Chiral amine-urea mediated asymmetric inverse-electron-demand cycloadditions of cyclic nitrones with *o*-hydroxystyrenes

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Experimental section

General.

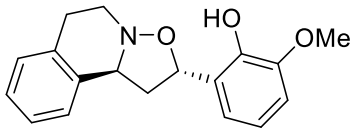
Melting points were determined on a Yanaco MP-13 melting point apparatus and are uncorrected. CD spectra were recorded on a Jasco J-1500 circular dichroism spectrophotometer. IR spectra were recorded on a JASCO FT/IR-4200 spectrophotometer and are reported in wavenumbers (cm^{-1}). ^{1}H NMR spectra were recorded on a BRUKER AVANCE III Fourier 300 (300 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. $^{13}C\{^{1}H\}$ NMR spectra were recorded on a BRUKER AVANCE III Fourier 300 (75 MHz) spectrometer using broadband proton decoupling. Chemical shifts are expressed in parts per million using the middle resonance of $CDCl_3$ (77.0 ppm) as an internal standard. Hydrogen multiplicity (C, CH, CH_2, CH_3) information was obtained from carbon DEPT spectra. High-resolution mass spectra were obtained on BRUKER micrOTOF II ESI-TOF spectrometer. Optical rotations were recorded with a JASCO P-1010 polarimeter. X-ray diffraction data were collected at 93 K using a Bruker SMART APEX2 diffractometer [Mo Kα radiation (λ = 0.71073 Å)]. Thin-layer chromatography (TLC) was performed using TLC aluminum sheets from Merck (silica gel 60 F254, 200 μm), and flash chromatography was performed using silica gel from Fuji Silysia Chemical (PSQ60B, 60 μm). Products were visualized by ultraviolet (UV) light and TLC stains. High performance liquid chromatography (HPLC) was performed using Daicel chiral columns (4.6 mm × 250 mm). Unless otherwise noted, all reactions were carried out under an argon atmosphere in dried glassware.

Materials.

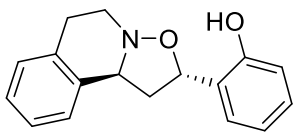
All reagents and solvents were commercial grade and purified prior to use, when necessary, except for the following. 3,4-Dihydroisoquinoline *N*-oxide, 2,3,4,5-tetrahydropyridine *N*-oxide, and 1-pyrroline *N*-oxide were prepared by the procedure reported previously.[1] Hydroxystyrenes[2] and amine-urea **2**[3] were prepared according to the reported procedure. Toluene was purified by distillation first from $CaCl_2$ and then from a sodium benzophenone still under argon.

General procedure A for the asymmetric cycloaddition reactions was exemplified by the reaction of nitrone 1a with 2-hydroxy-3-methoxystyrene in the presence of amine-urea 2.

A solution of nitrone **1a** (29.4 mg, 0.20 mmol) in toluene (0.5 mL) was added to 2-hydroxy-3-methoxystyrene (60.1 mg, 0.40 mmol, 2.0 equiv) and amine-urea **2** (115.7 mg, 0.20 mmol, 100 mol%), and then the mixture was stirred at 35 °C for 12 h. The reaction mixture was filtered through a plug of silica gel (0.8 g) with CH_2Cl_2 (20 mL) as an eluent. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (silica gel 6 g, Hexane:EtOAc = 80:20, v/v) to provide isoxazolidine **3b** (53.6 mg, 90%, 89% ee) as colorless powder.

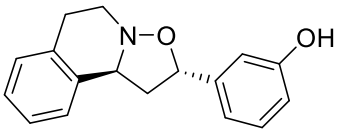


2-Methoxy-6-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3b): Mp 125-126 °C; R_f = 0.21 (Hexane:EtOAc = 75:25, v/v); $[\alpha]_D^{23}$ -81.9 (c 0.71, CHCl3 for 94% ee); IR (KBr) 3495, 2937, 1612, 1480, 1353, 1276, 1082, 1008, 855, 737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.14 (br s, 1H), 7.25-7.09 (m, 4H), 6.84 (dd, *J* = 7.6, 2.4 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.72 (dd, *J* = 7.6, 2.4 Hz, 1H), 5.21 (dd, *J* = 7.7, 6.8 Hz, 1H), 4.80 (t, *J* = 6.0 Hz, 1H), 3.89 (s, 3H), 3.65 (dt, *J* = 12.7, 4.5 Hz, 1H), 3.39-3.14 (m, 2H), 3.00-2.85 (m, 2H), 2.71 (dt, *J* = 16.2, 4.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.5 (C), 144.0 (C), 135.1 (C), 133.2 (C), 128.5 (CH), 128.3 (C), 127.0 (CH), 126.73 (CH), 126.65 (CH), 120.2 (CH), 118.6 (CH), 111.2 (CH), 77.6 (CH), 61.7 (CH), 56.0 (CH_3), 47.2 (CH_2), 44.2 (CH_2), 23.8 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{19}NNaO_3$ $[M+Na]^+$ 320.1257, found 320.1257. The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-3, Hexane:^{i}PrOH = 30:70, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C): t_{minor} = 16.4 min, t_{major} = 24.5 min.



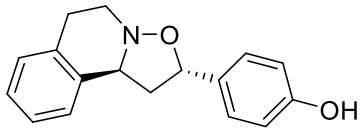
2-((2*S*,10b*S*)-1,5,6,10b-Tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3a): Isolated as colorless powder (50.4 mg, 94%, 81% ee) after silica gel column chromatography (6 g, Hexane:EtOAc

= 91:9, v/v) following the general procedure **A** using 2-hydroxystyrene (48.1 mg, 0.40 mmol, 2.0 equiv) at 35 °C for 24 h. Mp 126-127 °C; R_f = 0.35 (Hexane:EtOAc = 75:25, v/v); $[\alpha]_D^{19}$ -88.1 (*c* 0.97, $CHCl_3$ for 81% ee); IR (KBr) 3430, 2926, 1602, 1461, 1361, 1287, 1240, 1119, 912, 749, 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.02 (br s, 1H), 7.31-7.09 (m, 5H), 6.95 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.91 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.74 (td, *J* = 7.5, 1.1 Hz, 1H), 5.03 (dd, *J* = 8.9, 6.1 Hz, 1H), 4.82 (d, *J* = 7.2 Hz, 1H), 3.86-3.71 (m, 1H), 3.40-3.25 (m, 2H), 3.07-2.89 (m, 2H), 2.66-2.50 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 155.1 (C), 134.8 (C), 133.3 (C), 129.7 (CH), 128.7 (CH), 128.6 (CH), 127.7 (C), 126.89 (CH), 126.86 (CH), 126.7 (CH), 118.6 (CH), 117.9 (CH), 79.0 (CH), 61.6 (CH), 46.9 (CH_2), 44.2 (CH_2), 22.2 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}NNaO_2$ $[M+Na]^+$ 290.1151, found 290.1139. The enantiomeric excess of was determined by HPLC analysis (Chiralcel OD-3, Hexane:^{i}PrOH = 30:70, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C): t_{minor} = 9.9 min, t_{major} = 13.5 min.

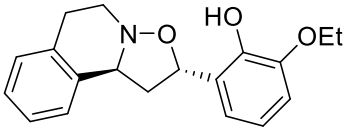


3-((2*S*,10b*S*)-1,5,6,10b-Tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (4): Isolated as colorless powder (32.3 mg, 60%, 21% ee) after silica gel column chromatography (8 g, Hexane:EtOAc = 80:20, v/v) following the general procedure **A** using 3-hydroxystyrene (48.9 mg, containing 2%wt EtOAc, 0.40 mmol, 2.0 equiv) at 50 °C for 48 h. Mp 144-147 °C; R_f = 0.10 (Hexane:EtOAc = 80:20, v/v); $[\alpha]_D^{28}$ +8.0 (*c* 0.50, $CHCl_3$ for 21% ee); IR (KBr) 3406, 3069, 2940, 2889, 2831, 2693, 2622, 2568, 1602, 1490, 1459, 1391, 1357, 1291, 1244, 1180, 1119, 998, 879, 768, 749, 723, 701, 673, 629, 460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22-7.11 (m, 5H), 7.08-6.99 (m, 1H), 6.82-6.72 (m, 2H), 5.33 (dd, *J* = 8.3, 6.0 Hz, 1H), 4.80 (t, *J* = 8.3 Hz, 1H,), 3.41 (dt, *J* = 10.2, 4.3 Hz, 1H), 3.36-3.24 (m, 1H), 3.15 (ddd, *J* = 16.0, 10.4, 4.5 Hz, 1H), 2.99-2.88 (m, 1H), 2.82-2.61 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 157.2 (C), 142.7 (C), 135.2 (C), 133.0 (C), 129.6 (CH), 128.3 (CH), 127.3 (CH), 126.8 (CH), 126.5 (CH), 118.1 (CH), 115.3 (CH), 112.6 (CH), 78.9 (CH), 62.6 (CH), 48.2 (CH_2), 45.5 (CH_2), 28.0 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{18}NO_2$ $[M+H]^+$ 268.1332, found 268.1324. The enantiomeric

excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 70:30, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C): t_{major} = 23.5 min, t_{minor} = 42.9 min.

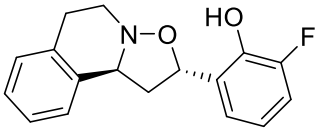


4-((2*S*,10b*S*)-1,5,6,10b-Tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (5): Isolated as colorless powder (28.7 mg, 54%, *exo*:*endo* = 92:8, 3% ee (*exo*), 3% ee (*endo*)) after silica gel column chromatography (8 g, Hexane:EtOAc = 80:20, v/v) following the general procedure **A** using 4-hydroxystyrene (48.1 mg, 0.40 mmol, 2.0 equiv) at 50 °C for 48 h. Mp 155-157 °C; R_f = 0.13 (Hexane:EtOAc = 80:20, v/v); $[\alpha]_D^{21}$ +1.1 (*c* 0.50, $CHCl_3$ for *exo*:*endo* = 92:8, 3% ee (*exo*), 3% ee (*endo*)); IR (KBr) 3062, 3020, 2947, 2844, 1612, 1516, 1492, 1455, 1427, 1358, 1270, 1236, 1204, 1170, 835, 769, 741, 719, 623 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.22 (m, 2H), 7.22-7.05 (m, 4H), 6.87-6.80 (m, 2H), 6.55 (br s, 1H), 5.28 (dd, *J* = 8.2, 5.9 Hz, 1H), 4.81 (t, *J* = 8.2 Hz, 1H), 3.41-3.23 (m, 2H), 3.07 (ddd, *J* = 16.3, 9.4, 5.0 Hz, 1H) , 2.94 (dt, *J* = 16.3, 4.0 Hz, 1H), 2.72 (dt, *J* = 12.5, 8.2 Hz, 1H), 2.66 (ddd, *J* =12.5, 8.2, 5.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 155.9 (C), 135.5 (C), 133.3 (C), 132.9 (C), 128.3 (CH), 127.9 (CH), 127.3 (CH), 126.7 (CH), 126.5 (CH), 115.6 (CH), 79.0 (CH), 62.9 (CH), 48.4 (CH_2), 45.3 (CH_2), 27.9 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{18}NO_2$ $[M+H]^+$ 268.1332, found 268.1322. The enantiomeric excess was determined by HPLC analysis (Chiralcel OZ-3, Hexane:EtOH = 95:5, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 59.1 min (*exo*), t_{minor} = 64.5 min (*exo*), t_{minor} = 100.8 min (*endo*), t_{major} = 111.6 min (*endo*).



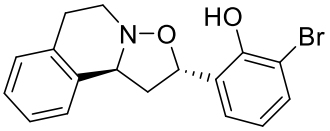
2-Ethoxy-6-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3c): Isolated as white powder (43.7 mg, 70%, 84% ee) after silica gel column chromatography (15 g, Hexane:EtOAc = 83:17, v/v) following the general procedure **A** using 3-ethoxy-2-hydroxystyrene (65.7 mg, 0.40 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 48-49 °C; R_f = 0.15 (Hexane:EtOAc = 83:17, v/v);

$[\alpha]_D^{25}$ -53.1 (*c* 1.0, $CHCl_3$ for 84% ee); IR (KBr) 2976, 2855, 1607, 1581, 1472, 1454, 1427, 1387, 1343, 1300, 1268, 1241, 1168, 1114, 1090, 1060, 1002, 911, 893, 837, 822, 782, 770, 739, 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.85 (br s, 1H), 7.24-7.07 (m, 4H), 6.87-6.79 (m, 1H), 6.78-6.70 (m, 2H), 5.23 (t, *J* = 6.9 Hz, 1H), 4.79 (t, *J* = 6.1 Hz, 1H), 4.10 (q, *J* = 7.0 Hz, 2H), 3.63 (dt, *J* = 12.8, 4.8 Hz, 1H), 3.32 (ddd, *J* = 12.8, 9.5, 4.8 Hz, 1H), 3.19 (ddd, *J* = 16.1, 9.5, 4.8 Hz, 1H), 2.99-2.84, (m, 2H), 2.73 (dt, *J* = 16.1, 4.8 Hz, 1H), 1.48 (t, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 147.6 (C), 144.0 (C), 135.2 (C), 133.3 (C), 128.5 (CH), 128.4 (C), 127.1 (CH), 126.7 (CH), 126.6 (CH), 120.0 (CH), 118.6 (CH), 112.2 (CH), 77.4 (CH), 64.3 (CH_2), 61.7 (CH), 47.3 (CH_2), 44.1 (CH_2), 24.1 (CH_2), 14.9 (CH_3); HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{21}NNaO_3$ $[M+Na]^+$ 334.1414, found 334.1437. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 12.4 min, t_{minor} = 20.2 min.

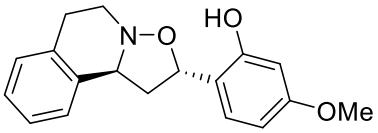


2-Fluoro-6-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3d): Isolated as white powder (51.2 mg, 90%, 86% ee) after silica gel column chromatography (15 g, Hexane:EtOAc = 83:17, v/v) following the general procedure **A** using 3-fluoro-2-hydroxystyrene (55.2 mg, containing 1wt% EtOAc and Et_2O, 0.40 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 177-178 °C; R_f = 0.21 (Hexane:EtOAc = 83:17, v/v); $[\alpha]_D^{24}$ -90.9 (*c* 1.0, $CHCl_3$ for 86% ee); IR (KBr) 2961, 2920, 2900, 2874, 2675, 1615, 1474, 1453, 1430, 1333, 1295, 1279, 1257, 1221, 1157, 1066, 999, 906, 896, 879, 859, 769, 756, 747, 734, 628 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.82 (br s, 1H), 7.32-7.18 (m, 2H), 7.18-7.10 (m, 2H), 7.07-6.98 (m, 1H), 6.74-6.61 (m, 2H), 5.07 (t, *J* = 7.0 Hz, 1H), 4.85 (dd, *J* = 6.7, 2.7 Hz, 1H), 3.90-3.74 (m, 1H), 3.41-3.25 (m, 2H), 3.08-2.92 (m, 2H), 2.67-2.51 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.9 (d, *J* = 242.6 Hz, C), 143.5 (d, *J* = 12.7 Hz, C), 134.6 (C), 133.1 (C), 130.6 (d, *J* = 1.7 Hz, C), 128.7 (CH), 127.0 (CH), 126.9 (CH), 128.8 (CH), 123.5 (d, *J* = 2.8 Hz, CH), 118.0 (d, *J* = 7.2, Hz, CH), 116.1 (d, *J* = 18.7 Hz, CH), 78.4 (d, *J* = 2.8 Hz, CH), 61.4 (CH), 46.8 (CH_2), 44.3 (CH_2), 22.0 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ -136.5; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}FNO_2$

$[M+H]^+$ 286.1238, found 286.1244. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 13.4 min, t_{minor} = 16.5 min.

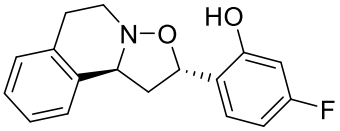


2-Bromo-6-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3e): Isolated as white powder (59.3 mg, 86%, 86% ee) after silica gel column chromatography (20 g, Hexane:EtOAc = 94:6, v/v) following the general procedure **A** using 3-bromo-2-hydroxystyrene (79.2 mg, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 59-60 °C; R_f = 0.22 (Hexane:EtOAc = 91:9, v/v); $[\alpha]_D^{25}$ -81.7 (*c* 1.0, $CHCl_3$ for 86% ee); IR (KBr) 3064, 2936, 2838, 2706, 2609, 1606, 1573, 1454, 1358, 1288, 1257, 1181, 1136, 992, 946, 911, 826, 745, 467 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 12.36 (br s, 1H), 7.47 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.30-7.18 (m, 2H), 7.18-7.10 (m, 2H), 6.89 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.63 (t, *J* = 7.9 Hz, 1H), 5.05 (dd, *J* = 7.8, 6.8 Hz, 1H), 4.84 (dd, *J* = 5.9, 3.8 Hz, 1H), 3.90-3.75 (m, 1H), 3.40-3.24 (m, 2H), 3.06-2.91 (m, 2H), 2.67-2.51 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 151.9 (C), 134.5 (C), 133.2 (CH), 133.1 (C), 129.4 (C), 128.7 (CH), 128.0 (CH), 127.0 (CH), 126.9 (CH×2), 119.4 (CH), 112.4 (C), 78.8 (CH), 61.3 (CH), 46.8 (CH_2), 44.1 (CH_2), 22.0 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}BrNO_2$ $[M+H]^+$ 346.0437, found 346.0426. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, detector: UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 7.4 min, t_{minor} = 8.8 min.



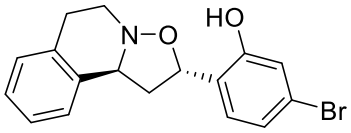
5-Methoxy-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3f): Isolated as white powder (40.5 mg, 68%, 86% ee) after silica gel column chromatography (15 g, CH_2Cl_2:Hexane = 10:1, v/v) following the general procedure **A** using 2-hydroxy-4-methoxystyrene (69.0 mg, containing 13wt% Toluene, 0.40 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 89-90 °C; R_f = 0.11

(CH_2Cl_2:Hexane = 91:9, v/v); $[\alpha]_D^{24}$ -82.4 (*c* 1.0, $CHCl_3$ for 86% ee); IR (KBr) 2997, 2957, 2934, 2909, 2833, 2620, 2578, 1623, 1582, 1511, 1442, 1402, 1313, 1275, 1171, 1155, 1110, 993, 902, 825, 753, 731, 694, 530 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.18 (br s, 1H), 7.31-7.09 (m, 4H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.52 (d, *J* = 2.6 Hz, 1H), 6.31 (dd, *J* = 8.3, 2.6 Hz, 1H), 4.99 (dd, *J* = 8.8, 6.0 Hz, 1H), 4.81 (br d, *J* = 7.2 Hz, 1H), 3.88-3.70 (m, 1H), 3.77 (s, 3H), 3.41-3.23 (m, 2H), 3.05-2.87 (m, 2H), 2.65-2.49 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 161.1 (C), 156.4 (C), 134.9 (C), 133.3 (C), 129.5 (CH), 128.6 (CH), 126.9 (CH x2), 126.7 (CH), 120.7 (C), 104.5 (CH), 103.2 (CH), 78.7 (CH), 61.5 (CH), 55.2 (CH_3), 46.9 (CH_2), 44.4 (CH_2), 22.1 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{19}NNaO_3$ $[M+Na]^+$ 320.1257, found 320.1250. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 13.5 min, t_{minor} = 21.2 min.

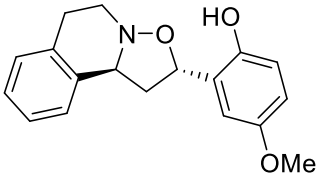


5-Fluoro-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3g): Isolated as white powder (40.1 mg, 70%, 82% ee) after silica gel column chromatography (25 g, Hexane:EtOAc = 10:1, Hexane:CH_2Cl_2 = 1:1, v/v) following the general procedure **A** using 4-fluoro-2-hydroxystyrene (64.1 mg, containing 14wt% EtOAc, 0.40 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 133-134 °C; R_f = 0.21 (Hexane:EtOAc = 83:17, v/v); $[\alpha]_D^{25}$ -82.5 (*c* 1.0, $CHCl_3$ for 82% ee); IR (KBr) 3066, 3006, 2985, 2955, 2928, 2852, 2560, 2520, 1613, 1519, 1445, 1371, 1359, 1292, 1236, 1198, 1171, 1159, 1113, 1095, 989, 973, 914, 858, 795, 767, 752, 670, 628 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.55 (br s, 1H), 7.30-7.17 (m, 2H), 7.17-7.09 (m, 2H), 6.83 (dd, *J* = 8.4, 6.6 Hz, 1H), 6.65 (dd, *J* = 10.8, 2.6 Hz, 1H), 6.44 (td, *J* = 8.4, 2.6 Hz, 1H), 5.00 (t, *J* = 6.9 Hz, 1H), 4.82 (dd, *J* = 5.8, 3.6 Hz, 1H), 3.86-3.71 (m, 1H), 3.40-3.24 (m, 2H), 3.03-2.89 (m, 2H), 2.64-2.49 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 163.8 (d, *J* = 244.8 Hz, C), 156.8 (d, *J* = 12.7 Hz, C), 134.7 (C), 133.2 (C), 129.5 (d, *J* = 10.5 Hz, CH), 128.7 (CH), 127.0 (CH), 126.9 (CH), 126.8 (CH), 124.1 (d, *J* = 2.8 Hz, C), 105.3 (CH), 105.0 (d, *J* = 1.1 Hz, CH), 78.6 (CH), 61.5 (CH), 46.9 (CH_2), 44.3 (CH_2), 22.0 (CH_2); ^{19}F NMR (282 MHz,

$CDCl_3$) δ -113.0; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}FNO_2$ $[M+H]^+$ 286.1238, found 286.1244. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 11.9 min, t_{minor} = 18.9 min.

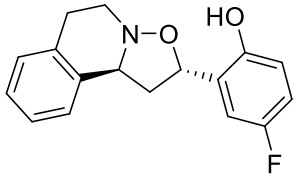


5-Bromo-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3h): Isolated as yellow solid (41.6 mg, 60%, 84% ee) after silica gel column chromatography (20 g, CH_2Cl_2) following the general procedure **A** using 4-bromo-2-hydroxystyrene (79.8 mg, 0.40 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 136-137 °C; R_f = 0.19 (CH_2Cl_2); $[\alpha]_D^{25}$ -84.5 (*c* 1.0, $CHCl_3$ for 84% ee); IR (KBr) 3056, 3016, 2981, 2925, 2851, 2656, 2555, 1590, 1498, 1452, 1424, 1368, 1263, 1234, 1121, 984, 969, 916, 889, 863, 802, 766, 748, 720, 682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.56 (br s, 1H), 7.31-7.17 (m, 2H), 7.17-7.09 (m, 3H), 6.86 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 4.98 (t, *J* = 7.3 Hz, 1H), 4.82 (t, *J* = 4.9 Hz, 1H), 3.86-3.72 (m, 1H), 3.39-3.24 (m, 2H), 3.01-2.90 (m, 2H), 2.64-2.49 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.2 (C), 134.6 (C), 133.2 (C), 129.8 (CH), 128.7 (CH), 127.1 (C), 127.0 (CH), 126.9 (CH×2), 122.7 (C), 121.5 (CH), 121.2 (CH), 78.6 (CH), 61.5 (CH), 46.9 (CH_2), 44.2 (CH_2), 22.0 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}BrNO_2$ $[M+H]^+$ 346.0437, found 346.0425. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 8.0 min, t_{minor} = 13.2 min.



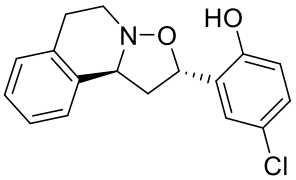
4-Methoxy-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3i): Isolated as white powder (43.2 mg, 72%, 79% ee) after silica gel column chromatography (15 g, Hexane:EtOAc:Et_3N = 82.5:16.5:1-74:25:1, v/v) following the general procedure **A** using 2-hydroxy-5-methoxystyrene (60.0 mg, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 50-51 °C; R_f = 0.30 (Hexane:EtOAc = 83:17, v/v); $[\alpha]_D^{25}$ -61.8 (*c* 1.0, $CHCl_3$ for 79% ee); IR (KBr) 3078, 3001, 2934, 2835,

2728, 2620, 1508, 1454, 1434, 1392, 1351, 1296, 1272, 1245, 1204, 1188, 1168, 1152, 1106, 1044, 1011, 984, 894, 813, 767, 750, 722, 697, 676 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.41 (br s, 1H), 7.30-7.09 (m, 4H), 6.88 (d, *J* = 8.8 Hz, 1H), 6.76 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.50 (d, *J* = 3.0 Hz, 1H), 4.98 (dd, *J* = 9.0, 6.0 Hz, 1H), 4.82 (br d, *J* = 7.4 Hz, 1H), 3.86-3.69 (m, 1H), 3.72 (s, 3H), 3.38-3.23 (m, 2H), 3.03 (ddd, *J* = 12.8, 7.4, 6.0 Hz, 1H), 2.94 (ddd, *J* = 12.8, 9.0, 2.3 Hz, 1H), 2.66-2.51, (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.0 (C), 148.9 (C), 134.8 (C), 133.3 (C), 128.6 (CH), 128.1 (C), 126.9 (CH×2), 126.7 (CH), 118.3 (CH), 114.6 (CH), 114.3 (CH), 79.0 (CH), 61.6 (CH), 55.8 (CH_3), 47.1 (CH_2), 44.3 (CH_2), 22.4 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{20}NO_3$ $[M+H]^+$ 298.1438, found 298.1433. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 27.8 min, t_{minor} = 47.6 min.

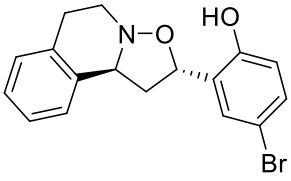


4-Fluoro-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3j): Isolated as white powder (46.6 mg, 82%, 79% ee) after silica gel column chromatography (15 g, CH_2Cl_2:Hexane = 3:1, v/v) following the general procedure **A** using 5-fluoro-2-hydroxystyrene (61.6 mg, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 47-48 °C; R_f = 0.16 (CH_2Cl_2:Hexane = 3:1); $[\alpha]_D^{25}$ -72.8 (*c* 1.0, $CHCl_3$ for 79% ee); IR (KBr) 3062, 3027, 3006, 2961, 2928, 2781, 2536, 1494, 1470, 1450, 1422, 1408, 1364, 1340, 1264, 1254, 1227, 1213, 1201, 1141, 1017, 997, 978, 911, 876, 822, 791, 771, 746, 730, 697, 470 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.87 (br s, 1H), 7.32-7.18 (m, 2H), 7.18-7.09 (m, 2H), 6.93-6.82 (m, 2H), 6.67-6.58 (m, 1H), 4.95 (dd, *J* = 8.7, 6.2 Hz, 1H), 4.82 (br d, *J* = 7.0 Hz, 1H), 3.87-3.71 (m, 1H), 3.40-3.23 (m, 2H), 3.07-2.90 (m, 2H), 2.66-2.50 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 155.5 (d, *J* = 236.6 Hz, C), 151.1 (d, *J* = 1.7 Hz, C), 134.6 (C), 133.3 (C), 128.7 (CH), 128.5 (d, *J* = 6.1 Hz, C), 127.0 (CH), 126.9 (CH×2), 118.6 (d, *J* = 8.3 Hz, CH), 115.8 (d, *J* = 22.6 Hz, CH), 114.8 (d, *J* = 23.1 Hz, CH), 78.5 (CH), 61.6 (CH), 47.0 (CH_2), 44.2 (CH_2), 22.1 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ -126.9; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}FNO_2$ $[M+H]^+$ 286.1238, found

286.1234. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C): t_{major} = 24.8 min, t_{minor} = 31.6 min.

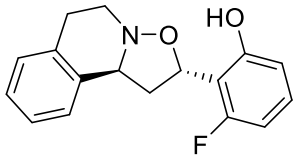


4-Chloro-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3k): Isolated as white powder (48.2 mg, 80%, 81% ee) after silica gel column chromatography (15 g, Hexane:EtOAc = 91:9, Toluene:Hexane = 75:25-Toluene:Hexane:Et_3N = 74:25:1) following the general procedure **A** using 5-chloro-2-hydroxystyrene (61.6 mg, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 99-100 °C; R_f = 0.38 (Hexane:EtOAc = 83:17); $[\alpha]_D^{24}$ -78.5 (*c* 1.0, $CHCl_3$ for 81% ee); IR (KBr) 3013, 2988, 2909, 2772, 2536, 1827, 1579, 1483, 1463, 1422, 1400, 1363, 1336, 1264, 1226, 1182, 1116, 1038, 1011, 996, 908, 882, 825, 754, 730, 700, 667 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.26 (br s, 1H), 7.32-7.18 (m, 2H), 7.18-7.08 (m, 3H), 6.92-6.82 (m, 2H), 4.94 (dd, *J* = 7.9, 7.0 Hz, 1H), 4.82 (dd, *J* = 5.9, 3.7 Hz, 1H), 3.87-3.71 (m, 1H), 3.41-3.23 (m, 2H), 3.05-2.89 (m, 2H), 2.65-2.49, (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 153.9 (C), 134.6 (C), 133.2 (C), 129.4 (CH), 129.3 (C), 128.7 (CH), 128.3 (CH), 127.1 (CH), 126.89 (CH), 126.86 (CH), 123.0 (C), 119.3 (CH), 78.5 (CH), 61.5 (CH), 47.0 (CH_2), 44.3 (CH_2), 22.0 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}ClNO_2$ $[M+H]^+$ 302.0942, found 302.0921. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 7.7 min, t_{minor} = 8.8 min.

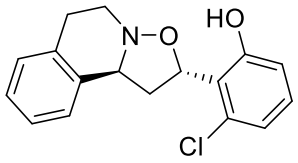


4-Bromo-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3l): Isolated as white powder (48.3 mg, 70%, 81% ee) after silica gel column chromatography (30 g, Toluene:Et_3N = 99:1, v/v) following the general procedure **A** using 5-bromo-2-hydroxystyrene (79.2 mg, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. Mp 109-110 °C; R_f = 0.26 (Toluene); $[\alpha]_D^{24}$ -67.8 (*c* 1.0, $CHCl_3$ for 81% ee); IR (KBr) 3076, 3032, 2956, 2909, 2881, 2704, 2591, 1586, 1497, 1453, 1437, 1420, 1360,

1281, 1264, 1248, 1011, 983, 983, 822, 763, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.32 (br s, 1H), 7.32-7.18 (m, 3H), 7.18-7.10 (m, 2H), 7.01 (d, *J* = 2.5 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 1H), 4.94 (dd, *J* = 7.9, 6.9 Hz, 1H), 4.82 (dd, *J* = 5.8, 3.6 Hz, 1H), 3.87-3.72 (m, 1H), 3.40-3.24 (m, 2H), 3.04-2.89 (m, 2H), 2.65-2.50, (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 154.4 (C), 134.5 (C), 133.2 (C), 132.3 (CH), 131.1 (CH), 129.9 (C), 128.7 (CH), 127.1 (CH), 126.88 (CH), 126.85 (CH), 119.9 (CH), 110.1 (C), 78.4 (CH), 61.4 (CH), 46.9 (CH_2), 44.3 (CH_2), 22.0 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}BrNO_2$ $[M+H]^+$ 346.0437, found 346.0444. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C): t_{major} = 27.8 min, t_{minor} = 30.6 min.



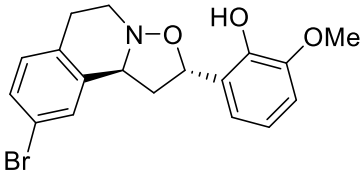
3-Fluoro-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3m): Isolated as orange oil (39.4 mg, 69%, 70% ee) after silica gel column chromatography (20 g, CH_2Cl_2:Hexane = 50:50, v/v) following the general procedure **A** using 6-fluoro-2-hydroxystyrene (56.0 mg, containing 2wt% EtOAc, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. R_f = 0.24 (CH_2Cl_2:Hexane = 50:50); $[\alpha]_D^{25}$ -71.3 (*c* 1.0, $CHCl_3$ for 70% ee); IR (KBr) 3057, 3012, 2947, 2857, 2740, 2657, 2579, 1628, 1577, 1470, 1425, 1359, 1296, 1223, 1051, 997, 974, 943, 826, 780, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.53 (br s, 1H), 7.31-7.18 (m, 2H), 7.18-7.05 (m, 3H), 6.72 (d, *J* = 8.3 Hz, 1H), 6.49 (ddd, *J* = 10.0, 8.2, 1.1 Hz, 1H), 5.61 (t, *J* = 7.7 Hz, 1H), 4.83 (t, *J* = 4.8 Hz, 1H), 3.87-3.71 (m, 1H), 3.40-3.24 (m, 2H), 3.04-2.90 (m, 2H), 2.67-2.51 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.3 (d, *J* = 244.3 Hz, C), 156.7 (d, *J* = 5.5 Hz, C), 134.6 (C), 133.2 (C), 129.3 (d, *J* = 11.0 Hz, CH), 128.6 (CH), 127.0 (CH), 126.9 (CH), 126.8 (CH), 116.0 (d, *J* = 14.3 Hz, C), 113.6 (d, *J* = 2.8 Hz, CH), 105.4 (d, *J* = 23.1 Hz, CH), 70.3 (d, *J* = 9.4 Hz, CH), 61.4 (CH), 47.1 (CH_2), 44.2 (CH_2), 22.2 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ -120.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{17}FNO_2$ $[M+H]^+$ 286.1238, found 286.1238. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:^{i}PrOH = 95:5, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 11.2 min, t_{minor} = 12.2 min.



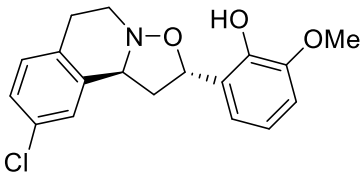
3-Chloro-2-((2*S*,10b*S*)-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3n): Isolated as yellow oil (39.6 mg, 66%, *exo*:*endo* = 97:3, 23% ee (*exo*), 16% ee (*endo*)) after silica gel column chromatography (18 g, CH_2Cl_2:Hexane = 75:25, v/v) following the general procedure **A** using 6-fluoro-2-hydroxystyrene (61.6 mg, 0.4 mmol, 2.0 equiv) at 35 °C for 48 h. R_f = 0.51 (CH_2Cl_2:Hexane = 75:25); $[\alpha]_D^{25}$ -52.1 (*c* 1.0, $CHCl_3$ for *exo*:*endo* = 97:3, 23% ee (*exo*), 16% ee (*endo*)); IR (KBr) 3064, 2936, 2838, 2706, 2609, 1606, 1573, 1454, 1358, 1288, 1257, 1181, 1136, 992, 946, 911, 826, 745, 467 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.49 (br s, 1H×97/100), 11.40 (br s, 1H×3/100), 7.32-7.19 (m, 2H), 7.18-7.12 (m, 2H), 7.07 (t, *J* = 8.1, Hz, 1H), 6.88-6.73 (m, 2H), 6.11 (dd, *J* = 9.2, 7.2 Hz, 1H×3/100), 5.80 (dd, *J* = 9.0, 6.0 Hz, 1H×97/100), 4.83 (dd, *J* = 7.8, 2.5 Hz, 1H), 3.95-3.69 (m, 1H), 3.41-3.23 (m, 2H), 3.23-3.08 (m, 2H×3/100), 3.04 (ddd, *J* = 12.8, 9.0, 2.5 Hz, 1H×97/100), 2.93 (ddd, *J* = 12.8, 7.8, 6.0 Hz, 1H×97/100), 2.70-2.54 (m, 1H×97/100), 2.45-2.33 (m, 1H×3/100); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.8 (C, *exo*+*endo*), 134.5 (C, *exo*), 133.4 (C, *endo*), 133.2 (C, *exo*), 132.9 (C, *endo*), 132.8 (C, *endo*), 132.7 (C, *exo*), 129.5 (CH, *endo*), 129.3 (CH, *exo*), 128.7 (CH, *exo*), 128.1 (CH, *endo*), 127.7 (CH, *endo*), 127.0 (CH, *exo*), 126.9 (CH×2, *exo*), 126.5 (CH, *endo*), 125.4 (CH, *endo*), 125.22 (C, *endo*), 125.17 (C, *exo*), 120.0 (CH, *exo*), 119.8 (CH, *endo*), 116.9 (CH, *exo*), 116.8 (CH, *endo*), 75.8 (CH, *endo*), 74.9 (CH, *exo*), 67.6 (CH, *endo*), 61.5 (CH, *exo*), 50.5 (CH_2, *endo*), 47.1 (CH_2, *exo*), 43.8 (CH_2, *exo*), 38.6 (CH_2, *endo*), 29.0 (CH_2, *endo*), 22.5 (CH_2, *exo*); HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{16}ClNNaO_2$ $[M+Na]^+$ 324.0762, found 324.0755. The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-3, Hexane:^{i}PrOH = 99:1, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{minor} = 23.1 min (*endo*), t_{minor} = 29.4 min (*exo*), t_{major} = 34.1 min (*endo*), t_{major} = 39.3 min (*exo*).

