Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information for

One-pot asymmetric synthesis of trihydro-quinoline scaffold containing five stereocenters via an organocatalytic quadruple-cascade reaction

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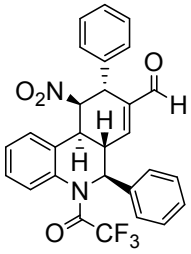
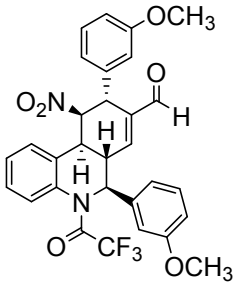
1 General information

The ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at 500 MHz and 125 MHz, respectively, with TMS as the internal standard. GC-MS experiments were performed on a GC system with a mass selective detector. HRMS data were measured on a LC/TOF-MS with ESI source. Column chromatography and flash chromatography experiments were performed on silica gel (200-300 mesh) eluting with ethyl ether and petroleum ether. TLC experiments were carried out on glass-backed silica plates. In each case, enantiomeric ratio was determined on a chiral column in comparison with authentic racemates by chiral HPLC. Chemicals were used without purification as commercially available.

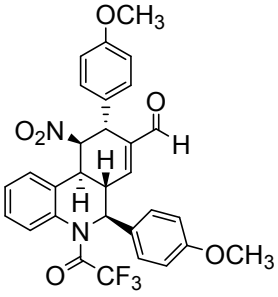
2 Typical procedure for the organocatalytic asymmetric Michael-Michael-Michael-aldol cyclization quadruple-cascade reaction.



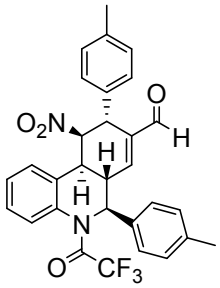
Compound (4a), yield: 63.76 mg, 63%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 10.32 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.53 (s, 1H), 7.48–7.44 (m, 5H), 7.43–7.40 (m, 4H), 7.40–7.36 (m, 2H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 5.56 (s, 1H), 5.31 (d, *J* = 11.5 Hz, 1H), 4.74 (s, 1H), 3.50 (t, *J* = 11.5 Hz, 1H), 3.08-3.05 (dd, J_1 = 11.5 Hz, J_2 = 2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.13, 156.78 (d, *J* = 36.5 Hz), 147.27, 138.96, 137.83, 137.53, 135.08, 133.10, 129.65×2, 129.23×2, 128.96, 128.53, 128.30, 128.28, 127.94×2, 127.71×2, 125.58, 122.76, 116.42 (dd, J_1 = 572.5 Hz, J_2 = 286.25 Hz), 85.66, 64.16, 45.75, 44.15, 34.78 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{21}F_3N_2O_4$ $[M+H]^+$ 507.2543, found 507.2564.



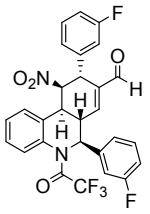
Compound (4b), yield: 63.41 mg, 56%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 12.55 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.53 (s, 1H), 7.41 (d, *J* = 4.5 Hz, 2H), 7.39–7.27 (m, 3H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 2.0 Hz, 1H), 7.00–6.93 (m, 3H), 6.91–6.87 (m, 2H), 6.85 (d, *J* = 7.5 Hz, 1H), 5.57 (s, 1H), 5.29 (d, *J* = 11.5 Hz, 1H), 4.70 (s, 1H), 3.83 (d, *J* = 1.0 Hz, 6H), 3.51–3.44 (m, 1H), 3.11-3.08 (dd, J_1 = 11.5 Hz, J_2 =2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.16, 160.41, 160.01, 156.81 (d, *J* = 37.5 Hz), 147.31, 140.56, 139.03, 137.73, 135.07, 133.14, 130.53, 130.28, 128.22×2, 125.53, 122.72, 119.85, 119.69, 116.58 (dd, J_1 = 573.25 Hz, J_2 = 286.25 Hz), 114.30, 113.98, 113.66, 113.53, 85.53, 63.96, 55.27×2, 45.69, 44.03, 34.87 ppm; HRMS: (ESI+) m/z calcd for $C_{30}H_{25}F_3N_2O_6$ $[M+H]^+$ 567.2733, found 567.2745.



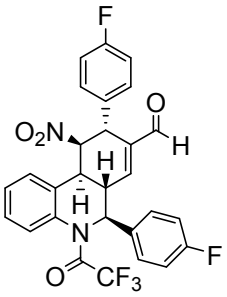
Compound (4c), yield: 65.68 mg, 58%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 17.97 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.51 (s, 1H), 7.43–7.33 (m, 5H), 7.28-7.19 (dd, J_1 = 14.5 Hz, J_2 =8.0 Hz, 3H), 6.98–6.94 (m, 5H), 5.51 (s, 1H), 5.28 (d, *J* = 11.5 Hz, 1H), 4.67 (s, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.47 (t, *J* = 11.5 Hz, 1H), 3.07-3.04 (dd, J_1 = 11.5 Hz, J_2 =2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.16, 160.03, 159.66, 156.79, 147.18, 138.05, 135.00, 133.37, 130.76, 129.45, 129.07×4, 128.21 (d, *J* = 8.7 Hz)×2, 125.62, 122.72, 115.00×2, 114.56×2, 85.88, 63.59, 55.35×2, 45.72, 43.53, 34.76 ppm; HRMS: (ESI+) m/z calcd for $C_{30}H_{25}F_3N_2O_6$ $[M+H]^+$ 567.2713, found 567.27334



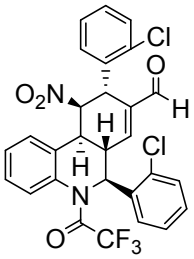
Compound (4d), yield: 69.45 mg, 65%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 252 nm; t_{major} = 65.62 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.51 (s, 1H), 7.40-7.38 (dd, J_1 = 10.0 Hz, J_2 = 1.0 Hz, 1H), 7.31–7.17 (m, 11H), 6.96 (d, J = 5.0 Hz, 1H), 5.46 (s, 1H), 5.25 (d, J = 15.0 Hz, 1H), 4.72 (s, 1H), 3.47 (t, J = 10.0 Hz, 1H), 3.01 (d, J = 15.0 Hz, 1H), 2.40 (s, 3H), 2.37 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.01, 156.64 (d, J = 36.5 Hz), 146.78, 139.13, 138.61, 137.94, 135.60, 135.01, 134.30, 134.25, 133.63, 130.36×2, 129.94×2, 128.35, 127.75×2, 127.57, 123.52, 115.93 (d, J = 287.5 Hz), 85.45, 63.88, 45.52, 43.81, 34.80, 29.71, 26.93, 21.21, 21.04 ppm; HRMS: (ESI+) m/z calcd for $C_{30}H_{25}F_3N_2O_4$ $[M+H]^+$ 535.1863, found 535.1894



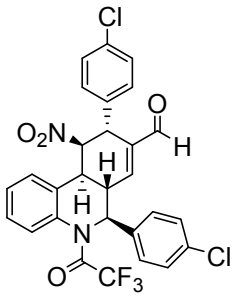
Compound (4e), yield: 58.55 mg, 54%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 10.32 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.55 (s, 1H), 7.47–7. 23 (m, 5H), 7.22 (d, J = 7.5 Hz, 2H), 7.17–7.11 (m, 2H), 7.08 (d, J = 7.5 Hz, 1H), 7.06–7.01 (m, 3H), 5.55 (d, J = 1.0 Hz, 1H), 5.34–5.30 (m, 1H), 4.71 (s, 1H), 3.49-3.44 (tt, J_1 = 11.5 Hz, J_2 =2.0 Hz, 1H), 3.06-3.44 (dd, J_1 = 11.5 Hz, J_2 =2.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.92, 164.08 (d, J = 35.5 Hz), 162.10 (d, J = 35.5 Hz), 157.00 (dd, J_1 = 75.0 Hz, J_2 = 37.5 Hz), 147.11, 141.43, 139.88 (d, J = 7.0 Hz), 137.65, 134.83, 132.71, 131.20 (d, J = 8.5 Hz), 130.97 (d, J = 8.0 Hz), 128.48 (d, J = 11.5 Hz)×2, 125.52, 123.47 (d, J = 2.5 Hz), 123.32, 122.87, 116.54 (dd, J_1 = 573.75 Hz, J_2 = 286.5 Hz), 116.07 (d, J = 21.0 Hz), 115.68 (d, J = 21.0 Hz), 115.27 (d, J = 22.0 Hz), 114.81 (d, J = 22.0 Hz), 85.32, 63.45, 45.56, 43.68, 34.74 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{19}F_5N_2O_4$ $[M+H]^+$ 543.1363, found 5543.1374



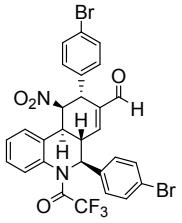
Compound (4f), yield: 91.08 mg, 84%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 29.15 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.52 (s, 1H), 7.45–7.37 (m, 5H), 7.3-7.22 (dd, J_1 = 8.0, J_2 = 5.0 Hz, 2H), 7.21 (d, J = 7.5 Hz, 1H), 7.16-7.09 (dt, J_1 = 17.0 Hz, J_2 = 8.5 Hz, 4H), 6.98 (d, J = 2.0 Hz, 1H), 5.51 (s, 1H), 5.30 (s, 1H), 4.70 (s, 1H), 3.47 (t, J = 11.5 Hz, 1H), 3.04-3.01 (dd, J_1 = 11.0, J_2 = 1.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.93, 163.71 (d, J = 42.0 Hz), 161.73 (d, J = 42.0 Hz), 156.73 (dd, J_1 = 75.0 Hz, J_2 = 37.5 Hz), 146.99, 137.93, 134.76, 134.60, 133.24 (d, J = 2.7 Hz), 132.89, 129.62 (d, J = 8.2 Hz)×4, 128.44 ×2, 125.56, 122.83, 116.72, 116.54, 116.56 (dd, J_1 = 46.25 Hz, J_2 = 22.5 Hz), 116.18, 85.53, 63.32, 53.42, 45.64, 43.40, 34.63 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{19}F_5N_2O_4$ $[M+H]^+$ 543.1343, found 543.1354



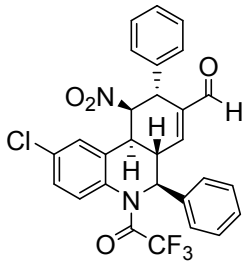
Compound (4g), yield: 83.82 mg, 73%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 7.85 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.56 (s, 1H), 7.59–7.54 (m, 2H), 7.49–7.43 (m, 2H), 7.41–7.28 (m, 6H), 7.25-7.24 (dd, J_1 = 7.5 Hz, J_2 =1.5 Hz, 1H), 7.19 (d, J = 2.0 Hz, 1H), 7.05 (t, J = 5.0 Hz, 1H), 5.83 (d, J = 12.0 Hz, 1H), 5.67 (s, 1H), 5.09 (s, 1H), 3.39 (t, J = 11.5 Hz, 1H), 3.05-3.02 (dd, J_1 = 11.5 Hz, J_2 =2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.95, 157.15 (d, J = 37.5 Hz), 147.63, 137.69, 137.41, 135.19, 134.61, 134.39, 133.53, 132.55, 130.96, 130.13, 129.93×2, 128.53×2, 128.22, 127.83, 127.53, 123.04, 115.84 (dd, J_1 = 573.75 Hz, J_2 = 287.5 Hz), 82.35, 60.47, 53.41, 46.79, 40.86, 35.34 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{19}Cl_2F_3N_2O_4$ $[M+H]^+$ 575.1762, found 575.1781



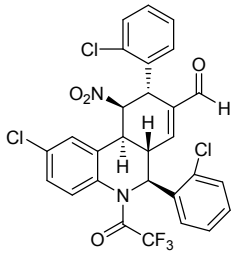
Compound (4h), yield: 86.12 mg, 75%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 13.47 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.51 (s, 1H), 7.45–7.42 (m, 3H), 7.41-7.28 (tt, J_1 = 4.5 Hz, J_2 =2.5 Hz, 6H), 7.24–7.19 (m, 3H), 6.99 (d, J = 2.0 Hz, 1H), 5.50 (d, J = 1.0 Hz, 1H), 5.28 (d, J = 11.5 Hz, 1H), 4.68 (s, 1H), 3.49-3.43 (tt, J_1 = 11.5 Hz, J_2 =2.0 Hz, 1H), 3.03 (dd, J_1 = 11.5 Hz, J_2 =2.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.88, 156.94 (d, J = 11.25 Hz), 147.00, 137.75, 137.32, 135.95, 135.06, 134.75, 134.62, 132.75, 129.79×2, 129.50×2, 129.28×2, 129.17, 128.51, 128.46, 125.51, 122.85, 115.81 (dd, J_1 = 572.5 Hz, J_2 = 286.25 Hz), 85.36, 63.41, 45.54, 43.51, 34.67 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{19}Cl_2F_3N_2O_4$ $[M+H]^+$ 575.1743, found 575.1755



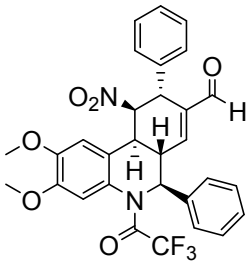
Compound (4i), yield: 90.03 mg, 68%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 15.65 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.50 (s, 1H), 7.60 (d, J = 2.5 Hz, 1H), 7.59–7.58 (m, 1H), 7.55–7.54 (m, 1H), 7.53–7.52 (m, 1H), 7.44-7.41 (dd, J_1 = 11.5 Hz, J_2 =4.0 Hz, 1H), 7.39-7.32 (dd, J_1 = 8.5 Hz, J_2 =7.0 Hz, 2H), 7.31 (d, J = 8.5 Hz, 2H), 7.21–7.16 (m, 3H), 6.98 (d, J = 2.0 Hz, 1H), 5.49 (d, J = 1.0 Hz, 1H), 5.26 (d, J = 11.5 Hz, 1H), 4.66 (s, 1H), 3.48–3.42 (m, 1H), 3.03-3.00 (dd, J_1 = 11.0 Hz, J_2 =2.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.79, 156.92 (dd, J_1 = 75.0 Hz, J_2 = 37.5 Hz), 146.94, 137.78, 137.67, 136.45, 134.72, 132.73×2, 132.69, 132.43×2, 129.54×2, 129.41, 128.49, 128.43, 125.49, 123.17, 122.82, 122.72, 117.11 (dd, J_1 = 573.5 Hz, J_2 = 287.25 Hz), 85.25, 63.43, 45.45, 43.56, 34.66 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{19}Br_2F_3N_2O_4$ $[M+H]^+$ 662.9765, found662.9771



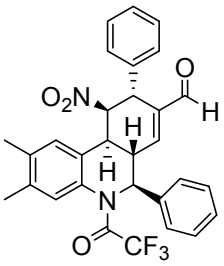
Compound (5a), yield: 79.94 mg, 74%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (87:13) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} =11.45 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.53 (s, 1H), 7.48–7.43 (m, 5H), 7.42–7.37 (m, 4H), 7.36-7.30 (dd, J_1 = 20.5 Hz, J_2 =9.5 Hz, 3H), 7.18 (d, *J* = 1.0 Hz, 1H), 6.99 (d, *J* = 2.0 Hz, 1H), 5.49 (s, 1H), 5.29 (d, *J* = 11.5 Hz, 1H), 4.77 (s, 1H), 3.50 (t, *J* = 11.5 Hz, 1H), 3.04-3.01 (dd, J_1 = 11.5 Hz, J_2 =2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.91, 156.71 (d, *J* = 37.5 Hz), 146.73, 138.60, 137.85, 137.26, 134.86, 134.33, 133.61, 129.71×2, 129.32×2, 129.13, 128.64, 128.42, 127.87×2, 127.62, 126.72, 123.57, 116.97 (d, *J* = 286.25 Hz), 85.29, 64.06, 45.50, 44.09, 34.76 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{20}ClF_3N_2O_4$ $[M+H]^+$ 541.1153, found 541.1162



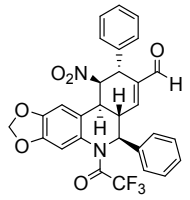
Compound (5b), yield: 75.40 mg, 62%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 252 nm; t_{major} = 16.04 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.55 (s, 1H), 7.58−7.55 (m, 2H), 7.44-7.42 (dd, J_1 = 10Hz, J_2 =5 Hz, 1H), 7.40−7.32 (m, 5H), 7.27 (s, 1H), 7.21-7.19 (dd, J_1 = 10Hz, J_2 =5 Hz, 1H), 7.16 (d, *J* =5 Hz, 1H), 7.02−7.01 (m, 1H), 5.81 (d, *J* =10 Hz,1H), 5.61 (s, 1H), 5.13 (s, 1H), 3.39 (t, *J* =10.0 Hz,1H), 2.98 (d, *J* =15.0 Hz,1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.71, 157.01 (dd, J_1=74.25 Hz, J_2=37.13 Hz), 147.13, 137.73, 137.04, 137.26, 134.63, 134.29, 134.16, 133.77, 133.51, 131.08, 130.29, 130.09×2, 128.59, 128.52, 128.30, 127.88, 127.51, 126.31, 123.86, 119.28, 115.84 (d, *J* = 286.38 Hz), 82.02, 60.55, 46.48, 40.90, 35.35 ppm; HRMS: (ESI+) m/z calcd for $C_{28}H_{18}Cl_3F_3N_2O_4$ $[M+H]^+$ 609.1003, found 609.1014



Compound (5c), yield: 86.06 mg, 76%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (85:15) as the eluent, Flow: 1.0 mL/min; UV = 236 nm; t_{major} = 13.11 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.52 (s, 1H), 7.48–7.41 (m, 7H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.92 (s, 1H), 6.78 (s, 1H), 5.56 (s, 1H), 5.32–5.26 (m, 1H), 4.67 (s, 1H), 3.88 (d, *J* = 2.0 Hz, 6H), 3.44-3.43 (tt, J_1 = 11.5Hz, J_2 =2.0 Hz, 1H), 3.04-3.01 (dd, J_1 =11.5 Hz, J_2 = 2.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.16, 156.70 (d, *J* = 36.25 Hz), 148.77, 148.35, 147.42, 138.95, 137.78, 137.55, 129.62×2, 129.22×2, 128.95, 128.52, 127.98×2, 127.80, 127.61, 125.26, 117.33 (d, *J* = 287.5 Hz), 109.79, 105.96, 86.18, 64.12, 56.25, 56.15, 46.02, 43.97, 34.59 ppm; HRMS: (ESI+) m/z calcd for $C_{30}H_{25}F_3N_2O_6$ $[M+H]^+$ 567.1785, found 567.1794



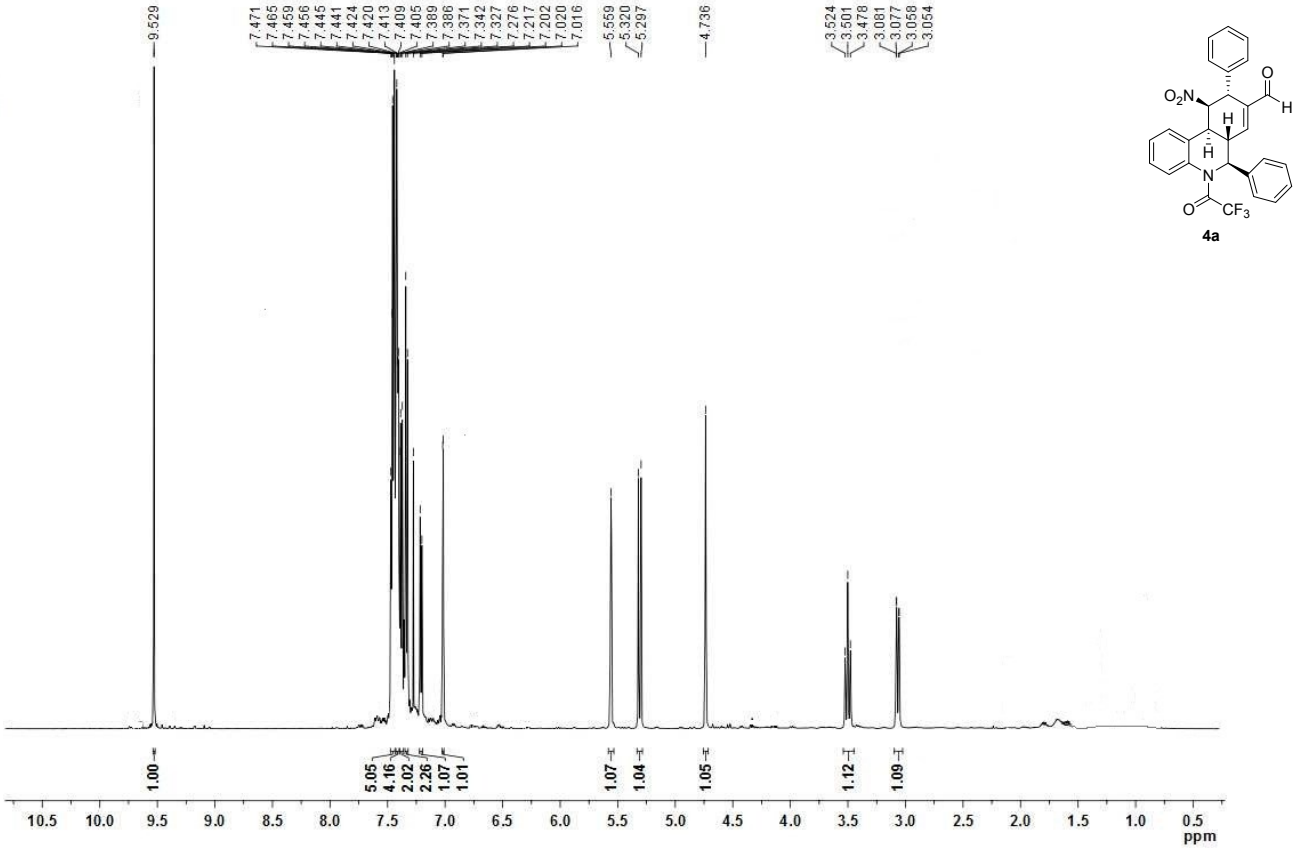
Compound (5d), yield: 76.93 mg, 72%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 1.0 mL/min; UV = 252 nm; t_{major} = 23.85 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.51 (s, 1H), 7.32 (d, *J*=7.5 Hz, 2H), 7.25 (t, *J*=8.5 Hz, 4H), 7.20-7.18 (m, 2H), 7.00 (d, *J*=2 Hz, 1H), 6.86 (s, 1H), 6.68 (s, 1H), 6.05 (s, 2H), 5.43 (s, 1H), 5.28 (d, *J* = 10.0 Hz, 1H), 4.68 (s, 1H), 3.47 (t, *J* = 15.0 Hz, 1H), 2.96 (d, *J* = 10.0 Hz, 1H), 2.41 (s, 3H), 2.37 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.20, 157.09 (dd, J_1=73 Hz, J_2=36.5 Hz), 147.53, 147.44, 147.01, 138.90, 138.40, 137.72, 134.46, 133.59, 130.22×2, 130.11, 129.82×2, 128.42, 127.78×2, 127.59, 127.29, 116.02 (dd, J_1=573.25 Hz, J_2=286.25 Hz), 103.44, 102.15, 86.06, 63.62, 43.86, 34.80, 29.66, 21.15, 20.98 ppm; HRMS: (ESI+) m/z calcd for $C_{30}H_{25}F_3N_2O_4$ $[M+H]^+$ 535.1872, found 535.1881

