Electronic Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

Asymmetric 5-*endo* chloroetherification of homoallylic alcohols toward the synthesis of chiral β-chlorotetrahydrofurans

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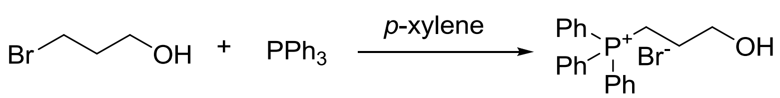
1. General Remarks

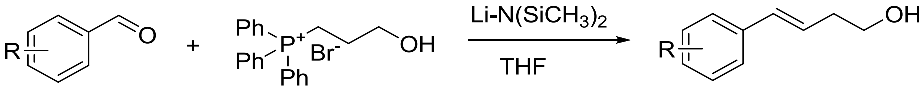
The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer. The chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. GC-MS was measured on Agilent 7890A /5975 C spectrometer. HRMS (ESI) was determined on a Bruker Daltonics micrOTOF-Q^{II} mass spectrometer. HPLC analysis was performed on Waters-Breeze (2487 Dual λ Absorbance Detector and 1525 Binary HPLC Pump). Chiralpak OD, AD, OJ columns were purchased from Daicel Chemical Industries, LTD. Column chromatography was generally performed on silica gel (200-300 mesh) and TLC inspections were on silica gel GF_{254} plates. Optical rotations were determined by using a Perkin-Elmer 341 LC polarimeter.

Unless otherwise stated, all commercial reagents and solvents were used as received. All the chiral starting materials were purchased from Aldrich, Alfa and Acros and used directly. Catalysts of **3a**[1], **3b**[2], **4a**[3], **4b**[4], **5a-5j**[5-8] were synthesized according to the reported methods.

2.1 General procedure for the preparation of but-3-en-1-ol compounds 1a-p.

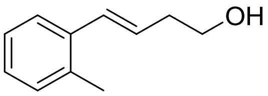


Under argon atmosphere, triphenylphosphine (9.5 g, 36.2 mmol), 3-bromopropan-1-ol (5.0 g, 36 mmol) and *p*-xylene (30 mL) were added in a round bottom flask equipped with a mechanical stirrer. The mixture was heated to 130 ^{o}C and stirred for 6 hours. After that, the reaction was then cooled to room temperature and ether (50 mL) was added. The solids were collected by filtration and dried under vacuum to afford 3-(triphenylphosphonium)propan-1-ol bromide as a white solid which was used in the next step without further purification.



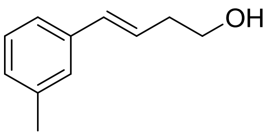
10.5 mmol of lithium bis(trimethylsilyl)amide was added dropwise at -20 °C or -78 °C to a suspension of 4.5 mmol of (3-propan-1-ol)triphenylphosphonium bromide in 10 mL of tetrahydrofuran. The solution was stirred at -20 °C for 1 hour and 3.75 mmol of aldehyde was added dropwise. After that, the mixture was stirred at the same temperature for 2 hours. The mixture was warmed to room temperature and stirred for another 12 hours, then saturated aqueous NH_4Cl solution was added. The organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/Petroleum = 1/5; v/v).

1a, (*E*)-4-o-tolylbut-3-en-1-ol:



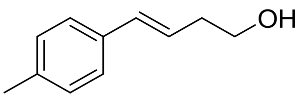
Colorless oil; 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12-7.21 (m, 4H), 6.69 (d, 1H, *J* = 15.6 Hz), 6.06 (dt, 1H, *J* = 7.2, 1.2 Hz), 3.72-3.75 (m, 2H), 2.47-2.52 (m, 2H), 2.33 (s, 3H), 1.75 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.4, 135.9, 130.3, 129.0, 127.2, 126.1, 125.5, 62.1, 36.7, 19.9 ppm; HRMS Calcd for $C_{11}H_{14}NaO$: $[M+Na]^+$, 185.0933. Found: m/z 185.0928.

1b, (*E*)-4-m-tolylbut-3-en-1-ol



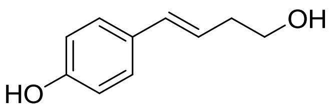
Colorless oil; 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10-7.23 (m, 3H), 7.03 (d, 1H, *J* = 6.8 Hz), 6.45 (d, 1H, *J* = 16.0 Hz), 6.18 (dt, 1H, dt, 1H, *J* = 7.2, 1.6 Hz), 3.71-3.74 (m, 2H), 2.45-2.48 (m, 2H), 2.33 (s, 3H), 1.83 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.1, 137.2, 132.9, 128.5, 128.1, 126.8, 126.1, 123.3, 62.1, 36.4, 21.4 ppm; HRMS Calcd for $C_{11}H_{14}NaO$: $[M+Na]^+$, 185.0937. Found: m/z 185.0935.

1c, (*E*)-4-p-tolylbut-3-en-1-ol:



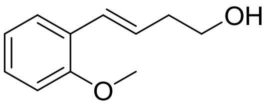
White solid; 65% yield.^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, 2H, *J* = 6.0), 7.11 (d, 2H, *J* = 8.0 Hz), 6.46 (d, 1H, *J* = 16.0 Hz), 6.14 (dt, 1H, *J* = 7.2, 1.6 Hz), 3.72-3.75 (m, 2H), 2.46-2.49 (m, 2H), 2.32 (s,3H), 1.62 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.1, 134.5, 132.7, 129.3, 126.0, 125.2, 62.1, 36.4, 21.2 ppm; HRMS Calcd for $C_{11}H_{14}NaO$: $[M+Na]^+$, 185. 0938. Found: m/z 185.0941.

1d, (*E*)-4-(4-hydroxybut-1-enyl)phenol:



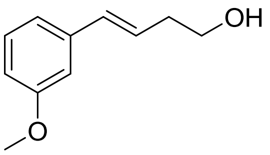
White solid; 52% yield. ^{1}H NMR (400 MHz, DMSO): δ = 9.30 (d, 1H, *J* = 8.0 Hz), 7.10 (d, 2H, *J* = 8.0 Hz), 6.61 (d, 2H, *J* = 8.4 Hz), 6.22 (d, 1H, *J* = 16.0 Hz), 5.91-5.99 (m, 1H), 4.47 (t, 1H, *J* = 4.0 Hz), 3.38-3.44 (q, 2H, *J* = 8.0 Hz), 2.18-2.33 (q, 2H, *J* = 8.0 Hz) ppm; ^{13}C NMR (100 MHz, DMSO): δ = 156.5, 130.6, 128.4, 126.9, 124.2, 115.3, 60.9, 36.4 ppm; HRMS Calcd for $C_{10}H_{12}NaO_2$: $[M+Na]^+$, 187.0721. Found: m/z 187.0717.

1e, (*E*)-4-(2-methoxyphenyl)but-3-en-1-ol:



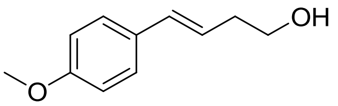
Colorless oil; 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27-7.30 (m, 1H), 7.07-7.12 (m, 1H), 6.66-6.79 (m, 3H), 6.06 (dt, 1H, *J* = 7.2, 1.6Hz), 3.70 (s, 3H), 3.60-3.63 (m, 2H), 2.34-2.39 (m, 2H), 1.62 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 128.3, 127.6, 127.0, 126.6, 126.3, 120.7, 110.9, 62.1, 55.4, 36.9 m; HRMS Calcd for $C_{11}H_{14}NaO_2$: $[M+Na]^+$, 201.0087. Found: m/z 201.0081.

1f, (*E*)-4-(3-methoxyphenyl)but-3-en-1-ol:



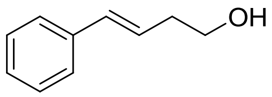
Colorless oil; 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19-7.23 (t, 1H, *J* = 8.0 Hz), 6.95 (d, 1H, *J* = 7.6 Hz), 6.89-6.90 (m, 1H), 6.78-6.79 (m, 1H), 6.76-6.77 (m, 1H), 6.46 (d, 1H, *J* = 15.6 Hz), 6.20 (dt, 1H, *J* = 7.2, 1.6Hz), 3.80 (s, 1H), 3.73-3.76 (m, 2H), 2.45-2.50 (m, 2H), 1.75 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 138.7, 132.7, 129.5, 126.8, 118.8, 112.9, 111.4, 62.0, 55.2, 36.4 ppm; HRMS Calcd for $C_{11}H_{14}NaO_2$: $[M+Na]^+$, 201.0086. Found: m/z 201.0083.

1g, (*E*)-4-(4-methoxyphenyl)but-3-en-1-ol:



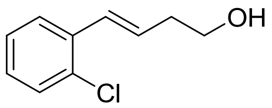
White solid; 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (dd, 2H, *J* = 4.8, 2.0 Hz), 6.84 (d, 2H, *J* = 8.8 Hz), 6.44 (d, 1H, *J* = 16.0 Hz), 6.05 (dt, 1H, *J* = 7.2, 1.2 Hz), 3.80 (s, 3H), 3.3 (t, 2H, *J* = 6.4 Hz), 2.48-2.43 (m, 2H), 1.63 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 132.3, 130.0, 127.2, 124.0, 114.0, 62.1, 55.3, 36.4 ppm; HRMS Calcd for $C_{11}H_{14}NaO_2$: $[M+Na]^+$, 201.0086. Found: m/z 201.0081.

1h, (*E*)-4-phenylbut-3-en-1-ol:



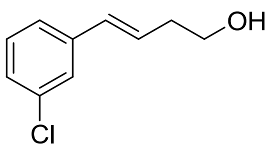
Colorless oil; 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20-7.38 (m, 5H), 6.50 (d, 1H, *J* = 16.0 Hz), 6.21 (dt, 1H, *J* = 7.2, 1.6Hz), 3.75-3.78 (m, 2H), 2.47-2.52 (m, 2H), 1.55 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.2, 132.9, 128.6, 127.3, 126.3, 126.1, 62.0, 36.4 ppm; HRMS Calcd for $C_{10}H_{12}NaO$: $[M+Na]^+$, 171.0775. Found: m/z 171.0779.

1i, (*E*)-4-(2-chlorophenyl)but-3-en-1-ol:



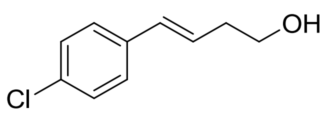
Colorless oil; 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50-7.52 (m, 1H), 7.32-7.34 (m, 1H), 7.15-7.20 (m, 2H), 6.87 (d, 1H, *J* = 8.0 Hz), 6.20 (dt, 1H, *J* = 7.2, 1.2Hz), 3.75-3.78 (m, 2H), 2.50-2.55 (m, 2H), 1.78 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.4, 132.66, 129.6, 129.5, 128.9, 128.3, 126.8, 126.7, 62.0, 36.5 ppm; HRMS Calcd for $C_{10}H_{11}ClNaO$: $[M+Na]^+$, 205.0389. Found: m/z 205.0381.

1j, (*E*)-4-(3-chlorophenyl)but-3-en-1-ol:



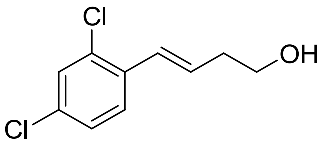
Colorless oil; 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (s, 1H), 7.15-7.21 (m, 3H), 6.40 (d, 1H, *J* = 16.0 Hz), 6.17-6.24 (m, 1H), 3.71-3.74 (m, 2H), 2.43-2.48 (m, 2H), 2.15 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.2, 134.5, 131.3, 129.8, 128.2, 127.2, 126.0, 124.4, 61.9, 36.3 ppm; HRMS Calcd for $C_{10}H_{11}ClNaO$: $[M+Na]^+$, 205.0391. Found: m/z 205.0386.

1k, (*E*)-4-(4-chlorophenyl)but-3-en-1-ol:



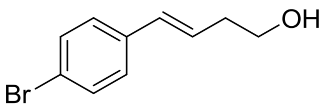
Colorless oil; 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (s, 4H), 6.39-6.44 (m, 1H), 6.17 (dt, 1H, *J* = 7.2, 1.6Hz), 3.71-3.75 (m, 2H), 2.43-2.48 (m, 2H), 2.09 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8, 132.8, 132.1, 131.4, 128.7, 127.3, 61.9, 36.4 ppm; HRMS Calcd for $C_{10}H_{11}ClNaO$: $[M+Na]^+$, 205.0385. Found: m/z 205.0379.

1l, (*E*)-4-(2,4-dichlorophenyl)but-3-en-1-ol:



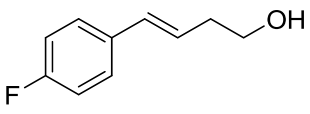
Colorless oil; 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ =7.43 (d, 1H, *J* = 8.8 Hz), 7.35 (d, 1H, *J* = 2.0 Hz), 7.16-7.18 (m, 1H), 6.79 (d, 1H, *J* = 15.6 Hz), 6.20 (dt, 1H, *J* = 7.2, 1.2 Hz), 3.76-3.79 (m, 2H), 2.49-2.55 (m, 2H), 1.76 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.0, 133.2, 131.2, 130.2, 129.4, 127.8, 127.4, 127.2, 61.9, 36.5 ppm; HRMS Calcd for $C_{10}H_{10}Cl_2NaO$: $[M+Na]^+$, 238.9991. Found: m/z 238.9986.

1m, (*E*)-4-(4-bromophenyl)but-3-en-1-ol:



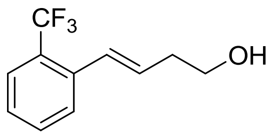
Yellow solid; 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.42 (m, 2H), 7.20-7.22 (m, 2H), 6.42 (d, 1H, *J* = 16.0 Hz), 6.19 (dt, 1H, *J* = 7.2, 1.6 Hz), 3.73-3.76 (m, 2H), 2.44-2.49 (m, 2H), 1.74 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.2, 131.6, 131.5, 127.6, 127.4, 120.9, 61.9, 36.4 ppm; HRMS Calcd for $C_{10}H_{11}BrNaO$: $[M+Na]^+$, 248.9876. Found: m/z248.9885.

1n, (*E*)-4-(4-fluorophenyl)but-3-en-1-ol:



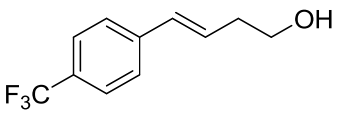
Colorless oil; 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.13-7.20 (m, 2H), 6.83-6.87 (m, 2H), 6.32 (d, 1H, *J* = 16.0 Hz), 5.95-6.05(m, 1H), 3.59-3.63 (m, 2H), 2.31-2.36 (m, 2H), 1.68 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1 (d, *J* = 270.0 Hz), 133.4 (d, *J* = 4.0 Hz), 131.5, 127.6 (d, *J* = 8.0 Hz), 126.1, 115.5(d, *J* = 21.0 Hz) , 62.0, 36.3 ppm; HRMS Calcd for $C_{10}H_{11}FNaO$: $[M+Na]^+$, 189.0678. Found: m/z 189.0674.

1o, (*E*)-4-(2-(trifluoromethyl)phenyl)but-3-en-1-ol:



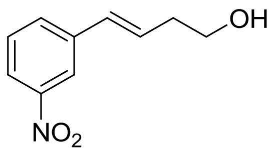
Colorless oil; 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, 2H, J = 8.4 Hz), 7.48 (d, 1H, J = 7.2 Hz), 7.33-7.36(m, 1H), 6.84-6.88(m, 1H), 6.17-6.24(m, 1H), 3.76-3.79 (m, 2H), 2.50-2.55 (m, 2H), 1.71 (br s, 1H) ppm; ^{113}C NMR (100 MHz, $CDCl_3$): δ = 136.5 (d, J = 2.0 Hz), 131.8, 131.0 (d, J = 1.0 Hz), 130.3, 128.7 (d, J = 1.0 Hz), 127.3, 127.0, 125.7 (dd, J = 6.0, 2.0 Hz), 123.0, 61.9, 36.5 ppm; HRMS Calcd for $C_{11}H_{11}F_3NaO$: $[M+Na]^+$, 239.0645. Found: m/z 239.0648.

1p, (*E*)-4-(4-(trifluoromethyl)phenyl)but-3-en-1-ol:



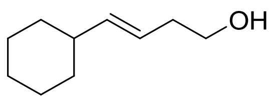
White solid; 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, 2H, J = 8.0 Hz), 7.39 (d, 2H, J = 8.0 Hz), 6.47 (d, 1H, J = 16.0 Hz), 6.30 (dt, 1H, J = 7.2, 1.5 Hz), 3.72-3.75 (m, 2H), 2.85 (s, br, 1H), 2.45-2.50 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.8, 131.1, 129.6, 128.9 (t, J = 160.0 Hz), 126.2, 125.5 (q, J = 4.0 Hz), 122.94, 60.9, 36.3 ppm; HRMS Calcd for $C_{11}H_{11}F_3NaO$: $[M+Na]^+$, 239.0649. Found: m/z 239.0645.

1q, (*E*)-4-(3-nitrophenyl)but-3-en-1-ol:



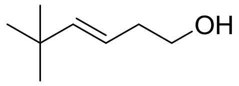
Yellow oil; 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (s, 1H), 8.05-8.07 (m, 1H), 7.63 (d, 1H, J = 7.2 Hz), 7.50(t, 1H, J = 8.0 Hz), 6.57 (d, 1H, J = 16.0 Hz), 5.85-5.91(m, 1H), 3.75-3.78 (m, 2H), 2.56-2.62 (m, 2H), 2.54 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 138.8, 134.8, 131.6, 129.2, 129.0, 123.3, 121.6, 61.9, 31.8 ppm; HRMS Calcd for $C_{10}H_{11}NNaO_3$: $[M+Na]^+$, 216.0628. Found: m/z 216.0615.

1r, (*E*)-4-cyclohexylbut-3-en-1-ol:



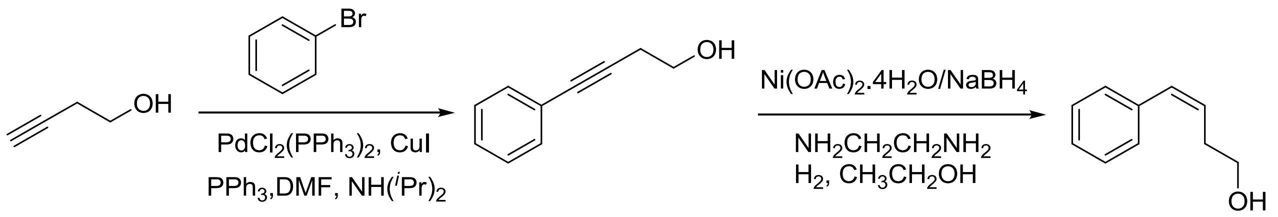
Colorless oil; 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.53-5.23 (m, 2H), 3.62 (t, 2H, J = 6.4 Hz), 2.31-2.22 (m, 2H), 1.72-1.62 (m, 7H), 1.30-1.04 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.4, 123.1, 62.0, 40.8, 36.0, 33.1, 31.0, 26.1 ppm; HRMS Calcd for $C_{10}H_{18}NaO$: $[M+Na]^+$, 177.1255. Found: m/z 177.1249.

1s , (*E*)-5,5-dimethylhex-3-en-1-ol:



Colorless oil; 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.46 (d, 1H, *J* = 12.0 Hz), 5.17-5.10 (m, 1H), 3.63 (t, 2H, *J* = 6.4 Hz), 2.49-2.43 (m, 2H), 1.79 (br, 1H), 1.10 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.9, 123.8, 62.8, 36.0, 33.3, 31.8, 31.2, 29.7 ppm; HRMS Calcd for $C_8H_{16}NaO$: $[M+Na]^+$, 151.1099. Found: m/z 151.1095.

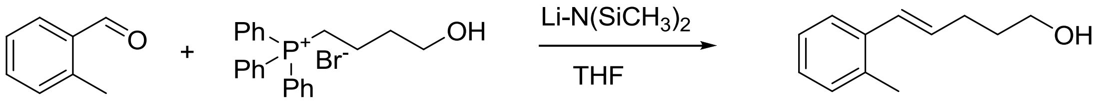
1t, (*Z*)-4-phenylbut-3-en-1-ol.[9,10]



To a solution of bromobenzene (0.5 mL, 4.75 mmol), bis(triphenylphosphine) palladium (II) chloride (0.167 g, 0.23 mmol), triphenylphosphine (0.09 g, 0.34 mmol), and copper(I) iodide (0.01 g, 0.052 mmol) were added to a dry round-bottomed flask, which was then sparged with argon and charged with diethylamine (1 mL) and DMF (10 mL). 3-Butyn-1-ol (0.3 mL, 4.75 mmol) was added via syringe. The stirred reaction mixture was heated at 80 °C for 6 h. After it was cooled to room temperature, the reaction mixture was diluted with diethyl ether (30 mL), and filtered. The filtrate was poured into water and the aqueous layer was extracted with diethyl ether (20 mL x 3). The combined organic layer was dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The product was isolated by chromatography on silica gel column (ethyl acetate / petroleum 1:3) to give an alkyne as a dark brown liquid (0.3 g, 43%).

To a solution of $Ni(OAc)_2{\bullet}H_2O$ (104 mg, 0.23 mmol) in EtOH (5 mL) under H_2 atmosphere (1 bar) was added a solution of $NaBH_4$ (16 mg, 1.67 mmol) in EtOH (1 mL) at room temperature. After being stirred for 1 h, a solution of alkyne (2.0 mmol) and ethylenediamine (80 mg, 1.46 mmol) in EtOH (2 mL) was added and the reaction was stirred overnight. Solvent was evaporated and the residue was purified by chromatography on silica gel column (ethyl acetate-petroleum 1:4) to give a colorless oil (0.2 g, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20-7.34 (m, 5H), 6.58 (d, 1H, *J* = 12.0 Hz), 5.66-5.73 (m, 1H), 3.75 (m, 2H), 2.60-2.67 (m, 2H), 1.55 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.2, 131.6, 128.8, 128.3, 128.2, 126.8, 62.5, 32.0 ppm.

1u, (*E*)-5-*o*-tolylpent-4-en-1-ol



Colorless oil; 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12-7.20 (m, 5H), 6.47 (d, 1H, *J* = 11.6 Hz), 5.67- 5.74 (m, 1H), 3.58 (t, 2H, *J* = 6.4 Hz), 2.19-2.24 (m, 5H), 1.60-1.68 (m, 1H), 1.50 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.6, 136.3, 131.8, 129.9, 129.0, 128.7, 126.9, 125.4, 62.4, 32.7, 24.7, 19.9 ppm; HRMS Calcd for $C_{12}H_{16}NaO$: $[M+Na]^+$, 200.1085. Found: m/z 200.1083.

2.2 General Procedure for the preparation of β-chlorotetrahydrofuran 2a-u

To a solution of but-3-en-1-ol **1** (0.2 mmol, 1.0 equiv), catalyst **5g** (10.7 mg, 0.02 mmol, 0.1 equiv), and 4-methylbenzenesulfonamide (17.1 mg, 0.1 mmol, 0.5 equiv) in THF (1 mL) at –20 °C under argon atmosphere was added *N*-chlorosuccinimide (54 mg, 0.4 mmol, 2 equiv). The resulting mixture was stirred at –20 °C for 12 hours. The reaction was quenched with water at –20 °C and then was warmed to room temperature. The solution was extracted with CH_2Cl_2 (3 × 5 mL). The combined extracts were washed with brine (5.0 mL), dried (Na_2SO_4), filtered and concentrated *in vacuum*. The residue was purified by flash column chromatography (EtOAc/Petroleum = 1/20; v/v) to yield the corresponding products **2**.

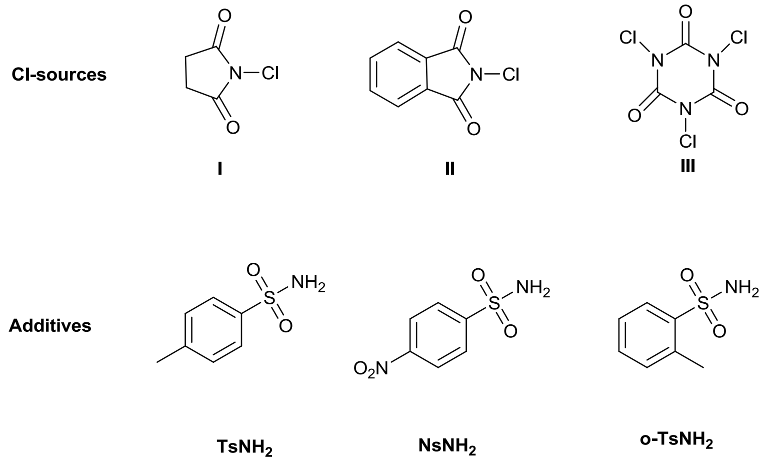
2.3 Optimization of solvent, Cl-sources and additives.

Table S1. Screening reaction conditions.[a]

Entry	Catalyst	Solvent and Additive	Cl-Sources	Yield (%)[b]	ee (%)[c]
1	**5a**	$CHCl_3$	I	75	78
2	**5a**	$(CH_3CH_2)_2O$	I	67	80
3	**5a**	CH_3CN	I	65	2
4	**5g**	$(^{i}Pr)_2O+TsNH_2$	I	<5	n.d
5	**5g**	$(CH_3CH_2)_2O+TsNH_2$	I	74	80
6	**5g**	$(^{n}Bu)_2O+TsNH_2$	I	<5	n.d
7	**5g**	$CH_3OC_6H_5+TsNH_2$	I	89	62
8	**5g**	$THF+NsNH_2$	I	82	35
9	**5g**	$THF+^{o}TsNH_2$	I	72	61
10	**5g**	$THF+TsNH_2$	II	80	82

11	**5g**	THF+$TsNH_2$	III	86	10
12[d]	-	THF+$TsNH_2$	I	87	-

[a] The reactions were carried out with **1a** (0.20 mmol), NCS (0.24 mmol), additive (0.10 mmol) and catalyst (0.02 mmol) in solvent (1.0 mL) under argon atmosphere at -20 ^{o}C for 12 h. *b* Isolated yield. [c] Determined by HPLC. [d] The reaction was carried out with **1h** (0.20 mmol), NCS (0.24 mmol), additive (0.10 mmol) in THF under argon atmosphere at rt for 12 h.



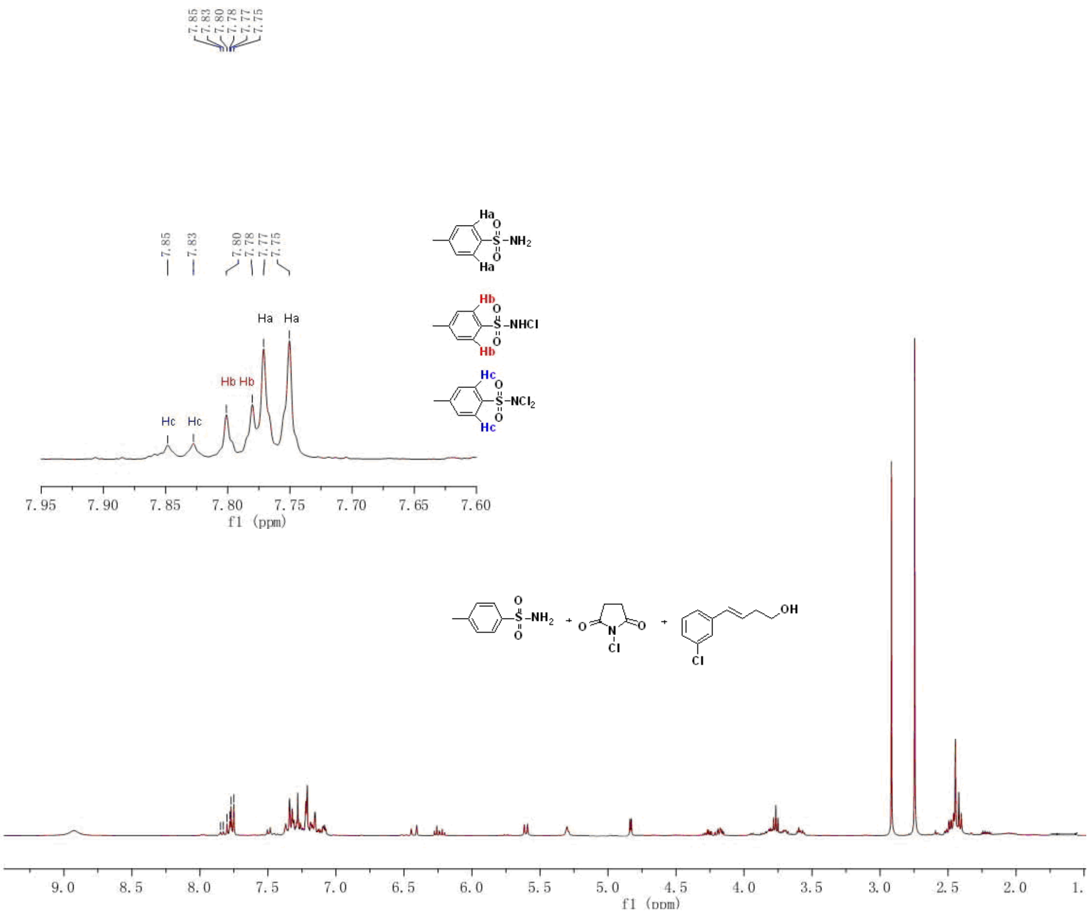


Fig. S1. The ^{1}H NMR spectrum of the reaction mixture of NCS, substrate **1j** and $TsNH_2$ in $CDCl_3$ at room temperature for 6 h.

2.4 Absolute stereochemical determination of β-chlorotetrahydrofurans

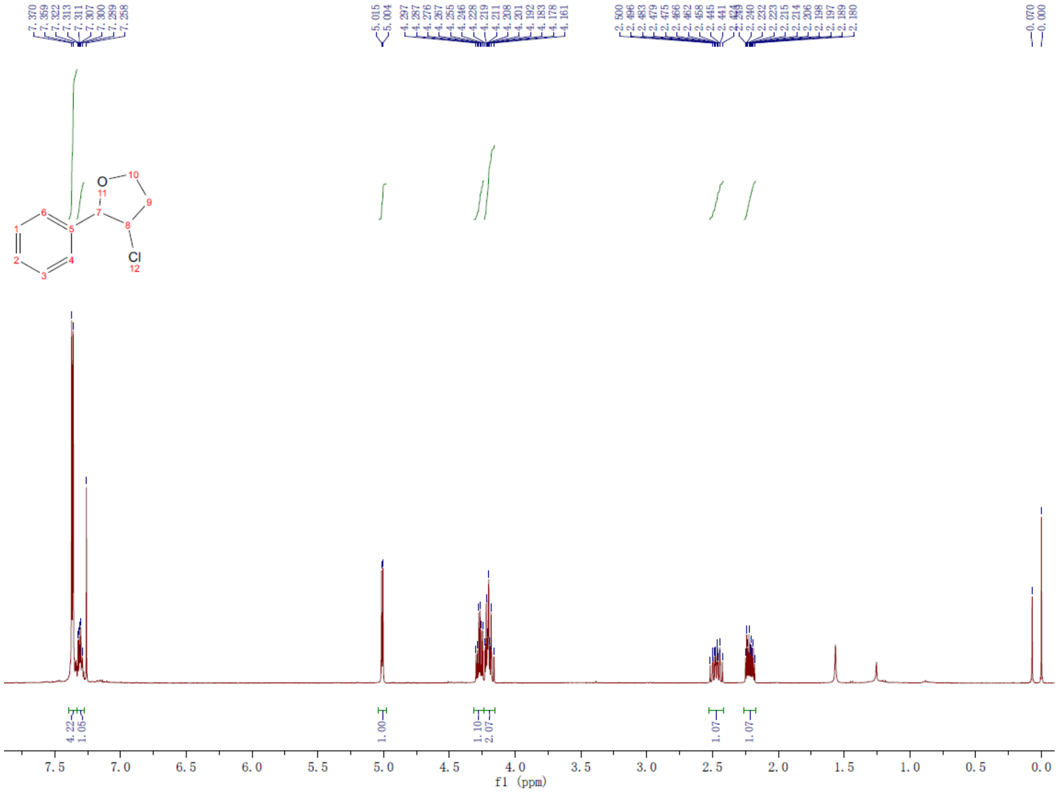
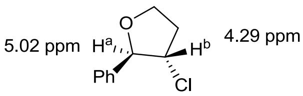


Fig. S2. The ^{1}H NMR spectrum of *trans*-**2h** (racemic), which was synthesized from *trans*-2,3-dichlorotetrahydrofuran and PhMgBr in Et_2O at room temperature according to reported method.[11] The data is well in accord with the NMR of product **2h**.



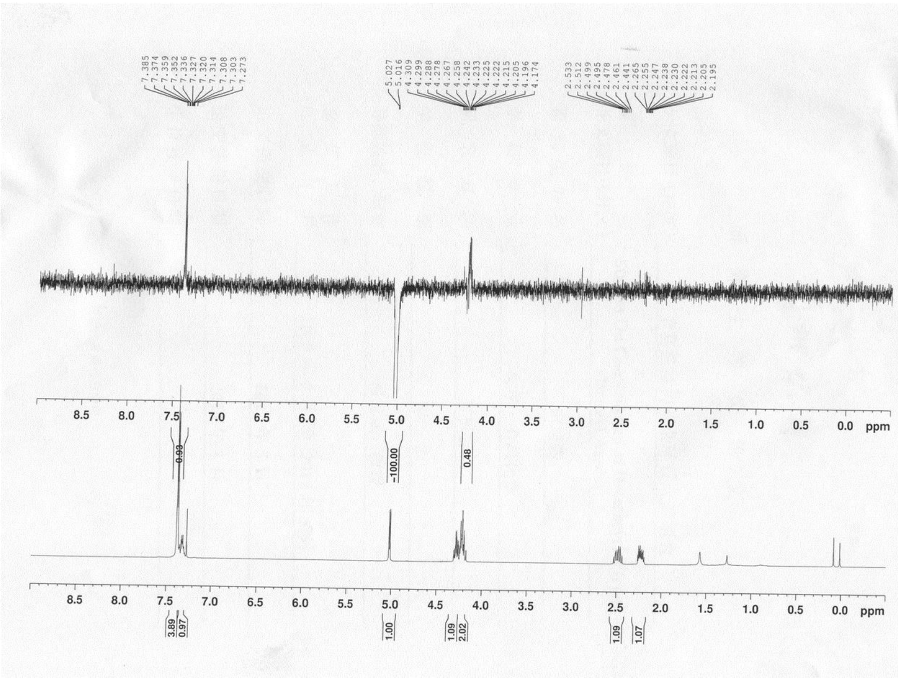
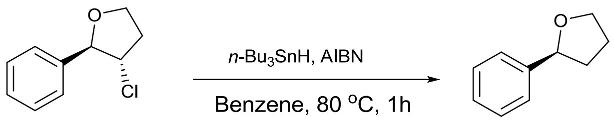
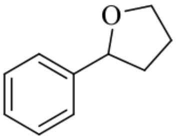


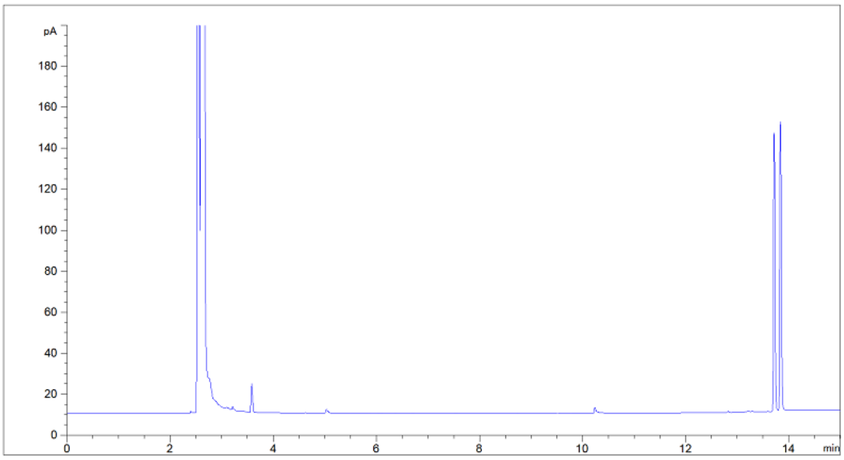
Fig. S3. NOE spectrum of the product **2h**. (There is no NOE between H[a] and H[b].)



