Supplementary Materials

Synthesis of D-Fructose-Based Bifunctional Primary Amine-Thiourea Organocatalysts and Their Applications in Asymmetric Reactions

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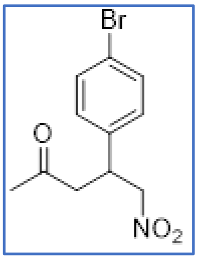
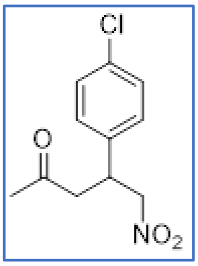
Typical procedure for asymmetric Michael Addition reaction:

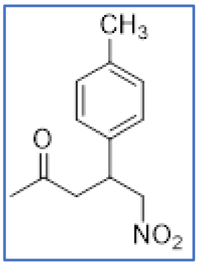
To a stirred solution of β-nitrostyrene (0.2 mmol) and ketone (3 equiv.) in dry dichloromethane (0.25 ml), 15 mol% saccharide-based amine-thiourea organocatalyst and benzoic acid were added. The reaction mixture was then stirred at room temperature for an appropriate reaction time, followed by concentration under vacuum. The reaction mixture was then subjected to purification by column chromatography using silica gel (60-120 mesh) with a hexane:EtOAc mixture as an eluent to obtain the desired product. The enantiomeric excess values of the product were determined by HPLC analysis on a chiral column using a mixture of n-hexane and iso-propanol as the mobile phase.



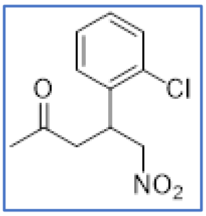
(*S*)-4-(4-bromophenyl)-5-nitropentan-2-one (**7a**): yield: 95% as yellow solid. $[\alpha]_D^{25}$ = -12.1 (c = 0.068, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=85/15, UV 220 nm, flow rate 1.0 ml/min, t_R=10.2 min (major, *S*), t_R=12.6 (minor, *R*), ee: >99%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.36 (m, 2H), 7.04-7.02 (m, 2H), 4.63-4.47 (m, 2H), 3.94-3.87 (m, 1H), 2.82 (d, 2H, *J* = 8 Hz), 2.06 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.95, 137.88, 132.21, 131.57, 131.18, 129.15, 121.87, 79.09, 45.91, 38.47, 30.37 ppm.



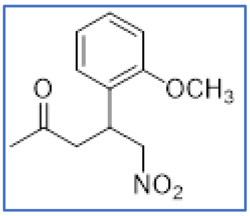
(*S*)-4-(4-chlorophenyl)-5-nitropentan-2-one (**7b**): yield: 90% as yellow solid. $[\alpha]_D^{25}$ = +5.9 (c = 0.052, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=85/15, UV 220 nm, flow rate 1.0 ml/min, t_R=9.8 min (major, *S*), t_R=11.5 (minor, *R*) ee: 91%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.24-7.20 (m, 2H), 7.11-7.07 (m, 2H), 4.63-4.47 (m, 2H), 4.06-3.88 (m, 1H), 2.82 (d, 2H, *J* = 8 Hz), 2.05 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.00, 137.36, 133.78, 130.86, 129.25, 128.82, 128.59, 79.18, 45.97, 38.41, 30.36 ppm.



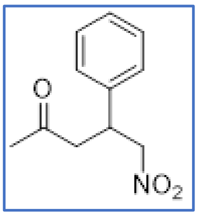
(*S*)-5-nitro-4-(*p*-tolyl)pentan-2-one (**7c**): yield: 81% as white solid. $[\alpha]_D^{25}$ = +1.2 (c = 0.045, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=85/15, UV 220 nm, flow rate 1.0 ml/min, t_R=7.4 min (major, *S*), t_R=8.2 (minor, *R*) ee:85%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.20-7.07 (m, 4H), 4.69-4.54 (m, 2H), 4.00-3.93 (m, 1H), 2.89 (d, 2H, *J* = 8 Hz), 2.31 (s, 3H), 2.10 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.56, 136.56, 134.75, 128.70, 127.91, 126.51, 126.21, 78.60, 45.18, 37.73, 29.34, 19.99 ppm.



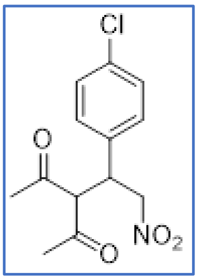
(*S*)-4-(2-chlorophenyl)-5-nitropentan-2-one (**7d**): yield: 88% as yellow oil. $[\alpha]_D^{25}$ = +6.8 (c = 0.062, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=90/10, UV 210 nm, flow rate 1.0 ml/min, t_R=9.817 min (major, *S*), t_R=12.583 min (minor, *R*) ee:83%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.34-7.12 (m, 4H), 4.73-4.64 (m, 2H), 4.43-4.36 (m, 1H), 3.02-2.86 (m, 2H), 2.09 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.24, 134.97, 132.71, 129.41, 128.03, 127.40, 126.38, 76.41, 43.50, 34.78, 29.18 ppm.



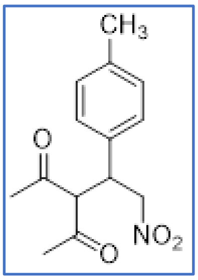
(*S*)-4-(2-methoxyphenyl)-5-nitropentan-2-one (**7e**): yield: 94% as pale-yellow oil. $[\alpha]_D^{25}$ = +15.3 (c = 0.034, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=48/2, UV 205 nm, flow rate 0.5 ml/min, t_R=31.2 min (major, *S*), t_R=32.7 (minor, *R*) ee: 81%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.17-7.15 (m, 1H), 7.07-7.05 (m, 1H), 6.84-6.80 (m, 2H), 4.69-4.63 (m, 2H), 4.17-4.12 (m, 1H), 3.78 (s, 3H), 2.98-2.84 (m, 2H), 2.04 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.15, 156.09, 128.27, 127.97, 125.45, 119.88, 109.99, 76.84, 54.32, 43.51, 34.34, 29.18 ppm.



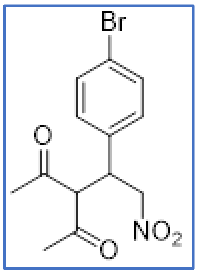
(*S*)-5-nitro-4-phenylpentane-2-one (**7f**): yield: 93% as white solid. $[\alpha]_D^{25}$ = +6.9 (c = 0.055, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=97/3, UV 220 nm, flow rate 1 ml/min, t_R=18.3 min (major, *S*), t_R=21.4 (minor, *R*) ee: 95%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.23 (m, 5H), 4.74-4.60 (m, 2H), 4.07-3.99 (m, 1H), 2.94 (d, *J* = 8 Hz, 2H), 2.14 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.39, 138.82, 129.09, 127.92, 127.39, 79.46, 46.18, 39.05, 30.40 ppm.



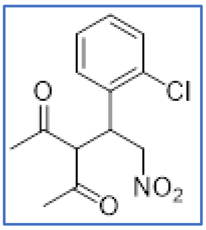
(*S*)-3-(1-(4-chlorophenyl)-2-nitroethyl)pentane-2,4-dione (**7g**): yield: 80% as white solid. $[\alpha]_D^{25}$ = +6.9 (c = 0.055, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=80/20, UV 205 nm, flow rate 1 ml/min, t_R=8.2 min (major, *S*), t_R=22.0 (minor, *R*) ee: 84%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32-7.29 (m, 2H), 7.15-7.11 (m, 2H), 4.65-4.58 (m, 2H), 4.34-4.20 (m, 2H), 2.30 (s, 3H), 1.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.38, 200.55, 134.58, 134.27, 133.22, 129.57, 129.33, 77.92, 70.56, 42.15, 30.41, 29.64 ppm.



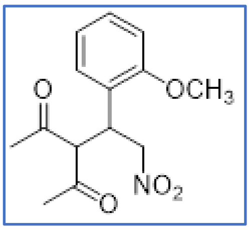
(*S*)-3-(2-nitro-1-(p-tolyl)ethyl)pentane-2,4-dione (**7h**): yield: 73% as white solid. $[\alpha]_D^{25}$ = +91.3 (c = 0.066, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=90/10, UV 210 nm, flow rate 1 ml/min, t_R=10.0 min (major, *S*), t_R=17.1 (minor, *R*) ee: 81%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.13-7.05 (m, 4H), 4.64-4.56 (m, 2H), 4.35 (d, 1H, *J* = 8 Hz), 4.23-4.17 (m, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 1.94 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.88, 201.08, 138.38, 132.85, 130.01, 127.78, 78.38, 70.88, 42.47, 30.38, 29.41, 21.05 ppm.



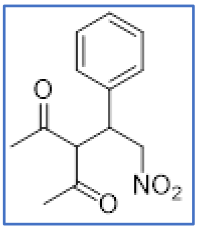
(*S*)-3-(1-(4-bromophenyl)-2-nitroethyl)pentane-2,4-dione (**7i**): yield: 78% as pale-yellow solid. $[\alpha]_D^{25}$ = +141.7 (c = 0.068, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=85/15, UV 210 nm, flow rate 1 ml/min, t_R=10.6 min (major, *S*), t_R=29.8 (minor, *R*) ee: 81%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48-7.45 (m, 2H), 7.09-7.05 (m, 2H), 4.65-4.58 (m, 2H), 4.32 (d, 1H, *J* = 12 Hz), 4.24-4.18 (m, 1H), 2.30 (s, 3H), 1.98 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.40, 200.56, 135.11, 132.58, 129.68, 122.71, 77.87, 70.54, 42.22, 30.42, 29.64 ppm.



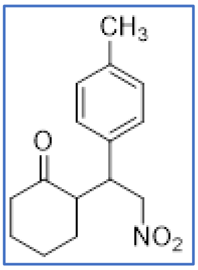
(S)-3-(1-(2-chlorophenyl)-2-nitroethyl)pentane-2,4-dione (**7j**): yield: 62% as pale-yellow solid. $[\alpha]_D^{25}$ = +200.1 (c = 0.048, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH= 49/1, UV 205 nm, flow rate 0.5 ml/min, t_R=33.9 min (major, S), t_R=36.1 (minor, R) ee: 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.07 (m, 4H), 4.79-4.75 (m, 1H), 4.70-4.65 (m, 1H), 4.61-4.52 (m, 2H), 2.23 (s, 3H), 1.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.89, 200.83, 133.78, 133.45, 130.67, 129.73, 129.04, 127.67, 77.33, 69.02, 38.86, 30.88, 28.43 ppm.



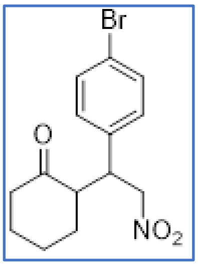
(S)-3-(1-(2-methoxyphenyl)-2-nitroethyl)pentane-2,4-dione (**7k**): yield: 52% as pale-yellow oil. $[\alpha]_D^{25}$ = +196.8 (c = 0.055, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH= 49/1, UV 210 nm, flow rate 0.5 ml/min, t_R=36.6 min (major, S), t_R=40.0 (minor, R) ee: 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.17 (m, 1H), 7.02-7.00 (m, 1H), 6.84-6.80 (m, 2H), 4.74-4.69 (m, 1H), 4.54-4.49 (m, 2H), 4.44-4.39 (m, 1H), 3.81 (s, 3H), 2.21 (s, 3H), 1.87 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.08, 202.27, 158.11, 139.57, 134.04, 131.20, 128.98, 79.57, 60.27, 52.90, 31.58, 30.60, 22.24 ppm.



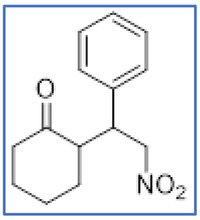
(S)-3-(2-nitro-1-phenylethyl)pentane-2,4-dione (**7l**): yield: 81% as pale-yellow solid. $[\alpha]_D^{25}$ = +173.1 (c = 0.048, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=45/5, UV 210 nm, flow rate 0.5 ml/min, t_R=21.8 min (major, S), t_R=29.5 (minor, R) ee: 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.10 (m, 5H), 4.59-4.52 (m, 2H), 4.32-4.16 (m, 2H), 2.22 (s, 3H), 1.87 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.80, 201.03, 135.99, 129.35, 129.17, 128.88, 128.57, 127.94, 78.19, 42.80, 30.44, 29.55 ppm.



(R)-2-[(S)-1-(4-methylphenyl)-2-nitroethyl] cyclohexanone (**7m**): yield: 46% as yellow solid. $[\alpha]_D^{25}$ = +13.1 (c = 0.05, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=48/2, UV 254 nm, flow rate 0.5 ml/min, retention time: 25.0 min (major, *syn*), 29.7 min (minor, *anti*), 31.3 min (major, *anti*) 38.8 min (minor, *syn*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15-7.03 (m, 4H), 4.96-4.80 (m, 1H), 4.65-4.60 (m, 1H) 4.01-3.96 (m, 1H for *anti*), 3.77-3.71 (m, 1H for *syn*), 2.76-2.66 (m, 1H), 2.52-1.20 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.08 (*syn*), 210.58 (*anti*), 137.46, 137.22, 135.22, 134.60, 129.63, 129.45, 128.24, 128.01, 79.03, 53.82, 52.59, 43.59, 42.76, 42.74, 33.19, 30.03, 28.54, 27.36, 25.03, 25.01, 21.06 ppm.



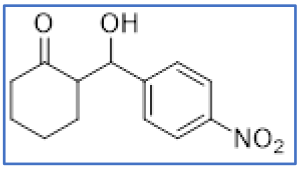
(S)-2-[(R)-1-(4-bromophenyl)-2-nitroethyl] cyclohexanone (**7n**): yield: 55% as white solid. Chiralpak AD-H, hexane/i-PrOH=90/10, UV 254 nm, flow rate 1 ml/min, retention time: 11.9 min (minor, *syn*), 13.6 min (major, *anti*), 15.3 min (minor, *anti*) 18.7 min (major, *syn*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65-7.44 (m, 2H), 7.18-7.06 (m, 2H), 4.97-4.85 (m, 1H), 4.84-4.58 (m, 1H), 3.96-3.78 (m, 1H for *anti*), 3.77-3.73 (m, 1H for *syn*), 2.75-2.63 (m, 1H), 2.51-1.25 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.55 (*syn*), 210.30 (*anti*), 137.37, 136.86, 133.75, 132.10, 131.87, 130.23, 129.93, 128.51, 121.73, 78.52, 53.55, 52.35, 43.44, 42.90, 42.74, 33.17, 30.32, 28.44, 27.35, 25.07 ppm.



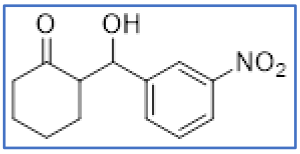
(*S*)-2-((*R*)-2-Nitro-1-phenylethyl)cyclohexan-1-one (**7o**): yield: 42% as white solid. $[\alpha]_D^{25}$ = -6.1 (c = 0.048, $CHCl_3$). Chiralpak AD-H, hexane/i-PrOH=90/10, UV 254 nm, flow rate 1 ml/min, retention time: 12.6 min (minor, *syn*), 14.5 min (minor, *anti*), 19.1 min (major, *anti*), 25.9 min (major, *syn*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.09 (m, 5H), 4.89-4.74 (m, 1H), 4.59-4.53 (m, 1H), 3.96-3.72 (m, 1H for *anti*), 3.71-3.66 (m, 1H for *syn*), 2.69-2.58 (m, 1H), 2.44-1.11 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.00 (*syn*), 210.52 (*anti*), 128.95, 128.76, 128.50, 128.18, 127.79, 127.56, 78.90, 53.78, 52.55, 43.95, 43.08, 42.33, 33.22, 30.00, 28.54, 27.35, 25.04 ppm.

Typical procedure for the asymmetric Aldol reaction:

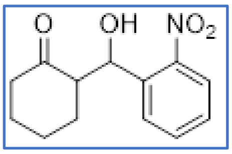
A solution of 20 mol% of the saccharide-based amine-thiourea organocatalyst **6a**, 20 mol% of benzoic acid, aldehydes (0.2 mmol), and ketone (4 equiv.) in water (0.5 ml) was stirred at 0 °C. The reaction mixture was then concentrated under vacuum, followed by purification with column chromatography using silica gel with hexane:EtOAc mixture. The enantiomeric excess values of the products were identified by HPLC analysis on a chiral column using a mixture of n-hexane and iso-propanol as the mobile phase.



(2*R*,1'*R*)-2-[Hydroxy-(4-nitro-phenyl)-methyl] cyclohexanone (**8a**): yield: 58% as white solid. Chiralpak OD-H, hexane/i-PrOH=95/5, UV 254 nm, flow rate 0.5 ml/min, *syn* product t_R (major) 56.6 min, t_R(minor) 66.6 min, ee: 30%, *anti* product t_R (major) 71.3 min, t_R(minor) 103.2 min, ee: 47%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29-8.24 (m, 2H), 7.56-7.50 (m, 2H) 5.53 (d, 1H for *syn*, *J* = 2 Hz), 4.95 (d, 1H for *anti*, *J* = 8 Hz), 3.21 (s, 1H), 2.88-1.30 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.65 (*anti*), 213.96 (*syn*), 142.25, 139.98, 130.69, 127.89, 126.63, 74.02 (*anti*), 70.15 (*syn*), 57.21 (*anti*), 56.82 (*syn*), 42.68, 40.44, 24.71, 23.77, 23.31 ppm.

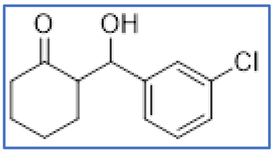


(2*R*,1'*R*)-2-[Hydroxy-(3-nitro-phenyl)-methyl] cyclohexanone (**8b**): yield: 52% as white solid. Chiralpak OD-H, hexane/i-PrOH=95/5, UV 254 nm, flow rate 0.5 ml/min, *syn* product t_R (major) 35.9 min, t_R(minor) 37.5 min, ee: 15%, *anti* product t_R (major) 42.6 min, t_R(minor) 61.8 min, ee: 52%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14-8.02 (m, 2H), 7.61-7.38 (m, 2H), 5.40 (d, 1H for *syn*, *J* = 2 Hz), 4.83 (d, 1H for *anti*, *J* = 8 Hz), 3.41 (s, 1H), 2.78-1.26 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.82 (*anti*), 214.03 (*syn*), 143.98, 143.37, 132.44, 132.01, 124.39, 123.02, 122.84, 73.99 (*anti*), 65.90 (*syn*), 57.14 (*anti*), 56.78 (*syn*), 30.74, 25.94, 24.75, 24.66 ppm.

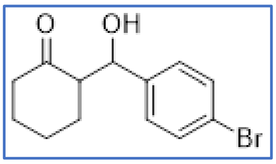


(2*R*,1'*R*)-2-[Hydroxy-(2-nitro-phenyl)-methyl] cyclohexanone (**8c**): 46% as pale-yellow solid. Chiralpak OD-H, hexane/i-PrOH=95/5, UV 254 nm, flow rate 0.5 ml/min, *syn* product t_R (minor) 20.3 min, t_R(major) 23.4 min, ee: 40%, *anti* product t_R (major)

32.2 min, t_R(minor) 38.6 min, ee: 67%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93-7.32 (m, 4H), 5.89 (s, 1H for *syn*), 5.37 (d, 1H for *anti*, J = 8 Hz), 3.27 (s, 1H), 2.82-0.81 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.87 (*anti*), 212.91 (*syn*), 147.27, 146.14, 132.12, 132.02, 128.03, 127.92, 127.43, 126.91, 68.72 (*anti*), 65.59 (*syn*), 56.34 (*anti*), 53.86 (*syn*), 41.79, 41.52, 27.67, 26.93, 26.74 ppm.



(2*R*,1'*R*)-2-[Hydroxy-(3-chloro-phenyl)-methyl] cyclohexanone (**8d**): 54% as white solid. Chiralpak OD-H, hexane/i-PrOH=95/5, UV 220 nm, flow rate 0.5 ml/min, *syn* product t_R (minor) 18.1 min, t_R(major) 19.0 min, ee: 23%, *anti* product t_R (major) 22.7 min, t_R(minor) 30.1 min, ee: 18%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.15 (m, 4H), 5.35 (d, 1H for *syn*, J = 2 Hz), 4.74 (d, 1H for *anti*, J = 8 Hz), 2.60-1.25 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.20 (*anti*), 214.46 (*syn*), 143.71, 143.12, 129.86, 129.62, 128.48, 128.39, 128.07, 127.18, 74.30 (*anti*), 70.11 (*syn*), 57.30 (*anti*), 57.00 (*syn*), 30.81, 25.96, 24.73, 23.83, 23.36 ppm.



(2*R*,1'*R*)-2-[Hydroxy-(4-bromo-phenyl)-methyl] cyclohexanone (**8e**): yield: 50% as white solid. Chiralpak OD-H, hexane/i-PrOH=90/10, UV 254 nm, flow rate 1 ml/min, *syn* product t_R (minor) 6.6 min, t_R(major) 7.8 min, ee: 69%, *anti* product t_R (major) 9.9 min, t_R(minor) 13.5 min, ee: 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.49 (m, 2H), 7.29-7.22 (m, 2H), 5.38 (d, 1H for *syn*, J = 4 Hz), 4.80 (d, 1H for *anti*, J = 8 Hz), 3.23 (s, 1H), 2.86-1.31 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.23 (*anti*), 214.52 (*syn*), 140.58, 140.08, 134.53, 134.25, 131.76, 131.51, 128.77, 127.58, 74.21 (*anti*), 70.19 (*syn*), 57.36 (*anti*), 57.02 (*syn*), 42.68, 40.33, 27.94, 26.00, 24.74, 23.83, 23.34 ppm.

Figure S1: ^{1}H NMR and ^{13}C NMR of **3.**

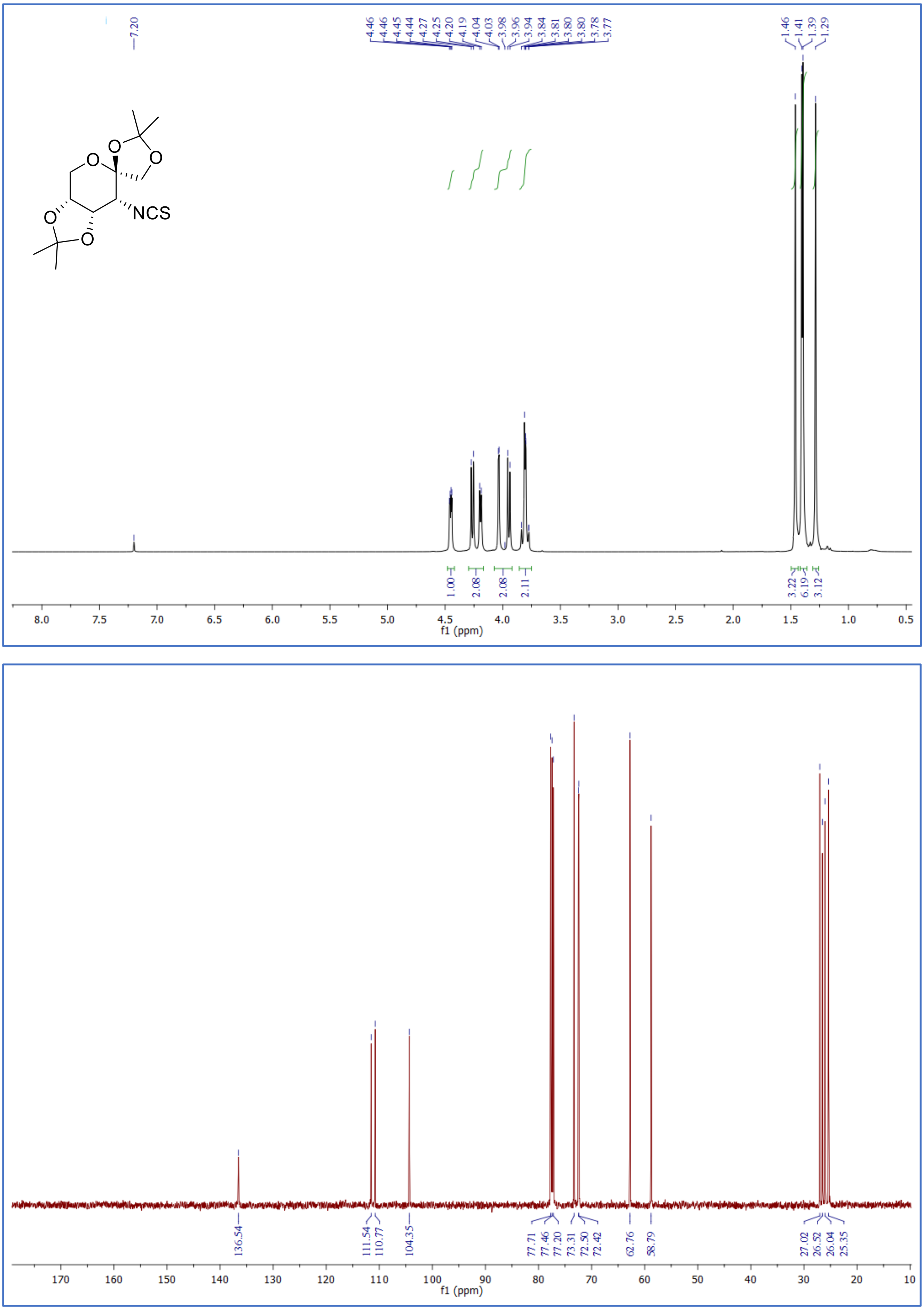
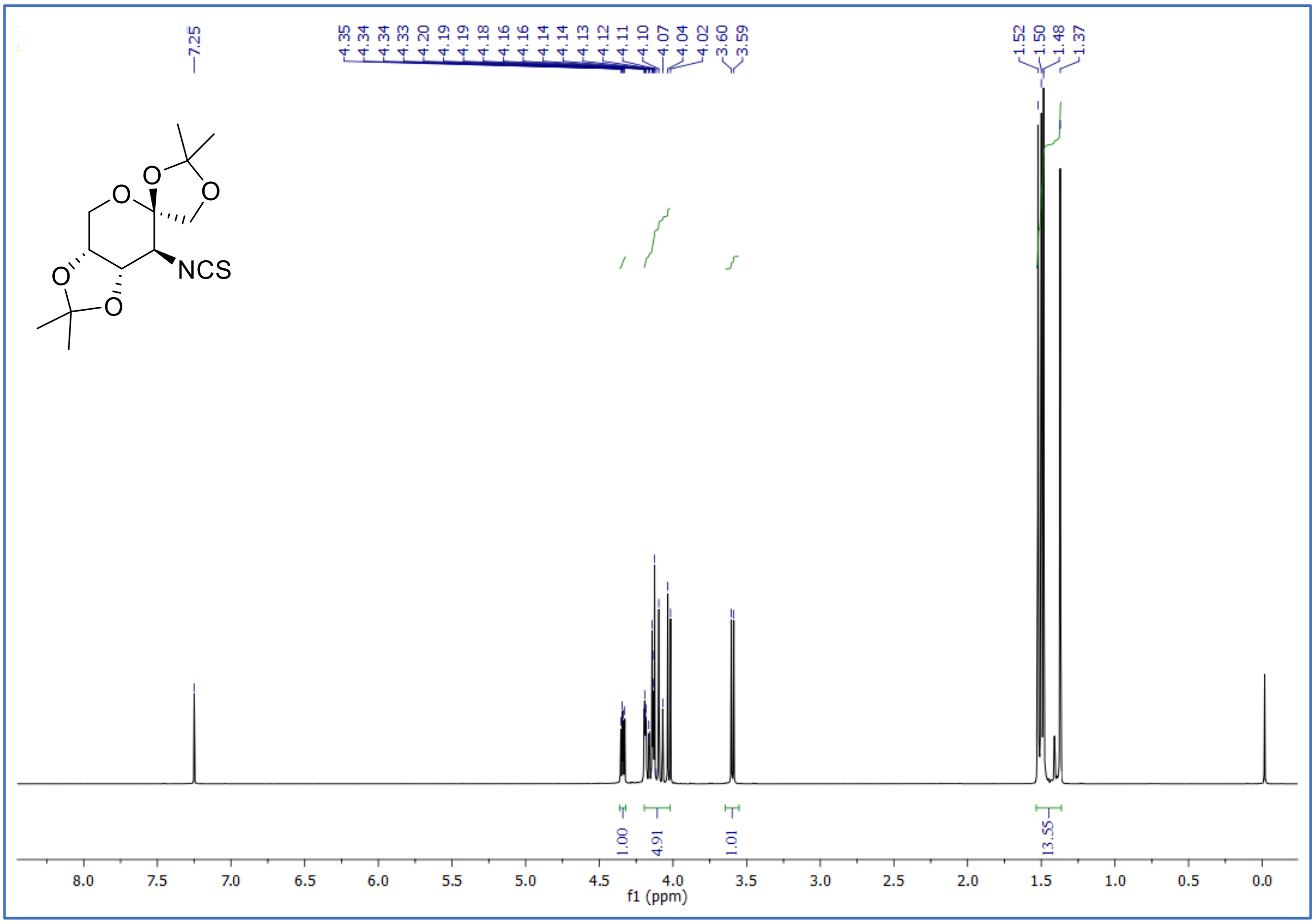


Figure S2: ^{1}H NMR and ^{13}C NMR of **4.**



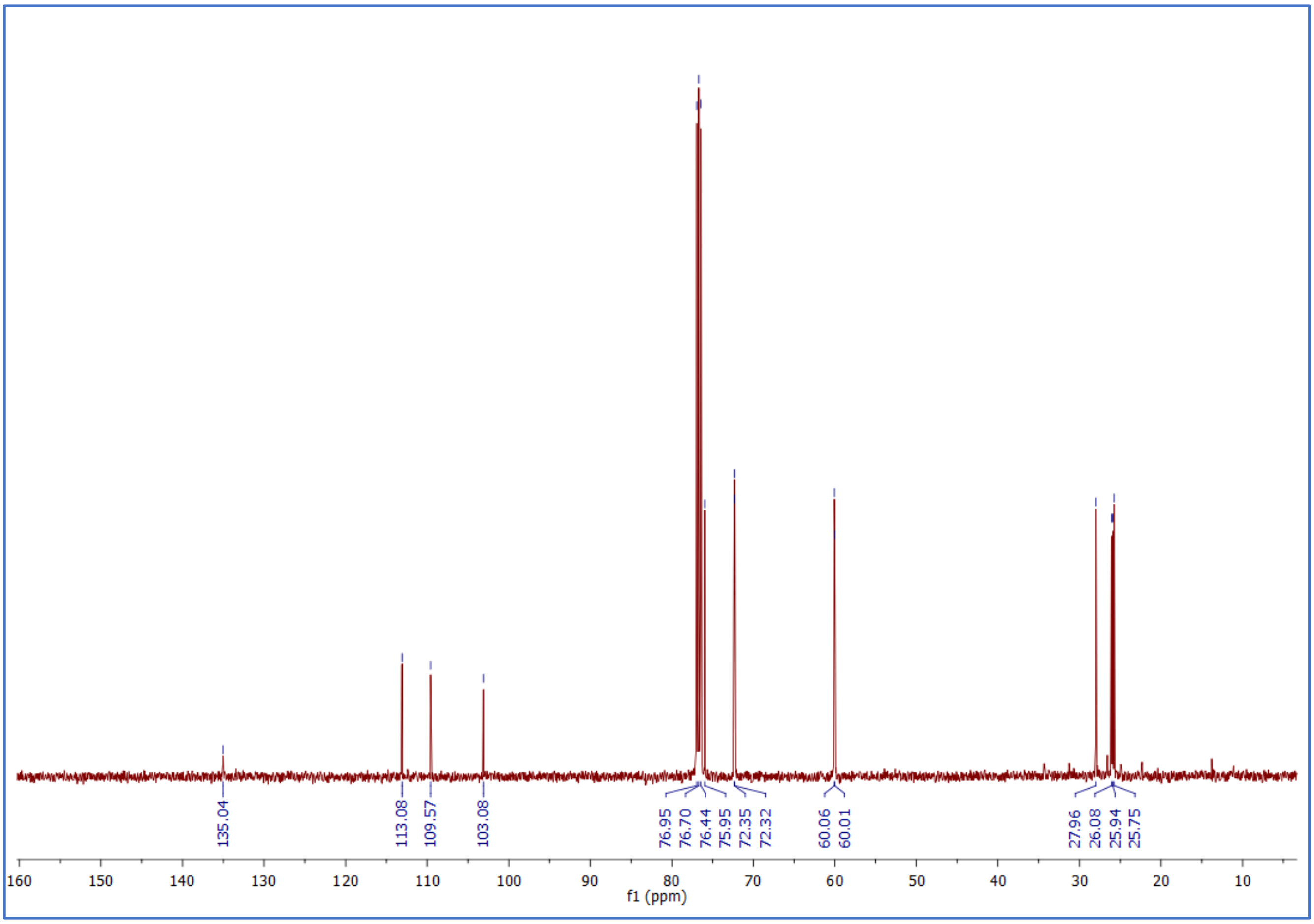
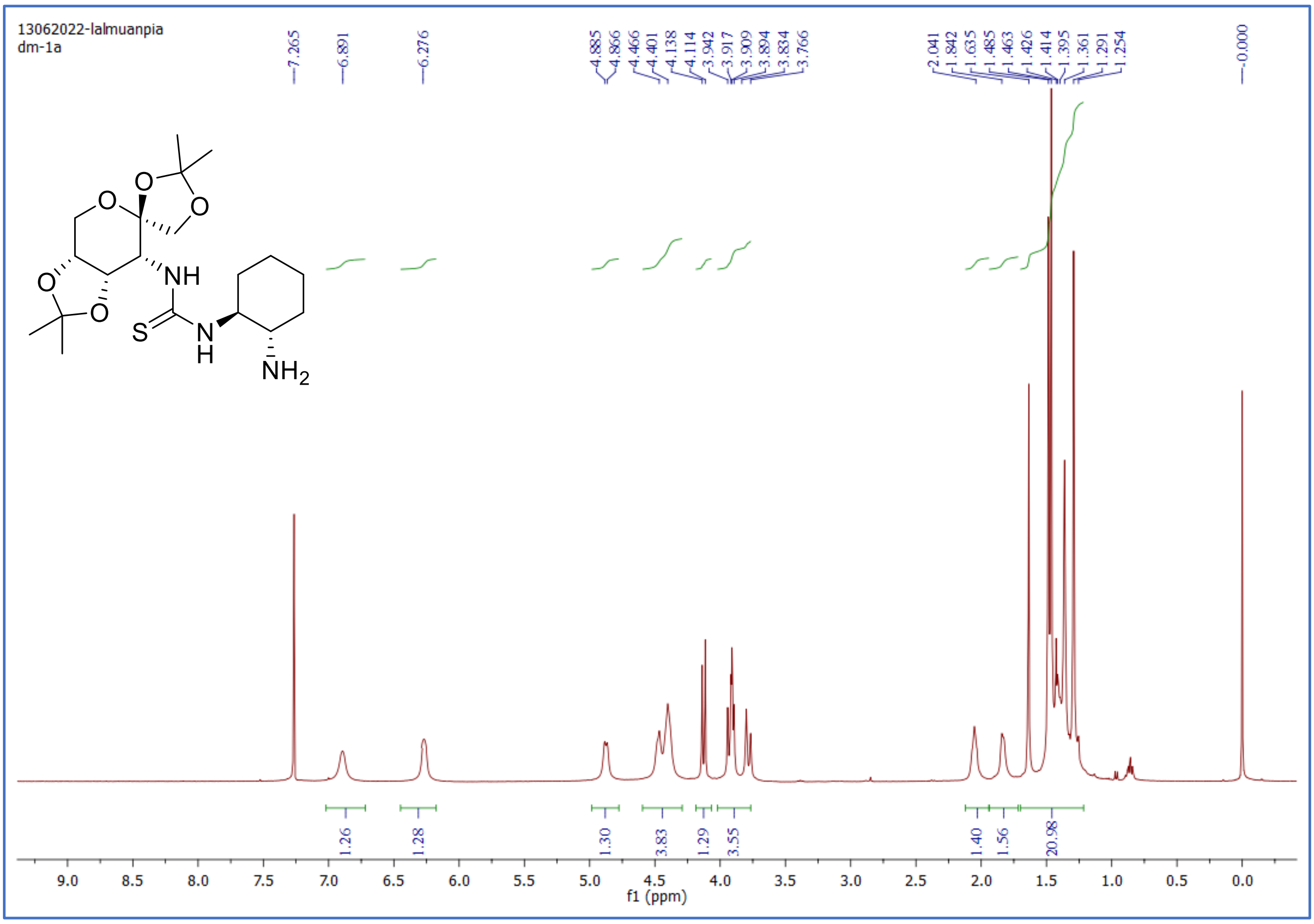


Figure S3: ^{1}H NMR and ^{13}C NMR of **5a.**



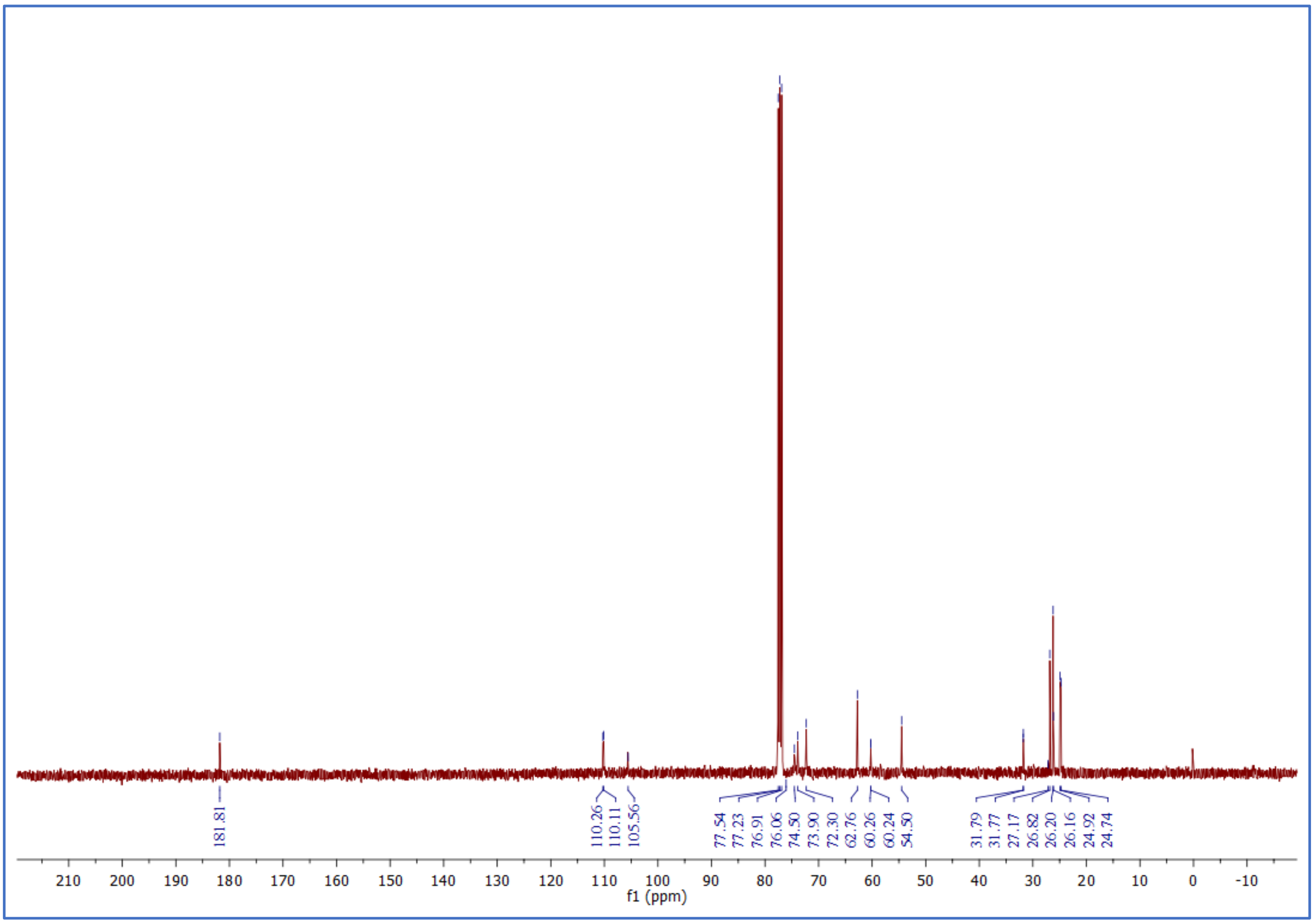
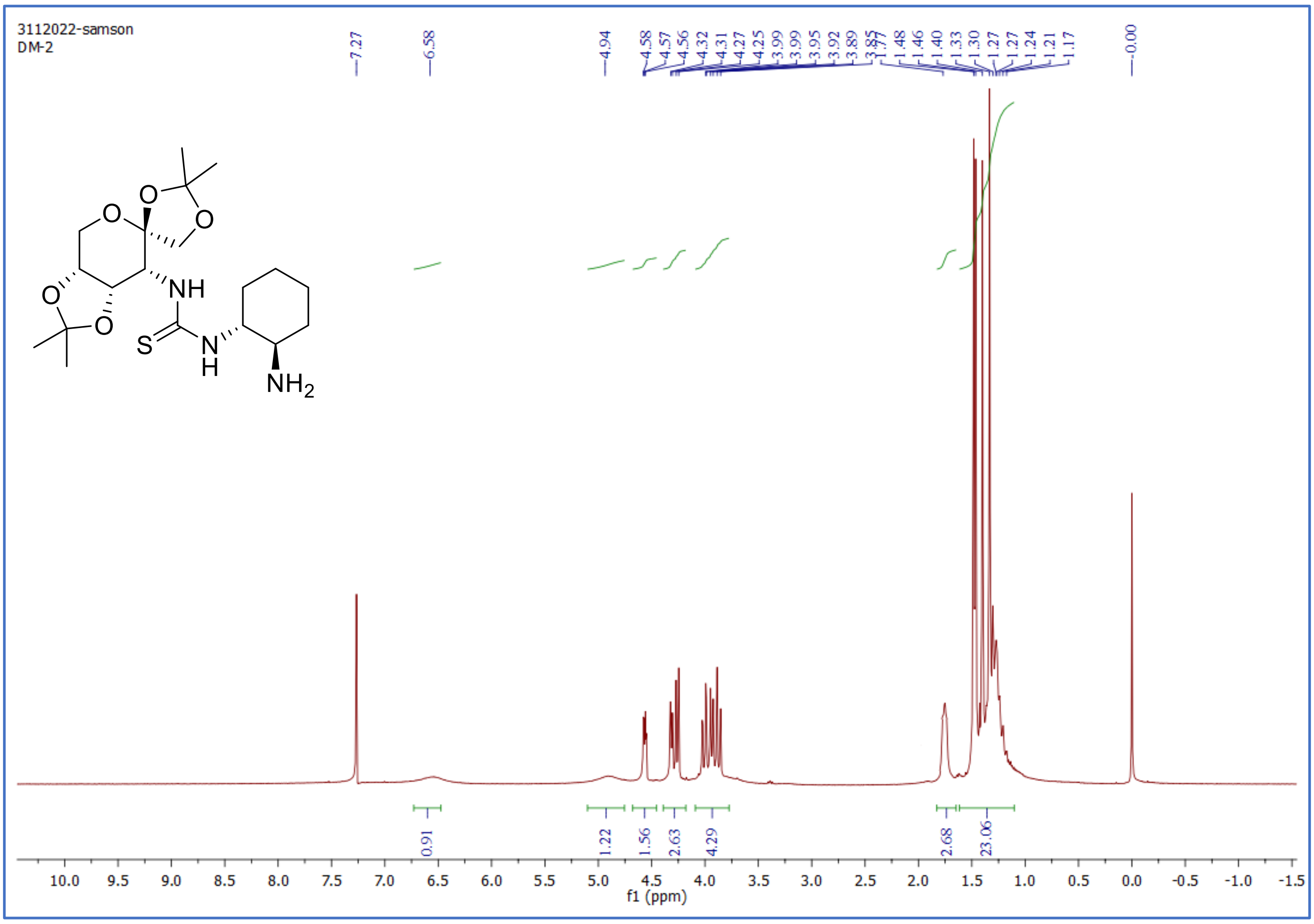


