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Communication

An eco-friendly procedure for the efficient synthesis of dialkyl α-aminophosphonates in aqueous media

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ABSTRACT

A new, convenient and high yielding procedure for the preparation of diethyl α-aminophosphonates in water by one-pot reaction of aldehydes, amines, tri/dialkyl phosphites in the presence of a low catalytic amount of [Cu(3,4-tmtppa)](MeSO$_4$)$_4$ (0.16 mol%) as a highly stable and re-usable catalyst is described.

1. Introduction

The synthesis of α-aminophosphonates which are considered as analogues of amino acids has been a focus of considerable attention in synthetic organic chemistry as well as in medicinal chemistry [1–4]. The addition of phosphorous nucleophiles to imines is a general reported synthetic method for the preparation of α-aminophosphonates. This reaction is usually catalyzed by Lewis acids such as $SnCl_2$, $SnCl_4$, $ZnCl_2$ and $MgBr_2$. However, these reactions can not proceed in one-pot from a carbonyl compound, an amine and a phosphite. Generation of water during the course of the reaction can decompose or deactivate these Lewis acids [5,6]. This drawback has been overcome by some recent methods using lanthanide triflates/magnesium sulfate [7], $InCl_3$ [8], $TaCl_5$–SiO_2 [9], $ZrCl_4$ [10], $Sc(DS)_3$ [11], $H_3PW_{12}O_{40}$ [12], $BiNO_3 \cdot 5H_2O$ [13], $Mg(ClO_4)_2$ [14,15] and β-cyclodextrine [16]. However, these methods involve either long reaction times, low yields of the products, required stoichiometric amount of reagents, use of additives or expensive catalysts.

One of the fundamental challenges and ultimate goals in organic synthesis is to perform the reactions in water [17,18]. Water is cheap, safe and reduces the use of harmful organic solvents. Therefore, it leads to the development of environmentally friendly chemical processes [19]. Although, today's environmental consciousness imposes the use of water as a solvent on both industrial and academic chemists, organic solvents are still used instead of water for mainly two reasons. First, most organic substances are insoluble in water and as a result, water does not act as a reasonable reaction medium. Second, many reaction substrates, reagents and catalysts are decomposed or deactivated in water. Therefore, efforts to carry out organic reactions in water pose an important challenge in the area of reaction design.

Metallophthalocyanines (Mpc), which are structurally similar to metal porphyrins, are easily accessible, more stable to degradation and cost effective than porphyrins. They have been extensively used as efficient catalysts in a variety of organic reactions [20–26]. Tetrapyridinoporphyrazines (tppa) are heterocyclic phthalocyanine (pc) derivatives in which benzene rings are replaced with electron-withdrawing pyridine rings. The presence of pyridine rings in these compounds not only increases the reactivity of tppa compared with pc, but also allows the facile quaternarization processes. The *N*,*N*′,*N*″,*N*‴-tetramethylated quaternized form of tetrapyridinoporphyrazine can be prepared easily by its reaction with dimethyl sulfate in dimethyl formamide [27]. The resulting tetramethyl-tetra-3,4-pyridinoporphyrazinato copper (II) methyl sulfate [Cu(3,4-tmtppa)](MeSO$_4$)$_4$ (**1**) (Fig. 1) is a water soluble compound and has considerable low solubility in common organic solvents. Unlike metallophthalocyanine, the reports on catalytic activity of metallotetrapyridinoporphyrazine in organic reactions are rare in the literature [28–30].

In continuation of our work on the development of new methods for the preparation of diethyl α-functionalized phosphonates [31–36], we have already reported one-pot synthesis of diethyl

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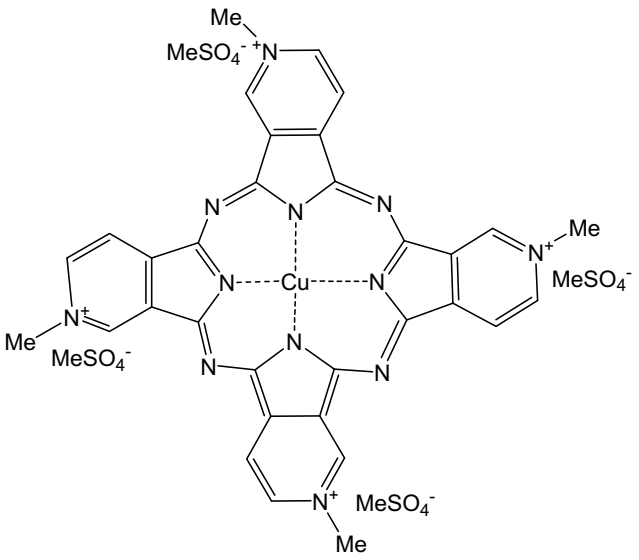


Fig. 1. [Cu(3,4-tmtppa)]$(MeSO_4)_4$ (**1**).

α-aminophosphonates catalyzed by metal triflates under solvent-free conditions [35].