2h **6**

Under an argon atmosphere, AIBN (4 mg, 0.02 mmol, 0.1 equiv) was added to a refluxing solution of **2h** (37 mg, 0.2 mmol, 1 equiv, 92% ee) and tributyltin hydride (0.24 mmol, 1.2 equiv) in anhydrous benzene (3 mL). The resulting mixture was refluxed for 1 h. The solvent was removed by rotory evaporator and the residue was purified by column chromatography to yield the corresponding product **6**. Optical rotation analysis and the chiral GC retention time revealed the isolated **6** to be *S* configuration as previous report ($[\alpha]^{D}_{20}$ = -2.3 (c = 0.3, $CHCl_3$)).[12] [Varian Capillary Column CP-Chirasil-Dex CB): carrier gas, N_2; injection temperature, 250 °C; detector temperature, 280 °C; column temperature, 50 °C, ramp 10 ^{o}C / min to 170 °C, then hold 15 min. t_R = 13.72 min (minor, *R*-isomer), 13.84 min (major, *S*-isomer)]. These data together with NOE data indicate that product **2h** should be 2*R*,3*S* configuration. The absolute stereochemistry of all other products was inferred by analogy.

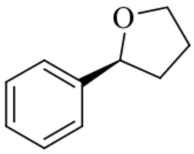


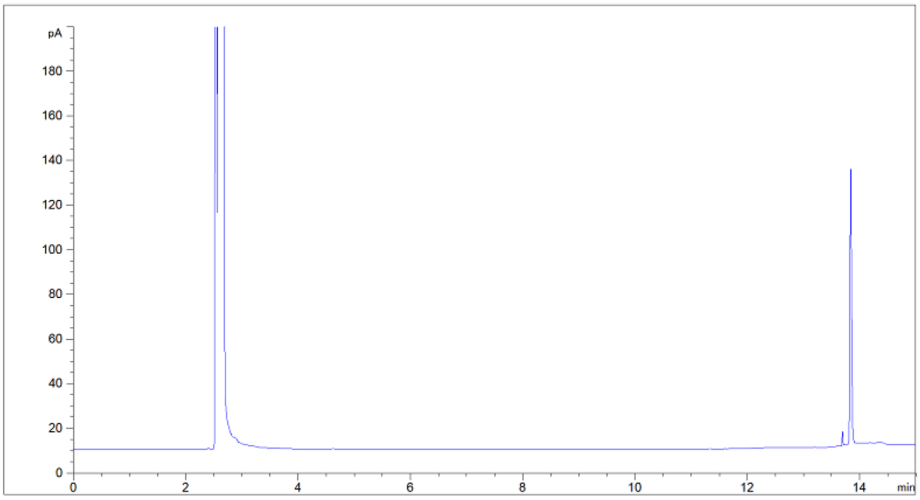


面积百分比报告

信号 1: FID1 A, 前部信号

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [pA*s]	峰高 [pA]	峰面积 %
1	13.712	BB	0.0305	261.71057	135.60086	48.54818
2	13.833	BB	0.0301	277.36334	140.38293	51.45182





面积百分比报告

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [pA*s]	峰高 [pA]	峰面积 %
1	13.715	MM T	8.75e-3	10.12156	9.28815	4.09816
2	13.836	BB	0.0295	236.85670	122.90540	95.90184

Fig. S4. GC analysis of **6,** Agilent 7890A GC, (Varian Capillary Column CP-Chirasil-Dex CB): carrier gas, N_2; injection temp, 250 °C; detector temperature, 280 °C; column temperature, 50 °C, ramp 10 ^{o}C/min to 170 °C, then hold 15 min.

2.5 Mechanism studies

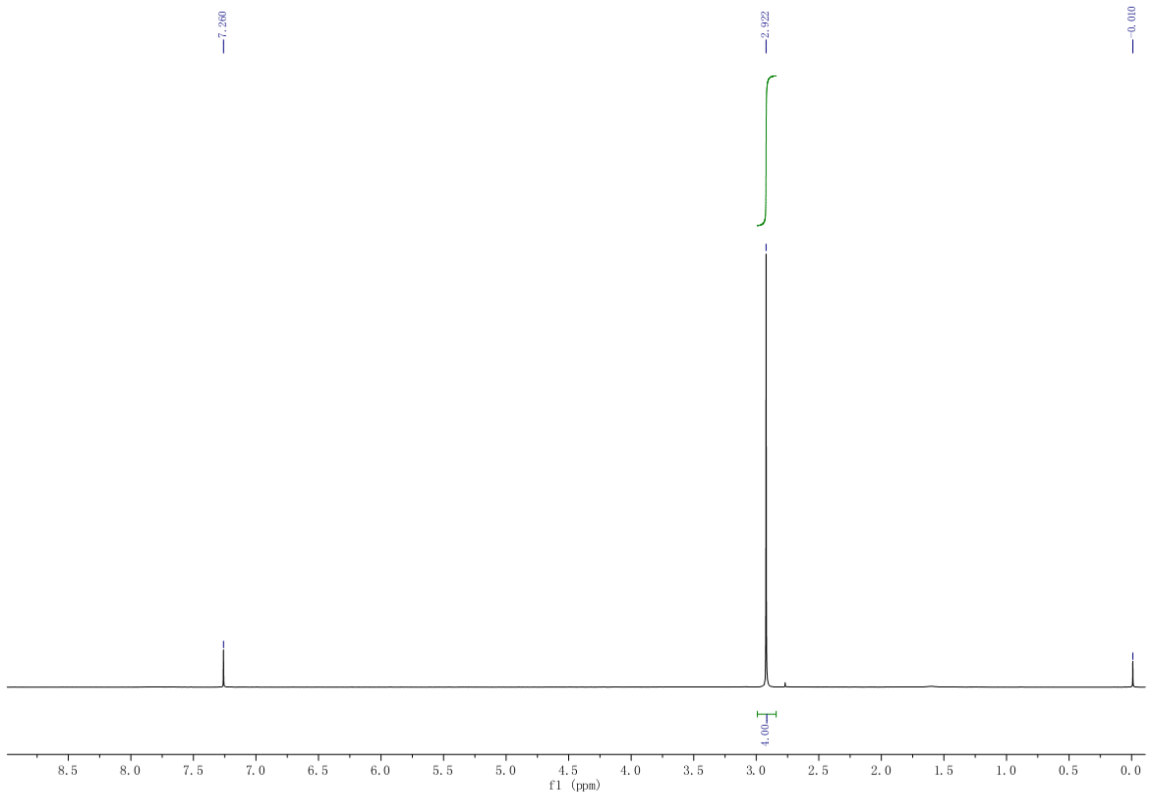


Fig. S5. ^{1}H NMR spectrum of NCS in $CDCl_3$.

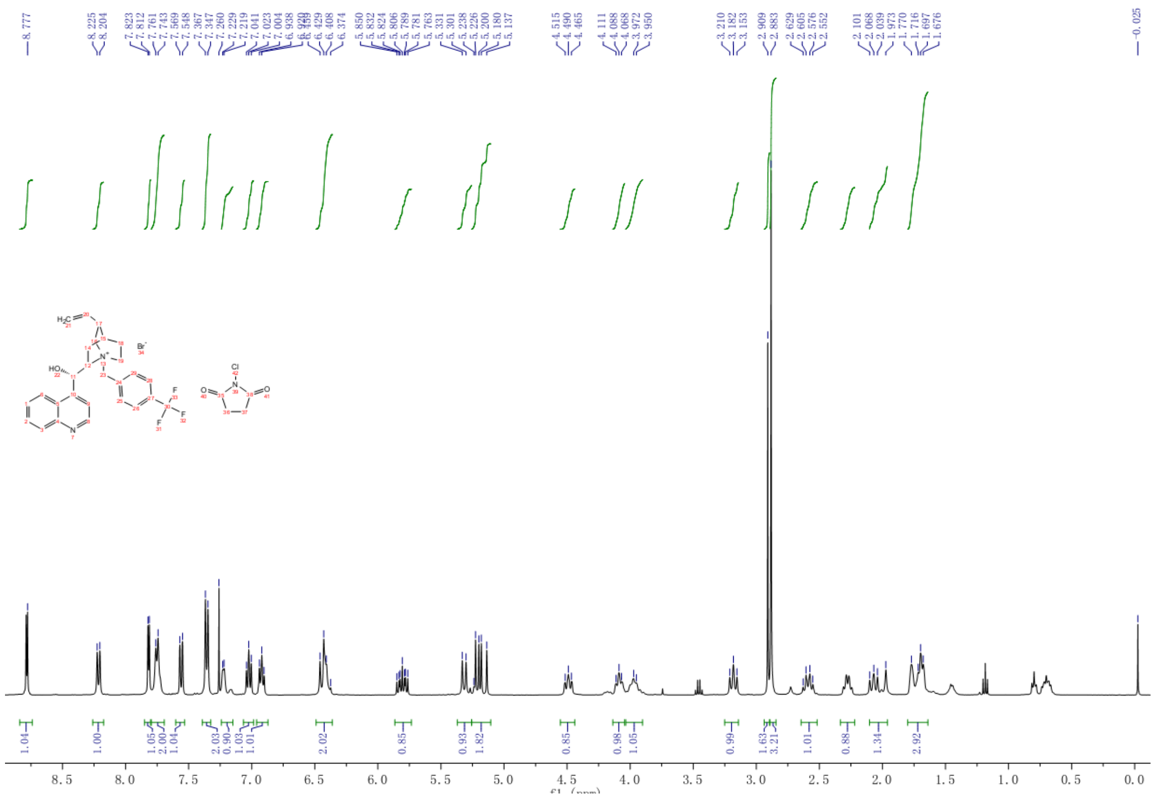


Fig. S6. ^{1}H NMR spectrum of NCS and **5g** (1:1) in $CDCl_3$.

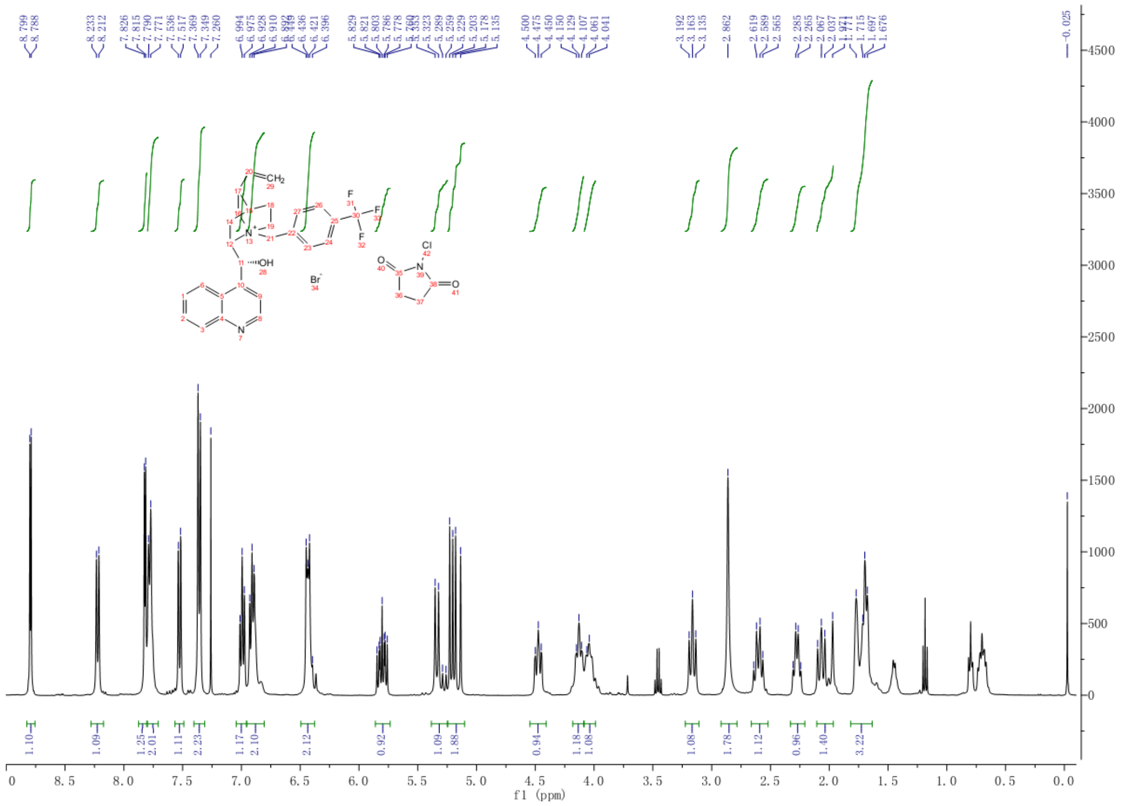
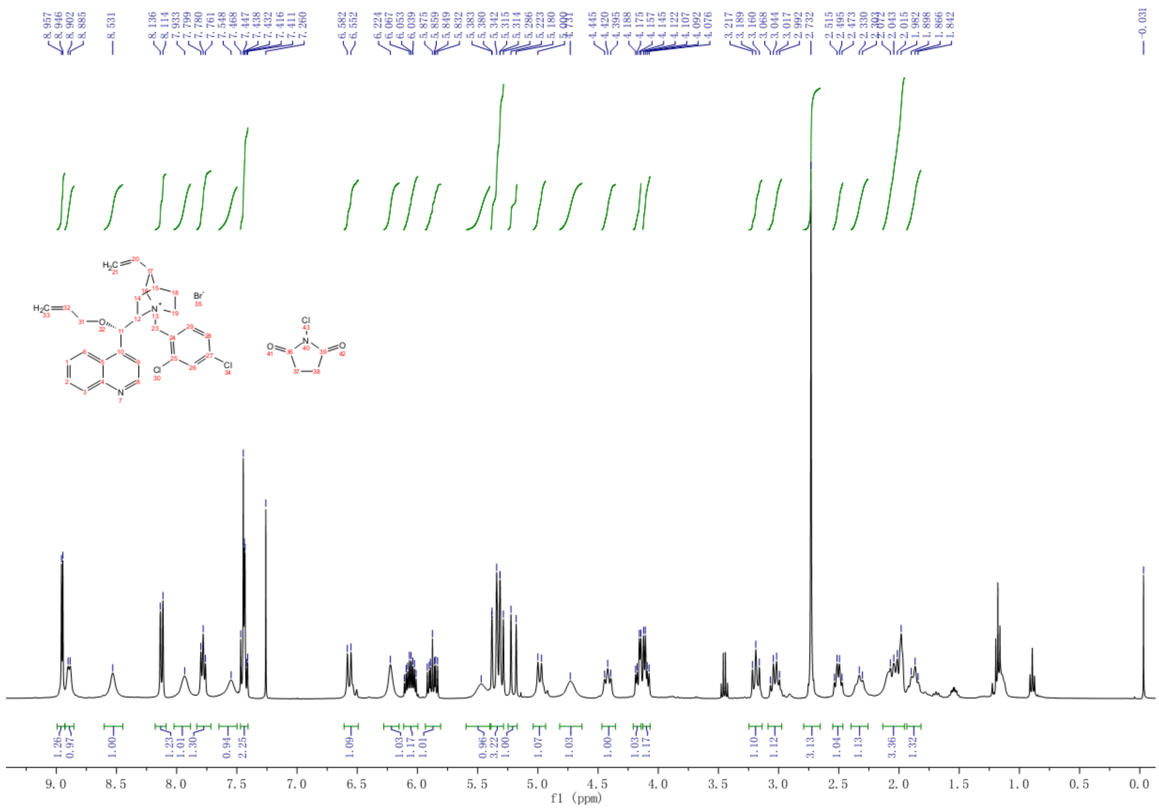
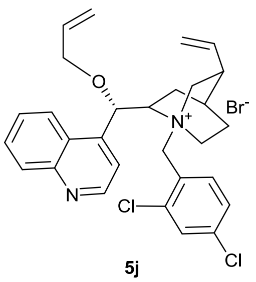


Fig. S7. ^{1}H NMR spectrum of NCS and **5g** (1:2) in $CDCl_3$.





5j

Fig. S8. [1]H NMR spectrum of NCS and **5j** (1:1) in $CDCl_3$ (The use of 5**j** as catalyst for the the 5-*endo* chloroetherification of **1a** under the optimized conditions, onlya 71% yield and 15% *ee* were observed).

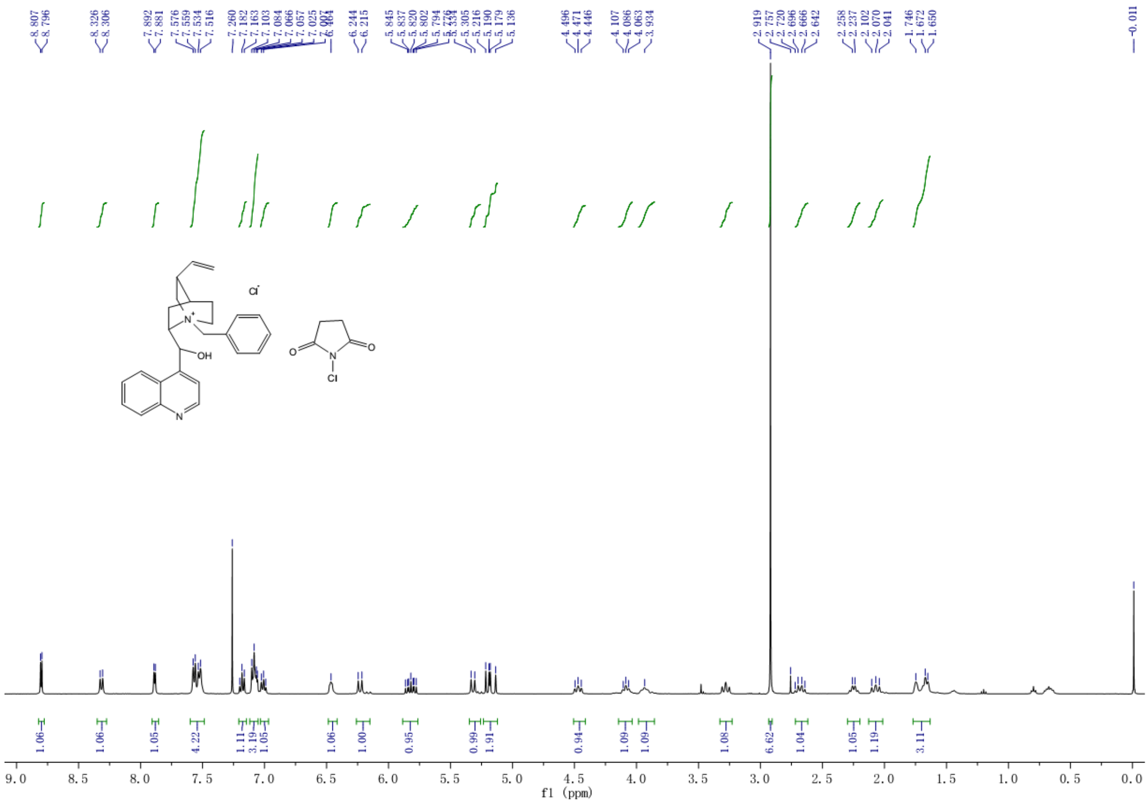


Fig. S9. [1]H NMR spectrum of NCS and **5b** in $CDCl_3$

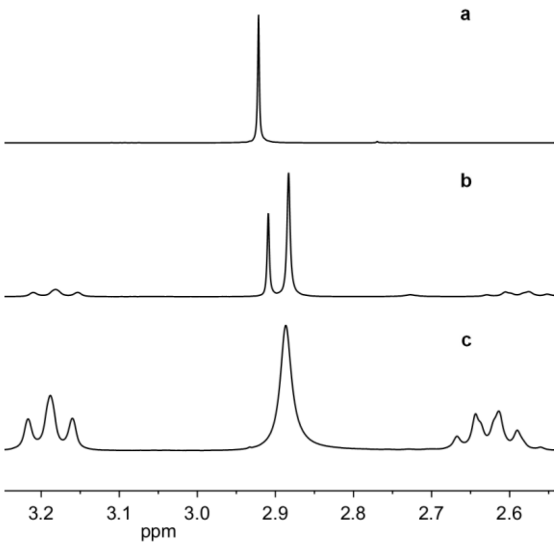


Fig. S10 ^{1}H NMR studies between NCS and catalyst 5g: (a) NCS; (b) 5g / NCS = 1; (c) 5g / NCS = 2.

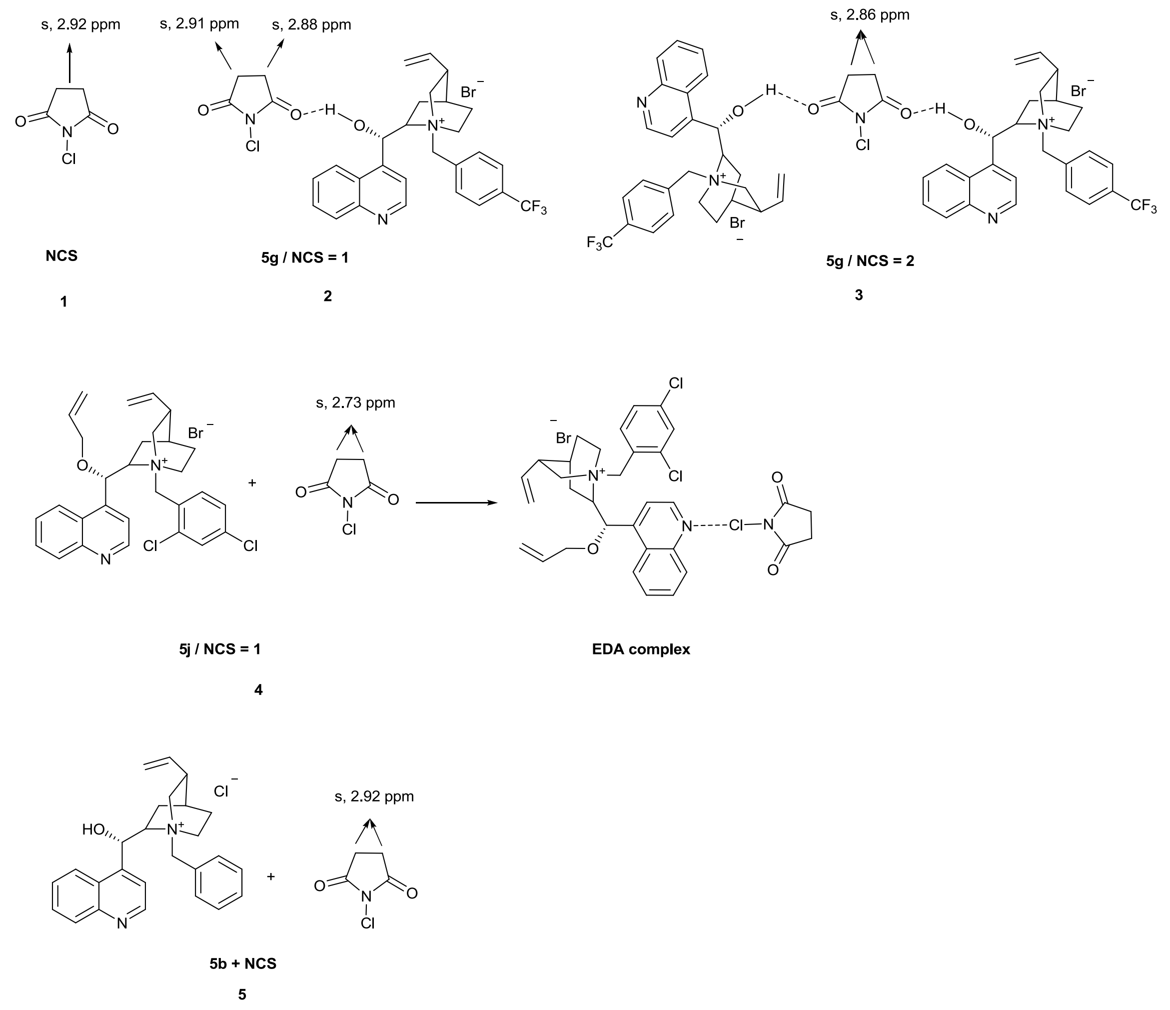


Fig. S11 Proposed interaction between chiral quaternary ammonium salts and NCS.

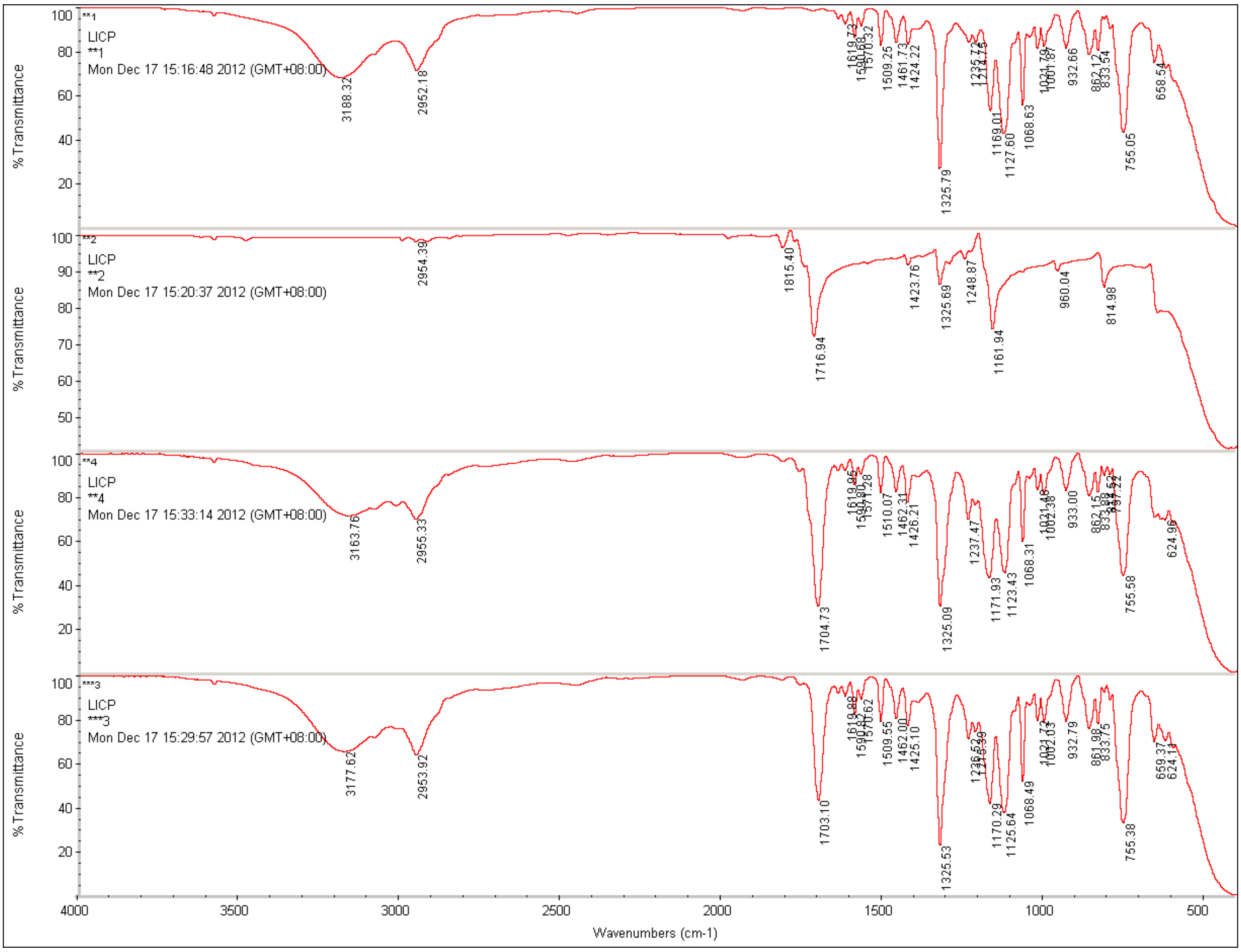


Fig. S12 (1) Catalyst 5g; (2) NCS; (3) 5g / NCS = 1; (c) 5g / NCS = 2.

In order to gain a better understanding of the reaction mechanism, we performed NMR studies while monitoring the reaction. Indeed, we were able to observe an association between NCS and the catalyst 5g in a stoichiometric ^{1}H NMR experiment (Fig. S10). Two peaks appear at 2.91 ppm and 2.88 ppm when the equal molar of 5g and NCS are added in $CDCl_3$ (Fig. S10b). It may indicate that the HB between one of the oxygen of the imide and OH of the catalyst is formed. We next examined the ^{1}H NMR spectra of 5g and NCS (with a molar ratio of 2:1) in $CDCl_3$ (Fig. S10c), only the resonance for the protons of NCS shifted upfield from δ 2.92 to 2.86 ppm. This observation shows the existence of HB between the OH of the catalyst and both O of NCS. With a cinchona quaternary ammonium salt 5j containing the *O*-allyl group in equal molar with NCS in $CDCl_3$, only the resonance for the protons of NCS significantly shifted upfield from δ 2.92 to 2.73 ppm. This result suggests that an electron-donor–acceptor (EDA) complex may be formed (Fig. S11, Scheme 4). Employing 5j as catalyst in the 5-*endo* chloroetherification of 1a, only 15% *ee* was observed. Based on these findings, we suggest the possible mechanism may involve a hydrogen bond mediated association between the catalyst and the chlorenium source (Fig. S12). On the other hand, the chiral ion pair of the quaternary ammonium salt may play a key role for the activation of homoallylic alcohol substrate.

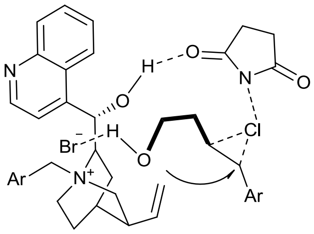
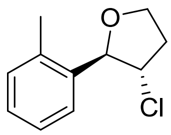


Fig. S12 Plausible reaction models for the 5-*endo* enantioselective chloroetherification.

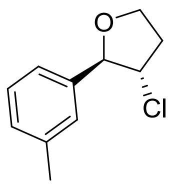
2.6 Analytical data for β-chlorotetrahydrofurans

2a, 3-chloro-2-o-tolyltetrahydrofuran



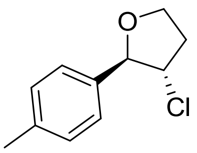
Colorless oil, 88% yield, 86% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.6 mL/min; detection wavelength = 254 nm; t_R = 10.98 (major), 11.79 (minor) min]. $[\alpha]_D^{20}$ = +30.5 (c = 0.27, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.34 (m, 1H), 7.16-7.21 (m, 3H), 5.30 (d, 1H, J = 4.0 Hz), 4.35-4.40 (m, 1H), 4.22-4.29 (m, 2H), 2.35-2.43 (m, 4H), 2.15-2.21 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 134.9, 130.5, 127.8, 126.1, 124.9, 86.5, 67.7, 63.2, 35.1, 19.5 ppm; HRMS Calcd for $C_{11}H_{13}ClNaO$: $[M+Na]^+$, 219.0547. Found: m/z 219.0537.

2b, 3-chloro-2-m-tolyltetrahydrofuran



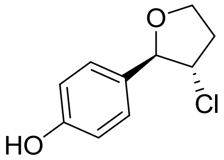
Colorless oil, 81% yield, 92% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.6 mL/min; detection wavelength = 254 nm; t_R = 11.26 (major), 11.92 (minor) min]. $[\alpha]_D^{20}$ = -5.2 (c = 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16-7.19 (m, 1H), 7.03-7.10 (m, 3H), 4.91 (d, 1H, J = 4.4 Hz), 4.17-4.22 (m, 1H), 4.08-4.16 (m, 2H), 2.35-2.45 (m, 1H), 2.29(s, 3H), 2.10-2.17(m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 137.2, 127.8, 127.4, 125.2, 121.6, 87.30, 66.3, 62.2, 34.6, 20.4 ppm; HRMS Calcd for $C_{11}H_{13}ClNaO$: $[M+Na]^+$, 219.0550. Found: m/z 219.0546.

2c, 3-chloro-2-p-tolyltetrahydrofuran



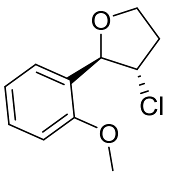
Colorless oil, 78% yield, 90% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 13.43 (minor), 15.21 (major) min]. $[\alpha]_D^{20}$ = +15.7 (c = 0.34, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (d, 2H, *J* = 8.0 Hz), 7.09 (d, 2H, *J* = 4.0 Hz), 4.89 (d, 1H, *J* = 4.4 Hz), 4.15-4.21 (m, 1H), 4.07-4.13 (m, 2H), 2.35-2.4 (m, 1H), 2.27 (s, 1H), 2.10-2.17 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.7, 135.9, 128.2, 124.5, 87.2, 66.2, 62.2, 34.6, 20.1 ppm; HRMS Calcd for $C_{11}H_{13}ClNaO$: $[M+Na]^+$, 219.0550. Found: m/z 219.0545.

2d, 3-chlorotetrahydrofuran-2-yl)phenol



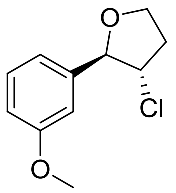
Colorless oil, 80% yield, 63% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 9.93 (minor), 15.77 (major) min]. $[\alpha]_D^{20}$ = -6.2 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.23 (m, 2H), 7.19 (s, 2H), 5.78 (s, 1H), 4.77 (d, 1H, *J* = 4.4 Hz), 4.15-4.20 (m, 1H), 4.06-4.12 (m, 1H), 4.01-4.05 (m, 1H), 2.35-2.44 (m, 1H), 2.12-2.19 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.5, 133.4, 130.9, 128.9, 125.5, 121.2, 86.7, 67.3, 62.6, 35.6 ppm; HRMS Calcd for $C_{10}H_{11}ClNaO_2$: $[M+Na]^+$, 221.0324. Found: m/z 221.0319.

