# endo-Selective Construction of Spiro-[butyrolactone-pyrrolidine] via Ag(I)/CAAA-Amidphos-Catalyzed 1,3-Dipolar Cycloaddition Between Azomethine Ylides and α-Methylene-γ-butyrolactone

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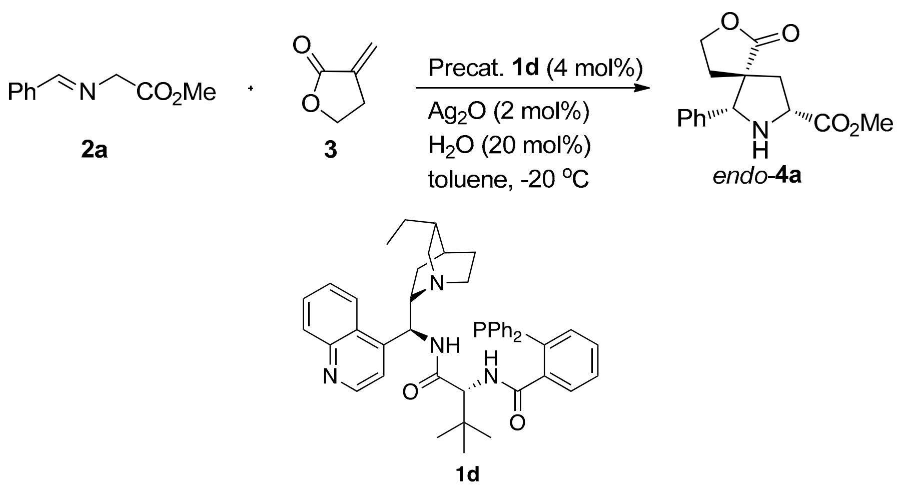
## contents

## A. General Information

$^1H$ and $^{13}C$ NMR spectra were recorded on Bruker AV-400 spectrometers in $CDCl_3$ unless otherwise noted. $CDCl_3$ served as internal standard ($\delta$ = 7.26) for $^1H$ NMR and ($\delta$ = 77.0) for $^{13}C$ NMR. Diastereomeric ratios were determined from $^1H$ NMR or HPLC analysis. High-performance liquid chromatography was carried out using a Agilent 1260 apparatuse which equipped with a spectrophotometric detector (monitoring at 205-230 nm) using a Daicel chiral AS-H 、AD-H column with hexane and i-PrOH as solvents . The toluene used for 1,3-Dipolar Cycloaddition of Imino Esters with α-methylene-γ-butyrolactone has not been dehydrated, and other solvents are used after reevaporation. The α-methylene-γ-butyrolactone were purchased from Adamas-beta® Co., Ltd.. Commercially available reagents were used without further purification. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates (qingdaohaiyang GF254). Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or potassium permanganate stains. Flash column chromatography was performed using silica gel 200-300 (particle size 0.0040–0.0750 mm) from Qingdaohaiyang. Precat. **1a-1d** were synthesized according to our previous work.[1] The absolute configuration of **6e** was determined unequivocally according to the XRD, and those of other product were deduced on the basis of these results.

## B. General Procedure for 1,3-Dipolar Cycloaddition of Imino Esters with α-methylene-γ-butyrolactone

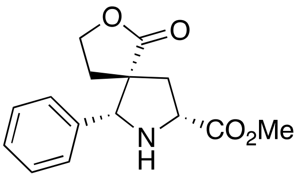



To a solution of Precat. **1d** (5.57 mg, 0.008 mmol) in toluene (1.4 mL) was added Ag2O

(0.92 mg, 0.004 mmol), followed by water dropwise (0.72 mg, 0.04 mmol) at room temperature under $N_2$ atmosphere. After the reaction mixture was stirred for 1 h, α-imino ester **2** (0.30 mmol) and α-methylene-γ-butyrolactone **3** (19.6 mg, 0.20 mmol) was successively added at -20 ºC. The reaction was monitored by TLC plate, and the residue was purified by silica gel column chromatography to afford the spiro *endo*-**4** adducts.

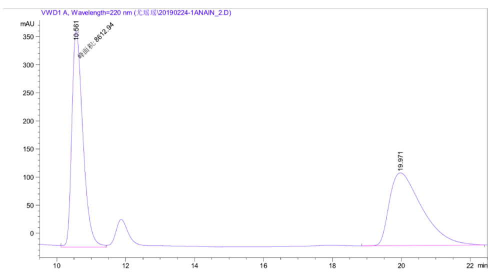
## C. Analytical data and HPLC chromatogram of the [3 + 2] cyclization products of α-iminoesters and the α-methylene-γ-butyrolactone

**(5S,6R,8R)-Methyl 1-oxo-6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4a)**

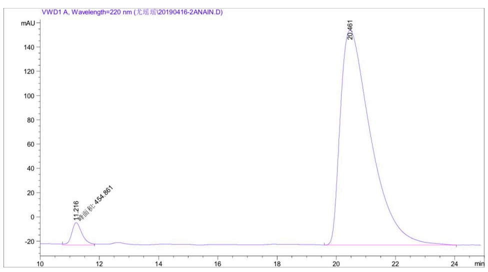



**4a**

White solid, yield: 51 mg (92%); Mp.110-115℃; $[\alpha]_D^{30}$ = -28.3 (*c* 0.40, $CH_2Cl_2$); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.01-7.34 (m, 5H), 4.16 (s, 1H), 4.08-4.02 (m, 2H), 3.84 (s, 3H), 3.51 (dd, J = 17.2, 9.2 Hz, 1H), 2.69 (dd, J = 13.2, 5.2 Hz, 1H), 2.51-2.43 (m, 1H), 2.33 (dd, J = 13.4, 8.4 Hz, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.7, 173.3, 136.6, 128.9, 127.1, 73.3, 65.2, 58.9, 53.7, 52.4, 40.4, 32.9; IR (film): *ν* (cm$^{-1}$) 3348，2950，2914，1769，1730，1459，1373，1173，1025，953，701，534; The ee value was 93%, $t_R$ (major) = 20.46 min, $t_R$(minor) =11.21 min (Chiralcel AS-H, λ = 220 nm, $^i$PrOH/hexanes 50:50, flow rate = 1 mL/min).

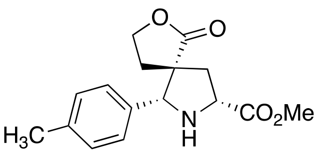



| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 10.561 | MM | 0.3731 | 8612.93555 | 384.77356 | 50.1695 |
| 2 | 19.971 | BV | 0.9754 | 8554.75000 | 129.60376 | 49.8305 |




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 11.216 | MM | 0.4085 | 454.86072 | 18.55841 | 3.4736 |
| 2 | 20.461 | BB | 1.0773 | 1.26399e4 | 177.09586 | 96.5264 |

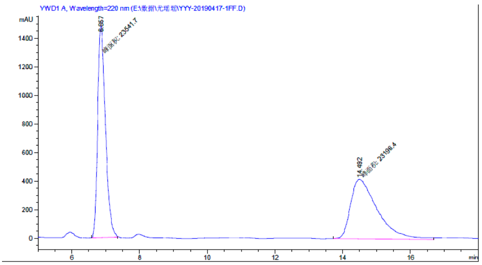
**(5S,6R,8R)-Methyl 1-oxo-6-(p-tolyl)-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4b)**



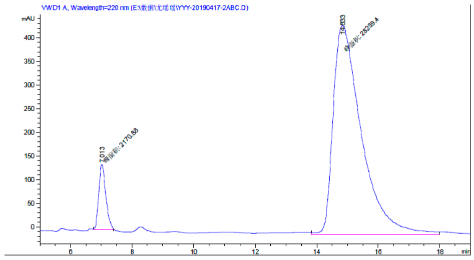

**4b**

Colorless oil, yield: 52 mg (90%); $[\alpha]_D^{30}$ = -6.27 (*c* 1.35, $CH_2Cl_2$); $^1$H-NMR (400 MHz,

$CDCl_3$) δ 7.27 (d, J = 7.2 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 4.12 (s, 1H), 4.07-4.01 (m, 2H), 3.83 (s, 1H), 3.52 (q, J = 8.4 Hz, 1H), 2.68 (dd, J = 13.2, 5.2 Hz, 1H), 2.50-2.40 (m, 1H), 2.34-2.28 (m, 6H),1.72(brs, 1H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.8, 173.3, 138.7, 133.5, 129.6, 127.0, 73.2, 65.2, 58.9, 53.6, 52.4, 40.4, 32.9, 21.1; IR (film): *ν* ($cm^{-1}$) 3328，2956，2863，1760，1745，1513，1376，1168，1028，778，647，531； The ee value was 86%, $t_R$ (major) = 14.83 min, $t_R$(minor) =7.01 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

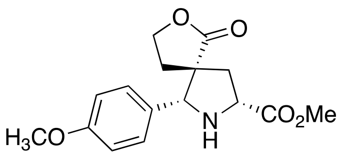


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.857 | MM | 0.2655 | 2.35417e4 | 1477.99475 | 50.3694 |
| 2 | 14.492 | MM | 0.9251 | 2.31964e4 | 417.91733 | 49.6306 |



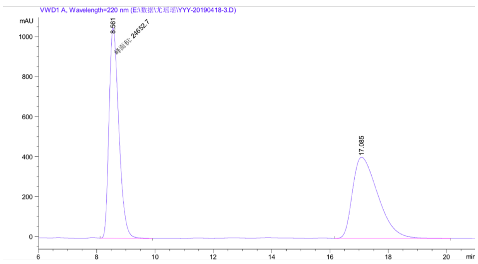
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 7.013 | MM | 0.2640 | 2170.87817 | 137.06865 | 7.1386 |
| 2 | 14.833 | MM | 1.0645 | 2.82394e4 | 442.13751 | 92.8614 |

**(5S,6R,8R)-Methyl 6-(4-methoxyphenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxyl-ate (4c)**

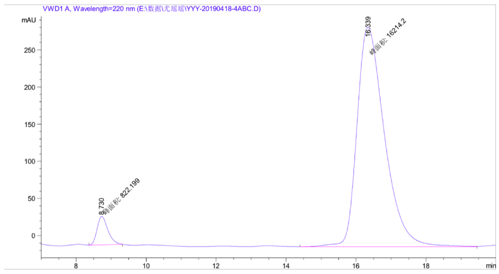


**4c**

Colorless oil, yield: 57 mg (91%); $[\alpha]_D^{30}$ = +8.414 (*c* 1.3, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 4.11 (s, 1H), 4.06-4.02 (m, 2H), 3.83-3.76 (m, 6H), 3.52 (dd, J = 17.2, 8.8 Hz, 1H), 2.68 (dd, J = 13.4, 4.8 Hz, 2H), 2.50-2.42 (m, 1H), 2.34-2.26 (m, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.9, 173.3, 159.9, 128.3, 114.2, 72.9, 65.2, 58.8, 55.2, 53.5, 52.4, 40.3, 32.9; IR (film): *ν* ($cm^{-1}$) 3331，2962，2840，1757，1742，1516，1379，1177，1028，781，644，537; The ee value was 90%, $t_R$ (major) = 16.33 min, $t_R$(minor) =8.73 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

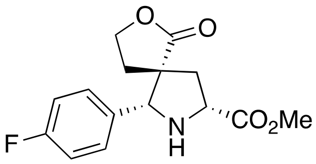


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.561 | MM | 0.3898 | 2.46527e4 | 1054.05408 | 50.0421 |
| 2 | 17.085 | BB | 0.9386 | 2.46112e4 | 406.89981 | 49.9579 |



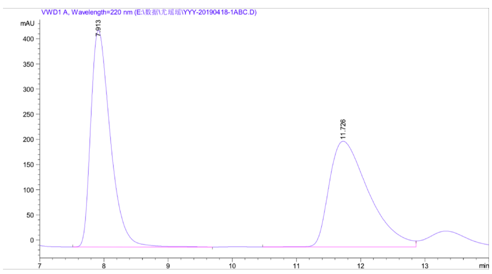
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.730 | MM | 0.3573 | 822.19867 | 38.35753 | 4.8261 |
| 2 | 16.339 | MM | 0.9147 | 1.62142e4 | 295.43259 | 95.1739 |

**(5*S*,6*R*,8*R*)-Methyl 6-(4-fluorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4d)**

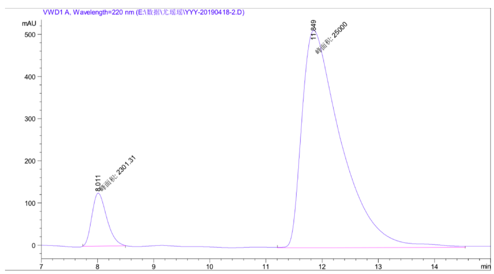


**4d**

White solid, yield: 53 mg (91%); Mp.125-127℃; $[\alpha]_D^{30}$ = -10.56 (*c* 0.8, $CH_2Cl_2$); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, J = 8.6, 5.4 Hz, 2H), 7.03 (t, J = 8.4 Hz, 2H), 4.16 (s, 1H), 4.09-4.00 (m, 2H), 3.82 (s, 3H), 3.58-3.52 (m, 1H), 2.77 (brs, 1H), 2.68 (dd, J = 13.4, 5.4 Hz, 1H), 2.49-2.41(m, 1H),2.34-2.28 (m, 1H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.5, 173. 2, 164.1, 161.7, 132.5, 128.9, 128.8, 115.9, 115.7, 72.3, 65.1, 58.7, 53.5, 52.4, 40.0, 32.9; IR (film): *v* (cm$^{-1}$) 3343, 2998, 2956, 1756, 1610, 1512, 1378, 1179, 1027, 849, 656, 543; The ee value was 83%, $t_R$ (major) = 11.84 min, $t_R$(minor) =8.01 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

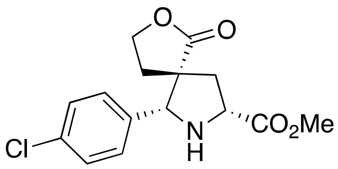


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 7.913 | BB | 0.3242 | 9120.29590 | 430.70453 | 50.2805 |
| 2 | 11.726 | BV | 0.6552 | 9018.54199 | 210.07019 | 49.7195 |



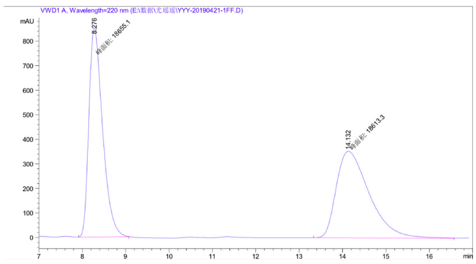
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.011 | MM | 0.3057 | 2301.30786 | 125.45576 | 8.4293 |
| 2 | 11.849 | MM | 0.8092 | 2.50000e4 | 514.91333 | 91.5707 |

**(5S,6R,8R)-Methyl 6-(4-chlorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4e)**

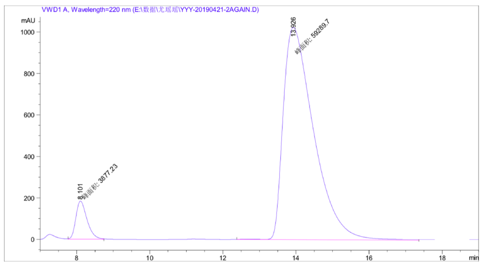


**4e**

Colorless oil, yield: 55 mg (88%); $[\alpha]_D^{30}$ = +17.922 (*c* 1.5, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.36-7.29 (m, 4H), 4.16 (s, 1H), 4.11-4.03 (m, 2H), 3.83 (s, 3H), 3.64-3.56 (m, 1H), 2.69 (dd, J = 13.4, 5.6 Hz, 1H), 2.50-2.42 (m, 2H), 2.35-2.29 (m, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.3, 173.2, 135.4, 134.7, 129.1, 128.6, 72.3, 65.2, 58.8, 53.6, 52.5, 40.1, 33.0; IR (film): *v* (cm$^{-1}$) 3337, 2953, 2917, 1763, 1438, 1212, 1177, 1028, 831, 671, 543; The ee value was 88%, $t_R$ (major) = 13.92 min, $t_R$(minor) =8.10 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

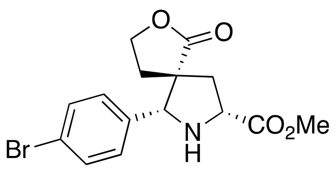


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.276 | MM | 0.3653 | 1.86551e4 | 851.14136 | 50.0560 |
| 2 | 14.132 | MM | 0.8800 | 1.86133e4 | 352.53094 | 49.9440 |



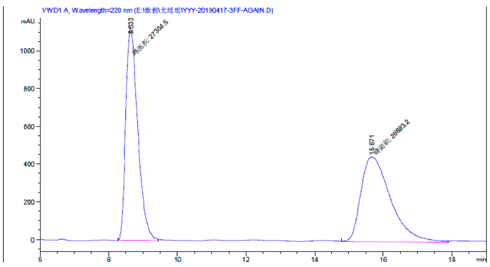
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.101 | MM | 0.3515 | 3877.22681 | 183.83273 | 6.1381 |
| 2 | 13.926 | MM | 0.9653 | 5.92897e4 | 1023.64642 | 93.8619 |

**(5S,6R,8R)-Methyl 6-(4-bromophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylat -e (4f)**

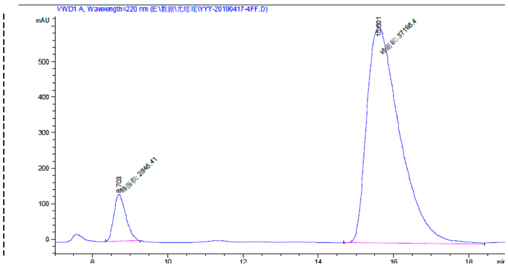


**4f**

Colorless oil, yield: 66 mg (93%); $[\alpha]_D^{30}$ = -10.19 (*c* 1.15, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7 .47 (d, J = 8.4 Hz, 2H), 7 .28 (d, J = 8.4 Hz, 2H), 4.14 (s, 1H), 4.11-4.02 (m, 2H), 3.82 (s, 3H), 3.63-3.57 (m, 1H), 2.68 (dd, J = 13.2, 5.6 Hz, 1H), 2.49-2.41 (m, 2H),, 2.35-2.28 (m, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ178.3,173.2,135.9,132.0,128.9,122.8, 72.3,65.2,53.5,52.5,40.1,33.0; IR (film): *v* (cm$^{-1}$) 3372, 2956, 2917, 1748, 1492, 1438, 1206, 1177, 1028, 820, 739, 537; The ee value was 85%, $t_R$ (major) = 15.60 min, $t_R$(minor) =8.70 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

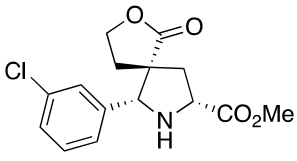


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.633 | MM | 0.4045 | 2.73045e4 | 1125.00171 | 50.3888 |
| 2 | 15.671 | MM | 0.9955 | 2.68832e4 | 450.08875 | 49.6112 |



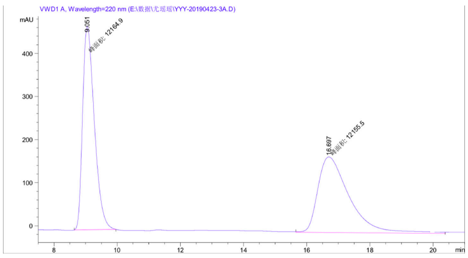
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.703 | MM | 0.3732 | 2946.41284 | 131.57155 | 7.3450 |
| 2 | 15.601 | MM | 1.0208 | 3.71684e4 | 606.86835 | 92.6550 |

**(5S,6R,8R)-Methyl 6-(3-chlorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4g)**

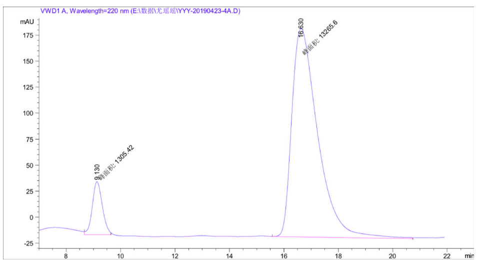


**4g**

Colorless oil, yield: 55 mg (89%); $[\alpha]_D^{30}$ = -14.751 (*c* 1.35, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H),7.32-7.30 (m, 4H), 4.14 (s, 1H), 4.13-4.03 (m, 2H), 3.83 (s, 3H), 3.68-3.61 (m, 1H), 2.69 (dd, J = 13.4, 5.4 Hz, 1H), 2.50-2.42 (m, 1H), 2.40-2.25 (m, 1H), 2.38-2.30 (m, 1H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.2, 173.1, 139.1, 134.6, 130.2, 129.0, 127.7, 125.2,72.3, 65.2, 58.8, 53.6, 52.5, 40.2, 33.1; IR (film): *ν* ($cm^{-1}$) 3387, 2965, 2714, 1763, 1733, 1572, 1450, 1367, 1177, 1028, 727, 540; The ee value was 82%, $t_R$ (major) = 16.63 min, $t_R$(minor) =9.13 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

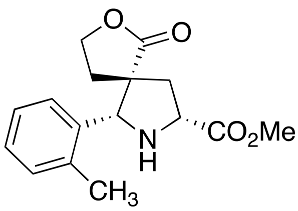


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 9.051 | MM | 0.4296 | 1.21649e4 | 471.93881 | 50.0194 |
| 2 | 16.697 | MM | 1.1536 | 1.21555e4 | 175.61247 | 49.9806 |



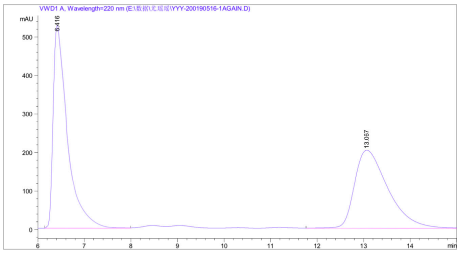
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 9.130 | MM | 0.4272 | 1305.41907 | 50.93499 | 8.9590 |
| 2 | 16.630 | MM | 1.1025 | 1.32656e4 | 200.53349 | 91.0410 |

**(5*S*,6*R*,8*R*)-Methyl 1-oxo-6-(*o*-tolyl)-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4h)**

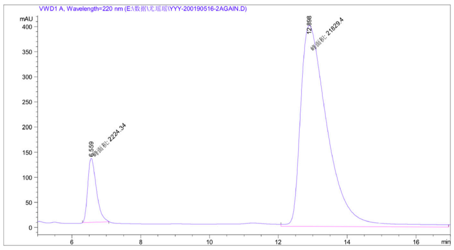


**4h**

White solid, yield: 54 mg (94%); Mp.103-105℃; $[\alpha]_D^{30}$ = -11.27 (*c* 1.83, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 7.2, 1.6 Hz, 1H), 7.24-7.13 (m, 3H), 4.58 (s, 1H), 4.08-4.00 (m, 2H), 3.82 (s, 3H), 3.55-3.49 (m, 1H), 2.89 (brs, 1H), 2.68 (dd, J = 13.6, 5.6 Hz, 1H), 2.46-2.29 (m, 6H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.8, 173.3, 135.5, 135.2, 130.7, 128.1, 126.9, 126.2, 66.9, 65.1, 58.8, 54.0, 52.4, 40.2, 33.1, 20.0; IR (film): *v* ($cm^{-1}$) 3372, 2982, 2959, 1757, 1736, 1489, 1489, 1379, 1263, 1174, 1019, 748, 683; The ee value was 82%, $t_R$ (major) = 12.89 min, $t_R$(minor) =6.55 min (Chiralcel AS-H, λ = 220 nm, $^i$PrOH/hexanes 50:50, flow rate = 1 mL/min).

