Enantioselective α-aminophosphonate functionalization of indole ring through an organocatalyzed Friedel-Crafts reaction.

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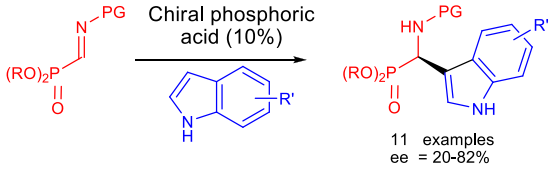


Abstract

Chiral phosphoric acids efficiently catalyze the asymmetric Friedel-Crafts reaction of several indoles with α-iminophosphonates to afford enantioenriched hybrid α-aminophosphonate functionalized indole derivatives.

Indole unit is a ubiquitous structural motif in nature that is frequently found in the structure of many proteins, in the form of the essential α-aminoacid tryptophan, as well as in numerous biologically active compounds such as pharmaceuticals, agrochemicals or alkaloids.[1] Indole framework is known to associate with multiple receptors and enzymes with high affinity and, for that reason, it is considered as one of the most important of all privileged structures in medicinal sciences.[2] Even, the chiral 3-indolyl methanamine moiety occurs widely in biologically active products.[3] Indole is an electron rich aromatic heterocycle containing ten π-electrons that govern its reactivity and

therefore it shows an intrinsic nucleophilic character.[4] Electrophilic aromatic substitution, usually at C-3, is the typical method chosen for the functionalization of the indole ring and asymmetric Friedel-Crafts reaction is the most direct way to the enantioselective synthesis of functionalized indole derivatives.[5] There are some precedents of asymmetric Friedel-Crafts reactions using aldimines and indoles as substrates.[5,6] Indolyl phosphoglycines **II** are the result of an isosteric substitution of a carboxylate group by a phosphonate moiety in indolylglycines **I** (Figure 1). This isosteric replacement is of great interest since, due to the tetrahedral configuration of the phosphorus atom, α-aminophosphonates can behave as stable analogs of the transition state of peptide cleavage, thus inhibiting enzymes engaged in proteolysis processes and, consequently, showing an assorted biological activity.[7] In fact, numerous phosphoglycine or α-aminophosphonic acid derivatives display activity as agrochemicals[8] and as antimicrobial,[9] antioxidant[10] or anticancer[11] agents and show promising biological properties for the treatment of infectious diseases[12].

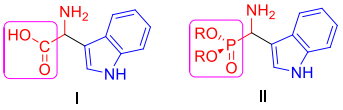


Figure 1. Indolylglycines **I** and their phosphorated isosters **II**.

The biological activity of drugs in general[13] and α-aminophosphonates in particular[14] is known to be strongly dependent on their absolute configuration and there are some examples in the literature reporting the enantioselective synthesis of indolyl glycine derivatives **I** through Friedel-Crafts reaction.[4 5] However, not much attention has been paid into the enantioselective synthesis of their phosphorated isosters, indolyl phosphoglycines **II**. Considering the high affinity of indole ring with biological receptors and the ability of α-aminophosphonates to inhibit enzymes, a general synthetic protocol to provide access to hybrid molecules[15] such as indolyl phosphoglycines in an enantioselective fashion would be of great interest in organic and medicinal chemistry. As far as we

know there are not examples that describe an enantioselective reaction for the functionalization of indole derivatives using phosphorated aldimines.

During the last years, our group has been involved in the synthesis of new aminophosphorus derivatives[16] and we reported the asymmetric preparation of α-aminophosphonate derivatives through an organocatalyzed nucleophilic addition of cyanide[17] or nitromethane[18] to phosphorated ketimines. In this case, we were intrigued about the possibility of functionalizing indoles with an α-aminophosphonate group using phosphorated aldimines as electrophiles and chiral Brönsted acids as organocatalysts. α-Phosphorated aldimines show an absolute lack of stability and their use as substrates is always a challenging task. This must be presumably the reason why, while there are a significant number of reports that describe the use of α-phosphorated ketimines,[19] there are only three examples in literature that describe enantioselective reactions using such substrates. Specifically, addition of enol ethers, enamines or alylsilanes to *in situ* generated 2,2,2-trichloroethoxycarbonyl (Troc) protected α-phosphorated aldimines, using Cu-diamine complexes as catalysts, were reported by Kobayashi *et al.*[20] However enantioselective reactions with α-phosphorated aldimines based in organocatalytic protocols have not been reported so far. Organocatalytic procedures are usually preferred when compared with metal catalysts due to their (relative) lack of sensitivity to moisture and oxygen, ready availability, low cost, and low toxicity, which confers a huge direct benefit in the production of pharmaceutical intermediates. Therefore, continuing with our interest in the enantioselective synthesis of aminophosphorated compounds, we report here an asymmetric Friedel-Crafts reaction of indoles with α-aldiminophosphonates using Brönsted acid catalysis.

Both, chiral phosphoric acids and bifunctional thioureas have demonstrated their capacity to catalyze electrophilic substitution reactions in indole ring.[5e] For this reason we first tested BINOL and VAPOL derived phosphoric acids **III-X** and thiourea alkaloids **XI-XII** (Figure 2) in the Friedel-Crafts reaction of indole **2** and diethyl α-iminophosphonate **1a** bearing a Troc protecting group (Table

1, Entries 1-10, R = Et). In order to overcome problems related to the instability of imine substrates, first, a clear solution of α-iminophosphonate **1a** is generated by treatment of α-bromo-α-aminophosphonate with a polymer supported base, followed by a quick filtration under inert atmosphere,[20] and then the catalyst and indole are added to the reaction flask.

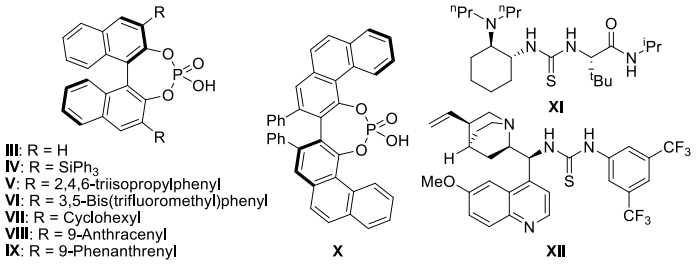
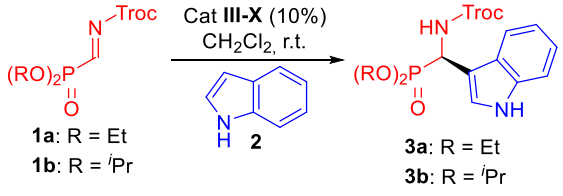


Figure 2. Brönsted acid catalysts tested.

Although non-substituted BINOL derived phosphoric acid **III** catalyzed efficiently the process, it did not show any enantioselectivity (Table 1, Entry 1). However, using 3-substituted BINOL derivatives **IV-IX** and VAPOL derivative **X** moderate enantiomeric excesses were observed (Table 1, Entries 2-8). Bifunctional thioureas **XI** and **XII** virtually did not catalyze the reaction and were discarded for the subsequent optimization of the conditions (Table 1, Entries 9-10).

Table 1 Screening of the catalyst and phosphorus substituent.



Entry	Comp.	Cat.	t (h)	R	%Conv.	%ee[a]
1	**3a**	**III**	12	Et	100	0
2	**3a**	**IV**	12	Et	100	45
3	**3a**	**V**	12	Et	100	29
4	**3a**	**VI**	12	Et	100	62
5	**3a**	**VII**	12	Et	100	40

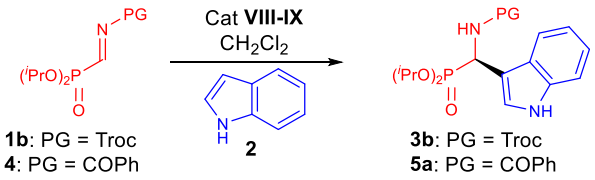
6	**3a**	**VIII**	12	Et	100	42
7	**3a**	**IX**	12	Et	100	32
8	**3a**	**X**	12	Et	100	17
9	**3a**	**XI**	24	Et	5	n.d.
10	**3a**	**XII**	24	Et	5	n.d.
11	**3b**	**III**	12	^{i}Pr	100	0
12	**3b**	**IV**	12	^{i}Pr	100	41
13	**3b**	**V**	12	^{i}Pr	100	47
14	**3b**	**VI**	12	^{i}Pr	100	55
15	**3b**	**VII**	12	^{i}Pr	100	40
16	**3b**	**VIII**	12	^{i}Pr	100	70
17	**3b**	**IX**	12	^{i}Pr	100	70
18	**3b**	**X**	12	^{i}Pr	100	19

a) Determined by chiral HPLC.

