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Asymmetric Synthesis of β-Hydroxy-α-amino Phosphonic Acid Derivatives via Organocatalytic Direct Aldol Reaction of α-Isothiocyanato Phosphonates with Aldehydes

Wen-Yong Han,[†,§] Jian-Qiang Zhao,[†,§] Zhi-Jun Wu,[‡] Xiao-Mei Zhang,[†] and Wei-Cheng Yuan*[,†]

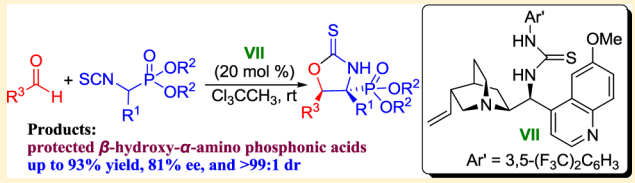
[†]National Engineering Research Center of Chiral Drugs, Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, China

[‡]Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, China

[§]University of Chinese Academy of Sciences, Beijing 100049, China

Supporting Information

ABSTRACT: α-Isothiocyanato phosphonates are first used as nucleophiles to react with aldehydes for the asymmetric synthesis of β-hydroxy-α-amino phosphonic acid derivatives. The process is catalyzed by a quinine-derived thiourea via cascade aldol/cyclization reaction, affording a wide range of protected β-hydroxy-α-amino phosphonates containing adjacent quaternary-tertiary stereocenters in up to 93% yield, up to 81% ee, and >99:1 dr. This work represents the first example of α-isothiocyanato phosphonates serving as nucleophiles that are used in the catalytic asymmetric synthesis.



Phosphonate analogues of α-amino acids have been a source of inspiration in bioorganic and medicinal chemistry due to their some biological activities and potential uses as peptide mimics and haptens of catalytic antibodies.[1] Developing efficient methods for preparing optically active α-amino phosphonic acid derivatives is becoming an important topic in organic synthesis.[2] Particularly, chiral β-hydroxy-α-amino phosphonates have found widespread applications as surrogates and structural analogues of β-hydroxy-α-amino acids, which are found widely in nature as useful building blocks for some complex natural products.[3] In this context and considering the fact that a defined spatial configuration of stereogenic center is an important issue for biologically active molecules, the development of an efficient and practical synthetic methodology to generate chiral β-hydroxy-α-amino phosphonic acids and their functionalized derivatives is an important objective in synthetic chemistry.[1c] However, to the best of our knowledge, only very few approaches to chiral β-hydroxy-α-amino phosphonic acid derivatives, especially those containing adjacent quaternary-tertiary stereocenters, have been reported.[4] Accordingly, an enantioselective and catalytic method for the construction of the optically active β-hydroxy-α-amino phosphonic acid derivatives containing adjacent quaternary-tertiary stereocenters has remained a formidable challenge and is highly desirable.

Recently, α-isothiocyanato nucleophiles, including α-isothiocyanato imides and esters, have been illustrated as valuable reagents for the synthesis of various enantioenriched β-hydroxy-α-amino acid derivatives,[5] α,β-diamino acid derivatives,[6] and spirocyclic compounds.[7] Notably, these α-isothiocyanato nucleophiles are able to smoothly react with aldehydes or ketones leading to masked chiral β-hydroxy-α-amino acid derivatives in a direct catalytic asymmetric aldol reaction.[5] In particular, we recently also reported a series of domino reactions of 3-isothiocyanato oxindoles with diverse electrophiles for the construction of spirocyclic oxindole compounds.[8] Motivated by the above-mentioned successes,[5−8] we envisioned that α-isothiocyanato phosphonates **1** might also serve as ideal nucleophilic reagents reacting with some appropriate electrophiles such as α-isothiocyanato imides or esters.[9] As a continuation of our study on the asymmetric organocatalysis,[8] we have found that a series of optically active β-hydroxy-α-amino phosphonic acid derivatives, containing adjacent quaternary-tertiary stereocenters, can be obtained from the reaction between α-isothiocyanato phosphonates **1** and aldehydes in up to 81% ee and >99:1 dr with quinine-derived thiourea **VII** as the catalyst via a cascade aldol/cyclization process. It is worthwhile to note that this work represents the first example regarding α-isothiocyanato phosphonates serving as nucleophiles for catalytic asymmetric transformation. Herein, we wish to present our research findings on this subject.

Preliminary optimization experiments were carried out with model substrates α-isothiocyanato phosphonate **1a** and benzaldehyde (Table 1).[10] The reactions could deliver the desired product **3a** in toluene at room temperature in the presence of 20 mol % readily available cinchona alkaloids **I**−**IV** (Figure 1), giving good diastereoselectivity and moderate enantioselectivity (Table 1, entries 1−4). And then, the 9-

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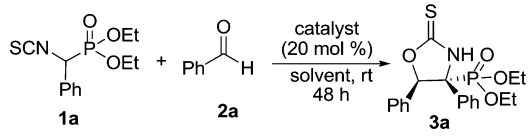
Table 1. Catalyst Screening and Optimization of Reaction Conditions[a]



entry	catalyst	solvent	yield (%)[b]	dr[c]	ee (%)[d]
1	**I**	toluene	74	88:12	66
2	**II**	toluene	13	87:13	58
3	**III**	toluene	65	90:10	−68
4	**IV**	toluene	26	86:14	−54
5	**V**	toluene	51	91:9	−71
6	**VI**	toluene	39	90:10	−72
7	**VII**	toluene	52	90:10	71
8	**VIII**	toluene	19	91:9	76
9	**IX**	toluene	85	86:14	−63
10	**X**	toluene	74	87:13	−61
11	**VII**	THF	trace	–	–
12	**VII**	hexane	68	85:15	59
13	**VII**	CH_2Cl_2	75	90:10	73
14	**VII**	$CHCl_3$	62	83:17	67
15	**VII**	CCl_4	82	90:10	68
16	**VII**	Cl_3CCH_3	78	91:9	75

[a]All reactions were carried out with **1a** (0.1 mmol) and **2a** (0.2 mmol) in 2.0 mL of solvent with 20 mol % catalyst at room temperature for 48 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Ee of major diastereoisomer as determined by chiral HPLC analysis.