2e, 3-chloro-2-(2-methoxyphenyl)tetrahydrofuran



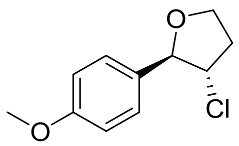
Colorless oil, 87% yield, 77% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 14.98 (major), 16.82 (minor) min]. $[\alpha]_D^{20}$ = -20.2 (c = 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.25-7.32 (m, 2H), 6.93-6.97 (m, 1H), 6.87 (d, 1H, *J* = 8.0 Hz), 5.38 (s, 1H), 4.42-4.44 (m, 1H), 4.25-4.36 (m, 2H), 3.87 (s, 1H), 2.23-2.33 (m, 1H), 2.10-2.16(m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 129.1, 128.9, 126.2, 120.5, 110.2, 84.9, 67.5, 63.2, 55.4, 34.7 ppm; HRMS Calcd for $C_{11}H_{13}ClNaO_2$: $[M+Na]^+$, 235.0589. Found: m/z 235.0585.

2f, 3-chloro-2-(3-methoxyphenyl)tetrahydrofuran



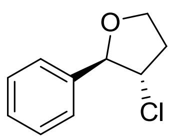
Colorless oil, 90% yield, 75% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 24.76 (major), 25.66 (minor) min]. $[\alpha]_D^{20}$ = -10.7 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.19-7.23 (m, 1H), 6.85-6.89 (m, 2H), 6.76 (dd, 1H, J = 8.0 Hz), 4.93 (d, 1H, J = 4.0 Hz), 4.11-4.22 (m, 3H), 3.75 (s, 1H), 2.34-2.44 (m, 1H), 2.11-2.16 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 141.7, 129.6, 117.8, 113.4, 111.1, 88.1, 67.3, 63.2, 55.3, 35.6 ppm; HRMS Calcd for $C_{11}H_{13}ClNaO_2$: $[M+Na]^+$, 235.0591. Found: m/z 235.0587.

2g, 3-chloro-2-(4-methoxyphenyl)tetrahydrofuran



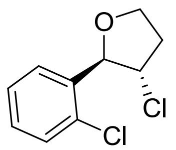
Colorless oil, 90% yield, 61% ee [Daicel CHIRALPAK OD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 16.31 (minor), 17.07 (major) min]. $[\alpha]_D^{20}$ = -16.2 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, 2H, J = 8.4 Hz), 6.88 (dd, 2H, J = 4.8, 2.0 Hz), 4.92 (d, 1H, J = 4.4 Hz), 4.17-4.19 (m, 1H), 4.14-4.16 (m, 3H), 3.80 (s, 3H), 2.43-2.52 (m, 1H), 2.11-2.16 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 130.8, 125.8, 112.9, 86.9, 66.1, 62.1, 54.3, 34.6 ppm; HRMS Calcd for $C_{11}H_{13}ClNaO_2$: $[M+Na]^+$, 235.0591. Found: m/z 235.0589.

2h, 3-chloro-2-phenyltetrahydrofuran



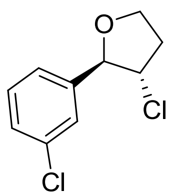
Colorless oil, 85% yield, 95% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.7 mL/min; detection wavelength = 254 nm; t_R = 9.62 (minor), 10.27 (major) min]. $[\alpha]_D^{20}$ = -25.1 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36-7.37 (m, 4H), 7.29-7.32 (m, 1H), 5.01 (d, 1H, J = 4.4 Hz), 4.24-4.31 (m, 1H), 4.13-4.26 (m, 2H), 2.43-2.52 (m, 1H), 2.18-2.25 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.0, 128.5, 128.0, 125.6, 88.3, 67.3, 63.2, 35.6 ppm; HRMS Calcd for $C_{10}H_{11}ClNaO$: $[M+Na]^+$, 205.0391. Found: m/z 205.0388.

2i, 3-chloro-2-(2-chlorophenyl)tetrahydrofuran



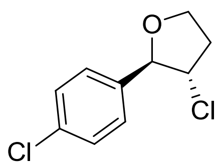
Colorless oil, 85% yield, 96% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 13.72 (major), 15.31 (minor) min]. $[\alpha]_D^{20}$ = -15.0 (c = 0.33, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28-7.35 (m, 2H), 7.16-7.21 (m, 2H), 5.39 (s, 1H), 4.31-4.37 (m, 2H), 4.22-4.28 (m, 1H), 2.16-2.26 (m, 1H), 2.07-2.13 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 131.0, 128.6, 128.1, 125.9, 125.9, 85.4, 67.1, 62.0, 33.4 ppm; HRMS Calcd for $C_{10}H_{10}Cl_2NaO$: $[M]^+$, 239.0007. Found: m/z 239.0004.

2j, 3-chloro-2-(3-chlorophenyl)tetrahydrofuran



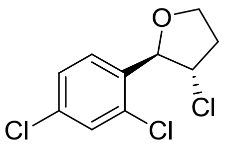
Colorless oil, 78% yield, 95% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 12.50 (minor), 14.19 (major) min]. $[\alpha]_D^{20}$ = +10.6 (c = 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (s, 1H), 7.26-7.28 (m, 3H), 4.96 (d, 1H, J = 4.4 Hz), 4.24-4.29 (m, 1H), 4.15-4.22 (m, 2H), 2.41-2.51 (m, 1H), 2.20-2.25 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 134.6, 129.8, 128.2, 125.7, 123.8, 87.5, 67.4, 62.9, 35.6 ppm; HRMS Calcd for $C_{10}H_{10}Cl_2NaO$: $[M+Na]^+$, 238.9998. Found: m/z 238.9995.

2k, 3-chloro-2-(4-chlorophenyl)tetrahydrofuran



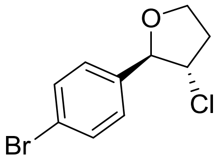
Colorless oil, 80% yield, 96% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.6 mL/min; detection wavelength = 254 nm; t_R = 13.84 (major), 15.18 (minorr) min]. $[\alpha]_D^{20}$ = -4.8 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.35 (m, 4H), 4.94 (d, 1H, J = 4.4 Hz), 4.18-4.27 (m, 1H), 4.11-4.17 (m, 2H), 2.42-2.51(m, 1H), 2.19-2.26 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 133.9, 128.7, 127.0, 87.5, 67.3, 62.8, 35.6 ppm; HRMS Calcd for $C_{10}H_{10}Cl_2NaO$: $[M+Na]^+$, 238.9998. Found: m/z 238.9996

2l, 3-chloro-2-(2,4-dichlorophenyl)tetrahydrofuran



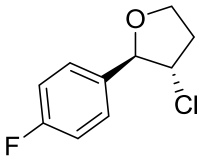
Colorless oil, 87% yield, 52% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.6 mL/min; detection wavelength = 254 nm; t_R = 17.08(major), 18.25 (minor) min]. $[\alpha]_D^{20}$ = -15.1 (c = 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26-7.31 (m, 1H), 7.17-7.19 (m, 1H), 5.32 (s, 1H), 4.29-4.34 (m, 2H), 4.26-4.26 (m, 1H), 2.08-2.19 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 137.2, 134.3, 132.7, 129.4, 127.9, 127.2, 86.0, 68.1, 62.7, 34.5 ppm; HRMS Calcd for $C_{10}H_9Cl_3NaO$: $[M+Na]^+$, 272.9609. Found: m/z 272.9605.

2m, 3-chloro-2-(4-bromophenyl)tetrahydrofuran



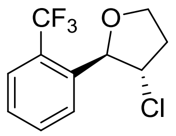
Colorless oil, 82% yield, 75% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 14.79 (major), 16.68 (minor) min]. $[\alpha]_D^{20}$ = +7.5 (c = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.50 (m, 2H), 7.25-7.27 (m, 2H), 4.92 (d, 1H, J = 4.4 Hz), 4.18-4.27 (m, 1H), 4.10-4.17 (m, 2H), 2.41-2.50 (m, 1H), 2.18-2.25 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 131.7, 127.3, 122.0, 87.5, 67.3, 62.8, 35.6 ppm; HRMS Calcd for $C_{10}H_{10}BrClNaO$: $[M+Na]^+$, 239.9489. Found: m/z 282.9481.

2n, 3-chloro-2-(4-fluorophenyl)tetrahydrofuran



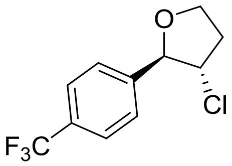
Colorless oil, 83% yield, 71% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 98/2; flow rate = 0.5 mL/min; detection wavelength = 254 nm; t_R = 13.01 (major), 16.86(minor) min]. $[\alpha]_D^{20}$ = -2.2 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.35 (m, 2H), 7.03-7.07 (m, 2H), 4.94 (d, 1H, J = 8.0 Hz), 4.20-4.38 (m, 1H), 4.22-4.29 (m, 2H), 4.11-4.18 (m, 2H), 2.43-2.53 (m, 1H), 2.19-2.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 135.5 (d, J = 4.0 Hz), 127.4 (d, J = 8.0 Hz), 115.5 (d, J = 22.0 Hz), 87.6, 67.2, 62.9, 35.6 ppm; HRMS Calcd for $C_{10}H_{10}ClFNaO$: $[M+Na]^+$, 223.0298. Found: m/z 223.0295.

2o, 3-chloro-2-(2-(trifluoromethyl)phenyl)tetrahydrofuran



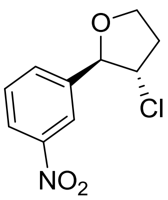
Colorless oil, 75% yield, 76% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.6 mL/min; detection wavelength = 254 nm; t_R = 13.06(minor), 13.78 (major) min]. $[\alpha]_D^{20}$ = -20.5 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, 1H, J = 8.0 Hz), 7.46-7.54 (m, 1H), 7.40 (d, 1H, J = 8.0 Hz), 7.31-7.36 (m, 1H), 5.48 (s, 1H), 4.34-4.38 (m, 1H), 4.21-4.27 (m, 2H), 2.29-2.38 (m, 1H), 2.10-2.16 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.5, 132.2, 131.6, 130.0, 128.2, 127.1, 126.2 (d, J = 5.0 Hz), 85.3 (d, J = 2.0 Hz), 68.2, 63.7, 34.7 ppm; HRMS Calcd for $C_{11}H_{10}F_3ClNaO$: $[M+Na]^+$, 273.0261. Found: m/z 273.0257.

2p, 3-chloro-2-(4-(trifluoromethyl)phenyl)tetrahydrofuran



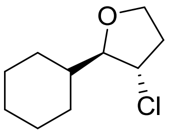
Colorless oil, 85% yield, 94% ee [Daicel CHIRALCEL OD-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 8.34 (minor), 9.39 (major) min]. $[\alpha]_D^{20}$ = -35.3 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, 2H, J = 8.0 Hz), 7.51 (d, 2H, J = 8.0 Hz), 5.02 (d, 1H, J = 4.8 Hz), 4.25-4.32 (m, 1H), 4.13-4.24 (m, 2H), 2.28-2.52 (m, 1H), 2.21-2.27 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 128.9, 125.9, 125.5 (d, J = 3 Hz), 87.5, 67.4, 62.7, 35.7 ppm; HRMS Calcd for $C_{11}H_{10}F_3ClNaO$: $[M+Na]^+$, 273.0258. Found: m/z 273.0254.

2q, 3-chloro-2-(3-nitrophenyl)tetrahydrofuran



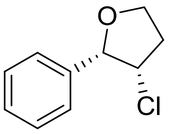
Colorless oil, 92% yield, 96% ee [Daicel CHIRALCEL OB-H (0.46 cm x 25 cm); hexane/2-propanol = 90/10; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 25.37 (major), 27.87 (minor) min]. $[\alpha]_D^{20}$ = -32.8 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.28 (s, 1H), 7.17-7.19 (m, 1H), 7.72-7.75 (m, 1H), 7.33-7.37 (m, 1H), 5.03 (d, 1H, J = 4.8 Hz), 4.29-4.33 (m, 1H), 4.14-4.29 (m, 2H), 2.44-2.56 (m, 1H), 2.24-2.32 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 142.1, 131.8, 129.6, 123.1, 120.6, 87.0, 67.5, 62.4, 35.7 ppm; HRMS Calcd for $C_{10}H_{10}ClNNaO_3$: $[M+Na]^+$, 250.0535. Found: m/z 250.0532.

2r, 3-chloro-2-cyclohexyltetrahydrofuran



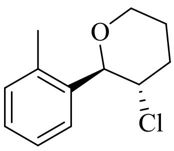
Colorless oil, 56% yield, 11% ee[(Varian Capillary Column CP-Chirasil-Dex CB): carrier gas, N_2; injection temperature, 250 °C; detector temperature, 280 °C; column temperature, 80 °C, ramp 10 °C / min to 170 °C, then hold 30 min. t_1 = 25.66 min, t_2 = 25.82 min,]. $[\alpha]_D^{20}$ = -5.3 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.12-4.16 (m, 1H), 3.87-3.99 (m, 2H), 3.69-3.72 (m, 1H), 2.28-2.34 (m, 1H), 2.10-2.15 (m, 1H), 1.68-1.79 (m, 7H), 1.17-1.25 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 91.7, 66.4, 58.7, 41.3, 37.1, 29.3, 28.6, 26.4, 26.0, 25.9 ppm; HRMS Calcd for $C_{10}H_{17}ClNaO$: $[M+Na]^+$, 211.0866. Found: m/z 211.0865.

2t, 3-chloro-2-phenyltetrahydrofuran



Colorless oil, 80% yield, 84% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 10.86 (major), 12.11 (minor) min]. $[\alpha]_D^{20}$ = +15.8 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36-7.37 (m, 4H), 7.29-7.34 (m, 1H), 5.02 (d, 1H, J = 4.4 Hz), 4.25-4.32 (m, 1H), 4.16-4.22 (m, 2H), 2.42-2.52 (m, 1H), 2.18-2.25 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 128.5, 128.0, 125.6, 88.3, 67.3, 63.2, 35.6 ppm; HRMS Calcd for $C_{10}H_{11}ClNaO$: $[M+Na]^+$, 205.0391. Found: m/z 205.0389.

2u, 3-chloro-2-o-tolyltetrahydro-2H-pyran



Colorless oil, 70% yield, 13% ee [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); hexane/2-propanol = 99/1; flow rate = 0.8 mL/min; detection wavelength = 254 nm; t_R = 13.21(minor), 14.96 (major) min]. $[\alpha]_D^{20}$ -11.5 (c = 0.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ= 7.10-7.32 (m, 4H), 4.81 (s, 1H), 4.01-4.45 (m, 1H), 3.97-4.00 (m, 1H), 3.51-3.56 (m, 1H), 2.33-2.45 (m, 5H), 2.17-2.28 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 135.6, 128.9, 128.7, 125.4, 125.2, 79.9, 67.6, 58.5, 34.3, 26.2, 20.5, 18.7 ppm; HRMS Calcd for $C_{12}H_{15}ClNaO$: $[M+Na]^+$, 234.0698. Found: m/z 234,0695.

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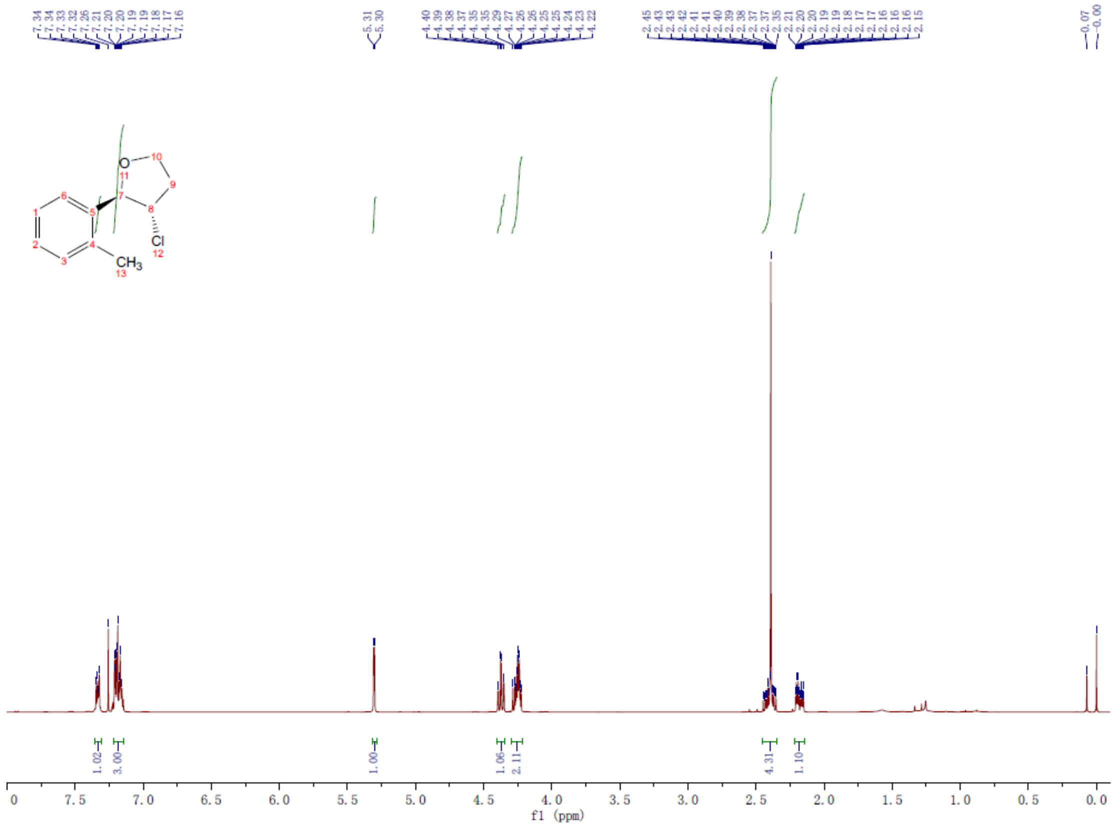
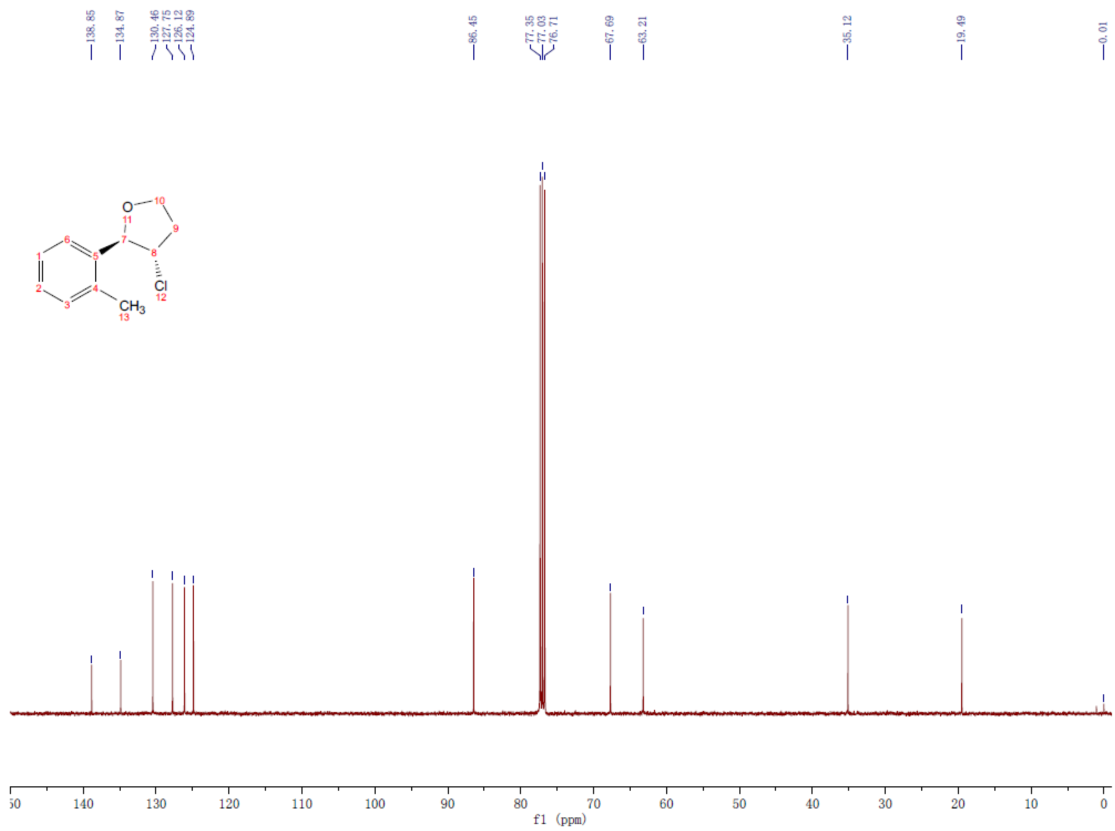
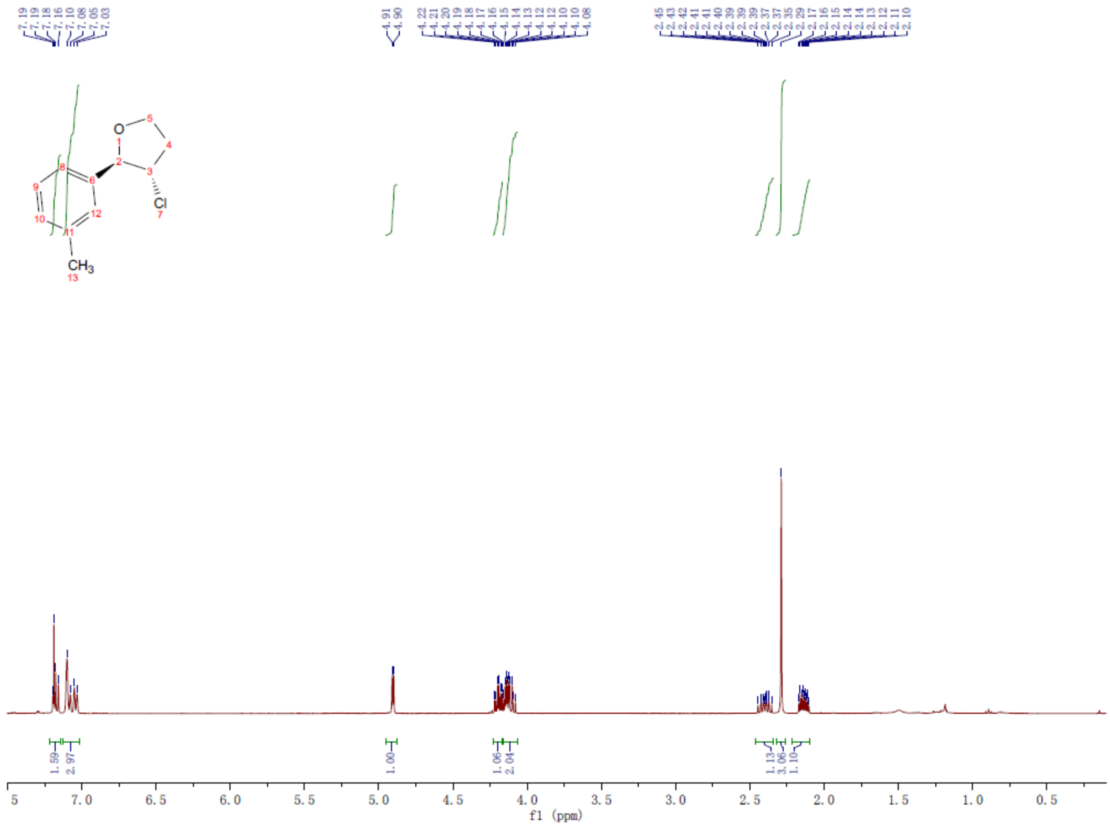
3. NMR Spectra of the products

2a





2b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7.19
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4.19
4.18
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4.16
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4.14
4.13
4.12
4.12
4.10
4.10
4.08
2.45
2.43
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2.35
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2.14
2.14
2.13
2.12
2.11
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1.13
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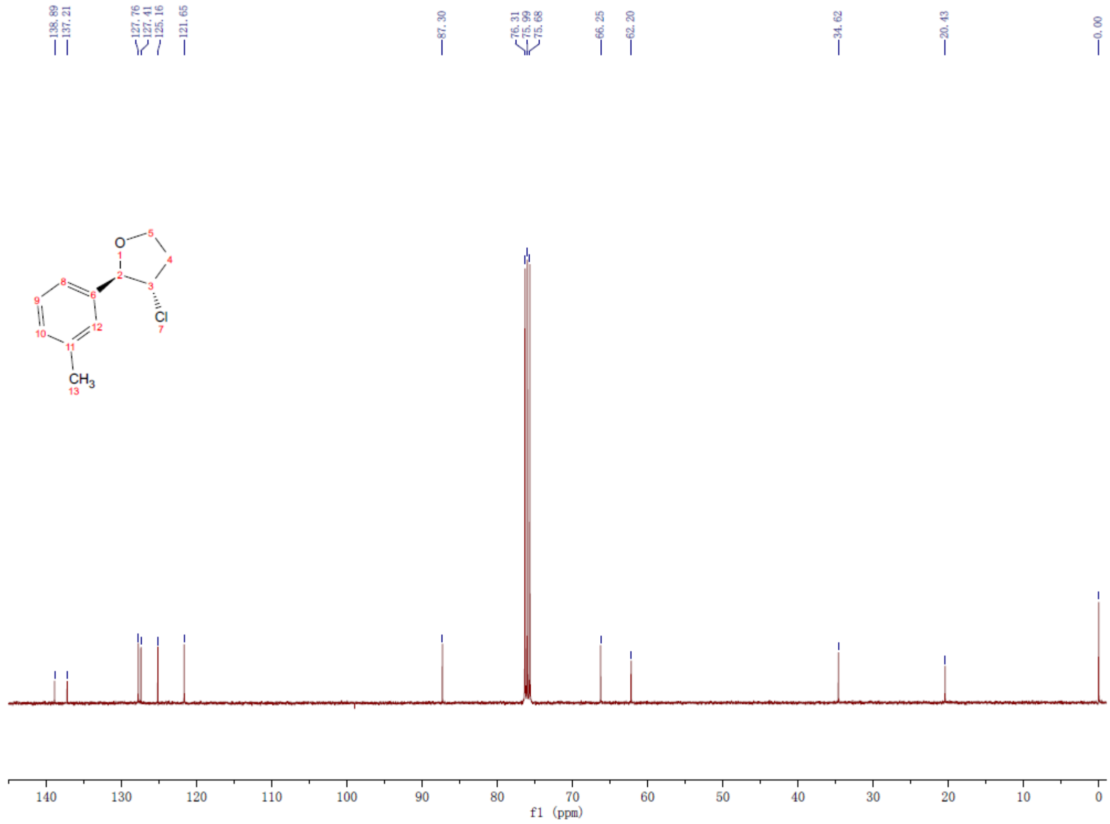
1.10
f1 (ppm)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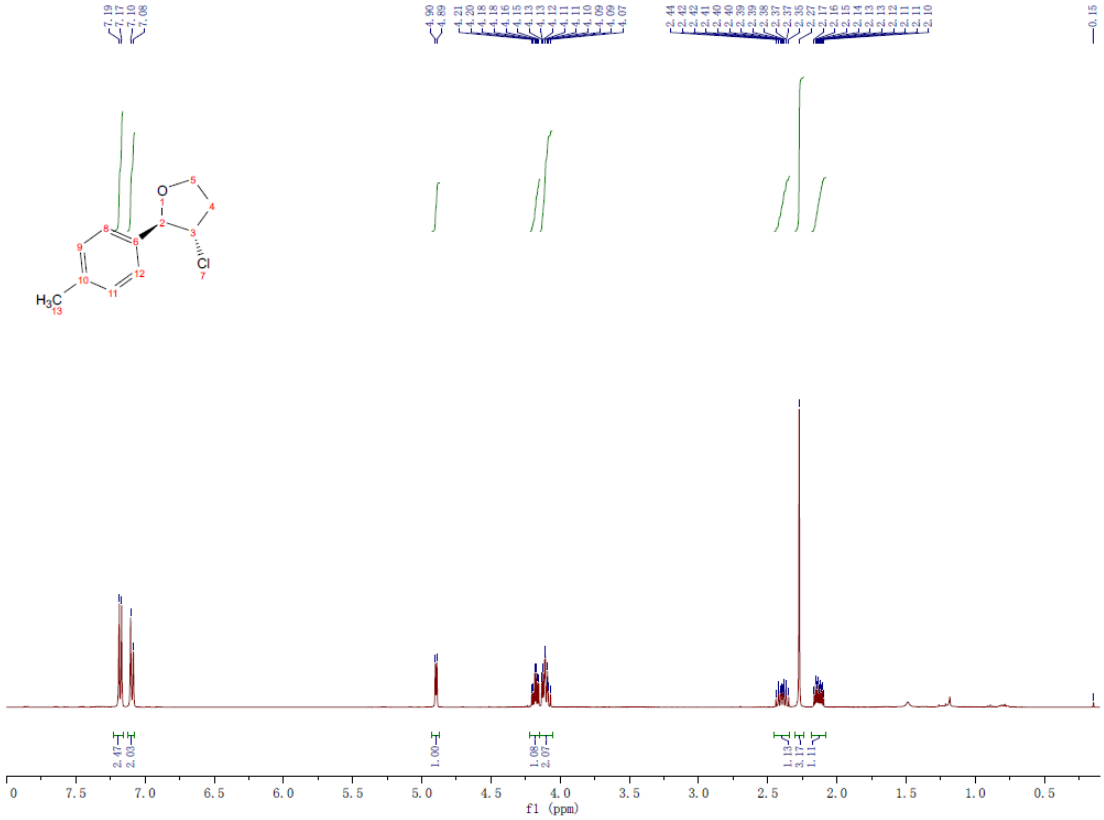
20.43
0.00
O
Cl
CH3
f1 (ppm)