2. Results and discussion

In this paper, we report the successful application of [Cu(3,4-tmtppa)]$(MeSO_4)_4$ for the preparation of various types of dialkyl α-aminophosphonates from the coupling reaction of aldehydes, amines, tri/dialkyl phosphites in water.

Initially, the coupling reaction of benzaldehyde, aniline and triethylphosphite in water with different catalytic amounts of [Cu(3,4-tmtppa)]$(MeSO_4)_4$ and at different reaction temperatures have investigated in order to optimize the reaction conditions. The best yield of the corresponding diethyl α-aminophosphonate was obtained in the presence of 0.16 mol% of [Cu(3,4-tmtppa)]-$(MeSO_4)_4$ and at 80 °C. Then, using optimized reaction conditions, the one-pot coupling reaction of a series of aldehydes and amines with different nucleophilic phosphorus reagents using [Cu(3,4-tmtppa)]$(MeSO_4)_4$ as a catalyst were examined (Scheme 1). The results of these studies are presented in Table 1.

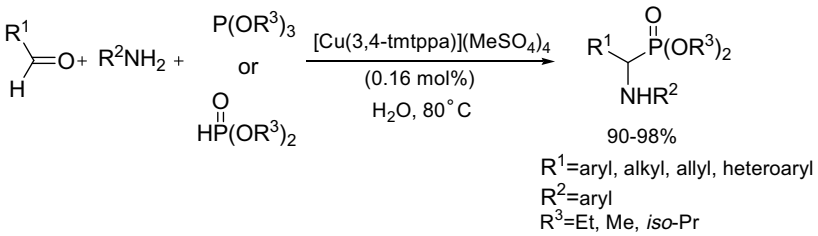
As shown in Table 1, the catalytic one-pot reaction of benzaldehyde and aniline proceeded well with different nucleophilic phosphorus reagents (Table 1, entries 1–5). These results demonstrate that both the yields and the reaction times are relatively independent of nucleophilic phosphorus compounds. Substituted benzaldehyde with electron-donating and electron-withdrawing groups underwent coupling reaction with different substituted anilines/benzyl amine and triethyl phosphite and gave the corresponding diethyl α-aminophosphonates in 90–98% yields (Table 1, entries 6–10, 16). Acid-sensitive aldehydes, such as furan-2-carbaldehyde, thiophene-2-carbaldehyde, and cinnamaldehyde underwent smooth reactions without any decomposition or polymerization under the present reaction conditions. The coupling reaction of *n*-butyraldehyde as an aliphatic aldehyde with aniline and triethyl phosphite gave the corresponding product in high yields (Table 1, entry 14). Naphthalene-2-carbaldehyde as a polynuclear aromatic aldehyde also reacted with triethyl phosphite to give the desired compound **14** in high yield. Difunctional aminophosphonates **16** and **17** were also prepared successfully by the presented method in 90% and 91% yields (Table 1, entries 17,18). In these transformations, turnover number (TON = mole of the product/mole of catalyst) is in the range of 562–612, which indicates the high efficiency of [Cu(3,4-tmtppa)]$(MeSO_4)_4$ for the preparation of a wide range of α-aminophosphonates. It should be noted that no competitive side reactions such as the formation of α-hydroxyphosphonates were observed in these transformations. We have also studied the reaction of ketones with aniline and triethyl phosphite under the same reaction conditions. However, the results were not as positive as those presented above.

To show the effect of the catalyst, one-pot reaction of benzaldehyde, aniline and triethyl phosphite was examined in the absence of the catalyst. However, this reaction remained incomplete and only 10% of the desired product **2** was obtained after 24 h.

After performing the preparation reaction of diethyl α-aminophosphonate (**2**) under the conditions described in Table 1, the reaction mixture was washed with CH_2Cl_2. The separated aqueous layer containing the catalyst was re-used for a consecutive run under the same reaction conditions. The average isolated yield of **2** for five consecutive runs was 95.2%, which clearly demonstrates the practical reusability of this catalyst as an aqueous solution (Fig. 2). In order to find out the yields of the catalyst recovered, the reusability test was repeated and in each run, the catalyst was isolated from the aqueous layer by evaporation of the solvent (Fig. 2). The average isolated yield of the catalyst **1** for five consecutive runs was 97.6%. This reusability demonstrates the high stability and turnover of [Cu(3,4-tmtppa)]$(MeSO_4)_4$ (**1**) under the employed conditions. It is worth to note that the recyclability test was stopped after five runs.

In order to show the unique behavior of [Cu(3,4-tmtppa)]$(MeSO_4)_4$ for the preparation of α-aminophosphonates, we studied the one-pot reaction of benzaldehyde, aniline and triethylphosphite in the presence of a catalytic amount of Cu-phthalocyanine tetrasulfate (0.16 mol%) as a water soluble phthalocyanine under the same reaction conditions. The results showed lower yield of the product with a longer reaction time (85%, 6 h). We have also investigated the reusability of Cu-phthalocyanine for the preparation of diethyl α-aminophosphonate (**2**) by the presented method. It was found that the reaction did not work well in the presence of recycled catalyst and the starting material remained intact.

