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A Simple and Green Procedure for the One-Pot Synthesis of α-Aminophosphonates with Quaternary Ammonium Salts as Efficient and Recyclable Reaction Media

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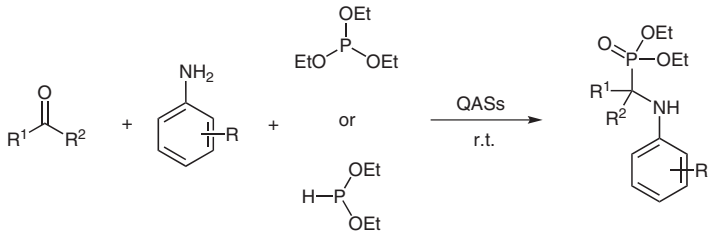

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Abstract A simple and highly efficient approach has been developed for a multicomponent one-pot reaction of aldehydes or ketones with amines and diethyl or triethyl phosphite to give the corresponding α-aminophosphonates. In the presence of quaternary ammonium salts, which are environmental friendly, inexpensive, and recyclable, α-aminophosphonates were obtained in excellent yields at room temperature within short times.

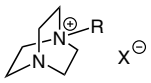
Key words aminophosphonates, multicomponent reactions, quaternary ammonium salts, green chemistry, phosphorylations

α-Aminophosphonates, an important class of organophosphorus compounds, have attracted considerable attention because of their wide range of applications in biological and medicinal chemistry.[1–8] Various synthetic methods have been developed for the preparation of α-aminophosphonates.[9] Of these methods, the multicomponent Kabachnik–Fields reaction, which uses an aldehyde, an amine, and a dialkyl or trialkyl phosphite as substrates, is one of the most efficient for the synthesis of α-aminophosphonates.[10] The transformations can be catalyzed by various acids, heterogeneous catalysts, or nanocatalysts.[11–13] Although some significant advances have been made, the reaction retains some drawbacks, such as inconvenient synthetic procedures, long reaction times, elevated temperatures, and expensive and moisture-sensitive catalysts. Typically, when Lewis acid catalysts such as zinc(II) chloride[14] are used, it is necessary to ensure the exclusion of water; furthermore, these catalysts cannot be reused because of the water that is formed by condensation of the amine with the carbonyl compound. In most cases, the range of carbonyl compounds is limited to aldehydes, and few examples have used ketones at room temperature with excellent yields.[15] As a result, the development of a simple, efficient, and green procedure for one-pot synthesis of α-aminophosphonate in excellent yields from a broad range of carbonyl compounds remains a major challenge in synthetic organic chemistry.

Multicomponent reactions (MCRs) are highly important reactions that are widely used in pharmaceutical chemistry for the production of structural scaffolds or combinatorial libraries for drug discovery.[16] MCRs provide powerful methods for obtaining complex structures from simple precursors by one-pot procedures.[17] Ionic liquids (ILs), acting as homogeneous catalysts, can be easily separated from reaction mixtures for reuse, and have consequently attracted significant attention as environmentally benign media for organic synthesis and catalytic reactions.[18] There have been many reports of the successful use of functionalized ILs as catalysts in various reactions, such as Michael reactions,[19] aldol reactions,[20] Mannich reactions,[21] Friedel–Crafts reactions,[22] or Henry reactions.[23]

We have designed a series of IL catalysts based on the 1,4-diazabicyclo[2.2.2]octane (DABCO) skeleton, and have shown them to be very effective catalysts for Michael addition reactions[24] and for Knoevenagel condensations.[25] Recently, other types of functionalized ILs based on DABCO have been designed and used in various reactions.[26] As part of our continuing interest in IL-mediated organic reactions, we report on our study of the use of quaternary ammonium salts base on DABCO as media for a multicomponent Kabachnik–Fields reaction of various aldehydes or ketones with amines and diethyl or triethyl phosphite to give the corresponding α-aminophosphonates.

The quaternary ammonium salts 1,4-diazabicyclo[2.2.2]octane hydroacetate ([H-DABCO][AcO]), hydrotetrafluoroborate ([H-DABCO][BF_4]), and hydrochloride ([H-DABCO]Cl) and 1-butyl-1,4-diazabicyclo[2.2.2]octanylium bromide ([C_4-DABCO]Br) (Figure 1) were synthesized by the reported methods.[25]



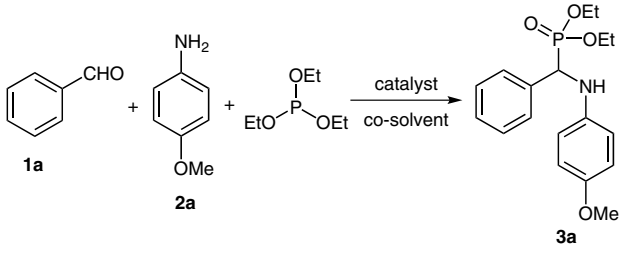
[H-DABCO][AcO], X = AcO, R = H
[H-DABCO][BF_4], X = BF_4, R = H
[H-DABCO]Cl, X = Cl, R = H
[C_4-DABCO]Br, X = Br, R = *n*-Bu

Figure 1 Structures of the DABCO-based quaternary ammonium salts.

With the quaternary ammonium salts in hand, we set out to optimize the conditions for the multicomponent reaction of benzaldehyde (1.0 mmol), 4-methoxyaniline (1.0 mmol), and trimethyl phosphite (2 mmol) at room temperature (Table 1). The yields of the α-aminophosphonate **3a** differed significantly when the quaternary ammonium salt [H-DABCO][AcO] was used with various solvents. When organic solvents such as tetrahydrofuran, dichloromethane, toluene, or acetonitrile were used, **3a** was obtained in poor to moderate yields (Table 1, entries 1–4). The strongly polar solvents ethanol and methanol gave fairly good yields in shorter times (entries 5 and 6); the α-aminophosphonate **3a** was obtained in 97% when two equivalents of methanol were added (entry 7). Other DABCO-based quaternary ammonium salts were also tested in the reaction under the same conditions (entries 8–10). We were pleased to observe that **3a** was obtained in near-quantitative yield in the presence of [H-DABCO]Cl within 30 minutes (entry 9). To confirm the efficient of [H-DABCO]Cl, other ILs and quaternary ammonium salts, such as 1-butyl-3-methylimidazolium tetrafluoroborate, hexadecyl(trimethyl)ammonium chloride, and triethylamine hydrochloride, were also investigated; however, only low to moderate yields were obtained (entries 11–13).

