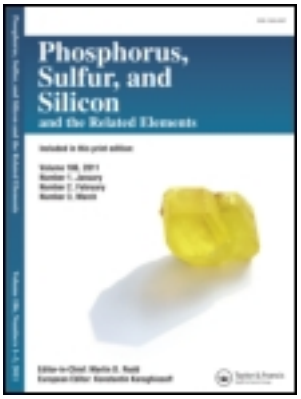

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A Simple and Effective Approach to the Via One-Pot Reactions in Water

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A SIMPLE AND EFFECTIVE APPROACH TO THE VIA ONE-POT REACTIONS IN WATER

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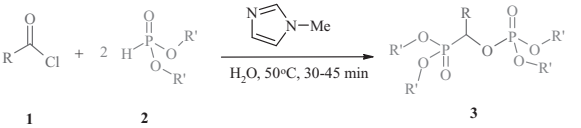
GRAPHICAL ABSTRACT



1 **2** **3**

1, 3	R	R'	Yield % of 3
a	4-Me-C_6H_4	Ph	87
b	4-Cl-C_6H_4	Ph	85
c	4-Br-C_6H_4	Ph	90
d	4-NO_2-C_6H_4	Ph	83
e	Ph	Ph	92
f	Et	Ph	89
g	4-OMe-C_6H_4	Ph	86
h	4-Me-C_6H_4	Et	90
i	Et	Me	78
j	Et	Et	
k	*t*Bu	Me	75
l	*t*Bu	Et	74

Abstract *Water-accelerated synthesis of organic target molecules has been used as a key method for the preparation of phosphoryloxy phosphonate derivatives. Condensation reactions of acid chlorides with dialkyl (aryl) phosphites in the presence of N-methyl imidazole in water have been developed as efficient and clean green synthetic procedures for the preparation of phosphoryloxy phosphonates in high yields. This synthetic protocol provides rapid access to novel and diversely substituted phosphoryloxy phosphonate derivatives.*

Keywords Acid chloride; dialkyl (aryl) phosphate; *N*-methyl imidazole; one-pot reactions; phosphoryloxy phosphonates

INTRODUCTION

Phosphorus compounds containing the P–C bond are not particularly frequent in nature; however, they have diverse biological activities and have attracted considerable

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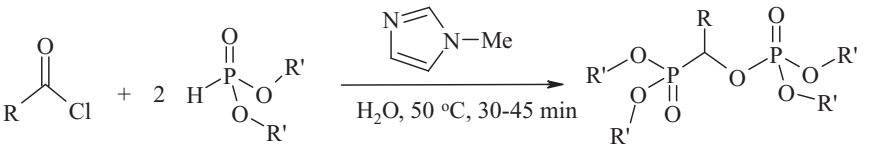
synthetic and pharmacological interest.[1,2] Besides valuable applications, their use in the production of the dangerous compounds sarin-, soman-, and VX-type chemical warfare agents (CWAs) must be noted.[3] Phosphonates have important applications in flame retardance,[4,5] organic synthesis,[6] and in biology.[7,8] Phosphonates also have been used as substitutes of the corresponding esters and acids of high biological activity[9,10] and as convenient probes for designing antibodies on the basis of transition state models. Addition of the phosphate–phosphonate compound as a flame retardant for polyurethanes or polyesters results in suitable flexibility and flame retardance.[11–13] Hence, a large number of methods have appeared describing novel syntheses of phosphonate systems.[14–17] In addition, performing organic reactions in water has become highly attractive in recent years due to environmental considerations.[18]

As part of our current studies on the development of new routes in the synthesis of organic compounds, we report an efficient synthetic route to phosphoryloxy phosphonate derivatives. Thus, the reaction of acid chlorides **1** with dialkyl (aryl) phosphites **2** in the presence of *N*-methyl imidazole in water leads to phosphoryloxy phosphonate derivatives **3** in good yield (Scheme 1).



