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PAPER

Multifunctional chiral phosphines-catalyzed highly diastereoselective and enantioselective substitution of Morita–Baylis–Hillman adducts with oxazolones†

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Multifunctional chiral phosphine (phosphine–thiourea type) **L2**-catalyzed allylic substitutions of MBH adducts **1** with oxazolones **2** produce the corresponding optically active adducts **3** in good to excellent yields and ee's as well as moderate to good de's under mild conditions. The synergistic interaction between hydrogen bond donor site and nucleophilic site has been discussed, indicating that finely tuning the active sites of the multifunctional phosphine organocatalysts is very important.

Introduction

Multifunctional chiral phosphines have proven to be powerful synthetic tools in asymmetric organocatalysis.[1–3] The combination of a hydrogen bonding motif with a highly nucleophilic phosphorus center within one molecule bearing a chiral framework can synergistically activate the substrates in a controlled chiral environment, providing highly effective access to optically active compounds. More importantly, the catalytic abilities and enantioselectivities of these multifunctional/bifunctional chiral phosphine organocatalysts can be finely tuned through enhancing or reducing the reactive center's nucleophilicity as well as varying and increasing hydrogen bond donors.

Recently, Chen and co-workers have reported the allylic substitution of Morita–Baylis–Hillman (MBH) adducts with various nucleophiles by the metal-free catalysis of tertiary amines based on the theory of "Lewis base-assisted Brønsted base catalysis".[4] Herein, we wish to report multifunctional chiral phosphine–thiourea/urea organocatalysts-catalyzed (Fig. 1) regiospecific and asymmetric allylic substitution of Morita–Baylis–Hillman (MBH) adducts with racemic oxazolones (masked amino acid fragments),[5] affording the functionalized amino acid derivatives in good to excellent yields, high regioselectivities, diastereoselectivities and enantioselectivities.

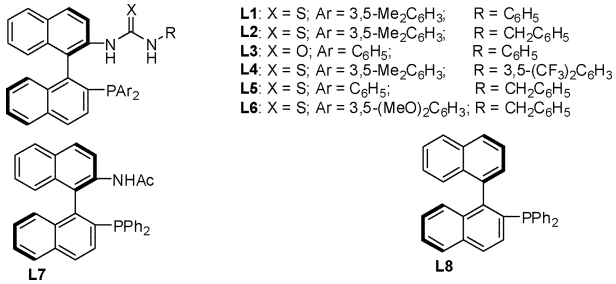

Fig. 1 Multifunctional chiral phosphines for asymmetric allylic substitutions.

Results and discussion

Initial examination was carried out by using Morita–Baylis–Hillman adduct **1a** (1.1 equiv.) and racemic oxazolone **2a** (1.0 equiv.) as the substrates in the presence of multifunctional chiral phosphines **L1–L6** (phosphine–thiourea/urea type) and **L7** (phosphine–amide type) (20 mol%) in toluene or dichloromethane (DCM) (Fig. 1). The results are summarized in Table 1. We found that the corresponding substitution product **3a** was produced in good chemical yields (63%–93%) and enantioselectivities (85–>99% ee's for *syn*-diastereomer **3a** and 50–98% ee's for *anti*-diastereomer **3a**) along with varying diastereoselectivities after the reaction was conducted for 24 h at room temperature (20 °C) by using multifunctional chiral phosphines **L1–L7** (entries 1–9). Under the above conditions the simple chiral phosphine **L8** was proven to give poor diastereoselectivity and enantioselectivity (Table 1, entries 10 and 11). These observations suggest that a hydrogen bonding motif of the catalyst is crucial for this asymmetric reaction and the polar solvent DCM favors the formation of the *anti*-diastereoisomer. In addition, the use of DCM as the solvent afforded **3a** in better yields and ee's than those of toluene (entries 1, 2 and 3, 4) and multifunctional chiral

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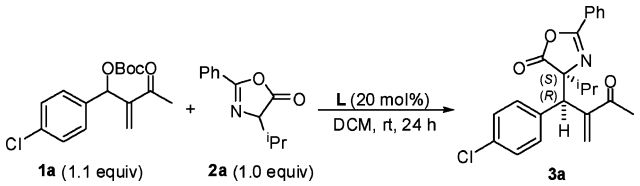
† Electronic supplementary information (ESI) available: Experimental procedures and spectroscopic data, NMR charts and chiral HPLC traces for all compounds and X-ray crystal data of **3b**. CCDC reference numbers 779521. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob00017a

Table 1 Multifunctional chiral phosphines catalyzed allylic substitution of MBH adduct **1a** with oxazolone **2a** in toluene or DCM



1a (1.1 equiv) **2a** (1.0 equiv) **3a**

Entry	Catalyst	Solvent	Yield (%)[a]	dr (*syn*/*anti*)	ee% (*syn*/*anti*)[b]
1	**L1**	DCM	81	4 : 1	95/81
2	**L1**	toluene	63	2 : 3	96/73
3	**L2**	toluene	81	1 : 1	85/50
4	***L2***	*DCM*	*87*	*16:1*	*97/80*
5	**L3**	DCM	93	3 : 1	97/96
6	**L4**	DCM	76	2 : 1	94/88
7	**L5**	DCM	86	3 : 1	98/96
8	**L6**	DCM	91	3 : 1	>99/98
9	**L7**	DCM	88	2 : 1	>99/95
10	**L8**	toluene	72	1 : 3	2/−3
11	**L8**	DCM	92	2 : 1	10/−23

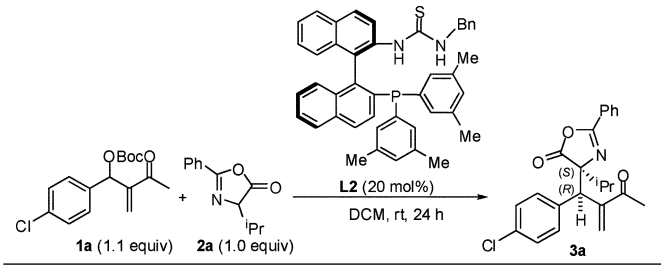
[a] Isolated yields. [b] Determined by chiral HPLC.

phosphines **L1–L6** (phosphine–thiourea/urea type) produced **3a** in higher diastereoselectivities than those of multifunctional chiral phosphine **L7** (phosphine–amide type) (entries 1, 4–8 and 9). Among these chiral phosphine–thiourea/urea organocatalysts **L1–L6**, it was found that Ar in the phosphorous center and R in the hydrogen bond donor site can significantly alter the diastereoselectivities and enantioselectivities of **3a** (entries 1, and 4–8). Chiral phosphine–thiourea catalyst **L2**, in which Ar is a 3,5-dimethylphenyl group and R is a benzyl group, afforded **3a** in 87% yield, 16 : 1 de (*syn*/*anti*), 97% ee for *syn*-diastereomer and 80% ee for *anti*-diastereomer (entry 4), suggesting that tuning the acidity of the hydrogen bonding motif as well as the nucleophilicity and the steric environment of the phosphorus center can significantly affect the stereochemical outcomes in this interesting asymmetric substitution reaction.

In the presence of **L2**, we continued screening various other solvents and examining the reaction temperatures for this reaction and the results are given in Table 2. We found that tetrahydrofuran (THF) and DCM are the solvents of choice (Table 2, entries 1–7) and reducing the reaction temperature to 0 °C gave the poorest result under otherwise identical conditions, suggesting that this reaction should be carried out at room temperature (Table 2, entries 8 and 9). In methanol, some byproducts derived from the reaction of **1a** or **2a** with methanol were also formed to give **3a** in low yield along with other complex product mixtures (Table 2, entry 6). As for solvents having a high dielectric constant such as DMF and MeCN, since they can strongly alter the hydrogen bonding interaction between the catalyst and the reacting partners, the corresponding adducts **3a** were obtained in moderate yields and moderate de values (Table 2, entries 3 and 5).

We next examined the generality of this reaction using a variety of MBH adducts **1** and oxazolones **2a**, **2b** (R^2 = ^{i}Bu), **2c** (R^2 = Me) and **2d** (R^2 = Ph). The results are indicated in Table 3. The corresponding products **3** were obtained in high yields and ee's as well as moderate to good de's whether they contain (R^1) aromatic, heteroaromatic or aliphatic groups (Table 3, entries 1–14). Only in

Table 2 Screening of solvent effects on the allylic substitution of MBH adduct **1a** with **2a** in the presence of **L2**

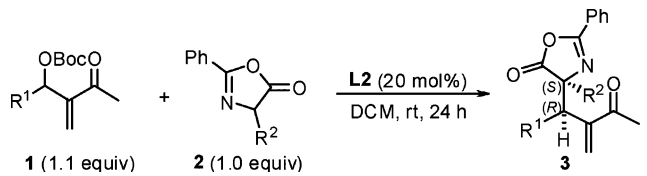


1a (1.1 equiv) **2a** (1.0 equiv) **3a**

Entry	Catalyst	Solvent	Yield (%)[a]	dr (*syn*/*anti*)	ee% (*syn*/*anti*)[b]
1	**L2**	DCF	75	5 : 1	96/94
2	**L2**	THF	81	10 : 1	96/72
3	**L2**	MeCN	63	6 : 1	96/82
4	**L2**	Et_2O	88	2 : 1	85/−15
5	**L2**	DMF	63	3 : 1	96/90
56	**L2**	MeOH	complex	—	—
7	**L2**	DCM	87	16 : 1	97/80
8[c]	**L2**	DCM	91	4 : 1	98/97
9[c]	**L2**	THF	88	5 : 1	96/82

[a] Isolated yields. [b] Determined by chiral HPLC. [c] The reaction was carried out at 0 °C

Table 3 Multifunctional chiral phosphine **L2**-catalyzed allylic substitution of various MBH adducts **1** with oxazolones **2a**, **2b**, **2c** and **2d**