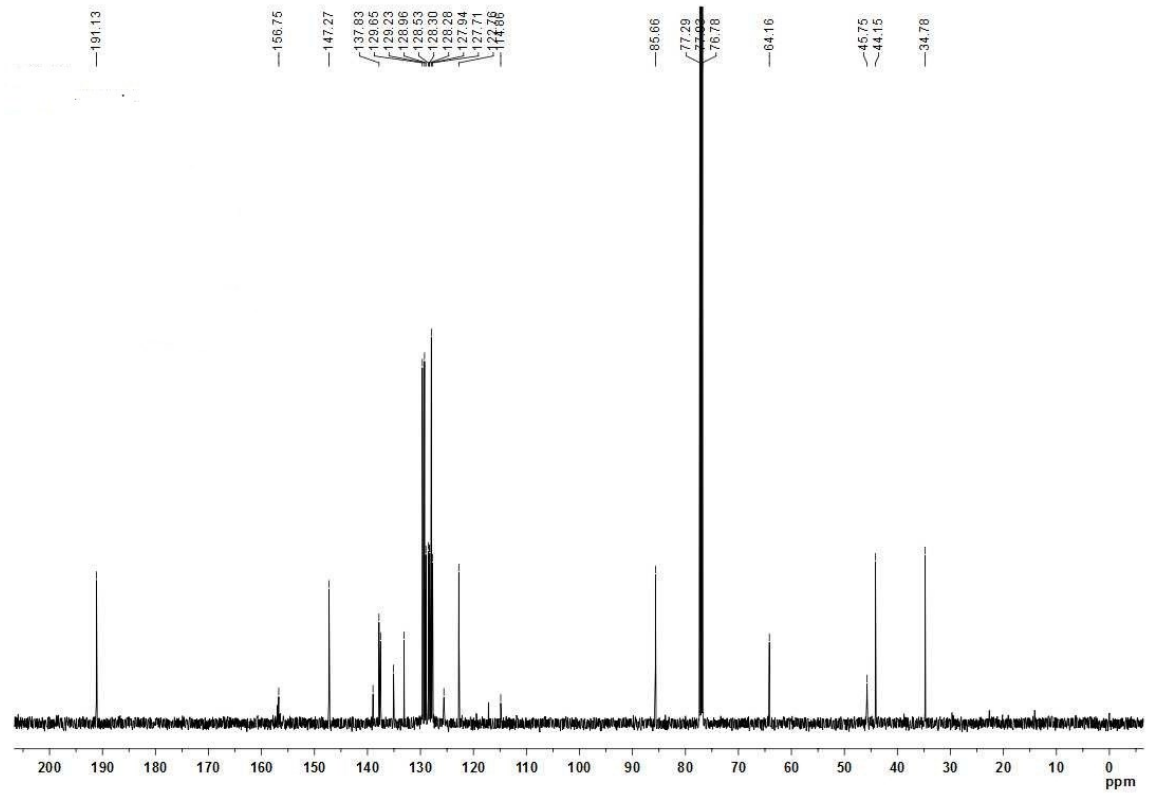


Compound (5e), yield: 64.63 mg, 86%; 99 % ee; > 99:1 dr; white solid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (80:20) as the eluent, Flow: 0.8 mL/min; UV = 236 nm; t_{major} = 18.51 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.52 (s, 1H), 7.47–7.42 (m, 5H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 2H), 7.01 (d, *J* = 1.5 Hz, 1H), 6.87 (s, 1H), 6.68 (s, 1H), 6.06 (s, 2H), 5.45 (s, 1H), 5.30 (d, *J* = 11.5 Hz, 1H), 4.71 (s, 1H), 3.52–3.46 (m, 1H), 2.94 (d, *J* = 10.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.16, 156.70 (d, *J* = 36.25 Hz), 148.77, 148.35, 147.42, 138.95, 137.95, 137.78, 137.55, 129.62×2, 129.22×2, 128.52, 127.98, 127.80×2, 127.61, 125.26, 116.53 (d, *J* = 287.5 Hz), 109.79, 105.96, 64.12, 56.25, 56.5, 46.02, 43.97, 34.83 ppm; HRMS: (ESI+) m/z calcd for $C_{29}H_{21}F_3N_2O_6$ $[M+H]^+$ 551.1885, found 551.1894

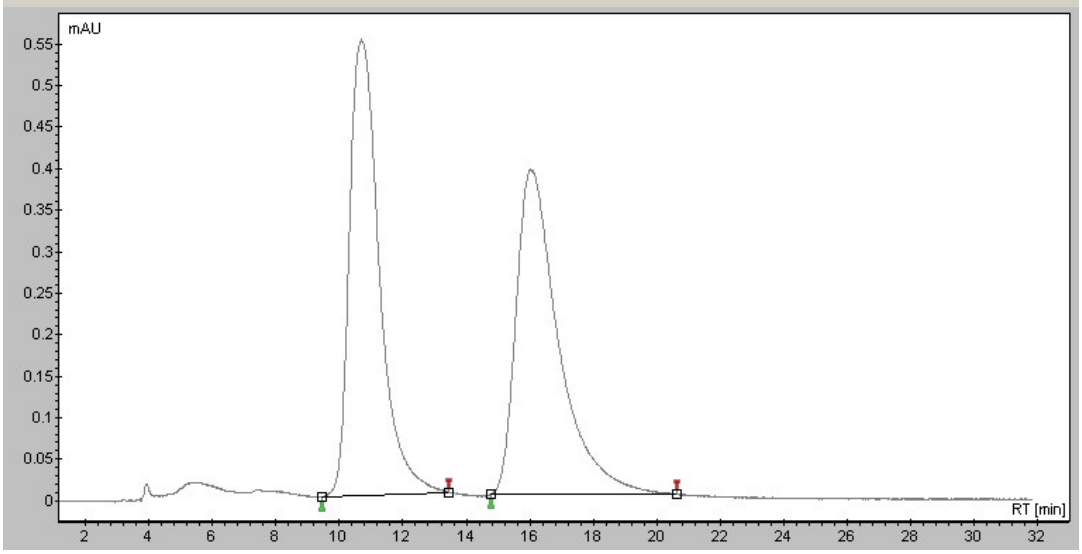
3. ^{1}H, ^{13}C NMR, and HPLC chromatograms of compounds 4a-4i and 5a-5e.

^{1}H NMR, ^{13}C NMR spectra of 4a



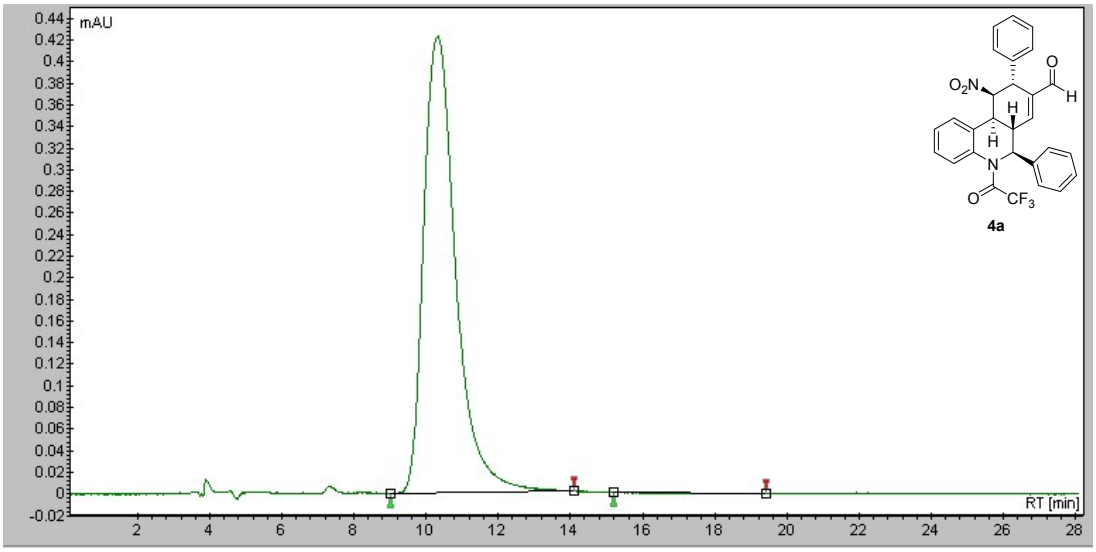


HPLC chromatogram of 4a (racemic)



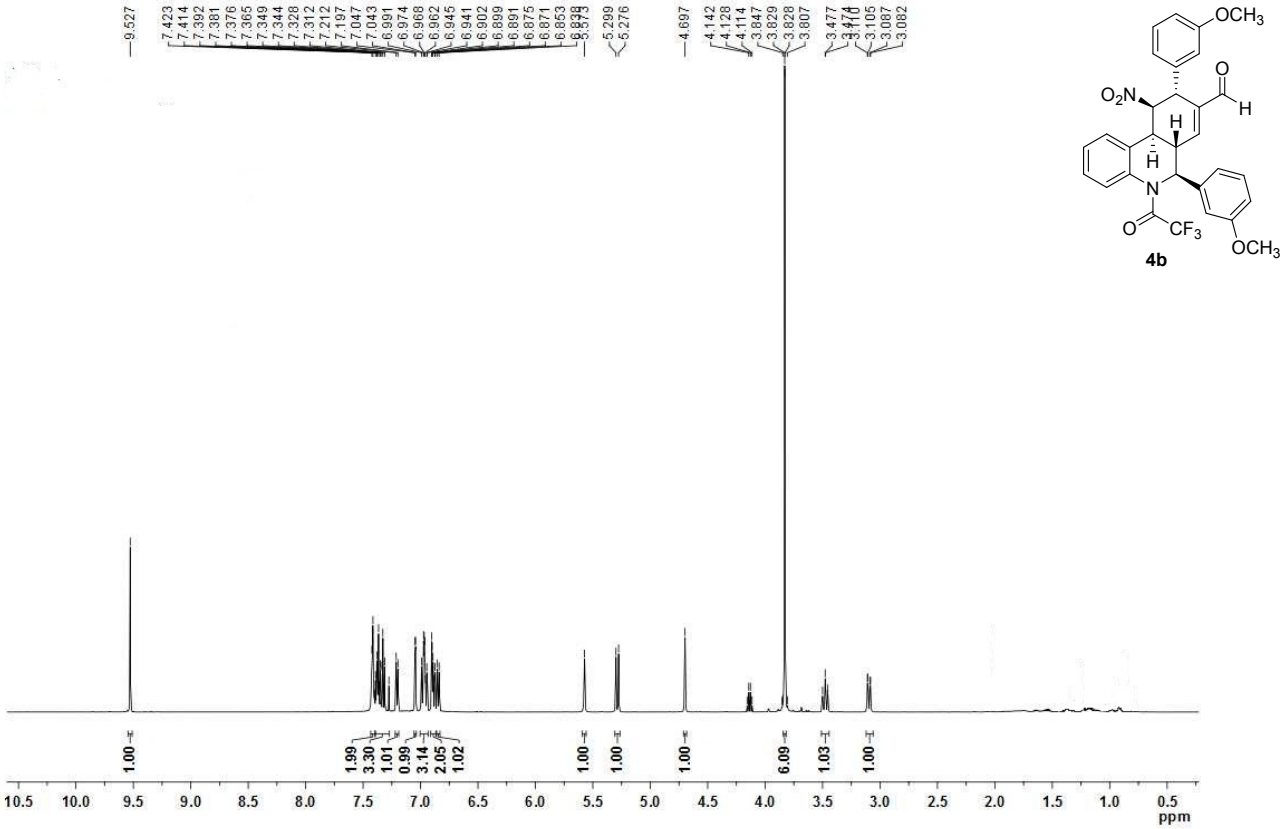
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	9.45	10.69	13.44	49.73
2	14.77	16.03	20.63	50.27

HPLC chromatogram of 4a (chiral)

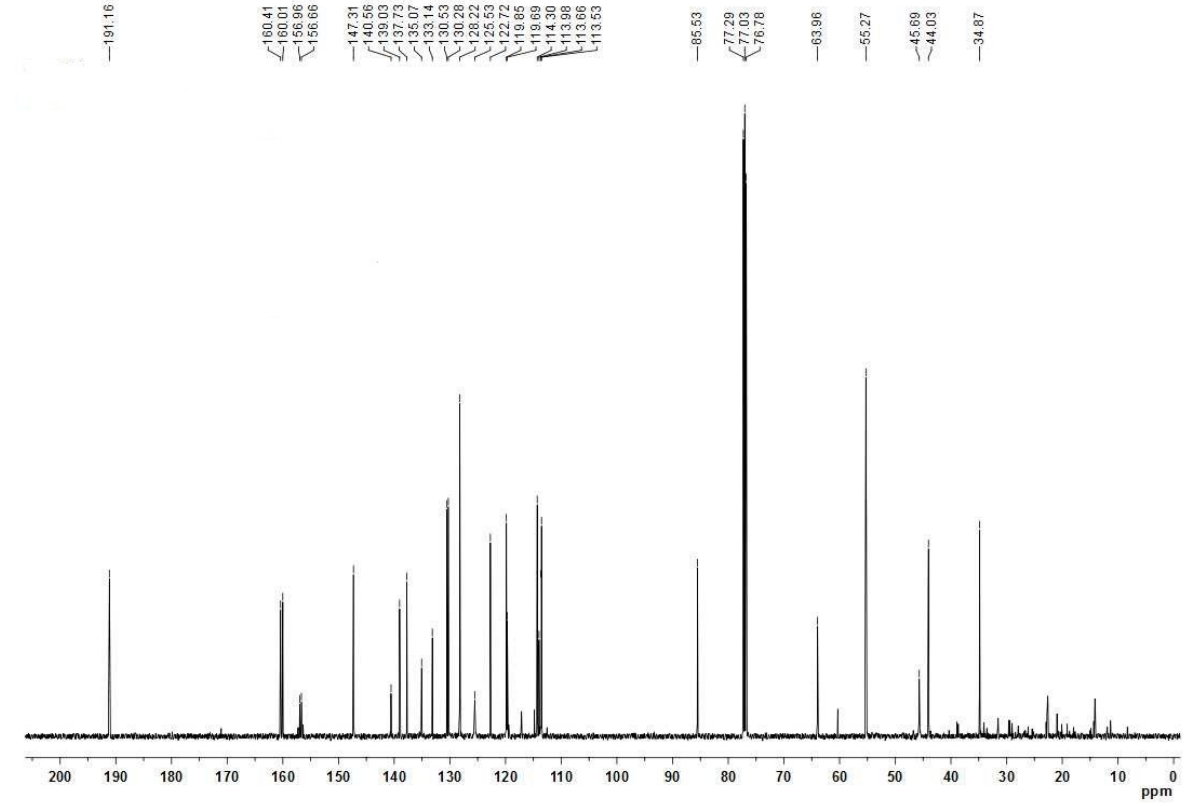


	Start [Min]	Time [Min]	End [Min]	Area [%]
1	9.01	10.32	14.10	99.87
2	15.20	17.24	19.43	0.13

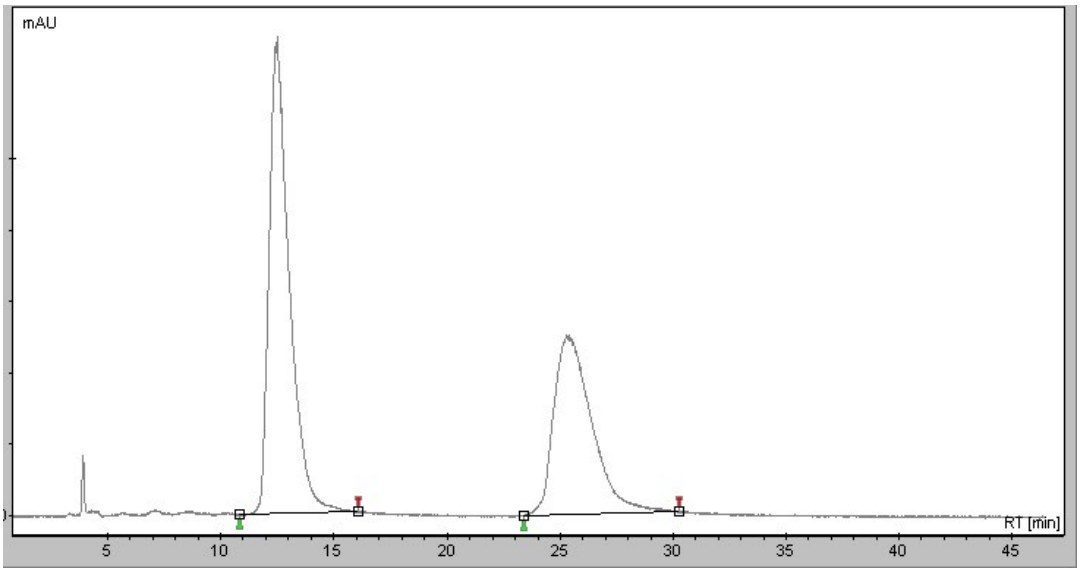
^{1}H NMR, ^{13}C NMR spectra of 4b



4b

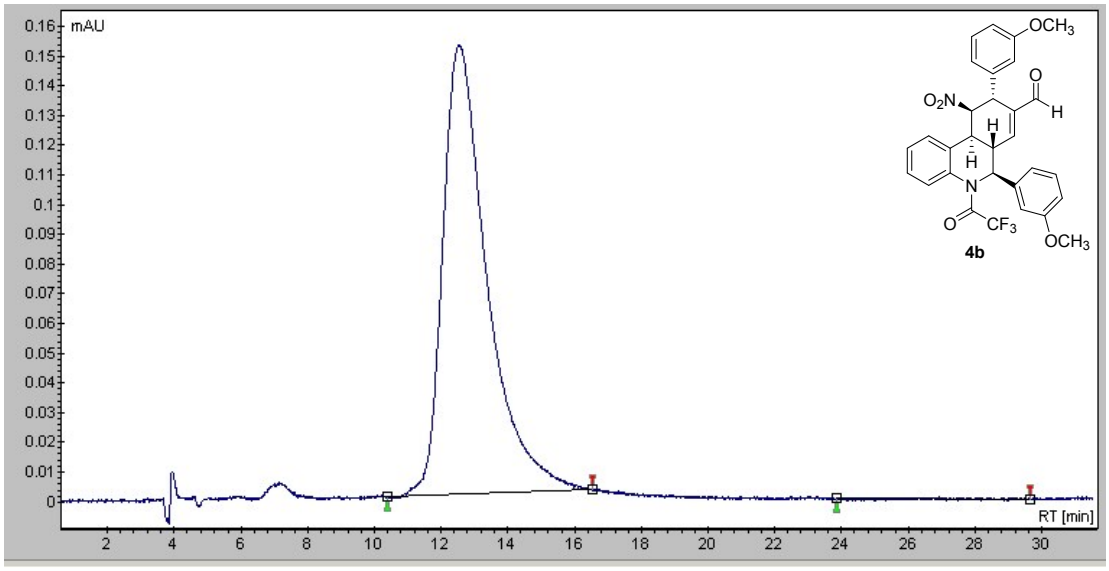


HPLC chromatogram of 4b (racemic)



