Supporting information

Efficient Synthesis of Cyclic P-Stereogenic Phosphinamides from Acyclic Chiral Precursors via Radical Oxidative Intramolecular Aryl C–H Phosphinamidation

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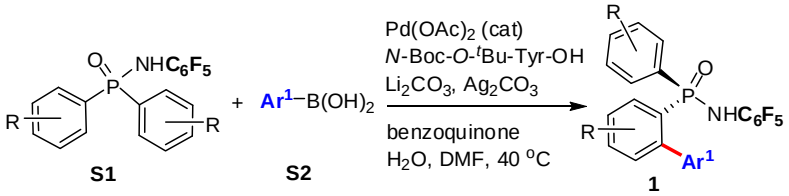
1. General information

Unless otherwise noted, all commercial materials were used without further purification. The ^{1}H NMR spectra were recorded at 300 MHz or 400 MHz (Bruker AV) with TMS as internal standard and the ^{13}C NMR spectra were recorded at 103 MHz, 126 MHz or 151 MHz. The ^{31}P NMR spectra were recorded at 162 MHz, 202 MHz or 243 MHz with 85% H_3PO_4 as external standard. All shifts are given in ppm. All coupling constants (*J* values) were reported in Hertz (Hz). X-ray crystallographic analysis was performed on a Bruker D8 ADVANCE diffractometer with Cu-Ka radiation (λ = 1.54178 Å) or Mo-Ka radiation (λ = 0.71073 Å). The structures were solved by direct methods using the program SHELXL-97 and refined anisotropically by full matrix least squares on F^2 values with SHELXL-97. Hydrogen atoms were located from the expected geometry and were refined only isotropically. High resolution mass was measured by using IonSpec 7.0T MALDI- FTICRMs. Column chromatography was performed on silica gel (purchased from SILICYCLE, 230-400 mesh) unless otherwise noted.

2. Experimental procedures and characterization data

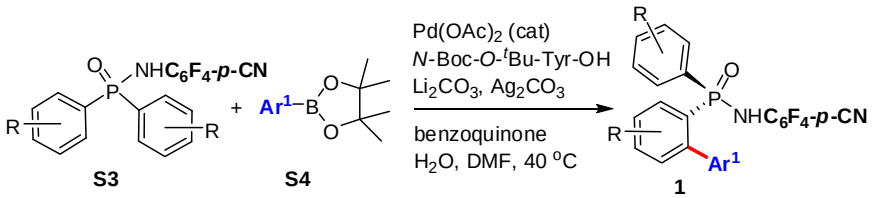
2.1 Preparation of substrates 1

2.1.1 General procedure for synthesizing N-C_6F_5 protected substrates 1[1]



To a dried 30 mL Schlenk tube equipped with a magnetic stirring bar was charged with $Pd(OAc)_2$ (10 mol%), diarylphosphinamide **S1** (1.0 equiv), Ag_2CO_3 (3.0 equiv), $KHCO_3$ (1.5 equiv), benzoquinone (0.1 equiv), arylboronic acid **S2** (1.75 equiv), *N*-Boc-*O*-^{t}Bu-Tyr-OH (20 mol %), and H_2O (60 equiv). Then anhydrous DMF was injected via syringe. The reaction mixture was stirred at 40 for 11 hours (or 50 °C for 2.5 hours) under vigorous stirring. The reaction mixture was cooled to room temperature and then quenched with aqueous NH_4Cl and water. The mixture was extracted with ethyl acetate for three times. The combined organic layer was washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography ethyl acetate/hexane as eluent to give the desired *ortho*-arylated products **1**. The substrates for the synthesis of **3d** and **3i** were recrystallized before use due to the containing a small amount byproducts.

2.1.2 General procedure for synthesizing N-C_6F_4-*p*-CN protected substrates 1[2]

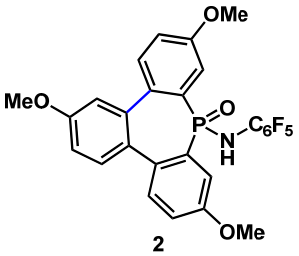


S3 **S4** **1**

To a dried 30 mL Schlenk tube equipped with a magnetic stirring bar was charged with $Pd(OAc)_2$ (10 mol%), *N*-Boc-*O*-^{t}Bu-Tyr-OH (20 mol %), diarylphosphinamide **S3** (0.20 mmol, 1.0 equiv), Ag_2CO_3 (1.5 equiv), Li_2CO_3 (3.0 equiv), BQ (0.5 equiv), aryboronic acid pinacol ester **S4** (2.0 equiv), water (40.0 equiv), and DMF. The reaction mixture was stirred at 40 °C for 12 hours under stirring. The reaction mixture was cooled to room temperature and then diluted with ethyl acetate and filtered through Celite. The filtrate was washed with aqueous NH_4Cl and then extracted with ethyl acetate. The combined organic layer was washed with water and brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated to dryness. The crude material was purified by flash column chromatography on silica gel using ethyl acetate/hexane as the eluent to give the desired *ortho*-arylated products **1**.

2.2 Experimental Procedure for synthesizing 2

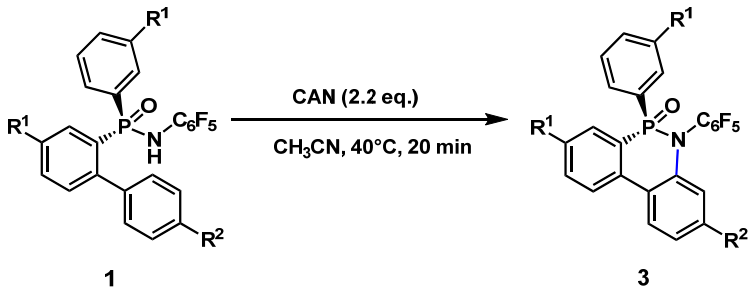
To a suspension of VOF_3 (62 mg, 0.5 mmol) in TFA (2 mL) was added Tf_2O (0.5 mL). The mixture was stirred at – 20 °C for 15 min, and then *ortho*-arylated phosphinamide **1a** (0.1 mmol, 85% ee) in TFA (3 mL) was slowly added via syringe. After warmed to room temperature, the reaction mixture was stirred overnight. Aq. $NaHCO_3$ was added to quench the reaction, and the aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic extracts were washed sequentially with H_2O (15 mL), brine (15 mL), and dried over Na_2SO_4. The organic phase was filtered and concentrated. The residue was purified by flash column chromatography on silica gel to give the racemic coupling product **2**.



2

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 14.7 Hz, 2H), 7.49 – 7.36 (m, 2H), 7.30 (d, *J* = 8.7 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.98 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 4.56 (d, *J* = 5.8 Hz, 1H), 3.90 (s, 3H), 3.90 (s, 3H), 3.88 (s, 3H); HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{20}F_5NO_4P$ $[M+H]^+$: 548.1045, Found: 548.1035; See Section **4.1** for crystallographic data of this compound.

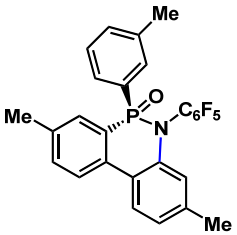
2.3 General procedure for the radical oxidative C–H phosphinamidation



1 **3**

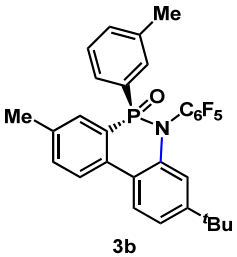
To a suspension of *ortho*-arylated phosphinamide **1** (0.1 mmol) in anhydrous CH_3CN (1 mL) was added $Ce(NH_4)_2(NO_3)_6$ (121 mg, 0.22 mmol). The reaction tube was charged with Ar and was heated at 40 ^oC for 20 min, and then was quenched by H_2O (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic extracts were washed sequentially with a mixture of aq. $NaHCO_3$ (10 mL) and aq. $Na_2S_2O_3$ (10 mL), brine (15 mL), and dried over Na_2SO_4. The organic phase was filtered and concentrated. The residue was purified by flash column chromatography on silica gel to give the desired cyclic phosphinamides **3**.

2.4. Characterization data of C–H phosphinamidation products 3



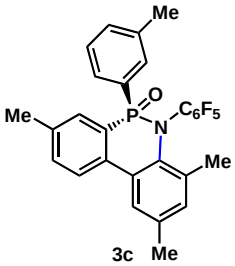
3a

3a was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (98% ee) in 93% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 6:1:1) to give a white solid. ^1H NMR (300 MHz, Acetone-d_6) δ 8.17 (dd, J = 8.3, 5.5 Hz, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 13.9 Hz, 1H), 7.45 (d, J = 13.4 Hz, 1H), 7.39–7.25 (m, 3H), 7.10 (d, J = 8.0 Hz, 1H), 6.78 (s, 1H), 2.42 (s, 3H), 2.28 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 145.9 (d, J = 255 Hz), 145.8 (d, J = 255 Hz), 139.9, 138.7, 138.1 (d, J = 12 Hz), 138.0 (d, J = 255 Hz), 137.7 (d, J = 14 Hz), 137.6 (d, J = 255 Hz), 134.0 (d, J = 4 Hz), 133.7, 133.3, 131.7 (d, J = 11 Hz), 130.8 (d, J = 128 Hz), 130.1 (d, J = 11 Hz), 128.3 (d, J = 11 Hz), 128.1 (d, J = 14 Hz), 125.9 (d, J = 128 Hz), 125.6, 124.7, 124.2 (d, J = 11 Hz), 122.0 (d, J = 8 Hz), 119.3 (d, J = 4 Hz), 21.2, 21.1, 20.9; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 18.66; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{19}F_5KNOP$ $[M+K]^+$: 538.0756, Found: 538.0746; HPLC chiralcel ID column (hexane/isopropanol = 80/20, 0.5 mL/min), t_r: 33.61 min (major), 38.45 min (minor): 97% ee.



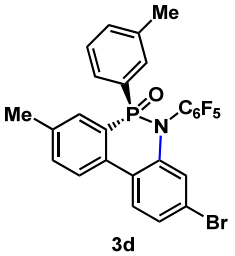
3b

3b was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (95% ee) in 91% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 6:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ8.15 (dd, J = 8.4, 5.6 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 14.0 Hz, 1H), 7.47 (d, J = 13.5 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.27 (td, J = 7.5, 4.0 Hz, 1H), 6.89 (s, 1H), 2.41 (s, 3H), 2.26 (s, 3H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 153.3, 146.1 (d, J = 255 Hz), 145.7 (d, J = 255 Hz), 140.9 (d, J = 255 Hz), 138.6, 138.2 (d, J = 14 Hz), 138.1 (d, J = 255 Hz), 137.8 (d, J = 14 Hz), 137.7 (d, J = 255 Hz), 134.1 (d, J = 6 Hz), 133.8, 133.4, 132.1 (d, J = 10 Hz), 130.7 (d, J = 129 Hz), 130.3 (d, J = 11 Hz), 128.7 (d, J = 14 Hz), 128.2 (d, J = 14 Hz), 126.1 (d, J = 129 Hz), 125.6, 124.4 (d, J = 10 Hz), 122.0 (d, J = 8 Hz), 121.2, 115.7 (d, J = 3 Hz), 115.0, 34.7, 31.0, 21.3, 21.1; ^{31}P NMR (202 MHz, Chloroform-*d*) δ 17.96; HRMS (MALDI-TOF) *m/z* Calcd for $C_{30}H_{25}F_5KNOP^+$ $[M+K]^+$: 580.1226, Found : 580.1221; HPLC chiralcel ID column (hexane/isopropanol = 90/10, 0.8 mL/min), t_r: 37.66 min (major), 40.86 min (minor): 94% ee.



3c

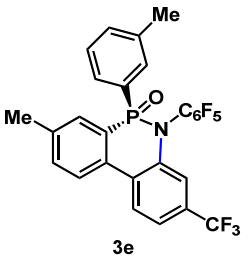
3c was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (86% ee) in 82% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 6:1:1) to give a white solid. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.04 (dd, J = 8.1, 5.3 Hz, 1H), 7.74 (d, J = 12.7 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.49 (d, J = 13.8 Hz, 1H), 7.40 – 7.24 (m, 3H), 6.98 (s, 1H), 2.50 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 145.5 (d, J = 252 Hz), 145.0 (d, J = 252 Hz), 139.6 (d, J = 252 Hz), 138.1, 138.0, 137.7 (d, J = 252 Hz), 136.2 (d, J = 8 Hz), 136.0, 133.9, 133.5 (d, J = 4 Hz), 133.3, 132.8, 131.0 (d, J = 11 Hz), 130.8 (d, J = 128 Hz), 130.5 (d, J = 8 Hz), 128.1 (d, J = 14 Hz), 127.9 (d, J = 14 Hz), 126.9 (d, J = 128 Hz), 125.6 (d, J = 11 Hz), 124.5, 116.5, 21.2, 21.0, 21.0, 18.1; ^{31}P NMR (202 MHz, Chloroform-*d*) δ 23.59; HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{21}F_5KNOP^+$ $[M+K]^+$: 552.0913, Found : 552.0907; HPLC chiralcel ID column (hexane/isopropanol = 80/20, 1.0 mL/min), t_r: 12.55 min (minor), 19.86 min (major): 86% ee.



3d

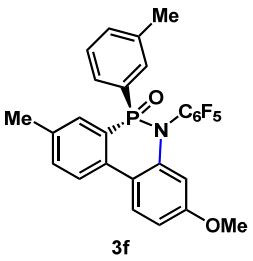
3d was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (98% ee) in 88% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.21 (dd,

J = 10.4, 5.6 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 13.4 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.40 – 7.29 (m, 3H), 7.14 (s, 1H), 2.43 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 146.0 (d, *J* = 257 Hz), 145.6 (d, *J* = 257 Hz), 140.1, 138.9 (d, *J* = 14 Hz), 138.4 (d, *J* = 14 Hz), 138.2 (d, *J* = 257 Hz), 138.1 (d, *J* = 257 Hz), 134.1 (d, *J* = 27 Hz), 133.8 (d, *J* = 27 Hz), 133.2 (d, *J* = 5 Hz), 132.1 (d, *J* = 11 Hz), 131.8 (d, *J* = 11 Hz), 130.6 (d, *J* = 11 Hz), 130.4 (d, *J* = 11 Hz), 130.2 (d, *J* = 129 Hz), 128.7 – 128.3 (m), 127.3 (d, *J* = 30 Hz), 127.0 (d, *J* = 19 Hz), 126.2 (d, *J* = 129 Hz), 124.7 (d, *J* = 11 Hz), 124.5 (d, *J* = 11 Hz), 123.7 (d, *J* = 8 Hz), 123.2, 121.8 (d, *J* = 30 Hz), 114.2, 21.4, 21.1; ^{31}P NMR (202 MHz, Chloroform-*d*) δ 18.01; HRMS (MALDI-TOF) *m/z* Calcd for $C_{26}H_{17}BrF_5NOP^+$ $[M+H]^+$: 564.0146, Found : 564.0156; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.0 mL/min), t_r: 6.82 min (minor), 8.47 min (major): 98% ee.



3e

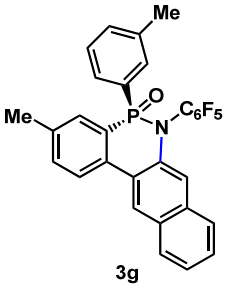
3e was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (88% ee) in 83% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a white solid. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.50 (d, *J* = 8.3 Hz, 1H), 8.31 (dd, *J* = 8.3, 5.5 Hz, 1H), 7.77–7.71 (m, 1H), 7.65–7.57 (m, 2H), 7.47 (d, *J* = 13.3 Hz, 1H), 7.42–7.28 (m, 3H), 7.27 (s, 1H), 2.47 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 145.8 (d, *J* = 246 Hz), 145.3 (d, *J* = 246 Hz), 141.2 (d, *J* = 246 Hz), 139.5 (d, *J* = 14 Hz), 139.1, 138.3 (d, *J* = 14 Hz), 134.0, 133.7, 132.5 (d, *J* = 6 Hz), 131.9 (d, *J* = 11 Hz), 131.3 (d, *J* = 33 Hz), 130.5 (d, *J* = 11 Hz), 129.6 (d, *J* = 130 Hz), 128.5 (d, *J* = 11 Hz), 128.3 (d, *J* = 15 Hz), 127.6 (d, *J* = 4 Hz), 126.8 (d, *J* = 129 Hz), 126.5, 125.0 (d, *J*= 11 Hz), 123.3 (d, *J*= 273 Hz), 120.2, 115.7, 114.0, 21.1, 21.0; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 17.42; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{16}F_8KNOP$ $[M+K]^+$: 592.0473, Found: 592.0469; HPLC chiralcel AD-H column (hexane/isopropanol = 90/10, 1.0 mL/min), t_r: 15.37 min (major), 21.49 min (minor): 85% ee.



3f

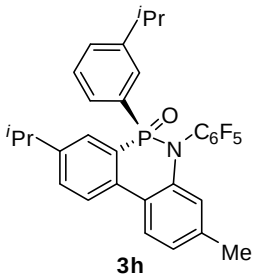
3f was prepared by using the general procedure above (10 equiv. H_2O was added) from corresponding *ortho*-arylated phosphinamide (90% ee) in 63% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a pale yellow solid. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.17 (d, *J* = 8.9 Hz, 1H), 8.10 (dd, *J* = 8.3, 5.6 Hz, 1H), 7.64–7.57 (m,

1H), 7.53 (d, *J* = 14.0 Hz, 1H), 7.46 (d, *J* = 13.4 Hz, 1H), 7.40–7.24 (m, 3H), 6.88 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.37 (s, 1H), 3.74 (s, 3H), 2.40 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 160.6, 145.9 (d, *J* = 251 Hz), 145.6 (d, *J* = 251 Hz), 140.2, 138.5 (d, *J* = 251 Hz), 138.1 (d, *J* = 14 Hz), 137.1 (d, *J* = 14 Hz), 134.0 (d, *J* = 6 Hz), 133.8, 133.3, 131.7 (d, *J* = 11 Hz), 130.8 (d, *J* = 128 Hz), 128.3 (d, *J* = 11 Hz), 128.1 (d, *J* = 14 Hz), 127.1, 125.0 (d, *J* = 128 Hz), 123.8 (d, *J* = 11 Hz), 117.6, 108.6, 104.9, 55.3, 21.1, 20.9; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 18.10; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{19}F_5KNO_2P$ $[M+K]^+$: 554.0705, Found: 554.0697; HPLC chiralcel AD-H column (hexane/isopropanol = 90/10, 1.0 mL/min), t_r: 28.37 min (minor), 67.25 min (major): 91% ee.



3g

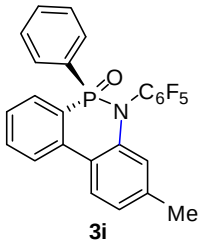
3g was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (94% ee) in 93% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.18 (dd, *J* = 8.2, 5.4 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.84 (d, *J* = 12.7 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.55 (d, *J* = 13.9 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.43 (dd, *J* = 13.5, 7.5 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.16 (td, *J* = 7.5, 3.7 Hz, 1H), 2.53 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 146.1 (d, *J* = 257 Hz), 145.0 (d, *J* = 257 Hz), 139.9 (d, *J* = 257 Hz), 138.9 (d, *J* = 13 Hz), 138.3 (d, *J* = 13 Hz), 136.9 (d, *J* = 15 Hz), 136.0 (d, *J* = 8 Hz), 134.4 (d, *J* = 5 Hz), 133.7 (d, *J* = 129 Hz), 133.6, 131.3 (d, *J* = 5 Hz), 131.2, 131.1 (d, *J* = 5 Hz), 131.0, 129.5 (d, *J* = 129 Hz), 129.0 (d, *J* = 9 Hz), 128.9, 128.6, 128.2 (d, *J* = 15 Hz), 128.1 (d, *J* = 13 Hz), 128.0 (d, *J* = 13 Hz), 127.7 (d, *J* = 30 Hz), 127.3 (d, *J* = 16 Hz), 126.4 (d, *J* = 30 Hz), 126.2 (d, *J* = 11 Hz), 123.0 (d, *J* = 30 Hz), 122.4 (d, *J* = 30 Hz), 117.4, 21.3, 21.1; ^{31}P NMR (202 MHz, Chloroform-*d*) δ 24.17; HRMS (MALDI-TOF) *m/z* Calcd for $C_{30}H_{19}F_5NNaOP^+$ $[M+Na]^+$: 558.1017, Found : 558.1029; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.0 mL/min), t_r: 10.05 min (minor), .20.37 min (major): 93% ee.



3h

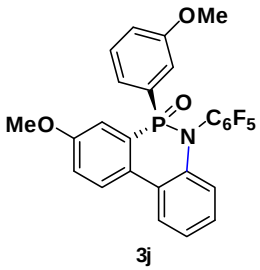
3h was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (95% ee) in 81% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 6:1:1) to give a white solid. ^{1}H NMR (300 MHz, Acetone-d6) δ 8.20 (dd, J = 8.4, 5.4 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 14.2 Hz, 1H),

7.49 (d, J = 13.6 Hz, 1H), 7.45 – 7.28 (m, 3H), 7.11 (d, J = 8.1 Hz, 1H), 6.81 (s, 1H), 3.03 (p, J = 6.9 Hz, 1H), 2.88 (p, J = 6.9 Hz, 1H), 2.24 (s, 3H), 1.26 (d, J = 6.9 Hz, 6H), 1.12 (dd, J = 6.9, 2.9 Hz, 6H); ^{13}C NMR (151 MHz, Chloroform-d) δ 148.9 (d, J = 12 Hz), 148.3 (d, J = 12 Hz), 146.0 (d, J = 255 Hz), 145.5 (d, J = 255 Hz), 140.7 (d, J = 255 Hz), 139.9, 138.7, 137.9 (d, J = 255 Hz), 137.6 (d, J = 255 Hz), 134.5 (d, J = 6 Hz), 131.0, 130.8, 130.3 (d, J = 128 Hz), 129.3 (d, J = 11 Hz), 129.1 (d, J = 11 Hz), 128.1 (d, J = 14 Hz), 127.7 (d, J = 14 Hz), 125.9 (d, J = 14 Hz), 125.7, 124.4 (d, J = 11 Hz), 122.2 (d, J = 6 Hz), 119.5, 115.1, 33.8, 33.7, 23.6, 23.5, 23.5, 23.4, 21.2; ^{31}P NMR (243 MHz, Chloroform-d) δ 18.87; HRMS (MALDI-TOF) m/z Calcd for $C_{31}H_{27}F_5KNOP^+$ $[M+K]^+$: 594.1382, Found : 594.1371; HPLC chiralcel OZ-H column (hexane/isopropanol = 90/10, 1.0 mL/min), tr: 5.70 min (major), 7.02 min (minor): 96% ee.



3i

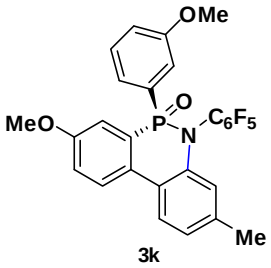
3i was prepared by using the general procedure above from corresponding ortho-arylated phosphinamide (96% ee) in 80% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a white solid. ^{1}H NMR (300 MHz, Acetone-d6) δ 8.27 (dd, J = 8.0, 5.4 Hz, 1H), 8.15 (d, J = 8.2 Hz, 1H), 7.86 – 7.69 (m, 2H), 7.67 – 7.49 (m, 4H), 7.43 (dd, J = 7.5, 3.4 Hz, 2H), 7.12 (d, J = 8.1 Hz, 1H), 6.83 (s, 1H), 2.25 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-d) δ 145.9 (d, J = 252 Hz), 145.6 (d, J = 252 Hz), 140.9 (d, J = 252 Hz), 140.5, 138.9, 137.9 (d, J = 252 Hz), 137.7 (d, J = 252 Hz), 136.8 (d, J = 4 Hz), 132.7, 132.5, 131.3 (d, J = 11 Hz), 130.7 (d, J = 128Hz), 130.0 (d, J = 11 Hz), 128.2 (d, J = 14 Hz), 127.5 (d, J = 14 Hz), 126.1 (d, J = 128 Hz), 126.0, 125.0, 124.3 (d, J = 11 Hz), 122.1 (d, J = 8 Hz), 119.5 (d, J = 3 Hz), 114.7, 21.3; ^{31}P NMR (243 MHz, Chloroform-d) δ 18.03; HRMS (MALDI-TOF) m/z Calcd for C25H15F5KNOP$^+$ $[M+K]^+$: 510.0443, Found : 510.0433; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.0 mL/min), tr: 9.44 min (minor), 17.67 min (major): 95% ee.



3j

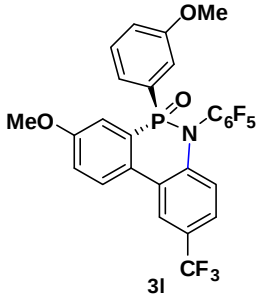
3j was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (87% ee) in 93% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 4:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.23 (dd, *J* = 8.9, 6.1 Hz, 1H), 8.19 – 8.14 (m, 1H), 7.39 (dd, *J* = 8.9, 2.8 Hz, 1H), 7.36 – 7.23 (m, 4H), 7.18 – 7.06 (m, 3H), 6.94 (d, *J* = 7.5 Hz, 1H), 3.89 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.3 (d, *J* = 17 Hz), 159.2 (d, *J* = 17 Hz), 145.9 (d, *J* = 257 Hz), 141.0 (d, *J* = 257 Hz), 138.5, 138.1 (d, *J* = 257 Hz), 137.7 (d, *J* = 257 Hz), 132.2 (d, *J* = 128 Hz), 129.5 (d, *J* = 17 Hz), 129.0, 127.6 (d, *J* = 128 Hz), 126.5 (d, *J* = 12 Hz), 125.5, 124.9 (d, *J* = 6 Hz), 123.9, 123.4

(d, *J* = 11 Hz), 120.5, 119.2, 119.0, 115.5 (d, *J* = 12 Hz), 114.6, 112.8 (d, *J* = 11 Hz), 55.3, 55.2; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 18.35; HRMS (MALDI-TOF) *m/z* Calcd for $C_{26}H_{17}F_5NNaO_3P^+$ $[M+Na]^+$: 540.0758, Found : 540.0754; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.5 mL/min), t_r: 11.21 min (major), 36.69 min (minor): 87% ee.



3k

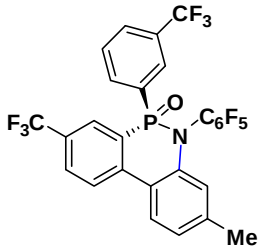
3k was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (87% ee) in 93% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a white solid. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.20 (dd, *J* = 8.9, 6.2 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.41–7.31 (m, 2H), 7.28 (dd, *J* = 14.8, 2.8 Hz, 1H), 7.20–7.06 (m, 4H), 6.81 (s, 1H), 3.90 (s, 3H), 3.72 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.7 (t, *J* = 16 Hz), 145.5 (d, *J* = 246 Hz), 140.5 (d, *J* = 246 Hz), 139.3, 137.8 (d, *J* = 246Hz), 137.2 (d, *J* = 246Hz), 132.0 (d, *J* = 138 Hz), 129.2 (d, *J* = 42 Hz), 129.1 (d, *J* = 16 Hz), 126.6 (d, *J* = 138 Hz), 125.0, 124.6, 123.0 (d, *J* = 11 Hz), 121.9 (d, *J* = 7 Hz), 120.1, 119.2, 118.5, 115.1 (d, *J* = 12 Hz), 114.3, 112.3 (d, *J* = 12 Hz), 55.2, 54.8, 20.8; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 18.75; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{20}F_5NO_3P$ $[M+H]^+$: 532.1095, Found : 532.1084; HPLC chiralcel OD-H column (hexane/isopropanol = 80/20, 0.5 mL/min), t_r: 12.35 min (major), 14.94 min (minor): 85% ee.



3l

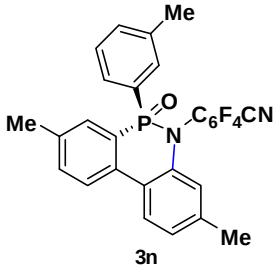
3l was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (90% ee) in 72% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.53 (s, 1H), 8.44 (dd, *J* = 9.0, 6.3 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.46 (dd, *J* = 8.9, 2.8 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.31 (dd, *J* = 15.2, 2.8 Hz, 1H), 7.18 – 7.07 (m, 4H), 3.92 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.9 (d, *J* = 17 Hz), 159.3 (d, *J* = 17 Hz), 145.9 (d, *J* = 257 Hz), 145.6 (d, *J* = 257 Hz), 141.4 (d, *J* = 257 Hz), 141.0, 138.2 (d, *J* = 257 Hz), 137.7 (d, *J* = 257 Hz), 131.5 (d, *J* = 128 Hz), 129.7 (d, *J* = 17 Hz), 128.0 (d, *J* = 6 Hz), 127.4 (d, *J* = 128 Hz), 126.7 (d, *J* = 12 Hz), 125.8 (d, *J* = 33 Hz), 125.6 (d, *J* = 3 Hz), 124.6 (d, *J* = 6 Hz), 123.6 (d, *J* = 272 Hz), 123.5 (d, *J* = 12 Hz), 122.6 (d, *J* = 4 Hz), 120.7, 119.2, 119.0 (d, *J* = 3 Hz), 115.7 (d, *J* = 12 Hz), 113.7, 113.2 (d, *J* = 12 Hz), 55.6, 55.2; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 18.01; HRMS

(MALDI-TOF) *m/z* Calcd for $C_{27}H_{16}F_8NNaO_3P^+$ $[M+Na]^+$: 608.0632, Found : 608.0643; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.5 mL/min), t_r: 5.49 min (minor), 29.92 min (major): 93% ee.



3m

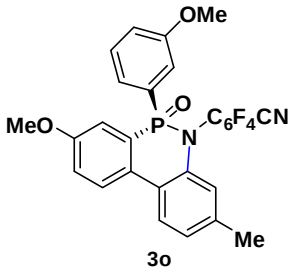
3m was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (99% ee) in 85% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 6:1:1) to give a white solid. ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.55 (dd, J = 8.3, 5.2 Hz, 1H), 8.27 (d, J = 8.2 Hz, 1H), 8.21–8.10 (m, 2H), 8.01–7.91 (m, 2H), 7.85 (dd, J = 12.7, 7.6 Hz, 1H), 7.71 (td, J = 8.0, 3.6 Hz, 1H), 7.23 (d, J = 8.1 Hz, 1H), 6.94 (s, 1H), 2.29 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 147.4 (d, J = 251 Hz), 145.7 (d, J = 251 Hz), 142.5, 142.5 (d, J = 251 Hz), 140.1 (d, J = 6 Hz), 139.0, 134.1 (d, J = 11 Hz), 132.1 (d, J = 130 Hz), 129.8, 129.5, 129.1 (d, J = 14 Hz), 127.7 (d, J = 11 Hz), 127.1 (d, J = 11 Hz), 126.5, 126.0 (d, J = 130 Hz), 125.7, 125.1 (d, J = 11 Hz), 123.3 (d, J = 272 Hz), 123.2 (d, J = 272 Hz), 121.1 (d, J = 8 Hz), 119.7 (d, J = 3 Hz), 21.4; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 14.81; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{13}F_{11}KNOP$ $[M+K]^+$: 646.0191, Found: 646.0182; HPLC chiralcel AD-H column (hexane/isopropanol = 90/10, 1.0 mL/min), t_r: 8.61 min (minor), 11.04 min (major): 98% ee.



3n

3n was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (95% ee) in 85% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 4:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.12 (dd, J = 8.2, 5.6 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 14.1 Hz, 1H), 7.49 (d, J = 13.5 Hz, 1H), 7.38 – 7.24 (m, 3H), 7.15 (d, J = 8.2 Hz, 1H), 6.90 (s, 1H), 2.43 (s, 3H), 2.27 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 147.7 (d, J = 263 Hz), 147.4 (d, J = 263 Hz), 145.1 (d, J = 263 Hz), 144.9 (d, J = 263 Hz), 140.2, 138.3 (d, J = 14 Hz), 138.2 – 138.0 (m), 133.9, 133.6, 131.5 (d, J = 12 Hz), 130.8, 129.9 (d, J = 11 Hz), 128.2 (d, J = 14 Hz), 128.1 (d, J = 14 Hz), 126.7, 126.2, 126.0, 125.9, 124.6 (d, J = 11 Hz), 123.6 (d, J = 11 Hz), 120.8 (d, J = 3 Hz), 107.2, 92.4, 21.2, 21.1, 20.9; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 20.04; HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{19}F_4N_2NaOP^+$ $[M+Na]^+$: 529.1063, Found : 529.1058; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.5 mL/min), t_r: 9.97 min (minor), 19.21

min (major): 94% ee.



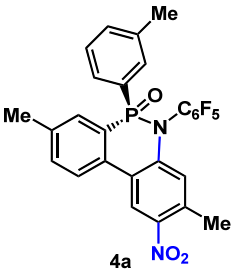
3o

3o was prepared by using the general procedure above from corresponding *ortho*-arylated phosphinamide (97% ee) in 88% yield. Purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 3:1:1) to give a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.15 (dd, J = 8.8, 6.2 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.40 – 7.28 (m, 3H), 7.20 – 7.05 (m, 4H), 6.92 (s, 1H), 3.89 (s, 3H), 3.70 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.3 (d, J = 17 Hz), 147.7 (d, J = 260 Hz), 147.4 (d, J = 260 Hz), 145.3 (d, J = 260 Hz), 144.9 (d, J = 260 Hz), 139.7, 137.6, 131.8 (d, J = 127 Hz), 129.7 (d, J = 17 Hz), 129.5 (d, J = 6 Hz), 127.4 (d, J = 126 Hz), 126.6 (d, J = 12 Hz), 126.2, 125.6, 119.0, 115.5 (d, J = 12 Hz), 112.7 (d, J = 12 Hz), 107.2, 92.5, 55.6, 55.2, 21.1; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 20.03; HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{19}F_4KN_2O_3P^+$ $[M+K]^+$: 577.0701, Found : 577.0703; HPLC chiralcel AD-H column (hexane/isopropanol = 70/30, 2.0 mL/min), t_r: 7.52 min (minor), 48.03 min (major): 97% ee.

2.5 Experimental procedure for synthesizing 4

2.5.1 Synthesis of 4a

To a suspension of *ortho*-arylated phosphinamide (50 mg, 0.1 mmol, 98% ee) in anhydrous CH_3CN (1 mL) was added $Ce(NH_4)_2(NO_3)_6$ (274 mg, 0.5 mmol). The reaction tube was charged with Ar and was heated to 60 °C for 2 hours. The reaction mixture was then quenched by addition of H_2O (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic extracts were washed with a mixture of aq. $NaHCO_3$ (10 mL) and aq. $Na_2S_2O_3$ (10 mL), brine (15 mL) sequentially and then dried over Na_2SO_4. The organic phase was filtered, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give to give the desired nitrated phosphinamide **4a** as a pale yellow solid in 65% Yield.