In previous work we have established a direct relationship between the size of the phosphorus substituents and the enantiomeric excesses observed for the addition of nucleophiles to α-iminophosphonates,[17,18] and in all the cases *iso*-propyl substituted phosphonates were far superior to other alkylic or aromatic substituents. For that reason, we tested di-*iso*-propyl iminophosphonate **1b** (Table 1, Entries 11-18, R = ^{i}Pr) as substrate in the Friedel-Crafts reaction with indole **2** using chiral phosphoric acids **III**-**X**. Again non-substituted BINOL derived phosphoric acid **III** did not show enantioselectivity but using other catalysts, the enantiomeric excesses were found ranging from moderate, for substituted BINOL derivatives **IV**-**VII** and VAPOL derivative **X** (Table 1, Entries 12-15 and 18), to good for chiral phosphoric acids with 9-phenanthrenyl or 9-anthracenyl substituents **VIII** and **IX** (Table 1, Entries 16-17). It is reasonable to think that the presence of bulkier groups in the phosphonate moiety would improve the enantioselectivity but, unfortunately, all attempts to synthesize α-iminophosphonates holding bulkier substituents than *iso*-propyl groups were unsuccessful.

In order to further improve the enantiomeric excesses, a study of the effect of the protecting group of the imine on the enantioselectivity of the process was performed (Table 2).

Table 2 Screening of the protecting group.



1b: PG = Troc
4: PG = COPh

3b: PG = Troc
5a: PG = COPh

Entry	Cat.	PG	Cat. loading (%)	Temp (ºC)	T (h).	Conv. (%)	%ee[a]
1	**VIII**	Cl_3CCH_2OCO (Troc)	10	r.t.	12	100	70
2	**IX**	Cl_3CCH_2OCO (Troc)	10	r.t	12	100	70
3	**VIII**	PhCO	10	r.t	12	100	60
4	**IX**	PhCO	10	r.t	12	100	75
5	**IX**	PhCO	10	0	48	81	58
6	**IX**	PhCO	10	-20	48	75	40
7	**IX**	PhCO	10	-40	48	70	20
8	**IX**	PhCO	10	40	12	0	n.d
9	**IX**	PhCO	5	r.t	12	85	62
10	**IX**	PhCO	20	r.t	48	100	75

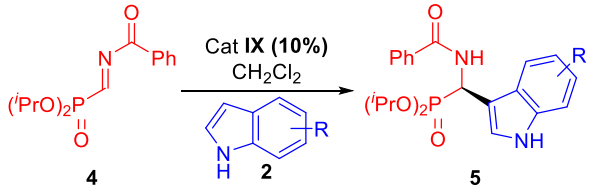
a) Determined by chiral HPLC.

Although lower enantiomeric excess was observed for phenylcarbonyl protected di-*iso*-propyl phosphonate derivative **4** (PG = PhCO) using 9-phenanthrenyl substituted BINOL phosphoric acid **VIII**, the results were improved to a 75% enantiomeric excess when 9-anthracenyl substituted catalyst **IX** was used (Table 2, Entries 3-4). Other attempts to improve the enantioselectivity at different temperatures were unsuccessful, probably due to the low solubility of the substrate at lower temperature (Table 2, Entries 5-7). Curiously, the reaction performed in refluxing dichloromethane afforded a complex mixture, derived presumably from degradation products from the unstable α-iminophosphonate substrate **4** (Table 2, Entry 8). Moreover, while a decrease in the catalyst loading resulted in a drop in both conversion and enantioselectivity (Table 2, Entry 9), an increase in the amount of the catalyst did not have any effect at all in the reaction performance (Table 2, Entry 10).

Since other attempts of improvement by optimization of the solvent were unsuccessful ($CHCl_3$, $ClCH_2CH_2Cl$, toluene, CH_2Cl_2, THF, DMF, DME and AcN were checked), the generalization of the organocatalyzed Friedel-Crafts reaction to several substituted indoles was

performed using phenylcarbonyl protected di-iso-propyl α-iminophosphonate **4** and catalyst **IX** (Table 3).

Table 3 Generalization of the Friedel-Crafts reaction.



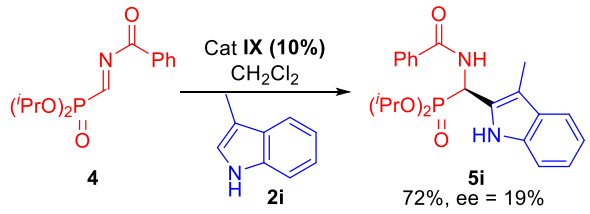
Entry	Comp.	R	t (h).	Yield (%)	%ee[a]
1	**5a**	H	12	69	75
2	**5b**	5-NO_2	12	64	68
3	**5c**	5-F	12	70	70
4	**5d**	6-F	12	68	70
5	**5e**	5-CH_3	12	72	75
6	**5f**	5-CH_3O	12	73	80
7	**5g**	7-CH_3O	12	75	82
8	**5h**	2-Me	18	70	39

a) Determined by chiral HPLC.

Slight differences can be observed for 5, 6 or 7 substituted indole substrates, with enantiomeric excesses ranging from 68 to 82%. The reaction can also be accomplished with indoles bearing strong and weak deactivating substituents (Table 3, Entries 2-4) as well as with weakly and strongly activated indole substrates (Table 3, Entries 5-7). Surprisingly, substitution on C-2 of the indole unit had an adverse effect on the enantioselectivity (Table 3, Entry 8).

Additionally, using 3-methyl substituted indole **2i**, electrophilic Friedel-Crafts reaction at the position 2 of the indole was observed, although with a low enantiomeric excess (Scheme 1). Therefore, the results obtained for indolyl phosphoglycines **5h** and **5i** indicate that an excess of steric hindrance by introducing substitution at the pyrrole unit may have a negative effect into the enantioselectivity of the process.

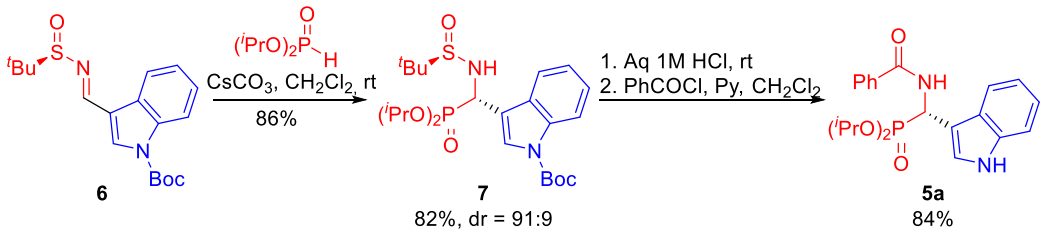
Scheme 1. Friedel-Crafts reaction of 3-substituted indole **2i**.



After several crystallizations, only crystals of the racemic mixture of indolyl phosphoglycine **5d** were obtained. Therefore, X-ray diffraction spectrum was not useful to determine the absolute configuration but served to confirm without doubt the structure of α-aminophosphonates **5** (See ESI). As far as we know, this strategy represents the first synthesis of acyclic indolyphospholglycines.

In order to determine the absolute configuration of the stereogenic carbon of the major enantiomer, an enriched mixture of indolyl phosphoglycine **5f** was analysed by Vibrational Circular Dichroism. However, due to the wide conformational space in compounds **5** no satisfactory correlation between the empirical and theoretical spectra was obtained. Deprotection of amine and/or phosphonate moieties would result in a reduced conformational space in indolyl phosphoglycines **5** but, in our case, the removal of phosphonate ester or amide groups in a reliable synthetic procedure was unfeasible. For this reason, we used the modified diastereoselective methodology reported by Ellman[21] and Yuan[22] for the preparation of compound **5a** using *tert*-butylsulfinyl group as chiral auxiliary (Scheme 2).

Scheme 2. Diastereoselective synthesis of **5a**.



The addition of di-*iso*-propylphospite to sulfinylimine **6**, in the presence of Cs_2CO_3, afforded indolyl phosphoglycine **7** in very good yield and diastereoselectivity (dr = 91:9). It should be noted that the basicity of indolyl group had to be deactivated with an electron withdrawing protecting group, since imines holding benzyl-protected indole moieties did not react with dialkylphosphites at all. Next, the selective simultaneous deprotection of amine and indole groups under mild acidic media, followed by a subsequent acylation of amine moiety with benzoyl chloride, afforded our model indolyl phosphoglycine **5a**. The crystal structure of the major isomer of aminophosphonate **7** shows an *S* configuration of the chiral carbon (See ESI). The comparison of the retention times in chiral HPLC with compound **5a** synthesized by the enantioselective Friedel-Crafts reaction showed that both compounds have the opposite configuration. Therefore, an *R* absolute configuration of our indolyl phosphoglycines **5** was unambiguously stablished.