Having optimized the conditions, we next explored the generality of this method by studying the reactions of aromatic aldehydes **1**, aromatic amines **2**, and triethyl phosphite in the presence of the quaternary ammonium salt [H-DABCO]Cl as a reaction medium at room temperature. The results are summarized in Table 2. Both aromatic aldehydes and amines with electron-withdrawing groups or electron-

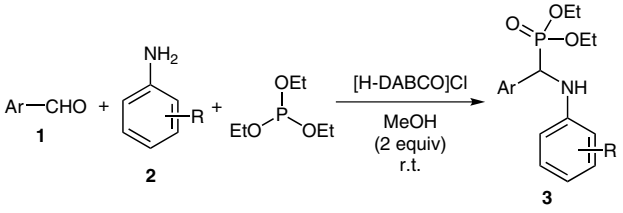
Table 1 Optimization of the Conditions for the Condensation of Benzaldehyde, 4-Methoxyaniline, and Triethyl Phosphite[a]



Entry	Catalyst	Solvent	Time (h)	Yield[b] (%)
1	[H-DABCO][AcO]	THF	48	17
2	[H-DABCO][AcO]	CH_2Cl_2	48	40
3	[H-DABCO][AcO]	toluene	48	35
4	[H-DABCO][AcO]	MeCN	48	53
5	[H-DABCO][AcO]	EtOH	24	85
6	[H-DABCO][AcO]	MeOH	12	94
7	[H-DABCO][AcO]	MeOH[c]	7	97
8	[H-DABCO][BF_4]	MeOH[c]	8	98
9	[H-DABCO]Cl	MeOH[c]	0.5	98
10	[C_4-DABCO]Br	MeOH[c]	24	10
11	[Bmim][BF_4][d]	MeOH[c]	24	53
12	[$Me(CH_2)_{15}N^+Me_3$]Cl^-	MeOH[c]	24	15
13	[Et_3N^+H]Cl^-	MeOH[c]	24	44

[a] Reaction conditions: aldehyde (1 mmol), amine (1 mmol), $P(OEt)_3$ (2 mmol), solvent (1 mL), catalyst (1 mmol), r.t.
[b] Isolated yield.
[c] MeOH (2 equiv) was used.
[d] 1-Butyl-3-methylimidazolium tetrafluoroborate.

Table 2 Scope of the Multicomponent Condensation Reactions of Aromatic Aldehydes, Aromatic Amines, and Triethyl Phosphite[a]



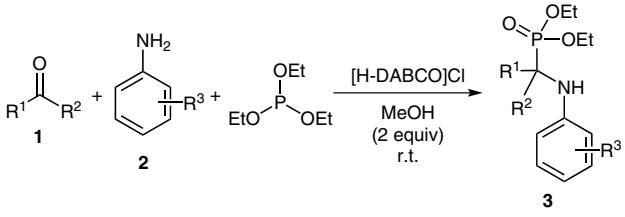
Entry	Ar	R	Product	Time (min)	Yield[b] (%)
1	Ph	4-MeO	**3a**	30	98
2	Ph	H	**3b**	10	96
3	Ph	4-F	**3c**	10	97
4	Ph	4-Cl	**3d**	100	93
5	Ph	4-Br	**3e**	3	98
6	Ph	4-Me	**3f**	25	98
7	4-ClC_6H_4	4-Me	**3g**	30	95
8	4-$MeOC_6H_4$	4-Me	**3h**	40	95
9	4-$O_2NC_6H_4$	4-Me	**3i**	40	98
10	3-$O_2NC_6H_4$	4-Me	**3j**	60	95
11	2-$O_2NC_6H_4$	4-Me	**3k**	60	91
12	4-$O_2NC_6H_4$	4-Cl	**3l**	120	90
13	4-$O_2NC_6H_4$	H	**3m**	8	98
14	4-ClC_6H_4	H	**3n**	20	97
15	4-$MeOC_6H_4$	H	**3o**	30	96
16	2-thienyl	H	**3p**	120	91
17	2-furyl	H	**3q**	20	98

[a] Reaction conditions: aldehyde (1 mmol), amine (1 mmol), $P(OEt)_3$ (2 mmol), [H-DABCO]Cl (1 mmol), r.t.
[b] Isolated yield.

donating groups were converted into the corresponding α-aminophosphonates in good to excellent yields (90–98%) within three minutes to two hours. The α-aminophosphonate products were obtained in higher yields when benzaldehyde was used as a substrate in the reaction than when substituted aromatic aldehydes were used (Table 2, entries 4 and 6–12). In reactions with the same aromatic amine, *para*-substituted aromatic aldehydes needed shorter reaction times and gave higher yields of the corresponding α-aminophosphonates than did substrates with *ortho*- or *meta*-substituents (entries 9–11). Hetaromatic aldehydes, such as thiophene-2-carbaldehyde or furan-2-carbaldehyde were also effective substrates for the Kabachnik–Fields reactions in [H-DABCO]Cl (entries 16 and 17).

Other carbonyl compounds, such as aliphatic aldehydes and cyclic/acyclic ketones were also found to be compatible with [H-DABCO]Cl and gave the corresponding α-aminophosphonates under the optimized conditions (Table 3). These carbonyl compounds smoothly gave the expected α-aminophosphonates in acceptable yields (Table 3, entries 1–4); however, little product was obtained in the case of an aromatic ketone (entry 5).

Table 3 Multicomponent Condensations of Various Carbonyl Compounds, Aromatic Amines, and Triethyl Phosphite[a]

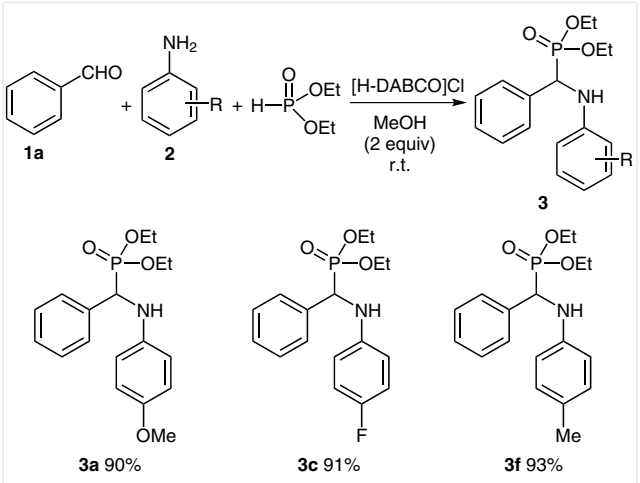


Entry	R^1	R^2	R^3	Product	Time (h)	Yield[b] (%)
1	*i*-Pr	H	4-Cl	**3r**	1	94
2	$(CH_2)_8Me$	H	H	**3s**	5	74
3	$(CH_2)_5$		4-Cl	**3t**	3	90
4	Et	Et	H	**3u**	12	62
5	Ph	Me	H	**3v**	12	<5

[a] Reaction conditions: carbonyl compound (1 mmol), amine (1 mmol), $P(OEt)_3$ (2 mmol), [H-DABCO]Cl (1 mmol), r.t.
[b] Isolated yield.

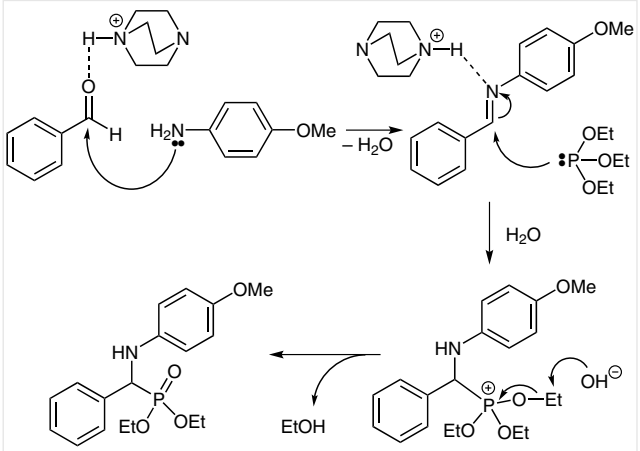
The α-aminophosphonates could be also prepared from diethyl phosphite instead of triethyl phosphite, under the same conditions. At room temperature, products **3a**, **3c**, and **3f** were obtained in yields of 90%, 91%, and 93%, respectively (Scheme 1).