1 **2** **3**

1, 3	R	R'	Yield % of **3**
a	4-Me-C_6H_4	Ph	87
b	4-Cl-C_6H_4	Ph	85
c	4-Br-C_6H_4	Ph	90
d	4-NO_2-C_6H_4	Ph	83
e	Ph	Ph	92
f	Et	Ph	89
g	4-OMe-C_6H_4	Ph	86
h	4-Me-C_6H_4	Et	90
i	Et	Me	78
j	Et	Et	75
k	^{t}Bu	Me	75
l	^{t}Bu	Et	74

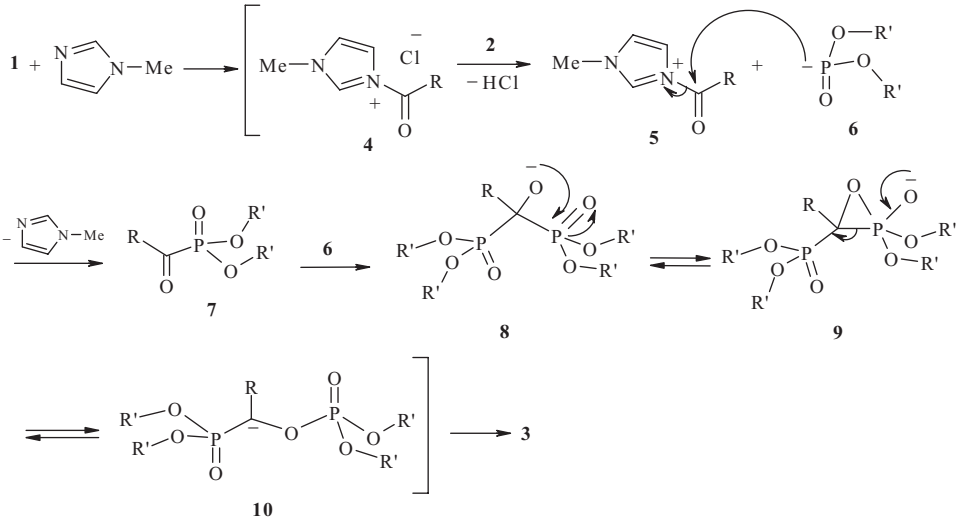
Scheme 1 Synthesis of phosphoryloxy phosphonate derivatives.

RESULTS AND DISCUSSION

The starting point for our experiments was to optimize the reaction conditions. Thus, after testing different reaction conditions, it was found that upon simple mixing of acid chlorides (5 mmol), dialkyl (aryl) phosphite (4 mmol), and *N*-methyl imidazole (4 mmol),

a quantitative conversion to phosphoryloxy phosphonate derivatives was observed with excellent yields in water. In addition, the reaction of acid chlorides and dialkyl (aryl) phosphite does not perform without *N*-methyl imidazole. However, the reaction of acid chlorides **1** with dialkyl (aryl) phosphites **2** in the presence of *N*-methyl imidazole in water leads to phosphoryloxy phosphonate derivatives **3** in excellent yields (Scheme 1). The product **3l** is a known compound.[17] The structures of compounds **3a–3l** were determined on the basis of their ^{1}H, ^{13}C, ^{31}P NMR, and IR spectra as well as elemental analysis data. The ^{1}H NMR spectrum of **3a** in $CDCl_3$ exhibited one singlet for the methyl protons at $\delta =$ 2.36 ppm and one doublet of doublets at $\delta = 6.11$ ($^{2}J_{PH} = 12.7$ Hz and $^{3}J_{PH} = 10.3$ Hz) for the methine proton, along with multiplets at $\delta = 6.62$–7.46 for the aromatic protons. The ^{13}C NMR spectrum of **3a** exhibited 32 signals in agreement with the proposed structure. The ^{1}H decoupled ^{31}P NMR spectrum of **3a** displayed two sharp doublets at $\delta = -10.5$ and $\delta = 7.9$ with $^{3}J_{PP} = 40.8$ Hz.

Mechanistically, it is reasonable to assume that the reaction involves the initial formation of a 1:1 zwitterionic intermediate **4** between acid chloride and *N*-methyl imidazole, which undergoes reaction with **2** to produce the cation **5** and the anion ion **6** after elimination of HCl. Intermediate **5** would be attacked by the negatively charged **6** and would lose *N*-methyl imidazole to produce **7**. This would be attacked by the negatively charged species **6** again, and finally compound **3** would be formed in good yield[17,19] (Scheme 2).



Scheme 2 Proposed mechanism for synthesis of phosphoryloxy phosphonates.

Because of the release of HCl during the reaction, a small quantity of *N*-methyl imidazole is protonated as the reaction proceeds. Also, decomposition of an insignificant quantity of the acid chloride occurs on the reaction timescale. For these reasons, an excess of *N*-methyl imidazole and of the acid chloride is used in these reactions.

Clearly, the results show that the reaction between acid chlorides and dialkyl (aryl) phosphites in the presence of *N*-methyl imidazole provides a simple one-pot entry into the synthesis of phosphoryloxy phosphonate derivatives of potential synthetic and pharmacological interest. The present method carries the advantage of being performed under

one-pot conditions, and requires no activation or modification of the educts. In addition, phosphoryloxy phosphonate derivatives using commercially available starting materials are synthesized.