1 (1.1 equiv) **2** (1.0 equiv) **3**

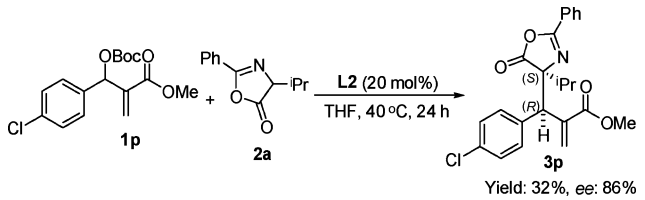
Entry	R^1	R^2	Yield (%)[a]	dr (*syn*/*anti*)	ee (%)[b]	Absolute configuration
1	*p*-BrC_6H_4	^{i}Pr	82 (**3b**)	16 : 1	97	*S*, *R*
2	*p*-$NO_2C_6H_4$	^{i}Pr	95 (**3c**)	4 : 1	98 (94)[d]	*S*, *R*
3	*p*-MeC_6H_4	^{i}Pr	91 (**3d**)	20 : 1	96	*S*, *R*
4	*o*-$MeOC_6H_4$	^{i}Pr	94 (**3e**)	5 : 1	95 (94)[d]	*S*, *R*
5	*m*-BrC_6H_4	^{i}Pr	91 (**3f**)	15 : 1	97	*S*, *R*
6	*p*-$CF_3C_6H_4$	^{i}Pr	86 (**3g**)	16 : 1	96	*S*, *R*
7	*m*-$MeOC_6H_4$	^{i}Pr	92 (**3h**)	12 : 1	99	*S*, *R*
8	*m*-$CF_3C_6H_4$	^{i}Pr	89 (**3i**)	16 : 1	97	*S*, *R*
9	*p*-BrC_6H_4	^{i}Bu (**2b**)	84 (**3j**)	3 : 1	91 (98)[d]	*S*, *R*
10	*p*-CLC_6H_4	Me (**2c**)	90 (**3k**)	4 : 1	97 (90)[d]	*S*, *R*
11	*p*-MeC_6H_4	Me (**2c**)	90 (**3l**)	10 : 1	96	*S*, *R*
12	*p*-BrC_6H_4	Me (**2d**)	85 (**3m**)	7 : 1	92	*R*, *R*
13		^{i}Pr	95 (**3n**)	12 : 1	95	*S*, *R*
14[c]	Et	^{i}Pr	96 (**3o**)	7 : 1	85	*S*, *R*

[a] Isolated yields. [b] Determined by chiral HPLC. [c] The reaction conditions: in THF at 35 °C. The two diastereomers cannot be separated by silica gel column chromatography. [d] The ee of *anti*-diastereomer.

entries 2, 4, 9 and 10 of Table 3 were the corresponding products **3c**, **3e**, **3j** and **3k** obtained in moderate de value.

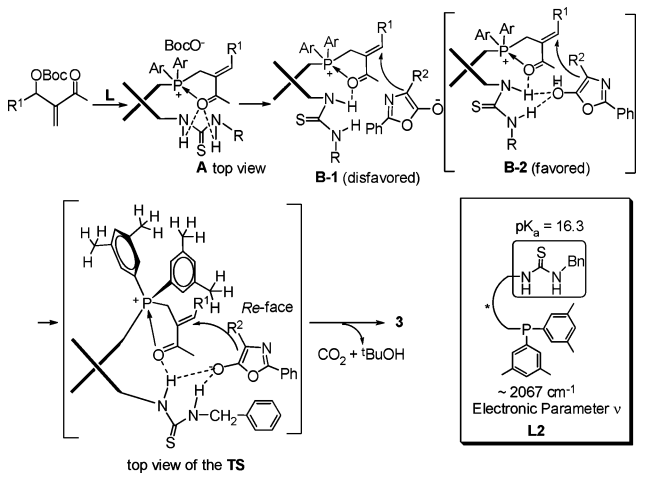
The relative and absolute configurations of the major diastereomers of **3** have been determined as *syn*-(*S*,*R*)-configurations by X-ray diffraction of **3b** containing a bromine atom on the benzene ring.[6] The CIF data of **3b** are presented in the ESI.†[7]

Using MBH adduct **1p** derived from methyl acrylate as the substrate afforded the corresponding product **3p** in 32% yield along with 86% ee under the standard conditions (Scheme 1). The inherent weaker reactivity accounts for its poor yield.



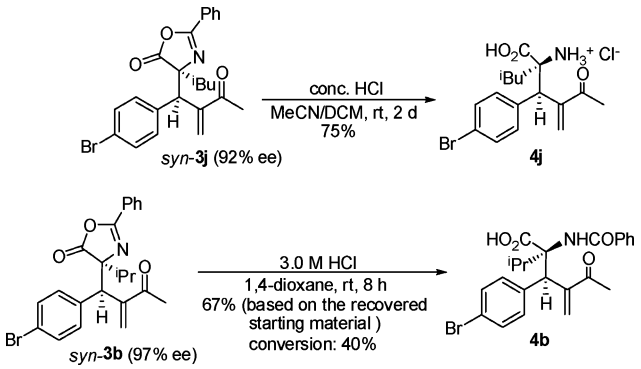
Scheme 1 Multifunctional chiral phosphine **L2**-catalyzed allylic substitution of MBH adduct **1p** with oxazolone **2a**.

A plausible mechanism for this asymmetric reaction is outlined in Scheme 2. As proposed by Krische,[8] the treatment of MBH adduct with **L** produces an electrophile–nucleophile ion pair **A** stabilized by intramolecular H-bonding, which reacts with the oxazolone anion generated from $BocO^-$ upon decomposition of the Boc residue with release of CO_2 and oxazolone to give intermediates **B-1** and **B-2**. Intermediate **B-2** is favored through intermolecular hydrogen bonding when compared with intermediate **B-1**, providing the addition product **3** in the *syn*-(*S*,*R*)-configuration from the *Re*-face attack due to the steric blocking of the two dimethylphenyl groups *via* the transition state **TS** shown in Scheme 2. The nucleophilicity (electronic parameter ν)[9] and steric bulkiness (steric parameter θ)[9] of the phosphorus center as well as the pK_a[10] value of the hydrogen bond donor site play significant roles in the stereochemical outcomes. As shown in Scheme 2 and Table 1, **L2** containing an *N*-benzyl thiourea functional group ($pK_a = 16.3$)[10c] and bis(3,5-dimethylphenylphosphine) group ($\nu \sim 2067\ cm^{-1}$) gave the best de value (Table 1, entry 4). It appears that subtly enhancing/reducing either acidity of the hydrogen bonding site or the reactive center's nucleophilicity caused significant alteration of the reaction outcome, suggesting that finely tuning the active sites of the multifunctional phosphines, which can synergistically activate the employed substrates, is very important. A detailed investigation on the combination of nucleophilicity of the phosphorus site and hydrogen bond donor site (pK_a value) will be carried out in due course.



Scheme 2 A plausible reaction mechanism.

The synthetic utility of these addition products was illustrated by nucleophilic ring opening of *syn*-**3** to give the corresponding optically active and diastereomeric pure quaternary α-amino acid derivatives.[11] For example, treatment of *syn*-**3j** and *syn*-**3b** with conc. or 3.0 M HCl aqueous solution afforded the corresponding quaternary amino acid **4j** as a hydrochloride salt and α-disubstituted amino acid **4b** (conversion: 40%) in good yields (Scheme 3).



Scheme 3 Transformation of the adducts to the corresponding amino acid derivatives.

In conclusion, we have established an efficient multifunctional chiral phosphine (phosphine–thiourea) **L2**-catalyzed allylic substitutions of MBH adducts **1** with oxazolones **2** to provide easy access to optically active adducts **3** under mild conditions. Good to excellent yields and ee's as well as moderate to good de's have been achieved. Finely tuning the active sites of these multifunctional phosphines is required to get good results. Further efforts are in progress regarding the scope and mechanistic details.

Experimental section

General remarks

^1H NMR spectra were recorded on a Bruker AM-300 or AM-400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; *J* values are in Hz. Mass spectra were recorded with a HP-5989 instrument. All of the compounds reported in this paper gave satisfactory HRMS analytic data. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin–Elmer-341 MC digital polarimeter; $[\alpha]_D$ values are given in units of 10 $deg^{-1}\ cm^2\ g^{-1}$. Infrared spectra were recorded on a Perkin–Elmer PE-983 spectrometer with absorption in cm^{-1}. Chiral HPLC was performed on a SHIMADZU SPD-10A vp series with chiral columns (Chiralpak AD-H, IC-H columns 4.6 × 250 mm, (Daicel Chemical Ind., Ltd.)). THF, toluene and Et_2O were distilled from sodium (Na) under argon (Ar) atmosphere. CH_3CN, 1,2-dichloroethane and dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF254 silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure. All the oxazolones were prepared according to the literature.[12]

Reaction procedure for the preparation of catalysts

The reaction procedure for the preparation of (*R*)-1-argio-3-(2′-(diargiophosphino)-1,1′-binaphthyl-2-yl)thiourea has been summarized in the ESI† and the spectroscopic data of **L1–L7** are shown below.

L1: (*R*)-1-(2′-(bis(3,5-dimethylphenyl)phosphino)-1,1′-binaphthyl-2-yl)-3-phenylthiourea. A white solid (620 mg, 61% yield). m.p. 112–115 °C; $[\alpha]_D^{20}$ = +158.2 (*c* 0.6, $CHCl_3$). IR (CH_2Cl_2) *ν* 3326, 3044, 2963, 1789, 1707, 1595, 1497, 1308, 1261, 1183, 1117, 840, 817, 748, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): *δ* 8.07 (1H, d, *J* = 8.8 Hz), 7.97 (2H, d, *J* = 8.8 Hz), 7.90 (2H, d, *J* = 8.4 Hz), 7.80 (1H, d, *J* = 8.0 Hz), 7.50–7.41 (3H, m) 7.30–7.19 (3H, m), 7.09–7.06 (3H, m), 6.91–6.88 (2H, m), 6.74 (4H, d, *J* = 7.8 Hz), 6.67 (1H, s), 6.62 (1H, d, *J* = 8.4 Hz), 6.53 (2H, d, *J* = 8.8 Hz), 2.18 (6H, s, $ArCH_3$), 2.04 (6H, s, $ArCH_3$); ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): *δ* −12.8; MS (ESI) *m/z* (%) 645.5 [M^+ + H]; HRMS (ESI) Calcd for $C_{43}H_{38}N_2PS$ [M^+ + H] requires 645.2488, Found 645.2483.

L2: (*R*)-1-benzyl-3-(2′-(bis(3,5-dimethylphenyl)phosphino)-1,1′-binaphthyl-2-yl)thiourea. White solid (580.0 mg, 56% yield). m.p. 116–119 °C; $[\alpha]_D^{20}$ = +190.5 (*c* 0.5, $CHCl_3$). IR (CH_2Cl_2) *ν* 3367, 3058, 2921, 1782, 1697, 1424, 1369, 1254, 1179, 1143, 1076, 848, 819, 747, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): *δ* 7.95 (1H, d, *J* = 8.8 Hz), 7.91–7.89 (2H, m), 7.84 (1H, d, *J* = 8.4 Hz), 7.55–7.46 (3H, m), 7.39–7.35 (1H, m), 7.22–7.17 (4H, m), 7.05–7.00 (4H, m), 6.98 (1H, s), 6.94 (1H, s), 6.83 (1H, d, *J* = 8.4 Hz), 6.75 (2H, d, *J* = 8.8 Hz), 6.56 (2H, d, *J* = 8.8 Hz), 6.40 (1H, brs), 4.77–4.74 (1H, m), 3.99 (1H, dd, J_1 = 14.8 Hz, J_2 = 4.0 Hz), 2.27 (6H, s, $ArCH_3$), 2.07 (6H, s, $ArCH_3$); ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): *δ* −14.0; MS (ESI) *m/z* (%) 659.6 [M^+ + H]; HRMS (ESI) Calcd for $C_{44}H_{40}N_2PS$ [M^+ + H] requires 659.2644, Found 659.2651.

