Organocatalytic Enantio- and Diastereoselective Synthesis of Highly Substituted δ-Lactones *via* Michael-Cyclization Cascade

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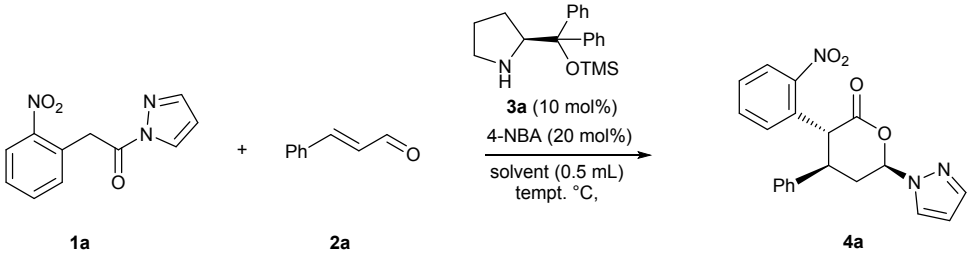
Supporting information

Table of contents:

General Methods

All reactions were carried out in oven dried glassware with magnetic stirring. All solvents were purified and dried according to standard methods prior to use. Catalysts **3a-c,** 3,5-dimethylpyrazole and α,β-unsaturated aldehydes are commercially available and used without further purification. Starting materials pyrazoleamides (**1a-f**) were prepared by earlier reported methods.[1] ^{1}H spectra were recorded on 400 MHz or 500 or 700 MHz in $CDCl_3$ and ^{13}C NMR spectra were recorded on 100 or 125 or 175 MHz in $CDCl_3$ using TMS or residual protio solvent signals as internal standard. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by the ESI (Q-TOF) ionization sources. IR spectra were measured with Bruker FT/IR Vector 22 spectrometer. Optical rotations were measured on a commercial automatic polarimeter and reported as follows: $[\alpha]\ ^{T}_{D}$ (c = g/100 mL, solvent). Routine monitoring of reactions were performed using precoated silica gel TLC plates from E-Merck. All the chromatographic separations were carried out by using silica gel (Acme's, 100-200 mesh). Melting points were recorded by using a melting point apparatus and are uncorrected. The enantioselectivity was determined by chiral HPLC analysis using chiralpak IA, IB, IC and OJH columns with a 200 UV-detector by using *iso*-propanol and *n*-hexane as eluents at 25 °C

Table S1. Optimization of reaction conditions for Michael-cyclization cascade[a].



1a 2a 4a

Entry	Solvent	Tempt. (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1	Toluene	35	12	89	85
2	Water	35	12	15	88
3	Tolune:water	35	12	87	82
4	Acetonitrile	35	12	74	72
5	1,4-dioxane	35	12	79	85
6	Chloroform	35	12	79	80
7	Mesitylene	35	12	88	88
8	Toluene	25	24	85	94
9	Toluene	0	24	40	96
10	Mesitylene	25	24	88	96

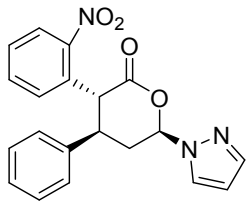
[a]All reactions were carried out using 0.2 mmol of **1a** and o.3 mmol of **2a**. [b] Isolated yield after column chromatography as single diastereomer (dr was determined by ^{1}H NMR). [c] Determined by HPLC using Diacel chiralpak IC column.

General Procedure for the Synthesis of highly substituted lactones:

The pyrazoleamide **1** (0.2 mmol) was added to a mixture of α,β–unsaturated aldehyde **3** (0.3 mmol) and the catalyst **3a** (6.5 mg, 0.02 mmol) and 4-NBA (0.04 mmol) in mesitylene (0.5 mL) at room temperature. The reaction mixture was stirred at 25 °C and the progress of the reaction was monitored by TLC (40% ethyl acetate in hexane). After complete conversion of the pyrazoleamide, the reaction mixture was diluted with CH_2Cl_2 and washed with saturated aq $NaHCO_3$ (2 times). Organic layer was dried over anhydrous $NaSO_4$, filtered and concentrated

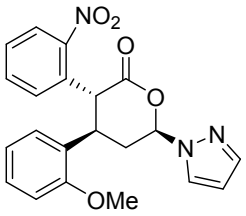
under reduced pressure. The product was purified by column chromatography over silica gel. (40% ethyl acetate in hexane). Enantiomeric excess of the lactones was determined by chiral HPLC analysis.

(*3R,4R,6R*)-3-(2-nitrophenyl)-4-phenyl-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (4a):



The compound **4a** was obtained as a white solid in 88% yield and 95.5% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 27.14 min, t_R(minor) = 34.32 min, $[\alpha]_D^{25}$ = -157.6 (*c* 0.25 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 2.4 Hz, 1H), 7.66 (d, *J* = 1.3 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.26 – 7.18 (m, 4H), 7.06 – 6.98 (m, 2H), 6.64 (dd, *J* = 11.1, 2.6 Hz, 2H), 6.40 – 6.34 (m, 1H), 3.92 (d, *J* = 61.3 Hz, 1H), 3.73 – 3.63 (m, 1H), 3.30 (td, *J* = 13.6, 11.3 Hz, 1H), 2.61 (dt, *J* = 14.1, 2.9 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.2, 146.5, 141.3, 139.9, 135.3, 133.8, 132.8, 130.3, 129.0, 128.9, 127.8, 127.3, 126.2, 107.0, 87.0, 56.1, 43.4, 34.4; IR (film): 2920, 2856, 1737, 1604, 1527, 1349, 1198, 1076 cm^{-1}; HRMS (ES+) calc. for $C_{20}H_{18}N_3O_4$ $[M+H]^+$: 364.1292 found: 364.1317

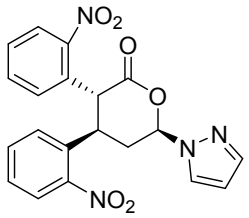
(*3R,4R,6R*)-4-(2-methoxyphenyl)-3-(2-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (4b):



The compound **4b** was obtained as a pale yellow solid in 84% yield and 85% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 19.91 min, t_R(minor) = 45.62 min, $[\alpha]_D^{25}$ = -131.20 (*c* 0.25 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.9 Hz, 1H), 7.73 (d, *J* = 2.3 Hz, 1H), 7.66 (d, *J* = 0.9 Hz, 1H), 7.39 – 7.26 (m, 2H), 7.17 – 7.11 (m, 1H), 6.89 (bs, 1H), 6.75 (d, *J* = 6.6 Hz, 1H), 6.63 (dd, *J* = 11.1, 2.5 Hz, 2H), 6.39 – 6.35 (m, 1H), 4.37 – 3.71 (m, 2H), 3.40 (bs, 4H), 2.47 (dt, *J* = 13.9, 2.6 Hz, 1H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 168.6, 156.4, 146.9, 141.2, 134.9, 133.6, 133.1, 130.2, 128.8, 125.7, 121.1, 110.4, 106.9, 87.4,

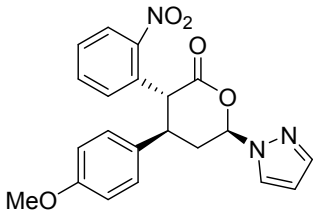
56.99, 54.85, 33.04; IR (film): 2930, 2851, 1738, 1599, 1525, 1387, 1344, 1246, 1081 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{20}N_3O_5$ $[M+H]^+$: 394.1397 found: 394.1424

(*3R,4R,6R*)-3,4-bis(2-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (4c):



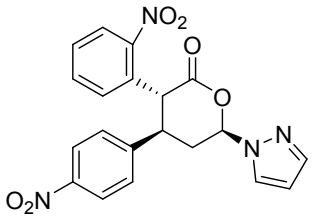
The compound **4c** was obtained as a pale yellow solid in 81% yield and 95% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 33.57 min, t_R(minor) = 51.07 min, $[\alpha]_D^{25}$ = -38.4 (*c* 0.25 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 2.3 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 1.3 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 6.67 (dd, *J* = 10.8, 2.4 Hz, 2H), 6.38 – 6.34 (m, 1H), 4.66 (t, *J* = 11.1 Hz, 1H), 4.05 (s, 1H), 3.43 – 3.27 (m, 1H), 2.71 – 2.55 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 149.9, 141.4, 134.3, 134.0, 133.4, 131.6, 130.7, 129.5, 128.7, 128.0, 126.6, 124.5, 107.1, 86.6, 53.4, 36.0, 34.1; IR (film): 2931, 2851, 1734, 1525, 1346, 1195, 1079 cm^{-1}; HRMS: calculated for $C_{20}H_{17}N_4O_6$ $[M+H]^+$: 409.1143 found: 409.1166

(*3R,4R,6R*)-4-(4-methoxyphenyl)-3-(2-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (4d):



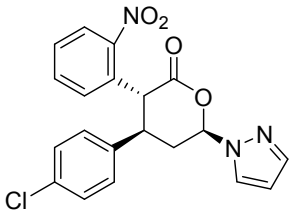
The compound **4d** was obtained as a pale yellow solid in 90% yield and 91% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 30.45 min, t_R(minor) = 36.57 min, $[\alpha]_D^{25}$ = -159.3 (*c* 0.15 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.7 Hz, 1H), 7.73 (bs, 1H), 7.65 (bs, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 2H), 6.76 – 6.66 (m, 3H), 6.63 (dd, *J* = 11.1, 2.4 Hz, 1H), 6.36 (d, *J* = 1.8 Hz, 1H), 3.85 (bs, 1H), 3.74 (s, 3H), 3.67 – 3.57 (m, 1H), 3.38 – 3.12 (m, 1H), 2.59 – 2.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 158.9, 141.1, 135.2, 133.8, 132.9, 132.0, 130.4, 128.9, 128.3, 126.2, 114.2, 107.0, 87.0, 56.2, 55.2, 42.6, 34.6, 31.5; IR (film): 2967, 2847, 1732, 1609, 1519, 1344, 1253, 1041, 953 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{20}N_3O_5$ $[M+H]^+$: 394.1397 found: 394.1419

(*3R,4R,6R*)-3-(2-nitrophenyl)-4-(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (**4e**):



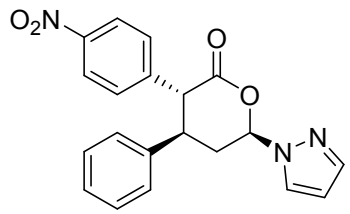
The compound **4e** was obtained as a white solid in 75% yield and 89% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 30.79 min, t_R(minor) = 53.37 min, $[\alpha]_D^{25}$ = -138.8 (*c* 0.17 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.2 Hz, 1H), 8.08 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 2.3 Hz, 1H), 7.63 (t, *J* = 3.0 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.66 (dd, *J* = 10.8, 2.4 Hz, 2H), 6.36 – 6.33 (m, 1H), 4.05 (bs, 1H), 3.94 – 3.82 (m, 1H), 3.43 – 3.31 (m, 1H), 2.60 (dt, *J* = 13.8, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 147.4, 147.3, 146.6, 141.4, 135.0, 134.2, 131.9, 130.5, 129.5, 128.5, 126.5, 124.1, 107.2, 86.7, 43.2, 33.9, 31.5; IR (film): 2883, 1731, 1609, 1519, 1349, 1193, 950 cm^{-1}; HRMS: calc. for $C_{20}H_{17}N_4O_6$ $[M+H]^+$: 409.1143 found: 409.1160

(*3R,4R,6R*)-4-(4-chlorophenyl)-3-(2-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (**4f**):



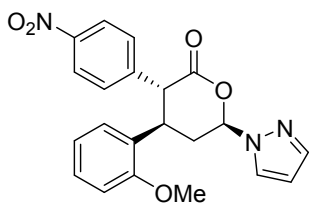
The compound **4f** was obtained as a pale yellow solid in 89% yield and 91% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 20.47 min, t_R(minor) = 35.28 min, $[\alpha]_D^{25}$ = -142.7 (*c* 0.11 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 2.1 Hz, 1H), 7.64 (s, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.20 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.72 – 6.53 (m, 2H), 6.36 (s, 1H), 3.94 (bs, 1H), 3.73 – 3.64 (m, 1H), 3.33 – 3.21 (m, 1H), 2.62 – 2.53 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 167.9, 146.4, 141.4, 138.5, 135.3, 134.1, 133.6, 132.4, 130.4, 129.2, 129.1, 129.1, 128.7, 126.4, 107.1, 86.8, 56.1, 42.8, 34.2; IR (film): 3085, 2857, 1732, 1522, 1344, 1193, 1088 cm^{-1}; HRMS (ES+) calc. for $C_{20}H_{17}ClN_3O_4$ $[M+H]^+$: 398.0902 found: 398.0932

(*3R,4R,6R*)-3-(4-nitrophenyl)-4-phenyl-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5a):



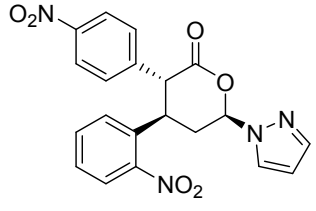
The compound **5a** was obtained as a pale yellow solid in 80% yield and 92% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 33.73 min, t_R(major) = 40.49 min, $[\alpha]_D^{25}$ = -196.6 (*c* 0.14 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.67 (bs, 2H), 7.27 – 7.11 (m, 5H), 7.07 – 7.01 (m, 2H), 6.53 (dd, *J* = 10.3, 4.1 Hz, 1H), 6.38 (bs, 1H), 4.16 (d, *J* = 12.0 Hz, 1H), 3.44 (td, *J* = 12.6, 2.8 Hz, 1H), 3.35 – 3.24 (m, 1H), 2.70 – 2.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 147.1, 144.2, 141.4, 139.0, 130.0, 129.9, 129.0, 127.9, 127.0, 123.7, 107.4, 87.1, 55.0, 44.7, 35.0; IR (film): 2924, 1732, 1517, 1349, 1182, 952 cm^{-1}; HRMS (ES+) calc. for $C_{20}H_{18}N_3O_3$ $[M+H]^+$: 364.1292 found: 364.1296

(*3R,4R,6R*)-4-(2-methoxyphenyl)-3-(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5b):



The compound **5b** was obtained as a pale yellow solid in 89% yield and 91% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 25.76 min, t_R(major) = 32.79 min, $[\alpha]_D^{25}$ = -70.0 (*c* 0.15 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.7 Hz, 2H), 7.69 – 7.63 (m, 2H), 7.21 (d, *J* = 8.7 Hz, 1H), 7.18 – 7.12 (m, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.50 (dd, *J* = 10.7, 4.0 Hz, 1H), 6.38 – 6.36 (m, 1H), 4.39 (d, *J* = 12.1 Hz, 1H), 3.97 – 3.87 (m, 1H), 3.68 (s, 3H), 3.31 (dd, *J* = 24.5, 13.3 Hz, 1H), 2.57 (dt, *J* = 14.1, 3.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 156.6, 147.0, 144.6, 141.3, 130.5, 129.9, 129.6, 128.9, 127.9, 126.9, 123.4, 122.9, 121.1, 110.9, 107.2, 87.5, 55.2, 53.1, 33.9; IR (film): 2918, 1739, 1522, 1346, 1246, 952 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{20}N_3O_5$ $[M+H]^+$: 394.1397 found: 394.1409

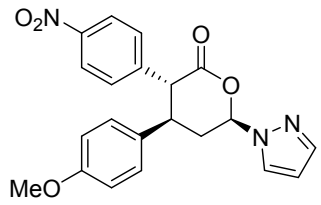
(*3R,4R,6R*)-4-(2-nitrophenyl)-3-(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5c):



The compound **5c** was obtained as a white solid in 85% yield and 92% ee. The optical purity was determined by chiral HPLC on

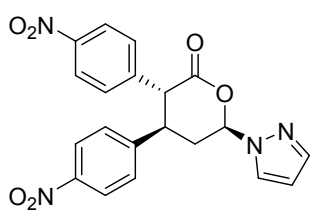
Chiralpak OJH column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 96.24 min, t_R(minor) = 145.23 min, $[\alpha]_D^{25}$ = +26.6 (*c* 0.15 in $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.7 Hz, 2H), 7.75 – 7.53 (m, 5H), 7.40 – 7.29 (m, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.54 (dd, *J* = 9.5, 4.9 Hz, 1H), 6.38 (t, *J* = 2.0 Hz, 1H), 4.42 – 4.26 (m, 2H), 3.38 – 3.20 (m, 1H), 2.92 – 2.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 149.8, 147.4, 142.8, 141.7, 133.6, 133.4, 130.6, 129.8, 128.7, 127.8, 124.8, 123.9, 107.4, 86.3, 53.6, 37.3, 34.6; IR (film): 2919, 1731, 1599, 1525, 1348, 1182, 949 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{17}N_4O_6$ $[M+H]^+$: 394.1397 found: 394.1403

(*3R,4R,6R*)-4-(4-methoxyphenyl)-3-(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5d):



The compound **5d** was obtained as a pale yellow solid in 74% yield and 92% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 69.74 min, t_R(major) = 81.69 min, $[\alpha]_D^{25}$ = -157.62 (*c* 0.42 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.7 Hz, 2H), 7.67 (d, *J* = 2.7 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 2H), 6.51 (dd, *J* = 10.4, 4.1 Hz, 1H), 6.39 – 6.36 (m, 1H), 4.09 (d, *J* = 12.0 Hz, 1H), 3.72 (s, 3H), 3.39 (td, *J* = 12.6, 2.8 Hz, 1H), 3.27 – 3.18 (m, 1H), 2.63 (dt, *J* = 14.1, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 159.0, 147.1, 144.4, 141.4, 131.0, 130.0, 129.8, 128.1, 123.7, 114.3, 107.3, 87.1, 55.3, 55.2, 44.0, 35.1, 31.5; IR (film): 2929, 2854, 1732, 1611, 1516, 1348, 1249, 1180, 1041, 952 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{20}N_3O_5$ $[M+H]^+$: 394.1397 found: 394.1403

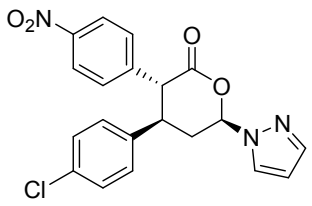
(*3R,4R,6R*)-3,4-bis(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5e):



The compound **5e** was obtained as a pale yellow solid in 65% yield and 91% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 67.32 min, t_R(major) = 91.97 min, $[\alpha]_D^{25}$ = -160.0 (*c* 0.10 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.03 (m, 4H), 7.69 (bs, 1H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.52 (dd, *J* =

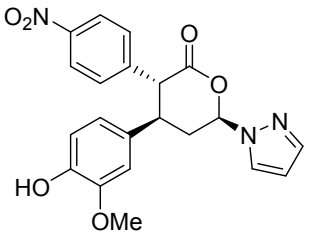
9.3, 4.8 Hz, 1H), 6.41 (bs, 1H), 4.26 (d, *J* = 12.3 Hz, 1H), 3.63 (td, *J* = 12.5, 3.6 Hz, 1H), 3.44 – 3.31 (m, 1H), 2.76 (dt, *J* = 14.2, 4.2 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.5, 147.5, 147.4, 146.4, 143.1, 141.7, 130.3, 129.9, 129.6, 128.2, 124.3, 124.0, 123.9, 107.6, 86.4, 54.3, 44.3, 34.3; IR (film): 2839, 1730, 1516, 1347, 1158, 1040 cm^{-1}; HRMS (ES+) calc. for $C_{20}H_{17}N_4O_6$ $[M+H]^+$: 409.1143 found: 409.1133

(*3R,4R,6R*)-4-(4-chlorophenyl)-3-(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5f):



The compound **5f** was obtained as a pale yellow solid in 90% yield and 90% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 44.47 min, t_R(major) = 58.11 min, $[\alpha]_D^{25}$ = -165.2 (*c* 0.17 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 2H), 7.69 – 7.65 (m, 2H), 7.22 – 7.13 (m, 4H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.49 (dd, *J* = 10.1, 4.4 Hz, 1H), 6.39 – 6.37 (m, 1H), 4.12 (d, *J* = 12.1 Hz, 1H), 3.44 (td, *J* = 12.6, 3.1 Hz, 1H), 3.33 – 3.20 (m, 1H), 2.66 (dt, *J* = 14.1, 3.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 147.2, 143.8, 141.5, 137.6, 133.8, 130.0, 129.9, 129.3, 128.4, 123.8, 107.4, 86.8, 54.9, 44.1, 34.7; IR (film): 3085, 2852, 1739, 1520, 1344, 1178, 1090, 950 cm^{-1}; HRMS (ES+) calc. for $C_{20}H_{17}ClN_3O_4$ $[M+H]^+$: 398.0902 found: 398.0918

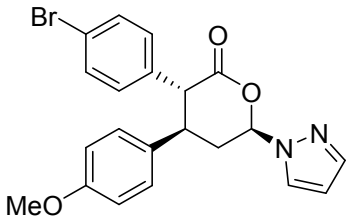
(*3R,4R,6R*)-4-(4-hydroxy-3-methoxyphenyl)-3-(4-nitrophenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (5g):



The compound **5g** was obtained as a pale yellow solid in 59% yield and 72% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 44.89 min, t_R(major) = 65.52 min, $[\alpha]_D^{25}$ = -95.5 (*c* 0.18 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.6 Hz, 2H), 7.67 (d, *J* = 1.9 Hz, 2H), 7.16 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.54 – 6.45 (m, 3H), 6.38 (t, *J* = 2.0 Hz, 1H), 5.56 (s, 1H), 4.08 (d, *J* = 11.8 Hz, 1H), 3.75 (s, 3H), 3.39 – 3.21 (m, 2H), 2.69 – 2.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 147.1, 146.8, 145.1, 144.4, 141.5, 130.9, 130.0, 123.7, 120.0, 114.8, 109.2, 107.4, 87.0, 55.9, 55.4, 44.5,

35.0; IR (film): 3015, 2901, 1739, 1519, 1347, 1247, 1158, 1014, 950 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{20}N_3O_6$ $[M+H]^+$: 410.1347 found: 410.1360

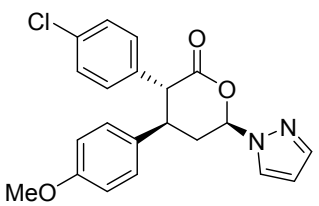
(*3R,4R,6R*)-3-(4-bromophenyl)-4-(4-methoxyphenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (6a):



The compound **6a** was obtained as a pale yellow solid in 75% yield and 96.7% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 20.71 min, t_R(minor) = 23.13 min, $[\alpha]_D^{25}$ = -204.4 (*c* 0.25 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.46 (dd, *J* = 10.6, 3.8 Hz, 1H), 6.39 – 6.33 (m, 1H), 3.87 (d, *J* = 11.8 Hz, 1H), 3.74 (s, 1H), 3.33 (td, *J* = 12.8, 2.8 Hz, 1H), 3.20 – 3.10 (m, 1H), 2.60 (dt, *J* = 14.0, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 158.8, 141.2, 136.1, 131.7, 130.5, 129.5, 128.1, 121.4, 114.2, 107.2, 87.2, 55.2, 55.1, 44.0, 35.3; IR (film): 3028, 2924, 2843, 1731, 1612, 1515, 1388, 1041 cm^{-1}; HRMS (ES+) calc. for $C_{21}H_{20}BrN_2O_3$ $[M+H]^+$: 427.0652, found: 429.0621

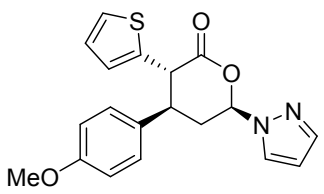
(*3R,4R,6R*)-3-(4-chlorophenyl)-4-(4-methoxyphenyl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (7a):

The compound **7a** was obtained as a pale yellow solid in 85% yield and 97% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 70:30];



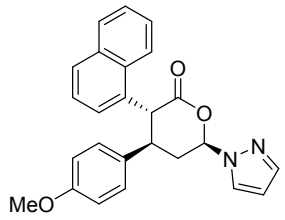
flow rate 1 mL/min; λ = 254 nm; t_R(major) = 20.36 min, t_R(minor) = 22.90 min, $[\alpha]_D^{25}$ = -182.4 (*c* 0.25 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 6.1, 1.7 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.96 – 6.89 (m, 4H), 6.74 (d, *J* = 8.6 Hz, 2H), 6.46 (dd, *J* = 10.6, 3.8 Hz, 1H), 6.37 – 6.35 (m, 1H), 3.88 (d, *J* = 11.8 Hz, 1H), 3.73 (s, 3H), 3.33 (td, *J* = 12.6, 2.9 Hz, 1H), 3.21 – 3.10 (m, 1H), 2.59 (dt, *J* = 14.0, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 158.8, 141.2, 135.7, 133.3, 131.7, 130.2, 129.6, 128.7, 128.1, 114.2, 107.2, 87.2, 55.2, 55.1, 44.1, 35.3; IR (film): 2909, 1745, 1513, 1265, 1088, 947 cm^{-1}; HRMS: calculated for $C_{21}H_{20}ClN_2O_3$ $[M+H]^+$ expected: 383.1157 found: 383.1163

(*3S,4R,6R*)-4-(4-methoxyphenyl)-6-(1H-pyrazol-1-yl)-3-(thiophen-2-yl)tetrahydro-2H-pyran-2-one (8a):



The compound **8a** was obtained as a yellow solid in 74% yield and 94% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 27.77 min, t_R(minor) = 33.29 min, $[\alpha]_D^{25}$ = -128.6 (*c* 0.15 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, 2H), 7.15 (d, *J* = 5.1 Hz, 1H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.85 – 6.71 (m, 4H), 6.45 (dd, *J* = 10.7, 3.6 Hz, 1H), 6.37 (d, *J* = 1.7 Hz, 1H), 4.26 (d, *J* = 11.5 Hz, 1H), 3.74 (s, 3H), 3.44 (td, *J* = 12.7, 3.2 Hz, 1H), 3.17 – 3.07 (m, 1H), 2.61 (dt, *J* = 14.2, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 158.8, 141.1, 138.5, 132.3, 129.6, 128.0, 127.5, 126.7, 125.0, 114.2, 107.2, 87.0, 55.2, 50.0, 44.5, 35.8; IR (film): 2909, 2844, 1738, 1613, 1515, 1388, 1251, 1041, 949 cm^{-1}; HRMS (ES+) calc. for $C_{19}H_{18}N_2O_3S$ $[M+H]^+$: 355.1111 found: 355.1103

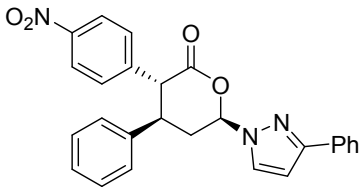
(*3R,4R,6R*)-4-(4-methoxyphenyl)-3-(naphthalen-1-yl)-6-(1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (9a):



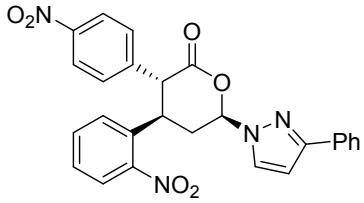
The compound **9a** was obtained as a white solid in 61% yield and 93% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 28.33 min, t_R(minor) = 44.05 min, $[\alpha]_D^{25}$ = -208.0 (*c* 0.15 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 1H), 7.75 (d, *J* = 2.1 Hz, 1H), 7.73 – 7.66 (m, 3H), 7.46 (td, *J* = 13.5, 6.6 Hz, 2H), 7.28 – 7.19 (m, 2H), 7.03 (d, *J* = 6.5 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.69 (dd, *J* = 10.9, 3.1 Hz, 1H), 6.62 (d, *J* = 8.6 Hz, 2H), 6.40 (bs, 1H), 4.40 (d, *J* = 11.2 Hz, 1H), 3.77 – 3.70 (m, 1H), 3.67 (s, 3H), 3.30 – 3.19 (m, 1H), 2.67 (dt, *J* = 14.0, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 158.6, 141.1, 134.2, 133.2, 132.3, 129.4, 129.3, 128.5, 127.9, 126.4, 125.5, 125.1, 123.2, 113.9, 107.3, 87.4, 55.1, 42.8, 35.5; IR (film): 2941, 1738, 1514, 1387, 1250, 1182, 1040, 950 cm^{-1}; HRMS (ES+) calc. for $C_{25}H_{23}N_2O_3$ $[M+H]^+$: 399.1703 found: 399.1726

(*3R,4R,6R*)-3-(4-nitrophenyl)-4-phenyl-6-(3-phenyl-1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (11a):

The compound **11a** was obtained as a white solid in 89% yield and 93.5% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 16.20 min, t_R(major) = 49.60 min, $[\alpha]_D^{25}$ = -113.20 (*c* 0.14 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 2H), 7.87 – 7.81 (m, 2H), 7.71 (d, *J* = 2.5 Hz, 1H), 7.46 – 7.32 (m, 3H), 7.28 – 7.19 (m, 3H), 7.16 (d, *J* = 8.7 Hz, 2H), 7.10 – 7.04 (m, 2H), 6.68 (d, *J* = 2.5 Hz, 1H), 6.51 (dd, *J* = 9.9, 4.2 Hz, 1H), 4.20 (d, *J* = 11.7 Hz, 1H), 3.49 – 3.42 (m, 1H), 3.36 (td, *J* = 13.2, 9.9 Hz, 1H), 2.77 – 2.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 153.4, 147.1, 144.2, 139.1, 132.7, 131.1, 129.9, 129.1, 128.7, 128.4, 127.9, 127.1, 126.0, 123.7, 104.8, 87.4, 55.0, 44.8, 34.9. IR (film): 3027, 2936, 2856, 1738, 1604, 1519, 1348, 1265, 1073 cm^{-1}; HRMS (ES+) calc. for $C_{26}H_{22}N_3O_4$ $[M+H]^+$: 440.1605 found: 440.1605



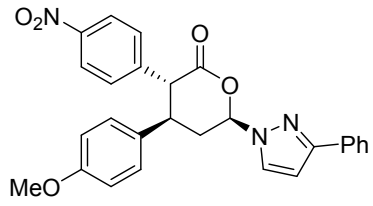
(*3R,4R,6R*)-4-(2-nitrophenyl)-3-(4-nitrophenyl)-6-(3-phenyl-1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (11c):



The compound **11c** was obtained as a white solid in 78% yield and 92% ee. The optical purity was determined by chiral HPLC on Chiralpak IA column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 25.07 min, t_R(minor) = 50.90 min, $[\alpha]_D^{25}$ = +37.8 (*c* 0.14 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.5 Hz, 2H), 7.86 – 7.80 (m, 2H), 7.78 – 7.57 (m, 4H), 7.46 – 7.34 (m, 4H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 2.3 Hz, 1H), 6.54 (dd, *J* = 9.3, 4.9 Hz, 1H), 4.46 – 4.31 (m, 2H), 3.46 – 3.32 (m, 1H), 2.92 (dd, *J* = 10.5, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 153.7, 149.8, 147.4, 142.8, 133.7, 133.4, 132.7, 131.9, 129.7, 128.7, 128.4, 127.9, 126.0, 124.8, 123.9, 104.9, 86.6, 53.6, 37.4, 34.5; IR (film): 3027, 2941, 2856, 1737, 1601, 1522, 1349, 1071 cm^{-1}; HRMS (ES+) calc. for $C_{26}H_{21}N_4O_6$ $[M+H]^+$: 485.1456 found: 485.1456

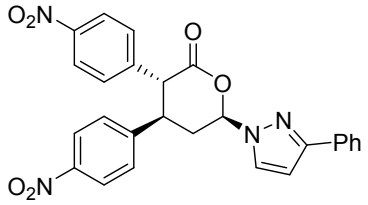
(*3R,4R,6R*)-4-(4-methoxyphenyl)-3-(4-nitrophenyl)-6-(3-phenyl-1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (11d):

The compound **11d** was obtained as a white solid in 88% yield and 87% ee. The optical purity was determined by chiral HPLC on Chiralpak IA column [*n*-hexane/2-propanol 60:40]; flow rate



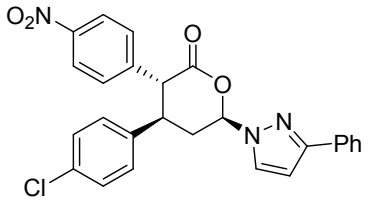
1 mL/min; λ = 254 nm; t_R(minor) = 42.54 min, t_R(major) = 46.55 min, $[\alpha]_D^{25}$ = +27.2 (*c* 0.25 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.86 – 7.81 (m, 2H), 7.70 (d, *J* = 2.3 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.68 (d, *J* = 2.3 Hz, 1H), 6.49 (dd, *J* = 9.8, 4.2 Hz, 1H), 4.14 (d, *J* = 11.6 Hz, 1H), 3.73 (s, 2H), 3.46 – 3.24 (m, 2H), 2.71 (d, *J* = 13.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 159.0, 153.4, 147.3, 147.1, 144.4, 132.7, 131.1, 130.0, 128.7, 128.3, 128.1, 126.0, 123.7, 114.4, 104.8, 87.4, 55.3, 55.2, 44.1, 35.0; IR (film): 3028, 2926, 2856, 1734, 1601, 1495, 1347, 1073 cm^{-1}; HRMS (ES+) calc. for $C_{27}H_{24}N_3O_5$ $[M+H]^+$: 470.1710 found: 470.1712