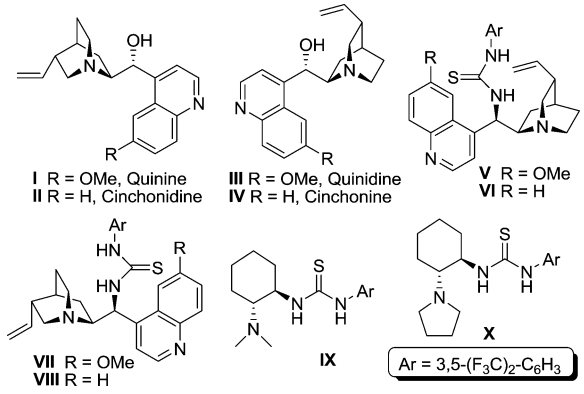
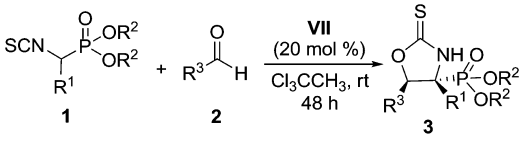


Figure 1. Structures of catalysts examined in this work.

thiourea cinchona alkaloids **V**–**VIII** (Figure 1) were found to afford slightly better diastereo- and enantioselectivity (Table 1, entries 5–8). We further examined the catalytic ability of chiral bifunctional thiourea-tertiary amines **IX** and **X** (Figure 1) bearing a *trans*-1,2-diaminocyclohexane scaffold (Table 1, entries 9–10). In general, the screening tests of catalysts revealed the quinine-derived thiourea **VII** to be the most selective and active for the reaction (Table 1, entry 7). To further optimize the reaction efficiency, various solvents were then examined. The reaction hardly took place with THF as solvent (Table 1, entry 11). After the survey of hexane and some chlorinated solvents (Table 1, entries 12–16), Cl_3CCH_3 emerged as a winner, showing a set of acceptable results in terms of yield as well as diastereo- and enantioselectivity (Table 1, entry 16).

With optimal conditions in hand (Table 1, entry 16), the reaction scope was next examined. As illustrated in Table 2, in the reactions of α-isothiocyanato phosphonate **1a** with various

Table 2. Scope of VII-Catalyzed Asymmetric Reaction of α-Isothiocyanato Phosphonates 1 and Aldehydes 2[a]



1a: R^1 = Ph, R^2 = Et
1b: R^1 = 4-MeC_6H_4, R^2 = Et
1c: R^1 = 4-$MeOC_6H_4$, R^2 = Et
1d: R^1 = 4-FC_6H_4, R^2 = Et
1e: R^1 = H, R^2 = Et
1f: R^1 = Ph, R^2 = -$CH(CH_3)_2$
1g: R^1 = Ph, R^2 = Ph

entry	1	2	3/yield (%)[b]	dr[c]	ee (%)[d]
1	**1a**	R^3 = 4-MeC_6H_4 (**2b**)	**3b**/62	88:12	75
2	**1a**	R^3 = 2-$MeOC_6H_4$ (**2c**)	**3c**/69	91:9	72
3	**1a**	R^3 = 2-FC_6H_4 (**2d**)	**3d**/78	99:1	78
4	**1a**	R^3 = 2-ClC_6H_4 (**2e**)	**3e**/72	>99:1	78
5	**1a**	R^3 = 2,4-$Cl_2C_6H_3$ (**2f**)	**3f**/70	99:1	74
6	**1a**	R^3 = 4-BrC_6H_4 (**2g**)	**3g**/85	91:9	74
7	**1a**	R^3 = 2-$NO_2C_6H_4$ (**2h**)	**3h**/80	>99:1	68
8	**1a**	R^3 = 4-$NO_2C_6H_4$ (**2i**)	**3i**/92	90:10	71
9	**1a**	R^3 = 2-CNC_6H_4 (**2j**)	**3j**/93	90:10	69
10	**1a**	R^3 = 1-naphthyl (**2k**)	**3k**/42	>99:1	70[e]
11	**1a**	R^3 = 2-thienyl (**2l**)	**3l**/73	89:11	75
12	**1a**	R^3 = 2-pyridinyl (**2m**)	**3m**/77	84:16	70
13	**1a**	R^3 = Me (**2n**)	**3n**/66	85:15[f]	55[g]
14	**1b**	R^3 = Ph (**2a**)	**3o**/38	90:10	78[e]
15	**1c**	R^3 = Ph (**2a**)	**3p**/36	92:8	81[h]
16	**1d**	R^3 = Ph (**2a**)	**3q**/86	93:7	76
17	**1e**	R^3 = Ph (**2a**)	**3r**/nr	–	–[h]
18	**1f**	R^3 = 4-$NO_2C_6H_4$ (**2i**)	**3s**/78	98:2	73
19	**1g**	R^3 = 4-$NO_2C_6H_4$ (**2i**)	**3t**/nr	–	–[e]

[a]Unless otherwise noted, all reactions were carried out with **1** (0.4 mmol) and **2** (0.8 mmol) in 8.0 mL of Cl_3CCH_3 with 20 mol % **VII** at room temperature for 48 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Ee of major diastereoisomer as determined by chiral HPLC analysis. [e]Run for 72 h. [f]The dr value was determined by ^{1}H NMR analysis. [g]Run for 120 h. [h]Run for 96 h. nr = No reaction.

aryl aldehydes (**2b**–**j**), the corresponding *trans*-adduct **3b**–**j** could be smoothly obtained in 88:12 to >99:1 dr, 68–78% ee, and 62–93% yield (Table 2, entries 1–9). The reactions proved insensitive to the substitution pattern, position, and electronic nature of the substituents on the aromatic ring of aldehydes. Nevertheless, sterically bulky 1-naphthaldehyde (**2k**) presented no problems in providing **3k** with >99:1 dr and 70% ee, though a reduced yield was observed (Table 2, entry 10). Additionally, the heteroaryl aldehydes **2l** and **2m** were also able to be converted into the desired products **3l** and **3m** with acceptable results (Table 2, entries 11–12). Much to our delight, alkyl aldehyde **2n** also underwent the desired transformation to furnish product **3n**, although a longer reaction time was needed for the reaction (Table 2, entry 13). On the other hand, we also evaluated the effect of various α-isothiocyanato phosphonates **1b**–**e** in the catalytic asymmetric reaction system (Table 2, entries 14–17). For **1b** and **1c** incorporating an electron-donating substituent at the phenyl ring reacting with benzaldehyde (**2a**), the reactions afforded the expected products **3o** and **3p** with high diastereoselectivity and good enantioselectivity, respectively, but the reactivity fell off remarkably for both reactions (Table 2, entries 14–15). Meanwhile, by incorporating an electron-withdrawing group at the phenyl ring, it was observed that the stereoselectivity could remain high and an up to 86% yield could be attained for