L3: (*R*)-1-(2′-(diphenylphosphino)-1,1′-binaphthyl-2-yl)-3-phenylurea. This is a known compound.[13] $[\alpha]_D^{20}$ = +72.3 (*c* 0.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS): *δ* 8.32 (1H, d, *J* = 8.8 Hz), 8.00 (1H, d, *J* = 8.8 Hz), 7.91 (2H, t, *J* = 8.4 Hz), 7.85 (1H, d, *J* = 8.8 Hz), 7.52 (1H, t, *J* = 7.6 Hz), 7.40 (1H, dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz), 7.32–6.95 (17H, m), 6.76 (1H, d, *J* = 8.8 Hz), 6.68 (2H, d, *J* = 7.6 Hz), 5.97 (1H, s), 5.94 (1H, s); ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): *δ* −14.3.

L4: (*R*)-1-(2′-(bis(3,5-dimethylphenyl)phosphino)-1,1′-binaphthyl-2-yl)-3-(3,5-bis(trifluoromethyl)phenyl)thiourea. A white solid. yield: 77%. m.p. 118–122 °C; $[\alpha]_D^{20}$ = +348.3 (*c* 0.5, $CHCl_3$). IR (CH_2Cl_2) *ν* 3052, 2921, 1779, 1707, 1580, 1473, 1383, 1277, 1250, 1178, 1134, 992, 883, 847 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): *δ* 8.28 (1H, d, *J* = 4.8 Hz), 8.11 (1H, d, *J* = 8.8 Hz), 7.97–7.93 (3H, m), 7.66–7.61 (4H, m), 7.54–7.46 (3H, m), 7.30–7.27 (2H, m), 7.11 (1H, d, *J* = 8.8 Hz), 7.08–7.04 (1H, m), 6.81 (1H, s), 6.78 (1H, s), 6.75 (1H, d, *J* = 8.8 Hz), 6.73 (1H, s), 6.71 (1H, s), 6.60 (1H, s), 6.58 (1H, s), 2.11 (6H, s, $ArCH_3$), 2.10 (6H, s, $ArCH_3$); ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): *δ* −13.5; ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$): *δ* −63.0; MS (ESI) *m/z* (%) 781.4 [M^+ + H]; HRMS (ESI) Calcd for $C_{45}H_{36}F_6N_2PS$ [M^+ + H] requires 781.2236, Found 781.2239.

L5: (*R*)-1-benzyl-3-(2′-(diphenyl)phosphino)-1,1′-binaphthyl-2-yl)thiourea. This is a known compound.[13]

L6: (*R*)-1-benzyl-3-(2′-(bis(3,5-dimethoxyphenyl)phosphino)-1,1′-binaphthyl-2-yl)thiourea. A white solid. yield: 58%. m.p. 103–105 °C; $[\alpha]_D^{20}$ = +123.8 (*c* 0.5, $CHCl_3$). IR (CH_2Cl_2) *ν* 2932, 1580, 1524, 1485, 1453, 1411, 1327, 1280, 1202, 1153, 1060, 1042, 817, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): *δ* 7.97 (1H, d, *J* = 8.8 Hz), 7.93 (2H, d, *J* = 8.8 Hz), 7.83 (1H, d, *J* = 8.0 Hz), 7.59 (1H, d, *J* = 8.4 Hz), 7.53–7.48 (2H, m), 7.37–7.28 (2H, m), 7.23–7.19 (3H, m), 7.13–7.11 (2H, m), 7.05–6.96 (3H, m), 6.71 (1H, d, *J* = 8.8 Hz), 6.47–6.42 (2H, m), 6.37 (1H, d, *J* = 2.4 Hz), 6.35 (1H, d, *J* = 2.4 Hz), 6.23 (1H, t, *J* = 2.4 Hz), 6.09 (1H, d, *J* = 2.4 Hz), 6.07 (1H, d, *J* = 2.4 Hz), 4.78 (1H, brs, CH_2Ph), 4.23 (1H, dd, J_1 = 12.8 Hz, J_2 = 3.6 Hz, CH_2Ph), 3.70 (6H, s, $ArOCH_3$), 3.55 (6H, s, $ArOCH_3$); ^{31}P NMR ($CDCl_3$, 162 MHz, 85% H_3PO_4): *δ* −10.4; MS (ESI) *m/z* (%) 723.4 [M^+ + H]; HRMS (ESI) Calcd for $C_{44}H_{40}O_4N_2PS$ [M^+ + H] requires 723.2448, Found 723.2441.

Typical procedure for the preparation of Boc-protected Morita–Baylis–Hillman adducts

The reaction procedure for the preparation of Boc-protected Morita–Baylis–Hillman adducts has been summarized in the ESI† and their spectroscopic data are shown below.

***tert*-Butyl 1-(4-chlorophenyl)-2-methylene-3-oxobutyl carbonate 1a.** A white solid; yield: 77%; m.p. 97–99 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) *δ* 7.34–7.27 (m, 4H), 6.50 (s, 1H), 6.23 (brs, 1H), 6.16 (d, *J* = 1.2 Hz, 1H), 2.31 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 197.2, 152.4, 147.4, 136.9, 134.1, 128.8, 128.6, 125.5, 82.8, 74.3, 27.7, 26.0; IR (neat) *ν* 3065, 3034, 2981, 2934, 1745, 1681, 1370, 1277, 1159 cm^{-1}; MS (%) *m/z* 254 (M-C_4H_8, 19), 209 (71), 195 (24), 193 (30), 192 (40), 175 (70), 115 (56), 57 (100), 43 (81); HRMS (EI) for $C_{12}H_{10}O_4Cl$ (M-C_4H_8): 253.0268; Found: 253.0265.

***tert*-Butyl 1-(4-bromophenyl)-2-methylene-3-oxobutyl *tert*-butyl carbonate 1b.** A white solid; yield: 67%; m.p. 101–103 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) *δ* 7.45–7.43 (m, 2H), 7.28–7.25 (m, 2H), 6.50 (s, 1H), 6.24 (s, 1H), 6.16 (s, 1H), 2.31 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 197.1, 152.1, 147.3, 137.4, 131.5, 129.1, 125.5, 122.2, 82.7, 74.2, 27.6, 26.0. IR (neat) *ν* 2981, 2934, 1746, 1681, 1370, 1488, 1370, 1280, 1157, 1084, 1073 cm^{-1}; MS (ESI) *m/z* 377 (M + Na); HRMS (ESI) for $C_{16}H_{19}BrNaO_4$ (M + Na): 377.0359; Found: 377.0359.

***tert*-Butyl 2-methylene-1-(4-nitrophenyl)-3-oxobutyl carbonate 1c.** A white solid; yield: 87%; m.p. 112–115 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) *δ* 8.19–8.17 (m, 2H), 7.62–7.59 (m, 2H), 6.61 (s, 1H), 6.33 (s, 1H), 6.27 (s, 1H), 2.35 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 197.0, 151.9, 147.5, 146.7, 145.4, 128.1, 126.4, 123.5, 83.1, 73.6, 27.5, 25.8. IR (neat) *ν* 3478, 3341, 3112, 2982, 2936, 1747, 1681, 1608, 1526, 1370, 1252, 1156, 1086, 975, 853 cm^{-1}; MS (ESI) *m/z* 344 (M + Na); HRMS (ESI) for $C_{16}H_{19}NNaO_6$ (M + Na): 344.1105; Found: 344.1105.

***tert*-butyl 2-methylene-3-oxo-1-p-tolylbutyl carbonate 1d.** A white solid; yield: 57%; m.p. 79–82 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) *δ* 7.27 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.53 (s, 1H), 6.20 (s, 1H), 6.12 (s, 1H), 2.31 (s, 3H), 2.30 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 197.2, 152.3, 147.7, 137.9, 134.9, 129.0, 127.3, 125.5, 82.3, 74.9, 27.6, 26.0, 21.0; IR (neat) *ν* 3476, 3348, 2981, 2932, 1745, 1682, 1515, 1370, 1276,

1160, 1083, 973, 884 cm^{-1}; MS (ESI) *m/z* 313 (M + Na); HRMS (ESI) for $C_{17}H_{22}NaO_4$ (M + Na): 313.1410; Found: 313.1414.

***tert*-Butyl 1-(2-methoxyphenyl)-2-methylene-3-oxobutyl carbonate 1e.** A white solid. yield: 52%; m.p 119–121 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.30–7.25 (m, 2H), 6.94–6.88 (m, 2H), 6.87 (d, 1H, J = 8.4 Hz), 6.22 (s, 1H), 5.82 (d, J = 1.2 Hz, 1H), 3.82 (s, 3H), 2.36 (s, 3H), 2.30 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197, 156.7, 152.5, 147.0, 129.4, 127.3, 126.7, 126.2, 120.4, 110.8, 82.3, 69.9, 55.5, 27.7, 26.3; IR (CH_2Cl_2) ν 2982, 1738, 1674, 1634, 1602, 1495, 1467, 1392, 1368, 1272, 1243, 1080, 985, 961, 942, 872 cm^{-1}; MS (EI) *m/z* (%) 306.(2.61) (M^+), 250 (6.02), 206 (41.08), 205 (94.30), 189 (23.01), 175 (35.34), 145 (23.06), 131 (36.81), 121 (13.11), 97 (28.71), 77 (19.60), 57 (87.43), 43 (100); HRMS (EI) Calcd for $C_{17}H_{22}O_5$ (M^+) requires 306.1467, Found 306.1460.

1-(3-Bromophenyl)-2-methylene-3-oxobutyl *tert*-butyl carbonate 1f. A white solid; yield: 52%; m.p. 100–103 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.52–7.51 (m, 1H), 7.42–7.39 (m, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 8.0 Hz, 1H), 6.50 (s, 1H), 6.25 (s, 1H), 6.17 (d, J = 1.2 Hz, 1H), 2.33 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 152.1, 147.2, 140.3, 131.3, 130.2, 130.0, 126.3, 125.8, 122.4, 82.9, 74.1, 27.7, 26.0; IR (neat) ν 2981, 2927, 1746, 1681, 1573, 1475, 1370, 1280, 1159, 1085, 971, 789 cm^{-1}; MS (ESI) *m/z* 377 (M + Na); HRMS (ESI) for $C_{16}H_{19}BrNaO_4$ (M + Na): 377.0359; Found: 377.0354.

