Metal-free and enantioselective synthesis of 1,4-benzoxazepines from *para*-quinone methides derivatives and α-bromohydroxamates

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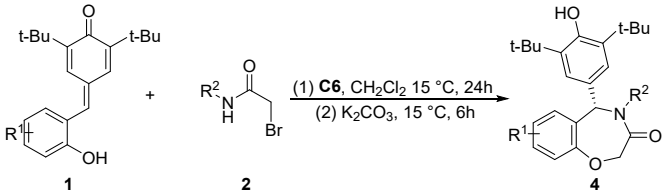
1. General information

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. [1] H NMR spectra were recorded on Bruker AVANCE III (500 MHz) or Bruker ASCEND (600 MHz) in $CDCl_3$ using residual solvent signals as the internal standard ($CDCl_3$ δ = 7.26 ppm). ^{13}C NMR spectra were recorded at 126 MHz (Bruker AVANCE III) or 151 MHz (Bruker ASCEND) in $CDCl_3$ using solvent signals as the internal standard ($CDCl_3$ δ = 77.16 ppm). HRMS data were measured on an Agilent 6120 LC/TOF-MS with ESI source. Melting points (m.p.) were obtained using a Büchi B-545 apparatus and uncorrected. Chiral HPLC analyses were performed using Agilent 1260 chromatography. Chiralpak IB, IC, ID, AD and IF columns were purchased from Daicel Chemical Industries (Shanghai, China). Optical rotations were measured on a Rudolph Autopol IV polarimeter. Column chromatography and flash chromatography experiments were conducted using silica gel GF254 (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC experiments were carried out on glass-backed silica plates. The *ortho*-hydroxyphenyl-substituted *p*-QMs[1] and α-bromohydroxamates[2] were prepared according to the reported literature procedures.

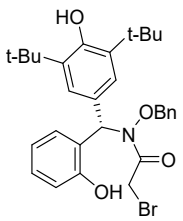
[1] (a) Zhao, K.; Zhi, Y.; Shu, T.; Valkonen, A.; Rissanen, K.; Enders, D. *Angew. Chem. Int. Ed*. **2016**, *55*, 12104. (b) Zhang, L.; Zhou, X.; Li, P.; Liu, Z.; Liu, Y.; Sun, Y.; Li, W. *RSC Adv.* **2017**, *7*, 39216.

[2] (a) 1. Singh, R.; Nagesh, K.; Yugandhar, D.; Prasanthi, A. V. G. *Org. Lett.* **2018**, 20, 4848. (b) Zhou, S.-J.; Cheng, X.; Hu, C.-X.; Xu, G.-Y.; Xiao, W.-J.; Xuan, J. *Sci. China. Chem.* **2021**, 64, 61-65.

2. Experimental procedures and characterization data of products

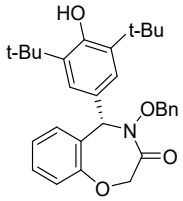


A flame-dried Schlenk-tube equipped with a magnetic stir bar was charged with **C6** (0.05 mmol, 10 mol%), **1** (0.1 mmol), **2** (1.2 equiv., 0.12 mmol) in 1.5mL DCM. The resulting mixture was stirred at 15 ℃ for 24 h. Then, the isolated conjugate adduct was treated with K_2CO_3 (2 equiv., 0.2 mmol) in CH_2Cl_2 (1 mL) at 15 °C for 6 h. The solvent was removed under reduced pressure, the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give the 1,4-Benzoxazepines **4**.

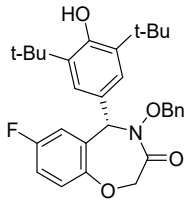


(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (3a). white solid, mp 100-102 ºC, 97% yield, 53.7 mg, 97:3 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IA-H with hexane/i-PrOH (96:4) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -34$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.32 (m, 4H), 7.28-7.27 (m, 3H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.11-7.10 (m, 2H), 6.94 (s, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 5.28 (s, 1H), 4.57 (d, *J* = 9.6 Hz, 1H), 4.46 (d, *J* = 9.6 Hz, 1H), 4.07 (s, 2H), 1.42 (s, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.6, 153.6, 136.0, 133.8, 130.1, 129.6, 129.1, 129.1, 129.0, 128.6, 126.6, 125.8, 124.6, 120.2, 116.7, 79.2,

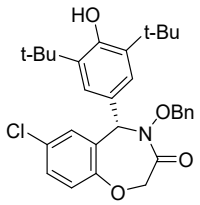
62.0, 41.6, 34.4, 30.3. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{36}BrNO_4Na$ 576.1720; Found 576.1728.



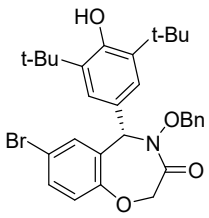
(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4a). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 112-114 ºC, 92% yield, 43.5 mg, 94:6 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -44$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36–7.34 (m, 2H), 7.32–7.27 (m, 4H), 7.08 (s, 2H), 7.05–7.00 (m, 2H), 6.81 (dd, *J* = 7.6, 1.4 Hz, 1H), 5.45 (s, 1H), 5.20 (s, 1H), 5.07 (d, *J* = 10.7 Hz, 1H), 4.96 (d, *J* = 10.7 Hz, 1H), 4.72 (d, *J* = 15.6 Hz, 1H), 4.43 (d, *J* = 15.6 Hz, 1H), 1.38 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.6, 156.6, 153.3, 135.9, 135.2, 131.3, 130.1, 129.9, 129.8, 128.7, 128.4, 123.7, 123.2, 121.0, 77.1, 72.3, 70.7, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{35}NO_4Na$ 496.2458; Found 496.2466.



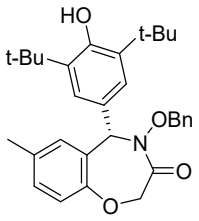
(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7-fluoro-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4b). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 67-59 ºC, 91% yield, 44.7 mg, 92.5:7.5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -41$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36–7.28 (m, 5H), 7.06 (s, 2H), 7.02–6.09 (m, 2H), 6.44 (dd, *J* = 8.3, 2.4 Hz, 1H), 5.32 (s, 1H), 5.22 (s, 1H), 5.08 (d, *J* = 10.8 Hz, 1H), 4.94 (d, *J* = 10.8 Hz, 1H), 4.71 (d, *J* = 15.8 Hz, 1H), 4.41 (d, *J* = 15.8 Hz, 1H), 1.38 (s, 16H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.4, 159.3, 157.4, 153.5, 152.6 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 136.1, 135.1, 130.7, 130.6 (d, $^2J_{C\text{-}F}$ = 7.5 Hz), 130.5, 129.9, 128.9, 128.5, 127.3 (d, $^1J_{C\text{-}F}$ = 196.7 Hz) 123.1, 122.3 (d, $^2J_{C\text{-}F}$ = 8.4 Hz), 116.4 (d, $^3J_{C\text{-}F}$ = 3.1 Hz), 116.2 (d, $^3J_{C\text{-}F}$ = 4.1 Hz), 77.1, 72.6, 70.4, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{34}FNO_4Na$ 514.2364; Found 514.2369.



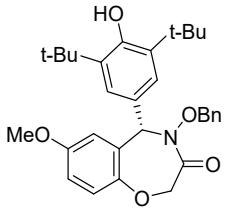
(S)-4-(benzyloxy)-7-chloro-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4c). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 57-59 ºC, 92% yield, 46.6 mg, 95:5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -59$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38–7.32 (m, 3H), 7.30–7.28 (m, 2H), 7.22 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.01 (s, 2H), 6.96 (d, *J* = 8.6 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 5.27 (s, 1H), 5.23 (s, 1H), 5.06 (d, *J* = 11.0 Hz, 1H), 4.97 (d, *J* = 11.0 Hz, 1H), 4.64 (d, *J* = 15.5 Hz, 1H), 4.40 (d, *J* = 15.5 Hz, 1H), 1.38 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.1, 155.0, 153.5, 136.1, 135.0, 130.7, 130.0, 129.8, 129.6, 129.3, 129.0, 128.5, 128.2, 123.0, 122.2, 77.2, 71.9, 70.2, 34.3, 30.1. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{34}ClNO_4Na$ 530.2069; Found 530.2070.



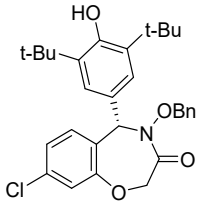
(S)-4-(benzyloxy)-7-bromo-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4d). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 90% yield, 49.6 mg, 94:6 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -44$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.39–7.32 (m, 4H), 7.30–7.28 (m, 2H), 7.01 (s, 2H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.73 (d, *J* = 1.9 Hz, 1H), 5.27 (s, 1H), 5.23 (s, 1H), 5.06 (d, *J* = 11.1 Hz, 1H), 4.98 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 15.4 Hz, 1H), 4.39 (d, *J* = 15.4 Hz, 1H), 1.38 (s, 18H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 167.1, 155.5, 153.5, 136.2, 135.0, 132.8, 132.6, 130.7, 130.0, 129.5, 129.0, 128.5, 123.0, 122.5, 115.6, 77.2, 71.8, 70.2, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{34}BrNO_4Na$ 574.1563; Found 574.1571.



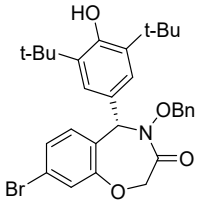
(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7-methyl-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4e). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 87% yield, 42.3 mg, 92.5:7.5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -26$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36–7.34 (m, 2H), 7.33–7.28 (m, 3H), 7.11 (s, 2H), 7.07 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.58 (d, *J* = 1.6 Hz, 1H), 5.37 (s, 1H), 5.19 (s, 1H), 5.07 (d, *J* = 10.7 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 4.74 (d, *J* = 15.8 Hz, 1H), 4.41 (d, *J* = 15.8 Hz, 1H), 2.28 (s, 3H), 1.38 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.6, 154.4, 153.3, 135.9, 135.3, 133.4, 131.3, 130.4, 130.4, 129.9, 129.0, 128.6, 128.4, 123.3, 120.7, 77.0, 72.7, 70.9, 34.3, 30.2, 20.6. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{31}H_{37}NO_4Na$ 510.2615; Found 510.2615.



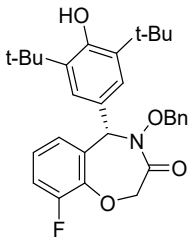
(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7-methoxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4f). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 85% yield, 42.7 mg, 91:9 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -17$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39-7.38 (m, 3H), 7.33-7.32 (m, 2H), 7.12 (s, 2H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.35 (d, *J* = 3.0 Hz, 1H), 5.36 (s, 1H), 5.20 (s, 1H), 5.08 (d, *J* = 10.7 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 4.76 (d, *J* = 16.0 Hz, 1H), 4.41 (d, *J* = 16.0 Hz, 1H), 3.76 (s, 3H), 1.39 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.7, 155.8, 153.3, 150.4, 135.9, 135.3, 130.9, 129.9, 128.7, 128.5, 128.4, 128.0, 123.3, 121.9, 114.9, 114.9, 78.0, 73.1, 71.0, 55.7, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{31}H_{37}BrNO_5Na$ 526.2564; Found 526.2577.



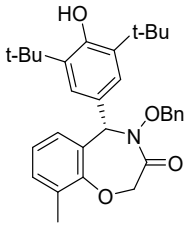
(S)-4-(benzyloxy)-8-chloro-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4g). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 88% yield, 44.6 mg, 92:8 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -57$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34–7.30 (m, 3H), 7.28–7.25 (m, 2H), 7.05 (d, *J* = 2.1 Hz, 1H), 7.02 (s, 2H), 6.96 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 5.38 (s, 1H), 5.22 (s, 1H), 5.06 (d, *J* = 11.0 Hz, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.63 (d, *J* = 15.3 Hz, 1H), 4.42 (d, *J* = 15.3 Hz, 1H), 1.38 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.2, 157.0, 153.4, 136.2, 135.2, 134.6, 131.1, 131.0, 129.9, 128.8, 128.5, 126.1, 123.4, 123.0, 121.2, 77.2, 71.8, 70.0, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{34}ClNO_4Na$ 530.2069; Found 530.2063.



(S)-4-(benzyloxy)-8-bromo-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4h). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 94% yield, 51.8 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -85$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 7.22 (s, 1H), 7.13–7.11 (m, 1H), 7.04 (s, 2H), 6.59 (d, *J* = 8.1 Hz, 1H), 5.38 (s, 1H), 5.26 (s, 1H), 5.07 (d, *J* = 11.0 Hz, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.65 (d, *J* = 15.4 Hz, 1H), 4.43 (d, *J* = 15.3 Hz, 1H), 1.39 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.0, 156.9, 153.3, 136.0, 135.0, 131.2, 130.7, 129.7, 128.7, 128.3, 126.5, 126.2, 124.0, 122.8, 122.1, 77.0, 71.7, 69.9, 34.2, 30.0. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{34}BrNO_4Na$ 574.1563; Found 574.1569.

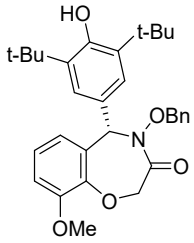


(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-9-fluoro-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4i). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 121-123 ºC, 95% yield, 46.6 mg, 97:3 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -85$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.7 Hz, 2H), 7.34-7.27 (m, 3H), 7.13-7.05 (m, 3H), 6.96 (td, *J* = 7.9, 4.8 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 5.50 (s, 1H), 5.26 (d, *J* = 2.9 Hz, 1H), 5.10 (dd, *J* = 10.8, 1.4 Hz, 1H), 5.00 (d, *J* = 10.9 Hz, 1H), 4.76 (dd, *J* = 15.6, 1.3 Hz, 1H), 4.53 (dd, *J* = 15.6, 1.1 Hz, 1H), 1.40 (s, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 167.2, 154.1 (d, $^1J_{C\text{-}F}$ = 247.1 Hz), 153.5, 144.4 (d, $^2J_{C\text{-}F}$ = 12.3 Hz), 136.2, 135.2, 131.2, 130.8, 129.9, 128.8, 128.5, 125.0 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 123.6 (d, $^3J_{C\text{-}F}$ = 7.3 Hz), 123.0, 116.6 (d, $^2J_{C\text{-}F}$ = 18.7 Hz), 77.2, 72.3, 70.3, 34.4, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{34}FNO_4Na$ 524.2364; Found 514.2367.

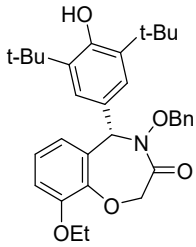


(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-9-methyl-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4j). Purified by silica gel

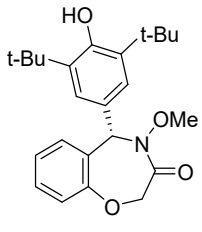
chromatography using PE/EA 6:1, white solid, mp 61-63 ºC, 87% yield, 42.3 mg, 90:10 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -66$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39-7.32 (m, 5H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.14 (s, 2H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 7.4 Hz, 1H), 5.49 (s, 1H), 5.23 (s, 1H), 5.13 (d, *J* = 10.6 Hz, 1H), 4.98 (d, *J* = 10.6 Hz, 1H), 4.86 (d, *J* = 16.0 Hz, 1H), 4.43 (d, *J* = 16.1 Hz, 1H), 2.26 (s, 3H), 1.42 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.6, 154.8, 153.2, 135.9, 135.3, 131.4, 131.2, 130.5, 130.4, 129.8, 128.8, 128.5, 127.6, 123.9, 123.2, 77.0, 72.1, 71.0, 34.4, 30.3, 15.7. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{31}H_{37}NO_4Na$ 510.2615; Found 510.2621.



(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-9-methoxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4k). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 89% yield, 44.7 mg, 94:6 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -21$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 4.5 Hz, 1H), 7.37–7.35 (m, 2H), 7.33–7.31 (m, 1H), 7.13 (s, 2H), 7.00 (t, *J* = 7.9 Hz, 1H), 6.90 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.51 (d, *J* = 7.6 Hz, 1H), 5.49 (s, 1H), 5.20 (s, 1H), 5.10 (d, *J* = 10.5 Hz, 1H), 4.94 (d, *J* = 10.5 Hz, 1H), 4.87 (d, *J* = 16.0 Hz, 1H), 4.49 (d, *J* = 16.0 Hz, 1H), 3.86 (s, 3H), 1.39 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.5, 153.2, 151.5, 145.4, 135.8, 135.2, 131.9, 130.7, 129.7, 128.7, 128.4, 128.3, 127.9, 124.3, 123.0, 121.2, 112.3, 77.9, 72.6, 70.8, 56.0, 34.2, 30.1. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{31}H_{37}NO_5Na$ 526.2564; Found 526.2569.

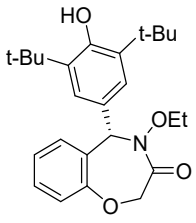


(S)-4-(benzyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-9-ethoxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4l). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 169-171 ºC, 91% yield, 47.0 mg, 95:5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -98$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37-7.36 (m, 2H), 7.34–7.29 (m, 3H), 7.09 (s, 2H), 6.97 (t, *J* = 7.9 Hz, 1H), 6.89 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 1H), 5.48 (s, 1H), 5.16 (s, 1H), 5.09 (d, *J* = 10.6 Hz, 1H), 4.95 (d, *J* = 10.5 Hz, 1H), 4.84 (d, *J* = 16.1 Hz, 1H), 4.46 (d, *J* = 16.1 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.0 Hz, 3H), 1.38 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.7, 153.2, 150.9, 145.9, 135.8, 135.3, 132.3, 130.9, 129.7, 128.7, 128.4, 124.3, 123.0, 121.3, 113.9, 77.1, 72.6, 70.8, 64.6, 34.3, 30.2, 14.8. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{32}H_{39}NO_5Na$ 540.2720; Found 540.2726.

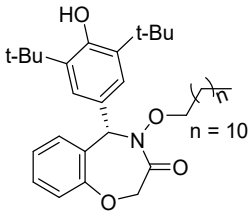


(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-methoxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4m). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 186-188 ºC, 96% yield, 38.1 mg, 94.5:5.5 er. The enantiomeric excess was determined by HPLC on

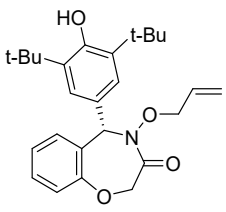
Daicel Chiralpak ID-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -31$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36–7.32 (m, 2H), 7.16 (td, *J* = 7.5, 1.2 Hz, 1H), 7.11 (s, 2H), 7.08 (dd, *J* = 8.0, 1.0 Hz, 1H), 5.77 (s, 1H), 5.22 (s, 1H), 4.77 (d, *J* = 15.8 Hz, 1H), 4.42 (d, *J* = 15.8 Hz, 1H), 3.85 (s, 3H), 1.39 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.2, 156.6, 153.3, 136.0, 131.0, 130.2, 129.9, 129.8, 124.2, 123.1, 121.4, 72.5, 69.2, 62.4, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{24}H_{31}NO_4Na$ 420.2145; Found 420.2149.



(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-ethoxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4n). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 168-170 ºC, 95% yield, 39.0 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak ID-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -32$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.15 (td, *J* = 7.5, 1.1 Hz, 1H), 7.12 (s, 2H), 7.08 (d, *J* = 8.0 Hz, 1H), 5.75 (s, 1H), 5.22 (s, 1H), 4.72 (d, *J* = 15.7 Hz, 1H), 4.42 (d, *J* = 15.7 Hz, 1H), 4.08 (ddq, *J* = 39.3, 9.0, 7.1 Hz, 2H), 1.39 (s, 18H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.4, 156.6, 153.3, 135.9, 131.3, 130.1, 129.2, 123.9, 123.2, 121.3, 72.3, 70.3, 69.9, 34.3, 30.2, 13.7. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{25}H_{33}NO_4Na$ 434.2302; Found 434.2300.

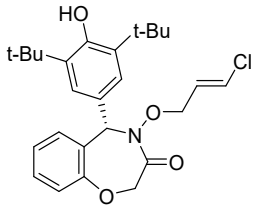


(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-(dodecyloxy)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4o). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 90% yield, 49.5 mg, 91:9 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IA-H with hexane/i-PrOH (95:5) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -37$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35-7.30 (m, 2H), 7.28 (s, 1H), 7.16-7.14 (m, 3H), 7.09 (dd, *J* = 8.0, 1.0 Hz, 1H), 5.74 (s, 1H), 5.21 (s, 1H), 4.72 (d, *J* = 15.7 Hz, 1H), 4.41 (d, *J* = 15.7 Hz, 1H), 4.05-3.96 (m, 2H), 1.68-1.69 (m, 2H), 1.40 (s, 18H), 1.33-1.28 (m, 18H), 0.91 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 167.2, 156.6, 153.3, 135.9, 131.4, 130.1, 129.3, 123.9, 123.4, 121.3, 75.0, 72.3, 69.9, 34.4, 31.9, 30.2, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 28.2, 26.0, 22.7, 14.1. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{35}H_{53}NO_4Na$ 574.3867; Found 574.3864.

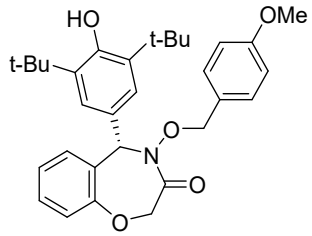


(S)-4-(allyloxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4p). Purified by silica gel chromatography using PE/EA 6:1, white solid, mp 118-120 ºC, 94% yield, 39.7 mg, 95.5:4.5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak ID-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -29$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34–7.28 (m, 2H), 7.14 (td, *J* = 7.5, 1.2 Hz, 1H), 7.12 (s, 2H), 7.08 (dd, *J* = 8.0,

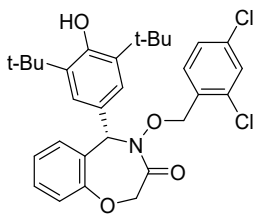
1.0 Hz, 1H), 6.00 (ddt, *J* = 17.0, 10.3, 6.5 Hz, 1H), 5.75 (s, 1H), 5.28– 5.22 (m, 2H), 5.22 (s, 1H), 4.72 (d, *J* = 15.7 Hz, 1H), 4.50 (ddd, *J* = 35.3, 11.6, 6.5 Hz, 2H), 4.41 (d, *J* = 15.7 Hz, 1H), 1.39 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.6, 156.7, 153.3, 136.0, 132.0, 131.2, 130.1, 130.1, 129.1, 123.9, 123.2, 121.2, 120.8, 76.0, 72.3, 70.2, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{26}H_{33}NO_4Na$ 446.2303; Found 446.2305.



(S,E)-4-((3-chloroallyl)oxy)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4q). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 91% yield, 41.6 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IF-H with hexane/i-PrOH (95:5) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -19$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.33 (dd, J = 20.9, 9.5 Hz, 2H), 7.17 (t, J = 7.4 Hz, 1H), 7.09 (d, J = 9.2 Hz, 3H), 6.23 (s, 1H), 6.09 (dt, J = 13.9, 7.2 Hz, 1H), 5.71 (s, 1H), 5.23 (s, 1H), 4.74 (d, J = 15.8 Hz, 1H), 4.56 – 4.51 (m, 1H), 4.45 – 4.41 (m, 2H), 1.40 (s, 18H). **^{13}C NMR** (101 MHz, CDCl3) δ 167.75, 156.61, 153.42, 136.03, 130.99, 130.21, 130.19, 128.96, 127.35, 125.18, 124.16, 123.13, 121.32, 72.86, 72.35, 70.73, 34.36, 30.19. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{26}H_{32}ClNO_4Na$ 480.1912; Found 480.1915.

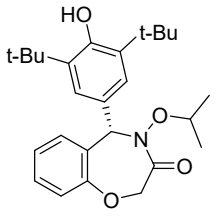


(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-((4-methoxybenzyl)oxy)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4r). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 88% yield, 44.2 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IA-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -13$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.25 (m, 3H), 7.07 (s, 2H), 7.04–6.99 (m, 2H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 2H), 5.42 (s, 1H), 5.22 (s, 1H), 5.05 (d, *J* = 10.7 Hz, 1H), 4.91 (d, *J* = 10.7 Hz, 1H), 4.69 (d, *J* = 15.5 Hz, 1H), 4.42 (d, *J* = 15.5 Hz, 1H), 3.79 (s, 3H), 1.38 (s, 18H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.4, 160.0, 156.5, 153.2, 135.9, 131.4, 130.2, 129.7, 128.1, 127.3, 123.3, 123.1, 120.8, 113.7, 76.6, 72.0, 70.6, 55.1, 34.3, 30.1. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{31}H_{37}BrNO_5Na$ 526.2564; Found 526.2562.



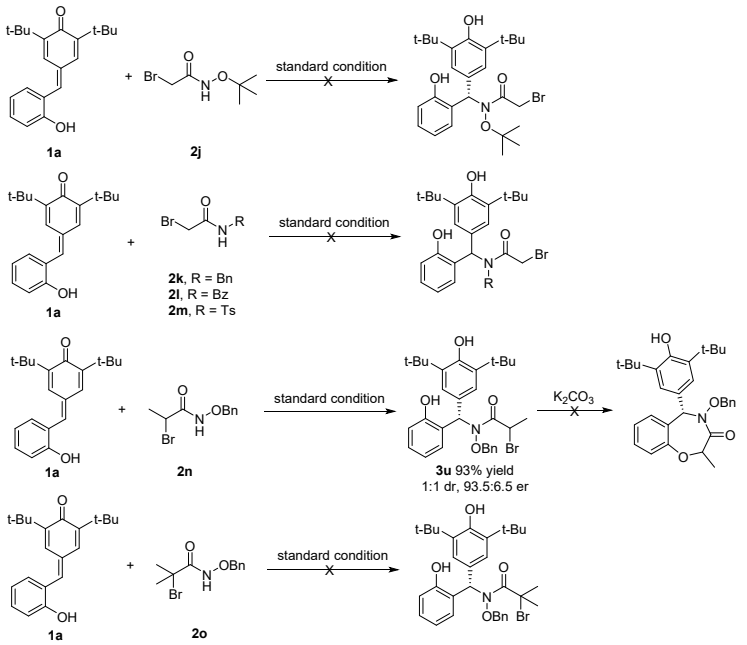
(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-((2,4-dichlorobenzyl)oxy)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4s). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 86% yield, 46.6 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IF-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -16$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 –7.21 (m, 3H), 7.07 – 7.02 (m, 5H), 6.88 (d, J = 7.3 Hz, 1H), 5.52 (s, 1H), 5.25 – 5.15 (m, 2H), 5.10 (d, J = 11.4 Hz, 1H), 4.64 (d, J = 15.3 Hz, 1H),

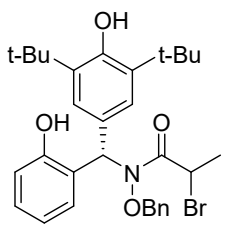
4.41 (d, J = 15.3 Hz, 1H), 1.37 (s, 18H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.44, 156.29, 153.39, 135.98, 135.47, 135.36, 132.95, 131.50, 131.34, 130.07, 129.91, 129.33, 127.15, 127.05, 123.33, 123.22, 120.82, 73.03, 71.63, 70.40, 34.34, 30.15. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{30}H_{33}Cl_2NO_4Na$ 564.1679; Found 564.1674.



(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-isopropoxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (4t). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 74% yield, 31.4 mg, 83:17 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -2.7$ (c = 1.0 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (ddd, *J* = 8.0, 7.3, 1.7 Hz, 1H), 7.27 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.13 (td, *J* = 7.4, 1.2 Hz, 1H), 7.09 – 7.07 (m, 3H), 5.74 (s, 1H), 5.22 (s, 1H), 4.59 (d, *J* = 15.2 Hz, 1H), 4.44 – 4.37 (m, 2H), 1.38 (s, 18H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.26 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.79, 156.62, 153.28, 135.93, 131.84, 130.52, 129.91, 127.13, 123.21, 123.09, 121.07, 76.82, 71.61, 70.44, 34.35, 30.18, 21.22, 20.80. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{26}H_{35}NO_4Na$ 448.2458; Found 448.2461.