(*3R,4R,6R*)-3,4-bis(4-nitrophenyl)-6-(3-phenyl-1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (11e):



The compound **11e** was obtained as a pale yellow solid in 80% yield and 89.7% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 20.60 min, t_R(major) = 41.19 min, $[\alpha]_D^{25}$ = -204.2 (*c* 0.26 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.07 (m, 4H), 7.86 – 7.81 (m, 2H), 7.71 (d, *J* = 2.5 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.40 – 7.29 (m, 3H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 2.5 Hz, 1H), 6.53 (dd, *J* = 9.3, 4.8 Hz, 1H), 4.31 (d, *J* = 12.2 Hz, 1H), 3.65 (td, *J* = 12.4, 3.8 Hz, 1H), 3.52 – 3.38 (m, 1H), 2.80 (dt, *J* = 14.3, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 153.7, 147.5, 146.5, 143.1, 132.5, 131.6, 129.9, 128.8, 128.6, 128.2, 126.0, 124.3, 124.0, 105.1, 86.7, 54.3, 44.4, 34.2; IR (film): 2936, 2856, 1734, 1604, 1517, 1344, 1158 cm^{-1}; HRMS (ES+) calc. for $C_{26}H_{21}N_4O_6$ $[M+H]^+$: 485.1456 found: 485.1470

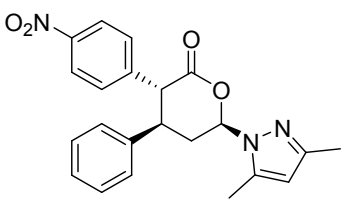
(*3R,4R,6R*)-4-(4-chlorophenyl)-3-(4-nitrophenyl)-6-(3-phenyl-1H-pyrazol-1-yl)tetrahydro-2H-pyran-2-one (11f):



The compound **11f** was obtained as a white solid in 83% yield and 91% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 60:40]; flow rate 1

mL/min; λ = 254 nm; t_R(minor) = 13.30 min, t_R(major) = 32.97 min, $[\alpha]_D^{25}$ = -183.2 (*c* 0.12 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.7 Hz, 2H), 7.86 – 7.80 (m, 2H), 7.69 (d, *J* = 2.5 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.36 (dd, *J* = 8.3, 6.3 Hz, 1H), 7.28 – 7.11 (m, 5H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 2.5 Hz, 1H), 6.49 (dd, *J* = 9.7, 4.4 Hz, 1H), 4.17 (d, *J* = 11.9 Hz, 1H), 3.45 (td, *J* = 12.3, 3.0 Hz, 1H), 3.39 – 3.28 (m, 1H), 2.75 – 2.68 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 153.5, 147.3, 143.8, 137.7, 133.8, 132.6, 131.3, 129.9, 129.3, 128.7, 128.4, 126.0, 123.8, 104.9, 87.1, 54.9, 44.2, 34.6; IR (film): 2936, 2856, 1737, 1604, 1522, 1453, 1347, 1084 cm^{-1}; HRMS (ES+) calc. for $C_{26}H_{21}N_4O_6$ $[M+H]^+$: 485.1456 found: 485.1470

(*3R,4R,6R*)-6-(3,5-dimethyl-1H-pyrazol-1-yl)-3-(4-nitrophenyl)-4-phenyltetrahydro-2H-pyran-2-one (12):



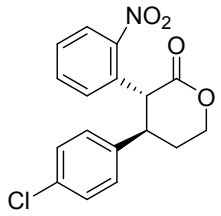
The compound **12** was obtained as a white solid in 35% yield and 94% ee. The optical purity was determined by chiral HPLC on Chiralpak IB column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 27.01 min, t_R(major) = 37.19 min, $[\alpha]_D^{25}$ = -135.0 (*c* 0.10 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.7 Hz, 2H), 7.24 – 7.12 (m, 5H), 7.10 – 7.04 (m, 2H), 6.37 (dd, *J* = 9.9, 4.1 Hz, 1H), 5.91 (s, 1H), 4.13 (dd, *J* = 12.0, 5.5 Hz, 1H), 3.57 – 3.37 (m, 2H), 2.60 – 2.51 (m, 1H), 2.39 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 150.1, 147.1, 144.5, 140.9, 139.3, 130.0, 128.9, 127.8, 127.1, 123.6, 107.5, 83.8, 55.2, 45.0, 34.2, 13.7, 10.7; IR (film): 2944, 2852, 1728, 1653, 1601, 1515, 1344, 1171, 1053 cm^{-1}; HRMS (ES+) calc. for $C_{22}H_{22}N_3O_4$ $[M+H]^+$: 392.1605 found: 392.1617

Procedure for the Cleavage of pyrazole and Synthesis Lactone (13): [1, 2]

To a 5 mL round bottom flask with magnetic stirring bar was added the lactone (0.2 mmol, 1.0 equiv) in $CHCl_3$ (1.6 mL) and MeOH (0.8 mL) at room temperature, then 20 mol% DABCO (0.04 mmol) was added to the solution. After 72 hours, evaporate the solvent and the crude reaction mixture was dissolved in MeOH (4.2 mL) and reaction mixture cooled to 0 °C. Then $NaBH_4$ (0.44 mmol) was added to the reaction mixture and stirred at this temperature for 10 minutes, then reaction mixture warmed to room temperature and allowed to stir for 1.30 hours,

then reaction mixture was quenched with ice cold water and extracted with DCM (thrice). The combined organic layers were washed with 10% HCl. Then organic layer dried over Na_2SO_4, filtered and concentrated in vacuo gave a crude product. The crude product was dissolved in DCM (8.0 mL) was added TFA (8 drops) and the solution stirred at room temperature for 1.30 hours. Then evaporate under vacuo and gave crude product. The crude product was purified by flash chromatography using 230-400 silica gel (25% EtOAc in hexane as an eluent) gave a colorless solid in 65% yield.

(*3R,4R*)-4-(4-chlorophenyl)-3-(2-nitrophenyl)tetrahydro-2H-pyran-2-one (13):



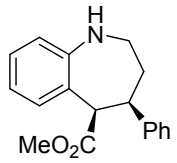
The compound **13** was obtained as a white solid in 65% yield and 92% ee. The optical purity was determined by chiral HPLC on Chiralpak OJH column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; t_R(major) = 28.60 min, t_R(minor) = 62.77 min, $[\alpha]_D^{25}$ = -165.6 (*c* 0.16 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.28 (m, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.67 (s, 1H), 4.76 (td, *J* = 11.9, 2.5 Hz, 1H), 4.63 (ddd, *J* = 11.4, 4.5, 2.3 Hz, 1H), 3.89 (s, 1H), 3.51 (td, *J* = 11.8, 3.7 Hz, 1H), 2.43 – 2.30 (m, 1H), 2.20 – 2.12 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.4, 146.8, 139.7, 134.7, 133.7, 133.2, 132.9, 129.0, 128.9, 128.6, 126.1, 68.7, 56.4, 44.7, 30.4; IR (film): 2930, 1724, 1586, 1530, 1344, 1262, 954 cm^{-1}; HRMS (ES+) calc. for $C_{17}H_{15}ClNO_4$ $[M+H]^+$: 332.0684 found: 332.0705

Procedure for the Synthesis of Benzazapine derivative (14):[1, 3]

To a 5 mL round bottom flask with magnetic stirring bar was added the lactone (0.2 mmol, 1.0 equiv) in $CHCl_3$ (1.6 mL) and MeOH (0.8 mL) at room temperature, then 20 mol% DABCO (0.04 mmol) was added to the solution. After 48 hours, evaporate the solvent and the crude reaction mixture was dissolved in THF/ACOH(10:1) 3.85 mL. To a stirred solution of ester in THF/ACOH was added Zn dust. Saturated aq. CuSO4 solution was added slowly at 0 °C and

then warm to RT. After 1.5 hours, the mixture was filtered, diluted with EtOAc, and washed twice with sat. aq. $NaHCO_3$ solution. The combined organic layers were dried over Na2SO4, filtered and concentrated in vacuo gave a crude product. The crude product was purified by flash chromatography using 230-400 silica gel (15% EtOAc in hexane as a eluent) gave a colorless semi solid in 50% yield.

methyl (*4R,5R*)-4-phenyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine-5-carboxylate (13):



The compound **14** was obtained as a colorless semisolid in 50% yield and 92% ee. The optical purity was determined by chiral HPLC on Chiralpak IC column [*n*-hexane/2-propanol 97:03]; flow rate 1 mL/min; λ = 254 nm; t_R(minor) = 44.47 min, t_R(major) = 58.11 min, $[\alpha]_D^{25}$ = 25.88 (*c* 0.34 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 4H), 7.27 – 7.08 (m, 3H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 4.02 (d, *J* = 1.9 Hz, 1H), 3.61 – 3.56 (m, 1H), 3.53 (s, 3H), 3.35 – 3.28 (m, 1H), 3.14 – 3.06 (m, 1H), 2.96 – 2.82 (m, 1H), 2.06 – 1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 149.8, 145.0, 132.3, 128.3, 128.1, 128.1, 127.9, 126.5, 120.8, 120.1, 57.0, 51.6, 47.8, 45.4, 31.7; IR (film): 3372, 2911, 1731, 1601, 1474, 1365, 1265, 1158, 1004 cm^{-1}; HRMS (ES+) calc. for $C_{18}H_{20}NO_2$ $[M+H]^+$: 282.1489 found: 282.1510

References:

1. B. B. Tan, G. Hernandez-Torres and C. F. Barbas III, *Angew. Chem. Int. Ed.* 2012, **51**, 5381.
2. S. R. Smith, S. M. Leckie, R. Holmes, J. Douglas, C. Fallan, P. Shapland, D. Pryde, A. M. Z. Slawin and A. D. Smith, *Org. Lett.* 2014, **16**, 2506.
3. L. D. Amico, X. Companyó, T. Naicker, T. M. Bräuer and K. A. Jørgensen, *Eur. J. Org. Chem.* 2013, 5262.

Figure 1. Molecular structure of **7a** shown with 50% ellipsoidal probability. (CCDC 1045015)

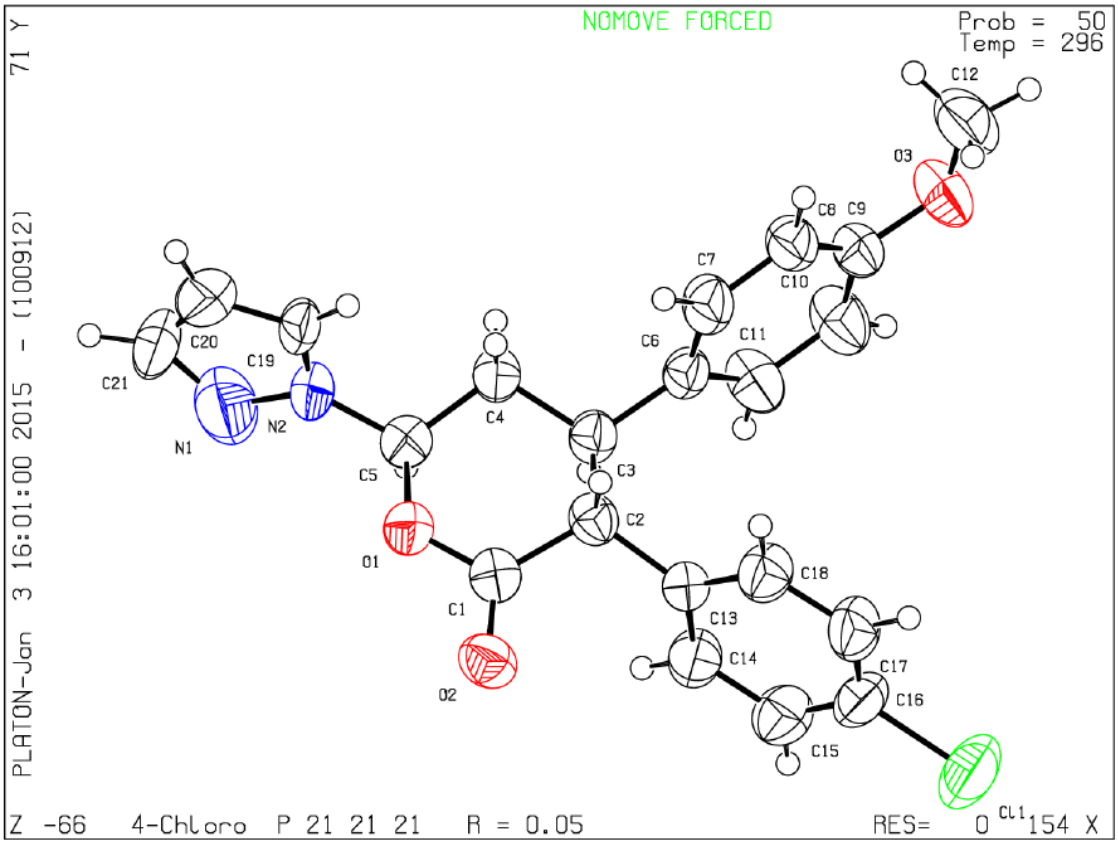


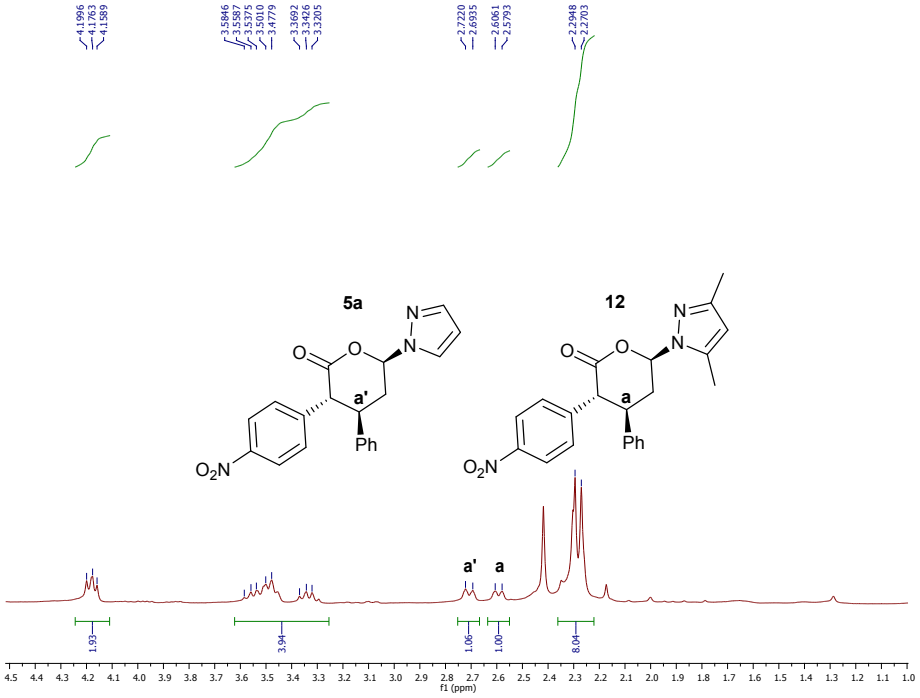
Table S2.

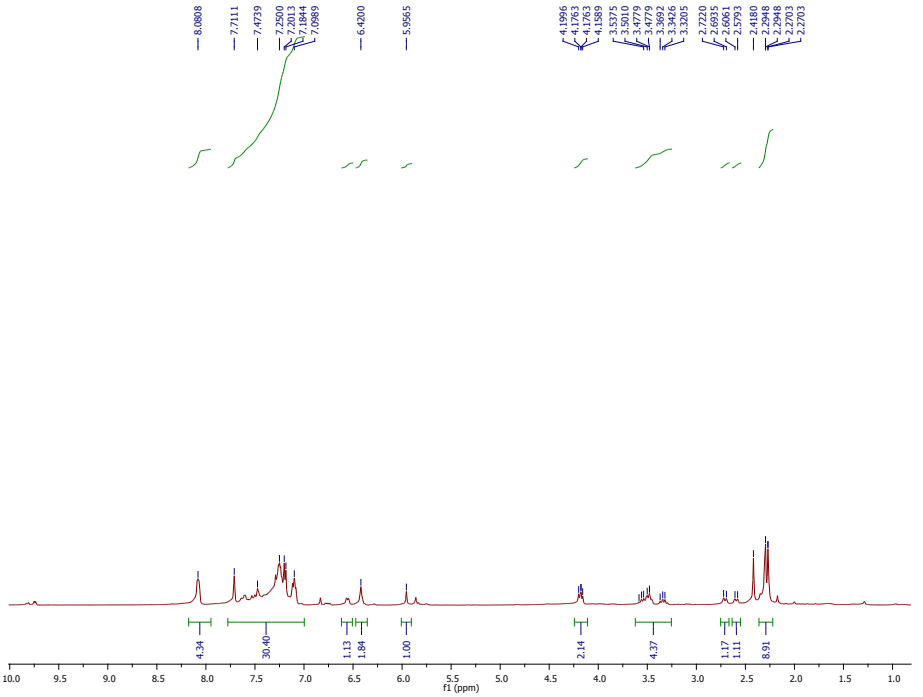
Experimental details

Crystal data	
Chemical formula	$C_{21}H_{19}ClN_2O_3$
M_r	382.83
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	296
a, b, c (Å)	6.1999 (5), 13.2765 (11), 23.277 (2)
V (Å^3)	1916.0 (3)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.22
Crystal size (mm)	× ×
Data collection	
Diffractometer	?
Absorption correction	–
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	11558, 3390, 2041
R_{int}	0.051
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.595
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.054, 0.152, 1.03
No. of reflections	3390
No. of parameters	245
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.19, −0.28
Absolute structure	Flack x determined using 643 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	0.07 (7)

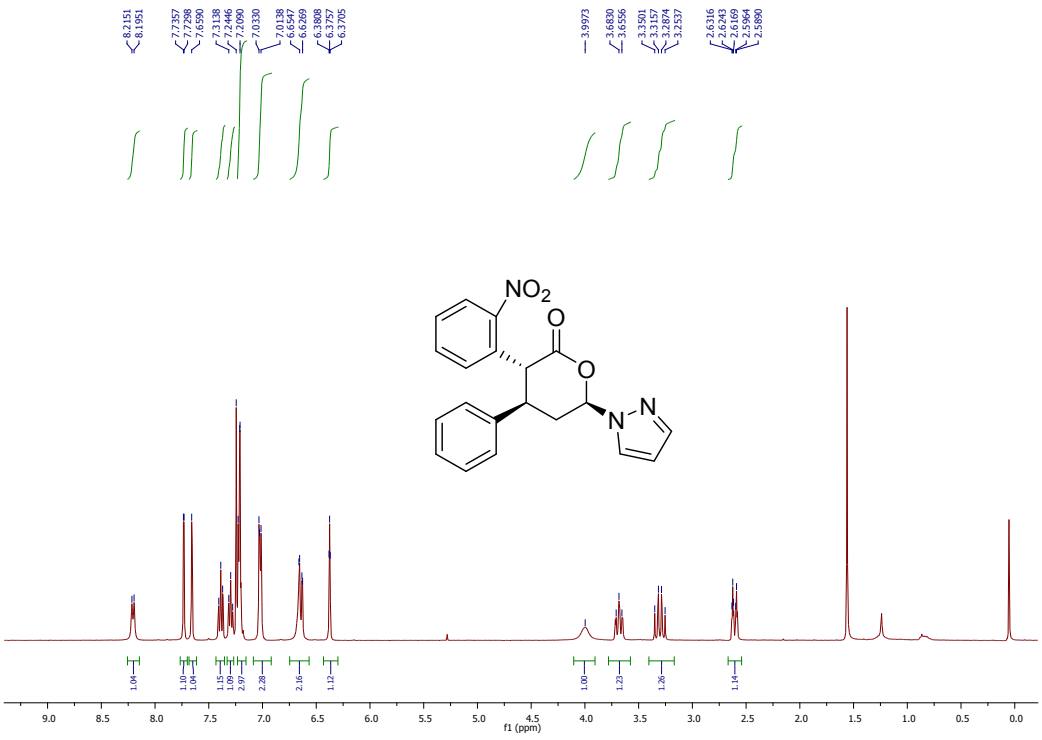
Computer programs: *SHELXL2014*/6 (Sheldrick, 2014).

Cross over experiment

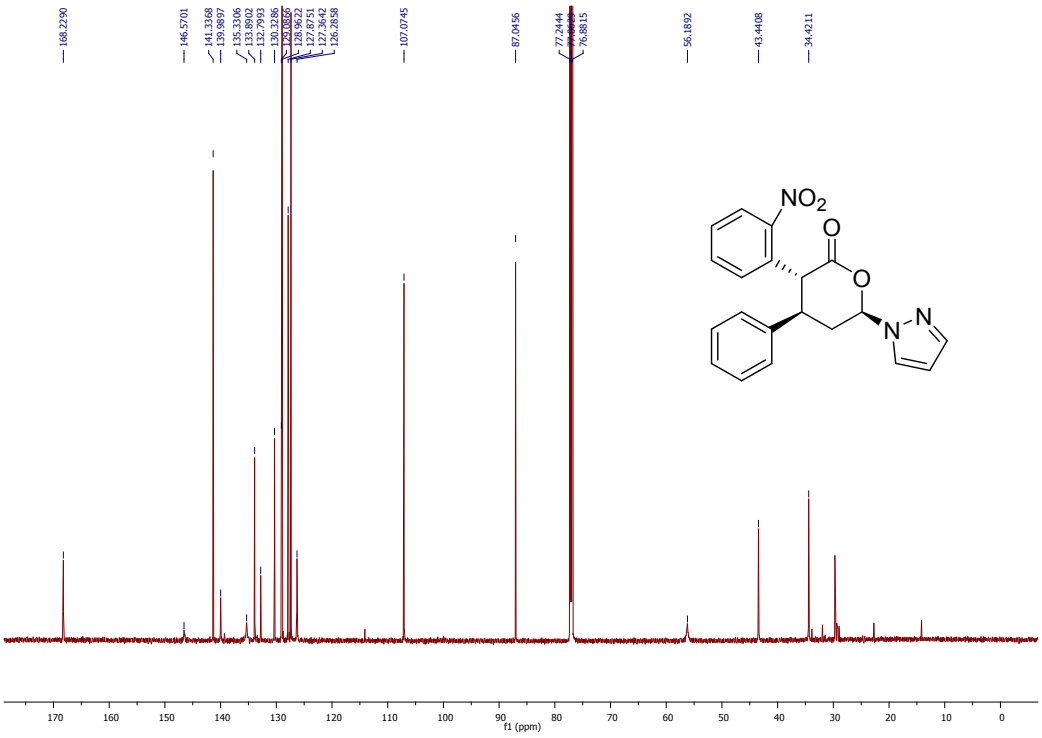




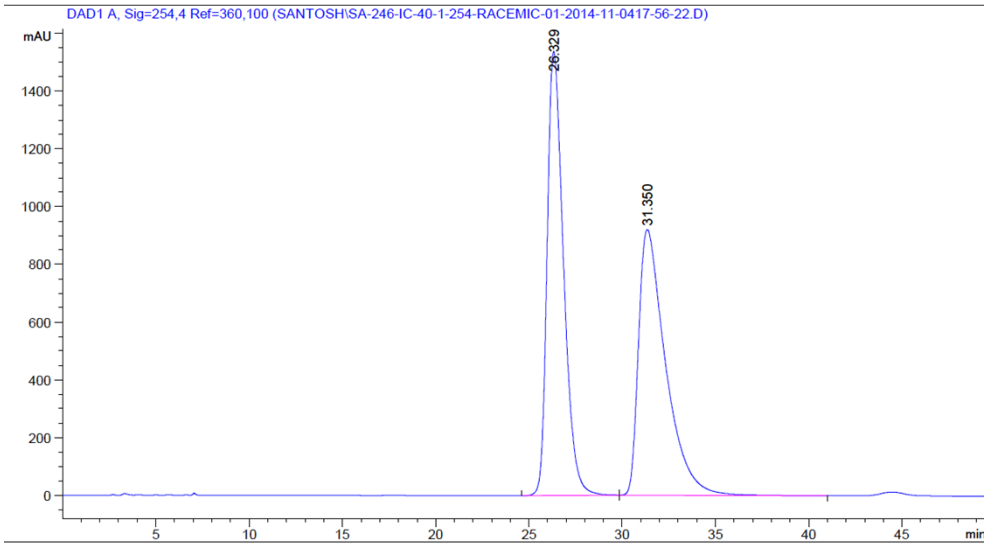
500 MHz ^{1}H NMR spectra of crude reaction mixture in $CDCl_3$



400 MHz ^{1}H NMR spectra of compound **4a** in $CDCl_3$

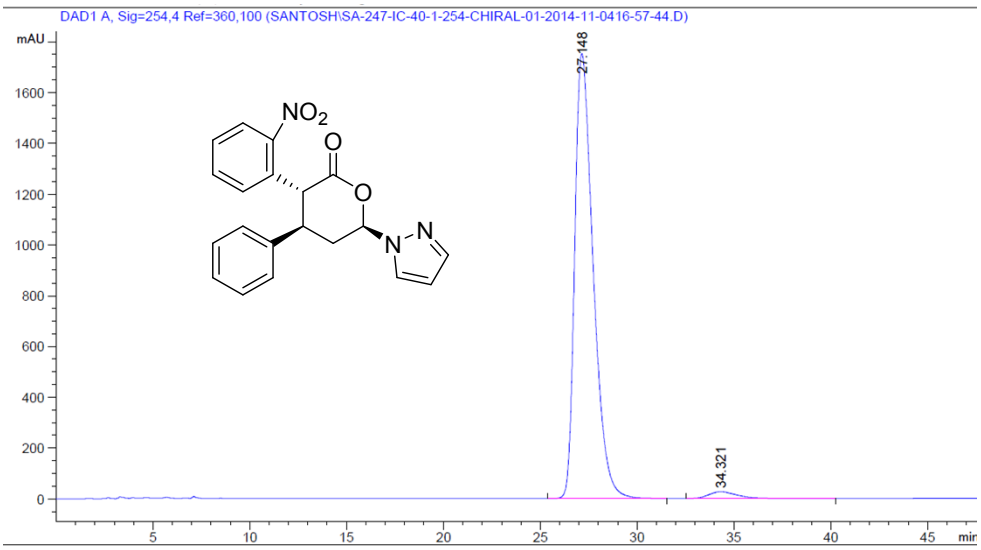


175 MHz ^{13}C NMR spectra of compound **4a** in $CDCl_3$



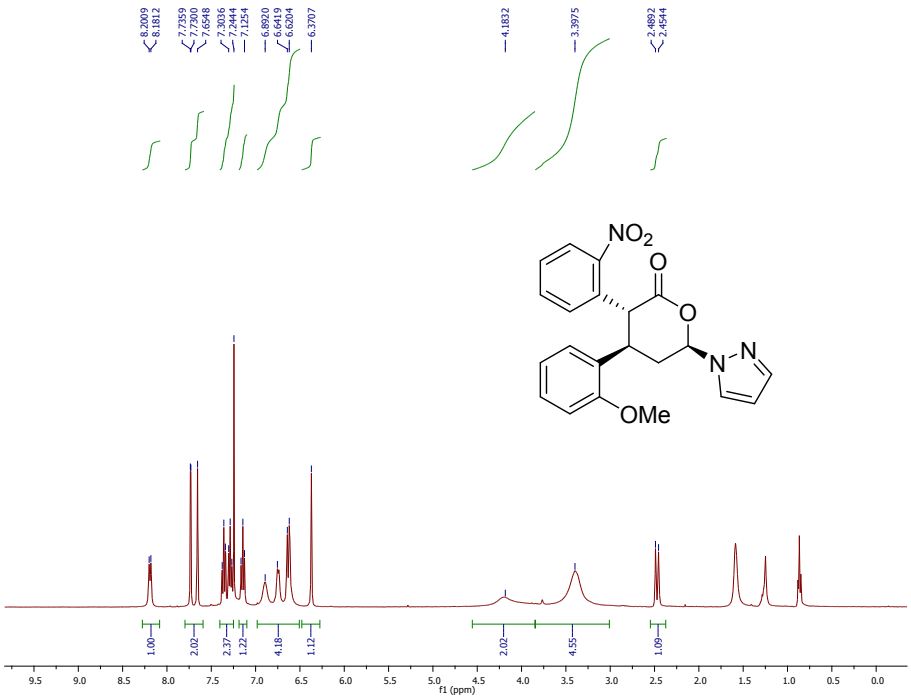
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.329	BB	0.9348	9.37363e4	1538.60864	50.2765
2	31.350	BB	1.4930	9.27051e4	920.45233	49.7235

HPLC graph of compound **4a** (racemic)

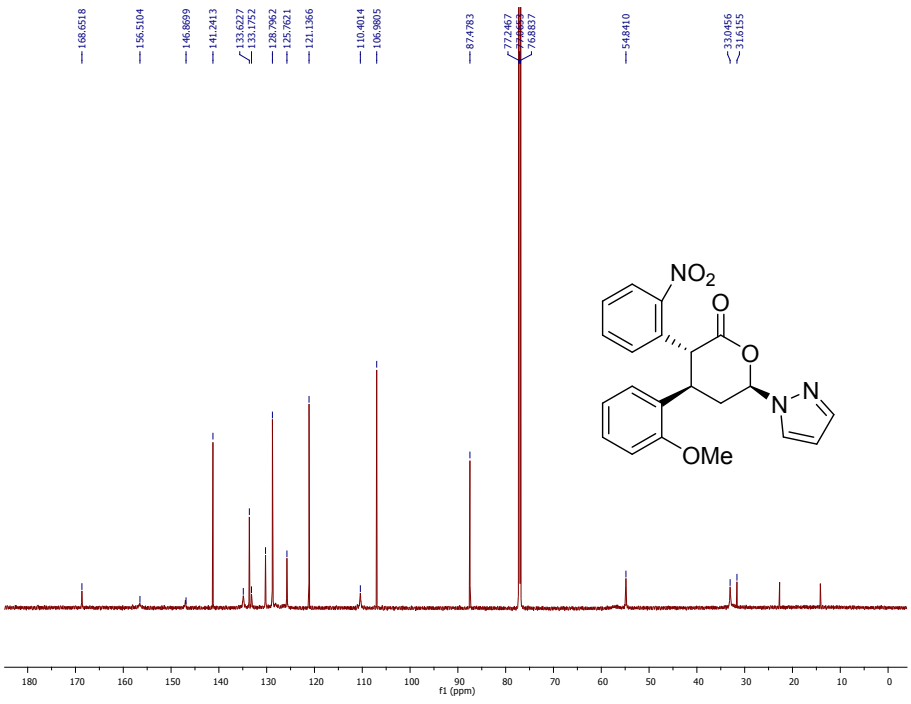


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.148	BB	1.0085	1.15733e5	1752.48999	97.7295
2	34.321	BB	1.5475	2688.78125	26.37119	2.2705

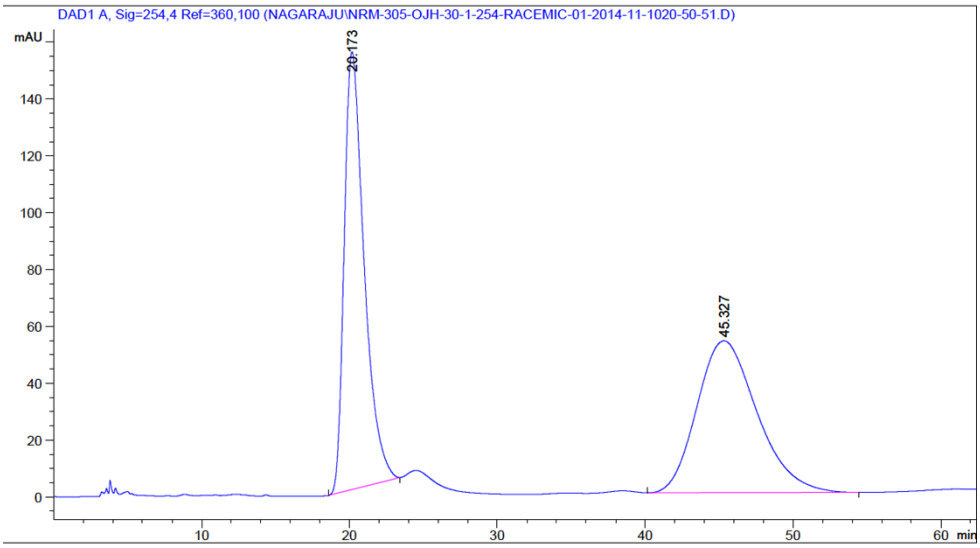
HPLC graph of compound **4a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **4b** in $CDCl_3$