A reasonable pathway for the reaction of an aldehyde with an amine and triethyl phosphite conducted in the presence of [H-DABCO]Cl is presented in Scheme 2. In the first stage of this reaction, an activated imine is formed from benzaldehyde and 4-methoxyaniline. Phosphite then



Scheme 1 Synthesis of α-aminophosphonates from diethyl phosphite

adds to the C=N bond of the imine to give a phosphonium intermediate that reacts with water to give the corresponding α-aminophosphonates **3a** and ethanol.



Scheme 2 Proposed mechanism for the three-component reaction

The recyclability and reusability of the quaternary ammonium salt [H-DABCO]Cl were examined for the reaction of benzaldehyde, aniline, and triethyl phosphite under the standard reaction conditions. When the reaction was complete, the mixture was concentrated and the residue was extracted three times with ethyl acetate. Removal of the solvent and purification by column chromatography gave the product **3a**. The residual quaternary ammonium salt [H-DABCO]Cl was treated with hydrochloric acid, more water was evaporated from the salt under vacuum, and the salt was reused in the same reaction with fresh reactants under similar conditions. The salt [H-DABCO]Cl could be used at least seven times without any significant change in reactivity (Figure 2).

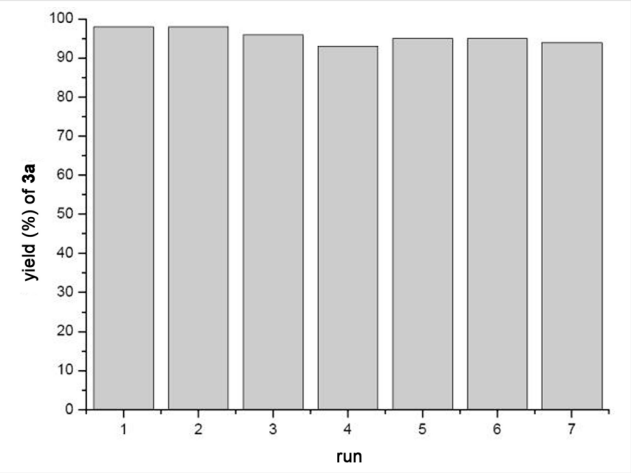


Figure 2 Recycling of the quaternary ammonium salt [H-DABCO]Cl in the synthesis of **3a**

In summary, we have shown that readily available and cheap DABCO-based quaternary ammonium salts can be use as reaction media for the multicomponent one-pot Kabachnik–Fields reaction of a wide range of carbonyl compounds (aromatic, heterocyclic, or aliphatic aldehydes and cyclic or acyclic ketones). The procedure offers several advantages, including short reaction times, mild reaction conditions, excellent yields, and easy workup procedures. The quaternary ammonium salt [H-DABCO]Cl can be easily recovered and reused at least seven times without loss of activity. In addition, either triethyl phosphite or diethyl phosphite can be used to carry out the condensation. We believe that this method is a useful addition to the available methods for the syntheses of α-aminophosphonates.

All chemicals were purchased from commercial suppliers and were used without further purification. Flash column chromatography was performed on silica gel (200–300 mesh). Melting points were determined with an X-4 apparatus and are uncorrected. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AV-400 spectrometer with $CDCl_3$ as the solvent. Chemical shifts are reported relative to TMS as internal standard.

α-Phosphonomalonates 3a–u; General Procedure

A 5 mL round-bottomed flask was charged with the carbonyl compound **1** (1.0 mmol), aromatic amine **2** (1 mmol), $P(OEt)_3$ (2 mmol), [H-DABCO]Cl (1 mmol), and MeOH (2.0 mmol), and the mixture was stirred at r.t. When the reaction was complete (TLC), the mixture was concentrated and the residue was extracted with EtOAc (3 × 2 mL). The combined extracts were washed with brine (3 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography [silica gel, PE–EtOAc (1:1)].

The residual quaternary ammonium salt [H-DABCO]Cl was treated with 5 M HCl, more H_2O was evaporated from the salt under vacuum, and the salt was reused in the next recycling run. [H-DABCO]Cl could be recovered and reused in this reaction at least seven times.

Diethyl {[(4-Methoxyphenyl)amino](phenyl)methyl}phosphonate (3a)[27]

White solid; yield: 342 mg (98%); mp 79–80 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.2 Hz, 3 H), 1.25 (t, *J* = 7.2 Hz, 3 H), 3.62 (s, 3 H), 3.64–3.72 (m, 1 H), 3.87–3.96 (m, 1 H), 4.05–4.15 (m, 2 H), 4.56 (br s, 1 H), 4.70 (d, *J* = 24.0 Hz, 1 H), 6.54 (d, *J* = 9.2 Hz, 2 H), 6.66 (d, *J* = 8.8 Hz, 2 H), 7.20–7.24 (m, 1 H), 7.29 (t, *J* = 7.6 Hz, 2 H), 7.46 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.20 (d, $^3J_{CP}$ = 5.7 Hz), 16.44 (d, $^3J_{CP}$ = 5.7 Hz), 56.54, 56.93 (d, J_{CP} = 149.7 Hz), 63.18 (d, $^2J_{CP}$ = 7.4 Hz), 63.25 (d, $^2J_{CP}$ = 7.2 Hz), 114.69, 115.21, 127.90, 127.96, 128.53, 136.11, 140.47, 152.61.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.90.

Diethyl [Anilino(phenyl)methyl]phosphonate (3b)[27]

White solid; yield: 306 mg (96%); mp 90–92 °C.

^{1}H NMR(400 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 3.61–3.71 (m, 1 H), 3.88–3.96 (m, 1 H), 4.05–4.16 (m, 2 H), 4.76 (d, *J* = 24.0 Hz, 1 H), 4.79 (br s, 1 H), 6.59 (d, *J* = 8.0 Hz, 2 H), 6.68 (t, *J* = 7.2 Hz, 1 H), 7.09 (t, *J* = 8.0 Hz, 2 H), 7.25–7.27 (m, 1 H), 7.32 (t, *J* = 7.6 Hz, 2 H), 7.47 (d, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.41 (d, $^3J_{CP}$ = 5.5 Hz), 16.65 (d, $^3J_{CP}$ = 5.5 Hz), 56.29 (d, J_{CP} = 149.3 Hz), 63.49, 114.06, 118.60, 128.03, 128.09, 128.80, 129.38, 136.10, 146.44, 146.58.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.79.

Diethyl {[(4-Fluorophenyl)amino](phenyl)methyl}phosphonate (3c)[27]

White solid; yield: 327 mg (97%); mp 110–111 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, *J* = 7.2 Hz, 3 H), 1.25 (t, *J* = 6.8 Hz, 3 H), 3.60–3.71 (m, 1 H), 3.86–3.96 (m, 1 H), 4.07–4.17 (m, 2 H), 4.72 (d, *J* = 24.0 Hz, 1 H), 5.02 (br s, 1 H), 6.53–6.56 (m, 2 H), 6.76 (t, *J* = 8.8 Hz, 2 H), 7.22 (t, *J* = 7.6 Hz, 1 H), 7.29 (t, *J* = 7.2 Hz, 2 H), 7.46–7.48 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.14 (d, $^3J_{CP}$ = 6.0 Hz), 16.39 (d, $^3J_{CP}$ = 5.9 Hz), 56.58 (d, J_{CP} = 150.0 Hz), 63.26 (d, $^2J_{CP}$ = 6.4 Hz), 63.32 (d, $^2J_{CP}$ = 6.4 Hz), 114.84, 115.41, 115.63, 127.98, 128.56, 135.80, 142.72, 142.87, 156.13 (d, J_{CF} = 234.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.61.