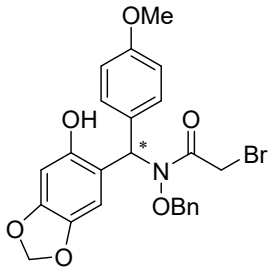
Scheme S1 List of unsuccessful α-haloamides





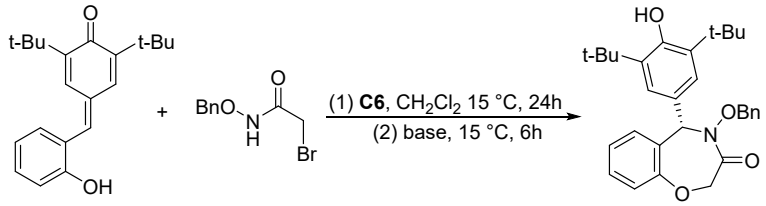
N-(benzyloxy)-2-bromo-N-((S)-(3,5-di-tert-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)propanamide (3u). Purified by silica gel chromatography using PE/EA 6:1, colorless oil, 93% yield, 52.8 mg, 1:1 dr, 93.5:6.5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IF-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = 8$ (c = 1.0 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 4H), 7.28 (s, 1H), 7.24 – 7.20 (m, 3H), 7.14 (d, *J* = 5.7 Hz, 2H), 6.90 (dd,

J = 16.3, 7.7 Hz, 2H), 6.73 (s, 1H), 5.27 (s, 1H), 4.82 (s, 1H), 4.69 (s, 1H), 4.53 (s, 1H), 1.68 (d, J = 6.7 Hz, 3H), 1.40 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.66, 133.31, 130.67, 129.81, 129.23, 129.10, 128.70, 126.00, 125.54, 119.99, 116.43, 77.24, 63.23, 37.13, 33.67, 30.27, 21.15. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{31}H_{38}NBrNO_4Na$ 590.1876; Found 590.1881.



N-(benzyloxy)-2-bromo-N-((6-hydroxybenzo[d][1,3]dioxol-5-yl)(4-methoxyphenyl)methyl)acetamide (**8a**). Purified by silica gel chromatography using PE/EA 3:1, colorless oil, 85% yield, 42.5 mg, 92.5:7.5 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IC-H with hexane/i-PrOH (80:20) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = 6$ (c = 1.0 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.37-7.34 (m, 4H), 7.18 (dd, J = 6.5, 3.2 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 6.83 (s, 1H), 6.79 (d, J = 2.1 Hz, 1H), 5.92-5.91 (m, 2H), 4.58-4.46 (m, 2H), 4.05 (d, J = 1.5 Hz, 1H), 3.82 (s, 3H), 1.73 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 149.6, 148.1, 141.2, 133.6, 129.8, 129.8, 129.4, 129.3, 129.2, 128.7, 116.3, 114.5, 114.1, 109.1, 101.2, 99.0, 79.5, 60.8, 55.3, 26.1. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{24}H_{22}BrNO_6Na$ 522.0523; Found 522.0519.

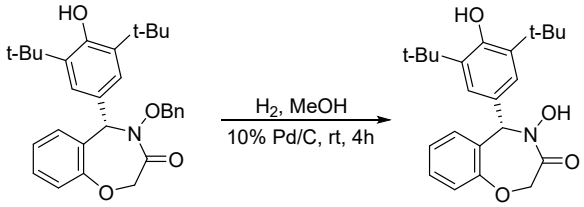
3. Scale-up experiment



1a 3 mmol | **2a** 3.6 mmol | **4a** 1.30 g, 92% yield, 93:7 er

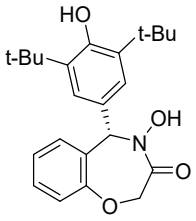
A Schlenk tube equipped with a magnetic stir bar was charged with **C6** (0.3 mmol), **1** (3 mmol), **2** (3.6 mmol) in 1.5mL DCM. The resulting mixture was stirred at 15 ℃ for 24 h. Then K_2CO_3 (6 mmol) was added to the solution and the resulting mixture was stirred at 15 °C for 6 h. The solvent was removed under reduced pressure, the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give the 1,4-Benzoxazepines **4a**.

4. Synthetic transformations of products

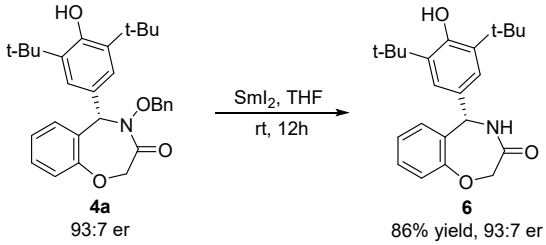


4a 93:7 er | **5** 95% yield, 93:7 er

Compound **4a** (0.1mmol) was dissolved in MeOH (2 mL) and then 10% Pd/ C (3 mg) was added. The reaction mixture was stirred under H_2 atmosphere for 4 h at room temperature. After filtration through a plug of Celite, the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give the **5**. (48 mg, 94% yield).



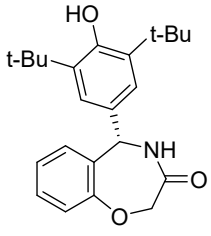
(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-hydroxy-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (5). Purified by silica gel chromatography using PE/EA 4:1, white solid, mp 173-175 ºC, 95% yield, 36.3 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IB-H with hexane/i-PrOH (95:5) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -60$ (c = 1.0 in CH_2Cl_2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.39-7.36 (m, 2H), 7.28 (s, 1H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.17 (s, 2H), 7.15 (d, *J* = 7.8 Hz, 1H), 5.88 (s, 1H), 5.22 (s, 1H), 5.00 (d, *J* = 15.8 Hz, 1H), 4.54 (d, *J* = 15.7 Hz, 1H), 1.41 (s, 18H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.6, 153.5, 135.9, 131.3, 130.5, 129.9, 129.7, 125.2, 123.3, 121.9, 72.0, 68.3, 34.3, 30.2. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{23}H_{29}NO_4Na$ 406.1989; Found 406.1995.



4a
93:7 er

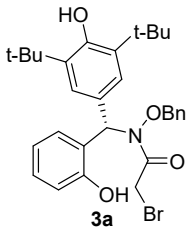
6
86% yield, 93:7 er

A 50 mL Schlenk tube equipped with a magnetic stir bar was charged with **4a** (0.1 mmol) under Argon, and anhydrous THF (2 mL) was added at room temperature. Then SmI_2 (3 mL, 0.1 M in THF) was added to the stirring solution dropwise via syringe. After the reaction is complete, the solution was diluted with CH_2Cl_2 (5 mL) and quenched with a 10% solution of $Na_2S_2O_3$ (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were washed with brine. The solvent was removed under reduced pressure, the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give the **6**.

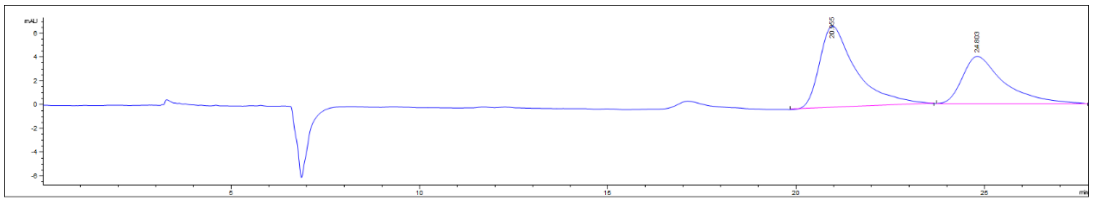


(S)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one (6), Purified by silica gel chromatography using PE/EA 3:1, colorless oil, 86% yield, 31.5 mg, 93:7 er. The enantiomeric excess was determined by HPLC on Daicel Chiralpak IA-H with hexane/i-PrOH (90:10) as the eluent, flow = 1.0 mL/min, UV = 254 nm, $[\alpha]_D^{25} = -23$ (c = 1.0 in CH_2Cl_2). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.34 (td, *J* = 7.7, 1.4 Hz, 1H), 7.31-7.28 (m, 1H), 7.26-7.23 (m, 1H), 7.17-7.16 (m, 1H), 7.10 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82-6.80 (m, 1H), 6.60 (d, *J* = 2.1, 1H), 5.89 (d, *J* = 2.9 Hz, 1H), 5.36 (s, 1H), 4.81 (d, *J* = 16.9 Hz, 1H), 4.51 (d, *J* = 16.9 Hz, 1H), 1.46 (s, 18H).^{13}C NMR (151 MHz, $CDCl_3$) δ 171.87, 157.51, 153.86, 136.66, 136.03, 129.88, 129.27, 128.32, 128.15, 127.98, 127.10, 124.85, 124.26, 121.11, 72.77, 57.09, 34.49, 30.26. HRMS (ESI) m/z: [M + Na]+ Calcd for $C_{23}H_{29}NO_3Na$ 390.2040; Found 390.2043.

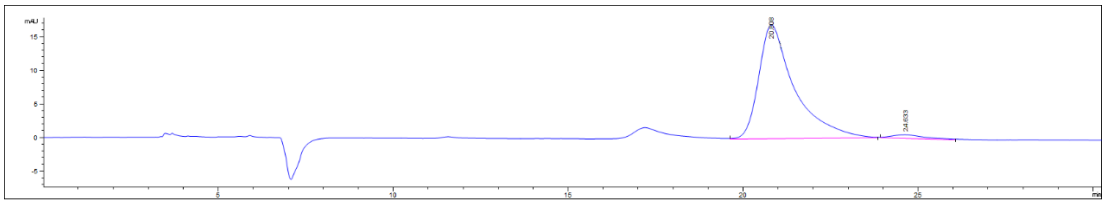
5. HPLC spectra of products



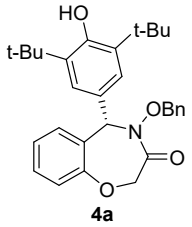
3a



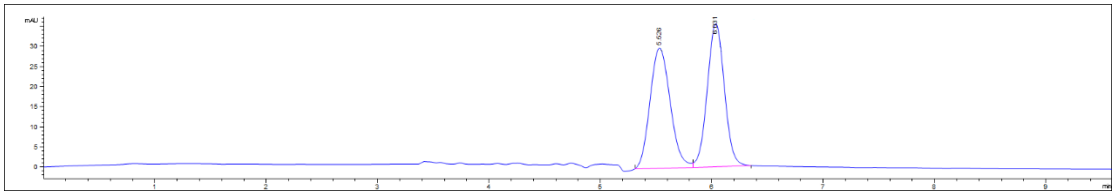
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	20.955	467.4	6.9	0.9655	0.509	59.426	BB
2	24.803	319.1	4	1.3155	0.531	40.574	MM



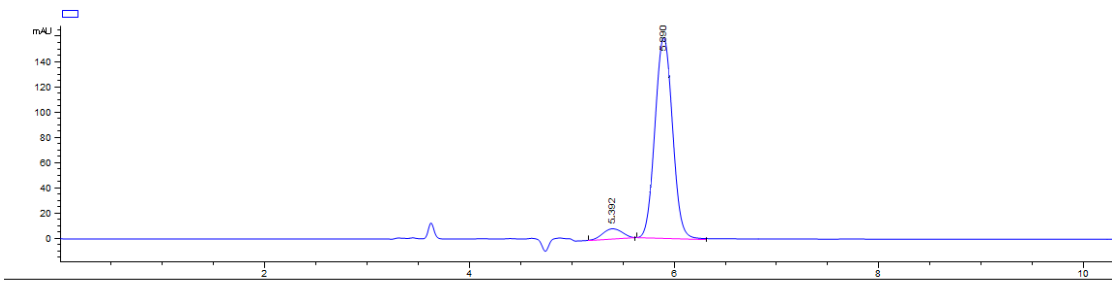
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	20.808	1218.4	16.9	1.1989	0.531	97.102	MM
2	24.633	36.4	5.5E-1	1.0959	0.657	2.898	MM



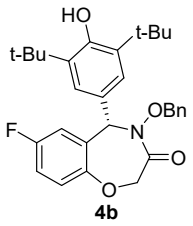
4a



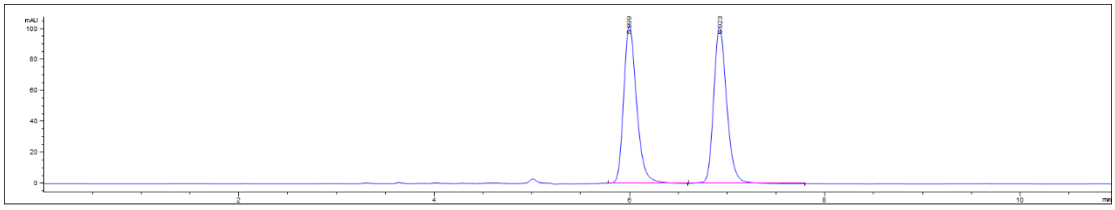
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.526	379.6	29.9	0.2116	0	49.901	MF
2	6.031	381.1	35.6	0.1784	0.957	50.099	FM



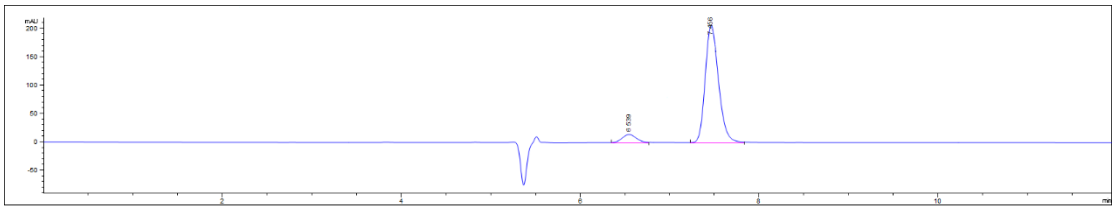
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.392	125.1	8.8	0.2379	1.011	6.112	MM
2	5.89	1922.2	160.2	0.2	0.949	93.888	MM



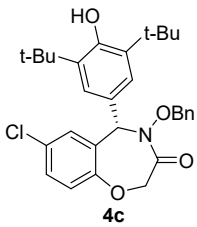
4b



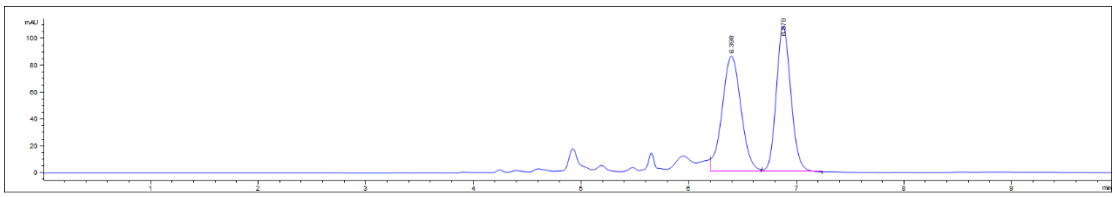
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.999	938.3	102.3	0.141	0.723	49.909	BB
2	6.923	941.7	101.6	0.1441	0.763	50.091	BB



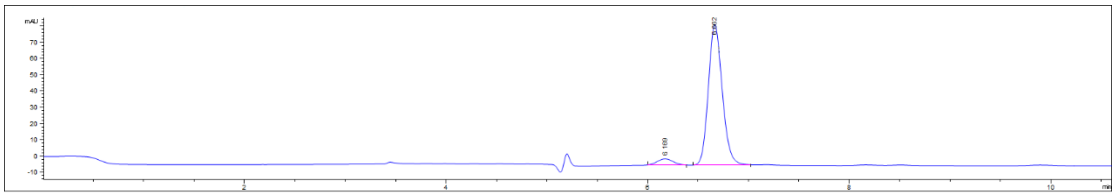
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.539	173.9	14.9	0.1947	0.892	7.473	MM
2	7.456	2152.7	207	0.1733	0.772	92.527	MM



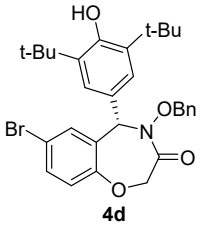
4c



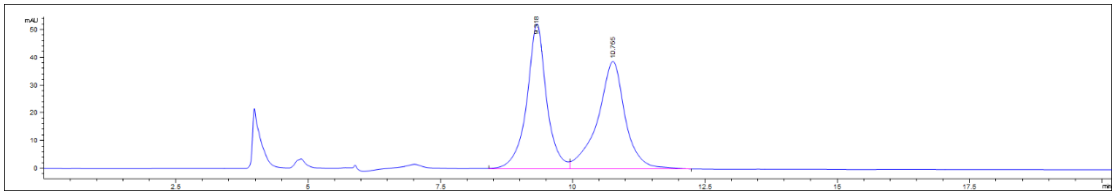
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.398	1045.2	85.7	0.2033	0.938	50.666	MM
2	6.879	1017.7	108.2	0.1457	0.85	49.334	VB



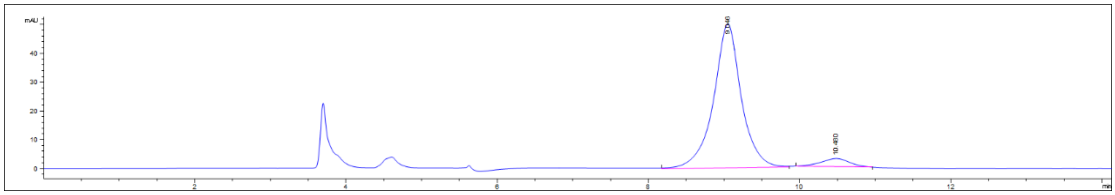
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.169	42.5	3.8	0.1853	0.939	4.883	MM
2	6.662	827.7	86	0.1604	0.837	95.117	MM



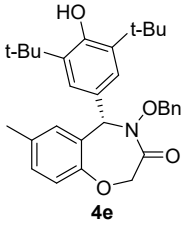
4d



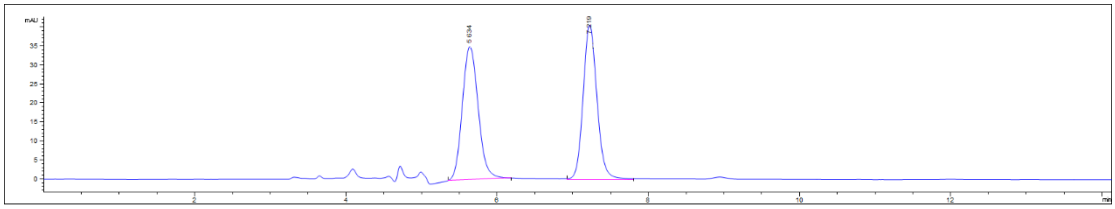
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.318	1379.6	52.3	0.4395	0	49.259	MF
2	10.755	1421.1	38.8	0.6102	1.172	50.741	FM



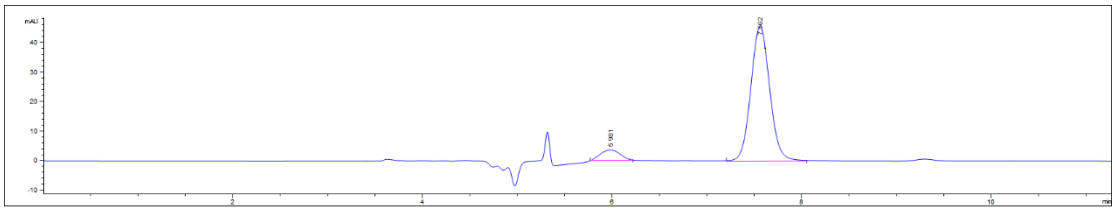
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.046	1281.6	49.9	0.4279	1.038	93.944	MM
2	10.48	82.6	3	0.4662	1.13	6.056	MM



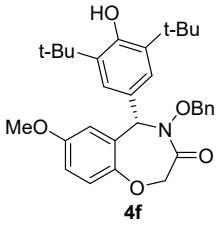
4e



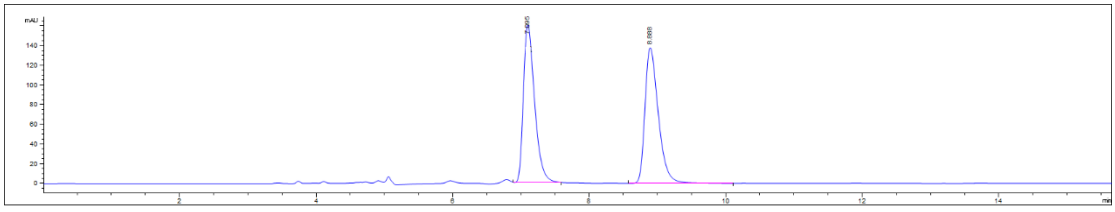
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.634	514.4	35.1	0.2444	0.864	49.586	MM
2	7.219	523	40.8	0.2138	0.858	50.414	MM



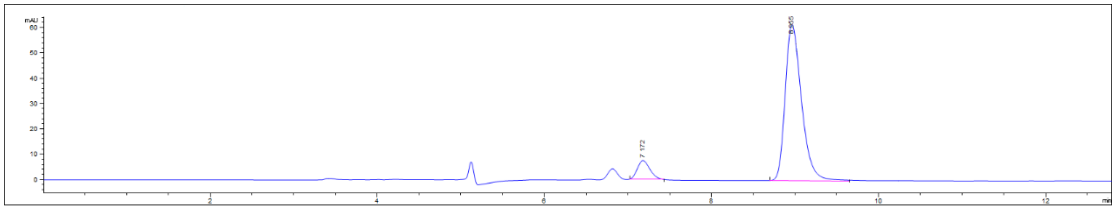
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.981	52.6	3.6	0.2453	0.96	7.522	MM
2	7.562	646.8	46	0.2343	0.923	92.478	MM



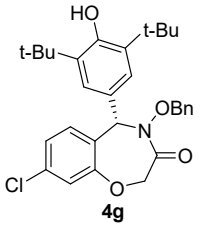
4f



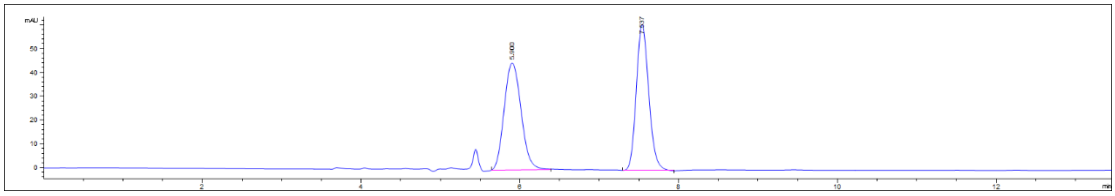
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.095	1844	160.6	0.1914	0.63	49.656	MM
2	8.888	1869.6	137.6	0.2085	0.608	50.344	BB



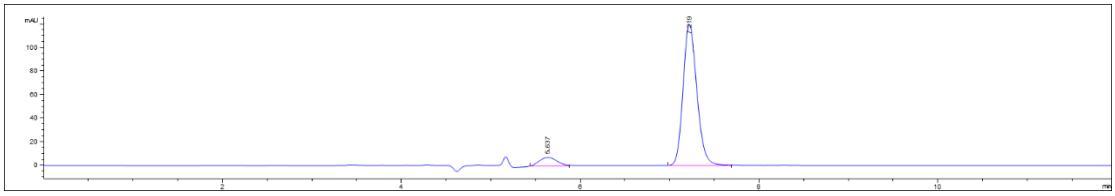
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.172	80.6	7.5	0.1783	0.785	8.749	MM
2	8.955	840.4	61.5	0.2276	0.685	91.251	MM



4g



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.9	673.9	45.1	0.2488	0.865	50.114	MM
2	7.537	670.8	61.4	0.1674	0.825	49.886	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.637	110	7.6	0.2405	0.858	7.850	MM
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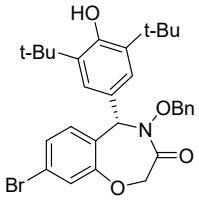
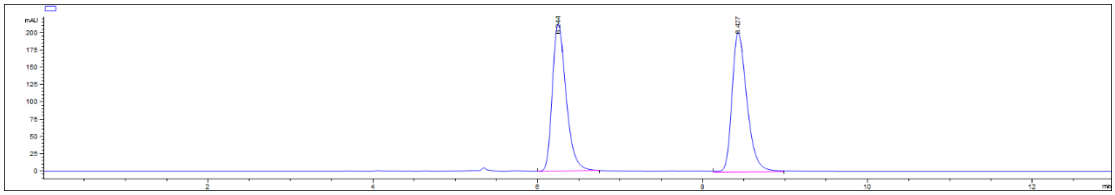
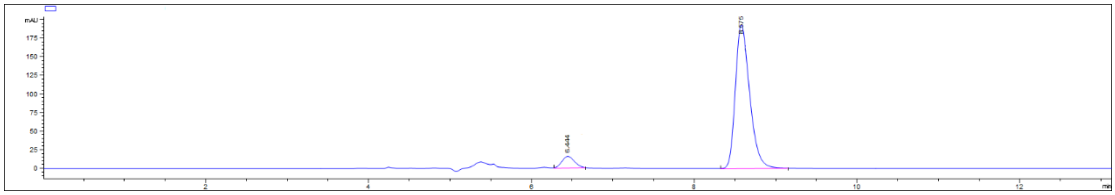


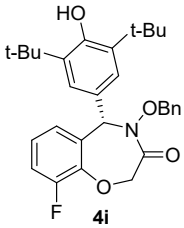
4h



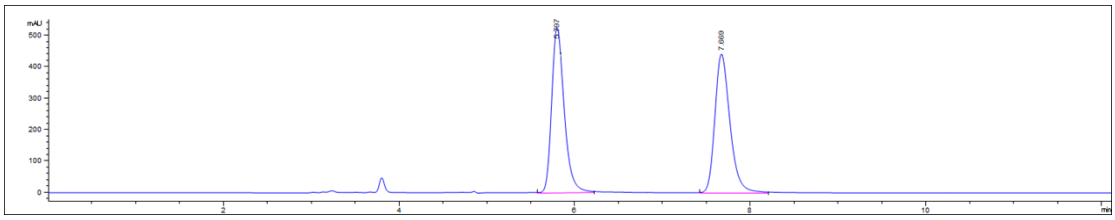
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.244	2480.5	212.9	0.1941	0.702	49.395	MM
2	8.427	2541.3	201.7	0.21	0.686	50.605	MM



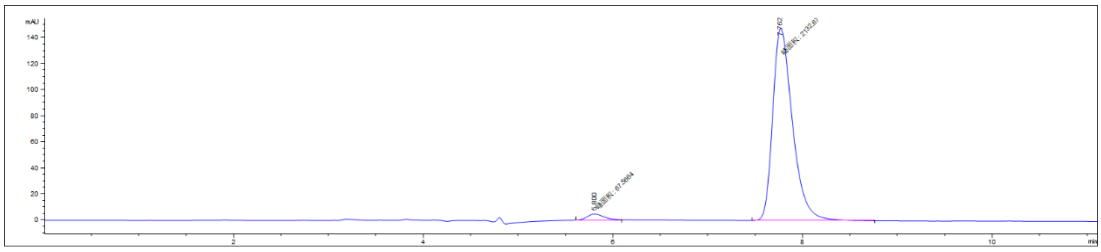
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.444	180.6	16.2	0.1858	0.882	6.959	MM
2	8.575	2414.7	195	0.2064	0.691	93.041	MM



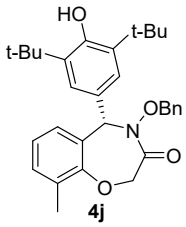
4i



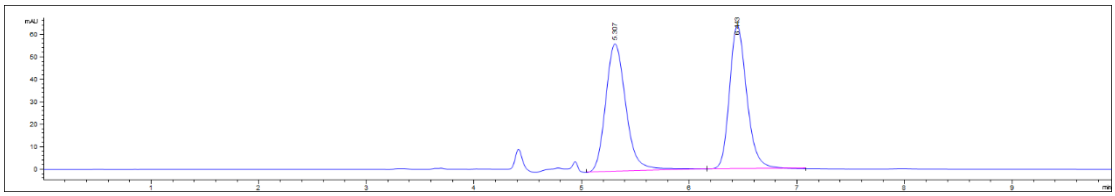
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.797	5288.8	527.7	0.1671	0.732	49.522	MM
2	7.669	5390.9	443.6	0.2026	0.734	50.478	MM



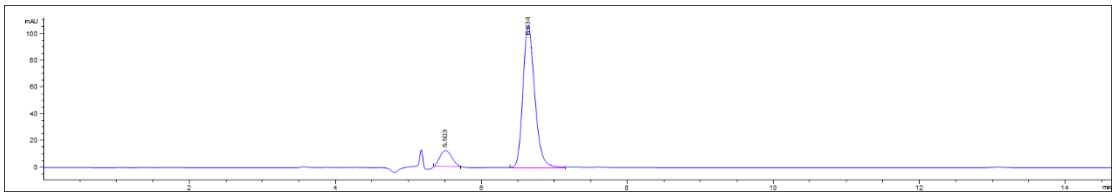
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.8	67.6	5	0.2238	0.771	3.071	MM
2	7.762	2132.7	147.6	0.2408	0.656	96.929	MM