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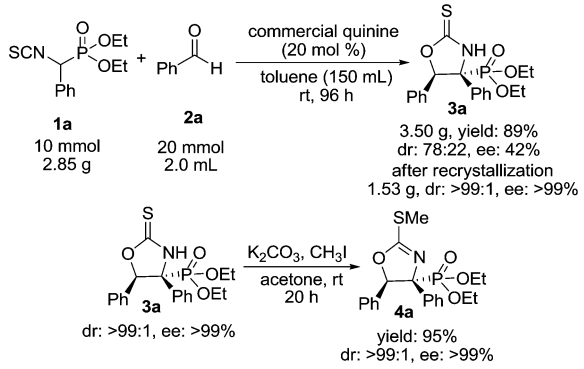
3q (Table 2, entry 16). As a limitation to the method, α-isothiocyanato phosphonate **1e** failed to react with benzaldehyde (**2a**) under the reaction conditions (Table 2, entry 17), presumably due to the fact that it is difficult to take off the hydrogen atom of the α-carbon atom of α-isothiocyanato phosphonate **1e**, thus depressing the aldol reaction. Ultimately, by changing the ester functionality from ethyl phosphonate (**1a**) to isopropyl phosphonate (**1f**), it was found that the reaction with **2i** proceeded smoothly and yielded the product **3s** in a set of good results (Table 2, entry 18). However, unfortunately the reaction of α-isothiocyanato phosphonate **1g** and **2i** did not provide the desired product **3t** under the standard conditions (Table 2, entry 19), presumably due to the more sterically hindered phosphate ester moiety on substrate **1g**.

In order to demonstrate the synthetic utility of this methodology, together with consideration of an easy source of catalyst and solvent, a large scale experiment with 20 mol % commercial available quinine (catalyst I in Figure 1) as the catalyst was tried in toluene under mild reaction conditions (Scheme 1). We were pleased to observe that the preparative-

Scheme 1. Preparative-Scale Experiment and Transformation of 3a



scale reaction proceeded smoothly and afforded the expected product **3a** in 89% yield with 78:22 dr and only 42% ee. Notably, the large scale experiment in Scheme 1 was performed at 10 mmol scale, which is 100 times larger than the scale of the original reaction shown in Table 1, entry 1, resulting in the product **3a** with an increased yield but with a decreased ee value. These results suggested that the 100-fold increase in scale led to some degree of change in the reaction performance, especially in the enantioselective control ability of the catalyst. However, much to our delight, the diastereo- and enantioselectivity of **3a** could be drastically enhanced to >99:1 dr and >99% ee by a simple recrystallization from a mixture of ethyl acetate and petroleum ether. Nevertheless, further transformation of the optically pure **3a** into compound **4a** could be readily achieved (Scheme 1). Upon treatment of **3a** with K_2CO_3 and iodomethane in acetone at room temperature for 20 h, the methylated product **4a** could be smoothly obtained in 95% yield without loss of dr and ee values.[11]

To determine the absolute configuration of the products, single crystals suitable for X-ray crystallographic analysis were fortunately obtained from optically pure **3a**. As shown in Figure 2, it contains a (*C2R*,*C3R*) configuration.[11] By assuming via a common reaction pathway in the construction of compounds **3**, the stereochemistry of the other products in this work was assigned by analogy.

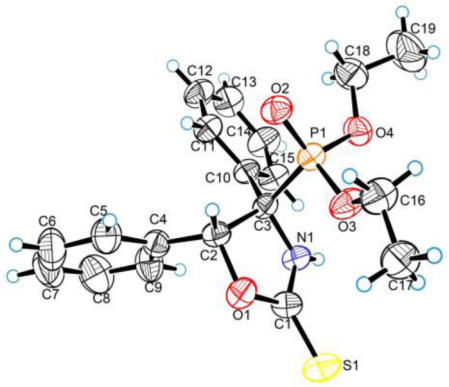
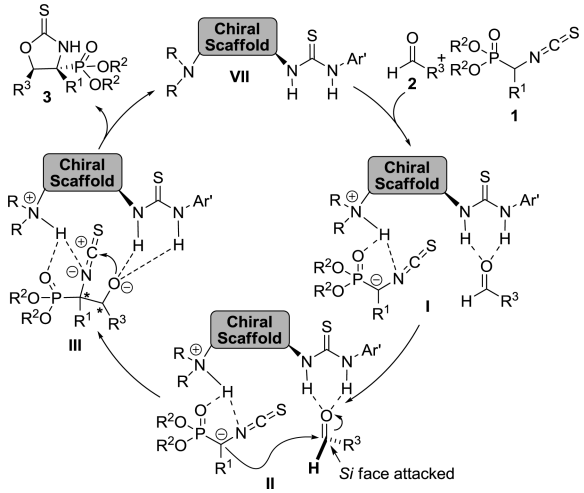


Figure 2. X-ray crystallographic structure of optically pure **3a**.

Based on recent studies on the asymmetric reactions of α-isothiocyanato nucleophiles and the above-illustrated experimental results, a possible pathway was assumed to understand the cascade aldol/cyclization reaction sequence and explain the stereochemistry (Scheme 2). We presume that the chiral

Scheme 2. Proposed Reaction Pathway for VII-Catalyzed Reaction of α-Isothiocyanato Phosphonates and Aldehydes



tertiary amine-thiourea **VII** should act in a bifunctional fashion. The tertiary amine moiety in the cinchona alkaloid serving as a base deprotonates the active hydrogen atom of the α-carbon atom of α-isothiocyanato phosphonates and then stabilizes the α-isothiocyanato phosphonates **1** by intermolecular hydrogen bonding interaction to form transition state **I**. Simultaneously, the thiourea moiety of **VII** activates the aldehydes **2** via double hydrogen bonding to the oxygen atom of the aldehydes. In the transition state **II**, the *Si* face of the aldehydes was attacked by the activated α-carbon anion of α-isothiocyanato phosphonates. And then, the oxygen anion of aldehydes approached the −NCS group of α-isothiocyanato phosphonates through a cyclization reaction in transition state **III**, leading to the (*C2R*,*C3R*) products **3** and releasing the organocatalyst **VII** into the next reaction cycle.

In conclusion, we have developed an organocatalytic asymmetric method for the synthesis of a series of optically active β-hydroxy-α-amino phosphonic acid derivatives. The reaction employs α-isothiocyanato phosphonates as nucleophilic reagents for addition to aldehydes with a quinine-derived

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thiourea as the catalyst via a cascade aldol/cyclization process, leading to protected β-hydroxy-α-amino phosphonates containing adjacent quaternary-tertiary stereocenters in up to 93% yield, up to 81% ee, and >99:1 dr. The potential synthetic utility of the methodology in this work was demonstrated by a large scale experiment and by the further conversion of one product. A plausible reaction pathway for the reaction of α-isothiocyanato phosphonates and aldehydes was also tentatively brought forward. Notably, this work represents the first example of α-isothiocyanato phosphonates serving as nucleophiles for the catalytic asymmetric transformation. We expect that insights gained from our present study are helpful for opening new opportunities to access enantioenriched β-hydroxy-α-amino phosphonic acid derivatives.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of 3. In an ordinary vial equipped with a magnetic stirring bar, compounds **1** (0.4 mmol), **2** (0.8 mmol), and catalyst **VII** (47.6 mg, 0.08 mmol) were dissolved in 8.0 mL of CH_3CCl_3 and stirred at room temperature. After the completion of the reaction, the mixture was subjected directly to flash column chromatography on silica gel using hexane/ethyl acetate (4:1−2:1) to purify the corresponding products.

