JOC The Journal of Organic Chemistry

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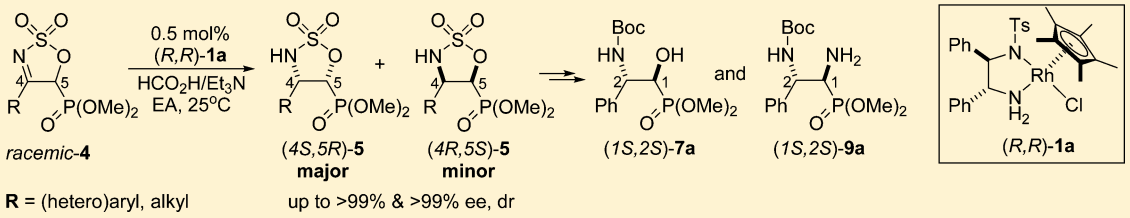
Stereoselective Synthesis of 4-Substituted Cyclic Sulfamidate-5-Phosphonates by Using Rh-Catalyzed, Asymmetric Transfer Hydrogenation with Accompanying Dynamic Kinetic Resolution

Yeon Ji Seo,[†,‡,§] Jin-ah Kim,[†,§] and Hyeon-Kyu Lee*[,†,‡]

[†]Korea Chemical Bank, Korea Research Institute of Chemical Technology, P.O. Box 107, Yuseong, Daejeon 305-600, Korea

[‡]Department of Medicinal Chemistry and Pharmacology, University of Science and Technology, 113 Gwahango, Yuseong, Daejeon 305-333, Korea

Supporting Information



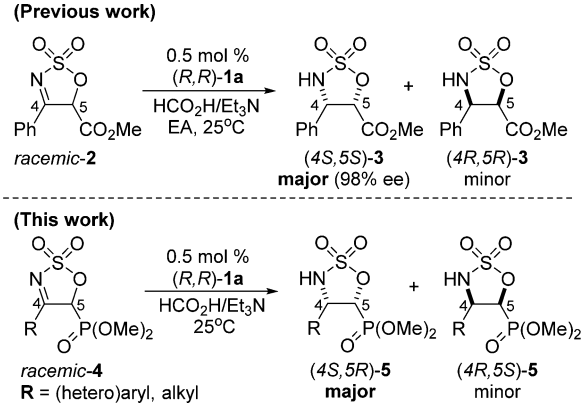
ABSTRACT: Dynamic kinetic resolution driven, asymmetric transfer hydrogenation of 4-substituted cyclic sulfamidate imine-5-phosphonates produces the corresponding cyclic sulfamidate-5-phosphonates. The process employs a HCO_2H/Et_3N mixture as the hydrogen source and the chiral Rh catalysts, (*R*,*R*)- or (*S*,*S*)-Cp*RhCl(TsDPEN), and it takes place at room temperature within 1 h with high yields and high levels of stereoselectivity.

Enantiomerically enriched *β*-amino-*α*-hydroxy phosphonates, which are isosteres of the corresponding *β*-amino-*α*-hydroxy carboxylates, have attracted great interest because of their wide range of biological activities.[1−5] These substances are also potentially important intermediates in the synthesis of renin inhibitors, HIV protease inhibitors, and haptens in the development of catalytic antibodies.[2,4] Although a number of methods have been described for the preparation of *β*-amino-*α*-hydroxy phosphonates,[1,2,6] most procedures targeted at enantiomerically enriched members of this family require the use of stoichiometric amounts of chiral starting materials such as chiral amino acids, amino aldehydes,[7] or aziridines.[3] Thus far, only a few catalytic asymmetric methods have been described to prepare these substances, one of which is Sharpless asymmetric aminohydroxylation (AA) of unsaturated phosphonates.[5,8] However, Sharpless AA of aryl-substituted unsaturated phosphonates proceeds in low yields (21−53%) and with variable levels of stereoselectivity (32−98% ee).[5]

Recently we described a new procedure for asymmetric transfer hydrogenation (ATH) of prochiral cyclic sulfamidate imines that uses HCO_2H/Et_3N as the hydrogen source and well-defined chiral Rh catalysts (Scheme 1).[9−11] In this early effort, we showed that ATH of the 4,5-disubstituted cyclic sulfamidate imine **2**, possessing a configurationally labile stereogenic C-5 center, is accompanied by dynamic kinetic resolution (DKR). It was also observed that DKR is caused by rapid racemization at the acidic stereogenic C-5 position under the reaction conditions.

We envisioned that introduction of a phosphonate group at C-5 of the 4,5-disubstituted cyclic sulfamidate imine framework would enhance the acidity of H-5 and, as a result, would promote high levels of stereoselectivity in the ATH−DKR reaction. Importantly, the cyclic sulfamidate-5-phosphonates **5** (Scheme 1) produced in these reactions could be potentially valuable intermediates in the synthesis of various chiral *β*-amino-*α*-hydroxy phosphonic acid derivatives. Below, we describe the results of a study guided by these proposals, which led to the development of a highly efficient ATH reaction of cyclic imine-5-phosphonates **4** that is accompanied by DKR and the application of this process

Scheme 1. Stereoselective Synthesis of 4,5-Disubstituted Cyclic Sulfamidates 3 and 5



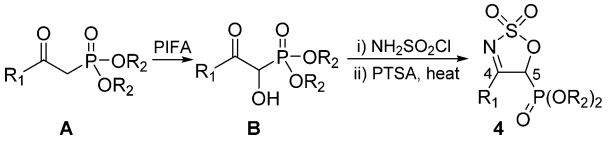
Received: June 24, 2015
Published: August 17, 2015

DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887−8902

to the preparation of stereochemically enriched, chiral cyclic sulfamidate-5-phosphonates **5**.

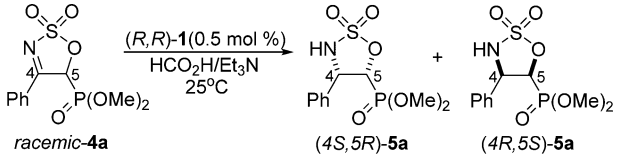
The racemic cyclic imine-5-phosphonates **4** used in this study were prepared from α-hydroxy-β-keto phosphonates (B) and sulfamoyl chloride using a modification of a previously described procedure (Scheme 2).[12]

Scheme 2. Synthesis of 4-Substituted Sulfamidate Imine-5-phosphonates 4



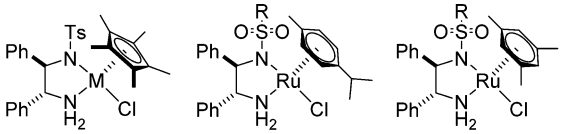
In initial studies aimed at identifying ideal catalyst systems for the ATH of these substrates, reaction of racemic 4-phenyl-cyclic imine-5-phosphonate dimethyl ester (**4a**) was carried out at rt using known chiral transition metal catalysts **1a**–**e** (0.5 mol %), HCO_2H/Et_3N (F/T = 5:2), as the hydrogen source and EtOAc as solvent. The results (Table 1) show that ATH reactions of **4a**

Table 1. Optimization of Chiral Catalysts 1 for ATH–DKR Reactions of 4a[a]



entry	cat-1	conv[b] (%)	dr[c] *syn*:*anti*	ee[d] (%)
1	(*R*,*R*)-**1a**	>99	>25:1	98
2	(*S*,*S*)-**1a**	>99	>25:1	97
3	(*R*,*R*)-**1b**	>99	>25:1	39
4	(*R*,*R*)-**1c**	>99	>25:1	96
5	(*R*,*R*)-**1d**	>99	>25:1	92
6	(*R*,*R*)-**1e**	>99	>25:1	94

[a]Reaction conditions: **4a** (0.5 mmol), **cat-1** (0.5 mol %), HCO_2H/Et_3N (F/*T* = 5:2, 0.5 mL), EtOAc (5 mL), at 25 °C. [b]Determined by using ^{1}H NMR analysis of crude product mixture. [c]Only 4,5-*cis* products were detected by using ^{1}H NMR analysis of crude product mixtures. [d]Determined by using chiral HPLC analysis.



(*R*,*R*)-**1a**: M=Rh
(*R*,*R*)-**1b**: M=Ir
(*R*,*R*)-**1c**: R= *p*-Tolyl
(*R*,*R*)-**1d**: R= F_5Ph
(*R*,*R*)-**1e**: R= *p*-Tolyl

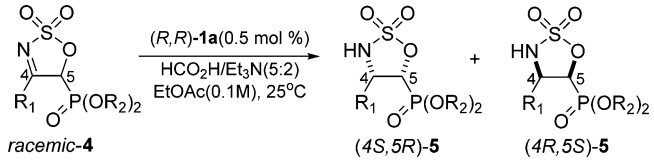
promoted by most of the chiral transition-metal catalysts, except Ir complex **1b**,[13] proceed rapidly and with high stereoselectivities. On the basis of the observation that the Rh catalyst (*R*,*R*)-**1a**[14] displayed the highest stereoselectivity (98% ee), it was used in further exploratory reactions. The influence of solvent on the ATH reaction of **4a** promoted by (*R*,*R*)-**1a** was investigated next (see the Supporting Information). In most of the solvents tested (EtOAc, CH_2Cl_2, $Cl(CH_2)_2Cl$, $CHCl_3$, toluene, DMF, MeOH, THF, and 2-propanol), ATH of **4a** takes place completely to form (4*S*,5*R*)-**5a** with high levels of stereoselectivity (>25:1 dr, 89–98% ee). For experimental convenience, all further ATH reactions were carried out in EtOAc as solvent.

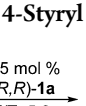
The scope and limitations of the ATH–DKR reaction were explored using a variety of cyclic sulfamidate imine 5-phosphonates **4** and optimized conditions involving (*R*,*R*)-**1a** (0.5 mol %) as the catalyst, a 5:2 mixture of HCO_2H/Et_3N as the hydrogen source, and EtOAc (25 °C) as the solvent. The results (Table 2) show that ATH reactions of **4a** catalyzed by (*R*,*R*)-**1a** under the optimized reaction conditions produce a mixture of stereoisomeric 4,5-*cis* sulfamidate 5-phosphonates in which the (4*S*,5*R*)-**5a** isomer predominates (98% ee, 99% yield, Table 2, entry 1). In a manner that is similar to our previous findings[9] for ATH of 4-substituted cyclic sulfamidate imine-5-carboxylates (**2**, Scheme 1), 4,5-*trans* sulfamidate 5-phosphonates are not detected (by using ^{1}H NMR analysis) in reactions of **4a**. ATH of 4-phenyl cyclic imine 5-phosphonate diethyl ester (**4b**) also produces the corresponding cyclic sulfamidates **5b** with excellent efficiency and stereoselectivity. The results also show that most of the ATH reactions of 4-aryl-5-phosphonate cyclic imine dimethyl esters take place completely at rt in short time periods. For example, ATH–DKR of cyclic sulfamidate imines possessing either electron-withdrawing or electron-donating groups at the *meta*- or *para*-position on the phenyl ring afford the corresponding sulfamidates in uniformly high yields and stereoselectivites. However, the ATH reaction of the cyclic imine **4i** containing an *ortho*-substituted phenyl group occurs slowly (50% conversion, 24 h). Because the HCO_2H/Et_3N (F/T) ratio is known to have a significant effect on both rates and enantioselectivities of ATH reactions,[15,16] a 1:1 instead of 5:2 mixture of F/T was employed as the hydrogen source. Under these conditions, ATH of **4i** is complete in 1 h (81% ee) (Table 2, entries 10 and 11). That cyclic imines containing heteroaromatic moieties are also suitable substrates for the ATH–DKR reaction was demonstrated by the finding that with respective furan and thiophene **4m** and **4n** derivatives participate in the process (Table 2, entries 15 and 17). As in the reaction of **4i**, employing a 1:1 instead of 5:2 mixture of F/T as the hydrogen source led to ATH reactions of **4m** and **4n** that are complete within 1 h and that take place with improved stereoselectivities (93 to 97% ee for **5m** and 97 to 99% ee for **5n**, Table 2, entries 15–18). Importantly, ATH reaction of **4g** under the optimized conditions, except using (*S*,*S*)-**1a** as the catalyst, produces the antipodal sulfamidate (4*R*,5*S*)-**5g** with an efficiency and stereoselectivity (98% ee, 97% yield) that match those associated with the reaction promoted by (*R*,*R*)-**1a** (Table 2, entry 8). We also observed that the catalyst loading can be reduced to 0.1 mol % (S/C = 1000) in the ATH–DKR reaction of **4a**, which requires a longer time (3 h) for completion but has a high efficiency and product enantiomeric purity (95% yield, 96% ee).

