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α-Amido sulphones as useful intermediates in the preparation of *C*-chiral α-aminophosphonates and α-aminophosphonic acids†

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α-Amido sulphones have been used as useful starting materials in the preparation of *C*-chiral α-aminophosphonates and α-aminophosphonic acids. The developed methodology is based on a one-pot, base-catalysed *in situ* generation of an imine intermediate followed by addition of a phosphorus nucleophile. The presented protocol is simple and effective and can be applied to a variety of structurally diverse α-amido sulphones and phosphorus nucleophiles, leading to the desired pure products after simple crystallization in very good yields. Importantly, the use of *H*-phosphonate bearing a chiral auxiliary allows the reaction to be performed with high diastereoselectivity (a single diastereoisomer is generated and isolated) and the possibility of precise control of the configuration at the newly generated *C*-chiral centre.

Introduction

α-Amido sulfones are considered very useful and stable precursors of *N*-acylimines and therefore they have found many applications in modern organic synthesis, including asymmetric synthesis.[1–3] Their utility stems from two aspects: the first one is their high stability and ease of preparation *via* simple acid-promoted three-component reactions of various aldehydes, sulfinates and carbamates,[2] and the second one is their very simple transformation into reactive *N*-acylimine derivatives under either acidic or basic conditions (Scheme 1a). Selected protocols where α-amido sulfones have been used as substrates include reactions with organometallic reagents leading to the generation the *N*-acylimines required for the subsequent nucleophilic addition,[4–7] reactions with allylating reagents leading to the synthesis of homoallylamino derivatives,[8,9] reactions with cyanide ions providing α-amido nitriles,[10–12] reactions with malonates and related derivatives,[13–15] reactions with enolates from simple carbonyl derivatives,[16–18] and finally reactions with nitronate anions leading to 2-nitroamine derivatives.[19–21]

Surprisingly, despite the extensive utility of α-amido sulfones in the preparation of structurally diverse compounds, their utility as imine precursors in the preparation of α-substituted aminophosphonates and aminophosphonic acids, important classes of compounds endowed with very interesting biological activities,[22–26] including excellent enzyme inhibitors,[27,28] drug candidates for antibiotics,[29,30] and antibacterial and antifungal agents,[31] is scarcely described in the literature.[32]

The only known applications include the reaction of α-amido sulfones with triethyl phosphite in the presence of indium(III) chloride[33] or dialkyl trimethylsilyl phosphites in the presence of iron(III) chloride. Both reactions proceed through an *N*-acylium ion, as the reaction intermediate, and lead to α-aminophosphonic acid esters as racemic mixtures with acceptable yields (Scheme 1b).[34] These methods, however, require the presence of metallic Lewis acid catalysts, malodorous or not easily available phosphorus nucleophiles, and dry conditions, under an inert atmosphere in a chlorinated solvent and the purification of the final products is tedious *via* column chromatography. In turn, the only known asymmetric preparation of optically active α-aminophosphonic acid derivatives with the use of α-amido sulfones is based on the reaction of dimethyl *H*-phosphonate under basic conditions in the presence of a chiral quaternary ammonium salt catalyst under phase-transfer catalytic conditions (Scheme 1c).[35] This protocol is based on the formation of an *N*-acylimine and its further reaction with dimethyl

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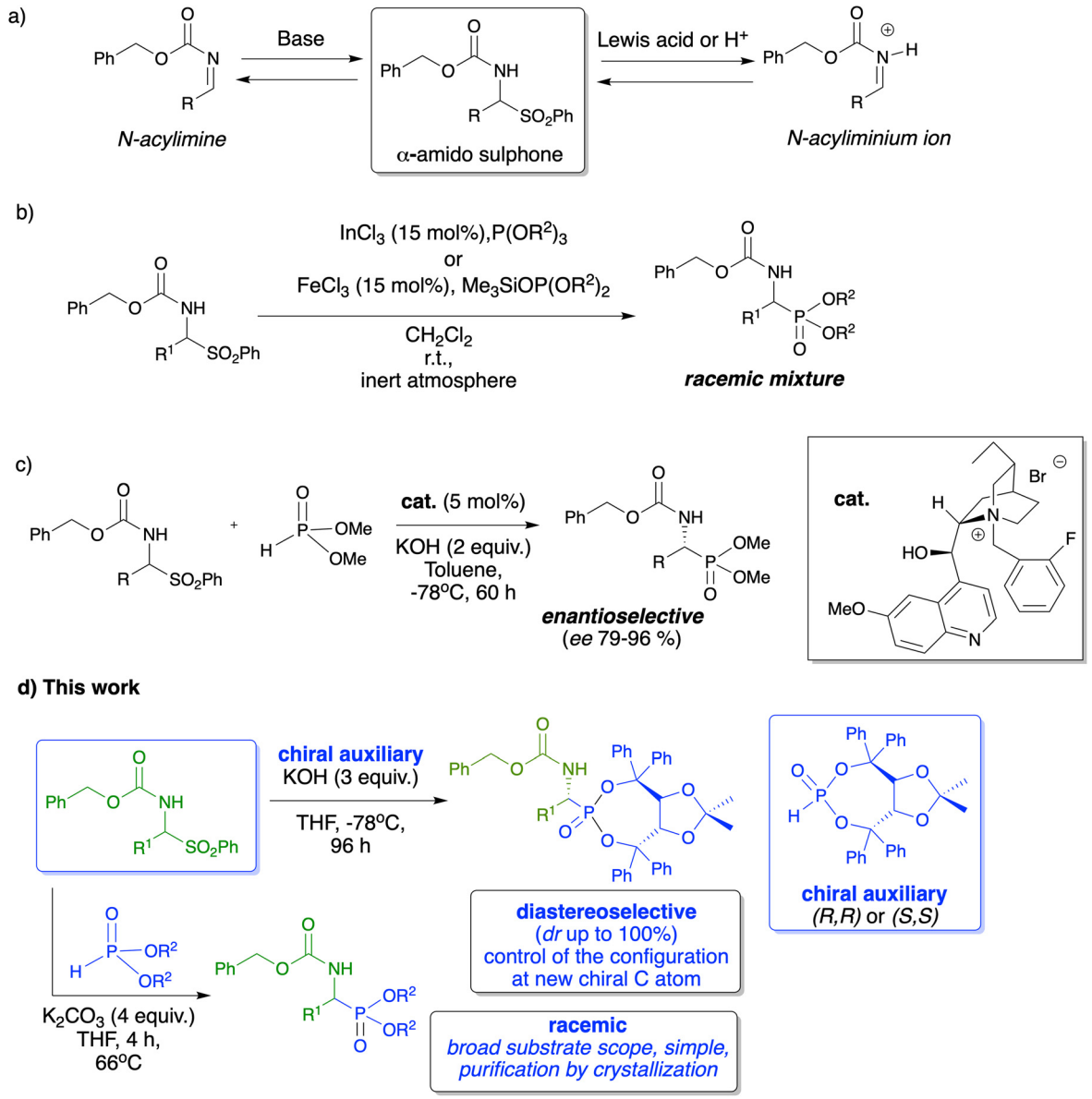


Scheme 1 Application of α-amido sulphones for the preparation of aminophosphonates. (a) Transformationioon of α-amido sulphones into reactive *N*-acylimines and *N*-acylium ions; (b) known protocols employing α-amido sulphones in the preparation of α-aminophopshonates; (c) known assymetric synthesis of α-aminophopshonates with the use of α-amido sulphones; (d) this work.

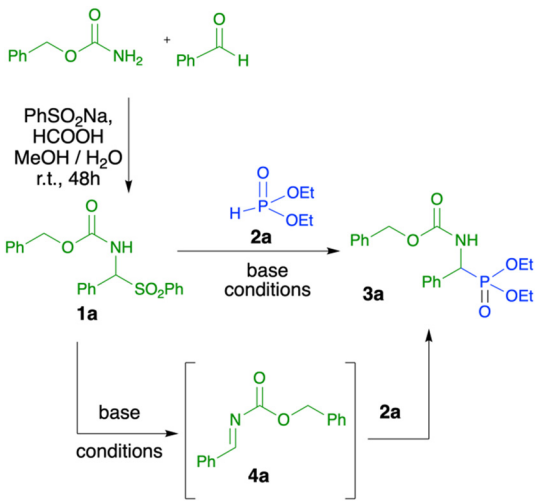
H-phosphonate, leading to the desired optically active α-aminophosphonic acids and their methyl esters, albeit with moderate enantioselectivity.

Our interest in the preparation of new α-aminophosphonic acids and their esters[36–40] prompted us to investigate the utility of α-amido sulphones as stable imine surrogates and practical intermediates in the preparation of these compounds. Herein we present the results of our research on the preparation of α-aminophosphonic acids and their esters not only as racemic mixtures but also in a highly diastereoselective fashion using a one-pot, effective and simple methodology based on the *in situ* generation of *N*-acylimines and their reaction with phosphorus nucleophiles (Scheme 1d).

