Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Enantioselective synthesis of 1,2,5,6-tetrahydropyridines (THPs) *via* proline-catalyzed direct Mannich-cyclization/domino oxidation-reduction sequence: Application for medicinally important *N*-heterocycles

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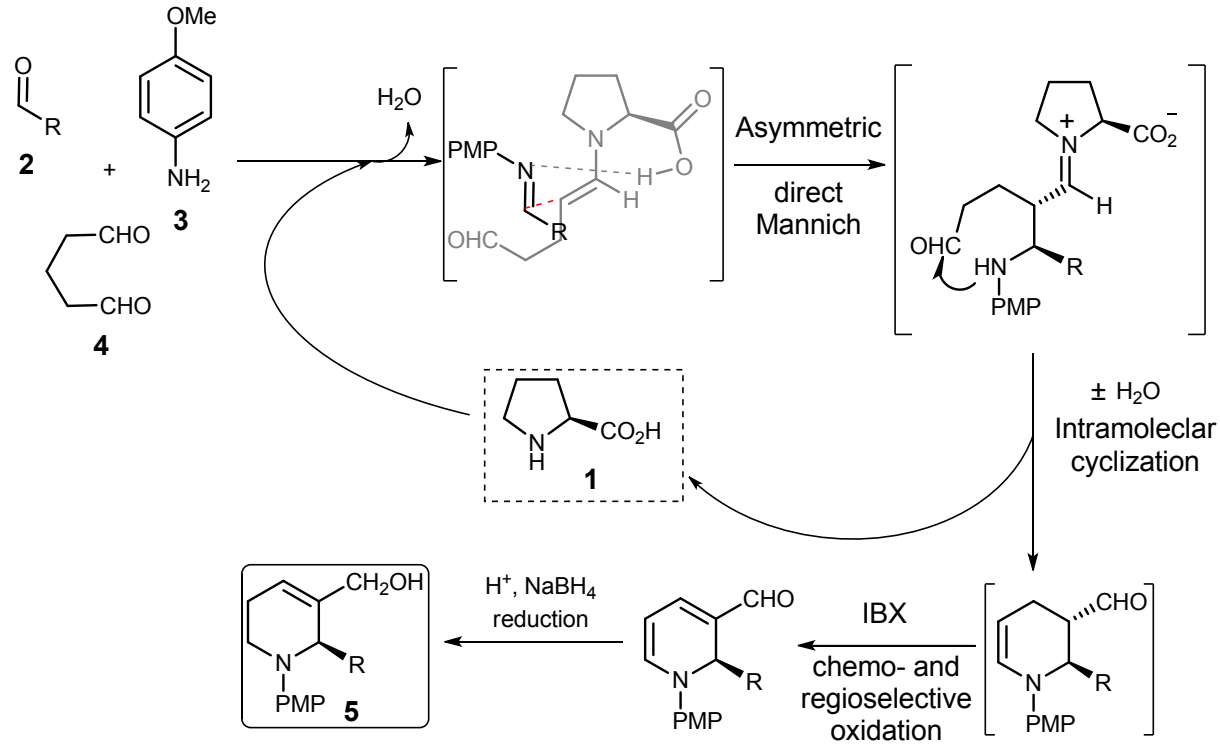
General Experimental Methods:

All reactions under standard conditions were monitored by thin-layer chromatography (TLC) through SiO_2 gel F-254 plates. All reagents were of analytical grade and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution and spectral data were reported in ppm relative to tetramethylsilane (TMS) as an internal standard. High-resolution mass spectra were recorded using the quadruple electrospray ionization (ESI) technique. HPLC was performed on Water-2998-instrument with CHIRALPAK-IA and IB columns using hexane/2-propanol.

General procedure for THPs 5:

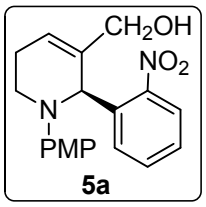
To a stirred solution of aryl aldehyde **2** (0.3 mmol) in DMSO (3.0 mL) at rt was added *p*-anisidine **3** (0.3 mmol) and stirred for additional 3 hr at the same temperature. To this mixture, was added glutaraldehyde **4** (25 % sol. in water, 0.360 mL, 0.9 mmol), and L-proline **1** (6.9 mg, 0.06 mmol) and taken to 10 °C. This reaction mixture was further stirred at the same temperature until the in situ generated imine was consumed completely as monitored by TLC. IBX (2-Iodoxybenzoic acid) (1.2 equiv, 0.36 mmol) was added into the same flask and further heated to 40 °C for 4 hrs. This reaction mixture was then cooled to 0 °C and Methanol (3.0 mL) was added followed by $NaBH_4$ (in excess and portion wise) along with CH_3CO_2H (200 mol %) until the dark red color of the solution turned into pale reddish yellow. The reaction was quenched slowly with saturated $NaHCO_3$ (5.0 mL, 20% sol.) and stirred with ethyl acetate (10 mL) for 10 min. at rt and organic layer was separated out. The aqueous layer was further extracted with ethyl acetate (10 mL) and the combined organic extracts were washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure after filtration. Purification was performed by a silica gel column and eluted with hexane/EtOAc to give product **5** (58-80% yields). The enantiomeric ratios (er) of the products were determined by stationary chiral phase HPLC analysis.

Scheme 1: Detailed plausible mechanism for the multicomponent asymmetric synthesis of 1,2,5,6-THPs



Analytical data of the synthesized compounds

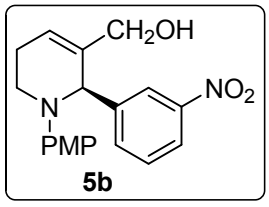
(*R*)-(1-(4-Methoxyphenyl)-2-(2-nitrophenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5a):



5a

Yellow viscous oil, (64 mg, 63% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.77–1.79 (bs, 1H), 2.18–2.23 (m, 1H), 2.25-2.32 (m, 1H), 3.00–3.07 (m, 1H), 3.15–3.19 (m, 1H), 3.73 (s, 3H), 4.06 (s, 2H), 5.80 (s, 1H), 6.16 (t, J = 4.2 Hz, 1H), 6.72 (d, J = 9.1 Hz, 2H), 6.84 (d, J = 9.1 Hz, 2H), 7.32–7.36 (m, 1H), 7.50–7.51 (m, 2H), 7.63 (d, J = 8.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.70, 44.50, 55.35, 55.57, 64.91, 114.20 (2C), 121.40 (2C), 124.16, 125.61, 128.02, 130.13, 131.66, 135.19, 136.73, 143.78, 150.57, 154.65; IR (KBr)/cm^{-1} 3448, 2924, 2854, 1520, 1466, 1350, 1242, 1180, 1034; HRMS (ESI): Calcd for $C_{19}H_{20}N_2O_4$ (MH^+) 341.1501; Found: 341.1504. $[\alpha]_D^{25}$ = – 81.4 (*c* 0.1, CH_2Cl_2). HPLC analysis: 97:3 er [Daicel Chiralpak-IB, *n*-hexane/2-propanol = 94/06), flow rate (0.8 mL/min), *t* (minor) = 15.224 min, *t* (major) = 22.808 min].

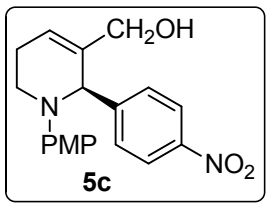
(*R*)-(1-(4-Methoxyphenyl)-2-(3-nitrophenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5b):



5b

Pale yellow viscous liquid, (75 mg, 74% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33–2.47 (m, 2H), 3.10–3.22 (m, 2H), 3.73 (s, 3H), 3.86 (d, J = 12.8 Hz, 1H), 4.01 (d, J = 12.8 Hz, 1H), 5.20 (s, 1H), 6.16 (t, J = 3.1 Hz, 1H), 6.75 (d, J = 9.1 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 7.37 (t, J = 7.9 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 8.02–8.08 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.68, 43.00, 55.40, 61.64, 64.78, 114.24 (2C), 121.24 (2C), 122.41, 123.23, 125.30, 128.76, 135.14, 136.77, 141.61, 143.76, 147.90, 154.34; IR (KBr)/cm^{-1} 3418, 2924, 2847, 1605, 1520, 1458, 1342, 1250, 1188, 1034; HRMS (ESI): Calcd for $C_{19}H_{20}N_2O_4$ (MH^+) 341.1501; Found: 341.1508. $[\alpha]_D^{25}$ = – 173 (*c* 0.5, CH_2Cl_2). HPLC analysis: 94:6 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 29.538 min, *t* (major) = 33.207 min].

(*R*)-(1-(4-Methoxyphenyl)-2-(4-nitrophenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5c):

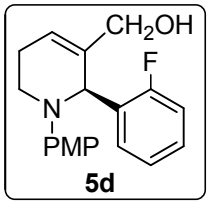


5c

Yellowish viscous oil, (82 mg, 80% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32–2.47 (m, 2H), 3.11–3.22 (m, 2H), 3.74 (s, 3H), 3.85 (d, J = 12.7 Hz, 1H), 3.99 (d, J = 12.8 Hz, 1H), 5.18 (s, 1H), 6.14 (t, J = 3.2 Hz, 1H), 6.75 (d, J = 9.1 Hz, 2H), 6.83 (d, J = 9.1 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 8.07

(d, J = 8.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.79, 42.96, 55.32, 61.74, 66.59, 114.15 (2C), 121.20 (2C), 122.98 (2C), 124.84, 129.48 (2C), 136.81, 143.68, 146.82, 147.80, 154.28; IR (KBr)/cm^{-1} 3446, 2925, 2854,1522, 1468, 1350, 1241, 1180, 1034; HRMS (ESI Calcd for $C_{19}H_{20}N_2O_4$ (MH^+) 341.1501; Found: 341.1495. $[\alpha]_D^{25}$ = – 198 (*c* 1.0, CH_2Cl_2). HPLC analysis: 97:3 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 80/20), flow rate (1.0 mL/min), *t* (minor) = 17.932 min, *t* (major) = 22.037 min].

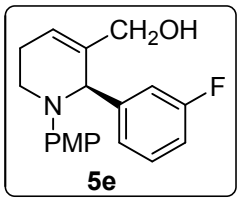
(*S*)-(2-(2-Fluorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5d):



5d

Reddish viscous oil, (57 mg, 61% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17–2.22 (m, 1H), 2.27–2.32 (m, 1H), 3.28–3.31 (m, 2H), 3.74 (s, 3H), 3.94 (s, 2H), 5.48 (s, 1H), 6.11 (t, J = 3.9 Hz, 1H), 6.77 (d, J = 8.9 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 7.17–7.22 (m, 2H), 7.32–7.34 (m, 1H) 7.39–7.41(m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.38, 44.79, 55.37, 57.34, 64.71, 114.08 (2C), 120.67 (2C), 124.84, 126.43, 128.51, 129.81, 129.96, 135.32, 137.64, 138.39, 144.27, 153.89; IR (KBr)/cm^{-1} 3140, 2916, 2850,1660, 1508, 1246, 1178; HRMS (ESI): Calcd for $C_{19}H_{20}FNO_2$ (MH^+) 314.1556; Found: 314.1559. $[\alpha]_D^{25}$ = – 46.1 (*c* 0.8, CH_2Cl_2). HPLC analysis: 98:2 er [Daicel Chiralpak-IB, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 11.835 min, *t* (major) = 14.871 min].

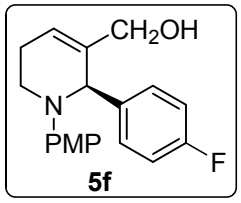
(*R*)-(2-(3-Fluorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5e)



5e

Yellow viscous liquid, (62 mg, 66% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26–2.31 (m, 1H), 2.39–2.47 (m, 1H), 3.18–3.21 (m, 2H), 3.74 (s, 3H), 3.91 (d, J = 12.4 Hz, 1H), 3.99 (d, J = 12.7 Hz, 1H), 5.08 (s, 1H), 6.10 (t, J = 4.3 Hz, 1H), 6.76 (d, J = 9.1 Hz, 2H), 6.86 (d, J = 9.2 Hz, 3H), 6.90–6.92 (m, 2H), 7.14–7.20 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.62, 42.63, 55.44, 61.87, 64.97, 114.15 (2C), 114.33, 115.41, 115.62, 120.88 (2C), 124.39, 124.67, 129.27, 129.35, 137.59, 144.24, 153.99; IR (KBr)/cm^{-1} 3420, 2924, 2848, 1655, 1589, 1247, 1170; HRMS (ESI Calcd for $C_{19}H_{20}FNO_2$ (MH^+) 314.1556; Found: 314.1562. $[\alpha]_D^{25}$ = – 41.3 (*c* 0.6, CH_2Cl_2). HPLC analysis: 81:19 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 17.480 min, *t* (major) = 20.078 min].

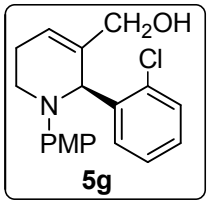
(*R*)-(2-(4-Fluorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5f):



5f

Yellowish viscous liquid, (64 mg, 68% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25–2.26 (m, 1H), 2.39–2.47 (m, 1H), 3.14–3.17 (m, 2H), 3.74 (s, 3H), 3.93 (m, 2H), 5.07 (s, 1H), 6.09 (t, J = 4.4 Hz, 1H), 6.75 (d, J = 9.2 Hz, 2H), 6.84 (d, J = 9.1 Hz, 2H), 6.89 (t, J = 8.7 Hz, 2H), 7.07 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.76, 42.35, 55.43, 61.80, 65.02, 114.10 (2C), 114.62, 114.83, 121.16 (2C), 124.14, 130.35, 130.43, 134.74, 137.93, 144.31, 154.04, 160.83; IR (KBr)/cm^{-1} 3426, 2924, 2854, 1643, 1597, 1512, 1242, 1034, 825, 725; HRMS (ESI): Calcd for $C_{19}H_{20}FNO_2$ (MH^+) 314.1556; Found: 314.1549. $[\alpha]_D^{25}$ = – 101 (*c* 0.2, CH_2Cl_2). HPLC analysis: 83:17 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 18.826 min, *t* (major) = 20.510 min].

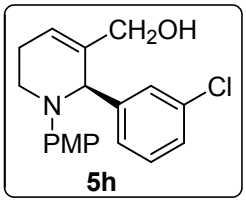
(*S*)-(2-(2-Chlorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5g):



5g

Dark red viscous liquid, (64 mg, 65% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16–2.23 (m, 1H), 2.25–2.34 (m, 1H), 3.28–3.31 (m, 2H), 3.74 (s, 3H), 3.93 (s, 2H), 5.48 (s, 1H), 6.11 (t, J = 3.8 Hz, 1H), 6.77 (d, J = 9.1 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 7.15–7.22 (m, 2H), 7.32–7.34 (m, 1H), 7.37–7.41 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.35, 44.76, 55.38, 57.30, 64.75, 114.07 (C), 120.64 (2C), 124.90, 126.44, 128.53, 129.83, 129.96, 153.33, 137.62, 138.38, 144.25, 153.87; IR (KBr)/cm^{-1} 3418, 2924, 2862, 1659, 1512, 1458, 1250, 1188, 1095, 1034; HRMS (ESI): Calcd for $C_{19}H_{20}ClNO_2$ (MH^+) 330.1261; Found : 330.1255. $[\alpha]_D^{25}$ = – 76.6 (*c* 0.3, CH_2Cl_2,). HPLC analysis: 97:3 er [Daicel Chiralpak-IB, *n*-hexane/2-propanol = 90/10), flow rate (0.6 mL/min), *t* (minor) = 8.278 min, *t* (major) = 11.601 min].

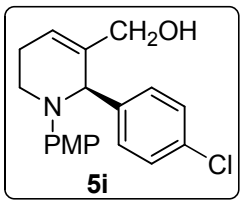
(*R*)-(2-(3-Chlorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5h):



5h

Pale yellow liquid, (67 mg, 68% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (bs, 1H), 2.25–2.30 (m, 1H), 2.40–2.46 (m, 1H), 3.17–3.20 (m, 2H), 3.78 (s, 3H), 3. 89 (d, J = 12.8 Hz, 1H), 3.98 (d, J = 12.8 Hz, 1H), 5.06 (s, 1H), 6.09

(t, J = 3.2 Hz, 1H), 6.76 (d, J = 9.1 Hz, 2H), 6.86 (d, J = 9.1 Hz, 2H), 6.98–7.01 (m, 1H), 7.08–7.13 (m, 1H), 7.15–7.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.47, 42.47, 55.42, 6180, 64.76, 114.14 (2C), 120.87 (2C), 124.36, 127.25, 127.46, 128.64, 129.12, 133.79, 137.33, 141.36, 144.03, 154.01; IR (KBr)/cm^{-1} 3464, 2924, 2947, 1643, 1512, 1242, 1188, 1088, 1034; HRMS (ESI): Calcd for $C_{19}H_{20}ClNO_2$ (MH^+) 330.1261; Found : 330.1267. $[\alpha]_D^{25}$ = – 97.6 (c 0.8, CH_2Cl_2). HPLC analysis: 85:15 er [Daicel Chiralpak-IA, n-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), t (minor) = 17.376 min, t (major) = 19.863 min].

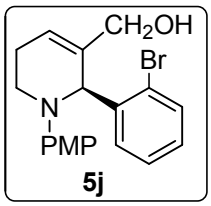


5i

(*R*)-(2-(4-Chlorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5i):

Colorless viscous liquid, (69 mg, 70% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25–2.30 (m, 1H), 2.38–2.46 (m, 1H), 3.12–3.17 (m, 2H), 3.74 (s, 3H), 3.87 (d, J = 13.1 Hz, 1H), 3.95 (d, J = 12.8 Hz, 1H), 5.06 (s, 1H), 6.08 (t, J = 3.2 Hz, 1H), 6.75 (d, J = 9.1 Hz, 2H), 6.84 (d, J = 9.1 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.71, 42.31, 55.38, 61.76, 64.78, 114.08 (2C), 121.09 (2C), 124.11, 127.99 (2C), 130.16 (2C), 133.02, 137.42, 137.60, 144.12, 154.02; IR (KBr)/cm^{-1} 3418, 2916, 2847, 1651, 1597, 1594, 1242, 1188, 1095, 1026; HRMS (ESI): Calcd for $C_{19}H_{20}ClNO_2$ (MH^+) 330.1261; Found : 330.1263. $[\alpha]_D^{25}$ = – 143.2 (c 0.7, CH_2Cl_2). HPLC analysis: 86:14 er [Daicel Chiralpak-IA, n-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), t (minor) = 20.054 min, t (major) = 23.154 min].

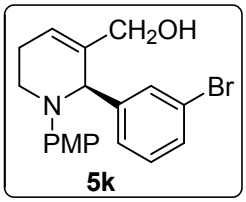
(*S*)-(2-(2-Bromophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5j)



5j

Reddish viscous liquid, (65 mg, 58% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30–2.35 (m, 2H), 3.14–3.19 (m, 1H), 3.23–3.30 (m, 2H), 3.52 (d, J = 13.9 Hz, 1H), 3.60 (d, J = 14.0 Hz, 1H), 3.76 (s, 3H), 5.55 (s, 1H), 5.91 (bs, 1H), 6.82 (d, J = 9.2 Hz, 2H), 6.90 (d, J = 9.1 Hz, 2H), 7.14–7.18 (m, 1H), 7.33–7.39 (m, 1H), 7.53–7.55 (m, 1H), 7.59–7.61 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.36, 45.13, 55.36, 59.75, 64.72, 114.04 (2C), 121.06 (2C), 124.97, 126.17, 127.03, 128.78, 130.19, 133.18, 137.67, 140.09, 144.35, 153.98; IR (KBr)/cm^{-1} 3317, 3055, 2916, 2847, 1512, 1450, 1242, 1180, 1034; HRMS (ESI): Calcd for $C_{19}H_{20}BrNO_2$ (MH^+) 374.0755; Found: 374.0759. $[\alpha]_D^{25}$ = – 32.3 (c 0.6, CH_2Cl_2). HPLC analysis: 98:2 er [Daicel Chiralpak-IB, n-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), t (minor) = 10.465 min, t (major) = 13.302 min].

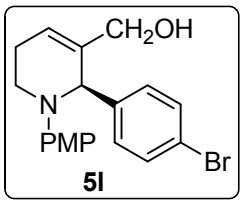
(*R*)-(2-(3-Bromophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5k)



5k

Yellow viscous liquid, (75 mg, 67% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27–2.28 (m, 1H), 2.41–2.48 (m, 1H), 3.19–3.22 (m, 2H), 3.77 (s, 3H), 3.92 (d, J = 12.9 Hz, 1H), 4.01 (d, J = 12.8 Hz, 1H), 5.07 (s, 1H), 6.12 (t, J = 4.2 Hz, 1H), 6.79 (d, J = 9.2 Hz, 2H), 6.88 (d, J = 9.1 Hz, 2H), 7.05–7.12 (m, 2H), 7.34–7.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.44, 42.35, 55.40, 61.75, 64.69, 114.12 (2C), 120.86 (2C), 122.09, 124.34, 127.66, 129.40, 130.34, 131.49, 137.24, 141.57, 144.01, 153.98; IR (KBr)/cm^{-1} 3302, 3055, 2916, 2839, 1566, 1512, 1458, 1242, 1180, 1034; HRMS (ESI): Calcd for $C_{19}H_{20}BrNO_2$ (MH^+) 374.0755; Found: 374.0762. $[\alpha]_D^{25}$ = – 113.3 (*c* 1.5, CH_2Cl_2). HPLC analysis: 90:10 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 17.692 min, *t* (major) = 19.870 min].

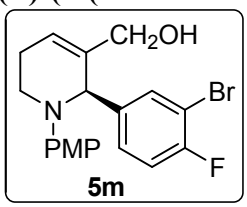
(*R*)-(2-(4-Bromophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5l):



5l

Colorless viscous liquid, (77 mg, 69% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25–2.30 (m, 1H), 2.38–2.46 (m, 1H), 3.13–3.16 (m, 2H), 3.74 (s, 3H), 3.87 (d, J = 12.0 Hz, 1H), 3.96 (d, J = 12.9 Hz, 1H), 5.04 (s, 1H), 6.08 (t, J = 4.2 Hz, 1H), 6.75 (d, J = 9.1 Hz, 2H), 6.83 (d, J = 9.1 Hz, 2H), 6.99 (d, J = 9.6 Hz, 2H), 7.33 (d, J = 9.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.70, 42.31, 55.37, 61.79, 64.70, 114.09 (2C), 121.05 (2C), 121.24, 124.07, 130.51 (2C), 130.91 (2C), 137.52, 137.94, 144.08, 154.01; IR (KBr)/cm^{-1} 3418, 2916, 2908, 1659, 1504, 1242, 1188, 1026, 818; HRMS (ESI): Calcd for $C_{19}H_{20}BrNO_2$ (MH^+) 374.0755; Found: 374.0757. $[\alpha]_D^{25}$ = – 187.5 (*c* 0.8, CH_2Cl_2). HPLC analysis: 92:8 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 21.191 min, *t* (major) = 25.148 min].

(*R*)-(2-(3-Bromo-4-fluorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5m):

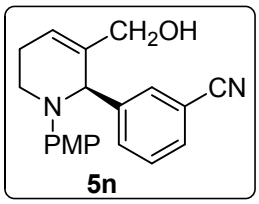


5m

Pale yellow viscous liquid, (83 mg, 71% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26–2.31 (m, 1H), 2.37–2.45 (m, 1H), 3.09–3.17 (m, 2H), 3.75 (s, 3H), 3.86–3.89 (d, J = 12.3 Hz, 1H), 3.98 (d, J = 12.9 Hz, 1H), 5.04 (s, 1H), 6.10 (t, J = 3.0 Hz, 1H),

6.77 (d, J = 9.1 Hz, 2H), 6.84 (d, J = 9.2 Hz, 2H), 6.92–6.96 (m, 1H), 6.98–7.02 (m, 1H), 7.32–7.34 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.56, 42.35, 55.40, 61.31, 64.64, 114.16 (2C), 121.18 (2C), 124.50, 129.45, 129.52, 133.41, 136.46, 137.22, 143.84, 154.21, 156.91, 159.36; IR (KBr)/cm^{-1} 3279, 3047, 2914, 2847, 1558, 1504, 1242, 1180, 1034; HRMS (ESI): Calcd for $C_{19}H_{19}BrFNO_2$ (MH^+) 392.0661; Found: 392.0667. $[\alpha]_D^{25}$ = – 95.4 (c 1.2, CH_2Cl_2). HPLC analysis: 87:13 er [Daicel Chiralpak-IA, n-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), t (minor) = 17.880 min, t (major) = 20.715 min].

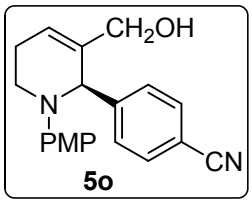
(*R*)-3-(3-(Hydroxymethyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-2-yl)benzonitrile (5n):



5n

Yellow viscous liquid, (71 mg, 74% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29–2.38 (m, 1H), 2.40–2.45 (m, 1H), 3.07–3.21 (m, 2H), 3.74 (s, 3H), 3.82–3.85 (m, 1H), 3.98 (d, J = 13.0 Hz, 1H), 5.11 (s, 1H), 6.13 (t, J = 3.1 Hz, 1H), 6.75 (d, J = 9.1 Hz, 2H), 6.83 (d, J = 9.1 Hz, 2H), 7.28–7.32 (m, 1H), 7.34–7.37 (m, 1H), 7.47–7.50 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.55, 42.70, 55.33, 61.53, 64.50, 111.65, 114.15 (2C), 118.85 121.11 (2C), 124.84, 128.62, 130.92, 132.02, 133.46, 136.75, 140.74, 143.70, 154.20; IR (KBr)/cm^{-1} 3418, 2924, 2947, 2230, 1605, 1512, 1458, 1242, 1188, 1034; HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ (MH^+) 321.1603; Found: 321.1609. $[\alpha]_D^{25}$ = – 143.3 (c 0.8, CH_2Cl_2). HPLC analysis: 88:12 er [Daicel Chiralpak-IA, n-hexane/2-propanol = 85/15), flow rate (0.5 mL/min), t (major) = 16.913 min, t (minor) = 21.912 min].

(*R*)-4-(3-(Hydroxymethyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-2-yl)benzonitrile (5o)

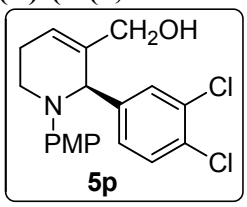


5o

Pale yellow viscous liquid, (74 mg, 78% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28–2.34 (m, 1H), 2.38–2.47 (m, 1H), 3.08–3.17 (m, 2H), 3.74 (s, 3H), 3.84 (d, J = 12.3 Hz, 1H), 3.97 (d, J = 12.9 Hz, 1H), 5.12 (s, 1H), 6.12 (t, J = 3.1 Hz, 1H), 6.75 (d, J = 9.1 Hz, 2H), 6.82 (d, J = 9.1 Hz, 2H), 7.25 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.62, 42.77, 55.28, 61.88, 64.42, 110.77, 114.09 (2C), 118.70, 121.02 (2C), 124.58, 129.36 (2C), 131.55 (2C), 136.78, 143.73, 144.74, 154.13; IR (KBr)/cm^{-1} 3418, 2924, 2862, 2230, 1659, 1512, 1458, 1250, 1188, 1095, 1034; HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ (MH^+) 321.1603; Found: 321.1605. $[\alpha]_D^{25}$ = –

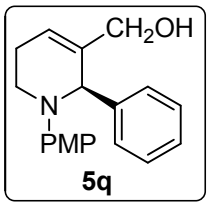
182.4 (*c* 1.5, CH_2Cl_2). HPLC analysis: 90:10 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 80/20), flow rate (0.5 mL/min), *t* (minor) = 16.974 min, *t* (major) = 18.771 min].

(*R*)-(2-(3,4-Dichlorophenyl)-1-(4-methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5p)



5p

Orange liquid, (76 mg, 70% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25–2.30 (m, 1H), 2.36–2.44 (m, 1H), 3.08–3.17 (m, 2H), 3.73 (s, 3H), 3.85 (d, *J* = 12.3 Hz, 1H), 3.97 (d, *J* = 12.9 Hz, 1H), 5.03 (s, 1H), 6.09 (t, *J* = 3.1 Hz, 1H), 6.75 (d, *J* = 9.1 Hz, 2H), 6.83 (d, *J* = 9.1 Hz, 2H), 6.93 (dd, *J* = 8.2 Hz, *J* = 2.0 Hz, 1H), 7.23–7.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.56, 42.53, 55.36, 61.33, 61.51, 114.19 (2C), 121.04 (2C), 124.49, 128.29, 129.70, 130.39, 131.13, 131.86, 137.03, 139.51, 143.81, 154.18; IR (KBr)/cm^{-1} 3410, 3055, 2916, 2839, 1605, 1512, 1458, 1396, 1242, 1188, 1034; HRMS (ESI): Calcd for $C_{19}H_{19}Cl_2NO_2$ (MH^+) 364.0871; Found: 364.0876. $[\alpha]_D^{25}$ = – 193 (*c* 1.3, CH_2Cl_2). HPLC analysis: 93:7 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 17.848 min, *t* (major) = 21.804 min].

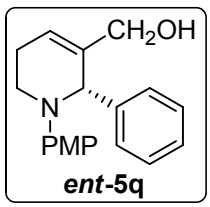


5q

(*R*)-(1-(4-Methoxyphenyl)-2-phenyl-1,2,5,6-tetrahydropyridin-3-yl)methanol (5q):

Yellow viscous oil, (51 mg, 58% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23–2.28 (m, 1H), 2.40–2.45 (m, 1H), 3.17–3.21 (m, 2H), 3.73 (s, 3H), 3.93 (m, 2H), 5.09 (s, 1H), 6.07 (bs, 1H), 6.75 (d, *J* = 9.1 Hz, 2H), 6.86 (d, *J* = 9.1 Hz, 2H), 7.12–7.15 (m, 2H), 7.20–7.22 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.54, 42.22, 55.39, 62.31, 64.94, 114.03 (2C), 120.73 (2C), 123.79, 127.27, 127.88 (2C), 128.87 (2C), 137.95, 139.10, 144.41, 153.73; IR (KBr)/cm^{-1} 3394, 2924, 2854, 1736, 1512, 1458, 1381, 1242, 1180, 1034, 875; HRMS (ESI): Calcd for $C_{19}H_{21}NO_2$ (MH^+) 296.1650; Found: 296.1658. $[\alpha]_D^{25}$ = – 140.5 (*c* 0.5, CH_2Cl_2). HPLC analysis: 85:15 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 88/12), flow rate (0.5 mL/min), *t* (minor) = 13.505 min, *t* (major) = 15.262 min].

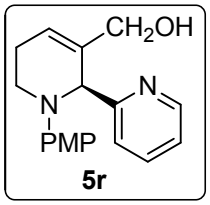
(S)-(1-(4-Methoxyphenyl)-2-phenyl-1,2,5,6-tetrahydropyridin-3-yl)methanol (*ent*-5q):



***ent*-5q**

$[\alpha]_D^{25}$ = + 42.3 (*c* 0.1, CH_2Cl_2). HPLC analysis: 18:82 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 88/12), flow rate (0.5 mL/min), *t* (major) = 13.397 min, *t* (minor) = 15.273 min].

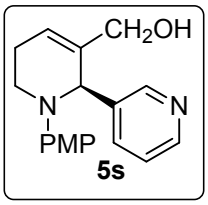
(*S*)-(1-(4-Methoxyphenyl)-2-(pyridin-2-yl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5r):



5r

Dark red viscous liquid, (56 mg, 63% yield), ^{1}H NMR ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33–2.37 (bs, 2H), 3.19–3.25 (m, 1H), 3.34-3.40 (m, 1H), 3.74 (s, 3H), 4.07 (d, J = 12.5 Hz, 1H), 4.14 (d, J = 12.4 Hz, 1H), 5.27 (s, 1H), 5.99 (t, J = 3.9 Hz, 1H), 6.79-6.80 (m, 2H), 6.82-6.83 (m, 2H), 7.16–7.19 (m, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 7.9 Hz, 1H), 8.50 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.81, 43.93, 55.49, 63.71, 65.88, 114.48 (2C), 117.45 (2C), 120.86, 122.50, 124.11, 124.93, 136.86, 137.42, 148.07, 159.26, 161.77; IR (KBr)/cm^{-1} 3294, 3055, 2924, 2839, 1466, 1242, 1034; HRMS (ESI): Calcd for $C_{18}H_{20}N_2O_2$ (MH^+) 297.1603; Found: 297.1608. $[\alpha]_D^{25}$ = – 111.5 (*c* 0.8, CH_2Cl_2). HPLC analysis: 91:9 er [Daicel Chiralpak-IB, *n*-hexane/2-propanol = 85/15), flow rate (0.5 mL/min), *t* (minor) = 22.747 min, *t* (major) = 28.847 min].

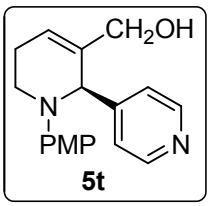
(*R*)-(1-(4-Methoxyphenyl)-2-(pyridin-3-yl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5s)



5s

Red viscous liquid, (64 mg, 72% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27–2.32 (m, 1H), 2.40–2.50 (m, 1H), 3.09–3.17 (m, 2H), 3.73 (s, 3H), 3.87 (d, J = 13.0 Hz, 1H), 3.99 (d, J = 12.9 Hz, 1H), 5.12 (s, 1H), 6.13 (s, 1H), 6.75 (d, J = 9.0 Hz, 2H), 6.84 (d, J = 9.1 Hz, 2H), 7.13–7.15 (m, 1H), 7.42–7.44 (m, 1H), 8.32 (s, 1H), 8.41 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.70, 42.52, 55.37, 60.18, 64.41, 141.18 (2C), 121.29 (2C), 123.07, 124.44, 135.00, 136.63, 136.92, 143.86, 148.23, 149.69, 154.24; IR (KBr)/cm^{-1} 3410, 2924, 2862, 1651, 1582, 1512, 1242, 1034; HRMS (ESI): Calcd for $C_{18}H_{20}N_2O_2$ (MH^+) 297.1603; Found: 297.1605. $[\alpha]_D^{25}$ = – 103 (*c* 0.4, CH_2Cl_2). HPLC analysis: 81:19 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 80/20), flow rate (1.0 mL/min), *t* (minor) = 19.082 min, *t* (major) = 22.508 min].

(*R*)-(1-(4-Methoxyphenyl)-2-(pyridin-4-yl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5t)

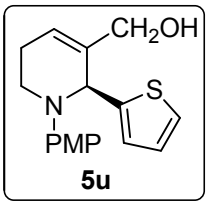


5t

Yellow viscous liquid, (67 mg, 76% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26–2.31 (m, 1H), 2.39–2.47 (m, 1H), 3.08–3.22 (m, 2H), 3.73 (s, 3H), 3.87 (d, J = 12.7 Hz, 1H), 3.98 (d, J = 12.8 Hz, 1H), 5.08 (s, 1H), 6.12 (t, J = 3.2 Hz, 1H), 6.74 (d, J = 9.1 Hz, 2H), 6.83 (d, J = 9.1 Hz, 2H), 7.05 (d, J = 6.0 Hz, 2H), 8.41 (d, J = 5.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.60, 42.79, 55.38, 61.26, 64.38, 114.17 (2C),

115.35, 118.22, 120.82 (2C), 123.89, 124.57, 136.73, 143.87, 148.52, 149.08, 154.08; IR (KBr)/cm^{-1} 3711, 3040, 2916, 2847, 1512, 1458, 1260, 1188; HRMS (ESI): Calcd for $C_{18}H_{20}N_2O_2$ (MH^+) 297.1603; Found: 297.1611. $[\alpha]_D^{25}$ = – 105.9 (*c* 0.7, CH_2Cl_2). HPLC analysis: 96:4 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 80/20), flow rate (1.0 mL/min), *t* (minor) = 20.044 min, *t* (major) = 24.477 min].

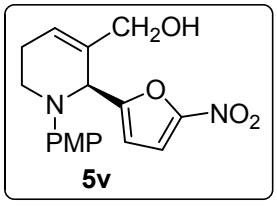
(*S*)-(1-(4-Methoxyphenyl)-2-(thiophen-2-yl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5u)



5u

Reddish viscous oil, (48 mg, 53% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24–2.29 (m, 1H), 2.43–2.52 (m, 1H), 3.21–3.24 (m, 2H), 3.75 (s, 3H), 4.02–4.09 (m, 2H), 5.41 (s, 1H), 6.03–6.05 (m, 1H), 6.66–6.68 (m, 1H), 6.78 (d, *J* = 9.2 Hz, 2H), 6.83–6.84 (m, 1H), 6.87 (d, *J* = 9.2 Hz, 2H), 7.12–7.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.98, 41.06, 55.41, 57.89, 64.97, 114.13 (2C), 120.69 (2C), 123.85, 124.81, 126.12, 126.64, 138.29, 141.57, 144.02, 153.97; IR (KBr)/cm^{-1} 3493, 2924, 2854, 1651, 1512, 1242, 1034; HRMS (ESI): Calcd for $C_{17}H_{19}NO_2S$ (MH^+) 302.1214; Found: 302.1219. $[\alpha]_D^{25}$ = – 123 (*c* 0.2, CH_2Cl_2). HPLC analysis: 86:14 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 90/10), flow rate (0.5 mL/min), *t* (minor) = 30.484 min, *t* (major) = 36.166 min].

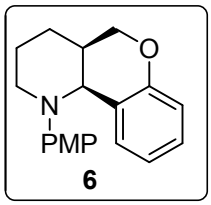
(*S*)-(1-(4-Methoxyphenyl)-2-(5-nitrofuran-2-yl)-1,2,5,6-tetrahydropyridin-3-yl)methanol (5v)



5v

Dark red viscous liquid, (62 mg, 63% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28–2.35 (m, 2H), 3.22–3.25 (m, 2H), 3.64 (s, 2H), 3.77 (s, 3H), 4.11 (s, 1H), 5.86 (bs, 1H), 6.85 (d, *J* = 9.0 Hz, 2H), 6.98 (m, 2H), 7.27–7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.03, 41.22, 55.48, 57.96, 65.05, 114.22 (2C), 120.89 (2C), 123.91, 124.84, 126.16, 126.63, 138.40, 141.83, 144.13, 154.04; IR (KBr)/cm^{-1} 3420, 2924, 2848, 1512, 1458, 1404, 1250, 1188; HRMS (ESI): Calcd for $C_{17}H_{18}N_2O_5$ (MH^+) 331.1294; Found: 331.1298. $[\alpha]_D^{25}$ = – 146 (*c* 0.4, CH_2Cl_2). HPLC analysis: 86:14 er [Daicel Chiralpak-IA, *n*-hexane/2-propanol = 85/15), flow rate (0.5 mL/min), *t* (minor) = 25.996 min, *t* (major) = 30.493 min].

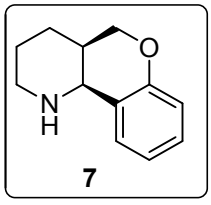
(4a*R*,10b*S*)-1-(4-Methoxyphenyl)-1,3,4,4a,5,10b-hexahydro-2*H*-chromeno[4,3-*b*]pyridine (6)



6

To a stirred solution of compound **5j** (160 mg, 0.43 mmol) in dry EtOH (4 mL) was added 10% Pd/C (10 wt %) and purged with H_2 and stirred under H_2 at room temperature for 4 hrs. Reaction mixture was filtered through celite and washed with ethanol. Solvent was evaporated under vacuo and crude material was used for further oxidation without purification at this stage. This crude material was taken in DMF (3.0 mL) and added $Pd(OAc)_2$ (18 mg, 20 mol%) and KO^{t}Bu (94 mg, 0.42 mmol) and PPh_3 (44 mg, 0.4 equivalents) and degassed the reaction mixture with nitrogen for 20 minutes. This reaction mixture was heated at 110 ^{o}C for 4 hrs and monitored by TLC. The reaction was quenched with saturated $NaHCO_3$ solution (5.0 mL) and extracted with EtOAc (2 × 8 mL). The combined organic layer was washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure to give crude mass which was purified by silica gel column chromatography by using hexane:EtOAc, gave **6** (62 mg, 61% yield) as colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47–1.59 (m, 1H), 1.84–1.87 (m, 2H), 2.03–2.07 (m, 1H), 2.77 (m, 1H), 3.29–3.40 (m, 3H), 3.66 (s, 3H), 4.31 (d, J = 3.9 Hz, 1H), 6.63 (d, J = 9.1 Hz, 2H), 6.94–7.00 (m, 3H), 7.08 (m, 1H), 7.13–7.16 (m, 1H), 7.52–7.54 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.85, 27.62, 47.45, 55.15, 58.37, 61.89, 64.56, 113.65 (2C), 125.39 (2C), 127.11, 127.80, 128.61 (2C), 129.95 (2C), 133.70 (2C); IR (KBr)/cm^{-1} 2932, 1597, 1298, 1180, 1034; HRMS (ESI): Calcd for $C_{19}H_{21}NO_2$ (MH^+) 296.1650; Found: 296.1655. $[\alpha]_D^{25}$ = – 31.7 (*c* 0.4, CH_2Cl_2).

(4a*R*,10b*S*)-1,3,4,4a,5,10b-Hexahydro-2*H*-chromeno[4,3-*b*]pyridine (7)

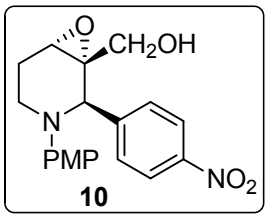


7

To a stirred solution of ceric ammonium nitrate (CAN) (441 mg, 0.8 mmol) in distilled H_2O (2.0 mL) at 0 °C was added compound **6** (95 mg, 0.32 mmol) in CH_3CN (3.0 mL) dropwise for 10 minutes. This reaction mixture was further stirred at rt for 1 hr and monitored by TLC. Once, compound **6** was consumed completely, reaction was quenched with saturated $NaHCO_3$ (5.0 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The crude mas was purified through a small pad of silica gel column using hexane:acetone as eluting solvent, afforded **7** (46 mg, 75% yield) as colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41–1.52 (m, 2H), 2.02–2.07 (m, 2H), 2.62 (s, 1H), 2.76–2.83 (m, 1H), 3.16–3.20 (m, 1H), 3.27–3.38 (m, 2H), 3.58–3.65 (m, 1H), 4.07 (d, J = 3.8 Hz, 1H), 7.18–7.22 (m, 1H), 7.28–7.30 (m, 1H), 7.35 (dd, J = 7.9 Hz, J = 1.3 Hz, 1H), 7.61 (dd, J = 7.7 Hz, J =

1.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.31, 28.04, 48.15, 58.59, 64.95, 70.16, 125.23, 128.05, 128.56, 130.85, 132.36, 156.15; IR (KBr)/cm^{-1} 3433, 2932, 1597, 1350, 1103; HRMS (ESI): Calcd for $C_{12}H_{15}NO$ (MH^+) 190.1232; Found: 190.1235 $[\alpha]_D^{25}$ = – 29.2 (*c* 0.1, CH_2Cl_2).

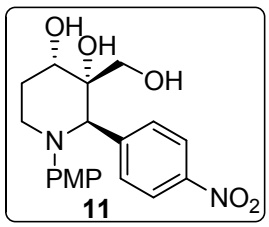
((1*S*,2*R*,6*S*)-3-(4-Methoxyphenyl)-2-(4-nitrophenyl)-7-oxa-3-azabicyclo[4.1.0] heptan-1-yl)methanol (10)



10

To a stirred solution of compound **5c** (64 mg, 0.19 mmol) in CH_2Cl_2 (2.0 mL) at 0 °C was added *m*-CPBA (56 mg, 0.38 mmol) predissolved in CH_2Cl_2 (1.0 mL) through syringe. This reaction mixture was further stirred for 3 hr at the same temperature and monitored by TLC. Once, compound **5c** was consumed, reaction was stirred with $NaHCO_3$ solution (3.0 mL, 10 mol % sol.) for 10 minutes. This reaction mixture was extracted with CH_2Cl_2 (5.0 mL) and combined organic layer was washed with brine solution and dried over Na_2SO_4. The crude mass after concentrated under vacuo was purified through column chromatography by unsing hexane/EtOAc as eluting solvents, which afford compound **10** (50 mg, 75% yield) as a colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (d, *J* = 4.2 Hz, 1H), 3.23 (d, *J* = 11.6 Hz, 1H), 3.44 (d, *J* = 11.7 Hz, 1H), 3.69–3.78 (m, 6H), 4.63–4.70 (m, 1H), 5.02 (s, 1H), 5.40 (s, 1H), 6.68 (d, *J* = 9.4 Hz, 2H), 7.03 (d, *J* = 8.9 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.84–7.95 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.17, 32.70, 43.34, 55.70, 58.15, 69.66, 72.58, 114.92 (2C), 121.97 (2C), 123.75 (2C), 130.25 (2C), 137.58, 144.45, 147.76, 155.05; IR (KBr)/cm^{-1} 3433, 2916, 2854, 1713, 1574, 1381, 1257, 1080, 756; HRMS (ESI): Calcd for $C_{19}H_{20}N_2O_5$ (MH^+) 357.1450; Found: 357.1455. $[\alpha]_D^{25}$ = + 43.8 (*c* 0.2, CH_2Cl_2).