EXPERIMENTAL

N-Methyl imidazole, acid chlorides, and dialkyl (aryl) phosphite were obtained from Fluka and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus *CHN–O*-Rapid analyzer. Mass spectra were recorded on a Finnigan-Matt 8430 spectrometer operating at an ionization potential of 70 eV. IR spectra were measured on a Shimadzu IR-460 spectrophotometer. ^{1}H, ^{13}C, and ^{31}P NMR spectra were measured with a Bruker DRX-500 Avance spectrometer at 500.1, 125.8, and 202.4 MHz, respectively. ^{1}H, ^{13}C, and ^{31}P spectra were obtained for solutions in $CDCl_3$ using TMS as internal standard and 85% H_3PO_4 as external standard, respectively.

Preparation of Compounds 3: General Procedure

N-Methyl imidazole (4 mmol) was added slowly to a mixture of the acid chloride **1** (5 mmol) and the repective dialkyl (aryl) phosphites **2** (4 mmol). Then, water (5 mL) was added to the reaction mixture, and the mixture was heated for 12 h at 50°C. After completion of the reaction (30–45 min) as indicated by TLC (*n*-hexane:EtOAc, 8:1), the resulting solid was removed by filtration, washed with water (5 mL) and diethylether (1 mL), and dried to afford the pure title compound. The dried product thus obtained showed a single spot on TLC and was pure enough for all analytical purposes.

Diphenyl[(diphenoxyphosphoryl)oxy](4-methylphenyl)methyl]phosphonate (3a)

White powder, mp 150–152°C; yield: 1.01 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 1510, 1324, 1295, 1248, and 1100. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 2.36$ (s, 3H, Me), 6.11 (dd, $^{2}J_{PH} = 12.7$ Hz, $^{3}J_{PH} = 10.3$ Hz, 1H, CH), 6.62–7.28 (m, 22H, CH), 7.46 (d, $^{3}J = 7.8$ Hz, 2H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 21.3$ (Me), 76.0 (dd, $^{1}J_{PC} = 175.2$ Hz, $^{2}J_{PC} = 7.2$ Hz, CH), 120.0 (d, $^{3}J_{PC} = 4.8$ Hz, CH), 120.1 (d, $^{3}J_{PC} = 4.7$ Hz, CH), 120.4 (d, $^{3}J_{PC} = 4.4$ Hz, CH), 120.5 (d, $^{3}J_{PC} = 4.1$ Hz, CH), 125.2 (CH), 125.3 (CH), 125.4 (CH), 128.5 (CH), 128.6 (CH), 129.3 (CH), 129.4 (CH), 129.6 (d, $^{3}J_{PC} = 4.2$ Hz, CH), 129.7 (CH), 139.6 (dd, $^{2}J_{PC} = 8.5$ Hz, $^{3}J_{PC} = 3.4$ Hz), 139.7, 150.1 (d, $^{2}J_{PC} = 9.0$ Hz), 150.2 (d, $^{2}J_{PC} = 9.2$ Hz), 150.3 (d, $^{2}J_{PC} = 7.8$ Hz), 150.5 (d, $^{2}J_{PC} = 7.6$ Hz). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -10.5$ (d, $^{3}J_{PP} = 40.8$ Hz), 7.9 (d, $^{3}J_{PP} = 40.8$ Hz). MS: *m*/*z* (%) = 586 (M^+, 15), 495 (48), 353 (64), 246 (58), 233 (100), 91 (68), 77 (47). Anal. Calcd. for $C_{32}H_{28}O_7P_2$ (586.41): C, 65.53; H, 4.81. Found: C, 65.38; H, 4.75%.

Diphenyl[(diphenoxyphosphoryl)oxy](4-chlorophenyl)methyl]phosphonate (3b)

Pale yellow powder, mp 158–160°C; yield: 1.03 g (85%). IR (KBr) (ν_{max}/cm^{-1}): 1587, 1462, 1387, 1290 and 1157. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 6.09$ (dd, $^{2}J_{PH} = 13.2$ Hz, $^{3}J_{PH} = 10.5$ Hz, 1H, CH), 6.92–7.28 (m, 22 CH), 7.47 (d, $^{3}J = 6.7$ Hz, 2H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 74.9$ (dd, $^{1}J_{PC} = 178.3$ Hz, $^{2}J_{PC} = 6.8$ Hz, CH), 119.8