Results and discussion

The starting *N*-benzyloxycarbonylamino sulfones were conveniently prepared *via* a formic acid promoted three-component reaction of aldehydes, benzenesulfinic acid sodium salt and benzyl carbamate.[41,42] α-Amido sulphones were conveniently obtained in pure form after simple crystallization. Subsequently, we selected α-amido sulfone **1a** and diethyl *H*-phosphonate (**2a**) as model substrates to perform the hydrophosphonylation of *N*-benzyloxycarbonylamino sulfones under basic conditions (Table 1). During the optimization of the reaction conditions, we quickly realized that the generated *N*-acylimine **4a** is highly unstable when removed from the reac-

Table 1 Optimization of the reaction conditions for hydrophosphonylation of α-amido sulphones[a]



Entry	Conditions	Conv.[b] (%)
1	No base, r.t., 24 h, THF	0
2	K_2CO_3 (4 equiv.), r.t., 24 h, THF	30%
3	**K_2CO_3 (4 equiv.), 66 °C, 4 h, THF**	**99%[b] [95%][c]**
4	Pyridine (4 equiv.), 66 °C, 4 h, THF	0
5	Cs_2CO_3 (4 equiv.), 66 °C, 4 h, THF	74
6	Et_3N (4 equiv.), 66 °C, 4 h, THF	0
7	NaOH (4 equiv.), 66 °C, 4 h, THF	81
8	Diisopropylamine (4 equiv.), 66 °C, 4 h, THF	5
9	L-Proline (4 equiv.), 66 °C, 4 h, THF	0
10	K_2CO_3 (4 equiv.), 64 °C, 4 h, MeOH	0
11	K_2CO_3 (4 equiv.), 77 °C, 4 h, ethyl acetate	42 (56)[d]
12	K_2CO_3 (4 equiv.), 80 °C, 4 h, 2-methyl THF	66 (89)[d]
13	K_2CO_3 (4 equiv.), 82 °C, 4 h, acetonitrile	50 (94)[d]
14	K_2CO_3 (4 equiv.), 101 °C, 4 h, 1,4-dioxane	54 (80)[d]
15	K_2CO_3 (2 equiv.), 66 °C, 4 h, THF	60
16	K_2CO_3 (6 equiv.), 66 °C, 4 h, THF	97

[a] General reaction conditions (unless otherwise stated): α-amido sulphone **1a** (2.4 mmol), *H*-phosphonate **2a** (2.4 mmol), and base (9.6 mmol, 4 equiv.). [b] Conversion based on the ^{31}P NMR spectra of the crude reaction mixture. [c] Isolated yield in square brackets. [d] Reaction time: 8 h.

tion mixture and undergoes decomposition to the starting benzaldehyde (to circumvent this, strictly anhydrous conditions and a protective atmosphere of argon should be used). Since we were interested in developing a simple and robust protocol, we decided to generate the imine *in situ* and therefore all reactions were performed in one pot by mixing α-amido sulfone **1a**, diethyl *H*-phosphonate **2a** and an appropriate base and solvent under different conditions.

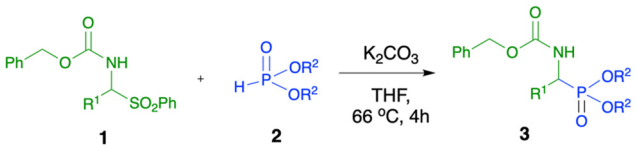
The nature of the base was important, and we discovered that its presence is crucial for the reaction to occur (Table 1, entry 1). The best results were obtained with solid inorganic bases (Table 1, entries 2, 3, 5, and 7) rather than with organic bases (Table 1, entries 4, 6, 8, and 9). The best results were obtained with K_2CO_3 (4 equiv.) after 4 h in THF at 66 °C (Table 1, entry 3), and the desired product **3a** was isolated in 95% yield after simple crystallization from diethyl ether. Using a greater amount of K_2CO_3 (6 equiv.) (Table 1, entry 16) did not improve the conversion and using a smaller amount of a base (2 equiv.) (Table 1, entry 15) lowered the reaction conversion. Furthermore, we also tested different solvents, and we selected THF for the examination of the substrate scope; however, quite good results were also obtained with acetonitrile (Table 1, entry 13), 2-methyl THF (Table 1, entry 12) and 1,4-dioxane (Table 1, entry 14), as representatives of "green solvents", but the reactions required a longer time.

Having established the optimized reaction conditions, we decided to examine the substrate scope of the developed protocol (Table 2). It was satisfying to see that our methodology worked well when we replaced diethyl *H*-phosphonate with other structurally variable phosphonates such as *n*-butyl *H*-phosphonate, i-propyl *H*-phosphonate or bulkier benzyl *H*-phosphonate (compounds **3b–d**, **3f–h**, **3k**, **3l**, **3m** and **3q**). Likewise, the reaction worked very well with other substituted benzaldehyde derived α-amido sulphones, including those with electron withdrawing or electron donating groups, and also with heteroaromatic 2-pyridine derived α-amido sulphone **3n** (Table 2). In all cases, the desired aromatic α-amino phosphonates were obtained in pure form in good to excellent isolated yields (74–95%) as white, bench-stable, non-hygroscopic solids, after simple crystallization from diethyl ether. Our methodology was also found to be suitable for the synthesis of aliphatic α-amino phosphonates **3o–r** prepared from suitable aliphatic α-amido sulphones, although the yields of the final products were slightly lower (58–77%) than in the case of the aromatic derivatives. Additionally, the aliphatic α-amino phosphonates **3o–r** were oils, but they were conveniently purified by simple filtration using a pad of silica gel.

Subsequently we became interested in performing the hydrophosphonylation of α-amido sulphones in an asymmetric fashion. To do that, we used the *H*-phosphonate (*R,R*)-**5**, derived from (*R,R*)-TADDOL, as the chiral auxiliary and phosphorus nucleophile in the reaction with α-amido sulphones. Such a chiral *H*-phosphonate is a bench-stable reagent that can be conveniently prepared on a multigram-scale *via* the reaction of the easily available (*R,R*)-TADDOL and PCl_3.[43] In our preliminary attempts to perform the diastereoselective hydrophosphonylation of the model α-amido sulphone **1a** with (*R,R*)-**5**, we applied the standard conditions used for the preparation of racemic α-amino phosphonates **3** with the hope that the presence of the chiral phosphorus nucleophile (*R,R*)-**5** will favour the formation of the desired product **6** in a diastereoselective fashion (Table 3, entry 1). Unfortunately, the dr observed in product **6** was only moderate (dr 35 : 65) and hence we tried to verify the influence of the base on the diastereoselectivity of the reaction by testing different inorganic and organic bases under similar reaction conditions (Table 3, entries 2–6), but the results were again disappointing. We also tested the effect of the solvent in the case when Cs_2CO_3 was used as the base, but there was no improvement in the dr (Table 3, entries 7–9).

We then decided to evaluate the possibility of performing the reaction under milder reaction conditions. To do so, we used the literature methodology for diastereoselective C–P

Table 2 Substrate scope of hydrophosphonylation of α-amido sulphones[a,b]



Entry	α-Amido sulphone **1**	*H*-Phosphonate **2**	α-Aminophosphonate **3**	Yield[a] (%)
1	**1a** R^1 = Ph	**2a** R^2 = Et	**3a** R^1 = Ph; R^2 = Et	95
2	**1a** R^1 = Ph	**2b** R^2 = *n*Bu	**3b** R^1 = Ph; R^2 = *n*Bu	87
3	**1a** R^1 = Ph	**2c** R^2 = iPr	**3c** R^1 = Ph; R^2 = iPr	94
4	**1a** R^1 = Ph	**2d** R^2 = Bn	**3d** R^1 = Ph; R^2 = Bn	91
5	**1b** R^1 = 4-Cl-Ph	**2a** R^2 = Et	**3e** R^1 = 4-Cl-Ph; R^2 = Et	95
6	**1b** R^1 = 4-Cl-Ph	**2b** R^2 = *n*Bu	**3f** R^1 = 4-Cl-Ph; R^2 = *n*Bu	82
7	**1b** R^1 = 4-Cl-Ph	**2c** R^2 = iPr	**3g** R^1 = 4-Cl-Ph; R^2 = iPr	95
8	**1b** R^1 = 4-Cl-Ph	**2d** R^2 = Bn	**3h** R^1 = 4-Cl-Ph; R^2 = Bn	95
9	**1c** R^1 = 4-F-Ph	**2a** R^2 = Et	**3i** R^1 = 4-F-Ph; R^2 = Et	82
10	**1d** R^1 = 4-Me-Ph	**2a** R^2 = Et	**3j** R^1 = 4-Me-Ph; R^2 = Et	82
11	**1d** R^1 = 4-Me-Ph	**2b** R^2 = *n*Bu	**3k** R^1 = 4-Me-Ph; R^2 = *n*Bu	74
12	**1d** R^1 = 4-Me-Ph	**2c** R^2 = iPr	**3l** R^1 = 4-Me-Ph; R^2 = iPr	77
13	**1d** R^1 = 4-Me-Ph	**2d** R^2 = Bn	**3m** R^1 = 4-Me-Ph; R^2 = Bn	91
14	**1e** R^1 = 2-Pyridyl	**2a** R^2 = Et	**3n** R^1 = 2-Pyridyl; R^2 = Et	87
15	**1f** R^1 = Et	**2a** R^2 = Et	**3o** R^1 = Et; R^2 = Et	62
16	**1g** R^1 = iPr	**2a** R^2 = Et	**3p** R^1 = iPr; R^2 = Et	77
17	**1g** R^1 = iPr	**2d** R^2 = Bn	**3q** R^1 = iPr; R^2 = Bn	62
18	**1h** R^1 = iBu	**2a** R^2 = Et	**3r** R^1 = iBu; R^2 = Et	58

[a] Yields are given for the purified, isolated products. [b] General procedure for the hydrophosphonylation of α-amido sulphones **1**: In a 50 mL flask, a suitable amount of *H*-phosphonate **2** (2.4 mmol, 1 equiv.) was added to a solution of α-amido sulphone **1** (2.4 mmol, 1 equiv.) and K_2CO_3 (9.6 mmol, 4 equiv.) in THF (15 mL). The mixture was heated at 66 °C for 4 h and then cooled and filtered. The solvent was removed under reduced pressure using a rotatory evaporator. The crude product was crystallized from diethyl ether in the case of solids and oily products were purified by column chromatography (eluent: hexane/ethyl acetate = 5 : 1 to 3 : 1) to obtain pure products **3a–r**.

