

Solvent-Free/Scalable Mechanochemical-Assisted Addition of Phosphine Oxides to Aldehydes: Sustainable Protocol for One-Pot Tandem P-C Bond Formation

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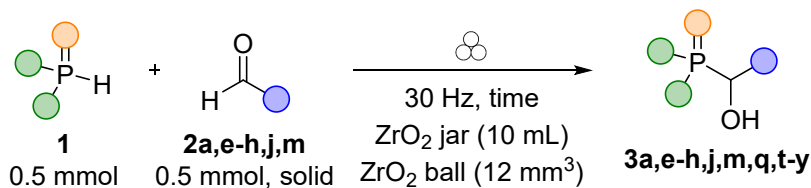
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I.- General information.

Commercially available reagents were used without further purification unless liquid aldehydes, which were distilled under reduced pressure. Secondary phosphine chalcogenides employed were carefully dried under vacuum before being used and stored under argon. Reactions were performed with Retsch MM400 or MM500 Vario ball mills using RETSCH ZrO₂ grinding jars and ZrO₂ ball bearings. ¹H and ³¹P{¹H}-NMR spectra (CDCl₃, DMSO-*d*⁶) were obtained using a Bruker NAV-300 (¹H, 300 MHz; ³¹P, 121 MHz) or a Bruker NAV-400 (¹H, 401 MHz; ³¹P, 162 MHz). ¹³C{¹H} spectra were obtained using a Bruker NAV-300 (75 MHz). All chemical shifts (δ) are given in parts per million (ppm). Calibration was made on the signal of the solvent (CDCl₃ ¹H: 7.26, ¹³C: 77.16, DMSO-*d*⁶ ¹H: 2.50; ¹³C: 39.52).^[1] Coupling constants (*J*-values) are given in hertz (Hz). Chemical shifts are reported as follows: value (description of absorption, coupling constant(s) where applicable, number of protons). The ¹H-NMR spectra are presented over the 0-10 ppm region. In the ¹³C-NMR spectra, the proximity of multiple aromatic signals and the presence of C–P couplings at different bond distances prevent unambiguous assignment in this region. Therefore, only the doublet signal of the CH(OH) group bound to phosphorus, characteristic of the C–P bond formed, and other signals derived from aliphatic carbons are reported in the product description. Full ¹³C-NMR spectra are available in Section IX.

II.- General procedures for the synthesis of α -hydroxyphosphine chalcogenides **3a-y**.

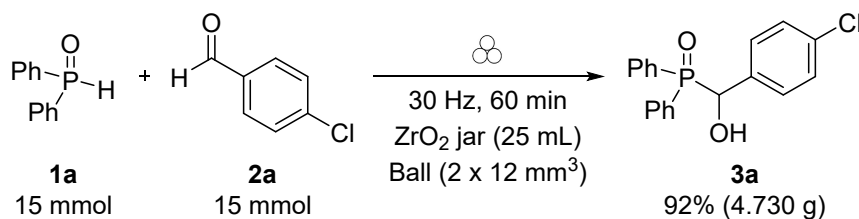
II.1.- Standard procedure for the synthesis of α -hydroxyphosphine chalcogenides **3a,e-h,j,m,q,t-y** obtained from solid aldehydes.



Scheme SI_1: Synthesis of products **3a,e-h,j,m,q,t-y**.

The corresponding secondary phosphine chalcogenide **1** (0.5 mmol, 1 equiv.), solid aldehyde **2a,e-h,j,m** (0.5 mmol, 1 equiv.) and a ZrO_2 bearing ball (12 mm³) were added to a ZrO_2 grinding jar (10 mL) which was milled at 30 Hz until reaction was completed (monitored by ¹H-NMR and ³¹P-NMR). Upon completion, the resulting α -hydroxyphosphine chalcogenide **3a,e-h,j,m,q,t-y** was directly scraped from the jar.

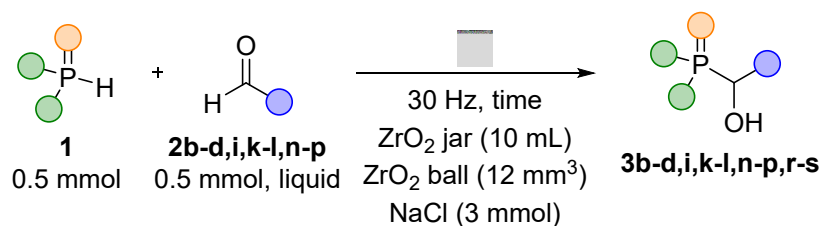
II.2.- Scaled-up procedure for the multigram synthesis of ((4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide **3a**.



Scheme SI_2: Multigram synthesis of product **3a**.

Diphenyl phosphine oxide **1a** (3.033 g, 15 mmol, 1 equiv.), 4-chlorobenzaldehyde **2a** (2.109 g, 15 mmol, 1 equiv.) and two ZrO_2 bearing balls (12 mm³) were added to a ZrO_2 grinding jar (25 mL) which was milled at 30 Hz for 60 min. Upon completion, the resulting ((4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide **3a** (4.730 g, 92% yield) was directly scraped from the jar.

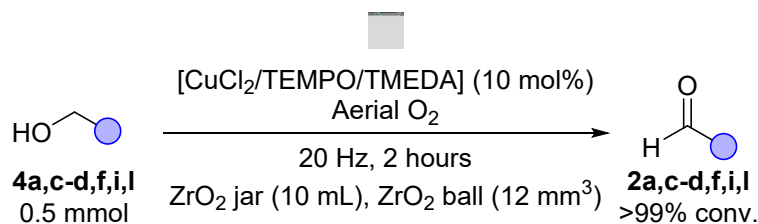
II.3.- Standard procedure for the synthesis of α -hydroxyphosphine chalcogenides **3b-d,i,k-l,n-p,r-s** obtained from liquid aldehydes.



Scheme SI_3: Synthesis of products **3b-d,i,k-l,n-p,r-s**.

The corresponding secondary phosphine chalcogenide **1** (0.5 mmol, 1 equiv.), liquid aldehyde **2b-d,i,k-l,n-p** (0.5 mmol, 1 equiv.), NaCl (174 mg, 3 mmol) and a ZrO_2 bearing ball (12 mm³) were added to a ZrO_2 grinding jar (10 mL) which was milled at 30 Hz until reaction was completed (¹H-NMR and ³¹P-NMR monitored). Upon completion, the resulting solid mixture was transferred to a vial (20 mL), the vial rinsed with distilled water, sonicated for 20 minutes, filtered and dried under vacuum affording α -hydroxyphosphine chalcogenides **3b-d,i,k-l,n-p,r-s**.

III.- Standard procedure for the mechanochemical oxidation of primary alcohols **4a,c-d,f,i,l** into aldehydes.



Scheme SI_4: Mechanochemical oxidation of primary alcohols **4a,c-d,f,i,l**.

The corresponding primary alcohol **4a,c-d,f,i,l** (0.5 mmol, 1 equiv.), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (9 mg, 0.05 mmol, 0.1 equiv.), 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO, 8 mg, 0.05 mmol, 0.1 equiv.), *N,N,N',N'*-tetramethylethylenediamine (TMEDA, 8 μL , 0.05 mmol, 0.1 equiv.) and a ZrO_2 bearing ball (12 mm^3) were added to a ZrO_2 grinding jar (10 mL) which was milled at 20 Hz for one hour. Then, the jar was opened for 10 seconds to allow air renewal, closed again, and milled at 20 Hz for one more hour. After that, the blue slurry formed in the jar was dissolved in dichloromethane (20 mL), poured in a separation funnel and washed with a saturated solution of NH_4Cl (20 mL). The aqueous phase was washed with dichloromethane (20 mL), the organic layers combined, dried with MgSO_4 and filtered. Finally, solvent was carefully removed under vacuum (750 to 400 mbar, 40 $^\circ\text{C}$) affording aldehydes **2a,c-d,f,i,l** in quantitative conversion (determined by $^1\text{H-NMR}$ as transformation of reactant **4** in product **2**).

To assess possible mass losses, alcohols **4a** and **4i** were selected as representative substrates and subjected to an internal standard-based $^1\text{H-NMR}$ analysis. After completing the procedure described above, the crude mixtures containing aldehydes **2a** and **2i** were dissolved in CDCl_3 and CHBr_3 (40 μL , 0.457 mmol) was added as an internal standard. $^1\text{H-NMR}$ spectra (**Figures SI_1** and **SI_2**) showed conversions of 81% (**2a**) and 83% (**2i**).

Moreover, the turnover number (TON) and turnover frequency (TOF) of the oxidative catalytic system were determined using product **2a** as a representative model substrate (81% conversion determined employing an internal standard).

$$\text{TON} = \text{mmol of product} / \text{mmol of catalyst} = 0.405 / 0.05 = 8.1.$$

$$\text{TOF} = \text{TON} / \text{reaction time} = 8.1 / 2 \text{ h} = 4.05 \text{ h}^{-1}.$$

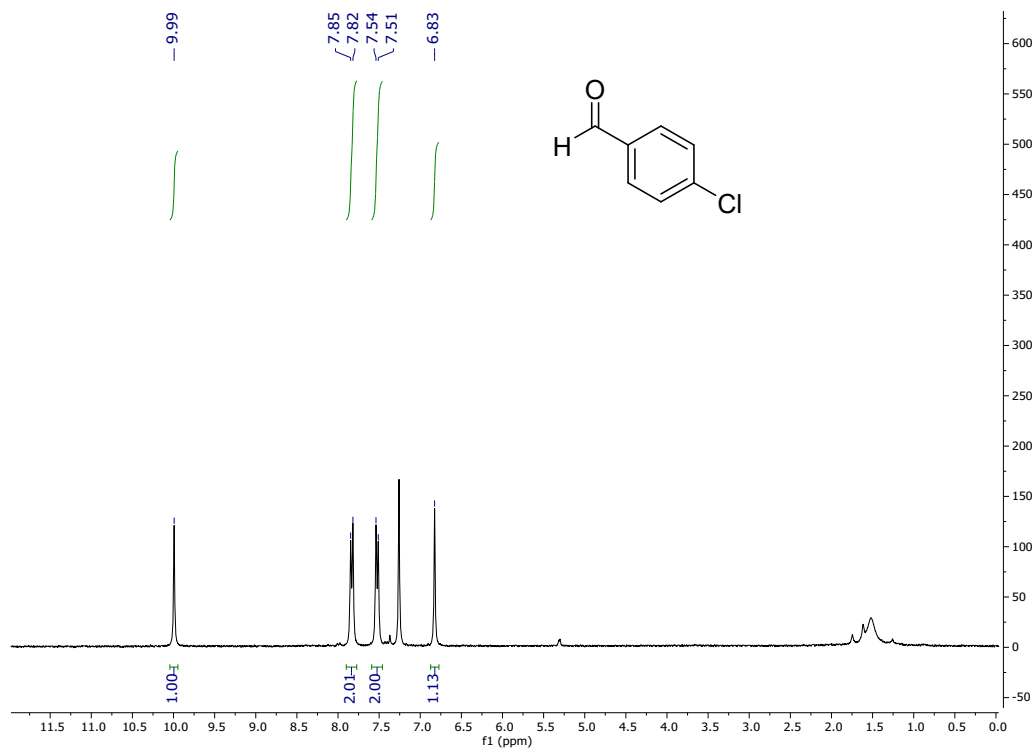


Figure SI_1: $^1\text{H-NMR}$ for **2a** in CDCl_3 (300 MHz) using CHBr_3 (40 μL , 0.457 mmol) as internal standard.

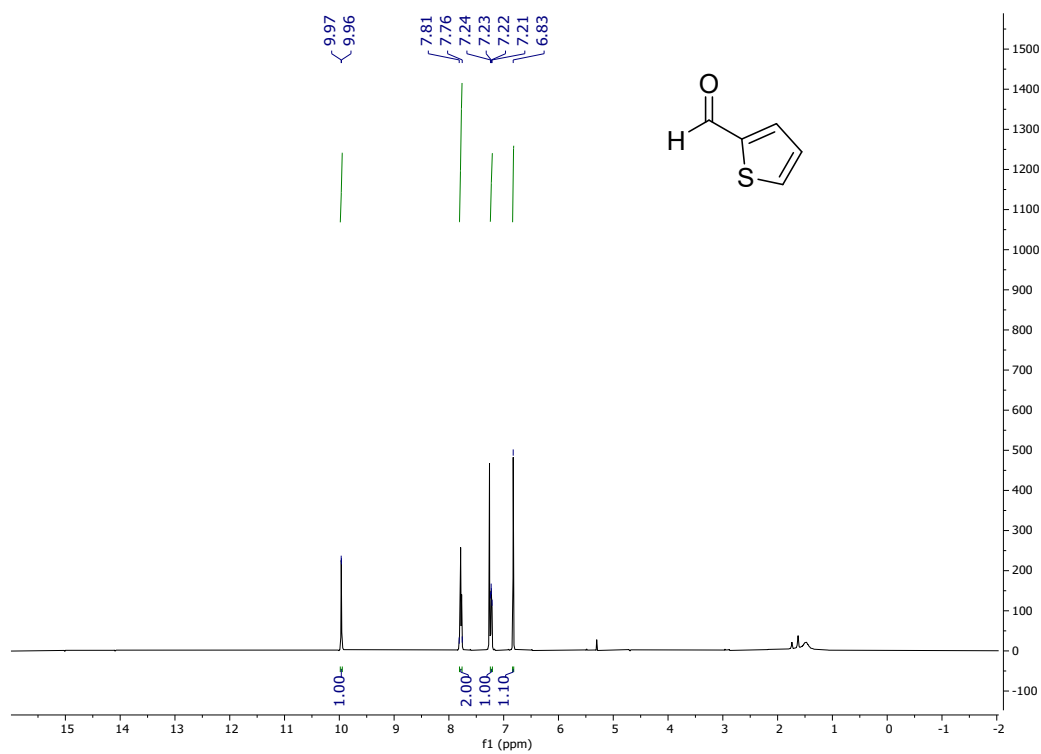
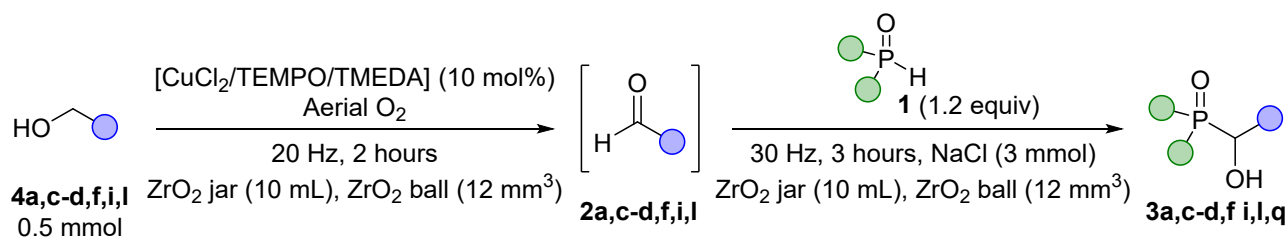


Figure SI_2: $^1\text{H-NMR}$ for **2i** in CDCl_3 (300 MHz) using CHBr_3 (40 μL , 0.457 mmol) as internal standard.

IV.- Standard procedure for the one-pot tandem synthesis of α -hydroxyphosphine oxides from primary alcohols.

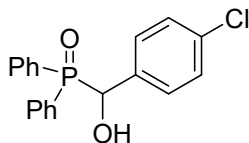


Scheme SI_5: One-pot synthesis of products **3a,c-d,f,i,l,q**.

The corresponding primary alcohol **4a,c-d,f,i,l** (0.5 mmol, 1 equiv.), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (9 mg, 0.05 mmol, 0.1 equiv.), 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO, 8 mg, 0.05 mmol, 0.1 equiv.), *N,N,N',N'*-tetramethylethylenediamine (TMEDA, 8 μL , 0.05 mmol, 0.1 equiv.) and a ZrO_2 bearing ball (12 mm³) were added to a ZrO_2 grinding jar (10 mL) which was milled at 20 Hz for one hour. Then, the jar was opened 10 seconds to allow air renewal, closed again, and milled at 20 Hz for one more hour, affording a blue slurry. Subsequently, the corresponding secondary phosphine oxide **1** (0.6 mmol, 1.2 equiv.) and NaCl (174 mg, 3 mmol) were added to the jar, which was milled at 30 Hz for 3 hours. Upon completion, the resulting solid mixture was transferred to a vial (20 mL), the vial rinsed with distilled water and sonicated for 20 minutes. Then, the solid was allowed to settle and the liquor decanted. The vial was rinsed again with distilled water, sonicated for 20 minutes and filtered. The filtered solid was washed with distilled water (60 mL) and dried under vacuum affording α -hydroxyphosphine oxides **3a,c-d,f,i,l,q**.

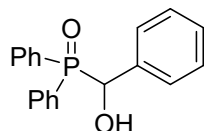
V.- Spectroscopic data of products 3a-y.

((4-Chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide 3a



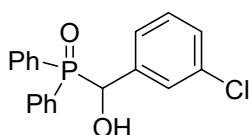
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.87 – 7.75 (m, 4H), 7.61 – 7.44 (m, 6H), 7.31 – 7.21 (m, 4H), 6.63 (dd, J = 17.4, 5.8 Hz, 1H), 5.68 (dd, J = 7.3, 5.8 Hz, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.93. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 71.6 (d, J = 86.0 Hz). The spectroscopic data were matched with the one reported in the literature.^[2]

(Hydroxy(phenyl)methyl)diphenylphosphine oxide 3b



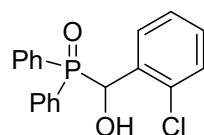
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.86 – 7.76 (m, 4H), 7.57 – 7.42 (m, 6H), 7.26 – 7.15 (m, 5H), 6.60 (dd, J = 17.8, 5.9 Hz, 1H), 5.63 (dd, J = 7.2, 5.9 Hz, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.09. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.3 (d, J = 86.7 Hz). The spectroscopic data were matched with the one reported in the literature.^[3]

((3-Chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide 3c



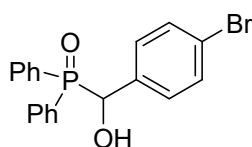
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.86 – 7.70 (m, 4H), 7.58 – 7.43 (m, 6H), 7.28 – 7.11 (m, 4H), 6.60 (dd, J = 17.3, 5.7 Hz, 1H), 5.71 – 5.60 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.40. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 71.8 (d, J = 85.3 Hz). The spectroscopic data were matched with the one reported in the literature.^[3]

((2-Chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide 3d



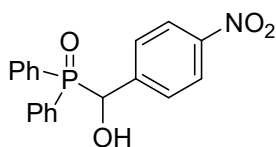
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.84 – 7.66 (m, 4H), 7.63 – 7.41 (m, 6H), 7.33 – 7.28 (m, 1H), 7.27 – 7.17 (m, 3H), 6.64 (dd, J = 18.0, 5.7 Hz, 1H), 5.96 – 5.89 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.82. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 68.7 (d, J = 87.6 Hz). The spectroscopic data were matched with the one reported in the literature.^[2]

((4-Bromophenyl)(hydroxy)methyl)diphenylphosphine oxide 3e



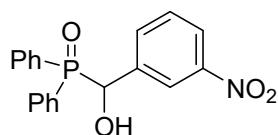
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.86 – 7.76 (m, 4H), 7.59 – 7.45 (m, 6H), 7.40 (d, J = 8.6 Hz, 2H), 7.18 (dd, J = 8.6, 2.1 Hz, 2H), 6.60 (dd, J = 17.4, 5.9 Hz, 1H), 5.66 (dd, J = 7.5, 5.9 Hz, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.79. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 71.7 (d, J = 85.9 Hz). The spectroscopic data were matched with the one reported in the literature.^[2]

(Hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide 3f



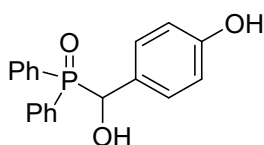
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 8.06 (d, J = 8.6 Hz, 2H), 7.88 – 7.71 (m, 4H), 7.58 – 7.43 (m, 8H), 6.82 (dd, J = 17.0, 5.7 Hz, 1H), 5.84 (dd, J = 9.1, 5.7 Hz, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.40. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.0 (d, J = 83.6 Hz). The spectroscopic data were matched with the one reported in the literature.^[4]

(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide 3g



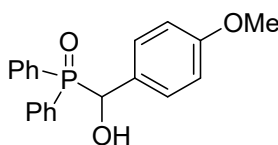
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 8.09 – 8.03 (m, 2H), 7.89 – 7.74 (m, 4H), 7.69 – 7.64 (m, 1H), 7.62 – 7.45 (m, 7H), 6.89 (dd, J = 16.8, 5.9 Hz, 1H), 5.92 (dd, J = 8.0, 5.9 Hz, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.46. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 71.4 (d, J = 84.6 Hz). The spectroscopic data were matched with the one reported in the literature.^[2]

(Hydroxy(4-hydroxyphenyl)methyl)diphenylphosphine oxide 3h



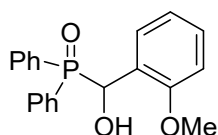
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 9.35 (*br s*, 1H), 7.88 – 7.72 (m, 4H), 7.59 – 7.42 (m, 6H), 7.04 (d, J = 8.5 Hz, 2H), 6.58 (d, J = 8.5 Hz, 2H), 6.32 (dd, J = 18.1, 5.7 Hz, 1H), 5.53 – 5.47 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.67. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.2 (d, J = 88.1 Hz). The spectroscopic data were matched with the one reported in the literature.^[4]

(Hydroxy(4-methoxyphenyl)methyl)diphenylphosphine oxide 3i



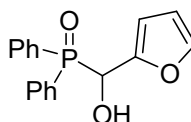
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.85 – 7.73 (m, 4H), 7.57 – 7.40 (m, 6H), 7.15 (dd, J = 8.8, 2.1 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 6.34 (dd, J = 17.8, 5.9 Hz, 1H), 5.58 – 5.49 (m, 1H), 3.67 (s, 3H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.68. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.0 (d, J = 87.6 Hz), 55.4. The spectroscopic data were matched with the one reported in the literature.^[3]

(Hydroxy(2-methoxyphenyl)methyl)diphenylphosphine oxide 3j



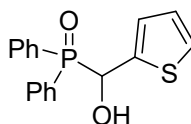
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.85 – 7.76 (m, 2H), 7.67 – 7.46 (m, 6H), 7.45 – 7.37 (m, 2H), 7.25 (dt, J = 7.6, 1.9 Hz, 1H), 7.18 (tt, J = 7.6, 1.9 Hz, 1H), 6.87 – 6.76 (m, 2H), 6.39 (dd, J = 16.2, 6.4 Hz, 1H), 5.96 (dd, J = 6.4, 4.2 Hz, 1H), 3.46 (s, 3H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.95. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 65.2 (d, J = 88.5 Hz), 55.5. The spectroscopic data were matched with the one reported in the literature.^[4]

(Furan-2-yl(hydroxy)methyl)diphenylphosphine oxide 3k



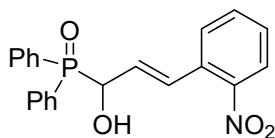
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.91 – 7.82 (m, 2H), 7.80 – 7.71 (m, 2H), 7.59 – 7.42 (m, 7H), 6.53 (dd, J = 14.3, 6.5 Hz, 1H), 6.34 – 6.31 (m, 1H), 6.23 – 6.20 (m, 1H), 5.65 – 5.58 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 26.74. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = $C_{\text{(hetero)aromatic}}$, 66.9 (d, J = 90.1 Hz). The spectroscopic data were matched with the one reported in the literature.^[2]

(Hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide 3l



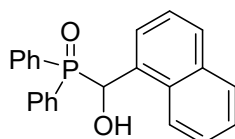
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.90 – 7.77 (m, 4H), 7.58 – 7.45 (m, 6H), 7.35 (dt, J = 4.9, 1.5 Hz, 1H), 6.99 – 6.87 (m, 3H), 5.94 – 5.88 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.14. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = $C_{\text{(hetero)aromatic}}$, 69.0 (d, J = 90.4 Hz). The spectroscopic data were matched with the one reported in the literature.^[3]

(E)-(1-Hydroxy-3-(2-nitrophenyl)allyl)diphenylphosphine oxide 3m



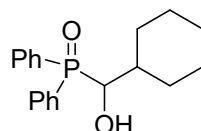
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.91 – 7.79 (m, 5H), 7.67 – 7.42 (m, 9H), 6.93 – 6.83 (m, 1H), 6.56 – 6.43 (m, 2H), 5.42 – 5.30 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.75. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , C_{vinyl} , 71.6 (d, J = 86.4 Hz).

(Hydroxy(naphthalen-1-yl)methyl)diphenylphosphine oxide 3n



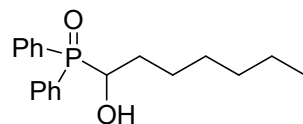
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 8.34 – 8.23 (m, 1H), 7.90 – 7.71 (m, 6H), 7.62 – 7.25 (m, 10H), 6.56 (dd, J = 19.5, 4.0 Hz, 1H), 6.45 – 6.36 (m, 1H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.80. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 68.9 (d, J = 87.9 Hz). The spectroscopic data were matched with the one reported in the literature.^[3]

(Cyclohexyl(hydroxy)methyl)diphenylphosphine oxide 3o



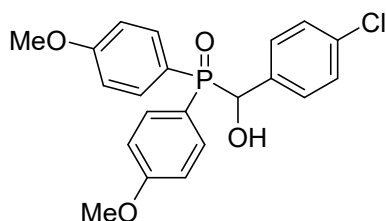
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.93 – 7.85 (m, 2H), 7.82 – 7.74 (m, 2H), 7.55 – 7.42 (m, 6H), 5.66 (dd, J = 11.7, 7.7 Hz, 1H), 4.24 – 4.16 (m, 1H), 1.77 – 1.45 (m, 6H), 1.23 – 0.95 (m, 5H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.97. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 73.7 (d, J = 88.2 Hz), 30.5 (d, J = 8.2 Hz), 28.1 (d, J = 5.7 Hz), 26.3 (d, J = 5.4 Hz), 26.0. The spectroscopic data were matched with the one reported in the literature.^[3]

(1-Hydroxyheptyl)diphenylphosphine oxide 3p



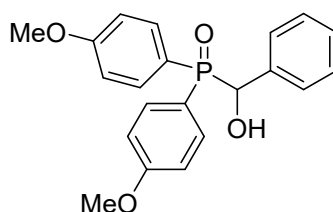
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.91 – 7.70 (m, 4H), 7.60 – 7.41 (m, 6H), 5.74 – 5.60 (m, 1H), 4.42 – 4.28 (m, 1H), 1.64 – 1.08 (m, 10H), 0.88 – 0.74 (m, 3H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 29.09. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 69.3 (d, J = 88.4 Hz), 31.6, 30.6 (d, J = 4.0 Hz), 28.8, 25.8 (d, J = 11.9 Hz), 22.4, 14.4.

((4-Chlorophenyl)(hydroxy)methyl)bis(4-methoxyphenyl)phosphine oxide 3q



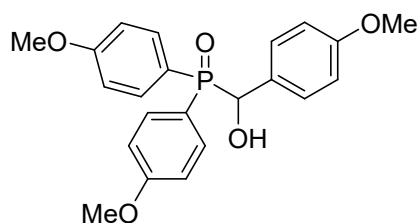
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.75 – 7.63 (m, 4H), 7.30 – 7.20 (m, 4H), 7.07 – 7.00 (m, 4H), 6.51 (dd, J = 17.6, 5.8 Hz, 1H), 5.54 (dd, J = 8.1, 5.8 Hz, 1H), 3.79 (s, 6H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.13. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.0 (d, J = 86.9 Hz), 55.7, 55.7.

(Hydroxy(phenyl)methyl)bis(4-methoxyphenyl)phosphine oxide 3r



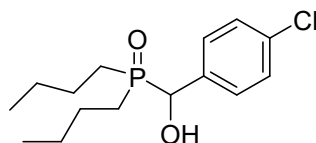
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.74 – 7.63 (m, 4H), 7.24 – 7.15 (m, 5H), 7.01 (dd, J = 8.8, 2.4 Hz, 4H), 6.48 (dd, J = 17.9, 5.8 Hz, 1H), 5.49 (dd, J = 8.1, 5.8 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 28.25. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.7 (d, J = 87.7 Hz), 55.7, 55.7. The spectroscopic data were matched with the one reported in the literature.^[5]

(Hydroxy(4-methoxyphenyl)methyl)bis(4-methoxyphenyl)phosphine oxide 3s



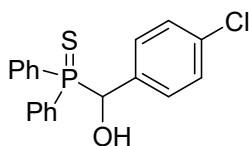
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.72 – 7.63 (m, 4H), 7.13 (dd, J = 8.8, 2.1 Hz, 2H), 7.05 – 6.98 (m, 4H), 6.76 (d, J = 8.8 Hz, 2H), 6.36 (dd, J = 17.9, 5.8 Hz, 1H), 5.46 – 5.40 (m, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.68 (s, 3H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 27.99. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = C_{aromatic} , 72.2 (d, J = 88.9 Hz), 55.7, 55.7, 55.4. The spectroscopic data were matched with the one reported in the literature.^[6]

Dibutyl((4-chlorophenyl)(hydroxy)methyl)phosphine oxide 3t



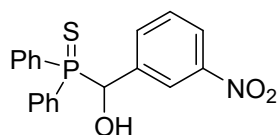
^1H NMR (300 MHz, $\text{DMSO-}d^6$): δ (ppm) = 7.42 – 7.37 (m, 4H), 6.33 (*br s*, 1H), 4.91 (d, J = 9.2 Hz, 1H), 1.76 – 1.61 (m, 2H), 1.55 – 1.27 (m, 8H), 1.25 – 1.14 (m, 2H), 0.86 (t, J = 6.8 Hz, 3H), 0.76 (t, J = 6.8 Hz, 3H). ^{31}P NMR (121 MHz, $\text{DMSO-}d^6$): δ (ppm) = 48.46. ^{13}C NMR (75 MHz, $\text{DMSO-}d^6$): δ (ppm) = 138.3, 132.1 (d, J = 2.5 Hz), 128.8 (d, J = 3.5 Hz), 128.2, 70.0 (d, J = 77.7 Hz), $C_{n\text{Bu}}$.

((4-Chlorophenyl)(hydroxy)methyl)diphenylphosphine sulfide 3u



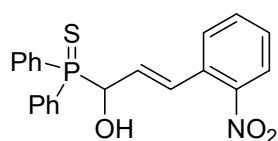
^1H NMR (300 MHz, CDCl_3): δ (ppm) = 8.00 – 7.89 (m, 2H), 7.66 – 7.44 (m, 6H), 7.39 – 7.30 (m, 2H), 7.12 (d, J = 8.6 Hz, 2H), 6.98 (dd, J = 8.6, 2.3 Hz, 2H), 5.56 (s, 1H), 4.09 (*br s*, 1H). ^{31}P NMR (121 MHz, CDCl_3): δ (ppm) = 52.59. ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) = C_{aromatic} , 72.8 (d, J = 54.8 Hz).

(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine sulfide 3v



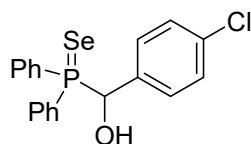
^1H NMR (401 MHz, CDCl_3): δ (ppm) = 8.05 – 8.01 (m, 1H), 7.99 – 7.92 (m, 2H), 7.73 – 7.71 (m, 1H), 7.65 – 7.59 (m, 1H), 7.58 – 7.43 (m, 6H), 7.36 – 7.29 (m, 3H), 5.70 (d, $J = 2.9$ Hz, 1H), 4.2 (*br s*, 1H). ^{31}P NMR (162 MHz, CDCl_3): δ (ppm) = 53.51. ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) = C_{aromatic} , 72.2 (d, $J = 53.6$ Hz).

(E)-(1-Hydroxy-3-(2-nitrophenyl)allyl)diphenylphosphine sulfide 3w



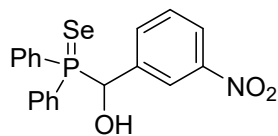
^1H NMR (401 MHz, CDCl_3): δ (ppm) = 8.01 – 7.93 (m, 2H), 7.92 – 7.82 (m, 3H), 7.59 – 7.45 (m, 7H), 7.41 – 7.35 (m, 1H), 7.32 (d, $J = 7.8$ Hz, 1H), 7.08 (dd, $J = 15.7, 4.9$ Hz, 1H), 6.18 – 6.09 (m, 1H), 5.25 – 5.19 (m, 1H), 3.52 (*br s*, 1H). ^{31}P NMR (162 MHz, CDCl_3): δ (ppm) = 49.13. ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) = C_{aromatic} , C_{vinyl} , 73.0 (d, $J = 58.6$ Hz).

((4-Chlorophenyl)(hydroxy)methyl)diphenylphosphine selenide 3x



^1H NMR (300 MHz, CDCl_3): δ (ppm) = 7.97 – 7.88 (m, 2H), 7.61 – 7.43 (m, 6H), 7.37 – 7.29 (m, 2H), 7.10 (d, $J = 8.6$ Hz, 2H), 6.96 (dd, $J = 8.6, 2.3$ Hz, 2H), 5.56 (m, 1H), 2.58 (s, 1H). ^{31}P NMR (121 MHz, CDCl_3): δ (ppm) = 50.60. ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) = C_{aromatic} , 71.7 (d, $J = 46.1$ Hz).

(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine selenide 3y



^1H NMR (300 MHz, CDCl_3): δ (ppm) = 8.08 – 8.02 (m, 1H), 8.00 – 7.91 (m, 2H), 7.73 – 7.68 (m, 1H), 7.65 – 7.43 (m, 7H), 7.38 – 7.30 (m, 3H), 5.71 (d, J = 2.7 Hz, 1H). ^{31}P NMR (121 MHz, CDCl_3): δ (ppm) = 51.99. ^{13}C NMR (75 MHz, CDCl_3): δ (ppm) = $\text{C}_{\text{aromatic}}$, 71.0 (d, J = 45.3 Hz).

VI.- Green chemistry metrics (GCM) calculations

Green Chemistry metrics (GCM) were calculated from α -hydroxy benzyl- and alkylphosphine oxides compounds **3a-3l**, **3o**.

In order to perform the Green Chemistry Metrics calculation, an *electrochemically oxidative process*^[2] was used for comparison except for compound **3c**, which comparison was performed using a *DES-assisted (Deep Eutectic Solvent) addition protocol*^[2] and for compounds **3f,3h** and **3j**, which comparison was performed using a conventional solution-based method^[3]. Note that the crude product obtained by the electrochemically oxidative process was purified by column chromatography (petroleum ether/ethyl acetate = 2/1, v/v) and the conventional solution-based product was purified by recrystallization (THF-Methanol) and this Energy usage calculations not been considered for the GCM calculations.