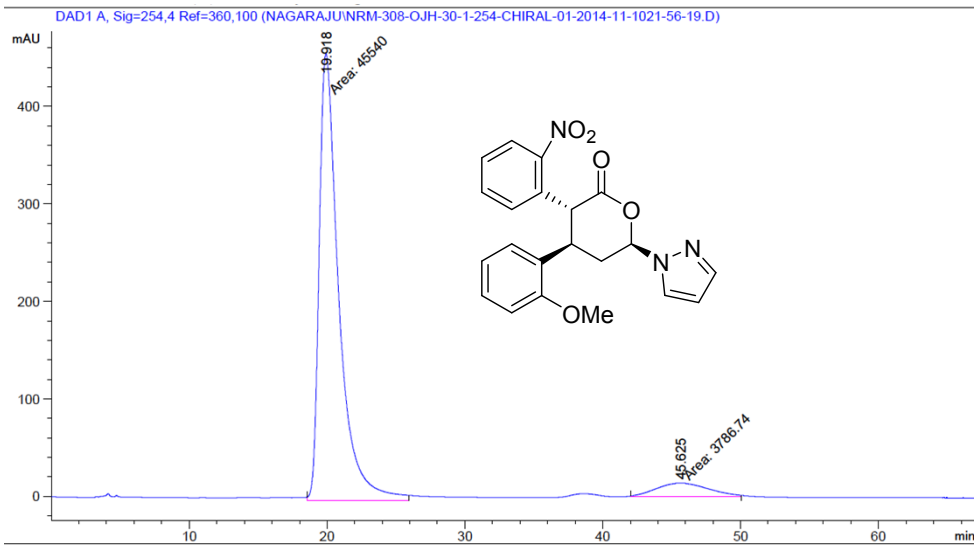


175 MHz ^{13}C NMR spectra of compound **4b** in $CDCl_3$



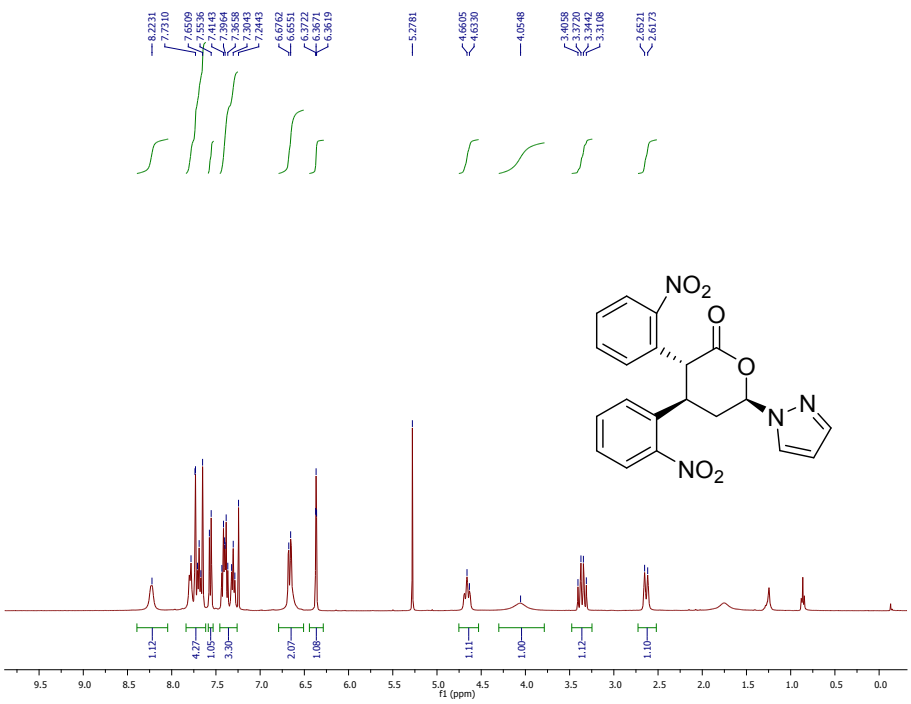
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.173	BB	1.4220	1.44722e4	154.04675	48.8925
2	45.327	BB	3.7677	1.51279e4	53.45546	51.1075

HPLC graph of compound **4b** (racemic)

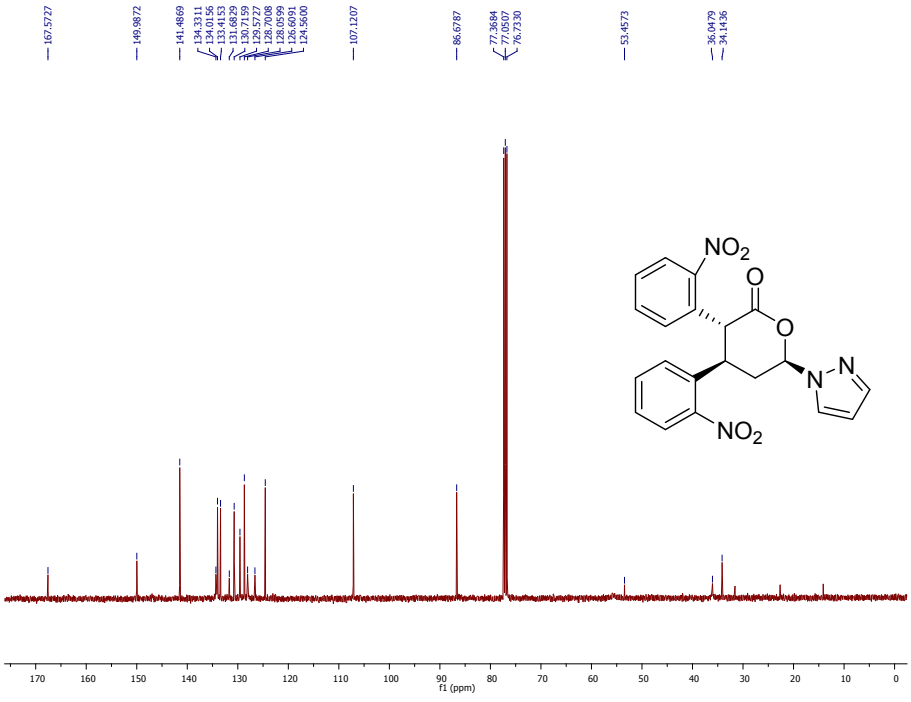


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.918	MM	1.6552	4.55400e4	458.55286	92.3232
2	45.625	MM	4.4947	3786.73706	14.04163	7.6768

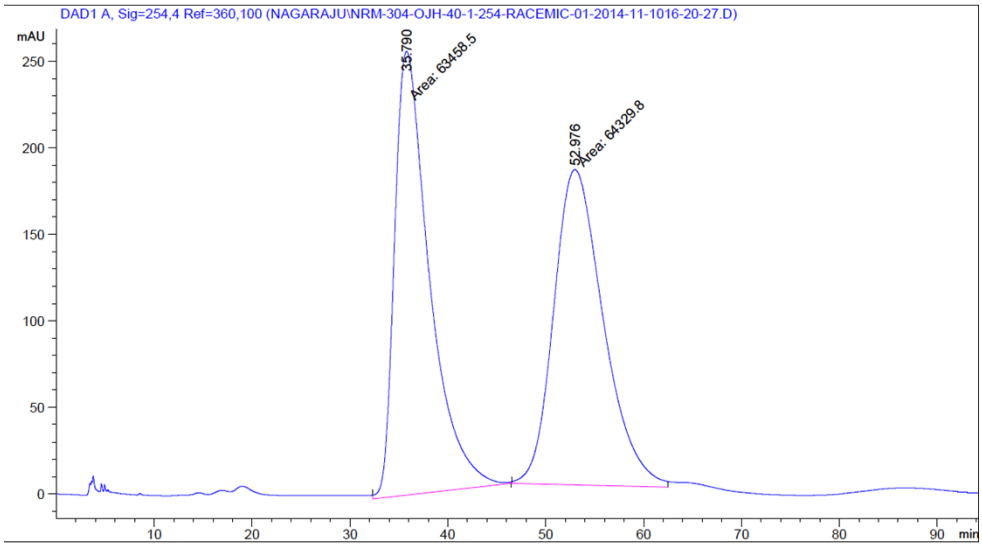
HPLC graph of compound **4b** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **4c** in $CDCl_3$

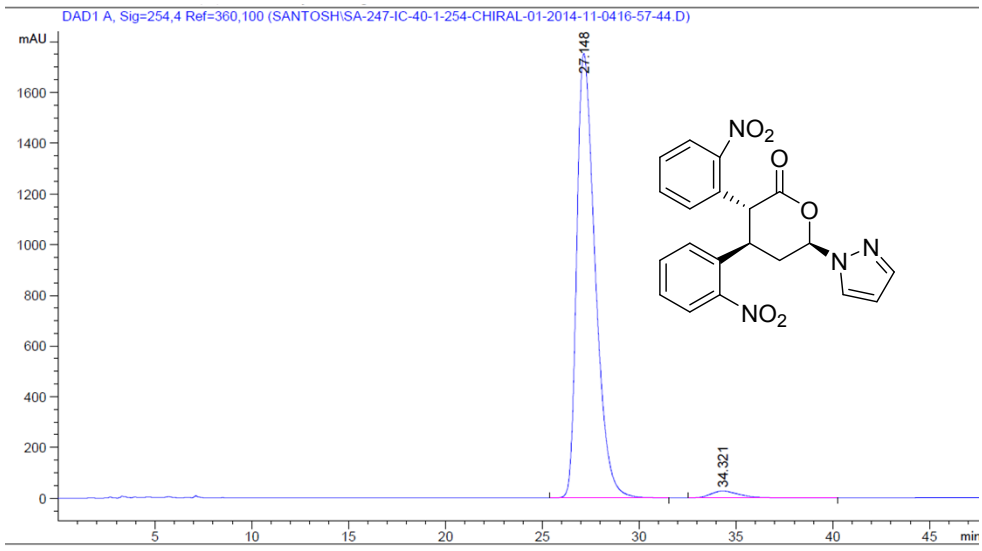


100 MHz ^{13}C NMR spectra of compound **4c** in $CDCl_3$



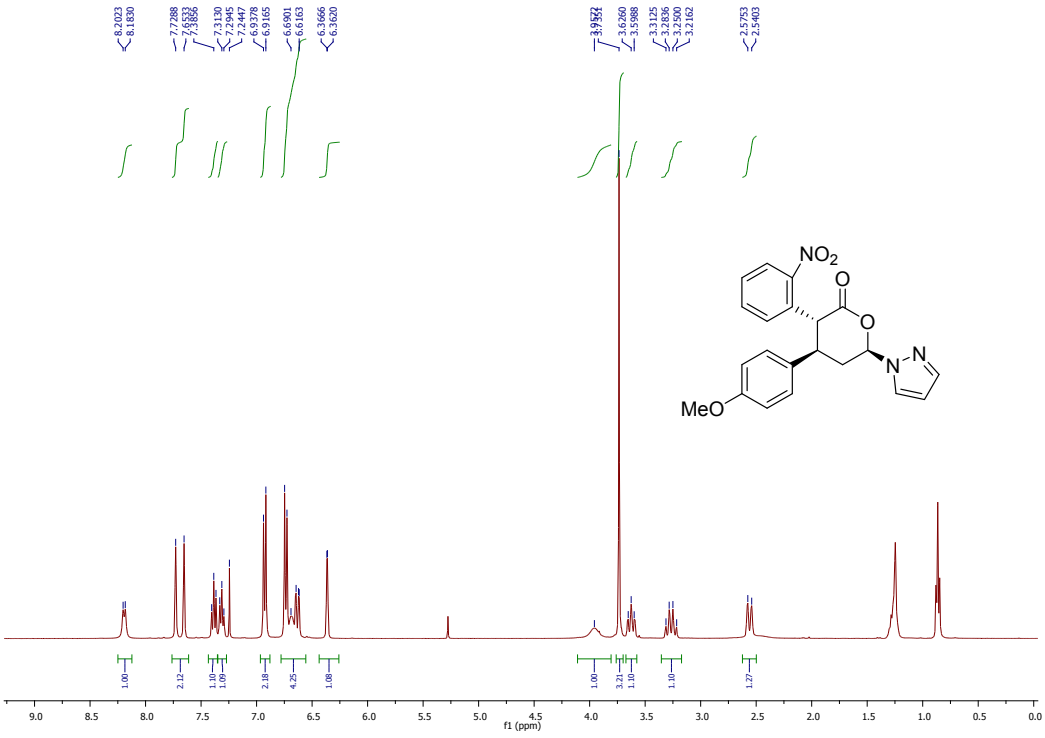
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.790	MM	4.1238	6.34585e4	256.47290	49.6591
2	52.976	MM	5.8814	6.43298e4	182.29631	50.3409

HPLC graph of compound **4c** (racemic)

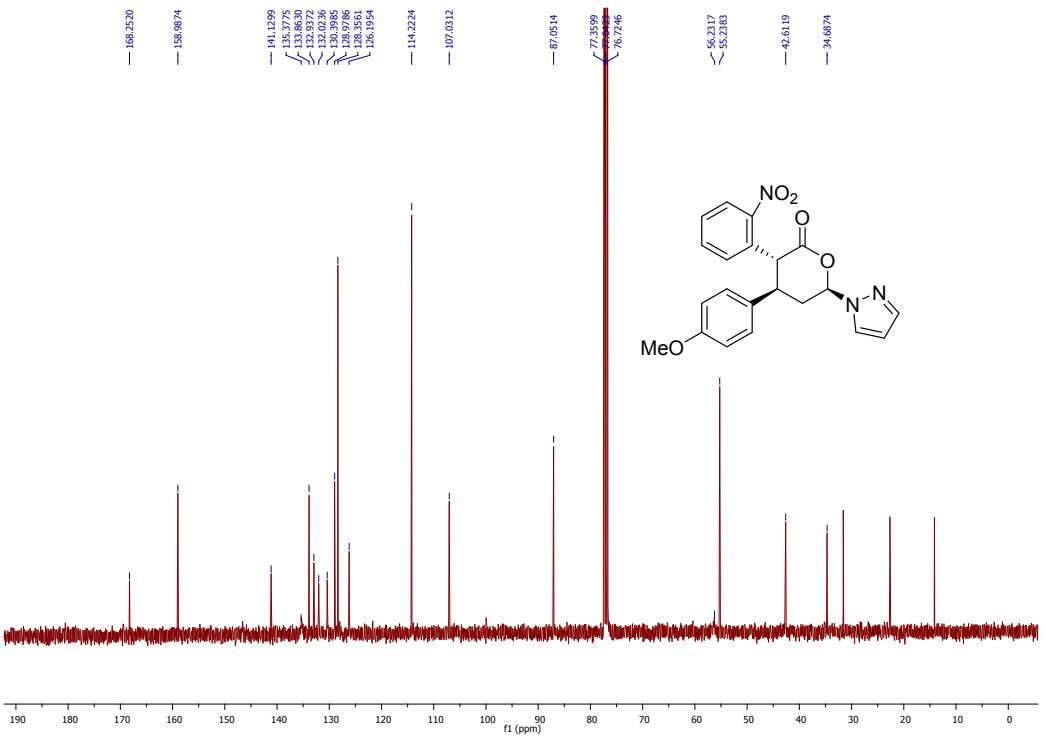


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.148	BB	1.0085	1.15733e5	1752.48999	97.7295
2	34.321	BB	1.5475	2688.78125	26.37119	2.2705

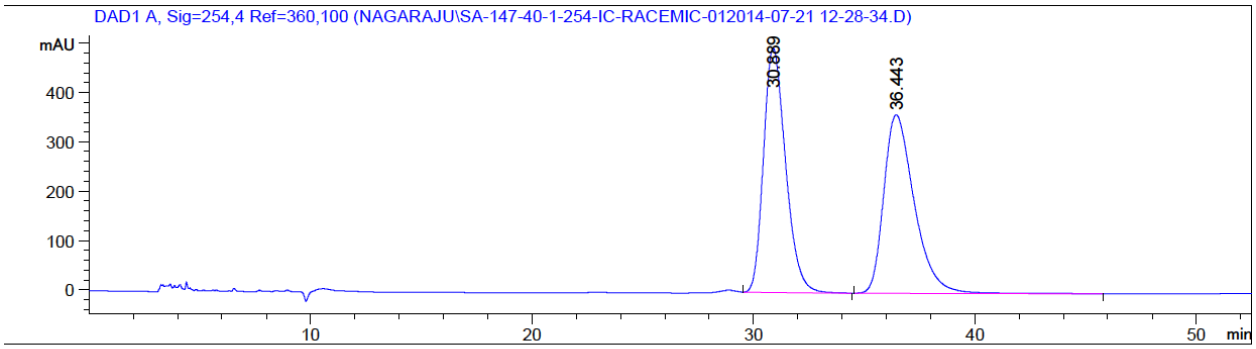
HPLC graph of compound **4c** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **4d** in $CDCl_3$

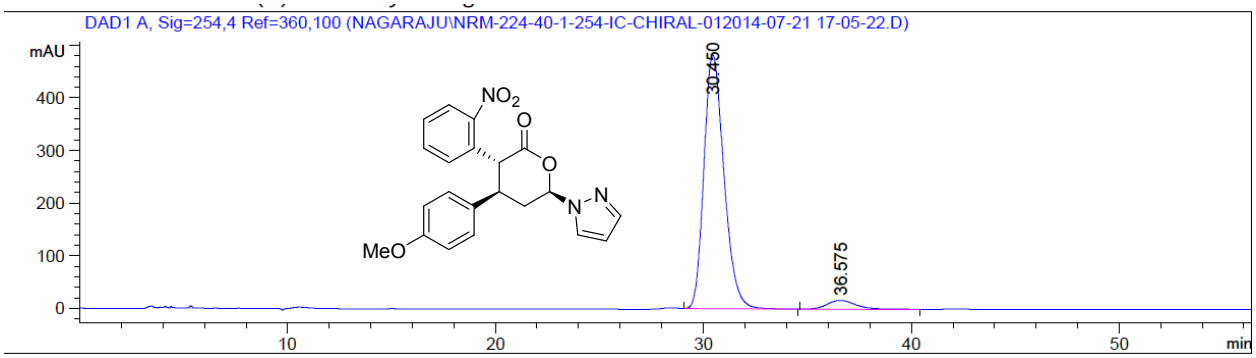


100 MHz ^{1}H NMR spectra of compound **4d** in $CDCl_3$



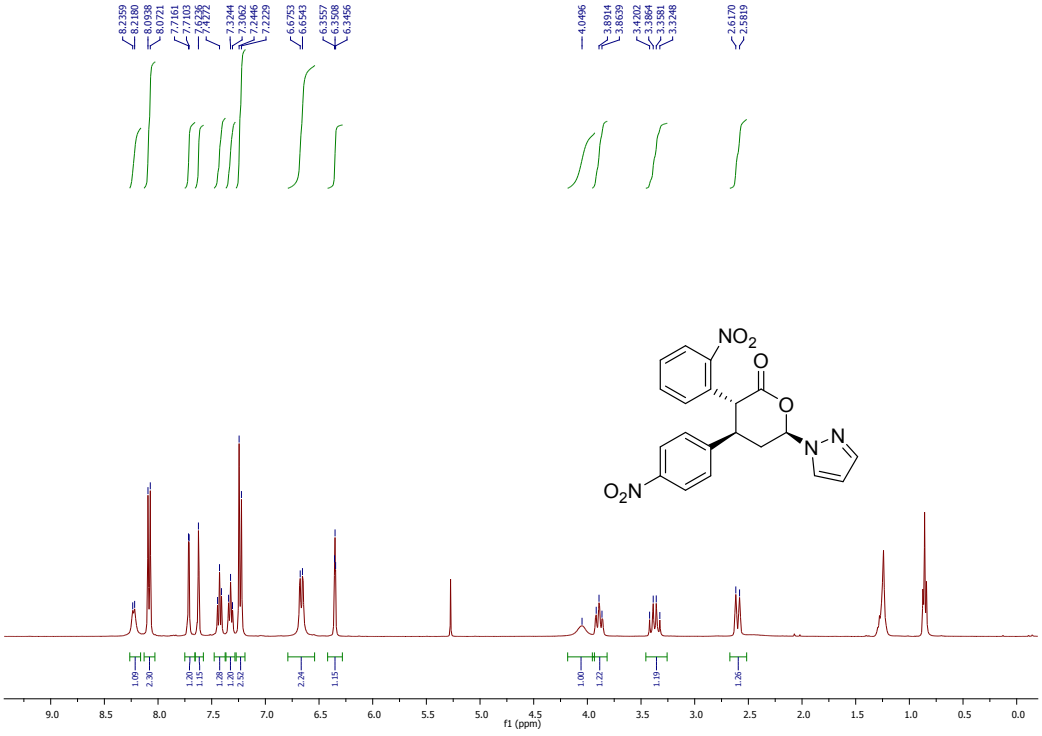
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.889	BB	1.0715	3.43396e4	494.93640	49.8486
2	36.443	BB	1.4625	3.45482e4	361.64319	50.1514

HPLC graph of compound **4d** (racemic)

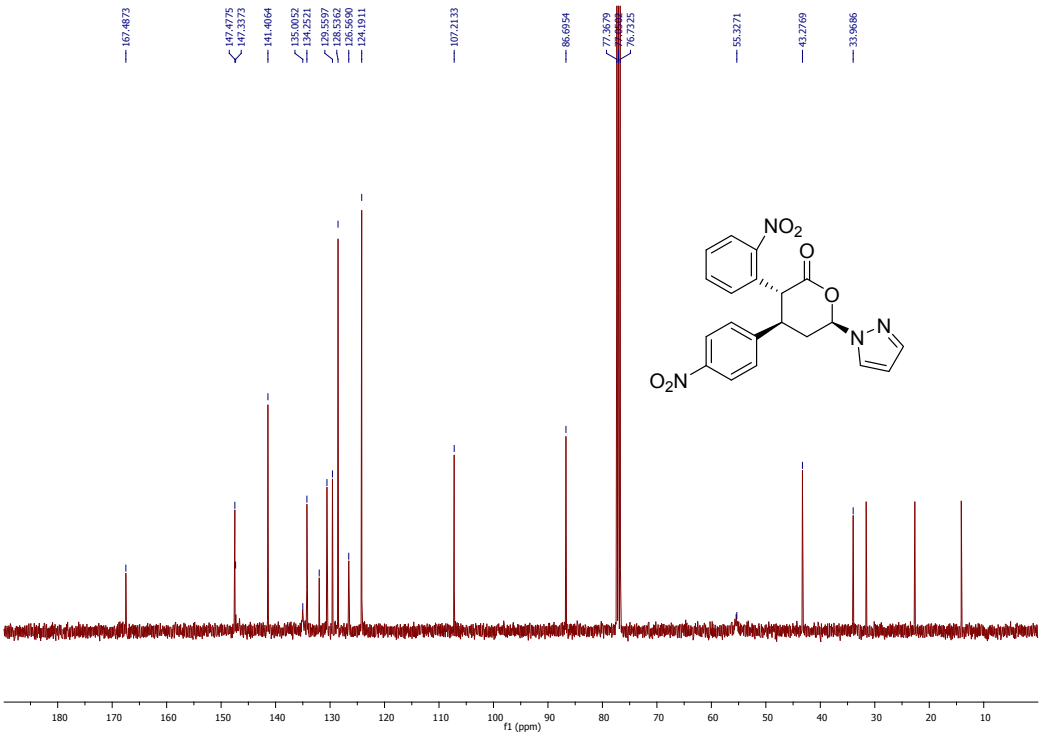


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.450	BB	1.0372	3.24136e4	482.84222	95.3344
2	36.575	BB	1.4395	1586.31470	16.83162	4.6656

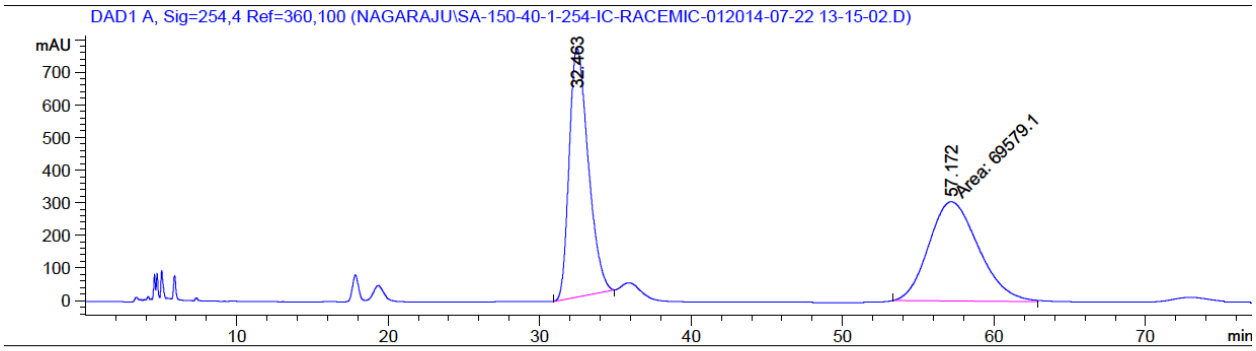
HPLC graph of compound **4d** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **4e** in $CDCl_3$

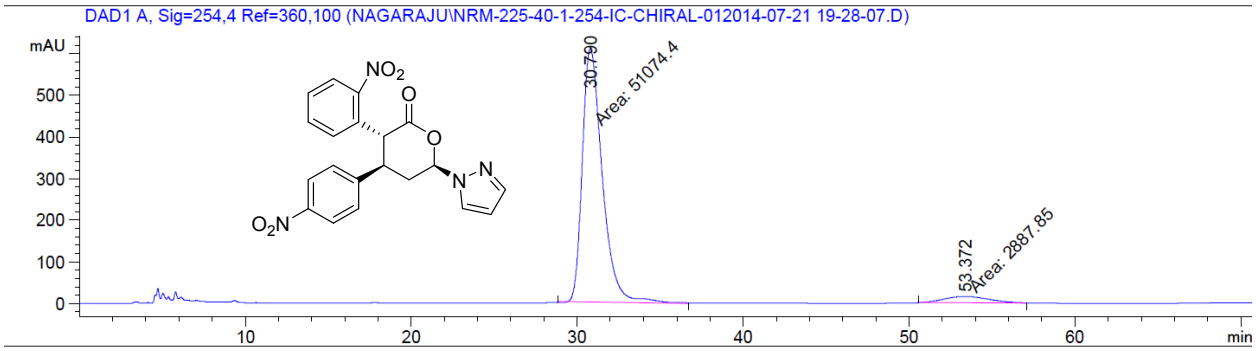


100 MHz ^{1}H NMR spectra of compound **4e** in $CDCl_3$



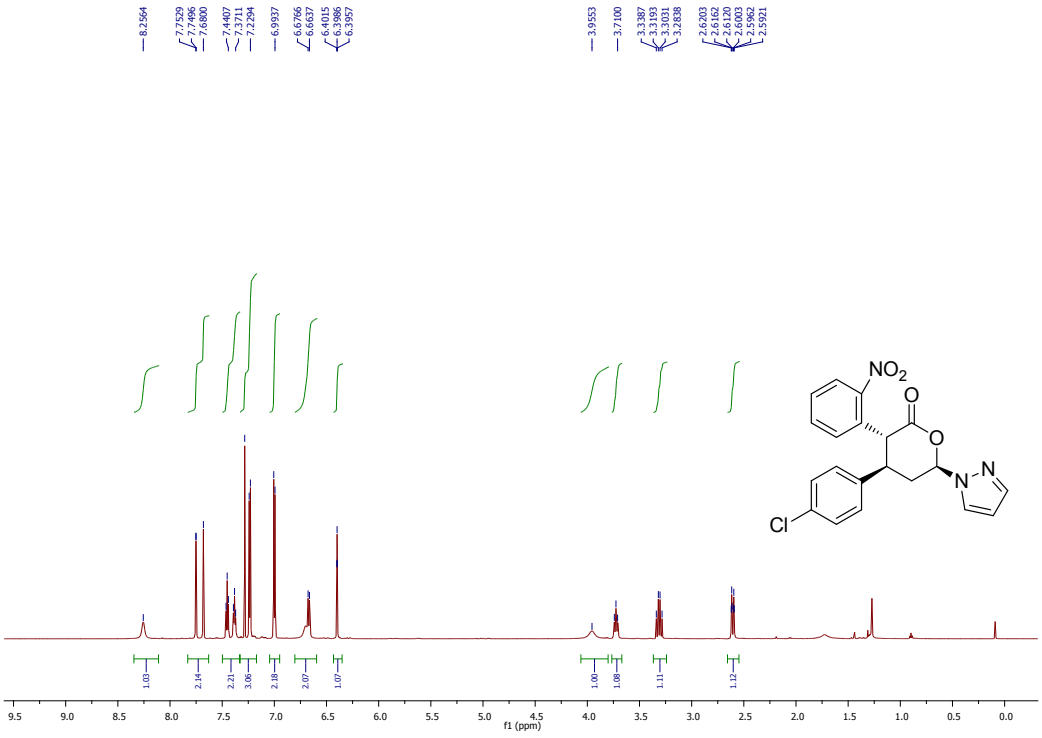
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.463	BB	1.3431	6.65310e4	761.62653	48.8802
2	57.172	MM	3.8136	6.95791e4	304.08118	51.1198

HPLC graph of compound **4e** (racemic)

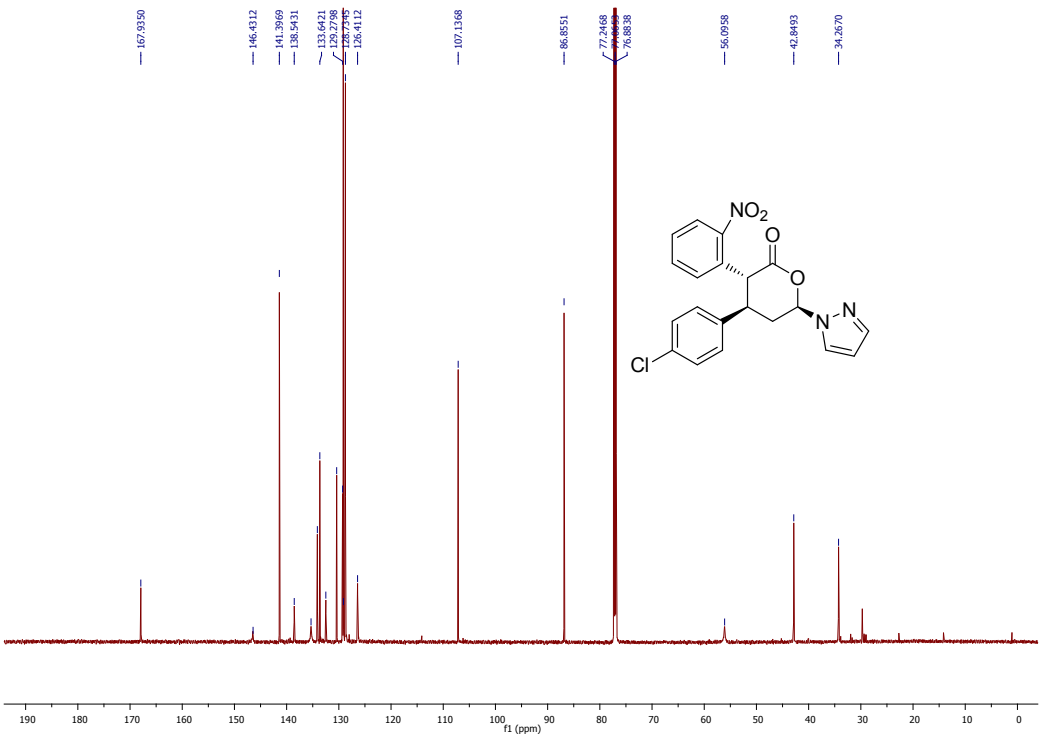


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.790	MM	1.3953	5.10744e4	610.09161	94.6484
2	53.372	MM	3.1000	2887.85010	15.52612	5.3516

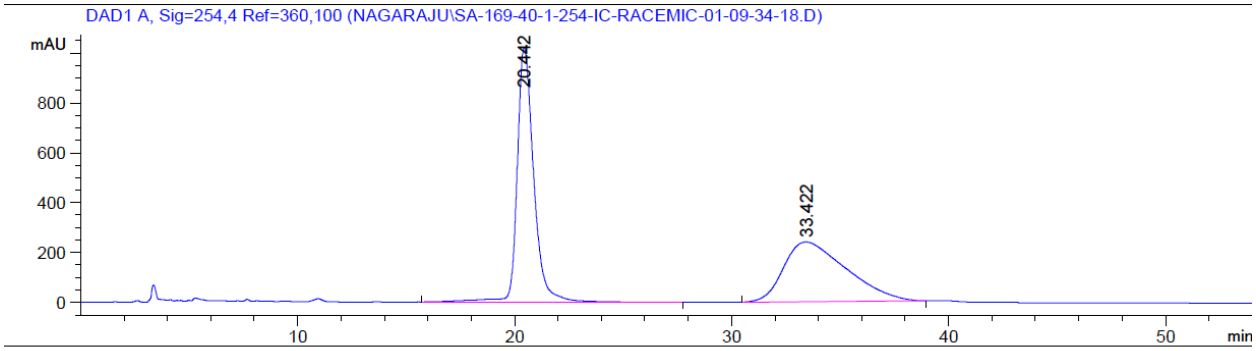
HPLC graph of compound **4e** (enantioenriched)



