

Diastereoselective Hydrophosphonylation of Imines Using a TADDOL Derived Phosphonate. Asymmetric Synthesis of α -Aminophosphonic acid derivatives.

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Electronic Supporting Information.

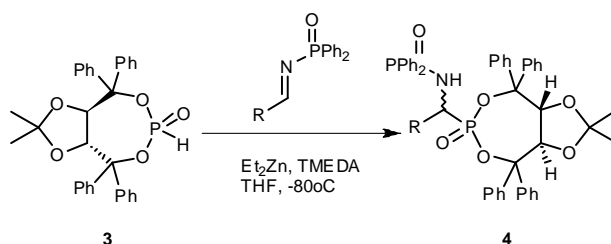
Experimental Procedures.

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1. General.

Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled prior to use. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with silica gel 60 F₂₅₄ plates. Visualization was accomplished by UV light. Flash chromatography was carried out using silica gel 60 (230–400 mesh ASTM). Melting points are uncorrected. ¹H (300 MHz), ¹³C (75 MHz) and ³¹P NMR (120 MHz) spectra were performed using CDCl₃ solutions with TMS as an internal reference ($\delta = 0.00$ ppm) for ¹H and ¹³C NMR spectra and phosphoric acid (50 %) as an external reference ($\delta = 0.0$ ppm) for ³¹P NMR spectra. Chemical shifts (δ) are reported in ppm. Coupling constants (*J*) are reported in Hertz. Low-resolution mass spectra (MS) were obtained chemical ionization (CI) (N₂). Data are reported in the form *m/z* (intensity relative to base = 100). Infrared spectra (IR) were taken as neat and only the most representative frequencies (in cm⁻¹) are given. *N*-diphenylphosphinoylimines¹ and TADDOL phosphite² **3** were prepared according to literature procedures.

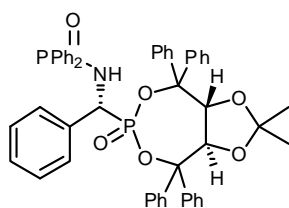
2. Hydrophosphonylation of N-diphenylphosphinoylimines with TADDOL phosphite **3**.



General procedure. The TADDOL phosphite **3** (1.0 equiv.) was dissolved in dry THF (15 mL) and the solution was cooled down to -80°C . Et₂Zn (1.2 equiv of 1.1 M solution in toluene) and TMEDA (1.0 equiv) were injected and the mixture was stirred for 15min at -80°C . After that time the solution of appropriate *N*-diphenylphosphinoylimine (1.0 equiv) in dry THF (15 mL) was added dropwise. The stirring was continued for 12h at -80°C before quenching with sat. aq. NH₄Cl (15mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 30mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated under reduced pressure affording desired products that were further purified by column chromatography (SiO₂, EtOAc/Hexane).

1 Lauzon, C.; Desrosiers, J.-N.; Charette, A. B. *J. Org. Chem.* 2005, **70**, 10579-10580.
2 Linghu, X.; Potnik, J. R.; Johnson, J. S. *J. Am. Chem. Soc.* 2004, **126**, 3070-3071.

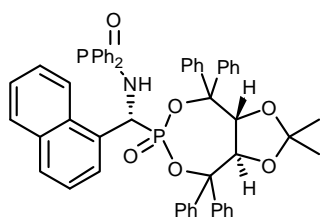
1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-1-phenylmethyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4a).



The title compound was prepared according to general procedure using 1.0 g (1.95 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (2.14 mL), 0.3 mL (1.95 mmol) of TMEDA and 0.6 g (1.95 mmol) of *N*-benzylidene-*P,P*-diphenylphosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 1.28 g (80%) of **4a** as white solid. Mp. 165-167°C. [α]_D²⁰ -111.4 (*c* 1.0, CH₂Cl₂). *R*_f (EtOAc / Pentane 2:1): 0.40. ¹H NMR (300 MHz, CDCl₃): δ 0.43

(s, 3H, CH₃), 0.88 (s, 3H, CH₃), 3.75-3.80 (m, 1H, NH), 4.68-4.83 (m, 1H, CHP), 4.96 (d, ³*J*_{HH} = 8.0 Hz, 1H, CHO), 5.54 (d, ³*J*_{HH} = 8.0 Hz, 1H, CHO), 6.96-7.90 (m, 35H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 26.4 (CH₃), 27.2 (CH₃), 53.4 (d, ¹*J*_{PC} = 161.7 Hz, CHP), 79.1 (d, ³*J*_{PC} = 2.0 Hz, CHO), 80.2 (d, ³*J*_{PC} = 2.0 Hz, CHO), 87.1 (d, ²*J*_{PC} = 8.4 Hz, CPh₂), 91.0 (d, ²*J*_{PC} = 13.4 Hz, CPh₂), 113.8 (C(CH₃)₂), 126.6 (2xCH_{ar}), 127.2 (2xCH_{ar}), 127.3 (2xCH_{ar}), 127.4 (2xCH_{ar}), 127.6 (CH_{ar}), 127.8 (CH_{ar}), 127.9 (CH_{ar}), 128.0 (2xCH_{ar}), 128.1 (d, ³*J*_{PC} = 5.4 Hz, 2xCH_{ar}), 128.3 (2xCH_{ar}), 128.4 (4xCH_{ar}), 128.5 (CH_{ar}), 128.6 (d, ³*J*_{PC} = 7.8 Hz, 2xCH_{ar}), 128.9 (2xCH_{ar}), 129.8 (2xCH_{ar}), 131.2 (d, ¹*J*_{PC} = 102.3 Hz, 2xCq), 131.9 (CH_{ar}), 132.0 (CH_{ar}), 132.1 (2xCH_{ar}), 132.2 (CH_{ar}), 132.3 (2xCH_{ar}), 132.6 (d, ³*J*_{PC} = 9.1 Hz, 2xCH_{ar}), 136.4 (C_q), 139.4 (C_q), 139.6 (C_q), 143.7 (C_q), 144.3 (d, ²*J*_{PC} = 7.6 Hz, C_q). ³¹P NMR (120 MHz, CDCl₃): δ 18.2 (d, ³*J*_{PP} = 39.7 Hz, PO(OR)₂), 25.2 (d, ³*J*_{PP} = 39.7 Hz, POPh₂). FTIR (neat) ν_{\max} (cm⁻¹): 3432 (N-H st), 1225 (P=O st). CIMS *m/z* (amu): 818 ([M+H], 100). HRMS (amu) Calcd for C₅₀H₄₆NO₆P₂ (M+H)⁺ 818.2800; Found, 818.2772.

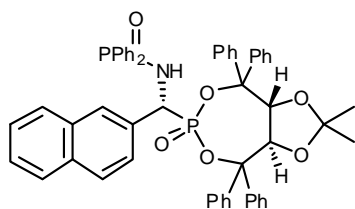
1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-1-naphthylmethyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4b).



The title compound was prepared according to general procedure using 0.5 g (1.0 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (1.1 mL), 0.15 mL (1.0 mmol) of TMEDA and 0.35 g (1.0 mmol) of *N*-(naphthalen-1-ylmethylene)-*P,P*-diphenylphosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.64 g (75%) of **4b** as yellowish solid. Mp. 176-178°C. *R*_f (EtOAc / Hexane 4:1): 0.37. [α]_D²⁰ -123.0 (*c* 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.44 (s, 3H, CH₃), 0.77 (s, 3H, CH₃), 4.62 (dt,

³*J*_{HH} = 8.0 Hz, ²*J*_{HP} = 12.8 Hz, 1H, CHP), 4.92 (d, ³*J*_{HH} = 8.0 Hz, 1H, CHO), 5.54 (d, ³*J*_{HH} = 7.9 Hz, 1H, CHO), 5.63-5.75 (m, 1H, NH), 6.36 (d, ³*J*_{HH} = 7.3 Hz, 1H, CH_{ar}), 6.96-7.90 (m, 36H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 26.5 (CH₃), 27.0 (CH₃), 50.0 (d, ¹*J*_{PC} = 150.0 Hz, CHP), 78.8 (CHO), 80.0 (CHO), 87.5 (d, ²*J*_{PC} = 7.1 Hz, CPh₂), 91.2 (d, ²*J*_{PC} = 13.1 Hz, CPh₂), 114.1 (C(CH₃)₂), 122.8 (C_{ar}), 125.5 (C_{ar}), 125.7 (C_{ar}), 126.0 (C_{ar}), 126.4 (C_{ar}), 126.5 (C_{ar}), 126.9 (C_{ar}), 127.4 (C_{ar}), 127.5 (C_{ar}), 127.9 (C_{ar}), 128.1 (C_{ar}), 128.3 (C_{ar}), 128.5 (C_{ar}), 128.7 (C_{ar}), 128.9 (C_{ar}), 129.0 (C_{ar}), 129.6 (C_{ar}), 131.0 (C_{ar}), 131.9 (C_{ar}), 132.0 (C_{ar}), 132.0 (C_{ar}), 132.2 (C_{ar}), 132.3 (C_{ar}), 132.7 (C_{ar}), 132.8 (C_{ar}), 134.2 (C_{ar}), 138.9 (d, ²*J*_{PC} = 10.0 Hz, C_{ar}), 139.8 (C_{ar}), 143.6 (C_{ar}), 144.4 (C_{ar}). ³¹P NMR (120 MHz, CDCl₃): δ 18.6 (d, ³*J*_{PP} = 33.1 Hz, PO(OR)₂), 25.1 (d, ³*J*_{PP} = 33.1 Hz, POPh₂). FTIR (neat) ν_{\max} (cm⁻¹): 3424 (N-H st), 1254 (P=O st). CIMS *m/z* (amu): 868 ([M+H], 100). HRMS (amu) Calcd for C₅₄H₄₈NO₆P₂ (M+H)⁺ 868.2957; Found, 868.2933.

1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-2-naphthylmethyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4c).