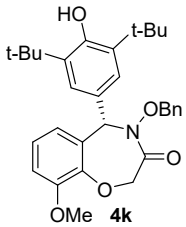
4j



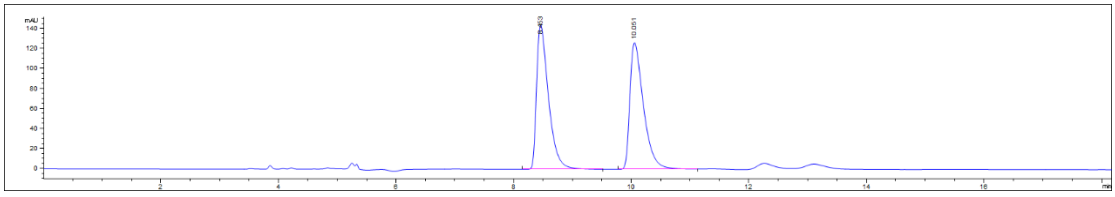
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.307	751.1	57	0.2038	0.783	51.322	BB
2	6.443	712.4	63.9	0.1702	0.759	48.678	BB



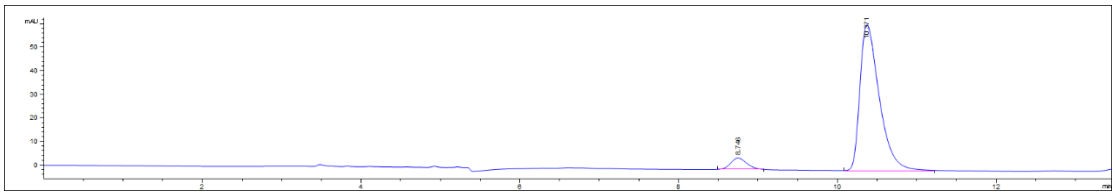
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.503	136.6	12	0.1905	0.834	10.117	MM
2	6.634	1213.5	106.8	0.1894	0.762	89.883	MM



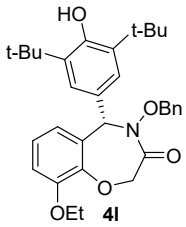
4k



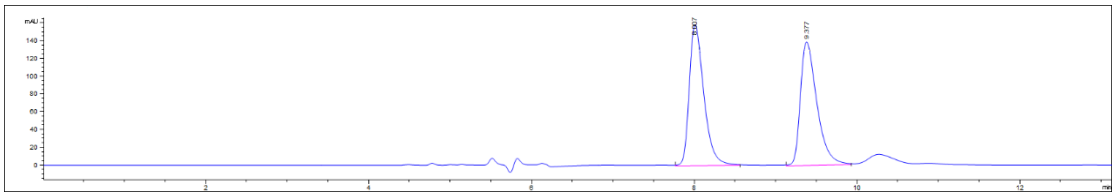
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.453	2039.2	144.8	0.2123	0.476	50.111	BB
2	10.051	2030.2	126.8	0.2427	0.487	49.889	BB



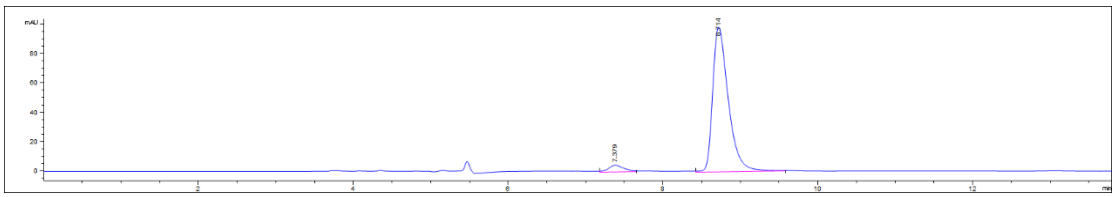
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.746	69.9	4.8	0.2402	0.818	6.163	MM
2	10.371	1063.6	62.1	0.2855	0.552	93.837	MM



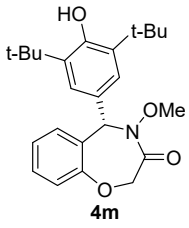
4l



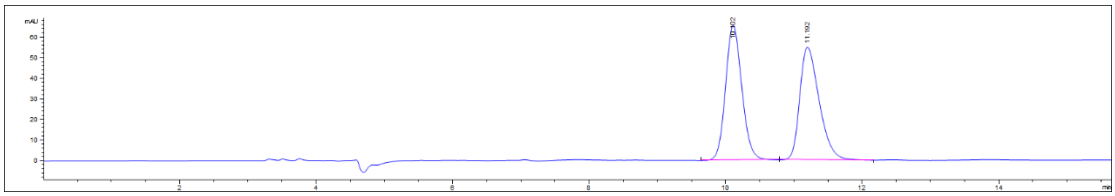
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.007	1988	158.5	0.209	0.643	50.190	MM
2	9.377	1972.9	139	0.2365	0.583	49.810	MM



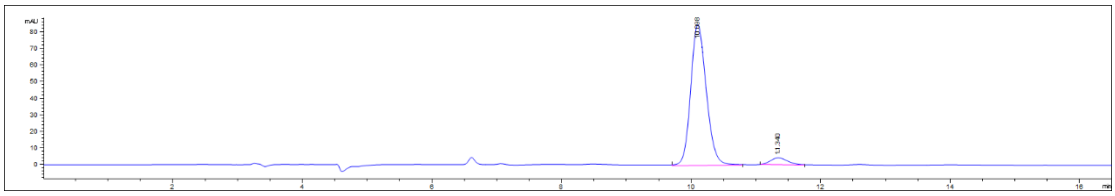
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.379	70.4	4.7	0.2476	0.785	4.790	MM
2	8.714	1399.8	99.2	0.2353	0.595	95.210	MM



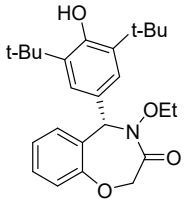
4m



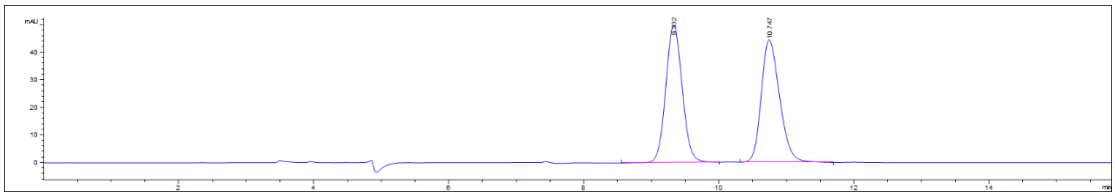
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.102	1088.5	65.4	0.2581	0.83	50.108	BB
2	11.192	1083.8	54.7	0.305	0.625	49.892	BB



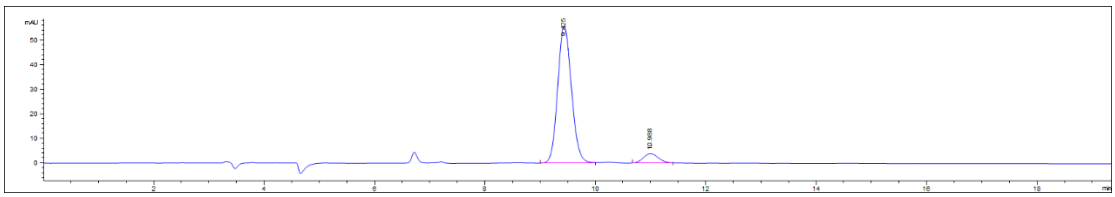
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.098	1435.8	84.8	0.2821	0.798	94.651	MM
2	11.34	81.1	4.2	0.3219	0.753	5.349	MM



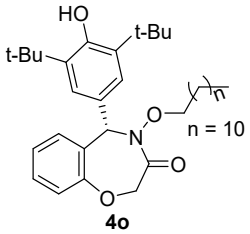
4n



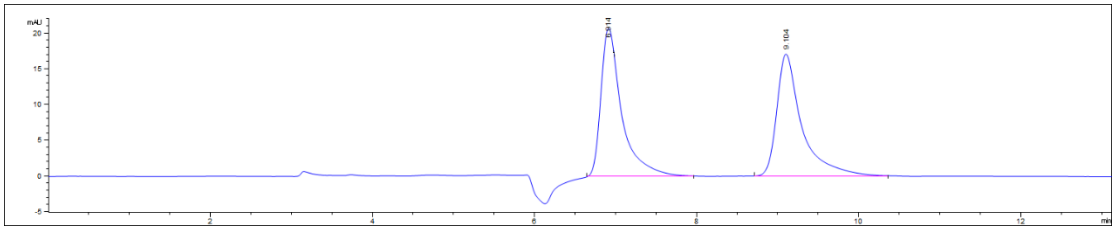
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.332	842	49.8	0.2634	0.901	50.059	BB
2	10.747	840	44.4	0.2929	0.718	49.941	BB



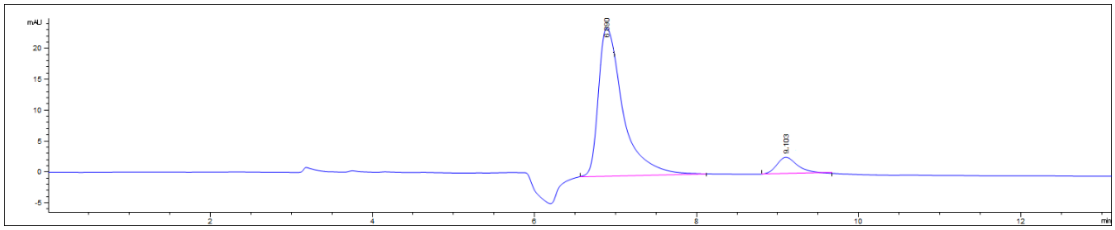
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.425	962.5	55.6	0.2886	0.856	93.050	MM
2	10.988	71.9	3.8	0.3131	0.868	6.950	MM



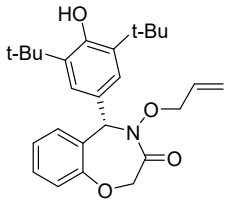
4o



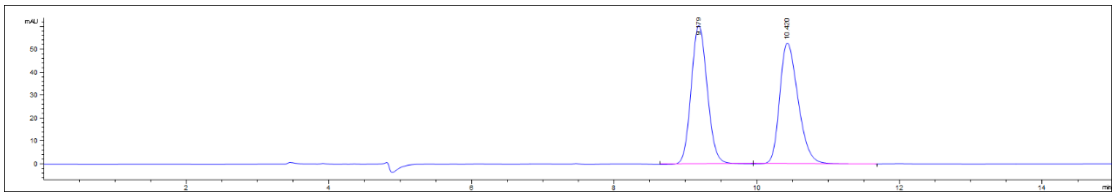
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.914	375.6	20.9	0.3	0.554	49.797	MM
2	9.104	378.6	17.2	0.3659	0.549	50.203	MM



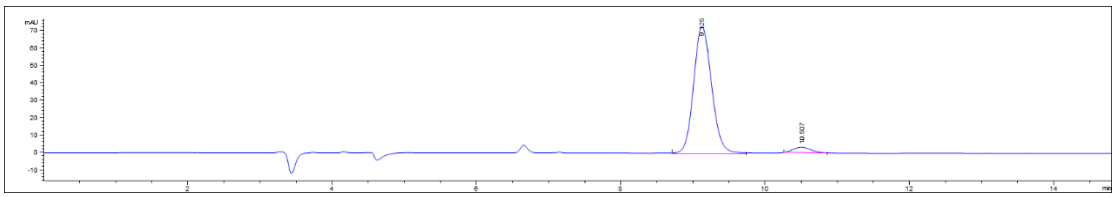
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.89	518.6	24.2	0.3571	0.488	91.005	MM
2	9.103	51.3	2.7	0.3118	0.746	8.995	MM



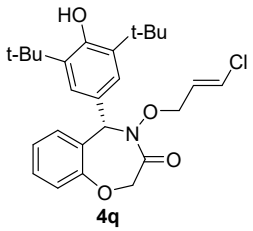
4p



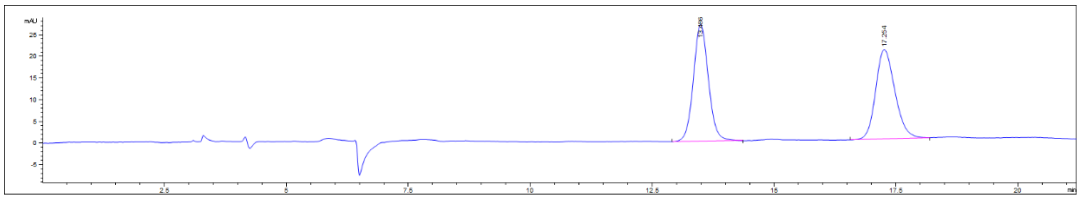
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.179	952	60.6	0.2453	0.863	50.181	BB
2	10.42	945.1	52.7	0.2791	0.678	49.819	BB



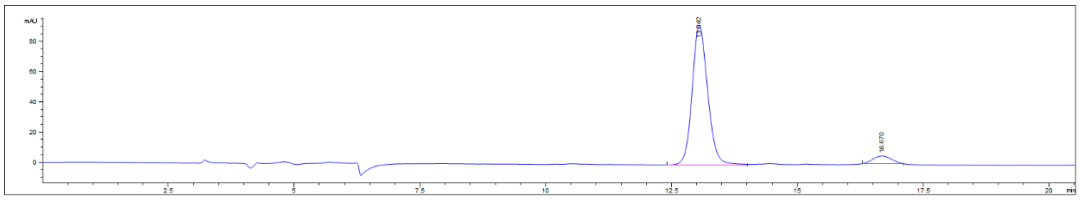
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.125	1284.1	73.3	0.2921	0.849	95.389	MM
2	10.507	62.1	3.3	0.3115	0.767	4.611	MM



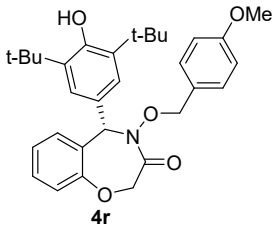
4q



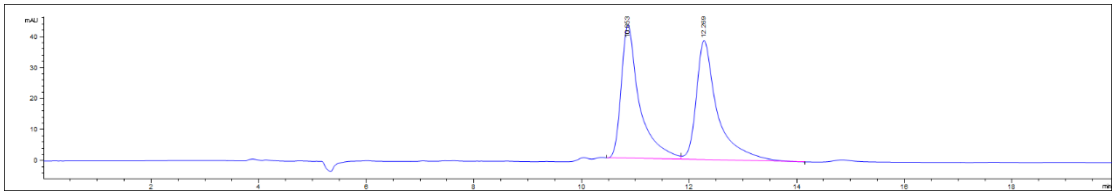
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.486	576.6	26.8	0.3289	0.891	50.552	BB
2	17.254	564	20.5	0.4229	0.786	49.448	BB



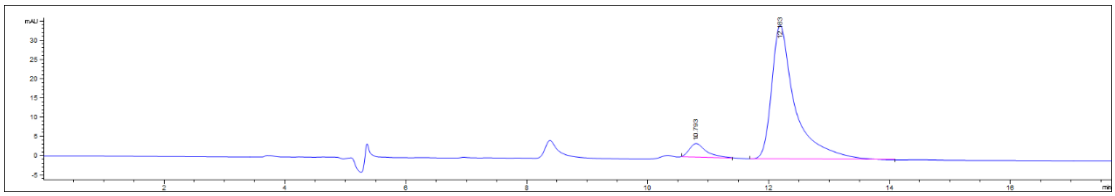
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.042	2020.1	93.2	0.3613	0.815	93.181	MM
2	16.67	147.8	5.5	0.452	0.9	6.819	MM



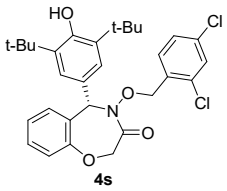
4r



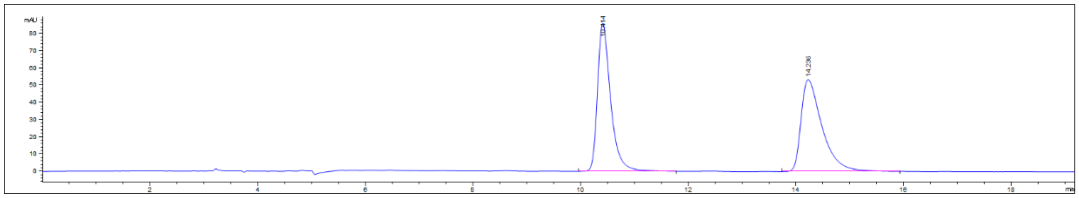
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.853	1021.7	43.1	0.3423	0.519	49.070	BV
2	12.269	1060.5	38.6	0.3943	0.527	50.930	VB



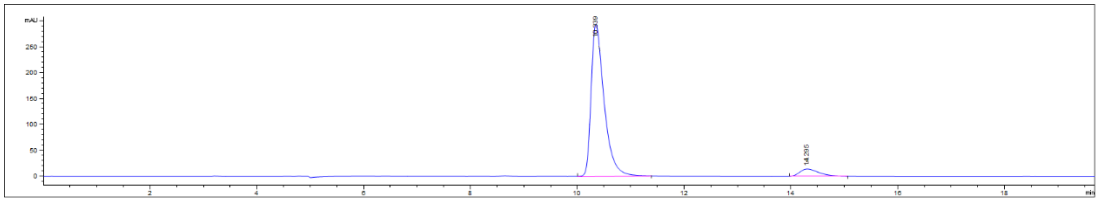
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.793	71.5	3.6	0.3345	0.605	7.074	MM
2	12.183	939.8	34.7	0.3876	0.508	92.926	BB



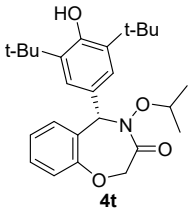
4s



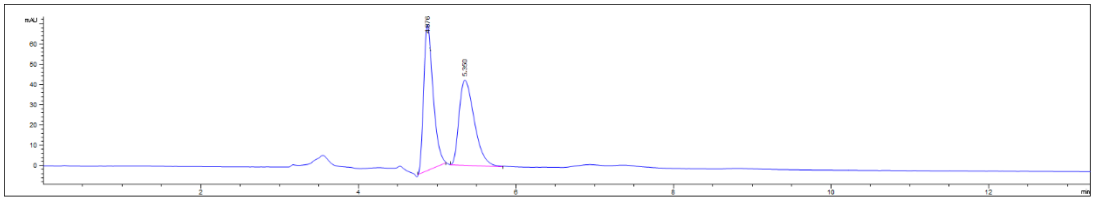
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.414	1449.9	85.5	0.2558	0.615	50.177	BB
2	14.236	1439.6	53.1	0.4043	0.478	49.823	BB



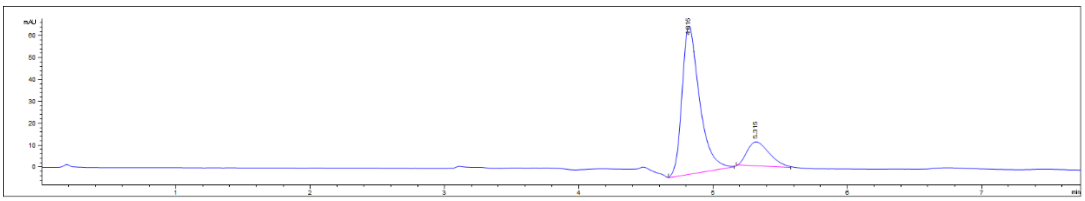
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.339	5035.8	294.2	0.2853	0.558	93.114	MM
2	14.295	372.4	14.5	0.4293	0.62	6.886	MM



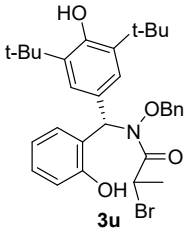
4t



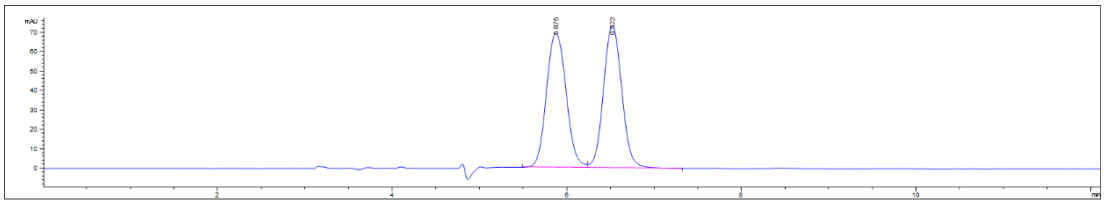
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	4.876	601.8	72.5	0.1384	0.659	51.432	MM
2	5.35	568.3	42.1	0.2248	0.592	48.568	MM



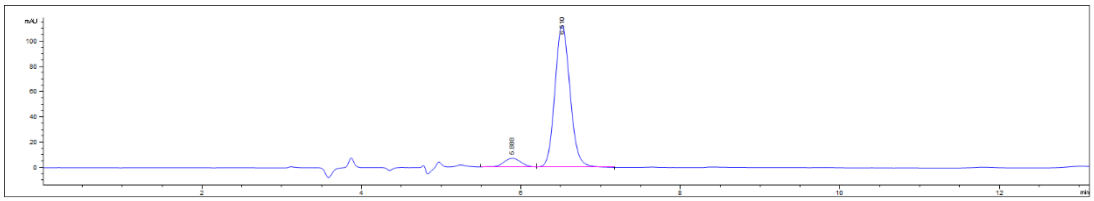
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	4.815	618.3	68	0.1515	0.64	82.961	MM
2	5.315	127	11	0.1929	0.646	17.039	MM



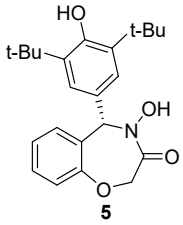
3u



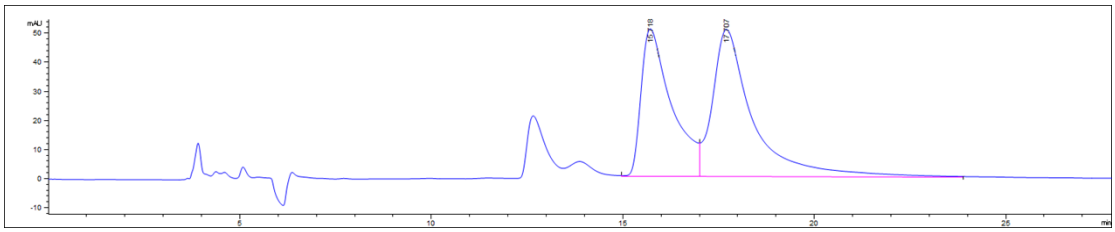
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.875	1085.1	69.2	0.251	0.878	50.301	BV
2	6.522	1072.1	73.3	0.2306	0.888	49.699	VB



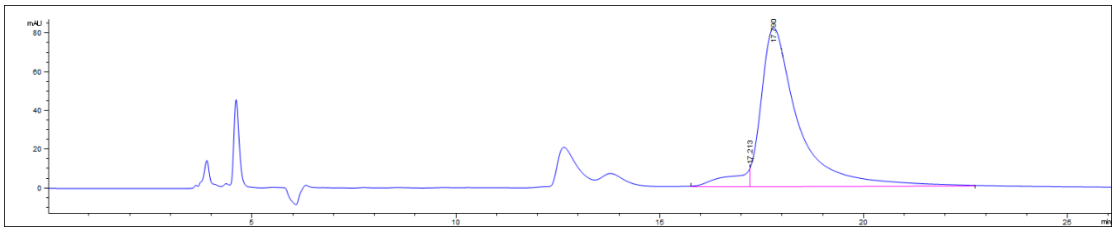
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.888	104	6.9	0.2423	0.997	6.558	BV
2	6.51	1481.9	112.4	0.2059	0.854	93.442	VB



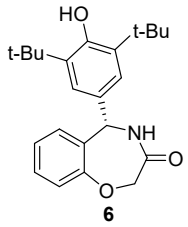
5



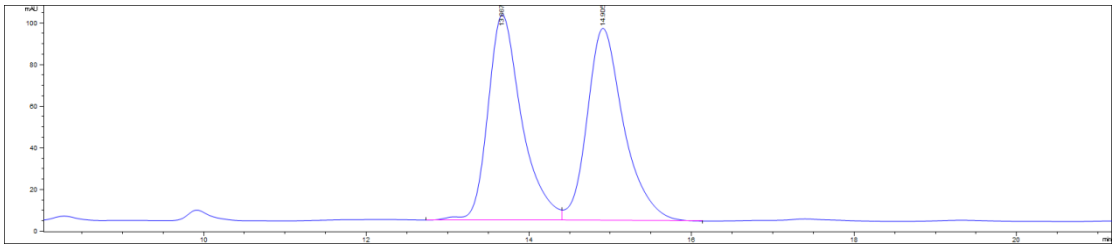
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	15.718	3078.1	51	1.0054	0	46.247	MF
2	17.707	3577.7	50.9	1.1717	0.388	53.753	FM



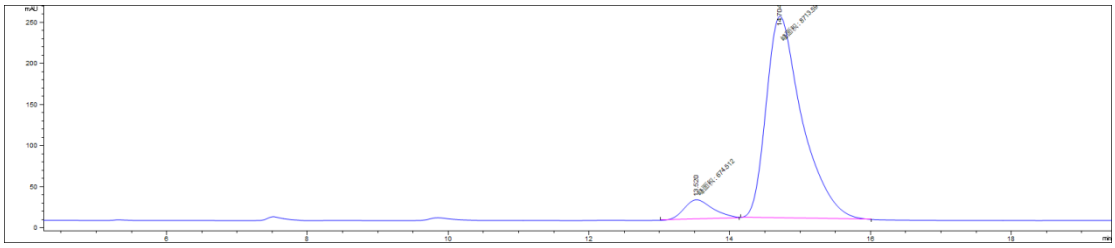
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	17.213	360.7	9.8	0.6108	7372.39	6.507	MF
2	17.79	5182.7	81.9	1.0542	0.468	93.493	FM



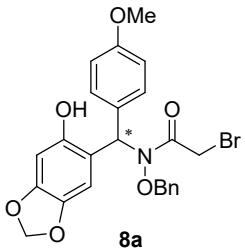
6



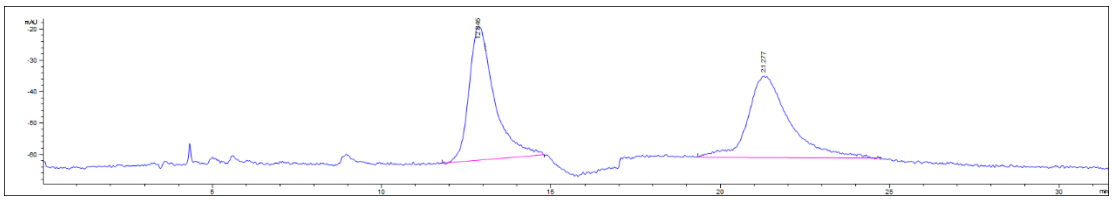
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.667	2844.8	98.4	0.4314	0.7	49.675	BV
2	14.905	2882	91.9	0.4697	0.72	50.325	VB



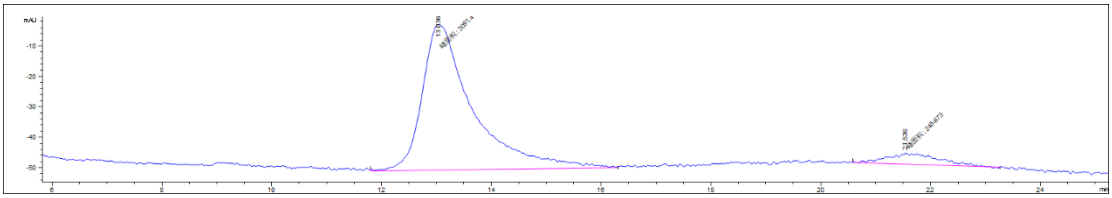
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.52	674.5	23.6	0.4764	0.709	7.185	MM
2	14.704	8713.6	246.1	0.5901	0.602	92.815	MM