(2*R*,3*S*,4*S*)-3-(Hydroxymethyl)-1-(4-methoxyphenyl)-2-(4-nitrophenyl) piperidine-3,4-diol (11)

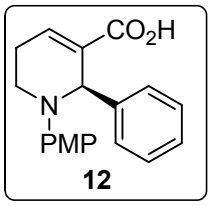


11

To a stirred solution of compound **5c** (60 mg, 0.18 mmol) in acetone (2.5 mL) and H_2O (0.5 mL) was added 4-Methylmorpholine *N*-oxide (NMO) (32 mg, 0.27 mmol) and OsO_4 (20 mol %, 1.76 mL, 0.02 M solution in *tert*-BuOH). This reaction mixture was stirred at room temperature for 12 hrs and monitored by TLC. The reaction mixture was evaporated under reduced pressure, once **6c** was completely consumed. The resulting mass was stirred with EtOAc (10 ml) and saturated $NaHCO_3$ (8.0 mL) for 10 minutes. Organic layer was separated and the aqueous

layer was again extracted with EtOAc (2 × 10 mL). The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure after filtration. The resulting mass was purified through column chromatography using hexane/EtOAc as eluting solvents, which afforded **11** (42 mg, 65 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.94–1.98 (m, 1H), 2.27–2.35 (m, 1H),3.11–3.21 (m, 2H), 3.56 (d, J = 11.6 Hz, 1H), 3.67 (s, 3H), 3.73 (bs, 1H), 3.75–3.79 (m, 1H), 4.19 (t, J = 3.7 Hz, 1H), 4.65 (s, 1H), 6.65 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 8.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.44, 51.47, 55.22, 63.94, 67.55, 69.20, 73.56, 114.14 (2C), 122.67 (2C), 125.11 (2C), 130.69 (2C), 144.11, 145.21, 146.74, 156.02; IR (KBr)/cm^{-1} 3441, 2939, 1597, 1520, 1350, 1250, 1103; HRMS (ESI): Calcd for $C_{19}H_{22}N_2O_6$ (MH^+) 375.1556; Found: 375.1560. $[\alpha]_D^{25}$ = – 61.5 (*c* 0.15, CH_2Cl_2).

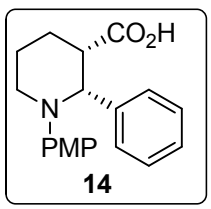
(*R*)-1-(4-Methoxyphenyl)-2-phenyl-1,2,5,6-tetra-hydropyridine-3-carboxylic acid (12)



12

To a stirred solution of compound **5q** (81 mg, 0.2 mmol) in acetonitrile (1.5 mL) and H_2O (0.5 mL) at 0 °C, was added slowly a freshly prepared solution (1.5 mL) of oxidizing agents [*prepared through reported procedure,*[26] *(2.3 mg of CrO_3 and 1.14 grams of H_5IO_6), in H_2O (12.0 mL)*] over a period of 30 minutes. The combined mixture was further stirred for additional 1 hr at rt and monitored by the TLC. The reaction was extracted with CH_2Cl_2 (2 × 10 mL), once **5q** was over. The combined organic fractions are passed through a small pad of Na_2SO_4 and concentrated under reduced pressure. The crude mass was purified through preparative TLC technique by eluting with CH_2Cl_2, to afford **12** (57 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (m, 1H), 2.60–2.73 (m, 1H), 3.20–3.28 (m, 1H), 3.30–3.35 (m, 1H), 3.76 (s, 3H), 5.23 (s, 1H), 6.12 (s, 1H), 6.76 (d, J = 9.1 Hz, 2H), 6.89 (d, J = 9.1 Hz, 2H), 7.01 (dd, J = 8.0, 1.4 Hz, 2H), 7.18–7.26 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.65, 44.12, 55.54, 63.54, 114.61 (2C), 123.49 (2C), 127.98, 128.67, 129.16, 130.46, 131.40, 131.74, 133.31, 134.18, 141.74, 160.01, 171.00; IR (KBr)/cm^{-1} 3441-3061 (br), 2939, 1690, 1582, 1512, 1126; HRMS (ESI): Calcd for $C_{19}H_{19}NO_3$ (MH^+) 310.1443; Found: 310.1439. $[\alpha]_D^{25}$ = – 127.4 (*c* 0.25, CH_2Cl_2).

(2*S*,3*R*)-1-(4-Methoxyphenyl)-2-phenylpiperidine-3-carboxylic acid (14)

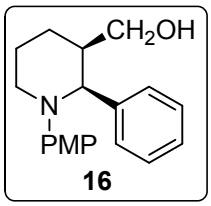


14

To a stirred solution of compound *ent*-**5q** (96 mg, 0.32 mmol) in dry EtOH (4 mL) was added 10% Pd/C (10 wt %) and purged with H_2 and stirred under H_2 at room temperature for 4 hrs. Reaction mixture was filtered through celite and

washed with ethanol. Solvent was evaporated under vacuo and crude material was used for further oxidation without purification at this stage. The oxidation of crude saturated *syn*-alcohol to corresponding acid was carried out by following the previous procedure, similar to compound **12**, to afford **14** (66 mg, 66% yield) after two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86–1.94 (m, 1H), 2.01–2.08 (m, 2H), 3.25–3.30 (m, 2H), 3.43–3.46 (m, 2H), 3.66 (s, 3H), 3.92 (d, J = 3.9 Hz, 1H), 6.63 (d, J = 9.1 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H), 7.15 (m, 3H), 7.38–7.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.68, 27.19, 29.68, 42.65, 55.24, 64.90, 113.85 (2C), 124.83, 127.32, 127.90 (2C), 128.28, 128.73, 131.23, 132.44, 135.92, 141.29, 170.16; IR (KBr)/cm^{-1} 3433–3063 (br), 2939, 1690, 1589, 1173, 1034; HRMS (ESI): Calcd for $C_{19}H_{21}NO_3$ (MH^+) 312.1599; Found: 312.1592 $[\alpha]_D^{25}$ = + 49.4 (*c* 0.1, CH_2Cl_2).

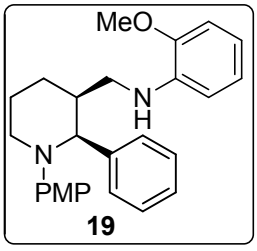
(2*S*,3*R*)-1-(4-Methoxyphenyl)-2-phenylpiperidin-3-yl)methanol (16)



16

Compound **5q** (140 mg, 0.32 mmol), was reduced by following previous procedure and purified through column chromatography to afford **16** as colorless viscous liquid with 90% yield (126 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62–1.69 (m, 2H), 1.83 (d, J = 6.4 Hz, 2H), 2.61–2.70 (m, 2H), 3.00–3.09 (m, 2H), 3.50–3.55 (m, 2H), 3.75 (s, 3H), 3.76–3.83 (m, 1H), 6.56 (d, J = 9.0 Hz, 2H), 6.78 (d, J = 8.9 Hz, 2H), 7.16–7.22 (m, 3H), 7.29 (t, J = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.51, 27.42, 45.96, 55.18, 56.60, 65.27, 67.46, 113.66 (2C), 125.11, 126.72 ,128.02 (2C) ,128.47 (2C), 139.24 , 142.13, 146.05, 155.21; HRMS (ESI): Calcd for $C_{19}H_{23}NO_2$ (MH^+) 298.1808, Found: 298.1813. $[\alpha]_D^{25}$ = – 56.3 (*c* 0.1, CH_2Cl_2).

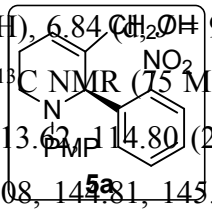
2-Methoxy-N-(((2*S*,3*S*)-1-(4-methoxyphenyl)-2-phenylpiperidin-3-yl)methyl) aniline (19)

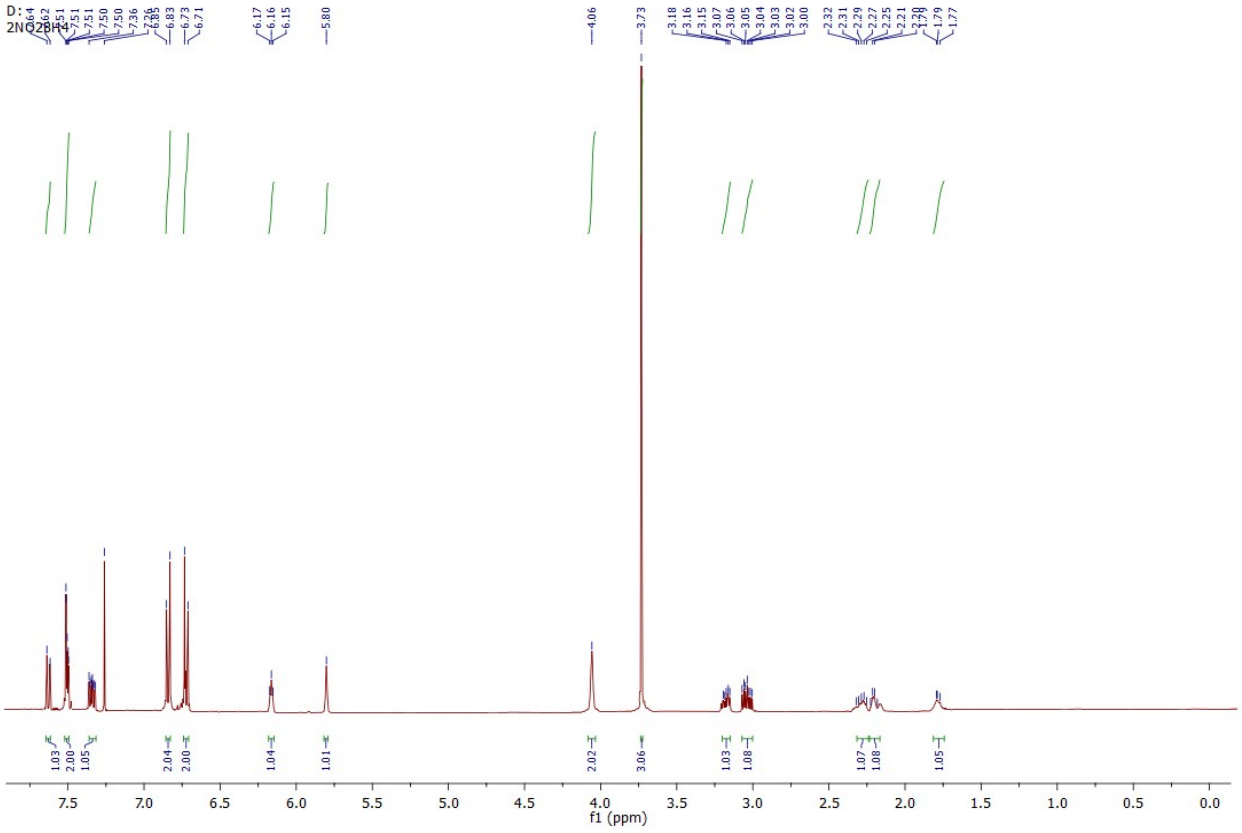


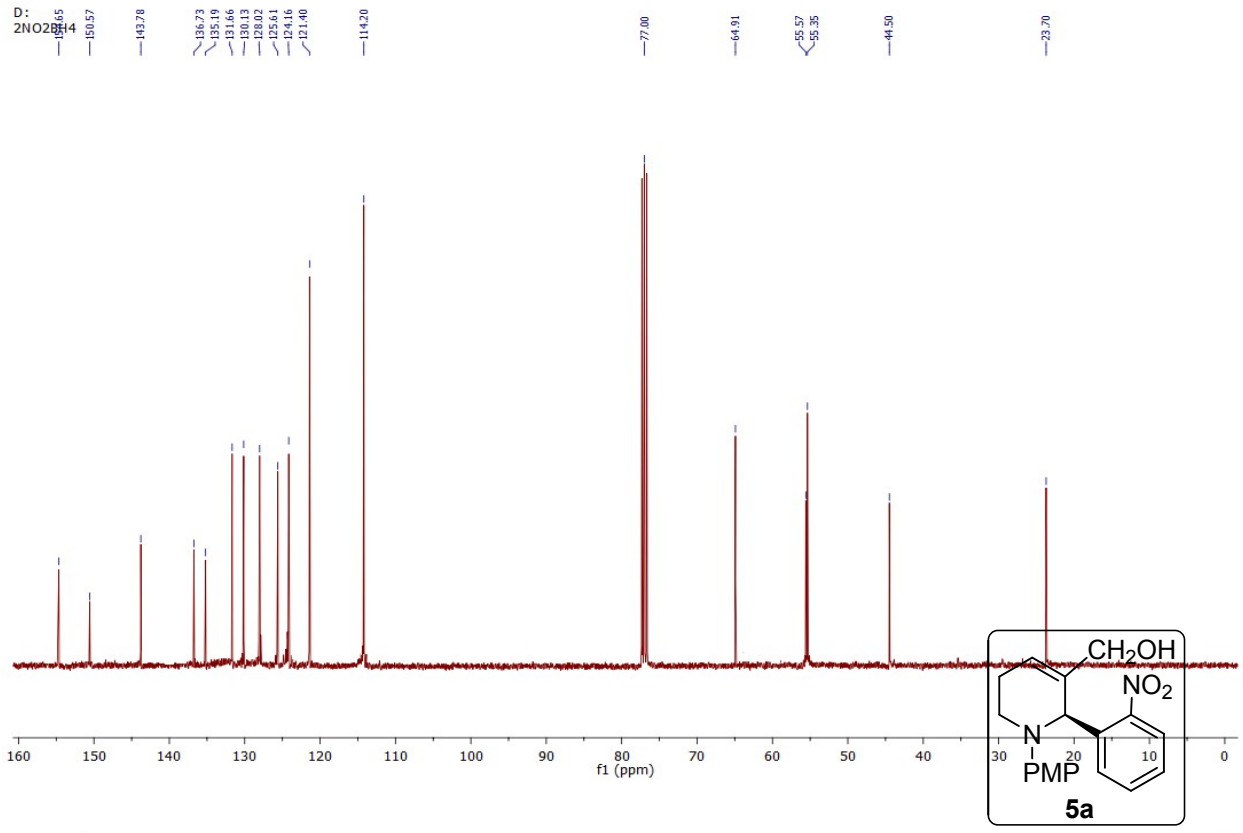
19

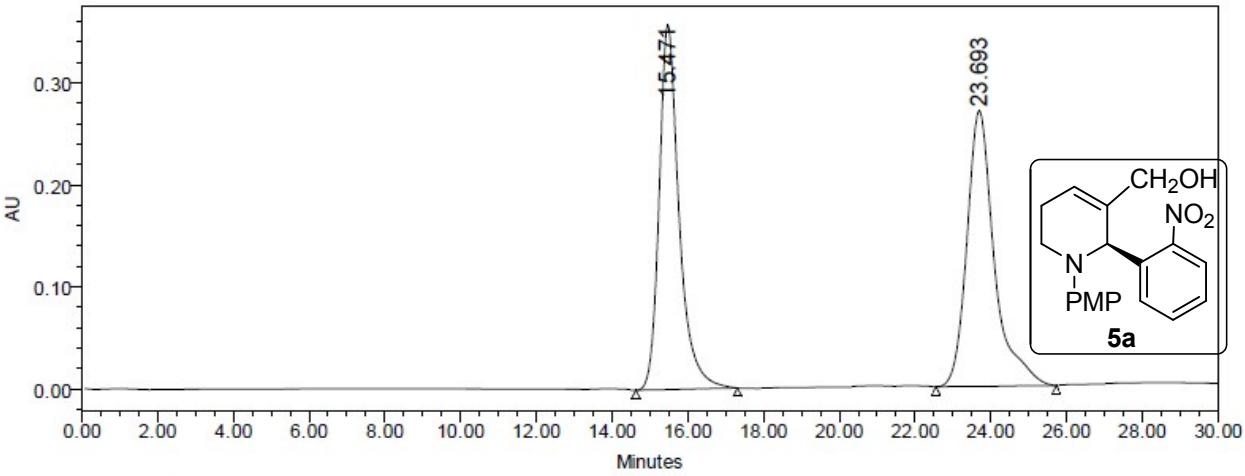
To a stirred solution of **20** (90 mg, 0.3 mmol) in dry CH_2Cl_2 (2.0 mL) at rt was added Et_3N (168 µL, 1.2 mmol) and TsCl (69 mg, 0.36 mmol) in dry CH_2Cl_2 (1.5 mL) by syringe. The resulting mixture was further stirred for 6 hrs at the same temperature and monitored by TLC. The reaction was quenched with saturated $NaHCO_3$ (3.0 mL) and extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in reduced pressure to give crude product, which was used further without isolation. The crude mass was taken in dry EtOH (3 mL) and added *o*-anisidine **18** (74 mg, 0.6 mmol) and further refluxed for additional 4 hrs. Once the reaction is over by TLC, EtOH was evaporated under reduced pressure and resulting residue was purified by column chromatography to afforded **19** (83 mg, 68% yield) as colorless

viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58–1.75 (m, 4H), 2.10–2.13 (m, 1H), 2.93–3.00 (m, 1H), 3.12–3.16 (m, 1H), 3.49–3.57 (m, 2H), 3.78 (s, 3H), 3.86 (s, 3H), 5.04 (d, J = 3.6, 1H), 6.47–6.49 (m, 1H), 6.56–6.60 (m, 1H), 6.72–6.76 (m, 2H), 6.78–6.81 (m, 2H), 6.84 (d, J = 9.2, 2H), 6.91(d, J = 9.2 Hz, 2H), 6.99–7.03 (m, 1H), 7.14 (d, J = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.28, 24.51, 31.47, 42.12, 46.55, 55.39, 55.75, 56.69, 110.37, 113.62, 114.80 (2C), 115.00, 115.94, 117.00, 118.46, 120.11, 121.03, 127.61 (2C), 128.07, 136.08, 144.81, 145.62, 147.28, 151.61; IR (KBr)/cm^{-1} 3393, 2932, 2831, 1598, 1512, 1366, 1180, 1034; Calcd for $C_{26}H_{30}N_2O_2$ (MH^+) 403.2385; Found: 403.2389. $[\alpha]_D^{25}$ = – 54.6 (*c* 0.15, CH_2Cl_2).









Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8363; Processing Method: 2 NO2 RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

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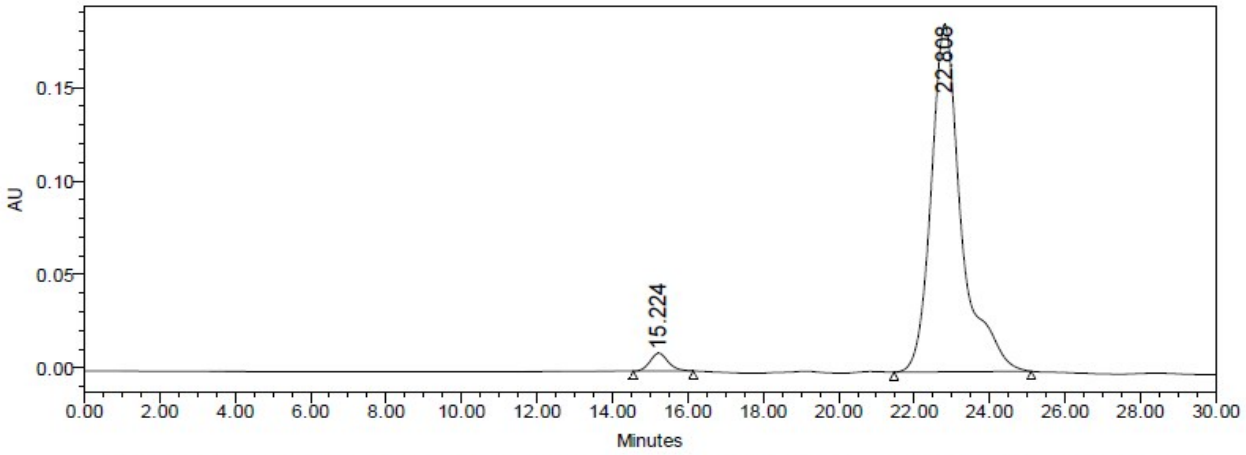

Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8361; Processing Method: 2 NITRO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

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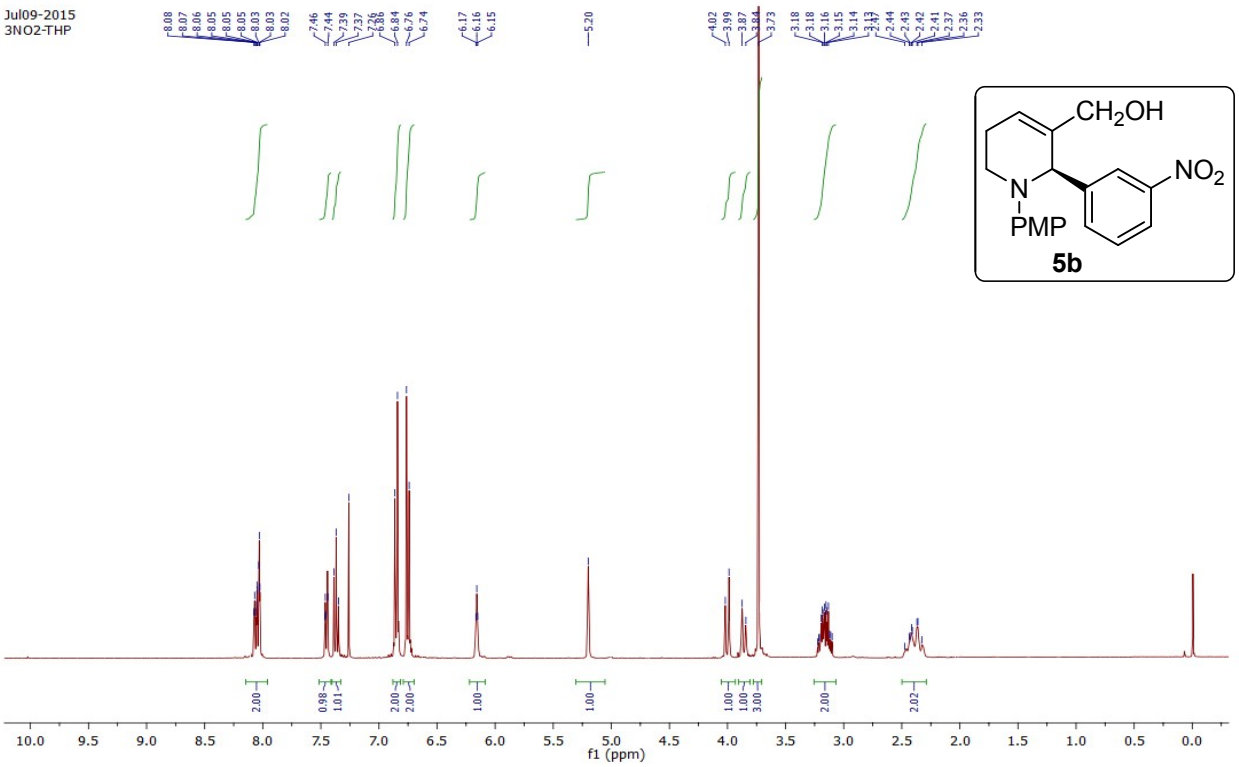

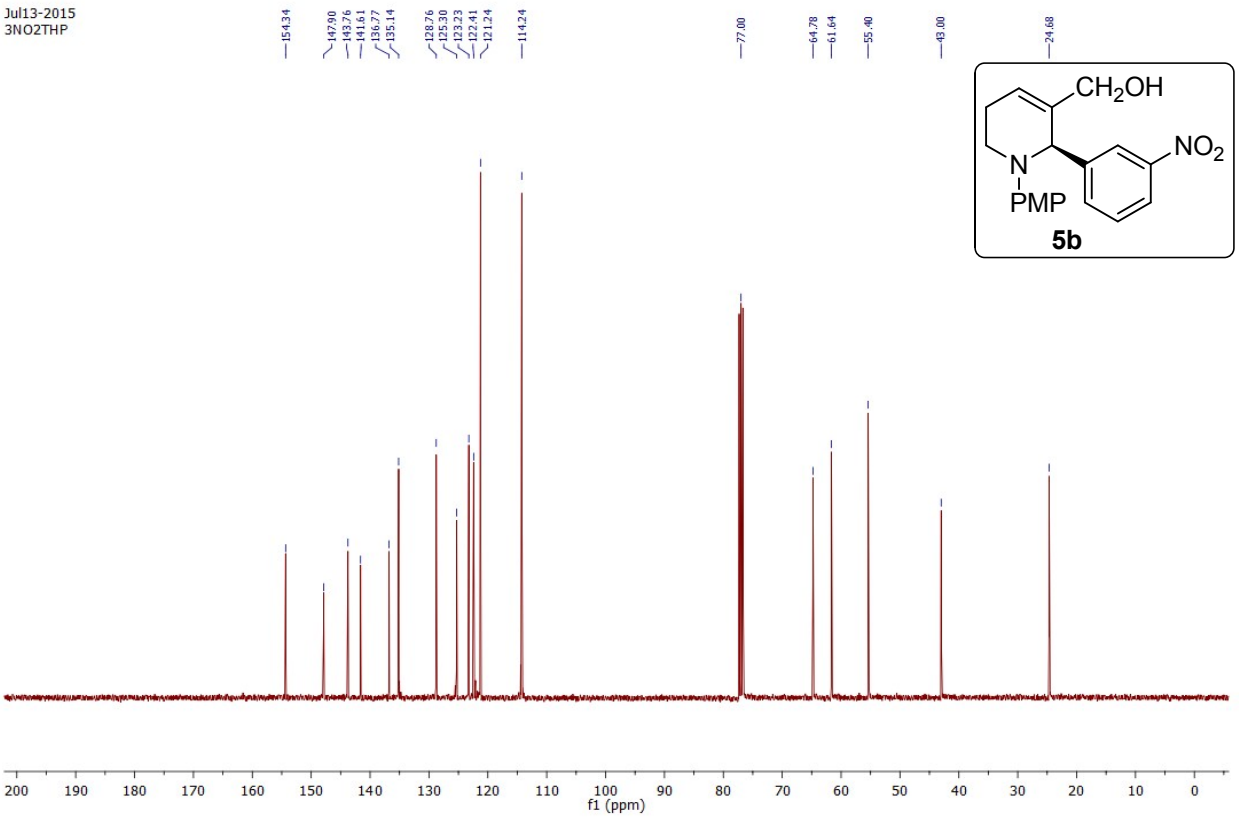

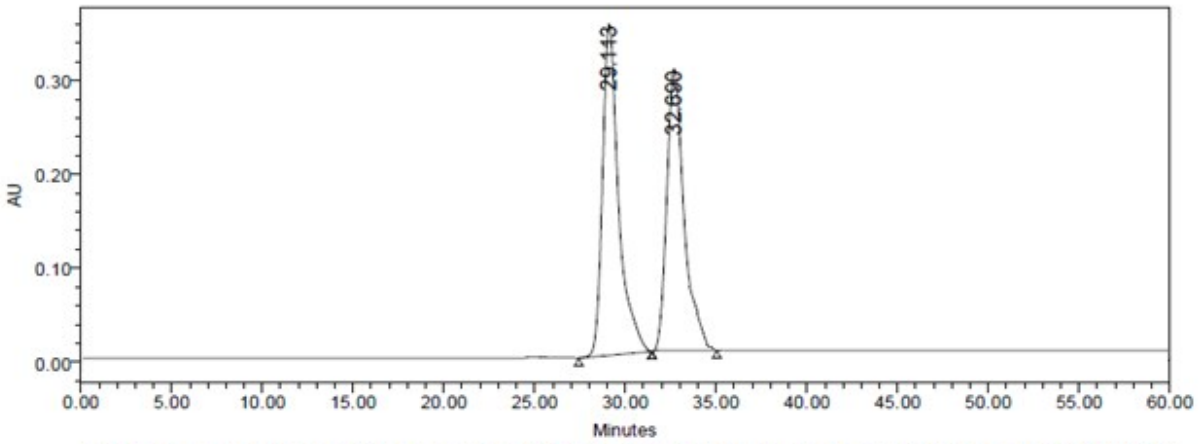

Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7898; Processing Method: 3 NITRO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

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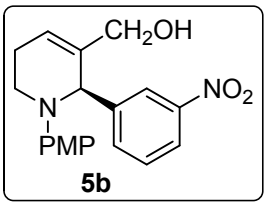

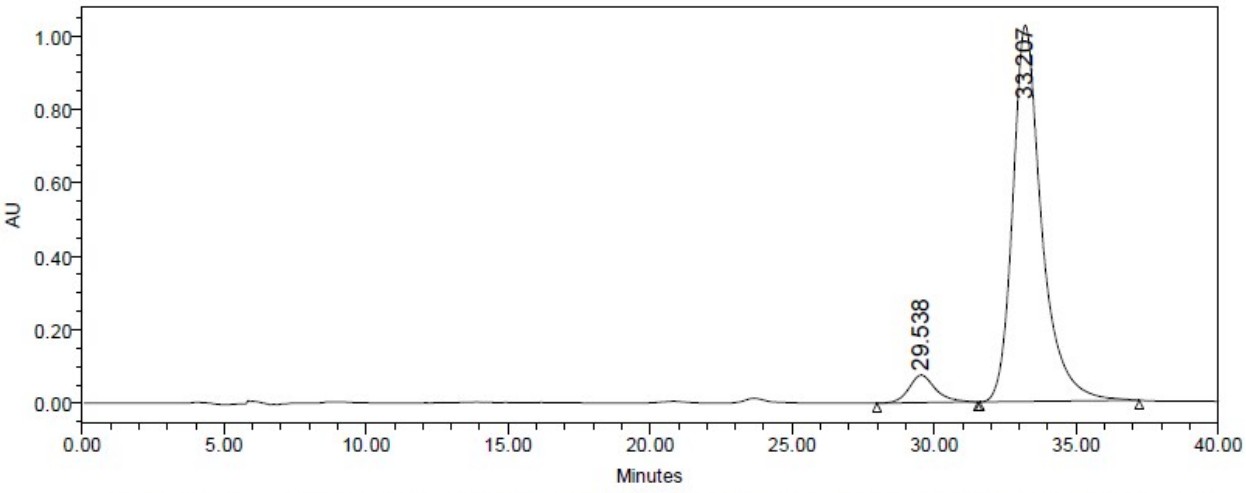

Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7896; Processing Method: 3 NITRO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

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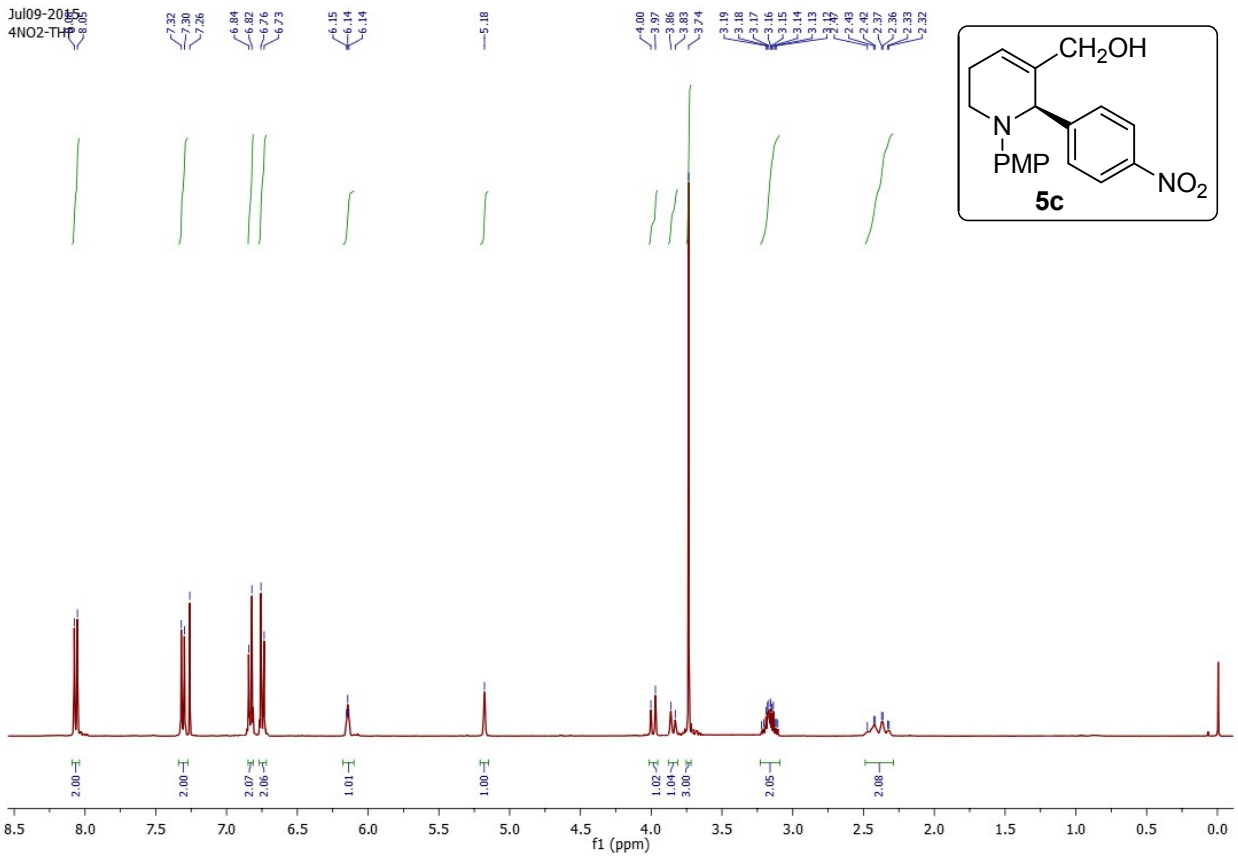
Jul09-2015
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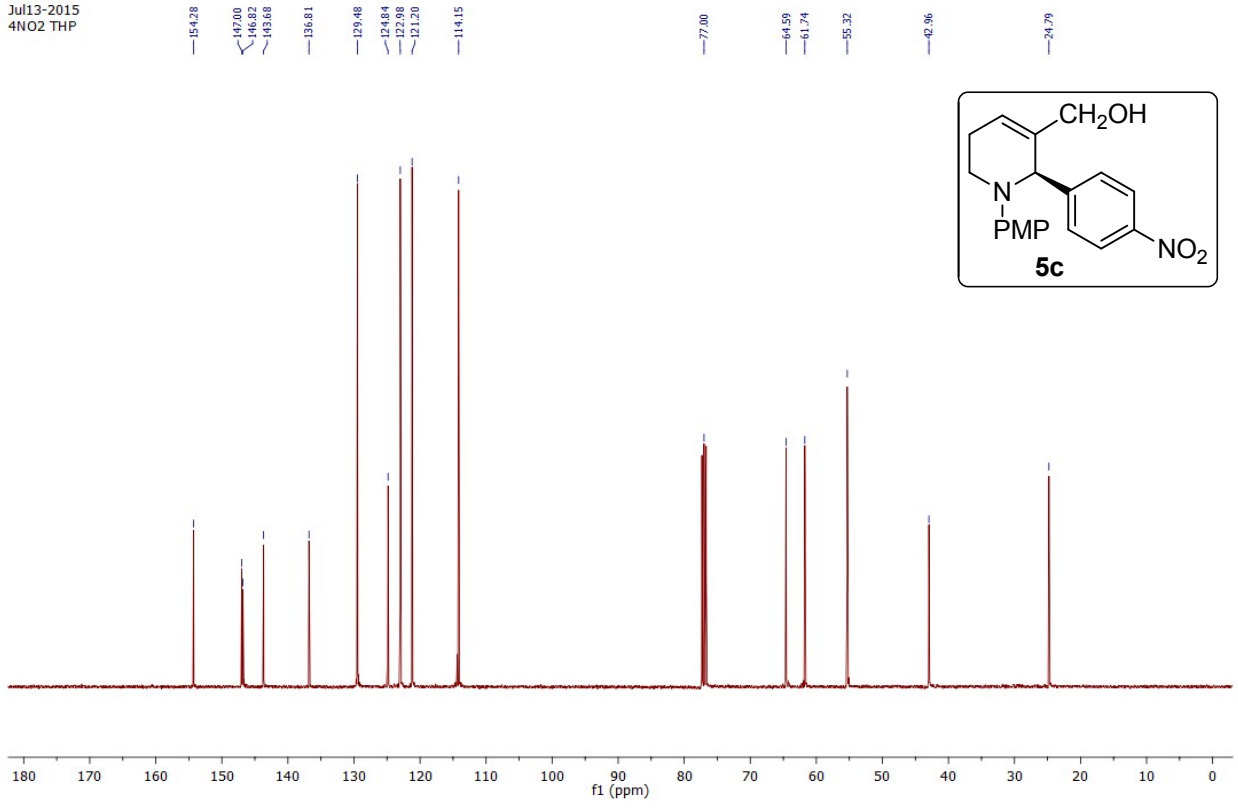
CH2OH
N
PMP
NO2
5c
f1 (ppm)


Jul13-2015
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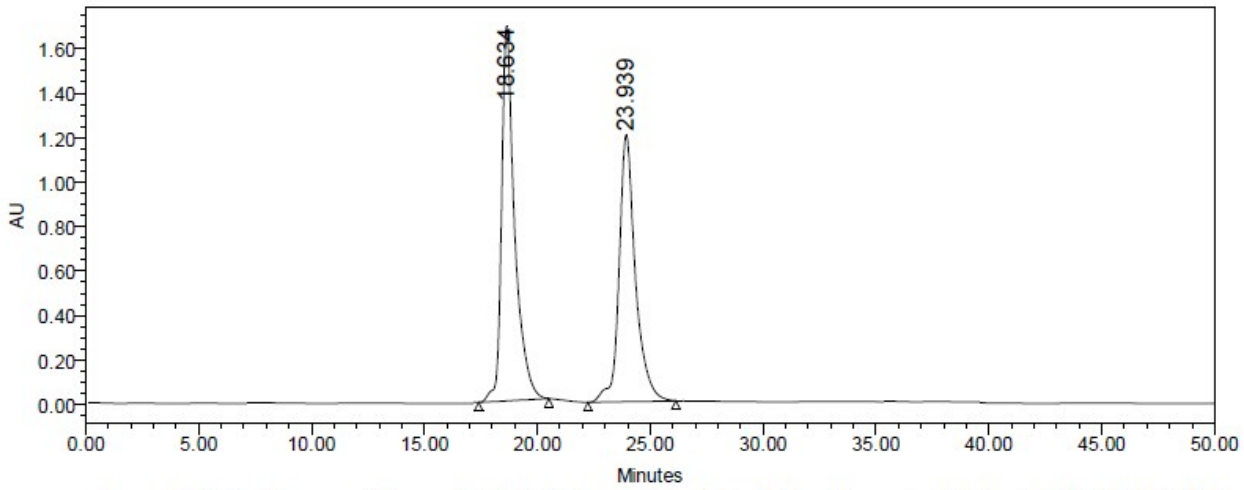
PMP
NO2
5c
f1 (ppm)



Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7863; Processing Method: 4 NITRO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

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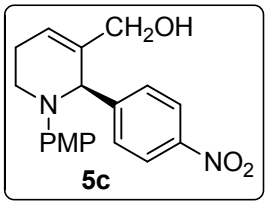
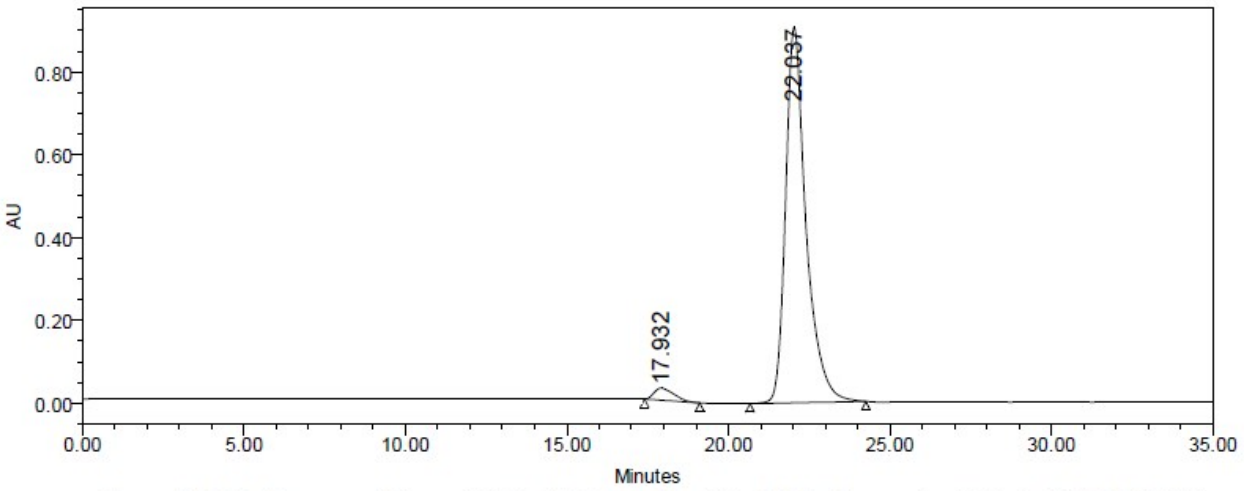
1	PDA 250.0 nm	18.634	67961973	52.87	1684220
2	PDA 250.0 nm	23.939	60575125	47.13	1200481