General procedure B for the asymmetric cycloaddition reactions was exemplified by the reaction of nitrone 1c with 2-hydroxy-3-methoxystyrene in the presence of amine-urea 2. To a

solution of 2-hydroxy-3-methoxystyrene (61.0 mg, 0.41 mmol, 2.0 equiv) and amine-urea **2** (115.7 mg, 0.20 mmol, 100 mol%) in toluene (0.5 mL) was added nitrone **1c** (45.2 mg, 0.20 mmol), and then the mixture was stirred at 35 °C for 24 h. The reaction mixture was filtered through a plug of silica gel (0.8 g) with CH_2Cl_2 (40 mL) as an eluent. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (silica gel 7 g, Hexane:EtOAc = 70:30, v/v) to provide isoxazolidine **3p** (70.4 mg, 94%, 87% ee) as colorless powder.

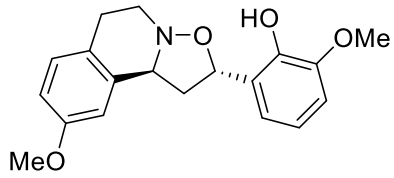


2-((2*S*,10b*S*)-9-Bromo-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)-6-methoxyphenol (3p): Mp 58-60 °C; R_f = 0.33 (Hexane:EtOAc = 70:30, v/v); $[\alpha]_D^{27}$ -107.7 (*c* 1.0, $CHCl_3$ for 94% ee); IR (KBr) 3510, 3404, 2937, 2838, 1613, 1593, 1481, 1441, 1353, 1274, 1227, 1165, 1079, 1032, 997, 969, 880, 859, 829, 782, 736, 454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.75 (br s, 1H), 7.34-7.28 (m, 1H), 7.28-7.26 (m, 1H), 7.01 (d, *J* = 8.1 Hz, 1H), 6.85 (dd, *J* = 7.4, 2.5 Hz, 1H), 6.80-6.70 (m, 2H), 5.21 (dd, *J* = 7.9, 6.3 Hz, 1H), 4.75 (t, *J* = 5.9 Hz, 1H), 3.89 (s, 3H), 3.64 (dt, *J* = 12.8, 4.7 Hz, 1H), 3.30 (ddd, *J* = 12.8, 9.9, 4.7 Hz, 1H), 3.12 (ddd, *J* = 16.4, 9.8, 4.5 Hz, 1H), 2.98-2.83 (m, 2H), 2.62 (dt, *J* = 16.4, 4.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.4 (C), 143.9 (C), 137.4 (C), 132.3 (C), 130.2 (CH), 129.9 (CH), 129.8 (CH), 128.0 (C), 120.1 (C), 120.1 (CH), 118.7 (CH), 111.2 (CH), 77.4 (CH), 61.4 (CH), 56.0 (CH_3), 47.0 (CH_2), 43.9 (CH_2), 23.4 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{18}BrNNaO_3$ $[M+Na]^+$ 398.0362, found 398.0363. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 16.1 min, t_{minor} = 25.6 min.



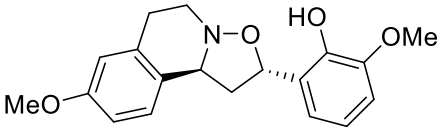
2-((2*S*,10b*S*)-9-Chloro-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)-6-methoxyphenol (3o): Isolated as colorless powder (65.6 mg, 99%, 88% ee) after silica gel column

chromatography (6 g, Hexane:EtOAc = 80:20, v/v) following the general procedure **B** using nitrone **1b** (36.3 mg, 0.20 mmol) and 2-hydroxy-3-methoxystyrene (60.1 mg, 0.40 mmol, 2.0 equiv) at 35 °C for 12 h. Mp 58-59 °C; R_f = 0.26 (Hexane:EtOAc = 67:23, v/v); $[\alpha]_D^{22}$ -104.0 (*c* 0.66, $CHCl_3$ for 88% ee); IR (KBr) 3420, 2938, 1599, 1483, 1441, 1353, 1274, 1227, 1084, 784, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.78 (br s, 1H), 7.17 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.12 (d, *J* = 1.9 Hz, 1H), 7.07 (d, *J* = 8.1 Hz, 1H), 6.85 (dd, *J* = 7.4, 2.4 Hz, 1H), 6.77 (t, *J* = 7.4 Hz, 1H), 6.73 (dd, *J* = 7.4, 2.4 Hz, 1H), 5.21 (dd, *J* = 8.3, 6.2 Hz, 1H), 4.80 (dd, *J* = 6.1, 5.5 Hz, 1H), 3.90 (s, 3H), 3.64 (dt, *J* = 12.9, 4.5 Hz, 1H), 3.36-3.25 (m, 1H), 3.22-3.08 (m, 1H), 2.99-2.83 (m, 2H), 2.68 (dt, *J* = 16.4, 4.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.4 (C), 143.9 (C), 136.9 (C), 132.2 (C), 131.7 (C), 129.9 (CH), 128.0 (C), 126.90 (CH), 126.87 (CH), 120.1 (CH), 118.7 (CH), 111.2 (CH), 77.3 (CH), 61.5 (CH), 56.0 (CH_3), 47.0 (CH_2), 43.9 (CH_2), 23.3 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{18}ClNNaO_3$ $[M+Na]^+$ 354.0867, found 354.0854. The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-3, Hexane:^{i}PrOH = 30:70, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C): t_{minor} = 18.3 min, t_{major} = 24.7 min.

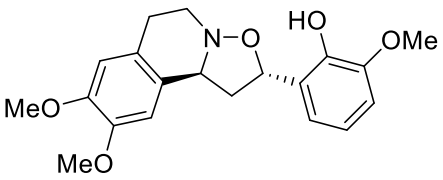


2-Methoxy-6-((2*S*,10b*S*)-9-methoxy-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3q): Isolated as colorless powder (59.7 mg, 90%, 86% ee) after silica gel column chromatography (8 g, Hexane:EtOAc = 70:30, v/v) following the general procedure **B** using nitrone **1d** (35.5 mg, 0.20 mmol) and 2-hydroxy-3-methoxystyrene (60.1 mg, 0.40 mmol, 2.0 equiv) at 35 °C for 24 h. Mp 49-50 °C; R_f = 0.27 (Hexane:EtOAc = 70:30, v/v); $[\alpha]_D^{23}$ -87.4 (*c* 1.0, $CHCl_3$ for 86% ee); IR (KBr) 3410, 2937, 2837, 1613, 1584, 1505, 1480, 1442, 1352, 1317, 1276, 1167, 1133, 1082, 1036, 1010, 971, 861, 823, 783, 737, 708, 462 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.03 (br s, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.84 (dd, *J* = 7.0, 2.6 Hz, 1H), 6.81-6.70 (m, 3H), 6.64 (d, *J* = 2.5 Hz, 1H), 5.21 (t, *J* = 7.2 Hz, 1H), 4.76 (t, *J* = 5.9 Hz, 1H), 3.90 (s, 3H), 3.79 (s, 3H), 3.63 (dt, *J* = 12.9, 4.7 Hz, 1H), 3.29 (ddd, *J* = 12.9, 9.9, 4.7 Hz 1H), 3.12 (ddd, *J* = 15.7, 9.9, 4.7 Hz, 1H), 2.97-2.86 (m, 2H), 2.65 (dt, *J* = 15.7, 4.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.5 (C), 144.0 (C), 136.1 (C), 129.5 (CH),

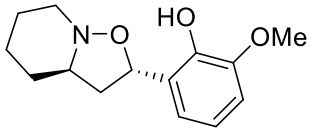
128.3 (C), 125.3 (C), 120.2 (CH), 118.6 (CH), 112.9 (CH), 111.8 (CH), 111.2 (CH), 77.4 (CH), 61.9 (CH), 56.0 (CH_3), 55.3 (CH_3), 47.5 (CH_2), 44.1 (CH_2), 23.1 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{22}NO_4$ $[M+H]^+$ 328.1543, found 328.1540. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 14.9 min, t_{minor} = 27.0 min.



2-Methoxy-6-((2*S*,10b*S*)-8-methoxy-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)phenol (3r): Isolated as colorless powder (49.5 mg, 76%, 90% ee) after silica gel column chromatography (8 g, Hexane:EtOAc = 70:30, v/v) following the general procedure **B** using nitrone **1e** (35.4 mg, 0.20 mmol) and 2-hydroxy-3-methoxystyrene (61.2 mg, 0.41 mmol, 2.0 equiv) at 35 °C for 24 h. Mp 140-142 °C; R_f = 0.16 (Hexane:EtOAc = 70:30, v/v); $[\alpha]_D^{25}$ -58.5 (*c* 1.0, $CHCl_3$ for 90% ee); IR (KBr) 3393, 2948, 2838, 1611, 1501, 1480, 1444, 1355, 1278, 1228, 1167, 1125, 1112, 1080, 1039, 1011, 990, 954, 892, 863, 821, 783, 737, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.15 (br s, 1H), 7.02 (d, *J* = 8.5 Hz, 1H), 6.85-6.68 (m, 4H), 6.65 (d, *J* = 2.6 Hz, 1H), 5.19 (dd, *J* = 7.7, 6.8 Hz, 1H), 4.74 (t, *J* = 5.8 Hz, 1H), 3.88 (s, 3H), 3.79 (s, 3H), 3.63 (dt, *J* = 12.5, 4.5 Hz, 1H), 3.30 (ddd, *J* = 12.5, 10.0, 4.5 Hz, 1H), 3.18 (ddd, *J* = 15.8, 10.0, 4.5 Hz, 1H), 2.94-2.80 (m, 2H), 2.66 (dt, *J* = 15.8, 4.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.1 (C), 148.5 (C), 144.0 (C), 134.5 (C), 128.3 (C), 128.1 (CH), 127.1 (C), 120.1 (CH), 118.5 (CH), 113.3 (CH), 112.8 (CH), 111.2 (CH), 77.6 (CH), 61.3 (CH), 55.9 (CH_3), 55.2 (CH_3), 47.1 (CH_2), 44.2 (CH_2), 24.1 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{22}NO_4$ $[M+H]^+$ 328.1543, found 328.1526. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 17.5 min, t_{minor} = 39.4 min.

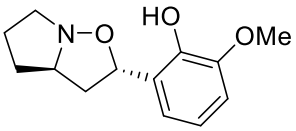


2-((2*S*,10b*S*)-8,9-Dimethoxy-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)-6-methoxyphenol (3s): Isolated as colorless powder (55.7 mg, 78%, 86% ee) after silica gel column chromatography (5 g, Hexane:EtOAc = 70:30, v/v) following the general procedure **B** using nitrone **1f** (41.4 mg, 0.20 mmol) and 2-hydroxy-3-methoxystyrene (60.8 mg, 0.40 mmol, 2.0 equiv) at 35 °C for 24 h. Mp 65-67 °C; R_f = 0.20 (Hexane:EtOAc = 50:50, v/v); $[\alpha]_D^{22}$ -66.4 (*c* 0.91, $CHCl_3$ for 86% ee); IR (KBr) 3432, 2937, 2836, 1612, 1517, 1480, 1360, 1257, 1224, 1117, 1082, 1019, 864, 782, 768, 735 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.09 (br s, 1H), 6.85 (dd, *J* = 7.7, 2.6 Hz, 1H), 6.76 (t, *J* = 7.7 Hz, 1H), 6.72 (dd, *J* = 7.7, 2.6 Hz, 1H), 6.61 (s, 1H), 6.57 (s, 1H), 5.22 (t, *J* = 7.1 Hz, 1H), 4.73 (t, *J* = 5.8 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.64 (dt, *J* = 12.9, 4.6 Hz, 1H), 3.29 (ddd, *J* = 12.9, 9.9, 4.6 Hz, 1H), 3.12 (ddd, *J* = 16.0, 9.9, 4.6 Hz, 1H), 2.94-2.84 (m, 2H), 2.62 (dt, *J* = 16.0, 4.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.6 (C), 148.1 (C), 147.9 (C), 144.1 (C), 128.5 (C), 126.7 (C), 125.4 (C), 120.2 (CH), 118.6 (CH), 111.2 (CH), 111.1 (CH), 109.6 (CH), 77.6 (CH), 61.5 (CH), 56.1 (CH_3), 56.0 (CH_3), 55.9 (CH_3), 47.4 (CH_2), 44.1 (CH_2), 23.5 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{23}NNaO_5$ $[M+Na]^+$ 380.1468, found 380.1481. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C): t_{major} = 21.1 min, t_{minor} = 29.5 min.

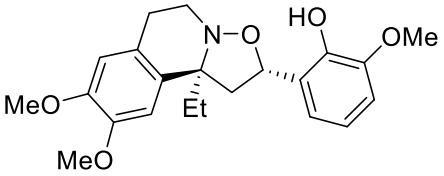


2-((2*S*,3a*R*)-Hexahydro-2*H*-isoxazolo[2,3-*a*]pyridin-2-yl)-6-methoxyphenol (3t): Isolated as colorless viscous oil (43.8 mg, 88%, 93% ee) after silica gel column chromatography (6 g, Hexane:EtOAc = 91:9, v/v) following the general procedure **B** using nitrone **1g** (19.8 mg, 0.20 mmol), 2-hydroxy-3-methoxystyrene (60.1 mg, 0.40 mmol, 2.0 equiv), and amine-urea **2** (34.7 mg, 0.06 mmol, 30 mol%) at 35 °C for 12 h. R_f = 0.35 (Hexane:EtOAc = 50:50, v/v); $[\alpha]_D^{21}$ -39.6 (*c* 0.65, acetone for 93% ee); IR (KBr) 3429, 2938, 2855, 1615, 1480, 1353, 1275, 1083, 992, 783, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.99 (br s, 1H×88/100), 7.03-6.96 (m, 1H×12/100), 6.87-6.76 (m, 1H×12/100), 6.82 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.69 (t, *J* = 7.8 Hz, 1H×88/100), 6.61 (dd, *J* = 7.8, 1.6 Hz, 1H×88/100), 6.17 (s,

1H×12/100), 5.37-5.29 (m, 1H×12/100), 5.11 (dd, *J* = 9.2, 5.8 Hz, 1H×88/100), 3.87 (s, 3H), 3.61-3.45 (m, 2H×88/100), 3.15-3.00 (m, 1H×88/100), 2.69-2.61 (m, 1H×12/100), 2.56 (ddd, *J* = 12.7, 6.7, 5.8 Hz, 1H×88/100), 2.47-2.35 (m, 2H×12/100), 2.37 (dd, *J* = 12.7, 9.2 Hz, 1H×88/100), 2.24-2.13 (m, 1H×12/100), 1.93-1.71 (m, 2H), 1.70-1.55 (m, 1H), 1.55-1.33 (m, 3H), a 88:12 mixture of *N*-invertomers was observed in $CDCl_3$; $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 149.3 (C), 144.9 (C), 129.0 (C), 120.6 (CH), 117.8 (CH), 111.6 (CH), 78.6 (CH), 59.7 (CH), 55.9 (CH_3), 49.2 (CH_2), 42.3 (CH_2), 25.9 (CH_2), 22.6 (CH_2), 19.0 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{14}H_{19}NNaO_3$ $[M+Na]^+$ 272.1257, found 272.1259. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:EtOH = 95:5, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{minor} = 23.4 min, t_{major} = 28.0 min.



2-((2*S*,3a*R*)-Hexahydropyrrolo[1,2-*b*]isoxazol-2-yl)-6-methoxyphenol (3u): Isolated as colorless viscous oil (31.7 mg, 67%, 91% ee) after silica gel column chromatography (5 g, Hexane:EtOAc = 91:9, v/v) following the general procedure **A** using nitrone **1h** (17.0 mg, 0.20 mmol), 2-hydroxy-3-methoxystyrene (60.1 mg, 0.40 mmol, 2.0 equiv), and amine-urea **2** (34.7 mg, 0.06 mmol, 30 mol%) at 35 °C for 12 h. R_f = 0.23 (Hexane:EtOAc = 50:50, v/v); $[\alpha]_D^{22}$ +48.5 (*c* 0.55, CH_2Cl_2 for 91% ee); IR (KBr) 3429, 2956, 1613, 1583, 1479, 1442, 1356, 1272, 1062, 782, 735 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.15 (br s, 1H), 6.81 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.71 (t, *J* = 7.7 Hz, 1H), 6.63 (dd, *J* = 7.7, 1.7 Hz, 1H), 5.20 (dd, *J* = 8.1, 5.8 Hz, 1H), 3.87 (s, 3H), 3.86-3.76 (m, 1H), 3.50 (ddd, *J* = 13.8, 7.7, 3.9 Hz, 1H), 3.15 (dt, *J* = 13.8, 8.2 Hz, 1H), 2.70-2.55 (m, 2H), 2.27-2.10 (m, 1H), 2.10-1.97 (m, 1H), 1.92-1.78 (m, 1H), 1.77-1.63 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 149.1 (C), 144.3 (C), 128.3 (C), 120.3 (CH), 118.3 (CH), 111.4 (CH), 79.0 (CH), 66.9 (CH), 56.0 (CH_3), 55.1 (CH_2), 42.9 (CH_2), 30.7 (CH_2), 24.5 (CH_2); HRMS (ESI-TOF) m/z: calcd for $C_{13}H_{17}NNaO_3$ $[M+Na]^+$ 258.1101, found 258.1100. The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-3, Hexane:EtOH = 95:5, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C): t_{minor} = 39.6 min, t_{major} = 47.8 min.



2-((*2S,10bS*)-10b-Ethyl-8,9-dimethoxy-1,5,6,10b-tetrahydro-2*H*-isoxazolo[3,2-*a*]isoquinolin-2-yl)-6-methoxyphenol (3v): Isolated as colorless powder (28.2 mg, 36%, *exo*:*endo* = 93:7, 81% ee (*exo*), 15% ee (*endo*)) after silica gel column chromatography (6 g, Hexane:EtOAc = 91:9-80:20, v/v) following the general procedure **B** using nitrone **1i** (47.2 mg, 0.20 mmol) and 2-hydroxy-3-methoxystyrene (60.7 mg, 0.40 mmol, 2.0 equiv) at 80 °C for 48 h. Mp 133-134 °C; R_f = 0.28 (Hexane:EtOAc = 67:33, v/v); $[\alpha]_D^{24}$ -36.1 (*c* 1.2, $CHCl_3$ for *exo*:*endo* = 93:7, 81% ee (*exo*), 15% ee (*endo*)); IR (KBr) 3420, 2938, 2834, 1611, 1584, 1516, 1465, 1354, 1256, 1211, 1081, 1008, 793, 737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.5 (br s, 1H), 6.98-6.53 (m, 6H×7/100), 6.83 (dd, *J* = 8.0, 1.5 Hz, 1H×93/100), 6.72 (t, *J* = 8.0 Hz, 1H×93/100), 6.66 (s, 1H×93/100), 6.63 (dd, *J* = 7.7, 1.5 Hz, 1H×93/100), 6.60 (s, 1H×93/100), 5.52-5.43 (m, 1H×7/100), 4.97 (dd, *J* = 9.1, 6.8 Hz, 1H×93/100), 3.90 (s, 3H×93/100), 3.88 (s, 6H×93/100), 3.86 (s, 3H×7/100), 3.84 (s, 3H×7/100), 3.83 (s, 3H×7/100), 3.65 (ddd, *J* = 13.6, 5.9, 2.7 Hz, 1H×93/100), 3.49-1.80 (m, 8H×7/100), 3.33 (ddd, *J* = 13.6, 11.0, 5.3 Hz, 1H×93/100), 3.16 (ddd, *J* = 16.5, 11.0, 5.9 Hz, 1H×93/100), 3.05 (dd, *J* = 12.8, 9.1 Hz, 1H×93/100), 2.66 (dd, *J* = 12.8, 6.8 Hz, 1H×93/100), 2.56 (ddd, *J* = 16.5, 5.3, 2.7 Hz, 1H×93/100), 2.04-1.86 (m, 2H×93/100), 0.99 (t, *J* = 7.5 Hz, 3H×93/100), 0.82 (t, *J* = 7.3 Hz, 3H×7/100); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.7 (C, *exo*), 147.8 (C, *endo*), 147.7 (C, *exo*), 147.6 (C, *exo*), 147.2 (C, *endo*), 146.4 (C, *endo*), 144.3 (C, *exo*), 142.6 (C, *endo*), 131.5 (C, *endo*), 129.7 (C, *exo*), 128.3 (C, *exo*), 127.9 (C, *endo*), 126.4 (C, *endo*), 125.4 (C, *exo*), 120.1 (CH, *exo*), 119.3 (CH, *endo*), 118.4 (CH, *exo*), 118.3 (CH, *endo*), 111.3 (CH, *exo*), 111.1 (CH, *exo*+*endo*), 110.5 (CH, *endo*), 110.0 (CH, *exo*), 109.6 (CH, *endo*), 76.9 (CH, *exo*), 76.3 (CH, *endo*), 70.2 (C, *endo*), 69.2 (C, *exo*), 56.1 (CH_3, *exo*), 56.0 (CH_3, *endo*), 55.9 (CH_3, *exo*+*endo*), 55.8 (CH_3, *exo*+*endo*), 50.6 (CH_2, *endo*), 49.4 (CH_2, *endo*), 48.2 (CH_2, *exo*), 44.4 (CH_2, *exo*), 32.9 (CH_2, *exo*), 32.6 (CH_2, *endo*), 27.4 (CH_2, *endo*), 22.9 (CH_2, *exo*), 9.6 (CH_3, *exo*), 8.8 (CH_3, *endo*); HRMS (ESI-TOF) m/z: calcd for $C_{22}H_{27}NNaO_5$ $[M+Na]^+$ 408.1781, found 408.1774. The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-3, Hexane:EtOH = 90:10, v/v, UV 220 nm,

flow rate = 1.0 mL/min, 35 °C): t_{minor} = 17.6 min (*endo*), t_{minor} = 19.2 min (*exo*), t_{major} = 24.6 min (*endo*), t_{major} = 28.2 min (*exo*).

***1.0 mmol scale procedure for the reaction of nitrone 1a with 2-hydroxy-3-methoxystyrene**:*

A solution of nitrone **1a** (147.1 mg, 1.0 mmol) in toluene (2.5 mL) was added to 2-hydroxy-3-methoxystyrene (301.3 mg, 2.0 mmol, 2.0 equiv) and amine-urea **2** (173.6 mg, 0.30 mmol, 30 mol%), and then the mixture was stirred at 35 °C for 24 h. The reaction mixture was filtered through a plug of silica gel (1.0 g) with CH_2Cl_2 (20 mL) as an eluent. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (silica gel 40 g, Hexane:EtOAc = 80:20, v/v) to provide isoxazolidine **3b** (258.8 mg, 87%, 84% ee) as colorless powder.

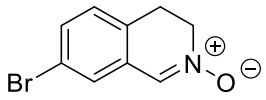
***1.0 mmol scale procedure for the reaction of nitrone 1a with 3-bromo-2-hydroxystyrene**:*

A solution of nitrone **1a** (147.1 mg, 1.0 mmol) in toluene (2.5 mL) was added to 3-bromo-2-hydroxystyrene (395.8 mg, 2.0 mmol, 2.0 equiv) and amine-urea **2** (578.8 mg, 1.0 mmol, 100 mol%), and then the mixture was stirred at 35 °C for 48 h. The reaction mixture was filtered through a plug of silica gel (1.0 g) with CH_2Cl_2 (40 mL) as an eluent. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (silica gel 20 g, Hexane:EtOAc = 94:6, v/v) to provide isoxazolidine **3e** (296.4 mg, 86%, 85% ee) as white powder.

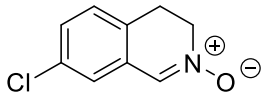
General procedure for the synthesis of nitrones 1b-1e was exemplified by the reaction of 7-bromo-1,2,3,4-tetrahydroisoquinoline.

Nitrones **1b-1e** were synthesized according to the reported procedure for the synthesis of 3,4-dihydroisoquinoline *N*-oxide (**1a**).[1] To a solution of 7-bromo-1,2,3,4-tetrahydroisoquinoline (214.0 mg, 1.0 mmol) and Na_2WO_4•$2H_2O$ (13.2 mg, 0.04 mmol, 4 mol%) in methanol (2.0 mL) was added 30% aqueous hydrogen peroxide (0.57 mL, 5.0 mmol, 5 equiv) dropwise at 0 °C over a period of 10 min. The mixture was stirred at 0 °C for 1 h and then at room temperature for 5 h. Methanol was removed under reduced pressure. To the residue was added saturated aqueous sodium chloride solution (5.0 mL) and extracted with CH_2Cl_2 (15 mL x 3). The combined organic layer was dried over Na_2SO_4 and

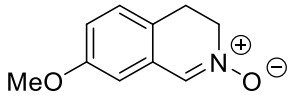
concentrated. The residue was purified by column chromatography (silica gel 8 g, EtOAc:Hexane = 97:3, v/v) to provide nitrone **1c** (85.1 mg, 38%) as pale yellow solid.



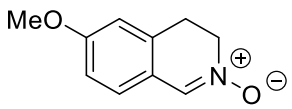
7-Bromo-3,4-dihydroisoquinoline 2-oxide (1c):[4] Mp 134-136 °C; R_f = 0.35 (EtOAc:Hexane = 91:9, v/v); IR (KBr) 3436, 3039, 3006, 1587, 1557, 1483, 1447, 1435, 1408, 1273, 1264, 1215, 1192, 1125, 1074, 918, 898, 825, 814, 761, 727, 677, 552, 519, 472, 435, 418 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.38 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.26 (d, *J* = 1.9 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 4.11 (t, *J* = 7.7 Hz, 2H), 3.13 (t, *J* = 7.7 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 132.5 (CH), 131.7 (CH), 130.2 (C), 128.7 (CH), 128.6 (C), 127.7 (CH), 121.1 (C), 58.0 (CH_2), 27.2 (CH_2); HRMS (ESI-TOF) m/z: calcd for C_9H_9BrNO $[M+H]^+$ 225.9862, found 225.9879.



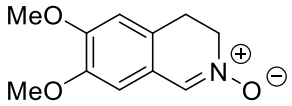
7-Chloro-3,4-dihydroisoquinoline 2-oxide (1b):[5] Isolated as yellow solid (75.4 mg, 42%) after silica gel column chromatography (10 g, EtOAc:MeOH = 98:2, v/v) following the general procedure using 7-chloro-1,2,3,4-tetrahydroisoquinoline (167.8 mg, 1.0 mmol). ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.24 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 2.1 Hz, 1H), 4.11 (t, *J* = 7.8 Hz, 2H), 3.16 (t, *J* = 7.8 Hz, 2H).



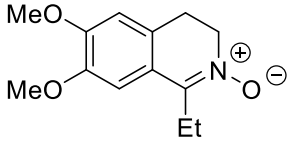
7-Methoxy-3,4-dihydroisoquinoline 2-oxide (1d):[6] Isolated as yellow solid (85.0 mg, 48%) after silica gel column chromatography (10 g, EtOAc:MeOH = 98:2, v/v) following the general procedure using 7-methoxy-1,2,3,4-tetrahydroisoquinoline[7] (163.7 mg, 1.0 mmol). ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.13 (d, *J* = 8.3, 1H), 6.82 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.66 (d, *J* = 2.6 Hz, 1H), 4.09 (td, *J* = 7.7, 0.9 Hz, 2H), 3.81 (s, 3H), 3.11 (t, *J* = 7.7 Hz, 2H).



6-Methoxy-3,4-dihydroisoquinoline 2-oxide (1e):[8] Isolated as pale yellow solid (175.3 mg, 99%) after silica gel column chromatography (13 g, EtOAc:MeOH = 95:5, v/v) following the general procedure using 6-methoxy-1,2,3,4-tetrahydroisoquinoline (0.15 mL, 1.0 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.82-6.74 (m, 2H), 4.07 (t, *J* = 7.7 Hz, 2H), 3.83 (s, 3H), 3.15 (t, *J* = 7.7 Hz, 2H).



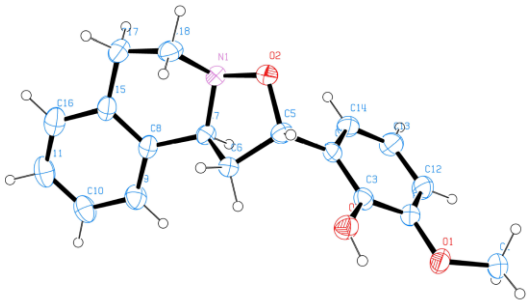
6,7-Dimethoxy-3,4-dihydroisoquinoline 2-oxide (1f):[8] Nitrone **1f** was synthesized by two step sequences from homoveratrylamine according to the literature.[1,9] To a solution of homoveratrylamine (725.0 mg, 4.0 mmol) in formic acid (2.0 mL) was added paraformaldehyde (360.0 mg, 4.0 mmol, 1.0 equiv) and the resulting suspension was stirred at 26 °C for 15 h. The solvent was evaporated in vacuo and the residue was basified by 2.0 M NaOH solution (25 mL) while cooling with ice water. The mixture was extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over Na_2SO_4 and concentrated to give crude 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline. To a solution of the crude tetrahydroisoquinoline and Na_2WO_4•$2H_2O$ (52.8 mg, 0.16 mmol, 4 mol%) in methanol (10 mL) was added 30% aqueous hydrogen peroxide (1.10 mL, 10 mmol, 5 equiv) dropwise at 0 °C over a period of 10 min. The mixture was stirred at 0 °C for 1 h and then at room temperature for 5 h. Methanol was removed under reduced pressure. To the residue was added saturated aqueous sodium chloride solution (10 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel 6 g, CH_2Cl_2:Hexane = 98:2, v/v) to provide nitrone **1f** (264.6 mg, 32%) as orange solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H), 6.73 (s, 1H), 6.63 (s, 1H), 4.08 (t, *J* = 8.0 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 3.12 (t, *J* = 8.0 Hz, 2H).

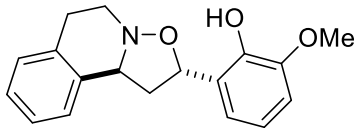


6,7-Dimethoxy-1-ethyl-3,4-dihydroisoquinoline 2-oxide (1i): Nitrone **1i** was synthesized by two step sequences from homoveratrylamine according to the literature.[1,10] To a solution of homoveratrylamine (906.2 mg, 5.0 mmol) in $CHCl_3$ (4.0 mL) was added propanal (0.44 mL, 6.0 mmol, 1.2 equiv) and trifluoroacetic acid (4.0 mL), and then the resulting solution was heated to reflux for 8 h. After cooling the mixture at room temperature, ice water (25 mL) was added, and then the mixture was basified (pH 9) by 1.0 M NaOH solution (30 mL). The mixture was extracted with $CHCl_3$ (30 mL×3). The combined organic layer was washed with brine (20 mL) and 1.0 M NaOH solution (50 mL×3), and then dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel 50 g, $CHCl_3$:MeOH = 94:6, v/v, silica gel 20 g, $CHCl_3$:MeOH = 88:12, v/v) to give 6,7-dimethoxy-1-ethyl-1,2,3,4-tetrahydroisoquinoline[11] (831.9 mg, 75%) as pale yellow oil. To a solution of 6,7-dimethoxy-1-ethyl-1,2,3,4-tetrahydroisoquinoline (222.3 mg, 1.0 mmol) and Na_2WO_4•$2H_2O$ (13.5 mg, 0.04 mmol, 4 mol%) in methanol (2.0 mL) was added 30% aqueous hydrogen peroxide (0.56 mL, 5.0 mmol, 5 equiv) dropwise at 0 °C over a period of 10 min. The mixture was stirred at 0 °C for 1 h and then at room temperature for 73 h. Methanol was removed under reduced pressure. To the residue was added saturated aqueous sodium chloride solution (20.0 mL) and extracted with CH_2Cl_2 (20 mL x 3). The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel 12 g, EtOAc:MeOH = 91:9, v/v, silica gel 8 g, CH_2Cl_2:MeOH = 97:3, v/v) to provide nitrone **1i** (74.0 mg, 31%) as brownish powder. Mp 113-114 °C; R_f = 0.11 (CH_2Cl_2:MeOH = 95:5, v/v); IR (KBr) 3420, 2989, 2966, 2940, 1606, 1593, 1518, 1464, 1446, 1330, 1285, 1219, 1201, 1148, 1072, 1014, 799 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.84 (s, 1H), 6.72 (s, 1H), 4.10 (t, *J* = 7.5 Hz, 2H), 3.92 (s, 6H), 3.04 (t, *J* = 7.5 Hz, 2H), 2.96 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 149.2 (C), 148.1 (C), 145.8 (C), 124.8 (C), 121.9 (C), 110.7 (CH), 107.6 (CH), 57.9 (CH_2), 56.2 (CH_3), 56.0 (CH_3), 27.5 (CH_2), 19.8 (CH_2), 9.8 (CH_3); HRMS (ESI-TOF) m/z: calcd for $C_{13}H_{17}NNaO_3$ $[M+Na]^+$ 258.1101, found 258.1103.

Determination of the relative and absolute configuration of cycloadduct 3

To determine the relative configuration of cycloadduct **3b**, X-ray crystallographic analysis was carried out using the single crystal which was grown in EtOH (Figure S1). The data has been deposited with the Cambridge Crystallographic Data Centre (CCDC 2498869).



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Temperature:     93 K

                 Calculated                Reported
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Hall group       P 2ac 2ab                 P 2ac 2ab
Moiety formula   C18 H19 N O3              ?
Sum formula      C18 H19 N O3              C18 H19 N O3
Mr               297.34                    297.34
Dx,g cm-3        1.287                     1.287
Z                4                         4
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F000             632.0                     632.0
F000'            632.30
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Nref             2724[ 1612]               2725
Tmin,Tmax        0.985,0.992               0.890,0.990
Tmin'            0.970

Correction method= # Reported T Limits: Tmin=0.890 Tmax=0.990
AbsCorr = MULTI-SCAN

Data completeness= 1.69/1.00      Theta(max)= 25.050

R(reflections)= 0.0539( 1556)     wR2(reflections)= 0.1166( 2725)

S = 0.997                 Npar= 202
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Figure S1. Single crystal X-ray analysis of **3b**.

