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ORIGINAL PAPER

Phosphorofluoridic acid promoted rapid protocol for the synthesis of fluorine-containing α-aminophosphonates under solvent-free conditions

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Abstract A simple and efficient method was developed for the synthesis of fluorine-containing α-aminophosphonates through a one-pot reaction of fluorine-containing aromatic aldehydes with anilines and phosphites in the presence of phosphorofluoridic acid as a catalyst. The products were obtained within short time periods in high yields under solvent-free reaction conditions.

Keywords Phosphorofluoridic acid · Fluorine-containing α-aminophosphonates · Multicomponent reactions · Kabachnik–Fields reaction

Introduction

Fluorine-containing organic compounds have received remarkable interest due to their various important applications in many areas, including medicinal and agricultural chemistry [1, 2]. The introduction of fluorine atoms into organic molecules usually promotes dramatic changes in their biological properties [3, 4]. Owing to their unique physical, chemical, and biological properties, fluorinated organic compounds have attracted much attention [4–6]. Many biologically important molecular scaffolds can be easily synthesized from readily available starting materials with the help of multicomponent reactions (MCRs) [7–9]. They allow the construction of several bonds in a single operation and are one of the most powerful synthetic tools for the creation of molecular complexity and diversity [10].

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One of the important reactions in the field of one-pot synthesis is the Kabachnik–Fields reaction. This three-component coupling of a carbonyl, an amine, and a hydrophosphoryl compound leads to α-aminophosphonates. The synthesis of α-aminophosphonates has attracted much attention recently due to their significant biological activities and structural analogy to α-amino acids [11–18]. For instance, the leucine surrogate **A** (Fig. 1) is a potent inhibitor of leucine aminopeptidase [19]. The proline analogue **B** (Fig. 1) is an angiotensin inhibitor, useful as an antihypertensive agent [20]. The aminophosphonate **C** (Fig. 1) possesses herbicidal activity [21]. Thus, a number of synthetic methods have been developed during recent decades for the formation of α-aminophosphonates [22–51]. Considering the wide range of biological properties of α-aminophosphonates, it is still necessary to develop a new method that is simple and efficient for this three-component reaction.

In recent decades, fluorine-containing catalytic applications have undergone rapid growth [52, 53, 54]. It is evident from the previous literature that phosphorofluoridic acid has invoked enormous interest as a potential green and acid catalyst to construct carbon–carbon and carbon–heteroatom bonds in various organic transformations [55–58]. In continuation of our ongoing effort to develop new environmentally benign methodology for the synthesis of useful precursors in the field of biology, industry, and key intermediates for multistep synthesis [59–62], we decided to investigate the efficiency of the phosphorofluoridic acid catalyst for the synthesis of fluorine-containing α-aminophosphonates. Herein, we report an MCR for the synthesis of fluorine-containing α-aminophosphonates from anilines, dialkylphosphites, and various aromatic fluorine-containing aldehydes using phosphorofluoridic acid catalyst in excellent yields (Scheme 1).

Results and discussion

The studies were initiated to optimize the reaction conditions for the model reaction of 4-fluorobenzaldehyde, 2,6-diisopropylaniline, and dimethyl phosphite in the presence of different catalysts. To demonstrate the capability of the catalyst, a catalyst-free reaction was done under solvent-free conditions. The product was obtained in only 50 % yield in the absence of catalyst even after 6 h (Table 1, entry 2). Surprisingly, the best result was obtained by using 5 mol% phosphorofluoridic acid (Table 1, entry 17) which afforded at the highest yield of 97 % in 10 min at 40 °C. To determine the effect of solvent, we screened different solvents such as ACN, EtOH, PEG-400, toluene, and aqueous medium. Under solvent conditions longer times (1–3 h) were required to afford comparable yields (Table 1, entries 9, 10, 12, 13). The reaction afforded only 65–75 % yield in the presence of catalysts such as Cu–Sn (200 mesh), $AlCl_3$, and $ZnCl_2$. It is interesting to note that the conversion rate of the intermediate imine to product in the presence of $AlCl_3$ and $ZnCl_2$ is slow in both neat and solvent conditions, although slightly better yields were obtained under neat conditions. However, more promising results were obtained with phosphorofluoridic acid in lesser time and with better yields. In terms of catalyst loading, 5 mol% was sufficient and mandatory for completion of the reaction. However no significant improvement was observed with 7 or 10 mol% of phosphorofluoridic acid (Table 1, entries 18, 19).

To study the scope and the limitations of this novel method, we investigated the reaction using several *ortho*-, *meta*-, and *para*-fluorine substituted benzaldehydes as well as anilines with dialkyl phosphites under the optimized solvent-free reaction conditions. The reaction was found to be compatible with various substitutents with excellent chemoselectivity. The results in Table 2 show that all the reactions proceeded cleanly to give the corresponding α-aminophosphonates in high yield.

Therefore, the advantages of our present methodology using phosphorofluoridic acid include: (i) use of solvent free condition, (ii) anhydrous condition need not to be maintained, and (iii) no base or any additional activator as well as additive is required. However, there is not a single report on the use of phosphorofluoridic acid as a catalyst for the synthesis of fluorine containing α-aminophosphonates. All the novel compounds were further characterized by spectral techniques (^1H, ^{13}C, ^{19}F, ^{31}P NMR, and HRMS). The main advantage of this present methodology is the residue was crystallized from ethanol to give the pure product without further purification.