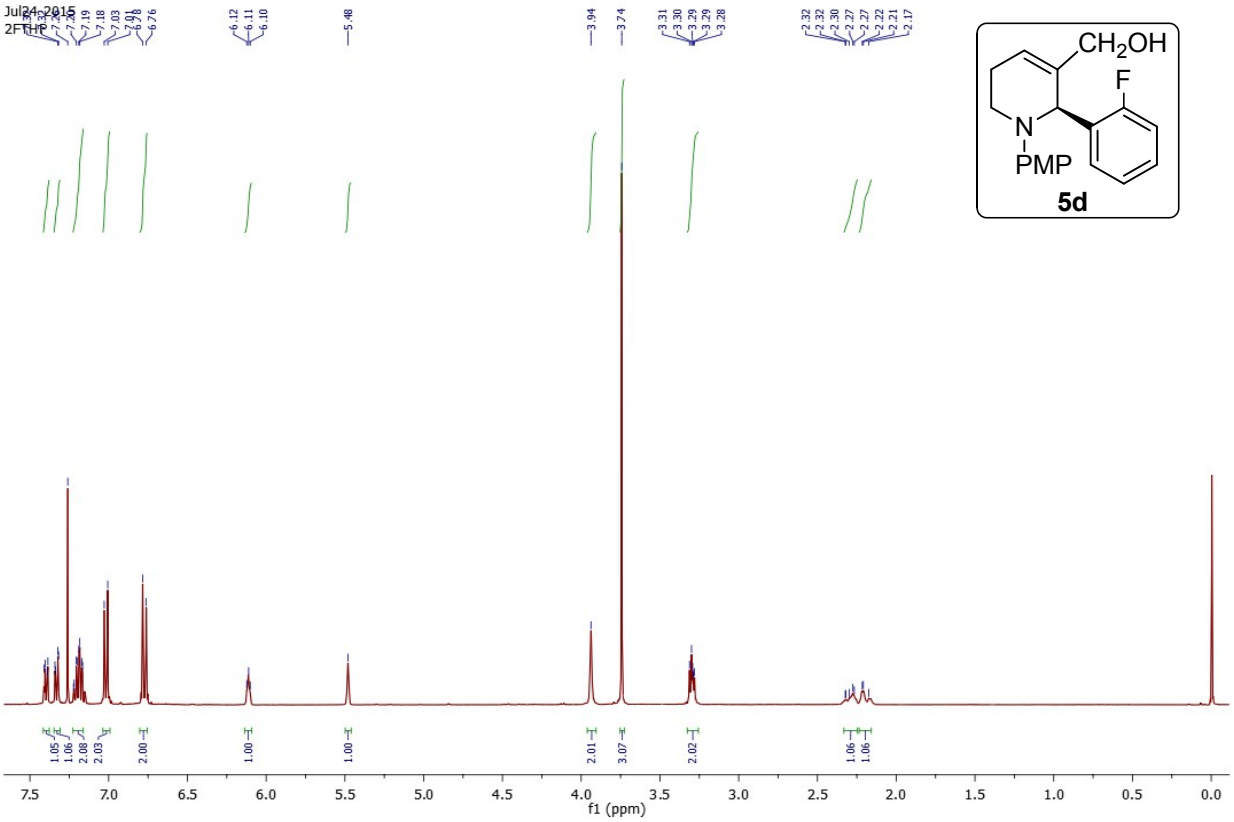
5c

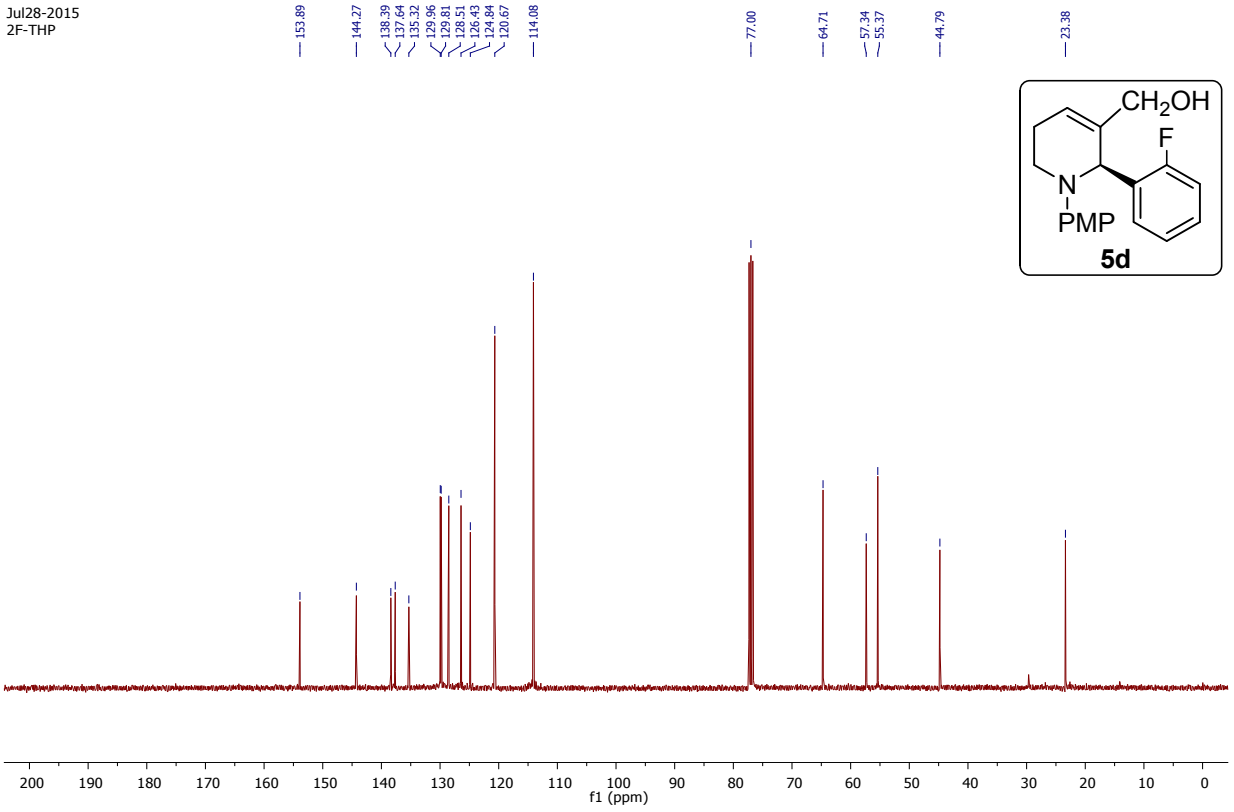


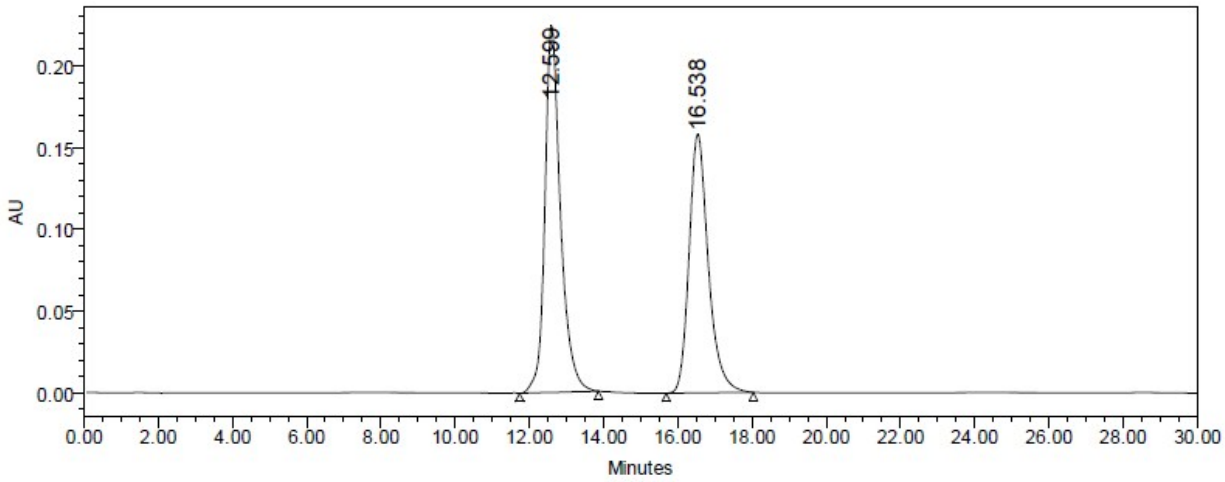
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7865; Processing Method: 4 NITRO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.932	1239998	3.01	29304
2	PDA 250.0 nm	22.037	39964344	96.99	907207


Jul24-2015
2FTHP
CH2OH
F
N
PMP
5d
f1 (ppm)

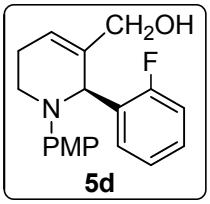

Jul28-2015
2F-THP
CH2OH
F
N
PMP
5d
f1 (ppm)



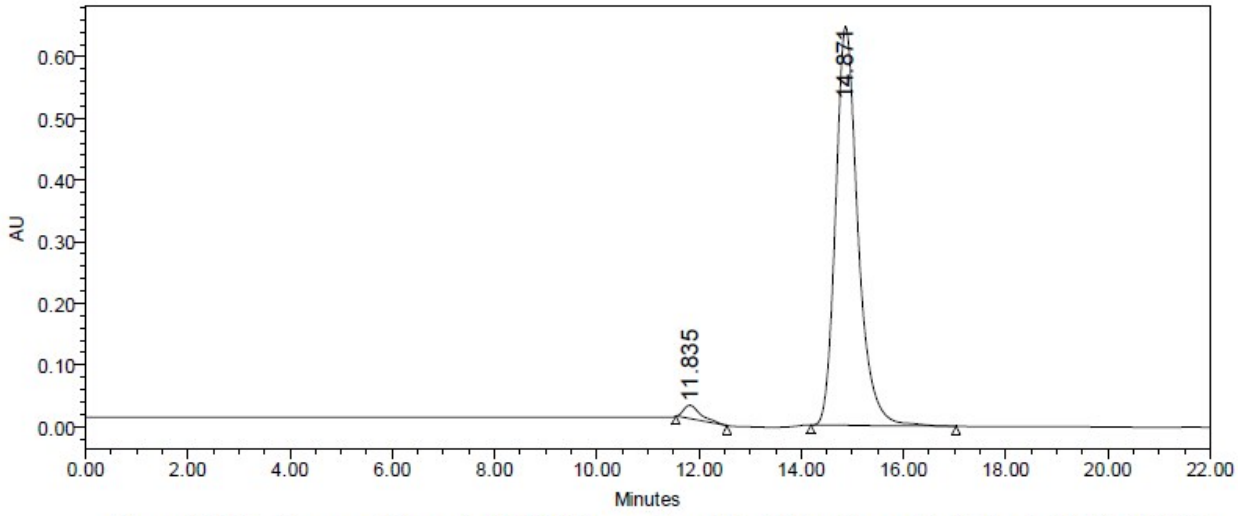
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8378; Processing Method: 2 FLURO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	12.599	6555802	53.51	224136
2	PDA 250.0 nm	16.538	5695813	46.49	158347



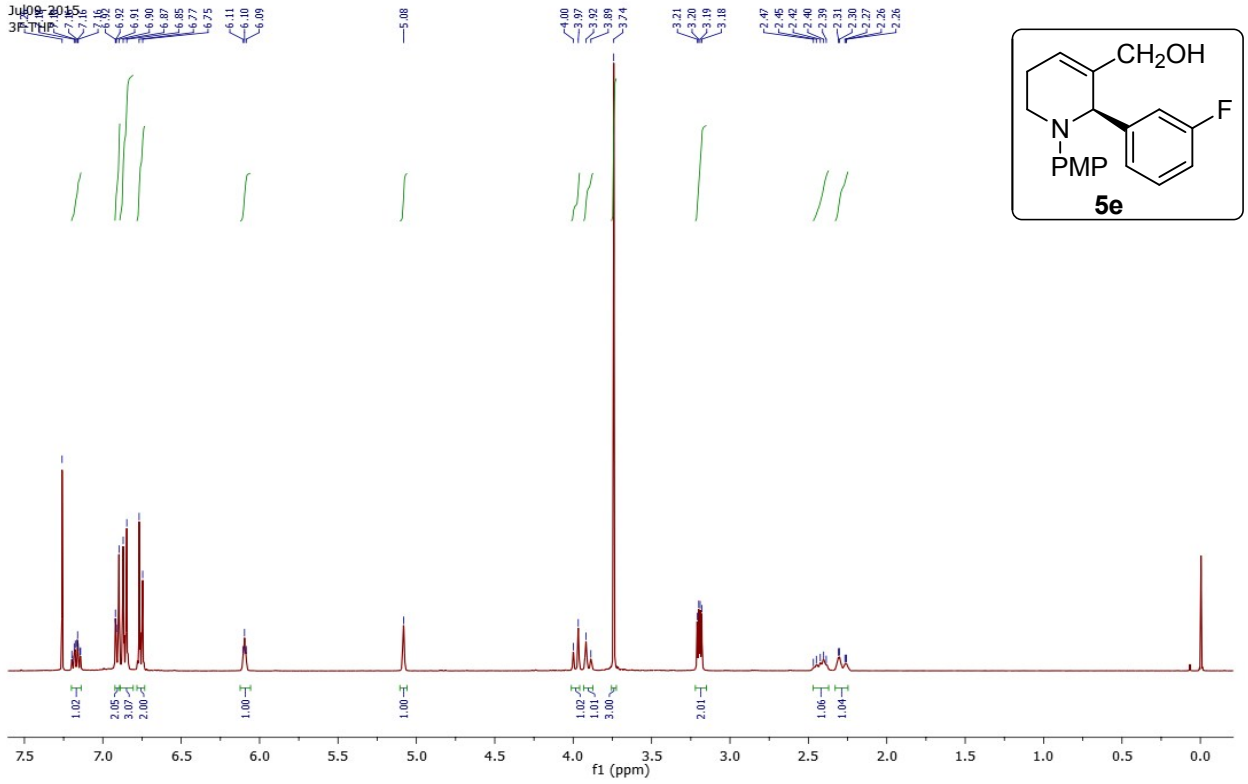
5d

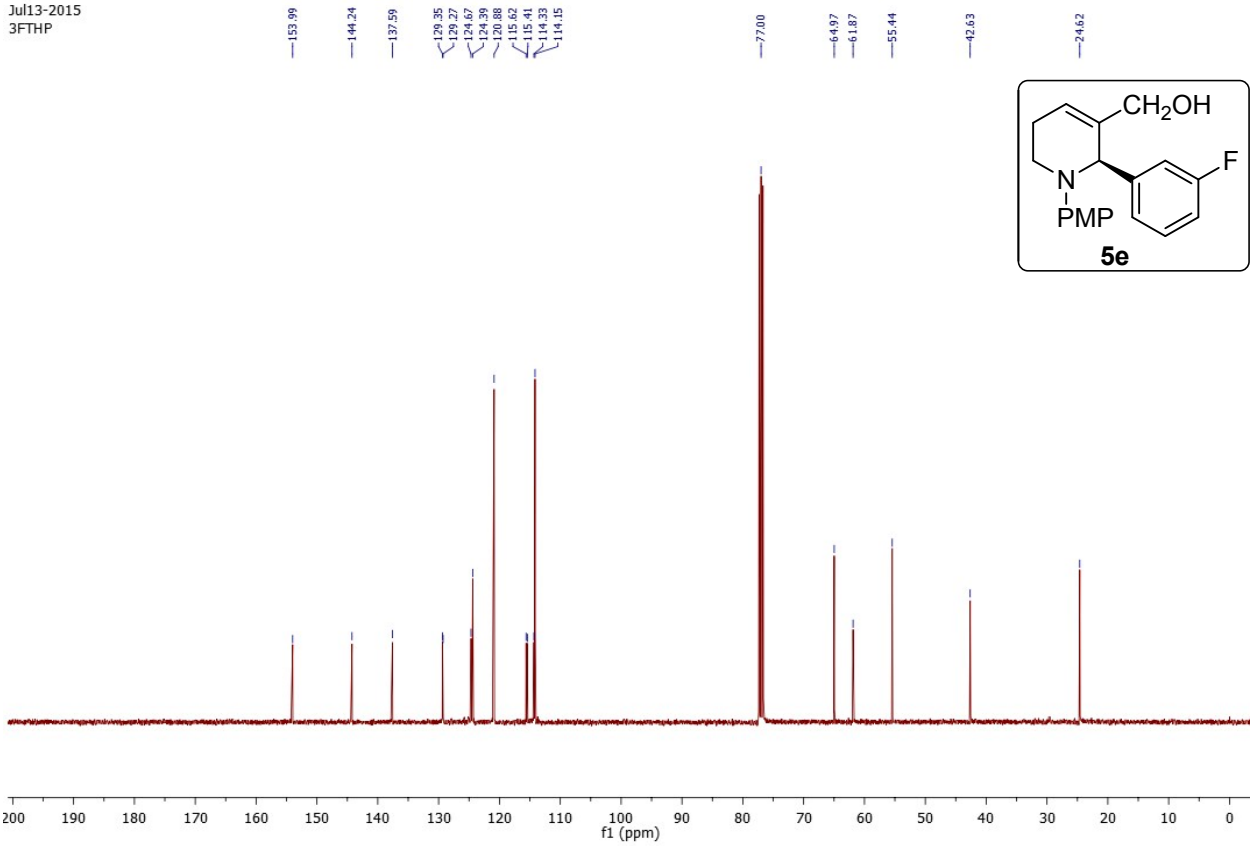


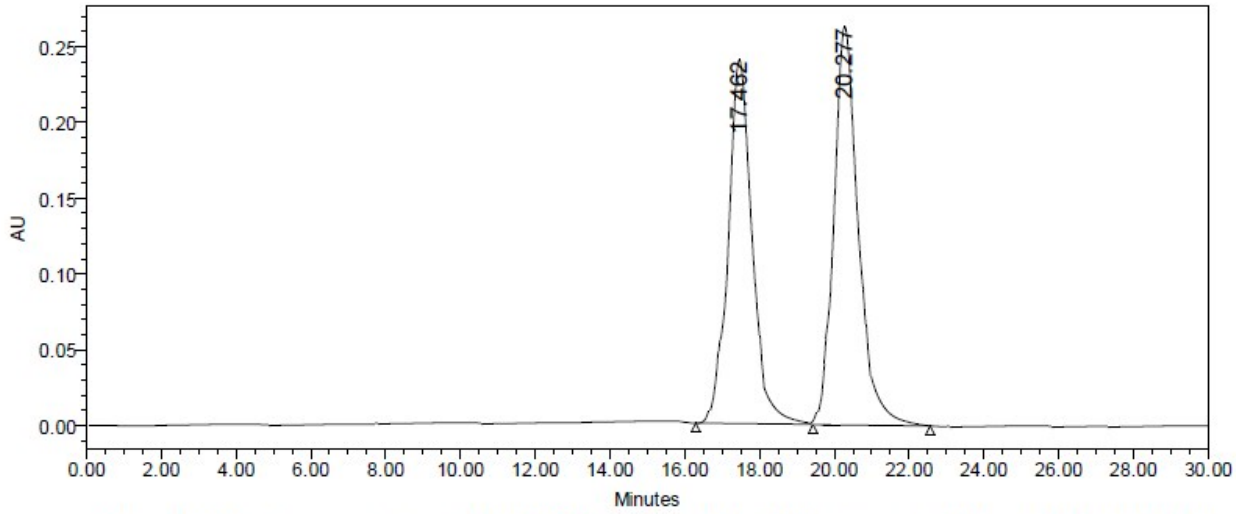
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8380; Processing Method: 2 F CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	11.835	499839	2.48	21526
2	PDA 250.0 nm	14.871	19661013	97.52	647097


Jul09-2015
3FTHP
CH2OH
F
N
PMP
5e
f1 (ppm)

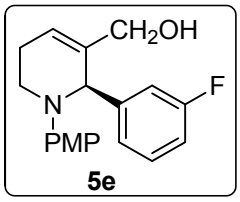

Jul13-2015
3FTHP
CH2OH
F
N
PMP
5e
f1 (ppm)



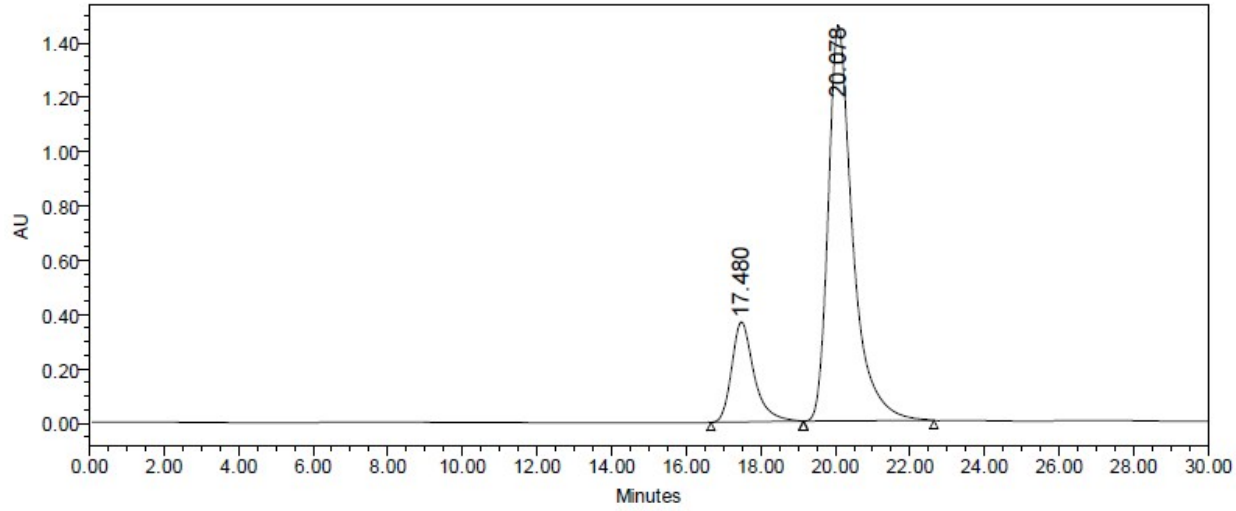
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7919; Processing Method: 3F RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.462	8831900	46.10	221128
2	PDA 250.0 nm	20.277	10325475	53.90	240103



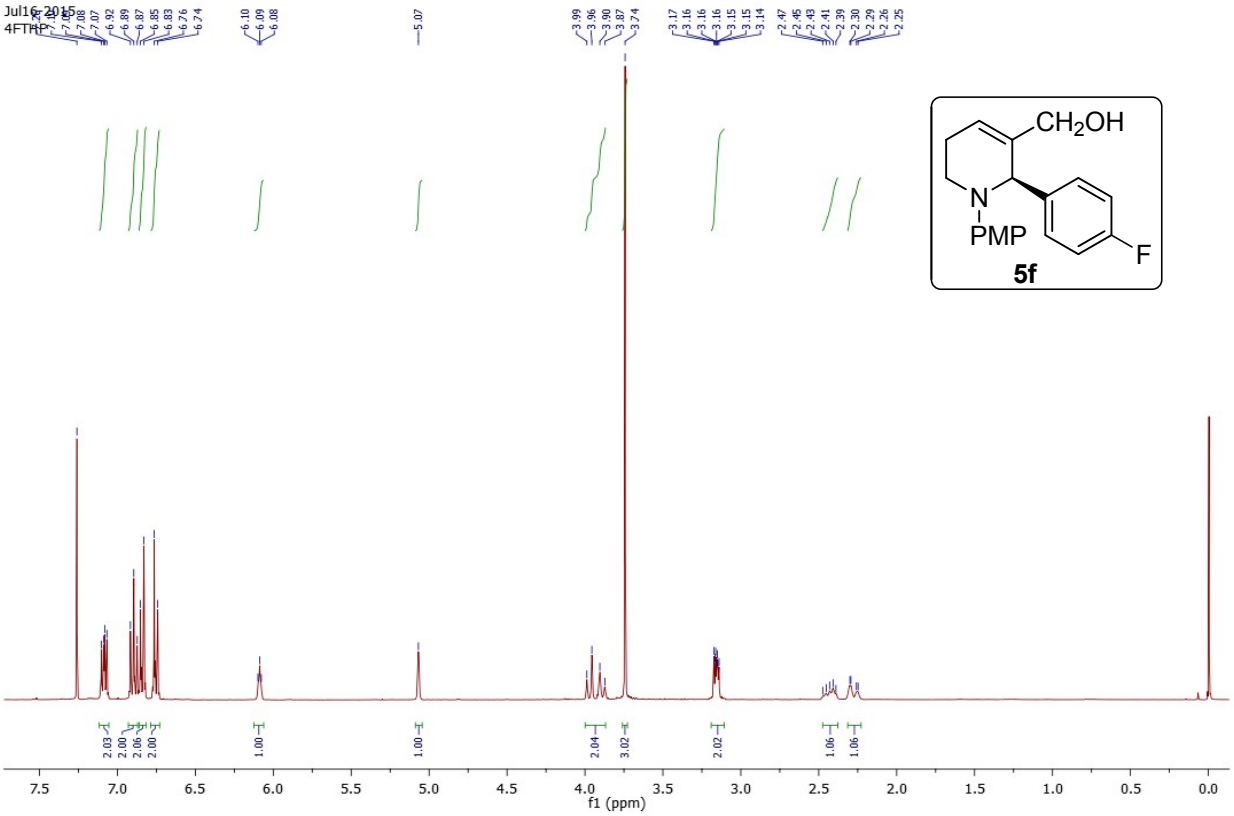
5e

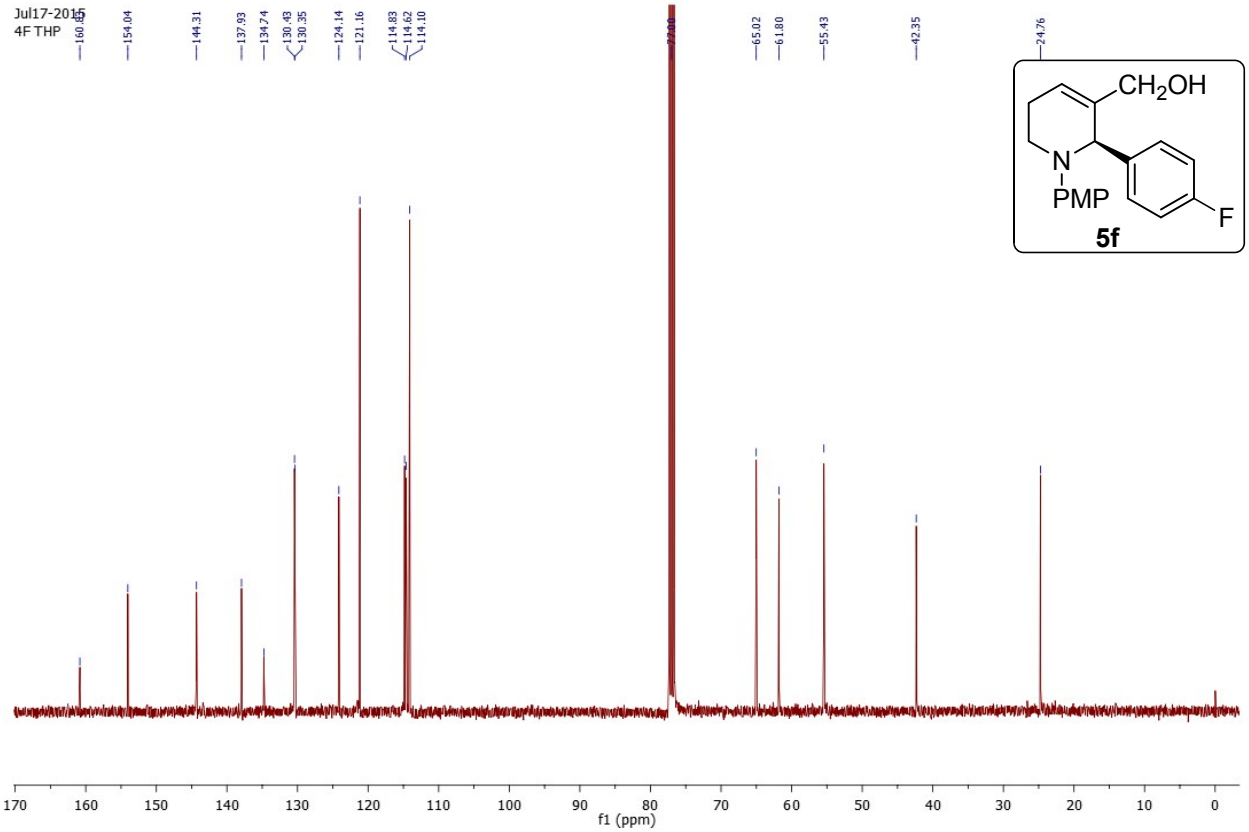


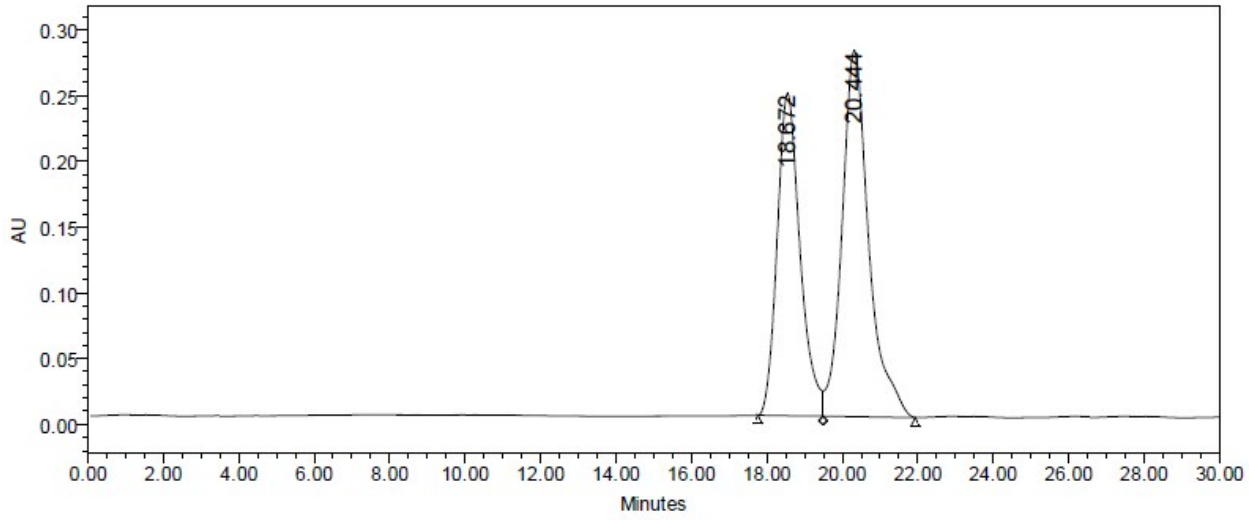
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7920; Processing Method: 3F CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.480	15290807	18.72	368440
2	PDA 250.0 nm	20.078	66384896	81.28	1456721


Jul16-2015
4FTHP
CH2OH
N
PMP
F
5f
f1 (ppm)

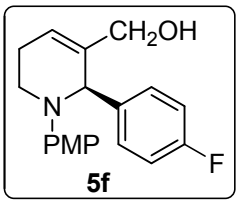

Jul17-2015
4F THP
CH2OH
N
PMP
F
5f
f1 (ppm)



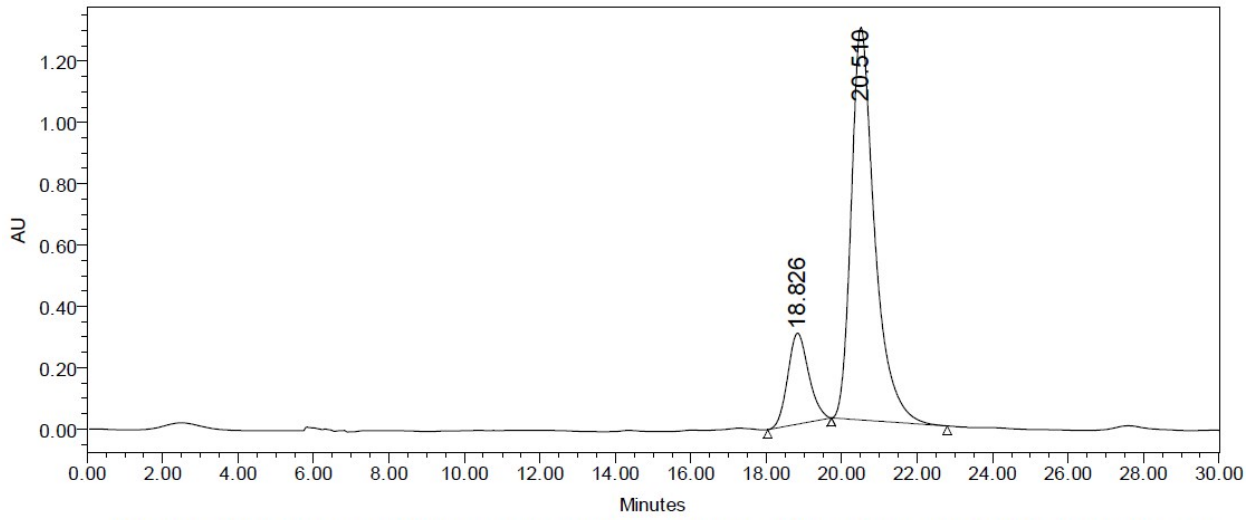
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7921; Processing Method: 4F RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	18.672	10349266	43.03	244926
2	PDA 250.0 nm	20.444	13701958	56.97	278431



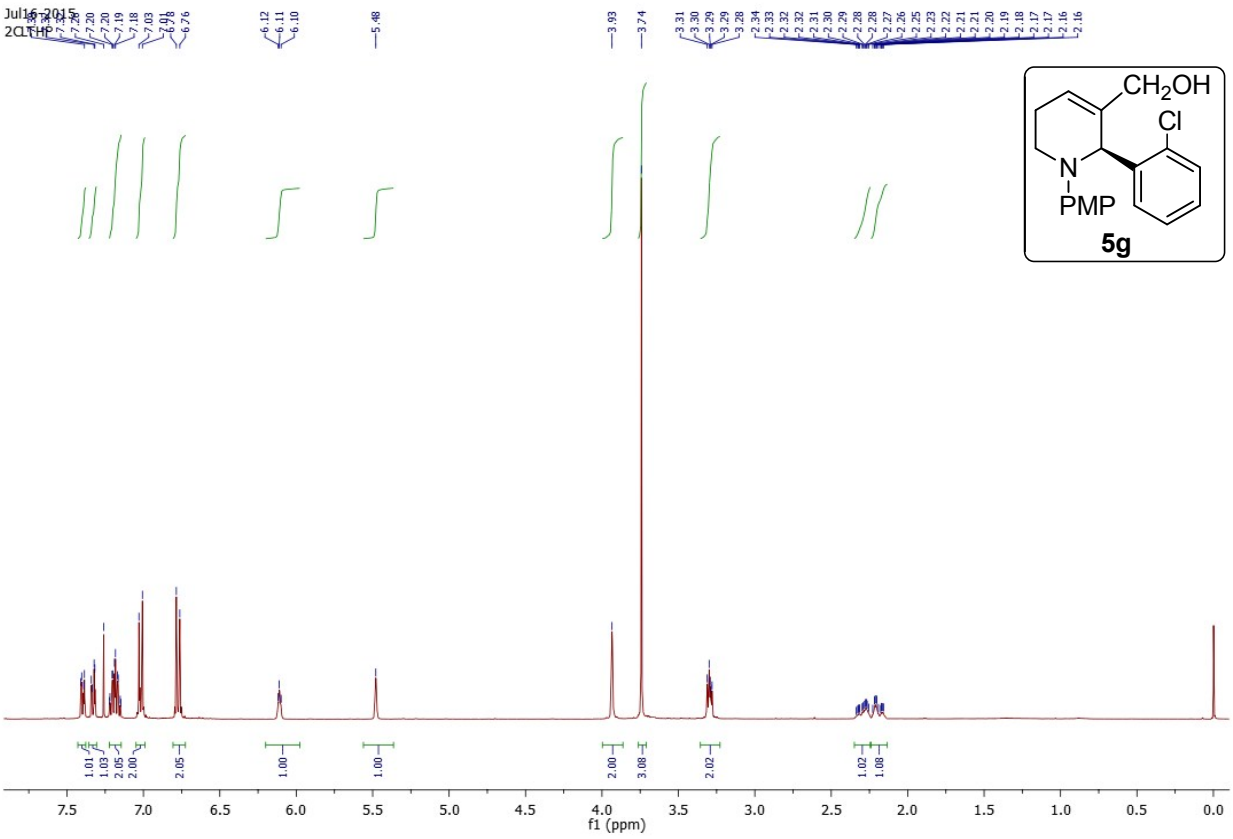
5f

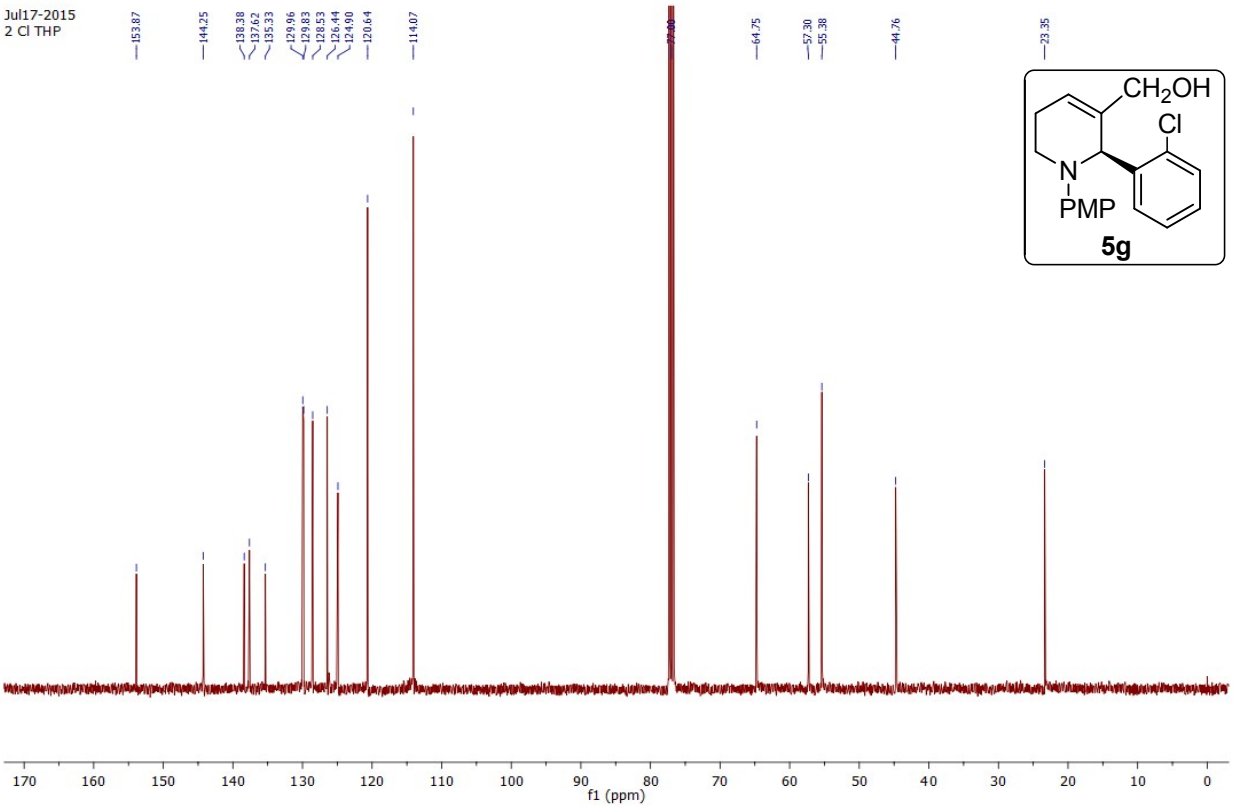


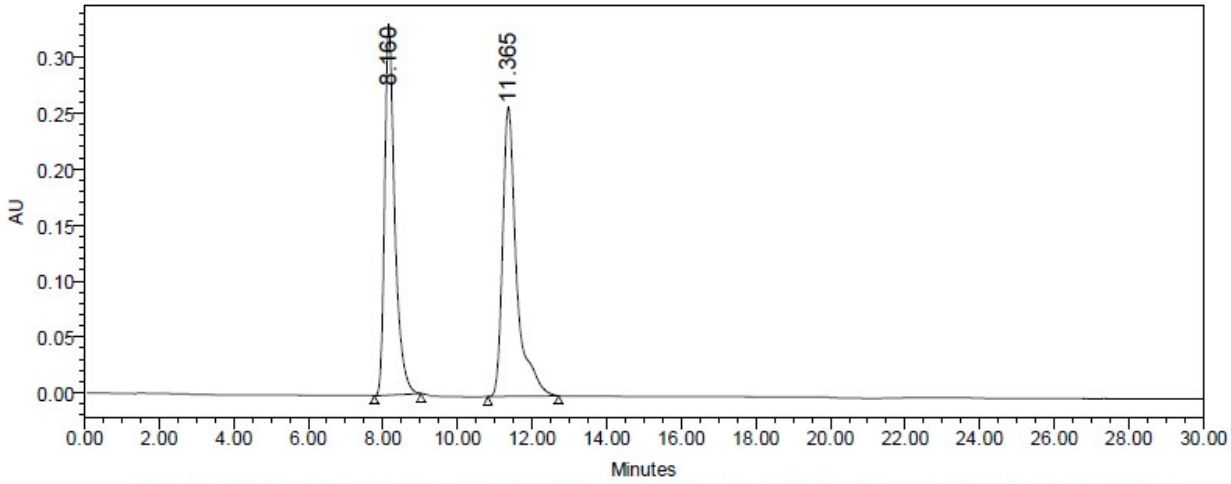
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7922; Processing Method: 4F CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	18.826	11418942	17.10	296796
2	PDA 250.0 nm	20.510	55370205	82.90	1280260


Jul16-2015
2Cl THP
CH2OH
Cl
N
PMP
5g
f1 (ppm)

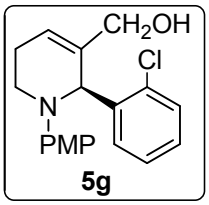

Jul17-2015
2 Cl THP
CH2OH
Cl
N
PMP
5g
f1 (ppm)



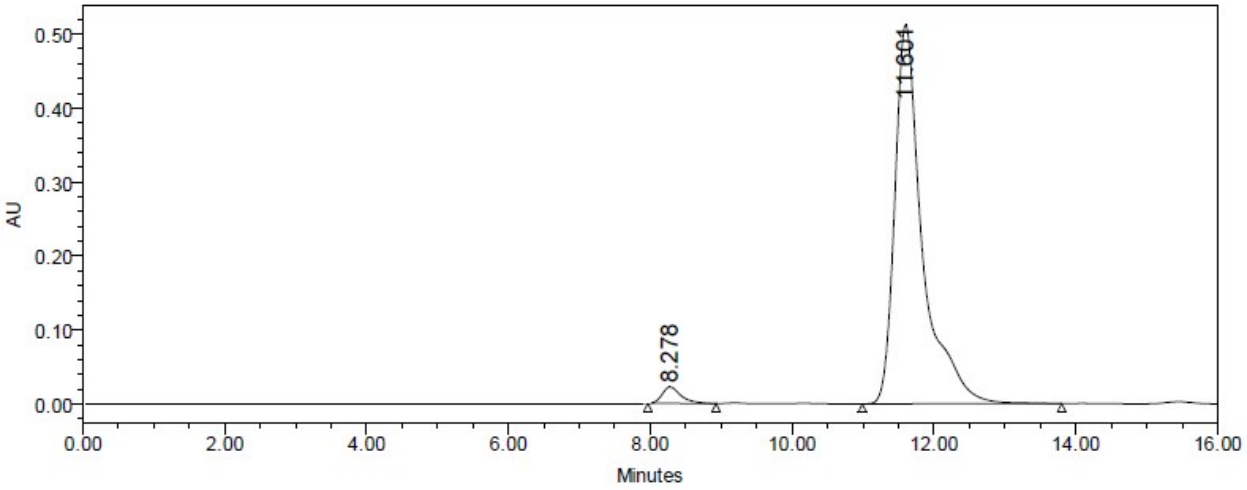
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8386; Processing Method: 2 CHLORO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	8.160	6240350	48.08	331077
2	PDA 250.0 nm	11.365	6739902	51.92	258215



