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Highly Enantioselective Synthesis of β-Aminophosphinates with Two Stereogenic Atoms and Their Conversion into Optically Pure Ethyl β-Amino-*H*-phosphinates

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Abstract: The first highly stereoselective synthesis of β-aminophosphinates has been realized by the nucleophilic attack of an anion generated from ethyl (1,1-diethoxyethyl)methylphosphinate and *n*BuLi on (*S*)-*N*-(*tert*-butanesulfinyl)imines at −78 °C. Subsequent removal of the protecting groups through pivotal metal-catalyzed thiophenolysis leads to optically pure ethyl β-amino-*H*-phosphinates. During this process, a pair of diastereoisomers with different configurations on the phosphorus atom can be obtained. Until now, Ellman *N*-(*tert*-butanesulfinyl)-imines have demonstrated excellent chirality-induced activity in the syntheses of both α-aminophosphinates and β-aminophosphinates. On the other hand, the Cram rules have been successfully applied to rationalize the highly enantioselective formation of (R_C)-α-aminophosphinates and (R_C)-β-aminophosphinates, whereas the phenomenon that the two pairs of diastereoisomers could both be efficiently isolated is tentatively discussed based on X-ray crystallographic and ^{1}H NMR spectroscopic analysis.

Keywords: aminophosphinates · Cram's rules · enantioselectivity · phosphorus · synthetic methods

Introduction

It is well known that nature uses α-amino acid building blocks to assemble the proteins that make life as we know it possible.[1] Recently, however, Schepartz and co-workers have reported evidence that nature could have used a different building block—β-amino acids—and have shown that peptides assembled from β-amino acids can fold into structures much like natural proteins. Because β-peptides are not processed in the cell like natural peptides or proteins, it may be possible in the future to design β-peptides that perform better or in more locations than current protein drugs.[2]

Organophosphorus compounds are important substrates in the study of biochemical processes;[3] therefore, as isosteres of β-amino acids, a lot of general synthetic methods have existed for the preparation of β-aminophosphonic acid derivatives, until recently, including efficient asymmetric syntheses.[4] However, it is usually overlooked that β-aminophosphonic acids are dibasic acids, whereas β-amino acids are monobasic acids. From this point of view, it is obvious that β-amino-*H*-phosphinic acids are much closer in structure to β-aminocarboxylic acids. It is well documented that β-aminophosphonic acids have shown diverse and interesting biological and biochemical properties, that is, antibacterial activity, enzyme inhibition, activity as haptens for catalytic antibodies, and anti-HIV activity.[5] Moreover, organophosphinic acids are a much better lipophiles than amino acids. Consequently, it is reasonable to forecast that β-amino-*H*-phosphinic acids may demonstrate an even higher biological activity, for example, as surrogates of β-aminocarboxylic acids and then act as or better than them. Unfortunately, probably as a result of their unique structure, it was most difficult to synthesize optically pure β-amino-*H*-phosphinic acids[6] and most of the synthetic methods available usually lead to racemates.[7]

The base-catalyzed hydrophosphonylation of aldehydes and imines is one of the most convenient and widely applied methods for the construction of P–C bonds.[8,9] This approach has always been an effective way to introduce hydroxy or amino groups into target molecules and with this strategy both α-hydroxyphosphonic acids and α-hydroxyphosphinates have been successfully obtained. Until now, this useful reaction has shown a broad scope because of the large variety of substrates that can be employed.[10,11] Our

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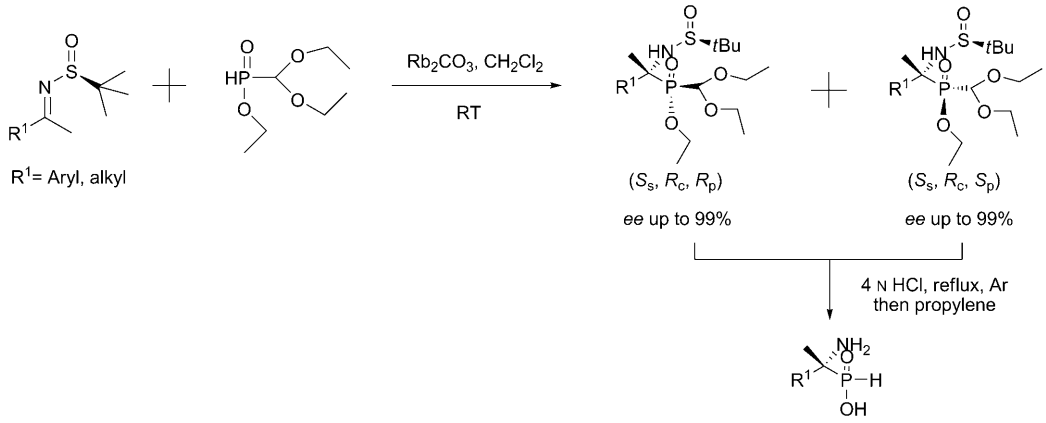


Scheme 1. Highly enantioselective synthesis of α-amino-*H*-phosphinic acids.

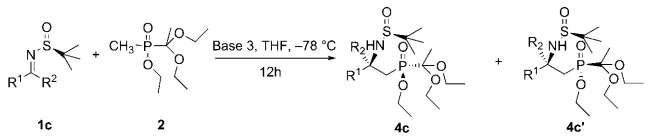
group has also been encouraged by this concept and has successfully accomplished the convenient synthesis of α-aminophosphonates.[12] Moreover, very recently, we reported the unprecedented nucleophilic attack of ethyl diethoxymethylphosphinate on Ellman *N*-(*tert*-butanesulfinyl)ketimines[13] by using the base Rb_2CO_3 followed by heating with 4N HCl to reflux, to realize the highly stereoselective and convenient synthesis of α-amino-*H*-phosphinic acids (Scheme 1).[14] This novel reaction has inaugurated a convenient route to the optically pure α-amino-*H*-phosphinic acids and makes it feasible to carry out investigations into these potential biologically active compounds. Inspired by the above successes, we further realized the importance of the synthesis of β-amino-*H*-phosphinic acids, which are always neglected by most but still have potential biological activities.

Herein, as part of our systematic efforts into the study of amino-*H*-phosphinic peptides, we disclose the highly stereoselective synthesis of β-aminophosphinates by nucleophilic attack of ethyl (diethoxyethyl)methylphosphinate on Ellman *N*-(*tert*-butanesulfinyl)imines, which can be subsequently converted into optically pure ethyl β-amino-*H*-phosphinates. During this process, a pair of diastereoisomers with different configurations at the phosphorus atom was obtained.

Results and Discussion

In the first set of experiments, (*S*)-(*tert*-butanesulfinyl)(*para*-methoxylphenyl)imine or -ketimine **1c** was chosen as the model compound to study the reaction with ethyl (diethoxyethyl)methylphosphinate (**2**). Lithium diisopropylamide (LDA) was inactive in this reaction probably as a result of the bulky diethoxymethyl group (see Table 1). When BuLi was used as the base, the situation remained unchanged when R^2 was a methyl group. It was disappointing that when the R^2 group was changed from a methyl group to a hydrogen atom, the reaction still seemed impossible. We were so astonished by the sluggish nucleophilic reagent that we decided to increase the dosage. To our delight, when the molar ratio of **2**/**1c** was doubled, the reaction ran smoothly and

Table 1. Screening of reaction conditions.



R^1=*p*-CH_3OPh
R^2=H, CH_3

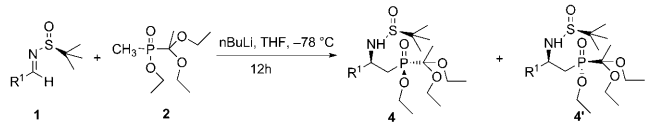
Entry	Base **3**	Molar ratio (**1c**/**2**/**3**)	R^2	Yield [%][a]		*de* [%][b]	
				4c	**4c′**	**4c**	**4c′**
1	LDA	1.0:0.8:1.2	CH_3	trace	trace	nd	nd
1	LDA	1.0:0.8:1.2	H	trace	trace	nd	nd
2	*n*BuLi	1.0:0.8:1.2	CH_3	<10	<10	nd	nd
3	*n*BuLi	1.0:0.8:1.2	H	<20	<20	nd	nd
4	*n*BuLi	0.8:1.0:1.2	H	<20	<20	nd	nd
5	*n*BuLi	1.0:2.0:2.2	H	49	48	>95	>95

[a] All the reactions were carried out at −78 °C for 12 h before quenching with saturated NH_4Cl at −78 °C. [b] The *de* values were determined by ^{31}P NMR spectroscopic analysis.

was completed within 12 h, and two isomers, which could be separated by chromatography on silica gel, were obtained. Initialized by the synthesis of α-aminophosphinates, we compared the ^1H NMR spectra of the two isomers and found that they had minor differences between $\delta = 2.0$ and 2.5 ppm, which can be assigned to the methylene groups of the two compounds. The ^{31}P NMR spectra indicated that the two isomers both possessed single configuration, that is, a single peak in the ^{31}P NMR spectra was observed.

To clarify the enantioselectivity of this reaction, further investigation into the reaction was then carried out (the results are summarized in Table 2). A variety of structurally diverse (*S*)-(*tert*-butanesulfinyl)imines **1** was treated with the ethyl (diethoxyethyl)methylphosphinate anion (generated from **2** and *n*BuLi in situ) to give the corresponding ethyl β-aryl-β-(*tert*-butylsulfinylamino) ethylphosphinates **4** and **4′** in excellent yields. The two isomers have slight differences in the ^{31}P NMR spectra but differ dramatically as far as the rotatory values are concerned, thus indicating that different configurations exist (Table 2).

Table 2. The synthesis of (S_S,R_C,S_P)-**4** and (S_S,R_C,R_P)-**4′**.



Entry	R^1	**4**		**4′**	
		Yield [%][a,b]	$[\alpha]_D^t$ [c]	Yield [%][a,b]	$[\alpha]_D^t$ [c]
1a	C_6H_5	42	+23.4	43	−9.18
		(47.84)[c]	(*c*=0.85)	(47.62)	(*c*=1.02)
1b	*p*-$CH_3C_6H_4$	47	+17.4	43	−5.65
		(47.80)	(*c*=1.02)	(47.81)	(*c*=1.04)
1c	*p*-$CH_3OC_6H_4$	49	+27.7	50	−3.47
		(47.81)	(*c*=0.75)	(47.83)	(*c*=1.02)
1d	$(CH_3)_2NC_6H_4$	49	+53.5	44	−1.02
		(47.94)	(*c*=1.05)	(45.69)	(*c*=0.93)
1e	*p*-$CH_3SC_6H_4$	46	+22.9	44	−6.74
		(47.79)	(*c*=0.65)	(44.64)	(*c*=0.96)
1f	*p*-FC_6H_4	47	+17.2	47	−3.37
		(47.72)	(*c*=1.00)	(47.41)	(*c*=0.96)
1g	*p*-ClC_6H_4	47	+12.2	48	−9.50
		(47.73)	(*c*=1.07)	(47.33)	(*c*=1.00)
1h	*p*-BrC_6H_4	47	+6.89	44	−3.50
		(47.71)	(*c*=1.00)	(47.28)	(*c*=1.03)
1i	thiophen-1-yl	48	+48.8	50	+32.8
		(47.45)	(*c*=1.04)	(47.47)	(*c*=0.97)
1j	2-naphthyl	41	+7.33	49	−7.99
		(47.96)	(*c*=1.10)	(47.88)	(*c*=1.00)
1k	biphenyl	45	+9.60	41	−6.0
		(47.79)	(*c*=1.02)	(47.63)	(*c*=1.00)
1l	2,4-dichloro-phenyl	48	+19.5	48	−47.7
		(48.09)	(*c*=1.10)	(47.56)	(*c*=1.08)
1m	tridecanyl	48	+30.4	48	+20.6
		(49.07)	(*c*=0.97)	(49.16)	(*c*=1.00)

[a] Yield of the isolated product. [b] All the optical values were measured with $CHCl_3$ as the solvent (see the Experimental Section). [c] The values in the parentheses are the yields obtained from ^{31}P NMR spectroscopic analysis, as each product gives a single peak.

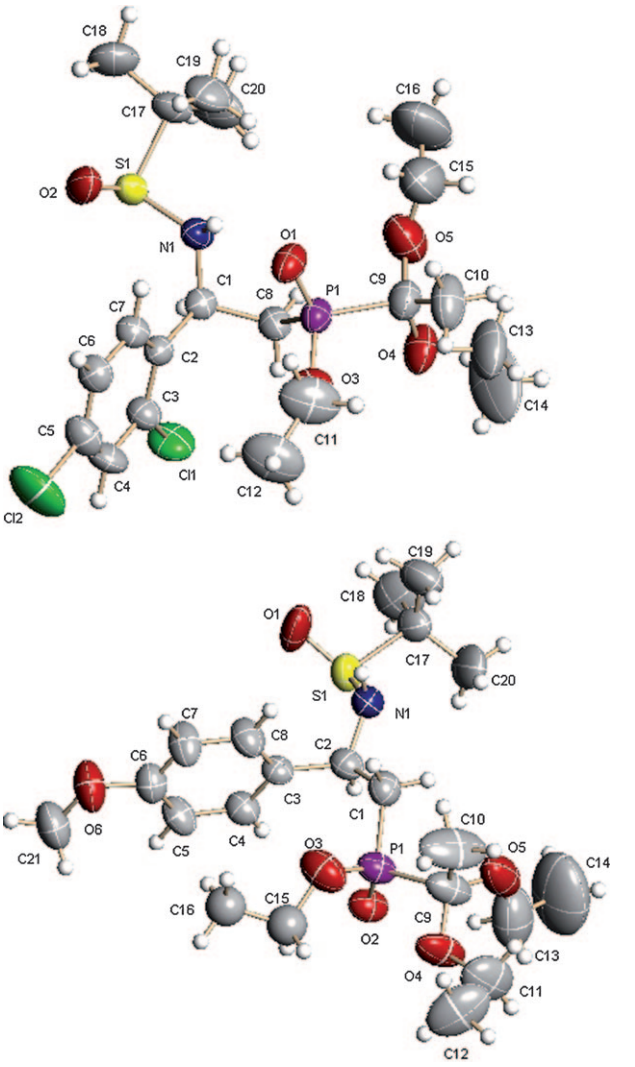


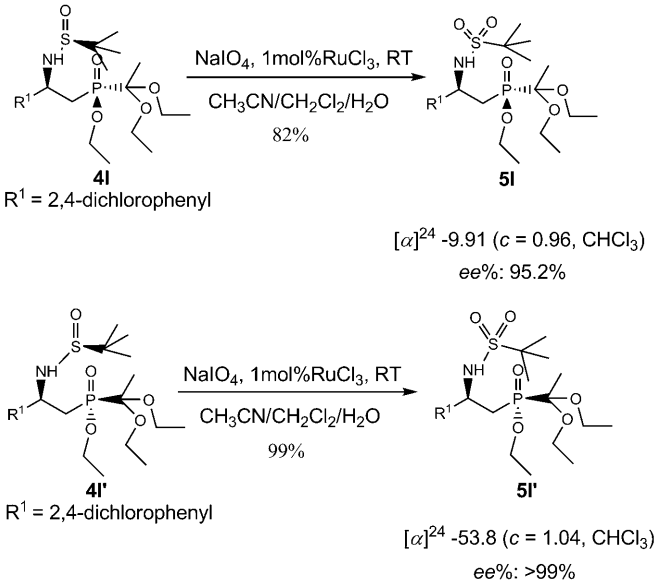
Figure 1. ORTEP drawings of (S_S,R_C,S_P)-**4l** (top) and (S_S,R_C,R_P)-**4c′** (bottom).