Green chemistry metrics formulas^[7] were customized for this reaction. Note that quantities are expressed in grams or grams/mol unless otherwise specified.

VI.1.- E-factor

Mechanosynthesis

General formula used for compounds **3a,3e-3h,3j**

$$E = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2a,2e - 2h,2j)} - \text{total product}}{\text{total product}}$$

General formula used for compounds **3b - 3d,3i,3k - 3l,3o**

$$E = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2b - 2d,3i, 2k - 2l,2o)} + \text{sodium chloride} - \text{total product}}{\text{total product}}$$

Mechanosynthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4 - \text{chlorobenzaldehyde (2a)} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0702 - 0.144}{0.144}$$

$$E = 0.188$$

Mechanosynthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{benzene (2b)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0391 + 0.174 - 0.143}{0.143}$$

$$E = 1.20$$

Mechanosynthesis of ((3-chlorophenyl)(hydroxy)diphenylphosphine oxide (**3c**):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 3\text{-chlorobenzaldehyde (2c)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0702 + 0.174 - 0.144}{0.144}$$

$$E = 1.39$$

Mechanosynthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3d):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 2\text{-chlorobenzaldehyde (2d)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0702 + 0.174 - 0.144}{0.144}$$

$$E = 1.39$$

Mechanosynthesis of (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-bromobenzaldehyde (2e)} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0925 - 0.156}{0.156}$$

$$E = 0.240$$

Mechanosynthesis of (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (3f):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-nitrobenzaldehyde (2f)} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0756 - 0.145}{0.145}$$

$$E = 0.217$$

Mechanosynthesis of (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (3g):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 3\text{-nitrobenzaldehyde (2g)} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0756 - 0.169}{0.169}$$

$$E = 0.0450$$

Mechanosynthesis of (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-hydroxybenzaldehyde (2h)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0611 + 0.174 - 0.148}{0.148}$$

$$E = 1.27$$

Mechanosynthesis of (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (3i):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-methoxybenzaldehyde (2i)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0680 + 0.174 - 0.189}{0.189}$$

$$E = 0.814$$

Mechanosynthesis of (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 2\text{-methoxybenzaldehyde (2j)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0680 + 0.174 - 0.160}{0.160}$$

$$E = 1.14$$

Mechanosynthesis of (furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{furan (2k)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0340 + 0.174 - 0.141}{0.141}$$

$$E = 1.19$$

Mechanosynthesis of (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (**3l**):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{thiophene (2l)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0421 + 0.174 - 0.151}{0.151}$$

$$E = 1.10$$

Mechanosynthesis of (cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (**3o**):

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{cyclohexane (2o)} + \text{NaCl} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.0421 + 0.174 - 0.137}{0.137}$$

$$E = 1.31$$

Electrochemistry, Deep Eutectic Solvent (DES) and conventional solution-based method

General formula used for compounds 3a-3b,3d-3e,3g,3i,3k,3l,3o obtained by electrochemically oxidative synthesis*

$$E = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2a - 2b,2d - 2e,2g,2i,2k,2l,2o)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

General formula used for compounds 3c

$$E = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2c)} + n - \text{BuLi} + \text{hexane} + \text{choline chloride} - \text{total product}}{\text{total product}}$$

General formula used for compounds 3f,3h,3j**

$$E = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2f,2h,2j)} + \text{THF} - \text{total product}}{\text{total product}}$$

*The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 2/1, v/v).

**The crude product was purified by recrystallization (THF-Methanol).

Electrochemically oxidative synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**):*

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4 - \text{chlorobenzaldehyde (2a)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.758 + 1.18 + 1.55 - 0.063}{0.063}$$

$$E = 55.96$$

Electrochemically oxidative synthesis of *(hydroxy(phenyl)methyl)diphenylphosphine oxide (3b)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{benzene (2b)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.2929 + 1.18 + 1.55 - 0.120}{0.120}$$

$$E = 25.03$$

Deep Eutectic Solvent (DES) synthesis of *(3-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3c)*:

$$E = \frac{\text{diphenylphosphine oxide} + 3\text{-chlorobenzaldehyde (2c)} + n\text{-BuLi} + \text{hexane} + \text{coline chloride} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.302 + 0.228 + 0.104 + 0.423 + 0.226 - 0.501}{0.501}$$

$$E = 1.56$$

Electrochemically oxidative synthesis of *(2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3d)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 2\text{-chlorobenzaldehyde (2d)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.758 + 1.18 + 1.55 - 0.0340}{0.0340}$$

$$E = 104.55$$

Electrochemically oxidative synthesis of *(4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-bromobenzaldehyde (2e)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.694 + 1.18 + 1.55 - 0.054}{0.054}$$

$$E = 64.28$$

Conventional solution synthesis of *(hydroxy(4-nitrophenyl)hydroxy)methyl)diphenylphosphine oxide (3f)***:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-nitrobenzaldehyde (2f)} + \text{THF} - \text{total product}}{\text{total product}}$$

$$E = \frac{1.01 + 0.756 + 17.76 - 1.17}{1.17}$$

$$E = 15.7$$

Electrochemically oxidative synthesis of *(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine Oxide (3g)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 3\text{-nitrobenzaldehyde (2g)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.5667 + 1.18 + 1.55 - 0.071}{0.071}$$

$$E = 46.86$$

Conventional solution synthesis of *(hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-hydroxibenzaldehyde (2h)} + \text{THF} - \text{total product}}{\text{total product}}$$

$$E = \frac{1.01 + 0.6106 + 17.76 - 1.542}{1.542}$$

$$E = 11.56$$

Electrochemically oxidative synthesis of *(Hydroxy(4-methoxy)methyl)diphenylphosphine Oxide (3i)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 4\text{-methoxybenzaldehyde (2i)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.511 + 1.18 + 1.55 - 0.291}{0.291}$$

$$E = 10.50$$

Conventional solution synthesis of *(hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j)***:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + 2\text{-methoxybenzaldehyde (2j)} + \text{THF} - \text{total product}}{\text{total product}}$$

$$E = \frac{1.01 + 0.6808 + 17.76 - 1.692}{1.692}$$

$$E = 10.50$$

Electrochemically oxidative synthesis of *(furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{furan (2k)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.2552 + 1.18 + 1.55 - 0.064}{0.064}$$

$$E = 47.22$$

Electrochemically oxidative synthesis of *(hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{thiophene (2l)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.3156 + 1.18 + 1.55 - 0.072}{0.072}$$

$$E = 42.70$$

Electrochemically oxidative synthesis of *(cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (3o)**:

Formula used:

$$E = \frac{\text{diphenylphosphine oxide} + \text{cyclohexane (2o)} + \text{MeCN} + \text{Dioxane} - \text{total product}}{\text{total product}}$$

$$E = \frac{0.101 + 0.3156 + 1.18 + 1.55 - 0.049}{0.049}$$

$$E = 63.21$$

VI.2. Energy usage calculations

Energy consumption and energy saved of the mechanochemistry (**3a-3l,3o**), and electrochemically oxidative (**3a-3b,3d-3e,3g,3i,3k,3l,3o**), Deep Eutectic Solvent (DES) (**3c**) or conventional solution-based synthesis (**3f,3h,3j**) processes were calculated based on the following equation (1 kWh = 3.6 MJ):

$$\text{Energy consumption by unit operation/process (kWh)} = \text{Power rating of the instrument (kW)} \times \text{Time of operation (h)}$$

$$\% \text{ Energy saved} = \frac{\text{Energy used (Conventional method)} - \text{Mechanosynthesis}}{\text{Energy used in Conventional method}} \times 100$$

Power consumption of:

- Vibratory shaker mill (Retsch, MM400) = 150 W (2 station)
- Hot plate stirrer (Hei-standard), = 800 W
- Electrochemically Power Supply (HYELEC HY-3010B) = 360 W
- Laboratory vacuum pump (conventional) = 1500 W

Reactions were calculated for 0.1 g scale reaction. Projections will show similar conclusions.

0.1 g:

Energy used for 0.1 g scale reaction:

Mechanosynthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**), (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**), (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3c**), (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3d**), (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3e**), (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (**3f**), (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (**3g**), (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (**3h**), (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (**3i**), (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (**3j**), (furan-2-yl)(hydroxy)methyl)diphenylphosphine oxide (**3k**), (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (**3l**), (cyclohexyl)(hydroxy)methyl)diphenylphosphine oxide (**3o**),

Energy used = (0.15 kW x 1.5 h) = 0.225 kwh/0.0001 kg = 2250 kwh/kg = 8100 MJ/kg (each product)

Electrochemically oxidative synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**), (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**), (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3e**), (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (**3g**), (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (**3i**), (furan-2-yl)(hydroxy)methyl)diphenylphosphine oxide (**3k**), (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (**3l**), (cyclohexyl)(hydroxy)methyl)diphenylphosphine oxide (**3o**),

Energy used = (0.36 kW x 1.5 h) + (1.5 kW x 1 h) = 2.04 kwh/0.0001 kg = 20400 kwh/kg = 73440 MJ/kg (each product)

Deep Eutectic Solvent (DES) synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3c**)

Energy used (**3c**) = (0.8 kW x 0.50 h) = 0.4 kwh/0.0001 kg = 4000 kwh/kg = 14400 MJ/kg (each product)

Conventional solution-based synthesis of (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (**3f**), (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (**3h**), (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (**3j**),

Energy used (3f) = (0.8 kW x 0.12 h) + (1.5 kW x 6 h) = 9.10 kwh/0.0001 kg = 90960 kwh/ kg = 327456 MJ/kg (each product)

Energy used (3h) = (0.8 kW x 0.83 h) + (1.5 kW x 6 h) = 9.66 kwh/0.0001 kg = 96640 kwh/ kg = 347904 MJ/kg (each product)

Energy used (3j) = (0.8 kW x 4 h) + (1.5 kW x 6 h) = 12.2 kwh/0.0001 kg = 122000 kwh/ kg = 439200 MJ/kg (each product)

To make the energy calculations easier to read and facilitate comparison between the mechanochemistry, electrochemically oxidative and solution-based synthesis, all the information has been summarised in Table SI_1:

Table SI_1. Energy consumption for the synthesis of compounds **3a** to **3j** using different methods.

Compound	Energy Consumption (kwh)	Energy Consumption (kwh.kg ⁻¹)	Energy Consumption (MJ.kg ⁻¹)
Mechanochemistry method			
3a-3l,3o	0.225	2250	8100
Electrochemically oxidative method			
3a-3b,3d-3e,3g,3i,3k,3l,3o	2.04	20400	73440
Deep Eutectic Solvent (DES) method			
3c	0.400	4000	14400
Conventional solution-based method			
3f	9.10	90960	327456
3h	9.66	96640	347904
3j	12.2	122000	439200

Energy saved

% Energy saved for the synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**), (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**), (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3e**), (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (**3g**), (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (**3i**), (furan-2-yl)(hydroxy)methyl)diphenylphosphine oxide (**3k**), (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (**3l**), (cyclohexyl)(hydroxy)methyl)diphenylphosphine oxide (**3o**):

$$\% \text{ Energy saved} = \frac{73440 \frac{\text{MJ}}{\text{Kg}} - 8100 \frac{\text{MJ}}{\text{Kg}}}{73440 \frac{\text{MJ}}{\text{Kg}}} \times 100$$

$$\% \text{ Energy saved} = 88.9 \% \text{ (each compound)}$$

% Energy saved for the synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3c**):

$$\% \text{ Energy saved} = \frac{14400 \frac{\text{MJ}}{\text{Kg}} - 8100 \frac{\text{MJ}}{\text{Kg}}}{14400 \frac{\text{MJ}}{\text{Kg}}} \times 100$$

$$\% \text{ Energy saved} = 43.7 \%$$

% Energy saved for the synthesis of (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (3f):

$$\% \text{ Energy saved} = \frac{327456 \frac{\text{MJ}}{\text{Kg}} - 8100 \frac{\text{MJ}}{\text{Kg}}}{327456 \frac{\text{MJ}}{\text{Kg}}} \times 100$$

$$\% \text{Energy saved} = 97.5 \%$$

% Energy saved for the synthesis of (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h):

$$\% \text{ Energy saved} = \frac{347904 \frac{\text{MJ}}{\text{Kg}} - 8100 \frac{\text{MJ}}{\text{Kg}}}{96640 \frac{\text{MJ}}{\text{Kg}}} \times 100$$

$$\% \text{Energy saved} = 97.7 \%$$

% Energy saved for the synthesis of (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j):

$$\% \text{ Energy saved} = \frac{439200 \frac{\text{MJ}}{\text{Kg}} - 43200 \frac{\text{MJ}}{\text{Kg}}}{691200 \frac{\text{MJ}}{\text{Kg}}} \times 100$$

$$\% \text{Energy saved} = 98.15 \%$$

VI.3.-. Process mass intensity (PMI)

Mechanosynthesis

General formula used for compounds 3a,3e-3h,3j

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2a,2e - 2h,2j)}}{\text{total product}}$$

General formula used for compounds 3b - 3d,3i,3k - 3l,3o

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2b - 2d,2i, 2k - 2l,2o)} + \text{sodium chloride}}{\text{total product}}$$

Mechanosynthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3a):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-chlorobenzaldehyde (2a)}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0702}{0.144}$$

$$PMI = 1.19$$

Mechanosynthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (3b):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{benzene (2b)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0391 + 0.174}{0.143}$$

$$PMI = 2.19$$

Mechanosynthesis of ((3-chlorophenyl)(hydroxy)diphenylphosphine oxide (3c):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 3\text{-chlorobenzaldehyde (2c)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0702 + 0.174}{0.144}$$

$$PMI = 2.39$$

Mechanosynthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3d):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 2\text{-chlorobenzaldehyde (2d)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0702 + 0.174}{0.144}$$

$$PMI = 2.39$$

Mechanosynthesis of (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-bromobenzaldehyde (2e)}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0925}{0.156}$$

$$PMI = 1.24$$

Mechanosynthesis of (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (3f):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-nitrobenzaldehyde (2f)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0756}{0.145}$$

$$PMI = 1.21$$

Mechanosynthesis of (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (3g):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 3\text{-nitrobenzaldehyde (2g)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0756}{0.169}$$

$$PMI = 1.04$$

Mechanosynthesis of (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-hydroxybenzaldehyde (2h)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0611 + 0.174}{0.148}$$

$$PMI = 2.27$$

Mechanosynthesis of (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (3i):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-methoxybenzaldehyde (2i)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0680 + 0.174}{0.189}$$

$$PMI = 1.81$$

Mechanosynthesis of (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 2\text{-methoxybenzaldehyde (2j)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0680 + 0.174}{0.160}$$

$$PMI = 2.14$$

Mechanosynthesis of (furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k):

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{furan (2k)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0340 + 0.174}{0.141}$$

$$PMI = 2.19$$

Mechanosynthesis of (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l):

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{thiophene (2l)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0421 + 0.174}{0.151}$$

$$PMI = 2.10$$

Mechanosynthesis of (cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (3o):

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{cyclohexane (2o)} + \text{NaCl}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.0421 + 0.174}{0.137}$$

$$PMI = 2.31$$

Electrochemistry, Deep Eutectic Solvent (DES) and conventional solution-based method

General formula used for compounds 3a-3b,3d-3e,3g,3i,3k,3l,3o obtained by electrochemically oxidative synthesis*

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2a - 2b,2d - 2e,2g,2i,2k,2l,2o)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

General formula used for compounds 3c

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2c)} + n - \text{BuLi} + \text{hexane} + \text{coline chloride}}{\text{total product}}$$

General formula used for compounds 3f,3h,3j**

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{aldehyde (2f,2h,2j)} + \text{THF}}{\text{total product}}$$

***The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 2/1, v/v).**

****The crude product was purified by recrystallization (THF-Methanol).**

Electrochemically oxidative synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3a)*:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4 - \text{chlorobenzaldehyde (1a)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.758 + 1.18 + 1.55}{0.063}$$

$$PMI = 56.94$$

Electrochemically oxidative synthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (3b)*:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{benzene (2b)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.2929 + 1.18 + 1.55}{0.120}$$

$$PMI = 25.03$$

Deep Eutectic Solvent (DES) synthesis of (3-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3c):

$$PMI = \frac{\text{diphenylphosphine oxide} + 3 - \text{chlorobenzaldehyde (2c)} + n - \text{BuLi} + \text{hexane} + \text{coline chloride}}{\text{total product}}$$

$$PMI = \frac{0.302 + 0.228 + 0.104 + 0.423 + 0.226}{0.501}$$

$$PMI = 2.56$$

Electrochemically oxidative synthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3d)*:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 2\text{-chlorobenzaldehyde (2d)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.758 + 1.18 + 1.55}{0.0340}$$

$$PMI = 105.6$$

Electrochemically oxidative synthesis of (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e)*:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-bromobenzaldehyde (2e)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.694 + 1.18 + 1.55}{0.054}$$

$$PMI = 65.3$$

Conventional solution synthesis of (hydroxy(4-nitrophenyl)hydroxy)methyl)diphenylphosphine oxide (3f)**:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-nitrobenzaldehyde (2f)} + \text{THF}}{\text{total product}}$$

$$PMI = \frac{1.01 + 0.756 + 17.76}{1.17}$$

$$PMI = 16.7$$

Electrochemically oxidative synthesis of (Hydroxy(3-nitrophenyl)methyl)diphenylphosphine Oxide (3g)*:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 3\text{-nitrobenzaldehyde (2g)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.5667 + 1.18 + 1.55}{0.071}$$

$$PMI = 47.86$$

Conventional solution synthesis of (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h)**:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-hydroxybenzaldehyde (2h)} + \text{THF}}{\text{total product}}$$

$$PMI = \frac{1.01 + 0.6106 + 17.76}{1.542}$$

$$PMI = 12.56$$

Electrochemically oxidative synthesis of *(Hydroxy(4-methoxy)methyl)diphenylphosphine Oxide (3i)**:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 4\text{-methoxybenzaldehyde (2i)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.511 + 1.18 + 1.55}{0.291}$$

$$PMI = 11.5$$

Conventional solution synthesis of *(hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j)***:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + 2\text{-methoxybenzaldehyde (2j)} + \text{THF}}{\text{total product}}$$

$$PMI = \frac{1.01 + 0.6808 + 17.76}{1.692}$$

$$PMI = 11.5$$

Electrochemically oxidative synthesis of *(furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k)**:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{furan (2k)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.2552 + 1.18 + 1.55}{0.064}$$

$$PMI = 48.2$$

Electrochemically oxidative synthesis of *(hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l)**:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{thiophene (2l)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.3156 + 1.18 + 1.55}{0.072}$$

$$PMI = 43.7$$

Electrochemically oxidative synthesis of *(cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (3o)**:

Formula used:

$$PMI = \frac{\text{diphenylphosphine oxide} + \text{cyclohexane (2o)} + \text{MeCN} + \text{Dioxane}}{\text{total product}}$$

$$PMI = \frac{0.101 + 0.3156 + 1.18 + 1.55}{0.049}$$

$$PMI = 64.2$$

VI.4.- Generalized reaction mass efficiency (RME)

Mechanosynthesis

General formula used for compounds 3a,3e-3h,3j

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{aldehyde (2a,2e - 2h,2j)}} \times 100$$

General formula used for compounds 3b - 3d,3i, 3k - 3l,3o

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{aldehyde (2b - 2d,2i,2k - 2l,2o)} + \text{sodium chloride}} \times 100$$

Mechanosynthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-chlorobenzaldehyde (2a)}} \times 100$$

$$RME = \frac{0.144}{0.101 + 0.0702} \times 100$$

$$RME = 84.1 \%$$

Mechanosynthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{benzene (2b)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.143}{0.101 + 0.0391 + 0.174} \times 100$$

$$RME = 45.6 \%$$

Mechanosynthesis of ((3-chlorophenyl)(hydroxy)diphenylphosphine oxide (**3c**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 3\text{-chlorobenzaldehyde (2c)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.144}{0.101 + 0.0702 + 0.174} \times 100$$

$$RME = 41.8 \%$$

Mechanosynthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3d**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 2\text{-chlorobenzaldehyde (2d)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.144}{0.101 + 0.0702 + 0.174} \times 100$$

$$RME = 41.8 \%$$

Mechanosynthesis of (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3e**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-bromobenzaldehyde (2e)}} \times 100$$

$$RME = \frac{0.156}{0.101 + 0.0925} \times 100$$

$$RME = 80.6 \%$$

Mechanosynthesis of (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (**3f**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-nitrobenzaldehyde (2f)}} \times 100$$

$$RME = \frac{0.145}{0.101 + 0.0756} \times 100$$

$$RME = 82.6 \%$$

Mechanosynthesis of (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (**3g**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 3\text{-nitrobenzaldehyde (2g)}} \times 100$$

$$RME = \frac{0.169}{0.101 + 0.0756} \times 100$$

$$RME = 96.2 \%$$

Mechanosynthesis of (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (**3h**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-hydroxybenzaldehyde (2h)}} \times 100$$

$$RME = \frac{0.148}{0.101 + 0.0611 + 0.174} \times 100$$

$$RME = 44.1 \%$$

Mechanosynthesis of (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (3i):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-methoxybenzaldehyde (2i)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.189}{0.101 + 0.0680 + 0.174} \times 100$$

$$RME = 55.2 \%$$

Mechanosynthesis of (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 2\text{-methoxybenzaldehyde (2j)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.160}{0.101 + 0.0680 + 0.174} \times 100$$

$$RME = 46.7 \%$$

Mechanosynthesis of (furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{furan (2k)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.141}{0.101 + 0.0340 + 0.174} \times 100$$

$$RME = 45.7 \%$$

Mechanosynthesis of (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{thiophene (2l)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.151}{0.101 + 0.0421 + 0.174} \times 100$$

$$RME = 47.6 \%$$

Mechanosynthesis of (cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (**3o**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{cyclohexane (2o)} + \text{NaCl}} \times 100$$

$$RME = \frac{0.137}{0.101 + 0.0421 + 0.174} \times 100$$

$$RME = 43.3 \%$$

Electrochemistry, Deep Eutectic Solvent (DES) and conventional solution-based method

General formula used for compounds 3a-3b,3d-3e,3g,3i,3k,3l,3o obtained by electrochemically oxidative synthesis*

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{aldehyde (2a - 2b,2d - 2e,2g,2i,2k,2l,2o)} + \text{MeCN} + \text{Dioxane}} \times 100$$

General formula used for compounds 3c

$$RME = \frac{\text{total product}}{\text{iphenylphosphine oxide} + \text{aldehyde (2c)} + n - \text{BuLi} + \text{hexane} + \text{coline chloride} - \text{total product}} \times 100$$

General formula used for compounds 3f,3h,3j**

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{aldehyde (2f,2h,2j)} + \text{THF}} \times 100$$

*The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 2/1, v/v).

**The crude product was purified by recrystallization (THF-Methanol).

Electrochemically oxidative synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4 - \text{chlorobenzaldehyde (1a)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.063}{0.101 + 0.758 + 1.18 + 1.55} \times 100$$

$$RME = 1.75 \%$$

Electrochemically oxidative synthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**):

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{benzene (2b)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.120}{0.101 + 0.2929 + 1.18 + 1.55} \times 100$$

$$RME = 4.00 \%$$

Deep Eutectic Solvent (DES) synthesis of (3-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3c):

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 3\text{-chlorobenzaldehyde(2c)} + n\text{-BuLi} + \text{hexane} + \text{collidine}}$$

$$RME = \frac{0.501}{0.302 + 0.228 + 0.104 + 0.423 + 0.226} \times 100$$

$$RME = 39.1 \%$$

Electrochemically oxidative synthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3d)*:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 2\text{-chlorobenzaldehyde (2d)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.0340}{0.101 + 0.758 + 1.18 + 1.55} \times 100$$

$$RME = 0.947 \%$$

Electrochemically oxidative synthesis of (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e)*:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-bromobenzaldehyde (2e)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.054}{0.101 + 0.694 + 1.18 + 1.55} \times 100$$

$$RME = 1.53 \%$$

Conventional solution synthesis of (hydroxy(4-nitrophenyl)hydroxy)methyl)diphenylphosphine oxide (3f)**:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-nitrobenzaldehyde (2f)} + \text{THF}} \times 100$$

$$RME = \frac{1.17}{1.01 + 0.756 + 17.76} \times 100$$

$$RME = 5.98 \%$$

Electrochemically oxidative synthesis of *(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine Oxide (3g)**:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 3\text{-nitrobenzaldehyde (2g)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.071}{0.101 + 0.5667 + 1.18 + 1.55} \times 100$$

$$RME = 2.09 \%$$

Conventional solution synthesis of *(hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h)***:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-hydroxibenzaldehyde (2h)} + \text{THF}} \times 100$$

$$RME = \frac{1.542}{1.01 + 0.6106 + 17.76} \times 100$$

$$RME = 7.96 \%$$

Electrochemically oxidative synthesis of *(Hydroxy(4-methoxy)methyl)diphenylphosphine Oxide (3i)**:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 4\text{-methoxybenzaldehyde (2i)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.291}{0.101 + 0.511 + 1.18 + 1.55} \times 100$$

$$RME = 8.69 \%$$

Conventional solution synthesis of *(hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j)***:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + 2\text{-methoxybenzaldehyde (2j)} + \text{THF}} \times 100$$

$$RME = \frac{1.692}{1.01 + 0.6808 + 17.76} \times 100$$

$$RME = 8.69 \%$$

Electrochemically oxidative synthesis of *(furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k)**:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{furan (2k)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.064}{0.101 + 0.2552 + 1.18 + 1.55} \times 100$$

$$RME = 2.07$$

Electrochemically oxidative synthesis of *(hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l)**:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{thiophene (2l)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.072}{0.101 + 0.3156 + 1.18 + 1.55} \times 100$$

$$RME = 2.29 \%$$

Electrochemically oxidative synthesis of *(cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (3o)**:

Formula used:

$$RME = \frac{\text{total product}}{\text{diphenylphosphine oxide} + \text{cyclohexane (2n)} + \text{MeCN} + \text{Dioxane}} \times 100$$

$$RME = \frac{0.049}{0.101 + 0.3156 + 1.18 + 1.55} \times 100$$

$$RME = 1.56 \%$$

VI.5.-. Real atom economy (RAE)

Mechanosynthesis

General formula used for compounds 3a,3e-3h,3j

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide} + \text{aldehyde (2a,2e - 2h,2j))}} \times 100$$

General formula used for compounds 3b - 3d,3i,3k - 3l,3o

$$RAE = \frac{\text{Weight of the desired product}}{\text{Weight (diphenylphosphine oxide} + \text{aldehyde (2b - 2d,2i,2k - 2l,2o)} + \text{sodium chloride)}} \times 100$$

Mechanosynthesis of *(4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3a)*:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide} + \text{4 - chlorobenzaldehyde (1a))}} \times 100$$

$$RAE = \frac{342.06 * 0.85}{202.19 + 140.57} \times 100$$

$$RAE = 85.0 \%$$

Mechanosynthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (3b):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + benzene (2b) + NaCl)}} \times 100$$

$$RAE = \frac{308.32 * 0.93}{202.19 + 78.11 + 55.44} \times 100$$

$$RAE = 85.4 \%$$

Mechanosynthesis of ((3-chlorophenyl)(hydroxy)diphenylphosphine oxide (3c):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 3 - chlorobenzaldehyde (2c) + NaCl)}} \times 100$$

$$RAE = \frac{329.74 * 0.84}{202.19 + 140.6 + 55.44} \times 100$$

$$RAE = 69.6 \%$$

Mechanosynthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (3d):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 2 - chlorobenzaldehyde (2d) + NaCl)}} \times 100$$

$$RAE = \frac{329.74 * 0.85}{202.19 + 140.6 + 55.44} \times 100$$

$$RAE = 70.4 \%$$

Mechanosynthesis of (4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - bromobenzaldehyde (2e))}} \times 100$$

$$RAE = \frac{387.21 * 0.81}{202.19 + 185.03} \times 100$$

$$RAE = 81.0 \%$$

Mechanosynthesis of (hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide (3f):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - nitrobenzaldehyde (2f))}} \times 100$$

$$RAE = \frac{353.32 * 0.78}{202.19 + 151.12} \times 100$$

$$RAE = 78.0 \%$$

Mechanosynthesis of (hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide (3g):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 3 - nitrobenzaldehyde (2g))}} \times 100$$

$$RAE = \frac{353.31 * 0.91}{202.19 + 151.12} \times 100$$

$$RAE = 91.0 \%$$

Mechanosynthesis of (hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h)

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - hydroxybenzaldehyde (2h) + NaCl)}} \times 100$$

$$RAE = \frac{324.32 * 0.88}{202.19 + 122.12 + 55.44} \times 100$$

$$RAE = 75.2 \%$$

Mechanosynthesis of (hydroxy(4-methoxy)methyl)diphenylphosphine oxide (3i):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - methoxybenzaldehyde (2i) + NaCl)}} \times 100$$

$$RAE = \frac{338.34 * 0.77}{202.19 + 136.15 + 55.44} \times 100$$

$$RAE = 66.2 \%$$

Mechanosynthesis of (hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j):

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 2 - methoxybenzaldehyde (2j) + NaCl)}} \times 100$$

$$RAE = \frac{338.34 * 0.91}{202.19 + 136.15 + 55.44} \times 100$$

$$RAE = 78.2 \%$$

Mechanosynthesis of (furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k):

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + furan (2k) + NaCl)}} \times 100$$

$$RAE = \frac{292.28 * 0.95}{202.19 + 66.07 + 55.44} \times 100$$

$$RAE = 85.8 \%$$

Mechanosynthesis of (hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l):

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + thiophene (2l) + NaCl)}} \times 100$$

$$RAE = \frac{314.34 * 0.94}{202.19 + 84.14 + 55.44} \times 100$$

$$RAE = 86.5 \%$$

Mechanosynthesis of (cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (3o):

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + cyclohexane (2o) + NaCl)}} \times 100$$

$$RAE = \frac{314.36 * 0.92}{202.19 + 84.16 + 55.44} \times 100$$

$$RAE = 84.6 \%$$

Electrochemistry, Deep Eutectic Solvent (DES) and conventional solution-based method

General formula used for compounds 3a-3b,3d-3e,3g,3i,3k,3l,3o obtained by electrochemically oxidative synthesis*

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + aldehyde (2a - 2b,2d - 2e,2g,2i,2k,2l,2o) + MeCN + Dioxane)}} \times 100$$

General formula used for compounds 3c

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + aldehyde (2c) + n - BuLi + hexane + coline chloride)}} \times 100$$

General formula used for compounds 3f,3h,3j**

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + aldehyde (2f,2h,2j) + THF)}} \times 100$$

*The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 2/1, v/v).

**The crude product was purified by recrystallization (THF-Methanol).

Electrochemically oxidative synthesis of (4-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3a**):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - chlorobenzaldehyde (1a) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{342.06 * 0.37}{202.19 + 140.57 + 41.05 + 88.11} \times 100$$

$$RAE = 27.8 \%$$

Electrochemically oxidative synthesis of (hydroxy(phenyl)methyl)diphenylphosphine oxide (**3b**):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + benzene (2b) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{308.32 * 0.78}{202.19 + 78.11 + 41.05 + 88.11} \times 100$$

$$RAE = 58.7 \%$$

Deep Eutectic Solvent (DES) synthesis of (3-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3c**):

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 3 - chlorobenzaldehyde (2c) + n - BuLi + hexane + coline chloride)}} \times 100$$

$$RAE = \frac{329.74 * 0.90}{202.19 + 140.6 + 64.1 + 86.2 + 139.7} \times 100$$

$$RAE = 46.9 \%$$

Electrochemically oxidative synthesis of (2-chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide (**3d**):

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 2 - chlorobenzaldehyde (2d) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{329.74 * 0.20}{202.19 + 140.6 + 41.05 + 88.11} \times 100$$

$$RAE = 14.0 \%$$

Electrochemically oxidative synthesis of *(4-bromophenyl)(hydroxy)methyl)diphenylphosphine oxide (3e)**:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - bromobenzaldehyde (2e) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{387.21 * 0.28}{202.19 + 185.03 + 41.05 + 88.11} \times 100$$

$$RAE = 21.0 \%$$

Conventional solution synthesis of *(hydroxy(4-nitrophenyl)hydroxy)methyl)diphenylphosphine oxide (3f)***:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - nitrobenzaldehyde (2f) + THF)}} \times 100$$

$$RAE = \frac{353.31 * 0.69}{202.19 + 151.12 + 72.11} \times 100$$

$$RAE = 57.3 \%$$

Electrochemically oxidative synthesis of *(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine Oxide (3g)**:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 3 - nitrobenzaldehyde (2g) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{353.31 * 0.40}{202.19 + 151.12 + 41.05 + 88.11} \times 100$$

$$RAE = 29.3 \%$$

Conventional solution synthesis of *(hydroxy(4-hydroxy)methyl)diphenylphosphine oxide (3h)**:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - hydroxibenzaldehyde (2h) + THF)}} \times 100$$

$$RAE = \frac{324.32 * 0.82}{202.19 + 122.12 + 72.11} \times 100$$

$$RAE = 67.1 \%$$

Electrochemically oxidative synthesis of *(Hydroxy(4-methoxy)methyl)diphenylphosphine Oxide (3i)**:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 4 - methoxybenzaldehyde (2i) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{338.34 * 0.30}{202.19 + 136.15 + 72.11} \times 100$$

$$RAE = 24.7 \%$$

Conventional solution synthesis of *(hydroxy(2-methoxy)methyl)diphenylphosphine oxide (3j)***:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + 2 - methoxybenzaldehyde (2j) + THF)}} \times 100$$

$$RAE = \frac{338.34 * 0.91}{202.19 + 136.15 + 72.11} \times 100$$

$$RAE = 75.0 \%$$

Electrochemically oxidative synthesis of *(furan-2-yl(hydroxy)methyl)diphenylphosphine oxide (3k)**:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + furan (2k) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{298.28 * 0.43}{202.19 + 66.07 + 41.05 + 88.11} \times 100$$

$$RAE = 32.3 \%$$

Electrochemically oxidative synthesis of *(hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide (3l)**:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + thiophene (2l) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{314.34 * 0.46}{202.19 + 84.14 + 41.05 + 88.11} \times 100$$

$$RAE = 34.8 \%$$

Electrochemically oxidative synthesis of *(cyclohexyl(hydroxy)methyl)diphenylphosphine oxide (3o)**:

Formula used:

$$RAE = \frac{\text{Weight total product}}{\text{Weight (diphenylphosphine oxide + cyclohexane (2o) + MeCN + Dioxane)}} \times 100$$

$$RAE = \frac{314.36 * 0.31}{202.19 + 84.16 + 41.05 + 88.11} * 100$$

$$RAE = 23.5 \%$$

VII.- Cost calculation

Table SI_2. Average Price of Electricity to household and non-household medium size consumer, by European Country, 2021 and 2022 (euro per Kilowatthour) reproduced from (<https://ec.europa.eu/eurostat/databrowser/bookmark/df2fd759-e5cb-4633-a73b-922ffce6bb7a?lang=en>) accessed in January 2024. Note that United Kingdom 2021 values have been reproduced from (https://www.ukpower.co.uk/home_energy/tariffs-per-unit-kwh) and (<https://www.gov.uk/government/statistical-data-sets/gas-and-electricity-prices-in-the-non-domestic-sector>) to household and non-household respectively. Data use for calculation in Table S3 and S4 are highlighted in yellow.