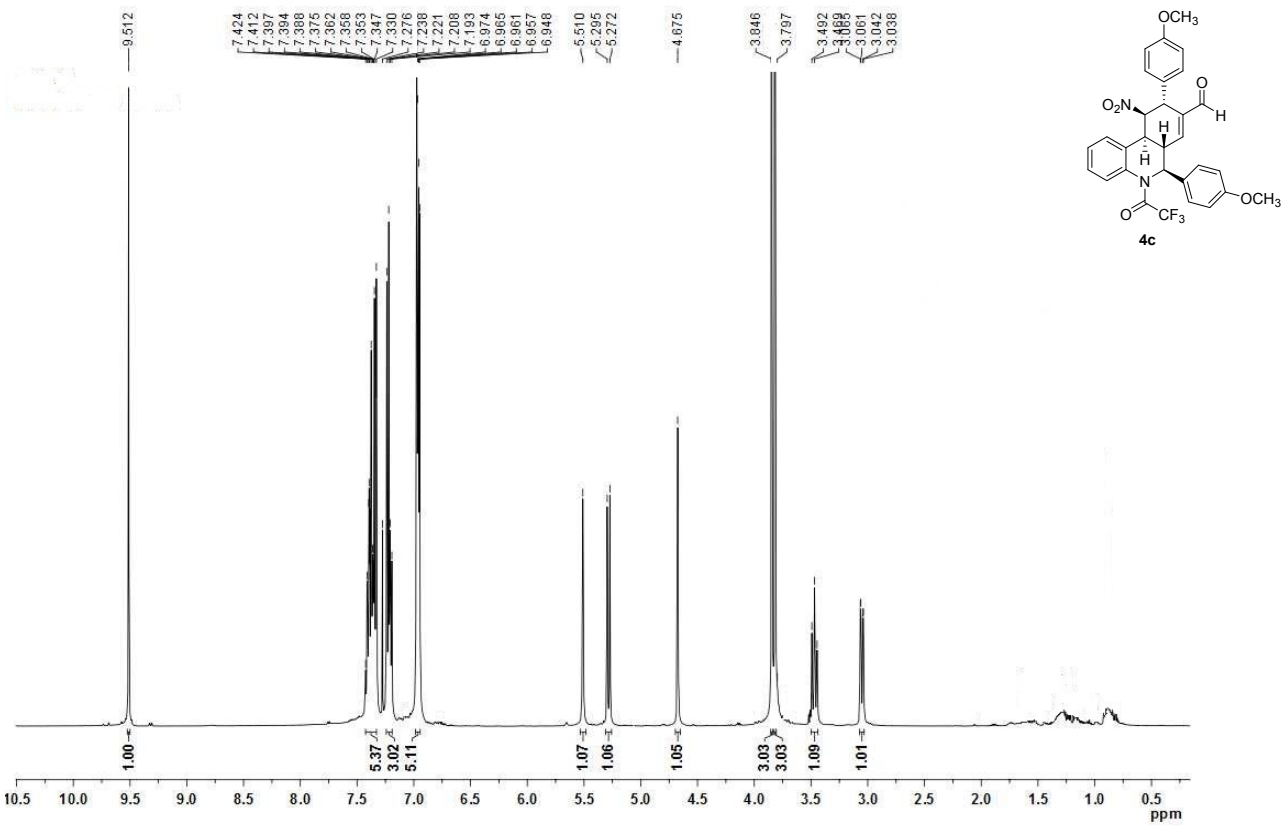
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	10.83	12.49	16.08	51.51
2	23.40	25.39	30.28	48.49

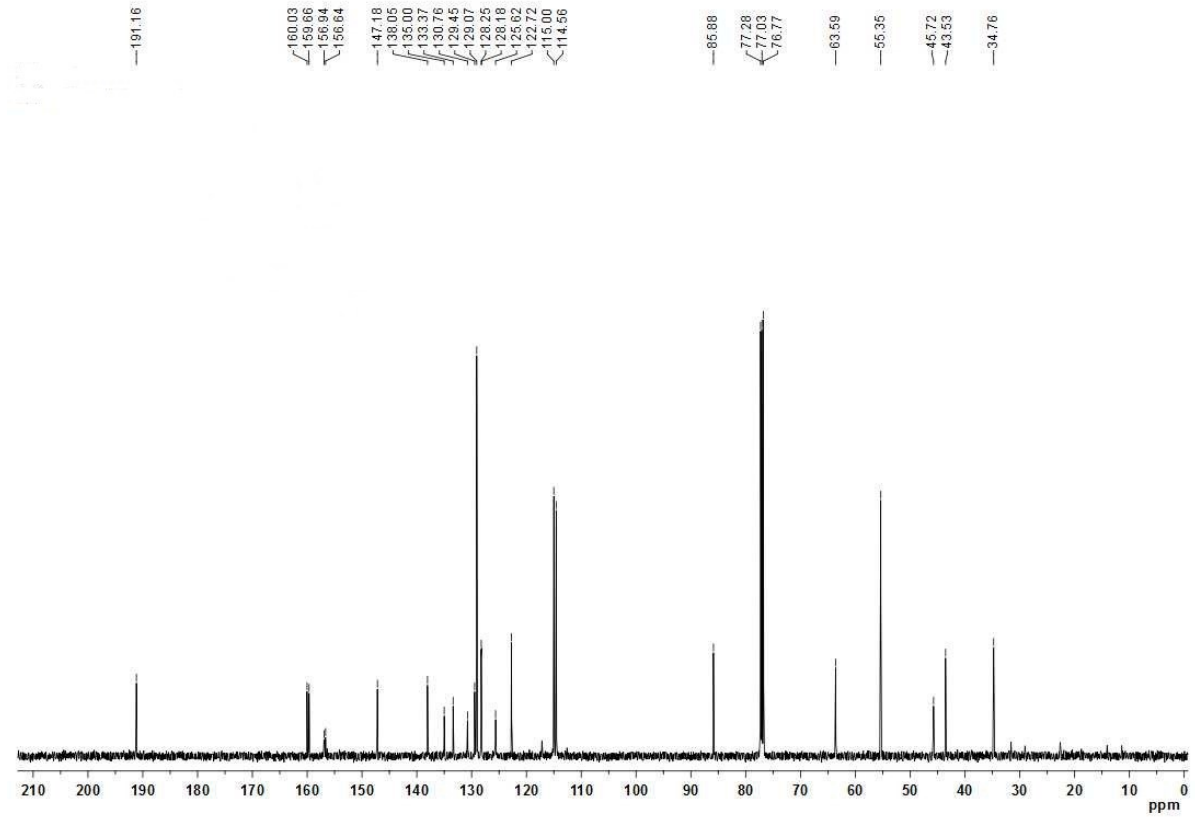
HPLC chromatogram of 4b (chiral)



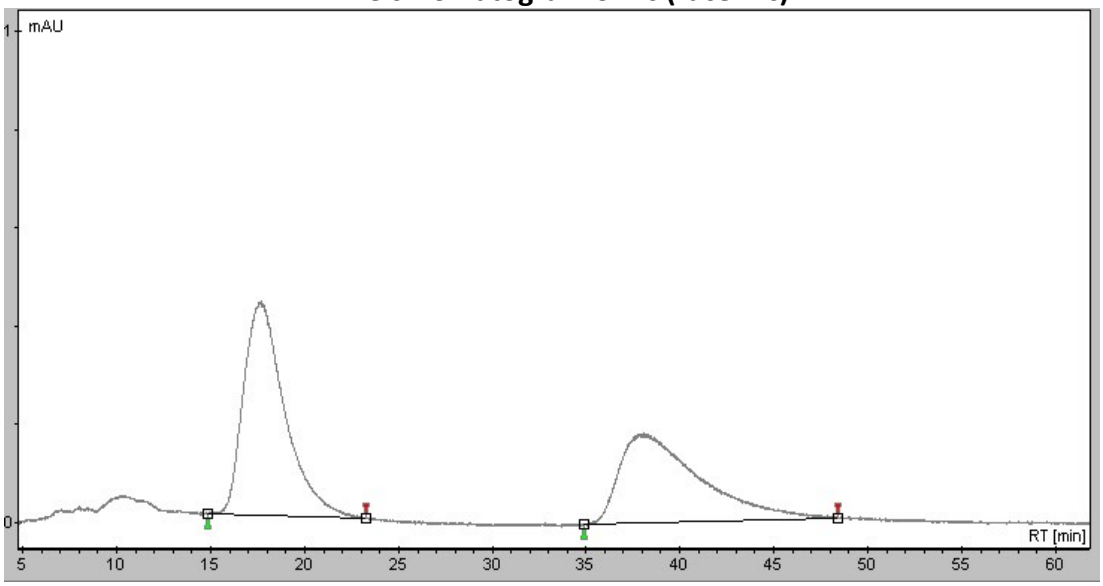
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	10.37	12.55	16.53	99.90
2	23.87	24.20	29.67	0.10

^{1}H NMR, ^{13}C NMR spectra of 4c



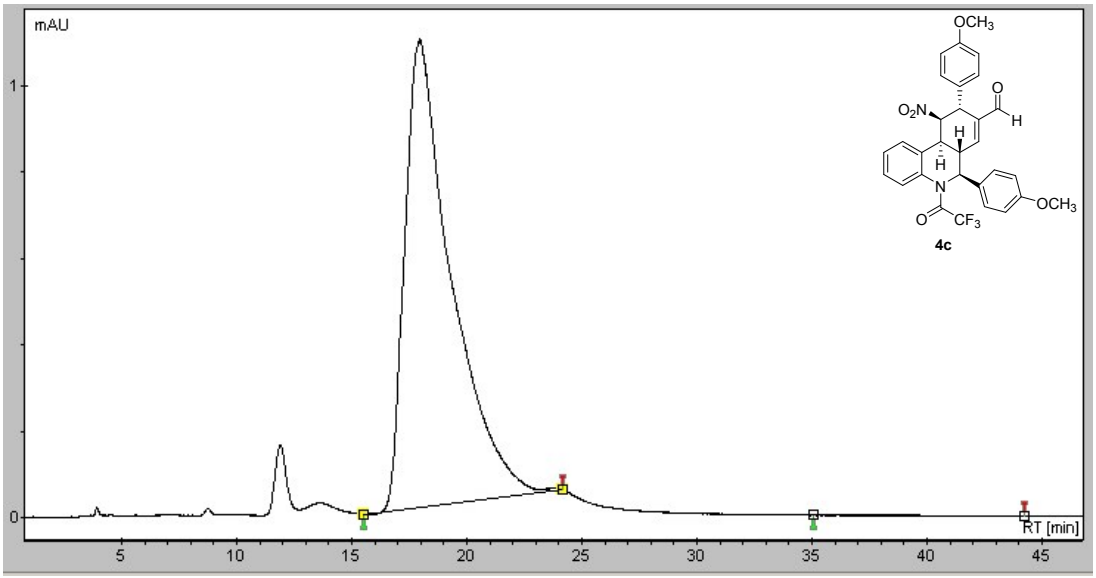


HPLC chromatogram of 4c (racemic)



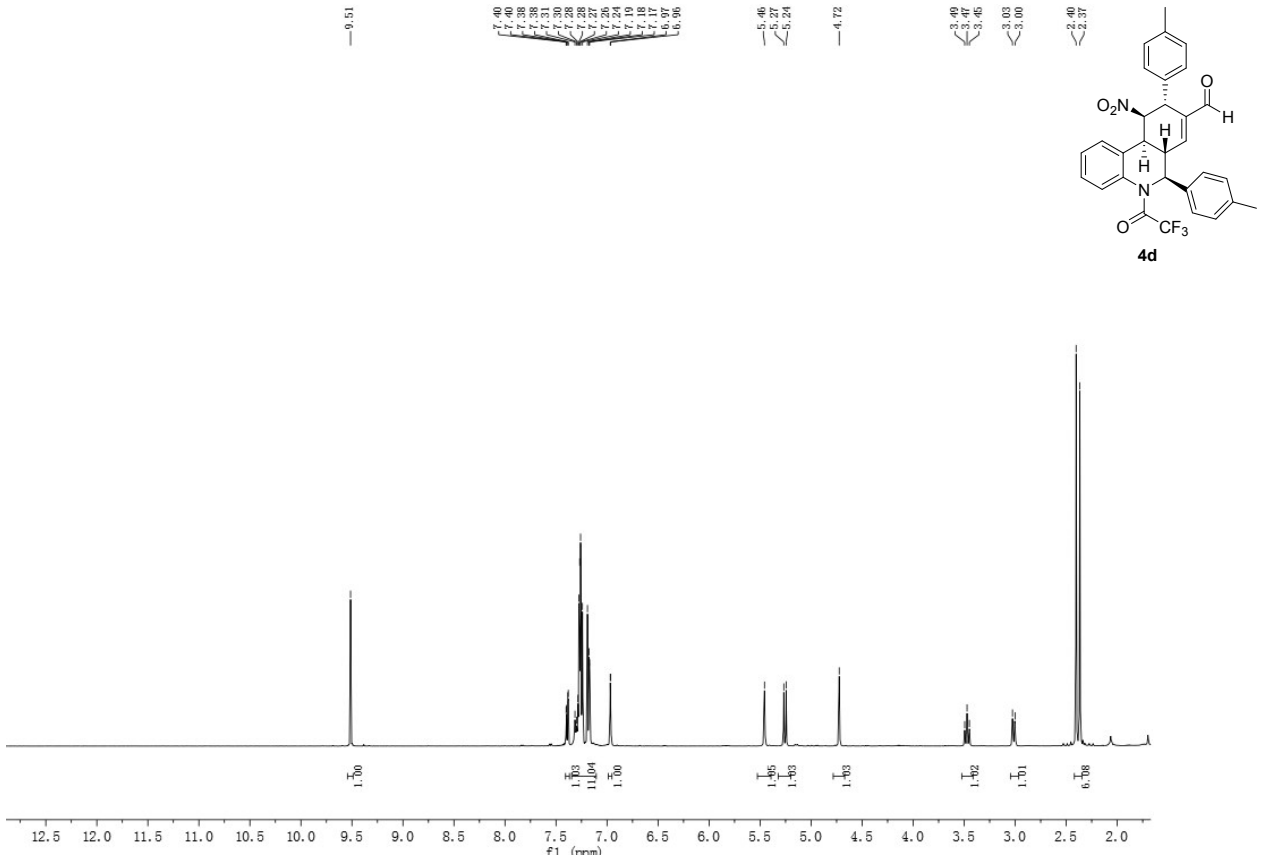
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	14.87	17.69	23.29	51.08
2	34.88	37.93	48.39	48.92

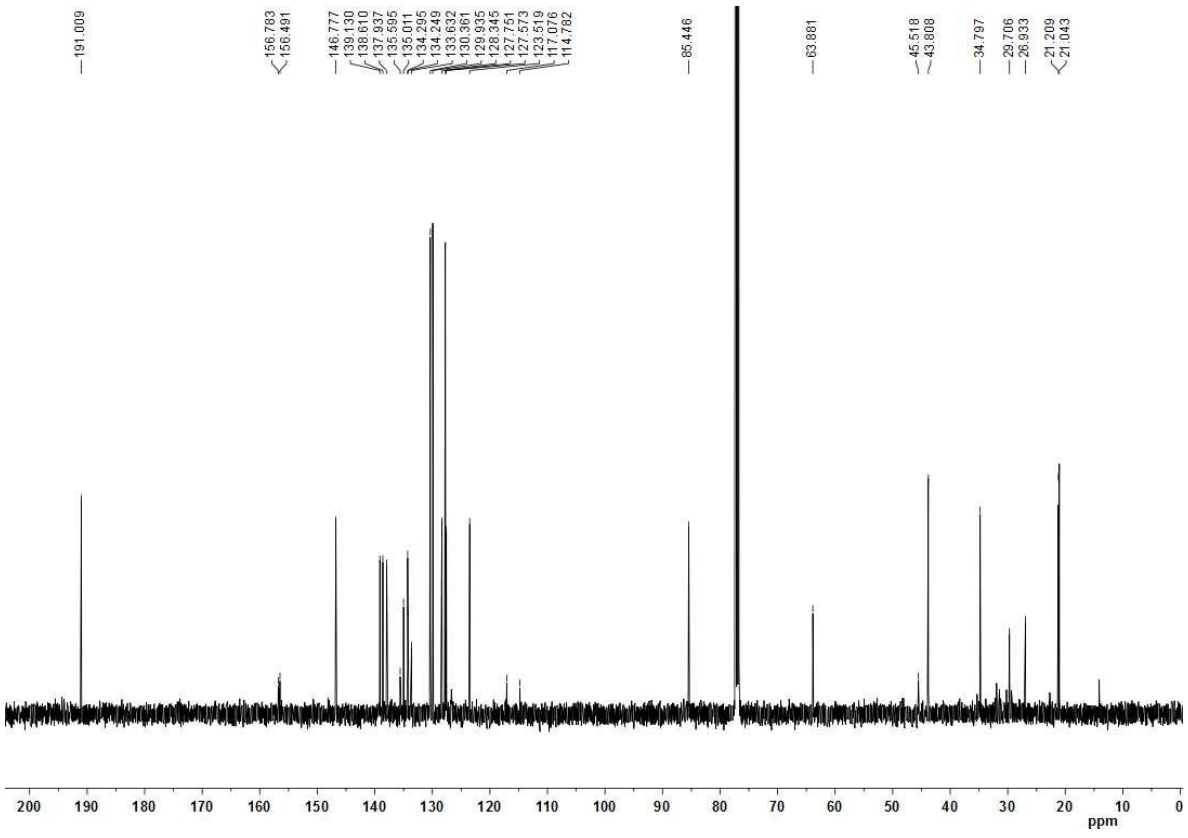
HPLC chromatogram of 4c (chiral)



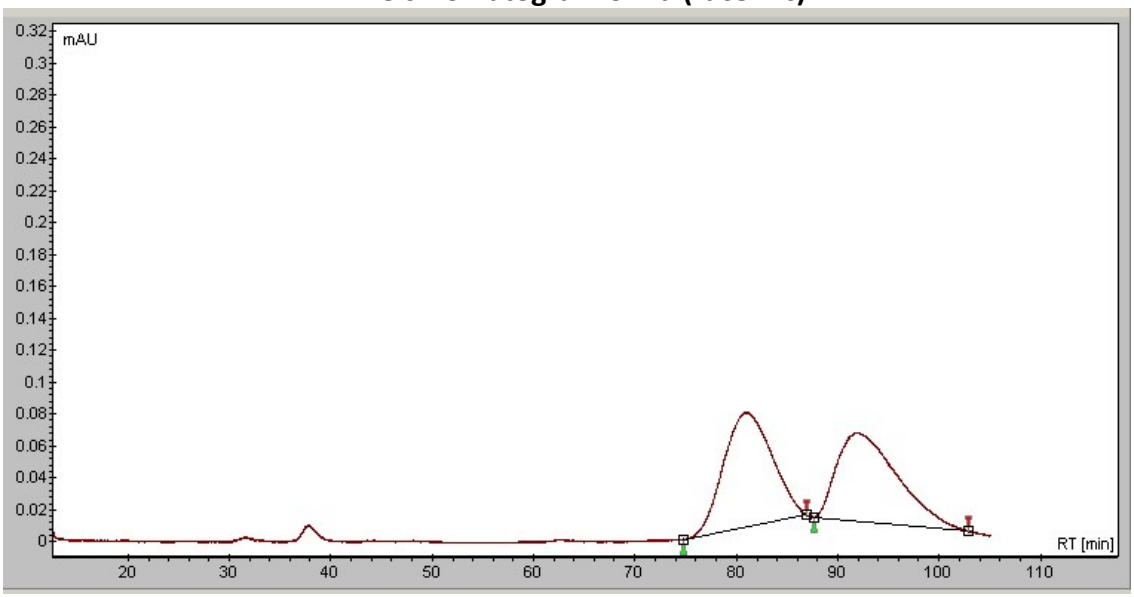
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	15.50	17.97	24.13	99.97
2	35.00	35.06	44.23	0.03

^{1}H NMR, ^{13}C NMR spectra of 4d



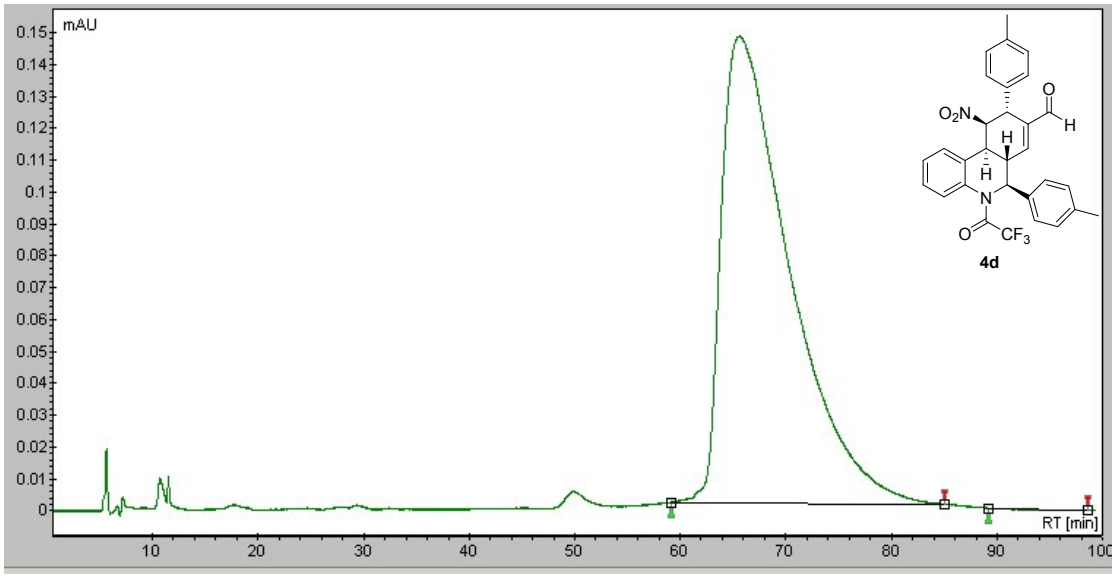


HPLC chromatogram of 4d (racemic)



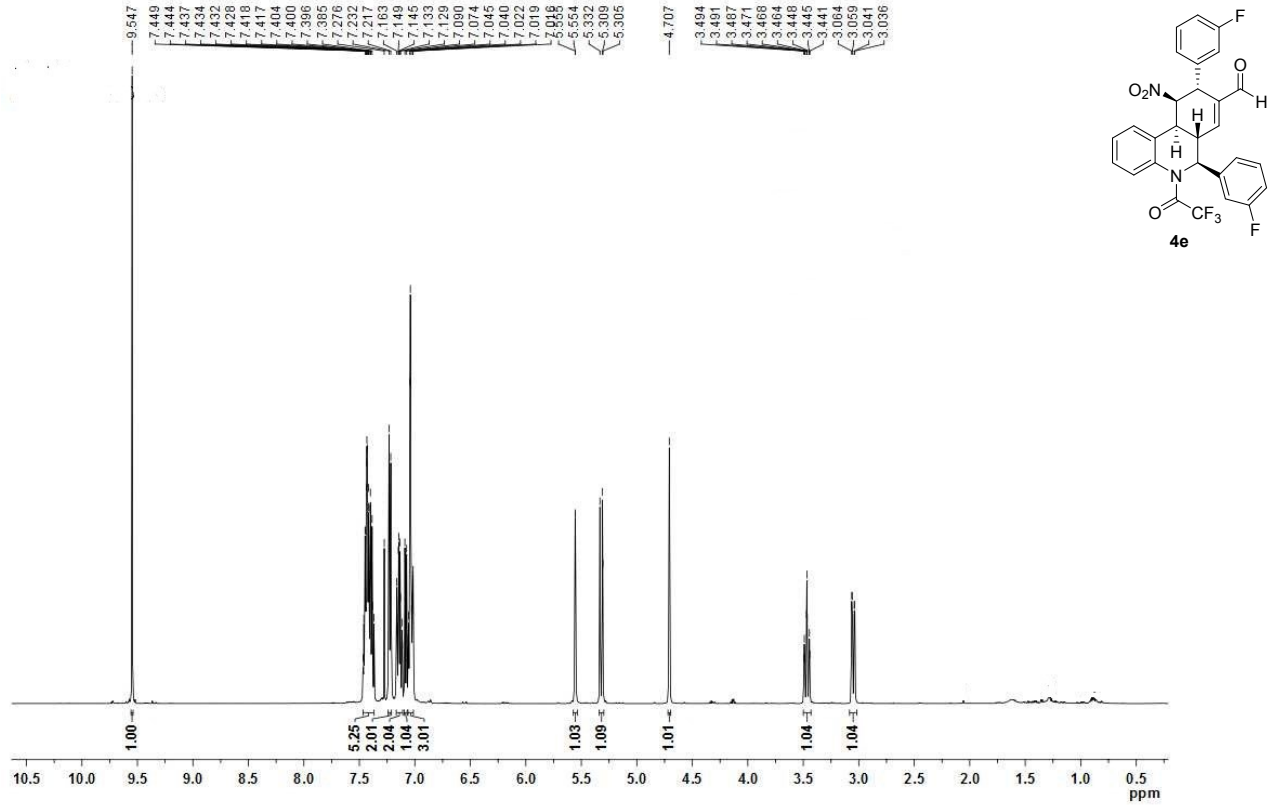
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	74.76	80.89	86.91	50.7
2	87.64	91.91	102.85	49.3

