dried two-necked flask charged with activated MS 5Å (1.25 g) under a nitrogen atmosphere were added (R)-10c (8.1 mg, 0.010 mmol) in dichloromethane (40 mL) at −78 °C. After 5 min, α-ketimino ester 7e (1.881 g, 5.00 mmol) in dichloromethane (10 mL), and 2-methoxyfuran (930 µL, 10.0 mmol) were added at −78 °C. The reaction mixture was allowed to warm to −60 °C and was then stirred at that temperature for 6 h. The resulting mixture was quenched with triethylamine (0.1 mL) at −60 °C, and concentrated under reduced pressure at room temperature. The residue was purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 3:1 to 1:1) to give the product 8e (2.187 g, 92% yield). The enantiomeric purity was determined by chiral HPLC analysis (95% ee).
(S)-4-(3-Bromophenyl)-4-(5-methoxyfuran-2-yl)oxazolidin-2-one (20): To a solution of 8e (2.187 g, 4.61 mmol, 95% ee) in ethanol (15 mL) was added sodium borohydride (0.698 g, 18.4 mmol). The mixture was stirred at room temperature for 5 h, and concentrated under reduced pressure. The resultant residue was dissolved in dichloromethane (30 mL). Saturated NH₄Cl aqueous solution (30 mL) was added, and the mixture was extracted with dichloromethane (10 mL × 3), and the combined organic layer was dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and purified by silica gel column chromatography (eluent: n-hexane:EtOAc = 2:1 to 1:1) to give the desired product 20 (1.302 g, 84% yield, 95% ee). Compound 20 was recrystallized from dichloromethane/diethyl ether/n-hexane (1:10:5) at room temperature (1.190 g, 76% yield, >99% ee). Coloreless oil. ¹H NMR (400 MHz, CDCl₃) δ 3.84 (s, 3H), 4.41 (d, J = 8.7 Hz, 1H), 4.91 (d, J = 8.7 Hz, 1H), 5.11 (d, J = 3.2 Hz, 1H), 6.09 (d, J = 3.7 Hz, 1H), 6.34 (s, 1H), 7.24-7.32 (m, 2H), 7.46-7.53 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 57.9, 62.5, 75.1, 80.2, 110.4, 122.9, 124.4, 128.9, 130.4, 131.6, 142.6, 142.7, 158.8, 162.1. IR (KBr) 3317, 3071, 1761, 1736, 1615, 1575, 1372, 1262, 1038 cm⁻¹. M.p. 122 °C. [α]D₂⁶ = +119.6 (c 1.00, CHCl₃, >99% ee). HPLC analysis; IA-3, CH₂Cl₂, 254 nm, 0.9 mL/min, tR = 14.0 min (major, S), 33.7 min (minor, R). HRMS (FAB+) calcd for C₁₄H₁₂BrNO₄ [M]+ 336.9950, found 336.9940.

(S)-4-(3-Bromophenyl)-2-oxooxazolidine-4-carboxylic acid (21): 21 was synthesized based on the literature procedure.²⁶ To a solution of 20 (1.190 g, 3.52 mmol) in acetonitrile (18 mL) and carbon tetrachloride (18 mL), water (35 mL) and sodium periodate (11.29 g, 52.8 mmol) were added at 0 °C. After stirred for 5 min, ruthenium(III) chloride (21.9 mg, 0.11 mmol) was added, and the mixture was stirred at 0 °C for 30 min. The mixture was filtered and the filtrate was extracted with ethyl acetate (15 mL × 3). Diethyl ether (10 mL) was added to the combined organic layer, and the solution was stirred at room temperature for 2 h. Ruthenium(IV) oxide was gradually precipitated. The suspension was dried over Na₂SO₄, and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure. The residue was dissolved in chloroform (20 mL), and extracted with NaHCO₃ aqueous solution (20 mL × 2). The combined aqueous layer was acidified with 3 M HCl aqueous solution (20 mL), and extracted with chloroform (15 mL × 3). The combined organic layer was dried over Na₂SO₄, and concentrated.
under reduced pressure to give the desired product 21 (0.893 g, 89% yield). Light brown oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.43 (d, \(J = 9.2\) Hz, 1H), 5.22 (d, \(J = 9.2\) Hz, 1H), 7.28 (t, \(J = 7.8\) Hz, 1H), 7.37 (d, \(J = 8.2\) Hz, 1H), 7.52 (d, \(J = 7.8\) Hz, 1H), 7.58 (t, \(J = 1.8\) Hz, 1H), 7.78 (s, 1H), 8.87 (brs, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 66.7, 74.2, 123.4, 123.5, 128.0, 130.9, 132.4, 139.6, 160.2, 172.9. IR (neat) 3291, 1739, 1475, 1421, 1261, 1052 cm\(^{-1}\). \([\alpha]_D^{27}\) = +106.0 (c 1.00, CHCl\(_3\), >99% ee). HRMS (FAB\(^+\) calcd for C\(_{10}\)H\(_9\)BrNO\(_4\) [M+H]\(^+\) 285.9715, found 285.9709.