Energy indicator	Medium size household		Non-household. medium size consumers	
	2021	2022	2021	2022
TIME				
GEO (Labels)				
European Union - 27 countries (from 2020)	0.2203	0.2525	0.0859	0.1604
Euro area - 20 countries (from 2023)	:	:	:	:
Euro area - 19 countries (2015-2022)	:	:	:	:
Belgium	0.2702	0.3437	0.081	0.1519
Bulgaria	0.1024	0.1093	0.0842	0.2372
Czechia	0.1802	0.2445	0.0739	0.1444
Denmark	0.29	0.4559	0.0725	0.1595
Germany (until 1990 former territory of the FRG)	0.3193	0.3279	0.0908	0.1512
Estonia	0.1324	0.2056	0.0834	0.1502
Ireland	0.2555	0.2324	0.1378	0.2104
Greece	0.168	0.2101	0.089	0.283
Spain	0.2323	0.3071	0.0931	0.1769
France	0.1946	0.2092	0.085	0.1203
Croatia	0.1291	0.1354	0.0881	0.141
Italy	0.2259	0.2115	0.0939	0.2354
Cyprus	0.1976	0.2607	0.1091	0.1722
Latvia	0.1403	0.1759	0.0849	0.1468
Lithuania	0.1348	0.1497	0.0932	0.1758
Luxembourg	0.1988	0.2017	0.0836	0.1230
Hungary	0.1003	0.0948	0.0818	0.1598
Malta	0.1285	0.1298	0.133	0.1332
Netherlands	0.1281	0.0451	0.0721	0.1339
Austria	0.2216	0.2249	0.0884	0.1437
Poland	0.1548	0.1464	0.0731	0.0988
Portugal	0.2089	0.2199	0.0755	0.1351
Romania	0.1536	0.2362	0.0824	0.2149
Slovenia	0.1662	0.1390	0.0757	0.1435
Slovakia	0.1668	0.1796	0.0929	0.1892
Finland	0.1767	0.1934	0.0669	0.0802
Sweden	0.2114	0.2278	0.0705	0.1115
Iceland	0.1355	0.1530	0.0449	0.0732
Liechtenstein	0.2071	0.2201	0.0863	0.1260
Norway	0.1826	0.1994	0.0715	0.1369
Switzerland	:	:	:	:
United Kingdom	0.2407*	0.2796*	0.1546**	0.2505**
Montenegro	0.098	0.0961	0.0773	0.0762
North Macedonia	0.0841	0.094	0.0752	0.1685
Albania	0.0925 (e)	0.0941 (e)	0.1039 (e)	0.1057 (e)
Serbia	0.0791	0.0808	0.0702	0.0893
Turkey	0.0834	0.0866	0.0648	0.1171
Bosnia and Herzegovina	0.0875	0.0887	0.0719	0.0714
Kosovo (under United Nations Security Council Resolution 1244/99)	0.0605 (e)	0.0611 (e)	0.0635 (e)	0.0659 (e)
Moldova	0.0851	0.1172	0.0633	0.0761
Ukraine	0.0485	:	0.0595	:
Georgia	0.0631	:	0.0713	:
Special value				
:		not available		
Available flags:				
e		estimated		
p		provisional		

* https://www.ukpower.co.uk/home_energy/tariffs-per-unit-kwh

** <https://www.gov.uk/government/statistical-data-sets/gas-and-electricity-prices-in-the-non-domestic-sector>

Table SI_3. Average costs calculation in euro to medium size household consumers in euro for the mechanochemical, deep eutectic solvents (DES), electrochemical and conventional solution-based method of 1 kg of the compounds **3a-l,3o**.

Year	2021	2022	2021	2022	2021	2022	2021	2022	2021	2022	2021	2022
	Mechanosynthesis 3a-3l,3o		Electrochemistry method 3a-3b,3d- 3e,3g,3i,3k,3l,3o		Deep Eutectic Solvent method (DES) 3c		Conventional solution-based method 3f		Conventional solution-based method 3h		Conventional solution-based method (3j)	
Spain	522.7	691.0	4738.9	6264.8	929.2	1228.4	21124.2	27970.4	22449.5	29678.1	28340.6	37466.2
Germany	718.4	737.8	6513.7	6689.2	1277.2	1311.6	29036.7	29814.3	30857.2	31688.3	38954.6	40003.8
France	437.9	470.7	3969.8	4267.7	778.4	836.8	17692.4	19022.3	18806.1	20217.1	23741.2	25522.4
UK	541.6	629.1	4910.3	5703.8	962.8	1118.4	21890.5	25425.2	23261.2	27020.5	29365.4	34111.2
Average	555.1	632.1	5033.2	5731.4	986.9	1098.8	22435.9	25557.9	23843.5	27151.0	30100.5	34275.9
Total average	593.6		5382.3		1042.9		25557.9		25497.3		32188.2	

Table SI_4. Average costs calculation to non-household, medium size consumers in euro for the mechanochemical, deep eutectic solvents (DES), electrochemical and conventional solution-based method of 1 kg of the compounds **3a-l,3o**.

<i>Year</i>	2021	2022	2021	2022	2021	2022	2021	2022	2021	2022	2021	2022
	Mechanosynthesis 3a-3l,3o		Electrochemistry method 3a-3b,3d- 3e,3g,3i,3k,3l,3o		Deep Eutectic Solvent method (DES) 3c		Conventional solution-based method 3f		Conventional solution-based method 3h		Conventional solution-based method 3j	
Spain	209.5	398.0	1899.2	3608.8	372.4	707.6	8468.6	16096.5	8997.2	17095.6	11358.2	21581.8
Germany	204.3	340.2	1852.3	3084.5	363.2	604.2	8259.2	13749.9	8774.9	14612.0	11077.6	18446.4
France	191.3	270.7	1734.0	2454.1	340.0	481.2	7731.6	10947.9	8214.4	11625.8	10370.0	14676.6
UK	347.9	563.6	3153.8	5110.2	618.4	1002.0	14060.2	22775.0	14940.5	24208.3	18861.2	30561.0
Average	238.2	393.1	2159.9	3564.4	423.5	698.9	9630.9	15892.8	10231.8	16885.4	12916.8	21316.5
Total average	593.6		2862.1		561.2		12761.8		13558.6		17116.6	

VIII.- References.

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IX.- Copy of NMR Spectra.

((4-Chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide 3a

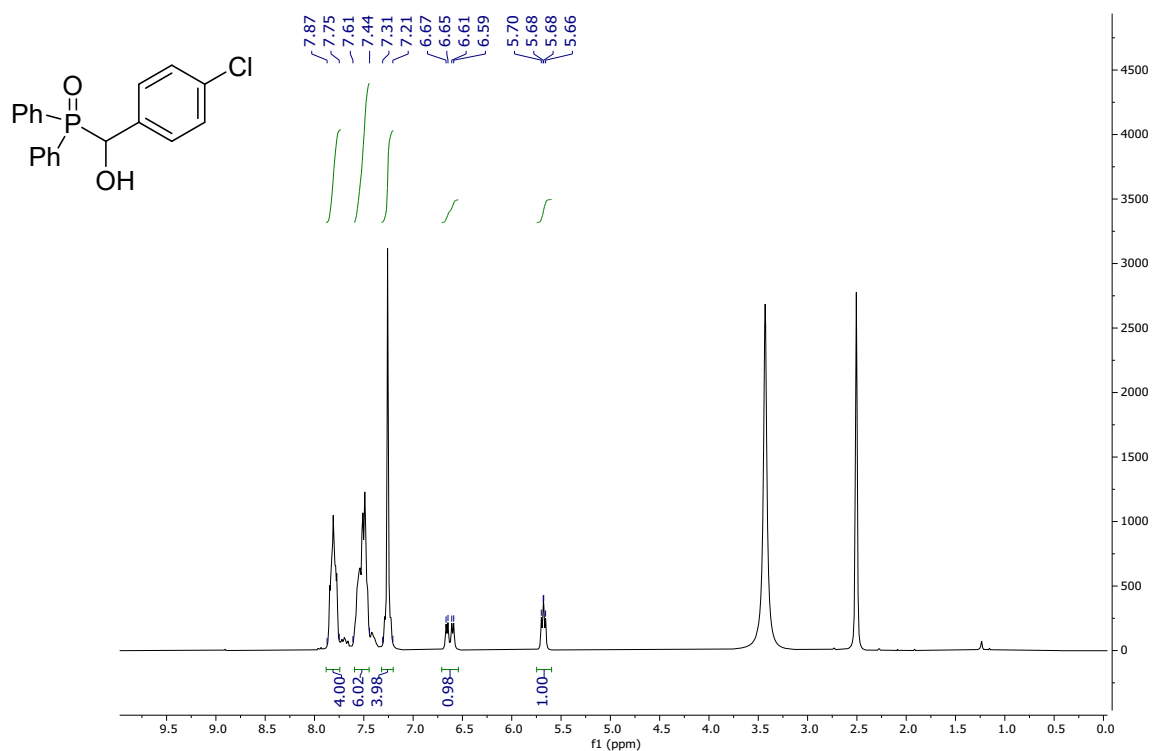


Figure SI_3: ¹H-NMR for 3a in DMSO-*d*⁶ (300 MHz).

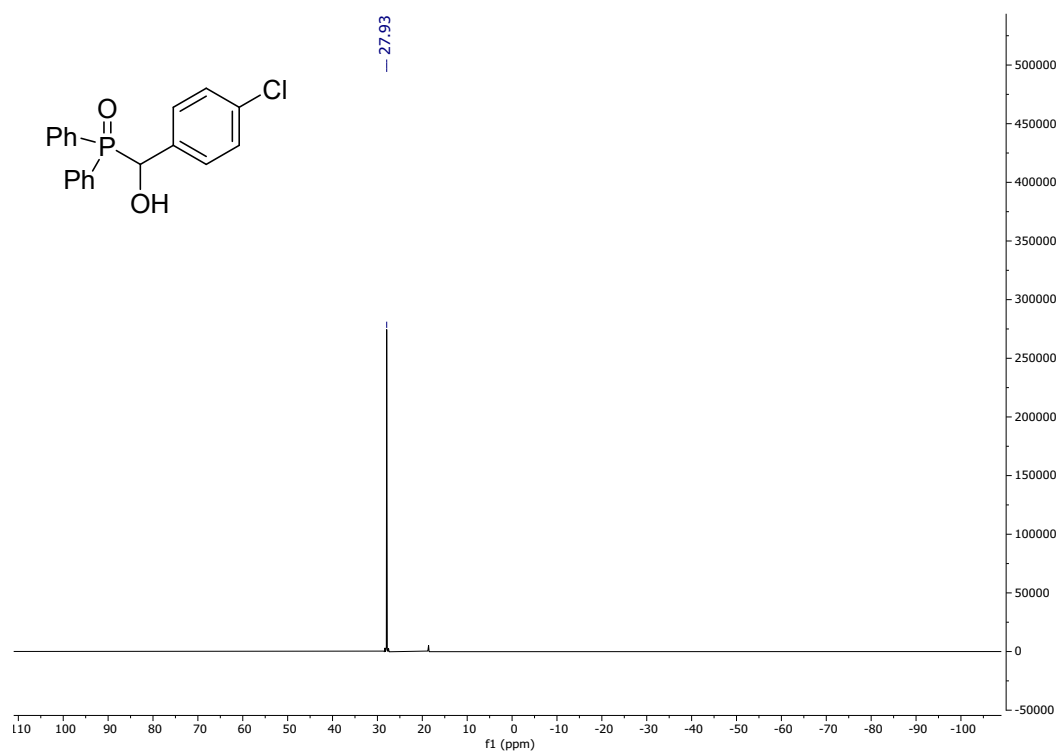


Figure SI_4: ³¹P-NMR for 3a in DMSO-*d*⁶ (121 MHz).

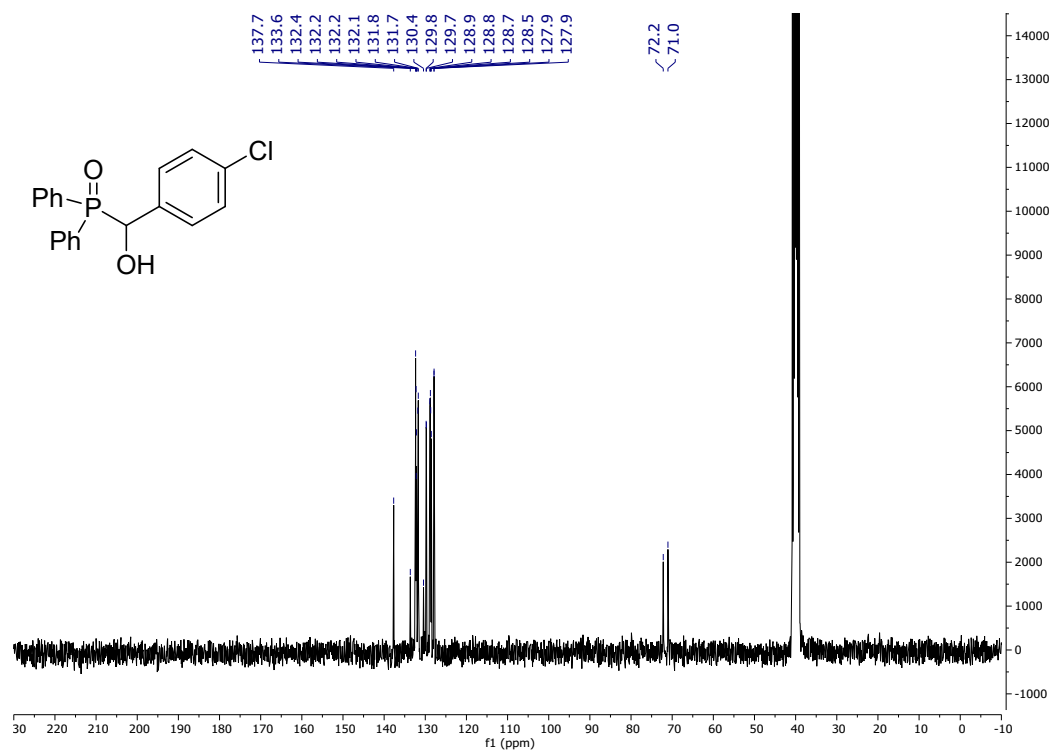


Figure SI_5: ¹³C-NMR for 3a in DMSO-*d*⁶ (75 MHz).

(Hydroxy(phenyl)methyl)diphenylphosphine oxide 3b

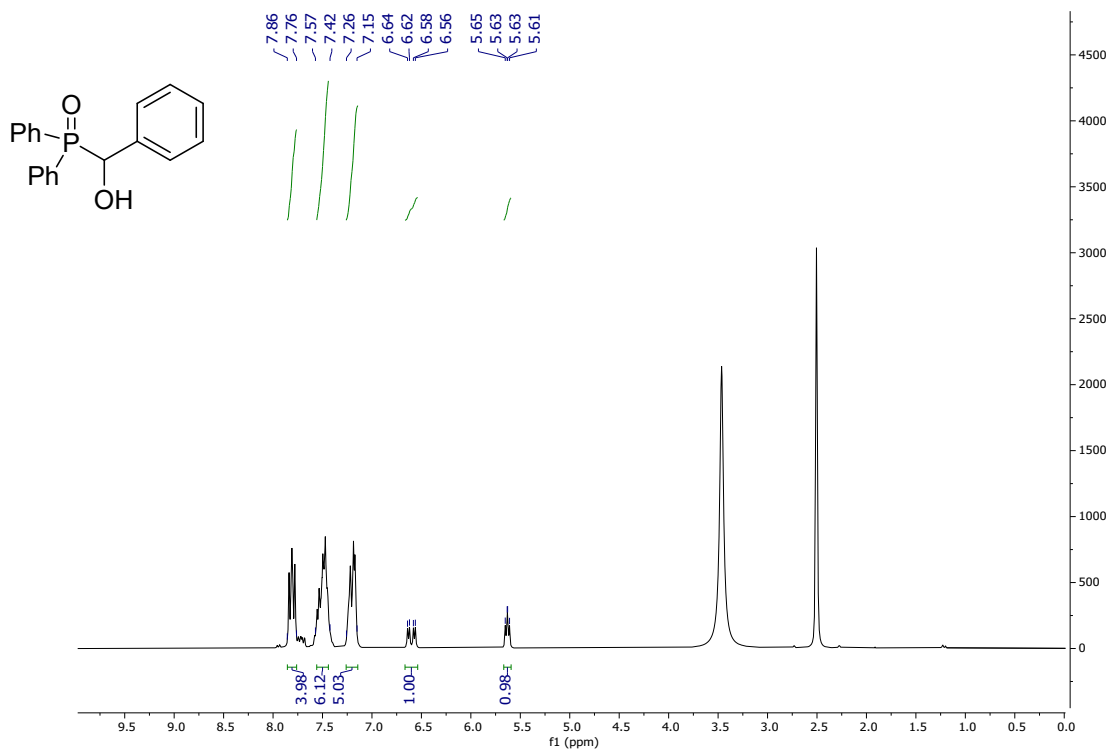


Figure SI_6: ¹H-NMR for 3b in DMSO-*d*⁶ (300 MHz).



Figure SI_7: ^{31}P -NMR for **3b** in $\text{DMSO-}d^6$ (121 MHz).

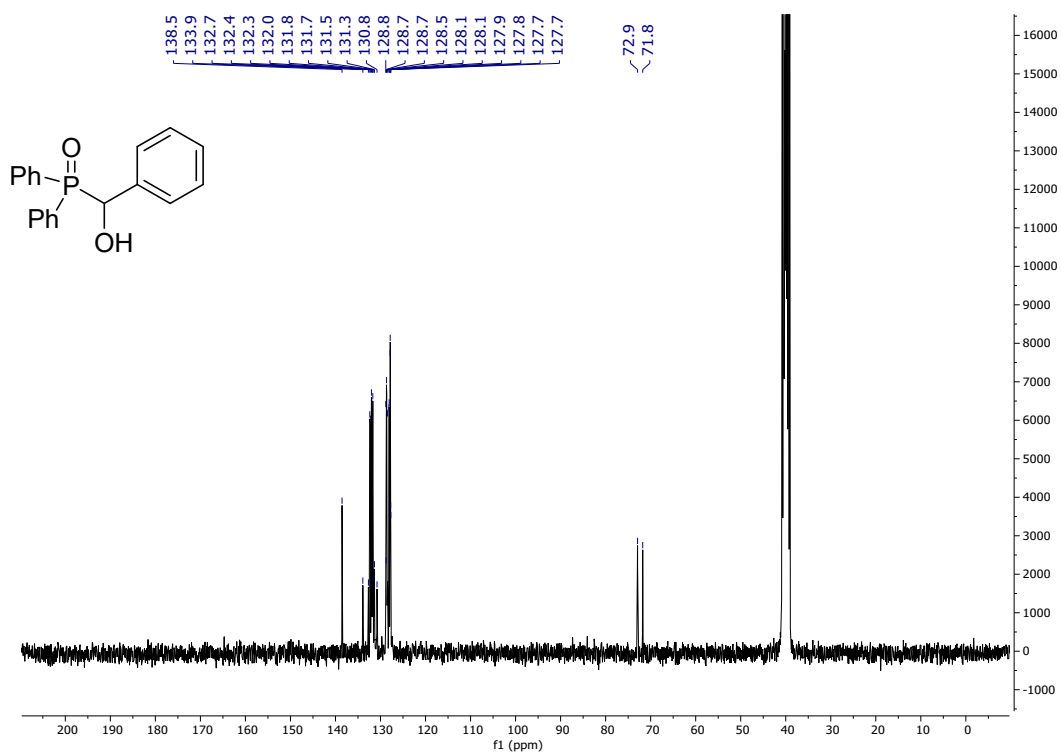


Figure SI_8: ^{13}C -NMR for **3b** in $\text{DMSO-}d^6$ (75 MHz).

((3-Chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide 3c

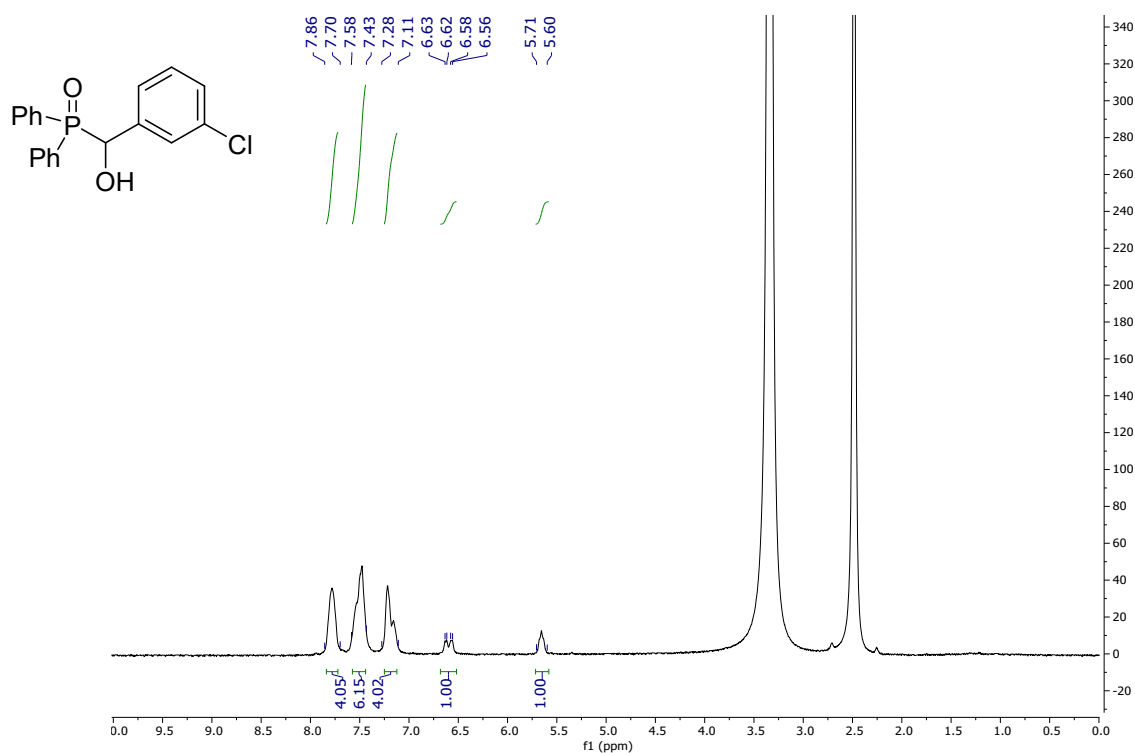


Figure SI_9: $^1\text{H-NMR}$ for **3c** in $\text{DMSO-}d^6$ (300 MHz).

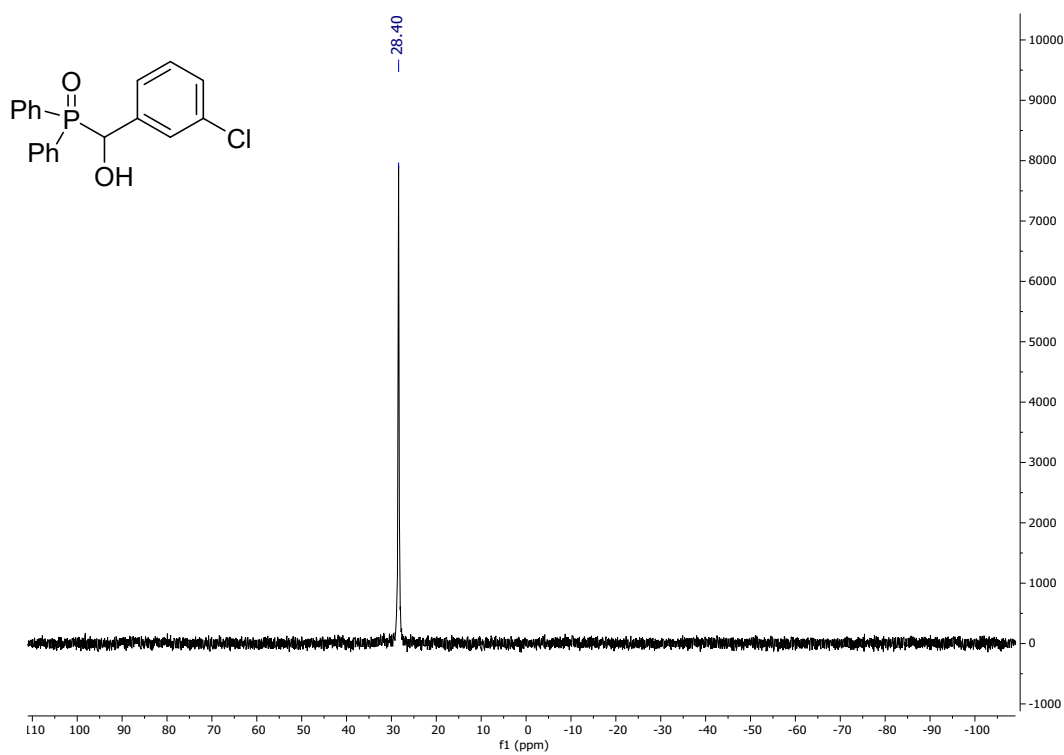


Figure SI_10: $^{31}\text{P-NMR}$ for **3c** in $\text{DMSO-}d^6$ (121 MHz).

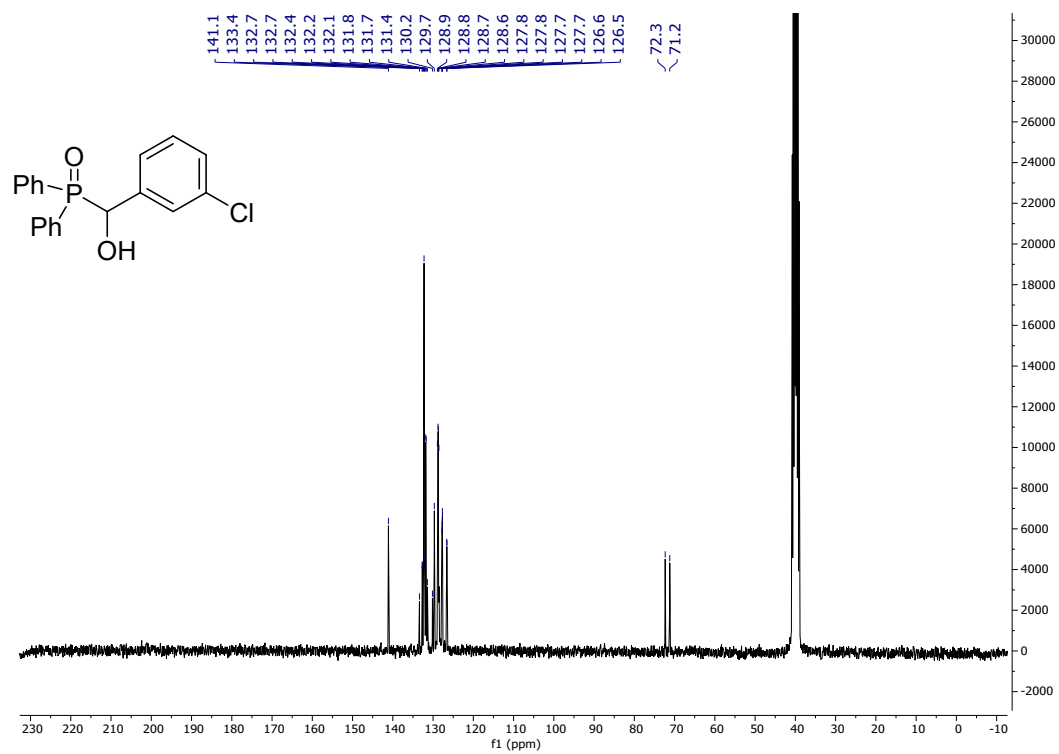


Figure SI_11: ¹³C-NMR for 3c in DMSO-*d*⁶ (75 MHz).

((2-Chlorophenyl)(hydroxy)methyl)diphenylphosphine oxide 3d

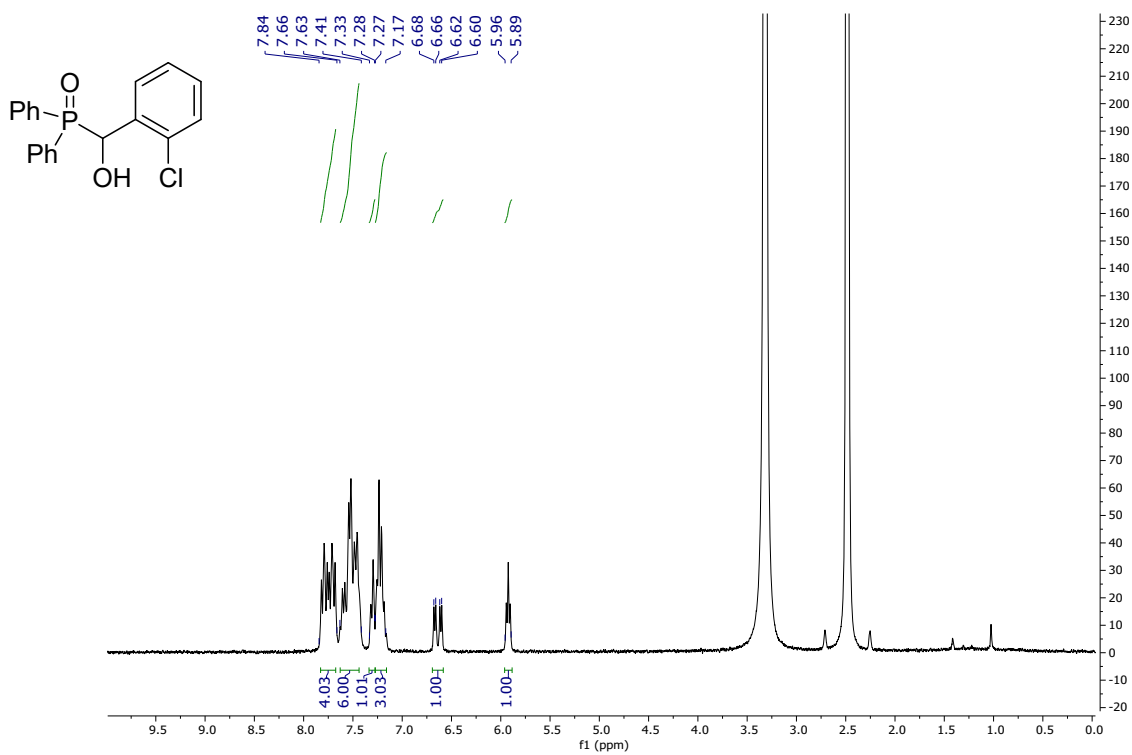


Figure SI_12: ¹H-NMR for 3d in DMSO-*d*⁶ (300 MHz).

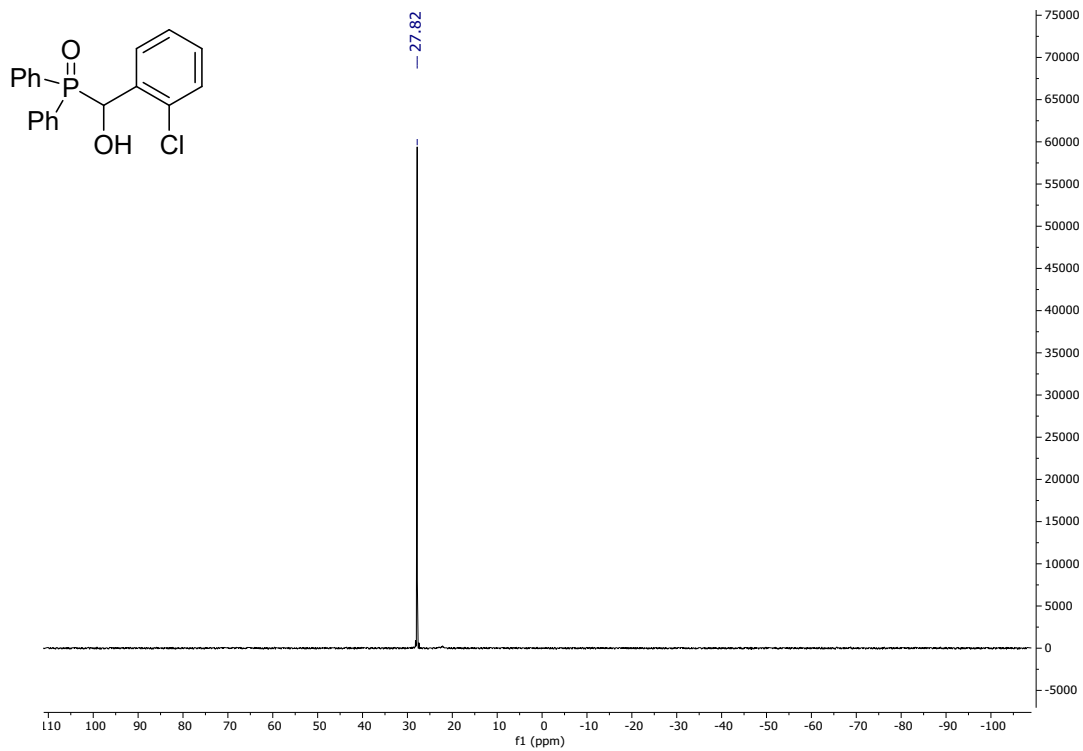


Figure SI_13: ³¹P-NMR for 3d in DMSO-*d*⁶ (121 MHz).