In conclusion, we have found that [Cu(3,4-tmtppa)]$(MeSO_4)_4$ can be used as a new, re-usable and efficient catalyst for the preparation of a variety of α-aminophosphonates by one-pot reactions



Scheme 1.

Table 1
One-pot synthesis of dialkyl α-aminophosphonates from aldehydes mediated by $[Cu(3,4\text{-tmtppa})](MeSO_4)_4$ in water at 80 °C

Entry	Aldehyde	Amine	P-Nucleophile	Product	Time (h)	Yield (%)[a]
1	C_6H_5CHO	$C_6H_5NH_2$	$P(OEt)_3$	**2**	0.5	96
2	C_6H_5CHO	$C_6H_5NH_2$	$HP(O)(OEt)_2$	**2**	1	90
3	C_6H_5CHO	$C_6H_5NH_2$	$P(OMe)_3$	**3**	0.5	95
4	C_6H_5CHO	$C_6H_5NH_2$	$P(O\text{-}iso\text{-}Pr)_3$	**4**	0.75	91
5	C_6H_5CHO	$C_6H_5NH_2$	$HP(O)(O\text{-}iso\text{-}Pr)_2$	**4**	1	93
6	4-(MeO)-C_6H_4CHO	$C_6H_5NH_2$	$P(OEt)_3$	**5**	3	90
7	4-Cl-C_6H_4CHO	$C_6H_5NH_2$	$P(OEt)_3$	**6**	0.5	95
8	2,6-Cl_2-C_6H_3CHO	$C_6H_5NH_2$	$P(OEt)_3$	**7**	1	98
9	C_6H_5CHO	4-Me-$C_6H_4NH_2$	$P(OEt)_3$	**8**	1	97
10	C_6H_5CHO	4-Cl-$C_6H_4NH_2$	$P(OEt)_3$	**9**	2	95
11	Thiophene-2-carbaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	**10**	1	90
12	Furan-2-carbaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	**11**	1.5	98
13	PhCH=CHCHO	$C_6H_5NH_2$	$P(OEt)_3$	**12**	2	91
14	$CH_3(CH_2)_2CHO$	$C_6H_5NH_2$	$P(OEt)_3$	**13**	1	96
15	Naphthalene-2-carbaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	**14**	2	91
16	C_6H_5CHO	$C_6H_5CH_2NH_2$	$P(OEt)_3$	**15**	1	95
17[b]	Terephethaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	**16**	2	90
18[c]	C_6H_5CHO	1,4-diaminobenzene	$P(OEt)_3$	**17**	2	91

[a] Yields refer to those of pure isolated products characterized by spectral data and elemental analysis.
[b] *Conditions:* aniline (2 equiv.), triethyl phosphite (2 equiv.).
[c] *Conditions:* benzaldehyde (2 equiv.), triethyl phosphite (2 equiv.).

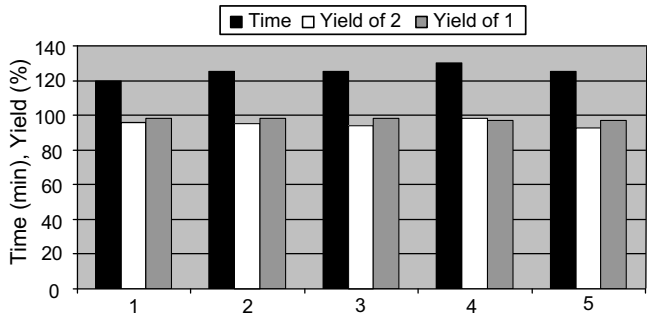


Fig. 2. Reusability of $[Cu(3,4\text{-tmtppa})](MeSO_4)_4$ (**1**) as a catalyst for the preparation of diethyl α-aminophosphonate (**2**).

of aldehydes, amines and tri/dialkyl phosphates in water. This reaction system not only provides a novel method for the synthesis of biologically important α-aminophosphonates, but also extends the applicability of $[Cu(3,4\text{-tmtppa})](MeSO_4)_4$ in organic synthesis in water which leads to environmentally friendly chemical processes. This property combined with ease of recovery and catalyst reusability makes this method an economic, benign and waste-free chemical process for the synthesis of dialkyl α-aminophosphonates.

3. Experimental

3.1. Materials and physical measurements

Chemicals were purchased from Merck and Fluka Chemical Companies. All of the products were identified by their physical and spectral data. IR spectra were run on a Perkin–Elmer 780 instrument. NMR spectra were recorded on a Bruker Avance DPX-250. Mass spectra were recorded on a Shimadzu GCMS-QP5050A. The purity of the products and the progress of the reactions were accomplished by TLC on silica-gel polygram SILG/UV_{254} plates.