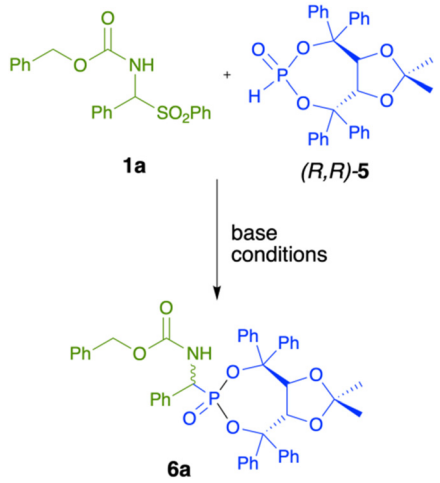
bond formation based on the use of a weak inorganic base in combination with a solid metal oxide.[44]

Such heterogeneous reactions have been found to be performed under mild conditions as the metal oxides can activate P(O)H groups so that deprotonation of the P–H bond occurs in the presence of weaker bases. In our case, however, different combinations of simple bases (KOH, K_2CO_3 or NaOH) with different metal oxides (Fe_2O_3, Al_2O_3, ZnO and MgO) led to good conversions at room temperature, but the diastereoselectivity was only moderate (Table 3, entries 10–15).

Next, we turned our attention towards the modification of the reaction conditions, and more specifically the reaction temperature, and we decided to lower the temperature as much as possible in order to favour the diastereoselective formation of one of the diastereoisomers (Table 3, entries 16–19). The preliminary attempts that we have performed required the generation of the imine from α-amido sulphone **1a** (K_2CO_3 [2 equiv.], 66 °C, 4 h, THF) and after the filtration of the base, the filtrate containing the crude imine was transferred to a separate flask and cooled to −78 °C, followed by the addition of a base and (*R*,*R*)-**5**. Such a reaction when performed with *n*-BuLi or LDA (Table 3, entries 16 and 17) did not produce the desired product; however, the use of $ZnEt_2$/(TMEDA)[45,46] resulted in the formation of a single diastereoisomer of **6a**, albeit with a low conversion (74%). Inspired by this result, we decided to perform the reaction directly at −78 °C but with the use of KOH (3 equiv.) as a simple, solid inorganic base (useful also in the synthesis of racemic α-aminophosphonates, Table 1) and α-amido sulfone **1a** in the presence of (*R*,*R*)-**5** (Table 3, entry 19). To our great satisfaction, during this reaction, the imine was generated *in situ* and reacted directly with (*R*,*R*)-**5**, producing the desired α-aminophosphonate **6a** as a single diastereoisomer after 4 days at −78 °C. Subsequently, the optimized reaction conditions were used in order to verify the substrate scope of this reaction (Table 4). We were pleased to see that aromatic α-amido sulphones **1a–f** reacted very well under such reaction conditions, producing the desired α-aminophosphonates **6a–f** as single diastereoisomers in good, isolated yields (85–95%). Importantly, neither the presence of electron-donating (**6d**) or electron-withdrawing (**6b** and **6c**) groups nor the place of substitution on the aromatic ring (**6e**) or the size of the aromatic substituent (**6f**) affected the diastereoselectivity of the reaction, and in each case, a single diastereoisomer of the desired α-aminophosphonates **6a–f** was formed. In the case of aliphatic α-amido sulfone **1k** and **1h**, presumably due to their lower reactivity, the yields were lower (65–75%) and the dr was up to 9 : 1. The absolute configuration of the newly formed asymmetric carbon in α-aminophosphonates (*R*,*R*,*R*)-**6a–h** was found to be (*R*), as determined by X-ray analysis of the crystals of compound (*R*,*R*,*R*)-**6a** (Fig. 1).[47]

Interestingly, when we used the opposite enantiomer of the chiral phosphorus auxiliary (*R*,*R*)-**5**, namely (*S*,*S*)-**5**, under similar reaction conditions, the absolute configuration at the

Table 3 Asymmetric hydrophosphonylation of α-amido sulphone **1a** with chiral TADDOL derived *H*-phosphonate (*R*,*R*)-**5** – optimization of the reaction conditions[a]



Entry	Conditions	dr[b] (%)/Conv.[b] [%]
1	K_2CO_3 (4 equiv.), 66 °C, 4 h, THF	35 : 65 [80]
2	Cs_2CO_3 (4 equiv.), 66 °C, 4 h, THF	33 : 67 [97]
3	NaOH (4 equiv.), 66 °C, 4 h, THF	36 : 64 [87]
4	KOH (4 equiv.), 66 °C, 4 h, THF	34 : 66 [90]
5	Pyridine (4 equiv.), 66 °C, 4 h, THF	—
6	Et_3N (4 equiv.), 66 °C, 4 h, THF	—
7	Cs_2CO_3 (4 equiv.), 80 °C, 4 h, 2-methyl THF	36 : 64 [89]
8	Cs_2CO_3 (4 equiv.), 110 °C, 4 h, toluene	65 : 35 [97]
9	Cs_2CO_3 (4 equiv.), 82 °C, 4 h, acetonitrile	45 : 55 [84]
10	KOH (2.5 equiv.), Fe_2O_3, r.t., 5 days, DCM	60 : 40 [80][c]
11	KOH (2.5 equiv.), Al_2O_3, r.t., 5 days, DCM	25 : 75 [89][c]
12	KOH (2.5 equiv.), ZnO, r.t., 5 days, DCM	30 : 70 [76][c]
13	KOH (2.5 equiv.), MgO, r.t., 5 days, DCM	35 : 65 [74][c]
14	K_2CO_3 (2.5 equiv.), Al_2O_3, r.t.,5 days, DCM	22 : 78 [98][c]
15	NaOH (2.5 equiv.), Al_2O_3, r.t.,5 days, DCM	40 : 60 [98][c]
16	*n*-BuLi (1 equiv.), 12 h, −78 °C, THF	—[d]
17	LDA (1 equiv.), 12 h, −78 °C, THF	—[d]
18	$ZnEt_2$/(TMEDA) (1 equiv.), 12 h, −78 °C, THF	100 [74][d]
19	**KOH (3 equiv.), −78 °C, 4 days, THF**	**100 [95]**

[a] General reaction conditions (unless otherwise stated): α-amido sulphone **1a** (2.4 mmol), *H*-phosphonate (*R*,*R*)-**5** (2.4 mmol), and base (9,6 mmol, 4 equiv.). [b] Diastereoselectivity and conversion based on the ^{31}P NMR spectra of the crude reaction mixture. — no reaction. [c] 6.5 g of metal oxide for 6 mmol of base. [d] The imine was first generated by reacting **1a** with K_2CO_3 (2 equiv.) at 66 °C for 4 h in THF and after filtration, the filtrate containing the imine was transferred to a separate flask and cooled to −78 °C followed by the addition of an appropriate base and (*R*,*R*)-**5**.

newly generated asymmetric α-carbon atom changed to (*S*). This was unambiguously confirmed by the X-ray analysis of the crystals of compound (*S*,*S*,*S*)-**6d** (Fig. 1).[47] Additionally, circular dichroism (CD) spectroscopy measurements performed for the solutions of compounds (*R*,*R*,*R*)-**6d** and (*S*,*S*,*S*)-**6d** revealed that the two compounds are enantiomers as their CD spectra were mirror images of each other.[47] The possibility of selective preparation of both enantiomers of α-aminophosphonates by simple use of either of the two easily available enantiomers of the chiral auxiliary (*R*,*R*)-**5** or (*S*,*S*)-**5** represents a real advantage of the developed methodology and clearly shows the influence of the chiral auxiliary on the diastereoselectivity of the hydrophosphonylation of α-amido sulphones.

Finally, to demonstrate the synthetic utility of the obtained α-aminophosphonates, we have shown that the model compounds **3a** and **3n** and the pure diastereoisomers of (*R*,*R*,*R*)-**6a, b** can be selectively and easily deprotected (Scheme 2).

The acid hydrolysis of **3a** afforded free α-aminophosphonic acid **7a** (89% yield). In turn, hydrogenation of acid labile heteroaromatic **3n** or benzaldehyde derived **3a** α-aminophosphonates in the presence of Pd/C led to α-aminophosphonate **8n** (92% yield) or **8a** (89% yield), phosphonic analogue of 2-phenylglycine, with a free amino group suitable for subsequent incorporation into the peptide sequence.

In the case of pure diastereoisomers of (*R*,*R*,*R*)-**6a,b**, acid hydrolysis led to pure enantiomers of free α-aminophosphonic acids (*R*)-**7a** (90% yield) and (*R*)-**7b** (87% yield) without racemisation.