27. Theoretical study on the E/Z-geometry of substrates 1b and 7a.

With regard to Eqs. 2 and 3 in the main text, we considered the E/Z-geometry of the substrates. According to the literature, 1b would have an E-geometry,\(^6\) whereas 7a would have a Z-geometry.\(^{27}\) Indeed, a preliminary theoretical study was preliminary performed by a molecular mechanics method (MM2, Chem3D for Windows) (Fig. S12). As a result, \((E)-1b\) was more stable than \((Z)-1b\) by 8.12 kcal/mol (Fig. S12a). On the other hand, \((Z)-7a\) was more stable than \((E)-7a\) by 2.97 kcal/mol (Fig. S12b). Moreover, \(^1\)H and \(^{13}\)C NMR analyses of either 1b or 7a showed a single geometric isomer in CDCl\(_3\) at room temperature, and thus the observed geometry (i.e., \((E)-1b\) and \((Z)-7a\)) should be quite stable.

![Theoretical study for the E/Z-geometry of substrates 1b and 7a.](image-url)
28. Possible transition states for the reactions.

Fig. S13a shows a possible transition state with the use of (R)-5b/1b/2. The imino nitrogen atom of 1b might coordinate to the $C_2$-symmetric chiral Brønsted acid center of (R)-5b. Under these conditions, the sterically hindered $i$-Pr$_3$Si moiety of 1b might be far from the 3,5-(o-Tol)C$_6$H$_3$ moiety and turned outward to avoid steric constraints. Nucleophile 2 would then selectively attack the activated 1b from the $si$-face. As a result, enantioenriched (S)-3b might be provided (up to 91% ee). The steric effect of the silyl moiety might play an important role in the orientation of the substrates, and the sterically more hindered silyl moiety could induce high enantioselectivity: Ph (76% ee) < Ph$_3$Si (79% ee) < $t$-BuMe$_2$Si (82% ee) < $t$-BuPh$_2$Si (88% ee) < $i$-Pr$_3$Si (91% ee) (see Table S5).

Fig. S13b shows a possible transition state with the use of (R)-10c/7a/2. The imino nitrogen atom of 7a might coordinate to the $C_1$-symmetric chiral Brønsted acid center of (R)-10c. Under these conditions, the sterically hindered phenyl moiety of 7a might avoid steric constraints from the outstandingly bulky 2,4,6-Cy$_3$C$_6$H$_2$ moiety of catalyst (R)-10c. Nucleophile 2 would then selectively attack the activated 7a from the $re$-face. As a result, enantioenriched (R)-8a might be provided (up to 95% ee).