3.2. Typical procedure for the synthesis of diethyl α-aminophosphonate (2)

Benzaldehyde (1.06 g, 10 mmol), aniline (0.931 g, 10 mmol) and triethyl phosphite (1.66 g, 10 mmol) were added to the stirring solution of $[Cu(3,4\text{-tmtppa})](MeSO_4)_4$ (0.018 g, 1.6 mmol) in water (20 mL). The resulting mixture was heated in an oil bath at 80 °C and stirred for an appropriate time (Table 1). Water (20 mL) was added to the cooled reaction mixture and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts was washed with water (2 × 10 mL), separated, dried over Na_2SO_4 and filtered. Pure product **2** was isolated by preparative plate chromatography eluted with *n*-hexane:EtOAc (1:1). Combined aqueous layers containing the catalyst was concentrated to appropriate volume (20 mL) and re-used for the preparation of diethyl α-aminophosphonate (**2**) following the above procedure.

3.3. Spectral data and elemental analysis of the products

3.3.1. Diethyl (phenyl)-N-(phenyl)aminomethylphosphonate (2)

^1H NMR ($CDCl_3$, TMS): δ 1.11 (t, 3H, $^2J_{H,H}$ = 7.1 Hz, OCH_2CH_3), 1.28 (t, 3H, $^2J_{H,H}$ = 7.1 Hz, OCH_2CH_3), 3.59–3.69 (m, 1H, OCH_2CH_3), 3.88–3.95 (m, 1H, OCH_2CH_3), 4.07–4.16 (m, 2H, OCH_2CH_3), 4.75 (d, 1H, $^2J_{P,H}$ = 26.4 Hz, CH), 4.79 (bs, 1H, NH), 6.59 (d, 2H, $^2J_{H,H}$ = 7.9 Hz, C_6H_5), 6.68 (t, 1H, $^2J_{H,H}$ = 7.3 Hz, C_6H_5), 7.10 (t, 2H, $^2J_{H,H}$ = 8.0 Hz, C_6H_5), 7.25–7.35 (m, 3H, C_6H_5), 7.47 (d, 2H, $^2J_{H,H}$ = 7.4 Hz, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 56.4 (d, $^1J_{C,P}$ = 150.4 Hz, CH), 63.7 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_2CH_3), 114.2, 118.8, 128.2–129.6, 136.3, 146.6–146.8 (C_6H_5) ppm; IR: 3305 (NH) cm^{-1}; MS (70 eV), *m*/*e*: 319 (M^+), 182 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{17}H_{22}NO_3P$: C, 63.94; H, 6.94. Found: C, 63.92; H, 6.92%.

3.3.2. Dimethyl (phenyl)-N-(phenyl)aminomethylphosphonate (3)

^1H NMR ($CDCl_3$, TMS): δ 3.40 (d, 3H, $^2J_{P,H}$ = 10.0 Hz, OCH_3), 3.69 (d, 3H, $^2J_{P,H}$ = 10.0 Hz, OCH_3), 4.66–4.79 (m, 2H, CH, NH), 6.51–6.63 (m, 3H, C_6H_5), 7.00–7.07 (m, 2H, C_6H_5), 7.19–7.31 (m, 3H, C_6H_5), 7.39–7.42 (m, 2H, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 52.78 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 54.62 (d, $^1J_{C,P}$ = 151.5 Hz, CH), 112.83, 117.51, 126.72, 126.81, 127.02, 127.69, 128.17, 134.53 (C_6H_5) ppm; IR: 3296 (NH) cm^{-1}; MS (70 eV), *m*/*e*: 291 (M^+), 154 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{15}H_{18}NO_3P$: C, 61.85; H, 6.23. Found: C, 61.83; H, 6.21%.

3.3.3. Di-iso-propyl (phenyl)-N-(phenyl)aminomethylphosphonate (4)

^1H NMR ($CDCl_3$, TMS): δ 0.83–1.09 (m, 3H, $OCH(CH_3)_2$), 1.16–1.26 (m, 9H, $OCH(CH_3)_2$), 4.36–4.40 (m, 2H, $OCH(CH_3)_2$),

4.55–4.67 (m, 2H, CH, NH), 6.50–6.63 (m, 5H, C_6H_5), 7.02 (t, 2H, $^2J_{H,H}$ = 7.5 Hz, C_6H_5), 7.19–7.27 (m, 1H, C_6H_5), 7.39 (d, 2H, $^2J_{H,H}$ = 7.4 Hz, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 23.20 (d, $^2J_{C,P}$ = 5.8 Hz, $OCH(CH_3)_2$), 23.77 (d, $^2J_{C,P}$ = 5.8 Hz, $OCH(CH_3)_2$), 56.48 (d, $^1J_{C,P}$ = 151.8 Hz, CH), 71.88 (d, $^2J_{C,P}$ = 7.6 Hz, $OCH(CH_3)_2$), 72.47 (d, $^2J_{C,P}$ = 7.6 Hz, $OCH(CH_3)_2$), 113.78, 118.20, 127.69, 127.96, 128.04, 128.39, 129.12, 136.24, 146.43, 146.66 (C_6H_5) ppm; IR: 3308 (NH) cm^{-1}; MS (70 eV), *m/e*: 347 (M^+), 210 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{19}H_{26}NO_3P$: C, 65.69; H, 7.54. Found: C, 65.65; H, 7.51%.