ATH reactions of 4-alkyl-substituted cyclic sulfamidate imine 5-phosphonates were explored. The results show that the efficiencies and stereoselectivities of the ATH–DKR reactions of these substrates are sensitive to the steric bulkiness of the 4-alkyl group. For example, ATH reaction of less hindered 4-phenethyl cyclic imine **4o** under the optimized conditions is completed in 0.5 h with an excellent level of stereoselectivity (97% ee, Table 2, entry 19) but that of the 4-isobutyl-cyclic imine **4p** requires 12 h for completion and occurs with a decreased level of stereoselectivity (75% ee, Table 2, entry 20). However, ATH reaction of sterically more demanding 4-alkyl cyclic imines such as 4-isopropyl **4q**, 4-cyclohexyl **4r**, and 4-*tert*-butyl **4s** is more sluggish, resulting in only 35–39% conversions even after 24 h (Table 2, entries 21–23). Since it is known that an attractive interaction between the arene ligand of the catalyst and the aryl substrate is of great importance in the favored transition state,[17]

DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887–8902

Table 2. ATH Reactions of 4-Substituted Cyclic Sulfamidate Imine-5-phosphonates 4[a]



entry	substrate 4,5	substrate R1	substrate R2	time (h)	conv (%)[b]	ee(*syn*) (%)[c]	conf.[d]
1	**a**		Me	0.5	>99(99)	98	*4S,5R*
2	**b**		Et	0.5	>99(96)	98[e]	*4S,5R*[f]
3	**c**		Me	0.5	>99(94)	96[g]	*4S,5R*
4	**d**		Me	0.5	>99(99)	97	*4S,5R*
5	**e**		Me	1.0	>99(95)	96	*4S,5R*
6	**f**		Me	1.5	>99(91)	94[h]	*4S,5R*
7	**g**		Me	1.0	>99(96)	97	*4S,5R*
8[i]	**g**		Me	1.0	>99(97)	98	*4R,5S*[i]
9	**h**		Me	0.5	>99(94)	97	*4S,5R*
10	**i**		Me	24	50	42	-
11	**i**		Me	1.0[j]	>99(95)[j]	81	-
12	**j**		Me	0.5	>99(95)	>99	*4S,5R*
13	**k**		Me	0.5	>99(93)	99	*4S,5R*[f]
14	**l**		Me	0.5	>99(97)	97	*4S,5R*
15	**m**		Me	1.5	>99(90)	93[k]	*4S,5R*
16	**m**		Me	1.0[j]	>99(90)[j]	97[k]	*4S,5R*
17	**n**		Me	2.0	>99(94)	97	*4S,5R*
18[i]	**n**		Me	1.0[j]	>99(90)[j]	99	*4S,5R*
19	**o**		Me	0.5	>99(99)	97	*4S,5R*[f]
20	**p**		Me	12[j]	>99(50)[j]	75[l]	ND[m]
21	**q**		Me	24[j]	39[j]	-	ND[m]
22	**r**		Me	30[j]	35[j]	-	ND[m]
23	**s**		Me	24[j]	35[j]	-	ND[m]

[a]Reaction conditions: **4** (0.5 mmol), (*R,R*)-**1a** (0.5 mol %), HCO_2H/Et_3N (5:2, 0.5 mL), EtOAc (5 mL), rt. [b]Determined by ^1H NMR analysis of the crude products (isolated yields in parentheses). [c]Determined by using chiral HPLC. Only 4,5-*cis* products were detected in ^1H NMR of crude products. [d]Absolute configurations of *N*-Boc-**5b**, **5k**, and **5o** were determined by using X-ray crystallographic analysis, and absolute configurations of the other products were determined by analogy to *N*-Boc-**5b**, **5k**, and **5o**. [e]ee of *N*-Boc-**5b**. [f]Determined by using X-ray crystallographic analysis (see the Supporting Information). [g]ee of *N*-Boc-**5c**. [h]ee of *N*-Boc-**5f**. [i](*S,S*)-**1a** (0.5 mol %) was used as catalyst. [j]1:1 mixture of HCO_2H/Et_3N was used as the hydrogen source. [k]ee of *N*-Boc-**5m**. [l]ee of ring-opened derivative derived from **5p** (see the Supporting Information). [m]ND: not determined.

low reactivity of 4-alkyl substrates which are absent from such attractive interaction in the transition state is not surprising.

Next, the scope of the process was explored by employing the 4-styryl-substituted cyclic imine-5-phosphonate dimethyl ester **4t** as the substrate (Scheme 3). ATH reaction of **4t** under the optimized reaction conditions using (*R,R*)-**1a** as the catalyst generates **5t** as the expected C=N reduction product with high enantiomeric purity (99% ee) along with the both C=N and C=C reduction product (4*S*,5*R*)-**5o** (94% ee) (**5t**:**5o** = 1:1). When **5t** is subjected to the same ATH reaction conditions, the unconjugated C=C bond does not undergo reduction. It is well-known that transfer hydrogenations promoted by Noyori-type diamine−transition-metal complexes are highly chemoselective, with C=O reduction being favored over C=C reduction.[18,19] However, it was reported recently that the use of Ru- or Rh-amido catalysts causes reversal of the typical C=O over C=C reduction selectivities in ATH reactions of α,β-unsaturated carbonyl compounds when the C=C double bond is activated by electron-withdrawing substituents or the reaction is performed in an aqueous medium.[20,21] Similar to the known transfer hydrogenation of substrates containing a C=C bond conjugated to C=O group with the Rh-amido catalysts,[20] the C=C bond conjugated to C=N group in **4t** is reduced under the ATH reaction conditions to produce **4o**, which is rapidly reduced to form **5o** (see entry 19 in Table 2 and Scheme 3).

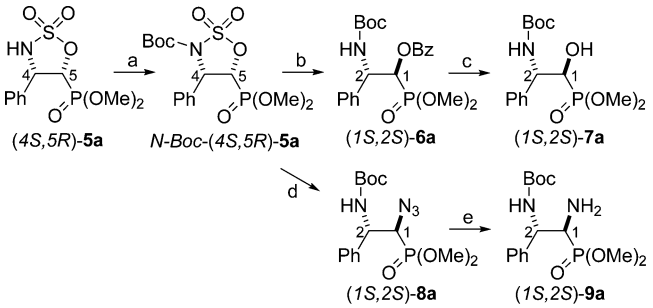
The cyclic sulfamidate-5-phosphonates **5** produced in these ATH reactions are valuable intermediates[22] in the synthesis of various chiral β-amino-α-hydroxy phosphonic acid derivatives and 1,2-functionalized aminophosphonic acid derivatives.

Scheme 3. ATH of 4-Styryl Cyclic Imine-5-phosphonate 4t

DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887−8902

In order to demonstrate the utility of the methodology developed in this study, the 4-phenyl cyclic sulfamidate-5-phosphonate **5a** was transformed to the corresponding 2-amino-1-hydroxy phosphonate **7a** and monoprotected 1,2-diamino phosphonate **9a** (Scheme 4). Treatment of *N*-Boc-**5a** with $PhCO_2H$ in the presence of CsF leads to smooth formation of the ring-opened product, *O*-benzoyl-*N*-Boc-**6a**, with inversion of configuration at C-1.[23] Selective removal of the *O*-benzoyl group in **6a** using KCN[12] in MeOH produces 2-(*N*-Boc-amino)-1-hydroxyphosphonate **7a**. Similarly, ring opening of *N*-Boc-**5a** with NaN_3 produces **8a**, which upon subsequent hydrogenation forms the monoprotected 1,2-diaminophosphonate **9a** (Scheme 4).

Scheme 4. Conversion of Cyclic Sulfamidate 5a to 1,2-Functionalized Phosphonates 7a and 9a[a]



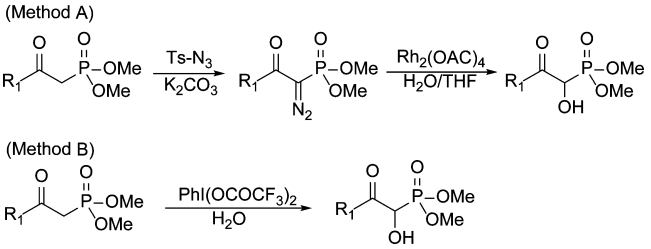
[a]Reaction conditions: (a) $(Boc)_2O$, Et_3N, cat. DMAP, CH_2Cl_2, 71%; (b) $PhCO_2H$, CsF, DMF, 60 °C, 3 h, 89%; (c) KCN, MeOH, rt, 3 h, 64%; (d) NaN_3, DMF, rt, 70%; (e) H_2, Pd/C, MeOH, rt, 12 h, 60%.

In summary, a convenient and highly stereoselective methodology for the preparation of 4-substituted cyclic sulfamidate 5-phosphonate esters **5** has been developed. This process, involving asymmetric transfer hydrogenation accompanied by dynamic kinetic resolution (ATH−DKR), uses HCO_2H/Et_3N as the hydrogen source and the well-defined chiral Rh catalysts (*S,S*)- or (*R,R*)-Cp*RhCl(TsDPEN). Most of the 4-substituted cyclic sulfamidate imine 5-phosphonate esters **4** probed in the effort undergo efficient and highly stereoselective ATH−DKR reactions rapidly (within 1 h) under mild and experimentally convenient conditions (room temperature, without the need for solvent degassing or an inert atmosphere).

EXPERIMENTAL SECTION

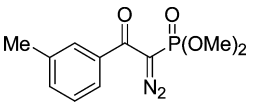
General Methods. All commercial reagents were used as obtained unless otherwise noted. Reactions were performed using oven-dried glassware under an atmosphere of nitrogen. Dichloromethane (DCM), ether, and THF were dried and purified using a solvent purification system. Flash column chromatography was carried out on silica gel (38−75 μm). Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} plates. Preparative thin-layer chromatography (PLC) was performed on silica gel 60 F_{254} 2 mm plates. Visualization of the developed chromatogram was accomplished with UV light and by staining with ethanolic phosphomolybdic acid (PMA) solution or ninhydrin solution followed by heating. Nuclear magnetic resonance (NMR) spectra were recorded using 500 MHz NMR instrument (^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz) or 300 MHz NMR instrument (^{1}H NMR at 300 MHz and ^{13}C NMR at 75 MHz). ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constants (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High-performance liquid chromatography (HPLC) was carried out on an HPLC system equipped with a Chiralpak IA, Chiralpak IB, Chiralpak IC, Chiralpak ID, Chiralpak AD-H, or Chiralpak OD-H column. HR-MS were measured with electron impact (EI) ionization via a double-focusing mass analyzer (magnetic and electric fields) or electrospray ionization (ESI) via time of flight (TOF) analyzer. The formic acid/triethylamine mixtures (molar ratio = 5:2 or 1:1) are commercially available. (*R,R*)-**1a**[14] and (*R,R*)-**1b**[13] were prepared according to the literature procedures. Chiral catalysts (*R,R*)-**1c**, (*R,R*)-**1d**, and (*R,R*)-**1e** are commercially available.

1. Synthesis of α-Hydroxy-β-keto Phosphonates.



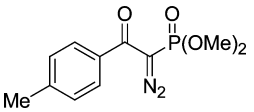
1.1. Synthesis of α-Diazo-β-keto Phosphonates. α-Diazo-β-keto phosphonates were prepared from the corresponding β-keto phosphonates[24] following the reported procedures.[25]

(1-Diazo-2-oxo-2-m-tolylethyl)phosphonic Acid Dimethyl Ester.



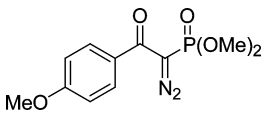
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:3): yield 79% (0.87 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.44 (m, 2H), 7.31−7.32 (m, 2H), 3.81 (s, 3H), 3.79(s, 3H), 2.37(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.5 (d, J_{CP} = 8.8 Hz), 138.7, 136.7 (d, J_{CP} = 3.2 Hz), 133.2, 128.5, 127.9, 124.3, 62.7 (d, J_{CP} = 217.2 Hz), 54.1, 54.0, 21.3; HRMS (EI) *m/z* calcd for $C_{11}H_{13}N_2O_4P$ 268.0613, found 268.0602.

(1-Diazo-2-oxo-2-p-tolylethyl)phosphonic Acid Dimethyl Ester.



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1 to 1:2): yield 71.6% (3.17 g as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57−7.60 (m, 2H), 7.27−7.28 (m, 2H), 3.86 (s, 3H), 3.82 (s, 3H), 2.41(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.0 (d, J_{CP} = 8.9 Hz), 143.3, 134.0 (d, J_{CP} = 3.5 Hz), 129.3, 127.5, 64.2 (d, J_{CP} = 217.0 Hz), 54.0, 53.9, 21.6; HRMS (EI) *m/z* calcd for $C_{11}H_{13}N_2O_4P$ 268.0613, found 268.0611.

[1-Diazo-2-(4-methoxyphenyl)-2-oxoethyl]phosphonic Acid Dimethyl Ester.



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2): yield 92% (0.92 g as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, 2H, *J* = 8.5 Hz), 6.82 (d, 2H, *J* = 8.6 Hz), 3.73 (s, 6H), 3.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.7 (d, J_{CP} = 9.2 Hz), 163.0, 129.7, 129.1 (d, J_{CP} = 2.8 Hz), 113.8, 62.0 (d, J_{CP} = 216.5 Hz), 55.4, 54.0, 53.8; HRMS (EI) *m/z* calcd for $C_{11}H_{13}N_2O_5P$ 284.0562, found 284.0554.

DOI: 10.1021/acs.joc.5b01434
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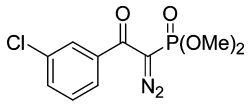
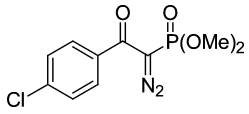
[2-(3-Chlorophenyl)-1-diazo-2-oxoethyl]phosphonic Acid Dimethyl Ester.



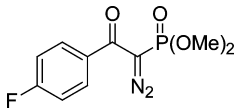
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1 to 1:3): yield 73% (1.6 g as a yellow oil), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.646−7.653 (m, 1H), 7.50−7.55 (m, 2H), 7.37−7.41 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.9 (d, J_{CP} = 10.0 Hz), 138.3, 134.8, 132.4, 129.9, 127.6, 125.4, 63.8 (d, J_{CP} = 217.9 Hz), 54.1, 54.0; HRMS (EI) *m*/*z* calcd for $C_{10}H_{10}ClN_2O_4P$ 288.0067, found 288.0064.

[2-(4-Chlorophenyl)-1-diazo-2-oxoethyl]phosphonic Acid Dimethyl Ester.



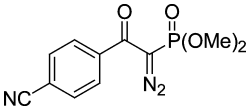
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1 to 1:3): yield 69.2% (3.03 g as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62−7.66 (m, 2H), 7.42−7.46 (m, 2H), 3.84 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.0 (d, J_{CP} = 9.9 Hz), 138.8, 135.06, 135.04, 128.9, 63.5 (d, J_{CP} = 217.0 Hz), 54.0, 53.9; HRMS (EI) *m*/*z* calcd for $C_{10}H_{10}ClN_2O_4P$ 288.0067, found 288.0065.

[1-Diazo-2-(4-fluorophenyl)-2-oxoethyl]phosphonic Acid Dimethyl Ester.



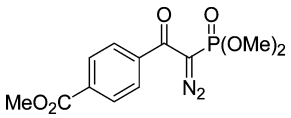
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1 to 1:3): yield 74% (0.81 g as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71−7.76 (m, 2H), 7.12−7.18 (m, 2H), 3.84 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.9 (d, J_{CP} = 9.8 Hz), 165.1 (d, J_{CF} = 252.5 Hz), 133.0 (d, J_{CF} = 5.6 Hz), 130.1 (d, J_{CF} = 9.0 Hz), 115.8 (d, J_{CF} = 21.9 Hz), 63.3 (d, J_{CP} = 218.6 Hz), 54.0, 54.0; HRMS (EI) *m*/*z* calcd for $C_{10}H_{10}FN_2O_4P$ 272.0362, found 272.0361.

[2-(4-Cyanophenyl)-1-diazo-2-oxoethyl]phosphonic Acid Dimethyl Ester.



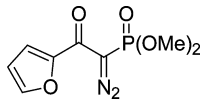
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1 to 1:2): yield 50% (1.0 g as a yellow oil), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77−7.78 (m, 4H), 3.82 (d, 3H, *J* = 1.9 Hz), 3.79 (d, 3H, *J* = 1.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.8 (d, J_{CP} = 10.8 Hz), 140.4, 132.3, 128.0, 117.7, 115.8, 64.8 (d, J_{CP} = 217.6 Hz), 54.1, 54.0; HRMS (EI) *m*/*z* calcd for $C_{11}H_{10}N_3O_4P$ 279.0409, found 279.0410.