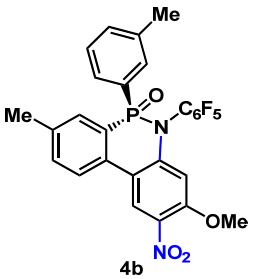
4a

^{1}H NMR (300 MHz, Acetone-d_6) δ 8.80 (s, 1H), 8.22 (dd, J = 8.4, 5.6 Hz, 1H), 7.61 (dd, J = 8.6,

1.8 Hz, 1H), 7.47 (d, *J* = 14.3 Hz, 1H), 7.35–7.13 (m, 4H), 6.87 (s, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 145.8 (d, *J* = 254 Hz), 145.3 (d, *J* = 254 Hz), 144.0, 142.6, 141.6 (d, *J* = 254 Hz), 139.5 (d, *J* = 14 Hz), 138.4 (d, *J* = 14 Hz), 138.1 (d, *J* = 254 Hz), 135.9, 134.4, 133.9, 131.9 (d, *J* = 11 Hz), 130.7 (d, *J* = 11 Hz), 129.9 (d, *J* = 130 Hz), 128.4 (d, *J* = 7 Hz), 128.3 (d, *J* = 11 Hz), 124.4 (d, *J* = 130 Hz), 123.4 (d, *J* = 11 Hz), 123.1, 122.2 (d, *J* = 7 Hz), 121.4, 113.0, 21.2, 21.1, 21.0; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 18.40; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{18}F_5KN_2O_3P$ $[M+K]^+$: 583.0607, Found: 583.0599; HPLC chiralcel OD-H column (hexane/isopropanol = 90/10, 1.0 mL/min), t_r: 10.74 min (major), 14.20 min (minor): 99% ee.

2.5.2 Synthesis of 4b

To a suspension of *ortho*-arylated phosphinamide (51 mg, 0.1 mmol, 90% ee) in anhydrous CH_3CN (1 mL) was added $Ce(NH_4)_2(NO_3)_6$ (121 mg, 0.22 mmol). The reaction tube was charged with Ar and was heated at 40 °C for 2 hours. After complete consumption of starting material (indicated by TLC), the reaction was quenched by H_2O (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic extracts were washed sequentially with a mixture of aq. $NaHCO_3$ (10 mL) and aq. $Na_2S_2O_3$ (10 mL), brine (15 mL), and then dried over Na_2SO_4. The organic phase was filtered, and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (Hexane/DCM/EtOAc = 8:10:1) to give the desired nitrated phosphinamide **4b** as a pale yellow solid in 78% Yield.



4b

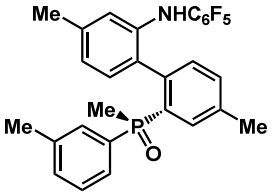
^{1}H NMR (400 MHz, Acetone) δ 8.81 (s, 1H), 8.25 (dd, *J* = 8.3, 5.8 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 14.2 Hz, 1H), 7.47 (d, *J* = 13.6 Hz, 1H), 7.42 – 7.30 (m, 3H), 6.64 (s, 1H), 3.80 (s, 3H), 2.44 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 154.5, 146.0 (d, *J* = 260 Hz), 145.5 (d, *J* = 260 Hz), 144.5, 141.8 (d, *J* = 260 Hz), 139.0 (d, *J* = 14 Hz), 138.6 (d, *J* = 260 Hz), 138.3 (d, *J* = 260 Hz), 137.8 (d, *J* = 260 Hz), 134.8, 134.6, 134.0, 132.1 (d, *J* = 5 Hz), 131.8 (d, *J* = 10 Hz), 130.7 (d, *J* = 10 Hz), 130.0 (d, *J* = 129 Hz), 128.6 (d, *J* = 14 Hz), 128.5 (d, *J* = 10 Hz), 116.6 (d, *J* = 10 Hz), 113.2, 102.5 (d, *J* = 3 Hz), 55.6, 21.3, 21.1; ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.51; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{18}F_5KN_2O_4P^+$ $[M+K]^+$: 599.0556, Found : 599.0566; HPLC chiralcel AD-H column (hexane/isopropanol = 80/20, 1.5 mL/min), t_r: 8.34 min (minor), 26.04 min (major): 89% ee.

2.6 Experimental procedure for derivatization

2.6.1 Experimental procedure for synthesizing 5

To a 1 mL anhydrous THF solution of **3a** (50 mg, 0.1 mmol, 98% ee) in a dried reaction tube

was added MeLi (0.187 mL, 1.6M in 2-Me-THF) dropwise at -78 °C. After complete consumption of **3a** (about 10 min, indicated by TLC), the reaction was quenched by addition of aq. NH_4Cl (1 mL) and H_2O. The aqueous phase was extracted with EtOAc (10 mL × 3) and the combined organic extracts were washed with brine (15 mL), and dried over Na_2SO_4. The organic phase was filtered, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (Hexane/DCM/EtOAc = 5:1:1) to give **5** as a yellow solid in 85% total yield as a mixture of two atropisomers (1.66:1, determined by ^{1}HNMR in $CDCl_3$ at 25 °C).



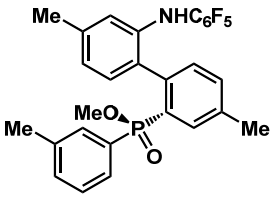
5

Two atropisomers exist in equilibrium and their ratio varies according to temperature and solvent. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 13.3 Hz, 1H, major atropisomer), 7.58 (br, 1H, major atropisomer), 7.47 (d, *J* = 12.2 Hz, 0.6H, minor atropisomer), 7.40–7.31 (m, 3.9H), 7.20–6.88 (m, 5.9H), 6.81 (d, *J* = 7.7 Hz, 0.6H, minor atropisomer), 6.77 (m, 1H, major atropisomer), 6.69 (s, 1H, major atropisomer), 6.64 (s, 0.6H, minor atropisomer), 6.36 (d, *J* = 7.7 Hz, 1H, major atropisomer), 6.11 (d, *J* = 7.7 Hz, 1H, major atropisomer), 2.47 (s, 3H, major atropisomer), 2.39 (s, 1.8H, minor atropisomer), 2.32 (m, 2.4H, minor atropisomer), 2.25 (s, 3H, major atropisomer), 2.18 (s, 3H, major atropisomer), 2.01 (d, *J* = 13.1 Hz, 3H, major atropisomer), 1.58 (d, *J* = 13.4 Hz, 1.8H, minor atropisomer); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 141.1, 141.0 (d, *J* = 251 Hz), 140.9, 140.8, 139.6 (d, *J* = 251 Hz), 139.2 (d, *J* = 9 Hz), 139.0, 138.2 (d, *J* = 12 Hz), 138.1 (d, *J* = 251 Hz), 137.8, 137.7 (d, *J* = 12 Hz), 137.6 (d, *J* = 251 Hz), 137.3 (d, *J* = 12 Hz), 137.1, 136.9 (d, *J* = 11 Hz), 135.7 (d, *J* = 251 Hz), 135.1 (d, *J* = 251 Hz), 133.2 (d, *J* = 122 Hz), 133.1 (d, *J* = 122 Hz), 132.9 (d, *J* = 120 Hz), 132.7, 132.6 (d, *J* = 121 Hz), 131.7 (d, *J* = 11 Hz), 131.5 (d, *J* = 11 Hz), 131.5, 131.4, 130.9, 130.6 (d, *J* = 9 Hz), 130.4, 130.3 (d, *J* = 12 Hz), 129.7, 128.2 (d, *J* = 12 Hz), 127.5 (d, *J* = 14 Hz), 126.4 (d, *J* = 12 Hz), 123.6, 123.0, 121.4, 121.3, 119.7, 119.3, 21.3, 21.2, 21.1, 21.0, 21.0, 20.9, 16.3 (d, *J* = 75 Hz), 16.2 (d, *J* = 75 Hz); ^{31}P NMR (243 MHz, Chloroform-*d*) δ 33.82 (minor atropisomer), 32.17 (major atropisomer); HRMS (MALDI-TOF) *m/z* Calcd for $C_{23}H_{28}F_5KNOP$ $[M+K]^+$: 554.1069, Found: 554.1066; HPLC chiralcel OZ-H column (hexane/isopropanol = 90/10, 1.0 mL/min), t_r: 7.22 min (major atropisomer, major enatiomer), 8.66 min (major atropisomer, minor enatiomer), ee: 97.8%; 12.68 min (minor atropisomer, major enatiomer), 15.64 min (minor atropisomer, minor enatiomer), ee: 98.5%.

2.6.2 Experimental procedure for synthesizing 6

To a 1 mL anhydrous MeOH solution of **3a** (50 mg, 0.1 mmol, 98% ee) was added NaOMe (27 mg, 0.5 mmol). The mixture was stirred at room temperature for 6 hours, and quenched by addition of aq. NH_4Cl (1 mL) and H_2O. The aqueous phase was extracted with EtOAc (10 mL × 3) and the combined organic extracts were washed with brine (15 mL), and dried over Na_2SO_4. The organic phase was filtered, and the filtrate was concentrated. The residue was purified by column

chromatography on silica gel (Hexane/EtOAc = 4:1) to give **6** as a white solid in 85% total yield as a mixture of two atropisomers (4.0:1 as determined by ^{1}HNMR in $CDCl_3$ at 25 ^{o}C).

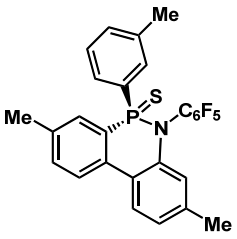


6

Two atropisomers exist in equilibrium and their ratio varies according to temperature and solvent. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 12.0 Hz, 1H, major atropisomer), 7.75 (d, *J* = 13.8 Hz, 0.25H, minor atropisomer), 7.34 (d, *J* = 7.5 Hz, 1.25H, major & minor atropisomer), 7.24–6.99 (m, 6.5H), 6.95 (d, *J* = 13.1 Hz, 1H, major atropisomer), 6.89 (d, *J* = 7.7 Hz, 0.25H, minor atropisomer), 6.77 (d, *J* = 8.7 Hz,, 0.25H, minor atropisomer), 6.73 (s, 1H, major atropisomer), 6.44 (d, *J* = 8.0 Hz, 1.25H, major & minor atropisomer), 6.15 (d, *J* = 7.7 Hz, 1H, major atropisomer), 3.71 (d, *J* = 11.0 Hz, 3H, major atropisomer), 3.54 (d, *J* = 11.0 Hz, 0.75H, minor atropisomer), 2.46 (s, 3H, major atropisomer), 2.40 (s, 0.75H, minor atropisomer), 2.31 (s, 0.75H, minor atropisomer), 2.29 (s, 3H, major atropisomer), 2.26 (s, 0.75H, minor atropisomer), 2.18 (s, 3H, major atropisomer); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 140.9, 140.6 (d, *J* = 12 Hz), 139.8, 139.3 (d, *J* = 249 Hz), 139.1 (d, *J* = 11 Hz), 138.3 (d, *J* = 249 Hz), 138.2, 138.0, 137.9 (d, *J* = 249 Hz), 137.8 (d, *J* = 14 Hz), 137.6 (d, *J* = 14 Hz), 137.4 (d, *J* = 249 Hz), 137.2, 137.1 (d, *J* = 12 Hz), 136.9 (d, *J* = 12 Hz), 133.6 (d, *J* = 249 Hz), 133.0 (d, *J* = 11 Hz), 132.8, 132.6, 132.5 (d, *J* = 11 Hz), 132.3, 132.2, 131.6, 131.5, 131.4 (d, *J* = 8 Hz), 131.2 (d, *J* = 14 Hz), 130.5, 129.8 (d, *J* = 133 Hz), 129.7 (d, *J* = 133 Hz), 128.8, 128.6 (d, *J* = 11 Hz), 128.1 (d, *J* = 11 Hz), 128.0 (d, *J* = 14 Hz), 127.8 (d, *J* = 14 Hz), 123.7, 123.1, 122.7, 122.3, 122.2, 117.8, 51.1 (d, *J* = 6 Hz), 51.0 (d, *J* = 6 Hz), 21.2, 21.1, 21.1, 21.0, 20.9; ^{31}P NMR (243 MHz, Chloroform-*d*) δ 35.33 (minor atropisomer), 33.11 (major atropisomer); HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{23}F_5NO_2P$ $[M+K]^+$: 570.1018, Found: 570.1006; HPLC chiralcel OZ-H column (hexane/isopropanol = 90/10, 1.0 mL/min), t_r: 9.61 min (major atropisomer, major enatiomer), 10.79 min (major atropisomer, minor enatiomer), ee: 92.2%; 12.96 min (minor atropisomer, major enatiomer), 17.47 min (minor atropisomer, minor enatiomer), ee: 95.4%.

2.6.3 Experimental procedure for synthesizing 7

To a suspension of **3a** (50 mg, 0.1 mmol, 98% ee) in anhydrous toluene (5 mL) was added Lawesson's reagent (40 mg, 0.1 mmol). The reaction tube was charged with Ar and was heated at 90 ^{o}C for 16 hours. After complete consumption of **3a** (indicated by TLC), the solvent was removed by rotary evaporation under reduced pressure. The residue was purified by column chromatography on silica gel (Hexane/DCM = 3:1) to give **7** as a white solid in 95% Yield.

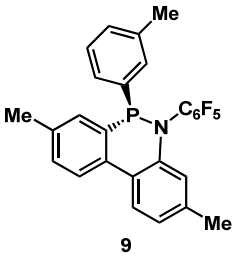


7

^{1}H NMR (300 MHz, Acetone-d_6) δ 8.05 (dd, J = 8.2, 5.5 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.90 (dd, J = 16.2 Hz, 0.6 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 15.0 Hz, 1H), 7.34 (dd, J = 14.2, 7.3 Hz, 1H), 7.28–7.16 (m, 2H), 7.07 (d, J = 7.6 Hz, 1H), 6.86 (s, 1H), 2.48 (s, 3H), 2.23 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 147.3 (d, J = 251 Hz), 146.0 (d, J = 251 Hz), 140.9 (d, J = 251 Hz), 139.9, 139.3, 138.3 (d, J = 14 Hz), 138.1 (d, J = 14 Hz), 137.9 (d, J = 251 Hz), 137.5 (d, J = 251 Hz), 134.2 (d, J = 100 Hz), 133.6, 133.3 (d, J = 4 Hz), 132.5, 131.2 (d, J = 12 Hz), 130.8 (d, J = 12 Hz), 127.9 (d, J = 15 Hz), 127.4 (d, J = 100 Hz), 127.3 (d, J = 11 Hz), 124.5 (d, J = 11 Hz), 121.8, 116.8, 21.3, 21.1, 21.0; ^{31}P NMR (243 MHz, Acetone-d_6) δ 54.42; HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{19}F_5NNaPS$ $[M+Na]^+$: 538.0788, Found: 538.0788; HPLC chiralcel AD-H column (hexane/isopropanol = 98/2, 0.5 mL/min), t_r: 9.87 min (minor), 10.86 min (major): 96% ee; See section **4.2** for crystallographic data of this compound.

2.6.4 Experimental procedure for synthesizing 8[3]

To an anhydrous DCM (10 mL) solution of **7** (52 mg, 0.1 mmol, 96% ee) was added methyl trifluoromethanesulfonate (22 μL, 0.2 mmol). The reaction tube was charged with Ar and was heated at 40 ^{o}C for 24 hours. The mixture was cooled to room temperature and *N,N,N',N',N'',N''*-hexamethylphosphanetriamine (36 μL, 0.2 mmol) was added via syringe. The reaction mixture was then stirred at 40 ^{o}C for an additional hour. Then the volatile materials were removed by evaporation and the residue was purified by column chromatography on silica gel (Hexane/DCM = 5:1) to give **8** as a white solid in 94% yield.

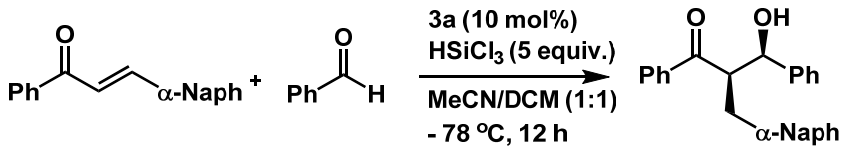


9

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.83 (d, J = 8.1 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.44 (dd, J = 12.9, 1.9 Hz, 1H), 7.36 (dd, J = 8.0, 1.9 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 7.02–6.92 (m, 3H), 6.85 (d, J = 1.7 Hz, 1H), 6.56 (s, 1H), 2.43 (s, 3H), 2.21 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 145.3 (d, J = 249 Hz), 140.9 (d, J = 4 Hz), 139.1 (d, J = 249 Hz), 138.5, 137.9 (d, J = 249 Hz), 137.8 (d, J = 14 Hz), 137.3 (d, J = 6 Hz), 136.4 (d, J = 14 Hz), 132.7 (d, J = 49 Hz), 132.2 (d, J = 65 Hz), 131.4, 131.2 (d, J = 22 Hz), 129.5, 127.7, 127.6 (d, J = 49 Hz), 126.0, 125.4, 125.0, 124.5, 123.2 (d, J = 22 Hz), 121.7, 21.3, 21.0, 20.9; ^{31}P NMR (202 MHz, Chloroform-*d*) δ 33.76 – 27.49 (m); HRMS (MALDI-TOF) *m/z* Calcd for $C_{17}H_{19}F_5NP$ $[M]^+$: 483.1175, Found:

483.1166; HPLC chiralcel AD-H column (hexane/isopropanol = 99/1, 0.5 mL/min), t_r: 8.55 min (minor), 9.06 min (major): 96% ee.

2.7 Experimental procedure for P-stereogenic phosphinamides catalyzed asymmetric reaction



9 **10** **11**

A dried reaction tube equipped with a magnetic stirring bar was charged with **9** (78.1 mg, 0.3 mmol), **10** (21.2 mg, 0.2 mmol), **3a** (10.0 mg, 0.02 mmol, 10 mol%), DCM (0.5 mL), and MeCN (0.5 mL) under argon atmosphere. The mixture was cooled to – 78 ^{o}C and then $HSiCl_3$ (135.4 mg, 1.0 mmol) was added slowly. The reaction mixture was stirred at – 78 ^{o}C until the complete consumption of **10** (indicated by TLC). The reaction was quenched by addition of aq. $NaHCO_3$ (1 mL) and H_2O. The aqueous phase was extracted with EtOAc (20 mL × 3) and the combined organic extracts were washed with brine (15 mL), and then dried over Na_2SO_4. The organic phase was filtered, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (Hexane/EtOAc = 10:1) to give **11** in 94% total yield as a mixture of diastereomer (*syn*:*anti* = 83:17, determined by HPLC)[4]. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.78 – 6.97 (m, 17+3.4H, *syn, anti*), 5.19 (d, *J* = 3.9 Hz, 0.2H, *anti*), 5.06 (t, *J* = 5.4 Hz, 1H, *syn*), 4.26 (dd, *J* = 15.0, 6.6 Hz, 1H, *syn*), 4.13 (dt, *J* = 11.2, 3.2 Hz, 0.2H, *anti*), 3.78–3.63 (m, 0.4H, *anti*), 3.44 (br, 1+0.2H, *syn, anti*), 3.37 (d, *J* = 4.8 Hz, 1H, *syn*), 3.35 (d, *J* = 1.9 Hz, 1H, *syn*); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 205.5 (*syn, anti*) , 142.5 (*syn*) , 141.4 (*anti*), 138.0 (*syn*), 137.0 (*anti*), 135.0 (*anti*), 134.4 (*syn*), 133.7 (*syn*), 133.6 (*anti*), 132.8 (*anti*), 132.7 (*syn*), 131.4 (*syn*), 128.7 (*syn*), 128.6 (*anti*) , 128.4 (*syn*), 128.3 (*anti*), 127.9 (*syn*), 127.8 (*anti*), 127.8 (*syn, anti*), 127.7 (*syn*), 127.6 (*anti*), 127.4 (*syn*), 127.2 (*anti*), 127.1 (*syn*), 126.8 (*anti*), 126.3 (*syn*), 126.2 (*anti*), 125.9 (*syn*), 125.8 (*anti*) , 125.3 (*syn*), 125.2 (*syn, anti*), 125.0 (*anti*), 123.1 (*anti*), 123.1 (*anti*), 123.1 (*syn*), 76.0 (*syn*), 73.9 (*anti*), 53.9 (*anti*), 53.6 (*syn*), 33.6 (*syn*), 30.4 (*anti*); HRMS (MALDI-TOF) *m/z* Calcd for $C_{26}H_{22}NaO_2$ $[M+Na]^+$: 389.1512, Found: 389.1509; HPLC chiralcel ID column (hexane/isopropanol = 95/5, 0.5 mL/min), t_r: 30.62 min (*syn*, major enatiomer), 43.47 min (*syn*, minor enatiomer), ee: 60%; 23.16 min (*anti*, minor enatiomer), 68.09 min (*anti*, major enatiomer), ee: 23%.

3. References

1. Y.-H. Chen, X.-L. Qin, J. Guan, Z.-J. Du and F.-S. Han, *Tetrahedron-Asymmetry*, DOI: 10.10.16/j.tetasy.2017.03.008

2. Z.-J. Du, J. Guan, G.-J. Wu, P. Xu, L.-X. Gao and F.-S. Han, *J. Am. Chem. Soc.*, 2015, **137**, 632.

3. H. el Hajjouji, E. Belmonte, J. Garcia-Lopez, I. Fernandez, M. J. Iglesias, L. Roces, S. Garcia-Granda, A. El Laghdach and F. Lopez Ortiz, *Org. Biomol. Chem.*, 2012, **10**, 5647.

4. K. Osakama, M. Sugiura, M. Nakajima and S. Kotani, *Tetrahedron Lett.*, 2012, **53**, 4199.

4. X-ray Crystallographic data

4.1 X-ray crystal data of compound 2 (racemic)

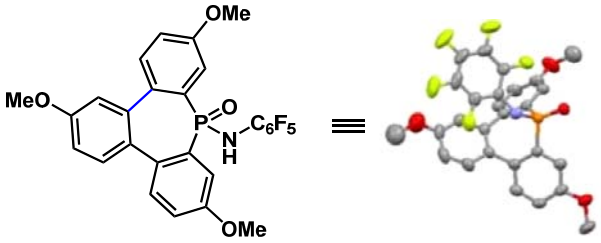


Table S1. Crystal data and structure refinement for 2

Identification code	**2**
Empirical formula	C27 H19 F5 N1 O4 P1
Formula weight	547.40
Temperature	273(2) K
Wavelength	0.71073 A
Crystal system, space group	triclinic
Unit cell dimensions	9.8498(6) A alpha = 103.6640(10) deg.
	b = 10.4837(7) A beta = 110.7240(10) deg.
	c = 13.4890(9) A gamma = 101.7210(10) deg.
Volume	1201.25(14) A^3
Z, Calculated density	2, 1.513 Mg/m^3
Absorption coefficient	0.190 mm^-1
F(000)	560.0
Crystal size	0.30 x 0.26 x 0.22 mm
Theta range for data collection	3.428 to 52.16 deg.
Limiting indices	-12<=h<=12, -12<=k<=12, -12<=l<=16
Reflections collected	7557
Completeness to theta = 26.08	99.3 %
Absorption correction	MULTI_SCAN
Max. and min. transmission	0.961 and 0.957
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4724 / 27 / 377
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0581, wR2 = 0.1596
R indices (all data)	R1 = 0.0811, wR2 = 0.1801
Largest diff. peak and hole	0.47 and -0.36 e.A^-3

4.2 X-ray crystal data of the enantiomerically enriched isomer 7 (>99% ee):

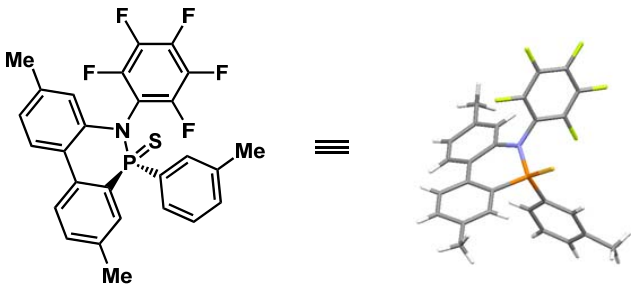


Table S2. Crystal data and structure refinement for 7

Identification code	**7**	
Empirical formula	C27 H19 F5 N1 P1 S1	
Formula weight	515.46	
Temperature	190(2) K	
Wavelength	1.54178 A	
Crystal system, space group	Monoclinic, C2	
Unit cell dimensions	a = 16.8922(4) A	alpha = 90 deg.
	b = 14.6238(3) A	beta = 108.6760(10) deg.
	c = 10.6886(2) A	gamma = 90 deg.
Volume	2501.35(9) A^3	
Z, Calculated density	4, 1.369 Mg/m^3	
Absorption coefficient	2.231 mm^-1	
F(000)	1056	
Crystal size	0.34 x 0.26 x 0.20 mm	
Theta range for data collection	4.09 to 66.58 deg.	
Limiting indices	-20<=h<=19, -17<=k<=17, -12<=l<=12	
Reflections collected / unique	12514 / 4366 [R(int) = 0.0396]	
Completeness to theta = 66.58	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.640 and 0.523	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4366 / 1 / 316	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	R1 = 0.0409, wR2 = 0.1042	
R indices (all data)	R1 = 0.0452, wR2 = 0.1071	
Absolute structure parameter	0.05(2)	
Largest diff. peak and hole	0.385 and -0.234 e.A^-3	