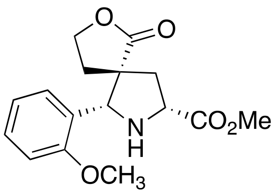


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.416 | BV | 0.2903 | 9953.96484 | 523.53442 | 49.6024 |
| 2 | 13.067 | BB | 0.7613 | 1.01135e4 | 202.65030 | 50.3976 |



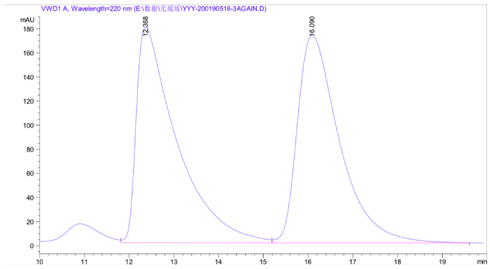
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.559 | MM | 0.2900 | 2224.33911 | 127.82899 | 9.2474 |
| 2 | 12.898 | MM | 0.9088 | 2.18294e4 | 400.32010 | 90.7526 |

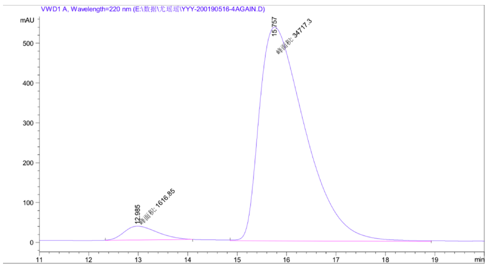
**(5*S*,6*R*,8*R*)-Methyl 6-(2-methoxyphenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4i)**



**4i**

White solid, yield: 57 mg (93%); Mp.122-125℃; $[\alpha]_D^{30}$ = -33.67 (*c* 1.20, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 2H), 7.28-7.24 (m, 1H),7.00 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H),4.82 (s, 1H), 4.19 (t, J = 8.8 Hz, 1H), 4.05 (t, J = 8.0 Hz, 1H), 3.96-3.80 (m, 6H), 2.58-2.53(m, 2H), 2.38-2.30(m, 1H), 2.23-2.17 (m, 1H)), 1.68 (brs, 1H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.3, 173.6, 156.6, 129.0, 127.4, 126.6, 121.1, 110.1, 65.3, 63.9, 59.0, 55.1, 53.9, 52.3, 40.1, 34.6; IR (film): *v* ($cm^{-1}$) 3390, 2950, 2840, 1745, 1602, 1489, 1379, 1200, 1135, 1025, 788, 632; The ee value was 91%, $t_R$ (major) = 15.75 min, $t_R$(minor) =12.98 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

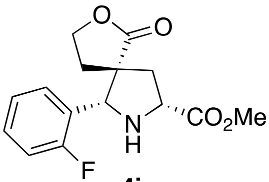




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 12.368 | VV | 0.8788 | 1.12661e4 | 179.25755 | 50.0830 |
| 2 | 16.090 | VB | 0.9828 | 1.12287e4 | 172.35782 | 49.9170 |

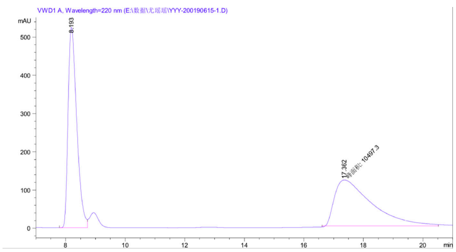
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 12.985 | MM | 0.7761 | 1616.84668 | 34.72333 | 4.4499 |
| 2 | 15.757 | MM | 1.0788 | 3.47173e4 | 536.37958 | 95.5501 |

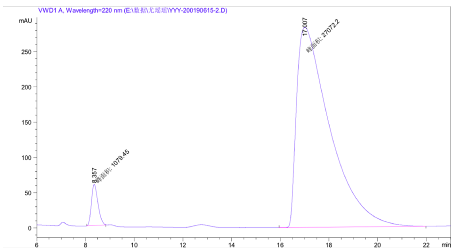
**(5*S*,6*S*,8*R*)-Methyl 6-(2-fluorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4j)**



**4j**

Colorless oil, yield: 53 mg (91%); $[\alpha]_D^{30}$ = +2.73 (*c* 1.20, $CH_2Cl_2$); $^1$H-NMR (400 MHz, CDCl3) δ 7.58 (t, J = 8.0 Hz, 1H), 7.30-7.25 (m, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 9.6 Hz, 1H), 4.69 (s, 1H), 4.15 (t, J = 9.2 Hz, 1H), 4.06 (t, J = 8.0 Hz, 1H), 3.86-3.79 (m, 4H), 2.65 (dd, J = 13.4, 6.8 Hz, 1H), 2.54-2.28 (m, 4H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.3, 173.2, 161.6, 159.1, 129.9, 129.8, 128.1, 124.8, 115.1, 114.9, 65.4, 63.4, 63.3, 58.8, 53.8, 52.4, 40.3, 33.4; IR (film): *ν* (cm$^{-1}$) 3345, 2922, 2852, 1765, 1736, 1456, 1387, 1209, 1171, 1024, 858, 711; The ee value was 92%, $t_R$ (major) = 17.00 min, $t_R$(minor) =8.35 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

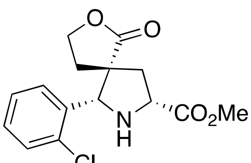




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.193 | BV | 0.3117 | 1.05964e4 | 523.96680 | 50.2349 |
| 2 | 17.362 | MM | 1.4547 | 1.04973e4 | 120.26815 | 49.7651 |

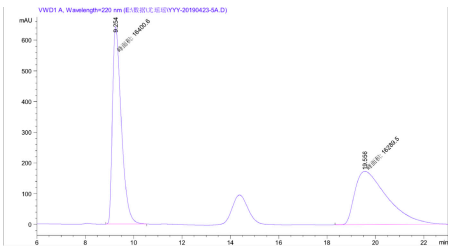
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.357 | MM | 0.3101 | 1079.45410 | 58.00867 | 3.8344 |
| 2 | 17.007 | MM | 1.5888 | 2.70722e4 | 283.98456 | 96.1656 |

**(5*S*,6*S*,8*R*)-Methyl 6-(2-chlorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4k)**

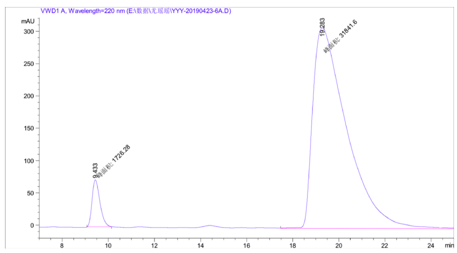


**4k**

White solid, yield: 53 mg (85%); Mp.118-122℃; $[\alpha]_D^{30}$ = -31.05 (*c* 1.95, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, J = 7.8, 1.6 Hz, 1H), 7.34-7.27 (m, 2H), 7.21 (td, J = 7.6, 2.0 Hz, 1H), 4.92 (s, 1H), 4.14 (td, J = 9.0, 2.4 Hz, 1H), 4.05 (dd, J = 7.2, 4.4 Hz, 1H), 3.81 (s, 3H), 2.70 (brs, 1H), 2.67-2.59 (m, 2H), 2.41-2.25 (m, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.0, 173.3, 135.6, 133.1, 129.4, 129.3, 128.7, 127.5, 66.3, 65.4, 58.7, 54.1, 52.3, 39.8, 33.7; IR (film): *ν* ($cm^{-1}$) 3378, 2980, 2953, 1775, 1727, 1438, 1376, 1203, 1178, 1031, 763, 680; The ee value was 90%, $t_R$ (major) = 19.28 min, $t_R$(minor) =9.43 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

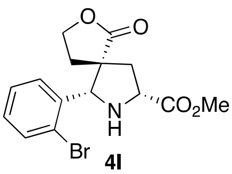



| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 9.254 | MM | 0.4255 | 1.64006e4 | 642.44452 | 50.1698 |
| 2 | 19.556 | MM | 1.5632 | 1.62895e4 | 173.68013 | 49.8302 |



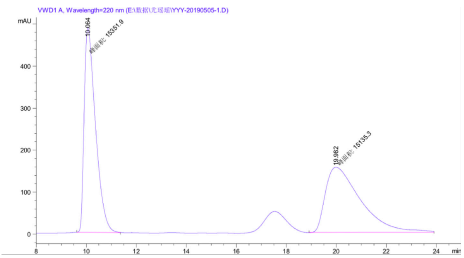

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 9.433 | MM | 0.3949 | 1726.28491 | 72.86068 | 5.1427 |
| 2 | 19.283 | MM | 1.7087 | 3.18416e4 | 310.58713 | 94.8573 |

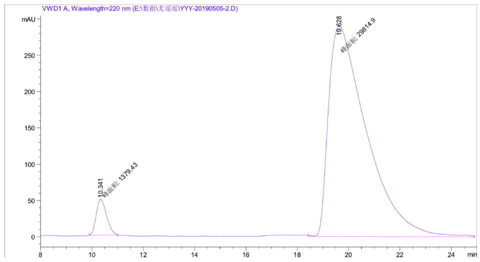
**(5*S*,6*S*,8*R*) -Methyl 6-(2-bromophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylat-e (4l)**




**4l**

White solid, yield: 65 mg (92%); Mp.115-118℃; $[\alpha]_D^{30}$ = -41.68 (*c* 1.25, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 7.8, 2.0 Hz, 1H), 7.52 (dd, J = 8.0, 1.2 Hz, 1H), 7.34 (td, J = 7.4, 1.6 Hz, 1H), 7.14 (td, J = 7.6, 1.6 Hz, 1H), 4.89 (s, 1H), 4.13 (td, J = 9.2, 2.0 Hz, 1H), 4.05 (dd, J = 8.8, 7.2 Hz, 1H), 3.94 – 3.83 (m, 1H), 3.81 (s, 3H),2.71 – 2.63 (m, 3H), 2.40 – 2.26 (m, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.0, 173.3, 137.2, 132.7, 129.7, 129.1, 128.2, 123.9, 69.0, 65.4, 58.7, 54.2, 52.3, 39.8, 33.7; IR (film): *ν* ($cm^{-1}$) 3372, 2974, 2950, 1766, 1727, 1436, 1376, 1203, 1174, 1025, 763, 668; The ee value was 91%, $t_R$ (major) = 19.62 min, $t_R$(minor) =10.31 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

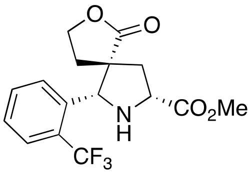




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 10.064 | MM | 0.5251 | 1.53519e4 | 487.27899 | 50.3553 |
| 2 | 19.982 | MM | 1.6264 | 1.51353e4 | 155.09763 | 49.6447 |

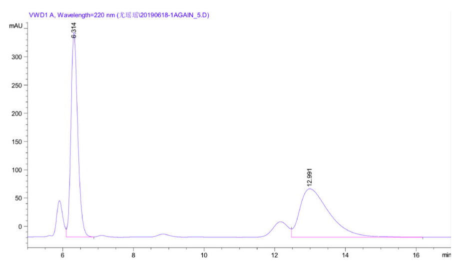
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 10.341 | MM | 0.4642 | 1379.42981 | 49.52673 | 4.4220 |
| 2 | 19.628 | MM | 1.7162 | 2.98149e4 | 289.53851 | 95.5780 |

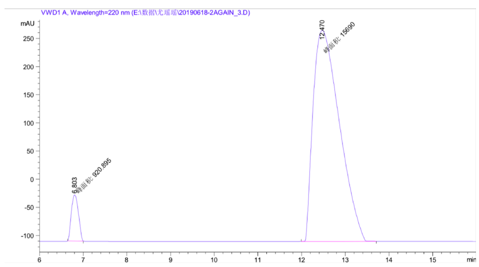
**(5*S*,6*S*,8*R*)-Methyl 6-(2-fluorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4m)**



**4m**

Colorless oil, yield: 62 mg (90%); $[\alpha]_D^{30}$ = +9.27 (*c* 2.00, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H),7.60 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 4.64 (s, 1H), 4.09-4.05 (m, 2H), 3.83 (s, 3H), 3.63-3.56 (m, 1H), 2.70 (dd, J = 13.2, 6.4 Hz, 1H), 2.61 (brs, 1H),2.42-2.30 (m, 3H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.5, 173.3, 137.1, 132.7, 129.1, 128.4, 126.1, 125.9, 66.3, 65.2, 58.7, 53.9, 52.5, 40.0, 33.7; IR (film): *v* (cm$^{-1}$) 3378, 2959, 2914, 1772, 1611, 1456, 1313, 1162, 1120, 1040, 772, 656; The ee value was 89%, $t_R$ (major) = 12.47 min, $t_R$(minor) =6.80 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

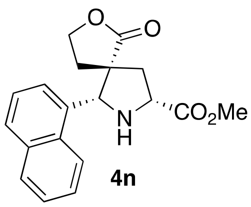




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.314 | VB | 0.2046 | 4858.60547 | 361.98715 | 49.4149 |
| 2 | 12.991 | VB | 0.8754 | 4973.66943 | 85.85242 | 50.5851 |

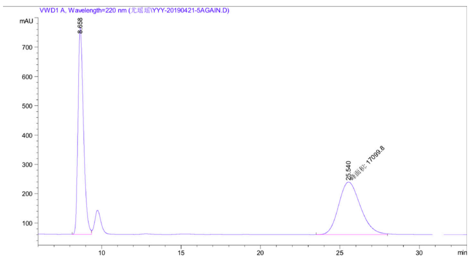
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.803 | MM | 0.1876 | 920.89520 | 81.80157 | 5.5439 |
| 2 | 12.470 | MM | 0.6979 | 1.56900e4 | 374.70883 | 94.4561 |

**(5S,6R,8R)-Methyl 6-(naphthalen-2-yl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylat-e (4n)**

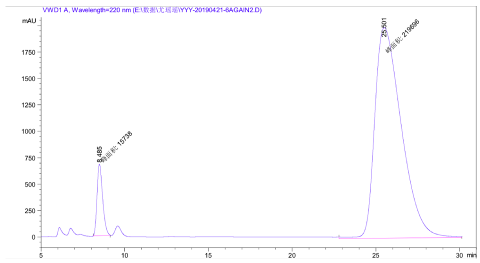


**4n**

White solid, yield: 58 mg (90%); Mp.141-143℃; $[\alpha]_D^{30}$ = -95.629 (*c* 1.1, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.87-7.82 (m, 4H), 7.53-7.47 (m, 3H), 4.34 (s, 1H), 4.12 (dd, J = 10.4, 5.4 Hz, 1H), 4.05-3.98 (m, 1H), 3.87 (s, 3H), 3.54-3.47 (m, 1H), 2.75 (dd, J = 13.6, 5.4 Hz, 1H), 2.51-2.35 (m, 3H), 2.17 (brs, 1H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.7, 173.3, 133.6, 133.2, 128.8, 128.1, 127.7, 126.6, 126.4, 124.6,73.4, 65.3, 65.2, 58.9, 53.7, 52.5, 40.5, 33.0; IR (film): *v* ($cm^{-1}$) 3345, 2956, 2917, 1763, 1441, 1373, 1209, 1177, 1028, 822, 742, 477; The ee value was 87%, $t_R$ (major) = 25.50 min, $t_R$(minor) =8.48 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

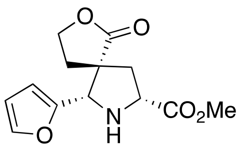


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.658 | VV | 0.3678 | 1.70308e4 | 704.80792 | 49.8988 |
| 2 | 25.540 | MM | 1.5905 | 1.70998e4 | 179.18639 | 50.1012 |



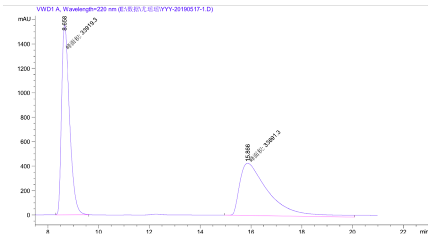
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.485 | MM | 0.3867 | 1.57380e4 | 678.22931 | 6.6847 |
| 2 | 25.501 | MM | 1.8386 | 2.19696e5 | 1991.51355 | 93.3153 |

**(5*S*,6*S*,8*R*)-Methyl 6-(furan-2-yl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4o)**

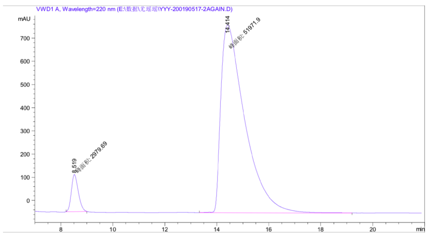


**4o**

Colorless oil, yield: 46 mg (87%); $[\alpha]_D^{30}$ = -1.65 (*c* 2.1, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 6.39 (s, 1H), 6.35 (s, 1H)，4.25 (s,1H), 4.04-4.00 (m, 1H), 3.90(dd, J = 13.4, 5.9 Hz, 1H), 4.81 (s, 3H), 2.65 (dd, J = 13.4, 6.0 Hz, 1H), 2.48-2.38 (m, 2H), 2.29 (dd, J = 12.8, 9.6 Hz, 1H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.4, 172.9, 150.7, 142.4, 110.7, 107.8, 65.9, 65.4, 58.9, 52.5, 40.3, 32.9; IR (film): *v* ($cm^{-1}$) 3313, 3119, 2953, 2917, 1763, 1435, 1379, 1215, 1182, 1028, 742, 605; The ee value was 89%, $t_R$ (major) = 14.41 min, $t_R$(minor) =8.51 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 50:50, flow rate = 1 mL/min).

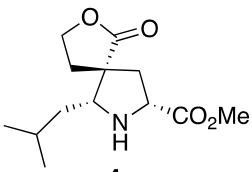


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.658 | MM | 0.3640 | 3.39193e4 | 1553.05872 | 50.1686 |
| 2 | 15.866 | MM | 1.3149 | 3.36913e4 | 427.04984 | 49.8314 |



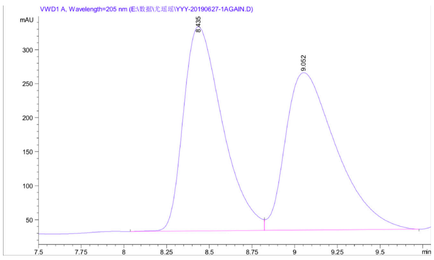
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.519 | MM | 0.3098 | 2979.69287 | 160.29471 | 5.4224 |
| 2 | 14.414 | MM | 1.0704 | 5.19719e4 | 809.19232 | 94.5776 |

**(5*S*,6*R*,8*R*)-Methyl 6-isopentyl-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (4p)**

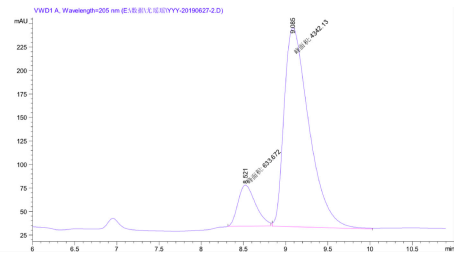



**4p**

Colorless oil, yield: 38 mg (75%); $[\alpha]_D^{30}$ = +28.77 (*c* 2.20, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 4.31-4.19 (m, 2H), 3.89 (dd, J = 9.0, 6.4 Hz, 1H), 3.74 (s, 3H), 3.04 (dd, J = 11.0, 3.2 Hz, 1H), 2.47 (dd, J = 13.4, 6.4 Hz, 1H), 2.40-2.32 (m, 1H), 2.27 (brs, 1H), 2.25-2.18 (m, 1H), 1.53-1.46 (m, 1H), 1.21-1.15 (m, 2H), 0.92 (dd, J = 10.4, 6.4 Hz, 6H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 179.5, 172.9, 66.8, 65.5, 59.4, 52.3, 51.5, 41.9, 39.6, 33.0, 25.9, 23.9, 21.4; IR (film): *v* ($cm^{-1}$) 3278, 2959, 2872, 1760, 1435, 1382, 1313, 1206, 1177, 1028, 876, 739; The ee value was 75%, $t_R$ (major) = 9.08 min, $t_R$(minor) =8.52 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 70:30, flow rate = 0.8 mL/min).

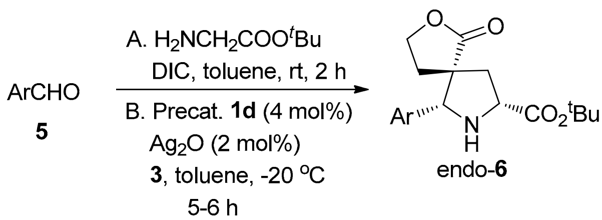


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰高 % |
|---|---|---|---|---|---|---|
| 1 | 8.435 | BV | 0.2450 | 4771.99219 | 300.50159 | 56.4702 |
| 2 | 9.052 | VB | 0.3163 | 4805.29297 | 231.64012 | 43.5298 |



| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.521 | MM | 0.2411 | 633.67188 | 43.80388 | 12.7351 |
| 2 | 9.085 | MM | 0.3415 | 4342.12549 | 211.91350 | 87.2649 |

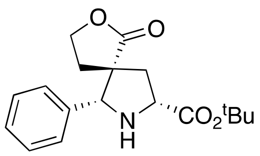
## D. General Procedure for 1,3-Dipolar Cycloaddition of Imino Esters with α-methylene-γ-butyrolactone via Three-component "One-pot"



To a solution of tert-butyl glycine (39.3 mg, 0.30 mmol) in toluene (1.0 mL) was added the aldehyde 5 (0.30 mmol) and *N*,*N*′-diisopropylcarbodiimide (37.8 mg, 0.30 mmol), which was stirred for 2 h at room temperature. Then, a solution of precat. **1d** (5.57 mg, 0.008 mmol) and $Ag_2O$ (0.92 mg, 0.004 mmol) in toluene (0.5 mL) stirred for 1 h, was mixed with the above solution, followed by α-methylene-γ-butyrolactone **3** dropwise (19.6 mg, 0.20 mmol) at -20 °C. The reaction was monitored by TLC plate, and the residue was purified by silica gel column chromatography to afford the spiro *endo*-**6** adducts.

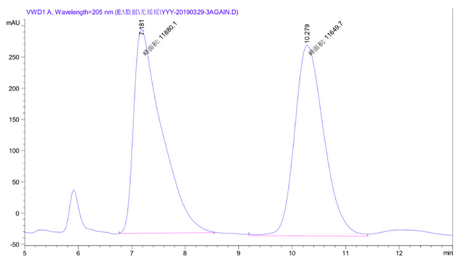
## E. Analytical data and HPLC chromatogram of the [3 + 2] cyclization products of α-iminoesters and the α-methylene-γ-butyrolactone via Three-component "One-pot"

**(5S,6R,8R)-tert-Butyl 1-oxo-6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (6a)**

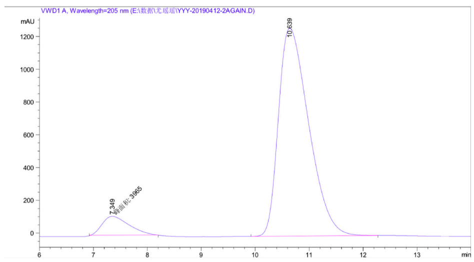


**6a**

Colorless oil, yield: 60 mg (95%); $[\alpha]_D^{30}$ = -26.77 (*c* 1.52, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.41-7.33 (m, 5H), 4.16 (s, 1H), 4.08-4.03 (m, 1H), 3.96 (dd, J = 9.6, 5.6 Hz, 1H), 3.57-3.50 (m, 1H), 2.64 (dd, J = 13.6, 5.6 Hz, 1H), 2.50-2.42 (m, 1H), 2.35-2.27 (m, 2H), 2.04 (brs, 1H), 1.54 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.8, 172.0, 136.9, 129.0, 128.9, 127.2, 82.0, 73.2, 65.3, 59.8, 53.8, 40.9, 33.1, 28.2; IR (film): *v* (cm$^{-1}$) 3307, 2977, 2914, 1750, 1730, 1456, 1373, 1275, 1162, 1028, 852, 757; The ee value was 85%, $t_R$ (major) = 10.63 min, $t_R$(minor) =7.34 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 70:30, flow rate = 1 mL/min).

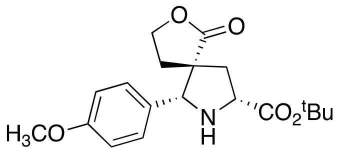


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 7.181 | MM | 0.6061 | 1.18801e4 | 326.66171 | 50.4896 |
| 2 | 10.279 | MM | 0.6350 | 1.16497e4 | 305.76019 | 49.5104 |



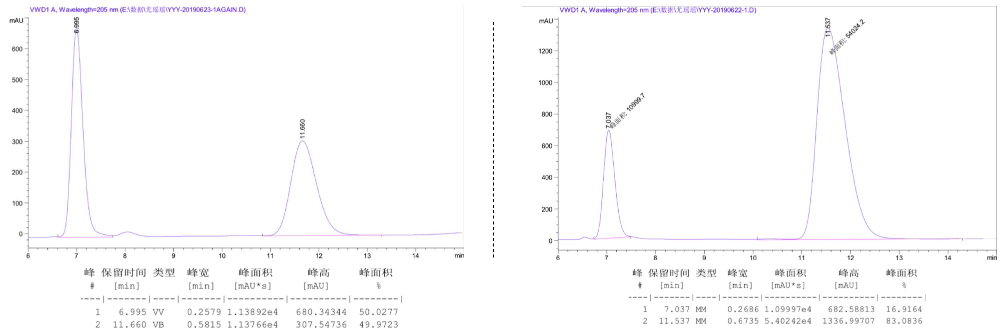
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 7.349 | MM | 0.5749 | 3965.00488 | 114.95587 | 7.4370 |
| 2 | 10.639 | VB | 0.5951 | 4.93495e4 | 1268.65320 | 92.5630 |

**(5S,6R,8R)-tert-Butyl 6-(4-chlorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxyl -ate (6b)**

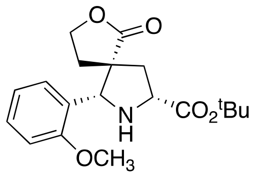


**6b**

Colorless oil, yield: 62 mg (90%); $[\alpha]_D^{30}$ = -6.34 ($c$ 1.22, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 4.13 (s, 1H), 4.08-4.03 (m, 1H), 3.95 (dd, J = 9.6, 5.2 Hz, 1H), 3.79 (s, 3H), 3.58-3.51 (m, 1H), 2.63 (dd, J = 13.2, 5.2 Hz, 1H), 2.49-2.41 (m, 1H), 2.32-2.26 (m, 2H), 1.97 (brs, 1H), 1.54 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.9, 171.9, 160.0, 132.2, 128.3, 114.3, 82.0, 73.0, 65.2, 59.7, 55.3, 53.7, 40.7, 33.1, 28.1; IR (film): $\nu$ (cm$^{-1}$) 3346, 2976, 2922, 1759, 1718, 1516, 1365, 1240, 1167, 1028, 825, 539; The ee value was 66%, $t_R$ (major) = 11.53 min, $t_R$(minor) =7.03 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 60:40, flow rate = 0.8 mL/min).