***tert*-Butyl 2-methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl carbonate 1g.** A white solid; yield: 45%; m.p. 89–93 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.58 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.8 Hz, 2H), 6.59 (s, 1H), 6.27 (s, 1H), 6.20 (s, 1H), 2.32 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197, 152.1, 147.1, 142.2 (d, J_{C-F} = 1.2 Hz), 130.2 (q, J_{C-F} = 32.4 Hz), 127.5, 125.9, 125.3 (q, J_{C-F} = 4.0 Hz), 123.9(q, J_{C-F} = 271.0 Hz), 82.8, 74.1, 27.5; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ –62.7. IR (neat) ν 2983, 2936, 1748, 1682, 1608, 1421, 1371, 1277, 1165, 1068, 974, 853 cm^{-1}; MS (ESI) *m/z* 367 (M + Na); HRMS (ESI) for $C_{17}H_{19}F_3NaO_4$ (M + Na): 367.1128; Found: 367.1126.

***tert*-Butyl 1-(3-methoxyphenyl)-2-methylene-3-oxobutyl carbonate 1h.** A colorless oil. yield: 75%; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.23 (t, J = 7.6 Hz, 1H), 6.98–6.95 (m, 1H), 6.92–6.91 (m, 1H), 6.83–6.81 (m, 1H), 6.54 (s, 1H), 6.22 (s, 1H), 6.10 (d, J = 1.2 Hz, 1H), 3.78 (s, 3H), 2.32 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 159.5, 152.3, 147.6, 139.5, 129.4, 125.7, 119.6, 113.7, 112.8, 82.5, 74.7, 55.2, 27.7, 26.1; IR (CH_2Cl_2) ν 2977, 2937, 1741, 1679, 1460, 1394, 1369, 1305, 1274, 1251, 1161, 1089, 1045, 942, 898 cm^{-1}; MS (EI) *m/z* (%) 306.(6.86) [M^+], 250 (4.51), 206 (42.71), 205 (55.37), 189 (16.61), 175 (59.06), 163 (6.09), 145 (10.07), 135 (11.34), 121 (20.08), 103 (15.47), 84 (11.10), 77 (13.19), 57 (100), 43 (87.19); HRMS (EI) Calcd for $C_{17}H_{22}O_5$ [M^+] requires 306.1467, Found 306.1462.

***tert*-butyl 2-methylene-3-oxo-1-(3-(trifluoromethyl)phenyl)butyl carbonate 1i.** A white solid; yield: 61%; m.p. 48–49 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.61 (t, J = 8.4 Hz, 2H), 7.54 (d, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 6.59 (s, 1H), 6.28 (s, 1H), 6.20 (s, 1H), 2.33 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197, 152.1, 147.1, 139.2, 131.0, 130.7 (q, J_{C-F} = 32.0 Hz), 128.9, 128.0,125.9, 125.0 (q, J_{C-F} = 3.7 Hz), 123.91 (q, J_{C-F} = 3.7 Hz), 123.90 (q, J_{C-F} = 270.7 Hz), 83.0, 74.2, 27.6; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ –62.6; IR (neat) ν 2983, 2972, 1749, 1675, 1327, 1285, 1272, 1251, 1160, 1119, 1072, 971, 956, 847 cm^{-1}; MS (ESI) *m/z* 367 (M + Na); HRMS (ESI) for $C_{17}H_{19}F_3NaO_4$ (M + Na): 367.1128; Found: 367.1130.

***tert*-Butyl 2-methylene-3-oxo-1-(thiophen-2-yl)butyl carbonate 1n.** A white solid. yield: 32%; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.27–7.25 (m, 1H), 7.08–7.07 (m, 1H), 6.94 (dd, J_1 = 5.2, J_2 = 3.6, 1H), 6.81 (s, 1H), 6.27 (s, 1H), 6.26 (d, J = 1.2 Hz, 1H), 2.35 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 152.1, 147.3, 140.7, 127.1, 126.8, 126.1, 125.2, 82.8, 70.2, 27.7, 26.0; IR (CH_2Cl_2) ν 2978, 2926, 1736, 1631, 1431, 1393, 1370, 1316, 1344, 1299, 1252, 1155, 1076, 1043, 962, 923, 868, 847 cm^{-1}; MS (EI) *m/z* (%) 306.(6.86) [M^+], 250 (4.51), 206 (42.71), 205 (55.37), 189 (16.61), 175 (59.06), 163 (6.09), 145 (10.07), 135 (11.34), 121 (20.08), 103 (15.47), 84 (11.10), 77 (13.19), 57 (100), 43 (87.19); MS (ESI) *m/z* 305 (M + Na); HRMS (ESI) for $C_{14}H_{18}NaO_4S$ (M + Na): 305.0818; Found: 305.0821.

***tert*-Butyl 1-(3-methoxyphenyl)-2-methylene-3-oxobutyl carbonate 1o.** A colorless oil. yield: 16%; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 6.14 (s, 1H), 6.03 (d, J = 0.8 Hz, 1H), 5.46–5.43 (m, 1H), 2.36 (s, 3H), 1.78–1.59 (m, 2H), 1.47 (s, 9H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 152.8, 148.3, 124.7, 82.1, 74.9, 27.7, 27.6, 26.0, 9.7; IR (CH_2Cl_2) ν 2976, 1741, 1679, 1459, 1394, 1369, 1305, 1275, 1251, 1161, 1089, 1044, 942, 898 cm^{-1}; MS (ESI) *m/z* 251 (M + Na); HRMS (ESI) for $C_{12}H_{20}NaO_4$ (M + Na): 251.1254; Found: 251.1260.

General procedure for the preparation of 3 from the reaction of 1a with 2a using 3a as an example in the presence of L2

To a mixture of **1a** (0.11 mmol, 34 mg), **2a** (0.10 mmol, 21 mg) and catalyst **L2** (13 mg, 0.020 mmol) was added 1.0 mL of dichloromethane at room temperature (20 °C) under argon. The reaction solution was monitored by TLC. After the reaction was complete, the solution was concentrated under reduced pressure and the residue was further purified by silica gel column chromatography (EtOAc/PE = 1/16) to give the target product **3a**.

Preparative thin layer chromatography was performed to obtain the pure *syn*-adduct for spectroscopic analyses (eluent: DCM/PE = 2/1).

(*S*)-4-((*R*)-1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-4-isopropy-2-phenyloxazol-5(4*H*)-one 3a. Following the general procedure, the *syn*/*anti* ratio (16 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major 2.46 ppm, δ minor: 2.79 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (34 mg, 86% overall yield in a diastereomeric ratio = 16 : 1). m.p. for *syn*-**3a** = 107–109 °C; $[\alpha]_D^{20}$ (*syn*-**3a**) = –52.0 (*c* 0.5, $CHCl_3$). IR (CH_2Cl_2): ν 2972, 1811, 1672, 1651, 1488, 1453, 1295, 1200, 1157, 1110, 1046, 1016, 961, 914, 887, 811, 783 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3a**: δ 7.87 (2H, d, J = 6.8 Hz, Ph–H), 7.56 (1H, t, J = 7.6 Hz, Ph–H), 7.45 (2H, t, J = 7.6 Hz, Ph–H), 7.27 (1H, s, $=CH_2$), 7.16 (2H, d, J = 8.4 Hz, Ar–H), 7.05 (2H, d, J = 8.4 Hz, Ar–H), 6.50 (1H, s, $=CH_2$), 4.90 (1H, s, Ar–CH), 2.46 (1H, qu, J = 6.8 Hz, $-CH(CH_3)_2$), 2.32 (3H, s, $COCH_3$), 1.10 (3H, d, J = 6.8 Hz, $-CH(CH_3)_2$), 0.81 (3H, d, J = 6.8 Hz, $-CH(CH_3)_2$); ^{13}C NMR

(100 MHz, $CDCl_3$) for *syn*-**3a**: δ 198.0, 177.9, 160.3, 145.9, 135.0, 133.3, 132.7, 131.5, 128.8, 128.7, 128.0, 127.8, 125.4, 79.8, 46.2, 32.3, 25.6, 17.5, 15.3; MS (EI(*syn*-**3a**)) *m*/*z* (%) 395 (1.86) [M^+], 193 (35.40), 105 (84.48), 86 (51.69), 84 (82.05), 77 (32.57), 71 (8.47), 57 (11.35), 43 (100); HRMS (EI) Calcd for $C_{23}H_{22}ClNO_3$ [M^+] requires 395.1292, Found 395.1288; The ee of the *syn*-diastereomer was determined to be 97% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 6.98 min, *t* (minor) = 8.57 min].

(*S*)-4-((*R*)-1-(4-Bromophenyl)-2-methylene-3-oxobutyl)-4-isopropy-2-phenyloxazol-5(4*H*)-one 3b. Following the general procedure, the *syn*/*anti* ratio (16 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 2.46 ppm, δ minor: 2.79 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomer along with a trace amount of impurity (36 mg, 82% overall yield in a diastereomeric ratio = 16 : 1); a white solid. m.p. for *syn*-**3b** = 103–105 °C; $[\alpha]_D^{20}$ (*syn*-**3b**) = –42.5 (c 1.0, $CHCl_3$). IR (CH_2Cl_2): ν 2922, 1811, 1678, 1651, 1485, 1454, 1342, 1296, 1157, 1113, 1072, 1047, 1022, 1010, 964, 911, 884, 811, 784 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3b**: δ 7.88–7.86 (2H, m, Ph–H), 7.57–7.52 (1H, m, Ph–H), 7.46–7.42 (2H, m, Ph–H), 7.28 (1H, s, $=CH_2$), 7.21 (2H, d, *J* = 8.8 Hz, Ar–H), 7.10 (2H, d, *J* = 8.8 Hz, Ar–H), 6.50 (1H, s, $=CH_2$), 4.89 (1H, s, Ar–CH), 2.46 (1H, qu, *J* = 6.8 Hz, -$CH(CH_3)_2$), 2.31 (3H, s, $COCH_3$), 1.10 (3H, d, *J* = 6.8 Hz, -$CH(CH_3)_2$), 0.81 (3H, d, *J* = 6.8 Hz, -$CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for *syn*-**3b**: δ 198.0, 177.9, 160.3, 145.9, 135.6, 132.9, 131.9, 130.9, 128.8, 128.7, 127.7, 125.3, 121.6, 79.7, 46.2, 32.3, 25.5, 17.5, 15.3; MS (EI(*syn*-**3b**)) *m*/*z* (%) 439 (2.07) [M^+], 239 (32.76), 237 (33.60), 202 (6.34), 158 (31.42), 115 (12.37), 105 (100.00), 77 (36.26), 43 (88.45); HRMS (EI) Calcd for $C_{23}H_{22}BrNO_3$ [M^+] requires 439.0783, Found 439.0785; The ee of the *syn*-diastereomer was determined to be 97% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 7.28 min, *t* (minor) = 8.61 min].