5. Copies of NMR Spectra

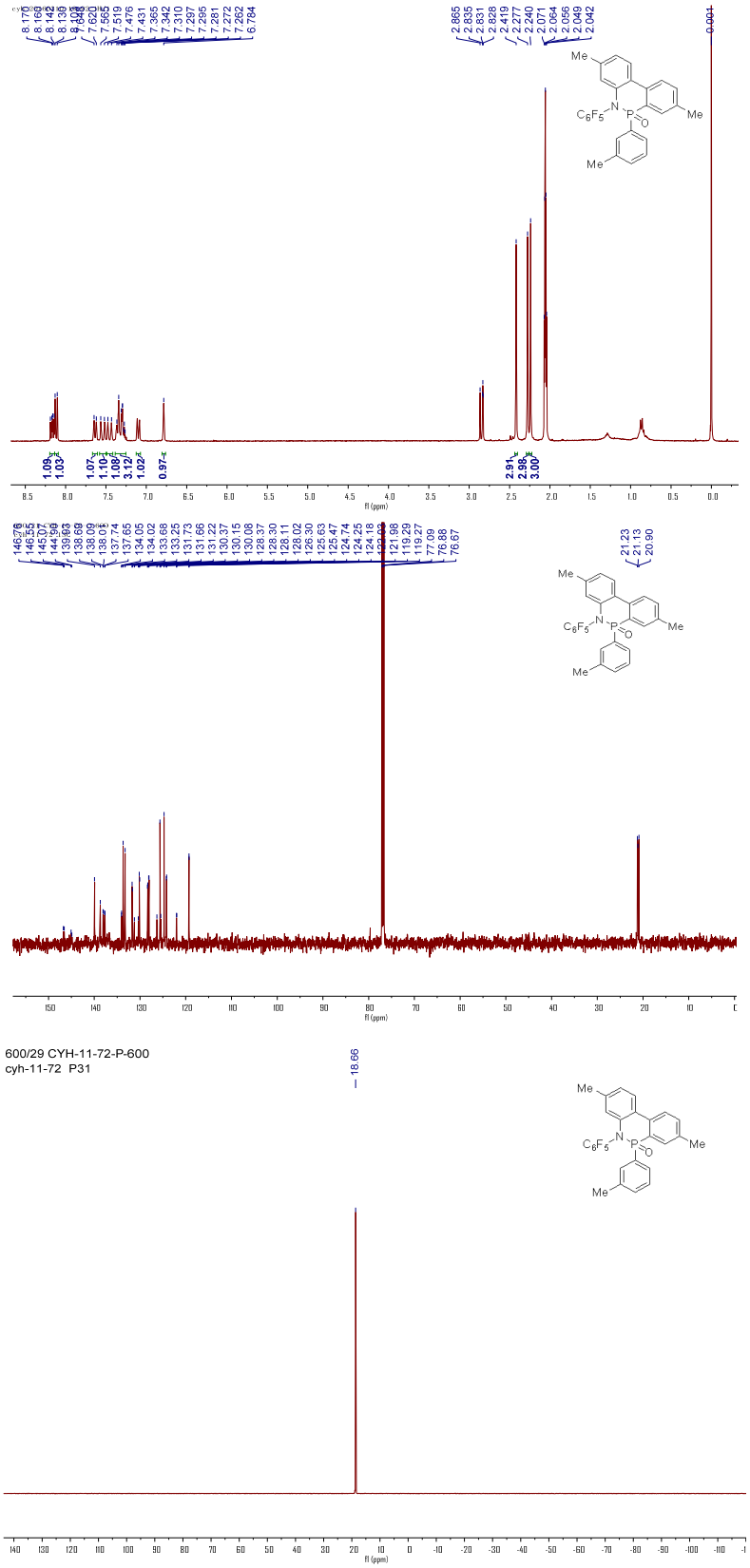


Figure S1. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3a

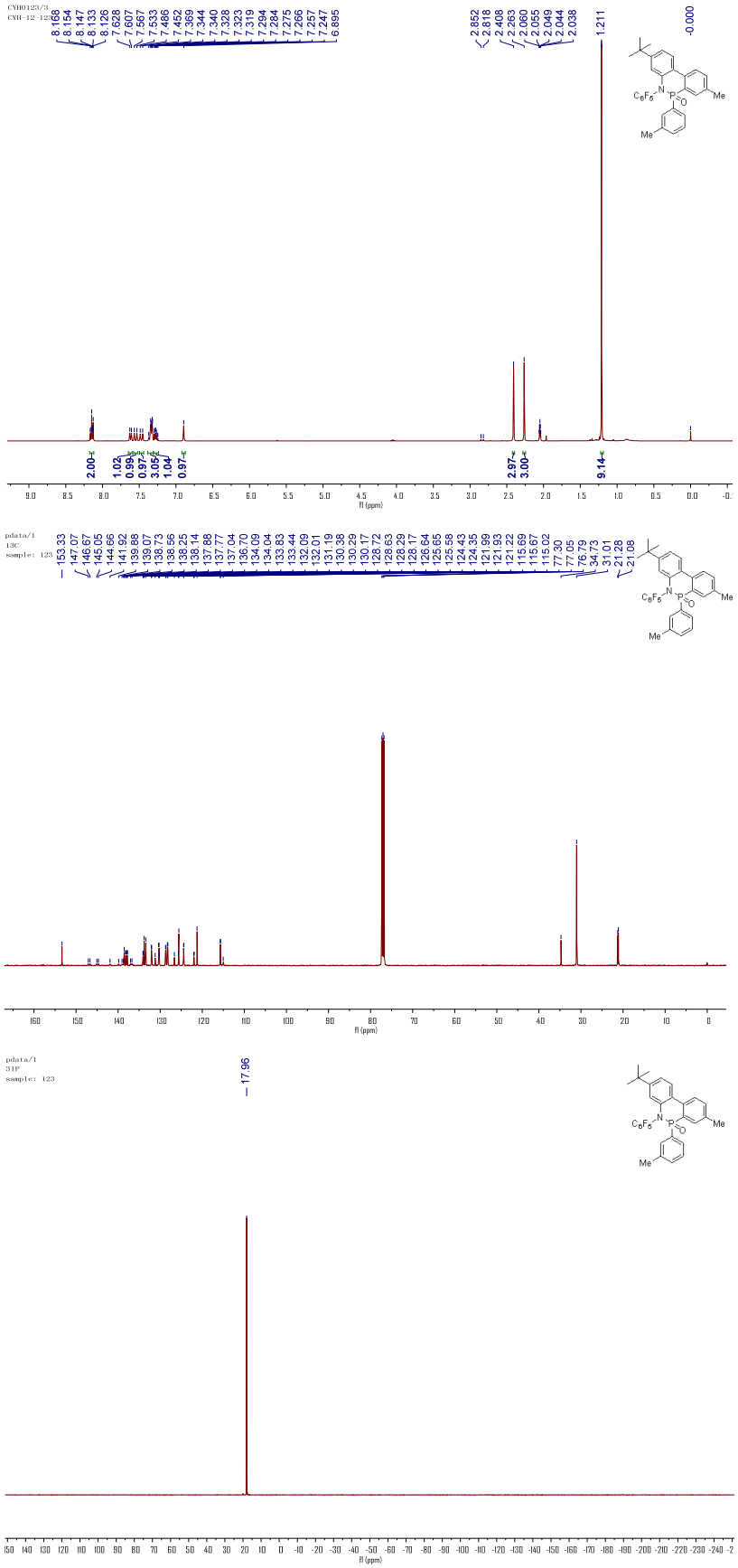


Figure S2. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3b

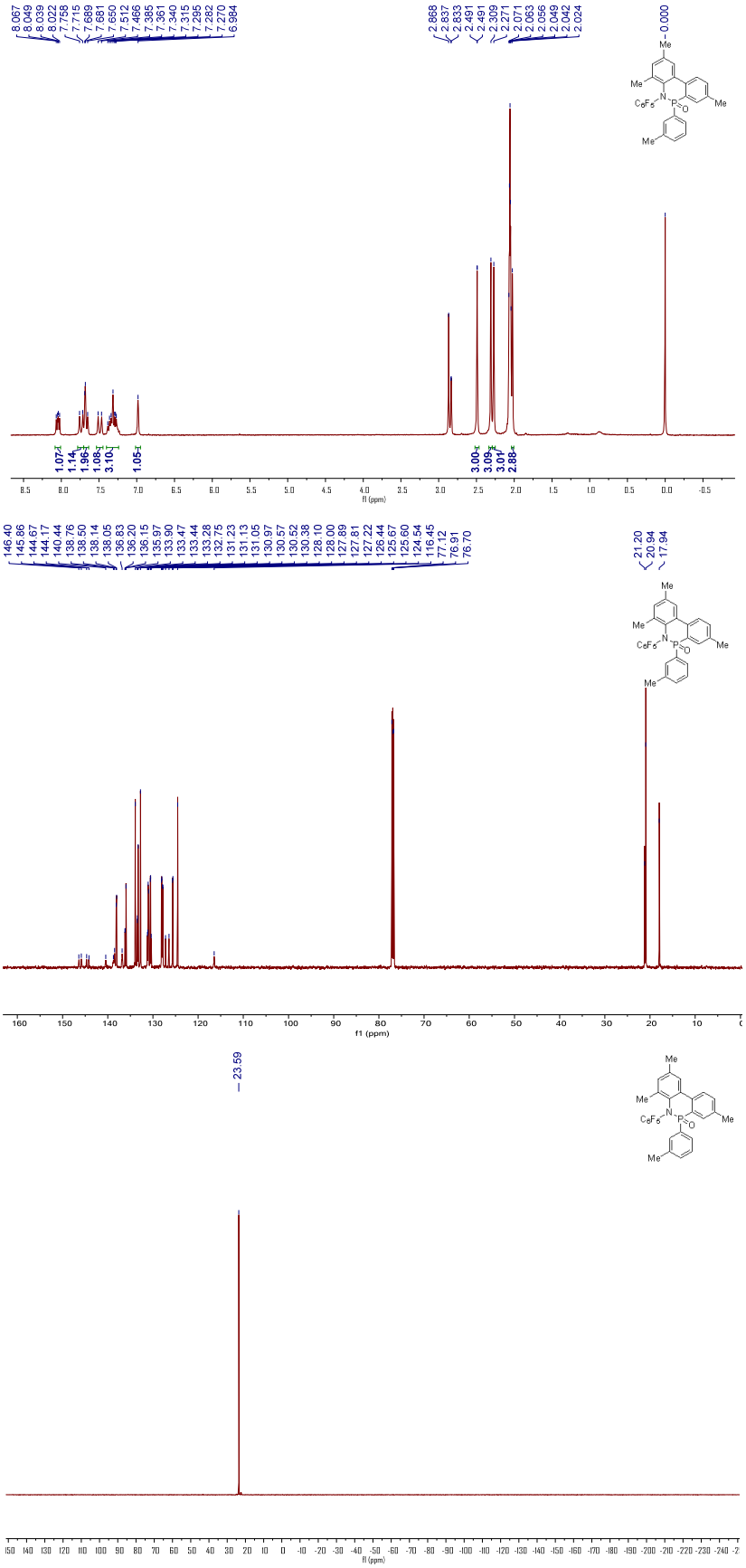


Figure S3. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3c

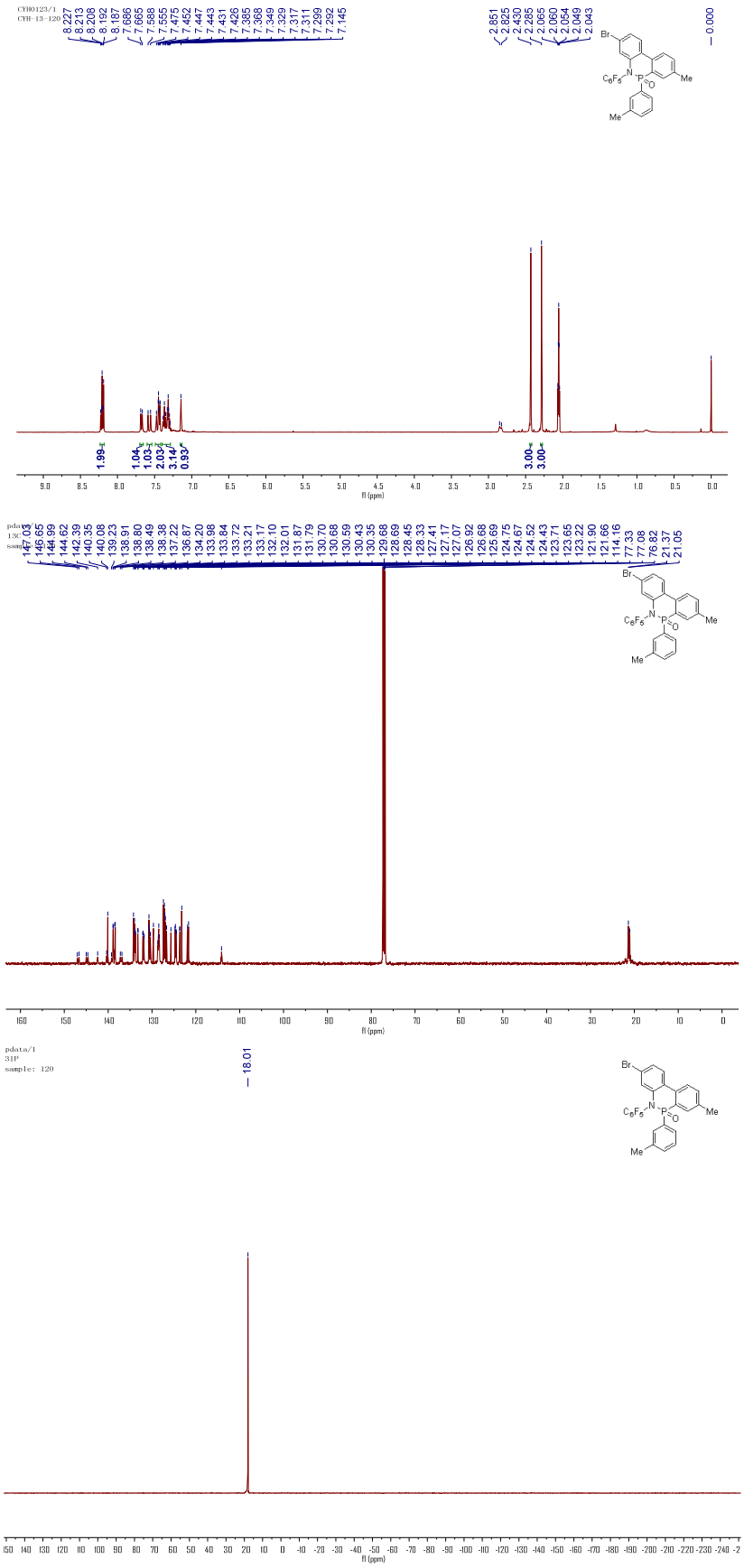


Figure S4. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3d

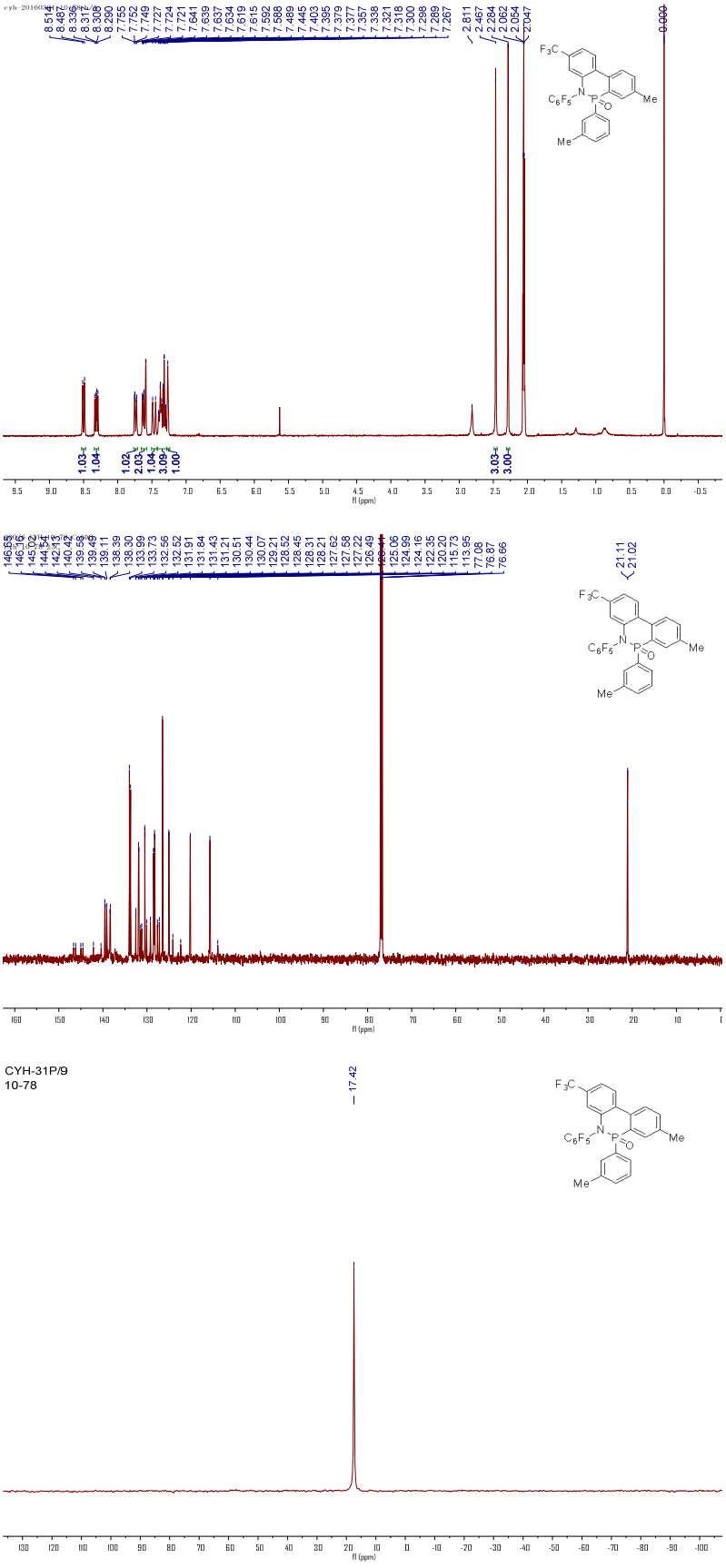


Figure S5. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3e

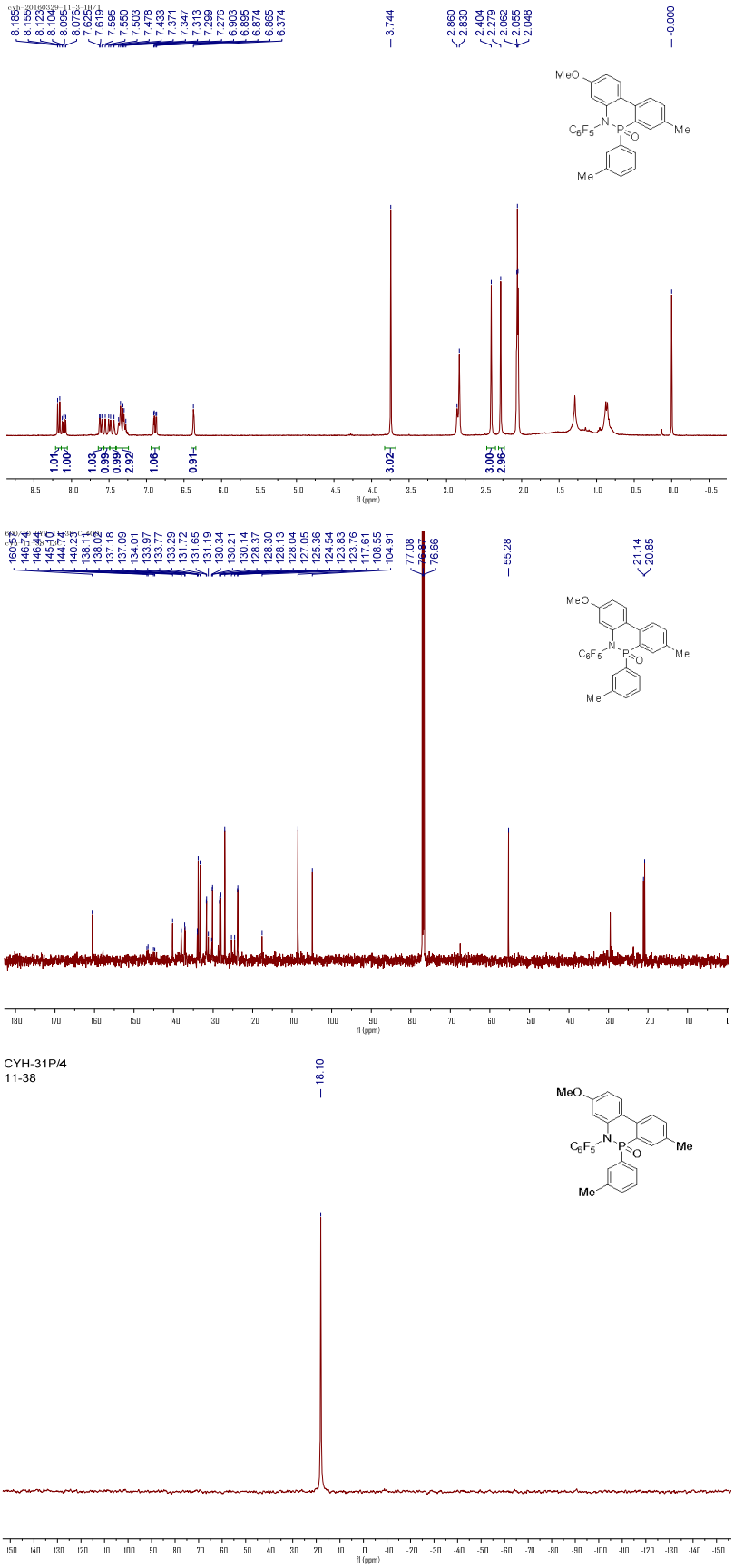


Figure S6. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3f

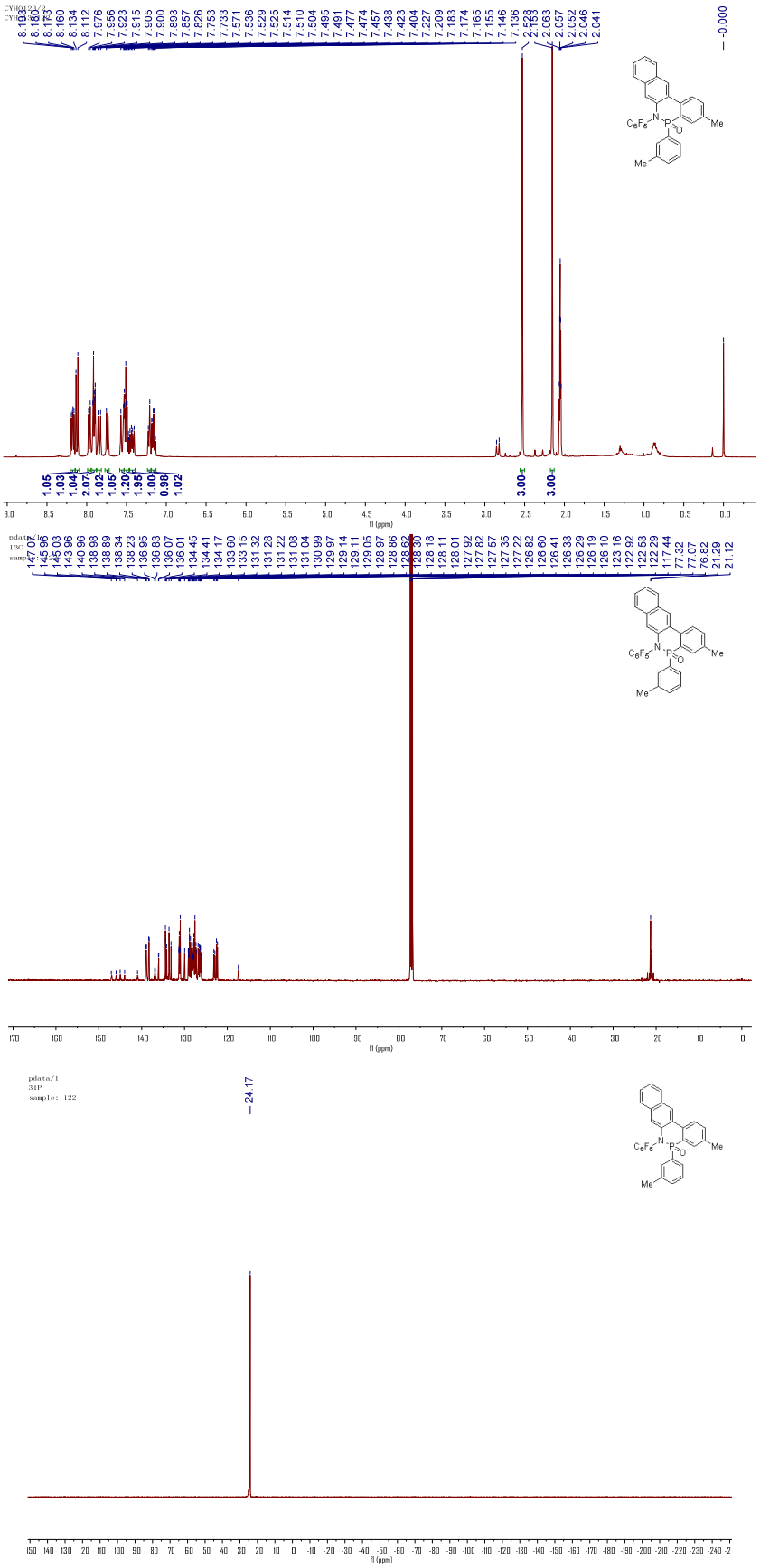


Figure S7. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3g

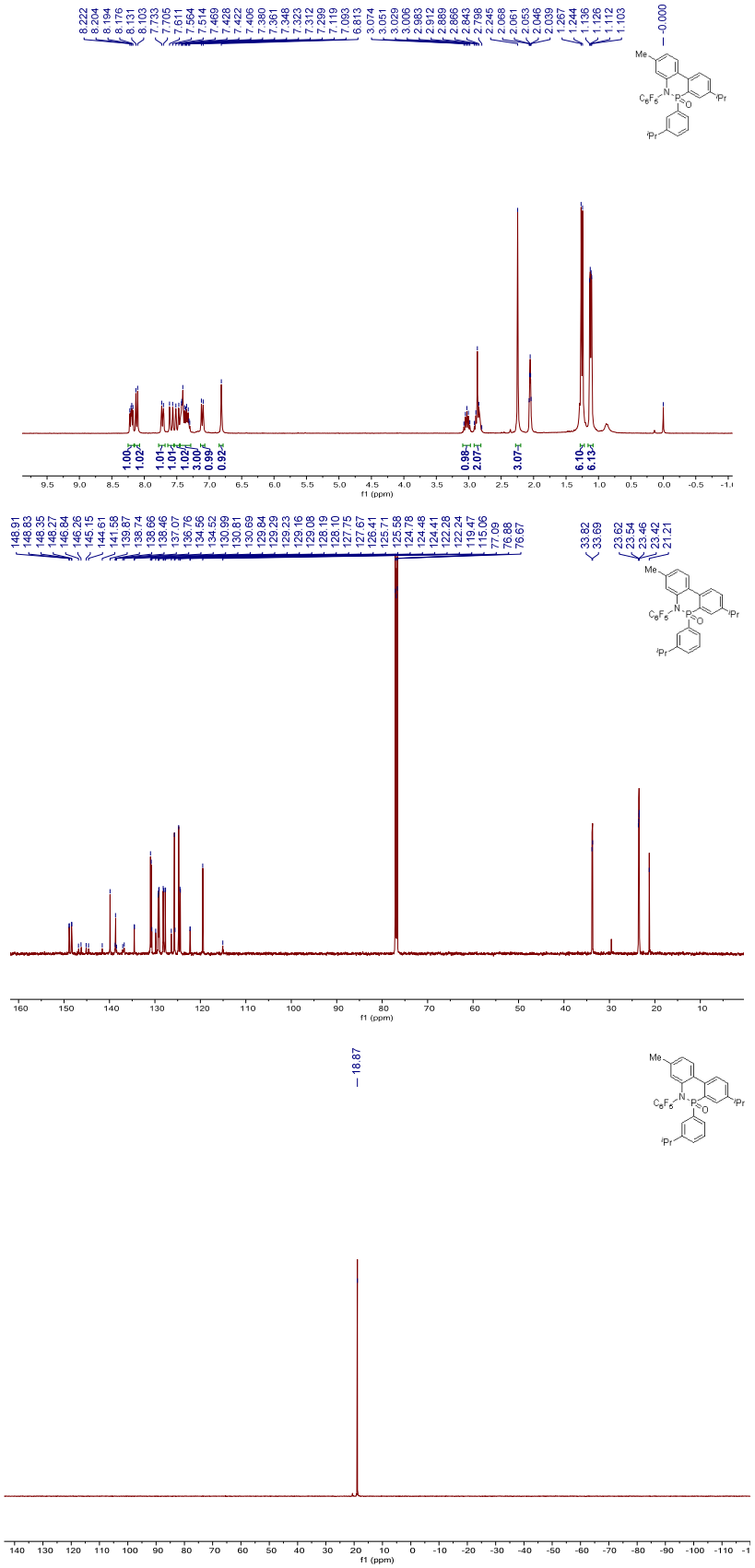


Figure S8. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3h

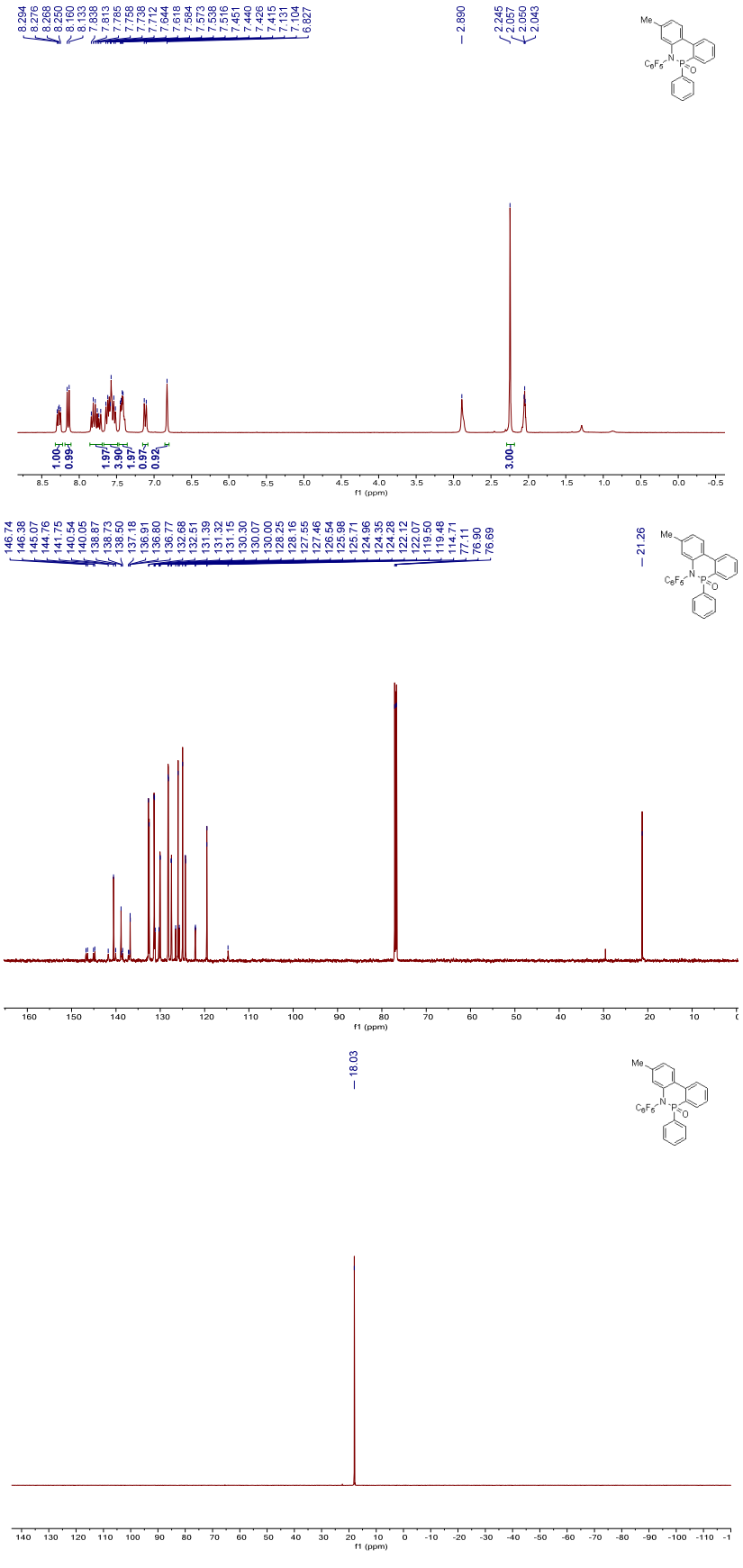


Figure S9. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3i

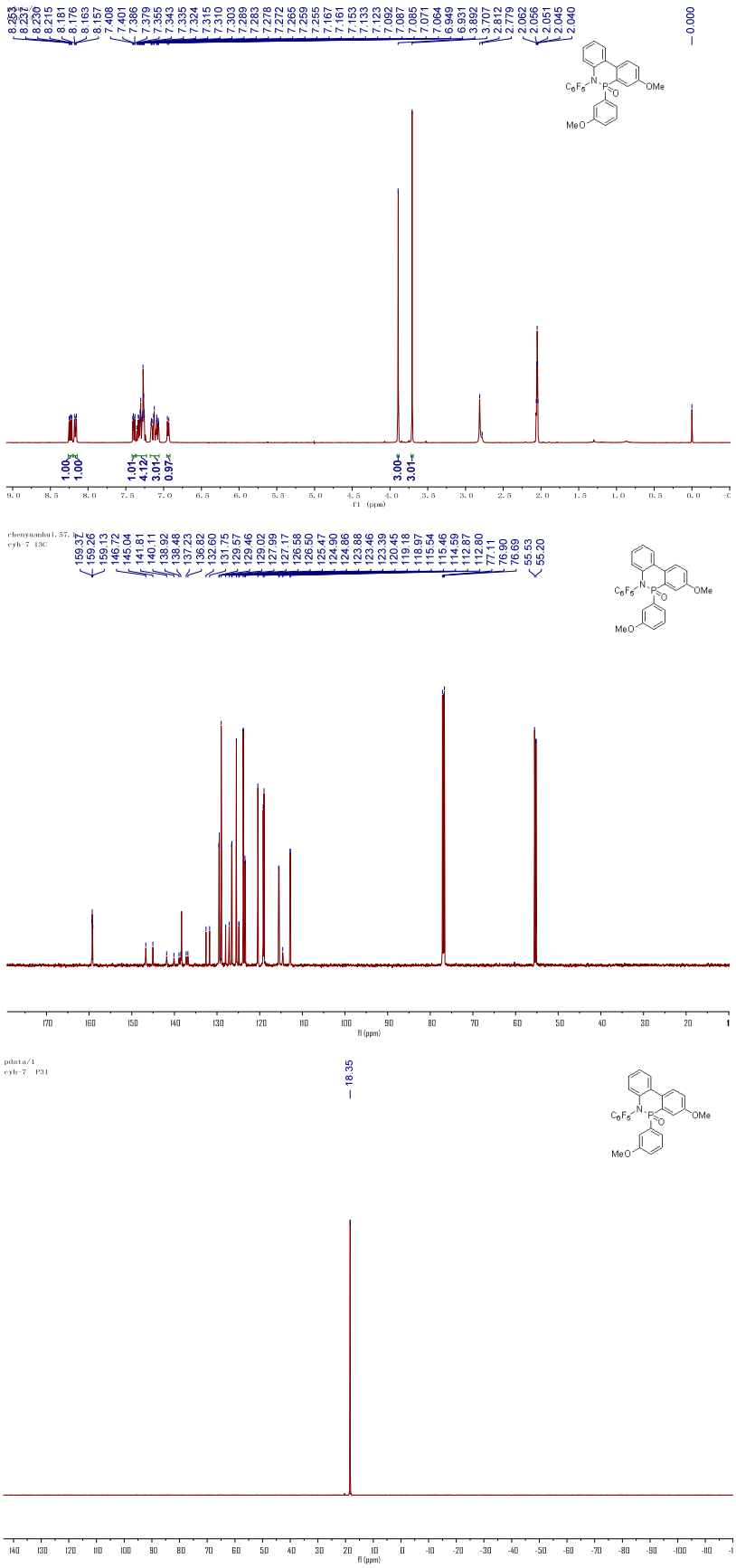


Figure S10. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3j

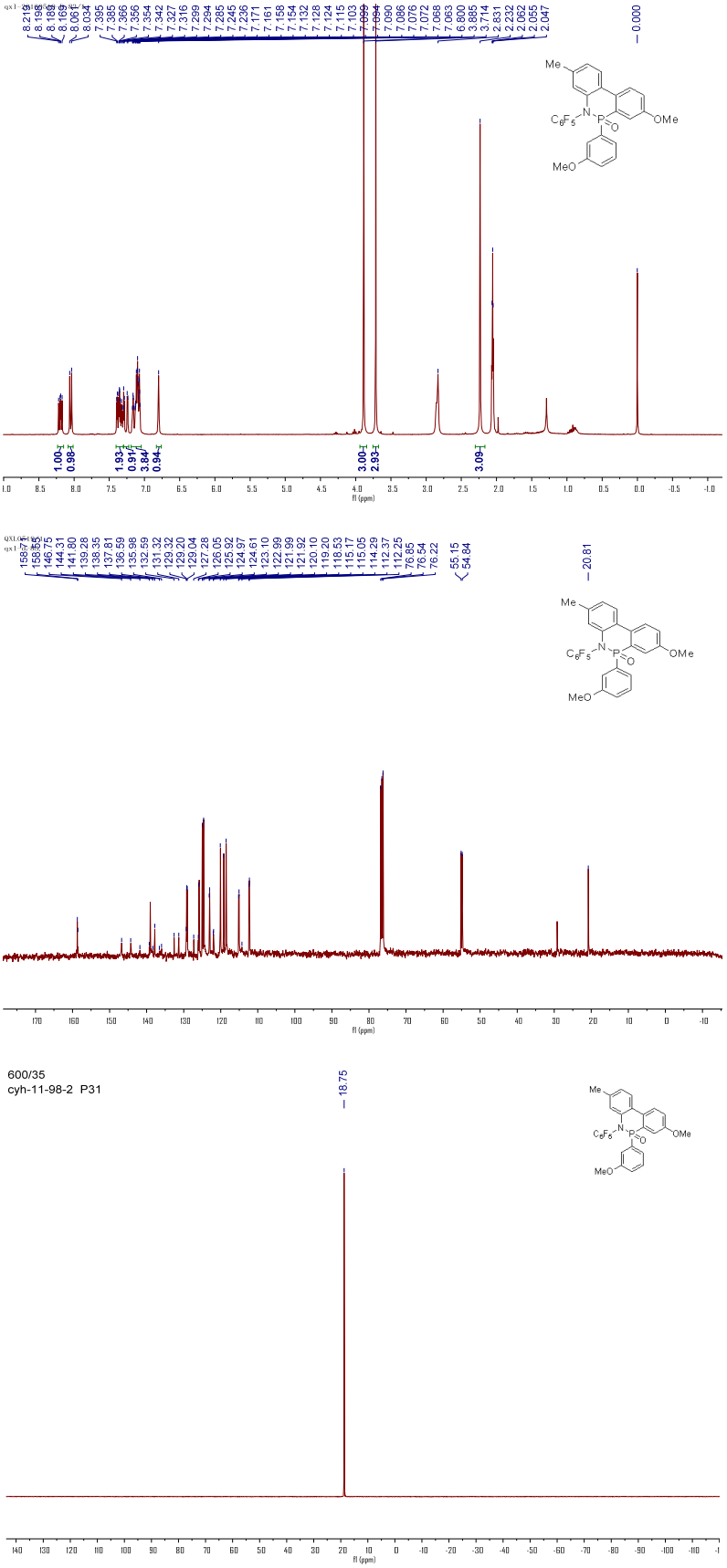