(d, $^3J_{PC} = 4.8$ Hz, CH), 120.1 (d, $^3J_{PC} = 4.5$ Hz, CH), 120.3 (d, $^3J_{PC} = 4.6$ Hz, CH), 120.4 (d, $^3J_{PC} = 4.3$ Hz, CH), 125.3 (CH), 125.4 (CH), 125.5 (CH), 128.9 (CH), 129.6 (CH), 129.7 (CH), 129.8 (CH), 129.9 (d, $^3J_{PC} = 4.5$ Hz, CH), 130.4 (CH), 135.7 (dd, $^2J_{PC} = 8.6$ Hz, $^3J_{PC} = 4.2$ Hz), 139.7, 150.0 (d, $^2J_{PC} = 10.2$ Hz), 150.1 (d, $^2J_{PC} = 10.2$ Hz, C), 150.3 (d, $^2J_{PC} = 8.2$ Hz). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -11.8$ (d, $^3J_{PP} = 39.9$ Hz), 7.7 (d, $^3J_{PP} = 39.8$ Hz). MS: *m/z* (%) = 606 (M^+, 20), 497 (68), 373 (74), 233 (100), 109 (52), 91 (45), 77 (78). Anal. Calcd. for $C_{31}H_{25}ClO_7P_2$ (606.93): C, 61.35; H, 4.15. Found: C, 61.28; H, 4.12%.

Diphenyl[[diphenoxyphosphoryl)oxy](4-bromophenyl)methyl]phosphonate (3c)

White powder, mp 165–167°C; yield: 1.17 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 1554, 1410, 1384, 1298. 1147 and 1025. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 6.84$ (dd, $^2J_{PH} = 14.5$ Hz, $^3J_{PH} = 10.9$ Hz, 1H, CH), 6.99–7.41 (m, 22H, CH), 7.52 (d, $^3J = 7.4$ Hz, 2H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 78.4$ (dd, $^1J_{PC} = 182.5$ Hz, $^2J_{PC} = 8.4$ Hz, CH), 118.4 (d, $^3J_{PC} = 5.2$ Hz, CH), 119.7 (d, $^3J_{PC} = 5.7$ Hz, CH), 120.1 (d, $^3J_{PC} = 4.9$ Hz, CH), 121.7 (d, $^3J_{PC} = 4.8$ Hz, CH), 125.1 (CH), 125.3 (CH), 125.4 (CH), 129.2 (CH), 129.4 (CH), 129.5 (CH), 129.7 (CH), 129.9 (d, $^3J_{PC} = 6.2$ Hz, CH), 130.1 (CH), 132.8 (dd, $^2J_{PC} = 9.4$ Hz, $^3J_{PC} = 5.8$ Hz, C), 138.6 (C), 149.8 (d, $^2J_{PC} = 9.8$ Hz, C), 150.0 (d, $^2J_{PC} = 9.8$ Hz, C), 151.4 (d, $^2J_{PC} = 8.7$ Hz, C). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -9.8$ (d, $^3J_{PP} = 38.8$ Hz), 8.5 (d, $^3J_{PP} = 38.5$ Hz). Anal. Calcd. for $C_{31}H_{25}BrO_7P_2$ (651.39): C, 57.16; H, 3.87. Found: C, 57.14; H, 3.86%.

Diphenyl[[diphenoxyphosphoryl)oxy](4-nitrophenyl)methyl]phosphonate (3d)

Yellow powder, mp 174–176°C; yield: 1.02 g (83%). IR (KBr) (ν_{max}/cm^{-1}): 1524, 1478, 1356, 1289, 1145 and 1087. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 6.25$ (dd, $^2J_{PH} = 14.3$ Hz, $^3J_{PH} = 10.7$ Hz, 1H, CH), 6.98–7.32 (m, 20H, CH), 7.66 (d, $^3J = 8.5$ Hz, 2H, CH), 8.12 (d, $^3J = 8.5$ Hz, 2H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 74.8$ (dd, $^1J_{PC} = 181.3$ Hz, $^2J_{PC} = 6.7$ Hz, CH), 119.8 (d, $^3J_{PC} = 5.1$ Hz, CH), 120.1 (d, $^3J_{PC} = 4.8$ Hz, CH), 120.3 (d, $^3J_{PC} = 4.1$ Hz, CH), 123.6 (d, $^3J_{PC} = 4.2$ Hz, CH), 125.7 (CH), 125.8 (CH), 126.4 (CH), 129.0 (CH), 129.1 (CH), 129.8 (CH), 129.9 (CH), 130.0 (d, $^3J_{PC} = 7.4$ Hz, CH), 131.0 (CH), 132.5 (dd, $^2J_{PC} = 10.2$ Hz, $^3J_{PC} = 6.4$ Hz, C), 148.4 (d, $^2J_{PC} = 8.7$ Hz, C), 149.8 (C), 149.9 (d, $^2J_{PC} = 9.6$ Hz, C), 150.0 (d, $^2J_{PC} = 8.5$ Hz, C), 150.3 (d, $^2J_{PC} = 8.6$ Hz, C). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -10.3$ (d, $^3J_{PP} = 40.2$ Hz), 12.4 (d, $^3J_{PP} = 40.2$ Hz). Anal. Calcd. for $C_{31}H_{25}NO_9P_2$ (617.48): C, 60.30; H, 4.08; N, 2.27. Found: C, 60.27; H, 3.94; N, 2.18%.