Conclusions

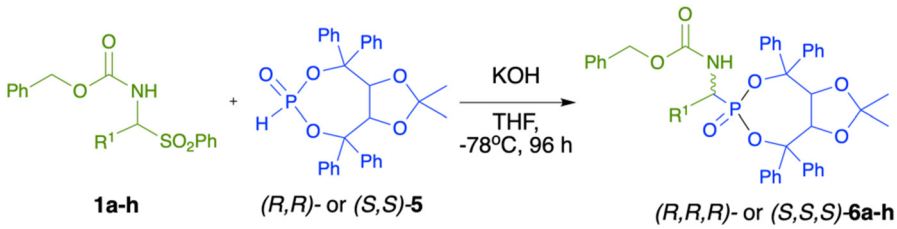
We have demonstrated that α-amido sulphones are easily available, bench-stable surrogates of imines and useful starting materials for the preparation of structurally diverse α-aminophosphonates and α-aminophosphonic acids. The developed methodology is based on the *in situ* generation of an imine during a three-component reaction of α-amido sulphones, *H*-phosphonates and a base under suitable conditions. The *in situ* generated imine undergoes hydrophosphonylation with various *H*-phosphonates in just 4 h in boiling THF, leading to α-aminophosphonates in high yields. In turn, when hydrophosphonylation is performed at −78 °C in the presence of a chiral *H*-phosphonate derived from easily available TADDOL, the desired α-aminophosphonates are obtained in a diastereoselective fashion (*dr* up to 100%). The asymmetric synthesis can be performed with precise control of the chirality at the newly generated α-carbon atom and selectively either (*R*)- or (*S*)-diastereoisomers can be produced. The developed methodology is operationally simple, and the products are obtained, in a majority of cases, in pure form after simple crystallization. The obtained α-aminophosphonates can be easily deprotected leading to α-aminophosphonic acids (also in enantiomerically pure form) that can find further application as useful building blocks in organic synthesis or medicinal chemistry.

Experimental

Materials and methods

All the substrates and solvents were of analytical grade purchased from Polish suppliers (Sigma-Aldrich and POCh) and

Table 4 Asymmetric hydrophosphonylation of α-amido sulphones **1** with TADDOL *H*-phosphonate **5** – substrate scope[a,b]



Entry	α-Amido sulphone **1**	*H*-Phosphonate **5**	α-Aminophosphonate **6**	Diastereomeric ratio (dr)	Yield[a] (%)
1	**1a** R^1 = Ph	(*R*,*R*)-**5**	(*R*,*R*,*R*)-**6a** R^1 = Ph	Single dia.	85
2	**1c** R^1 = 4-F-Ph	(*R*,*R*)-**5**	(*R*,*R*,*R*)-**6b** R^1 = 4-F-Ph	Single dia.	93
3	**1b** R^1 = 4-Cl-Ph	(*R*,*R*)-**5**	(*R*,*R*,*R*)-**6c** R^1 = 4-Cl-Ph	Single dia.	95
4	**1d** R^1 = 4-Me-Ph	(*R*,*R*)-**5**	(*R*,*R*,*R*)-**6d** R^1 = 4-Me-Ph	Single dia.	91
5	**1i** R^1 = 2,4-MeO-Ph	(*R*,*R*)-**5**	(*R*,*R*,*R*)-**6e** R^1 = 2,4-MeO-Ph	Single dia.	89
6	**1j** R^1 = 2-naphthyl	(*R*,*R*)-**5**	(*R*,*R*,*R*)-**6f** R^1 = 2-naphthyl	Single dia.	90
7	**1k** R^1 = Me	(*R*,*R*)-**5**	**6g** R^1 = Me	9 : 1	65
8	**1h** R^1 = iBu	(*R*,*R*)-**5**	**6h** R^1 = R^1 = iBu	9 : 1	75
9	**1a** R^1 = Ph	(*S*,*S*)-**5**	(*S*,*S*,*S*)-**6a** R^1 = Ph	Single dia.	88
10	**1c** R^1 = 4-F-Ph	(*S*,*S*)-**5**	(*S*,*S*,*S*)-**6b** R^1 = 4-F-Ph	Single dia.	91
11	**1d** R^1 = 4-Me-Ph	(*S*,*S*)-**5**	(*S*,*S*,*S*)-**6d** R^1 = 4-Me-Ph	Single dia.	93

[a] Yields are given for the purified, isolated products. [b] General procedure for the asymmetric hydrophosphonylation of α-amido sulphones **1**: In a 50 mL flask, a suitable amount of TADDOL derived *H*-phosphonate **5** (1 equiv.) was added to a solution of the appropriate α-amido sulphone **1** (1 equiv.) in THF (15 mL). After the resulting mixture was cooled to −78 °C, finely ground KOH (3 equiv.) was added to one portion to the mixture. The reaction mixture was stirred vigorously at the same temperature without any precaution to exclude air or moisture. After 4 days, saturated aq. NH_4Cl (*ca.* 15 mL) was added, and then the mixture was allowed to warm to room temperature. The organic layer was separated, and the aqueous layer was extracted three times with toluene (3 × 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and the filtrate was concentrated to give the crude product. The concentrated crude product was then purified by column chromatography using CH_2Cl_2 (100%) to CH_2Cl_2/MeOH 97 : 3 to afford the desired pure products **6a–h**.

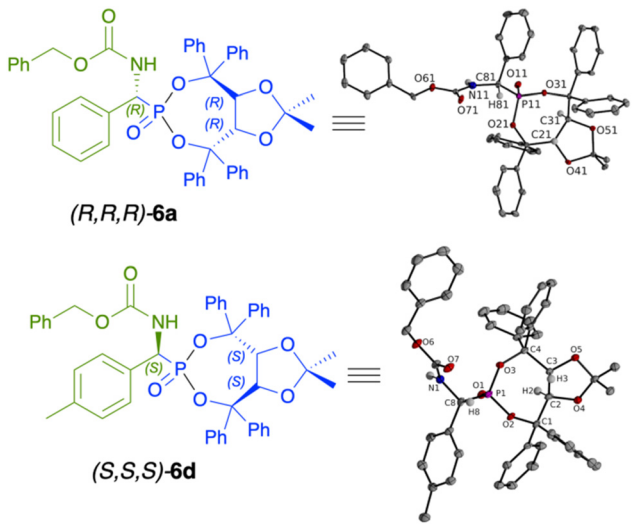
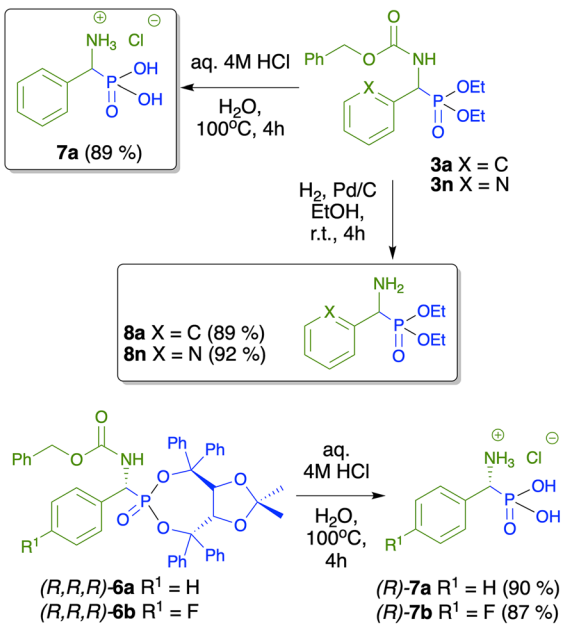


Fig. 1 Determination of the absolute configuration in compounds (*R*,*R*,*R*)-**6a** and (*S*,*S*,*S*)-**6d** by X-ray analysis.



Scheme 2 Further transformations of the obtained α-aminophosphonates.

used without further purification. Unless otherwise specified solvents were removed using a rotary evaporator. The ^1H, ^{13}C and ^{31}P NMR spectra were collected on a Jeol 400yh instrument (400 MHz for ^1H NMR, 162 MHz for ^{31}P NMR and 101 MHz for ^{13}C NMR) and were processed using dedicated software (Delta 5.0.5). Samples of the product were diluted with $CDCl_3$, DMSO-d_6 or D_2O with reference to the respective residual ^1H or ^{13}C signals of the solvents. Coupling constant are reported in hertz (Hz). Multiplicities are reported with the abbreviations: s (singlet), brs (broad singlet), d (doublet),

t (triplet), and m (multiplet) and the reported J values are those observed from the splitting patterns in the spectrum and may not reflect the true coupling constant values. Analytical thin layer chromatography was performed on SIL G/UV254 plates and visualization was accomplished using UV light (254 nm). Column chromatography (FC) was performed using Sigma-Aldrich® silica gel high purity-grade (SiO_2 70–230 mesh). The optical rotations were measured on a Bellingham + Stanley ADP440 + polarimeter and $[\alpha]_D^T$ values are given in deg cm^3 g^{-1} dm^{-1}; concentrations, c, are listed in 0.05 g/5 mL^{-1}. Mass spectra were recorded using a Waters LCT Premier XE mass spectrometer (electrospray ionization, ESI) (Waters, Milford, MA, USA) and melting points were determined using SRS melting point apparatus OptiMelt MPA 100 (Stanford Research System, Sunnyvale, CA, USA) and are reported at the Faculty of Chemistry, Wroclaw University of Science and Technology. CCDC 2248672 for (*R,R,R*)-**6a** and 2248673† for (*S,S,S*)-**6d** contain the supplementary crystallographic data for this paper.

General procedure for hydrophosphonylation of α-amido sulphones 1. In a 50 mL flask, a suitable amount of *H*-phosphonate **2** (2.4 mmol, 1 equiv.) was added to a solution of α-amido sulphone **1** (2.4 mmol, 1 equiv.) and K_2CO_3 (9.6 mmol, 4 equiv.) in THF (15 mL). The mixture was heated at 66 °C for 4 h and then cooled and filtered. The solvent was removed under reduced pressure using a rotatory evaporator. The crude products were crystallized from diethyl ether in the case of solids and oily products were purified by column chromatography (eluent: hexane/ethyl acetate = 5 : 1 to 3 : 1) to obtain the pure products **3a–r**.