Diethyl {[(4-Chlorophenyl)amino](phenyl)methyl}phosphonate (3d)[28]

White solid; yield: 329 mg (93%); mp 118–120 °C.

^{1}H NMR (400 MHz, $CDCl_3$,): δ = 1.09 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 3.59–3.68 (m, 1 H), 3.86–3.96 (m, 1 H), 4.05–4.16 (m, 2 H), 4.68 (d, *J* = 24.0 Hz, 1 H), 6.49 (d, *J* = 9.2 Hz, 2 H), 7.02 (d, *J* = 8.8 Hz, 2 H), 7.25–7.28 (m, 1 H), 7.32 (t, *J* = 7.2 Hz, 2 H), 7.42–7.44 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.40 (d, $^3J_{CP}$ = 5.7 Hz), 16.39 (d, $^3J_{CP}$ = 5.6 Hz), 56.40 (d, J_{CP} = 149.5 Hz), 63.47 (d, $^2J_{CP}$ = 6.4 Hz), 63.62 (d, $^2J_{CP}$ = 6.8 Hz), 115.21, 123.27, 128.03, 128.28, 128.89, 129.22, 135.63, 145.01.

^{31}P NMR (162 MHz, $CDCl_3$,): δ = 23.43.

Diethyl {[(4-Bromophenyl)amino](phenyl)methyl}phosphonate (3e)[9]

White solid; yield: 390 mg (98%); mp 121–122 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 7.2 Hz, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H), 3.58–3.68 (m, 1 H), 3.85–3.94 (m, 1 H), 4.07–4.19 (m, 2 H), 4.74 (d, *J* = 24.4 Hz, 1 H), 5.54 (br s, 1 H), 6.51 (d, *J* = 8.8 Hz, 2 H), 7.12 (d, *J* = 8.8 Hz, 2 H), 7.19–7.23 (m, 1 H), 7.27 (t, *J* = 7.2 Hz, 2 H), 7.47 (d, *J* = 6.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.24 (d, $^3J_{CP}$ = 5.9 Hz), 16.50 (d, $^3J_{CP}$ = 5.5 Hz), 56.92 (d, J_{CP} = 150.4 Hz), 63.30 (d, $^2J_{CP}$ = 7.4 Hz), 63.36 (d, $^2J_{CP}$ = 8.0 Hz), 109.75, 115.50, 128.02, 128.62, 131.76, 135.65, 145.66, 145.81.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.35

Diethyl {Phenyl[(4-tolyl)amino]methyl}phosphonate (3f)[28]

White solid; yield: 327 mg (98%); mp 119–120 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.2 Hz, 3 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 2.17 (s, 3 H), 3.62–7.32 (m, 1 H), 3.88–3.98 (m, 1 H), 4.05–4.16 (m, 2 H), 4.58 (br s, 1 H), 4.73 (d, *J* = 24.4 Hz, 1 H), 6.50 (d, *J* = 8.0 Hz, 2 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 7.23–7.26 (m, 1 H), 7.31 (t, *J* = 7.6 Hz, 2 H), 7.46 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.42 (d, $^3J_{CP}$ = 5.6 Hz), 16.65 (d, $^3J_{CP}$ = 5.7 Hz), 20.57, 56.55 (d, J_{CP} = 149.4 Hz), 63.47 (d, $^2J_{CP}$ = 5.9 Hz), 63.48 (d, $^2J_{CP}$ = 6.0 Hz), 114.18, 127.81, 128.03, 128.07, 128.77, 129.87, 136.22, 144.25.

^{31}P NMR (162 MHz, $CDCl_3$,): δ = 23.91.

Diethyl {(4-Chlorophenyl)[(4-tolyl)amino]methyl}phosphonate (3g)[12h]

White solid; yield: 350 mg (95%); mp 111–113 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 2.18 (s, 3 H), 3.72–3.82 (m, 1 H), 3.93–4.01 (m, 1 H), 4.08–4.16 (m, 2 H), 4.66 (br s, 1 H), 4.69 (d, *J* = 25.6 Hz, 1 H), 6.46 (d, *J* = 8.4 Hz, 2 H), 6.91 (d, *J* = 8.4 Hz, 2 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 7.38–7.41 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.47 (d, $^3J_{CP}$ = 5.6 Hz), 16.65 (d, $^3J_{CP}$ = 5.6 Hz), 20.56, 56.06 (d, J_{CP} = 149.6 Hz), 63.46 (d, $^2J_{CP}$ = 6.8 Hz), 63.63 (d, $^2J_{CP}$ = 6.6 Hz), 114.19, 128.14, 128.96, 129.38, 129.93, 133.86, 134.95, 143.96.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.23.

Diethyl {(4-Methoxyphenyl)[(4-tolyl)amino]methyl}phosphonate (3h)[12h]

White solid; yield: 345 mg (95%); mp 95–96 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ =1.13 (t, *J* = 7.2 Hz, 3 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 2.17 (s, 3 H), 3.64–3.72 (m, 1 H), 3.76 (s, 3 H), 3.89–3.97 (m, 1 H), 4.04–4.15 (m, 2 H), 4.56 (br s, 1 H), 4.65 (d, *J* = 23.6 Hz, 1 H), 6.51 (d, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.48 (d, $^3J_{CP}$ = 5.8 Hz), 16.65 (d, $^3J_{CP}$ = 5.7 Hz), 20.57, 55.41, 56.17 (d, J_{CP} = 151.1 Hz), 63.36 (d, $^2J_{CP}$ = 5.3 Hz), 63.41 (d, $^2J_{CP}$ = 5.2 Hz), 114.23, 127.76, 128.00, 129.12, 129.84, 144.13, 144.28, 159.43.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.11.

Diethyl {(4-Nitrophenyl)[(4-tolyl)amino]methyl}phosphonate (3i)[9j]

Yellow solid; yield: 371 mg (98%); mp 159–161 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.2 Hz, 3 H), 1.29 (t, *J* = 7.2 Hz, 3 H), 2.17 (s, 3 H), 3.82–3.92 (m, 1 H), 3.98–4.06 (m, 1 H), 4.10–4.18 (m, 2 H), 4.58 (br, s, 1 H), 4.82 (d, *J* = 25.2 Hz, 1 H), 6.44 (d, *J* = 8.4 Hz, 2 H), 6.90 (d, *J* = 8.0 Hz, 2 H), 7.64 (d, *J* = 8.8 Hz, 2 H), 8.17 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.47 (d, $^3J_{CP}$ = 5.4 Hz), 16.64 (d, $^3J_{CP}$ = 5.4 Hz), 56.32 (d, J_{CP} = 147.3 Hz), 63.62 (d, $^2J_{CP}$ = 7.0 Hz), 63.94 (d, $^2J_{CP}$ = 6.7 Hz), 114.16, 123.95, 128.89, 130.05, 143.38, 144.42, 147.79.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 21.99.