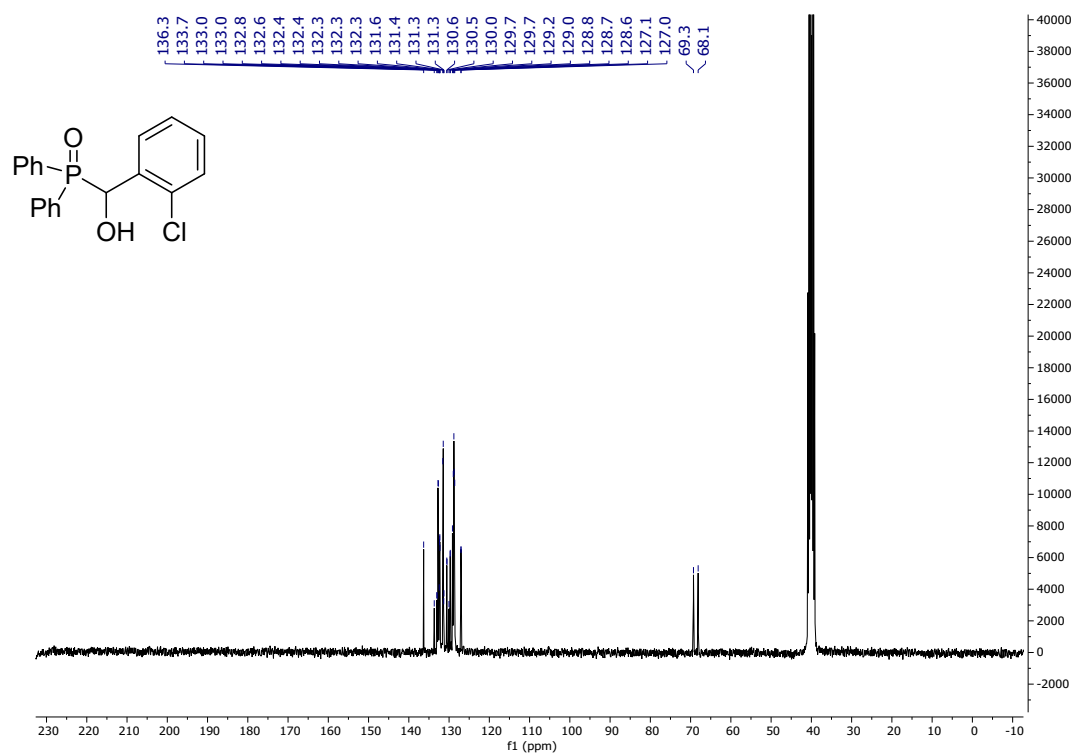


Figure SI_14: ¹³C-NMR for 3d in DMSO-*d*⁶ (75 MHz).

((4-Bromophenyl)(hydroxy)methyl)diphenylphosphine oxide 3e

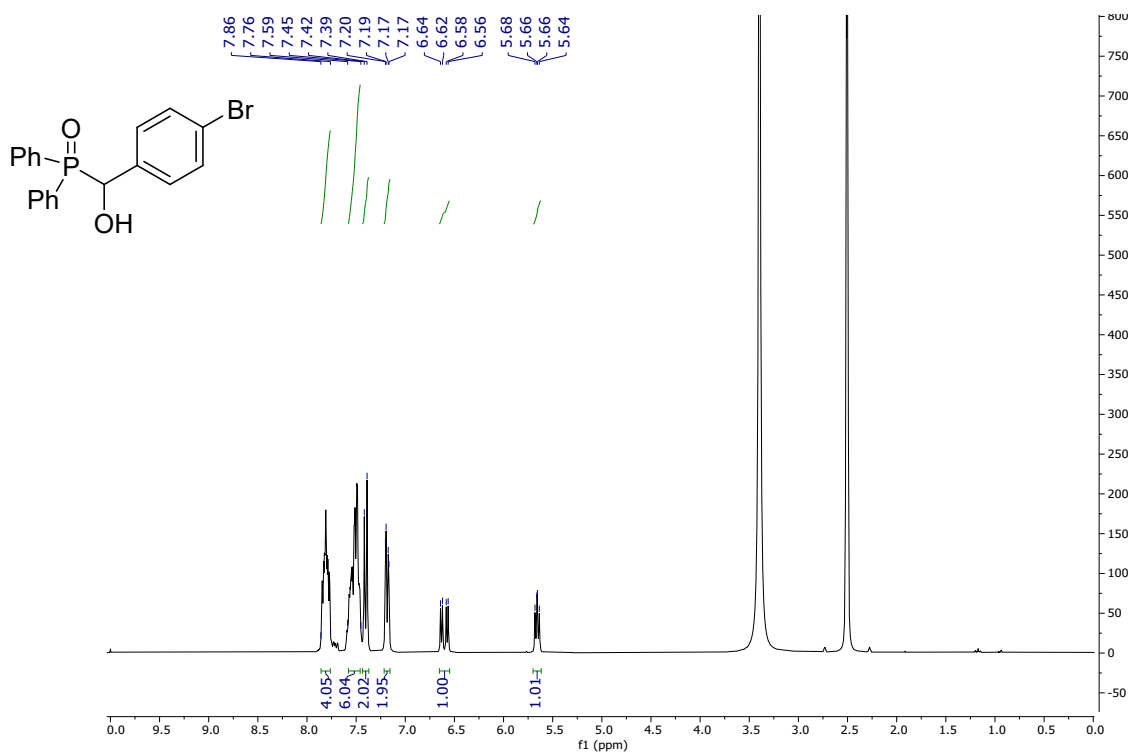


Figure SI_15: ¹H-NMR for 3e in DMSO-*d*₆ (300 MHz).

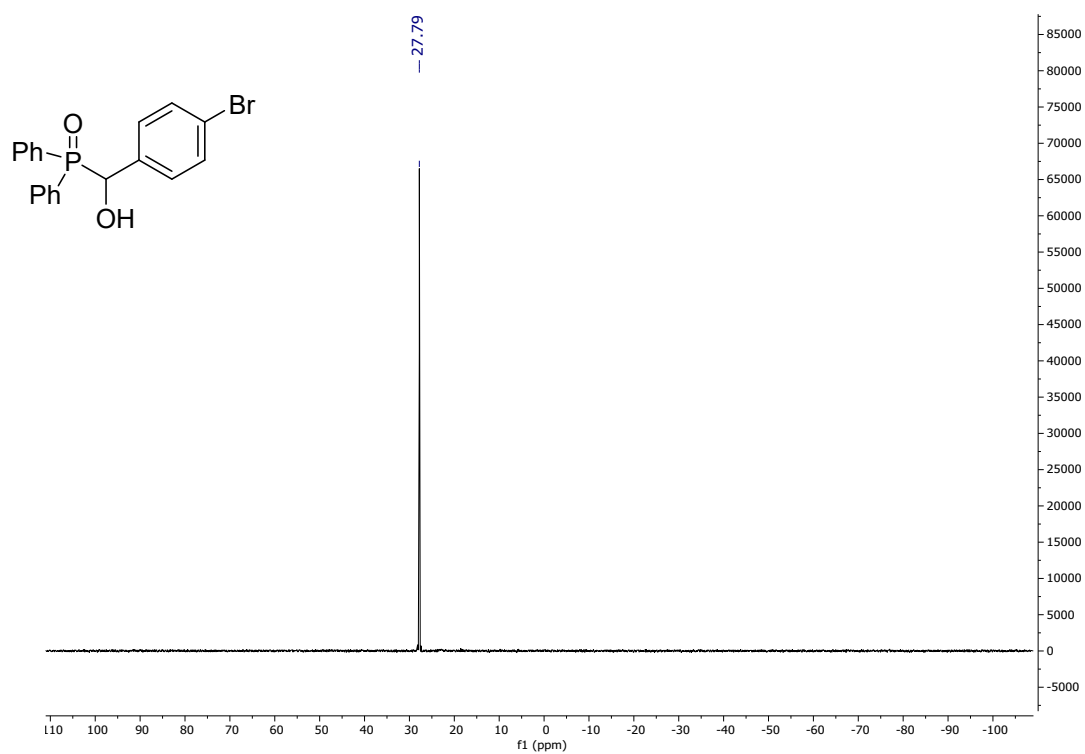


Figure SI_16: ³¹P-NMR for 3e in DMSO-*d*₆ (121 MHz).

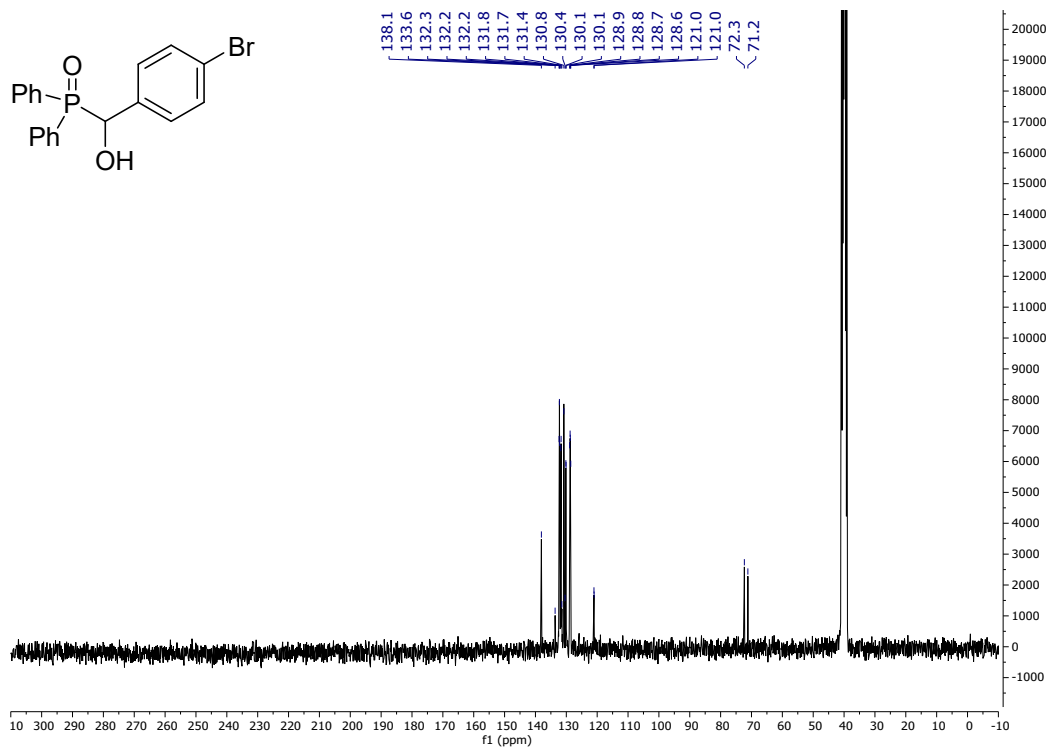


Figure SI_17: $^{13}\text{C-NMR}$ for **3e** in $\text{DMSO-}d^6$ (75 MHz).

(Hydroxy(4-nitrophenyl)methyl)diphenylphosphine oxide 3f

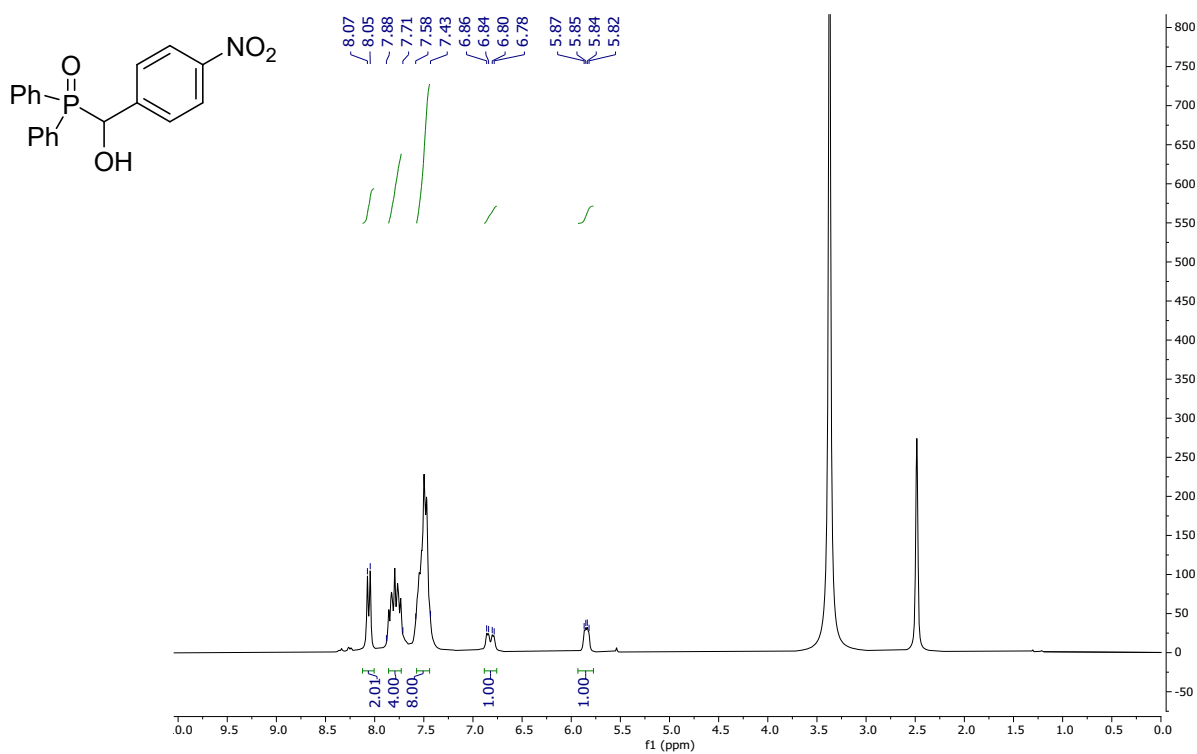


Figure SI_18: $^1\text{H-NMR}$ for **3f** in $\text{DMSO-}d^6$ (300 MHz).

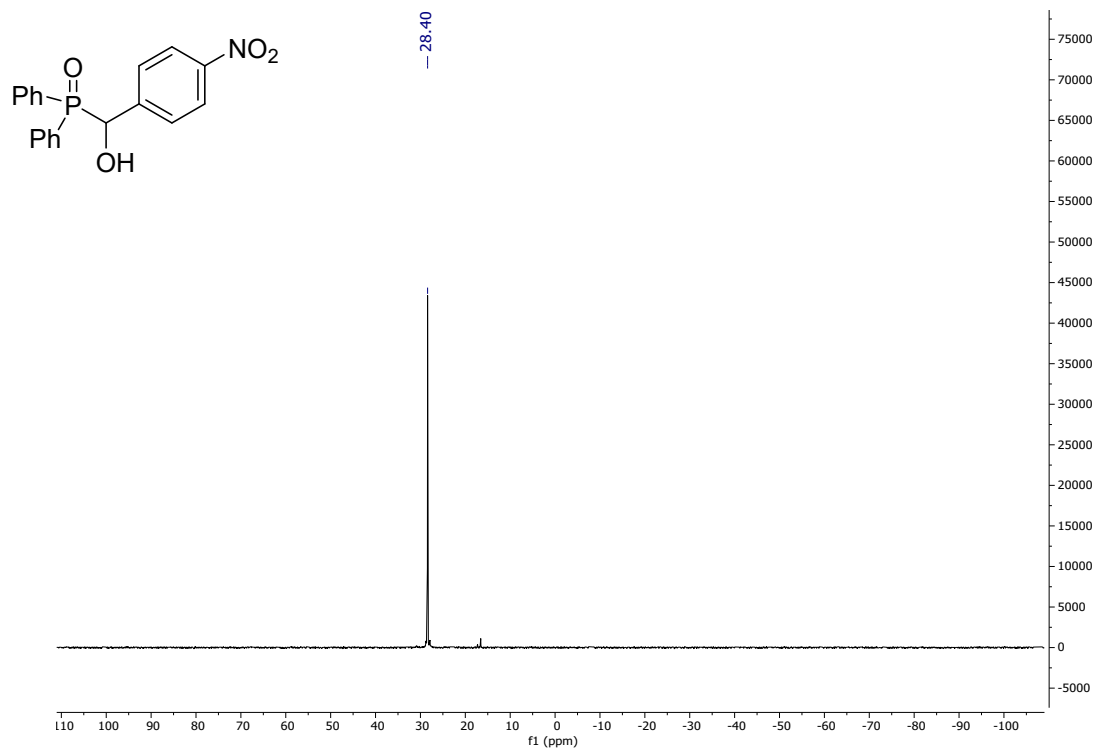


Figure SI_19: ^{31}P -NMR for **3f** in $\text{DMSO-}d_6$ (121 MHz).

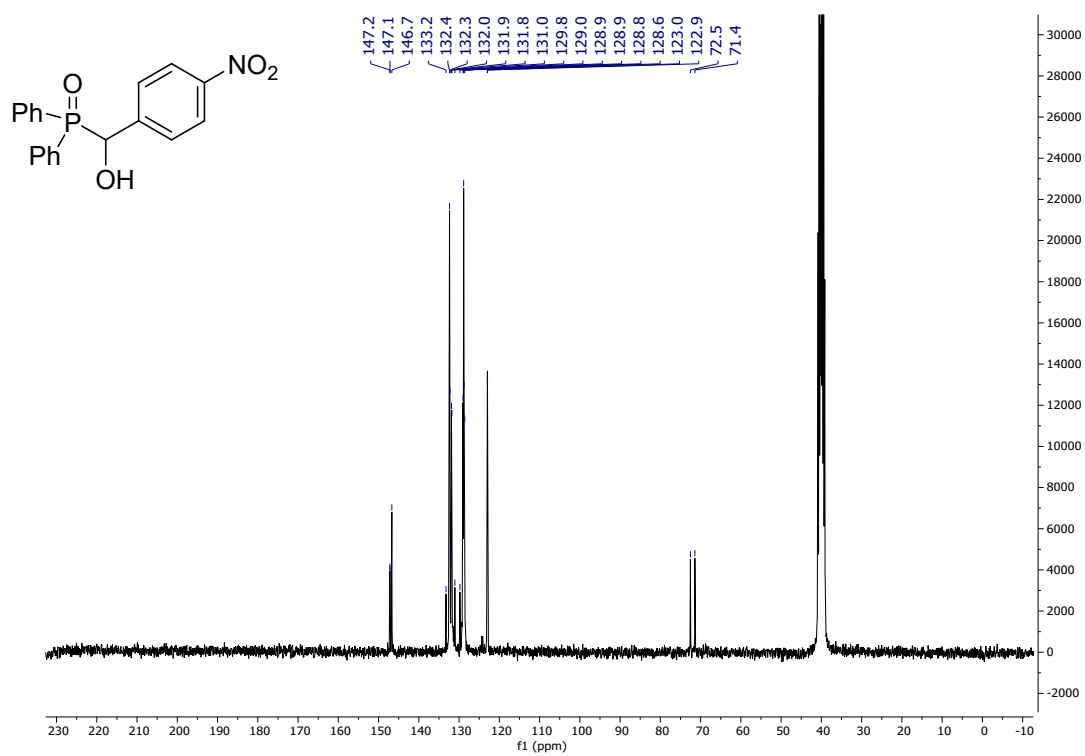


Figure SI_20: ^{13}C -NMR for **3f** in $\text{DMSO-}d_6$ (75 MHz).

(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine oxide 3g

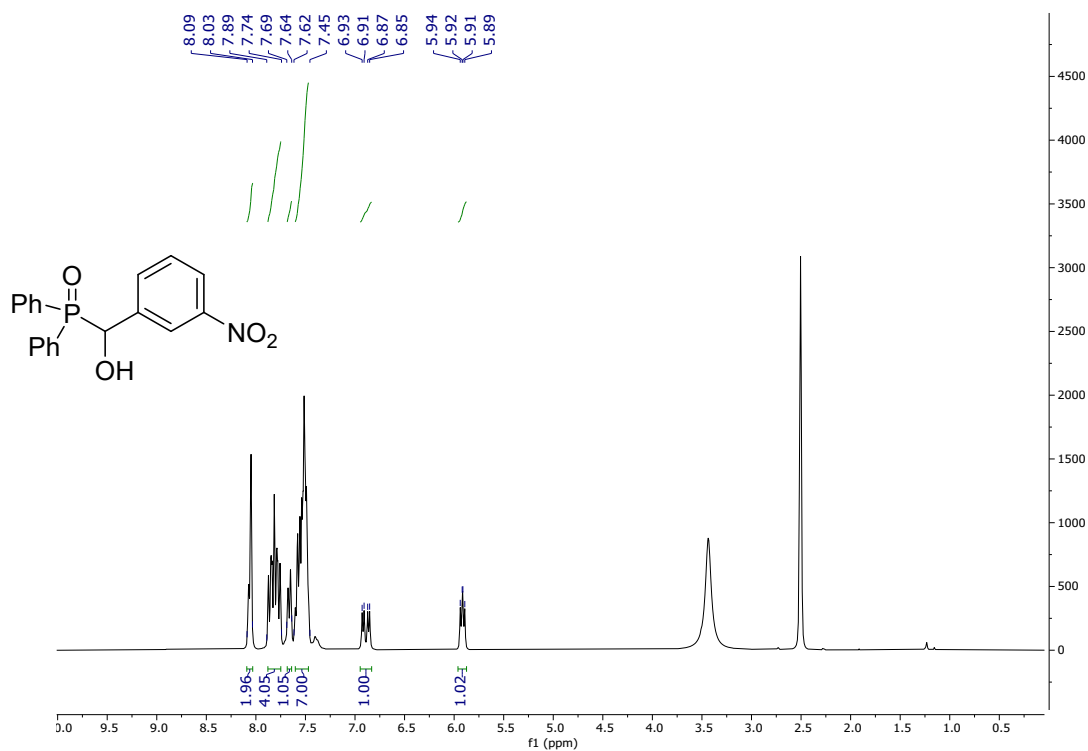


Figure SI_21: ¹H-NMR for **3g** in DMSO-*d*₆ (300 MHz).

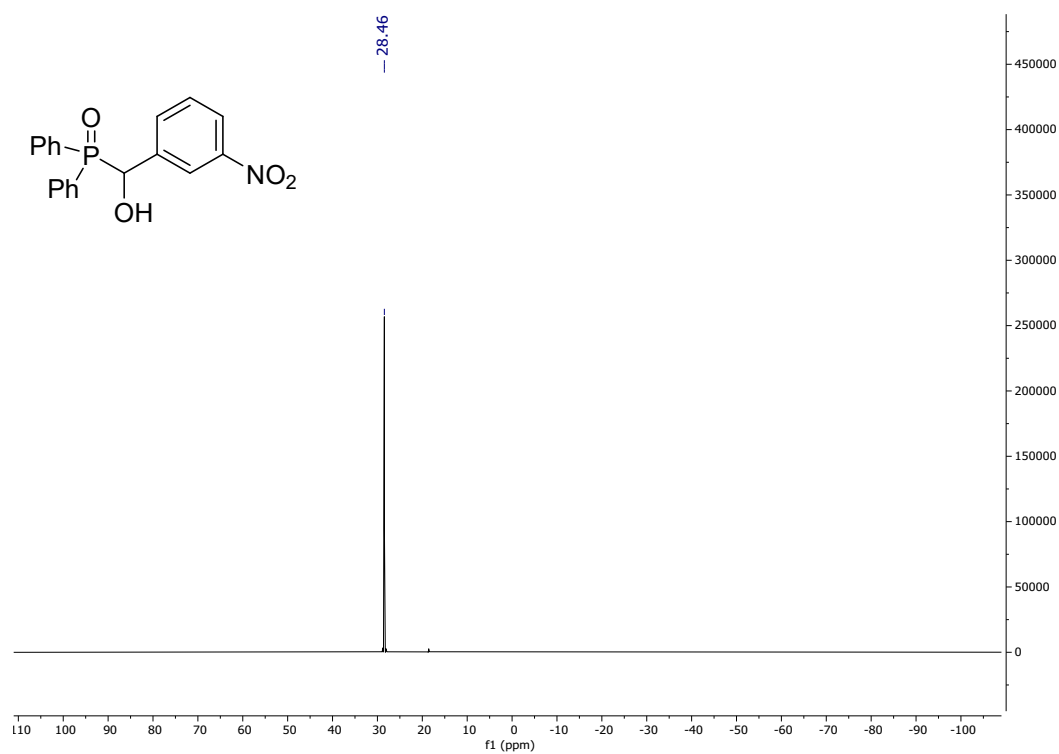


Figure SI_22: ³¹P-NMR for **3g** in DMSO-*d*₆ (121 MHz).

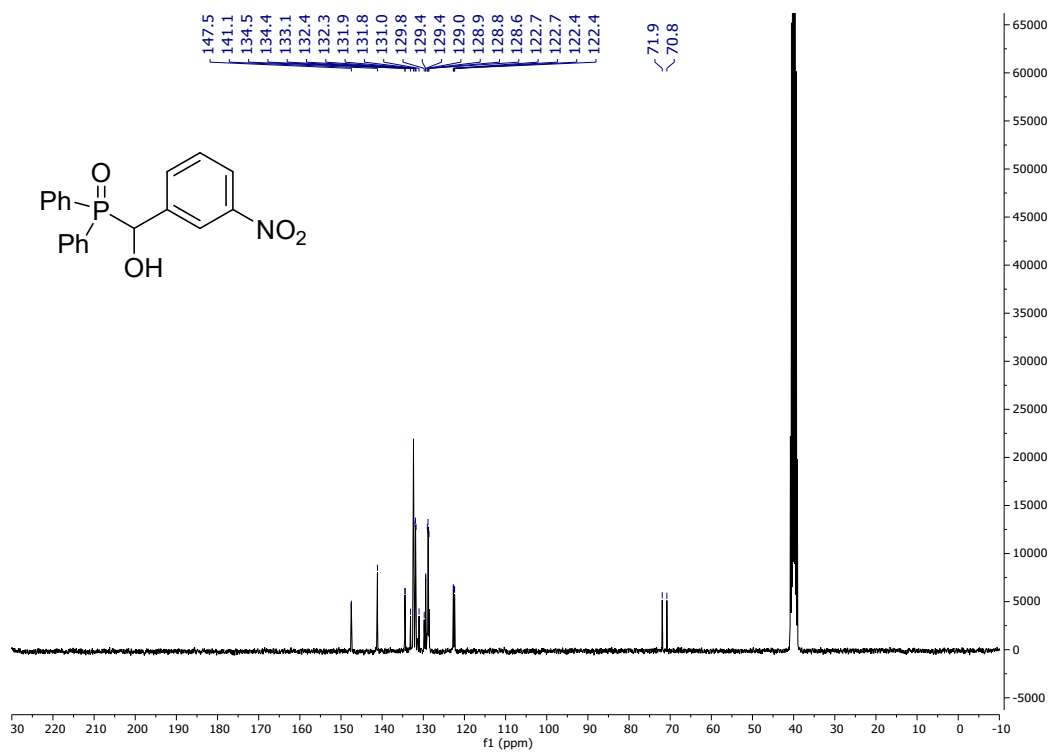


Figure SI_23: ¹³C-NMR for 3g in DMSO-*d*⁶ (75 MHz).

(Hydroxy(4-hydroxyphenyl)methyl)diphenylphosphine oxide 3h

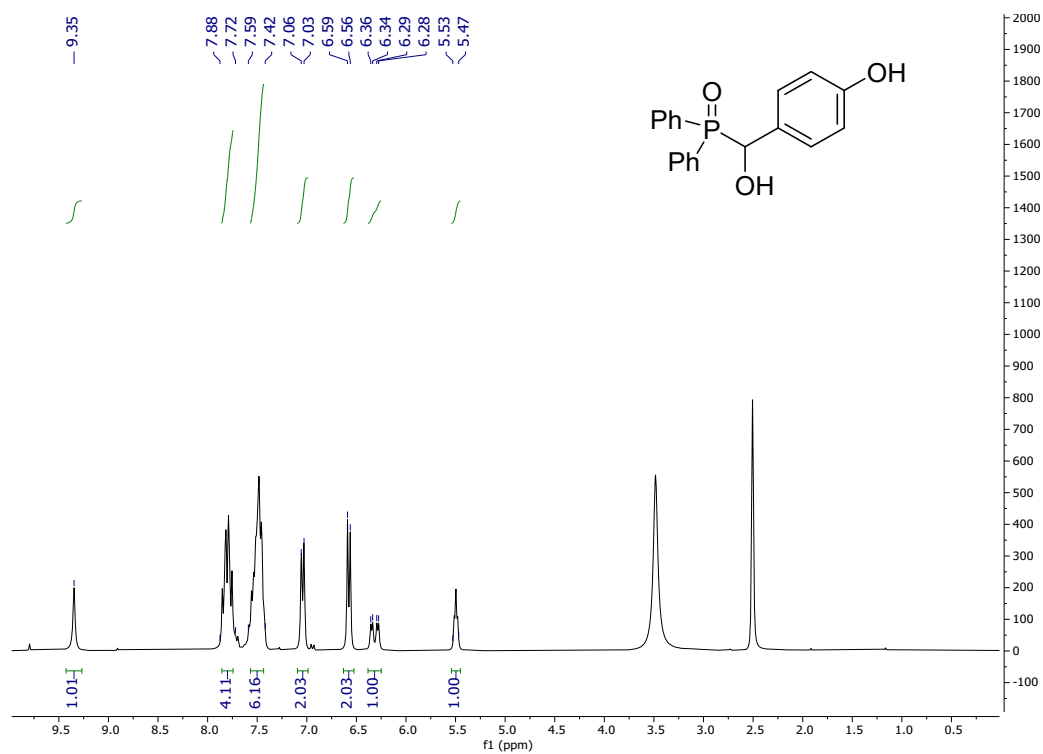


Figure SI_24: ¹H-NMR for 3h in DMSO-*d*⁶ (300 MHz).

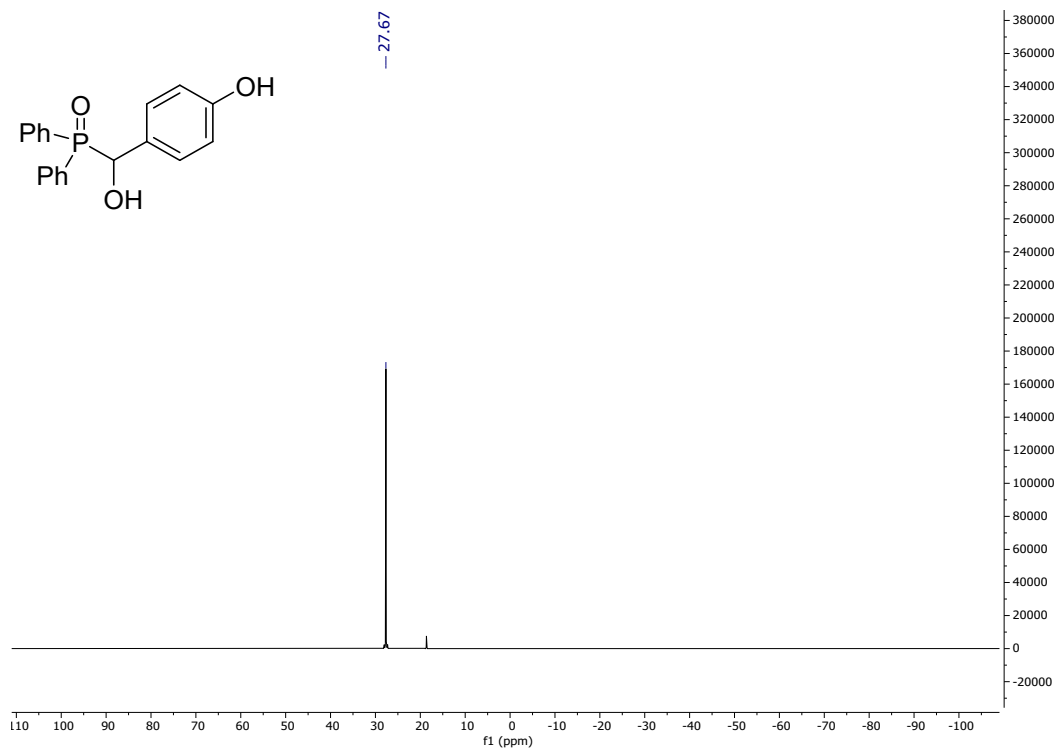


Figure SI_25: ³¹P-NMR for **3h** in DMSO-*d*⁶ (121 MHz).

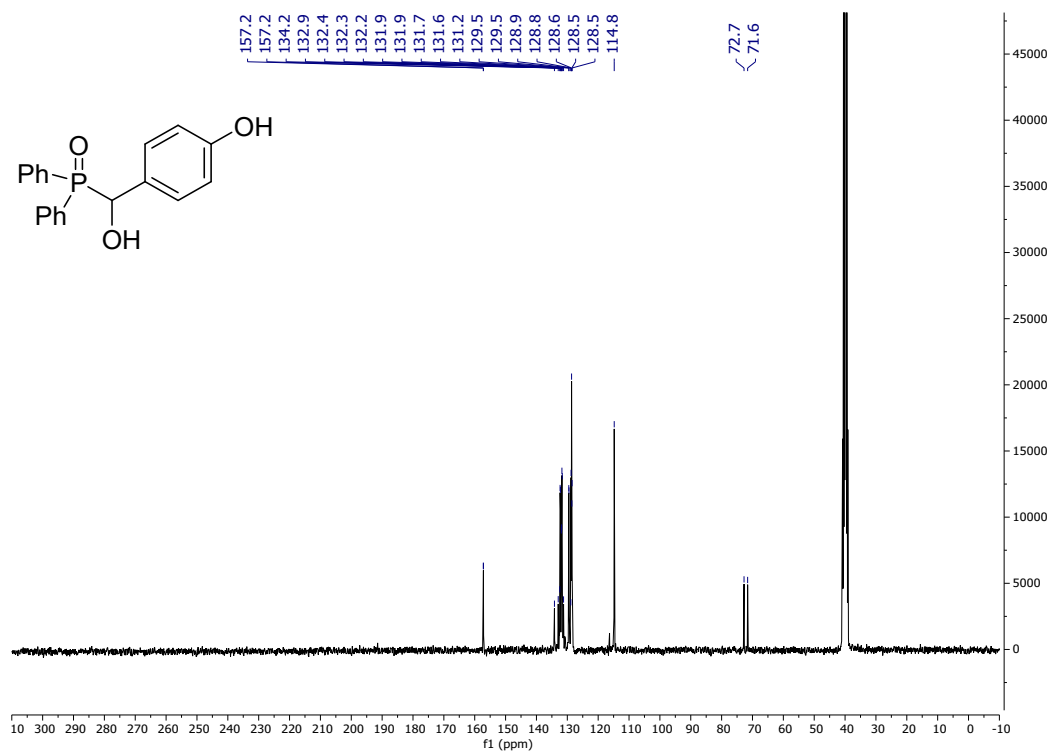


Figure SI_26: ¹³C-NMR for **3h** in DMSO-*d*⁶ (75 MHz).