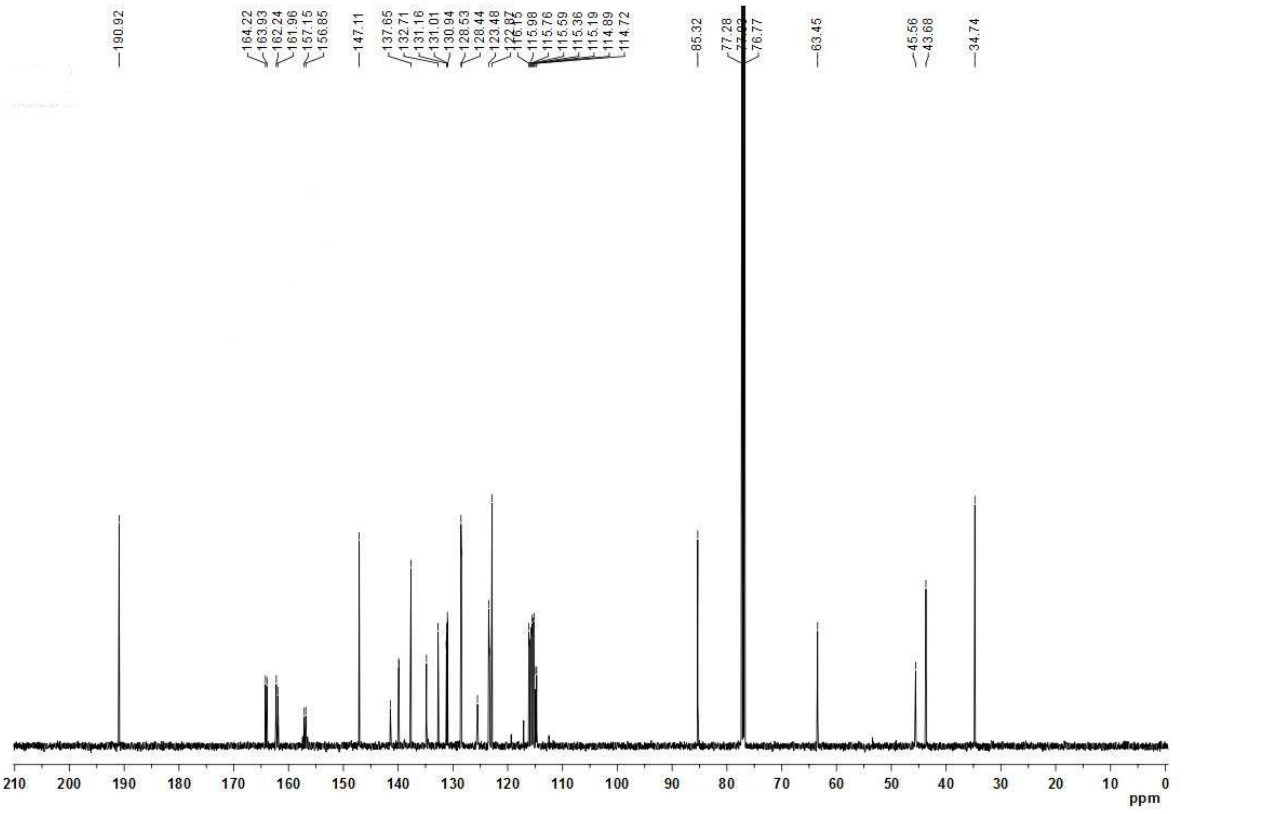
HPLC chromatogram of 4d (chiral)



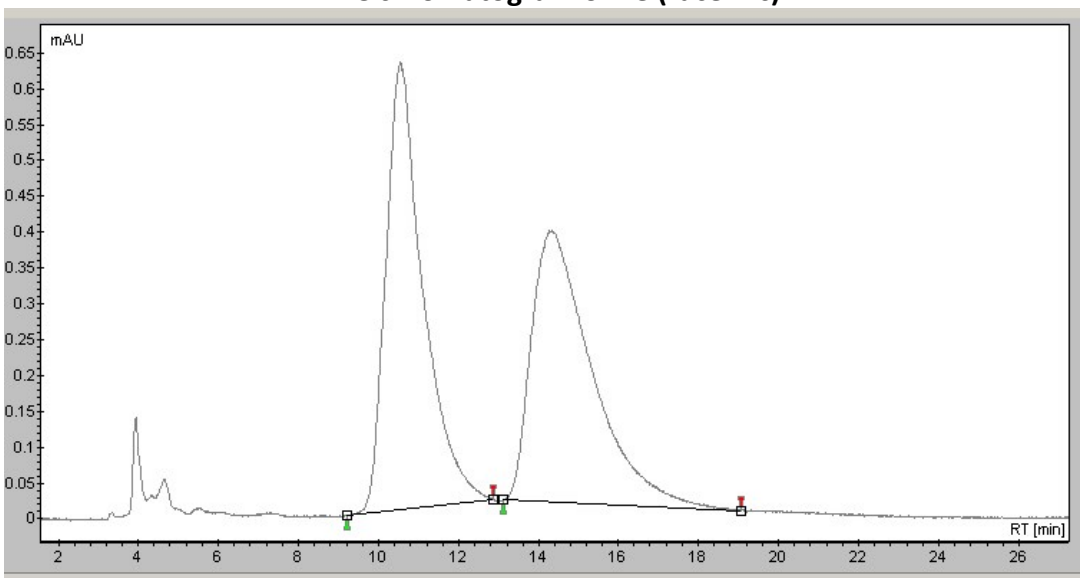
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	59.15	65.62	85.05	99.93
2	89.20	95.73	98.62	0.07

^{1}H NMR, ^{13}C NMR spectra of 4e



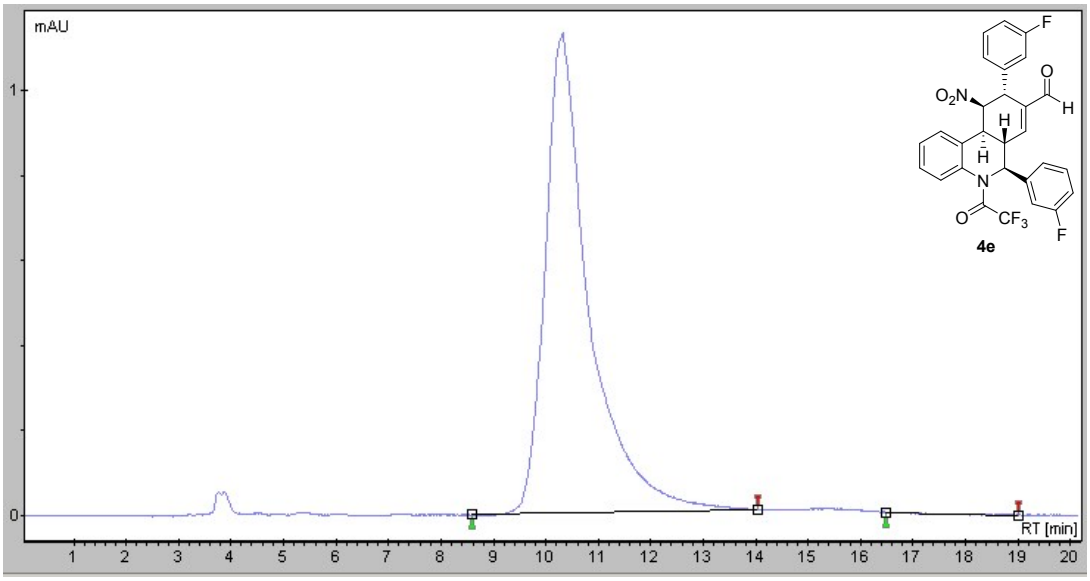


HPLC chromatogram of 4e (racemic)



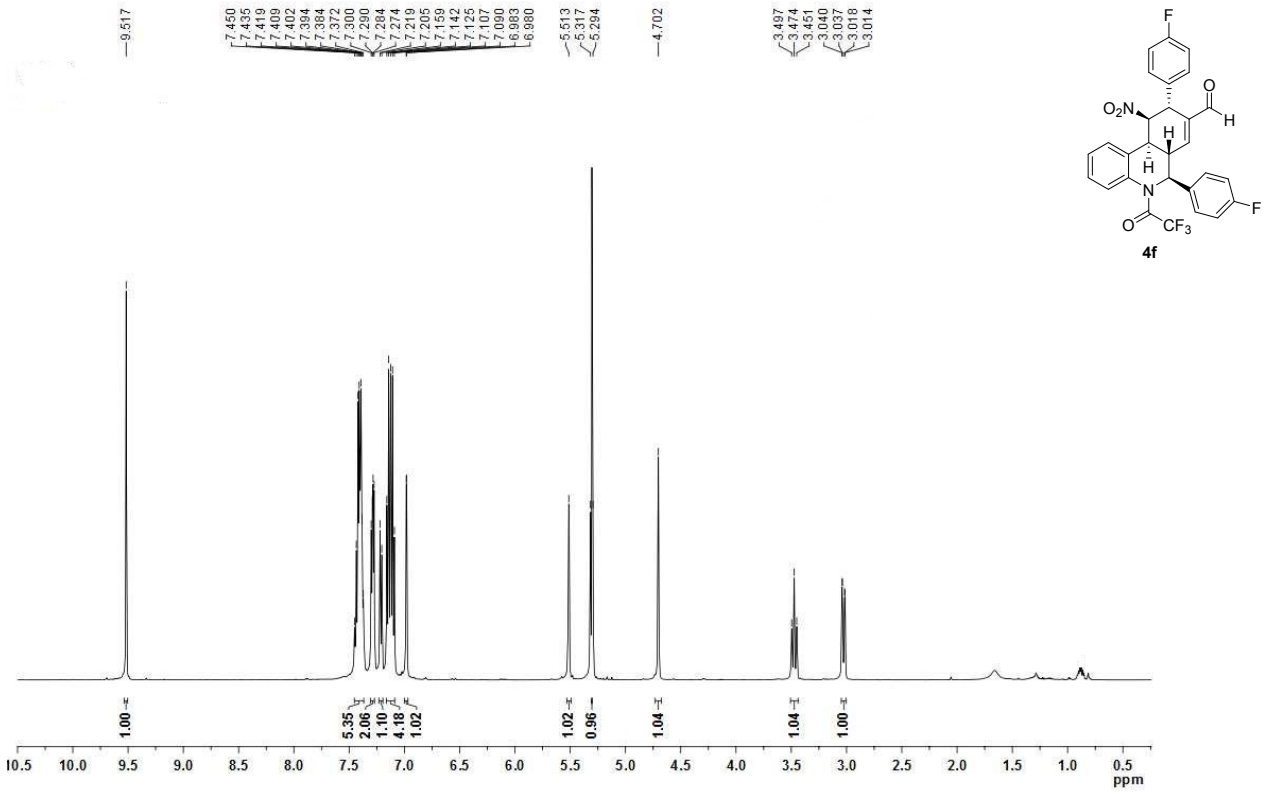
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	9.21	10.55	12.86	50.28
2	13.11	14.32	19.07	49.72

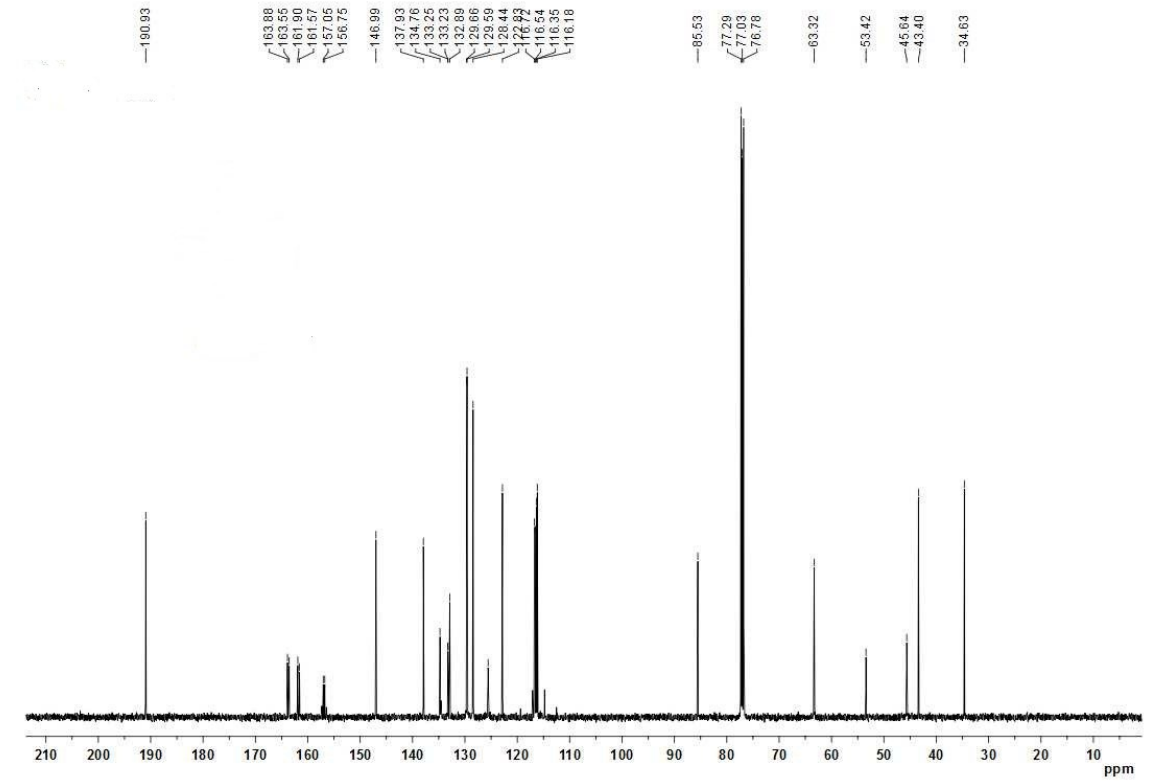
HPLC chromatogram of 4e (chiral)



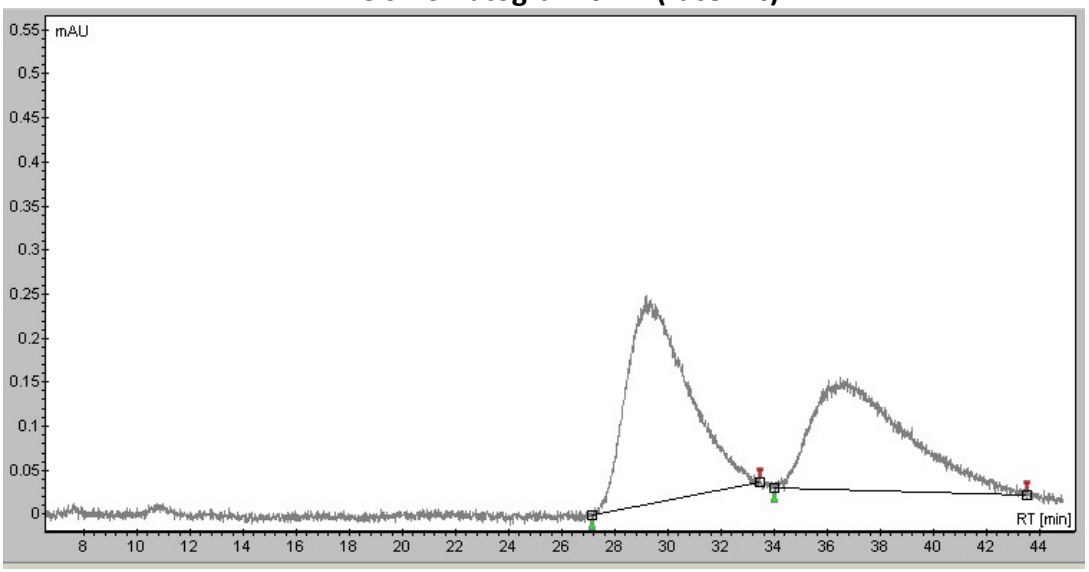
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	8.59	10.32	14.04	99.86
2	16.48	17.52	19.01	0.14

^{1}H NMR, ^{13}C NMR spectra of 4f



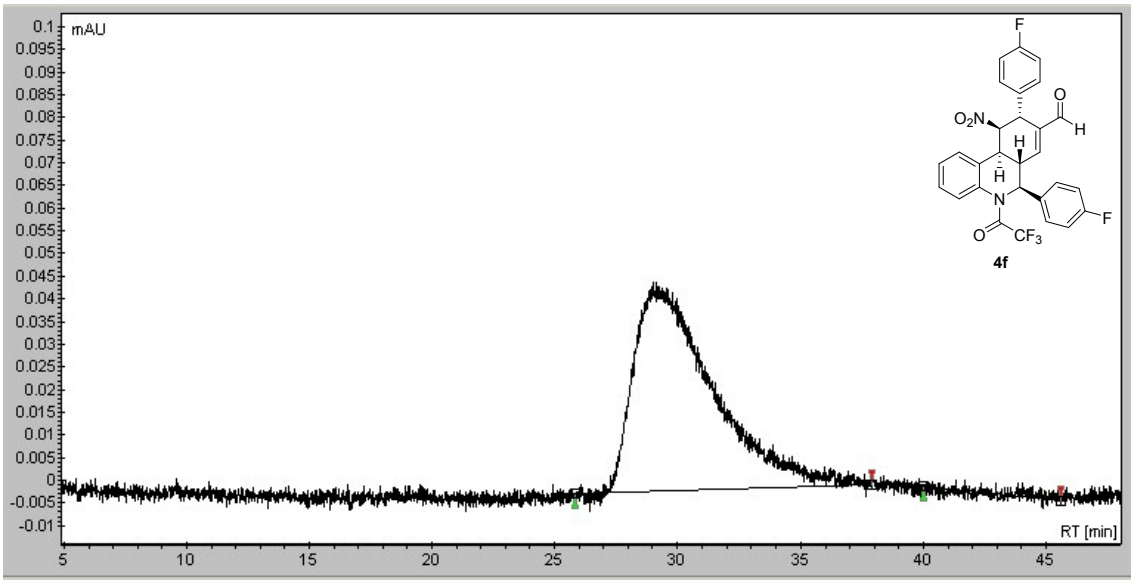


HPLC chromatogram of 4f (racemic)



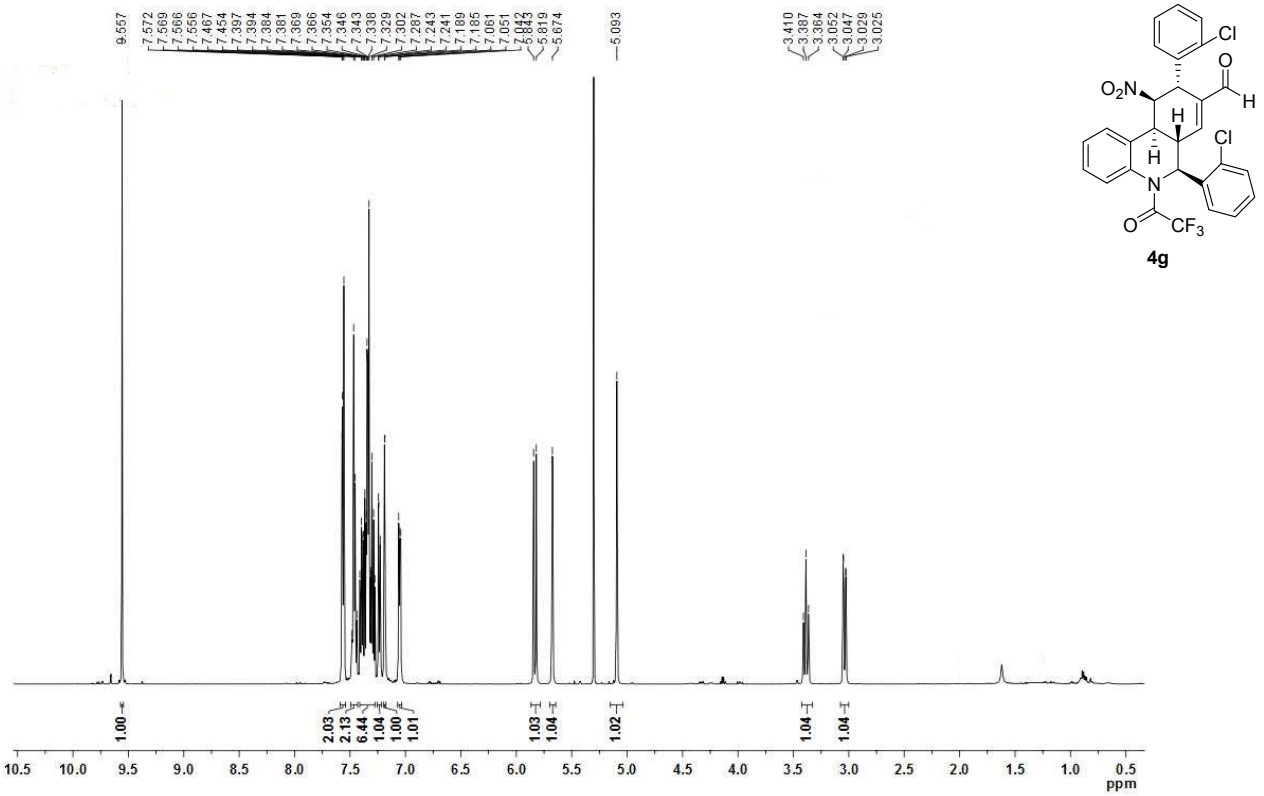
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	27.13	29.20	33.44	52.63
2	33.98	36.60	43.53	47.37