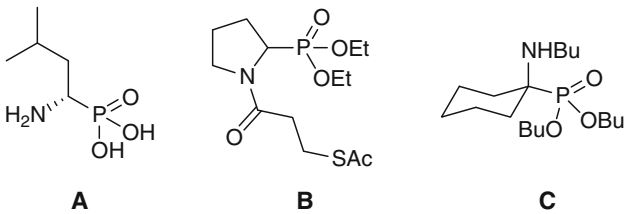


Fig. 1 Biologically active α-aminophosphonates

Conclusion

We have developed a new method for the synthesis of fluorine-containing α-aminophosphonates by a three-component one-pot reaction in good to excellent yields under mild and solvent-free conditions. This methodology uses phosphorofluoridic acid as a simple, novel, and highly efficient catalyst. Cleaner conversion, solvent-free conditions, higher yields, very short duration, avoidance of tedious work-up procedures, and the simplicity of operation are some of the advantages of this protocol.

Experimental

Chemicals were purchased from Aldrich and Alfa Aesar chemical companies. NMR spectra were recorded in ppm in $CDCl_3$ on a Jeol JNM ECP 400 NMR instrument using TMS as the internal standard. Infrared spectra were obtained using a Shimadzu IR Prestige-21 FT-IR spectrometer. HRMS was recorded on Jeol JMS-700 mass

Scheme 1

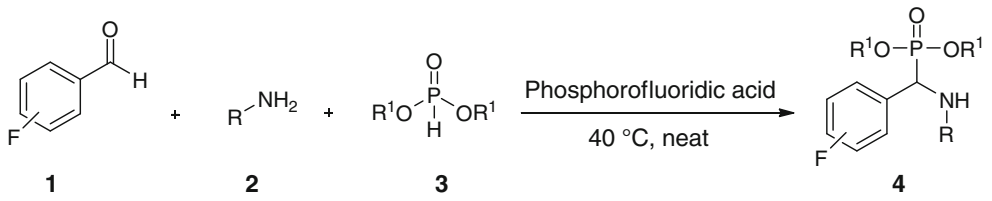
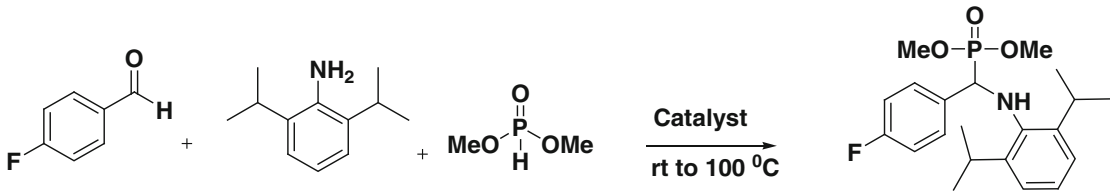


Table 1 Optimization of the reaction conditions for the synthesis of dimethyl (2,6-diisopropylphenylamino)(4-fluorophenyl)methylphosphonate (**4a**)



Entry	Catalyst loading (5 mol%)	Solvent	Temp/°C	Time	Yield[a]/%
1	–	Toluene	rt	8 h	45
2	–	Neat	90	6 h	50
3	Cu–Sn (200 mesh)	Toluene	rt	8 h	65
4	Cu–Sn (200 mesh)	Neat	80	4 h	72
5	$AlCl_3$	ACN	90	6 h	65
6	$AlCl_3$	Neat	80	4.5 h	70
7	$ZnCl_2$	Neat	90	5 h	75
8	$ZnCl_2$	EtOH	rt	6 h	70
9	Phosphorofluoridic acid	Toluene	90	1.5 h	88
10	Phosphorofluoridic acid	MeCN	90	1 h	90
11	Phosphorofluoridic acid	Neat	40	10 min	97
12	Phosphorofluoridic acid	H_2O	100	2 h	90
13	Phosphorofluoridic acid	PEG-400	100	3 h	88
14	Phosphorofluoridic acid	Neat	90	10 h	92
15	Phosphorofluoridic acid	Neat	80	10 min	92
16	Phosphorofluoridic acid	Neat	60	10 min	95
17	Phosphorofluoridic acid	Neat	rt	30 min	85
18	Phosphorofluoridic acid (7 mol%)	Neat	40	10 min	96
19	Phosphorofluoridic acid (10 mol%)	Neat	40	15 min	95

All reactions were carried out at rt to 100 °C by using 4-fluorobenzaldehyde (1 mmol), 2,6-diisopropylaniline (1 mmol), dimethyl phosphite (1 mmol), and catalyst

rt room temperature

[a] Isolated yields

spectrometer. Melting points were measured in open capillaries on an Electrothermal-9100 (Japan) instrument.

General experimental procedure

A mixture of fluorine-containing aromatic aldehydes (1 mmol), anilines (1 mmol), dialkyl phosphites (1 mmol), and phosphorofluoridic acid (5 mol%) was stirred at 40 °C under solvent-free conditions for the appropriate time (Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with water and extracted with chloroform. The organic layer was evaporated, and the crude product was recrystallized from ethanol to afford pure fluorine-containing α-aminophosphonates in good to excellent yields.

Dimethyl (2,6-diisopropylphenylamino)(4-fluorophenyl)-methylphosphonate (**4a**, $C_{21}H_{29}FNO_3P$)

Yellow solid; yield: 381.38 mg (97 %); m.p.: 78–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.37$ (dd, $J_{H,H} = 1.6$ Hz, 5.3 Hz, 1H, Ar–H), 7.34 (dd, $J_{H,H} = 1.6$ Hz, 5.3 Hz, 1H, Ar–H), 7.00–6.95 (m, 5H, Ar–H), 4.87 (br s, 1H, NH), 4.21 (d, $^2J_{P,H} = 22.3$ Hz, 1H, P–CH), 3.84 (d, $^2J_{P,H} = 10.6$ Hz, 3H, OCH_3), 3.47 (d, $^2J_{P,H} = 10.6$ Hz, 3H, OCH_3), 3.13–3.07 (m, 2H, $(CH_3)_2CH$), 1.18 (d, $J = 7.0$ Hz, 6H, $CH(CH_3)_2$), 0.97 (d, $J = 6.6$ Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 25.31$ and 25.34 (both s,