(Hydroxy(4-methoxyphenyl)methyl)diphenylphosphine oxide 3i

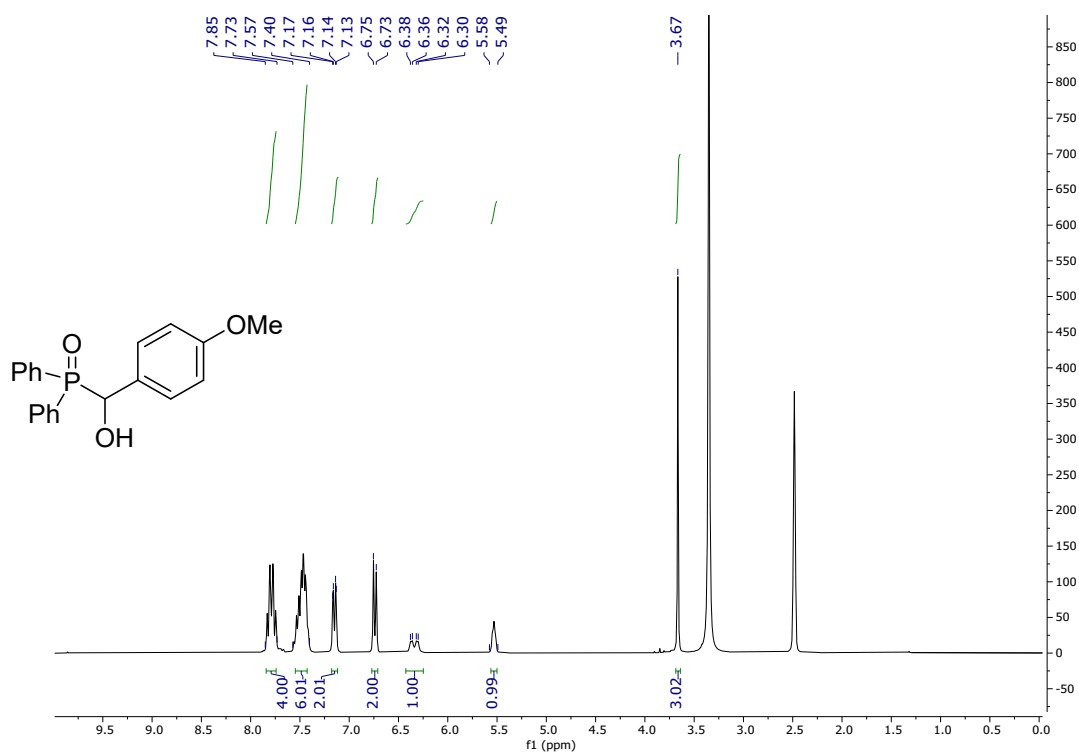


Figure SI_27: ¹H-NMR for **3i** in DMSO-*d*₆ (300 MHz).

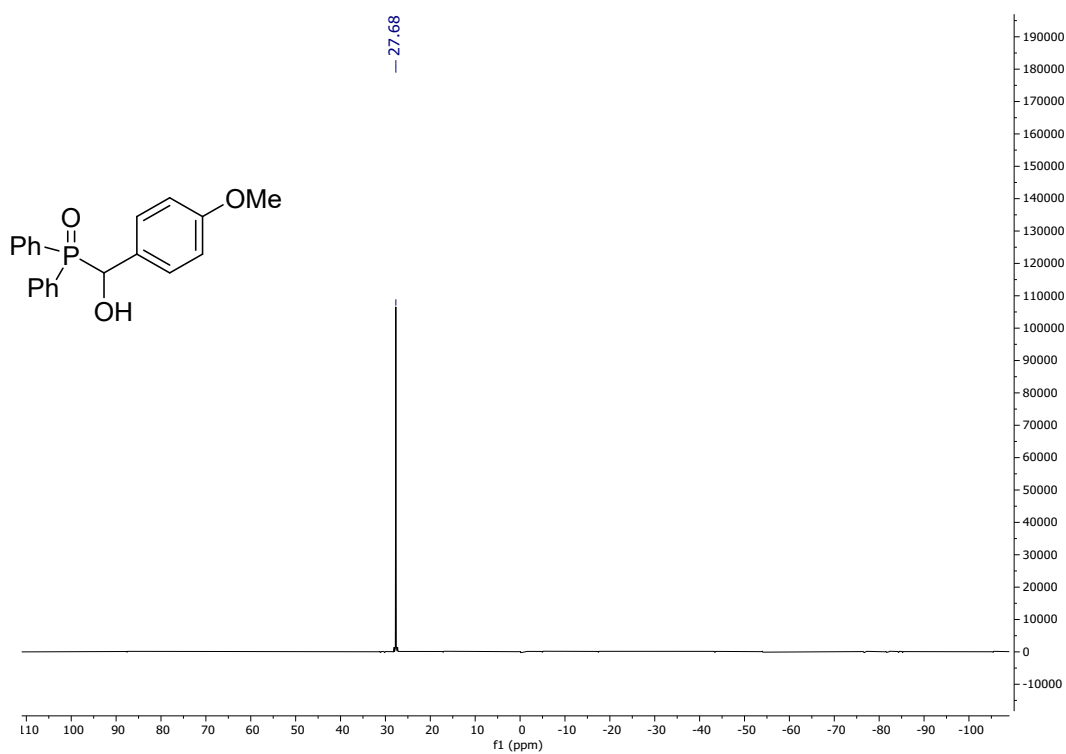


Figure SI_28: ³¹P-NMR for **3i** in DMSO-*d*₆ (121 MHz).

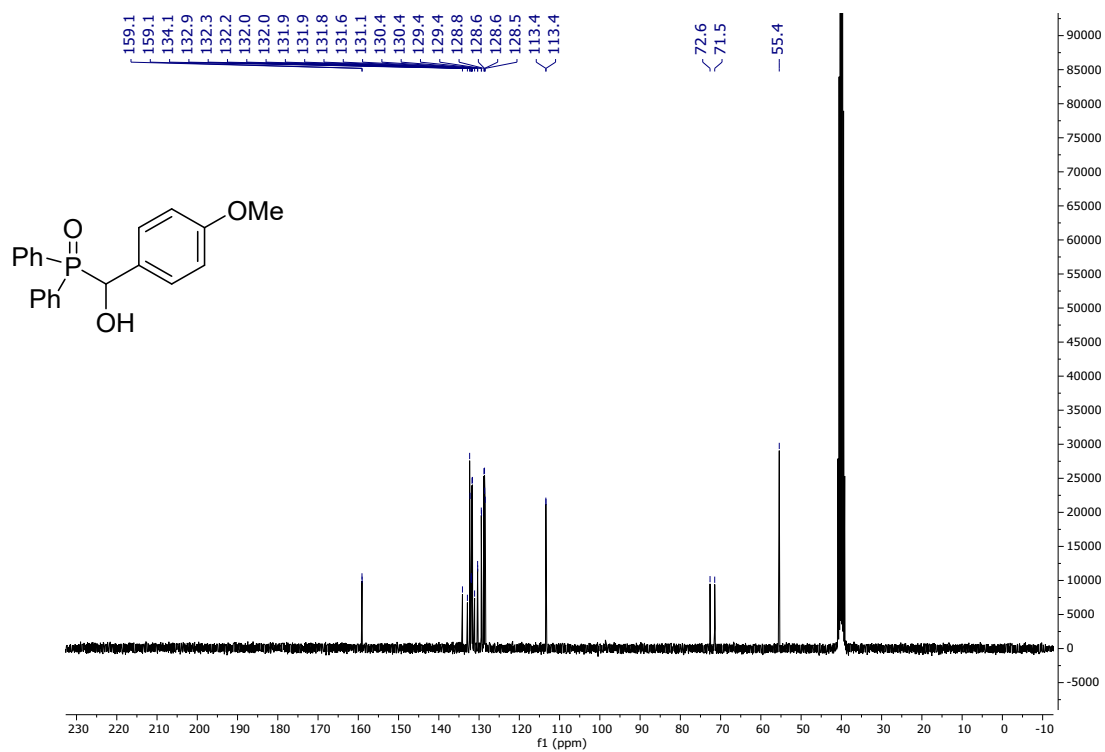


Figure SI_29: ¹³C-NMR for 3i in DMSO-*d*⁶ (75 MHz).

(Hydroxy(2-methoxyphenyl)methyl)diphenylphosphine oxide 3j

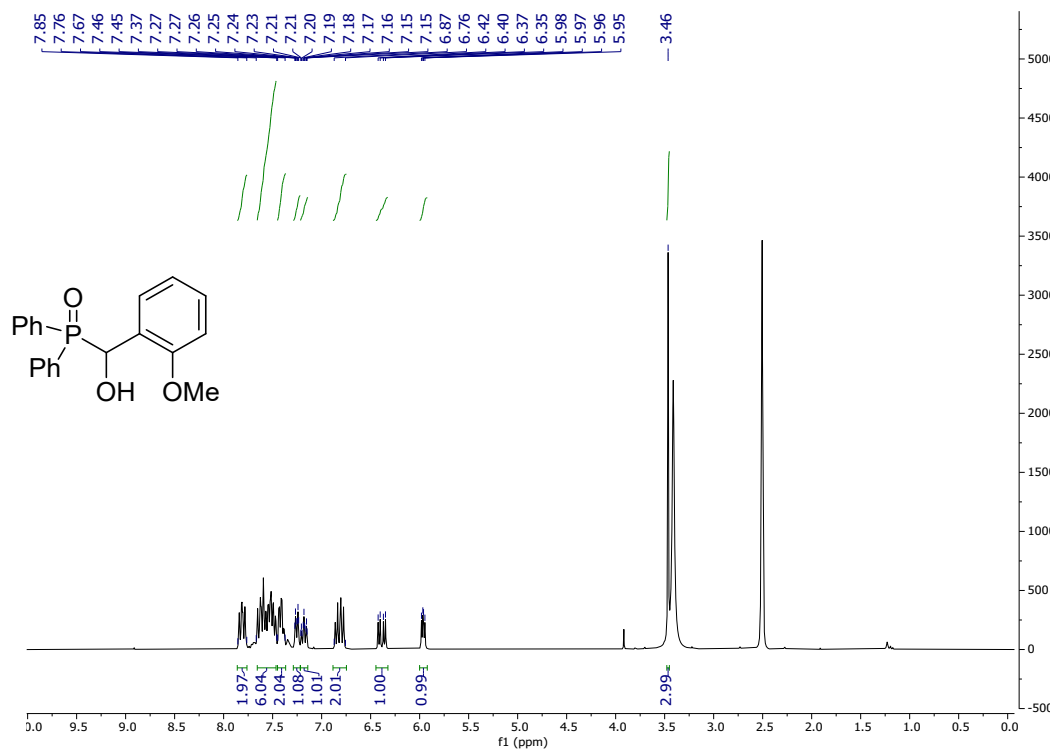
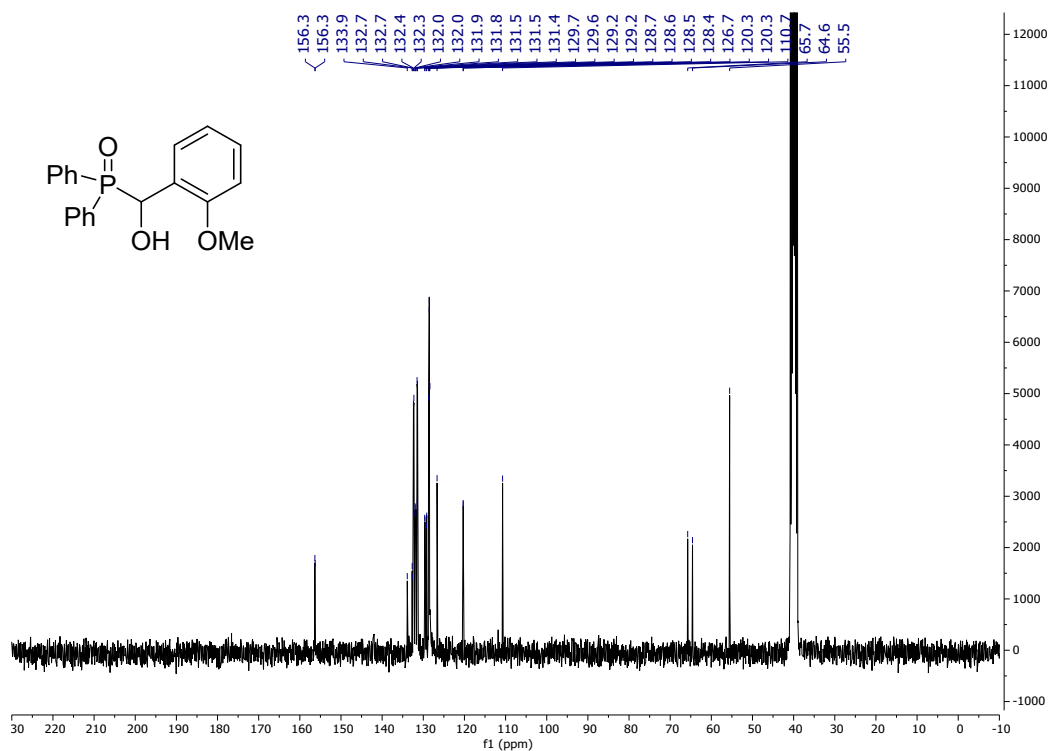
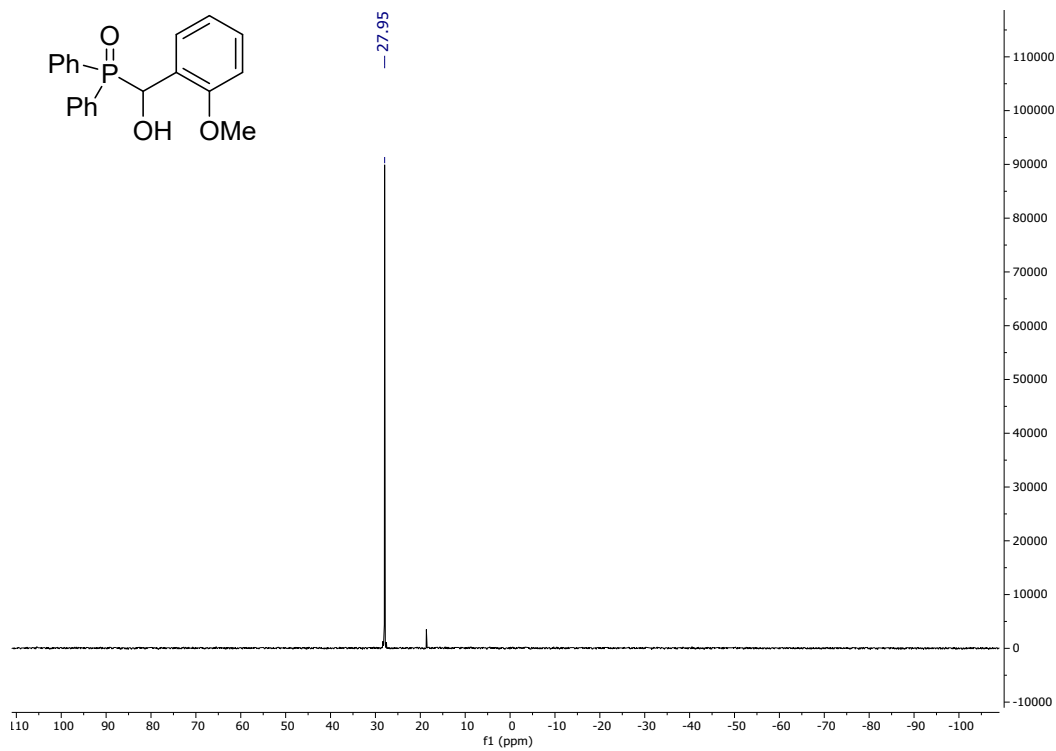


Figure SI_30: ¹H-NMR for 3j in DMSO-*d*⁶ (300 MHz).



(Furan-2-yl(hydroxy)methyl)diphenylphosphine oxide 3k

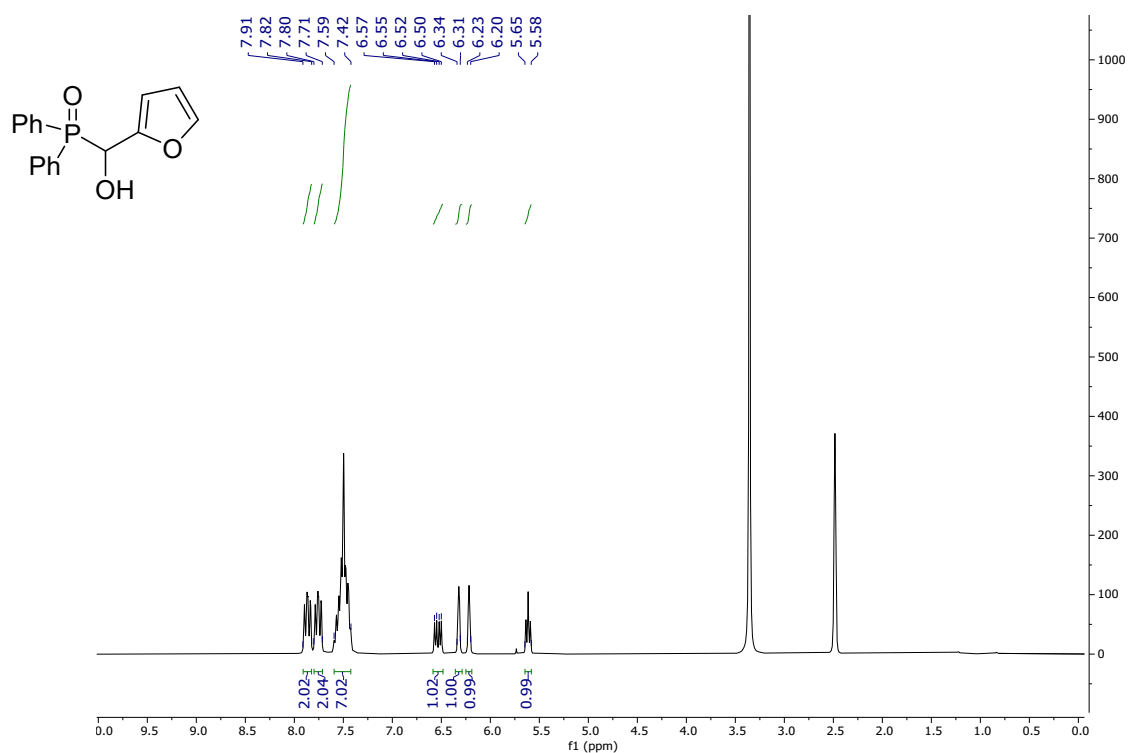


Figure SI_33: ¹H-NMR for 3k in DMSO-*d*₆ (300 MHz).

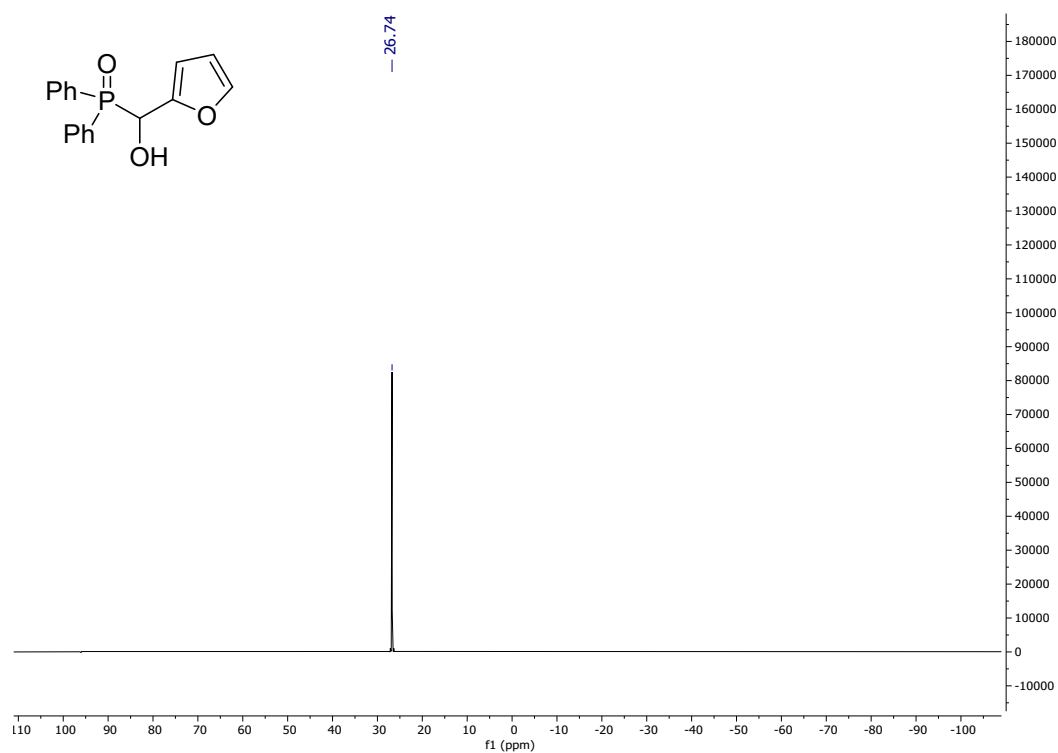


Figure SI_34: ³¹P-NMR for 3k in DMSO-*d*₆ (121 MHz).

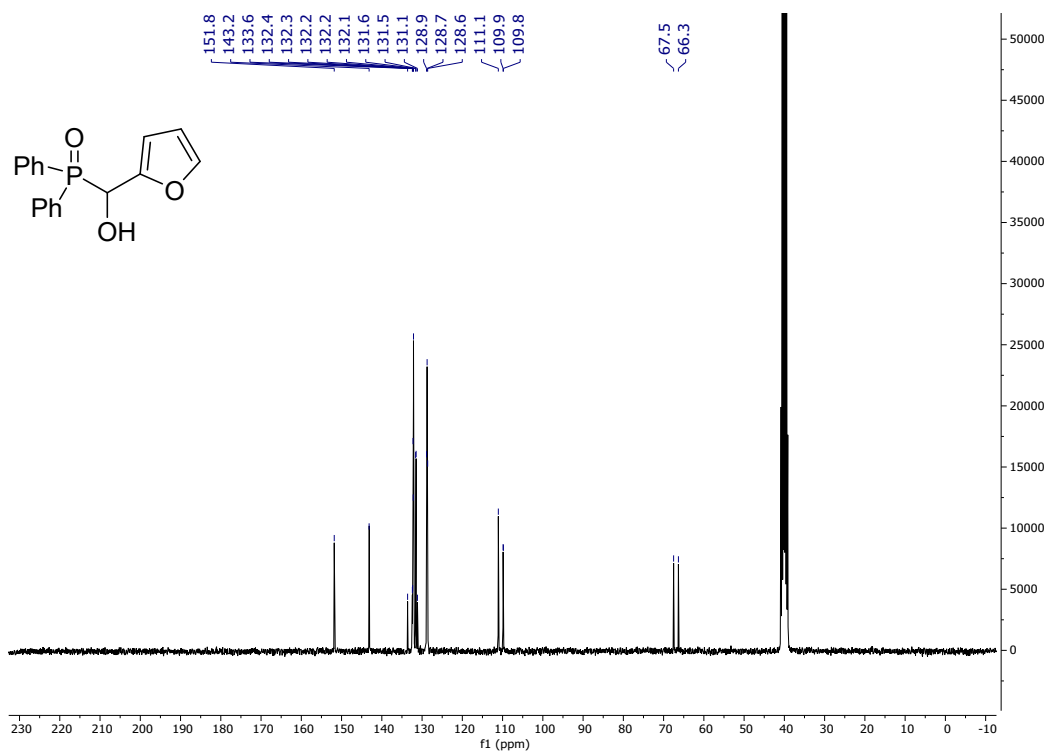


Figure SI_35: ¹³C-NMR for 3k in DMSO-*d*⁶ (75 MHz).

(Hydroxy(thiophen-2-yl)methyl)diphenylphosphine oxide 3l

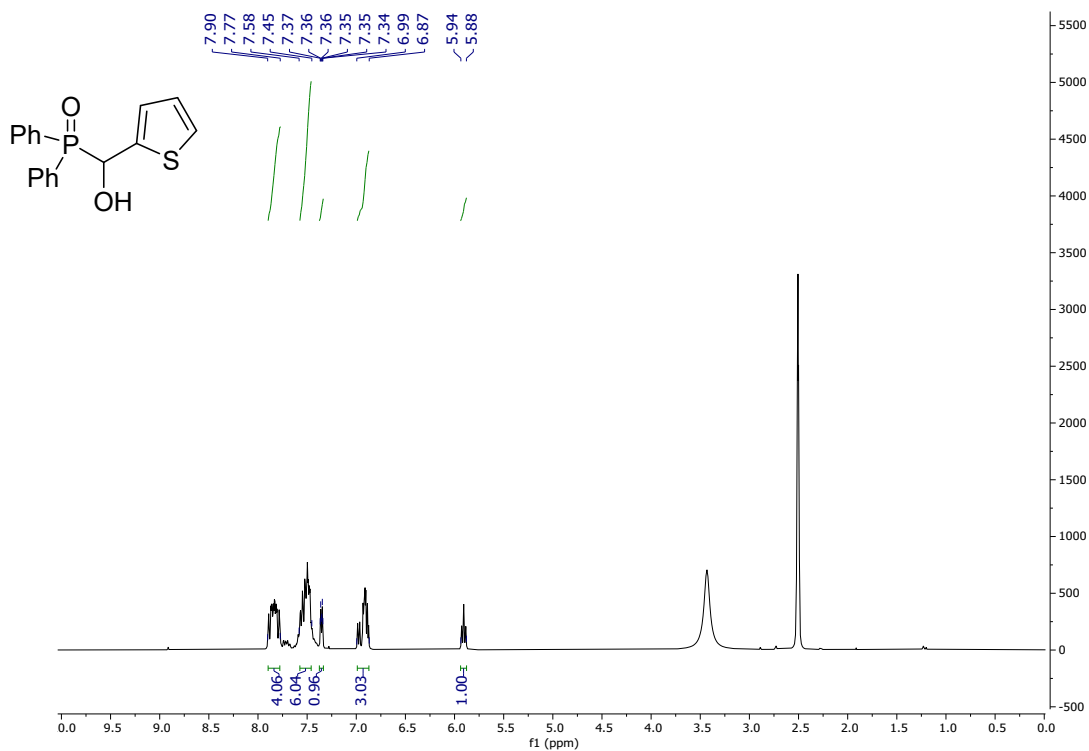


Figure SI_36: ¹H-NMR for 3l in DMSO-*d*⁶ (300 MHz).

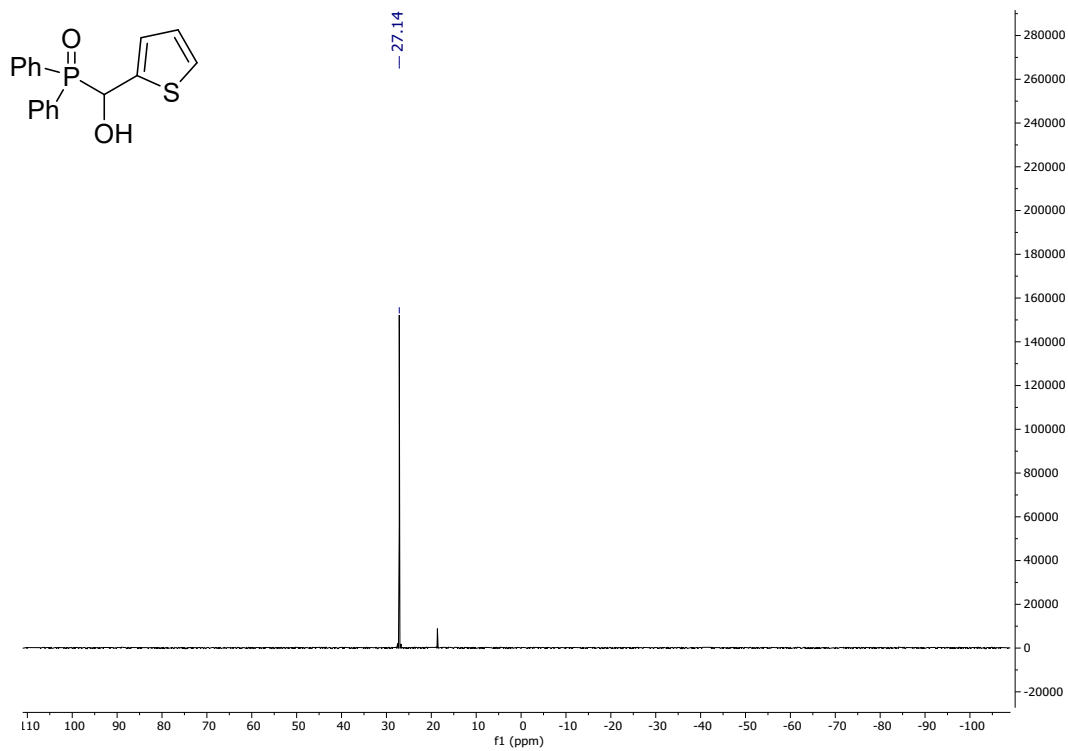


Figure SI_37: ^{31}P -NMR for 31 in $\text{DMSO-}d^6$ (121 MHz).

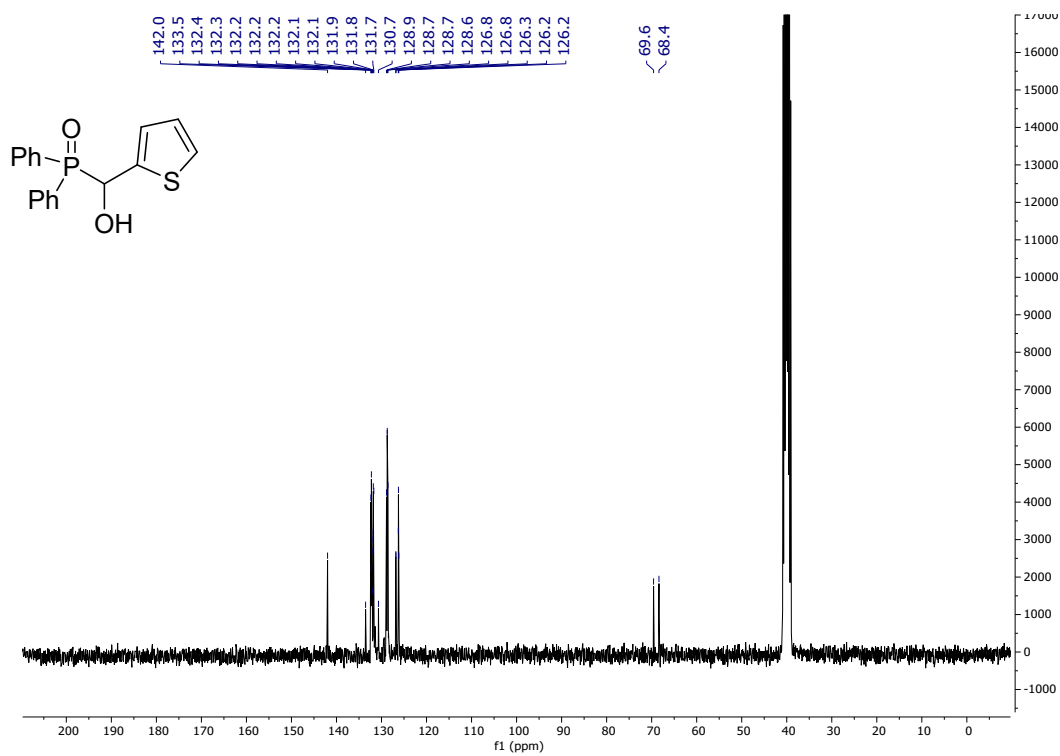


Figure SI_38: ^{13}C -NMR for 31 in $\text{DMSO-}d^6$ (75 MHz).

(E)-(1-Hydroxy-3-(2-nitrophenyl)allyl)diphenylphosphine oxide 3m

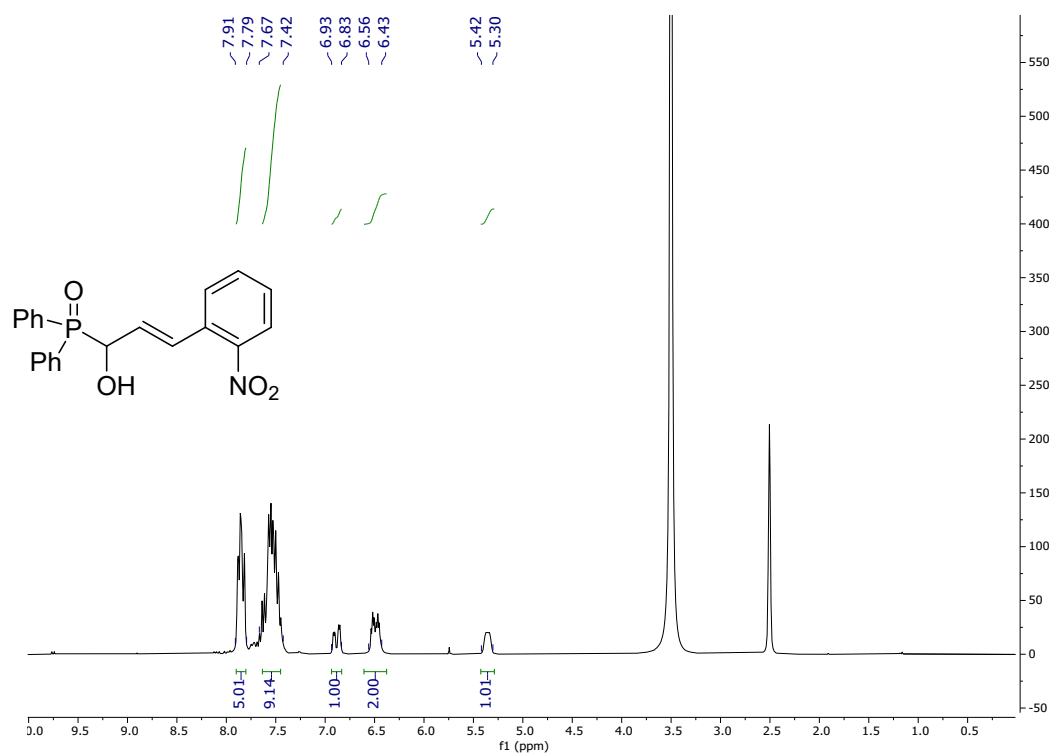


Figure SI_39: ¹H-NMR for 3m in DMSO-*d*₆ (300 MHz).