(*S*)-4-((*R*)-1-(4-Nitrophenyl)-2-methylene-3-oxobutyl)-4-isopropyl-2-phenyloxazol-5(4*H*)-one 3c. Following the general procedure, the *syn*/*anti* ratio (4 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 2.51 ppm, δ minor: 2.79 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomer along with a trace amount of impurity (39 mg, 95% overall yield in a diastereomeric ratio = 4 : 1); a white solid. m.p. for *syn*-**3c** = 114–117 °C; $[\alpha]_D^{20}$ (*syn*-**3c**) = –79.7 (*c* 1.0, $CHCl_3$); $[\alpha]_D^{20}$ (*anti*-**3c**) = –139.5 (c 0.5, $CHCl_3$). IR (CH_2Cl_2): ν(*syn*-**3c**) 2922, 1813, 1676, 1645, 1604, 1522, 1453, 1367, 1342, 1320, 1289, 1163, 1106, 1044, 1025, 973, 910, 877, 855, 833, 783 cm^{-1}; R (CH_2Cl_2): ν(*anti*-**3c**) 2961, 2925, 1782, 1680, 1646, 1605, 1522, 1493, 1450, 1347, 1258, 1174, 1070, 1015, 964, 859. ^1H NMR (300 MHz, $CDCl_3$, TMS) for *syn*-**3c**: δ 7.95 (2H, d, *J* = 9.0 Hz, Ar–H), 7.87 (2H, d, *J* = 7.2 Hz, Ar–H), 7.57 (1H, t, *J* = 7.2 Hz, Ph–H), 7.48–7.39 (5H, m, Ph–H and $=CH_2$), 6.60 (1H, s, $=CH_2$), 5.03 (1H, s, Ar–CH), 2.51 (1H, qu, *J* = 7.2 Hz, -$CH(CH_3)_2$), 2.35 (3H, s, $COCH_3$), 1.11 (3H, d, *J* = 7.2 Hz, -$CH(CH_3)_2$), 0.81 (3H, d, *J* = 7.2 Hz, -$CH(CH_3)_2$); ^1H NMR (400 MHz, $CDCl_3$, TMS) for *anti*-**3c**: δ 8.10–8.05 (2H, m), 7.56–7.41 (4H, m), 7.36–7.31 (3H, m), 6.79 (1H, s), 6.41 (1H, s), 5.55 (1H, s), 2.79 (1H, qu, *J* = 6.8 Hz), 2.21 (3H, s), 1.22 (3H, d, *J* = 6.8 Hz), 1.10 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) for *syn*-**3c**: δ 198.0, 177.6, 160.5, 147.0, 145.1, 144.2, 133.0, 131.1, 129.8, 128.8, 127.7, 124.9, 123.0, 79.4, 46.5, 32.4, 25.5, 17.4, 15.2; ^{13}C NMR (100 MHz, $CDCl_3$) for *anti*-**3c**: δ 197.2, 169.4, 163.3, 147.2, 144.5, 142.8, 137.1, 131.5, 130.8, 129.2, 128.5, 126.6, 123.1, 106.7, 51.2, 28.1, 25.1, 18.9; MS (EI(*syn*-**3c**)) *m*/*z* (%) 406 (0.12) [M^+], 202 (19.95), 174 (5.82), 115 (1.70), 105 (100.00), 77 (15.77), 51 (2.09), 43 (11.30); HRMS (EI) Calcd for $C_{23}H_{22}N_2O_5$ [M^+] requires 406.1529, Found 406.1531; MΣ (ESI(*anti*-**3c**)) *m*/*z* 407 (M^+ + H); HRMS (ESI) for $C_{23}H_{23}N_2O_5$ (M + H): 407.1610, Found: 407.1602; The ee of the *syn*-diastereomer was determined to be 98% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 9.77 min, *t* (minor) = 12.36 min]; the ee of the *anti*-diastereomer was determined to be 94% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.5 mL min^{-1}, λ = 230 nm, *t* (major) = 21.78 min, *t* (minor) = 20.54 min].

(*S*)-4-Isopropyl-4-((*R*)-2-methylene-3-oxo-1-*p*-tolylbutyl)-2-phenyloxazol-5(4*H*)-one 3d. Following the general procedure, the *syn*/*anti* ratio (20 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 2.46 ppm, δ minor: 2.75 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (34 mg, 91% overall yield in a diastereomeric ratio = 20 : 1); a white solid. m.p. for *syn*-**3d** = 90–93 °C; $[\alpha]_D^{20}$ (*syn*-**3d**) = –53.3 (*c* 0.7, $CHCl_3$). IR (CH_2Cl_2): ν 2921, 1812, 1679, 1652, 1322, 1294, 1046, 1022, 963, 909, 882, 810, 785 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3d**: δ 7.88–7.85 (2H, m, Ph–H), 7.55–7.51 (1H, m, Ph–H), 7.46–7.41 (2H, m, Ph–H), 7.24 (1H, s, $=CH_2$), 7.10 (2H, d, *J* = 8.0 Hz, Ar–H), 6.88 (2H, d, *J* = 7.6 Hz, Ar–H), 6.46 (1H, s, $=CH_2$), 4.90 (1H, s, Ar–CH), 2.46 (1H, qu, *J* = 6.8 Hz, -$CH(CH_3)_2$), 2.30 (3H, s, $COCH_3$), 2.15 (3H, s, $PhCH_3$), 1.11 (3H, d, *J* = 6.8 Hz, -$CH(CH_3)_2$), 0.81 (3H, d, *J* = 6.8 Hz, -$CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3d**: δ 198.2, 178.1, 160.0, 146.4, 136.9, 133.3, 132.4, 130.0, 128.6, 128.5, 128.3, 127.7, 125.7, 80.1, 46.5, 32.3, 25.7, 20.9, 17.6, 15.4; MS (EI(*syn*-**3d**)) *m*/*z* (%) 375 (1.26) [M^+], 173 (41.78), 131 (8.05), 115 (4.62), 105 (33.00), 86 (14.60), 84 (22.95), 77 (22.56), 43 (100); HRMS (EI) Calcd for $C_{24}H_{25}NO_3$ [M^+] requires 375.1834, Found 375.1834; the ee of the *syn*-diastereomer was determined to be 96% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 6.78 min, *t* (minor) = 7.78 min].

(*S*)-4-Isopropyl-4-((*R*)-1-(2-methoxyphenyl)-2-methylene-3-oxobutyl)-2-phenyloxazol-5(4*H*)-one 3e. Following the general procedure, the *syn*/*anti* ratio (5 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 2.45 ppm, δ minor: 2.79 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (37 mg, 94% overall yield in a diastereomeric ratio = 5 : 1). m.p. for *syn*-**3e** = 119–121 °C; $[\alpha]_D^{20}$ (*syn*-**3e**) = + 55.5 (*c* 0.7, $CHCl_3$); $[\alpha]_D^{20}$ (*anti*-**3e**) = –7.7 (*c* 0.5, $CHCl_3$). IR (CH_2Cl_2): ν(*syn*-**3e**) 2921, 1817, 1676, 1647, 1489, 1461, 1449, 1344, 1290, 1240, 1198, 1154, 1109, 1043, 1023, 955, 910, 882, 787, 728 cm^{-1}; IR (CH_2Cl_2): ν(*anti*-**3e**) 2961, 2926, 2854, 1826, 1780, 1685, 1655, 1599, 1492, 1258, 1216, 1169, 1105, 1072, 1022, 951, 881, 800. ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3e**: δ 7.88 (2H, d, *J* = 8.4 Hz, Ph–H), 7.53 (1H, t, *J* = 7.2 Hz, Ph–H),

7.44 (2H, t, J = 7.2 Hz, Ph–H), 7.31 (1H, dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, Ar–H), 7.09–7.04 (1H, m, Ar–H), 6.97 (1H, s, $=CH_2$), 6.83–6.81 (1H, m, Ar–H), 6.63–6.60 (1H, m, Ar–H), 6.37 (1H, s, $=CH_2$), 5.71 (1H, s, Ar–CH), 3.87 (3H, s, Ar–OCH_3), 2.45 (1H, qu, J = 6.8 Hz, -$CH(CH_3)_2$), 2.27 (3H, s, $COCH_3$), 1.12 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$), 0.84 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) for *anti*-**3e**: δ 7.57–7.55 (2H, m), 7.34–7.24 (5H, m), 6.88–6.73 (2H, m), 6.60 (1H, s), 6.29 (1H, s), 6.01 (1H, s), 3.84 (3H, s), 2.79 (1H, qu, J = 6.8 Hz), 2.21 (3H, s), 1.22 (3H, d, J = 6.8 Hz), 1.13 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3e**: δ 198.5, 177.7, 159.9, 157.1, 147.4, 132.4, 130.9, 128.6, 128.4, 128.3, 127.7, 125.8, 125.3, 119.4, 111.4, 80.0, 56.0, 38.1, 32.5, 26.0, 17.4, 15.8; ^{13}C NMR (100 MHz, $CDCl_3$) for *anti*-**3e**: δ 197.7, 168.5, 158.1, 146.1, 137.8, 130.5, 129.9, 128.7, 128.3, 128.1, 127.3, 126.7, 126.1, 119.6, 111.3, 69.9, 56.1, 43.3, 28.0, 27.7, 25.7, 19.0, 18.8; MS (EI(*syn*-**3e**)) m/z (%) 391 (0.51) [M^+], 190 (6.62), 189 (47.94), 147 (20.16), 131 (6.13), 115 (4.41), 105 (31.61), 86 (61.28), 84 (100.00), 77 (23.16), 43 (89.95); HRMS (EI) Calcd for $C_{24}H_{25}NO_4$ [M^+] requires 391.1784, Found 391.1785; MS (ESI(*anti*-**3e**)) m/z 392 (M^+ + H); HRMS (ESI) for $C_{24}H_{26}NO_4$ (M^+ + H): 392.1861, Found: 392.1856. The ee of the *syn*-diastereomer was determined to be 95% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, t (major) = 7.02 min, t (minor) = 8.57 min]; The ee of the *anti*-diastereomer was determined to be 94% [determined by HPLC, Chiralpak IC-H, n-hexane/isopropanol = 95 : 5, 0.3 mL min^{-1}, λ = 230 nm, t (major) = 31.09 min, t (minor) = 31.33 min].