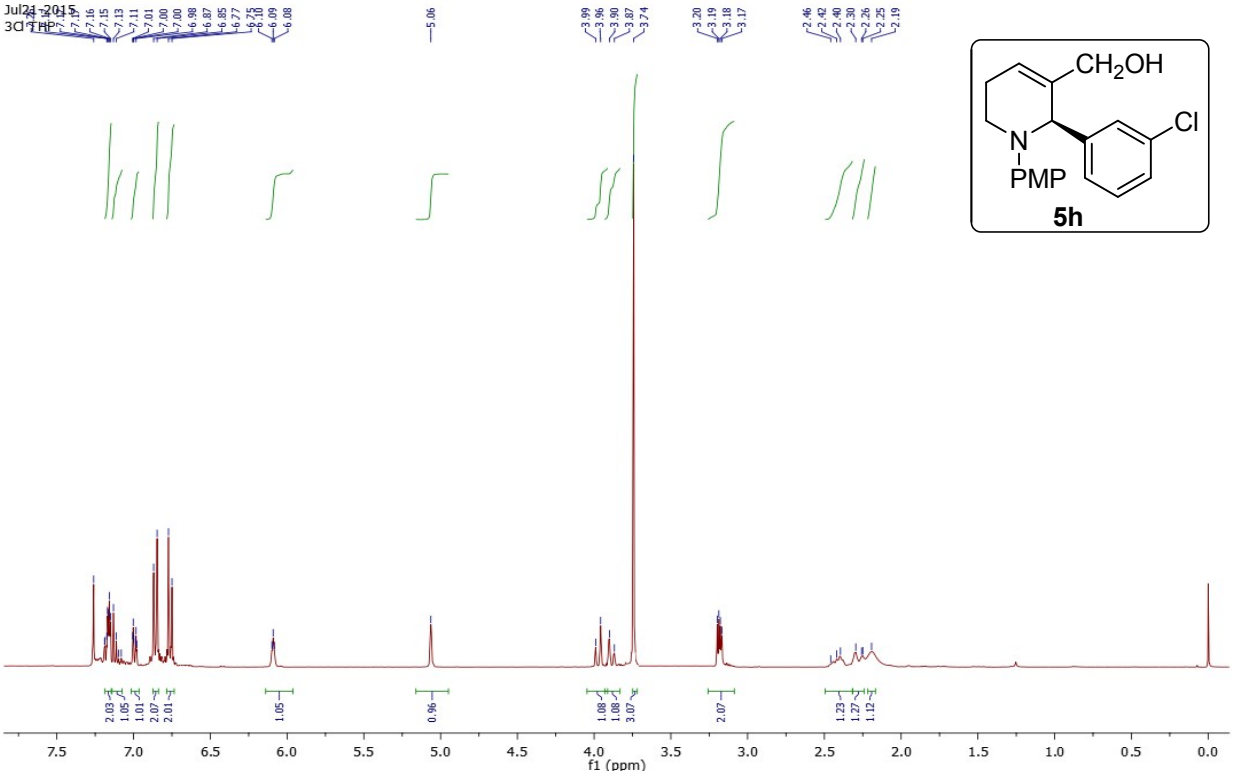
5g

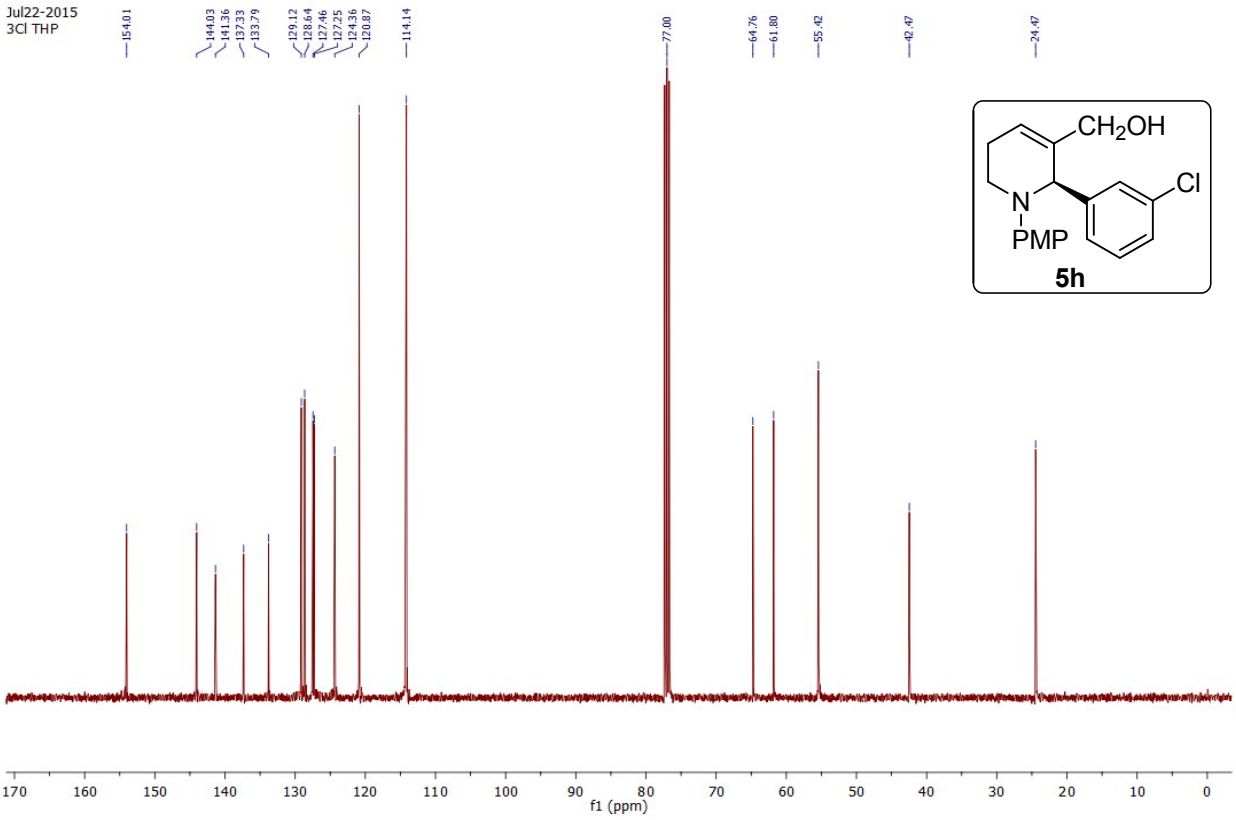


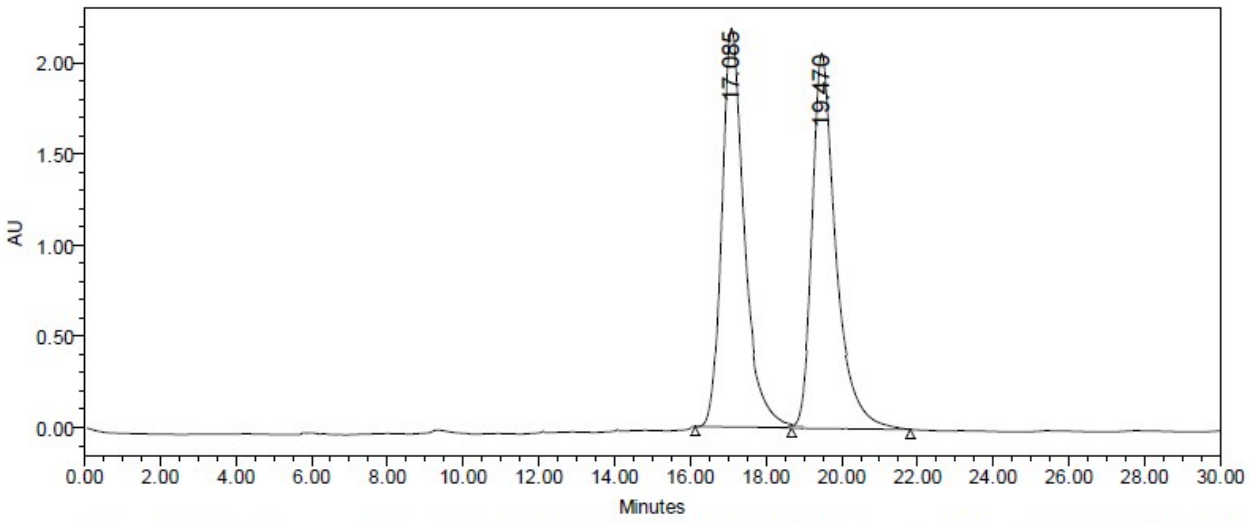
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8388; Processing Method: 2 CHLRO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	8.278	403096	2.82	22153
2	PDA 250.0 nm	11.601	13905371	97.18	512154


Jul21-2015
3Cl THP
CH2OH
Cl
N
PMP
5h
f1 (ppm)

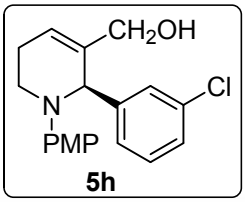

Jul22-2015
3Cl THP
CH2OH
Cl
N
PMP
5h
f1 (ppm)



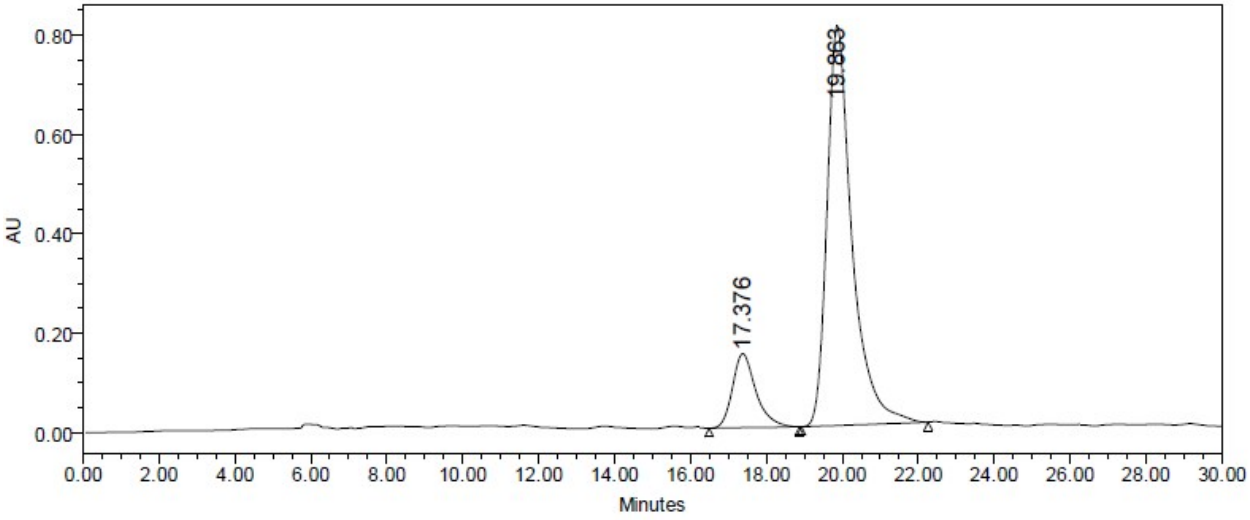
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7955; Processing Method: 3 CL RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.085	89914368	52.74	2185644
2	PDA 250.0 nm	19.470	80576338	47.26	1985008



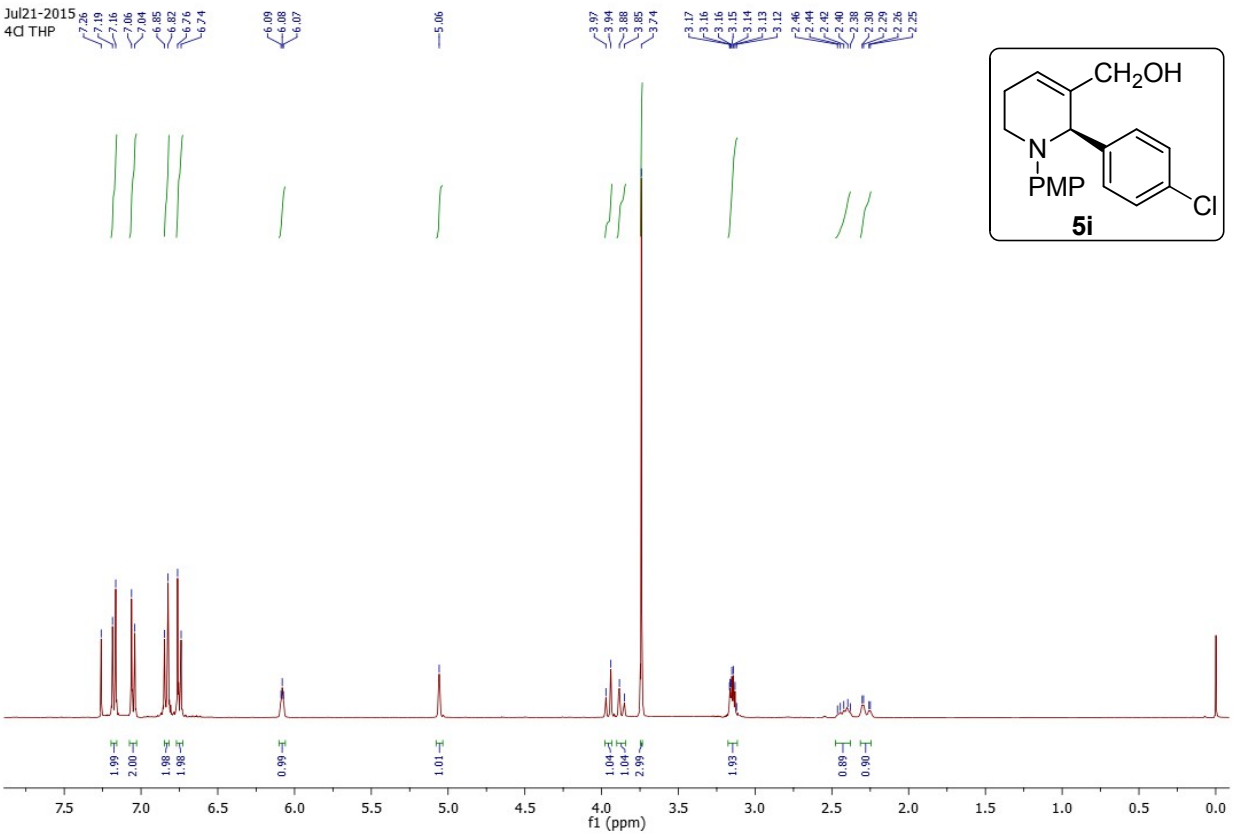
5h

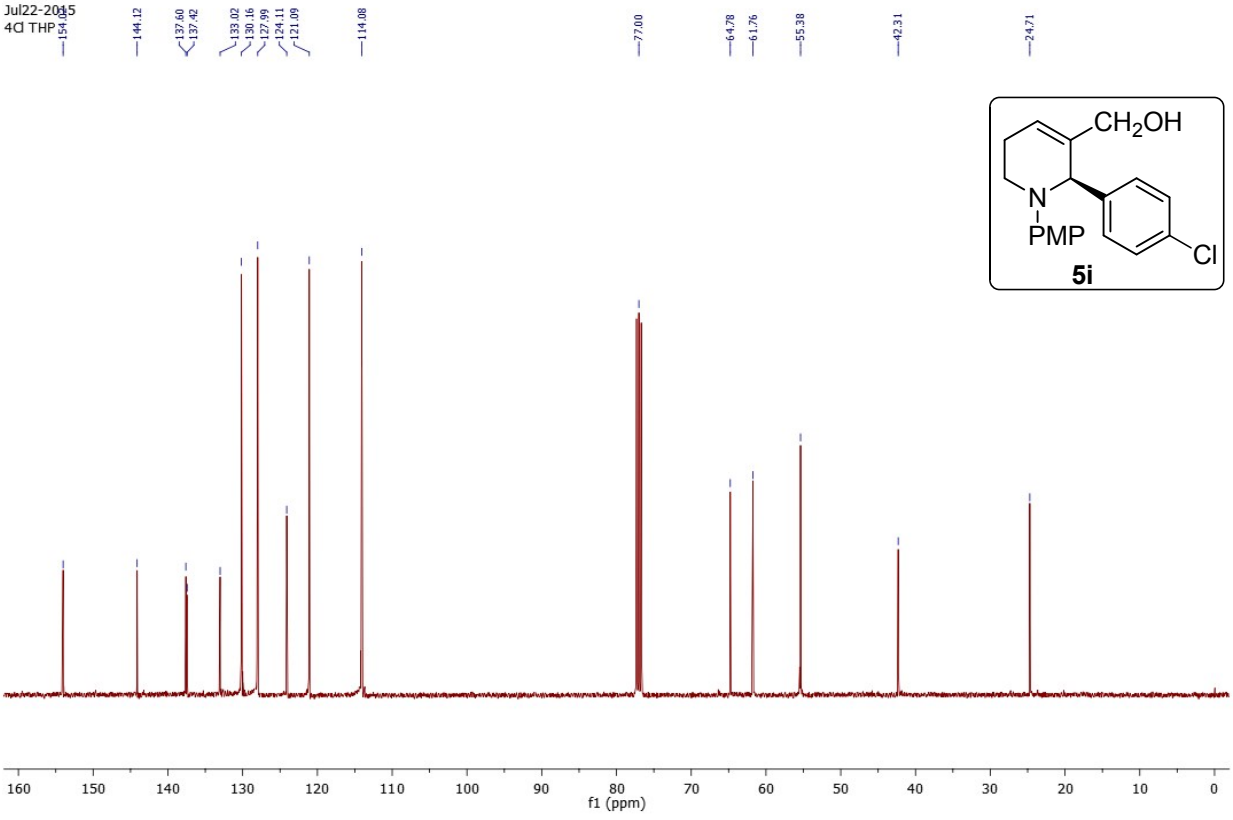


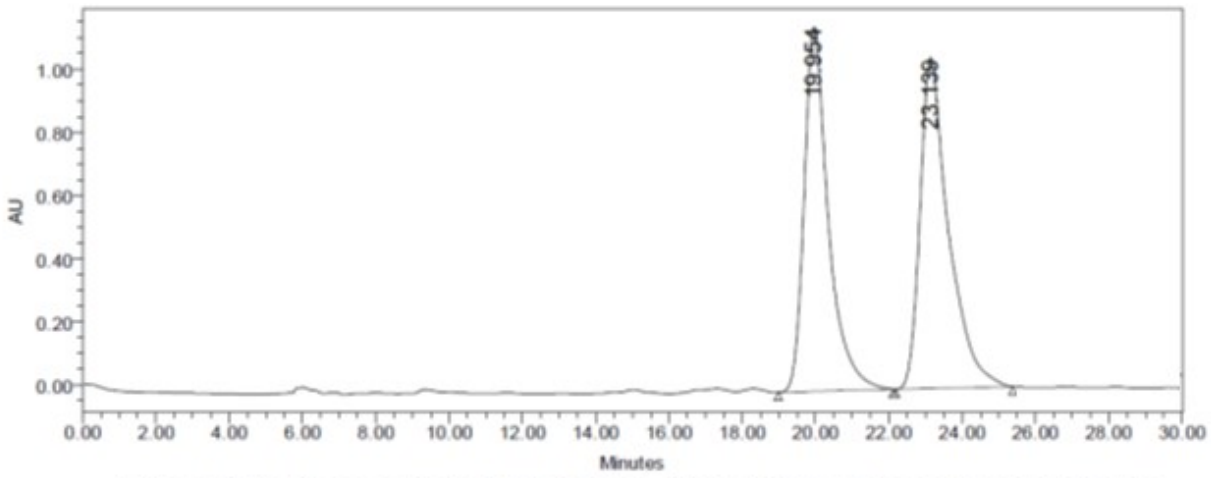
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7953; Processing Method: 3 CL CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.376	6365899	14.72	148767
2	PDA 250.0 nm	19.863	36871615	85.28	804214


Jul21-2015
4Cl THP
7.26
7.19
7.16
7.06
7.04
6.85
6.82
6.76
6.74
6.09
6.08
6.07
5.06
3.97
3.94
3.88
3.85
3.74
3.17
3.16
3.16
3.15
3.14
3.13
3.12
2.46
2.44
2.42
2.40
2.38
2.30
2.29
2.26
2.25
1.99
2.00
1.98
1.98
0.99
1.01
1.04
1.04
2.99
1.93
0.89
0.90
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
CH2OH
N
PMP
Cl
5i

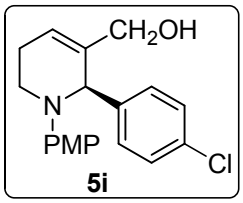

Jul22-2015
4Cl THP
154.04
144.12
137.60
137.42
133.02
130.16
127.99
124.11
121.09
114.08
77.00
64.78
61.76
55.38
42.31
24.71
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
CH2OH
N
PMP
Cl
5i



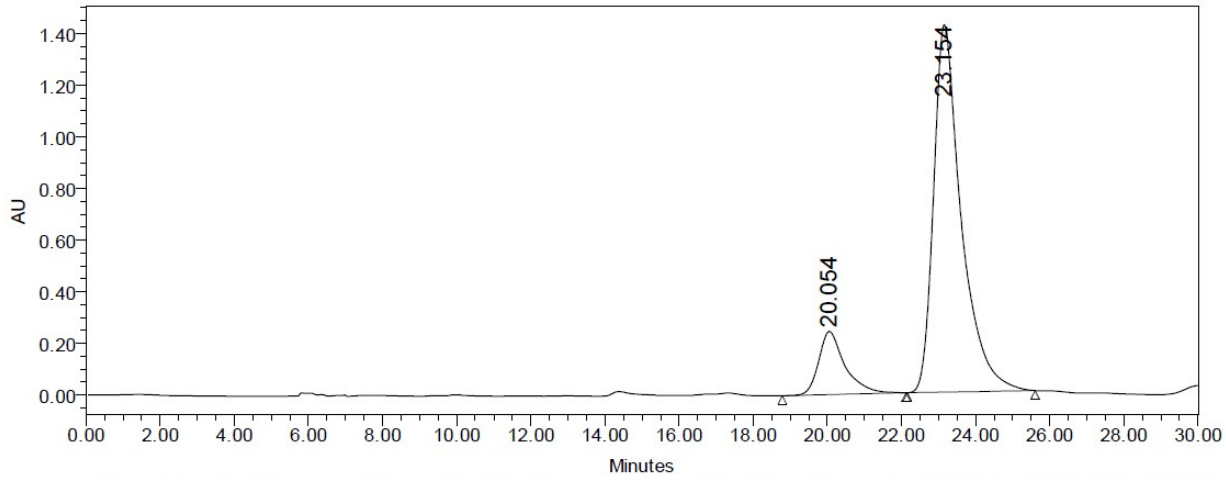
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7960; Processing Method: 4 CHLORO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	19.954	53061234	48.36	1154391
2	PDA 250.0 nm	23.139	56668222	51.64	1048413



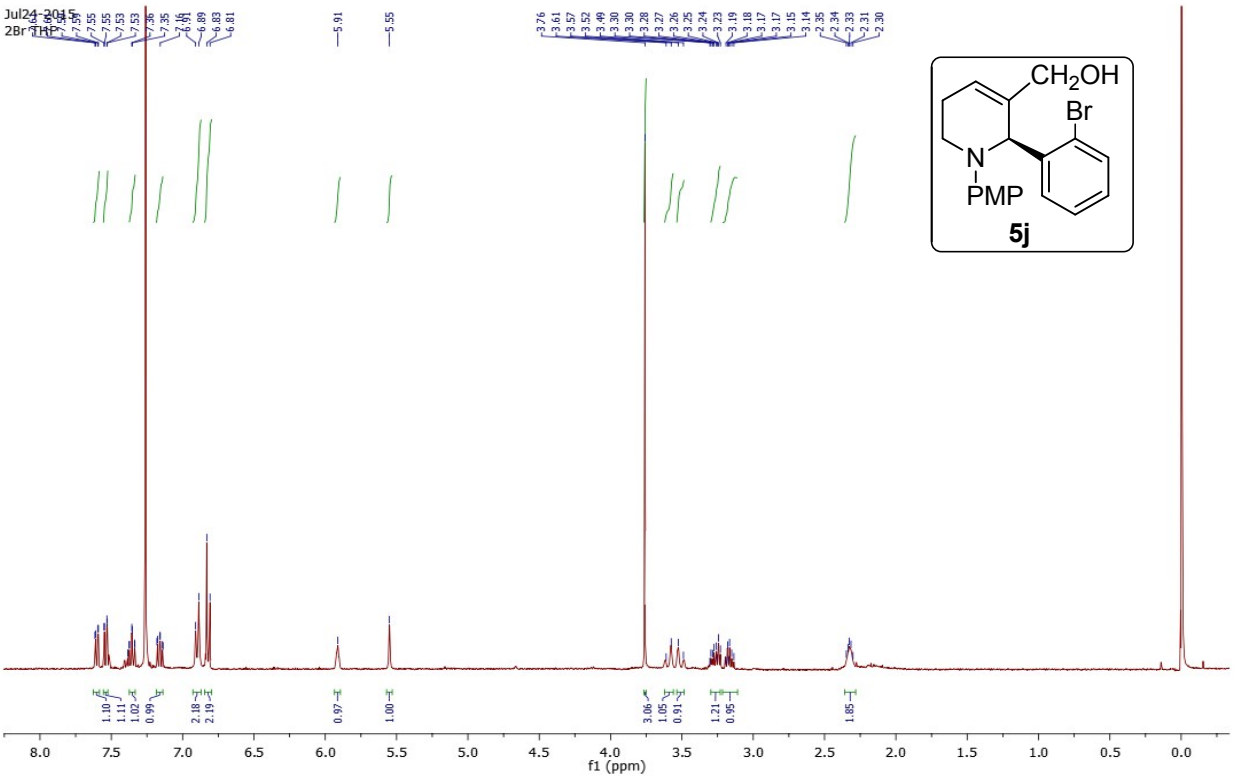
5i

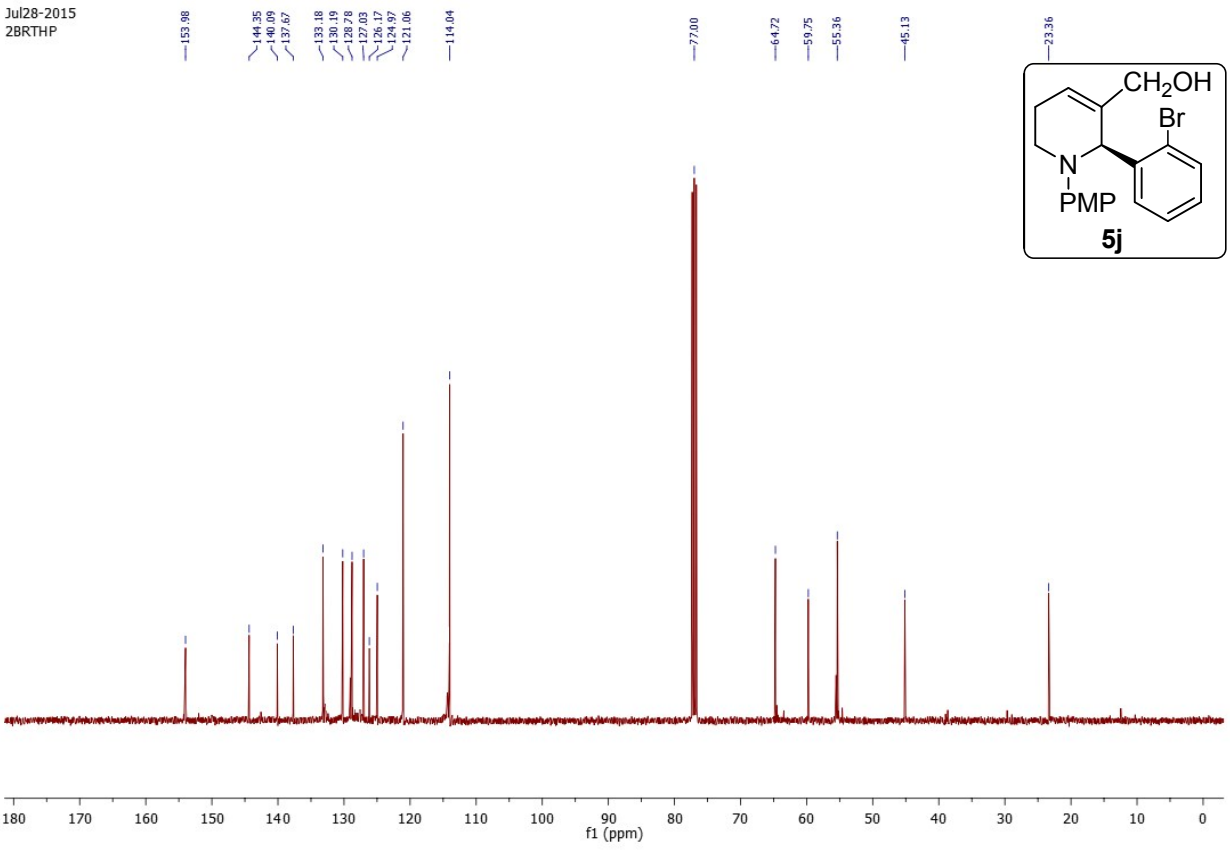


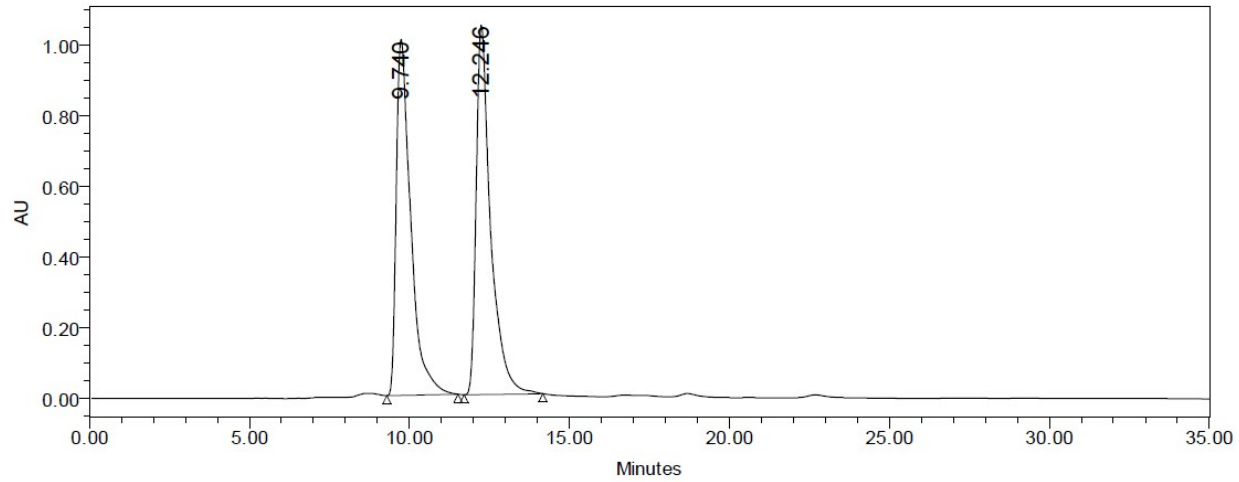
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7962; Processing Method: 4 CHLORO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	20.054	11970301	13.96	244304
2	PDA 250.0 nm	23.154	73804689	86.04	1421144


Jul24-2015
2Br THF
CH2OH
Br
N
PMP
5j
f1 (ppm)

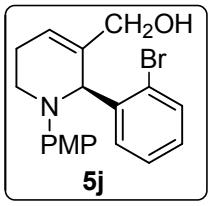

Jul28-2015
2BRTHP
CH2OH
Br
N
PMP
5j
f1 (ppm)



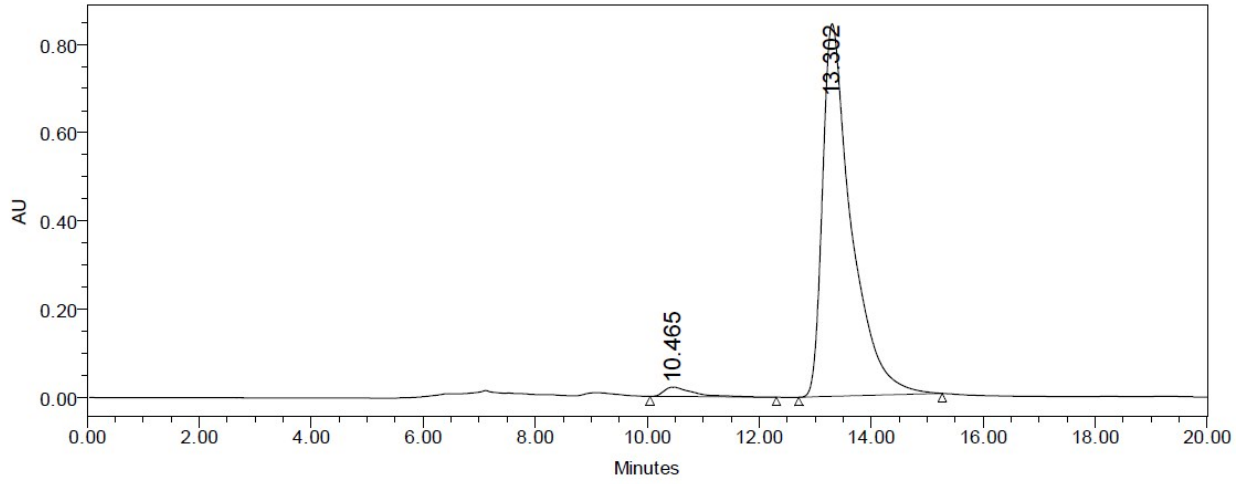
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8314; Processing Method: 2 BROMO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	9.740	31666174	49.12	1008518
2	PDA 250.0 nm	12.246	32794376	50.88	1046111



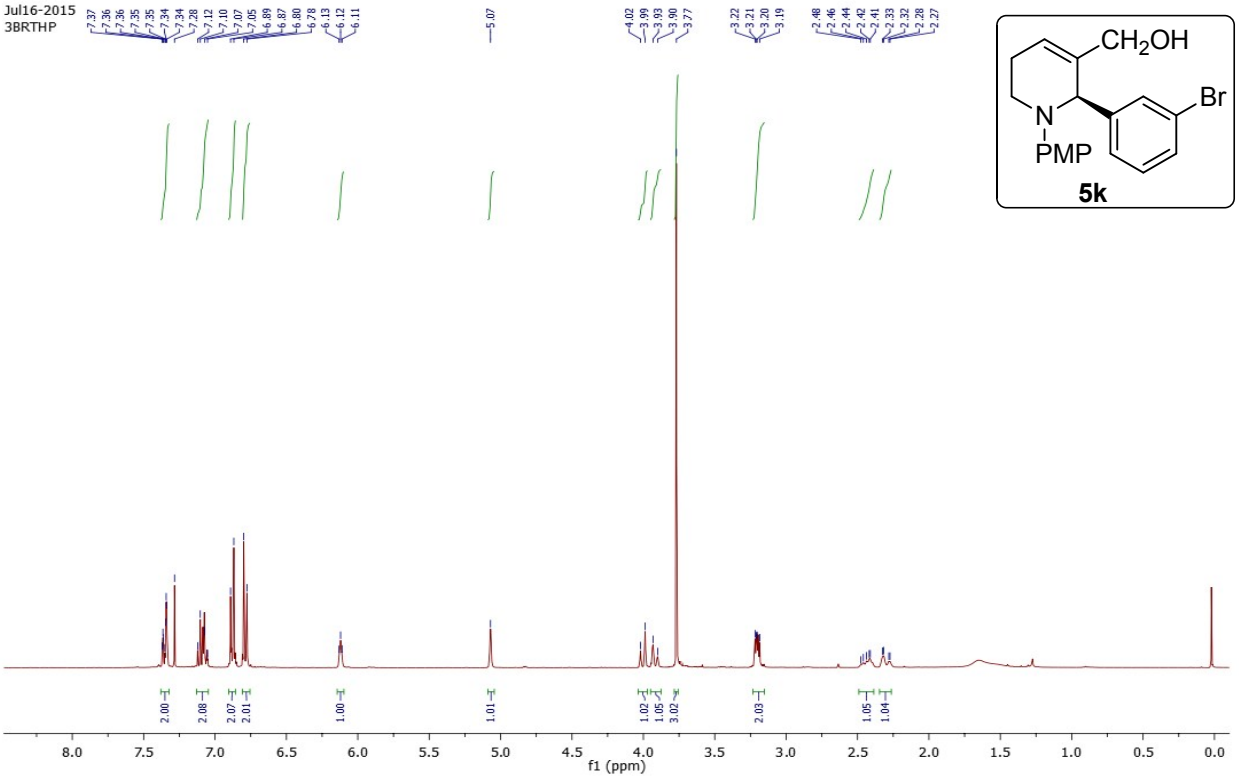
5j



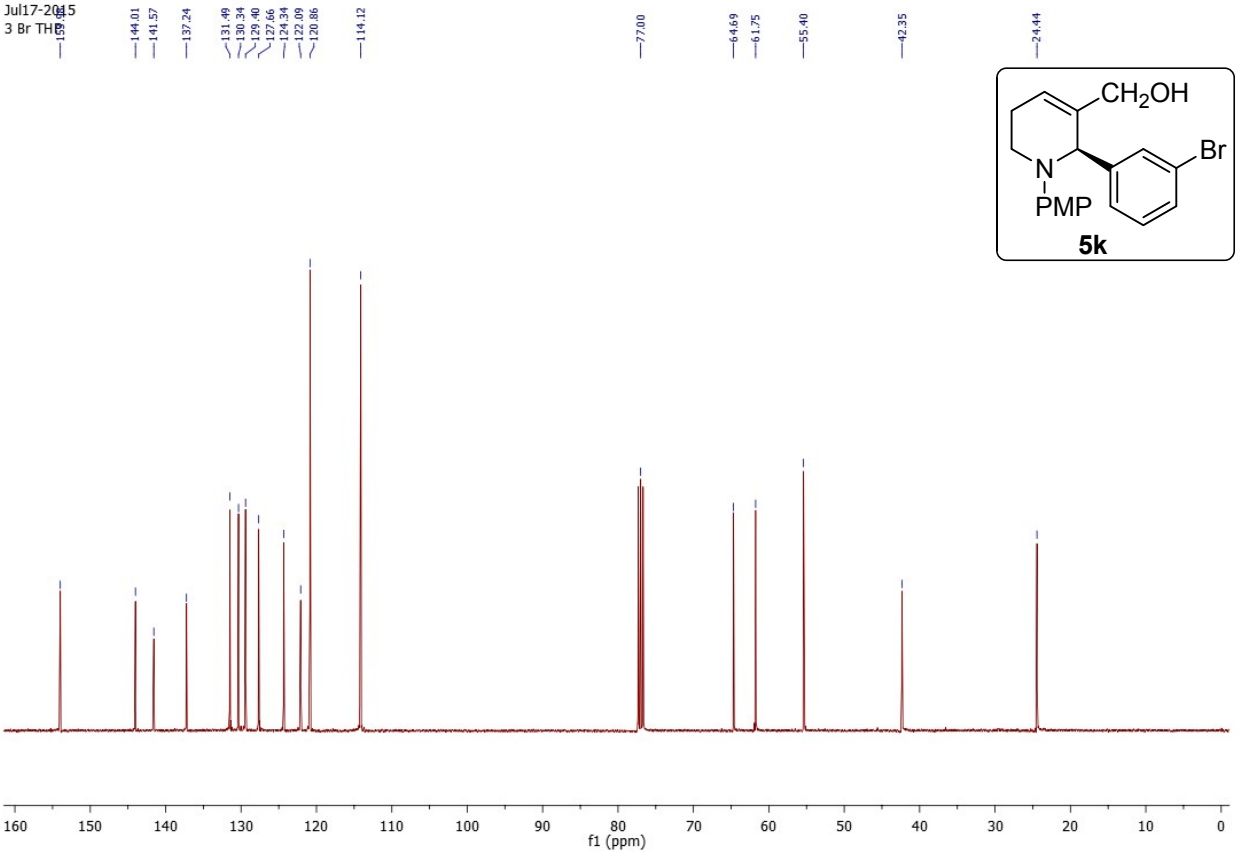
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8312; Processing Method: 2 BROMO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

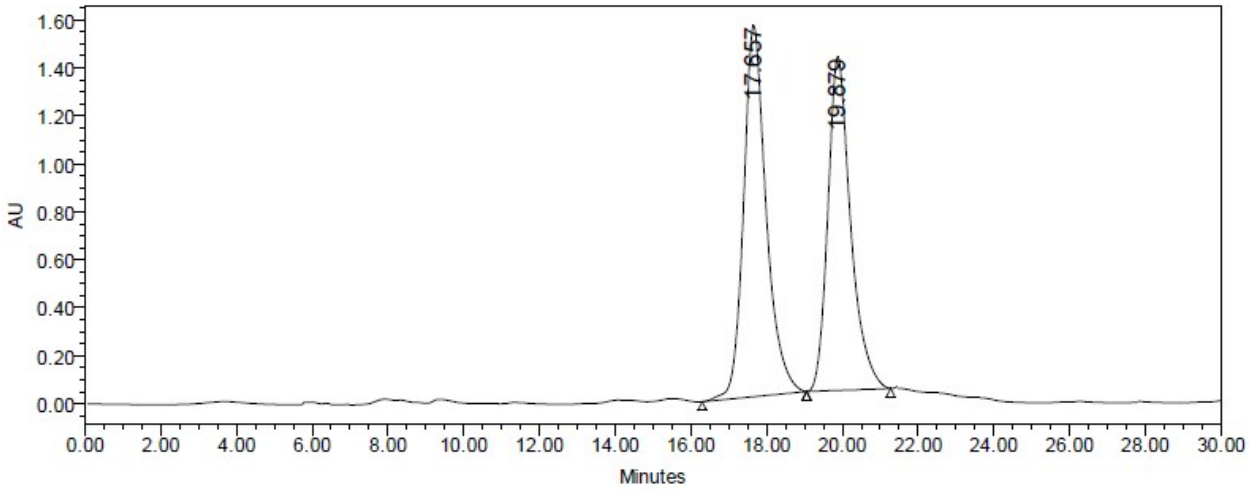
	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	10.465	768403	2.49	21397
2	PDA 250.0 nm	13.302	30106963	97.51	843809


Jul16-2015
3BRTHP
f1 (ppm)

CH2OH
Br
N
PMP
5k


Jul17-2015
3 Br THP
f1 (ppm)

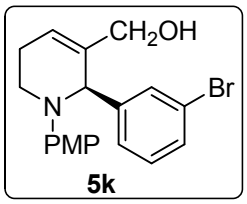
CH2OH
Br
N
PMP
5k



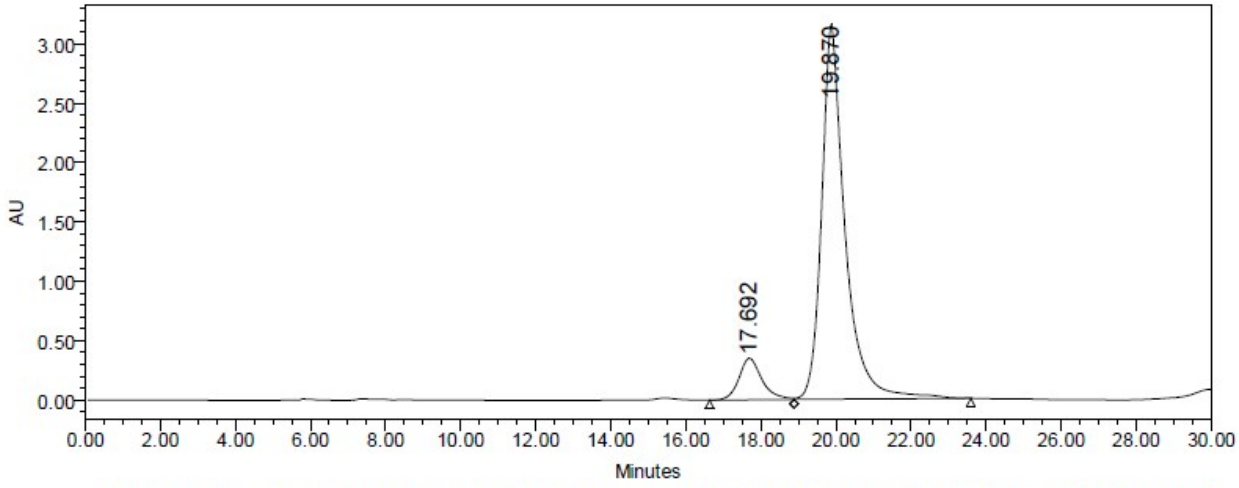
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8000; Processing Method: 3 BROMO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.657	64363439	52.54	1547168
2	PDA 250.0 nm	19.879	58147067	47.46	1391268