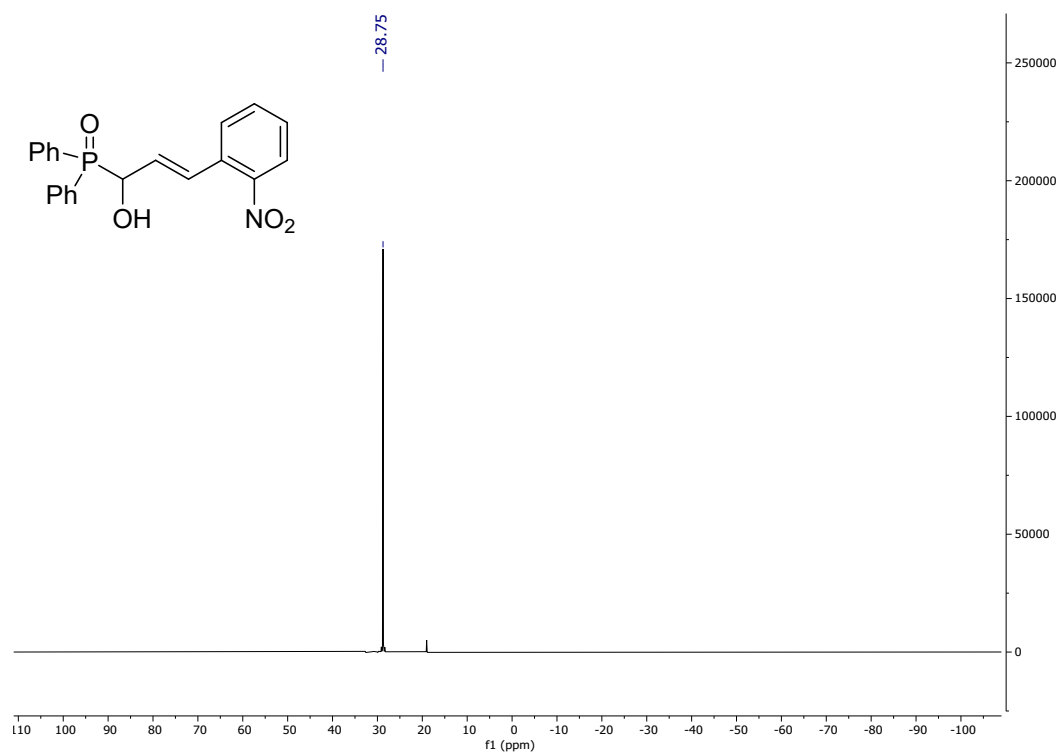


Figure SI_40: ³¹P-NMR for 3m in DMSO-*d*₆ (121 MHz).

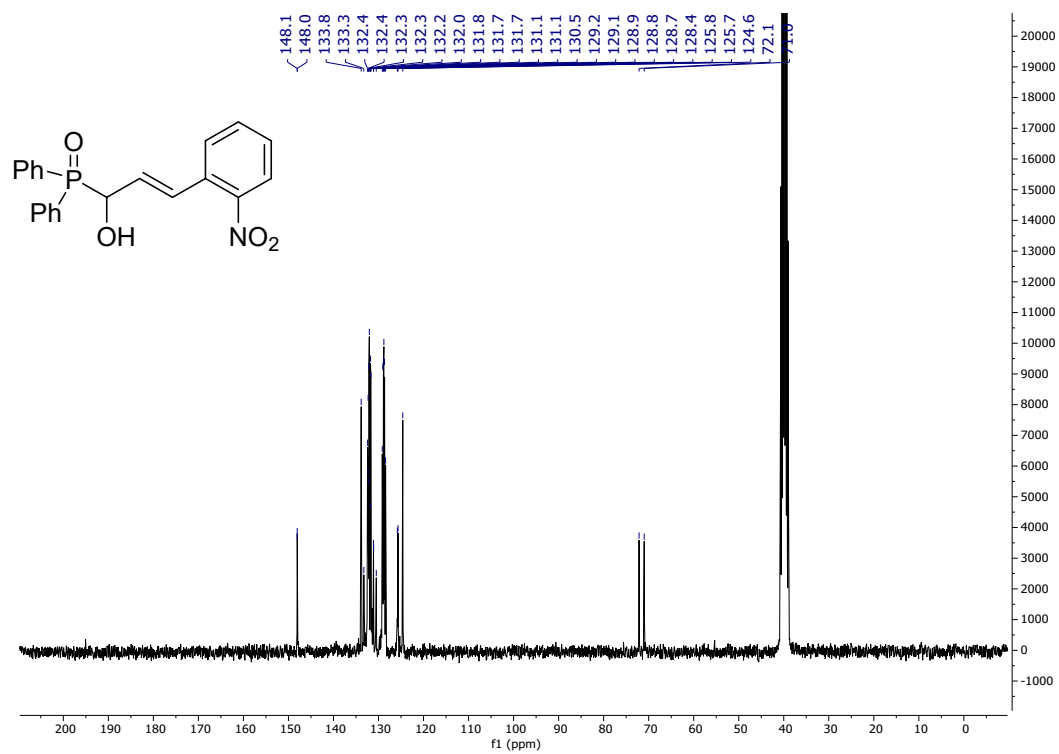


Figure SI_41: ¹³C-NMR for **3m** in DMSO-*d*⁶ (75 MHz).

(Hydroxy(naphthalen-1-yl)methyl)diphenylphosphine oxide **3n**

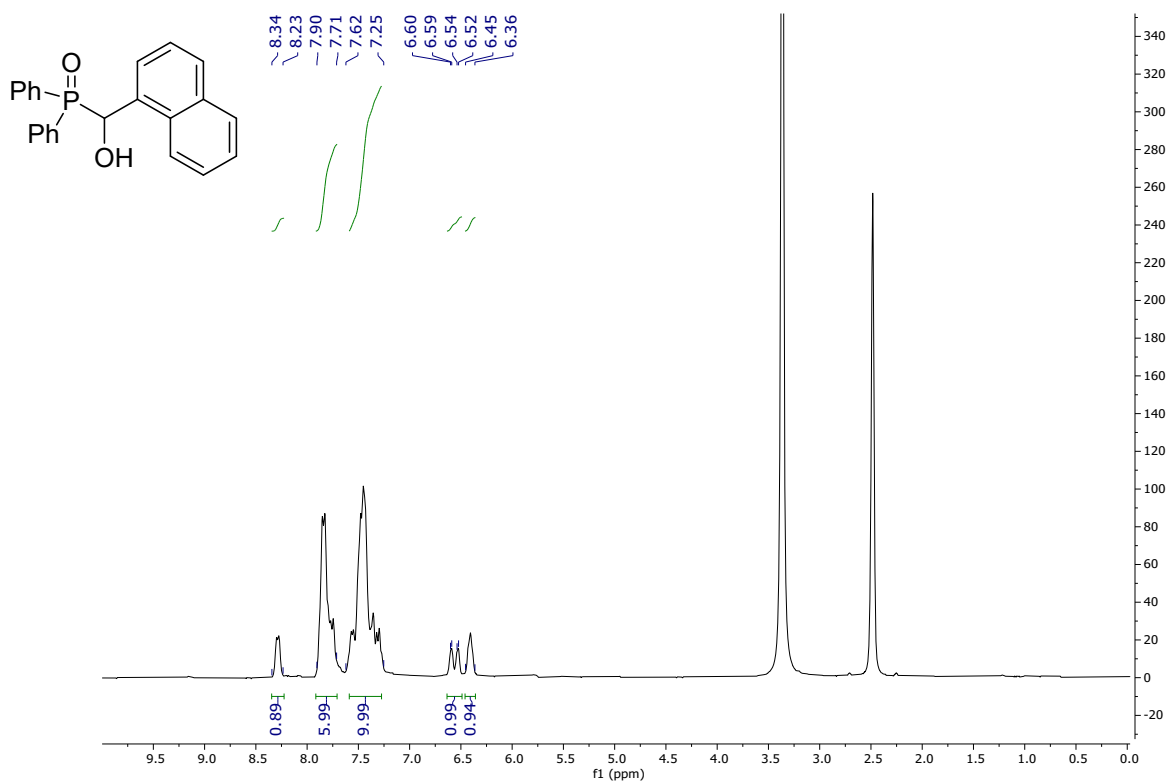


Figure SI_42: ¹H-NMR for **3n** in DMSO-*d*⁶ (300 MHz).

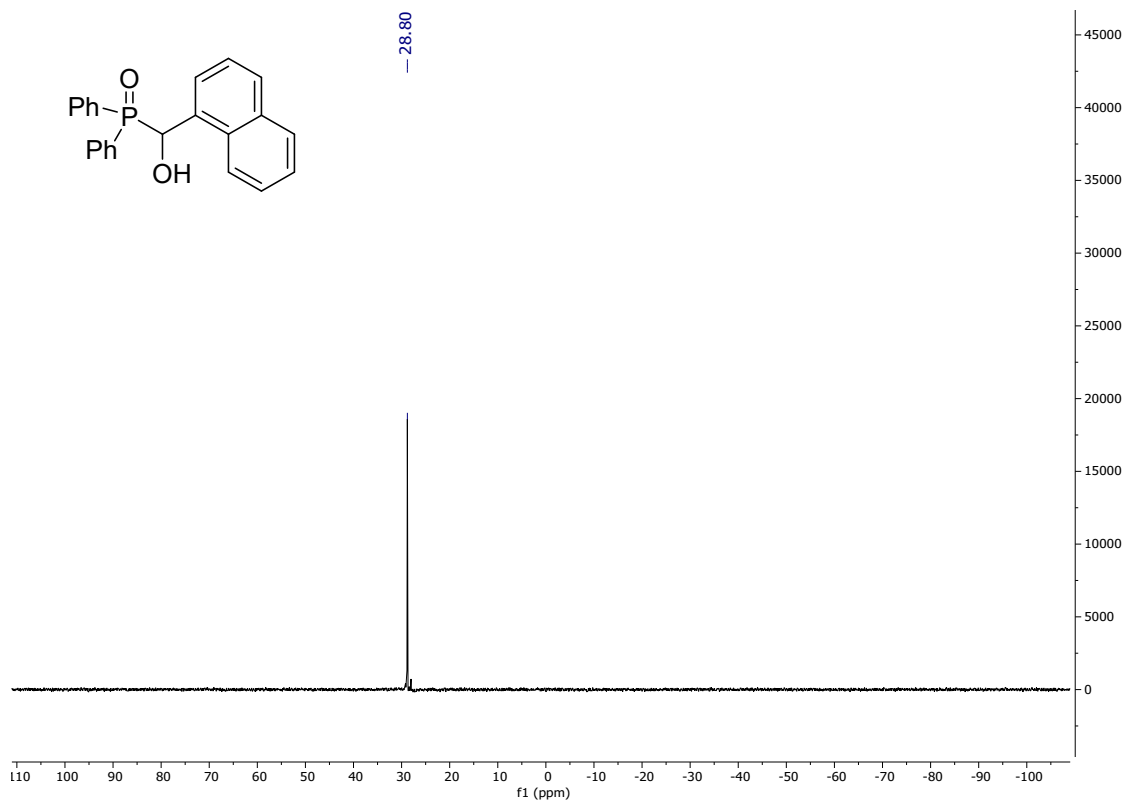


Figure SI_43: ^{31}P -NMR for **3n** in $\text{DMSO-}d^6$ (121 MHz).

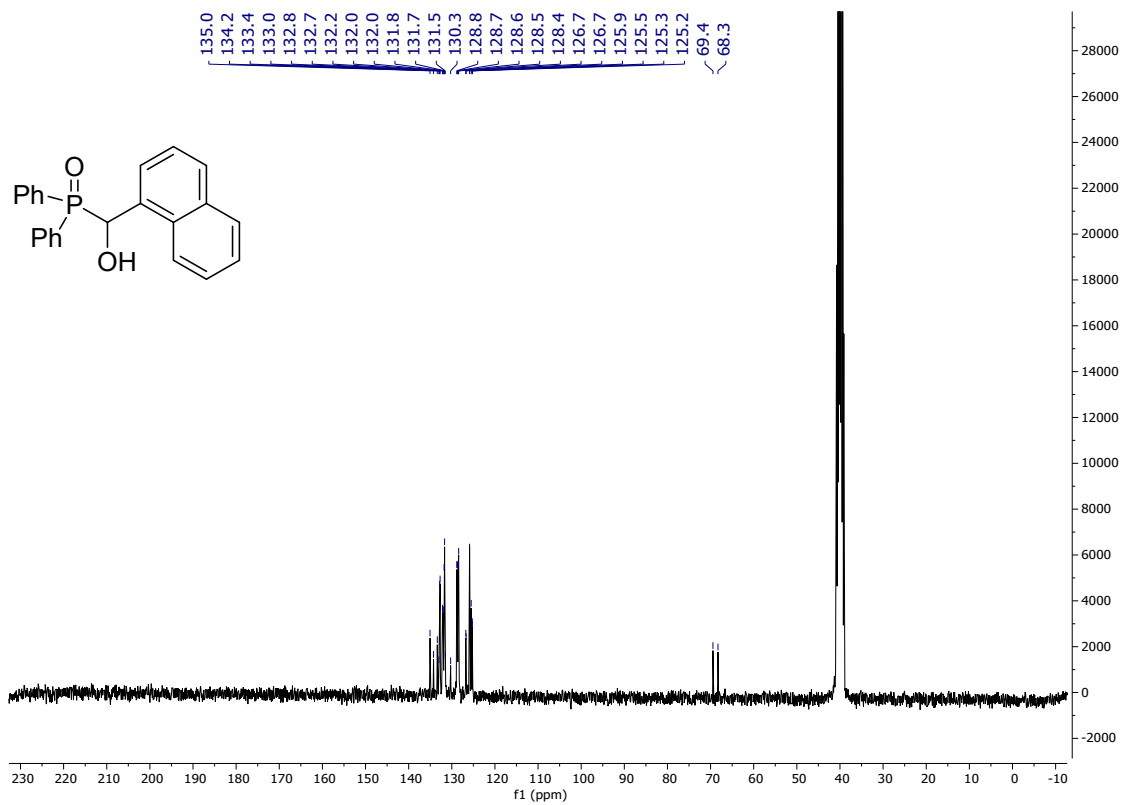


Figure SI_44: ^{13}C -NMR for **3n** in $\text{DMSO-}d^6$ (75 MHz).

(Cyclohexyl(hydroxy)methyl)diphenylphosphine oxide 3o

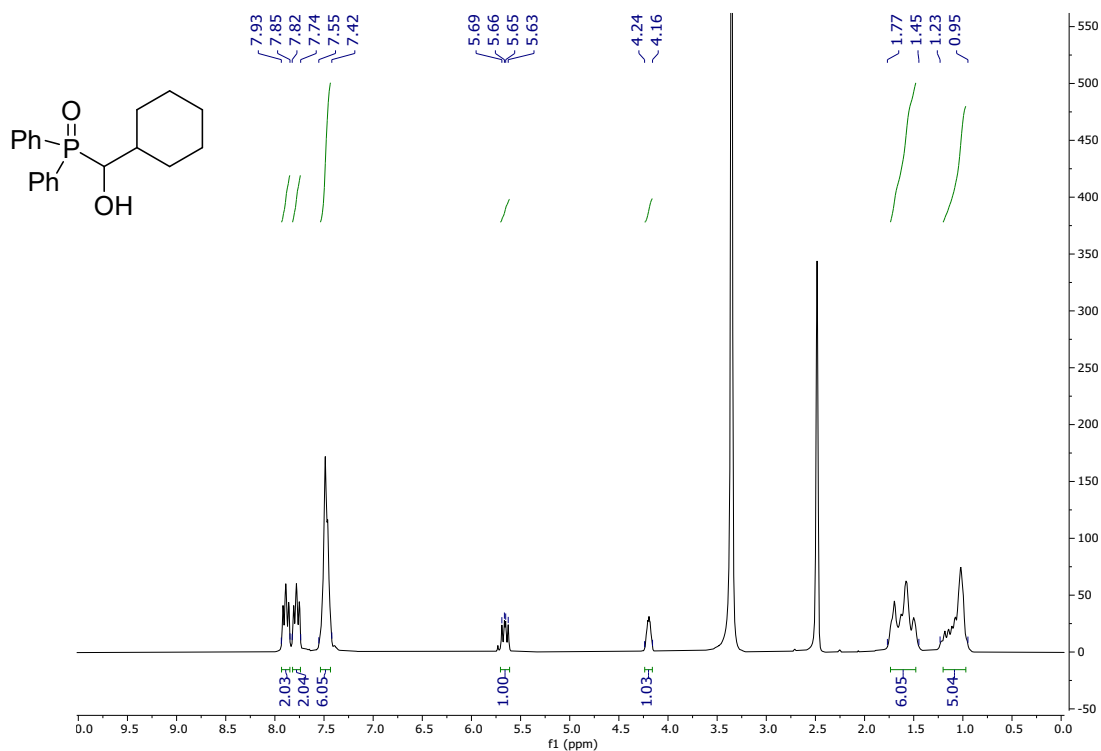


Figure SI_45: $^1\text{H-NMR}$ for **3o** in $\text{DMSO-}d^6$ (300 MHz).



Figure SI_46: $^{31}\text{P-NMR}$ for **3o** in $\text{DMSO-}d^6$ (121 MHz).

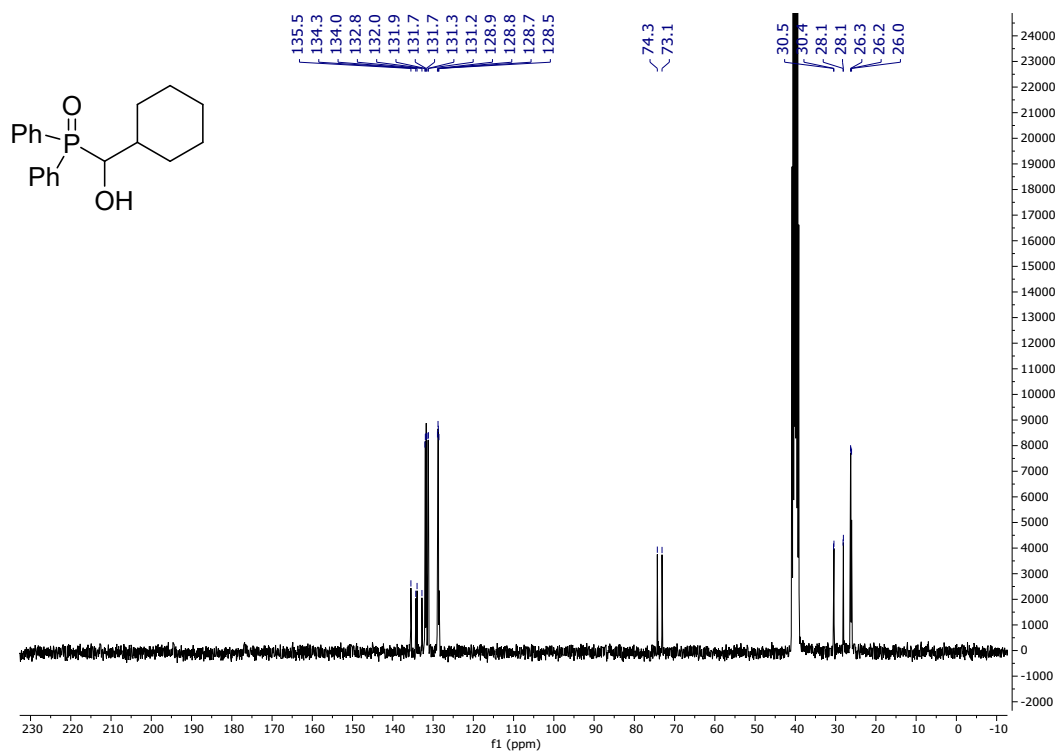


Figure SI_47: $^{13}\text{C-NMR}$ for **3o** in $\text{DMSO-}d^6$ (75 MHz).

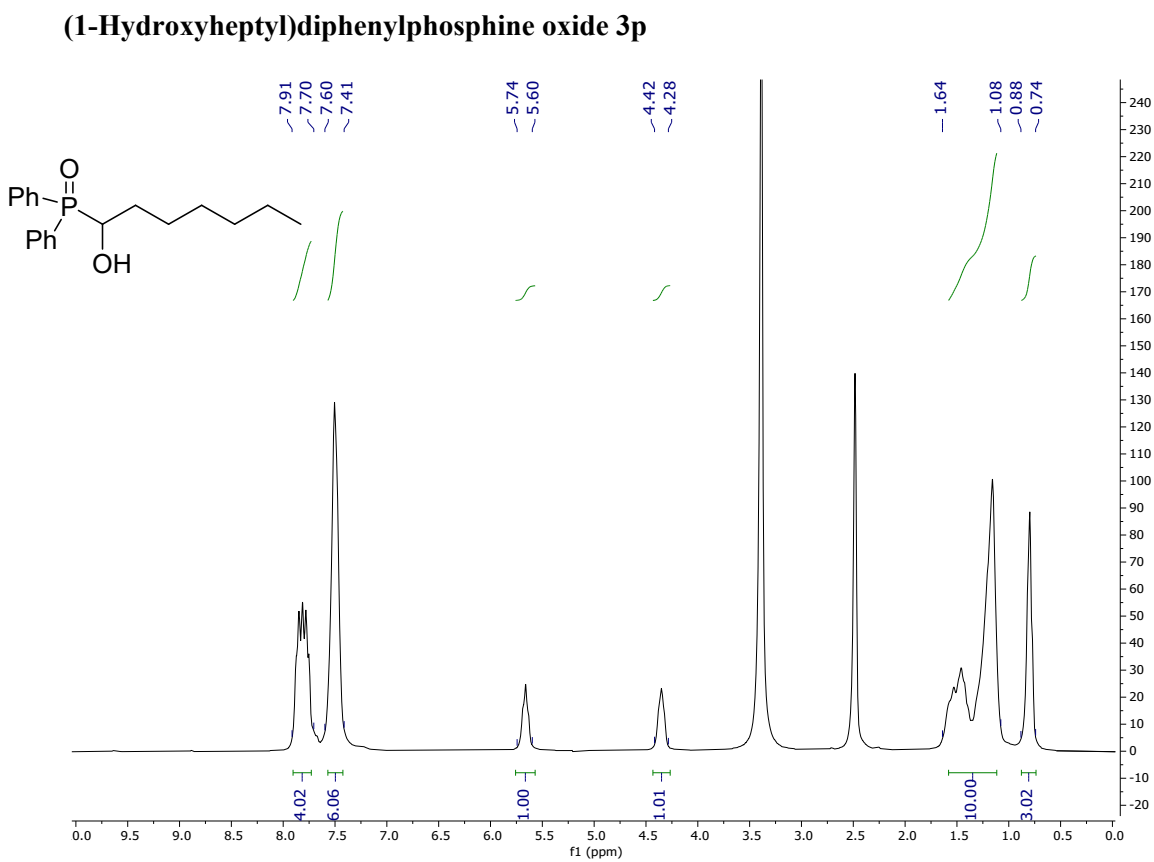


Figure SI_48: $^1\text{H-NMR}$ for **3p** in $\text{DMSO-}d^6$ (300 MHz).

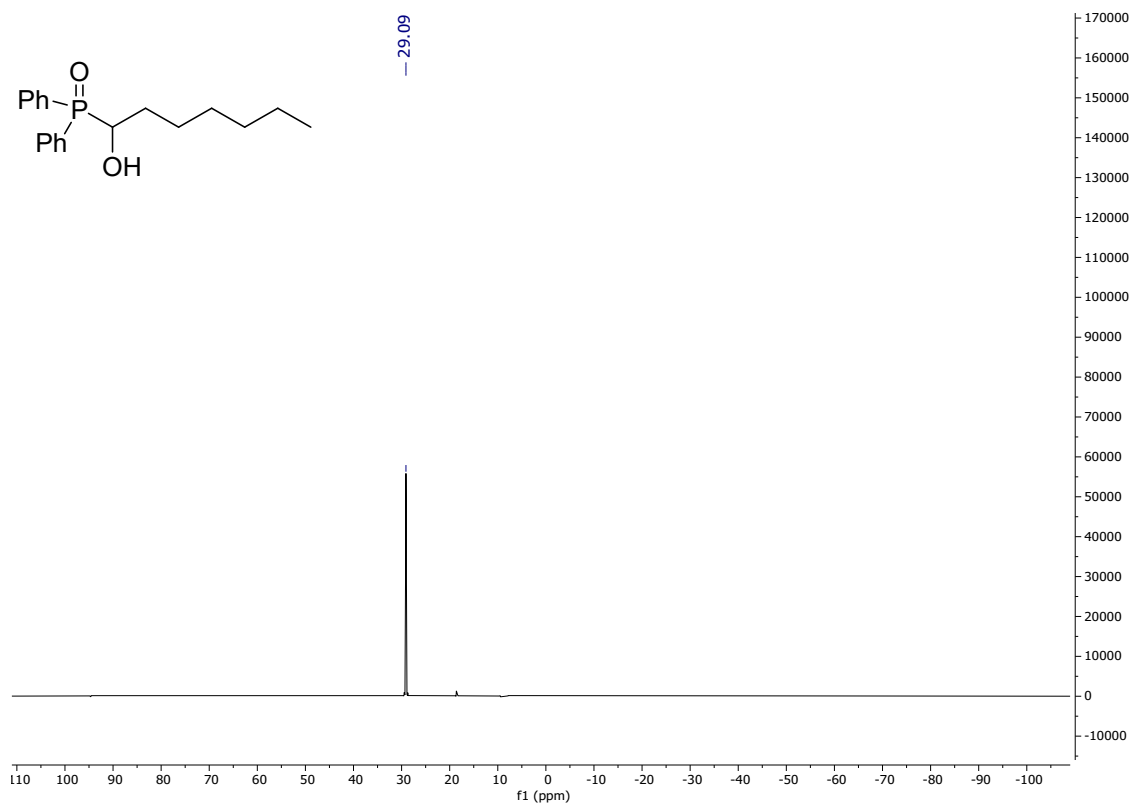


Figure SI_49: ^{31}P -NMR for 3p in $\text{DMSO-}d^6$ (121 MHz).

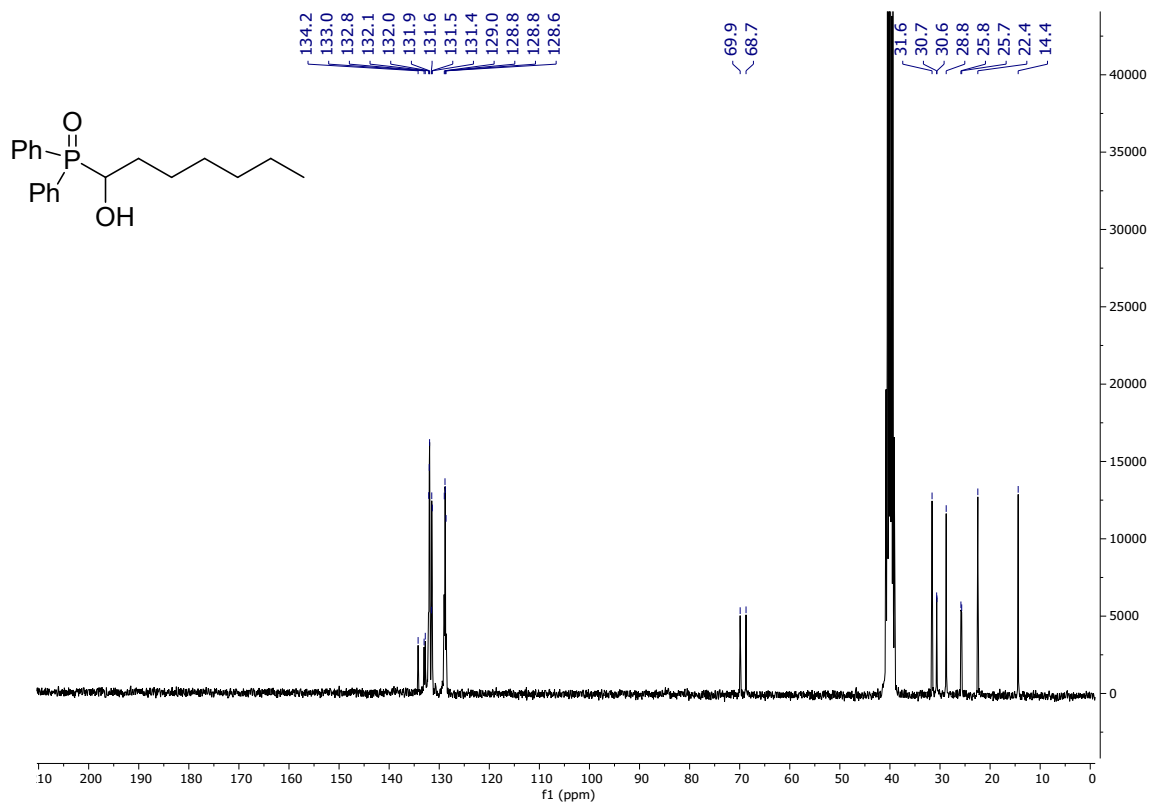


Figure SI_50: ^{13}C -NMR for 3p in $\text{DMSO-}d^6$ (75 MHz).

((4-Chlorophenyl)(hydroxy)methyl)bis(4-methoxyphenyl)phosphine oxide 3q

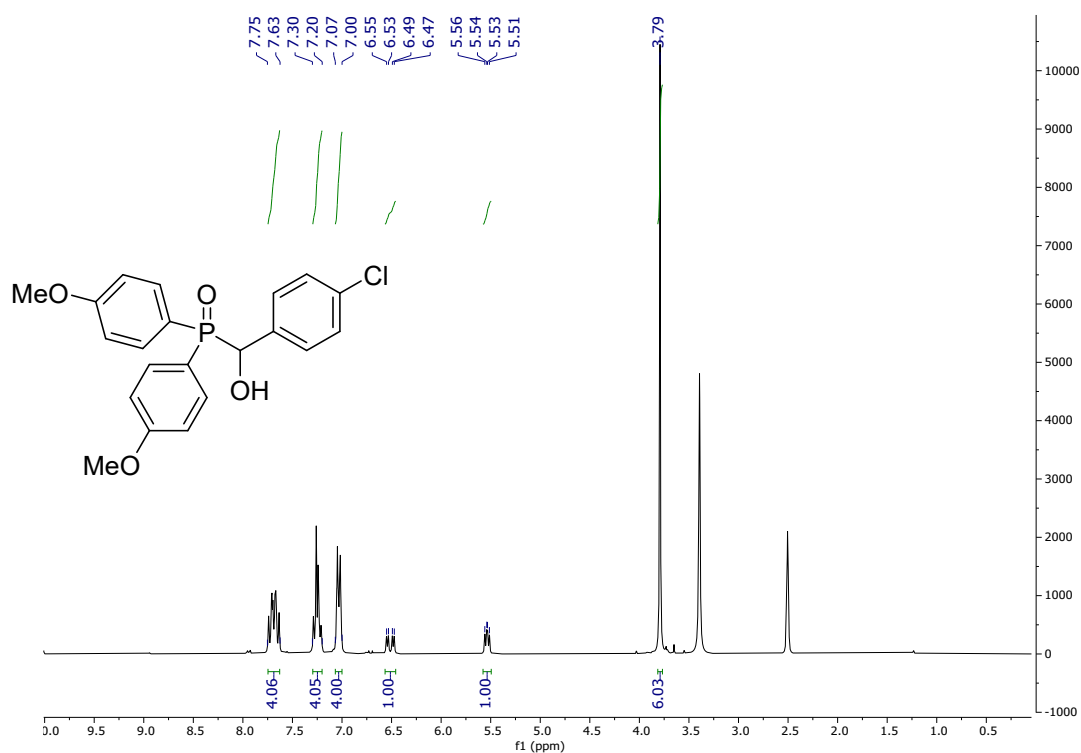


Figure SI_51: ¹H-NMR for **3q** in DMSO-*d*⁶ (300 MHz).

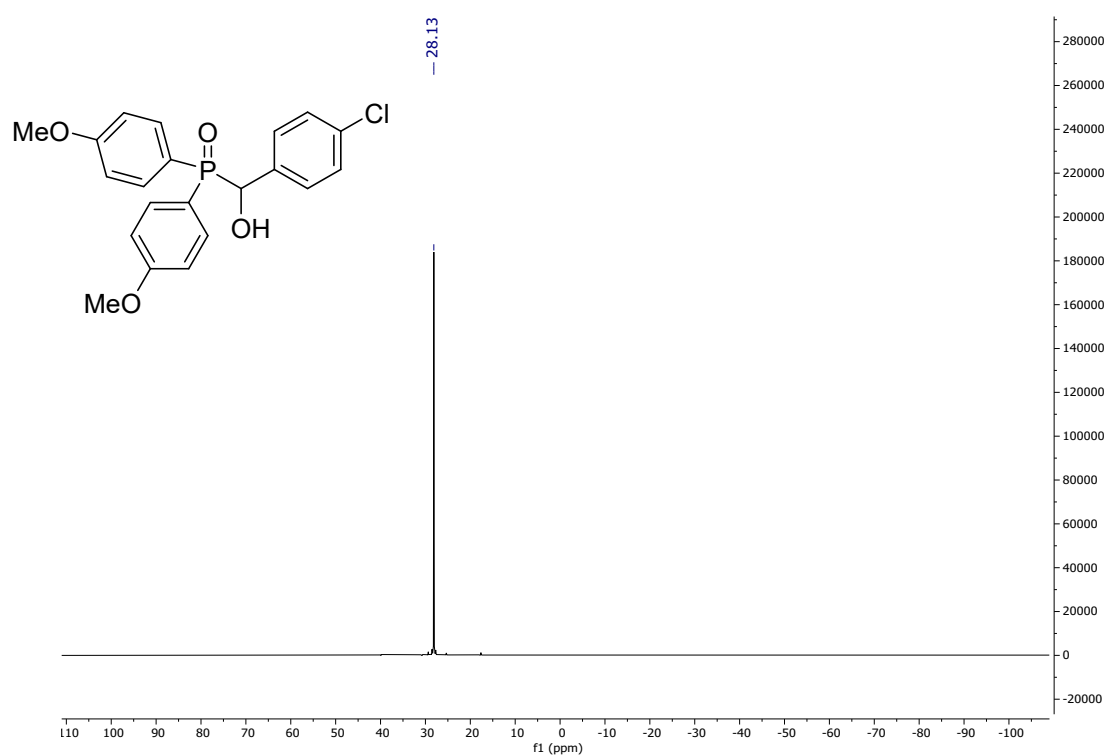


Figure SI_52: ³¹P-NMR for **3q** in DMSO-*d*⁶ (121 MHz).