2c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7.17
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7.08
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4.89
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4.20
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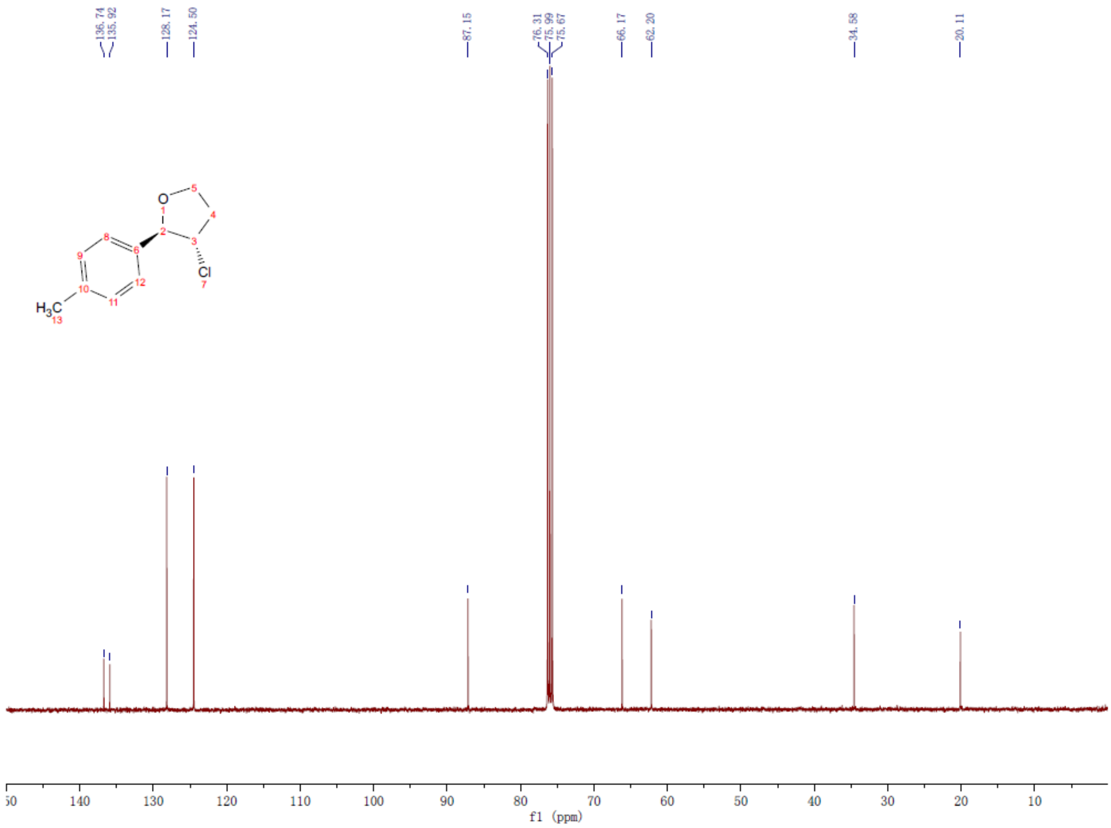
4.15
4.13
4.13
4.12
4.11
4.11
4.10
4.09
4.09
4.07
2.44
2.42
2.42
2.41
2.40
2.39
2.39
2.38
2.37
2.37
2.35
2.27
2.17
2.16
2.15
2.14
2.13
2.13
2.12
2.11
2.11
2.10
0.15
2.47
2.03
1.00
1.08
2.07
1.13
3.17
1.11
f1 (ppm)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135.92
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124.50
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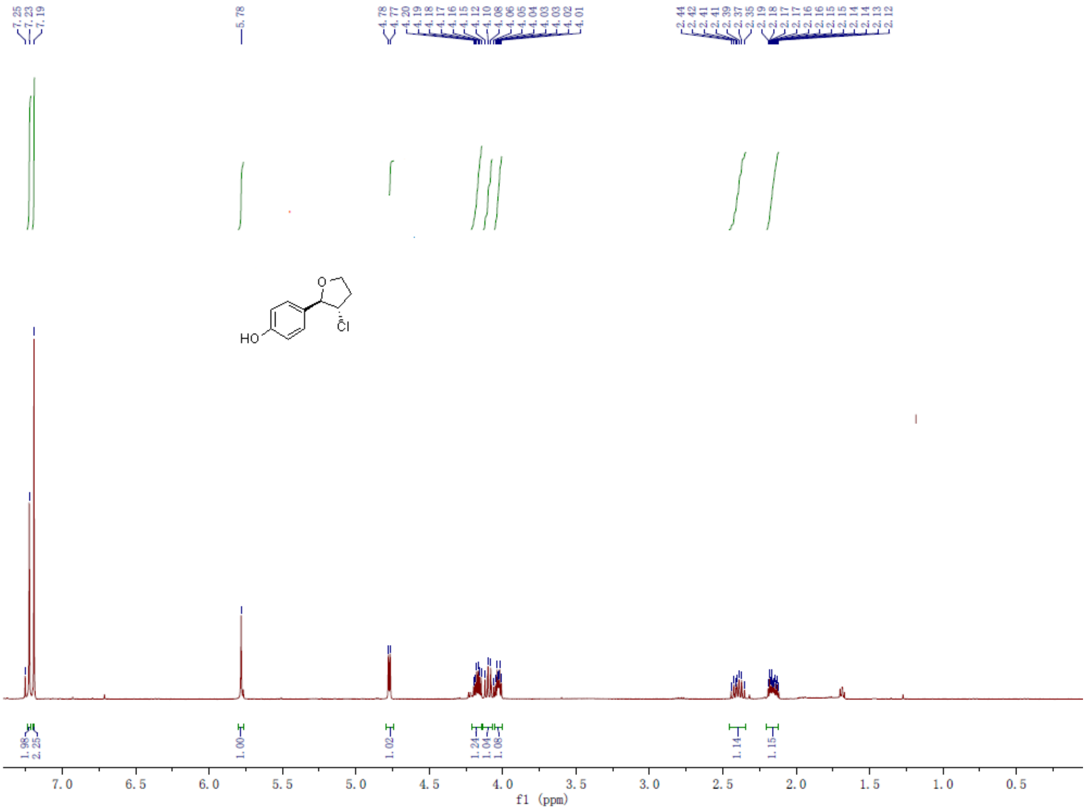
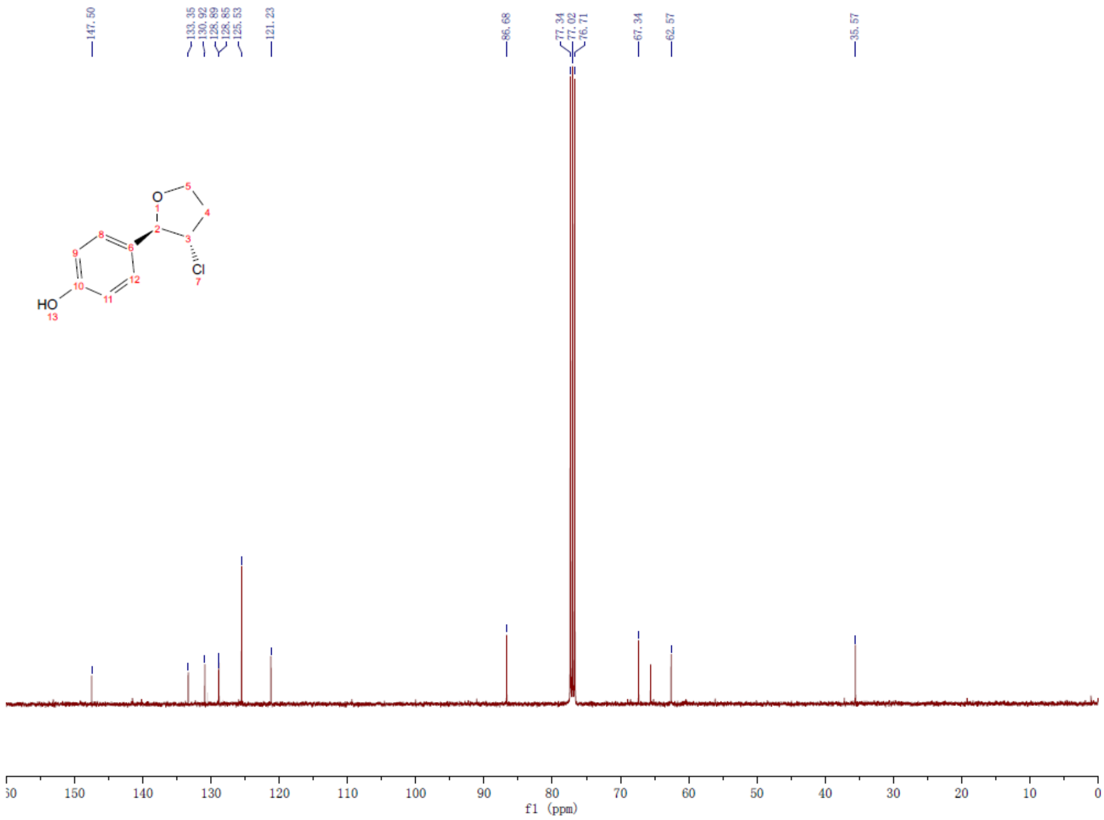
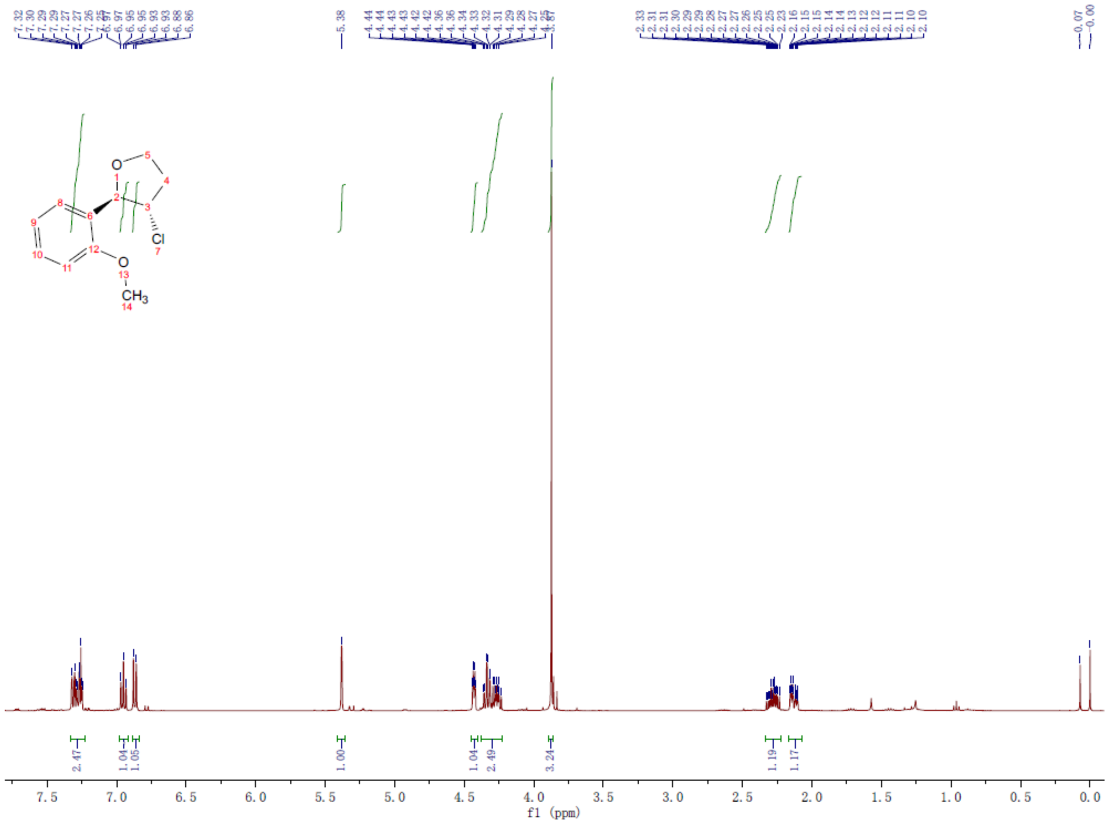
76.31
75.99
75.67
66.17
62.20
34.58
20.11
f1 (ppm)

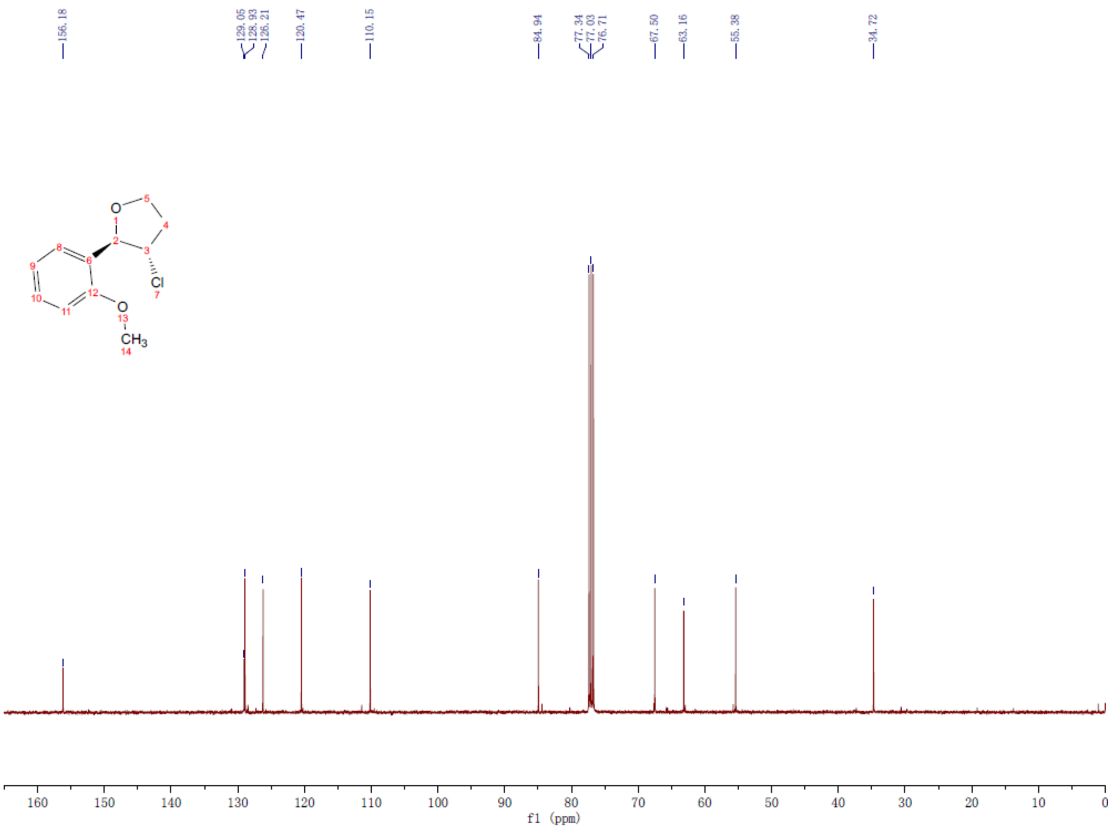
2d



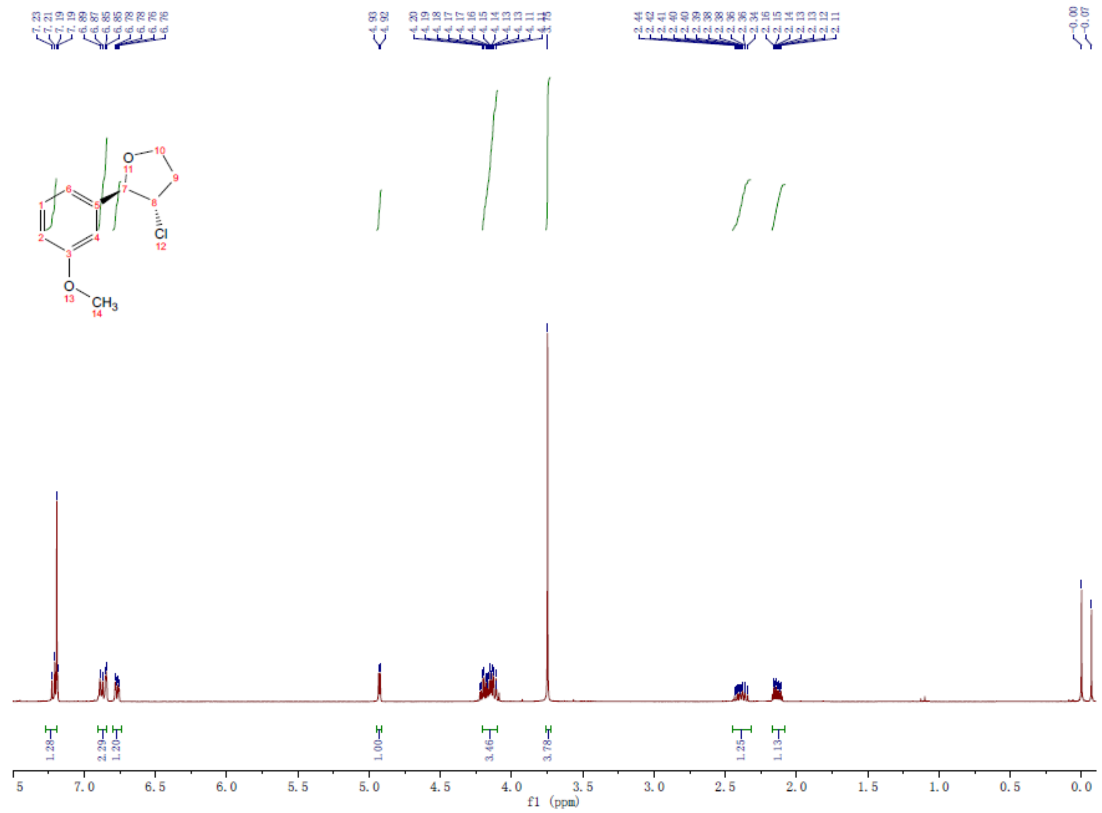


2e





2f


O
Cl
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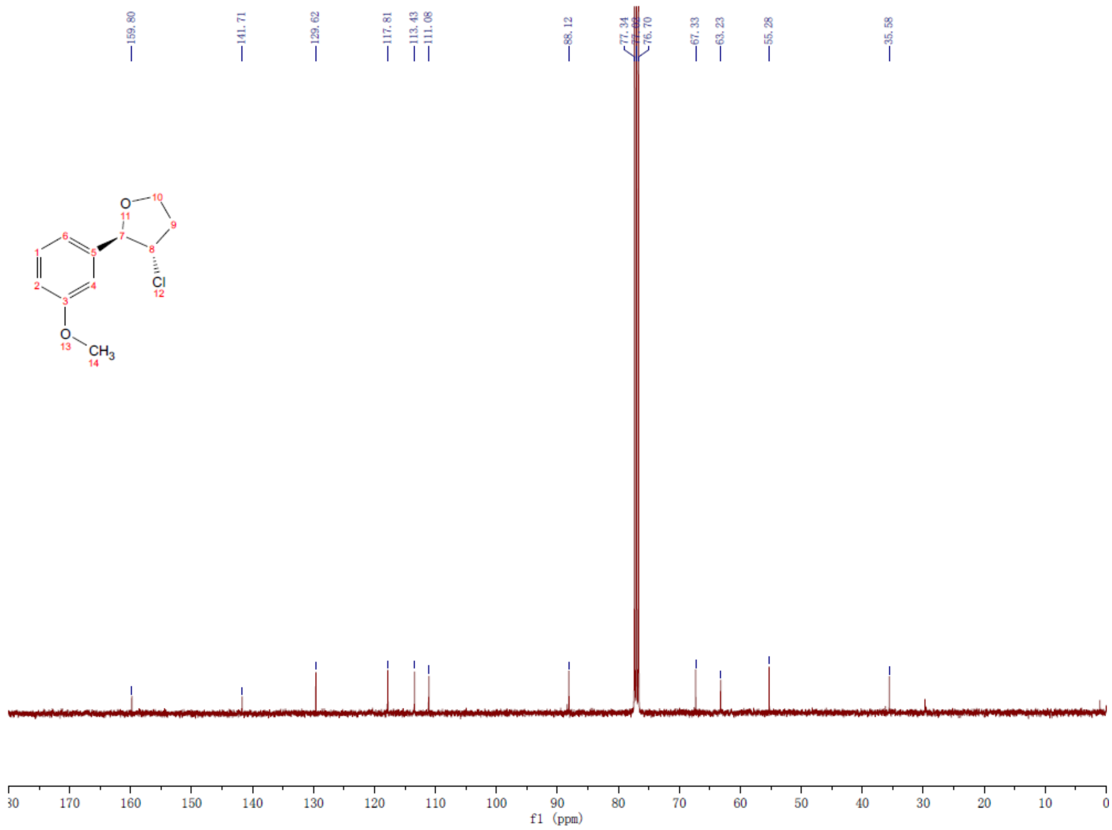
1.20
1.00
3.46
3.78
1.25
1.13
f1 (ppm)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67.33
63.23
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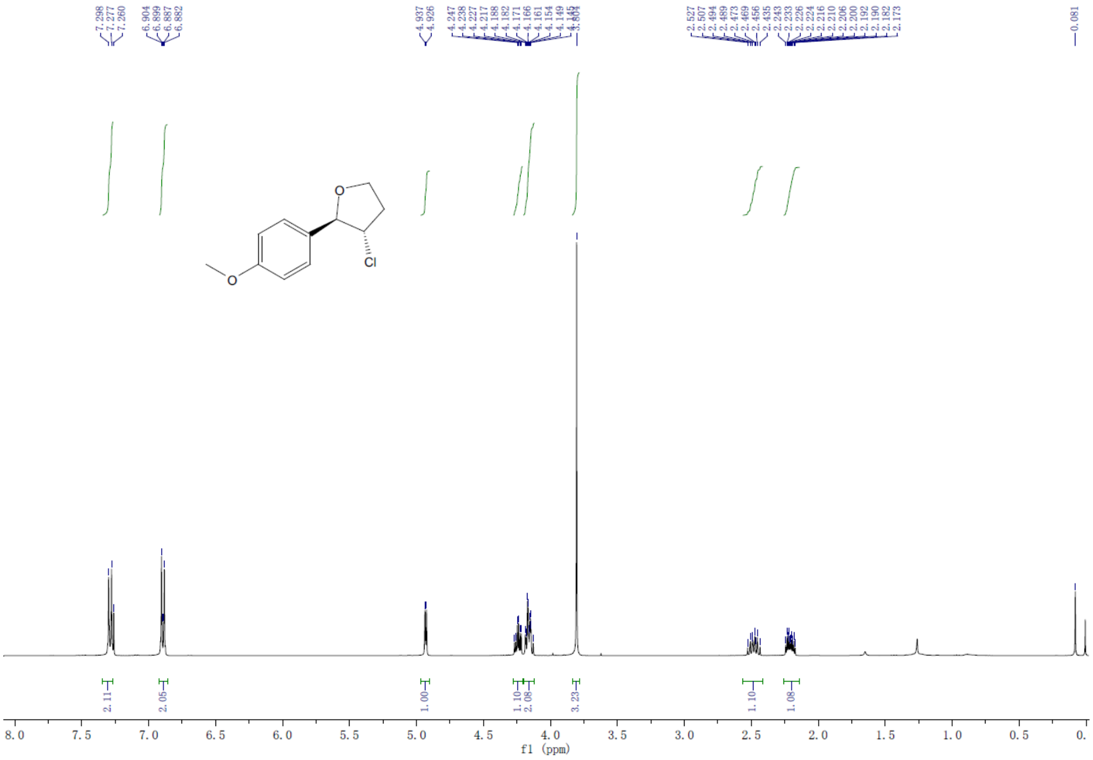
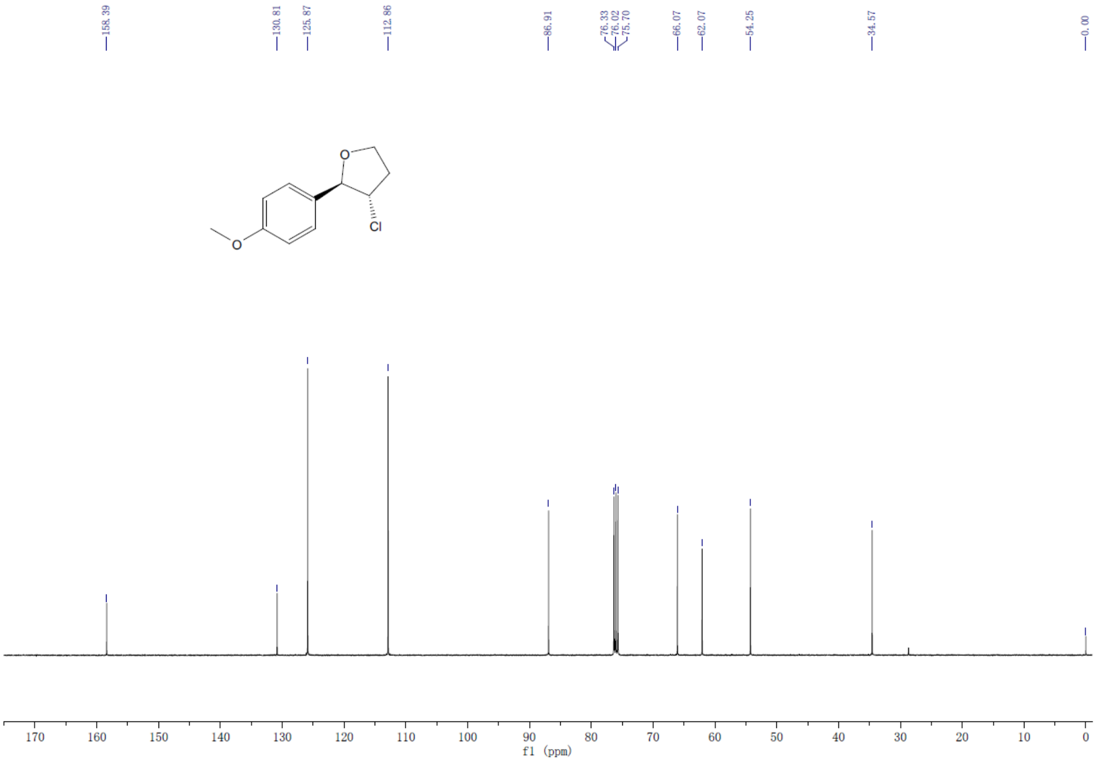
35.58
O
Cl
CH_3
f1 (ppm)

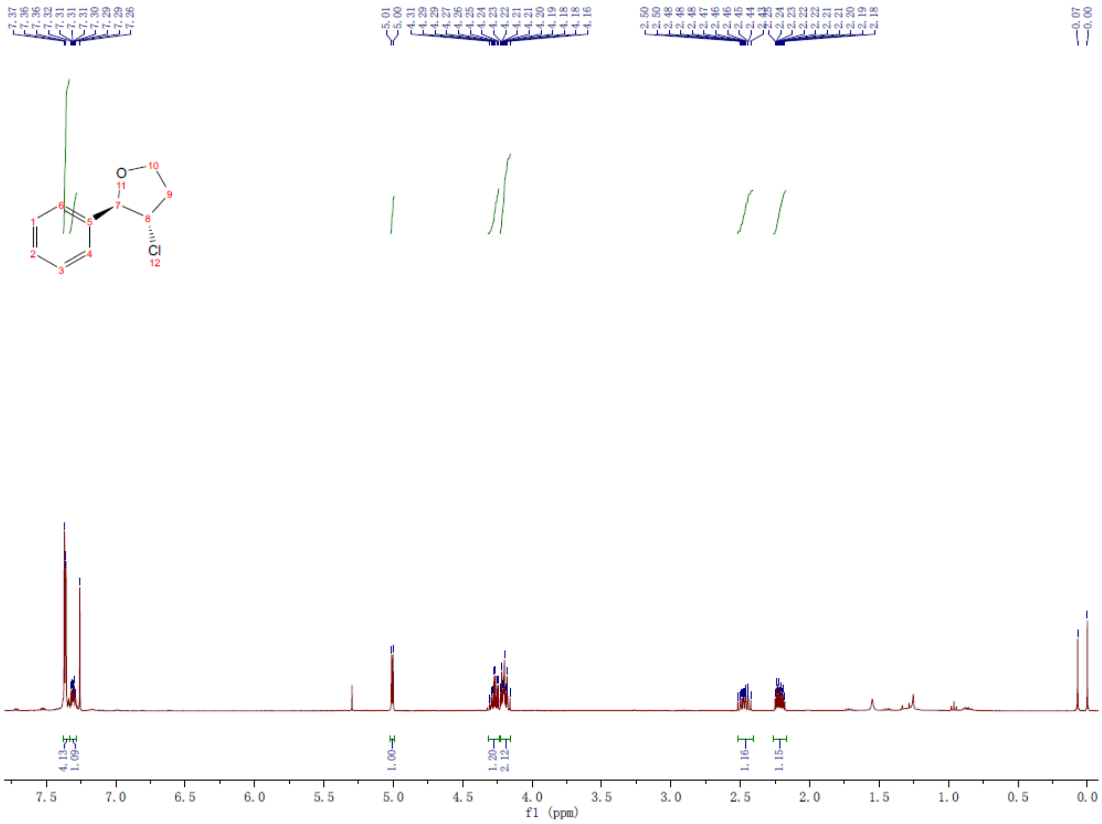
2g

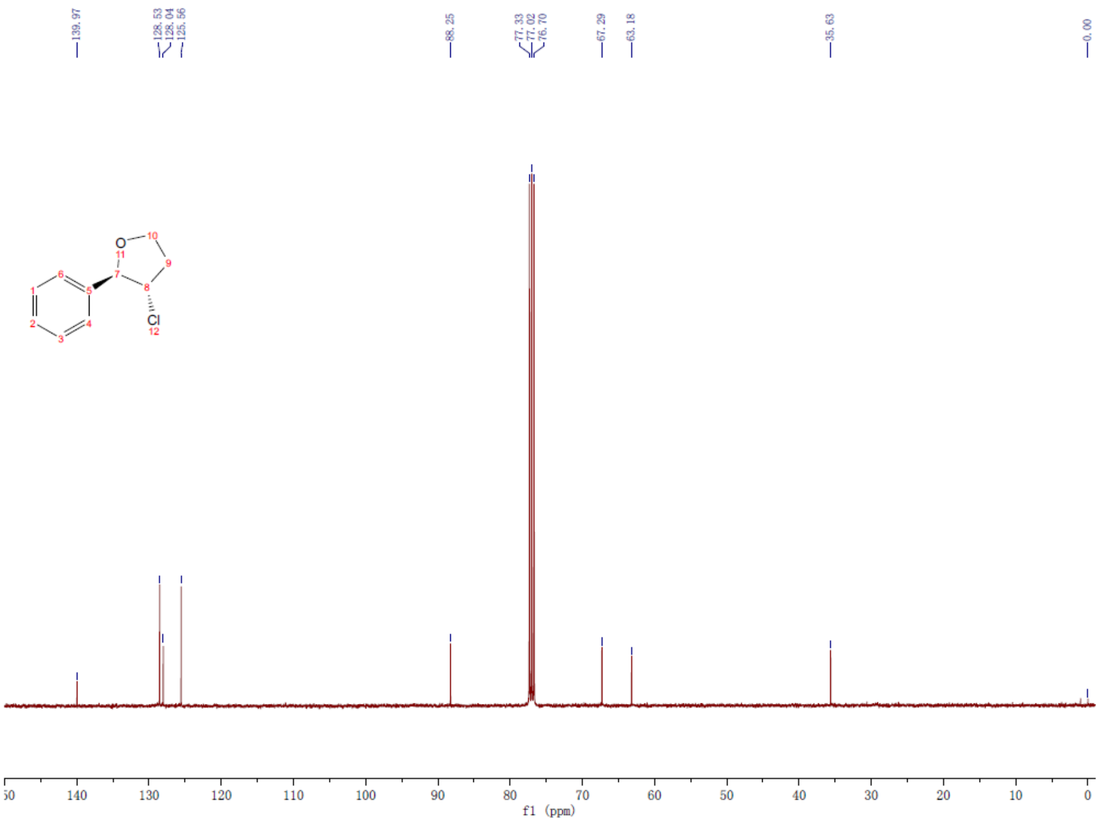




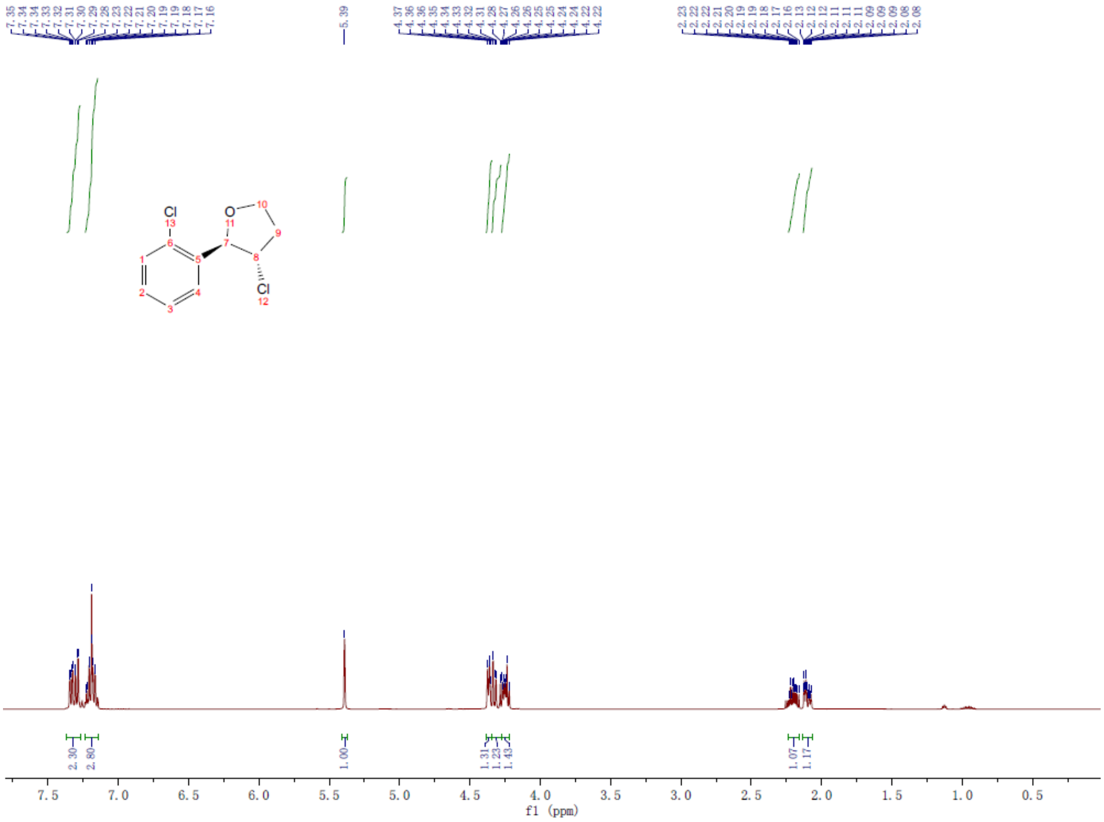
Electronic Supplementary Material (ESI) for Chemical Communications