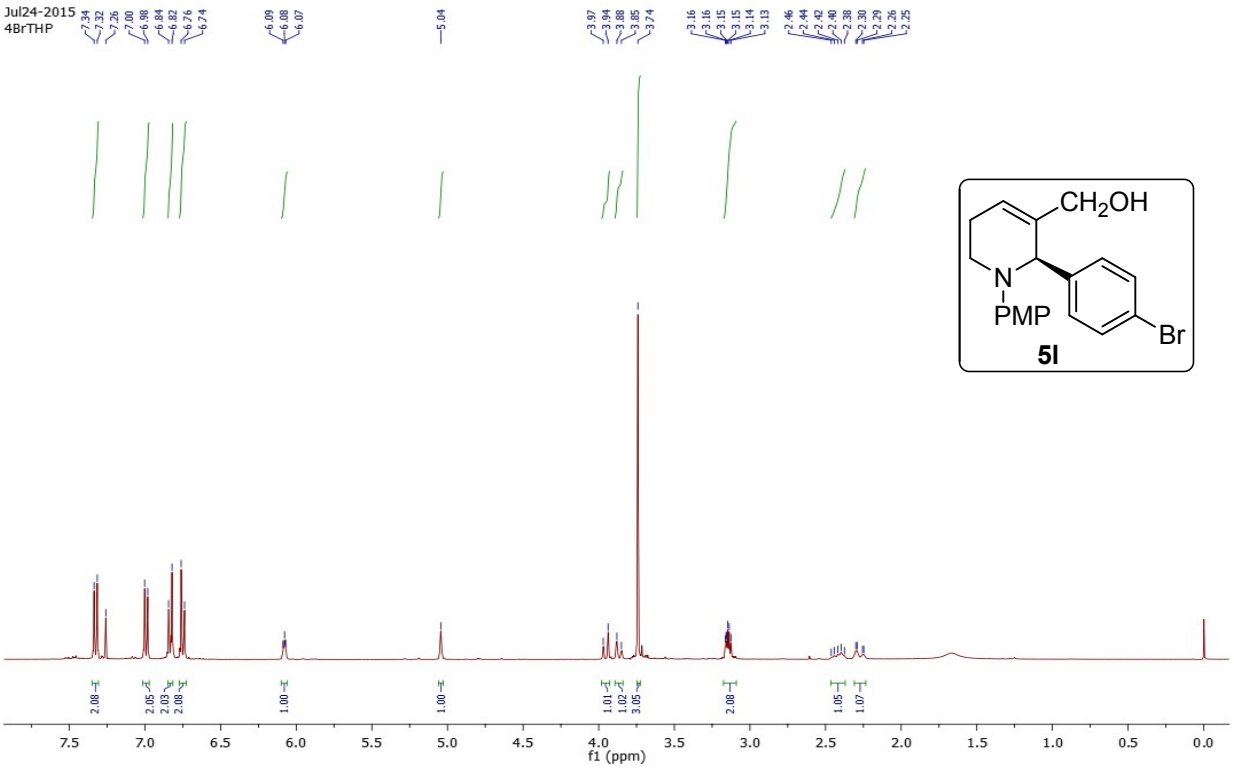
5k

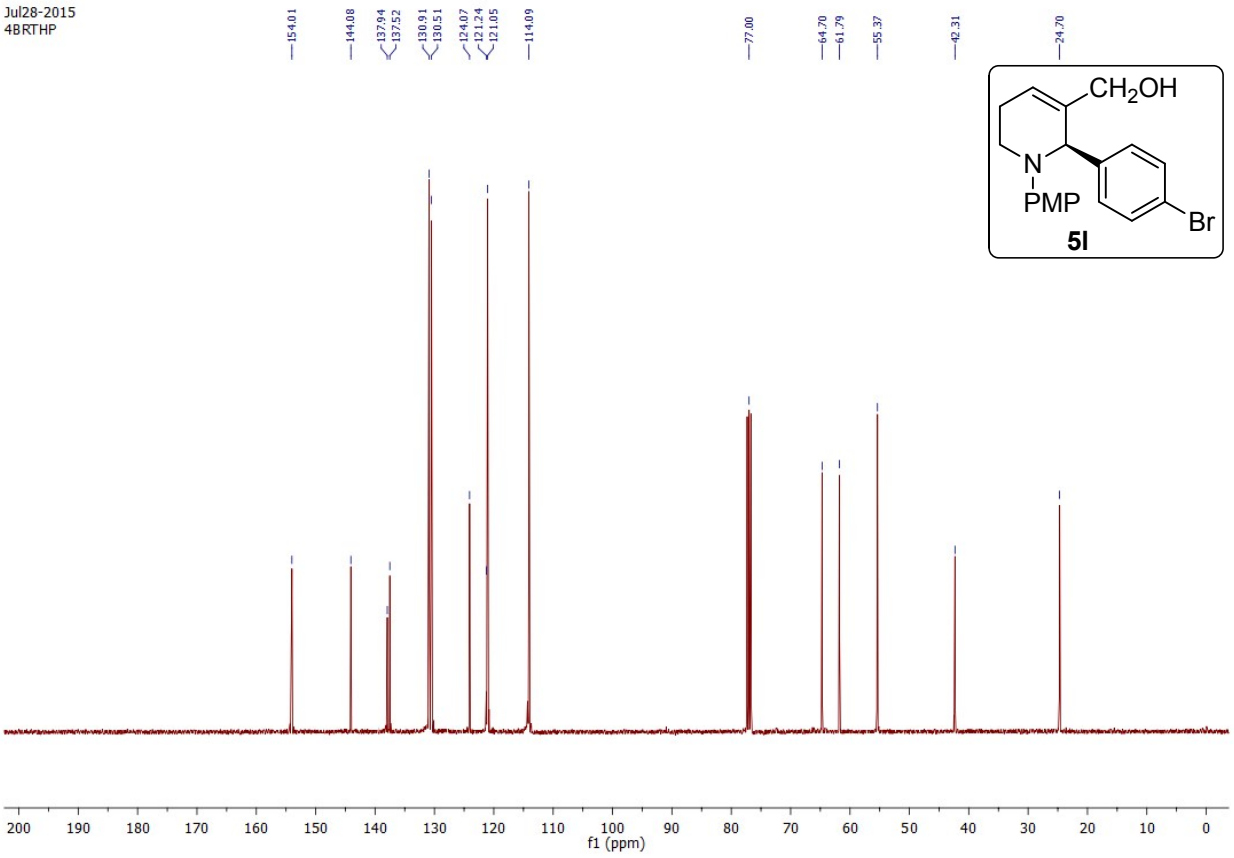


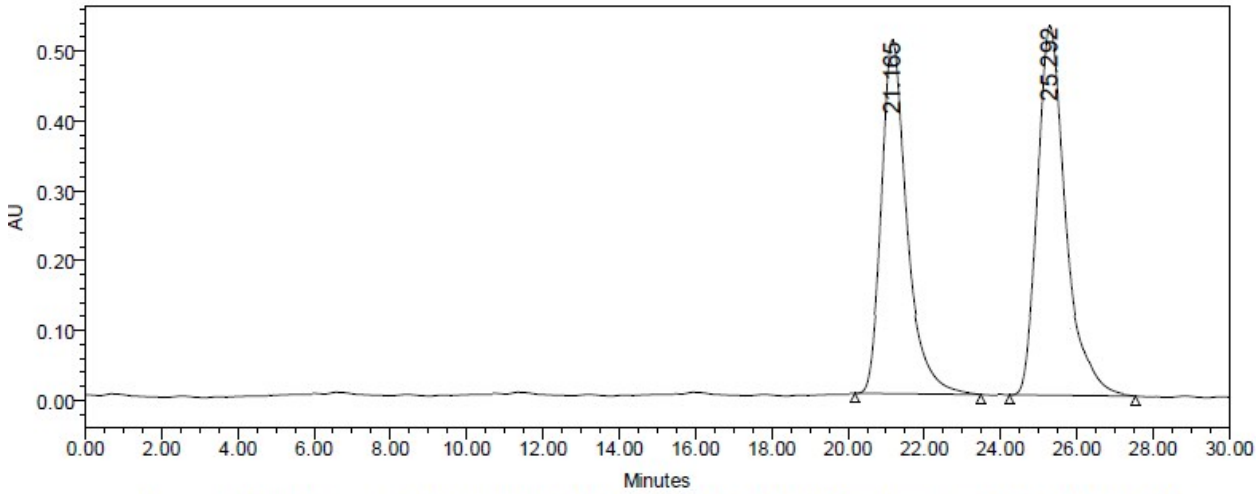
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7990; Processing Method: 3 BROMO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.692	14880585	9.84	350042
2	PDA 250.0 nm	19.870	136420501	90.16	3160055


Jul24-2015
4BrTHP
CH2OH
N
PMP
Br
5l
f1 (ppm)

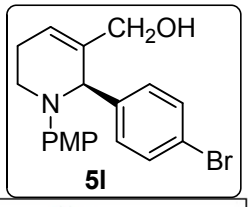

Jul28-2015
4BRTHP
CH2OH
N
PMP
Br
5l
f1 (ppm)



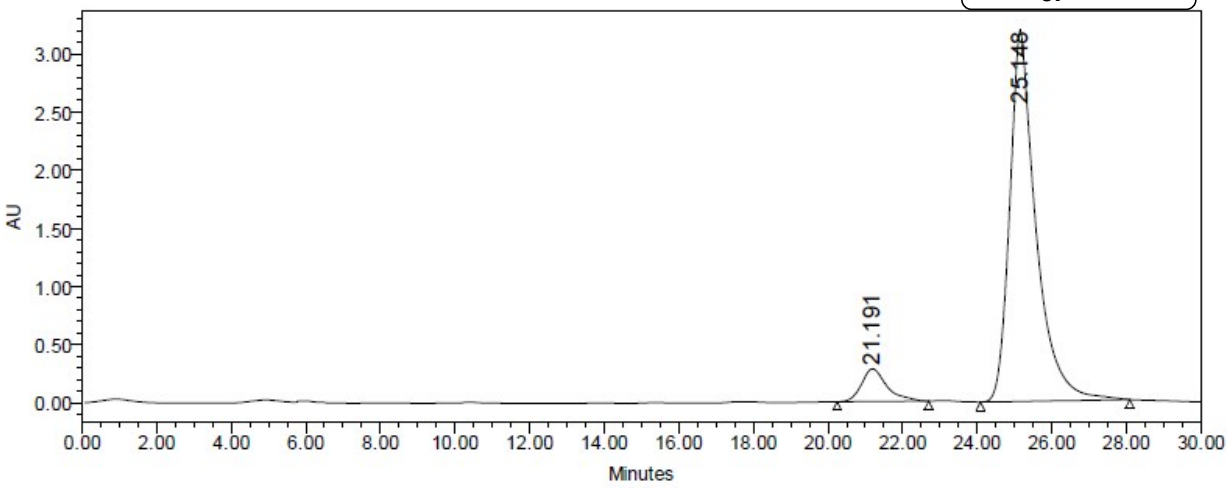
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8002; Processing Method: 4 BROMO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	21.165	22638925	46.48	494607
2	PDA 250.0 nm	25.292	26069312	53.52	525883



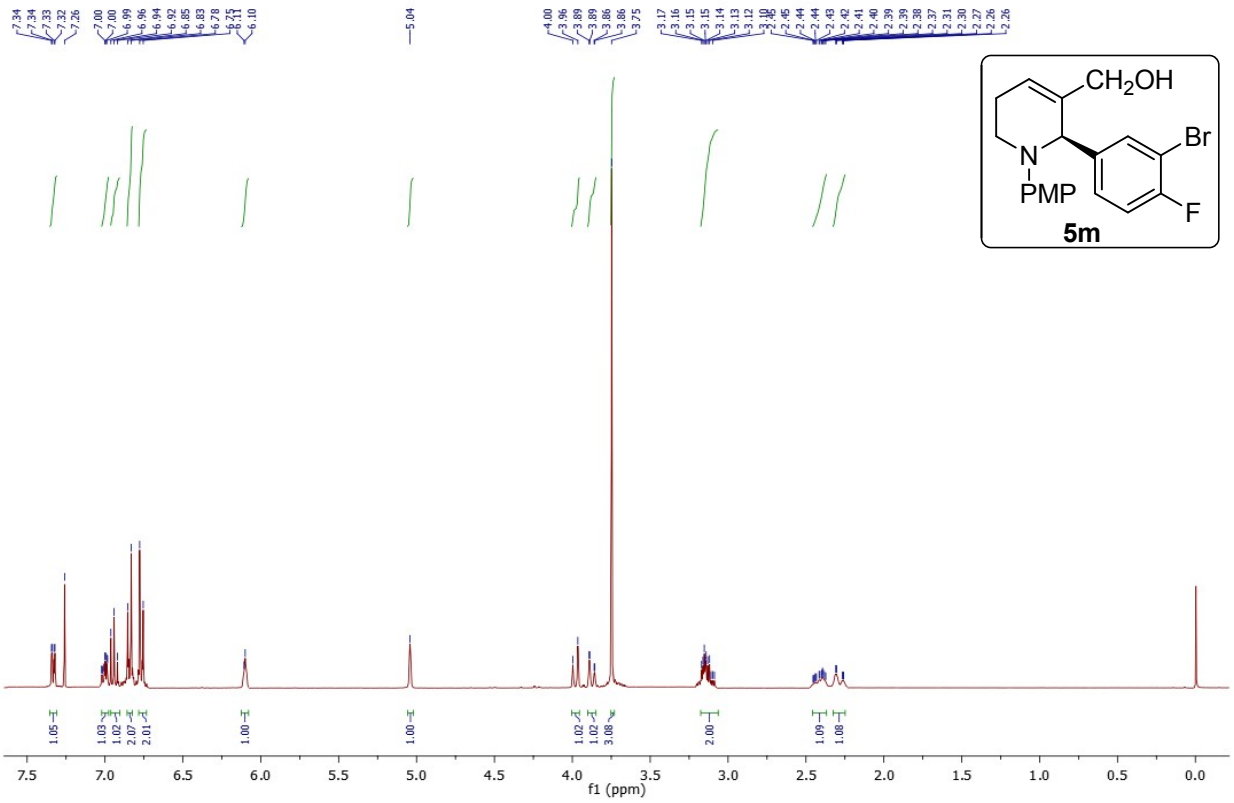
5l

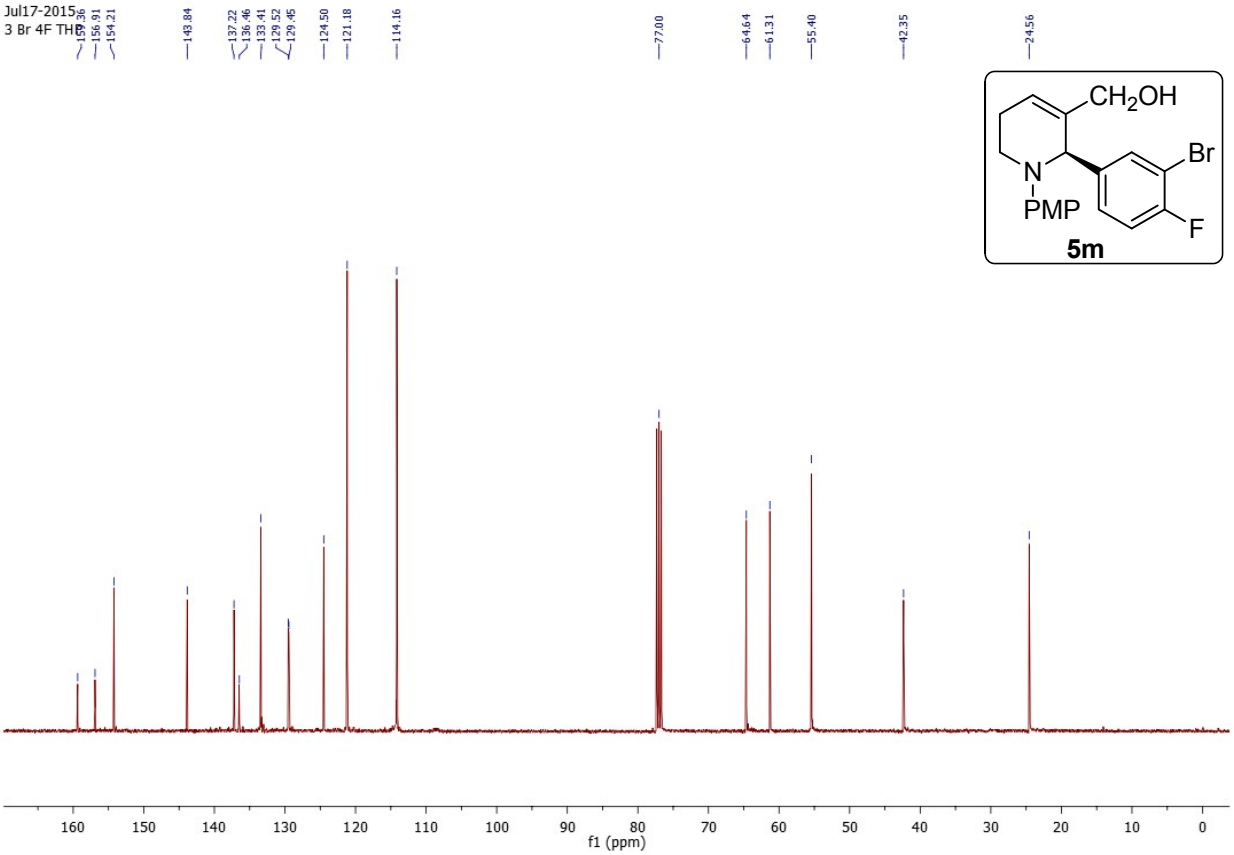


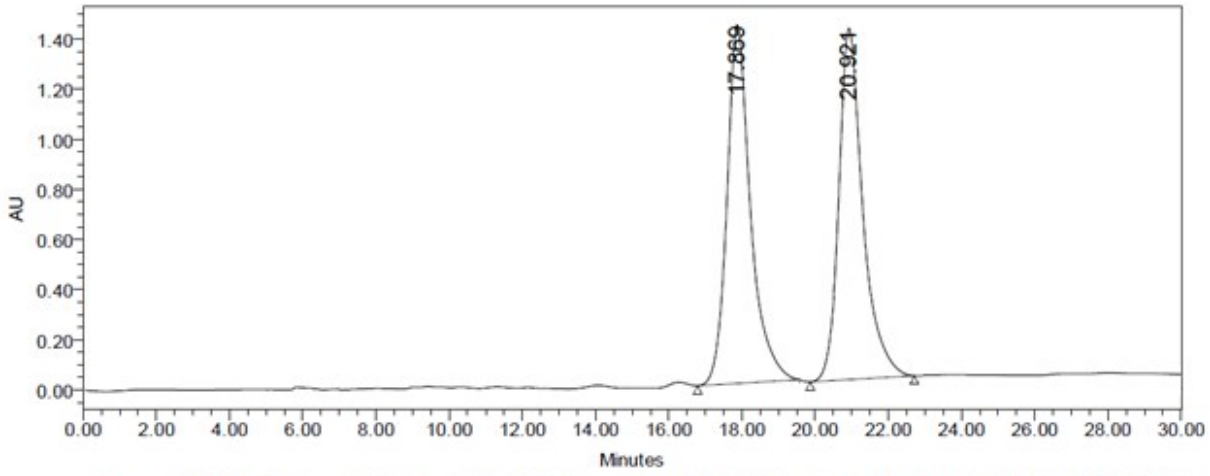
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 7998; Processing Method: 4 BROMO CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	21.191	13203192	7.81	280793
2	PDA 250.0 nm	25.148	155825705	92.19	3192249


CH2OH
Br
N
PMP
F
5m
f1 (ppm)

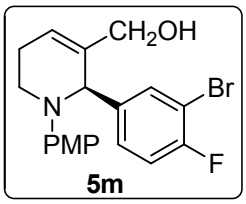

Jul17-2015
3 Br 4F THB
CH2OH
Br
N
PMP
F
5m
f1 (ppm)

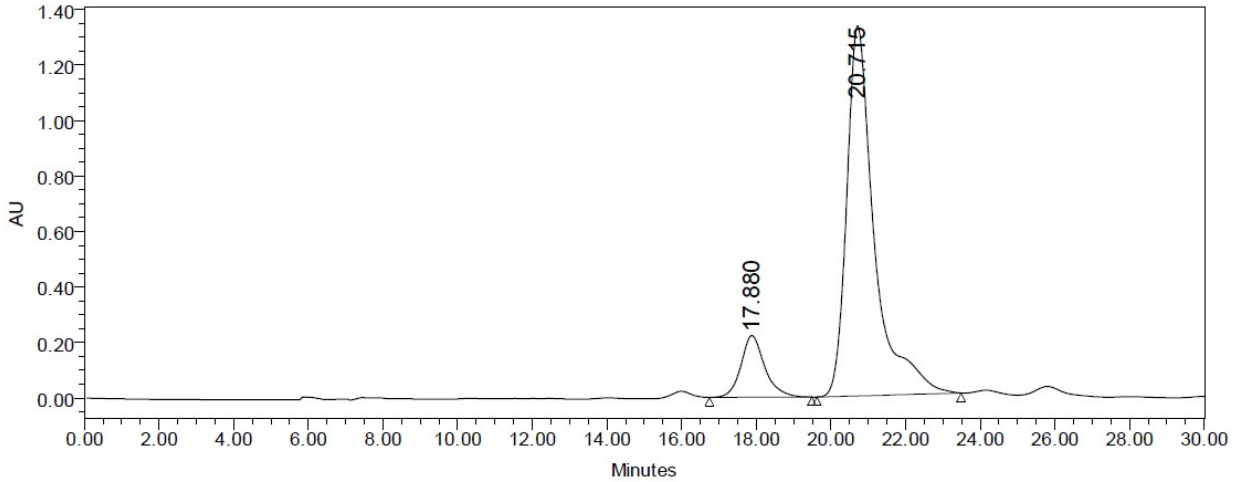


Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8056; Processing Method: 3BR 4F RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.869	64069717	55.00	1430273
2	PDA 250.0 nm	20.921	52410682	45.00	1314742

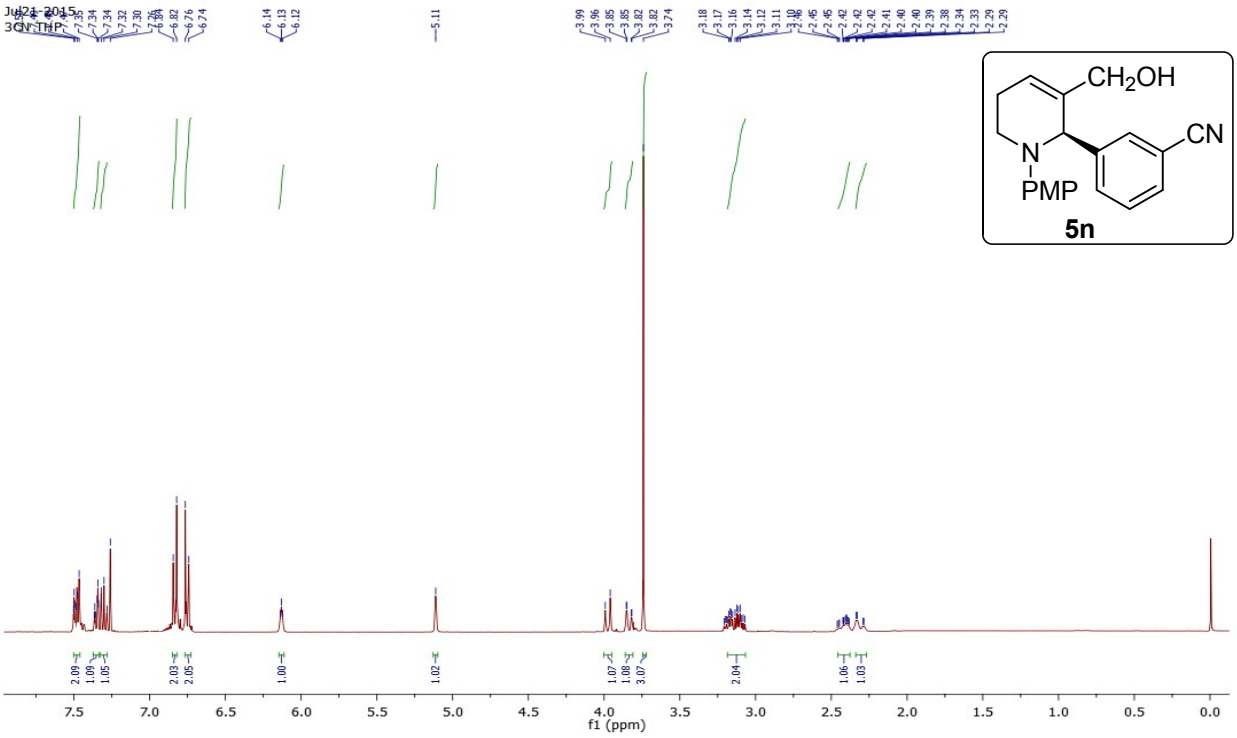


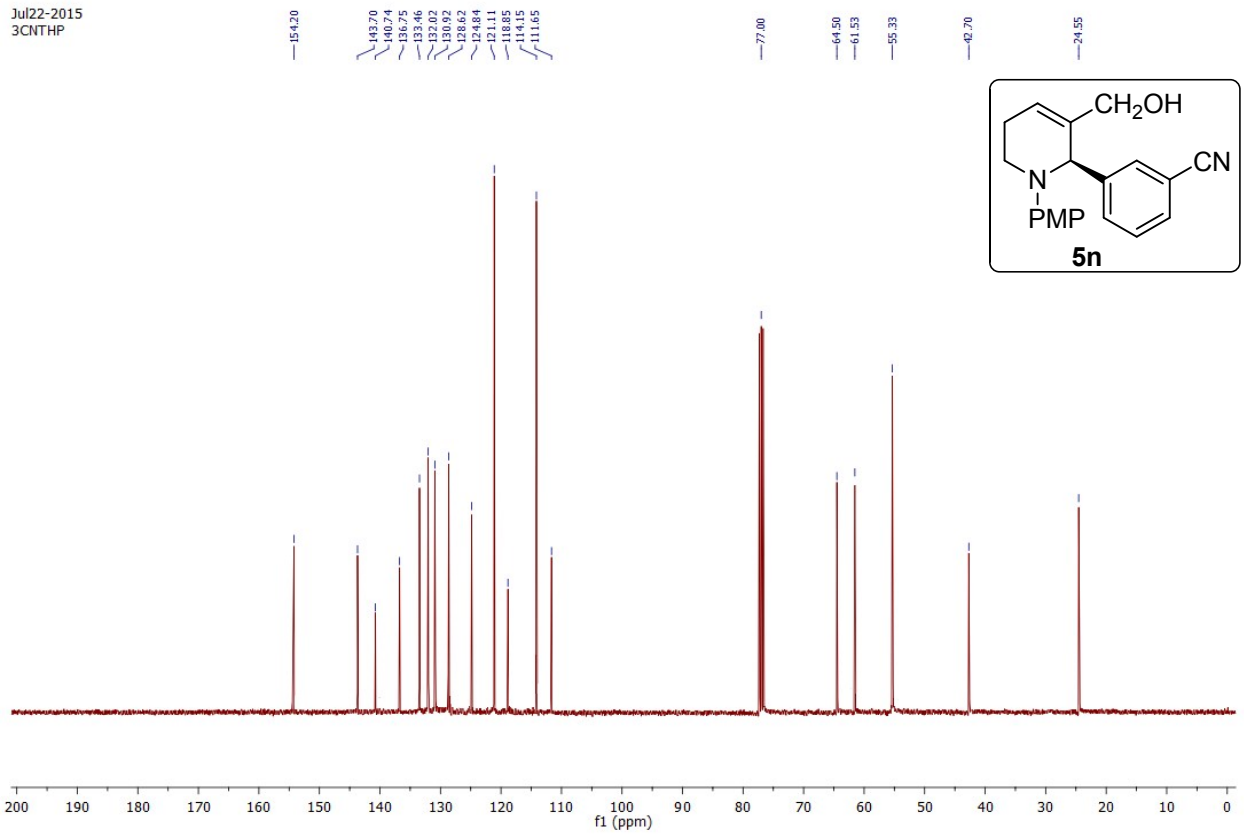


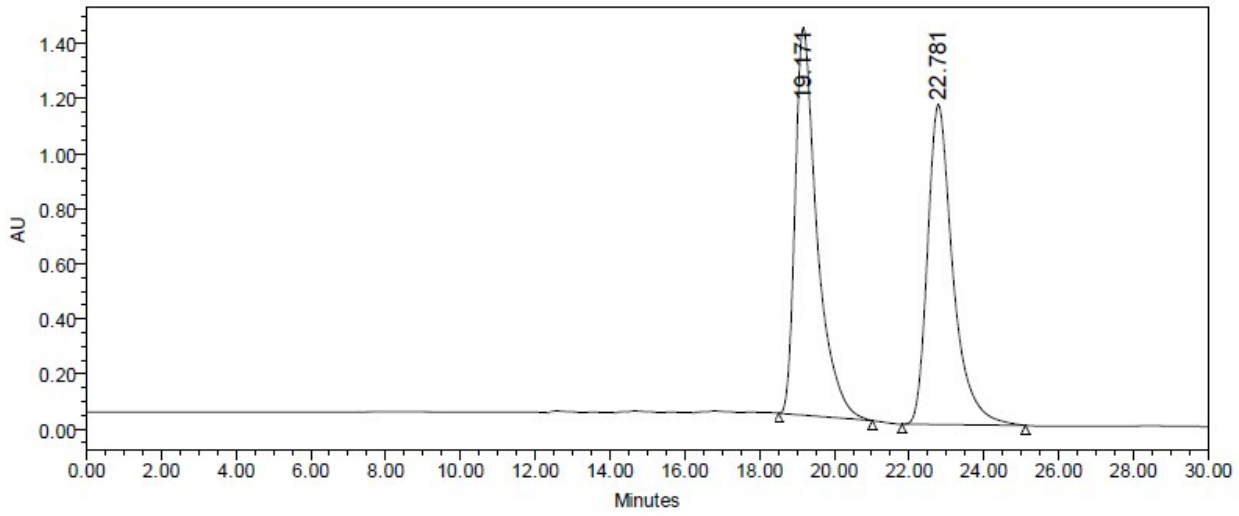
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8045; Processing Method: 3 BR 4 F CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.880	9838697	12.52	222367
2	PDA 250.0 nm	20.715	68715444	87.48	1333644


Jul21-2015
3CNTHP
CH2OH
CN
N
PMP
5n
f1 (ppm)

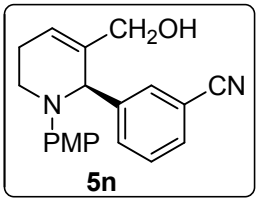

Jul22-2015
3CNTHP
CH2OH
CN
N
PMP
5n
f1 (ppm)



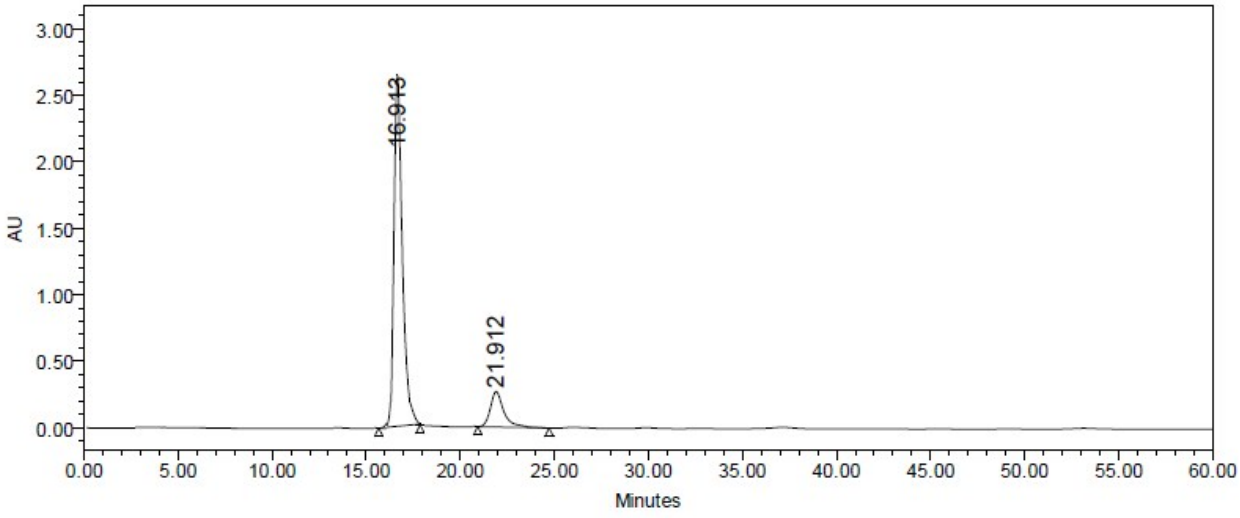
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8287; Processing Method: 3 CN RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	19.171	57318668	51.14	1407707
2	PDA 250.0 nm	22.781	54760710	48.86	1162400



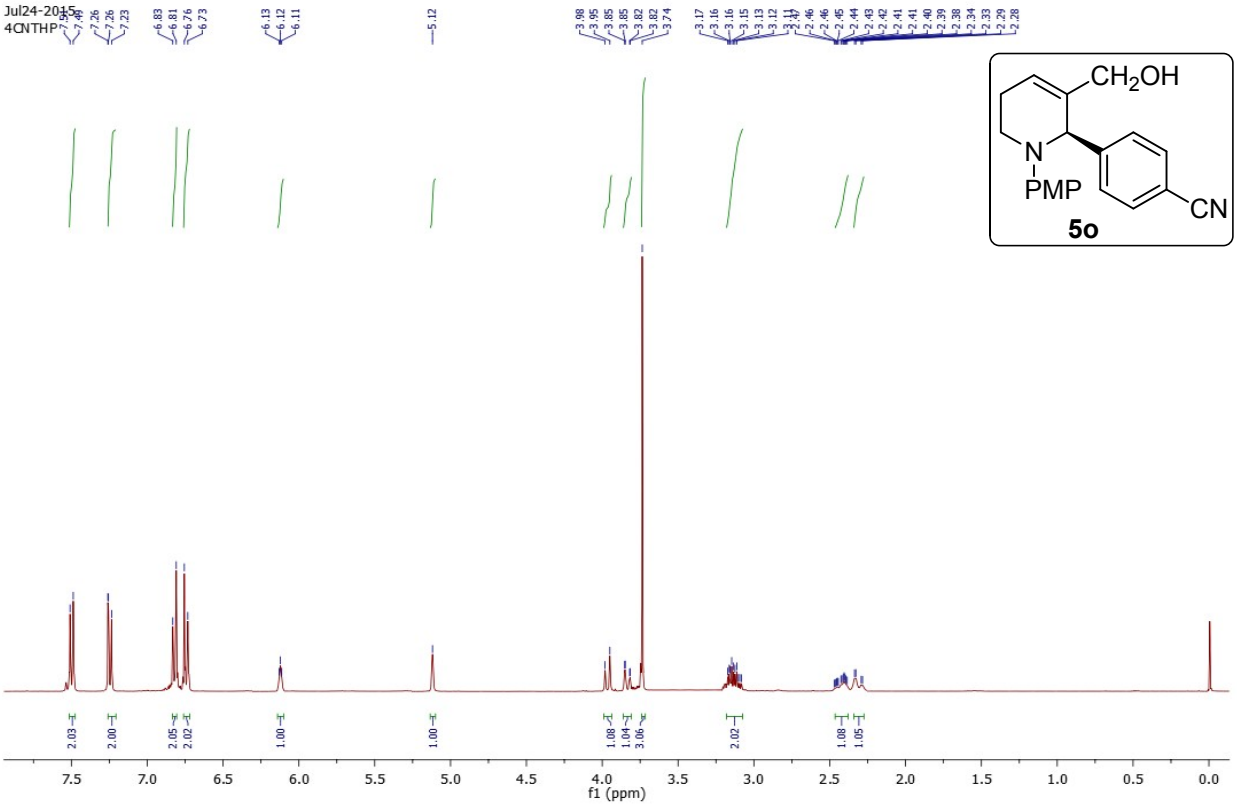
5n

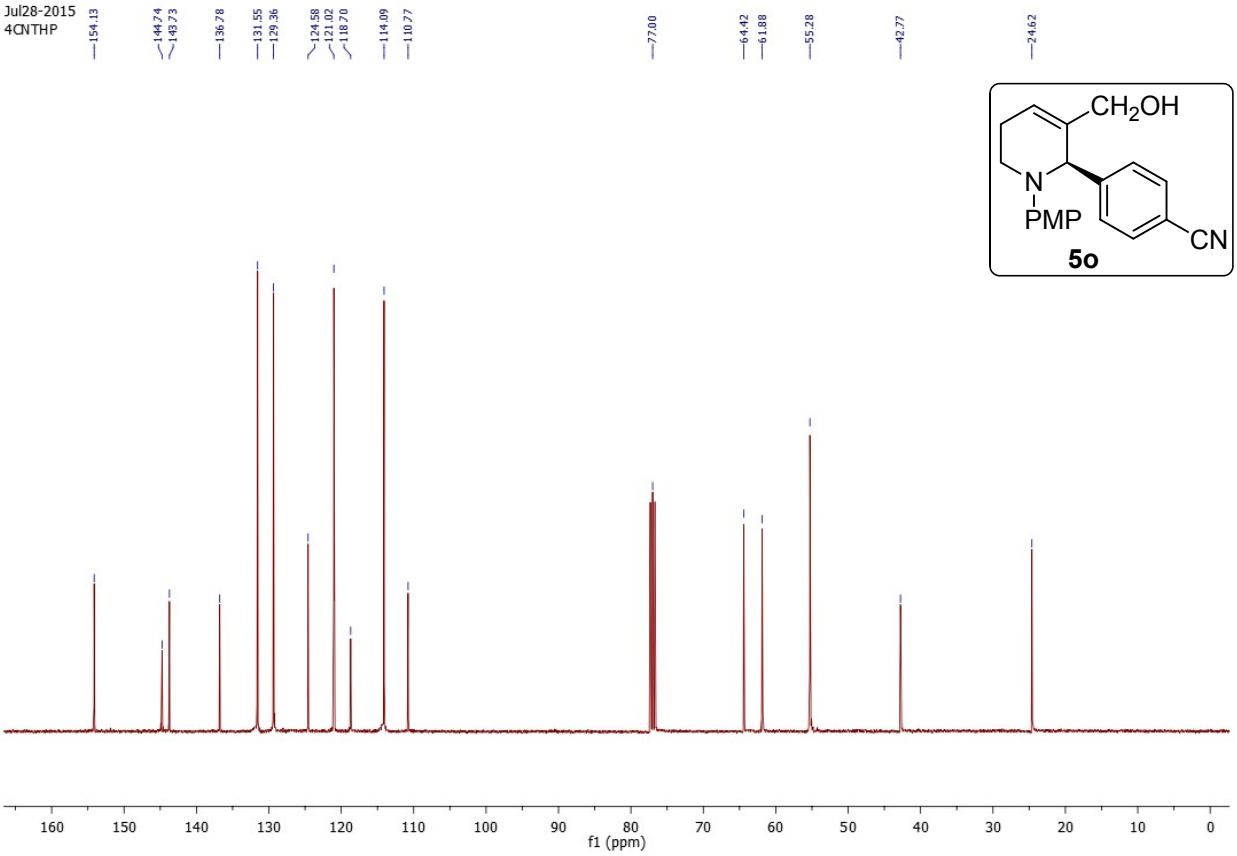


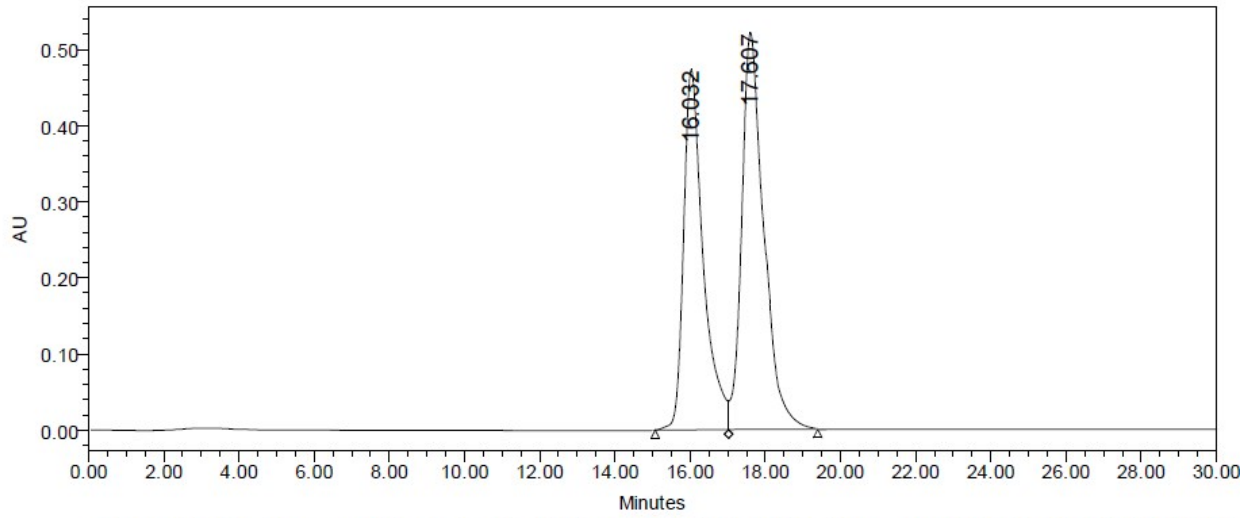
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8285; Processing Method: 3 CN CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	16.913	98406714	88.09	2907512
2	PDA 250.0 nm	21.912	13300190	11.91	267504


Jul24-2015
4CNTHP
CH2OH
N
PMP
CN
5o
f1 (ppm)

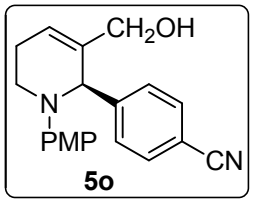

Jul28-2015
4CNTHP
CH2OH
N
PMP
CN
5o
f1 (ppm)

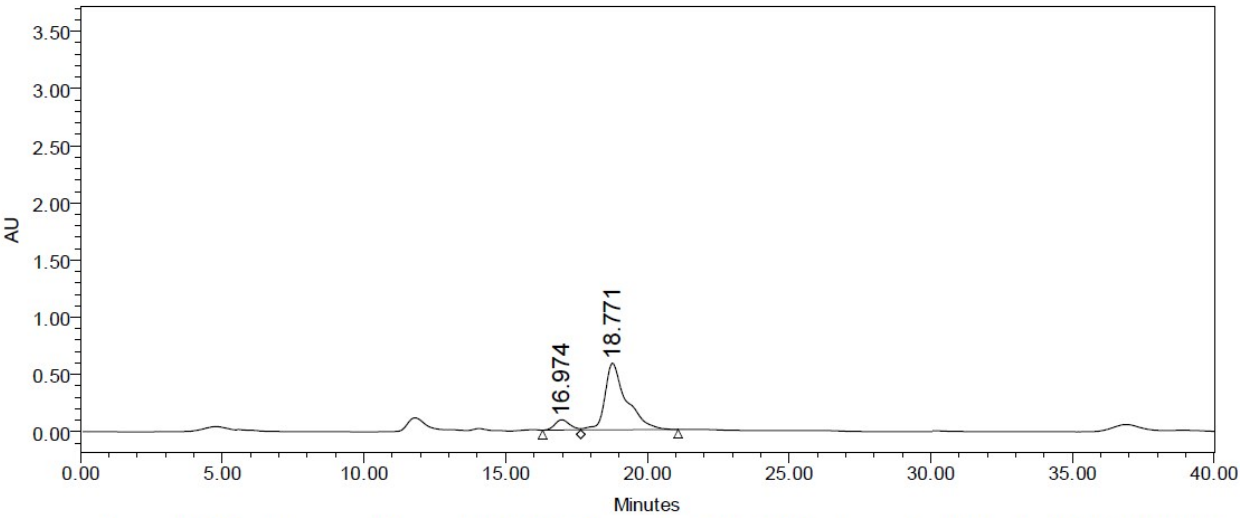


Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8122; Processing Method: 4CN RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	16.032	17238920	36.88	473417
2	PDA 250.0 nm	17.607	29507228	63.12	521904