Table 2 Synthesis of different α-aminophosphonates in the presence of 5 mol% phosphorofluoridic acid (Scheme 1)

Benzaldehyde **1**	Amine **2**	R^1	Product	*t*/min	Yield/%[a]	M.p./°C
4-F	2,6-Diisopropylaniline	Me	**4a**	10	97	78–79
2-F	2,6-Diisopropylaniline	Me	**4b**	15	96	82–83
3-F	2,6-Diisopropylaniline	Me	**4c**	12	95	80–81
2-Cl–6-F	2,6-Diisopropylaniline	Me	**4d**	10	96	76–77
4-F	2,6-Diisopropylaniline	Et	**4e**	10	96	97–98
2-F	2,6-Diisopropylaniline	Et	**4f**	15	95	73–74
3-F	2,6-Diisopropylaniline	Et	**4g**	10	94	71–72
2-Cl–6-F	2,6-Diisopropylaniline	Et	**4h**	15	94	73–74
4-F	5-Aminoindan	Me	**4i**	10	96	121–122
2-F	5-Aminoindan	Me	**4j**	15	94	108–110
3-F	5-Aminoindan	Me	**4k**	15	93	114–115
2-Cl–6-F	5-Aminoindan	Me	**4l**	15	92	109–110
4-F	5-Aminoindan	Et	**4m**	10	94	95–96
2-F	5-Aminoindan	Et	**4n**	10	95	120–122
3-F	5-Aminoindan	Et	**4o**	10	96	118–119
2-Cl–6-F	5-Aminoindan	Et	**4p**	15	92	116–117
4-F	Aniline	Et	**4q**	10	97	85–86 (85–86 [63])
2-F	Aniline	Et	**4r**	11	96	82–83
3-F	Aniline	Et	**4s**	10	95	89–90
2-Cl–6-F	Aniline	Et	**4t**	10	95	78–79 (85–86 [64])

All reactions were carried out at 40 °C by using aldehydes (1 mmol), amines (1 mmol), dialkyl phosphites (1 mmol), and phosphorofluoridic acid (5 mol%) under solvent-free conditions

[a] Isolated yields

$CH(CH_3)_2$), 28.63, 54.35 (d, $J = 7.1$ Hz, OCH_3), 55.13 (d, $J = 7.1$ Hz, OCH_3), 62.60 (d, $^1J_{C,P} = 165.3$ Hz, P–CH), 116.47, 116.69, 124.83, 125.07, 131.39, 131.46, 131.54, 133.48, 141.46, 141.59, 143.01, 162.50, 164.96 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -114.84$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 26.2$ ppm; IR: $\bar{\nu} = 3{,}205$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{21}H_{29}FNO_3P$ $m/z = 393.1869$, found 393.1878.

Dimethyl (2,6-diisopropylphenylamino)(2-fluorophenyl)-methylphosphonate (**4b**, $C_{21}H_{29}FNO_3P$)

White solid; yield: 377.45 mg (96 %); m.p.: 82–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.82$ (t, $J_{H,H} = 16.0$ Hz, 1H, Ar–H), 7.23–7.16 (m, 2H, Ar–H), 7.00 (s, 3H, Ar–H), 6.94 (t, $J_{H,H} = 16.0$ Hz, 1H, Ar–H), 4.89 (br s, 1H, NH), 4.75 (d, $^2J_{P,H} = 22.7$ Hz, 1H, P–CH), 3.82 (d, $^2J_{P,H} = 10.9$ Hz, 3H, OCH_3), 3.47 (d, $^2J_{P,H} = 10.9$ Hz, 3H, OCH_3), 3.24–3.13 (m, 2H, $(CH_3)_2CH$), 1.19 (d, $J = 6.9$ Hz, 6H, $CH(CH_3)_2$), 0.99 (d, $J = 6.9$ Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 25.28$ and 25.45 (both s, $CH(CH_3)_2$), 28.69, 54.40 (d, $J = 7.1$ Hz, OCH_3), 55.07 (d, $J = 7.1$ Hz, OCH_3), 61.53 (d, $^1J_{C,P} = 155.2$ Hz, P–CH), 116.39, 116.62, 124.79, 125.03, 125.15, 125.66, 141.60, 141.71, 143.00, 160.27, 162.73 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -118.55$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 27.1$ (d, $^4J_{P,F} = 5.2$ Hz) ppm; IR: $\bar{\nu} = 3{,}275$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{21}H_{29}FNO_3P$ $m/z = 393.1869$, found 393.1869.

Dimethyl (2,6-diisopropylphenylamino)(3-fluorophenyl)-methylphosphonate (**4c**, $C_{21}H_{29}FNO_3P$)

Brown solid; yield: 373.52 mg (95 %); m.p.: 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J_{H,H} = 2.2$ Hz, 1H, Ar–H), 7.15 (t, $J_{H,H} = 9.8$ Hz, 2H, Ar–H), 7.00 (t, $J_{H,H} = 9.8$ Hz, 3H, Ar–H), 6.96 (d, $J_{H,H} = 2.2$ Hz, 1H, Ar–H), 4.88 (br s, 1H, NH), 4.21 (d, $^2J_{P,H} = 22.3$ Hz, 1H, P–CH), 3.84 (d, $^2J_{P,H} = 10.6$ Hz, 3H, OCH_3), 3.47 (d, $^2J_{P,H} = 10.6$ Hz, 3H, OCH_3), 3.21–3.11 (m, 2H, $(CH_3)_2CH$), 1.19 (d, $J = 6.6$ Hz, 6H, $CH(CH_3)_2$), 0.98 (d, $J = 6.6$ Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 25.15$ and 25.22 (both s, $CH(CH_3)_2$), 28.60, 54.10 (d, $J = 7.2$ Hz, OCH_3), 54.26 (d, $J = 7.2$ Hz, OCH_3), 61.84 (d, $^1J_{C,P} = 152$ Hz, P–CH), 116.47, 123.83, 125.07, 131.39, 131.46, 132.54, 133.48, 141.46, 141.59, 144.01, 162.50, 165.96 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -114.48$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 26.5$ ppm; IR: $\bar{\nu} = 3{,}229$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{21}H_{29}FNO_3P$ $m/z = 393.1869$, found 393.1878.