[1-Diazo-2-(4-methoxycarbonylphenyl)-2-oxoethyl]phosphonic Acid Dimethyl Ester.



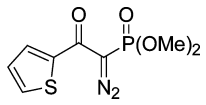
Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 10:1): yield 67% (1.83 g as a yellow oil), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, 2H, *J* = 8.5 Hz), 7.72 (d, 2H, *J* = 8.4 Hz), 3.95(s, 3H), 3.82 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.8 (d, J_{CP} = 9.9 Hz), 166.0, 140.5, 133.4, 129.8, 127.3, 62.5(d, J_{CP} = 188.6 Hz), 54.1, 54.0, 52.5; HRMS (EI) *m*/*z* calcd for $C_{12}H_{13}N_2O_6P$ 312.0511, found 312.0506.

(1-Diazo-2-furan-2-yl-2-oxoethyl)phosphonic Acid Dimethyl Ester.



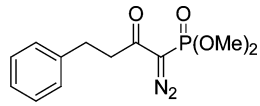
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:3 to 1:4): yield 84.2% (1.9 g as a dark-brown oil), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.57 (m, 1H), 7.26−7.28 (m, 1H), 6.58−6.60 (dd, 1H, *J* = 1.74, 3.63 Hz), 3.91 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (d, J_{CP} = 8.2 Hz), 151.5, 145.3, 117.4, 112.6, 61.0 (d, J_{CP} = 236.4 Hz), 54.3, 54.2; HRMS (EI) *m*/*z* calcd for $C_8H_9N_2O_5P$ 244.0249, found 244.0258.

(1-Diazo-2-oxo-2-thiophene-2-yl-ethyl)phosphonic Acid Dimethyl Ester.



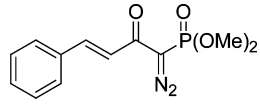
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:4): yield 62.8% (1.08 g as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75−7.76 (m, 1H), 7.66−7.67 (m, 1H), 7.12−7.14 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2 (d, J_{CP} = 9.7 Hz), 141.5(d, J_{CP} = 2.3 Hz), 133.5, 131.1, 128.0, 62.5 (d, J_{CP} = 216.6 Hz), 54.1, 54.1; HRMS (EI) *m*/*z* calcd for $C_8H_9N_2O_4PS$ 260.0021, found 260.0019.

(1-Diazo-2-oxo-4-phenylbutyl)phosphonic Acid Dimethyl Ester.



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 2:1): yield 63% (0.73 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26−7.29 (m, 2H), 7.18−7.20 (m, 3H), 3.77 (s, 3H), 3.74 (s, 3H), 2.94−2.97 (m, 2H), 2.83−2.76 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.7 (d, J_{CP} = 13.1 Hz), 140.5, 128.5, 128.4, 126.3, 63.5 (d, J_{CP} = 220.1 Hz), 53.56, 53.52, 40.9, 30.3; HRMS (EI) *m*/*z* calcd for $C_{12}H_{15}N_2O_4P$ 282.0769, found 282.0792.

(1-Diazo-2-oxo-4-phenylbut-3-enyl)phosphonic Acid Dimethyl Ester.



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1): yield 68.8% (2.27 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, 1H, *J* = 15.5 Hz), 7.58−7.60 (m, 2H), 7.41−7.42 (m, 3H), 7.12−7.15 (d, 1H, *J* = 15.5 Hz), 3.90 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.8 (d, J_{CP} = 13.0 Hz), 143.2, 134.2, 130.8, 129.0, 128.6, 120.8, 64.2 (d, J_{CP} = 213.9 Hz), 53.6, 53.6; HRMS (EI) *m*/*z* calcd for $C_{12}H_{13}N_2O_4P$ 280.0613, found 280.0614.

DOI: 10.1021/acs.joc.5b01434
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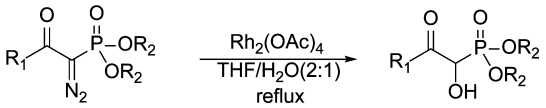
1.2. Synthesis of α-Hydroxy-β-keto Phosphonates. Method A.[26]

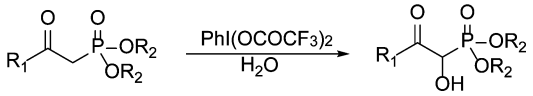
(Method A)



A solution of the diazo compound (1.0 equiv) in THF and H_2O (2:1 ratio) was refluxed with $Rh_2(OAc)_4$ (0.03 equiv) overnight and allowed to cool to room temperature. The mixture was concentrated in vacuo, and the aqueous residue was extracted with EtOAc (×3). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and evaporated to dryness. The residue was purified by chromatography to give the α-hydroxy-β-ketophosphonates.

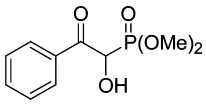
Method B.[27]

(Method B)



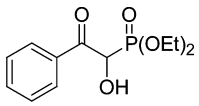
To a suspension of β-ketophosphonate in H_2O was added PIFA (2.0 equiv) portionwise within 10 min. The reaction mixture was stirred at room temperature until TLC indicated the total consumption of the β-ketophosphonate. The reaction mixture was treated with saturated $NaHCO_3$ (aq) and extracted with EtOAc (×3). The combined organic layers were washed with water and brine and dried over $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by chromatography to give the desired product.

(1-Hydroxy-2-oxo-2-phenylethyl)phosphonic Acid Diethyl Ester (Method B).



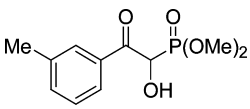
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:4): yield 59% (1.30 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δδ 8.02−8.03 (d, 2H, J = 7.35 Hz), 7.61−7.64 (m, 1H), 7.47−7.50 (m, 2H), 5.52−5.56 (d, 1H, J = 16.15 Hz), 3.69−3.73 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.0, 134.7, 133.5, 129.5, 128.6, 72.6 (d, J_{CP} = 149.8 Hz), 54.3 (d, J_{CP} = 7.1 Hz), 54.0 (d, J_{CP} = 7.1 Hz); HRMS(EI) m/z calcd for $C_{10}H_{13}O_5P$ 244.0501, found 244.0489

(1-Hydroxy-2-oxo-2-phenylethyl)phosphonic Acid Diethyl Ester (Method B).



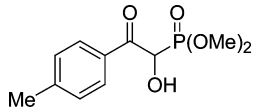
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:3): yield 37% (40 mg as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03−8.06 (m, 2H), 7.61−7.64 (m, 1H), 7.48−7.53 (m, 2H), 5.53 (d, 1H, J = 16.2 Hz), 4.03−4.19 (m, 4H), 1.17−1.27 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2 (d, J_{CP} = 2.0 Hz), 134.6, 133.8, 129.5, 128.5, 72.7 (d, J_{CP} = 149.8 Hz), 63.8 (d, J_{CP} = 7.1 Hz), 63.6 (d, J_{CP} = 7.2 Hz), 16.2 (d, J_{CP} = 6.0 Hz); HRMS (EI) m/z calcd for $C_{12}H_{17}O_5P$ 272.0814, found 272.0813.

(1-Hydroxy-2-oxo-2-m-tolylethyl)phosphonic Acid Dimethyl Ester (Method A).



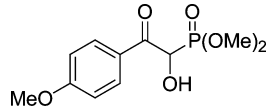
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:3): yield 57% (0.47 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83−7.86 (m, 2H), 7.45−7.46 (m, 1H), 7.38−7.41 (m, 1H), 5.55 (d, 1H, J = 16.1 Hz), 3.75 (d, 3H, J = 9.2 Hz), 3.73 (d, 3H, J = 9.1 Hz), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.1 (d, J_{CP} = 2.2 Hz), 138.7, 135.6, 133.6, 129.9, 128.6, 126.9, 72.6 (d, J_{CP} = 150.1 Hz), 54.4 (d, J_{CP} = 7.1 Hz), 54.2 (d, J_{CP} = 7.1 Hz), 21.4; HRMS (EI) m/z calcd for $C_{11}H_{15}O_5P$ 258.0657, found 258.0655.

(1-Hydroxy-2-oxo-2-p-tolylethyl)phosphonic Acid Dimethyl Ester (Method A).



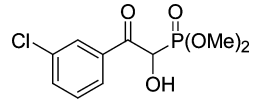
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:3): yield 67% (0.75 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, 2H, J = 8.3 Hz), 7.33 (d, 2H, J = 8.12 Hz), 5.56 (d, 1H, J = 15.7 Hz), 3.79 (d, 3H, J = 10.8 Hz), 3.74 (d, 3H, J = 10.8 Hz), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5 (d, J_{CP} = 2.4 Hz), 139.4, 134.1, 132.8, 131.9, 129.5, 125.5, 74.0 (d, J_{CP} = 152.7 Hz), 54.2 (d, J_{CP} = 7.0 Hz), 53.6 (d, J_{CP} = 7.0 Hz), 20.7; HRMS (EI) m/z calcd for $C_{11}H_{15}O_5P$ 258.0657, found 258.0646.

[2-(4-Methoxyphenyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method A).



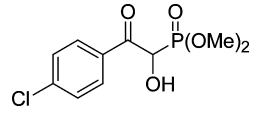
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:3): yield 44% (0.3 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, 2H, J = 9.0 Hz), 6.93 (d, 2H, J = 9.0 Hz), 5.48 (d, 1H, J = 15.2 Hz), 3.84 (s, 3H), 3.75 (d, 3H, J = 10.8 Hz), 3.67 (d, 3H, J = 10.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.7 (d, J_{CP} = 2.1 Hz), 164.8, 132.5, 126.2, 114.1, 72.0 (d, J_{CP} = 149.5 Hz), 55.6, 54.2 (d, J_{CP} = 7.1 Hz), 54.0 (d, J_{CP} = 7.1 Hz); HRMS (EI) m/z calcd for $C_{11}H_{15}O_6$ P 274.0606, found 274.0602.

[2-(3-Chlorophenyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method A).



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2): yield 99.2% (1.34 g as a yellow oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03−8.04 (m, 1H), 7.93−7.96 (m, 1H), 7.60−7.64 (m, 1H), 7.44−7.49 (m, 1H), 5.51 (d, 1H, J = 16.5 Hz), 3.79 (d, 3H, J = 11.0 Hz), 3.75 (d, 3H, J = 9.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0 (d, J_{CP} = 2.1 Hz), 135.1, 135.0, 134.6, 129.9, 129.3, 127.7, 72.8 (d, J_{CP} = 150.0 Hz), 54.4 (d, J_{CP} = 7.1 Hz), 54.2 (d, J_{CP} = 7.0 Hz); HRMS (EI) m/z calcd for $C_{10}H_{12}ClO_5P$ 278.0111, found 278.0100.

[2-(4-Chlorophenyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method A).



DOI: 10.1021/acs.joc.5b01434
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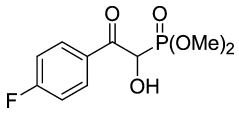
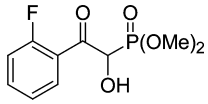
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2): yield 62% (1.2 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, 2H, J = 8.7 Hz), 7.49 (d, 2H, J = 8.7 Hz), 5.51 (d, 1H, J = 16.2 Hz), 3.80 (d, 3H, J = 10.9 Hz), 3.73 (d, 3H, J = 10.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 141.5, 131.7, 130.9, 129.1, 72.6 (d, J_{CP} = 149.6 Hz), 54.3 (d, J_{CP} = 7.2 Hz), 54.2 (d, J_{CP} = 7.2 Hz); HRMS (EI) m/z calcd for $C_{10}H_{12}ClO_5P$ 278.0111, found 278.0130.

[2-(4-Fluorophenyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method A).



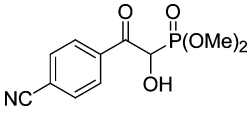
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2): yield 91% (0.7 g as a yellow solid), mp =101.4−102.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10−8.12 (m, 2H), 7.16−7.19 (m, 2H), 5.48−5.52 (dd, 1H, J = 5.4, 16.0 Hz), 4.15−4.16 (brs, 1H), 3.79 (d, 3H, J = 10.8 Hz), 3.71 (d, 3H, J = 10.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.3 (d, J_{CP} = 2.1 Hz), 166.7 (d, J_{CF} = 256.2 Hz), 132.4 (d, J_{CF} = 9.7 Hz), 129.8 (d, J_{CF} = 2.9 Hz), 115.9 (d, J_{CF} = 22.0 Hz), 72.5 (d, J_{CP} = 149.5 Hz), 54.3 (d, J_{CP} = 7.1 Hz), 54.1 (d, J_{CP} = 7.1 Hz); HRMS (EI) m/z calcd for $C_{10}H_{12}FO_5P$ 262.0406, found 262.0396.

[2-(2-Fluorophenyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method B).



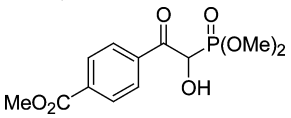
Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1): yield 42% (0.42 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90−7.93 (m, 1H), 7.60−7.94 (m, 1H), 7.28−7.31 (m, 1H), 7.18−7.21 (m, 1H), 5.65 (d, 1H, J = 18.7 Hz), 3.88−3.92 (brs, 1H), 3.77 (d, 3H, J = 10.7 Hz), 3.72 (d, 3H, J = 11.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.5, 162.0 (d, J_{CF} = 254.4 Hz), 136.1 (d, J_{CF} = 9.5 Hz), 131.0 (d, J_{CF} = 1.9 Hz), 124.7 (d, J_{CF} = 3.2 Hz), 122.9 (d, J_{CF} = 12.3 Hz), 116.6 (d, J_{CF} = 23.4 Hz), 75.8 (dd, J_{CP} = 10.7, 148.7 Hz), 54.4 (d, J_{CP} = 7.3 Hz), 53.9 (d, J_{CP} = 7.3 Hz) ; HRMS (EI) m/z calcd for $C_{10}H_{12}FO_5P$ 262.0406, found 262.0405.

[2-(4-Cyanophenyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method A).



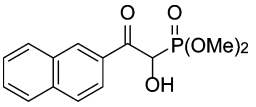
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:3): yield 56% (0.53 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, 2H, J = 8.0 Hz), 7.80 (d, 2H, J = 8.0 Hz), 5.54 (d, 1H, J = 17.2 Hz), 3.79 (d, 3H, J = 10.9 Hz), 3.73 (d, 3H, J = 10.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3 (d, J_{CP} = 2.0 Hz), 136.6, 132.4, 129.9, 117.7, 117.6, 73.2 (d, J_{CP} = 149.4 Hz), 54.4 (d, J_{CP} = 7.3 Hz), 54.2 (d, J_{CP} = 7.1 Hz); HRMS (EI) m/z calcd for $C_{11}H_{12}NO_5P$ 269.0453, found 269.0441.