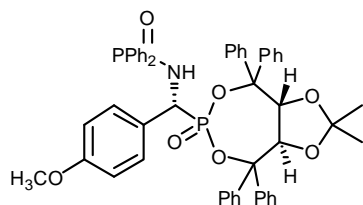


The title compound was prepared according to general procedure using 0.5 g (1.0 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (1.1 mL), 0.15 mL (1.0 mmol) of TMEDA and 0.35 g (1.0 mmol) of *N*-(naphthalen-2-ylmethylene)-*P,P*-diphenylphosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.62 g (73%) of **4c** as yellowish solid. Mp. 172-173°C *R*_f (EtOAc / Hexane 3:1): 0.48. [α]_D²⁰ -129.1 (*c* 1.0,

CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.39 (s, 3H, CH₃), 0.87 (s, 3H, CH₃), 3.87-3.94 (m, 1H, NH), 4.85-5.00 (m, 2H, CHP, CHO), 5.54 (d, ³*J*_{HH} = 7.9 Hz, 1H, CHO), 6.84-7.93 (m, 37H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 26.3 (CH₃), 27.2 (CH₃), 54.0 (d, ¹*J*_{PC} = 161.7 Hz, CHP), 79.1 (d, ³*J*_{PC} = 2.0 Hz, CHO), 80.3 (d, ³*J*_{PC} = 2.0 Hz, CHO), 87.0 (d, ²*J*_{PC} = 8.5 Hz, CPh₂), 90.1 (d, ²*J*_{PC} = 13.2 Hz, CPh₂), 113.8 (C(CH₃)₂), 125.0 (d, ³*J*_{PC} = 4.5 Hz, C_{ar}), 126.2 (d, ³*J*_{PC} = 6.2 Hz, C_{ar}), 126.6 (C_{ar}), 127.2 (C_{ar}), 127.5 (C_{ar}), 127.6 (C_{ar}), 127.7 (C_{ar}), 127.8 (C_{ar}), 128.0 (C_{ar}), 128.2 (C_{ar}), 128.3 (C_{ar}), 128.5 (C_{ar}), 128.6

(C_{ar}), 128.7 (C_{ar}), 128.8 (C_{ar}), 128.9 (C_{ar}), 129.7 (C_{ar}), 132.0 (C_{ar}), 132.1 (C_{ar}), 132.2 (C_{ar}), 132.3 (C_{ar}), 132.4 (C_{ar}), 132.6 (d, ²J_{PC} = 10.0 Hz, C_{ar}), 133.2 (C_{ar}), 133.3 (C_{ar}), 133.4 (C_{ar}), 134.1 (C_{ar}), 138.9 (d, ²J_{PC} = 9.7 Hz, C_{ar}), 139.6 (C_{ar}), 143.7 (C_{ar}), 144.3 (d, ²J_{PC} = 7.5 Hz, C_{ar}). ³¹P NMR (120 MHz, CDCl₃): δ 18.0 (d, ³J_{PP} = 39.5 Hz, PO(OR)₂), 25.1 (d, ³J_{PP} = 39.5 Hz, POPh₂). FTIR (neat) ν_{max} (cm⁻¹): 3434 (N-H st), 1251 (P=O st). CIMS m/z (amu): 868 ([M+H], 100). HRMS (amu) Calcd for C₅₄H₄₈NO₆P₂ (M+H)⁺ 868.2957; Found, 868.2969.

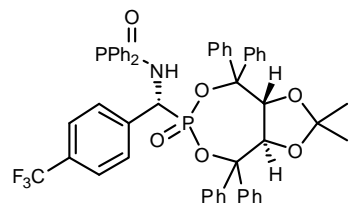
1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-*p*-methoxyphenylmethyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4d).



The title compound was prepared according to general procedure using 0.5 g (1.0 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (1.1 mL), 0.15 mL (1.0 mmol) of TMEDA and 0.33 g (1.0 mmol) of *N*-(4-methoxybenzylidene)-*P,P*-diphenylphosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.68 g (82%) of **4d** as white solid. Mp. 156-158°C. [α]_D²⁰ -132.1 (c 1.0, CH₂Cl₂). R_f (EtOAc / Hexane 3:1): 0.38.

¹H NMR (300 MHz, CDCl₃): δ 0.44 (s, 3H, CH₃), 0.89 (s, 3H, CH₃), 3.41-3.46 (m, 1H, NH), 3.78 (s, 3H, OCH₃), 4.72 (dt, ³J_{HH} = 7.8 Hz, ²J_{HP} = 15.8 Hz, 1H, CHP), 5.05 (d, ³J_{HH} = 8.0 Hz, 1H, CHO), 5.55 (d, ³J_{HH} = 8.0 Hz, 1H, CHO), 6.69 (d, ³J_{HH} = 8.4 Hz, 2H, CH_{ar}), 7.05-7.90 (m, 32H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 26.4 (CH₃), 27.2 (CH₃), 53.4 (d, ¹J_{PC} = 159.7 Hz, CHP), 55.5 (OCH₃), 79.1 (d, ³J_{PC} = 2.0 Hz, CHO), 80.3 (d, ³J_{PC} = 1.9 Hz, CHO), 87.1 (d, ²J_{PC} = 8.2 Hz, CPh₂), 90.8 (d, ²J_{PC} = 12.4 Hz, CPh₂), 113.8 (C(CH₃)₂), 126.7 (C_{ar}), 127.2 (C_{ar}), 128.2 (C_{ar}), 127.3 (C_{ar}), 127.4 (C_{ar}), 127.6 (C_{ar}), 127.9 (C_{ar}), 128.2 (C_{ar}), 128.3 (C_{ar}), 128.4 (C_{ar}), 128.6 (C_{ar}), 128.9 (C_{ar}), 129.2 (C_{ar}), 129.3 (C_{ar}), 129.5 (C_{ar}), 129.8 (C_{ar}), 132.0 (C_{ar}), 132.1 (C_{ar}), 132.2 (C_{ar}), 132.3 (C_{ar}), 132.5 (C_{ar}), 132.6 (C_{ar}), 132.7 (C_{ar}), 139.5 (C_{ar}), 139.7 (C_{ar}), 143.8 (C_{ar}), 144.4 (d, ³J_{PC} = 7.6 Hz, C_{ar}), 159.5 (C_{ar}). ³¹P NMR (120 MHz, CDCl₃): δ 18.3 (d, ³J_{PP} = 40.7 Hz, PO(OR)₂), 24.5 (d, ³J_{PP} = 40.7 Hz, POPh₂). FTIR (neat) ν_{max} (cm⁻¹): 3442 (N-H st), 1253 (P=O st). CIMS m/z (amu): 848 ([M+H], 100). HRMS (amu) Calcd for C₅₁H₄₈NO₇P₂ (M+H)⁺ 848.2906; Found, 848.2914.

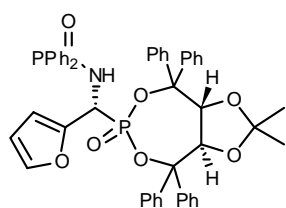
1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-*p*-trifluoromethylphenylmethyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4e).



The title compound was prepared according to general procedure using 0.5 g (1.0 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (1.1 mL), 0.15 mL (1.0 mmol) of TMEDA and 0.37 g (1.0 mmol) of *N*-(4-trifluoromethylbenzylidene)-*P,P*-diphenylphosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.64 g (75%) of **4e** as yellowish solid. Mp. 149-150°C. [α]_D²⁰ -141.0 (c 1.0, CH₂Cl₂). R_f (EtOAc / Hexane 3:1): 0.53.

¹H NMR (300 MHz, CDCl₃): δ 0.43 (s, 3H, CH₃), 0.85 (s, 3H, CH₃), 4.80 (dt, ³J_{HH} = 8.0 Hz, ²J_{HP} = 16.0 Hz, 1H, CHP), 4.90 (d, ³J_{HH} = 7.9 Hz, 1H, CHO), 5.53 (d, ³J_{HH} = 8.0 Hz, 1H, CHO), 6.90 (d, ³J_{HH} = 7.7 Hz, 2H, CH_{ar}), 7.20-7.92 (m, 32H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 26.4 (CH₃), 27.2 (CH₃), 53.8 (d, ¹J_{PC} = 161.3 Hz, CHP), 78.8 (d, ³J_{PC} = 2.0 Hz, CHO), 79.7 (d, ³J_{PC} = 1.9 Hz, CHO), 87.5 (d, ²J_{PC} = 8.3 Hz, CPh₂), 91.6 (d, ²J_{PC} = 13.2 Hz, CPh₂), 114.1 (C(CH₃)₂), 125.3 (CF₃), 126.7 (C_{ar}), 127.2 (C_{ar}), 127.4 (C_{ar}), 127.5 (C_{ar}), 127.6 (C_{ar}), 127.8 (C_{ar}), 127.9 (C_{ar}), 128.0 (C_{ar}), 128.4 (C_{ar}), 128.6 (C_{ar}), 128.7 (C_{ar}), 128.8 (C_{ar}), 128.9 (C_{ar}), 129.3 (C_{ar}), 129.5 (C_{ar}), 129.8 (C_{ar}), 131.9 (C_{ar}), 132.1 (C_{ar}), 132.3 (C_{ar}), 132.4 (C_{ar}), 132.5 (C_{ar}), 132.6 (C_{ar}), 132.8 (C_{ar}), 139.2 (C_{ar}), 139.4 (C_{ar}), 140.4 (C_{ar}), 143.5 (C_{ar}), 144.0 (d, ³J_{PC} = 7.5 Hz, C_{ar}). ³¹P NMR (120 MHz, CDCl₃): δ 17.2 (d, ³J_{PP} = 40.7 Hz, PO(OR)₂), 25.3 (d, ³J_{PP} = 40.7 Hz, POPh₂). FTIR (neat) ν_{max} (cm⁻¹): 3362 (N-H st), 1254 (P=O st). CIMS m/z (amu): 886 ([M+H], 100). HRMS (amu) Calcd for C₅₁H₄₅F₃NO₆P₂ (M+H)⁺ 886.2674; Found, 886.2676.

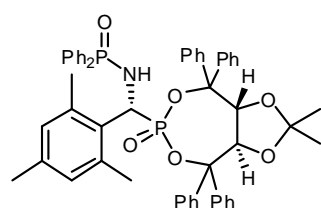
1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-2-furylmethyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4f).