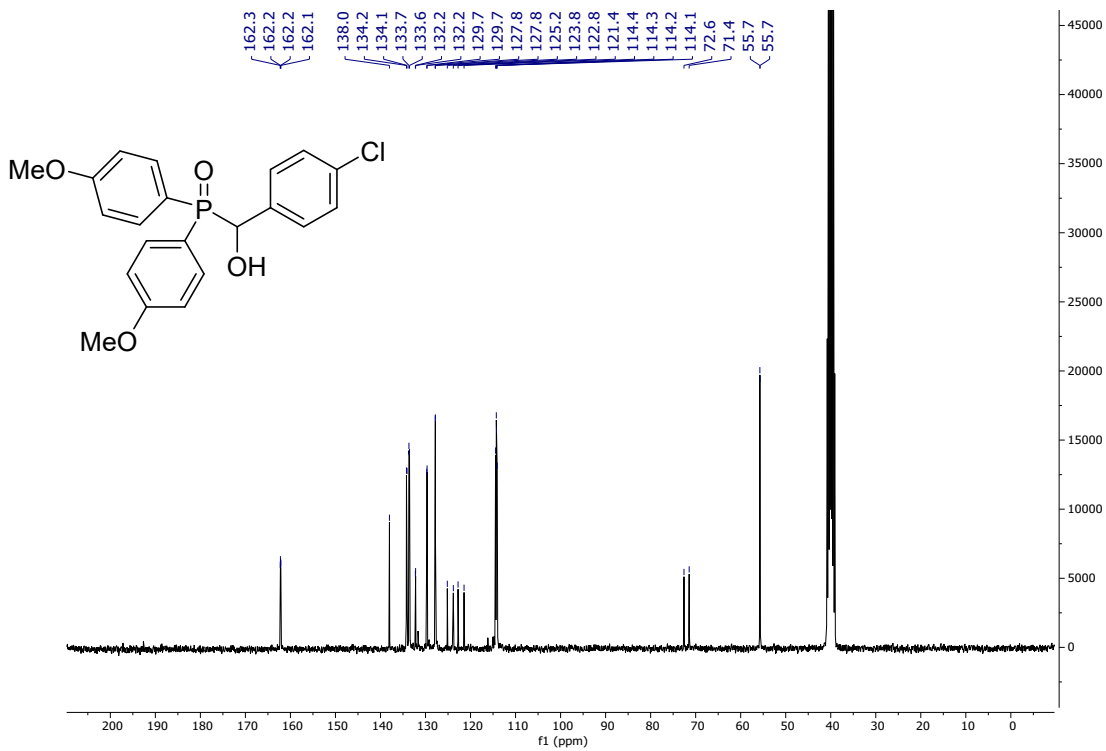


Figure SI_53: ¹³C-NMR for **3q** in DMSO-*d*⁶ (75 MHz).

(Hydroxy(phenyl)methyl)bis(4-methoxyphenyl)phosphine oxide **3r**

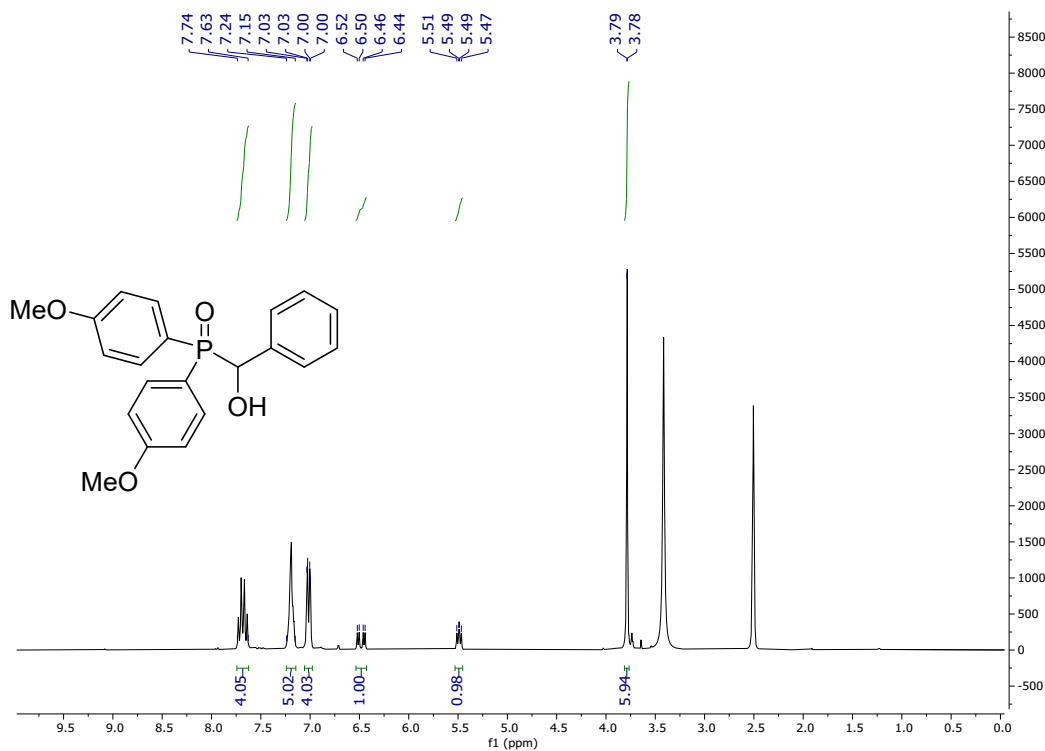
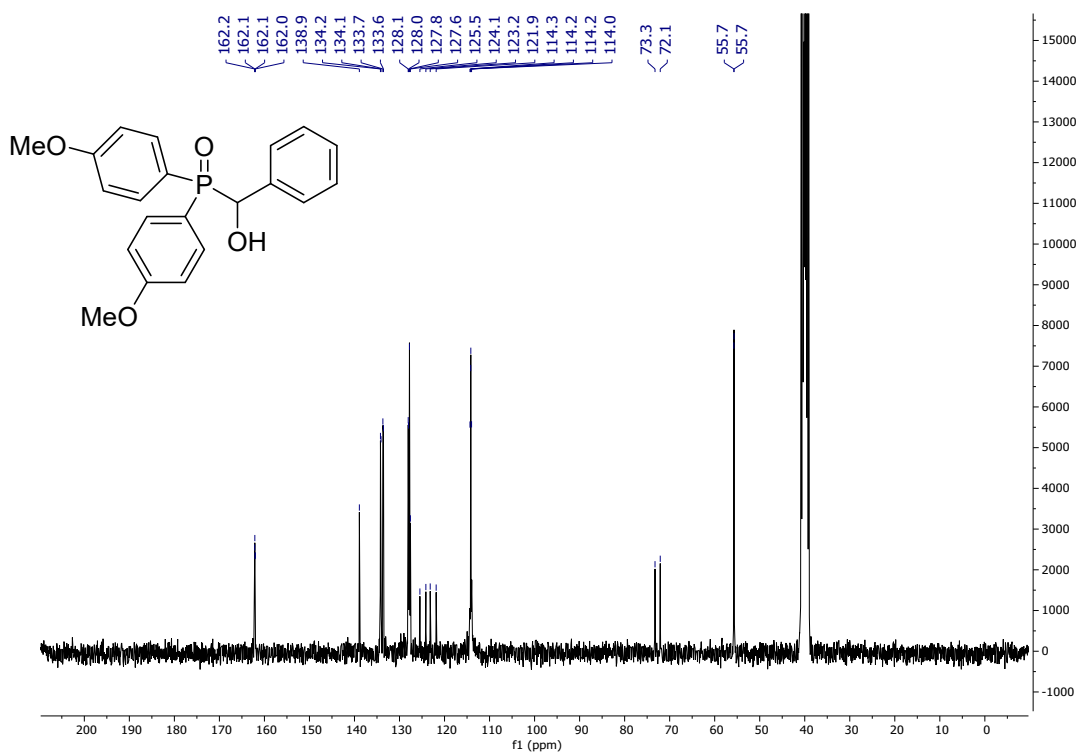
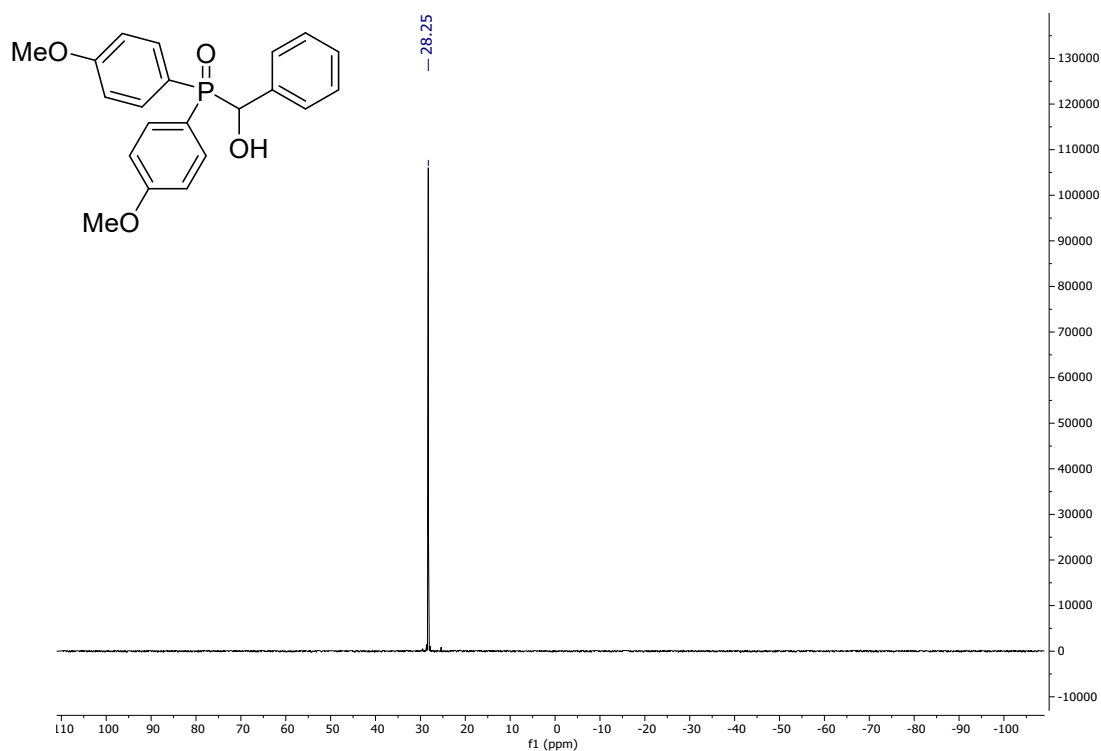


Figure SI_54: ¹H-NMR for **3r** in DMSO-*d*⁶ (300 MHz).



(Hydroxy(4-methoxyphenyl)methyl)bis(4-methoxyphenyl)phosphine oxide 3s

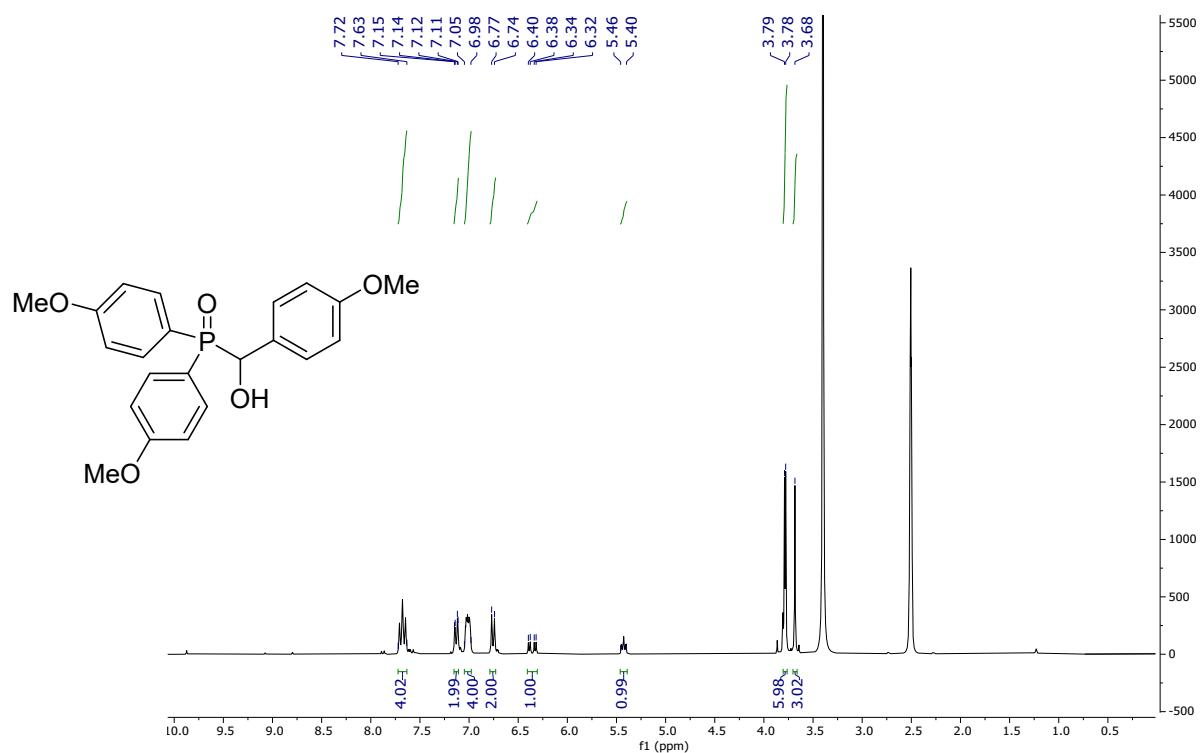


Figure SI_57: $^1\text{H-NMR}$ for 3s in $\text{DMSO-}d^6$ (300 MHz).

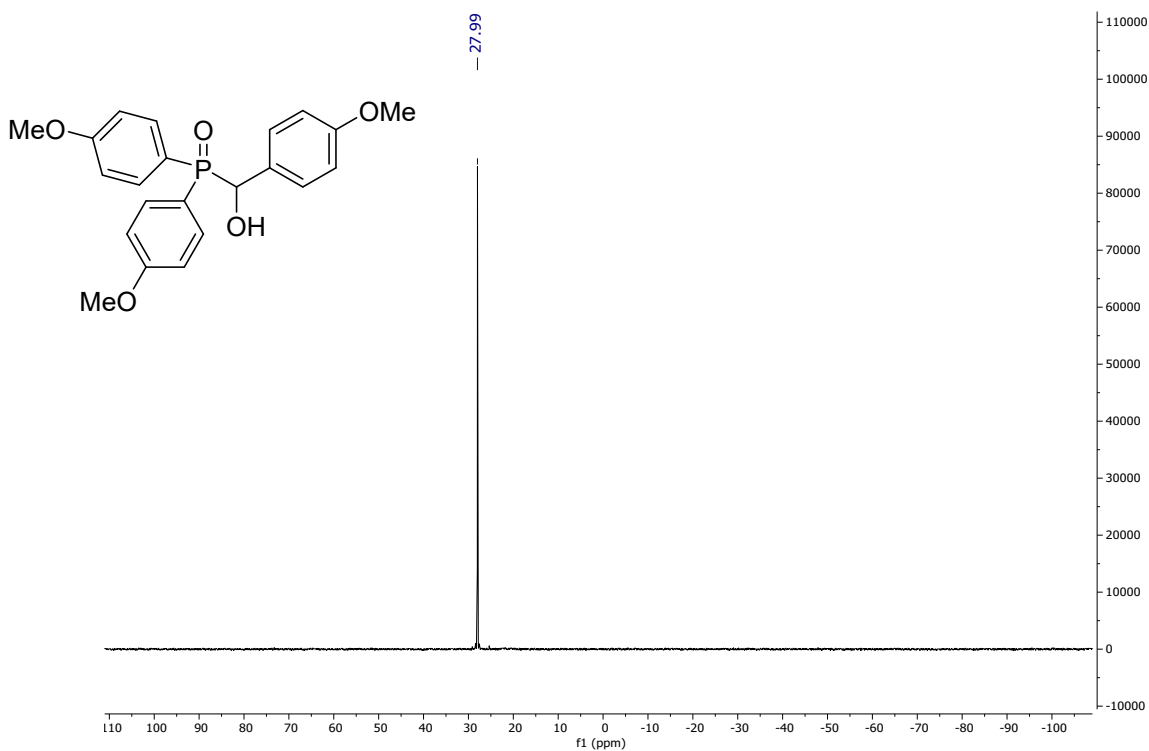


Figure SI_58: $^{31}\text{P-NMR}$ for 3s in $\text{DMSO-}d^6$ (121 MHz).

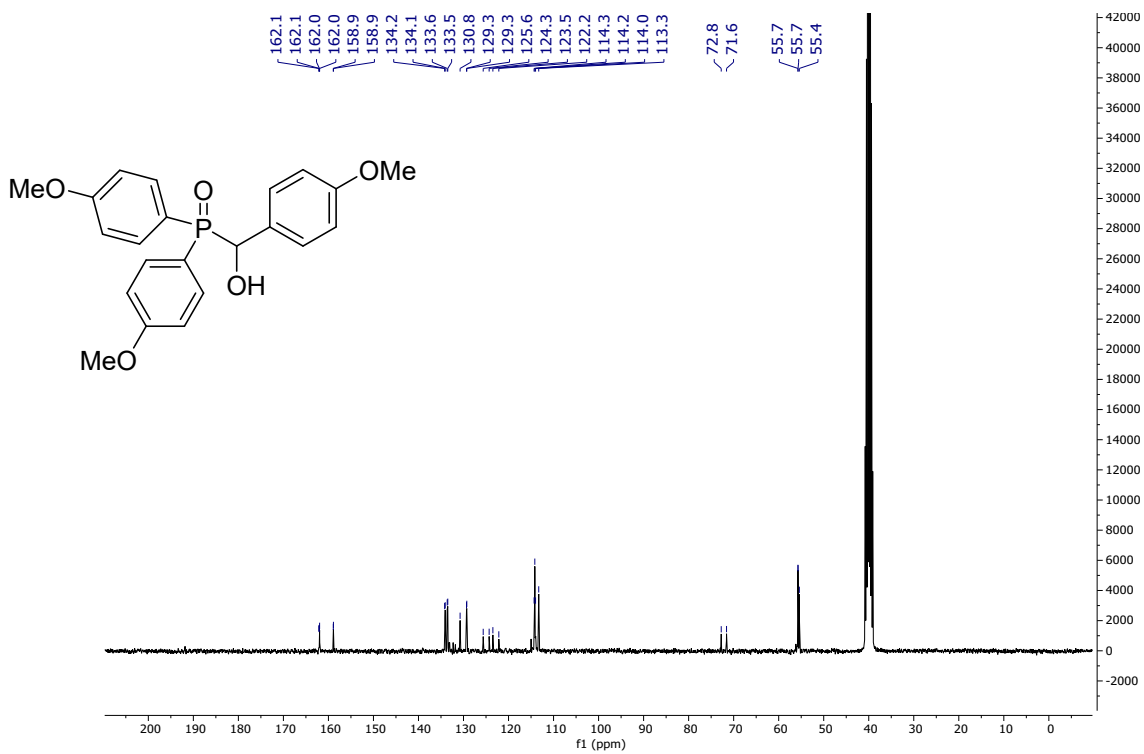


Figure SI_59: ¹³C-NMR for 3s in DMSO-*d*⁶ (75 MHz).

Dibutyl((4-chlorophenyl)(hydroxy)methyl)phosphine oxide 3t

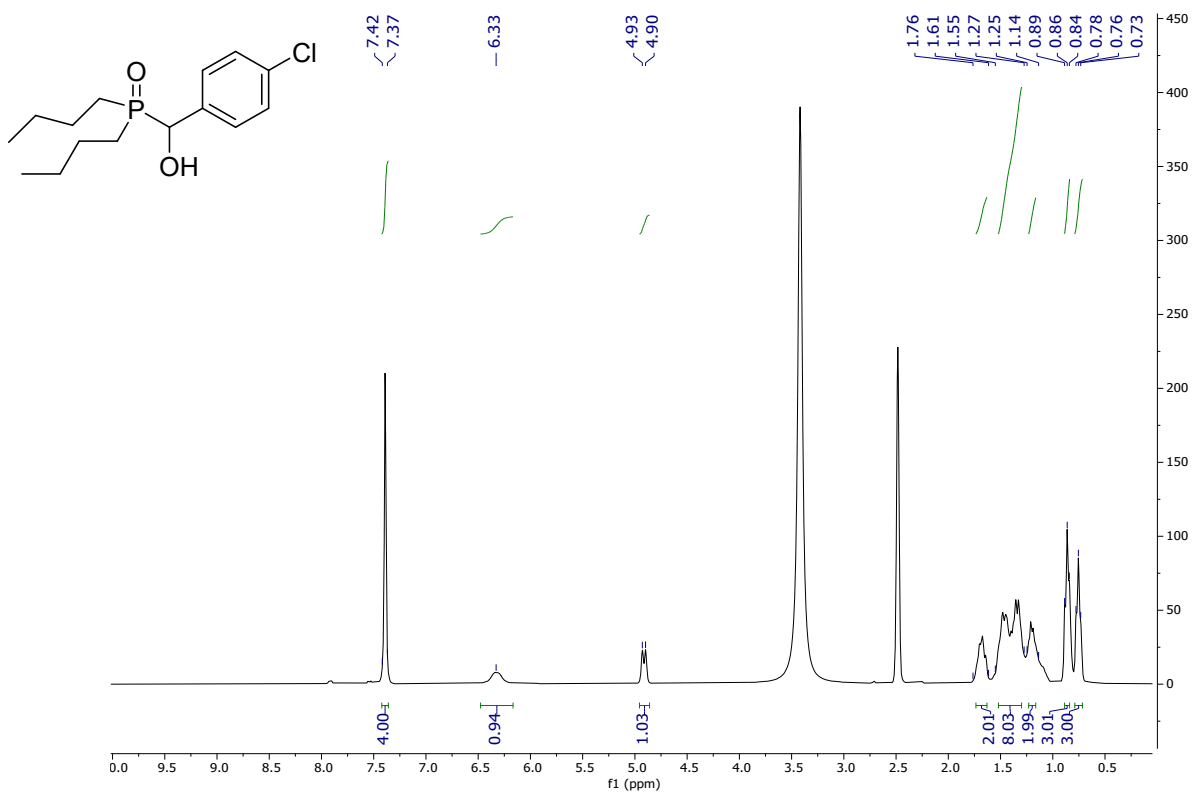


Figure SI_60: ¹H-NMR for 3t in DMSO-*d*⁶ (300 MHz).

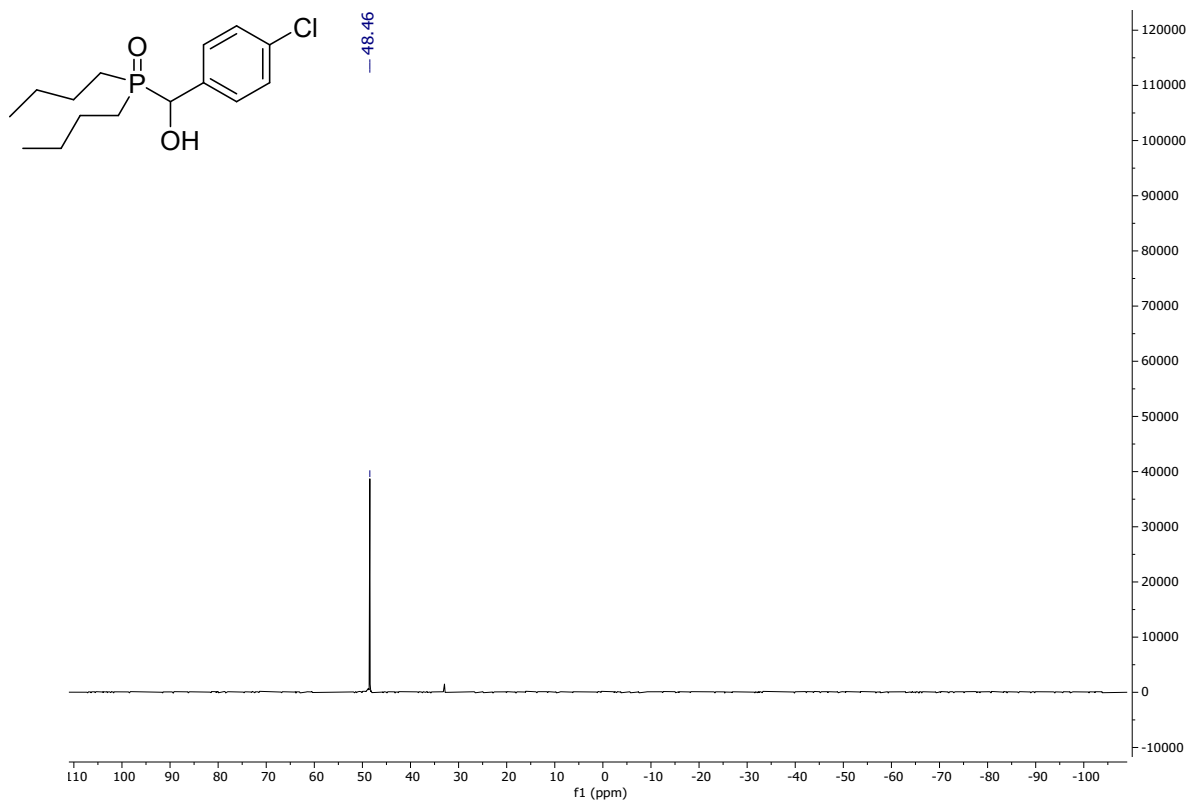


Figure SI_61: ^{31}P -NMR for 3t in $\text{DMSO-}d^6$ (121 MHz).

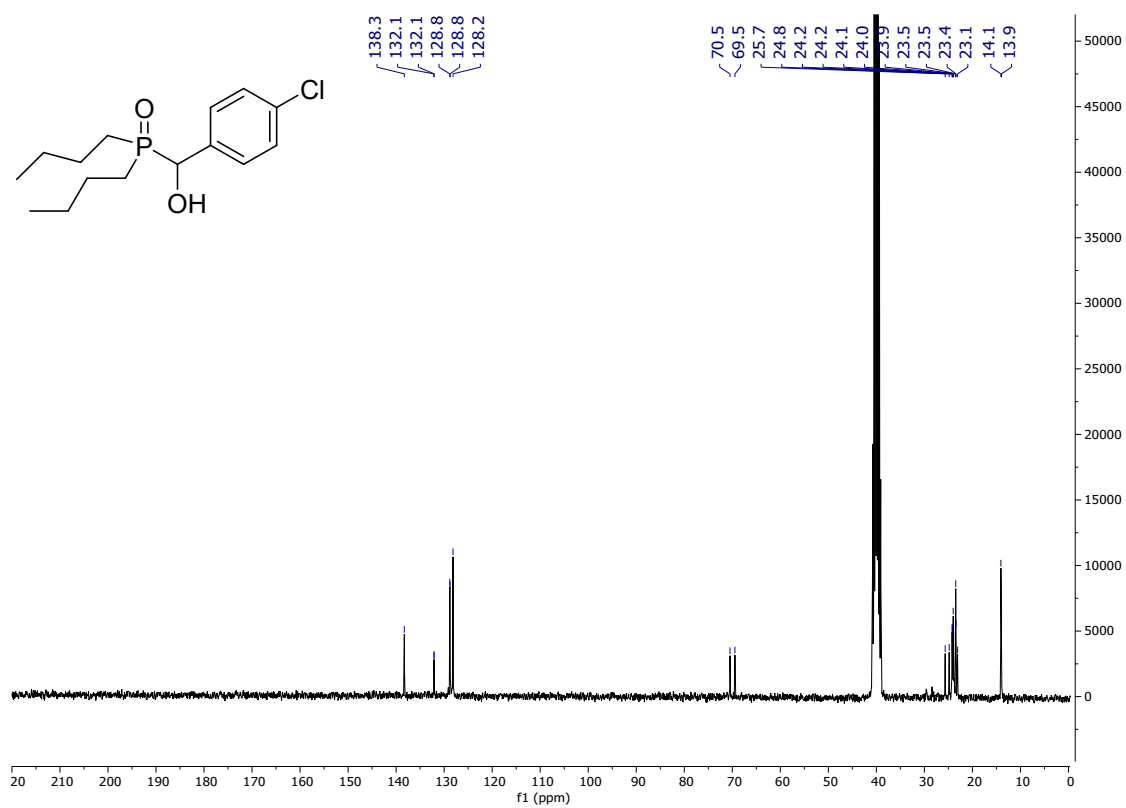


Figure SI_62: ^{13}C -NMR for 3t in $\text{DMSO-}d^6$ (75 MHz).

((4-Chlorophenyl)(hydroxy)methyl)diphenylphosphine sulfide 3u

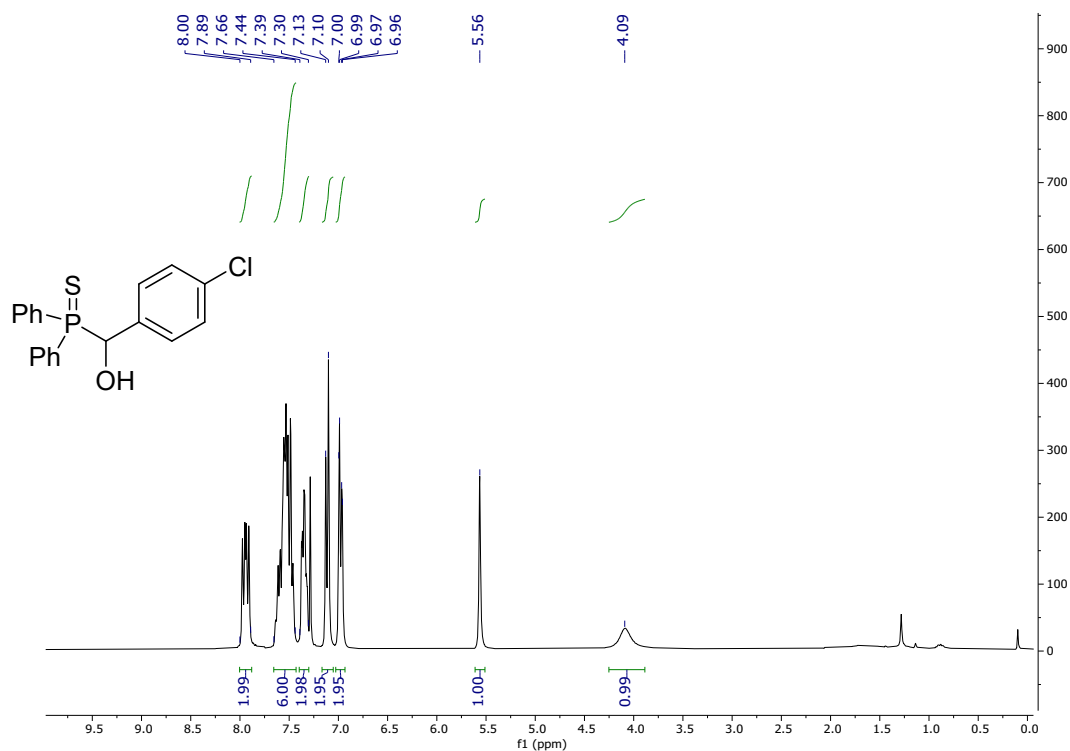


Figure SI_63: $^1\text{H-NMR}$ for 3u in CDCl_3 (300 MHz).

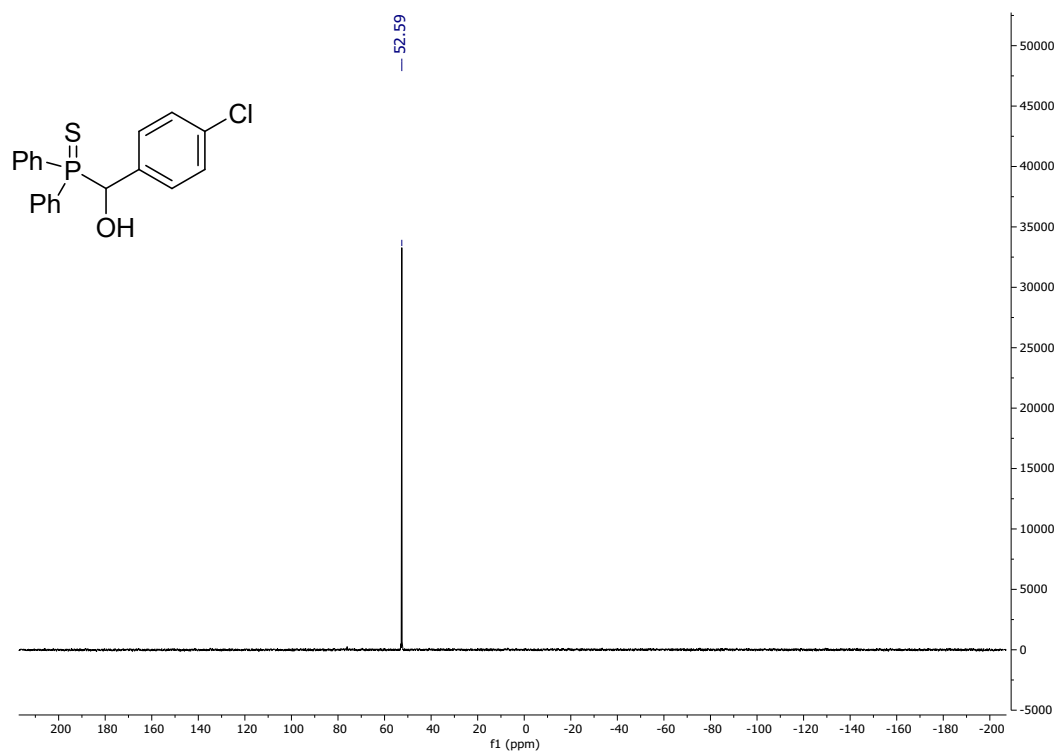


Figure SI_64: $^{31}\text{P-NMR}$ for 3u in CDCl_3 (121 MHz).