8a



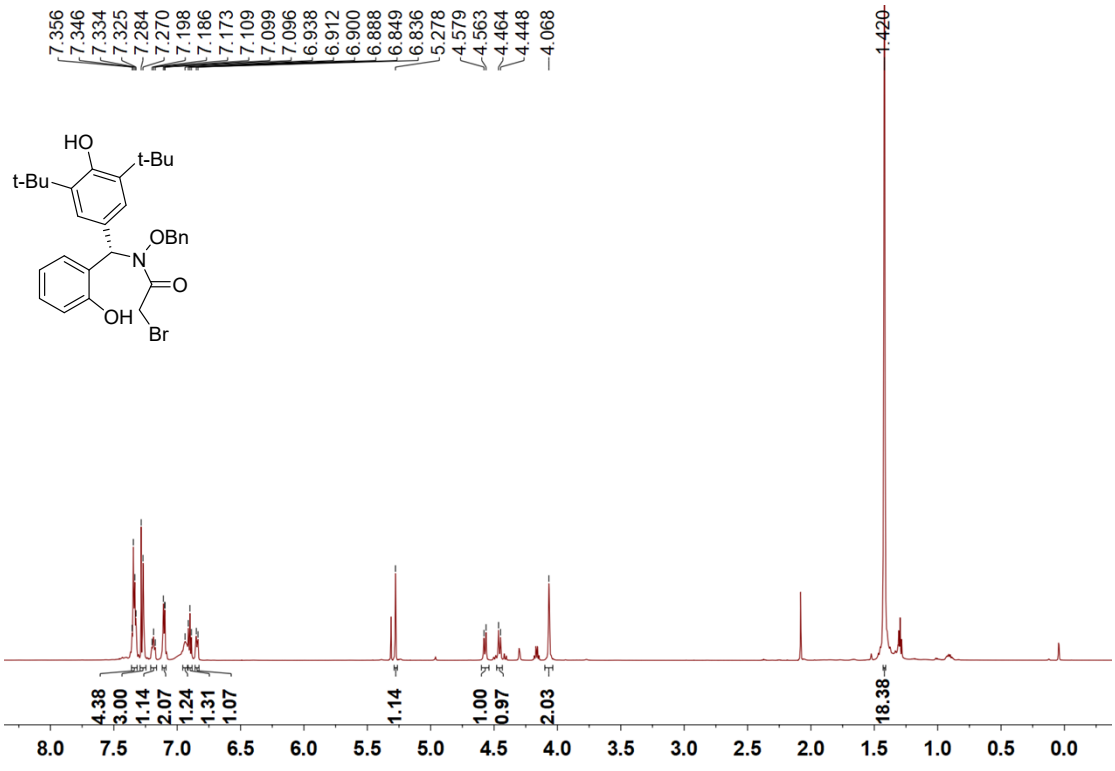
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.845	2238.3	42.7	0.8728	0.569	49.632	MM
2	21.277	2271.4	26.2	1.4434	0.628	50.368	MM



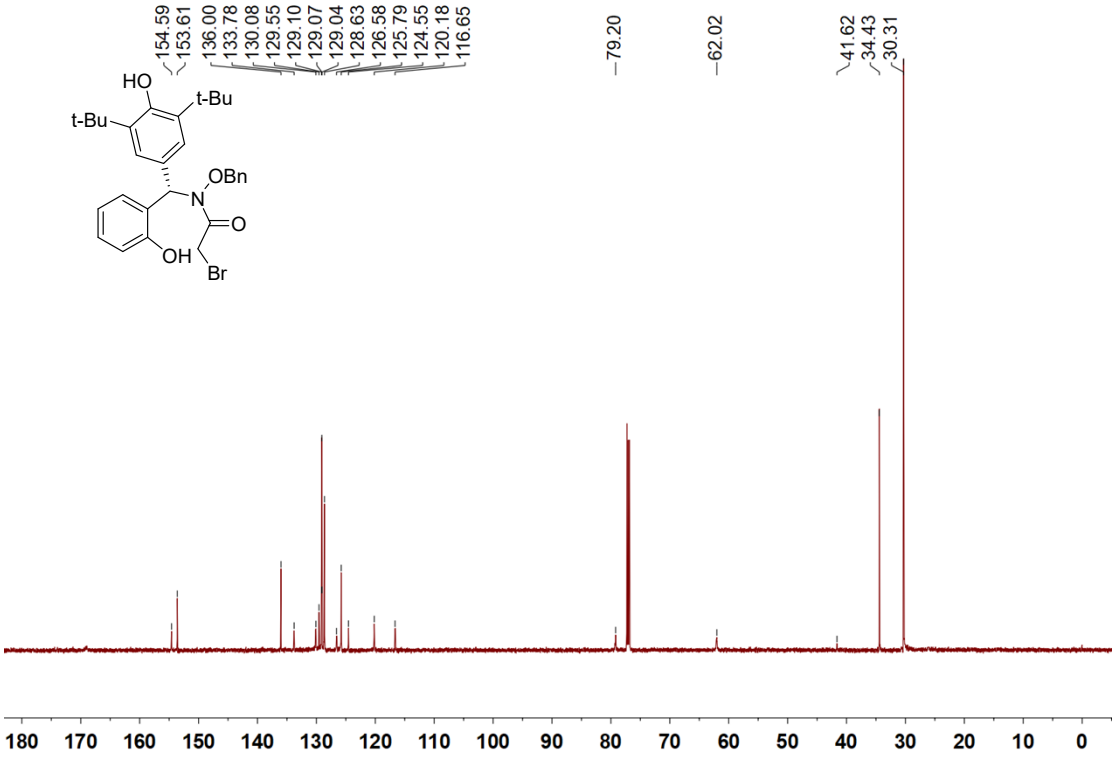
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.036	3091.4	48	1.0734	0.484	92.630	MM
2	21.536	246	3.8	1.0917	0.583	7.370	MM

6. NMR spectra of products

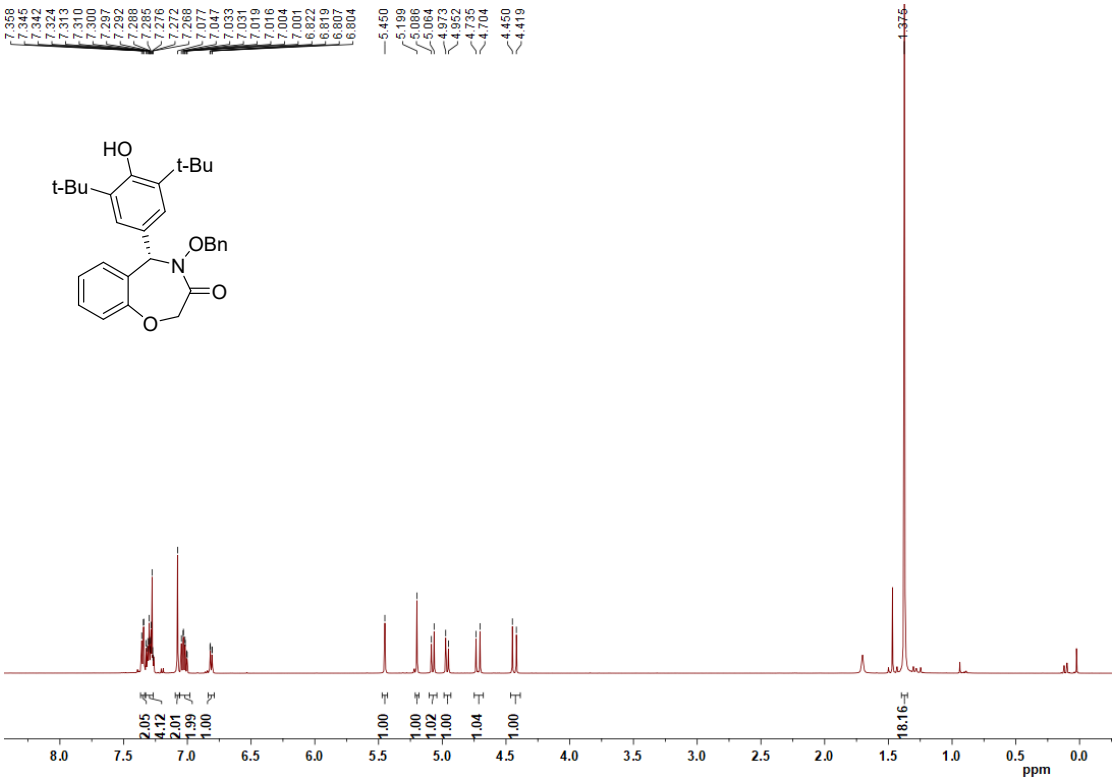
^{1}H NMR of compound 3a (600 MHz in $CDCl_3$)



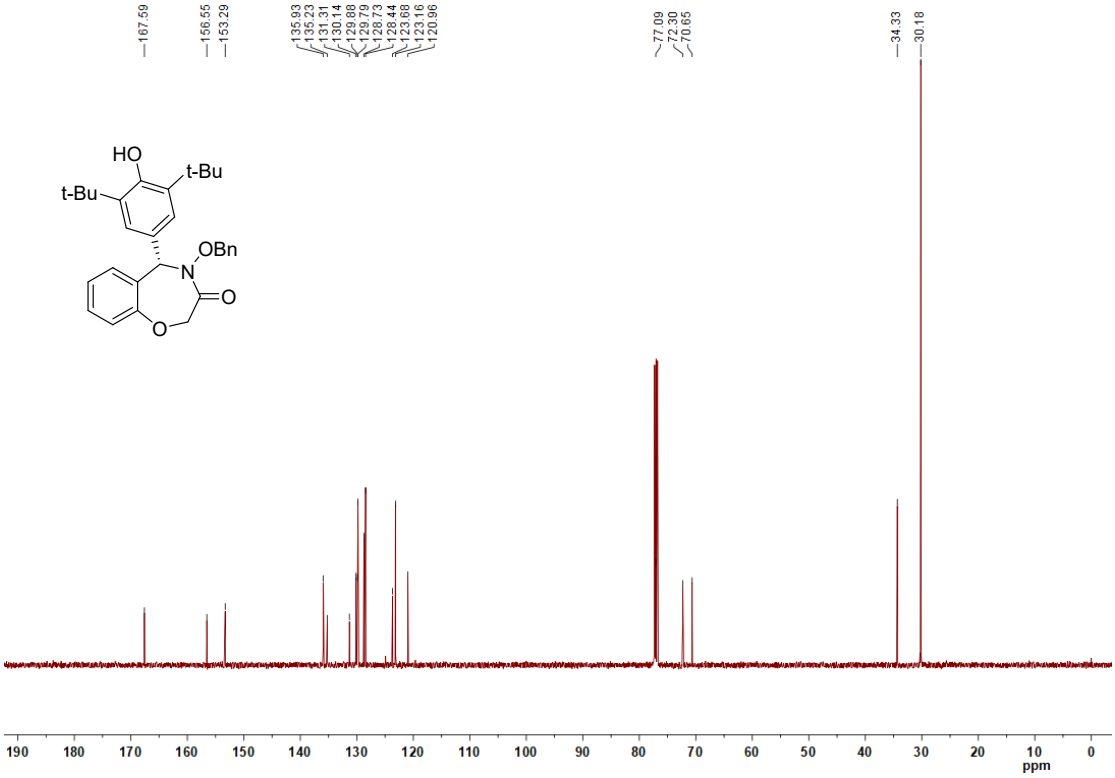
^{13}C NMR of compound 3a (150 MHz in $CDCl_3$)



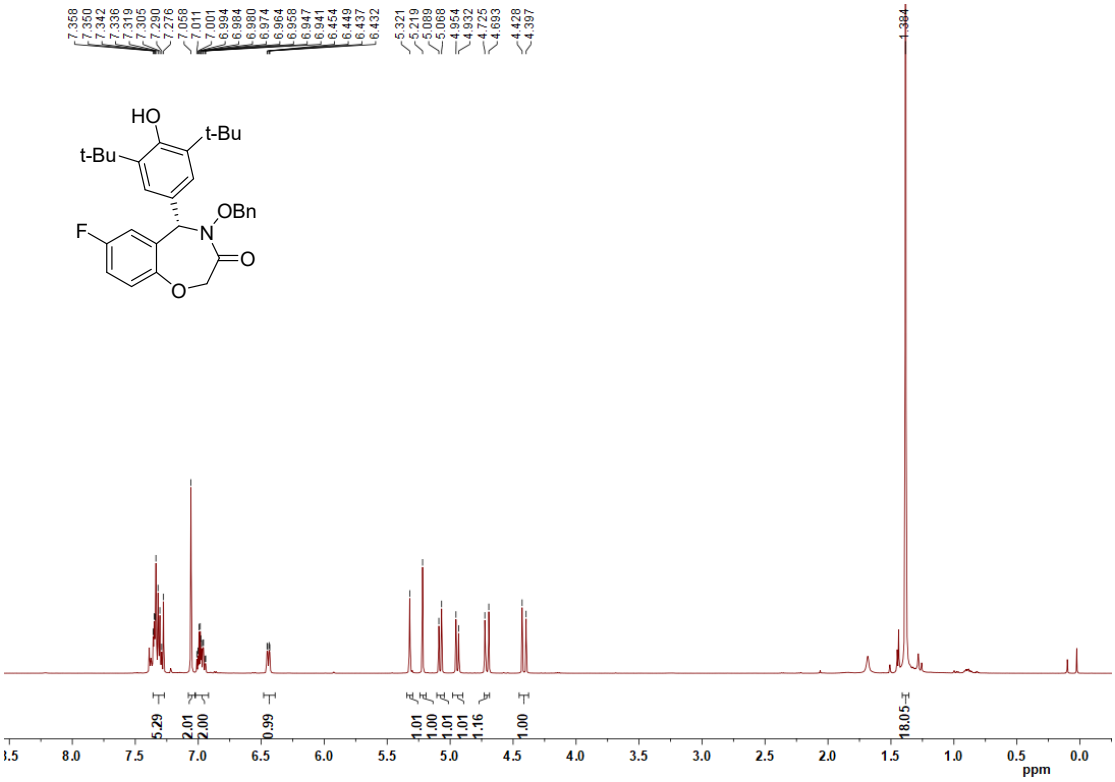
^{1}H NMR of compound 4a (500 MHz in $CDCl_3$)



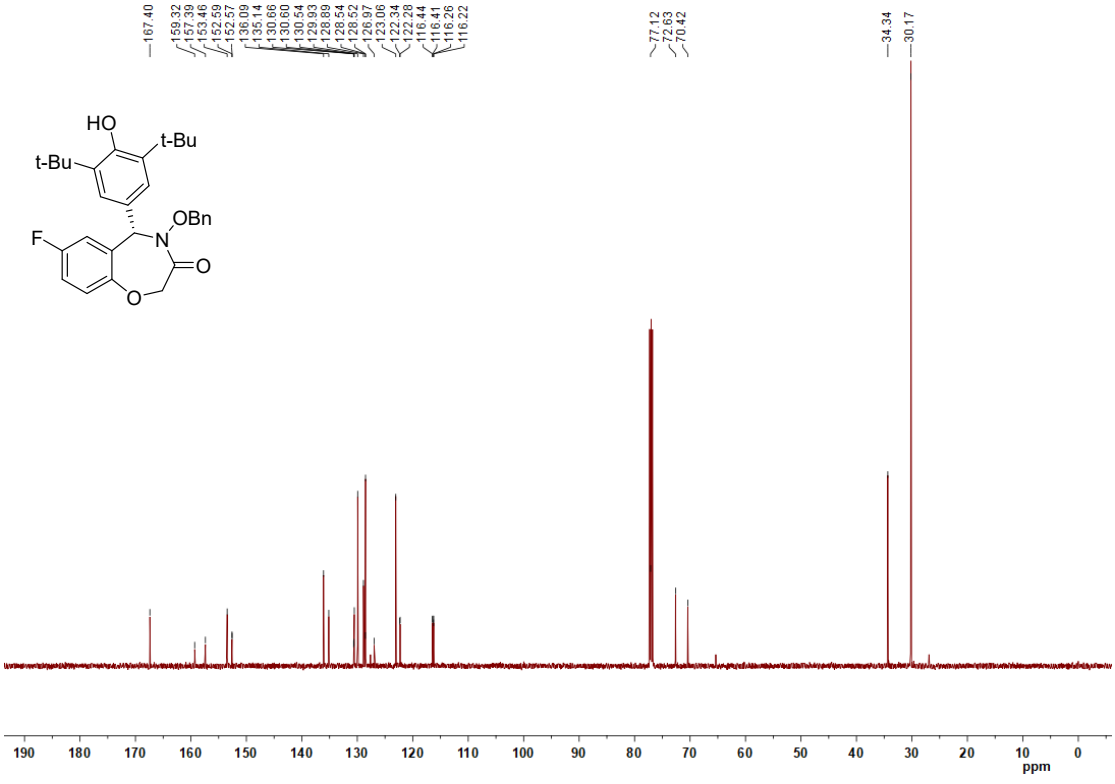
^{13}C NMR of compound 4a (125 MHz in $CDCl_3$)



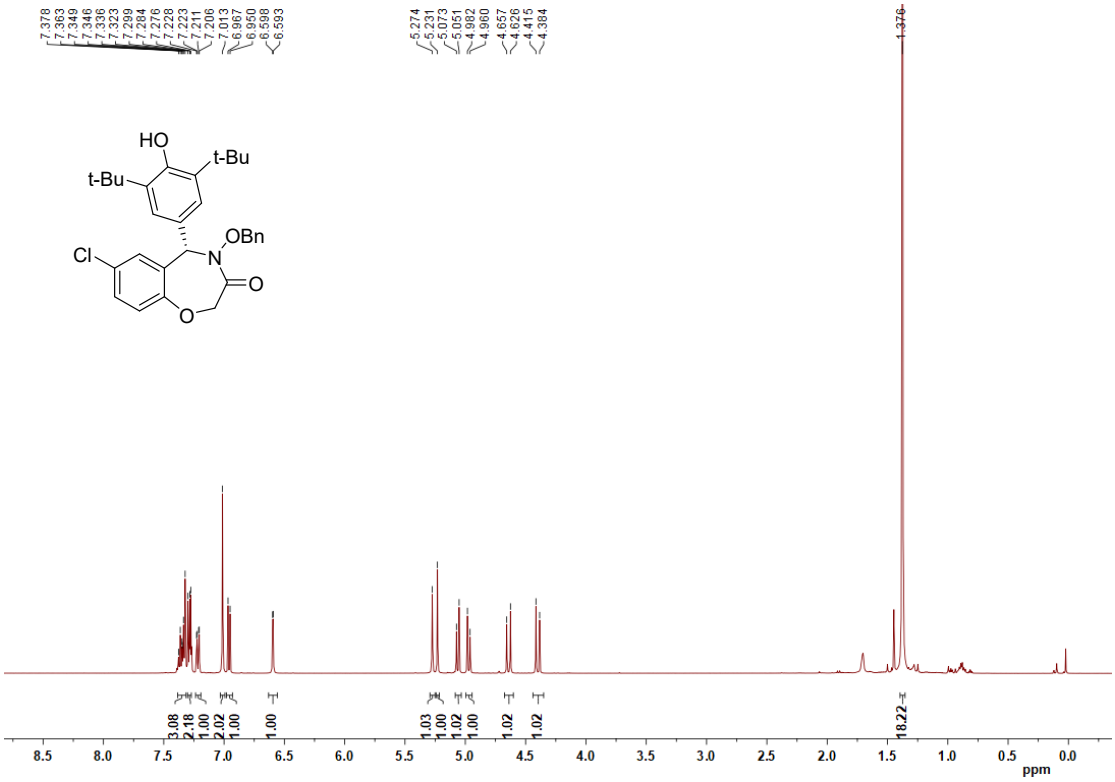
^{1}H NMR of compound 4b (500 MHz in $CDCl_3$)



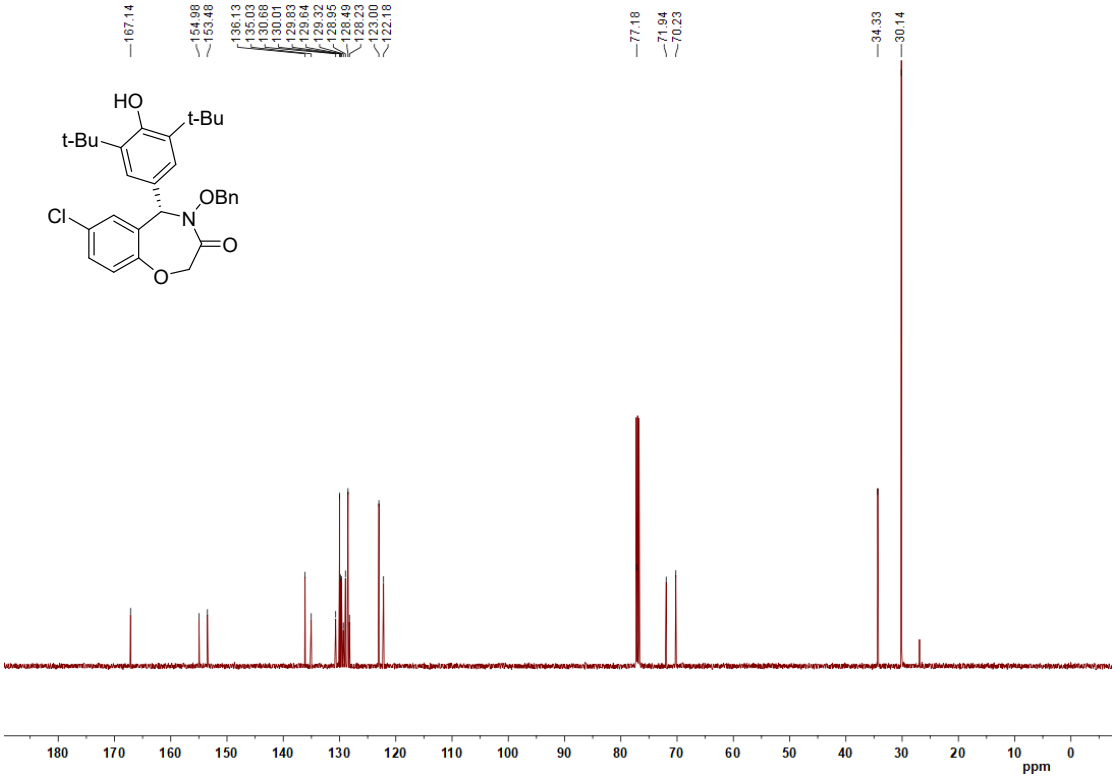
^{13}C NMR of compound 4b (125 MHz in $CDCl_3$)



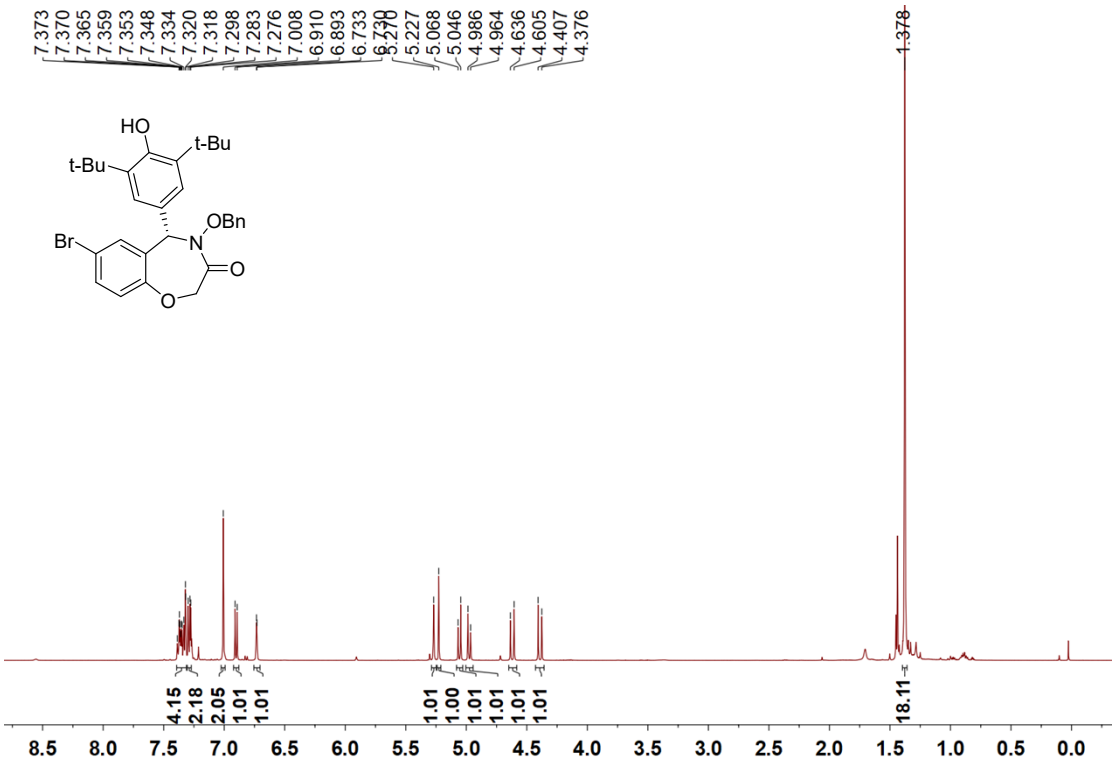
^{1}H NMR of compound 4c (500 MHz in $CDCl_3$)



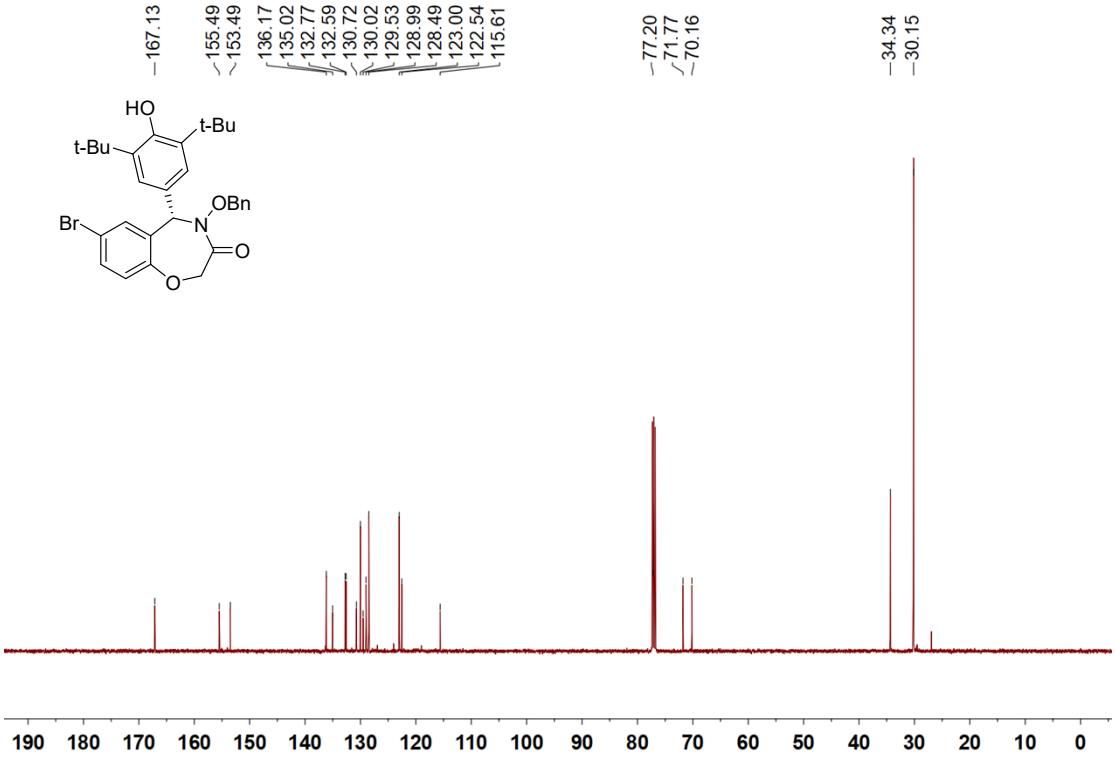
^{13}C NMR of compound 4c (125 MHz in $CDCl_3$)