The comparison between experimental and calculated ECD spectra allows the absolute configuration assignment of cycloadduct **3b** (Figure S2).[12] The experimental UV and ECD spectra (1.0 mg/mL in acetonitrile) was obtained as the average of four spectra measured in the 245–400 nm region at 100 nm min^{-1} (Figure S3). The UV spectra are dominated by the absorption bands of the phenol moiety. A positive Cotton effect was observed at around 290 nm and a negative Cotton effect was observed at around 280 nm. To simulate the experimental ECD spectrum, the spectra of possible four conformations were simulated and then mixed using the Boltzmann distribution (Figure S4). TD-DFT calculations on (3*S*,5*S*)-**3b** were performed at the PCM(MeCN)-CAM-B3LYP/6-311++G(2d,p)//B3LYP/6-31+G(d) level of theory.

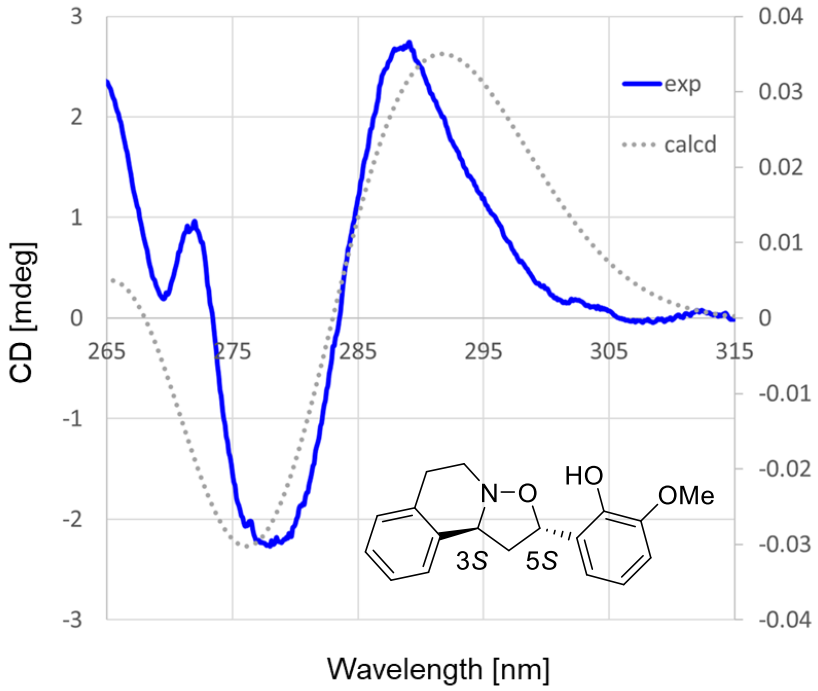

Figure S2. ECD spectra of **3b** (blue solid line: experimental, gray dotted line: calculated).

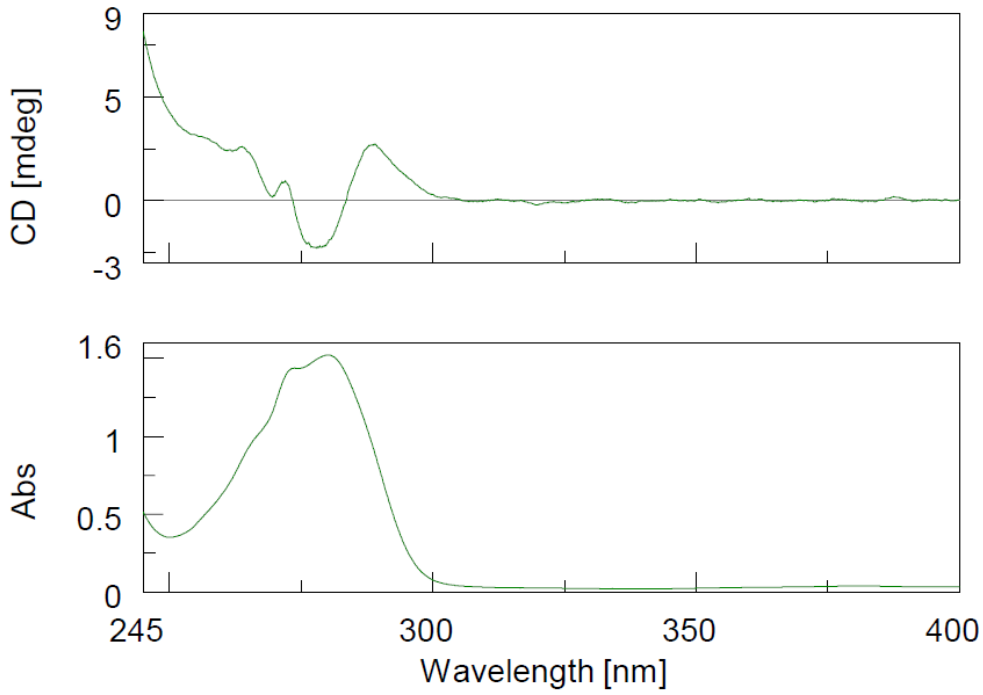

Figure S3. Experimental UV (bottom) and ECD (top) spectra of **3b**.

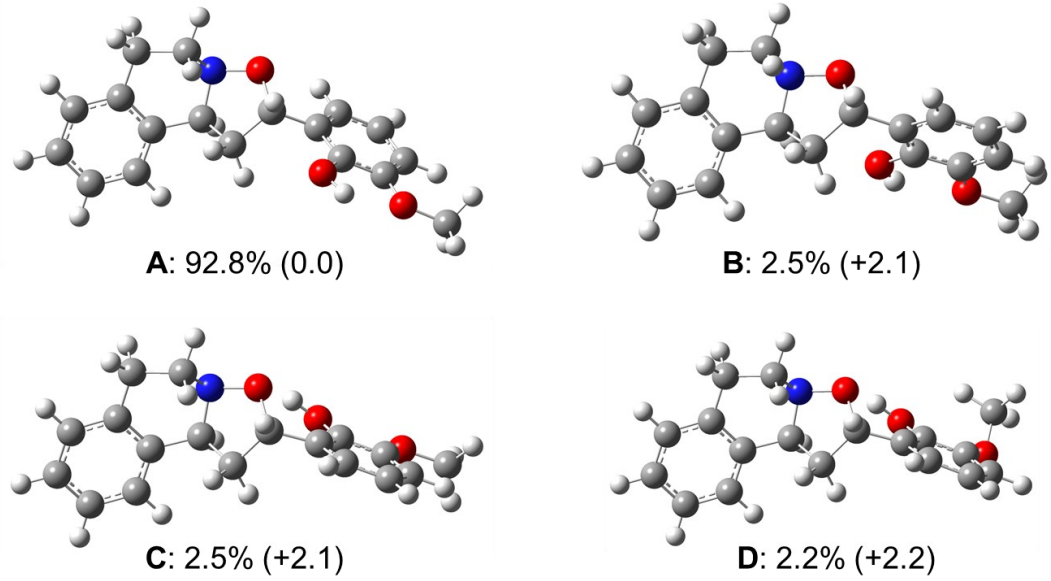

Figure S4. Optimized 3D-strucutres of (3*S*,5*S*)-**3b**.
Relative energies (kcal mol^{-1}) are shown in parentheses.

DFT calculations

Quantum mechanical calculations were performed using Gaussian 16 (Revision C.01).[13,14] All geometries were optimized using the M06-2X density functional, the 6-31G(d) basis set, the IEFPCM(Toluene) solvation model, and an ultrafine integration grid. The intrinsic reaction coordinate (IRC) approach was used to search for reactants and products. Single point energies were calculated using M06-X, the def2tzvpp basis set, the IEFPCM(Toluene) solvation model, and an ultrafine integration grid. The energies were converted to zero-point energy-corrected free energies at 298.15 K and 1 atm with use of the IEFPEM(Tolunen)-M06-2X/6-31G(d) harmonic frequencies. Non-covalent interaction analysis was performed using Multiwfn,[15] and the result was visualized by VMD.[16]

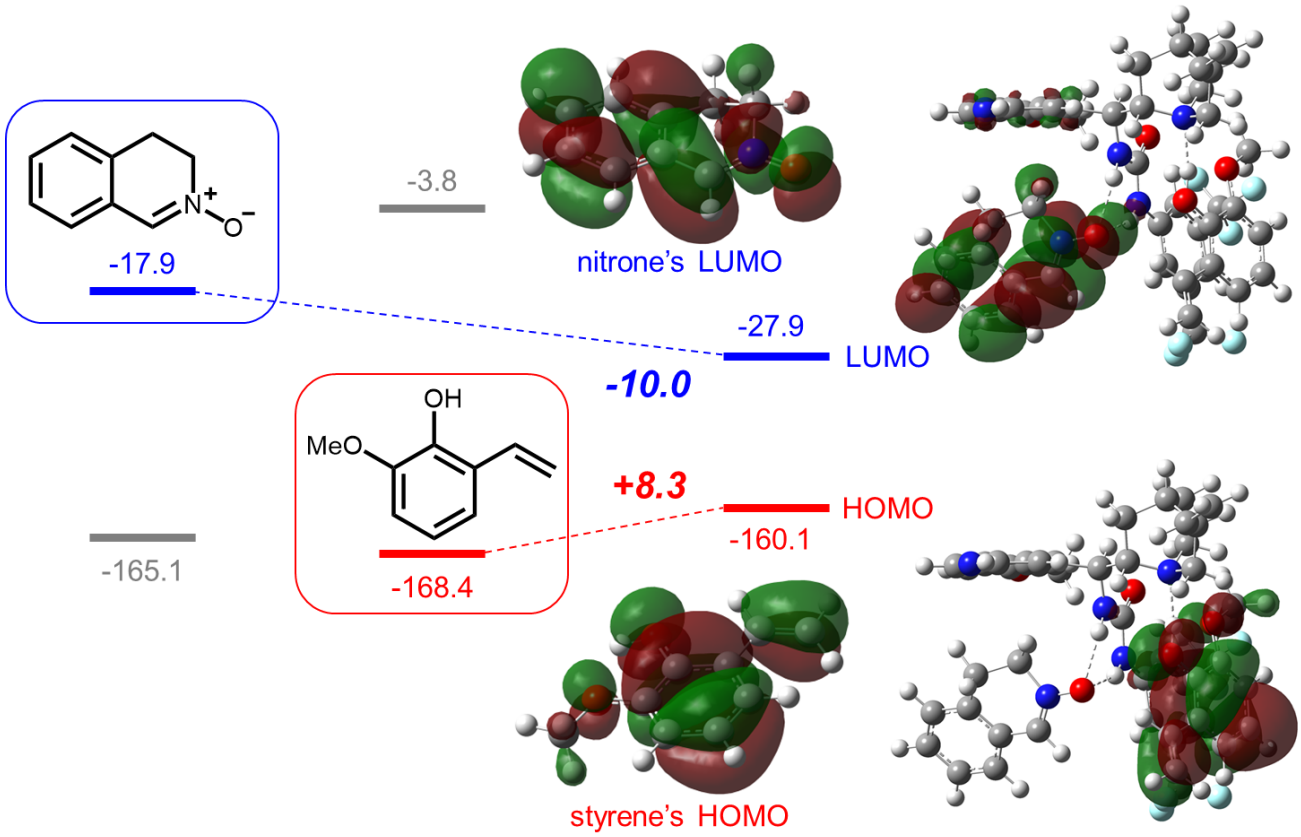

Figure S5. HOMO-LUMO energy levels by DFT calculations. All calculations were performed at M06-2X/def2tzvpp-IEFPCM(toluene)//M06-2X/6-31G(d)-IEFPCM(toluene). All energies are in kcal mol^{-1}.

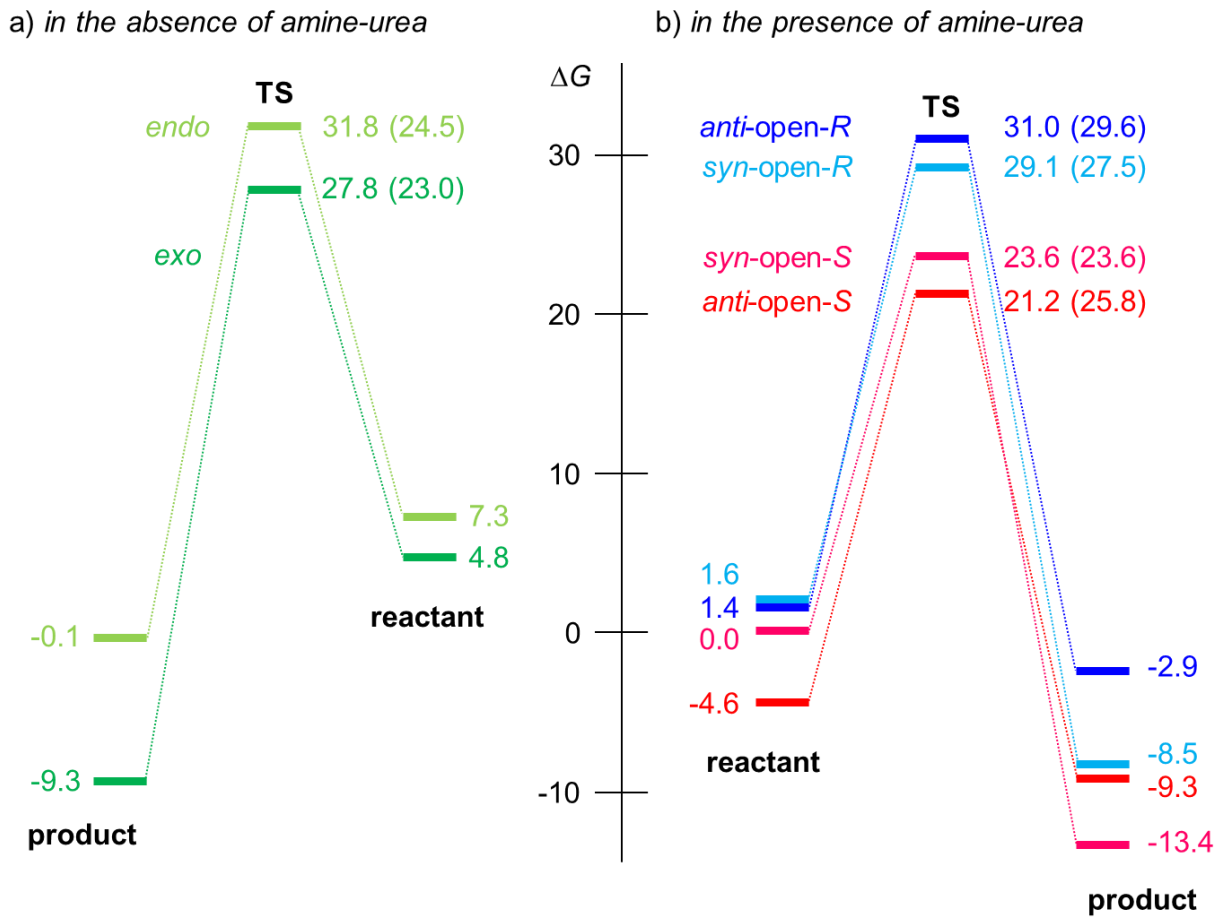

Figure S6. Computed energy profiles for the cycloaddition. All calculations were performed at M06-2X/def2tzvpp-IEFPCM(toluene)//M06-2X/6-31G(d)-IEFPCM(toluene). All energies are in kcal mol^{-1}. The energy of the sum of nitrone **1a** and 2-hydroxy-3-methoxystyrene is set to zero for the cycloaddition in the absence of amine-urea **2** (a, left). The energy of the sum of nitrone **1a**, 2-hydroxy-3-methoxystyrene, and amine-urea **2** is set to zero for the cycloaddition in the presence of **2** (b, right).

Anti-Open-S-Reactant

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.025649 a.u.

Thermal correction to Gibbs Free Energy = 0.794345 a.u.

Sum of electronic and thermal Free Energies = -3066.231303 a.u.

The lowest frequency = 6.89 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.253573 a.u.

C	2.5455491853	0.7615444187	2.7923674443
N	2.9102021404	1.6074308416	1.6389793236
C	4.3751200548	1.7273118094	1.6038648489
C	3.0365689555	1.3991170524	4.1230496856
C	4.9242683724	2.498176318	2.8440774626
C	3.7303368034	2.729082687	3.8007766818
C	2.3320869612	2.9597515036	1.7443766273
C	2.7095833932	3.6278076122	3.0915676313
C	1.0358952658	0.4691191279	2.7934089339
N	0.6212873168	-0.0618576687	1.5126019138
C	-0.1691458249	0.6003902435	0.6231785467
O	-0.6900553776	1.6943984498	0.8430256827
N	-0.3691110318	-0.1476117323	-0.5227151752
H	3.0626869688	-0.1909317405	2.6142085466
H	4.7906946331	0.7143566108	1.5555404093
H	4.6497322662	2.2332761164	0.67297191
H	3.7141449805	0.7244256382	4.6564197724
H	2.1905152828	1.5863953401	4.7962824868
H	5.2880985214	3.4846201944	2.5289598355
H	4.0863472177	3.1999228039	4.7222956152
H	1.2512407917	2.8894724021	1.5963175734
H	2.7316120351	3.5264428817	0.8985746455
H	1.8264313214	3.7509076214	3.7293984002
H	0.4919578217	1.4083014809	2.943496185
H	1.059942886	-0.9271186271	1.1932066492
H	3.1295912013	4.6252907115	2.9250764387
O	0.9112499848	-2.6028098019	0.0896416848
N	-0.1500432979	-3.2763139673	0.4069456694
C	2.7142333125	-0.6815145451	-2.8459300378
C	1.7124766964	1.8641929152	-3.5097899683
C	2.4658122897	-0.3274326328	-4.1839875897
C	2.4658187639	0.2629115819	-1.8429329961
C	1.9305263015	1.5234989541	-2.1829977872
C	1.9920901288	0.9297435168	-4.5140762537
H	2.6169818081	-1.070071481	-4.9613488271
H	1.7939939657	1.1847849522	-5.5495700335
H	1.2976922779	2.8319261869	-3.7693405659
O	2.7094887654	-0.0610502391	-0.5541083368
C	3.1774217723	-2.0248952321	-2.4547146752
H	2.9677022019	-2.3058812572	-1.4252936857
H	2.5887535561	0.7067452041	0.0727398357
H	4.0875867174	-3.8735318352	-2.906756661
H	0.1865621825	-1.008460711	-0.5719075406
C	-0.9014075532	0.289133466	-1.7279532577
C	-1.8192639807	1.035631205	-4.2812502135
C	-1.6130248181	1.4793540835	-1.8944977612
C	-0.6837204188	-0.5406926026	-2.8402193296
C	-1.1320212045	-0.1630516444	-4.0905710873
C	-2.0491009307	1.8339268368	-3.1714506679
H	-1.7953855443	2.1236234881	-1.0442308951
H	-0.1100315819	-1.4551678794	-2.7190469328
H	-2.1589471367	1.3339844317	-5.2668445352
C	-2.7158582167	3.1679275995	-3.3406830834

C	-0.8756105555	-1.0398363889	-5.2821165665
F	-2.0210208909	-1.5450848938	-5.7732308118
F	-0.0777597812	-2.0763000322	-4.9947706351
F	-0.3031219228	-0.3548982638	-6.2851187625
F	-1.8084896788	4.1644646979	-3.3839910698
F	-3.5431472115	3.4492913989	-2.3240371679
F	-3.4259103239	3.2423474789	-4.4740206209
H	2.55688817	-1.2513807185	4.3999846194
C	1.4843599365	-1.3505937331	4.5240506182
C	0.602913963	-0.532759145	3.8597571449
C	-0.795680507	-0.7476753147	4.0785031398
C	0.9973544241	-2.3762612549	5.3723526392
C	-1.1721918204	-1.8171868772	4.9343782593
C	-1.8037652777	0.0156181127	3.4281073401
H	1.7061174199	-3.0221332212	5.8869806341
H	-2.8170261709	-2.9135810525	5.7862566048
C	-3.1319569749	-0.2975690645	3.6157867682
H	-1.5251525567	0.8273750166	2.7672022527
C	-3.5114666234	-1.3658324189	4.476450588
H	-4.56990086	-1.5712384292	4.5977719467
C	-2.556136877	-2.096122573	5.1214960957
N	-0.2745926606	-2.6228690834	5.5701444784
C	-2.0748020919	-4.64469296	-0.0731923365
C	-4.4343334854	-5.9213810886	0.6576897496
C	-2.366280323	-4.8421130556	1.2864482666
C	-2.9561643581	-5.0986149894	-1.0581654897
C	-4.1365938569	-5.735003757	-0.6908456508
C	-3.5491887545	-5.4788047989	1.640662827
H	-4.8245477418	-6.0815421678	-1.454760086
H	-3.7786995042	-5.6314401383	2.6916634755
O	-4.1610917032	0.3459620484	3.0224064105
C	-3.8359763263	1.3760494337	2.1027525221
H	-3.203799151	0.9975911362	1.2918130678
H	-3.3101486611	2.197582323	2.6019605944
H	-4.7848253354	1.7330989553	1.7045875312
O	1.6269625931	2.3069846088	-1.107694802
C	1.0497904943	3.5712123868	-1.3692657543
H	1.7701715559	4.2321198825	-1.8670876995
H	0.7706230358	3.9836175216	-0.4001990514
H	0.1539265119	3.479313776	-1.9899513265
C	6.0648700344	1.770469877	3.4946963038
H	5.8749937385	0.73438024	3.7815531956
C	7.2643331527	2.2965949772	3.7269832834
H	8.0563729099	1.7272104895	4.2029789089
H	7.4962353704	3.320882029	3.4443938265
C	-1.3285188741	-4.400969585	2.2865420556
H	-0.5960091897	-5.2069460618	2.4257354765
H	-1.7754503588	-4.1979681856	3.2641394227
H	-2.7178360668	-4.9416518511	-2.1063871814
H	-5.357267681	-6.4140697661	0.946330746
C	-0.6093070307	-3.1488008209	1.8124433575
H	0.2893629611	-2.9455743677	2.3962881388
H	-1.25549226	-2.2624245898	1.8401050597
C	-0.8453069024	-3.9576102321	-0.448041351
H	-0.4751705344	-3.9524704286	-1.4680534879
C	3.8009672863	-2.8882583352	-3.2595344796
H	4.0592192127	-2.6435977747	-4.2864431909

Anti-Open-S-TS

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3066.992162 a.u.

Thermal correction to Gibbs Free Energy = 0.798218 a.u.

Sum of electronic and thermal Free Energies = -3066.193944 a.u.

The lowest frequency = -487.48 cm^{-1}

Number of imaginary frequencies = 1

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.216344 a.u.

C	-0.9523521891	1.3088220975	-0.5147481247
N	-0.5752065734	2.1498789166	-1.6694353003
C	0.8920541662	2.1385328172	-1.7847306828
C	-0.3830582611	1.8974113074	0.8058568788
C	1.5858797006	2.7522627476	-0.5295251699
C	0.4644893506	3.1312717672	0.4657193277
C	-1.022466086	3.5452575478	-1.505908341
C	-0.4446221678	4.1681687738	-0.2065103702
C	-2.4778968309	1.094905034	-0.4382150996
N	-3.0282723595	0.7212821842	-1.7220125302
C	-3.7034054657	1.5821453232	-2.5243389989
O	-4.085249425	2.6981306302	-2.168106787
N	-3.9527640749	1.0452363269	-3.7755038826
H	-0.4948327235	0.334283721	-0.7296211653
H	1.2057729274	1.0993836654	-1.9361296399
H	1.1553011488	2.6902247543	-2.6925563503
H	0.2106978084	1.1546662403	1.3481933005
H	-1.1993858347	2.1931372453	1.477592345
H	2.103235319	3.6780776496	-0.8113172355
H	0.9101282319	3.5428279061	1.3766508438
H	-2.113212349	3.5686033212	-1.5226622681
H	-0.6777671514	4.0859609091	-2.3929619573
H	-1.2509086493	4.449310953	0.4803426358
H	-2.9514061269	2.0404508817	-0.1493427917
H	-2.7021039344	-0.1522640856	-2.1351734494
H	0.1233731139	5.0781007903	-0.4276178466
O	-3.0855942362	-1.6503252763	-3.3384806148
N	-3.7193830848	-2.7324503587	-2.9970112212
C	-1.22089254	-1.4170912483	-5.1841223409
C	-1.2209647544	0.7663428559	-6.9614845441
C	-1.3985437815	-1.6123206004	-6.5629663375
C	-1.0180604454	-0.1111753078	-4.7136477785
C	-1.0568508904	0.9800839208	-5.5981834256
C	-1.3850802918	-0.537824134	-7.4398793693
H	-1.5338588301	-2.618464347	-6.9473088701
H	-1.5254018267	-0.6969024922	-8.5035178214
H	-1.2567194698	1.6018839533	-7.6510065126
O	-0.8286647464	0.0783353937	-3.3922026848
C	-1.3218625967	-2.4845797207	-4.1801922852
H	-0.8189689293	-2.2822844825	-3.2406615517
H	-0.8754279424	1.0333826007	-3.1113217907
H	-1.4637078276	-4.5685293686	-3.7421306863
H	-3.6821325812	0.0678464263	-3.9039263958
C	-4.3128643938	1.7398385447	-4.9209623672
C	-4.9256563858	3.0016693975	-7.3659732452
C	-4.6793824249	3.0902896651	-4.9444103015
C	-4.2681453137	1.0248950438	-6.129730874
C	-4.5724457259	1.6534122176	-7.3246345327
C	-4.9692331454	3.6956373285	-6.1653017137
H	-4.7216027185	3.6538413859	-4.0222710847
H	-3.9594920955	-0.0182429461	-6.1232677023
H	-5.1612276153	3.4892552245	-8.3050682918
C	-5.248736511	5.1710052166	-6.1636019895
C	-4.4438094805	0.9044013696	-8.6197309404
F	-5.4459577869	1.2005668464	-9.4613183455
F	-4.4391151579	-0.4229102404	-8.446577881

F	-3.302729704	1.2223571178	-9.2615748658
F	-4.1099943532	5.8766615716	-6.0389780873
F	-6.0386348891	5.5313553748	-5.1425251851
F	-5.8399655308	5.576952952	-7.2957086405
H	-0.9330636585	-0.791975582	0.9652330197
C	-2.0039359393	-0.8871335899	1.104359587
C	-2.8887729571	0.0030875932	0.5453639958
C	-4.2841395658	-0.2074488125	0.7882049418
C	-2.4876932871	-1.9861531397	1.8573521655
C	-4.6582160815	-1.3498495874	1.5448689864
C	-5.29094345	0.654752085	0.276318656
H	-1.7770323237	-2.6914892729	2.2844518287
H	-6.3023691755	-2.484315881	2.3471364309
C	-6.6181405492	0.3711500617	0.5032224462
H	-5.0106251928	1.5251046436	-0.3042151243
C	-6.9962794566	-0.7742341983	1.258320993
H	-8.0547268748	-0.956317886	1.4127484552
C	-6.0409328279	-1.6065618996	1.765198913
N	-3.7584044961	-2.234001243	2.0629942976
C	-4.2606347961	-5.0153961329	-3.5770417672
C	-5.1175385299	-7.5535759003	-2.8256608983
C	-4.0682129118	-5.4510639868	-2.256576496
C	-4.8698969719	-5.8508503355	-4.5125742243
C	-5.2967150344	-7.1216330797	-4.1376601789
C	-4.506833463	-6.7188828431	-1.8900187522
H	-5.7734350029	-7.7699281473	-4.8656304119
H	-4.3687559684	-7.0564598008	-0.866281736
O	-7.6492052183	1.1166730078	0.0442945738
C	-7.3259070737	2.2556527361	-0.7357938929
H	-6.7483872586	1.9787142113	-1.6248868036
H	-6.7471837146	2.9801336876	-0.1518043922
H	-8.2768419777	2.6968237396	-1.0316453219
O	-0.9710611824	2.1981670239	-4.9875025182
C	-1.2114872601	3.3344920992	-5.7970293132
H	-0.4037088772	3.476189202	-6.5243987025
H	-1.2522543592	4.1891152664	-5.1216350891
H	-2.1680116561	3.2449271322	-6.3260787396
C	2.5996613414	1.8160333182	0.0630935561
H	2.2523690909	0.8035391739	0.2789846634
C	3.8636908836	2.136124234	0.3261050875
H	4.5569280548	1.4219678109	0.7591700759
H	4.250261484	3.1302321003	0.1136161825
C	-3.3637032076	-4.5127469684	-1.3061434377
H	-2.2774876721	-4.6078874531	-1.4397654707
H	-3.583183982	-4.7666487141	-0.2649373074
H	-5.0125918503	-5.5009372002	-5.5316426416
H	-5.4550133564	-8.5413327698	-2.5280424597
C	-3.7769281189	-3.0674502201	-1.5639383071
H	-3.1117267809	-2.3623542592	-1.0600699527
H	-4.7996208824	-2.8853901428	-1.2138219612
C	-3.767828634	-3.6764289611	-3.9512110303
H	-4.0042394363	-3.2931067632	-4.9399995277
C	-1.765693497	-3.7816470193	-4.427337592
H	-1.9212215617	-4.1198414564	-5.4482722573

Anti-Open-S-Product

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.048326 a.u.

Thermal correction to Gibbs Free Energy = 0.801674 a.u.

Sum of electronic and thermal Free Energies = -3066.246652 a.u.

The lowest frequency = 8.37 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.268363 a.u.

C	1.974057891	0.8067332671	2.6673572148
N	2.4100129634	1.6200760676	1.5105807959
C	3.8788943698	1.5375868895	1.4179735135
C	2.5575810732	1.382895527	3.9879939749
C	4.5802977458	2.1397970836	2.6726994466
C	3.46275716	2.5749252137	3.6483228444
C	2.029190338	3.0385438713	1.6494272518
C	2.6081564726	3.6439928169	2.9554958319
C	0.4392269541	0.67401575	2.7342717937
N	-0.1329267143	0.2831312606	1.4573675201
C	-0.7211146538	1.1958482887	0.6324119186
O	-1.0756934048	2.3156827042	0.9987555604
N	-0.9121768809	0.7132770048	-0.6492006881
H	2.3876415327	-0.1913839083	2.4687629699
H	4.1440789928	0.4819627429	1.2895505482
H	4.1778490812	2.0584094349	0.5031818857
H	3.1094501074	0.6182210741	4.5432232075
H	1.7482186228	1.7207071349	4.6476093835
H	5.1366422047	3.0407058456	2.3847478273
H	3.9123942406	2.9751189601	4.5622151543
H	0.9420095784	3.1182480049	1.6065993134
H	2.4228400458	3.5481901072	0.7645549163
H	1.8015311354	3.9596478955	3.6264569928
H	0.0221685867	1.6589130025	2.9705757006
H	0.2752366753	-0.5326407718	1.0051820202
H	3.214839779	4.5297716462	2.7398791974
O	-0.0546175692	-2.1219392956	-0.4583460076
N	-0.746647902	-3.1809777699	0.1746554616
C	1.5188388459	-1.6149235763	-2.1487610995
C	2.0482168846	0.5981163549	-3.7890743471
C	1.4510463145	-1.7331621385	-3.5405115448
C	1.9146537628	-0.3961429377	-1.588583653
C	2.1274455841	0.7267056798	-2.4074812041
C	1.7343711061	-0.6421788945	-4.3512266563
H	1.1730847878	-2.676459205	-3.9975142787
H	1.6719041965	-0.7355312572	-5.4294208339
H	2.2023929388	1.4565787305	-4.4333772318
O	2.0440316944	-0.319524189	-0.2498589605
C	1.0976903941	-2.6718660054	-1.1590428474
H	1.8939463748	-2.8082157287	-0.4161136012
H	2.096196491	0.6165687482	0.1152485194
H	1.3236013004	-4.8183055094	-1.4658978711
H	-0.6897977222	-0.2709895418	-0.7989739578
C	-1.1303914411	1.4743640376	-1.7930166768
C	-1.4341351842	2.8704598896	-4.221859586
C	-1.2999793434	2.8632302546	-1.7909199015
C	-1.1249166867	0.7903926638	-3.0195652352
C	-1.2749523617	1.4858213388	-4.2060584172
C	-1.441346582	3.5339006336	-3.0039263706
H	-1.3124115837	3.406042831	-0.8559911736
H	-0.9659167568	-0.2848966573	-3.0348601485
H	-1.5483825294	3.4093641899	-5.1559499718
C	-1.4942997755	5.034274752	-2.9755228919
C	-1.1994876824	0.7687184769	-5.5229797671
F	-2.2163038005	1.1127607787	-6.3283808036
F	-1.2230430415	-0.5625323065	-5.3889132754

F	-0.0694706381	1.0838419888	-6.1845312376
F	-0.2578304008	5.5557600196	-2.8623567526
F	-2.2035153856	5.4949055772	-1.9366436758
F	-2.0313919893	5.5433042283	-4.0925164727
H	1.8438898907	-1.2986634472	4.1598470583
C	0.7825308846	-1.2500778868	4.3785761611
C	-0.0357488042	-0.3156204892	3.7914504424
C	-1.4223883314	-0.3322774095	4.1423331911
C	0.2416955851	-2.1877100003	5.2924758498
C	-1.8563651622	-1.3157880593	5.071302757
C	-2.3639970499	0.5813365073	3.5971941546
H	0.8995148481	-2.9249295703	5.7495811283
H	-3.5382495201	-2.1140090043	6.1509068647
C	-3.686581925	0.5061086858	3.9690305047
H	-2.0412166969	1.3253808412	2.8796727955
C	-4.123648385	-0.4730386763	4.9040521837
H	-5.1758427646	-0.4917725852	5.1683602852
C	-3.2309896494	-1.3563688554	5.4376061088
N	-1.0222989251	-2.2345497371	5.6347077791
C	-0.8396002128	-5.6261646537	-0.2521091013
C	-0.9273885003	-8.1840329827	0.8504700026
C	-0.0712354643	-5.9234119095	0.8803135039
C	-1.650053854	-6.6049218983	-0.8215263475
C	-1.6899886772	-7.8861350596	-0.2762171095
C	-0.1273332672	-7.2015373458	1.4303416615
H	-2.3219533484	-8.6463698713	-0.724235441
H	0.4562982819	-7.4267670468	2.3193238579
O	-4.6600173879	1.3197445933	3.4982785147
C	-4.2775866114	2.2986859203	2.5474543004
H	-3.8348979158	1.837176789	1.6578686409
H	-3.5536633102	3.0014247077	2.9753323078
H	-5.1903879368	2.8281518322	2.277090228
O	2.3629300488	1.8838142876	-1.7245887578
C	2.3112700629	3.0838037883	-2.475861836
H	3.1551042462	3.1491535882	-3.1719562367
H	2.3683849534	3.9000596441	-1.7557585159
H	1.3690094704	3.1561665705	-3.0320604308
C	5.55015098	1.1729086935	3.2893117078
H	5.1591393021	0.1805310952	3.5227274942
C	6.8249186007	1.4452370711	3.553847334
H	7.4852227229	0.7116099899	4.0053447915
H	7.2536823414	2.4181285265	3.3248644102
C	0.7434837512	-4.799746334	1.4658195048
H	1.6659722353	-4.6534282044	0.8885435943
H	1.0443064113	-5.0323680544	2.4925269422
H	-2.2520756181	-6.362132299	-1.6935360455
H	-0.9627665168	-9.1784275773	1.2844739899
C	-0.0991661814	-3.5170511147	1.4634025092
H	0.4998407497	-2.6496686771	1.755851408
H	-0.8990879712	-3.6234762929	2.2036344228
C	-0.7241099646	-4.249146492	-0.8499301528
H	-1.5723747969	-4.0625966348	-1.514784298
C	0.5942393403	-4.0278043517	-1.6573124782
H	0.3676234357	-4.0290827558	-2.7244206845

Anti-Open-R-Reactant

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.015833 a.u.