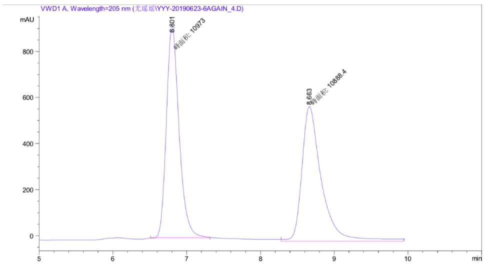

**(5S,6R,8R)-tert-Butyl 6-(2-methoxyphenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carbo-xylate (6c)**



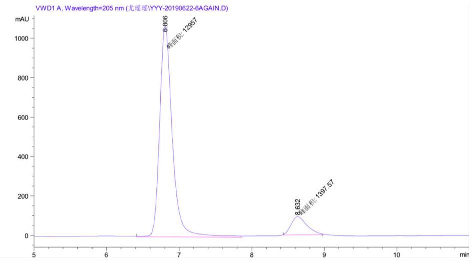
**6c**

White solid, yield: 64 mg (92%); Mp.135-141℃; $[\alpha]_D^{30}$ = -8.99 ($c$ 2.03, $CH_2Cl_2$); $^1$H-NMR (400 MHz, CDCl3) δ 7.56 (d, J = 7.6 Hz, 1H), 7.27-7.23 (m, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 4.81 (s, 1H), 4.23-4.18 (m, 1H), 4.01-3.91 (m, 2H), 3.86-3.83 (m, 1H), 3.79 (s, 3H), 3.58-2.53 (m, 1H), 2.50-2.45 (m, 1H), 2.14 (dd, J = 13.2, 8.0 Hz, 1H), 1.53 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.3, 172.4, 156.5, 128.9, 127.2, 121.0, 110.0, 81.8, 65.2, 63.9, 59.8, 55.1, 54.0, 42.2, 40.3, 34.9, 28.1, 23.5; IR (film): $\nu$ (cm$^{-1}$) 3340, 2974, 2923, 1760, 1715, 1620, 1465, 1370, 1242, 1165, 1025, 837, 760; The ee value was 81%, $t_R$ (minor)

= 8.63 min, $t_R$(major) =6.80 min (Chiralcel AD-H, λ = 220 nm, iPrOH/hexanes 70:30, flow rate = 0.6 mL/min).

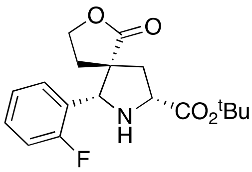


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.801 | MM | 0.1994 | 1.09730e4 | 917.33063 | 50.1935 |
| 2 | 8.663 | MM | 0.3101 | 1.08884e4 | 585.26471 | 49.8065 |



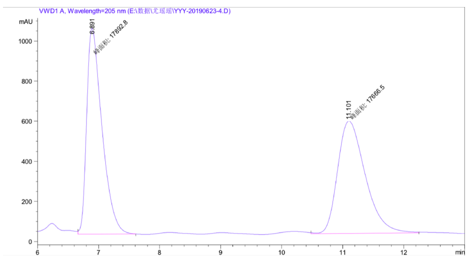
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.806 | MM | 0.2017 | 1.29570e4 | 1070.81616 | 90.2639 |
| 2 | 8.632 | MM | 0.2514 | 1397.56860 | 92.64329 | 9.7361 |

**(5S,6S,8R)-tert-Butyl 6-(2-fluorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxyl Ate (6d)**

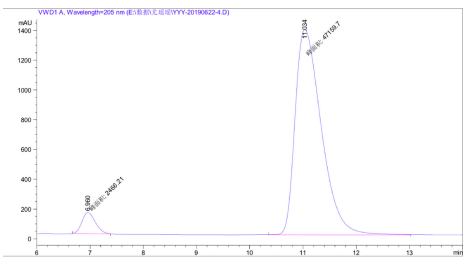


**6d**

Colorless oil, yield: 68 mg (96%); $[\alpha]_D^{30}$ = +15.30 (*c* 0.85, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.58 (t, J = 7.6 Hz, 1H), 7.28-7.26 (m, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.05-7.00 (m, 1H), 4.69 (s, 1H), 4.16 (t, J = 9.2 Hz, 1H), 3.97-3.93 (m, 1H), 3.89-3.79 (m, 1H), 2.61-2.56 (m, 1H), 2.53-2.48 (m, 1H), 2.44-2.39 (m, 1H), 2.30-2.24 (m, 1H), 1.53 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.3, 171.9, 161.6, 159.1, 129.8, 129.7, 128.0, 128.0, 124.8, 124.8, 115.1, 114.9, 81.9, 65.3, 63.5, 63.4, 59.7, 53.9, 40.7, 33.6, 28.0; IR (film): *v* ($cm^{-1}$) 3381, 2977, 2935, 1763, 1718, 1459, 1367, 1227, 1156, 1028, 835, 757; The ee value was 90%, $t_R$ (major) = 11.03 min, $t_R$(minor) =6.96 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 60:40, flow rate = 0.8 mL/min).

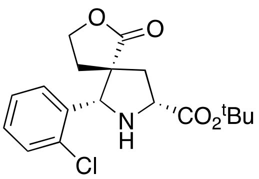


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.891 | MM | 0.2906 | 1.78928e4 | 1026.21729 | 50.3181 |
| 2 | 11.101 | MM | 0.5255 | 1.76665e4 | 560.25671 | 49.6819 |



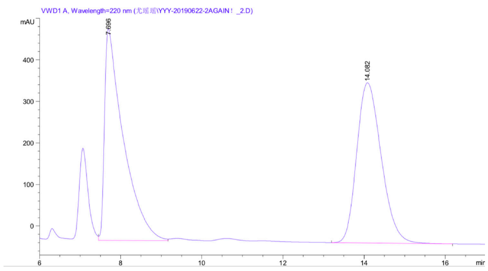
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 6.960 | MM | 0.2903 | 2466.21387 | 141.59065 | 4.9696 |
| 2 | 11.034 | MM | 0.5700 | 4.71597e4 | 1378.92065 | 95.0304 |

**(5S,6S,8R)-tert-Butyl 6-(2-chlorophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxyl -ate (6e)**

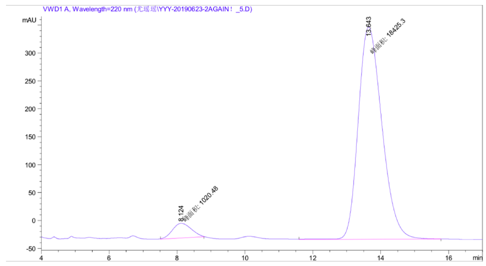


**6e**

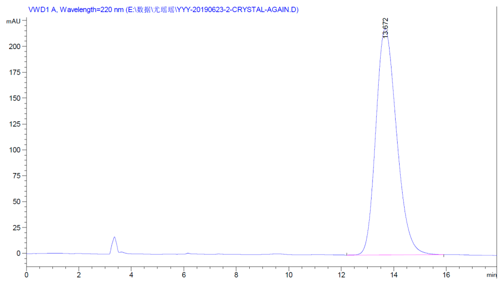
White solid, yield: 68 mg (97%); Mp.121-126℃;$[\alpha]_D^{30}$ = -20.78 ($c$ 1.60, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 1H), 7.36-7.30 (m, 2H), 7.22 (d, J = 7.6 Hz, 1H), 4.94 (s, 1H), 4.18 (t, J = 9.2 Hz, 1H), 4.00-3.88 (m, 2H), 2.66-2.58 (m, 2H), 2.43-2.35 (m, 1H), 2.30-2.24 (m, 1H), 1.69 (brs, 1H), 1.54 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.1, 172.1, 135.9, 133.3, 129.5, 129.4, 128.7, 127.6, 82.0, 66.6, 65.4, 59.7, 54.3, 40.4, 34.1, 28.1; IR (film): $\nu$ (cm$^{-1}$) 3381, 2974, 2923, 1766, 1724, 1456, 1370, 1206, 1153, 1043, 849, 751; The ee value was 90% (100% ee after recrystallization), $t_R$ (major) = 13.64 min, $t_R$(minor) =8.12 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 70:30, flow rate = 0.8 mL/min).




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 7.696 | VV | 0.4398 | 1.63940e4 | 509.09299 | 50.2662 |
| 2 | 14.082 | BB | 0.6509 | 1.62204e4 | 385.59082 | 49.7338 |



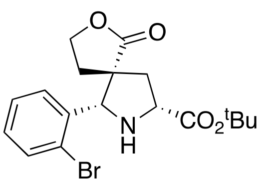

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 8.124 | MM | 0.6421 | 1020.47760 | 26.48889 | 5.2478 |
| 2 | 13.643 | MM | 0.8071 | 1.84253e4 | 380.46976 | 94.7522 |




| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 13.672 | BB | 0.8562 | 1.20250e4 | 218.48022 | 100.0000 |

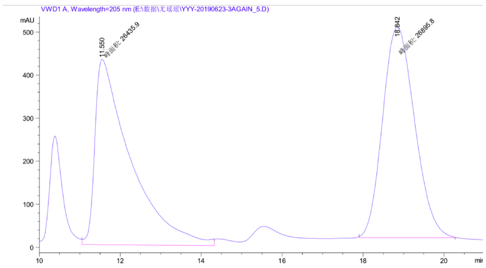
After recrystallization

**(5S,6S,8R)-tert-Butyl 6-(2-bromophenyl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxyl-ate (6f)**

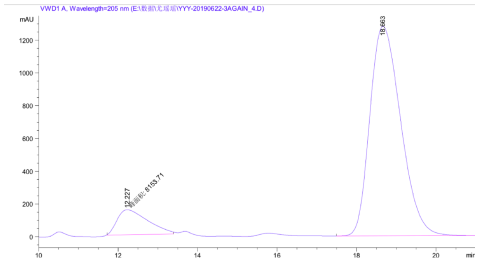


**6f**

Colorless oil, yield: 74 mg (94%); $[\alpha]_D^{30}$ = -23.17 ($c$ 2.03, $CH_2Cl_2$); $^1$H-NMR (400 MHz, CDCl3) δ 7.66 (dd, J = 8.0, 1.6 Hz, 1H), 7.54 (dd, J = 8.0, 1.6 Hz, 1H), 7.38-7.33 (m, 1H), 7.18-7.13 (m, 1H), 4.90 (s, 1H), 4.16 (td, J = 10.0, 2.0 Hz, 1H), 3.99-3.88 (m, 2H), 2.71-2.66 (m, 1H), 2.61 (dd, J = 13.2, 11.2 Hz, 1H), 2.42-2.34 (m, 1H), 2.27 (dd, J = 13.2, 8.8 Hz, 1H), 1.53 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 177.9, 171.9, 137.4, 132.7, 129.7, 128.9, 128.1, 123.9, 81.8, 69.1, 65.3, 59.6, 54.2, 40.2, 33.9, 28.0; IR (film): *v* ($cm^{-1}$) 3378, 2977, 2932, 1766, 1733, 1456, 1367, 1260, 1129, 1031, 843,760; The ee value was 79%, $t_R$ (major) = 18.66 min, $t_R$(minor) =12.22 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 70:30, flow rate = 0.6 mL/min).

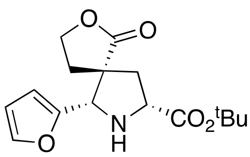


| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 11.550 | MM | 1.0226 | 2.64359e4 | 430.85706 | 49.5688 |
| 2 | 18.842 | MM | 0.9176 | 2.68958e4 | 488.52686 | 50.4312 |



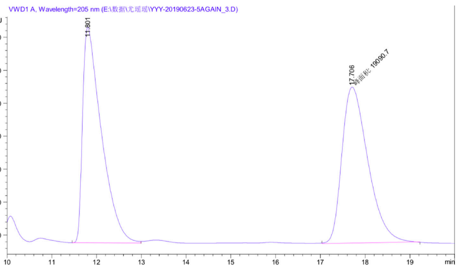
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 12.227 | MM | 0.8891 | 8153.70703 | 152.85008 | 10.5532 |
| 2 | 18.663 | BBA | 0.8468 | 6.91091e4 | 1280.05725 | 89.4468 |

**(5S,6S,8R)-tert-Butyl 6-(furan-2-yl)-1-oxo-2-oxa-7-azaspiro[4.4]nonane-8-carboxylate (6g)**

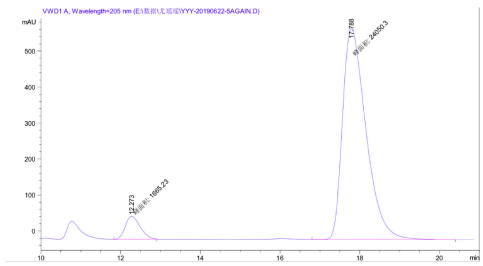


**6g**

Colorless oil, yield: 55 mg (89%); $[\alpha]_D^{30}$ = +55.92 (*c* 1.55, $CH_2Cl_2$); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, J = 1.6, 0.8 Hz, 1H), 6.39 (d, J = 3.2 Hz, 1H), 6.35 (dd, J = 3.2, 1.6 Hz, 1H), 4.25 (s, 1H), 4.24-4.20 (m, 1H), 3.97-3.89 (m, 2H), 2.59 (dd, J = 13.2, 5.6 Hz, 1H), 2.44-2.40 (m, 2H), 2.25 (dd, J = 13.2, 9.2 Hz, 1H), 1.51 (s, 9H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.3, 171.6, 151.1, 142.3, 110.7, 107.6, 82.0, 65.9, 65.3, 59.7, 52.6, 40.5, 33.2, 28.0; IR (film): *v* ($cm^{-1}$) 3342, 2968, 2932, 1763, 1724, 1459, 1373, 1248, 1168, 1028, 881, 754; The ee value was 87%, $t_R$ (major) = 17.78 min, $t_R$(minor) = 12.27 min (Chiralcel AS-H, λ = 220 nm, iPrOH/hexanes 70:30, flow rate = 0.6 mL/min).



| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 11.801 | BV | 0.4243 | 1.91064e4 | 653.11798 | 50.0205 |
| 2 | 17.706 | MM | 0.6729 | 1.90907e4 | 472.87402 | 49.9795 |



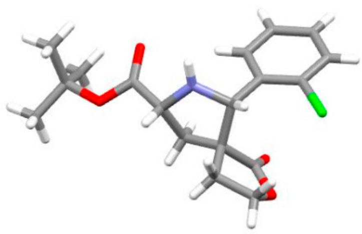
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 % |
|---|---|---|---|---|---|---|
| 1 | 12.273 | MM | 0.4308 | 1665.23096 | 64.42223 | 6.4756 |
| 2 | 17.788 | MM | 0.6844 | 2.40503e4 | 585.66888 | 93.5244 |

Reference:

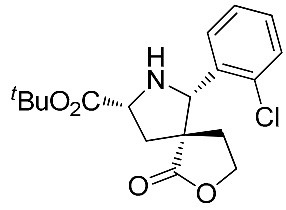

1. Wang, H.; Deng, Q.; Zhou, Z.; Hu, S.; Liu, Z.; Zhou, L.-Y. $Ag_2CO_3$/CA-AA-AmidPhos Multifunctional Catalysis in the Enantioselective 1,3-Dipolar Cycloaddition of Azomethine Ylides. *Org. Lett.* **2016**, *18*, 404–407.

## F. Crystallographic data for 6e

The crystal **6e** was measured on a Bruker Apex-II CCD diffractometer with monochromatic Mo Kα radiation (λ = 0.71073 Å) at 296(2) K. Absorption and scaling correction were undertaken with the SADABS program, and the direct method was used to resolve the crystal structure; except for hydrogen atoms, other atoms were refined by the full-matrix least-squares procedure employing the free Olex2 program embedded with SHELXL-2015. The refinement details for *endo*-**6e** have been explained in the CIF document, and the crystallographic data and refinement parameters for **6e** have been summarized in Table 1 (CCDC 1970670).



≡



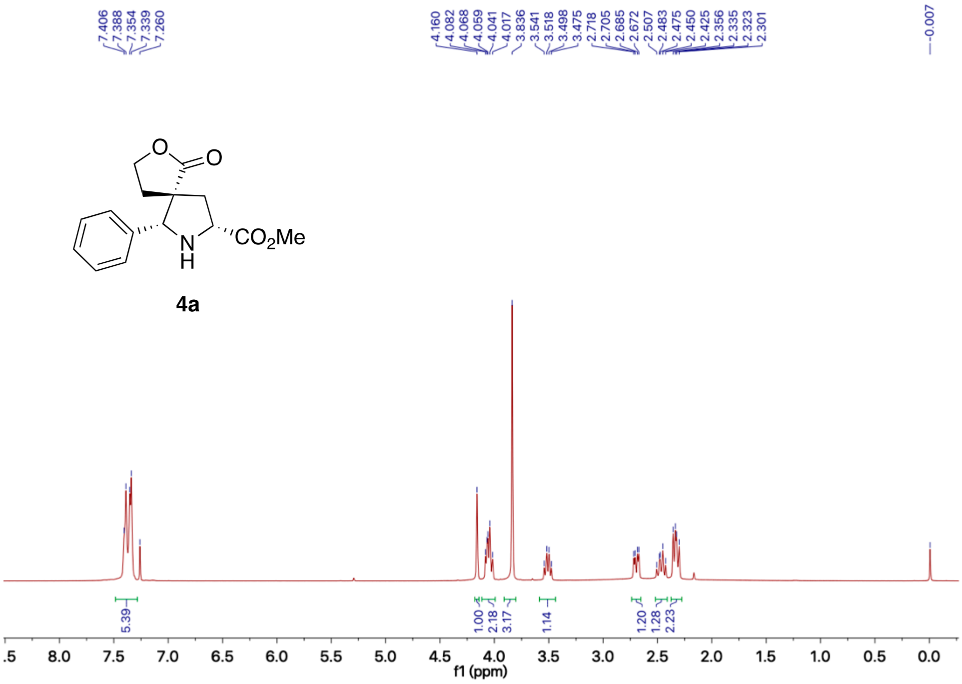

**6e**

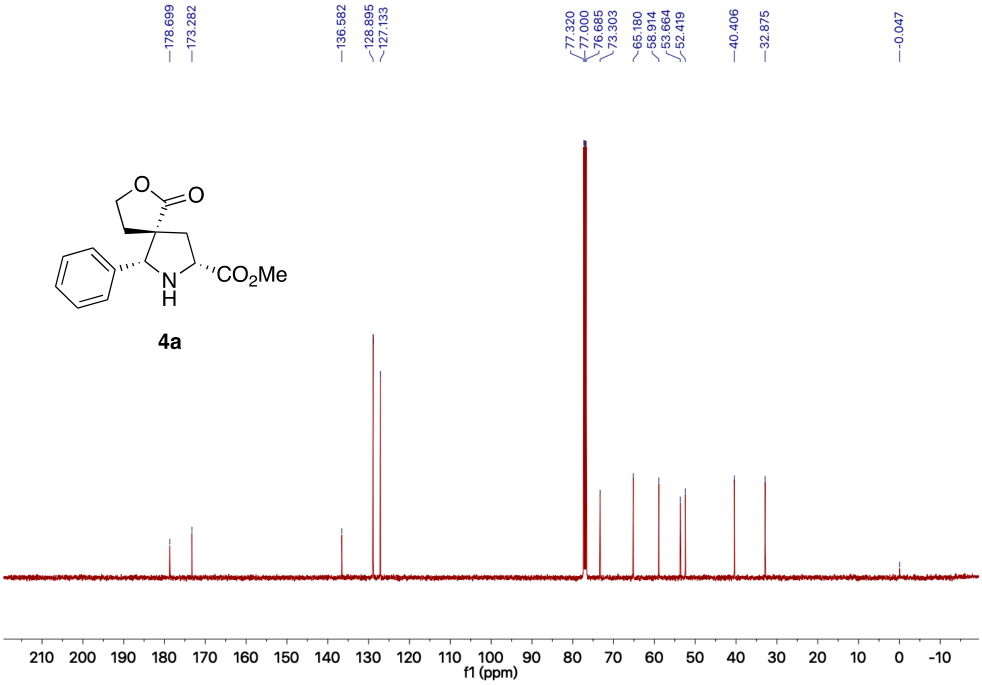
**6e** (CCDC 1970670)

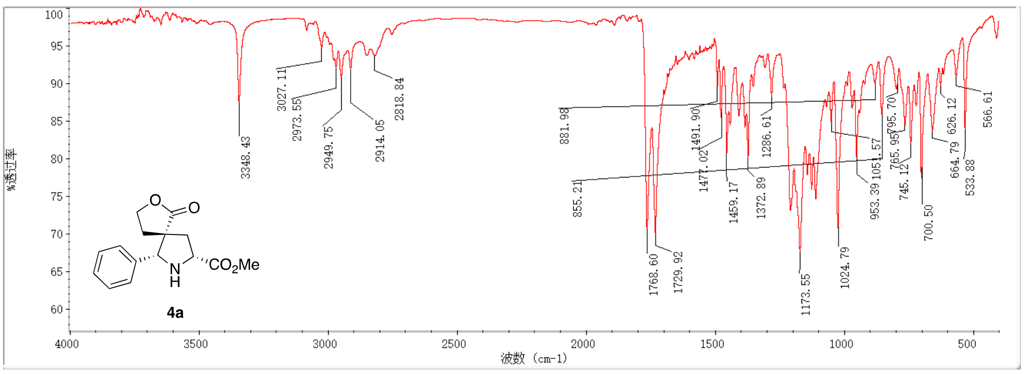
**Table 1. Crystal data and structure refinement for 6e**

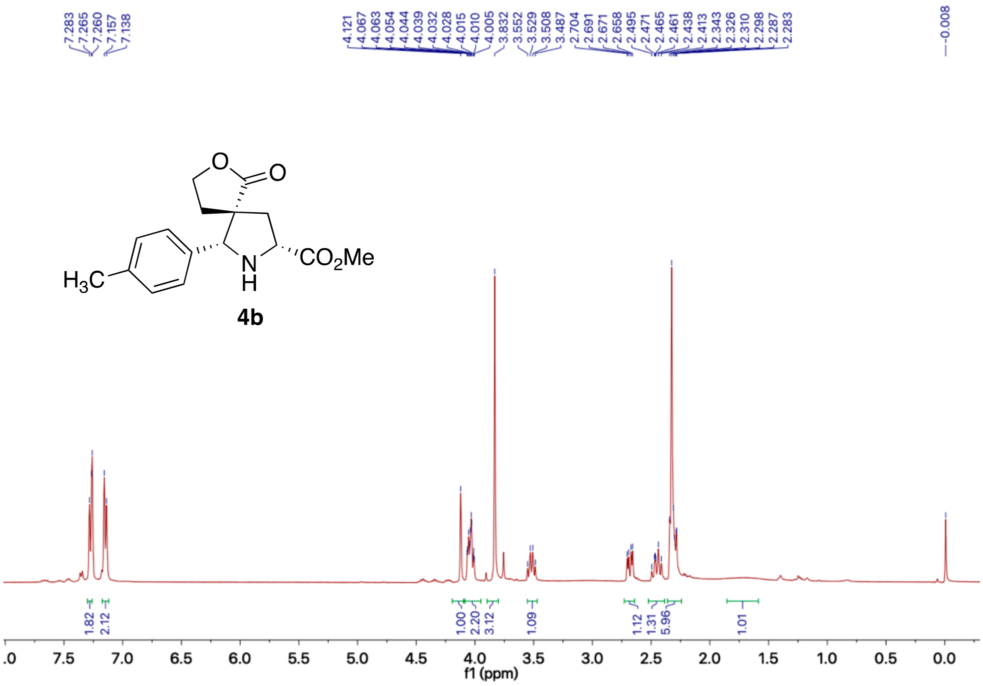
| | | |
|---|---|---|
| Empirical formula | C18H22ClNO4 | |
| Formula weight | 351.81 g/mol | |
| Temperature | 296.00(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | monoclinic | |
| Space group | P 1 2(1)/n 1 | |
| Unit cell dimensions | a = 13.497(8) Å | α = 90°. |
| | b = 6.376(4) Å | β =102.085(8)°. |
| | c = 21.471(13) Å | γ = 90°. |
| Volume | 1806.78 (190) Å$^3$ | |
| Z | 4 | |
| Density (calculated) | 1.2933 g/cm$^3$ | |
| Absorption coefficient | 0.232mm$^{-1}$ | |
| F(000) | 744 | |
| Crystal size | 0.32 x 0.28 x 0.22 mm$^3$ | |
| $\theta$range for data collection | 2.996 to 25.009°. | |
| Index ranges | $-15 \le h \le 15$, $-7 \le k \le 7$, $-25 \le l \le 25$ | |
| Reflections collected | 13306 | |
| Independent reflections | 3180 [$R_{int}$ = 0.0719] | |
| Completeness to theta = 25.009° | 100 % | |
| Refinement method | Full-matrix least-squares on F2 | |
| Max. and min. transmission | 0.7454 and 0.4246 | |
| Data/restraints/parameters | 3180/ 0 / 220 | |
| Goodness-of-fit on $F^2$ | 1.032 | |
| Final $R$ indices [I>2σ(I)] | $R1$ = 0.0621, $wR2$ = 0.1555 | |
| $R$ indices (all data) | $R1$ = 0.0843, $wR2$ = 0.1779 | |
| Largest diff. peak and hole | 0.310 and -0.409 e.Å$^{-3}$ | |