700 MHz ^{1}H NMR spectra of compound **4f** in $CDCl_3$

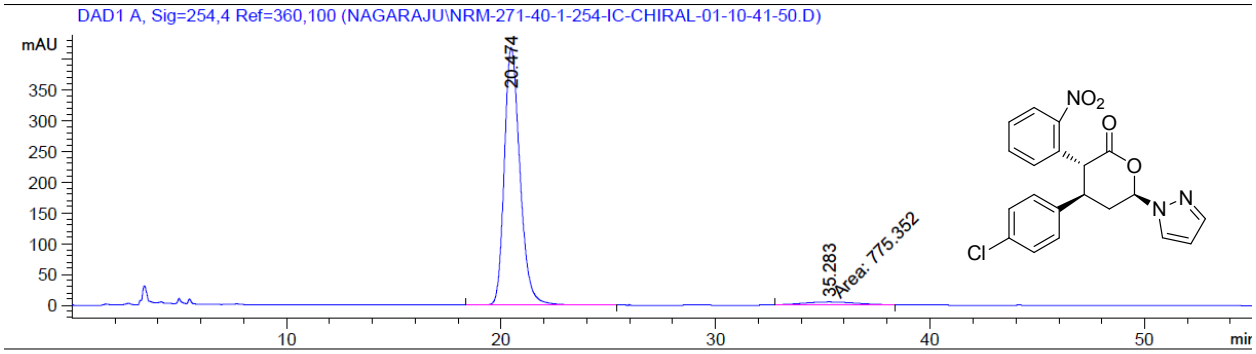


175 MHz ^{13}C NMR spectra of compound **4f** in $CDCl_3$



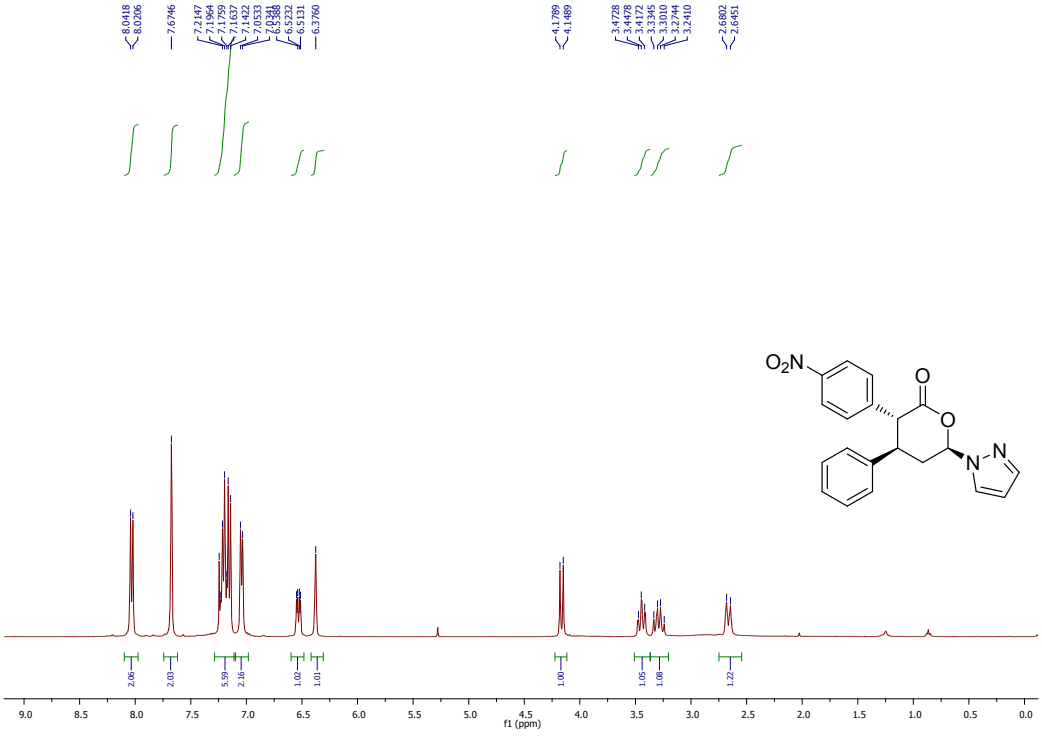
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.442	BB	0.8097	5.47669e4	1021.10571	53.2279
2	33.422	BB	2.8298	4.81245e4	239.75557	46.7721

HPLC graph of compound **4f** (racemic)

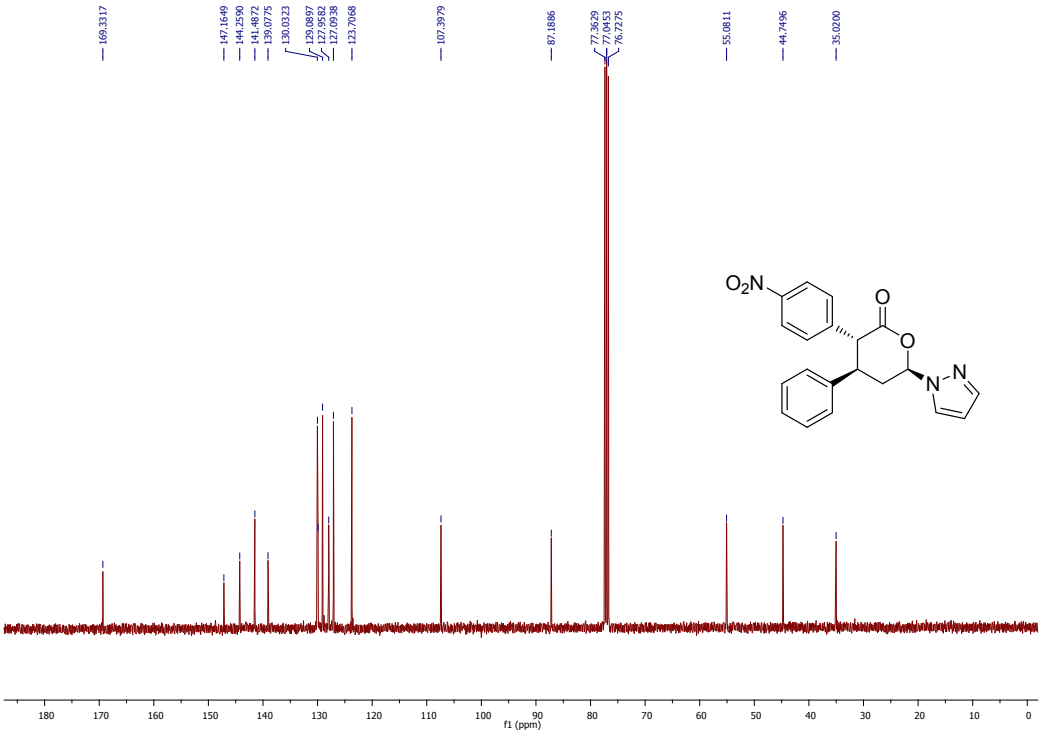


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.474	BB	0.7808	2.12224e4	417.67935	96.4753
2	35.283	MM	2.6813	775.35168	4.81957	3.5247

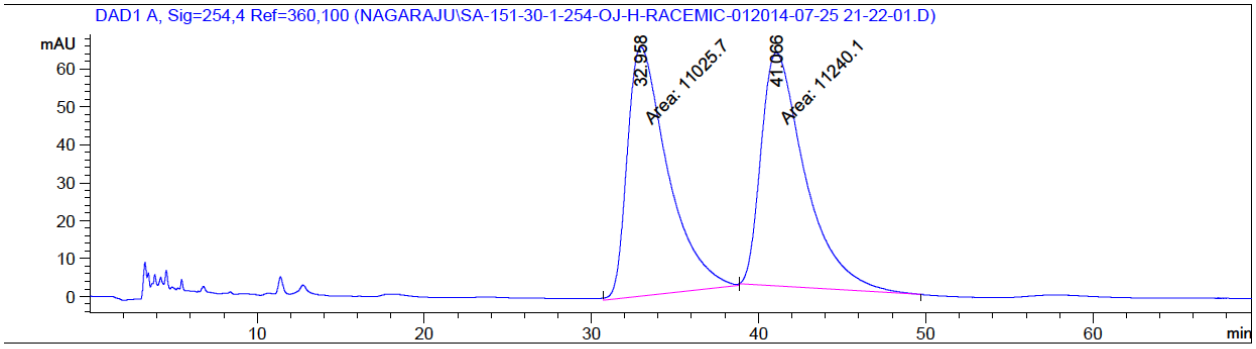
HPLC graph of compound **4f** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5a** in $CDCl_3$

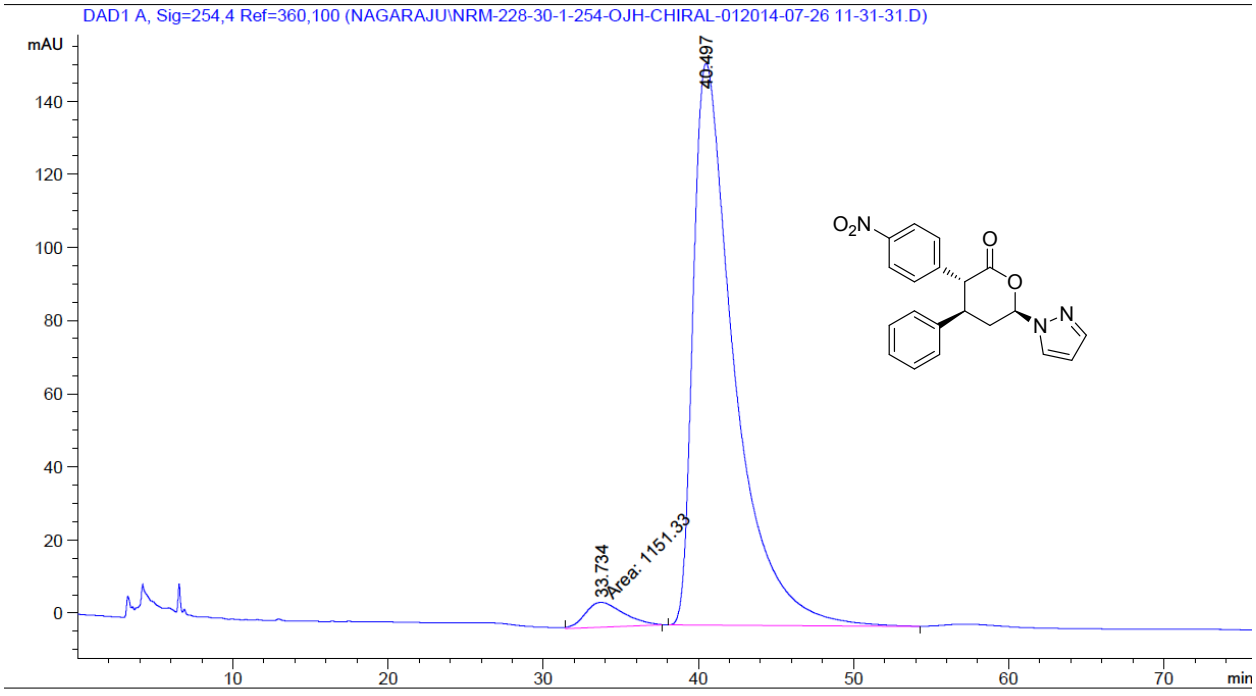


100 MHz ^{13}C NMR spectra of compound **5a** in $CDCl_3$



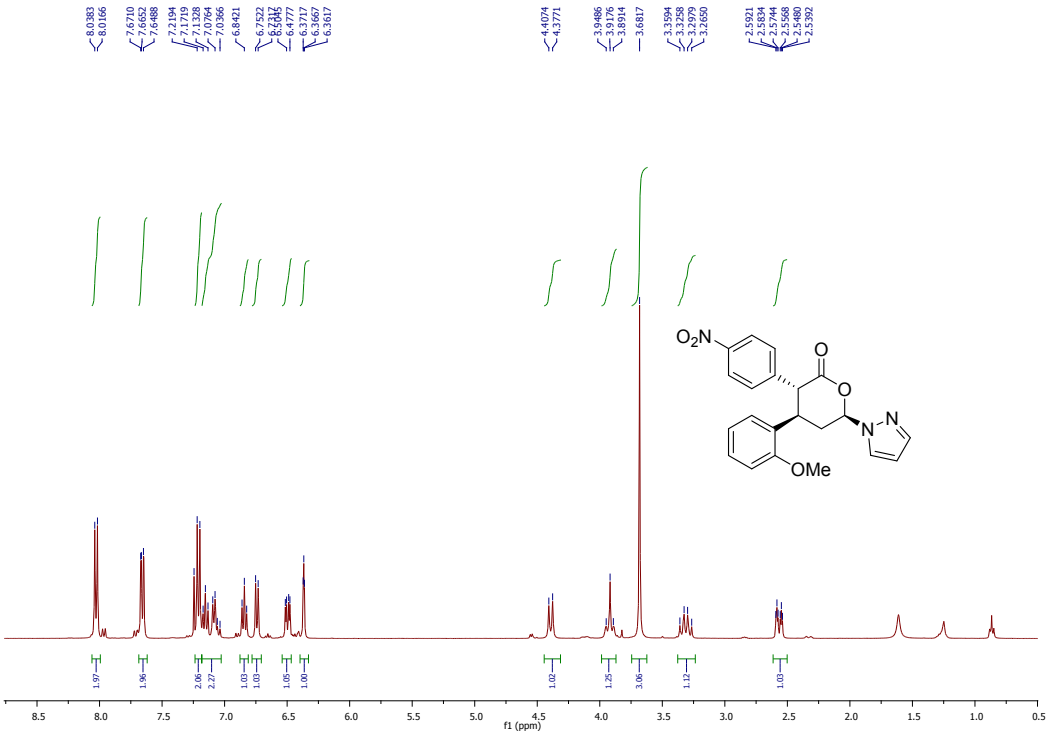
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.958	MM	2.8008	1.10257e4	65.61076	49.5185
2	41.066	MM	3.0475	1.12401e4	61.47256	50.4815

HPLC graph of compound **5a** (racemic)

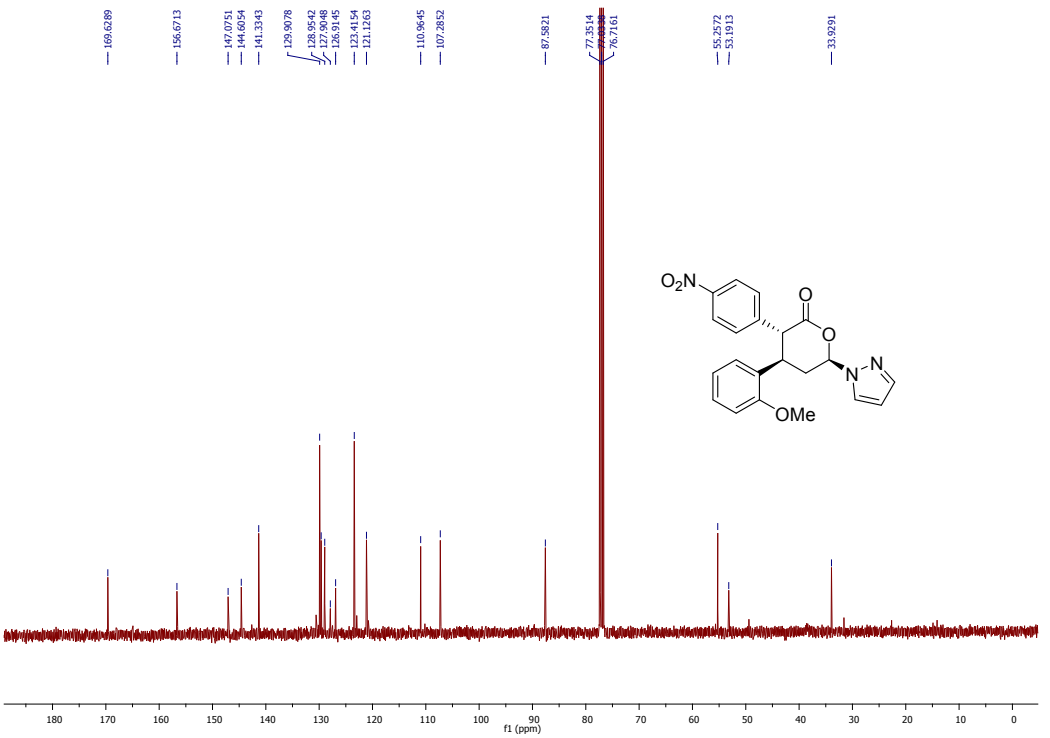


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.734	MM	1.9986	1151.33105	6.76537	3.9098
2	40.497	BB	2.6859	2.82961e4	153.69820	96.0902

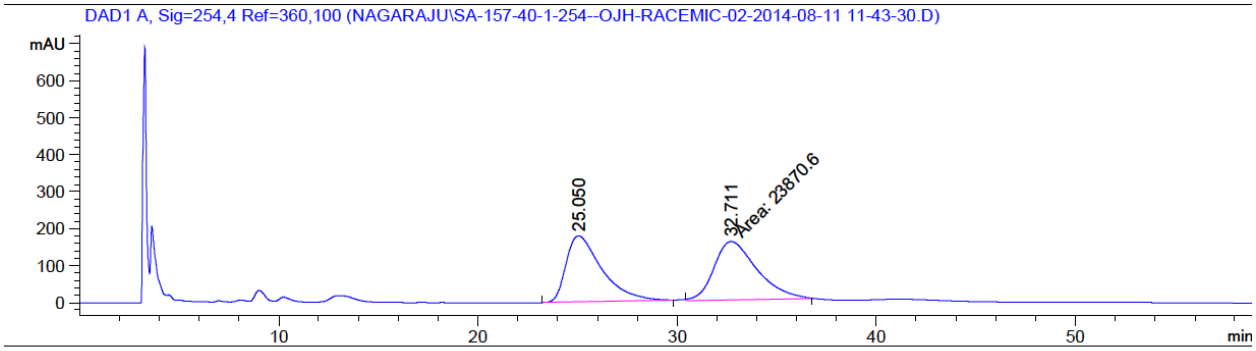
HPLC graph of compound **5a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5b** in $CDCl_3$

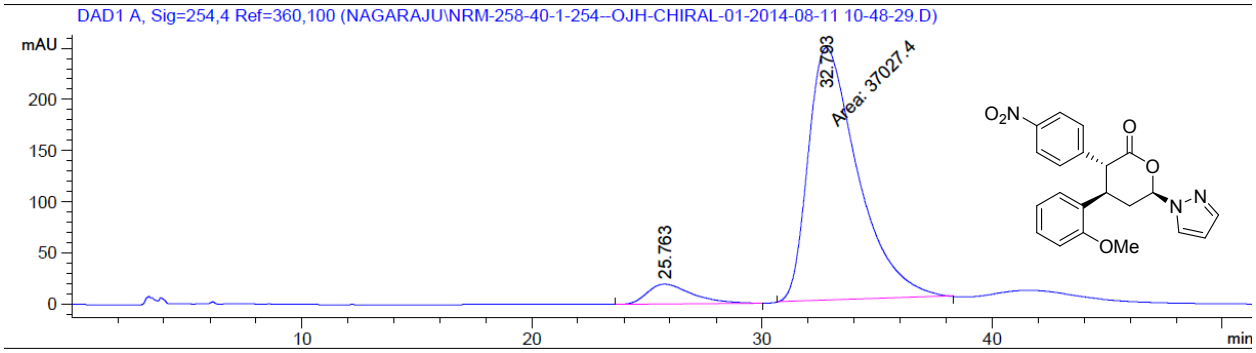


100 MHz ^{13}C NMR spectra of compound **5b** in $CDCl_3$



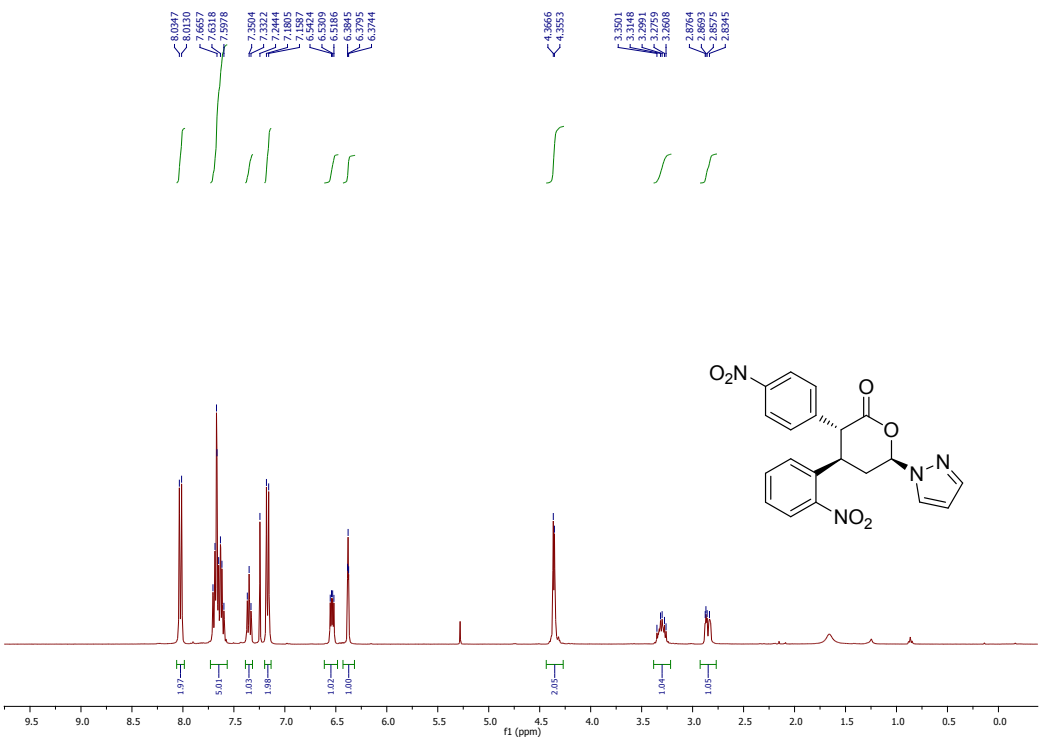
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.050	BB	1.8573	2.21975e4	178.69200	48.1841
2	32.711	MM	2.5100	2.38706e4	158.50026	51.8159

HPLC graph of compound **5b** (racemic)

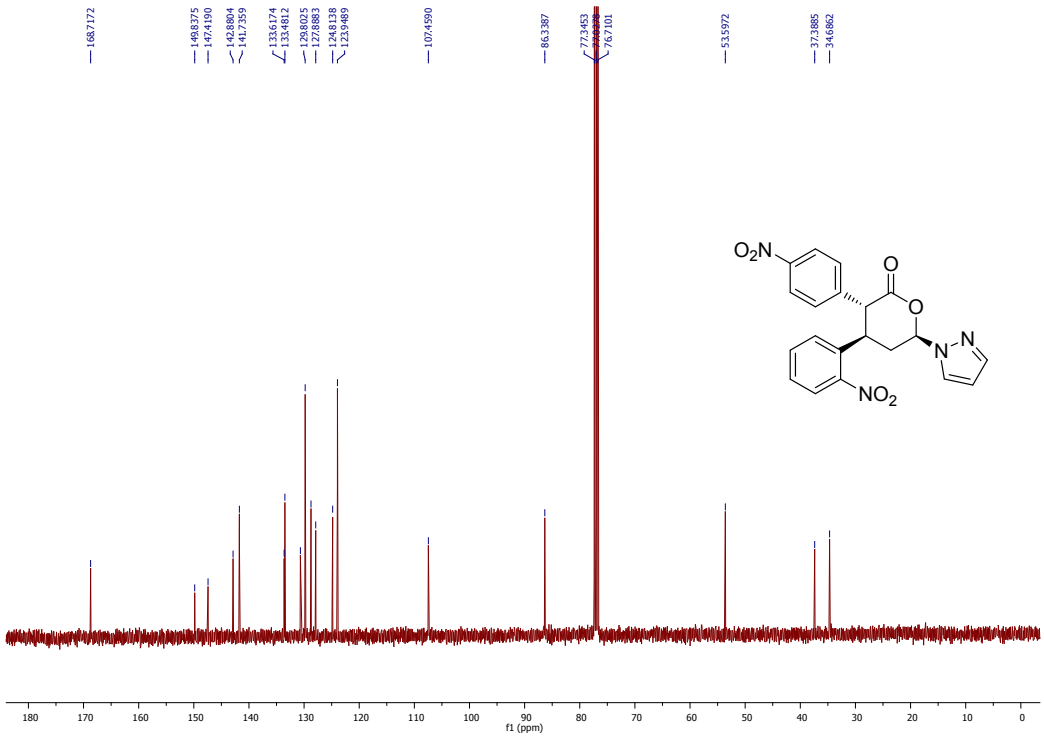


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.763	BB	1.9850	2660.49976	19.63227	6.7036
2	32.793	MM	2.4986	3.70274e4	246.98943	93.2964

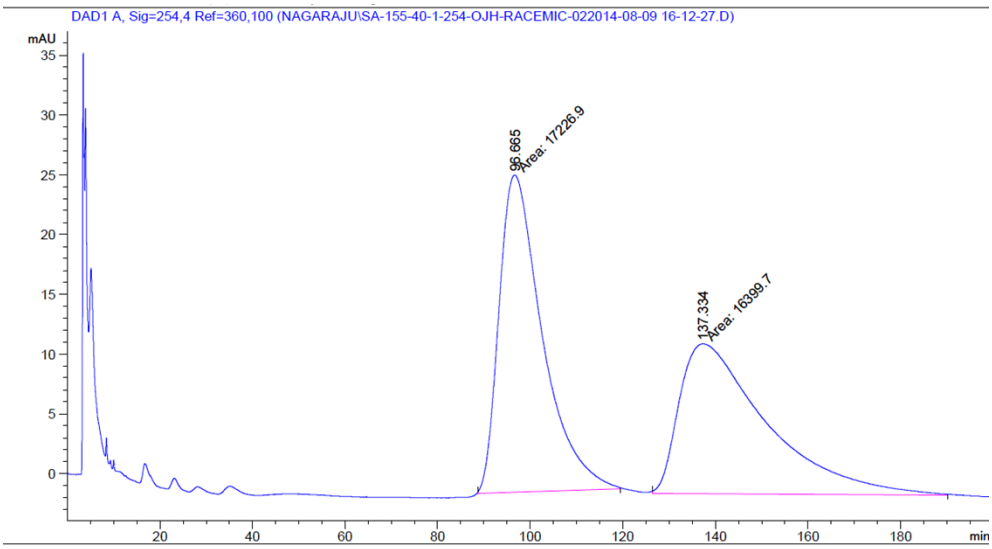
HPLC graph of compound **5b** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5c** in $CDCl_3$

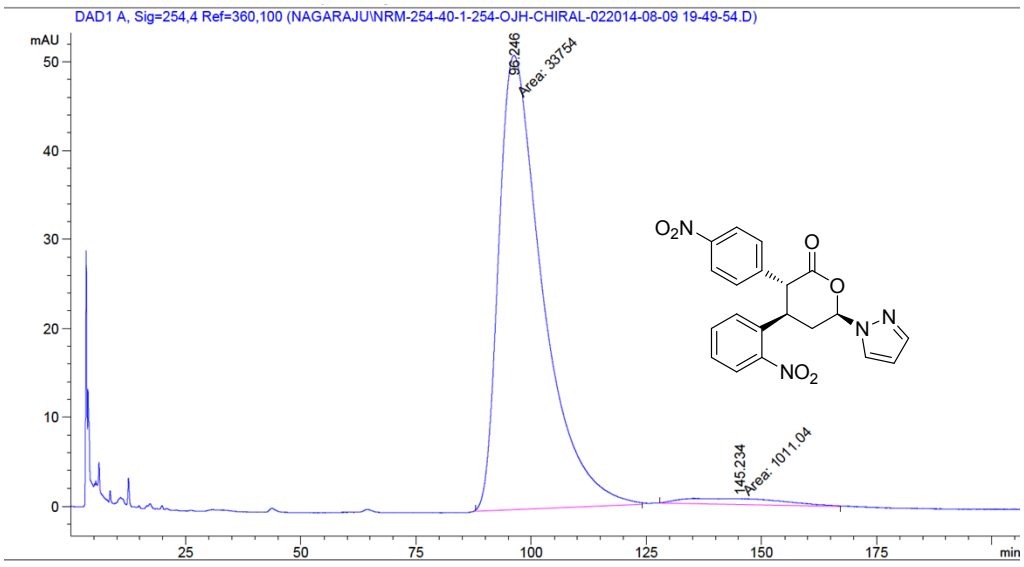


100 MHz ^{13}C NMR spectra of compound **5c** in $CDCl_3$



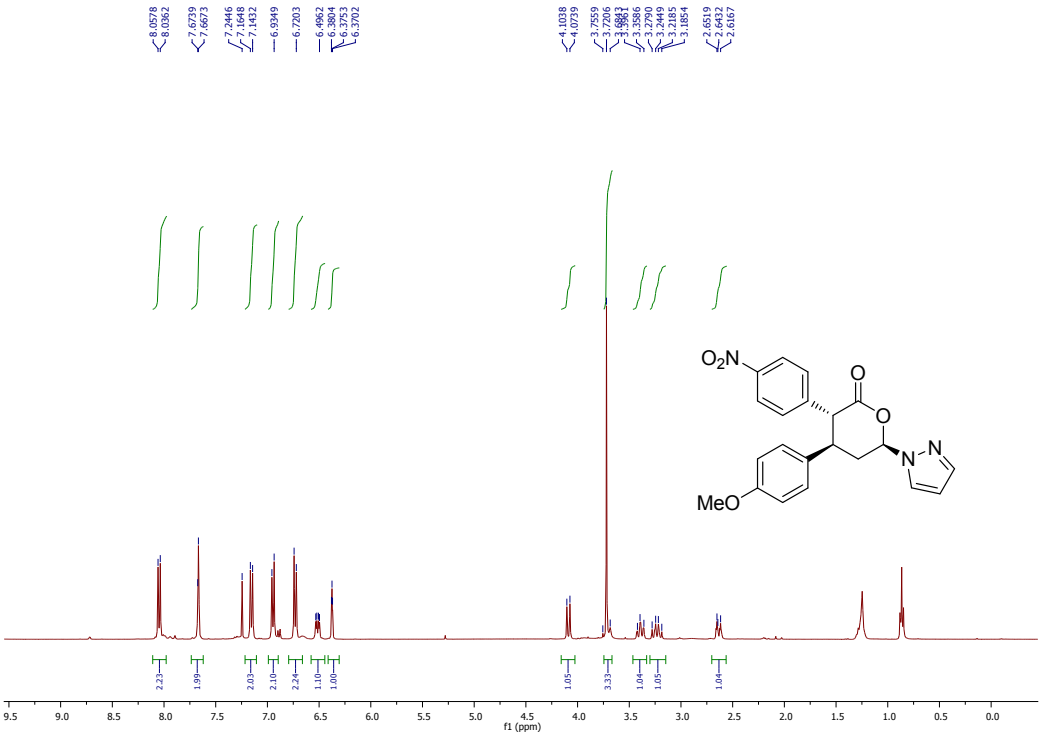
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	96.665	MM	10.8175	1.72269e4	26.54159	51.2300
2	137.334	MM	21.7938	1.63997e4	12.54156	48.7700

HPLC graph of compound **5c** (racemic)

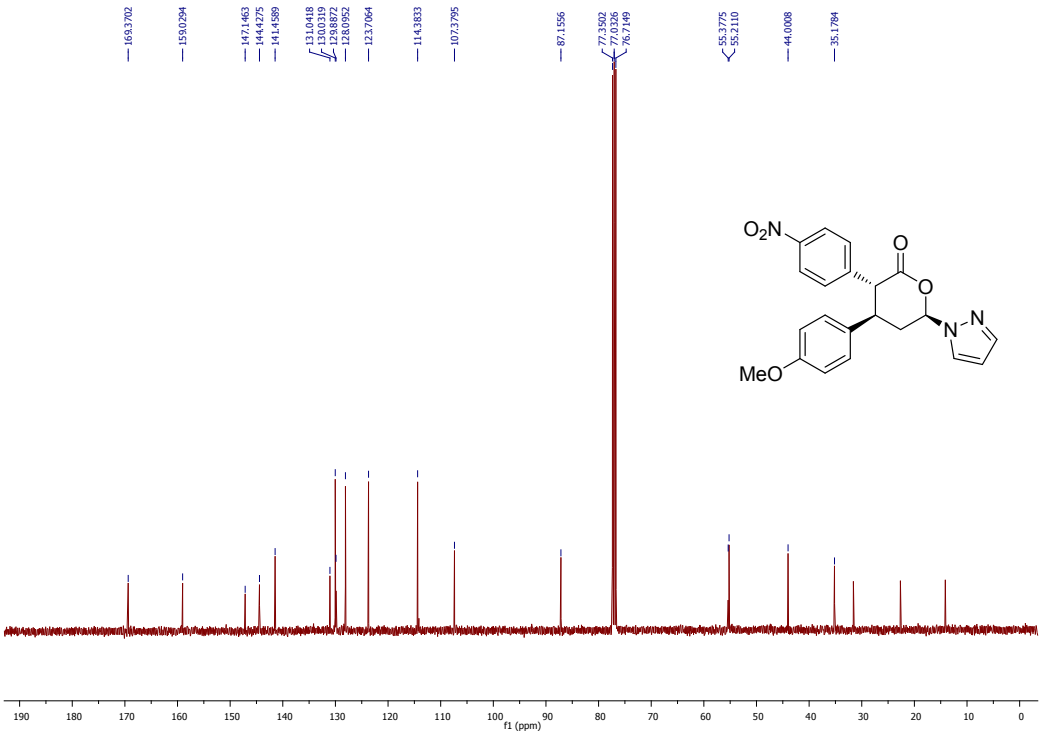


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	96.246	MM	11.0113	3.37540e4	51.08987	97.0918
2	145.234	MM	25.3842	1011.03809	6.63825e-1	2.9082