[2-[4-(Methoxycarbonyl)phenyl]-1-hydroxy-2-oxoethyl]-phosphonic Acid Dimethyl Ester (Method A).



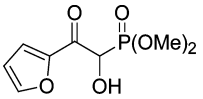
Purified by column chromatography on silica gel (CH_2Cl_2 only): yield 42% (0.71 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15−8.17 (m, 2H), 8.09−8.11 (m, 2H), 5.73 (brs, 1H), 5.62 (d, 1H, J = 16.9 Hz), 3.96 (s, 3H), 3.77 (d, 3H, J = 7.5 Hz), 3.75 (d, 3H, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ194.8, 165.9, 136.7, 135.2, 129.7, 129.4, 73.0 (d, J_{CP} = 150 Hz), 54.4 (d, J_{CP} = 7.2 Hz), 54.2 (d, J_{CP} = 7.2 Hz), 52.62; HRMS (EI) m/z calcd for $C_{12}H_{15}O_7P$ 302.0555, found 302.0551.

[2-(2-Naphthyl)-1-hydroxy-2-oxoethyl]phosphonic Acid Dimethyl Ester (Method B).



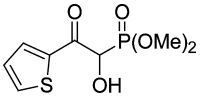
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2): yield 88.9% (1.28 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.05−8.07 (m, 1H), 7.99−8.01 (d, 1H, J = 8.15 Hz), 7.86−7.92 (m, 2H), 7.55−7.64 (m, 2H), 5.68−5.72 (m, 1H), 4.26−4.28 (m, 1H), 3.70−3.75 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.72−194.74 (d, J_{CP} = 2.2 Hz), 136.3, 132.2, 132.2, 130.7, 130.0, 129.4, 128.6, 127.9, 127.1, 124.25, 72.1−73.3 (d, J_{CP} = 149.9 Hz), 54.26−54.32 (d, J_{CP} = 7.15 Hz), 54.08−54.13 (d, J_{CP} = 7.18 Hz); HRMS (EI) m/z calcd for $C_{14}H_{15}O_5P$ 294.0657, found 294.0649.

(2-Furan-2-yl-1-hydroxy-2-oxoethyl)phosphonic Acid Dimethyl Ester (Method A).



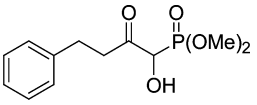
Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:2 to 1:4): yield 42% (0.76 g as a dark-brown oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, 1H, J = 1.2 Hz), 7.44 (d, 1H, J = 3.7 Hz), 6.54 (dd, 1H, J = 1.7, 3.7 Hz), 5.27 (d, 1H, J = 16.2 Hz), 4.29 (brs, 1H), 3.74 (d, 3H, J = 10.8 Hz), 3.69 (d, 3H, J = 10.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.6 (d, J_{CP} = 1.6 Hz), 149.8, 148.1, 121.3, 112.9, 72.3 (d, J_{CP} = 149.4 Hz), 54.2 (d, J_{CP} = 7.0 Hz), 54.1 (d, J_{CP} = 7.0 Hz); HRMS (EI) m/z calcd for $C_8H_{11}O_6P$ 234.0293, found 234.0293.

(1-Hydroxy-2-oxo-2-thiophene-2-yl-ethyl)phosphonic Acid Dimethyl Ester (Method A).



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:3): yield 93.3% (0.7 g as a dark-brown oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, 1H, J = 3.6 Hz), 7.81 (d, 1H, J = 5.1 Hz), 7.21 (t, 1H, J = 4.8 Hz), 5.35 (d, 1H, J = 15.0 Hz), 3.86 (d, 3H, J = 10.8 Hz), 3.77 (d, 3H, J = 10.8 Hz), 2.05−2.54 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.0 (d, J_{CP} = 1.8 Hz), 139.6, 136.1, 135.6, 128.6, 73.1 (d, J_{CP} = 149.8 Hz), 54.3 (d, J_{CP} = 6.7 Hz), 54.2 (d, J_{CP} = 6.6 Hz); HRMS (EI) m/z calcd for $C_8H_{11}O_5PS$ 250.0065, found 250.0063.

(1-Hydroxy-2-oxo-4-phenylbutyl)phosphonic Acid Dimethyl Ester (Method A).



Purified by column chromatography on silica gel (*n*-hexane/EtOAc, 1:1 to 1:3): yield 87.6% (1.86 g as a pale yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26−7.29 (m, 2H), 7.17−7.21 (m, 3H), 4.65 (d, 1H, J = 18.4 Hz), 3.83 (d, 3H, J = 10.9 Hz), 3.73

DOI: 10.1021/acs.joc.5b01434
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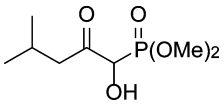
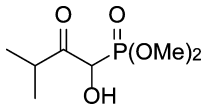
(d, 3H, J = 10.7 Hz), 3.21−3.26 (m, 1H), 2.90−2.99 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.5, 140.2, 128.5, 128.4, 126.3, 75.5 (d, J_{CP} = 150.6 Hz), 54.2 (d, J_{CP} = 7.3 Hz), 54.0 (d, J_{CP} = 7.3 Hz), 40.9, 29.4; HRMS (EI) m/z calcd for $C_{12}H_{17}O_5P$ 272.0814, found 272.0821.

Dimethyl (1-Hydroxy-4-methyl-2-oxopentyl)phosphonate (Method B).



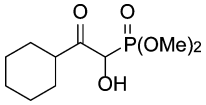
Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2): yield 70.6% (756 mg as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.64 (d, 1H, J = 18 Hz), 3.88 (d, 3H, J = 10.9 Hz), 3.8 (d, 3H, J = 10.65 Hz), 2.70−2.75 (m, 1H), 2.54−2.59 (m, 1H), 2.22−2.26 (m, 1H), 0.95 (d, 6H, J = 6.75 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.7 (d, J_{CP} = 1.5 Hz), 128.1, 75.7 (d, J_{CP} = 125 Hz), 54.2 (d, J_{CP} = 7.3 Hz), 54.0 (d, J_{CP} = 7.0 Hz), 48.2, 24.7, 22.4 (d, J_{CP} = 30 Hz); HRMS (EI) m/z calcd for $C_8H_{17}O_5P$ 224.0814, found 224.0808.

Dimethyl (1-Hydroxy-3-methyl-2-oxobutyl)phosphonate (Method B).



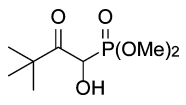
Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2): yield 52.2% (1.18 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.84 (d, 1H, J = 18.15 Hz), 3.88 (d, 3H, J = 10.85 Hz), 3.8 (d, 3H, J = 10.65 Hz), 3.20−3.25 (m, 1H), 1.16−1.2 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6 (d, J_{CP} = 2.1 Hz), 73.9 (d, J_{CP} = 151 Hz), 54.2 (d, J_{CP} = 7.25 Hz), 54.0 (d, J_{CP} = 6.95 Hz), 37.5, 19.7, 17.3; HRMS (EI) m/z calcd for $C_7H_{15}O_5P$ 210.0657, found 210.0617

(2-Cyclohexyl-1-hydroxy-2-oxoethyl)phosphonic Acid Dimethyl Ester (Method B).



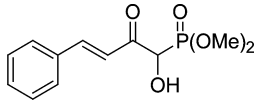
Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2 to 1:4): yield 74.3% (288.1 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.78−4.82(d, 1H, J = 17.95 Hz), 3.86−3.88 (d, 3H, J = 10.85 Hz), 3.77−3.79(d, 3H, J = 10.8 Hz), 2.93−2.98 (m, 1H), 1.32−1.89 (m, 10H), 5.68−5.72 (m, 1H), 4.26−4.28 (m, 1H), 3.70−3.75 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.37, 73.35−74.56 (d, J_{CP} = 151.1 Hz), 54.16−54.22 (d, J_{CP} = 7.3 Hz), 53.93−53.98 (d, J_{CP} = 6.91 Hz), 47.2, 30.1, 27.2, 25.8, 25.6, 24.9; HRMS (EI) m/z calcd for $C_{10}H_{19}O_5P$ 250.0970, found 250.0961.

Dimethyl (1-Hydroxy-3,3-dimethyl-2-oxobutyl)phosphonate (Method B).



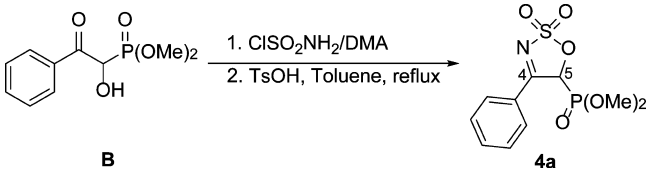
Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2): yield 40.1% (771 mg as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (d, 1H, J = 15.4 Hz), 3.87 (d, 3H, J = 10.9 Hz), 3.8 (d, 3H, J = 10.85 Hz), 1.29 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.2, 71.6 (d, J_{CP} = 147.1 Hz), 54.2 (d, J_{CP} = 7.4 Hz), 53.9 (d, J_{CP} = 7.0 Hz), 43.8, 26.7; HRMS (EI) m/z calcd for $C_8H_{17}O_5P$ 224.0814, found 224.0801.

(1-Hydroxy-2-oxo-4-phenylbut-3-enyl)phosphonic Acid Dimethyl Ester (Method A).



Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:1): yield 66.2% (1.27 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, 1H, J = 15.9 Hz), 7.58 (d, 2H, J = 7.3 Hz), 7.35−7.40 (m, 3H), 7.18 (d, 1H, J = 15.9 Hz), 4.92 (d, 1H, J = 17.7 Hz), 4.26 (brs, 1H), 3.86 (d, 3H, J = 10.8 Hz), 3.76 (d, 3H, J = 10.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.9 (d, J_{CP} = 1.9 Hz), 145.6, 133.9, 131.4, 129.0, 120.6, 75.1 (d, J_{CP} = 150.7 Hz), 54.3 (d, J_{CP} = 7.3 Hz), 54.1 (d, J_{CP} = 6.6 Hz); HRMS (EI) m/z calcd for $C_{12}H_{15}O_5P$ 270.0657, found 270.0659.

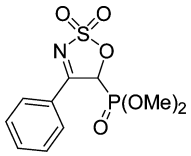
2. Typical Procedure for the Synthesis of 4-Substituted Cyclic Imine-5-phosphonates 4 from α-Hydroxy-β-keto Phosphonates.[9]



B **4a**

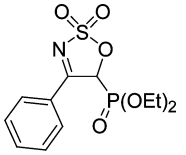
To the solution of 2-phenyl-1-hydroxy-2-oxoethylphosphonic acid dimethyl ester (**B**, 1.3 g, 5.32 mmol) in DMA (*N*,*N*-dimethylacetamide, 20 mL) was added chlorosulfamide[12] (1.3 g, 10.64 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, and the solvent was removed. The residue was redissolved in toluene (10 mL), and a catalytic amount of PTSA (*p*-toluenesulfonic acid) was added. The reaction mixture was heated to reflux for 2 h and cooled to room temperature. The solvent was removed, and the reaction mixture was diluted with EtOAc (30 mL) and washed brine. The organics were dried over $MgSO_4$ and evaporated. The residue was recrystallized from EtOAc/n-hexane to give the desired imine as white crystals **4a** (0.85 g, 54% yield).

*Dimethyl 4-Phenyl-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, **4a**. Recrystallized from EtOAc/n-hexane:*



yield 54% (0.86 g as a white solid); mp = 160.5−162.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14−8.16 (m, 2H), 7.74−7.76 (m, 1H), 7.59−7.62 (m, 2H), 6.19 (d, 1H, J = 10.8 Hz), 3.95 (d, 3H, J = 11.1 Hz), 3.71 (d, 3H, J = 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 136.0, 130.7, 129.2, 126.9, 82.7 (d, J_{CP} = 155.3 Hz), 55.4 (d, J_{CP} = 7.0 Hz), 55.3 (d, J_{CP} = 6.1 Hz); HRMS (EI) m/z calcd for $C_{10}H_{12}NO_6PS$ 305.0123, found 305.0096.

*Diethyl 4-Phenyl-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, **4b**. Recrystallized from EtOAc/n-hexane:*



yield 57% (0.41 g as a white solid); mp = 146.8−147.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01−8.12 (m, 2H), 7.69−7.72 (m, 1H), 7.53−7.56 (m, 2H), 6.10 (d, 1H, J = 10.7 Hz), 4.16−4.25 (m, 2H), 3.88−4.09 (m, 2H), 1.37 (t, 3H, J = 7.2 Hz), 1.16 (t, 3H, J = 7.1 Hz); ^{13}C NMR

DOI: 10.1021/acs.joc.5b01434
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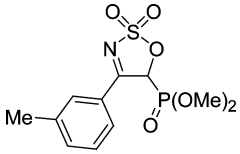
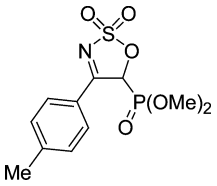
(75 MHz, $CDCl_3$) δ 173.8, 135.8, 130.7, 129.1, 127.1, 83.2 (d, J_{CP} = 154.5 Hz), 65.4 (d, J_{CP} = 7.1 Hz), 65.2 (d, J_{CP} = 7.3 Hz), 16.3 (d, J_{CP} = 5.7 Hz), 16.0 (d, J_{CP} = 5.8 Hz); HRMS (EI) m/z calcd for $C_{12}H_{16}NO_6PS$ 333.0436, found 333.0434.

Dimethyl 4-(3-Methylphenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4c****. Recrystallized from EtOAc/n-hexane:*



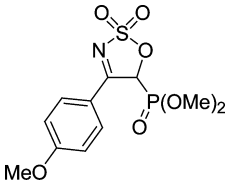
yield 55% (0.66 g as a white solid); mp = 155.4−157.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.89 (d, 1H, J = 7.9 Hz), 7.52 (d, 1H, J = 7.7 Hz), 7.45 (t, 1H, J = 7.8 Hz), 6.12 (d, 1H, J = 10.7 Hz), 3.91 (d, 3H, J = 11.1 Hz), 3.71 (d, 3H, J = 11.1 Hz), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 139.3, 136.9, 130.9, 129.0, 128.0, 126.8, 82.8 (d, J_{CP} = 155.4 Hz), 55.3 (d, J_{CP} = 7.0 Hz), 55.2 (d, J_{CP} = 7.3 Hz), 21.3; HRMS (EI) m/z calcd for $C_{11}H_{14}NO_6PS$ 319.0279, found 319.0284.