Thermal correction to Gibbs Free Energy = 0.795213 a.u.

Sum of electronic and thermal Free Energies = -3066.22062 a.u.

The lowest frequency = 11.31 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.244868 a.u.

C	-2.572268739	-1.1112137401	2.7560954545
N	-3.3224626322	-1.1243491746	1.4824157753
C	-4.7138240507	-0.7227547564	1.7642271552
C	-3.2846919609	-2.0023517395	3.8137147191
C	-5.479255181	-1.8038087362	2.5792382433
C	-4.4132534437	-2.7816589308	3.1221949659
C	-3.3500854044	-2.476647632	0.8819154786
C	-3.8149755099	-3.5275026753	1.9215354973
C	-1.099537182	-1.5350684543	2.5738868045
N	-0.4847608763	-0.9240503273	1.4085960493
C	-0.0910271474	-1.6589752722	0.3293414508
O	-0.1152900273	-2.8927006119	0.3113357716
N	0.3541152216	-0.8964002641	-0.7270631693
H	-2.58433962	-0.0603372146	3.0592023771
H	-4.6795901498	0.2208592683	2.3150616118
H	-5.2113819988	-0.5227415011	0.8098197223
H	-3.6766292061	-1.3958970468	4.6379472494
H	-2.5752747858	-2.7088063876	4.2606974476
H	-6.1399310051	-2.3698407974	1.9096189294
H	-4.8736947607	-3.4822918797	3.8254187681
H	-2.3648466888	-2.721448817	0.4837739964
H	-4.0408858669	-2.4250661528	0.0346281746
H	-2.9713566224	-4.1452936841	2.2516593885
H	-1.0722661671	-2.6145249135	2.3853653604
H	-0.4529856167	0.0908082413	1.3421467298
H	-4.5563871262	-4.20243852	1.4820665832
O	0.6851667387	1.6544164786	0.3684873081
N	1.0913706967	2.7027196552	-0.2626072484
C	0.4255883773	3.8123016895	-0.3245401468
O	-2.2051126772	0.5584163249	-0.3441746999
C	-1.4176038193	1.7762258178	-2.6852388133
C	-0.6194692114	2.3219027932	-3.6087215489
H	-2.6557539262	0.0901817345	0.4289362352
H	-0.141027119	1.7127372823	-4.3680097833
H	-0.4153137129	3.3909356897	-3.6344468373
H	0.323632906	0.1195121752	-0.5835734478
C	1.1270831406	-1.341683473	-1.7885477467
C	2.8675543651	-2.0306034163	-3.9086606736
C	1.463174782	-2.6837310737	-2.0268685613
C	1.6273981813	-0.3644219416	-2.6612756783
C	2.4950901983	-0.7097831044	-3.6873376592
C	2.3250099023	-2.9986265534	-3.0709077842
H	1.059799547	-3.459894519	-1.3913454038
H	1.3213641036	0.6711237413	-2.5292829465
H	3.5543947376	-2.2947329987	-4.7031304755
C	2.6412735335	-4.4499548543	-3.3014450535
C	3.0917116795	0.3995330885	-4.5026131657
F	3.7579695196	-0.0483931664	-5.5704122541
F	3.9552538055	1.1289434117	-3.7688218384
F	2.1563803441	1.2618886	-4.9413454533
F	3.7597597799	-4.6123514417	-4.021312603
F	1.6529812965	-5.073667334	-3.9602124857
F	2.8082674559	-5.1099625104	-2.1426055028
H	-1.6755330891	0.0197519493	4.8321090156
C	-0.6979045642	-0.4479760384	4.8487434139
C	-0.2627466375	-1.2573338074	3.8265684339

C	1.0430978838	-1.8328799314	3.9573389775
C	0.1296128292	-0.2064712335	5.9713918474
C	1.7891726741	-1.5214692599	5.1279938926
C	1.6159938872	-2.6886546198	2.9782958633
H	-0.2336191488	0.437752168	6.7701988197
H	3.6328051369	-1.8254164366	6.1922115743
C	2.8854408159	-3.1899802537	3.1575004795
H	1.0512968283	-2.9477588817	2.0925074865
C	3.6286458745	-2.8864315173	4.3306771245
H	4.622171155	-3.310807936	4.4313136595
C	3.0895795727	-2.0765641665	5.2871265278
N	1.3277500038	-0.712689053	6.122374825
C	0.9237988284	4.9662821805	-1.0616679051
C	1.8499994293	7.1577792047	-2.5055776092
C	1.9943907862	4.8078633466	-1.9571209089
C	0.3156486023	6.2153735145	-0.9041139357
C	0.7820981073	7.310150643	-1.6224587359
C	2.448672862	5.9097338557	-2.6732752533
H	0.314131523	8.2808401601	-1.4953304829
H	3.2751880248	5.7902320291	-3.368578422
O	3.5264020346	-3.9850411833	2.268051832
C	2.8953798776	-4.1931621126	1.016295275
H	1.9467136106	-4.7303961357	1.1281969848
H	3.5881285088	-4.7857711899	0.4203926271
H	2.6969303861	-3.2373936943	0.5165728609
C	-6.3272860998	-1.1862345742	3.6521677129
H	-5.8056211962	-0.5589152451	4.3778805198
C	-7.6434054545	-1.3449297009	3.7627353682
H	-8.2114361501	-0.8760349139	4.5600015785
H	-8.2002700396	-1.9540396044	3.0545773076
H	-1.5588548065	0.6975577457	-2.663693932
C	-2.1038816484	2.5373246021	-1.6299485394
C	-3.1885243004	3.9863491054	0.5136980173
C	-2.4296663581	1.8778506407	-0.4361968986
C	-2.3920731269	3.9055734601	-1.7609913459
C	-2.9386522865	4.6207027966	-0.7097753847
C	-2.9253550125	2.6286598739	0.6512518138
H	-2.1836552817	4.3996909475	-2.7049819186
H	-3.1707231417	5.6746020091	-0.8235148238
H	-3.5913224184	4.5556789949	1.3434657519
O	-3.1016120067	1.9133469252	1.8015254075
C	-3.5699854594	2.6180486628	2.9329519055
H	-2.8771293152	3.4197286789	3.2124171002
H	-3.6279538154	1.8909780138	3.7456687653
H	-4.5659395036	3.0392656866	2.7539405167
C	2.5536529555	3.4191062488	-2.1367627413
H	3.5973399092	3.4501856244	-2.4604358868
H	1.9922576906	2.9024299319	-2.9281108247
H	2.2160512858	8.0110613775	-3.0675833321
H	-0.5204632219	6.3161452057	-0.2176702255
H	-0.5202268212	3.8324922984	0.2057753653
C	2.4568470344	2.6269397871	-0.8427529995
H	2.663787609	1.5662833242	-0.9805019195
H	3.1348363807	3.0176556008	-0.0765147623

Anti-Open-R-TS

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3066.975977 a.u.

Thermal correction to Gibbs Free Energy = 0.798826 a.u.

Sum of electronic and thermal Free Energies = -3066.177151 a.u.

The lowest frequency = -499.67 cm^{-1}

Number of imaginary frequencies = 1

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.201416 a.u.

C	-1.6572484715	-2.0143398343	2.3703245048
N	-2.3491837665	-2.1421782738	1.06702028
C	-3.8031011034	-2.022717512	1.3053560388
C	-2.2595216748	-3.0101370527	3.4036428945
C	-4.3807136812	-3.2529347234	2.0602519288
C	-3.1707539912	-3.9998545927	2.661167374
C	-2.1127975921	-3.4724194558	0.4606211037
C	-2.3821119534	-4.6001070482	1.4892537862
C	-0.127870439	-2.2164724082	2.2647742243
N	0.4644858417	-1.5545228767	1.1131839603
C	0.9842230213	-2.2638590287	0.0718949568
O	1.1393292041	-3.4870792171	0.1039589328
N	1.337063713	-1.4879096114	-1.0107390184
H	-1.8455405935	-0.9786057956	2.6690104985
H	-3.9720769822	-1.1110496878	1.8801451023
H	-4.29747886	-1.8901388234	0.3378933196
H	-2.8159213921	-2.4765484973	4.1828715639
H	-1.4620608149	-3.5606544819	3.9162650367
H	-4.8692342327	-3.9280366874	1.3453646914
H	-3.512941024	-4.7834587532	3.3439565017
H	-1.0970381195	-3.533582647	0.0732095329
H	-2.7933305005	-3.5489162418	-0.3931306225
H	-1.4394514232	-5.0278227233	1.851145579
H	0.0641179639	-3.2841021976	2.1113411984
H	0.2770365413	-0.566122963	0.9685367785
H	-2.9477991839	-5.4148611747	1.0259381027
O	1.2096227758	1.3339088553	-0.5190285972
N	2.2241637117	2.0519157919	-0.9085352565
C	1.8938430177	3.2400976644	-1.4561373686
O	-1.323238323	0.0670974419	-0.3467109369
C	-0.1850901457	1.776162988	-2.153977068
C	0.6427823324	2.6532317454	-2.8599681641
H	-1.8558398324	-0.5818401648	0.1971932214
H	1.2652119188	2.2444118944	-3.6535717801
H	0.3059014816	3.6653448539	-3.06730334
H	1.1648513695	-0.4771611997	-0.9374792161
C	1.986413049	-1.9333804363	-2.1577941376
C	3.3657805366	-2.6313334061	-4.5244783446
C	2.5182885529	-3.219579896	-2.319902123
C	2.1427750539	-1.0087113095	-3.2044143086
C	2.8227283354	-1.3593990146	-4.3600701007
C	3.1985656276	-3.5405672062	-3.4905269187
H	2.3976273861	-3.9558323939	-1.5385412455
H	1.7226921216	-0.0120485202	-3.1007121448
H	3.8984698256	-2.8998384661	-5.4294939362
C	3.7314592941	-4.9404793053	-3.6219401233
C	3.0364366172	-0.3441771959	-5.4460635299
F	2.8873079735	-0.8789386293	-6.6633373792
F	4.2775066289	0.1714993702	-5.3971089873
F	2.1838305522	0.6901625206	-5.349336056
F	4.6644518961	-5.0344658918	-4.5788924242
F	2.7601511841	-5.8135672086	-3.9270675612
F	4.2856973147	-5.3640392527	-2.4741597571
H	-1.0271537894	-0.7080862397	4.4532953873
C	0.0052475943	-1.0308005724	4.5247097803
C	0.5971618761	-1.7925808195	3.5460685784

C	1.9640985979	-2.1723525442	3.7483297676
C	0.7403194161	-0.6455697529	5.6719200459
C	2.6071886175	-1.7263478207	4.9357430463
C	2.6936418878	-2.9644495904	2.8214994009
H	0.2537625607	-0.0411237552	6.4353623717
H	4.4295891012	-1.7312528189	6.0769305563
C	4.0126134803	-3.2735035643	3.0642461908
H	2.2084589986	-3.3280184791	1.9258031571
C	4.6558773615	-2.8320592129	4.2525381378
H	5.6947824552	-3.1055846011	4.4049220494
C	3.9663279246	-2.0827114644	5.1608932766
N	1.9913954258	-0.9681227628	5.8855123643
C	2.9798838078	4.0534481671	-2.0450656526
C	5.0202910387	5.5315002502	-3.2251825307
C	4.089204769	3.3930050534	-2.5917773484
C	2.8926225632	5.443880387	-2.0971414158
C	3.9122946828	6.1838254274	-2.6893174713
C	5.1072358458	4.1406669153	-3.1740974224
H	3.8452094188	7.2662646061	-2.7268850366
H	5.9716486521	3.6321734884	-3.5927347027
O	4.7948027257	-3.9951755958	2.2255439168
C	4.2373299147	-4.3522076612	0.9727883567
H	3.3723786892	-5.0141735579	1.0927682477
H	5.0249138038	-4.8678176847	0.4241952999
H	3.9185746021	-3.4604546672	0.4196617241
C	-5.4029651241	-2.8428800085	3.078959603
H	-5.0603858791	-2.1625770753	3.8613413576
C	-6.6725264474	-3.2403076647	3.0800216271
H	-7.3740981883	-2.9134761271	3.8410566292
H	-7.0548105427	-3.9113658594	2.314404045
H	-0.190879124	0.7149542906	-2.3758975351
C	-1.2274114143	2.2525412231	-1.2436482301
C	-2.9991585422	3.1483843526	0.7449967311
C	-1.7379062467	1.351977261	-0.2959779079
C	-1.6447000365	3.5932717937	-1.1970421328
C	-2.531068987	4.0328485527	-0.2282899141
C	-2.5884368446	1.8209760985	0.7201661969
H	-1.2836662888	4.2927821943	-1.9440651358
H	-2.8586987625	5.0668050671	-0.2140108869
H	-3.6705358001	3.5018093305	1.5186826864
O	-2.9331174481	0.8866924114	1.6555581556
C	-3.6482288529	1.3393392208	2.787759799
H	-3.1041074758	2.1403461295	3.3005183237
H	-3.742004519	0.4796938895	3.455099074
H	-4.6483378751	1.6927164111	2.5127478362
C	4.0934414134	1.8852583288	-2.5348884362
H	5.1061806107	1.488802191	-2.6522149061
H	3.5026779784	1.4961508016	-3.372507675
H	5.8197486611	6.1053892638	-3.6830351554
H	2.0270975429	5.9432418057	-1.668742028
H	1.1161588568	3.7684232732	-0.9041515715
C	3.5047767747	1.3970032583	-1.2143339908
H	3.3185912921	0.3217206476	-1.2199616191
H	4.1935367854	1.6137044588	-0.38970243111

Anti-Open-R-Product

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.039158 a.u.

Thermal correction to Gibbs Free Energy = 0.802837 a.u.

Sum of electronic and thermal Free Energies = -3066.236321 a.u.

The lowest frequency = 7.24 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.259293 a.u.

C	-2.688602469	-1.3911660146	2.7058673773
N	-3.2109935509	-1.245131583	1.3273596186
C	-4.6667002084	-1.004674719	1.4143869198
C	-3.4708807833	-2.4913237653	3.4769574908
C	-5.441215199	-2.2567022279	1.9159436166
C	-4.385619207	-3.2284129233	2.4879451846
C	-3.0084738749	-2.4823226026	0.5393007312
C	-3.5264613621	-3.719768958	1.3152719506
C	-1.1679434358	-1.6605122986	2.7495565543
N	-0.4378500823	-0.8743000065	1.762235121
C	0.1282995972	-1.4788413194	0.6741382108
O	0.344007285	-2.6905307053	0.6282760014
N	0.4557425533	-0.6260099701	-0.360260794
H	-2.8633878207	-0.4110709806	3.15056424
H	-4.8210226407	-0.1594764682	2.0901436766
H	-5.019671914	-0.6976924212	0.424697444
H	-4.0523620631	-2.0557717006	4.2975675086
H	-2.7770859067	-3.2057617121	3.9357003827
H	-5.9242563276	-2.7540865926	1.0648129917
H	-4.8816050054	-4.0675308645	2.9849602639
H	-1.9543913248	-2.5968969795	0.2877220135
H	-3.5546805515	-2.3467988484	-0.3993140108
H	-2.6877277931	-4.3160920444	1.69330563
H	-0.9893648961	-2.7065153343	2.4752017241
H	-0.6826148665	0.1072463158	1.6792472123
H	-4.1127990716	-4.3682341035	0.6565197937
O	0.0793664802	2.2407141697	-1.1574688446
N	0.9956240738	3.3216778643	-0.8193900974
C	0.5948906844	4.4804597702	-1.6860723105
O	-1.9993311178	1.0261191872	0.258255863
C	-1.130440346	2.8445758446	-1.6089929919
C	-0.5929504953	3.9463808183	-2.5105133638
H	-2.5675785632	0.3262700676	0.7053983435
H	-0.2285264362	3.4932107581	-3.437696705
H	-1.3070444941	4.7290319446	-2.7703523067
H	0.0385373599	0.307111773	-0.3754054545
C	1.1231742211	-1.0366682157	-1.5199455655
C	2.5068012155	-1.7035231827	-3.8884993728
C	1.9826702702	-2.140391663	-1.5557734071
C	0.9543052408	-0.2804233026	-2.6871813201
C	1.649246272	-0.6079847979	-3.8417699779
C	2.6525697355	-2.4578662755	-2.7326588763
H	2.1156657971	-2.7524369483	-0.6760167499
H	0.293064273	0.5773214643	-2.6724971786
H	3.0432294833	-1.9572230762	-4.7962045232
C	3.5227749058	-3.6831309634	-2.7391004841
C	1.5168249927	0.2506783825	-5.0673101021
F	1.300904062	-0.4834193855	-6.1671671971
F	2.6364067978	0.9603446484	-5.2914212414
F	0.508745389	1.132606657	-4.9642607532
F	4.4464953655	-3.6362052699	-3.708748708
F	2.8043468663	-4.7996644274	-2.9319612603
F	4.1695492055	-3.8368114055	-1.5715425918
H	-2.3033439432	-0.4361127069	5.0015452143
C	-1.2973410579	-0.8083586448	5.153630196
C	-0.5965880906	-1.4435371861	4.1558077253

C	0.7210039631	-1.9071069041	4.4782211246
C	-0.7202097878	-0.6273145428	6.4331624428
C	1.1990863272	-1.6779580298	5.7990459387
C	1.5559202701	-2.583573806	3.5486546552
H	-1.292762976	-0.1183210162	7.2065334881
H	2.8306923599	-1.9528385038	7.1711999815
C	2.811088673	-3.0035108059	3.9277473044
H	1.1990170068	-2.7713580584	2.5444841987
C	3.285457353	-2.7845237276	5.2493495102
H	4.2798017867	-3.1379192123	5.5016980469
C	2.496855045	-2.1386547263	6.1557451639
N	0.478063825	-1.0391305919	6.762015187
C	1.6824469491	5.0404939498	-2.5713221747
C	3.5964127051	6.0397812336	-4.3368151512
C	2.6573209724	4.1855529124	-3.0987806176
C	1.6808723957	6.3910428594	-2.9174541102
C	2.6301930446	6.8911344865	-3.804142836
C	3.6128590662	4.6948873117	-3.9761594172
H	2.6201661153	7.9426377611	-4.0735352296
H	4.3750089024	4.0301105453	-4.3749442695
O	3.6850786825	-3.6386722299	3.1102504966
C	3.3289571387	-3.7421913637	1.7438032591
H	2.4203051362	-4.339464699	1.6075652558
H	4.1683644037	-4.2244603023	1.2444396494
H	3.1623018816	-2.7461841962	1.3157139617
C	-6.5105023037	-1.8843804567	2.9008600135
H	-6.1803944051	-1.3464412774	3.7918470784
C	-7.8043097974	-2.1549611356	2.7515764051
H	-8.5392341672	-1.8644231648	3.4956216394
H	-8.1738464387	-2.6810146715	1.8744752053
H	-1.6467484806	2.0562190969	-2.1672423108
C	-1.9855670818	3.2922408374	-0.4407733917
C	-3.5049998281	4.003179808	1.8059308566
C	-2.3826224666	2.3128765404	0.4734018356
C	-2.3785239022	4.617744623	-0.233709172
C	-3.1372829352	4.9707571819	0.8722382744
C	-3.1180208655	2.6820173513	1.6136453488
H	-2.0906674735	5.3855931797	-0.9437320671
H	-3.4398582858	6.0015258962	1.0218260212
H	-4.0792988044	4.2870139623	2.6798549838
O	-3.3961007977	1.6606199846	2.4754892309
C	-4.1441875971	1.9756582154	3.6337631447
H	-3.610385551	2.6952882164	4.2638528306
H	-4.2710103872	1.0386470398	4.1809192063
H	-5.1302517308	2.3750368917	3.3713060678
C	2.6438086977	2.7613478291	-2.6173040992
H	3.5982594913	2.2640249975	-2.8161234789
H	1.8669614387	2.1904877571	-3.1368229205
H	4.3435064643	6.4257336201	-5.0234146736
H	0.9290369943	7.0520271056	-2.4918691617
H	0.2430072807	5.2673875261	-1.0103866632
C	2.3196816307	2.7704163876	-1.1214982622
H	2.3456279886	1.7665057104	-0.6886134215
H	3.0475177563	3.3874854834	-0.5848957708

Syn-Open-S-Reactant

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.020101 a.u.

Thermal correction to Gibbs Free Energy = 0.797125 a.u.

Sum of electronic and thermal Free Energies = -3066.222976 a.u.

The lowest frequency = 10.21 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.249020 a.u.

C	1.8294663766	1.7094276771	2.7813257374
N	2.3428330297	2.1265794984	1.4635188626
C	3.8009838877	1.9189206965	1.464238968
C	2.2715119156	2.706510492	3.8808296502
C	4.4901249239	2.6390256091	2.6659726681
C	3.4211831483	3.5528220068	3.3114883104
C	2.0679901822	3.5532007831	1.2088366084
C	2.8434100209	4.4513749698	2.2091560079
C	0.2906442756	1.4833180815	2.7987480855
N	-0.2775136841	0.9904971411	1.5620717024
C	-0.979248985	1.8120778339	0.7317703759
O	-1.07974217	3.0253092772	0.8941909532
N	-1.5743818021	1.1311016868	-0.3161520149
H	2.3208470798	0.7538299705	2.9819826097
H	3.9908811906	0.8392542014	1.4923214532
H	4.1844451088	2.2918779432	0.509150503
H	2.5710514698	2.172782878	4.7883561441
H	1.4426325155	3.3707589949	4.1599297879
H	5.2958458137	3.2816461783	2.290178863
H	3.8830802749	4.1524527697	4.1016693763
H	0.9883581326	3.7041403711	1.2709652498
H	2.3651968574	3.7553697709	0.1755920824
H	2.1774378209	5.2025264757	2.6465022972
H	-0.1854591215	2.4537912368	2.969912284
H	-0.2920628665	-0.0108747369	1.3771139983
H	3.6558605997	4.9898703061	1.7079305511
O	-1.3091421952	-1.4813994264	0.5897749921
N	-1.3745872333	-2.7578918043	0.4458863106
C	1.2898933545	-1.6635922273	-1.6533604804
C	0.8154762366	0.4536898013	-3.4339727823
C	0.8956225457	-1.9146876943	-2.9778481091
C	1.437082732	-0.3386229273	-1.2270558692
C	1.1681389699	0.7214136699	-2.1166361651
C	0.6753917844	-0.8715294147	-3.8625601698
H	0.7526665612	-2.9453305381	-3.2929243062
H	0.3640753784	-1.0679801323	-4.8827964238
H	0.6104571024	1.2638601934	-4.1242693905
O	1.8777669148	-0.1041710118	0.0262143647
C	1.5402809847	-2.7449969256	-0.6857681667
H	1.3162873181	-2.497673238	0.3515481336
H	1.854656111	0.8635709884	0.3001633973
H	2.1356893372	-4.710322199	-0.206709979
H	-1.447381275	0.1171879794	-0.3320288232
C	-2.0500571831	1.7088764884	-1.4838188492
C	-2.9105249991	2.7252950209	-3.9697432659
C	-2.423780562	3.0533077466	-1.6051951848
C	-2.1470549021	0.87517611	-2.6082734116
C	-2.5627009979	1.3837803138	-3.8268456266
C	-2.8377639389	3.5357718197	-2.8444753903
H	-2.3679595819	3.7072863459	-0.746007136
H	-1.8465528438	-0.1656413003	-2.527556492
H	-3.23376716	3.1202776843	-4.9261010628
C	-3.1325657655	5.0034962985	-2.9666942505
C	-2.5307621196	0.506097603	-5.0434914347
F	-3.5547767931	0.7603254114	-5.8703267602
F	-2.5698859217	-0.7973526803	-4.7352770975

F	-1.404531552	0.7032837457	-5.7580046216
F	-2.0003440403	5.7159394996	-3.1056163835
F	-3.7595973786	5.4816390474	-1.8834323215
F	-3.899471922	5.2767987341	-4.032124964
H	-1.2631307721	2.0377275107	4.9452539562
C	-0.9240724569	1.0062996486	4.9372916489
C	-0.1077562973	0.5520923469	3.9326475948
C	0.3084069184	-0.820707805	3.978446577
C	-1.3497831855	0.1268306807	5.9619096229
C	-0.1848285688	-1.6144514771	5.0529675695
C	1.1893803908	-1.4227772351	3.0332731159
H	-2.0033143293	0.4983958292	6.7488219105
H	-0.1986735385	-3.5581018343	5.9694881993
C	1.6042762829	-2.7248101393	3.1994633647
H	1.5423420293	-0.8707406374	2.168635511
C	1.0877512884	-3.5229591135	4.2526887627
H	1.4272706345	-4.5507238996	4.3335677438
C	0.2048423672	-2.9799001559	5.1446733802
N	-1.0110614827	-1.1369810795	6.0267382528
C	-1.4431173085	-4.8133034069	-0.7990716558
C	-1.3893547476	-7.5876539346	-0.9914919648
C	-1.0730928257	-5.5808205711	0.3184594856
C	-1.7696706985	-5.4358430938	-2.0065733842
C	-1.746165994	-6.8230394432	-2.1004726945
C	-1.0507072465	-6.9661301964	0.21048404
H	-2.0058891731	-7.3067861926	-3.0362804653
H	-0.7637678214	-7.5640025183	1.0713405431
O	2.5040225668	-3.3367525478	2.3791273831
C	3.5573186934	-2.5168509498	1.8740563542
H	4.0571411736	-2.0041287011	2.7047533534
H	3.1984591671	-1.7832373325	1.1472450522
H	4.2526481341	-3.1960102184	1.3805233846
O	1.2711179828	1.9641605012	-1.5633467835
C	1.0045114191	3.0697785667	-2.4067050934
H	1.7703314903	3.1578893053	-3.1865533448
H	1.0198328564	3.9509489817	-1.765137281
H	0.0166633793	2.9868857302	-2.8733521146
C	5.0908840837	1.6673809307	3.6430096244
H	4.4320721412	0.8790065234	4.0138534052
C	6.3504284861	1.7077928845	4.0691215891
H	6.7381187985	0.984570343	4.7796442823
H	7.0406496312	2.4716920204	3.7183274324
C	-0.6590878167	-4.8378646006	1.5642997903
H	0.4141724009	-4.6034395519	1.5112470617
H	-0.8122141945	-5.4475105733	2.4596091634
H	-2.0454847559	-4.8293374059	-2.8650393634
H	-1.3713018466	-8.670542778	-1.0619086012
C	-1.4433965157	-3.5438115545	1.702642198
H	-1.0454765831	-2.888077401	2.4757002797
H	-2.5055220718	-3.7278910417	1.8959090705
C	-1.4293345023	-3.3602761804	-0.6987842972
H	-1.4194373883	-2.7228572757	-1.5767721959
C	1.9986428695	-3.9628004596	-0.983053117
H	2.2638948853	-4.2472184621	-1.9981329721

Syn-Open-S-TS

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3066.991770 a.u.

Thermal correction to Gibbs Free Energy = 0.800374 a.u.

Sum of electronic and thermal Free Energies = -3066.191397 a.u.

The lowest frequency = -489.38 cm^{-1}

Number of imaginary frequencies = 1

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.214699 a.u.

C	-0.8867782662	1.7389314587	-0.3945197403
N	-0.5405988106	2.3630544762	-1.6857176207
C	0.9264157637	2.3042393638	-1.8273929297
C	-0.456618638	2.6485824297	0.7810313963
C	1.6555598772	2.9145046936	-0.5893376672
C	0.5785325691	3.6505418599	0.242686856
C	-0.9569775302	3.7791848677	-1.7217644793
C	-0.1500122988	4.6196586961	-0.6980632205
C	-2.3810023971	1.3212403398	-0.280862982
N	-2.9764641992	0.7896834404	-1.4895139928
C	-3.6001748894	1.6173525429	-2.3781310118
O	-3.8680722929	2.7918381228	-2.1431893779
N	-3.9212203567	0.9801706294	-3.5637212925
H	-0.2764858312	0.8340096257	-0.352943347
H	1.2139746936	1.2559894229	-1.9716295371
H	1.1846640587	2.8419712717	-2.7452992443
H	-0.0543382986	2.0493712885	1.6040963202
H	-1.3180578703	3.2014886315	1.1799517573
H	2.382432651	3.6618468815	-0.9306571323
H	1.0563289868	4.1887170774	1.0667937689
H	-2.029177842	3.8175108654	-1.5271036396
H	-0.8030012397	4.1331175041	-2.7453395316
H	-0.8192761893	5.2714318832	-0.1269298731
H	-2.9619667656	2.216881438	-0.0401258778
H	-2.732528789	-0.144933335	-1.8123951099
H	0.5796139913	5.2641358771	-1.2017839549
O	-3.0725591445	-1.7017743224	-3.1086368088
N	-3.7041457958	-2.8287155228	-2.9380880283
C	-1.1805148724	-1.364648105	-5.0162480527
C	-1.2074043403	0.8089661026	-6.8048593995
C	-1.3301192766	-1.5681914185	-6.3987413152
C	-1.0133200421	-0.0527862307	-4.5482593389
C	-1.0686974385	1.0331321324	-5.4402559406
C	-1.3267927796	-0.5001187078	-7.2806836991
H	-1.4320878391	-2.5778694642	-6.7829540732
H	-1.4456297453	-0.6691175969	-8.3451253552
H	-1.2557898108	1.6401914497	-7.4989750913
O	-0.8365333686	0.1501940573	-3.2252717991
C	-1.2648033533	-2.4455024428	-4.0297869483
H	-0.8197741422	-2.2571527951	-3.0631527594
H	-0.8876558514	1.1138597206	-2.9527433976
H	-1.3868166682	-4.5315375223	-3.6294442405
H	-3.6711419788	-0.0099375052	-3.6314260552
C	-4.3140548315	1.5970552949	-4.7434527125
C	-5.0062535776	2.6950003804	-7.2472553933
C	-4.7325034642	2.9294395544	-4.8387139033
C	-4.2601250399	0.8168210906	-5.9112917979
C	-4.604527428	1.3644316185	-7.1343176846
C	-5.0594722401	3.4538785716	-6.087687986
H	-4.7813727958	3.5439262637	-3.9505674732
H	-3.9074401646	-0.2106403337	-5.8511060175
H	-5.2681424948	3.1200876306	-8.2095822457
C	-5.3870416044	4.9169589688	-6.163522384
C	-4.4692020929	0.5546898702	-8.3908012941
F	-5.5337465978	0.7098286921	-9.1936393269
F	-4.333581373	-0.7550641268	-8.1491302855

F	-3.3957770434	0.9392083899	-9.1085620074
F	-4.2719186285	5.6643908145	-6.0664866708
F	-6.1971185727	5.3038575413	-5.1687261382
F	-5.9800927537	5.2461269529	-7.3197934603
H	-3.8089666764	1.6150123029	2.0025752695
C	-3.3534763088	0.6326098404	1.9235619285
C	-2.5717167005	0.3154938998	0.8419456601
C	-1.9957739953	-0.9973703655	0.7948052432
C	-3.5969760972	-0.3299961837	2.9328483809
C	-2.3294327842	-1.8921371785	1.8515784539
C	-1.1256319085	-1.4560106484	-0.2365777828
H	-4.2222645274	-0.0669953388	3.7838567711
H	-2.1008148676	-3.8769675922	2.6410347982
C	-0.5858423663	-2.7202380943	-0.1830178871
H	-0.8891950653	-0.8311873689	-1.0904825809
C	-0.9532015463	-3.6237328879	0.8462361879
H	-0.5225248686	-4.6198311686	0.8359101032
C	-1.8121059804	-3.2167888622	1.8297716656
N	-3.1245057996	-1.5516169086	2.9055355346
C	-4.1549771962	-5.0424948848	-3.8012841455
C	-4.9532298377	-7.6756258757	-3.3916203834
C	-3.9876877006	-5.630388063	-2.5374260512
C	-4.7096684633	-5.7732082138	-4.8508930589
C	-5.1086869008	-7.0912891579	-4.6462804626
C	-4.3960489478	-6.9453078245	-2.3420654745
H	-5.5440995492	-7.6584818447	-5.4625017976
H	-4.277172405	-7.4018858909	-1.3630161666
O	0.3039777718	-3.1909462447	-1.1023048547
C	1.265493719	-2.2554911258	-1.5850851612
H	1.7779612768	-1.7764414927	-0.7428564391
H	0.8167910389	-1.4856629408	-2.2212550439
H	1.9772038238	-2.835097989	-2.1729459858
O	-1.0257940759	2.2592218807	-4.84159431
C	-1.3205291932	3.3748406024	-5.6632228544
H	-0.5116273124	3.5587825749	-6.3797926727
H	-1.4238287287	4.23093781	-4.9964739195
H	-2.2622914768	3.225722316	-6.204189987
C	2.3995427063	1.8780121223	0.2058849185
H	1.8252583438	1.0101938628	0.5375900295
C	3.690284806	1.9525614724	0.5192891347
H	4.1844171378	1.1795192964	1.0993665928
H	4.2999156899	2.7962229791	0.2038065339
C	-3.3582285448	-4.7845190681	-1.4567531576
H	-2.2634932305	-4.801808487	-1.5540053763
H	-3.5955109275	-5.1741294582	-0.4624028927
H	-4.8311965611	-5.3063312037	-5.8248581009
H	-5.2678282023	-8.7014256979	-3.2275468022
C	-3.8478344112	-3.3444280398	-1.5660033249
H	-3.2784413119	-2.6698253289	-0.9261899675
H	-4.9071109036	-3.2797026459	-1.2934882408
C	-3.671536473	-3.6607261639	-3.9934983716
H	-3.8524658805	-3.1741358749	-4.9494281489
C	-1.6698482652	-3.7442432111	-4.3222297981
H	-1.7559550985	-4.0739970804	-5.353977867

Syn-Open-S-Product

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.059116 a.u.

Thermal correction to Gibbs Free Energy = 0.803476 a.u.

Sum of electronic and thermal Free Energies = -3066.255640 a.u.

The lowest frequency = 7.81 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.276675 a.u.