Benzyl ((diethoxyphosphoryl)(phenyl)methyl)carbamate (3a). White solid, 860 mg, 95% yield; mp: 112–114 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.43 (d, J = 10.8 Hz, 1H), 7.43 (d, J = 7.9 Hz, 2H), 7.34–7.22 (m, 8H), 5.11–4.96 (m, 3H), 4.02–3.71 (m, 4H), 1.10 (t, J = 7.0 Hz, 3H), 1.03 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 156.48 (d, J = 8.6 Hz), 137.38, 136.24, 128.86, 128.74, 128.69, 128.64, 128.40, 128.31, 128.13 126.01, 66.38, 62.99 (d, J = 7.1 Hz), 62.77 (d, J = 6.8 Hz), 52.72 (d, J = 153.6 Hz), 16.72 (d, J = 5.4 Hz), 16.58 (d, J = 5.6 Hz); ^{31}P NMR (162 MHz, DMSO-d_6) δ: 21.97. HRMS (ESI) calculated for $C_{19}H_{24}NO_5PNa$ $[M + Na]^+$: 400.1290 found 400.1289.

Benzyl ((dibutoxyphosphoryl)(phenyl)methyl)carbamate (3b). White solid, 905 mg, 87% yield; mp: 104–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, J = 7.4 Hz, 2H), 7.37–7.23 (m, 8H), 5.89 (s, 1H, NH), 5.20–5.00 (m, 3H), 4.07–3.93 (m, 2H), 3.90–3.80 (m, 1H), 3.67–3.57 (m, 1H), 1.63–1.51 (m, 2H), 1.44–1.27 (m, 4H), 1.24–1.13 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H), 0.80 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.74 (d, J = 12.1 Hz), 136.19, 135.41, 128.70 (d, J = 2.0 Hz), 128.59, 128.33–128.14 (m), 127.97 (d, J = 5.8 Hz), 67.35, 67.05 (d, J = 7.1 Hz), 66.85 (d, J = 7.3 Hz), 52.51 (d, J = 153.3 Hz), 32.56 (d, J = 5.8 Hz), 32.35 (d, J = 5.9 Hz), 18.62 (d, J = 13.1 Hz), 13.61 (d, J = 7.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 21.94. HRMS (ESI) calculated for $C_{23}H_{32}NO_5PNa$ $[M + Na]^+$: 456.1916 found 456.1819.

Benzyl ((diisopropoxyphosphoryl)(phenyl)methyl)carbamate (3c). White solid, 919 mg, 94% yield; mp: 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, J = 7.5 Hz, 2H), 7.35–7.24 (m, 8H), 5.85 (s, 1H NH), 5.17–4.99 (m, 3H), 4.70–4.59 (m, 1H), 4.47–4.37 (m, 1H), 1.28 (d, J = 6.2 Hz, 3H), 1.21 (d, J = 6.2 Hz, 3H), 1.18 (d, J = 6.2 Hz, 3H), 0.89 (d, J = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.80 (d, J = 9.5 Hz), 128.27 (d, J = 3.8 Hz), 128.18–128.05 (m), 72.31 (d, J = 7.2 Hz), 71.87 (d, J = 7.4 Hz), 67.31, 53.12 (d, J = 154.1 Hz), 24.28 (d, J = 3.1 Hz), 24.19 (d, J = 3.5 Hz), 23.79 (d, J = 5.2 Hz), 23.21 (d, J = 5.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 20.18. HRMS (ESI) calculated for $C_{21}H_{28}NO_5PNa$ $[M + Na]^+$: 428.1603 found 428.1613.

Benzyl ((bis(benzyloxy)phosphoryl)(phenyl)methyl)carbamate (3d). White solid, 1101 mg, 91% yield; mp: 124–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49–7.20 (m, 18H), 7.09 (dd, J = 6.3, 2.8 Hz, 2H), 6.02 (s, 1H, NH), 5.27 (dd, J = 21.8, 9.6 Hz, 1H), 5.12–4.92 (m, 4H), 4.83 (dd, J = 11.7, 7.2 Hz, 1H), 4.60 (dd, J = 11.6, 8.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.73 (d, J = 11.3 Hz), 136.14, 135.78, 135.03, 128.81 (d, J = 2.1 Hz), 128.68–128.00 (m), 127.95, 68.67 (d, J = 6.7 Hz), 68.52 (d, J = 7.1 Hz), 67.40, 52.77 (d, J = 154.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 22.89. HRMS (ESI) calculated for $C_{29}H_{28}NO_5PNa$ $[M + Na]^+$: 524.1603 found 524.1605.

Benzyl ((4-chlorophenyl)(diethoxyphosphoryl)methyl)carbamate (3e). White solid, 938 mg, 95% yield; mp: 116–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.24 (m, 9H), 5.98 (s, 1H, NH), 5.17–4.99 (m, 3H), 4.13–3.98 (m, 2H), 3.98–3.88 (m, 1H), 3.82–3.70 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.82 (d, J = 12.9 Hz), 136.09, 134.19 (d, J = 3.3 Hz), 134.01, 129.25 (d, J = 2.0 Hz), 128.56, 128.24, 128.02 (d, J = 6.0), 129.57–127.99 (m), 67.46 (s), 63.54 (d, J = 6.9 Hz), 63.35 (d, J = 7.2 Hz), 52.02 (d, J = 156.0 Hz), 16.44 (d, J = 5.7 Hz), 16.27 (d, J = 5.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 21.38 (s); HRMS (ESI) calculated for $C_{19}H_{23}ClNO_5PNa$ $[M + Na]^+$: 434.0900 found 434.0899.

Benzyl ((4-chlorophenyl)(dibutoxyphosphoryl)methyl)carbamate (3f). White solid, 921 mg; 82% yield; mp: 95–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.23 (m 9H), 5.89 (brs, 1H), 5.16–5.01 (m, 3H), 4.06–3.94 (m, 2H), 3.92–3.83 (m, 1H), 3.73–3.64 (m, 1H), 1.61–1.52 (m, 2H), 1.47–1.39 (m, 2H), 1.37–1.27 (m, 2H), 1.26–1.16 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H), 0.82 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.74 (d, J = 12.4 Hz), 136.06, 134.20, 129.32, 128.87, 128.62, 128.37, 128.22, 67.48, 67.13 (d, J = 7.1 Hz), 67.03 (d, J = 7.5 Hz), 51.98 (d, J = 156.2 Hz), 32.54 (d, J = 5.8 Hz), 32.37 (d, J = 5.8 Hz), 18.68, 18.58, 13.63, 13.56; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 21.35. HRMS (ESI) calculated for $C_{23}H_{31}ClNO_5PNa$ $[M + Na]^+$: 490.1526 found 490.1534.

Benzyl ((4-chlorophenyl)(diisopropoxyphosphoryl)methyl) carbamate (3g). White solid, 938 mg; 95% yield; mp:132–134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.14 (m, 9H), 5.91 (brs, 1H), 5.16–4.97 (m, 3H, CHP and CH2Ph), 4.69–4.59 (m, 1H), 4.52–4.42 (m, 1H), 1.28 (d, J = 6.2 Hz, 3H), 1.23 (d, J = 6.2 Hz, 3H), 1.18 (d, J = 6.2 Hz, 3H), 0.96 (d, J = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.83 (d, J = 9.6 Hz), 136.15, 134.46, 134.02, 129.47, 128.71, 128.60, 128.35, 128.27, 72.39 (d, J = 7.2 Hz), 72.12 (d, J = 7.4 Hz), 67.42, 52.58 (d, J = 157.0 Hz), 24.21 (d, J = 3.3 Hz), 24.16 (d, J = 3.5 Hz), 23.78 (d, J

= 5.2 Hz), 23.36 (d, J = 5.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ: 19.47; HRMS (ESI) calculated for $C_{21}H_{27}ClNO_5PNa$ $[M + Na]^+$: 462.1213 found 462.1208.

Benzyl ((bis(benzyloxy)phosphoryl)(4-chlorophenyl)methyl) carbamate (3h). White solid, 1.221 mg; 95% yield; mp: 148–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.20 (m, 17H), 7.10 (dd, J = 7.3, 1.9 Hz, 2H), 5.94 (brs, 1H), 5.18 (dd, J = 22.2, 9.4 Hz, 1H), 5.09–4.91 (m, 4H), 4.83 (dd, J = 11.7, 7.7 Hz, 1H), 4.70 (dd, J = 11.6, 9.1 Hz, 1H); ^{13}C NMR (101 MHz, DMSO), δ: 156.48 (d, J = 8.5 Hz), 137.21, 136.78 (d, J = 14.4 Hz), 135.08, 133.10, 130.65, 129.13–127.82 (m, aromatic carbon atoms), 68.17 (d, J = 6.9 Hz), 67.91 (d, J = 6.6 Hz), 66.56, 52.23 (d, J = 154.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 22.38. HRMS (ESI) calculated for $C_{29}H_{27}ClNO_5PNa$ $[M + Na]^+$: 558.1213 found 538.1221.

Benzyl ((diethoxyphosphoryl)(4-fluorophenyl)methyl)carbamate (3i). White solid, 808 mg; 82% yield; mp: 124–126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40 (brs, 2H), 7.31 (brs, 5H), 7.01 (t, J = 8.6 Hz, 2H), 6.05 (brs, 1H), 5.17–5.01 (m, 3H), 4.14–3.99 (m, 2H), 3.98–3.87 (m, 1H), 3.79–3.68 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.82 (d, J = 11.1 Hz), 136.13, 131.30, 129.77, 128.59, 128.33, 128.22, 115.74 (d, J = 2.0 Hz), 115.53 (d, J = 2.0 Hz), 67.42, 63.48 (d, J = 6.9 Hz), 63.26 (d, J = 7.1 Hz), 51.90 (d, J = 155.6 Hz), 16.43 (d, J = 5.7 Hz), 16.25 (d, J = 5.7 Hz).; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 21.66. HRMS (ESI) calculated for $C_{19}H_{23}FNO_5PNa$ $[M + Na]^+$: 418.1196 found 418.1190.