HPLC chromatogram of 4f (chiral)

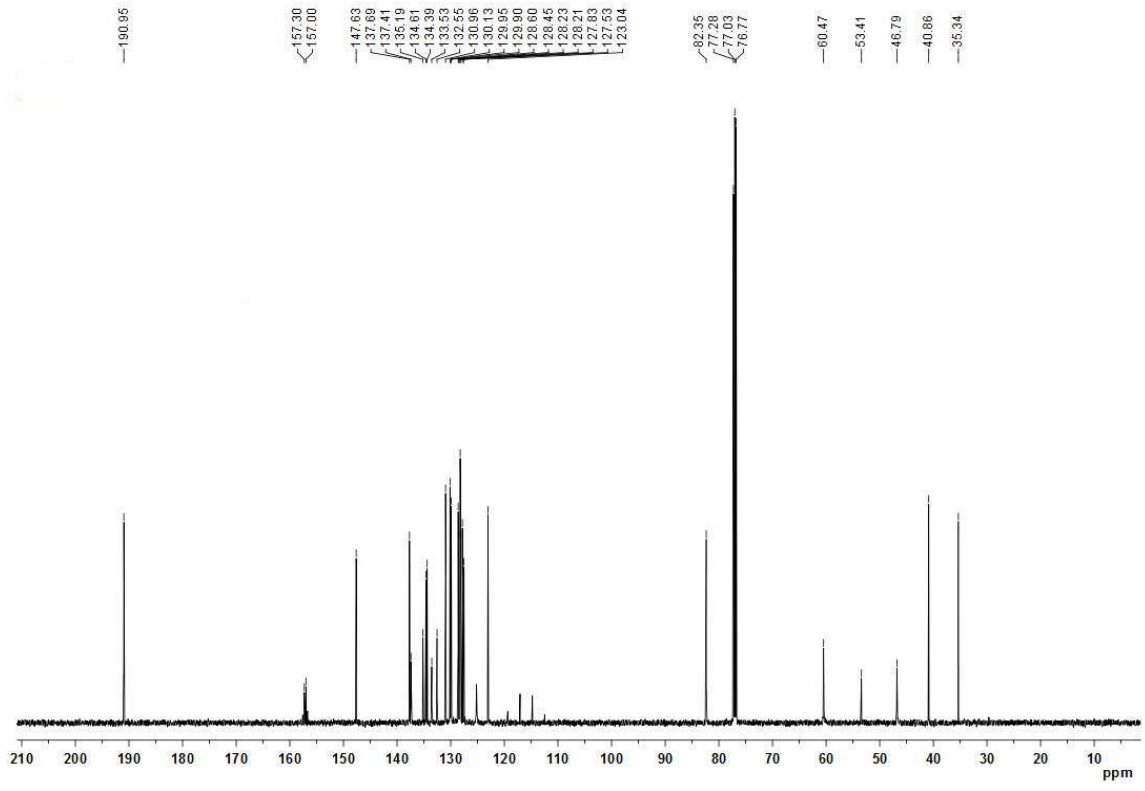


	Start [Min]	Time [Min]	End [Min]	Area [%]
1	25.83	29.15	37.91	99.97
2	40.00	45.62	45.63	0.03

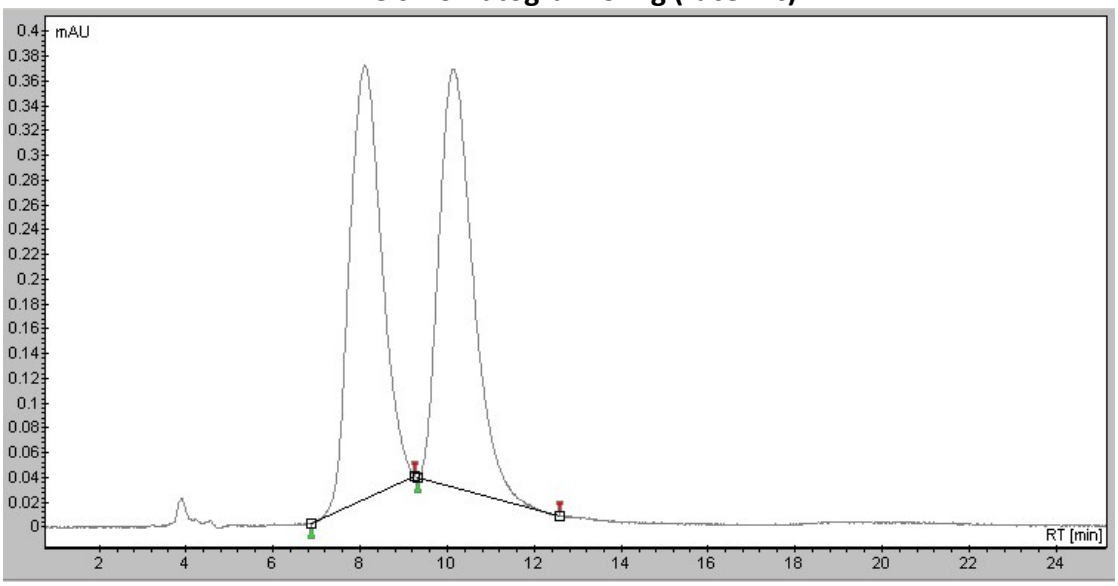
^{1}H NMR, ^{13}C NMR spectra of 4g



4g

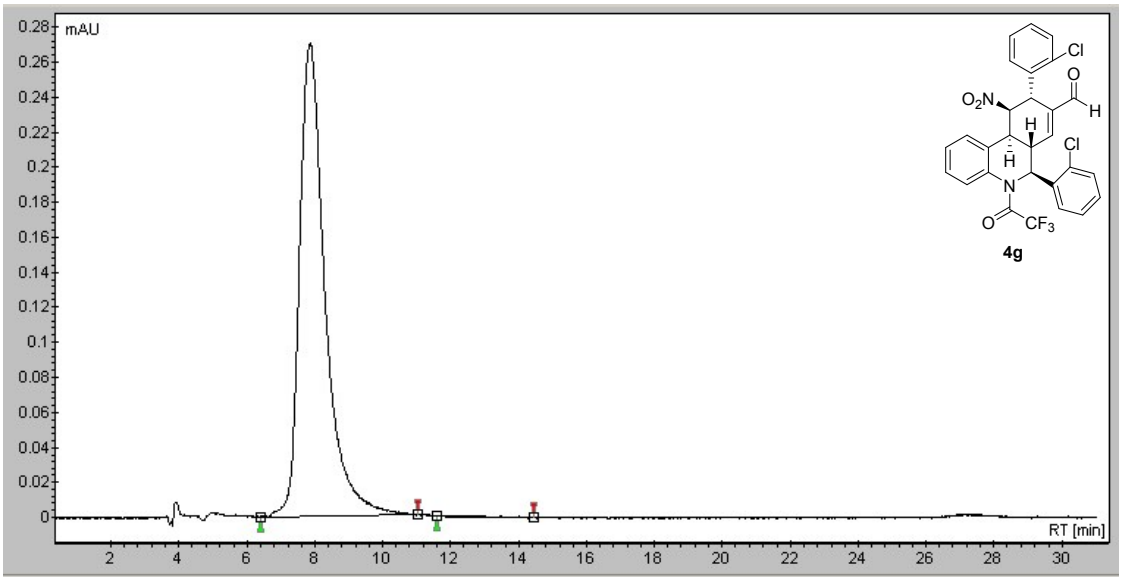


HPLC chromatogram of 4g (racemic)



	Start [Min]	Time [Min]	End [Min]	Area [%]
1	6.86	8.11	9.26	49.60
2	9.34	10.15	12.57	50.40

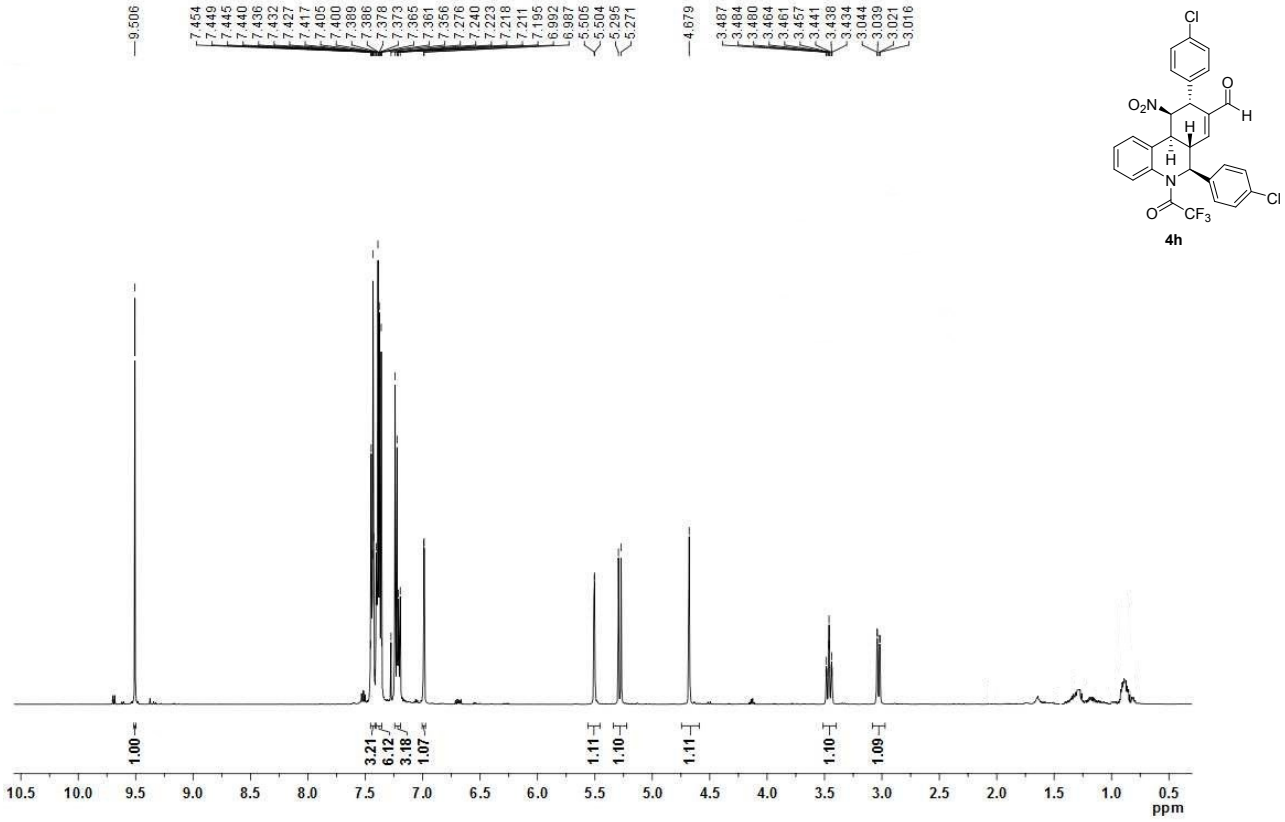
HPLC chromatogram of 4g (chiral)



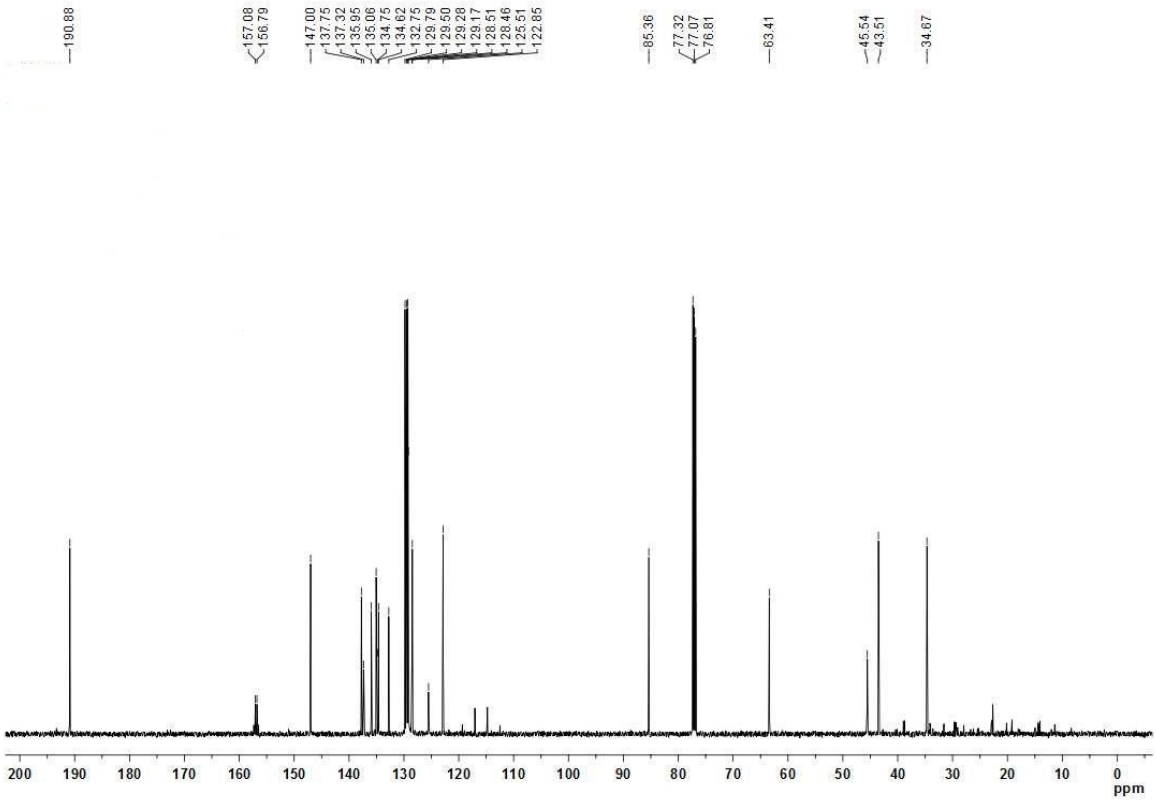
4g

	Start [Min]	Time [Min]	End [Min]	Area [%]
1	6.4	7.85	11.03	99.66
2	11.59	12.67	14.45	0.34

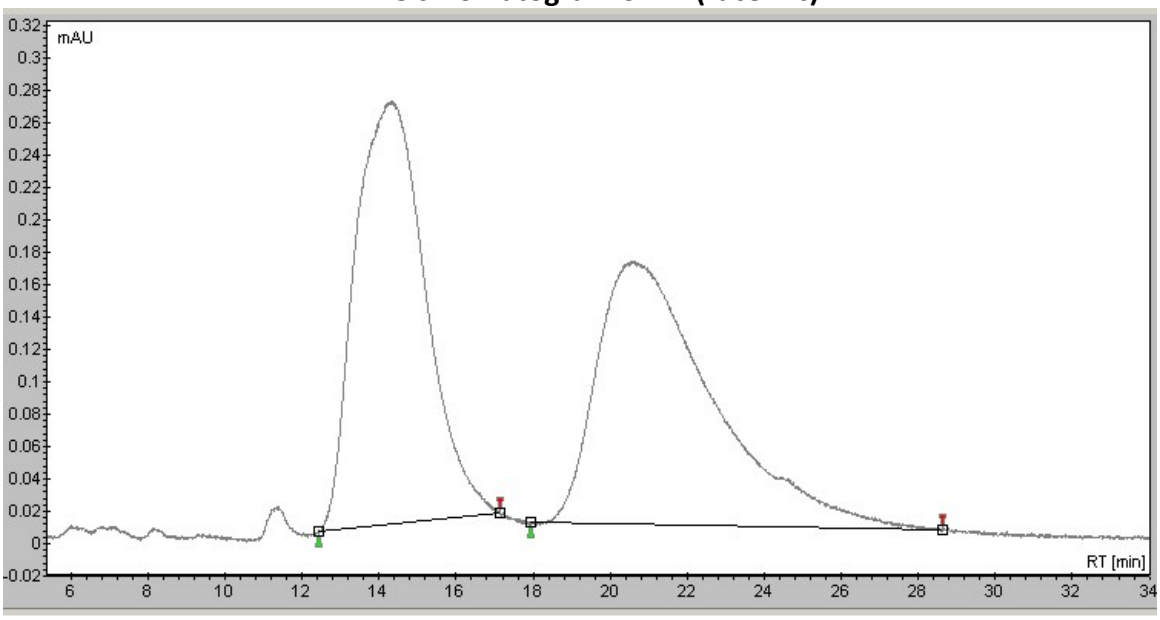
^{1}H NMR, ^{13}C NMR spectra of 4h



4h

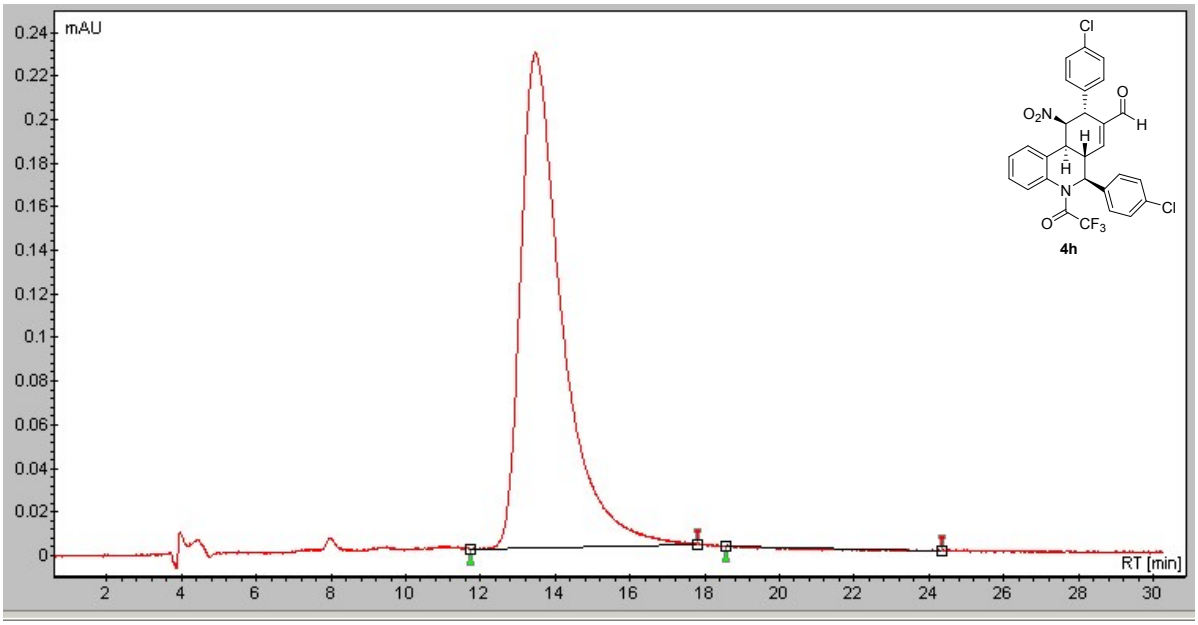


HPLC chromatogram of 4h (racemic)



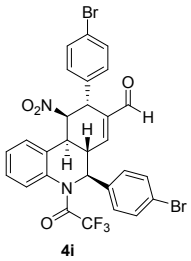
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	12.44	14.31	17.13	49.50
2	17.95	20.67	28.65	50.50

HPLC chromatogram of 4h (chiral)