Diethyl (4*R*,5*R*)-4,5-Diphenyl-2-thioxooxazolidin-4-ylphosphonate (3a). White solid, 122.1 mg, yield 78%; dr 91:9, 75% ee, $[\alpha]_D^{20}$ = −24.4 (*c* 2.06, $CHCl_3$); mp 109.8−111.2 °C. HPLC analysis Chiralpak AD-H (80/20 hexane/*i*-PrOH; 1.0 mL/min; for major diastereoisomer: t_{major} = 5.59 min, t_{minor} = 10.21 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.11 (t, *J* = 6.9 Hz, 3H), 1.46 (t, *J* = 6.9 Hz, 3H), 3.83−3.86 (m, 1H), 4.05−4.11 (m, 1H), 4.31−4.38 (m, 2H), 6.37 (d, *J* = 16.8 Hz, 1H), 7.00−7.12 (m, 8H), 7.20−7.22 (m, 2H), 9.36 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3 (d, *J* = 5.3 Hz, 1C), 16.5 (d, *J* = 5.5 Hz, 1C), 64.3 (d, *J* = 7.8 Hz, 1C), 65.0 (d, *J* = 7.2 Hz, 1C), 70.3 (d, *J* = 158.1 Hz, 1C), 89.1 (d, *J* = 1.7 Hz, 1C), 127.3 (d, *J* = 4.7 Hz, 1C), 127.7, 127.9, 128.1 (d, *J* = 2.1 Hz, 1C), 128.9, 132.1 (d, *J* = 5.6 Hz, 1C), 133.4 (d, *J* = 7.6 Hz, 1C), 189.2 (d, *J* = 4.5 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$): δ (ppm): 18.17; HRMS (ESI-TOF) calcd for $C_{19}H_{22}NNaO_4PS$ $[M+Na]^+$: 414.0899; found: 414.0884.

Diethyl (4*R*,5*R*)-4-Phenyl-2-thioxo-5-*p*-tolyloxazolidin-4-ylphosphonate (3b). White solid, 100.6 mg, yield 62%; dr 88:12, 75% ee, $[\alpha]_D^{20}$ = −26.9 (*c* 1.37, $CHCl_3$); mp 41.0−42.8 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 9.15 min, t_{minor} = 13.21 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.10 (t, *J* = 6.9 Hz, 3H), 1.46 (t, *J* = 6.9 Hz, 3H), 2.19 (s, 3H), 3.80−3.84 (m, 1H), 4.03−4.08 (m, 1H), 4.30−4.35 (m, 2H), 6.34 (d, *J* = 16.8 Hz, 1H), 6.88 (s, 4H), 7.04−7.08 (m, 3H), 7.19−7.21 (m, 2H), 8.83 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, *J* = 5.3 Hz, 1C), 16.5 (d, *J* = 5.5 Hz, 1C), 21.1, 64.2 (d, *J* = 7.9 Hz, 1C), 64.9 (d, *J* = 7.2 Hz, 1C), 70.1 (d, *J* = 157.9 Hz, 1C), 89.2 (d, *J* = 1.8 Hz, 1C), 127.2 (d, *J* = 4.7 Hz, 1C), 127.6, 127.9 (d, *J* = 1.4 Hz, 1C), 128.1 (d, *J* = 2.1 Hz, 1C), 128.5, 130.2 (d, *J* = 7.4 Hz, 1C), 132.2 (d, *J* = 5.6 Hz, 1C), 138.9, 189.2 (d, *J* = 4.4 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$): δ (ppm): 18.34; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NNaO_4PS$ $[M+Na]^+$: 428.1056; found: 428.1043.

Diethyl (4*R*,5*R*)-5-(2-Methoxyphenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3c). White solid, 116.3 mg, yield 69%; dr 91:9, 72% ee, $[\alpha]_D^{20}$ = −13.2 (*c* 2.64, $CHCl_3$); mp 49.5−50.3 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 10.90 min, t_{minor} = 19.55 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.13 (t, *J* = 6.9 Hz, 3H), 1.45 (t, *J* = 6.9 Hz, 3H), 3.65 (s, 3H), 3.81−3.88 (m, 1H), 4.05−4.10 (m, 1H), 4.29−4.34 (m, 2H), 6.52 (d, *J* = 8.4 Hz, 1H), 6.67−6.75 (m, 2H), 7.00−7.10 (m, 5H), 7.26−7.28 (m, 2H), 9.17 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3 (d, *J* = 5.2 Hz, 1C), 16.5 (d, *J* = 5.6 Hz, 1C), 54.9, 64.1 (d, *J* = 7.9 Hz, 1C), 64.7 (d, *J* = 7.2, Hz, 1C), 70.3 (d, *J* = 156.3 Hz, 1C), 84.8, 109.9, 120.1, 122.4 (d, *J* = 9.4 Hz, 1C), 127.0 (d, *J* = 4.6 Hz, 1C), 127.3, 127.9 (d, *J* = 2.0, Hz, 1C), 128.6, 130.4, 132.0 (d, *J* = 5.6 Hz, 1C), 156.3, 189.3; ^{31}P NMR (121 MHz, $CDCl_3$): δ (ppm): 18.74; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NNaO_5PS$ $[M+Na]^+$: 444.1005; found: 444.0990.