The structure and absolute configuration of **4l** and **4c′** were determined by single-crystal X-ray analysis (Figure 1).[15] As shown in the ORTEP drawings, it can be readily seen that the configuration of the β-C atoms in **4l** and **4c′** are both *R*, thus indicating, in combination with ^{31}P NMR spectroscopic analysis, that high enantioselectivity at the β-C atom was achieved (>95% *de*). What is more interesting is that, according to the ORTEP drawings, two isomers that differed at the phosphorus atom were again obtained just as their homologues, namely, α-aminophosphinates! (The configuration of the phosphorus atom is *S* in **4l** and *R* in **4c′**.) That is to say, in this novel reaction, the high enantioselectivities at both the β-C and P atoms were realized simultaneously, and we can still call this process "one stone, two birds". Yokomatsu and co-workers reported the synthesis of ethyl (1*R*,2*S*)-(dibenzylamino)-1-hydroxy-3-phenylpropylphosphinate and determined its relative configuration by X-ray analysis;[16] consequently, we have obtained direct experimental evidence of the absolute configuration of β-aminophosphinates to further elucidate the stereogenic nature of the phosphorus atoms.

To further determine the accurate *ee* value of the products, we oxidized (S_S,R_C,S_P)-**4l** and (S_S,R_C,R_P)-**4l′** into their corresponding sulfonylamide derivatives (R_C,S_P)-**5l** and-(R_C,R_P)-**5l′**(Scheme 2).[17,18] The high optical purity of (R_C,S_P)-**5l** and (R_C,R_P)-**5l′** were determined by HPLC (95.2 and >99% *ee*, respectively), thus indicating that this synthetic method promises to be a general and convenient approach for the preparation of enantiomerically pure β-aminophosphinates.

Unlike α-amino-*H*-phosphinic acids, β-amino-*H*-phosphinic acids are found to be more sensitive to oxidation, especially under acidic conditions. Therefore, attempts to obtain β-amino-*H*-phosphinic acids by means of hydrolysis in HCl proved to be a failure. The product could not even withstand the usual workup procedure after the reaction was completed, that is, removal of the solvent (Scheme 3).

To run the reaction under milder conditions, we decided to remove the protecting groups one by one. However, the traditional conditions seemed to be inefficient for our sub-

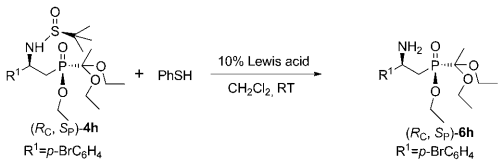


Scheme 2. Oxidation of (S_S,R_C,S_P)-**4l** and (S_S,R_C,R_P)-**4l′** into their corresponding sulfonylamide derivatives (R_C,S_P)-**5l** and (R_C,R_P)-**5l′**.

strates: attempts to remove the *tert*-butanesulfinyl group from the amino group (4N HCl in dioxane/MeOH)[19] and diethoxyethyl group from the phosphorus atom (TMSCl/EtOH/CH_2Cl_2)[20] both led to inseparable mixtures. Through several trials, we found that $BF_3{\cdot}Et_2O$ worked well for the removal of the diethoxymethyl group; however, subsequent attempts to eliminate the *tert*-butanesulfinyl group proved to be another failure (Scheme 4).

From the above trials, it seemed obvious that the removal of the *tert*-butylsulfinyl group first was indispensable. We assumed that there may be some substances generated during the reaction (e.g., acyl chloride), which led to decomposition of the product. Unfortunately, only one option remained for the removal of the *tert*-butylsulfinyl group, that is, 4N HCl in dioxane.[21] We needed to find another mild condition. Fortunately, the work of Hou and co-workers aroused our interests and afforded a mild and efficient procedure for the removal of the *para*-toluenesulfinyl group in the sulfonamide by means of thiophenolysis in the presence of a Lewis acid.[22] Considering that there may be some similarities in the chemical behavior between the *para*-toluenesulfinyl group and *tert*-butanesulfinyl group, we began to apply this strategy to our substrates (the results are summarized in Table 3).

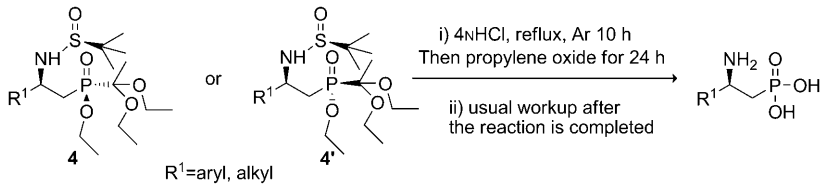
Table 3. The removal of the *tert*-butylsulfinyl group[a].



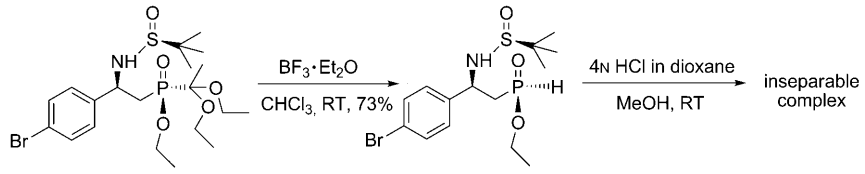
Entry	Catalyst	t [h]	Yield [%]
1	$ZnCl_2$	24	complex
2	$CuSO_4$	48	NR
3	$ZnCl_2/CuSO_4$[b]	24	complex
4	$Yb(OTf)_3$	24	<30 and complex[c]
5	$NbCl_5$	24	40 and clean[c]
6	$NbCl_5/CuSO_4$[b]	24	72[d,e]

[a] Reagents and conditions: (R_C,S_P)-**4h** (1 equiv), PhSH (3 equiv), Lewis acid (0.1 equiv), solvent: CH_2Cl_2, room temperature. [b] Both the catalysts are added as 0.1 equivalents. [c] Determined by TLC analyis. [d] Yield of the isolated product based on (R_C,S_P)-**4h**. [e] The yield of (R_C, R_P)-**6h′** was 71% based on (R_C,R_P)-**4h′**.

Reagents $ZnCl_2$ and $CuSO_4$, which demonstrated high activity towards the desulfinylation of *para*-toluenesulfinylamines, proved to be ineffective toward (R_C,S_P)-**4h** (Table 3). The excellent Lewis acid $Yb(OTf)_3$ did catalyze this reaction but the result was still far from our expectations. However, when the strong Lewis acid $NbCl_5$ was used, **6h** was obtained in only 40% yield but as a clean product after 24 hours. It is interesting that when 10 mol% $NbCl_5$ with 10 mol% $CuSO_4$ was added to the reaction system, the reaction ran smoothly and was completed within 24 h, thus resulting in 72% yield of the isolated product.[23] With the products (R_C,S_P)-**6h** and (R_C,R_P)-**6h′** bearing exposed NH_2 groups in hand, we successfully realized the synthesis of ethyl β-amino-*H*-phosphinates (Scheme 5), which also proved our assumption that the *tert*-butylsulfinyl group should be removed preferentially to avoid decomposition of the product.

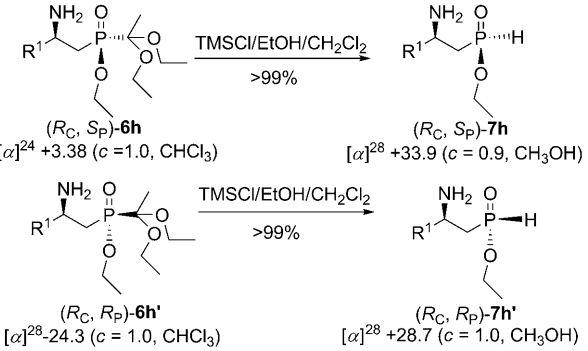


Scheme 3. Hydrolysis of β-aminophosphinates by using 4N HCl.

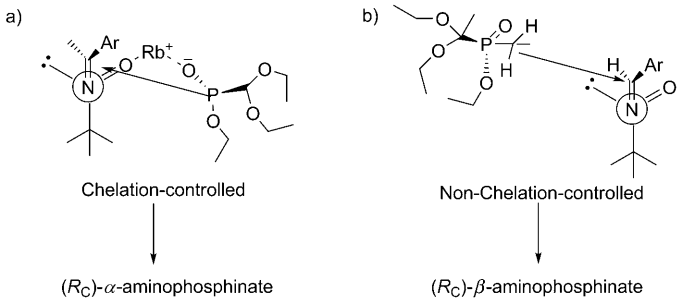


Scheme 4. Attempts to remove the protecting groups.

During the study of the removal of the protecting group, we found another interesting



Scheme 5. The final synthesis of ethyl β-amino-*H*-phosphinates ($R^1 = p$-BrC_6H_4). TMSCl = trimethylsilyl chloride.

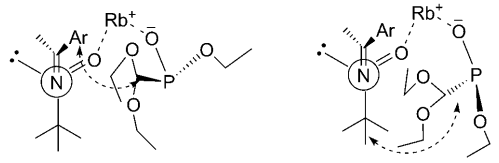


Scheme 7. Depiction of the stereoselectivities controlled by the Cram rules.

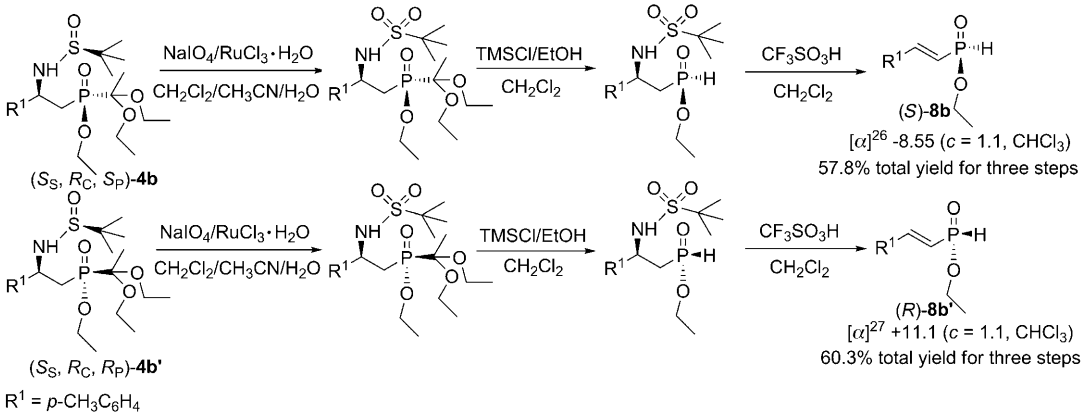
phenomenon: Although we did not obtain the desired products, the elimination products (*S*)-**8b** and (*R*)-**8b′** were obtained in three steps (Scheme 6).[24] The opposite optical rotation values demonstrated that the phosphorus atoms possessed the opposite configuration in these two compounds.

Mechanistic investigation: stereoselectivity controlled by the Cram rules: In the process of synthesizing α-amino-*H*-phosphinic acids and β-amino-*H*-phosphinic acids, we noticed that the reactions usually afforded high enantiomeric excess. Moreover, it is interesting to find that (*S*)-(*tert*-butanesulfinyl)imines as substrates afforded both R_C products of α-aminophosphinates and β-aminophosphinates. This phenomenon can be perfectly interpreted by applying the Cram rules.[13a,f,25] When (*S*)-(*tert*-butanesulfinyl)imines or -ketimines were treated with ethyl diethoxymethylphosphinate in the presence of Rb_2CO_3, the rubidium ion chelated with oxygen atoms on both the phosphoryl and sulfinyl groups, as a result of which the phosphorus atom attacked from the oxygen side to afford (R_C)-α-aminophosphinate (see Scheme 7). However, when ethyl (diethoxyethyl)methylphosphinate was used as the nucleophilic reagent, the carbanion did not chelate well with the lithium ion, so the reaction took a non-chelation-controlled form to result in (R_C)-β-aminophosphinate (see Scheme 7).

For (R_C)-α-aminophosphinates, it was also expected that enantioselectivity at the phosphorus atom could be realized; that is, instead of two, only a single phosphorus product was obtained. It can be concluded that this idea is difficult to be realized in this reaction system because the bulky diethoxymethyl group is repelled both by the aryl and *tert*-butylsulfinyl groups so that poor enantioselectivity was obtained at the phosphorus atom (see Scheme 8). Actually, in the synthesis of α-aminophosphinates, taking no account of the reaction time and yield, when a weak base was used, such as K_2CO_3, the two isomers could be obtained in the ratio of approximately 2:1 to 3:1 (see Figure 2). There was no indication that the synthesis of β-aminophosphinates involved enantioselectivity at the phosphorus atom because this atom



Scheme 8. Explanation for the poor enantioselectivity at the phosphorus atom during the formation of (R_C)-α-aminophosphinates.