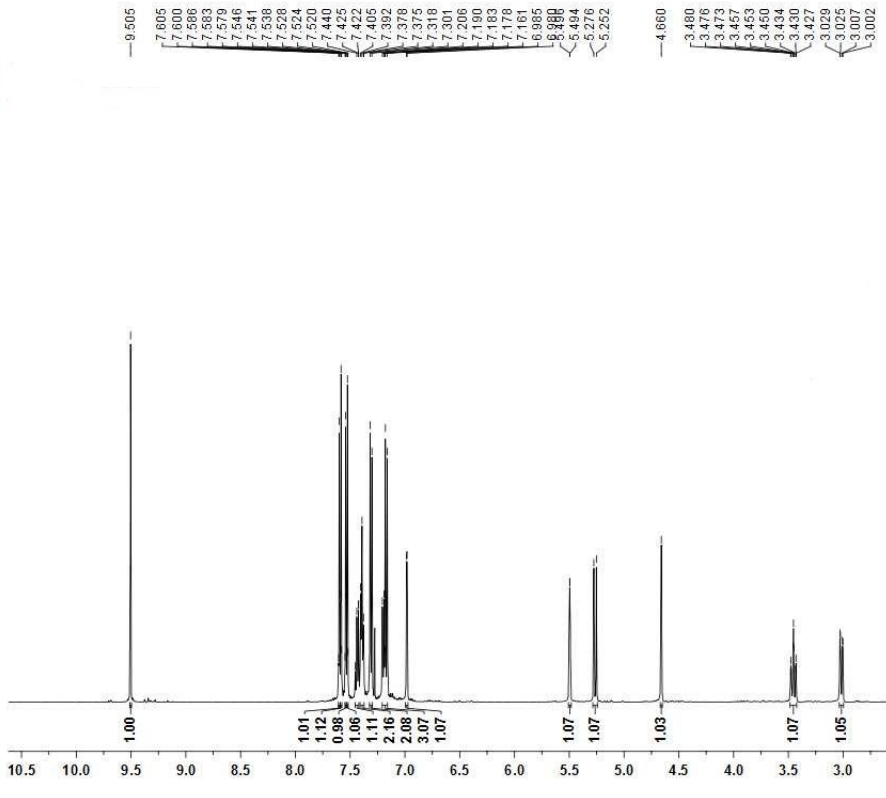


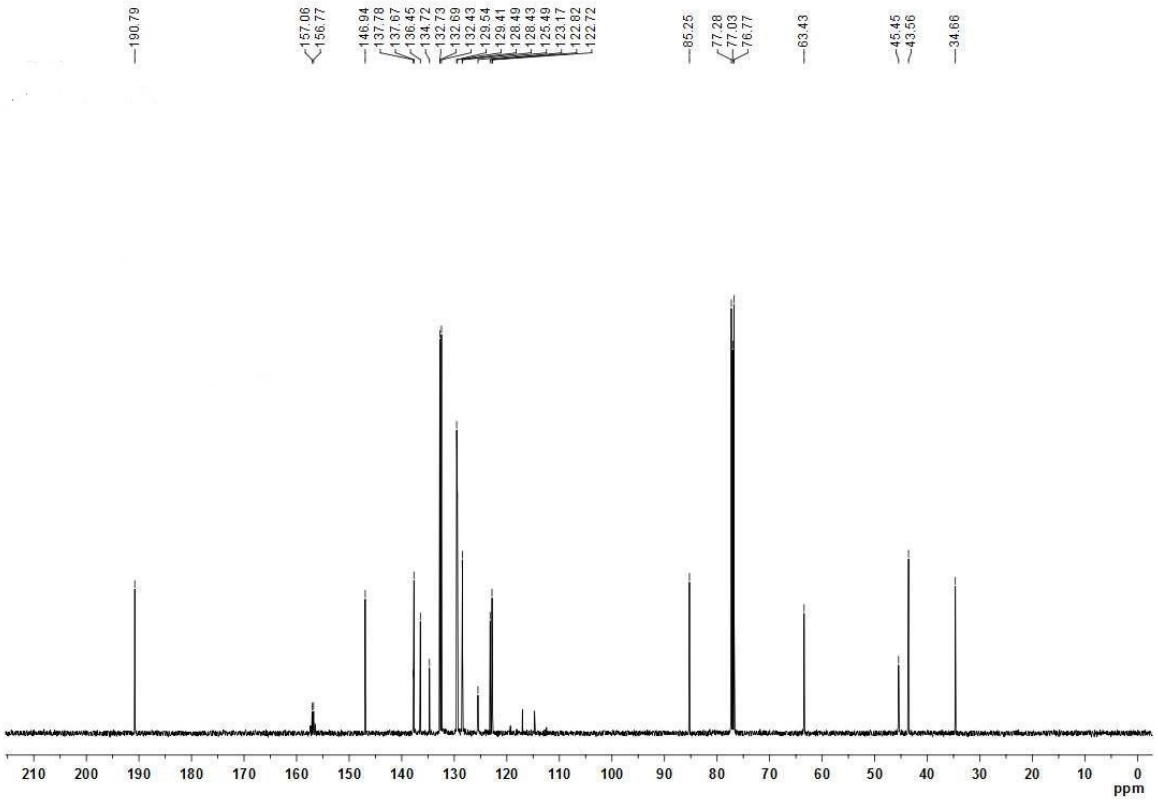
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	11.73	13.47	17.81	99.81
2	18.56	20.85	24.34	0.19

^{1}H NMR, ^{13}C NMR spectra of 4i

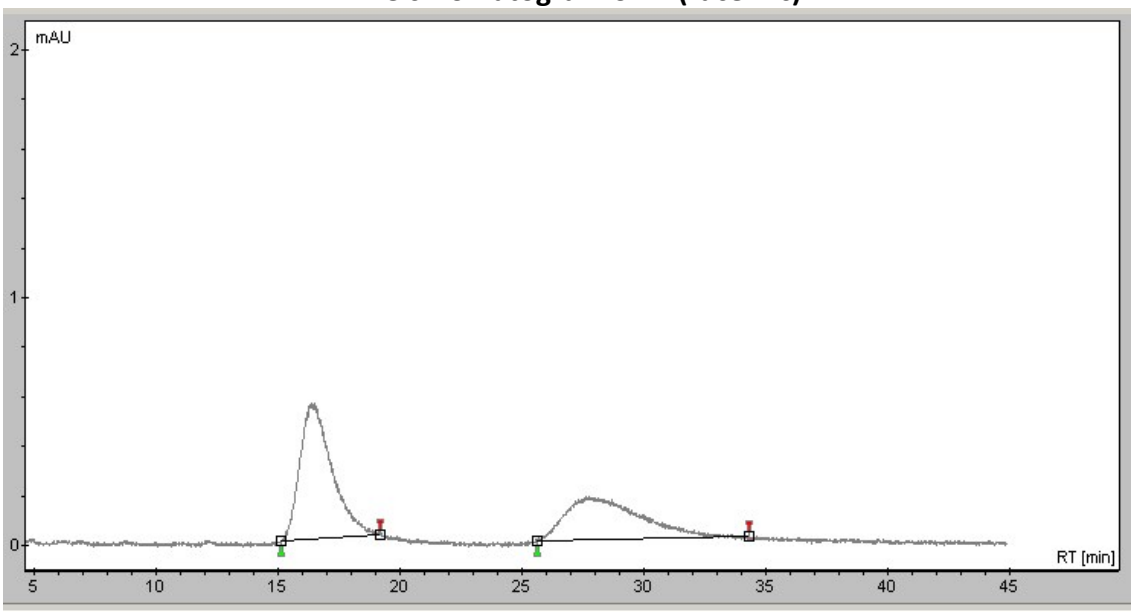


4i



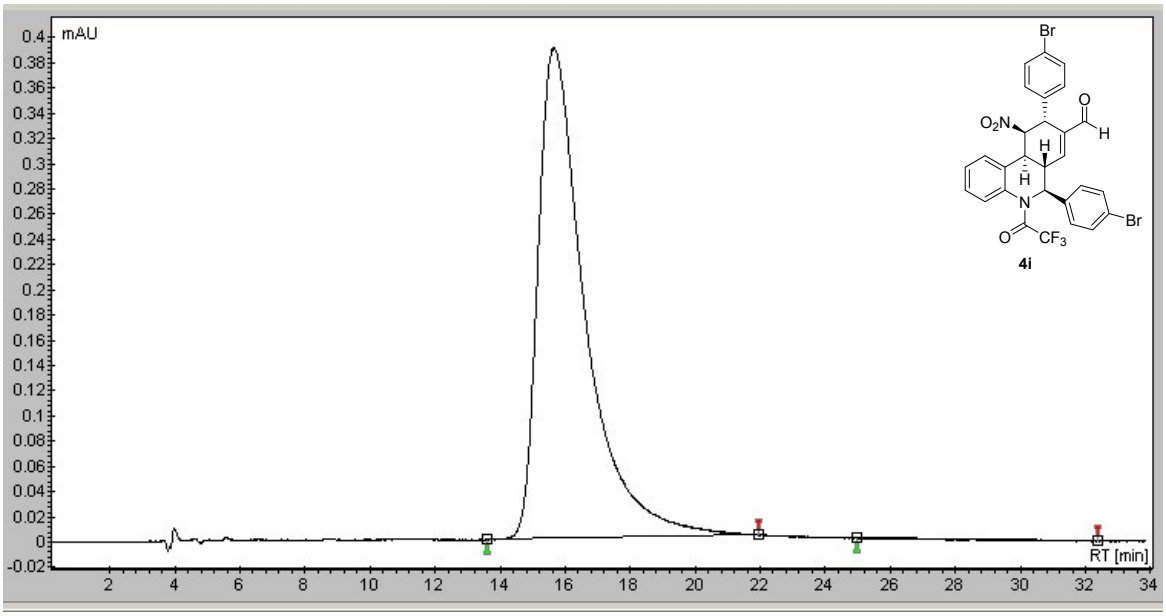


HPLC chromatogram of 4i (racemic)



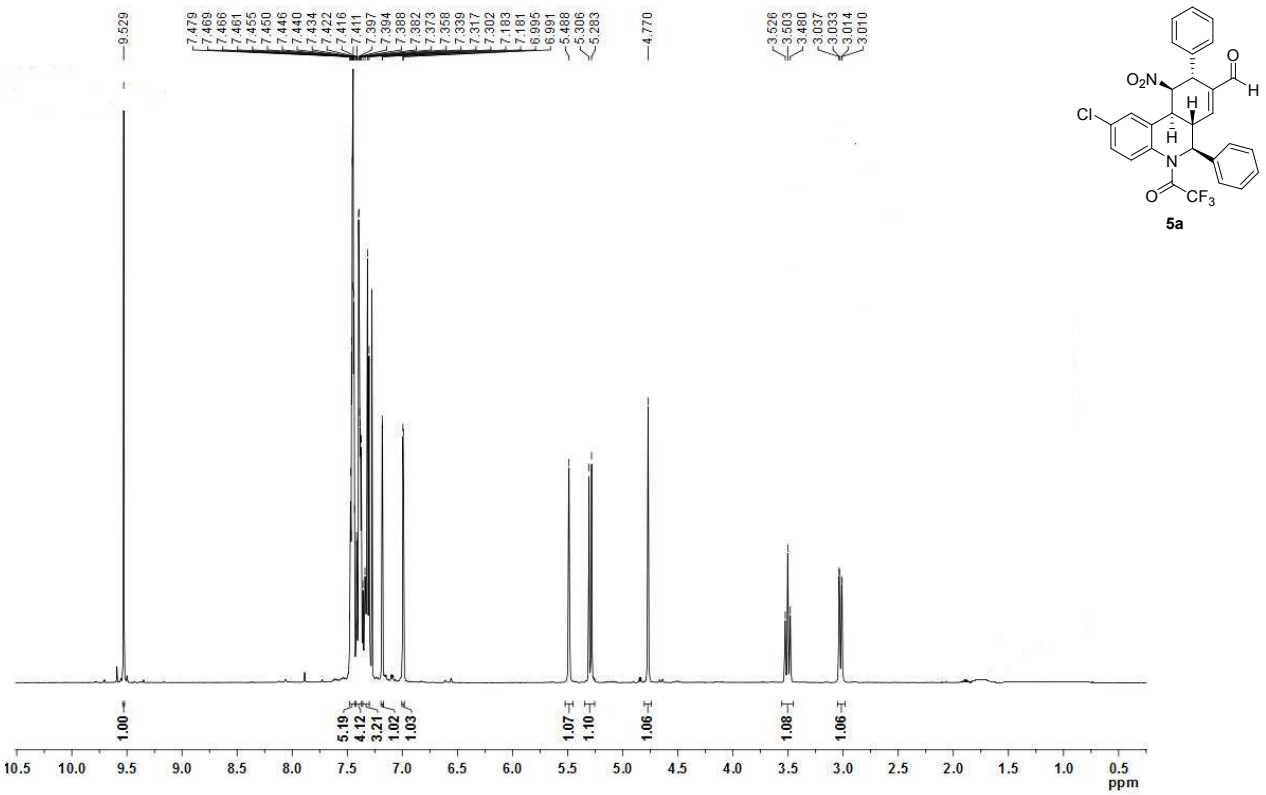
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	15.13	16.40	19.19	52.23
2	25.63	27.71	34.32	47.77

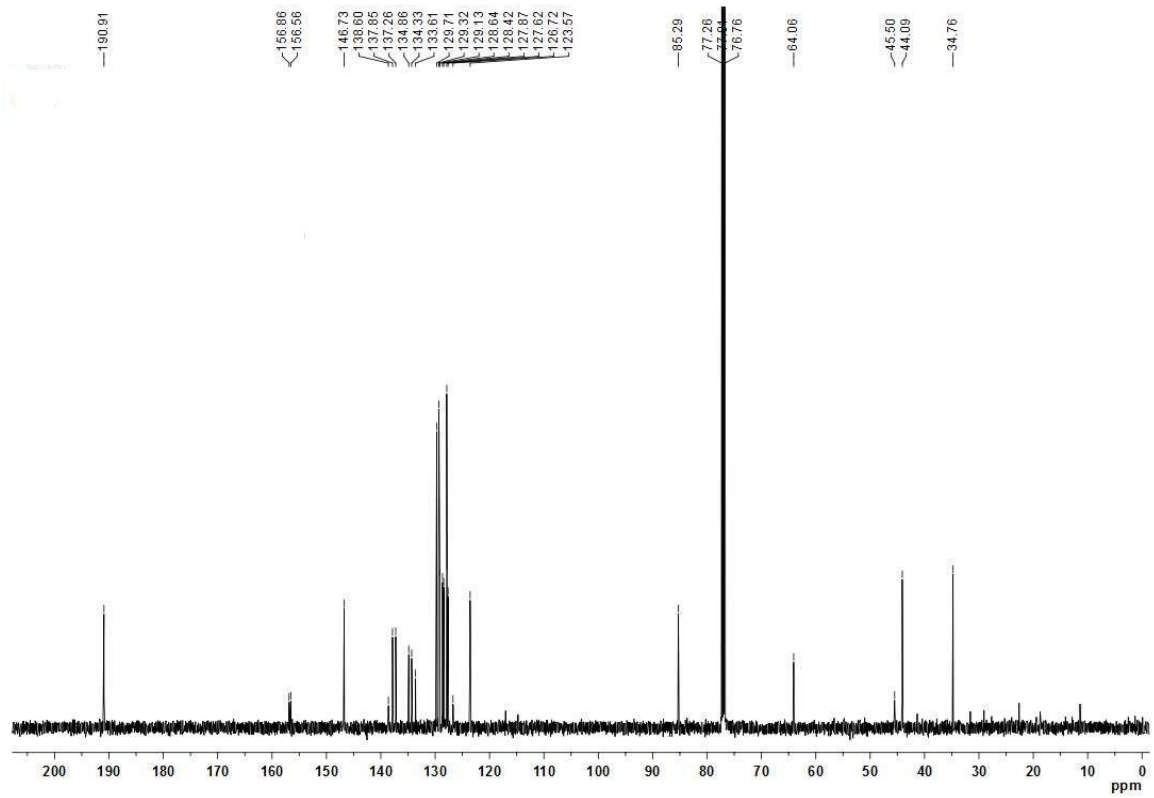
HPLC chromatogram of 4i (chiral)



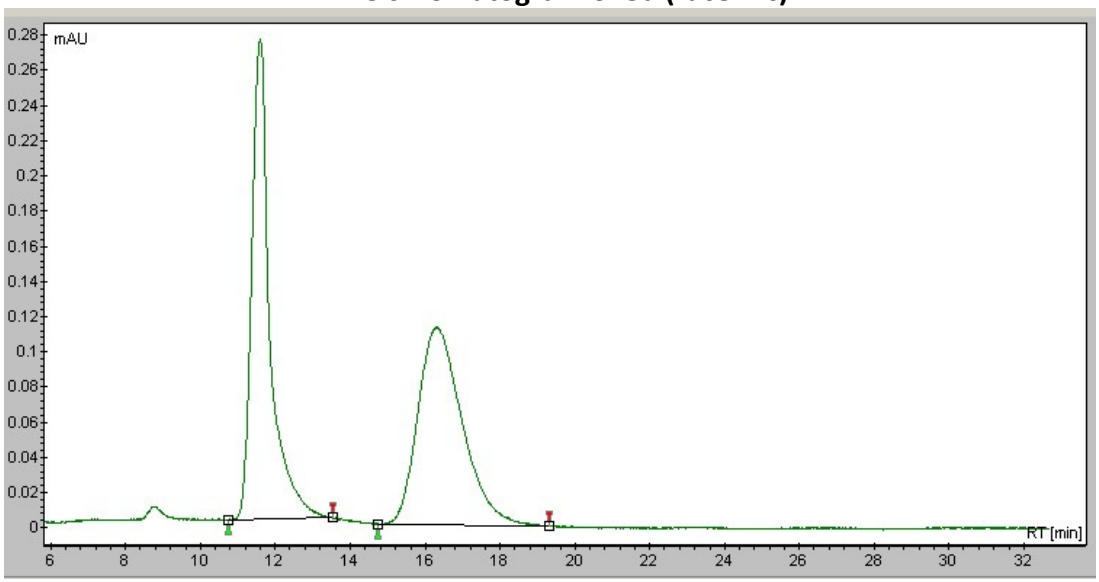
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	13.60	15.65	21.95	99.84
2	24.97	27.88	32.38	0.16

^{1}H NMR, ^{13}C NMR spectra of 5a



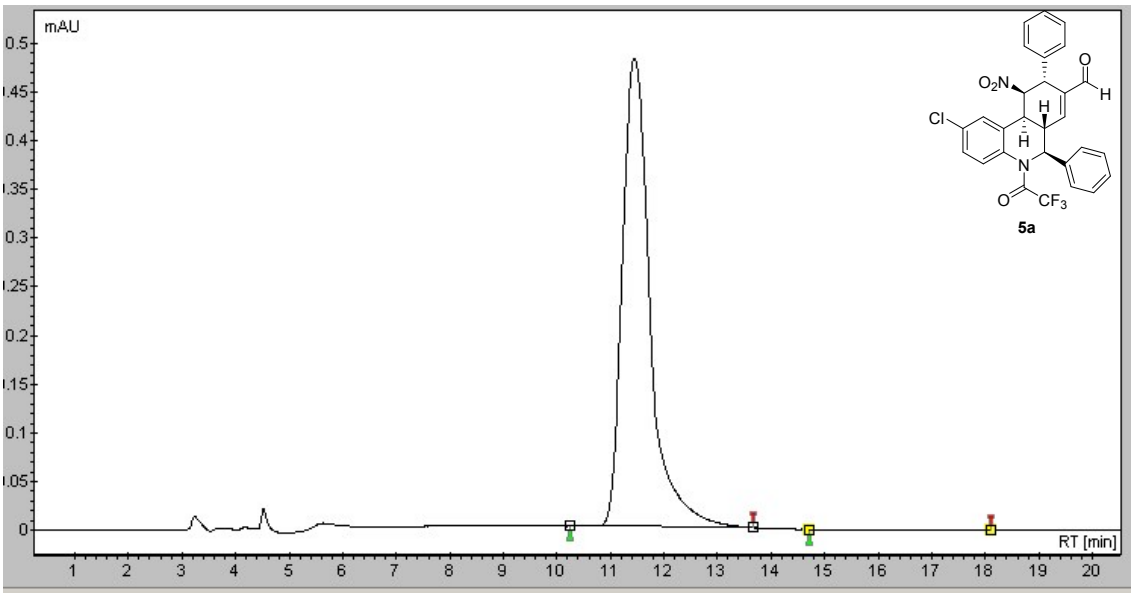


HPLC chromatogram of 5a (racemic)



	Start [Min]	Time [Min]	End [Min]	Area [%]
1	10.75	11.60	13.52	50.00
2	14.75	16.31	19.31	49.445

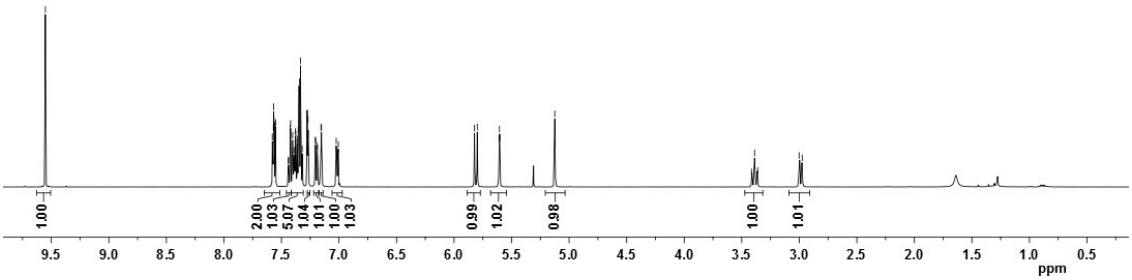
HPLC chromatogram of 5a (chiral)

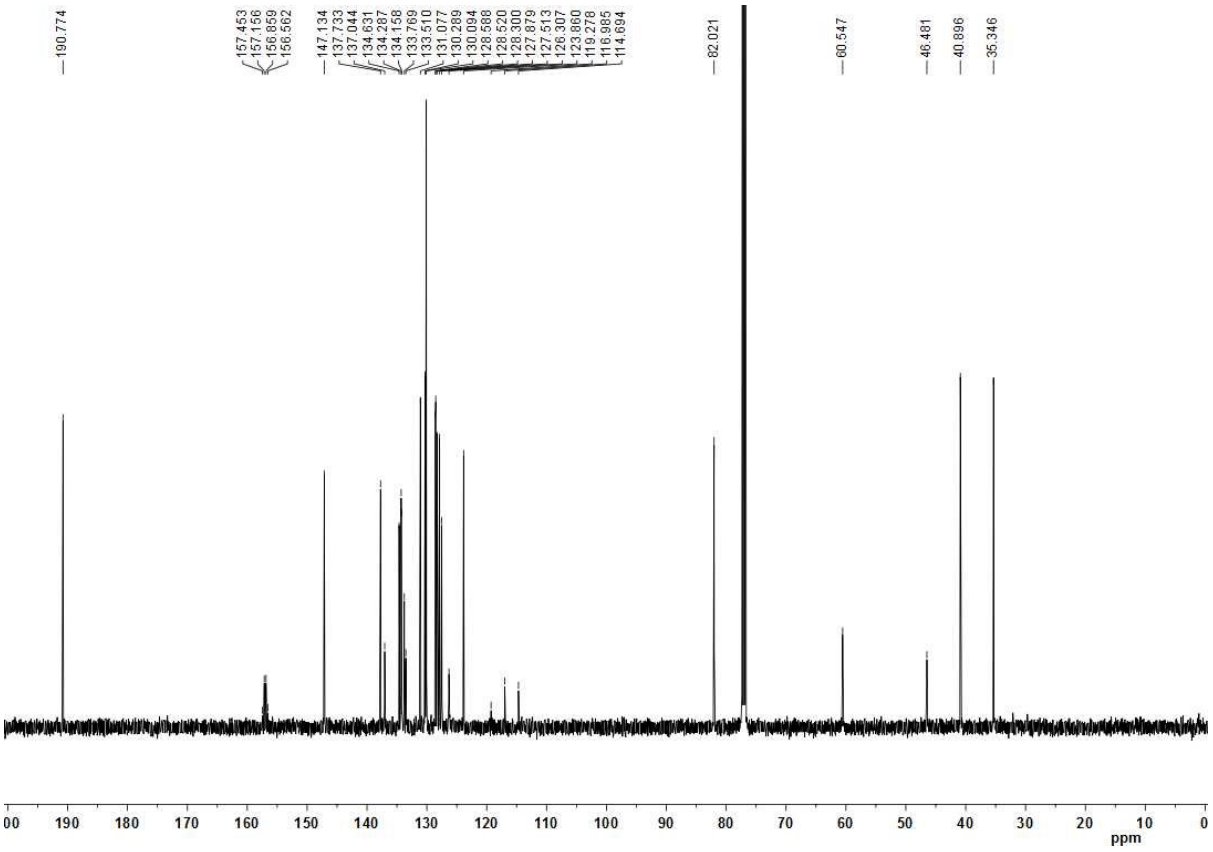


	Start [Min]	Time [Min]	End [Min]	Area [%]
1	10.25	11.45	13.66	99.93
2	14.70	17.08	18.11	0.07