Diethyl {(3-Nitrophenyl)[(4-tolyl)amino]methyl}phosphonate (3j)[9j]

Yellow solid; yield: 359 mg (95%); mp 102–103 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, *J* = 7.2 Hz, 3 H), 1.29 (t, *J* = 7.2 Hz, 3 H), 2.18 (s, 3 H), 3.84–3.94 (m, 1 H), 3.99–4.06 (m, 1 H), 3.11–4.18 (m, 2 H), 4.61 (br s, 1 H), 4.80 (d, *J* = 24.8 Hz, 1 H), 6.47 (d, *J* = 8.0 Hz, 2 H), 6.92 (d, *J* = 8.0 Hz, 2 H), 7.50 (t, *J* = 8.0 Hz, 1 H), 7.81 (d, *J* = 7.2 Hz, 1 H), 8.11 (d, *J* = 8.4 Hz, 1 H), 8.32 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.43 (d, $^3J_{CP}$ = 5.6 Hz), 16.62 (d, $^3J_{CP}$ = 5.3 Hz), 56.20 (d, J_{CP} = 148.8 Hz), 63.56 (d, $^2J_{CP}$ = 7.0 Hz), 63.94 (d, $^2J_{CP}$ = 6.6 Hz), 114.16, 122.98, 123.08, 128.58, 129.72, 130.05, 134.00, 139.22, 143.43, 148.67.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.17.

Diethyl {(2-Nitrophenyl)[(4-tolyl)amino]methyl}phosphonate (3k)[9j]

Yellow solid; yield: 344 mg (91%); mp 160–162 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.2 Hz, 3 H), 1.29 (t, *J* = 7.2 Hz, 3 H), 2.19 (s, 3 H), 3.75–3.85 (m, 1 H), 3.89–3.97 (m, 1 H), 4.11–4.21 (m, 2 H), 4.86 (br s, 1 H), 6.13 (d, *J* = 26.4 Hz, 1 H), 6.58 (d, *J* = 8.4 Hz, 2 H), 6.94 (d, *J* = 8.4 Hz, 2 H), 7.40 (t, *J* = 8.0 Hz, 1 H), 7.53 (t, *J* = 7.6 Hz, 1 H), 7.71–7.73 (m, 1 H), 7.98 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.16 (d, $^3J_{CP}$ = 5.5 Hz), 16.58 (d, $^3J_{CP}$ = 5.5 Hz), 20.57, 50.34 (d, J_{CP} = 150.1 Hz), 63.50 (d, $^2J_{CP}$ = 7.2 Hz), 64.07 (d, $^2J_{CP}$ = 7.1 Hz), 113.85, 125.43, 128.29, 128.68, 129.02, 130.14, 132.33, 133.71, 143.28, 149.71.

^{31}P NMR (162 MHz, $CDCl_3$,): δ = 22.14.

Diethyl {[(4-Chlorophenyl)amino](4-nitrophenyl)methyl}phosphonate (3l)[9j]

Yellow solid; yield: 359 mg (90%); mp 165–167 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, *J* = 7.2 Hz, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 3.80–3.90 (m, 1 H), 3.99–4.05 (m, 1 H), 4.10–4.18 (m, 2 H), 4.59 (br s, 1 H), 4.76 (d, *J* = 25.2 Hz, 1 H), 6.44 (d, *J* = 8.8 Hz, 2 H), 7.02 (d, *J* = 8.8 Hz, 2 H), 7.61 (d, *J* = 7.6 Hz, 2 H), 8.17 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.46 (d, $^3J_{CP}$ = 5.6 Hz), 16.64 (d, $^3J_{CP}$ = 5.0 Hz), 56.32 (d, J_{CP} = 147.8 Hz), 63.79 (d, $^2J_{CP}$ = 6.9 Hz), 63.98 (d, $^2J_{CP}$ = 7.1 Hz), 115.15, 124.02, 128.78, 129.43, 143.76, 144.36, 144.50, 147.87.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 21.53.

Diethyl [Anilino(4-nitrophenyl)methyl]phosphonate (3m)[27]

Yellow solid; yield: 357 mg (98%); mp 142–144 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 3.82–3.91 (m, 1 H), 3.98–4.06 (m, 1 H), 4.08–4.18 (m, 2 H), 4.58 (br s, 1 H), 4.85 (d, *J* =25.2 Hz, 1 H), 6.56 (d, *J* = 8.0 Hz, 2 H), 6.72 (t, *J* = 7.2 Hz, 1 H), 7.10 (t, *J* = 8.0 Hz, 2 H), 7.65 (d, *J* = 6.8 Hz, 2 H), 8.18 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.47 (d, $^3J_{CP}$ = 5.8 Hz), 16.64 (d, $^3J_{CP}$ = 5.8 Hz), 56.24 (d, J_{CP} = 147.2 Hz), 63.70 (d, $^2J_{CP}$ = 7.1 Hz), 63.97 (d, $^2J_{CP}$ = 6.8 Hz), 114.04, 119.32, 123.96, 128.85, 129.56, 144.25, 145.88, 147.79.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 21.85.

Diethyl [Anilino(4-chlorophenyl)methyl]phosphonate (3n)[28]

White solid; yield: 343 mg (97%); mp 72–74 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 3.72–3.82 (m, 1 H), 3.93–4.01 (m, 1 H), 4.05–4.16 (m, 2 H), 4.07 (br s, 1 H), 4.76 (d, *J* = 24.4 Hz, 1 H), 6.56 (d, *J* = 8.0 Hz, 2 H), 6.71 (t, *J* = 7.2 Hz, 1 H), 7.10 (t, *J* = 7.6 Hz, 2 H), 7.29 (d, *J* = 8.4 Hz, 2 H), 7.41 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.47 (d, $^3J_{CP}$ = 5.4 Hz), 16.65 (d, $^3J_{CP}$ = 5.6 Hz), 55.83 (d, J_{CP} = 149.4 Hz), 63.57 (d, $^2J_{CP}$ = 7.6 Hz), 63.64 (d, $^2J_{CP}$ = 7.6 Hz), 109.99, 114.16, 118.97, 129.01, 129.43, 133.96, 134.75, 146.21.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.04.

Diethyl [Anilino(4-methoxyphenyl)methyl]phosphonate (3o)[27]

White solid; yield: 336 mg (96%); mp 98–100 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.2 Hz, 3 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 3.65–3.71 (m, 1 H), 3.75 (s, 3 H), 3.90–3.96 (m, 1 H), 4.06–4.15 (m, 2 H), 4.70 (d, *J* = 23.6 Hz, 1 H), 4.73 (br s, 1 H), 6.58 (d, *J* = 8.0 Hz, 2 H), 6.67 (t, *J* = 7.2 Hz, 1 H), 6.85 (d, *J* = 6.8 Hz, 2 H), 7.09 (t, *J* = 7.6 Hz, 2 H), 7.37 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.48 (d, $^3J_{CP}$ = 5.6 Hz), 16.66 (d, $^3J_{CP}$ = 5.6 Hz), 55.43, 55.58 (d, J_{CP} = 151.3 Hz), 63.39 (d, $^2J_{CP}$ = 4.8 Hz), 63.97 (d, $^2J_{CP}$ = 4.2 Hz), 114.09, 114.26, 118.54, 127.89, 129.18, 129.35, 146.63, 159.51.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.02.