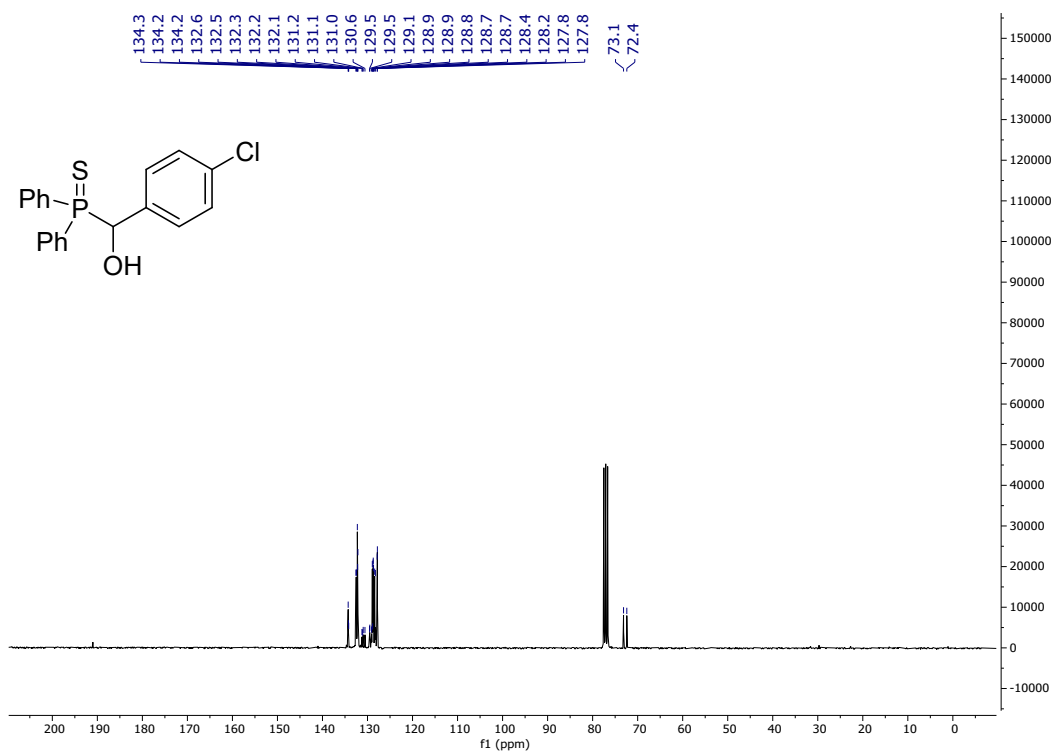


Figure SI_65: ¹³C-NMR for 3u in CDCl₃ (75 MHz).

(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine sulfide 3v

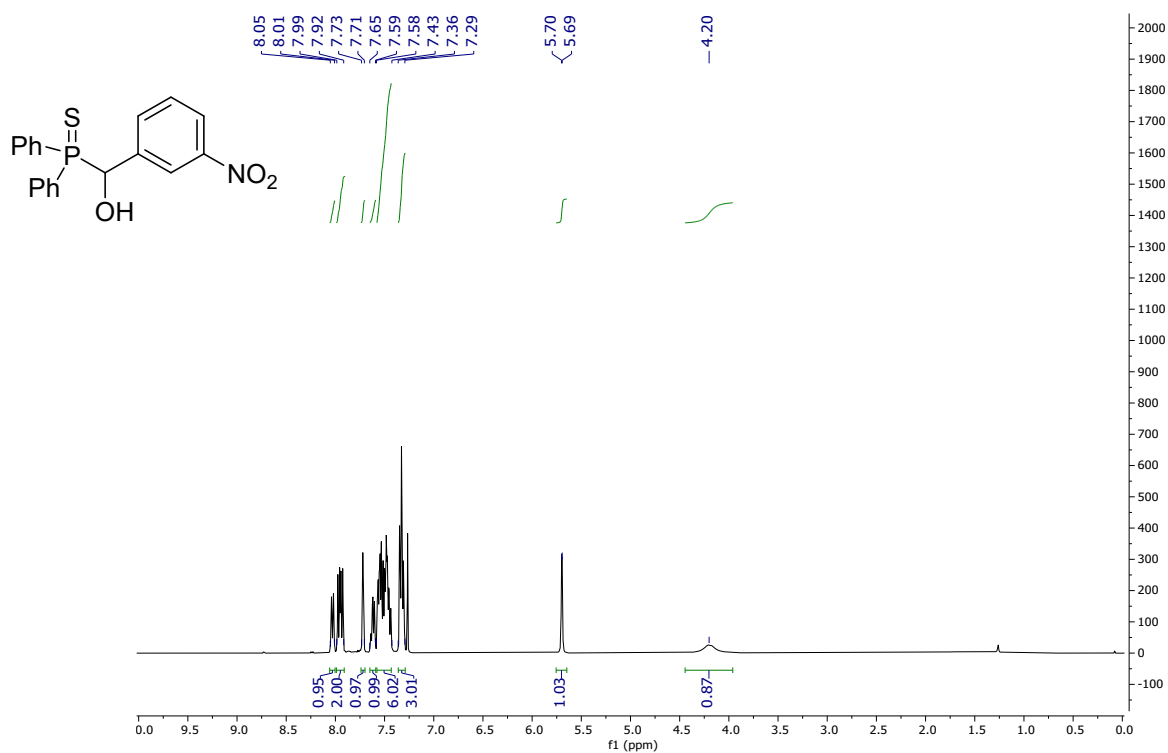
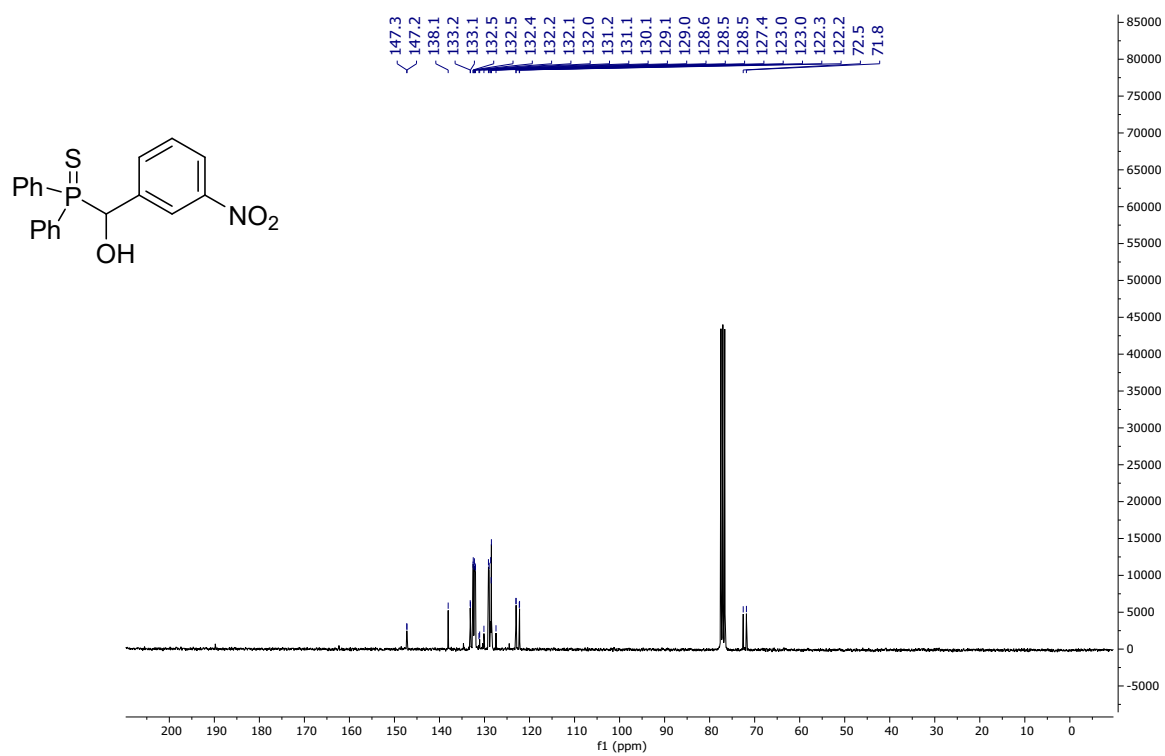
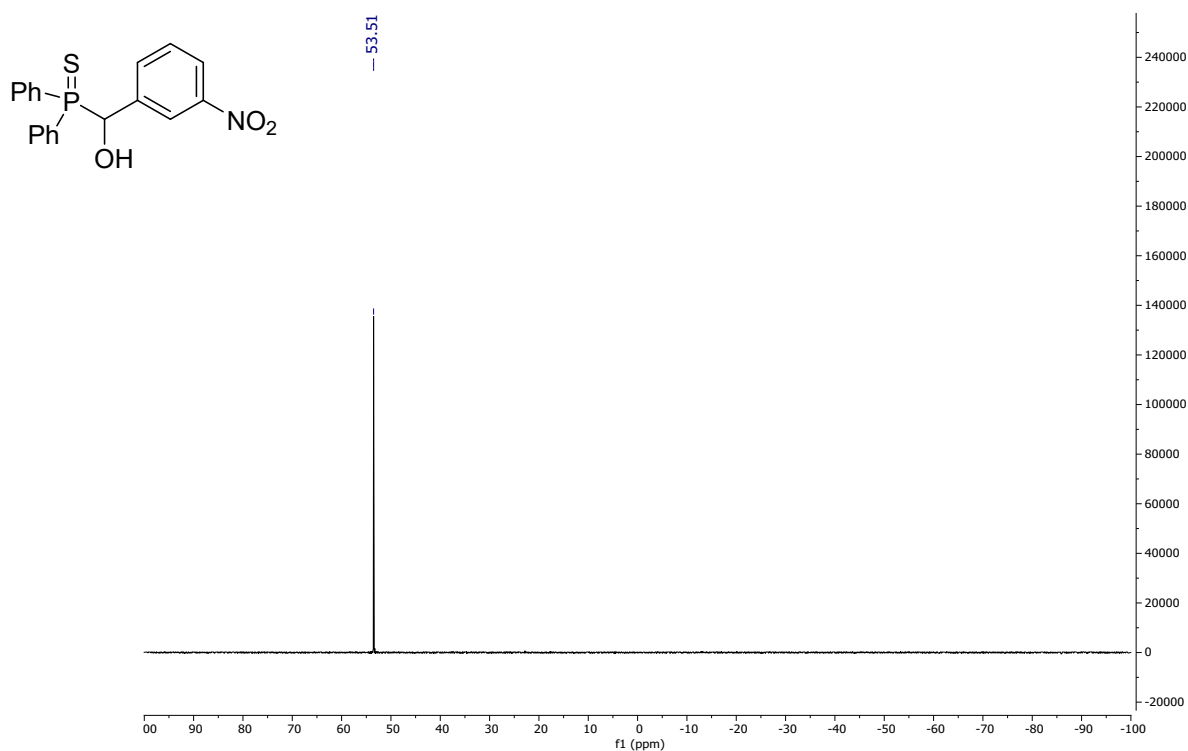


Figure SI_66: ¹H-NMR for 3v in CDCl₃ (401 MHz).



(E)-(1-Hydroxy-3-(2-nitrophenyl)allyl)diphenylphosphine sulfide 3w

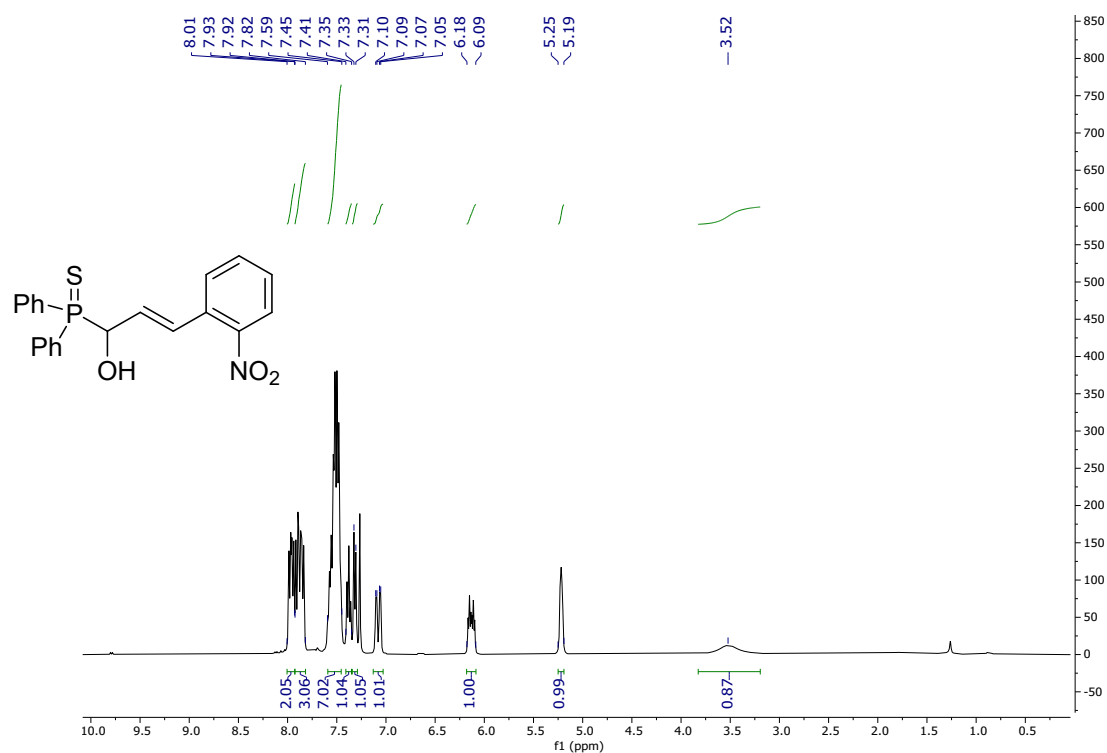


Figure SI_69: ¹H-NMR for 3w in CDCl₃ (401 MHz).

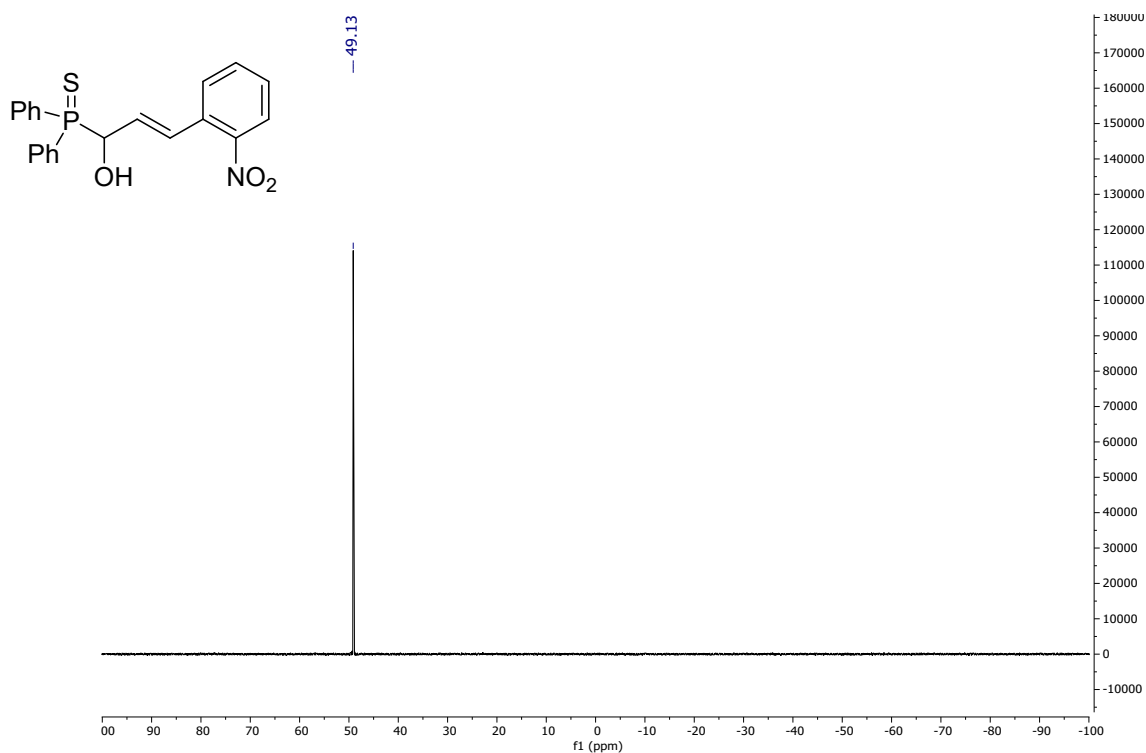


Figure SI_70: ³¹P-NMR for 3w in CDCl₃ (162 MHz).

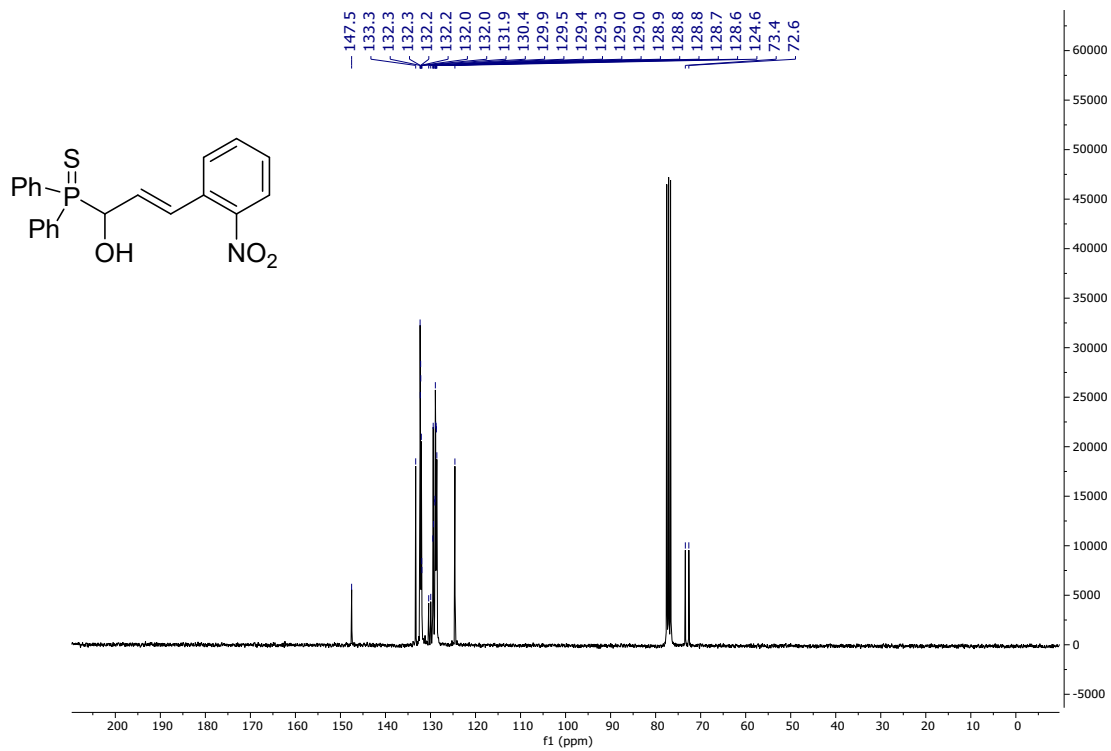


Figure SI_71: ¹³C-NMR for **3w** in CDCl₃ (75 MHz).

((4-Chlorophenyl)(hydroxy)methyl)diphenylphosphine selenide 3x

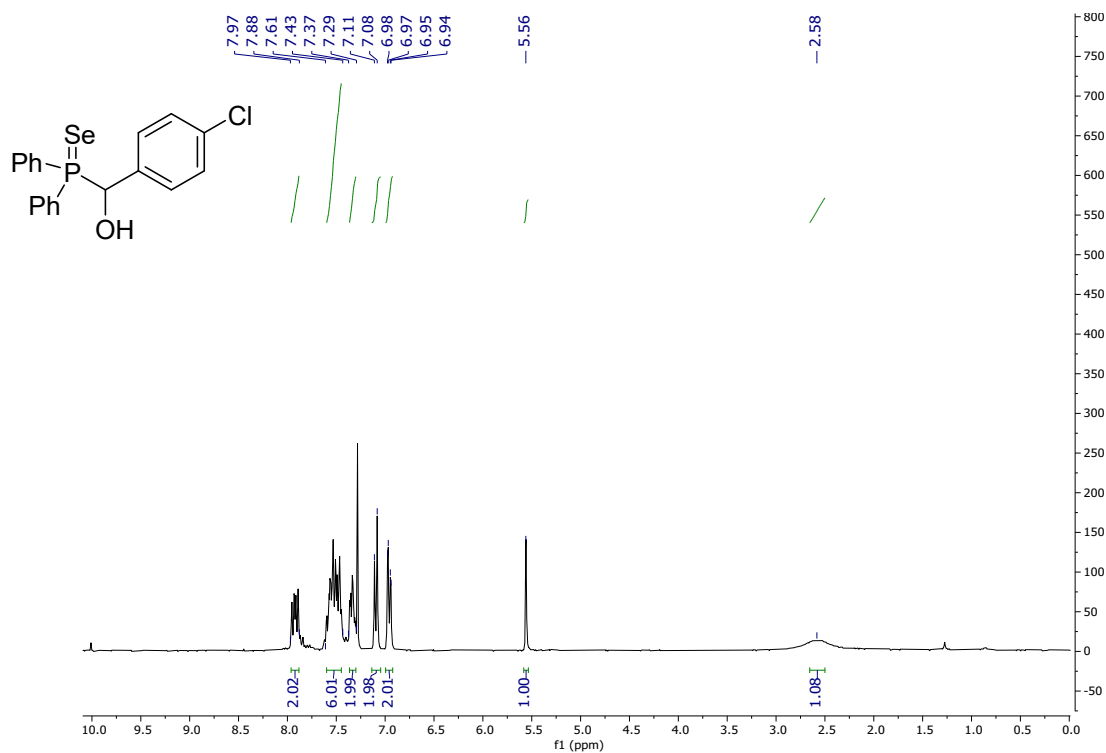
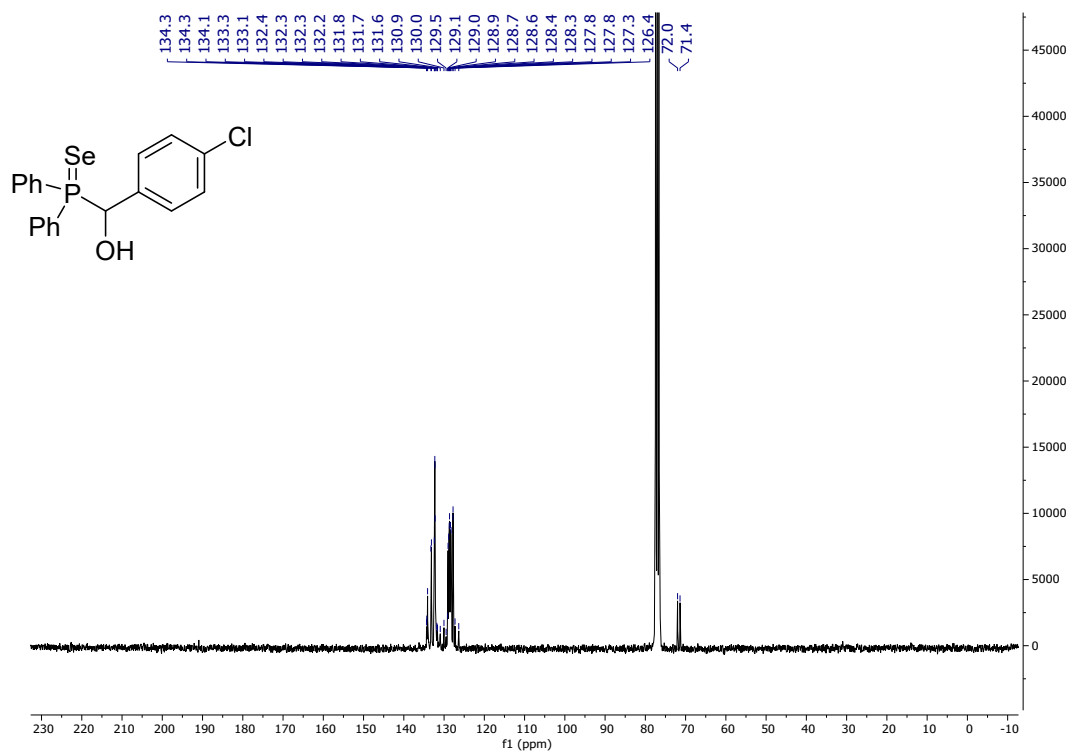
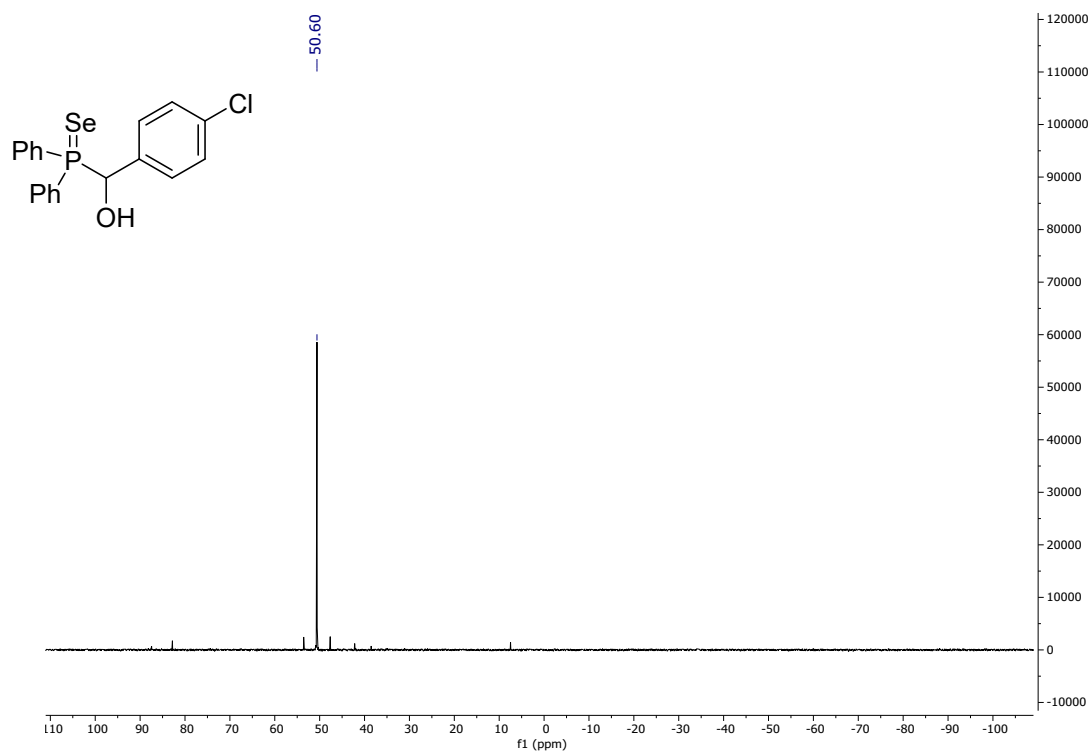


Figure SI_72: ¹H-NMR for **3x** in CDCl₃ (300 MHz).



(Hydroxy(3-nitrophenyl)methyl)diphenylphosphine selenide **3y**

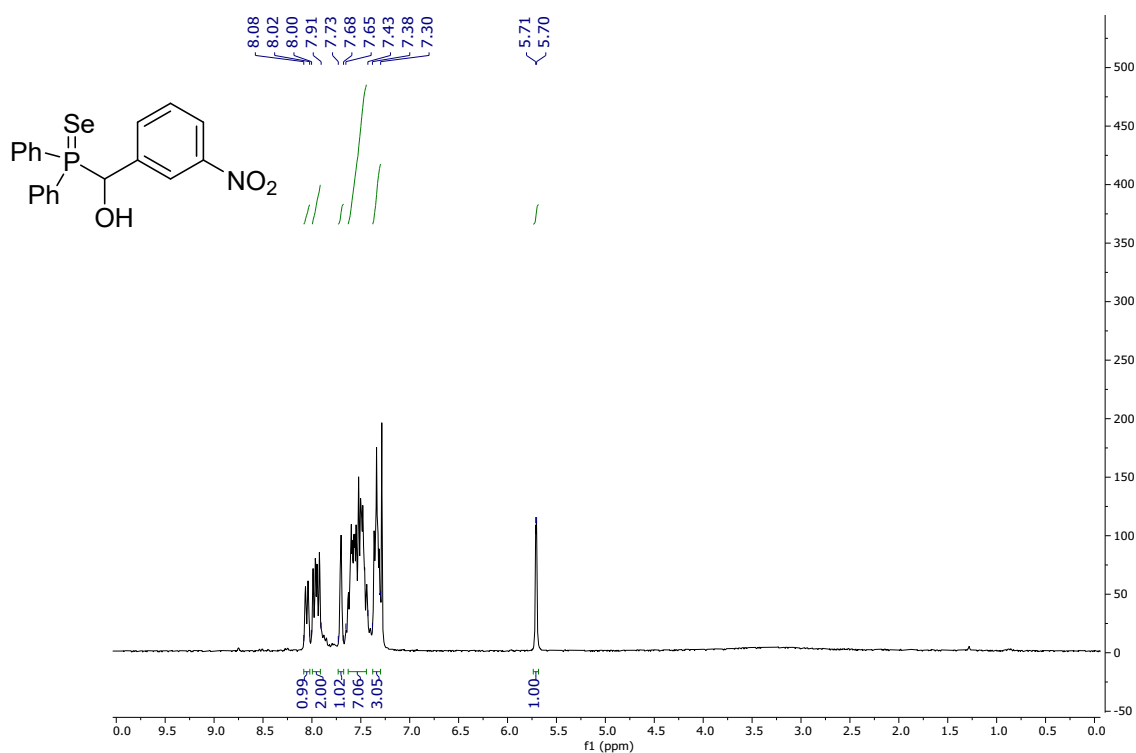


Figure SI_75: $^1\text{H-NMR}$ for **3y** in CDCl_3 (300 MHz).

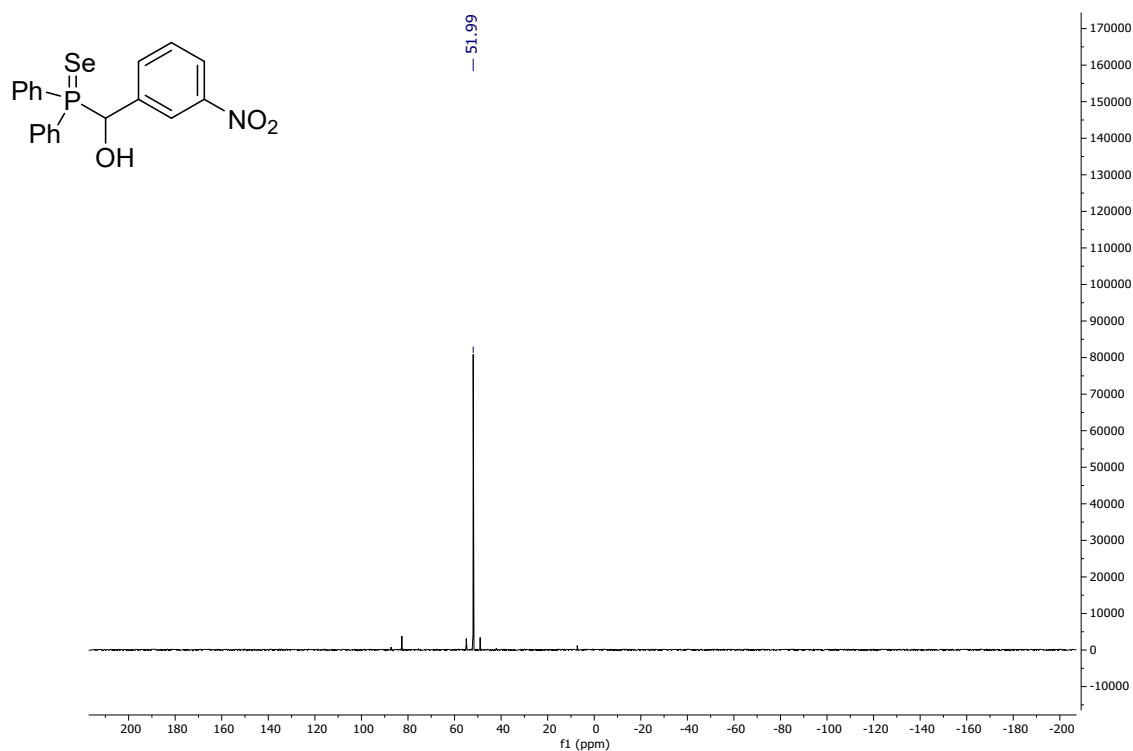


Figure SI_76: $^{31}\text{P-NMR}$ for **3y** in CDCl_3 (121 MHz).

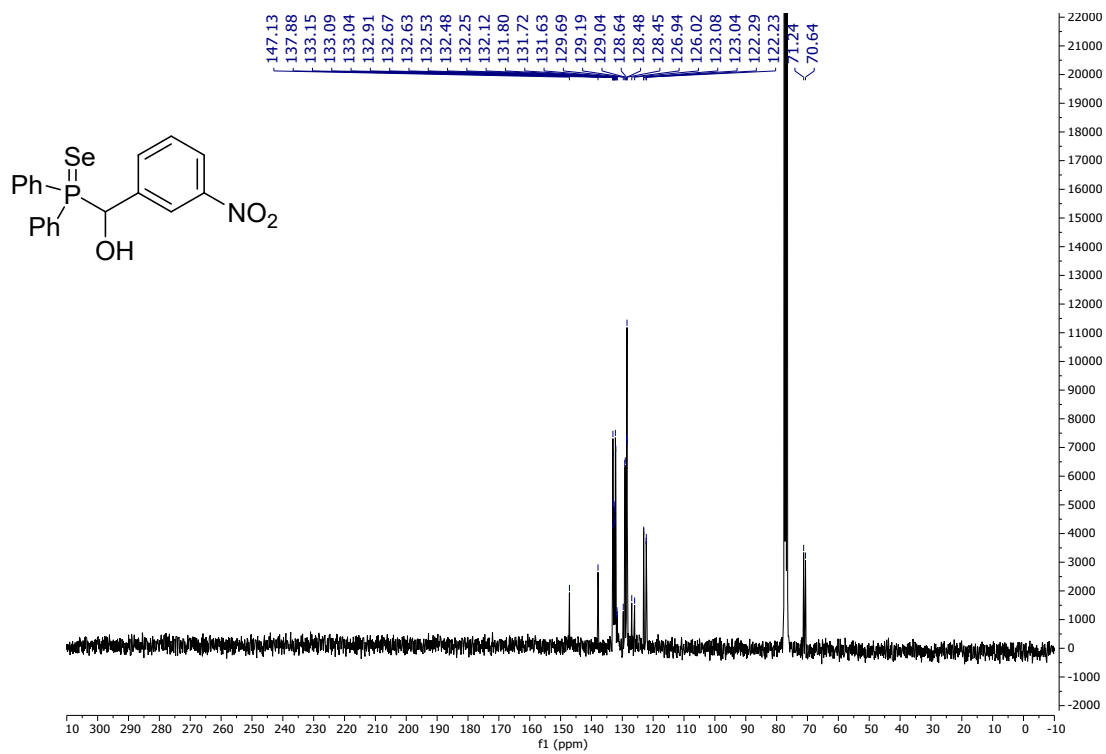


Figure SI_77: $^{13}\text{C-NMR}$ for **3y** in CDCl_3 (75 MHz).