Dimethyl (2,6-diisopropylphenylamino)(2-chloro-6-fluorophenyl)methylphosphonate (**4d**, $C_{21}H_{28}ClFNO_3P$)
Yellow solid; yield: 410.05 mg (96 %); m.p.: 76–77 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.13 (m, 2H, Ar–H), 7.09–6.98 (m, 4H, Ar–H), 5.12 (d, $^2J_{P,H}$ = 29.6 Hz, 1H, P–CH), 4.85 (br s, 1H, NH), 3.65 (d, $^2J_{P,H}$ = 11.0 Hz, 3H, OCH_3), 3.50 (d, $^2J_{P,H}$ = 10.6 Hz, 3H, OCH_3), 3.38–3.28 (m, 2H, $(CH_3)_2CH$), 1.23 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$), 1.07 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.93 and 24.47 (both s, $CH(CH_3)_2$), 27.32, 52.88 (d, J = 7.1 Hz, OCH_3), 53.24 (d, J = 7.1 Hz, OCH_3), 57.36 (d, $^1J_{C,P}$ = 150 Hz, P–CH), 115.05, 115.28, 123.52, 123.80, 125.51, 129.70, 129.78, 135.13, 140.42, 140.50, 161.31, 163.82 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −109.92 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 24.7 (d, $^4J_{P,F}$ = 5.3 Hz) ppm; IR: $\bar{\nu}$ = 3,289 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{21}H_{28}ClFNO_3P$ m/z = 427.1479, found 427.1476.

Diethyl (2,6-diisopropylphenylamino)(4-fluorophenyl)-methylphosphonate (**4e**, $C_{23}H_{33}FNO_3P$)
Green solid; yield: 404.36 mg (96 %); m.p.: 97–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37(d, $J_{H,H}$ = 1.4 Hz, 1H, Ar–H), 7.35 (t, $J_{H,H}$ = 3.2 Hz, 1H, Ar–H), 7.34 (d, $J_{H,H}$ = 1.4 Hz, 1H, Ar–H), 6.99 (d, $J_{H,H}$ = 1.8 Hz, 4H, Ar–H), 4.75 (br s, 1H, NH), 4.22 (d, $^2J_{P,H}$ = 28.4 Hz, 1H, P–CH), 4.20–4.17 (m, 2H, OCH_2CH_3), 3.99–3.89 (m, 1H, OCH_2CH_3), 3.76–3.66 (m, 1H, OCH_2CH_3), 3.17–3.11 (m, 2H, $(CH_3)_2CH$), 1.32 (t, J = 14.2 Hz, 3H, OCH_2CH_3), 1.18 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), 1.04 (t, J = 13.9 Hz, 3H, OCH_2CH_3), 0.97 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.32 (dd, J = 5.5 Hz, 27.02 Hz, OCH_2CH_3), 25.30 and 25.38 (both s, $CH(CH_3)_2$), 28.59, 62.77 (d, $^1J_{C,P}$ = 151 Hz, P–CH), 64.01 (d, J = 7.1 Hz, OCH_2), 64.23 (d, J = 7.1 Hz, OCH_2), 116.36, 116.56, 124.80, 124.89, 131.43, 131.51, 131.59, 133.81, 141.75, 141.87, 162.46, 164.91 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −115.48 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 22.5 ppm; IR: $\bar{\nu}$ = 3,196 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{23}H_{33}FNO_3P$ m/z = 421.2182, found 421.2186.

Diethyl (2,6-diisopropylphenylamino)(2-fluorophenyl)-methylphosphonate (**4f**, $C_{23}H_{33}FNO_3P$)
Yellow solid; yield: 400.14 mg (95 %); m.p.: 73–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (t, $J_{H,H}$ = 17.9 Hz, 1H, Ar–H), 7.22–7.15 (m, 2H, Ar–H), 6.99 (d, $J_{H,H}$ = 2.5 Hz, 3H, Ar–H), 6.92 (t, $J_{H,H}$ = 17.9 Hz, 1H, Ar–H), 4.87 (br s, 1H, NH), 4.33 (d, $^2J_{P,H}$ = 28.6 Hz, 1H, P–CH), 4.20–4.12 (m, 2H, OCH_2CH_3), 3.97–3.87 (m, 1H, OCH_2CH_3), 3.76–3.66 (m, 1H, OCH_2CH_3), 3.28–3.18 (m, 2H, $(CH_3)_2CH$), 1.28 (t, J = 13.9 Hz, 3H, OCH_2CH_3), 1.19 (d, J = 6.5 Hz, 6H, $CH(CH_3)_2$), 1.02 (t, J = 12.8 Hz, 3H, OCH_2CH_3), 1.01 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.30 (d, J = 6.3 Hz, OCH_2CH_3), 17.53 (d, J = 6.3 Hz, OCH_2CH_3), 25.30 and 25.45 (both s, $CH(CH_3)_2$), 28.63, 55.47 (d, $^1J_{C,P}$ = 153 Hz, P–CH), 64.04 (d, J = 7.1 Hz, OCH_2), 64.20 (d, J = 7.1 Hz, OCH_2), 116.30, 116.53, 124.76, 124.86, 125.57, 130.68, 130.76, 131.26, 141.89, 142.01, 142.90, 160.35, 162.85 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −118.47 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 23.4 (d, $^4J_{P,F}$ = 5.1 Hz) ppm; IR: $\bar{\nu}$ = 3,296 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{23}H_{33}FNO_3P$ m/z = 421.2182, found 421.2182.