**Fig. S13** Possible transition states for the reactions with the use of (R)-5b and (R)-10c.
29. References.
1. D. G. Manly and E. D. Amstutz, *J. Org. Chem.*, 1956, **21**, 516.
2. B. Wang, C. M. Yu, Z. W. Chen and W. K. Su, *Chinese Chem. Lett.*, 2008, **19**, 904.
3. T. Harada and K. Kanda, *Org. Lett.*, 2006, **8**, 3817.
4. I. Mizota, Y. Matsuda, S. Kamimura, H. Tanaka and M. Shimizu, *Org. Lett.*, 2013, **15**, 4206.
5. M. Guo, D. Li and Z. Zhang, *J. Org. Chem.*, 2003, **68**, 10172.
6. M. Hatano, K. Yamashita, M. Mizuno, O. Ito and K. Ishihara, *Angew. Chem., Int. Ed.*, 2015, **54**, 2707.
7. W. Yan, D. Wang, J. Feng, P. Li, D. Zhao and R. Wang, *Org. Lett.*, 2012, **14**, 2512.
8. P. Cali and M. Begtrup, *Synthesis*, 2002, **2002**, 2515.
9. D. Uraguchi and M. Terada, *J. Am. Chem. Soc.*, 2004, **126**, 5356.
10. M. Terada, K. Machioka and K. Sorimachi, *Angew. Chem., Int. Ed.*, 2009, **48**, 2553.
11. T. Akiyama, H. Morita, J. Itoh and K. Fuchibe, *Org. Lett.*, 2005, **7**, 2583.
12. (a) S. Hoffmann, A. M. Seayad, B. List, *Angew. Chem., Int. Ed.* 2005, **44**, 7424; (b) M. Klussmann, L. Ratjen, S. Hoffmann, V. Wakchaure, R. Goddard, B. List, *Synlett*, 2010, **2010**, 2189.
13. M. Hatano, T. Ozaki, K. Nishikawa and K. Ishihara, *J. Org. Chem.*, 2013, **78**, 10405.
14. S. Liu and L. G. Pedersen, *J. Phys. Chem. A*, 2009, **113**, 3648.
15. F. Krasovec and J. Jan, *Croat. Chem. Acta*, 1963, **35**, 183.
16. D. Shamir, I. Zilbermann, E. Maimon, A. I. Shames, H. Cohen and D. Meyerstein, *Inorg. Chim. Acta*, 2010, **363**, 2819.
17. P. Christ, A. G. Lindsay, S. S. Vormittag, J.-M. Neudröffl, A. Berkessel and A. M. C. O’Donoghue, *Chem. Eur. J.*, 2011, **17**, 8524.
18. Y. Qian, C. Jing, C. Zhai and W.-h. Hua, *Adv. Synth. Catal.*, 2012, **354**, 301.
19. H. M. L. Davies, T. Hansen and M. R. Churchill, *J. Am. Chem. Soc.*, 2000, **122**, 3063.
20. K. Dolbeare, G. F. Pontoriero, S. K. Gupta, R. K. Mishra and R. L. Johnson, *J. Med. Chem.*, 2003, **46**, 727.
21. D. Uraguchi, K. Sorimachi and M. Terada, *J. Am. Chem. Soc.*, 2004, **126**, 11804.
22. B. Prasad, R. Adepu, S. Sandra, D. Rambabu, G. R. Krishna, C. M. Reddy, G. S. Deora, P. Misra and M. Pal, *Chem. Commun.*, 2012, **48**, 10434.
23. E. Chong and S. A. Blum, *J. Am. Chem. Soc.*, 2015, **137**, 10144.
24. (a) T. Kurisaki, T. Naniwa, H. Yamamoto, H. Imagawa and M. Nishizawa, *Tetrahedron Lett.*, 2007, **48**, 1871; (b) B. C. J. van Esseveldt, F. L. van Delft, J. M. M. Smits, R. de Gelder, H. E. Schoemaker and F. P. J. T. Rutjes, *Adv. Synth. Catal.*, 2004, **346**, 823.
25. G. E. Collis and A. K. Burrell, *Tetrahedron Lett.*, 2005, **46**, 3653.
26. (a) F. Köhler, H.-J. Gais and G. Raabe, *Org. Lett.*, 2007, **9**, 1231; (b) H. Liu, J. Xu and D.-M. Du, *Org. Lett.*, 2007, **9**, 4725.
27. T. Hashimoto, K. Yamamoto and K. Maruoka, *Chem. Lett.*, 2011, **40**, 326.
\( ^1H \text{ NMR, 400 MHz, THF-}\text{d}_6 \)

\( ^{13}C \text{ NMR, 100 MHz, THF-}\text{d}_6 \)
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, THF-$d_8$
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, THF-$d_8$
\(^{1}H\) NMR, 400 MHz, THF-\(d_8\)

\(^{13}C\) NMR, 100 MHz, THF-\(d_8\)
\(^1\)H NMR, 400 MHz, THF-\(d_8\)

\(^{13}\)C NMR, 100 MHz, THF-\(d_8\)
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, THF-$d_8$
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, THF-$d_8$
$^{1}H$ NMR, 400 MHz, THF-$d_{8}$

$^{13}C$ NMR, 100 MHz, THF-$d_{8}$
$^{1}H$ NMR, 400 MHz, THF-$d_{8}$

$^{13}C$ NMR, 100 MHz, THF-$d_{8}$
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, THF-$d_8$
$^{1}H$ NMR, 400 MHz, THF-$d_{8}$