Benzyl ((diethoxyphosphoryl)(*p*-tolyl)methyl)carbamate (3j). White solid, 771 mg, 83% yield; mp: 115–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36–7.24 (m, 7H), 7.14 (d, J = 8.2 Hz, 2H), 5.74 (brs, 1H), 5.16–5.00 (m, 3H), 4.13–4.00 (m, 2H), 3.97–3.87 (m, 1H), 3.78–3.65 (m, 1H), 2.32 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.75 (d, J = 11.0 Hz), 138.08, 136.22, 132.20, 129.43, 128.58, 128.28, 127.89, 67.33, 63.45 (d, J = 6.9 Hz), 63.16 (d, J = 7.1 Hz), 52.25 (d, J = 154.7 Hz), 21.25 (s), 16.45 (d, J = 5.8 Hz), 16.26 (d, J = 5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 22.14. HRMS (ESI) calculated for $C_{20}H_{26}NO_5PNa$ $[M + Na]^+$: 414.1446 found 414.1448

Benzyl ((dibutoxyphosphoryl)(*p*-tolyl)methyl)carbamate (3k). White solid, 835 mg; 74% yield; mp: 108–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38–7.22 (m, 7H), 7.14 (d, J = 8.2 Hz, 2H), 5.77 (brs, 1H), 5.20–4.96 (m, 3H), 4.06–3.95 (m, 2H), 3.86 (1H), 3.69–3.58 (m, 1H), 2.32 (s, 3H), 1.64–1.53 (m, 2H), 1.46–1.28 (m, 4H), 1.26–1.14 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H), 0.80 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$), δ: 155.70 (d, J = 10.7 Hz), 138.03, 136.23, 132.33, 129.97–127.77 (m), 67.31, 67.04 (d, J = 7.1 Hz), 66.81 (d, J = 7.4 Hz), 52.20 (d, J = 154.7 Hz), 32.57 (d, J = 5.8 Hz), 32.37 (d, J = 5.8 Hz), 21.22, 18.64 (d, J = 11.8 Hz), 13.62 (d, J = 7.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$), δ: 22.13. HRMS (ESI) calculated for $C_{24}H_{34}NO_5PNa$ $[M + Na]^+$: 470.2072 found 470.2079.

Benzyl ((diisopropoxyphosphoryl)(*p*-tolyl)methyl)carbamate (3l). White solid; 812 mg; 77% yield; mp: 126–128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.22 (m, 7H), 7.12 (d, J = 8.3 Hz, 2H), 5.77 (brs, 1H), 5.20–4.95 (m, 3H), 4.71–4.59 (m, 1H), 4.51–4.36 (m, 1H), 2.31 (s, 3H), 1.28 (d, J = 6.2 Hz, 3H), 1.22 (d, J = 6.2 Hz, 3H), 1.19 (d, J = 6.2 Hz, 3H), 0.92 (d, J = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$), δ: 155.78 (d, J = 11.0 Hz), 137.85, 136.30, 132.68, 130.19–127.62 (m), 72.21 (d, J = 7.2 Hz), 71.80 (d, J = 7.5 Hz), 67.24, 52.82 (d, J = 156.8 Hz), 24.29 (d, J = 3.1 Hz), 24.19 (d, J = 3.4 Hz), 23.80 (d, J = 5.3 Hz), 23.27 (d, J = 5.7 Hz), 21.23; ^{31}P NMR (162 MHz, $CDCl_3$), δ: 20.35. HRMS (ESI) calculated for $C_{22}H_{30}NO_5PNa$ $[M + Na]^+$: 442.1759 found 442.1758.

Benzyl ((bis(benzyloxy)phosphoryl)(*p*-tolyl)methyl)carbamate (3m). White solid, 1115 mg; 91% yield; mp: 128–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.22 (m, 15H), 7.15–7.07 (m, 4H), 5.84 (brs, 1H), 5.21 (dd, J = 21.5, 9.6 Hz, 1H), 5.11–4.92 (m, 4H), 4.83 (dd, J = 11.7, 7.3 Hz, 1H), 4.62 (dd, J = 11.7, 8.5 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.75 (d, J = 10.8 Hz), 138.15, 136.33–135.70 (m), 132.00, 129.52, 128.84–127.69 (m, aromatic carbon atom), 68.64 (d, J = 6.9 Hz), 68.47 (d, J = 7.2 Hz), 52.50 (d, J = 155.7 Hz), 21.27; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 23.08. HRMS (ESI) calculated for $C_{30}H_{30}NO_5PNa$ $[M + Na]^+$: 538.1759 found 538.1765.

Benzyl ((diethoxyphosphoryl)(pyridin-2-yl)methyl)carbamate (3n). white solid, 790 mg, 87% yield, mp: 110–112 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.48 (d, J = 4.7 Hz, 1H), 8.21 (d, J = 9.8 Hz, 1H), 7.77 (t, J = 7.7 Hz, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.37–7.24 (m, 5H), 5.25 (dd, J = 21.7, 10.0 Hz, 1H), 5.10–4.98 (m, 2H), 4.02–3.79 (m, 4H), 1.12 (t, J = 7.0 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.86, 167.53, 156.42 (d, J = 8.0 Hz), 155.71, 149.18, 137.33, 132.26, 128.85, 128.39, 128.28, 123.47 (d, J = 2.4 Hz), 123.33 (d, J = 3.9 Hz), 66.48, 63.07 (d, J = 6.8 Hz), 62.91 (d, J = 6.7 Hz), 54.91 (d, J = 148.0 Hz), 16.69 (d, J = 5.5 Hz), 16.56 (d, J = 5.6 Hz); ^{31}P NMR (162 MHz, DMSO-d_6) δ: 20.97. HRMS (ESI) calculated for $C_{19}H_{24}NO_5PNa$ $[M + Na]^+$: 401.1294 found 401.1291.

Benzyl (1-(diethoxyphosphoryl)propyl)carbamate (3o). Colourless oil, 585 mg, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.06 (m, 5H), 5.17–5.02 (m, 3H), 4.14–3.91 (m, 4H), 1.94–1.84 (m, 1H), 1.63–1.51 (m, 1H), 1.25 (dt, J = 17.9, 7.1 Hz, 6H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.29 (d, J = 6.2 Hz), 136.41 (s), 128.64–128.10 (m), 67.16 (s), 62.67 (d, J = 7.1 Hz), 62.49 (d, J = 6.7 Hz), 49.11 (d, J = 155.8 Hz), 23.35 (s), 16.41 (s), 10.49 (s); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.41 (s). HRMS (ESI) calculated for $C_{15}H_{24}NO_5PNa$ $[M + Na]^+$: 352.1290 found 352.1286.

Benzyl (1-(diethoxyphosphoryl)-2-methylpropyl)carbamate (3p). Yellowish oil, 588 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.19–5.04 (m, 3H), 4.13–3.94 (m, 4H), 2.23–2.13 (m, 1H), 1.32–1.19 (m, 6H), 1.02–0.95 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.46 (d, J = 6.5 Hz), 136.39 (s), 129.44–127.29 (m), 67.23 (s), 62.42 (m), 52.68 (d, J = 152.9 Hz), 29.03 (d, J = 4.5 Hz), 20.51 (d, J = 12.7 Hz), 17.78 (d, J = 4.2 Hz), 16.42 (d, J = 6.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.83 (s). HRMS (ESI) calculated for $C_{16}H_{26}NO_5PNa$ $[M + Na]^+$: 366.1446 found 366.1450.

Benzyl (1-(bis(benzyloxy)phosphoryl)-2-methylpropyl)carbamate (3q). White solid; 728 mg, 62% yield; mp: 82–84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.21 (m, 15H), 5.13–5.03 (m, 3H), 5.02–4.92 (m, 4H), 4.19–4.06 (m, 1H), 2.26–2.15 (m, 1H),

1.04–0.93 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 156.40 (d, J = 6.5 Hz), 136.35–136.05 (m), 128.74–128.02 (m), 67.85 (t, J = 6.8 Hz), 67.29, 53.00 (d, J = 152.4 Hz), 29.07 (d, J = 4.6 Hz), 20.51 (d, J = 12.8 Hz), 17.87 (d, J = 4.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ: 25.77. HRMS (ESI) calculated for $C_{25}H_{30}NO_5PNa$ [M + Na]$^+$: 490.1759 found 490.1760.

Benzyl (1-(diethoxyphosphoryl)-3-methylbutyl)carbamate (3r). White solid, 497 mg, 58% yield; 88–90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 5.17–4.93 (m, 3H), 4.17–3.99 (m, 4H), 1.72 (m, 1H), 1.58–1.51 (m, 2H), 1.24 (dt, J = 19.6, 7.1 Hz, 6H), 0.91 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.04 (d, J = 5.0 Hz), 136.43 (s), 128.56 (s), 128.24 (s), 128.14 (s), 62.67 (d, J = 7.1 Hz), 62.49 (d, J = 6.6 Hz), 46.00 (d, J = 156.4 Hz), 38.61 (s), 24.47 (d, J = 13.3 Hz), 23.40 (s), 21.20 (s), 16.45 (dd, J = 5.8, 3.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.00 (s). HRMS (ESI) calculated for $C_{17}H_{28}NO_5PNa$ [M + Na]$^+$: 380.1603 found 380.1603.