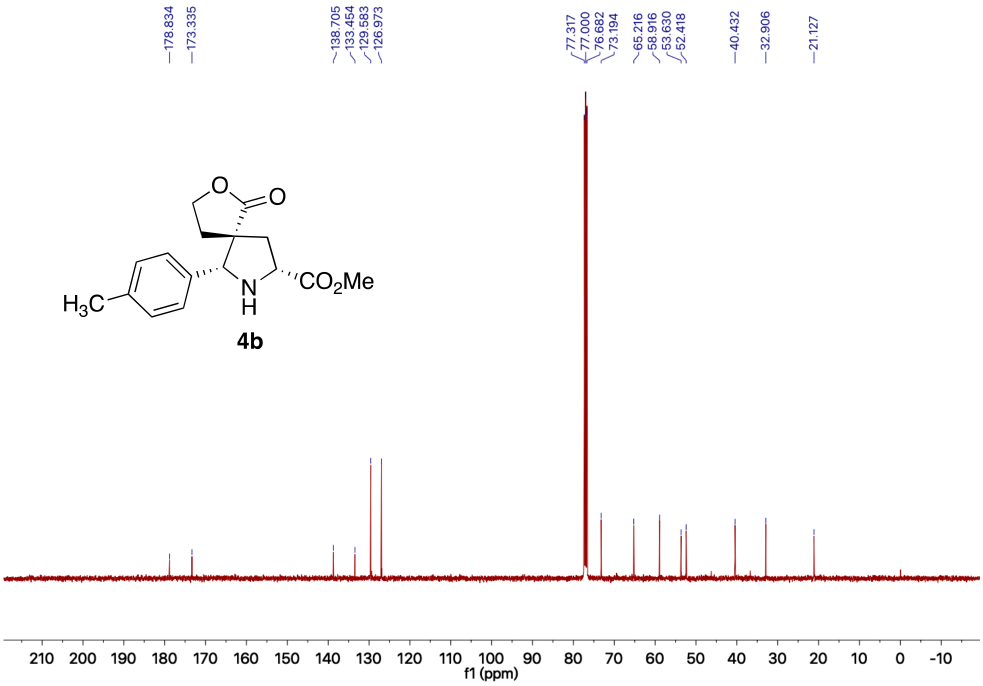
# G. NMR Spectra of the Products

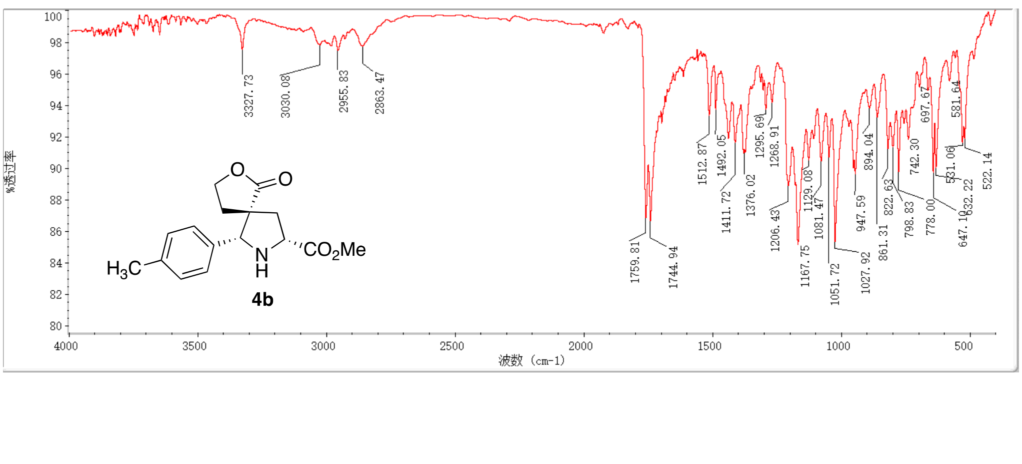


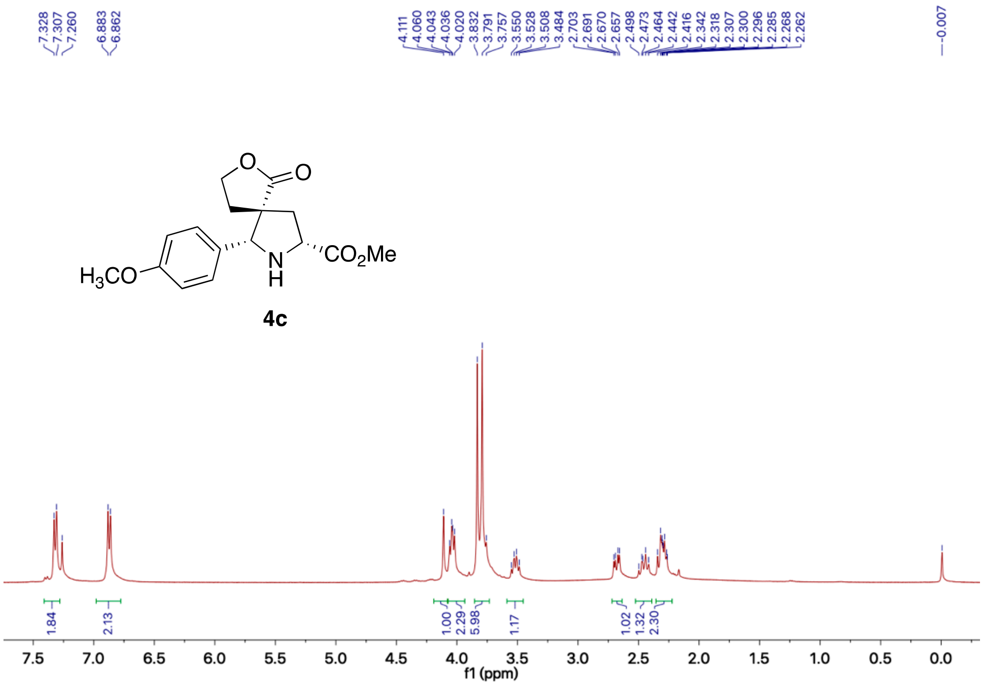







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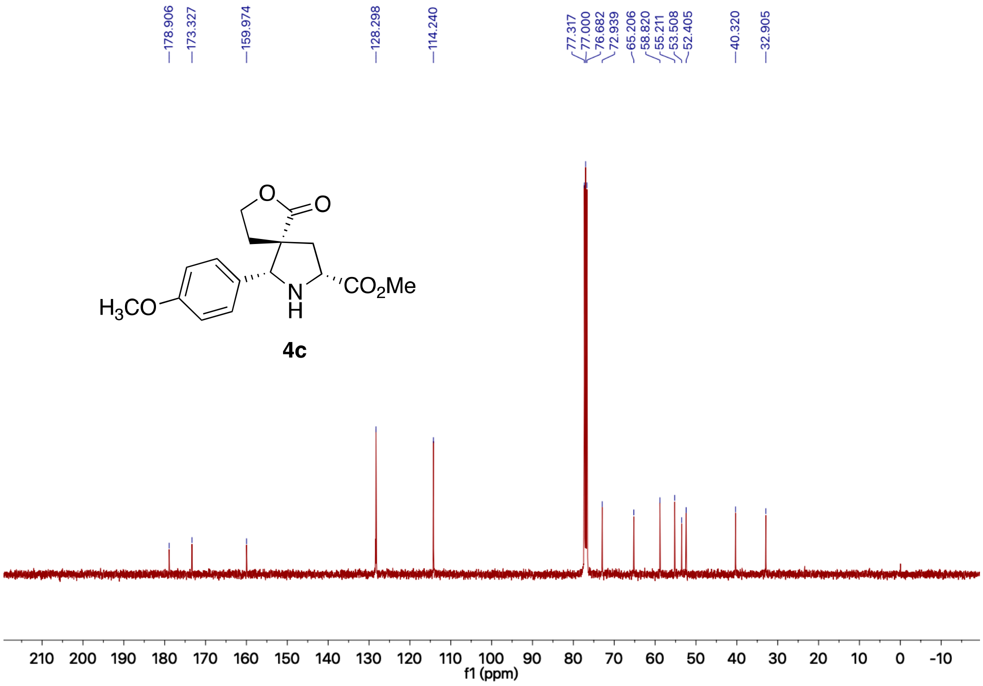
7.307
7.260
6.883
6.862
4.111
4.060
4.043
4.036
4.020
3.832
3.791
3.757
3.550
3.528
3.508
3.484
2.703
2.691
2.670
2.657
2.498
2.473
2.464
2.442
2.416
2.342
2.318
2.307
2.300
2.296
2.285
2.268
2.262
-0.007
H3CO
CO2Me
N
H
O
O
4c
1.84
2.13
1.00
2.29
5.98
1.17
1.02
1.32
2.30
f1 (ppm)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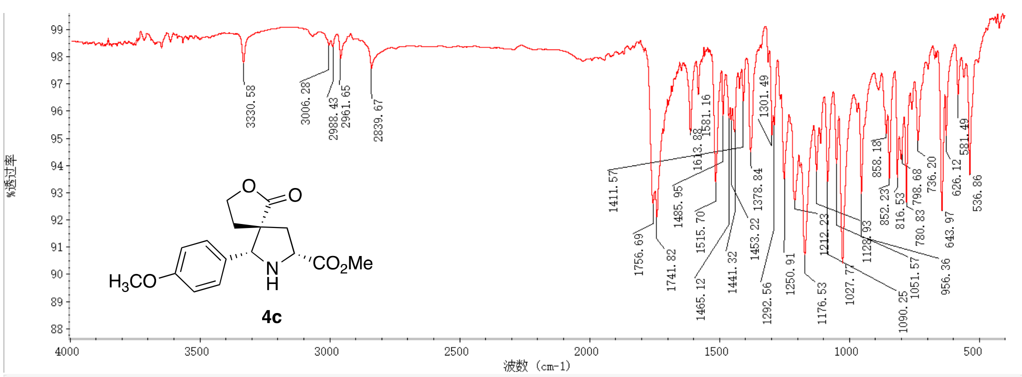
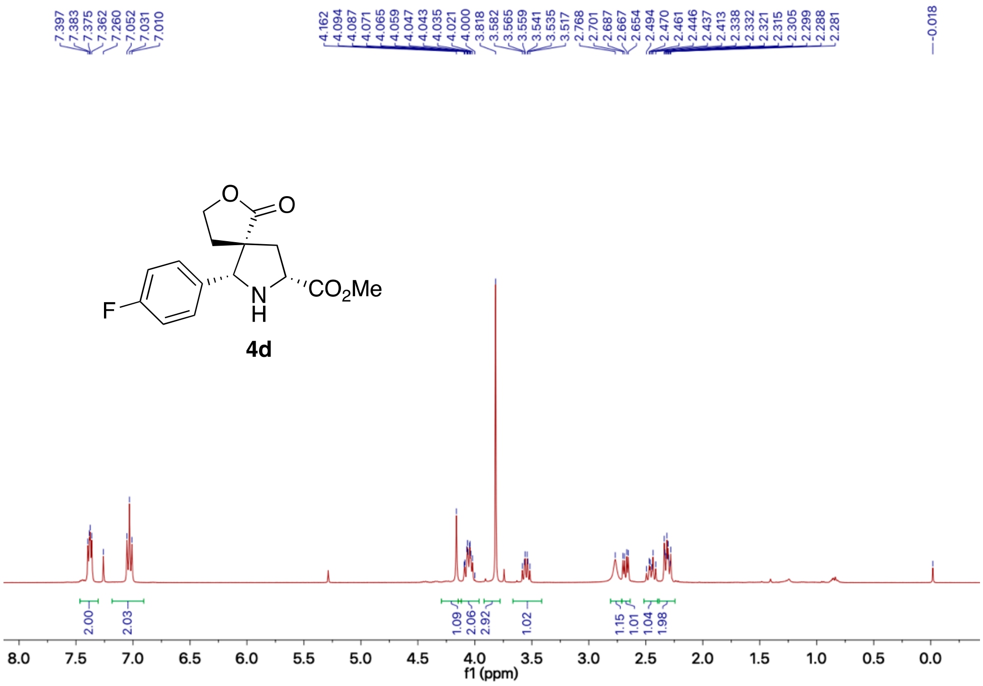
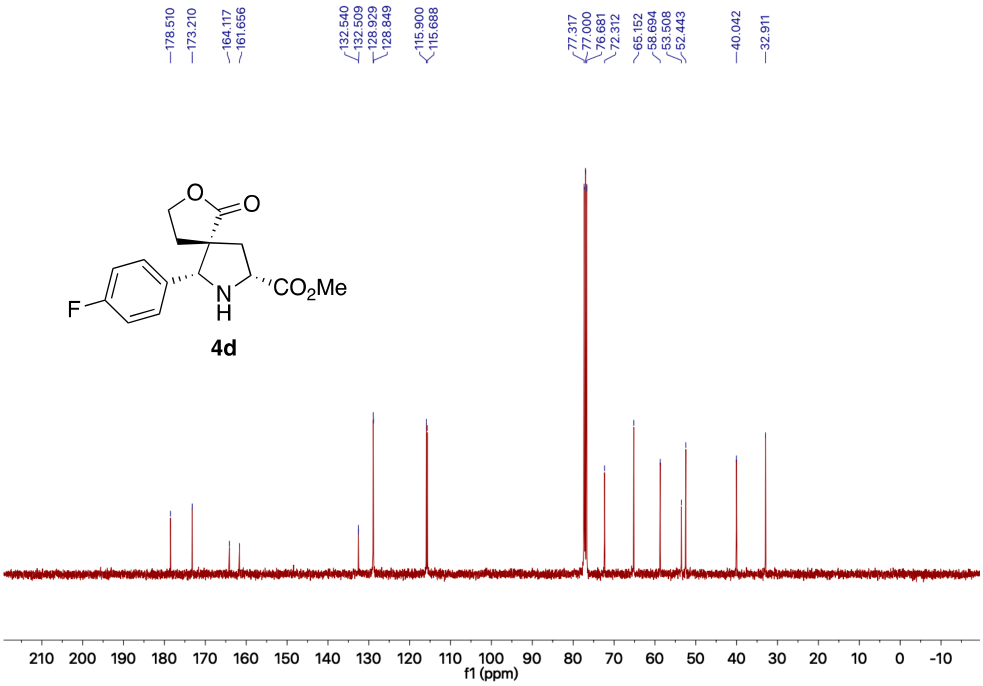
173.327
159.974
128.298
114.240
77.317
77.000
76.682
72.939
65.206
58.820
55.211
53.508
52.405
40.320
32.905
4c
f1 (ppm)

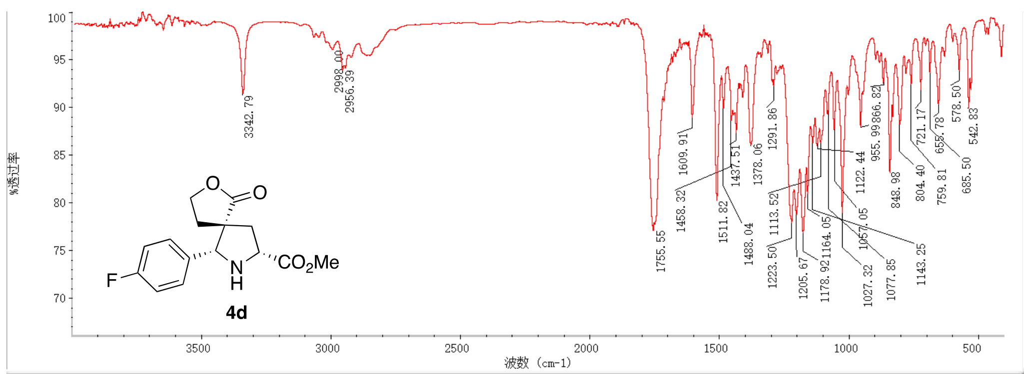

3330.58
3006.28
2988.43
2961.65
2839.67
1756.69
1741.82
1613.88
1581.16
1515.70
1485.95
1465.12
1453.22
1441.32
1411.57
1378.84
1301.49
1292.56
1250.91
1212.23
1176.53
1128.93
1090.25
1051.57
1027.77
956.36
858.18
852.23
816.53
798.68
780.83
736.20
643.97
626.12
581.49
536.86
%透过率
波数 (cm-1)
4c



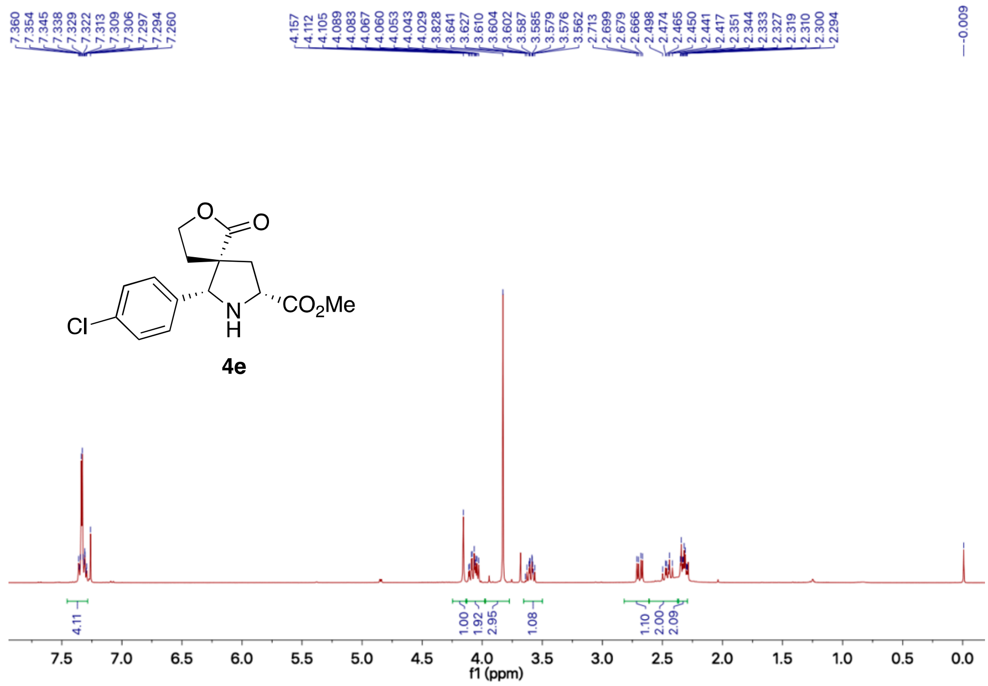
O
O
F
N
H
CO2Me
4d
f1 (ppm)

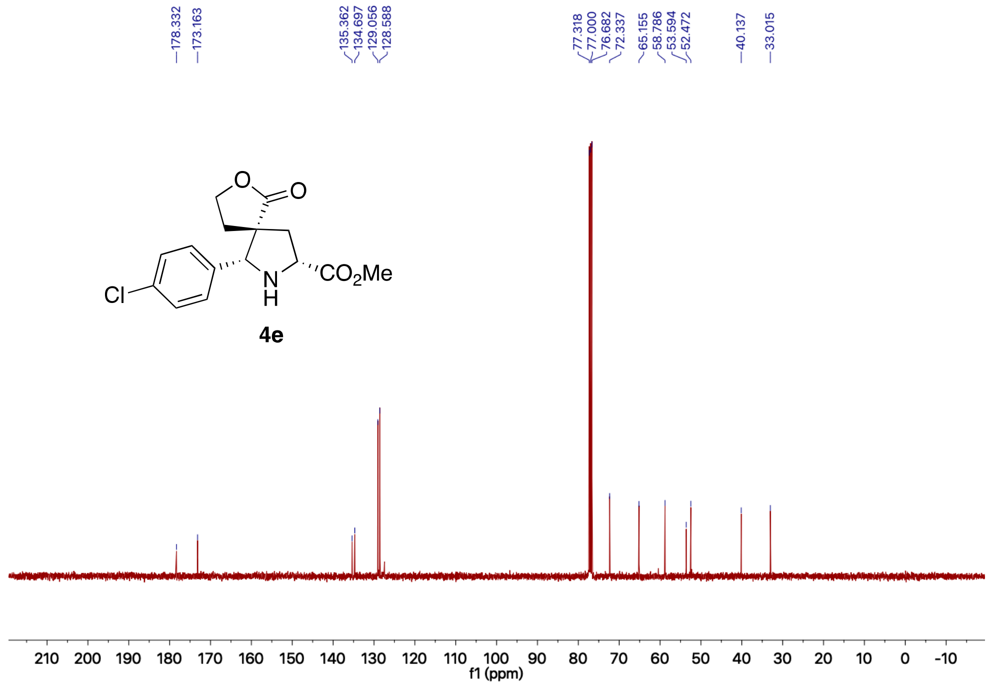



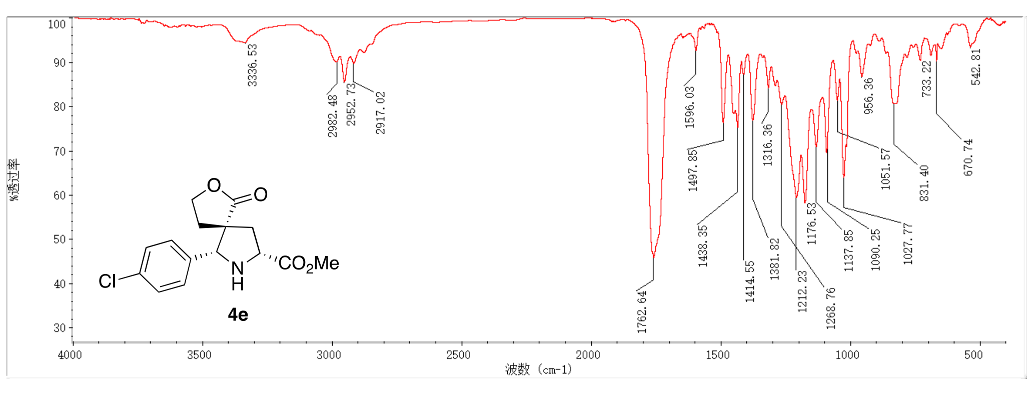
O
O
F
N
H
CO2Me
4d
f1 (ppm)