It is interesting that *N*-substituted indoles did not show any Friedel-Crafts reaction with α-iminophosphonates. Bifunctional catalysis on indole by the Lewis basic site of phosphoric acids, has been discarded by some authors[6] on the basis that some examples regarding *N*-substituted indoles have been reported.[23] However, the lack of reactivity of *N*-methylindole in our case and the absence or substantial decreasing of enantioselectivity in several others,[24] might indicate a crucial role for the NH group at the indole ring in the transition state, which may establish an hydrogen bond with the phosphoryl oxygen of the catalyst. Similar activation has been proposed by other authors for the nucleophilic addition of indoles to nitroalkenes.[25]

Based upon these results and the models proposed for similar processes we suggest a tentative transition state where a double activation of the imine and the indole by the phosphoric acid catalyst could happen. According to this model, the phosphoryl oxygen would establish a hydrogen bond with the indole NH proton, while a simultaneous second hydrogen bond between the phosphoric acidic proton and the imine nitrogen would activate the electrophile (Figure 3). Moreover, the fact that improved enantiomeric excesses are observed for aromatic substituted BINOL derived phosphoric acids, might suggest a contribution of those aromatic substituents into the transition state by means of a π-stacking effect with the indole ring.

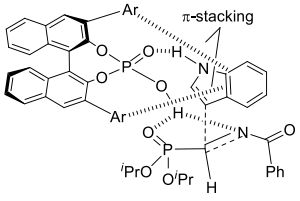


Figure 3. Tentative transition state.

As a conclusion, we report the first enantioselective functionalization of indole ring with α-aminophosphonates. Enantioenriched indolyl phosphoglycines are efficiently obtained by a Brönsted acid catalyzed Friedel-Crafts reaction using α-iminophosphonates and indole derivatives. This is also the first example reported of an enantioselective functionalization of phosphorated aldimines that avoids the use of metal catalysts.

Experimental section.

General. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with silica gel 60 F_{254} plates. Visualization was

accomplished by UV light. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Varian Unity Plus (at 300 MHz, 75 MHz and 120 MHz respectively) and on a Bruker Avance 400 (at 400 MHz, 100 MHz and 160 MHz respectively). Chemical shifts (δ) are reported in ppm relative to residual $CHCl_3$ (δ = 7.26 ppm for ^{1}H and δ = 77.16 ppm for ^{13}C NMR) and using phosphoric acid (50 %) as an external reference (δ = 0.0 ppm) for ^{31}P NMR spectra. Coupling constants *(J)* are reported in Hertz. Data for ^{1}H NMRspectra are reported as follows: chemical shift, multiplicity, coupling constant, integration). Multiplicity abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). ^{13}C NMR peak assignments were supported by Distortionless Enhanced Polarization Transfer (DEPT).High resolution mass spectra (HRMS) were obtained by positive-ion electrospray ionization (ESI). Data are reported in the form *m/z* (intensity relative to base = 100). Infrared spectra (IR) were taken in a Nicolet iS10 Termo Scientific spectrometer as neat solids. Peaks are reported in cm^{-1}. Iminophosphonate substrates were prepared from α-bromo α-aminophosphonates and used without purification. 2,2,2-Trichloroethyl bromo(diethoxyphosphoryl)methylcarbamate[26] was synthesized following literature procedures.

Synthesis of di-*iso*-propyl (dibenzylaminomethyl)phosphonate. Following a modified literature procedure,[27]a solution of di-*iso*-propyl phosphite (33.1 g, 0.25 mol), dibenzylamine (39.5 g, 0.20 mol) and 37% aqueous formaldehyde (20 g, 0.24 mol) in THF (100 mL) was stirred for 1 h at room temperature. The reaction was then heated at 50 ºCovernight. The resulting solution was concentrated under reduced pressure and the crude residue was dissolved in hexanes (300 mL), washed with water (3 × 100 mL) and dried over $MgSO_4$. The solvent was evaporated under vacuum affording 74.3 g (99 %) of pure di-*iso*-propyl dibenzylaminomethylphosphonate as a colorless oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (d, $^{3}J_{HH}$ = 8.0 Hz, 6H), 7.30 (t, $^{3}J_{HH}$ = 7.6 Hz, 6H), 7.21 (t, $^{3}J_{HH}$ = 7.6 Hz, 3H), 4.93–4.48 (m, 2H),

3.81 (s, 4H), 2.86 (d, $^{2}J_{PH}$ = 10.5 Hz, 2H), 1.31 (t, $^{3}J_{HH}$ = 5.7 Hz, 12H) (ppm). (75 MHz, $CDCl_3$) δ 138.8 (C_{quat}), 129.1 (CH), 128.2 (CH), 127.0 (CH), 70.2 (d, $^{2}J_{PC}$ = 7.0 Hz, 2xCH), 59.2 (d, $^{3}J_{PC}$ = 8.3 Hz, 2xCH_2), 49.7 (d, $^{1}J_{PC}$ = 159.4 Hz, CH_2), 24.2 (d, $^{3}J_{PC}$ = 3.3 Hz, 2xCH_3). 24.1 (d, $^{3}J_{PC}$ = 4.5 Hz, 2xCH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 24.9.FTIR (neat) ν_{max} 3027(C-H_{Ar}), 1450 (CH_2), 1251 (P=O), 1220 (P-O-C), 1049 (P-O-C) (cm^{-1}). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{31}NO_3P$ 376.2036, Found 376.2042.

Synthesis of di-*iso*-propyl aminomethylphosphonate. Following a modified literature procedure,[27]a mixture of di-*iso*-propyl dibenzylaminomethylphosphonate(75.08 g, 200mmol), 37% aqueous hydrochloric acid (19.7 mL, 0.200 mol) and 10% palladium on carbon (10.6 g, 10 mmol Pd) in ethanol (300 mL) was stirred for 6 hours under hydrogen pressure at 80 psi. A solution of NaOH 2M (100 mL, 200mmol) was added, and the reaction mixture was filtered through Celite. The volatiles were distilled off at reduced pressure, and the residue was dissolved in diethyl ether. The resulting solution was dried over $MgSO_4$ and concentrated at reduced pressure to afford 35.1 g (90%) of di-*iso*-propyl aminomethylphosphonate as a yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 4.78 – 4.58 (m, 2H, 2xCH), 2.91 (d, $^{3}J_{HH}$ = 10.1 Hz, 2H, CH_2), 1.67 (s, 2H, NH_2), 1.30 (d, $^{3}J_{HH}$ = 6.2 Hz, 12H, 4xCH_3) . ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): 70.3 (d, $^{2}J_{PC}$ = 7.0 Hz, 2xCH), 38.6 (d, $^{1}J_{PC}$ = 149.3 Hz, CH), 23.9 (d, $^{3}J_{PC}$ = 4.2 Hz, 2xCH_3), 23.8 (d, $^{3}J_{PC}$ = 3.5 Hz, 2x CH_3) ^{31}P NMR (120 MHz, $CDCl_3$): δ 26.8. FTIR (neat) ν_{max}3436, 3398 (N-H), 1243 (P=O), 1160 (P-O-C), 1045 (P-O-C).

General procedure for the acylation of di-*iso*-propyl aminomethylphosphonate. Pyridine (3.55 mL, 44mmol) was added to a solution di-*iso*-propyl aminomethylphosphonate(7,8 g, 40mmol) in CH_2Cl_2 (80 mL) at room temperature. The solution was cooled to 0ºC and the corresponding chloride (44 mmol) was slowly added. The reaction was stirred at room temperature for 2h and was then washed with a 1M aqueous solution of HCl (2×30 mL). The

combined organic layers were dried over $MgSO_4$ and volatiles were distilled off at reduced pressure to yield the crude product, which was purified by crystallization.