Dimethyl 4-(4-Methylphenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4d****. Recrystallized from EtOAc/n-hexane:*



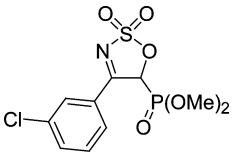
yield 73% (0.42 g as a white solid); mp = 208.8−211.5 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.10 (d, 2H, J = 7.8 Hz), 7.48 (d, 2H, J = 7.9 Hz), 6.97 (d, 1H, J = 11.3 Hz), 3.87 (d, 3H, J = 11.1 Hz), 3.73 (d, 3H, J = 11.1 Hz), 2.49 (s, 3H); ^{13}C NMR (75 MHz,, acetone-d_6) δ 175.4, 147.3, 130.7, 129.7, 123.9, 83.7 (d, J_{CP} = 151.1 Hz), 54.7 (d, J_{CP} = 6.9 Hz), 54.6 (d, J_{CP} = 6.6 Hz), 21.5; HRMS (EI) m/z calcd for $C_{11}H_{14}NO_6PS$ 319.0279, found 319.0300.

Dimethyl 4-(4-Methoxyphenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4e****. Recrystallized from EtOAc/n-hexane:*



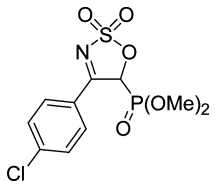
yield 75% (1.185 g as a white solid); mp = 178.8−180.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, 2H, J = 9.0 Hz), 7.06 (d, 2H, J = 9.0 Hz), 6.12 (d, 1H, J = 10.1 Hz), 3.98 (d, 3H, J = 11.1 Hz), 3.95 (s, 3H), 3.74 (d, 3H, J = 11.0 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.2, 165.6, 133.4, 118.7, 114.7, 83.4 (d, J_{CP} = 151.0 Hz), 56.0, 54.7 (d, J_{CP} = 7.0 Hz), 54.6 (d, J_{CP} = 6.8 Hz); HRMS (EI) m/z calcd for $C_{11}H_{14}NO_7PS$ 335.0229, found 335.0234.

Dimethyl 4-(3-Chlorophenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4f****. Recrystallized from EtOAc/n-hexane:*



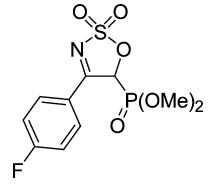
yield 78% (0.94 g as a white solid); mp = 176.7−180.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14−8.15 (m, 1H), 8.00−8.03 (m, 1H), 7.68−7.71 (m, 1H), 7.53 (t, 1H, J = 7.9 Hz), 6.10 (d, 1H, J = 10.9 Hz), 3.94 (d, 3H, J = 11.2 Hz), 3.76 (d, 3H, J = 11.1 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 179.7, 140.4, 139.6, 136.0, 135.5, 134.5, 134.3, 88.9 (d, J_{CP} = 152.8 Hz), 59.7 (d, J_{CP} = 9.3 Hz), 59.6 (d, J_{CP} = 6.7 Hz); HRMS (EI) m/z calcd for $C_{10}H_{11}ClNO_6PS$ 338.9733, found 338.9734.

Dimethyl 4-(4-Chlorophenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4g****. Recrystallized from EtOAc/n-hexane:*



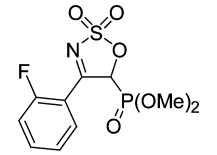
yield 83.3% (1.0 g as a white solid); mp = 174.7−177.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, 2H, J = 8.7 Hz), 7.54 (d, 2H, J = 8.7 Hz), 6.10 (d, 1H, J = 10.7 Hz), 3.94 (d, 3H, J = 11.1 Hz), 3.72 (d, 3H, J = 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 142.9, 132.0, 129.6, 125.2, 82.6 (d, J_{CP} = 154.9 Hz), 55.4 (d, J_{CP} = 7.0 Hz), 55.3 (d, J_{CP} = 7.4 Hz); HRMS (EI) m/z calcd for $C_{10}H_{11}ClNO_6PS$ 338.9733, found 338.9737.

Dimethyl 4-(4-Fluorophenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-dioxide, ***4h****. Recrystallized from EtOAc/n-hexane:*



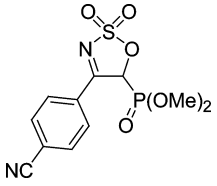
yield 67% (0.98 g as a white solid); mp = 138.4−142.9 °C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21−8.24 (m, 2H), 7.27−7.30 (m, 2H), 6.15 (d, 1H, J = 10.6 Hz), 3.98 (d, 3H, J = 11.2 Hz), 3.77 (d, 3H, J = 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 167.4 (d, J_{CF} = 259.5 Hz), 133.7 (d, J_{CF} = 9.9 Hz), 123.1 (d, J_{CF} = 3.0 Hz), 116.8 (d, J_{CF} = 22.3 Hz), 82.5 (d, J_{CP} = 154.7 Hz), 55.4 (d, J_{CP} = 7.1 Hz), 55.3 (d, J_{CP} = 7.3 Hz); HRMS (EI) m/z calcd for $C_{10}H_{11}FNO_6PS$ 323.0029, found 323.0033.

Dimethyl 4-(2-Fluorophenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4i****. Recrystallized from EtOAc/n-hexane:*



yield 60% (1.19 g as a white solid); mp = 117.9−118.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03−8.06 (m, 1H), 7.69−7.74 (m, 1H), 7.35−7.38 (m, 1H), 7.23−2.27 (m, 1H), 6.30 (dd, 1H, J = 1.4, 151.2 Hz), 3.87 (d, 3H, J = 11.3 Hz), 3.74 (d, 3H, J = 11.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 162.4 (d, J_{CF} = 256.0 Hz), 137.5 (d, J_{CF} = 9.6 Hz), 131.5, 125.4 (d, J_{CF} = 3.1 Hz), 116.7 (d, J_{CF} = 21.6 Hz), 116.4 (d, J_{CF} = 11.0 Hz), 84.4 (dd, J_{CP} = 11.1, 156.1 Hz), 55.2 (d, J_{CP} = 7.3 Hz), 55.2 (d, J_{CP} = 7.4 Hz); HRMS (EI) m/z calcd for $C_{10}H_{11}FNO_6PS$ 323.0029, found 323.0029.

Dimethyl 4-(4-Cyanophenyl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4j****. Recrystallized from EtOAc/n-hexane:*



yield 78% (1.12 g as a white solid); mp = 158.5−161.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, 2H, J = 7.9 Hz), 7.88 (d, 2H, J = 7.9 Hz), 6.17 (d, 1H, J = 11.1 Hz), 3.97 (d, 3H, J = 11.1 Hz), 3.76 (d, 3H, J = 11.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 132.7, 131.0, 130.5, 118.9, 117.2, 82.7 (d, J_{CP} = 154.8 Hz), 55.5 (d, J_{CP} = 7.2 Hz), 55.4 (d, J_{CP} = 7.4 Hz); HRMS (EI) m/z calcd for $C_{11}H_{11}N_2O_6PS$ 330.0075, found 330.0088.

DOI: 10.1021/acs.joc.5b01434
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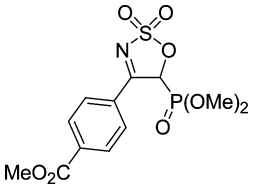
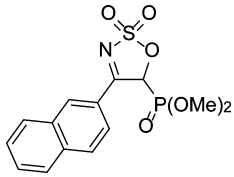
Dimethyl 4-[4-(Methoxycarbonyl)phenyl]-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4k****. Recrystallized from EtOAc/n-hexane:*



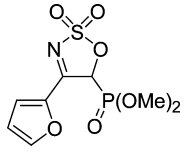
yield 44.4% (0.4 g as a white solid); mp = 149.5−152.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16−8.17 (m, 4H), 6.14 (d, 1H, J = 11.1 Hz), 3.94 (s, 3H), 3.89 (d, 3H, J = 11.2 Hz), 3.69 (d, 3H, J = 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 165.5, 136.2, 130.6, 130.4, 130.0, 82.9 (d, J_{CP} = 155.3 Hz), 55.4 (d, J_{CP} = 6.9 Hz), 55.2 (d, J_{CP} = 7.2 Hz), 52.8; HRMS (EI) m/z calcd for $C_{12}H_{14}NO_8PS$ 363.0178, found 363.0159.

Dimethyl [4-(Naphthalen-2-yl)-5H-1,2,3-oxathiazol-5-yl]-phosphonate 2,2-Dioxide, ***4l****. Recrystallized from EtOAc/n-hexane:*



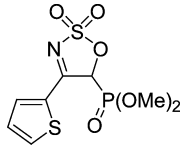
yield 43% (681.7 mg as a ivory solid); mp = 219.3−220.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11−8.13 (m, 1H), 7.90−8.02 (m, 3H), 7.60−7.71 (m, 2H) 6.27 (d, 1H, J = 10.45 Hz), 3.95 (d, 3H, J = 11.1 Hz), 3.69 (d, 3H, J = 11.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 136.8, 134.1, 132.2, 130.3, 130.1, 129.3, 128.1, 127.7, 124.7, 124.1,82.8 (d, J_{CP} = 29.88 Hz), 55.44 (d, J_{CP} = 7.16 Hz), 55.22 (d, J_{CP} = 7.17 Hz); HRMS (EI) m/z calcd for $C_{14}H_{14}NO_6PS$ 355.0279, found 355.0248.

Dimethyl 4-(Furan-2-yl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4m****. Recrystallized from EtOAc/n-hexane:*



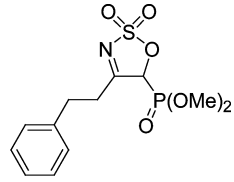
yield 48.4% (0.61 g as a ivory solid); mp = 138.0−142.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, 1H, J = 1.3 Hz), 7.82 (d, 1H, J = 3.8 Hz), 6.72 (dd, 1H, J = 1.7, 3.8 Hz), 5.87 (d, 1H, J = 10.1 Hz), 3.94 (d, 3H, J = 11.2 Hz), 3.77 (d, 3H, J = 11.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 150.8, 143.1, 126.1, 114.3, 81.4 (d, J_{CP} = 155.9 Hz), 55.4 (d, J_{CP} = 3.9 Hz), 55.3 (d, J_{CP} = 3.7 Hz); HRMS (EI) m/z calcd for $C_8H_{10}NO_7PS$ 294.9916, found 294.9918.

Dimethyl 4-(Thiophene-2-yl)-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4n****. Recrystallized from EtOAc/n-hexane:*



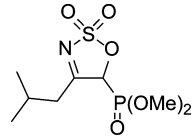
yield 43% (73.6 mg as a ivory solid); mp = 145.3−146.7 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 8.40−8.41 (m, 1H), 8.29−8.30 (m, 1H), 7.42−7.44 (m, 1H), 6.87 (d, 1H, J = 10.6 Hz), 3.96 (d, 3H, J = 11.1 Hz), 3.79 (d, 3H, J = 11.0 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 173.0, 145.5, 144.1, 135.5, 134.9, 88.2 (d, J_{CP} = 153.2 Hz), 59.8 (d, J_{CP} = 7.1 Hz), 59.7 (d, J_{CP} = 6.6 Hz); HRMS (EI) m/z calcd for $C_8H_{10}NO_6PS_2$ 310.9687, found 310.9689.

Dimethyl 4-Phenethyl-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, ***4o****. Recrystallized from EtOAc/n-hexane:*



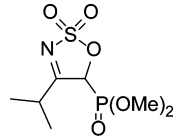
yield 67% (1.8 g as a white solid); mp = 100.5−101.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23−7.33 (m, 5H), 5.33 (d, 1H, J = 12.5 Hz), 3.91 (d, 3H, J = 11.2 Hz), 3.80 (d, 3H, J = 11.0 Hz), 3.24−3.31 (m, 1H), 3.03−3.18 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.1, 138.8, 128.8, 128.5, 126.9, 83.9 (d, J_{CP} = 157.4 Hz), 55.3 (d, J_{CP} = 7.4 Hz), 55.1 (d, J_{CP} = 6.9 Hz), 33.7, 31.4; HRMS (EI) m/z calcd for $C_{12}H_{16}NO_6PS$ 333.0436, found 333.0436.

Dimethyl (4-Isobutyl-2,2-dioxido-5H-1,2,3-oxathiazol-5-yl)-phosphonate, ***4p****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



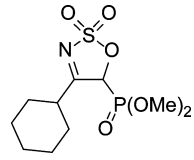
yield 20% (180 mg as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.42 (d, 1H, J = 12.4 Hz), 3.95 (d, 3H, J = 11.1 Hz), 3.89 (d, 3H, J = 11 Hz), 2.76−2.8 (m, 1H), 2.63−2.68 (m, 1H), 2.29−2.30 (m, 1H), 1.03−1.06 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.9, 83.9 (d, J_{CP} = 158 Hz), 55.4 (d, J_{CP} = 7.4 Hz), 55.2 (d, J_{CP} = 6.8 Hz), 40.5, 26.3, 22.6, 22.0; HRMS (EI) m/z calcd for $C_8H_{16}NO_6PS$ 285.0436, found 285.0422

Dimethyl (4-Isopropyl-2,2-dioxido-5H-1,2,3-oxathiazol-5-yl)-phosphonate, ***4q****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



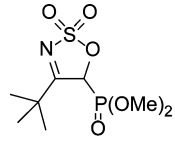
yield 9.8% (324 mg as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.58 (d, 1H, J = 12.45 Hz), 3.94 (d, 3H, J = 11.15 Hz), 3.83 (d, 3H, J = 11 Hz), 3.19−3.24 (m, 1H), 1.32−1.36 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.2, 82.8 (d, J_{CP} = 158 Hz), 55.4 (d, J_{CP} = 7.5 Hz), 55.1 (d, J_{CP} = 6.8 Hz), 31.7, 20.7, 18.9; HRMS (EI) m/z calcd for $C_7H_{14}NO_6PS$ 271.0279, found 271.0264

Dimethyl (4-Cyclohexyl-5H-1,2,3-oxathiazol-5-yl)phosphonate 2,2-Dioxide, ***4r****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



yield 48.45% (1.25 g as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.53−5.56 (m, 1H), 3.83−3.93 (m, 6H), 2.87−2.89 (m, 1H), 1.26−2.01 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.17 (d, J_{CP} = 5.3 Hz), 82.74 (d, J_{CP} = 157.8 Hz), 55.32−55.37 (d, J_{CP} = 7.37), 55.08 (d, J_{CP} = 6.7), 40.6, 31.5, 25.7, 28.8, 25.3, 24.8; HRMS (EI) m/z calcd for $C_{10}H_{18}NO_6PS$ 311.0592, found 311.0583.