Diethyl (2,6-diisopropylphenylamino)(3-fluorophenyl)-methylphosphonate (**4g**, $C_{23}H_{33}FNO_3P$)
Yellow solid; yield: 395.93 mg (94 %); m.p.: 71–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, $J_{H,H}$ = 2.2 Hz, 1H, Ar–H), 7.15 (t, $J_{H,H}$ = 9.8 Hz, 2H, Ar–H), 7.01–6.99 (m, 3H, Ar–H), 4.89 (br s, 1H, NH), 4.43 (d, $^2J_{P,H}$ = 26.2 Hz, 1H, P–CH), 4.24–4.18 (m, 2H, OCH_2CH_3), 3.99–3.92 (m, 1H, OCH_2CH_3), 3.75–3.69 (m, 1H, OCH_2CH_3), 3.21–3.11 (m, 2H, $(CH_3)_2CH$), 1.32 (t, J = 13.9 Hz, 3H, OCH_2CH_3), 1.19 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$), 1.04 (t, J = 14.3 Hz, 3H, OCH_2CH_3), 0.98 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.31 (d, J = 5.5 Hz, OCH_2CH_3), 17.61 (d, J = 5.5 Hz, OCH_2CH_3), 25.33 and 25.36 (both s, $CH(CH_3)_2$), 28.61, 63.12 (d, $^1J_{C,P}$ = 151 Hz, P–CH), 64.13 (d, J = 6.3 Hz, OCH_2), 64.30 (d, J = 6.3 Hz, OCH_2), 116.17, 116.63, 116.78, 123.94, 124.83, 124.89, 125.60, 131.05, 140.44, 141.85, 142.83, 162.62, 165.07 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −115.86 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 22.6 ppm; IR: $\bar{\nu}$ = 3,145 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{23}H_{33}FNO_3P$ m/z = 421.2182, found 421.2188.

Diethyl (2,6-diisopropylphenylamino)(2-chloro-6-fluorophenyl)methylphosphonate (**4h**, $C_{23}H_{32}ClFNO_3P$)
Green solid; yield: 427.85 mg (94 %); m.p.: 73–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.14 (m, 2H, Ar–H), 7.04 (d, $J_{H,H}$ = 2.9 Hz, 2H, Ar–H), 7.02 (d, $J_{H,H}$ = 2.9 Hz, 2H, Ar–H), 4.87 (br s, 1H, NH), 4.51 (d, $^2J_{P,H}$ = 27.1 Hz, 1H, P–CH), 4.05–3.91 (m, 4H, OCH_2CH_3), 3.42–3.32 (m, 2H, $(CH_3)_2CH$), 1.23 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$), 1.19 (t, J = 13.9 Hz, 3H, OCH_2CH_3), 1.08 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), 1.03 (t, J = 13.9 Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.27 (d, J = 6.3 Hz, OCH_2CH_3), 17.36 (d, J = 6.3 Hz, OCH_2CH_3), 25.16 and 25.72 (both s, $CH(CH_3)_2$), 28.48, 58.89 (d, $^1J_{C,P}$ = 151 Hz, P–CH), 63.10 (d, J = 7.1 Hz, OCH_2), 63.65 (d, J = 7.1 Hz, OCH_2), 116.24, 116.47, 124.72, 124.82, 130.77, 130.85, 136.45, 141.95, 142.02, 142.98, 162.55, 165.06 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −108.34 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 23.2 (d, $^4J_{P,F}$ = 5.4 Hz)

ppm; IR: $\bar{\nu}$ = 3,223 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{23}H_{32}ClFNO_3P$ *m/z* = 455.1792, found 455.1793.

Dimethyl (2,3-dihydro-1H-inden-5-ylamino) (4-fluorophenyl)methylphosphonate (**4i**, $C_{18}H_{21}FNO_3P$)
Faint brown solid; yield: 355.15 mg (96 %); m.p.: 121–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.43 (m, 2H, Ar–H), 7.02 (t, $J_{H,H}$ = 16.8 Hz, 2H, Ar–H), 6.95 (d, $J_{H,H}$ = 8.0 Hz, 1H, Ar–H), 6.48 (s, 1H, Ar–H), 6.37 (dd, $J_{H,H}$ = 1.8 Hz, 8.0 Hz, 1H, Ar–H), 4.85 (br s, 1H, NH), 4.76 (d, $^2J_{P,H}$ = 24.2 Hz, 1H, P–CH), 3.76 (d, J = 10.6 Hz, 3H, OCH_3), 3.52 (d, J = 10.6 Hz, 3H, OCH_3), 2.73 (t, J = 13.9 Hz, 4H, CH_2), 2.01–1.94 (m, 2H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.51, 31.80, 32.98, 53.69 (d, J = 7.1 Hz, OCH_3), 53.90 (d, J = 7.1 Hz, OCH_3), 55.27 (d, $^1J_{C,P}$ = 151 Hz, P–CH), 110.04, 112.01, 115.48, 115.69, 124.66, 129.25, 129.30, 129.38, 131.54, 134.44, 144.41, 144.56, 145.39, 161.18, 163.63 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −116.28 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 20.8 ppm; IR: $\bar{\nu}$ = 3,165 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{18}H_{21}FNO_3P$ *m/z* = 349.1243, found 349.1246.