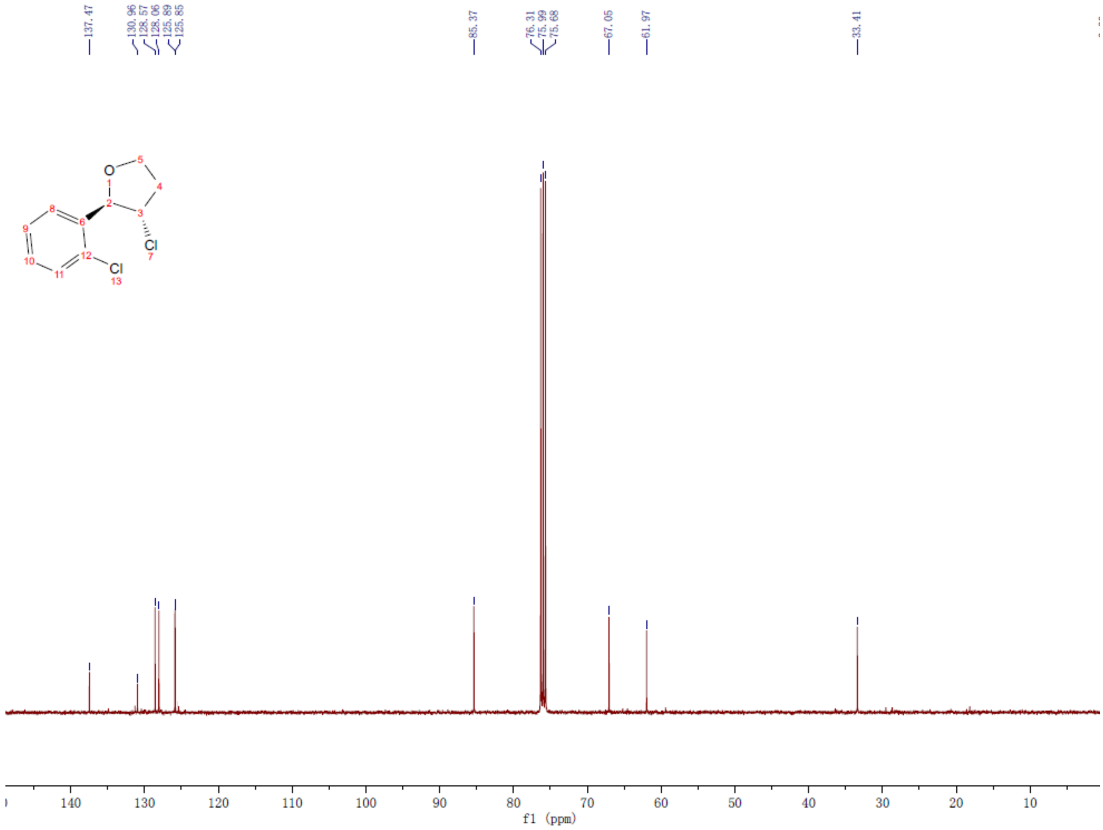
2h



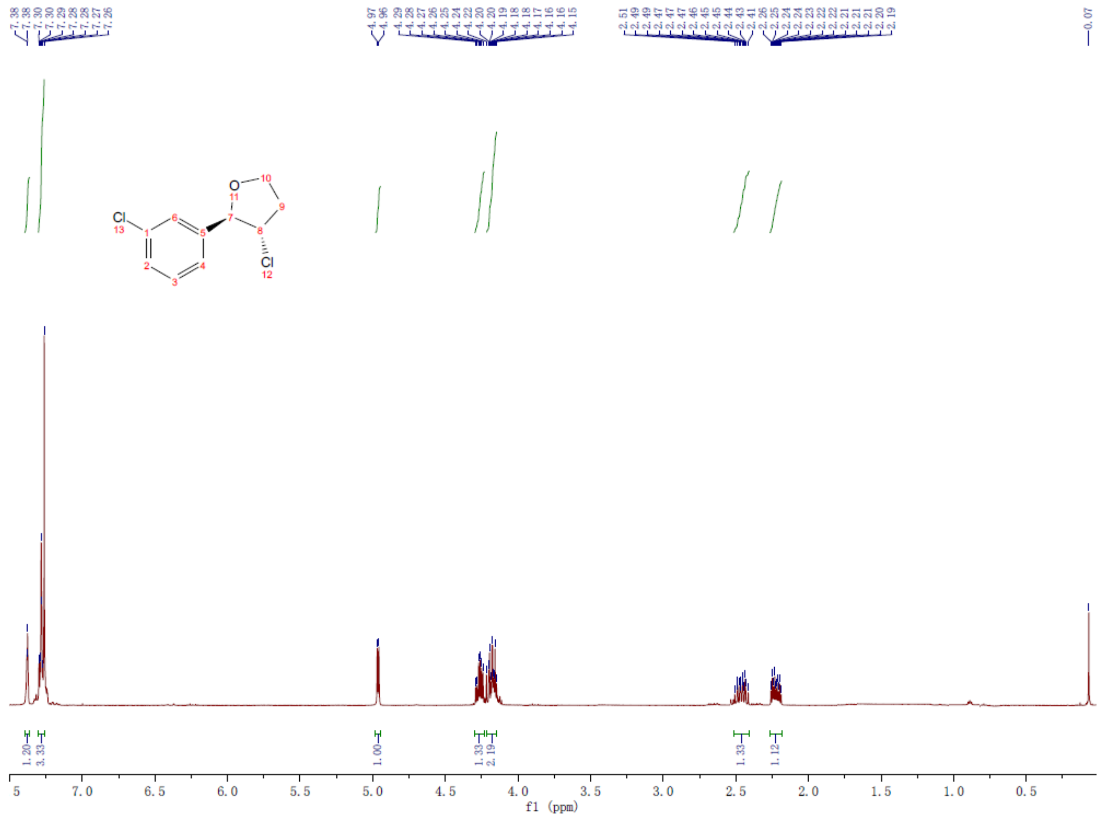


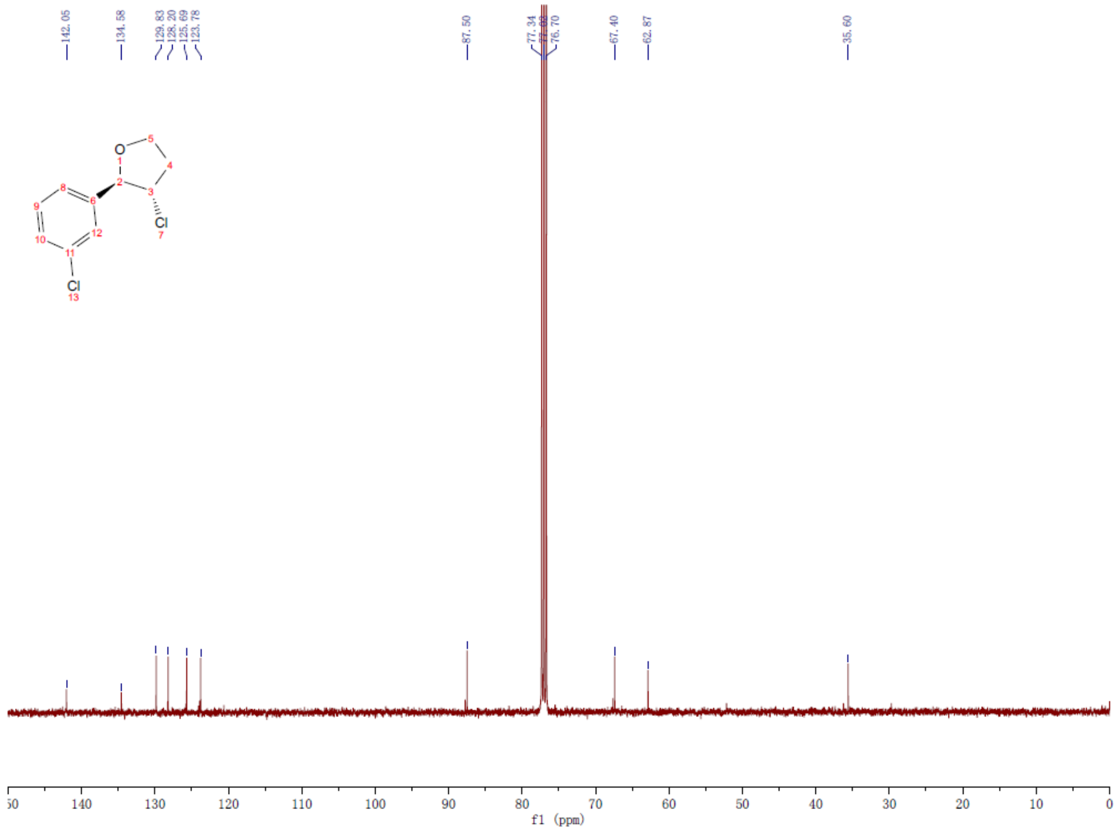
2i



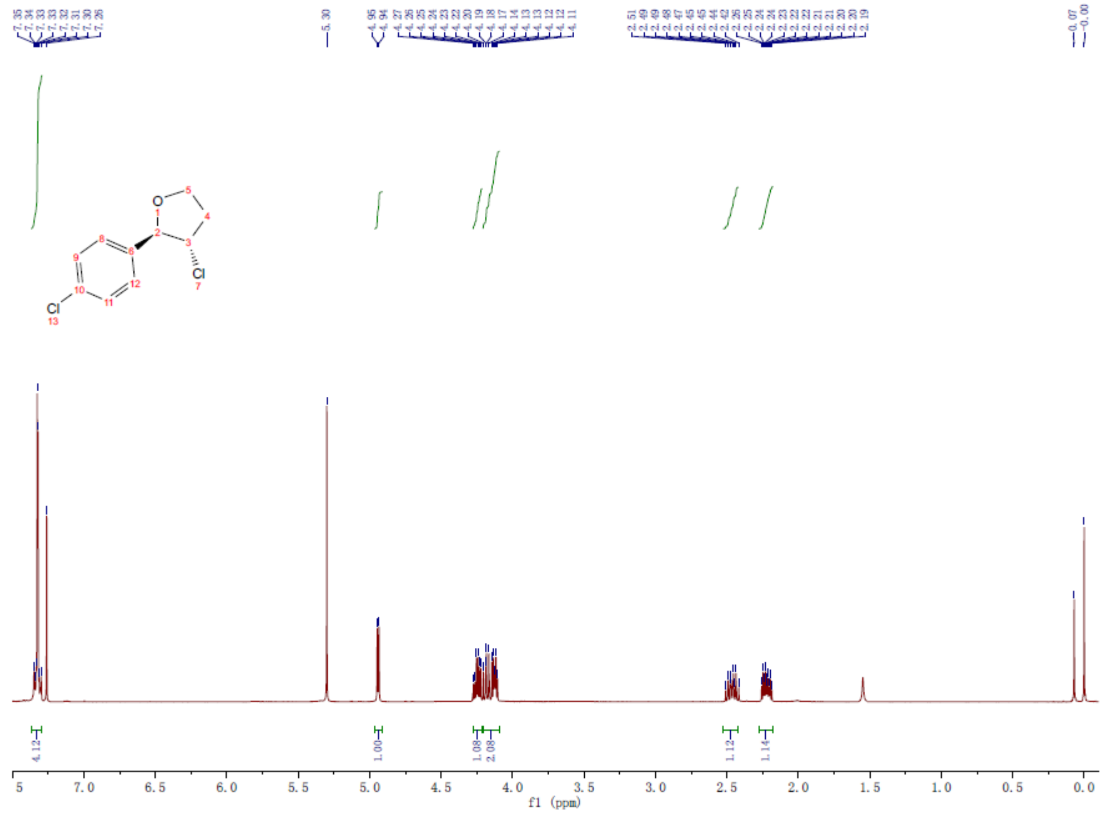


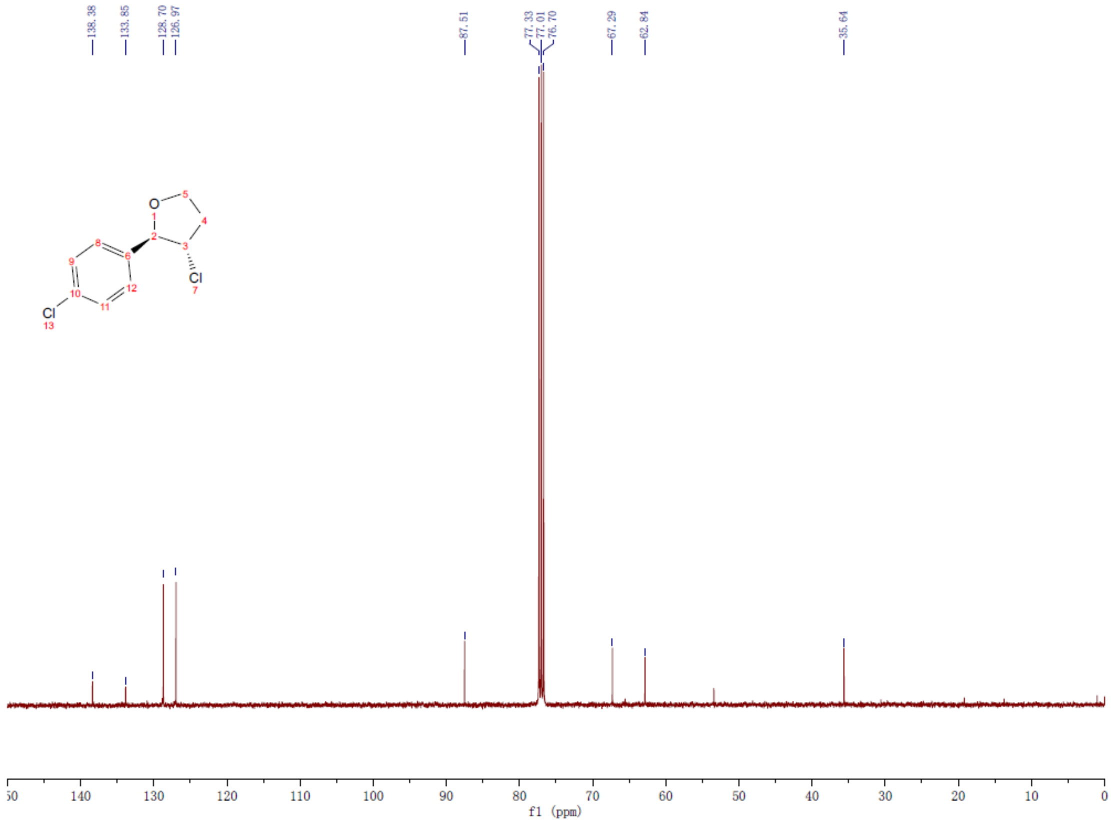
2j





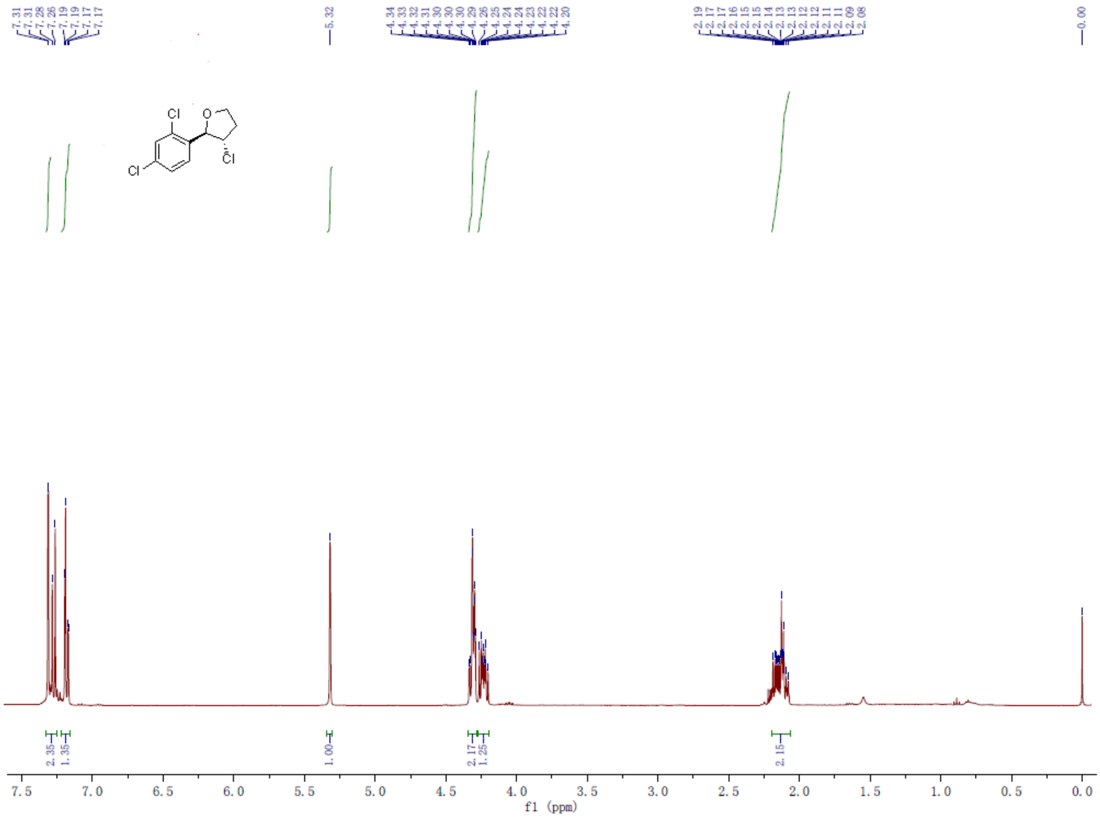
2k

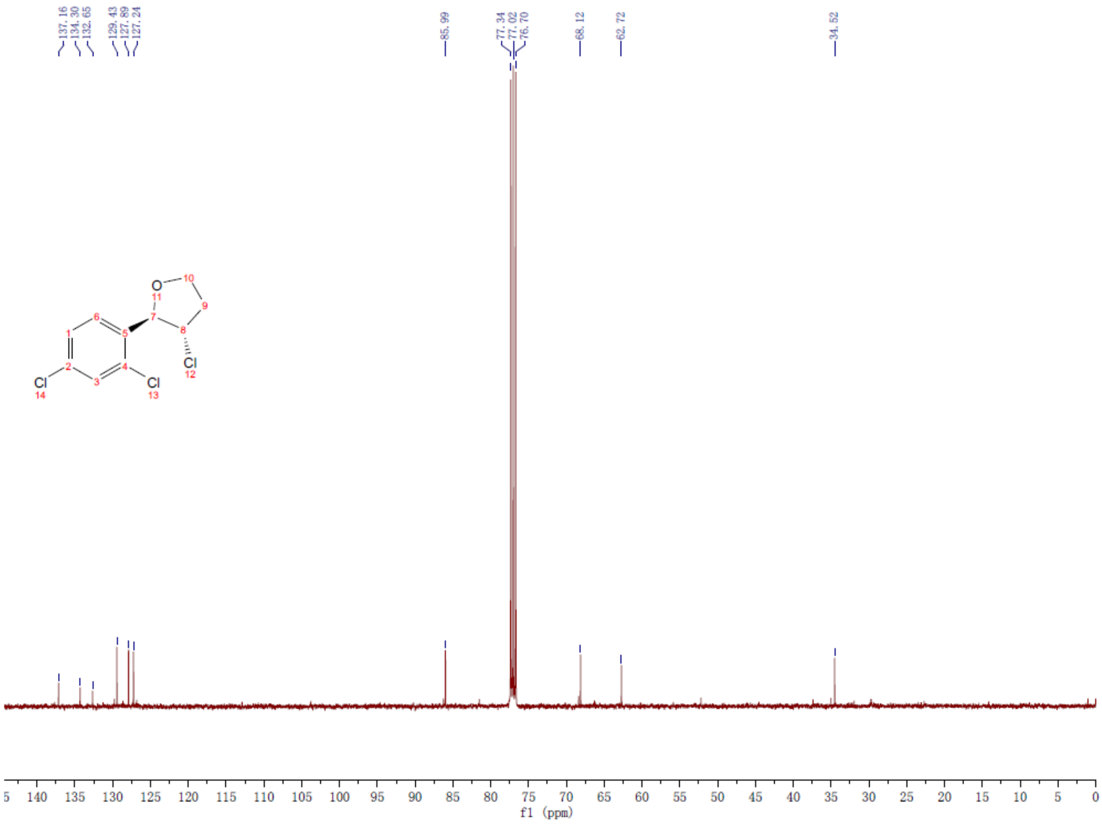




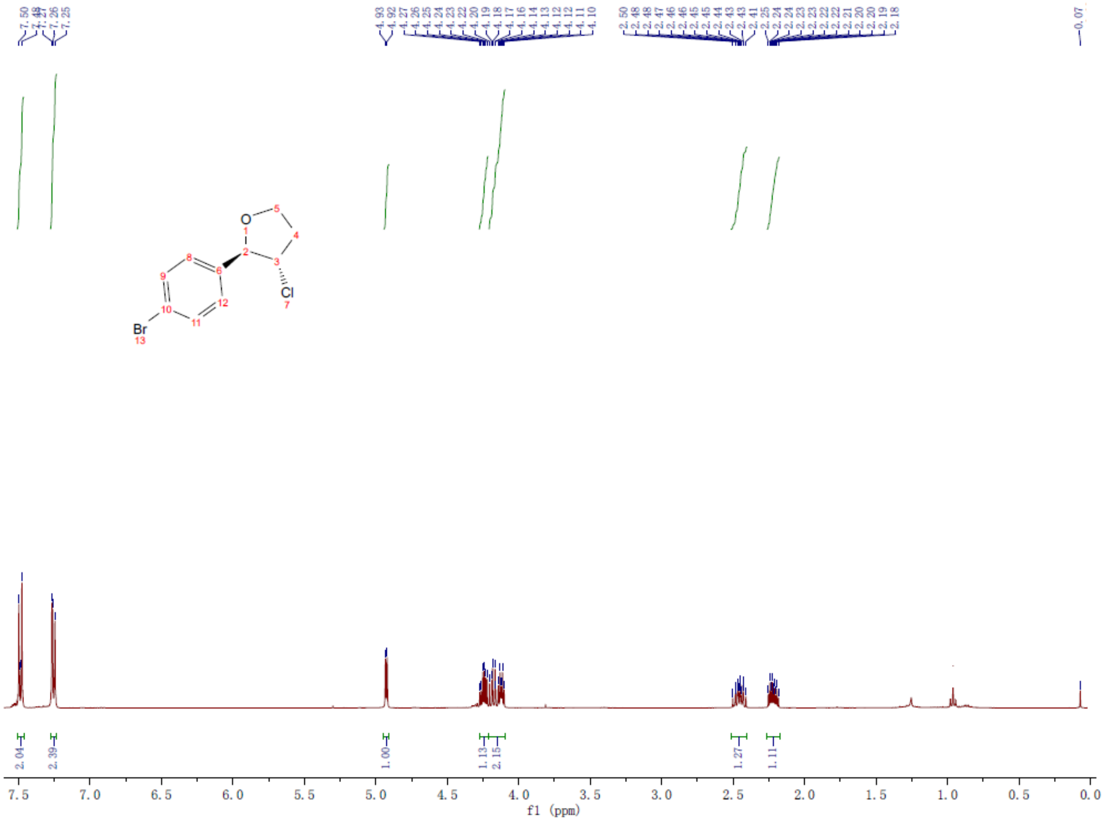
Electronic Supplementary Material (ESI) for Chemical Communications

2l





2m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7.49
7.48
7.27
7.26
7.25
4.93
4.92
4.27
4.26
4.25
4.24
4.23
4.22
4.20
4.19
4.18
4.17
4.16
4.14
4.13
4.12
4.12
4.11
4.10
2.50
2.48
2.48
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2.46
2.46
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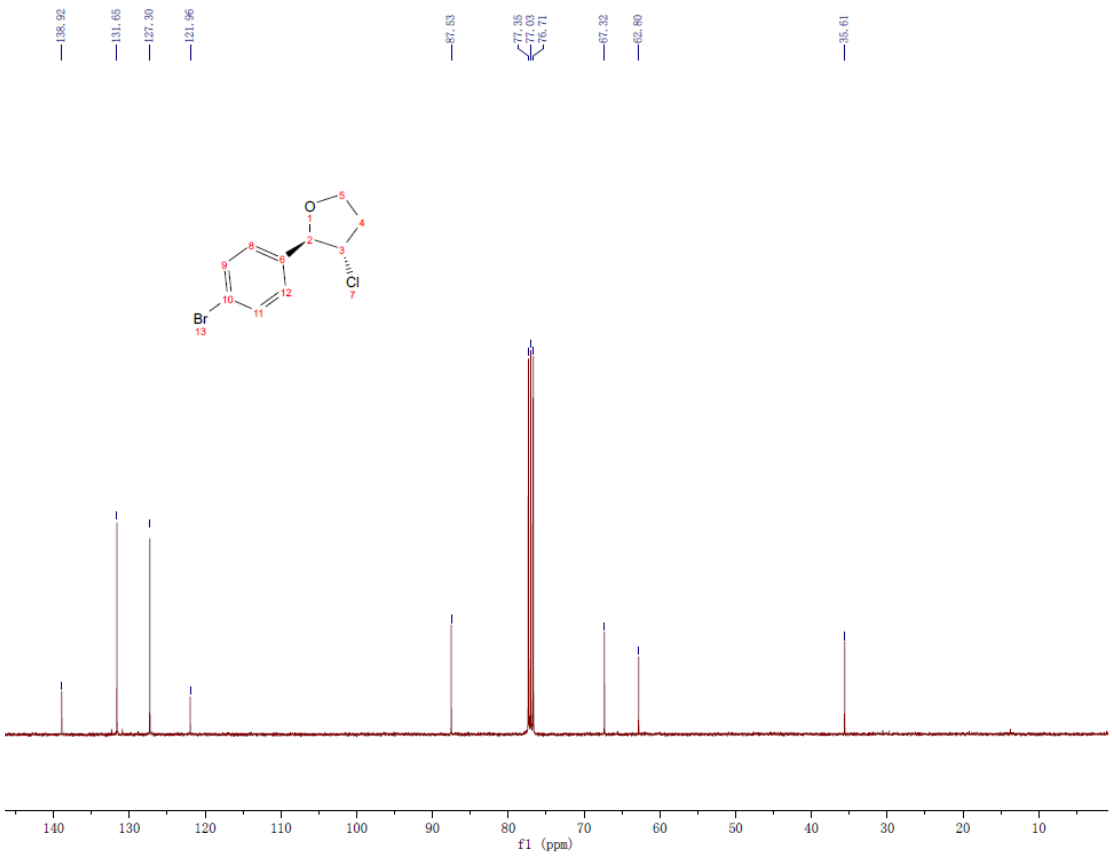
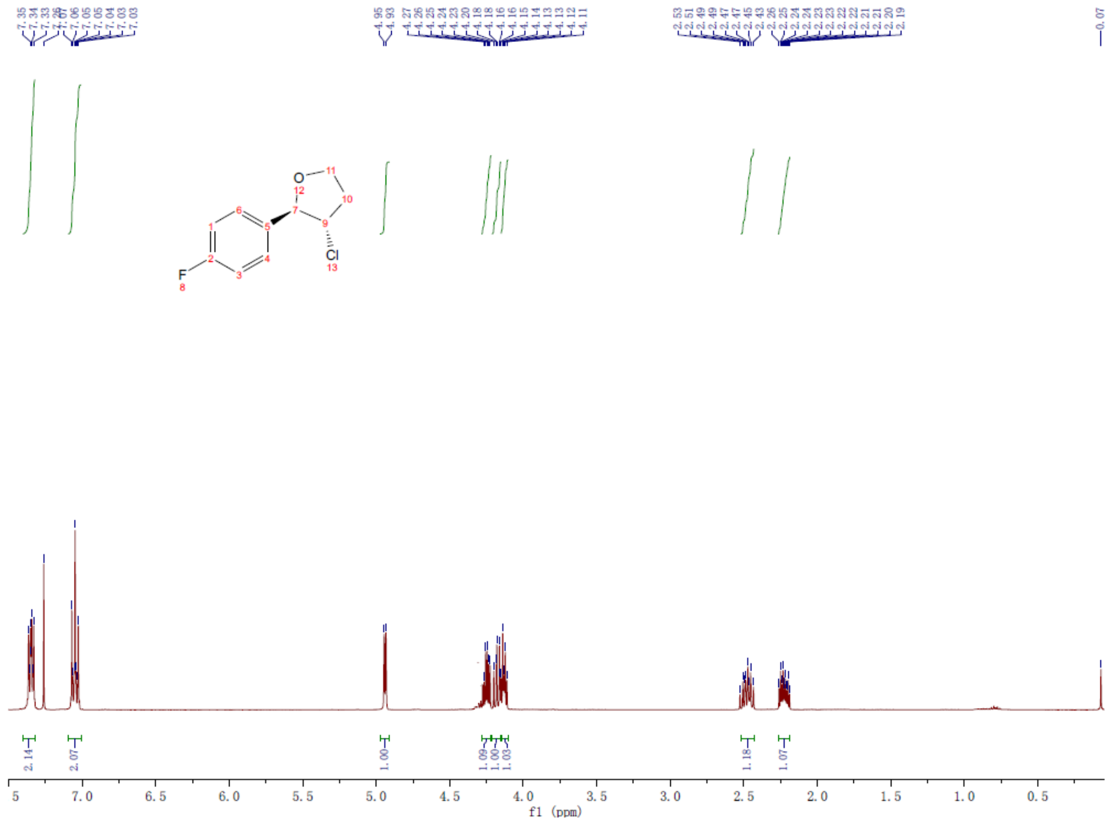
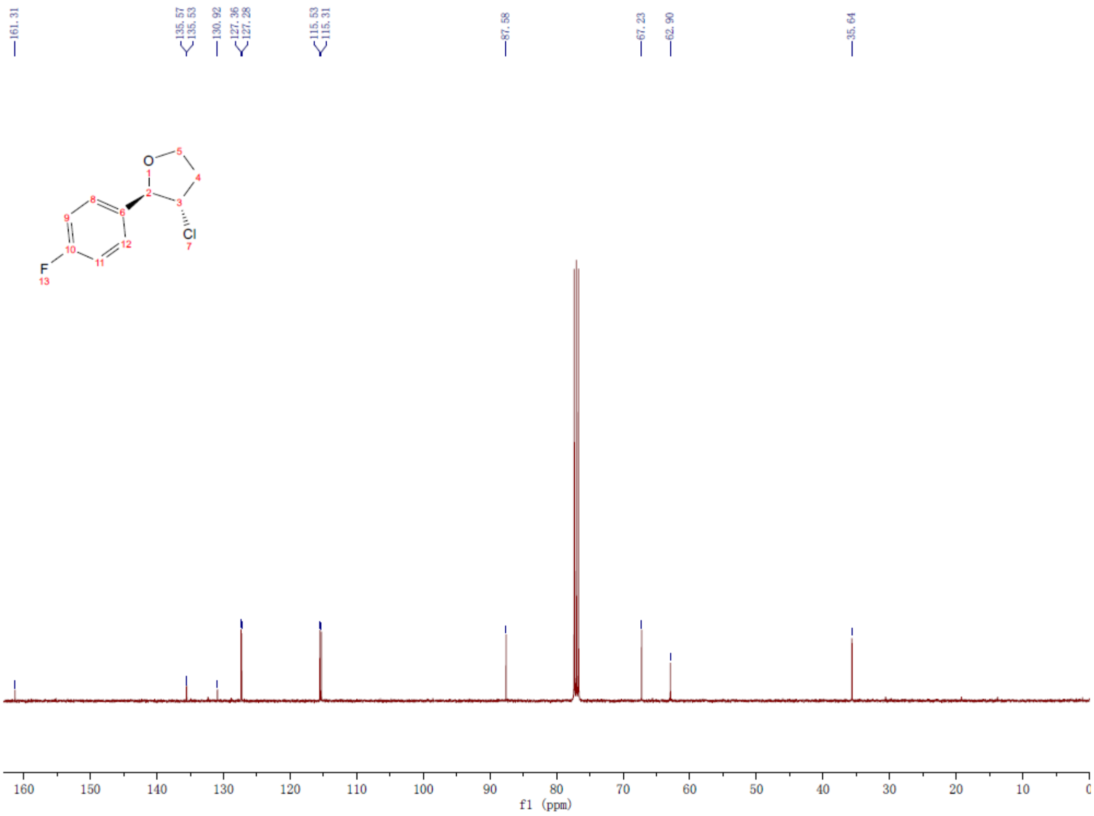
2.25
2.24
2.24
2.23
2.23
2.22
2.22
2.21
2.20
2.20
2.19
2.18
0.07
2.04
2.39
1.00
1.13
2.15
1.27
1.11
f1 (ppm)

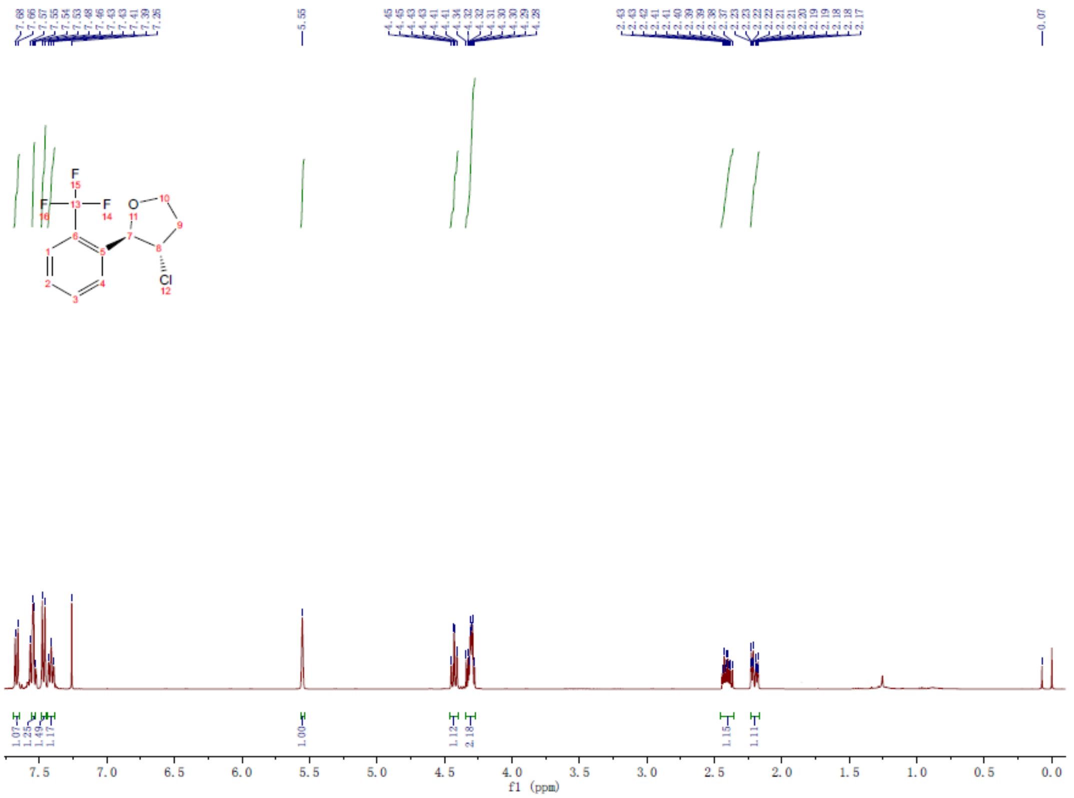

138.92
131.65
127.30
121.96
87.53
77.35
77.03
76.71
67.32
62.80
35.61
f1 (ppm)

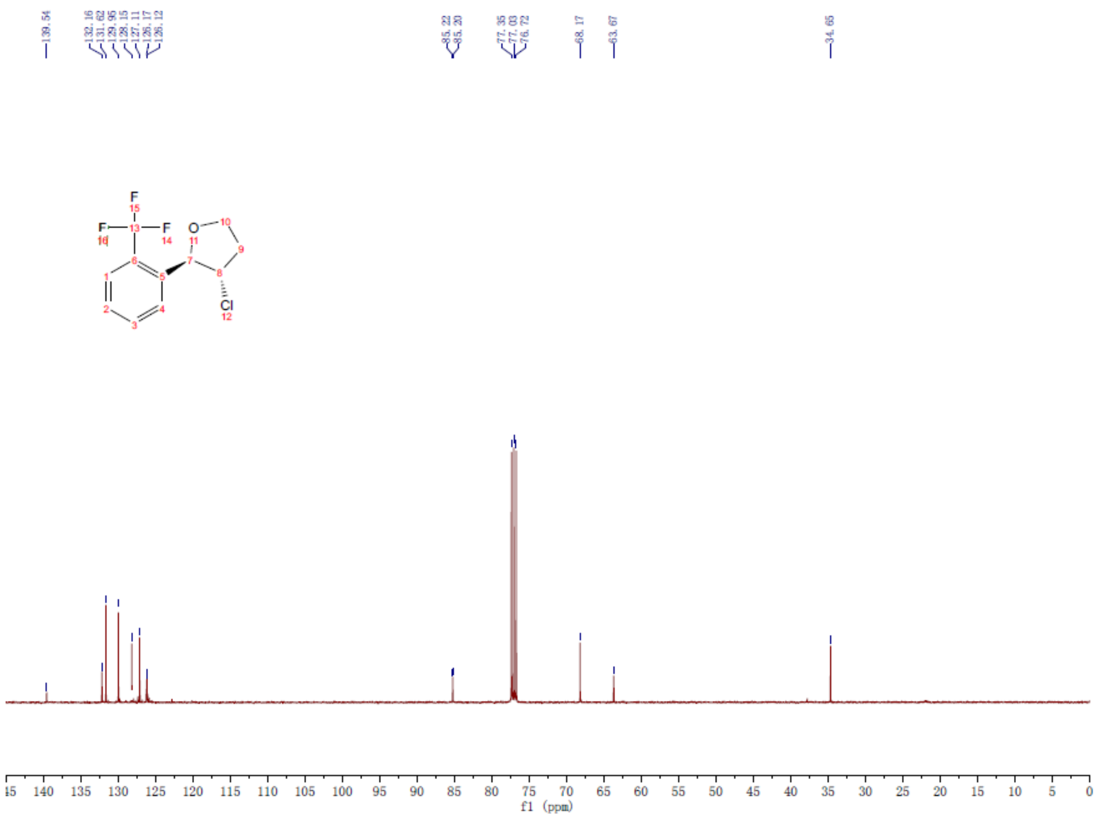
2n


f1 (ppm)

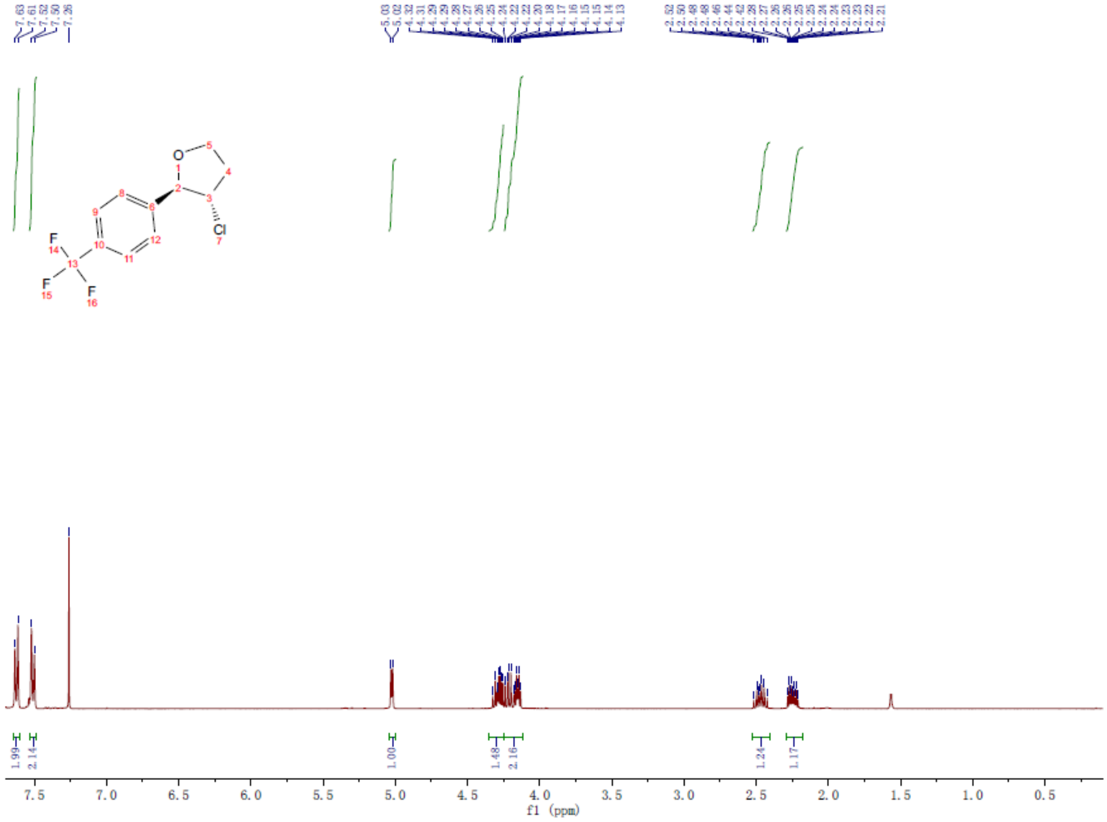

161.31
135.57
135.53
130.92
127.36
127.28
115.53
115.31
87.58
67.23
62.90
35.64
f1 (ppm)