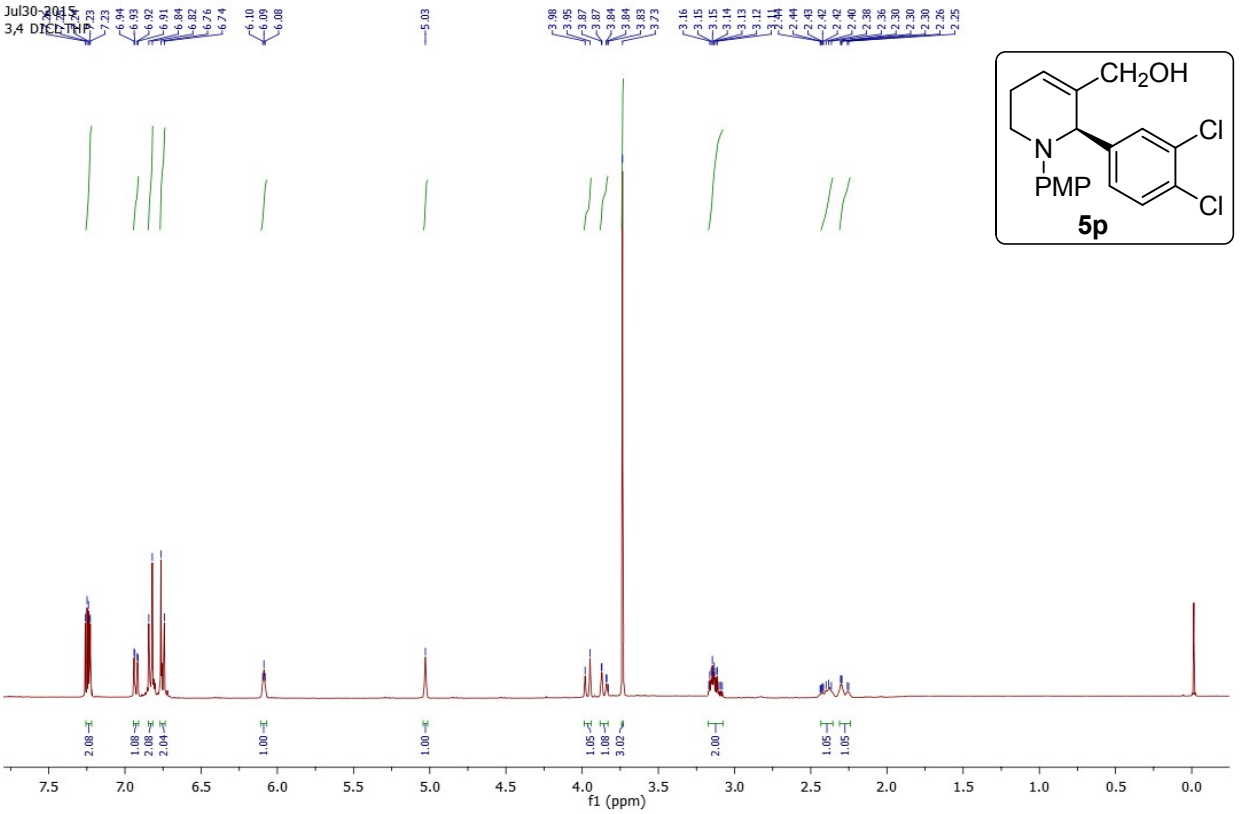


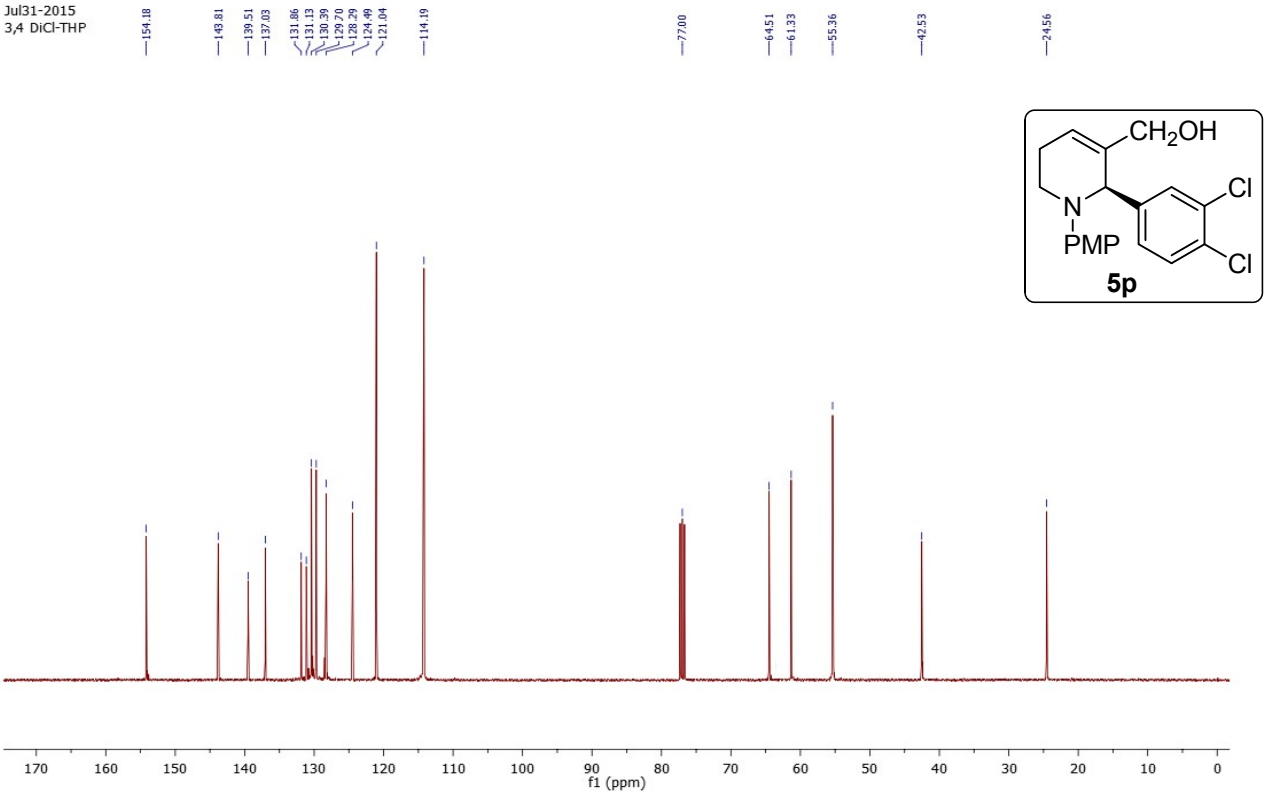


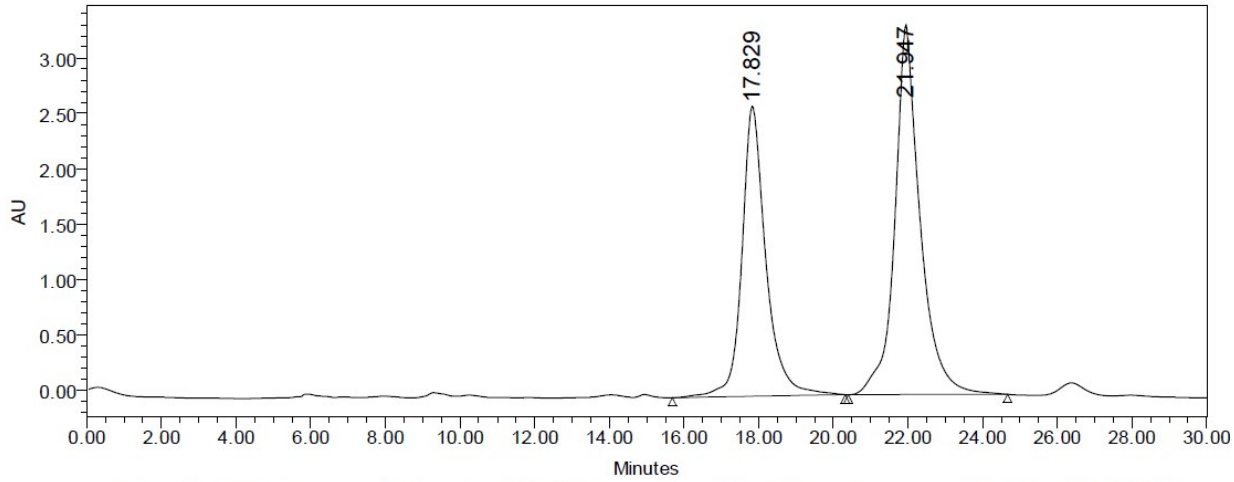
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8120; Processing Method: 4CN CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	16.974	3333045	9.80	91005
2	PDA 250.0 nm	18.771	30667437	90.20	581946


Jul30-2015
3,4 DiCl-THP
CH2OH
Cl
N
PMP
Cl
5p
f1 (ppm)

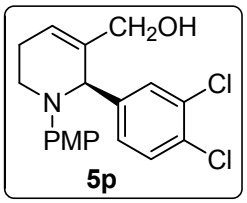

Jul31-2015
3,4 DiCl-THP
CH2OH
Cl
N
PMP
Cl
5p
f1 (ppm)



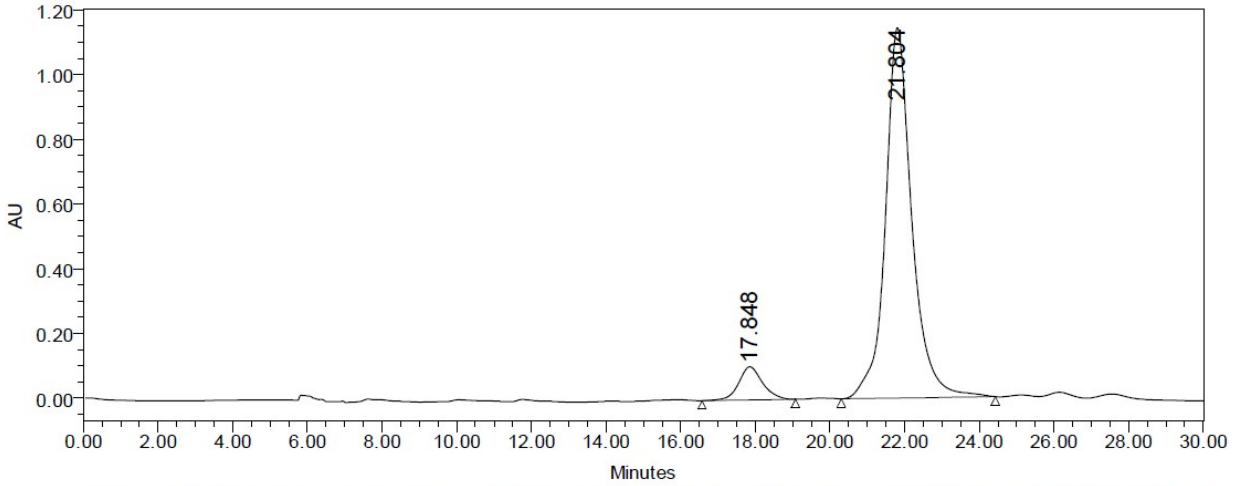
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8043; Processing Method: 3 4 DICHLORO RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.829	117093886	42.72	2615794
2	PDA 250.0 nm	21.947	157000148	57.28	3343128



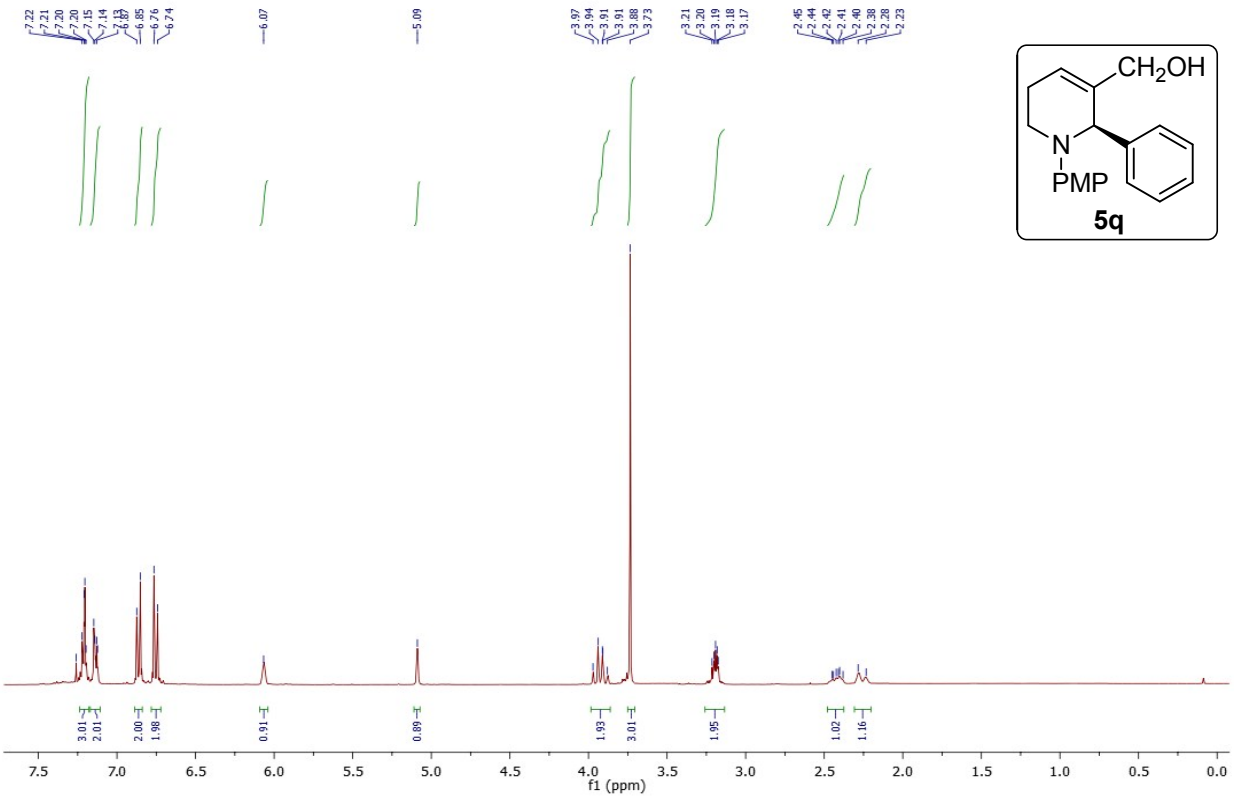
5p

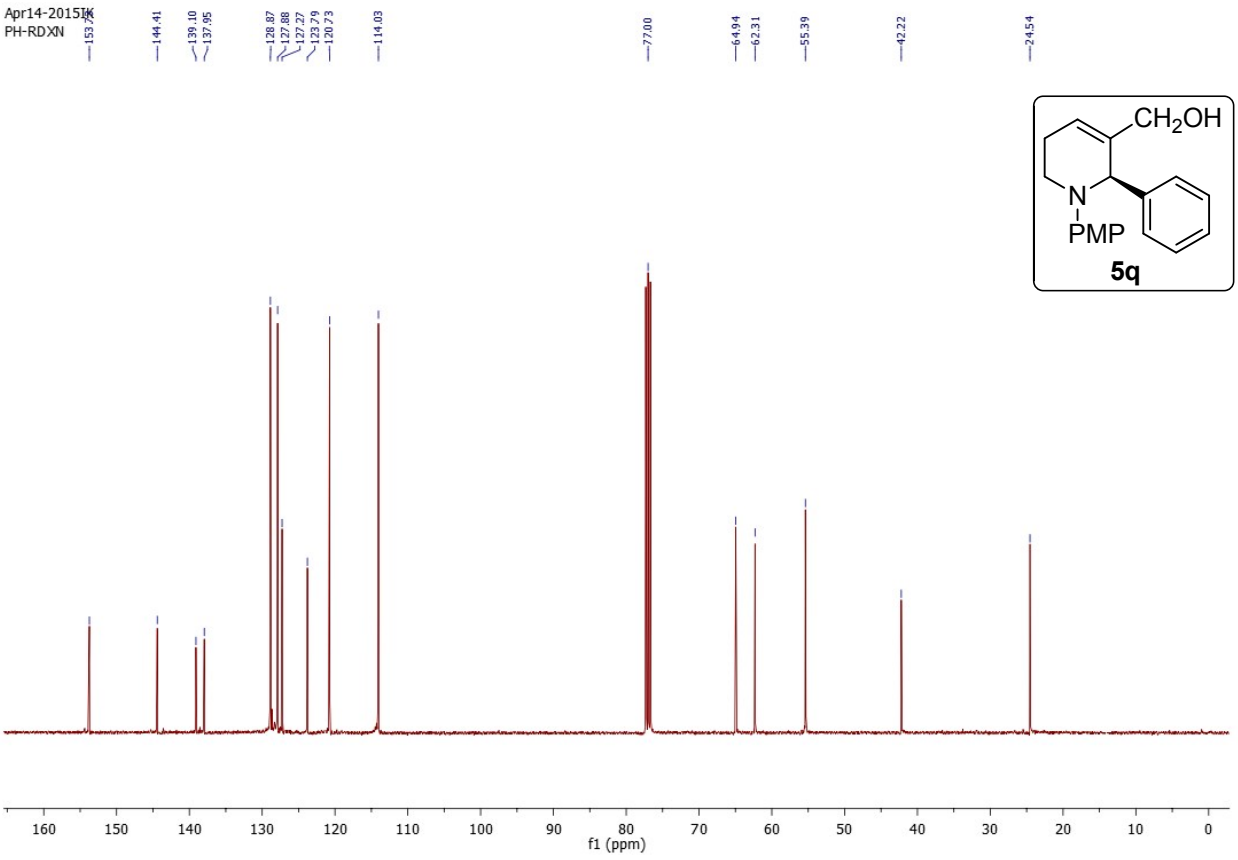


Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8041; Processing Method: 3 4 DICHLORO THP CHIRAL

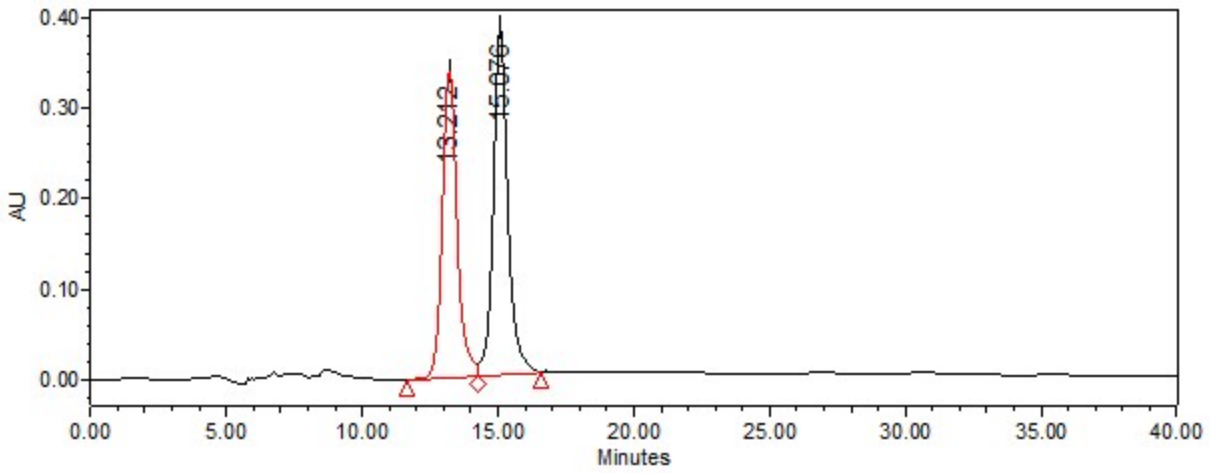
Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	17.848	4566887	7.48	102766
2	PDA 250.0 nm	21.804	56495197	92.52	1144218

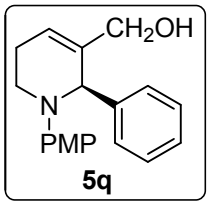

7.22
7.21
7.20
7.20
7.15
7.14
7.13
6.87
6.85
6.76
6.74
6.07
5.09
3.97
3.94
3.91
3.91
3.88
3.73
3.21
3.20
3.19
3.18
3.17
2.45
2.44
2.42
2.41
2.40
2.38
2.28
2.23
CH2OH
N
PMP
5q
3.01
2.01
2.00
1.98
0.91
0.89
1.93
3.01
1.95
1.02
1.16
f1 (ppm)


Apr14-2015IK
PH-RDXN
153.27
144.41
139.10
137.95
128.87
127.88
127.27
123.79
120.73
114.03
77.00
64.94
62.31
55.39
42.22
24.54
CH2OH
N
PMP
5q
f1 (ppm)

Racemic phenyl thp

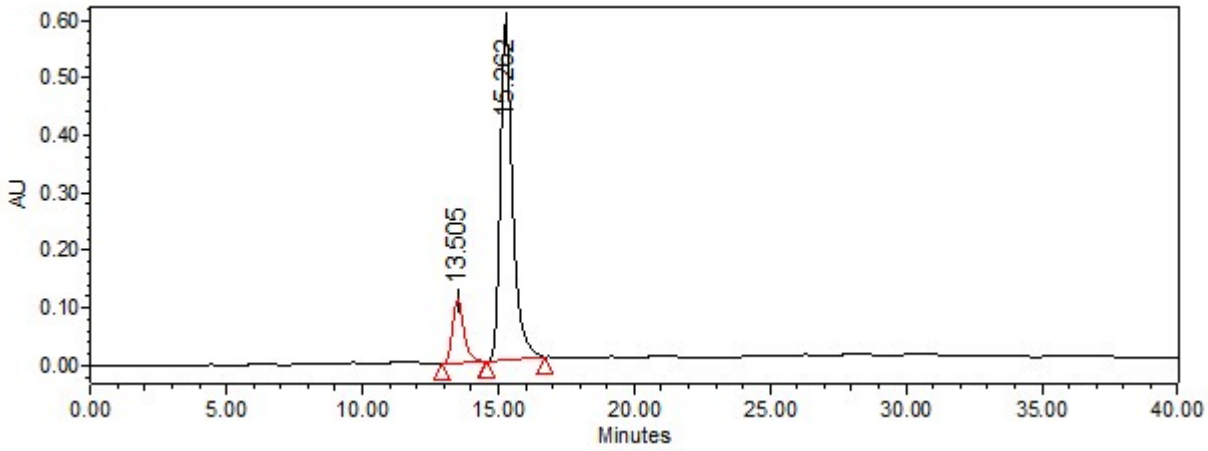


	Retention Time	Area	% Area	Height
1	13.212	13027787	47.57	339344
2	15.076	14361165	52.43	383744



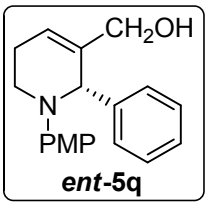
5q

Chiral **5q**

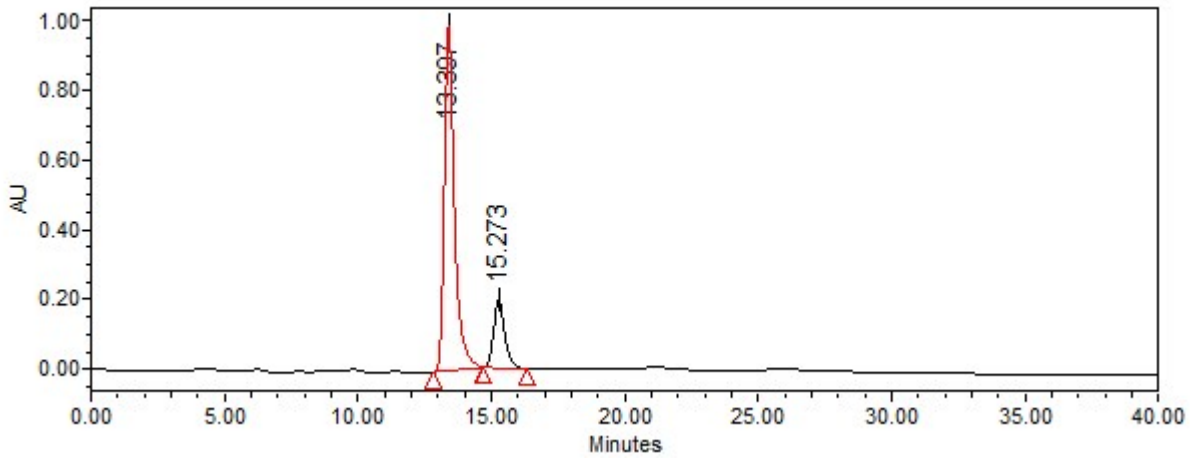


	Retention Time	Area	% Area	Height
1	13.505	3275267	15.03	109433
2	15.262	18522896	84.97	583829

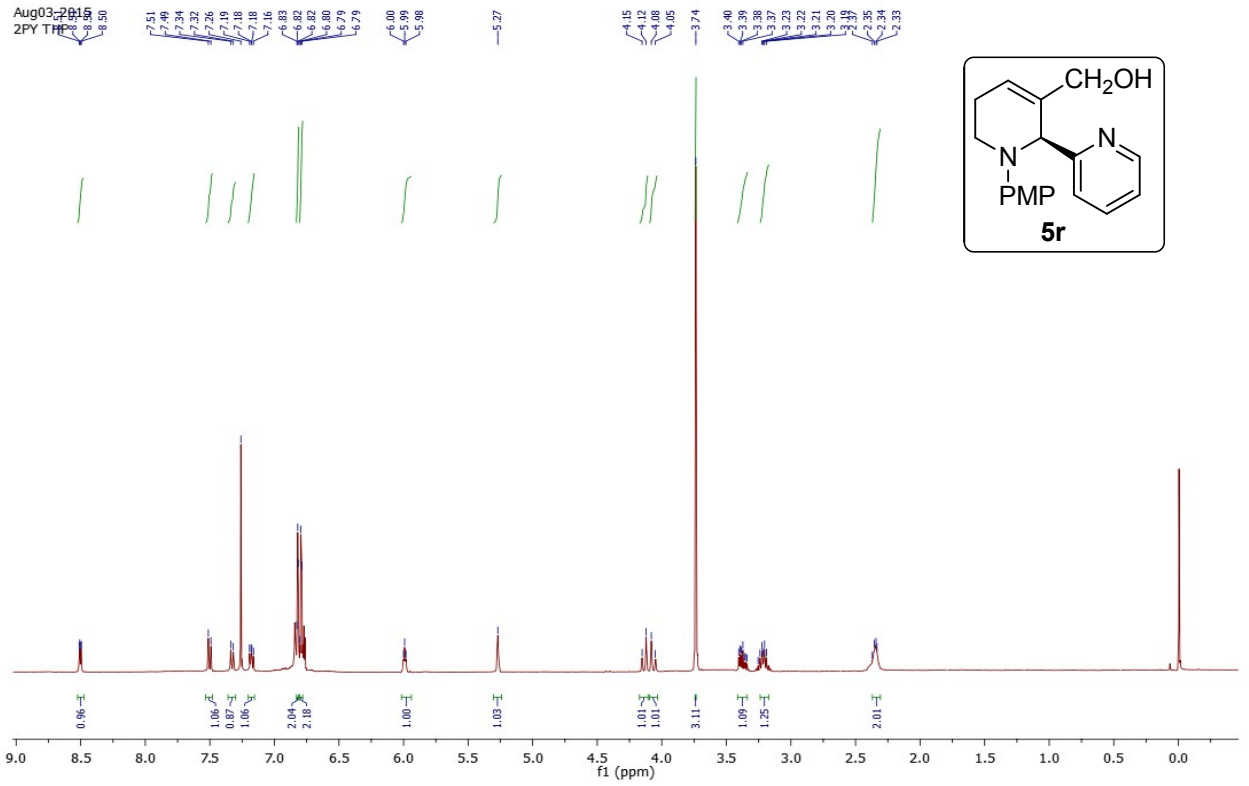
Chiral *ent*-**5q**

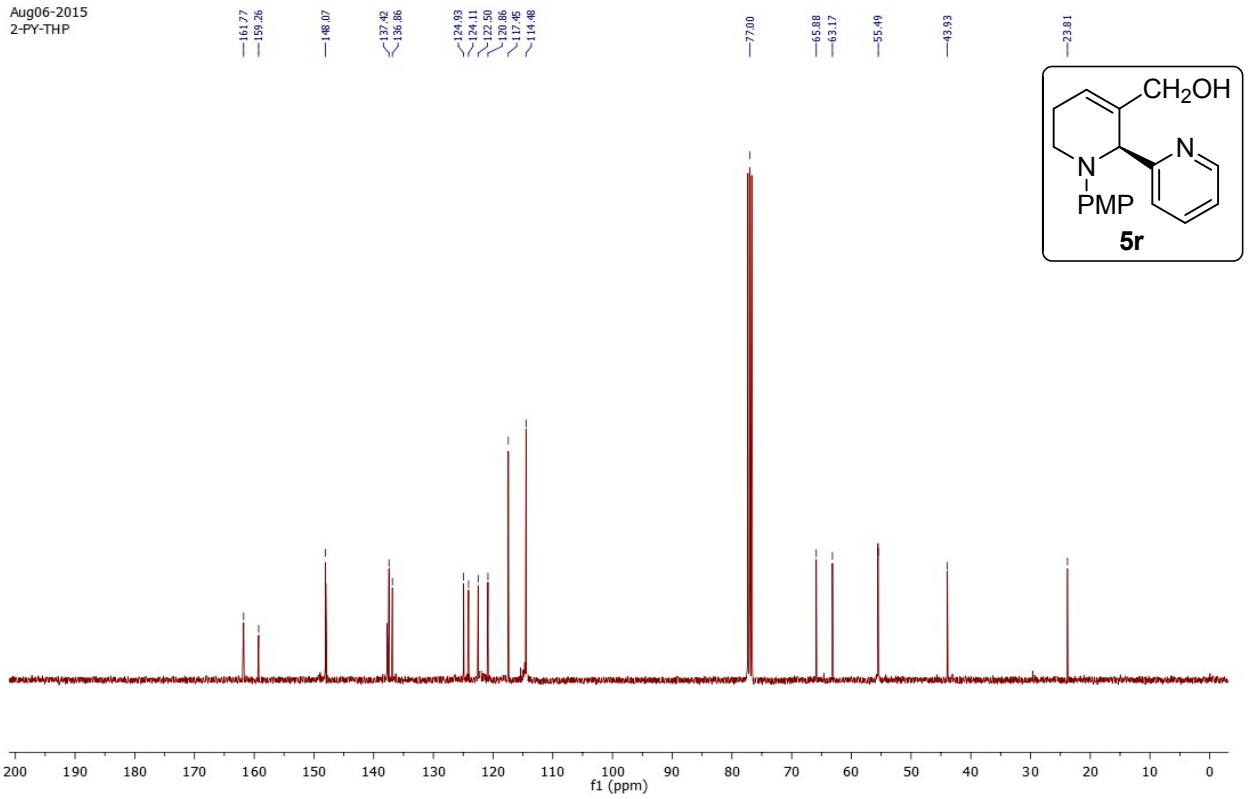


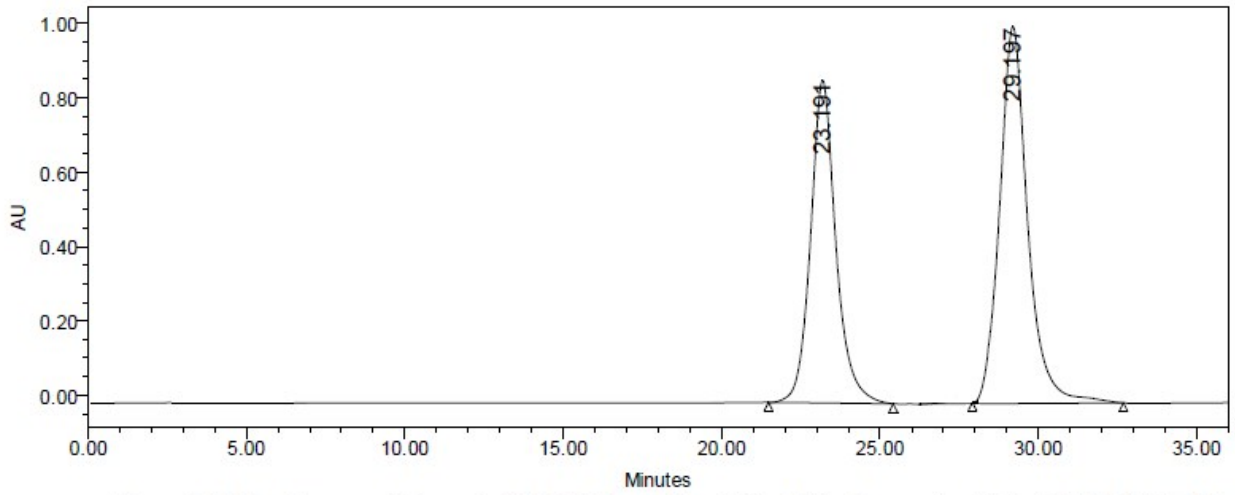
***ent*-5q**



	Retention Time	Area	% Area	Height	Int Type
1	13.397	25885435	81.91	991350	BB
2	15.273	5715748	18.09	197306	BB


Aug03-2015
2PY THP
CH2OH
N
N
PMP
5r
f1 (ppm)

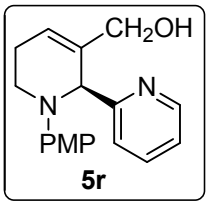

Aug06-2015
2-PY-THP
CH2OH
N
N
PMP
5r
f1 (ppm)



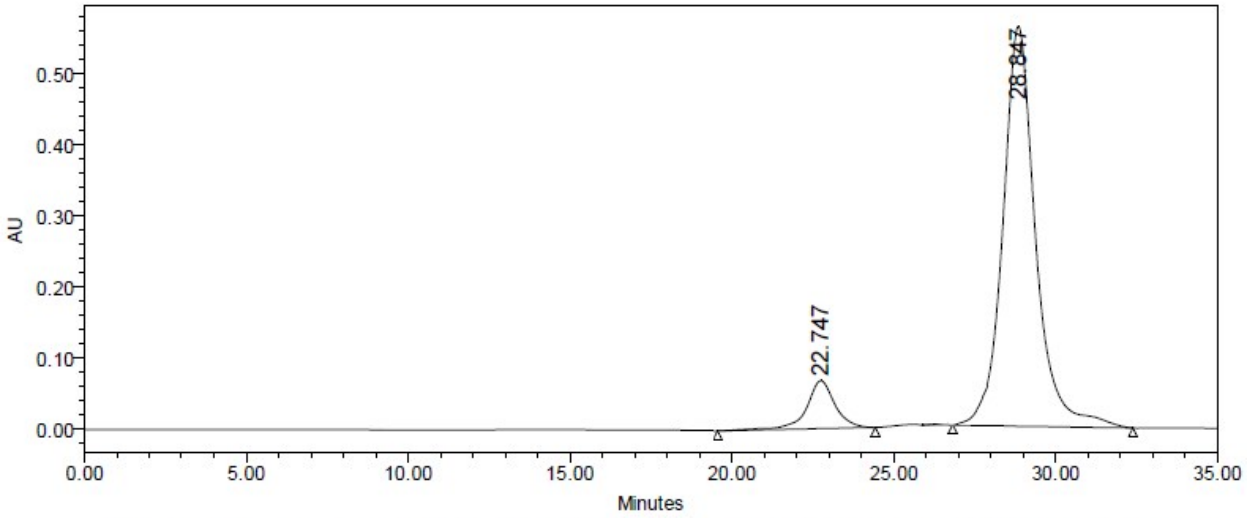
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8341; Processing Method: 2 PY RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	23.191	48295556	42.30	868004
2	PDA 250.0 nm	29.197	65883976	57.70	1014510



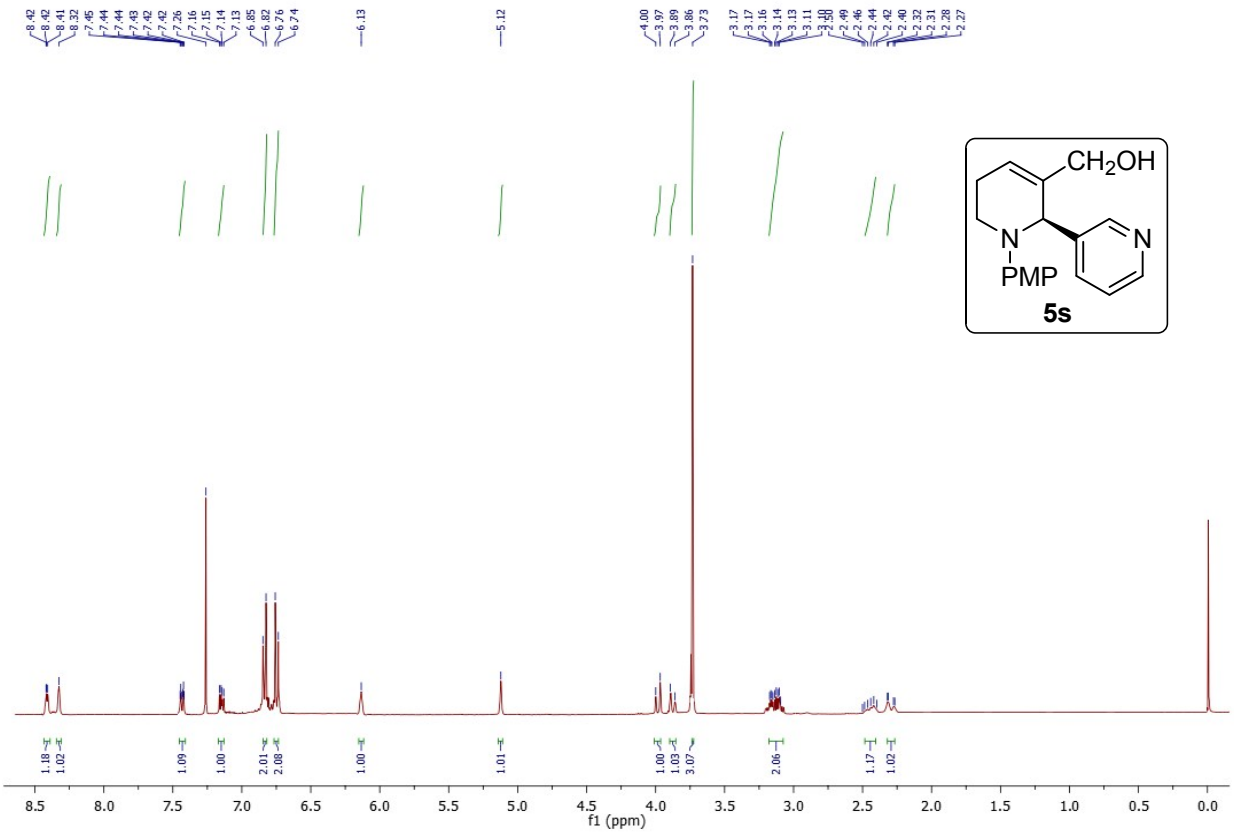
5r

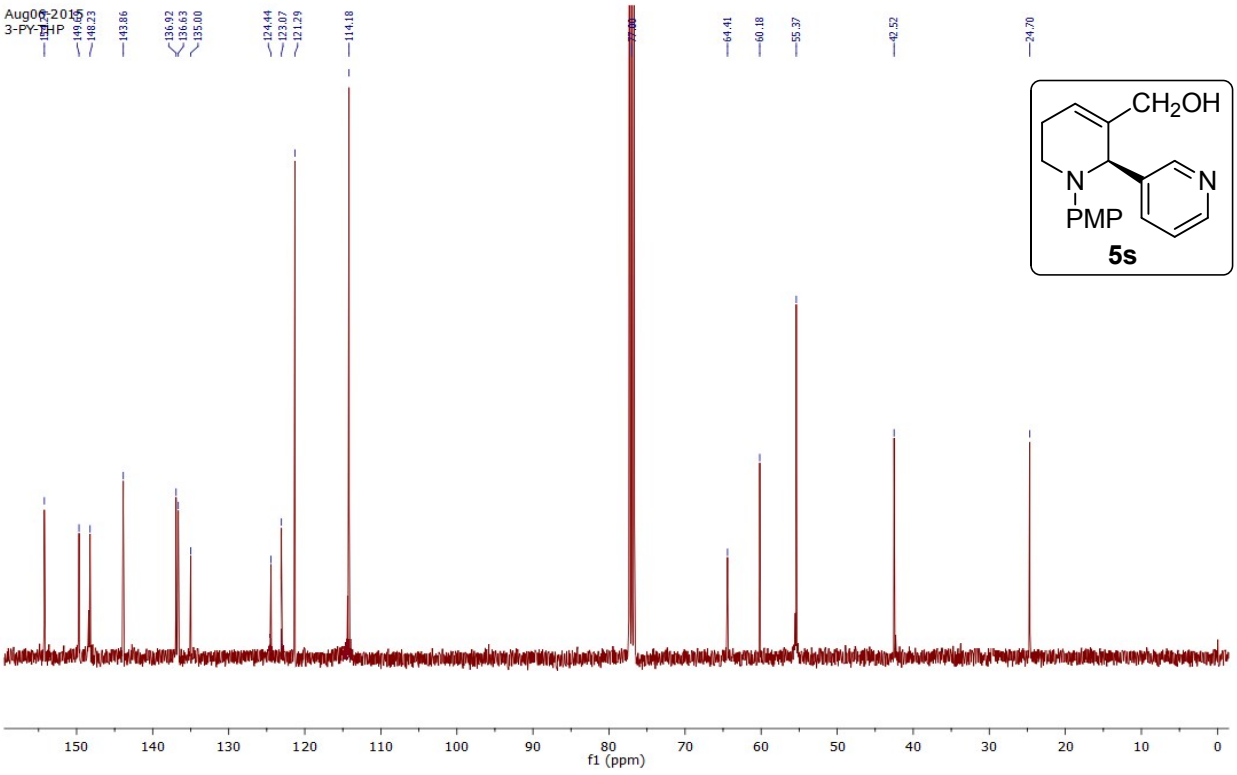


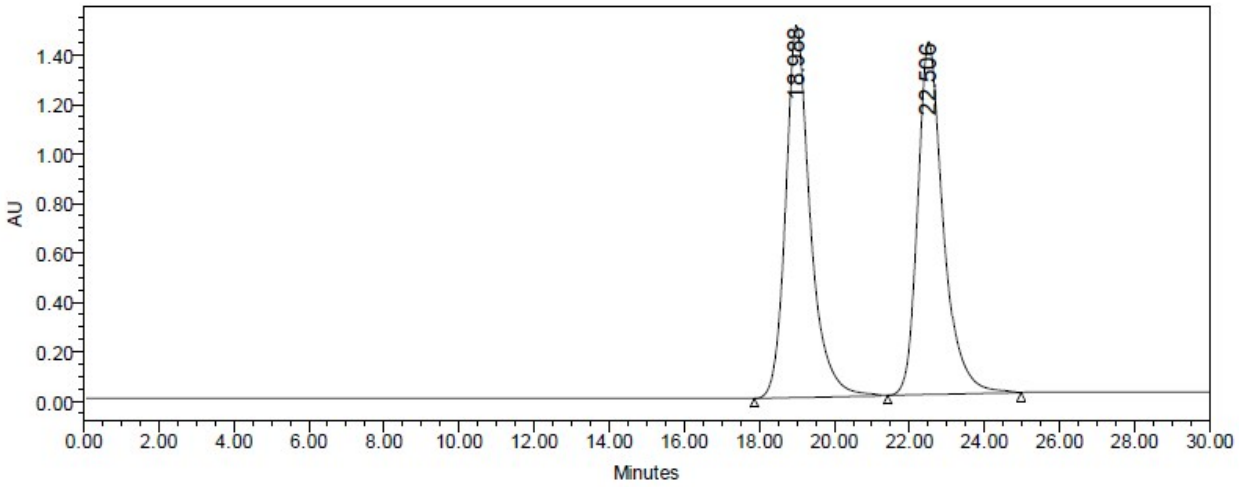
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8350; Processing Method: PY CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	22.747	4125038	9.17	67417
2	PDA 250.0 nm	28.847	40870051	90.83	562472


CH2OH
N
N
PMP
5s
f1 (ppm)

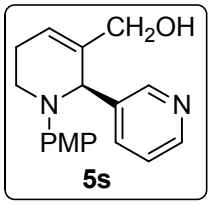

Aug06-2015
3-PY-THP
CH2OH
N
N
PMP
5s
f1 (ppm)



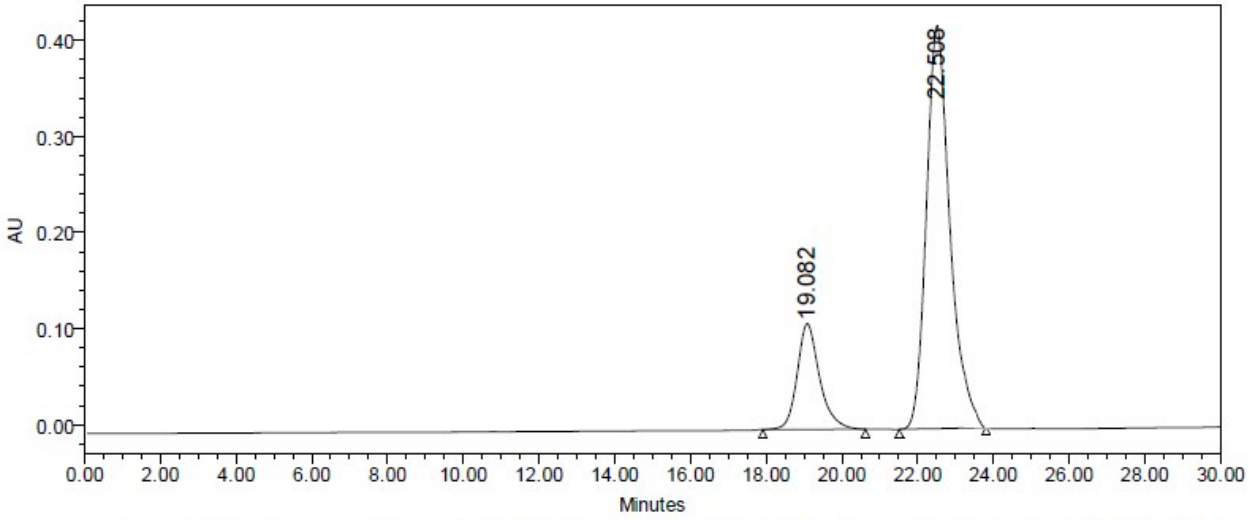
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8199; Processing Method: 3 PY RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	18.988	68858155	55.03	1504567
2	PDA 250.0 nm	22.506	56273885	44.97	1347839



