

Supplementary Information

Synthesis of Phosphonates from Phenylphosphonic Acid and its Monoesters

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General information

The MW-assisted reactions were carried out in a CEM[®] Discover (300 W) focused MW reactor equipped with a stirrer and a pressure controller applying 10–150 W irradiation. The ³¹P, ¹³C and ¹H NMR spectra were obtained in CDCl₃ or DMSO-*d*₆ solution on a Bruker AV-300 spectrometer operating at 121.5, 75.5, 300 and 500 MHz, respectively. The ³¹P NMR chemical shifts are referred to H₃PO₄, while the ¹³C and ¹H chemical shifts are referred to TMS. The couplings are given in Hz. The exact mass measurements were performed using an Agilent 6545 Q-TOF mass spectrometer in high resolution, positive electrospray mode.

General procedure for the esterification of phenylphosphonic acid and its monoesters

1. General procedure for the direct esterification of phenylphosphonic acid (1)

A mixture of 0.10 g (0.63 mmol) of phenylphosphonic acid (**1**) and 9.45 mmol of an alcohol (0.55 mL of ethanol, 0.87 mL of *n*-butanol, or 1.5 mL of *n*-octanol) was measured in a sealed tube, and irradiated in the MW reactor applying 50–150 W irradiation in the presence of 0.012 mL (0.060 mmol) [bmim][BF₄] at the temperatures and for the times shown in Table 1. (The pressure developed was in the range of 1–18 bar.) The excess of alcohol was removed under reduced pressure, and the residue purified by column chromatography (silica gel/ethyl acetate) to afford products **2a-c**.

Phenylphosphonic acid monobutyl ester (2a): ³¹P NMR (CDCl₃, 121.5 MHz) δ: 20.5, δ_P^[S1,S2] (CDCl₃, 202.4 MHz): 21.8, δ_P^[S3] (CDCl₃, 121.5 MHz): 21.8; [M+Na]⁺ = 237.0652, C₁₀H₁₅O₃PNa requires 237.0656.

Phenylphosphonic acid monoethyl ester (2b): ³¹P NMR (CDCl₃, 121.5 MHz) δ: 20.3, δ_P^[S4] (CDCl₃, 500 MHz): 20.7, δ_P^[S3] (CDCl₃, 121.5 MHz): 21.0; [M+H]⁺ = 187.0521, C₈H₁₂O₃P requires 187.0524.

Phenylphosphonic acid monoethyl ester (2c): ^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 20.5, $\delta_{\text{P}}^{[\text{S1}]}$ (CDCl_3 , 202.4 MHz): 22.8, $\delta_{\text{P}}^{[\text{S2}]}$ (CDCl_3 , 202.4 MHz): 22.6; $[\text{M}+\text{H}]^+ = 271.1460$, $\text{C}_{14}\text{H}_{24}\text{O}_3\text{P}$ requires 271.1463.

2. General procedure for the alkylating esterification of phenylphosphonic acid (1)

A: A mixture of 0.10 g (0.63 mmol) of phenylphosphonic acid (**1**), 0.068 mL (0.63 mmol) or 0.15 mL (1.4 mmol) of butyl bromide, and 0.10 mL (0.69 mmol) or 0.19 mL (1.4 mmol) of triethylamine in a closed vial was irradiated in the MW reactor at 10–20 W at the given temperature for the appropriate time. The resulting mixture was filtered, and removal of the volatile components provided the crude product that was analyzed by ^{31}P NMR spectroscopy. See Table 2, entries 1 and 3, as well as Table 3, entries 1–5.

B: The phenylphosphonic acid (**1**) and the butyl bromide were measured in as above (see Method A), but in 1 mL of acetonitrile, and instead of triethylamine 0.095 g (0.69 mmol) or 0.19 g (1.4 mmol) of potassium carbonate and 0.0072 g (0.032 mmol) or 0.014 g (0.063 mmol) of benzyltriethylammonium chloride was used. The mixture was irradiated in the microwave reactor as above at 10–30 W. The resulting reaction mixture was filtered, and removal of the volatile components gave the crude product that was analyzed by ^{31}P NMR spectroscopy. See Table 2, entry 4, and Table 3, entry 6.

3. General procedure for the direct esterification of phenylphosphonic acid monoesters (2)

A mixture of 0.47 mmol of phenylphosphonic acid monoester (**2a**: 0.10 g, **2c**: 0.13 g) and 7.05 mmol of an alcohol (0.65 mL of *n*-butanol or 1.1 mL of *n*-octanol) was measured in a sealed tube, and irradiated in the MW reactor using 50–150 W irradiation in the presence of 0.0088 mL (0.047 mmol) or 0.017 mL (0.094 mmol) of $[\text{bmim}][\text{BF}_4]$, or 0.0097 mL (0.047 mmol) of $[\text{bmim}][\text{PF}_6]$ at the temperatures and for the times shown in Table 4. (The

pressure developed was in the range of 1–10 bar.) The excess of alcohol was removed under reduced pressure, and the residue purified by column chromatography (silicagel/ethyl acetate) to afford the corresponding phosphonates as shown in [Table 4](#).