Scheme 6. The unexpected reactions that led to (*S*)-**8b** and (*R*)-**8b′**. $R^1 = p$-$CH_3C_6H_4$.

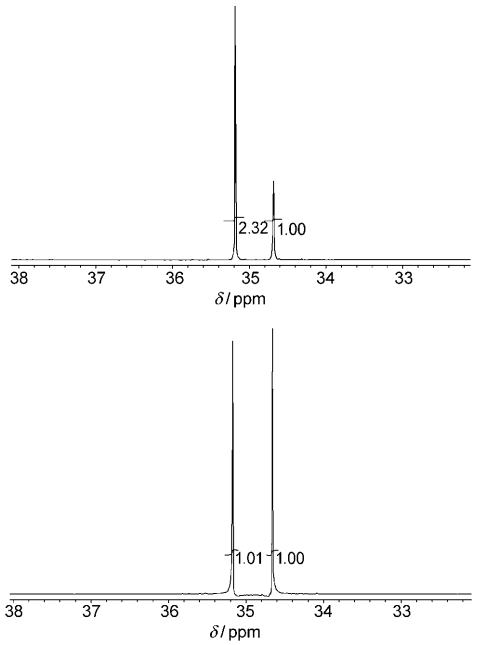


Figure 2. Top: K_2CO_3 was used as the base (the ratio of the two products was approximately 2:1 and the yield was poor (<40%), but slightly better enantioselectivity at the phosphorus atom was achieved even after 5 days). Bottom: Rb_2CO_3 was used as the base (the ratio of the two products was approximately 1:1 and the yield was excellent (99%), but no enantioselectivity at phosphorus atom was obtained within 3 days). For the structures of the two diastereoisomers, see Scheme 1 when R^1 is *p*-$OCH_3C_6H_4$.

is not involved in the core of the reaction and the material was also racemic at the phosphorus atom.

There was another phenomenon that aroused our interest: Besides the high enantioselectivity at the carbon atom and beyond our expectations, we simultaneously obtained two products that were optically pure at the phosphorus atom (see Scheme 1 and Table 2). To give a rational explanation for this outcome, we refer to the X-ray structures of these products (see Figure 3 and Figure 4). It can be clearly seen in Figure 3 that the two α-aminophosphinates formed intramolecular hydrogen bonds, which resulted in bond polarities that differed from each other to a relatively large extent. (Please pay careful attention to the different configurations at the phosphorus atoms and the formation of the hydrogen bonds in Figure 3.) However, the situation changed dramatically for the β-aminophosphinates. Probably because of the longer distance between the sulfinylamino and diethoxyethyl groups, the hydrogen atom could only form a hydrogen bond with the P=O unit. Also because the *tert*-sulfinylamino and diethoxyethyl groups are bulky, they must be located on different sides of the molecule. Therefore, the product (S_S,R_C,S_P)-**4l** formed a configuration with intramolecular hydrogen bonding and the bulky *tert*-sulfinylamino and diethoxyethyl groups on different sides. However, the situation became too difficult for (S_S,R_C,R_P)-**4c′** to form the same configuration because of distance and spatial hindrance factors, thus compelling (S_S,R_C,R_P)-**4c′** to form intermolecular hy-

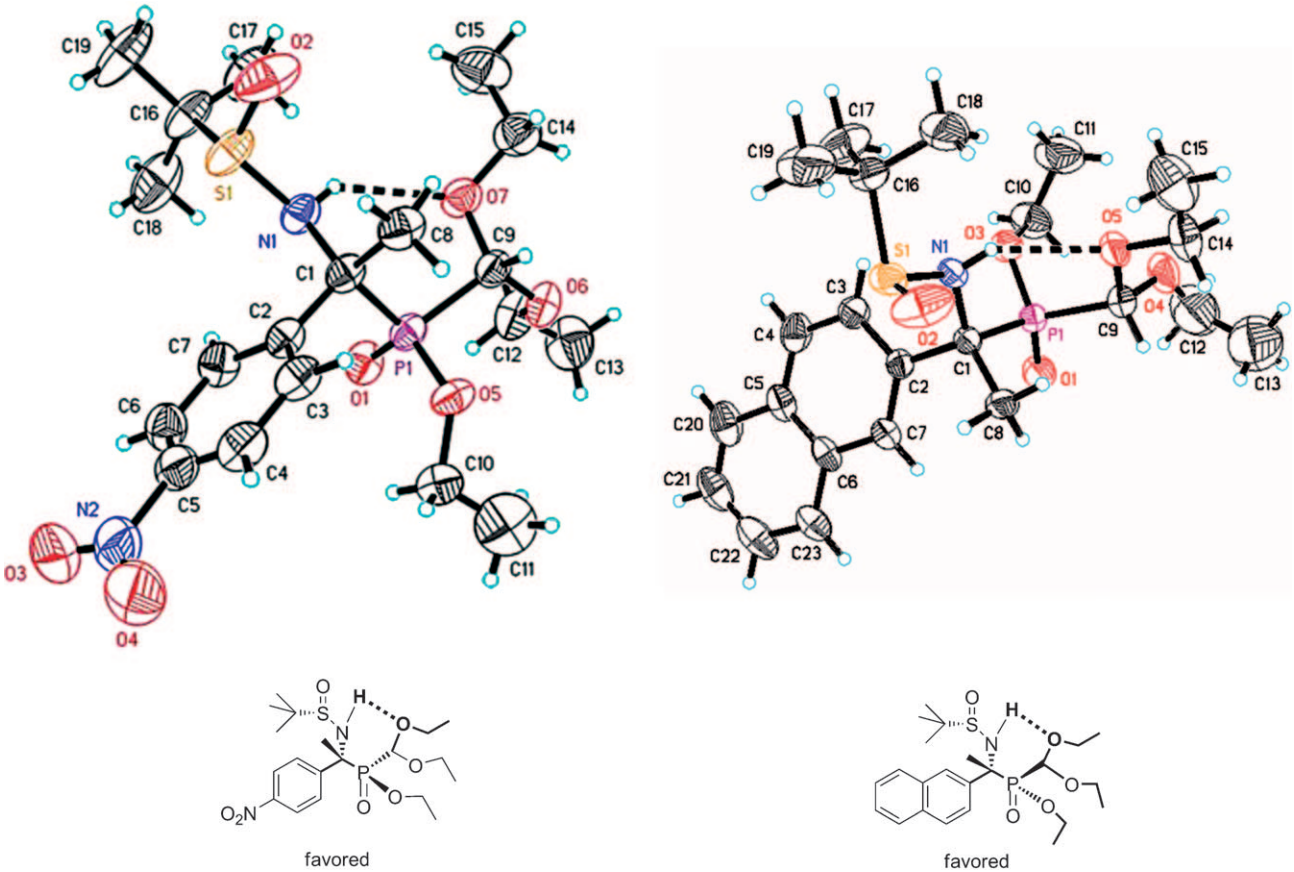


Figure 3. The X-ray structure of two α-aminophosphinates with different configurations at the phosphorus atom; left: S_S,R_C,R_P, right: S_S,R_C,S_P[26]

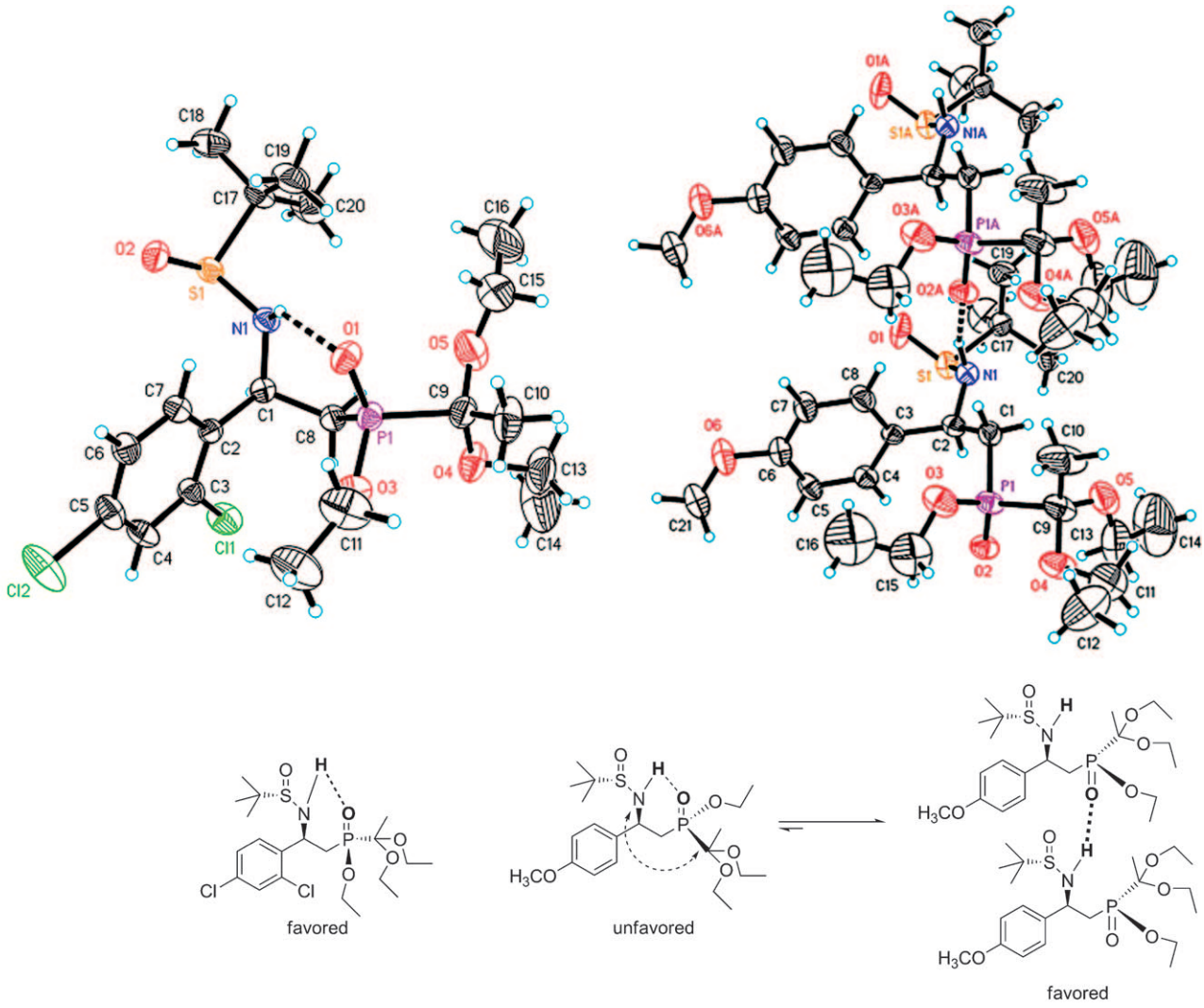


Figure 4. The X-ray structure of two β-aminophosphinates with different configurations at the phosphorus atom; left: (S_S,R_C,S_P)-**4l**, right: (S_S,R_C,R_P)-**4c′**.[15]

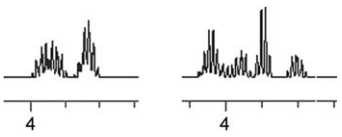


Figure 5. ^{1}H NMR spectrum of $3\times CH_2$ in (O)P(OCH_2CH$_3$) and CH-(OCH_2CH$_3$)$_2$ of (R_C)-α-aminophosphinates (R^1 = *p*-BrC_6H_4; Scheme 1). Left: S_S,R_C,R_P (two sets of peaks), right: S_S,R_C,S_P (four sets of peaks).

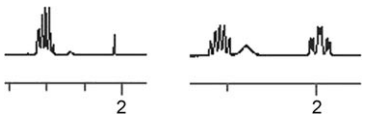


Figure 6. ^{1}H NMR spectrum of α-CH_2 of (R_C)-β-aminophosphinates (R^1 = *p*-BrC_6H_4; Table 2). Left: S_S,R_C,S_P (single set of peak), right: S_S,R_C,R_P (two sets of peaks).

drogen bonds (see Figure 4). This behavior is probably why β-aminophosphinates can be separated more readily on silica gel than α-aminophosphinates, taking no account of the material ethyl (diethoxyethyl)methylphosphinate (**2**). Although the above discussion seems to be limited to the solid phase, it is helpful for us to learn more about the interior of the molecules. We assumed that the intramolecular hydrogen bond may still exist when the molecules are surrounded by aprotic solvents.

To further understand the results of the X-ray analysis, we can turn to the ^{1}H NMR spectra of the diastereoisomers. In the ^{1}H NMR spectra, the groups near the chiral center in the two diastereoisomers, either in (R_C)-α-aminophosphinate or (R_C)-β-aminophosphinate, differ dramatically from each other, thus indicating that their ambient chemical environment also differs sharply (Figure 5 and Figure 6). This observation is in accord with the X-ray structures.

Conclusion

In summary, the nucleophilic attack of ethyl (diethoxyethyl)-methylphosphinate on Ellman *N*-(*tert*-butanesulfinyl)imines followed by subsequent removal of the protecting groups through pivotal metal-catalyzed thiophenolysis has been shown to be a highly stereoselective and convenient synthesis of β-amino-*H*-phosphinates. Because of the high similarity of β-amino-*H*-phosphinic acids to the β-aminocarboxylic acids in terms of chemical structure, namely, they are both monobasic acids, it is reasonable to look forward to the potential biological activity of the optically pure β-amino-*H*-phosphinates. Additionally, we have also demonstrated that the stereoselectivities of both α-aminophosphinates and β-aminophosphinates are perfectly consistent with our prediction based on the Cram rules. With our efforts, the optically pure α-amino-*H*-phosphinic acids and β-amino-*H*-phosphinic acids are now more accessible and the application of the optically pure amino-*H*-phosphinic acids to the synthesis of amino-*H*-phosphinic peptides is currently under investigation.