3.3.4. Diethyl (4-methoxyphenyl)-N-(phenyl) aminomethylphosphonate (**5**)

^{1}H NMR ($CDCl_3$, TMS): δ 1.02–1.08, (m, 3H, OCH_2CH_3), 1.18–1.22 (m, 3H, OCH_2CH_3), 3.70 (s, 3H, OCH_3), 3.63–3.69, 3.84–3.89, 4.01–4.06 (m, 4H, OCH_2CH_3), 4.58–4.67 (m, 2H, CH, NH), 6.50–6.63 (m, 3H, C_6H_4, C_6H_5), 6.77–6.81 (m, 2H, C_6H_4, C_6H_5), 7.00–7.03 (m, 2H, C_6H_4, C_6H_5), 7.29–7.31 (m, 2H, C_6H_4, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.7 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 16.8 (d, $^3J_{C,P}$=5.8 Hz, OCH_2CH_3), 55.7 (d, $^1J_{C,P}$ = 152.1 Hz, CH), 55.61 (OCH_3), 63.5 (OCH_2CH_3), 114.3–114.4, 118.7, 129.3–129.5 (C_6H_5, C_6H_4) ppm; IR: 3303 (NH) cm^{-1}; MS (70 eV), *m/e*: 349 (M^+), 212 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{18}H_{24}NO_4P$: C, 61.88; H, 6.92. Found: C, 61.85; H, 6.90%.

3.3.5. Diethyl (4-cholorophenyl)-N-(phenyl) aminomethylphosphonate (**6**)

^{1}H NMR ($CDCl_3$, TMS): δ 1.09 (t, 3H, $^2J_{H,H}$ = 7.1 Hz, OCH_2CH_3), 1.21 (t, 3H, $^2J_{H,H}$ = 7.1 Hz, OCH_2CH_3), 3.69–4.09 (m, 4H, OCH_2CH_3), 4.60–4.70 (m, 2H, CH, NH), 6.48 (d, 2H, $^2J_{H,H}$ = 7.8 Hz, C_6H_4, C_6H_5), 6.63 (t, 1H, $^2J_{H,H}$ = 7.3 Hz, C_6H_4, C_6H_5), 7.03 (t, 2H, $^2J_{H,H}$ = 7.8 Hz, C_6H_4, C_6H_5), 7.23 (d, 2H, $^2J_{H,H}$ = 8.4 Hz, C_6H_4, C_6H_5), 7.32–7.36 (m, 2H, C_6H_4, C_6H_5), ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 55.9 (d, $^1J_{C,P}$ = 150.5 Hz, CH), 63.7–63.9 (OCH_2CH_3), 114.2, 119.1, 129.2–129.6, 134.1, 135.0, 146.3–146.5 (C_6H_5, C_6H_4) ppm; IR: 3299 (NH) cm^{-1}; MS (70 eV), *m/e*: 353 (M^+), 355 (M+2), 216 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{17}H_{21}ClNO_3P$: C, 57.71; H, 5.98. Found: C, 57.69; H, 5.95%.

3.3.6. Diethyl (2,6-dichlorophenyl)-N-(phenyl)aminomethylphosphonate (**7**)

^{1}H NMR ($CDCl_3$, TMS): δ 1.02–1.07 (m, 3H, OCH_2CH_3), 1.24–1.29 (m, 3H, OCH_2CH_3), 3.81–3.84 (m, 1H, OCH_2CH_3), 3.94–4.01 (m, 1H, OCH_2CH_3), 4.10–4.19 (m, 2H, OCH_2CH_3), 5.40 (t, 1H, NH), 5.77 (dd, 1H, $^3J_{H,H}$ = 9.95 Hz, $^2J_{P,H}$ = 28.6 Hz), 6.56–6.66 (m, 3H, C_6H_5, C_6H_3), 7.01–7.27 (m, 5H, C_6H_5, C_6H_3) ppm; δ ^{13}C NMR ($CDCl_3$, TMS): 16.11 (d, $^3J_{P,C}$ = 5.8 Hz, OCH_2CH_3), 16.46 (d, $^3J_{P,C}$ = 5.8 Hz, OCH_2CH_3), 53.14 (d, $^1J_{P,C}$ = 157.9 Hz, CH), 63.07 (d, $^2J_{P,C}$ = 6.8 Hz, OCH_2CH_3), 63.39 (d, $^2J_{P,C}$ = 6.8 Hz, OCH_2CH_3), 113.28, 113.51, 118.71, 128.34, 129.26, 129.30, 130.47, 130.52, 145.61, 145.86 (C_6H_5, C_6H_3) ppm; IR: 3322 (NH) cm^{-1}; MS (70 eV): *m/e* = 391 [M^++4], 389 [M^++2], 387 [M^+], 250 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{17}H_{20}Cl_2NO_3P$: C, 52.59; H, 5.19. Found: C, 52.56; H, 5.15%.