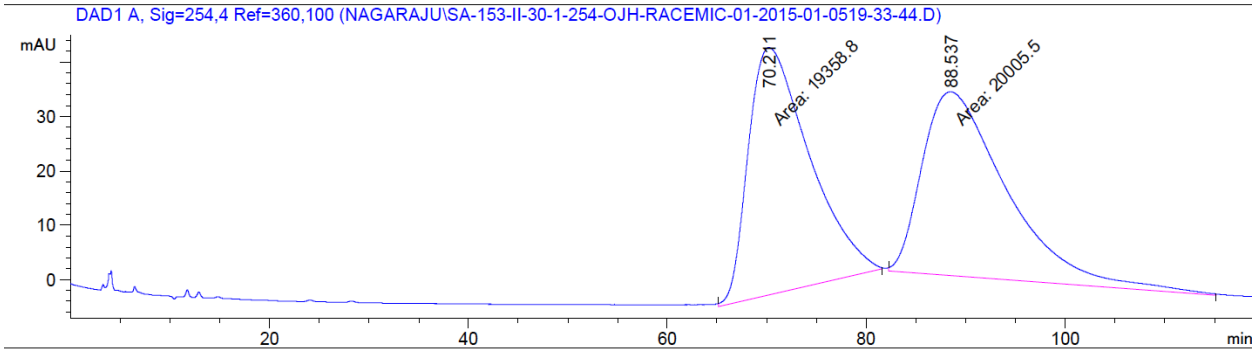
HPLC graph of compound **5c** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5d** in $CDCl_3$

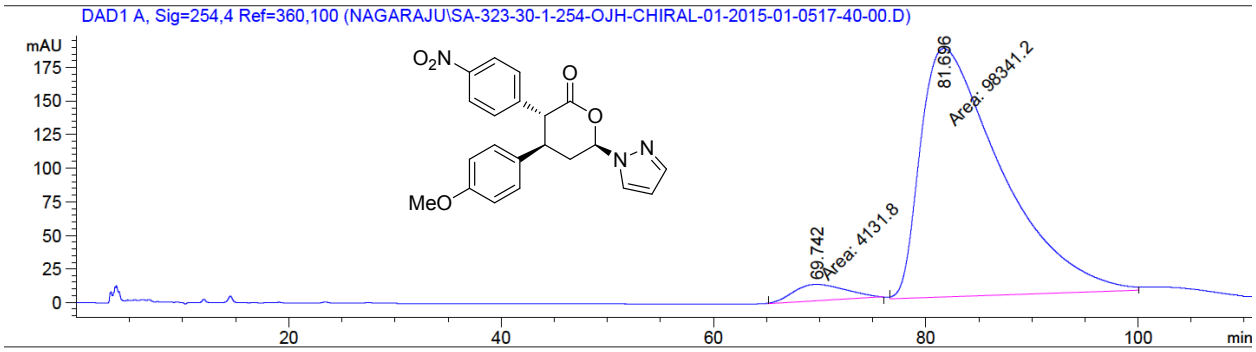


100 MHz ^{13}C NMR spectra of compound **5d** in $CDCl_3$



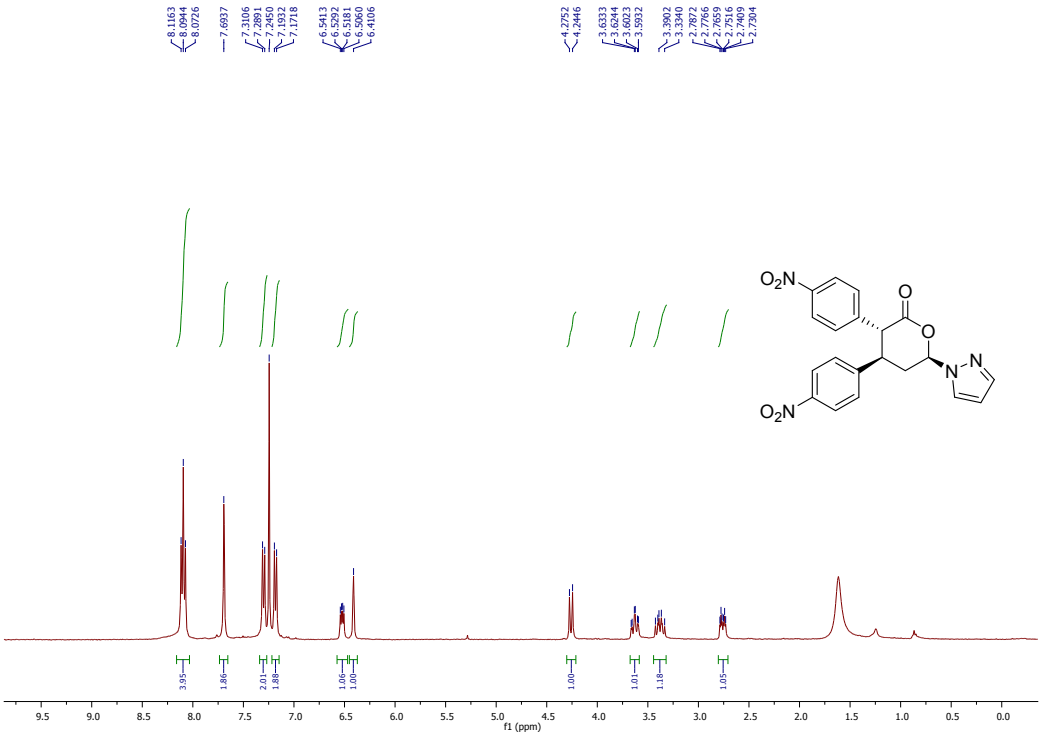
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	70.211	MM	7.0998	1.93588e4	45.44457	49.1785
2	88.537	MM	9.8741	2.00055e4	33.76781	50.8215

HPLC graph of compound **5d** (racemic)

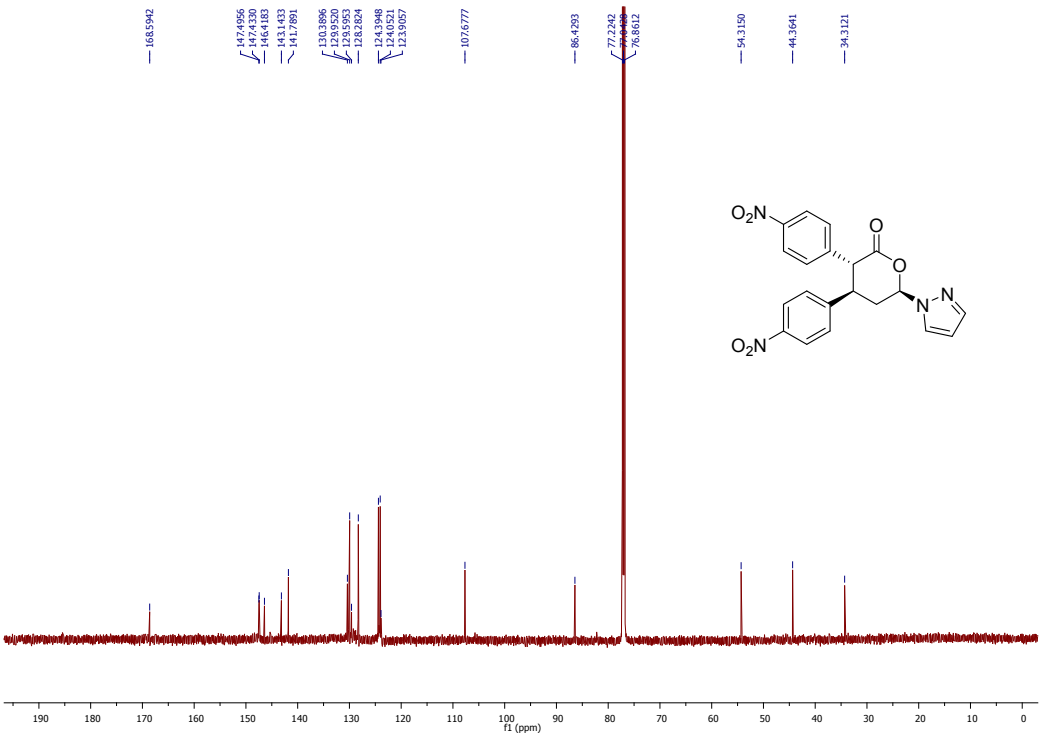


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	69.742	MM	3.9893	4131.79688	12.13707	4.0321
2	81.696	MM	8.8554	9.83412e4	185.08794	95.9679

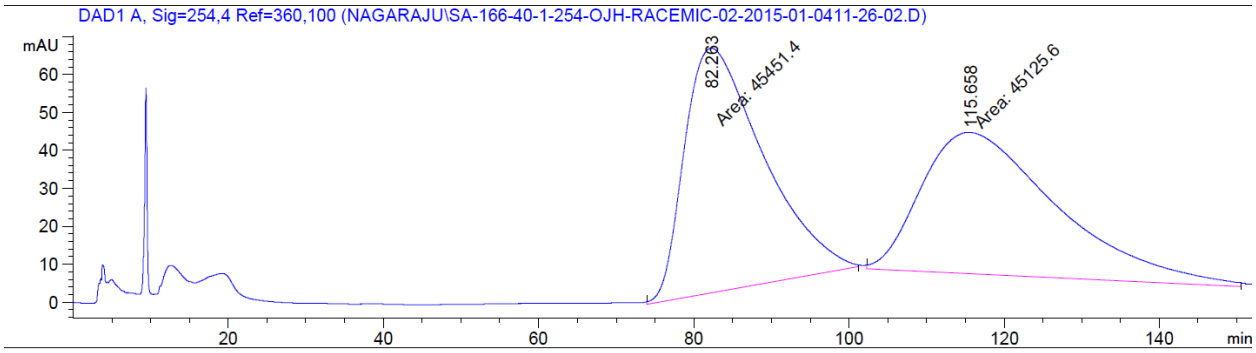
HPLC graph of compound **5d** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5e** in $CDCl_3$

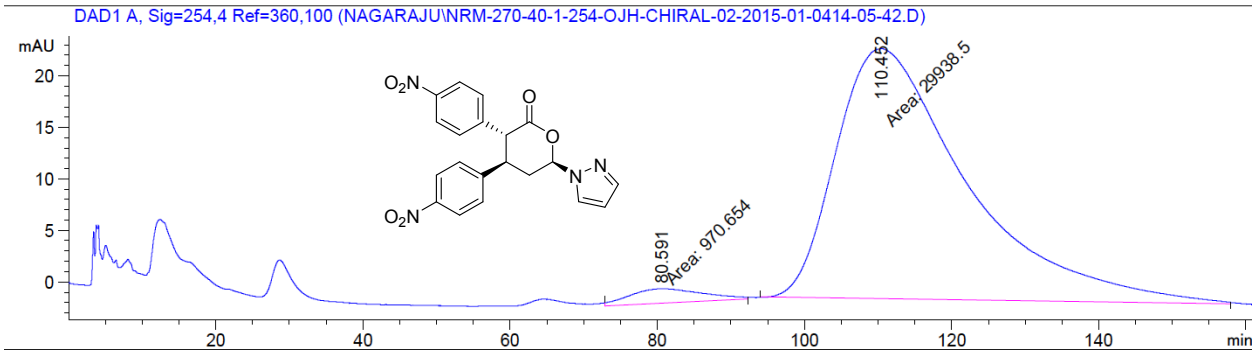


175 MHz ^{13}C NMR spectra of compound **5e** in $CDCl_3$



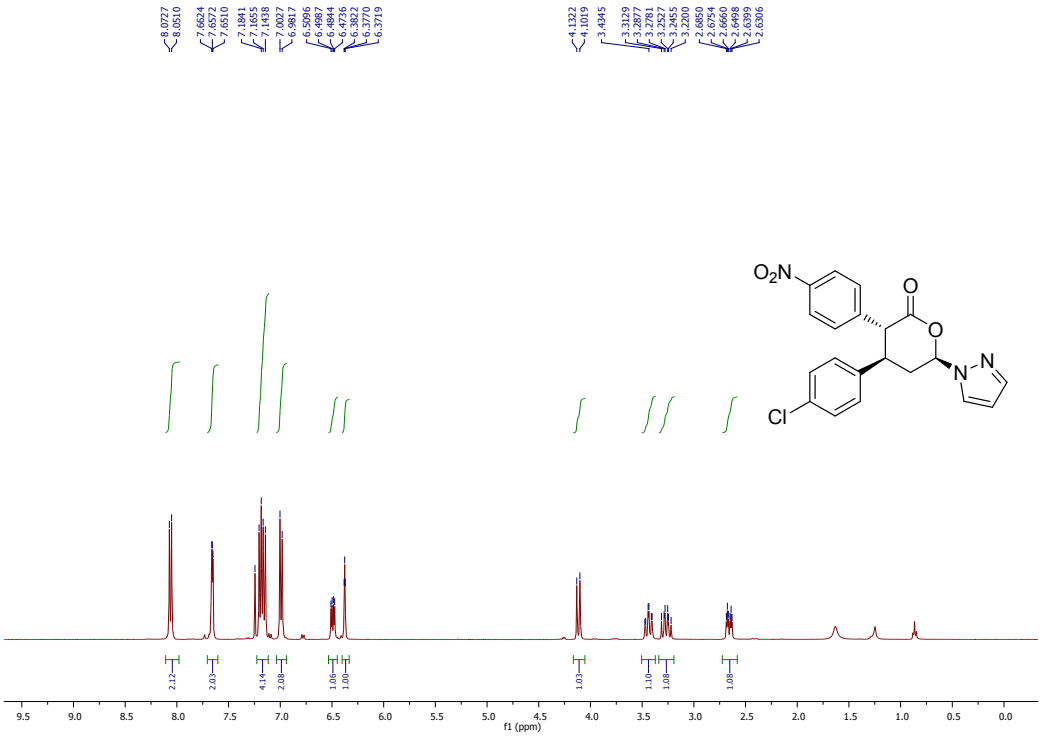
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	82.263	MM	8.2526	4.54514e4	64.42590	50.1799
2	115.658	MM	20.2442	4.51256e4	37.15102	49.8201

HPLC graph of compound **5e** (racemic)

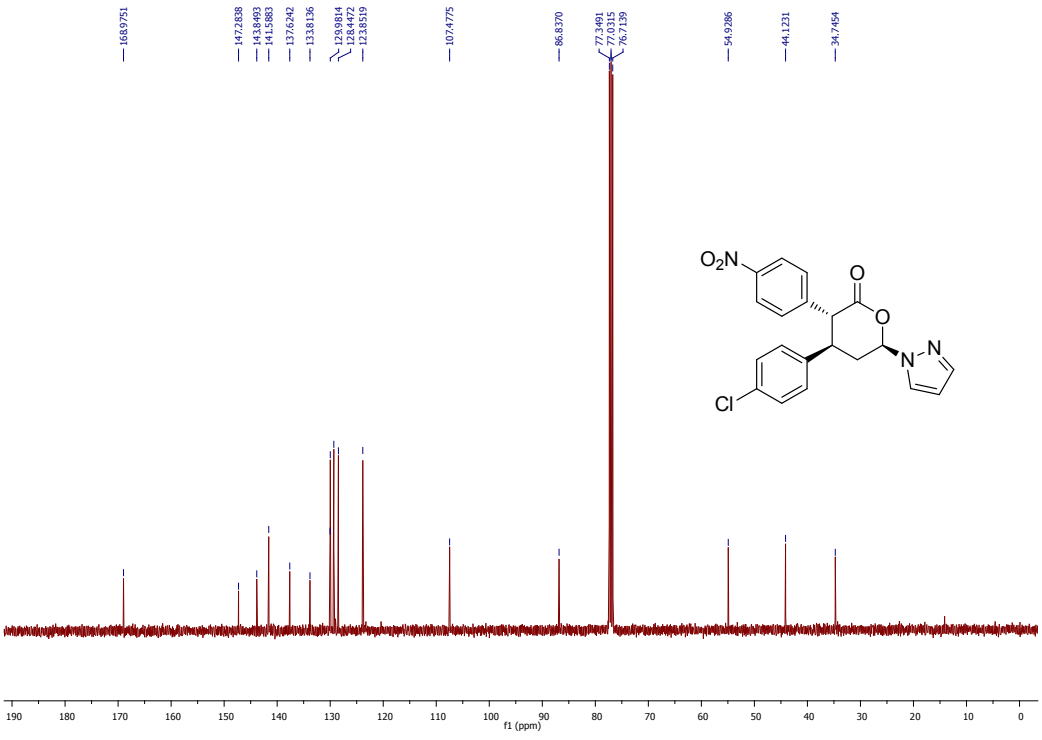


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	80.591	MM	11.6038	970.65424	1.39416	3.1403
2	110.452	MM	20.5841	2.99385e4	24.24086	96.8597

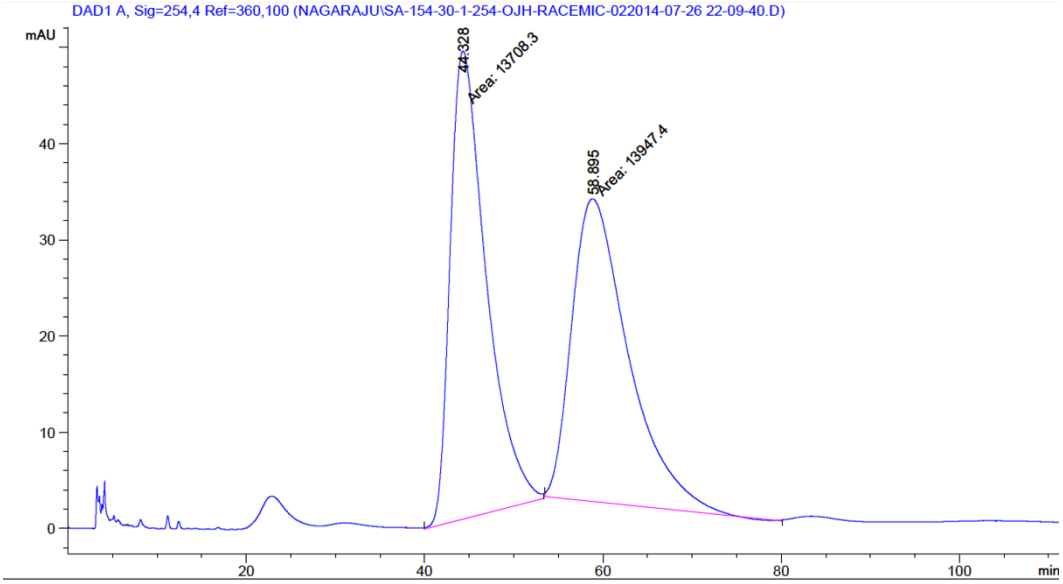
HPLC graph of compound **5e** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5f** in $CDCl_3$

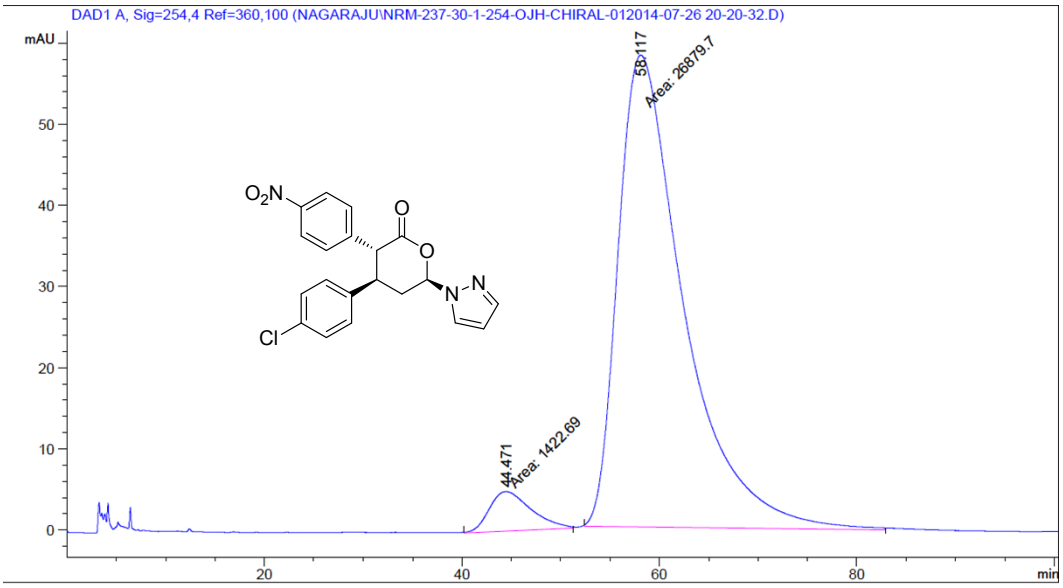


100 MHz ^{13}C NMR spectra of compound **5f** in $CDCl_3$



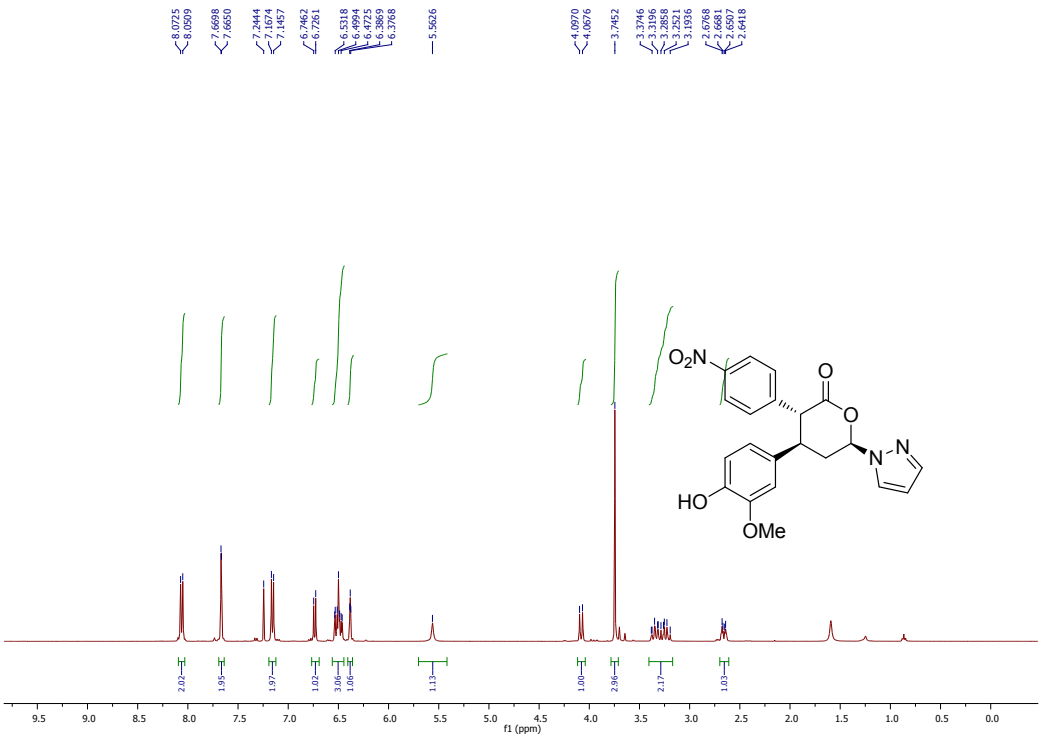
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	44.328	MM	4.6932	1.37083e4	48.68120	49.5677
2	58.895	MM	7.3850	1.39474e4	31.47661	50.4323

HPLC graph of compound **5f** (racemic)

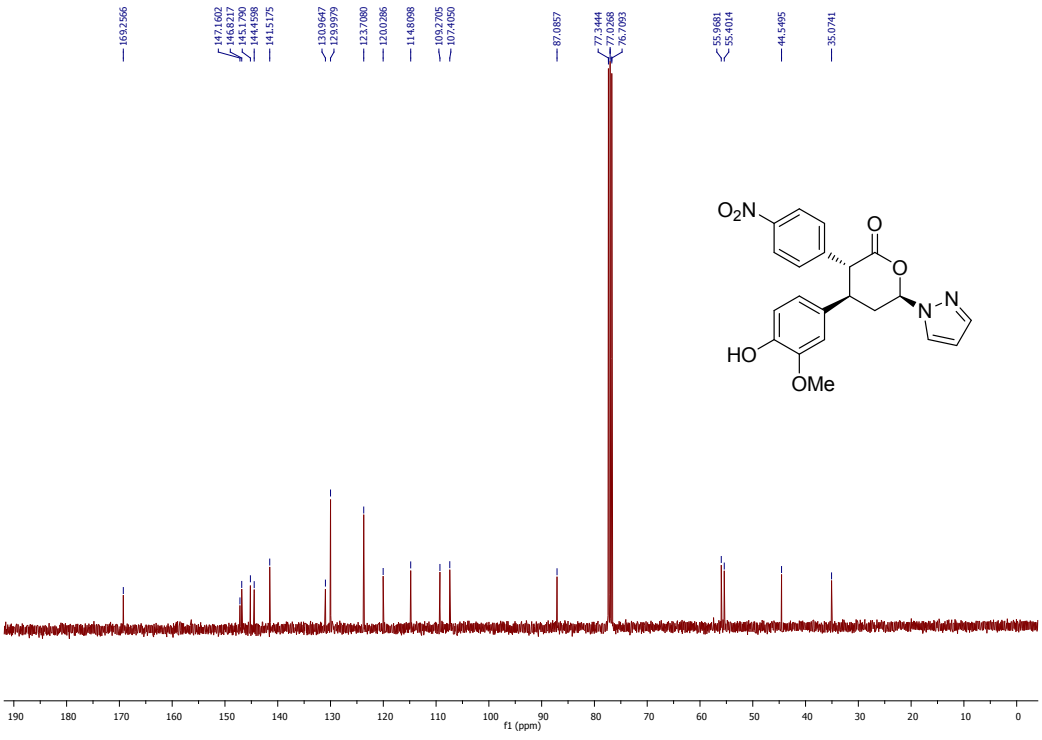


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	44.471	MM	4.8775	1422.69238	4.86136	5.0268
2	58.117	MM	7.6999	2.68797e4	58.18158	94.9732

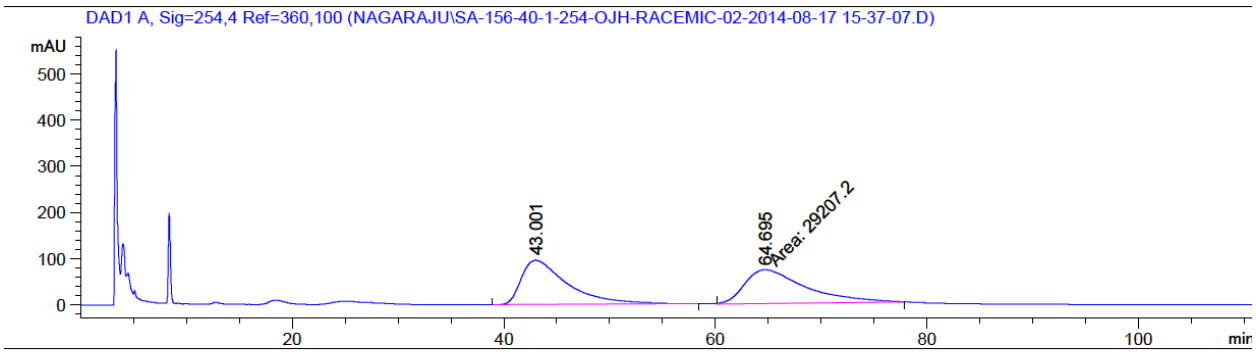
HPLC graph of compound **5f** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **5g** in $CDCl_3$

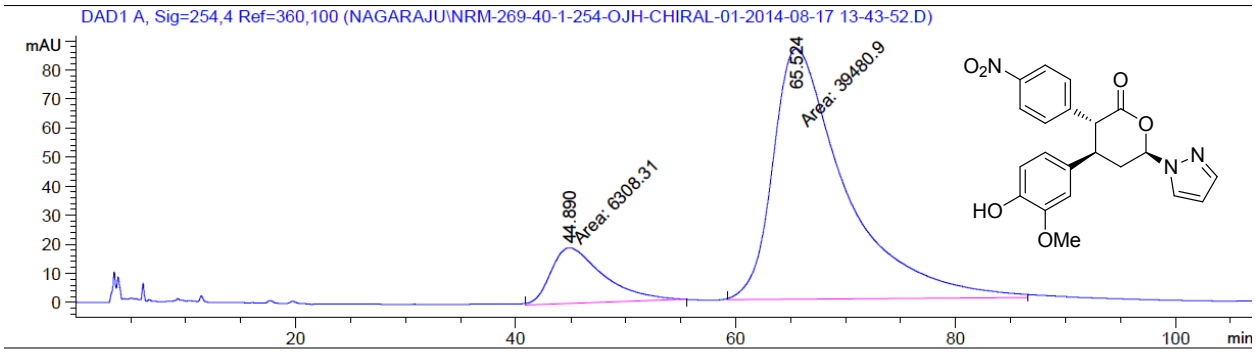


100 MHz ^{13}C NMR spectra of compound **5g** in $CDCl_3$



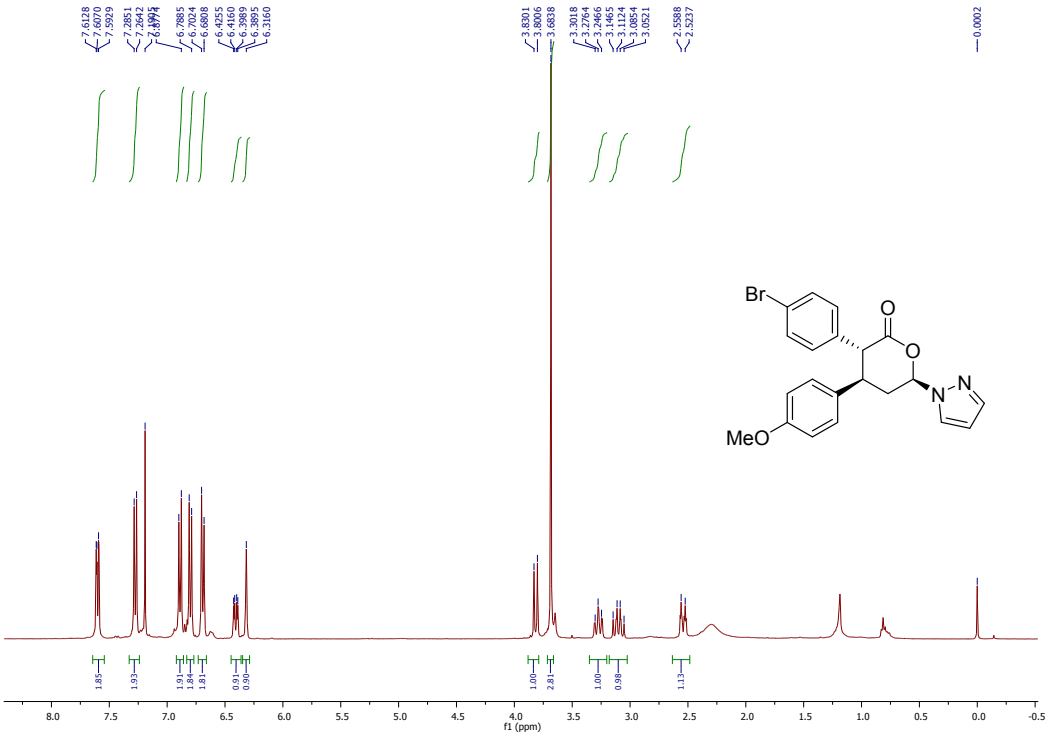
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.001	BB	4.0849	2.91866e4	95.78594	49.9824
2	64.695	MM	6.6468	2.92072e4	73.23571	50.0176

HPLC graph of compound **5g** (racemic)

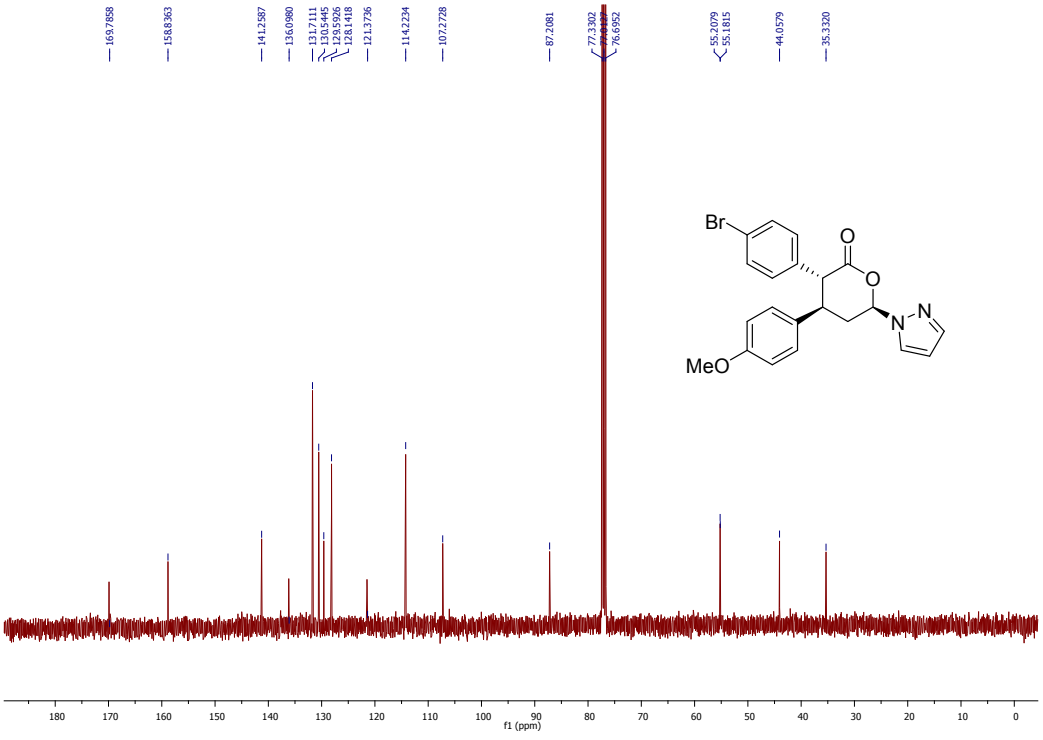


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	44.890	MM	3.8820	6308.30859	19.07043	13.7768
2	65.524	MM	7.6467	3.94809e4	86.05203	86.2232