4. General procedure for the alkylating esterification of phenylphosphonic acid monoesters (2)

A: To 0.75 mmol of phenylphosphonic acid monoalkyl ester (**2a**: 0.16 g, **2b**: 0.14 g, **2c**: 0.20 g) was added 0.75 mmol of an alkyl halide (0.060 mL of ethyl iodide, 0.068 mL of propyl bromide, 0.070 mL of isopropyl bromide, 0.081 mL of butyl bromide, or 0.13 mL of octyl bromide) and 0.12 mL (0.83 mmol) of triethylamine. The contents of the closed vial were irradiated in the MW reactor at 10–20 W. The resulting mixture was filtered, and removal of the volatile components provided the crude product that was purified by column chromatography (Brockmann I type neutral aluminium oxide/ethyl acetate–hexane) to afford diesters **3a-h** in purities of >99% as colorless oils ([Table 5](#), entries 1, 3 and 5, as well as [Table 6](#), entries 1, 3, 5, 7, 9 and 11).

B: The monoesters (**2**) and alkyl halides were used as above, but in 1 mL of acetonitrile, and instead of triethylamine 0.095 g (0.069 mmol) of potassium carbonate and 0.0072 g (0.032 mmol) of benzyltriethylammonium chloride were measured in. After carrying out the reaction as above, the resulting mixture was filtered, and removal of the volatile components provided the crude product that was purified as described above to give diesters **3a-h** ([Table 5](#), entries 2, 4 and 6, as well as [Table 6](#), entries 2, 4, 6, 8, 10 and 12).

The following products were prepared by Method A:

Dibutyl phenylphosphonate (3a): ^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 18.8, $\delta_{\text{P}}^{[\text{S5}]}$ (CDCl_3) 19.4; $\delta_{\text{P}}^{[\text{S6}]}$ (CDCl_3 , 162 MHz) 19.4; $[\text{M}+\text{Na}]^+ = 293.1284$, $\text{C}_{14}\text{H}_{23}\text{O}_3\text{PNa}$ requires 293.1283.

Diethyl phenylphosphonate (3b): ^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 18.9, $\delta_{\text{P}}^{[\text{S5}]}$ (CDCl_3) 19.7, $\delta_{\text{P}}^{[\text{S7}]}$ (CDCl_3 , 162 MHz) 18.4; $[\text{M}+\text{H}]^+ = 215.0834$, $\text{C}_{10}\text{H}_{16}\text{O}_3\text{P}$ requires 215.0837.

Diocetyl phenylphosphonate (3c): ^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 18.0, $\delta_{\text{P}}^{[\text{S1}]}$ (CDCl_3 , 202.4 MHz) 18.8, $\delta_{\text{P}}^{[\text{S2}]}$ (CDCl_3 , 202.4 MHz) 18.0; $[\text{M}+\text{H}]^+ = 383.2718$, $\text{C}_{22}\text{H}_{40}\text{O}_3\text{P}$ requires 383.2715.

Characterization data for the new compounds 3d-h

Butyl ethyl phenylphosphonate (3d):

^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 17.7; ^{13}C NMR (CDCl_3 , 75.5 MHz) δ : 13.6 (CH_3)^a, 16.4 (d, $J = 6.4$; CH_2CH_3), 18.8 (CH_3)^a, 32.5 (d, $J = 6.5$; OCH_2CH_2), 62.2 (d, $J = 5.4$; OCH_2)^b, 65.9 (d, $J = 5.7$; OCH_2)^b, 128.48 (d, $J = 188.0$; C_1), 128.51 (d, $J = 15.0$; C_2)^c, 131.8 (d, $J = 9.8$; C_3)^c, 132.4 (d, $J = 3.0$; C_4); ^1H NMR (CDCl_3 , 300 MHz) δ : 0.87 (t, $J = 7.4$, 3H; CH_3)^a, 1.22–1.43 (m, 5H; OCH_2CH_2 ^b and CH_3 ^a), 1.55–1.68 (m, 2H; OCH_2CH_2)^b, 3.91–4.19 (m, 4H; 2x OCH_2), 7.38–7.55 (m, 3H; ArH), 7.72–7.83 (m, 2H; ArH),^{a,b,c} may be reversed; $[\text{M}+\text{Na}]^+ = 265.0967$, $\text{C}_{12}\text{H}_{19}\text{O}_3\text{PNa}$ requires 265.0970.