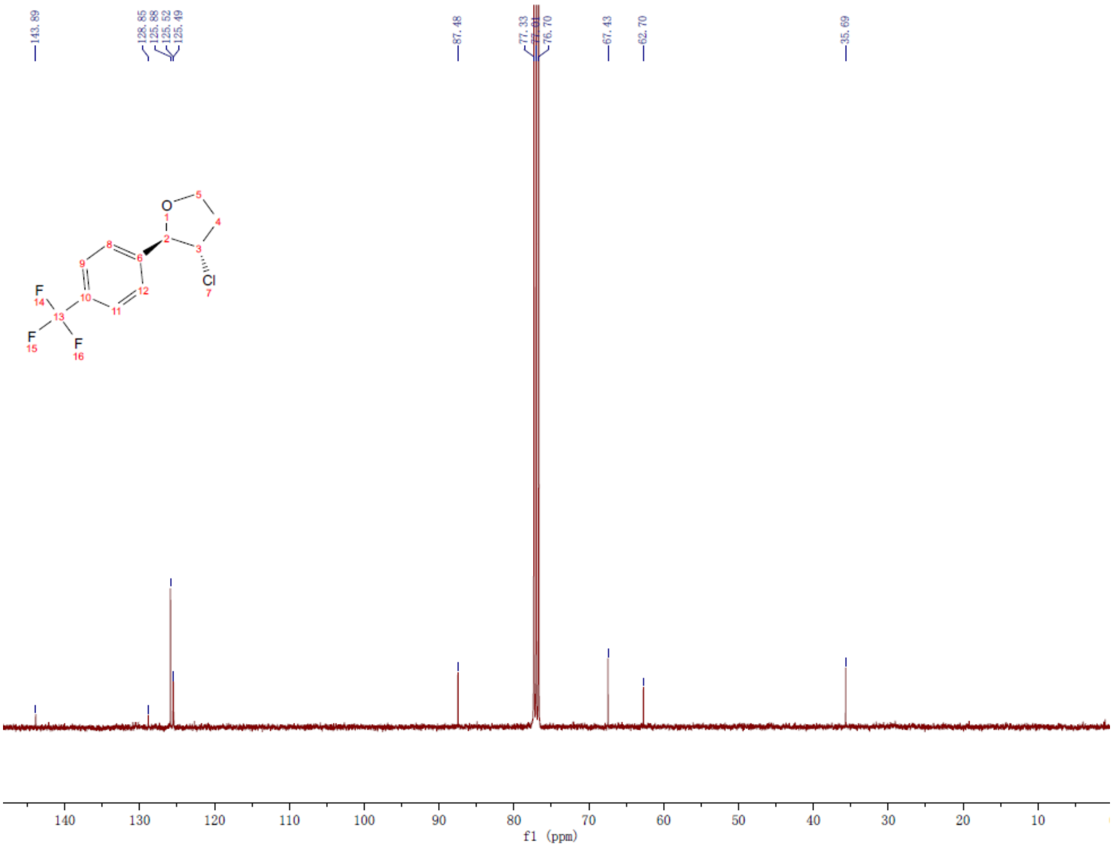
2o


5.55
0.07
F
F
F
O
Cl
1.07
1.25
1.49
1.17
1.00
1.12
2.18
1.15
1.11
f1 (ppm)

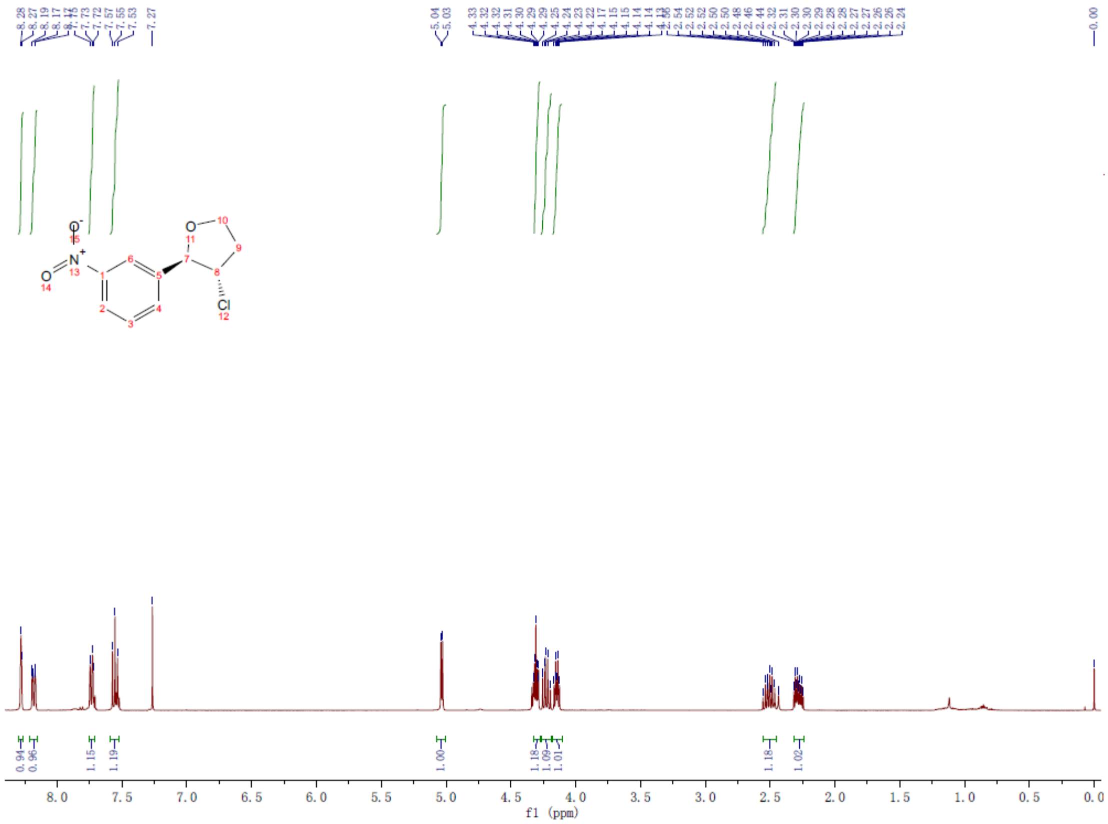

139.54
132.16
131.62
129.95
128.15
127.11
126.17
126.12
85.22
85.20
77.35
77.03
76.72
68.17
63.67
34.65
F
F
F
O
Cl
f1 (ppm)

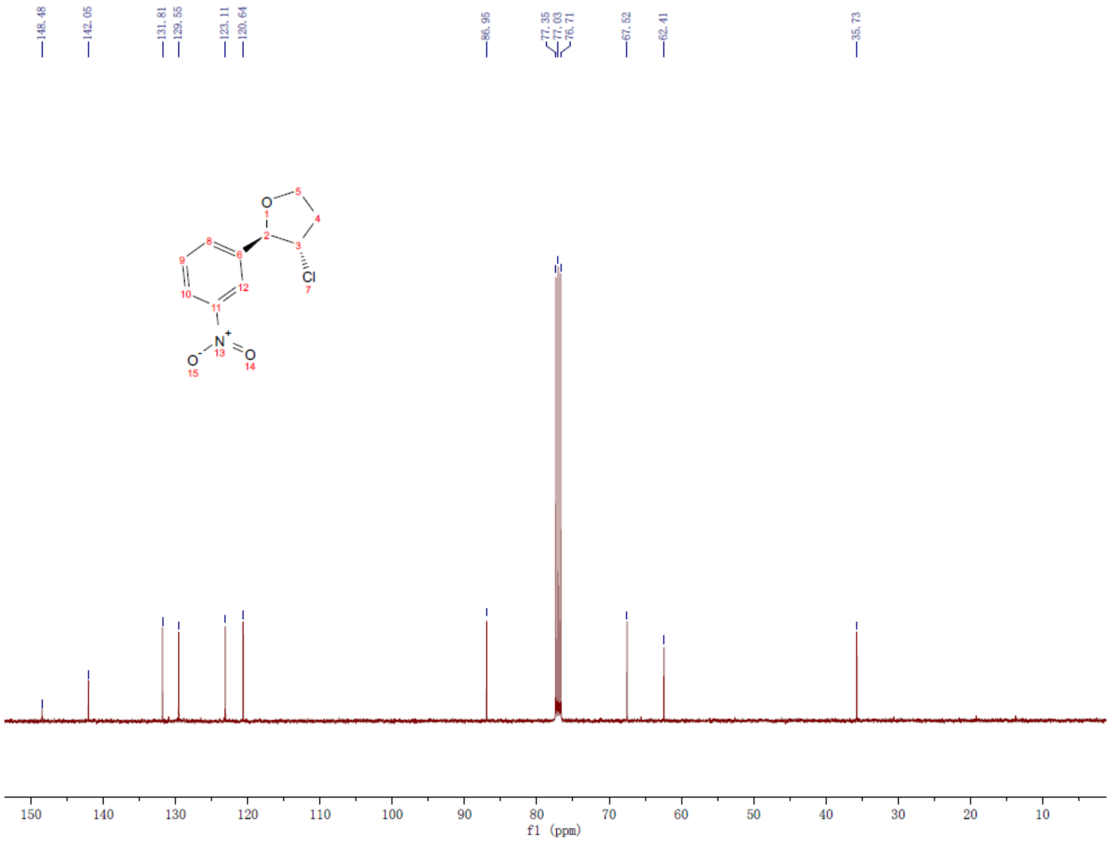
2p


O
Cl
F
F
F
1.99
2.14
1.00
1.48
2.16
1.24
1.17
f1 (ppm)


143.89
128.85
125.88
125.52
125.49
87.48
77.33
77.01
76.70
67.43
62.70
35.69
O
Cl
F
F
F
f1 (ppm)

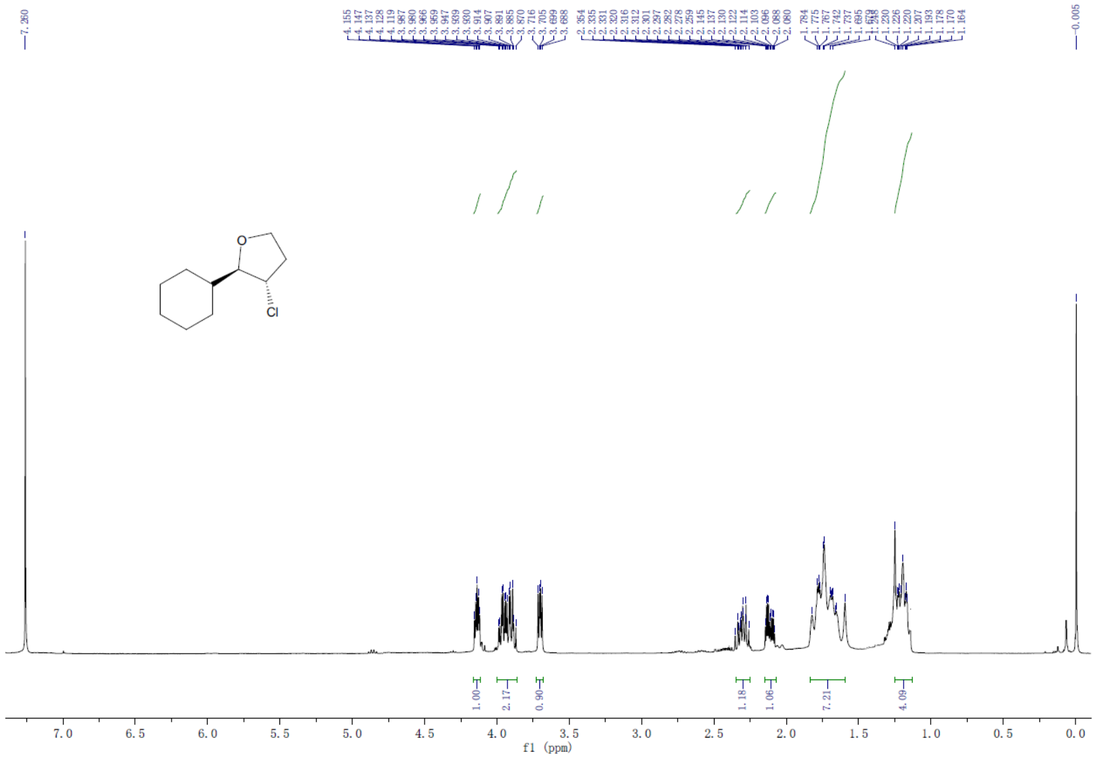
2q

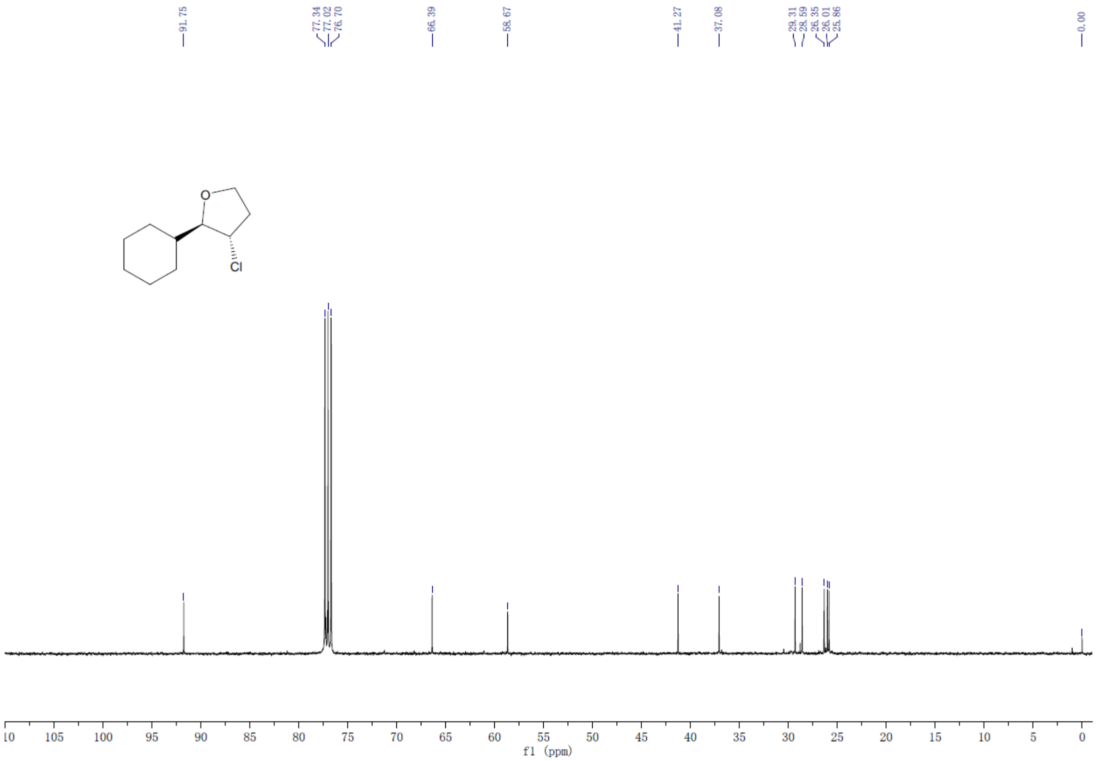

0.94
0.96
1.15
1.19
1.00
1.18
1.09
1.01
1.18
1.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


148.48
142.05
131.81
129.55
123.11
120.64
86.95
77.35
77.03
76.71
67.52
62.41
35.73
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

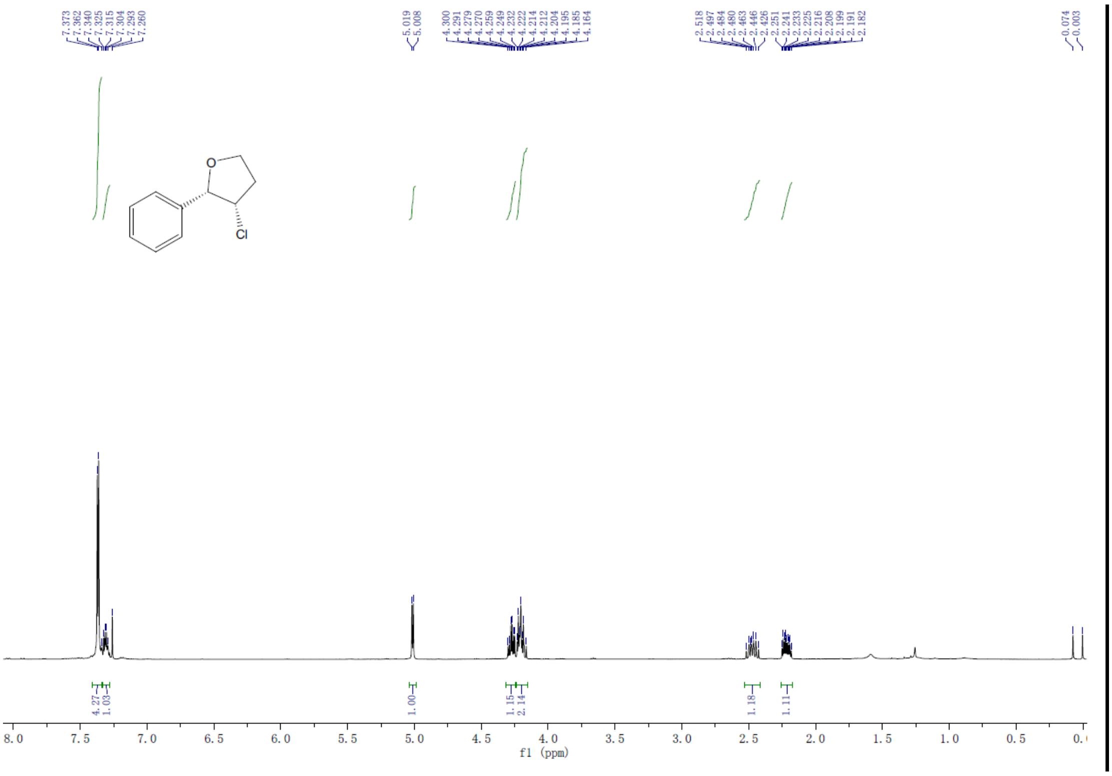
Electronic Supplementary Material (ESI) for Chemical Communications

2r





2t


7.373
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7.325
7.315
7.304
7.293
7.260
5.019
5.008
4.300
4.291
4.279
4.270
4.259
4.249
4.232
4.222
4.214
4.212
4.204
4.195
4.185
4.164
2.518
2.497
2.484
2.480
2.463
2.446
2.426
2.251
2.241
2.233
2.225
2.216
2.208
2.199
2.191
2.182
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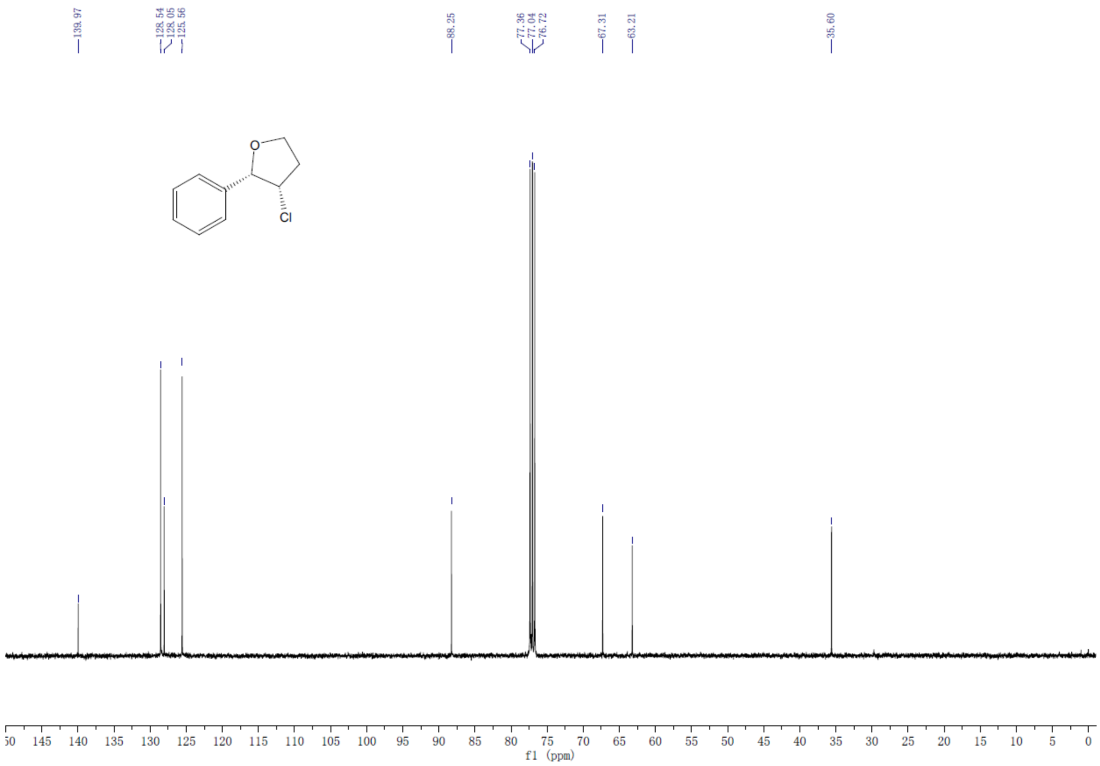
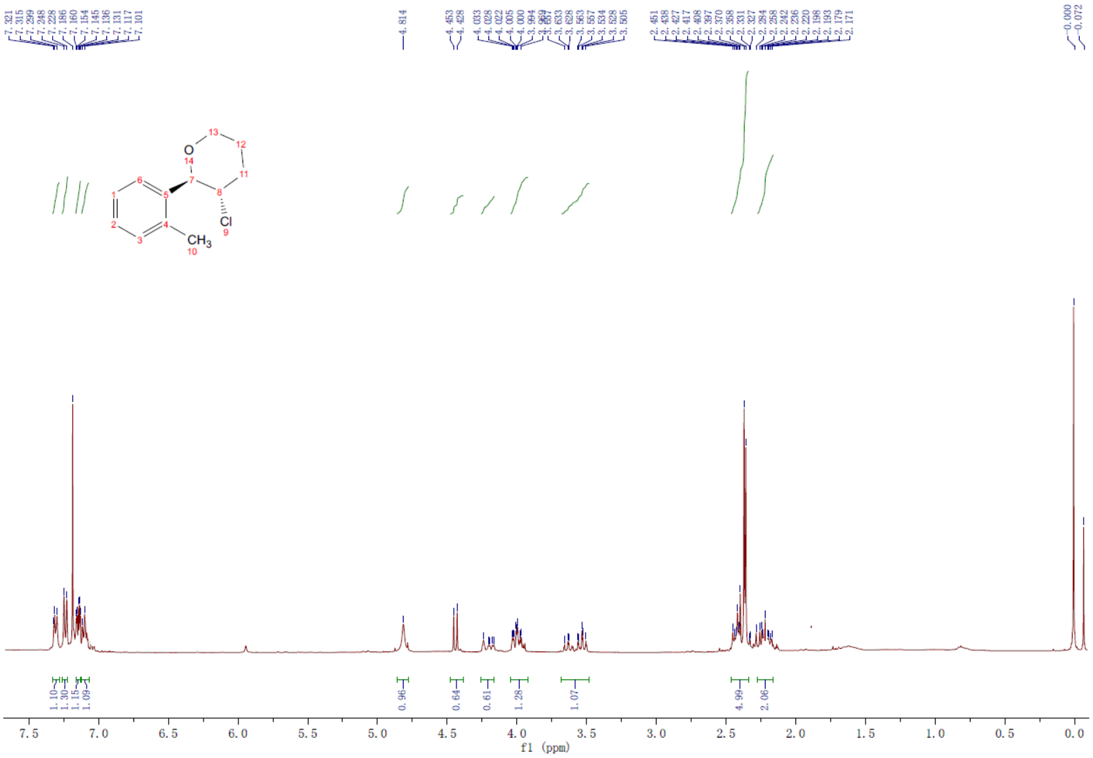
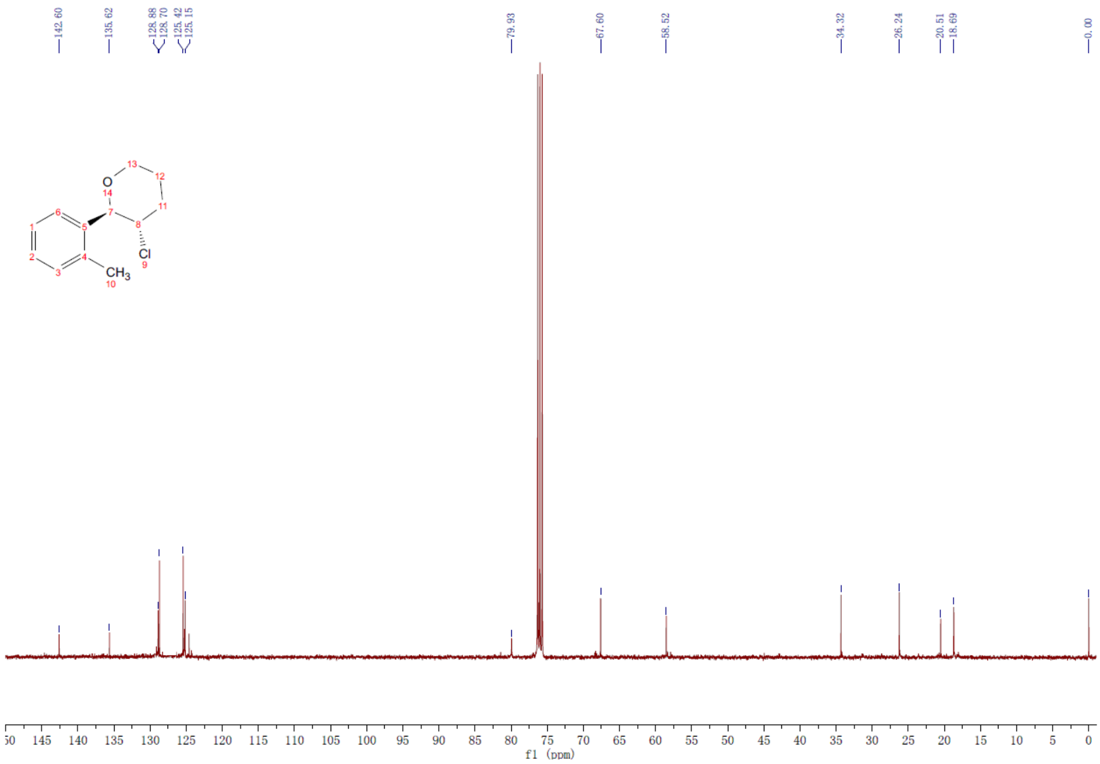
0.003
O
Cl
4.27
1.03
1.00
1.15
2.14
1.18
1.11
f1 (ppm)


139.97
128.54
128.05
125.56
88.25
77.36
77.04
76.72
67.31
63.21
35.60
O
Cl
f1 (ppm)

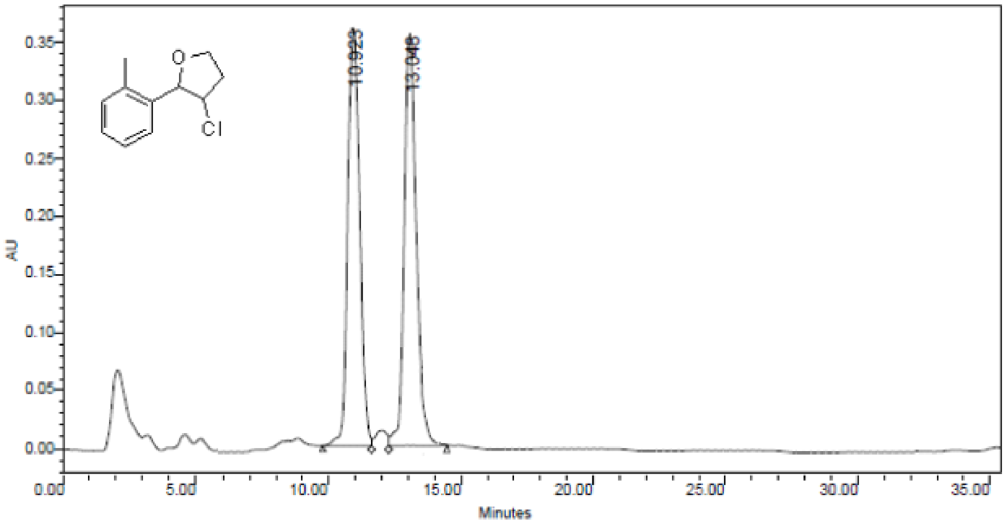
2u



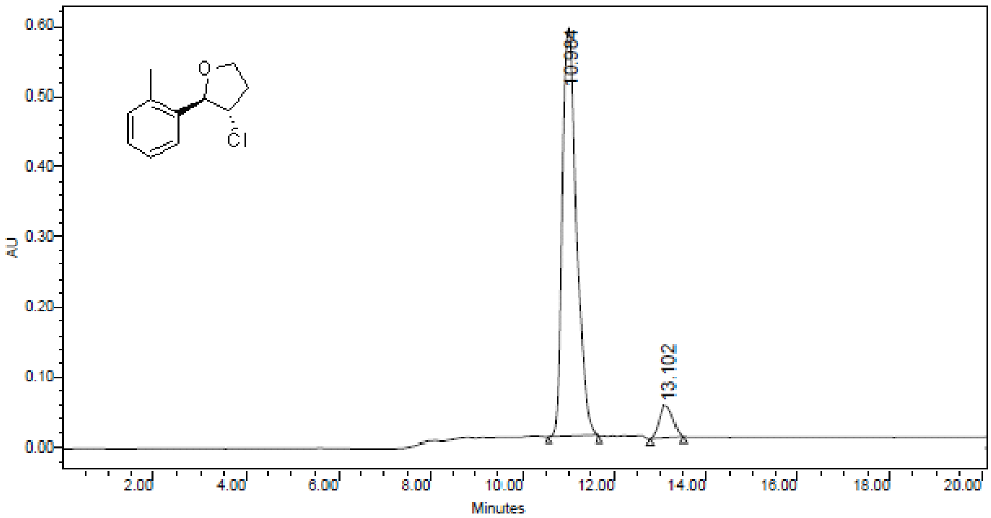


HPLC Spectra of the Chiral Compounds

2a

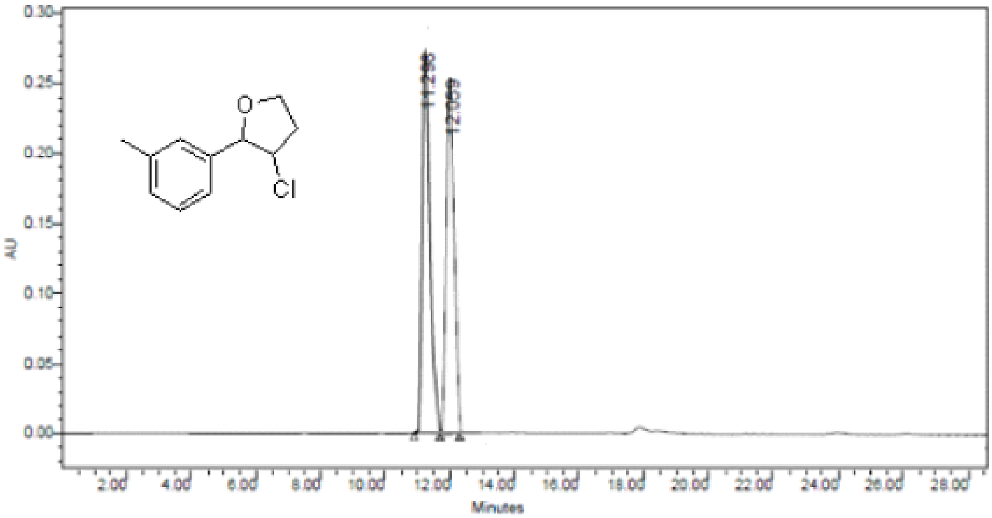


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	10.923	11232098	50.44	359764	50.37
2	13.048	11035166	49.56	354442	49.63

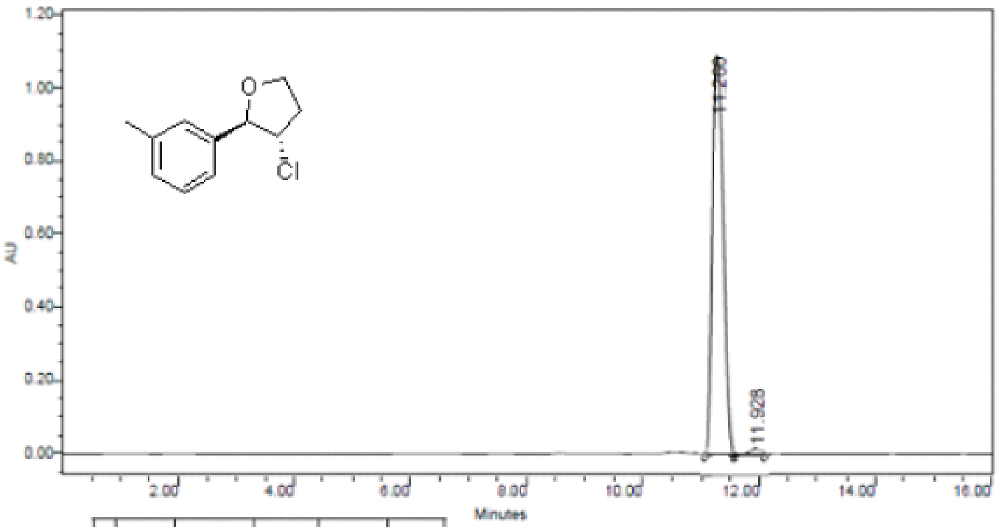


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	10.984	12651883	93.19	582271	92.60
2	13.102	923938	6.81	46510	7.40