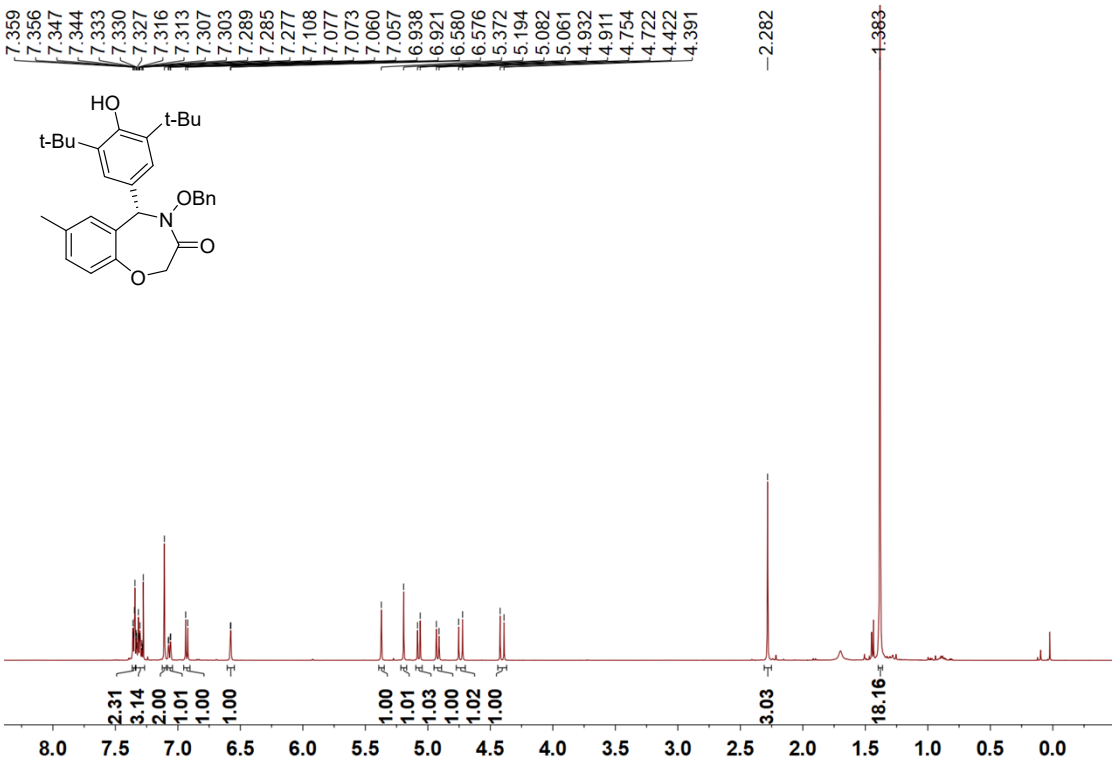
^{1}H NMR of compound 4d (500 MHz in $CDCl_3$)



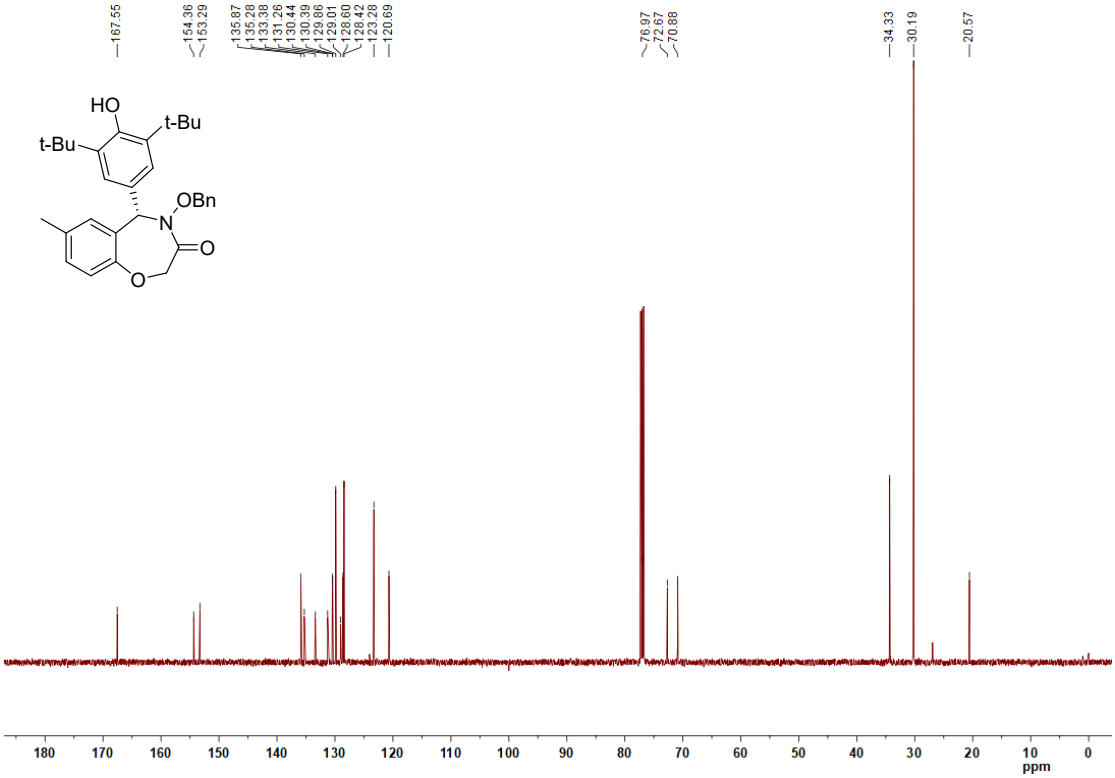
^{13}C NMR of compound 4d (125 MHz in $CDCl_3$)



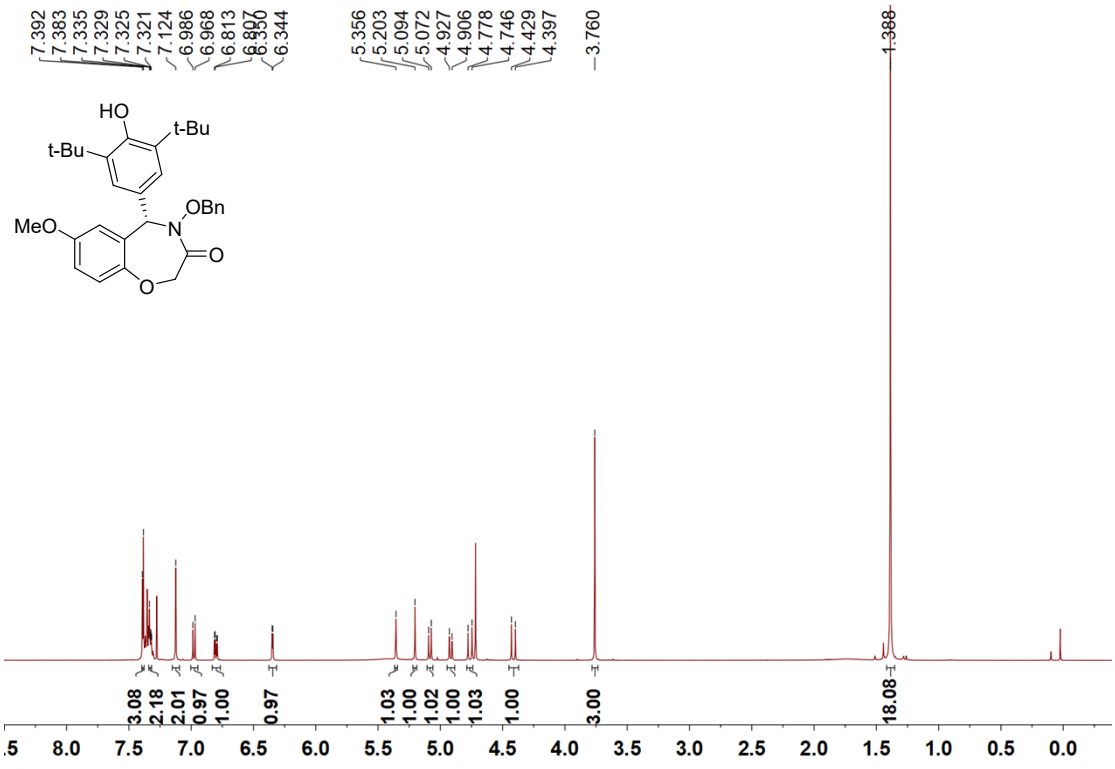
^{1}H NMR of compound 4e (500 MHz in $CDCl_3$)



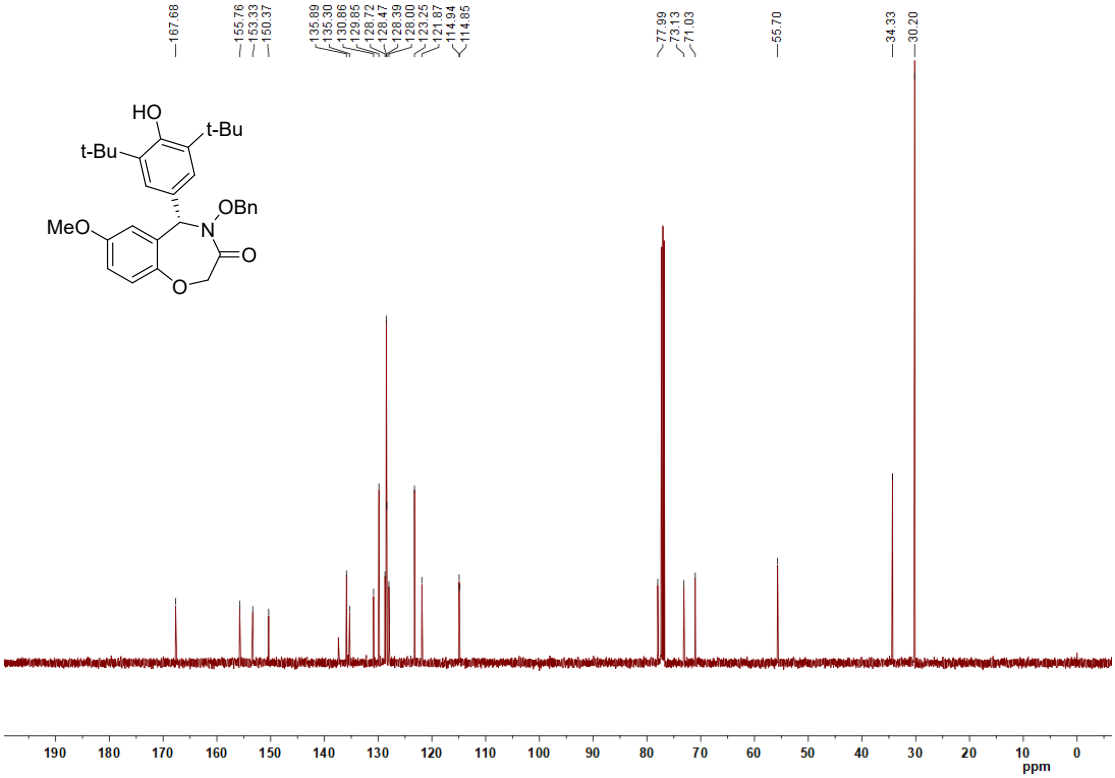
^{13}C NMR of compound 4e (125 MHz in $CDCl_3$)



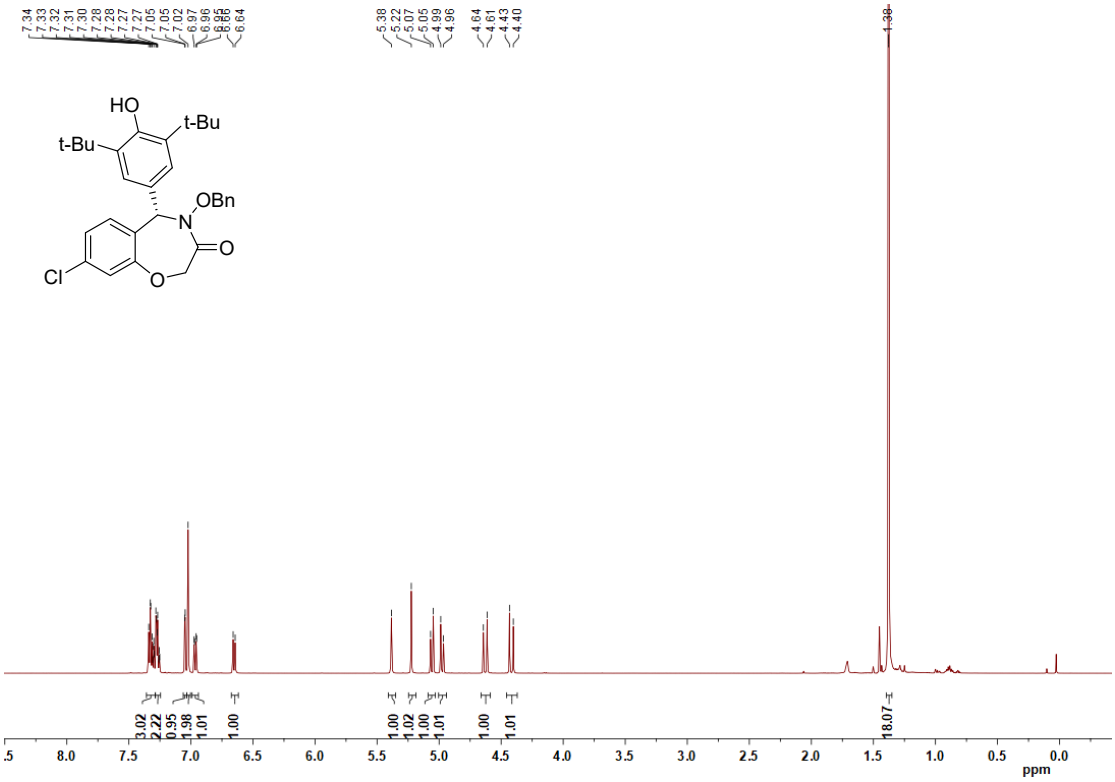
^{1}H NMR of compound 4f (500 MHz in $CDCl_3$)



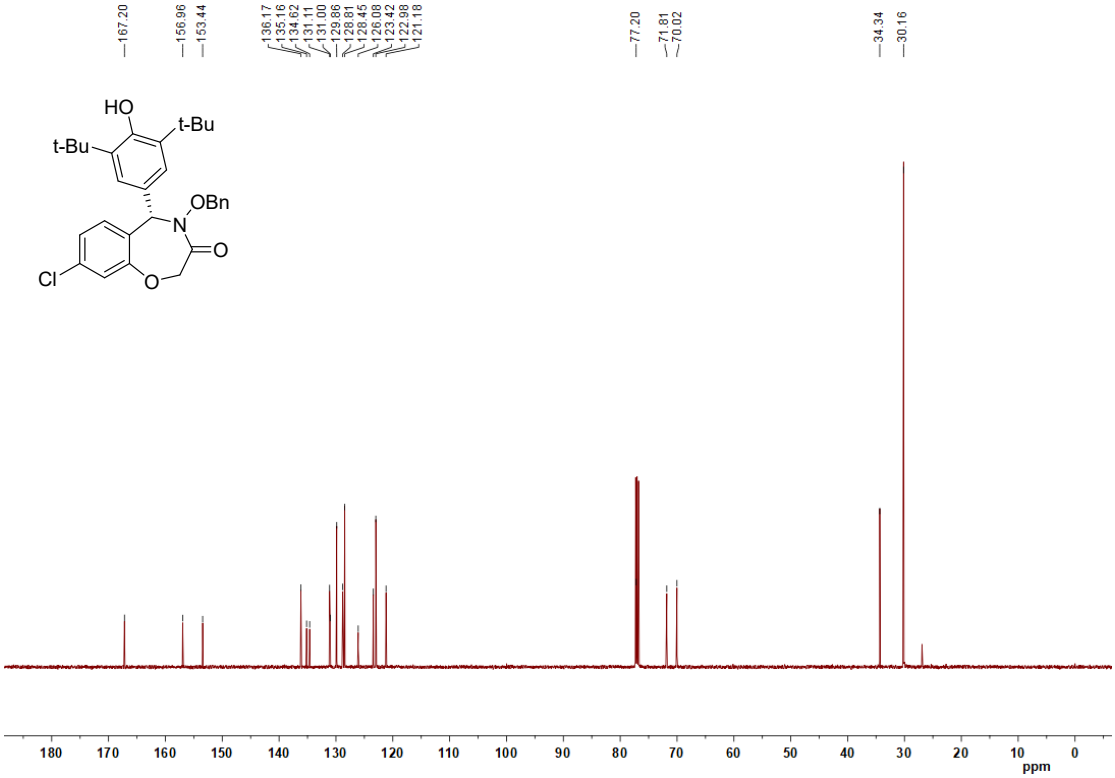
^{13}C NMR of compound 4f (125 MHz in $CDCl_3$)



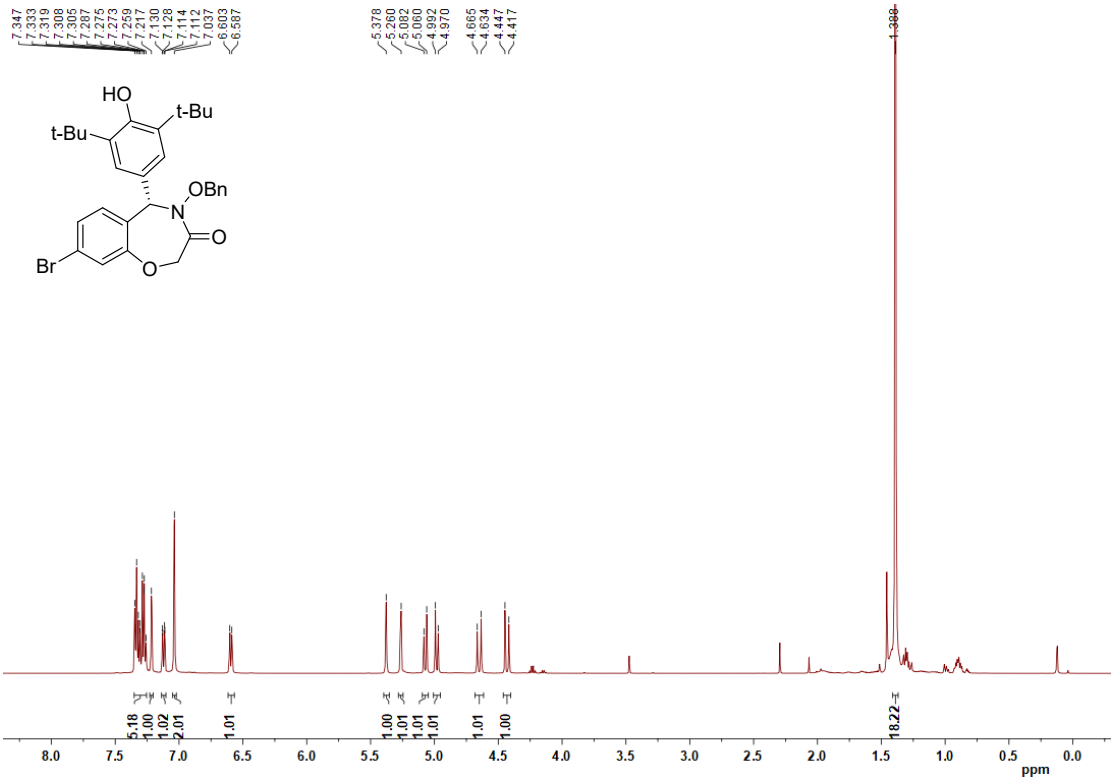
^{1}H NMR of compound 4g (500 MHz in $CDCl_3$)



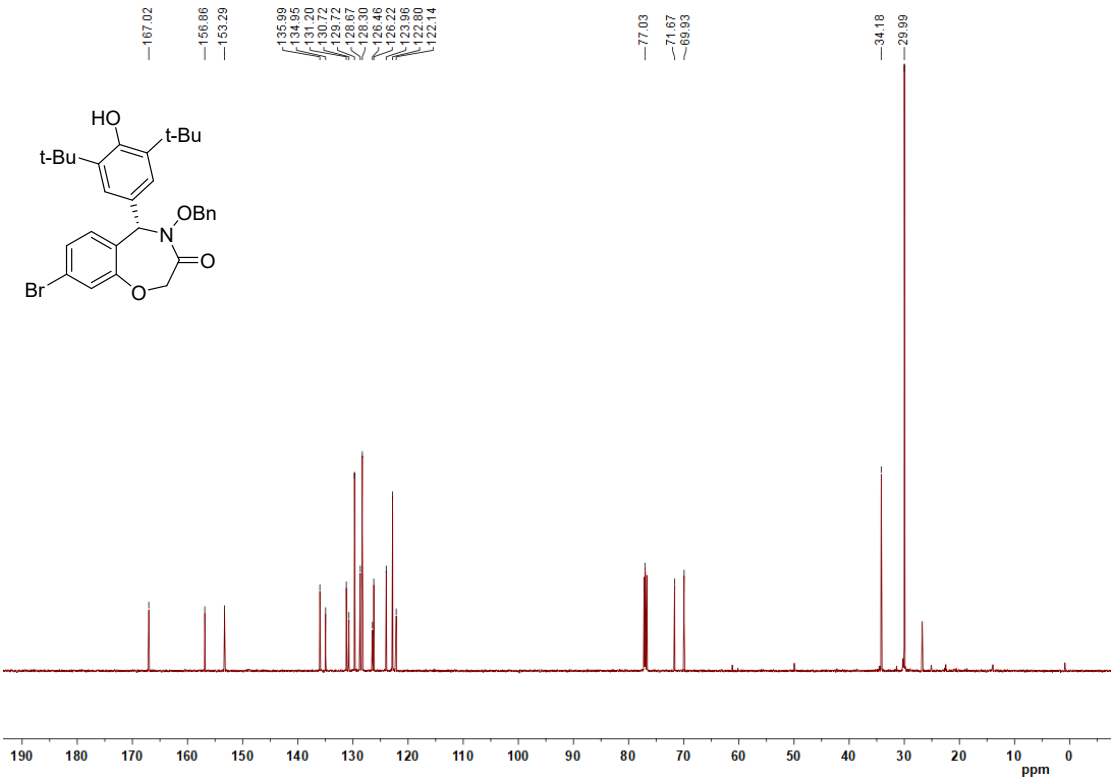
^{13}C NMR of compound 4g (125 MHz in $CDCl_3$)



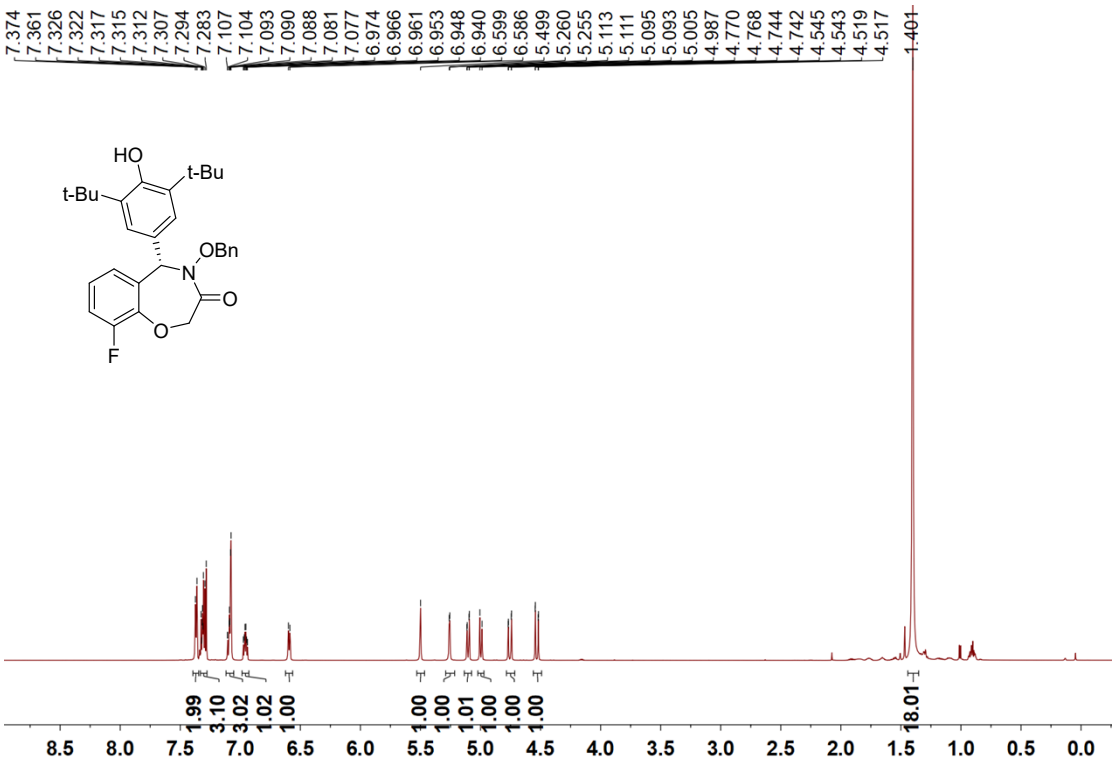
^{1}H NMR of compound 4h (500 MHz in $CDCl_3$)



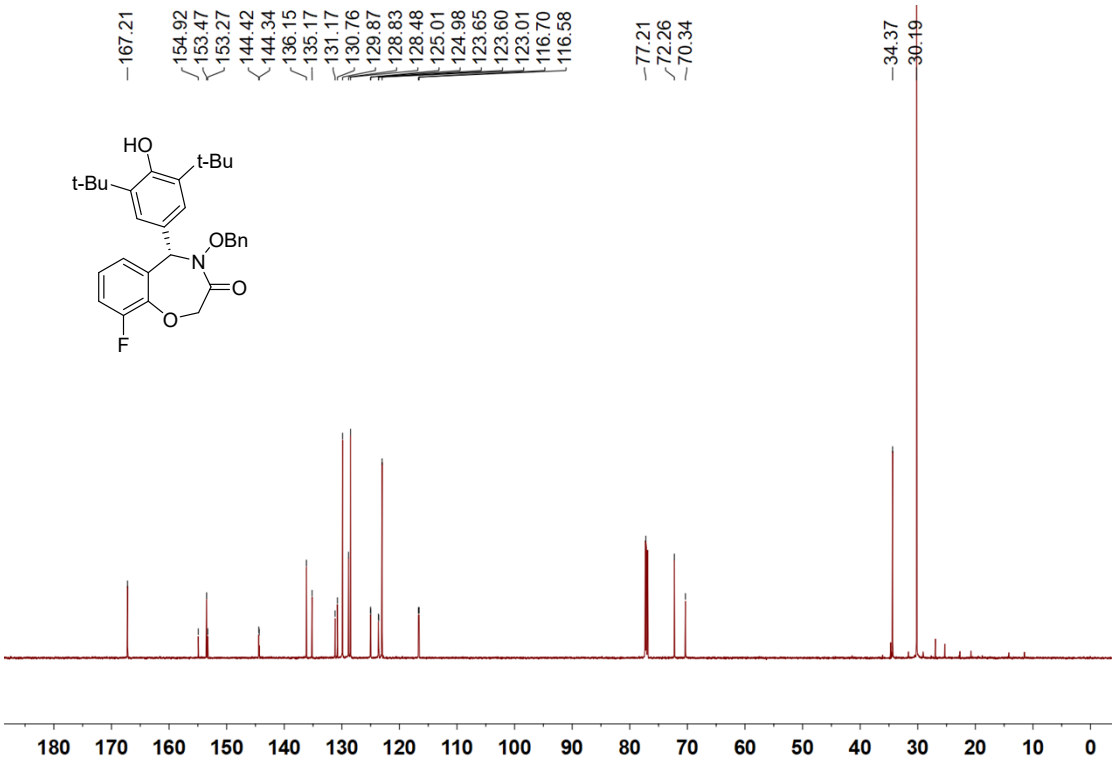
^{13}C NMR of compound 4h (125 MHz in $CDCl_3$)