Butyl propyl phenylphosphonate (3e):

^{31}P NMR (CDCl_3) δ : 18.8; ^{13}C NMR (CDCl_3 , 75.5 MHz) δ : 10.1 (CH_3)^a, 13.6 (CH_3)^a, 18.8 (CH_2CH_3), 23.8 (d, $J = 6.6$; OCH_2CH_2)^b, 32.5 (d, $J = 6.5$; OCH_2CH_2)^b, 65.8 (d, $J = 5.7$; OCH_2)^c, 67.6 (d, $J = 5.7$; OCH_2)^c, 128.41 (d, $J = 188.2$; C_2)^d, 128.46 (d, $J = 15.0$; C_1), 131.8 (d, $J = 9.8$; C_3)^d, 132.4 (d, $J = 3.0$; C_4); ^1H NMR (CDCl_3 , 300 MHz) δ 0.81–0.94 (m, 6H; 2x CH_3), 1.27–1.42 (m, 2H; CH_2CH_3), 1.55–1.72 (m, 4H; 2x OCH_2CH_2), 3.86–4.10 (m, 4H; 2x OCH_2), 7.37–7.54 (m, 3H; ArH), 7.71–7.82 (m, 2H; ArH),^{a,b,c,d} may be reversed; $[\text{M}+\text{H}]^+ = 257.1307$, $\text{C}_{13}\text{H}_{22}\text{O}_3\text{P}$ requires 257.1307.

Butyl isopropyl phenylphosphonate (3f):

^{31}P NMR (CDCl_3) δ : 17.8; ^{13}C NMR (CDCl_3 , 75.5 MHz) δ : 13.7 (CH_2CH_3)^a, 18.8 (CH_2CH_3), 23.9 (d, J = 4.9; CHCH_3)^a, 24.2 (d, J = 3.9; CHCH_3)^a, 32.5 (d, J = 6.7; OCH_2CH_2), 65.7 (d, J = 5.7; OCH)^b, 71.0 (d, J = 5.6; OCH_2)^b, 128.4 (d, J = 14.9; C_2)^c, 129.2 (d, J = 188.4; C_1), 131.8 (d, J = 9.8; C_3)^c, 132.2 (d, J = 3.0; C_4); ^1H NMR (CDCl_3 , 300 MHz) δ : 0.87 (t, J = 7.4, 3H; CH_2CH_3), 1.22 (d, J = 6.2; 3H; CHCH_3)^a, 1.28–1.42 (m, 5H; CH_2CH_3 and CHCH_3)^a, 1.55–1.66 (m, 2H; OCH_2CH_2), 3.87–4.08 (m, 2H; OCH_2), 4.60–4.78 (m, 1H; OCH), 7.36–7.56 (m, 3H; ArH), 7.71–7.85 (m, 2H; ArH),^{a,b,c} may be reversed; $[\text{M}+\text{H}]^+ = 257.1307$, $\text{C}_{13}\text{H}_{22}\text{O}_3\text{P}$ requires 257.1307.

Ethyl propyl phenylphosphonate (3g):

^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 18.9; ^{13}C NMR (CDCl_3 , 75.5 MHz) δ : 10.1 (CH_2CH_3), 16.4 (d, J = 6.4; OCH_2CH_3), 23.9 (d, J = 6.6; OCH_2CH_2), 62.1 (d, J = 5.5; OCH_2)^a, 67.6 (d, J = 5.7; OCH_2)^a, 128.49 (d, J = 188.0; C_1), 128.50 (d, J = 15.0; C_2)^b, 131.8 (d, J = 9.8; C_3)^b, 132.4 (d, J = 3.0; C_4); ^1H NMR (CDCl_3 , 300 MHz) δ : 0.91 (t, J = 7.4, 3H; CH_3)^c, 1.29 (t, J = 7.1, 3H; CH_3)^c, 1.66 (h, J = 7.1, 2H; OCH_2CH_2), 3.88–4.19 (m, 4H; $2\times\text{OCH}_2$), 7.38–7.57 (m, 3H; ArH), 7.72–7.84 (m, 2H; ArH),^{a,b,c} may be reversed; $[\text{M}+\text{Na}]^+ = 251.0809$, $\text{C}_{11}\text{H}_{17}\text{O}_3\text{PNa}$ requires 251.0813.

Ethyl isopropyl phenylphosphonate (3h):

^{31}P NMR (CDCl_3 , 121.5 MHz) δ : 17.7; ^{13}C NMR (CDCl_3 , 126 MHz) δ : 16.4 (d, J = 6.6; CH_2CH_3), 23.9 (d, J = 4.8; CHCH_3)^a, 24.1 (d, J = 3.9; CHCH_3)^a, 61.9 (d, J = 5.3; OCH_2)^b, 71.0 (d, J = 5.6; OCH)^b, 128.4 (d, J = 14.9; C_2)^c, 129.2 (d, J = 187.8; C_1), 131.8 (d, J = 9.8; C_3)^c, 132.3 (d, J = 3.0; C_4); ^1H NMR (CDCl_3 , 500 MHz) δ : 1.20 (d, J = 6.2, 3H; CHCH_3)^a, 1.27 (t, J = 7.0, 3H; CH_2CH_3), 1.34 (d, J = 6.1, 3H; CHCH_3)^a, 3.96–4.13 (m, 2H; OCH_2), 4.63–4.73 (m, 1H; OCH), 7.39–7.45 (m, 2H; ArH), 7.47–7.53 (m, 1H; ArH), 7.75–7.82 (m, 2H; ArH),^{a,b,c} may be reversed; $[\text{M}+\text{Na}]^+ = 251.0814$, $\text{C}_{11}\text{H}_{17}\text{O}_3\text{PNa}$ requires 251.0813.

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Spectra for compounds 2a-c, 3a-h





