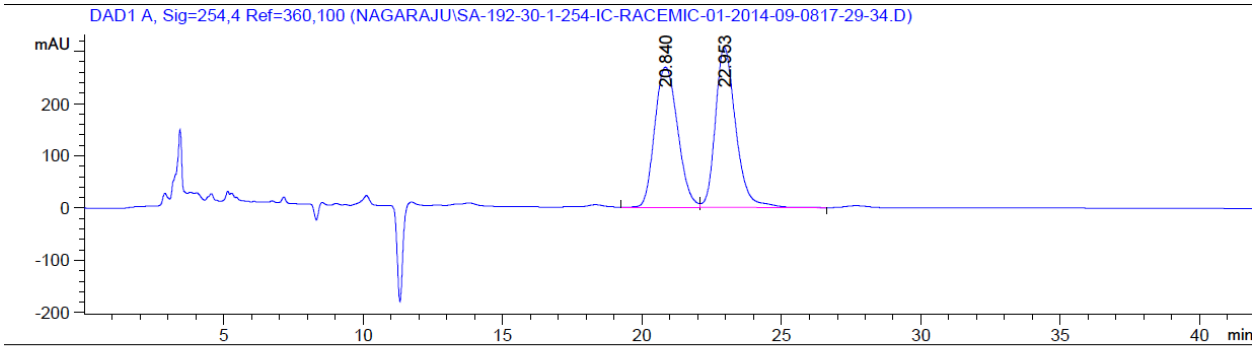
HPLC graph of compound **5g** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **6a** in $CDCl_3$

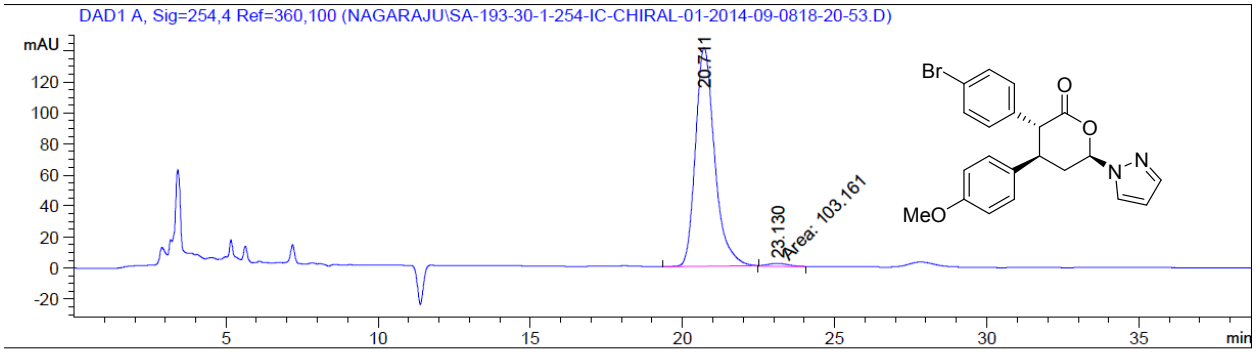


100 MHz ^{13}C NMR spectra of compound **6a** in $CDCl_3$



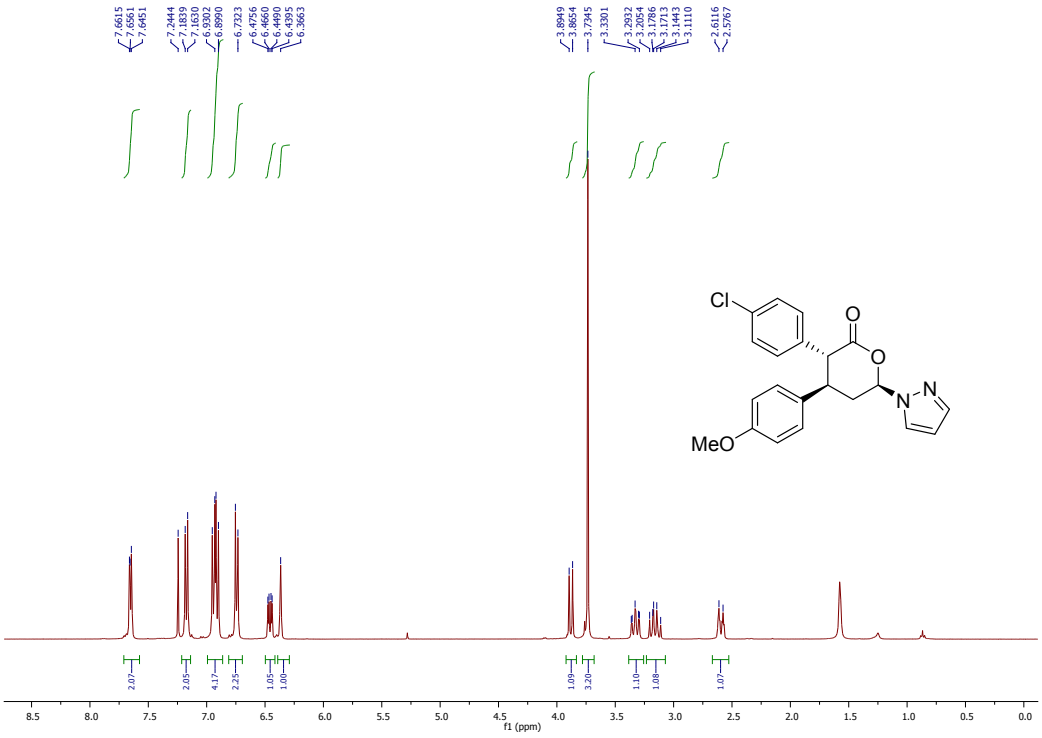
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.840	BV	0.9112	1.52855e4	268.08002	49.6953
2	22.953	VB	0.7757	1.54729e4	306.12219	50.3047

HPLC graph of compound **6a** (racemic)

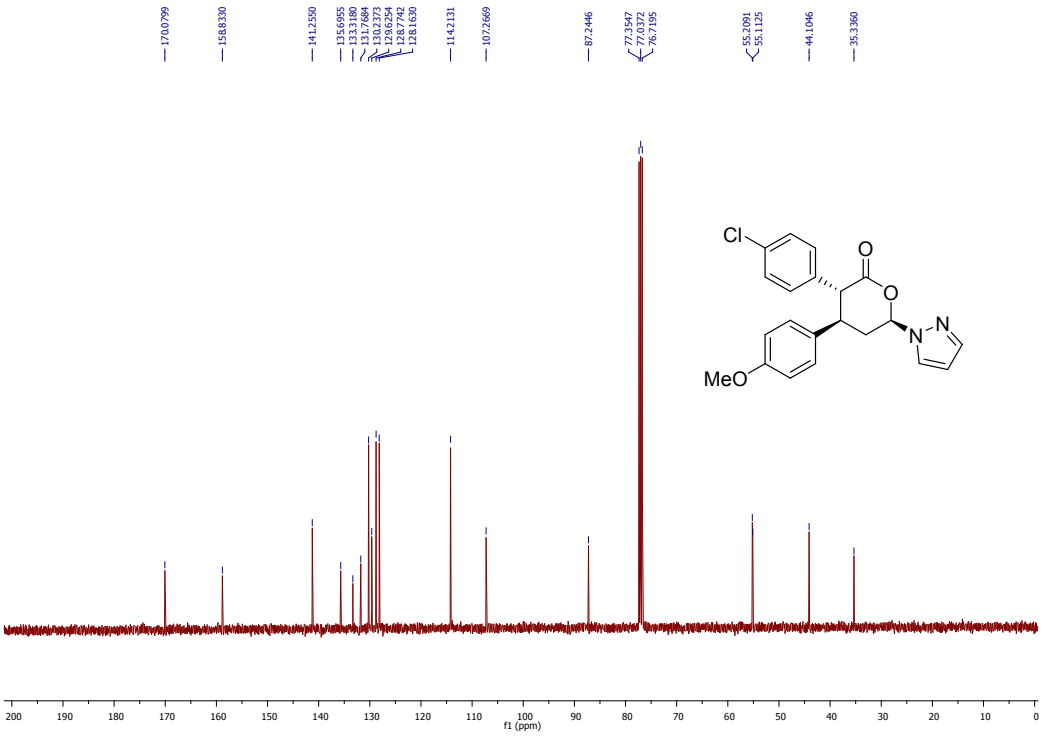


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.711	BB	0.6707	6164.95313	140.83859	98.3542
2	23.130	MM	0.8354	103.16142	2.05809	1.6458

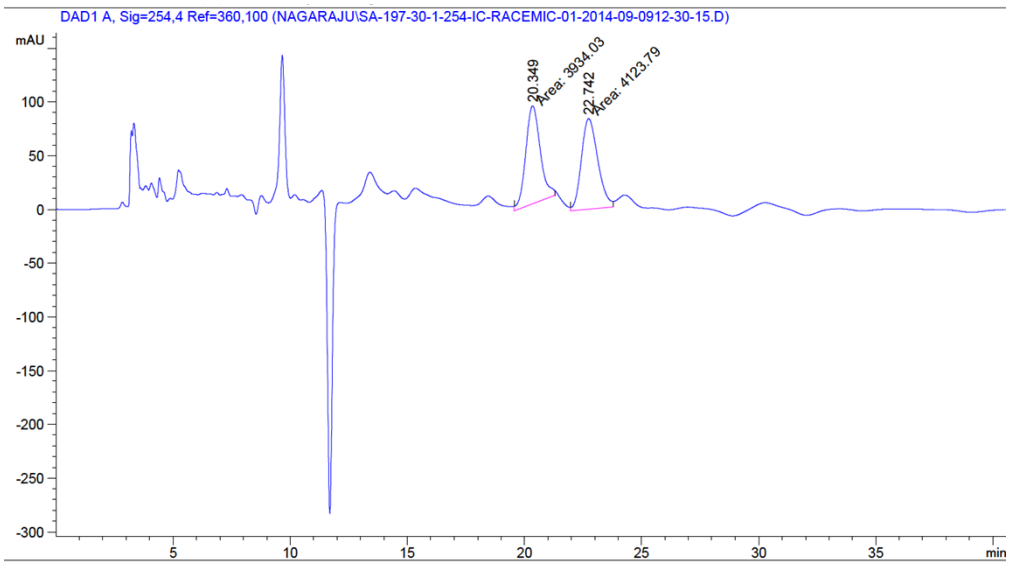
HPLC graph of compound **6a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **7a** in $CDCl_3$

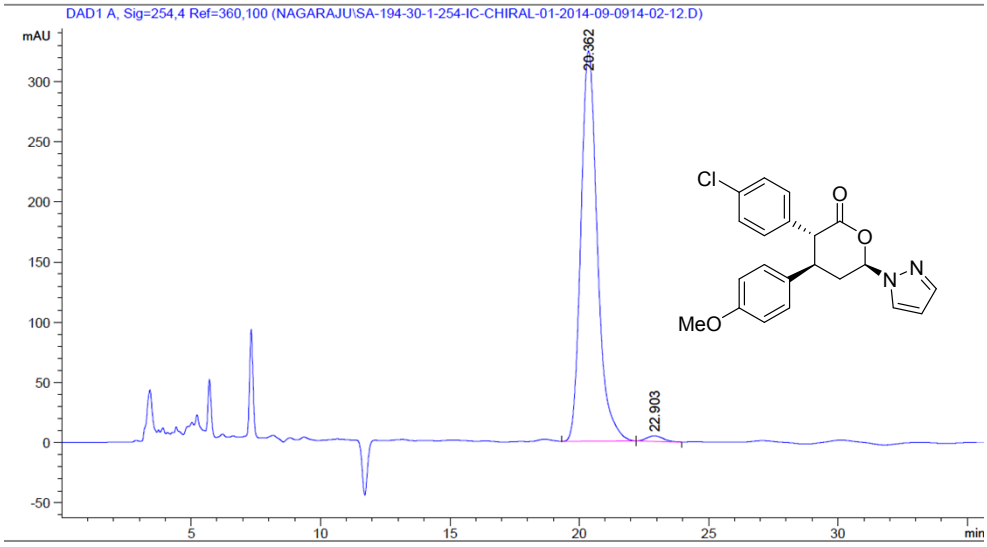


100 MHz ^{13}C NMR spectra of compound **7a** in $CDCl_3$



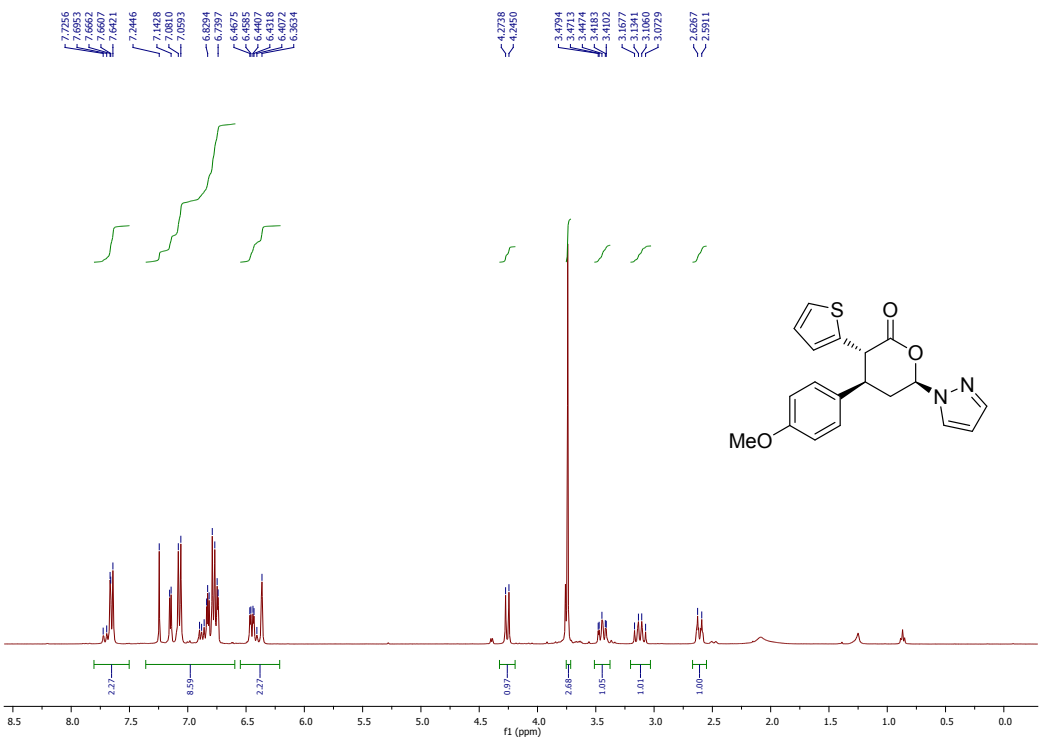
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.349	MM	0.7194	3934.03296	91.14014	48.8226
2	22.742	MM	0.8145	4123.78516	84.38293	51.1774

HPLC graph of compound **7a** (racemic)

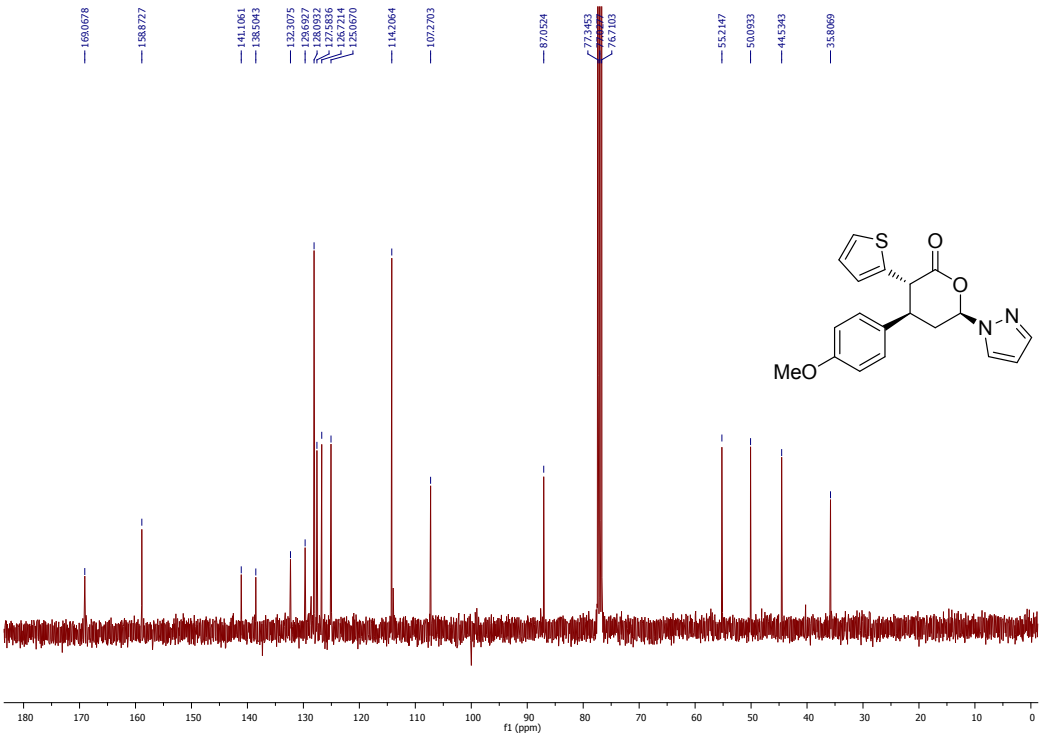


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.362	BB	0.6800	1.43320e4	324.02551	98.6708
2	22.903	BB	0.6638	193.07199	4.48895	1.3292

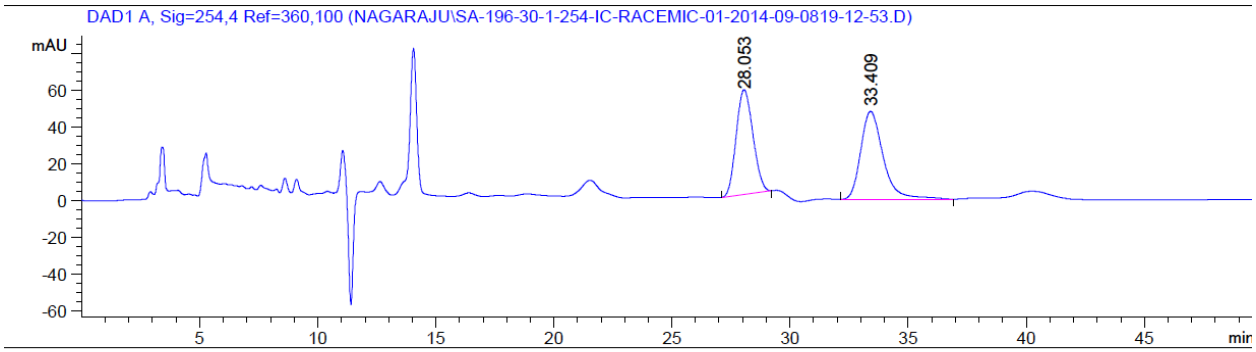
HPLC graph of compound **7a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **8a** in $CDCl_3$

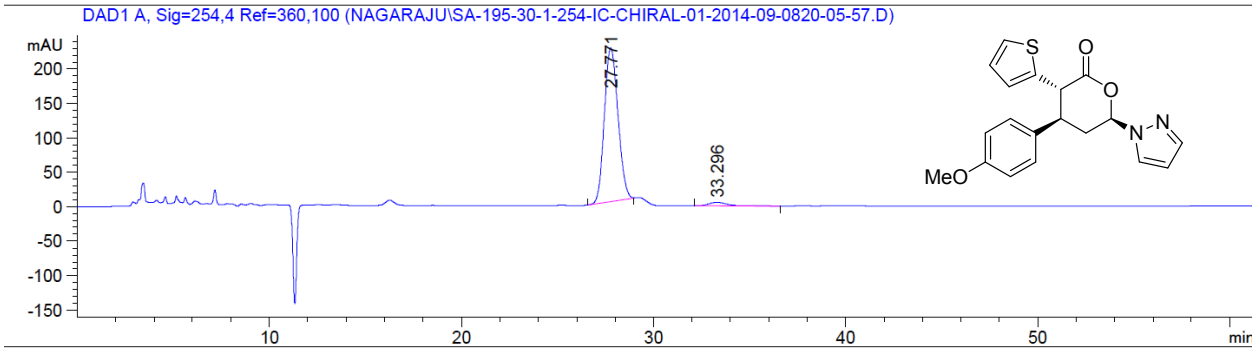


100 MHz ^{13}C NMR spectra of compound **8a** in $CDCl_3$



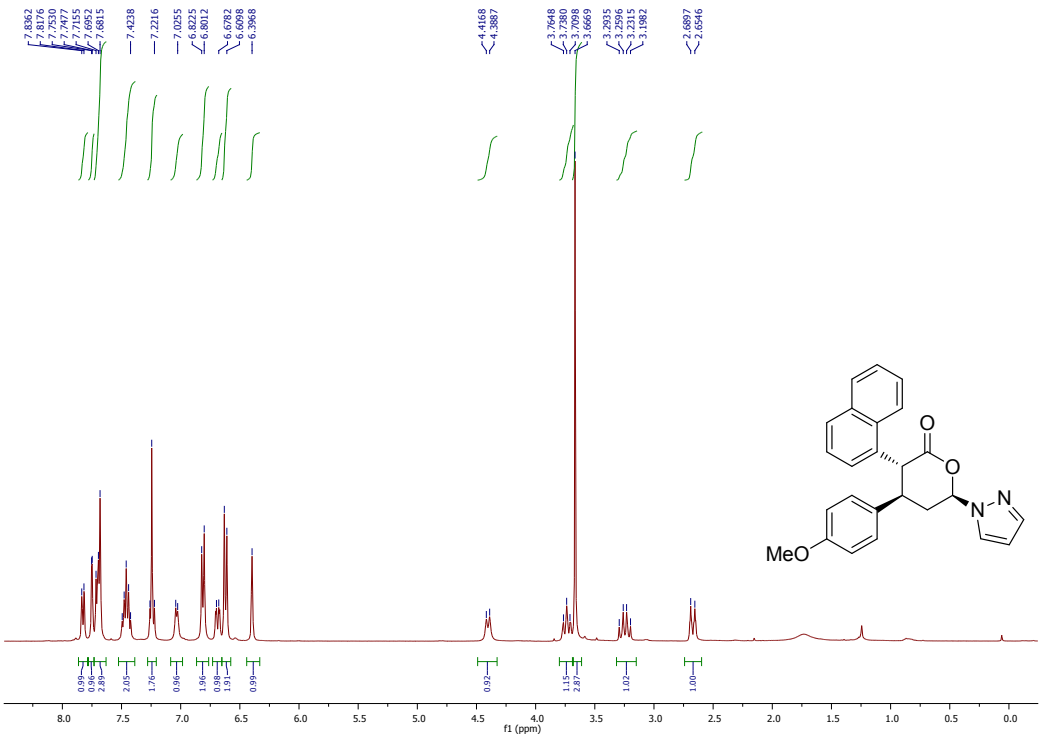
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.053	BB	0.7798	2810.26440	56.94290	47.1477
2	33.409	BB	1.0093	3150.28516	47.77608	52.8523

HPLC graph of compound **8a** (racemic)

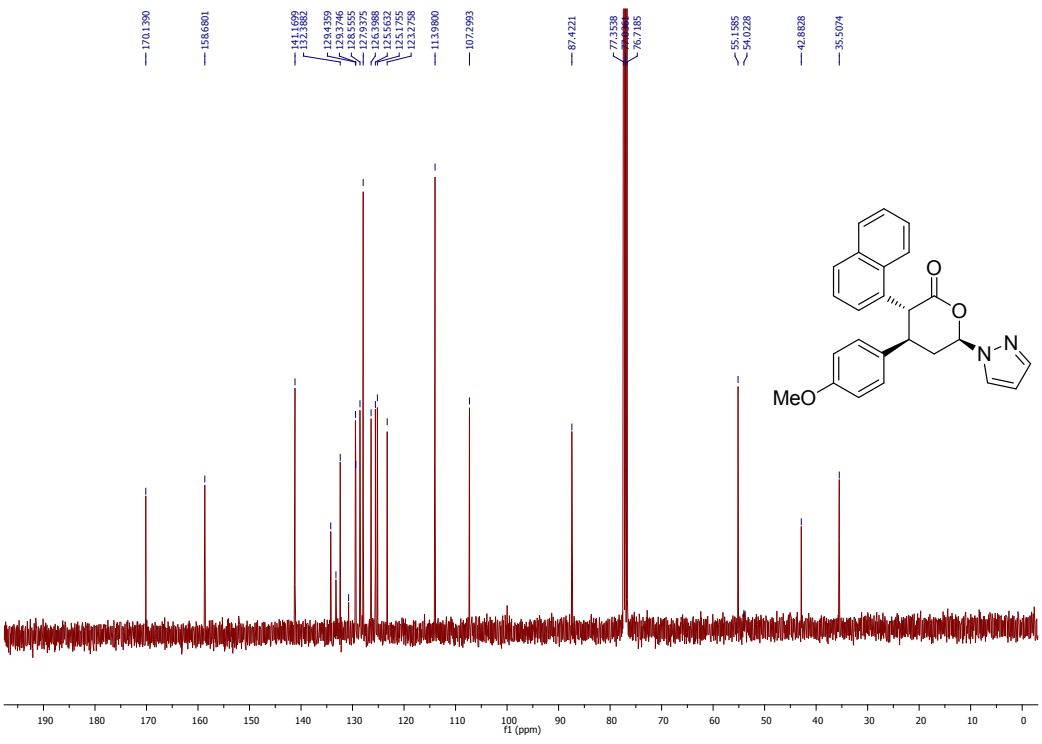


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.771	BB	0.7719	1.09614e4	222.82465	96.9673
2	33.296	BB	0.9804	342.81912	5.09867	3.0327

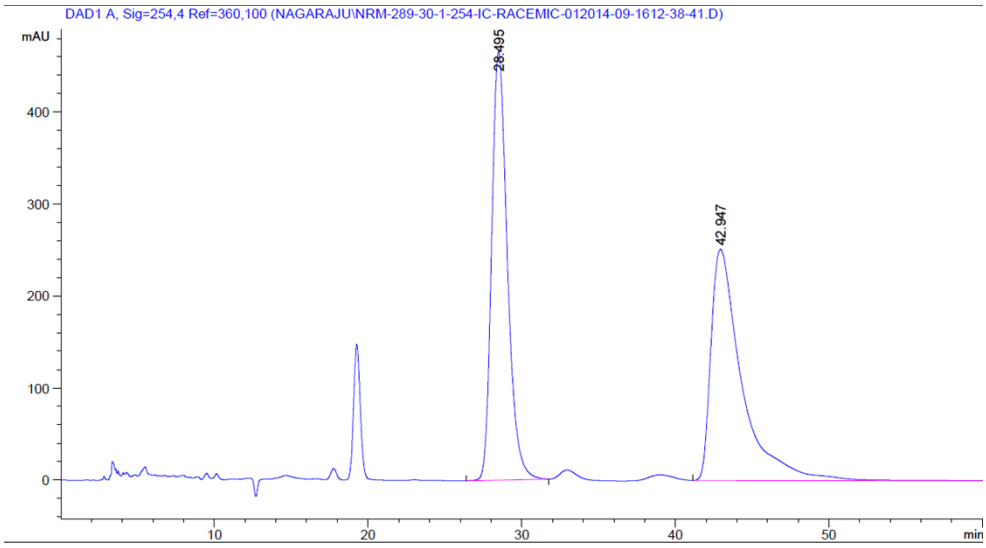
HPLC graph of compound **8a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **9a** in $CDCl_3$

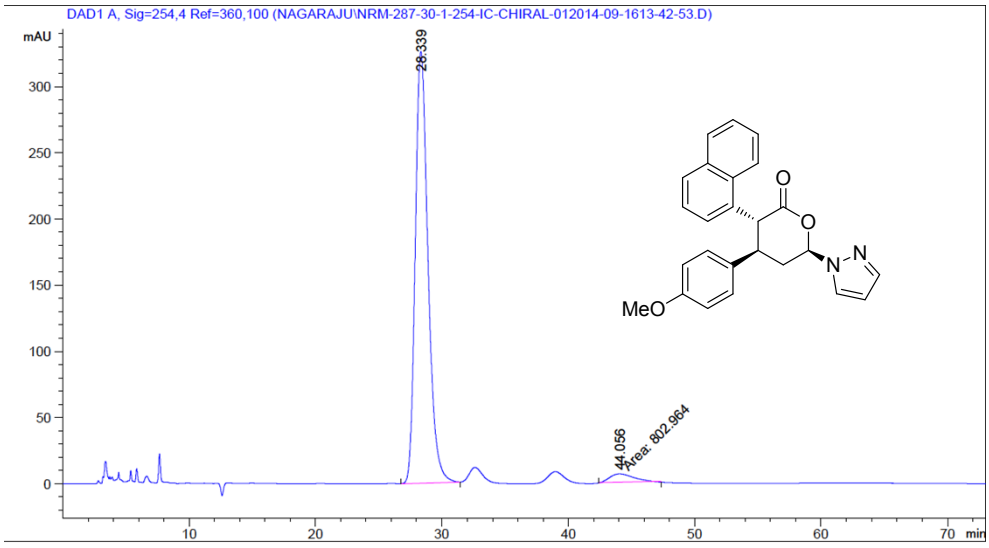


100 MHz ^{13}C NMR spectra of compound **9a** in $CDCl_3$



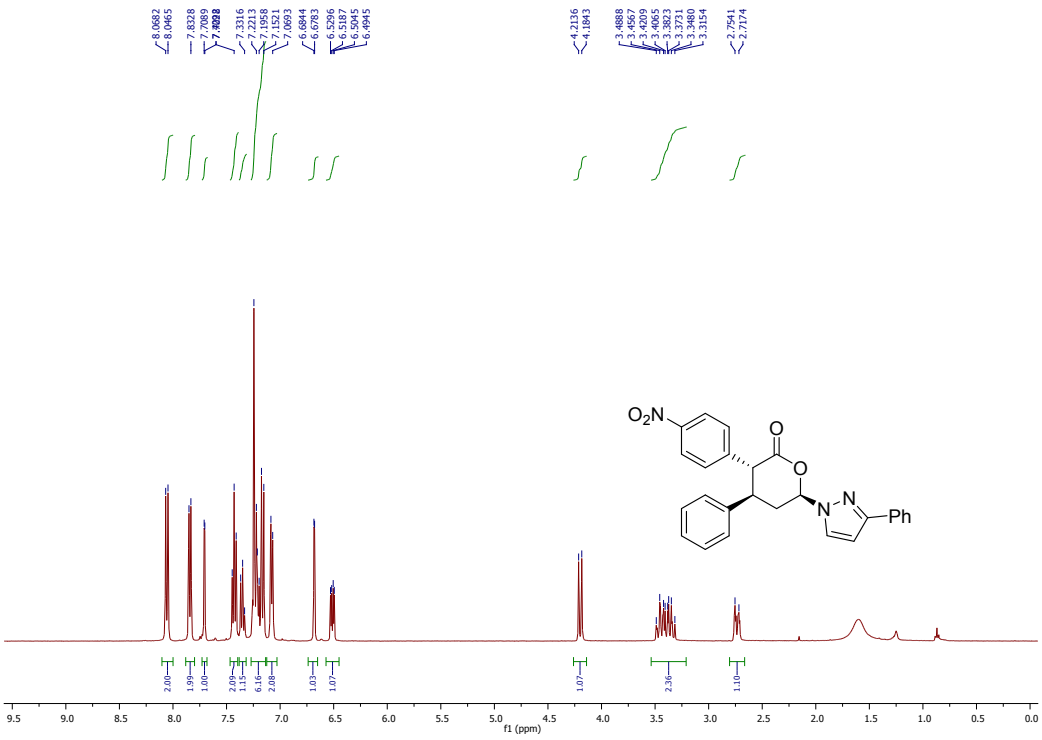
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.495	BB	1.0905	3.30943e4	465.99896	48.6040
2	42.947	BBA	2.0320	3.49954e4	251.41054	51.3960

HPLC graph of compound **9a** (racemic)