(*S*)-4-((*R*)-1-(3-Bromophenyl)-2-methylene-3-oxobutyl)-4-isopropyl-2-phenyloxazol-5(4*H*)one 3f. Following the general procedure, the *syn*/*anti* ratio (15 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 2.47 ppm, δ minor: 2.80 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (40 mg, 91% overall yield in a diastereomeric ratio = 15 : 1); a white solid. m.p. for *syn*-**3f** = 154–156 °C; $[\alpha]_D^{20}$ (*syn*-**3f**) = −71.8 (c 0.8, $CHCl_3$). IR (CH_2Cl_2): ν 2974, 2954, 1811, 1673, 1655, 1470, 1288, 1196, 1159, 1111, 1041, 1019, 978, 916, 888, 876, 800, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3f**: δ 7.87 (2H, d, J = 6.8 Hz, Ph–H), 7.55 (1H, t, J = 7.6 Hz, Ph–H), 7.45 (2H, t, J = 7.2 Hz, Ph–H), 7.35 (1H, s, Ar–H), 7.28 (1H, s, $=CH_2$), 7.19 (2H, dd, J_1 = 8.0 Hz, J_1 = 2.0 Hz, Ar–H), 6.97 (1H, t, J = 8.0 Hz, Ar–H), 6.52 (1H, s, $=CH_2$), 4.89 (1H, s, Ar–CH), 2.47 (1H, qu, J = 6.8 Hz, -$CH(CH_3)_2$), 2.34 (3H, s, $COCH_3$), 1.10 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$), 0.82 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for *syn*-**3f**: δ 198.0, 177.8, 160.4, 145.6, 138.8, 133.0, 132.7, 130.5, 129.5, 129.1, 129.0, 128.7, 127.8, 125.3, 121.6, 79.7, 46.6, 32.2, 25.6, 17.5, 15.3; MS (EI(*syn*-**3f**)) m/z (%) 439 (2.18) [M^+], 237 (5.17), 202 (20.39), 174 (5.64), 158 (8.15), 115 (6.41), 105 (100.00), 84 (11.45), 77 (25.88), 43 (39.26); HRMS (EI) Calcd for $C_{23}H_{22}BrNO_3$ [M^+] requires 439.0783, Found 439.0790; The ee of the *syn*-diastereomer was determined to be 97% [determined by HPLC, Chiralpak IC-H, n-hexane/isopropanol = 99 : 1, 0.7 mL min^{-1}, λ = 230 nm, t (major) = 15.63 min, t (minor) = 8.57 min].

(*S*)-4-Isopropyl-4-((*R*)-2-methylene-3-oxo-1-(4-(trifluorophenyl))butyl)-2-phenyloxazol-5(4*H*)-one 3g. Following the general procedure, the *syn*/*anti* ratio (16 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 2.50 ppm, δ minor: 2.78 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (37 mg, 86% overall yield in a diastereomeric ratio = 16 : 1); a white solid. m.p. for *syn*-**3g** = 122–123 °C; $[\alpha]_D^{20}$ (*syn*-**3g**) = −57.3 (c 0.8, $CHCl_3$). IR (CH_2Cl_2): ν 2978, 2881, 1813, 1673, 1650, 1617, 1493, 1451, 1323 1292, 1251, 1198, 1128, 1110, 1043, 1018, 986, 969, 911, 881, 821, 781 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3g**: δ 7.86 (2H, d, J = 7.2 Hz, Ph–H), 7.55 (1H, t, J = 7.8 Hz, Ph–H), 7.44 (2H, t, J = 7.2 Hz, Ph–H), 7.33–7.38 (5H, m, Ar–H and $=CH_2$), 6.54 (1H, s, $=CH_2$), 5.00 (1H, s, Ar–CH), 2.50 (1H, qu, J = 6.8 Hz, -$CH(CH_3)_2$), 2.33 (3H, s, $COCH_3$), 1.11 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$), 0.82 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3g**: δ 198.0, 177.8, 160.4, 145.6, 140.7, 132.8, 130.6, 129.5 (q, J_{C-F} = 32.0 Hz), 129.2, 128.7, 127.7, 125.3, 124.8 (q, J_{C-F} = 3.7 Hz), 123.9 (q, J_{C-F} = 207.7 Hz), 79.7, 46.6, 32.3, 25.5, 17.4, 15.3; ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$): δ (*syn*-**3g**) −62.7; MS (EI(*syn*-**3g**)) m/z (%) 429 (1.67) [M^+], 202 (24.30), 174 (5.44), 165 (0.60), 106 (8.18), 105 (100.00), 84 (9.37), 77 (23.72), 43 (26.76); HRMS (EI) Calcd for $C_{24}H_{22}F_3NO_3$ [M^+] requires 429.1552, Found 429.1557; the ee of the *syn*-diastereomer was determined to be 96% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 95 : 5, 0.7 mL min^{-1}, λ = 230 nm, t (major) = 7.02 min, t (minor) = 8.57 min].

(*S*)-4-Isopropyl-4-((*R*)-1-(3-methoxyphenyl)-2-methylene-3-oxobutyl)-2-phenyloxazol-5(4*H*)-one 3h. Following the general procedure, the *syn*/*anti* ratio (12 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 2.47 ppm, δ minor: 2.77 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (36 mg, 92% overall yield in a diastereomeric ratio = 12 : 1); a white solid. m.p. for *syn*-**3h** = 117–119 °C; $[\alpha]_D^{20}$ (*syn*-**3h**) = −49.8 (c 0.7, $CHCl_3$). IR (CH_2Cl_2): ν 2974, 1818, 1680, 1651, 1597, 1491, 1467, 1451, 1294, 1259, 1244, 1199, 1154, 1111, 1045, 1021, 969, 902, 864, 794, 779, 729 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) for *syn*-**3h**: δ 7.87 (2H, d, J = 7.2 Hz, Ph–H), 7.53 (1H, t, J = 7.5 Hz, Ph–H), 7.43 (2H, t, J = 7.2 Hz, Ph–H), 7.26 (1H, s, $=CH_2$), 7.00 (1H, t, J = 7.8 Hz, Ar–H), 6.82 (1H, d, J = 6.8 Hz, Ar–H), 6.78–6.76 (1H, m), 6.61 (1H, dd, J_1 = 10.8 Hz, J_2 = 3.2 Hz, Ar–H), 6.49 (1H, s, $=CH_2$), 4.92 (1H, s, Ar–CH), 3.57 (3H, s, Ar–OCH_3), 2.47 (1H, qu, J = 7.2 Hz, -$CH(CH_3)_2$), 2.32 (3H, s, $COCH_3$), 1.12 (3H, d, J = 7.2 Hz, -$CH(CH_3)_2$), 0.84 (3H, d, J = 7.2 Hz, -$CH(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) for *syn*-**3h**: δ 198.2, 178.0, 160.1, 158.9, 146.1, 137.9, 132.5, 128.7, 128.6, 127.7, 125.6, 122.7, 115.3, 113.5, 80.0, 55.0, 46.9, 32.3, 25.7, 17.6, 15.4; MS (EI(*syn*-**3h**)) m/z (%) 391 (4.95) [M^+], 203 (4.09), 189 (77.39), 147 (45.34), 132 (6.29), 115 (8.73), 105 (100.00), 77 (52.88), 51 (5.77), 43 (84.84); HRMS (EI) Calcd for $C_{24}H_{25}NO_4$ [M^+] requires 391.1784, Found 391.1788; The ee of the *syn*-diastereomer was determined to be >99% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, t (major) = 7.21 min, t (minor) = 17.78 min].

(*S*)-4-Isopropyl-4-((*R*)-2-methylene-3-oxo-1-(3-(trifluorophenyl))butyl)-2-phenyloxazol-5(4*H*)-one 3i. Following the general procedure, the *syn*/*anti* ratio (16 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major:

2.50 ppm, δ minor: 2.75 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (38 mg, 89% overall yield in a diastereomeric ratio = 16 : 1). Awhite solid. m.p. for *syn*-**3i** = 80–83 °C; $[\alpha]_D^{20}$ (*syn*-**3i**) = –45.2 (*c* 0.9, $CHCl_3$). IR (CH_2Cl_2): *v* 2924, 1806, 1673, 1655, 1620, 1449, 1366 1288, 1161, 1177, 1131, 1096, 1042, 1021, 979, 968, 918, 891, 814, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3i**: δ 7.82 (2H, d, J = 9.6 Hz, Ar–H), 7.56–7.51 (1H, m, Ar–H), 7.45–7.40 (4H, m, Ar–H), 7.35 (1H, s, $=CH_2$), 7.32 (1H, d, J = 10.8, Ar–H), 7.22–7.27 (1H, m, Ar–H), 6.56 (1H, s, $=CH_2$), 5.00 (1H, s, Ar–CH), 2.50 (1H, qu, J = 6.8 Hz, -$CH(CH_3)_2$), 2.35 (3H, s, $COCH_3$), 1.12 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$), 0.83 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for *syn*-**3i**: δ 197.9, 177.8, 160.6, 145.8, 137.7, 134.1 (d, J_{C-F} = 1.5 Hz), 132.7, 130.1 (q, J_{C-F} = 30.0 Hz), 129.0, 128.6, 128.5, 126.7 (q, J_{C-F} = 3.7 Hz), 125.3, 124.2 (q, J_{C-F} = 3.7 Hz), 123.8 (q, J_{C-F} = 270.6 Hz), 79.8, 46.9, 32.3, 25.4, 17.5, 15.3; ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$): δ –62.8; MS (EI(*syn*-**3i**)) *m*/*z* (%) 429 (0.65) [M^+], 227 (0.91), 202 (23.69), 174 (5.14), 128 (0.71), 115 (3.23), 105 (100.00), 77 (23.72), 51 (2.72), 43 (26.76); HRMS (EI) Calcd for $C_{24}H_{22}F_3NO_3$ [M^+] requires 429.1552, Found 429.1554; the ee of the *syn*-diastereomer was determined to be 97% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 5.38 min, *t* (minor) = 8.78 min].