Synthesis of 2,2,2-trichloroethyl (di-*iso*-propyloxyphosphoryl)methylcarbamate. The general procedure was followed, affording 9.3 g (63%) of 2,2,2-trichloroethyl (di-*iso*-propyloxyphosphoryl)methylcarbamate as a white solid after crystallization in Et_2O / pentane. M.p. (Et_2O / pentane) 72-75 ºC.^{1}H NMR (400 MHz, $CDCl_3$): δ 5.65 (broad s, 1H), 4.72 (s, 2H), 4.77 – 4.65 (m, 2H), 3.57 (dd, $^2J_{PH}$ = 11.9 Hz, $^3J_{HH}$ = 5.9 Hz, 2H), 1.30 (t, $^3J_{HH}$ = 6.0 Hz, 12H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): 154.7 (d, $^3J_{PC}$ = 7.9 Hz, C_{quat}), 95.43 (C_{quat}), 74.88 (CH_2), 71.67 (d, $^2J_{PC}$ = 6.8 Hz, CH), 38.01 (d, $^1J_{PC}$ = 159.5 Hz, CH_2), 24.12 (d, $^3J_{PC}$ = 3.9 Hz, CH_3), 24.05 (d, $^3J_{PC}$ = 4.7 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 20.8.FTIR (neat) ν_{max}3391 (N-H), 1714 (C=O), 1213 (P=O), 1018 (P-O-C), 1005 (P-O-C) (cm^{-1}). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{20}Cl_3NO_5P$ 370.0139; Found 370.0147.

Synthesis of di-*iso*-propyl benzamidomethylphosphonate. The general procedure was followed, affording 7.7 g (64%) of di-*iso*-propyl benzamidomethylphosphonate as a white solid after crystallization in AcOEt / hexanes. M.p. (AcOEt / hexanes) 87-89 ºC.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.55 – 7.40 (m, 3H), 6.53 (s, 1H), 4.90 – 4.53 (m, 2H), 3.88 (dd, $^2J_{PH}$ = 13.2 Hz, $^3J_{HH}$ = 5.7 Hz, 2H), 1.34 (t, $^3J_{HH}$ = 6.7 Hz, 12H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 167.4 (d, $^3J_{CP}$ = 6.7 Hz, C_{quat}), 134.1 (C_{quat}), 131.9 (C_{Ar}), 128.8 (C_{Ar}), 127.1 (C_{Ar}), 71.7 (d, $^2J_{PC}$ = 6.7 Hz, CH), 36.4 (d, $^1J_{PC}$ = 157.5 Hz, CH_2), 24.2 (d, $^3J_{PC}$ = 5.9 Hz, CH_3), 24.1 (d, $^3J_{PC}$ = 6.5 Hz, CH_3).^{31}P NMR (120 MHz, $CDCl_3$): δ 21.9.FTIR (neat) ν_{max}3279 (N-H), 3044 (C-H_{Ar}), 1753 (C=O), 1245 (P=O), 1197 (P-O-C), 1102 (P-O-C) (cm^{-1}). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{22}NO_4PNa$ 322.1179; Found 322.1191.

General procedure for thehalogenation ofα-aminomethylphosphonates.[23] *N*-Bromosuccinimide (0.89 g, 5 mmol) was added to a solution of the corresponding α-

aminomethylphosphonate (5 mmol) in CCl_4. The mixture was stirredin a quartz flask under UV light until observing the disappearance of starting α-aminomethylphosphonateby ^{31}P-RMN. Then, the mixture was filtered and the volatiles were distilled off at reduced pressure to yield the crude product, which was purified by crystallization in Et_2O.

Synthesis of 2,2,2-trichloroethyl bromo(di-*iso*-propyloxyphosphoryl)methylcarbamate. The general procedure was followed, affording 2.1 g (95 %) of 2,2,2-Trichloroethyl bromo(di-*iso*-propyloxyphosphoryl)methylcarbamate as a white solid.^{1}H NMR (300 MHz, $CDCl_3$): δ 6.99 (s, 1H), 6.02 (dd, $^3J_{HH}$ = 11.7 Hz, $^3J_{HH}$ = 8.8 Hz, 1H), 5.05 – 4.57 (m, 4H), 1.36 (m, 12H, 4xCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): 154.0 (d, $^3J_{PC}$ = 15.9 Hz, C_{quat}), 94.9 (C_{quat}), 75.2 (CH_2), 74.4 (d, $^2J_{PC}$ = 7.2 Hz, CH), 73.8 (d, $^3J_{PC}$ = 7.0 Hz, CH), 51.5 (d, $^1J_{PC}$ = 194.0 Hz, CH), 24.4 (d, $^3J_{PC}$ = 2.7 Hz, CH_3), 24.3 (d, $^3J_{PC}$ = 3.1 Hz, CH_3), 23.7 (d, $^3J_{PC}$ = 6.0 Hz, CH_3), 23.6 (d, $^3J_{PC}$ = 6.5 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 10.9.No reliable HRMS or M.p. was obtained due to fast dehalogenation of substrate.

Synthesis of di-*iso*-propyl bromobenzamidomethylphosphonate. The general procedure was followed, affording 1.8 g (95 %) of di-*iso*-propyl bromobenzamidomethylphosphonate as a colorless oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, $^3J_{HH}$ = 10.8 Hz, $^3J_{HH}$= 5.2 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.57 – 7.51 (m, 1H), 7.48 – 7.42 (m, 2H), 6.36 (dd, $^3J_{HH}$ = 11.0 Hz, $^3J_{HH}$ = 9.0 Hz, 1H), 4.94 – 4.75 (m, 2H), 1.39 (d, $^3J_{HH}$ = 6.2 Hz, 6H), 1.32 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 1.28 (d, $^3J_{HH}$ = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.0 (d, $^3J_{PC}$ = 10.1 Hz, C_{quat}), 132.8 (C_{quat}), 132.68 (CH), 128.8 (CH), 128.01 (CH), 74.3 (d, $^2J_{PC}$ = 7.2 Hz, CH), 73.6 (d, $^2J_{PC}$ = 7.2 Hz, CH), 58.3 (d, $^1J_{PC}$ = 194.8 Hz, CH), 24.6 (d, $^3J_{PC}$ = 2.7 Hz, CH_3), 24.4 (d, $^3J_{PC}$ = 3.3 Hz, CH_3), 23.9 (d, $^3J_{PC}$ = 5.4 Hz, CH_3), 23.8 (d, $^3J_{PC}$ = 6.1 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): 11.9δ.No reliable HRMS or M.p. was obtained due to fast dehalogenation of substrate.

General for the asymmetric Friedel-Crafts reaction of iminophosphonates 1 or 4 and indole derivatives 2. A mixture of bromomethylphosphonate (0.1 mmol) piperidinomethyl

polystyrene and $MgSO_4$ was stirred in CH_2Cl_2 (1 mL) for 20 min. The reaction was filtered through a nylon filter to afford a clear solution of pure α-iminophosphonate **1**, which formation was determined by ^{31}P NMR. Next, indole derivative **2** (1 mmol) and (11bR)-2,6-di-9-phenanthrenyl-4-hydroxy-dinaphtho[2,1-d:1′,2′-f][1,3,2]dioxaphosphepin-4-oxide **IX** (7 mg, 0.01 mmol) was added and the solution was stirred at room temperature for 12-18 h(See table 2). The resulting solution was concentrated under vacuum and the crude residue was purified by column chromatography (AcOEt / Hexanes).

(*R*)-2,2,2-Trichloroethyl (diethylphosphoryl)(1*H*-indole-3-yl)methylcarbamate (3a). The general procedure was followed, using 2,2,2-Trichloroethyl bromo(diethoxyphosphoryl)methylcarbamate (41.9 mg, 0.1 mmol), affording 31.9 mg (70%) of **3a** as a white solid.M.p. (hexanes/CH_2Cl_2) = 105-106 ºC. Formation of α-iminophosphonate **1a** was evidenced by ^{31}P NMR (δ = 1.7 ppm). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.15 (broad s, 1H), 7.71 (d, $^{3}J_{HH}$ = 7.7 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.21 – 7.06 (m, 2H), 6.25 (broad d, $^{3}J_{HH}$ = 9.4 Hz, 1H), 5.57 (dd, $^{2}J_{PH}$= 20.2 Hz, $^{3}J_{HH}$ = 10.0 Hz, 1H), 4.85 (d, $^{3}J_{HH}$ = 12.0 Hz, 1H), 4.65 (d, $^{3}J_{HH}$ = 12.0 Hz, 1H), 4.34 – 4.17 (m, 2H), 4.02 (m, 1H), 3.80 (m, 1H),1.35 (t, $^{3}J_{HH}$ = 6.9 Hz, 3H), 1.08 (t, $^{3}J_{HH}$ = 7.0 Hz, 3H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): 154.4 (d, $^{3}J_{PC}$ = 8.0 Hz, C_{quat}), 136.1 (C_{quat}), 126.2 (d, $^{2}J_{PC}$ = 8.8 Hz, C_{quat}), 124.5 (d, $^{3}J_{PC}$ = 5.3 Hz, CH), 122.4 (CH), 119.96 (CH), 118.96 (CH), 111.62 (CH), 108.7 (C_{quat}), 95.5 (C_{quat}), 74.9 (CH_2), 63.4 (d, $^{2}J_{PC}$ = 6.2 Hz, CH_2), 63.4 (d, $^{2}J_{PC}$ = 7.1 Hz, CH_2), 45.0 (d, $^{1}J_{PC}$ = 162.9 Hz, CH), 16.6 (d, $^{3}J_{PC}$ = 5.9 Hz, CH_3), 16.3 (d, $^{3}J_{PC}$ = 5.7 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 23.1.FTIR (neat) ν_{max} 3391 (N-H), 1727 (C=O), 1236 (P=O), 1220 (P-O-C), 1101 (P-O-C) (cm^{-1}). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}Cl_3N_2O_5P$ 457.0248; Found 457.0250. Ee (32%) was determined by HPLC analysis (Chiracel-IC, Heptane/Ethanol 90:10, 1 mL/min). Retention time (min): 8.10 (minor) and 10.04 (major).