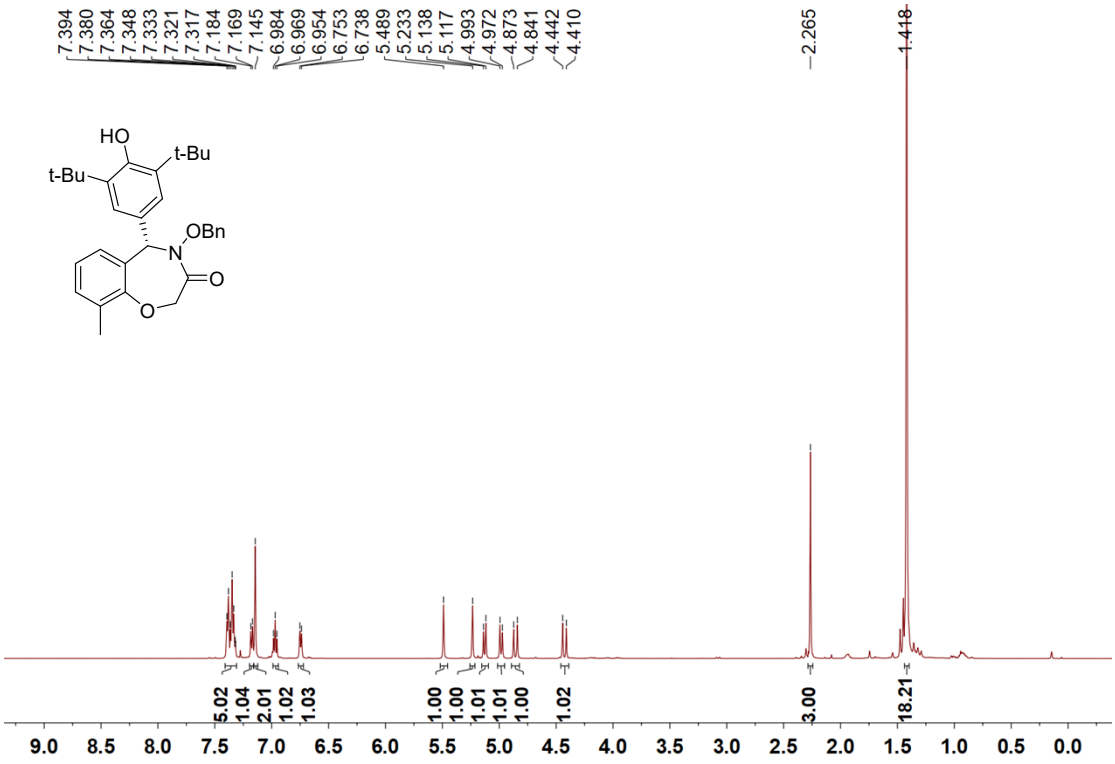
^{1}H NMR of compound 4i (600 MHz in $CDCl_3$)



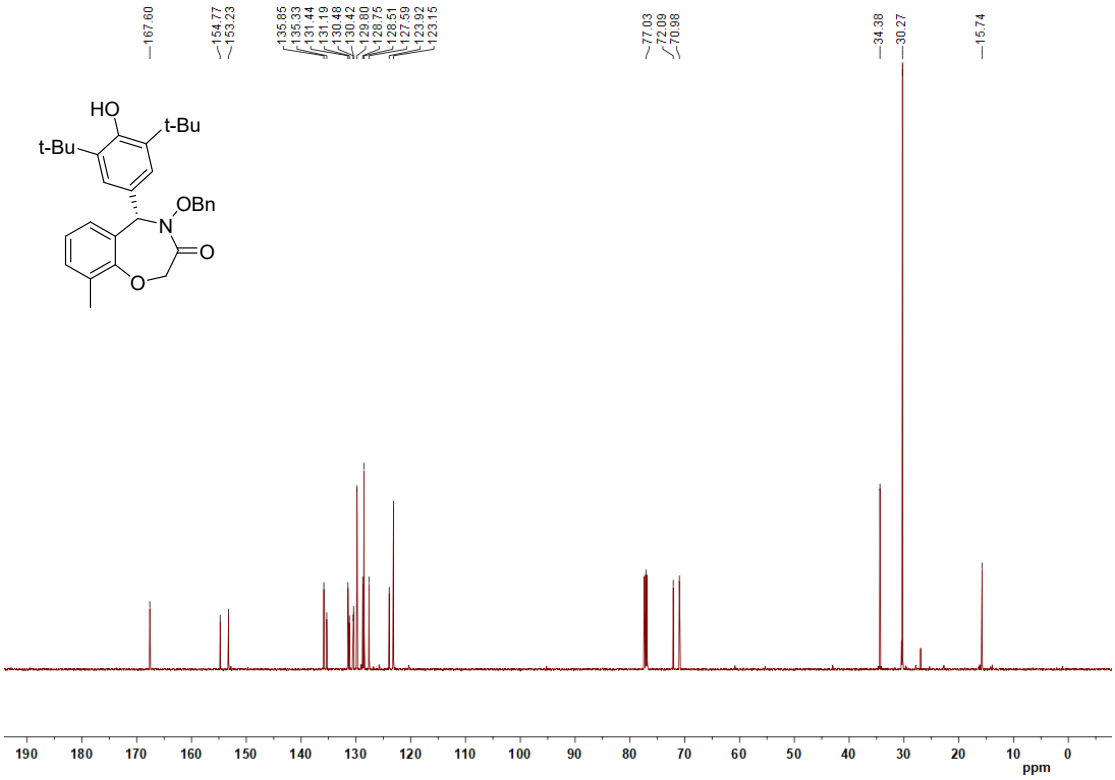
^{13}C NMR of compound 4i (150 MHz in $CDCl_3$)



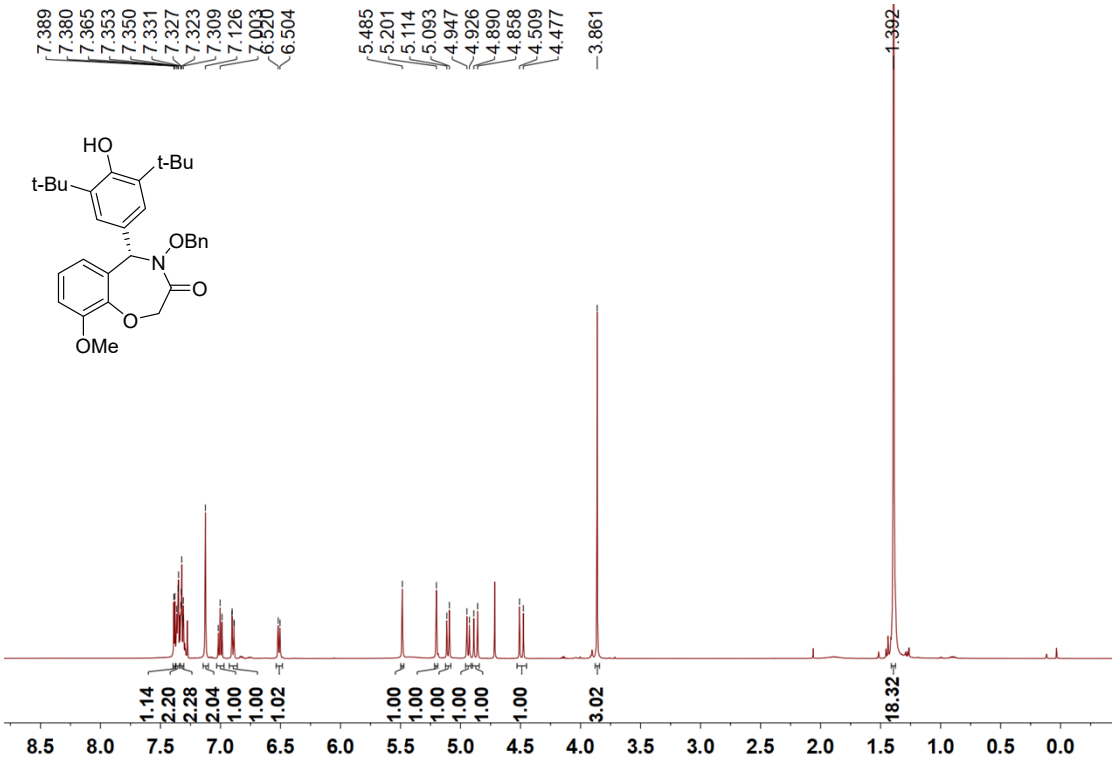
^{1}H NMR of compound 4j (500 MHz in $CDCl_3$)



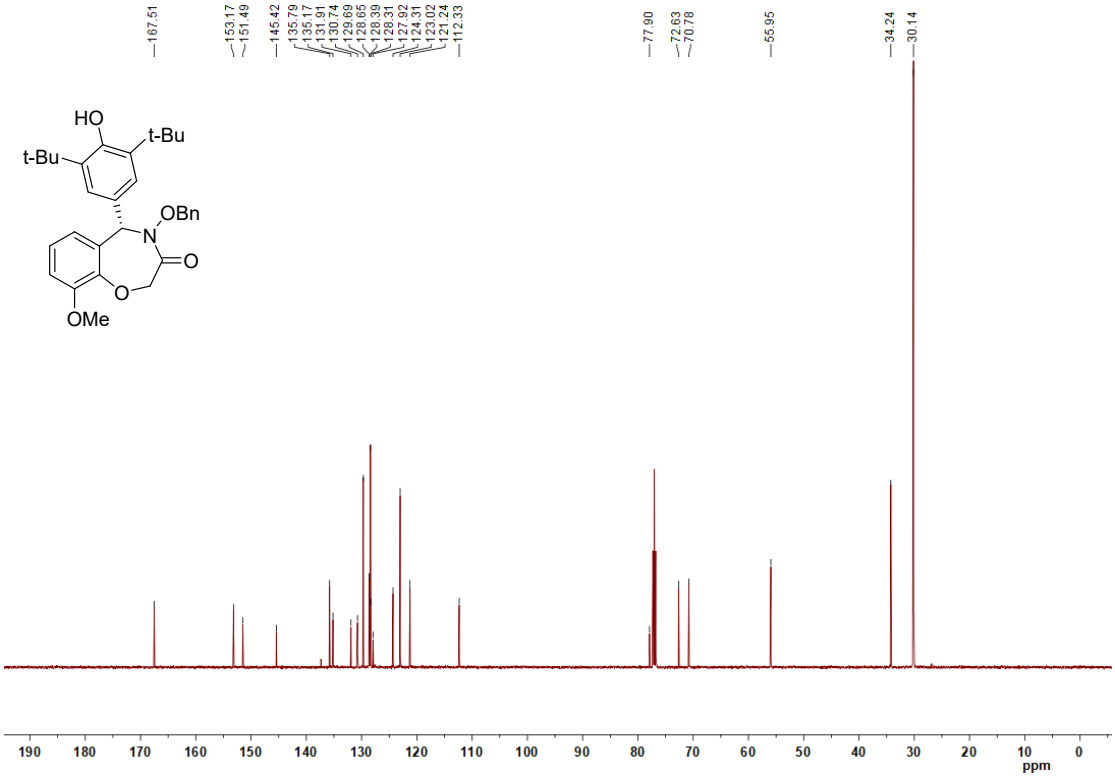
^{13}C NMR of compound 4j (125 MHz in $CDCl_3$)



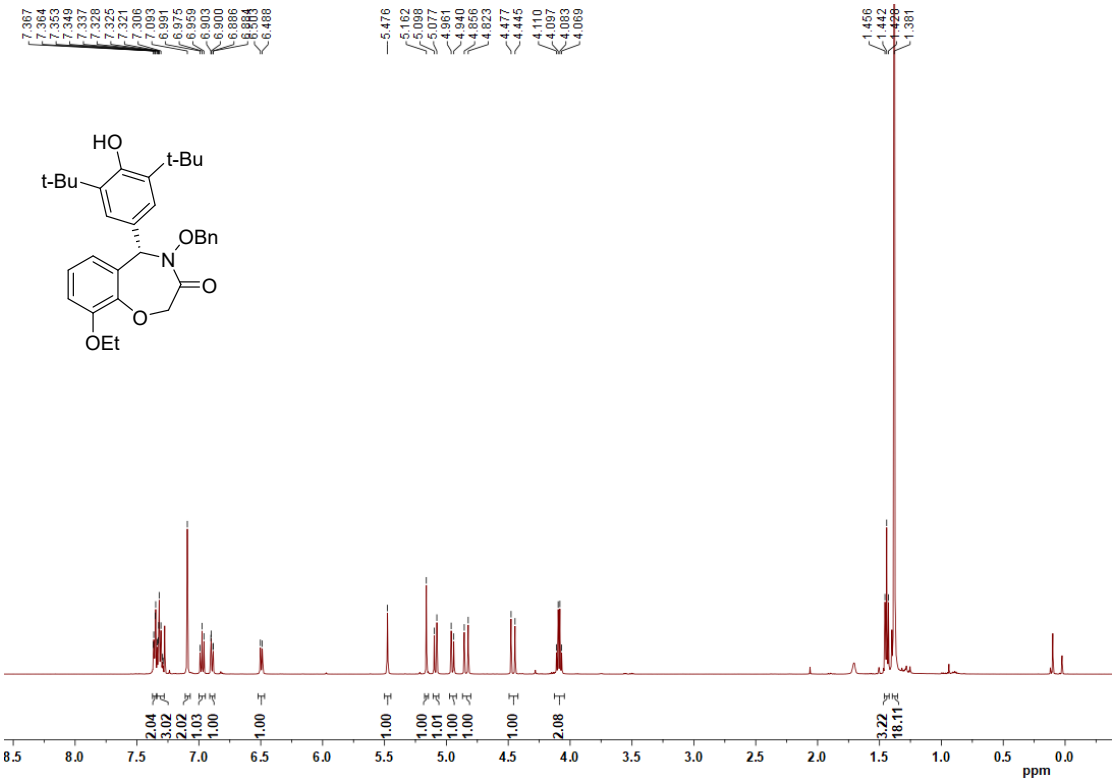
^{1}H NMR of compound 4k (500 MHz in $CDCl_3$)



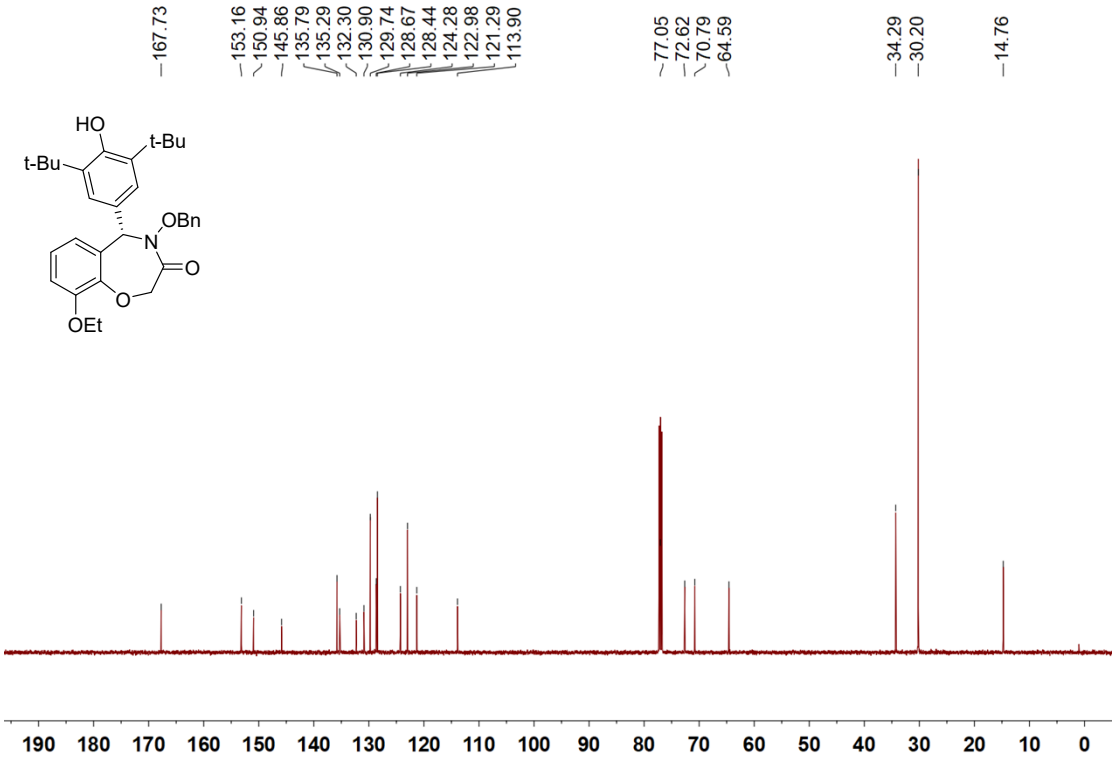
^{13}C NMR of compound 4k (125 MHz in $CDCl_3$)



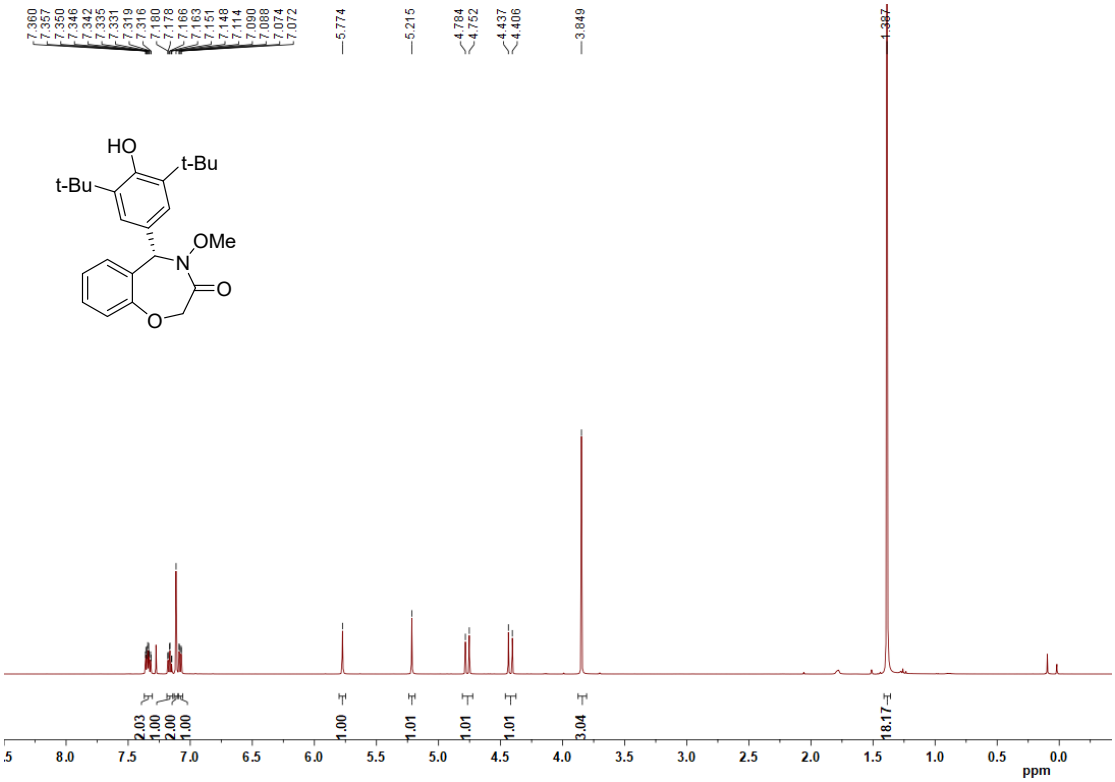
^{1}H NMR of compound 4l (500 MHz in $CDCl_3$)



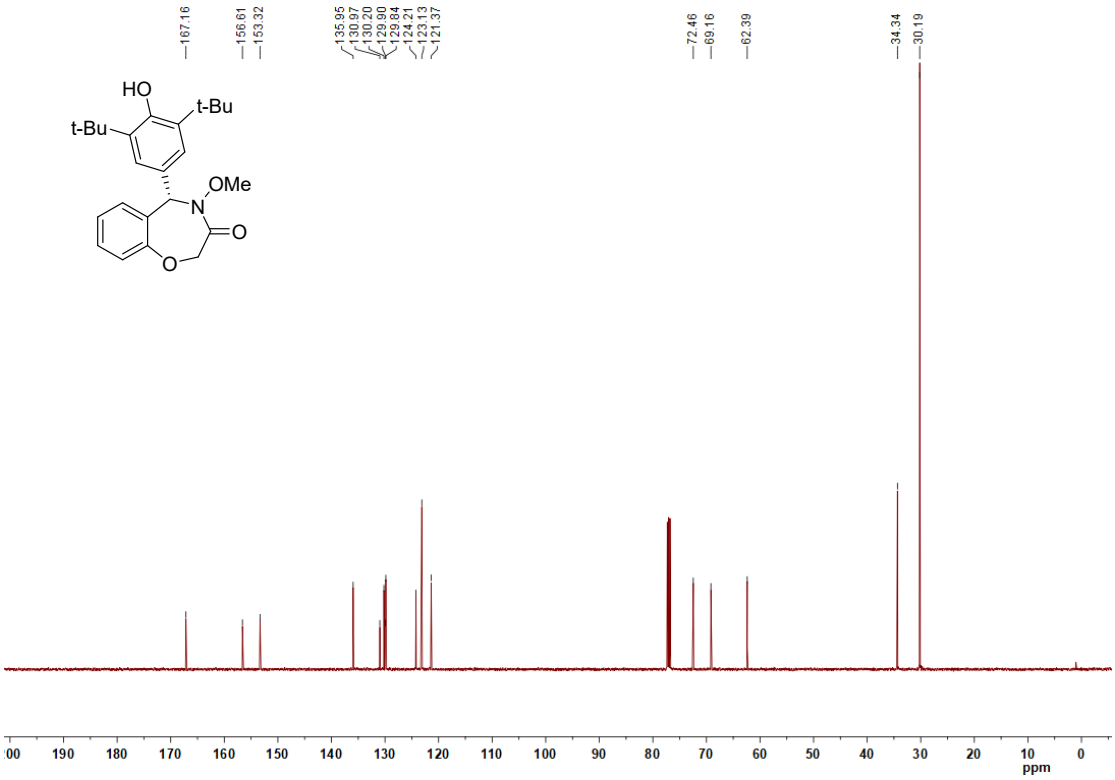
^{13}C NMR of compound 4l (125 MHz in $CDCl_3$)



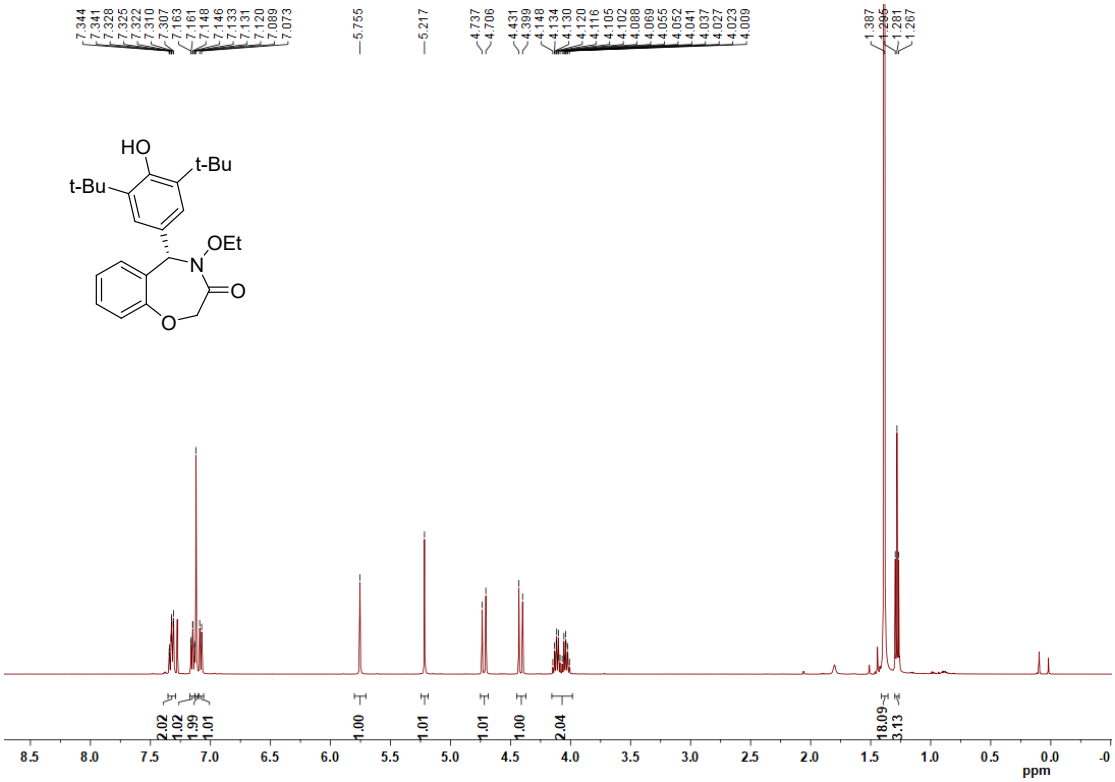
^{1}H NMR of compound 4m (500 MHz in $CDCl_3$)



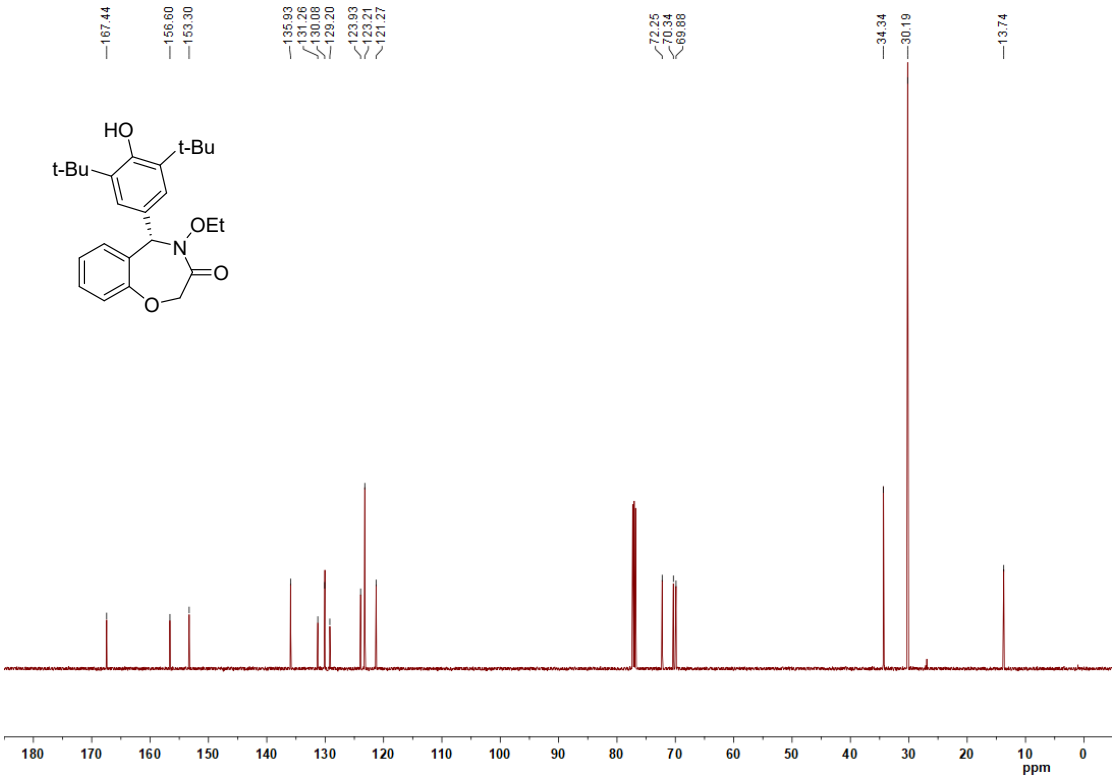
^{13}C NMR of compound 4m (125 MHz in $CDCl_3$)