Experimental Section

General: Reactions were performed in a nitrogen or argon atmosphere, unless otherwise mentioned. All the reagents were purchased from commercial sources and used as received. THF was freshly distilled over sodium. Column chromatography was performed on silica gel (300–400 mesh). All the yields given refer to the yield of the isolated products. IR spectra were obtained on a Shimadzu IR-440 spectrometer. ^{1}H NMR spectra (400 MHz) were recorded on Bruker AM-400 spectrometer with $CDCl_3$ as the solvent and trimethylsilane (TMS) as an internal standard, unless otherwise indicated. ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AM-400 spectrometer with $CDCl_3$ as the solvent, unless otherwise indicated. ^{19}F NMR spectra (282 MHz) were recorded on a Bruker AM-300 spectrometer with $CDCl_3$ as the solvent with CF_3COOH as an external standard; the downfield shifts are designated as negative unless otherwise indicated. ^{31}P NMR (121 MHz) spectra were recorded on a Bruker AM-400 spectrometer with $CDCl_3$ as the solvent with 85% H_3PO_4 as external standard otherwise indicated. Mass spectra were performed at 2020 eV on a Hewlett-Pack 5989 A apparatus. HRMS data were recorded on a MAT 8430 spectrometer. Elemental analyses were conducted in a Heraeus Rapid CHNO apparatus. Optical rotation values were measured on a Perkin-Elmer 241M spectrometer. All the reactions were monitored by TLC.

Synthesis

(*S*)-*N*-tert-Butylsulfinylimines **1** were prepared according to reported procedures[14] and the spectra of **1a**, **1b**, **1c**, **1d**, **1f**, **1g**, **1h**, **1i**, **1j**, and **1l** are identical to reported data.[27]

(*S*)-(+)-*N*-(*para*-methylsulfylphenylidene)-*tert*-butanesulfinamide (1e): Obtained as a yellow solid; m.p. 84–86 °C; $[\alpha]_D^{26}=+21.3$ ($c=1.06$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=8.52$ (s, 1H), 7.76 (dd, $J_1=2.0$, $J_2=6.8$ Hz, 2H), 7.29 (dd, $J_1=2.0$, $J_2=6.8$ Hz, 2H), 2.53 (s, 3H), 1.26 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=162.13$ (s), 145.32 (s), 130.85 (s), 129.86 (s), 125.78 (s), 57.98 (s), 22.82 (s), 15.14 ppm (s); IR (KBr) $\tilde{\nu}=2984$, 1585, 1550, 1448, 1438, 1362, 1175, 1083 cm^{-1}; MS (ESI): *m*/*z* (%): 199.9, 256.0 $[M+H]^+$, 277.9 $[M+Na]^+$, 310.0 $[M+MeOH+Na]^+$, 319.0; elemental analysis (%) calcd for $C_{12}H_{17}NOS_2$: C 56.43, H 6.71, N 5.48; found: C 56.30, H 6.61, N 5.38.

(*S*)-(+)-*N*-(*para*-Biphenylidene)-*tert*-butanesulfinamide (1k): Obtained as a yellow solid; m.p. 111–112 °C; $[\alpha]_D^{26}=+13.4$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=8.63$ (s, 1H), 7.92 (dd, $J_1=2.0$, $J_2=6.8$ Hz, 2H), 7.69 (dd, $J_1=1.6$, $J_2=6.8$ Hz, 2H), 7.62 (m, 2H), 7.46 (td, $J_1=1.2$, $J_2=8.4$ Hz, 2H), 7.40 (m, 1H), 1.28 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=162.26$ (s), 145.16 (s), 139.95 (s), 132.97 (s), 129.85 (s), 128.94 (s), 128.14 (s), 127.60 (s), 127.19 (s), 57.83 (s), 22.61 ppm (s); IR (KBr): $\tilde{\nu}=2983$, 1593, 1556, 1486, 1450, 1363, 1184, 1082, 1008 cm^{-1}; MS (ESI): *m*/*z* (%): 230.0, 286.0 $[M+H]^+$, 308.1 $[M+Na]^+$, 340.0 $[M+MeOH+Na]^+$, 349.0; elemental analysis (%) calcd for $C_{17}H_{19}NOS$: C 71.54, H 6.71, N, 4.91; found: C 71.56; H 6.81, N 4.77.

(*S*)-(+)-*N*-(Tridecanylidene)-*tert*-butanesulfinamide (1m): Obtained as a colorless oil; $[\alpha]_D^{26}=+116.1$ ($c=1.06$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=8.04$ (t, $J=4.8$ Hz, 1H), 2.48 (m, 2H), 1.58 (m, 2H), 1.27 (m, 27H), 0.85 ppm (d, $J=6.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.01$ (s), 56.58 (s), 36.32 (s), 32.12 (s), 29.63 (s), 25.71 (s), 22.89 (s), 22.54 (s), 14.31 ppm (s); IR (KBr): $\tilde{\nu}=2926$, 2856, 1623, 1459, 1363, 1226, 1186, 1089 cm^{-1}; MS (ESI): *m*/*z* (%): 246.1, 302.2 $[M+H]^+$, 334.2 $[M+Na]^+$, 356.2 $[M+MeOH+Na]^+$, 388.2 $[M+2MeOH+Na]^+$, 397.1; elemental analysis (%) calcd for $C_{17}H_{35}NOS$: C 67.72, H 11.70, N 4.65; found: C 67.76, H 11.71, N 4.83.

Ethyl 1,1-(diethoxyethyl)methylphosphinate (2): Prepared according to ref. [20,28]. B.p. 70–75 °C/0.05 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=4.21$ (m, 2H), 3.70 (m, 4H), 1.51 (d, $J=7.2$ Hz, 3H), 1.47 (d, $J=9.9$ Hz, 3H), 1.33 (t, $J=7.2$ Hz, 3H), 1.22 ppm (t, $J=7.2$ Hz, 6H); ^{31}P NMR (121 MHz, $CHCl_3$): $\delta=49.00$ ppm (s).

Typical procedure for the stereoselective synthesis of ethyl −1′,1′-diethoxyethyl-(S_S,S_C,R or S_P)-(+ or −)-2-(*tert*-butylsulfinylamino)-2-aryl or alkyl ethylphosphinate (S_S,R_C,S_P)-4 and (S_S,R_C,R_P)-4′: A Schlenk flask (20 mL) was flushed with argon and ethyl (diethoxymethyl)methylphosphinate (**2**; 0.2 mL, 224 mg, 1 mmol) in freshly distilled THF (3 mL) was added. The resulting mixture was cooled to −78 °C and *n*BuLi (0.75 mL, 1.2 mmol) was added dropwise. After stirring at this temperature for approximately 1 h, a (*S*)-*N*-*tert*-butylsulfinyl imine **1** (0.5 mmol) in freshly distilled THF (2 mL) was carefully added, with the temperature kept below −70 °C. The mixture was then stirred for 12 h at −78 °C. TLC analysis indicated that the reaction had gone to completion. Saturated NH_4Cl solution (5 mL) was added at −78 °C to quench the reaction. The whole mixture was warmed to room temperature, the organic layer was separated, and the aqueous layer was washed with Et_2O (3×10 mL). The organic layers were washed with brine and dried over anhydrous Na_2SO_4 overnight. The solvent was removed under reduced pressure and the residue was subjected to chromatography on silica gel (300–400 mesh, EtOAc/CH_2Cl_2/petroleum ether = 2:1:1 to EtOAc/CH_2Cl_2 = 2:1 with 1% NEt_3) to afford pure (S_S,R_C,S_P)-**4** and (S_S,R_C,R_P)-**4′**.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-phenylethylphosphinate (4a): Obtained as a colorless oil (91 mg, 42%); $[\alpha]_D^{25}=+23.4$ ($c=0.85$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.43$ (d, $J=6.9$ Hz, 2H), 7.35 (d, $J=6.9$ Hz, 2H), 7.27 (m, 1H), 5.40 (d, $J=4.8$ Hz, 1H), 4.91 (m, 1H), 4.00 (m, 2H), 3.67 (m, 4H), 2.47 (m, 2H), 1.46 (d, $J=11.4$ Hz, 3H), 1.21 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=141.17$ (d, $J=7.00$ Hz), 128.47 (s), 127.75 (s), 127.46 (s), 101.16 (d, $J=142.9$ Hz), 61.54 (d, $J=7.3$ Hz), 58.20 (d, $J=5.6$ Hz), 57.86 (d, $J=6.8$ Hz), 56.13 (s), 55.38 (d, $J=4.4$ Hz), 33.26 (d, $J=81.2$ Hz), 22.50 (s), 19.82 (d, $J=12.1$ Hz), 16.33 (d, $J=5.7$ Hz), 15.42 (s), 15.28 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.84$ ppm (s); IR (KBr): $\tilde{\nu}=3457$, 3227, 2980, 1456, 1392, 1299, 1226, 1186, 1158, 1038 cm^{-1}; MS (ESI): *m*/*z* (%): 456.1 $[M+Na]^+$; HRMS (ESI): *m*/*z*: calcd for $C_{20}H_{36}NO_5PSNa$: 456.1944 $[M^++23]$; found: 456.1938.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-phenylethylphosphinate (4a′): Obtained as a colorless oil (93 mg, 43%); $[\alpha]_D^{23}=-9.18$ ($c=1.02$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.46$ (m, 2H), 7.34 (m, 3H), 5.13 (d, $J=2.4$ Hz, 1H), 4.80 (m, 1H), 4.09 (m, 2H), 3.69 (m, 4H), 2.66 (m, 1H), 2.09 (m, 1H), 1.44 (d, $J=11.7$ Hz, 3H), 1.19 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=141.10$ (d, $J=9.7$ Hz), 128.56 (s, 2C), 128.01 (s), 127.62 (s), 101.00 (d, $J=140.0$ Hz), 61.76 (d, $J=6.7$ Hz), 57.99 (d, $J=4.5$ Hz), 57.76 (d, $J=7.4$ Hz), 56.09 (s), 54.90 (d, $J=4.4$ Hz), 32.82 (d, $J=82.7$ Hz), 22.37 (s), 20.20 (d, $J=12.7$ Hz), 16.36 (d, $J=5.2$ Hz), 15.36 (s), 15.17 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.62$ ppm (s); IR (KBr): $\tilde{\nu}=3227$, 2980, 1456, 1391, 1226, 1185, 1156, 1039 cm^{-1}; MS (ESI): *m*/*z* (%): 456.1 $[M+Na]^+$;