The title compound was prepared according to general procedure using 0.5 g (1.0 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (1.1 mL), 0.15 mL (1.0 mmol) of TMEDA and 0.29 g (1.0 mmol) of *N*-(furan-2-ylmethylene)-*P,P*-diphenylphosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.62 g (80%) of **4f** as yellowish solid. Mp. 161-163°C. [α]_D²⁰ -133.3 (c 1.0, CH₂Cl₂). R_f (EtOAc / Hexane 3:1): 0.25. ¹H NMR (300 MHz, CDCl₃): δ

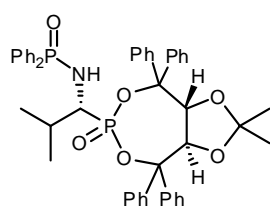
0.53 (s, 3H, CH₃), 0.81 (s, 3H, CH₃), 3.72-3.81 (m, 1H, NH), 4.85 (dt, ³J_{HH} = 7.8 Hz, ²J_{HP} = 16.2 Hz, 1H, CHP), 5.10 (d, ³J_{HH} = 7.9 Hz, 1H, CHO), 5.55 (d, ³J_{HH} = 8.0 Hz, 1H, CHO), 6.04-6.16 (m, 2H, CH_{ar}), 7.23-7.89 (m, 31H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 26.6 (CH₃), 27.1 (CH₃), 48.4 (d, ¹J_{PC} = 173.1 Hz, CHP), 79.0 (CHO), 80.1 (CHO), 87.4 (d, ²J_{PC} = 8.6 Hz, CPh₂), 90.8 (d, ²J_{PC} = 13.7 Hz, CPh₂), 109.4 (d, ³J_{PC} = 8.5 Hz, C_{ar}), 110.8 (C_{ar}), 114.1 (C(CH₃)₂), 126.9 (C_{ar}), 127.3 (C_{ar}), 127.4 (C_{ar}), 127.5 (C_{ar}), 127.9 (C_{ar}), 128.0 (C_{ar}), 128.3 (C_{ar}), 128.5 (C_{ar}), 128.6 (C_{ar}), 128.8 (C_{ar}), 128.9 (C_{ar}), 129.0 (C_{ar}), 129.8 (C_{ar}), 132.1 (C_{ar}), 132.2 (C_{ar}), 132.3 (C_{ar}), 132.4 (C_{ar}), 132.5 (C_{ar}), 132.6 (d, ²J_{PC} = 9.9 Hz, C_{ar}), 132.7 (C_{ar}), 139.4 (C_{ar}), 139.6 (C_{ar}), 142.4 (C_{ar}), 143.8 (C_{ar}), 144.4 (C_{ar}), 149.0 (C_{ar}). ³¹P NMR (120 MHz, CDCl₃): δ 14.5 (d, ³J_{PP} = 40.3 Hz, PO(OR)₂), 25.4 (d, ³J_{PP} = 40.3 Hz, POPh₂). FTIR (neat) ν_{max} (cm⁻¹): 3369 (N-H st), 1264 (P=O st). CIMS m/z (amu): 808 ([M+H], 100). HRMS (amu) Calcd for C₄₈H₄₄NO₇P₂ (M+H)⁺ 808.2593; Found, 808.2590.

1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-1-(2,3,6-trimethylphenyl)methyl]-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4g).



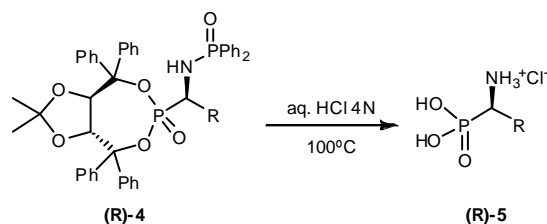
The title compound was prepared according to general procedure using 1.0 g (1.95 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (2.14 mL), 0.3 mL (1.95 mmol) of TMEDA and 0.68 g (1.95 mmol) of *P,P*-diphenyl-*N*-(2,4,6-trimethylbenzylidene)phosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.98 g (59%) of **4g** as white solid. Mp. 184-186°C. [α]_D²⁰ -119.2 (c 1.12, CH₂Cl₂). *R*_f (EtOAc / Pentane 2:1): 0.52. ¹H NMR (300 MHz, CDCl₃): δ 0.44 (s, 3H, CH₃), 0.88 (s, 3H, CH₃), 2.25 (s, 3H, CH₃), 2.29 (s, 6H, 2xCH₃), 3.42 (d, ²J_{PH} = 22.3 Hz, 1H, NH), 4.62 (m, 1H, CHP), 4.98 (d, ³J_{HH} = 8.1 Hz, 1H, CHO), 5.55 (d, ³J_{HH} = 8.1 Hz, 1H, CHO), 6.98 (d, ³J_{HH} = 7.5 Hz, 2H, 2xCH_{ar}), 6.96-7.90 (m, 30H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 19.3 (2xCH₃), 21.9 (CH₃), 26.4 (CH₃), 27.2 (CH₃), 50.3 (d, ¹J_{PC} = 161.7 Hz, CHP), 79.0 (d, ³J_{PC} = 2.1 Hz, CHO), 80.2 (d, ³J_{PC} = 2.0 Hz, CHO), 87.0 (d, ²J_{PC} = 8.5 Hz, CPh₂), 91.2 (d, ²J_{PC} = 13.4 Hz, CPh₂), 114.7 (C(CH₃)₂), 126.6 (2xCH_{ar}), 127.2 (2xCH_{ar}), 127.3 (2xCH_{ar}), 127.4 (2xCH_{ar}), 127.6 (CH_{ar}), 127.8 (CH_{ar}), 127.9 (CH_{ar}), 128.0 (2xCH_{ar}), 128.3 (2xCH_{ar}), 128.4 (4xCH_{ar}), 128.7 (CH_{ar}), 128.8 (d, ³J_{PC} = 7.8 Hz, 2xCH_{ar}), 129.1 (2xCH_{ar}), 130.7 (2xCH_{ar}), 131.2 (d, ¹J_{PC} = 102.3 Hz, 2xCq), 131.9 (CH_{ar}), 132.0 (CH_{ar}), 132.1 (2xCH_{ar}), 132.3 (2xCH_{ar}), 132.8 (d, ³J_{PC} = 9.1 Hz, 2xCH_{ar}), 133.3 (CH_q), 134 (d, ³J_{PC} = 5.1 Hz, 2xC_q), 136.4 (C_q), 140.3 (C_q), 140.5 (C_q), 143.9 (C_q), 145.0 (d, ²J_{PC} = 7.8 Hz, C_q). ³¹P NMR (120 MHz, CDCl₃): δ 18.6 (d, ³J_{PP} = 31.6 Hz, PO(OR)₂), 24.7 (d, ³J_{PP} = 31.6 Hz, POPh₂). FTIR (neat) ν_{max} (cm⁻¹): 3428 (N-H st), 1221 (P=O st). CIMS m/z (amu): 674 ([M+H], 100). HRMS (amu) Calcd for C₅₃H₅₁NO₆P₂ (M+H)⁺ 859.3186; Found, 859.3192.

1,3-Dioxolo[4,5-e][1,3,2]dioxaphosphepin, tetrahydro-2,2-dimethyl-6-[diphenylphosphinoylamino-1-(2-methylpropyl)-4,4,8,8-tetraphenyl-, 6-oxide, (3aR,8aR) (4g).



The title compound was prepared according to general procedure using 1.0 g (1.95 mmol) of **3** in 15 mL of THF, 1.1 M solution of Et₂Zn in toluene (2.14 mL), 0.3 mL (1.95 mmol) of TMEDA and 0.68 g (1.95 mmol) of *P,P*-diphenyl-*N*-(2,4,6-trimethylbenzylidene)phosphinic amide in 15 mL of THF. The crude product was purified by column chromatography (SiO₂, EtOAc/Hexane) to afford 0.99 g (65%) of **4g** as white solid. Mp. 163-165°C. [α]_D²⁰ -101.2 (c 1.01, CH₂Cl₂). *R*_f (EtOAc / Pentane 2:1): 0.61. ¹H NMR (300 MHz, CDCl₃): δ 0.44 (s, 3H, CH₃), 0.88 (s, 3H, CH₃), 1.06 (d, ³J_{HH} = 6.6 Hz, 3H, CH₃), 1.10 (d, ³J_{HH} = 6.6 Hz, 3H, CH₃), 2.60 (m, 1H, CH), 3.52 (s, 1H, NH), 3.63 (m, 1H, CHP), 5.01 (d, ³J_{HH} = 8.0 Hz, 1H, CHO), 5.57 (d, ³J_{HH} = 8.10 Hz, 1H, CHO), 7.13-7.62 (m, 30H, CH_{ar}). ¹³C NMR (75 MHz, CDCl₃): δ 19.4 (CH₃), 19.7 (CH₃), 26.4 (CH₃), 27.5 (CH₃), 31.5 (d, ²J_{PC} = 6.6 Hz, CH), 57.0 (d, ¹J_{PC} = 164.8 Hz, CHP), 79.0 (d, ³J_{PC} = 2.2 Hz, CHO), 80.5 (d, ³J_{PC} = 2.1 Hz, CHO), 86.7 (d, ²J_{PC} = 8.7 Hz, CPh₂), 91.4 (d, ²J_{PC} = 13.0 Hz, CPh₂), 114.0 (C(CH₃)₂), 124.3 (2xCH_{ar}), 124.5 (2xCH_{ar}), 124.7 (2xCH_{ar}), 125.9 (CH_{ar}), 126.0 (CH_{ar}), 127.2 (CH_{ar}), 127.3 (2xCH_{ar}), 127.5 (d, ²J_{PC} = 5.4 Hz, 2xCH_{ar}), 128.1 (2xCH_{ar}), 128.3 (4xCH_{ar}), 128.4 (CH_{ar}), 128.6 (d, ³J_{PC} = 7.8 Hz, 2xCH_{ar}), 130.2 (2xCH_{ar}), 131.1 (d, ¹J_{PC} = 102.3 Hz, 2xCq), 131.8 (CH_{ar}), 132.1 (2xCH_{ar}), 132.2 (CH_{ar}), 132.3 (2xCH_{ar}), 136.4 (C_q), 139.4 (C_q), 139.6 (C_q), 143.1 (C_q). ³¹P NMR (120 MHz, CDCl₃): δ 19.1 (d, ³J_{PP} = 40.1 Hz, PO(OR)₂), 23.0 (d, ³J_{PP} = 40.1 Hz, POPh₂). FTIR (neat) ν_{max} (cm⁻¹): 3433 (N-H st), 1212 (P=O st). CIMS m/z (amu): 783 ([M+H], 100). HRMS (amu) Calcd for C₄₇H₄₇NO₆P₂ (M+H)⁺ 783.2883; Found, 783.2879.