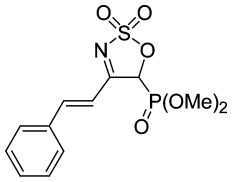
Dimethyl (4-tert-Butyl-2,2-dioxido-5H-1,2,3-oxathiazol-5-yl)-phosphonate, ***4s****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887−8902

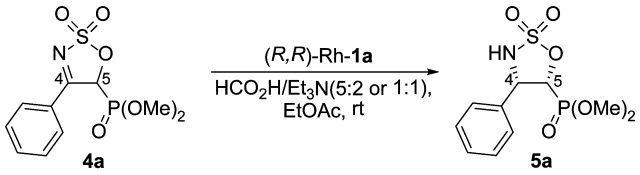
yield 36% (348 mg as a yellow oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.61 (d, 1H, J = 12.15 Hz), 3.95 (d, 3H, J = 11.1 Hz), 3.89 (d, 3H, J = 11.1 Hz), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 83.5 (d, J_{CP} = 156 Hz), 55.3 (d, J_{CP} = 7.8 Hz), 55.0 (d, J_{CP} = 7.0 Hz), 38.2, 28.0; HRMS (EI) m/z calcd for $C_8H_{16}NO_6PS$ 285.0436, found 285.0427.

*Dimethyl 4-(E)-Styryl-5H-1,2,3-oxathiazole-5-phosphonate 2,2-Dioxide, **4t**. Recrystallized from EtOAc/n-hexane:*



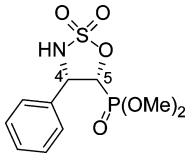
yield 67% (0.57 g as a ivory solid); mp = 157.0−158.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, 1H, J = 16.0 Hz), 7.63−7.65 (m, 2H), 7.44−7.49 (m, 3H), 7.09 (d, 1H, J = 16.0 Hz), 5.69 (d, 1H, J = 11.3 Hz), 3.97 (d, 3H, J = 11.1 Hz), 3.84 (d, 3H, J = 11.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 150.3, 133.5, 132.5, 129.4, 129.3, 114.2, 82.6 (d, J_{CP} = 155.9 Hz), 55.5 (d, J_{CP} = 7.2 Hz), 55.3 (d, J_{CP} = 7.0 Hz); HRMS (EI) m/z calcd for $C_{12}H_{14}NO_6PS$ 331.0279, found 331.0282.

3. Typical Procedure for the ATH−DKR of 4,5-Disubstituted Cyclic Imine 4.



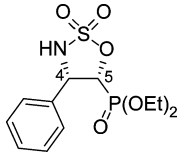
To the solution of 4,5-disubstituted cyclic imine **4a** (70 mg, 0.23 mmol) in EtOAc (2.3 mL) was added (*R*,*R*)-Cp*RhCl(TsDPEN) (**1a**) catalyst (0.5 mol %) and then HCO_2H/Et_3N (5:2 azeotropic mixture, 0.23 mL) via a syringe, and the reaction mixture was stirred for 0.5 h at room temperature and diluted with EtOAc. The reaction mixture was washed with water and brine. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1) to give a white solid **5a** (69.5 mg, 98.6%).

*Dimethyl (4S,5R)-4-Phenyl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, **5a**. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



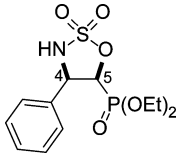
yield 98.6% (69.5 mg as a white solid); mp = 166.8−170.8 °C; 98% ee; Chiralpak IB, 20% ethanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(minor) = 8.9 min, t_R(major) = 9.9 min; $[\alpha]^{29}_D$ = +8.49 (c 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23−7.43 (m, 5H), 5.69 (brs, 1H), 5.33 (d, 1H, J = 26.4 Hz), 5.12 (dd, 1H, J = 2.3, 6.2 Hz), 3.71 (d, 3H, J = 10.7 Hz), 3.17 (d, 3H, J = 11.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.2 (d, J_{CP} = 6.0 Hz), 129.3, 128.8, 127.1, 162.8, 61.0, 55.1 (d, J_{CP} = 6.5 Hz), 52.7 (d, J_{CP} = 6.8 Hz); HRMS (EI) m/z calcd for $C_{10}H_{14}NO_6PS$ 307.0279, found 307.0276.

*Diethyl (4S,5R)-4-Phenyl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, **5b**. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



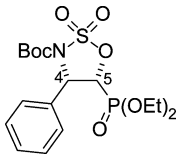
yield 95% (31.9 mg as a white solid); mp = 172.9−176.0 °C; $[\alpha]^{22}_D$ = +116.61 (c 0.33, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.46 (m, 5H), 6.27−6.29 (m, 1H), 5.27−5.36 (m, 1H), 5.07 (dd, 1H, J = 2.4, 6.4 Hz), 4.01−4.12 (m, 2H), 3.71−3.76 (m, 1H), 3.42−3.47 (m, 1H).1.21 (t,3H, J = 7.0 Hz), 0.92 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.5 (d, J_{CP} = 2.6 Hz), 129.1, 128.6, 127.3, 81.3 (d, J_{CP} = 168.6 Hz), 64.9 (d, J_{CP} = 6.7 Hz), 62.7 (d, J_{CP} = 7.0 Hz), 61.2, 16.3 (d, J_{CP} = 5.5 Hz), 15.9 (d, J_{CP} = 6.0 Hz); HRMS (EI) m/z calcd for $C_{12}H_{18}NO_6PS$ 335.0592, found 335.0591.

*Diethyl (4R,5S)-4-Phenyl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ent-**5b**. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



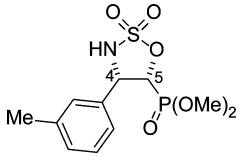
yield 92.2% (28.39 mg as a white solid); mp = 173−174.2 °C; $[\alpha]^{29}_D$ = −92.26 (c 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.65−7.67 (m, 2H), 7.44−7.46 (m, 3H), 5.45−5.51 (m, 2H), 3.65−4.01 (m, 4H), 1.09 (m, 3H), 1.07 (m, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 134.7 (d, J_{CP} = 2.9 Hz), 129.5, 129.0, 129.0, 81.3 (d, J_{CP} = 168.4 Hz), 64.1 (d, J_{CP} = 6.6 Hz), 63.1 (d, J_{CP} = 6.6 Hz), 61.9, 16.5 (d, J_{CP} = 5.5 Hz), 16.3 (d, J_{CP} = 5.9 Hz).

*(4S,5R)-N-Boc-4-phenyl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide Diethyl Ester, (4S,5R)-N-Boc-**5b**.*



To a stirred mixture of (4*S*,5*R*)-**5b** (41 mg, 0.12 mmol) and triethylamine (0.05 mL, 0.36 mmol) in anhydrous CH_2Cl_2 (2 mL) at 0 °C were added di-*tert*-butyl dicarbonate (49 mg, 0.18 mmol) and DMAP (cat). The mixture was stirred for 2 h at room temperature, diluted with diethyl ether (10 mL), and washed successively with cold 1 N HCl, aqueous saturated $NaHCO_3$ solution, and brine. The organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 20:1) to give 50.1 mg (96% yield) as a white solid: yield 96% (50 mg as a white solid); mp = 127.2−127.5 °C; $[\alpha]^{22}_D$ = −11.17 (c 0.17, $CHCl_3$); 97.8% ee; Chiralcel OD-H, 10% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm, t_R(minor) = 11.0 min, t_R(major) = 16.1 min; ^{1}H NMR (500 MHz, acetone-d_6) δ 7.43−7.56 (m, 5H), 5.67 (d, 1H, J = 5.8 Hz), 5.54−5.57 (m, 1H), 4.06−4.12 (m, 2H), 3.69−3.75 (m, 1H), 3.38−3.48 (m, 1H), 1.39 (s 9H), 1.3 (t, 3H, J = 7.1 Hz), 1.04 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 134.4, 129.3, 128.5, 128.2, 86.0, 75.2 (d, J_{CP} = 172.6 Hz), 63.8 (d, J_{CP} = 4.5 Hz), 63.8 (d, J_{CP} = 4.1 Hz), 63.0, 27.8, 16.3 (d, J_{CP} = 5.9 Hz), 16.1 (d, J_{CP} = 5.6 Hz); HRMS (EI) m/z calcd for $C_{17}H_{26}NO_8PS$ 435.1117, found 435.1118.

*Dimethyl (4S,5R)-4-(3-Methylphenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, **5c**. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2):*



yield 94.17% (47.19 mg as a white solid); mp = 163.3−164.4 °C; $[\alpha]^{21}_D$ = +125.40 (c 0.33, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.44−7.48 (m, 2H), 7.35 (t, 1H, J = 7.6 Hz), 7.24 (d, 1H, J = 7.6 Hz), 5.50−5.52 (m, 1H), 5.41−5.46 (m, 1H), 3.52 (d, 3H, J = 10.8 Hz), 3.40 (d, 3H, J = 11.0 Hz), 2.40 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 138.7, 134.4 (d, J_{CP} = 3.2 Hz), 130.2, 129.4, 129.0, 125.9, 81.2

DOI: 10.1021/acs.joc.5b01434
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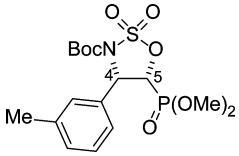
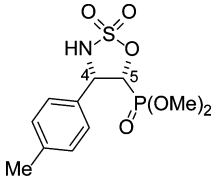
(d, J_{CP} = 169.0 Hz), 61.7, 54.2 (d, J_{CP} = 6.7 Hz), 53.2 (d, J_{CP} = 6.6 Hz), 21.4; HRMS (EI) *m*/*z* calcd for $C_{11}H_{16}NO_6PS$ 321.0436, found 321.0426.

*N-Boc-(4S,5R)-4-(3-methylphenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide Dimethyl Ester, N-Boc-**5c**. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:3):*



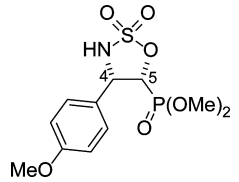
yield 98.4% (62.2 mg as a yellow oil); 96.4% ee; Chiralpak AD-H, 10% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(minor) = 9.9 min, t_R(major) = 11.5 min; $[\alpha]^{22}_D$ = +5.99 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.36−7.38 (m, 3H), 7.26−7.28 (m, 1H), 5.29−5.64 (m, 2H), 3.73 (d, 3H, *J* = 11.1 Hz), 3.20 (d, 3H, *J* = 11.0 Hz), 2.41 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.5, 138.7, 136.2, 130.5, 129.8, 129.1, 126.2, 85.8, 76.1 (d, J_{CP} = 172.6 Hz), 64.0, 53.9 (q, J_{CP} = 6.4 Hz), 27.9, 21.4; HRMS (EI) *m*/*z* calcd for $C_{16}H_{24}NO_8PS$ 421.0960, found 421.0968.

*Dimethyl (4S,5R)-4-(4-Methylphenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, **5d**. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2):*



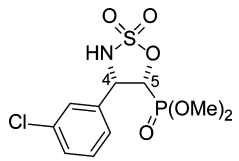
yield 99.6% (32 mg as a white solid); mp = 134.5−136.0 °C; 96.7% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(major) = 9.2 min, t_R(minor) = 11.8 min; $[\alpha]^{21}_D$ = +126.27 (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.55 (d, 2H, *J* = 8.2 Hz), 7.30 (d, 2H, *J* = 8.0 Hz), 7.15−7.20 (brs, 1H), 5.50−5.52 (m, 1H), 5.43−5.48 (m, 1H), 3.53 (d, 3H, *J* = 10.8 Hz), 3.43 (d, 3H, *J* = 1.6 Hz), 2.40 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 139.4, 131.6, 129.7, 128.8, 81.2 (d, J_{CP} = 169.0 Hz), 61.6, 54.2 (d, J_{CP} = 6.6 Hz), 53.2 (d, J_{CP} = 6.6 Hz), 21.1; HRMS (EI) *m*/*z* calcd for $C_{11}H_{16}NO_6PS$ 321.0436, found 321.0408.

*Dimethyl (4S,5R)-4-(4-Methoxyphenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, **5e**. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2):*



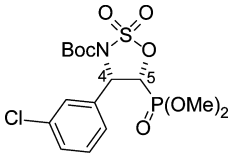
yield 96% (33 mg as a white solid); mp = 132.5−134.1 °C; 96% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(major) = 10.5 min, t_R(minor) = 15.0 min; $[\alpha]^{21}_D$ = +107.68 (*c* 0.44, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, 2H, *J* = 8.7 Hz), 7.00 (d, 2H, *J* = 8.8 Hz), 5.45 (dd, 1H, *J* = 3.4, 6.5 Hz), 5.40 (dd, 1H, *J* = 6.5, 17.2 Hz), 3.84 (s, 3H), 3.52 (d, 3H, *J* = 10.8 Hz), 3.44 (d, 3H, *J* = 11.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 128.7, 123.8, 114.0, 80.9 (d, J_{CP} = 169.8 Hz), 60.7, 55.4, 54.8 (d, J_{CP} = 6.6 Hz), 53.0 (d, J_{CP} = 6.9 Hz); HRMS (EI) *m*/*z* calcd for $C_{11}H_{16}NO_7PS$ 337.0385, found 337.0383.

*Dimethyl (4S,5R)-4-(3-Chlorophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, **5f**. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:2):*



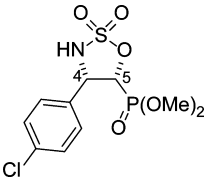
yield 90.9% (31 mg as a white solid); mp = 96.8−98.5 °C; $[\alpha]^{21}_D$ = +118.13 (*c* 0.33, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.74 (s, 1H), 7.60−7.62 (m, 1H), 7.47−7.51 (m, 2H), 5.50−5.56 (m, 2H), 3.56 (d, 3H, *J* = 3.6 Hz), 3.53 (d, 3H, *J* = 3.4 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 137.7, 134.5, 130.7, 129.6, 129.1, 127.7, 80.3 (d, J_{CP} = 169.3 Hz), 61.1, 54.2 (d, J_{CP} = 6.7 Hz), 53.5 (d, J_{CP} = 6.6 Hz); HRMS (EI) *m*/*z* calcd for $C_{10}H_{13}ClNO_6PS$ 340.9890, found 340.9895.

*N-Boc-(4S,5R)-4-(3-chlorophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide Dimethyl Ester, N-Boc-**5f**. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



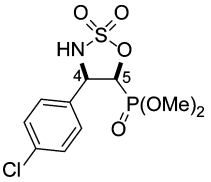
yield 88.7% (78 mg as a white solid); mp = 106.7−108.4 °C; 94% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(minor) = 10.4 min, t_R(major) = 13.2 min; $[\alpha]^{22}_D$ = +6.85 (*c* 0.35, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.59−7.60 (m, 1H), 7.49−7.55 (m, 3H), 5.73 (d, 1H, *J* = 5.9 Hz), 5.64−5.67 (m, 1H), 3.77 (d, 3H, *J* = 11.1 Hz), 3.37 (d, 3H, *J* = 11.0 Hz), 1.42 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.1, 138.5, 138.5, 131.0, 130.0, 129.1, 127.6, 86.2, 75.7 (d, J_{CP} = 173.0 Hz), 62.2, 54.2 (d, J_{CP} = 2.7 Hz), 54.1 (d, J_{CP} = 2.9 Hz), 27.9; HRMS (EI) *m*/*z* calcd for $C_{15}H_{21}ClNO_8PS$ 441.0414, found 441.0383.