Diphenyl[[diphenoxyphosphoryl)oxy](phenyl)methyl]phosphonate (3e)

Yellow powder, mp 142–144°C; yield: 1.05 g (92%). IR (KBr) (ν_{max}/cm^{-1}): 1541, 1487, 1456, 1358, 1290 and 1148. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 6.16$ (dd, $^2J_{PH} = 13.0$ Hz, $^3J_{PH} = 10.4$ Hz, 1H, CH), 6.73–7.38 (m, 25H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 76.1$ (dd, $^1J_{PC} = 176.5$ Hz, $^2J_{PC} = 6.7$ Hz, CH), 120.1 (d, $^3J_{PC} = 6.2$ Hz,

CH), 120.2 (d, $^3J_{PC} = 5.8$ Hz, CH), 120.4 (d, $^3J_{PC} = 4.7$ Hz, CH), 121.5 (d, $^3J_{PC} = 4.7$ Hz, CH), 125.4 (CH), 125.6 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 129.6 (d, $^3J_{PC} = 6.8$ Hz, CH), 129.7 (CH), 129.9 (CH), 131.7 (dd, $^2J_{PC} = 10.8$ Hz, $^3J_{CP} = 5.7$ Hz, C), 150.0 (d, $^2J_{PC} = 9.4$ Hz, C), 150.1 (d, $^2J_{PC} = 9.2$ Hz, C), 150.3 (d, $^2J_{PC} = 8.7$ Hz, C), 150.5 (d, $^2J_{PC} = 9.5$ Hz, C). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -11.7$ (d, $^3J_{PP} = 40.1$ Hz), 8.4 (d, $^3J_{PP} = 40.1$ Hz). Anal. Calcd. for $C_{31}H_{26}O_7P_2$ (572.49): C, 65.49; H, 4.58. Found: C, 65.38; H, 4.48%.

Diphenyl[[diphenoxyphosphoryl)oxy]propyl]methyl]phosphonate (3f)

Yellow powder,mp 154–156°C; yield: 0.93 g (89%). IR (KBr) (ν_{max}/cm^{-1}): 1654, 1547, 1325, 1245, 1189 and 1048. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.16$ (t, $^3J = 7.2$ Hz, 3H, CH_3), 2.18 (m, 2H, CH_2), 5.22 (m, 1H, CH), 6.79–7.37 (m, 20H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 9.9$ (d, $^2J_{PC} = 10.7$ Hz, CH_3), 24.6 (dd, $^2J_{PC} = 14.2$ Hz, $^3J_{PC} = 8.4$ Hz, CH_2), 75.6 (dd, $^1J_{PC} = 171.6$ Hz, $^2J_{PC} = 7.4$ Hz, CH_2), 120.1 (d, $^3J_{PC} = 6.5$ Hz, CH), 120.2 (d, $^3J_{PC} = 6.8$ Hz, CH), 120.5 (d, $^3J_{PC} = 5.7$ Hz, CH), 120.7 (d, $^3J_{PC} = 5.8$ Hz, CH), 125.5 (CH), 125.7 (CH), 129.4 (CH), 129.7 (CH), 129.8 (CH), 128.9 (CH), 149.9 (d, $^2J_{PC} = 10.4$ Hz, C), 150.1 (d, $^2J_{PC} = 10.3$ Hz, C), 150.4 (d, $^2J_{PC} = 9.8$ Hz, C), 150.5 (d, $^2J_{PC} = 9.5$ Hz, C). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -10.2$ (d, $^3J_{PP} = 39.0$ Hz), 9.5 (d, $^3J_{PP} = 39.1$ Hz). Anal. Calcd. for $C_{27}H_{26}O_7P_2$ (524.44): C, 61.84; H, 5.00. Found: C, 61.74; H, 4.87%.