Diethyl [Anilino(2-thienyl)methyl]phosphonate (3p)[13b]

Wax; yield: 296 mg (91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, *J* = 6.8 Hz, 3 H), 1.26 (t, *J* = 6.8 Hz, 3 H), 3.80–3.90 (m, 1 H), 3.99–4.07 (m, 1 H), 4.10–4.20 (m, 2 H), 4.93 (br s, NH, 1 H), 5.05 (d, *J* = 24.0 Hz, 1 H), 6.68 (d, *J* = 8.0 Hz, 2 H), 6.72 (t, *J* = 7.2 Hz, 1 H), 6.94 (t, *J* = 4.8 Hz, 1 H), 7.10–7.16 (m, 3 H), 7.19 (dt, *J* = 1.2, 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.28 (d, $^3J_{CP}$ = 6.0 Hz), 16.45 (d, $^3J_{CP}$ = 5.9 Hz), 56.58 (d, J_{CP} = 157.4 Hz), 63.54 (d, $^2J_{CP}$ = 6.7 Hz), 63.76 (d, $^2J_{CP}$ = 7.1 Hz), 113.99, 118.88, 125.29, 126.21, 127.11, 129.23, 139.79, 146.30.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.89.

Diethyl [Anilino(2-furyl)methyl]phosphonate (3q)[27]

Wax; yield: 303 mg (98%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 6.8 Hz, 3 H), 1.25 (t, *J* = 6.8 Hz, 3 H), 3.82–3.88 (m, 1 H), 4.00–4.07 (m, 1 H), 4.13–4.20 (m, 2 H), 4.91 (d, *J* = 24.0 Hz, 1 H), 5.11 (br s, 1 H), 6.27 (s, 1 H), 6.38 (t, *J* = 3.2 Hz, 1 H), 6.65–6.72 (m, 3 H), 7.11 (t, *J* = 8.0 Hz, 2 H), 7.34 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.26 (d, $^3J_{CP}$ = 5.7 Hz), 16.39 (d, $^3J_{CP}$ = 5.3 Hz), 50.12 (d, J_{CP} = 158.7 Hz), 63.29 (d, $^2J_{CP}$ = 6.6 Hz), 63.32 (d, $^2J_{CP}$ = 6.6 Hz), 108.76, 110.78, 113.91, 118.75, 129.14, 142.42, 146.28, 149.49.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.30.

Diethyl {1-[(4-Chlorophenyl)amino]-2-methylpropyl}phosphonate (3r)[9j]

White solid; yield: 301 mg (94%); mp 88–89 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03–1.35 (m, 12 H), 2.20–2.31 (m, 1 H), 3.50–3.70 (m, 1 H), 3.89–4.16 (m, 5 H), 6.57–6.63 (m, 2 H), 7.09–7.16 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.40 (d, $^3J_{CP}$ = 7.8 Hz), 16.47 (d, $^3J_{CP}$ = 6.9 Hz), 17.97 (d, $^3J_{CP}$ = 15.8 Hz), 20.67 (d, $^3J_{CP}$ = 16.2 Hz), 29.84 (d, $^2J_{CP}$ = 7.4 Hz), 56.49 (d, J_{CP} = 201.4 Hz), 61.85 (d, $^2J_{CP}$ = 9.8 Hz), 62.59 (d, $^2J_{CP}$ = 9.6 Hz), 114.33, 122.33, 129.06, 146.44.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.18.

Diethyl (1-Anilinoundecyl)phosphonate (3s)[9f]

Colorless oil; yield: 273 mg (74%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.8 Hz, 3 H), 1.18 (t, *J* = 7.2 Hz, 3 H), 1.24–1.31 (m, 16 H), 1.53–1.57 (m, 1 H), 1.63–1.71 (m, 1 H), 1.88–1.95 (m, 1 H), 3.66–3.76 (m, 2 H), 3.96–4.04 (m, 1 H), 4.08–4.13 (m, 3 H), 6.66 (d, *J* = 8.0 Hz, 2 H), 6.71 (t, *J* = 7.6 Hz, 1 H), 7.17 (t, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.10, 16.36 (d, $^3J_{CP}$ = 5.6 Hz), 16.46 (d, $^3J_{CP}$ = 4.0 Hz), 17.09, 20.44, 22.65, 26.05, 29.36, 30.73, 31.85, 35.94, 39.19, 50.87 (d, J_{CP} = 155.3 Hz), 61.99 (d, $^2J_{CP}$ = 7.4 Hz), 63.01 (d, $^2J_{CP}$ = 7.1 Hz), 113.24, 117.82, 129.21, 147.37.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 26.51.

Diethyl {1-[(4-Chlorophenyl)amino]cyclohexyl}phosphonate (3t)[12h]

White solid; yield: 311 mg (90%); mp 133–135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 9.6 Hz, 6 H), 1.38–1.68 (m, 6 H), 1.79 (t, *J* = 16.8 Hz, 2 H), 2.14–2.19 (m, 2 H), 3.32 (br s, 1 H), 4.05 (q, J_1 = 9.2 Hz, J_2 = 18.8 Hz, 4 H), 6.98 (d, *J* = 11.6 Hz, 2 H), 7.10 (d, *J* = 11.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.53, 16.65, 19.99, 20.14, 25.36, 30.06, 56.12, 58.24, 62.25, 62.37, 119.55, 124.25, 128.59, 144.35.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 27.44.

Diethyl (1-Anilino-2-ethylbutyl)phosphonate (3u)[29]

White solid; yield: 186 mg (62%); mp 116–117 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.2 Hz, 6 H), 1.24 (t, *J* = 6.8 Hz, 6 H), 1.91–2.01 (m, 4 H), 3.63–3.67 (m, 2 H), 4.02–4.10 (m, 3 H), 6.80 (t, *J* = 7.2 Hz, 1 H), 6.94 (d, *J* = 8.0 Hz, 2 H), 7.12–7.17 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.83, 16.41, 16.46 (d, $^3J_{CP}$ = 5.6 Hz), 26.46, 61.11 (d, J_{CP} = 148.8 Hz), 62.04 (d, $^2J_{CP}$ = 7.6 Hz), 62.21 (d, $^2J_{CP}$ = 8.0 Hz), 118.90, 119.64, 128.74, 145.69.

^{31}P NMR (162 MHz, $CDCl_3$): δ = 29.14.