3.3.7. Diethyl (phenyl)-N-(4-methylphenyl)aminomethylphosphonate (**8**)

^{1}H NMR ($CDCl_3$, TMS): δ 1.15 (t, 3H, $^2J_{H,H}$ = 7.0 Hz, OCH_2CH_3), 1.31 (t, 3H, $^2J_{H,H}$ = 7.0 Hz, OCH_2CH_3), 2.21 (s, 3H, CH_3), 3.70–3.76 (m, 1H, OCH_2CH_3), 3.92–4.02 (m, 1H, OCH_2CH_3), 4.11–4.20 (m, 2H, OCH_2CH_3), 4.72–4.82 (m, 2H, CH, NH), 6.55 (d, 2H, $^2J_{H,H}$ = 8.2 Hz, C_6H_4, C_6H_5), 6.94 (d, 2H, $^2J_{H,H}$ = 8.1 Hz, C_6H_4, C_6H_5), 7.29–7.38 (m, 3H, C_6H_4, C_6H_5), 7.48–7.51 (m, 2H, C_6H_4, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 16.8 (d, $^3J_{C,P}$=5.8 Hz, OCH_2CH_3), 20.76 (CH_3), 56.7 (d, $^1J_{C,P}$ = 150.4 Hz, CH), 63.6–63.7 (OCH_2CH_3), 114.4, 128.0–130.1, 136.4, 144.2–144.5 (C_6H_5, C_6H_4) ppm; IR: 3303 (NH) cm^{-1}; MS (70 eV), m/e: 333 (M^+), 196 [M−*diethyl(phenyl)-N-(phenyl)aminomethylphosphonate* P(O)$(OEt)_2$]. Anal. Calc. for $C_{18}H_{24}NO_3P$: C, 64.85; H, 7.26. Found: C, 64.82; H, 7.24%.

3.3.8. Diethyl (phenyl)-N-(4-chlorophenyl)aminomethylphosphonate (**9**)

^{1}H NMR ($CDCl_3$, TMS): δ 0.99–1.03 (m, 3H, OCH_2CH_3), 1.18–1.24 (m, 3H, OCH_2CH_3), 3.45–3.70 (m, 1H, OCH_2CH_3), 3.80–4.00 (m, 1H, OCH_2CH_3), 4.02–4.04 (m, 3H, OCH_2CH_3, NH), 4.62 (d, 1H, $^2J_{P,H}$ = 24.1 Hz, CH), 6.41–6.45 (m, 2H, C_6H_5, C_6H_4), 6.93–6.98 (m, 2H, C_6H_5, C_6H_4), 7.21–7.26 (m, 3H, C_6H_5, C_6H_4), 7.34–7.38 (m, 2H, C_6H_5, C_6H_4) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 15.15 (d, $^3J_{P,C}$ = 5.8 Hz, OCH_2CH_3), 15.40 (d, $^3J_{P,C}$ = 5.8 Hz, OCH_2CH_3), 55.14 (d, $^1J_{P,C}$ = 150.9 Hz, CH), 62.19–62.44 (m, OCH_2CH_3), 113.97, 122.02, 126.73–127.08, 127.63–127.98, 134.39, 143.76, 143.99 (C_6H_5, C_6H_4) ppm; IR: 3287 (NH) cm^{-1}; MS (70 eV): *m/e* = 355 [M^++2], 353 [M^+], 216 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{17}H_{21}ClNO_3P$: C, 57.71; H, 5.98. Found: C, 57.69; H, 5.95%.

3.3.9. Diethyl (2-thienyl)-N-(phenyl)aminomethylphosphonate (**10**)

^{1}H NMR ($CDCl_3$, TMS): δ 0.78–0.85 (m, 3H, OCH_2CH_3), 1.10–1.24 (m, 3H, OCH_2CH_3), 3.82–4.11 (m, 4H, OCH_2CH_3), 4.5 (bs, 1H, NH), 4.97 (d, 1H, $^2J_{P,H}$ = 23.65 Hz, OCH_2CH_3), 6.68–6.70 (m, 3H, C_6H_5, C_4H_3S), 6.89–6.91 (m, 1H, C_6H_5, C_4H_3S), 7.04–7.15 (m, 4H, C_6H_5, C_4H_3S) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.26 (d, $^3J_{P,C}$ = 5.8 Hz, OCH_2CH_3), 16.43 (d, $^3J_{P,C}$ = 5.8 Hz, OCH_2CH_3), 52.08 (d, $^1J_{P,C}$ = 158.2 Hz, CH), 63.43 (d, $^2J_{P,C}$ = 7.0 Hz, OCH_2CH_3), 63.61 (d, $^2J_{P,C}$ = 7.0 Hz, OCH_2CH_3), 113.97, 118.93, 123.99, 125.25, 126.14, 127.07, 129.22, 139.86, 146.11 (C_6H_5, C_4H_3S) ppm; IR: 3291 (NH) cm^{-1}; MS (70 eV): *m/e* = 325 [M^+], 188 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{15}H_{20}NO_3PS$: C, 55.37; H, 6.20. Found: C, 55.35; H, 6.17%.