Figure S4: ^{1}H NMR and ^{13}C NMR of **5b.**



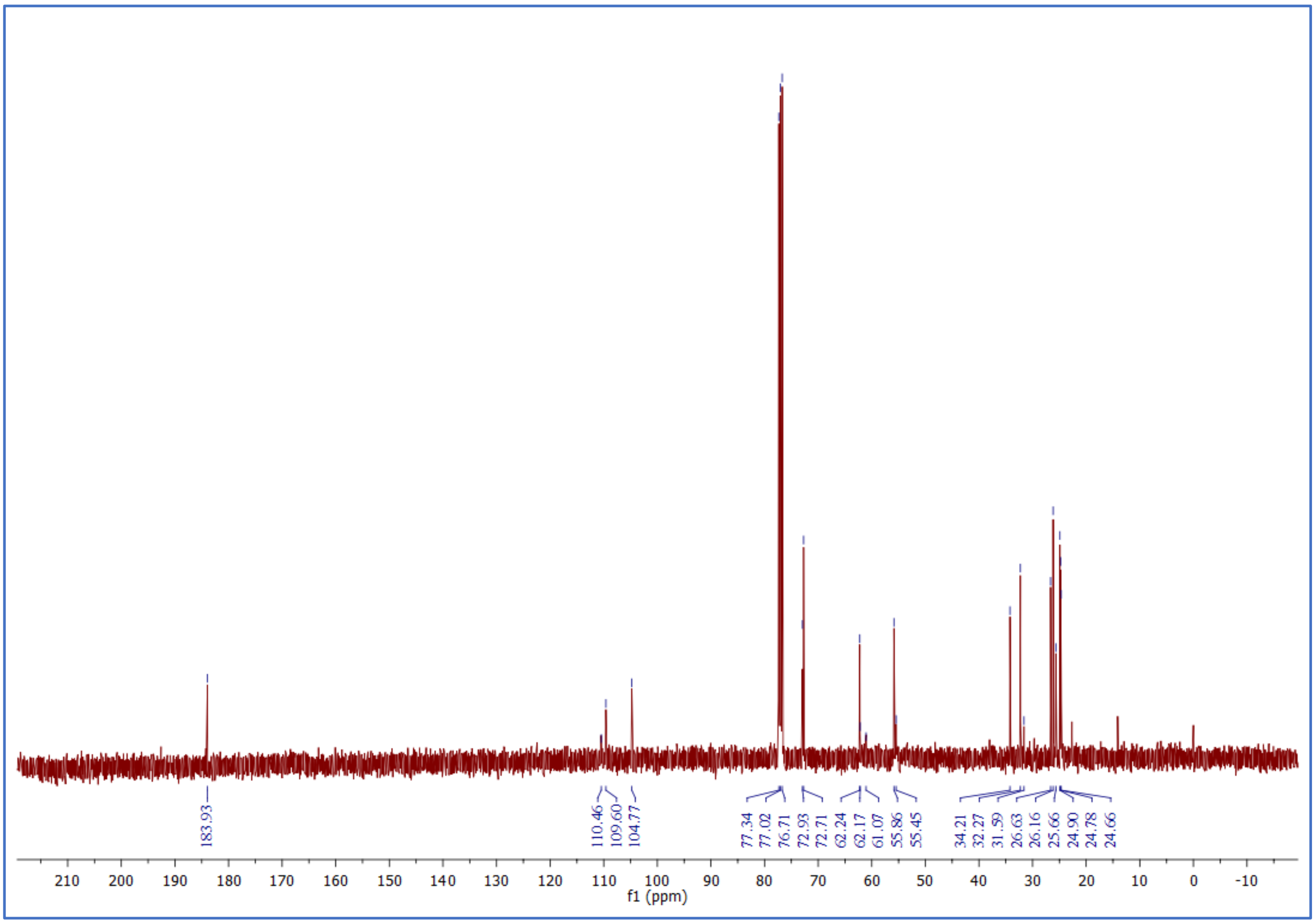
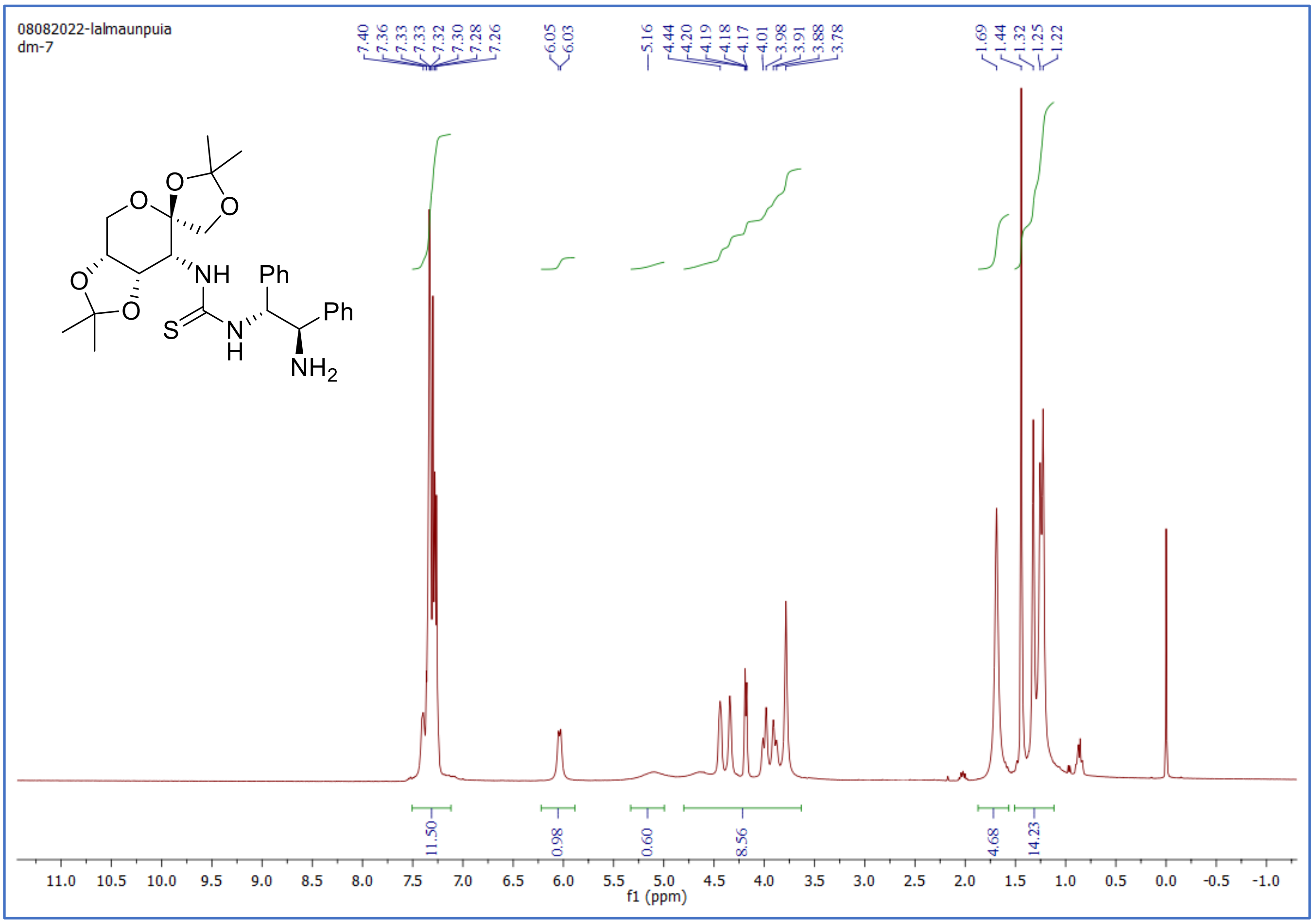


Figure S5: ^{1}H NMR and ^{13}C NMR of **5c.**



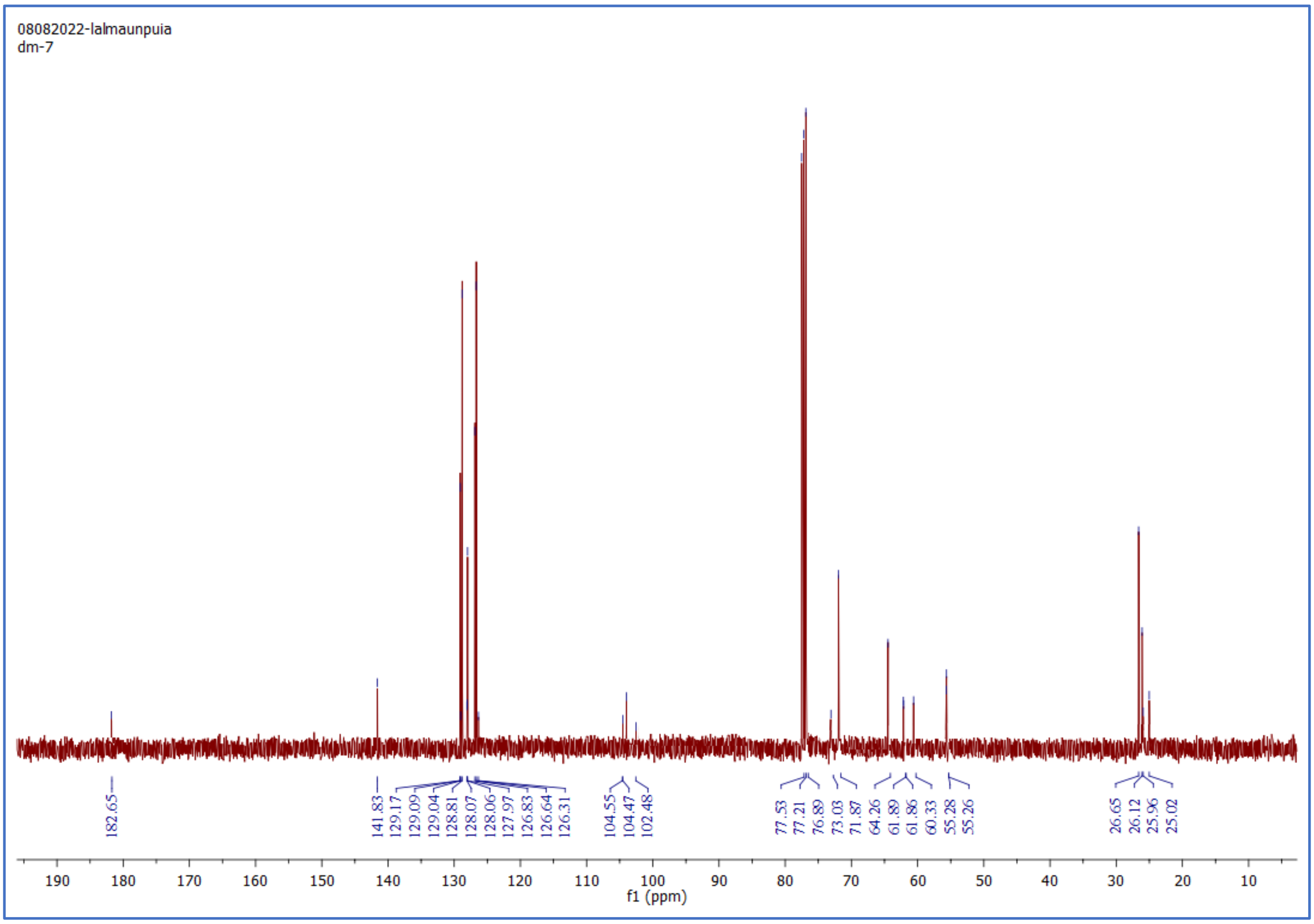
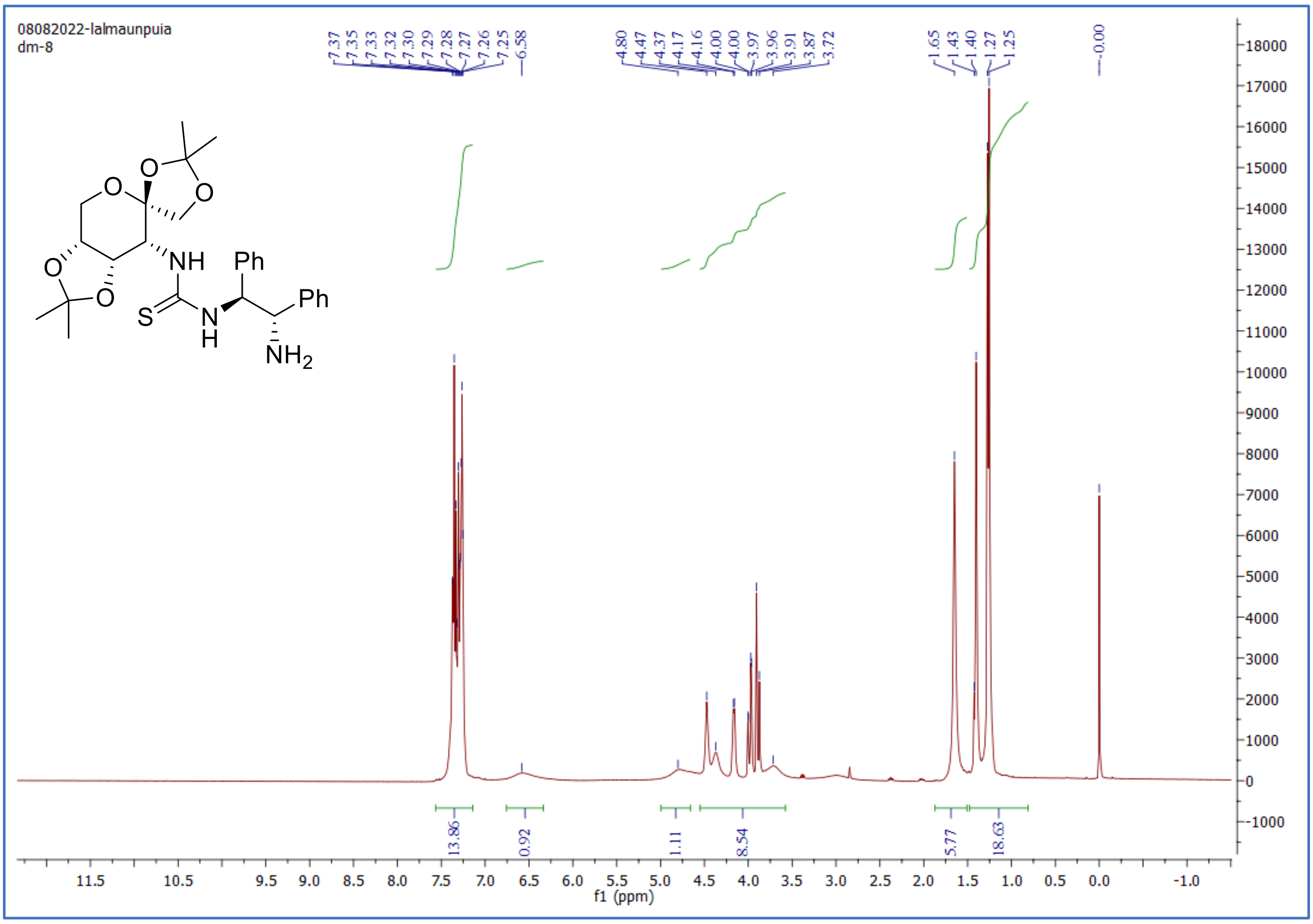


Figure S6: ^{1}H NMR and ^{13}C NMR of **5d.**



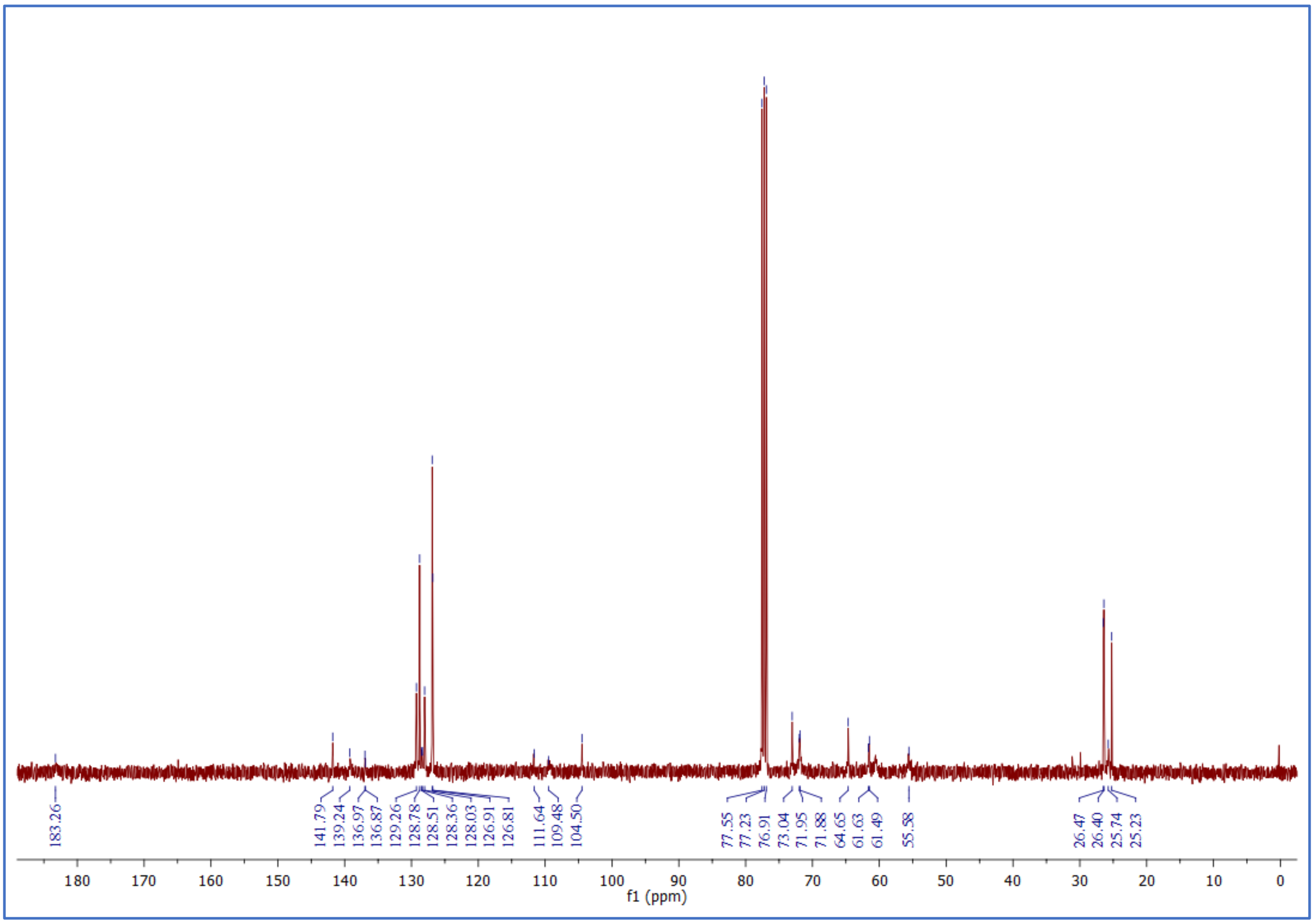
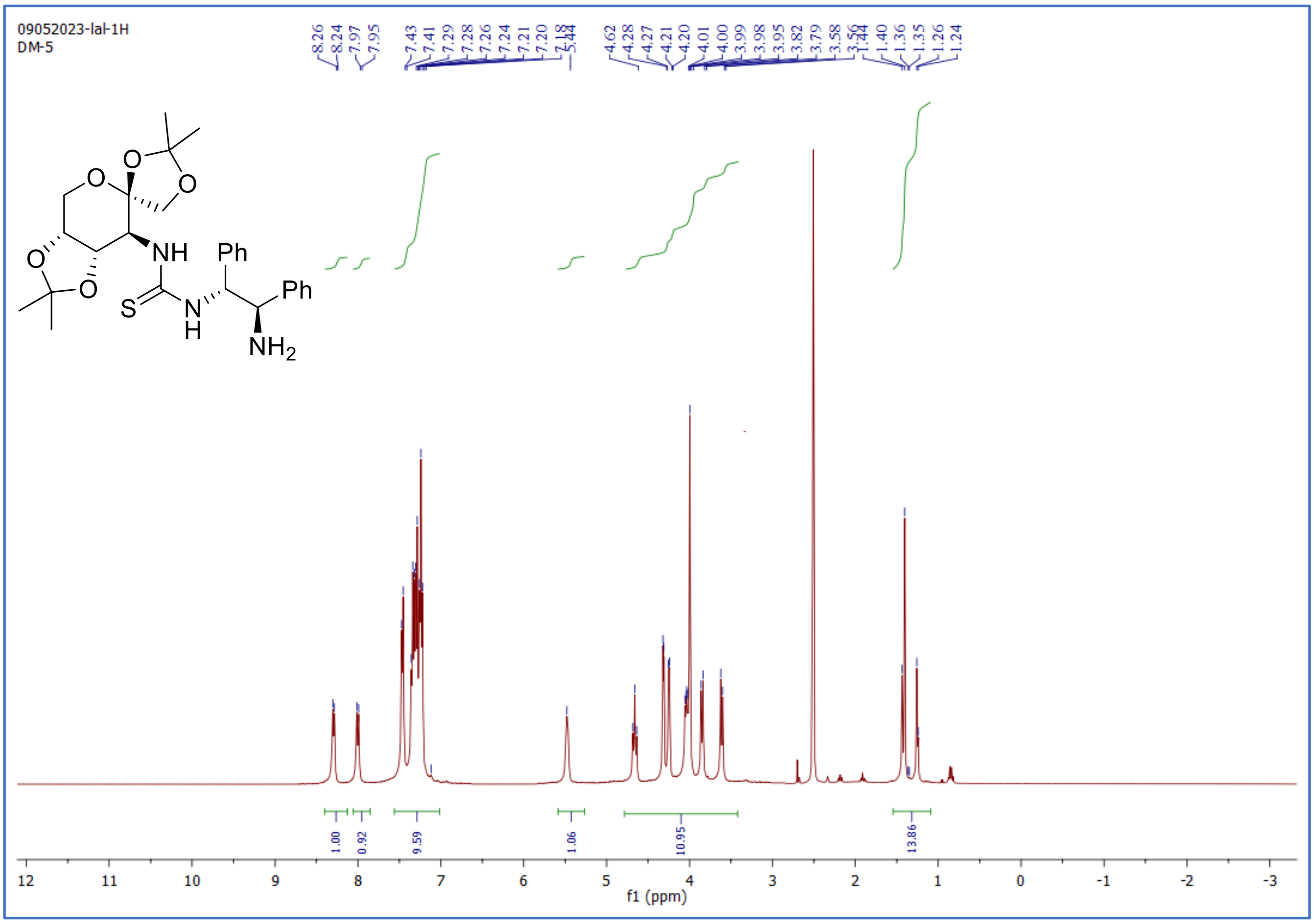


Figure S7: ^{1}H NMR and ^{13}C NMR of **6a.**



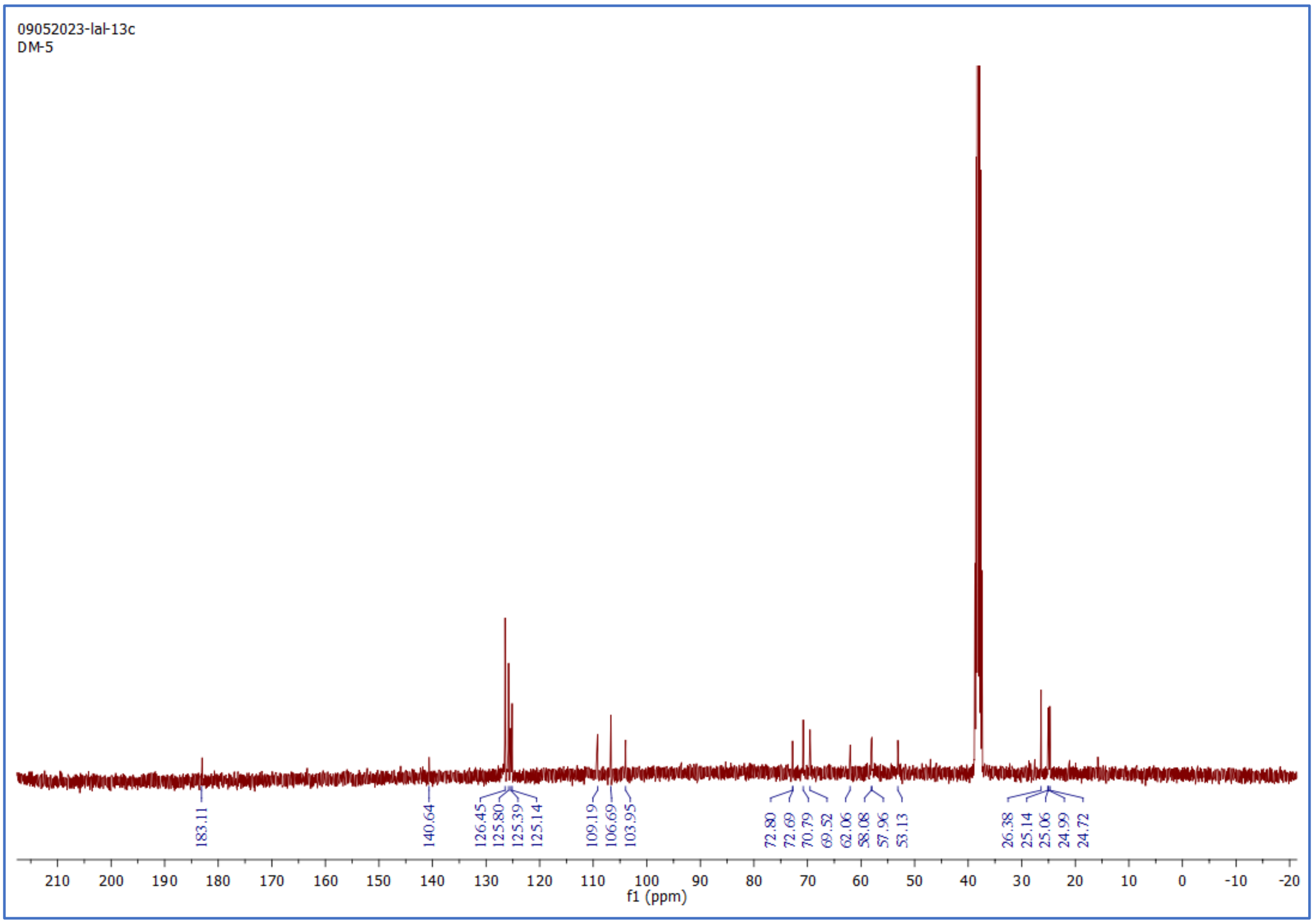
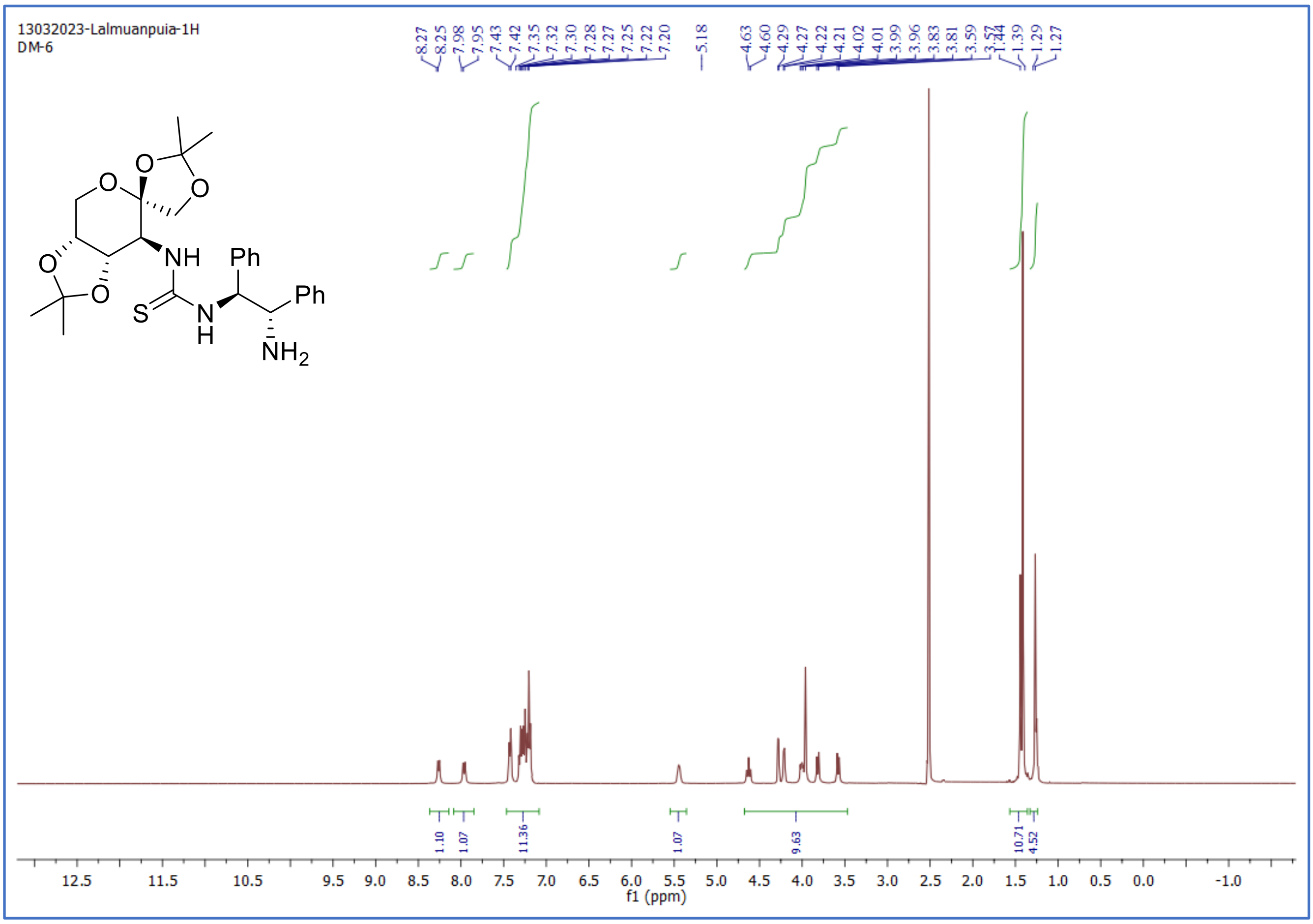


Figure S8: ^{1}H NMR and ^{13}C NMR of **6b.**



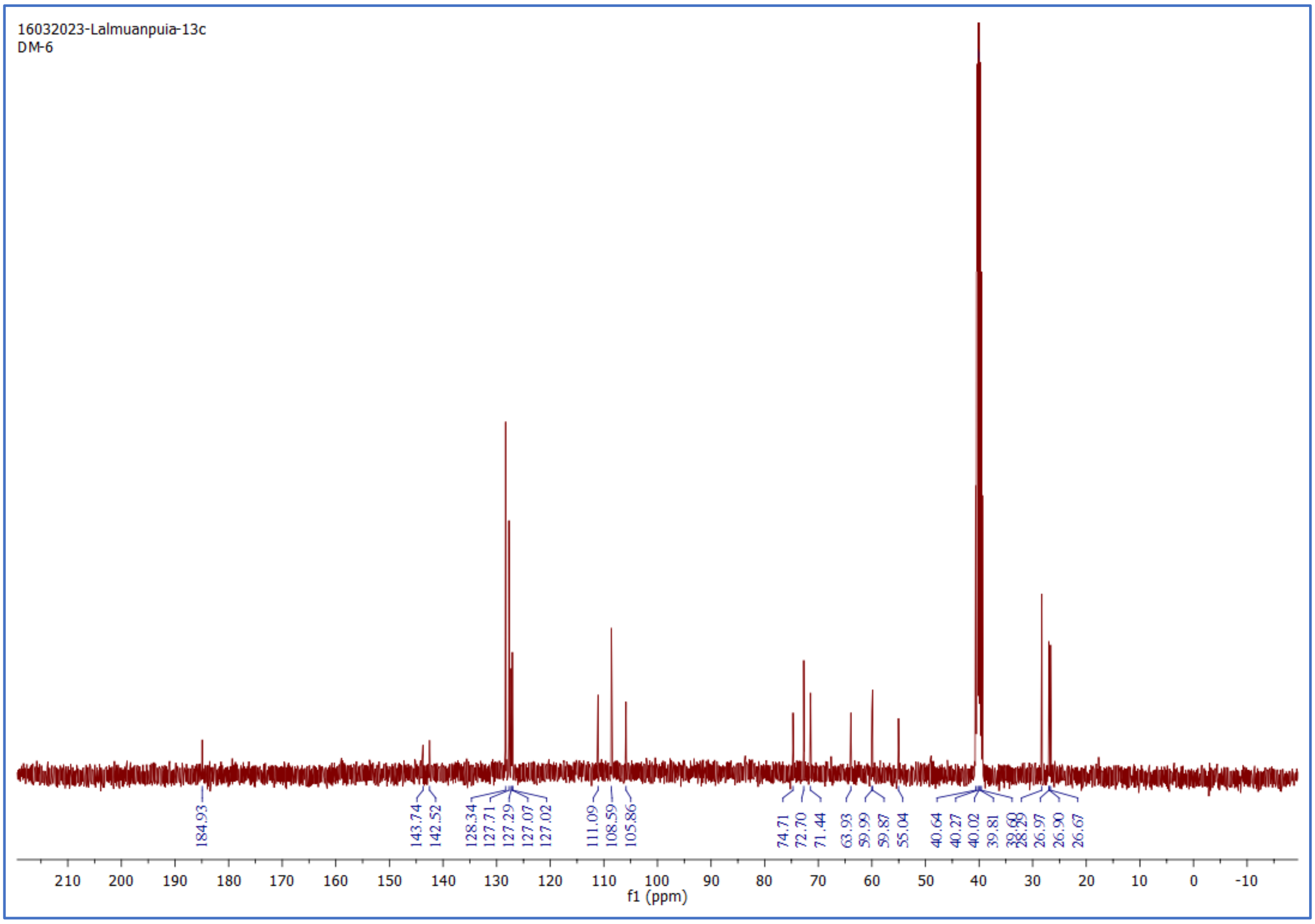


Figure S9: HRMS data of **3.**

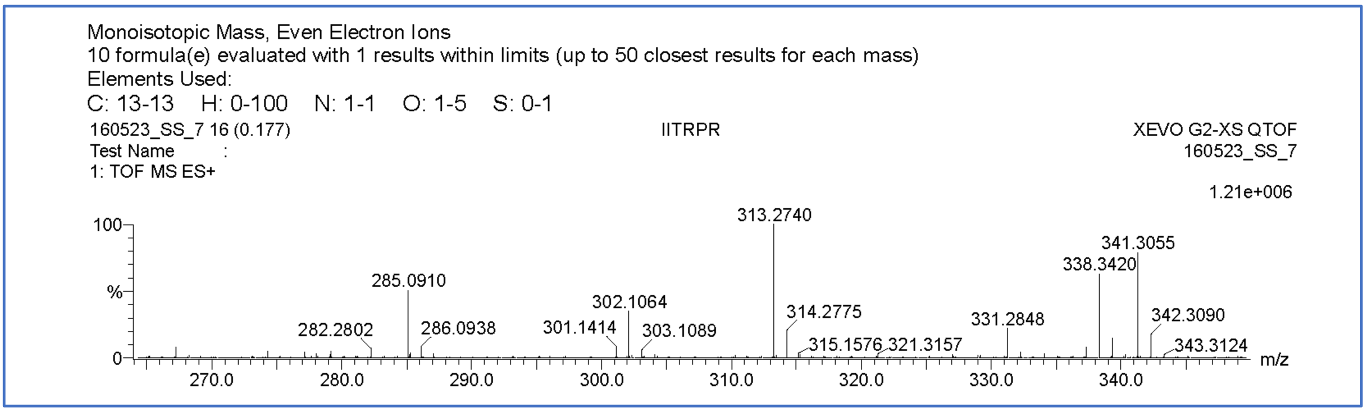


Figure S10: HRMS data of **4**.

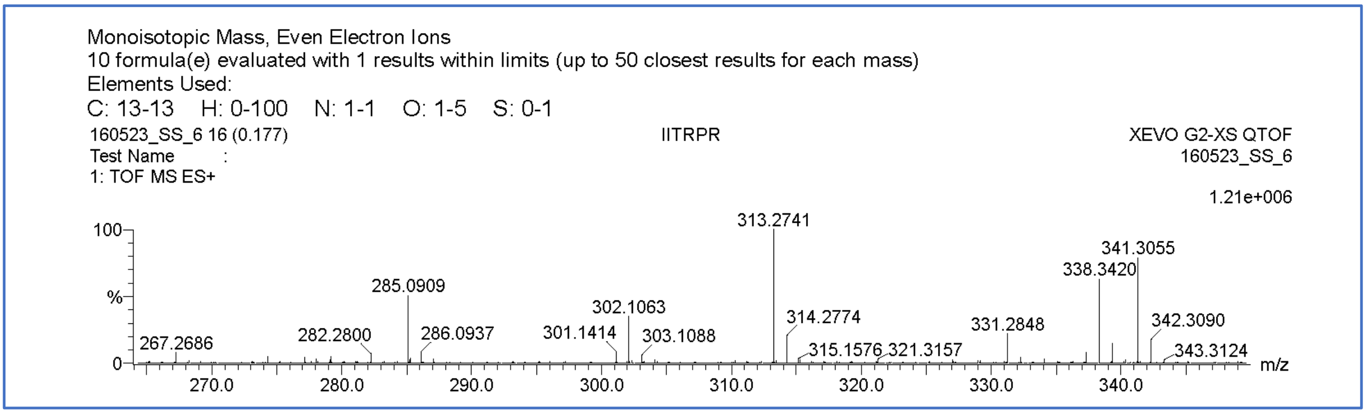


Figure S11: HRMS data of **5a**.

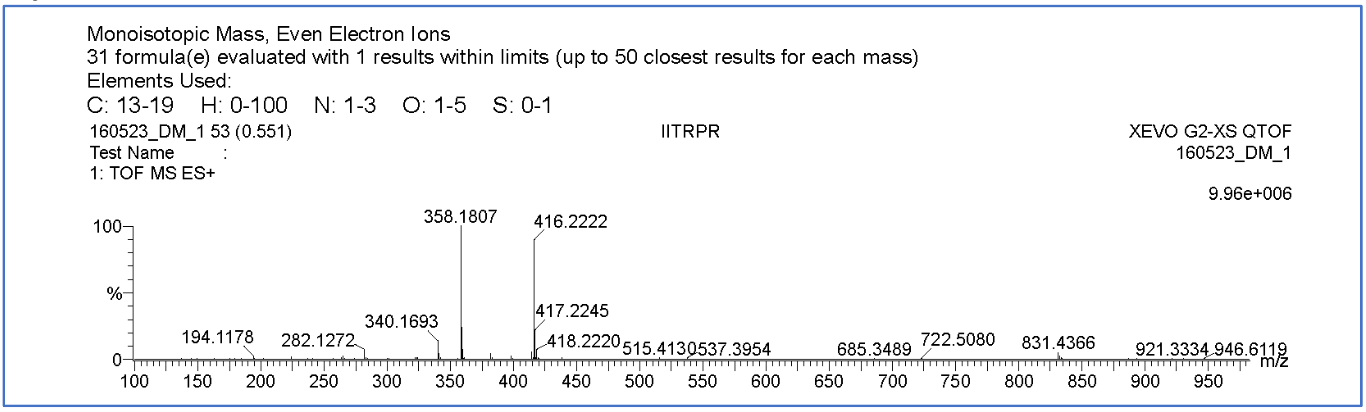


Figure S12: HRMS data of **5b.**

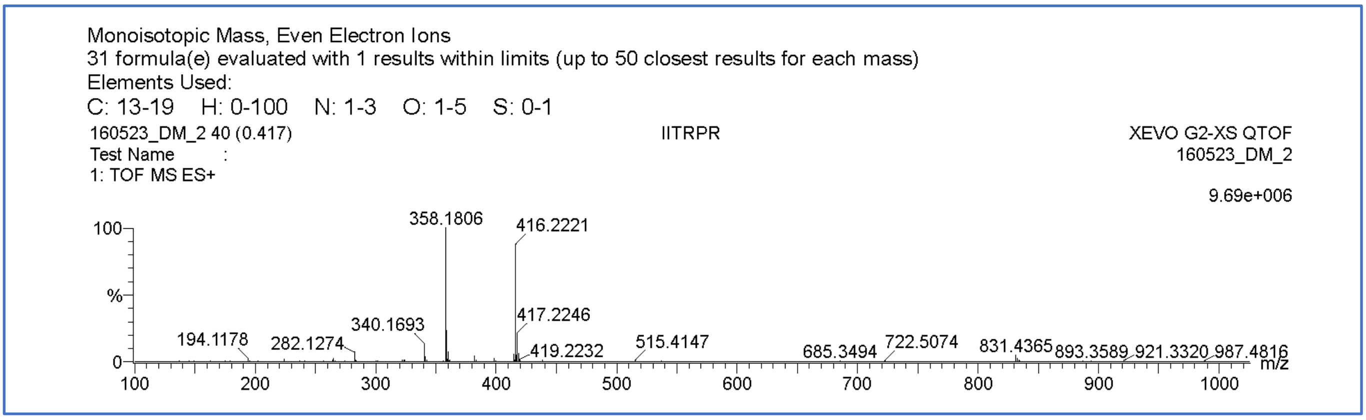


Figure S13: HRMS data of **5c**.

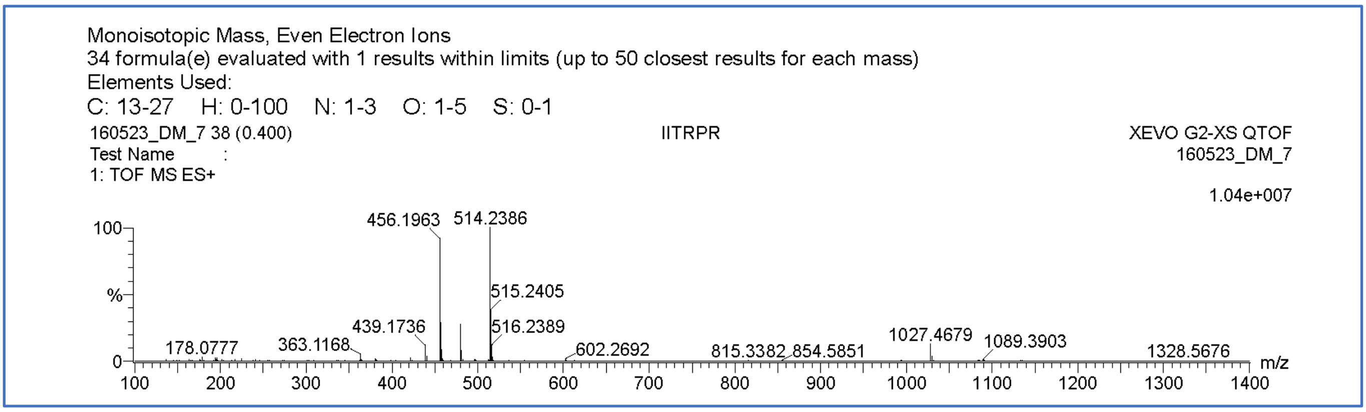


Figure S14: HRMS data of **5d**.

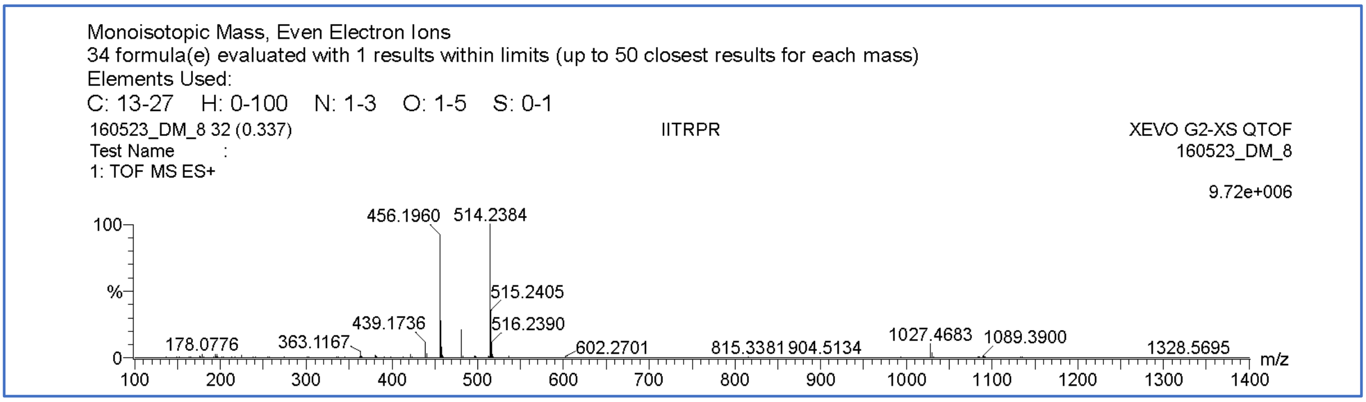


Figure S15: HRMS data of **6a**.