General procedure of the asymmetric hydrophosphonylation of α-amido sulphones. In a 50 mL flask, a suitable amount of TADDOL derived *H*-phosphonate **5** (1 equiv.) was added to a solution of the appropriate α-amido sulphone **1** (1 equiv.) in THF (15 mL). After the resulting mixture was cooled to −78 °C, finely ground KOH (3 equiv.) was added in one portion to the mixture. The reaction mixture was stirred vigorously at the same temperature without any precaution to exclude air or moisture. After 4 days, saturated aq. NH_4Cl (*ca.* 15 mL) was added, and then the mixture was allowed to warm to room temperature. The organic layer was separated, and the aqueous layer was extracted three times with toluene (3 × 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and the filtrate was concentrated to give the crude product. The concentrated crude product was then purified by column chromatography using CH_2Cl_2 (100%) to CH_2Cl_2/MeOH 97 : 3 to afford the desired pure products **6a–h**.

Benzyl (((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2] dioxaphosphepin-6-yl)(phenyl)methyl)carbamate (*R,R,R*)-6a. White solid; 187 mg, 85% yield; mp: 123–125 °C; $[\alpha]_D^{20}$ = −145.8 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$), δ: 7.58–7.53 (m, 2H), 7.52–7.47 (m, 2H), 7.42–7.15 (m, 24H), 7.02–6.97 (m, 2H), 5.73 (br, s, 1H), 5.51 (d, J = 7.9 Hz, 1H), 5.36–4.96 (m, 4H) 0.81 (s, 3H), 0.53 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$), δ: 155.70 (d, $^1J_{CO}$ = 14.0 Hz), 144.14, 143.31, 139.33 (d, J = 9.9 Hz), 135.15, 129.82, 129.62, 128.63, 128.57, 128.54, 128.24, 128.12, 127.97, 127.91, 127.78, 127.40, 127.30, 126.62, 114.10, 90.93 (d, J = 12.6 Hz), 87.39 (d, J = 8.2 Hz), 79.94, 79.08, 67.40, 53.91 (d, $^1J_{CP}$ = 161.2 Hz), 27.02, 26.53; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 15.07; HRMS (ESI) calculated for $C_{46}H_{42}NO_7PNa$ [M + Na]$^+$: 774.2596 found 774.2600.

Benzyl (((3aS,8aS)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2] dioxaphosphepin-6-yl)(phenyl)methyl)carbamate (*S,S,S*)-6a. White solid, 194 mg, 88% yield; mp: 124–126 °C; $[\alpha]_D^{20}$ = +171.0 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$), δ: 7.58–7.53 (m, 2H), 7.52–7.44 (m, 2H), 7.42–7.13 (m, 24H), 7.03–6.96 (m, 2H), 5.70 (br, s, 1H), 5.51 (d, J = 7.9 Hz), 5.36–4.96 (m, 4H), 0.80 (s, 3H), 0.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$), δ: 155.69 (d, $^1J_{CO}$ = 12.6 Hz), 144.22, 143.31, 139.34 (d, $^2J_{CP}$ = 9.9 Hz), 135.17, 129.63, 128.64, 128.62, 128.56, 128.54, 128.23, 128.12, 128.09, 127.90, 127.77, 127.39, 127.29, 126.61, 114.10, 90.94 (d, $^2J_{CP}$ = 13.0 Hz), 87.37 (d, $^2J_{CP}$ = 9.7 Hz), 79.91, 79.05, 67.39, 53.92 (d, $^1J_{CP}$ = 161.9 Hz), 27.01, 26.54; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 15.05 HRMS (ESI) calculated for $C_{46}H_{42}NO_7PNa$ [M + Na]$^+$: 774.2596 found 774.2594.

Benzyl(((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetra-phenyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2]dioxaphosphepin-6-yl)(4-fluorophenyl)methyl)carbamate (*R,R,R*)-6b. White solid, 210 mg, 93% yield; mp: 174–176 °C; $[\alpha]_D^{20}$ = −139.2 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$), δ: 7.54–7.48 (m, 2H), 7.47–7.41 (m, 2H), 7.38–7.12 (m, 21H), 7.03–6.88 (m, 4H), 5.64 (br, s, 1H), 5.49 (d, J = 7.6), 5.33–4.89 (m, 4H), 0.76 (s, 3H), 0.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$), δ: 163.87 (d, J_{CF} = 3.1 Hz), 161.41 (d, $^1J_{CO}$ = 3.3 Hz), 144.05 (d, $^2J_{CP}$ = 6.2 Hz), 143.14, 139.21 (d, $^3J_{CF}$ = 9.9 Hz), 131.11, 129.78, 129.57, 128.68, 128.64, 128, 56, 128.48, 128.36, 128.26, 128.17, 127.95, 127.87, 127.39, 127.30, 127.25, 126.60, 115.51 (d, $^2J_{CF}$ = 21.7 Hz), 114.22, 91.14 (d, $^2J_{CP}$ = 11.7 Hz), 87.57 (d, $^2J_{CP}$ = 10.4 Hz), 79.68, 78.93, 67.45, 53.21 (d, J_{CP} = 161.4 Hz), 26.96, 26.52; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.69; HRMS (ESI) calculated for $C_{46}H_{41}FNO_7PNa$ [M + Na]$^+$: 792.2502 found 792.2498.

Benzyl (((3aS,8aS)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*] [1,3,2] dioxaphosphepin-6-yl)(4-fluorophenyl)methyl)carbamate (*S,S,S*)-6b. White solid, 205 mg, 91% yield; mp:208–210 °C; $[\alpha]_D^{20}$ = + 169.2 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$), δ: 7.56–7.51 (m, 2H), 7.49–7.43 (m, 2H), 7.41–7.15 (m, 21H), 7.01–6.91 (m, 2H), 5.70 (br, s 1H), 5.49 (d, J = 7.8 Hz, 1H), 5.31–4.94 (m, 4H), 78, 0.52; ^{13}C NMR (101 MHz, $CDCl_3$), δ: 163.87 (d, $^1J_{CF}$ = 3.1 Hz), 161.42 (d, $^1J_{CO}$ = 3.1 Hz), 155.68, 144.10 (d, $^2J_{CP}$ = 6.2 Hz), 143.16, 139.25 (d, $^3J_{CF}$ = 9.9 Hz), 131.12, 129.59, 128.68, 128.64, 128.57, 128.50, 128.36, 128.25, 127.94, 127.88, 127.40, 127.31, 127.26, 126.62, 115.50 (d, $^2J_{CF}$ = 19.5 Hz), 114.22, 91.15 (d, $^2J_{CP}$ = 13.5 Hz), 87.54 (d, $^2J_{CP}$ = 9.0 Hz), 79.77, 78.95, 67.45, 53.24 (d, $^1J_{CP}$ = 167.8 Hz), 26.98, 26.54; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.65; HRMS (ESI) calculated for $C_{46}H_{42}NO_7PNa$ [M + Na]$^+$: 792.2502 found 792.2498.

Benzyl((4-chlorophenyl)((3aR,8aR)-2,2-dimethyl-6-oxido 4,4,8,8-tetraphenyltetrahydro [1,3]dioxolo[4,5-*e*][1,3,2] dioxaphosphepin-6-yl)methyl)carbamate (*R,R,R*)-6c. White solid 219 mg, 95% yield; mp: 236–238 °C; $[\alpha]_D^{20}$ = −135.5 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56–7.49 (m, 2H), 7.49–7.43 (m, 2H), 7.41–7.14 (m, 23H), 6.94–6.89 (m, 2H), 5.70 (s, br, 1H), 5.48 (d, J = 7.9 Hz, 1H), 5.29–4.94 (m, 4H), 0.77 (s, 3H), 0.52 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 155.71 (d, $^1J_{CO}$ = 14.1 Hz), 144.06 (d, J_{CCl} = 6.2 Hz), 143.11, 139.19 (d, $^2J_{CCl}$ = 9.9 Hz), 136.08, 134.03 (d, $^2J_{CP}$ = 3.6 Hz), 129.84, 129.62, 129.13, 128.73, 128.59, 128.50, 128.40, 128.28, 127.93 (d, $^3J_{CP}$ = 6.2 Hz), 127.40, 127.32, 126.61, 114.26, 92.02 (d, $^1J_{CP}$ = 13.5 Hz), 91.33 (d, $^1J_{CP}$ = 12.7 Hz), 79.66, 78.90, 67.49, 53.46 (d, J_{CP} = 161.5 Hz), 26.98, 26.55; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 14.51; HRMS (ESI) calculated for C46H41ClNO$_7$PNa [M + Na]$^+$: 808.2207 found 808.2220.

Benzyl (((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2] dioxaphosphepin-6-yl)(*p*-tolyl)methyl)carbamate (*R,R,R*)-6d. White solid; yield = 91%; mp; 128–130 °C; $[\alpha]_D^{20}$ = −122.7 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.58–7.52 (m, 2H), 7.50–7.45 (m, 2H), 7.40–7.14 (m, 21H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.01 (d, *J* = 6.9 Hz, 2H), 5.65 (br, s, 1H), 5.50 (d, *J* = 7.9 Hz, 1H), 5.37–4.97 (m, 4H), 2.35 (s, 3H), 0.80 (s, 3H), 0.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 155.62 (d, $^1J_{CO}$ = 12.3 Hz), 144.18 143.36, 139.38 (d, *J* = 9.9 Hz), 137.80 132.12, 129.62, 129.31, 128.59, 128.51, 128.21, 127.88, 127.75, 127.37, 127.27 (d, $^3J_{CP}$ = 4.5 Hz), 126.63, 114.06, 90.80 (d, $^2J_{CP}$ = 14.2 Hz), 87.29 (d, $^3J_{CP}$ = 9.2 Hz), 79.96, 79.09, 67.33, 53.64 (d, $^1J_{CP}$ = 165.6 Hz), 27.01, 26.53, 21.28; ^{31}P NMR (162 MHz, $CDCl_3$) *δ*: 15.23; HRMS (ESI) calculated for $C_{47}H_{44}NO_7PNa$ [M + Na]$^+$: 788.2753 found 788.2749.