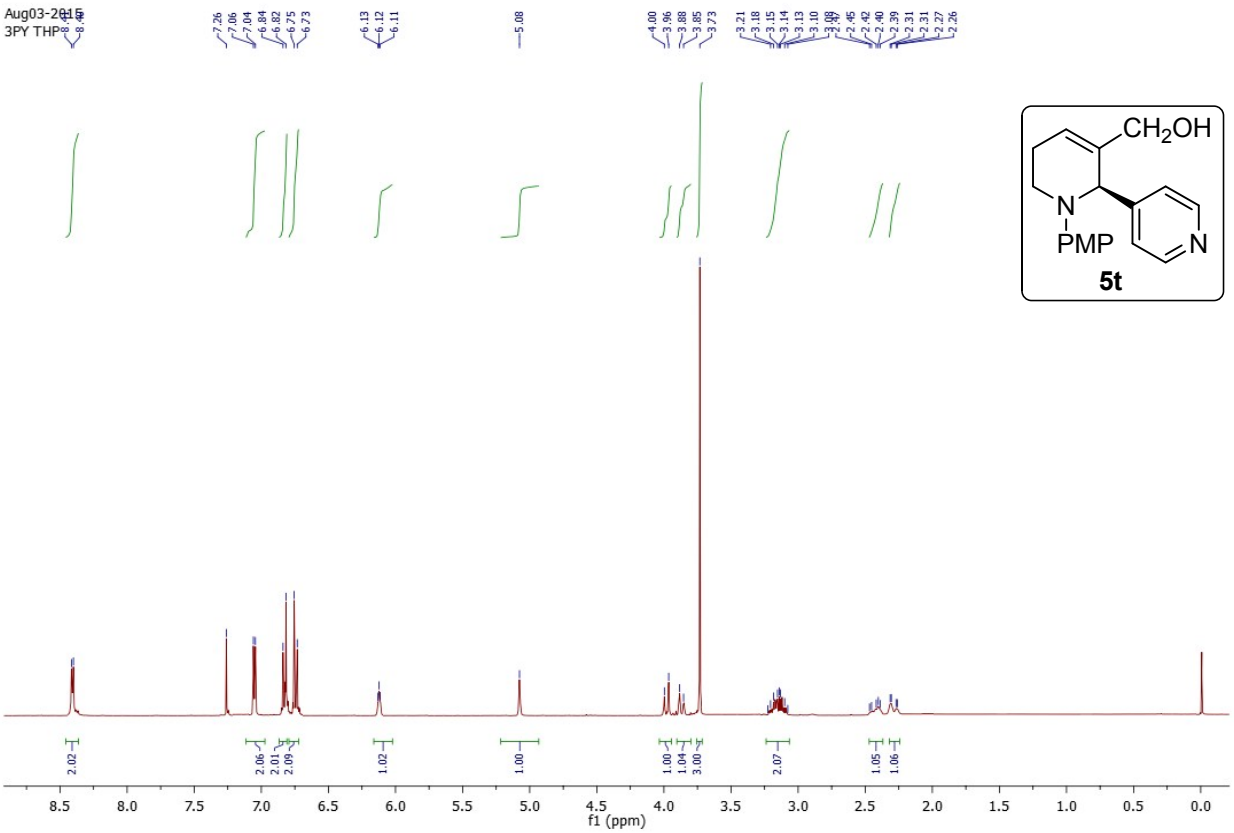
5s

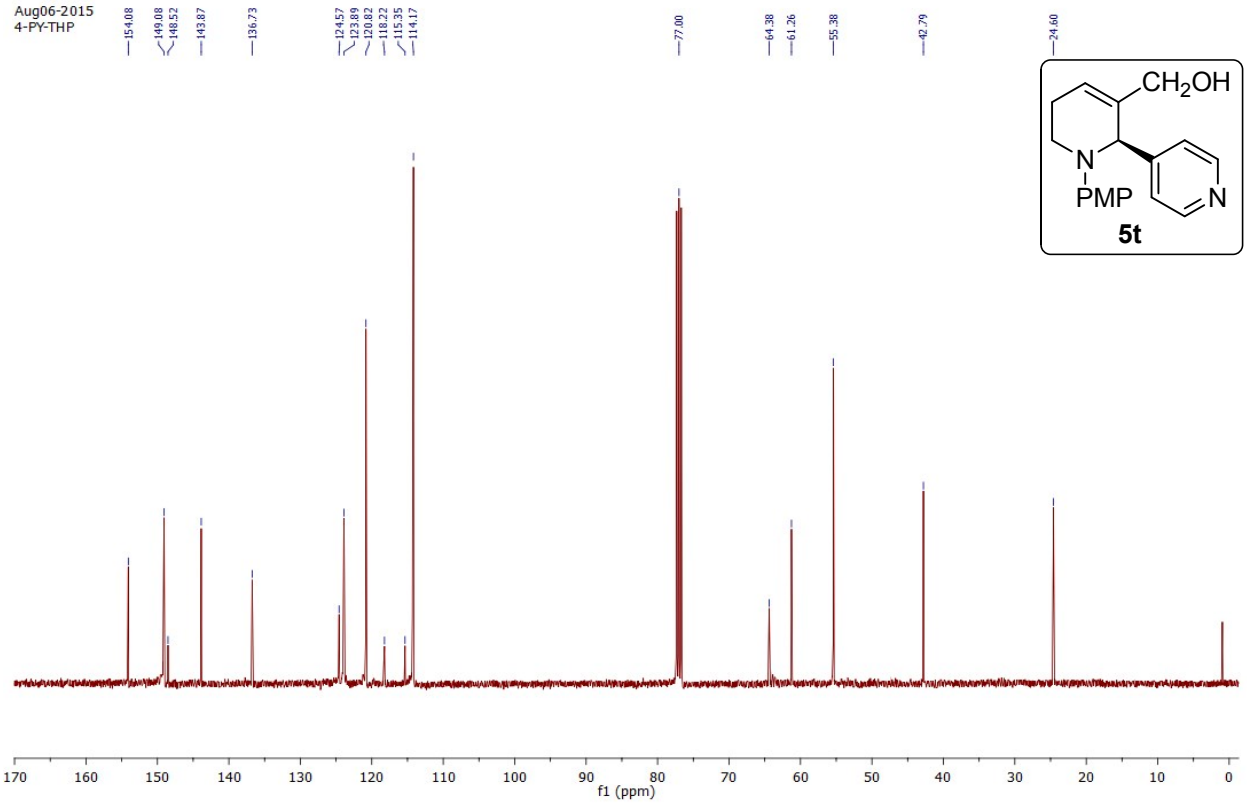


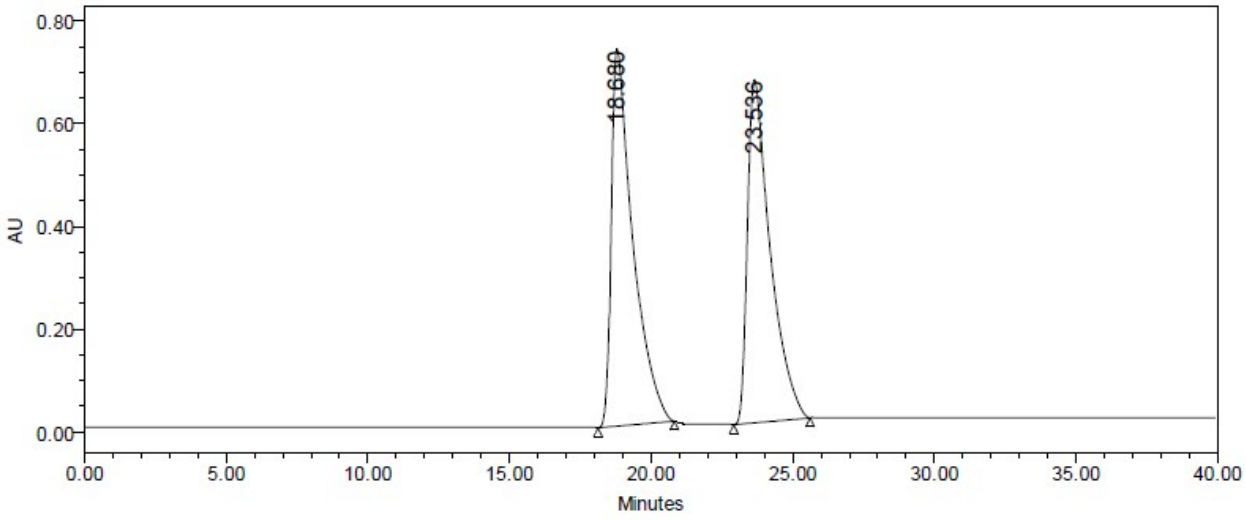
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8197; Processing Method: 3 PY CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	19.082	4513431	18.56	109892
2	PDA 250.0 nm	22.508	19809305	81.44	418745


Aug03-2015
3PY THP
8.47
8.46
7.26
7.06
7.04
6.84
6.82
6.75
6.73
6.13
6.12
6.11
5.08
4.00
3.96
3.88
3.85
3.73
3.21
3.18
3.15
3.14
3.13
3.10
3.08
2.45
2.42
2.40
2.39
2.31
2.31
2.27
2.26
CH2OH
N
PMP
N
5t
2.02
2.06
2.01
2.09
1.02
1.00
1.00
1.04
3.00
2.07
1.05
1.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

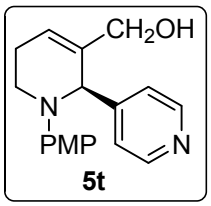

Aug06-2015
4-PY-THP
154.08
149.08
148.52
143.87
136.73
124.57
123.89
120.82
118.22
115.35
114.17
77.00
64.38
61.26
55.38
42.79
24.60
CH2OH
N
PMP
N
5t
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



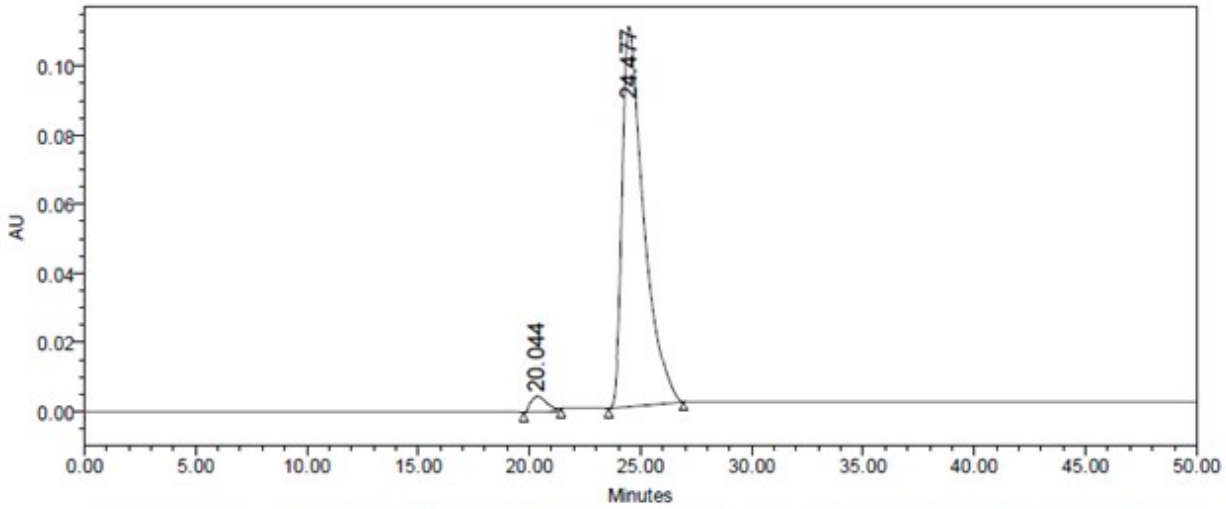
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8152; Processing Method: 4PY RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	18.680	31793344	45.99	707083
2	PDA 250.0 nm	23.536	37339115	54.01	668271



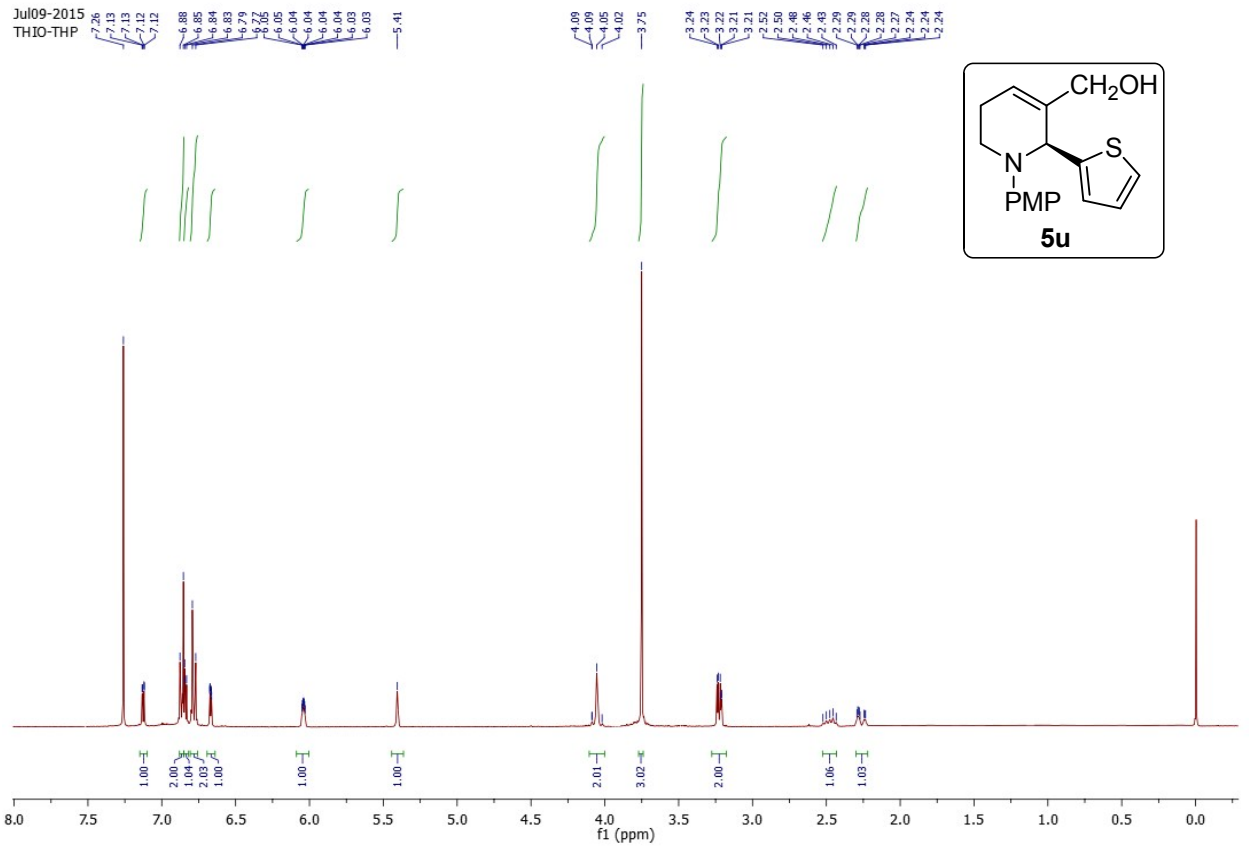
5t

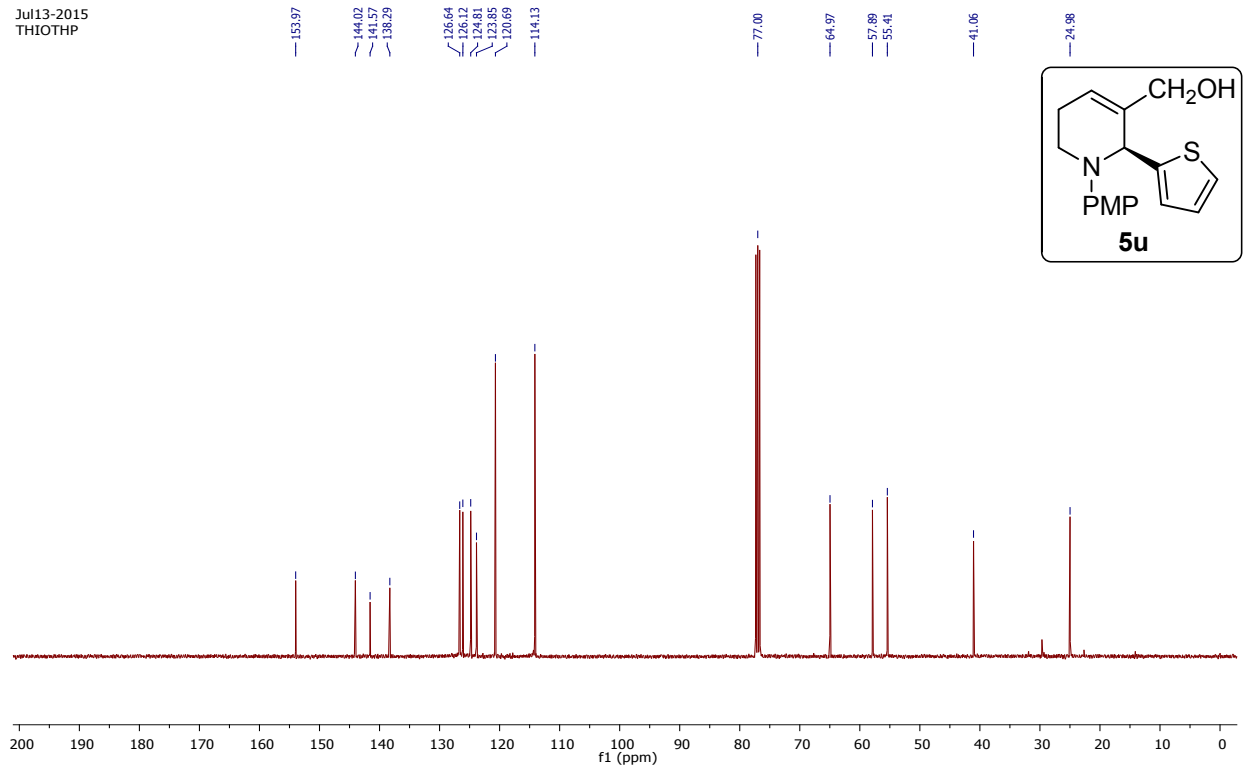


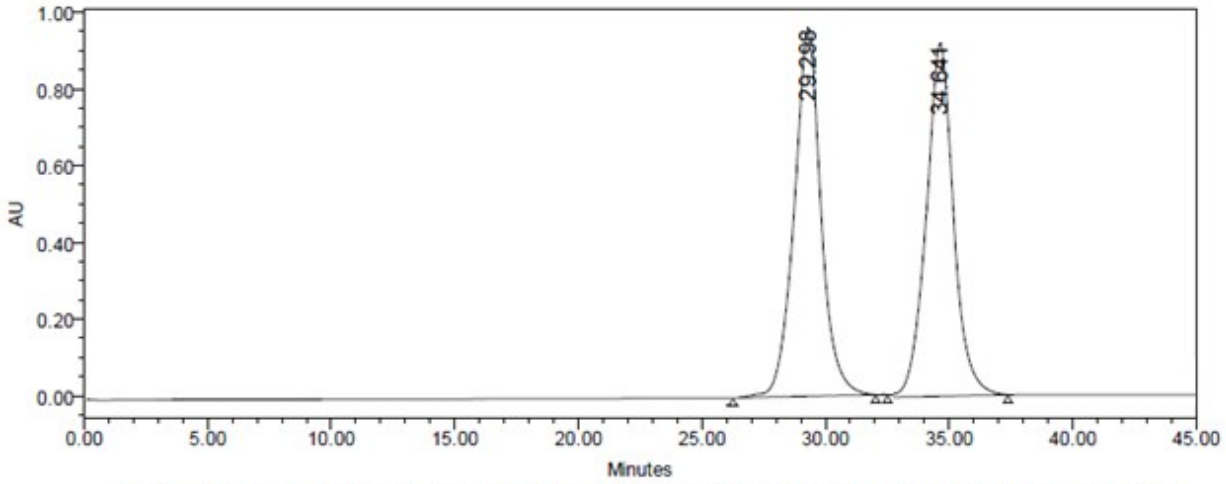
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8150; Processing Method: 4PY CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	20.044	296556	4.24	5200
2	PDA 250.0 nm	24.477	6694887	95.76	107102


Jul09-2015
THIO-THP
CH2OH
N
S
PMP
5u
f1 (ppm)

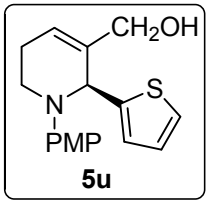

Jul13-2015
THIOTHP
CH2OH
N
S
PMP
5u
f1 (ppm)



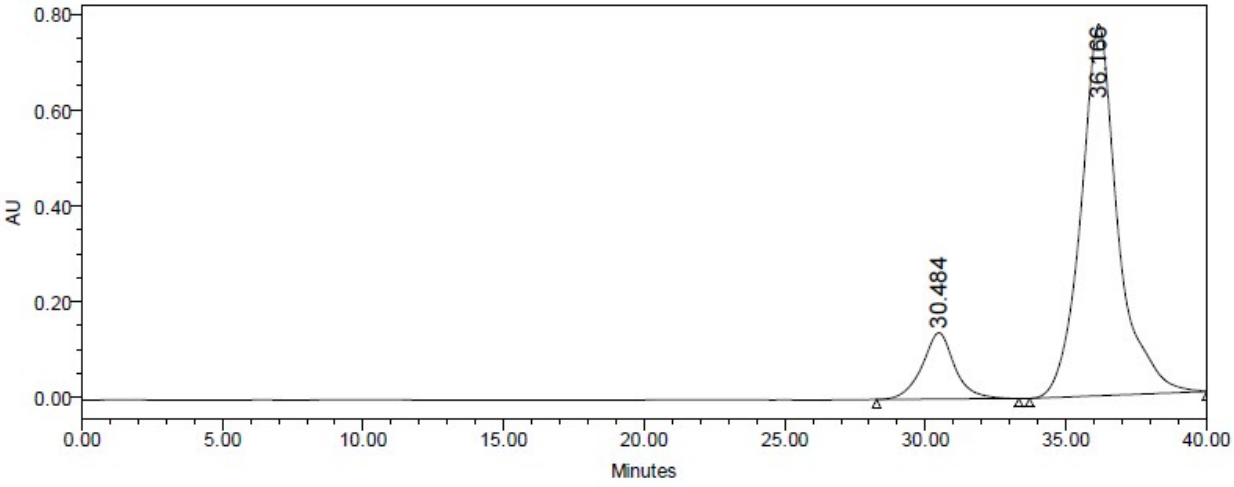
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8079; Processing Method: THIOPHENE 2 RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	29.298	72536719	50.02	959798
2	PDA 250.0 nm	34.641	72465682	49.98	902550



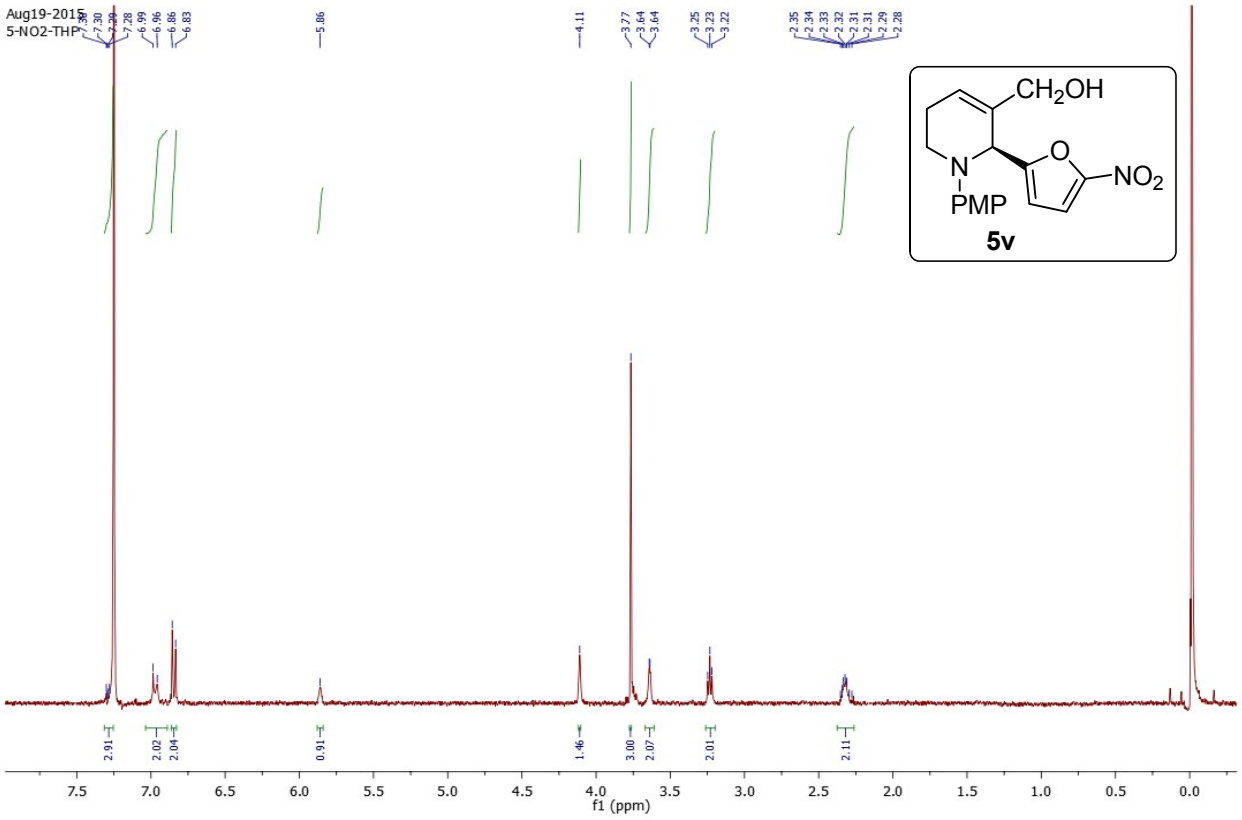
5u

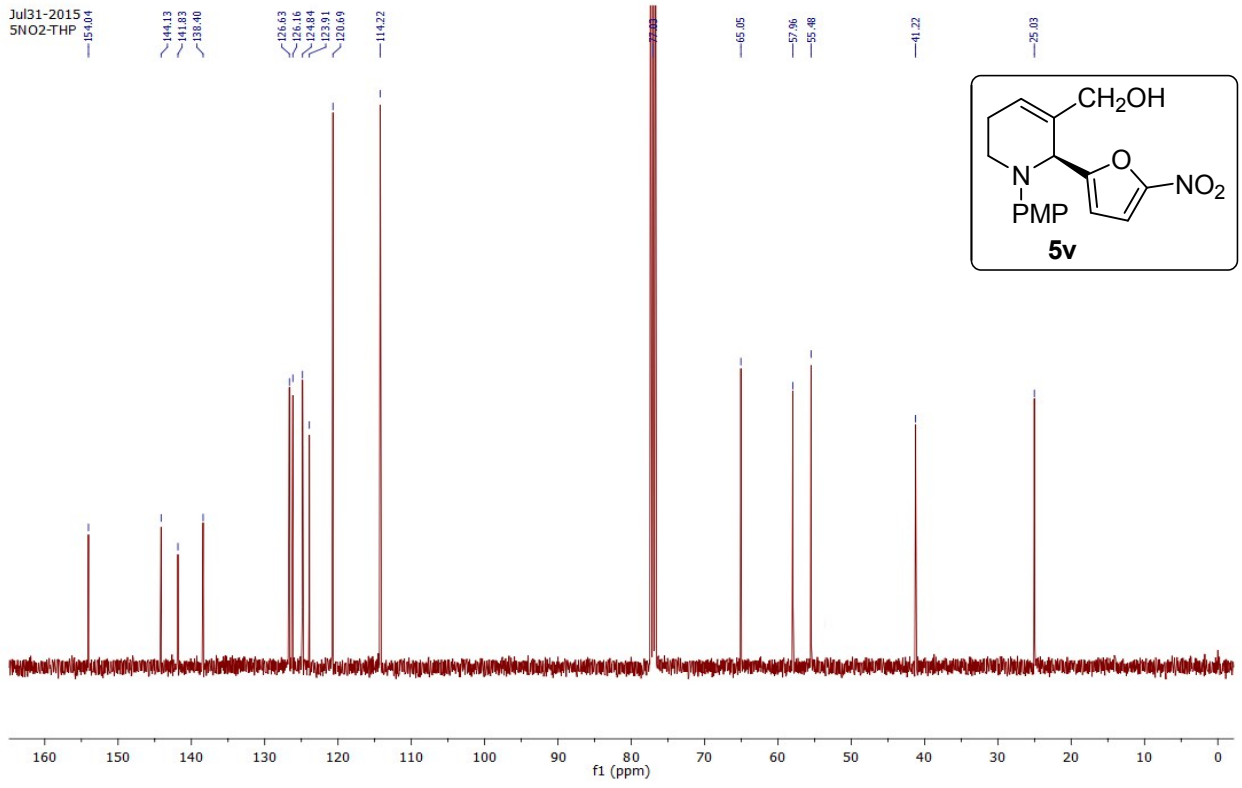


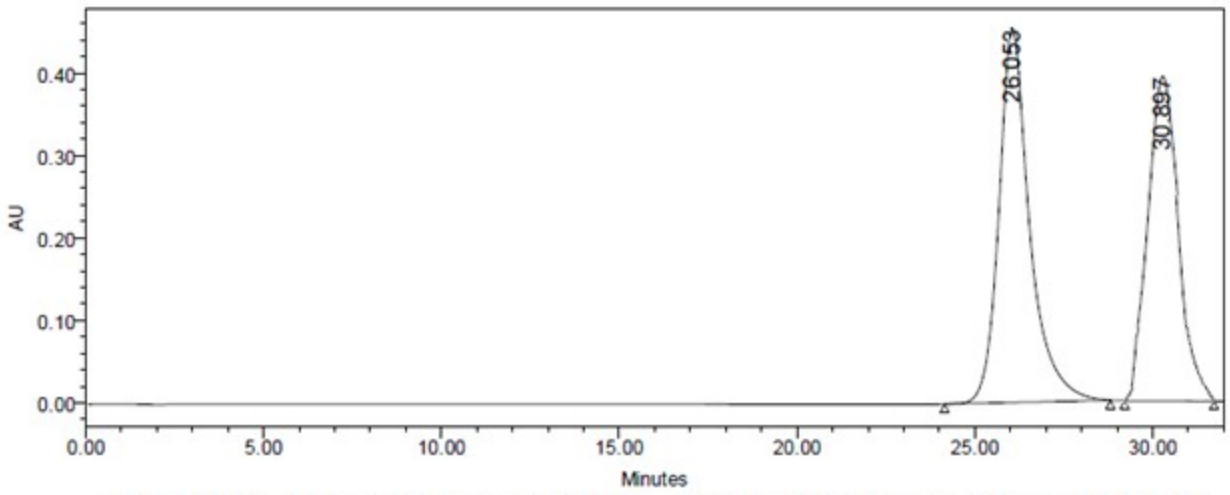
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8074; Processing Method: THIOPHENE 2 CHIRAL THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	30.484	11179571	13.60	138282
2	PDA 250.0 nm	36.166	71039168	86.40	774084


Aug19-2015
5-NO2-THP
CH2OH
O
NO2
N
PMP
5v
f1 (ppm)

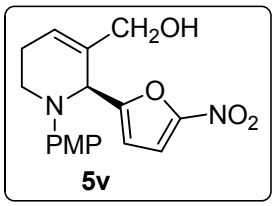

Jul31-2015
5NO2-THP
CH2OH
O
NO2
N
PMP
5v
f1 (ppm)



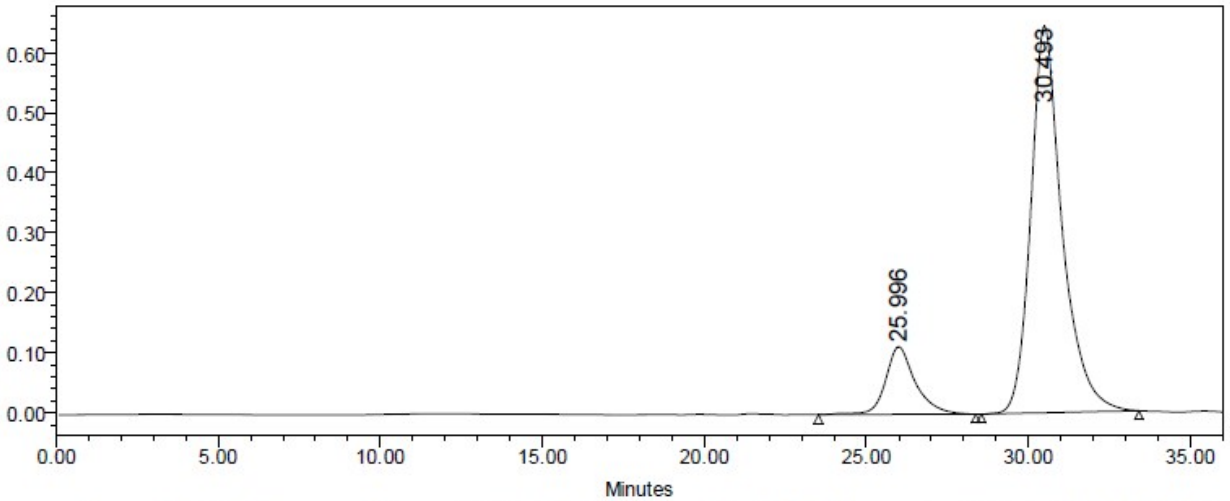
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8334; Processing Method: 5 NO2 FURYL RACEMIC THP

Processed Channel Descr.: PDA 250.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	26.053	27305834	56.77	454071
2	PDA 250.0 nm	30.897	20793365	43.23	350452



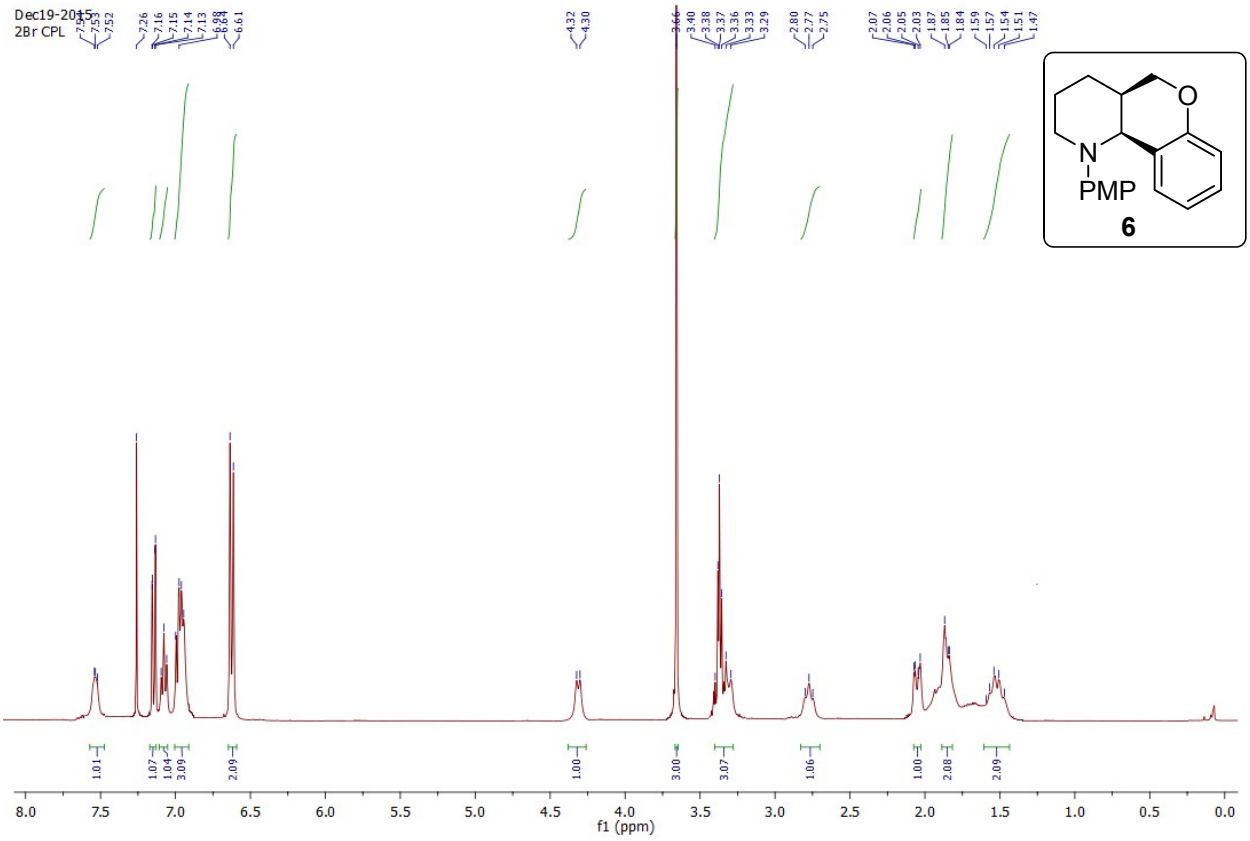
5v

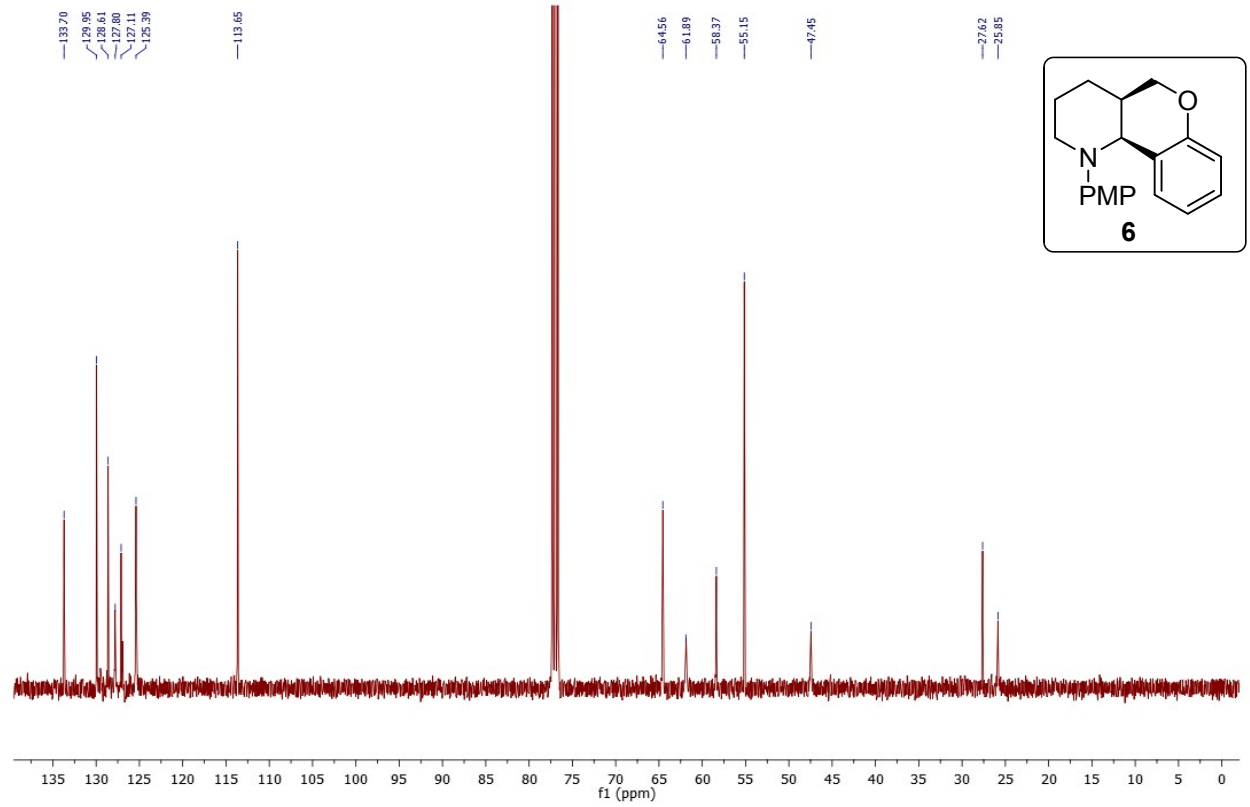


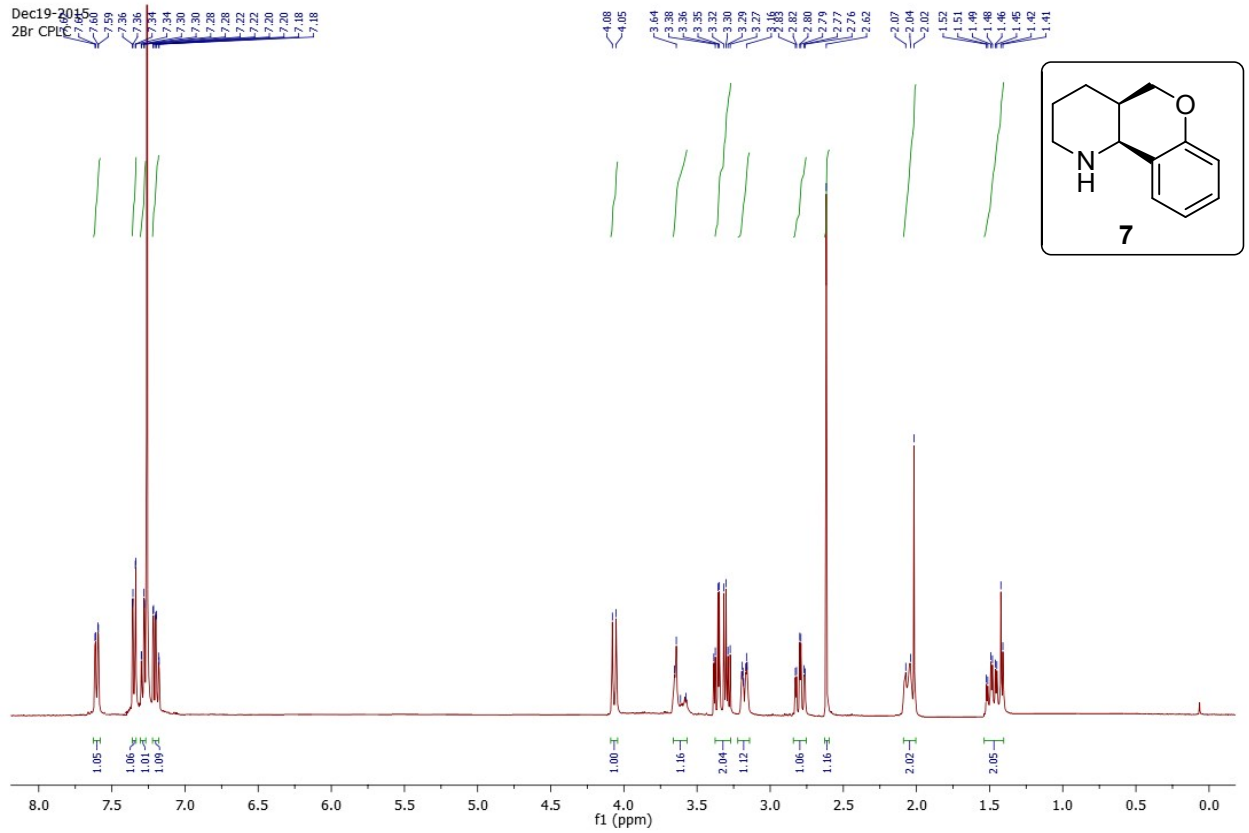
Channel: 2998; Processed Channel: PDA 250.0 nm; Result Id: 8336; Processing Method: 5 NITRO FURYL CHIRAL THP