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Supporting Information

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References

(1) Peyman, A.; Budt, K.-H.; Spanig, J. S.; Stowasser, B.; Ruppert, D. *Tetrahedron Lett.* **1992**, *33*, 4549.
(2) Alonso, E.; Alonso, E.; Solis, A.; del Pozo, C. *Synlett* **2000**, 698.
(3) Kafarski, P.; Lejczak, B. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *63*, 193.
(4) Allerberger, F.; Klare, I. J. *J. Antimicrob. Chemother.* **1999**, *43*, 211.
(5) Maier, L. *Phosphorus, Sulfur Silicon Relat. Elem.* **1990**, *47*, 43.
(6) Maier, L.; Spörri, H. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *61*, 69.
(7) Emsley, J.; Hall, D. *The Chemistry of Phosphorus: Environmental, Organic, Inorganic, Biochemical and Spectroscopic Aspects*; Harper & Row: London, **1976**.
(8) Chung, S.-K.; Kang, D.-H. *Tetrahedron: Asymmetry* **1996**, *7*, 21.
(9) (a) Kukhar, V. P.; Solodenko, V. A. *Russ. Chem. Rev. (Engl. Transl.)* **1987**, *56*, 859. (b) Laschat, S.; Kunz, H. *Synthesis* **1992**, 90. (c) Matveeva, E. D.; Podrugina, T. A.; Tishkovskaya, E. V.; Tomilova, L. G.; Zefirov, N. S. *Synlett* **2003**, 2321. (d) Pavlov, V. Y.; Kabachnik, M. M.; Zobnina, E. V.; Timofeev, V. P.; Konstantinov, I. O.; Kimel, B. G.; Ponomarev, G. V.; Beletskaya, I. P. *Synlett* **2003**, 2193. (e) Van Meenen, E.; Moonen, K.; Acke, D.; Stevens, C. V. *ARKIVOC* **2006**, *(i)*, 31. (f) Yadav, J. S.; Reddy, B. V. S.; Sreedhar, P. *Green Chem.* **2002**, *4*, 436. (g) Sobhani, S.; Safaei, E.; Asadi, M.; Jalili, F. *J. Organomet. Chem.* **2008**, *693*, 3313. (h) Dake, S. A.; Raut, D. S.; Kharat, K. R.; Mhaske, R. S.; Deshmukh, S. U.; Pawar, R. P. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2527. (i) Reddy, C. B.; Kumar, K. S.; Kumar, M. A.; Reddy, M. V. N.; Krishna, B. S.; Naveen, M.; Arunasree, M. K.; Reddy, C. S.; Raju, C. N.; Reddy, C. D. *Eur. J. Med. Chem.* **2012**, *47*, 553. (j) Yu, Y.-Q. *Synthesis* **2013**, *45*, 2545. (k) Sharghi, H.; Ebrahimpourmoghaddam, S.; Doroodmand, M. M. *Tetrahedron* **2013**, *69*, 4708. (l) Milen, M.; Ábrányi-Balogh, P.; Dancsó, A.; Frigyes, D.; Pongó, L.; Keglevich, G. *Tetrahedron Lett.* **2013**, *54*, 5430.
(10) (a) Kabachnik, M. I.; Medved, T. Y. *Dokl. Akad. Nauk SSSR* **1952**, *83*, 689. (b) Fields, E. K. *J. Am. Chem. Soc.* **1952**, *74*, 1528. (c) Keglevich, G.; Bálint, E. *Molecules* **2012**, *17*, 12821. (d) Zefirov, N. S.; Matveeva, E. D. *ARKIVOC* **2008**, *(i)*, 1.
(11) (a) Qian, C.; Huang, T. *J. Org. Chem.* **1998**, *63*, 4125. (b) Ranu, B. C.; Hajra, A.; Jana, U. *Org. Lett.* **1999**, *1*, 1141. (c) Manabe, K.; Kobayashi, S. *Chem. Commun.* **2000**, 669. (d) Chandrasekhar, S.; Prakash, S. J.; Jagadeshwar, V.; Narsihmulu, C. *Tetrahedron Lett.* **2001**, *42*, 5561. (e) Heydari, A.; Zarei, M.; Alijanianzadeh, R.; Tavakol, H. *Tetrahedron Lett.* **2001**, *42*, 3629. (f) Akiyama, T.; Sanada, M.; Fuchibe, K. *Synlett* **2003**, 1463. (g) Xu, F.; Luo, Y.; Deng, M.; Shen, Q. *Eur. J. Org. Chem.* **2003**, 4728. (h) Paraskar, A. S.; Sudalai, A. *ARKIVOC* **2006**, *(x)*, 183. (i) Bhagat, S.; Chakraborti, A. K. *J. Org. Chem.* **2008**, *73*, 6029. (j) Rezaei, Z.; Firouzabadi, H.; Iranpoor, N.; Ghaderi, A.; Jafari, M. R.; Jafari, A. A.; Zare, H. R. *Eur. J. Med. Chem.* **2009**, *44*, 4266. (k) Thirumurugan, P.; Nandakumar, A.; Priya, N. S.; Muralidaran, D.; Perumal, P. T. *Tetrahedron Lett.* **2010**, *51*, 5708. (l) Gallardo-Macias, R.; Nakayama, K. *Synthesis* **2010**, 57. (m) Tang, J.; Wang, L.; Wang, W.; Zhang, L.; Wu, S.; Mao, D. *J. Fluorine Chem.* **2011**, *132*, 102. (n) Disale, S. T.; Kale, S. R.; Kahandal, S. S.; Srinivasan, T. G.; Jayaram, R. V. *Tetrahedron Lett.* **2012**, *53*, 2277. (o) Fang, D.; Jiao, C.; Ni, C. *Heteroat. Chem.* **2010**, *21*, 546. (p) Hou, J.-T.; Gao, J.-W.; Zhang, Z.-H. *Appl. Organomet. Chem.* **2011**, *25*, 47. (q) Zhang, G.; Zi, Y.; Xia, Y.; Fei, Y.; Wang, Y. *Huaibei Shifan Daxue Xuebao, Ziran Kexueban* **2011**, *32*, 38.
(12) (a) Yadav, J. S.; Subba Reddy, B. V.; Madan, C. *Synlett* **2001**, 1131. (b) Kaboudin, B.; Nazari, R. *Tetrahedron Lett.* **2001**, *42*, 8211. (c) Kabachnik, M. M.; Zobnina, E. V.; Beletskaya, I. P. *Synlett* **2005**, 1393. (d) Xia, M.; Lu, Y.-d. *Ultrason. Sonochem.* **2007**, *14*, 235. (e) Zahouily, M.; Elmakssoudi, A.; Mezdar, A.; Rayadh, A.; Sebti, S. *Catal. Commun.* **2007**, *8*, 225. (f) Ambica, S. K.; Taneja, S. C.; Hundal, M. S.; Kapoor, K. K. *Tetrahedron Lett.* **2008**, *49*, 2208. (g) Bhattacharya, A. K.; Rana, K. C. *Tetrahedron Lett.* **2008**, *49*, 2598. (h) Dar, B.; Singh, A.; Sahu, A.; Patidar, P.; Chakraborty, A.; Singh, B.; Sharma, M. *Tetrahedron Lett.* **2012**, *53*, 5497. (i) Olszewski, T. K.; Boduszek, B. *Tetrahedron* **2010**, *66*, 8661. (j) Ordóñez, M.; Sayago, F. J.; Cativiela, C. *Tetrahedron* **2012**, *68*, 6369. (k) Boduszek, B.; Olszewski, T. K.; Goldeman, W.; Grzegolec, K.; Blazejewska, P. *Tetrahedron* **2012**, *68*, 1223. (l) Olszewski, T. K.; Boduszek, B. *Synthesis* **2011**, 437. (m) Tibhe, G. D.; Bedolla-Medrano, M.; Cativiela, C.; Ordóñez, M. *Synlett* **2012**, *23*, 1931. (n) Michalska, J.; Boduszek, B.; Olszewski, T. K. *Heteroat. Chem.* **2011**, *22*, 617.
(13) (a) Kassaee, M. Z.; Movahedi, F.; Masrouri, H. *Synlett* **2009**, 1326. (b) Vinu, A.; Kalita, P.; Balasubramanian, V. V.; Oveisi, H.; Selvan, T.; Mano, A.; Chari, M. A.; Subba Reddy, B. V. *Tetrahedron Lett.* **2009**, *50*, 7132. (c) Subba Reddy, B. V.; Siva Krishna, A.; Ganesh, A. V.; Narayana Kumar, G. G. K. S. *Tetrahedron Lett.* **2011**, *52*, 1359. (d) Kidwai, M.; Bhardwaj, S.; Mishra, N. K.; Jain, A.; Kumar, A.; Mozzumdar, S. *Catal. Sci. Technol.* **2011**, *1*, 426. (e) Patil, A. B.; Patil, D. S.; Bhanage, B. M. *Mater. Lett.* **2012**, *86*, 50.
(14) Zon, J. *Pol. J. Chem.* **1981**, *55*, 643.
(15) (a) Sheykhan, M.; Mohammadnejad, H.; Akbari, J.; Heydari, A. *Tetrahedron Lett.* **2012**, *53*, 2959. (b) Fang, D.; Yang, J.; Ni, C. *Heteroat. Chem.* **2011**, *22*, 5. (c) Heydari, A.; Khaksar, S.; Tajbakhsh, M. *Tetrahedron Lett.* **2009**, *50*, 77. (d) Bhagat, S.; Chakraborti, A. K. *J. Org. Chem.* **2007**, *72*, 1263. (e) Chandrasekhar, S.; Narsihmulu, C.; Sultana, S. S.; Saritha, B.; Prakash, S. J. *Synlett* **2003**, 505.
(16) (a) Dömling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168. (b) Armstrong, R. W.; Combs, A. P.; Tempest, P. A.; Brown, S. D.; Keating, T. A. *Acc. Chem. Res.* **1996**, *29*, 123. (c) Ugi, I. *Pure Appl. Chem.* **2001**, *73*, 187. (d) Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439. (e) Sunderhaus, J. D.; Martin, S. F. *Chem. Eur. J.* **2009**, *15*, 1300.
(17) *Multicomponent Reactions*; Zhu, J.; Bienaymé, H., Eds.; Wiley-VCH: Weinheim, **2005**.
(18) (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071. (b) Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459. (c) Sheldon, R. *Chem. Commun.* **2001**, 2399. (d) *Ionic Liquids in Synthesis*, 2nd ed. Wasserscheid, P.; Welton, T., Eds.; Wiley-VCH: Weinheim, **2008**.
(19) (a) Luo, S. Z.; Mi, X. L.; Zhang, L.; Liu, S.; Xu, H.; Cheng, J.-P. *Angew. Chem. Int. Ed.* **2006**, *45*, 3093. (b) Ni, B.; Zhang, Q. Y.; Headley, A. D. *Green Chem.* **2007**, *9*, 737. (c) Ranu, B. C.; Banerjee, S. *Org. Lett.* **2005**, *7*, 3049. (d) Xu, J.-M.; Qian, C.; Liu, B.-K.; Wu, Q.; Lin, X.-F. *Tetrahedron* **2007**, *63*, 986. (e) Xu, J.-M.; Wu, Q.; Zhang, Q.-Y.; Zhang, F.; Lin, X.-F. *Eur. J. Org. Chem.* **2007**, 1798.
(20) (a) Zhou, L.; Wang, L. *Chem. Lett.* **2007**, *36*, 628. (b) Luo, S.; Mi, X.; Zhang, L.; Liu, S.; Xu, H.; Cheng, J.-P. *Tetrahedron* **2007**, *63*, 1923. (c) Hu, S.; Jiang, T.; Zhang, Z.; Zhu, A.; Han, B.; Song, J.; Xie, Y.; Li, W. *Tetrahedron Lett.* **2007**, *48*, 5613.