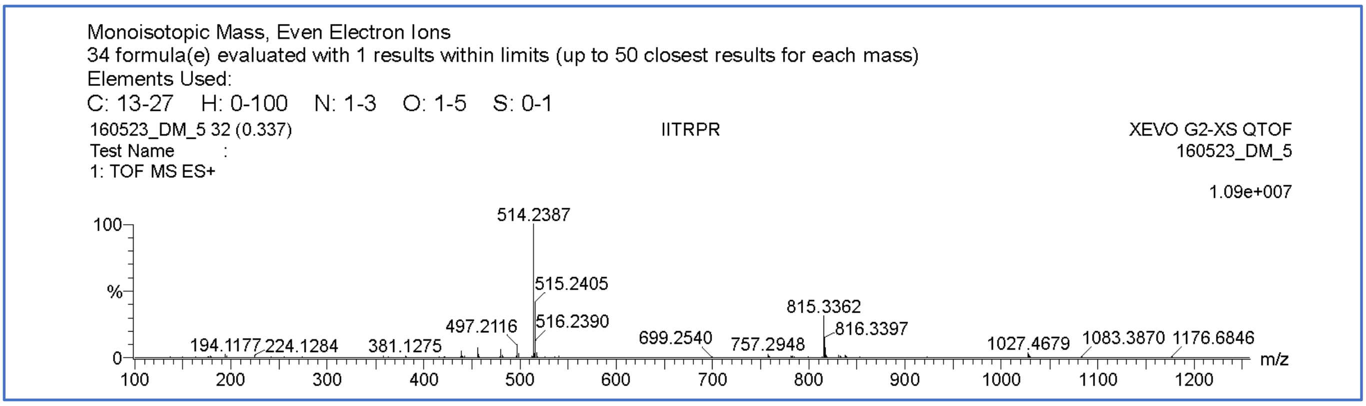


Figure S16: HRMS data of **6b**.

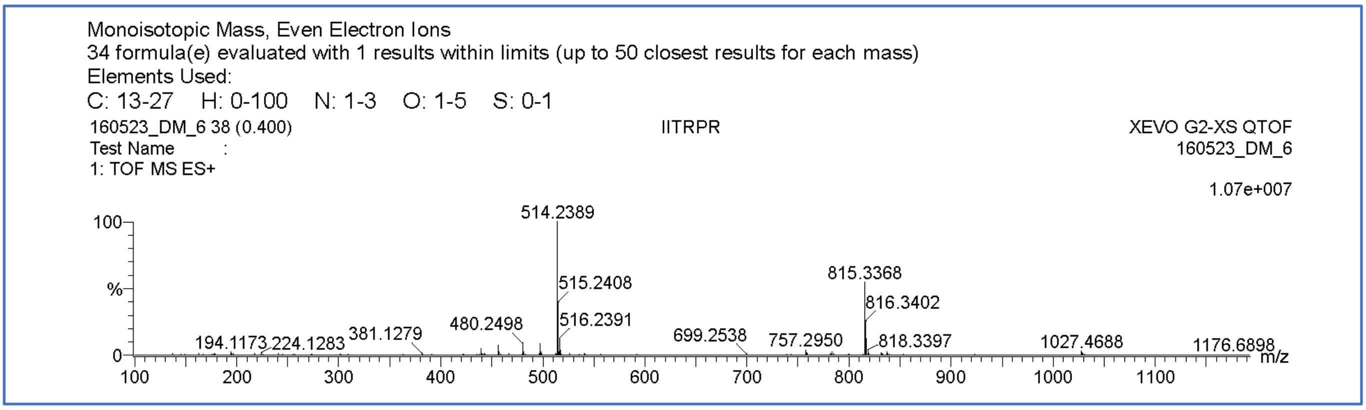
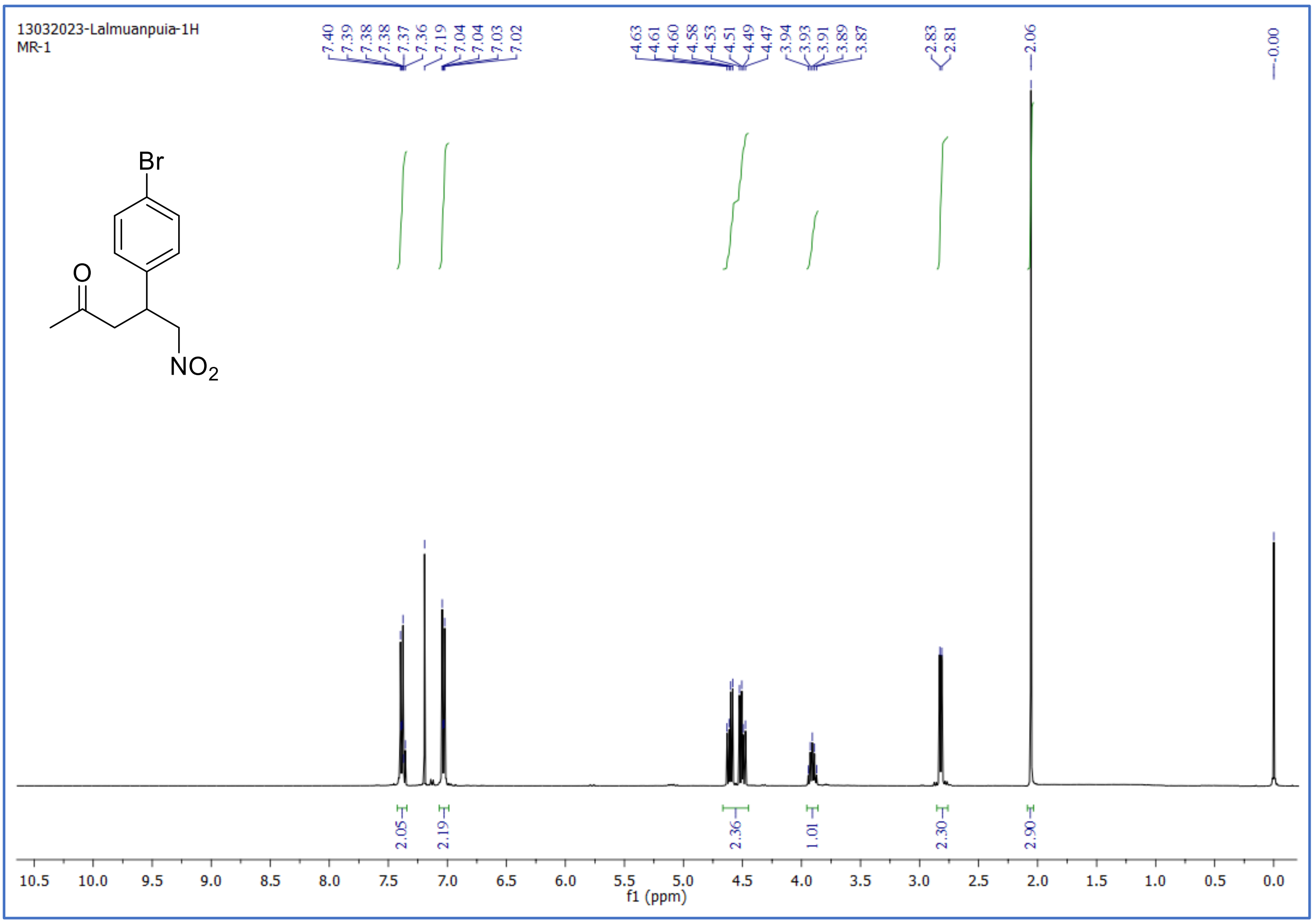


Figure S17: ^{1}H NMR and ^{13}C NMR of **8a.**



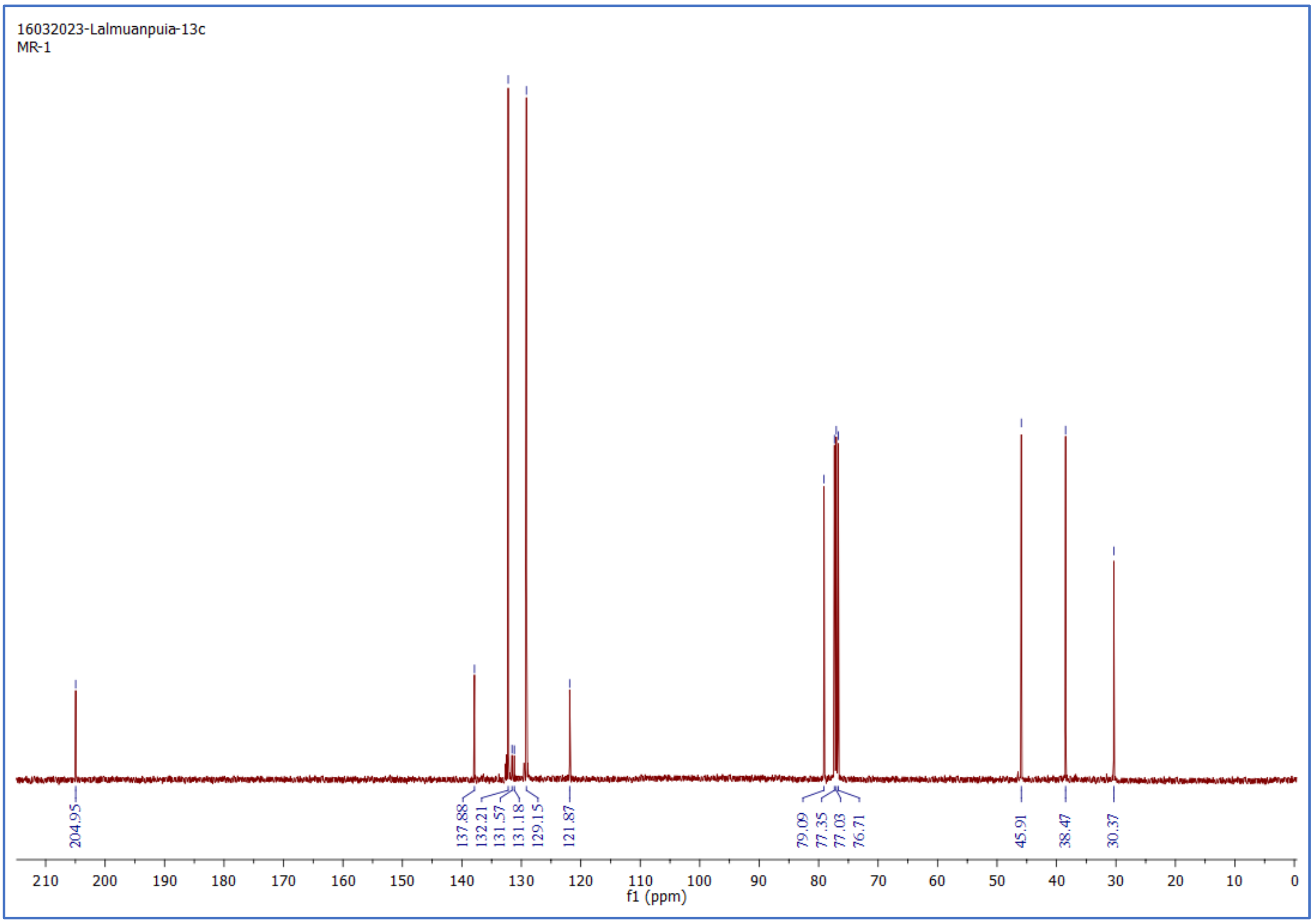
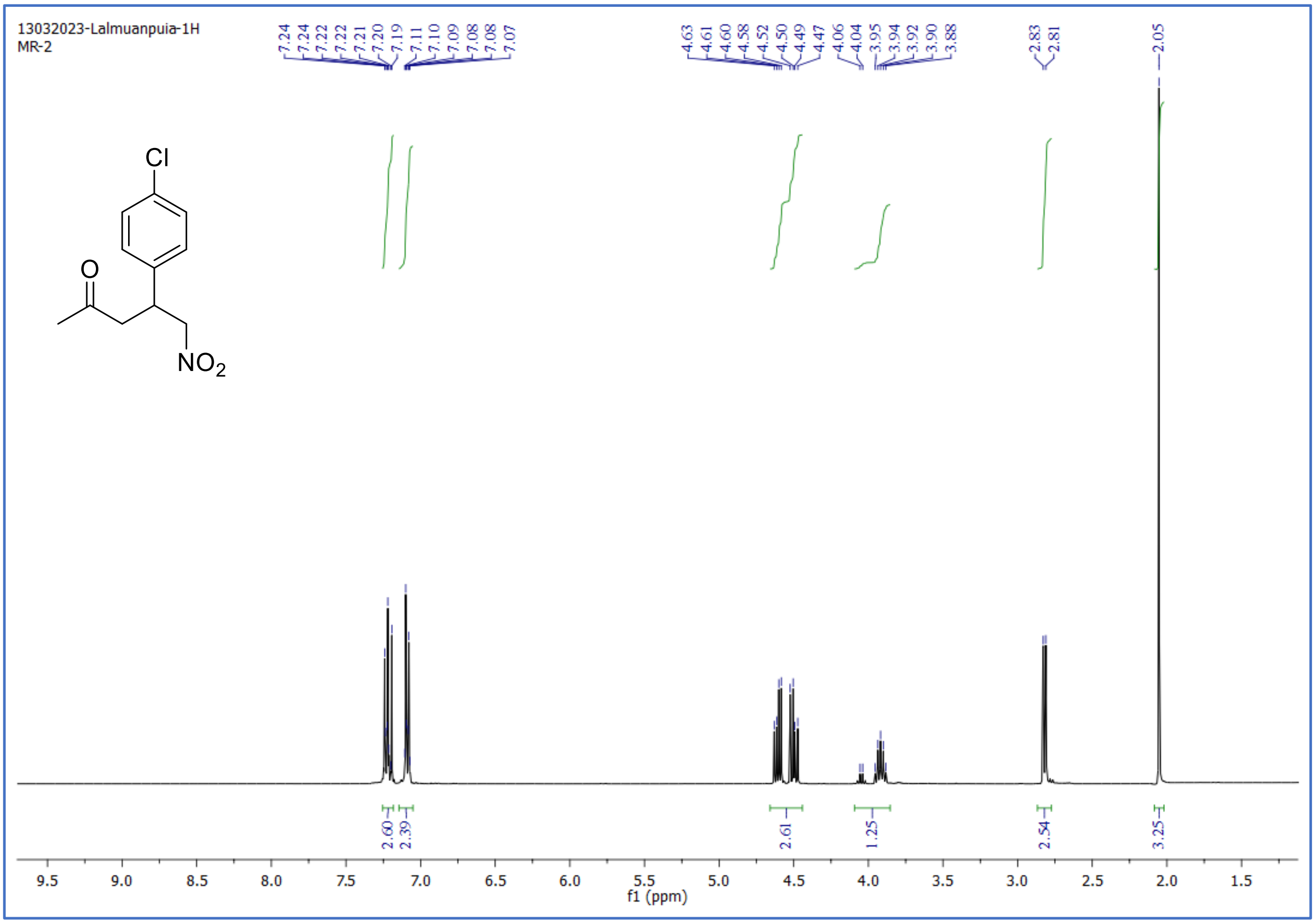


Figure S18: ^{1}H NMR and ^{13}C NMR of **8b.**



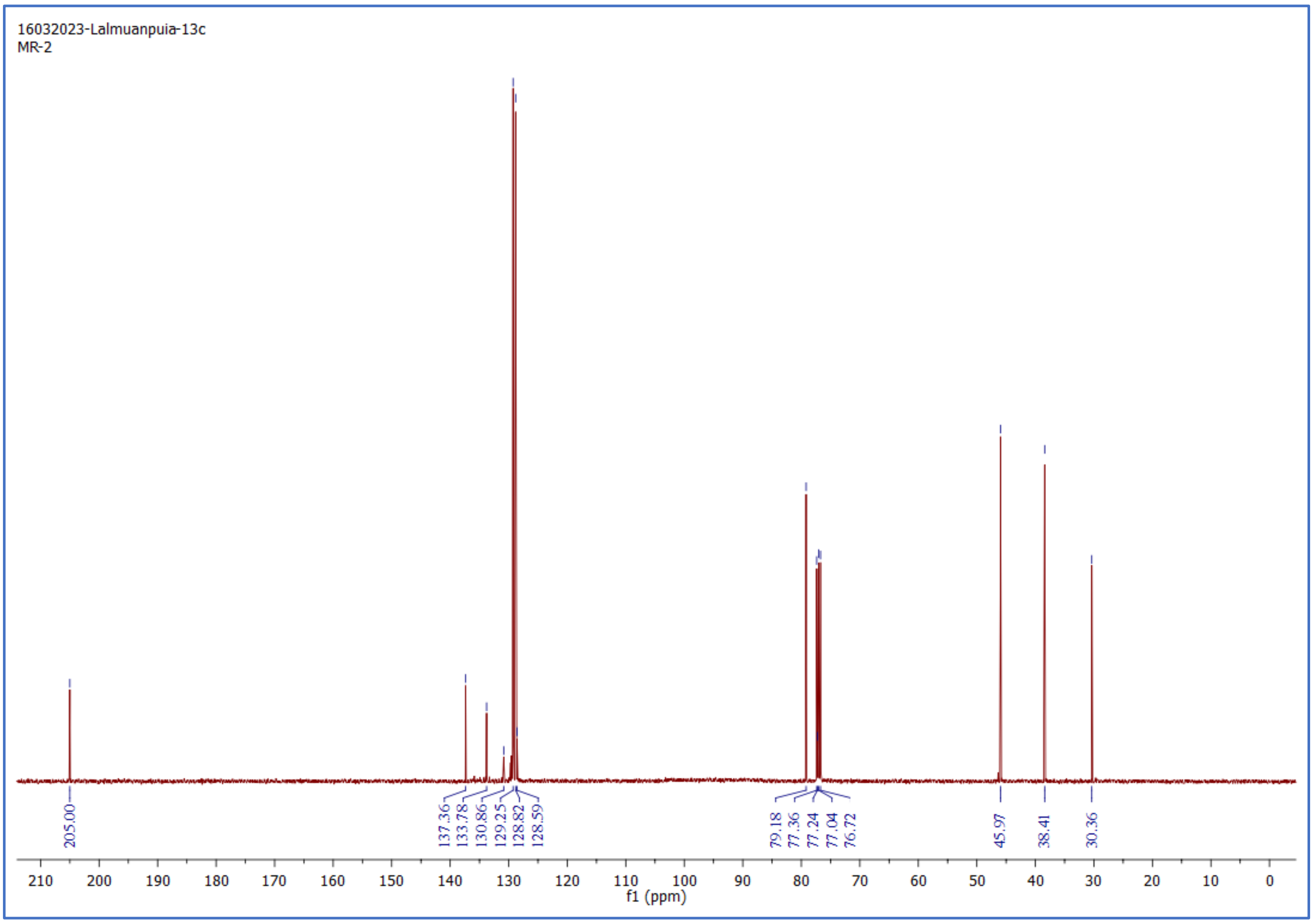
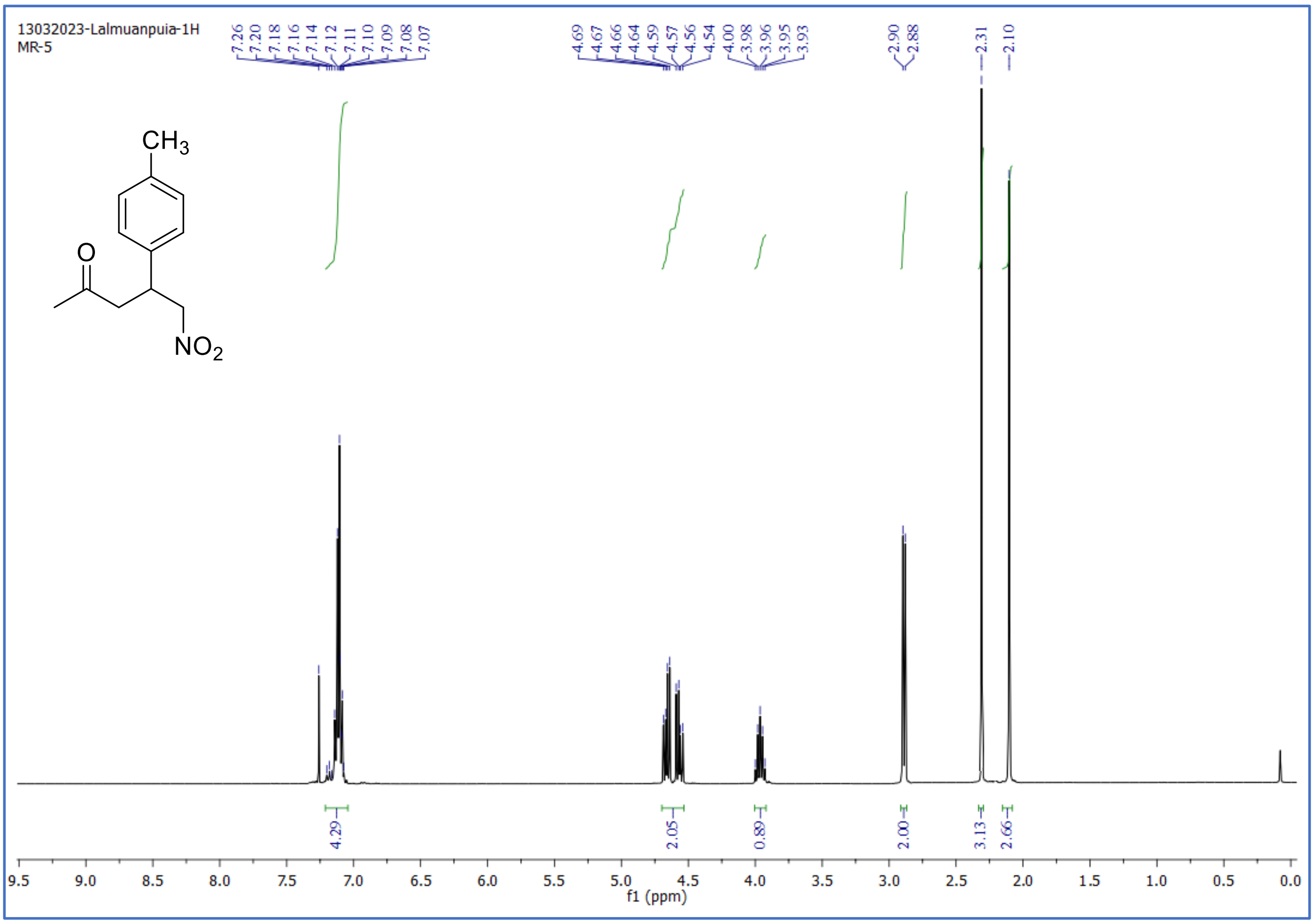


Figure S19: ^{1}H NMR and ^{13}C NMR of **8c.**



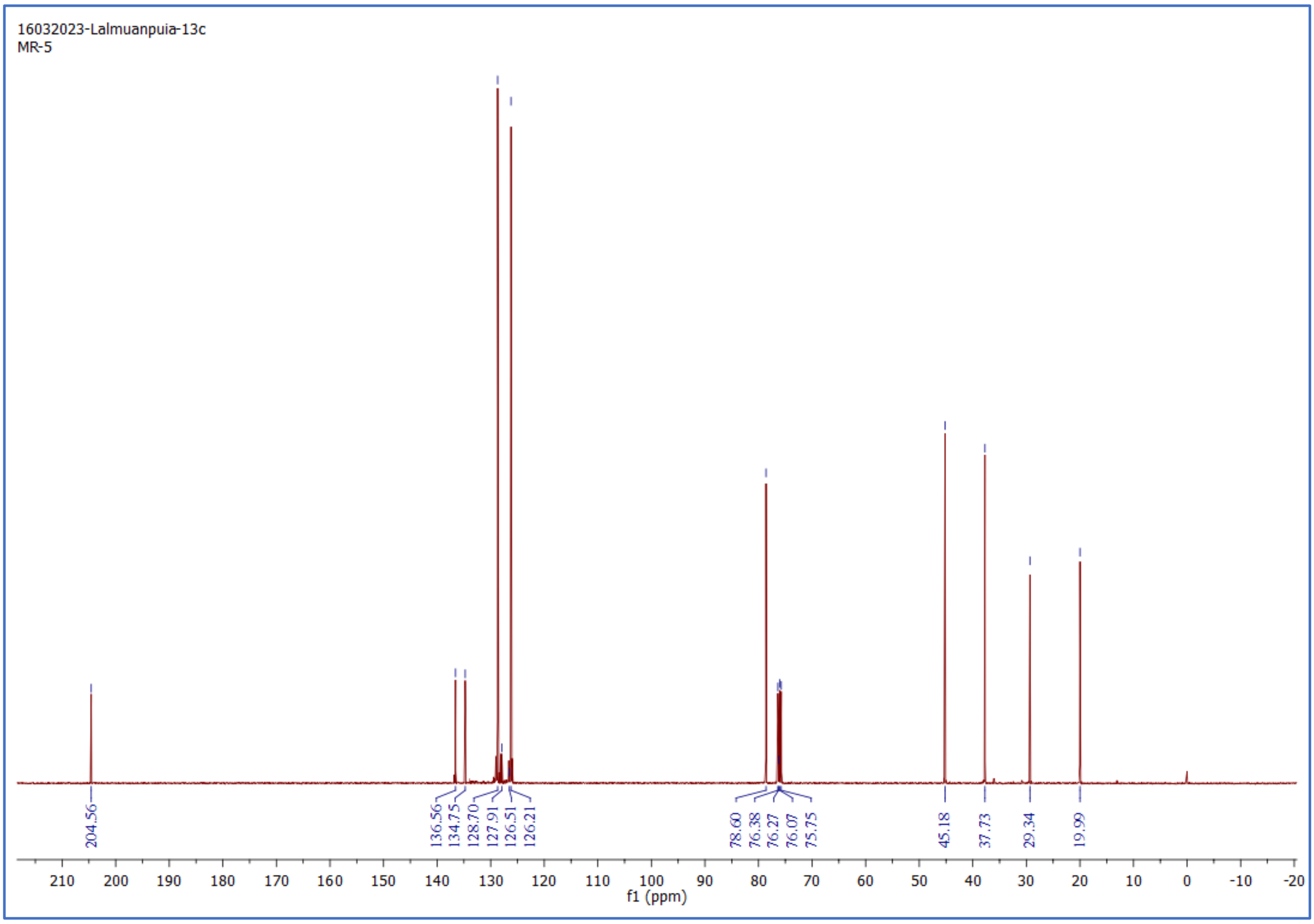
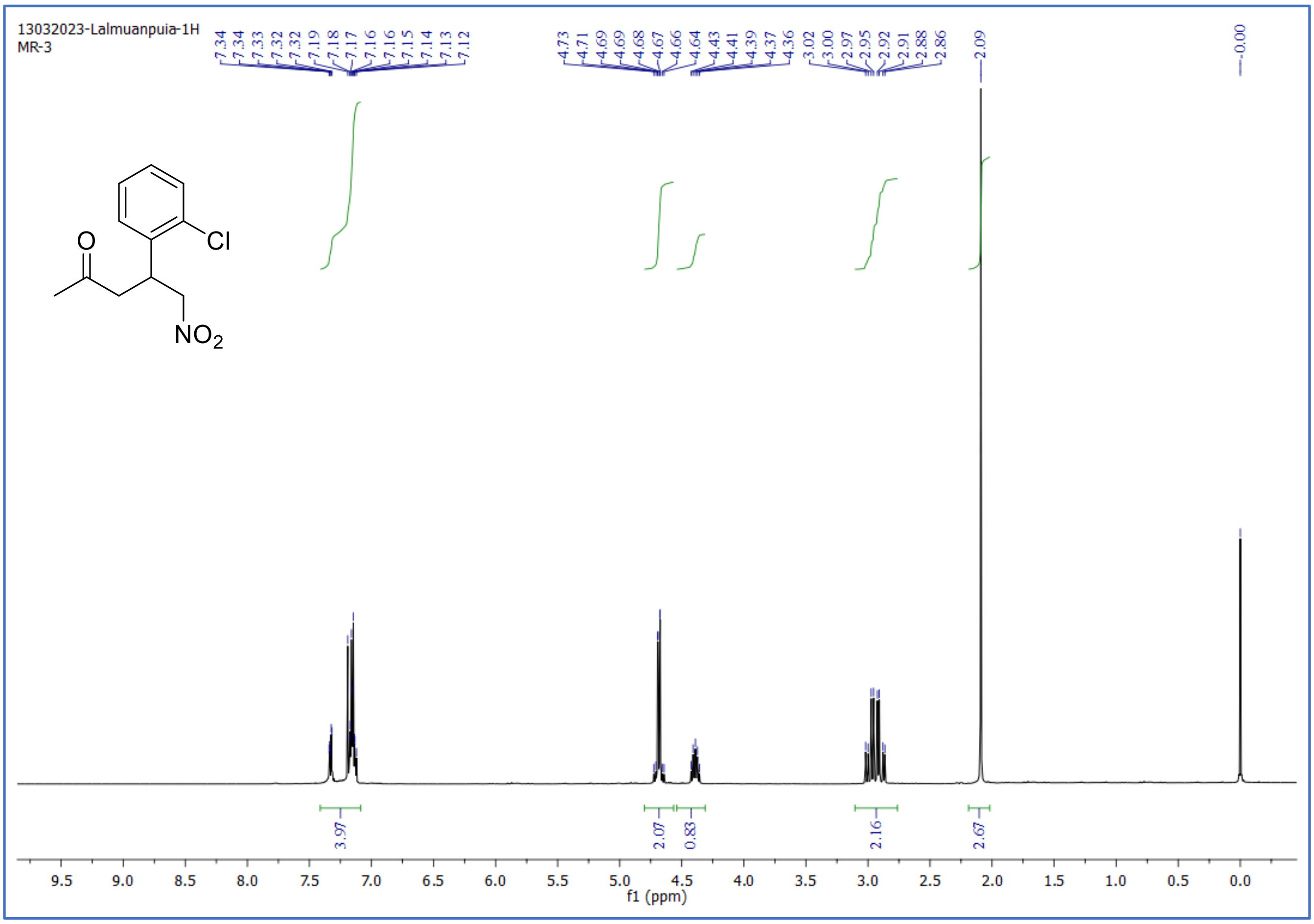


Figure S20: ^{1}H NMR and ^{13}C NMR of **8d.**



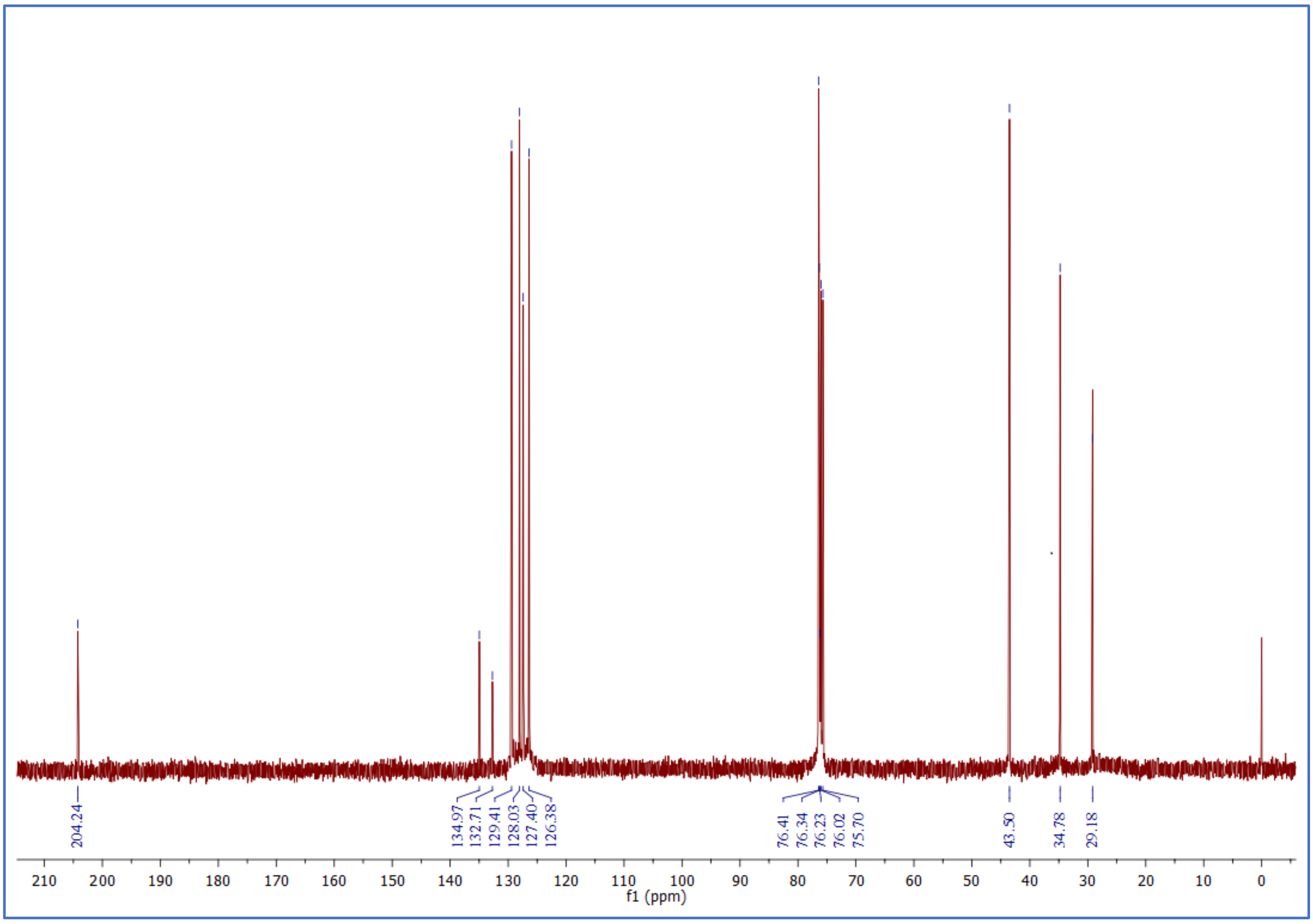
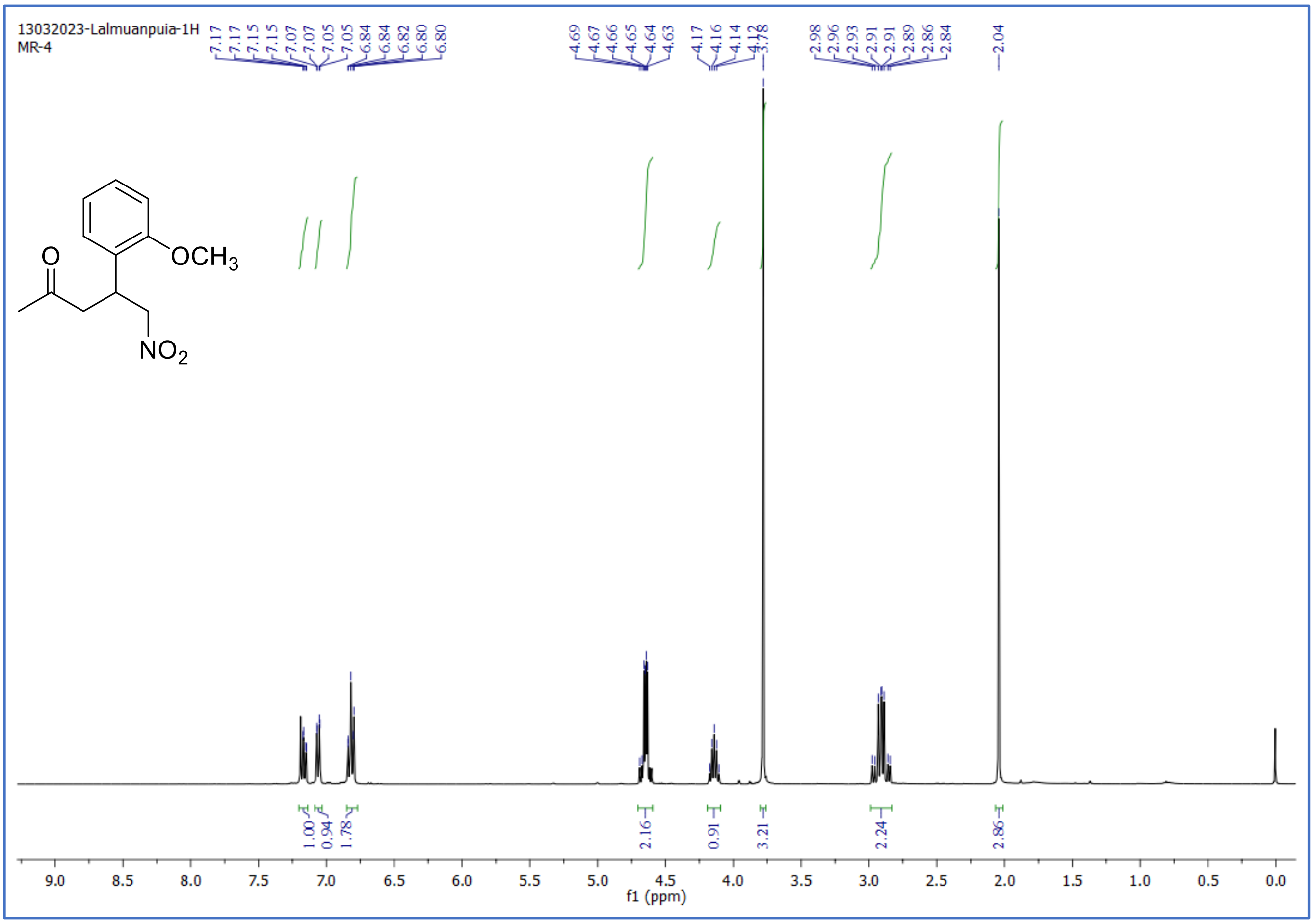


Figure S21: ^{1}H NMR and ^{13}C NMR of **8e.**



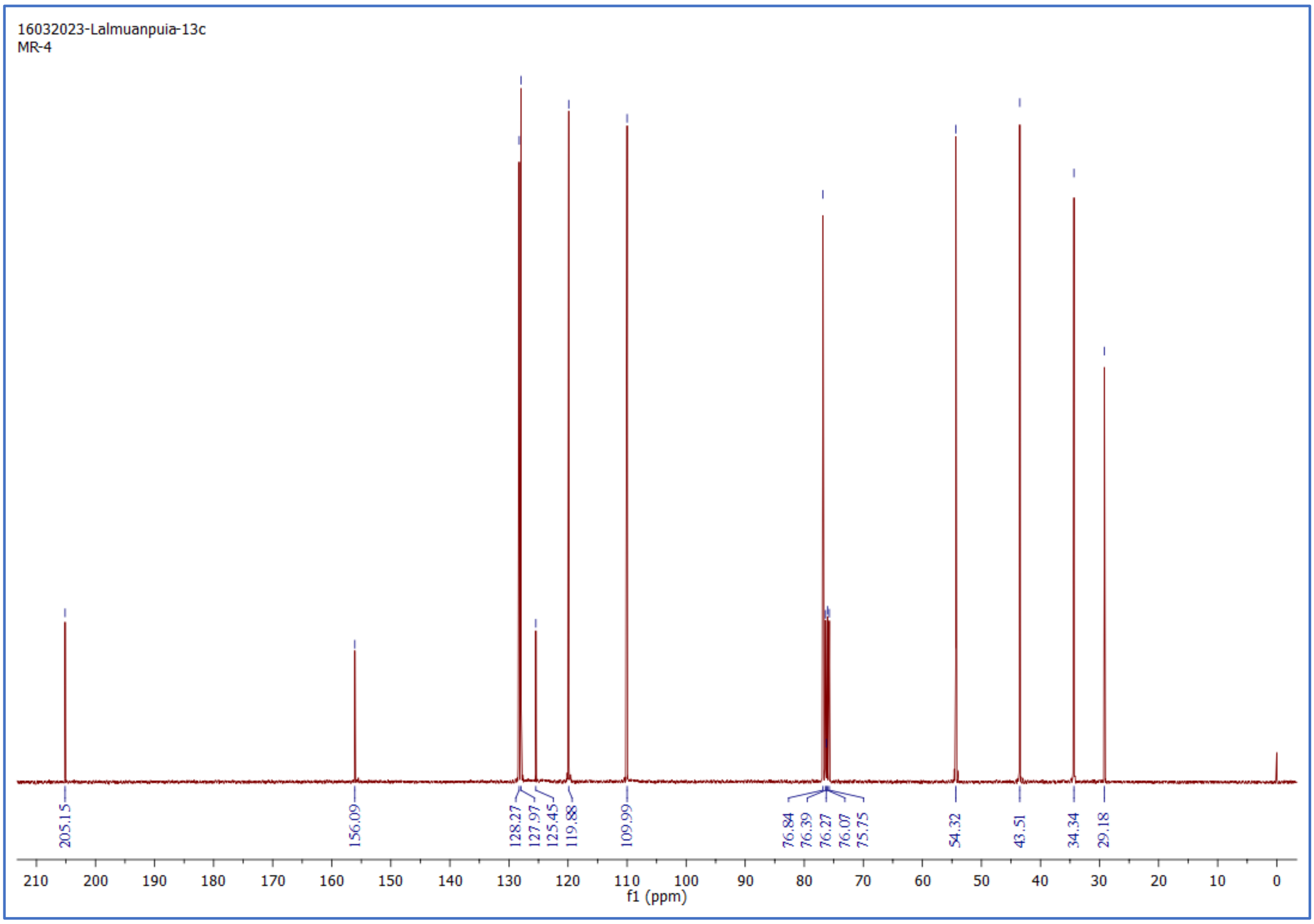
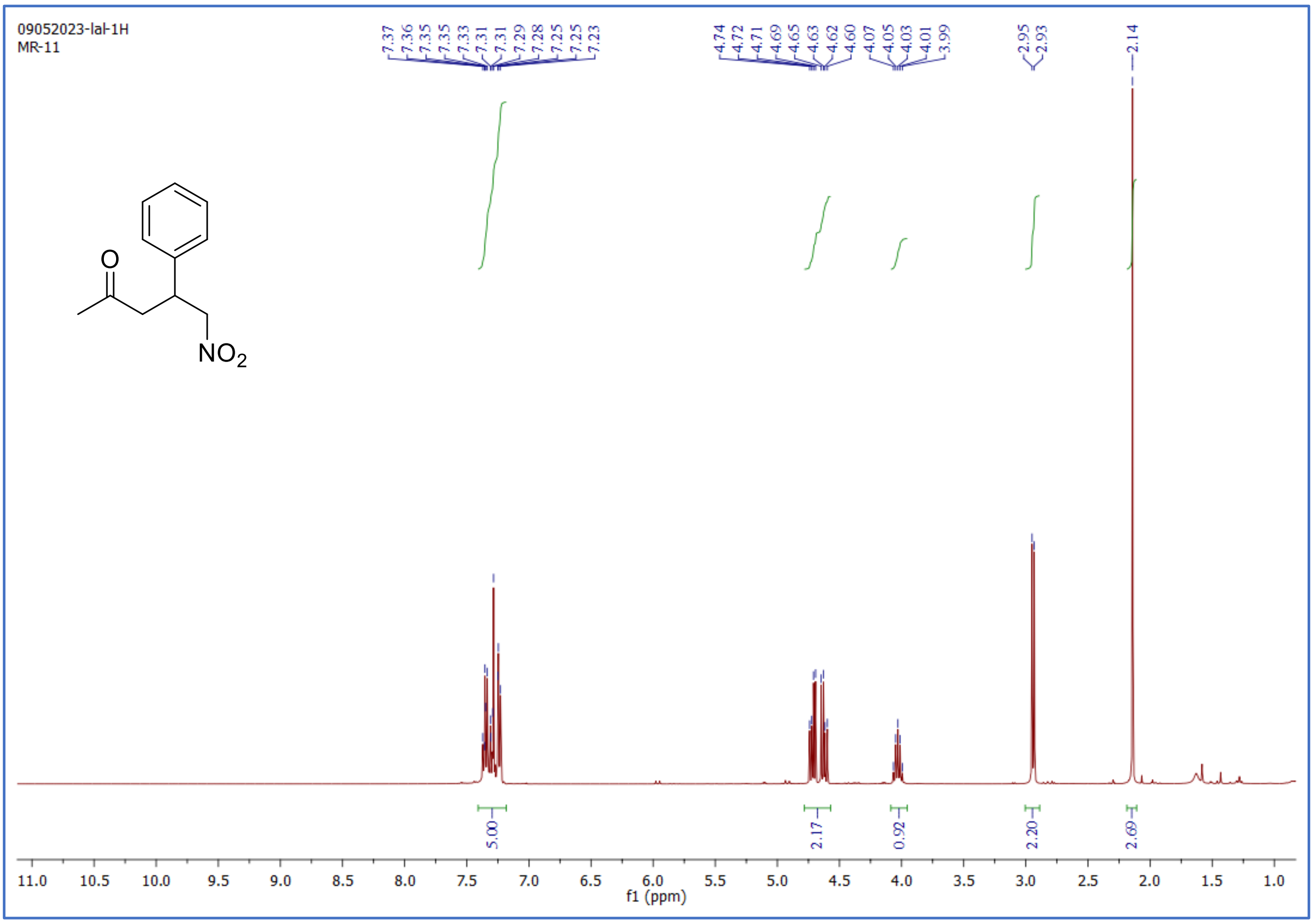