3. Preparation of aminophosphonic acids (*R*)-(+)-5.



The compound **4** (1.22 mmol) was dissolved in dioxane (15 mL) and aq. 4N HCl (5 mL) was added. The mixture was brought to 100°C and stirred at that temperature for 12 h. After that time the solution was cooled down to room temperature, diluted with H₂O (15 mL) and extracted with CH₂Cl₂ (3 x 10mL). The aqueous layer was evaporated to dryness affording the crude product that was purified by crystallization from EtOH yielding the desired acids (*R*)-**5a-b** as white solids. **5a** (R = Ph): 0.22 g (82%). Mp. 281-283°C (lit.³ 282-283°C). [α]_D²⁰ +16.0 (c 1.0, 1N NaOH) [lit.³ [α]_D²⁵ +17.0 (c 0.42, 1N NaOH); lit.⁴ [α]_D²⁰ +15.0 (c 2.0, 1N NaOH)]. **5b** (R = i-Pr): 0.18 g (78%). Mp. 264-266°C (lit.⁴ 262-264°C). [α]_D²⁰ +1.2 (c 1.0, 1N NaOH) [lit.⁵ [α]_D²⁵ +0.9]. The spectroscopic data were in agreement with values described in the literature^{3,4,6}

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 - 5 Lavielle, G. *J. Med. Chem.* **1991**, *34*, 1998-2003.
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Diastereoselective Hydrophosphonylation of Imines Using a TADDOL Derived Phosphonate. Asymmetric Synthesis of α -Aminophosphonic acid derivatives.

Francisco Palacios*^a, Tomasz K. Olszewski^a and Javier Vicario.^a

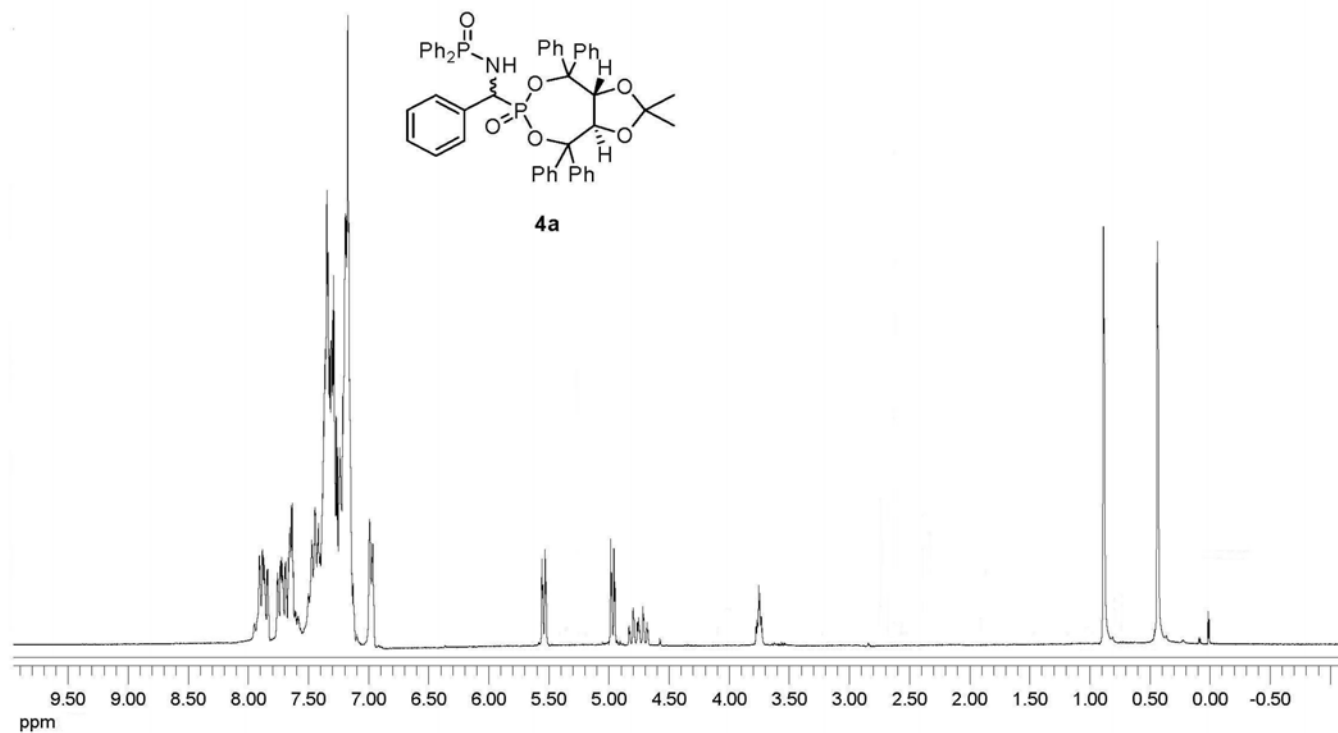
Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco, Apartado 450, 01080 Vitoria, Spain. Fax: 34-945-013049, Tel: (+34) 945 183103, E-mail: francisco.palacios@ehu.es

Electronic Supporting Information.

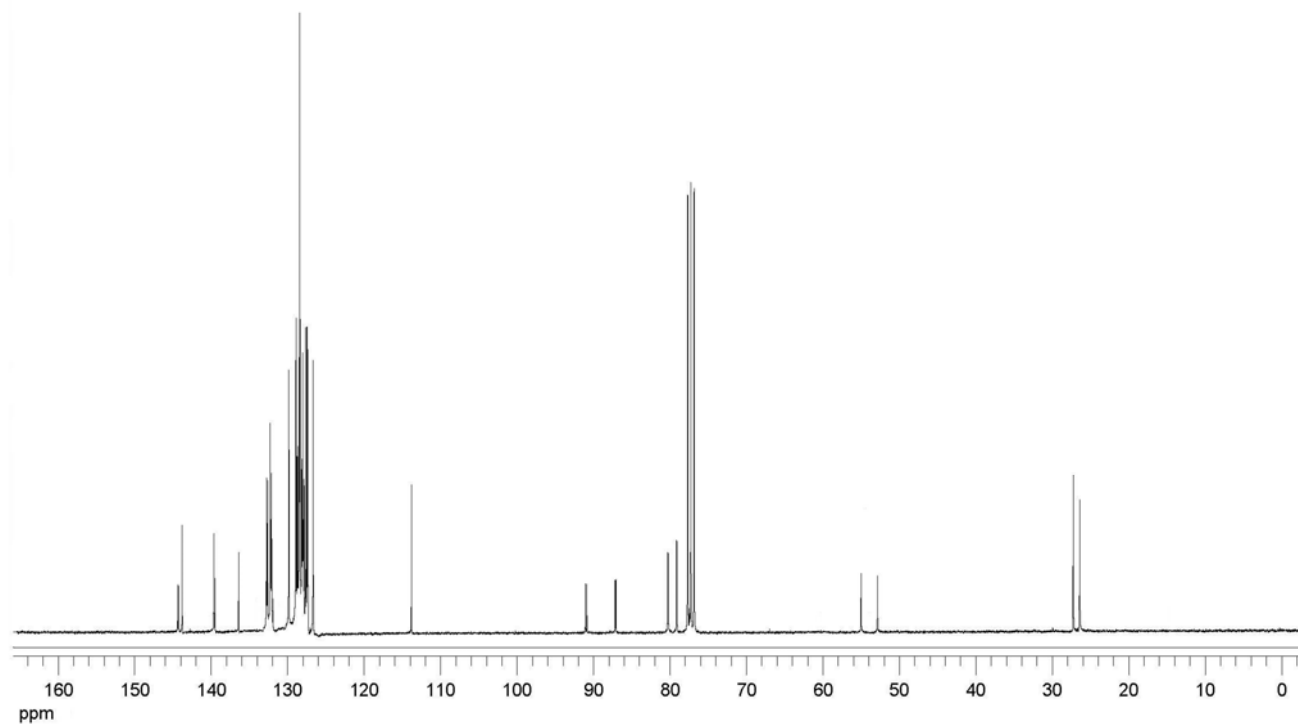
1H, 13C NMR spectra.

1. ^1H and ^{13}C NMR of aminophosphonates 4a-f.

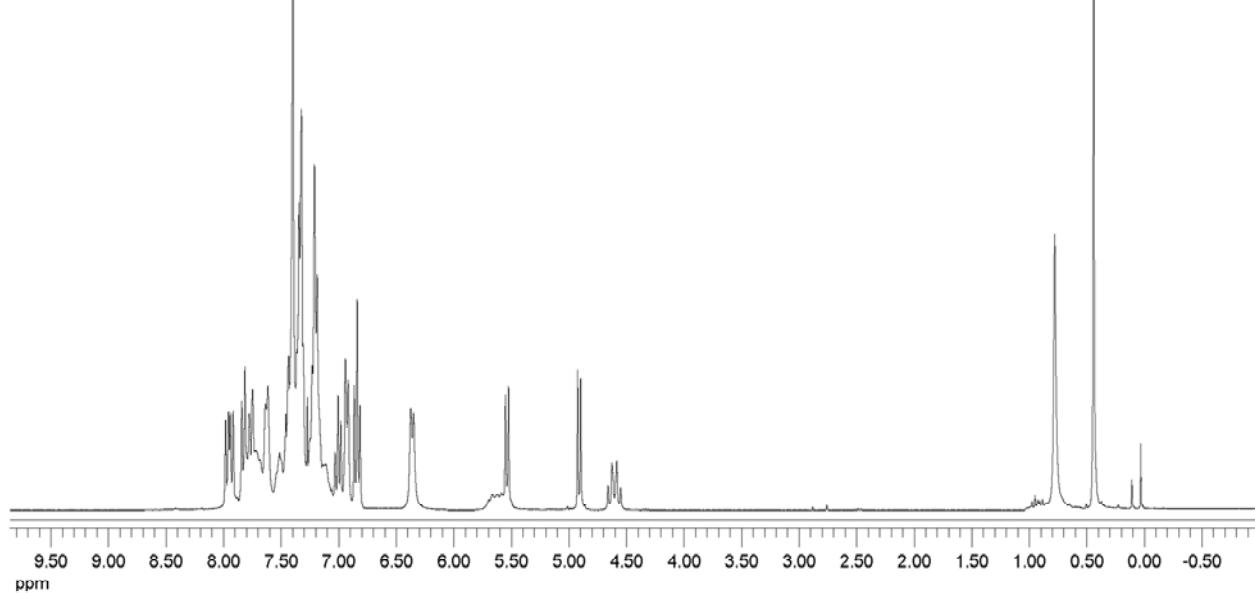
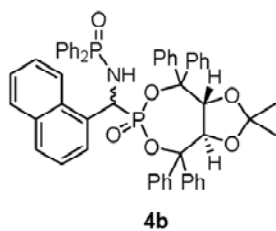
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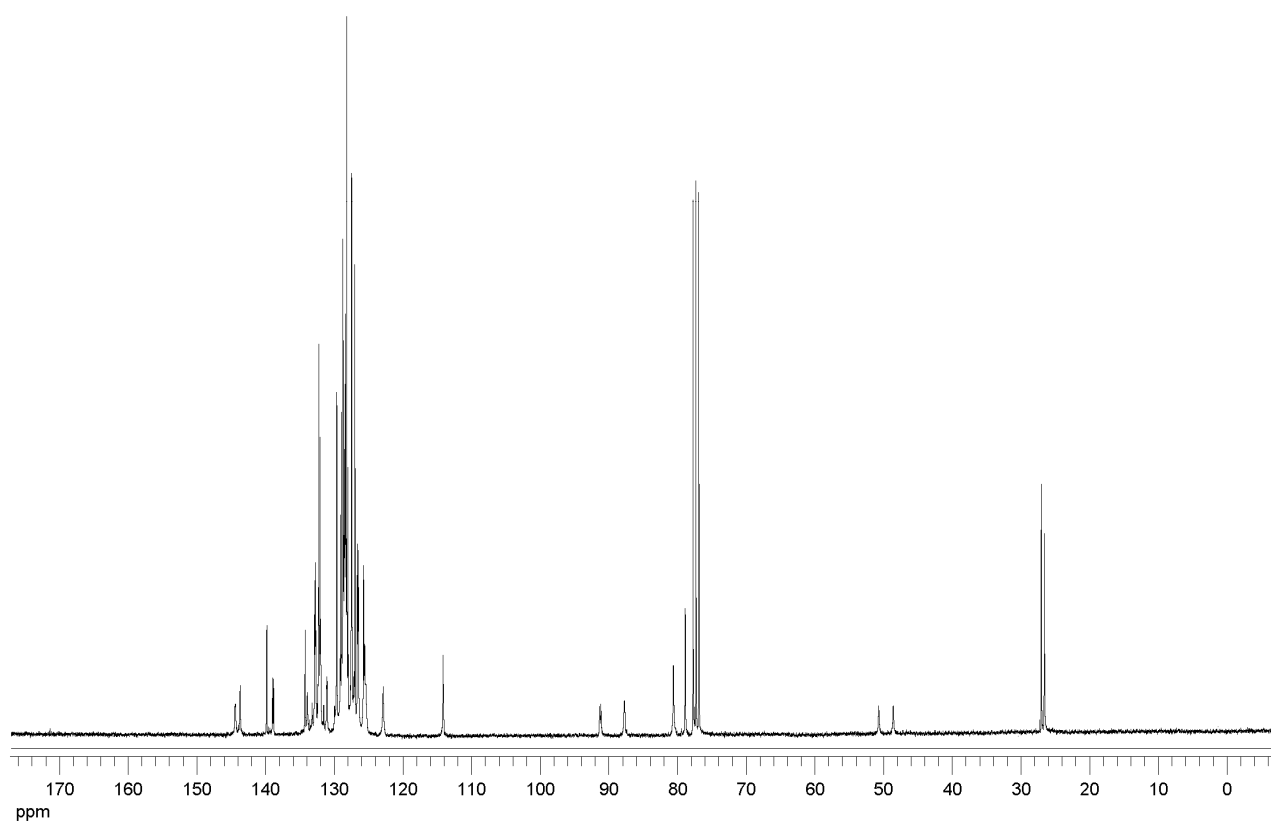
^{13}C NMR (75 MHz)