$^{13}C$ NMR, 100 MHz, THF-$d_{8}$
$^{1}$H NMR, 400 MHz, THF-$d_6$

$^{13}$C NMR, 100 MHz, THF-$d_6$
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, THF-$d_8$

$^{13}$C NMR, 100 MHz, THF-$d_8$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^{1}H$ NMR, 400 MHz, CDCl$_3$

$^{13}C$ NMR, 100 MHz, CDCl$_3$
$^{1}$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^1$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
\[^{1}H\text{ NMR, 400 MHz, CDCl}\_3\]

\[^{13}C\text{ NMR, 100 MHz, CDCl}\_3\]
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$  

$^{13}$C NMR, 100 MHz, DMSO-$d_6$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
\[ \text{MeO}_2\text{CH} \text{N-CO}_2\text{Bn} \]

\[ \text{MeO} \]

\((8h)\)

\(\text{H NMR, 400 MHz, CDCl}_3\)

\(\text{C NMR, 100 MHz, CDCl}_3\)
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$ 

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^{1}$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^{1}H$ NMR, 400 MHz, CDCl$_3$

$^{13}C$ NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
${}^1H$ NMR, 400 MHz, CDCl$_3$

${}^{13}C$ NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
\(^1\)H NMR, 400 MHz, CDCl\(_3\)

\(^{13}\)C NMR, 100 MHz, CDCl\(_3\)
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl₃

$^{13}$C NMR, 100 MHz, CDCl₃
$^1$H NMR, 400 MHz, CDCl$_3$  

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
\(^1\text{H NMR, 400 MHz, CDCl}_3\)

\(^{13}\text{C NMR, 100 MHz, CDCl}_3\)
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
Racemic 3a

3a by the catalysis

| Peak No. | RT (min) | Area   | Height (mV) | % Area |
|----------|----------|--------|-------------|--------|
| 1        | 15.87    | 46139871 | 1443911    | 58.011 |
| 2        | 32.372   | 42850531 | 36331      | 11.389 |
| Total    |          | 5242542 | 1542242    | 100.000 |

AD-H, 
n-hexane/i-PrOH = 1/1, 
1.0 mL/min, 254 nm
Racemic 3b

3b by the catalysis

| Peak No. | RT (min) | Area (LU) | Height (mV) | % Area |
|----------|----------|-----------|-------------|--------|
| 1        | 10.272   | 15150786  | 526106      | 95.343 |
| 2        | 11.488   | 340249    | 42983       | 4.657  |
| 合計     |          | 15594005  | 971999      | 100.000|

AD-H,
n-hexane/i-PrOH = 9/1,
0.6 mL/min, 254 nm
Racemic 8a

8a by the catalysis

Peak Table

| Peak No. | RT (min) | Area   | Height (mV) | % Area |
|----------|----------|--------|-------------|--------|
| 1        | 13.911   | 275847 | 11579       | 2.532  |
| 2        | 17.548   | 10619890 | 328836     | 87.688 |
| Total    |          | 10895553 | 344315     | 100.000 |
Racemic 8b

8b by the catalysis

PDA Multi 10/240nm 4nm

Peak No. | RT (min) | Area  | Height (mV) | % Area | Area  | Height (mV) | % Area |
--- | --- | --- | --- | --- | --- | --- | --- |
1 | 12.610 | 38.6459 | 17820 | 1.648 | 19833422 | 718381 | 100.000 |
2 | 15.528 | 19469932 | 700562 | 98.152 |
Total | | | | | 19833422 | 718381 | 100.000 |

AD-H,
n-hexane/i-PrOH = 1/1,
0.6 mL/min, 240 nm
MeO₂CHN CO₂Bn
\[ \text{Racemic 8c} \]

OD-3,
\[ n\text{-hexane/i-PrOH }= 1/1, \]
1.0 mL/min, 254 nm

**8c by the catalysis**

| Peak No. | RT (min) | Area    | Height | % Area |
|----------|----------|---------|--------|--------|
| 1        | 10.023   | 2625834 | 91803  | 98.56% |
| 2        | 18.159   | 96616   | 9181   | 1.44%  |
| Total    |          | 2635450 | 92694  | 100.00%|