C	1.8766852726	1.4898356296	2.8126213888
N	2.2700846869	2.2333151951	1.5966291423
C	3.7423857862	2.2525088355	1.524348747
C	2.2951056569	2.2726371523	4.0854394044
C	4.3818519352	2.8880357969	2.7960242575
C	3.2197008061	3.4229265645	3.6639283871
C	1.7810905206	3.6239577251	1.6229364867
C	2.3952774324	4.4029140177	2.8171800296
C	0.3662251263	1.1699100716	2.8317402435
N	-0.1340665268	0.5591411901	1.6149777476
C	-0.9444386339	1.2845665641	0.7751408752
O	-1.2753569392	2.4483000469	0.9727673478
N	-1.3887695691	0.5355711058	-0.2936674486
H	2.4401414649	0.5506315409	2.7661469343
H	4.084199439	1.2204490095	1.3857736834
H	4.0138729712	2.8070162059	0.6205590285
H	2.7749135373	1.606927182	4.8094523795
H	1.4125705598	2.6930020088	4.5841445934
H	5.002655113	3.7441941781	2.5043941297
H	3.6267698982	3.9243082042	4.5472709212
H	0.6894445546	3.6041976568	1.6473849748
H	2.066750831	4.0697705841	0.6669310294
H	1.6081384038	4.8517622868	3.4323043856
H	-0.1634721638	2.1240499263	2.9020354289
H	0.3797381577	-0.2103788763	1.18768322
H	3.035034755	5.2188941015	2.4634485764
O	0.6478795167	-1.9886204322	0.0351880174
N	-0.7136078554	-2.3646611667	-0.2948066015
C	1.1977647725	-0.8745509758	-2.0585472924
C	0.8200611648	1.5044420331	-3.4878794371
C	0.6934792492	-0.9049834223	-3.3622341008
C	1.5521451473	0.3502542418	-1.4861040587
C	1.3334924673	1.5454706428	-2.1947950905
C	0.5179099412	0.27402806	-4.074647587
H	0.416513877	-1.8495255351	-3.8208152326
H	0.0998696898	0.2489250192	-5.0761995927
H	0.6262640164	2.4222287907	-4.0325155779
O	2.1001513177	0.3495909891	-0.2535684692
C	1.3974083555	-2.0920312628	-1.1843619487
H	2.4409972407	-2.1436335232	-0.8599526837
H	2.0231319562	1.2328917791	0.2311341797
H	1.3666335275	-4.2321253133	-1.1605864581
H	-1.1842760416	-0.4698632013	-0.3001988118
C	-1.9198572547	1.0180083586	-1.481943468
C	-2.8114302603	1.7751902278	-4.042056337
C	-2.040700162	2.3749319505	-1.8086903605
C	-2.2912231884	0.0540714455	-2.4273350679
C	-2.7117416775	0.4333376898	-3.6896298673
C	-2.4815249245	2.7244535037	-3.0812928136
H	-1.7782438369	3.1315316753	-1.081177372
H	-2.1919060471	-0.9962352052	-2.1725117163
H	-3.1269444532	2.0722050165	-5.0362842981
C	-2.4904347421	4.1722241598	-3.4763426997
C	-3.0272804205	-0.6228748687	-4.7079764772
F	-4.3427472081	-0.8622825911	-4.8075731549
F	-2.436927254	-1.7952267887	-4.4131244544

F	-2.6035648228	-0.2635172463	-5.9307128313
F	-1.3396148806	4.5100073853	-4.0999739696
F	-2.6103949733	4.9906879066	-2.4246844996
F	-3.4816392225	4.4560865703	-4.331901397
H	-1.2003978743	1.9776055258	4.8484703574
C	-0.861793641	0.955228719	4.9890764074
C	-0.040913145	0.3637411945	4.058756529
C	0.3621394753	-0.989558009	4.2920398739
C	-1.2879274405	0.2378936487	6.1292955913
C	-0.131365709	-1.6170735904	5.4723268904
C	1.2190489985	-1.7317728969	3.426395184
H	-1.9397336077	0.719440169	6.85560868
H	-0.162551414	-3.4125285074	6.6530143344
C	1.5841041714	-3.0200984492	3.7516017175
H	1.5874071438	-1.2876722756	2.5102421846
C	1.073025502	-3.6482600757	4.9195224567
H	1.3790012613	-4.6689274263	5.1238079477
C	0.2376992331	-2.9629252748	5.7504499134
N	-0.9463137477	-1.0035348744	6.3739713899
C	-1.1475815871	-4.7505048237	-1.0660319996
C	-1.9831361335	-7.3511284716	-0.5065959959
C	-1.1242996099	-5.21792396	0.254253745
C	-1.6024198313	-5.578563237	-2.0920654242
C	-2.0128012525	-6.8793269639	-1.8176057165
C	-1.5509785639	-6.5184700084	0.5217153833
H	-2.3621430795	-7.5191686537	-2.6217347631
H	-1.5501757667	-6.8751188552	1.548625318
O	2.4330807107	-3.791811778	3.030560673
C	3.105731656	-3.1769592664	1.9459545872
H	3.6813908185	-2.3074952299	2.2877027027
H	2.3908797972	-2.8614092498	1.1807764796
H	3.781745479	-3.9305773607	1.5427726964
O	1.6507530569	2.679364001	-1.5049468109
C	1.4490212145	3.9078432866	-2.1769862365
H	2.0711117085	3.968484693	-3.0776950836
H	1.741940951	4.6922884978	-1.4794087701
H	0.3987990043	4.0409305219	-2.4558767031
C	5.252560247	1.9121337743	3.5361901376
H	4.8018847774	0.9464480464	3.7753662708
C	6.5086822339	2.1488455295	3.9039584562
H	7.0957376816	1.4122034173	4.4432084212
H	6.9949199487	3.0945065451	3.675450654
C	-0.717405226	-4.2498161202	1.3352276978
H	0.3748856381	-4.1818826183	1.4294780341
H	-1.1019676965	-4.5673754954	2.309674084
H	-1.6322930668	-5.1992138606	-3.1112526557
H	-2.3105566796	-8.3618130803	-0.2836658886
C	-1.2691350449	-2.8746783867	0.9647623374
H	-1.0589093175	-2.1232921572	1.731798922
H	-2.3539237085	-2.9254108823	0.8257419326
C	-0.6112078285	-3.3778562413	-1.3985676551
H	-1.1588841445	-2.971206513	-2.2570562425
C	0.8957131841	-3.4218603881	-1.7253598555
H	1.0854499134	-3.5884949455	-2.7865096735

Syn-Open-R-Reactant

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.014767 a.u.

Thermal correction to Gibbs Free Energy = 0.794280 a.u.

Sum of electronic and thermal Free Energies = -3066.220487 a.u.

The lowest frequency = 7.62 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.243597 a.u.

C	-2.3696926792	-1.9411421854	2.4758571125
N	-3.2542265886	-1.9095654121	1.2900895407
C	-4.6444182781	-1.8470620263	1.7748147893
C	-2.8009794767	-3.0832652687	3.4423747444
C	-5.1032300788	-3.1847768361	2.4180791109
C	-3.8155376797	-3.9830562092	2.7189075213
C	-3.0956594394	-3.1388222559	0.4821353754
C	-3.2177315971	-4.4042359925	1.3691170251
C	-0.8821510456	-2.1023111936	2.0811796209
N	-0.5089779001	-1.3712818578	0.8934923989
C	0.1352198971	-1.9791567767	-0.1424340734
O	0.4374124927	-3.1669740428	-0.1698872344
N	0.391994852	-1.0850637042	-1.1716138348
H	-2.5066676487	-0.9726363724	2.9693319885
H	-4.6845212614	-1.0449356059	2.5160598367
H	-5.2962212379	-1.5568736306	0.9447197353
H	-3.2300028226	-2.6728545378	4.3621746082
H	-1.9323317151	-3.6789748631	3.7457802959
H	-5.6922585402	-3.7585952146	1.6904463205
H	-4.0500224316	-4.8588565014	3.3316682411
H	-2.1371710795	-3.1107921099	-0.0392223801
H	-3.8798294736	-3.1126871376	-0.2809553384
H	-2.2363564545	-4.8688263857	1.521475271
H	-0.7116433262	-3.1528319051	1.8270589345
H	-0.6205809371	-0.3628688794	0.8396086959
H	-3.8557011426	-5.1515108957	0.8863881679
O	-0.1524712269	1.39953337	0.0607587421
N	0.9379238789	2.088684624	-0.0082894357
C	0.9910354805	3.2586772677	-0.5647702851
O	-2.5544810997	0.0863023217	-0.5112226796
C	-1.5326855093	1.5525001354	-2.6258531919
C	-0.7479384496	2.2411338852	-3.4622831503
H	-2.9614651073	-0.4462301635	0.2322164783
H	-0.0782098048	1.7368150259	-4.1510985276
H	-0.7482162629	3.327646939	-3.5018843869
H	0.0592014559	-0.1314151682	-1.0004728507
C	1.3714744027	-1.2129806278	-2.1457751879
C	3.3771889618	-1.2582130595	-4.1274714574
C	1.9411974172	-2.4307430457	-2.542908309
C	1.8107647215	-0.0293639172	-2.7526774448
C	2.7973523141	-0.0602972961	-3.7272581441
C	2.9309662523	-2.4284435526	-3.5198825196
H	1.6178783577	-3.3517547322	-2.0762433174
H	1.3727427351	0.919809612	-2.4503337431
H	4.158084989	-1.2794594733	-4.8780842292
C	3.4921264291	-3.7477841402	-3.9738517663
C	3.2054495863	1.2429891884	-4.3497001026
F	4.3750997311	1.1552138526	-4.9928113948
F	3.3218286646	2.2126674537	-3.423407929
F	2.2942818325	1.6747083268	-5.2390896001
F	4.7341551245	-3.6183988944	-4.4645972643
F	2.7431365739	-4.2912423264	-4.9467408932
F	3.5425919989	-4.6403543897	-2.9762147267
H	0.665765613	-3.8022193453	3.4789265798
C	0.7774624183	-2.7776595925	3.8219999059
C	0.0498403185	-1.7695060036	3.2382307339

C	0.2574754495	-0.4314211997	3.7076085961
C	1.7012798374	-2.487753824	4.8518770004
C	1.2358930443	-0.2547426367	4.7278084087
C	-0.429629779	0.7144015132	3.2055537354
H	2.2688645433	-3.295760145	5.3093445443
H	2.2744237284	1.1586248629	5.970459341
C	-0.1329414259	1.9701132242	3.6925485894
H	-1.1893762825	0.6134697648	2.4402281998
C	0.8615293306	2.1412309369	4.6952720909
H	1.0619482877	3.1487414079	5.0446432525
C	1.5193465962	1.0580170927	5.1978476285
N	1.9391085352	-1.2762981551	5.2913607059
C	2.221926044	4.0368265299	-0.5991645572
C	4.5798930359	5.5088775733	-0.6514535647
C	3.4416490088	3.4058144281	-0.3043452262
C	2.1896988327	5.3944939534	-0.9285319686
C	3.3691972553	6.1299117412	-0.9520740751
C	4.6136030259	4.1514099066	-0.3327476082
H	3.344511699	7.1850349338	-1.2033201071
H	5.5600667887	3.6672157657	-0.108527266
O	-0.724549242	3.1196127793	3.2980903975
C	-1.7651136958	3.0307255376	2.3356221185
H	-1.3944902791	2.6304257015	1.385042061
H	-2.1374202684	4.0459358728	2.1973001175
H	-2.5751380885	2.387290832	2.7018395679
C	-5.9631176652	-2.94507098	3.6238642798
H	-5.5028375562	-2.3875504981	4.4418947525
C	-7.2247096265	-3.3494095849	3.7461796366
H	-7.8060005841	-3.1476408075	4.6403876061
H	-7.7209057393	-3.9010979048	2.9511271475
H	-1.4754010026	0.4657211936	-2.618263319
C	-2.5021263876	2.1403949732	-1.6856856875
C	-4.3229411309	3.2339908432	0.1501361305
C	-2.9931748054	1.3531099665	-0.6319138763
C	-2.9464407873	3.4653678984	-1.8116184727
C	-3.8414045616	4.0100619328	-0.9075769915
C	-3.900476442	1.9170347402	0.2878317969
H	-2.5995583527	4.0605704636	-2.6507212445
H	-4.1859543532	5.0323730425	-1.0216775159
H	-5.0248389204	3.6643314782	0.8545074149
O	-4.2851578773	1.0854437967	1.3073901974
C	-5.2918402622	1.5806162602	2.1695718106
H	-4.9411209664	2.4588939256	2.7247964499
H	-5.5247192623	0.782508303	2.8737863275
H	-6.1942208579	1.8445041958	1.6069514157
C	3.4133423198	1.9204000792	-0.0458118403
H	4.2676196952	1.6090393844	0.561115384
H	3.4898441754	1.3959642473	-1.0074791388
H	5.5019311405	6.0810209649	-0.6683201189
H	1.2394224712	5.8686078944	-1.1577523201
H	0.0498674825	3.6257715447	-0.9631814351
C	2.1284172594	1.5019612507	0.6540917759
H	1.9706024784	0.4222436246	0.6302045402
H	2.0894099829	1.8348440003	1.6981552954

Syn-Open-R-TS

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3066.979624 a.u.

Thermal correction to Gibbs Free Energy = 0.800078 a.u.

Sum of electronic and thermal Free Energies = -3066.179546 a.u.

The lowest frequency = -499.87 cm^{-1}

Number of imaginary frequencies = 1

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.205666 a.u.

C	-1.8303115324	-2.4796720483	2.4229908593
N	-2.643933594	-2.446589632	1.185936833
C	-4.0590025751	-2.4095296232	1.5980318657
C	-2.3004787964	-3.6372159332	3.3535563938
C	-4.5375336196	-3.757930969	2.2018098308
C	-3.2609948545	-4.5435175428	2.5686981027
C	-2.4312825547	-3.6697961081	0.3802642512
C	-2.5813580503	-4.943083941	1.2513851456
C	-0.3137988719	-2.6146137416	2.1356891883
N	0.1528810905	-1.8767033507	0.9822990132
C	0.7616652934	-2.5211342839	-0.0525052436
O	0.9618987892	-3.7310774482	-0.0886380933
N	1.1119987565	-1.6506118631	-1.0697820314
H	-2.0154946639	-1.5209576314	2.9178863798
H	-4.1502038158	-1.6118974937	2.3417828498
H	-4.6687260267	-2.1235024257	0.7355810591
H	-2.7831858582	-3.2401067402	4.2523802432
H	-1.4425984346	-4.2251726343	3.6989201932
H	-5.0780042552	-4.3296162245	1.4357148796
H	-3.516867418	-5.4280915753	3.1599889483
H	-1.4491418615	-3.6333635106	-0.0919575846
H	-3.1784111332	-3.6485391177	-0.4194660571
H	-1.6008066191	-5.3899725385	1.4543045108
H	-0.1149021082	-3.660520019	1.8853245111
H	0.041398933	-0.8692928526	0.9123284007
H	-3.1768779674	-5.6979429868	0.7278234947
O	0.6647710356	0.9957467584	0.0514121346
N	1.7200247707	1.7650537202	-0.0021781027
C	1.4842218367	2.9977871837	-0.4937771313
O	-1.7822410308	-0.2400445077	-0.3584740176
C	-0.2983917922	1.5766171017	-1.8282432331
C	0.6421087967	2.5325774006	-2.2203635611
H	-2.3097921604	-0.8728746659	0.20764592
H	1.461250426	2.223732871	-2.8660636213
H	0.3279806629	3.5556353071	-2.4049177382
H	0.9035659641	-0.6652568873	-0.8896971746
C	1.8777699815	-1.9386963339	-2.1903109324
C	3.464504399	-2.3072414632	-4.4962431676
C	2.2652923753	-3.2264154122	-2.5826750965
C	2.2847727949	-0.8467594795	-2.9715547052
C	3.0703123538	-1.0336618611	-4.0966398217
C	3.0459479055	-3.3833226612	-3.7247458635
H	1.9625596125	-4.0825594081	-1.9951593157
H	1.9769691102	0.154175718	-2.683406906
H	4.0751038929	-2.4528003362	-5.3791839395
C	3.4023761815	-4.7857521328	-4.1350667517
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C	3.8830024849	3.3172724535	-1.0181899809
C	2.5042942591	5.2767897031	-0.6393204412
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Syn-Open-R-Product

Optimization: IEFPCM(Toluene)-M06-2X/6-31G(d)

E = -3067.047456 a.u.

Thermal correction to Gibbs Free Energy = 0.803322 a.u.

Sum of electronic and thermal Free Energies = -3066.244134 a.u.

The lowest frequency = 3.58 cm^{-1}

Number of imaginary frequencies = 0

Single-point energy calculation: IEFPCM(Toluene)-M06-2X/def2tzvpp

E(RM06) = -3068.268664 a.u.

C	-2.2889872344	-2.0144840544	2.4270765265
N	-3.1338338196	-1.9218838505	1.2126993695
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C	-4.9646770682	-3.3681427527	2.1553646751
C	-3.6537192047	-4.1287742547	2.4456279972
C	-2.8795995801	-3.07165727	0.3168339383
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C	0.0602445946	-1.8799927805	3.349948745

C	0.1528690978	-0.6067657888	3.993122545	C	-7.1490446159	-3.6813765306	3.3458191436
C	1.5595859892	-2.7265649657	5.0453467824	H	-7.7801939414	-3.5713851754	4.2219949722
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C	-0.5138135897	0.5633378369	3.5309651384	H	-1.0369909764	1.3210348799	-1.9663023504
H	2.1221468876	-3.5602045315	5.4611171128	C	-2.2357735244	2.6393641302	-0.7700783482
H	1.7131056533	0.7588100935	6.7136710059	C	-4.6757955265	3.2443152557	0.4703224502
C	-0.3794700206	1.7542827444	4.2103259337	C	-2.9366041951	1.6482494943	-0.0777557671
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C	0.4329455959	1.8339904293	5.3751755757	C	-3.9686365015	4.2342195992	-0.2138313899
H	0.5115745798	2.7929568962	5.8765108427	C	-4.1587219228	1.9556566973	0.5451258685
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C	2.2136402712	3.9975545146	-1.4644597931	H	-5.6169417752	3.4871695315	0.9495834889
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C	2.5939538459	4.8800067244	-2.4797420578	H	-5.9309149185	1.917820567	2.5891463918
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C	4.4836615517	3.1955882829	-1.3561008788	H	-6.7258786337	1.4761028946	1.0481983068
H	4.1840410787	5.5996314043	-3.7330582594	C	2.7849295923	2.2835372811	0.2889318192
H	5.2247610763	2.5409327991	-0.9036881948	H	3.6324123803	2.1804246689	0.9743431665
O	-0.9792133312	2.9119827001	3.8522310162	H	2.5366008983	1.2679900527	-0.0452937785
C	-1.8296650236	2.8633822308	2.7174182574	H	5.8746896932	4.0636702857	-2.7434313168
H	-1.2707909567	2.5829490561	1.8182282005	H	1.8470220883	5.5396397035	-2.9174828102
H	-2.2336090686	3.8676106472	2.5885019996	H	0.4193714653	4.9821690791	-0.8319421812
H	-2.6505644172	2.1520781286	2.8793893206	C	1.592910938	2.8859887864	1.0302143843
C	-5.8872484957	-3.2592261159	3.3334343728	H	1.2426195495	2.2298516646	1.8335919381
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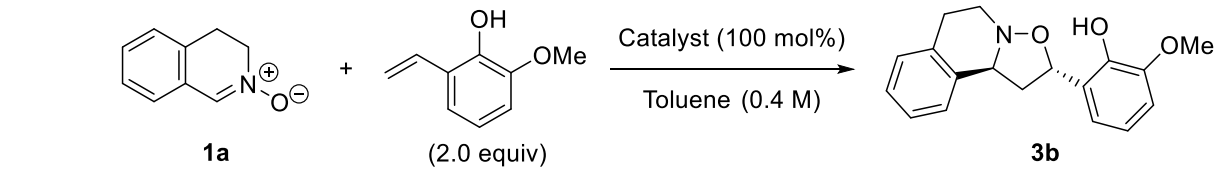
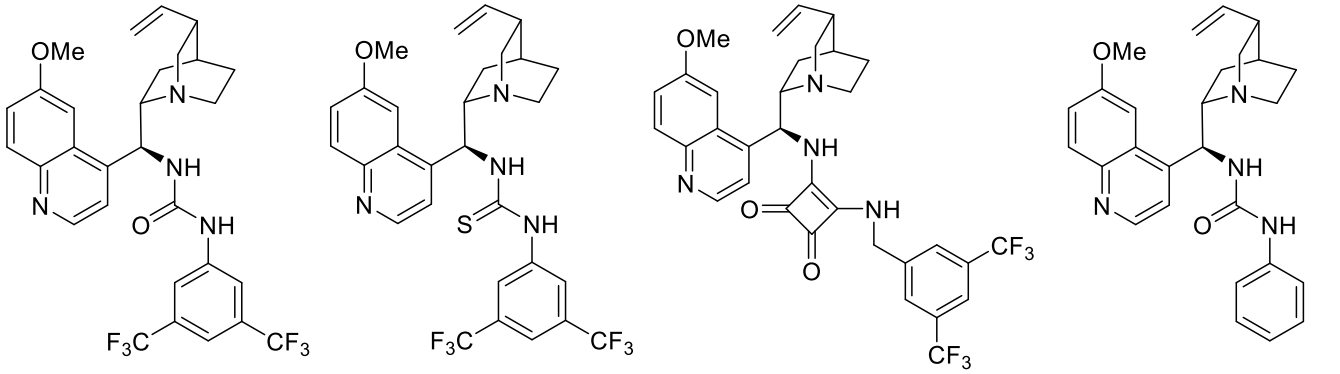
Appendix





amine-urea **2**
65%, 94% ee (0 °C, 48 h)
90%, 89% ee (35 °C, 12 h)

amine-thiourea
57%, 94% ee (0 °C, 48 h)

amine-squaramide
16%, 85% ee (0 °C, 48 h)

amine-urea **2'**
36%, 59% ee (35 °C, 12 h)

Scheme S1. Screening of catalysts.

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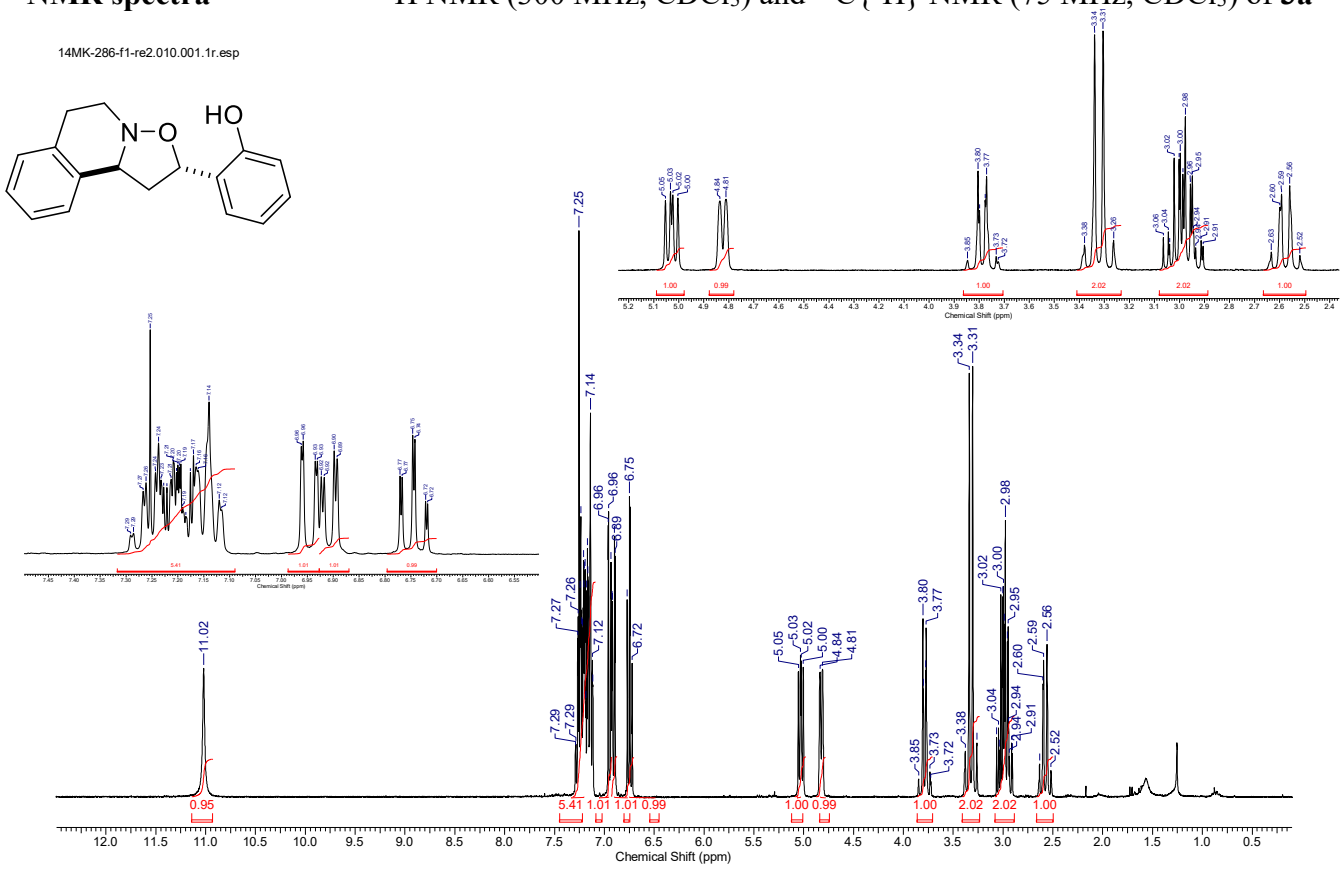
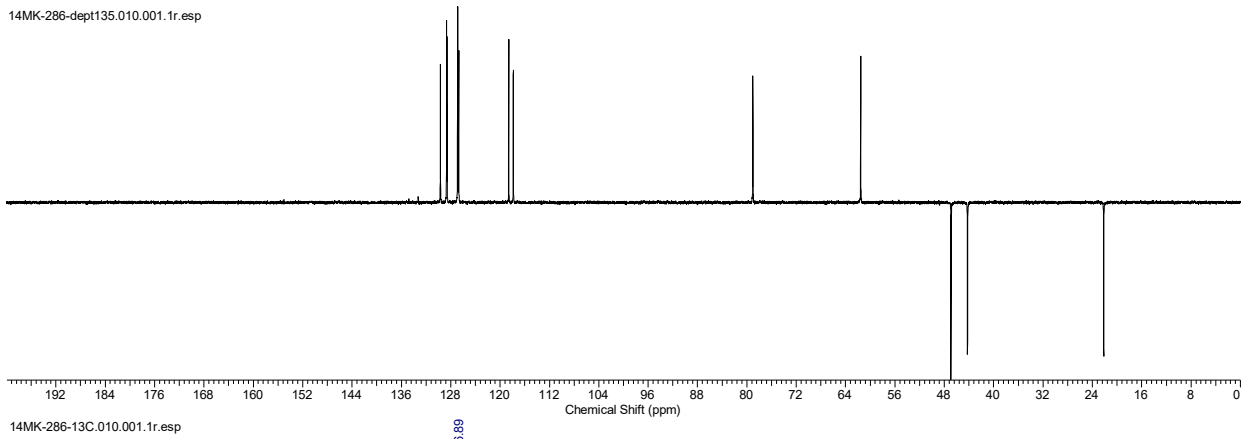
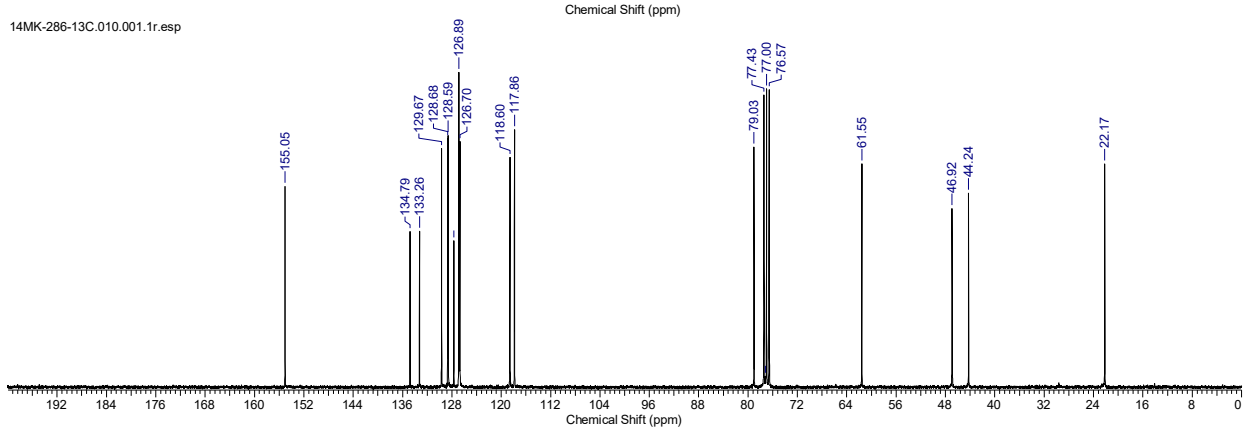
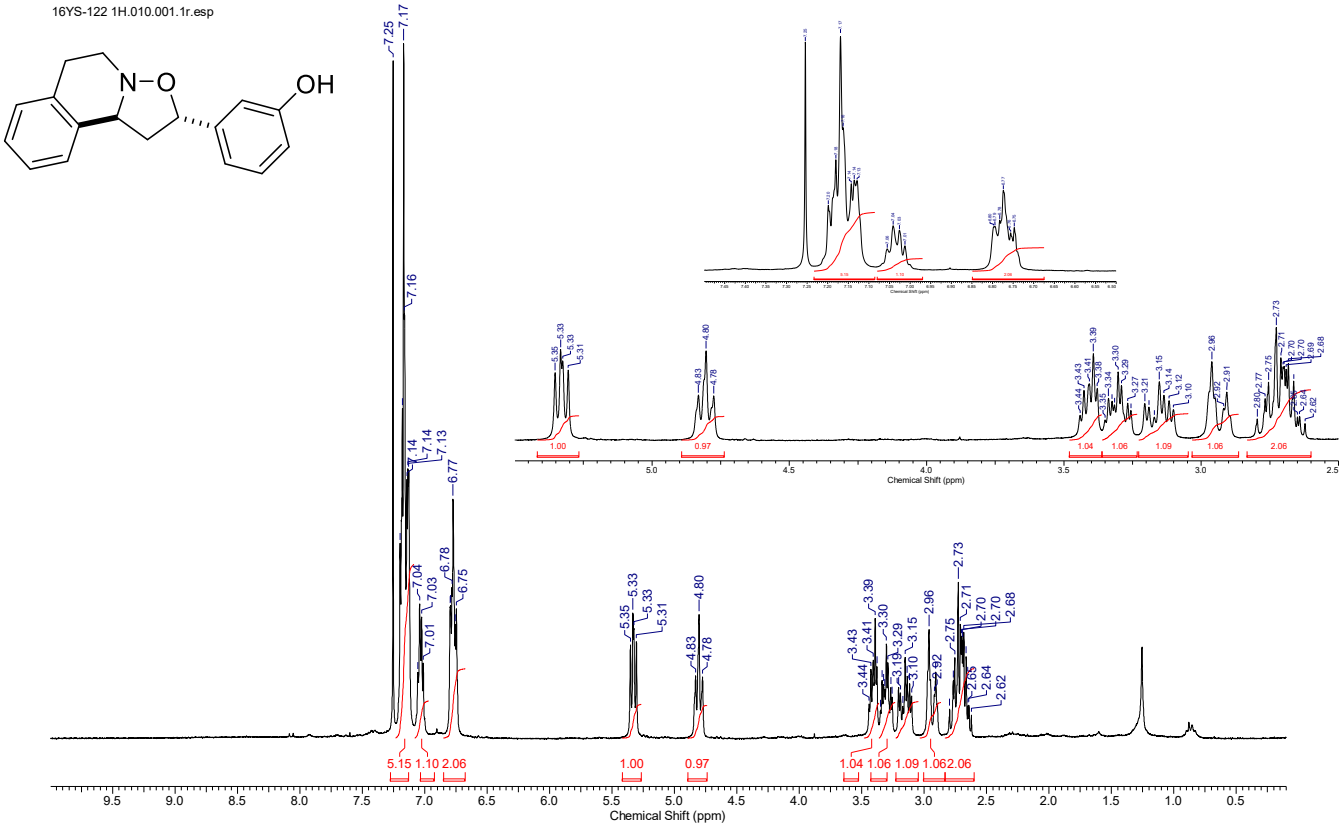
NMR spectra ^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3a**