Dimethyl (2,3-dihydro-1H-inden-5-ylamino) (2-fluorophenyl)methylphosphonate (**4j**, $C_{18}H_{21}FNO_3P$)
White solid; yield: 328.17 mg (94 %); m.p.: 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.51 (m, 1H, Ar–H), 7.24–7.21 (m, 1H, Ar–H), 7.10 (t, $J_{H,H}$ = 15.7 Hz, 1H, Ar–H), 7.04 (d, $J_{H,H}$ = 8.0 Hz, 1H, Ar–H), 6.95 (d, $J_{H,H}$ = 8.0 Hz, 1H, Ar–H), 6.53 (s, 1H, Ar–H), 6.42 (dd, $J_{H,H}$ = 2.2 Hz, 8.0 Hz, 1H, Ar–H), 5.21 (d, $^2J_{P,H}$ = 24.9 Hz, 1H, P–CH), 4.87 (br s, 1H, NH), 3.83 (d, J = 11 Hz, 3H, OCH_3), 3.50 (d, J = 10.6 Hz, 3H, OCH_3), 2.78–2.71 (m, 4H, CH_2), 2.01–1.93 (m, 2H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.80, 33.09, 34.25, 49.37 (d, $^1J_{C,P}$ = 155 Hz, P–CH), 54.90 (d, J = 6.3 Hz, OCH_3), 55.32 (d, J = 6.3 Hz, OCH_3), 111.10, 113.03, 116.39, 116.61, 124.64, 124.78, 125.90, 125.98, 130.07, 130.72, 130.83, 135.81, 145.39, 145.53, 146.72, 160.72, 163.14 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −119.69 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 22.5 (d, $^4J_{P,F}$ = 5.1 Hz) ppm; IR: $\bar{\nu}$ = 3,227 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{18}H_{21}FNO_3P$ *m/z* = 349.1243, found 349.1245.

Dimethyl (2,3-dihydro-1H-inden-5-ylamino) (3-fluorophenyl)methylphosphonate (**4k**, $C_{18}H_{21}FNO_3P$)
Brown solid; yield: 324.68 mg (93 %); m.p.: 114–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, $J_{H,H}$ = 7.7 Hz, 1H, Ar–H), 7.79 (d, $J_{H,H}$ = 7.7 Hz, 1H, Ar–H), 7.43–7.38 (m, 1H, Ar–H), 7.21 (d, $J_{H,H}$ = 8.0 Hz, 2H, Ar–H), 6.96 (d, $J_{H,H}$ = 8.0 Hz, 1H, Ar–H), 6.54 (s, 1H, Ar–H), 6.43 (d, $J_{H,H}$ = 8.0 Hz, 1H, Ar–H), 4.89 (br s, 1H, NH), 4.82 (d, $^2J_{P,H}$ = 25.2 Hz, 1H, P–CH), 3.80 (d, $^2J_{P,H}$ = 10.6 Hz, 3H, OCH_3), 3.55 (d, $^2J_{P,H}$ = 10.6 Hz, 3H, OCH_3), 2.78–2.72 (m, 4H, CH_2), 2.01–1.93 (m, 2H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.83, 33.12, 34.29, 55.12 (d, J = 7.1 Hz, OCH_3), 55.55 (d, J = 7.1 Hz, OCH_3), 56.95 (d, $^1J_{C,P}$ = 147 Hz, P–CH), 111.33, 113.31, 115.97, 116.34, 118.19, 121.39, 124.76, 125.98, 126.98, 131.13, 131.44, 135.76, 139.85, 145.70, 145.86, 146.69, 162.55, 165.49 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −114.45 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 20.7 ppm; IR: $\bar{\nu}$ = 3,289 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{18}H_{21}FNO_3P$ *m/z* = 349.1243, found 349.1246.

Dimethyl (2,3-dihydro-1H-inden-5-ylamino)(2-chloro-6-fluorophenyl)methylphosphonate(**4l**, $C_{18}H_{20}ClFNO_3P$)
White solid; yield: 352.43 mg (92 %); m.p.: 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.11 (m, 2H, Ar–H), 6.97 (d, $J_{H,H}$ = 8.0 Hz, 2H, Ar–H), 6.59 (s, 1H, Ar–H), 6.48 (dd, $J_{H,H}$ = 1.8 Hz, 8.0 Hz, 1H, Ar–H), 5.55 (d, $^2J_{P,H}$ = 28 Hz, 1H, P–CH), 4.85 (br s, 1H, NH), 3.86 (d, $^2J_{P,H}$ = 8.0 Hz, 3H, OCH_3), 3.62 (d, $^2J_{P,H}$ = 12.0 Hz, 3H, OCH_3), 2.79–2.71 (m, 4H, CH_2), 2.03–1.93 (m, 2H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.44, 31.75, 32.90, 53.23 (d, J = 7.1 Hz, OCH_3), 54.08 (d, J = 7.1 Hz, OCH_3), 57.12 (d, $^1J_{C,P}$ = 152 Hz, P–CH), 109.93, 111.73, 115.16, 124.29, 124.66, 129.54, 129.61, 134.70, 144.20, 144.35, 145.40, 160.85, 163.36 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −112.68 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 21.3 (d, $^4J_{P,F}$ = 5.3 Hz) ppm; IR: $\bar{\nu}$ = 3,206 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{18}H_{20}ClFNO_3P$ *m/z* = 383.0853, found 383.0856.