Figure S11. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3k

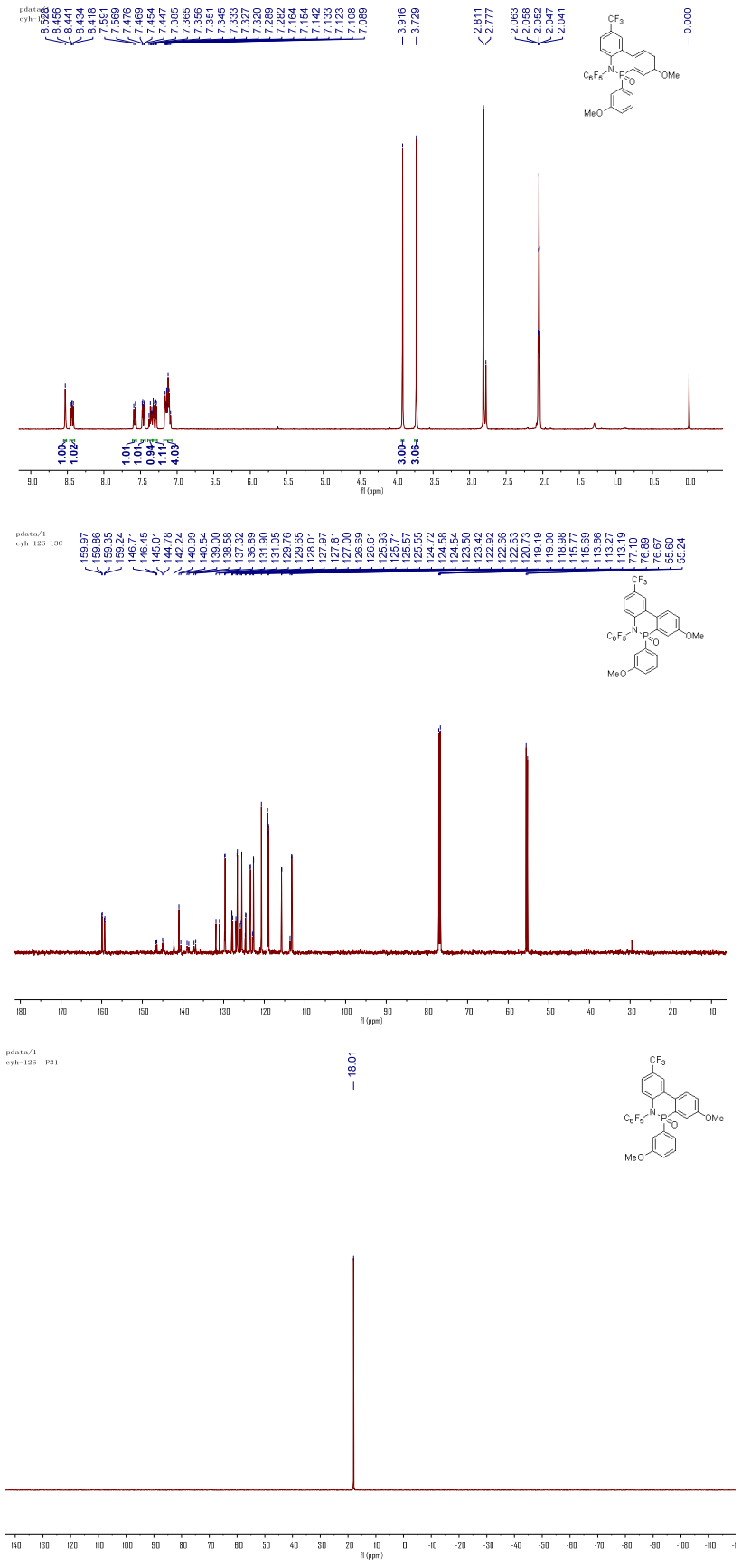


Figure S12. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3l

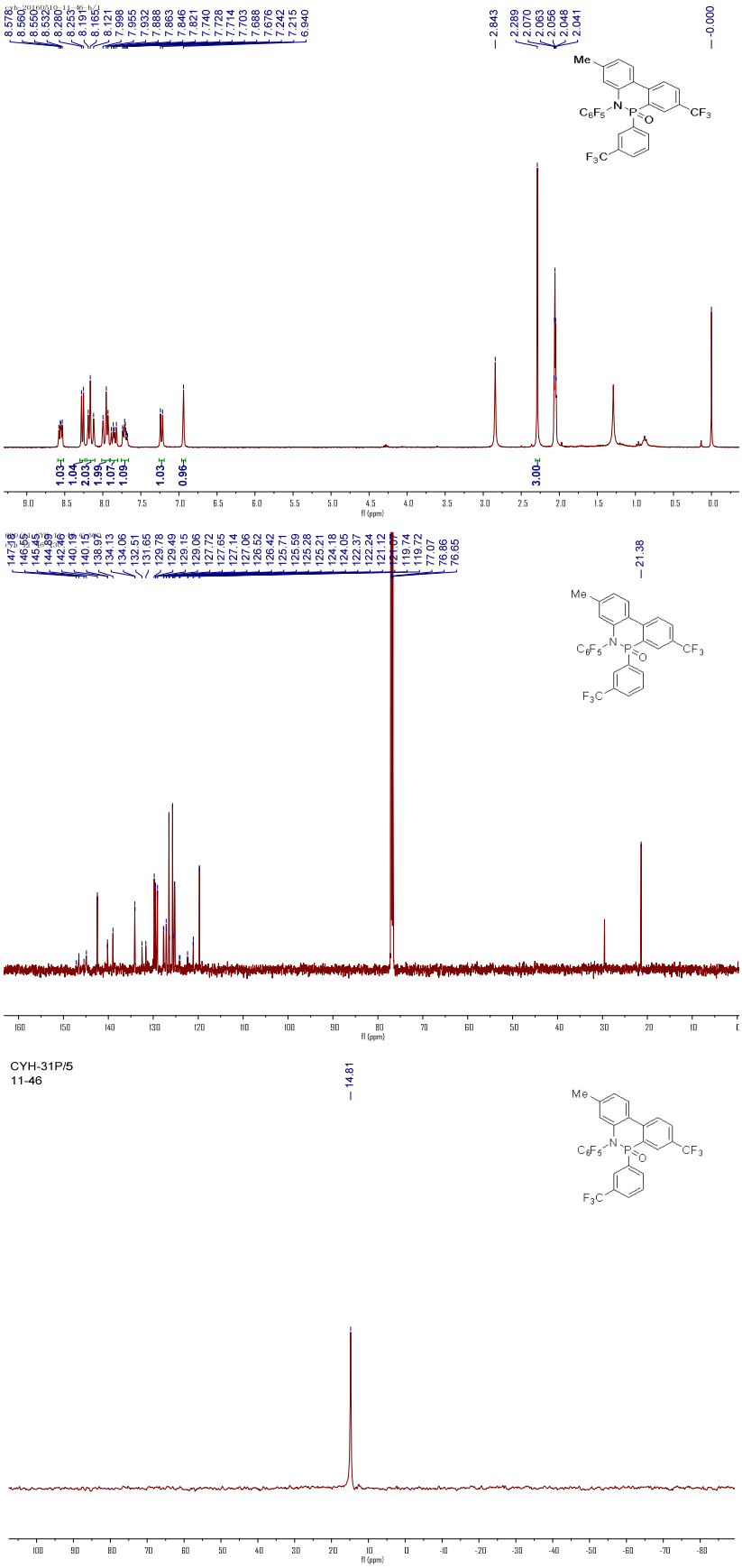


Figure S13. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3m

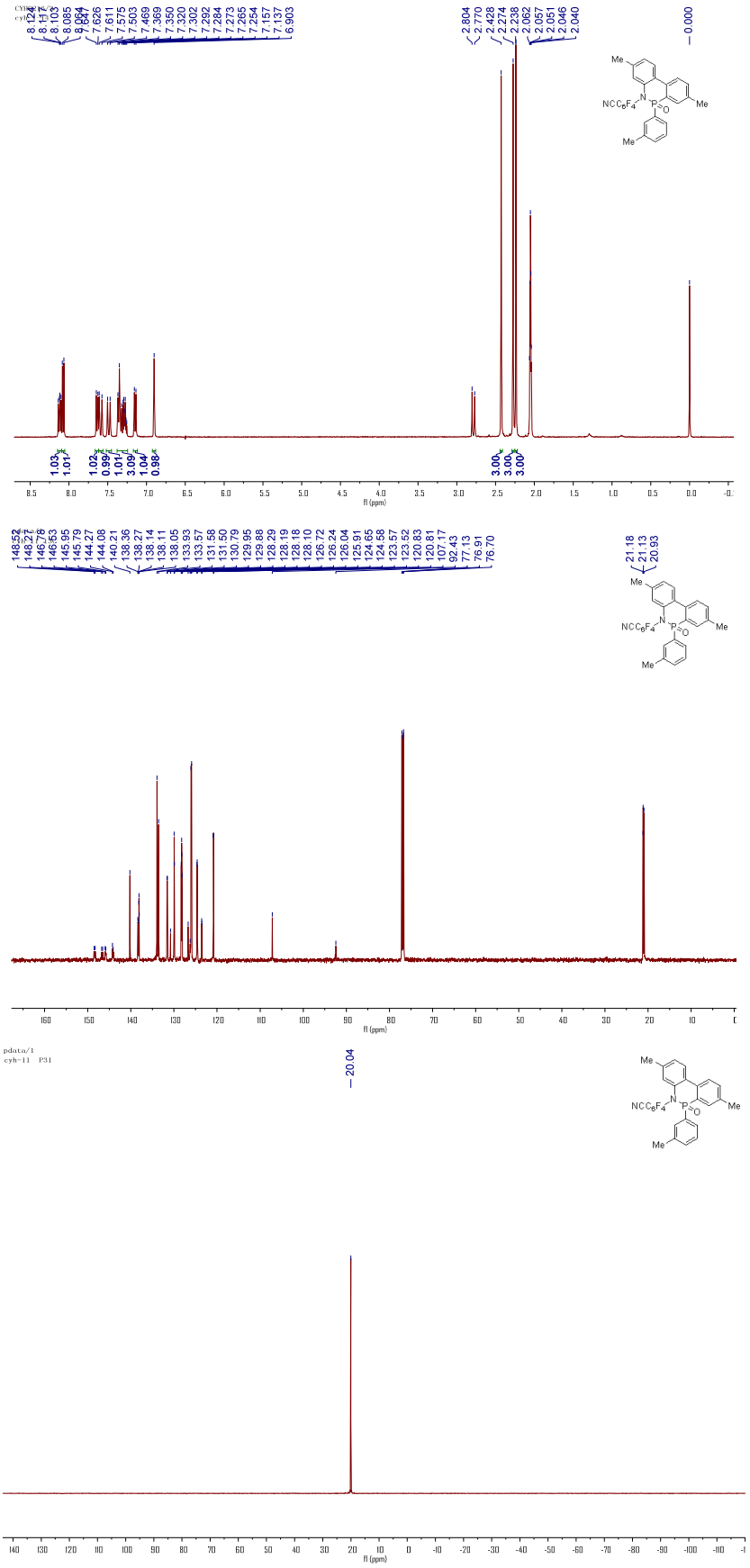


Figure S14. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3n

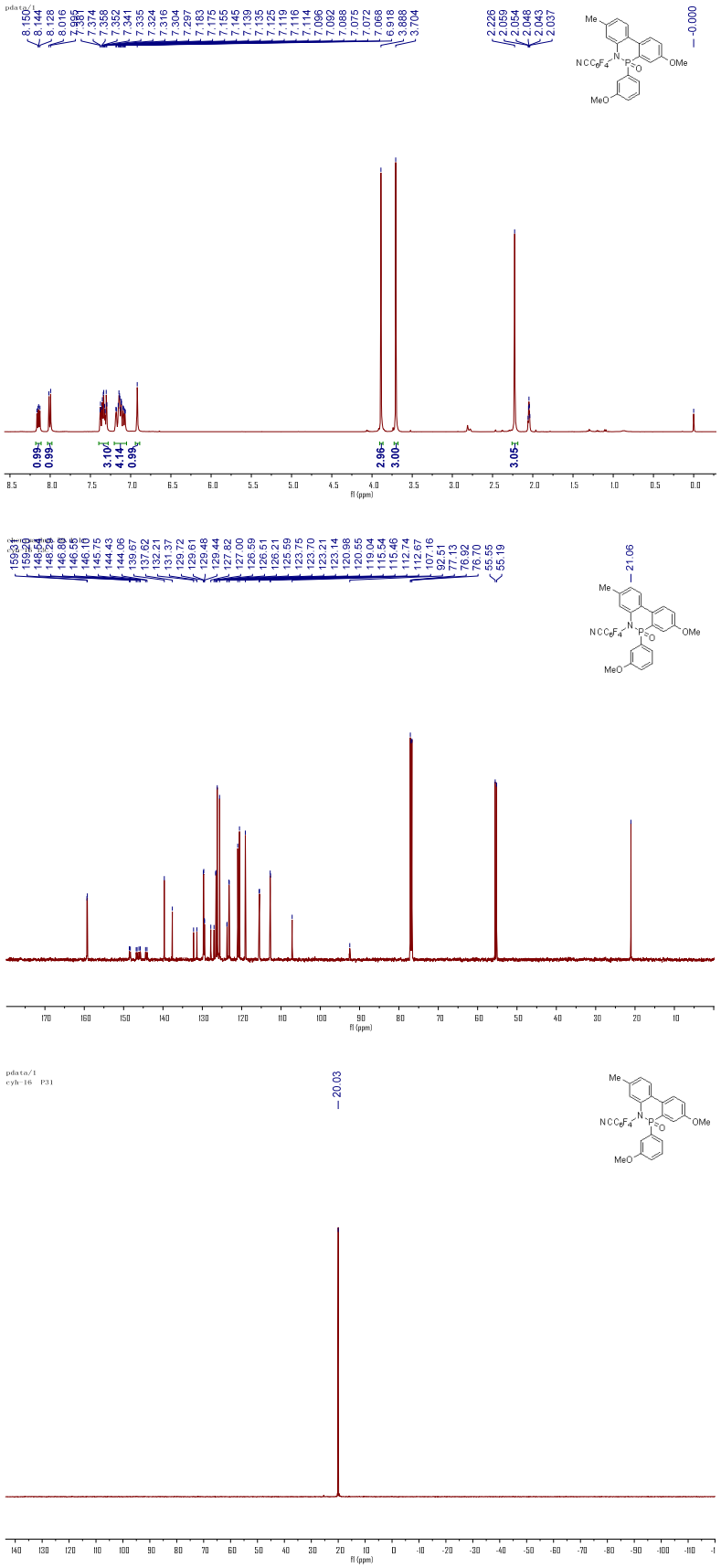


Figure S15. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 3o

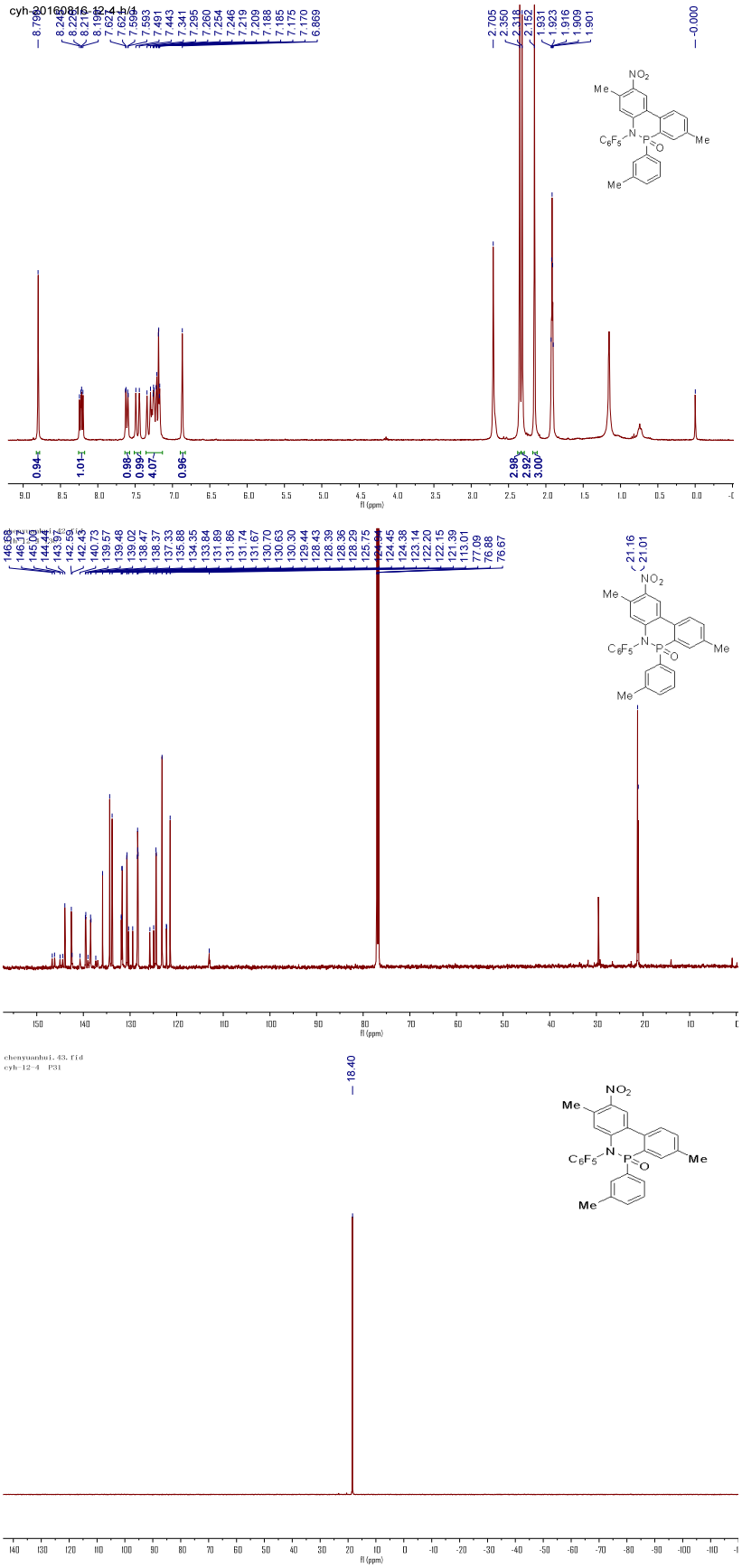


Figure S16. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 4a

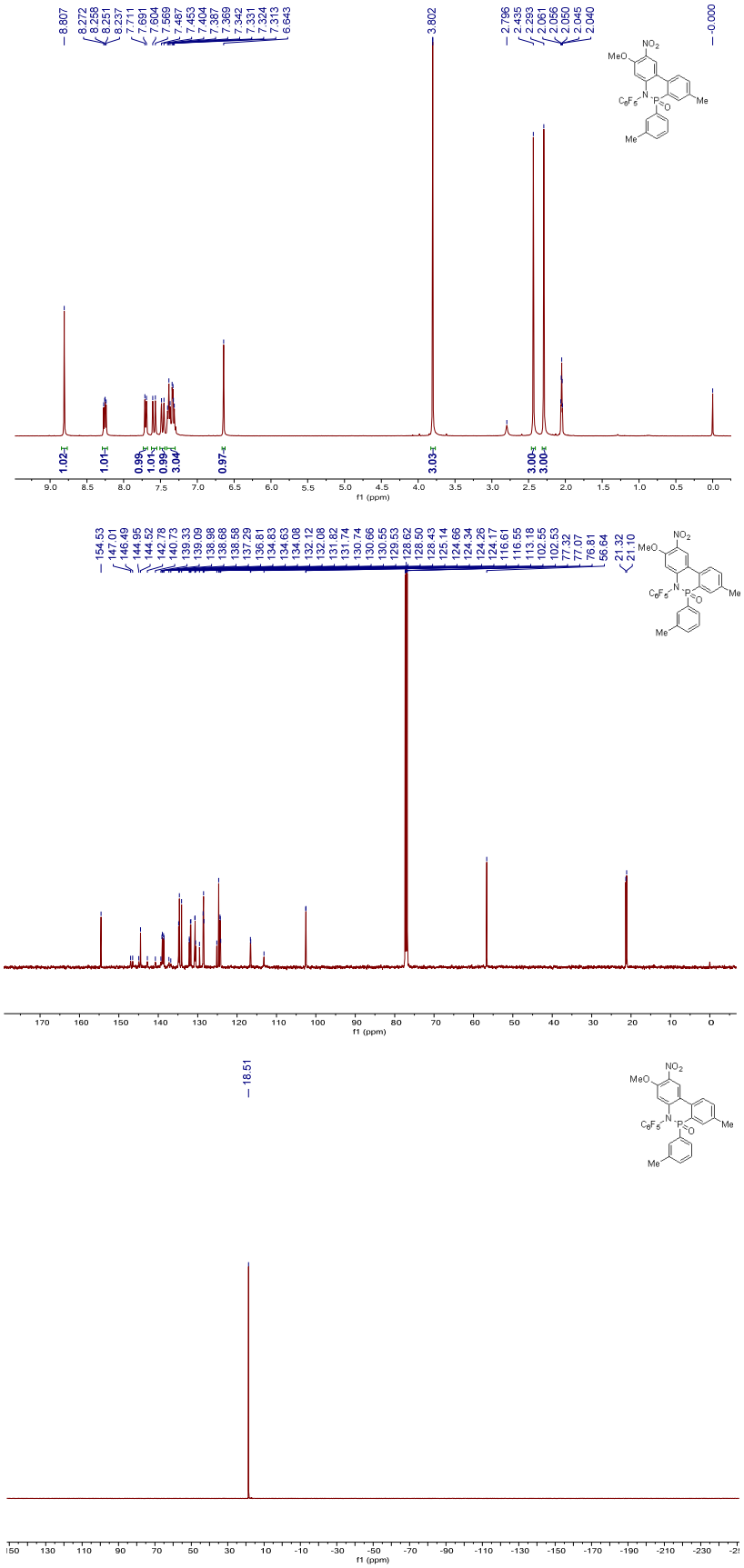


Figure S17. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 4b

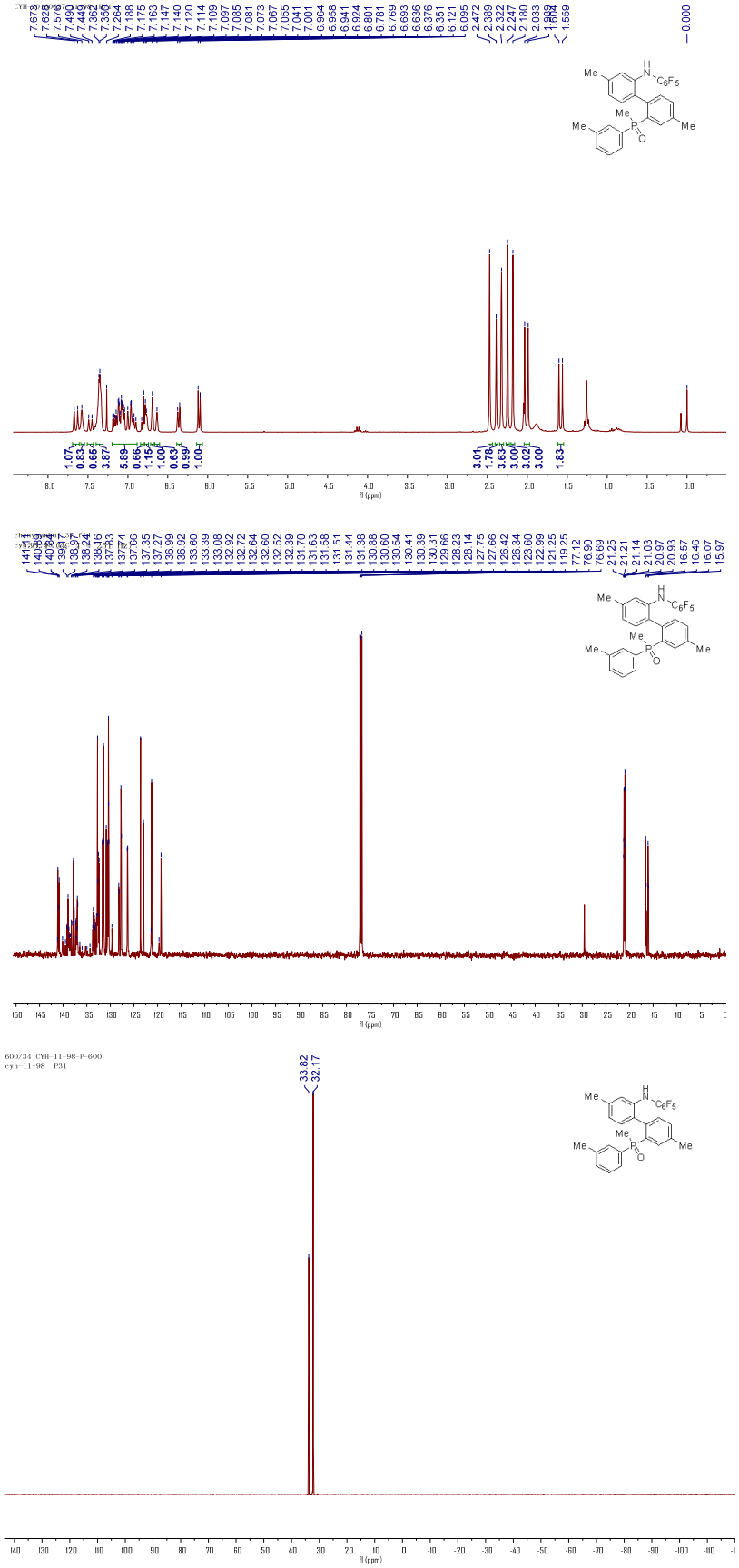


Figure S18. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 5

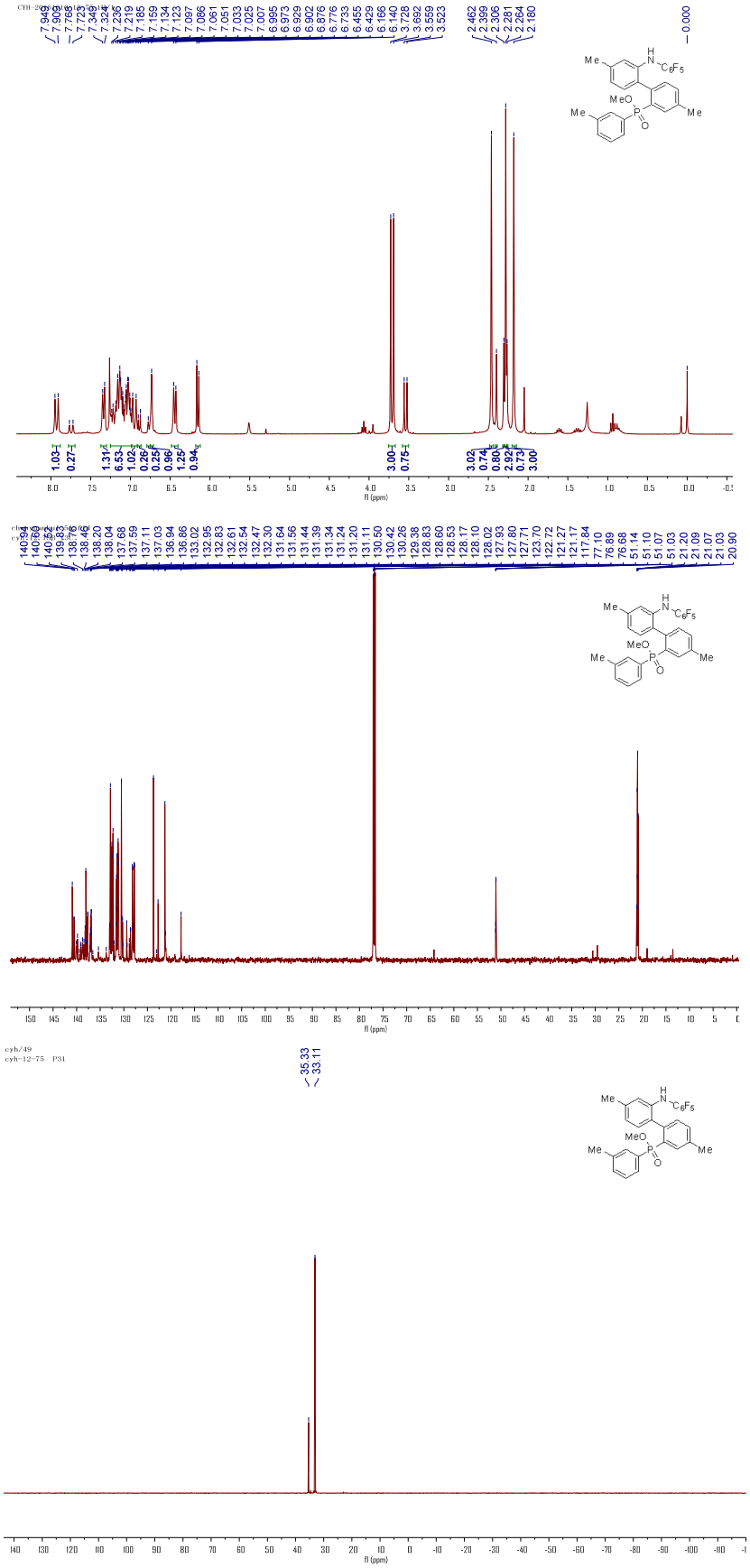


Figure S19. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 6

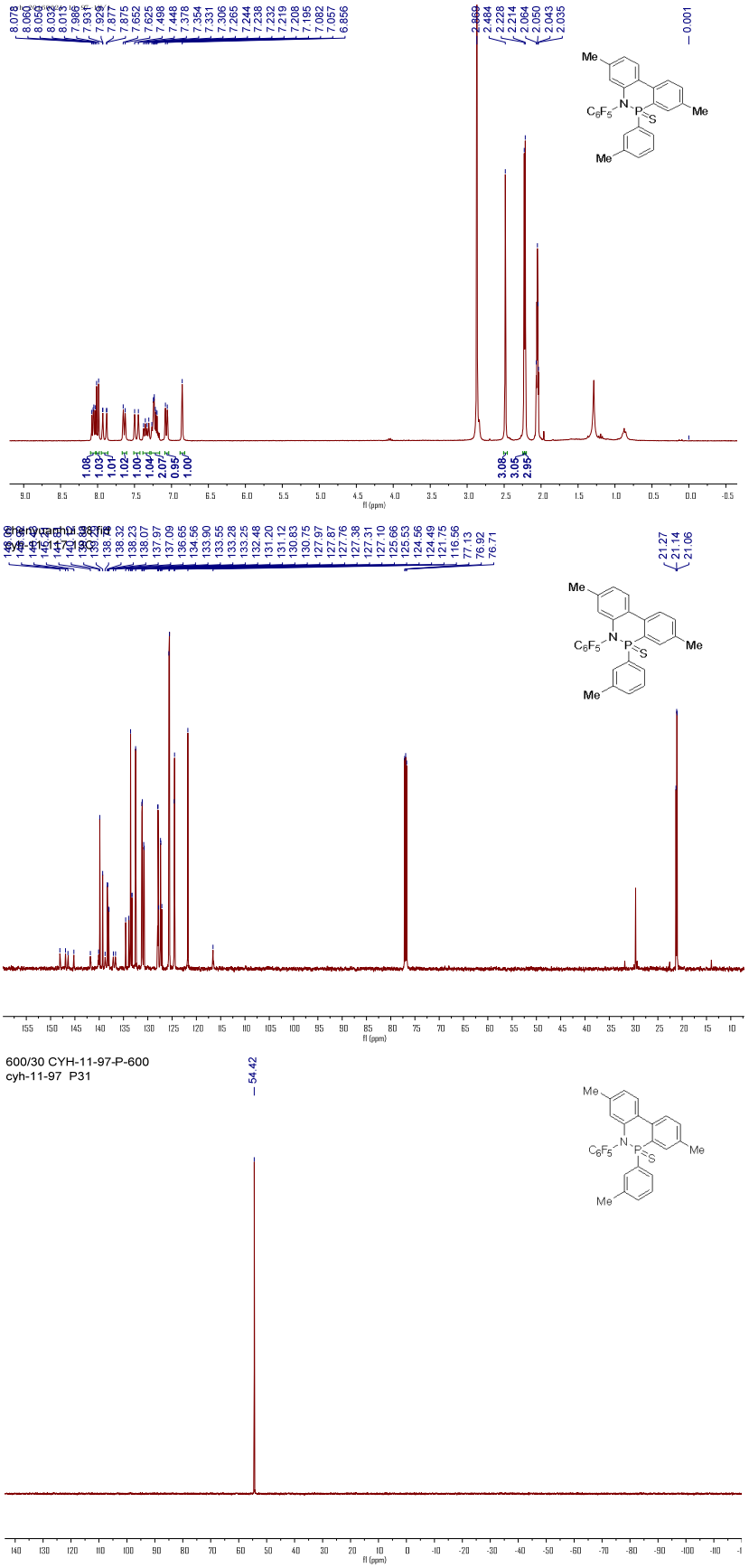


Figure S20. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 7

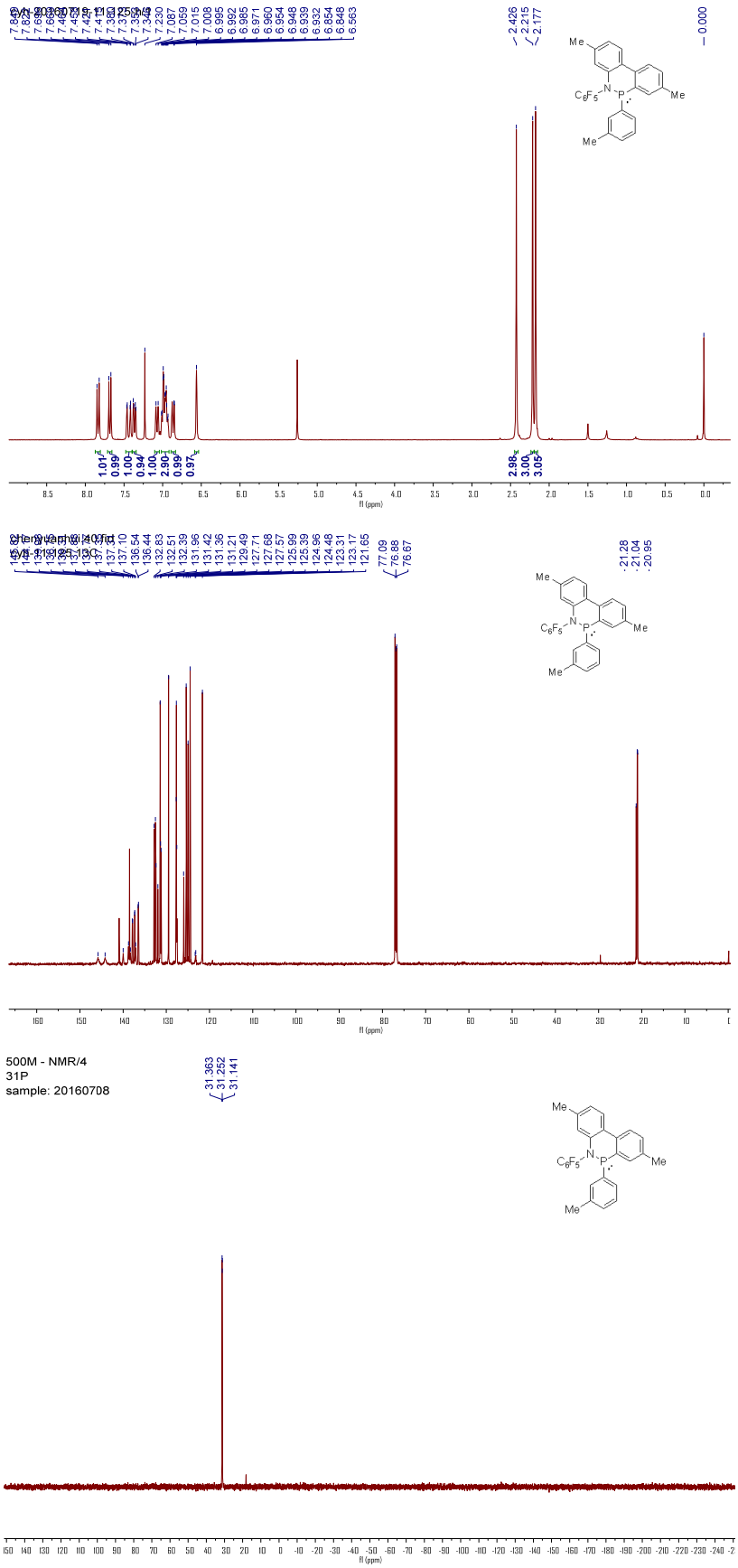


Figure S21. ^{1}H (upper), ^{13}C (middle), and ^{31}P-NMR (bottom) of compound 8