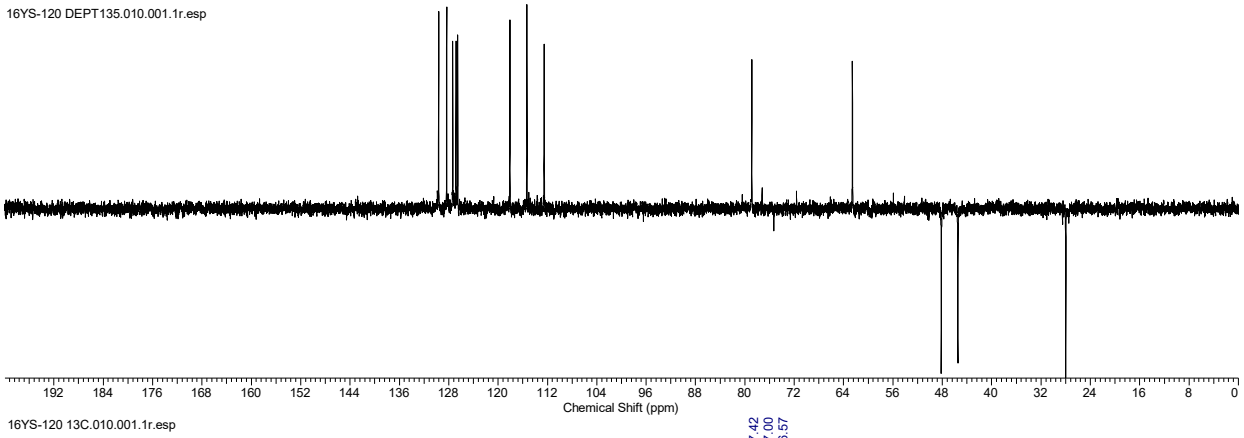


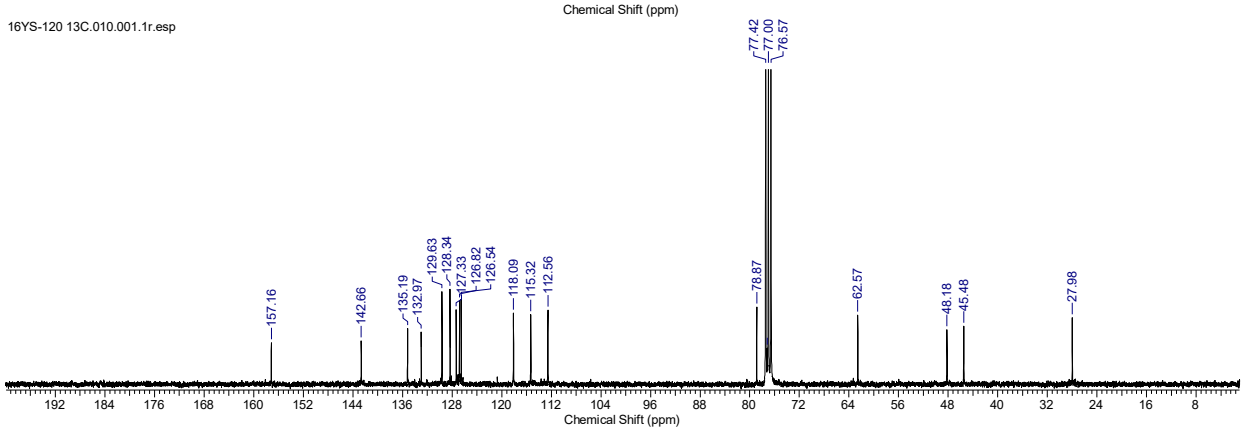




^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **4**







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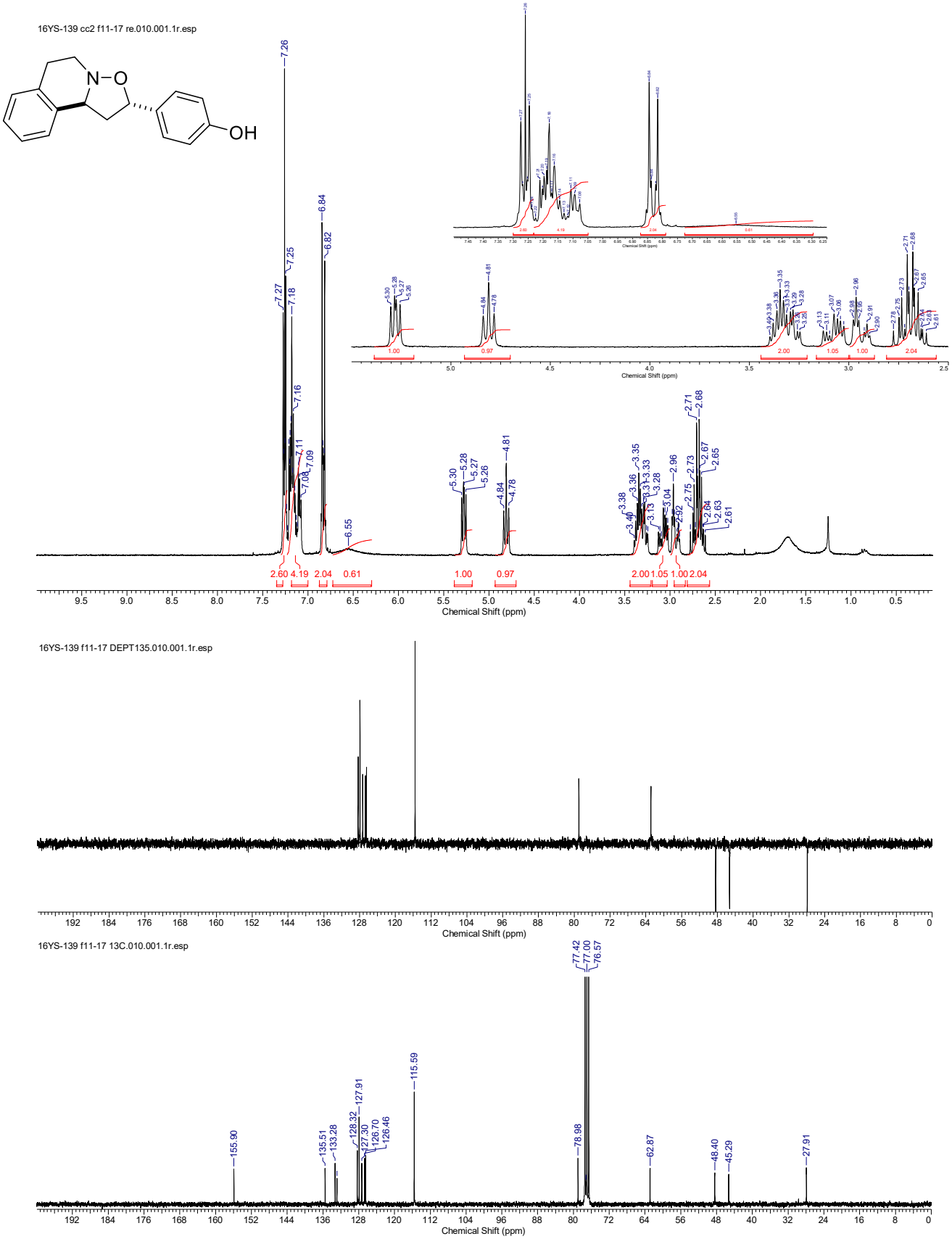
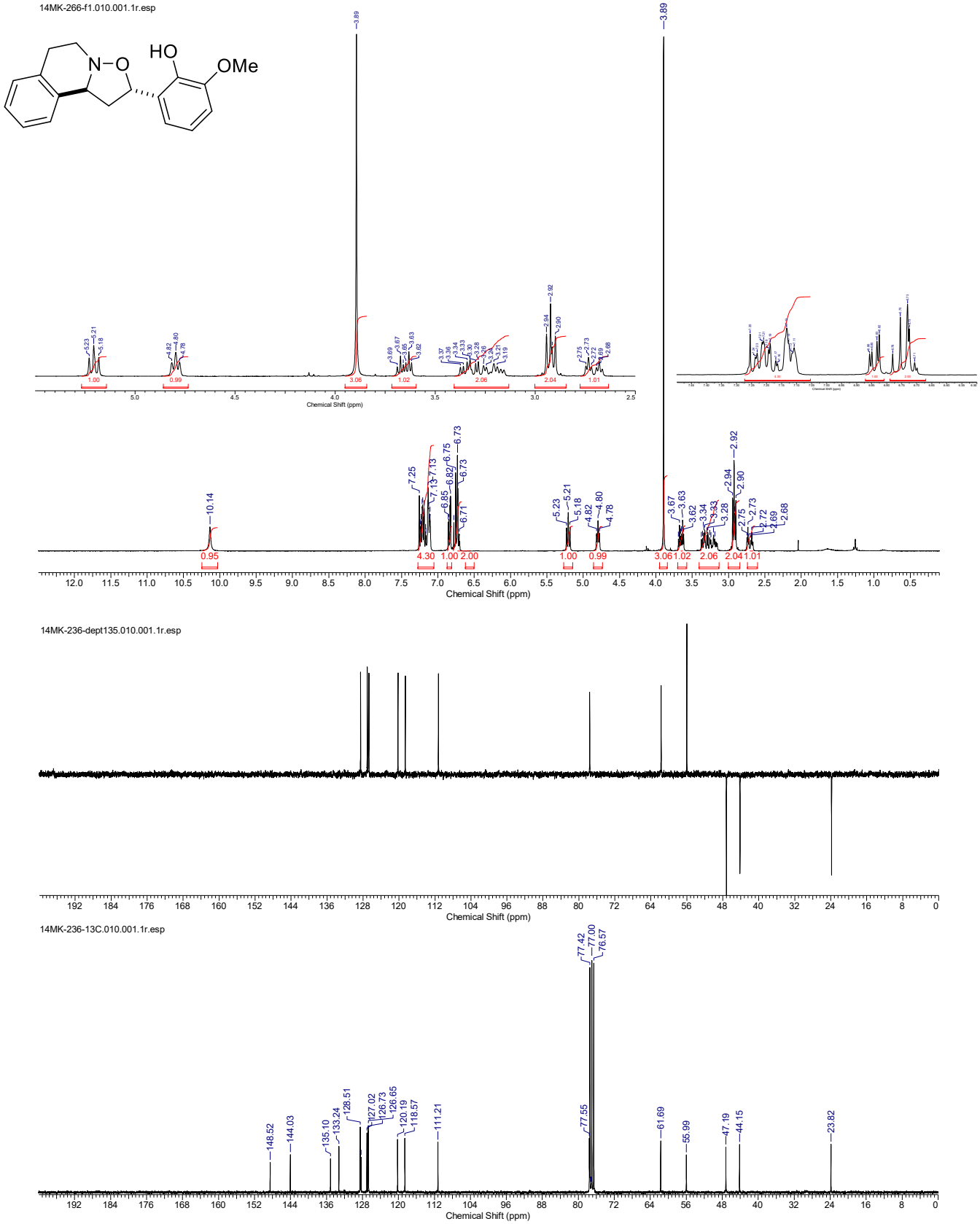
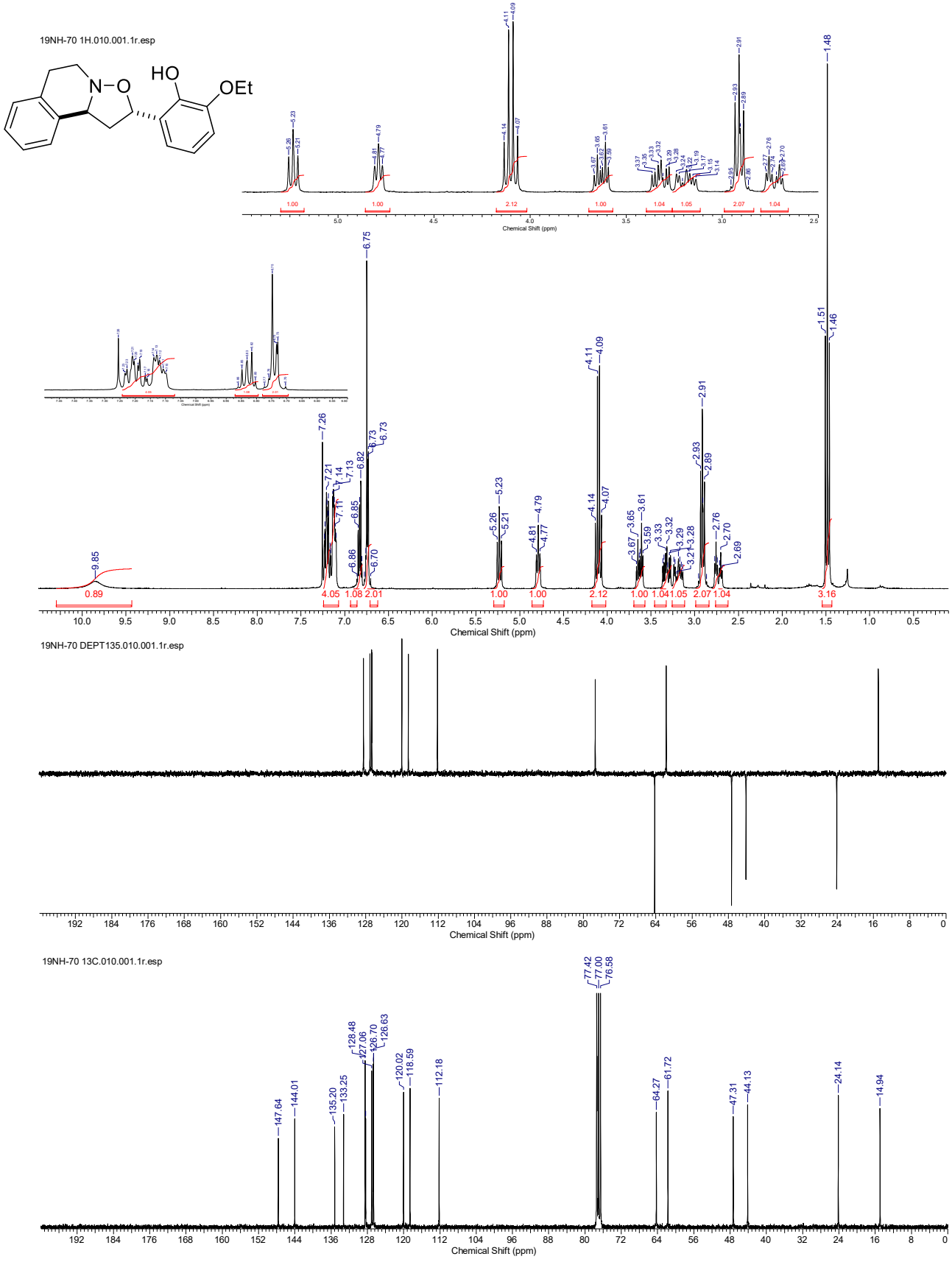


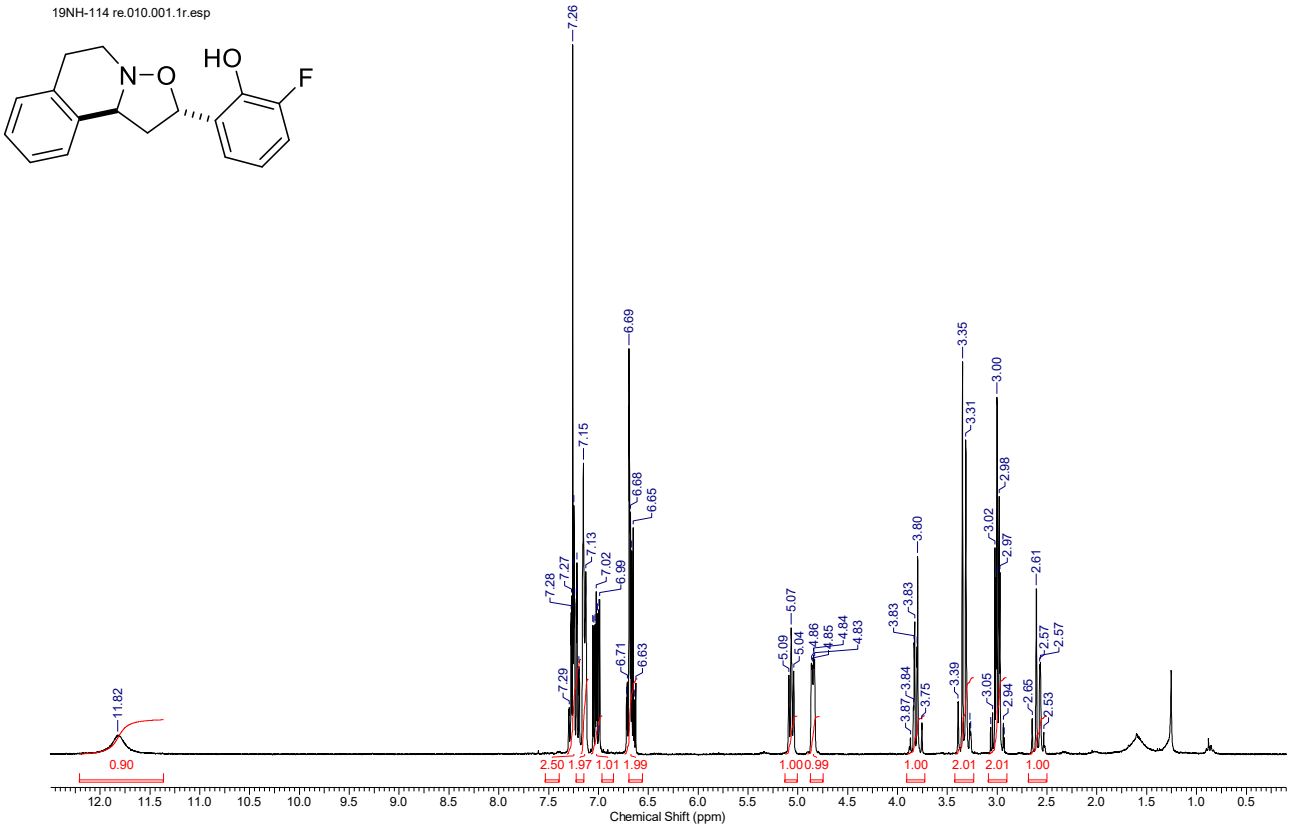
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3b**

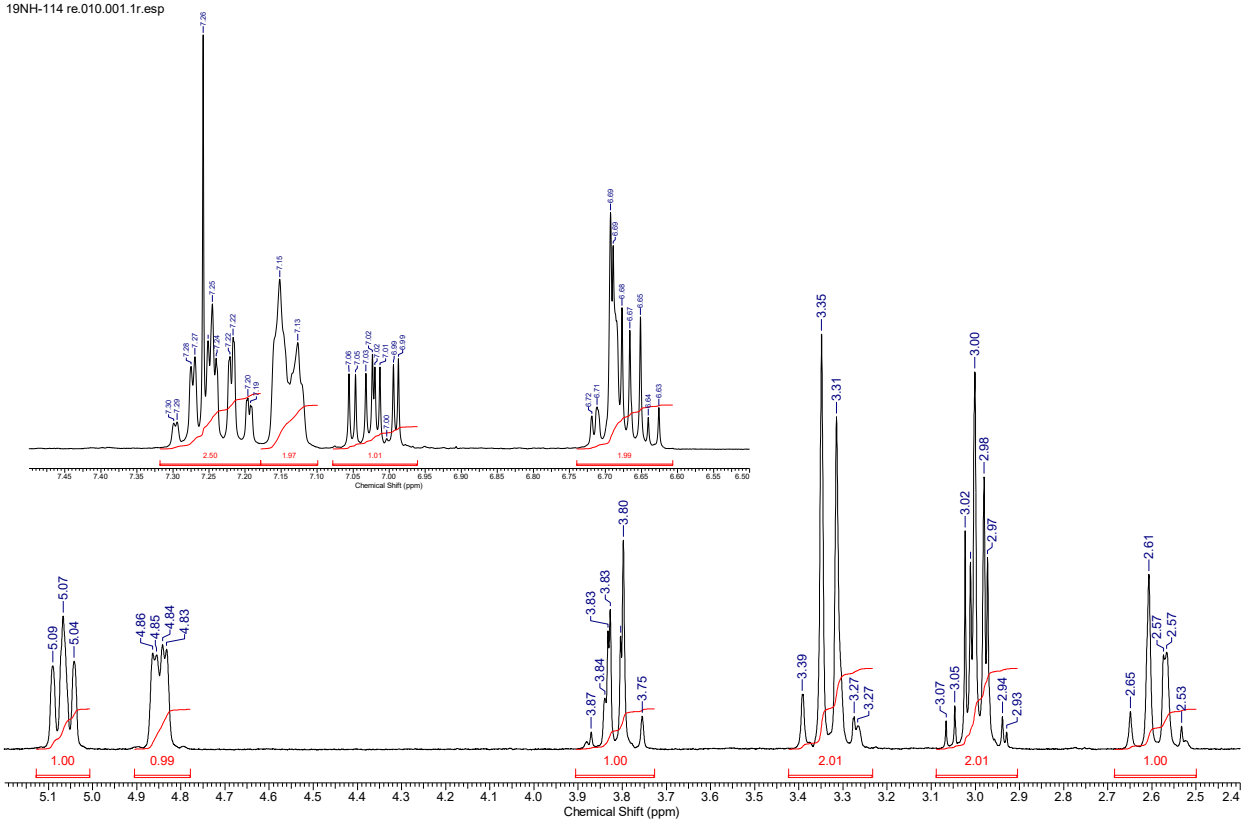


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3c**

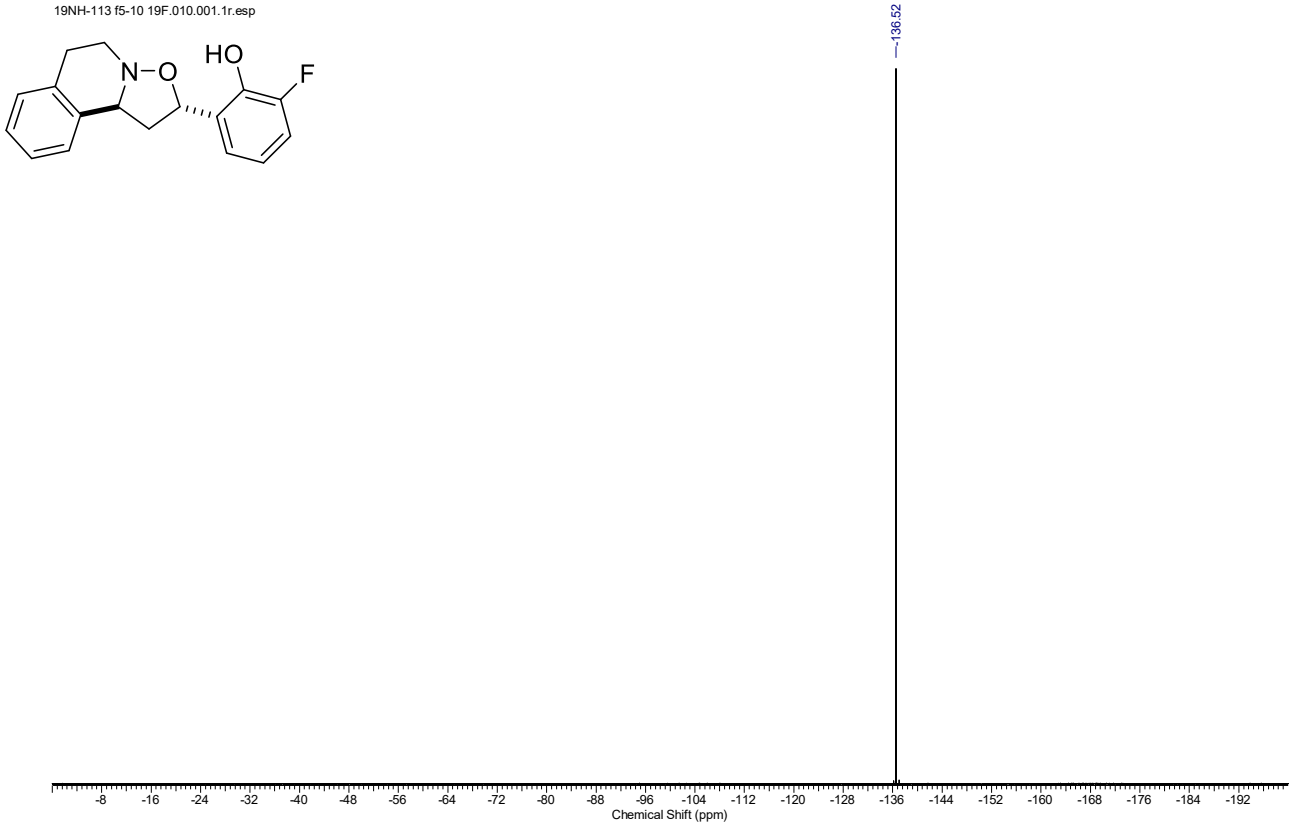


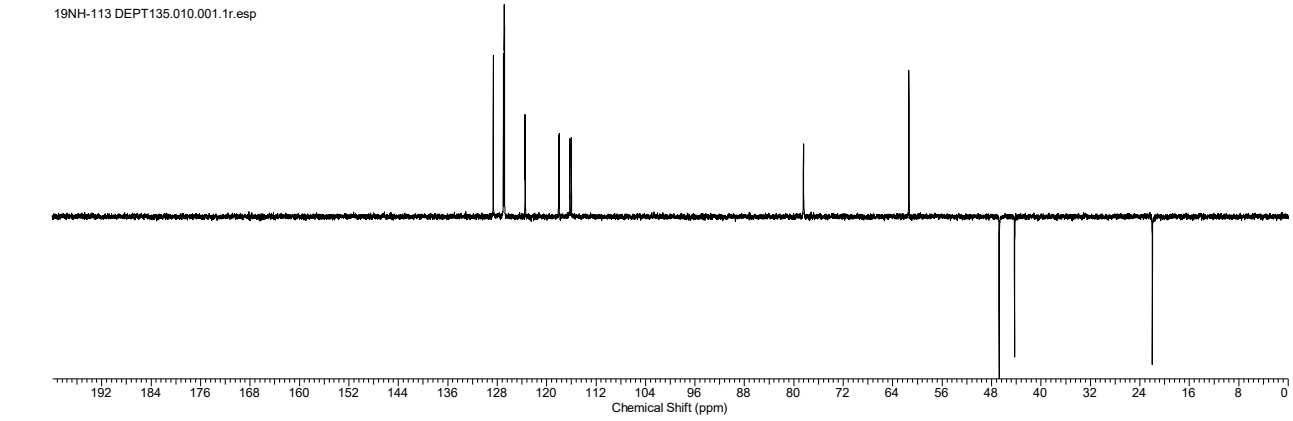
^{1}H NMR (300 MHz, $CDCl_3$) of **3d**

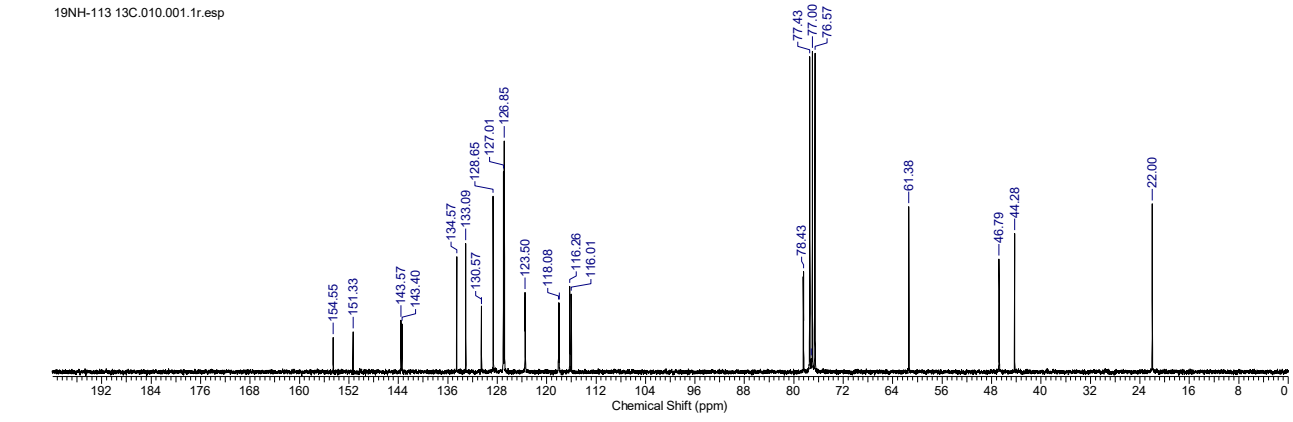




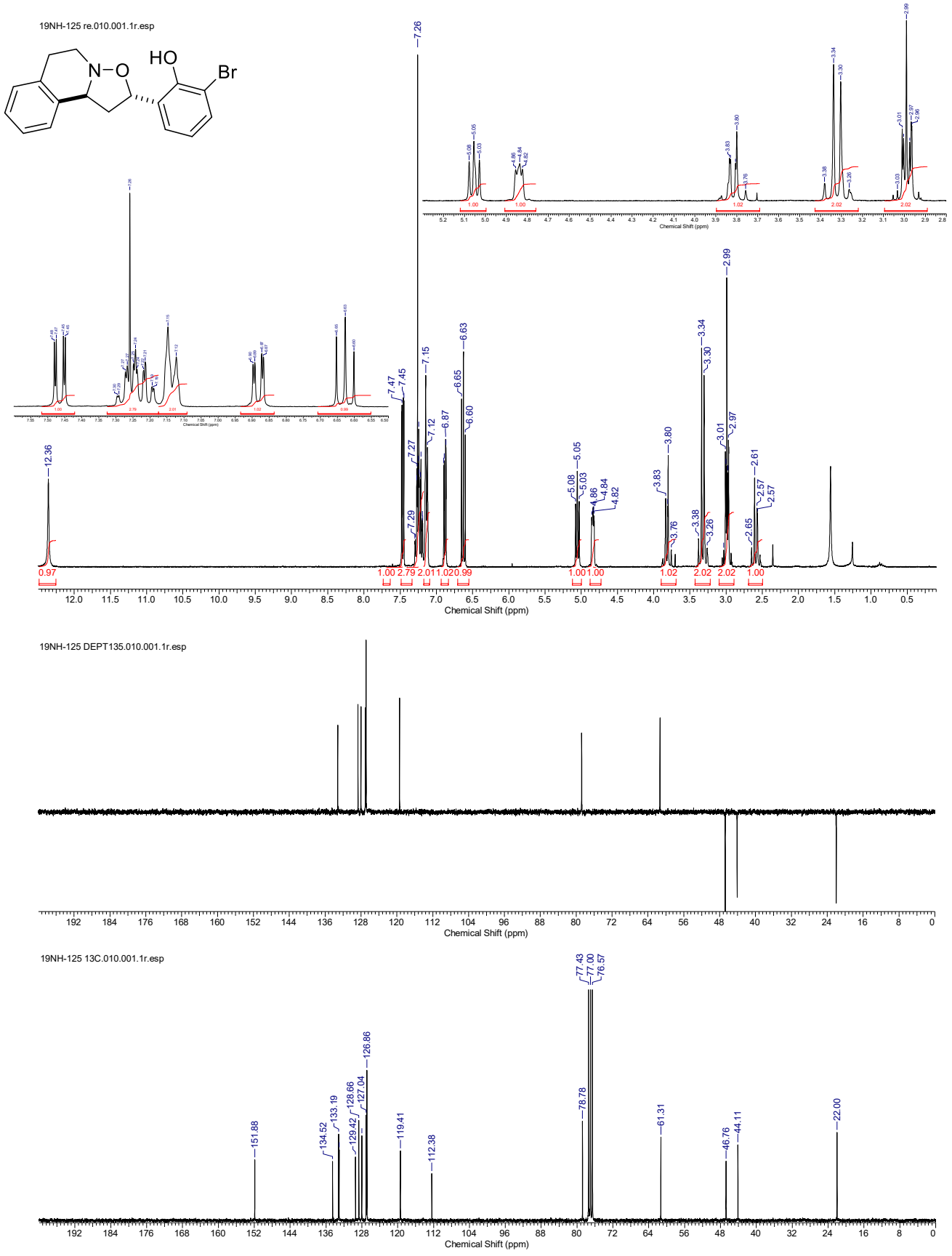
^{19}F NMR (282 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) of **3d**



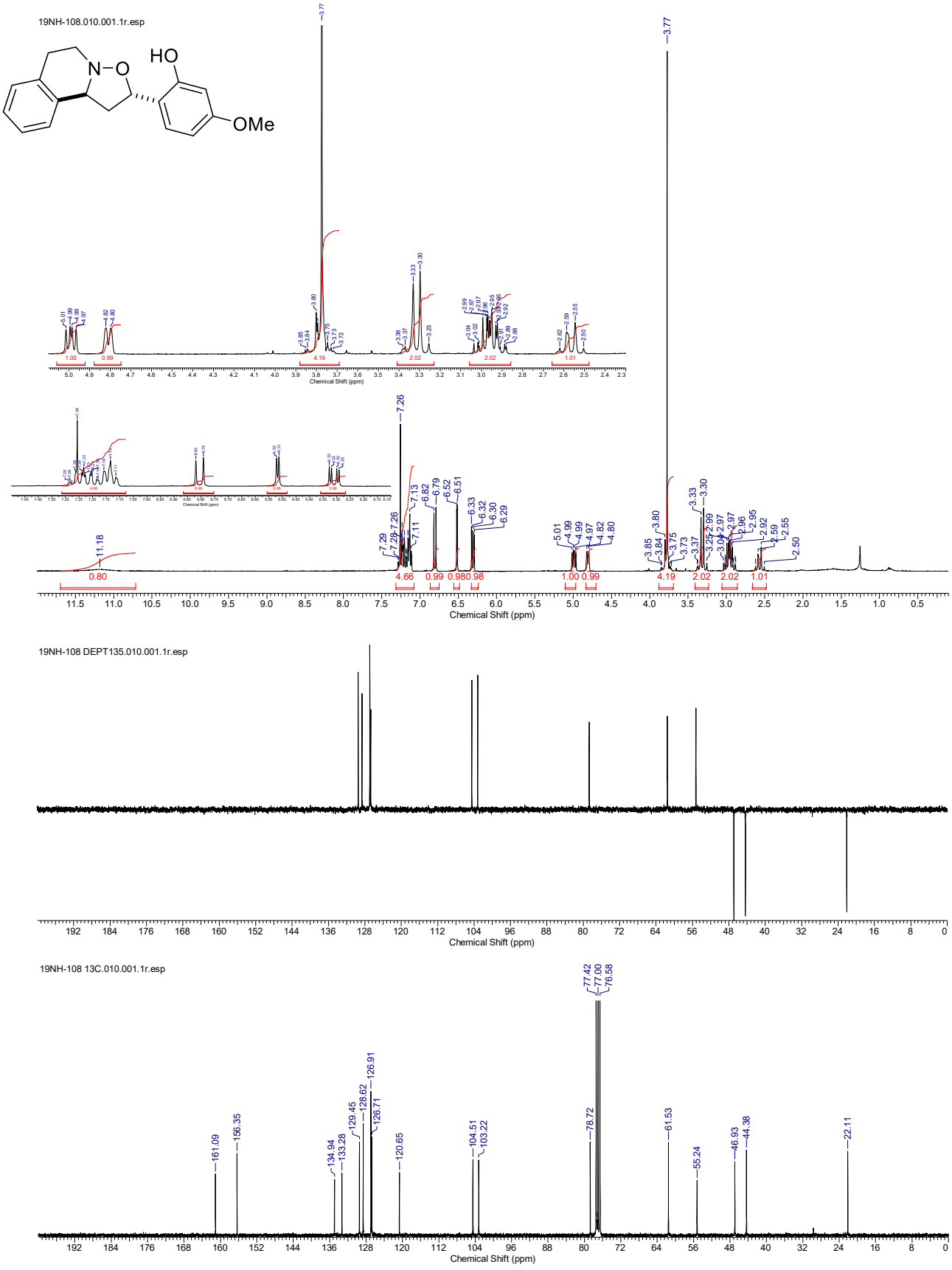




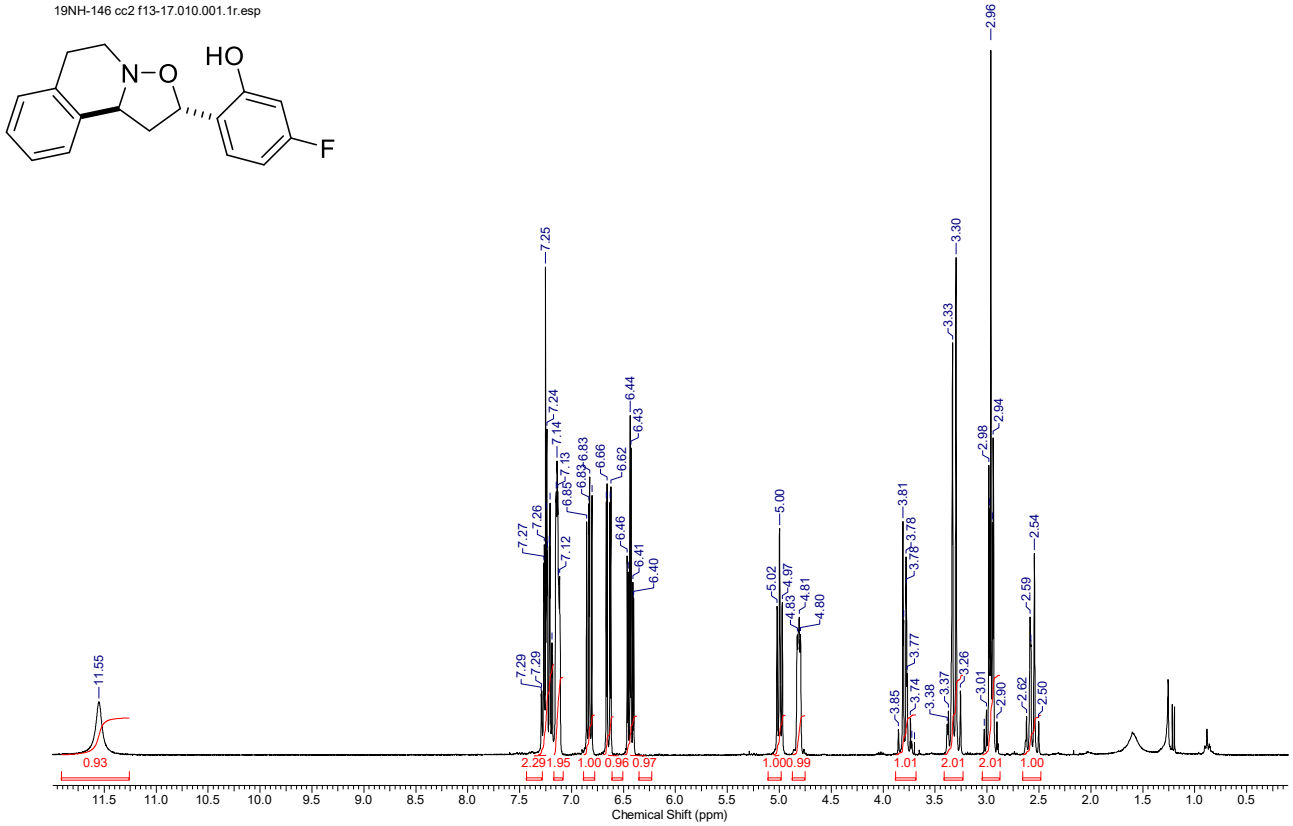
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3e**