HRMS (ESI): *m/z*: calcd for $C_{20}H_{36}NO_5PSNa$: 456.1944 [M^++23]; found: 456.1945.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-methylphenyl)ethylphosphinate (4b): Obtained as a colorless oil (105 mg, 47%); $[\alpha]_D^{25}=+17.4$ ($c=1.02$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.29$ (d, $J=7.8$ Hz, 2H), 7.13 (d, $J=8.1$ Hz, 2H), 5.30 (d, $J=5.6$ Hz, 1H), 4.83 (m, 1H), 4.02 (m, 2H), 3.63 (m, 4H), 2.42 (m, 2H), 2.29 (s, 3H), 1.43 (dd, $J_1=15.2$, $J_2=4.5$ Hz, 3H), 1.15 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.14$ (d, $J=10.4$ Hz), 137.80 (s), 129.29 (s), 127.58 (s), 101.06 (d, $J=140.0$ Hz), 61.81 (d, $J=6.7$ Hz), 58.03 (d, $J=5.2$ Hz), 57.80 (d, $J=6.7$ Hz), 56.09 (s), 54.70 (d, $J=4.5$ Hz), 33.00 (d, $J=82.6$ Hz), 22.44 (s), 21.08 (s), 20.27 (d, $J=12.7$ Hz), 16.43 (d, $J=5.2$ Hz), 15.41 (s), 15.23 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=$ 47.80 ppm (s); IR (KBr): $\tilde{\nu}=3226$, 2980, 1516, 1457, 1390, 1225, 1185, 1155, 1038 cm^{-1}; MS (ESI): *m/z* (%): 470.2 [M+Na]$^+$; elemental analysis (%) calcd for $C_{21}H_{38}NO_5PS$: C 56.35, H 8.56, N 3.13; found: C 56.55, H 8.47, N 3.02.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-methylphenyl)ethylphosphinate (4b′): Obtained as a colorless oil (96 mg, 43%); $[\alpha]_D^{25}=-5.65$ ($c=1.04$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.30$ (d, $J=8.0$ Hz, 2H), 7.13 (d, $J=8.0$ Hz, 2H), 5.13 (d, $J=2.8$ Hz, 1H), 4.70 (d, $J=4.0$ Hz, 1H), 4.06 (m, 2H), 3.63 (m, 4H), 2.59 (m, 1H), 2.29 (s, 3H), 2.04 (m, 1H), 1.44 (d, $J=8.7$ Hz, 3H), 1.14 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.18$ (d, $J=$ 10.4 Hz), 137.52 (s), 129.21 (s), 127.44 (s), 101.23 (d, $J=142.9$ Hz), 61.58 (d, $J=7.5$ Hz), 58.22 (d, $J=5.2$ Hz), 57.88 (d, $J=6.7$ Hz), 56.08 (s), 55.20 (d, $J=4.4$ Hz), 33.33 (d, $J=80.4$ Hz), 22.54 (s), 21.09 (s), 19.90 (d, $J=$ 11.9 Hz), 16.40 (d, $J=5.9$ Hz), 15.46 (s), 15.31 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.81$ ppm (s); IR (KBr): $\tilde{\nu}=3234$, 2980, 1226, 1186, 1158, 1040 cm^{-1}; MS (ESI): *m/z* (%): 470.1 [M+Na]$^+$; elemental analysis (%) calcd for $C_{21}H_{38}NO_5PS$: C 56.35, H 8.56, N 3.13; found: C 56.58, H 8.59, N 3.23.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-methoxylphenyl)ethylphosphinate (4c): Obtained as a colorless oil (113 mg, 49%); $[\alpha]_D^{25}=+27.7$ ($c=0.75$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.30$ (d, $J=8.7$ Hz, 2H), 6.83 (d, $J=8.7$ Hz, 2H), 5.26 (d, $J=4.2$ Hz, 1H), 4.81 (m, 1H), 4.00 (m, 2H), 3.73 (s, 3H), 3.62 (m, 4H), 2.38 (m, 2H), 1.42 (d, $J=11.4$ Hz, 3H), 1.14 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=159.05$ (s), 133.09 (d, $J=9.7$ Hz), 128.57 (d, $J=8.2$ Hz), 113.81 (d, $J=11.9$ Hz), 101.12 (d, $J=142.9$ Hz), 61.51 (d, $J=7.5$ Hz), 58.11 (d, $J=5.3$ Hz), 57.78 (d, $J=6.7$ Hz), 55.92 (s), 55.11 (s), 54.81 (d, $J=3.7$ Hz), 33.18 (d, $J=81.1$ Hz), 22.44 (s), 19.77 (d, $J=$ 12.7 Hz), 16.32 (d, $J=6.0$ Hz), 15.35 (s), 15.21 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.81$ ppm (s); IR (KBr): $\tilde{\nu}=3217$, 2979, 1614, 1517, 1390, 1249, 1183, 1078, 1031 cm^{-1}; MS (ESI): *m/z* (%): 486.1 [M+Na]$^+$; elemental analysis (%) calcd for $C_{21}H_{38}NO_6PS$: C 54.41, H 8.26, N 3.02; found: C 54.28, H 8.36, N 3.03.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-methoxylphenyl)ethylphosphinate (4c′): Obtained as a white solid (115 mg, 49%); m.p. 112–113 °C; $[\alpha]_D^{24}=-3.47$ ($c=1.02$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.38$ (d, $J=9.0$ Hz, 2H), 6.90 (d, $J=9.0$ Hz, 2H), 5.13 (d, $J=2.7$ Hz, 1H), 4.76 (m, 1H), 4.11 (m, 2H), 3.81 (s, 3H), 3.68 (m, 4H), 2.36 (m, 1H), 2.06 (m, 1H), 1.49 (d, $J=11.7$ Hz, 3H), 1.23 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=159.38$ (s), 133.12 (d, $J=8.7$ Hz), 128.93 (s), 113.99 (s), 101.12 (d, $J=140.2$ Hz), 61.88 (d, $J=7.1$ Hz), 58.10 (d, $J=3.9$ Hz), 57.87 (d, $J=6.9$ Hz), 56.08 (s), 55.25 (s), 54.37 (d, $J=3.5$ Hz), 32.90 (d, $J=82.3$ Hz), 22.52 (s), 20.33 (d, $J=$ 12.1 Hz), 16.52 (d, $J=5.1$ Hz), 15.48 (s), 15.29 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.83$ ppm (s); IR (KBr): $\tilde{\nu}=3217$, 2978, 1614, 1517, 1250, 1183, 1078, 1030 cm^{-1}; MS (ESI): *m/z* (%): 486.3 [M+Na]$^+$; elemental analysis (%) calcd for $C_{21}H_{38}NO_6PS$: C 54.41, H 8.26, N 3.02; found: C 54.31, H 8.16, N 2.95.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-dimethylamino)ethylphosphinate (4d): Obtained as a light-yellow oil (117 mg, 49%); $[\alpha]_D^{24}=+53.5$ ($c=1.05$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.27=$(d, $J=8.7$ Hz, 2H), 6.69 (d, $J=9.0$ Hz, 2H), 5.20 (d, $J=3.6$ Hz, 1H), 4.79 (m, 1H), 4.09 (m, 2H), 3.67 (m, 4H), 2.92 (s, 6H), 2.51 (m, 1H), 2.33 (m, 1H), 1.46 (d, $J=11.1$ Hz, 3H), 1.20 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=149.84$ (s), 128.25 (d, $J=$ 10.5 Hz), 128.03 (d, $J=11.9$ Hz), 111.98 (d, $J=6.7$ Hz), 100.95 (d, $J=$ 142.9 Hz), 61.23 (d, $J=6.7$ Hz), 57.89 (d, $J=6.0$ Hz), 57.53 (d, $J=7.5$ Hz), 55.54 (s), 54.62 (d, $J=3.7$ Hz), 40.17 (s), 33.03 (d, $J=80.4$ Hz), 22.27 (s), 19.61 (d, $J=12.0$ Hz), 16.19 (d, $J=6.0$ Hz), 15.16 (s), 15.00 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.94$ ppm (s); IR (KBr): $\tilde{\nu}=3213$, 2979, 1616, 1524, 1476, 1363, 1222, 1185, 1116, 1070, 1037 cm^{-1}; MS (ESI): *m/z* (%): 499.2 [M+Na]$^+$; HRMS (ESI): *m/z*: calcd for $C_{22}H_{41}N_2O_5PSNa$: 499.2366 [M^++23]; found: 499.2361; elemental analysis (%) calcd for $C_{22}H_{41}N_2O_5PS$: C 55.44, H 8.67, N 5.88; found: C 55.10, H 9.15, N 5.73.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-dimethylamino)ethylphosphinate 4d′: Obtained as a light-brown solid (105 mg, 44%); m.p. 57–59 °C; $[\alpha]_D^{24}=-1.02$ ($c=0.93$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.24$ (d, $J=8.1$ Hz, 2H), 6.66 (d, $J=8.4$ Hz, 2H), 5.12 (d, $J=0.9$ Hz, 1H), 4.64 (m, 1H), 4.05 (m, 2H), 3.61 (m, 4H), 2.88 (s, 6H), 2.59 (m, 1H), 1.96 (m, 1H), 1.43 (d, $J=11.1$ Hz, 3H), 1.13 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=150.02$ (s), 128.24 (s), 128.05 (s), 112.07 (s), 100.82 (d, $J=138.5$ Hz), 61.50 (d, $J=$ 6.7 Hz), 57.73 (d, $J=5.2$ Hz), 57.50 (d, $J=6.7$ Hz), 55.64 (s), 54.08 (d, $J=$ 4.5 Hz), 40.18 (s), 32.65 (d, $J=81.9$ Hz), 22.25 (s), 20.03 (d, $J=12.7$ Hz), 16.23 (d, $J=5.2$ Hz), 15.16 (s), 14.97 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=45.69$ ppm (s); IR (KBr): $\tilde{\nu}=3215$, 2978, 1616, 1525, 1362, 1223, 1186, 1167, 1038 cm^{-1}; MS (ESI): *m/z* (%): 499.2 [M+Na]$^+$; elemental analysis (%) calcd for $C_{22}H_{41}N_2O_5PS$: C 55.44, H 8.67, N 5.88; found: C 55.19, H 8.77, N 5.89.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-methylsulfylphenyl)ethylphosphinate (4e): Obtained as a colorless oil (110 mg, 46%); $[\alpha]_D^{25}=+23.4$ ($c=0.85$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.37$ (d, $J=8.1$ Hz, 2H), 7.25 (d, $J=8.7$ Hz, 2H), 5.40 (d, $J=4.5$ Hz, 1H), 4.88 (m, 1H), 4.05 (m, 2H), 3.69 (m, 4H), 2.53 (s, 3H), 2.43 (m, 2H), 1.48 (d, $J=11.1$ Hz, 3H), 1.25 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.04$ (s), 137.97 (d, $J=4.0$ Hz), 127.96 (s), 126.55 (s), 101.16 (d, $J=143.3$ Hz), 61.60 (d, $J=6.9$ Hz), 58.18 (d, $J=$ 5.6 Hz), 57.87 (d, $J=6.8$ Hz), 56.12 (s), 55.04 (d, $J=4.4$ Hz), 33.13 (d, $J=$ 80.7 Hz), 22.50 (s), 19.82 (d, $J=11.7$ Hz), 16.35 (d, $J=5.7$ Hz), 15.71 (s), 15.41 (s), 15.27 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.79$ ppm (s); IR (KBr): $\tilde{\nu}=3457$, 3230, 2979, 1477, 1444, 1391, 1228, 1186, 1158, 1039 cm^{-1}; MS (ESI): *m/z* (%): 502.1 [M+Na]$^+$; HRMS (ESI): *m/z*: calcd for $C_{21}H_{38}NO_5PS_2Na$: 502.1821 [M^++23]; found: 502.1823.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-methylsulfylphenyl)ethylphosphinate (4e′): Obtained as a white solid (105 mg, 44%); m.p. 99—100 °C; $[\alpha]_D^{22}=-9.18$ ($c=1.02$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.33$ (d, $J=8.0$ Hz, 2H), 7.20 (d, $J=8.4$ Hz, 2H), 5.13 (d, $J=2.0$ Hz, 1H), 4.70 (m, 1H), 4.06 (m, 2H), 3.62 (m, 4H), 2.58 (m, 1H), 2.42 (s, 3H), 2.01 (td, $J_1=4.4$, $J_2=13.8$ Hz, 1H), 1.44 (d, $J=12.0$ Hz, 3H), 1.16 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.42$ (s), 137.90 (d, $J=9.7$ Hz), 128.14 (s), 126.60 (s), 101.05 (d, $J=140.0$ Hz), 61.87 (d, $J=6.7$ Hz), 58.05 (d, $J=5.2$ Hz), 57.82 (d, $J=$ 6.7 Hz), 56.14 (s), 54.56 (d, $J=4.4$ Hz), 32.83 (d, $J=82.6$ Hz), 22.43 (s), 20.26 (d, $J=12.6$ Hz), 16.44 (d, $J=5.2$ Hz), 15.65 (s), 15.42 (s), 15.23 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.64$ ppm (s); IR (KBr): $\tilde{\nu}=3220$, 3188, 2978, 1600, 1498, 1441, 1408, 1359, 1236, 1217, 1076, 1035 cm^{-1}; MS (ESI): *m/z* (%): 502.1 [M+Na]$^+$; HRMS (ESI): *m/z*: calcd for $C_{21}H_{38}NO_5PS_2Na$: 502.1821 [M^++23]; found: 502.1820.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-fluorophenyl)ethylphosphinate (4f): Obtained as a colorless oil (106 mg, 47%); $[\alpha]_D^{24}=+17.2$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.32$ (m, 2H), 6.97 (t, $J=8.8$ Hz, 2H), 5.41 (d, $J=$ 5.2 Hz, 1H), 4.85 (m, 1H), 3.97 (m, 2H), 3.89 (m, 1H), 3.63 (m, 3H), 2.36 (m, 2H), 1.42 (d, $J=24.8$ Hz, 3H), 1.18 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=162.11$ (d, $J=244.9$ Hz), 136.96 (d, $J=9.7$ Hz), 129.09 (d, $J=8.2$ Hz), 115.19 (d, $J=21.6$ Hz), 101.07 (d, $J=143.6$ Hz), 61.52 (d, $J=6.7$ Hz), 58.11 (d, $J=5.2$ Hz), 57.81 (d, $J=6.7$ Hz), 56.06 (s), 54.85 (d, $J=4.4$ Hz), 33.13 (d, $J=81.2$ Hz), 22.42 (s), 19.71 (d, $J=$ 11.9 Hz), 16.25 (d, $J=5.1$ Hz), 15.32 (s), 15.19 ppm (s); ^{19}F NMR (282 MHz, $CHCl_3$): $\delta=-110.41$ ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.72$ ppm (s); IR (KBr): $\tilde{\nu}=3241$, 2980, 1605, 1512, 1476, 1392, 1226, 1161, 1039 cm^{-1} (s); MS (ESI): *m/z* (%): 474.1 [M+Na]$^+$; elemental anal-