2b

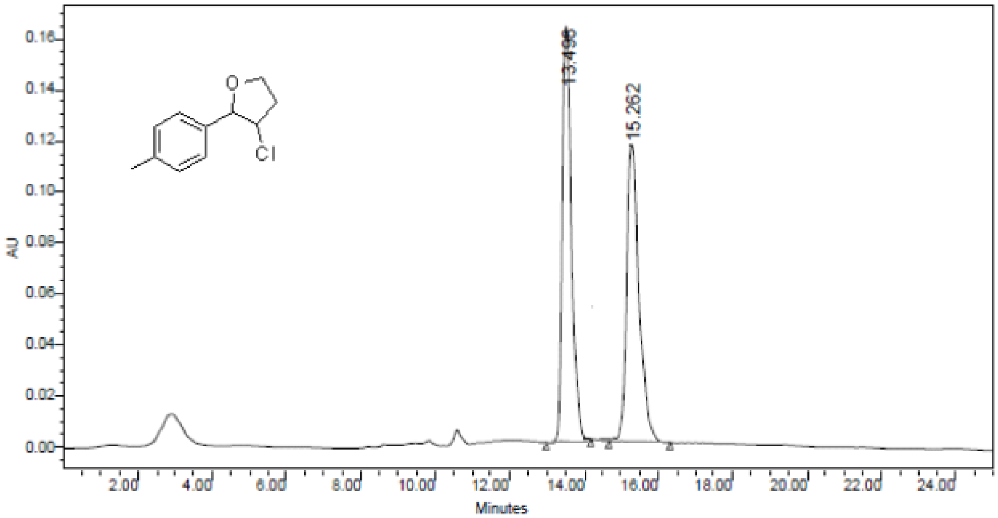


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	11.298	4616468	51.66	272279	51.46
2	12.059	4320033	48.34	256875	48.54

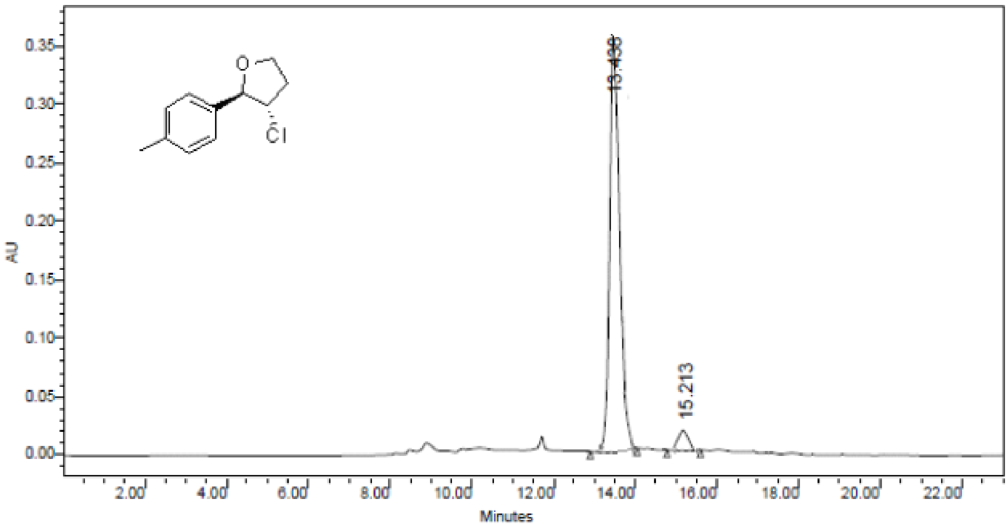


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	11.260	6358764	96.16	155289	96.78
2	11.928	653979	3.84	38403	3.22

2c

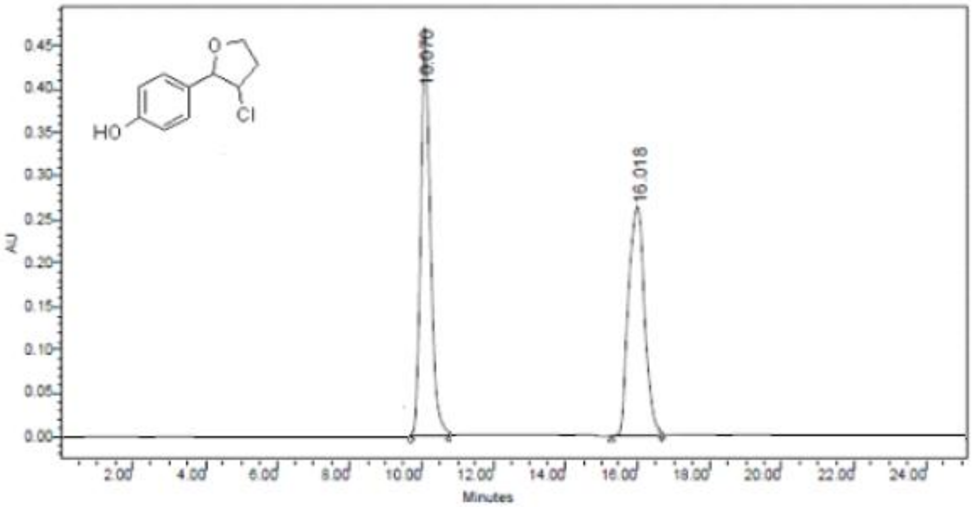


	RT (min)	Area (µV*sec)	%Area	Heigh (µV)	% Heigh
1	13.498	2756607	50.82	164327	58.10
2	15.262	2667727	49.18	118526	41.90

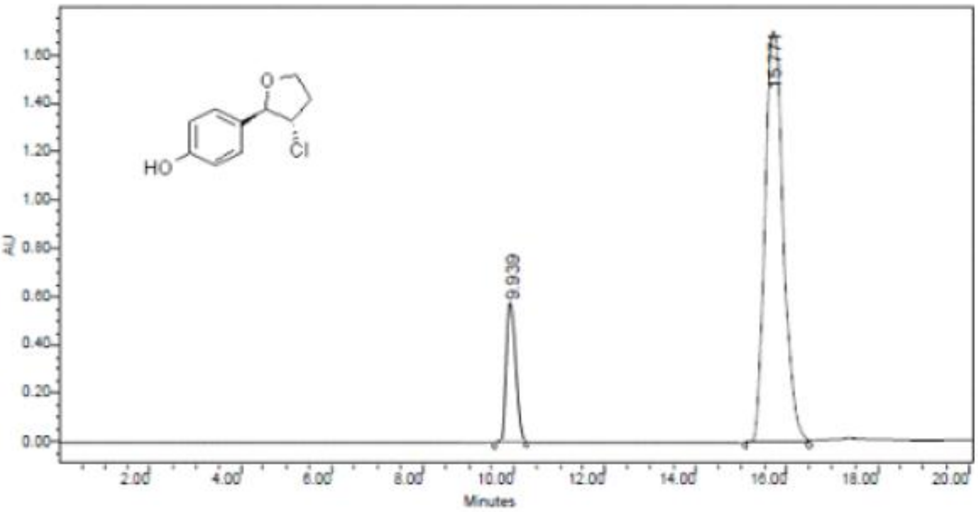


	RT (min)	Area (µV*sec)	%Area	Heigh (µV)	% Heigh
1	13.438	5732372	95.17	360172	96.43
2	15.213	291057	4.83	13333	3.57

2d

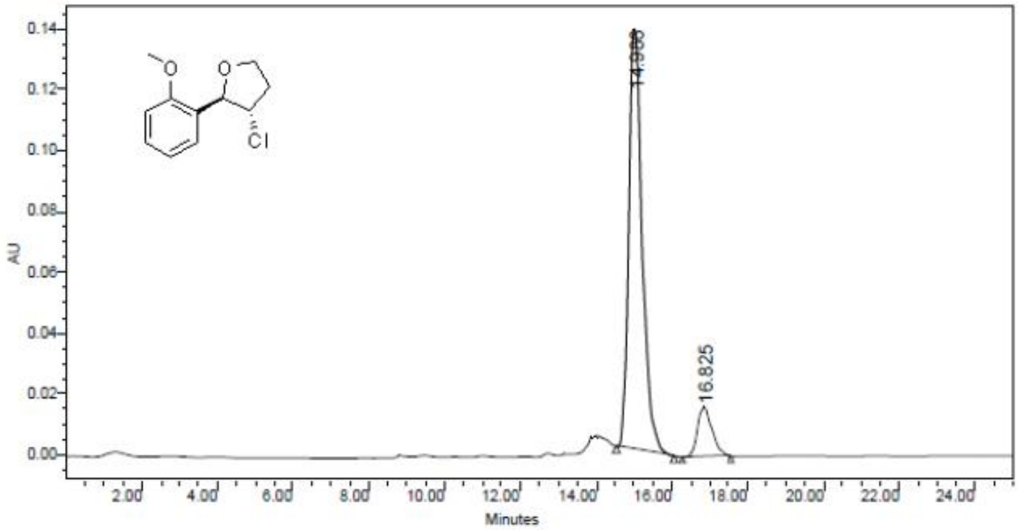


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	10.070	6830620	51.59	468795	64.03
2	16.018	6284736	48.41	263298	35.97

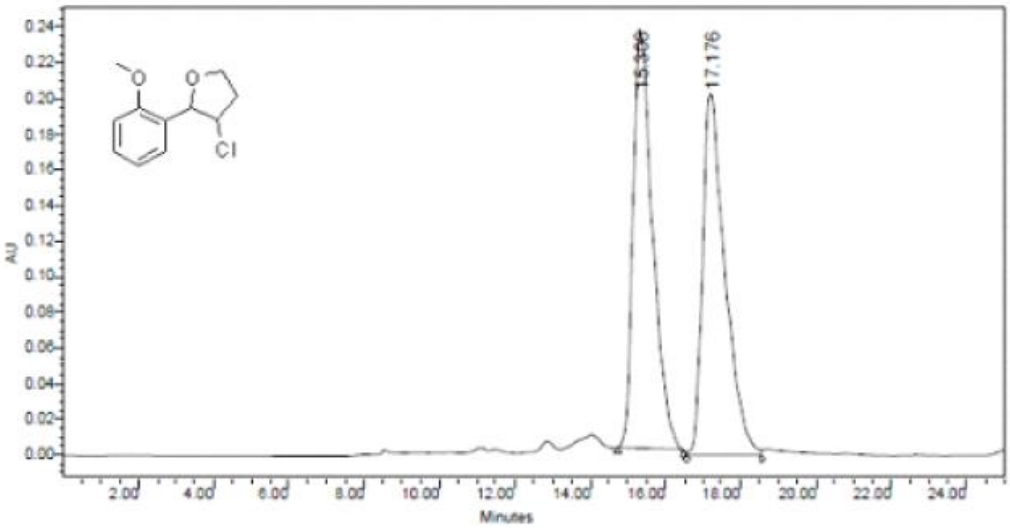


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	9.939	10673785	18.21	636914	27.23
2	15.771	47938269	81.79	1702403	72.77

2e

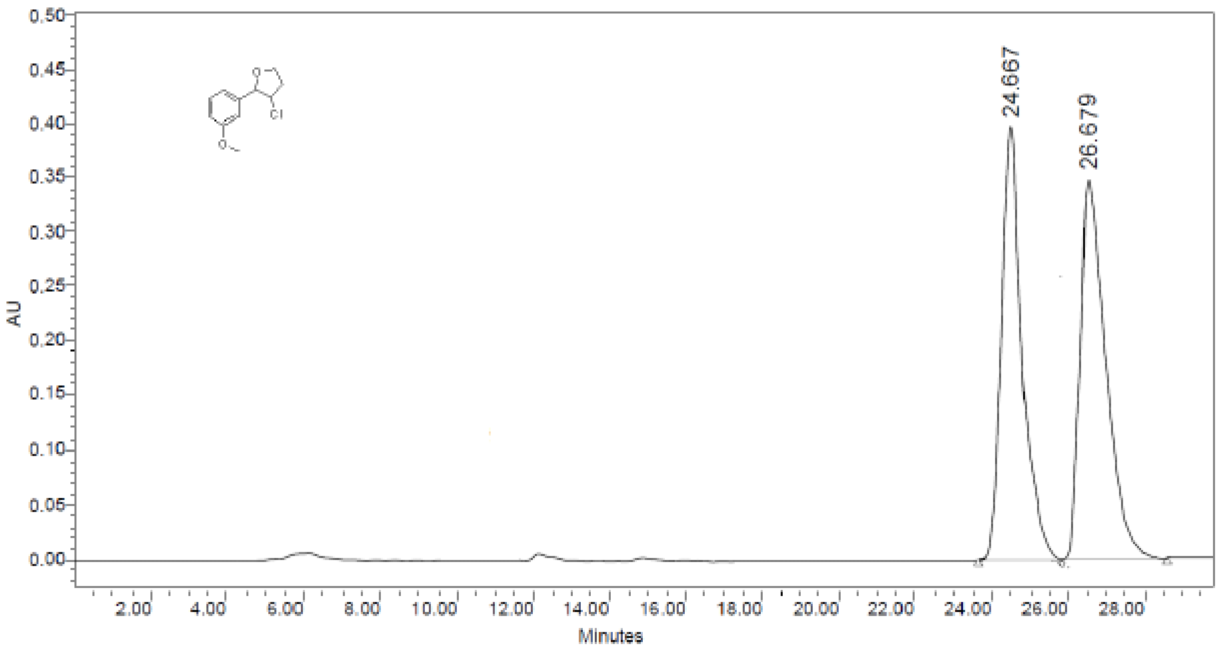


	RT (min)	Area (□V*sec)	%Area	Height (□V)	% Height
1	14.986	3394354	88.55	137865	89.56
2	16.825	439038	11.45	16078	10.44

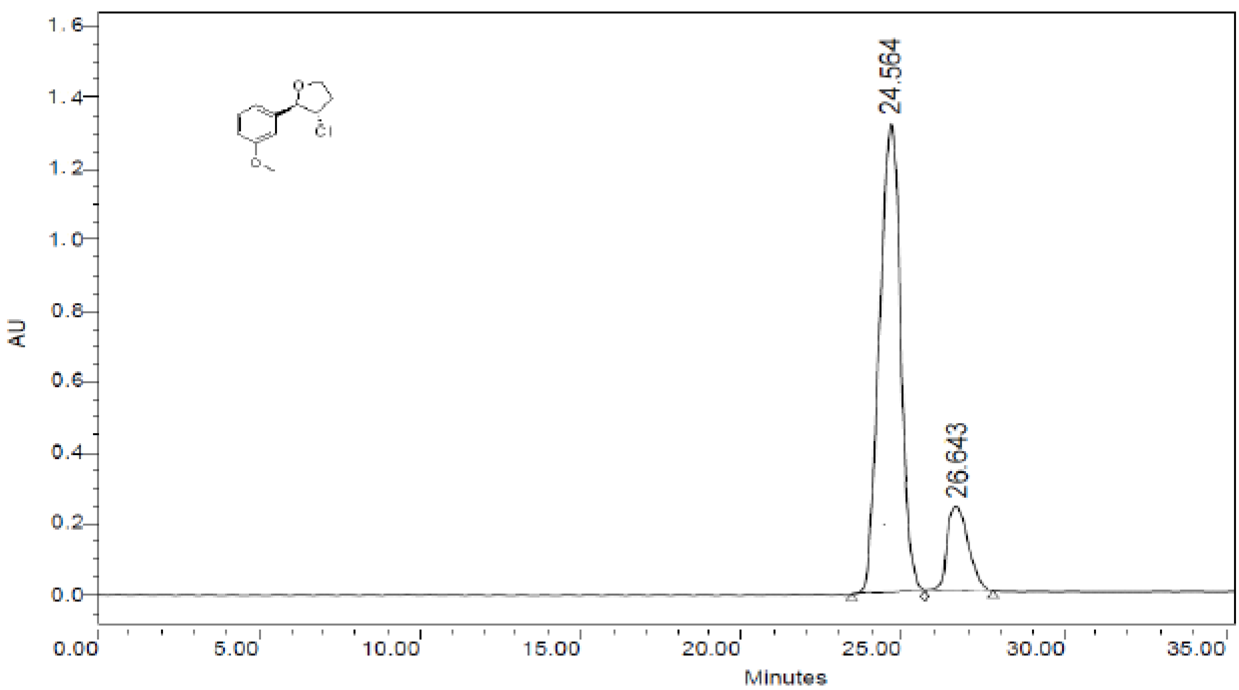


	RT (min)	Area (□V*sec)	%Area	Height (□V)	% Height
1	15.306	6465406	50.08	234748	53.60
2	17.176	6436704	49.92	203195	46.40

2f

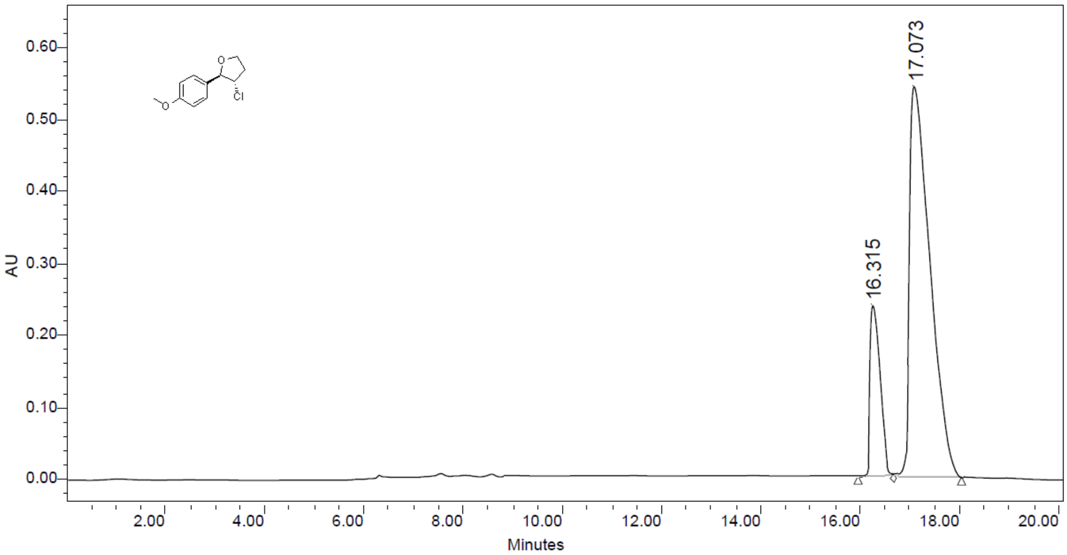


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	24.667	862591	50.53	31876	54.35
2	26.679	848762	49.47	26835	45.65

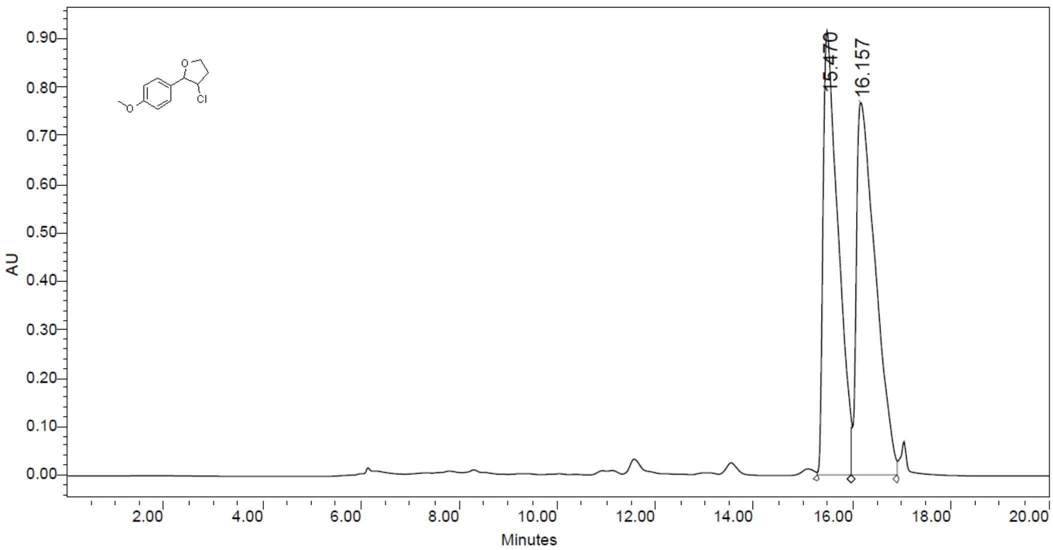


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	24.564	3418901	87.62	85183	85.59
2	26.643	489483	12.38	14336	14.41

2g

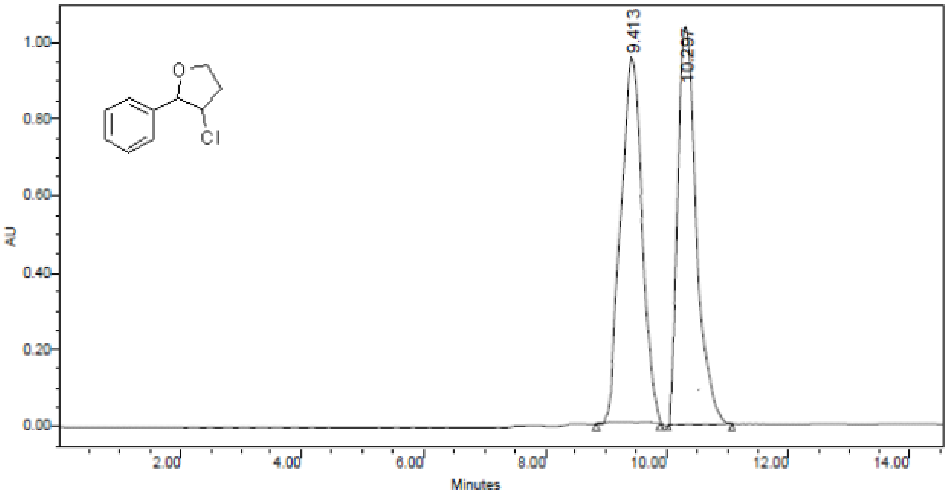


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	16.315	3739251	19.27	316147	31.73
2	17.073	15666163	80.73	544665	68.27

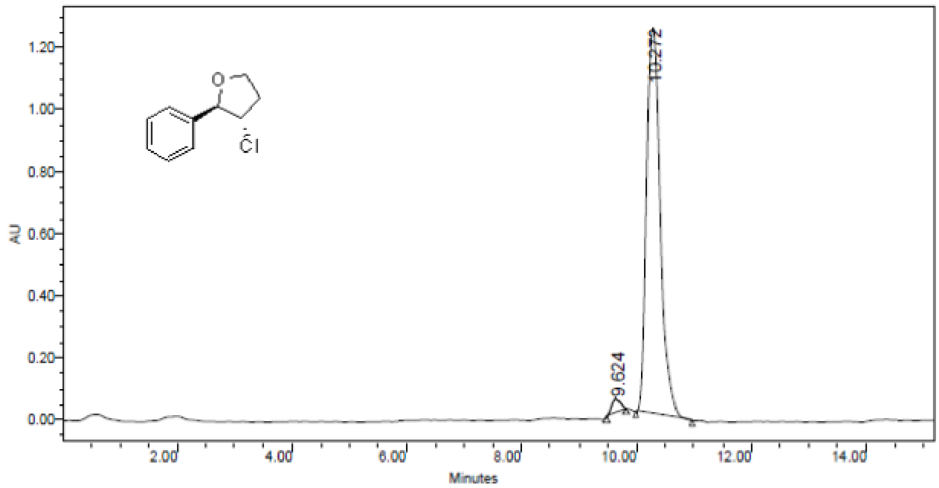


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	15.470	19615509	48.52	918666	54.33
2	16.157	20814418	51.48	772149	45.67

2h

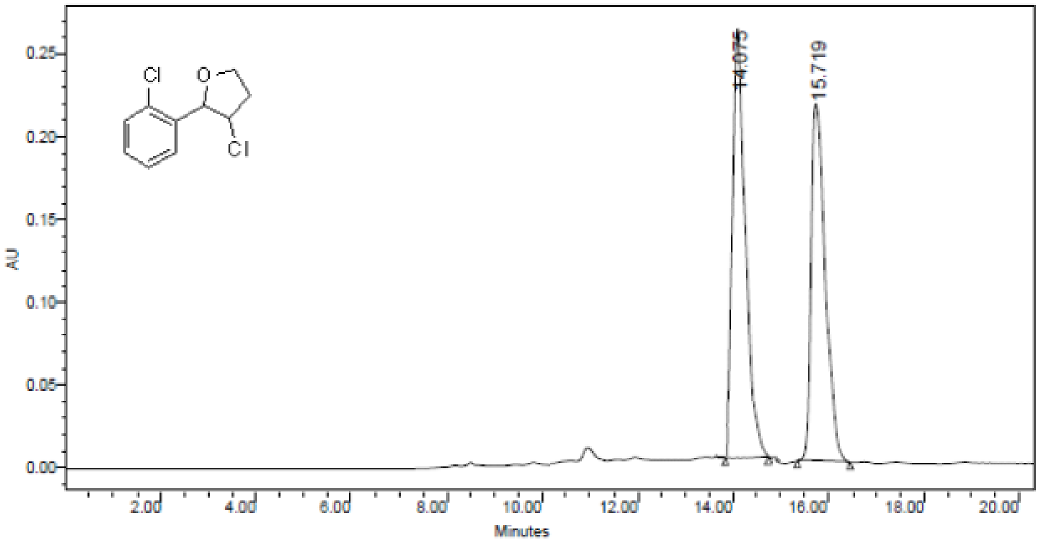


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	9.413	18333059	49.92	825365	46.59
2	10.297	18394369	50.08	946277	53.41

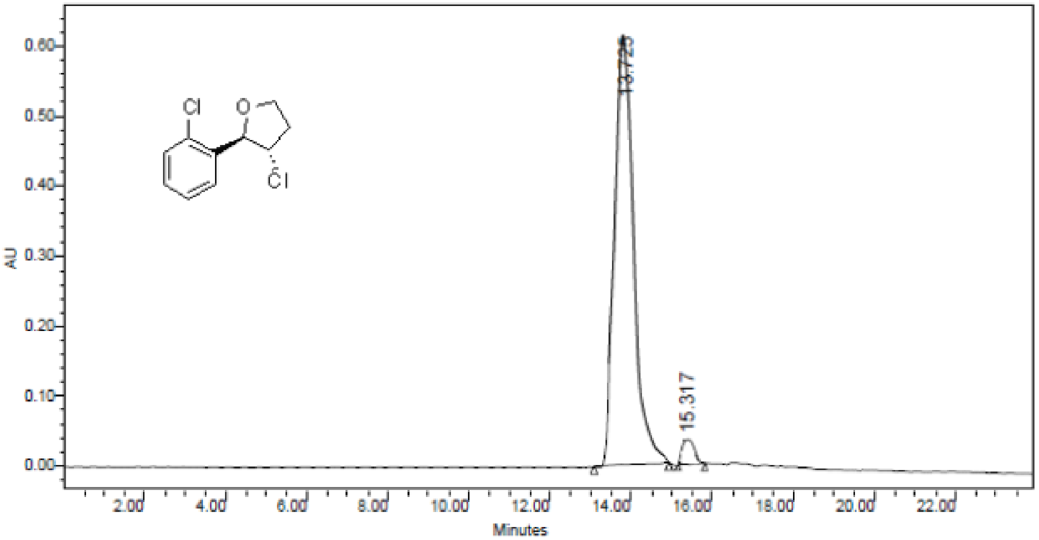


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	9.624	501899	2.37	45802	3.54
2	10.272	20696783	97.63	1248066	96.46

2i

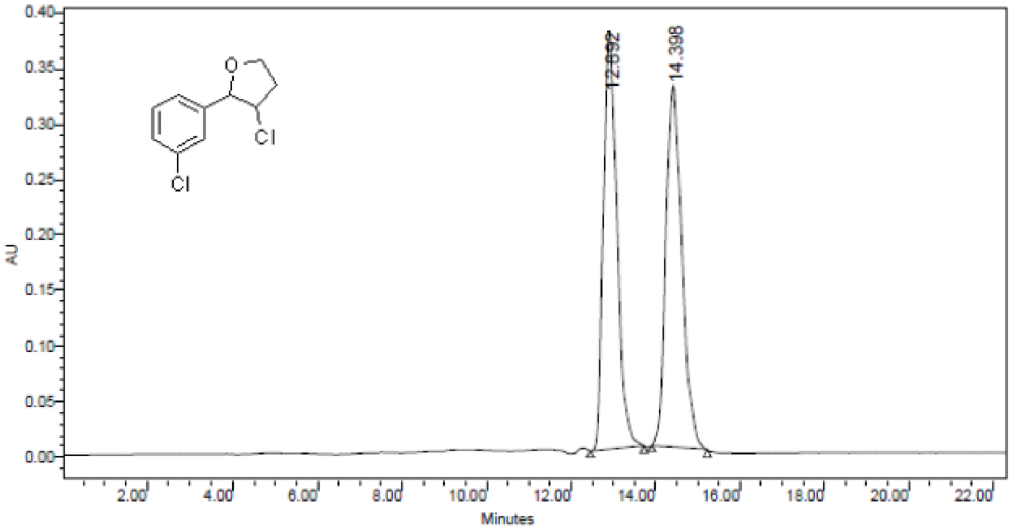


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	14.075	4429594	49.98	249970	53.71
2	15.719	4433705	50.02	215422	46.29

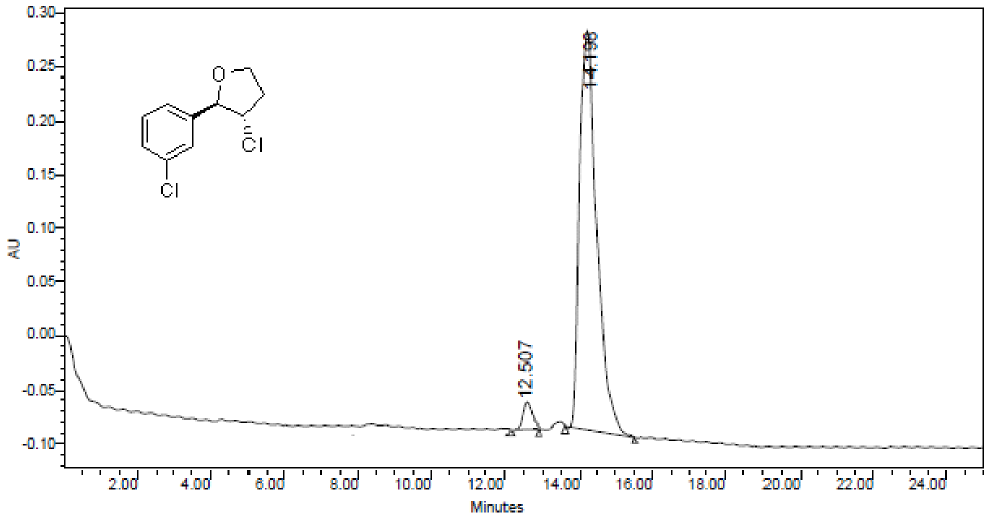


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	13.725	20508720	97.67	615647	95.64
2	15.317	490263	2.33	28080	4.36

2j

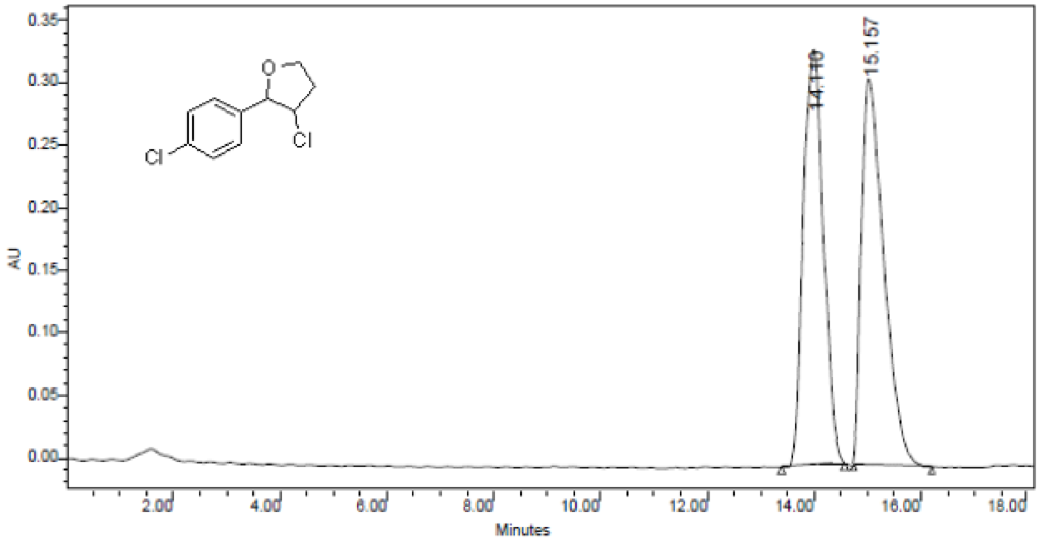


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	12.892	8379830	49.33	377515	53.73
2	14.398	8606311	50.67	325110	46.27

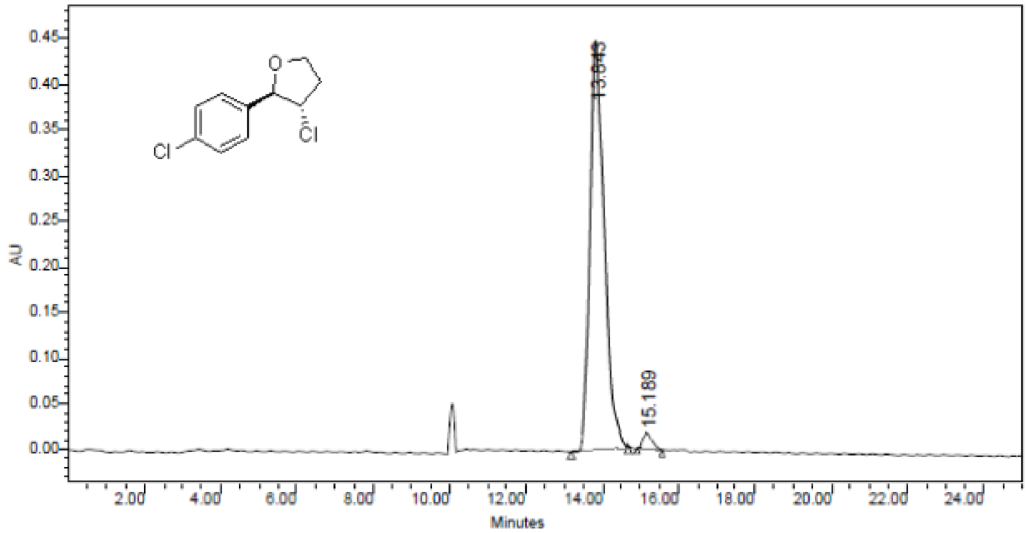


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	12.507	290959	2.33	13805	3.58
2	14.198	12194377	97.67	371330	96.42

2k

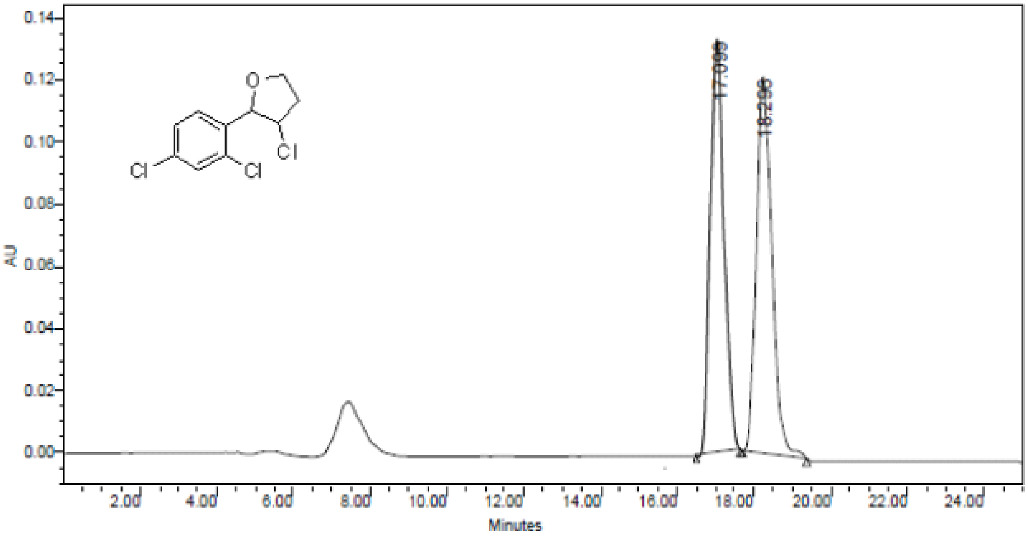


	RT (min)	Area (□V*sec)	%Area	Heigh (□V)	% Heigh
1	14.110	2969176	49.70	179788	54.15
2	15.157	3004894	50.30	152213	45.85