Diethyl (4*R*,5*R*)-5-(2-Fluorophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3d). White solid, 127.7 mg, yield 78%; dr 99:1, 78% ee, $[\alpha]_D^{20}$ = −1.1 (*c* 2.22, $CHCl_3$); mp 136.8−138.1 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 10.55 min, t_{minor} = 11.68 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.21 (t, *J* = 6.9 Hz, 3H), 1.45 (t, *J* = 6.9 Hz, 3H), 4.00−4.03 (m, 1H), 4.21−4.33 (m, 3H), 6.64 (d, *J* = 17.7 Hz, 1H), 6.78−6.86 (m, 2H), 6.94−7.08 (m, 5H), 7.22−7.26 (m, 2H), 9.82 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3, 16.4 (d, *J* = 5.1 Hz, 1C), 64.3 (d, *J* = 8.0 Hz, 1C), 65.2 (d, *J* = 7.2 Hz, 1C), 70.4 (d, *J* = 157.4 Hz, 1C), 82.9, 115.0 (d, *J* = 21.3 Hz, 1C), 121.9 (dd, J_1 = 9.7 Hz, J_2 = 12.2 Hz, 1C), 123.9 (d, *J* = 3.4 Hz, 1C), 126.9 (d, *J* = 4.4 Hz, 1C), 127.8 (d, *J* = 1.7 Hz, 1C), 128.0 (d, *J* = 2.2 Hz, 1C), 129.1 (d, *J* = 2.9 Hz, 1C), 130.9 (d, *J* = 8.3 Hz, 1C), 131.8 (d, *J* = 5.0 Hz, 1C), 159.7 (d, *J* = 247.5 Hz, 1C), 189.1 (d, *J* = 2.6 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 18.04; HRMS (ESI-TOF) calcd for $C_{19}H_{22}FNO_4PS$ $[M+H]^+$: 410.0986; found: 410.1004.

Diethyl (4*R*,5*R*)-5-(2-Chlorophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3e). Yellow solid, 122.7 mg, yield 72%; dr >99:1, 78% ee, $[\alpha]_D^{20}$ = −45.6 (*c* 1.78, $CHCl_3$); mp 153.8−155.2 °C. HPLC analysis Chiralpak AS-H (90/10 hexane/ethanol: 1.0 mL/min; for major diastereoisomer; t_{major} = 6.38 min, t_{minor} = 8.78 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.16 (t, *J* = 6.9 Hz, 3H), 1.48 (t, *J* = 6.9 Hz, 3H), 3.91−3.96 (m, 1H), 4.09−4.15 (m, 1H), 4.30−4.39 (m, 2H), 6.89−6.97 (m, 3H), 6.99−7.16 (m, 5H), 7.33−7.61 (m, 2H), 7.76 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.4, 16.5 (d, *J* = 5.6 Hz, 1C), 64.3 (d, *J* = 7.6 Hz, 1C), 65.0 (d, *J* = 7.1 Hz, 1C), 70.4 (d, *J* = 157.5 Hz, 1C), 84.7, 126.7, 126.9 (d, *J* = 4.6 Hz, 1C), 128.0 (d, *J* = 1.6 Hz, 1C), 128.3 (d, *J* = 2.2 Hz, 1C), 129.1, 129.3, 130.2, 132.2, 132.3, 133.0, 189.2; ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 18.12; HRMS (ESI-TOF) calcd for $C_{19}H_{21}ClNNaO_4PS$ $[M+Na]^+$: 448.0510; found: 448.0517.

Diethyl (4*R*,5*R*)-5-(2,4-Dichlorophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3f). White solid, 128.9 mg, yield 70%; dr 99:1, 74% ee, $[\alpha]_D^{20}$ = −44.5 (*c* 3.75, $CHCl_3$); mp 182.7−184.0 °C. HPLC analysis Chiralpak AS-H (80/20 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 4.04 min, t_{minor} = 4.77 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.28 (t, *J* = 6.9 Hz, 3H), 1.45 (t, *J* = 6.9 Hz, 3H), 4.14−4.36 (m, 4H), 6.77−6.83 (m, 2H), 6.88−7.06 (m, 4H), 7.17−7.21 (m, 3H), 9.91 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.4 (d, *J* = 5.7 Hz, 1C), 16.5 (d, *J* = 5.2 Hz, 1C), 64.4 (d, *J* = 8.1 Hz, 1C), 65.4 (d, *J* = 7.4 Hz, 1C), 70.6 (d, *J* = 158.2 Hz, 1C), 83.8, 126.8 (d, *J* = 4.5 Hz, 1C), 127.2, 128.0 (d, *J* = 1.7 Hz, 1C), 128.3 (d, *J* = 2.2 Hz, 1C), 128.8, 130.2, 131.2 (d, *J* = 10.2 Hz, 1C), 131.5 (d, *J* = 4.9 Hz, 1C), 133.6, 135.4, 188.8 (d, *J* = 2.3 Hz, 1C) ; ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.67; HRMS (ESI-TOF) calcd for $C_{19}H_{21}Cl_2NO_4PS$ $[M+H]^+$: 460.0300; found: 460.0294.

Diethyl (4*R*,5*R*)-5-(4-Bromophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3g). White solid, 159.9 mg, yield 85%; dr 91:9, 74% ee, $[\alpha]_D^{20}$ = −39.9 (*c* 5.30, $CHCl_3$); mp 171.1−172.9 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 10.88 min, t_{minor} = 15.62 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.09 (t, *J* = 6.9 Hz, 3H), 1.42 (t, *J* = 6.9 Hz, 3H), 3.83−3.87 (m, 1H), 4.04−4.10 (m, 1H), 4.27−4.32 (m, 2H), 6.30 (d, *J* = 16.8 Hz, 1H), 6.86−6.89 (m, 2H), 7.00−7.09 (m, 3H), 7.16−7.21 (m, 4H), 9.87 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, *J* = 5.3 Hz, 1C), 16.4 (d, *J* = 5.6 Hz, 1C), 64.3 (d, *J* = 7.9 Hz, 1C), 65.2 (d, *J* = 7.3 Hz, 1C), 70.2 (d, *J* = 158.8 Hz, 1C), 88.1, 123.1, 127.2 (d, *J* = 4.6 Hz, 1C), 128.0, 128.3, 129.3, 131.0, 131.7 (d, *J* = 5.6 Hz, 1C), 132.4 (d, *J* = 7.5 Hz, 1C), 188.9 (d, *J* = 4.7 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.83; HRMS (ESI-TOF) calcd for $C_{19}H_{21}BrNNaO_4PS$ $[M+Na]^+$: 492.0004; found: 492.0010.