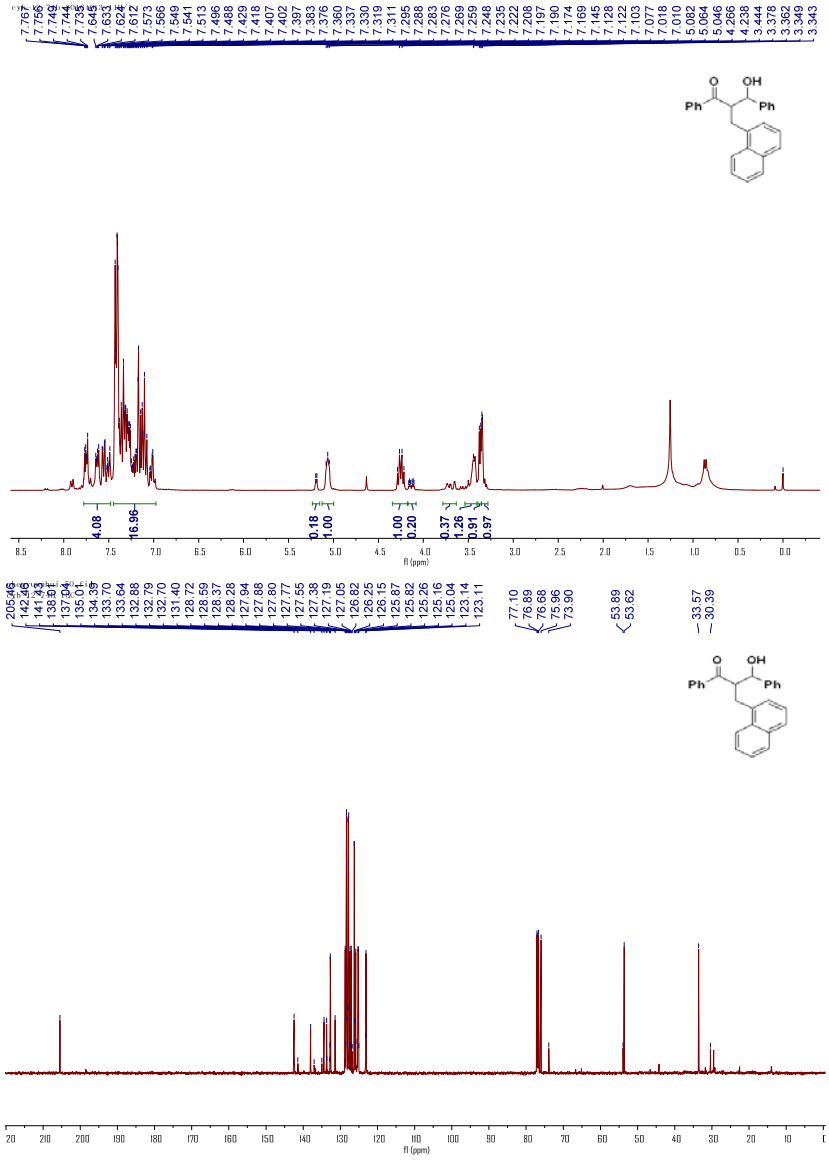
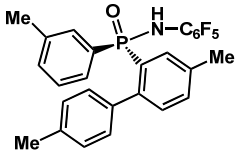
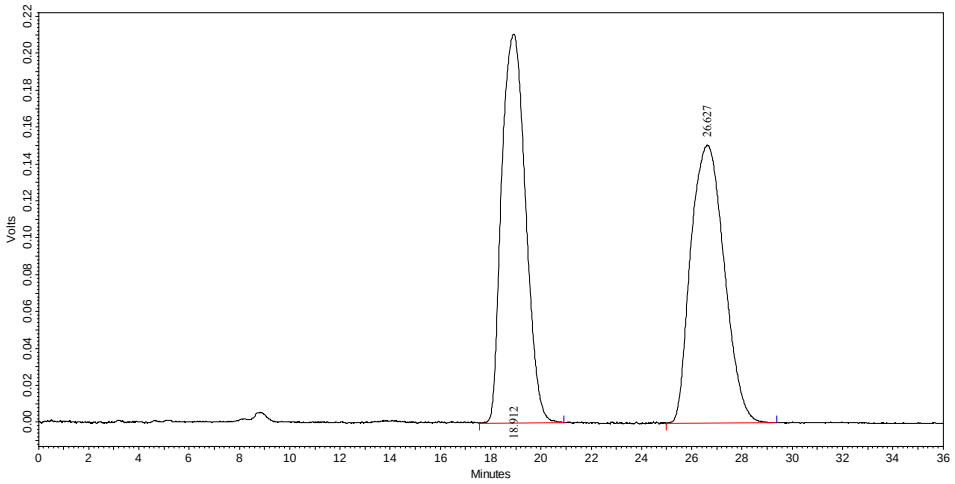


Figure S22. ^{1}H (upper) and ^{13}C (bottom) of compound 11

6. Copies of HPLC charts

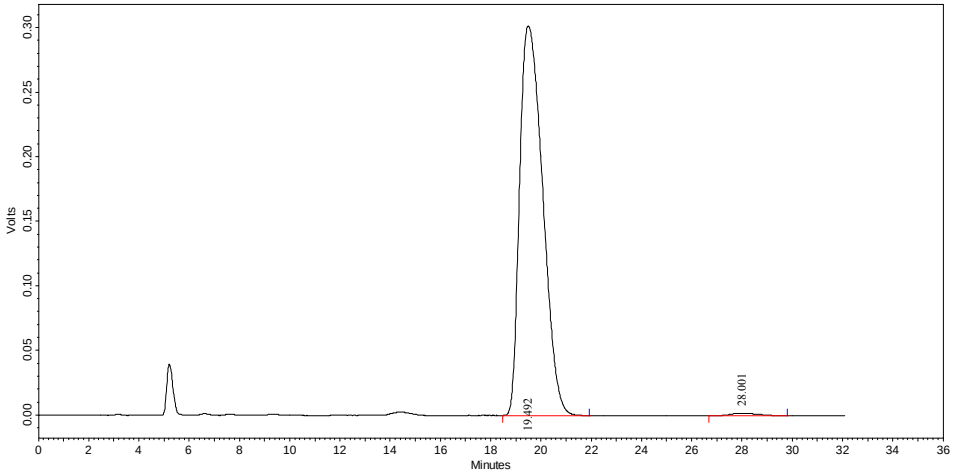
6.1 HPLC chart of 3a (substrate and product)





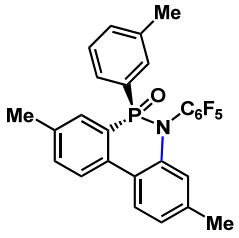
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.912	13895899	49.878	210780	58.300
2	26.627	13964031	50.122	150762	41.700
Total		27859930	100.000	361542	100.000

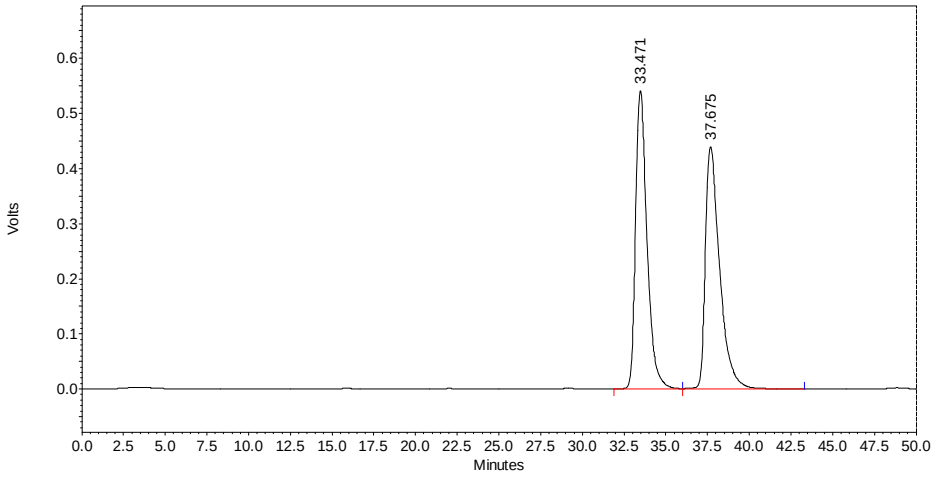


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.492	19209677	99.142	301827	99.359
2	28.001	166167	0.858	1947	0.641
Total		19375844	100.000	303774	100.000

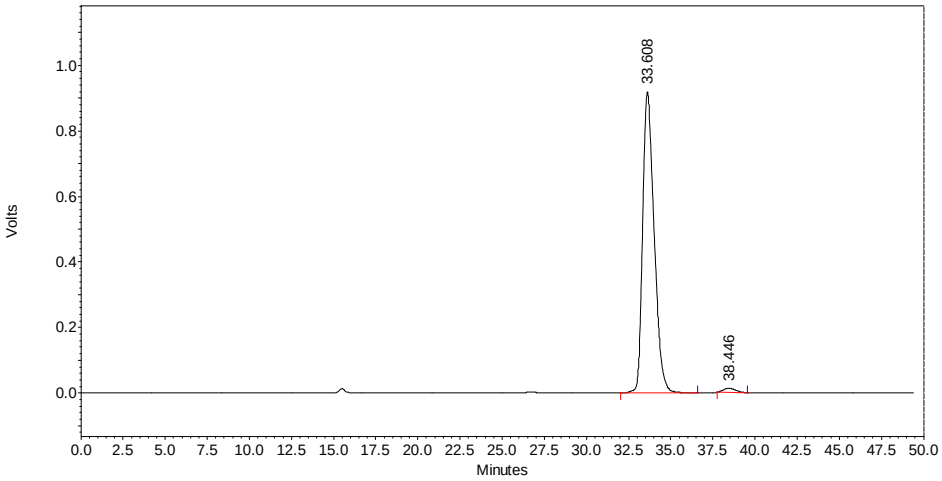


3a



Detector A (254nm)

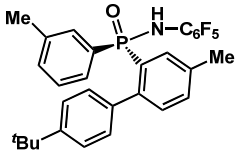
Pk #	Retention Time	Area	Area %	Height	Height %
1	33.471	25824075	49.721	540286	55.184
2	37.675	26113614	50.279	438769	44.816
Total		51937689	100.000	979055	100.000

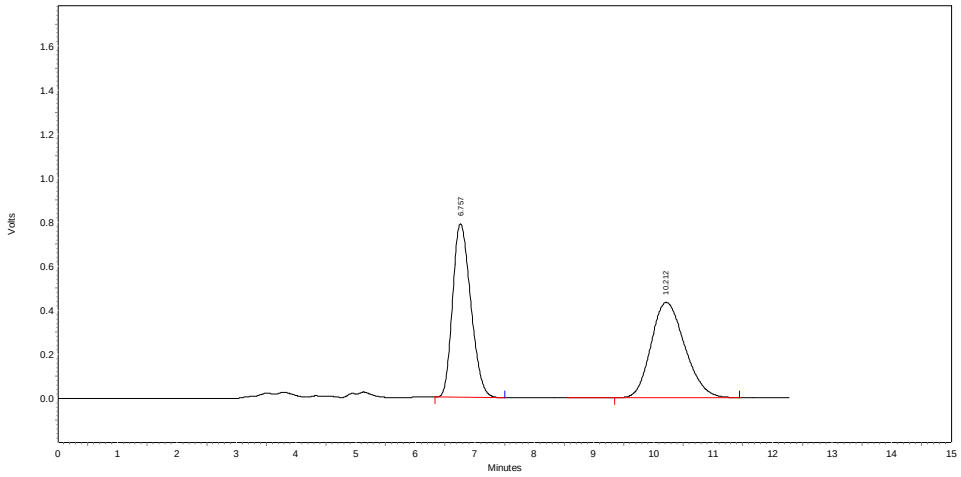


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	33.608	43516835	98.511	916567	98.587
2	38.446	657688	1.489	13139	1.413
Total		44174522	100.000	929706	100.000

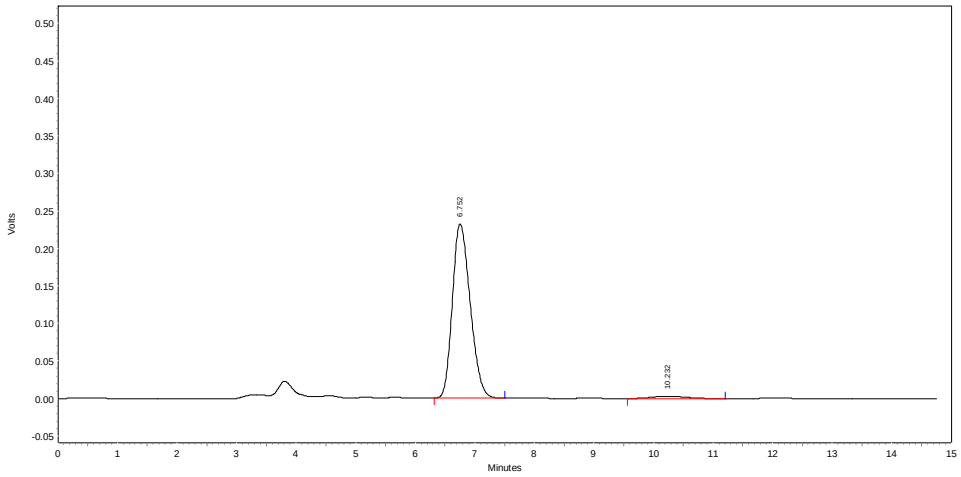
6.2 HPLC chart of 3b (substrate and product)





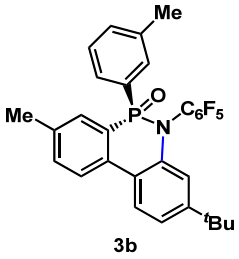
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	6.757	16735453	49.571	788562	64.552
2	10.212	17025030	50.429	433027	35.448
Total		33760482	100.000	1221589	100.000

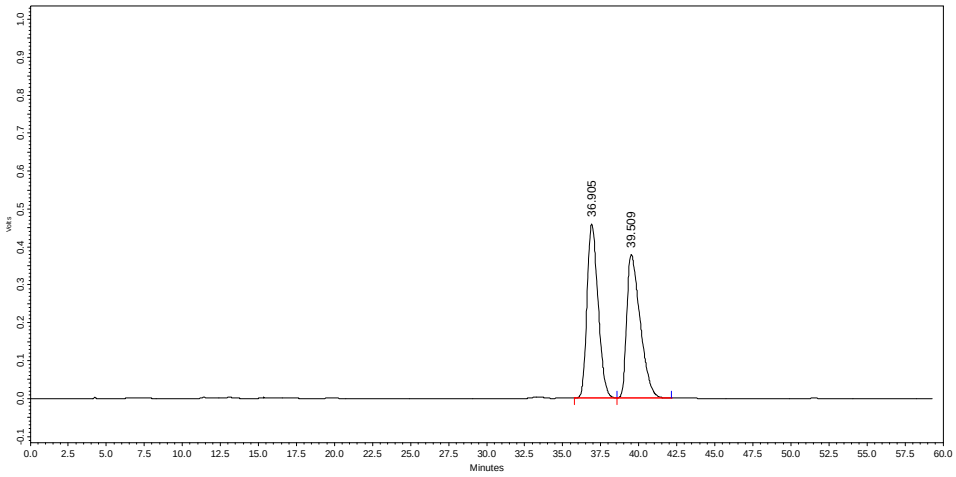


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	6.752	4823845	97.575	231633	98.658
2	10.232	119910	2.425	3152	1.342
Total		4943755	100.000	234785	100.000

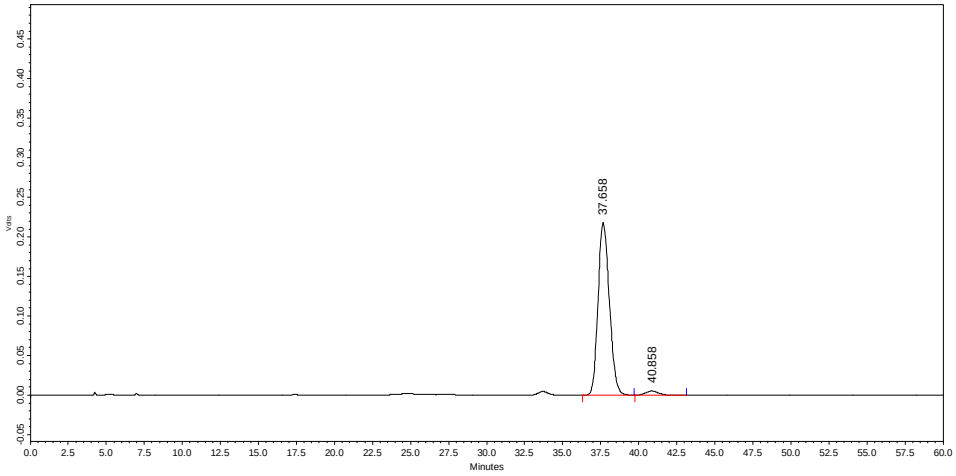


3b



Detector A (254nm)

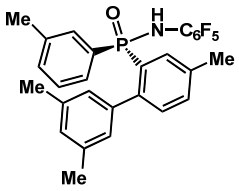
Pk #	Retention Time	Area	Area %	Height	Height %
1	36.905	23254850	50.002	459786	54.884
2	39.509	23252901	49.998	377948	45.116
Total		46507751	100.000	837735	100.000

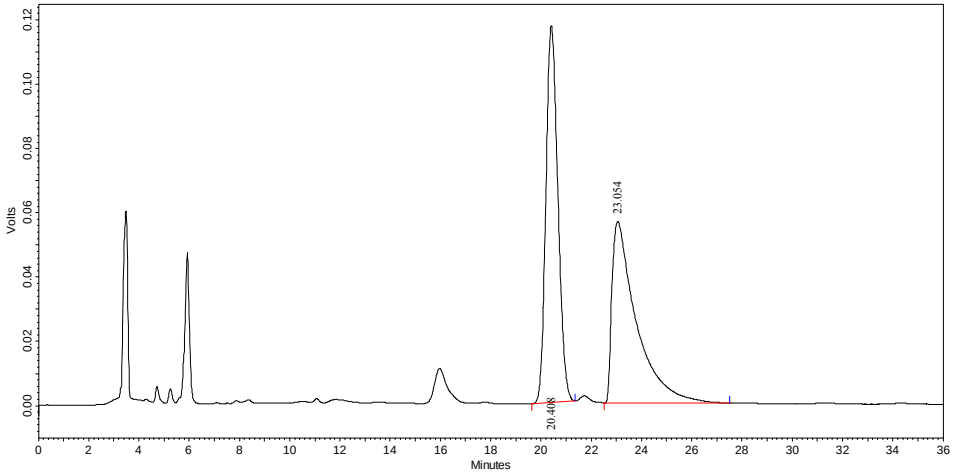


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	37.658	11302211	97.223	218133	97.611
2	40.858	322787	2.777	5339	2.389
Total		11624999	100.000	223473	100.000

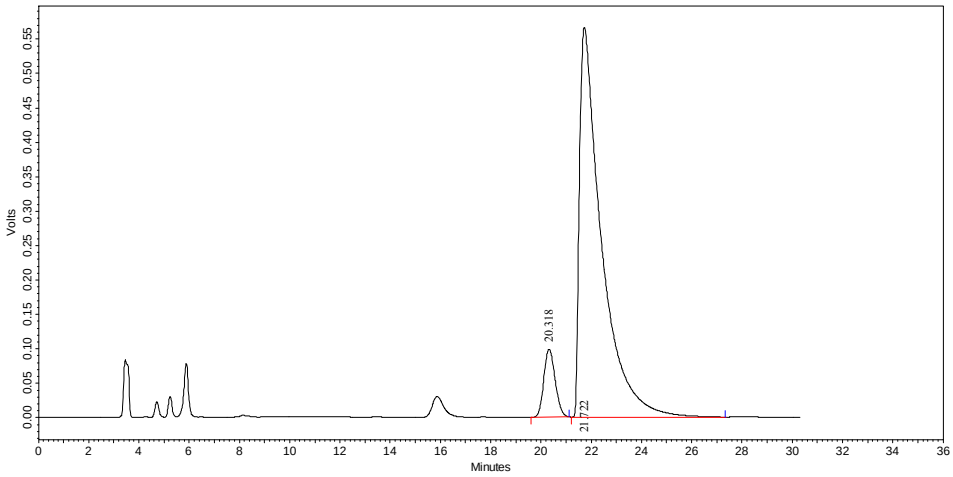
6.3 HPLC chart of 3c (substrate and product)





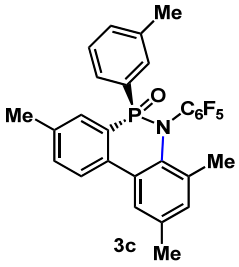
Detector A (254nm)

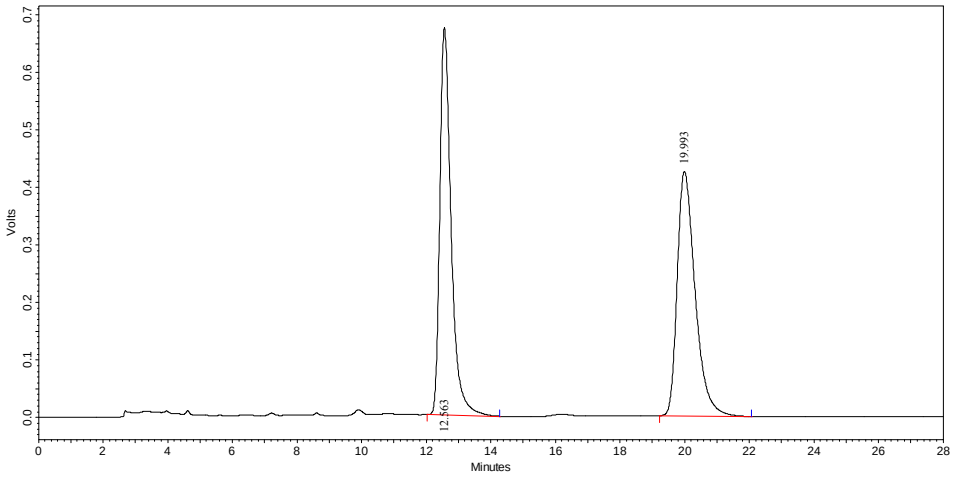
Pk #	Retention Time	Area	Area %	Height	Height %
1	20.408	3884720	50.519	117260	67.477
2	23.054	3804826	49.481	56518	32.523
Total		7689546	100.000	173777	100.000



Detector A (254nm)

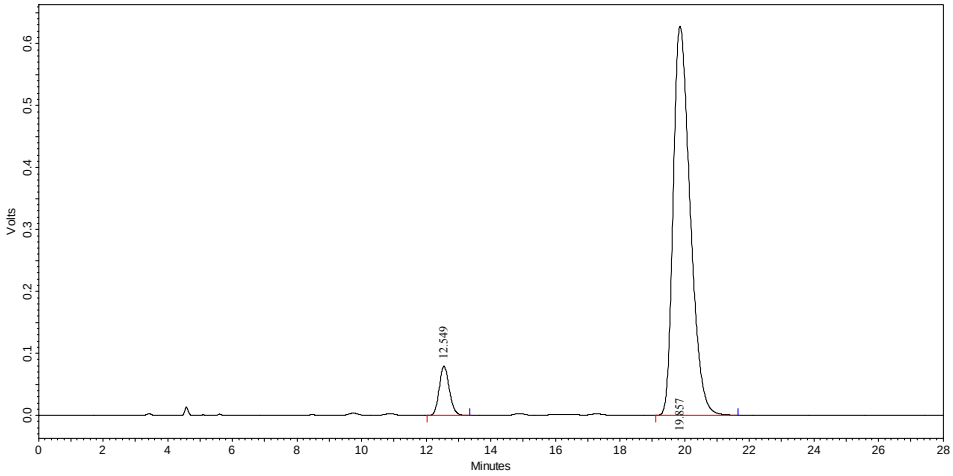
Pk #	Retention Time	Area	Area %	Height	Height %
1	20.318	3091906	8.281	98717	14.848
2	21.722	34245338	91.719	566139	85.152
Total		7689546	100.000	173777	100.000





Detector A (254nm)

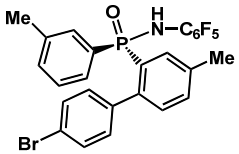
Pk #	Retention Time	Area	Area %	Height	Height %
1	12.563	16348210	50.009	674087	61.337
2	19.993	16342067	49.991	424904	38.663
Total		32690277	100.000	1098991	100.000

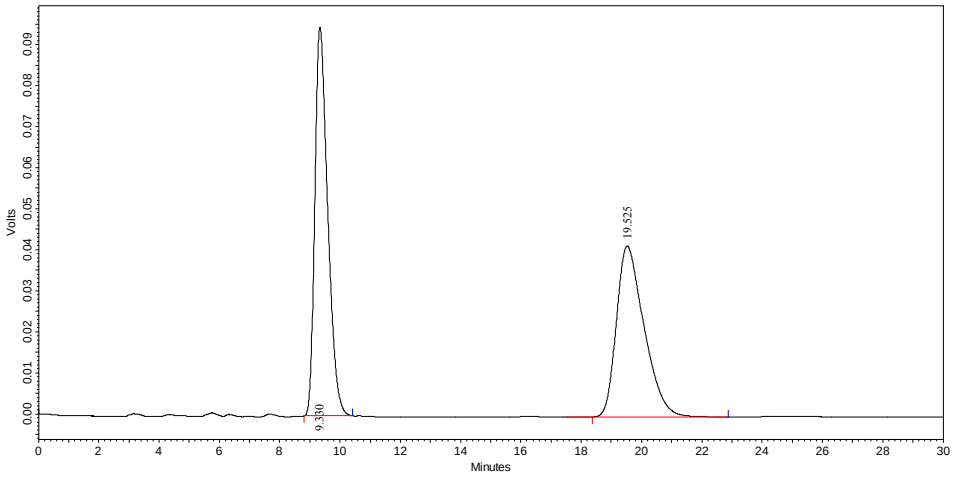


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.549	1731045	7.030	79389	11.211
2	19.857	22891388	92.970	628735	88.789
Total		24622433	100.000	708124	100.000

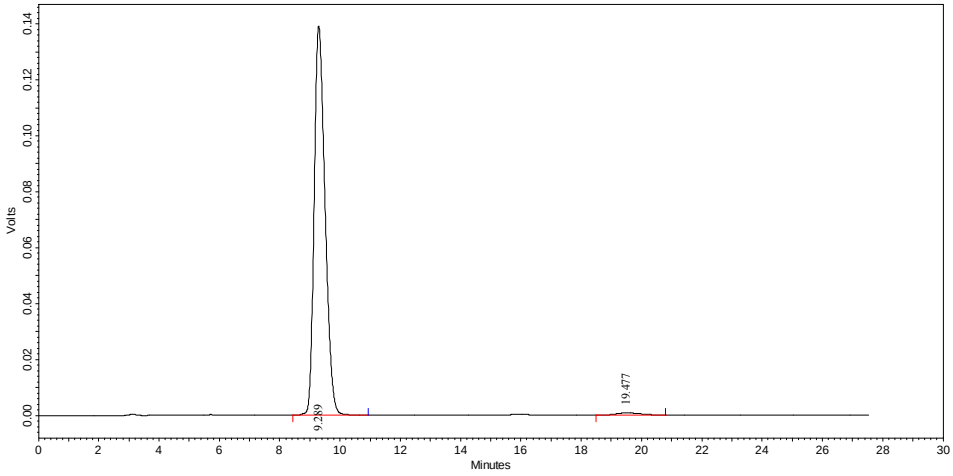
6.4 HPLC chart of 3d (substrate and product)





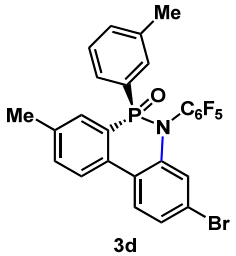
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.330	2816448	51.286	94823	69.414
2	19.525	2675153	48.714	41782	30.586
Total		5491601	100.000	136605	100.000

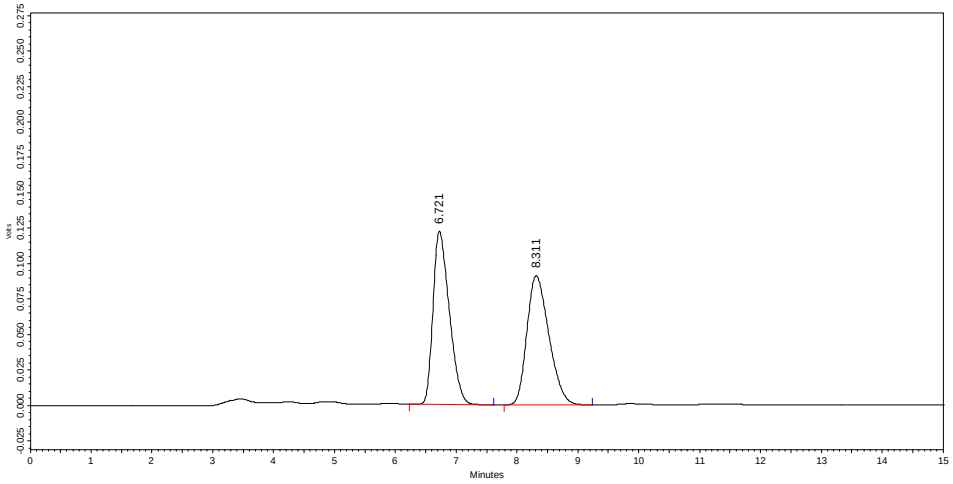


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.289	3495925	98.781	139203	99.434
2	19.477	43131	1.219	792	0.566
Total		3539056	100.000	139995	100.000

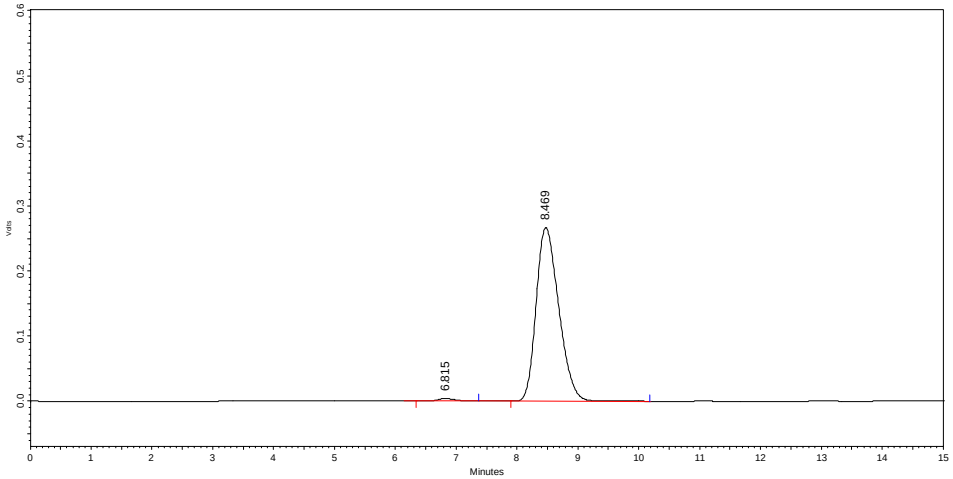


3d



Detector A (254nm)

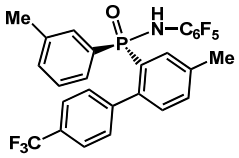
Pk #	Retention Time	Area	Area %	Height	Height %
1	6.721	2275013	49.826	122426	57.302
2	8.311	2290903	50.174	91224	42.698
Total		4565916	100.000	213651	100.000

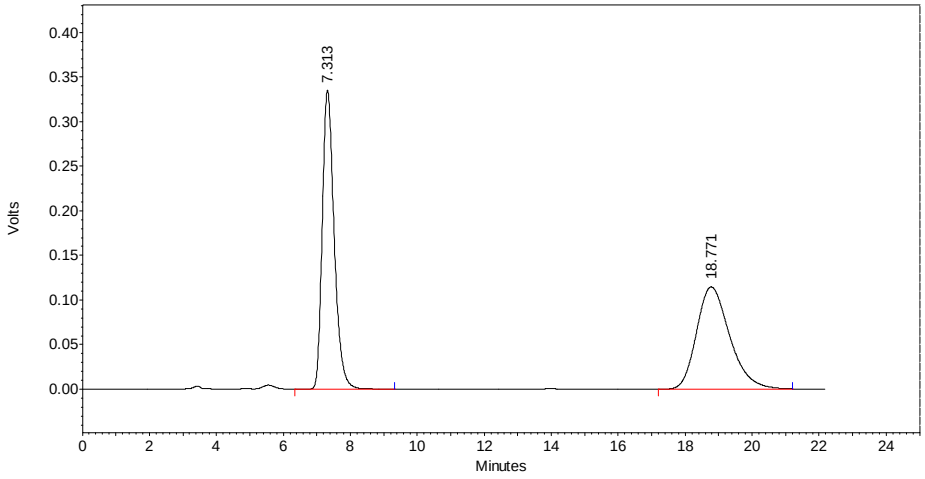


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	6.815	78633	1.131	3881	1.435
2	8.469	6870942	98.869	266626	98.565
Total		6949575	100.000	270507	100.000

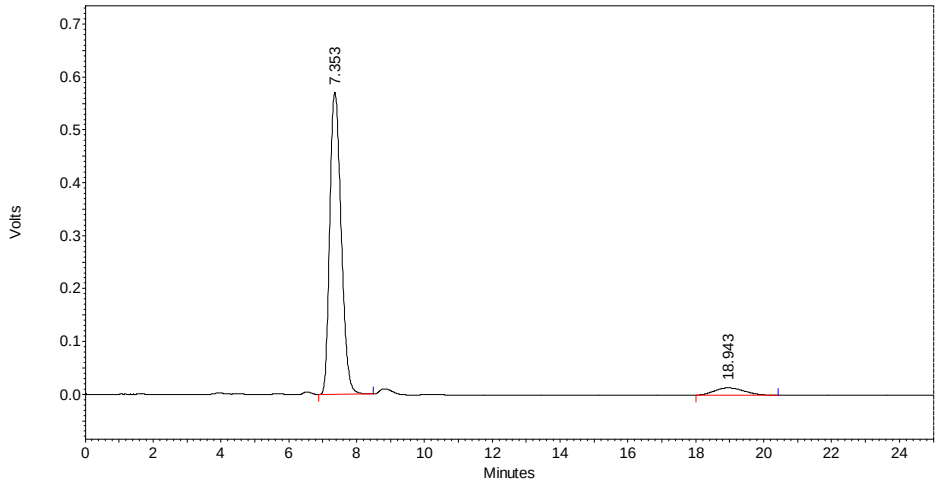
6.5 HPLC chart of 3e (substrate and product)





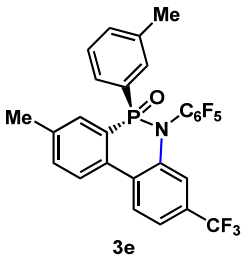
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	7.313	8270120	51.058	334944	74.487
2	18.771	7927309	48.942	114725	25.513
Total		16197429	100.000	449669	100.000