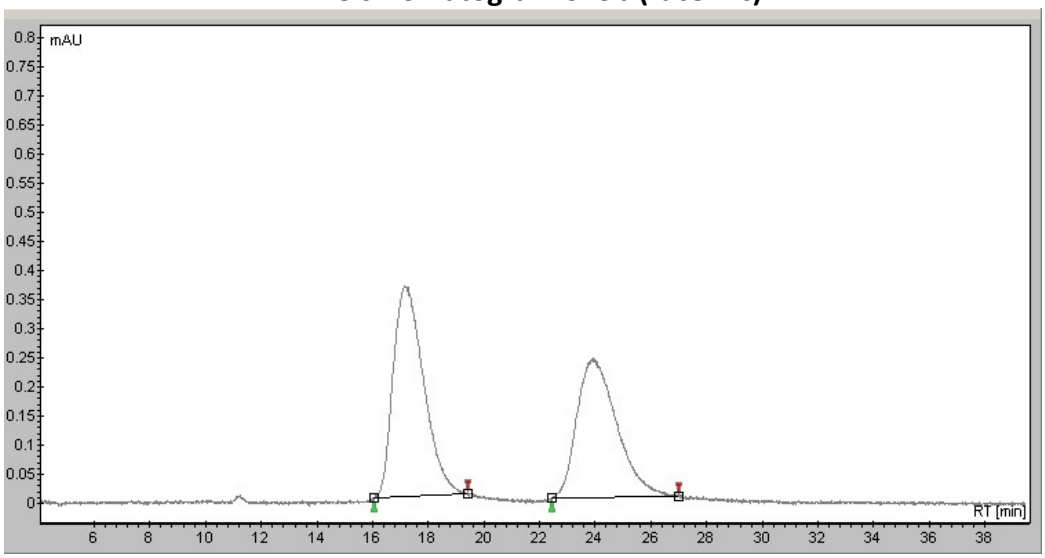
^{1}H NMR, ^{13}C NMR spectra of 5b

5b



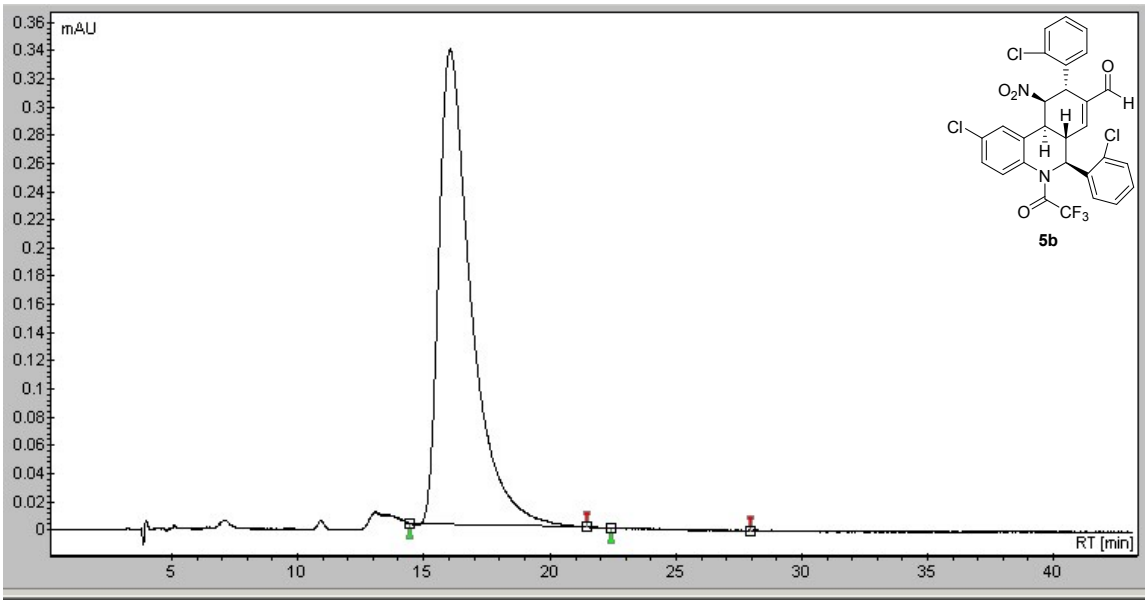


HPLC chromatogram of 5b (racemic)



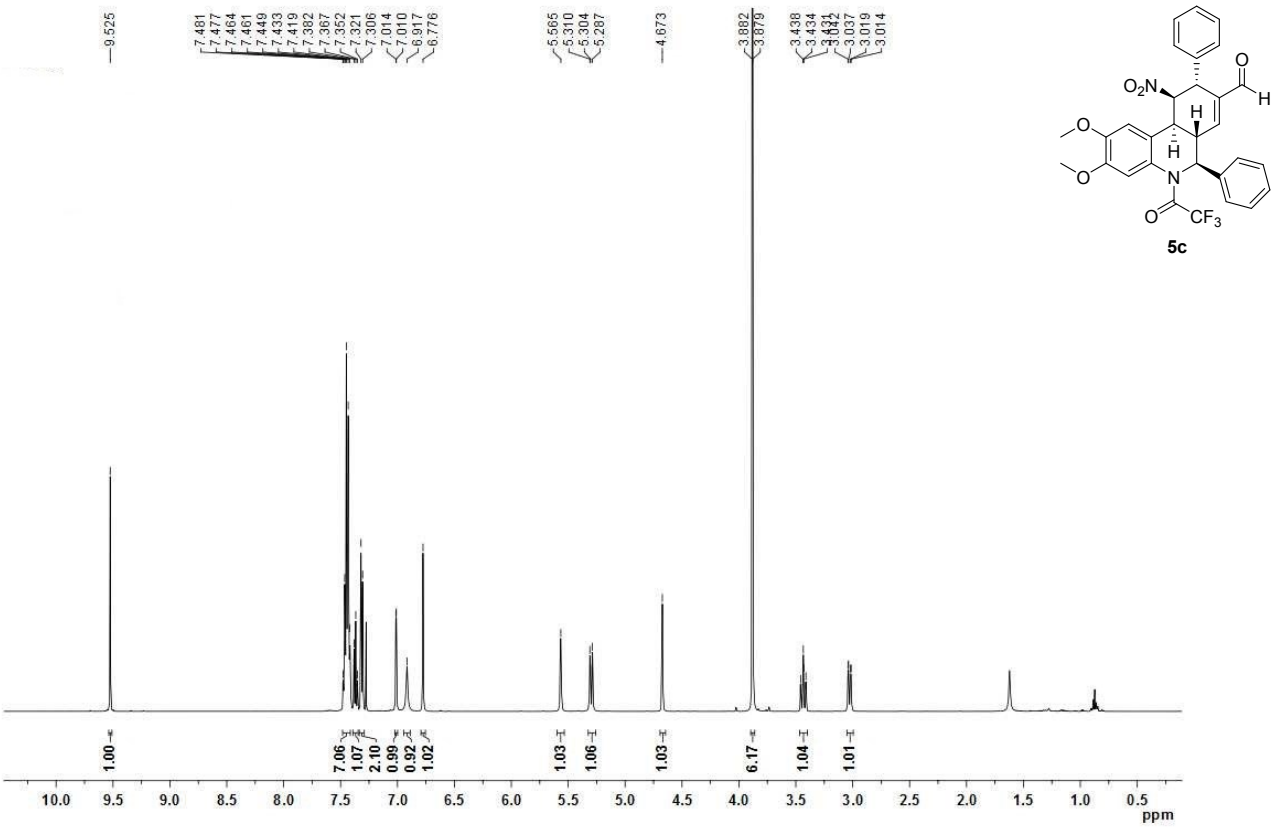
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	16.05	17.19	19.41	51.88
2	22.43	23.93	26.99	48.12

HPLC chromatogram of 5b (chiral)

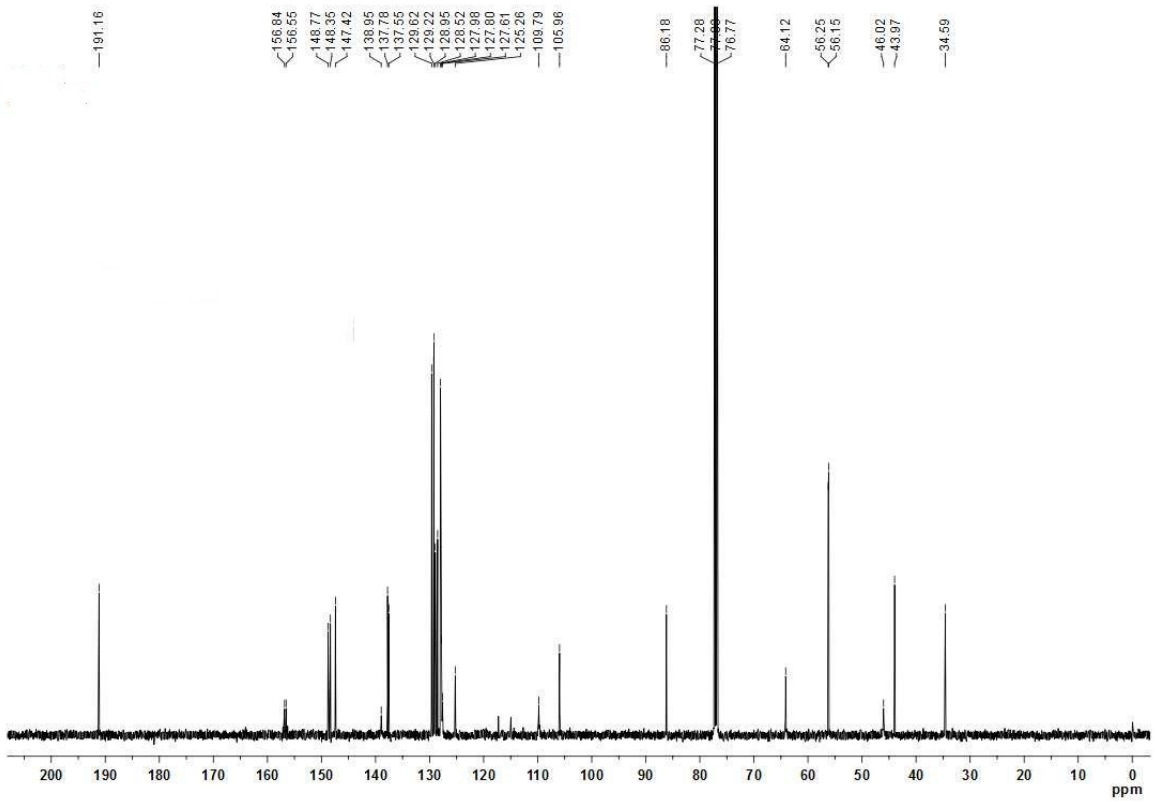


	Start [Min]	Time [Min]	End [Min]	Area [%]
1	14.44	16.04	21.47	99.62
2	22.44	25.45	27.97	0.38

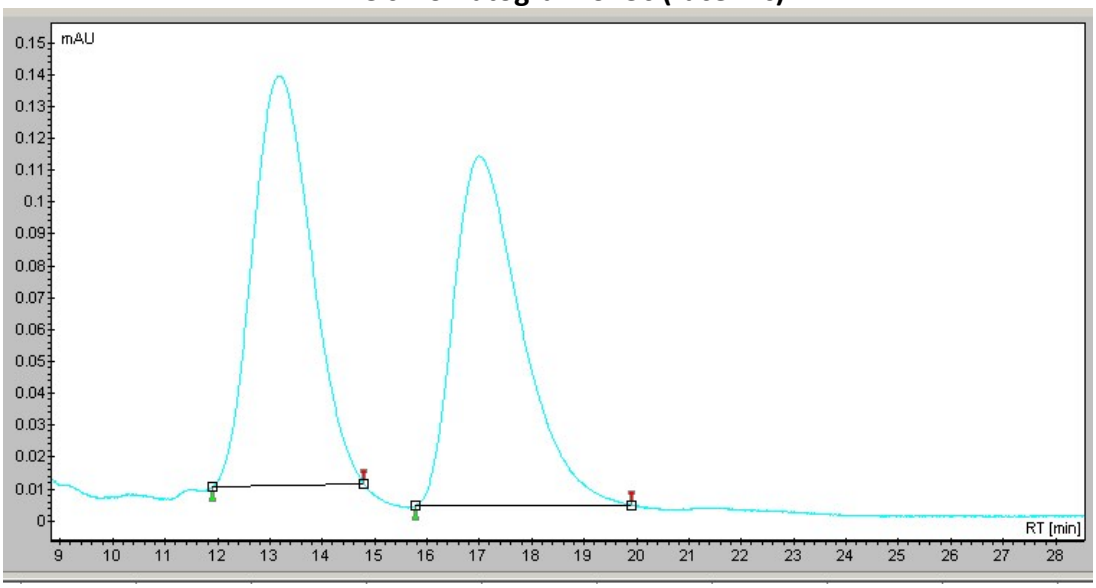
^{1}H NMR, ^{13}C NMR spectra of 5c



5c

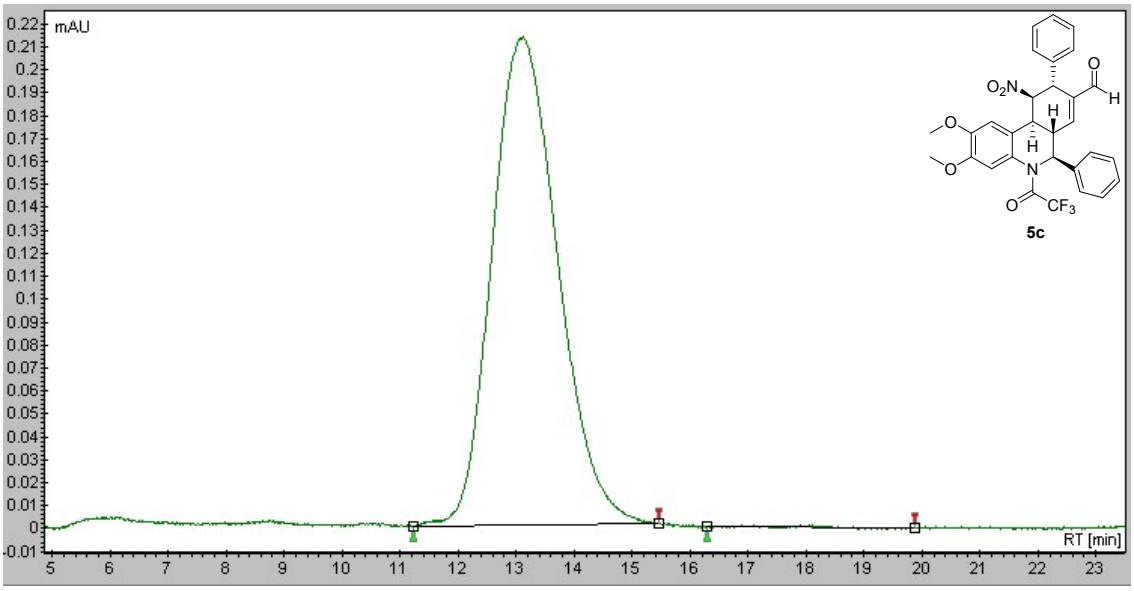


HPLC chromatogram of 5c (racemic)



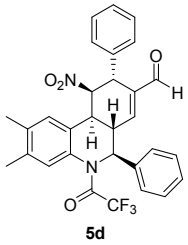
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	11.90	13.19	14.79	50.47
2	15.78	17.00	19.90	49.53

HPLC chromatogram of 5c (chiral)

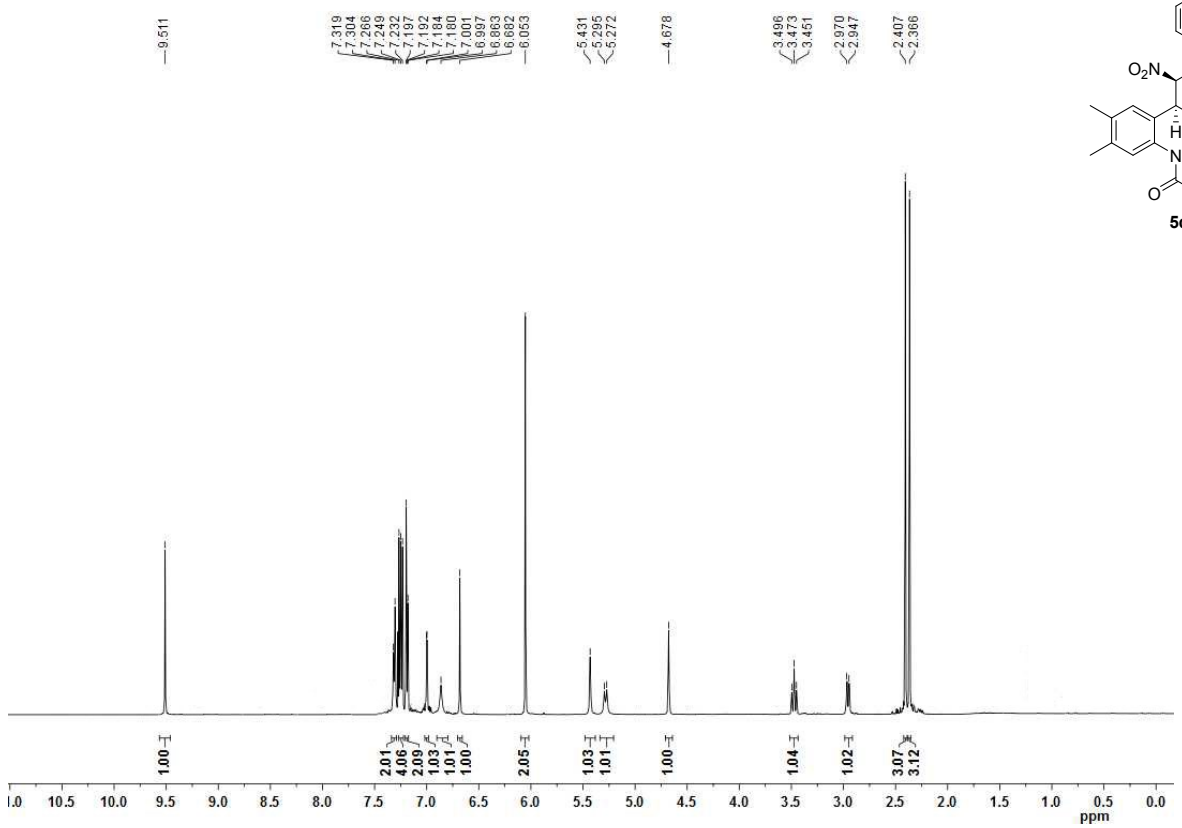


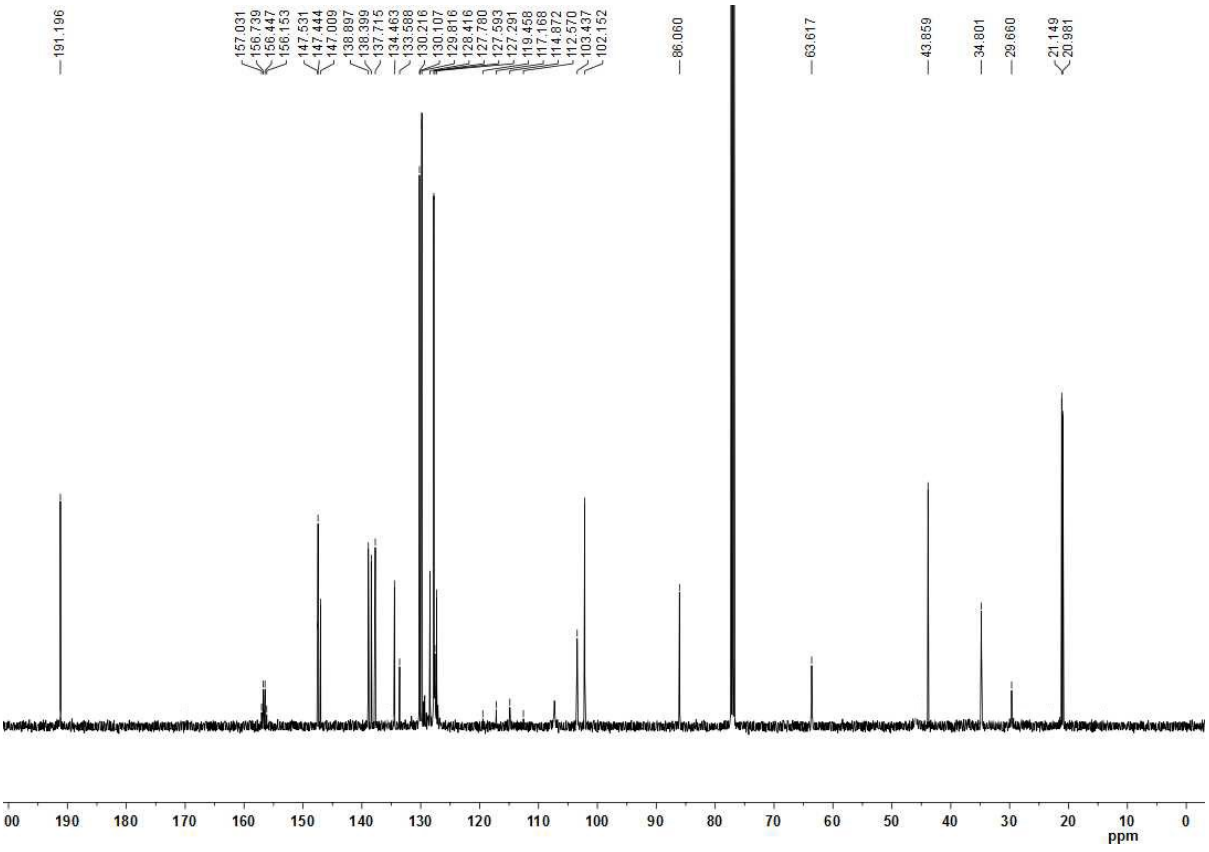
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	11.23	13.11	15.47	99.80
2	16.30	18.01	19.88	0.23