3.3.10. Diethyl (2-furyl)-N-(phenyl)aminomethylphosphonate (**11**)

^{1}H NMR ($CDCl_3$, TMS): δ 1.18–1.36 (m, 6H, OCH_2CH_3), 3.85–4.21 (m, 4H, OCH_2CH_3), 4.52 (bs, 1H, NH), 4.67 (dd, 1H, $^2J_{H,H}$ = 7.0 Hz, $^2J_{P,H}$ = 22.5 Hz, CH), 6.32–6.38 (m, 2H, C_4H_3O, C_6H_5), 6.65–6.77 (m, 3H, C_4H_3O, C_6H_5), 7.12–7.38 (m, 2H, C_4H_3O, C_6H_5), 8.20 (s, 1H, C_4H_3O, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.30 (d, $^3J_{C,P}$ = 5.7 Hz, OCH_2CH_3), 16.4 (d, $^3J_{C,P}$ = 5.7 Hz, OCH_2CH_3), 50.3 (d, $^1J_{C,P}$ = 159.5 Hz, CH), 63.3 (d, $^2J_{C,P}$=7.0 Hz, OCH_2CH_3), 63.5 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_2CH_3), 108.8, 110.8, 114.0, 118.9, 129.2, 142.5, 149.4 (C_4H_3O, C_6H_5) ppm; IR: 3298 (NH) cm^{-1}; MS (70 eV), *m/e*: 309 (M^+), 172 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{15}H_{20}NO_4P$: C, 58.25; H, 6.52. Found: C, 58.23; H, 6.50%.

3.3.11. Diethyl 3-phenyl-1-(phenylamino)allylphosphonate (**12**)

^{1}H NMR ($CDCl_3$, TMS): δ 1.26–1.33 (m, 6H, OCH_2CH_3), 4.10–4.23 (m, 5H, OCH_2CH_3, NH), 4.47 (dd, 1H, $^2J_{H,H}$ = 6.0 Hz, $^2J_{P,H}$ = 27.5 Hz, CH), 6.24–6.30 (m, 1H, CH=CH), 6.68–6.77 (m, 4H, C_6H_5, CH=CH), 7.14–7.37 (m, 7H, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 22.9–23.1 (OCH_2CH_3), 60.5 (d, $^1J_{C,P}$=153.3 Hz, CH), 69.5 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_2CH_3), 70.0 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_2CH_3), 120.3, 124.9–139.6 (C_6H_5) ppm; IR: 3297 (NH) cm^{-1}; MS (70 eV), *m/e*: 345 (M^+), 208 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{19}H_{24}NO_3$ P: C, 66.07; H, 7.00. Found: C, 66.00; H, 6.68%.

3.3.12. Diethyl (n-propyl)-N-(phenyl)aminomethylphosphonate (**13**)

^{1}H NMR ($CDCl_3$, TMS): δ 0.84 (t, 3H, $^2J_{H,H}$ = 7.2 Hz, CH_3), 1.09–1.24 (m, 6H, OCH_2CH_3), 1.50–1.82 (m, 4H, $(CH_2)_2CH_3$), 3.60–3.65 (m, 2H, NH, CH), 3.94–4.09 (m, 4H, OCH_2CH_3), 6.58 (d, 2H, $^2J_{H,H}$ = 8.2 Hz, C_6H_5), 6.65 (d, 1H, $^2J_{H,H}$ = 7.4 Hz, C_6H_5), 7.09 (t, 2H, $^2J_{H,H}$ = 7.6 Hz, C_6H_5) ppm; MS (70 eV), *m/e*: 285 (M^+), 148 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{14}H_{24}NO_3P$: C, 58.93; H, 8.48. Found: C, 58.90; H, 8.45%.

*3.3.13. Diethyl (2-naphthyl)-N-(phenyl)aminomethylphosphonate (**14**)*

^{1}H NMR ($CDCl_3$, TMS): δ 1.13 (t, 3H, $^2J_{H,H}$ = 6.8 Hz, OCH_2CH_3), 1.33 (t, 3H, $^3J_{H,H}$ = 6.8 Hz, OCH_2CH_3), 3.63–3.75 (m, 1H, OCH_2CH_3), 3.90–4.06 (m, 1H, OCH_2CH_3), 4.14–4.21 (m, 2H, OCH_2CH_3), 4.92–5.04 (m, 1H, CH), 6.66–6.75 (m, 3H, $C_{10}H_7$, C_6H_5), 7.10–7.16 (m, 2H, $C_{10}H_7$, C_6H_5), 7.48–7.67 (m, 3H, $C_{10}H_7$, C_6H_5), 7.85 (s, 3H, $C_{10}H_7$, C_6H_5), 7.98 (s, 1H, $C_{10}H_7$, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.63 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 16.87 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 56.7 (d, $^1J_{C,P}$ = 150.1 Hz, CH), 63.73 (d, $^3J_{C,P}$ = 7.0 Hz, OCH_2CH_3), 114.30, 118.86, 126.0–129.60, 133.51–133.95, 146.63–146.87 ($C_{10}H_7$, C_6H_5) ppm; IR: 3301 (NH) cm^{-1}; MS (70 ev), *m/e*: 369 (M^+), 232 [M−P(O)$(OEt)_2$]. Anal. Calc. for **$C_{21}H_{24}NO_3P$**: C, 68.29; H, 6.50. Found: C, 68.24; H, 6.45%.