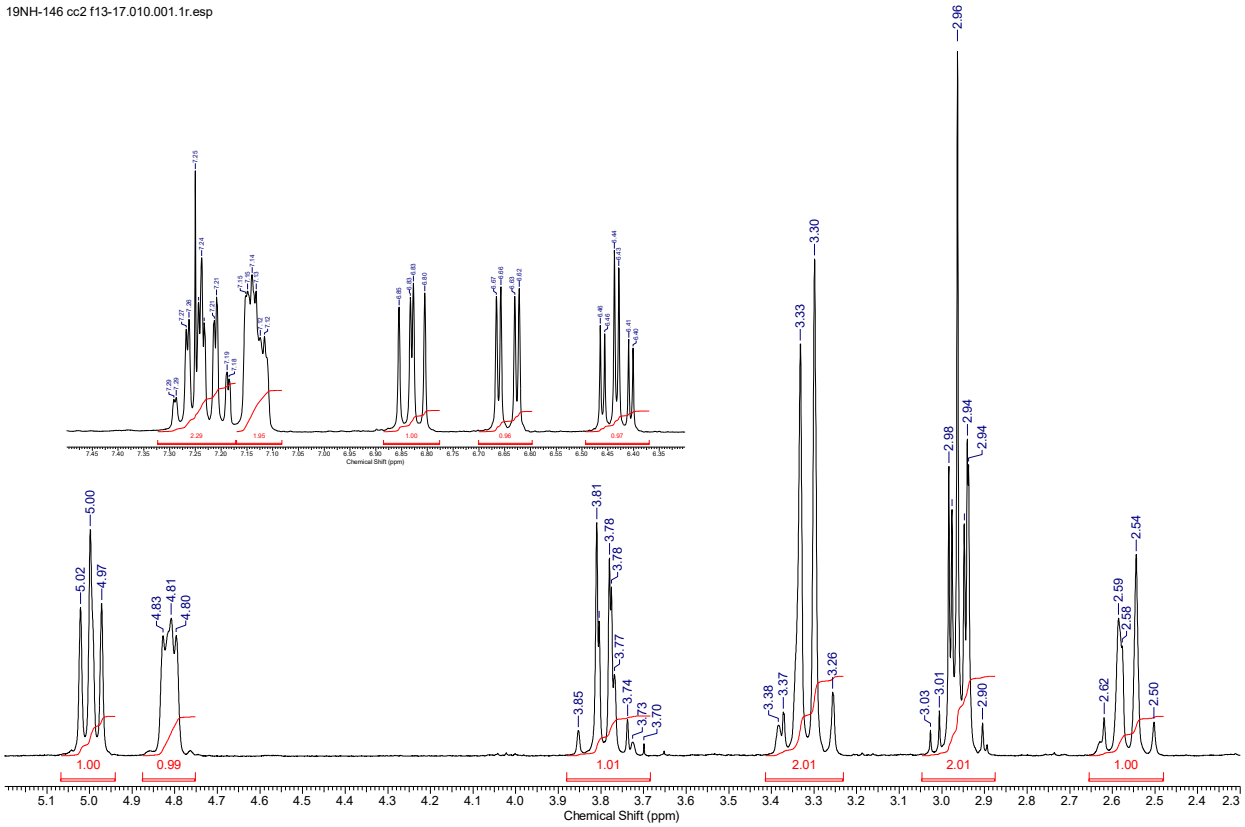


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3f**

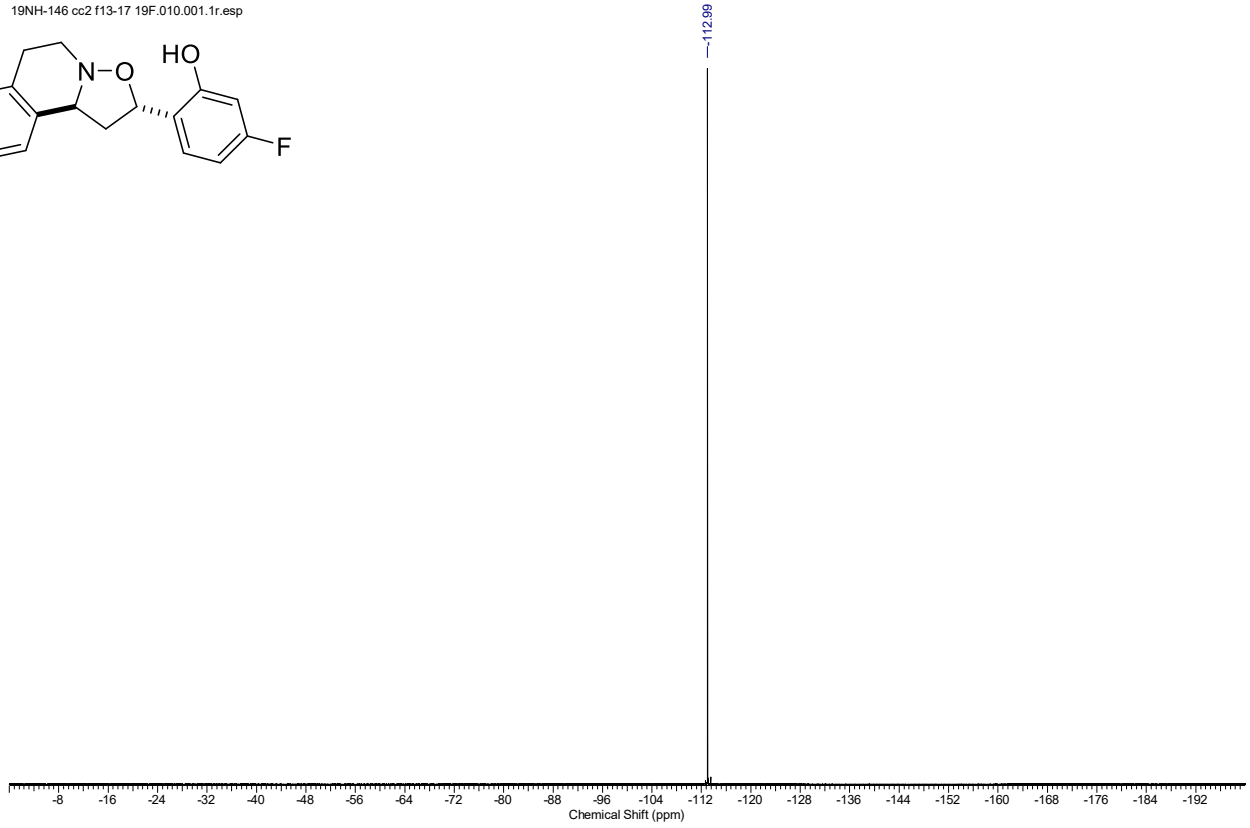


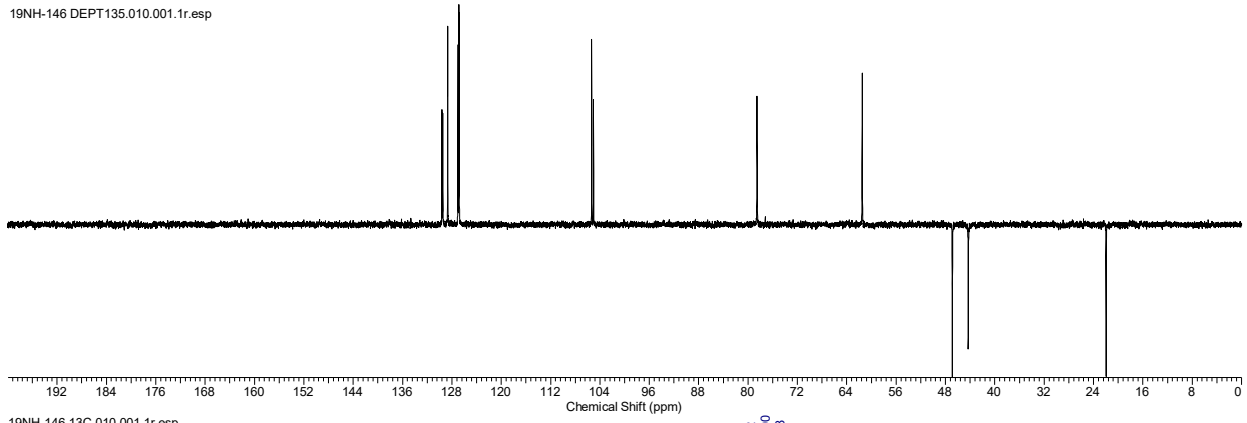
^{1}H NMR (300 MHz, $CDCl_3$) of **3g**

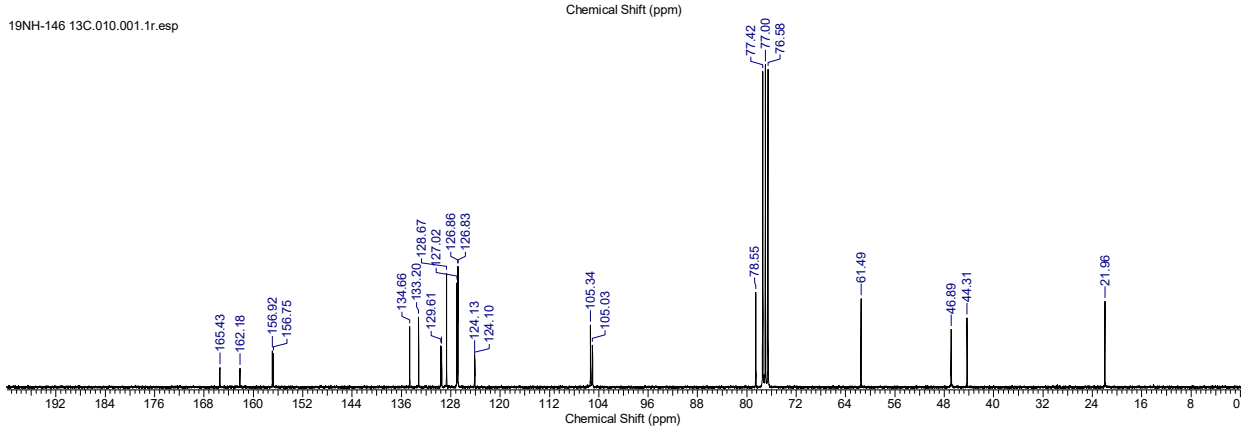




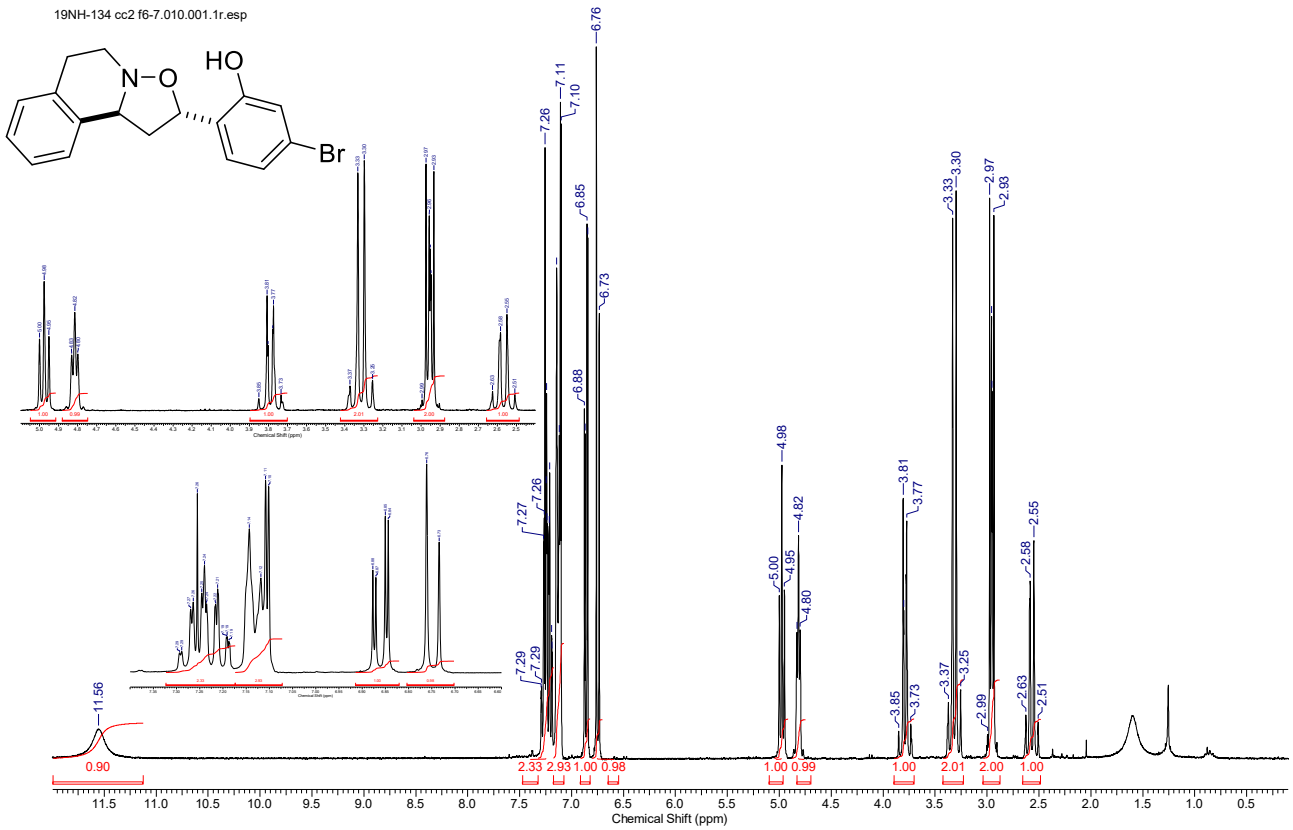
^{19}F NMR (282 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) of **3g**

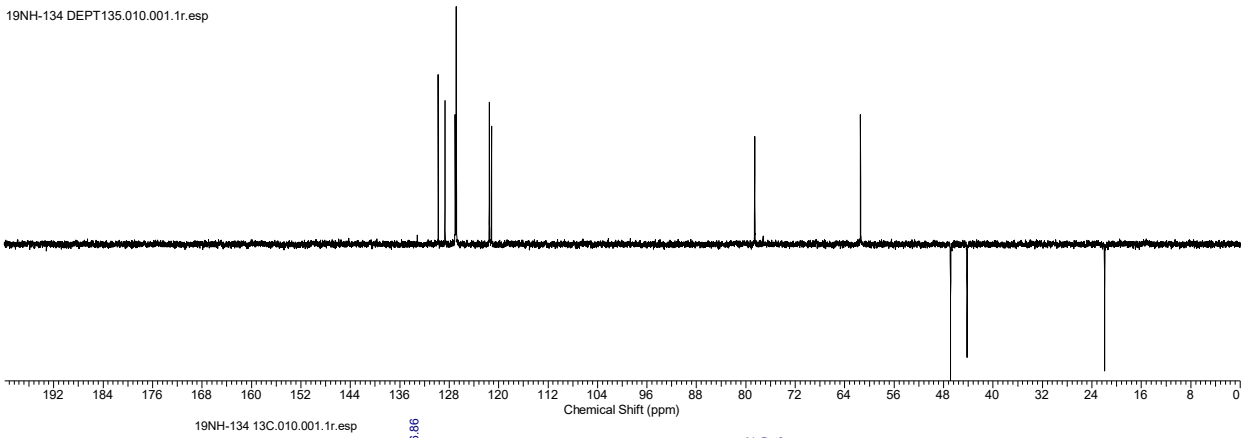


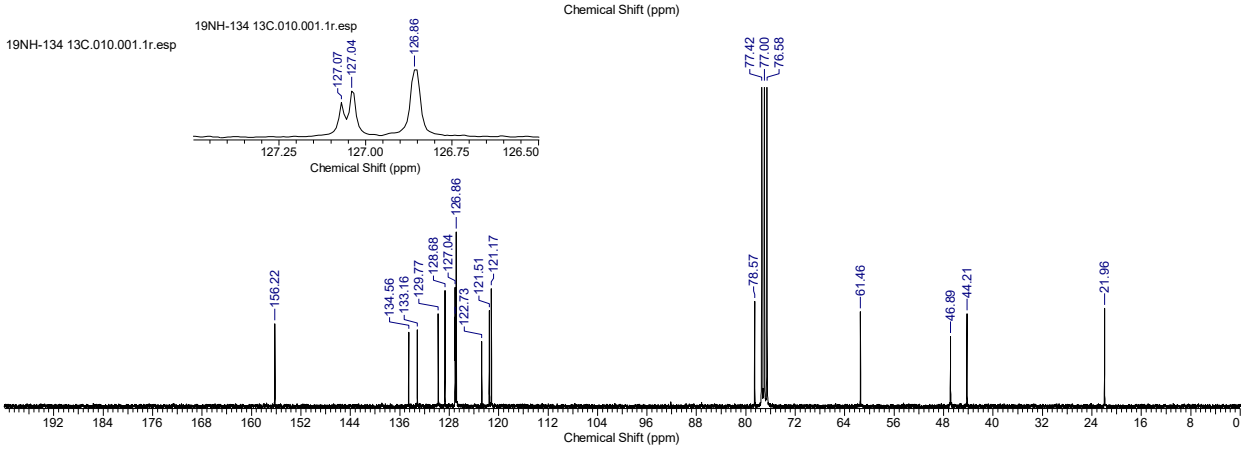




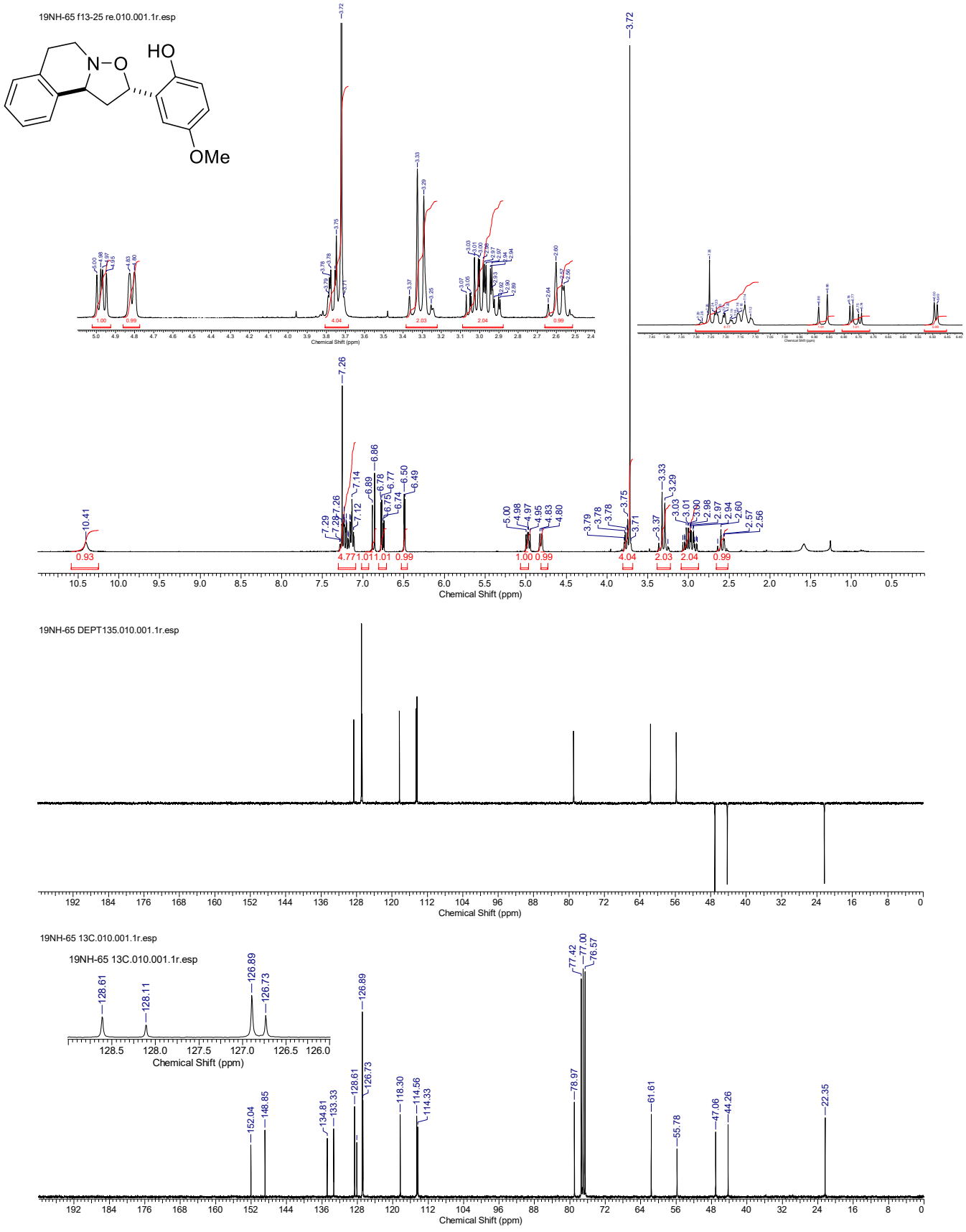
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3h**



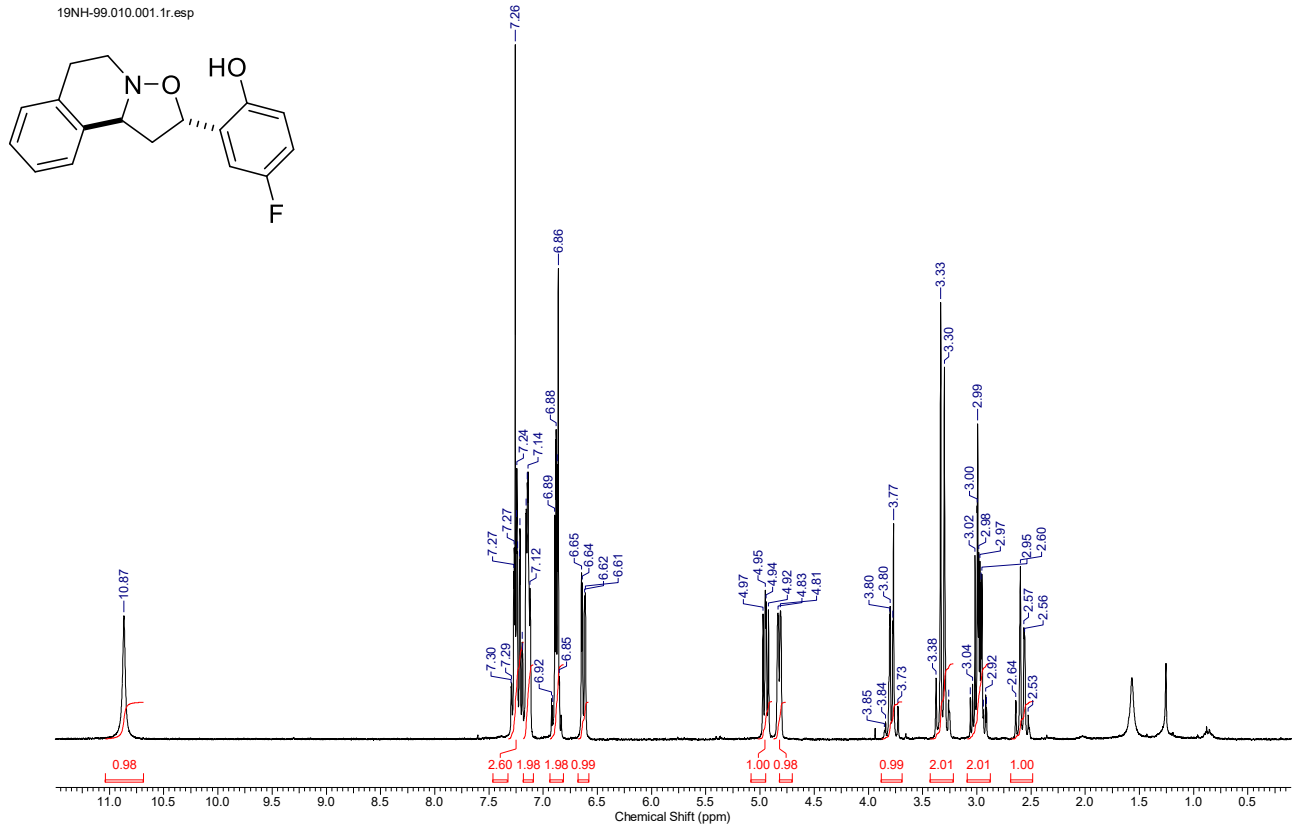


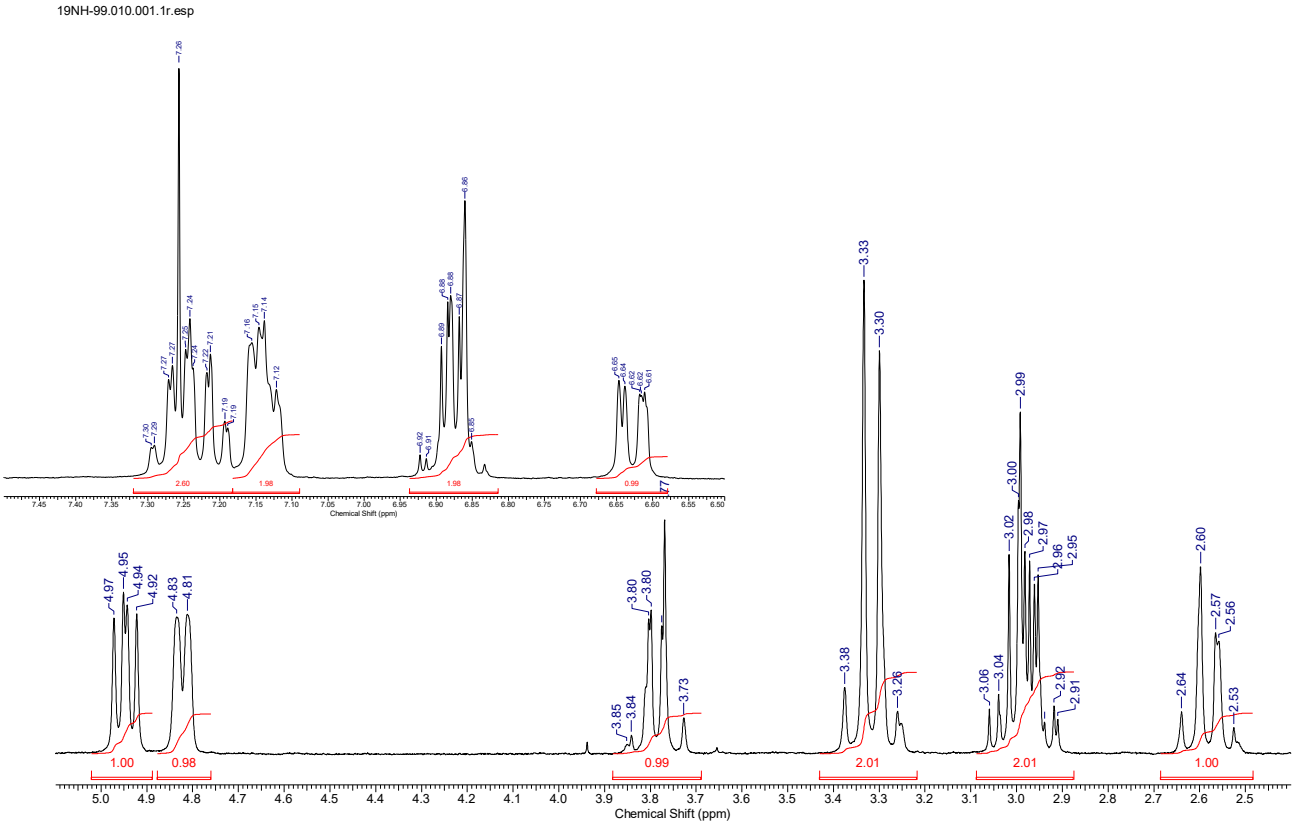


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3i**

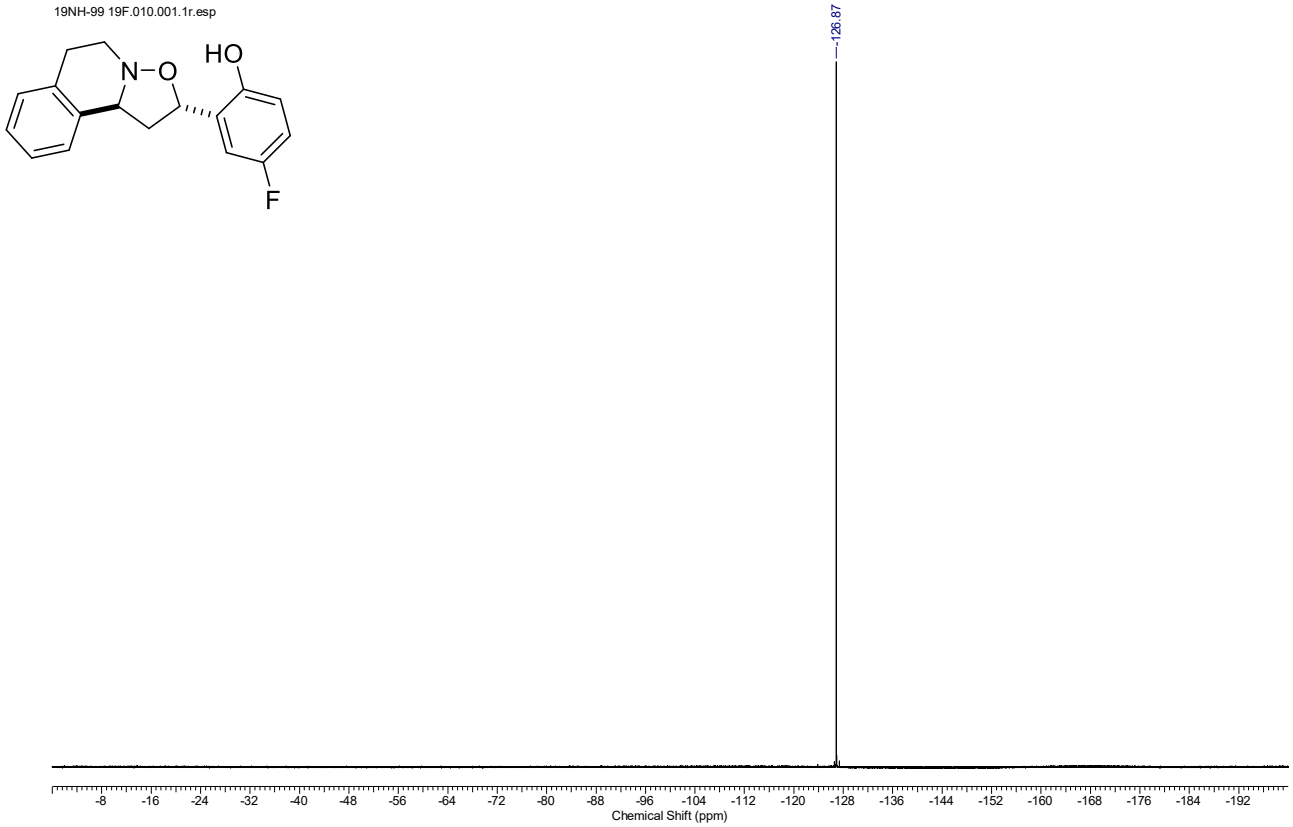


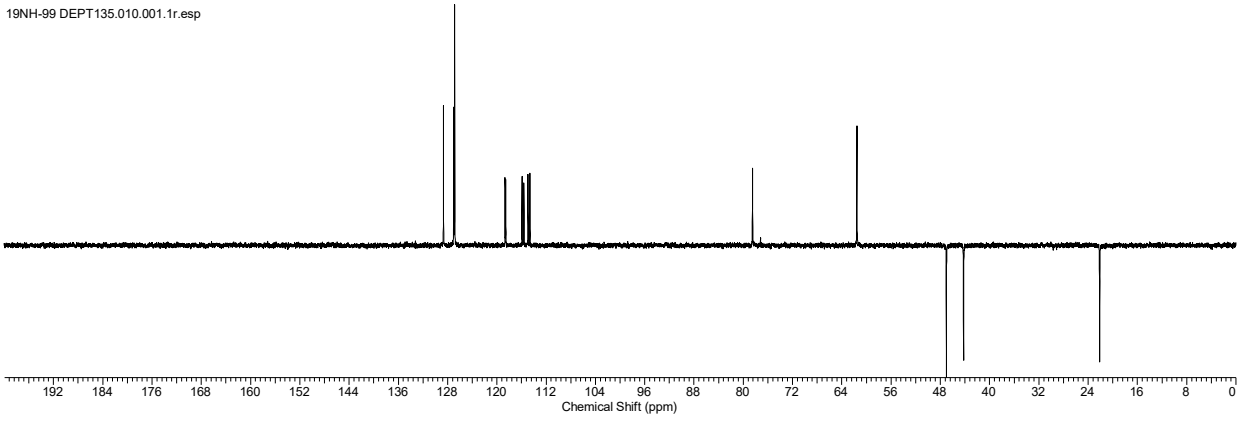
^{1}H NMR (300 MHz, $CDCl_3$) of **3j**

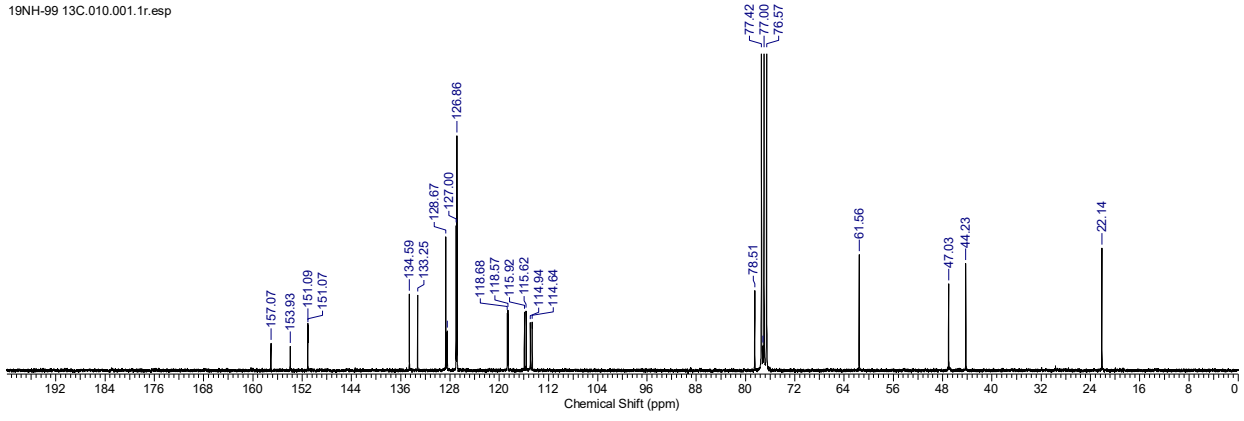




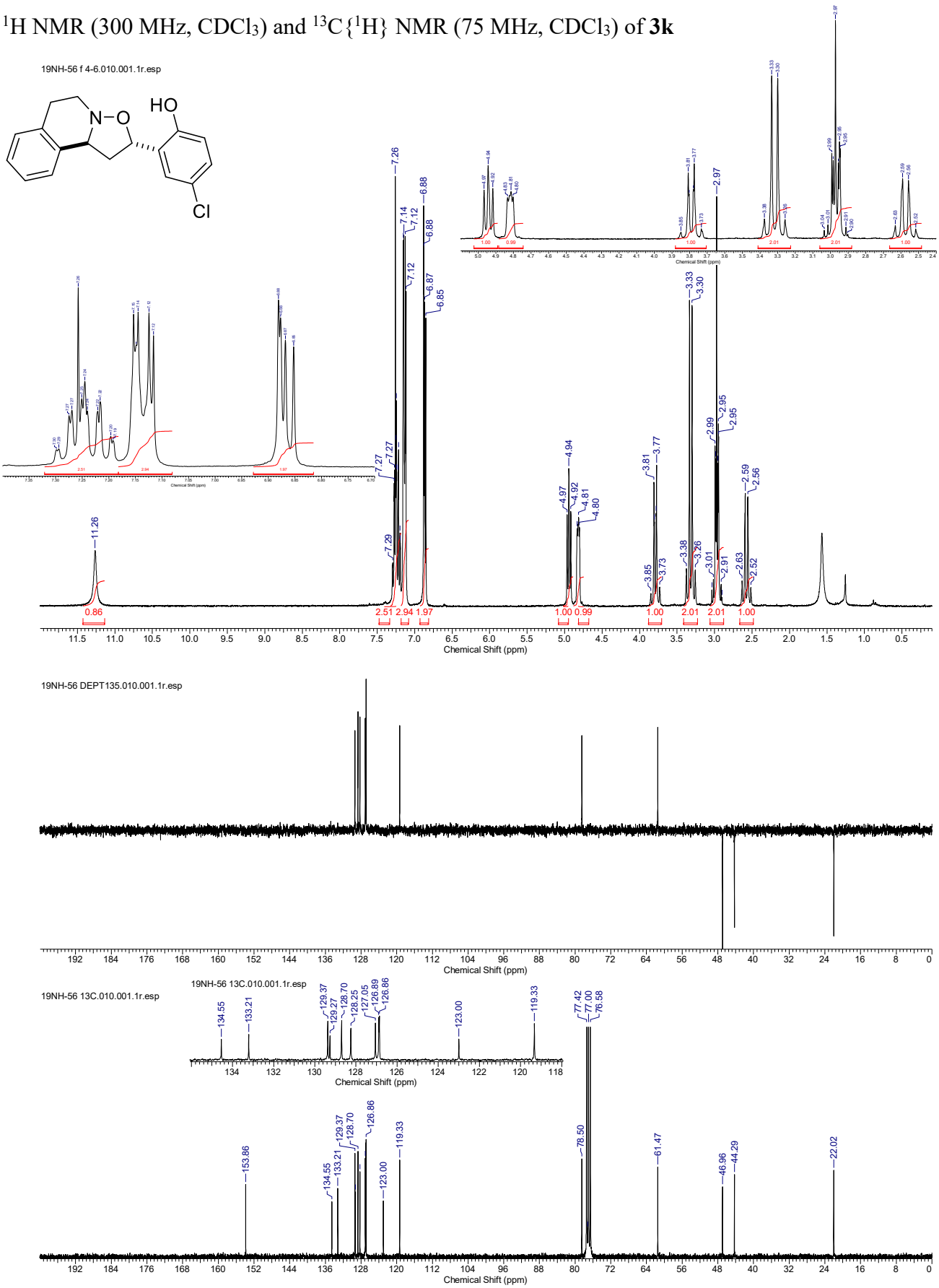
^{19}F NMR (282 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) of **3j**