S-B5
Racemic 8d

\[
\text{AD-H,} \\
n\text{-hexane/i-PrOH = 1/1,} \\
0.6 \text{ mL/min, 254 nm}
\]

8d by the catalysis

Peak Table

| Peak No. | RT (min) | Area         | Height (mV) | % Area |
|----------|----------|--------------|-------------|--------|
| 1        | 13.151   | 965076       | 44652       | 1.797  |
| 2        | 18.863   | 52257762     | 1327733     | 88.003 |
| Total    |          | 53029538     | 1397564     | 100.000|

S-B6
Racemic 8e

8e by the catalysis

Peak Table

| Peak No. | RT (min) | Area  | Height (mV) | % Area |
|----------|----------|-------|-------------|--------|
| 1        | 10.692   | 352914| 19075       | 1.311  |
| 2        | 12.548   | 28568332| 1197815    | 98.689 |
| Total    |          | 22992245| 1216980    | 100.000|
Racemic 8f

\[ \text{IC-3,} \]
\[ n\text{-hexane/i-PrOH = 1/1,} \]
\[ 0.6 \text{ mL/min, 254 nm} \]

---

**8f by the catalysis**

---

**S-B8**
Racemic 8g

AD-H, 
n-hexane/i-PrOH = 1/1, 
0.6 mL/min, 254 nm

8g by the catalysis
MeO₂CHN CO₂Bn

(8h)

AD-H,
n-hexane/i-PrOH = 1/1,
0.6 mL/min, 254 nm

Racemic 8h

8h by the catalysis
Racemic 8i

AD-H,

$n$-hexane/$i$-PrOH = 1/1,

0.6 mL/min, 254 nm

8i by the catalysis
Racemic 8j

\[
\begin{align*}
\text{MeO}_2\text{CHN} & \text{-} \text{CO}_2\text{Bn} \\
\text{Me} & \text{-} \text{O}\text{Me}
\end{align*}
\]

AD-H, 
\[n\text{-hexane}/i\text{-PrOH = 1/1,}
\]
0.6 mL/min, 254 nm

8j by the catalysis

**Chart 1**

| Peak No. | RT (min) | Area   | Height (mV) | % Area |
|----------|----------|--------|-------------|--------|
| 1        | 11.37    | 176537 | 88857       | 2.209  |
| 2        | 15.45    | 32039379 | 903043 | 97.691 |
| Total    | 33217916 | 941700 | 100,000    |

S-B12
MeO₂CHN₅CO₂Bn

(81)

AD-H,
n-hexane/i-PrOH = 1/1,
0.6 mL/min, 254 nm

Racemic 81

81 by the catalysis

Peak Table

| Peak No | RT (min) | Area  | Height (mV) | % Area |
|---------|----------|-------|-------------|--------|
| 1       | 18.057   | 686747| 20163       | 4.919  |
| 2       | 28.276   | 2396589| 452466      | 97.081 |
| Total   |          | 23175463| 453129     | 100.000|

S-B13
Racemic 8m

8m by the catalysis

| Peak No. | RT (min) | Area   | Height | % Area |
|----------|----------|--------|--------|--------|
| 1        | 9.633    | 7927118| 270428 | 95.037 |
| 2        | 22.883   | 417514 | 4901   | 4.963  |
| Total    |          | 9332512| 280329 | 100.000|
MeO₂CH₅ \text{CO}_₂\text{Bn} \quad \text{AD-H,}
\text{n-hexane/i-PrOH = 1/1,}
0.6\, \text{mL/min, 254 nm}

\textbf{Racemic 8n}

\textbf{8n by the catalysis}

| Peak No | RT (min) | Area  | Height (mV) | % Area |
|---------|----------|-------|-------------|--------|
| 1       | 14.553   | 1273484 | 45498     | 6.415  |
| 2       | 16.489   | 17702462 | 522753   | 93.585 |
| Total   |          | 18915936 | 603251   | 100.000 |

S-B15
Racemic 8p

8p by the catalysis

Peak Table

| Peak No. | RT (min) | Area   | Height (mV) | % Area |
|----------|----------|--------|-------------|--------|
| 1        | 11.741   | 20030458 | 86386      | 2.850  |
| 2        | 12.854   | 68787049 | 2544829    | 91.120 |
| Total    |          | 79805505 | 2831015    | 100.000|

AD-H,

$n$-hexane/$i$-PrOH = 1/1,

0.6 mL/min, 230 nm