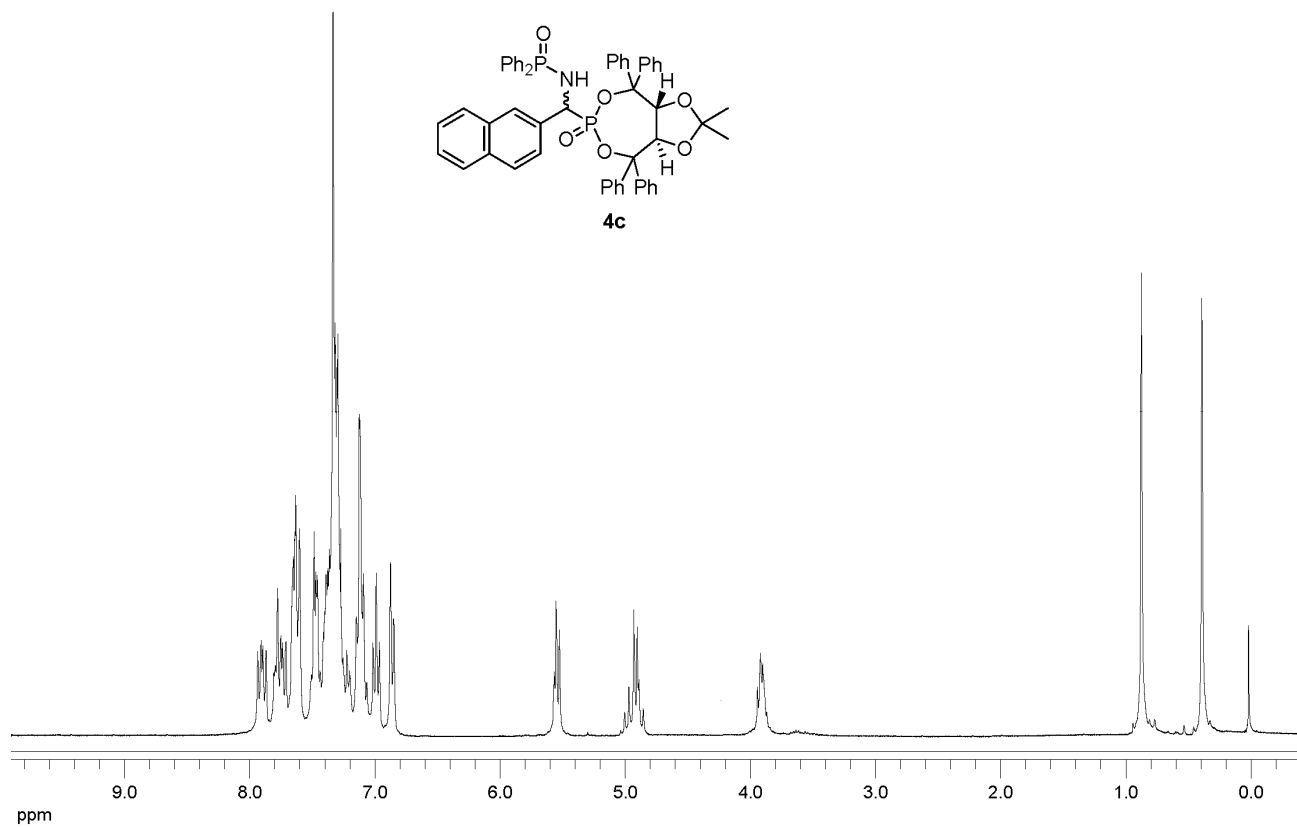
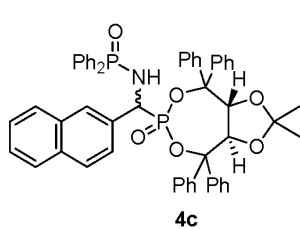
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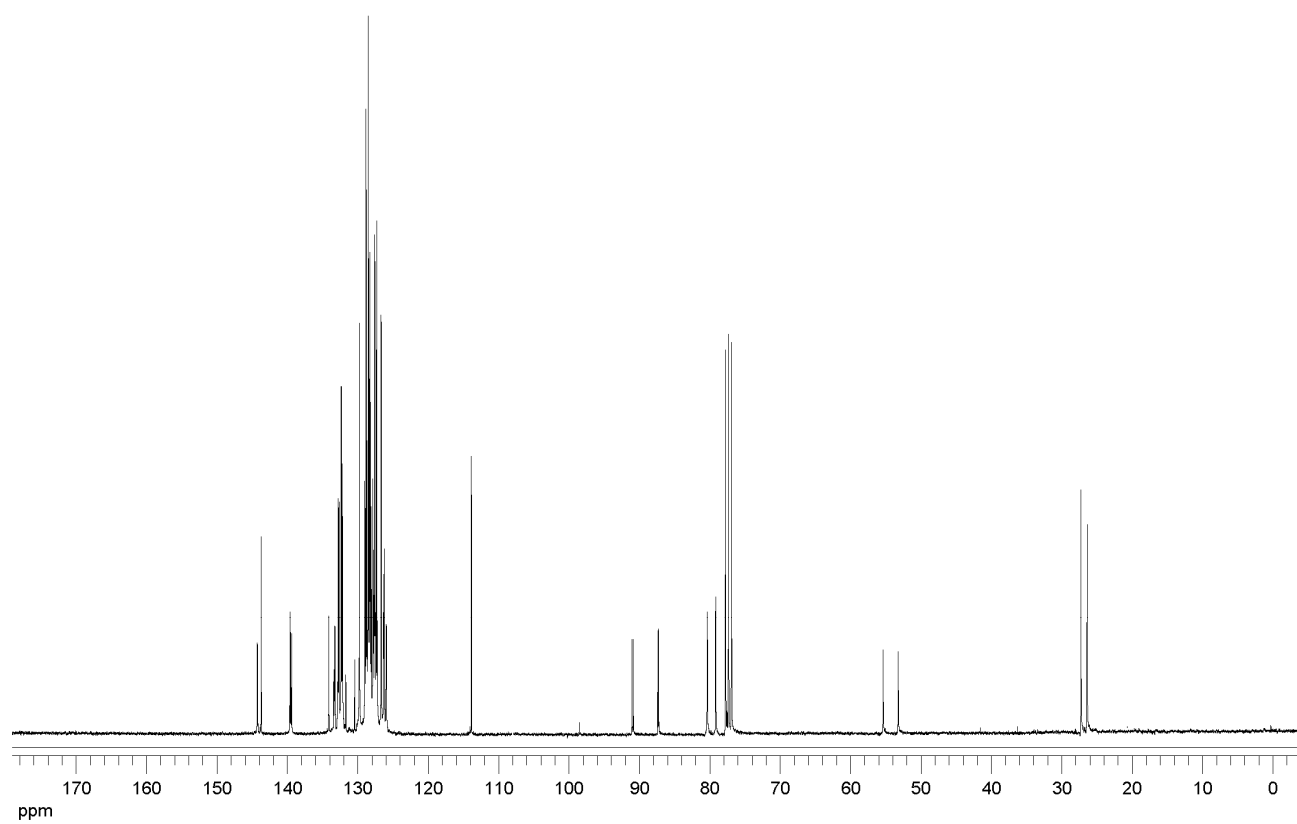
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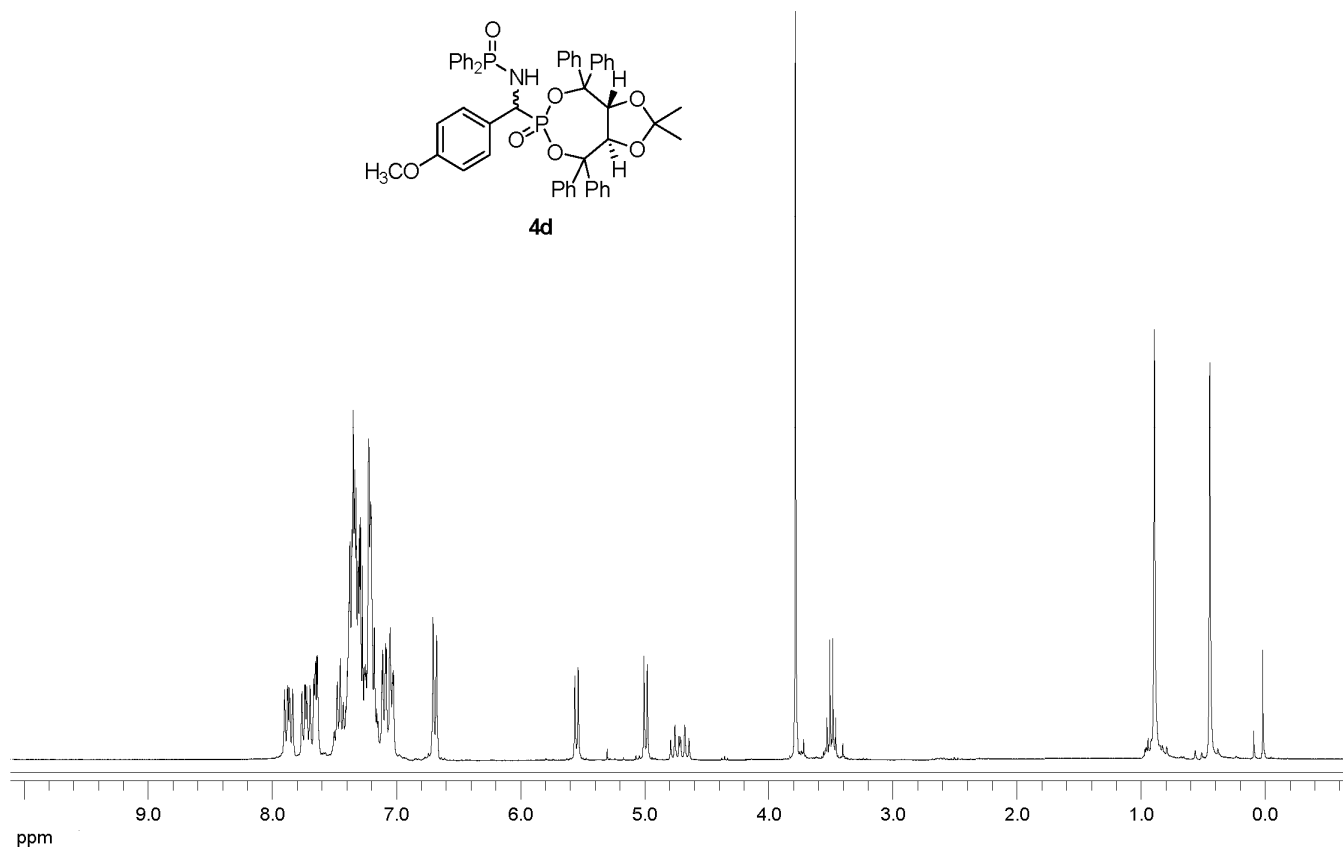
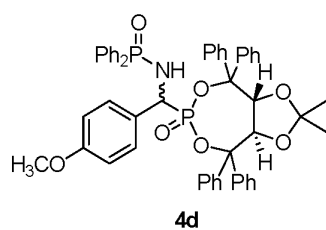