*Dimethyl (4S,5R)-4-(4-Chlorophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-dioxide, **5g**. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1) and recrystallized from EtOAc/n-hexane:*



yield 95.6% (65.5 mg as a white solid); mp = 128.7−130.8 °C; 96.8% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(major) = 10.0 min, t_R(minor) = 13.9 min; $[\alpha]^{25}_D$ = +60.54 (*c* 0.52, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (m, 4H), 5.29 (dd, 1H, *J* = 6.4, 22.0 Hz), 5.16 (dd, 1H, *J* = 3.1, 6.3 Hz), 3.65 (d, 3H, *J* = 10.8 Hz), 3.37 (d, 3H, *J* = 10.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.3, 130.5, 128.8, 128.8, 80.5 (d, J_{CP} = 169.8 Hz), 60.5, 55.0 (d, J_{CP} = 6.8 Hz), 53.0 (d, J_{CP} = 7.0 Hz); HRMS (EI) *m*/*z* calcd for $C_{10}H_{13}ClNO_6PS$ 340.9890, found 340.9898.

*Dimethyl (4R,5S)-4-(4-Chlorophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ent-**5g**. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



yield 97% (27.4 mg as a white solid); mp = 132−133.2 °C; 97.9% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(minor) = 10.1 min, t_R(major) = 12.9 min; $[\alpha]^{30}_D$ = −86.26 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (m, 4H), 6.20 (brs, 1H), 5.29 (dd, 1H, *J* = 6.4, 22.1 Hz), 5.16 (dd, 1H, *J* = 3.1, 6.3 Hz), 3.65 (d, 3H, *J* = 10.8 Hz), 3.37 (d, 3H, *J* = 10.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.3, 130.5, 128.9, 128.8, 80.6 (d, J_{CP} = 169.7 Hz), 60.5, 55.0 (d, J_{CP} = 6.8 Hz), 53.0 (d, J_{CP} = 7.0 Hz); HRMS (EI) *m*/*z* calcd for $C_{10}H_{13}ClNO_6PS$ 340.9890, found 340.9889.

DOI: 10.1021/acs.joc.5b01434
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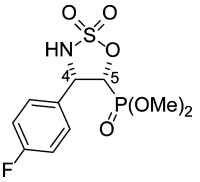
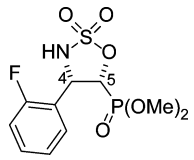
Dimethyl (4S,5R)-4-(4-Fluorophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5h****. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



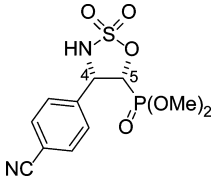
yield 94% (30.5 mg as a white solid); mp = 181.0−185.4 °C; 96% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(major) = 9.2 min, t_R(minor) = 11.8 min; $[\alpha]^{22}_D$ = +100.22 (*c* 0.38, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.68−7.72 (m, 2H), 7.40−7.41 (brs, 1H), 7.20−7.25 (m, 2H), 5.49−5.52 (m, 2H), 3.54 (d, 3H, *J* = 8.7 Hz), 3.45 (d, 3H, *J* = 8.8 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 165.4, 162.1, 131.3 (q, J_{CF} = 8.5 Hz), 115.8 (d, J_{CF} = 21.6 Hz), 80.6 (d, J_{CP} = 169.9 Hz), 61.1, 54.2 (d, J_{CP} = 6.6 Hz), 53.4 (d, J_{CP} = 6.6 Hz); HRMS (EI) *m*/*z* calcd for $C_{10}H_{13}FNO_6PS$ 325.0185, found 325.0195.

Dimethyl (4S,5R)-4-(2-Fluorophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5i****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4) and recrystallized from EtOAc/n-hexane:*



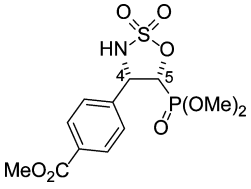
yield 95.4% (47.19 mg as a ivory solid); mp = 173.1−175.8 °C; 81.4% ee; Chiralpak AD-H, 10% 2-propanol/*n*-hexane, 1.5 mL/min, 215 nm t_R(major) = 9.6 min, t_R(minor) = 13.1 min; $[\alpha]^{29}_D$ = +117.6 (*c* 0.3, $CHCl_3$);[1] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.48 (m, 2H), 7.27−7.30 (m, 1H), 7.14−7.18 (m, 1H), 6.14 (brs, 1H), 5.58 (dd, 1H, *J* = 6.2, 30.0 Hz), 5.29−5.31 (m, 1H), 3.88 (d, 3H, *J* = 10.6 Hz), 3.21 (d, 3H, *J* = 11.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2 (d, J_{CF} = 245.7 Hz), 131.0 (d, J_{CF} = 8.4 Hz), 127.5 (d, J_{CF} = 3.1 Hz), 124.7 (d, J_{CF} = 3.2 Hz), 118.5 (d, J_{CF} = 13.9 Hz), 115.2 (d, J_{CF} = 20.9 Hz), 81.0 (dd, J_{CP} = 3.4, 168.1 Hz), 55.9 (d, J_{CP} = 4.2 Hz), 55.5 (d, J_{CP} = 6.4 Hz), 52.6 (d, J_{CP} = 7.1 Hz); HRMS (EI) *m*/*z* calcd for $C_{10}H_{13}FNO_6PS$ 325.0185, found 325.0171.

Dimethyl (4S,5R)-4-(4-Cyanophenyl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5j****. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



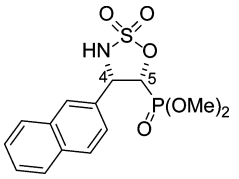
yield 95% (31.5 mg as a white solid); mp = 188.1−189.0 °C; 100% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.5 mL/min, 215 nm t_R(minor) = 9.2 min, t_R(major) = 13.8 min; $[\alpha]^{30}_D$ = +110.79 (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, 2H, *J* = 8.0 Hz), 7.56 (d, 2H, *J* = 8.0 Hz), 6.02 (brs, 1H), 5.36 (dd, 1H, *J* = 6.2, 21.7 Hz), 5.19−5.21 (m, 1H), 3.69 (d, 3H, *J* = 10.7 Hz), 3.39 (d, 3H, *J* = 11.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.0, 132.3, 128.2, 117.9, 113.3, 80.3 (d, J_{CP} = 169.1 Hz), 60.6, 55.3 (d, J_{CP} = 6.5 Hz), 53.0 (d, J_{CP} = 6.9 Hz); HRMS (EI) *m*/*z* calcd for $C_{11}H_{13}N_2O_6PS$ 332.0232, found 332.0232.

Dimethyl (4S,5R)-4-[4-(Methoxycarbonyl)phenyl]-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5k****. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



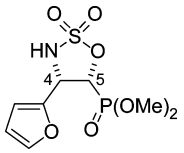
yield 93.4% (46.7 mg as a white solid); mp = 153.5−156.1 °C; 99.2% ee; Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm t_R(major) = 12.9 min, t_R(minor) = 15.2 min; $[\alpha]^{20}_D$ = +91.05 (*c* 0.33, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 8.07 (d, 2H, *J* = 8.5 Hz), 7.77 (d, 2H, *J* = 8.4 Hz), 7.45 (brs, 1H), 5.56−5.61 (m, 2H), 3.91 (s, 3H), 3.50 (d, 3H, *J* = 10.8 Hz), 3.47 (d, 3H, *J* = 11.0 Hz); ^{13}C NMR (125 MHz, acetone-d_6) δ 166.8, 140.2, 131.4, 129.9, 129.3, 80.4 (d, J_{CP} = 169.0 Hz), 61.4, 54.2 (d, J_{CP} = 6.8 Hz), 53.4 (d, J_{CP} = 6.6 Hz), 52.5; HRMS (EI) *m*/*z* calcd for $C_{12}H_{16}NO_8PS$ 365.0334, found 365.0334.

Dimethyl (4S,5R)-4-(Naphthalen-2-yl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5l****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



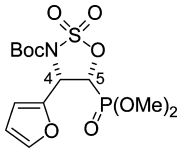
yield 96.6%; mp = 60.5 °C, 96.6% ee; Chiralpak IB, 20% ethanol/*n*-hexane, 1.0 mL/min, 215 nm, t_R(minor) = 14.8 min, t_R(major) = 18.3 min; $[\alpha]^{21}_D$ = +57.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83−7.89 (m, 4H), 7.53(m, 3H), 6.19 (d, 1H, *J* = 9.5 Hz) 5.44−5.53 (m, 1H), 5.22−5.24 (m, 1H), 3.64 (d, 3H, *J* = 10.7 Hz), 3.05 (d, 3H, *J* = 11.05 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.3, 132,8,128.5, 128.2, 127.7, 127.1, 126.9, 128.4, 126.5, 124.2, 81.51 (d, J_{CP} = 76.01 Hz), 61.2, 55.15 (d, J_{CP} = 6.46 Hz), 52.65 (d, J_{CP} = 6.8 Hz); HRMS (EI) *m*/*z* calcd for $C_{14}H_{16}NO_6PS$ 357.0436, found 357.0467.

Dimethyl (4S,5R)-4-(Furan-2-yl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5m****. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1) and recrystallized from EtOAc/n-hexane:*



yield 90% (45 mg as a white solid); mp = 98.0−100.2 °C, $[\alpha]^{31}_D$ = +45.2 (*c* 0.25, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.63−7.64 (m, 1H), 6.70 (d, 1H, *J* = 3.4 Hz), 6.49−6.50 (m, 1H), 5.45 (dd, 1H, *J* = 6.3, 13.2 Hz), 5.39 (dd, 1H, *J* = 4.2, 6.3 Hz), 3.69 (d, 3H, *J* = 10.9 Hz), 3.67 (d, 3H, *J* = 10.9 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.1, 144.2, 111.5, 111.1, 79.7 (d, J_{CP} = 169.8 Hz), 55.9, 54.4 (d, J_{CP} = 6.6 Hz), 53.9 (d, J_{CP} = 6.6 Hz); HRMS (EI) *m*/*z* calcd for $C_8H_{12}NO_7PS$ 297.0072, found 297.0076.

*N-Boc-(4S,5R)-4-(furan-2-yl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide Dimethyl Ester, N-Boc-****5m****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:1):*



yield 90% (35.1 mg as a brown oil); 97.2% ee: Chiralpak IB-H, 30% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm, t_R(minor) = 7.0 min, t_R(major) = 8.4 min; $[\alpha]^{31}_D$ = +7.8 (*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.653−7.651 (m, 1H), 6.58 (d, 1H, *J* = 3.3 Hz), 6.51−6.52 (m, 1H), 5.76 (d, 1H, *J* = 5.5 Hz), 5.53 (dd, 1H, *J* = 5.6, 8.2 Hz), 3.78 (d, 3H, *J* = 11.0 Hz), 3.62 (d, 3H, *J* = 11.0 Hz), 1.45 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.6, 148.4, 144.4, 111.6, 111.3, 86.0, 75.3 (d, J_{CP} = 174.0 Hz), 57.5, 54.5 (d, J_{CP} = 6.6 Hz), 54.3 (d, J_{CP} = 6.2 Hz), 27.9; HRMS (EI) *m*/*z* calcd for $C_{13}H_{20}NO_9PS$ 397.0596, found 397.0599.

DOI: 10.1021/acs.joc.5b01434
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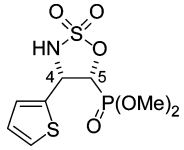
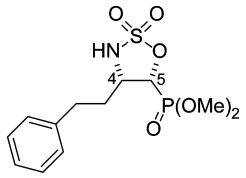
Dimethyl (4S,5R)-4-(Thiophene-2-yl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5n****. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



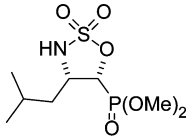
yield 93.9% (29.4 mg as a white solid); mp = 130.1−134.6 °C; 99% ee: Chiralpak AD-H, 20% 2-propanol/*n*-hexane, 1.0 mL/min, 215 nm, t_R(major) = 10.1 min, t_R(minor) = 11.1 min; $[\alpha]^{21}_D$ = +106.04 (*c* 0.46, $CHCl_3$); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.53−7.54 (m, 1H), 7.41−7.42 (m, 1H), 7.08−7.10 (m, 1H), 5.70 (dd, 1H, *J* = 6.2, 12.8 Hz), 5.44 (dd, 1H, *J* = 5.0, 6.2 Hz), 3.60 (d, 3H, *J* = 11.0 Hz), 3.55 (d, 3H, *J* = 10.8 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 137.6, 129.0, 127.7, 127.5, 80.7 (d, J_{CP} = 170.0 Hz), 57.9, 54.3 (d, J_{CP} = 6.8 Hz), 53.5 (d, J_{CP} = 6.6 Hz); HRMS (EI) *m*/*z* calcd for $C_8H_{12}NO_6PS_2$ 312.9844, found 312.9835.

Dimethyl (4S,5R)-4-Phenethyl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5o****. Purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1):*



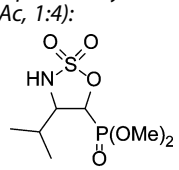
yield 99.4% (49.7 mg as a ivory solid); mp = 134.9−138.8 °C; 96.5% ee; Chiralpak AD-H, 10% 2-propanol/*n*-hexane, 1.5 mL/min, 215 nm, t_R(minor) = 10.3 min, t_R(major) = 12.7 min; $[\alpha]^{30}_D$ + 67.61 (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22−7.34 (m, 5H), 5.48 (brs, 1H), 4.84 (d, 1H, *J* = 6.2 Hz), 4.10−4.13 (m, 1H), 3.94 (d, 3H, *J* = 10.5 Hz), 3.84 (d, 3H, *J* = 10.9 Hz), 2.89−2.95 (m, 1H), 2.74−2.80 (m, 1H), 2.30−2.37 (m, 1H), 2.13−2.20 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 128.7, 128.5, 126.6, 80.8 (d, J_{CP} = 166.3 Hz), 57.7, 55.6 (d, J_{CP} = 6.7 Hz), 53.1 (d, J_{CP} = 6.8 Hz), 32.6, 30.1 (d, J_{CP} = 1.8 Hz); HRMS (EI) *m*/*z* calcd for $C_{12}H_{18}NO_6PS$ 335.0592, found 335.0593.