Diethyl (2,3-dihydro-1H-inden-5-ylamino) (4-fluorophenyl)-methylphosphonate(**4m**, $C_{20}H_{25}FNO_3P$)
Brown solid; yield: 354.52 mg (94 %); m.p.: 95–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.43 (m, 2H, Ar–H), 7.02 (t, $J_{H,H}$ = 17.2 Hz, 2H, Ar–H), 6.94 (d, $J_{H,H}$ = 8.0 Hz, 1H, Ar–H), 6.48 (s, 1H, Ar–H), 6.37 (dd, $J_{H,H}$ = 2.2 Hz, 8.0 Hz, 1H, Ar–H), 4.87 (br s, 1H, NH), 4.72 (d, $^2J_{P,H}$ = 24.0 Hz, 1H, P–CH), 4.15–4.07 (m, 2H, OCH_2CH_3), 4.01–3.92 (m, 1H, OCH_2CH_3), 3.80–3.70 (m, 1H, OCH_2CH_3), 2.76–2.72 (m, 4H, CH_2), 2.01–1.93 (m, 2H, CH_2), 1.27 (t, J = 14.2 Hz, 3H, OCH_2CH_3), 1.13 (t, J = 13.9 Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.18 (d, J = 5.5 Hz, OCH_2CH_3), 16.33 (d, J = 5.5 Hz, OCH_2CH_3), 25.50, 31.78, 32.96, 55.64 (d, $^1J_{C,P}$ = 151 Hz, P–CH), 63.09 (d, J = 7.1 Hz, OCH_2), 63.30 (d, J = 7.1 Hz, OCH_2), 109.98, 111.96, 115.28, 115.50, 124.61, 129.26, 129.40, 131.85, 134.22, 144.65, 144.80, 145.32, 161.08, 163.60 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −115.48 (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): δ = 23.8 ppm; IR: $\bar{\nu}$ = 3,277 (NH) cm^{-1}; HRMS (ESI): calcd for $C_{20}H_{25}FNO_3P$ *m/z* = 377.1556, found 377.1560.

Diethyl (2,3-dihydro-1H-inden-5-ylamino)(2-fluorophenyl)-methylphosphonate (**4n**, $C_{20}H_{25}FNO_3P$)
White solid; yield: 358.29 mg (95 %); m.p.: 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.57$ (t, $J_{H,H} = 14.6$ Hz, 1H, Ar–H), 7.23–7.18 (m, 1H, Ar–H), 7.10–7.01 (m, 2H, Ar–H), 6.94 (d, $J_{H,H} = 8.0$ Hz, 1H, Ar–H), 6.53 (s, 1H, Ar–H), 6.42 (d, $J_{H,H} = 8.0$ Hz, 1H, Ar–H), 5.17 (d, $^2J_{P,H} = 24.5$ Hz, 1H, P–CH), 4.86 (br s, 1H, NH), 4.24-4.17 (m, 2H, OCH_2CH_3), 3.99–3.89 (m, 1H, OCH_2CH_3), 3.78–3.68 (m, 1H, OCH_2CH_3), 2.76–2.71 (m, 4H, CH_2), 2.00–1.92 (m, 2H, CH_2), 1.31 (t, $J = 14.2$ Hz, 3H, OCH_2CH_3), 1.07 (t, $J = 13.9$ Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.07$ (d, $J = 5.5$ Hz, OCH_2CH_3), 16.36 (d, $J = 5.5$ Hz, OCH_2CH_3), 25.52, 31.81, 32.98, 48.42 (d, $^1J_{C,P} = 150.3$ Hz, P–CH), 63.19 (d, $J = 7.1$ Hz, OCH_2), 63.43 (d, $J = 7.1$ Hz, OCH_2), 109.76, 111.69, 114.94, 115.18, 123.72, 123.84, 124.51, 124.67, 128.78, 129.27, 134.30, 144.34, 144.49, 145.38, 159.59, 162.02 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -119.31$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 23.1$ (d, $^4J_{P,F} = 5.1$ Hz) ppm; IR: $\bar{\nu} = 3{,}208$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{20}H_{25}FNO_3P$ $m/z = 377.1556$, found 377.1556.

Diethyl (2,3-dihydro-1H-inden-5-ylamino) (3-fluorophenyl)methylphosphonate (**4o**, $C_{20}H_{25}FNO_3P$)
Brown solid; yield: 362.06 mg (96 %); m.p.: 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.29$ (s, 2H, Ar–H), 7.19 (d, $J_{H,H} = 9.1$ Hz, 1H, Ar–H), 6.95 (d, $J_{H,H} = 7.7$ Hz, 2H, Ar–H), 6.48 (s, 1H, Ar–H), 6.38 (d, $J_{H,H} = 9.1$ Hz, 1H, Ar–H), 4.87 (br s, 1H, NH), 4.73 (d, $^2J_{P,H} = 24.5$ Hz, 1H, P–CH), 4.15–4.09 (m, 2H, OCH_2CH_3), 4.01–3.93 (m, 1H, OCH_2CH_3), 3.82–3.73 (m, 1H, OCH_2CH_3), 2.74 (t, $J = 13.2$ Hz, 4H, CH_2), 2.01–1.94 (m, 2H, CH_2), 1.28 (t, $J = 13.9$ Hz, 3H, OCH_2CH_3), 1.14 (t, $J = 13.9$ Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.11$ (d, $J = 5.5$ Hz, OCH_2CH_3), 16.34 (d, $J = 5.5$ Hz, OCH_2CH_3), 25.52, 31.80, 32.98, 56.05 (d, $^1J_{C,P} = 149.4$ Hz, P–CH), 63.20 (d, $J = 7.1$ Hz, OCH_2), 63.39 (d, $J = 7.1$ Hz, OCH_2), 109.95, 111.92, 114.62, 114.79, 123.45, 124.65, 129.89, 129.97, 134.33, 139.09, 144.62, 144.76, 145.36, 161.74, 164.20 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -113.58$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 23.2$ ppm; IR: $\bar{\nu} = 3{,}278$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{20}H_{25}FNO_3P$ $m/z = 377.1556$, found 377.1560.