Diphenyl[[diphenoxyphosphoryl)oxy](4-methoxyphenyl)methyl] phosphonate (3g)

White powder, mp 158–160°C; yield: 1.03 g (86%). IR (KBr) (ν_{max}/cm^{-1}): 1525, 1455, 1324, 1247 and 1187. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 3.54$ (s, 3H, OCH_3), 6.24 (dd, $^2J_{PH} = 12.5$ Hz, $^3J_{PH} = 10.4$ Hz, 1H, CH), 6.54–7.36 (m, 20H, CH), 7.52 (d, $^3J = 7.5$ Hz, 2H, CH), 7.64 (d, $^3J = 7.3$ Hz, 2H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 52.4$ (OCH_3), 68.8 (dd, $^1J_{PC} = 185.4$ Hz, $^2J_{PC} = 9.5$ Hz, CH), 120.1 (d, $^3J_{PC} = 4.8$ Hz, CH), 121.2 (d, $^3J_{PC} = 4.7$ Hz, CH), 121.9 (d, $^3J_{PC} = 4.4$ Hz, CH), 122.4 (d, $^3J_{PC} = 4.1$ Hz, CH), 126.3 (CH), 126.8 (CH), 127.0 (CH), 128.6 (CH), 129.1 (CH), 129.7 (CH), 130.0 (CH), 130.1 (d, $^3J_{PC} = 6.3$ Hz, CH), 130.2 (CH), 140.2 (dd, $^2J_{PC} = 8.5$ Hz, $^3J_{PC} = 3.4$ Hz, C), 152.2 (d, $^2J_{PC} = 8.9$ Hz, C), 152.6 (d, $^2J_{PC} = 8.9$ Hz, C), 152.8 (d, $^2J_{PC} = 7.9$ Hz, C), 153.0 (d, $^2J_{PC} = 8.1$ Hz, C), 158.8 (C). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -11.2$ (d, $^3J_{PP} = 38.4$ Hz), 8.54 (d, $^3J_{PP} = 38.4$ Hz). Anal. Calcd. for $C_{32}H_{28}O_8P_2$ (602.51): C, 63.79; H, 4.64. Found: C, 63.64; H, 4.58%.

Diethyl[[diethoxyphosphoryl)oxy](4-methylphenyl)methyl]phosphonate (3f)

White powder, mp 165–167°C; yield: 0.64 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 1524, 1487, 1347, 1310 and 1298. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.25$ (t, $^3J_{HH} = 7.2$ Hz, 6H, CH_3), 1.35 (t, $^3J_{HH} = 7.4$ Hz, 6H, CH_3), 2.37 (s, 3H, CH_3), 4.25 (m, 2H, CH_2), 4.28 (m, 2H, CH_2), 4.45 (m, 2H, CH_2), 4.47 (m, 2H, CH_2), 6.27 (dd, $^2J_{PH} = 14.3$ Hz, $^3J_{PH} = 11.5$ Hz, 1H, CH), 7.36 (d, $^3J_{HH} = 8.5$ Hz, 2H, CH), 8.24 (d, $^3J_{HH} = 8.4$ Hz, 2H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 13.4$ (d, $^3J_{PC} = 5.6$ Hz, CH_3), 14.6 (d, $^3J_{PC} = 6.4$ Hz, CH_3), 22.3 (CH_3), 62.1 (d, $^2J_{PC} = 8.5$ Hz, CH_2), 62.3 (d, $^2J_{PC} = 8.6$ Hz, CH_2), 62.5 (d,

$^{2}J_{PC}$ = 7.4 Hz, CH_2), 62.7 (d, $^{2}J_{PC}$ = 7.6 Hz, CH_2), 75.6 (dd, $^{1}J_{PC}$ = 187.4 Hz, $^{2}J_{PC}$ = 9.7 Hz, CH), 129.4 (d, $^{3}J_{PC}$ = 6.8 Hz, CH), 129.7 (d, $^{3}J_{PC}$ = 6.7 Hz, CH), 131.8 (CH), 132.0 (CH), 132.8 (dd, $^{2}J_{PC}$ = 9.5 Hz, $^{3}J_{PC}$ = 4.7 Hz, C), 140.1 (C). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -12.0$ (d, $^{3}J_{PP}$ = 38.4 Hz), 10.3 (d, $^{3}J_{PP}$ = 38.4 Hz). Anal. Calcd. for $C_{16}H_{28}O_7P_2$ (394.34): C, 48.73; H, 7.16. Found: C, 48.65; H, 6.98%.