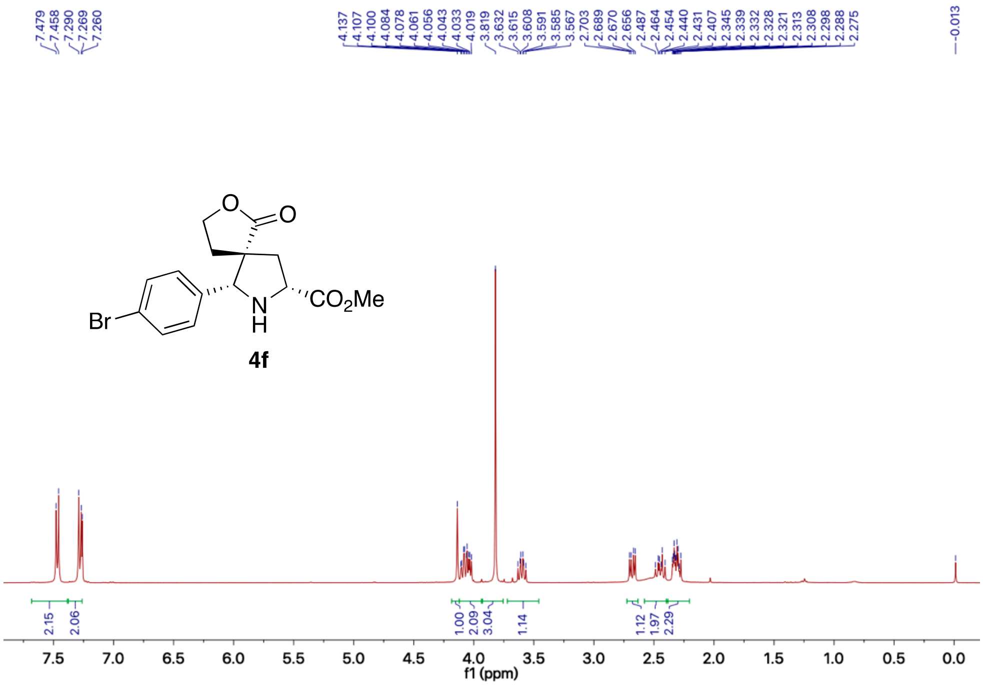



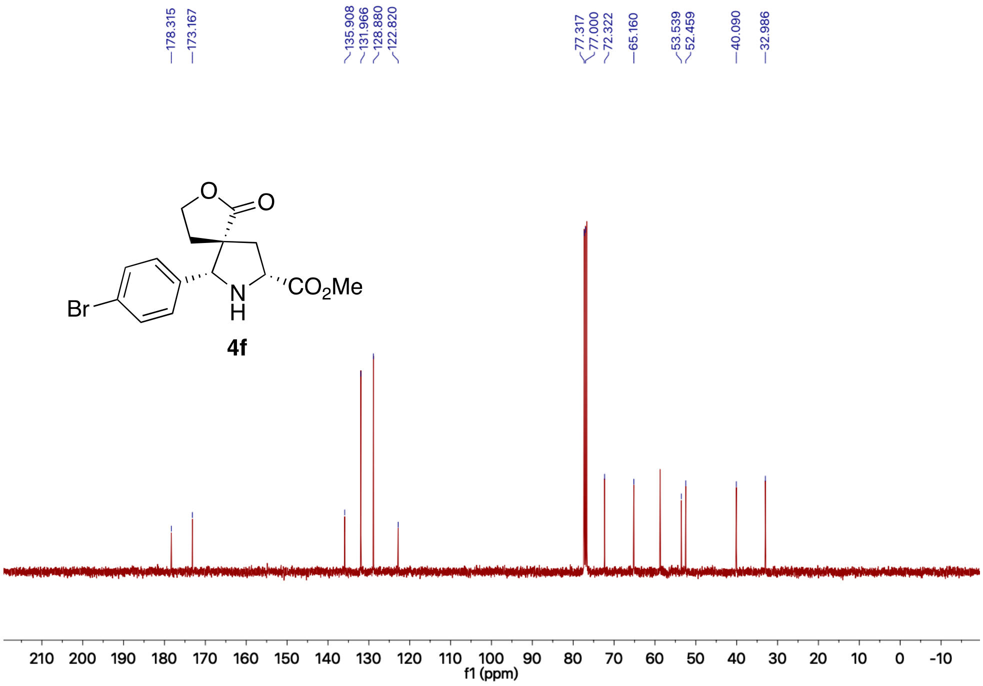
%透过率
波数 (cm-1)
O
O
F
N
H
CO2Me
4d

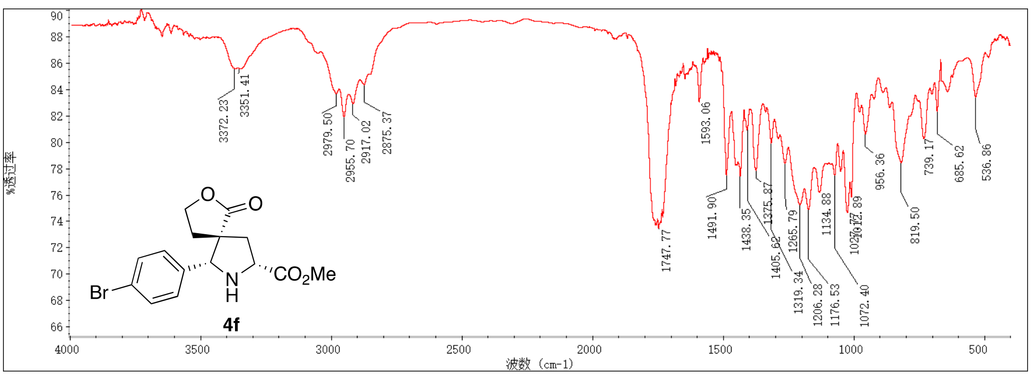


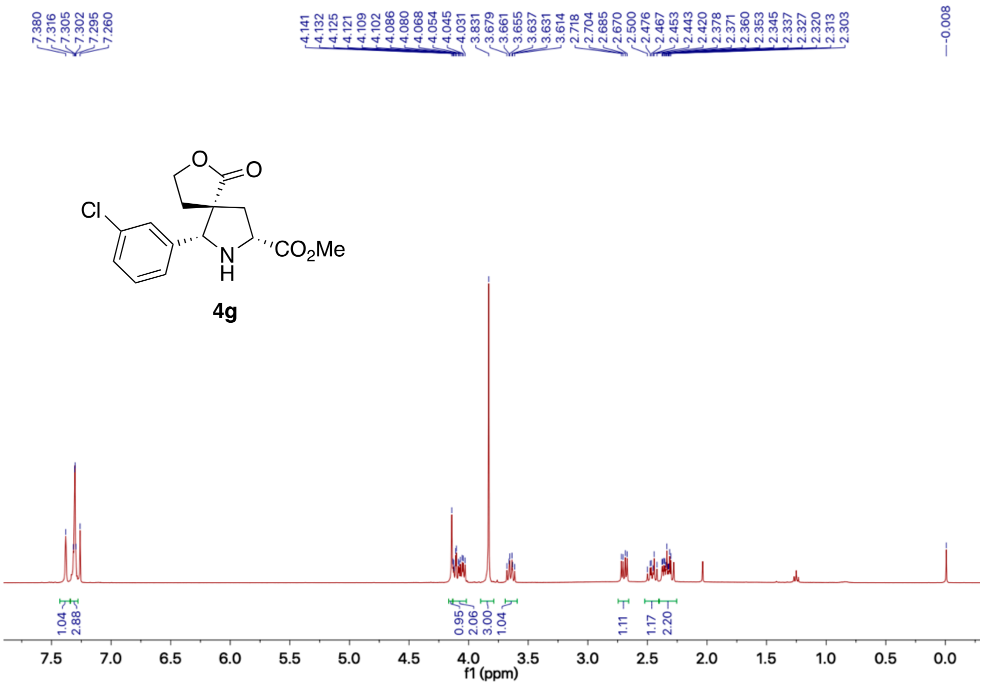


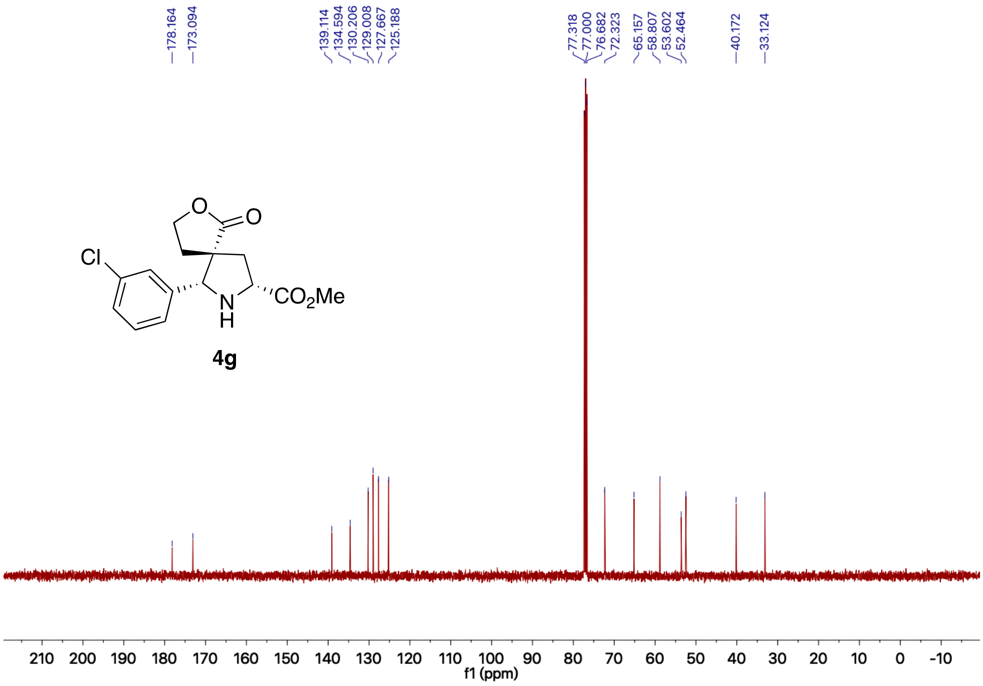


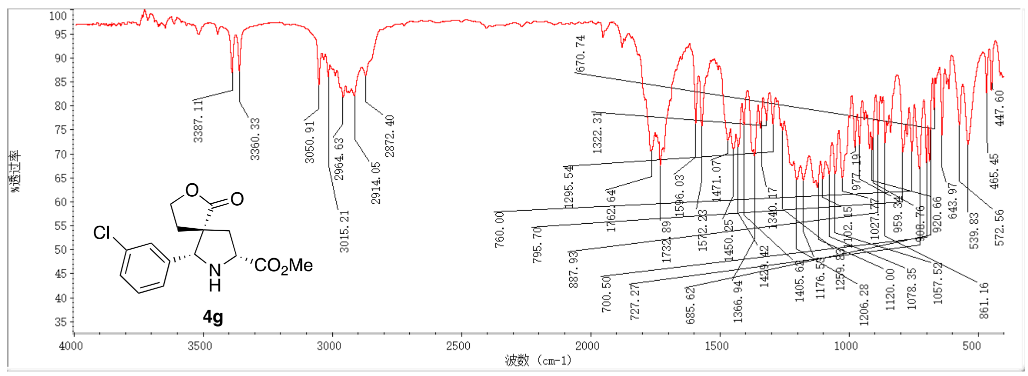

4f
f1 (ppm)

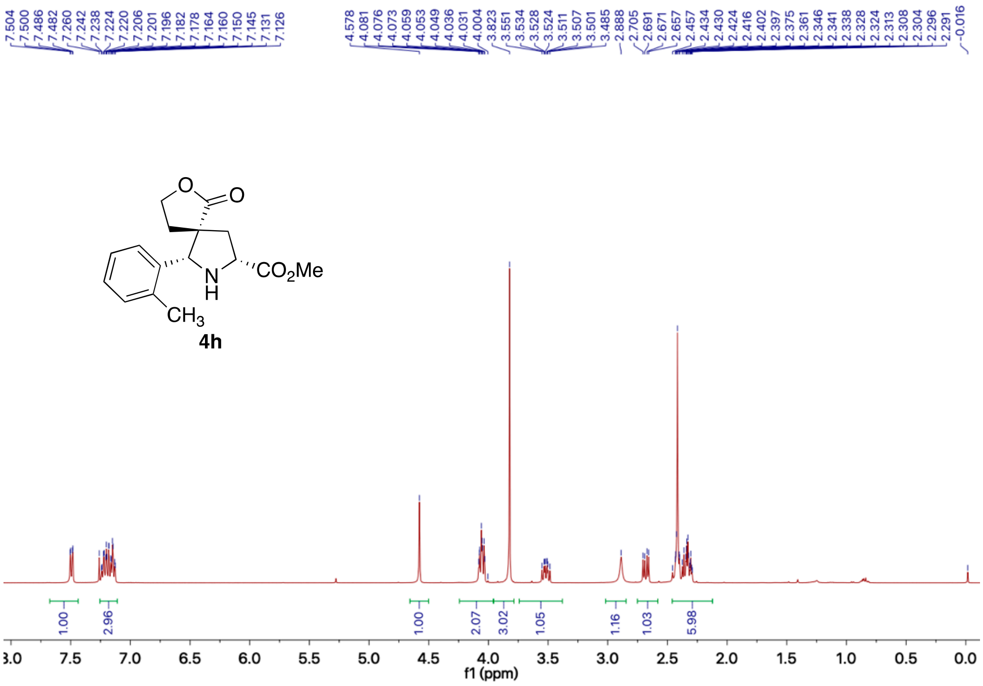

4f
f1 (ppm)


4f
%透过率
波数 (cm-1)


4g
f1 (ppm)


4g
f1 (ppm)


4g
%透过率
波数 (cm-1)



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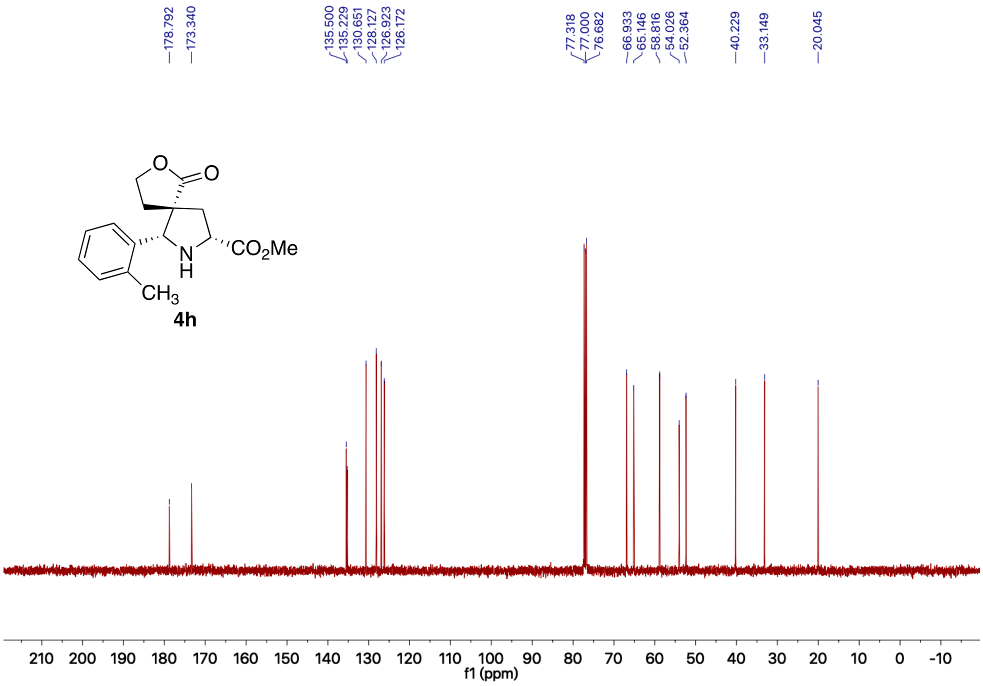
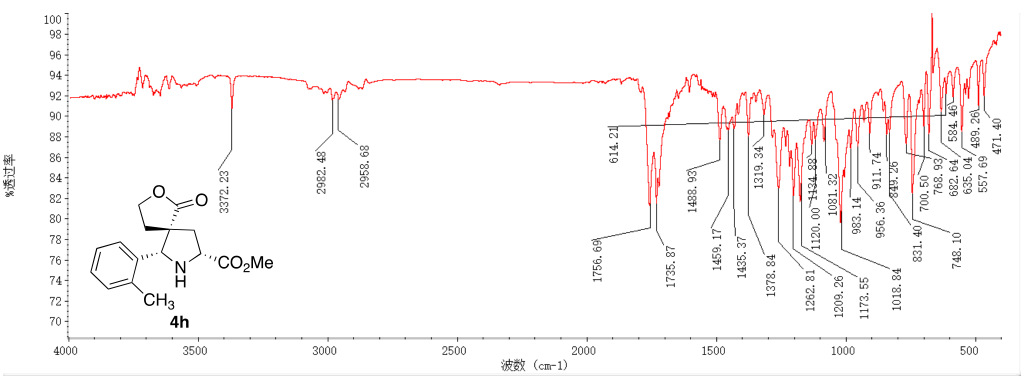
4.578 4.081 4.076 4.073 4.059 4.053 4.049 4.036 4.031 4.004 3.823 3.551 3.534 3.528 3.524 3.511 3.507 3.501 3.485 2.888 2.705 2.691 2.671 2.657 2.457 2.434 2.430 2.424 2.416 2.402 2.397 2.375 2.361 2.346 2.341 2.338 2.328 2.324 2.313 2.308 2.304 2.296 2.291 -0.016
CO2Me
H
N
O
O
CH3
4h
1.00 2.96 1.00 2.07 3.02 1.05 1.16 1.03 5.98
f1 (ppm)

178.792 173.340 135.500 135.229 130.651 128.127 126.923 126.172 77.318 77.000 76.682 66.933 65.146 58.816 54.026 52.364 40.229 33.149 20.045
CO2Me
4h
f1 (ppm)

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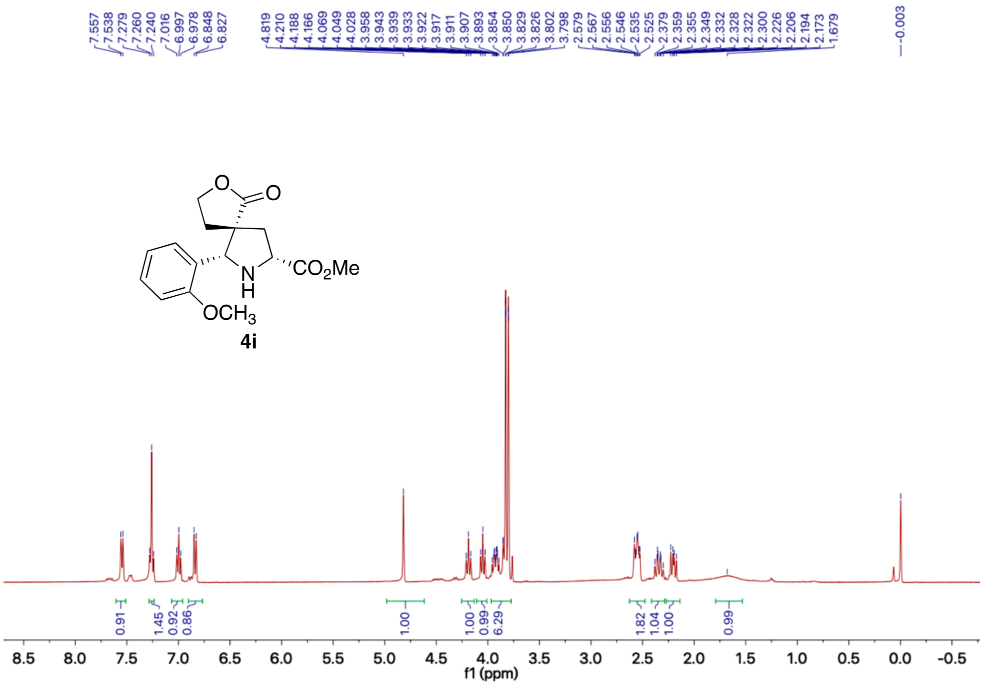
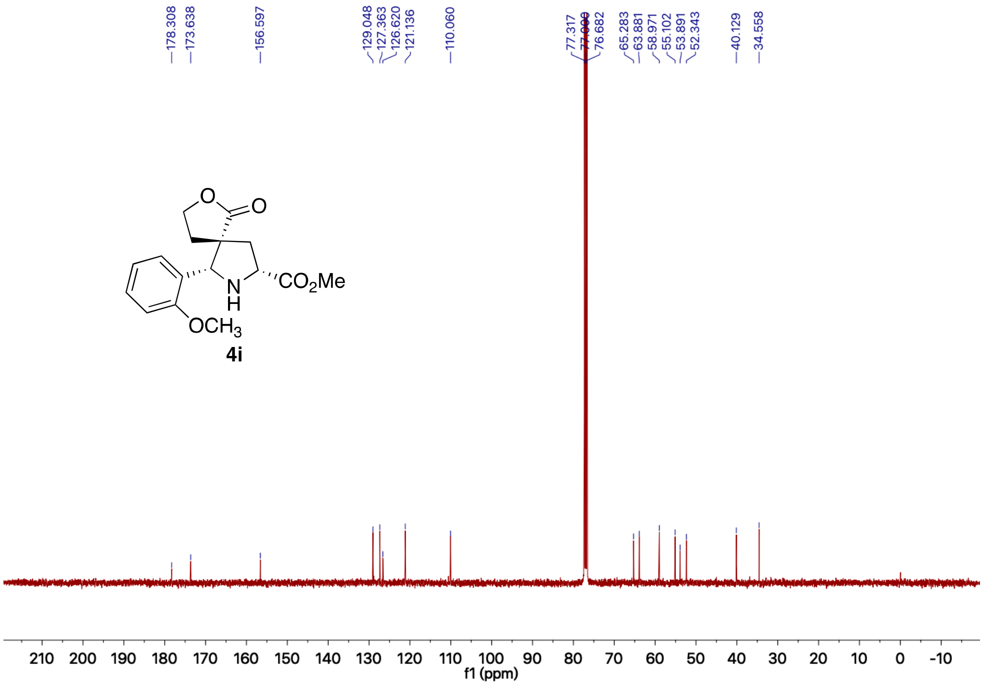
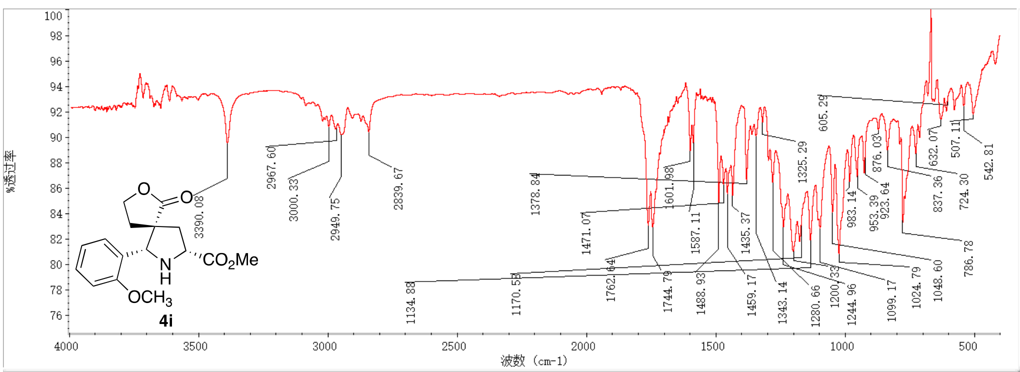
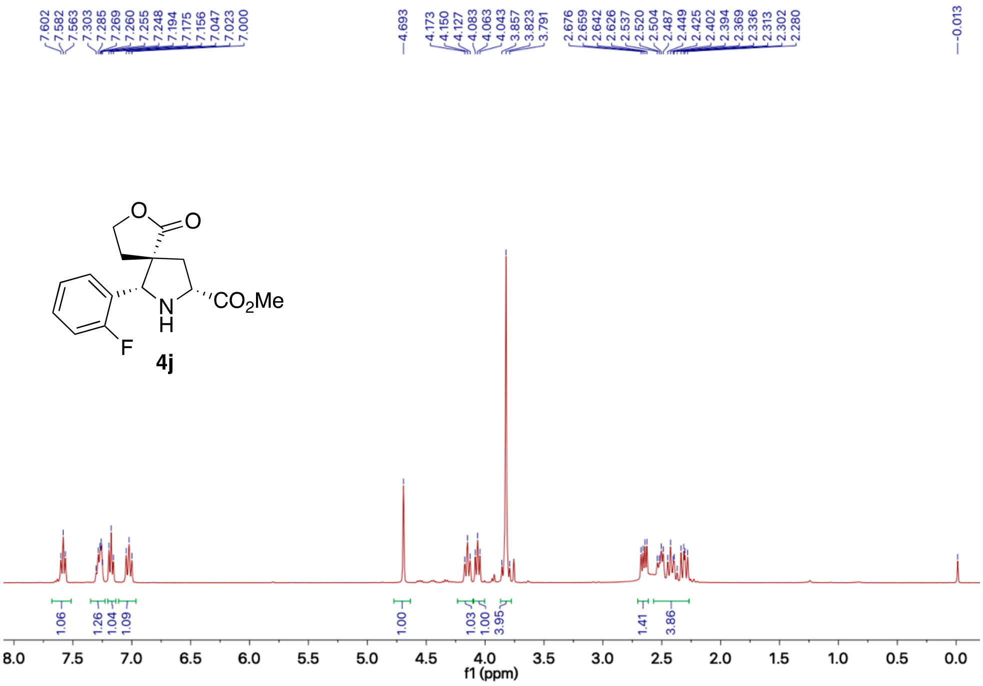
CO2Me
4h
%透过率
波数 (cm-1)