Diethyl (2,3-dihydro-1H-inden-5-ylamino)(2-chloro-6-fluorophenyl)methylphosphonate (**4p**, $C_{20}H_{24}ClFNO_3P$)
White solid; yield: 378.22 mg (92 %); m.p.: 116–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.14$–7.09 (m, 2H, Ar–H), 6.97-6.89 (m, 2H, Ar–H), 6.59 (s, 1H, Ar–H), 6.47 (dd, $J_{H,H} = 2.2$ Hz, 8.0 Hz, 1H, Ar–H), 5.53 (d, $^2J_{P,H} = 27.0$ Hz, 1H, P–CH), 4.87 (br s, 1H, NH), 4.26–4.19 (m, 2H, OCH_2CH_3), 4.08–4.02 (m, 1H, OCH_2CH_3), 3.94–3.88 (m, 1H, OCH_2CH_3), 2.79–2.71 (m, 4H, CH_2), 2.03–1.93 (m, 2H, CH_2), 1.31 (t, $J = 13.9$ Hz, 3H, OCH_2CH_3), 1.13 (t, $J = 14.2$ Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.02$ (d, $J = 5.5$ Hz, OCH_2CH_3), 16.34 (d, $J = 5.5$ Hz, OCH_2CH_3), 25.47, 31.78, 32.92, 51.67 (d, $^1J_{C,P} = 165.3$ Hz, P–CH), 62.80 (d, $J = 6.3$ Hz, OCH_2), 63.48 (d, $J = 6.3$ Hz, OCH_2), 109.90, 111.71, 124.65, 125.22, 129.33, 129.44, 144.47, 144.63, 145.37, 160.92, 162.32, 163.44 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -112.50$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 21.7$ (d, $^4J_{P,F} = 5.4$ Hz) ppm; IR: $\bar{\nu} = 3{,}265$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{20}H_{24}ClFNO_3P$ $m/z = 411.1166$, found 411.1169.

Diethyl (2-fluorophenyl)(phenylamino)methylphosphonate (**4r**, $C_{17}H_{21}FNO_3P$)
Yellow solid; yield: 323.82 mg (96 %); m.p.: 82–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.42$–7.36 (m, 4H, Ar–H), 7.20–7.23 (m, 2H, Ar–H), 7.12 (t, $J_{H,H} = 8.0$ Hz, 1H, Ar–H), 6.98–6.86 (m, 2H, Ar–H), 5.17 (d, $^2J_{P,H} = 23.5$ Hz, 1H, P–CH), 4.86 (br s, 1H, NH), 4.11–3.92 (m, 2H, OCH_2CH_3), 4.03–3.96 (m, 1H, OCH_2CH_3), 3.76–3.70 (m, 1H, OCH_2CH_3), 1.25 (t, $J = 14.2$ Hz, 3H, OCH_2CH_3), 1.14 (t, $J = 13.9$ Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.6$ (d, $J = 5.8$ Hz, OCH_2CH_3), 16.8 (d, $J = 5.8$ Hz, OCH_2CH_3), 55.9 (d, $^1J_{C,P} = 150.5$ Hz, P–CH), 63.73 (d, $J = 6.3$ Hz, OCH_2), 64.91 (d, $J = 6.3$ Hz, OCH_2), 114.2, 119.13, 129.25, 129.68, 134.12, 135.07, 146.34, 159.58, 160.43 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -116.48$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 22.7$ (d, $^4J_{P,F} = 5.4$ Hz) ppm; IR: $\bar{\nu} = 3{,}299$ (NH) cm^{-1}; HRMS (ESI): calcd for $C_{17}H_{21}FNO_3P$ $m/z = 337.1243$, found: 337.1246.

Diethyl (3-fluorophenyl)(phenylamino)methylphosphonate (**4s**, $C_{17}H_{21}FNO_3P$)
Pale yellow solid; yield: 320.26 mg (95 %); m.p.: 89–90 °C; ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 7.23$–7.12 (m, 3H, Ar–H), 7.05–6.99 (m, 2H, Ar–H), 6.86 (s, 1H, Ar–H), 6.72 (t, $J_{H,H} = 8.0$ Hz, 1H, Ar–H), 6.66 (dd, $J_{H,H} = 2.2$ Hz, 8 Hz, 2H, Ar–H), 5.23 (d, $^2J_{P,H} = 21.6$ Hz, 1H, P–CH), 4.79 (br s, 1H, NH), 4.21-3.98 (m, 2H, OCH_2CH_3), 3.92-3.86 (m, 1H, OCH_2CH_3), 3.73–3.68 (m, 1H, OCH_2CH_3), 1.21 (t, $J = 12.0$ Hz, 3H, OCH_2CH_3), 1.21 (t, $J = 12.0$ Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.4$ (d, $J = 5.8$ Hz, OCH_2CH_3), 16.8 (d, $J = 5.8$ Hz, OCH_2CH_3), 54.8 (d, $^1J_{C,P} = 150.5$ Hz, P–CH), 63.68 (d, $J = 6.3$ Hz, OCH_2), 64.96 (d, $J = 6.3$ Hz, OCH_2), 115.6, 119.42, 128.26, 129.98, 135.62, 136.56, 146.85, 160.55, 162.89 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -115.64$ (m, 1F) ppm; ^{31}P NMR (161.7 MHz, $CDCl_3$): $\delta = 23.4$ ppm; IR: $\bar{\nu} = 3{,}322$

(NH) cm^{-1}; HRMS (ESI): calcd for $C_{17}H_{21}FNO_3P$ $m/z = 337.1243$, found: 337.1248.

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