Figure S22: ^{1}H NMR and ^{13}C NMR of **8f.**



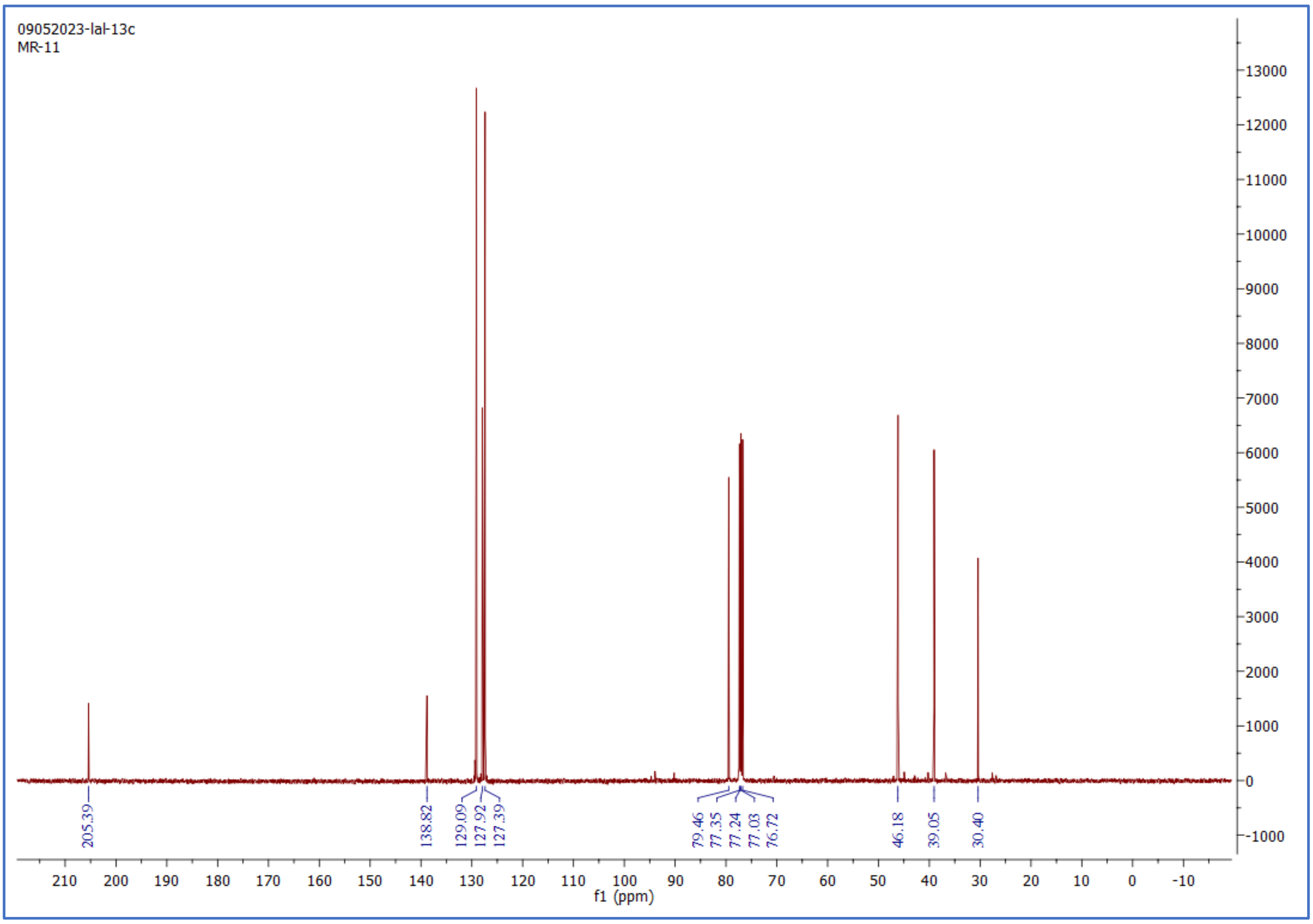
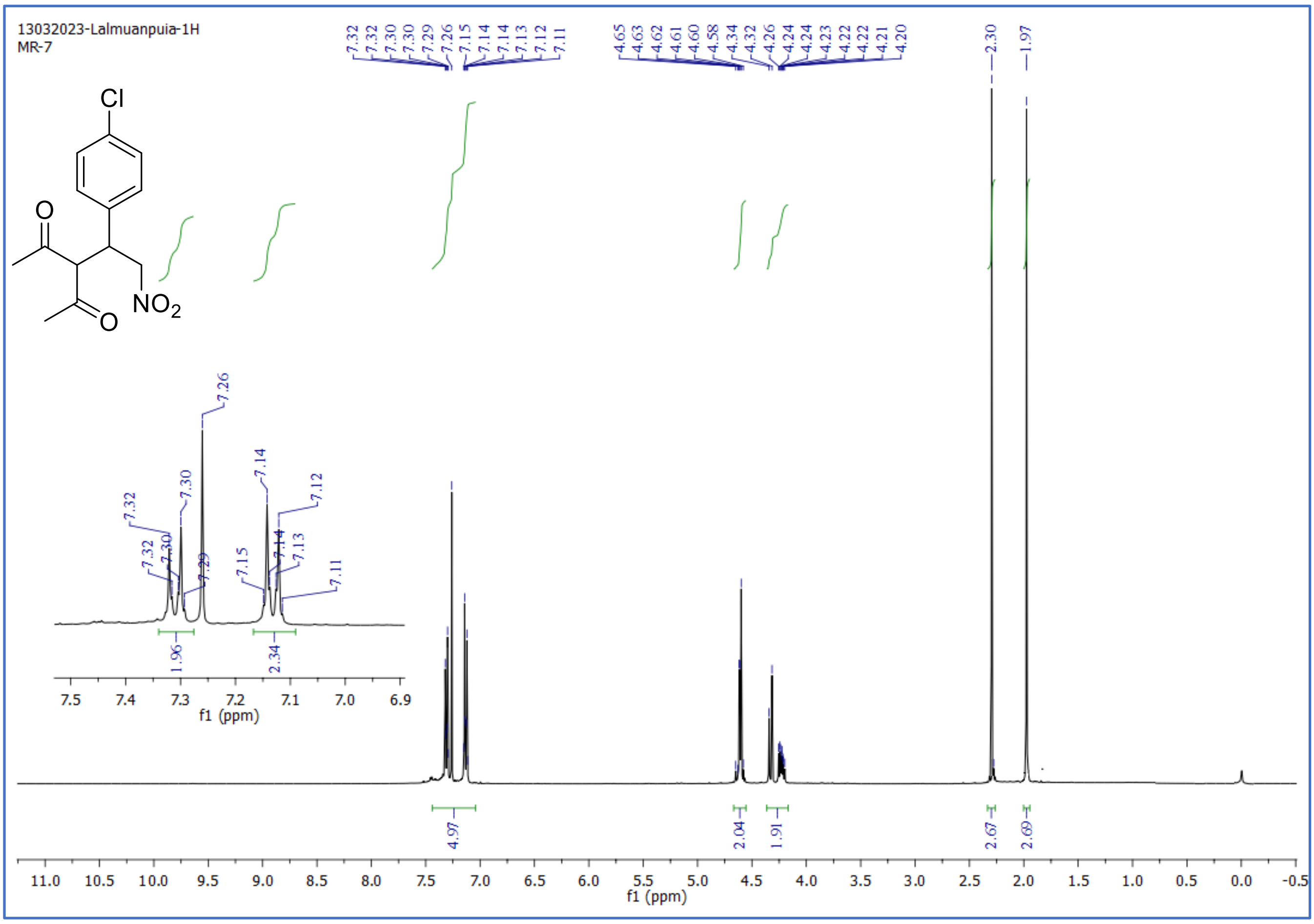


Figure S23: ^{1}H NMR and ^{13}C NMR of **8g.**



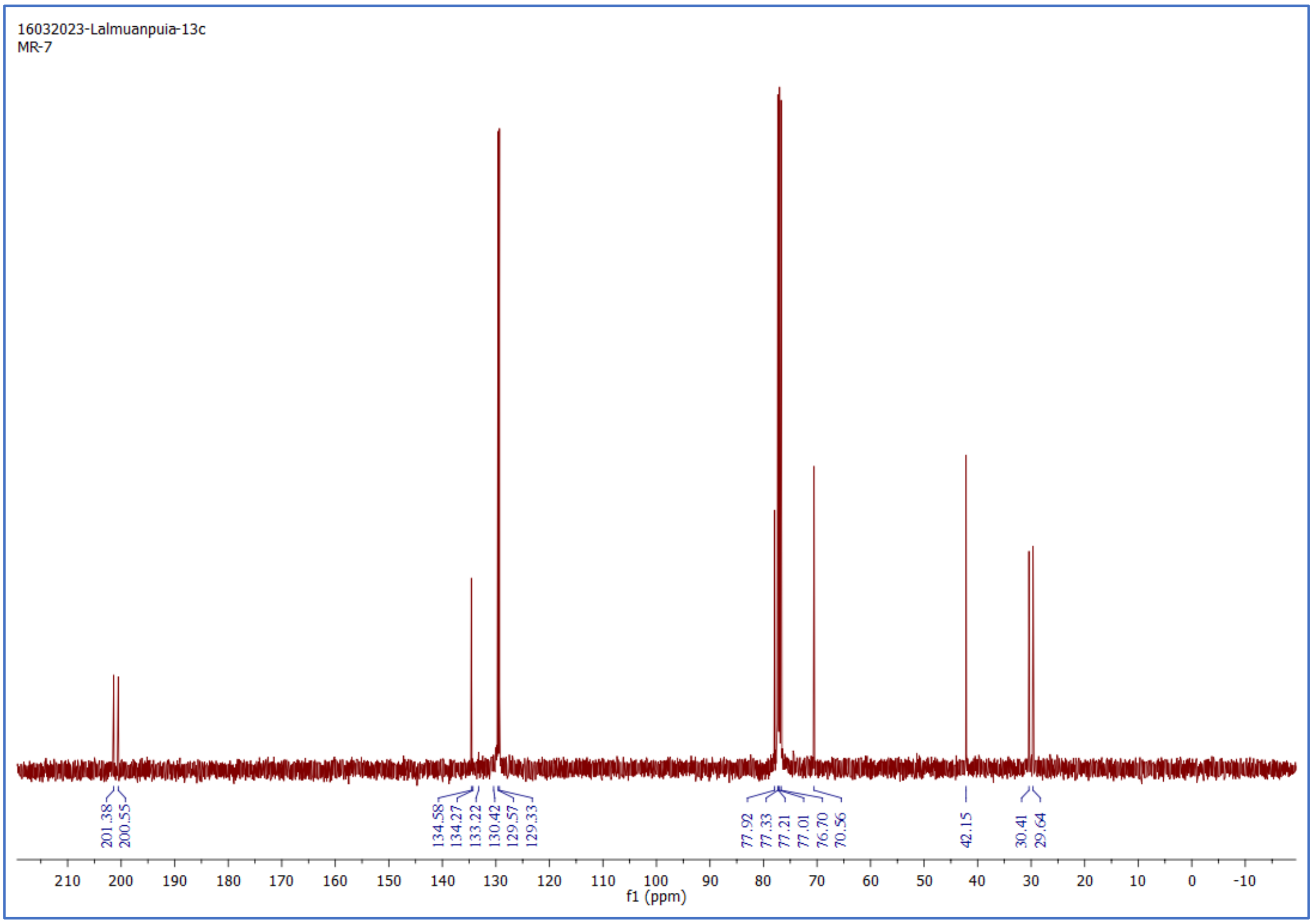
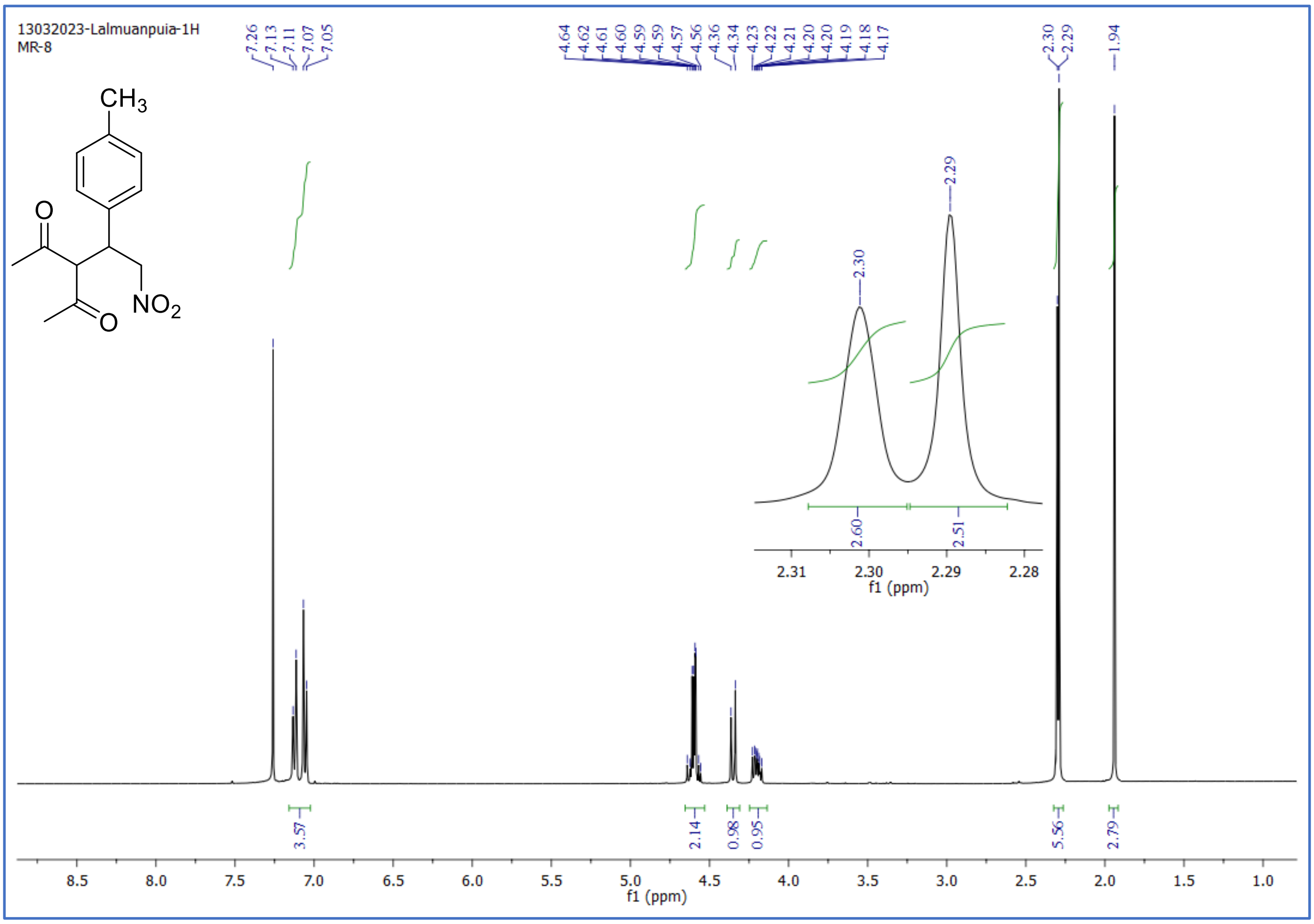


Figure S24: ^{1}H NMR and ^{13}C NMR of **8h.**



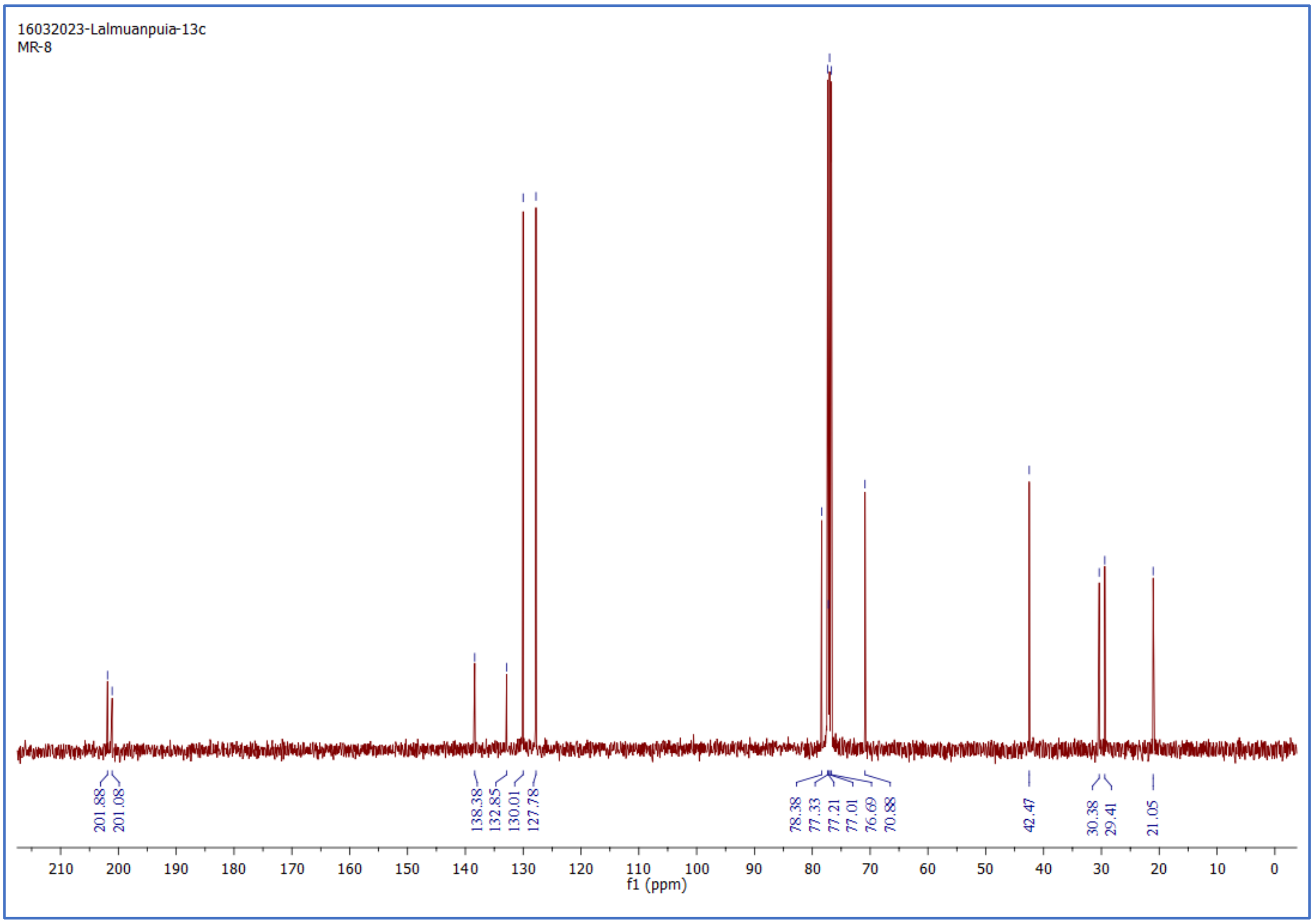
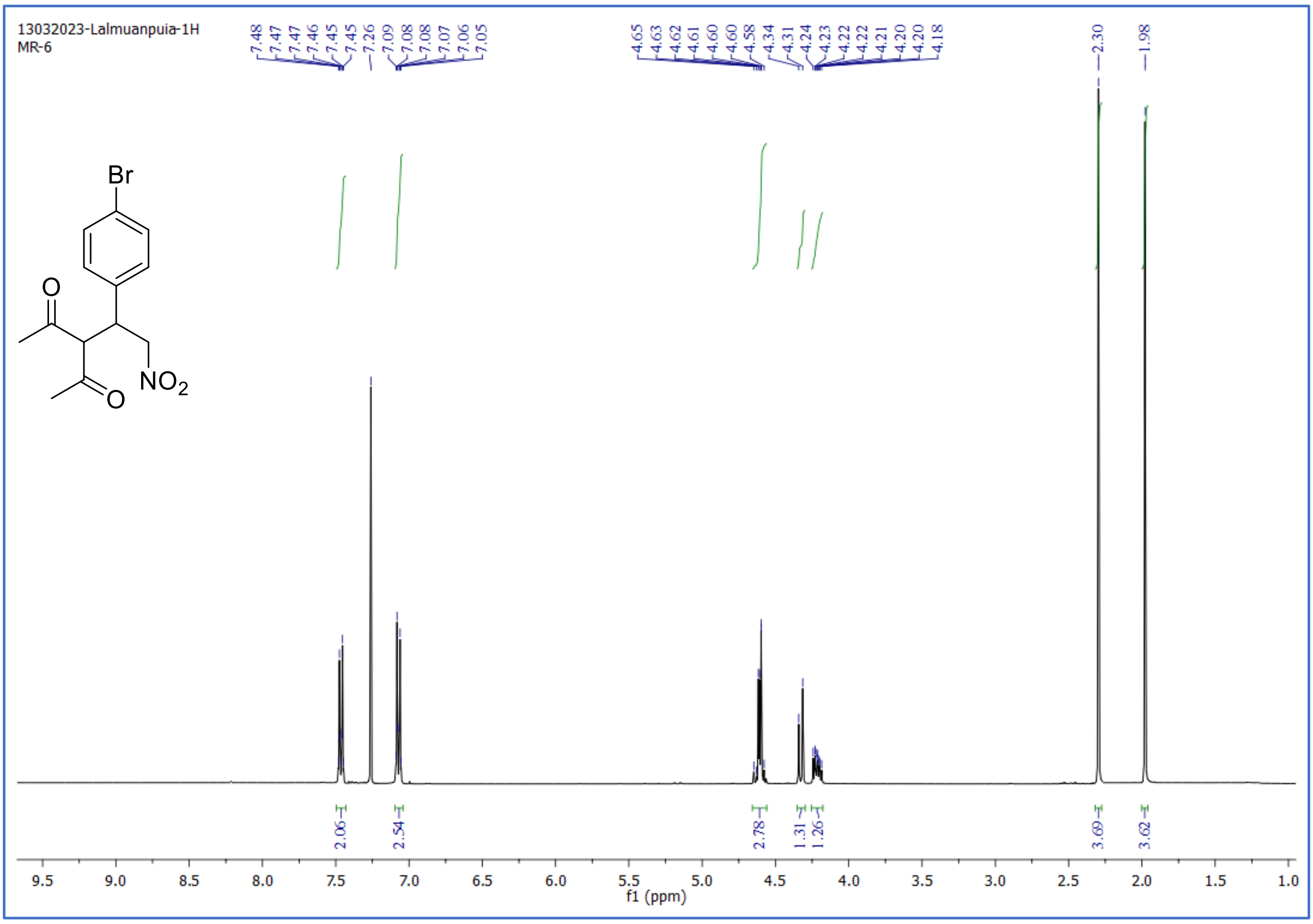


Figure S25: ^{1}H NMR and ^{13}C NMR of **8i.**



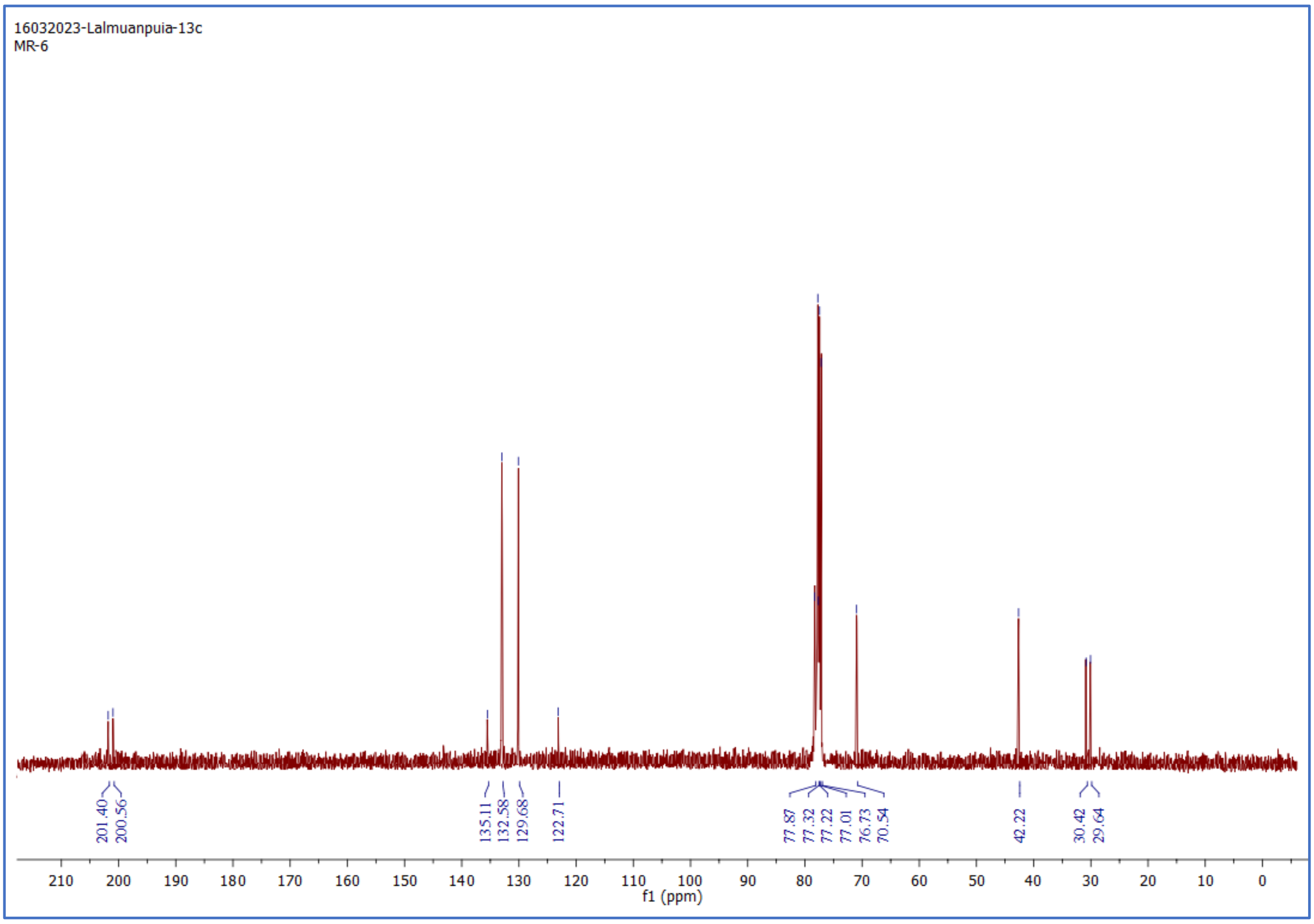
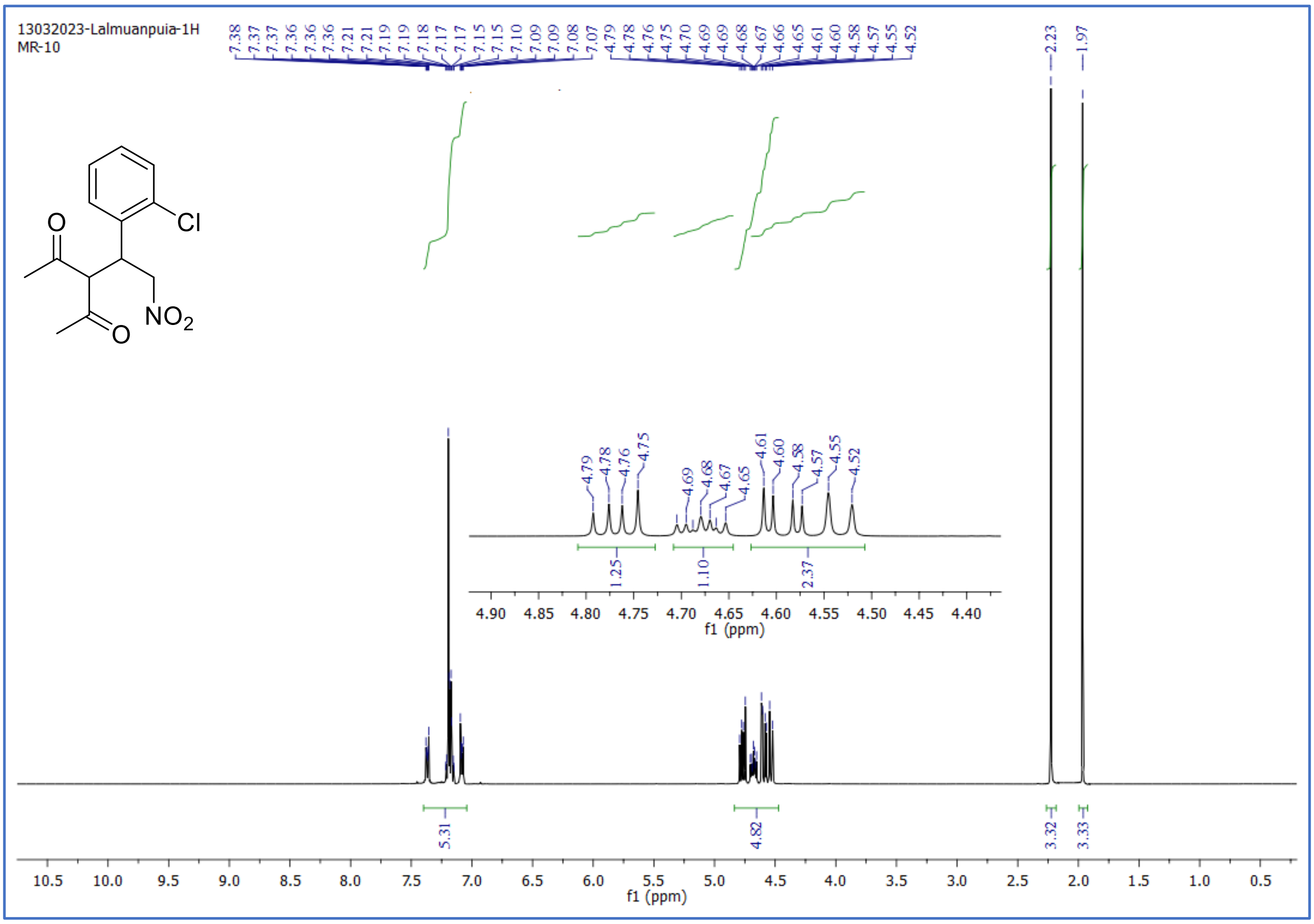


Figure S26: ^{1}H NMR and ^{13}C NMR of **8j.**



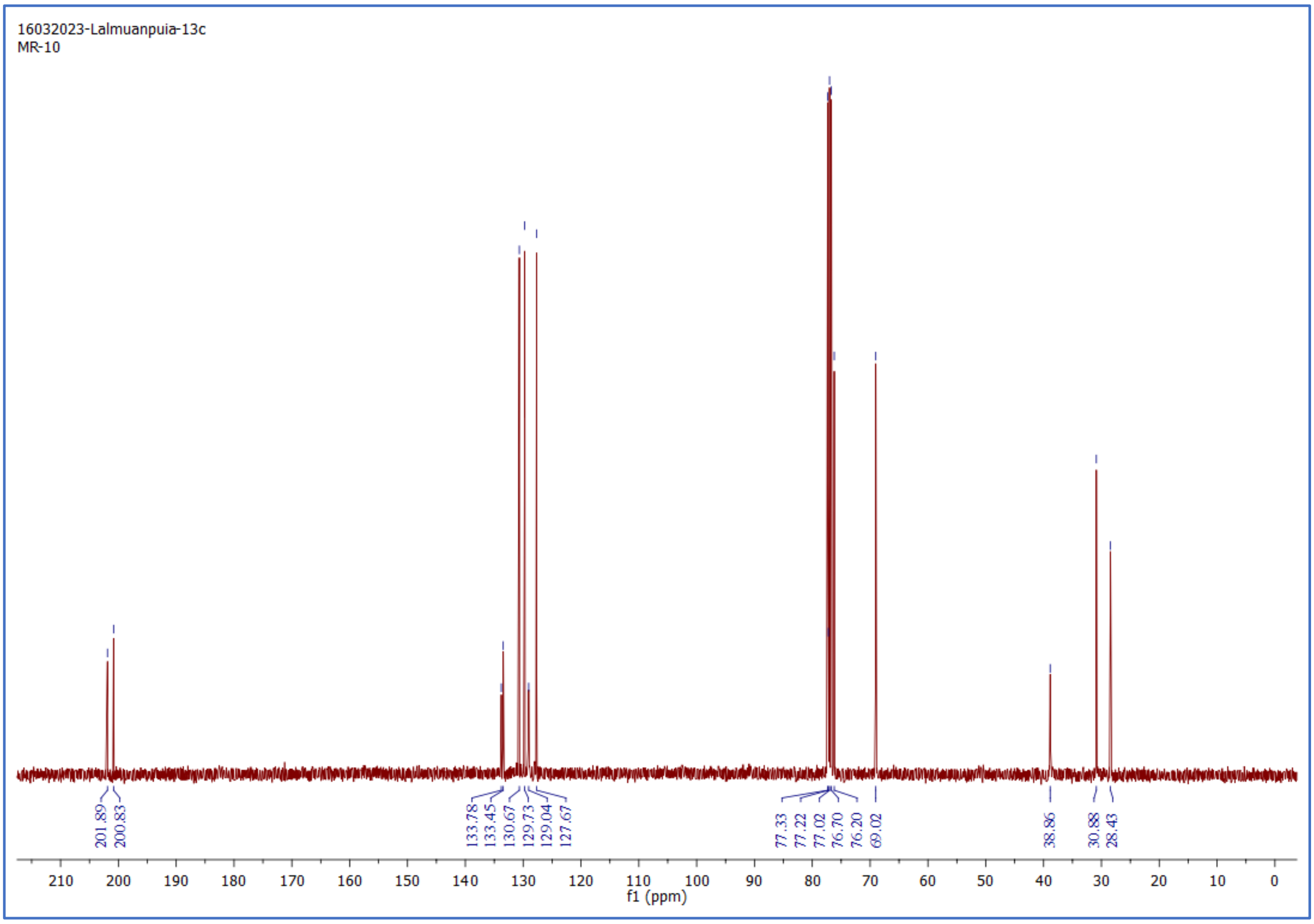
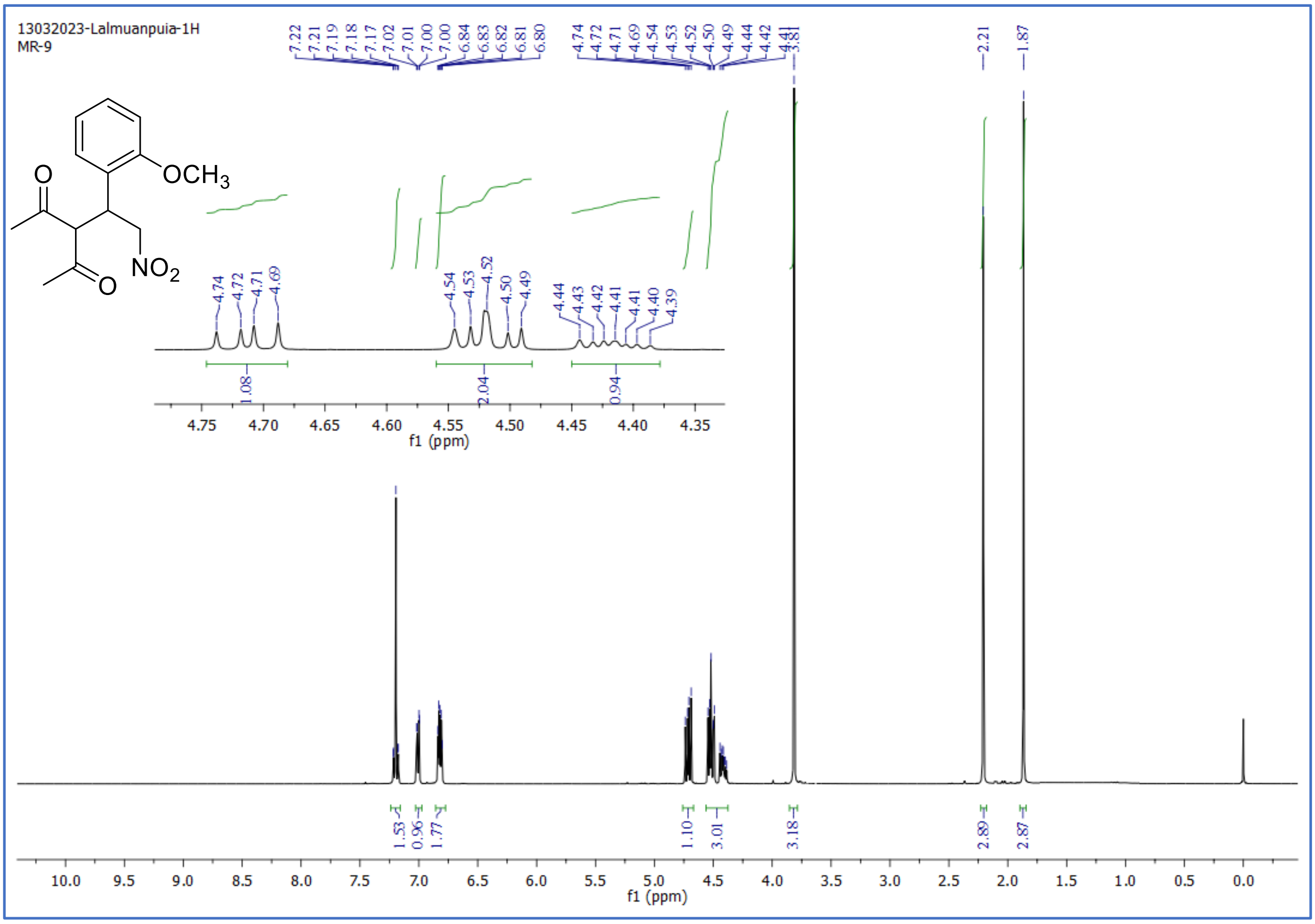


Figure S27: ^{1}H NMR and ^{13}C NMR of **8k.**



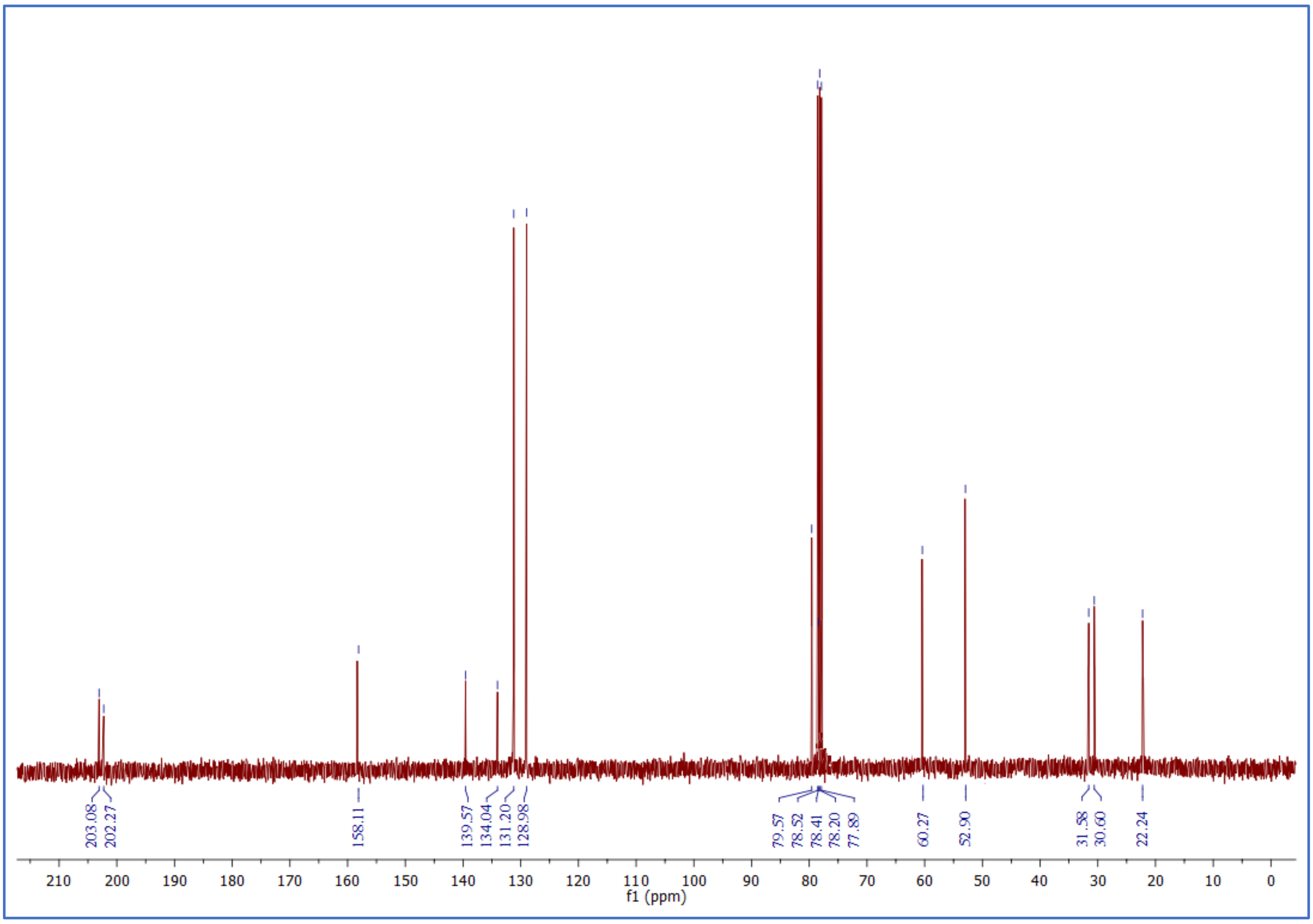
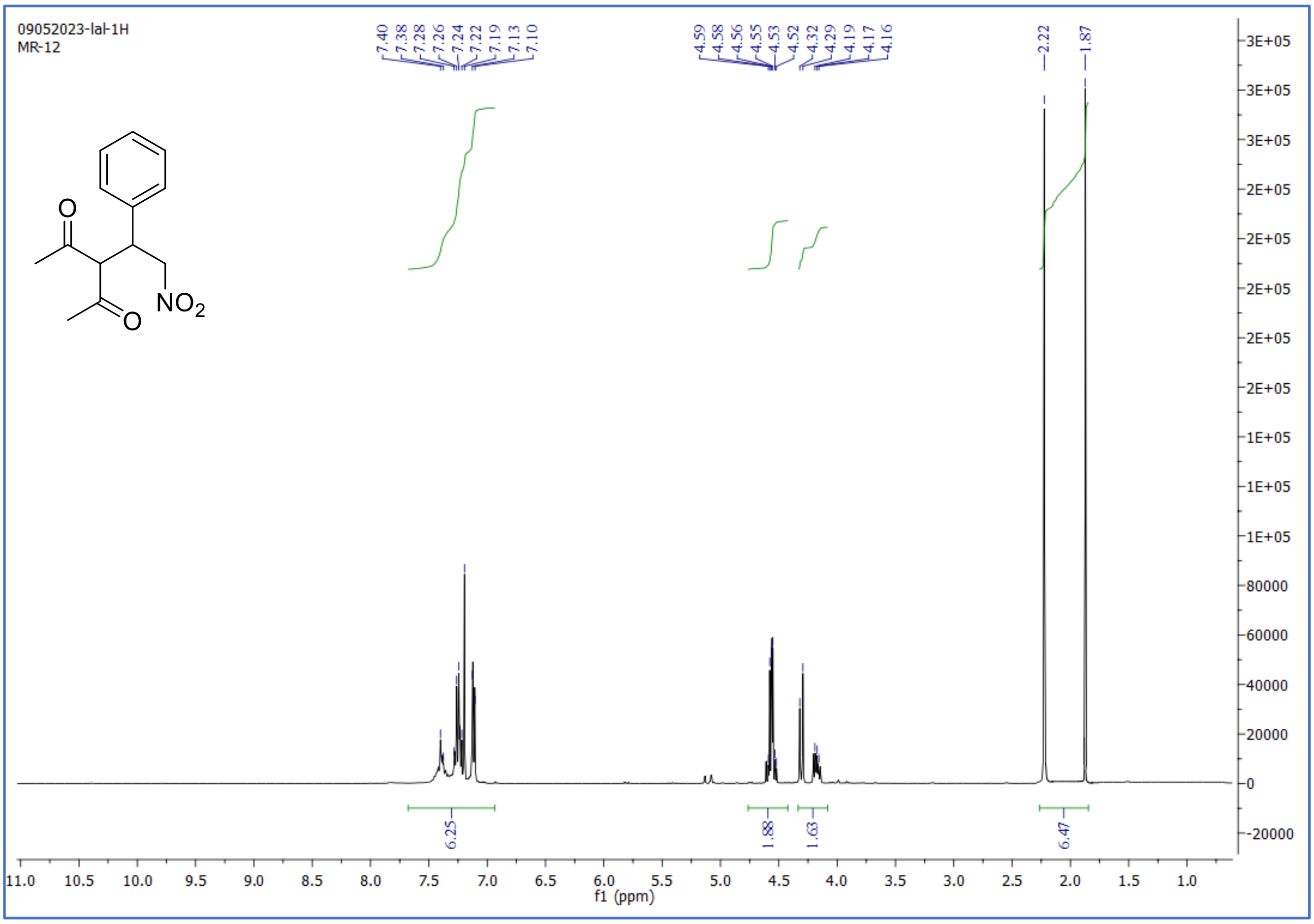