(*S*)-4-((*R*)-1-(4-Bromophenyl)-2-methylene-3-oxobutyl)-4-isobutyl-2-phenyloxazol-5(4*H*)-one 3j. Following the general procedure, the *syn*/*anti* ratio (3 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 4.68 ppm, δ minor: 4.86 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (38 mg, 84% overall yield in a diastereomeric ratio = 3 : 1); a white solid. m.p. for *syn*-**3j** = 123–126 °C; $[\alpha]_D^{20}$ (*syn*-**3j**) = –28.1 (c 0.6, $CHCl_3$); $[\alpha]_D^{20}$ (*anti*-**3j**) = –2.1 (*c* 0.4, $CHCl_3$). IR (CH_2Cl_2): *v*(*syn*-**3j**) 2920, 1808, 1671, 1652, 1486, 1452, 1357, 1318, 1293, 1157, 1242, 1148, 1114, 1073, 1045, 1023, 1014, 988, 975, 928, 891, 853, 818, 779 cm^{-1}; IR (CH_2Cl_2): *v*(*anti*-**3j**) 2969, 1816, 1683, 1653, 1487, 1451, 1141, 1320, 1291, 1261, 1216, 1095, 1021, 869. ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3j**: δ 7.89–7.87 (2H, m, Ph–H), 7.59–7.55 (1H, m, Ph–H), 7.48–7.44 (2H, m, Ph–H), 7.24 (1H, s, $=CH_2$), 7.22–7.19 (2H, m, Ar–H), 7.07–7.04 (2H, m, Ar–H), 6.48 (1H, s, $=CH_2$), 4.68 (1H, s, Ar–CH), 2.31 (3H, s, $COCH_3$), 2.13 (1H, dd, J_1 = 14.4 Hz; J_2 = 6.4 Hz, $CH_2CH(CH_3)_2$), 1.86 (1H, dd, J_1 = 14.4 Hz; J_2 = 6.0 Hz, $CH_2CH(CH_3)_2$), 1.49 (1H, qu, J = 6.8 Hz, $CH_2CH(CH_3)_2$), 0.86 (3H, d, J = 6.8 Hz, $CH_2CH(CH_3)_2$), 0.81 (3H, d, J = 6.8 Hz, $CH_2CH(CH_3)_2$); ^1H NMR (400 MHz, $CDCl_3$, TMS) for *anti*-**3j**: δ 8.05–8.03 (2H, m), 7.64–7.60 (1H, m), 7.55–7.49 (4H, m), 7.44–7.41 (2H, m), 6.21 (1H, s), 6.15 (1H, s), 4.86 (1H, s), 2.26 (3H, s), 1.84 (2H, d, J = 6.4 Hz), 1.45 (1H, qu, J = 6.8 Hz), 0.79 (6H, t, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3j**: δ 198.2, 179.8, 160.1, 146.7, 135.2, 132.7, 131.6, 131.1, 128.8, 128.5, 127.7, 125.5, 121.7, 49.9, 44.1, 25.6, 25.2, 23.8, 23.5; ^{13}C NMR (100 MHz, $CDCl_3$) for *anti*-**3j**: δ 197.6, 179.8, 160.3, 146.9, 138.1, 132.8, 131.6, 131.4, 129.0, 128.9, 127.9, 125.6, 121.3, 75.9, 47.8, 45.3, 25.3, 25.0, 23.9, 23.3; MS (EI(*syn*-**3j**)) *m*/*z* (%) 453 (0.34) [M^+], 366 (1.68), 239 (25.08), 237 (25.26), 216 (4.96), 202 (6.34), 158 (31.42), 115 (16.91), 105 (100.00), 77 (34.68), 43 (51.45); HRMS (EI) Calcd for $C_{24}H_{24}BrNO_3$ [M^+] requires 453.0940, Found 453.0941; MS (ESI(*anti*-**3j**)) *m*/*z* 454 (M^+ + H); HRMS (ESI) for $C_{24}H_{25}NO_3Br$ (M^+ + H): 454.1029, Found: 454.1012; The ee of the *syn*-diastereomer was determined to be 91% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 7.55 min, *t* (minor) = 9.14 min]; The ee of the *anti*-diastereomer was determined to be 98% [determined by HPLC, Chiralpak IC-H, n-hexane/isopropanol = 98 : 2, 0.3 mL min^{-1}, λ = 230 nm, *t* (major) = 41.25 min, *t* (minor) = 51.36 min].

(*S*)-4-((*R*)-1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-4-methyl-2-phenyloxazol-5(4*H*)-one 3k. Following the general procedure, the *syn*/*anti* ratio (4 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 4.75 ppm, δ minor: 4.86 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (33 mg, 90% overall yield in a diastereomeric ratio = 4 : 1); a white solid. m.p. for *syn*-**3k** = 123–125 °C; $[\alpha]_D^{20}$ (*syn*-**3k**) = –0.7 (c 0.7, $CHCl_3$); $[\alpha]_D^{20}$ (*anti*-**3k**) = –11.2 (*c* 0.4, $CHCl_3$). IR(CH_2Cl_2): *v*(*syn*-**3k**) 1818, 1789, 1658, 1620, 1492, 1450, 1323, 1295, 1168, 1092, 1072, 1017, 982, 898, 818, 782 cm^{-1}; IR(CH_2Cl_2): *v*(*anti*-**3k**) 2958, 2925, 2854, 1822, 1742, 1683, 1652, 1491, 1452, 1375, 1292, 1259, 1216, 1199, 1091, 917, 876. ^1H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3k**: δ 7.90–7.87 (2H, m, Ph–H), 7.58–7.54 (1H, m, Ph–H), 7.47–7.43 (2H, m, Ph–H), 7.25 (1H, s, $=CH_2$), 7.16–7.13 (2H, m, Ar–H), 7.08–7.06 (2H, m, Ar–H), 6.52 (1H, s, $=CH_2$), 4.75 (1H, s, Ar–CH), 2.33 (3H, s, $COCH_3$), 1.58 (3H, s, $PhCH_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) for *anti*-**3k**: δ 8.05–8.03 (2H, m), 7.64–7.51 (5H, m), 7.31–7.29 (2H, m), 6.23 (1H, s), 6.16 (1H, s), 4.86 (1H, s), 2.26 (3H, s), 1.45 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3k**: δ 198.3, 179.7, 160.2, 146.2, 135.1, 133.4, 132.8, 131.0, 128.7, 128.5, 128.1, 127.8, 125.5, 72.9, 48.9, 25.5, 22.5; ^{13}C NMR (100 MHz, $CDCl_3$) for *anti*-**3k**: δ 179.6, 179.7, 160.5, 147.4, 136.9, 133.2, 133.0, 131.1, 128.9, 128.6, 128.3, 127.9, 125.6, 72.0, 47.0, 25.3, 23.9; MS (EI) *m*/*z* (%) 367 (2.11) [M^+], 339 (1.06), 195 (19.54), 193 (58.52), 158 (3.08), 151 (3.21), 141 (2.81), 115 (21.09), 105 (69.94), 77 (44.95), 43 (100); HRMS (EI(*syn*-**3k**)) Calcd for $C_{21}H_{18}ClNO_3$ [M^+] requires 367.0975, Found 367.0973; MS (ESI(*anti*-**3k**)) *m*/*z* 368 (M^+ + H); HRMS (ESI) for $C_{21}H_{19}NO_3Cl$ (M^+ + H): 368.1057, Found: 368.1048; the ee of the *syn*-diastereomer was determined to be 97% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 9.13 min, *t* (minor) = 12.97 min]; the ee of the *anti*-diastereomer was determined to be 90% [determined by HPLC, Chiralpak IC-H, n-hexane/isopropanol = 95 : 5, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 15.92 min, *t* (minor) = 17.68 min].

(*S*)-4-Methyl-4-((*R*)-2-methylene-3-oxo-1-*p*-tolylbutyl)-2-phenyloxazol-5(4*H*)-one 3l. Following the general procedure, the *syn*/*anti* ratio (10 : 1) was determined by ^1H NMR spectroscopic analysis of the crude product (δ major: 4.75 ppm, δ minor: 5.29 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (31 mg, 90% overall yield in a diastereomeric ratio = 10 : 1); a white solid. m.p. for *syn*-**3l** = 113–114 °C; $[\alpha]_D^{20}$ (*syn*-**3l**) = +13.2 (*c* 0.9, $CHCl_3$). IR (CH_2Cl_2): *v* 2924, 1820, 1672, 1651, 1450, 1289, 1170, 1008, 969, 900, 814, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.90–7.8 (2H, m, Ph–H),

7.57–7.53 (1H, m, Ph–H), 7.47–7.43 (2H, m, Ph–H), 7.21 (1H, s, =CH_2), 7.09 (2H, dd, J_1 = 6.4 Hz; J_2 = 2.0 Hz, Ar–H), 6.90 (2H, d, J = 7.6 Hz, Ar–H), 6.45 (1H, s, =CH_2), 4.75 (1H, s, Ar–CH), 2.32 (3H, s, $COCH_3$), 2.17 (3H, s, $ArCH_3$), 1.58 (3H, s, $PhCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3l**: δ 198.5, 180.0, 160.0, 146.6, 137.0, 133.4, 132.5, 129.4, 128.7, 128.6, 128.1, 127.8, 125.8, 73.2, 49.2, 25.5, 22.5, 20.9; MS (EI(*syn*-**3l**)) *m*/*z* (%) 347(1.42) [M^+], 319 (1.82), 173 (74.97), 141 (3.11), 131 (14.80), 115 (12.13), 105 (37.01), 97 (3.87), 77 (34.49), 43 (100); HRMS (EI) Calcd for $C_{22}H_{21}NO_3$ [M^+] requires 347.1521, Found 347.1523; The ee of the *syn*-diastereomer was determined to be 96% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 8.52 min, *t* (minor) = 11.32 min].

(*R*)-4-((*R*)-1-(4-Bromophenyl)-2-methylene-3-oxobutyl)-2,4-diphenyloxazol-5(4*H*)-one 3m. Following the general procedure, the *syn*/*anti* ratio (7 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 6.25 ppm, δ minor: 6.22 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (40 mg, 85% overall yield in a diastereomeric ratio = 7 : 1); a white solid. m.p. for *syn*-**3m** = 93–95 °C; $[\alpha]_D^{20}$ (*syn*-**3m**) = –192.6 (*c* 0.6, $CHCl_3$). IR (CH_2Cl_2): ν 2922, 1809, 1650, 1486, 1449, 1365, 1324, 1297, 1065, 1011, 988, 961, 925, 905, 883, 814, 786 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.97 (2H, d, J = 7.2 Hz, Ar–H), 7.65–7.58 (3H, m, Ar–H), 7.49 (2H, t, J = 6.8 Hz, Ar–H), 7.35–7.20 (7H, m, Ar–H), 7.07 (1H, s, =CH_2), 6.25 (1H, s, =CH_2), 5.37 (1H, s, Ar–CH), 2.12 (3H, s, $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) for *syn*-**3m**: δ 198.1, 177.7, 161.0, 145.5, 136.8, 134.8, 133.1, 131.9, 131.1, 129.3, 128.9, 128.7, 128.4, 128.0, 126.0, 125.3, 121.9, 77.4, 50.6, 25.4; MS (EI(*syn*-**3m**)) *m*/*z* (%) 428.(56.76) [$M^+ - COCH_3$], 386 (100.00), 307 (16.38), 304 (37.96), 227 (16.95), 202 (88.69), 193 (10.03), 173 (21.15), 152 (16.34), 105 (67.55), 77 (37.81), 43 (56.29); HRMS (EI) Calcd for $C_{26}H_{20}BrNO_3$ [M^+] requires 473.0627, Found 473.0625; The ee of the *syn*-diastereomer was determined to be 92% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 13.75 min, *t* (minor) = 14.80 min].