Dimethyl[[dimethoxyphosphoryl)oxy]propyl]phosphonate (3i)

Yellow powder, mp 115–117°C; yield: 0.43 g (78%). IR (KBr) (ν_{max}/cm^{-1}): 1541, 1487, 1452, 1328, and 1254. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.28 (m, 3H, CH_3), 1.65 (m, 2H, CH_2), 3.72 (d, $^{3}J_{PH}$ = 5.4 Hz, 3H, CH_3), 3.78 (d, $^{3}J_{PH}$ = 5.6 Hz, 3H, CH_3), 3.80 (d, $^{3}J_{PH}$ = 6.2 Hz, 3H, CH_3), 3.82 (d, $^{3}J_{PH}$ = 6.2 Hz, 3H, CH_3), 5.24 (m, 1H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 12.5 (d, $^{3}J_{PC}$ = 4.8 Hz, CH_3), 28.3 (dd, $^{2}J_{PC}$ = 7.4 Hz, $^{3}J_{PC}$ = 4.2 Hz, CH_2), 51.4 (d, $^{2}J_{PC}$ = 6.0 Hz, OCH_3), 51.8 (d, $^{2}J_{PC}$ = 6.2 Hz, OCH_3), 52.0 (d, $^{2}J_{PC}$ = 5.8 Hz, OCH_3), 52.3 (d, $^{2}J_{PC}$ = 5.8 Hz, OCH_3), 78.4 (dd, $^{1}J_{PC}$ = 195.2 Hz, $^{2}J_{PC}$ = 9.7 Hz, CH). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -11.7$ (d, $^{3}J_{PP}$ = 34.5 Hz), 12.3 (d, $^{3}J_{PP}$ = 34.5 Hz). Anal. Calcd. for $C_7H_{18}O_7P_2$ (276.16): C, 30.44; H, 6.57. Found: C, 30.34; H, 6.40%.

Diethyl[[diethoxyphosphoryl)oxy]propyl]phosphonate (3j)

Pale yellow powder, mp 121–123°C; yield: 0.50 g (75%). IR (KBr) (ν_{max}/cm^{-1}): 1537, 1462, 1447, 1320 and 1212. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.25–1.27 (m, 3H, CH_3), 1.32 (t, $^{3}J_{HH}$ = 7.2 Hz, 3H, CH_3), 1.36 (t, $^{3}J_{HH}$ = 7.2 Hz, 3H, CH_3), 1.40 (t, $^{3}J_{HH}$ = 7.3 Hz, 3H, CH_3), 1.42 (t, $^{3}J_{HH}$ = 7.3 Hz, 3H, CH_3), 1.62–1.64 (m, 1H, CH), 1.75–1.77 (m, 1H, CH), 4.25–4.27 (m, 2H, OCH_2), 4.28–4.30 (m, 2H, OCH_2), 4.35–4.37 (m, 2H, OCH_2), 4.40–4.42 (m, 2H, OCH_2), 4.82–4.85 (m, 1H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 12.3 (d, $^{3}J_{PC}$ = 4.5 Hz, CH_3), 15.2 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 15.3 (d, $^{3}J_{PC}$ = 5.0 Hz, CH_3), 16.4 (d, $^{3}J_{PC}$ = 4.8 Hz, CH_3), 16.5 (d, $^{3}J_{PC}$ = 4.8 Hz, CH_3), 26.5 (dd, $^{2}J_{PC}$ = 8.2 Hz, $^{3}J_{PC}$ = 5.4 Hz, CH_2), 62.2 (d, $^{2}J_{PC}$ = 8.7 Hz, OCH_2), 62.3 (d, $^{2}J_{PC}$ = 8.7 Hz, OCH_2), 63.4 (d, $^{2}J_{PC}$ = 8.5 Hz, OCH_2), 63.5 (d, $^{2}J_{PC}$ = 8.5 Hz, OCH_2), 74.6 (dd, $^{1}J_{PC}$ = 187.4 Hz, $^{2}J_{PC}$ = 9.2 Hz, CH). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -11.5$ (d, $^{3}J_{PP}$ = 34.2 Hz), 11.3 (d, $^{3}J_{PP}$ = 34.2 Hz). Anal. Calcd. for $C_{11}H_{26}O_7P_2$ (332.27): C, 39.76; H, 7.89. Found: C, 39.65; H, 7.78%.