*3.3.14. Diethyl (phenyl)-N-(benzyl)aminomethylphosphonate (**15**)*

^{1}H NMR ($CDCl_3$, TMS): δ 1.05 (t, $^2J_{H,H}$=7.0 Hz, 3H, OCH_2CH_3), 1.17–1.32 (m, 3H, OCH_2CH_3), 2.95 (brs, 1H, NH), 3.44–4.07 (m, 7H, OCH_2CH_3, $CH_2C_6H_5$, CH), 7.19–7.34 (m, 10H, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.63 (d, $^3J_{C,P}$ = 5.8 Hz, OCH_2CH_3), 16.82 (d, $^3J_{C,P}$ = 6.1 Hz, OCH_2CH_3), 51.59 (d, $^3J_{C,P}$ = 17.5 Hz, CH_2), 59.98 (d, $^1J_{C,P}$ = 153.4 Hz, CH), 63.17 (d, $^2J_{C,P}$ = 6.8 Hz, CH_2CH_3), 63.34 (d, $^2J_{C,P}$ = 7.2 Hz, OCH_2CH_3), 127.50–129.12, 136.09, 139.72 (C_6H_5). IR: 3309 (NH) cm^{-1}. MS (70 eV), *m/e:* 333 (M^+), 196 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{18}H_{24}NO_3P$: C, 64.86; H, 7.21. Found: C, 64.85; H, 7.15%.

*3.3.15. Diethyl {4-[N-(phenyl)amino-(diethoxyphosphoryl)methyl]phenyl}-N-(phenyl)aminomethylphosphonate (**16**)*

^{1}H NMR ($CDCl_3$, TMS): δ 0.84–0.92 (m, 3H, OCH_2CH_3), 0.93–0.98 (m, 3H, OCH_2CH_3), 1.11–1.20 (m, 6H, OCH_2CH_3), 3.30–3.55 (m, 2H, OCH_2CH_3), 3.65–3.80 (m, 2H, OCH_2CH_3), 3.96–4.03 (m, 4H, OCH_2CH_3), 4.65–4.73 (m, 4H, CH, NH), 6.45–6.49 (m, 4H, C_6H_5), 6.57–6.61 (m, 2H, C_6H_5), 6.93–6.99 (m, 4H, C_6H_5), 7.36 (s, 4H, C_6H_4) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 15.97–16.38 (OCH_2CH_3), 55.81 (d, $^1J_{P,C}$ = 150.8 Hz, CH), 63.13–63.35 (OCH_2CH_3), 113.89, 118.33, 128.19–129.49, 135.56, 146.07–146.30 (C_6H_5, C_6H_4) ppm; IR: 3285 (NH) cm^{-1}; MS (70 eV): *m/e* = 560 [M^+], 423 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{28}H_{38}N_2O_6P_2$: C, 59.99; H, 6.83. Found: C, 59.90; H, 6.80%.

*3.3.16. Diethyl phenyl-N-{4-[N-(phenyl)amino-(diethoxyphosphoryl)methyl]phenyl}aminomethylphosphonate (**17**)*

^{1}H NMR ($CDCl_3$, TMS): δ 0.98–1.03 (m, 6H, OCH_2CH_3), 1.14–1.22 (m, 6H, OCH_2CH_3), 3.45–3.59 (m, 2H, OCH_2CH_3), 3.78–3.85 (m, 2H, OCH_2CH_3), 3.95–4.04 (m, 6H, OCH_2CH_3, NH), 4.53 (d, 2H, $^2J_{P,H}$ = 23.9 Hz, CH), 6.33 (s, 4H, C_6H_4), 7.14–7.35 (m, 10H, C_6H_5) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.15 (d, $^3J_{C,P}$ = 5.9 Hz, OCH_2CH_3), 16.38 (d, $^3J_{C,P}$ = 5.9 Hz, OCH_2CH_3), 56.96 (d, $^1J_{C,P}$ = 150.5 Hz, CH), 63.19 (d, $^2J_{P,C}$ = 6.7 Hz, OCH_2CH_3), 63.20 (d, $^2J_{P,C}$ = 6.7 Hz, OCH_2CH_3), 115.39, 127.07–128.49, 135.23, 138.86–139.23 (C_6H_5, C_6H_4) ppm; IR: 3291 (NH) cm^{-1}; MS (70 eV): *m/e* = 560 [M^+], 423 [M−P(O)$(OEt)_2$]. Anal. Calc. for $C_{28}H_{38}N_2O_6P_2$: C, 59.99; H, 6.83. Found: C, 59.93; H, 6.81%.

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