Diethyl (4*R*,5*R*)-5-(2-Nitrophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3h). Red oil, 139.7 mg, yield 80%; dr >99:1, 68% ee, $[\alpha]_D^{20}$ = −56.5 (*c* 1.83, $CHCl_3$); HPLC analysis Chiralpak AD-H (80/20 hexane/ethanol; 1.0 mL/min; for major diaster-

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eoisomer: t_{major} = 9.64 min, t_{minor} = 14.45 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.34 (t, J = 6.9 Hz, 3H), 1.43 (t, J = 6.9 Hz, 3H), 4.24−4.34 (m, 3H), 4.38−4.44 (m, 1H), 6.77−6.82 (m, 2H), 6.90−6.93 (m, 1H), 7.07−7.26 (m, 6H), 7.73−7.75 (m, 1H), 10.41 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, J = 5.7 Hz, 1C), 16.6 (d, J = 5.2 Hz, 1C), 64.6 (d, J = 8.2 Hz, 1C), 65.4 (d, J = 7.4 Hz, 1C), 71.1 (d, J = 160.1 Hz, 1C), 82.1, 124.2, 126.8 (d, J = 4.6 Hz, 1C), 127.9 (d, J = 1.4 Hz, 1C), 128.0 (d, J = 2.1 Hz, 1C), 129.6 (d, J = 2.6 Hz, 1C), 130.3 (d, J = 10.9 Hz, 1C), 131.5 (d, J = 4.9 Hz, 1C), 133.1, 147.6, 188.7 (d, J = 2.2 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.00; HRMS (ESI-TOF) calcd. for $C_{19}H_{21}N_2NaO_6PS$ $[M+Na]^+$: 459.0750; found: 459.0758.

Diethyl (4*R*,5*R*)-5-(4-Nitrophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3i). White solid, 160.6 mg, yield 92%; dr 90:10, 71% ee, $[\alpha]_D^{20}$ = −39.9 (*c* 6.61, $CHCl_3$); mp 70.8−72.2 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 18.11 min, t_{minor} = 22.02 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.13 (t, J = 6.9 Hz, 3H), 1.46 (t, J = 6.9 Hz, 3H), 3.90−3.94 (m, 1H), 4.10−4.16 (m, 1H), 4.29−4.39 (m, 2H), 6.41 (d, J = 16.5 Hz, 1H), 7.00−7.09 (m, 3H), 7.18−7.22 (m, 4H), 7.93 (d, J = 8.7 Hz, 2H), 9.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, J = 5.3 Hz, 1C), 16.5 (d, J = 5.5 Hz, 1C), 64.4 (d, J = 7.9 Hz, 1C), 65.4 (d, J = 7.3 Hz, 1C), 70.3 (d, J = 159.8 Hz, 1C), 87.3 (d, J = 2.0 Hz, 1C), 123.0, 127.0 (d, J = 4.8 Hz, 1C), 128.3, 128.5, 128.7, 131.5 (d, J = 5.8 Hz, 1C), 140.4 (d, J = 7.1 Hz, 1C), 147.8, 188.7 (d, J = 4.9 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.45; HRMS (ESI-TOF) calcd for $C_{19}H_{21}N_2NaO_6PS$ $[M+Na]^+$: 459.0750; found: 459.0729.

Diethyl (4*R*,5*R*)-5-(2-Cyanophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3j). White solid, 154.9 mg, yield 93%; dr 90:10, 69% ee, $[\alpha]_D^{20}$ = −43.8 (*c* 2.40, $CHCl_3$); mp 166.6−168.1 °C. HPLC analysis Chiralpak AD-H (80/20 hexane/*i*-PrOH; 1.0 mL/min; for major diastereoisomer: t_{major} = 8.08 min, t_{minor} = 17.20 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.12 (t, J = 6.9 Hz, 3H), 1.46 (t, J = 6.9 Hz, 3H), 3.85−3.93 (m, 1H), 4.08−4.14 (m, 1H), 4.34 (q, J = 7.2 Hz, 2H), 6.37 (d, J = 16.5 Hz, 1H), 7.01−7.19 (m, 7H), 7.36−7.38 (m, 2H), 9.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, J = 5.2 Hz, 1C), 16.5 (d, J = 5.6 Hz, 1C), 64.5 (d, J = 7.8 Hz, 1C), 65.4 (d, J = 7.2 Hz, 1C), 70.3 (d, J = 159.5 Hz, 1C), 87.6, 112.7, 118.1, 127.0 (d, J = 4.8 Hz, 1C), 128.2, 128.3, 128.7, 131.7, 138.6 (d, J = 11.2 Hz, 1C), 188.8 (d, J = 4.8 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.49; HRMS (ESI-TOF) calcd for $C_{20}H_{21}N_2NaO_4PS$ $[M+Na]^+$: 439.0852; found: 439.0839.

Diethyl (4*R*,5*R*)-5-(Naphthalen-1-yl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3k). White solid, 74.2 mg, yield 42%; dr >99:1, 70% ee, $[\alpha]_D^{20}$ = −104.5 (*c* 1.07, $CHCl_3$); mp 75.3−76.9 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 10.04 min, t_{minor} = 16.38 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.15 (t, J = 6.9 Hz, 3H), 1.53 (t, J = 6.9 Hz, 3H), 3.92−3.94 (m, 1H), 4.14−4.16 (m, 1H), 4.41−4.46 (m, 2H), 6.77−6.87 (m, 3H), 7.19−7.29 (m, 4H), 7.42−7.70 (m, 5H), 8.13 (d, J = 8.4 Hz, 1H), 8.59 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3 (d, J = 5.2 Hz, 1C), 16.6 (d, J = 5.5 Hz, 1C), 64.4 (d, J = 7.8 Hz, 1C), 65.0 (d, J = 7.3 Hz, 1C), 70.6 (d, J = 157.1 Hz, 1C), 85.3, 123.1, 124.7, 125.7, 126.0, 126.4, 126.8 (d, J = 4.9 Hz, 1C), 127.4, 128.2, 128.5, 129.5, 129.8 (d, J = 8.4 Hz, 1C), 130.4, 131.7, 132.9, 189.3; ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 19.04; HRMS (ESI-TOF) calcd for $C_{23}H_{24}NNaO_4PS$ $[M+Na]^+$: 464.1056; found: 464.1056.

Diethyl (4*R*,5*S*)-4-Phenyl-5-(thiophen-2-yl)-2-thioxooxazolidin-4-ylphosphonate (3l). White solid, 116.1 mg, yield 73%; dr 89:11, 75% ee, $[\alpha]_D^{20}$ = +7.8 (*c* 3.04, $CHCl_3$); mp 89.5−91.1 °C. HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 9.78 min, t_{minor} = 13.86 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.12 (t, J = 6.9 Hz, 3H), 1.44 (t, J = 6.9 Hz, 3H), 3.83−3.86 (m, 1H), 4.07−4.10 (m, 1H), 4.27−4.33 (m, 2H), 6.65 (d, J = 16.2 Hz, 1H), 6.73−6.76 (m, 1H), 6.93−6.94 (m, 1H), 7.06−7.15 (m, 4H), 7.28−7.31 (m, 2H), 9.84 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, J = 5.4 Hz, 1C), 16.5 (d, J = 5.5 Hz, 1C), 64.4 (d, J = 7.9 Hz, 1C), 65.1 (d, J = 7.3 Hz, 1C), 70.2 (d, J = 156.2 Hz, 1C), 84.8 (d, J = 2.3 Hz, 1C), 126.0, 127.3 (d, J = 4.5 Hz, 1C), 128.0, 128.2 (d, J = 2.2 Hz, 1C), 129.0, 131.8 (d, J = 4.5 Hz, 1C), 135.8 (d, J = 10.4 Hz, 1C), 188.6 (d, J = 3.4 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 18.11; HRMS (ESI-TOF) calcd for $C_{17}H_{20}NNaO_4PS_2$ $[M+Na]^+$: 420.0464; found: 420.0460.