^{1}H NMR, ^{13}C NMR spectra of 5d

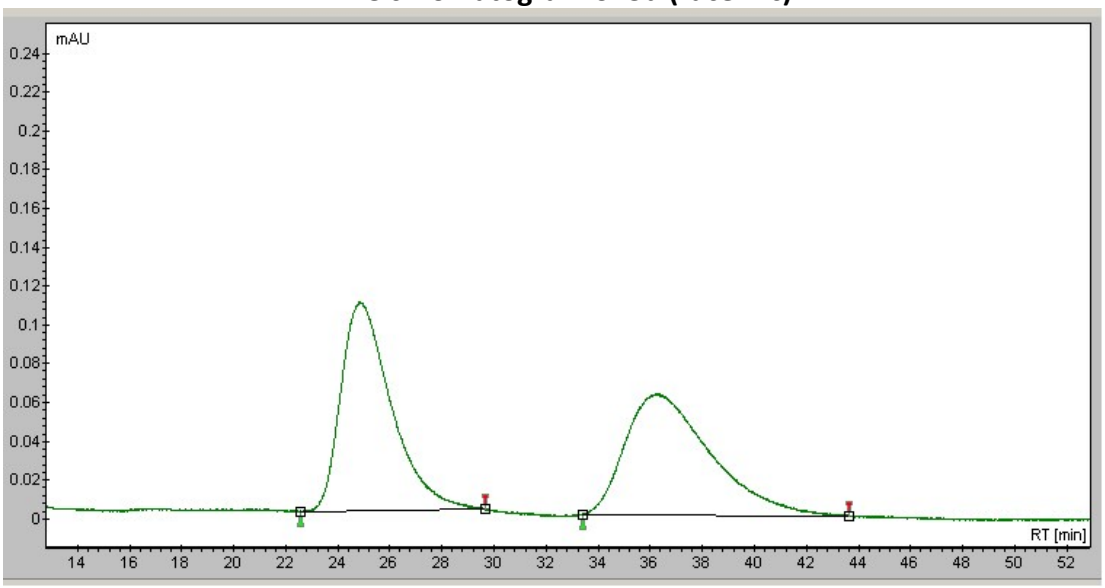


5d



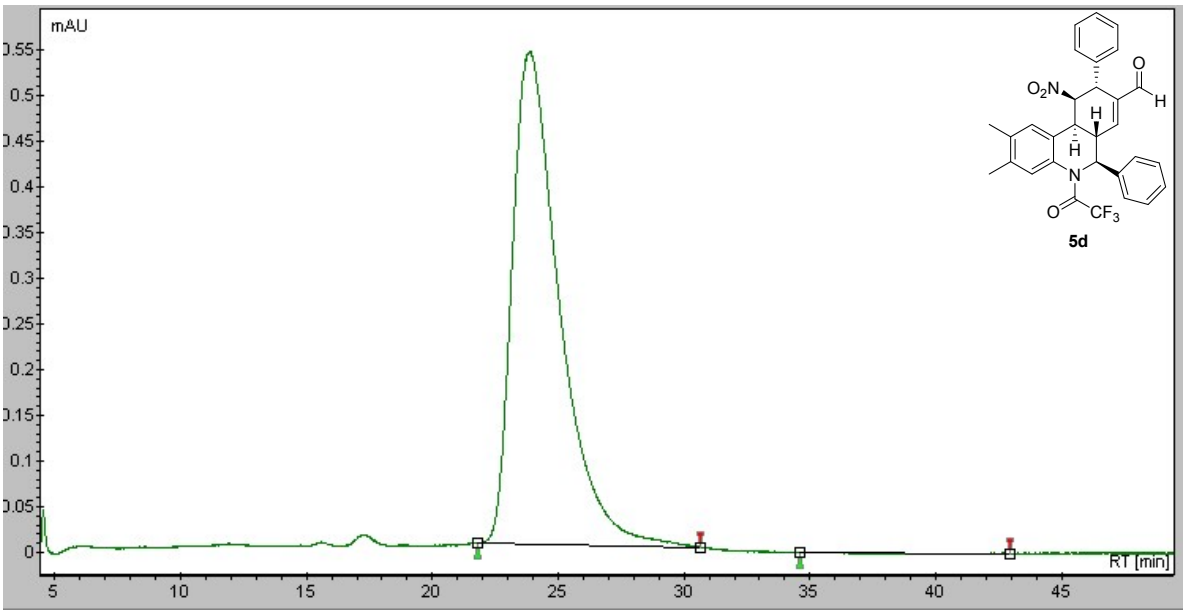


HPLC chromatogram of 5d (racemic)



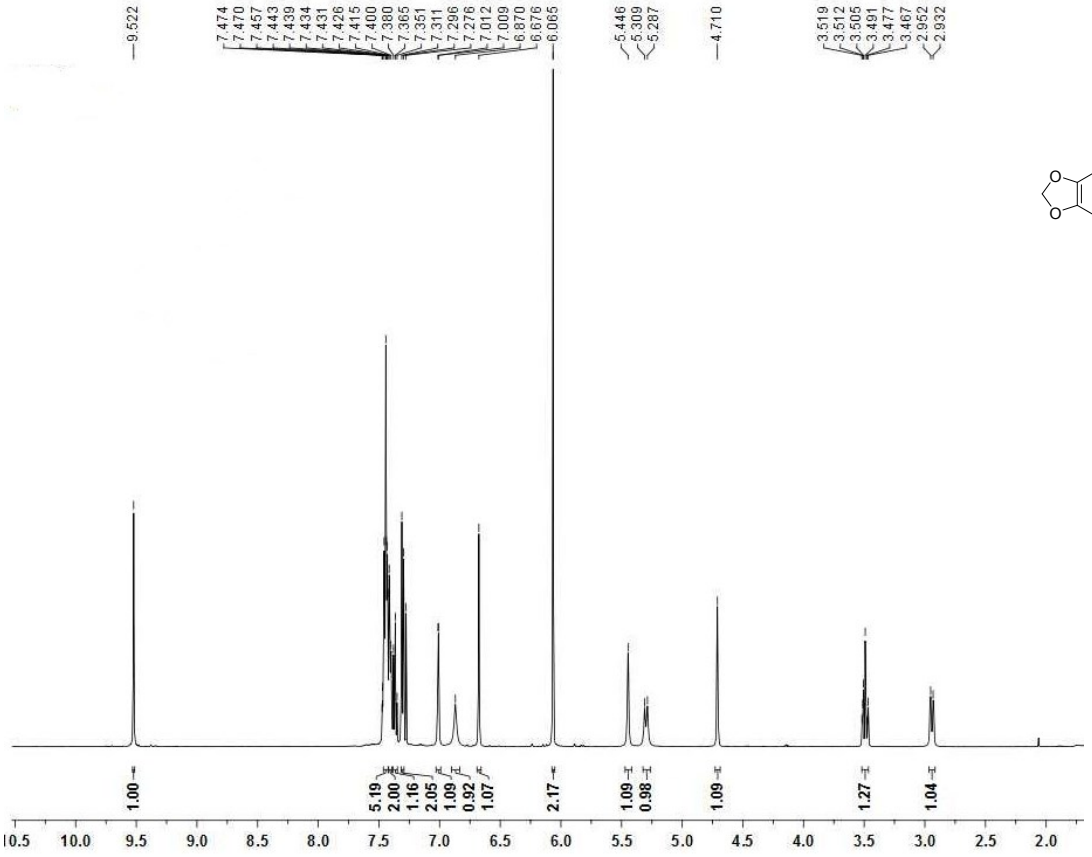
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	22.58	24.87	29.69	50.58
2	33.39	36.24	43.61	49.42

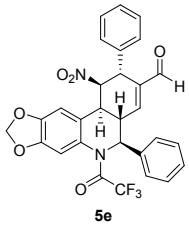
HPLC chromatogram of 5d (chiral)



	Start [Min]	Time [Min]	End [Min]	Area [%]
1	21.80	23.85	30.65	99.67
2	34.61	38.97	42.96	0.33

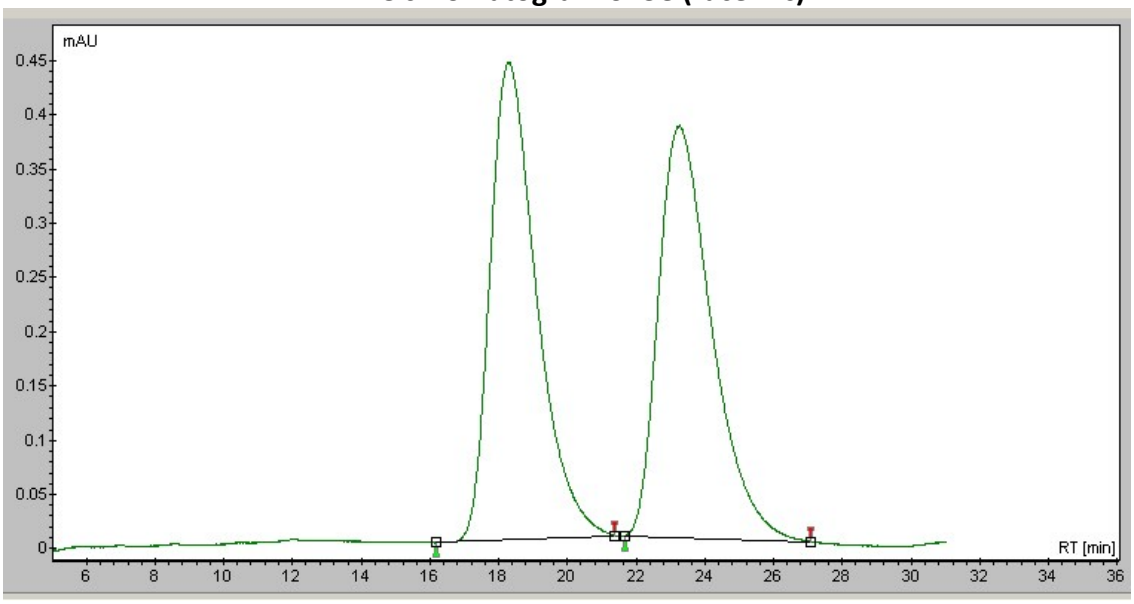
^{1}H NMR, ^{13}C NMR spectra of 5e





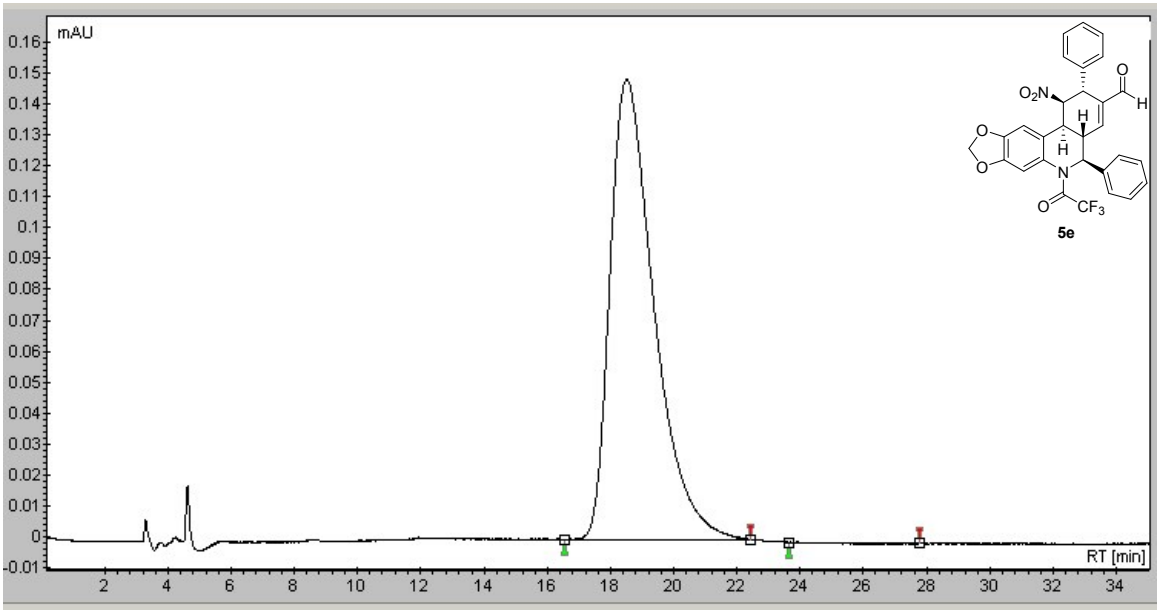
5e

HPLC chromatogram of 5e (racemic)



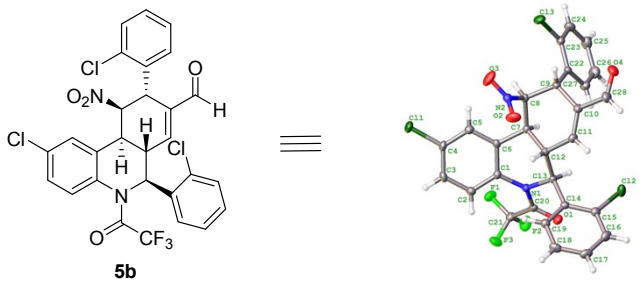
	Start [Min]	Time [Min]	End [Min]	Area [%]
1	16.18	18.28	21.37	50.22
2	21.67	23.92	27.08	49.78

HPLC chromatogram of 5e (chiral)



	Start [Min]	Time [Min]	End [Min]	Area [%]
1	16.53	18.51	22.42	99.74
2	23.62	25.10	27.76	0.26

4. X-ray crystal structure of compound 5b.



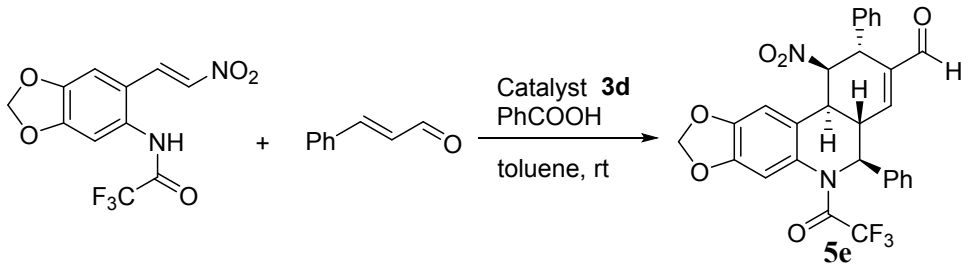
5b

Table 1. Crystal data and structure refinement parameters of compound (**5b**)

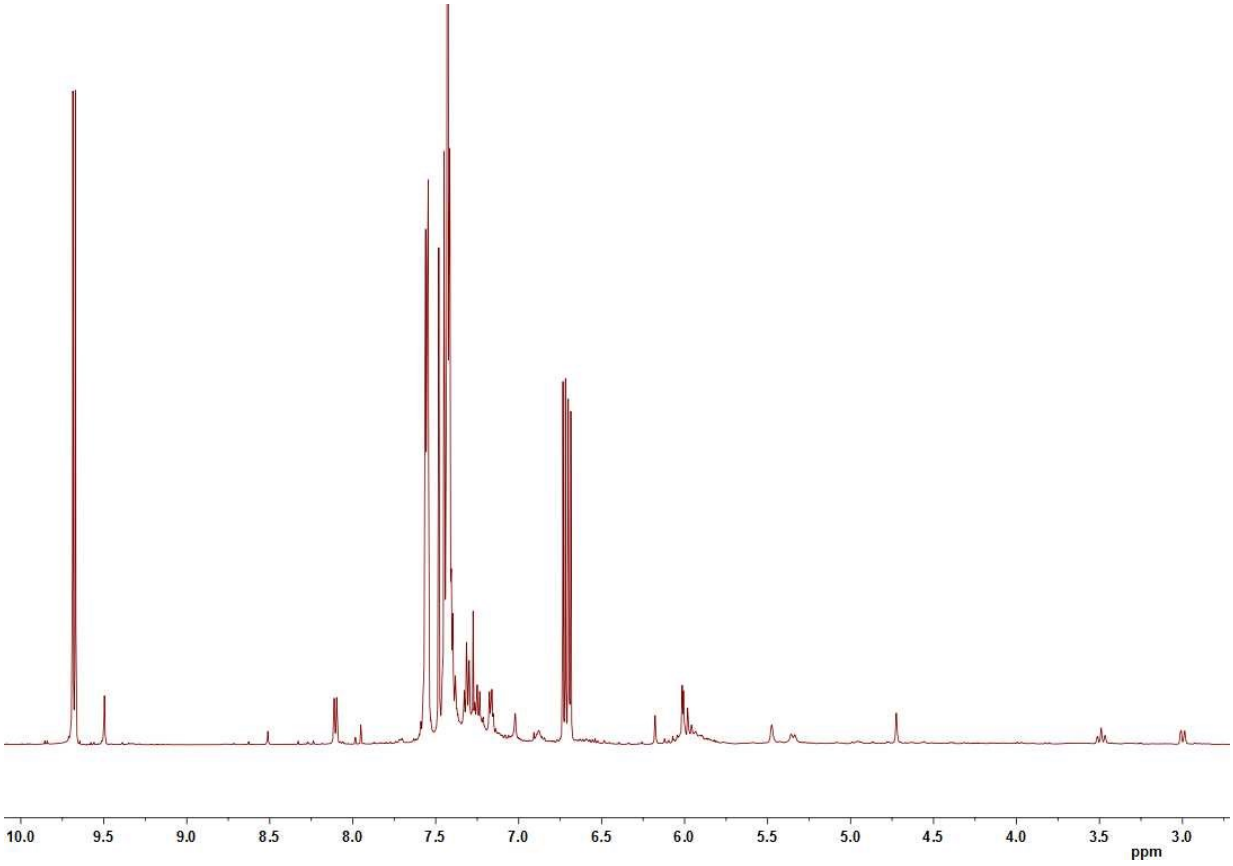
Parameter	Value
CCDC deposition number	1957856
Empirical formula	$C_{28}H_{18}Cl_3F_3N_2O_4$
Formula weight	609.79
Temperature	273.15 K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P 21 21 21
Cell dimensions	a = 8.3488(9) Å α= 90°
	b = 10.4603(11) Å β= 90°
	c = 29.766(3) Å γ= 90°
Volume	2599.5(5) $Å^3$
Z	4
Density (calculated)	1.558 Mg /m^3
Absorption coefficient	0.414 mm^{-1}
F_{000}	1240
Crystal size	0.2 × 0.08 × 0.08 mm^3
Theta range for data collection	2.064 to 28.910°
Index ranges	-11 ≤ *h* ≤ 10
	-14 ≤ *k* ≤ 13
	-40 ≤ *l* ≤ 40
Reflections collected	23723
Independent reflections	6831 [$R_{(int)}$ = 0.0536]
Absorption correction	Semi-empirical from equivalents

Refinement method	Full-matrix least-squares on F2
Data /restraints /parameters	6831 / 0 / 361
Goodness of fit on F^2	0.971
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0367, ωR_2 = 0.0669
R indices (all data)	R_1 =0.0551, ωR_2 =0.0727
Absolute structure parameter	0.09(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.247 and -0.243 e.Å $^{-3}$

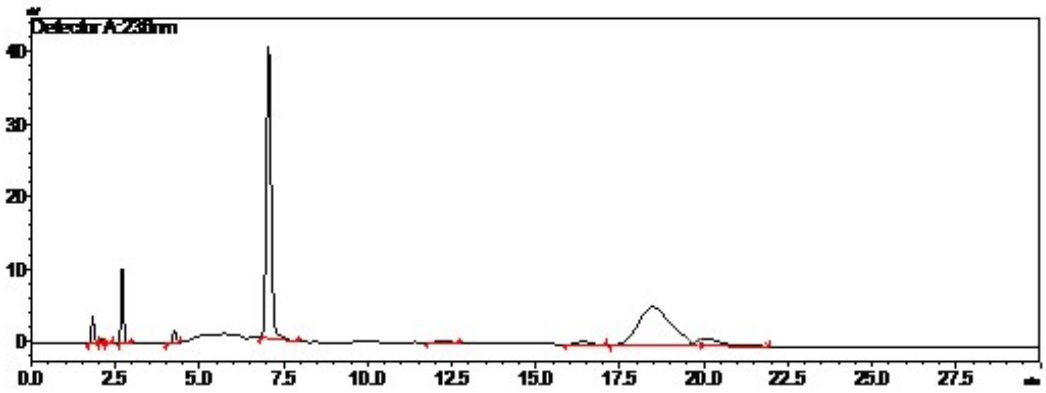
5. ^{1}H, ^{13}C NMR, and HPLC chromatograms of the crude reaction mixture



^{1}H NMR, ^{13}C NMR spectra of the crude reaction mixture



HPLC chromatogram of 5e in crude reaction mixture (chiral)



	Start [Min]	Time [Min]	End [Min]	Area [%]
1	1.63	1.75	1.92	2.14
2	2.69	2.83	2.95	4.67
3	4.11	4.29	4.47	0.39
4	6.86	7.42	7.97	44.5
5	11.62	12.25	12.87	0.61
	15.87	16.25	16.64	1.24
6	17.49	18.50	19.95	43.5
7	20.13	20.65	21.60	2.24