Benzyl (((3aS,8aS)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2] dioxaphosphepin-6-yl)(*p*-tolyl)methyl)carbamate (*S,S,S*)-6d. White solid, 208 mg, 93% yield; mp: 154–156 °C; $[\alpha]_D^{20}$ = +142.2 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.57–7.51 (m, 2H), 7.50–7.45 (m, 2H), 7.40–7.12 (m, 21H), 7.09 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 7.6 Hz, 2H), 5.61 (br, s, 1H), 5.48 (d, *J* = 7.9 Hz, 1H), 5.50–4.99, (m, 4H), 2.34 (s, 3H), 0.79 (s, 3H), 0.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*:155.62 (d, $^1J_{CO}$ = 12.4 Hz), 144.16, 143.38, 139.37 (d, $^2J_{CP}$ = 9.9 Hz), 137.85, 132.11, 129.62, 129.28, 128.58, 128.50, 128.21, 127.87, 127.73, 127.36 127.26, 127.24, 126.61, 114.05, 90.82 (d, $^2J_{CP}$ = 9.9 Hz), 87.27 (d, $^2J_{CP}$ = 7.9 Hz), 79.93, 79.07, 67.33, 53.61 (d, $^1J_{CP}$ = 162.8 Hz), 27.00, 26.52, 21.26; ^{31}P NMR (162 MHz, $CDCl_3$) *δ*: 15.21; HRMS (ESI) calculated for $C_{47}H_{44}NO_7PNa$ [M + Na]$^+$: 788.2753 found 788.2757.

Benzyl ((2,5-dimethoxyphenyl)((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*]-[1,3,2] dioxaphosphepin-6-yl)methyl)carbamate (*R,R,R*)-6e. White solid, 212 mg, 89% yield; mp: 120–122 °C $[\alpha]_D^{20}$ = −133.5 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.57–7.52 (m, 2H), 7.50–7.46 (m, 2H), 7.38–7.15 (m, 19H), 7.07–7.03 (m, 2H), 6.95–6.84 (m, 2H), 6.79 (d, *J* = 6.7 Hz, 1H), 5.68–5.58 (br, s, 1H), 5.51 (d, *J* = 8.0 Hz), 5.30–4.93 (m, 4H), 3.86 (s, 3H), 3.69 (s, 3H), 0.82 (s, 3H), 0.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 155.63 (d, $^1J_{CO}$ = 13.6 Hz), 149.09 (d, $^3J_{CP}$ = 2.0 Hz), 149.03 (d, $^3J_{CP}$ = 2.7 Hz), 129.47, 128.63, 128.53, 128.47, 128.17, 127.90, 127.82, 127.42, 127.29, 127.14, 126.61, 120.57 (d, $^2J_{CP}$ = 7.2 Hz), 113.92, 111.08, 90.60 (d, $^1J_{CP}$ = 11.7 Hz), 87.21 (d,$^1J_{CP}$ = 11.5 Hz), 80.35, 79.09, 67.39, 56.01, 55.90, 53.50 (d, $^1J_{CP}$ = 164.1 Hz), 26.99, 26.47; ^{31}P NMR (162 MHz, $CDCl_3$) *δ*:15.29; HRMS (ESI) calculated for $C_{48}H_{46}NO_9PNa$ [M + Na]$^+$: 834.2808 found 834.2809.

Benzyl (((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2] dioxaphosphepin-6-yl)-(naphthalen-2-yl)methyl)carbamate (*R,R,R*)-6f. White solid; 211 mg, 90% yield; mp: 126–128 °C; $[\alpha]_D^{20}$ = −119.0 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.83 (d, *J* = 5.7 Hz, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.71–7.60 (m, 2H), 7.58–7.07 (m, 24H), 7.06–6.91 (m, 2H), 6.82 (d, *J* = 7.9 Hz, 2H), 5.77(s, br, 1H), 5.49 (d, *J* = 7.7 Hz, 1H), 5.41–4.94 (m, 4H), 0.77 (s, 3H), 0.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*:155.76 (d, $^1J_{CO}$ = 14.0 Hz), 144.18, 143.23, 139.25, 133.20 (d, $^2J_{CP}$ = 10.6 Hz), 129.65, 128.61, 128.47, 128.24, 127.92, 127.70, 127.39, 127.16, 126.83, 126.60, 126.32, 125.58, 114.14, 91.15 (d, $^2J_{CP}$ = 13.6 Hz), 87.43 (d, $^2J_{CP}$ = 8.9 Hz), 79.77, 78.98, 67.46, 54.21 (d, $^1J_{CP}$ = 162.9 Hz), 26.98, 26.54; ^{31}P NMR (162 MHz, $CDCl_3$) *δ*: 15.05; HRMS (ESI) calculated for $C_{50}H_{44}NO_7PNa$ [M + Na]$^+$: 824.2753 found 824.2769.

Benzyl (1-((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*] [1,3,2]dioxaphosphepin-6-yl) ethyl)carbamate (6g). White solid; 131 mg, 65% yield; mp: 156–158 °C; dr = 9 : 1; $[\alpha]_D^{20}$ = −163.7 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.60–7.46 (m, 4H), 7.45–7.13 (m, 21H), 5.54 (d, *J* = 7.9 Hz, 1H), 5.35–4.93 (m, 4H), 4.34–4.18 (m, 1H), 1.38 (dd, *J* = 17.7, 7.3 Hz, 3H), 0.77 (s, 3H), 0.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 155.64 (d, $^1J_{CO}$ = 6.4 Hz), *155.41 (d, $^1J_{CO}$ = 8.8 Hz), 144.44, 143.73, 143.38, 139.55, 136.24, 129.75, 128.84, 128.76, 128.64, 128.58, 128.39, 128.36, 128.28, 128.22, 128.12, 127.92, 127.83, 127.39, 127.33, 127.20, 127.08, 126.87, 126.65, *114.4, 114.12, 90.87 (d, $^2J_{CP}$ = 13.5 Hz), 86.87 (d, $^2J_{CP}$ = 8.8 Hz), 79.68, 78.99, 67.19, *67.02, 45.04 (d, ^1JCP = 167.66 Hz), *44.44 (d, $^1J_{CP}$ = 166.65 Hz), 26.94 (d, $^2J_{CP}$ = 6.3 Hz), *26.66 (d, $^2J_{CP}$ = 7.9 Hz), 16.20, 15.71; ^{31}P NMR (162 MHz, $CDCl_3$) *δ*: 19.38, *18.88; HRMS (ESI) calculated for $C_{41}H_{40}NO_7PNa$ [M + Na]$^+$: 712.2440 found 721.2435.

Benzyl (1-((3aR,8aR)-2,2-dimethyl-6-oxido-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-*e*] [1,3,2] dioxaphosphepin-6-yl)-3-methylbutyl)carbamate (6h). White solid; 161 mg, 75% yield; mp: 114–116 °C; dr = 1 : 9; $[\alpha]_D^{20}$ = −153.8 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.61–7.48 (m, 4H), 7.42–7.06 (m, 21H), 5.54 (d, *J* = 7.9 Hz, 1H), 5.27–5.07 (m, 2H), 5.01 (d, *J* = 10.5 Hz, 1H), 4.94 (d, *J* = 12.1 Hz, 1H), 4.30–4.16 (m, 1H), 1.77–1.56 (m, 2H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 6.4 Hz, 3H), 0.74 (s, 3H), 0.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 156.03 (d, $^1J_{CO}$ = 4.3 Hz), *155.73 (d, $^1J_{CO}$ = 5.1 Hz), 144.69 (d, $^3J_{CP}$ = 7.2 Hz), *144.52 (d, $^3J_{CP}$ = 5.8 Hz), 143.78, 139.56, 136.26, 129.82, 128.94, 128.73, 128.65, 128.60, 128.54, 128.44, 128.39, 128.35, 128.26, 128.17, 128.06, 127.77, 127.36, 127.32, 127.23, 126.95, 126.67, *114.33, 114.16, 91.10 (d, $^2J_{CP}$ = 13.8 Hz), *90.61 (d, $^2J_{CP}$ = 14.1 Hz), *87.07 (d, $^2J_{CP}$ = 9.1 Hz), 86.80 (d, $^2J_{CP}$ = 8.9 Hz), *80.21, 79.79, *79.49, 78.93, 67.23, *67.06, 47.97 (d, $^1J_{CP}$ = 165.64 Hz, *47.31 (d, $^1J_{CP}$ = 165.64 Hz), *38.36 (d, $^2J_{CP}$ = 4.1 Hz), 37.82 (d, $^2J_{CP}$ = 3.4 Hz), 26.94, *26.72, 24.63, *24.46, *24.32, *23.52, 23.48, *21.27, 21.18; ^{31}P NMR (162 MHz, $CDCl_3$) *δ*: *19.21, 18.90; HRMS (ESI) calculated for $C_{44}H_{46}NO_7PNa$ [M + Na]$^+$: 754.2910 found 754.2913.

Conflicts of interest

There are no conflicts to declare.

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