Di(*tert*-butyl)[[(dimethoxyphosphoryl)oxy]2,2-dimethylpropyl]phosphonate (3k)

White powder, mp 111–113°C; yield: 0.46 g (75%). IR (KBr) (ν_{max}/cm^{-1}): 1557, 1480, 1467, 1334 and 1228. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.14 (s, 9H, Me_3C), 3.74 (d, $^{3}J_{PH}$ = 5.5 Hz, 3H, CH_3), 3.76 (d, $^{3}J_{PH}$ = 5.5 Hz, 3H, CH_3), 3.82 (d, $^{3}J_{PH}$ = 5.8 Hz, 3H, CH_3), 3.85 (d, $^{3}J_{PH}$ = 5.8 Hz, 3H, CH_3), 5.22 (dd, $^{3}J_{PH}$ = 5.8 Hz, $^{3}J_{PH}$ = 4.2 Hz, 1H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 28.7 (d, $^{3}J_{PC}$ = 5.6 Hz, Me_3C), 34.6 ($^{2}J_{PC}$ = 8.5 Hz, $^{3}J_{PC}$ = 5.0 Hz, Me_3C), 52.3 (d, $^{2}J_{PC}$ = 7.4 Hz, OCH_3), 52.5 (d, $^{2}J_{PC}$ = 7.4 Hz, OCH_3), 53.4 (d, $^{2}J_{PC}$ = 8.0 Hz, OCH_3), 53.5 (d, $^{2}J_{PC}$ = 8.0 Hz, OCH_3), 80.4 (dd, $^{1}J_{PC}$ = 194.3 Hz, $^{2}J_{PC}$ = 8.6 Hz, CH). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -12.0$ (d, $^{3}J_{PP}$ = 35.1 Hz), 11.5 (d, $^{3}J_{PP}$ = 35.1 Hz). Anal. Calcd. for $C_9H_{22}O_7P_2$ (304.21): C, 35.53; H, 7.29. Found: C, 35.58; H, 7.32%.

Di(*tert*-butyl)[[(diethoxyphosphoryl)oxy]2,2-dimethylpropyl] phosphonate (3l)

White powder, mp 115–117°C; yield: 0.53 g (74%). IR (KBr) (ν_{max}/cm^{-1}): 1562, 1480, 1475, 1345 and 1260. ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.14$ (s, 9H, *Me*$_3$C), 1.28 (t, $^3J_{HH} = 7.2$ Hz, 3H, CH_3), 1.30 (t, $^3J_{HH} = 7.2$ Hz, 3H, CH_3), 1.32 (t, $^3J_{HH} = 7.3$ Hz, 3H, CH_3), 1.34 (t, $^3J_{HH} = 7.3$ Hz, 3H, CH_3), 4.06–4.10 (m, 2H, OCH_2), 4.12–4.15 (m, 2H, OCH_2), 4.17–4.20 (m, 2H, OCH_2), 4.23–4.27 (m, 2H, OCH_2), 4.45 (dd, $^3J_{PH} = 11.7$ Hz, $^3J_{PH} = 8.5$ Hz, 1H, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 15.7$ (d, $^3J_{PC} = 4.6$ Hz, CH_3), 15.8 (d, $^3J_{PC} = 4.6$ Hz, CH_3), 16.4 (d, $^3J_{PC} = 5.2$ Hz, CH_3), 16.5 (d, $^3J_{PC} = 5.2$ Hz, CH_3), 29.4 (d, $^3J_{PC} = 5.4$ Hz, *Me*$_3$C), 35.1 (dd, $^2J_{PC} = 8.9$ Hz, $^3J_{PC} = 6.0$ Hz, Me_3C), 61.8 (d, $^2J_{PC} = 8.5$ Hz, OCH_2), 62.2 (d, $^2J_{PC} = 8.5$ Hz, OCH_2), 62.5 (d, $^2J_{PC} = 8.7$ Hz, OCH_2), 63.6 (d, $^2J_{PC} = 8.7$ Hz, OCH_2), 74.6 (dd, $^1J_{PC} = 150.2$ Hz, $^2J_{PC} = 7.0$ Hz, CH). ^{31}P NMR (202 MHz, $CDCl_3$): $\delta = -11.5$ (d, $^3J_{PP} = 15.5$ Hz), 19.6 (d, $^3J_{PP} = 15.5$ Hz). Anal. Calcd. for $C_{13}H_{30}O_7P_2$ (360.32): C, 43.33; H, 8.39. Found: C, 43.42; H, 8.42%.

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