ysis (%) calcd for $C_{20}H_{35}FNO_5PS$: C 53.20, H 7.81, N 3.10; found: C 53.07, H, 8.06, N 2.82.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-fluorophenyl)ethylphosphinate (4f′): Obtained as a white solid (106 mg, 47%); m.p. 88—90°C; $[\alpha]_D^{24}=-3.37$ ($c=0.96$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.33$ (m, 2H), 7.00 (t, $J=8.8$ Hz, 2H), 5.10 (d, $J=2.8$ Hz, 1H), 4.73 (m, 1H), 4.05 (m, 2H), 3.63 (m, 4H), 2.58 (m, 1H), 2.00 (m, 1H), 1.52 (d, $J=8.7$ Hz, 3H), 1.14 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=162.35$ (d, $J=245.6$ Hz), 136.89 (d, $J=9.7$ Hz), 129.41 (d, $J=8.2$ Hz), 115.44 (d, $J=21.6$ Hz), 101.03 (d, $J=140.7$ Hz), 61.86 (d, $J=6.7$ Hz), 58.06 (d, $J=5.2$ Hz), 57.82 (d, $J=6.7$ Hz), 56.11 (s), 54.33 (d, $J=4.5$ Hz), 32.88 (d, $J=82.7$ Hz), 22.39 (s), 20.22 (d, $J=13.4$ Hz), 16.40 (d, $J=5.2$ Hz), 15.39 (s), 15.19 ppm (s); ^{19}F NMR (282 MHz, $CDCl_3$): $\delta=-109.74$ ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.41$ ppm (s); IR (KBr): $\tilde{\nu}=3187$, 2978, 1607, 1515, 1359, 1218, 1163, 1076, 1035 cm^{-1} (s); MS (ESI): m/z (%): 474.1 $[M+Na]^+$; elemental analysis (%) calcd for $C_{20}H_{35}FNO_5PS$: C 53.20, H 7.81, N 3.10; found: C 53.03, H 7.69, N 3.07.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-chlorophenyl)ethylphosphinate (4g): Obtained as a colorless oil (110 mg, 47%); $[\alpha]_D^{24}=+12.2$ ($c=1.07$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.36$ (d, $J=8.4$ Hz, 2H), 7.29 (d, $J=8.4$ Hz, 2H), 5.47 (d, $J=5.2$ Hz, 1H), 4.87 (m, 1H), 3.99 (m, 2H), 3.64 (m, 4H), 2.37 (m, 2H), 1.44 (d, $J=15.2$ Hz, 3H), 1.15 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=139.73$ (d, $J=8.9$ Hz), 133.45(s), 128.84 (s), 128.53 (s), 101.09 (d, $J=142.9$ Hz), 61.61 (d, $J=6.7$ Hz), 58.16 (d, $J=6.0$ Hz), 57.86 (d, $J=6.7$ Hz), 56.18 (s), 54.91 (d, $J=3.4$ Hz), 33.00 (d, $J=81.1$ Hz), 22.45 (s), 19.74 (d, $J=12.6$ Hz), 16.26 (d, $J=5.2$ Hz), 15.37 (s), 15.23 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.73$ ppm (s); IR (KBr): $\tilde{\nu}=3236$, 2980, 2233, 1494, 1444, 1391, 1224, 1186, 1039 cm^{-1}; MS (ESI): m/z (%): 490.1 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{20}H_{35}NO_5PSClNa$: 490.1554 $[M^++23]$; found: 490.1556.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-chlorophenyl)ethylphosphinate (4g′): Obtained as a white solid (112 mg, 48%); m.p. 74–75°C; $[\alpha]_D^{24}=-9.50$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.36$ (d, $J=8.8$ Hz, 2H), 7.29 (t, $J=8.8$ Hz, 2H), 5.14 (d, $J=3.2$ Hz, 1H), 4.72 (m, 1H), 4.06 (m, 2H), 3.63 (m, 4H), 2.57 (m, 1H), 2.01 (m, 1H), 1.44 (d, $J=12.0$ Hz, 3H), 1.17 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=139.66$ (d, $J=9.6$ Hz), 133.78 (s), 129.05 (s), 128.72 (s), 101.00 (d, $J=140.7$ Hz), 61.89 (d, $J=6.7$ Hz), 58.05 (d, $J=5.2$ Hz), 57.81 (d, $J=7.5$ Hz), 56.17 (s), 54.41 (d, $J=3.7$ Hz), 32.75 (d, $J=82.7$ Hz), 22.35 (s), 20.19 (d, $J=12.7$ Hz), 16.37 (d, $J=5.2$ Hz), 15.36 (s), 15.17 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.33$ ppm (s); IR (KBr): $\tilde{\nu}=3219$, 2980, 2233, 1493, 1444, 1391, 1225, 1185, 1155, 1090, 1037 cm^{-1}; MS (ESI): m/z (%): 490.0 $[M+Na]^+$, 548.6 $[M+K]^+$; HRMS (ESI): m/z: calcd for $C_{20}H_{35}NO_5PSClNa$: 490.1554 $[M^++23]$; found: 490.1560.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(*para*-bromophenyl)ethylphosphinate (4h): Obtained as a colorless oil (120 mg, 47%); $[\alpha]_D^{22}=+6.89$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.45$ (d, $J=8.4$ Hz, 2H), 7.30 (d, $J=8.4$ Hz, 2H), 5.48 (d, $J=5.6$ Hz, 1H), 4.85 (m, 1H), 3.97 (m, 2H), 3.64 (m, 4H), 2.38 (m, 2H), 1.43 (d, $J=11.2$ Hz, 3H), 1.17 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=140.31$ (s, $J=9.7$ Hz), 131.53 (s), 129.22 (s), 121.65 (s), 101.13 (d, $J=143.6$ Hz), 61.57 (d, $J=7.4$ Hz), 58.20 (d, $J=6.0$ Hz), 57.91 (d, $J=6.7$ Hz), 56.24 (s), 55.00 (d, $J=4.5$ Hz), 33.00 (d, $J=81.9$ Hz), 22.49 (s), 19.79 (d, $J=11.9$ Hz), 16.30 (d, $J=5.2$ Hz), 15.41 (s), 15.28 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.71$ ppm (s); IR (KBr): $\tilde{\nu}=3235$, 2979, 2231, 1489, 1391, 1365, 1224, 1186, 1038 cm^{-1}; MS (ESI): m/z (%): 534.1 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{20}H_{35}NO_5PSBrNa$: 534.1049 $[M^++23]$; found: 534.1058.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(*para*-bromophenyl)ethylphosphinate (4h′): Obtained as a white solid (112 mg, 44%); m.p. 75–77°C; $[\alpha]_D^{22}=-3.50$ ($c=1.03$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.36$ (d, $J=8.4$ Hz, 2H), 7.29 (d, $J=8.4$ Hz, 2H), 5.47 (d, $J=5.2$ Hz, 1H), 4.87 (m, 1H), 3.99 (m, 2H), 3.64 (m, 4H), 2.37 (m, 2H), 1.44 (d, $J=15.2$ Hz, 3H), 1.15 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=139.73$ (s, $J=8.9$ Hz), 133.45(s), 128.84 (s), 128.53 (s), 101.09 (d, $J=142.9$ Hz), 61.61 (d, $J=6.7$ Hz), 58.16 (d, $J=6.0$ Hz), 57.86 (d, $J=6.7$ Hz), 56.18 (s), 54.91 (d, $J=3.4$ Hz), 33.00 (d, $J=81.1$ Hz), 22.45 (s), 19.74 (d, $J=12.6$ Hz), 16.26 (d, $J=5.2$ Hz), 15.37 (s), 15.23 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.73$ ppm (s); IR (KBr): $\tilde{\nu}=3236$, 2980, 2233, 1494, 1444, 1391, 1224, 1186, 1039 cm^{-1}; MS (ESI): m/z (%): 490.1 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{20}H_{35}NO_5PSClNa$: 490.1554 $[M^++23]$; found: 490.1556.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(1-thiophenyl)ethylphosphinate (4i):Obtained as a colorless oil (105 mg, 48%); $[\alpha]_D^{25}=+48.8$ ($c=1.04$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.28$ (d, $J=4.2$ Hz, 1H), 7.14 (d, $J=3.3$ Hz, 1H), 6.98 (dd, $J_1=3.9$, $J_2=5.1$ Hz, 1H), 5.50 (d, $J=4.2$ Hz, 1H), 5.18 (m, 1H), 4.12 (m, 2H), 3.70 (m, 4H), 2.60 (m, 2H), 1.50 (d, $J=11.4$ Hz, 3H), 1.22 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=144.73$ (d, $J=12.6$ Hz), 126.63 (s), 125.85 (s), 125.41 (s), 101.22 (d, $J=145.0$ Hz), 61.71 (d, $J=7.3$ Hz), 58.15 (d, $J=5.7$ Hz), 57.97 (d, $J=6.9$ Hz), 56.11 (s), 51.47 (d, $J=4.0$ Hz), 33.35 (d, $J=81.2$ Hz), 22.59 (s), 19.63 (d, $J=12.1$ Hz), 16.45 (d, $J=5.6$ Hz), 15.44 (s), 15.31 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.45$ ppm (s); IR (KBr): $\tilde{\nu}=3468$, 3219, 2979, 1633, 1444, 1392, 1227, 1185, 1157, 1038 cm^{-1}; MS (ESI): m/z (%): 462.1 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{18}H_{34}NO_5PS_2Na$: 462.1508 $[M^++23]$; found: 462.1524.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(1-thiophenyl)ethylphosphinate (4i′): Obtained as a colorless oil (109 mg, 50%); $[\alpha]_D^{24}=+32.8$ ($c=0.97$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.24$ (d, $J=5.2$ Hz, 1H), 7.10 (dd, $J_1=1.2$, $J_2=2.8$ Hz, 1H), 6.92 (d, $J=3.6$ Hz, 1H), 5.14 (d, $J=2.4$ Hz, 1H), 5.05 (m, 1H), 4.09 (m, 2H), 3.62 (m, 4H), 2.77(m, 1H), 2.18 (m, 1H), 1.47 (d, $J=11.1$ Hz, 3H), 1.17 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=144.40$ (d, $J=11.9$ Hz), 126.48 (s), 126.06 (s), 125.62 (s), 101.09 (d, $J=140.7$ Hz), 61.87 (d, $J=6.7$ Hz), 58.03 (d, $J=5.2$ Hz), 57.72 (d, $J=6.7$ Hz), 55.96 (s), 50.43 (d, $J=3.7$ Hz,), 33.19 (d, $J=83.4$ Hz), 22.46 (s), 20.13 (d, $J=12.6$ Hz), 16.41 (d, $J=5.2$ Hz), 15.36 (s), 15.13 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.47$ ppm (s); IR (KBr): $\tilde{\nu}=3218$, 2980, 1476, 1444, 1391, 1226, 1185, 1166, 1037 cm^{-1}; MS (ESI): m/z (%): 462.1 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{18}H_{34}NO_5PS_2Na$: 462.1508 $[M^++23]$; found: 462.1512.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(2-naphthyl)ethylphosphinate (4j): Obtained as a colorless oil (99 mg, 41%); $[\alpha]_D^{23}=+7.33$ ($c=1.10$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.92$ (s, 1H), 7.84 (m, 3H), 7.51 (m, 3H), 5.55 (d, $J=4.5$ Hz, 1H), 5.10 (m, 1H), 4.04 (m, 2H), 3.70 (m, 4H), 2.58 (m, 2H), 1.50 (d, $J=11.1$ Hz, 3H), 1.22 (m, 15H), 1.12 ppm (t, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.48$ (d, $J=10.4$ Hz), 133.15 (s), 132.94 (s), 128.29 (s), 128.12 (s), 127.53 (s), 126.35 (s), 126.14 (s), 126.05 (s), 125.55 (s), 101.22 (d, $J=143.7$ Hz), 61.62 (d, $J=6.7$ Hz), 58.22 (d, $J=5.9$ Hz), 57.91 (d, $J=6.7$ Hz), 56.16 (s), 55.48 (d, $J=3.7$ Hz), 32.99 (d, $J=80.4$ Hz), 22.52 (s), 19.84 (d, $J=11.9$ Hz), 16.29 (d, $J=5.2$ Hz), 15.44 (s), 15.30 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.96$ ppm (s); IR (KBr): $\tilde{\nu}=3188$, 2985, 1478, 1390, 1221, 1192, 1163, 1072, 1041, 1026 cm^{-1}; MS (ESI): m/z (%): 506.1 $[M+Na]^+$; elemental analysis (%) calcd for $C_{24}H_{38}NO_5PS$: C 59.61, H 7.92, N 2.90; found: C 59.47, H 7.94, N 2.92.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(2-naphthyl)ethylphosphinate (4j′): Obtained as a white solid (118 mg, 49%); m.p. 84–85°C; $[\alpha]_D^{25}=-7.99$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.92$ (s, 1H), 7.84 (m, 3H), 7.48 (m, 2H), 5.34 (d, $J=4.0$ Hz, 1H), 4.98 (m, 1H), 4.11 (m, 2H), 3.69 (m, 4H), 2.77 (m, 1H), 2.19 (m, 1H), 1.51 (d, $J=15.6$ Hz, 3H), 1.20 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.37$ (d, $J=10.4$ Hz), 133.16 (s), 128.53 (s), 128.07 (s), 127.59 (s), 126.66 (s), 126.19 (s), 126.16 (s), 125.42 (s), 101.11 (d, $J=140.0$ Hz), 61.91 (d, $J=6.7$ Hz), 58.07 (d, $J=5.3$ Hz), 57.86 (d, $J=6.7$ Hz), 56.19 (s), 55.06 (d, $J=3.8$ Hz), 32.70 (d, $J=82.7$ Hz), 22.45 (s), 20.29 (d, $J=13.4$ Hz), 16.39 (d, $J=5.2$ Hz), 15.43 (s), 15.24 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.88$ ppm (s); IR (KBr): $\tilde{\nu}=3217$, 2978, 1614, 1517, 1250, 1183, 1078, 1030 cm^{-1}; MS (ESI): m/z (%): 506.2 $[M+Na]^+$; elemental analysis (%) calcd for $C_{21}H_{38}NO_6PS$: C 59.61, H 7.92, N 2.90; found: C 59.71, H 7.84, N 2.97.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(4-biphenyl)ethylphosphinate (4k): Obtained as a colorless oil (114.5 mg, 45%); $[\alpha]_D^{25}=+9.60$ ($c=1.02$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.57$ (m, 4H), 7.51 (d, $J=8.4$ Hz, 2H), 7.41 (td, $J_1=7.2$, $J_2=1.6$ Hz, 2H), 7.32 (tt, $J_1=7.6$, $J_2=1.2$ Hz, 1H), 5.49 (d, $J=5.2$ Hz, 1H), 4.96 (m, 1H), 4.03 (m, 2H), 3.69 (m, 4H), 2.45 (m, 2H), 1.50 (d, $J=9.6$ Hz, 3H), 1.17 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=140.71$ (s), 140.66 (s), 140.31 (d, $J=8.9$ Hz), 128.72 (s), 127.91 (s), 127.27 (s), 127.23 (s), 127.05 (s), 101.22 (d, $J=142.9$ Hz), 61.62 (d, $J=7.4$ Hz), 58.25 (d, $J=5.2$ Hz), 57.92 (d, $J=6.7$ Hz), 56.23 (s), 55.29 (d, $J=4.5$ Hz), 33.38 (d, $J=81.2$ Hz), 22.57 (s), 19.89 (d, $J=1.9$ Hz), 16.36 (d, $J=5.9$ Hz), 15.48 (s), 15.34 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.79$ ppm (s); IR (KBr): $\tilde{\nu}=3240$, 2980, 1714, 1488, 1391, 1224, 1186, 1154, 1039 cm^{-1}; MS (ESI): m/z (%): 532.2 $[M+Na]^+$; elemental analysis (%) calcd for $C_{26}H_{40}NO_5PS$: C 61.27, H 7.91, N 2.75; found: C 60.90, H 7.68, N 2.85.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(4-biphenyl)ethylphosphinate (4k′):Obtained as a white solid (103 mg, 41%); m.p. 113–114°C; $[\alpha]_D^{25}=-6.02$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.54$ (m, 6H), 7.39 (t, $J=8.0$ Hz, 2H), 7.30 (t, $J=8.0$ Hz, 2H), 5.19 (d, $J=2.8$ Hz, 1H), 4.81 (m, 1H), 4.08 (m, 2H), 3.66 (m, 4H), 2.65 (m, 1H), 2.10 (m, 1H), 1.47 (d, $J=12.0$ Hz, 3H), 1.19 ppm (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=140.91$ (s), 140.53 (s), 140.13 (d, $J=9.7$ Hz), 128.62 (s), 128.02 (s), 127.28 (s), 127.22 (s), 126.95 (s), 101.00 (d, $J=140.0$ Hz), 61.79 (d, $J=6.7$ Hz), 57.99 (d, $J=5.2$ Hz), 57.77 (d, $J=6.7$ Hz), 56.13 (s), 54.68 (d, $J=4.5$ Hz), 32.89 (d, $J=81.9$ Hz), 22.38 (s), 20.20 (d, $J=12.7$ Hz), 16.36 (d, $J=6.0$ Hz), 15.36 (s), 15.18 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.63$ ppm (s); IR (KBr): $\tilde{\nu}=3194$, 2975, 1601, 1489, 1238, 1222, 1188, 1074, 1040 cm^{-1}; MS (ESI): m/z (%): 532.3 $[M+Na]^+$, 548.6 $[M+K]^+$; elemental analysis (%) calcd for $C_{26}H_{40}NO_5PS$: C 61.27, H 7.91, N 2.75; found: C 61.47, H 8.08, N 2.82.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)-2-(2,4-dichlorophenyl)ethylphosphinate (4l): Obtained as a white solid (120.5 mg, 48%); m.p. 99—101°C; $[\alpha]_D^{25}=+19.5$ ($c=1.10$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.73$ (d, $J=8.1$ Hz, 1H), 7.37 (d, $J=2.4$ Hz, 1H), 7.31 (dd, $J_1=2.1$, $J_2=8.4$ Hz, 1H), 6.10 (d, $J=6.60$ Hz, 1H), 5.23 (m, 1H), 3.96 (m, 2H), 3.69 (m, 4H), 2.40 (m, 2H), 1.47 (d, $J=16.0$ Hz, 3H), 1.20 (m, 15H), 1.09 ppm (t, $J=9.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=137.48$ (d, $J=8.4$ Hz), 133.92 (s), 133.02 (s), 130.54 (s), 129.11 (s), 127.16 (s), 101.02 (d, $J=143.0$ Hz), 61.57 (d, $J=6.9$ Hz), 58.30 (d, $J=5.6$ Hz), 57.87 (d, $J=7.2$ Hz), 56.44 (s), 52.40 (d, $J=5.7$ Hz), 31.25 (d, $J=81.9$ Hz), 22.49 (s), 19.93 (d, $J=12.2$ Hz), 16.18 (d, $J=5.6$ Hz), 15.38 (s), 15.22 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=48.09$ ppm (s); IR (KBr): $\tilde{\nu}=3230$, 2978, 1587, 1561, 1474, 1388, 1177, 1168, 1076, 1032 cm^{-1}; MS (ESI): m/z (%): 525.1 $[M+Na]^+$; elemental analysis (%) calcd for $C_{20}H_{34}Cl_2NO_5PS$: C 47.81, H 6.82, N 2.79; found: C 47.81, H 6.95, N 2.55.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(−)-2-(*tert*-butylsulfinylamino)-2-(2,4-dichlorophenyl)ethylphosphinate (4l′): Obtained as a colorless oil (120.5 mg, 48%); $[\alpha]_D^{25}=-47.7$ ($c=1.08$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.68$ (d, $J=8.1$ Hz, 1H), 7.38 (d, $J=1.5$ Hz, 1H), 7.32 (dd, $J_1=2.1$ Hz, $J_2=8.4$ Hz, 1H), 5.62 (d, $J=4.2$ Hz, 1H), 5.13 (m, 1H), 4.21 (m, 2H), 3.66 (m, 4H), 2.48 (m, 1H), 2.14 (m, 1H), 1.47 (d, $J=12.0$ Hz, 3H), 1.33 (t, $J=6.0$ Hz, 3H), 1.19 ppm (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=137.20$ (d, $J=11.3$ Hz), 134.21 (s), 133.37 (s), 130.32 (s), 129.42 (s), 127.55 (s), 101.03 (d, $J=140.5$ Hz), 62.08 (d, $J=6.9$ Hz), 58.06 (d, $J=5.2$ Hz), 57.84 (d, $J=6.8$ Hz), 56.45 (s), 51.84 (d, $J=4.5$ Hz), 31.61 (d, $J=82.0$ Hz), 22.28 (s), 20.17 (d, $J=12.9$ Hz), 16.48 (d, $J=5.6$ Hz), 15.34 (s), 15.15 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.56$ ppm (s); IR (KBr): $\tilde{\nu}=3221$, 2981, 2233, 1590, 1561, 1475, 1390, 1226, 1185, 1039 cm^{-1}; MS (ESI): m/z (%): 525.1 $[M+Na]^+$; elemental analysis (%) calcd for $C_{20}H_{34}Cl_2NO_5PS$: C 47.81, H 6.82, N 2.79; found: C 47.85, H 6.89, N 2.58.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,S_P)-(+)-2-(*tert*-butylsulfinylamino)tetradecylphosphinate (4m): Obtained as a colorless oil (126 mg, 48%); $[\alpha]_D^{25}=+30.4$ ($c=0.97$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=4.79$ (d, $J=6.0$ Hz, 1H), 4.18 (m, 2H), 3.63 (m, 5H), 2.07 (m, 2H), 1.88 (m, 1H), 1.70 (m, 1H), 1.43 (t, $J=11.2$ Hz, 3H), 1.21 (m, 38H), 0.83 ppm (t, $J=11.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=101.19$ (d, $J=141.5$ Hz), 61.60 (d, $J=7.4$ Hz), 58.08 (d, $J=5.2$ Hz), 57.89 (d, $J=6.7$ Hz), 55.72 (s), 53.29 (d, $J=5.2$ Hz), 36.19 (d, $J=9.6$ Hz), 31.90 (s), 31.26 (d, $J=82.6$ Hz), 22.70 (s), 19.97 (d, $J=11.9$ Hz), 16.64 (d, $J=5.2$ Hz), 15.47 (s), 15.32 (s), 14.10 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=49.07$ ppm (s); IR (KBr): $\tilde{\nu}=3226$, 2927 (s), 1465, 1390, 1364, 1186, 1157, 1040 cm^{-1}; MS (ESI): m/z (%): 480.3 $[M\text{-OEt}]^+$, 526.4 $[M+H]^+$, 548.3 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{26}H_{56}NO_5PSNa$: 548.3509 $[M^++23]$; found: 548.3503.