Diethyl (4*R*,5*R*)-4-Phenyl-5-(pyridin-2-yl)-2-thioxooxazolidin-4-ylphosphonate (3m). Light brown solid, 120.9 mg, yield 77%; dr 84:16, 70% ee, $[\alpha]_D^{20}$ = −8.1 (*c* 2.70, $CHCl_3$); mp 105.7−107.1 °C. HPLC analysis Chiralpak AD-H (80/20 hexane/*i*-PrOH; 1.0 mL/min; for major diastereoisomer: t_{major} = 10.05 min, t_{minor} = 14.64 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.22 (t, J = 6.9 Hz, 3H), 1.43 (t, J = 6.9 Hz, 3H), 3.90−4.11 (m, 1H), 4.23−4.32 (m, 3H), 6.44 (d, J = 17.7 Hz, 1H), 6.91−7.01 (m, 5H), 7.17−7.20 (m, 2H), 7.32−7.37 (m, 1H), 8.36−8.37 (m, 1H), 9.77 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3, 16.5 (d, J = 5.5 Hz, 1C), 64.5 (d, J = 7.8 Hz, 1C), 65.1 (d, J = 7.3 Hz, 1C), 70.5 (d, J = 157.8 Hz, 1C), 88.8, 122.6, 123.4, 127.3, 127.4, 127.8, 131.7 (d, J = 4.7 Hz, 1C), 136.2, 148.5, 154.0 (d, J = 10.7 Hz, 1C), 189.1 (d, J = 2.8 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.89; HRMS (ESI-TOF) calcd for $C_{18}H_{21}N_2NaO_4PS$ $[M+Na]^+$: 415.0852; found: 415.0860.

Diethyl (4*R*,5*R*)-5-Methyl-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3n). White solid, 86.9 mg, yield 66%; dr 85:15, 55% ee, $[\alpha]_D^{20}$ = +46.3 (*c* 2.11, $CHCl_3$); mp 159.2−160.6 °C. HPLC analysis Chiralpak AD-H (after the *N*-H was protected by acetyl group, 80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 5.74 min, t_{minor} = 7.81 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.03−1.11 (m, 6H), 1.32−1.42 (m, 3H), 3.79−4.05 (m, 2H), 4.24−4.29 (m, 2H), 5.49−5.52 (m, 1H), 7.32−7.37 (m, 3H), 7.54−7.56 (m, 2H), 9.10 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.2 (d, J = 5.3 Hz, 1C), 16.4 (d, J = 5.6 Hz, 1C), 17.5 (d, J = 6.8 Hz, 1C), 64.0 (d, J = 7.8 Hz, 1C), 64.8 (d, J = 7.1 Hz, 1C), 69.3 (d, J = 157.4 Hz, 1C), 83.8, 125.8 (d, J = 4.0 Hz, 1C), 127.1 (d, J = 4.9 Hz, 1C), 128.6, 132.2 (d, J = 6.0 Hz, 1C), 189.0; ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 18.67; HRMS (ESI-TOF) calcd For $C_{14}H_{20}NNaO_4PS$ $[M+Na]^+$: 352.0743; found: 352.0759.

Diethyl (4*R*,5*R*)-5-Phenyl-2-thioxo-4-*p*-tolyloxazolidin-4-ylphosphonate (3o). White solid, 61.6 mg, yield 38%; dr 90:10, 78% ee, $[\alpha]_D^{20}$ = −23.3 (*c* 1.52, $CHCl_3$); mp 145.9−147.2 °C. HPLC analysis Chiralpak AD-H (80/20 hexane/*i*-PrOH; 1.0 mL/min; for major diastereoisomer: t_{major} = 5.69 min, t_{minor} = 7.97 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.12 (t, J = 6.9 Hz, 3H), 1.46 (t, J = 6.9 Hz, 3H), 2.17 (s, 3H), 3.82−3.84 (m, 1H), 4.04−4.10 (m, 1H), 4.29−4.34 (m, 2H), 6.35 (d, J = 16.8 Hz, 1H), 6.82−6.85 (m, 2H), 7.00−7.14 (m, 7H), 9.04 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3 (d, J = 5.3 Hz, 1C), 16.5 (d, J = 5.5 Hz, 1C), 20.9, 64.3 (d, J = 8.0 Hz, 1C), 65.0 (d, J = 7.2 Hz, 1C), 70.2 (d, J = 158.3 Hz, 1C), 89.1 (d, J = 2.1 Hz, 1C), 126.2 (d, J = 4.0 Hz, 1C), 127.1 (d, J = 4.8 Hz, 1C), 127.8 (d, J = 13.8 Hz, 1C), 128.6 (d, J = 1.5 Hz, 1C), 128.9, 133.4 (d, J = 7.5 Hz, 1C), 137.9 (d, J = 2.2 Hz, 1C), 189.2 (d, J = 4.6 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 18.24; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NNaO_4PS$ $[M+Na]^+$: 428.1056; found: 428.1069.

Diethyl (4*R*,5*R*)-4-(4-Methoxyphenyl)-5-phenyl-2-thioxooxazolidin-4-ylphosphonate (3p). White solid, 60.7 mg, yield 36%; dr 92:8, 81% ee, $[\alpha]_D^{20}$ = −31.5 (*c* 1.10, $CHCl_3$); mp 52.9−54.5 °C. HPLC analysis Chiralpak AD-H (80/20 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 8.22 min, t_{minor} = 10.00 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.14 (t, J = 6.9 Hz, 3H), 1.46 (t, J = 6.9 Hz, 3H), 3.67 (s, 3H), 3.83−3.88 (m, 1H), 4.06−4.11 (m, 1H), 4.28−4.35 (m, 2H), 6.33 (d, J = 16.5 Hz, 1H), 6.56 (d, J = 8.7 Hz, 2H), 6.99−7.03 (m, 2H), 7.08−7.15 (m, 5H), 8.87 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3 (d, J = 5.3 Hz, 1C), 16.5 (d, J = 5.5 Hz, 1C), 55.1, 64.2 (d, J = 8.0 Hz, 1C), 65.1 (d, J = 7.2 Hz, 1C), 69.8 (d, J = 159.3 Hz, 1C), 89.2 (d, J = 2.7 Hz, 1C), 113.3, 123.9 (d, J = 5.6 Hz, 1C), 127.7, 127.9, 128.6 (d, J = 4.9 Hz, 1C), 129.0, 133.3 (d, J = 7.0 Hz, 1C), 159.3, 189.2 (d, J = 5.0 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 18.26; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NNaO_5PS$ $[M+Na]^+$: 444.1005; found: 444.1000.