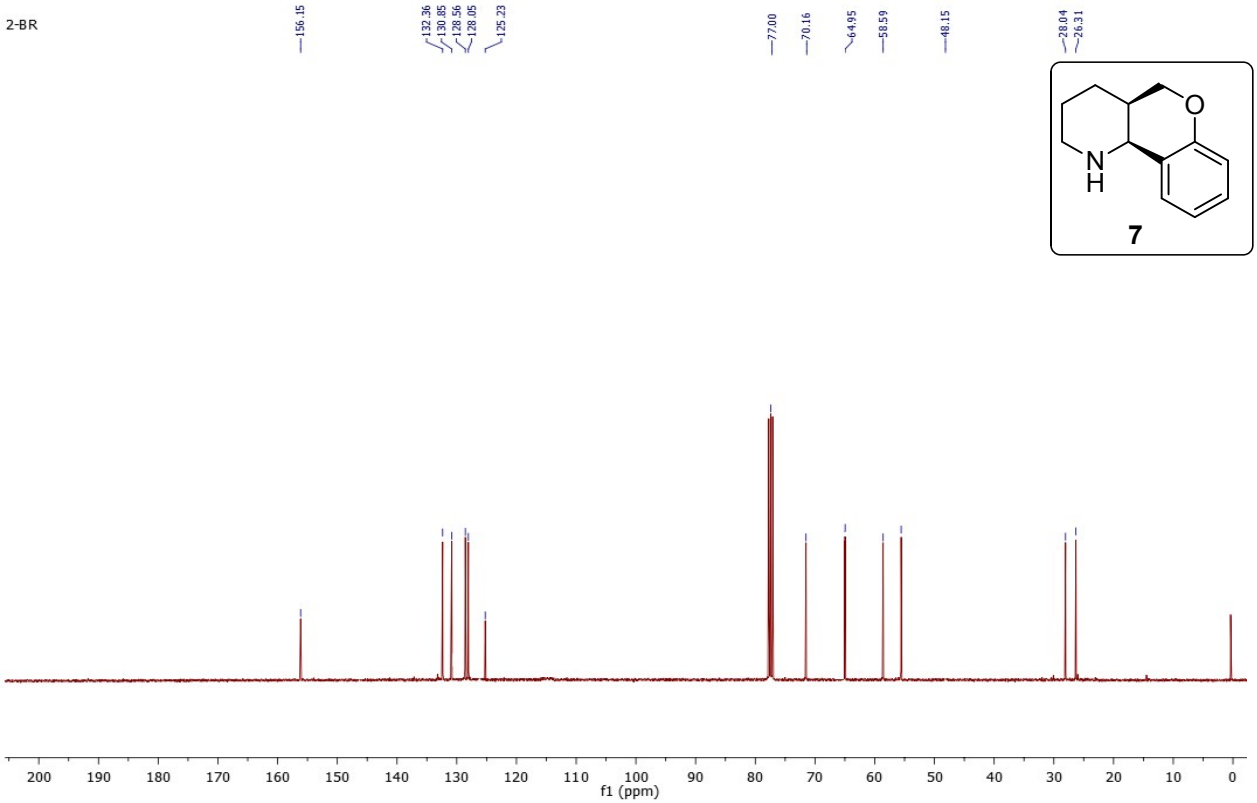
Processed Channel Descr.: PDA 250.0 nm

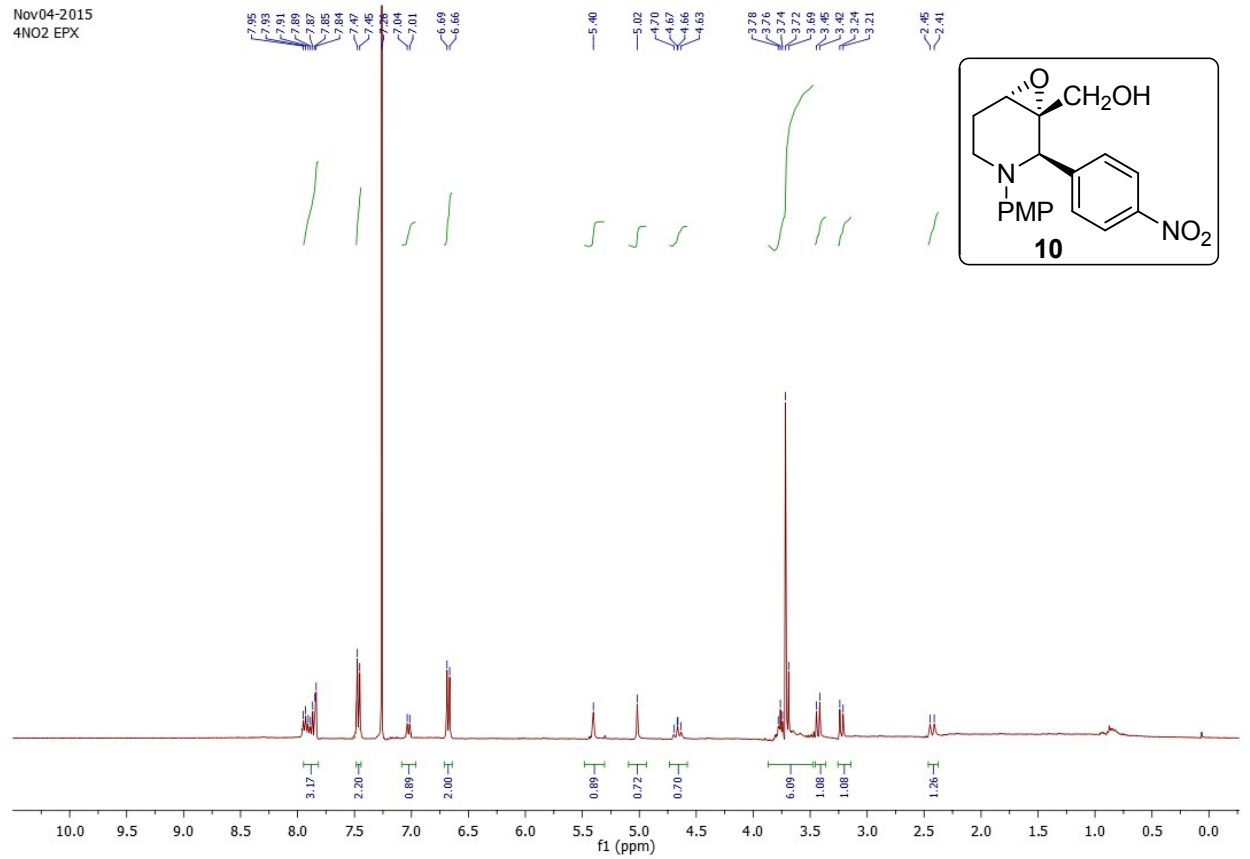
	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 250.0 nm	25.996	7216186	14.25	112766
2	PDA 250.0 nm	30.493	43430027	85.75	644159

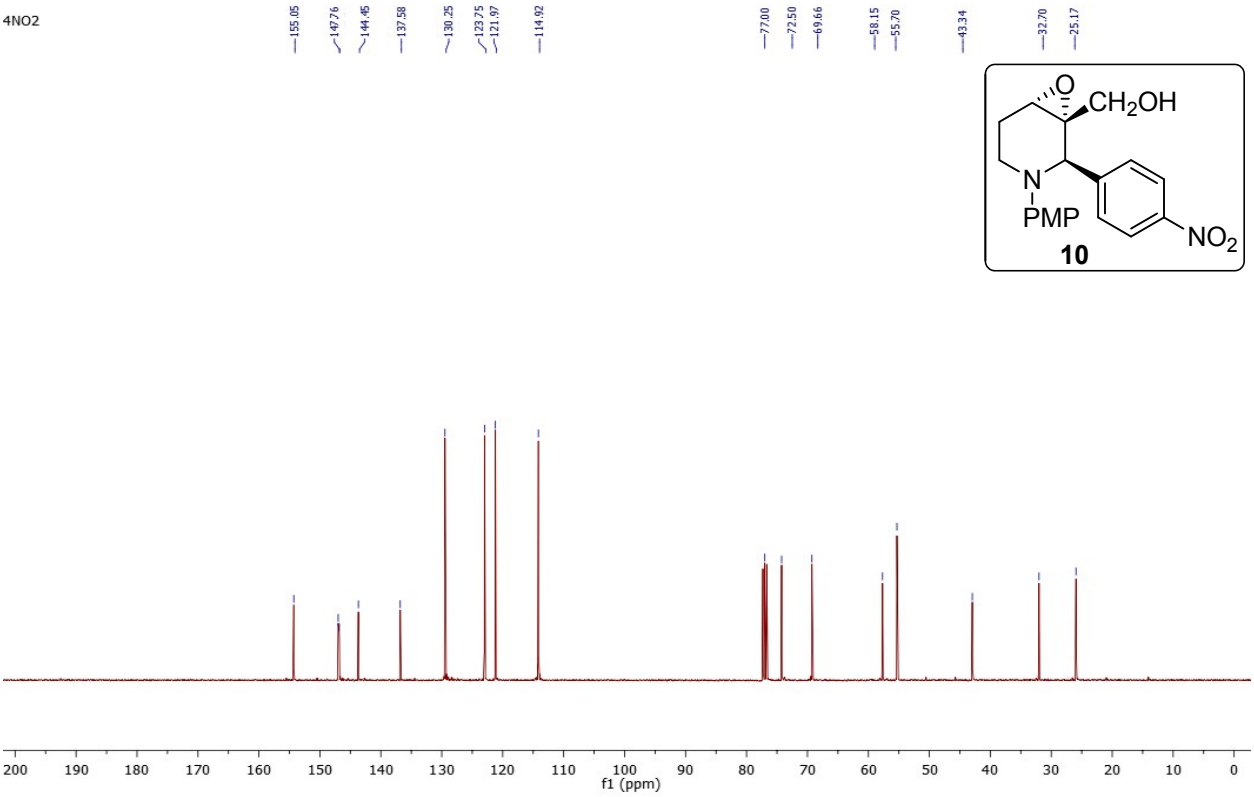

Dec19-2015
2Br CPL
7.55
7.53
7.52
7.26
7.16
7.15
7.14
7.13
6.84
6.61
4.32
4.30
3.66
3.40
3.38
3.37
3.36
3.33
3.29
2.80
2.77
2.75
2.07
2.06
2.05
2.03
1.87
1.85
1.84
1.59
1.57
1.54
1.51
1.47
1.01
1.07
1.04
3.09
2.09
1.00
3.00
3.07
1.06
1.00
2.08
2.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
N
PMP
6

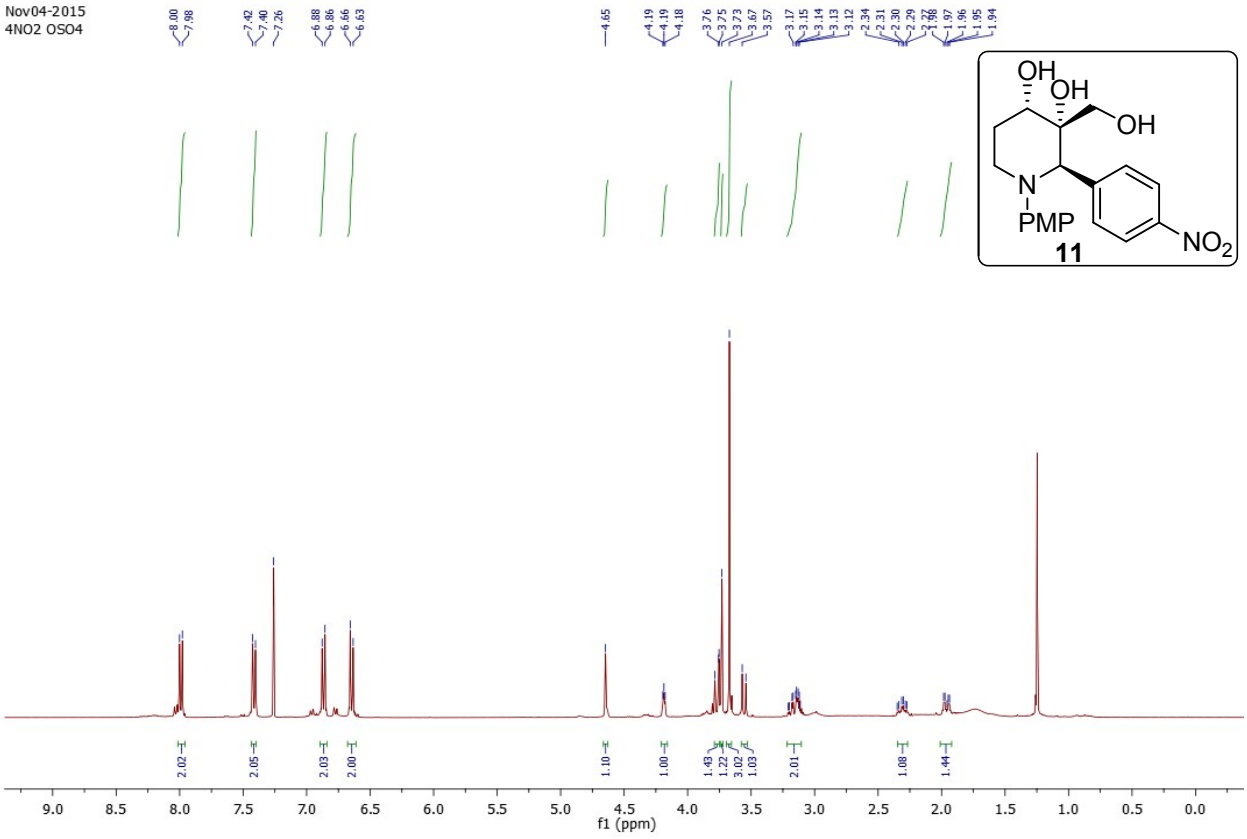

133.70
129.95
128.61
127.80
127.11
125.39
113.65
64.56
61.89
58.37
55.15
47.45
27.62
25.85
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)
O
N
PMP
6

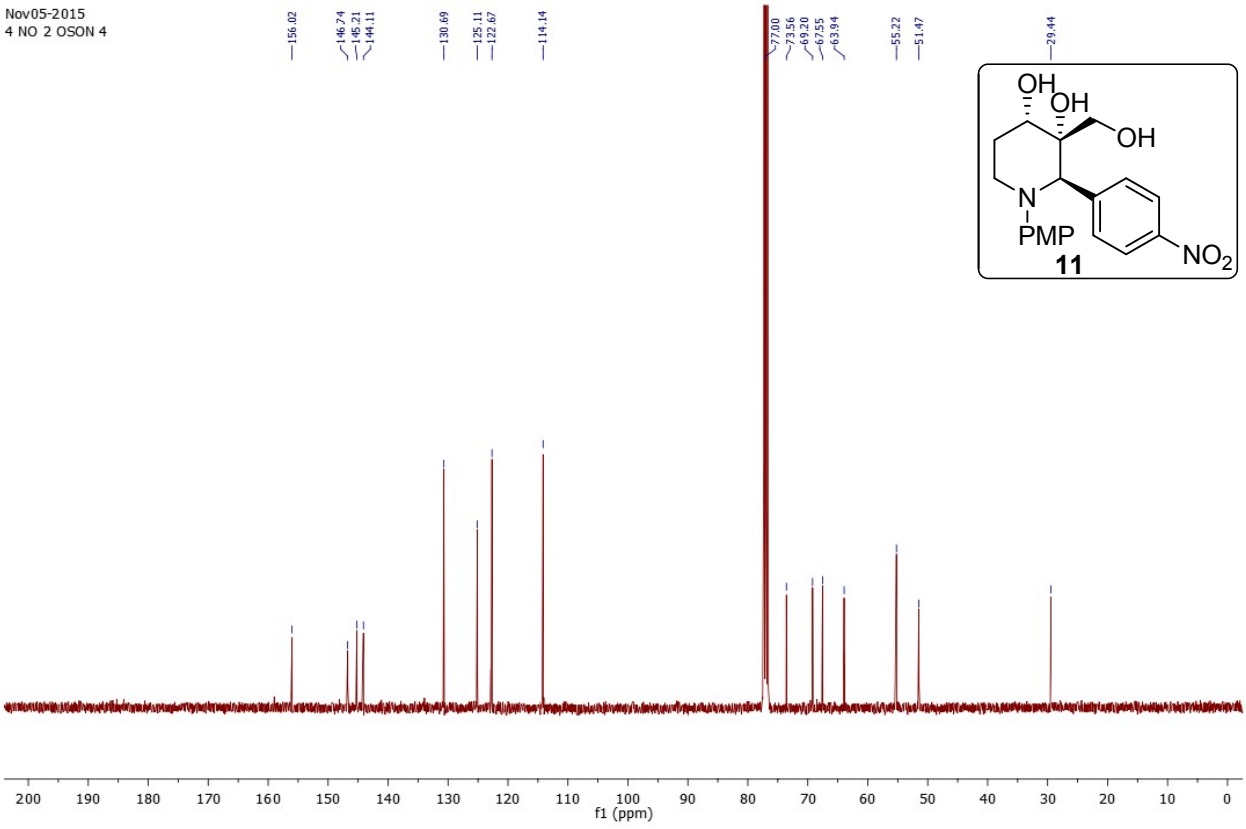

Dec19-2015
2Br CPLC 5
7.60
7.59
7.36
7.36
7.34
7.34
7.30
7.30
7.28
7.28
7.22
7.22
7.20
7.20
7.18
7.18
4.08
4.05
3.64
3.38
3.36
3.35
3.32
3.30
3.29
3.27
3.16
3.03
2.82
2.80
2.79
2.77
2.76
2.62
2.07
2.04
2.02
1.52
1.51
1.49
1.48
1.46
1.45
1.42
1.41
1.05
1.06
1.01
1.09
1.00
1.16
2.04
1.12
1.06
1.16
2.02
2.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
N
H
7

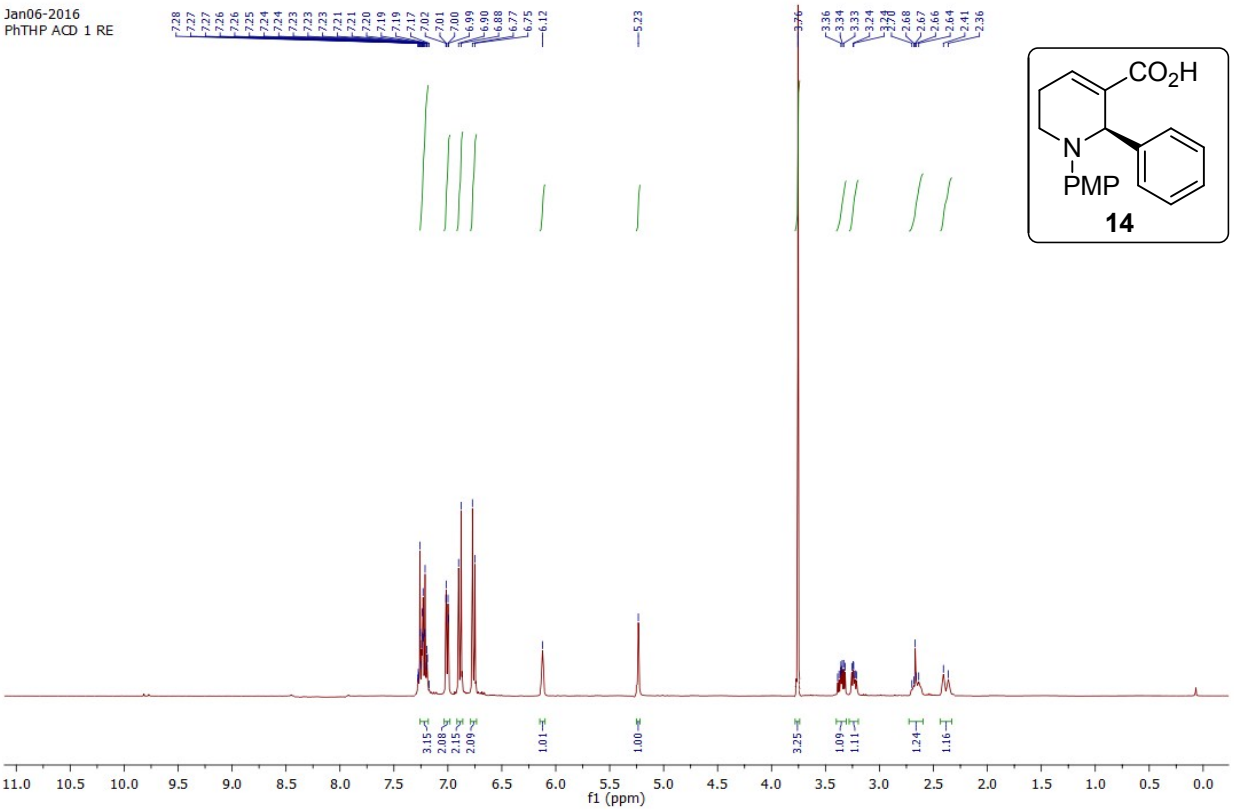

2-BR
156.15
132.36
130.85
128.56
128.05
125.23
77.00
70.16
64.95
58.59
48.15
28.04
26.31
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
O
N
H
7

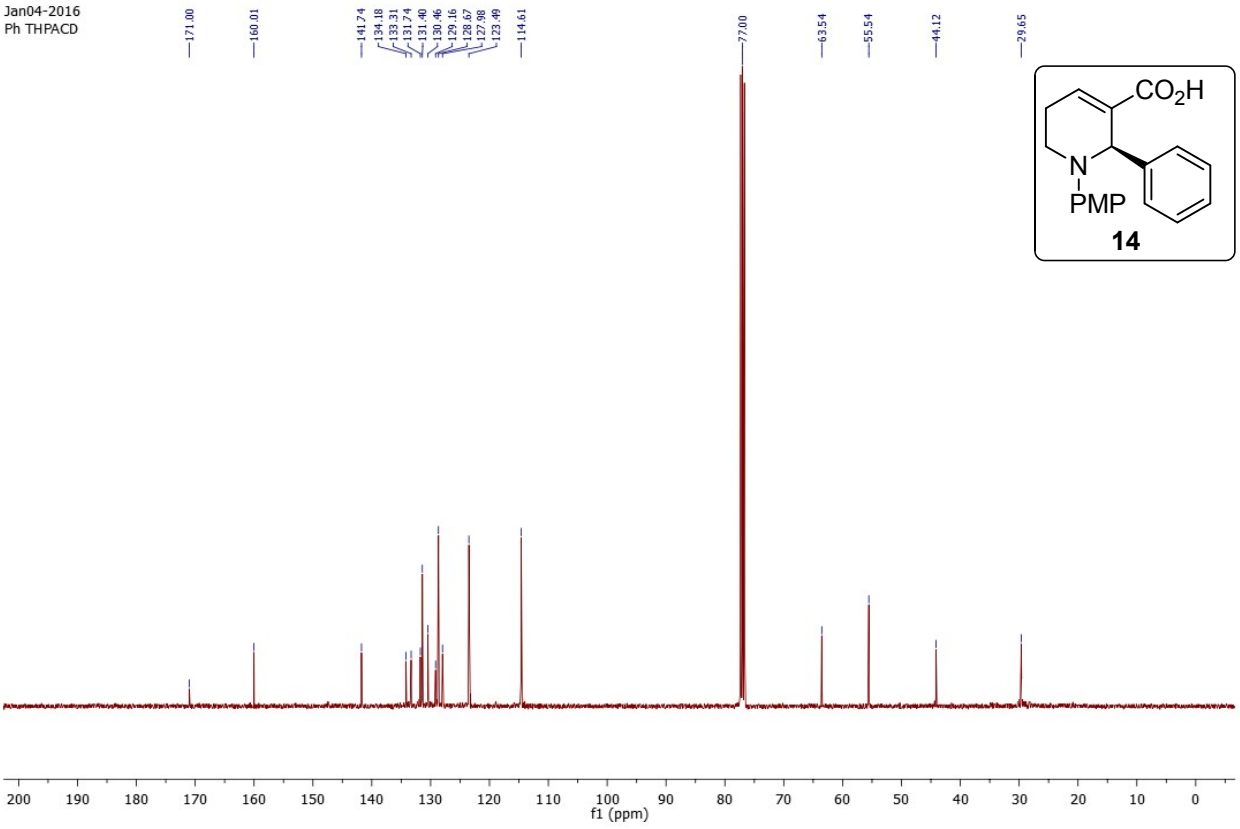

Nov04-2015
4NO2 EPX
7.95
7.93
7.91
7.89
7.87
7.85
7.84
7.47
7.45
7.04
7.01
6.69
6.66
5.40
5.02
4.70
4.67
4.66
4.63
3.78
3.76
3.74
3.72
3.69
3.45
3.42
3.24
3.21
2.45
2.41
3.17
2.20
0.89
2.00
0.89
0.72
0.70
6.09
1.08
1.08
1.26
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
O
CH2OH
N
PMP
NO2
10

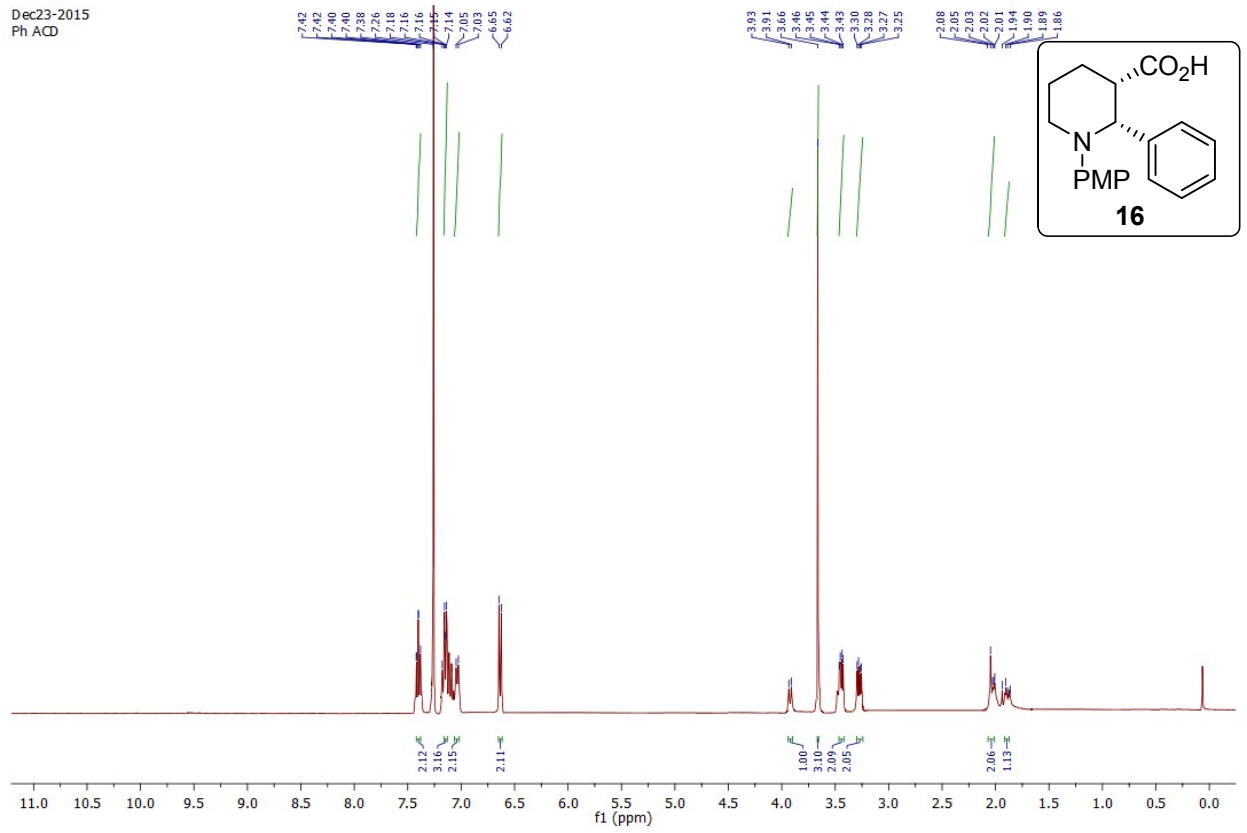

4NO2
155.05
147.76
144.45
137.58
130.25
123.75
121.97
114.92
77.00
72.50
69.66
58.15
55.70
43.34
32.70
25.17
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
O
CH2OH
N
PMP
NO2
10

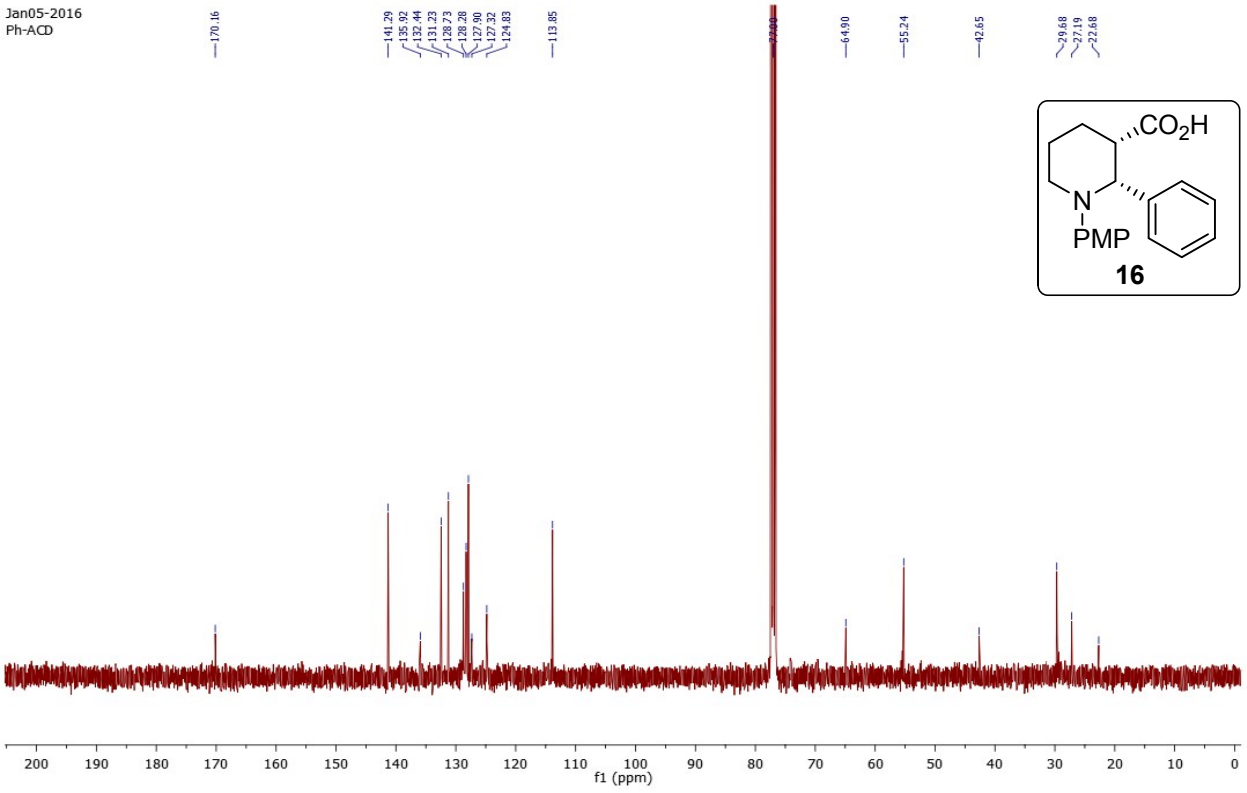

Nov04-2015
4NO2 OSO4
OH
OH
OH
N
PMP
NO2
11
f1 (ppm)

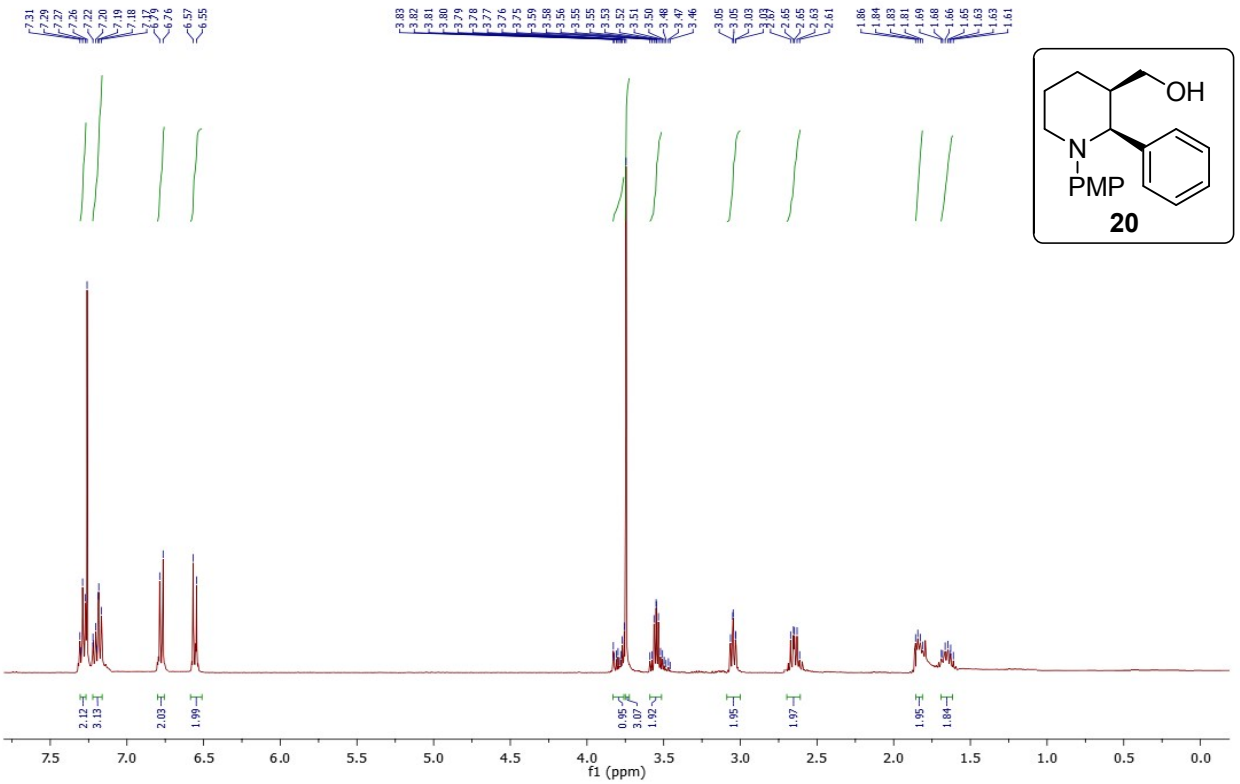

Nov05-2015
4 NO 2 OSON 4
OH
OH
OH
N
PMP
NO2
11
f1 (ppm)

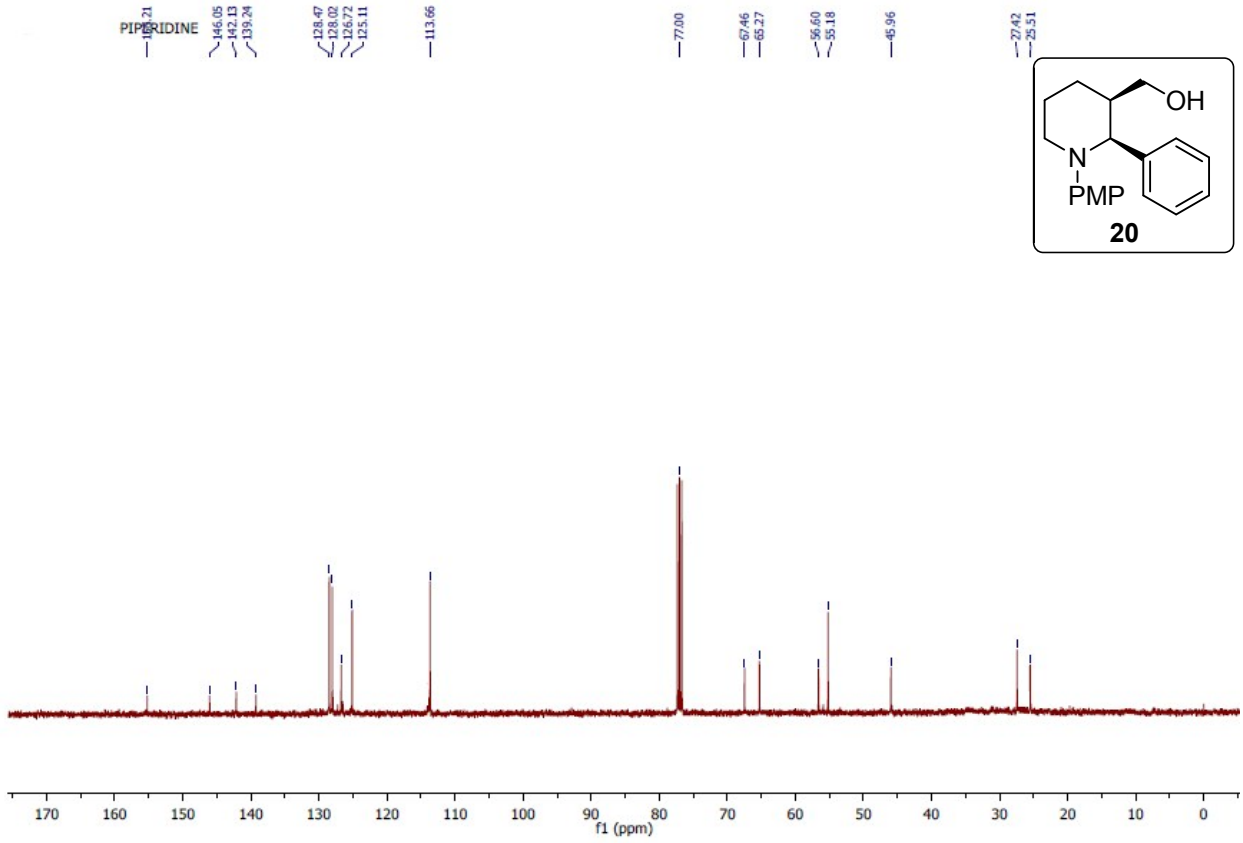

Jan06-2016
PhTHP ACD 1 RE
CO2H
N
PMP
14
f1 (ppm)

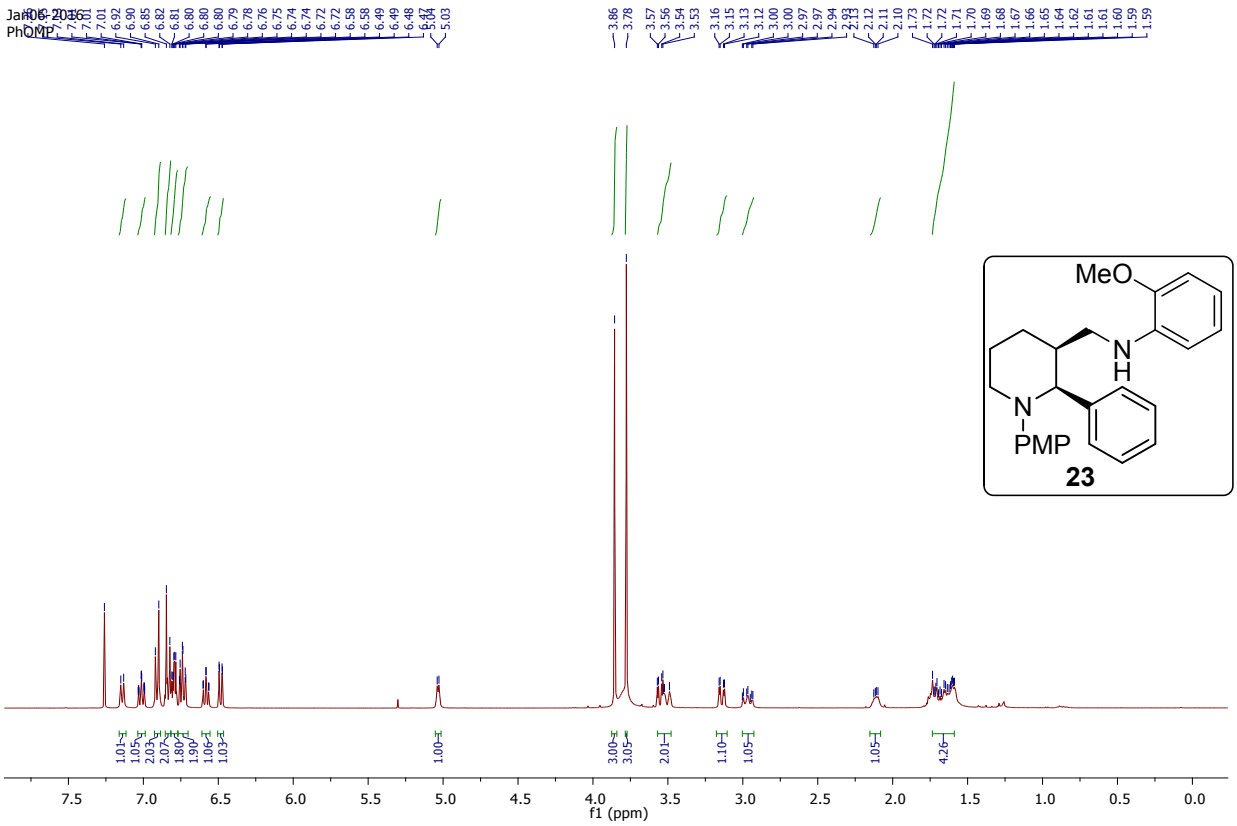

Jan04-2016
Ph THPACD
CO2H
N
PMP
14
f1 (ppm)

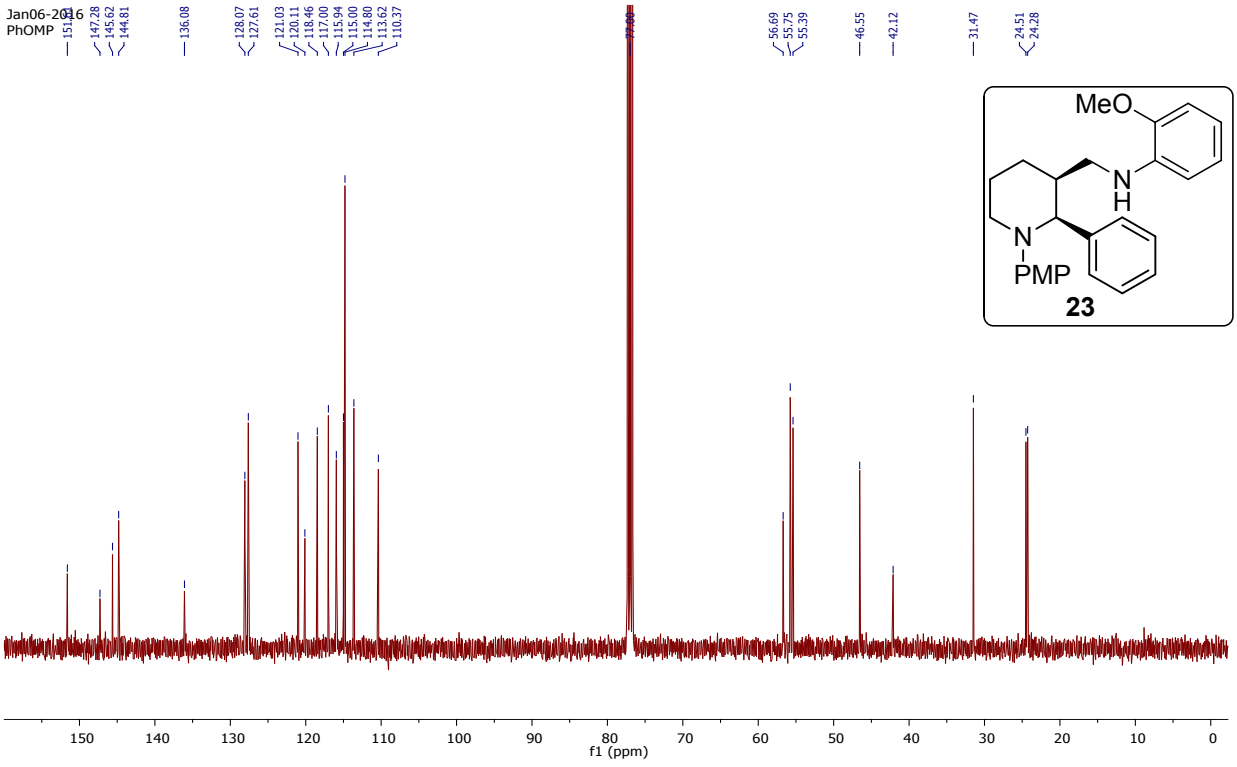

Dec23-2015
Ph ACD
CO2H
N
PMP
16
f1 (ppm)


Jan05-2016
Ph-ACD
CO2H
N
PMP
16
f1 (ppm)


OH
N
PMP
20
f1 (ppm)


PIPERIDINE
OH
N
PMP
20
f1 (ppm)


Jan06-2016
PhOMP
MeO
N
H
N
PMP
23
f1 (ppm)


Jan06-2016
PhOMP
MeO
N
H
N
PMP
23
f1 (ppm)