Ethyl 1′,1′-diethoxyethyl-(S_S,R_C,R_P)-(+)-2-(*tert*-butylsulfinylamino)tetradecylphosphinate (4m′): Obtained as a colorless oil (126 mg, 48%); $[\alpha]_D^{25}=+20.6$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=4.58$ (d, $J=4.4$ Hz, 1H), 4.15 (m, 2H), 3.63 (m, 5H), 2.25 (m, 1H), 1.86 (m, 1H), 1.77 (td, $J_1=4.0$, $J_2=14.8$ Hz, 1H), 1.67 (m, 1H), 1.43 (t, $J=12.0$ Hz, 3H), 1.21 (m, 15H), 0.81 ppm (t, $J=6.4$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta=101.69$ (d, $J=137.7$ Hz), 61.67 (d, $J=6.7$ Hz), 58.04 (d, $J=4.5$ Hz), 57.66 (d, $J=6.7$ Hz), 55.67 (s), 51.88 (d, $J=4.5$ Hz), 35.75 (d, $J=9.7$ Hz), 32.01 (d, $J=94.8$ Hz), 31.83 (s), 29.39 (s), 25.94 (s,), 22.61 (s), 20.22 (d, $J=13.4$ Hz), 16.59 (d, $J=5.2$ Hz), 15.42 (s), 15.17 (s), 14.02 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=49.22$ ppm (s); IR (KBr): $\tilde{\nu}=3220$, 2928 (s), 1465, 1390, 1364, 1228, 1187, 1157, 1039 cm^{-1}; MS (ESI): m/z (%): 548.3 $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{26}H_{56}NO_5PSNa$: 548.3509 $[M^++23]$; found: 548.3500.

Preparation of (R_C,S_P)-5l and (R_C,R_P)-5l′: $[RuCl_3]\cdot H_2O$ (1 mol%) was added to $NaIO_4$ (15 equiv) in CH_2Cl_2/MeCN/H_2O (1.0:0.04:0.7), and the mixture was stirred for 1 h. A solution of **4l** or **4l′** (0.5 mmol) in CH_2Cl_2 was added rapidly to the mixture by cannula. The final concentration of **4l** or **4l′** was 0.03 M. Upon completion, as determined by TLC, H_2O (5 mL) and EtOAc (10 mL) were added, the organic layer was separated, the aqueous layer was washed with EtOAc (3×10 mL), and the organic layers were combined, washed with brine, and dried over anhydrous Na_2SO_4 overnight. The solvent was removed under reduced pressure and the residue was then subjected to the flash chromatography (EtOAc/petroleum ether=1:1) to afford pure **5l** or **5l′** in good yield.

Ethyl 1′,1′-diethoxyethyl-(R_C,S_P)-(−)-2-(*tert*-butylsulfonylamino)-2-(2,4-dichlorophenyl)ethylphosphinate (5l): Obtained as a white solid (212 mg, 82%, 95.2% *ee*); m.p. 74–76°C; $[\alpha]_D^{29}=-9.91$ ($c=0.96$, in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.74$ (d, $J=8.4$ Hz, 1H), 7.37 (s, 1H), 7.31 (d, $J=8.4$ Hz, 1H), 6.88 (d, $J=9.2$ Hz, 1H), 5.32 (m, 1H), 3.84 (m, 1H), 3.69 (m, 5H), 2.64 (m, 1H), 2.34 (m, 1H), 1.44 (d, $J=11.6$ Hz, 3H), 1.32 (s, 9H), 1.21 (m, 6H), 0.92 ppm (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=137.65$ (d, $J=4.4$ Hz), 133.80 (s), 132.29 (s), 130.09 (s), 129.15 (s), 127.13 (s), 100.80 (d, $J=142.2$ Hz), 61.61 (d, $J=7.5$ Hz), 59.77 (s), 58.21 (d, $J=5.9$ Hz), 58.10 (d, $J=6.7$ Hz), 51.59 (d, $J=7.5$ Hz), 30.27 (d, $J=82.7$ Hz), 24.02 (s), 20.00 (s, $J=11.9$ Hz), 15.99 (d, $J=6.0$ Hz), 15.39 (s), 15.30 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=49.43$ ppm (s); IR(KBr): $\tilde{\nu}=3158$, 2978, 1590, 1475, 1392, 1314, 1216, 1132, 1037, 1129, 1060, 1028 cm^{-1}; MS (ESI): m/z (%): 540.1 $[M+Na]^+$; HPLC analysis (performed at room temperature): Chiralpak IA (4.6×250 mm), *n*-hexane/2-propanol 90:10, $\lambda=214$ nm, flow rate=0.8 mL min^{-1}, retention time=13.25 min (minor), 22.01 min (major); elemental analysis (%) calcd for $C_{20}H_{34}Cl_2NO_6PS$: C 46.33, H 6.61, N 2.70; found: C 46.46, H 6.84, N 2.52.

Ethyl 1′,1′-diethoxyethyl-(R_C,R_P)-(−)-2-(*tert*-butylsulfonylamino)-2-(2,4-dichlorophenyl)ethylphosphinate (5l′): Obtained as a colorless oil (259 mg, >99%, >99% *ee*); $[\alpha]_D^{29}=-53.8$ ($c=1.04$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta=7.61$ (d, $J=8.4$ Hz, 1H), 7.33 (d, $J=1.6$ Hz, 1H), 7.26 (dd, $J_1=2.0$, $J_2=8.4$ Hz, 1H), 6.27 (s, 1H), 5.30 (m, 1H), 4.19 (m, 2H), 3.65 (m, 1H), 3.54 (m, 3H), 2.35 (m, 2H), 1.34 (m, 18H), 1.12 ppm (m, $J=7.2$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.44$ (s), 133.69 (s), 132.06 (s), 130.05 (s), 129.22 (s), 127.32 (s), 100.79 (d, $J=142.2$ Hz), 62.08 (d, $J=6.7$ Hz), 60.09 (s), 58.15 (d, $J=6.0$ Hz), 57.88 (d, $J=7.4$ Hz), 51.21 (s), 31.56 (d, $J=79.6$ Hz), 23.92 (s), 19.77 (d, $J=12.6$ Hz), 16.37 (d, $J=6.0$ Hz), 15.20 (s), 15.04 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta=47.20$ ppm (s); IR(KBr): $\tilde{\nu}=3139$, 2981, 1590, 1475, 1307, 1218, 1186, 1128, 1030 cm^{-1}; MS (ESI): m/z (%): 540.1 $[M+Na]^+$; HPLC analysis (performed at room temperature): Chiralpak IA (4.6×250 mm), hexane/2-propanol 90:10, $\lambda=214$ nm, flow rate=

0.9 mL min^{-1}, retention time = 10.73 min (major), 12.33 min (minor); elemental analysis (%) calcd for $C_{20}H_{34}Cl_2NO_6PS$: C 46.33, H 6.61, N 2.70; found: C 46.48, H 6.60, N 2.38.

Conversion of compound (S_S,R_C,S_P)-4h or (S_S,R_C,R_P)-4h′ into (R_C,S_P)-6h or (R_C,R_P)-6h′: [$NbCl_5$] (6 mg, 0.021 mmol, 10 mmol %) and $CuSO_4$ (4 mg, 0.021 mmol, 10 mmol %) were added to solution of (S_S,R_C,S_P)-**4h** (108 mg, 0.21 mmol) in CH_2Cl_2 (1.0 mL) with stirring in an argon atmosphere. After stirring for 5 min at room temperature, PhSH (69 mg, 0.07 mL, 0.63 mmol, 300 mol %) was added. The reaction mixture was stirred at room temperature, and TLC analysis demonstrated that the reaction was completed after 24 h. The slurry was diluted with EtOAc (1 mL) and subjected to flash chromatography directly, first eluting with EtOAc (1% NEt_3) to remove excess PhSH then with $CHCl_3$/MeOH/NEt_3 100:5:1, to afford the desired product **6h**. The synthesis of **6h′** was the same as the above.