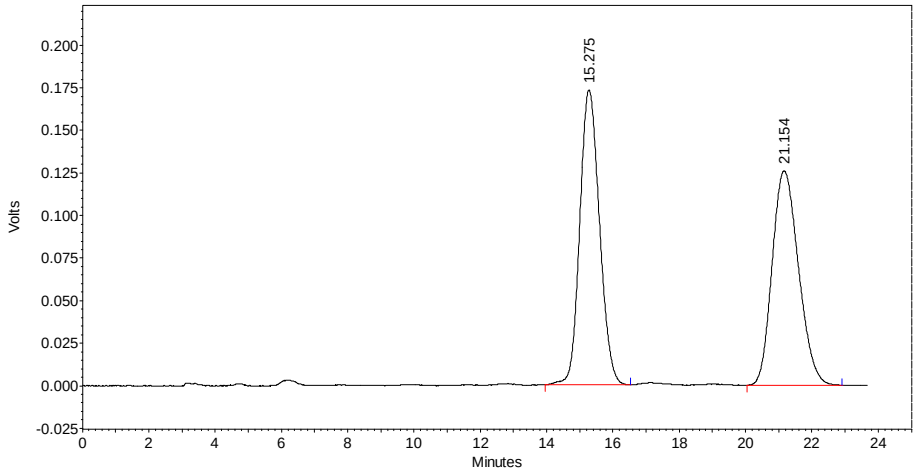


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	7.353	13343025	93.908	571700	97.611
2	18.943	865525	6.092	13994	2.389
Total		14208550	100.000	5856493	100.000

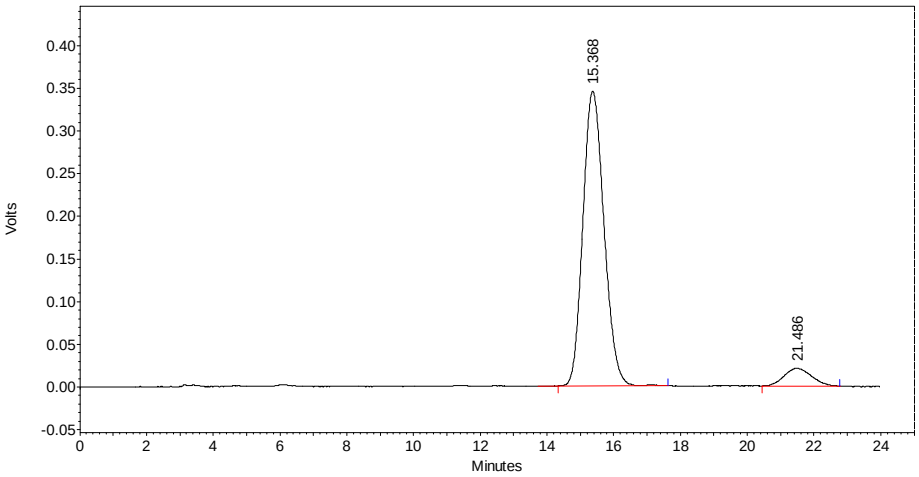


3e



Detector A (254nm)

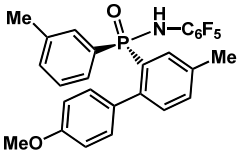
Pk #	Retention Time	Area	Area %	Height	Height %
1	15.275	7156838	50.719	173282	57.915
2	21.154	6953869	49.281	125919	42.085
Total		14110707	100.000	299201	100.000

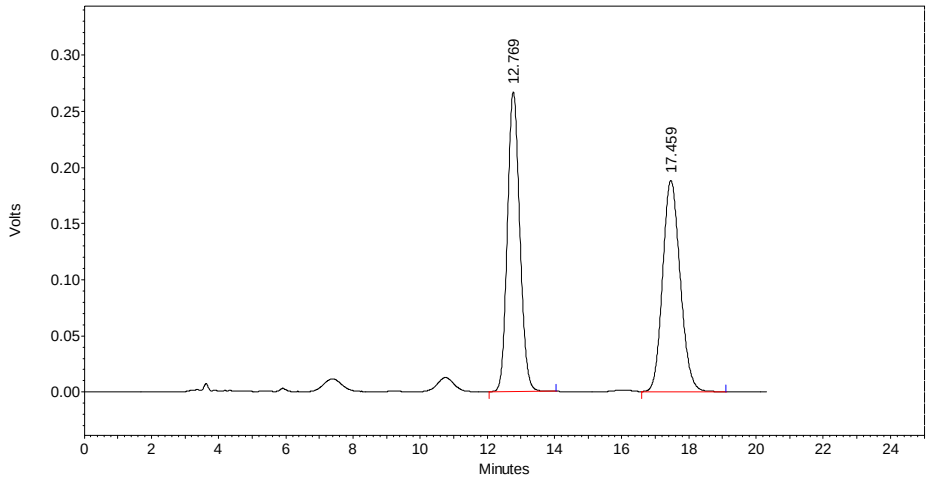


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	15.368	15175892	92.671	345284	94.348
2	21.486	1200165	7.329	20686	5.652
Total		16376057	100.000	365970	100.000

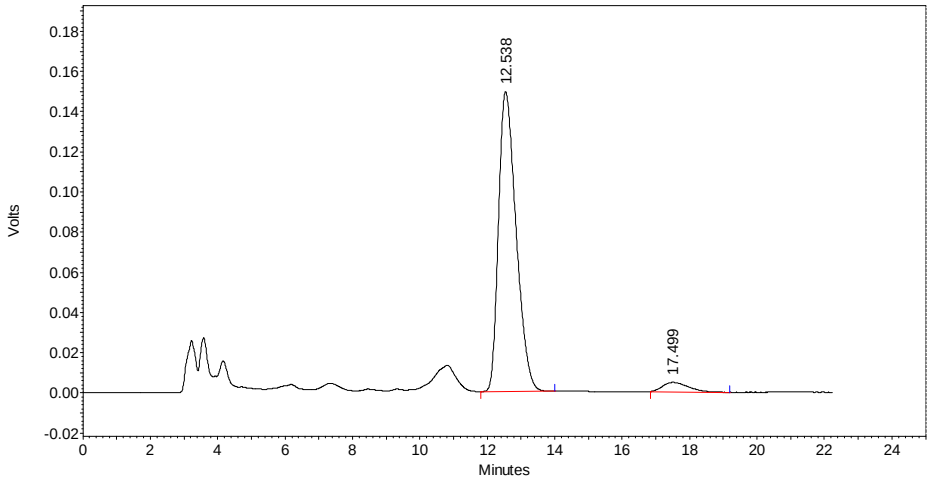
6.6 HPLC chart of 3f (substrate and product)





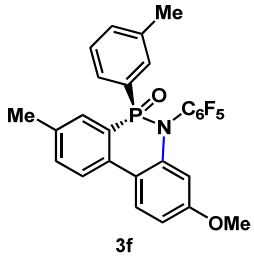
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.769	6830020	50.057	265812	58.651
2	17.459	6814347	49.943	187395	41.349
Total		13644367	100.000	453207	100.000

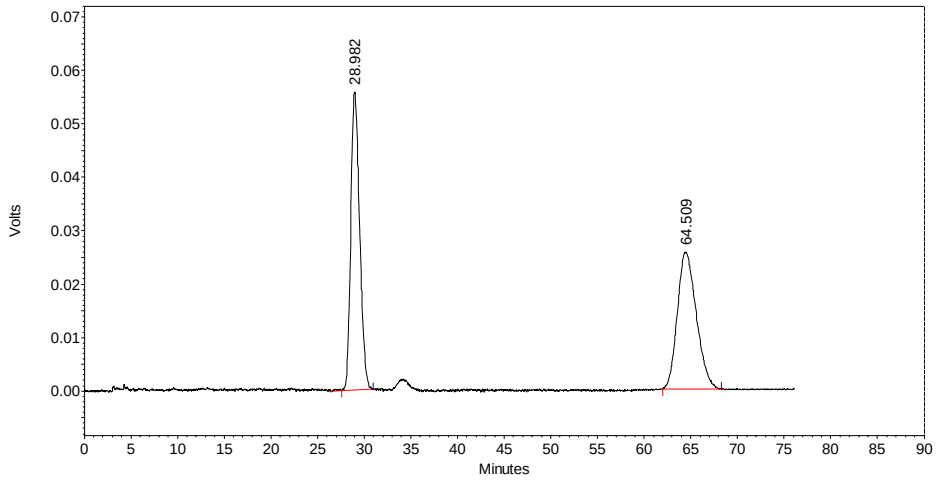


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.538	5415962	95.622	149043	96.925
2	17.499	247963	4.378	4729	3.075
Total		5663925	100.000	153772	100.000

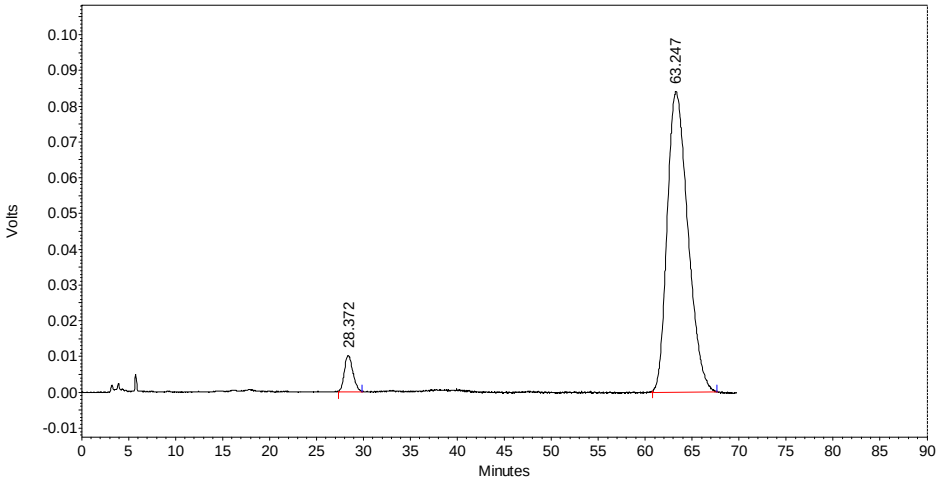


3f



Detector A (254nm)

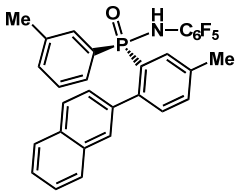
Pk #	Retention Time	Area	Area %	Height	Height %
1	28.982	3673683	50.251	55814	68.518
2	64.509	3637053	49.749	25645	31.482
Total		7310736	100.000	81459	100.000

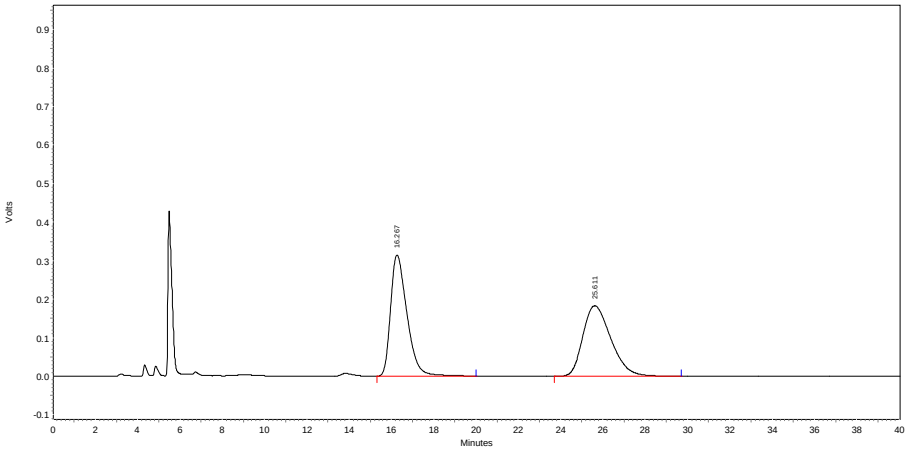


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	28.372	633244	4.685	10125	10.744
2	63.247	12881915	95.315	84114	89.256
Total		13515159	100.000	94238	100.000

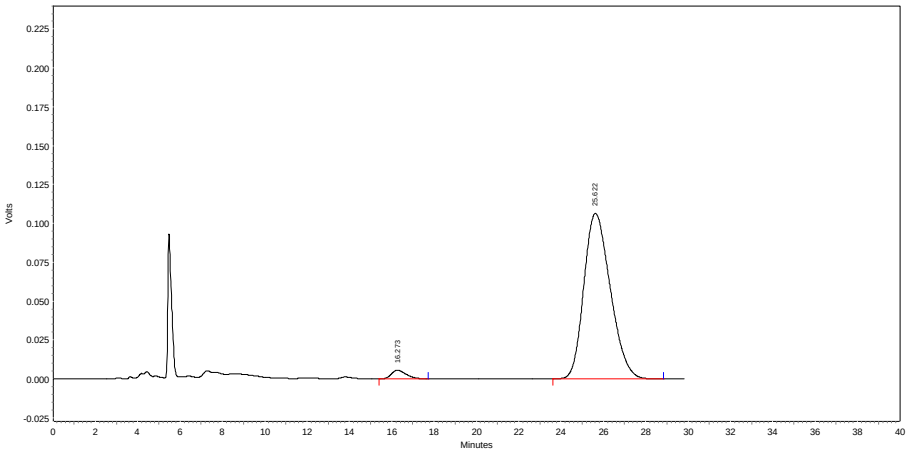
6.7 HPLC chart of 3g (substrate and product)





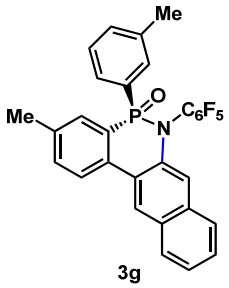
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.267	16713748	49.892	314907	63.226
2	25.611	16786182	50.108	183161	36.774
Total		33499930	100.000	498068	100.000

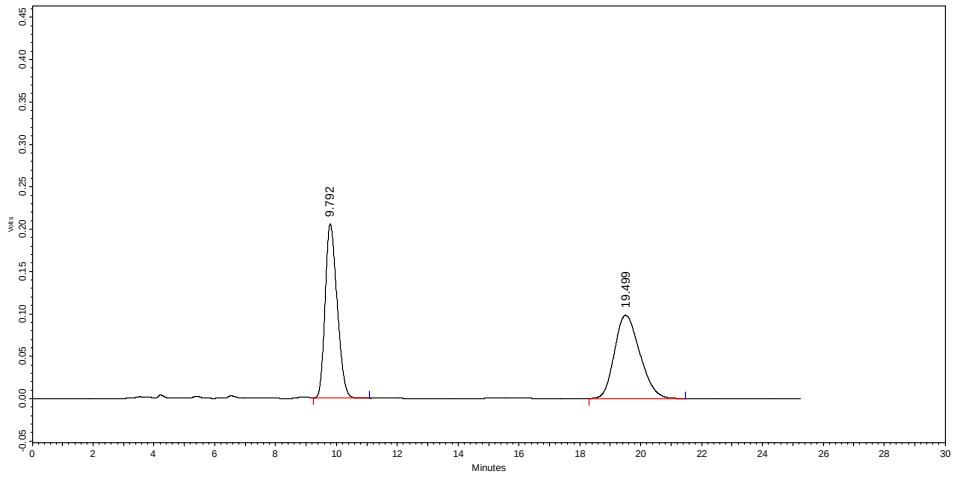


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.273	269516	2.834	5573	4.976
2	25.622	9242194	97.166	106431	95.024
Total		9511711	100.000	112004	100.000

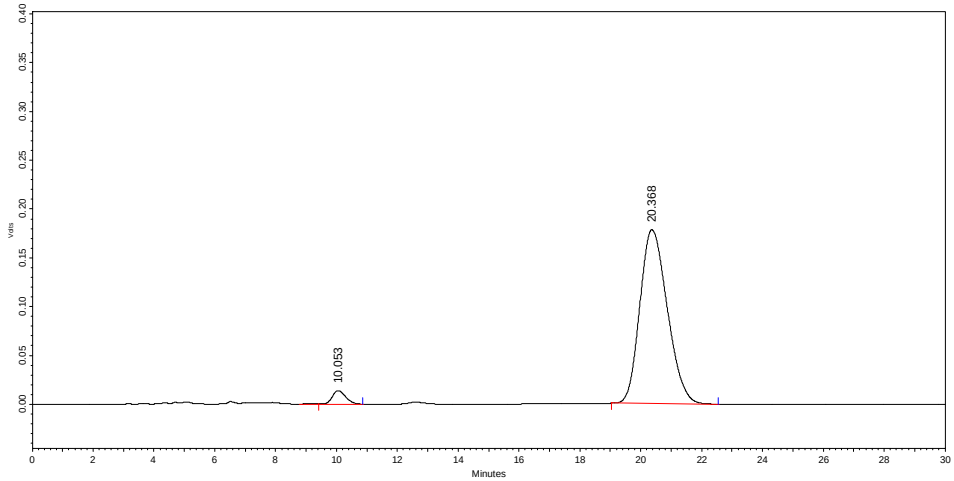


3g



Detector A (254nm)

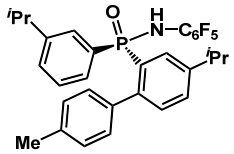
Pk #	Retention Time	Area	Area %	Height	Height %
1	9.792	5633241	49.890	205401	67.690
2	19.499	5658191	50.110	98042	32.310
Total		11291432	100.000	303443	100.000

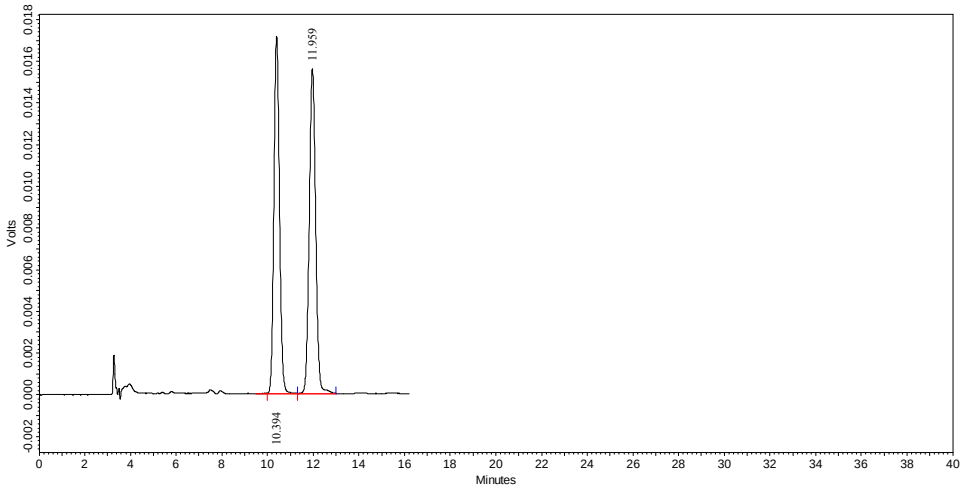


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	10.053	414502	3.580	13848	7.211
2	20.368	11162421	96.420	178191	92.789
Total		11576923	100.000	192039	100.000

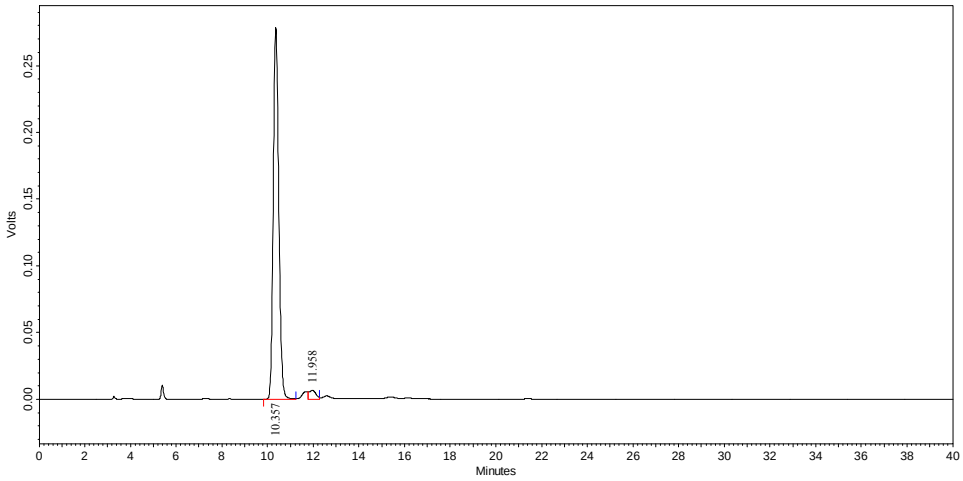
6.8 HPLC chart of 3h (substrate and product)





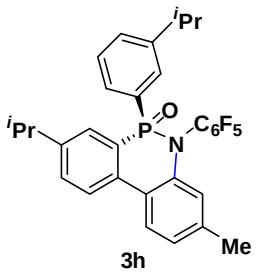
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	10.394	293487	49.190	17172	52.432
2	11.959	303151	50.810	15579	47.568
Total		596638	100.000	32750	100.000

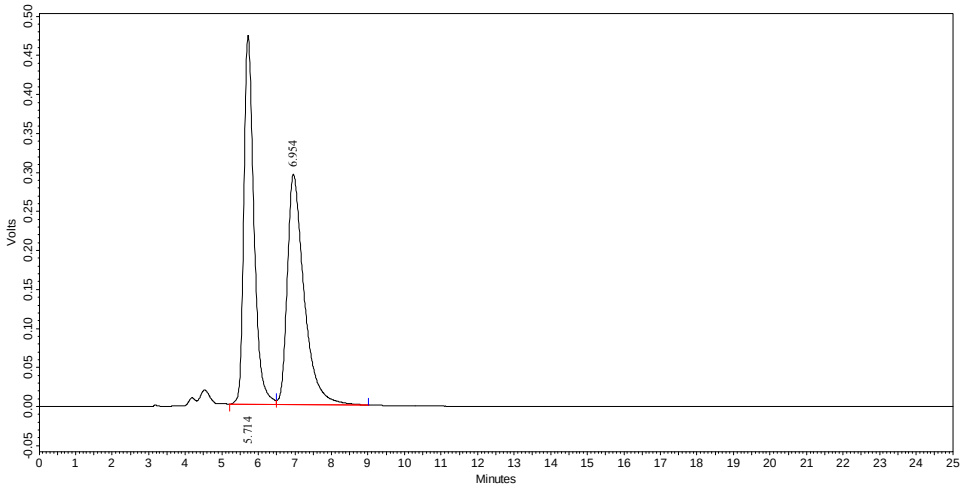


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	10.357	4710614	97.214	278760	97.696
2	11.958	135013	2.786	6575	2.304
Total		4845627	100.000	285335	100.000

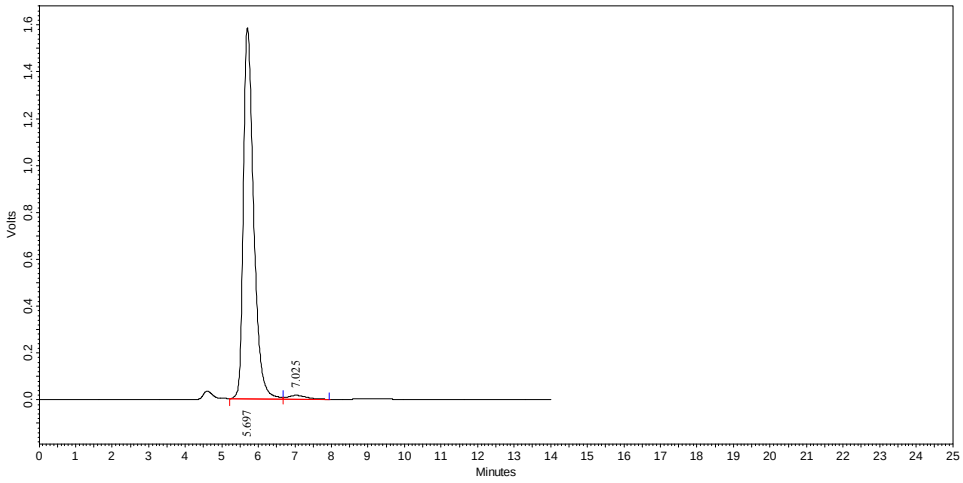


3h



Detector A (254nm)

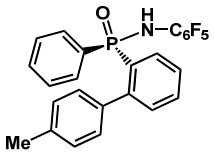
Pk #	Retention Time	Area	Area %	Height	Height %
1	5.714	9176949	49.336	473329	61.568
2	6.954	9424140	50.664	295464	38.432
Total		18601089	100.000	768793	100.000

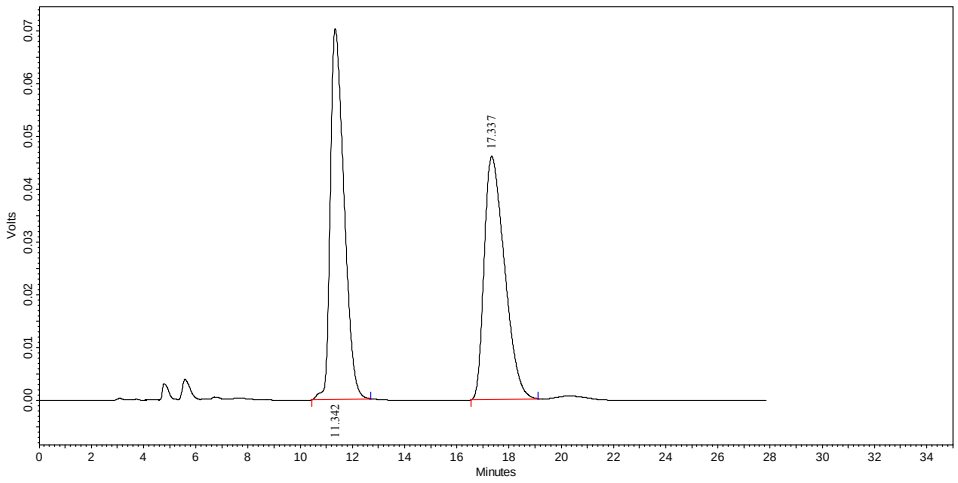


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	5.697	31162483	98.310	1585089	98.994
2	7.025	535822	1.690	16109	1.006
Total		31698304	100.000	1601198	100.000

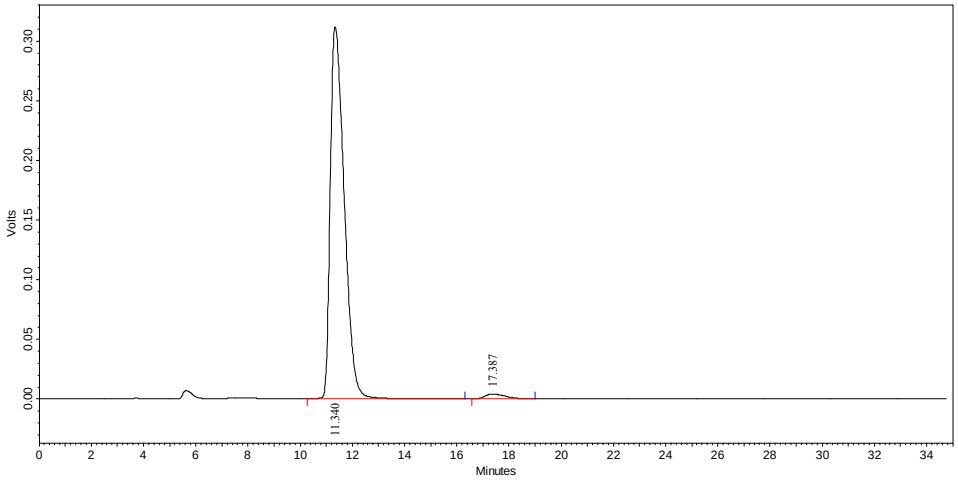
6.9 HPLC chart of 3i (substrate and product)





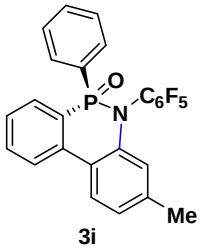
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.342	2558762	50.641	70254	60.402
2	17.337	2493958	49.359	46057	39.598
Total		5052720	100.000	116310	100.000

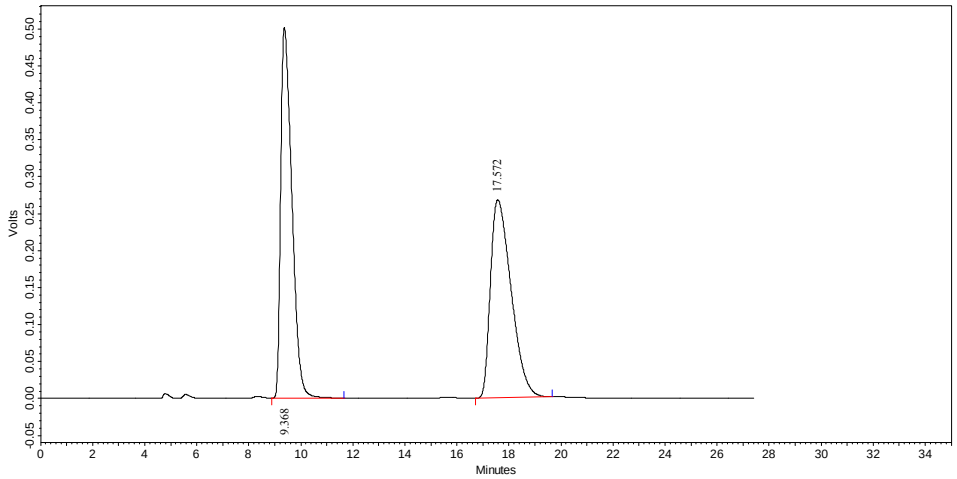


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.340	11580552	98.055	312136	98.666
2	17.387	229731	1.945	4220	1.334
Total		11810283	100.000	316356	100.000

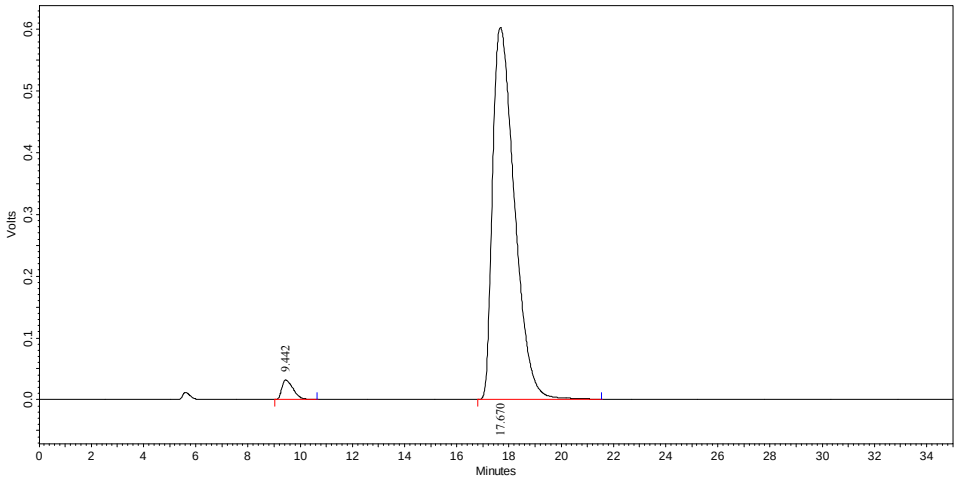


3i



Detector A (254nm)

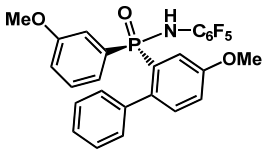
Pk #	Retention Time	Area	Area %	Height	Height %
1	9.368	14975718	50.264	501998	65.180
2	17.572	14818126	49.736	268175	34.820
Total		29793844	100.000	770173	100.000

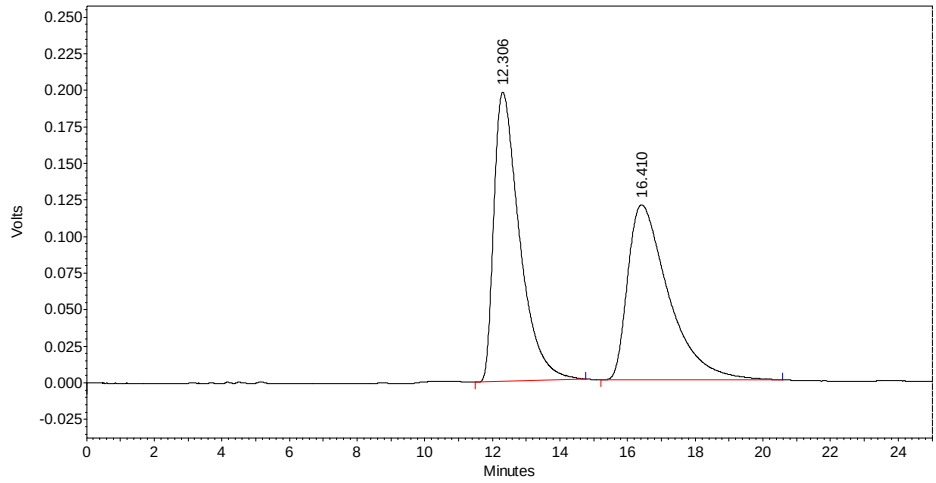


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.442	952699	2.644	31702	4.995
2	17.670	35084482	97.356	602971	95.005
Total		36037181	100.000	634673	100.000

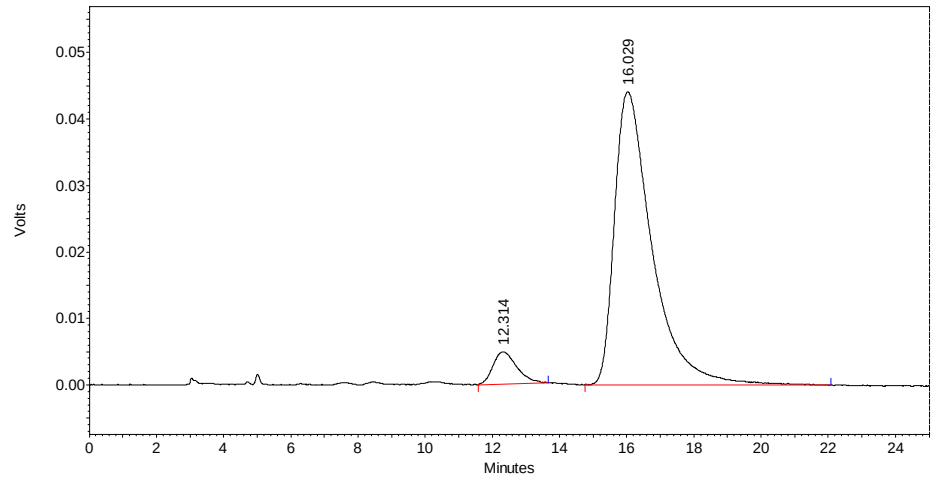
6.10 HPLC chart of 3j (substrate and product)





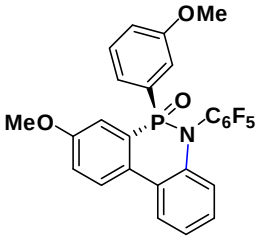
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.306	10463106	50.935	197739	62.292
2	16.410	10078787	49.065	119698	37.708
Total		20541894	100.000	317437	100.000