Figure S28: ^{1}H NMR and ^{13}C NMR of **8l.**



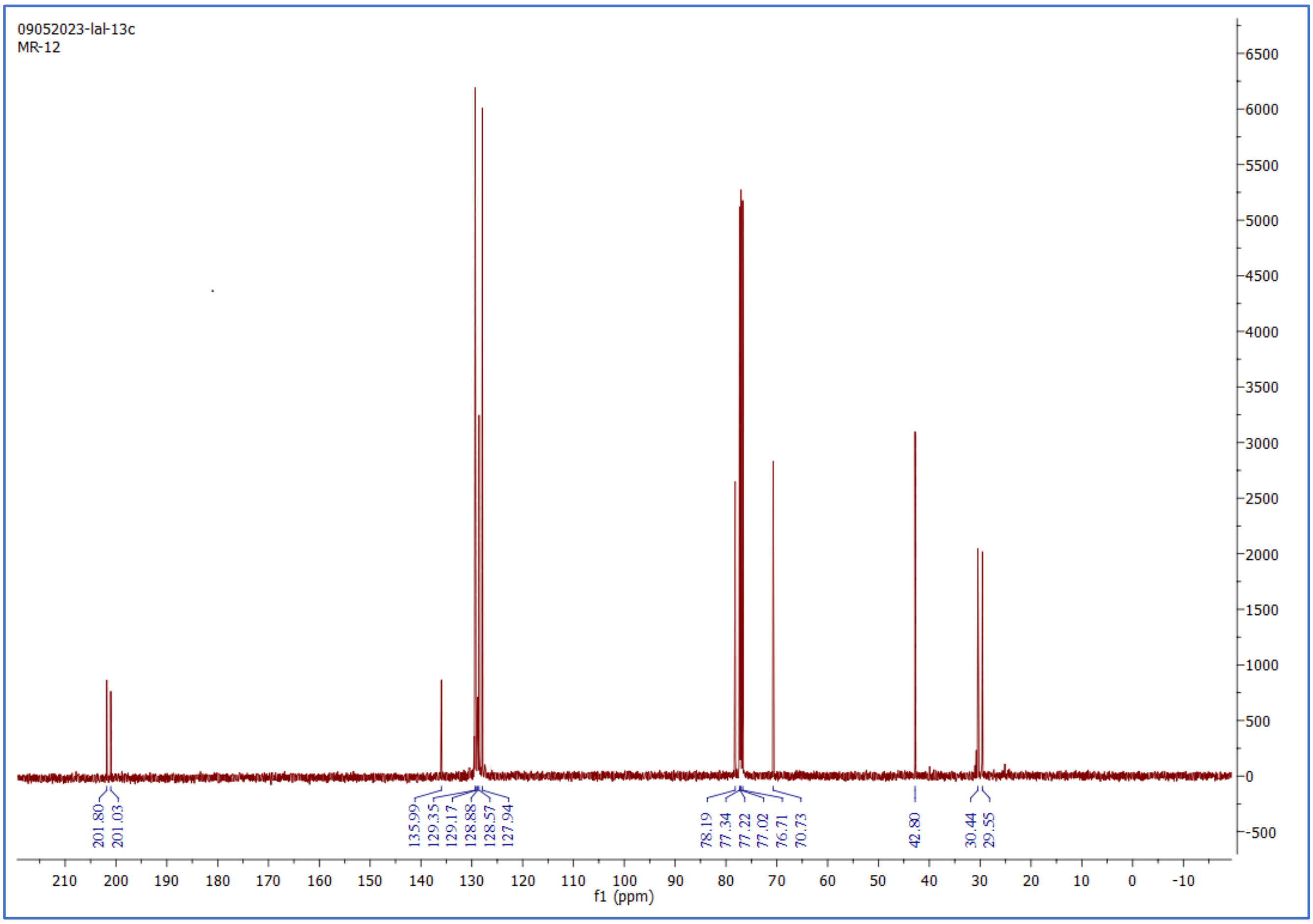
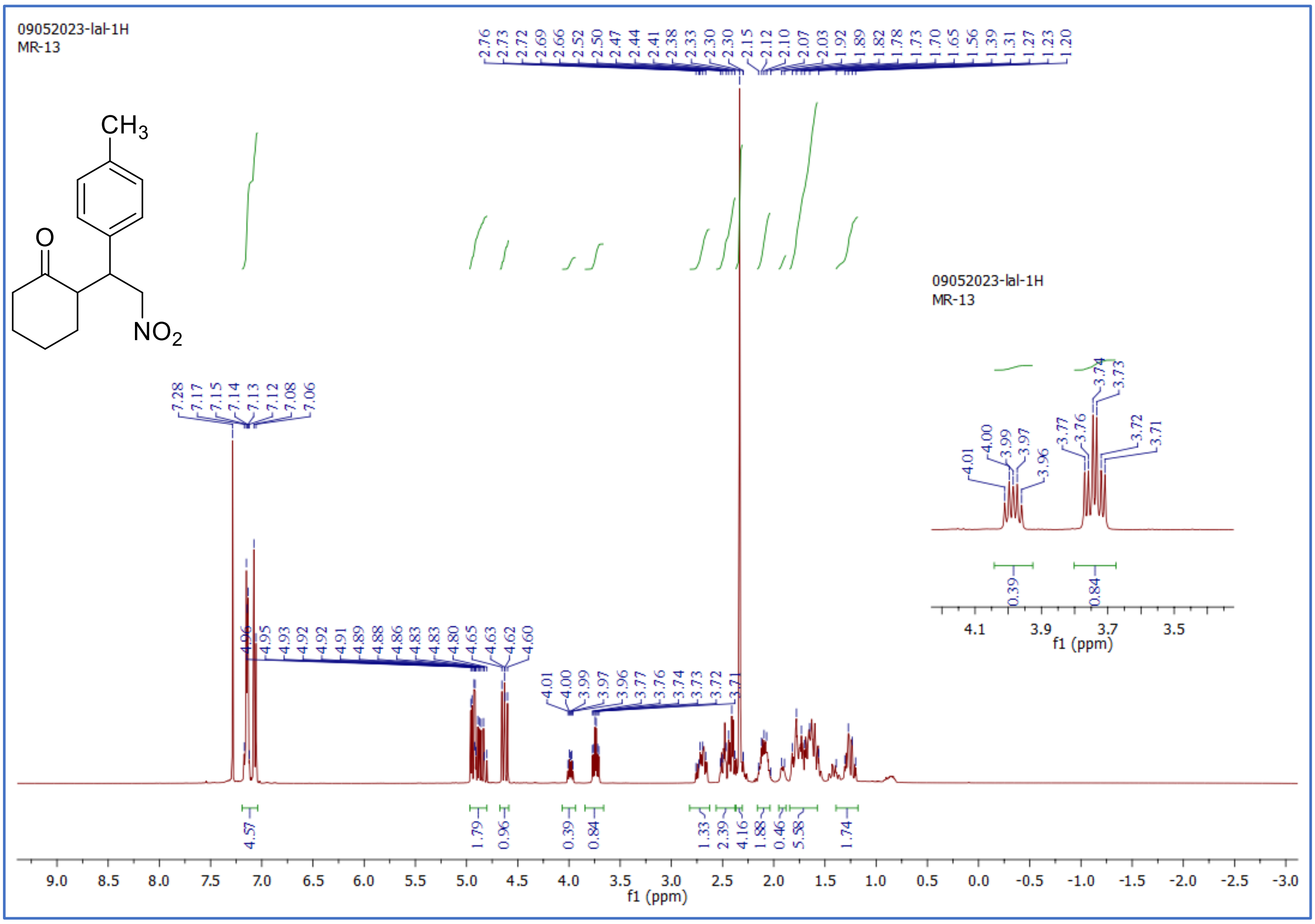


Figure S29: ^{1}H NMR and ^{13}C NMR of **8m.**



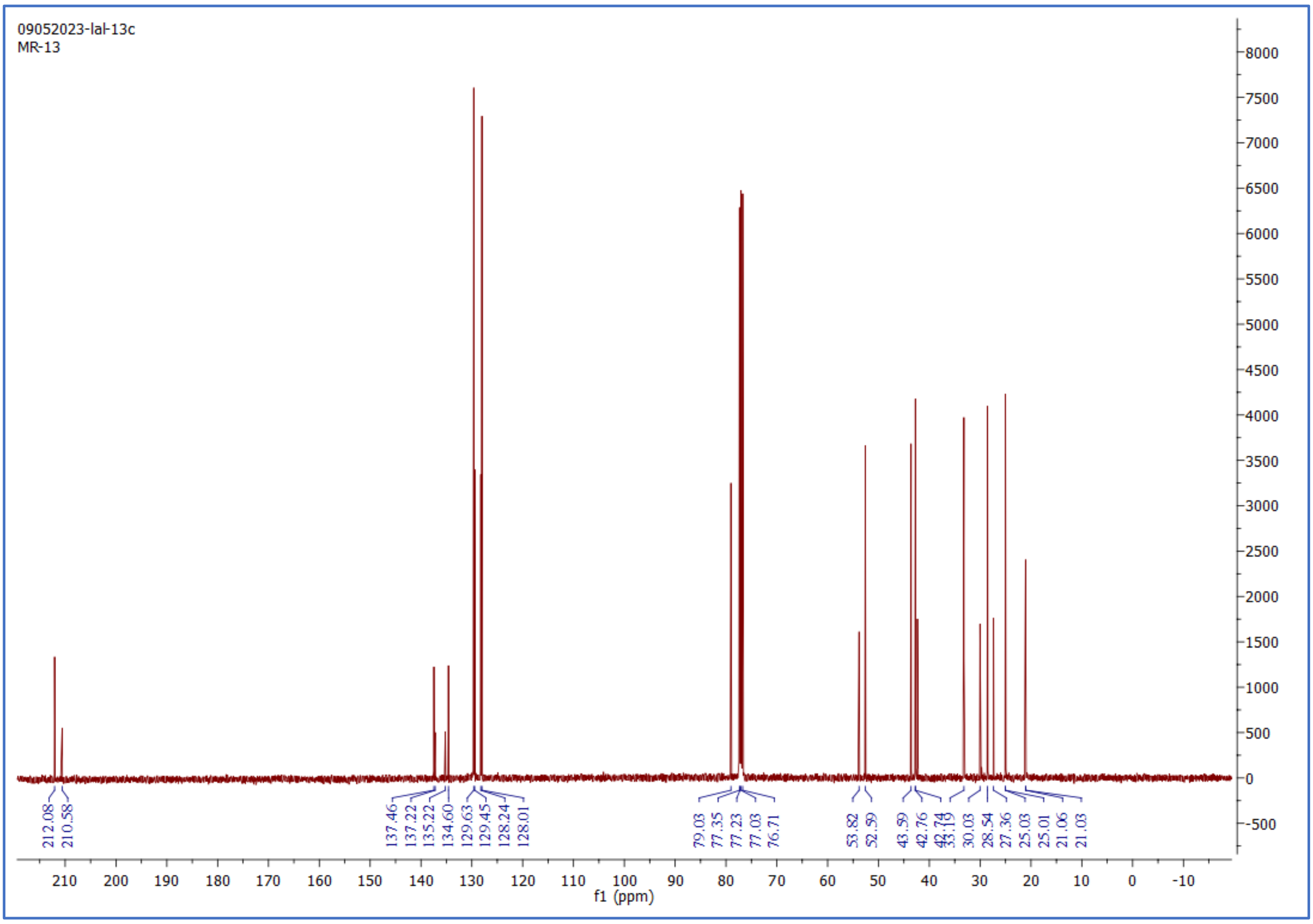
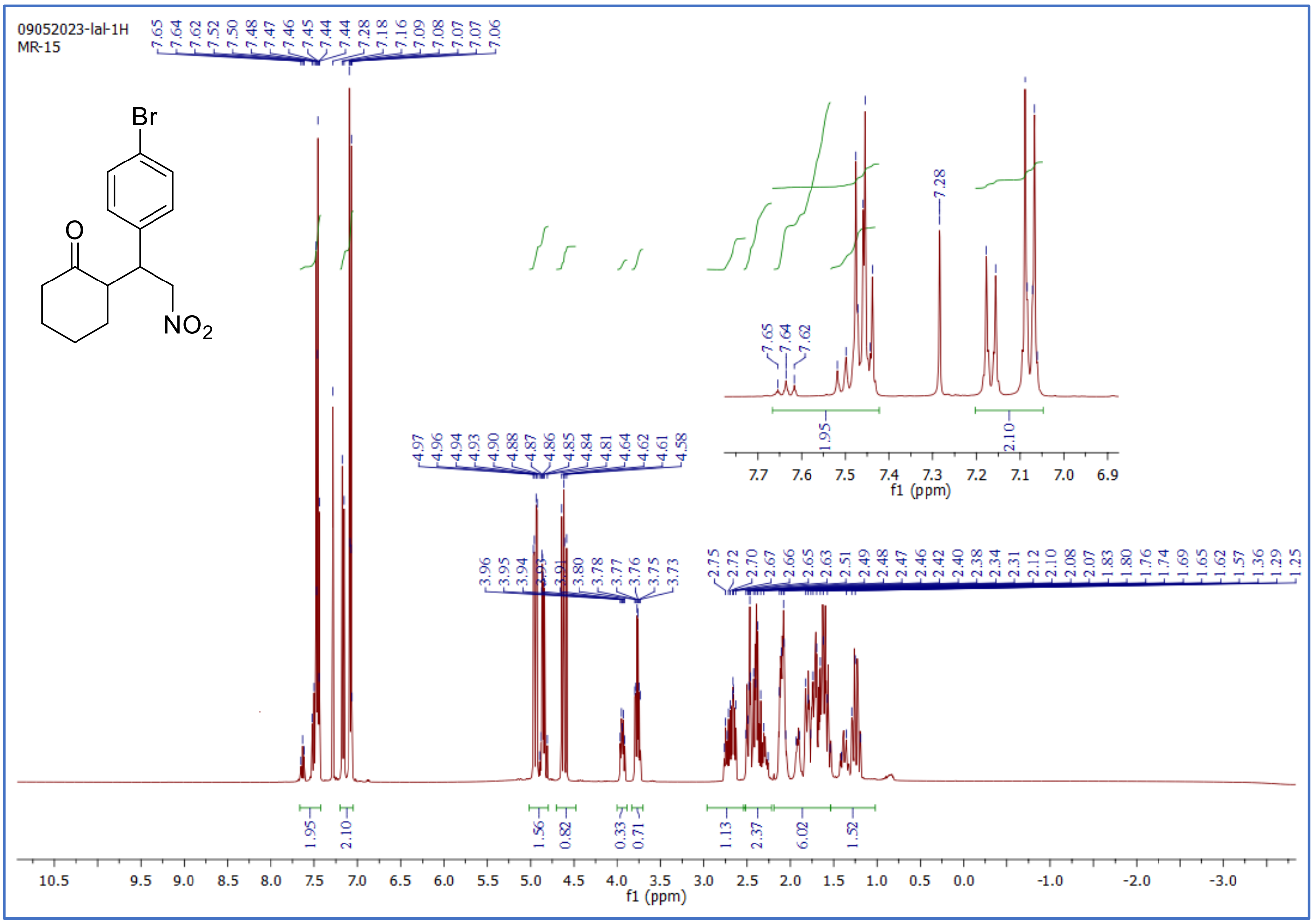


Figure 30: ^{1}H NMR and ^{13}C NMR of **8n.**



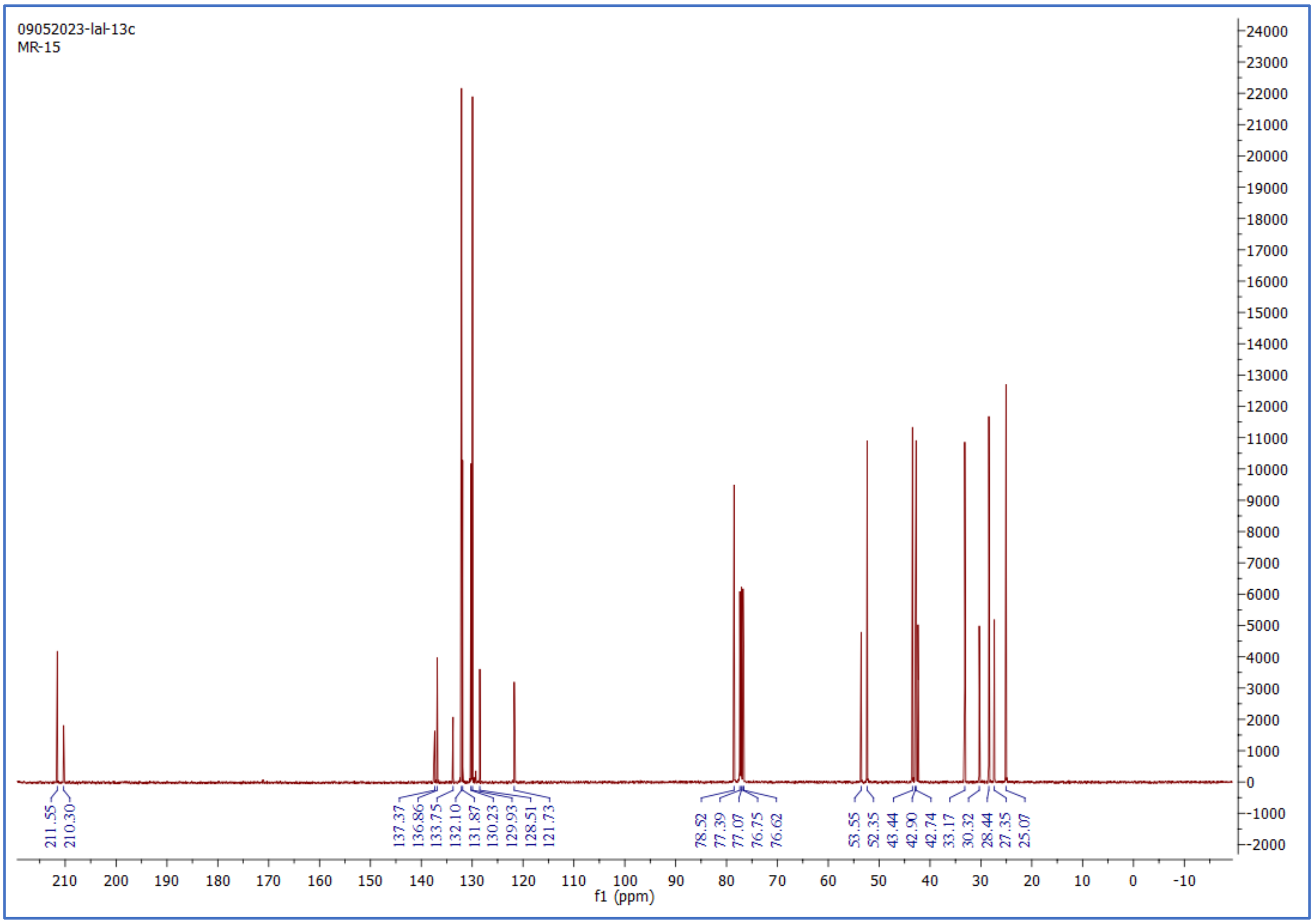


Figure S31: ^{1}H NMR and ^{13}C NMR of **8o.**

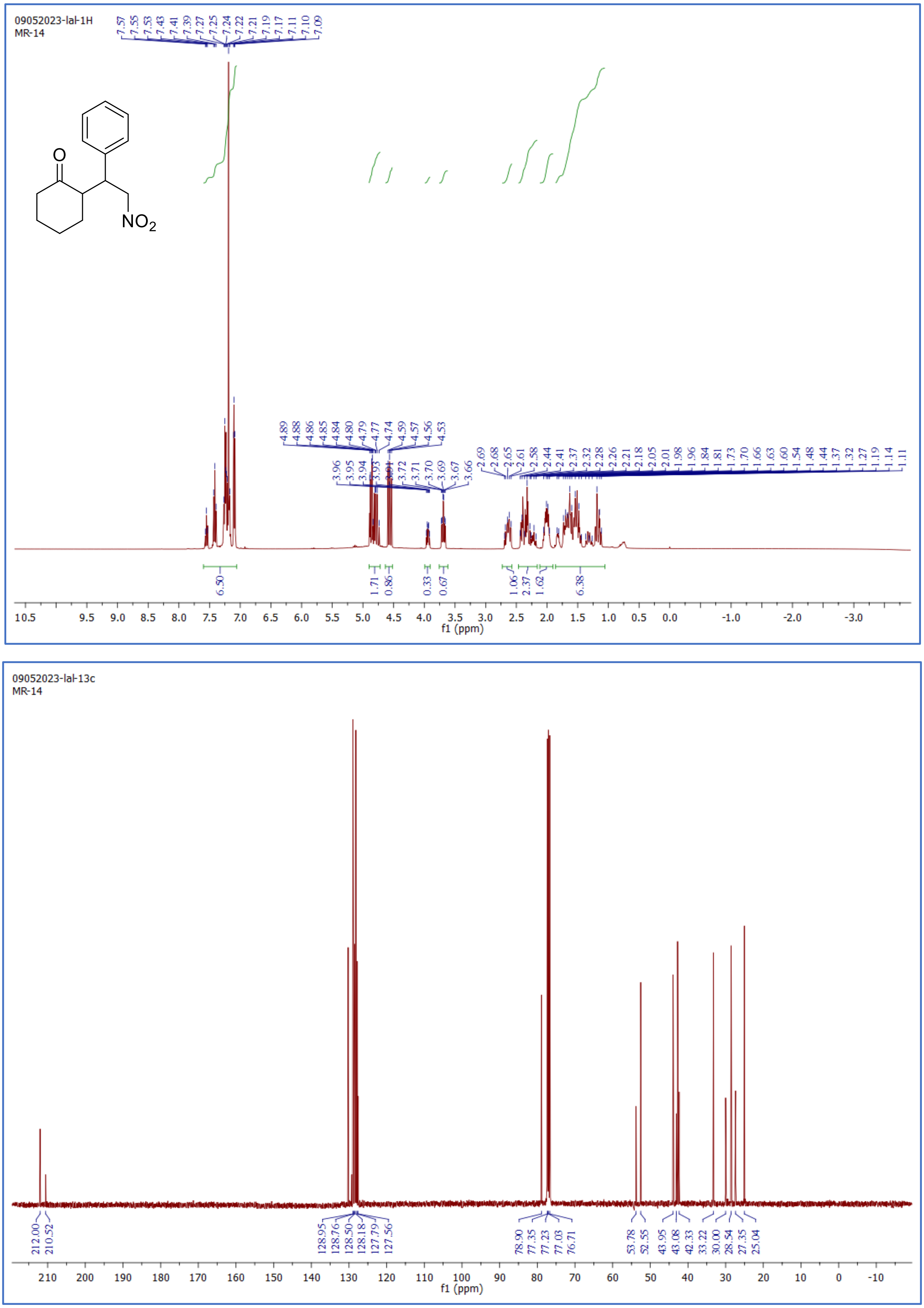
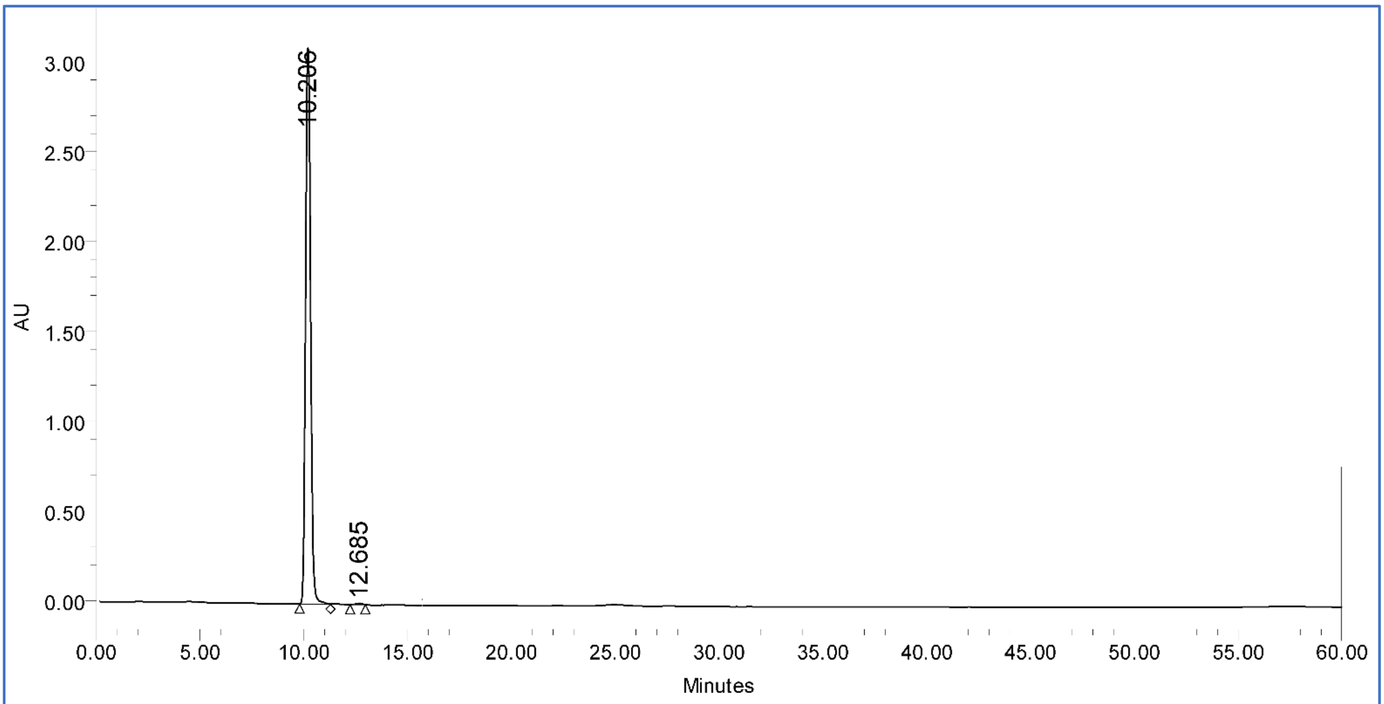
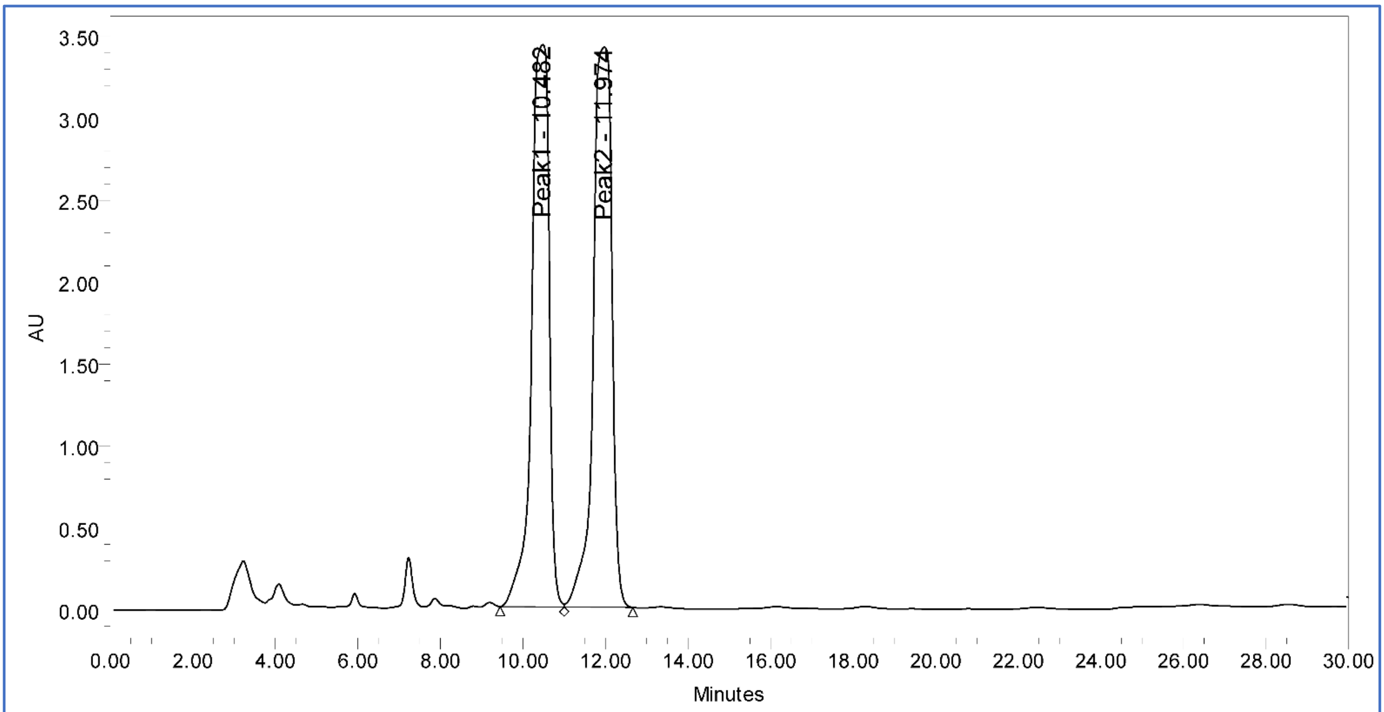


Figure S32: HPLC data of enantioenriched and racemic of **8a**.

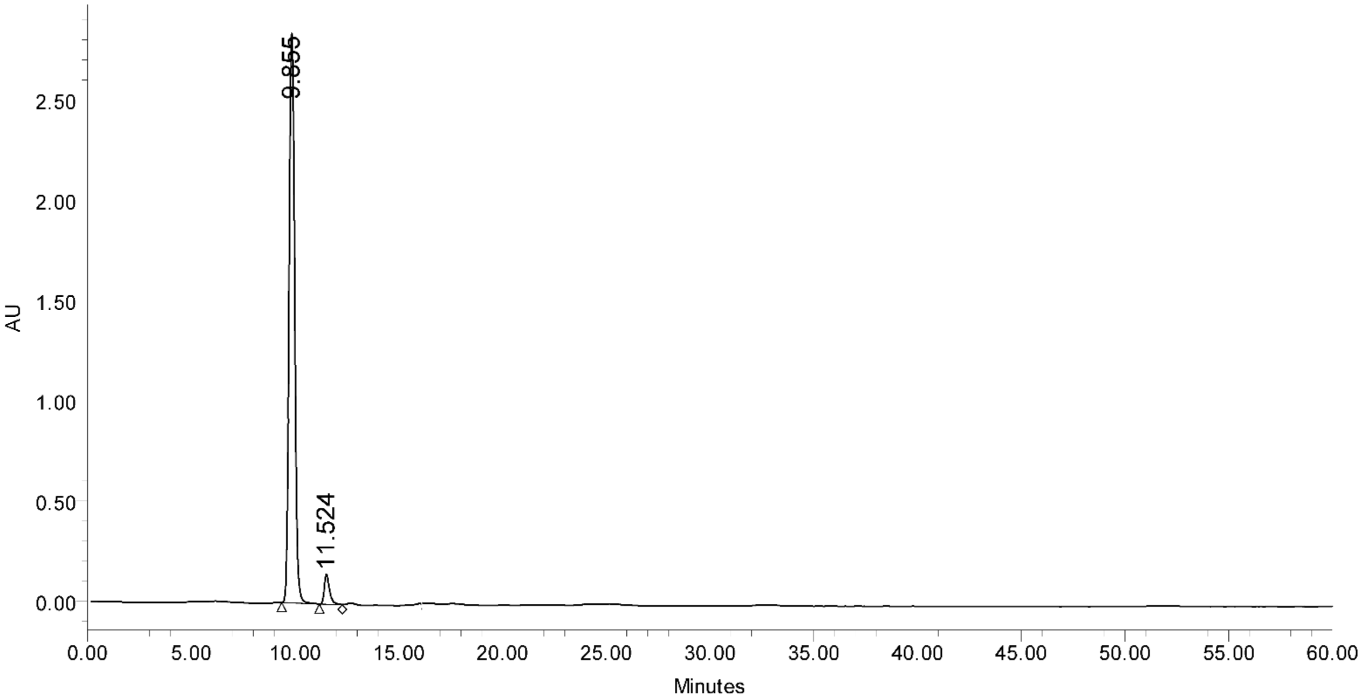


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	10.206	53262120	99.75	3149779	99.81
2	12.685	136040	0.25	5954	0.19

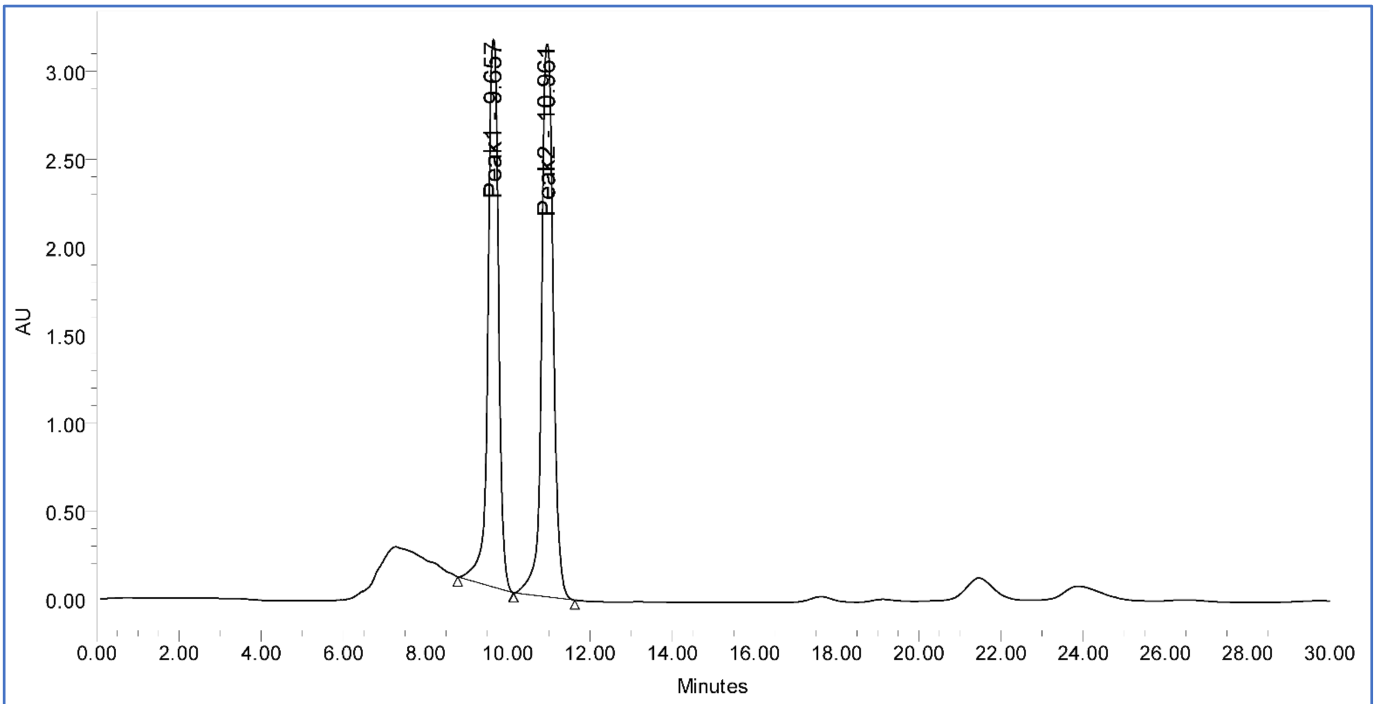


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	10.482	101301673	48.53	3431092	50.09
2	Peak2	11.974	107431124	51.47	3419129	49.91

Figure S33: HPLC data of enantioenriched and racemic of **8b**.

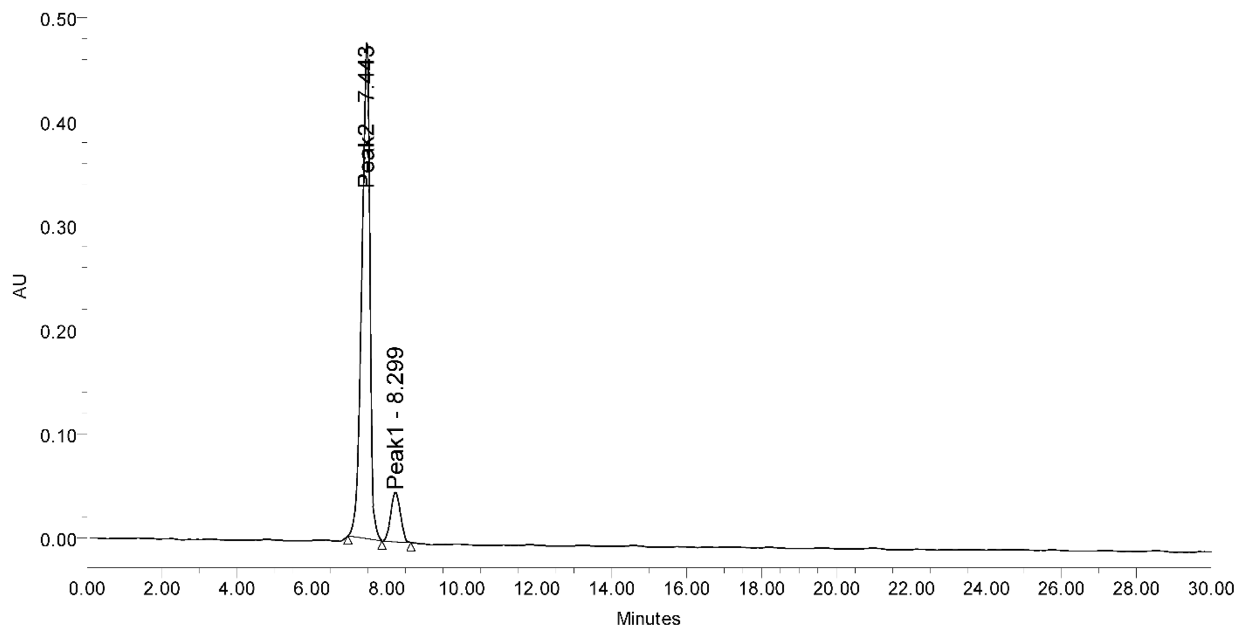


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	9.855	52242348	95.25	2813104	94.96
2	11.524	2607285	4.75	149316	5.04

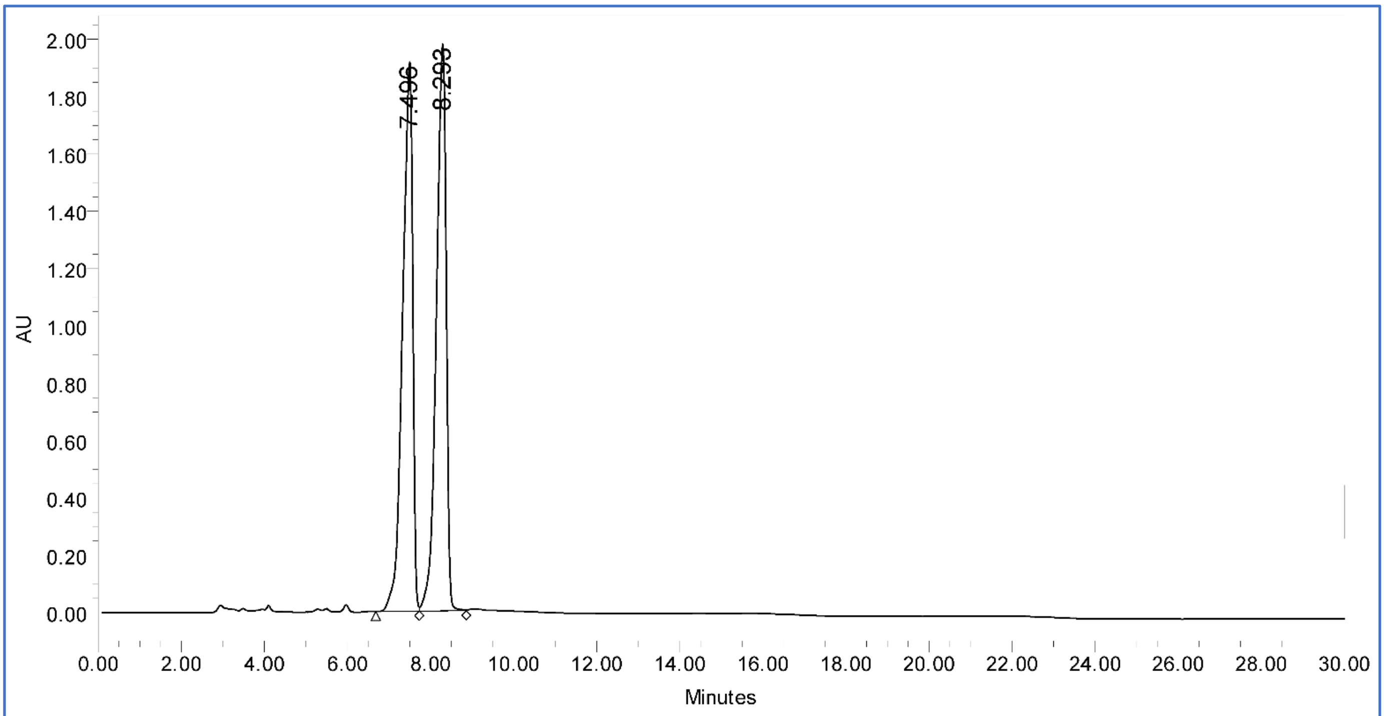


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	9.657	56091124	47.44	3116884	49.77
2	Peak2	10.961	62155094	52.56	3145415	50.23

Figure S34: HPLC data of enantioenriched and racemic of **8c**.