(*S*)-4-Isopropyl-4-((*R*)-2-methylene-3-oxo-1-(thiophen-2-yl)-butyl)-2-phenyloxazol-5(4*H*)-one 3n. Following the general procedure, the *syn*/*anti* ratio (12 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 5.35 ppm, δ minor: 5.70 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with trace amount of impurity (35 mg, 95% overall yield in a diastereomeric ratio = 12 : 1); a white solid. m.p. for *syn*-**3n** = 78–80 °C; $[\alpha]_D^{20}$ (*syn*-**3n**) = –79.5 (c 0.4, $CHCl_3$). IR (CH_2Cl_2): ν 2922, 1817, 1653, 1622, 1451, 1427, 1390, 1361, 1336, 1322, 1293, 1254, 1234, 1198, 1156, 1111, 1069, 1042, 1020, 967, 904, 879, 856, 783 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) for *syn*-**3n**: δ 7.96–7.92 (2H, m, Ph–H), 7.59–7.54 (1H, m, Ph–H), 7.49–7.44 (2H, m, Ph–H), 7.21 (1H, s, =CH_2), 7.01 (1H, d, J = 7.2 Hz, thiophen-H), 6.94 (1H, d, J = 3.0 Hz, thiophen-H), 6.76 (1H, dd, J_1 = 6.8 Hz; J_2 = 3.2 Hz, thiophen-H), 6.47 (1H, s, =CH_2), 5.35 (1H, s, Ar–CH), 2.32–2.45 (4H, m, $COCH_3$, $CH(CH_3)_2$), 1.09 (3H, d, J = 6.6 Hz, $CH(CH_3)_2$), 0.84 (3H, d, J = 6.6 Hz, $CH(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) for *syn*-**3n**: δ 197.8, 178.0, 160.9, 146.7, 140.3, 132.6, 129.4, 128.7, 128.0, 127.9, 126.3, 125.7, 80.3, 41.6, 32.6, 25.5, 17.6, 15.4; MS (EI(*syn*-**3n**)) *m*/*z* (%) 367 (1.45) [M^+], 339 (1.65), 324 (2.02), 165 (89.62), 123 (23.90), 105 (57.74), 97 (3.87), 77 (43.30), 57 (6.77), 43 (100); HRMS (EI) Calcd for $C_{21}H_{20}NO_3S$ [M^+] requires 367.1242, Found 367.1248; the ee of the *syn*-diastereomer was determined to be 95% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 90 : 10, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 6.91 min, *t* (minor) = 8.57 min].

(*S*)-4-Isopropyl-4-((*R*)-3-methylene-4-oxopentan-2-yl)-2-phenyloxazol-5(4*H*)-one 3o. Following the general procedure, the *syn*/*anti* ratio (7 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 0.76 ppm, δ minor: 0.68 ppm). The mixture was purified by column chromatography using silica gel to give a mixture of diastereoisomers along with a trace amount of impurity (30 mg, 96% overall yield in a diastereomeric ratio = 7 : 1); a colorless liquid. $[\alpha]_D^{20}$ = +16.9 (*c* 1.0, $CHCl_3$). IR (CH_2Cl_2): ν 2965, 2916, 1817, 1774, 1681, 1655, 1580, 1451, 1371, 1336, 1321, 1293, 1261, 1163, 1094, 1022, 954, 920, 880, 799, 761 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.98–7.95 (2H, m, Ar–H), 7.59–7.54 (1H, m, Ar–H), 7.50–7.46 (2H, m, Ar–H), 7.36–7.32 (0.5H, (*anti*-**3o**), m, Ar–H), 6.23 (0.14H (*anti*-**3o**), s, =CH_2), 6.20 (1H, s, =CH_2), 6.18 (1H, s, =CH_2), 5.91 (0.14H (*anti*-**3o**), s, =CH_2), 3.89 (0.14H (*anti*-**3o**), dd, J_1 = 11.6 Hz; J_2 = 3.2 Hz, CH_2CH), 3.69 (1H, dd, J_1 = 11.6 Hz; J_2 = 4.0 Hz, CH_2CH), 2.92–2.85 (0.14H (*anti*-**3o**), m), 2.30–2.20 (4.4H, m, $CH(CH_3)_2$, $COCH_3$), 1.69–1.51 (2H, m, CH_3CH_2), 1.33–1.28 (0.28H (*anti*-**3o**), m, CH_3CH_2), 1.23 (0.42H (*anti*-**3o**), d, J = 6.8 Hz, $CH(CH_3)_2$), 1.19 (0.42H (*anti*-**3o**), d, J = 6.8 Hz, $CH(CH_3)_2$), 0.97 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$), 0.89 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$), 0.76 (3H, t, J = 7.2 Hz, CH_3CH_2), 0.68 (0.42H (*anti*-**3o**), t, J = 7.2 Hz, CH_3CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (major) 199.3, 179.5, 159.5, 148.0, 132.6, 128.7, 127.8, 126.2, 125.7, 80.2, 41.8, 32.3, 25.7, 22.6, 16.8, 16.6, 11.5; MS (EI) *m*/*z* (%) 313 (1.43) [M^+], 271 (4.10), 242 (8.07), 203 (11.73), 188 (2.29), 174 (3.13), 155 (1.12), 105 (100), 77 (24.27), 57 (11.42), 43 (25.48); HRMS (EI) Calcd for $C_{19}H_{23}NO_3$ [M^+] requires 313.1678, Found 313.1679; the ee of the *syn*-diastereomer was determined to be 85% [determined by HPLC, Chiralpak IC-H, n-hexane/isopropanol = 99 : 1, 0.5 mL min^{-1}, λ = 214 nm, *t* (major) = 34.31 min, *t* (minor) = 22.87 min].

Methyl 2-((*R*)-(4-chlorophenyl)((*S*)-4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)methyl)acrylate 3p. To a mixture of **1p** (0.11 mmol, 36 mg), **2a** (0.10 mmol, 21 mg) and catalyst **L2** (13 mg, 0.020 mmol) was added 1.0 mL of THF at room temperature under argon. The resulting mixture was heated to 40 °C and monitored by TLC. After the reaction complete, the solution was concentrated under reduced pressure and the residue was further purified by silica gel column chromatography (EtOAc/PE = 1/20) to give the desired product **3p** (13 mg, 32% yield), a white solid, m.p. for *syn*-**3p** = 98–100 °C. The *syn*/*anti* ratio (2 : 1) was determined by ^{1}H NMR spectroscopic analysis of the crude product (δ major: 2.79 ppm, δ minor: 2.62 ppm). $[\alpha]_D^{20}$ (*syn*-**3p**) –100.3 (*c* 0.6, $CHCl_3$). IR (CH_2Cl_2): ν 2967, 1772, 1717, 1649, 1491, 1441, 1408, 1386, 1157, 1122, 1090, 1071, 1013, 1002, 969, 947, 921, 885, 782 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) for *syn*-**3p**: δ 7.52–7.50 (2H, m), 7.33–7.31 (3H, m), 7.21 (4H, s), 6.49 (1H, s), 5.23 (1H, s), 3.65 (3H, S) 2.79 (1H, qu, J = 6.8 Hz, -$CH(CH_3)_2$), 1.21 (3H, d, J = 6.8 Hz, -$CH(CH_3)_2$), 1.08 (3H, d, J = 6.8 Hz,

-$CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) for *syn*-**3p**: δ 169.3, 166.5, 163.4, 137.4, 136.6, 133.7, 132.0, 130.3, 129.0, 128.4, 128.2, 126.7, 106.8, 53.4, 52.3, 28.0, 18.9, 18.7; MS (EI(*syn*-**3p**)) *m/z* (%) 411 (1.64) [M^+], 308 (14.13), 266 (5.64), 209 (69.26), 177 (4.46), 149 (38.93), 130 (13.74), 115 (22.47), 105 (100.00), 77 (33.65), 59 (11.86); HRMS (EI) Calcd for $C_{23}H_{22}ClNO_4$ [M^+] requires 411.1237, Found 411.1248; the ee of the *syn*-diastereomer was determined to be 86% [determined by HPLC, Chiralpak AD-H, n-hexane/isopropanol = 95 : 5, 0.7 mL min^{-1}, λ = 230 nm, *t* (major) = 11.42 min, *t* (minor) = 10.17 min].

General procedure for the hydrolysis of addition products 3j and 3b to the corresponding amino acid

The addition product *syn*-**3j** (30 mg, 60 μmol) was dissolved in a mixed solvent of MeCN/DCM (0.20 mL/0.10 mL), then 0.10 mL conc. HCl was added. The resulting mixture was stirred at room temperature for two days. The solvent was removed under reduced pressure and the residue was purified by column chromatography on SiO_2 gel (DCM/EtOH = 40/1–10/1 as eluent) to give the corresponding amido acid **4j** as a white solid (18 mg, 45 μmol, 75% yield). m.p. 95–97 °C; $[\alpha]_D^{20}$ = +75.2 (*c* 0.7, $CHCl_3$). IR (neat): ν 2954, 2922, 2851, 1815, 1697, 1487, 1464, 1382, 1328, 1211, 1154, 1106, 1073, 1009, 909, 821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.42 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 5.54 (1H, s), 5.01 (1H, s), 3.81 (1H, s), 2.31–2.04 (4H, m), 1.80–1.75 (1H, m), 1.42–1.29 (1H, m), 0.92 (3H, d, *J* = 6.6 Hz), 0.86 (3H, d, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.5, 170.8, 152.8, 139.9, 131.1, 130.8, 119.9, 111.8, 84.6, 58.1, 48.3, 25.0, 24.6, 23.5, 15.6; MS (ESI) *m/z* 350 ($M - H_2O$–HCl)$^+$; HRMS (ESI) for $C_{17}H_{21}NO_2Br$ ($M - H_2O$–HCl)$^+$: 350.0750, Found: 350.0757.

The addition product *syn*-**3b** (65.0 mg, 148 μmol) was dissolved in 500 μL 1,4-dioxane, then 80.0 μL, 3.0 M HCl aqueous solution was added. The resulting mixture was stirred at room temperature for 8 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography on SiO_2 gel (DCM/EtOH = 40/1–20/1 as eluent) to give the corresponding amino acid derivative **4b** as white solid (18.0 mg, 39 μmol, 67% yield based on the recovered **3b**, 39.0 mg starting material was recovered). m.p. 139–141 °C; $[\alpha]_D^{20}$ = +28.3 (*c* 0.9, $CHCl_3$). IR (CH_2Cl_2): ν 2927, 2855, 1780, 1714, 1674, 1520, 1487, 1394, 1365, 1264, 1218, 1074, 1011, 895, 801 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 8.51 (1H, bs), 7.87 (2H, d, *J* = 7.2 Hz), 7.57 (1H, d, *J* = 6.8 Hz), 7.48 (2H, d, *J* = 6.8 Hz), 7.36 (2H, d, *J* = 8.7 Hz), 7.22 (2H, d, *J* = 8.7 Hz), 6.43 (1H, s), 5.12 (1H, s), 4.78 (1H, bs), 2.81 (1H, qu, *J* = 7.2 Hz), 2.39 (3H, s), 1.08 (3H, d, *J* = 7.2 Hz), 1.05 (3H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.1, 169.6, 162.5, 147.6, 137.9, 133.8, 132.9, 132.2, 131.4, 130.8, 128.8, 127.3, 121.0, 72.6, 51.2, 33.4, 26.8, 18.7, 18.0; MS (ESI) *m/z* 458 (M^+ + H); HRMS (ESI) for $C_{23}H_{25}NO_4Br$ (M^+ + H): 458.0952, Found: 458.0961.

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