(*R*)-2,2,2-Trichloroethyl (di-*iso*-propoxyphosphoryl)(1*H*-indole-3-yl)methylcarbamate (3b). The general procedure was followed, using 2,2,2-Trichloroethyl bromo(di-*iso*-propoxyphosphoryl)methylcarbamate (44.7 mg, 0.1 mmol), affording 35.3 mg (73%) of **3b** as a white solid.M.p. (AcOEt / hexanes) = 118-120 ºC. Formation of α-iminophosphonate **1b** was evidenced by ^{31}P NMR (δ = 0.9ppm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.07 (broad s, 1H), 7.74 (d, $^{3}J_{HH}$ = 7.9 Hz, 1H), 7.43 – 7.30 (m, 2H), 7.18 (ddd, $^{3}J_{HH}$ = 8.2 Hz, $^{3}J_{HH}$ = 7.0 Hz, $^{4}J_{HH}$ = 1.2 Hz, 1H), 7.11 (ddd, $^{3}J_{HH}$ = 8.0 Hz, $^{3}J_{HH}$ = 7.0 Hz, $^{4}J_{HH}$ = 1.1 Hz, 1H), 6.13 (broad d, $^{3}J_{HH}$ = 10.9 Hz, 1H), 5.49 (dd, $^{2}J_{PH}$ = 21.1 Hz, $^{3}J_{HH}$ = 9.9 Hz, 1H), 4.82 (d, $^{3}J_{HH}$ = 12.0 Hz, 1H), 4.80 (m, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.53 (m, 1H), 1.37 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.33 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.20 (d, $^{3}J_{HH}$ = 6.1 Hz, 3H), 0.88 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): 154.3 (d, $^{3}J_{PC}$ = 9.0 Hz, C_{quat}), 136.1(C_{quat}),126.5 (d, $^{2}J_{PC}$ = 9.7 Hz, C_{quat}), 124.4 (d, $^{3}J_{PC}$ = 5.5 Hz, CH), 122.5(CH), 120.0(CH), 119.3(CH), 111.5(CH), 109.5(C_{quat}), 95.5(C_{quat}), 74.91 (CH_2), 72.4 (d, $^{2}J_{PC}$ = 7.3 Hz, CH), 72.1 (d, $^{2}J_{PC}$ = 7.6 Hz, CH), 45.5 (d, $^{1}J_{PC}$ = 165.1 Hz, CH), 24.3 (d, $^{3}J_{PC}$ = 3.6 Hz, CH_3), 24.27 (d, $^{3}J_{PC}$ = 4.8 Hz, CH_3), 24.0 (d, $^{3}J_{PC}$ = 5.1 Hz, CH_3), 23.4 (d, $^{3}J_{PC}$ = 5.2 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 21.1.FTIR (neat) ν_{max} 3389 (N-H), 1729 (C=O), 1239 (P=O), 1216 (P-O-C), 1103 (P-O-C) (cm^{-1}). HRMS (ESI-TOF) m/z: [M + H]$^{+}$ Calcd for $C_{18}H_{24}Cl_3N_2O_5P$ 485.0561; Found 485.0563. Ee (70%) was determined by HPLC analysis (Chiracel-IC, Heptane/Ethanol 90:10, 1 mL/min). Retention time (min): 5.08 (minor) and 6.93 (major).

(*R*)-Di-*iso*-propyl benzamido(1*H*-indole-3-yl)methylphosphonate (5a). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and indole (11.7 mg, 0.1 mmol), affording 28.6 mg (69 %) of **5a** as a white solid M.p. (AcOEt / hexanes) = 76-78 ºC.Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm).^{1}H NMR (400 MHz, $CDCl_3$): δ 9.06 (broad s, 1H), 7.84(m, 1H), 7.77 –

7.72 (m, 2H), 7.52 – 7.42 (m, 2H), 7.41 – 7.32 (m, 3H), 7.20 – 7.06 (m, 2H), 6.90 (d, $^{3}J_{HH}$ = 10.2 Hz, 1H), 6.13 (dd, $^{2}J_{PH}$ = 20.5 Hz, $^{3}J_{HH}$ = 9.7 Hz, 1H), 4.84 (m, 1H), 4.57 (m, 1H), 1.36 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.27 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.20 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 0.93 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6 (d, $^{3}J_{PC}$ = 6.5 Hz, C_{quat}), 136.2 (CH), 134.2 (C_{quat}), 131.8 (CH), 128.7 (CH), 127.2 (CH), 126.7 (d, $^{3}J_{PC}$ = 9.9 Hz, C_{quat}), 124.6 (d, $^{3}J_{PC}$ = 5.3 Hz, CH), 122.5 (CH), 120.11 (CH), 119.6 (CH), 111.5 (CH), 110.0 (C_{quat}), 72.3 (d, $^{2}J_{PC}$ = 7.3 Hz, CH), 72.0 (d, $^{2}J_{PC}$ = 7.6 Hz, CH), 43.3 (d, $^{1}J_{PC}$ = 163.5 Hz, CH), 24.4 (d, $^{3}J_{PC}$ = 3.5 Hz, CH_3), 24.3 (d, $^{3}J_{PC}$ = 3.2 Hz, CH_3), 24.0 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 23.5 (d, $^{3}J_{PC}$ = 5.2 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 21.9.FTIR (neat) ν_{max} 3385 (N-H), 1714 (C=O), 1263 (P=O), 1220 (P-O-C), 1030 (P-O-C) (cm^{-1}). HRMS (ESI-TOF) m/z: $[M + H]^{+}$ Calcd for $C_{22}H_{28}N_2O_4P$ 415.1781; Found 415.1781. Ee (75%) was determined by HPLC analysis (Chiracel-IA, Heptane/CH_2Cl_2/Ethanol 50:49:1, 1 mL/min). Retention time (min): 8.88 (minor) and 9.89 (major).

(*R*)-Di-*iso*-propyl benzamido(5-nitro-1*H*-indole-3-yl)methylphosphonate (5b). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 5-nitroindole (16.2 mg, 0.1 mmol), affording 29.4 mg (64 %) of **5b** as a pale yellow solid.M.p. (hexanes/CH_2Cl_2) = 190-192 ºC.Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.45 (broad s, 1H), 8.84 (d, $^{4}J_{HH}$ = 2.2 Hz, 1H), 8.03 (dd, $^{3}J_{HH}$ = 9.0, $^{4}J_{HH}$ = 2.2 Hz, 1H), 7.82 – 7.78 (m, 2H), 7.51 (m, 1H), 7.47 – 7.39 (m, 3H), 7.30 (d, $^{3}J_{HH}$ = 9.0 Hz, 1H), 7.10 (dd, $^{3}J_{HH}$ = 9.3 Hz, $^{3}J_{PH}$ = 3.8 Hz, 1H), 6.04 (dd, $^{2}J_{PH}$ = 21.2 Hz, $^{3}J_{HH}$ = 9.3 Hz, 1H), 4.83 (m, 1H), 4.63 (m, 1H), 1.41 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.32 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.28 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 0.99 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H).$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$ / Acetone-D6): δ 166.3 (d, $^{3}J_{PC}$ = 6.9 Hz, C_{quat}), 141.2 (C_{quat}), 138.9 (C_{quat}), 133.7 (C_{quat}), 131.1 (CH), 127.9 (CH), 127.7 (d, $^{3}J_{PC}$ = 7.9 Hz, C_{quat}), 126.9

(CH), 125.5 (d, $^{3}J_{PC}$ = 8.1 Hz, CH), 116.9 (CH), 116.6 (CH), 112.3 (C_{quat}), 111.2 (CH), 71.4 (d, $^{2}J_{PC}$ = 7.3 Hz, CH), 42.8 (d, $^{1}J_{PC}$ = 163.5 Hz, CH), 23.6 (d, $^{3}J_{PC}$ = 3.5 Hz, CH_3), 23.5 (d, $^{3}J_{PC}$ = 3.5 Hz, CH_3), 23.3 (d, $^{3}J_{PC}$ = 5.1 Hz, CH_3), 22.8 (d, $^{3}J_{PC}$ = 5.1 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 21.0. FTIR (neat) ν_{max} 3233 (N-H), 1628 (C=O), 1230 (P=O), 1096 (P-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{27}N_3O_6P$ 460.1632; Found 460.1631. Ee (68%) was determined by HPLC analysis (Chiracel-IA, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 8.33 (major) and 10.95 (minor).