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7.255
7.248
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7.047
7.023
7.000
4.693
4.173
4.150
4.127
4.083
4.063
4.043
3.857
3.823
3.791
2.676
2.659
2.642
2.626
2.537
2.520
2.504
2.487
2.449
2.425
2.402
2.394
2.369
2.336
2.313
2.302
2.280
-0.013
CO2Me
F
4j
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1.26
1.04
1.09
1.00
1.03
1.00
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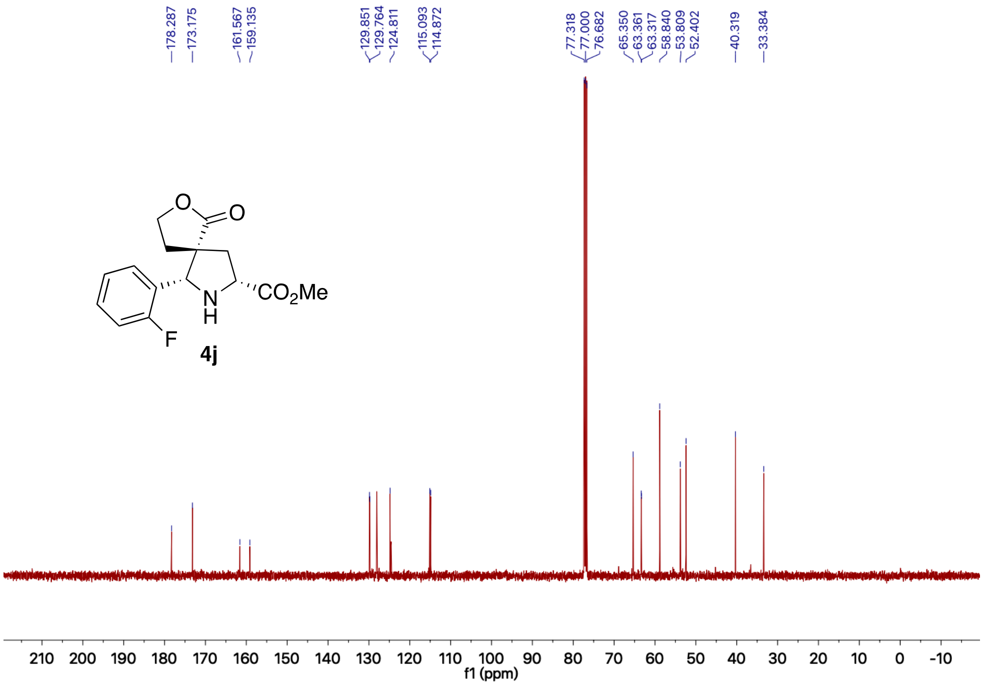
1.41
3.86
f1 (ppm)

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159.135
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129.764
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77.318
77.000
76.682
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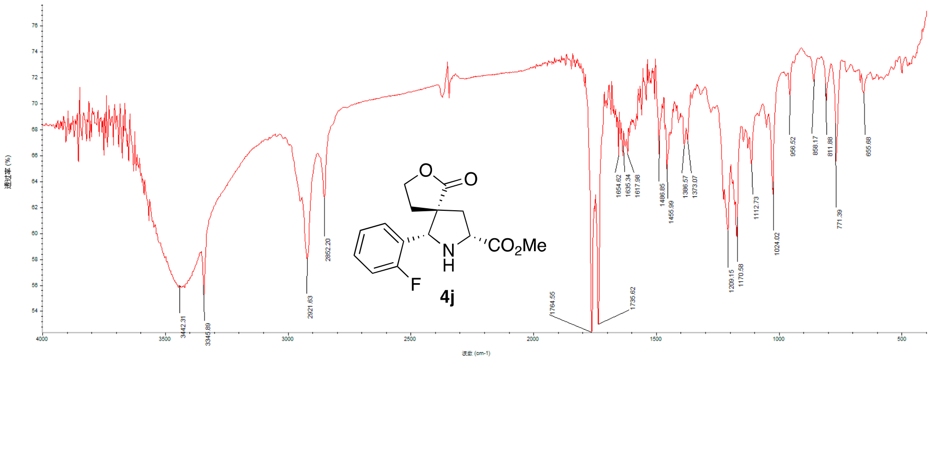
63.361
63.317
58.840
53.809
52.402
40.319
33.384
CO2Me
F
4j
f1 (ppm)

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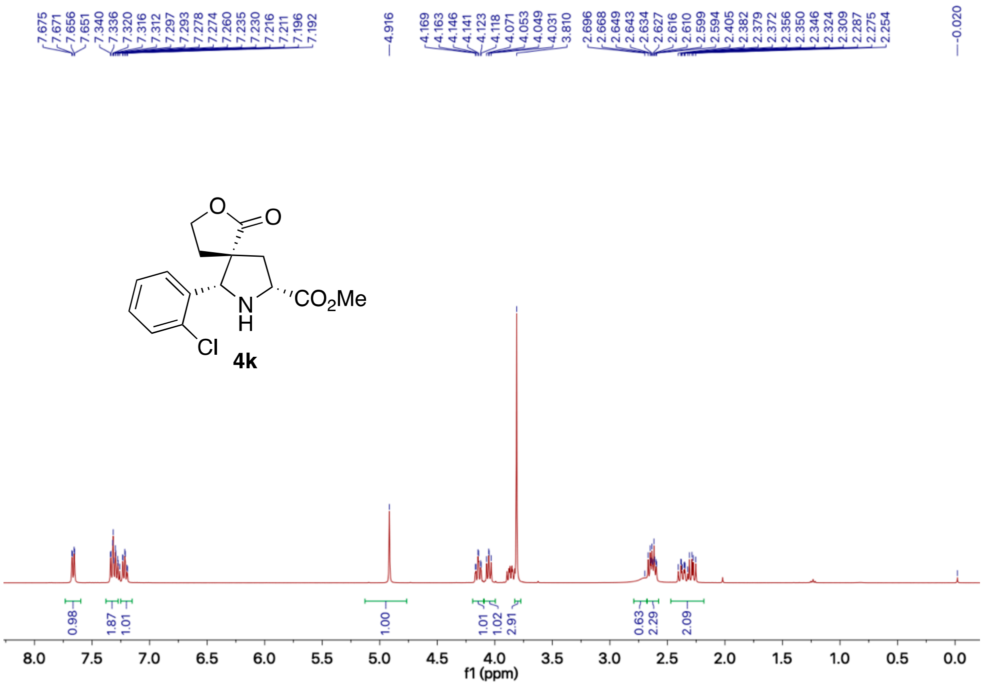
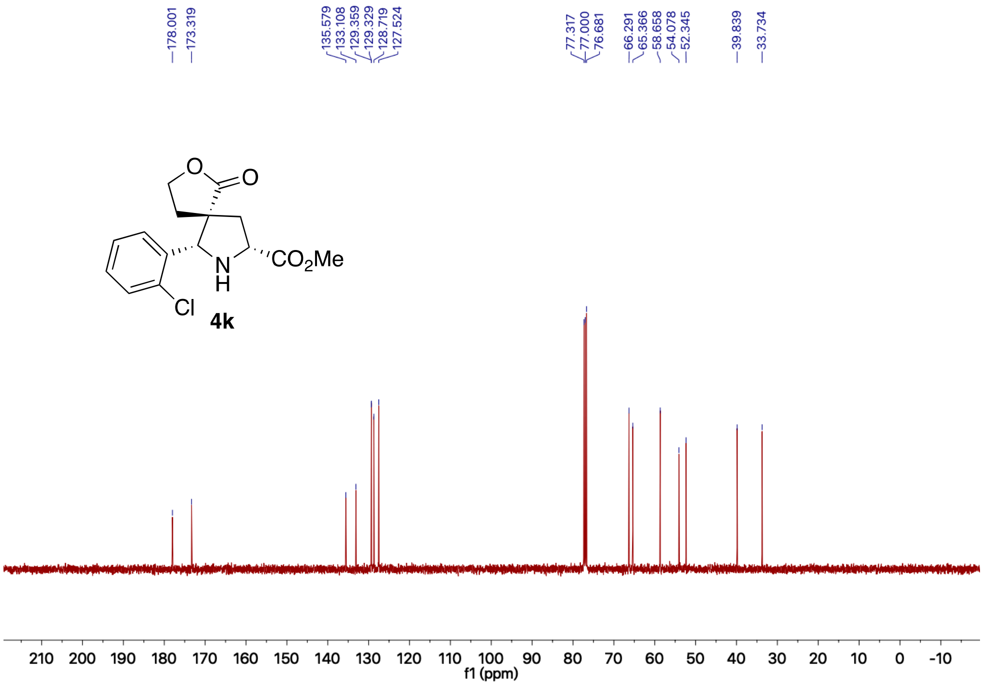
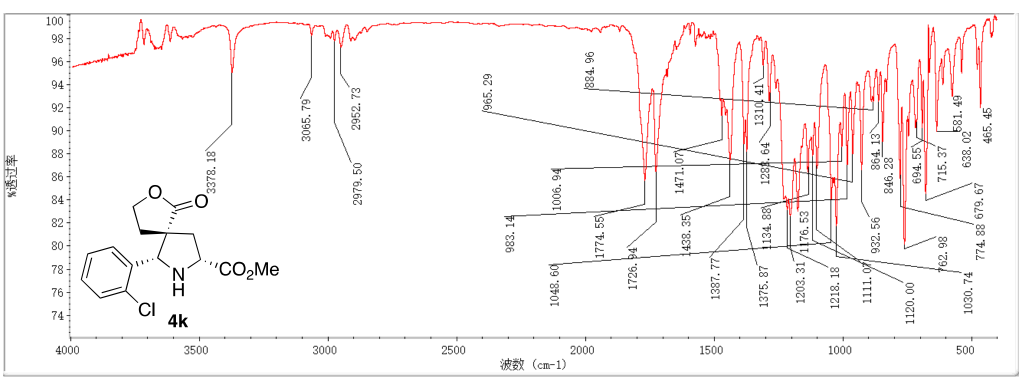
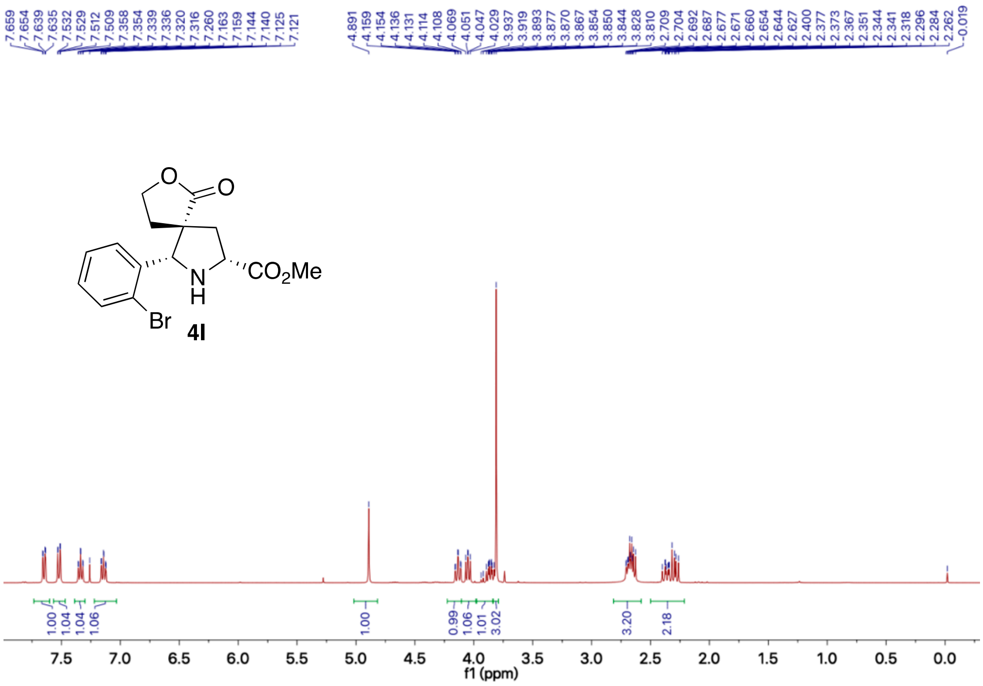
2921.63
2852.20
1764.55
1735.62
1654.62
1635.34
1617.98
1486.85
1455.99
1386.57
1373.07
1209.15
1170.58
1112.73
1024.02
956.52
856.17
811.88
771.39
655.68
CO2Me
F
4j





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7.316
7.260
7.163
7.159
7.144
7.140
7.125
7.121
4.891
4.159
4.154
4.136
4.131
4.114
4.108
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4.029
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3.870
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3.850
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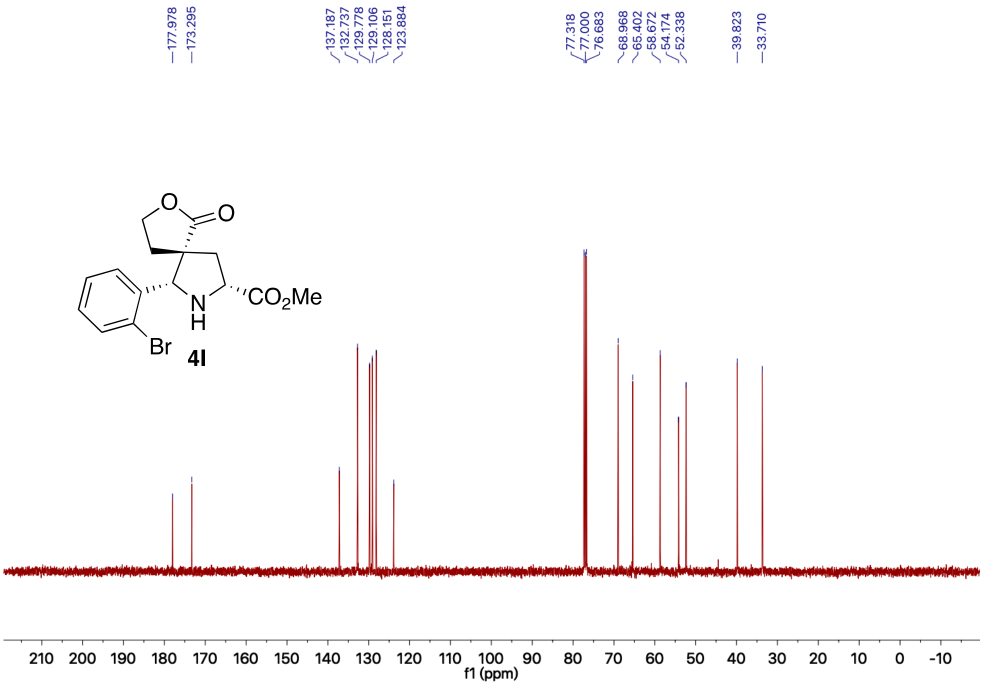
3.828
3.810
2.709
2.704
2.692
2.687
2.677
2.671
2.660
2.654
2.644
2.627
2.400
2.377
2.373
2.367
2.351
2.344
2.341
2.318
2.296
2.284
2.262
-0.019
CO2Me
N
H
Br
4l
1.00
1.04
1.04
1.06
1.00
0.99
1.06
1.01
3.02
3.20
2.18
f1 (ppm)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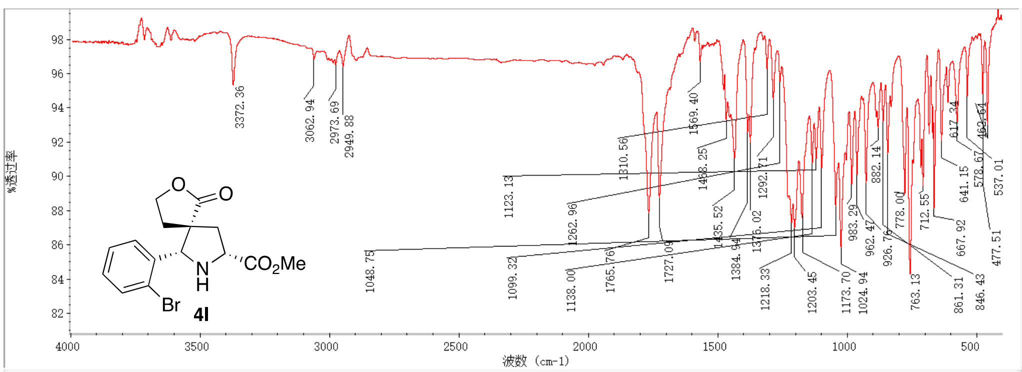
129.106
128.151
123.884
77.318
77.000
76.683
68.968
65.402
58.672
54.174
52.338
39.823
33.710
CO2Me
N
H
Br
4l
f1 (ppm)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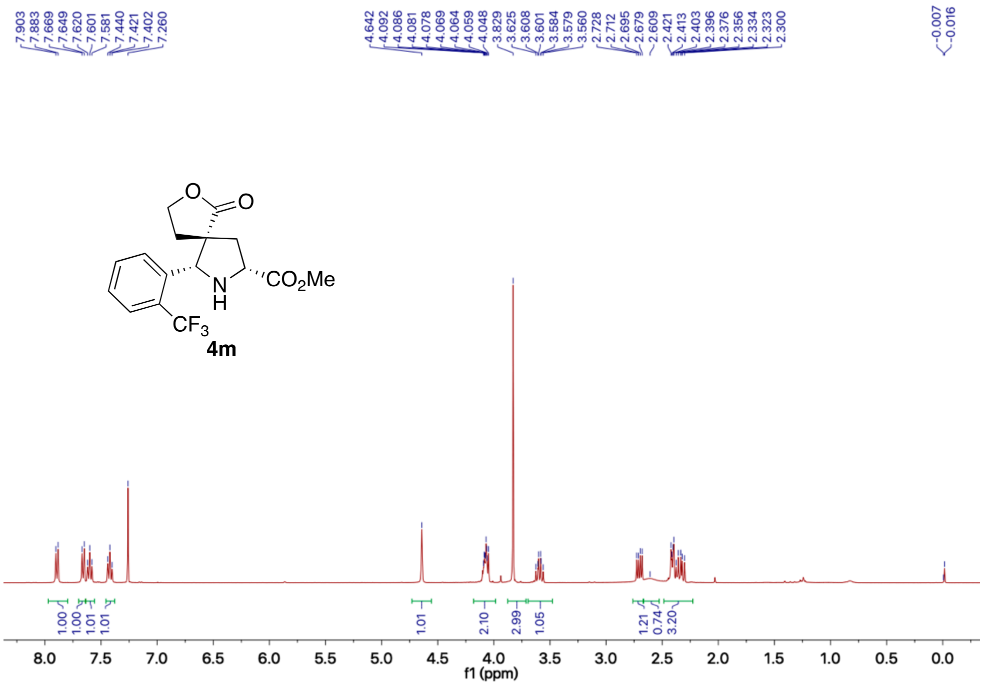
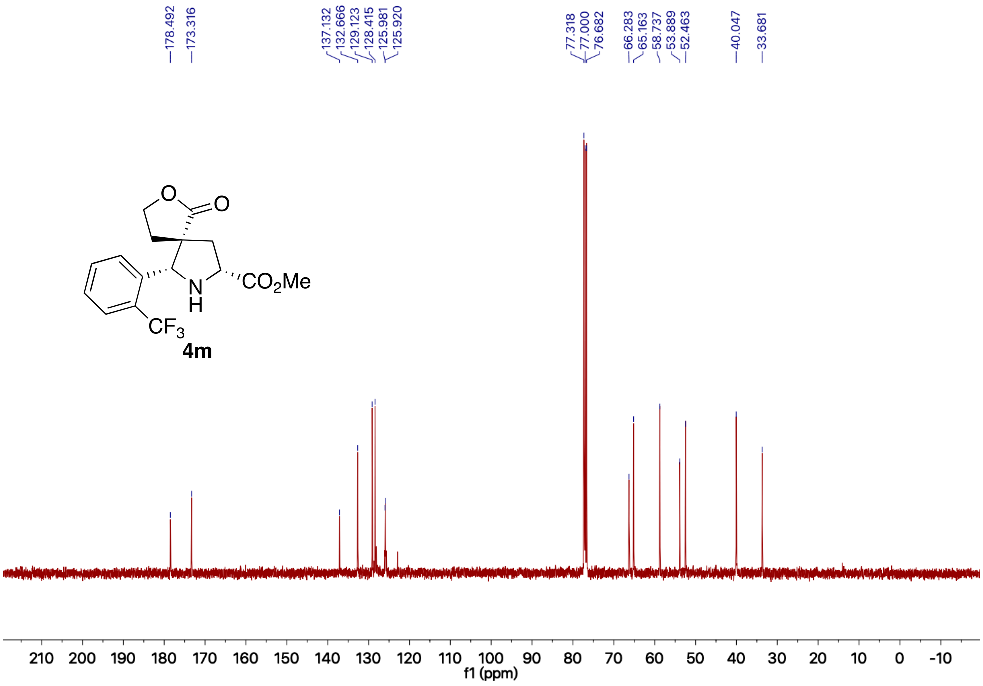
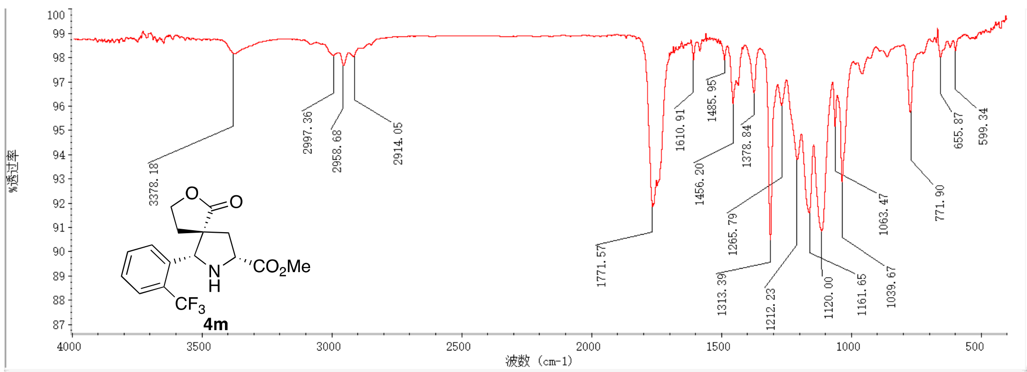
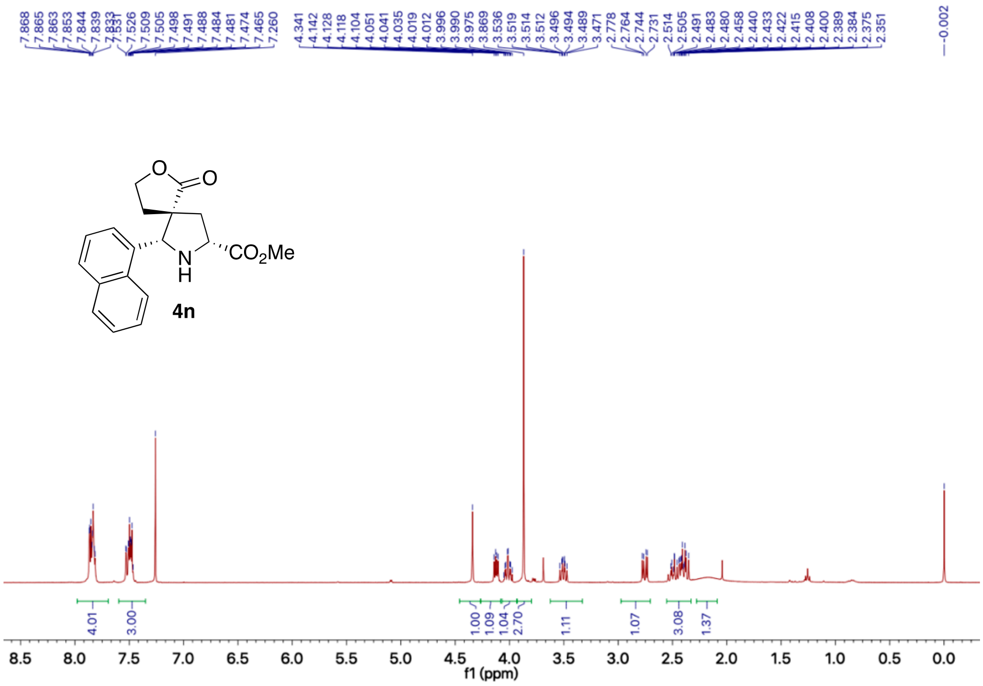
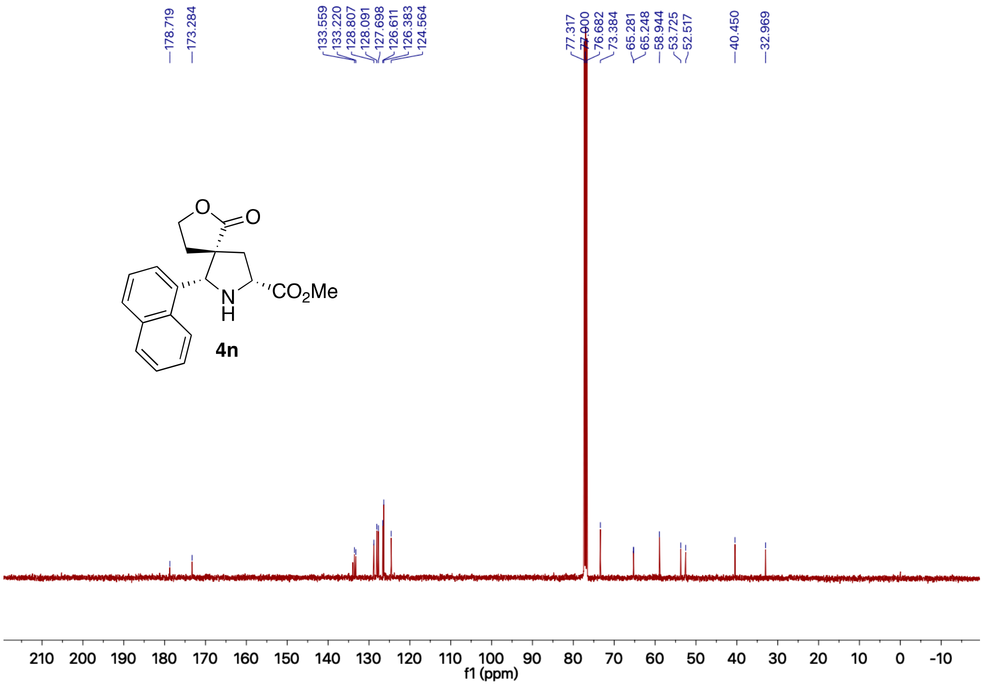
1435.52
1376.02
1048.75
1099.32
1138.00
1765.76
1727.09
1384.94
1218.33
1203.45
1173.70
1024.94
983.29
962.47
926.75
882.14
778.00
712.55
763.13
667.92
861.31
846.43
641.15
617.34
578.67
537.01
477.51
%透过率
波数 (cm-1)
CO2Me
N
H
Br
4l