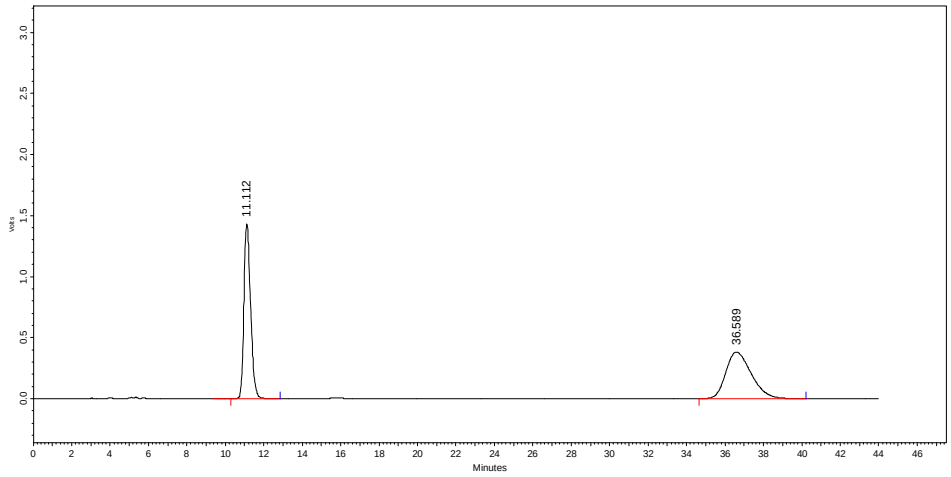


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.314	236112	6.448	4810	9.854
2	16.029	3425573	93.552	44005	90.146
Total		3661685	100.000	48815	100.000

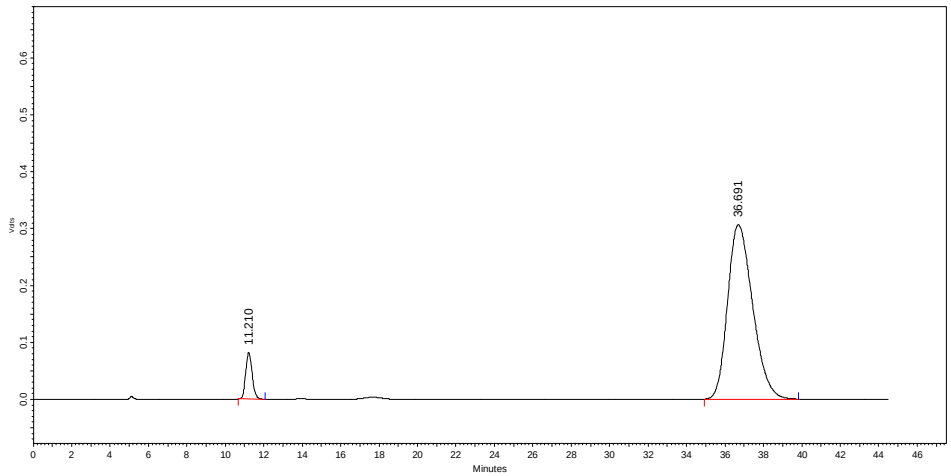


3j



Detector A (254nm)

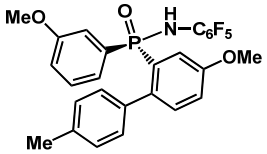
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.112	34452761	49.630	1430474	78.962
2	36.589	34966812	50.370	381131	21.038
Total		69419573	100.000	1811605	100.000

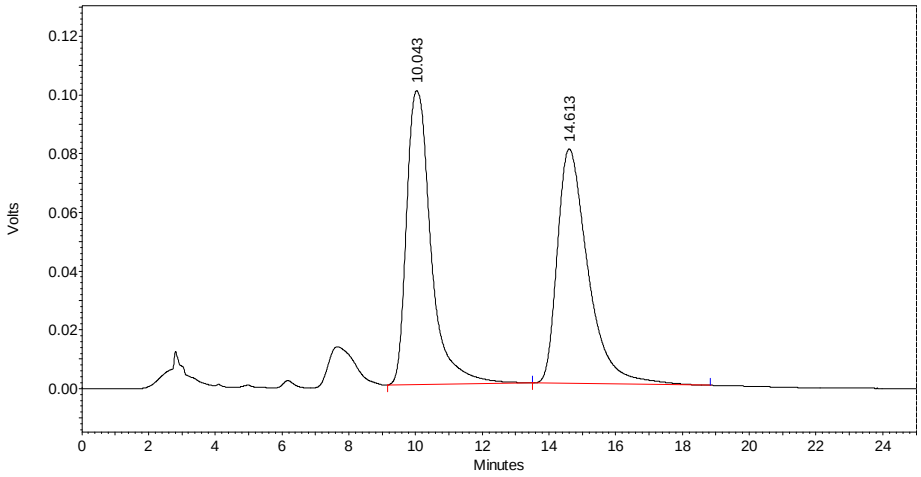


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.210	1916800	6.467	82245	21.149
2	36.691	27724940	93.533	306648	78.851
Total		29641740	100.000	388893	100.000

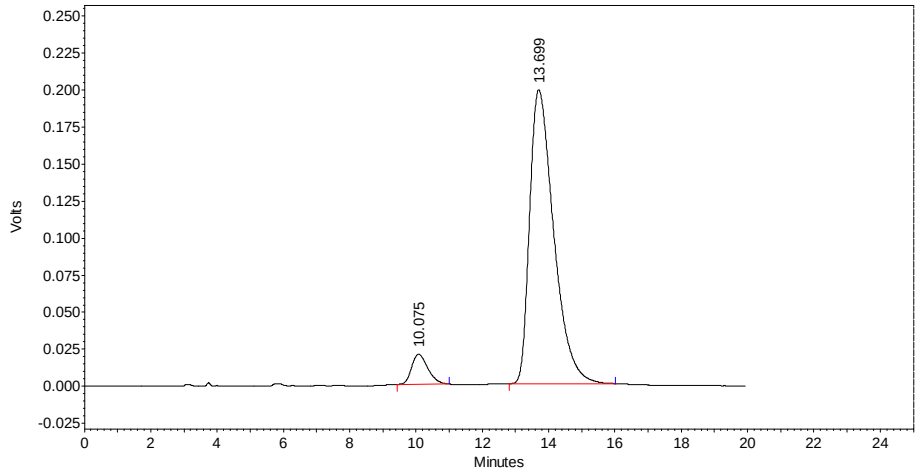
6.11 HPLC chart of 3k (substrate and product)





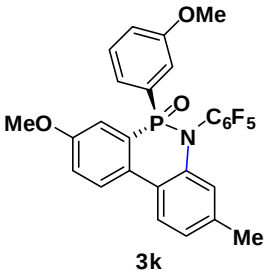
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	10.043	5110804	50.015	98805	55.530
2	14.613	5107802	49.985	79125	44.470
Total		10218607	100.000	177930	100.000

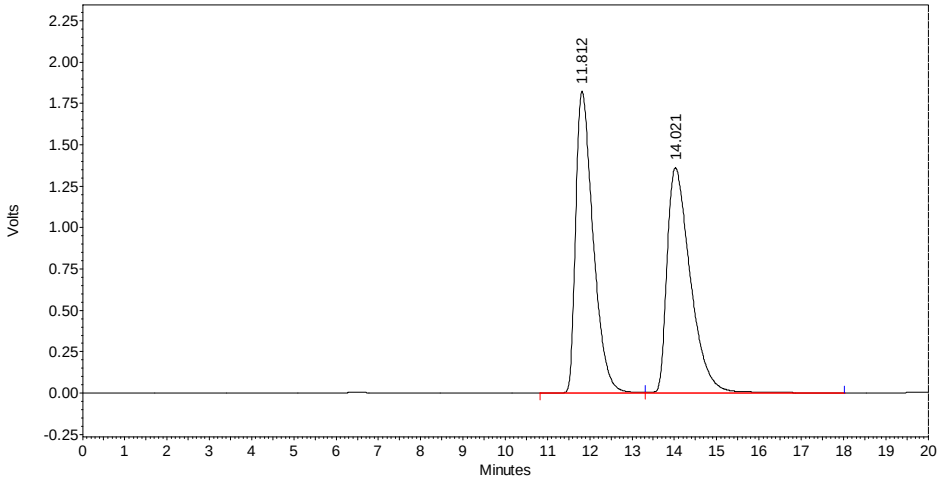


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	10.075	688071	6.439	20257	9.273
2	13.699	9998739	93.562	198183	90.727
Total		10686809	100.000	218440	100.000

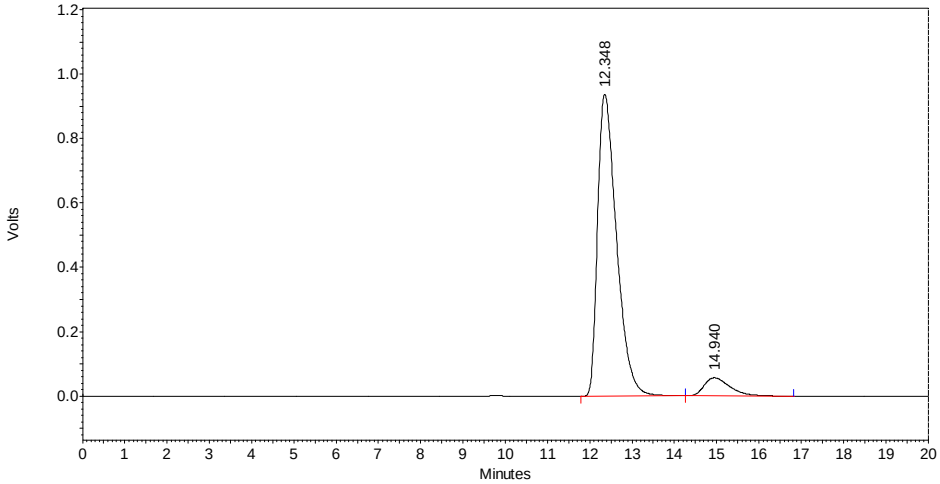


3k



Detector A (254nm)

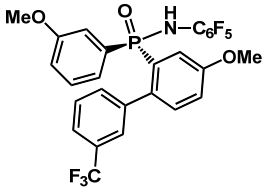
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.812	52120917	49.970	1824610	57.301
2	14.021	52183624	50.030	1359622	42.699
Total		104304540	100.000	3184232	100.000

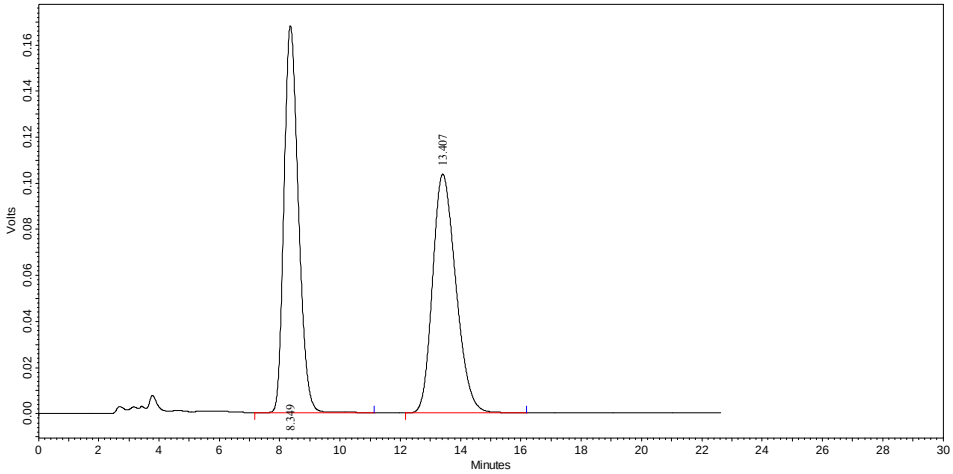


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.348	29165086	92.352	937685	94.306
2	14.940	2415180	7.648	56618	5.694
Total		31580266	100.000	994303	100.000

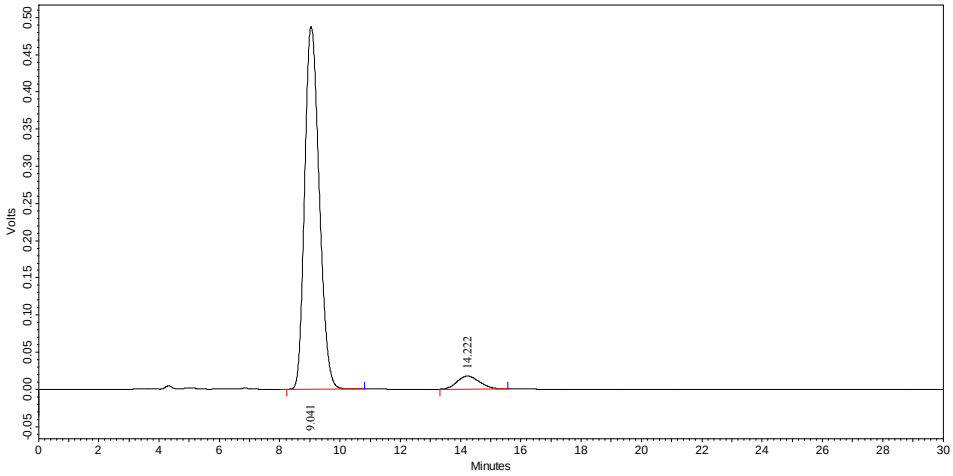
6.12 HPLC chart of 3l (substrate and product)





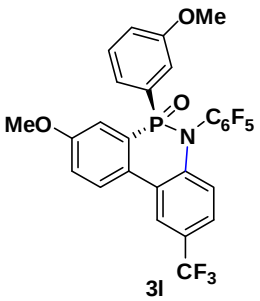
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.349	5562122	50.012	168072	61.854
2	13.407	5559531	49.988	103651	38.146
Total		11121653	100.000	271723	100.000

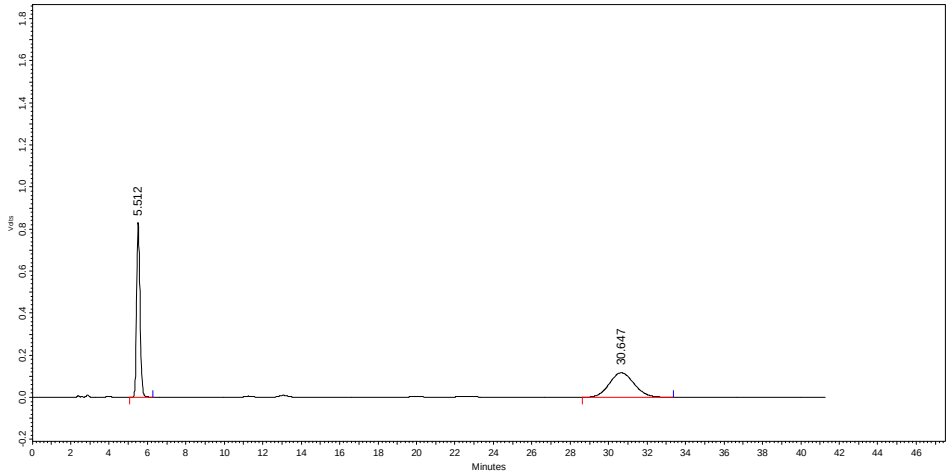


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.041	16304892	94.709	487900	96.547
2	14.222	910929	5.291	17450	3.453
Total		17215821	100.000	505350	100.000

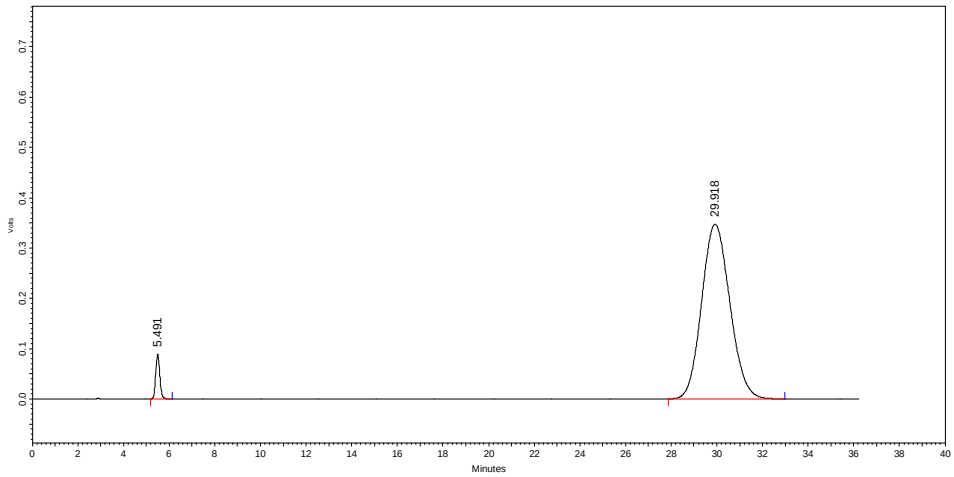


3l



Detector A (254nm)

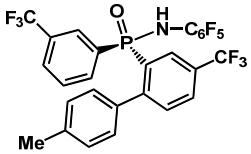
Pk #	Retention Time	Area	Area %	Height	Height %
1	5.512	10182456	49.394	830168	87.736
2	30.647	10432187	50.606	116040	12.264
Total		20614643	100.000	946208	100.000

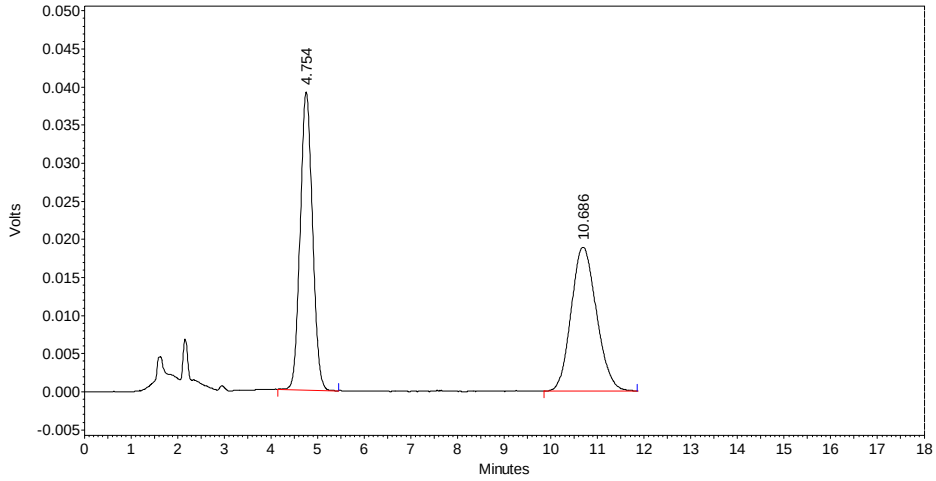


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	5.491	1093829	3.539	88980	20.401
2	29.918	29817508	96.461	347172	79.599
Total		30911337	100.000	436151	100.000

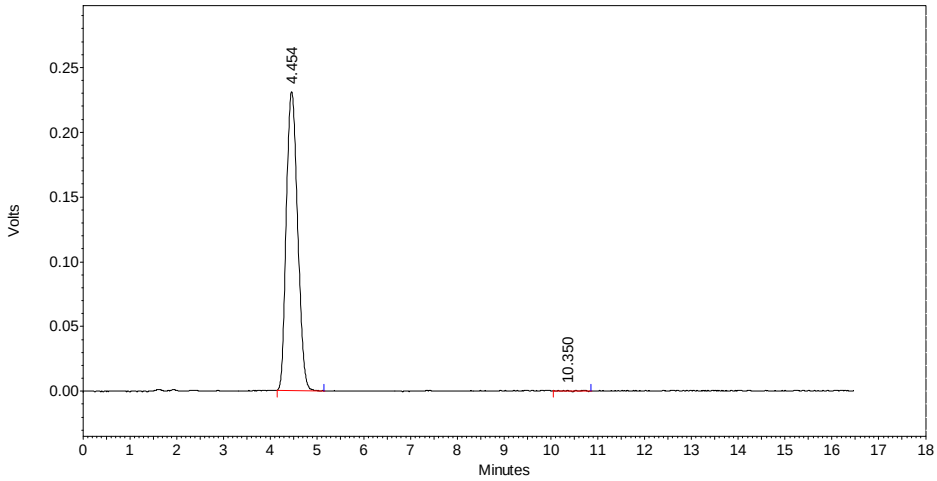
6.13 HPLC chart of 3m (substrate and product)





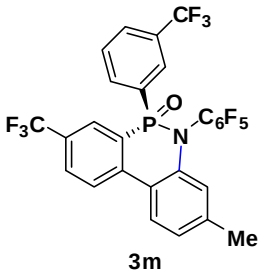
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.754	717086	50.238	38294	67.047
2	10.686	710290	49.762	18822	32.953
Total		1427375	100.000	57116	100.000

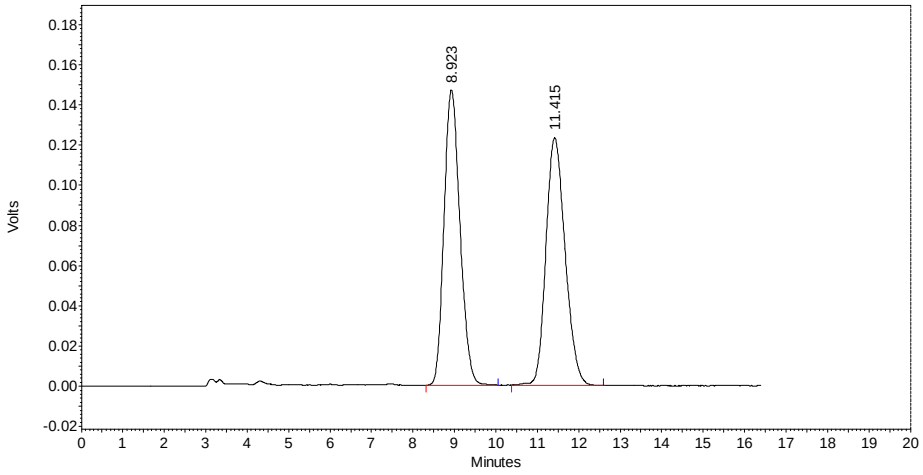


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.454	3872149	99.843	225500	99.896
2	10.350	6102	0.157	234	0.104
Total		3878251	100.000	225733	100.000

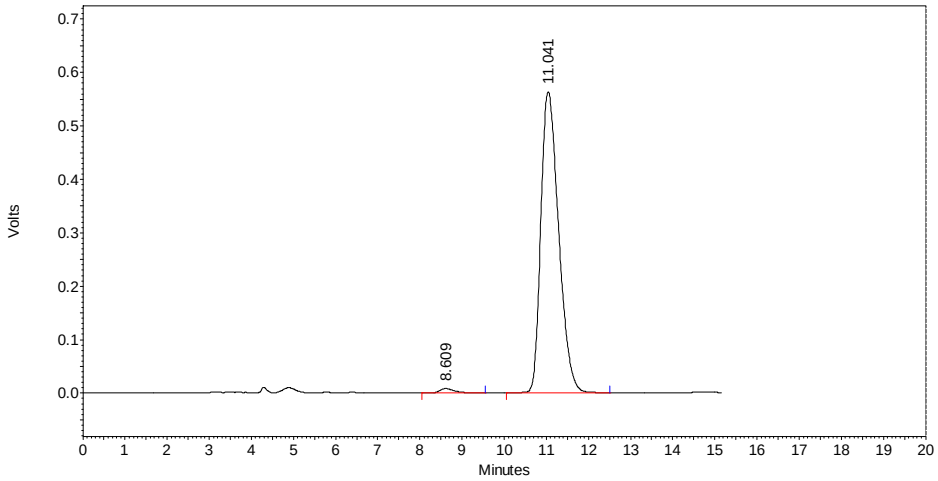


3m



Detector A (254nm)

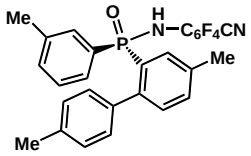
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.923	3942086	49.867	147047	54.451
2	11.415	3963143	50.133	123007	45.549
Total		7905229	100.000	270054	100.000

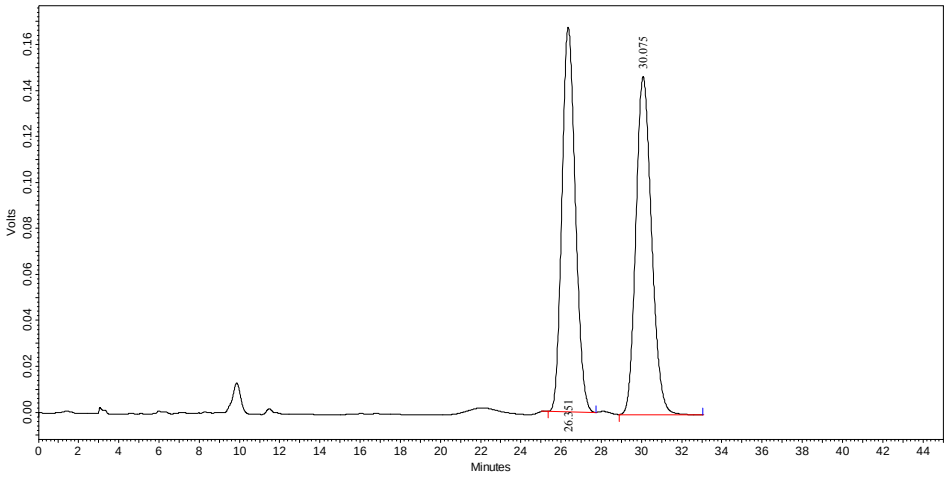


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.609	195600	1.169	8185	1.439
2	11.041	16542722	98.831	560528	98.561
Total		16738322	100.000	568713	100.000

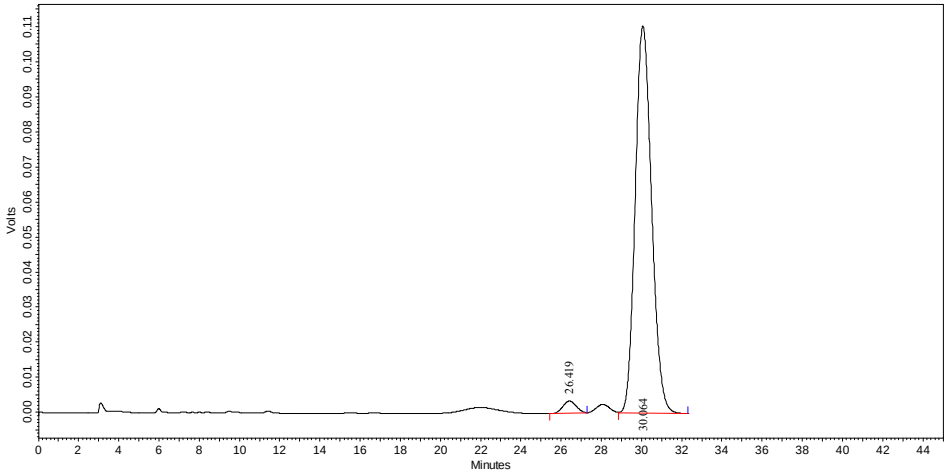
6.14 HPLC chart of 3n (substrate and product)





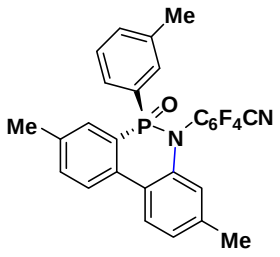
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	26.351	7789902	49.418	167396	53.264
2	30.075	7973274	50.582	146880	46.736
Total		15763176	100.000	314276	100.000

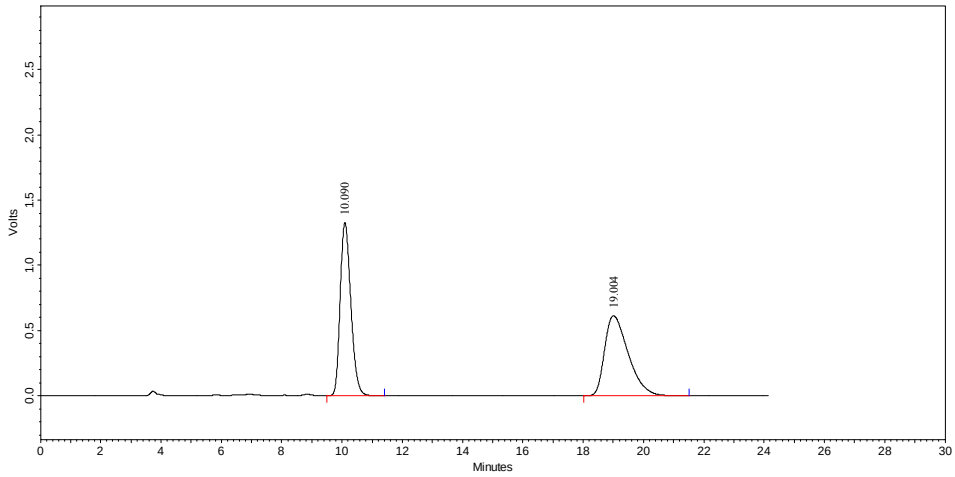


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	26.419	160126	2.504	3477	3.052
2	30.064	6235822	97.496	110446	96.948
Total		6395948	100.000	113923	100.000

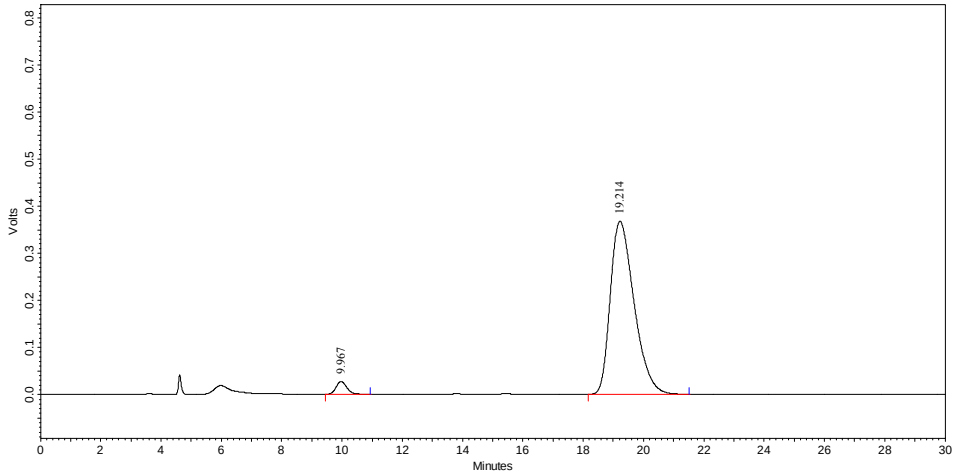


3n



Detector A (254nm)

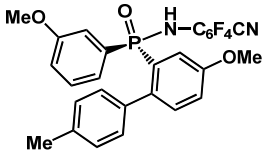
Pk #	Retention Time	Area	Area %	Height	Height %
1	10.090	32368398	49.113	1327908	68.401
2	19.004	33538207	50.887	613455	31.599
Total		65906605	100.000	1941363	100.000

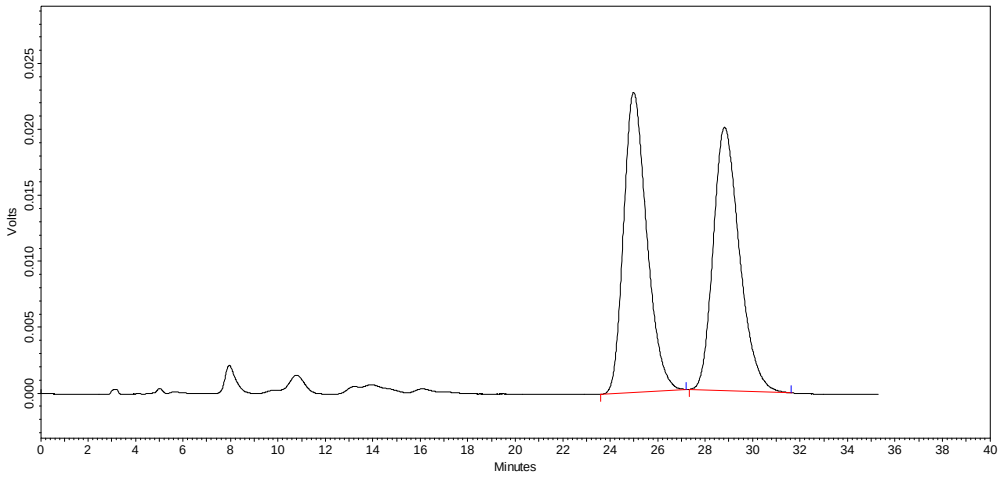


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.967	672279	3.221	26933	6.818
2	19.214	20197838	96.779	368093	93.182
Total		20870117	100.000	395026	100.000

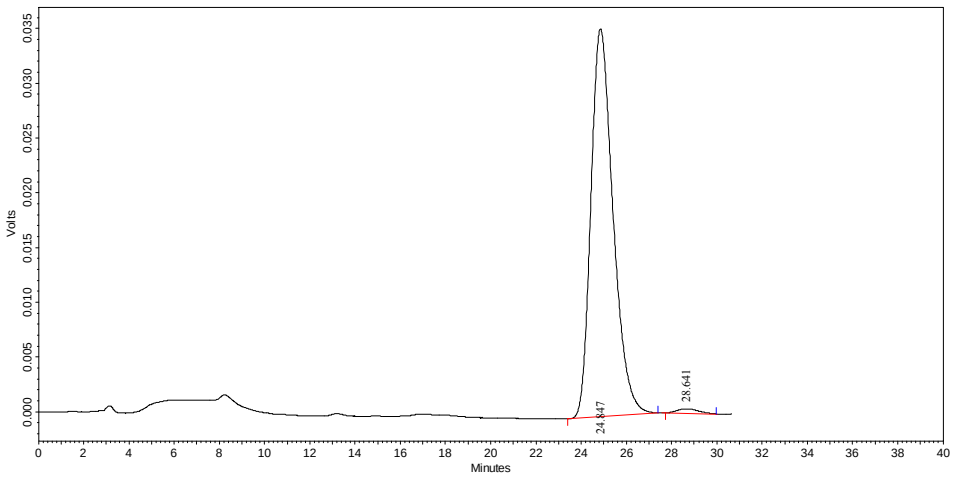
6.15 HPLC chart of 3o (substrate and product)





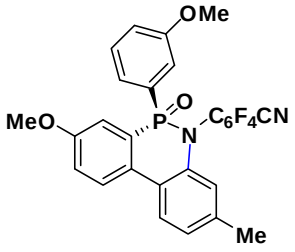
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	24.984	1539109	50.050	22762	53.269
2	28.818	1536032	49.950	19968	46.731
Total		3075141	100.000	42730	100.000