Ethyl 1′,1′-diethoxyethyl-(R_C,S_P)-(+)-2-amino-2-(*para*-bromophenyl)ethylphosphinate (6h): Obtained as a white solid (62 mg, 72 %); m.p. 75–77 °C; $[\alpha]_D^{24} = +3.38$ ($c = 1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta = 7.42$ (d, $J = 9.0$ Hz, 2H), 7.26 (d, $J = 9.0$ Hz, 2H), 4.55 (t, $J = 8.7$ Hz, 1H), 4.19 (m, 2H), 3.68 (m, 4H), 2.14 (m, 3H), 1.98 (m, 1H), 1.46 (t, $J = 11.7$ Hz, 3H), 1.29 (t, $J = 7.5$ Hz, 3H), 1.18 ppm (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 144.90$ (d, $J = 19.1$ Hz), 131.57 (s), 127.84 (s), 120.89 (s), 101.18 (d, $J = 186.2$ Hz), 61.67 (d, $J = 9.2$ Hz), 58.21 (d, $J = 6.9$ Hz), 57.68 (d, $J = 9.2$ Hz), 50.10 (d, $J = 6.1$ Hz), 35.65 (d, $J = 107.6$ Hz), 20.23 (d, $J = 16.0$ Hz), 16.64 (d, $J = 6.8$ Hz), 15.45 (s), 15.26 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 47.87$ ppm (s); IR (KBr): $\tilde{\nu} = 3354$, 3292, 2978, 2931, 1489, 1390, 1363, 1219, 1157, 1034, 968 cm^{-1}; MS (ESI): *m*/*z* (%): 408.2 [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{16}H_{28}NO_4PBr$ [M^++H]: 408.0942; found: 408.0939.

Ethyl 1′,1′-diethoxyethyl-(R_C,R_P)-(−)-2-amino-2-(*para*-bromophenyl)ethylphosphinate (6h′): Obtained as a light-brown oil (61 mg, 71 %); $[\alpha]_D^{24} = -24.3$ ($c = 1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta = 7.46$ (d, $J = 8.7$ Hz, 2H), 7.34 (d, $J = 8.7$ Hz, 2H), 4.51 (td, $J_1 = 3.6$, $J_2 = 9.3$ Hz, 1H), 4.15 (m, 2H), 3.68 (m, 4H), 3.56 (br, 2H, NH_2), 2.33 (m, 1H), 1.99 (m, 1H), 1.48 (t, $J = 7.5$ Hz, 3H), 1.48 ppm (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 143.52$ (d, $J = 16.0$ Hz), 131.61 (s), 128.30 (s), 121.28 (s), 100.94 (d, $J = 186.3$ Hz), 61.89 (d, $J = 9.1$ Hz), 58.25 (d, $J = 6.1$ Hz), 57.69 (d, $J = 9.9$ Hz), 49.99 (d, $J = 5.4$ Hz), 34.52 (d, $J = 109.9$ Hz), 20.18 (d, $J = 16.8$ Hz), 16.50 (d, $J = 7.6$ Hz), 15.42 (s), 15.21 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 48.00$ ppm (s); IR (KBr): $\tilde{\nu} = 3350$, 2979, 2931, 1591, 1488, 1453, 1391, 1225, 1159, 1037, 959 cm^{-1}; MS (ESI): *m*/*z* (%): 408.1 [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{16}H_{28}NO_4PBr$ [M^++H]: 408.0942; found: 408.0934.

Conversion of (R_C,S_P)-6h and (R_C,R_P)-6h′ into (R_C,S_P)-7h and (R_C,R_P)-7h′: EtOH (40 μL) and freshly distilled TMSCl (30 μL) were added to a solution of **6h** (40 mg, 0.098 mmol) in CH_2Cl_2 (1 mL) with stirring in an argon atmosphere. The solution was stirred at room temperature for 2 h. EtOAc (1 mL) was added to the solution and the reaction mixture was evaporated to nearly dryness below 25 °C (this step is strongly recommended because the P–H bond is susceptible to oxidation at high temperature). The residue was subjected to high vacuum to remove excess solvent to afford pure **7h**. The synthesis of **7h′** was the same as the above.

Ethyl (R_C,S_P)-(+)-2-amino-2-(*para*-bromophenyl)-*H*-ethylphosphinate (7h): Obtained as a light-yellow gum (32 mg, >99 %; >95 % *ee*); $[\alpha]_D^{24} = +33.9$ ($c = 0.90$, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta = 7.57$ (d, $J = 8.1$ Hz, 2H), 7.40 (dd, $J_1 = 1.8$, $J_2 = 8.1$ Hz, 2H), 6.85 (dd, $J_1 = 3.3$, $J_2 = 572.7$ Hz, 1H), 4.68 (m, 1H), 4.00 (m, 2H), 3.44 (br, 2H, NH_2), 2.56 (m, 2H), 1.19 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 133.48$ (s), 131.29 (s), 128.31 (s), 122.67(s), 62.53 (s), 48.39 (d, $J = 19.3$ Hz), 31.18 (d, $J = 107.2$ Hz), 14.04 ppm (s); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 35.03$ ppm (dm, $J = 333.8$ Hz); IR (KBr): $\tilde{\nu} = 2908$(br), 2077, 1731, 1595, 1521, 1492, 1283, 1213, 1070, 1012, 829 cm^{-1}; MS (ESI): *m*/*z* (%): 292.0 [*M*+H]$^+$; HRMS (EI): *m*/*z*: calcd for $C_{10}H_{16}NO_2PBr$: 292.0097 [M^++H]; found: 292.0088.

Ethyl (R_C,R_P)-(+)-2-amino-2-(*para*-bromophenyl)-*H*-ethylphosphinate (7h′): Obtained as a light-yellow gum (32 mg, >99 %, >95 % *ee*); $[\alpha]_D^{24} = +28.7$ ($c = 1.00$, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta = 7.57$ (d, $J = 8.7$ Hz, 2H), 7.42 (d, $J = 8.7$ Hz, 2H), 6.87 (dd, $J = 573.9$ Hz, 1H), 4.67 (m, 1H), 4.00 (m, 2H), 3.21 (br, 2H, NH_2), 2.61 (m, 2H), 1.13 ppm (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 134.57$ (s, $J = 4.5$ Hz), 132.23 (s), 129.36 (s), 133.60 (s), 63.43 (d, $J = 6.7$ Hz), 48.14 (d, $J = 21.6$ Hz), 32.40 (d, $J = 96.1$ Hz), 15.01 ppm (d, $J = 5.9$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 34.36$ ppm (dm, $J = 358.2$ Hz); IR (KBr): $\tilde{\nu} = 2933$ (br), 2077, 1731, 1595, 1492, 1417, 1210, 1071, 1040, 1012, 968, 826, 750 cm^{-1}; MS (ESI): *m*/*z* (%): 292.0 [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{10}H_{16}NO_2PBr$: 292.0097 [M^++H]; found: 292.0090.

Conversion of (S_S,R_C,S_P)-4b and (S_S,R_C,R_P)-4b′ into (*S*)-8b and (*R*)-8b′:

Step 1: [$RuCl_3$]·H_2O (1 mol %) was added to $NaIO_4$ (15 equiv) in CH_2Cl_2/MeCN/H_2O (1.0:0.04:0.7) and stirred for 1 h. A solution of **4b** or **4b′** (0.25 mmol) in CH_2Cl_2 (3 mL) was added rapidly to the mixture by cannula. The final concentration of **4b** or **4b′** was 0.03 M. Upon completion, as determined by TLC, H_2O (5 mL) and EtOAc (10 mL) were added, the organic layer was separated, the aqueous layer was washed with EtOAc (3×10 mL), and the organic layers were combined, washed with brine, and dried over anhydrous Na_2SO_4 overnight. The solvent was removed under reduced pressure and the residue was then subjected to the flash chromatography (EtOAc/petroleum ether = 1:1) to afford pure (R_C,S_P)-**5b** or (R_C,R_P)-**5b′**.

Step 2: EtOH (100 μL) and freshly distilled TMSCl (75 μL) were added to a solution of (R_C,S_P)-**5b** or (R_C,R_P)-**5b′** in CH_2Cl_2 (2 mL) with stirring in an argon atmosphere. The solution was stirred at room temperature for 2 h. EtOAc (1 mL) was added to the solution and the reaction mixture was evaporated to nearly dryness below 25 °C (this step is strongly recommended because that the P–H bond is susceptible to oxidation at high temperature). The residue was subjected to high vacuum to remove excess solvent. The residue was used directly without further purification.

Step 3: The residue obtained in Step 2 was added to a 25-mL flask under argon, and the system was cooled to 0 °C. A cold solution of CF_3SO_3H (15 mL) in CH_2Cl_2 (0.1 M) was added to the residue slowly. The solution was stirred at this temperature for 1 h and room temperature for another 2 h until TLC analysis indicated that the reaction was completed. The reaction mixture was washed with saturated $NaHCO_3$ solution (3×15 mL) and brine (10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was subjected to high vacuum to afford pure (*S*)-**8b** or (*R*)-**8b′** in good yield over the three steps.

Ethyl (*S*)-(−)-2-(*para*-methylphenyl)vinylphosphinate (8b): Obtained as a brown oil (30.3 mg; total yield over 3 steps: 57.8 %); $[\alpha]_D^{26} = -8.55$ ($c = 1.10$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta = 7.46$ (dd, $J_1 = 17.4$, $J_2 = 23.7$ Hz, 1H), 7.40 (d, $J = 7.5$ Hz, 2H), 7.32 (d, $J = 560.1$ Hz, 1H), 7.19 (d, $J = 7.8$ Hz, 2H), 6.29 (dd, $J_1 = 18.0$, $J_2 = 21.9$ Hz, 1H), 4.16 (m, 2H), 2.36 (s, 3H), 1.38 ppm (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 149.65$ (d, $J = 7.3$ Hz), 141.09 (s), 131.79 (s, $J = 21.2$ Hz), 129.63 (s), 127.86 (s), 114.99 (d, $J = 132.8$ Hz), 61.93 (d, $J = 6.6$ Hz), 21.44 (s), 16.49 ppm (d, $J = 6.5$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 26.13$ ppm (s); IR (KBr): $\tilde{\nu} = 2924$, 2364, 1612, 1512, 1459, 1357, 1192, 978, 782 cm^{-1}; MS (ESI): *m*/*z* (%): 211.2 [*M*+H]$^+$, 233.0 [*M*+Na]$^+$; HRMS (EI): *m*/*z*: calcd for $C_{11}H_{15}O_2P$: 210.0810; found: 210.0811.

Ethyl (*R*)-(+)-2-(*para*-methylphenyl)vivylphosphinate (8b′): Obtained as a brown oil (31.6 mg, total yield for 3 steps: 60.3 %); $[\alpha]_D^{27} = +11.1$ ($c = 1.13$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): $\delta = 7.46$ (dd, $J_1 = 17.6$, $J_2 = 23.6$ Hz, 1H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 560.4$ Hz, 1H), 7.18 (d, $J = 7.6$ Hz, 2H), 6.29 (ddd, $J_1 = 1.2$, $J_1 = 17.6$, $J_2 = 18.8$ Hz, 1H), 4.15 (m, 2H), 2.36 (s, 3H), 1.38 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 149.62$ (d, $J = 7.3$ Hz), 141.08 (s), 131.78 (s, $J = 21.2$ Hz), 129.61 (s), 127.84 (s), 114.98 (d, $J = 133.6$ Hz), 61.91 (d, $J = 6.6$ Hz), 21.43 (s), 16.39 ppm (d, $J = 6.6$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 26.12$ ppm (s); IR (KBr): $\tilde{\nu} = 2926$, 2365, 1612, 1513, 1181, 977, 783 cm^{-1}; MS (ESI): *m*/*z* (%): 211.0 [*M*+H]$^+$, 233.0 [*M*+Na]$^+$; HRMS (EI): *m*/*z*: calcd for $C_{11}H_{15}O_2P$: 210.0810; found: 210.0808.

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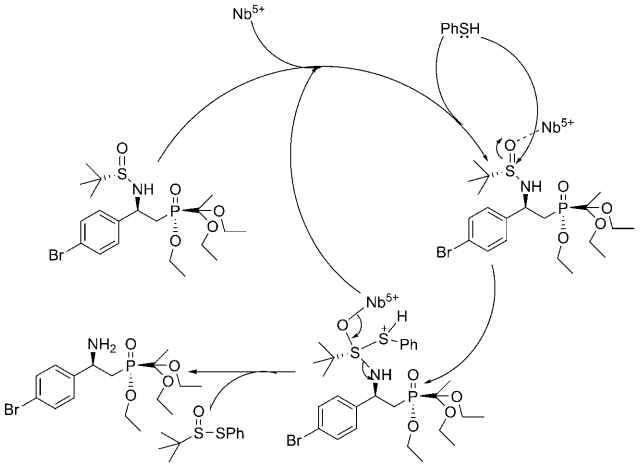

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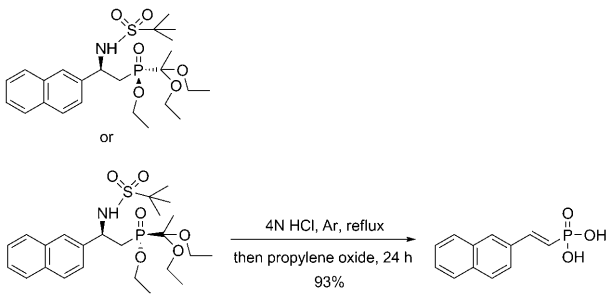

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