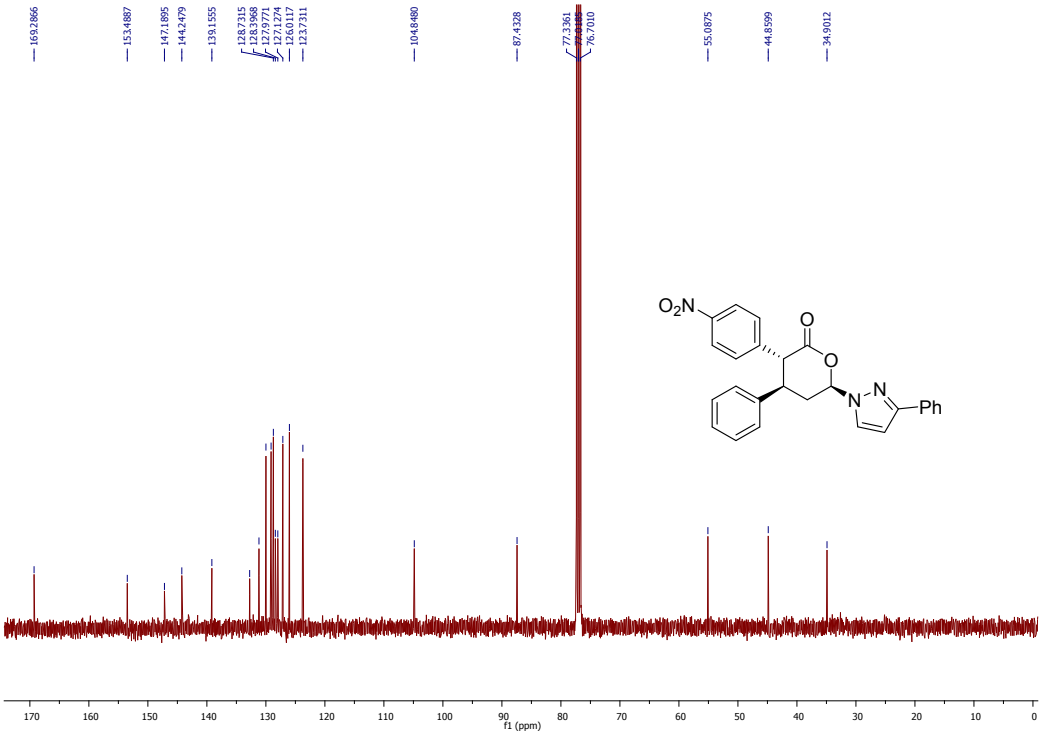


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.339	BB	1.0716	2.27390e4	326.07532	96.5892
2	44.056	MM	2.1239	802.96448	6.30090	3.4108

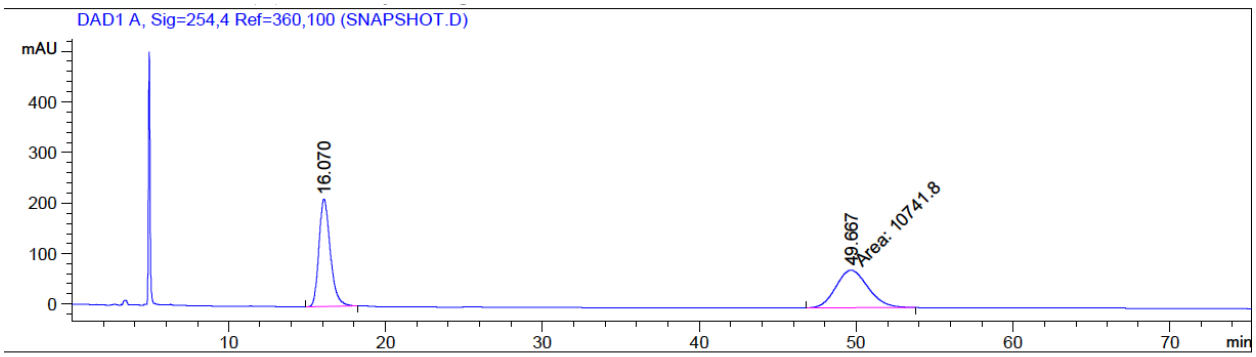
HPLC graph of compound **9a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **11a** in $CDCl_3$

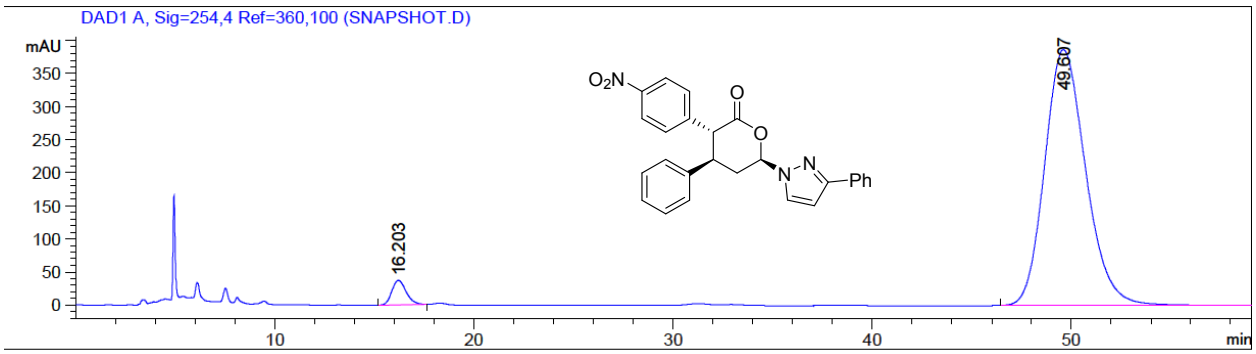


100 MHz ^{13}C NMR spectra of compound **11a** in $CDCl_3$



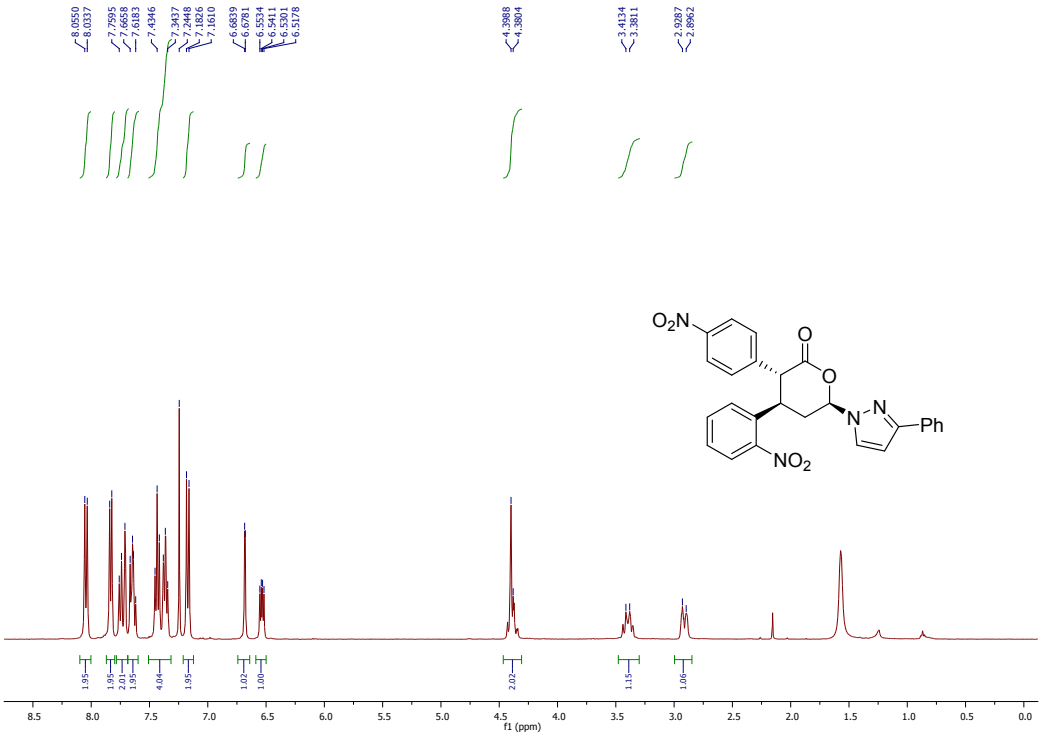
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.070	BB	0.7722	1.07350e4	212.94171	49.9841
2	49.667	MM	2.4013	1.07418e4	74.55523	50.0159

HPLC graph of compound **11a** (racemic)

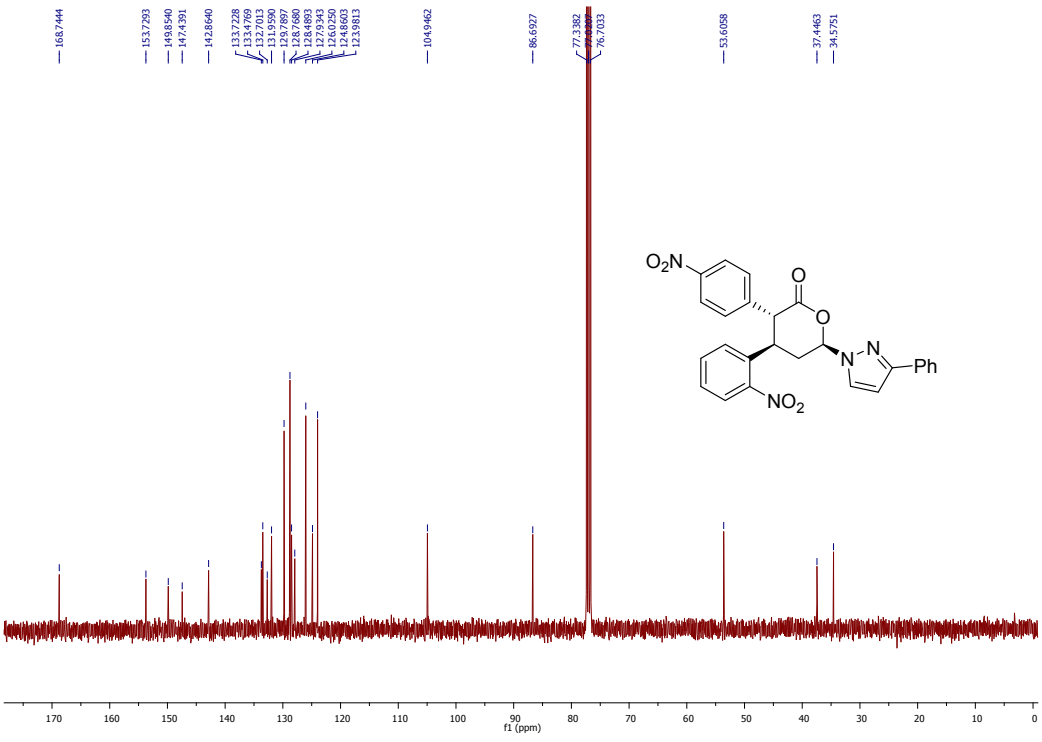


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.203	BB	0.7739	1875.61011	37.34915	3.2756
2	49.607	BBA	2.1235	5.53851e4	386.58389	96.7244

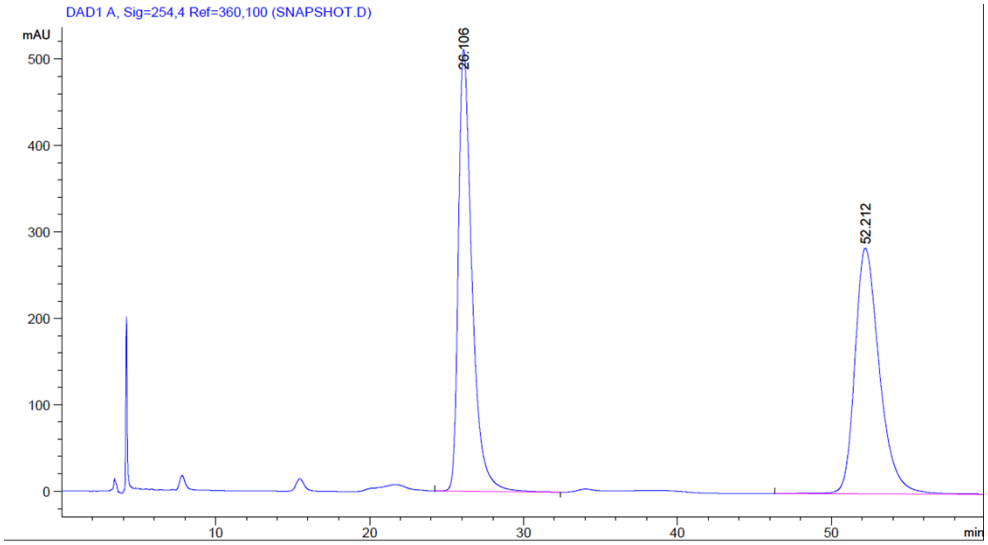
HPLC graph of compound **11a** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **11c** in $CDCl_3$

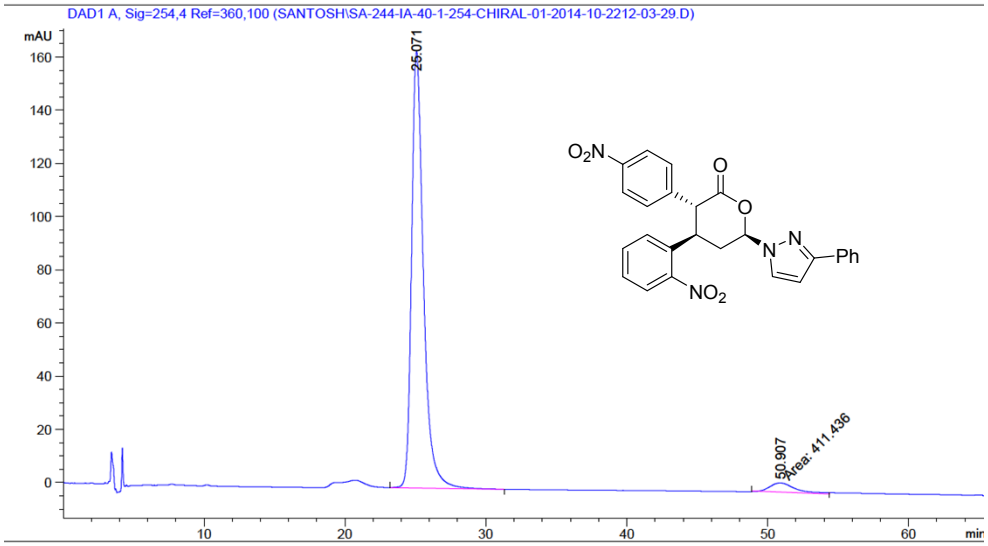


100 MHz ^{13}C NMR spectra of compound **11c** in $CDCl_3$



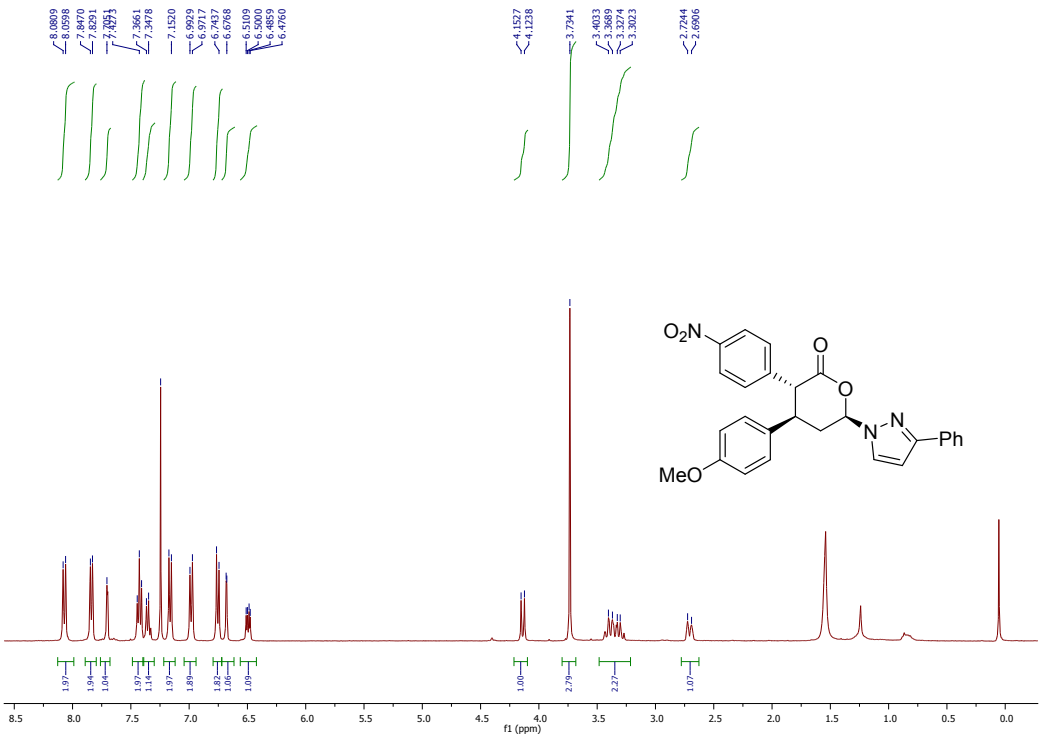
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.106	BB	0.9283	3.14569e4	510.94553	49.9772
2	52.212	BBA	1.6859	3.14856e4	284.32440	50.0228

HPLC graph of compound **11c** (racemic)

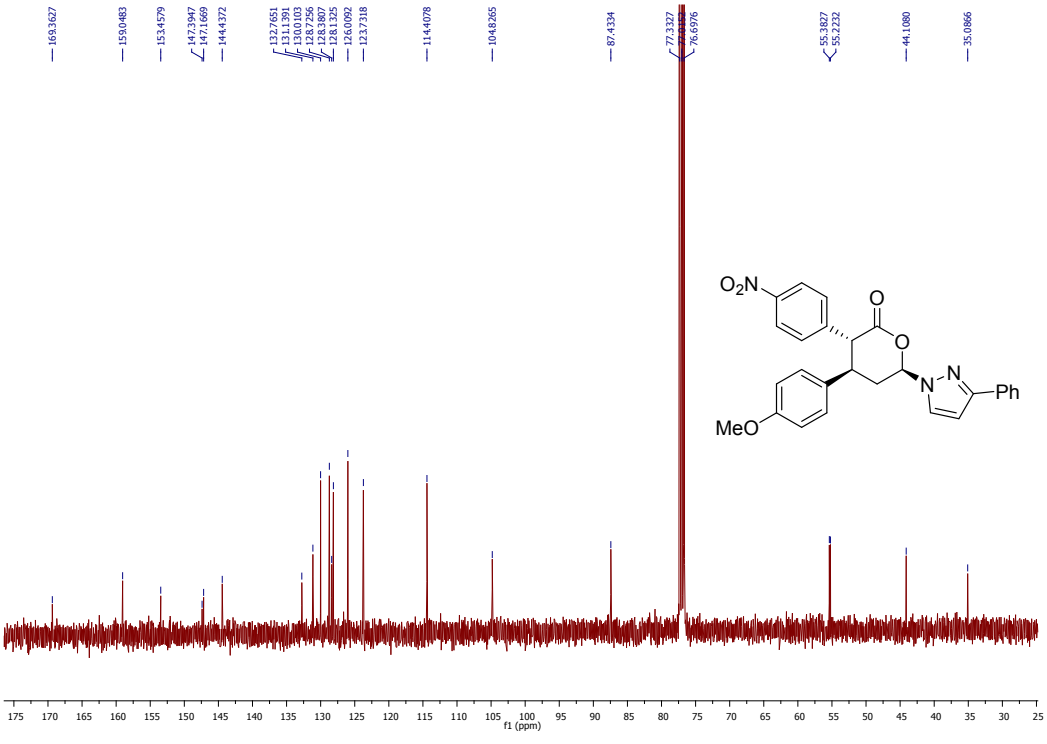


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.071	BB	0.8803	9607.15918	164.28012	95.8933
2	50.907	MM	2.0265	411.43637	3.38387	4.1067

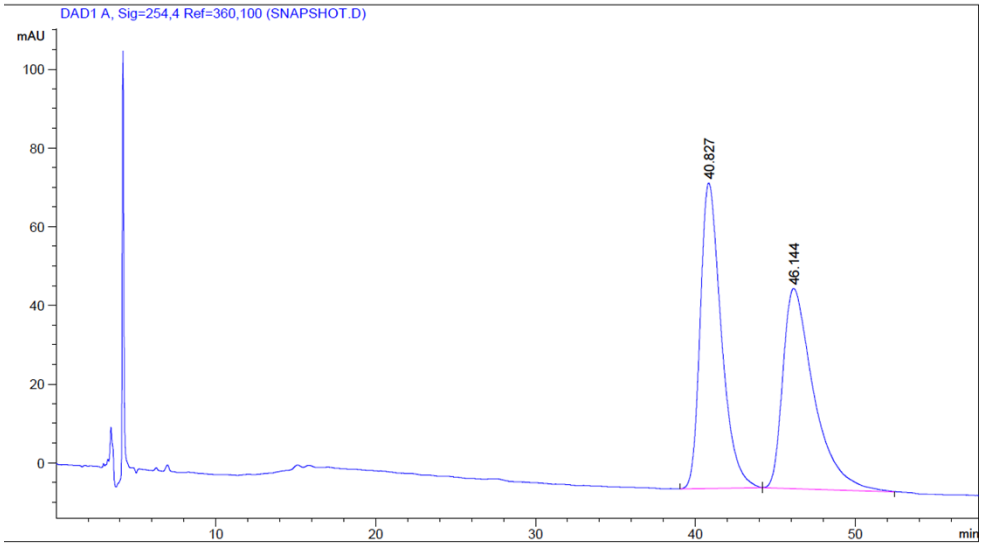
HPLC graph of compound **11c** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **11d** in $CDCl_3$

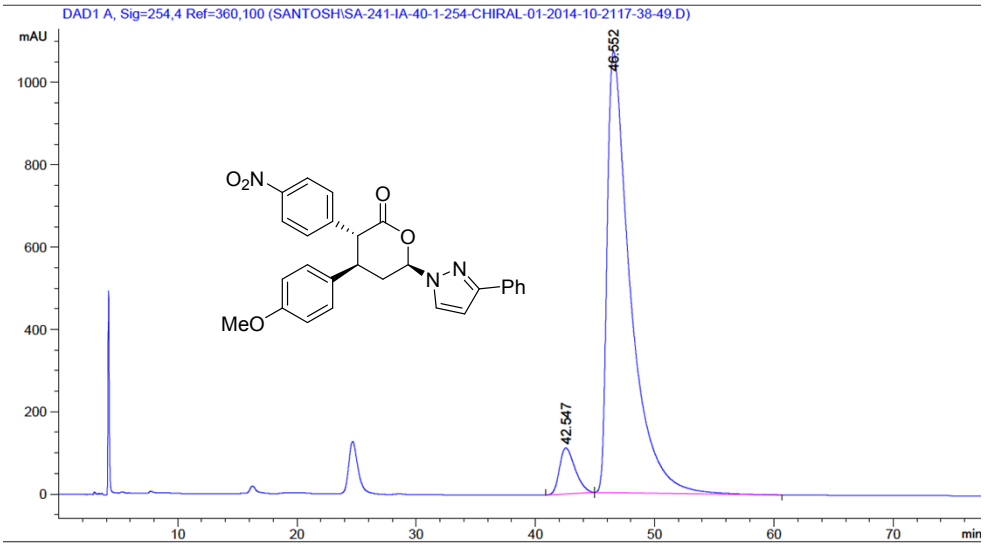


100 MHz ^{13}C NMR spectra of compound **11d** in $CDCl_3$



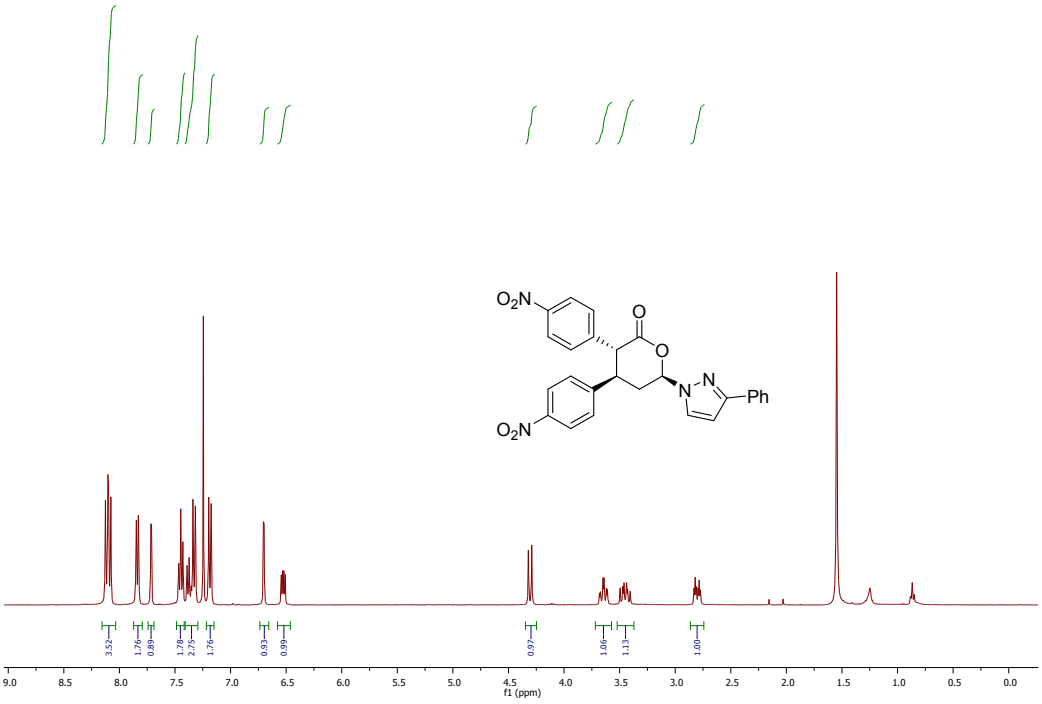
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.827	BB	1.3908	7099.03271	77.63568	50.9805
2	46.144	BB	1.9891	6825.96631	50.81886	49.0195

HPLC graph of compound **11d** (racemic)

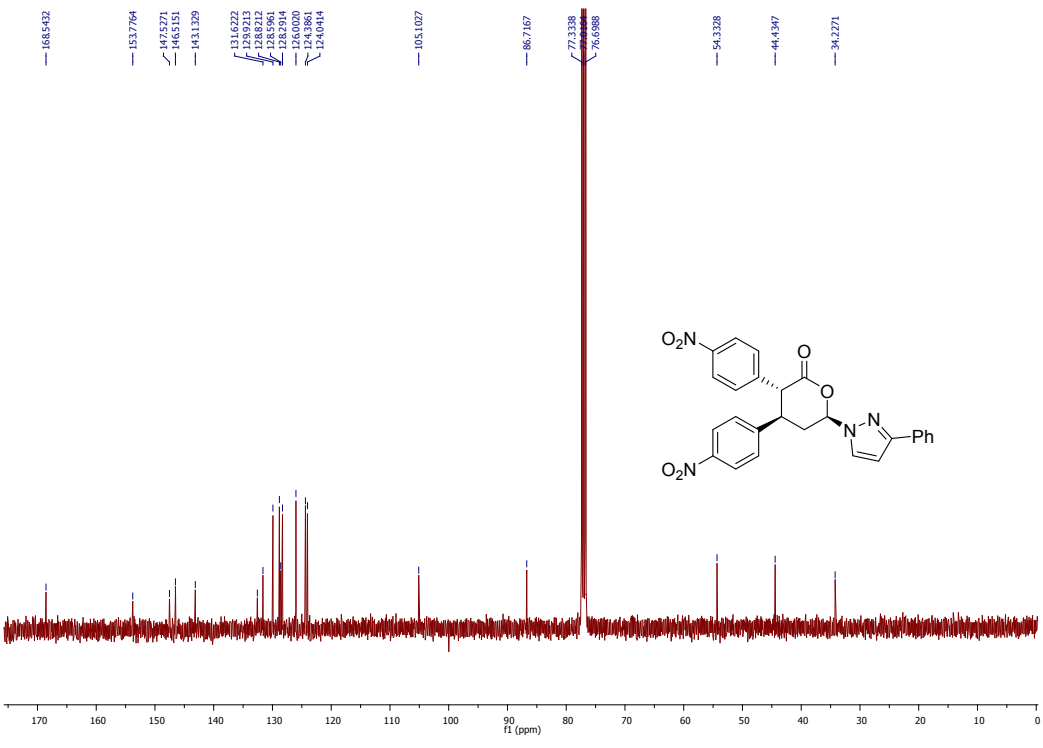


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	42.547	BB	1.3940	1.01566e4	111.78680	6.5777
2	46.552	BB	1.9505	1.44252e5	1071.61877	93.4223

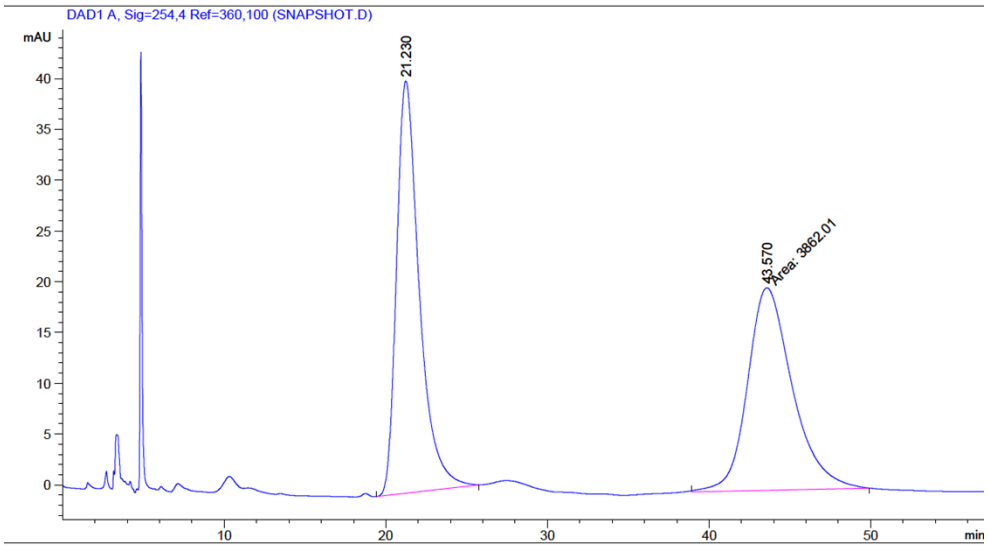
HPLC graph of compound **11d** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **11e** in $CDCl_3$

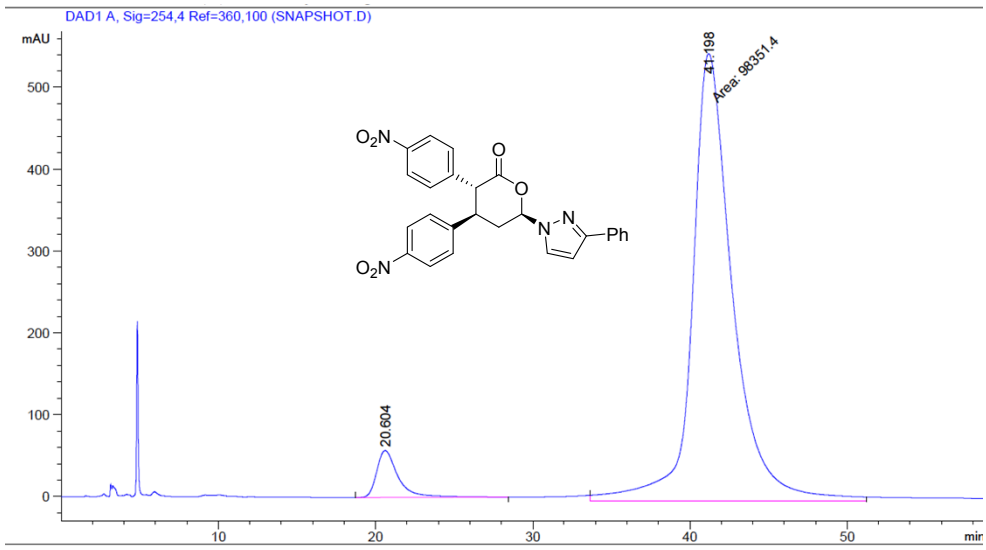


100 MHz ^{13}C NMR spectra of compound **11e** in $CDCl_3$



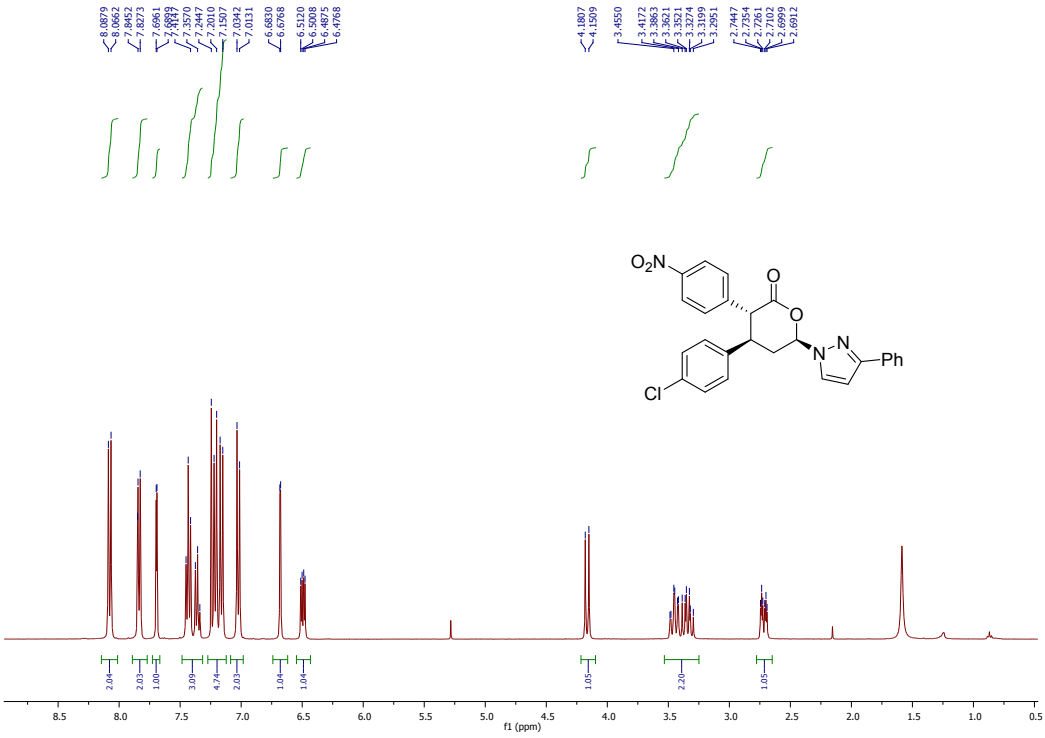
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.230	BB	1.4450	3966.74512	40.55978	50.6689
2	43.570	MM	3.2267	3862.00928	19.94848	49.3311