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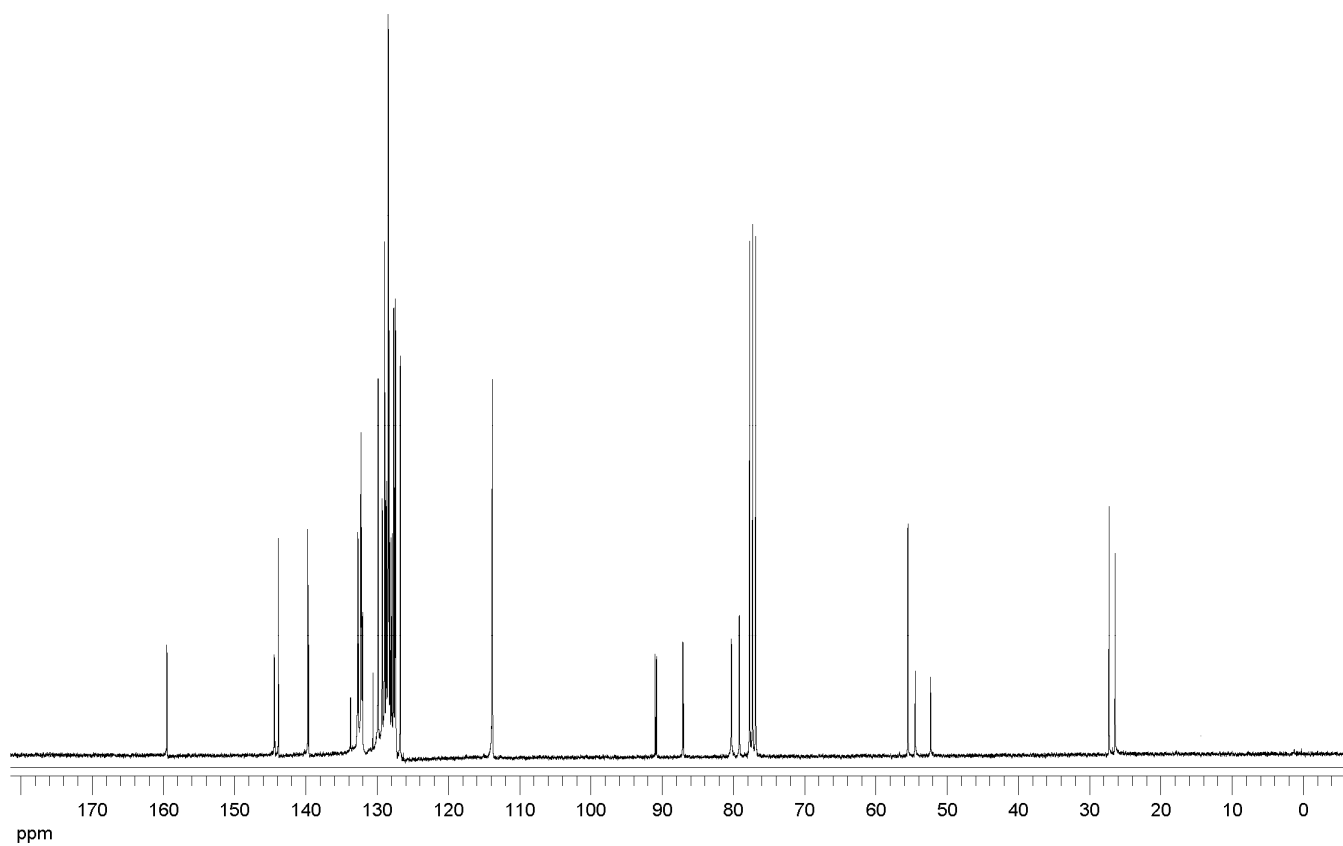
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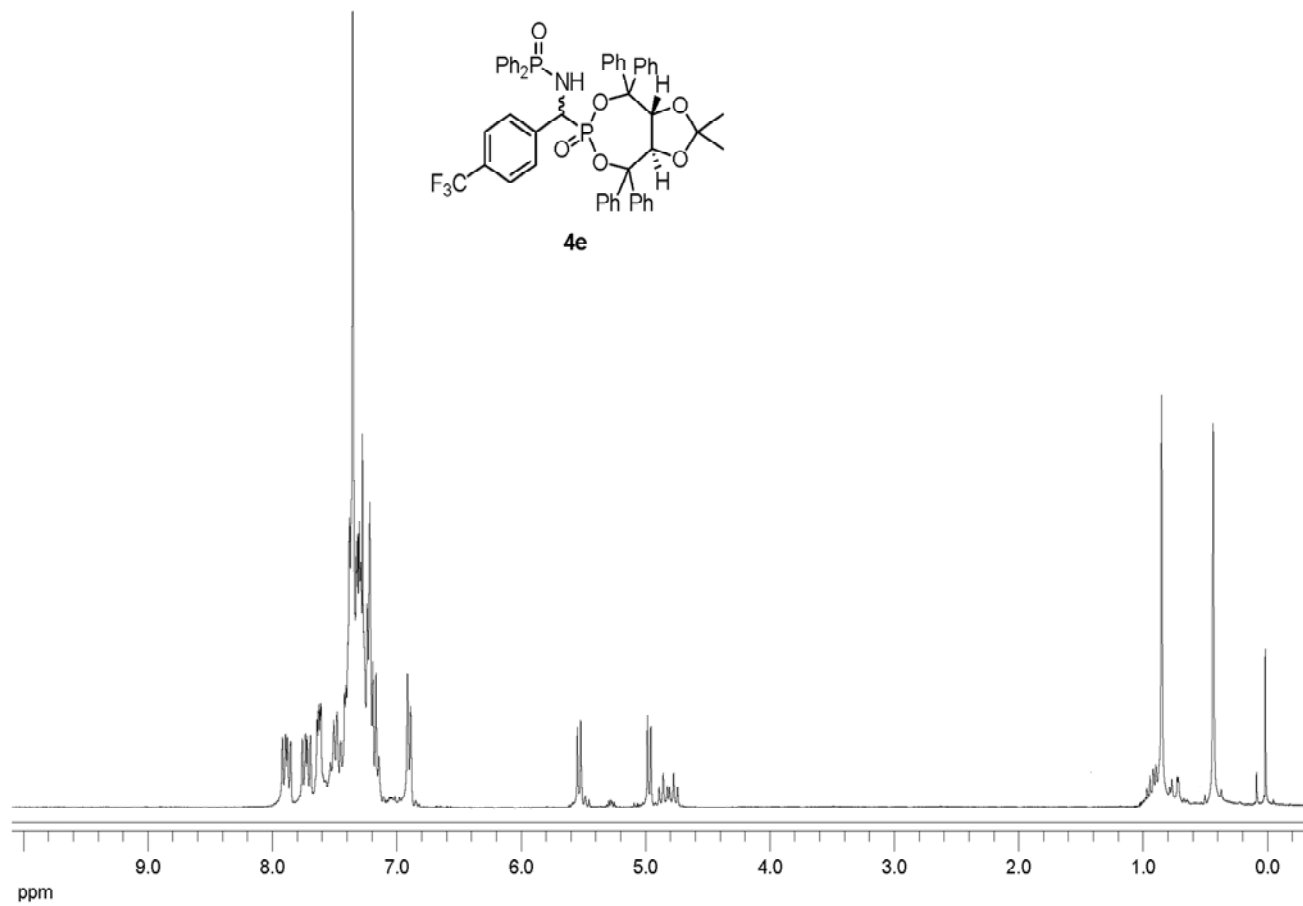
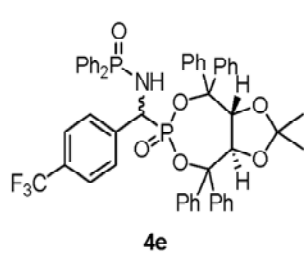
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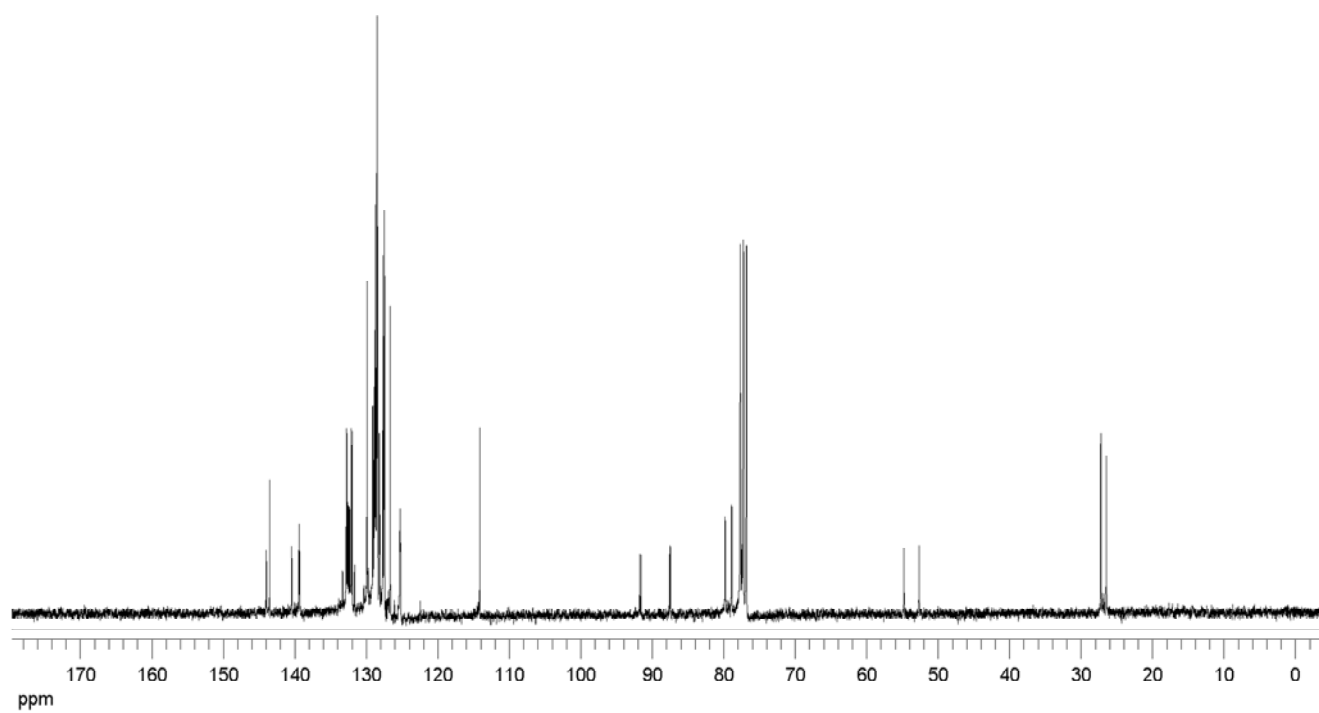