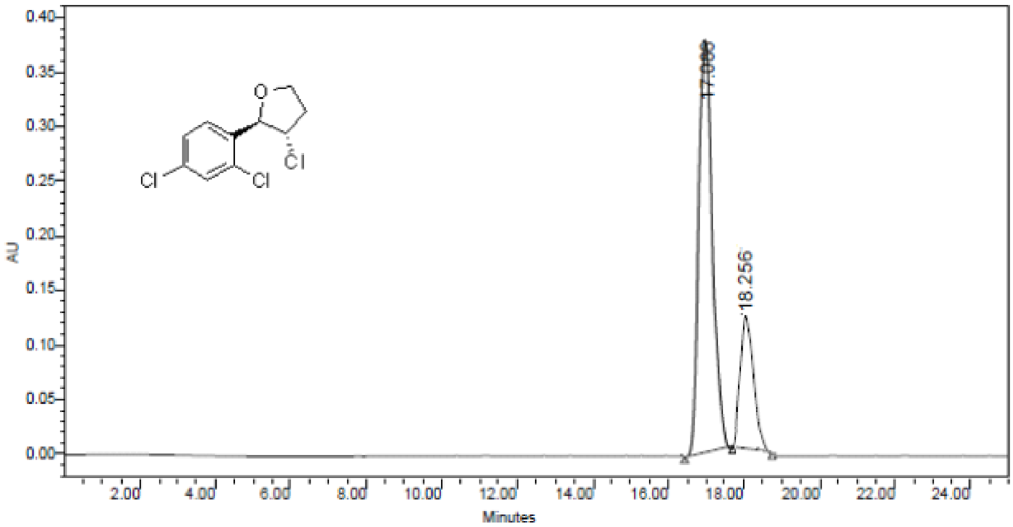


	RT (min)	Area (□V*sec)	%Area	Heigh (□V)	% Heigh
1	13.843	11817789	98.18	446629	96.67
2	15.189	219483	1.82	15376	3.33

2l



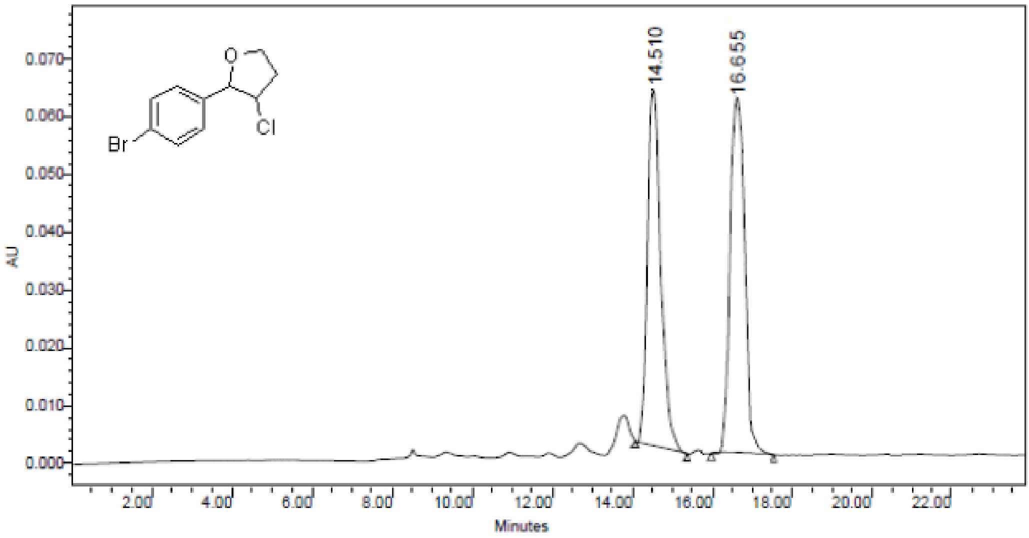
	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	17.099	3327926	49.47	132909	52.33
2	18.296	3399031	50.53	121077	47.67



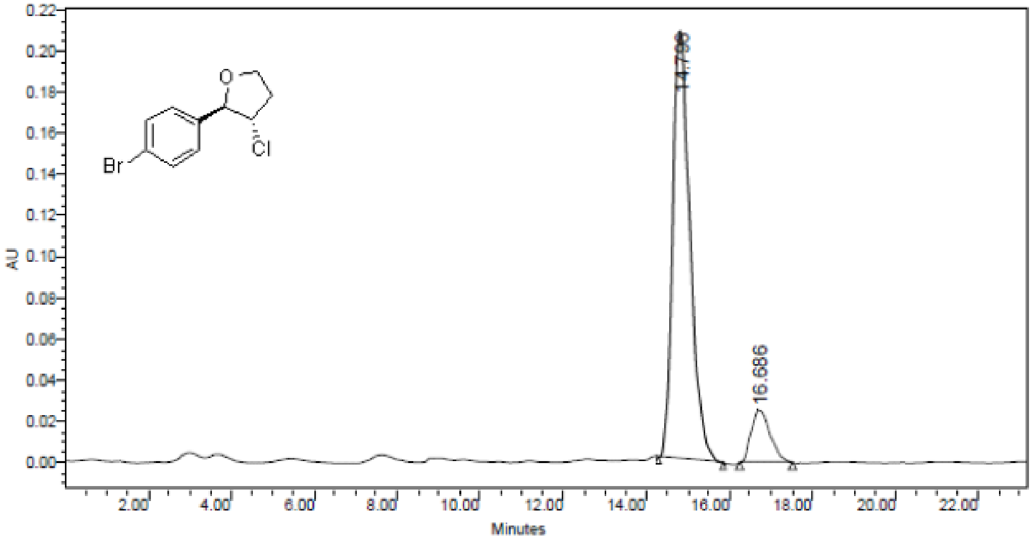
	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	17.086	9559437	76.23	377944	67.28
2	18.256	2980285	23.77	183823	32.72

Electronic Supplementary Material (ESI) for Chemical Communications

2m

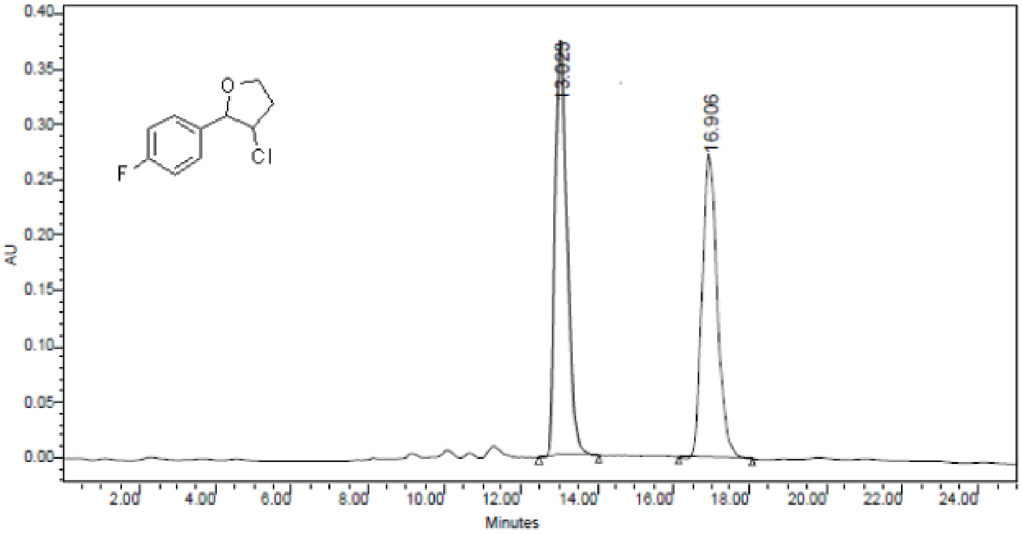


	RT (min)	Area (μV*sec)	%Area	Heigh (μV)	% Heigh
1	14.510	1439506	49.65	61700	50.31
2	16.655	1459546	50.35	60930	49.69

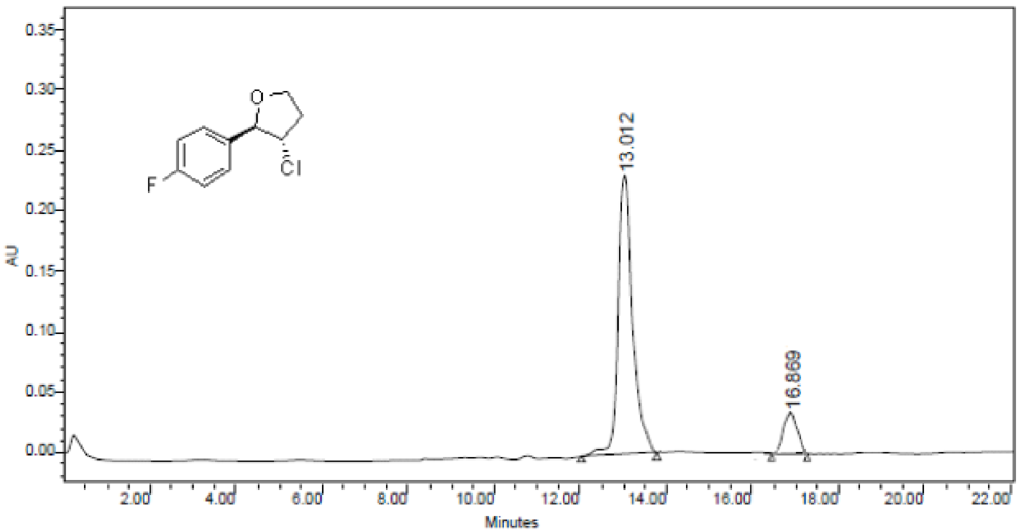


	RT (min)	Area (μV*sec)	%Area	Heigh (μV)	% Heigh
1	14.796	6033948	87.89	208381	88.97
2	16.686	831166	12.11	25840	11.03

2n

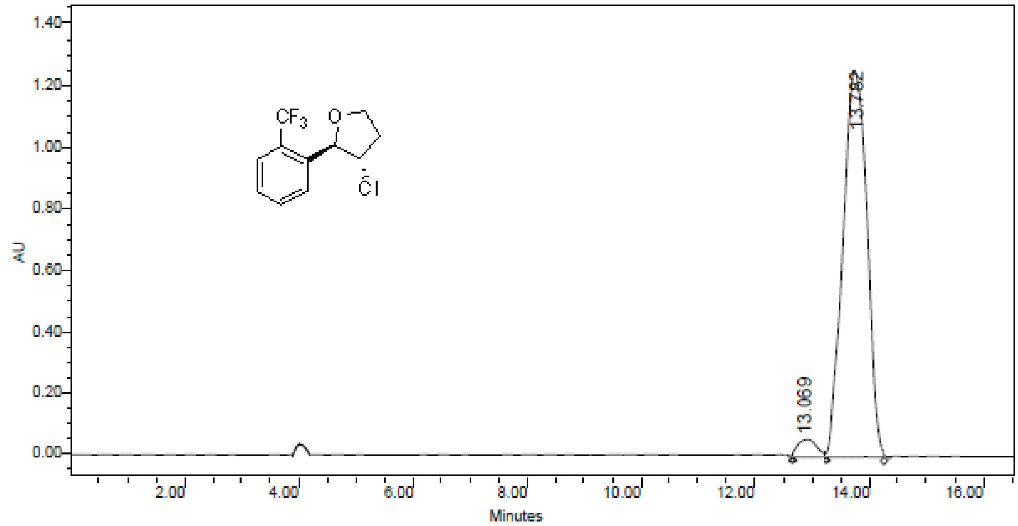


	RT (min)	Area (μV*sec)	%Area	Heigh (μV)	% Heigh
1	13.023	7764916	50.52	367585	57.47
2	16.906	7606255	49.48	272000	42.53

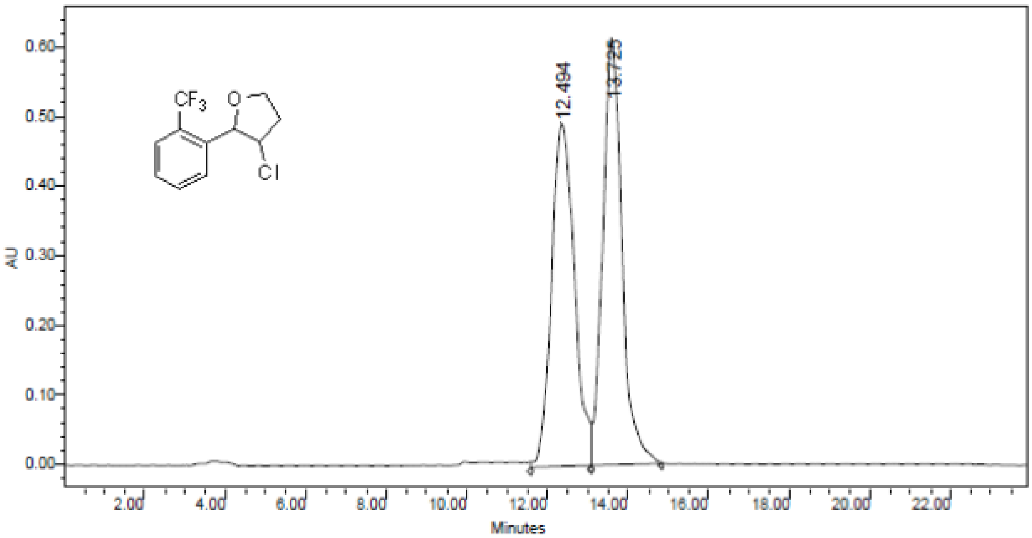


	RT (min)	Area (μV*sec)	%Area	Heigh (μV)	% Heigh
1	13.012	5452249	85.21	230808	86.15
2	16.869	946384	14.79	37109	13.85

2o

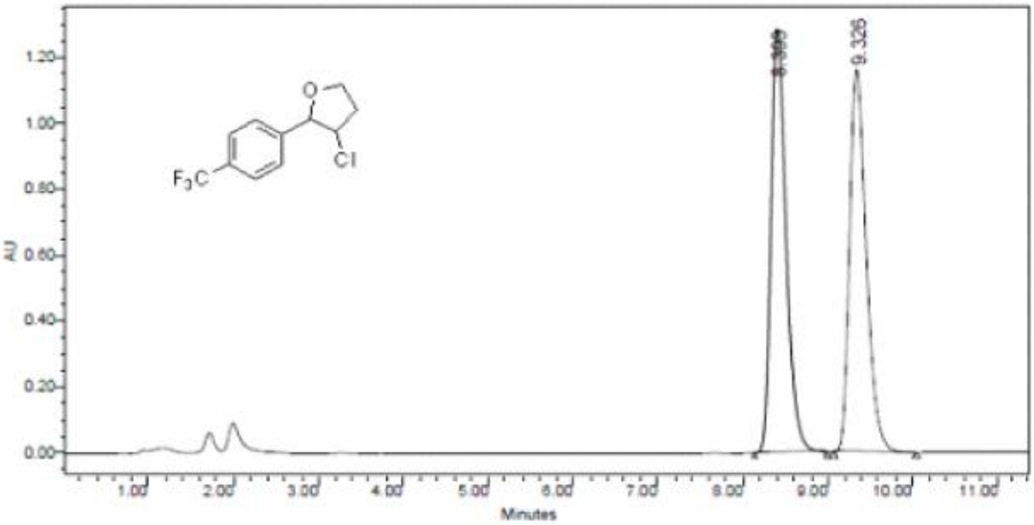


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	13.069	6058162	11.84	178000	11.39
2	13.782	45091749	88.16	1384461	88.61

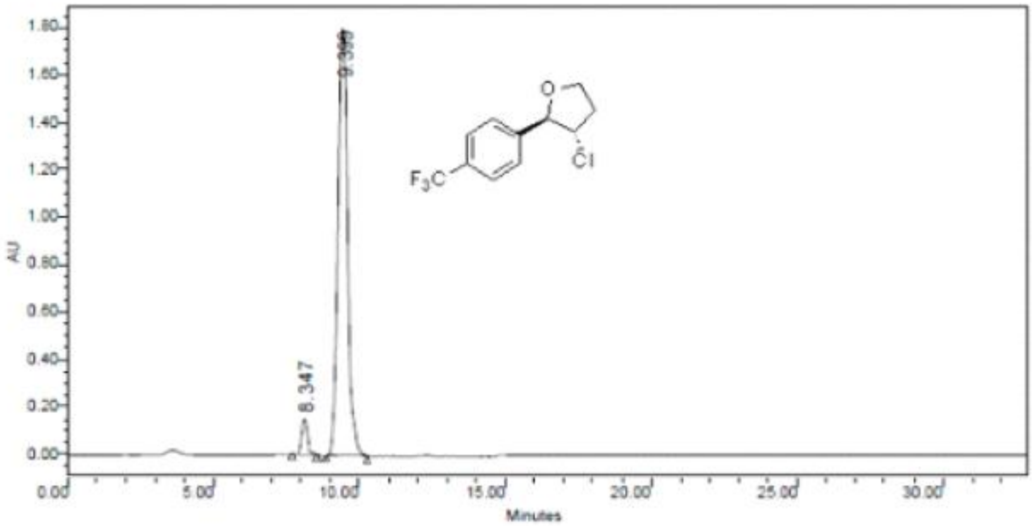


	RT (min)	Area (μV*sec)	%Area	Height (μV)	% Height
1	12.494	19741725	49.05	494665	44.55
2	13.725	20508720	50.95	615647	55.45

2p

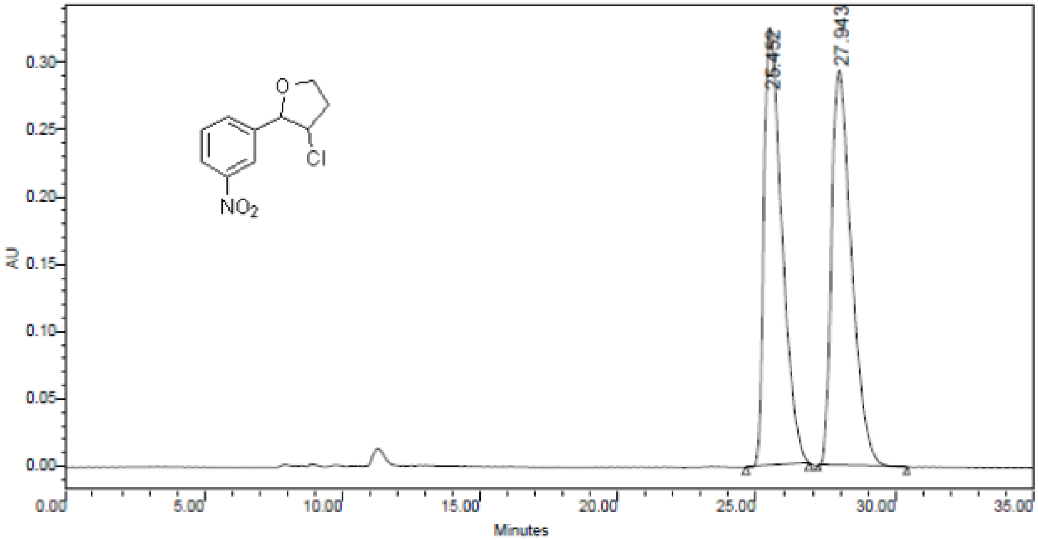


	RT (min)	Area (□V*sec)	% Area	Height (□V)	% Height
1	8.393	15917659	50.12	1288558	52.55
2	9.326	15841584	49.88	1163428	47.45

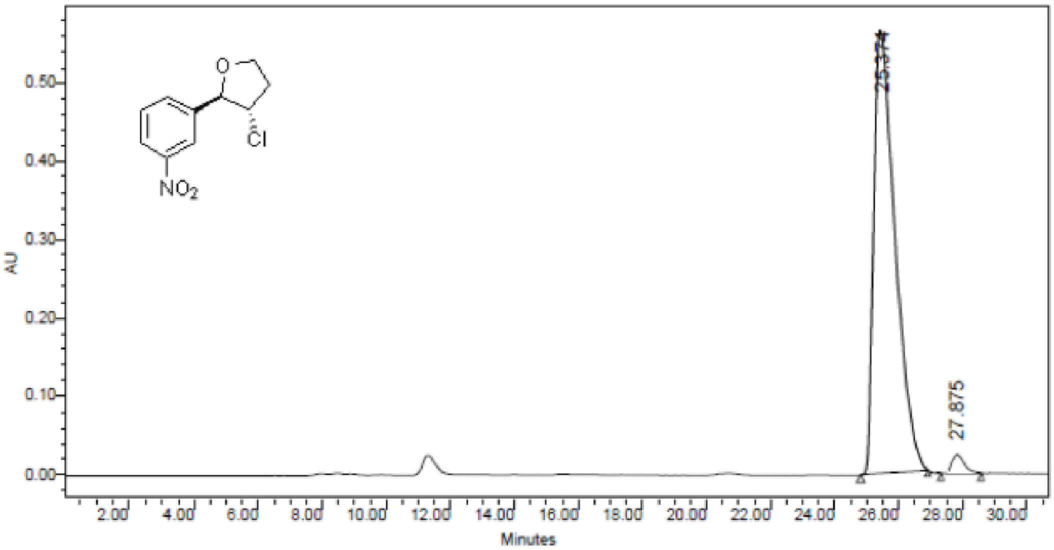


	RT (min)	Area (□V*sec)	% Area	Height (□V)	% Height
1	8.347	895081	2.59	34769	2.03
2	9.399	33692063	97.41	1673989	97.97

2q

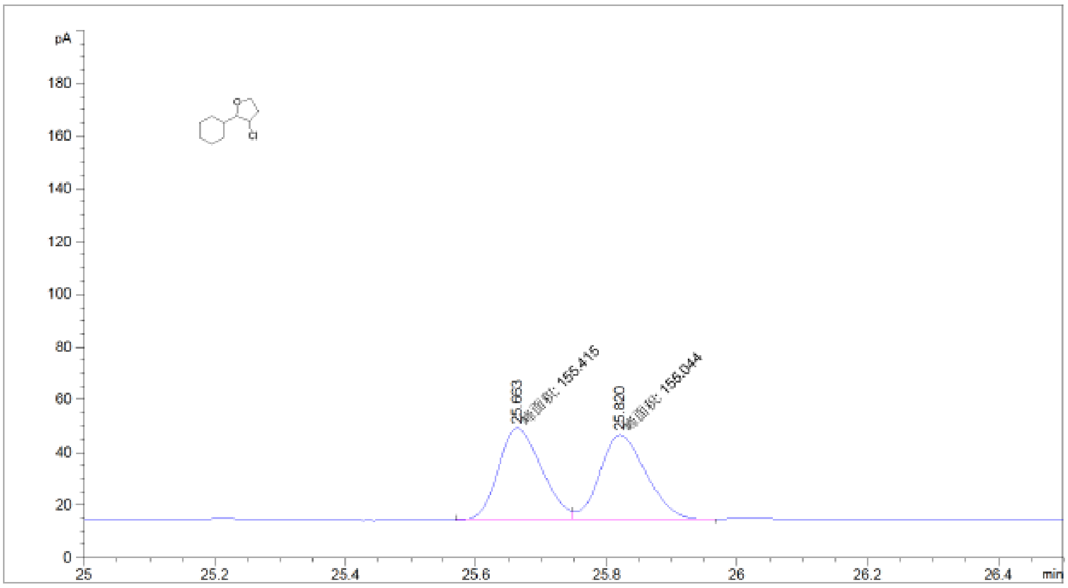


	RT (min)	Area (□V*sec)	%Area	Height (□V)	% Height
1	25.452	14765074	49.98	325081	52.54
2	27.943	14774384	50.02	293704	47.46

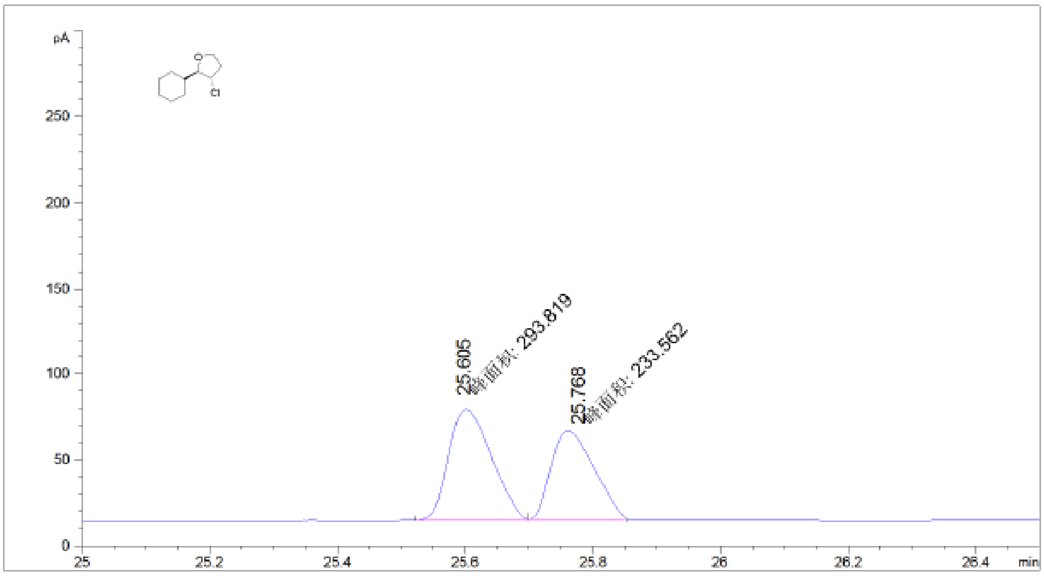


	RT (min)	Area (□V*sec)	%Area	Height (□V)	% Height
1	25.374	26177984	98.13	566184	92.30
2	27.875	498759	1.87	47224	7.70

2r

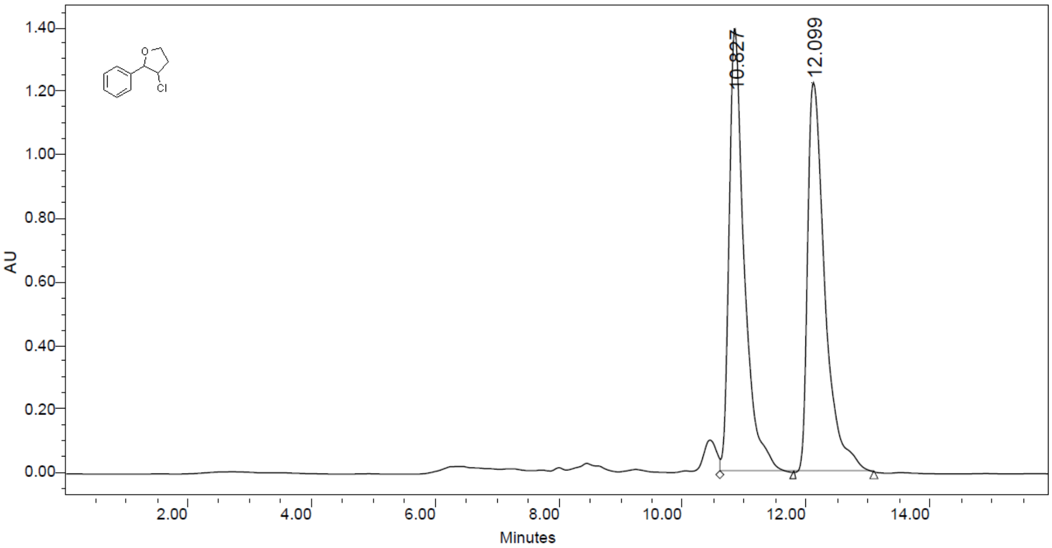


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [pA*s]	峰高 [pA]	峰面积 %
1	25.663	MF T	0.0756	155.41458	34.26678	50.05974
2	25.820	FM T	0.0815	155.04362	31.71597	49.94026

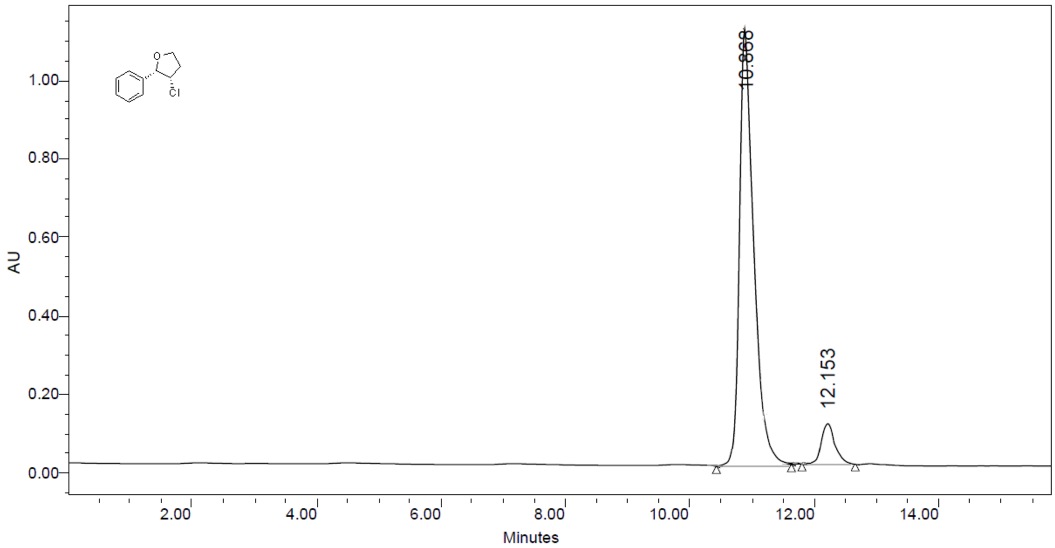


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [pA*s]	峰高 [pA]	峰面积 %
1	25.605	MM	0.0771	293.81860	63.47786	55.71279
2	25.768	MM	0.0763	233.56227	50.98784	44.28721

2t

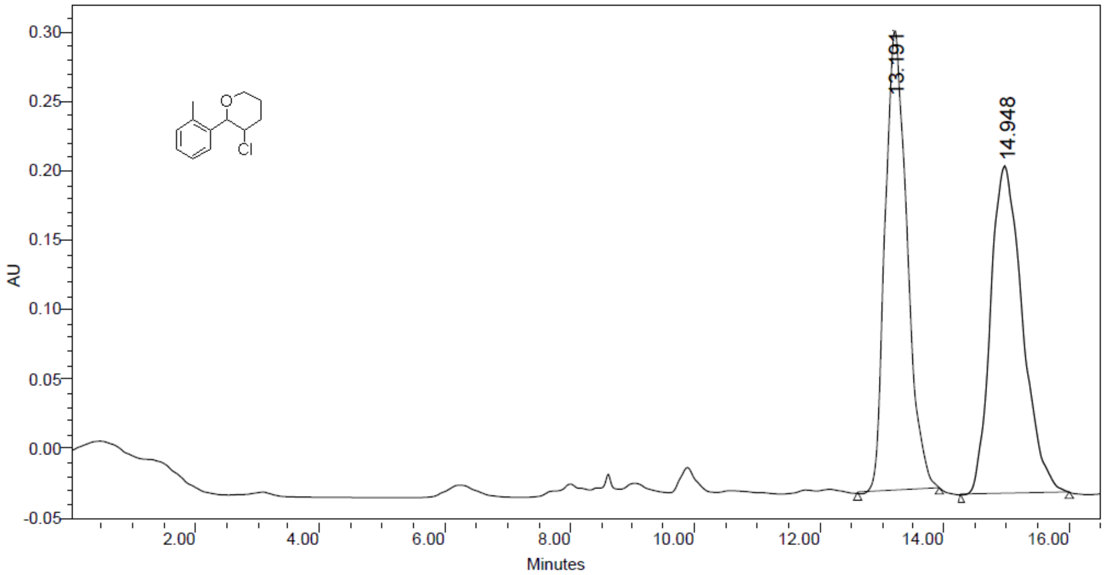


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Heigh
1	10.827	23812576	49.85	1395584	53.23
2	12.099	23951561	50.15	1226077	46.77

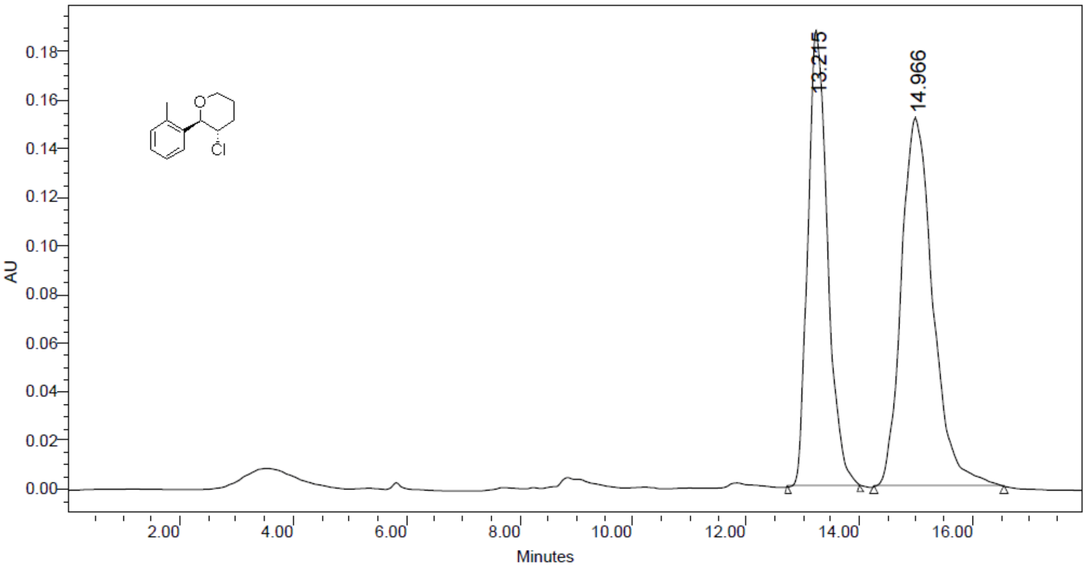


	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Heigh
1	10.868	17630369	91.92	1125905	82.48
2	12.153	1549137	8.08	239128	17.52

2u



	RT (min)	Area (□V*sec)	%Area	Heigh (□V)	% Heigh
1	13.191	8148714	49.19	332095	58.46
2	14.948	8418298	50.81	235998	41.54



	RT (min)	Area (□V*sec)	%Area	Heigh (□V)	% Heigh
1	13.215	4556043	43.49	187678	55.29
2	14.966	5919571	56.51	151792	44.71