(*R*)-Di-*iso*-propyl benzamido(5-fluoro-1*H*-indole-3-yl)methylphosphonate (5c). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 5-fluoroindole (13.5 mg, 0.1 mmol), affording 30.3 mg (70 %) of **5c** as a white solid.M.p. (hexanes/CH_2Cl_2) = 157-158 ºC. Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (broad s, 1H), 7.81 – 7.75 (m, 2H), 7.59 – 7.39 (m, 4H), 7.29 – 7.24 (m, 2H), 6.94 (dt, $^{3}J_{FH}$ = 9.0, $^{4}J_{HH}$ = 2.5 Hz, 1H), 6.81 (d, $^{3}J_{HH}$ = 9.6 Hz, 1H), 6.01 (dd, $^{2}J_{PH}$ = 20.8 Hz, $^{3}J_{HH}$ = 9.7 Hz, 1H), 4.80 (m, 1H), 4.59 (m, 1H), 1.37 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.29 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.23 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 0.96 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.6 (d, $^{3}J_{PC}$ = 6.9 Hz, C_{quat}), 158.2 (d, $^{1}J_{FC}$ = 235.6 Hz, C_{quat}), 134.1 (C_{quat}), 132.6 (C_{quat}), 131.9 (CH), 128.8 (CH), 127.2 (CH), 127.2 (C_{quat}), 126.1 (d, $^{3}J_{PC}$ = 6.1 Hz, CH), 112.0 (d, $^{3}J_{FC}$ = 9.7 Hz, CH), 111.3 (d, $^{2}J_{FC}$ = 26.5 Hz, CH), 110.9 (d, $^{4}J_{FC}$ = 4.1 Hz, C_{quat}), 104.9 (d, $^{2}J_{FC}$ = 24.2 Hz, CH), 72.4 (d, $^{2}J_{PC}$ = 7.3 Hz, CH), 72.1 (d, $^{2}J_{PC}$ = 7.6 Hz, CH), 43.3 (d, $^{1}J_{PC}$ = 163.4 Hz, CH), 24.4 (d, $^{3}J_{PC}$ = 3.3 Hz, CH_3), 24.3 (d, $^{3}J_{PC}$ = 3.3 Hz, CH_3), 24.1 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 23.5 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 21.6 (ppm). ^{19}F NMR (282 MHz, $CDCl_3$) δ -123.8. FTIR (neat) ν_{max} 3354 (N-H), 1634 (C=O), 1216 (P=O), 1093 (P-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{27}FN_2O_4P$ 433.1687; Found 433.1689. Ee (70%) was determined by HPLC

analysis (Chiracel-IC, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 9.30 (major) and 12.09 (minor).

(*R*)-Di-*iso*-propyl benzamido(6-fluoro-1*H*-indole-3-yl)methylphosphonate (5d). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 6-fluoroindole (13.5 mg, 0.1 mmol), affording 29.4 mg (68 %) of **5d** as a white solid.M.p. (hexanes/CH_2Cl_2) = 171-173 ºC.Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.00 (broad s, 1H), 7.78 – 7.72 (m, 3H), 7.48 (m, 1H), 7.44 – 7.36 (m, 3H), 7.02 (dd, $^{3}J_{FH}$ = 9.5, $^{4}J_{HH}$ = 2.3 Hz, 1H), 6.93 – 6.84 (m, 2H), 6.06 (dd, $^{2}J_{PH}$= 20.7, $^{3}J_{HH}$ = 9.6 Hz, 1H), 4.80 (m, 1H), 4.57 (m, 1H), 1.36 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.28 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.22 (d, $^{3}J_{HH}$ = 6.1 Hz, 3H), 0.94 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.7 (d, $^{3}J_{PC}$ = 6.7 Hz, C_{quat}), 160.3 (d, $^{1}J_{FC}$ = 238.1 Hz, C_{quat}), 136.1 (d, $^{3}J_{FC}$ = 12.5 Hz, C_{quat}), 134.1 (C_{quat}), 131.9 (CH), 128.8 (CH), 127.2 (CH), 124.8 (dd, $^{3}J_{PC}$ = 6.0, $^{5}J_{FC}$ = 3.4 Hz, CH), 123.2 (d, $^{3}J_{PC}$ = 9.6 Hz, C_{quat}), 120.5 (d, $^{3}J_{PC}$ = 10.1 Hz, CH), 110.3 (C_{quat}), 109.0 (d, $^{2}J_{FC}$ = 24.5 Hz, CH), 97.7 (d, $^{2}J_{FC}$ = 26.1 Hz, H), 72.4 (d, $^{2}J_{PC}$ = 7.3 Hz, CH), 72.1 (d, $^{2}J_{PC}$ = 7.7 Hz, CH), 43.3 (d, $^{1}J_{PC}$ = 163.3 Hz, CH), 24.4 (d, $^{3}J_{PC}$ = 3.6 Hz, CH_3), 24.3 (d, $^{3}J_{PC}$ = 3.3 Hz, CH_3), 24.0 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 23.5 (d, $^{3}J_{PC}$ = 5.2 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 21.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -121.1. FTIR (neat) ν_{max} 3300 (N-H), 1641 (C=O), 1233 (P=O), 1097 (P-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{27}FN_2O_4P$ 433.1687; Found 433.1692. Ee (70%) was determined by HPLC analysis (Chiracel-IC, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 7.39 (major) and 12.20 (minor).

(*R*)-Di-*iso*-propyl benzamido(5-methyl-1*H*-indole-3-yl)methylphosphonate (5e). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 5-methylindole (13.1 mg, 0.1 mmol), affording 30.8 mg (72 %) of **5e**

as a white solid.M.p. (hexanes/CH_2Cl_2) = 96-98 ºC.Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.72 (broad s, 1H), 7.80 – 7.69 (m, 2H), 7.61 (s, 1H), 7.51 – 7.32 (m, 4H), 7.25 (m, 1H), 6.99 (m, 1H), 6.77 (d, $^{3}J_{HH}$ = 9.7 Hz, 1H), 6.09 (dd, $^{2}J_{PH}$ = 20.3 Hz, $^{3}J_{HH}$ = 9.7 Hz, 1H), 4.84 (m, 1H), 4.53 (m, 1H), 2.43 (s, 3H), 1.37 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.28 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.21 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 0.94 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$): δ 166.6 (d, $^{3}J_{PC}$ = 6.3 Hz, C_{qua}), 134.5 (C_{quat}), 134.3 (C_{quat}), 131.7 (CH) , 129.4 (C_{qua}), 128.7 (CH), 127.2 (CH), 126.9 (d, $^{2}J_{PC}$ = 10.3 Hz, C_{quat}), 124.7 (d, $^{3}J_{PC}$ = 5.8 Hz, CH), 124.2 (CH), 119.1 (CH), 111.1 (CH), 109.6 (C_{qua}), 72.2 (d, $^{2}J_{PC}$ = 7.2 Hz, CH), 71.9 (d, $^{2}J_{PC}$ = 7.6 Hz, CH), 43.2 (d, $^{1}J_{PC}$ = 163.5 Hz, CH), 24.4 (d, $^{3}J_{PC}$ = 3.6 Hz, CH_3), 24.3 (d, $^{3}J_{PC}$ = 3.3 Hz, CH_3), 24.0 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 23.5 (d, $^{3}J_{PC}$ = 5.2 Hz, CH_3), 21.7 (CH_3).^{31}P NMR (120 MHz, $CDCl_3$): δ 21.9. FTIR (neat) ν_{max} 3303 (N-H), 1638 (C=O), 1223 (P=O), 1099 (P-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{30}N_2O_4P$ 429.1938; Found 429.1943. Ee (75%) was determined by HPLC analysis (Chiracel-IC, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 9.49 (major) and 11.61 (minor).