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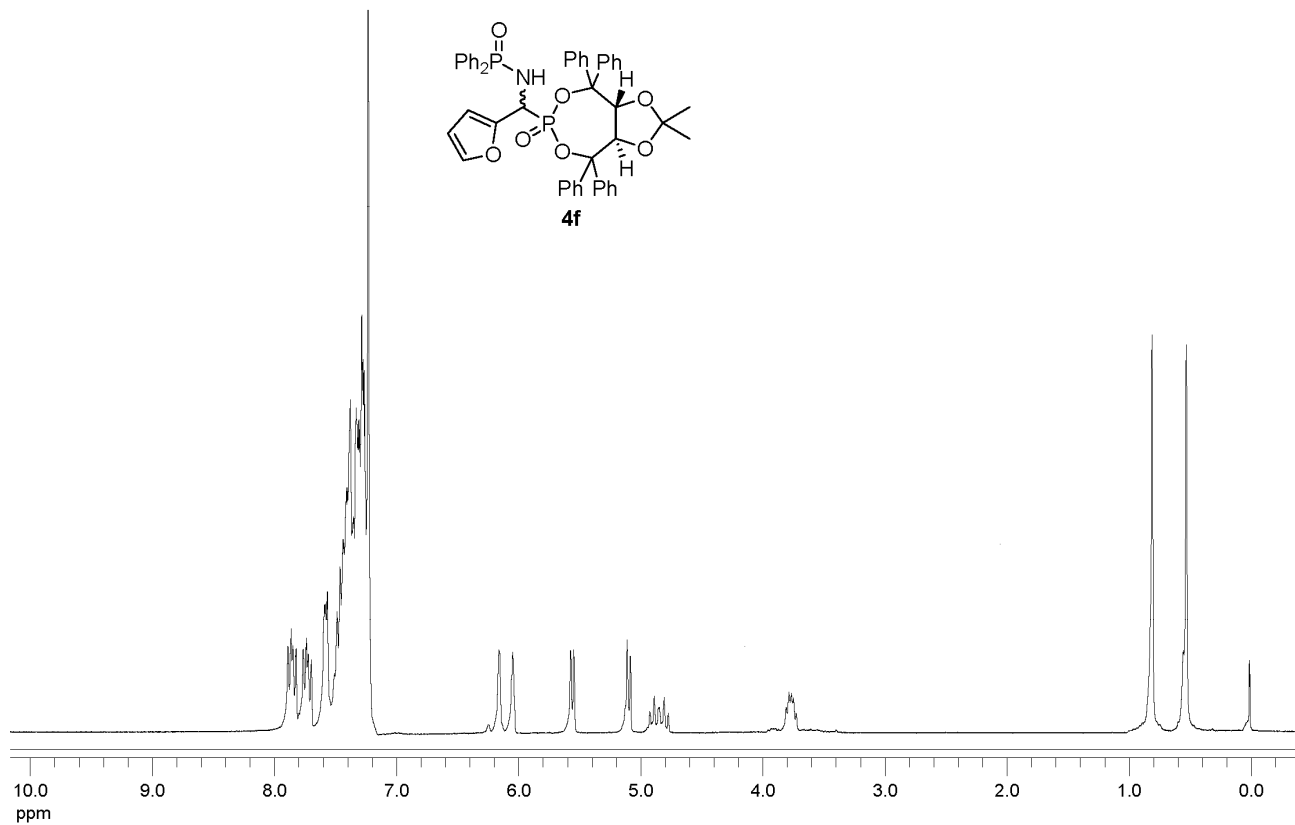
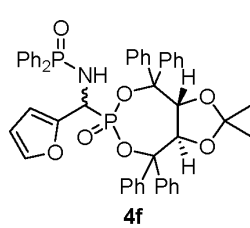
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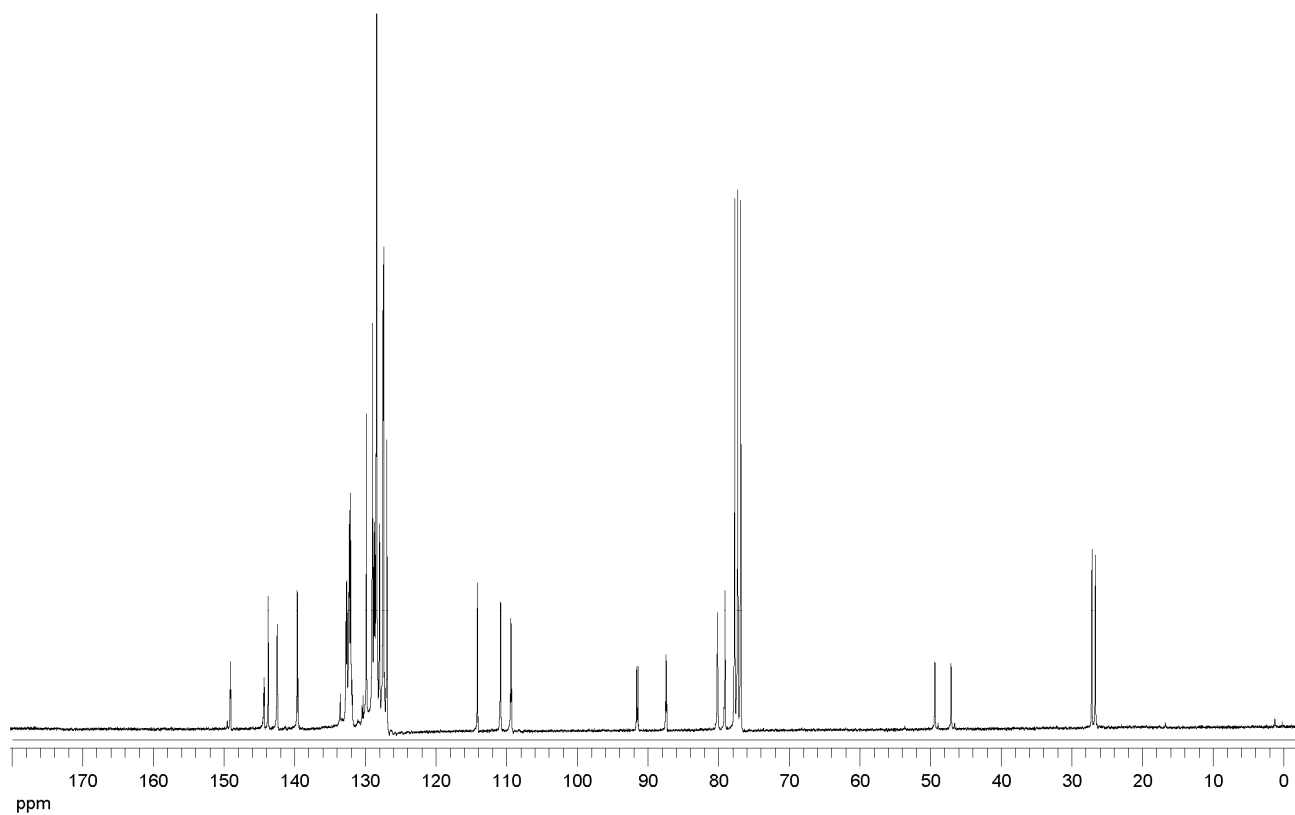
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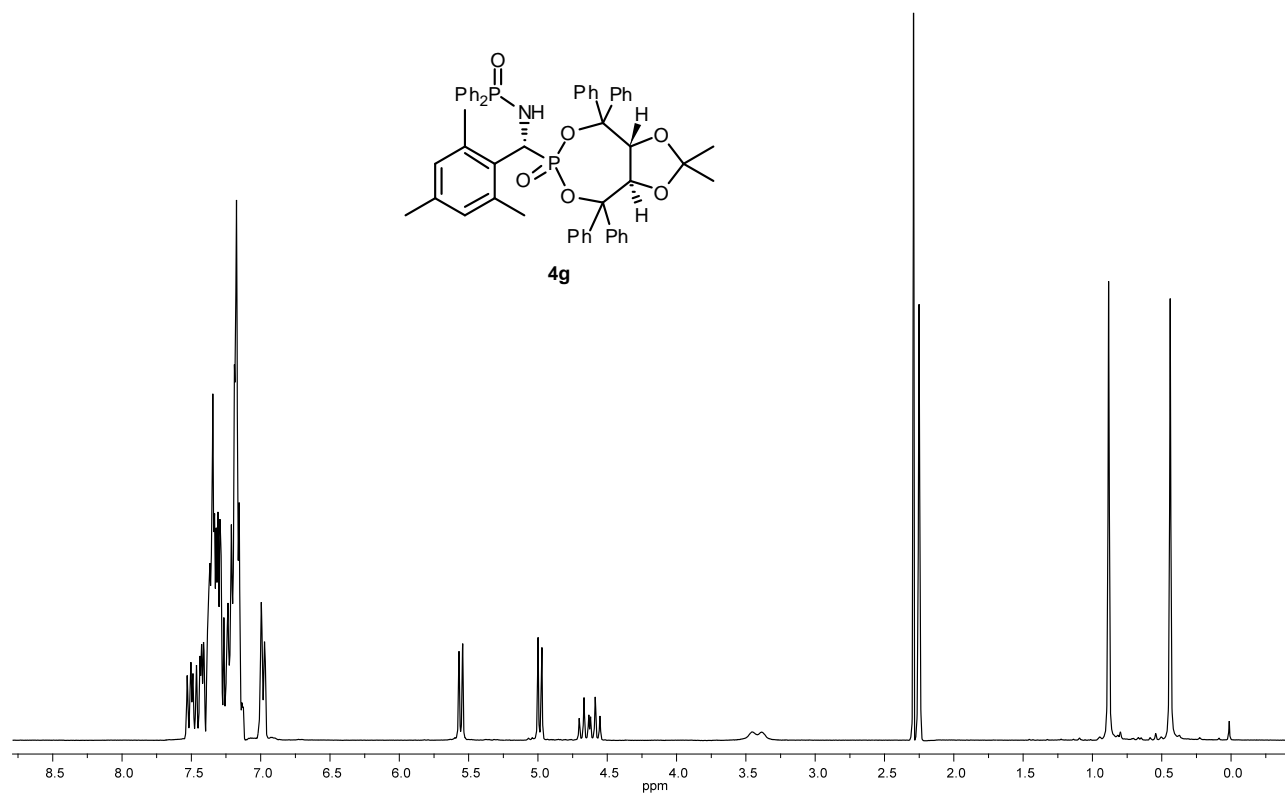