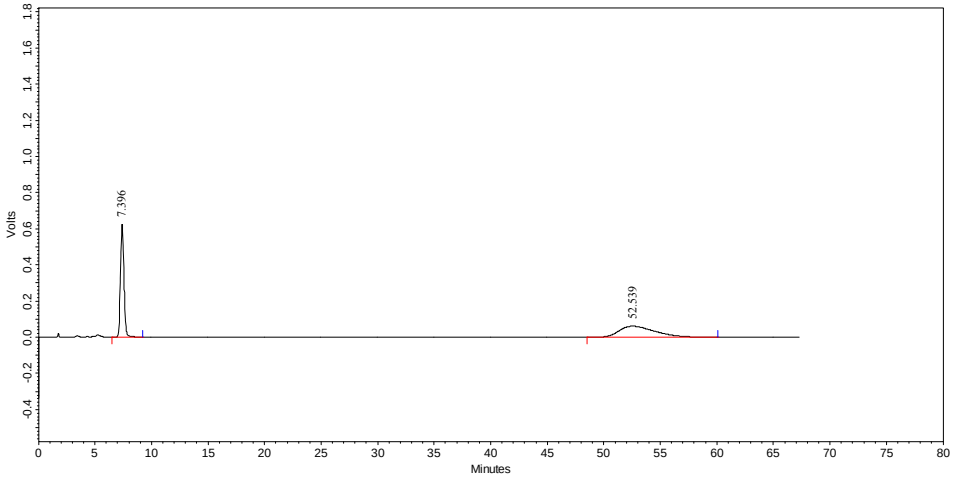


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	24.847	2409105	98.809	35438	98.787
2	28.641	29035	1.191	435	1.213
Total		2438140	100.000	35874	100.000

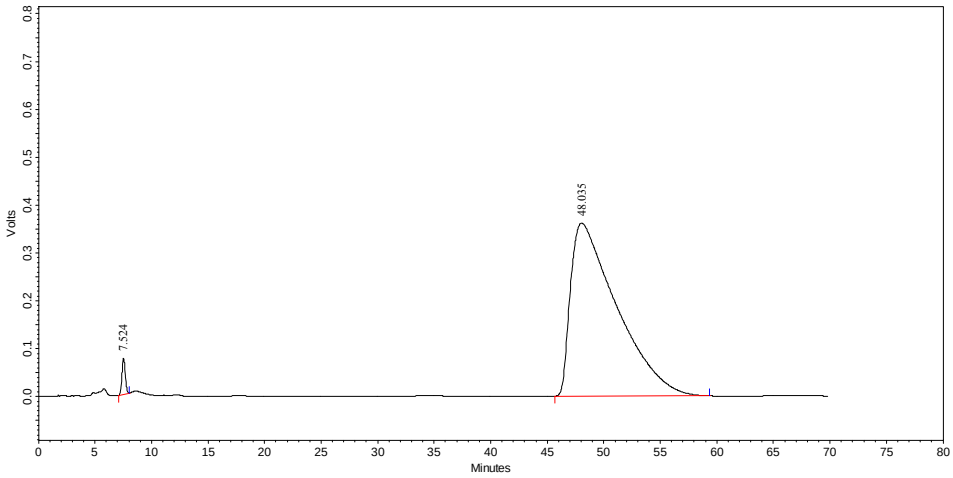


3o



Detector A (254nm)

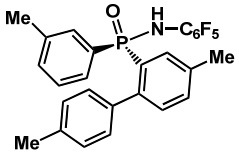
Pk #	Retention Time	Area	Area %	Height	Height %
1	7.396	13323594	49.605	622991	91.050
2	52.539	13535930	50.395	61236	8.950
Total		26859524	100.000	684227	100.000

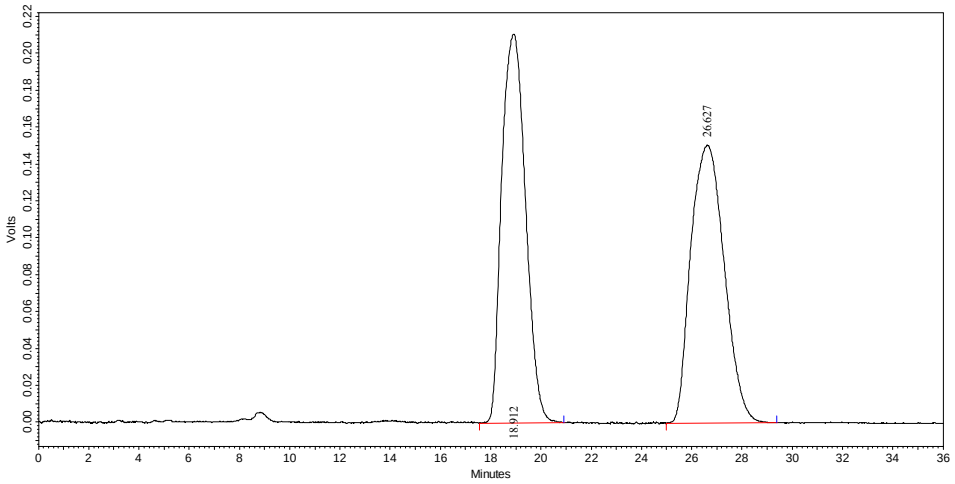


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	7.524	1550530	1.486	75696	17.306
2	48.035	102775711	98.514	361695	82.694
Total		104326241	100.000	437391	100.000

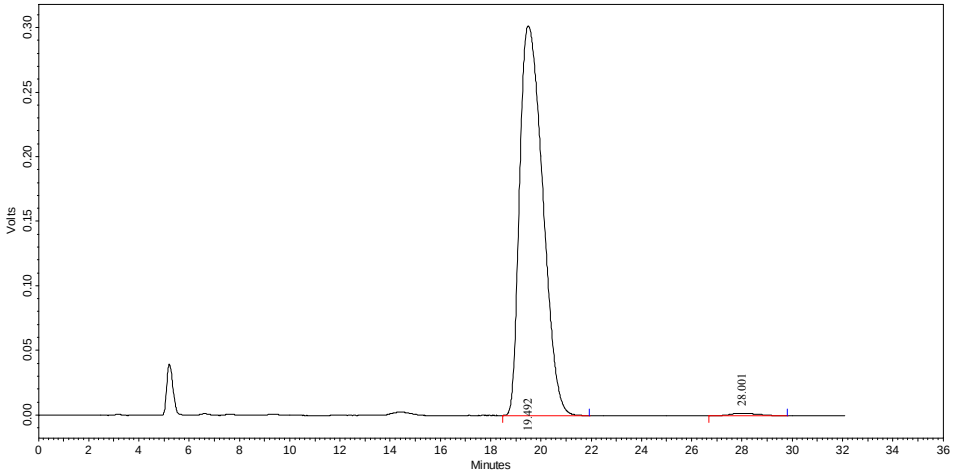
6.16 HPLC chart of 4a (substrate and product)





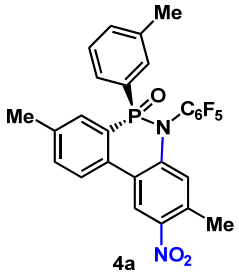
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.912	13895899	49.878	210780	58.300
2	26.627	13964031	50.122	150762	41.700
Total		27859930	100.000	361542	100.000

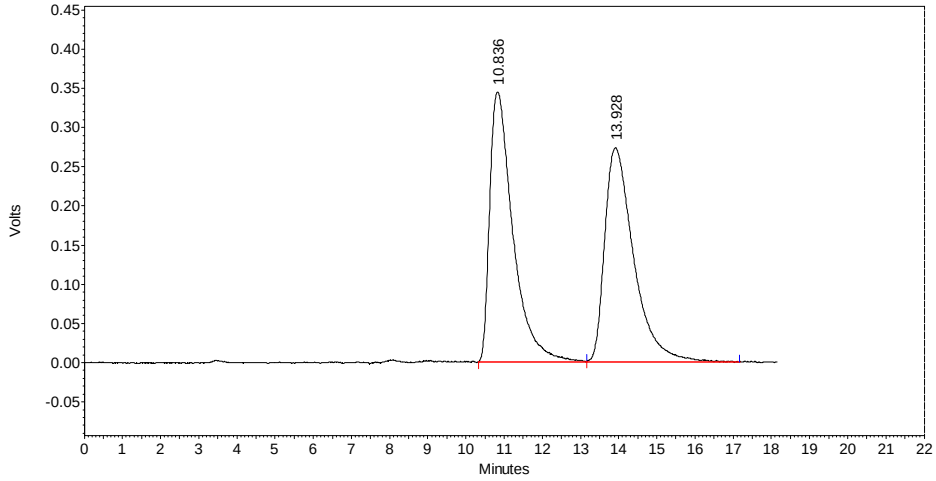


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.492	19209677	99.142	301827	99.359
2	28.001	166167	0.858	1947	0.641
Total		19375844	100.000	303774	100.000

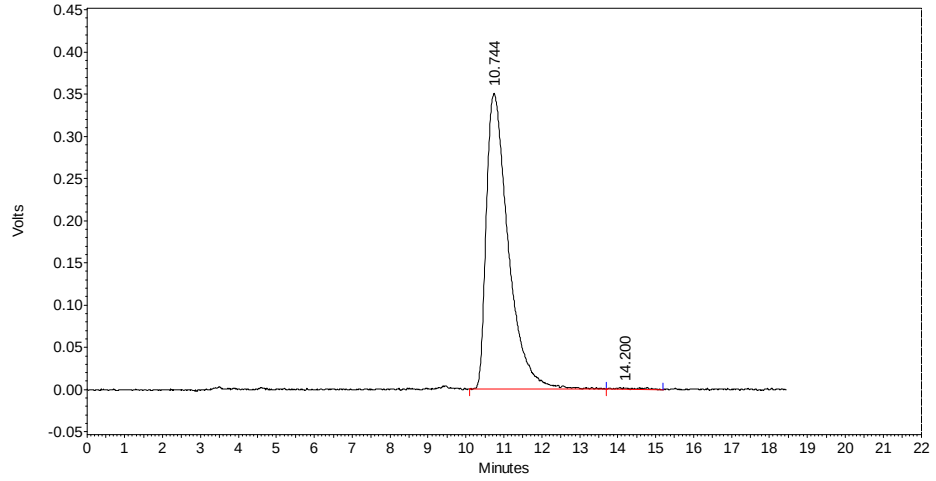


4a



Detector A (254nm)

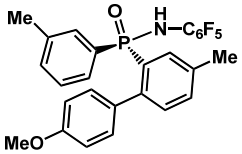
Pk #	Retention Time	Area	Area %	Height	Height %
1	10.836	14529106	50.197	321678	54.369
2	13.928	14415340	49.803	269978	45.631
Total		28944446	100.000	591655	100.000

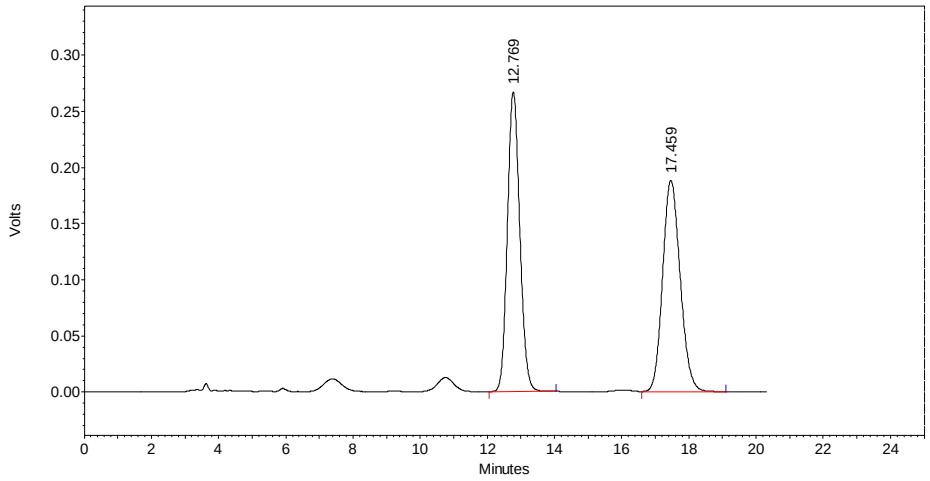


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	10.744	14036181	99.632	346552	99.775
2	14.200	51862	0.368	783	0.225
Total		14088042	100.000	347335	100.000

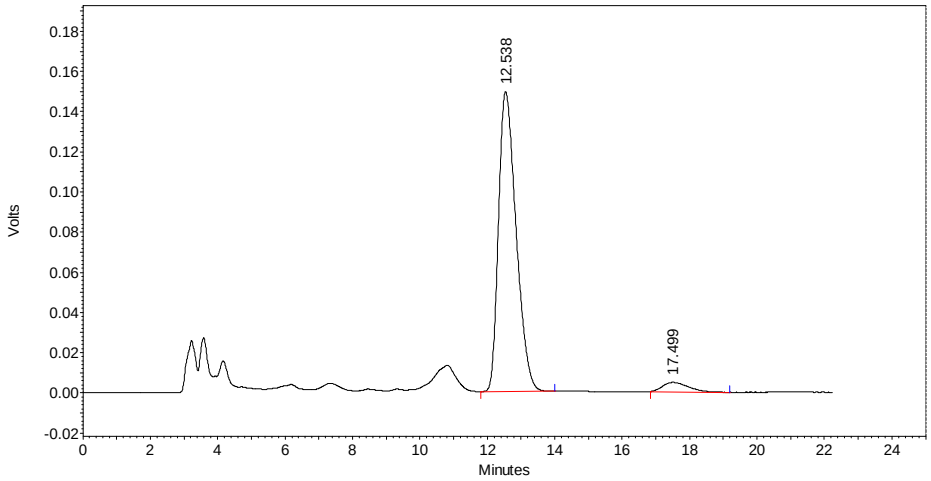
6.17 HPLC chart of 4b (substrate and product)





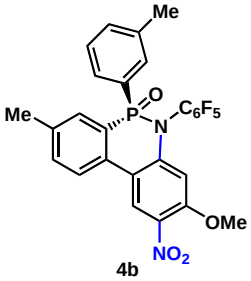
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.769	6830020	50.057	265812	58.651
2	17.459	6814347	49.943	187395	41.349
Total		13644367	100.000	453207	100.000

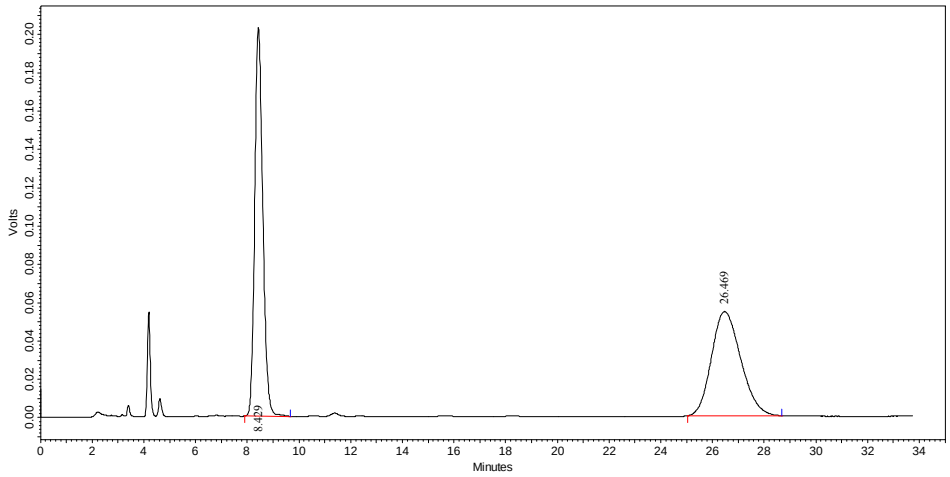


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.538	5415962	95.622	149043	96.925
2	17.499	247963	4.378	4729	3.075
Total		5663925	100.000	153772	100.000

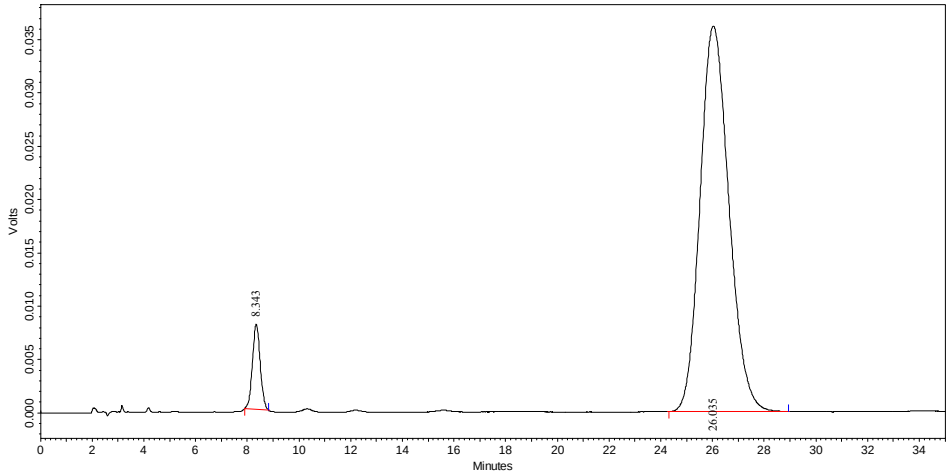


4b



Detector A (254nm)

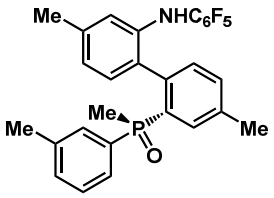
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.429	4413619	50.768	203095	78.885
2	26.469	4280018	49.232	54362	21.115
Total		8693637	100.000	257458	100.000



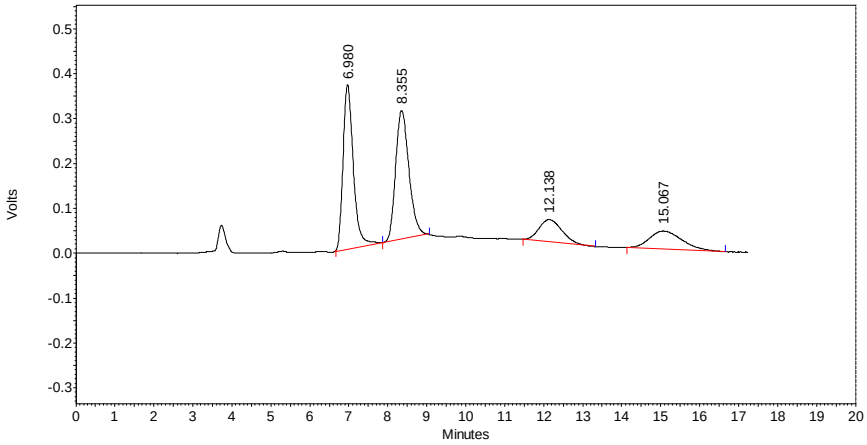
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.343	165943	5.571	7966	18.038
2	26.035	2812818	94.429	36195	81.962
Total		2978761	100.000	44161	100.000

6.18 HPLC chart of 5

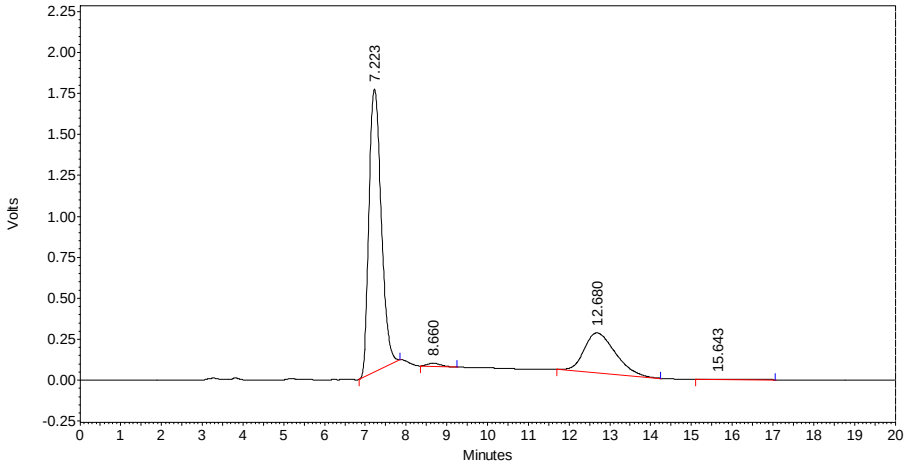


5



Detector A (254nm)

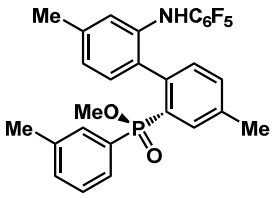
Pk #	Retention Time	Area	Area %	Height	Height %
1	7.001	5768190	36.889	289607	47.367
2	8.382	5769122	36.895	234963	38.430
3	12.148	2024719	12.949	48803	7.982
4	15.136	2074478	13.267	38031	6.220
Total		15636510	100.000	611404	100.000



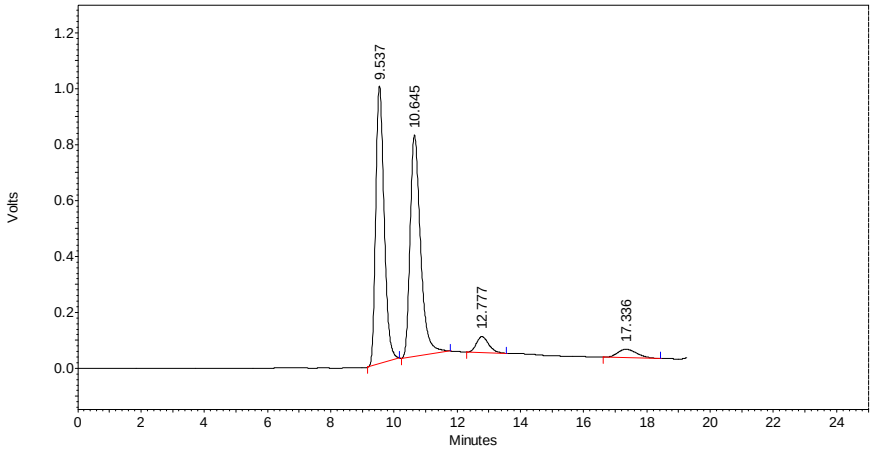
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	7.223	25714790	69.431	1260948	84.875
2	8.660	284570	0.768	12819	0.863
3	12.680	10959107	29.590	210508	14.169
4	15.643	77973	0.211	1380	0.093
Total		37036439	100.000	1485654	100.000

6.19 HPLC chart of 6

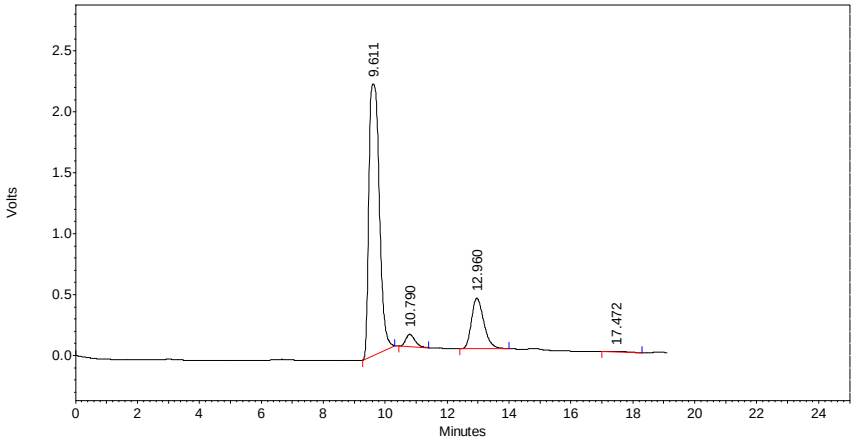


6



Detector A (254nm)

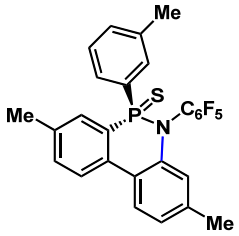
Pk #	Retention Time	Area	Area %	Height	Height %
1	9.537	18277928	46.582	994997	53.081
2	10.645	18120872	46.182	791898	42.246
3	12.777	1546611	3.942	56996	3.041
4	17.336	1292854	3.295	30609	1.633
Total		39238265	100.000	1874500	100.000



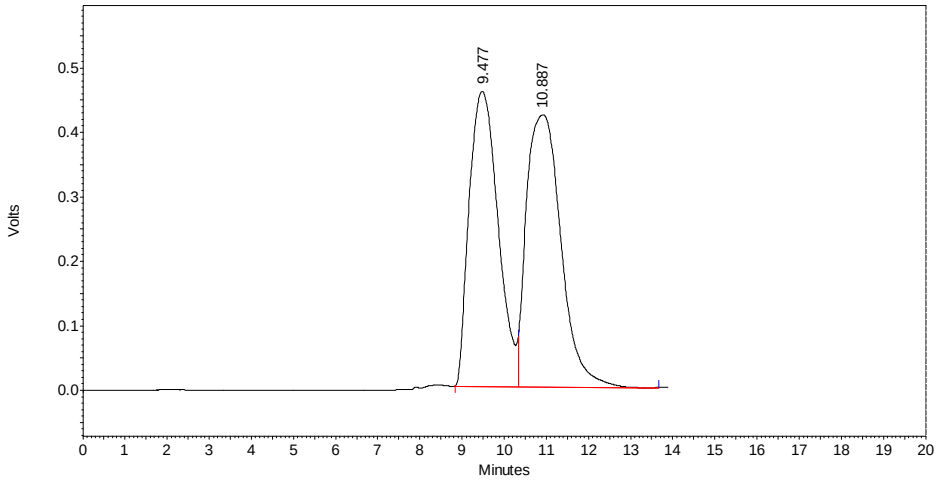
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.611	52099246	78.883	2229671	80.975
2	10.790	2104994	3.187	101313	3.679
3	12.960	11569657	17.518	415689	15.097
4	17.472	272241	0.412	6849	0.249
Total		66046139	100.000	2753521	100.000

6.20 HPLC chart of 7

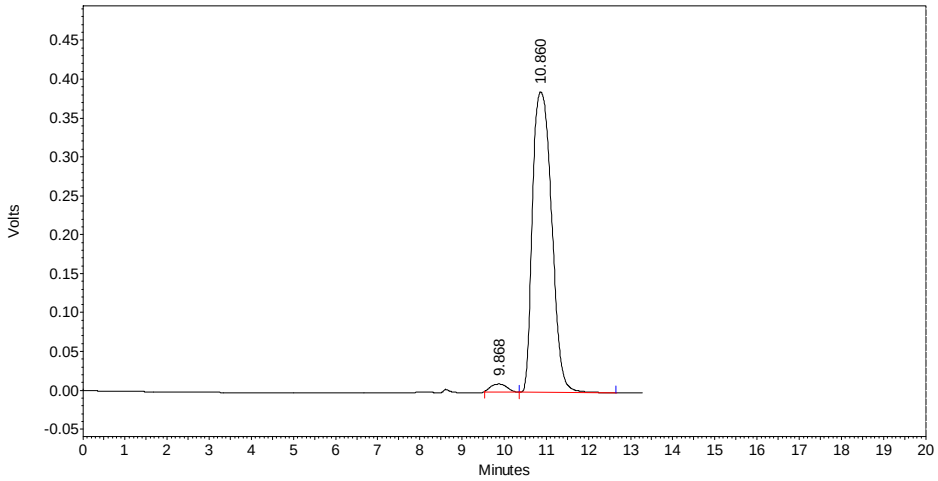


7



Detector A (254nm)

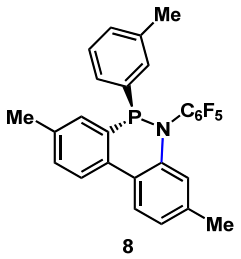
Pk #	Retention Time	Area	Area %	Height	Height %
1	9.477	21857370	47.698	447320	51.560
2	10.887	23967112	52.302	420257	48.440
Total		45824482	100.000	867578	100.000



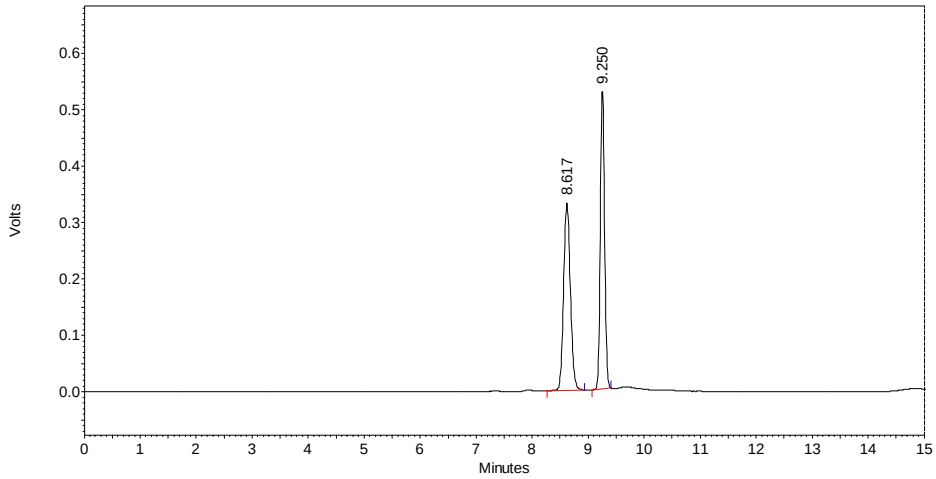
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.868	266097	2.137	10039	2.533
2	10.860	12186270	97.863	386276	97.467
Total		12452366	100.000	396315	100.000

6.21 HPLC chart of 8

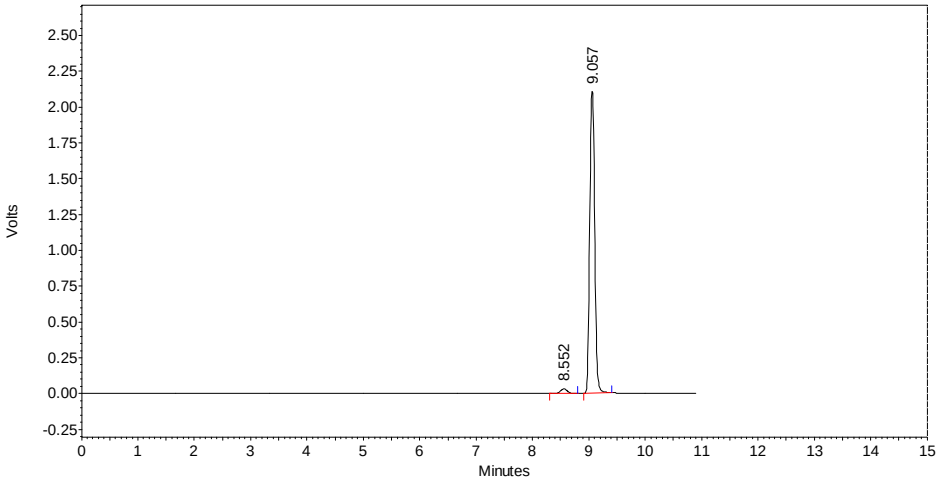


8



Detector A (254nm)

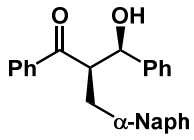
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.617	2817394	50.478	331808	38.625
2	9.250	2764077	49.522	527233	61.375
Total		5581471	100.000	859041	100.000



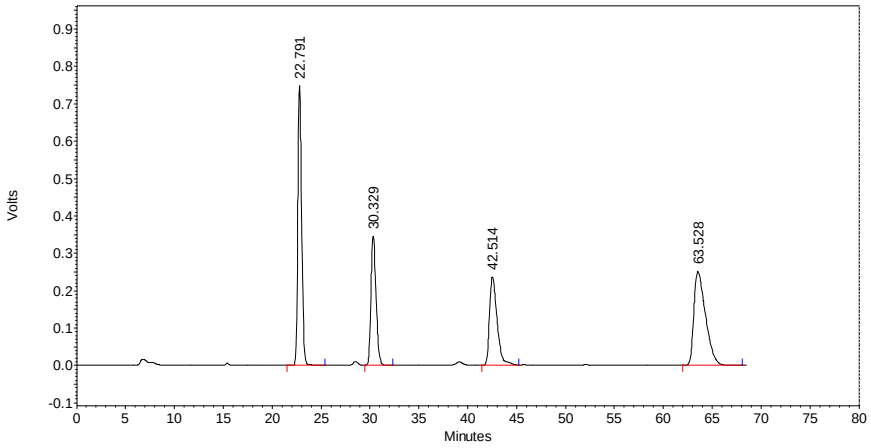
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.552	272295	2.052	32307	1.509
2	9.057	12997654	97.948	2108976	98.491
Total		13269950	100.000	2141283	100.000

6.22 HPLC chart of 11

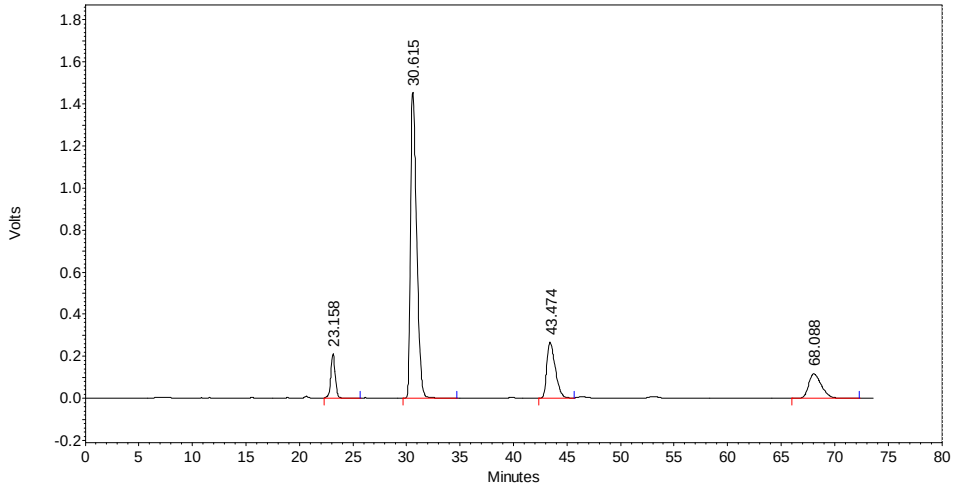


11



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	22.791	20524794	30.797	743579	47.179
2	30.329	12493559	18.746	345399	21.915
3	42.514	12813906	19.227	236513	15.006
4	63.528	20812923	31.229	250588	15.899
Total		66645182	100.000	1576079	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.158	5914944	6.711	181626	10.168
2	30.615	58094548	65.915	1242210	69.541
3	43.474	14609741	16.576	250734	14.036
4	68.088	9516141	10.797	111741	6.255
Total		88135374	100.000	1786310	100.000