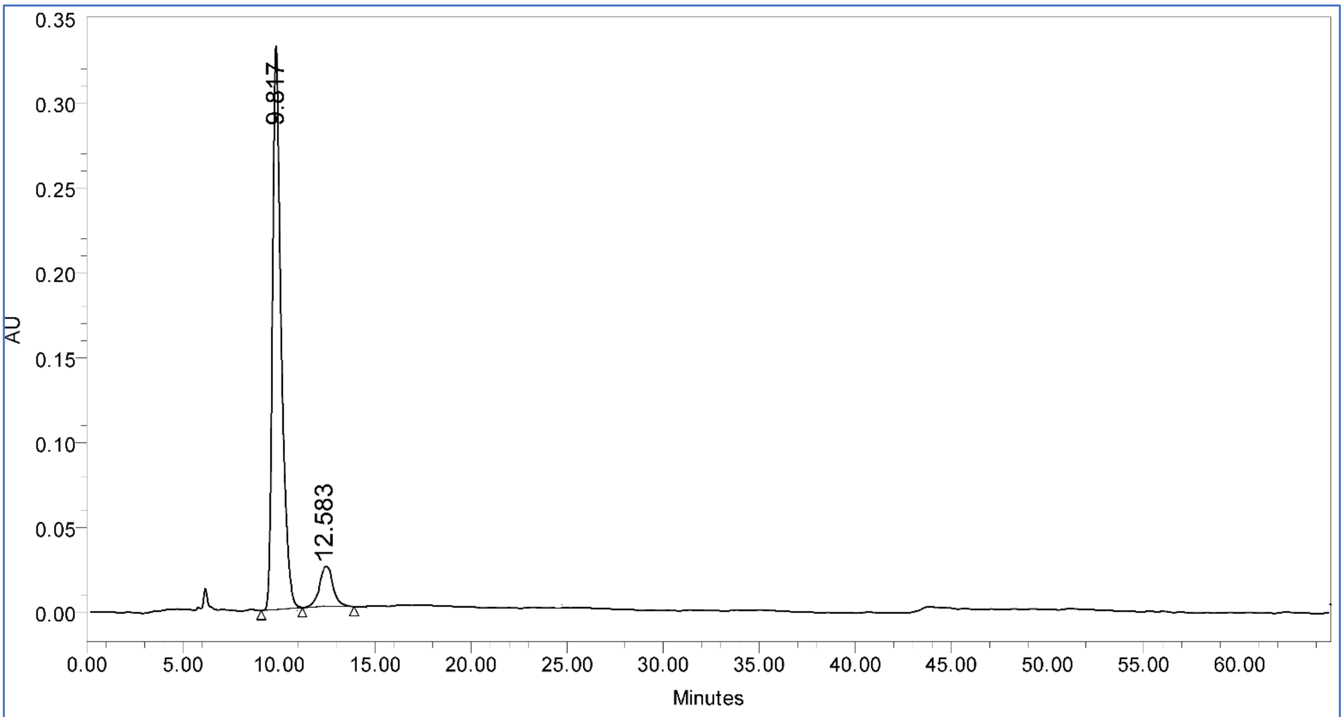


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	7.443	7245344	92.30	479125	91.44
2	Peak2	8.299	604349	7.70	44873	8.56

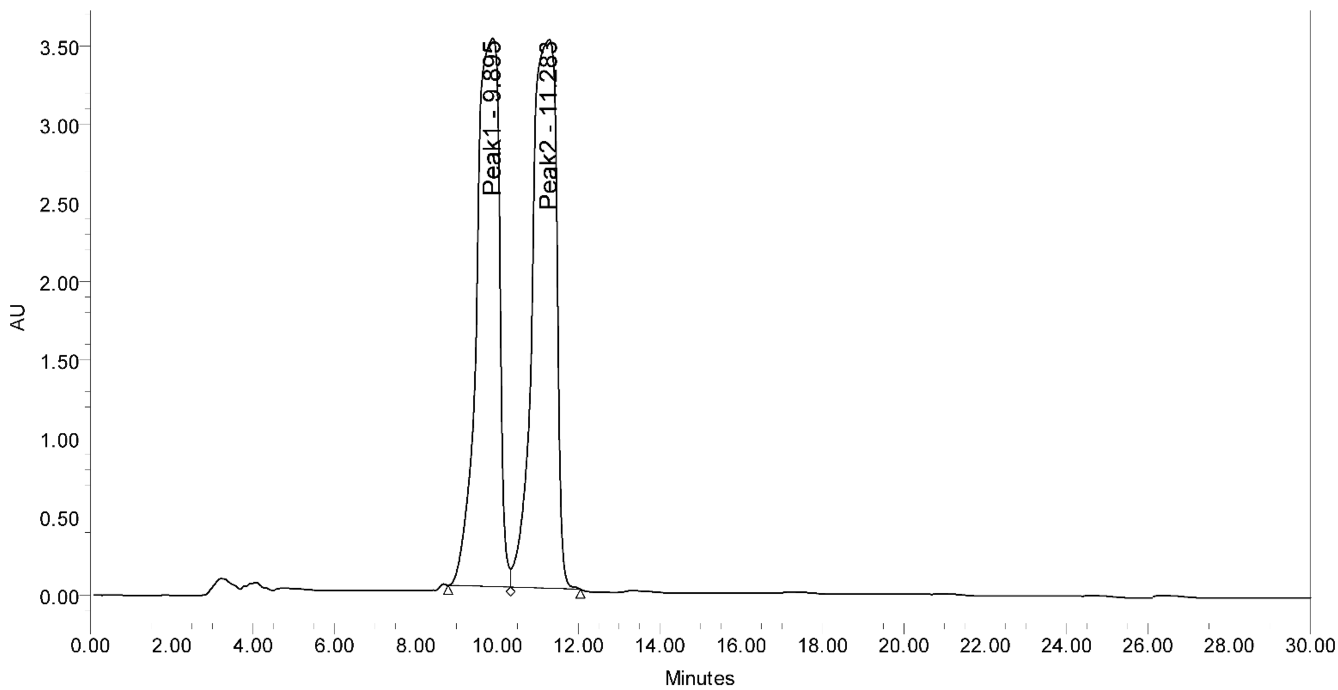


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	7.496	32358794	49.81	1917931	49.18
2	8.293	32601966	50.19	1981868	50.82

Figure S35: HPLC data of enantioenriched and racemic of **8d**.

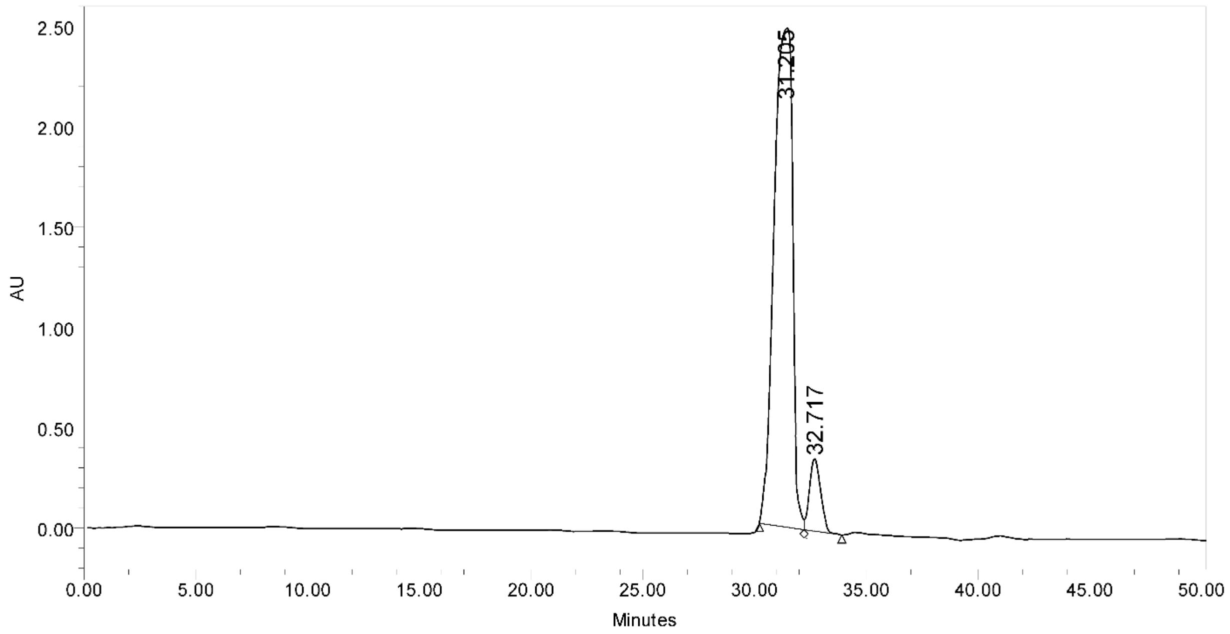


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	9.817	10452148	91.60	332082	94.70
2	12.583	959075	8.40	18587	5.30

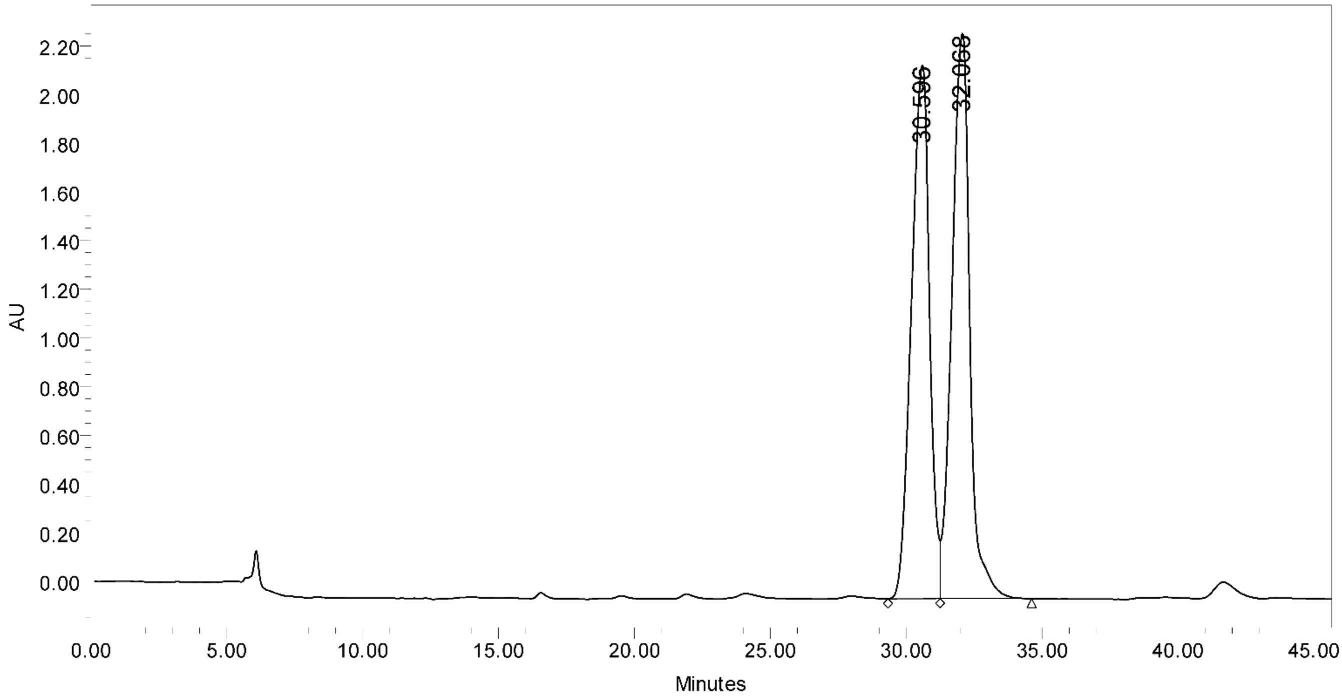


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	9.895	135720219	48.43	3493625	49.98
2	Peak2	11.283	144515065	51.57	3496102	50.02

Figure S36: HPLC data of enantioenriched and racemic of **8e**.

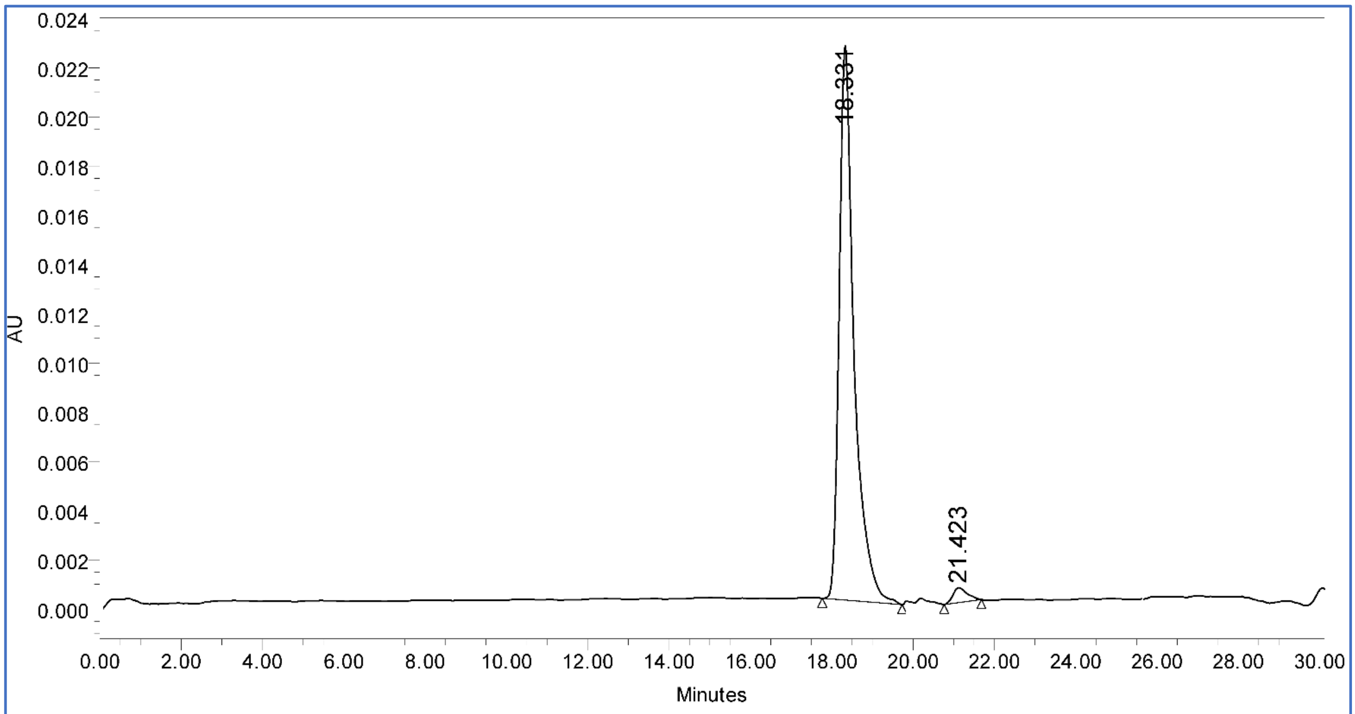


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	31.205	144636815	90.54	2502999	86.25
2	32.717	15106988	9.46	399001	13.75

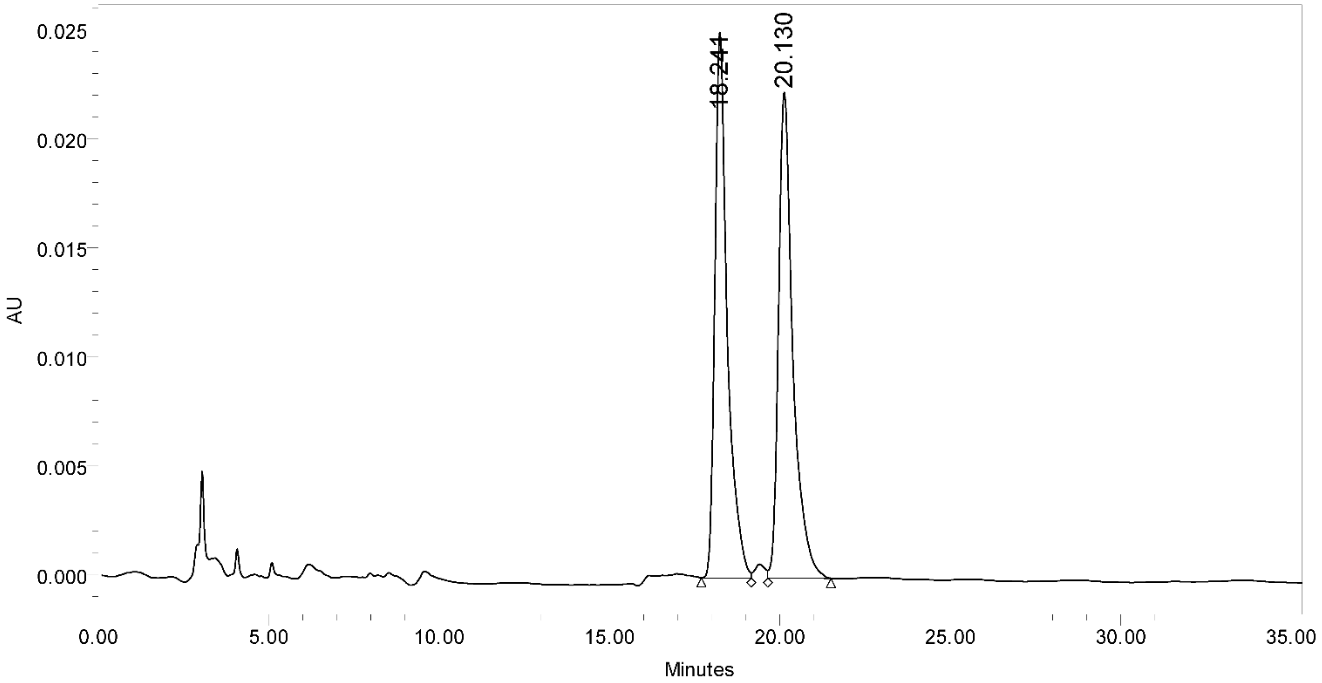


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	30.596	101282099	48.81	2193136	48.58
2	32.068	106217028	51.19	2321643	51.42

Figure S37: HPLC data of enantioenriched and racemic of **8f**.

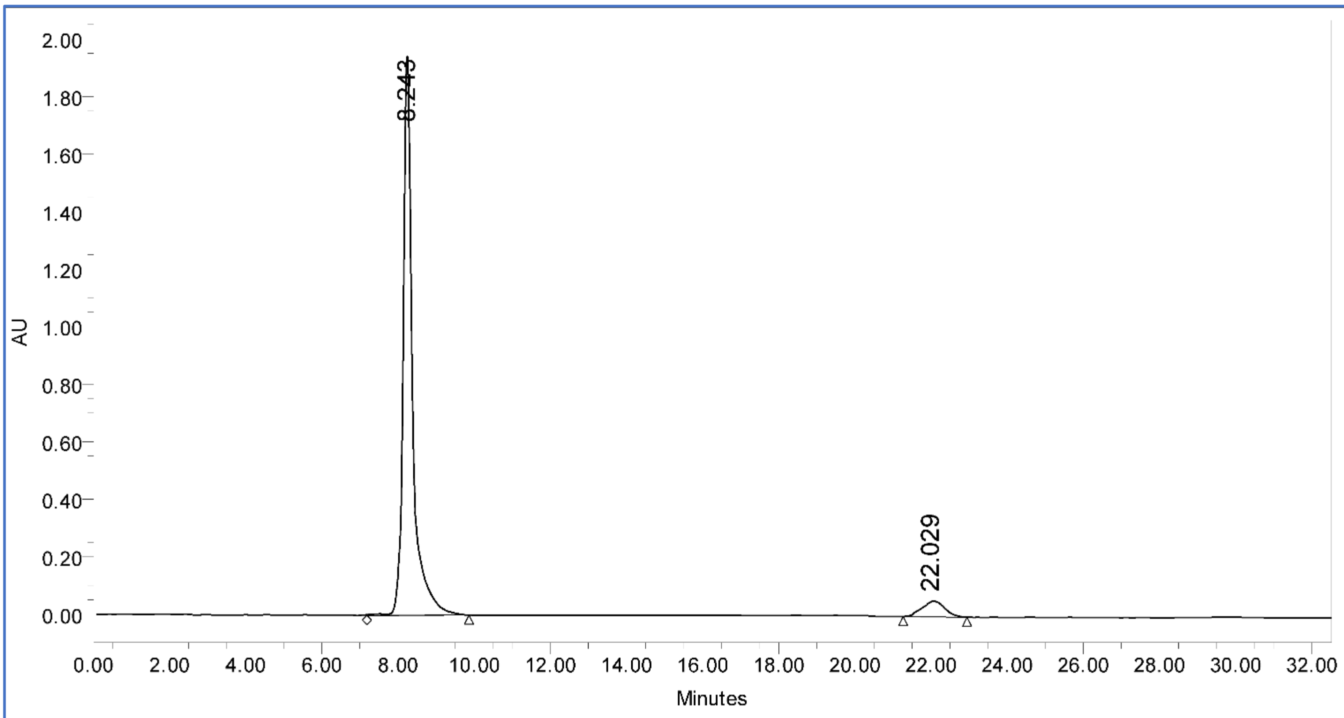


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	18.331	574350	97.49	22510	97.39
2	21.423	14771	2.51	604	2.61

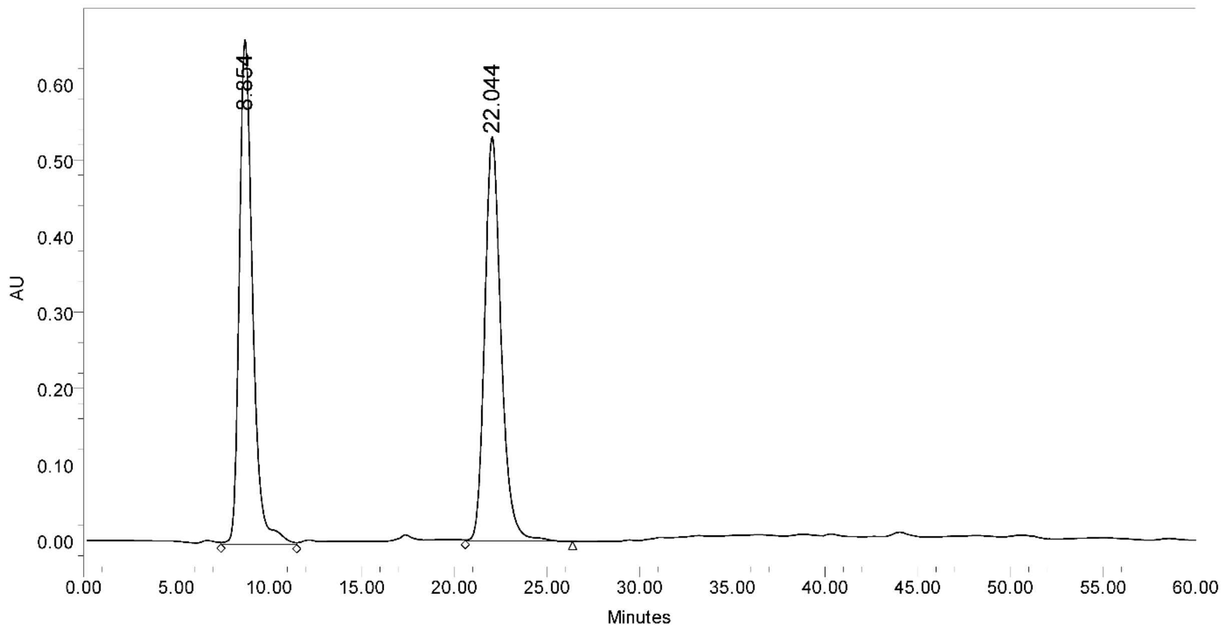


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	18.241	636301	49.38	25051	52.92
2	20.130	652184	50.62	22283	47.08

Figure S38: HPLC data of enantioenriched and racemic of **8g**.

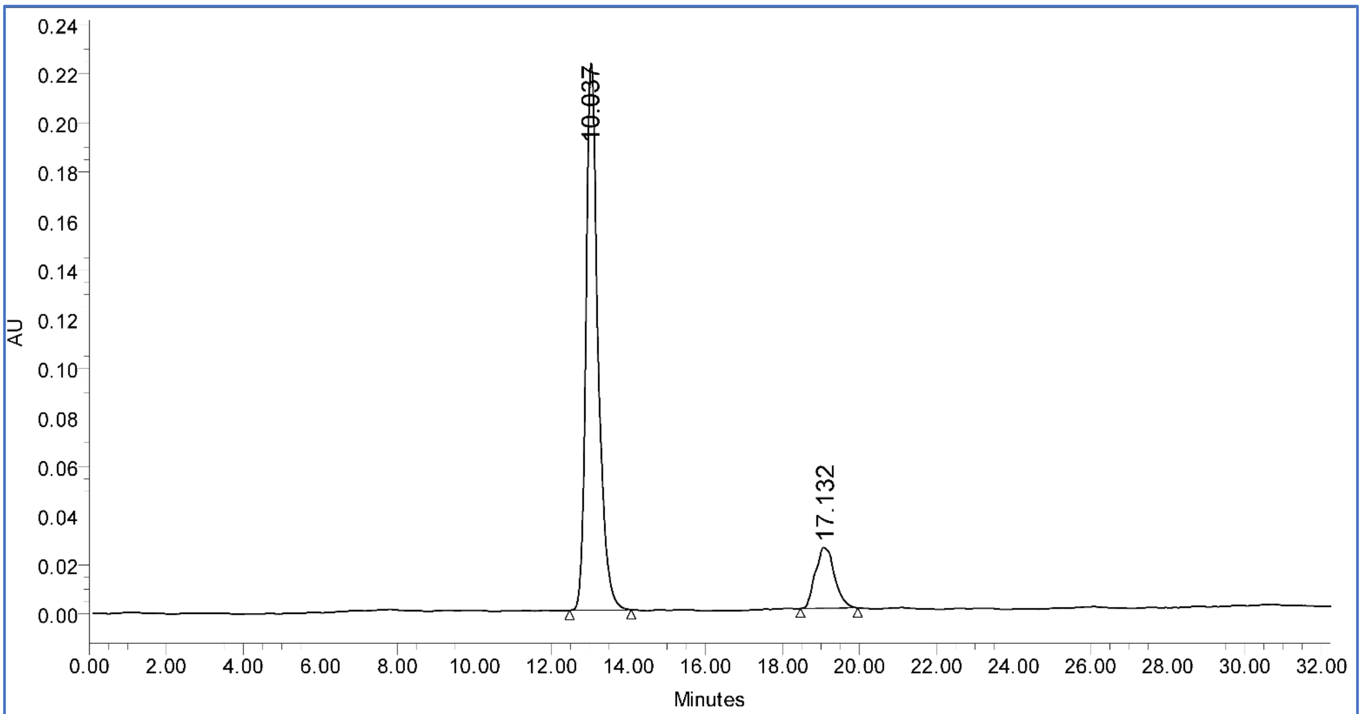


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	8.243	24735059	91.96	1812656	97.05
2	22.029	2163079	8.04	55105	2.95

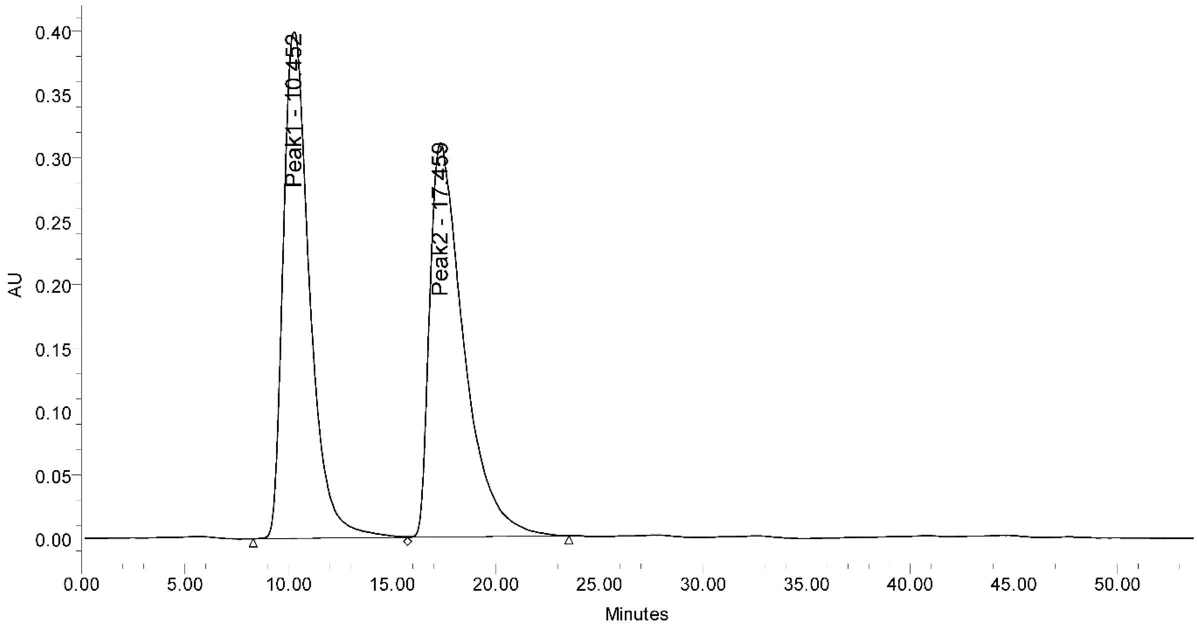


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	8.854	33857570	50.46	634752	55.55
2	22.044	32524095	49.54	520362	44.45

Figure S39: HPLC data of enantioenriched and racemic of **8h**.

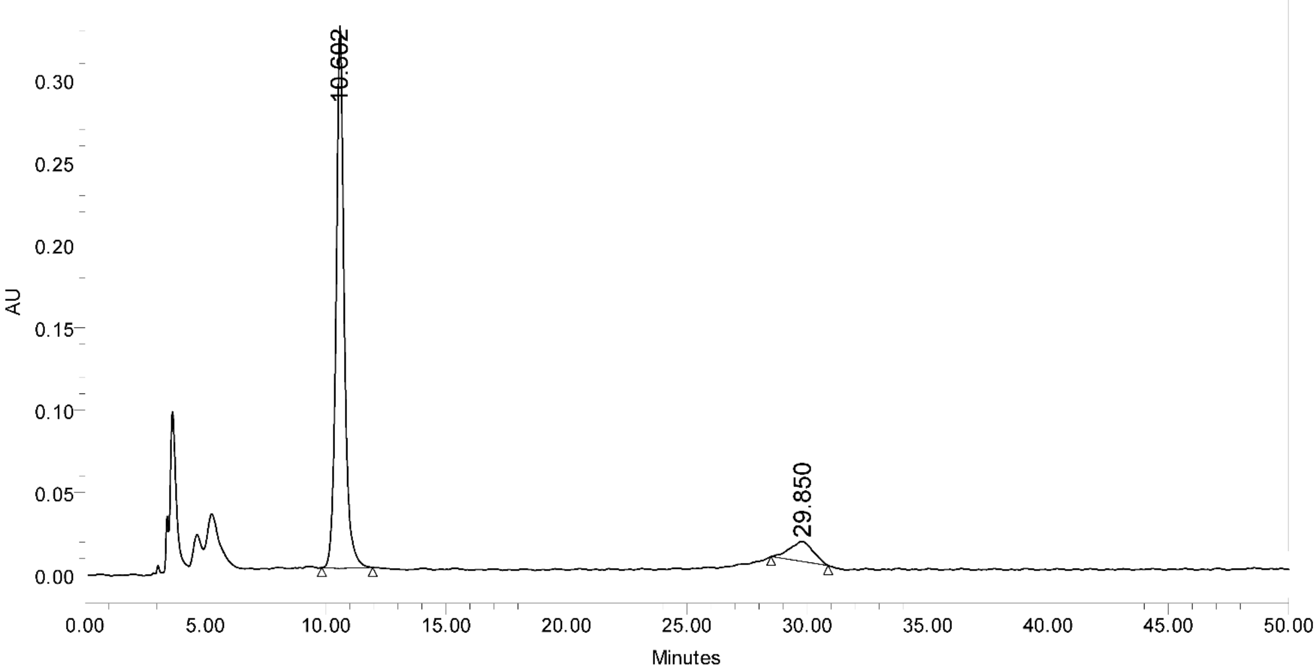


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	10.037	4742229	90.31	221594	92.06
2	17.132	508957	9.69	19118	7.94

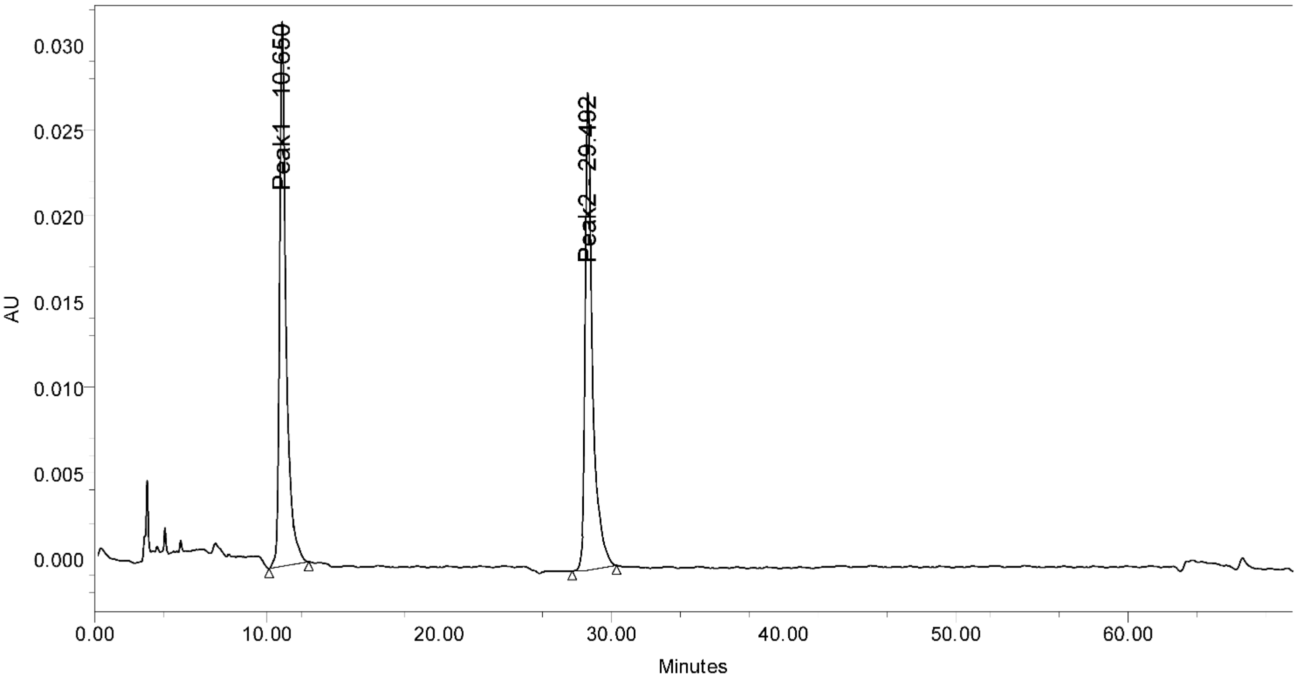


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	10.452	34458734	50.00	409111	55.22
2	Peak2	17.459	34461031	50.00	320815	44.78

Figure S40: HPLC data of enantioenriched and racemic of **8i**.

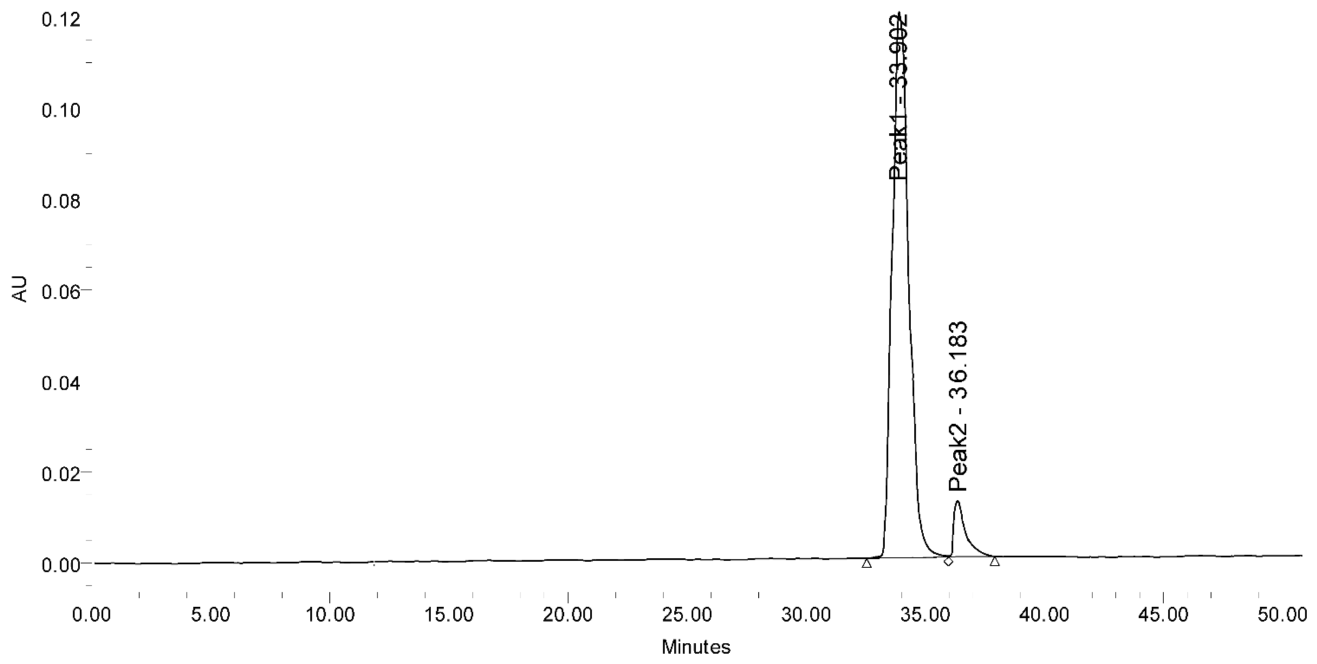


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	10.602	7624034	90.30	328481	96.47
2	29.850	818537	9.70	12017	3.53

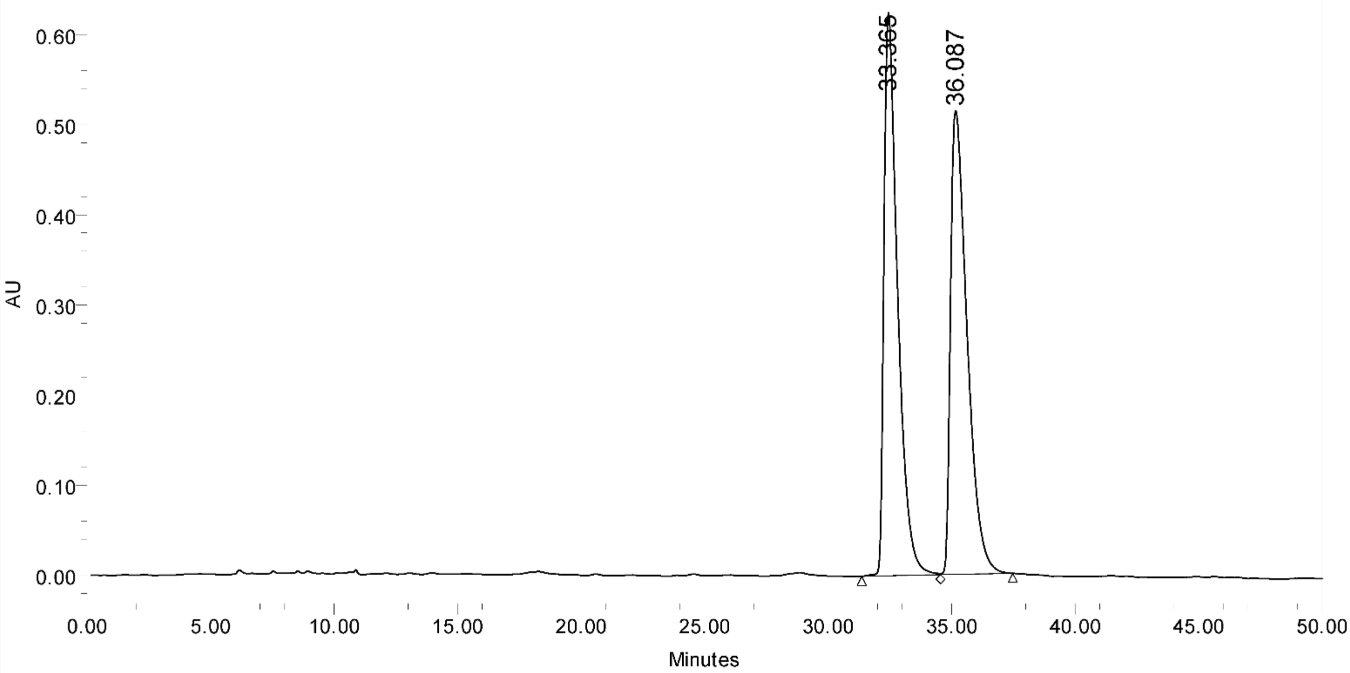


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	10.650	832626	49.84	31773	53.24
2	Peak2	29.492	837892	50.16	27907	46.76

Figure S41: HPLC data of enantioenriched and racemic of **8j**.

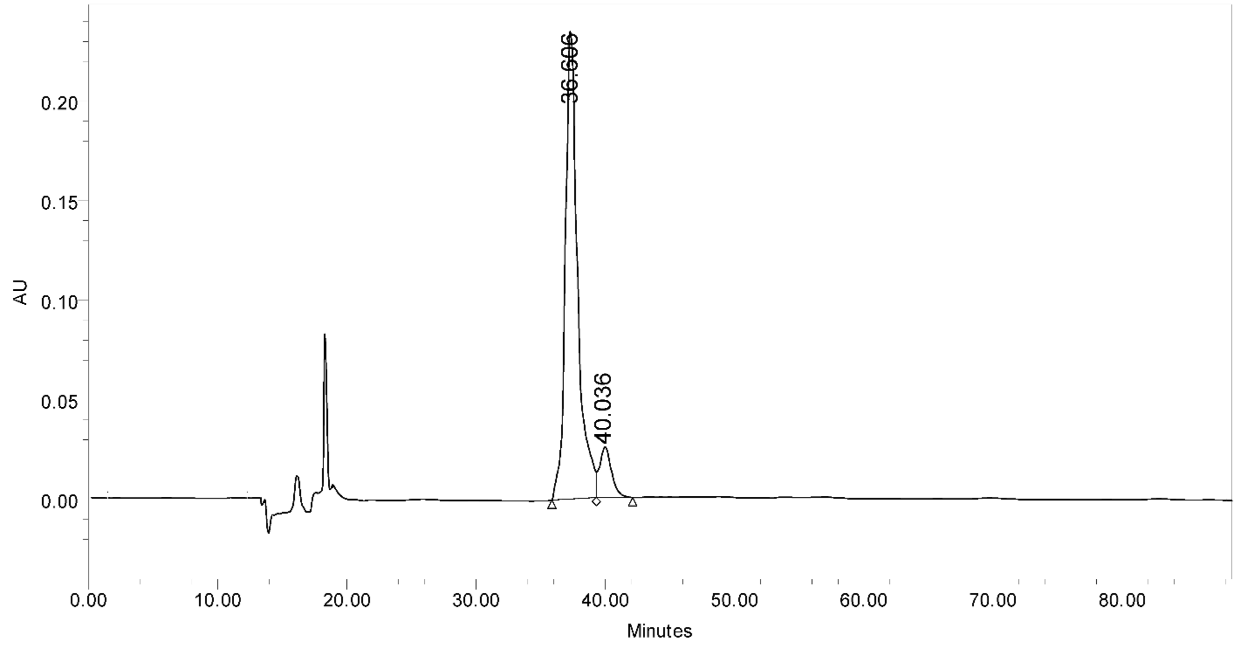


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	33.902	5721230	85.36	118781	87.21
2	Peak2	36.183	981363	14.64	17414	12.79

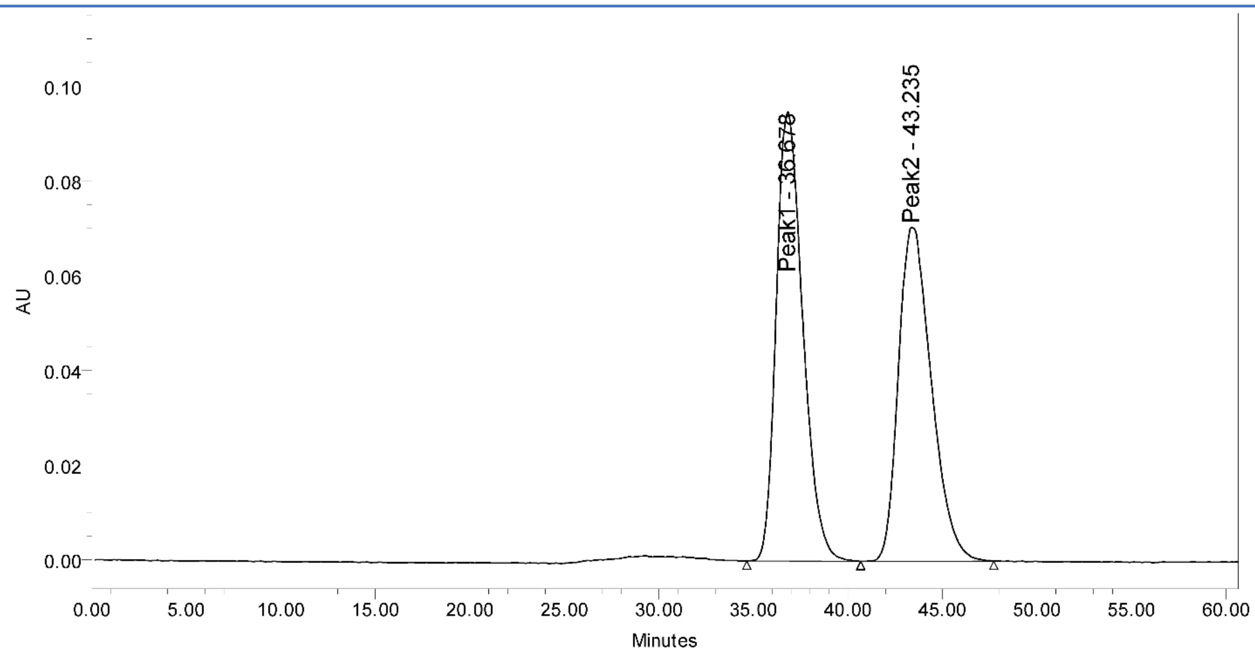


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	33.365	24080034	50.10	624600	54.82
2	36.087	23987219	49.90	514796	45.18

Figure S42: HPLC data of enantioenriched and racemic of **8k**.