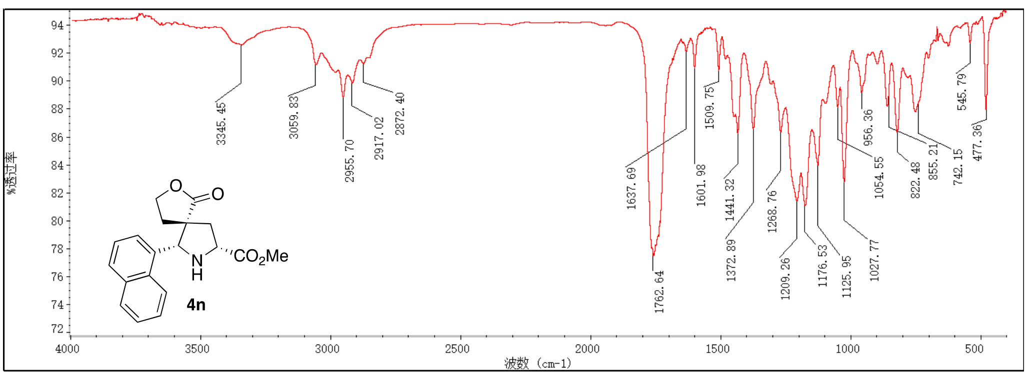


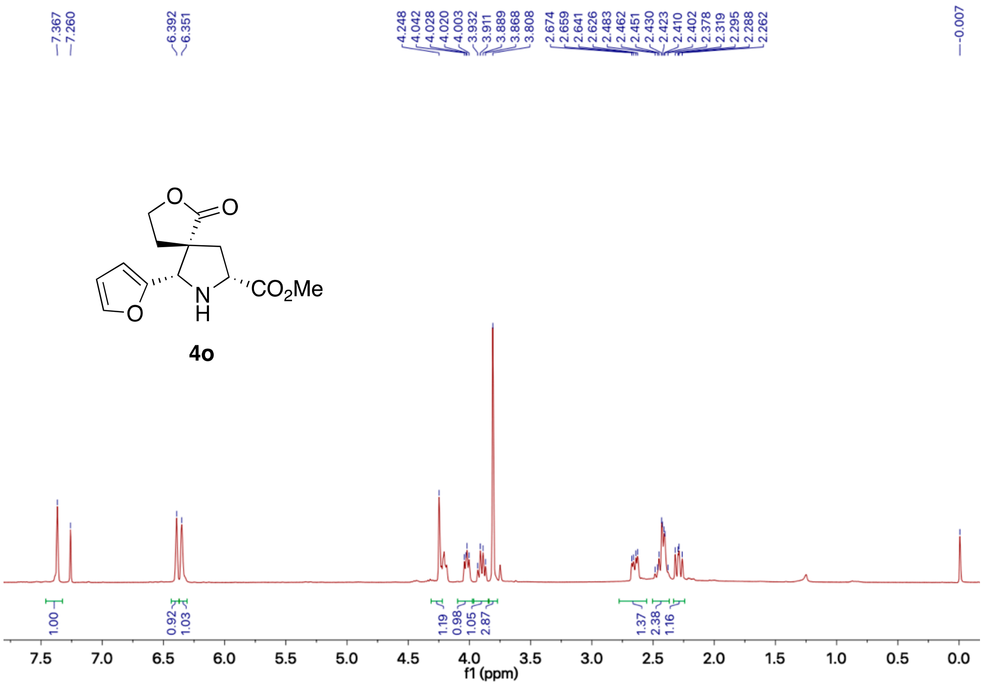








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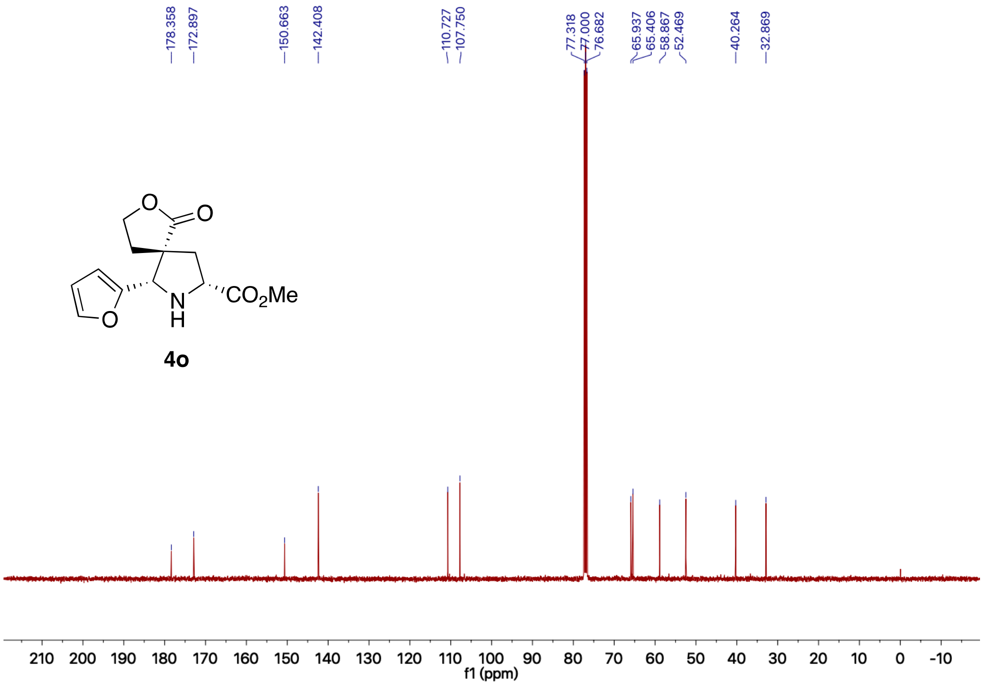
f1 (ppm)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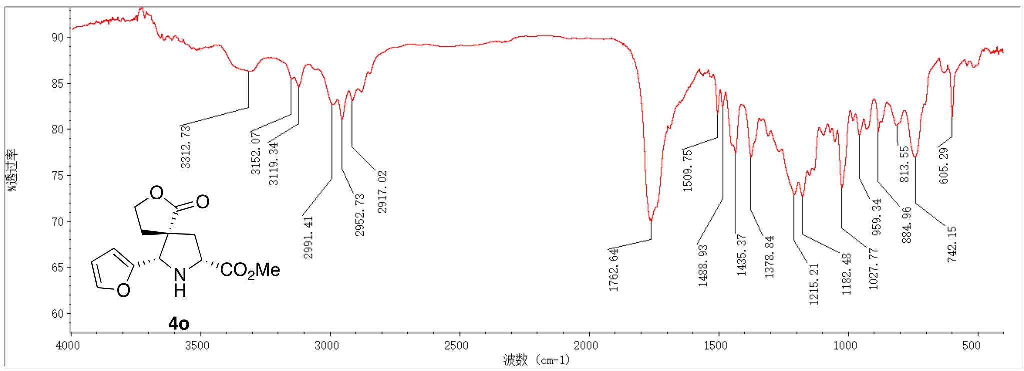
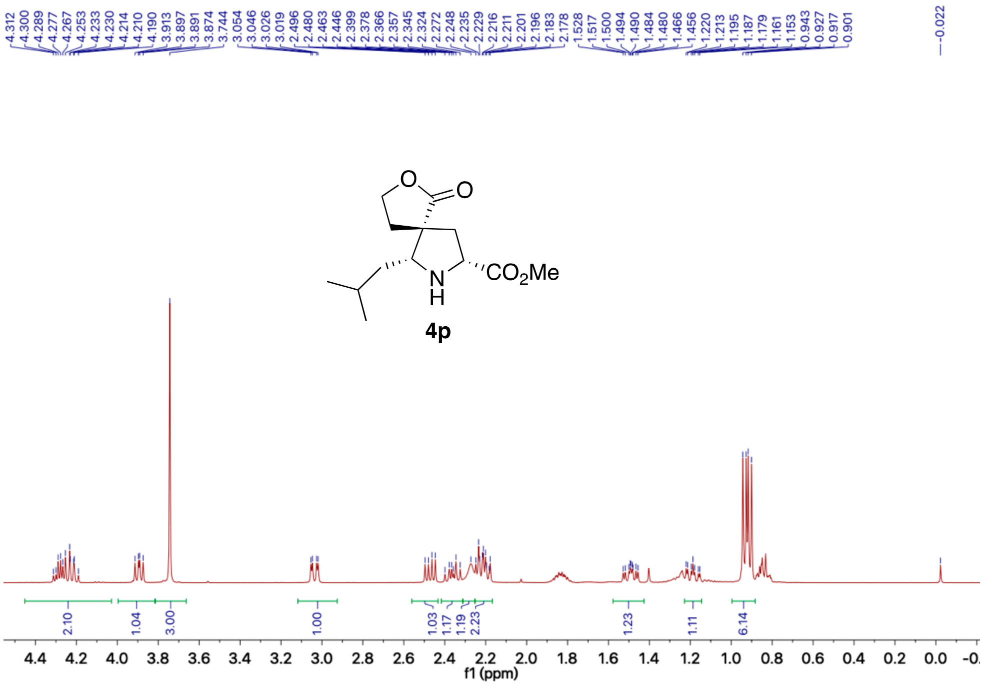
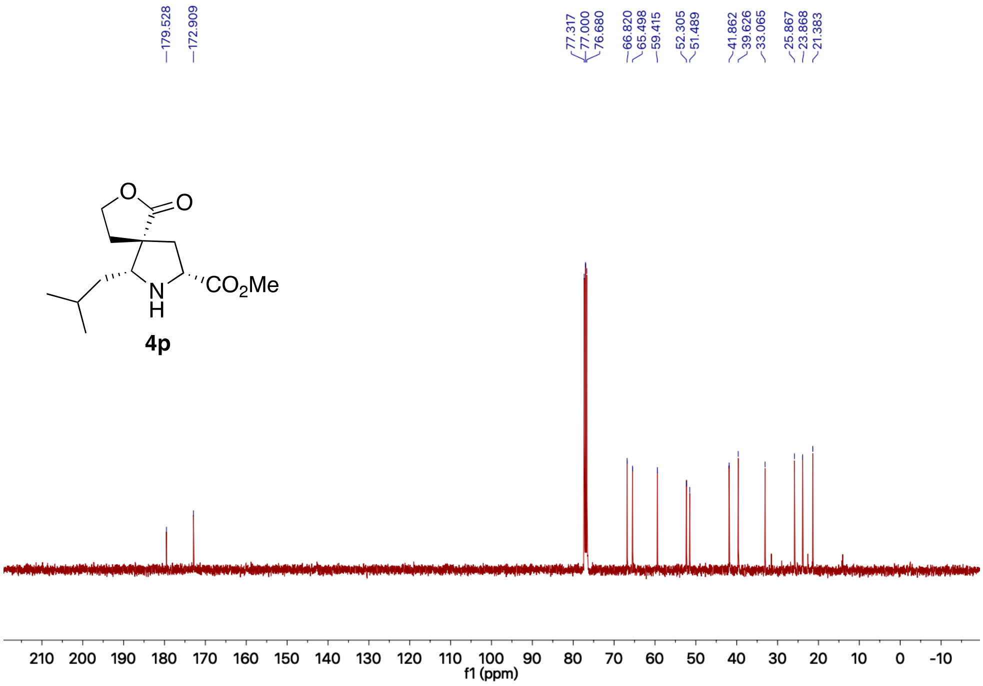
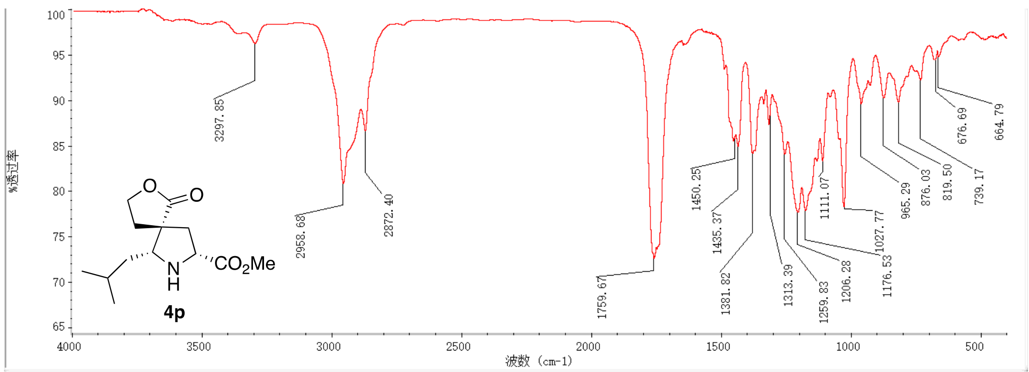
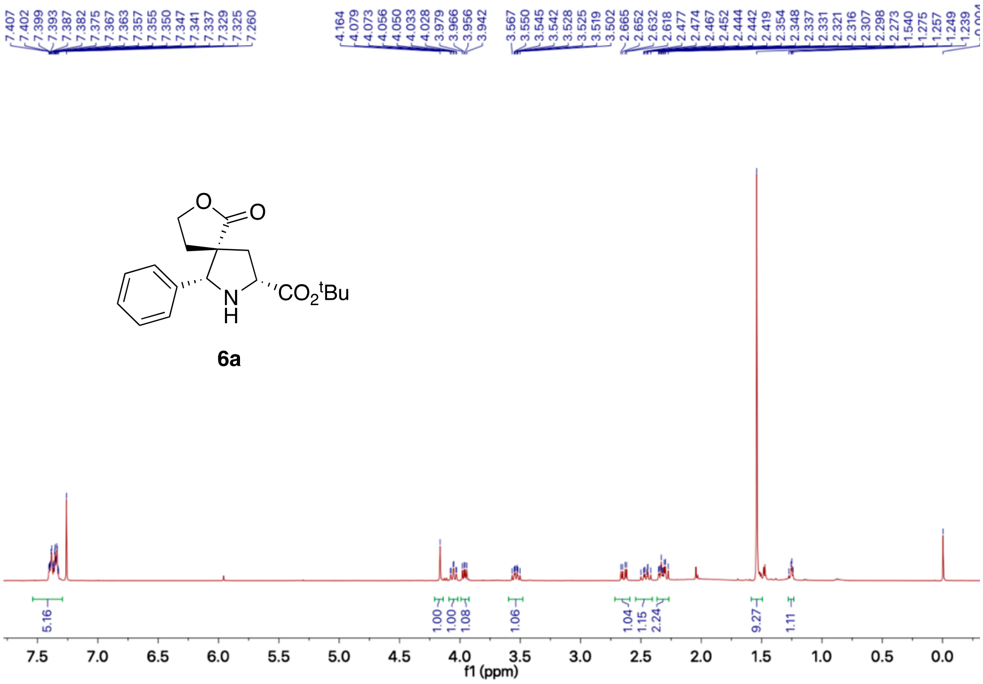
f1 (ppm)

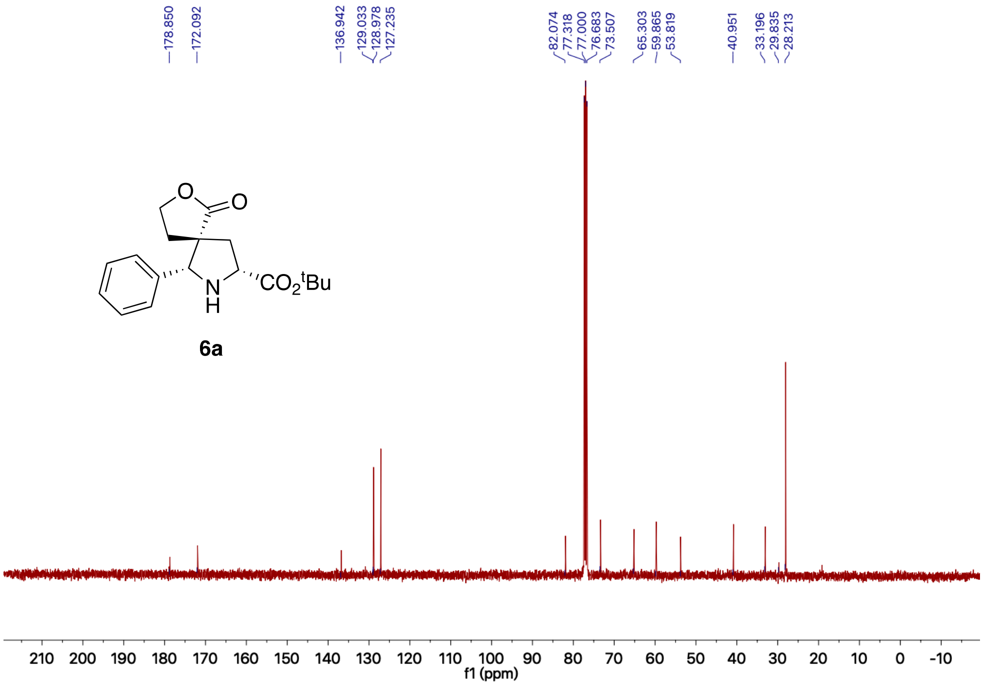

4o
%透过率
波数 (cm-1)

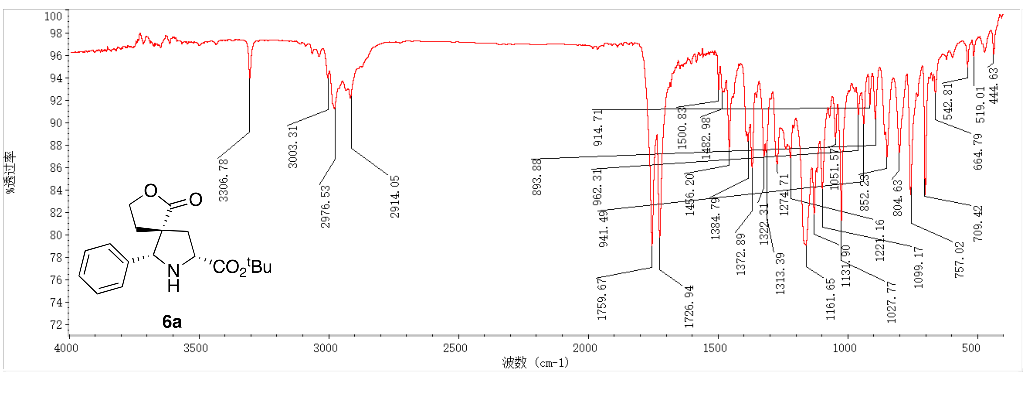


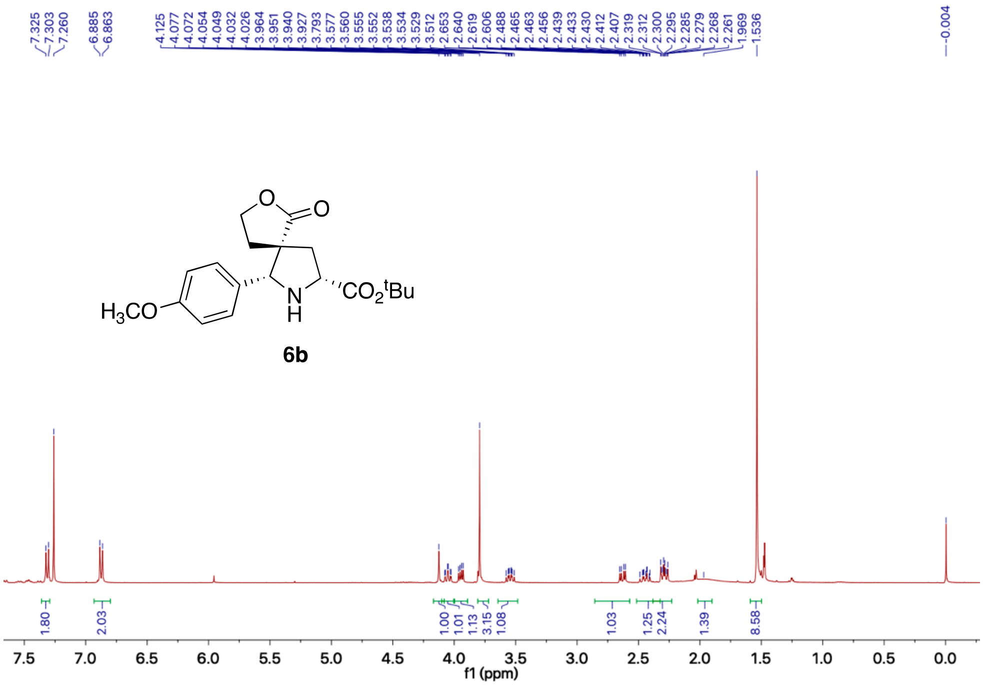








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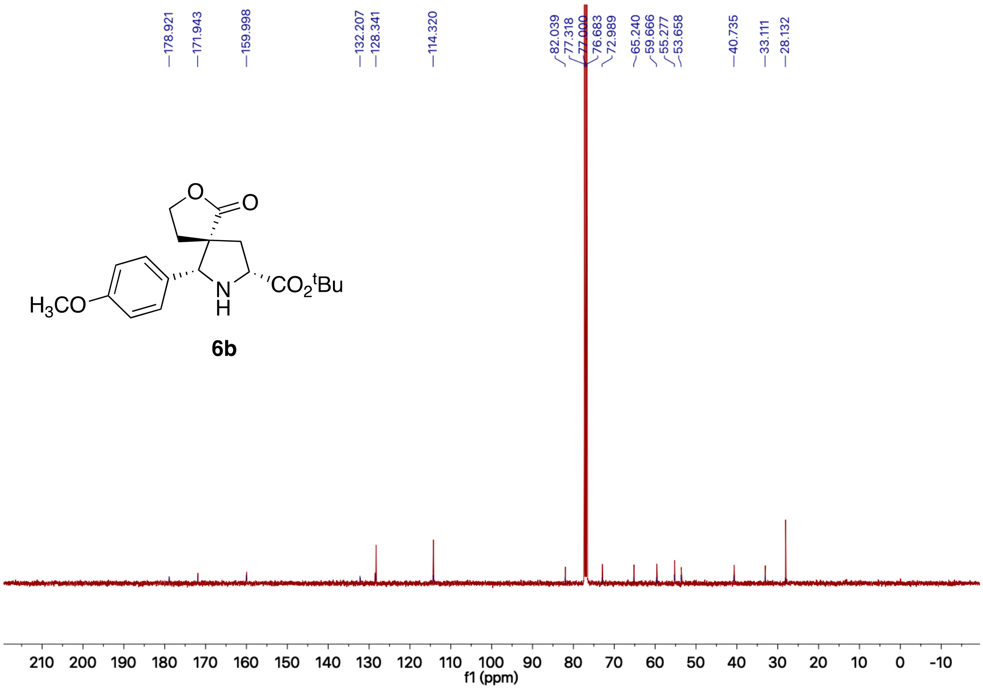
7.260
6.885
6.863
4.125
4.077
4.072
4.054
4.049
4.032
4.026
3.964
3.951
3.940
3.927
3.793
3.577
3.560
3.555
3.552
3.538
3.534
3.529
3.512
2.653
2.640
2.619
2.606
2.488
2.465
2.463
2.456
2.439
2.433
2.430
2.412
2.407
2.319
2.312
2.300
2.295
2.285
2.279
2.268
2.261
1.969
1.536
-0.004
H3CO
O
O
N
H
CO2tBu
6b
1.80
2.03
1.00
1.01
1.13
3.15
1.08
1.03
1.25
2.24
1.39
8.58
f1 (ppm)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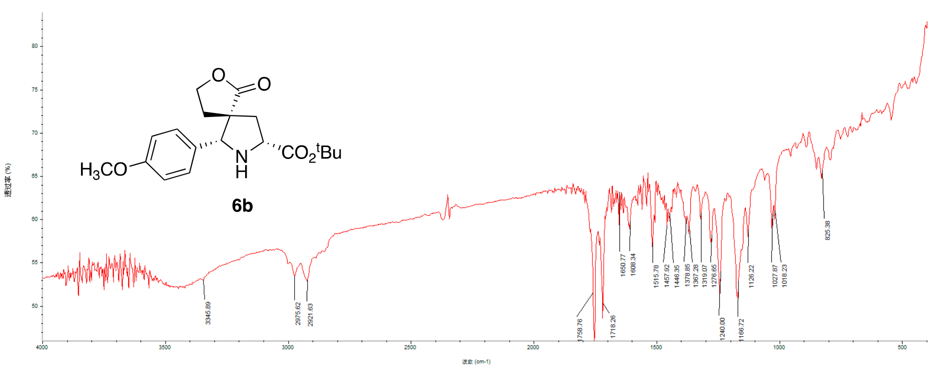
159.998
132.207
128.341
114.320
82.039
77.318
77.000
76.683
72.989
65.240
59.666
55.277
53.658
40.735
33.111
28.132
H3CO
O
O
N
H
CO2tBu
6b
f1 (ppm)