Dimethyl (4-Isobutyl-2,2-dioxido-1,2,3-oxathiazolidin-5-yl)-phosphonate, ***5p****. Purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



yield 50% (90 mg as a colorless oil); $[\alpha]^{28}_D$ = +57.2 (*c* 0.23, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.00 (d, 1H, *J* = 12.7 Hz), 4.79 (d, 1H, *J* = 6.2 Hz), 4.14−4.23 (m, 1H), 3.95 (d, 3H, *J* = 13.5 Hz), 3.83 (d, 3H, *J* = 11 Hz), 1.78−1.91 (m, 2H), 1.33−1.40 (m, 1H), 0.96−1.00 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.5 (d, J_{CP} = 166 Hz), 57.1, 55.7 (d, J_{CP} = 6.6 Hz), 52.9 (d, J_{CP} = 7.4 Hz), 36.9, 25.8, 22.9, 21.8; HRMS (EI) *m*/*z* calcd for $C_8H_{18}NO_6PS$ 287.0592, found 287.0574.

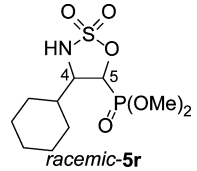
Dimethyl (4-Isopropyl-2,2-dioxido-1,2,3-oxathiazolidin-5-yl)-phosphonate, ***5q****. Prepared from* ***4q*** *by employing $NaBH_4$ reduction in MeOH/H_2O at rt and purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



*racemic-***5q**

yield 60.4% (33 mg as a colorless oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (d, 1H, *J* = 12.9 Hz), 4.88 (d, 1H, *J* = 5.65 Hz), 3.94 (d, 3H, *J* = 10.5 Hz), 3.82 (d, 3H, *J* = 11 Hz), 3.73−3.79 (m, 1H), 2.2−2.3 (m, 1H), 1.13 (d, 3H, *J* = 6.5 Hz), 1.04 (d, 3H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.0 (d, J_{CP} = 164 Hz), 65.7, 55.8 (d, J_{CP} = 6.6 Hz), 52.8 (d, J_{CP} = 7.5 Hz), 27.8 (d, J_{CP} = 2.2 Hz), 21.3, 19.2; HRMS (EI) *m*/*z* calcd for $C_7H_{16}NO_6PS$ 273.0436, found 273.0408.

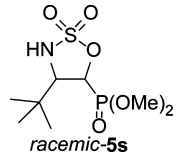
Dimethyl 4-Cyclohexyl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, ***5r****. Prepared from* ***4r*** *by employing $NaBH_4$ reduction in MeOH/H_2O at rt and purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



*racemic-***5r**

yield 13% (24 mg as a colorless oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.21 (d, 1H, *J* = 13.1 Hz), 4.89 (d, 1H, *J* = 5.4 Hz), 3.82−3.96 (m, 6H), 0.86−2.04 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.0 (d, J_{CP} = 164 Hz), 64.4, 56.0 (d, J_{CP} = 6.5 Hz), 52.9 (d, J_{CP} = 7.4 Hz), 36.8, 31.2, 29.8, 25.9, 25.2, 25.1; HRMS (EI) *m*/*z* calcd for $C_{10}H_{20}NO_6PS$ 313.0749, found 313.0725.

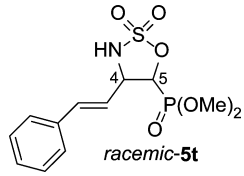
Dimethyl (4-tert-Butyl-2,2-dioxido-1,2,3-oxathiazolidin-5-yl)-phosphonate, ***5s****. Prepared from* ***4s*** *by employing $NaBH_4$ reduction in MeOH/H_2O at rt and purified by column chromatography on silica gel (n-hexane/EtOAc, 1:4):*



*racemic-***5s**

yield 86% (47 mg as a colorless oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 (d, 1H, *J* = 14 Hz), 4.85−4.86 (m, 1H), 3.92 (d, 3H, *J* = 10.8 Hz), 3.83 (d, 3H, *J* = 11 Hz), 1.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.4 (d, J_{CP} = 163.1 Hz), 69.1, 55.4 (d, J_{CP} = 7.0 Hz), 53.3 (d, J_{CP} = 7.4 Hz), 32.3, 26.8; HRMS (EI) *m*/*z* calcd for $C_8H_{18}NO_6PS$ 287.0592, found 287.0621

Dimethyl (4-(E)-Styryl)-1,2,3-oxathiazolidine-5-phosphonate 2,2-dioxide, ***5t****. Prepared from* ***4t*** *by employing $NaBH_4$ reduction in MeOH at rt and purified by column chromatography on silica gel (n-hexane/EtOAc, 1:1):*



*racemic-***5t**

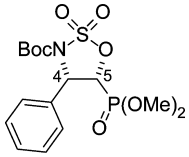
yield 42% (14 mg as a ivory solid); mp = 130.1−134.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.45 (m, 5H), 6.80 (d, 1H, *J* = 15.8 Hz), 6.43 (dd, 1H, *J* = 8.1, 15.7 Hz), 4.92−4.93 (m, 1H), 4.77−4.89 (m, 1H), 3.90 (d, 3H, *J* = 10.6 Hz), 3.73 d, 3H, *J* = 11.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 135.0, 129.0, 128.9, 126.9, 118.5 (d, J_{CP} = 3.5 Hz), 80.7 (d, J_{CP} = 168.8 Hz), 60.1, 55.5 (d, J_{CP} = 6.6 Hz), 53.2 (d, J_{CP} = 7.1 Hz); HRMS (EI) *m*/*z* calcd for $C_{12}H_{16}NO_6PS$ 333.0436, found 333.0441.

4. ATH Reactions of Dimethyl 4-(*E*)-Styryl-1,2,3-oxathiazolidine-5-phosphonate 2,2-Dioxide, 4t. To the solution of **4t** (35 mg, 0.1 mmol) in EtOAc (1.0 mL) was added (*R*,*R*)-**1a** (0.5 mol %) and then HCO_2H/Et_3N (5:2, 0.1 mL) via a syringe, and the reaction mixture was stirred at room temperature for 0.5 h. The reaction mixture was diluted with EtOAc and washed with brine. The organic layer was dried over anhydrous $MgSO_4$ and concentrated to produce a mixture of **5t** and **5o** which were inseparable by silica gel column chromatography. Analyis of ^{1}H NMR and chiral HPLC of the crude product revealed that the ratio of **5t** and **5o** was 1:1 (see the Supporting Information). Combined yield 97.8 mg (97.5%). **5t**: 99% ee; Chiralpak AD-H, 10% 2-propanol/*n*-hexane, 1.5 mL/min, 215 nm, t_R(minor) = 15.2 min, t_R(major) = 16.9 min. **5o**: 94.4% ee; Chiralpak AD-H, 10% 2-propanol/*n*-hexane, 1.5 mL/min, 215 nm, t_R(minor) = 10.2 min, t_R(major) = 12.5 min.

5. Conversion of Cyclic Sulfamidate 5a to 1,2-Functionalized Phosphonates 7a and 9a. *Dimethyl N-Boc-(4S,5R)-4-phenyl-1,2,3-oxathiazolidine-5-phosphonate, N-Boc-(4S,5R)-***5a***. Prepared from*

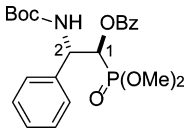
DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887−8902

*(4S,5R)-**5a** by using the procedure for (4S,5R)-**5b** from (4S,5R)-**5b** and purified by preparative TLC (CH_2Cl_2/MeOH = 20:1):*



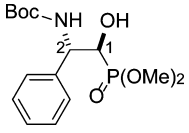
yield 70.83% (101 mg as colorless oil); $[\alpha]^{25}_D$ = +4.8 (*c* 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, 2H, *J* = 7.1 Hz), 7.37−7.41 (m, 3H), 5.43 (s, 1H), 5.2−5.23 (m, 1H), 3.71 (d, 3H, *J* = 11 Hz), 3.09 (d, 3H, *J* = 11 Hz), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 134.4, 129.4, 128.7, 128.1, 86.1, 74.9 (d, J_{CP} = 175 Hz), 62.8, 53.8 (d, J_{CP} = 6.9 Hz), 53.7 (d, J_{CP} = 6.7 Hz), 27.8; HRMS (EI) *m*/*z* calcd for $C_{15}H_{22}NO_8PS$ 407.0804, found 407.0804.

*(1S,2S)-2-(N-Boc-amino)-1-(dimethoxyphosphoryl)-2-phenylethyl Benzoate, (1S,2S)-**6a**.*



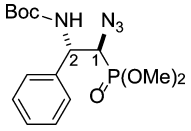
Benzoic acid (30 mg, 0.25 mmol, 2.0 equiv) and CsF (37.2 mg 0.25 mmol, 2.0 equiv) were added to a solution of (4*S*,5*R*)-***N*-Boc-5a** (50 mg, 0.12 mmol) in dry DMF (3 mL). The solution was heated to 60 °C for 3 h. Upon completion, the reaction mixture was poured into saturated NaCl solution and extracted with Et_2O. The combined organic layer was dried ($MgSO_4$) and concentrated. The resulting colorless oil was purified by flash column chromatography (silica gel, *n*-hexane/EtOAc, 1:2): yield 88.82% (49.1 mg as colorless oil); $[\alpha]^{24}_D$ = +31.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, 2H, *J* = 1.9 Hz), 7.25−7.61 (m, 8H), 5.78−5.81 (m, 1H), 5.68 (d, 1H, *J* = 8.6 Hz), 5.35 (brs, 1H), 3.7 (d, 3H, *J* = 10.85 Hz), 3.6 (d, 3H, *J* = 10 Hz), 1.35 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 154.9, 138.1, 133.7, 130.1, 130.0, 128.7, 128.6, 128.4, 128.0, 127.1, 79.9, 70.2 (d, J_{CP} = 160 Hz), 53.4 (d, J_{CP} = 108 Hz), 53.3 (d, J_{CP} = 6.3 Hz), 28.2; HRMS (EI) *m*/*z* calcd for $C_{22}H_{28}NO_7P$ 449.1603, found 449.1603.

*Dimethyl (1S,2S)-[2-(N-Boc-amino)-1-hydroxy-2-phenylethyl]-phosphonate, (1S,2S)-**7a**.*



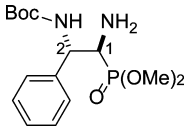
Potassium cyanide (11.6 mg, 0.2 mmol) was added to a stirred solution of (1*S*,2*S*)-**6a** (160 mg, 0.36 mmol) in MeOH (3 mL). The resulting mixture was stirred at 25 °C for 3 h. After removal of the solvent, the residue was dissolved in CH_2Cl_2 and then washed with brine. The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica-gel (*n*-hexane/EtOAc, 1:2): yield 64% (80 mg as colorless oil); $[\alpha]^{29}_D$ = +1.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25−7.39 (m, 5H), 6.01−6.08 (m, 1H), 5.1(brs, 1H), 4.37 (d, 1H, *J* = 39 Hz), 3.72−3.79 (m, 6H), 3.36 (d, 1H, *J* = 9 Hz), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 128.5, 127.8, 127. 6, 126.9, 84.3, 72.1, 53.5 (d, J_{CP} = 32 Hz), 53.3 (d, J_{CP} = 7 Hz), 29.7, 28.3; HRMS (EI) *m*/*z* calcd for $C_{15}H_{24}NO_6P$ 345.1341, found 345.1350

*Dimethyl (1S,2S)-[2-(N-Boc-amino)-1-azido-2-phenylethyl]-phosphonate, (1S,2S)-**8a**.*



NaN_3 (40 mg, 0.61 mmol, 5.0 equiv) was added in a single portion to a solution of (4*S*,5*R*)-***N*-Boc-5a** (50 mg, 0.12 mmol, 1.0 equiv) in DMF (3 mL) at 25 °C. The resulting mixture was stirred for 3 h. Upon completion, the reaction mixture was poured into saturated NaCl solution and extracted with Et_2O. The combined organic layer was dried ($MgSO_4$) and concentrated. The resulting colorless oil was purified by flash column chromatography (silica gel, CH_2Cl_2/MeOH, 20:1): yield 70.1% (26.5 mg as colorless oil); $[\alpha]^{26}_D$ = +10.4 (*c* 1.0, $CHCl_3$); IR 3409, 2108, 1683, 1507, 1247, 1033 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.39 (m, 5H), 5.61 (brs, 1H), 5.26 (s, 1H), 4.00 (d, 1H, *J* = 12 Hz), 3.76−3.86 (m, 6H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 139.4, 128.7, 128.0, 126.5, 80.0, 62.5 (d, J_{CP} = 158 Hz), 53.5 (d, J_{CP} = 16.3 Hz), 53.0, 28.3, 28.0; HRMS (EI) *m*/*z* calcd for $C_{15}H_{23}N_4O_5P$ 370.1406, found 370.1400.

*Dimethyl (1S,2S)-[2-(N-Boc-amino)-1-amino-2-phenylethyl]-phosphonate, (1S,2S)-**9a**.*



A mixture of (1*S*,2*S*)-**8a** (55 mg, 0.15 mmol) and 10% palladium on carbon (55.3 mg) in MeOH (1 mL) was stirred under an atmosphere of H_2 for 12 h. The reaction mixture was filtered over Celite and washed three times with dichloromethane. After concentration of the solution under reduced pressure, the crude product was purified by silica gel column chromatography (*n*-hexane/EtOAc, 2:1): yield 60% (31 mg as colorless oil); $[\alpha]^{29}_D$ = +4.1 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24−7.35 (m, 5H), 6.04 (brs, 1H), 5.06(brs, 1H), 3.63−3.83 (m, 6H), 3.26 (brs, 1H), 1.41 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 128.6, 128.4, 127. 6, 126.8, 126.6, 79.6, 53.1 (d, J_{CP} = 24 Hz), 29.7, 28.3; HRMS (EI) *m*/*z* calcd for $C_{15}H_{25}N_2O_5P$ 344.1501, found 344.1482.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01434.

X-ray data for *N*-Boc-(4*S*,5*R*)-**5b** (CIF)

X-ray data for (4*S*,5*R*)-**5k** (CIF)

X-ray data for (4*S*,5*R*)-**5o** (CIF)

Optimization studies and X-ray crystallographic analysis data (PDF)

^{1}H and ^{13}C NMR spectra and chiral HPLC chromatograms for new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: leehk@krict.re.kr.

Author Contributions

§Y.J.S. and J.-a.K. contributed equally to this work.

DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887−8902

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This investigation was supported financially by a grant from the Ministry of Science, ICT & Future Planning of Korea, through the National Research Foundation of Korea (NRF-2008-2004732) and the Korea Research Institute of Chemical Technology.

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DOI: 10.1021/acs.joc.5b01434
J. Org. Chem. 2015, 80, 8887−8902