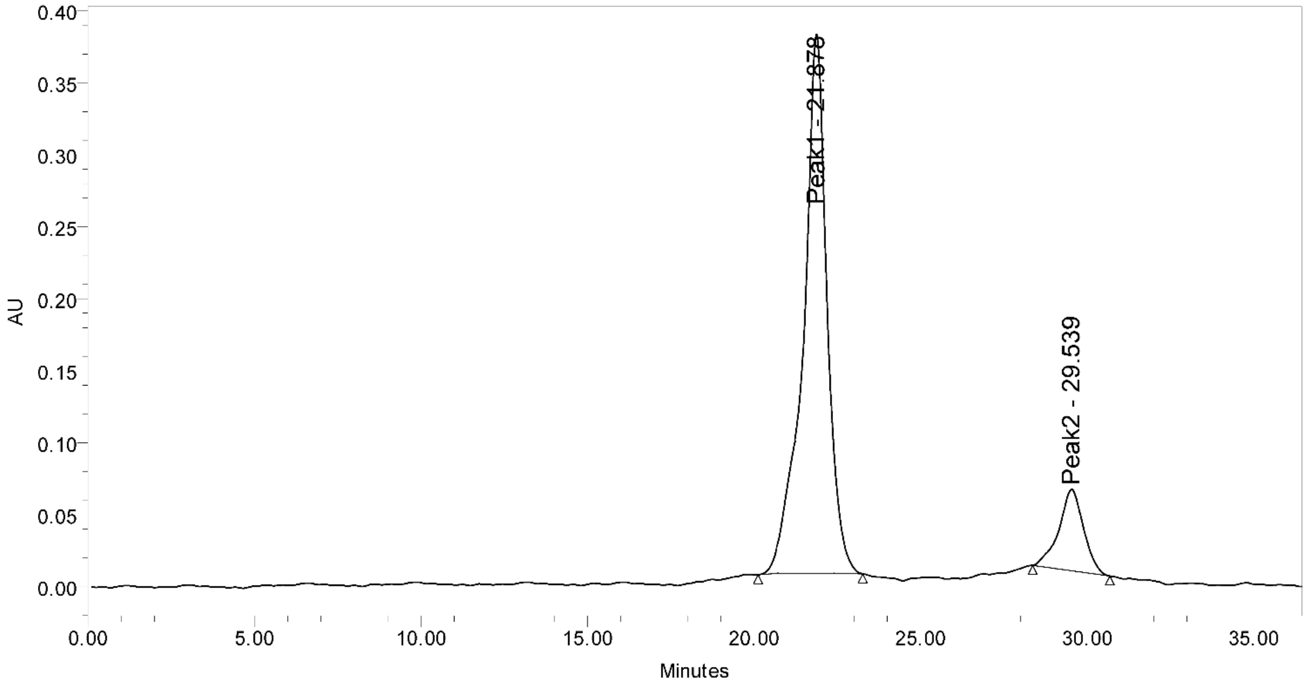


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	36.606	16230359	87.81	232237	91.35
2	40.036	2253740	12.19	21989	8.65

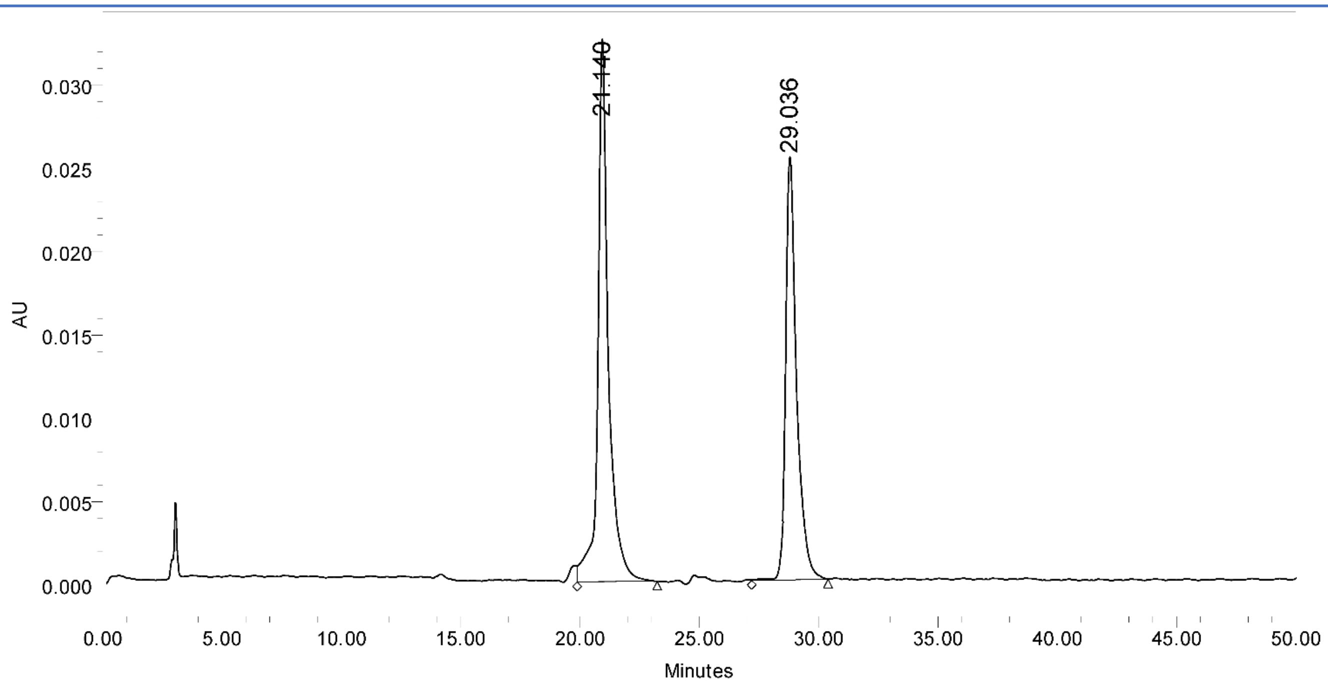


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	36.678	9271940	51.03	94826	56.37
2	Peak2	43.235	8549610	48.97	70462	43.63

Figure S43: HPLC data of enantioenriched and racemic of **8l**.

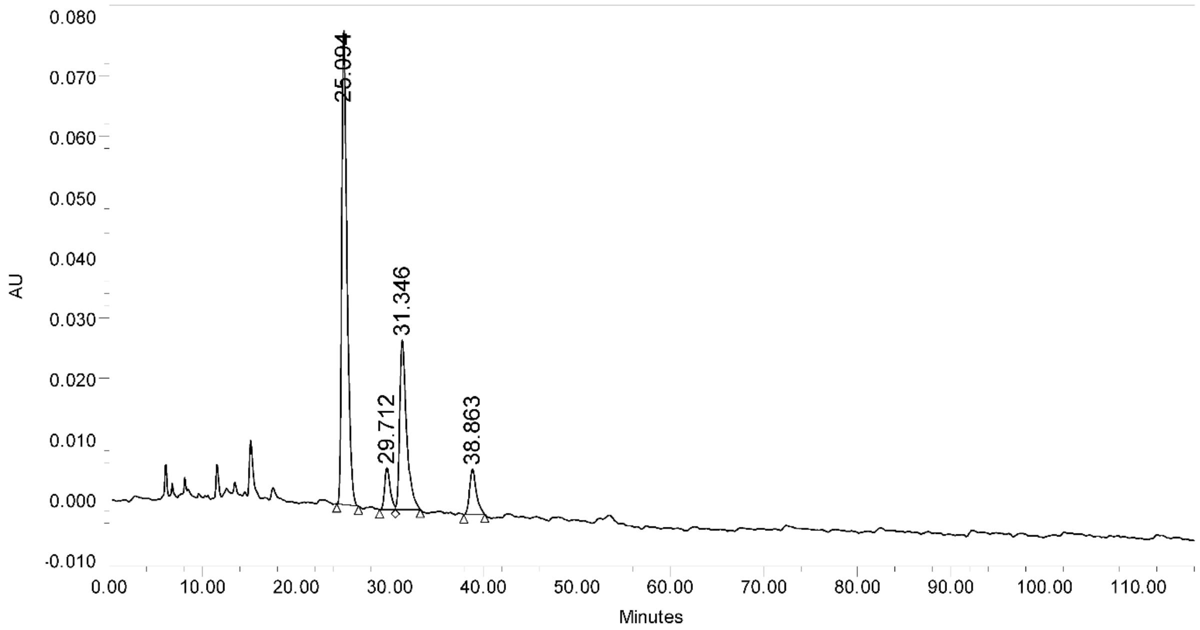


	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	21.878	19565886	87.03	374157	86.87
2	Peak2	29.539	2914727	12.97	56561	13.13

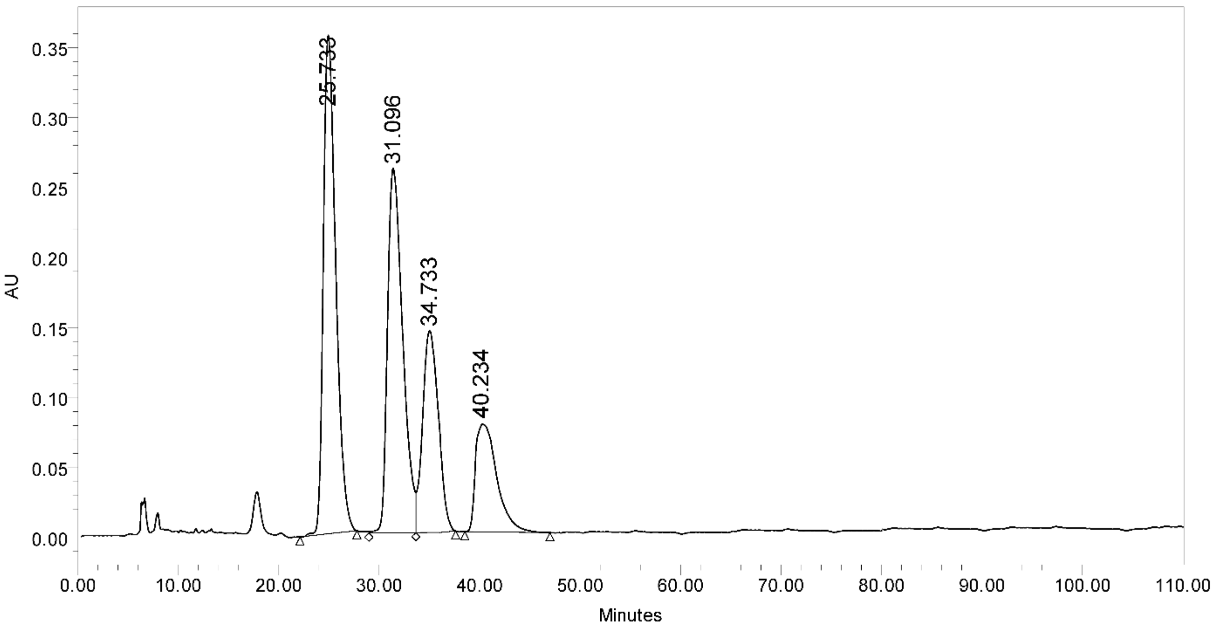


	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	21.140	991813	55.25	32569	56.23
2	29.036	803257	44.75	25355	43.77

Figure S44: HPLC data of enantioenriched and racemic of **8m**.

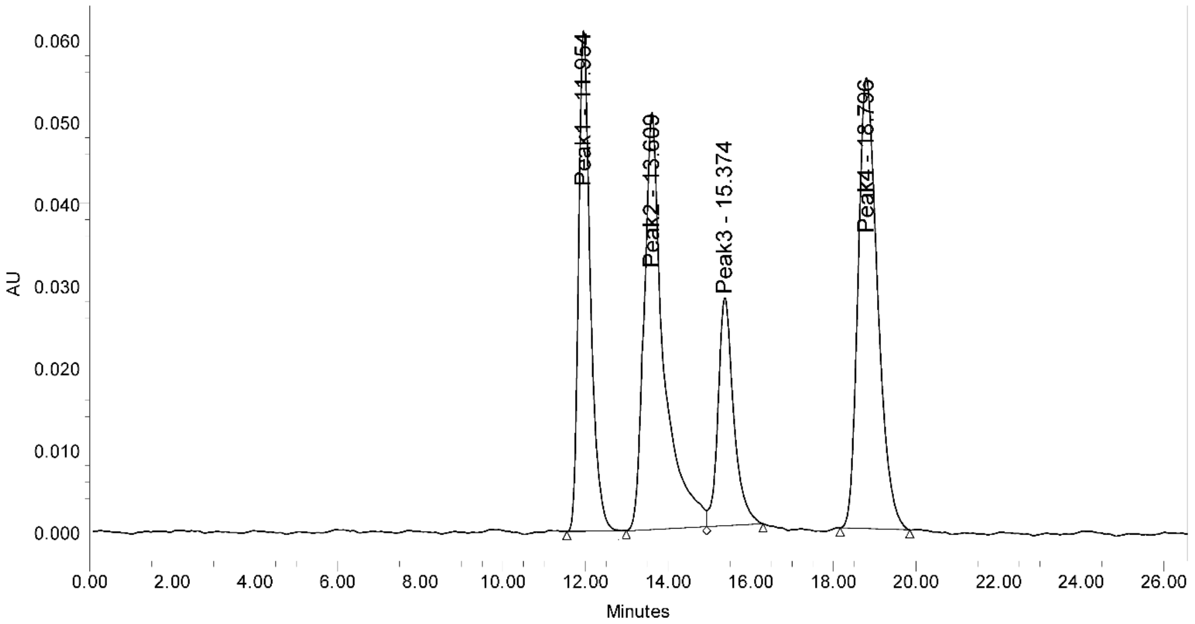


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	25.094	154998	60.93	3921	64.90
2	29.712	14343	5.64	345	5.72
3	31.346	66099	25.98	1401	23.19
4	38.863	18941	7.45	374	6.19

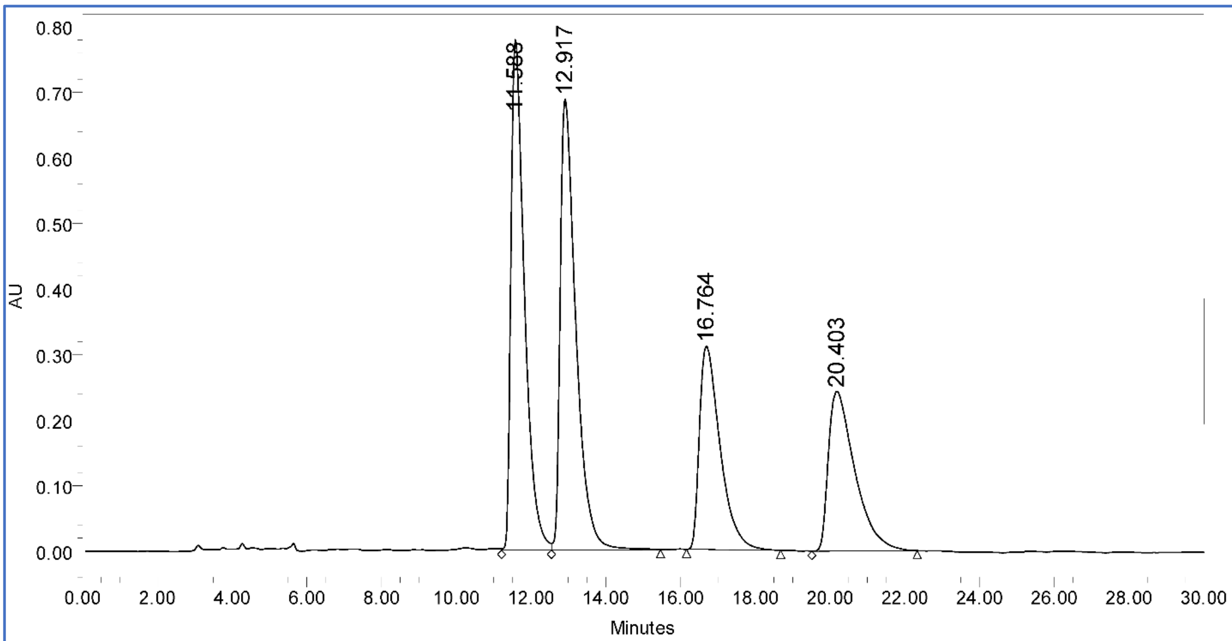


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	25.733	30618838	34.70	356037	42.57
2	31.096	27474430	31.14	260447	31.14
3	34.733	17273019	19.58	144102	17.23
4	40.234	12865415	14.58	75739	9.06

Figure S45: HPLC data of enantioenriched and racemic of **8n**.

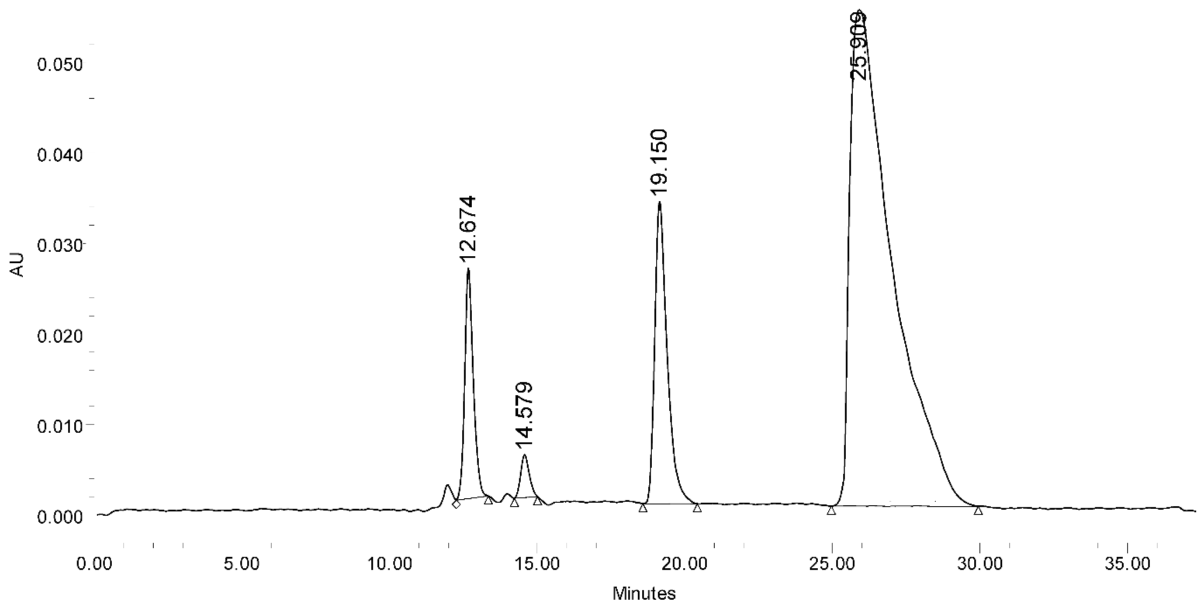


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	11.954	121701	21.46	6105	31.35
2	Peak2	13.609	191802	33.82	5090	26.14
3	Peak3	15.374	73409	12.94	2779	14.27
4	Peak4	18.796	180261	31.78	5497	28.23

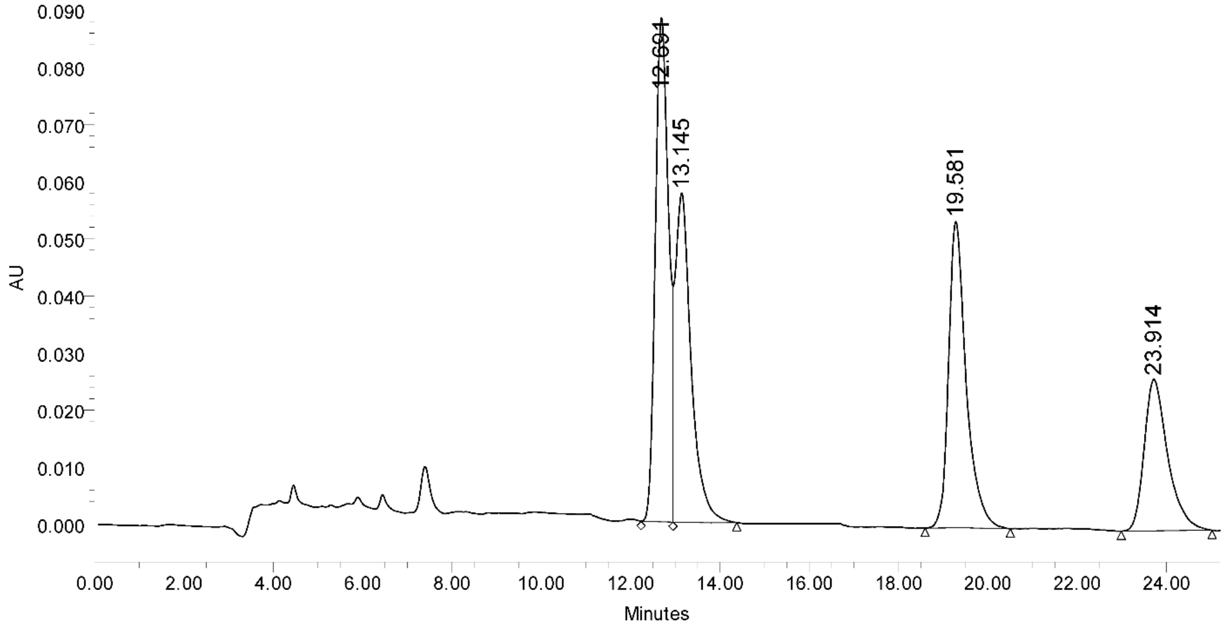


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	11.588	19570841	30.79	778853	38.54
2	12.917	20043150	31.53	687765	34.04
3	16.764	11944654	18.79	310018	15.34
4	20.403	12011183	18.89	244042	12.08

Figure S46: HPLC data of enantioenriched and racemic of **8o**.

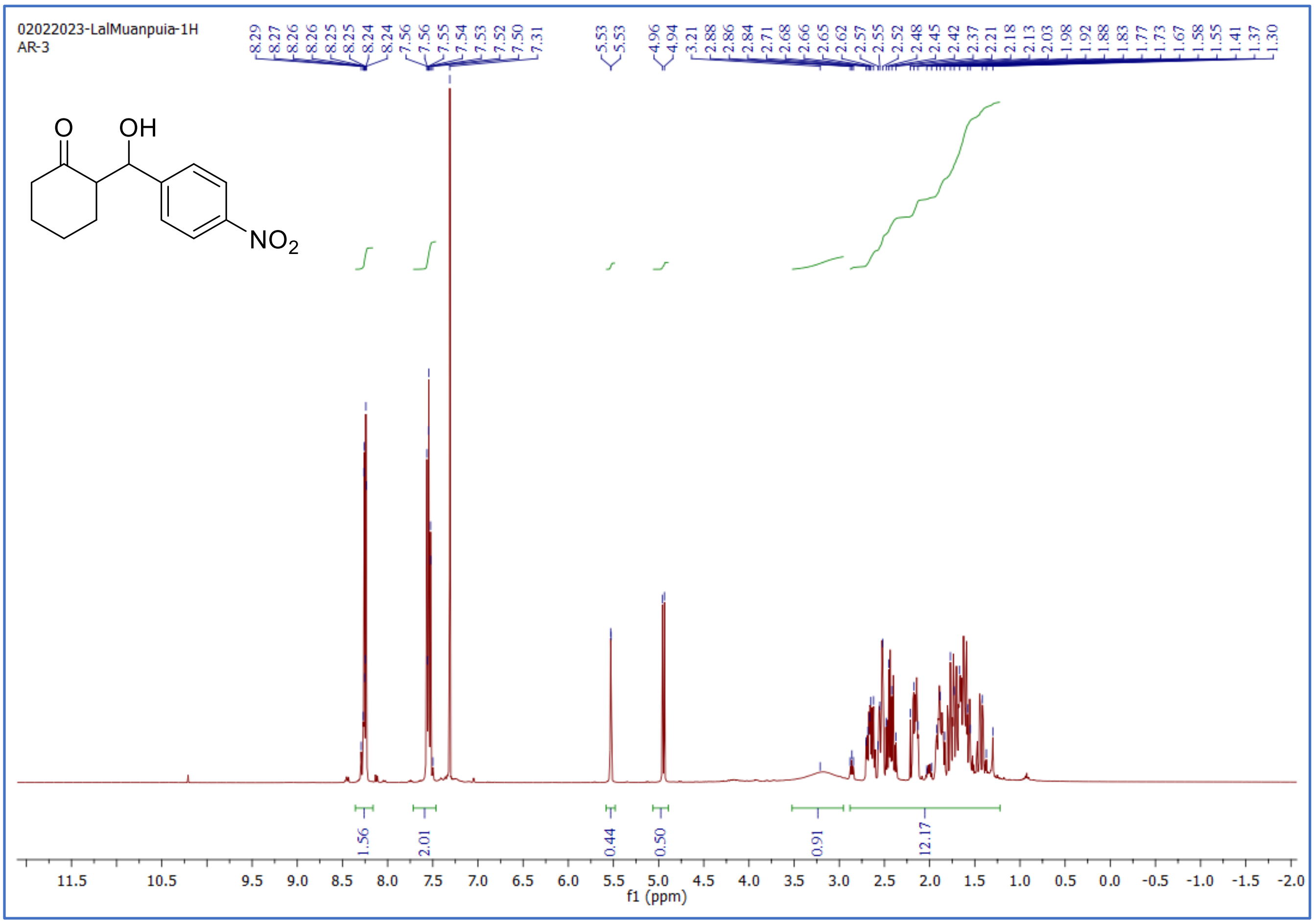


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	12.674	51333	8.65	2548	21.88
2	14.579	9516	1.60	473	4.07
3	19.150	97910	16.51	3337	28.66
4	25.909	434443	73.24	5286	45.39



	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	12.691	1806830	31.75	88364	39.08
2	13.145	1450364	25.48	57634	25.49
3	19.581	1460765	25.67	53572	23.69
4	23.914	973103	17.10	26530	11.73

Figure S47: ^{1}H NMR and ^{13}C NMR of **9a.**



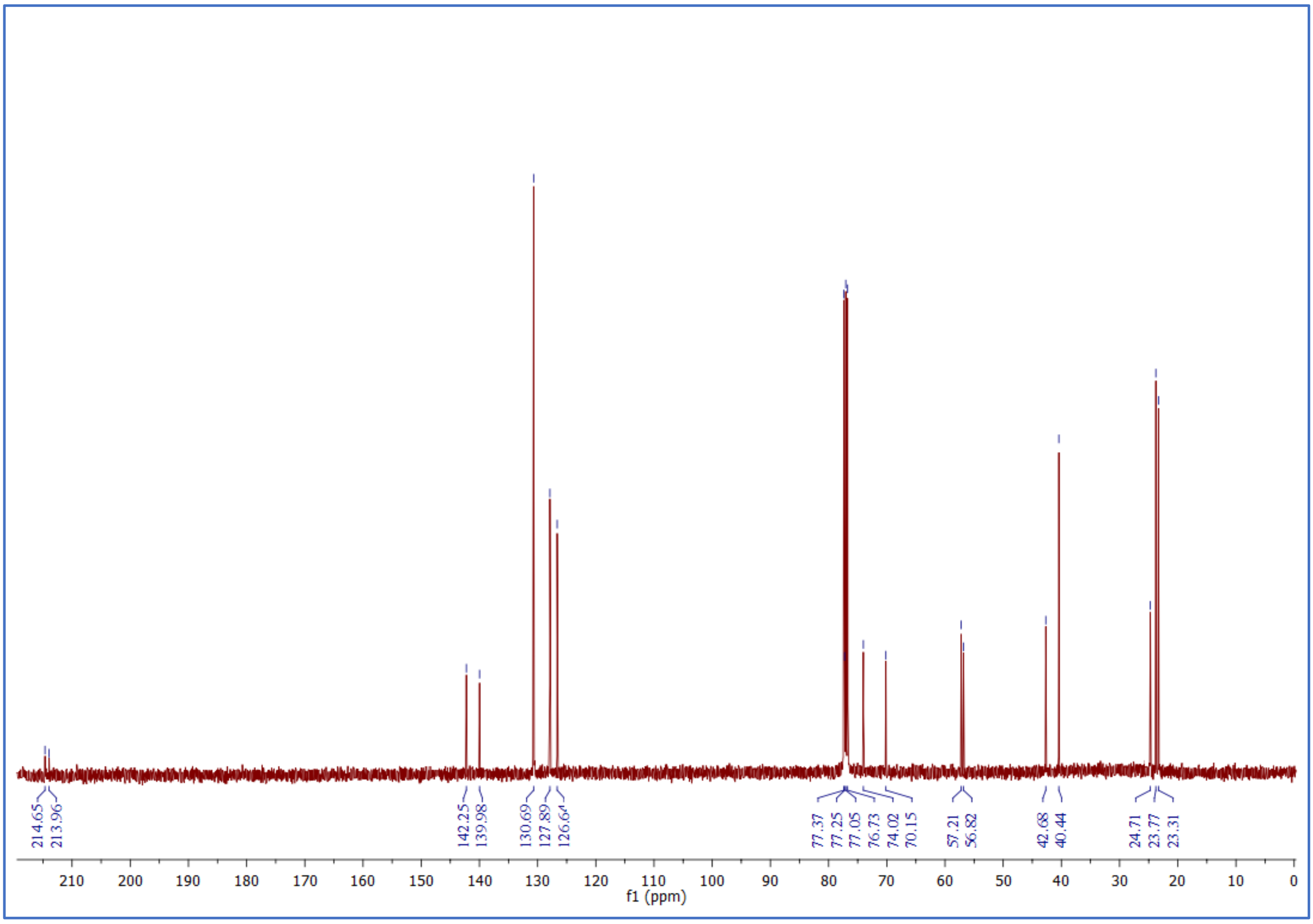
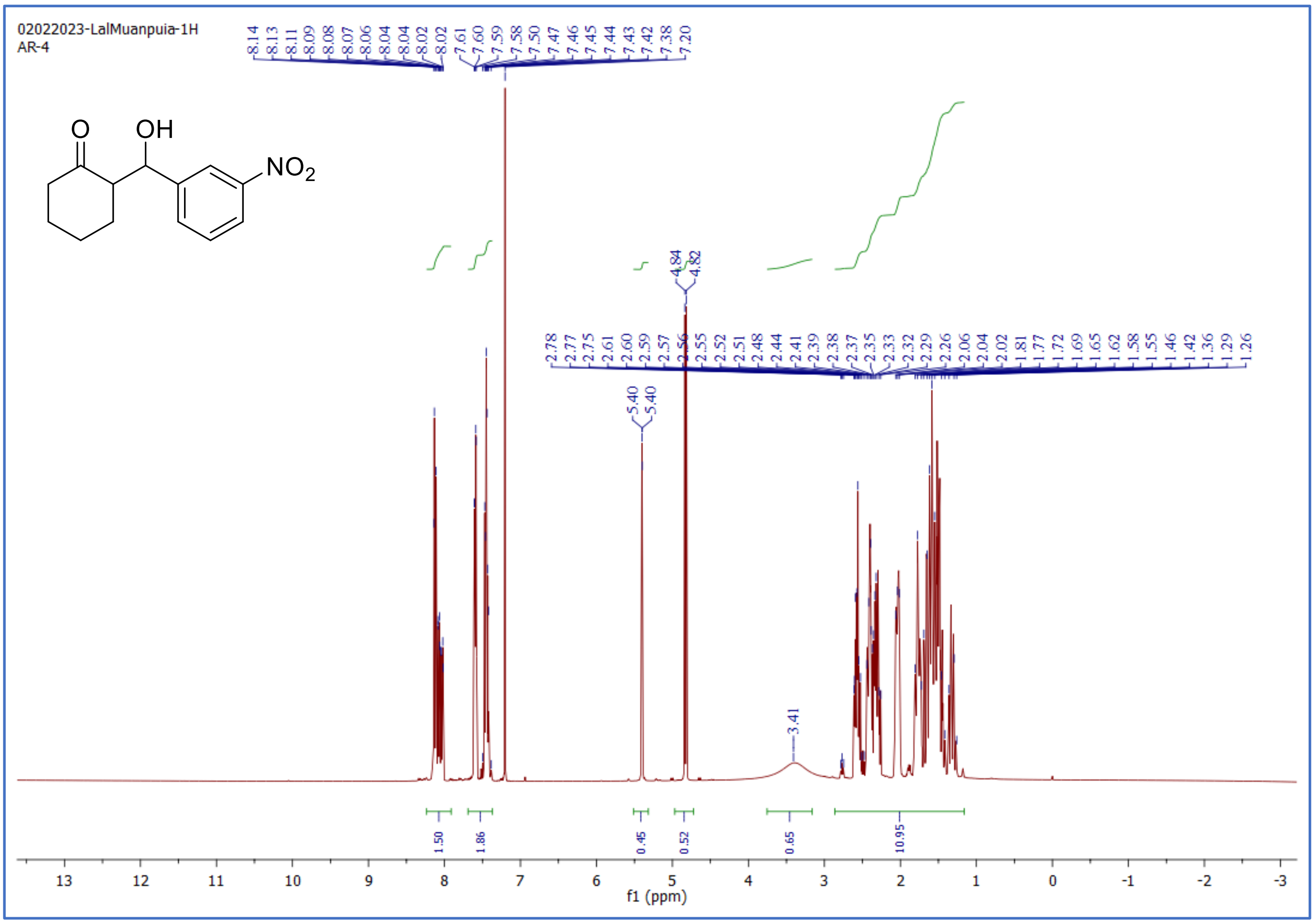


Figure S48: ^{1}H NMR and ^{13}C NMR of **9b.**



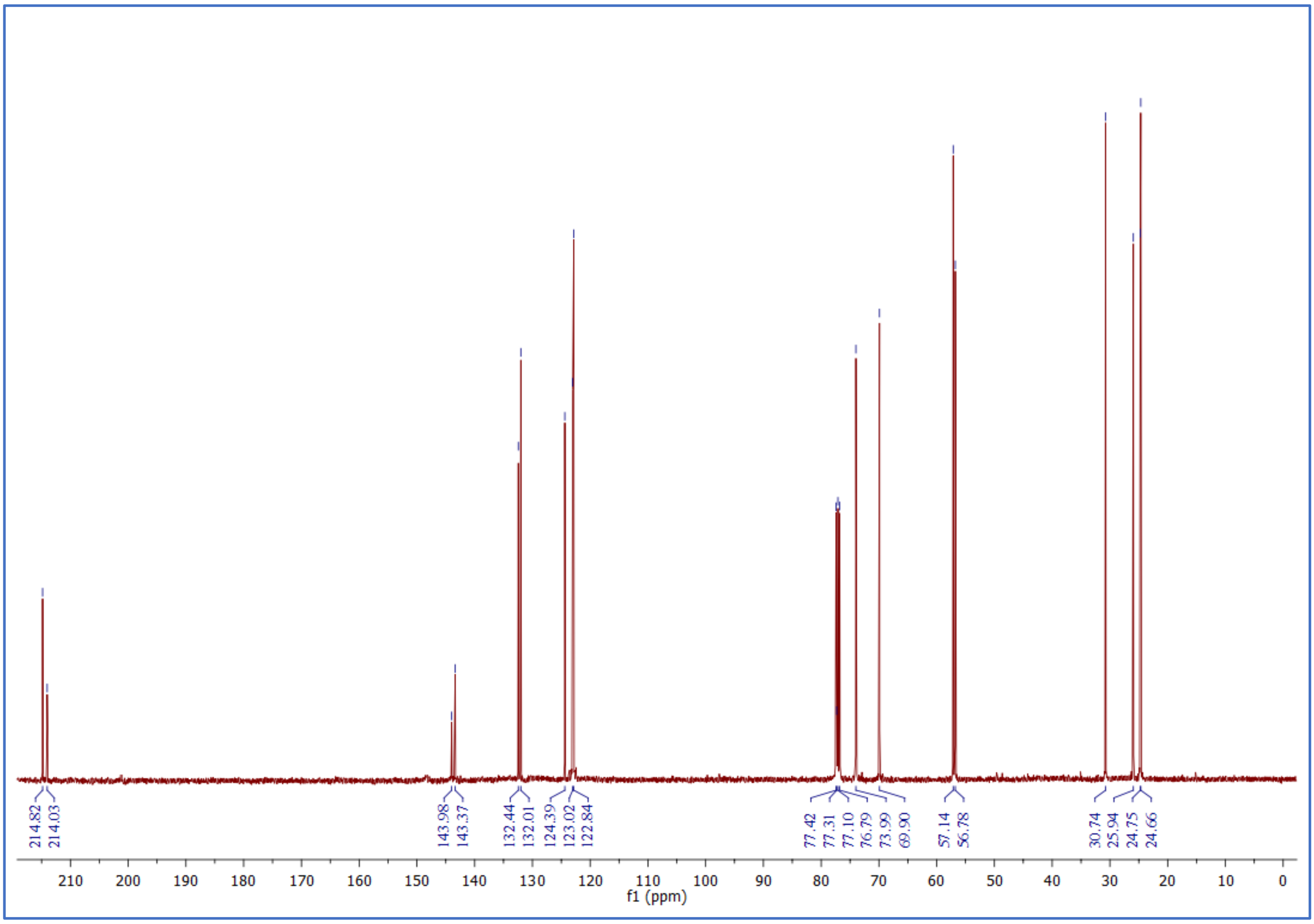
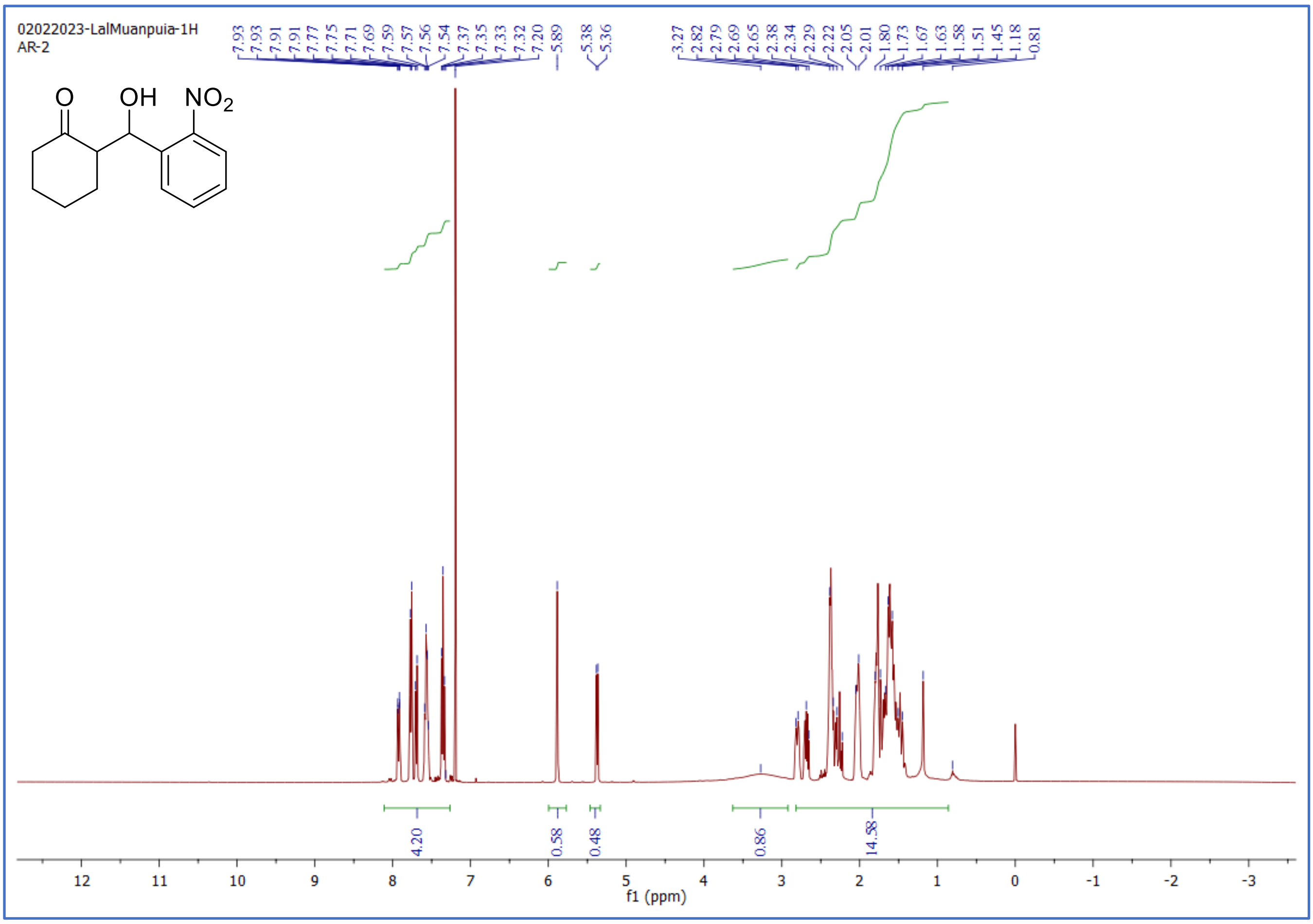