(*R*)-Di-*iso*-propyl benzamido(5-methoxy-1*H*-indole-3-yl)methylphosphonate (5f). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 5-methoxylindole (14.7 mg, 0.1 mmol), affording 32.4 mg (73 %) of **5f** as a white solid.M.p. (hexanes/CH_2Cl_2) = 126-127 ºC. Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (broad s, 1H), 7.82 – 7.66 (m, 2H), 7.57 – 7.35 (m, 4H), 7.30 (d, $^{4}J_{HH}$ = 2.4 Hz, 1H), 7.24 (d, $^{3}J_{HH}$ = 8.8 Hz, 1H), 6.84 (dd, $^{3}J_{HH}$ = 8.8 Hz, $^{4}J_{HH}$ = 2.4 Hz, 1H), 6.77 (d, $^{3}J_{HH}$ = 9.6 Hz, 1H), 6.08 (dd, $^{2}J_{PH}$ = 20.6 Hz, $^{3}J_{HH}$ = 9.7 Hz, 1H), 4.82 (m, 1H), 4.60 (m, 1H), 3.84 (s, 3H), 1.37 (d, $^{3}J_{HH}$ = 6.1 Hz, 3H), 1.29 (d, $^{3}J_{HH}$ = 6.1 Hz, 3H), 1.22 (d, $^{3}J_{HH}$ = 6.1 Hz, 3H), 0.96 (d, $^{3}J_{HH}$ = 6.1 Hz, 3H).

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 166.7 (d, $^{3}J_{PC}$ = 6.4 Hz, C_{quat}), 154.6 (C_{quat}), 134.3 (C_{quat}), 131.8 (CH), 131.1 (C_{quat}), 128.7 (CH), 127.3 (C_{quat}), 127.2 (CH), 125.0 (d, $^{3}J_{PC}$ = 5.1 Hz, CH), 113.4 (CH), 112.1 (CH), 110.2 (C_{quat}), 100.9 (CH), 72.2 (d, $^{2}J_{PC}$ = 7.1 Hz, CH), 72.0 (d, $^{2}J_{PC}$ = 7.6 Hz, CH), 55.9 (CH_3), 43.2 (d, $^{1}J_{PC}$ = 163.5 Hz, CH), 24.4 (d, $^{3}J_{PC}$ = 3.3 Hz, CH_3), 24.3 (d, $^{3}J_{PC}$ = 3.0 Hz, CH_3), 24.1 (d, $^{3}J_{PC}$ = 4.8 Hz, CH_3), 23.5 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3).^{31}P NMR (120 MHz, $CDCl_3$): δ 21.9. FTIR (neat) ν_{max} 3310 (N-H), 1638 (C=O), 1229 (P=O), 1005 (C-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{30}N_2O_5P$ 445.1887; Found 445.1890. Ee (80%) was determined by HPLC analysis (Chiracel-IC, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 12.25 (major) and 14.91 (minor).

(*R*)-Di-*iso*-propyl benzamido(7-methoxy-1*H*-indole-3-yl)methylphosphonate (5g). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 6-methoxylindole (14.7 mg, 0.1 mmol), affording 33.3 mg (75 %) of **5g** as a white solid.M.p. (hexanes/CH_2Cl_2) = 134-136 ºC. Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.66 (broad s, 1H), 7.81 – 7.75 (m, 2H), 7.58 (m, 1H), 7.46 – 7.40 (m, 2H), 7.40 – 7.29 (m, 2H), 7.17 (d, $^{3}J_{HH}$ = 9.7 Hz, 1H), 7.05 (t, $^{3}J_{HH}$ = 7.9 Hz, 1H), 6.63 (d, $^{3}J_{HH}$ = 7.7 Hz, 1H), 6.14 (dd, $^{2}J_{PH}$ = 20.6, $^{3}J_{HH}$ = 9.8 Hz, 1H), 4.78 (m, 1H), 4.55 (m, 1H), 3.90 (s, 3H), 1.36 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 1.27 (d, $^{3}J_{HH}$ = 5.6 Hz, 3H), 1.21 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H), 0.93 (d, $^{3}J_{HH}$ = 6.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5 (d, $^{3}J_{PC}$ = 6.6 Hz, C_{quat}), 146.2 (C_{quat}), 134.3 (C_{quat}), 131.8 (CH), 128.7 (CH), 128.3 (d, $^{3}J_{PC}$ = 10.4 Hz, C_{quat}), 127.4 (CH), 126.6 (C_{quat}), 123.9 (d, $^{3}J_{PC}$ = 5.7 Hz, CH), 120.8 (CH), 112.4 (CH), 110.9 (C_{quat}), 102.4 (CH), 72.2 (d, $^{2}J_{PC}$ = 7.5 Hz, CH), 72.0 (d, $^{2}J_{PC}$ = 7.4 Hz, CH), 55.5 (CH_3), 43.3 (d, $^{1}J_{PC}$ = 163.3 Hz, CH), 24.4 (d, $^{3}J_{PC}$ = 3.6 Hz, CH_3), 24.3 (d, $^{3}J_{PC}$ = 3.1 Hz, CH_3), 24.0 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 23.6 (d, $^{3}J_{PC}$ = 5.2 Hz, CH_3).^{31}P NMR (120 MHz, $CDCl_3$): δ 21.9. FTIR (neat) ν_{max} 3315 (N-H), 1637 (C=O), 1233 (P=O), 1004 (C-O-C).

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{30}N_2O_5P$ 445.1887, Found 445.1893. Ee (82%) was determined by HPLC analysis (Chiracel-IA, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 6.43 (minor) and 8.49 (major).

(*R*)-Di-*iso*-propyl benzamido(2-methyl-1*H*-indole-3-yl)methylphosphonate (5h). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate (37.8 mg, 0.1 mmol) and 2-methylindole (13.1 mg, 0.1 mmol), affording 30.0 mg (70 %) of **5h** as a purple solid.M.p. (hexanes/CH_2Cl_2) = 167-169 ºC. Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (broad s, 1H), 7.97 (m, 1H), 7.88 – 7.65 (m, 2H), 7.50 (m, 1H), 7.44 – 7.35 (m, 2H), 7.26 (m, 1H), 7.18 (dd, $^3J_{HH}$ = 9.3 Hz, $^3J_{PH}$ = 3.9 Hz, 1H), 7.13 – 7.02 (m, 2H), 5.87 (dd, $^2J_{PH}$ = 22.1 Hz, $^3J_{HH}$ = 9.3 Hz, 1H), 4.77 (m, 1H), 4.37 (m, 1H), 2.46 (d, $^4J_{HH}$ = 2.1 Hz, 3H), 1.37 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 1.29 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 1.19 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 0.74 (d, $^3J_{HH}$ = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.8 (d, $^3J_{PC}$ = 8.1 Hz, C_{quat}), 135.4 (C_{quat}), 134.3 (d, $^3J_{PC}$ = 11.4 Hz, C_{quat}), 134.3 (C_{quat}), 131.8 (CH), 128.8 (CH), 127.2 (CH), 127.1 (C_{quat}), 121.4 (CH), 120.0 (CH), 119.7 (CH), 110.6 (CH), 106.0 (C_{quat}), 72.3 (d, $^2J_{PC}$ = 7.1 Hz, CH), 71.6 (d, $^2J_{PC}$ = 7.5 Hz, CH), 44.8 (d, $^1J_{PC}$ = 165.7 Hz, CH), 24.5 (d, $^3J_{PC}$ = 2.7 Hz, CH_3), 24.3 (d, $^3J_{PC}$ = 3.5 Hz, CH_3), 24.1 (d, $^3J_{PC}$ = 5.0 Hz, CH_3), 23.0 (d, $^3J_{PC}$ = 6.0 Hz, CH_3), 12.2 (d, $^4J_{PC}$ = 1.6 Hz, CH_3). ^{31}P NMR (120 MHz, $CDCl_3$): δ 22.6. FTIR (neat) ν_{max} 3294 (N-H), 1635 (C=O), 1245 (P=O), 1206 (P-O-C), 1106 (P-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{30}N_2O_4P$ 429.1938; Found 429.1944. Ee (39%) was determined by HPLC analysis (Chiracel-IA, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 4.63 (major) and 6.33 (minor).