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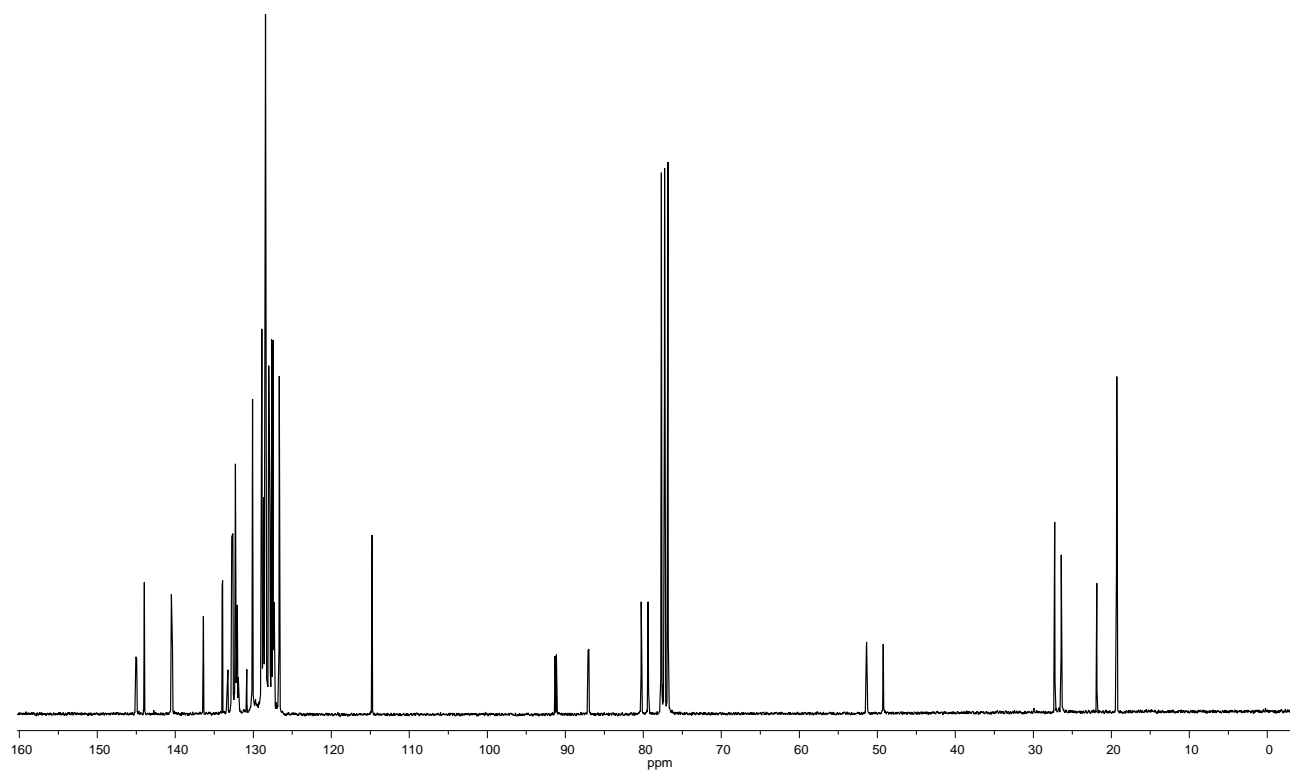
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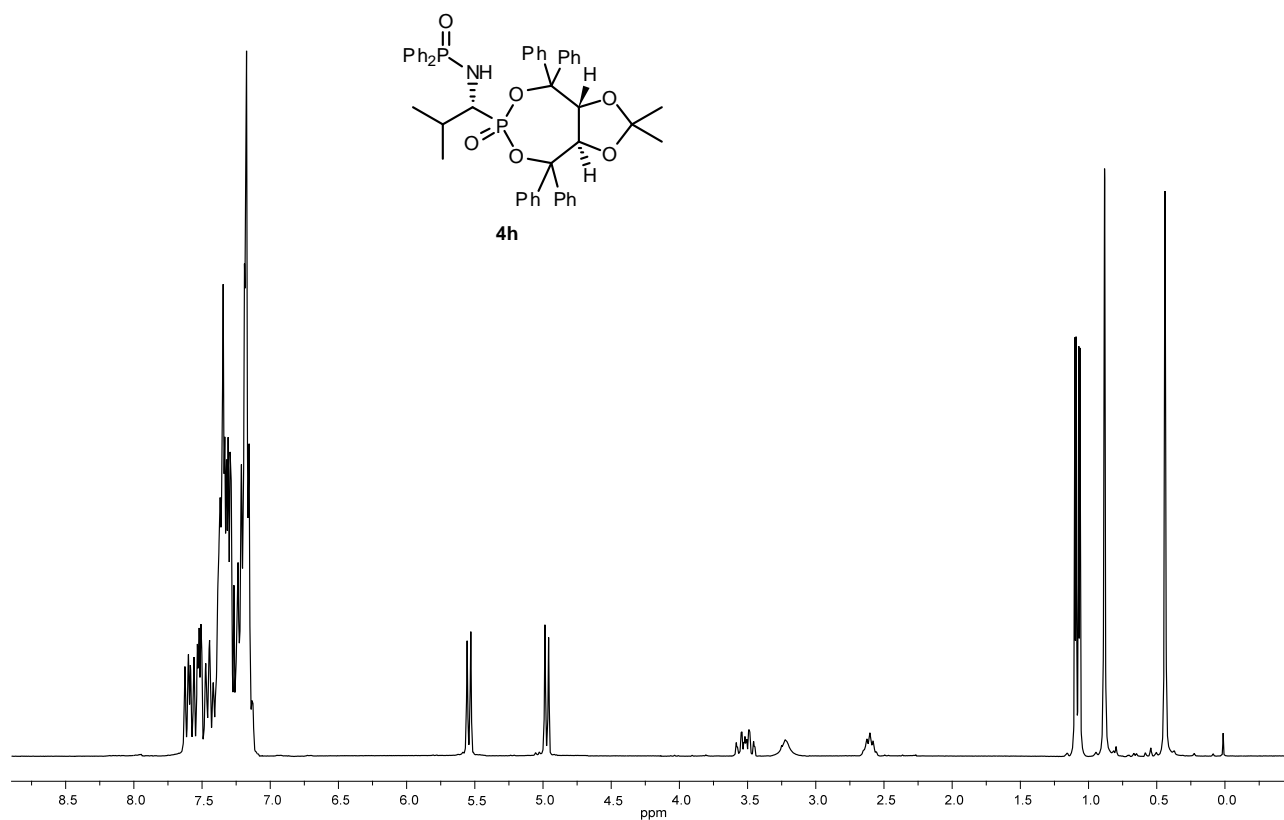
¹H NMR (300 MHz)



¹³C NMR (75 MHz)



^1H NMR (300 MHz)



^{13}C NMR (75 MHz)