(21) (a) Feng, L.-C.; Sun, Y.-W.; Tang, W.-J.; Xu, L.-J.; Lam, K.-L.; Zhou, Z.; Chan, A. S. C. *Green Chem.* **2010**, *12*, 949. (b) Sayin, S.; Yilmaz, M. *RSC Adv.* **2014**, *4*, 2219. (c) Petrović, V. P.; Simijonović, D.; Živanović, M. N.; Košarić, J. V.; Petrović, Z. D.; Marković, S.; Marković, S. D. *RSC Adv.* **2014**, *4*, 24635.
(22) (a) Wasserscheid, P.; Sesing, M.; Korth, W. *Green Chem.* **2002**, *4*, 134. (b) Luo, Y.; Pan, A. X.; Xing, M.; Chen, M.; Xie, J. M. *Adv. Mater. Res. (Durnten-Zurich, Switz.)* **2012**, *443–444*, 917. (c) Tran, P. H.; Duus, F.; Le, T. N. *Tetrahedron Lett.* **2012**, *53*, 222.
(23) (a) Ying, A. G.; Xu, S. L.; Liu, S.; Ni, Y. X.; Yang, J. G.; Wu, C. L. *Ind. Eng. Chem. Res.* **2014**, *53*, 547. (b) Epishina, M. A.; Ovchinnikov, I. V.; Kulikov, A. S.; Makhova, N. N.; Tartakovsky, V. A. *Mendeleev Commun.* **2011**, *21*, 21. (c) Li, Z.-H.; Zhou, Z.-M.; Hao, X.-Y.; Zhang, J.; Dong, X.; Liu, Y.-Q.; Sun, W.-W.; Cao, D. *Appl. Catal., A* **2012**, *425*, 28.
(24) Xu, D.-Z.; Liu, Y.; Shi, S.; Wang, Y. *Tetrahedron: Asymmetry* **2010**, *21*, 2530.
(25) (a) Xu, D.-Z.; Liu, Y.; Shi, S.; Wang, Y. *Green Chem.* **2010**, *12*, 514. (b) Xu, D.-Z.; Shi, S.; Wang, Y. *RSC Adv.* **2013**, *3*, 23075.
(26) (a) Ying, A.; Li, Z.; Yang, J.; Liu, S.; Xu, S.; Yan, H.; Wu, C. *J. Org. Chem.* **2014**, *79*, 6510. (b) Safaei, S.; Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V. *Adv. Synth. Catal.* **2012**, *354*, 3095. (c) Keithellakpam, S.; Laitonjam, W. S. *Chin. Chem. Lett.* **2014**, *25*, 767. (d) Chiappe, C.; Rajamani, S.; D'Andrea, F. *Green Chem.* **2013**, *15*, 137. (e) Munshi, M. K.; Gade, S. M.; Rane, V. H.; Kelkar, A. A. *RSC Adv.* **2014**, *4*, 32127. (f) Singh, A.; Singh, P.; Goel, N. *Struct. Chem.* **2014**, *25*, 821. (g) Khalafi-Nezhad, A.; Mohammadi, S. *Synthesis* **2012**, *44*, 1725.
(27) Hamadi, H.; Kooti, M.; Afshari, M.; Ghiasifar, Z.; Adibpour, N. *J. Mol. Catal. A: Chem.* **2013**, *373*, 25.
(28) Agawane, S. M.; Nagarkar, J. M. *Tetrahedron Lett.* **2011**, *52*, 3499.
(29) Pudovik, A. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1952**, 940.