(*R*)-Di-*iso*-propyl benzamido(3-methyl-1*H*-indole-2-yl)methylphosphonate (5i). The general procedure was followed, using di-*iso*-propyl bromobenzamidomethylphosphonate

(37.8 mg, 0.1 mmol) and 3-methylindole (13.1 mg, 0.1 mmol), affording 30.1 g (72%) of **5i** as a white solid.M.p. (hexanes/CH_2Cl_2) = 144-145 ºC.Formation of α-iminophosphonate **4** was evidenced by ^{31}P NMR (δ = 2.8 ppm). ^1H NMR (300 MHz, $CDCl_3$) δ 10.05 (broad s, 1H), 8.52 (d, $^3J_{HH}$ = 9.9 Hz, 1H), 7.82 (d, $^3J_{HH}$ = 8.4, 2H), 7.54 (d, $^3J_{HH}$ = 7.9 Hz, 1H), 7.41 (m, 1H), 7.33 – 7.23 (m, 2H), 7.04 (m, 1H), 6.94 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 6.79 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 6.30 (dd, $^2J_{PH}$ = 21.2 Hz, $^3J_{HH}$ = 9.9 Hz, 1H), 4.72 (m, 1H), 4.46 (m, 1H), 2.45 (s, 3H), 1.33 – 1.18 (m, 9H), 0.95 (d, $^3J_{HH}$ = 6.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 167.0 (d, $^3J_{PC}$ = 6.9 Hz, C_{quat}), 136.2 (C_{quat}), 134.2 (C_{quat}), 131.6 (CH), 128.4 (CH), 127.7 (CH), 127.4 (C_{quat}), 127.4 (C_{quat}), 122.2 (CH), 119.1 (CH), 118.9 (CH), 111.4 (CH), 110.6 (d, $^3J_{PC}$ = 10.0 Hz, C_{quat}), 73.2 (d, $^2J_{PC}$ = 7.8 Hz, CH), 72.9 (d, $^2J_{PC}$ = 7.8 Hz, CH), 42.9 (d, $^1J_{PC}$ = 163.2 Hz, CH), 24.4 (d, $^3J_{PC}$ = 3.3 Hz, CH_3), 24.1 (d, $^3J_{PC}$ = 5.0 Hz, CH_3), 24.0 (d, $^3J_{PC}$ = 3.9 Hz, CH_3), 23.4 (d, $^3J_{PC}$ = 5.5 Hz, CH_3), 9.0 (CH_3).^{31}P NMR (120 MHz, $CDCl_3$): δ 20.7. FTIR (neat) ν_{max} 3316 (N-H), 1667 (C=O), 1213 (P=O), 1123 (P-O-C). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd $C_{23}H_{30}N_2O_4P$ 429.1938; Found 429.1943. Ee (19%) was determined by HPLC analysis (Chiracel-IA, Heptane/CH_2Cl_2/Ethanol 50:48:2, 1 mL/min). Retention time (min): 3.71 (minor) and 4.10 (major).

Determination of the absolute configuration of 5a.

Synthesis of *tert*-butyl (*R*,*E*)-3-(((tert-*butyl*-sulfinyl)imino)methyl)-1*H*-indole-1-carboxylate (6). A mixture of the starting aldehyde (4.91 g, 20.0 mmol), (*R*)-*tert*-butanesulfinamide (2.91 g, 24.0 mmol) and $Ti(OEt)_4$ (5.48 g, 24.0 mmol) was stirred at rt for 12 h. 1 mL of water was added to quench the reaction and the suspended solid was filtered through celite. The filtrate was washed with Et_2O, dried over $MgSO_4$ and the product was crystallized in Et_2O to afford the pure imine as a white solid in quantitative yield. The spectroscopic data are in agreement with those of the literature.[28]

Synthesis of *tert*-butyl 3-((*S*)-(((*R*)-*tert*-butylsulfinyl)amino)(diisopropoxyphosphoryl)methyl)-1*H*-indole-1-carboxylate (7).

A mixture of imine **6**(1.05 g, 3.0 mmol), di-*iso*-propyl phosphite (0.60 mL, 3.6 mmol) and $CsCO_3$ (5.86g, 18.0 mmol) was stirred at rt for 120 h in CH_2Cl_2 (10 mL). Then, the reaction was washed with water (3×40 mL) and sat. NH_4Cl (1×40 mL), the organic layer was dried over $MgSO_4$ and the volatiles were distilled off under reduced pressure to give the crude product which was purified by flash chromatography (hexanes/AcOEt) to give 1.26 g (82%) of pure α-aminophosphonate**7** as a white solid. The major diastereomer was obtained after crystallization in hexanes/AcOEt.M.p. (hexanes/AcOEt) = 104-105 ºC.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.77 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.69 (d, $^4J_{HH}$ = 4.1 Hz, 1H), 7.30 (m, 1H), 7.20 (m, 1H), 4.93 (dd, $^2J_{PH}$ = 17.7 Hz, $^3J_{HH}$ = 1.9 Hz, 1H), 4.70 (m, 1H), 4.59 (m, 1H), 4.08 (dd, $^3J_{PH}$ = 5.6 Hz, $^3J_{HH}$ = 1.9 Hz, 1H), 1.66 (s, 9H), 1.31 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 1.27 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 1.24 (d, $^3J_{HH}$ = 6.2 Hz, 3H), 1.22 (s, 9H), 1.11 (d, $^3J_{HH}$ = 6.2 Hz, 3H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ149.5 (C_{quat}), 135.9 (C_{quat}), 129.1 (d, $^3J_{PC}$ = 2.9 Hz, C_{quat}), 126.7 (d, $^3J_{PC}$ = 9.5 Hz, CH), 124.8 (CH), 122.5 (CH), 121.7 (CH), 115.2 (CH), 113.3 (d, $^2J_{PC}$ = 8.5 Hz, C_{quat}), 84.0 (C_{quat}), 72.6 (d, $^2J_{PC}$ = 7.2 Hz, CH), 72.2 (d, $^2J_{PC}$ = 7.6 Hz, CH), 55.9 (C_{quat}), 49.3 (d, $^1J_{PC}$ = 161.4 Hz, CH), 28.3 (CH_3), 24.3 (d, $^3J_{PC}$ = 3.5 Hz, CH_3), 24.2 (d, $^3J_{PC}$ = 3.7 Hz, CH_3), 24.1 (d, $^3J_{PC}$ = 5.2 Hz, CH_3), 23.7 (d, $^3J_{PC}$ = 5.4 Hz, CH_3), 22.7 (CH_3).^{31}P RMN (120 MHz, $CDCl_3$) δ 19.34. FTIR (neat) ν_{max} 3262 (N-H), 1736 (C=O), 1451 (CH_3), 1254 (P=O), 1066 (S=O). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{40}N_2O_6PS$ 515.2339; Found 515.2345.

(*S*)-Di-*iso*-propyl benzamido(1*H*-indole-3-yl)methylphosphonate (5a). Following a modified literature procedure,[22] α-aminophosphonate **7** (257 mg, 0.5 mmol) was dissolved in ^{i}PrOH (2 mL) and 4N HCl (2 mL) was added. The reaction mixture was stirred at room temperature until the starting material was totally consumed (TLC). Then, the mixture was

extracted with CH_2Cl_2 (2×15 mL), the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was again dissolved in CH_2Cl_2 (5 mL), cooled to 0 ºC, and pyridine (44 μL, 0.55 mmol) and benzoyl chloride (64 μL, 0.55 mmol) were sequentially added. The reaction mixture was stirred at room temperature for 2 h and then was quenched with 0.1 M HCl (5 mL) and extracted with CH_2Cl_2 (10 mL). The organic layerwas dried over $MgSO_4$ and concentrated under reduced pressure to give the crude product, which was purified by flash chromatography (hexanes/AcOEt) to give 174.1 mg of pure **5a** (84 %) as a white solid. Ee (90%) was determined by HPLC analysis (Chiracel-IA, Heptane/CH_2Cl_2/Ethanol 50:49:1, 1 mL/min). Retention time (min): 8.14 (major) and 9.24 (minor).Comparison of the retention times with compound **5a** synthesized by the enantioselective Friedel-Crafts reaction from **4** showed that both compounds have the opposite configuration.

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Supporting Information Available: Copies of ^{1}H and ^{13}C $\{^{1}H\}$ NMR spectra for indolyl phosphoglycines **3**, **5**, **7** and their precursors, chiral chromatograms of compounds **5** and thermal ellipsoid plots for (rac)-**5d** and **7**. This material is available free of charge via the Internet at http://pubs.acs.org. CCDC 1564848 and CCDC 1877404 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

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