Figure S49: ^{1}H NMR and ^{13}C NMR of **9c.**



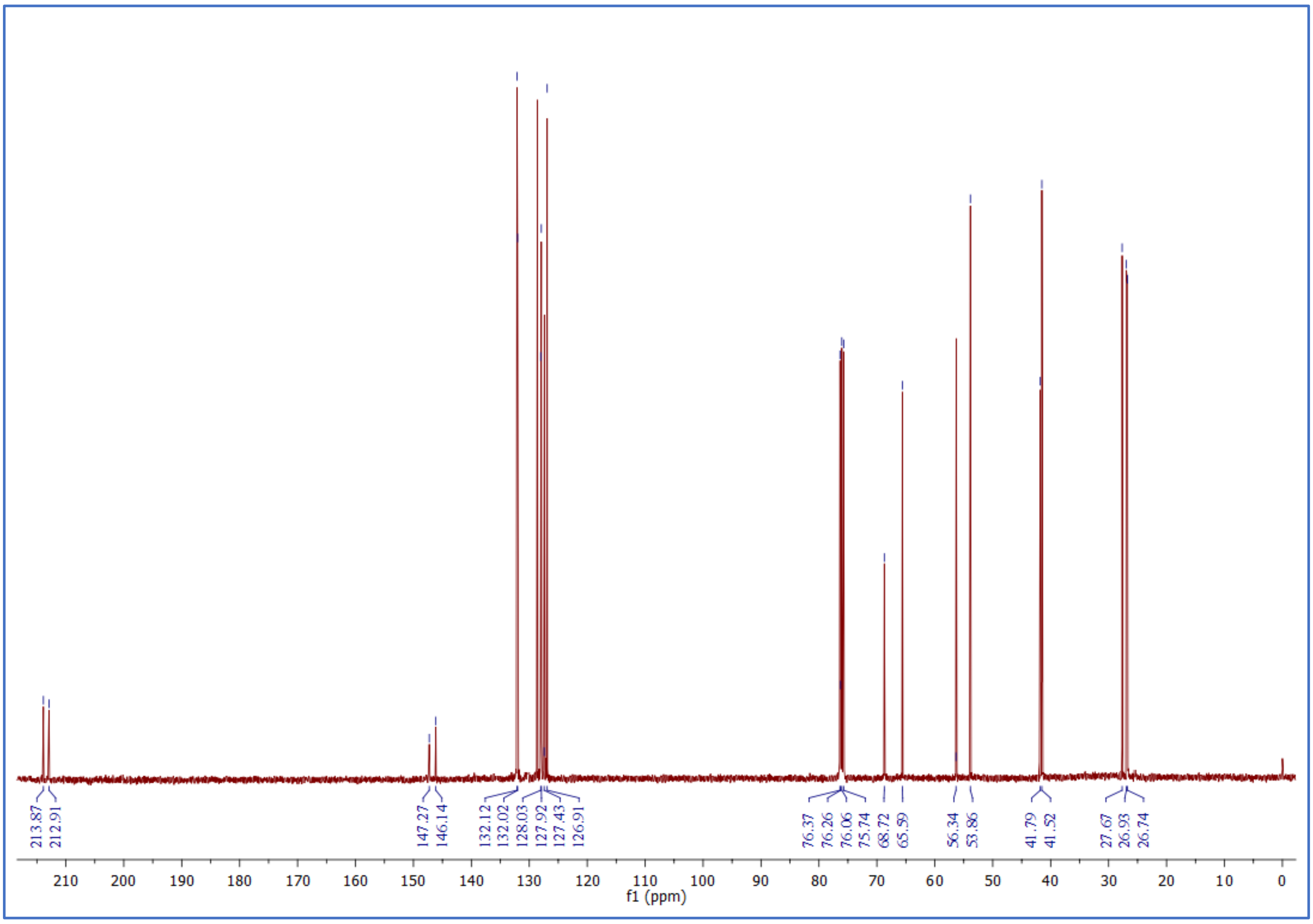
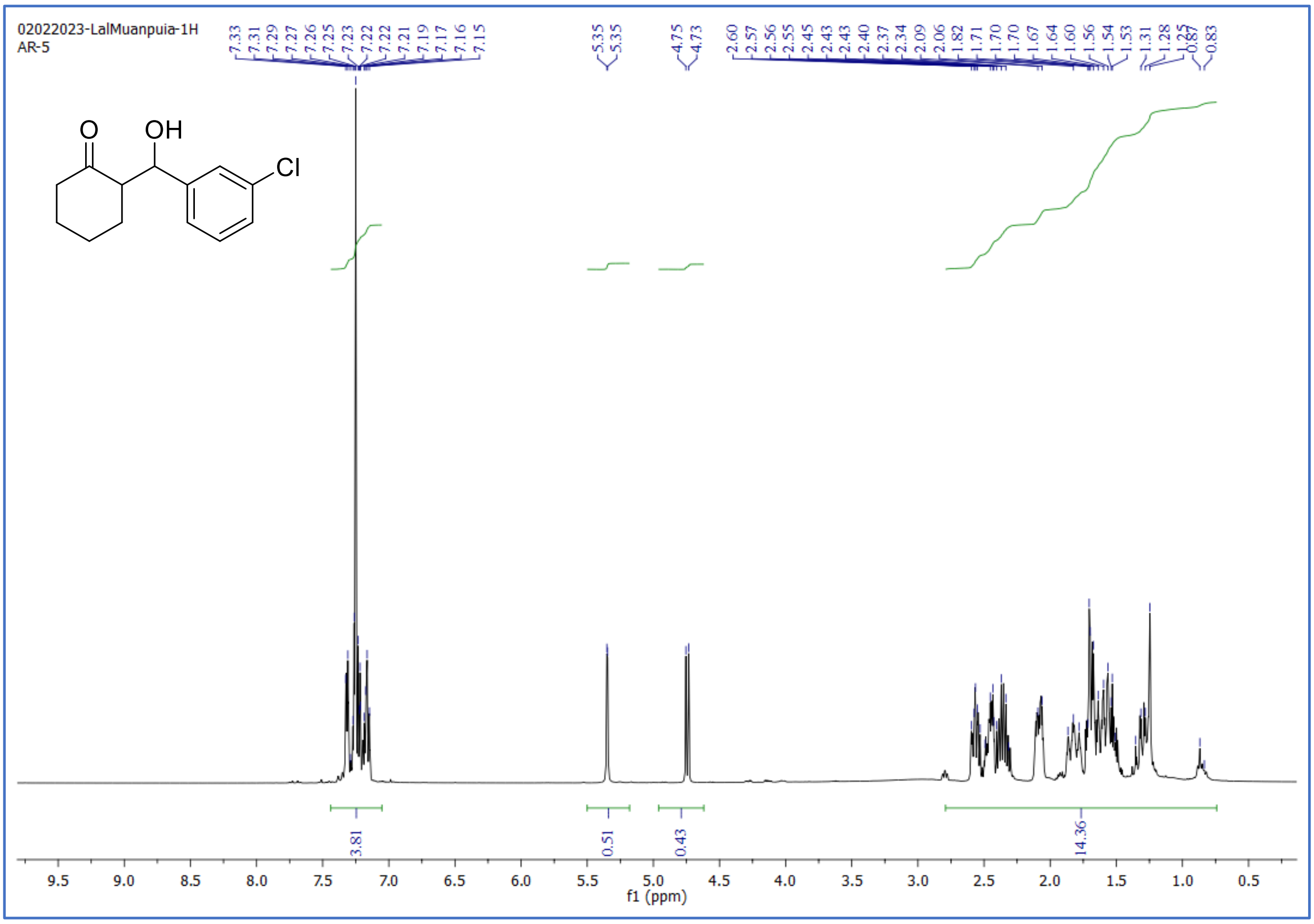


Figure S50: ^1H NMR and ^{13}C NMR of **9d.**



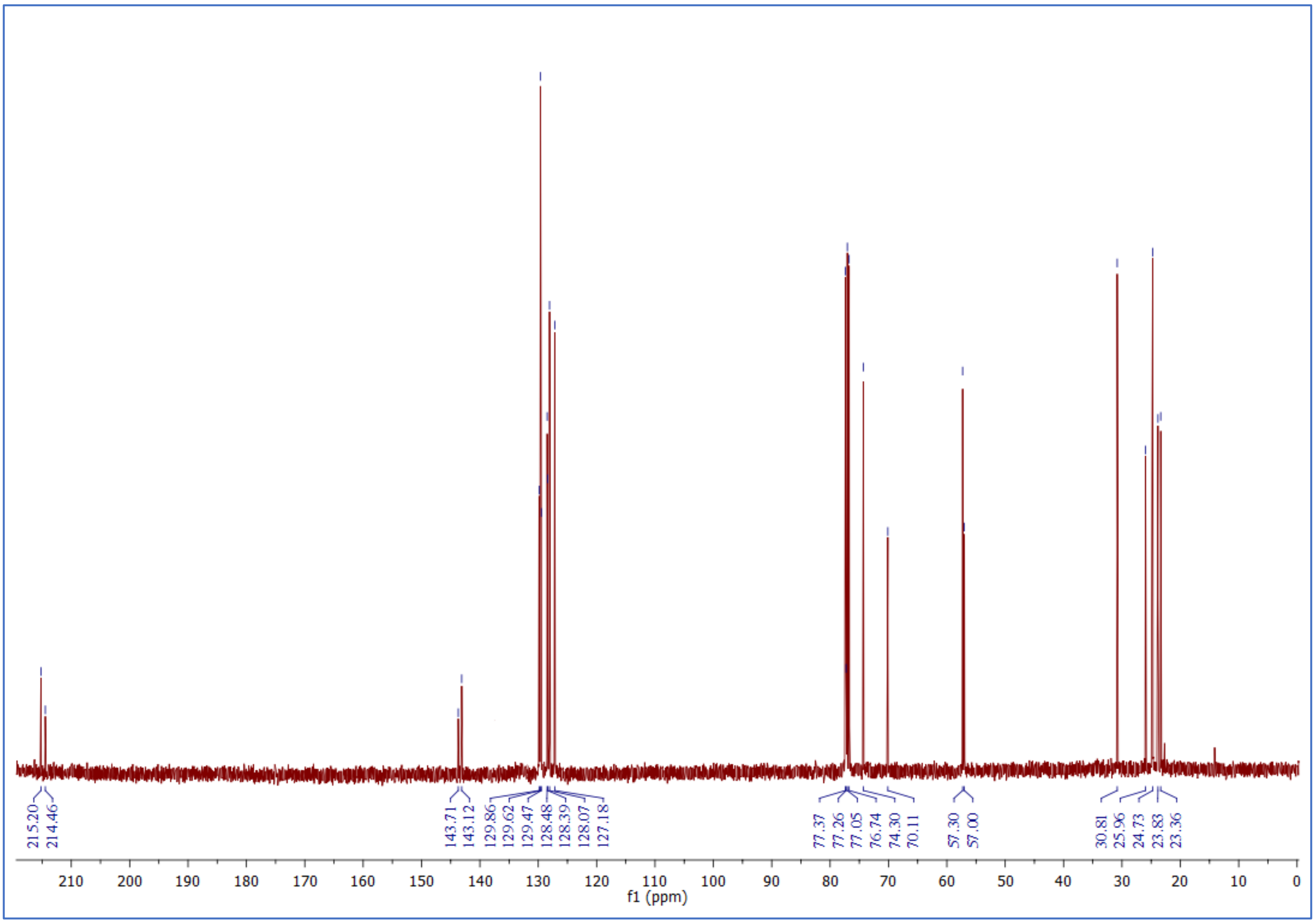
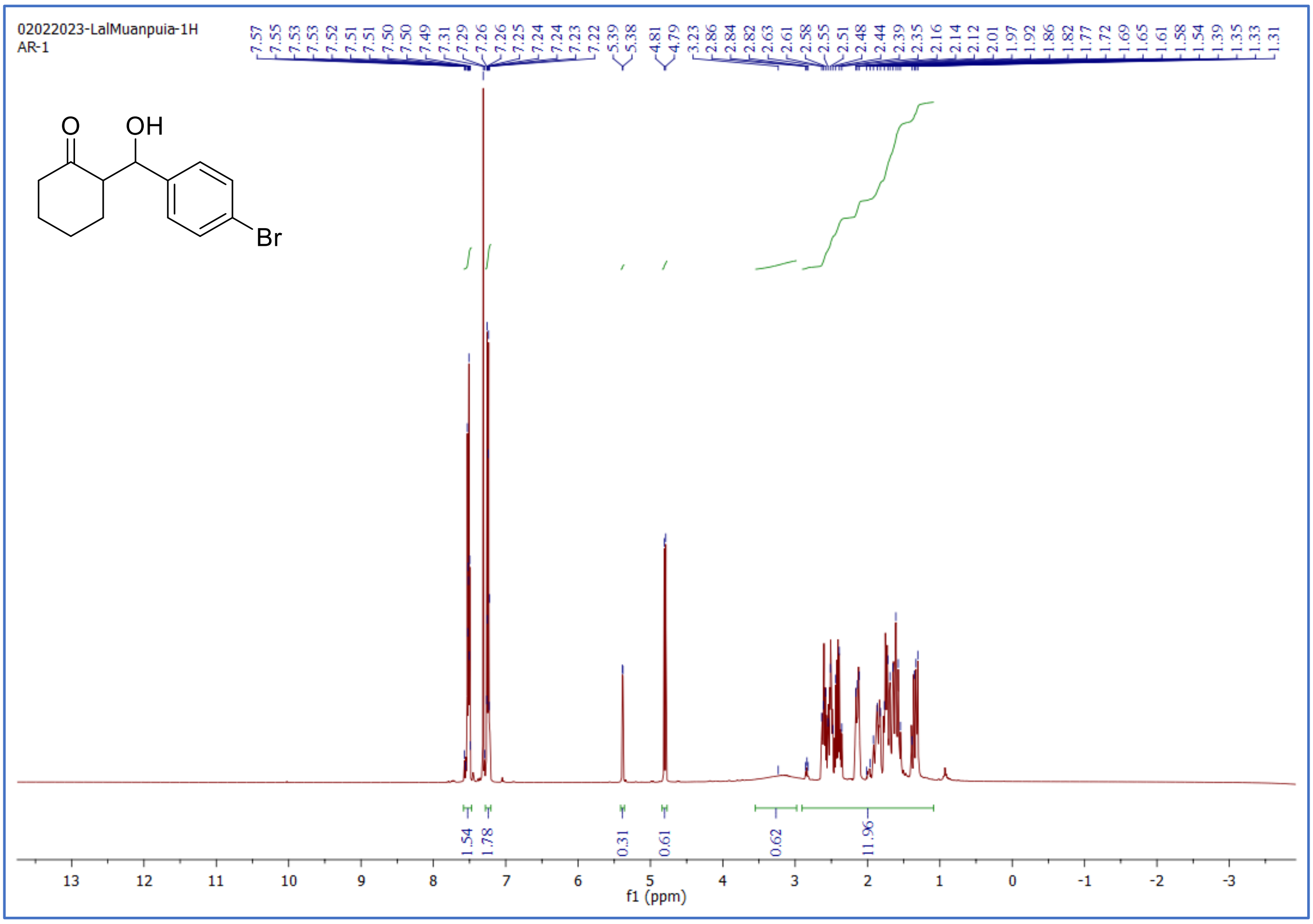


Figure S51: ^{1}H NMR and ^{13}C NMR of **9e.**



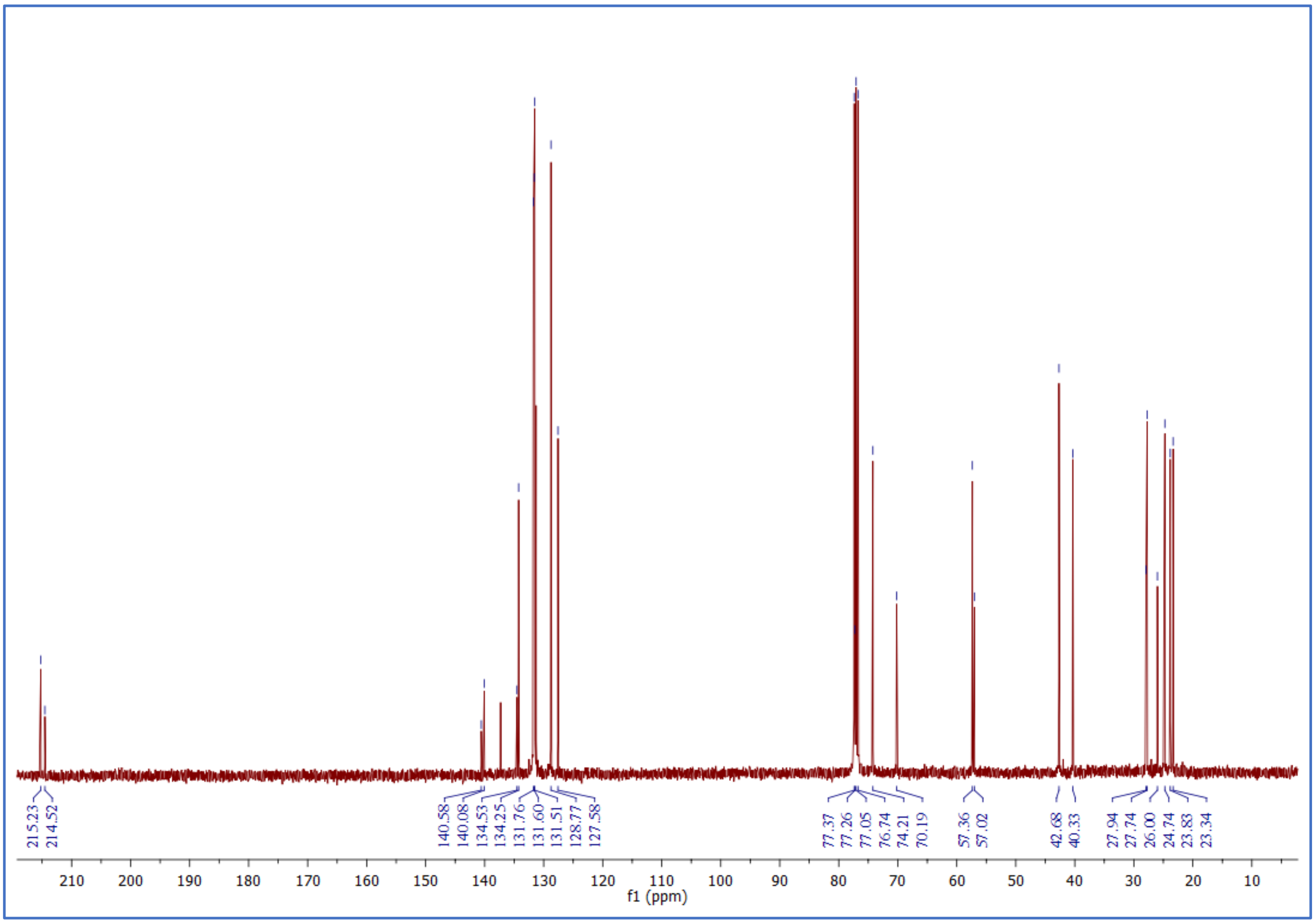
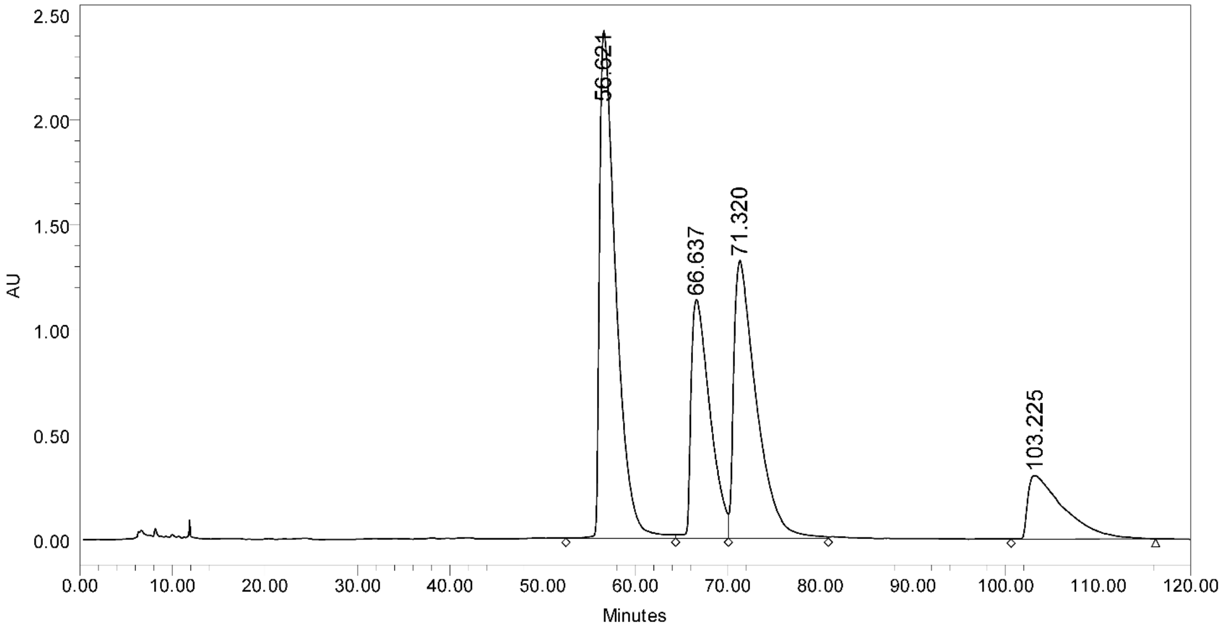
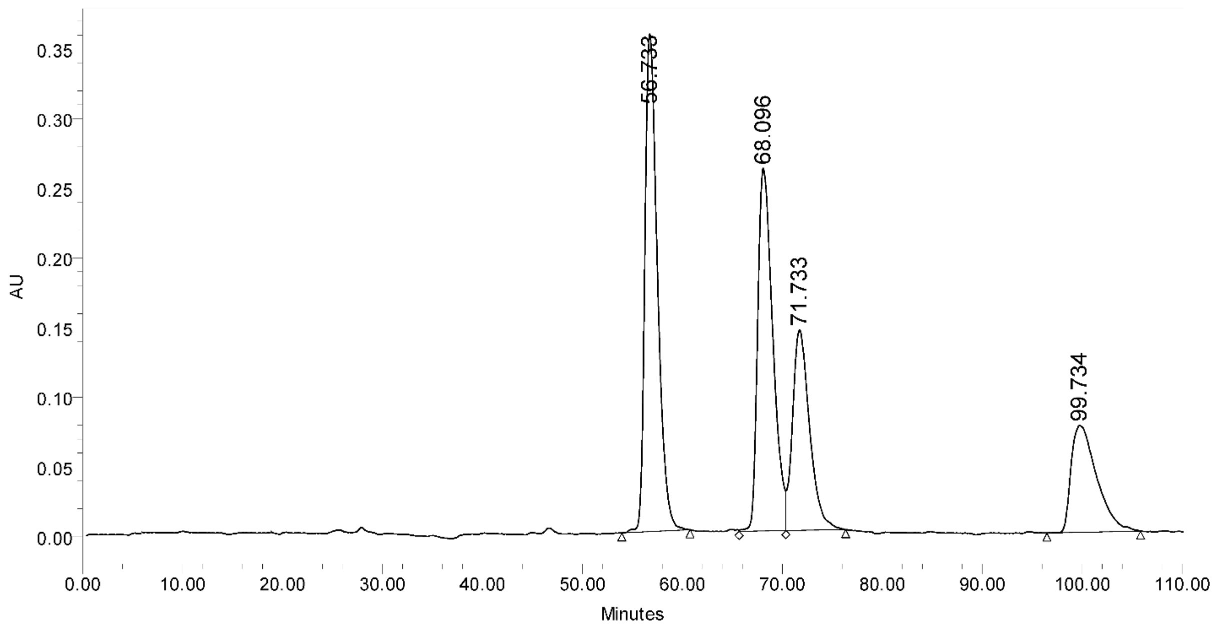


Figure S52: HPLC data of enantioenriched and racemic of **9a**.

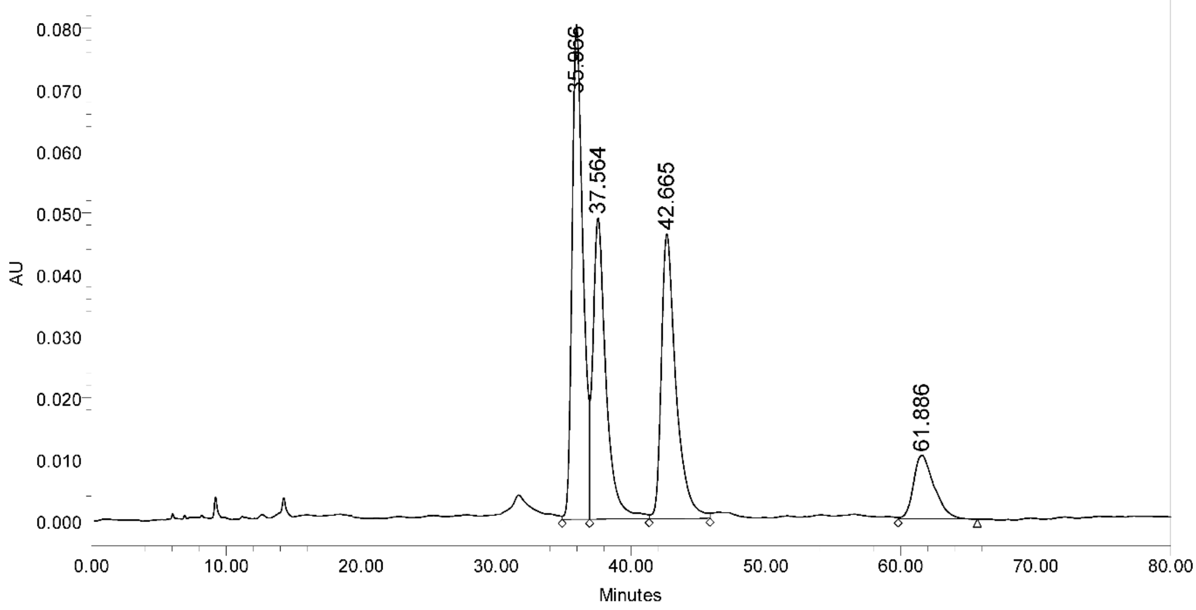


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	56.621	296858961	38.96	2417901	46.70
2	66.637	160738967	21.09	1135534	21.93
3	71.320	223134519	29.28	1322194	25.54
4	103.225	81277284	10.67	301908	5.83

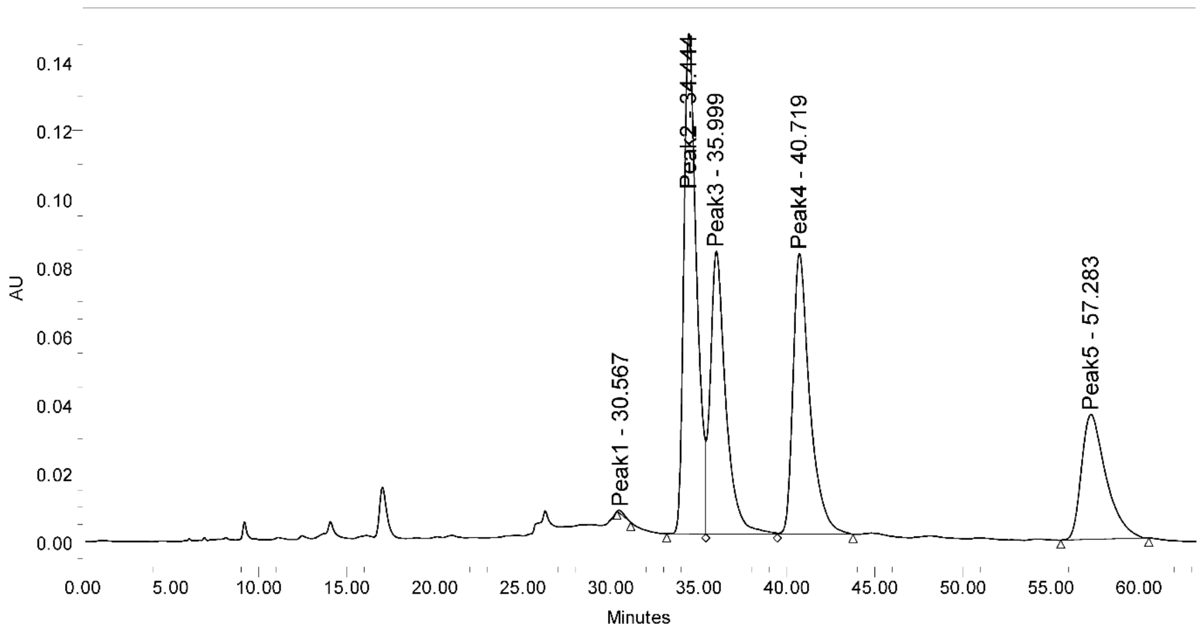


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	56.733	31134594	34.84	357318	42.63
2	68.096	27431818	30.70	260293	31.06
3	71.733	17139110	19.18	143808	17.16
4	99.734	13649457	15.28	76744	9.16

Figure S53: HPLC data of enantioenriched and racemic of **9b**.

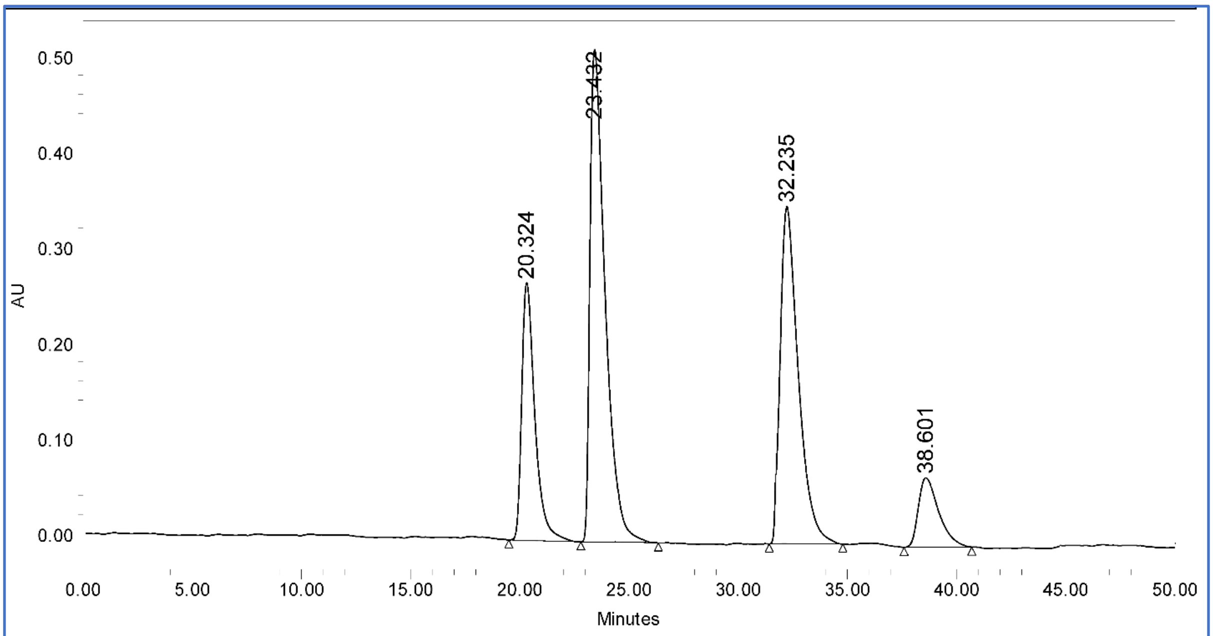


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	35.966	4472898	36.11	80329	43.26
2	37.564	3334456	26.92	48851	26.31
3	42.665	3477300	28.07	46222	24.89
4	61.886	1101166	8.89	10301	5.55

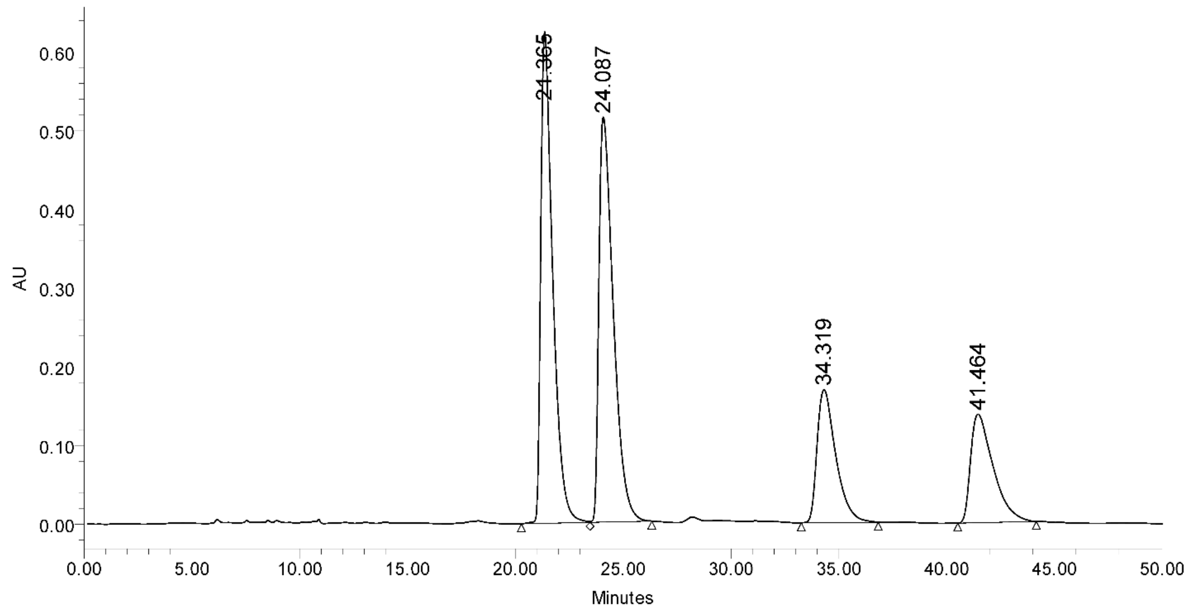


	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	Peak1	30.567	21371	0.10	888	0.26
2	Peak2	34.444	7299108	34.18	145969	41.99
3	Peak3	35.999	5065586	23.72	82431	23.71
4	Peak4	40.719	5433032	25.44	81928	23.57
5	Peak5	57.283	3536640	16.56	36435	10.48

Figure S54: HPLC data of enantioenriched and racemic of **9c**.

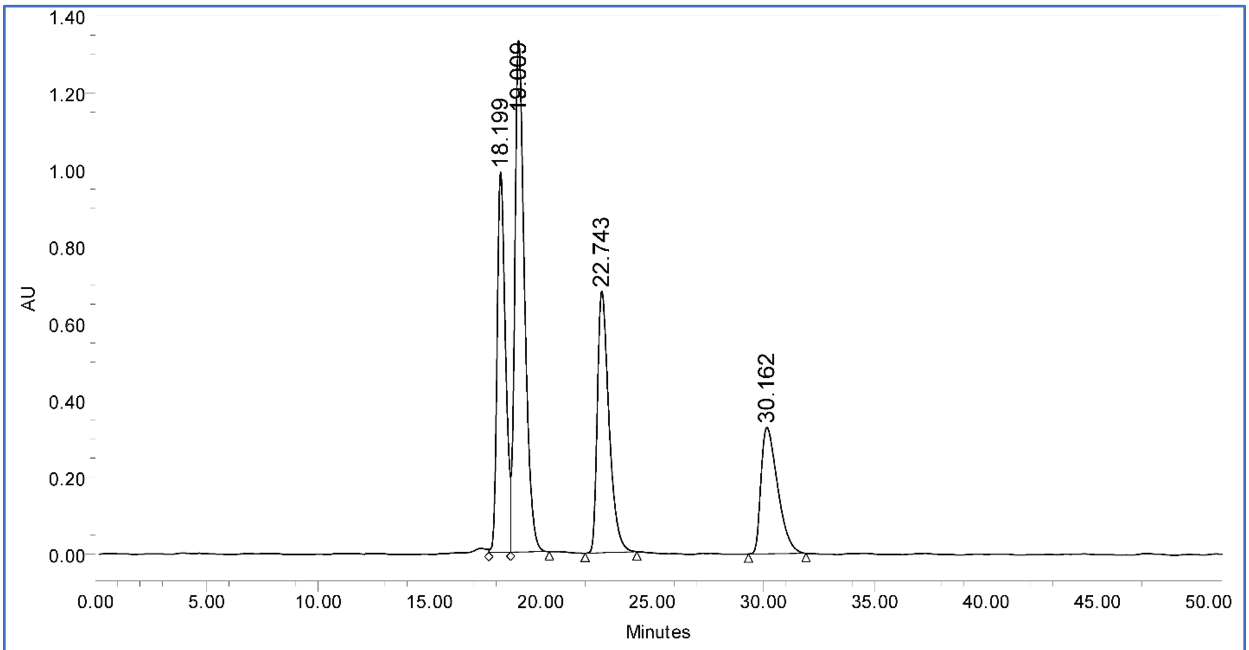


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	20.324	11305378	18.34	269633	22.27
2	23.432	24977567	40.52	515460	42.58
3	32.235	20644129	33.49	352800	29.14
4	38.601	4717473	7.65	72717	6.01

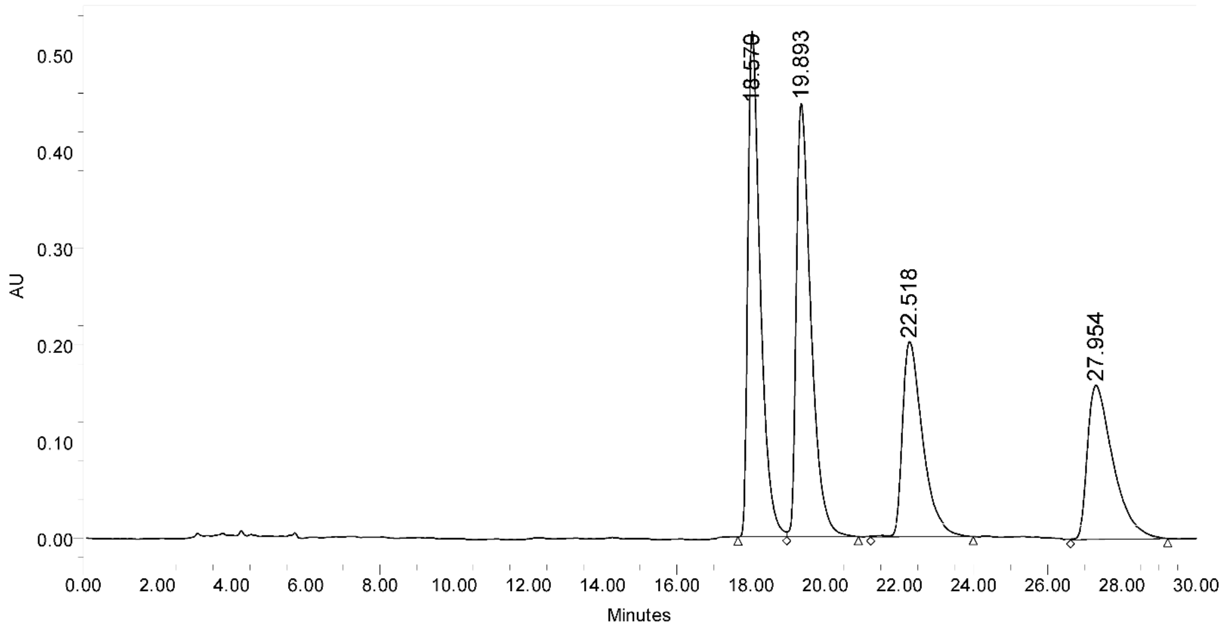


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	21.365	24071037	35.26	624568	43.19
2	24.087	23963364	35.10	514684	35.59
3	34.319	10209475	14.95	169031	11.69
4	41.464	10032024	14.69	137962	9.54

Figure S55: HPLC data of enantioenriched and racemic of **9d**.

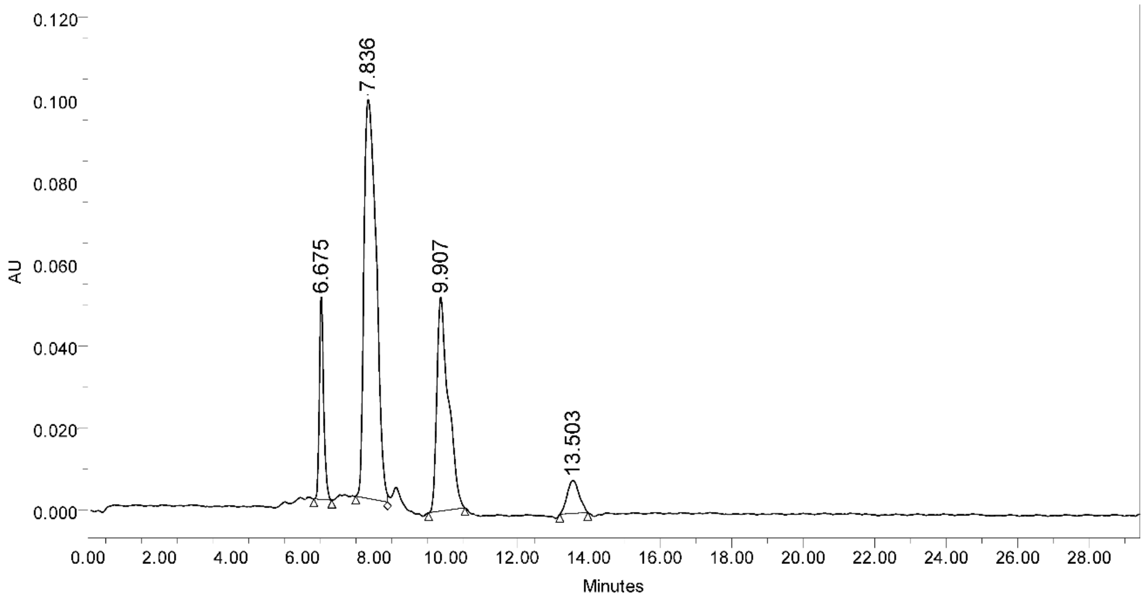


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	18.199	25680908	23.72	988211	29.70
2	19.009	40780636	37.67	1330480	39.99
3	22.743	24698290	22.81	680015	20.44
4	30.162	17095304	15.79	328501	9.87

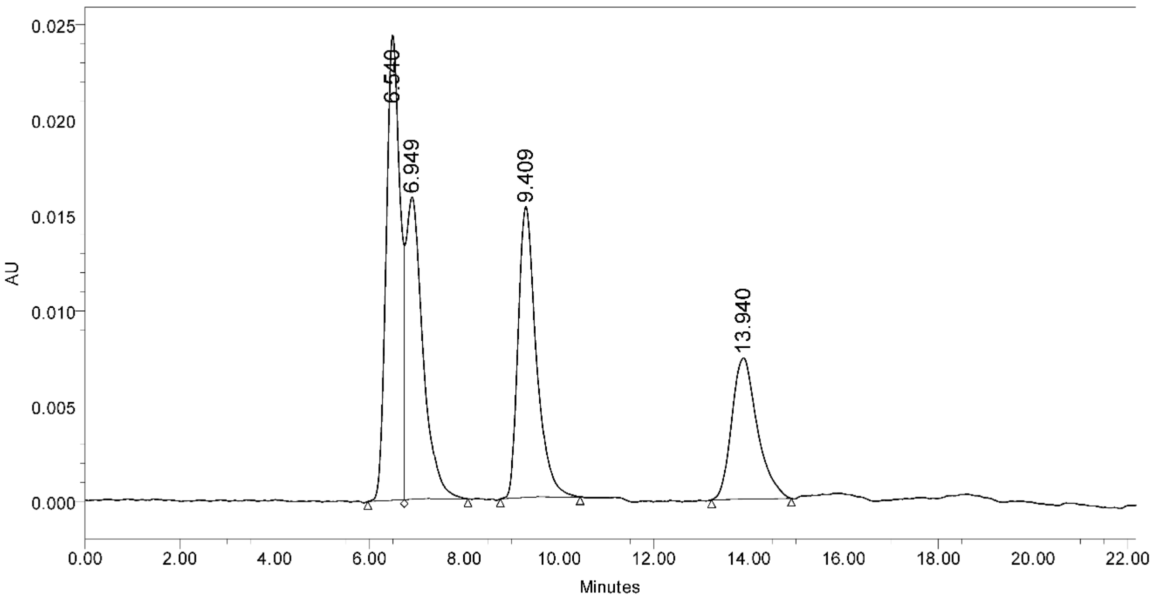


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	18.570	12124923	30.64	522545	39.30
2	19.893	12273599	31.01	447915	33.69
3	22.518	7596967	19.20	200691	15.10
4	27.954	7582068	19.16	158313	11.91

Figure S56: HPLC data of enantioenriched and racemic of **9e**.



	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	6.675	41248	10.37	4976	23.75
2	7.836	220911	55.52	9962	47.55
3	9.907	117060	29.42	5216	24.89
4	13.503	18652	4.69	799	3.81



	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	6.540	499513	31.79	24402	38.78
2	6.949	397273	25.28	15850	25.19
3	9.409	396939	25.26	15262	24.25
4	13.940	277671	17.67	7410	11.78