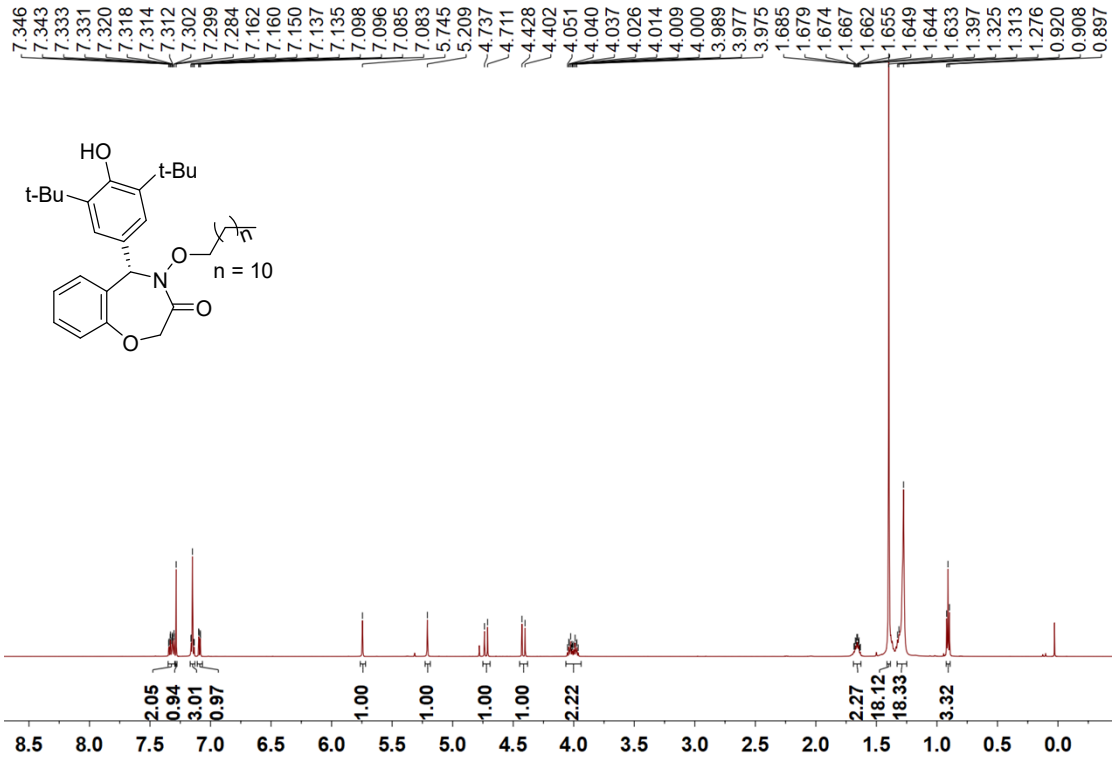
^{1}H NMR of compound 4n (500 MHz in $CDCl_3$)



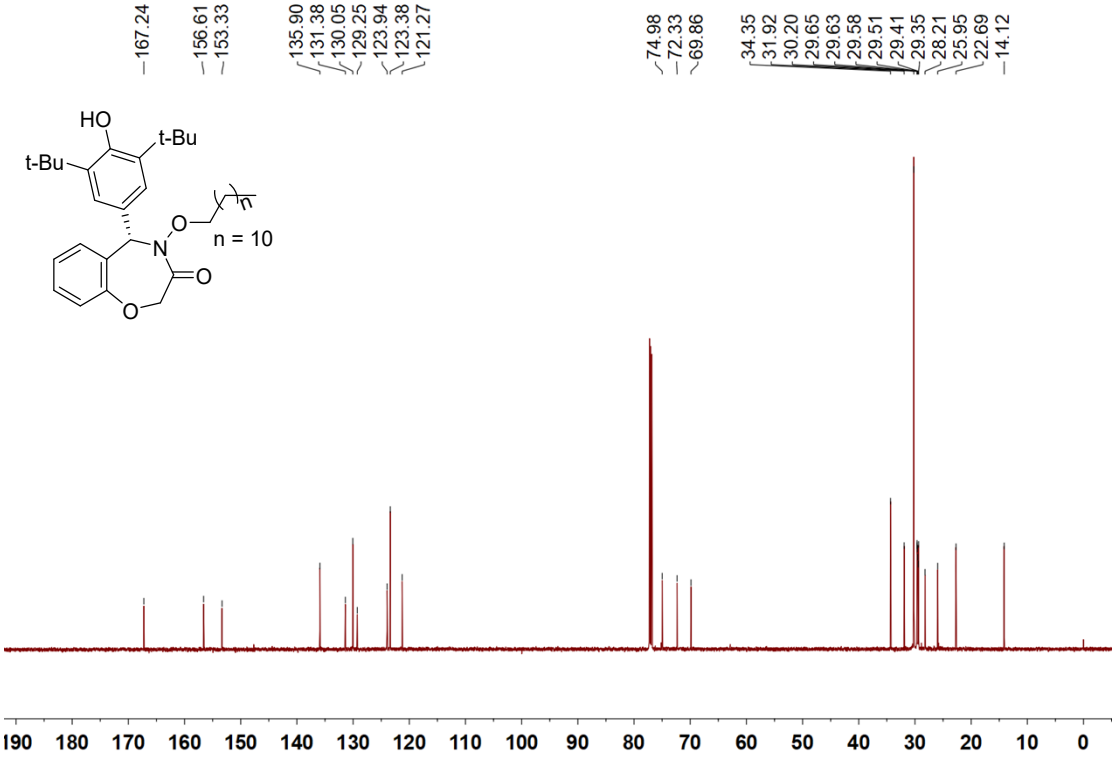
^{13}C NMR of compound 4n (125 MHz in $CDCl_3$)



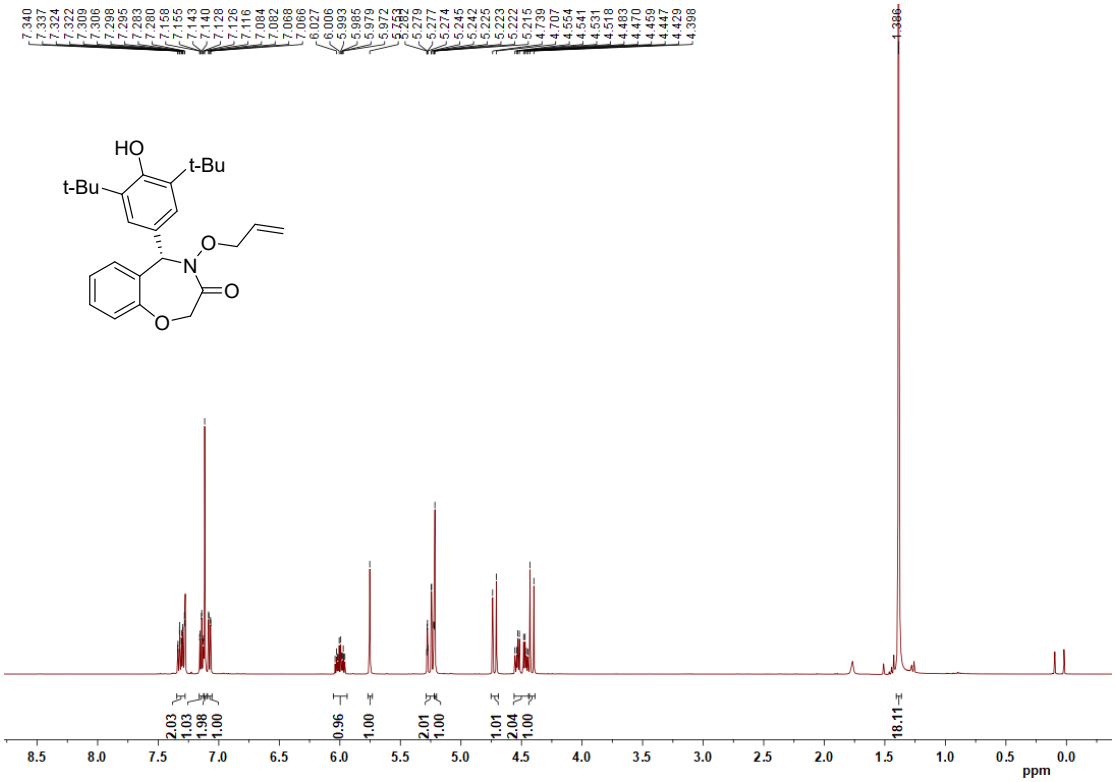
^{1}H NMR of compound 4o (600 MHz in $CDCl_3$)



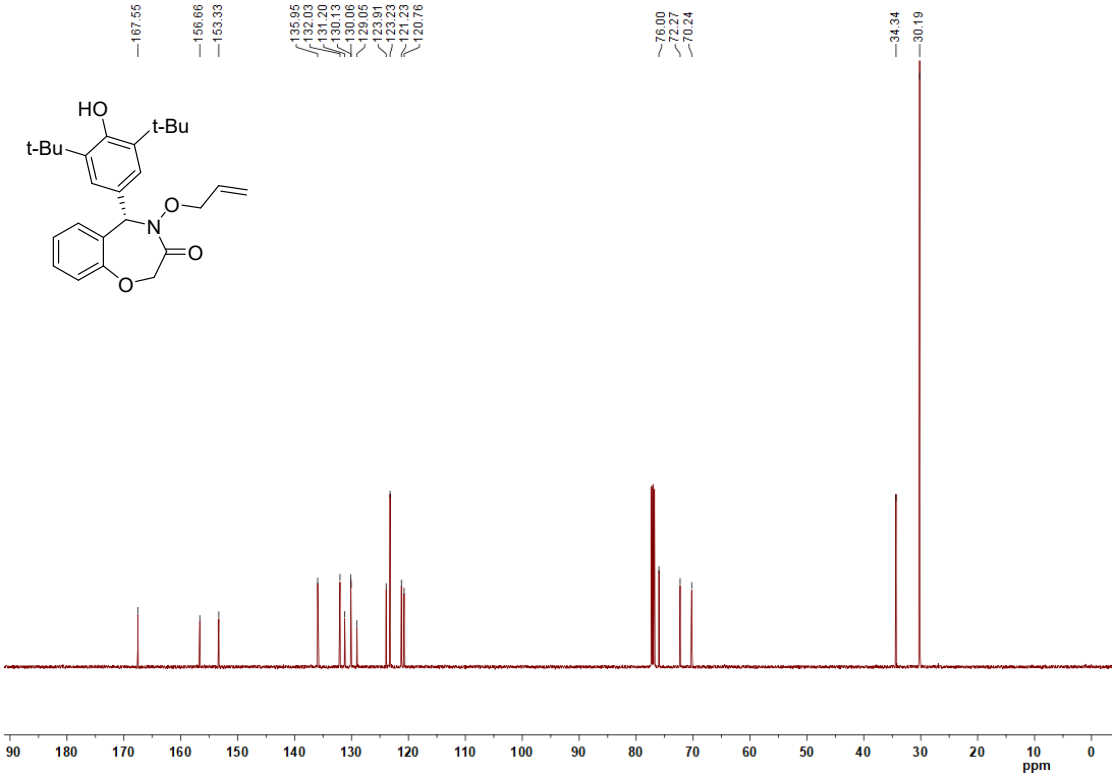
^{13}C NMR of compound 4o (150 MHz in $CDCl_3$)



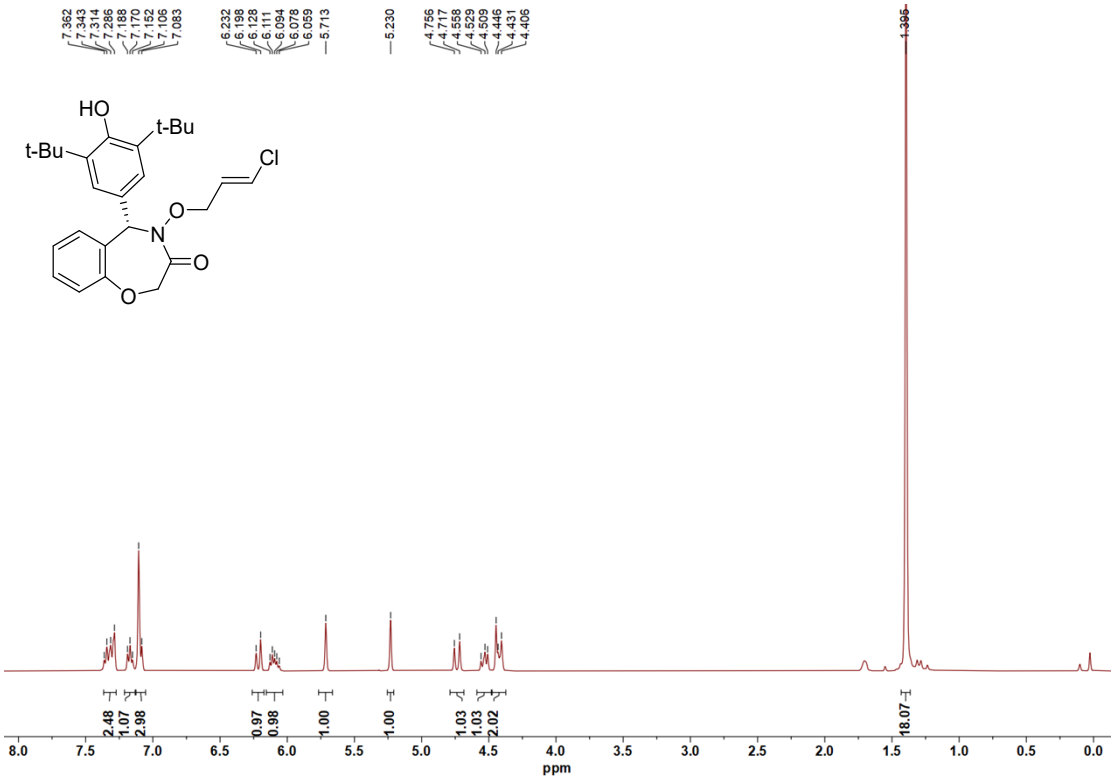
^{1}H NMR of compound 4p (600 MHz in $CDCl_3$)



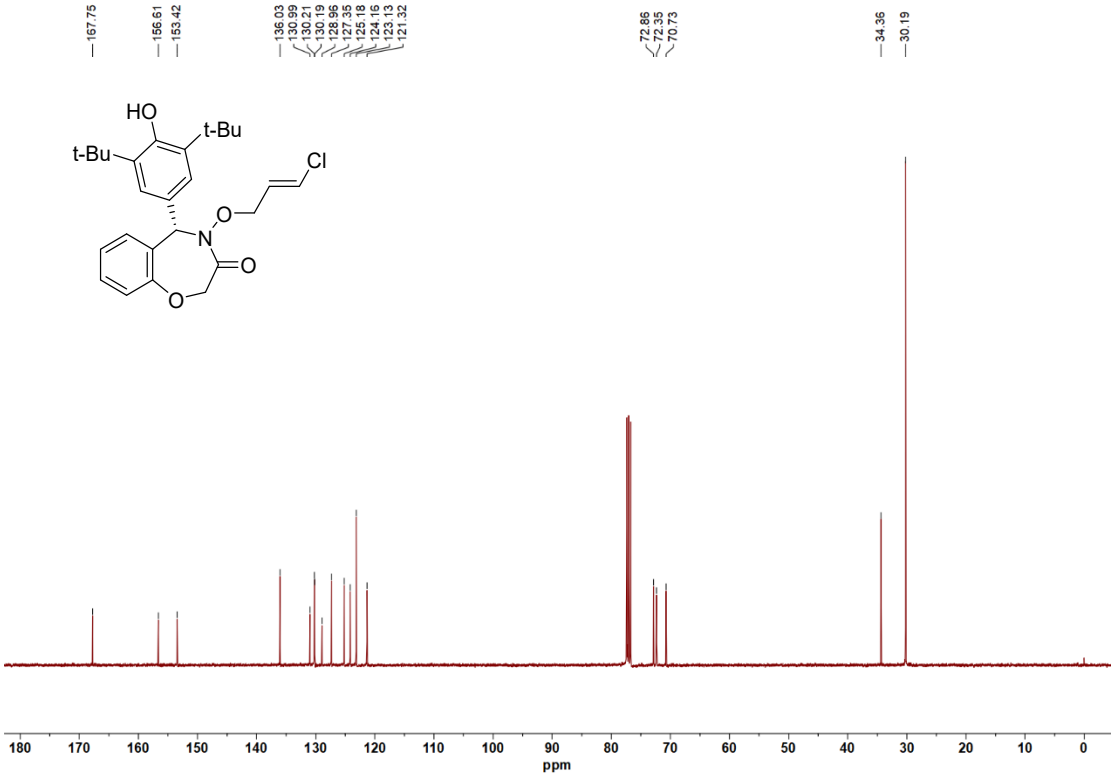
^{13}C NMR of compound 4p (150 MHz in $CDCl_3$)



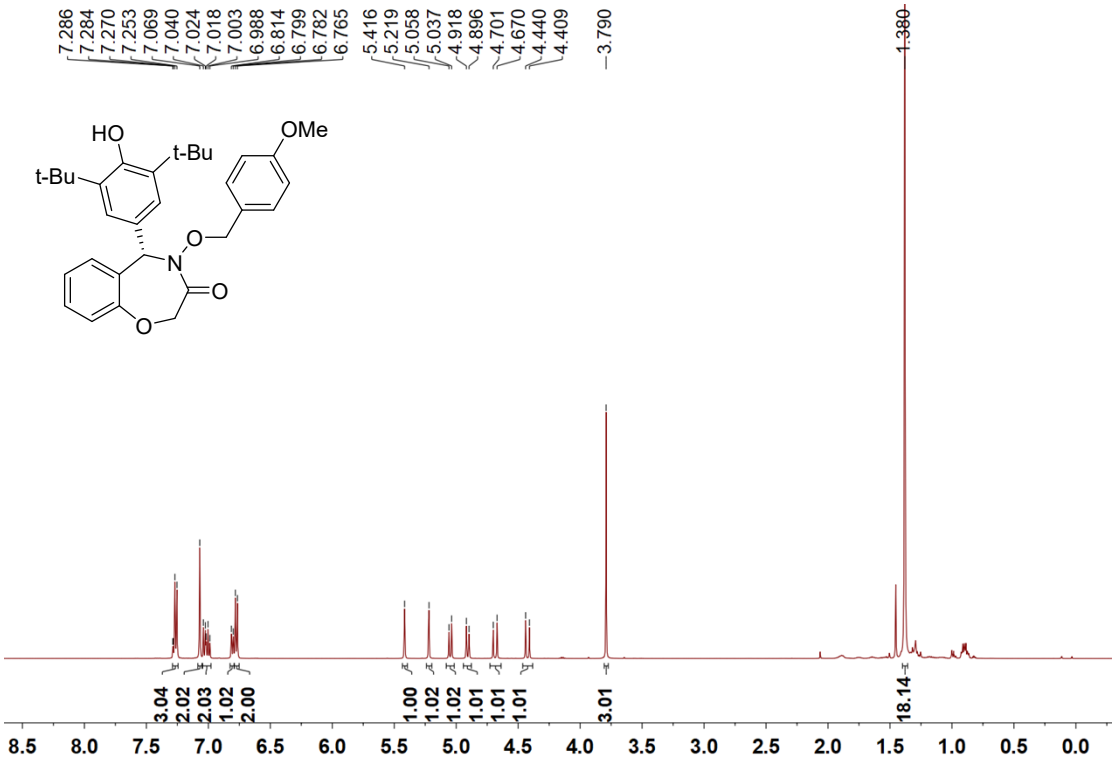
^{1}H NMR of compound 4q (400 MHz in $CDCl_3$)



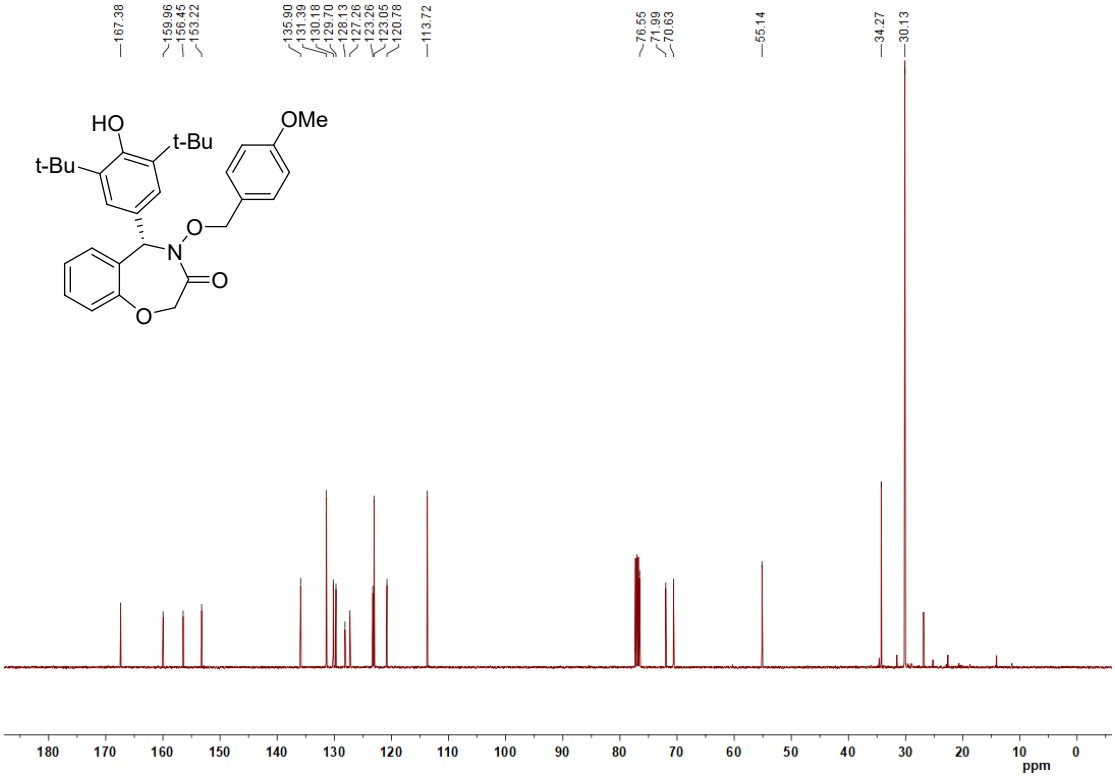
^{13}C NMR of compound 4q (100 MHz in $CDCl_3$)



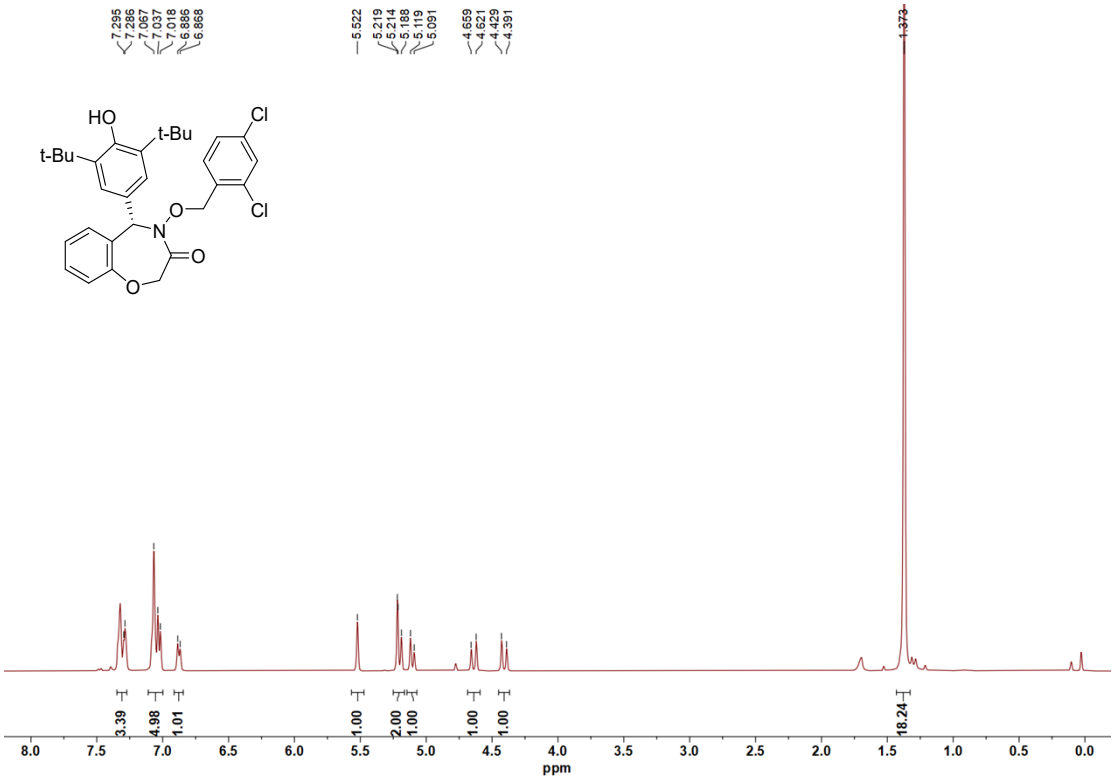
^{1}H NMR of compound 4r (500 MHz in $CDCl_3$)



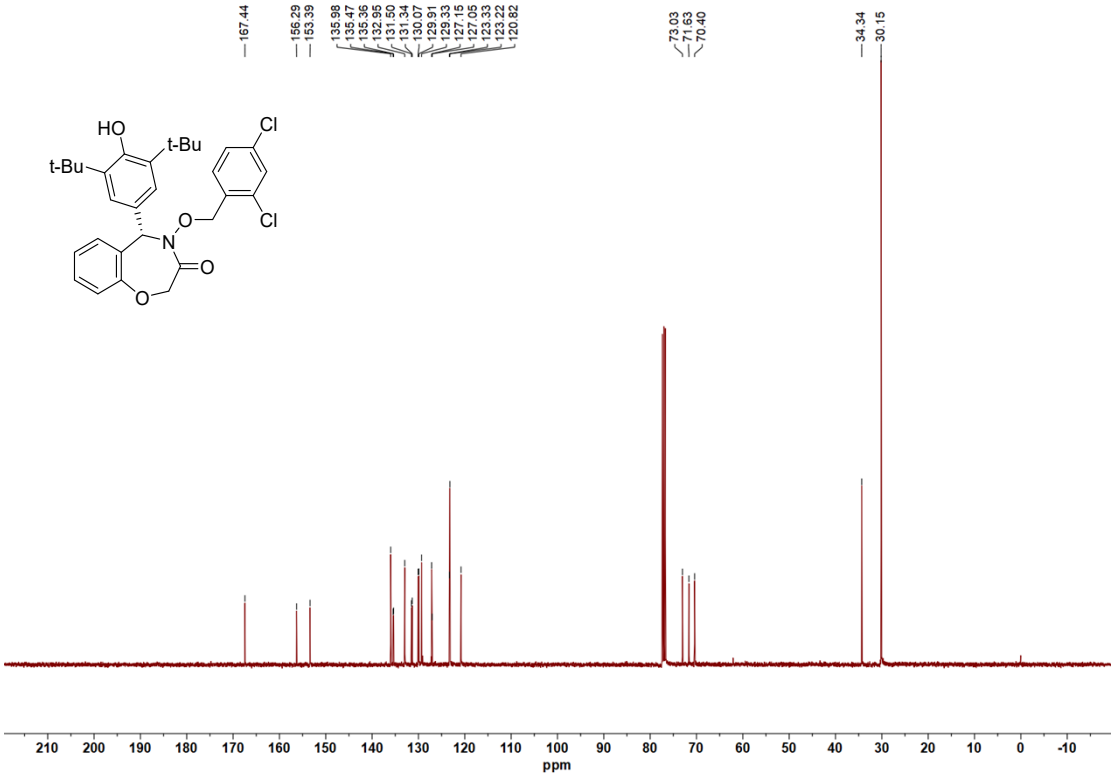
^{13}C NMR of compound 4r (125 MHz in $CDCl_3$)



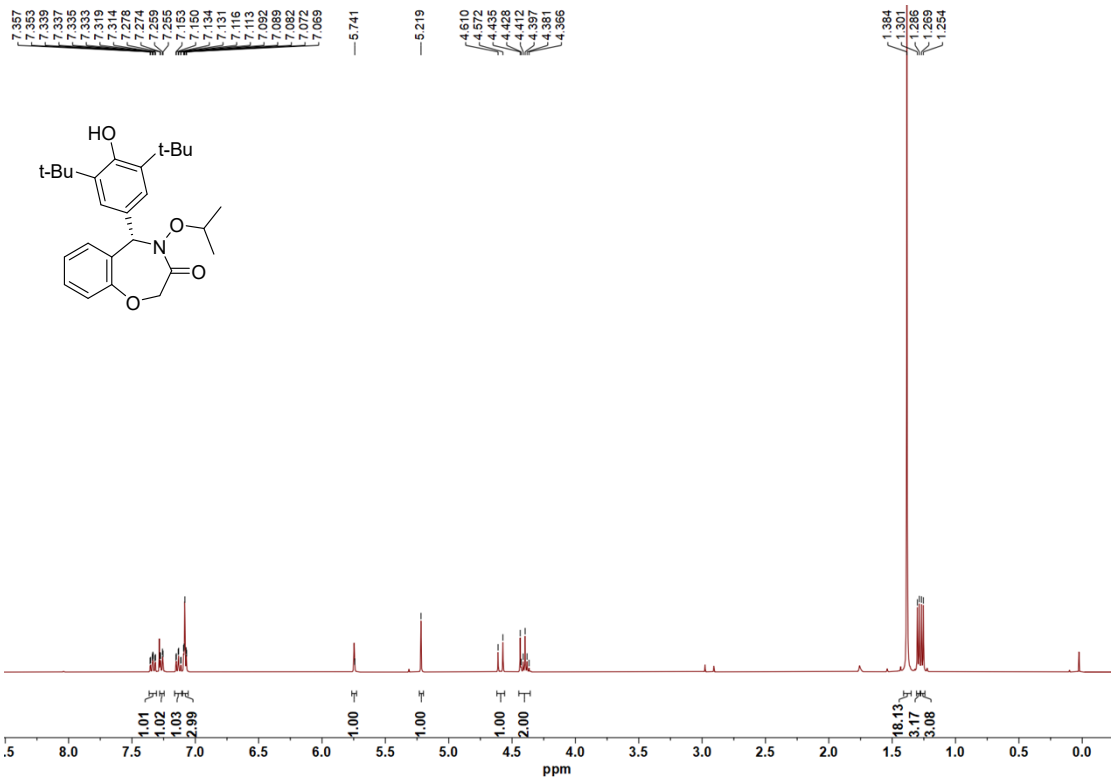
^{1}H NMR of compound 4s (400 MHz in $CDCl_3$)