Diethyl (4*R*,5*R*)-4-(4-Fluorophenyl)-5-phenyl-2-thioxooxazolidin-4-ylphosphonate (3q). White solid, 140.8 mg, yield 86%; dr 93:7, 76% ee, $[\alpha]_D^{20}$ = −24.8 (*c* 1.01, $CHCl_3$); mp 47.7−49.0 °C.

HPLC analysis Chiralpak AD-H (85/15 hexane/*i*-PrOH; 1.0 mL/min; for major diastereoisomer: t_{major} = 7.12 min, t_{minor} = 10.09 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.19 (t, J = 6.9 Hz, 3H), 1.45 (t, J = 6.9 Hz, 3H), 3.96−4.00 (m, 1H), 4.13−4.19 (m, 1H), 4.30−4.37 (m, 2H), 6.32 (d, J = 16.8 Hz, 1H), 6.64−6.69 (m, 2H), 6.96−6.99 (m, 2H), 7.06−7.16(m, 5H), 9.88 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 16.3 (d, J = 7.1 Hz, 1C), 16.5 (d, J = 7.3 Hz, 1C), 64.3 (d, J = 7.9 Hz, 1C), 65.2 (d, J = 7.3 Hz, 1C), 69.9 (d, J = 159.7 Hz, 1C), 88.9, 114.7 (d, J = 21.4 Hz, 1C), 127.6, 128.0, 129.1, 129.2 (d, J = 3.5 Hz, 1C), 129.3, 133.2 (d, J = 7.4 Hz, 1C), 162.2 (d, J = 247.5 Hz, 1C), 189.1 (d, J = 4.5 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 17.95; HRMS (ESI-TOF) calcd for $C_{19}H_{21}FNNaO_4PS$ $[M+Na]^+$: 432.0805; found: 432.0821.

Diisopropyl (4*R*,5*R*)-5-(4-Nitrophenyl)-4-phenyl-2-thioxooxazolidin-4-ylphosphonate (3s). Gray solid, 144.9 mg, yield 78%; dr 98:2, 73% ee, $[\alpha]_D^{20}$ = −46.5 (*c* 1.15, $CHCl_3$); mp 172.1−173.5 °C. HPLC analysis Chiralpak AS-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 5.81 min, t_{minor} = 8.56 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.80 (d, J = 6.0 Hz, 3H), 1.31 (d, J = 6.0 Hz, 3H), 1.49 (d, J = 6.0 Hz, 6H), 4.48−4.57 (m, 1H), 4.88−4.98 (m, 1H), 6.42 (d, J = 16.5 Hz, 1H), 7.05−7.14 (m, 3H), 7.22−7.26 (m, 4H), 7.95 (d, J = 8.7 Hz, 2H), 8.88 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 22.9 (d, J = 6.2 Hz, 1C), 24.1 (d, J = 5.1 Hz, 1C), 24.2, 24.5 (d, J = 2.3 Hz, 1C), 70.2 (d, J = 160.7 Hz, 1C), 73.7 (d, J = 8.2 Hz, 1C), 74.7 (d, J = 7.4 Hz, 1C), 87.7 (d, J = 2.6 Hz, 1C), 123.0, 127.1 (d, J = 4.8 Hz, 1C), 128.4 (d, J = 8.9 Hz, 1C), 128.8 (d, J = 1.7 Hz, 1C), 131.9 (d, J = 6.2 Hz, 1C), 140.5 (d, J = 6.5 Hz, 1C), 147.9, 188.7 (d, J = 5.0 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 15.58; HRMS (ESI-TOF) calcd for $C_{21}H_{25}N_2NaO_6PS$ $[M+Na]^+$: 487.1063; found: 487.1051.

Experimental Procedure for the Synthesis of 4a. To a mixture of **3a** (100 mg, 0.26 mmol) and anhydrous K_2CO_3 (43.7 mg, 0.32 mmol) in 12.0 mL of acetone was added CH_3I (45.0 mg, 0.32 mmol) at 0 °C. Then the reaction was stirred at room temperature overnight and then concentrated in vacuo. The residue mixture was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 4:1) to give compound **4a**.

Diethyl (4*R*,5*R*)-2-(Methylthio)-4,5-diphenyl-4,5-dihydrooxazol-4-ylphosphonate (4a). Colorless oil, 98.0 mg, yield 95%; dr >99:1, >99% ee, $[\alpha]_D^{20}$ = −24.0 (*c* 2.08, $CHCl_3$). HPLC analysis Chiralpak AD-H (90/10 hexane/ethanol; 1.0 mL/min; for major diastereoisomer: t_{major} = 4.18 min, t_{minor} = 5.50 min); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.10 (t, J = 6.9 Hz, 3H), 1.36 (t, J = 6.9 Hz, 3H), 2.64 (s, 3H), 3.79−3.82 (m, 1H), 3.97−4.03 (m, 1H), 4.21−4.27 (m, 2H), 6.25 (d, J = 18.9 Hz, 1H), 6.93−6.96 (m, 2H), 6.98−7.01 (m, 3H), 7.04−7.06 (m, 3H), 7.25−7.28(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 14.5, 16.1 (d, J = 5.2 Hz, 1C), 16.3 (d, J = 5.8 Hz, 1C), 63.4 (d, J = 7.9 Hz, 1C), 64.1 (d, J = 7.3 Hz, 1C), 80.2 (d, J = 158.9 Hz, 1C), 88.7 (d, J = 4.7 Hz, 1C), 126.9 (d, J = 2.5 Hz, 1C), 127.1 (d, J = 2.0 Hz, 1C), 127.6 (d, J = 2.7 Hz, 1C), 128.1, 128.2, 135.1, 135.6 (d, J = 10.1 Hz, 1C), 167.9 (d, J = 11.2 Hz, 1C); ^{31}P NMR (121 MHz, $CDCl_3$), δ (ppm): 21.11; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NNaO_4PS$ $[M+Na]^+$: 428.1056; found: 428.1070.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, characterization data for new compounds, X-ray crystal structure and the CIF file of **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: yuanwc@cioc.ac.cn.

Notes

The authors declare no competing financial interest.

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