HPLC graph of compound **11e** (racemic)

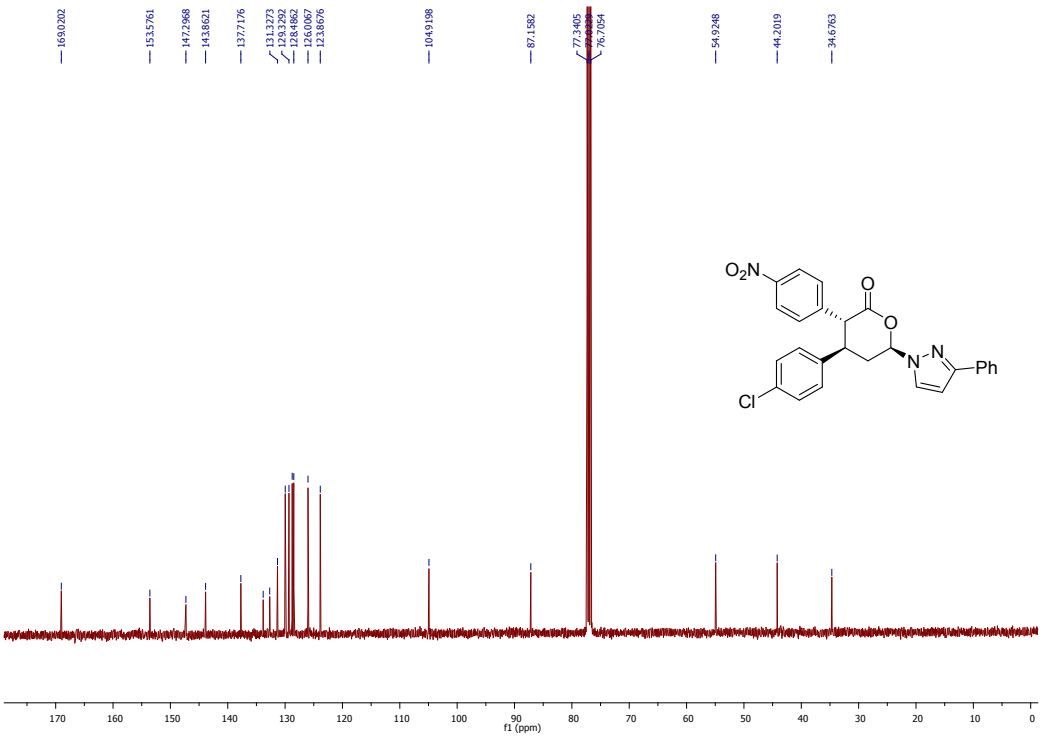


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.604	BB	1.3947	5379.58789	57.22547	5.1861
2	41.198	MM	2.9963	9.83514e4	547.07758	94.8139

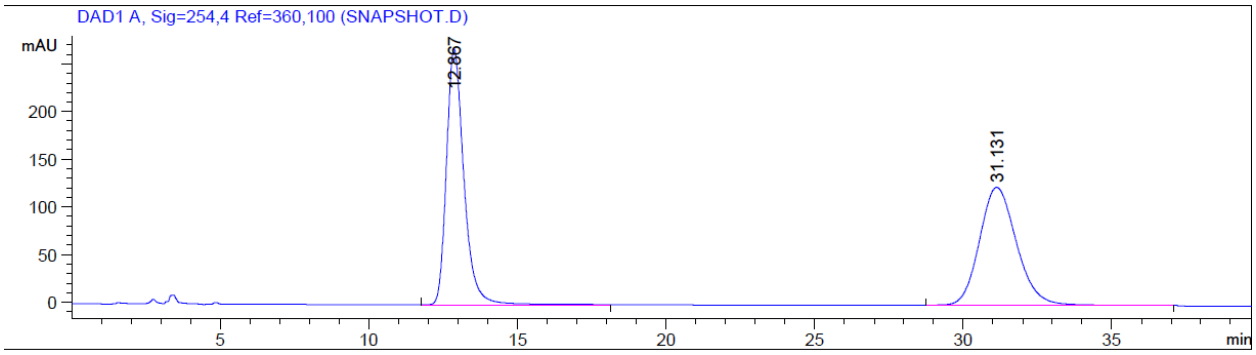
HPLC graph of compound **11e** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **11f** in $CDCl_3$

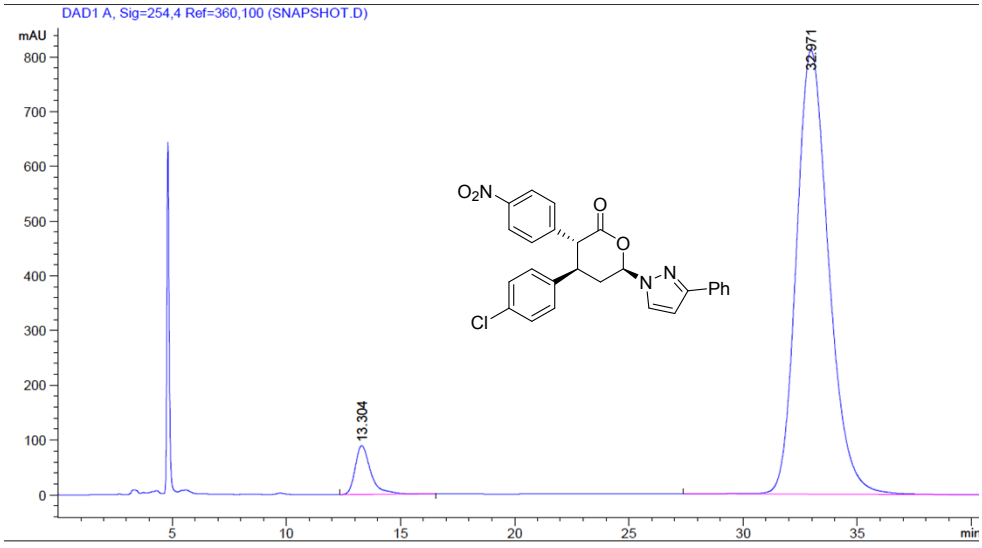


100 MHz ^{1}H NMR spectra of compound **11f** in $CDCl_3$



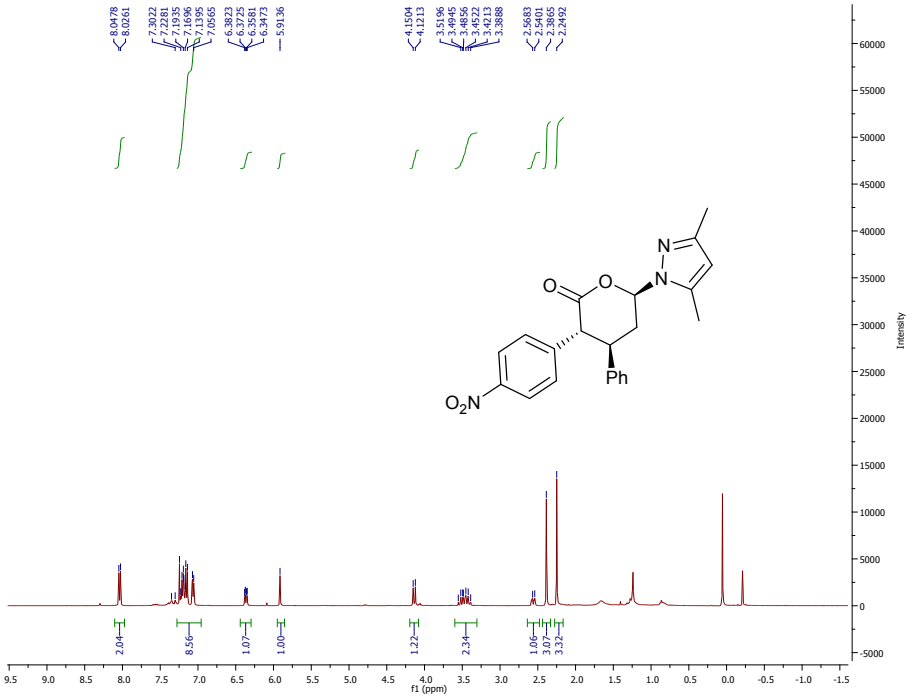
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.867	BB	0.6234	1.09882e4	268.54688	50.6048
2	31.131	BB	1.3356	1.07256e4	123.70191	49.3952

HPLC graph of compound **11f** (racemic)

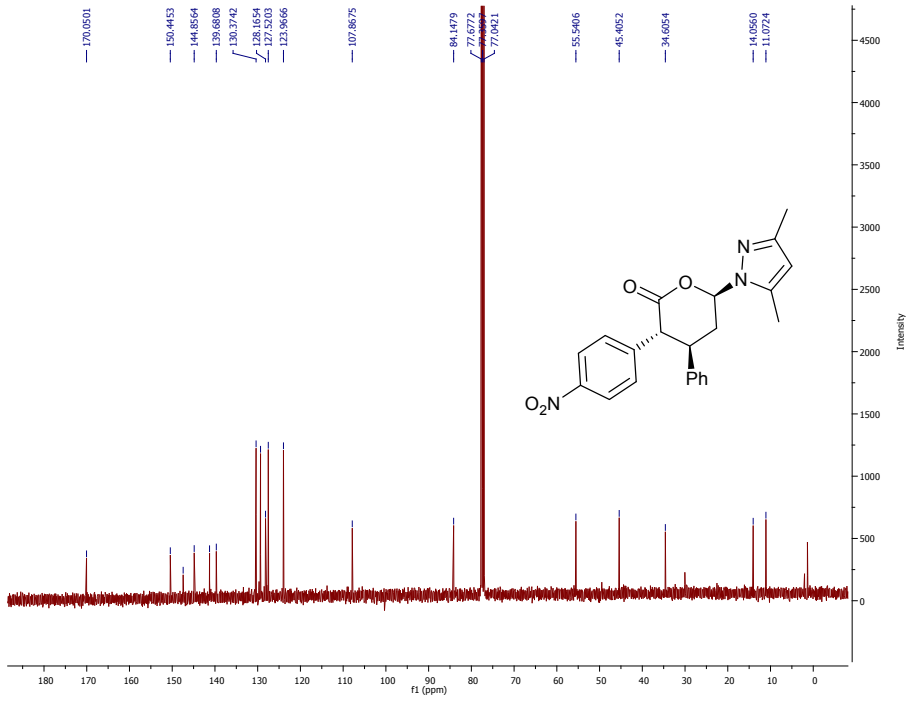


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.304	BB	0.7136	4191.96729	88.99210	5.0052
2	32.971	BBA	1.5110	7.95605e4	810.68866	94.9948

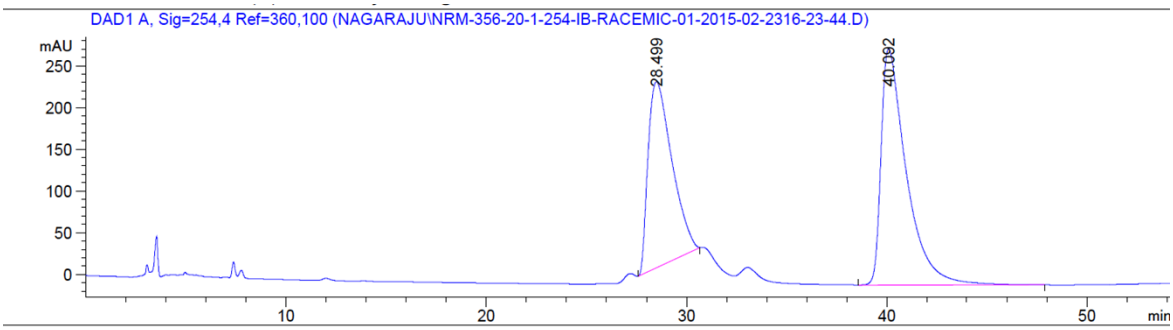
HPLC graph of compound **11f** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **12** in $CDCl_3$

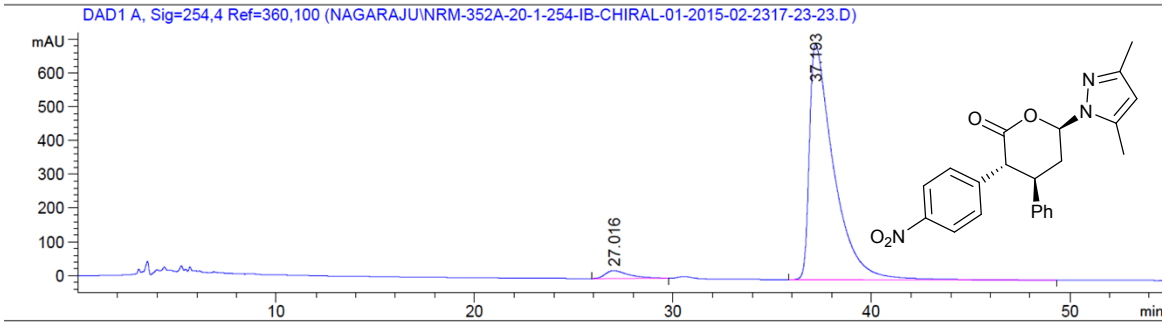


100 MHz ^{1}H NMR spectra of compound **12** in $CDCl_3$



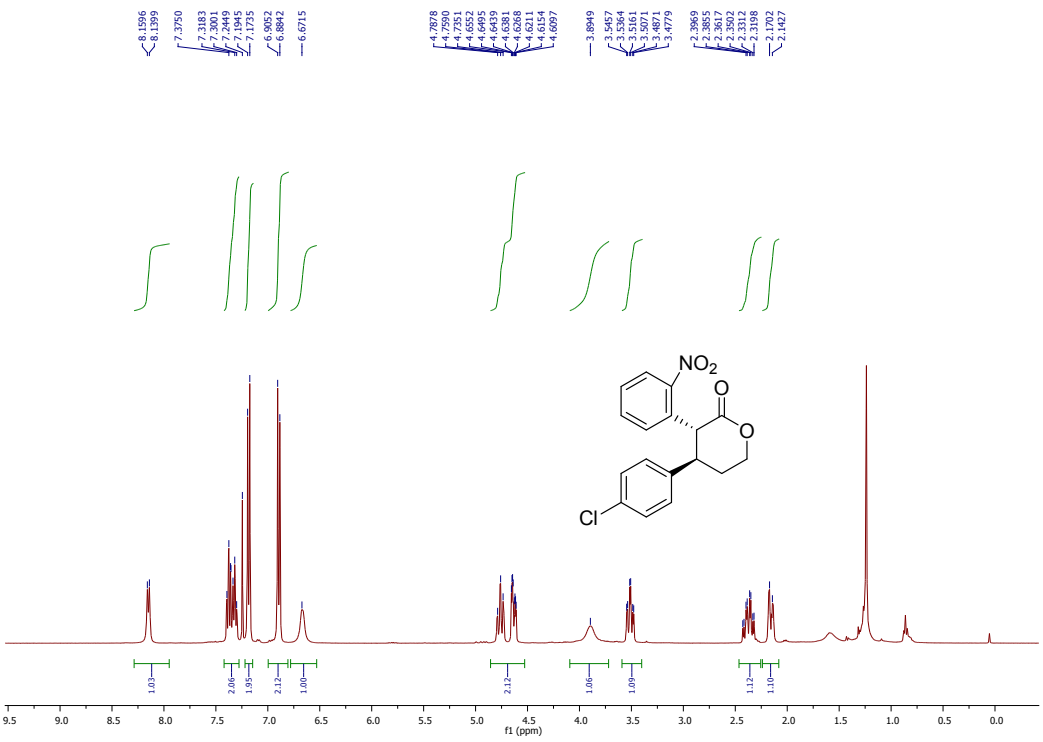
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.499	BB	1.2724	1.84248e4	223.34415	42.5153
2	40.092	BB	1.2882	2.49120e4	283.21628	57.4847

HPLC graph of compound **12** (racemic)

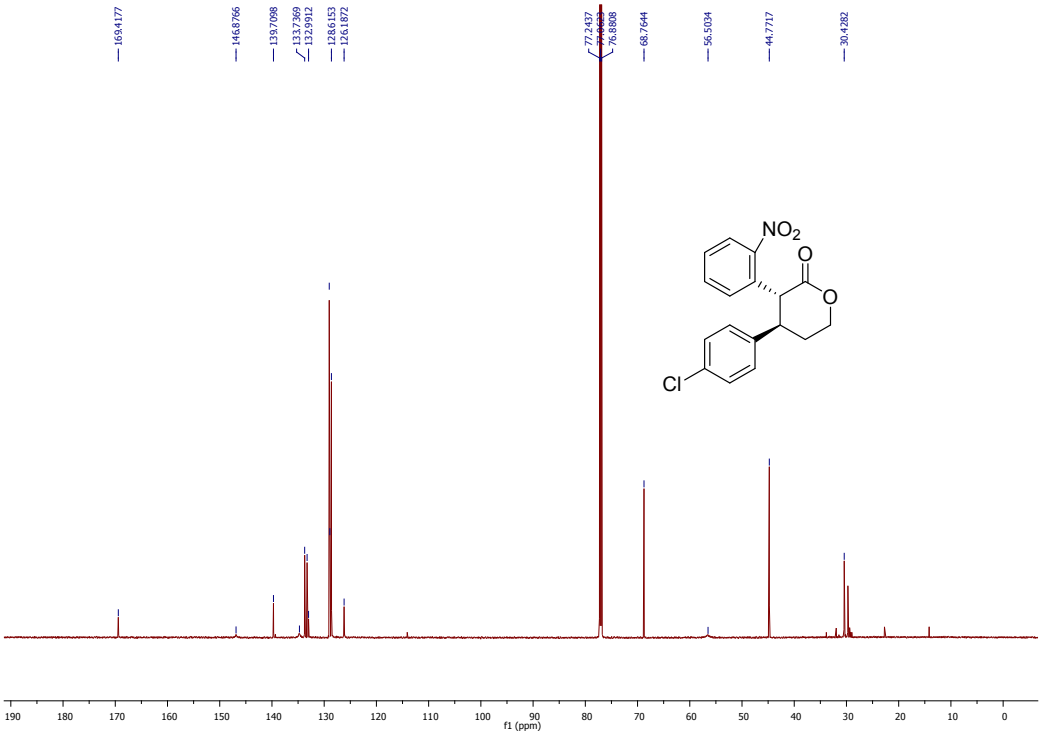


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.016	BB	1.2160	1916.48901	23.14667	3.1179
2	37.193	BB	1.2250	5.95500e4	696.82025	96.8821

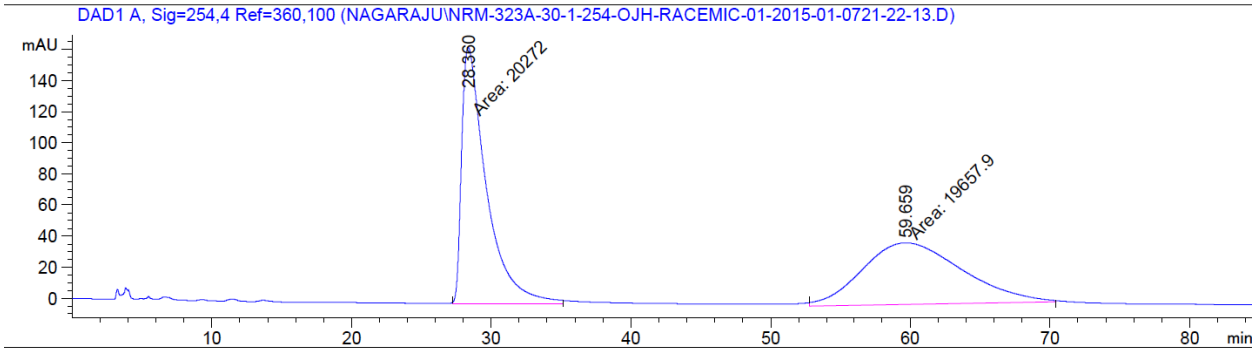
HPLC graph of compound **12** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **13** in $CDCl_3$

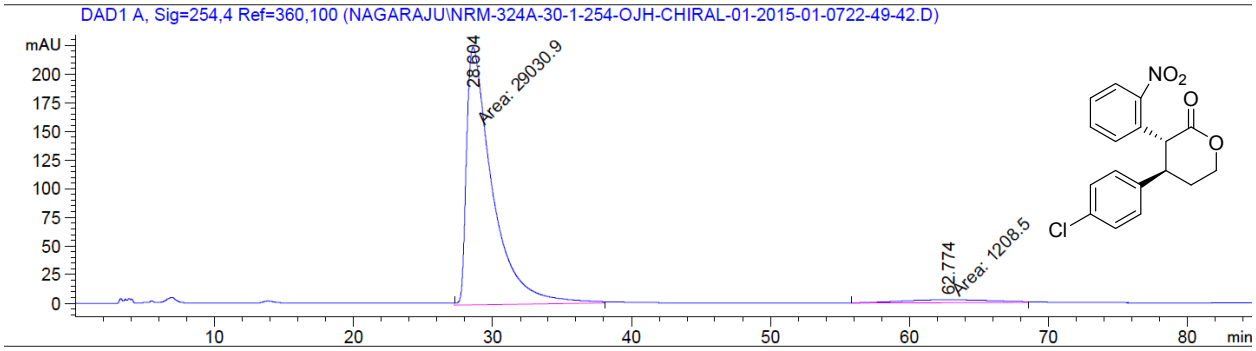


175 MHz ^{1}H NMR spectra of compound **13** in $CDCl_3$



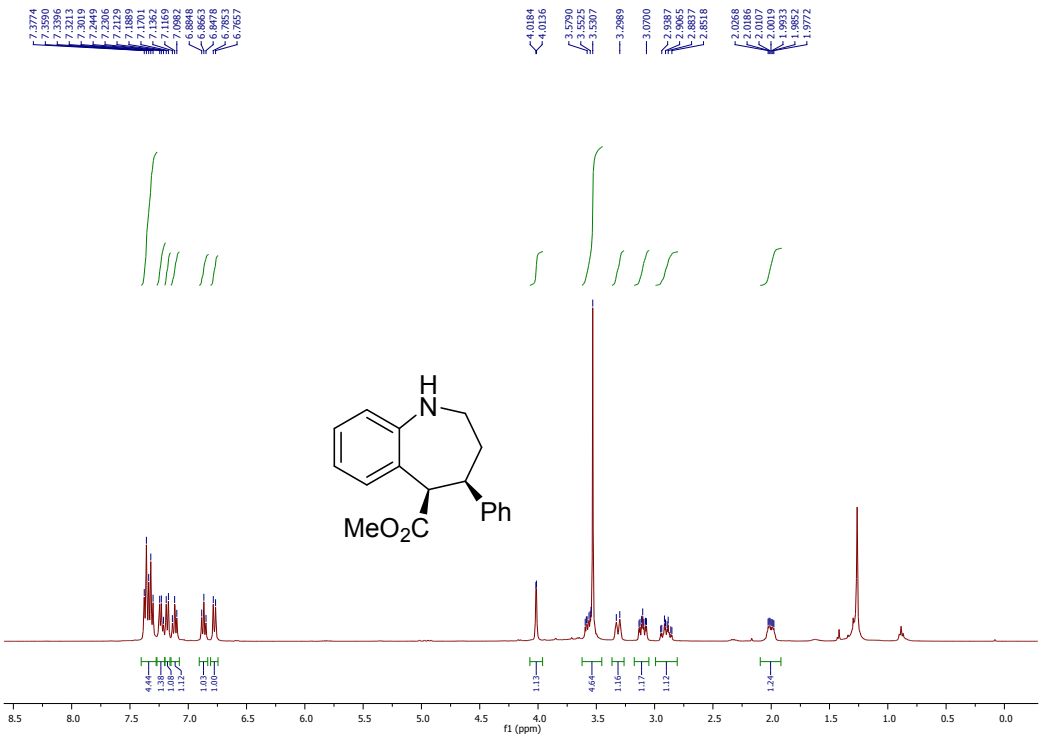
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.360	MM	2.0510	2.02720e4	164.73222	50.7689
2	59.659	MM	8.2977	1.96579e4	39.48466	49.2311

HPLC graph of compound **13** (racemic)

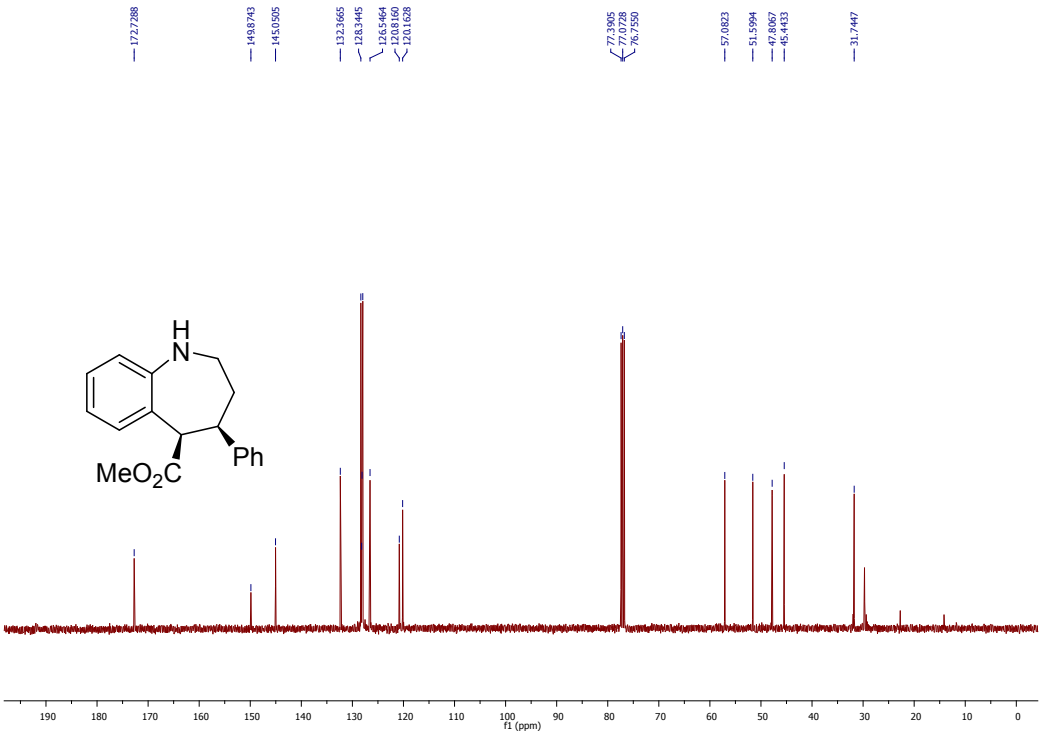


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.604	MM	2.1538	2.90309e4	224.64540	96.0036
2	62.774	MM	7.8945	1208.50012	2.55136	3.9964

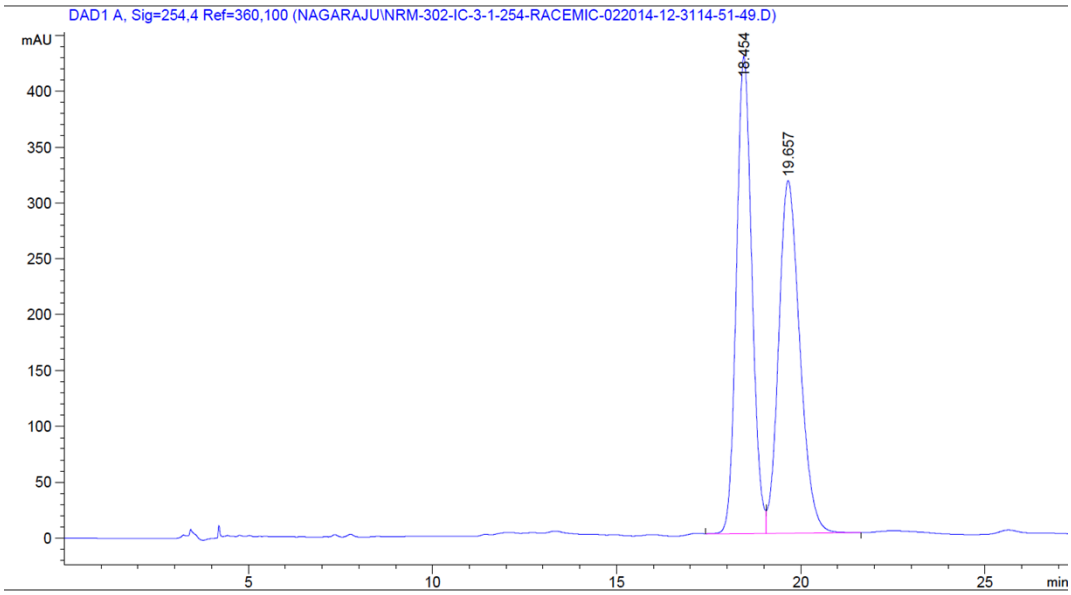
HPLC graph of compound **13** (enantioenriched)



400 MHz ^{1}H NMR spectra of compound **14** in $CDCl_3$

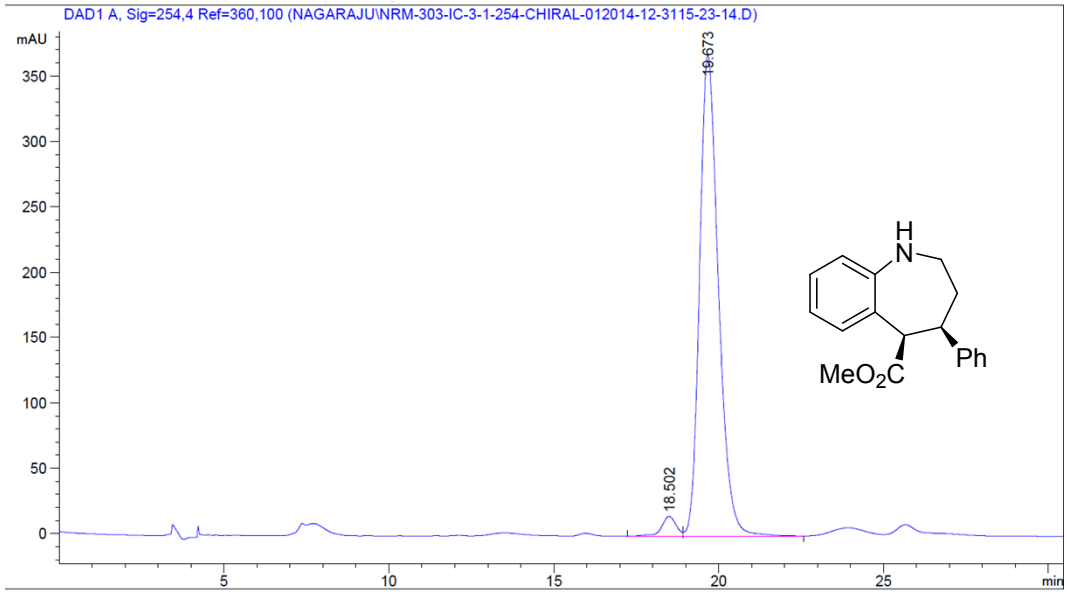


100 MHz ^{13}C NMR spectra of compound **14** in $CDCl_3$



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.454	BV	0.4526	1.24673e4	427.06335	49.7048
2	19.657	VB	0.6128	1.26154e4	315.26758	50.2952

HPLC graph of compound **14** (racemic)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.502	BV	0.4728	472.79605	15.20524	3.1301
2	19.673	VB	0.6101	1.46320e4	367.85938	96.8699

HPLC graph of compound **14** (enantioenriched)