H3CO
O
O
N
H
CO2tBu
6b
3345.89
2975.62
2921.63
1758.76
1718.26
1650.77
1608.34
1515.78
1457.92
1446.35
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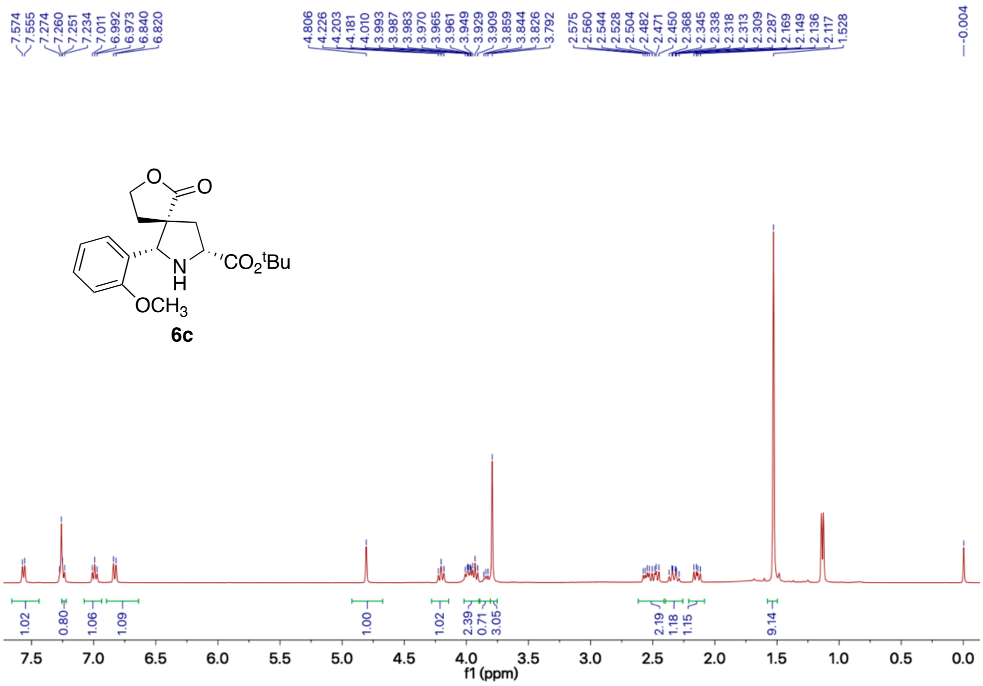
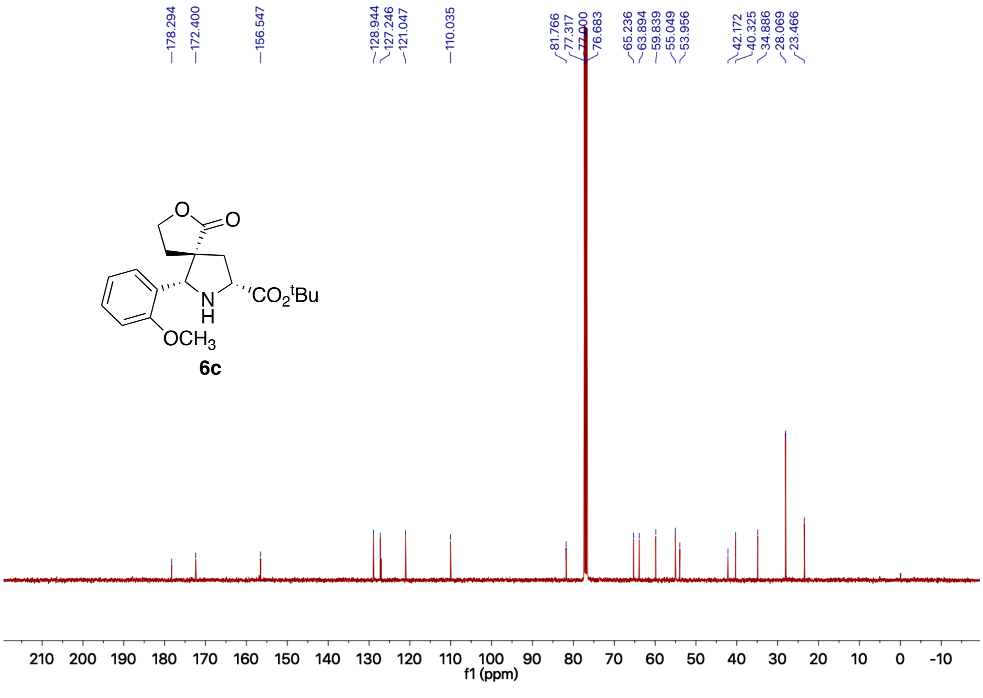
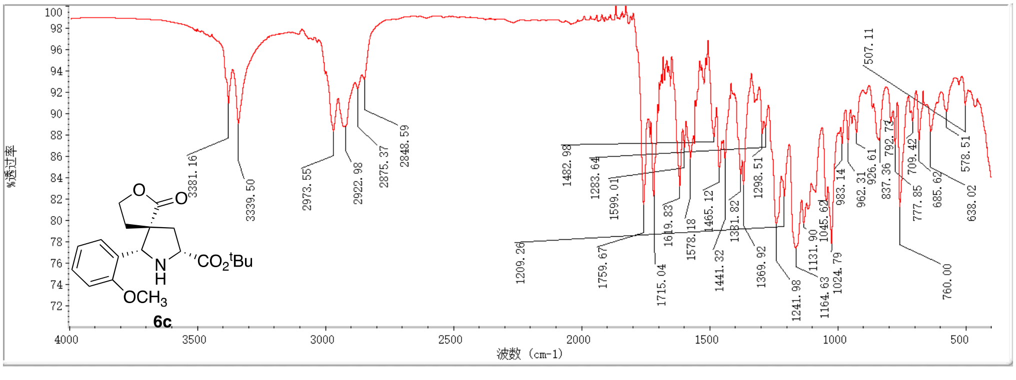
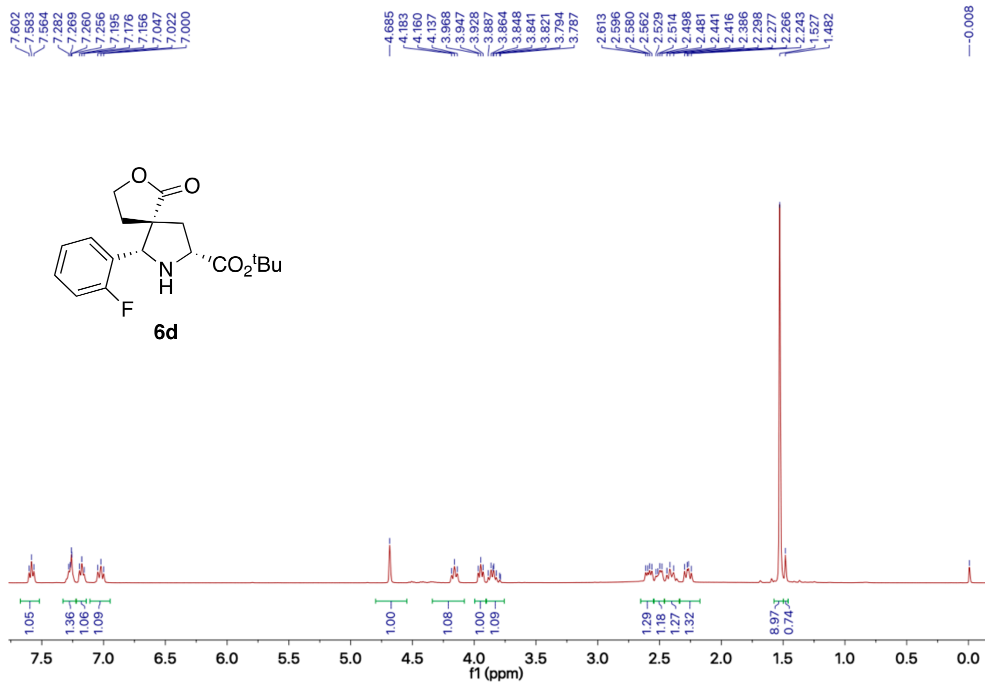
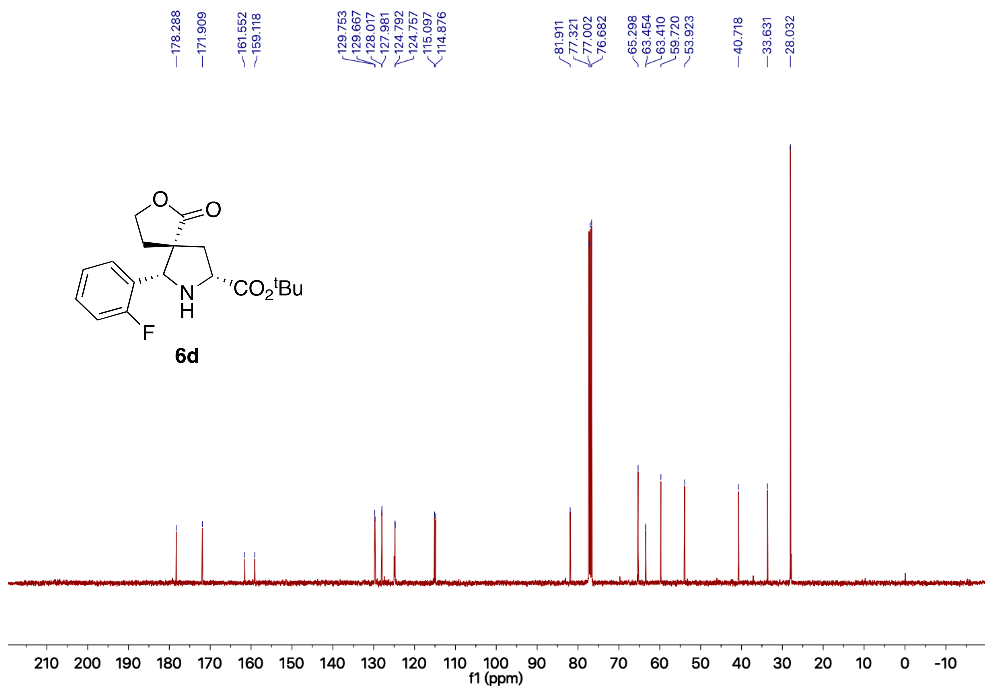
1367.28
1310.07
1276.65
1240.00
1166.72
1126.22
1027.87
1018.23
825.38

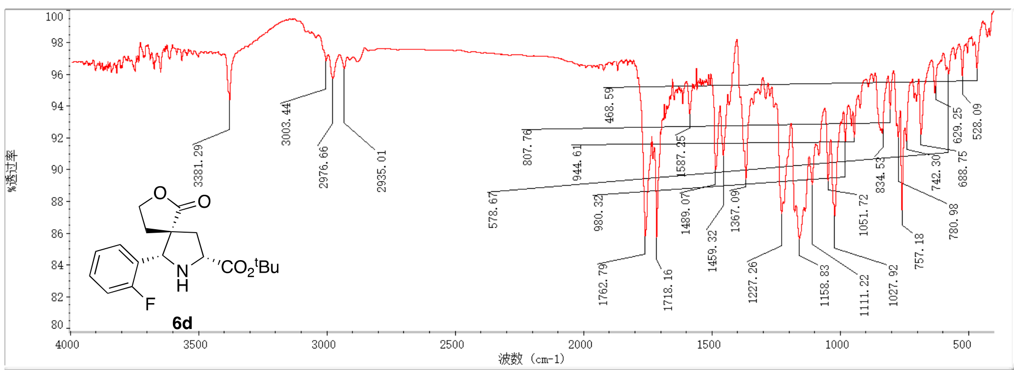


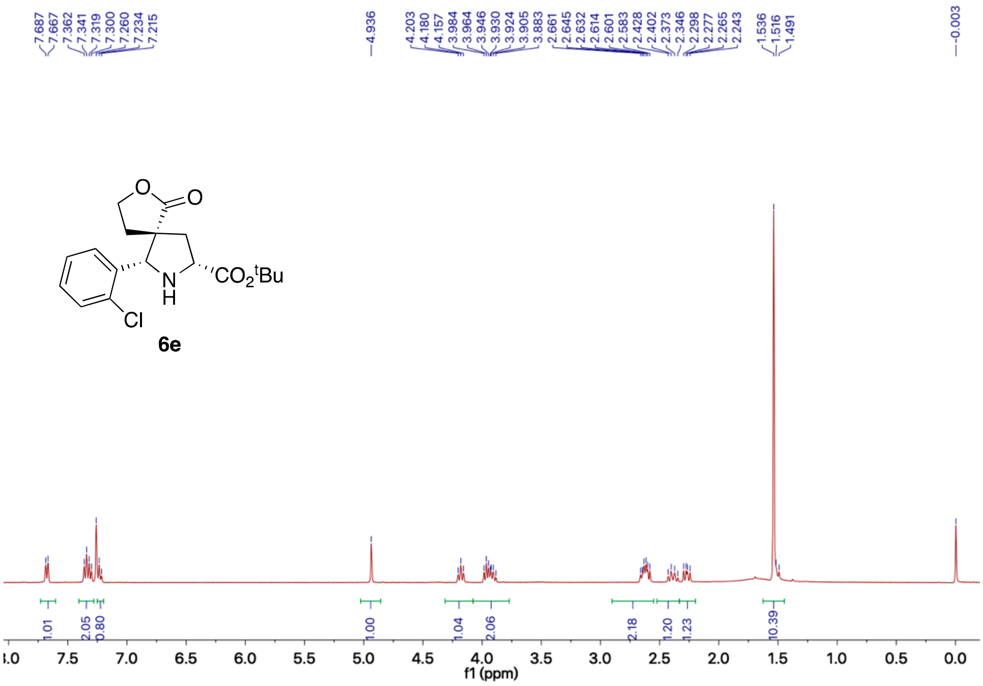


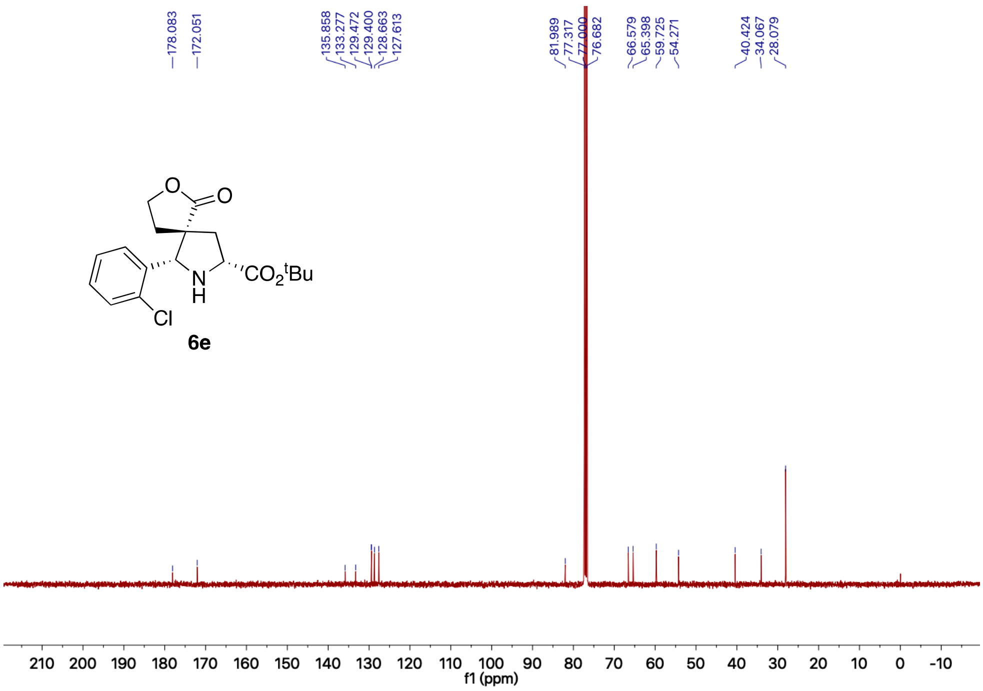


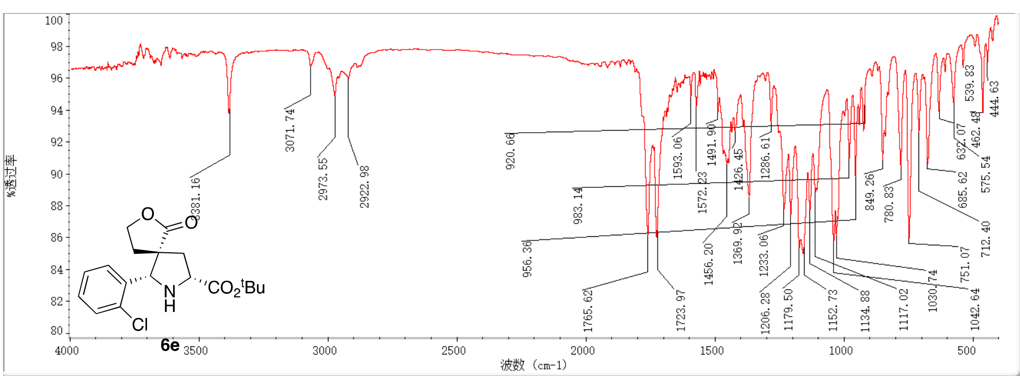


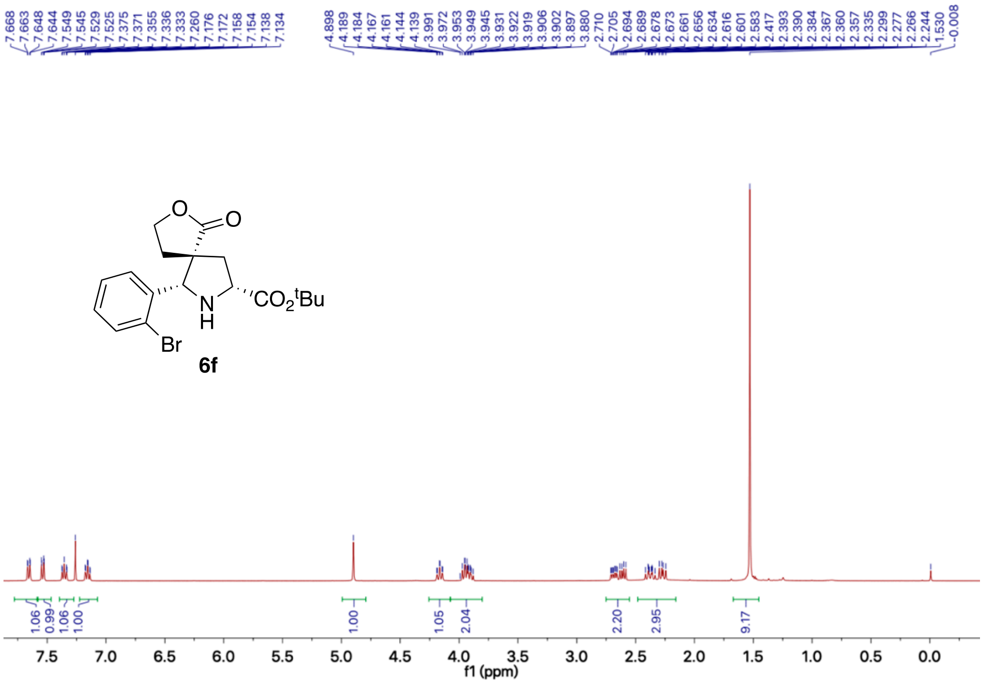












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7.644
7.549
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7.529
7.525
7.375
7.371
7.355
7.336
7.333
7.260
7.176
7.172
7.158
7.154
7.138
7.134
4.898
4.189
4.184
4.167
4.161
4.144
4.139
3.991
3.972
3.953
3.949
3.945
3.931
3.922
3.919
3.906
3.902
3.897
3.880
2.710
2.705
2.694
2.689
2.678
2.673
2.661
2.656
2.634
2.616
2.601
2.583
2.417
2.393
2.390
2.384
2.367
2.360
2.357
2.335
2.299
2.277
2.266
2.244
1.530
-0.008
CO2tBu
Br
6f
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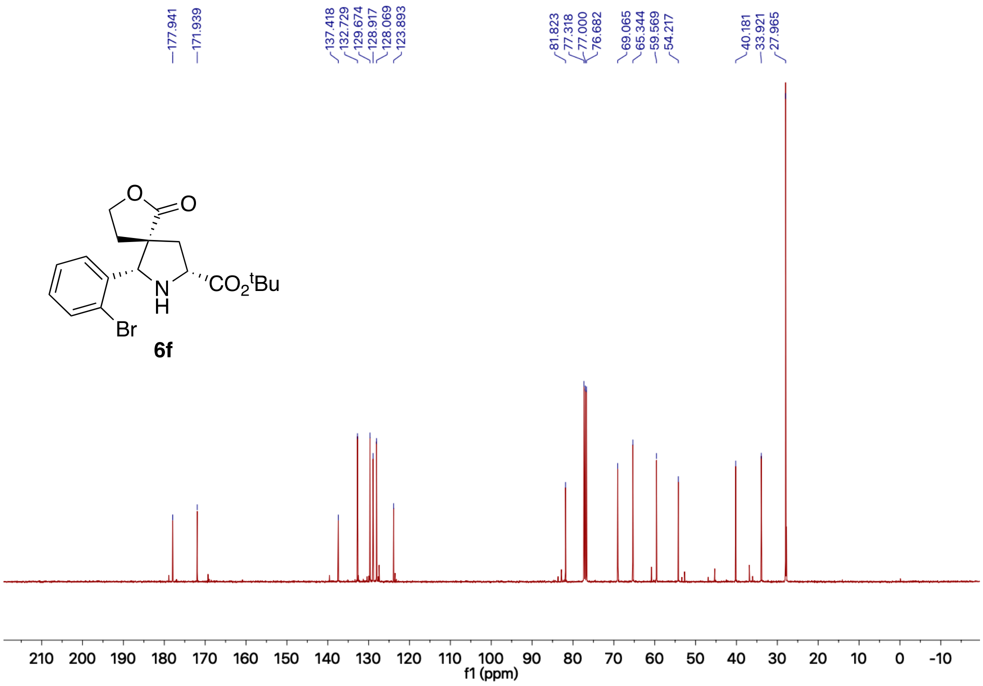
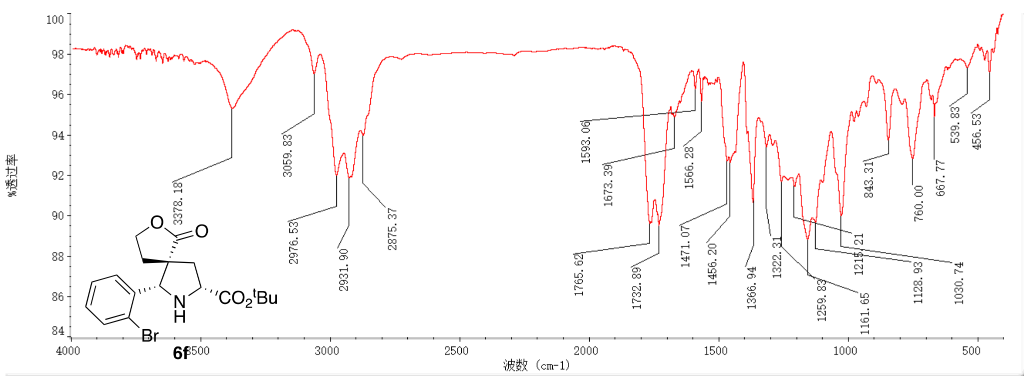
0.99
1.06
1.00
1.00
1.05
2.04
2.20
2.95
9.17
f1 (ppm)

177.941
171.939
137.418
132.729
129.674
128.917
128.069
123.893
81.823
77.318
77.000
76.682
69.065
65.344
59.569
54.217
40.181
33.921
27.965
CO2tBu
Br
6f
f1 (ppm)

%透过率
3378.18
3059.83
2976.53
2931.90
2875.37
1765.62
1732.89
1673.39
1593.06
1566.28
1471.07
1456.20
1366.94
1322.31
1259.83
1215.21
1161.65
1128.93
1030.74
843.31
760.00
667.77
539.83
456.53
CO2tBu
Br
6f
波数 (cm-1)