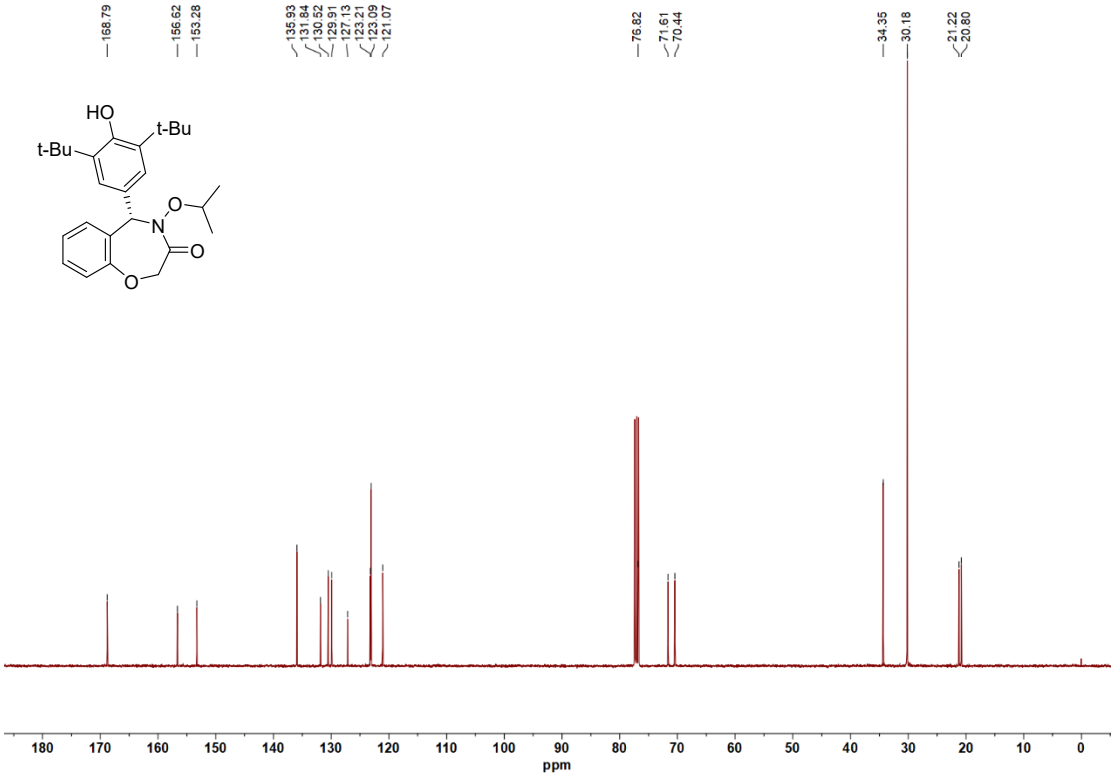
^{13}C NMR of compound 4s (100 MHz in $CDCl_3$)



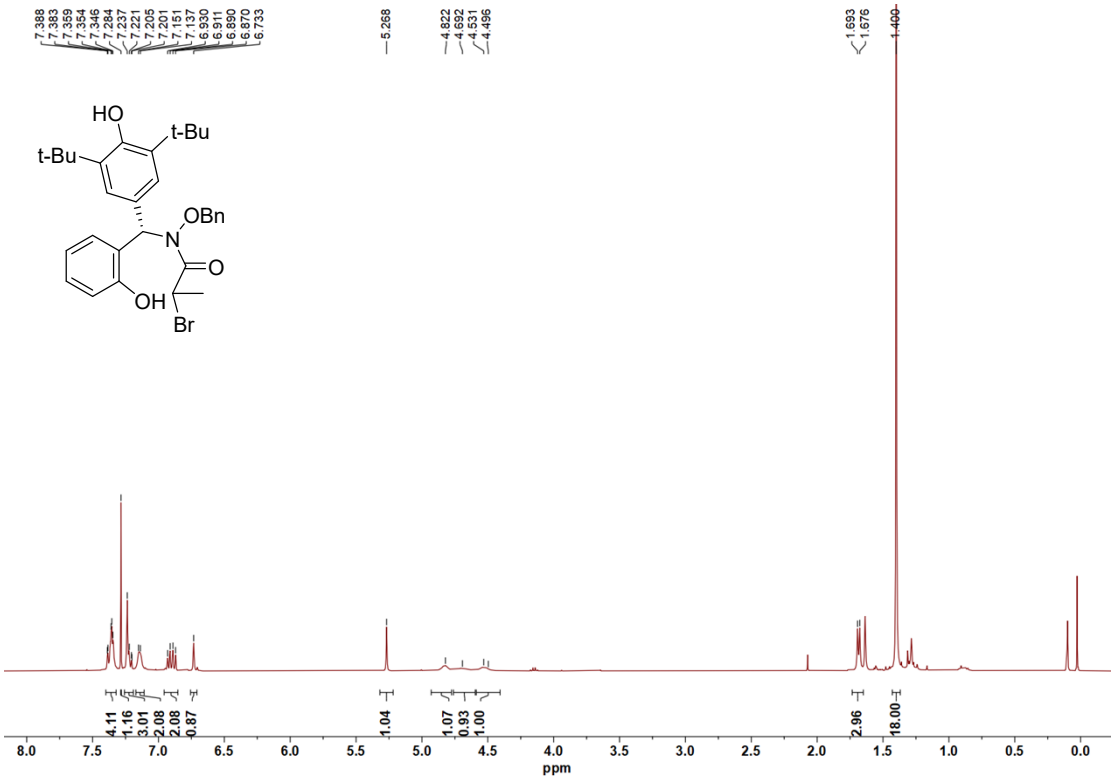
^{1}H NMR of compound 4t (400 MHz in $CDCl_3$)



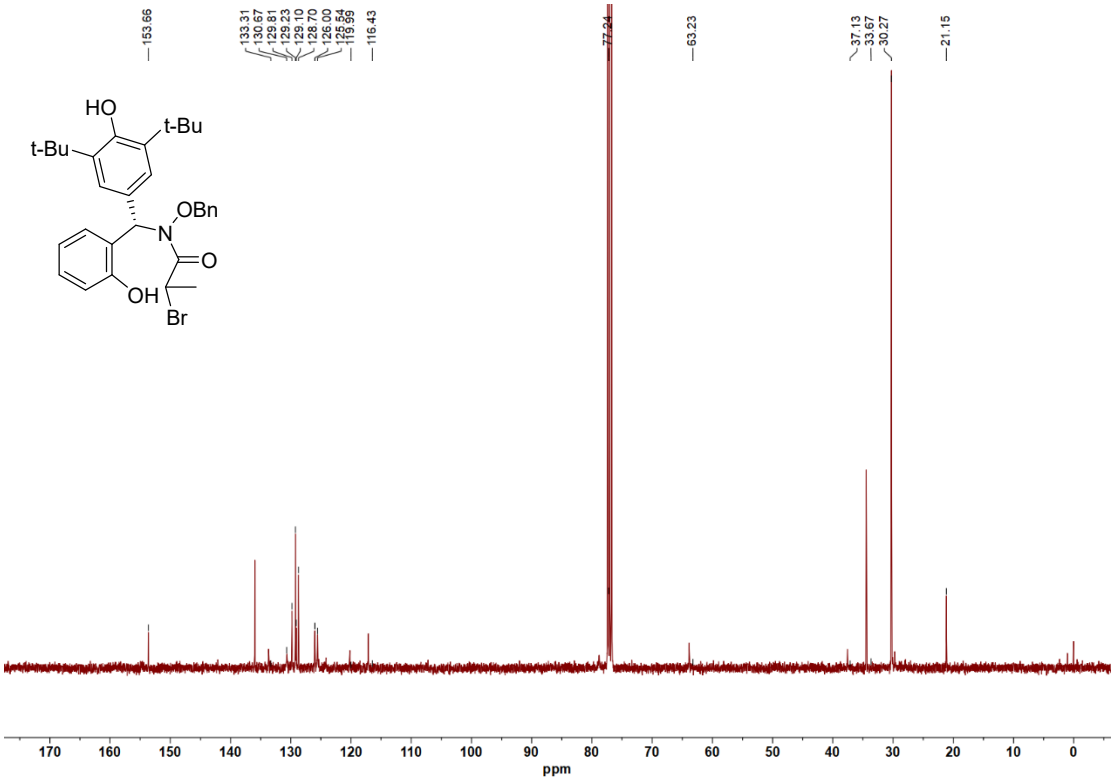
^{13}C NMR of compound 4t (100 MHz in $CDCl_3$)



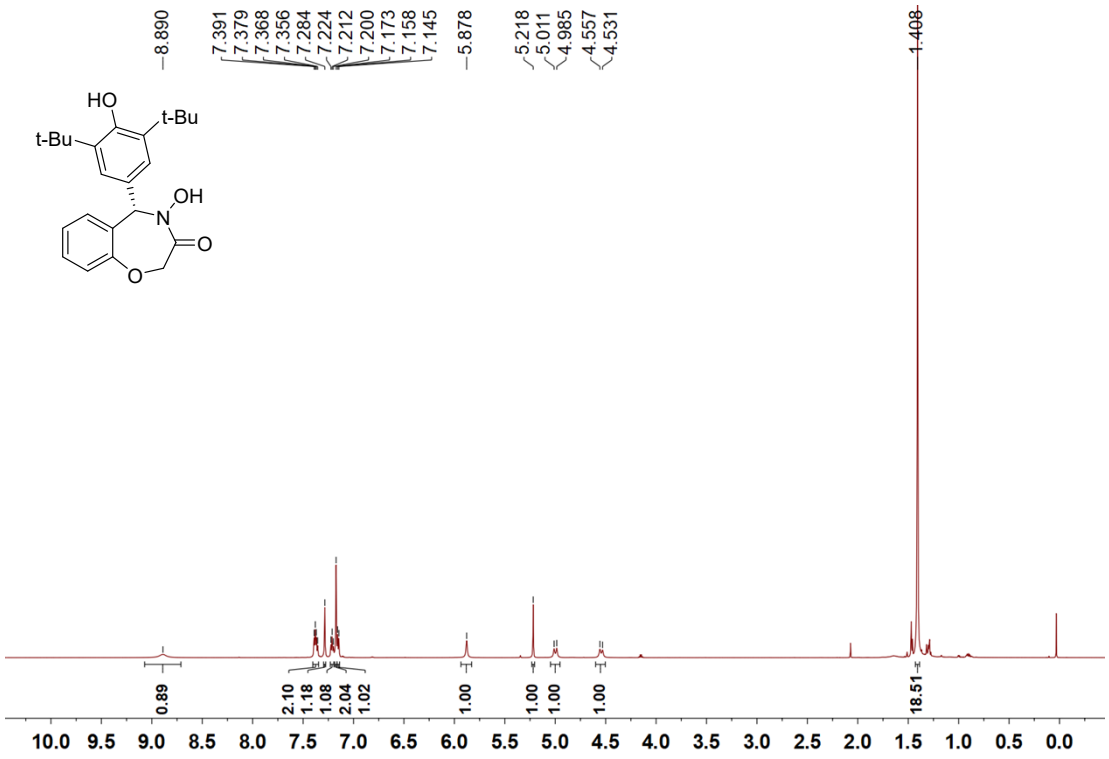
^{1}H NMR of compound 3u (400 MHz in $CDCl_3$)



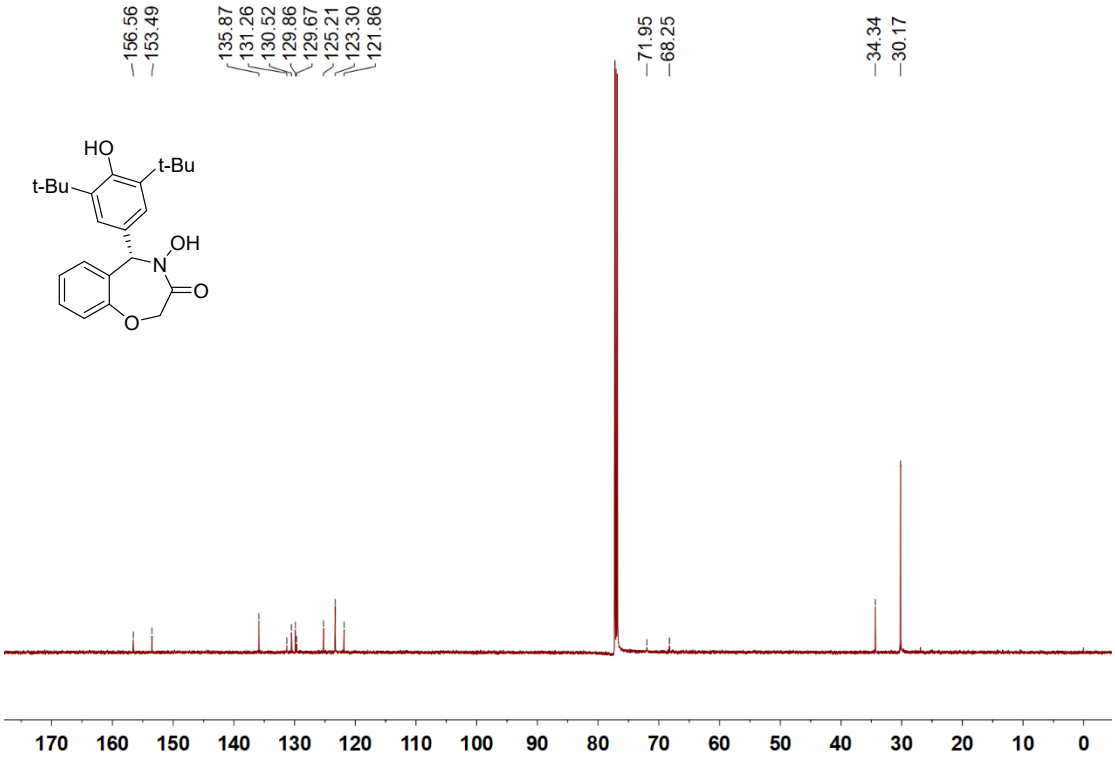
^{13}C NMR of compound 3u (100 MHz in $CDCl_3$)



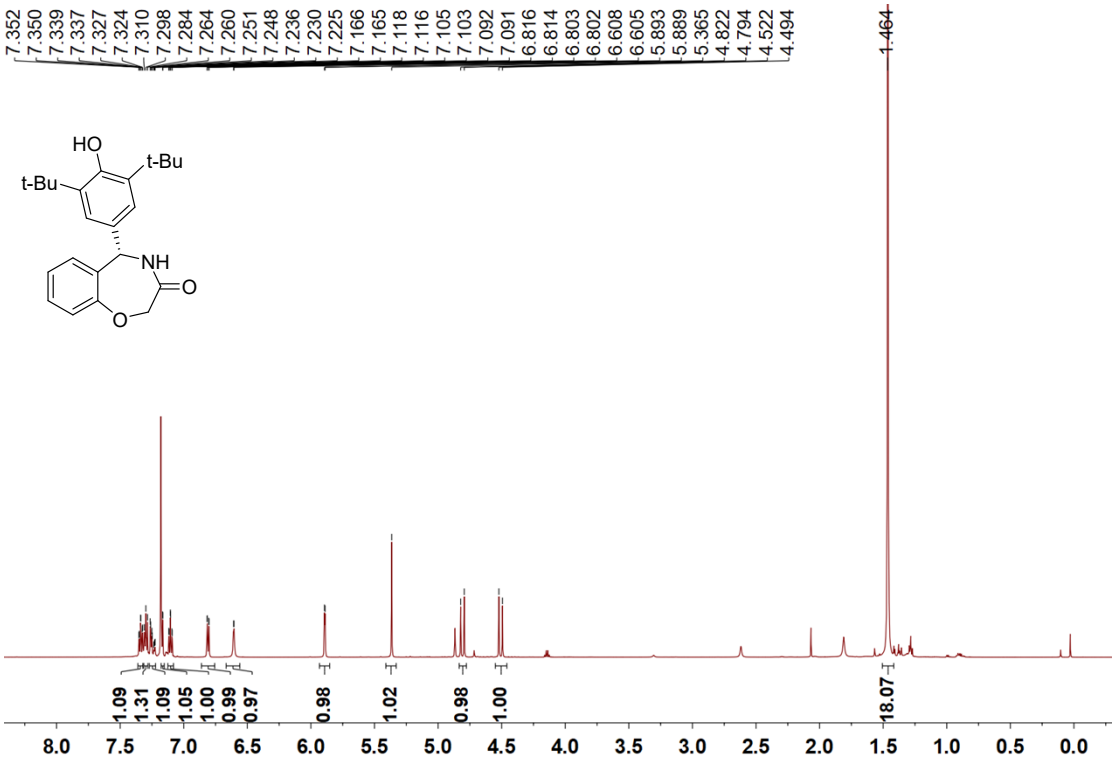
^{1}H NMR of compound 5 (600 MHz in $CDCl_3$)



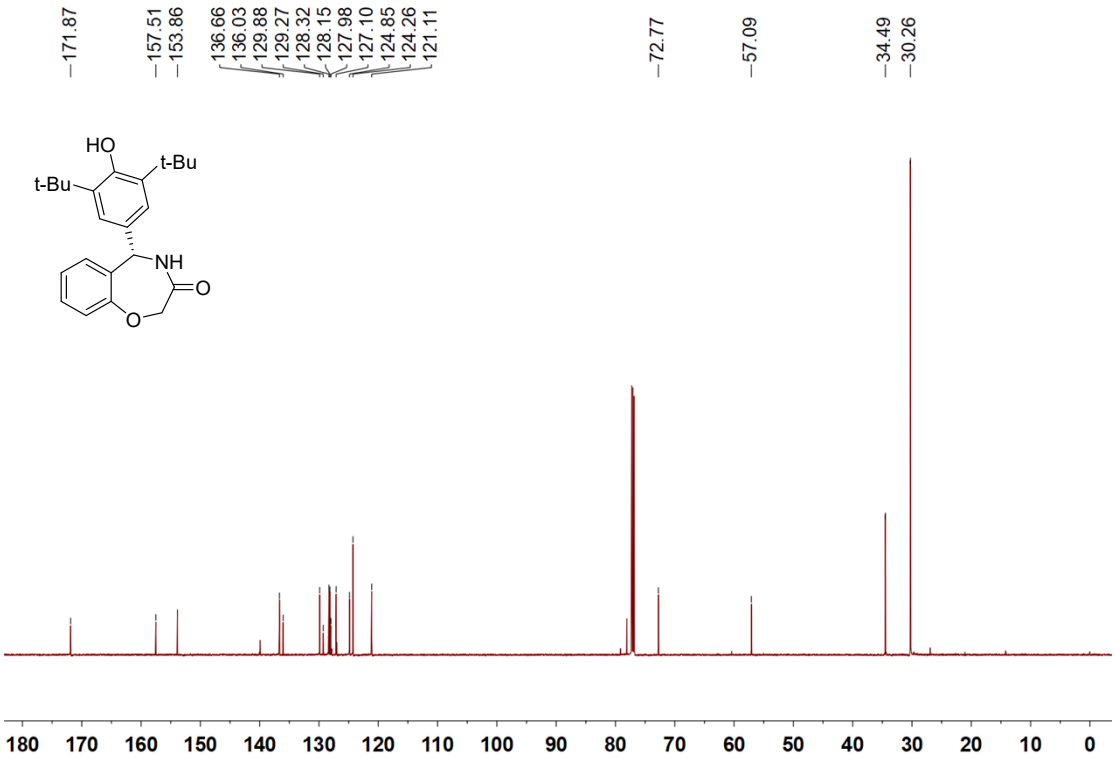
^{13}C NMR of compound 5 (150 MHz in $CDCl_3$)



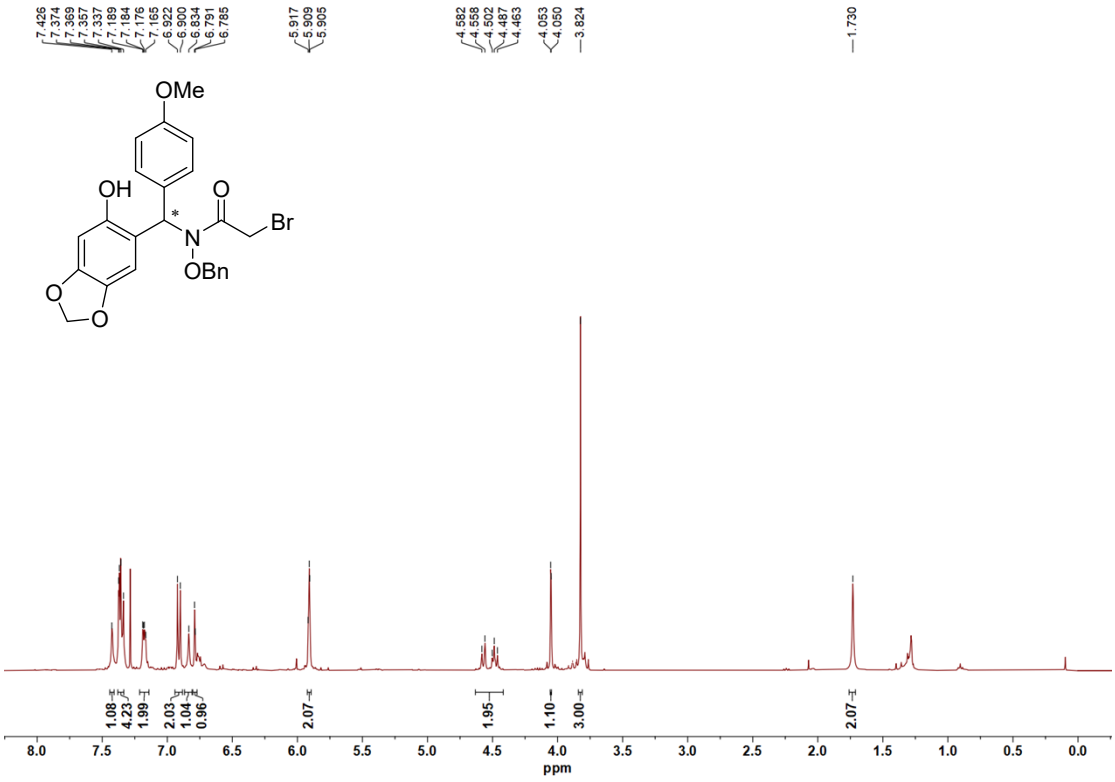
^{1}H NMR of compound 6 (600 MHz in $CDCl_3$)



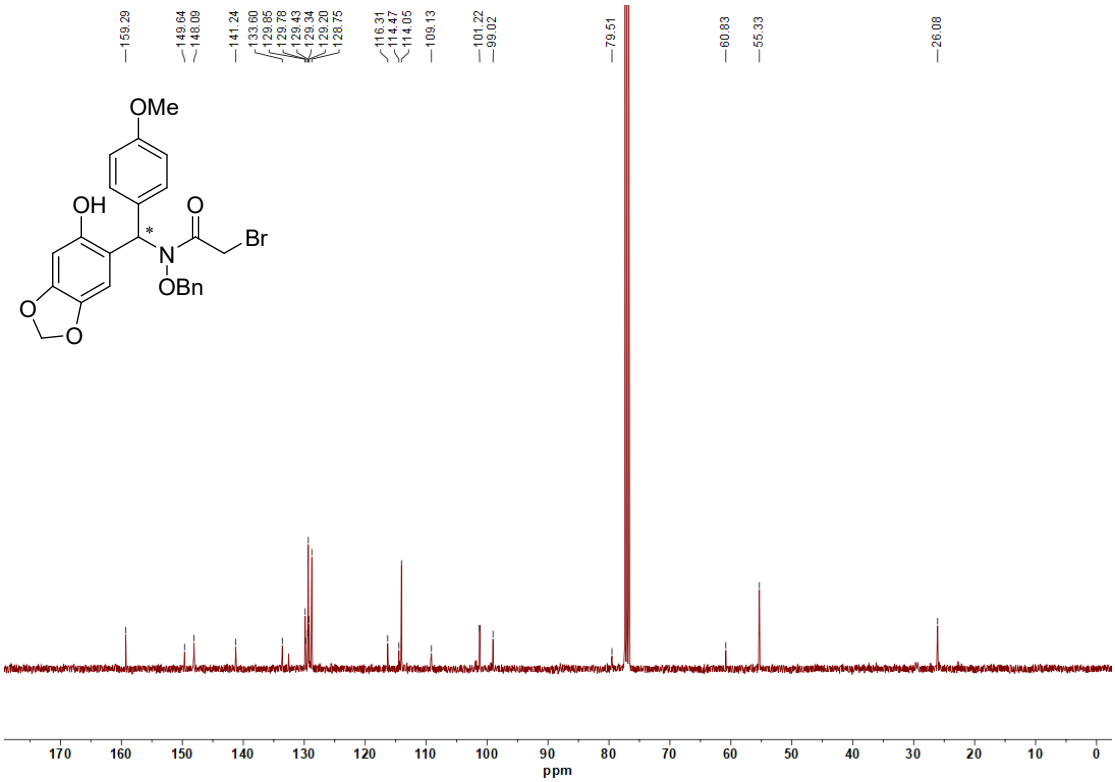
^{13}C NMR of compound 6 (150 MHz in $CDCl_3$)



^{1}H NMR of compound 8a (400 MHz in $CDCl_3$)

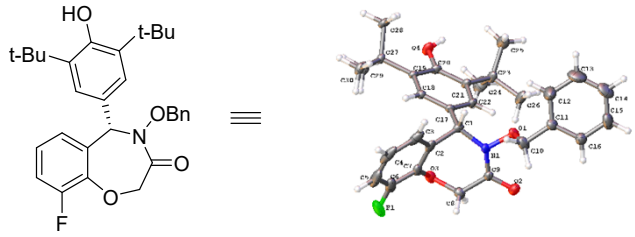


^{13}C NMR of compound 8a (100 MHz in $CDCl_3$)



9. Crystal data and structure refinement for enantiopure 4i.

Crystals of enantiopure **4i** suitable for X-ray analysis were obtained from crystallization in a solution of CH_2Cl_2 and n-hexan



CCDC deposition number	2226867	
Empirical formula	C_{30} H_{34} F N O_4	
Formula weight	491.60	
Temperature	213.00 K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 10.13420(10) Å	α= 90°.
	b = 10.9767(2) Å	β= 90°.
	c = 27.3919(4) Å	γ = 90°.
Volume	3047.08(8) $Å^3$	
Z	4	
Density (calculated)	1.257 Mg/m^3	
Absorption coefficient	1.486 mm^{-1}	
F(000)	1216	
Crystal size	0.1 x 0.07 x 0.07 mm^3	
Theta range for data collection	3.774 to 54.997°.	
Index ranges	-12<=h<=9, -13<=k<=13, -33<=l<=33	
Reflections collected	32680	
Independent reflections	5782 [R(int) = 0.0460]	
Completeness to theta = 25.242°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.5934	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5782 / 1 / 362	
Goodness-of-fit on F^2	1.064	
Final R indices [I>2sigma(I)]	R1 = 0.0754, wR2 = 0.2166	
R indices (all data)	R1 = 0.0910, wR2 = 0.2322	
Absolute structure parameter	0.032(11)	
Extinction coefficient	n/a	

Largest diff. peak and hole	1.123 and -0.939 e.Å^{-3}