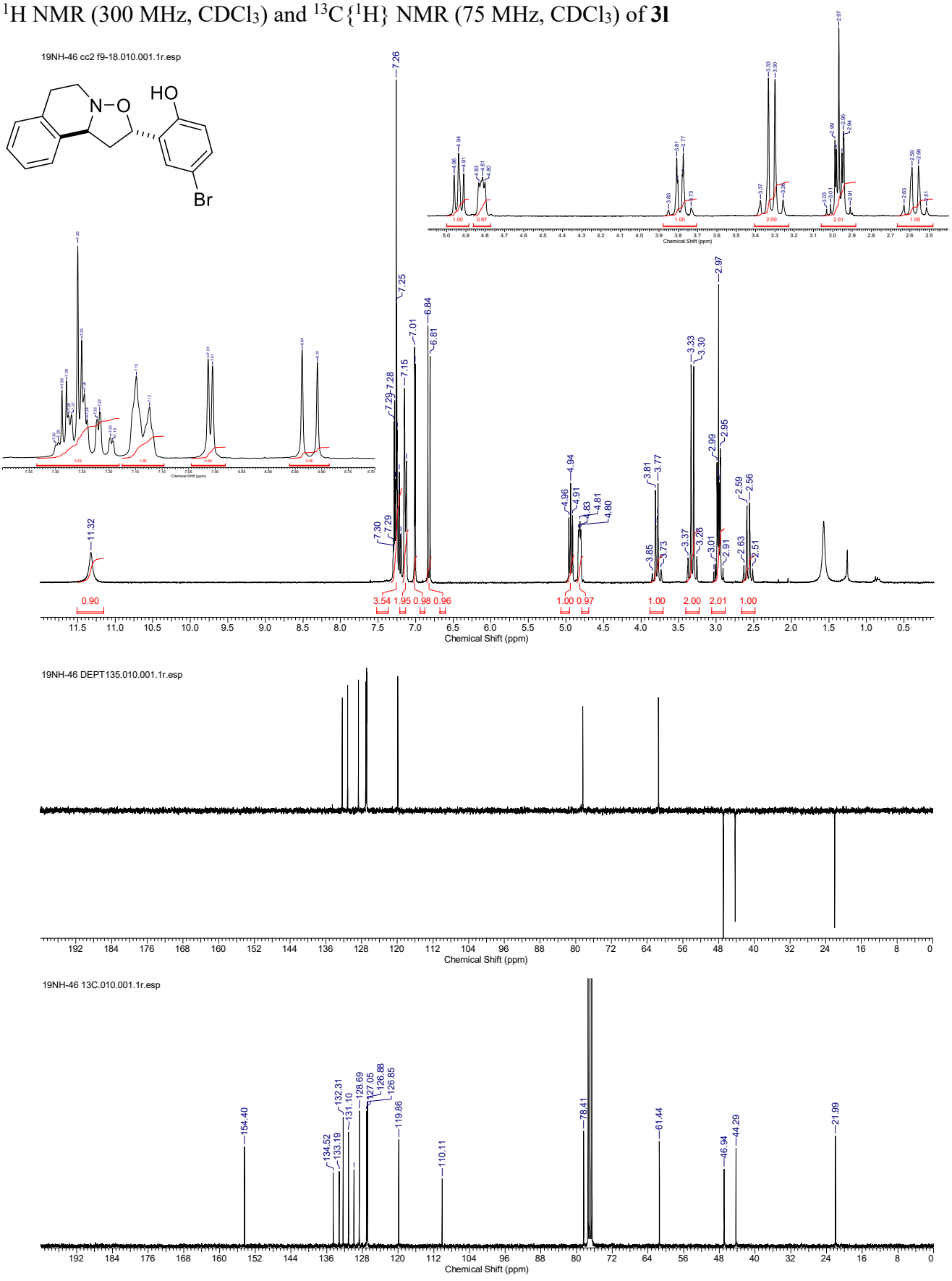




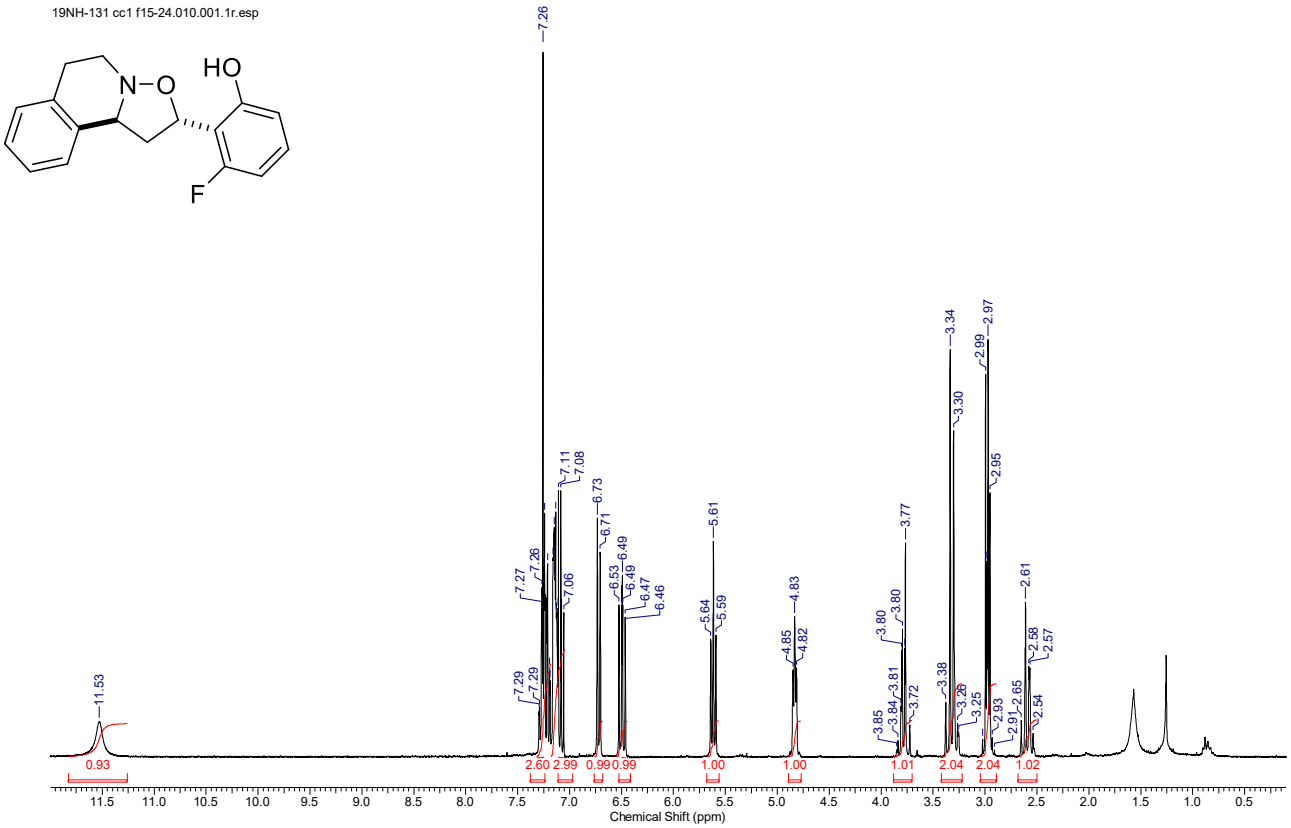
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3k**

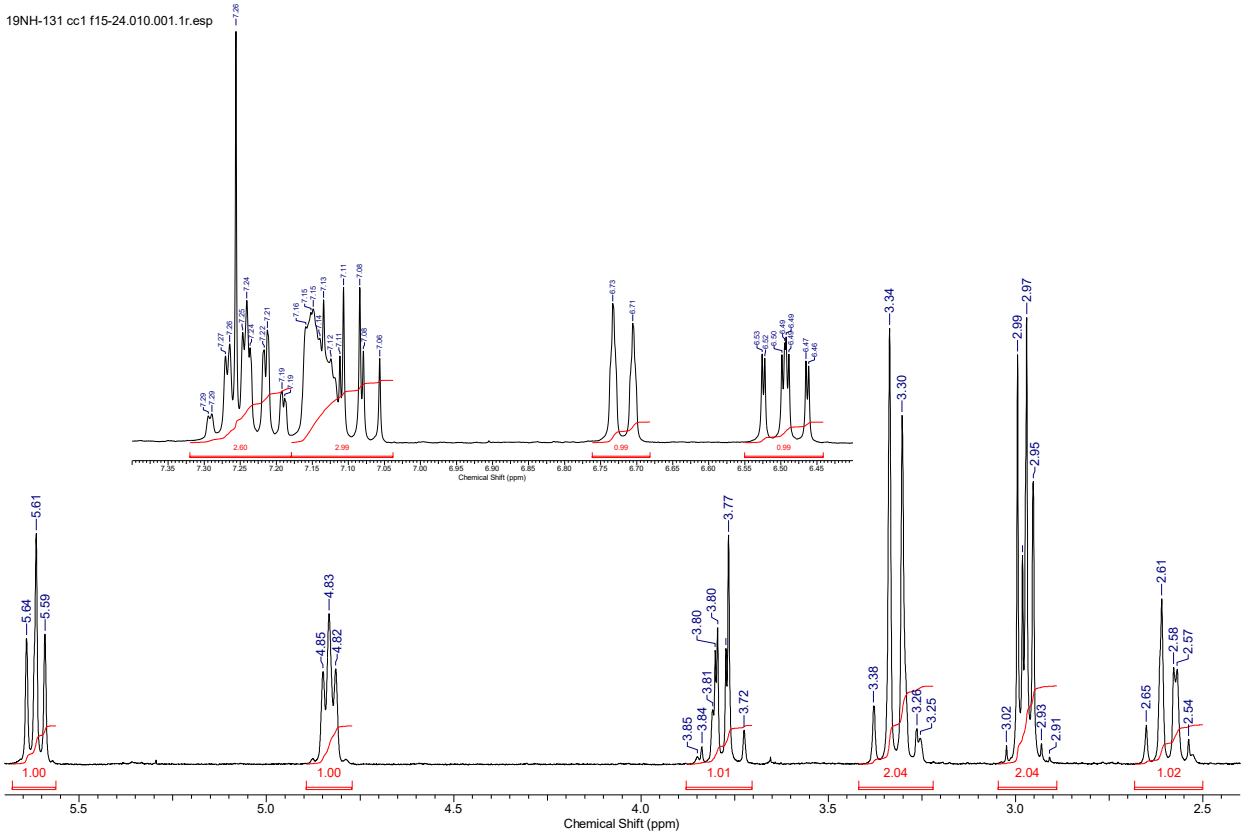


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3l**

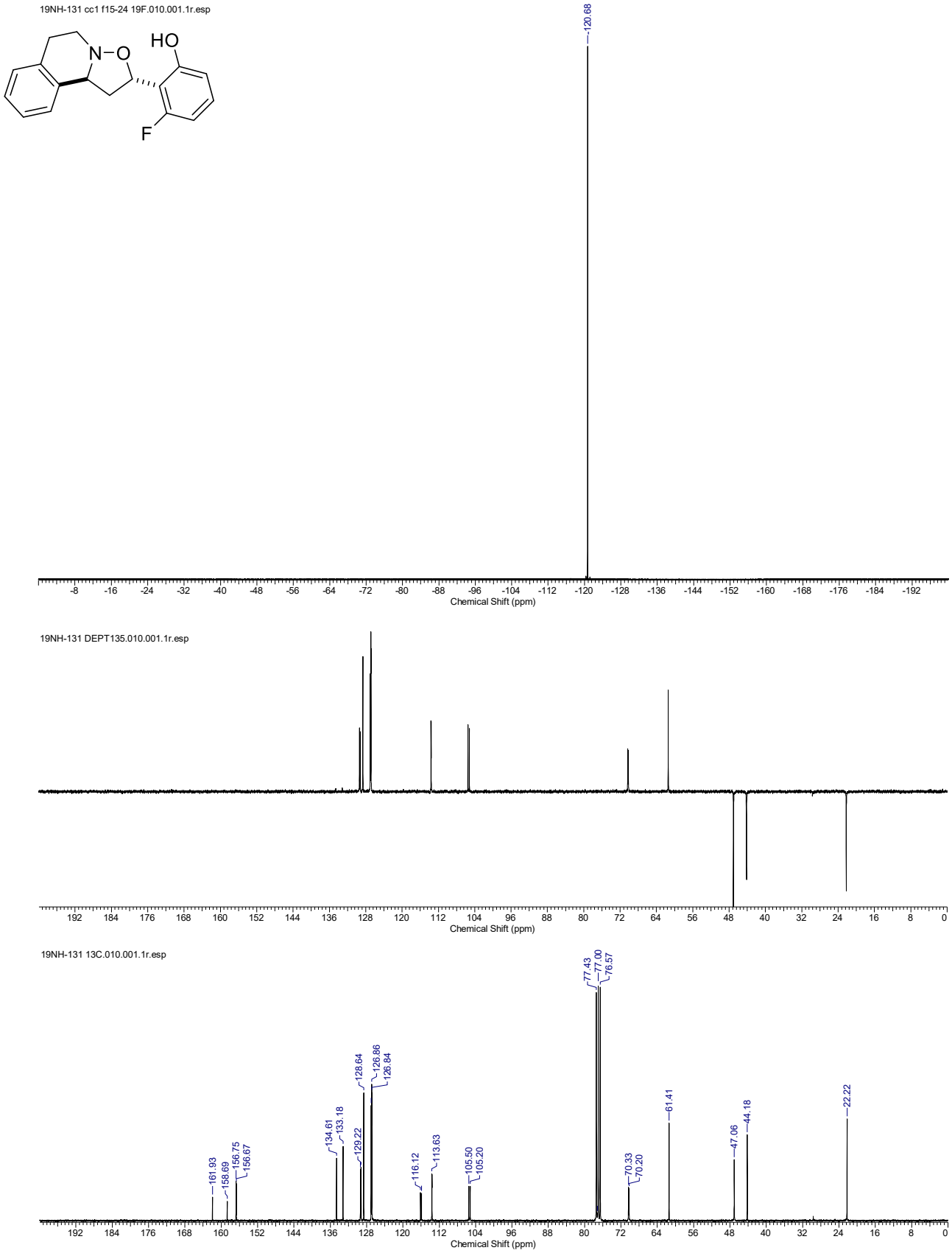


^{1}H NMR (300 MHz, $CDCl_3$) of **3m**

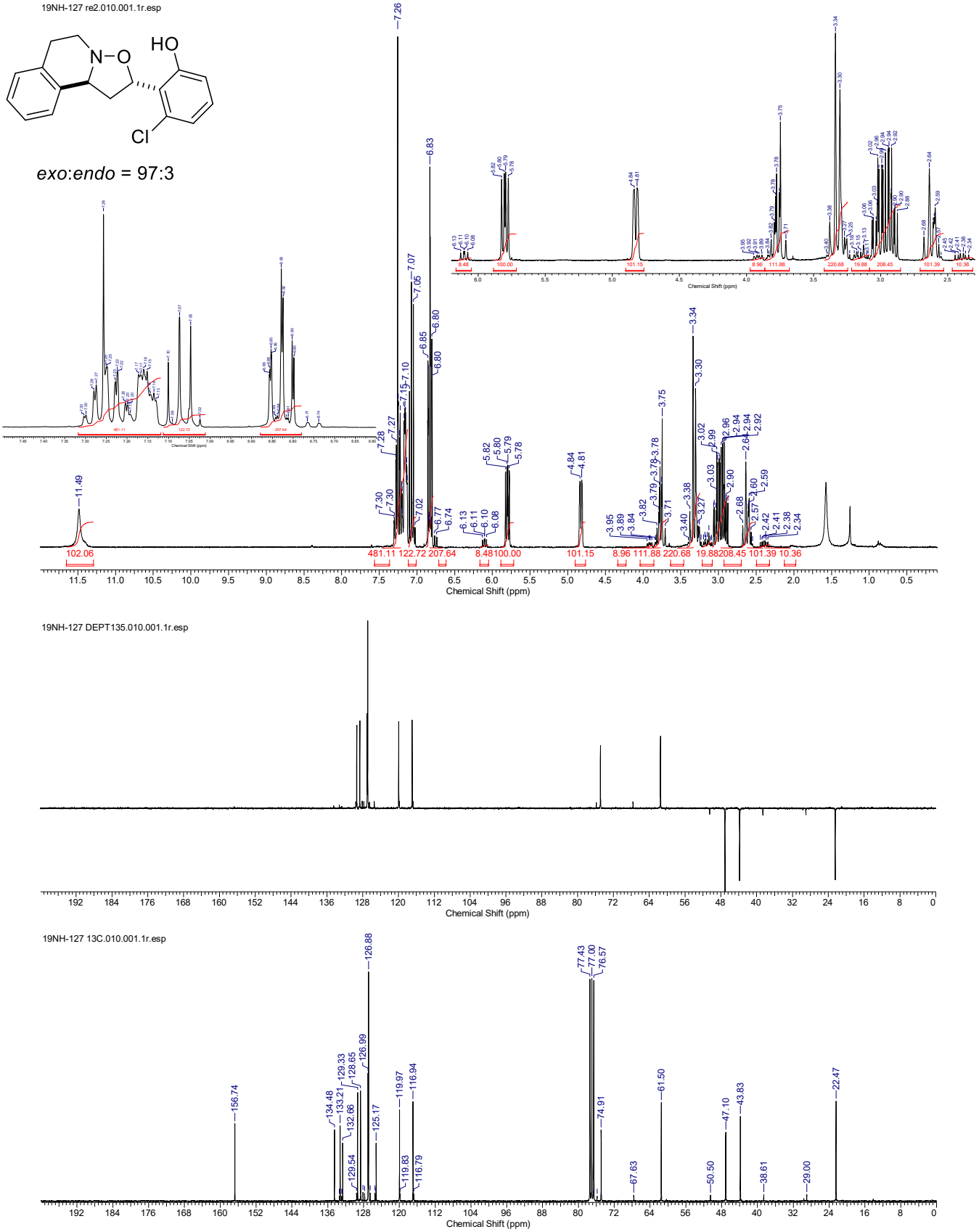




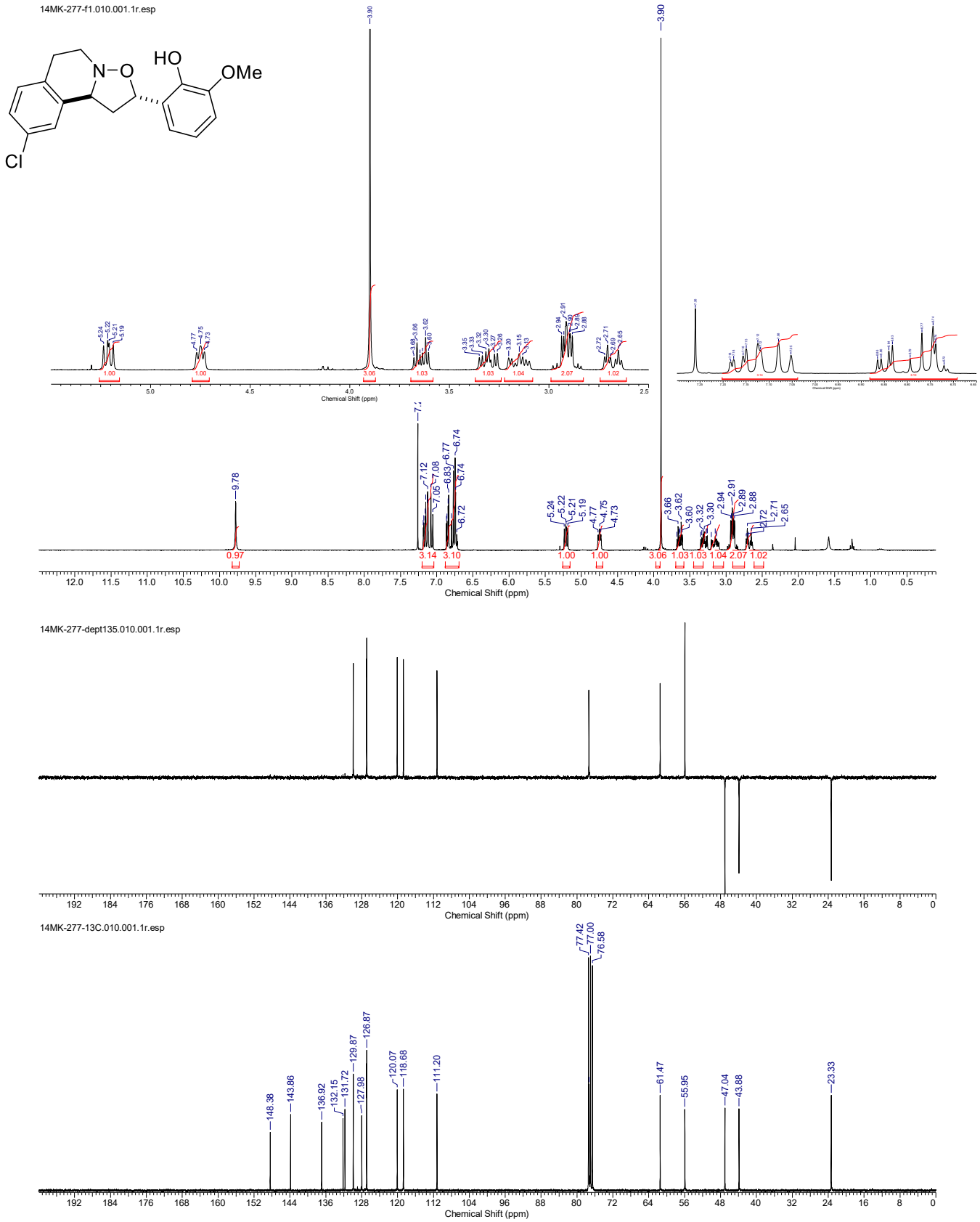
^{19}F NMR (282 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) of **3m**



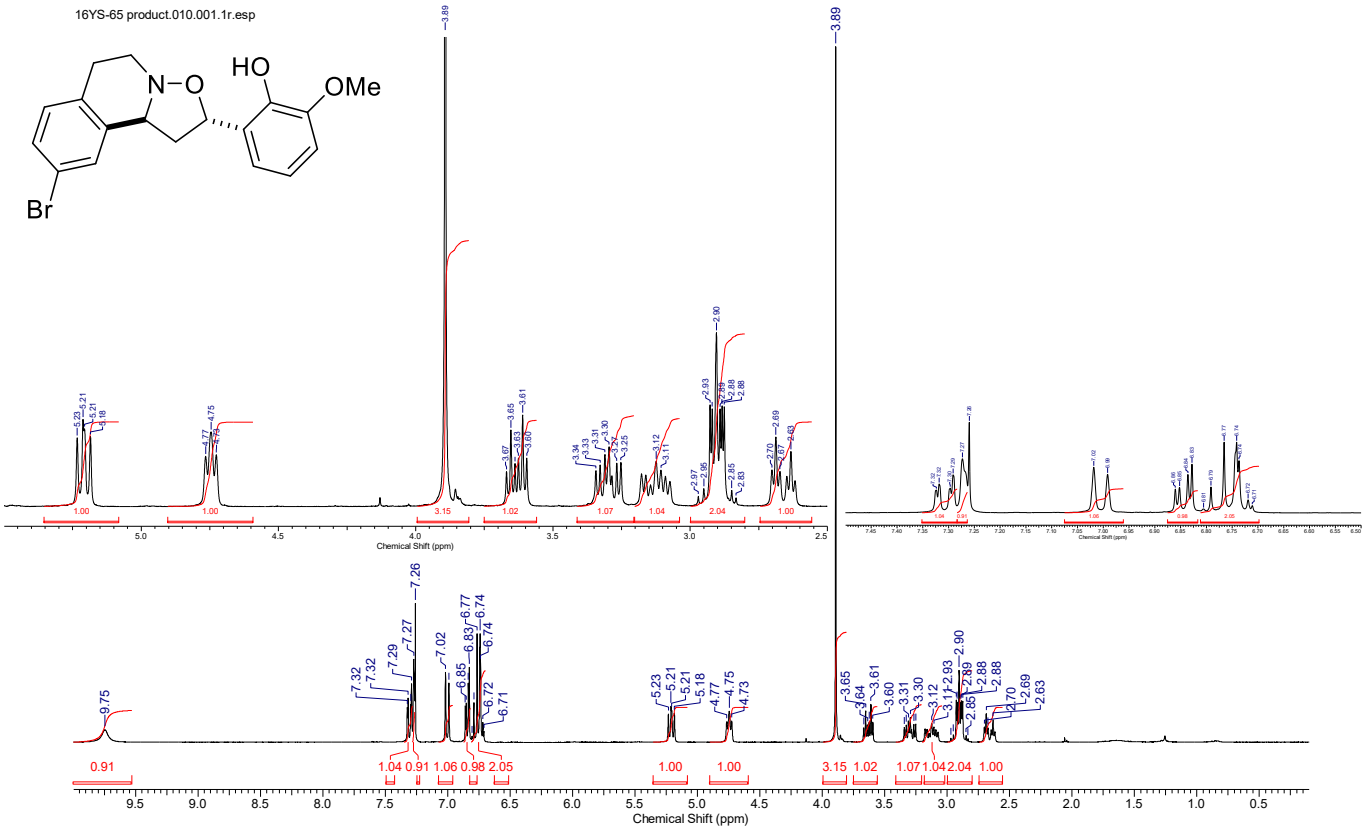
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3n**

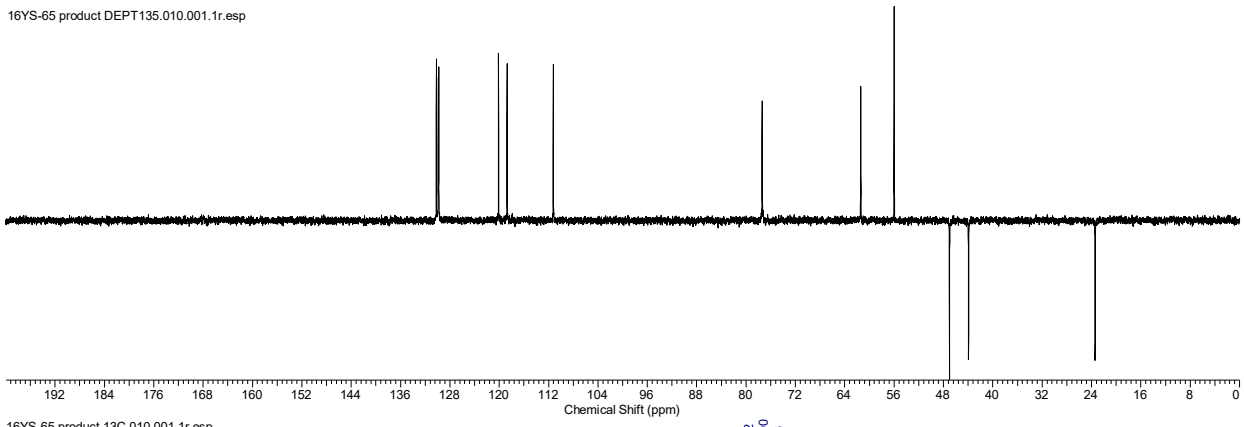


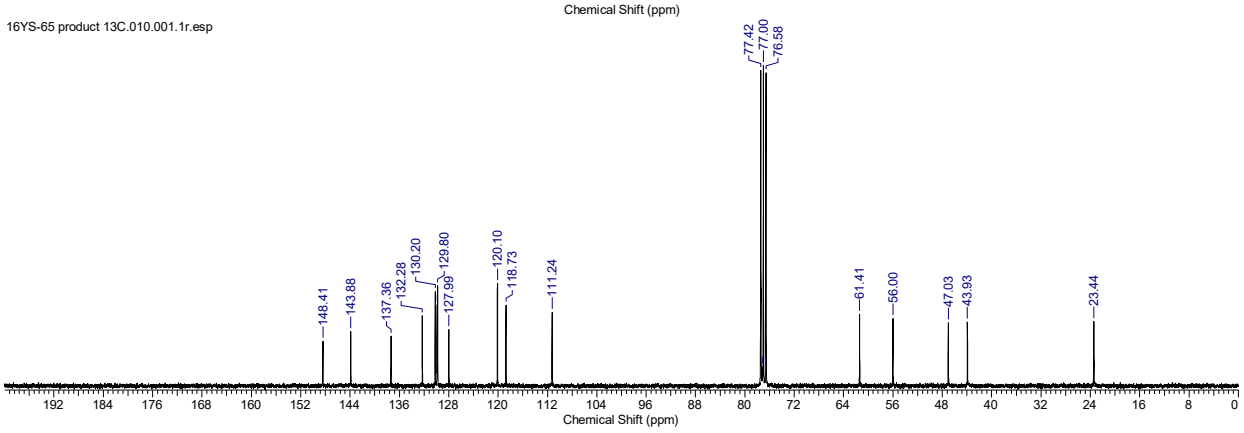
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3o**



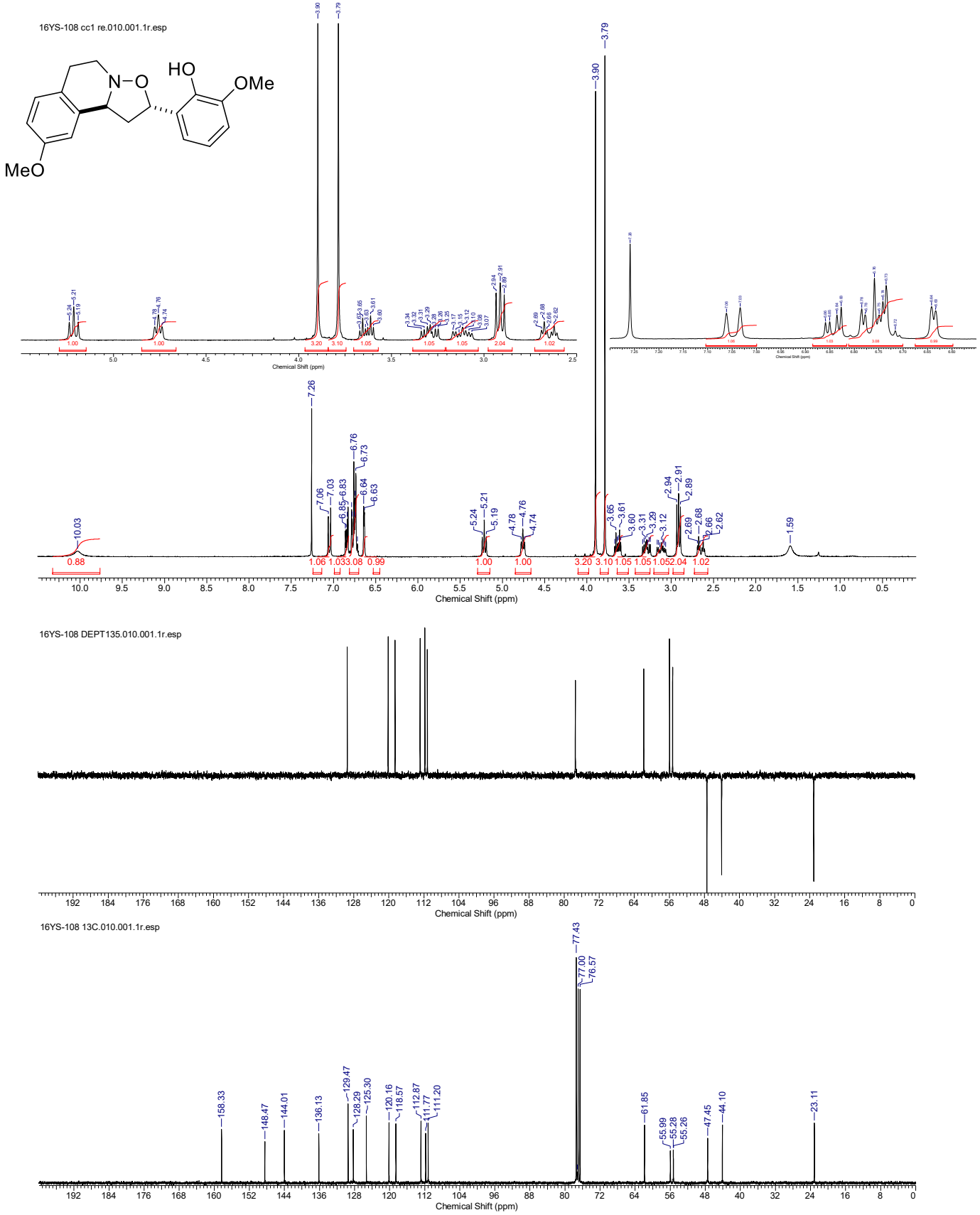
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3p**



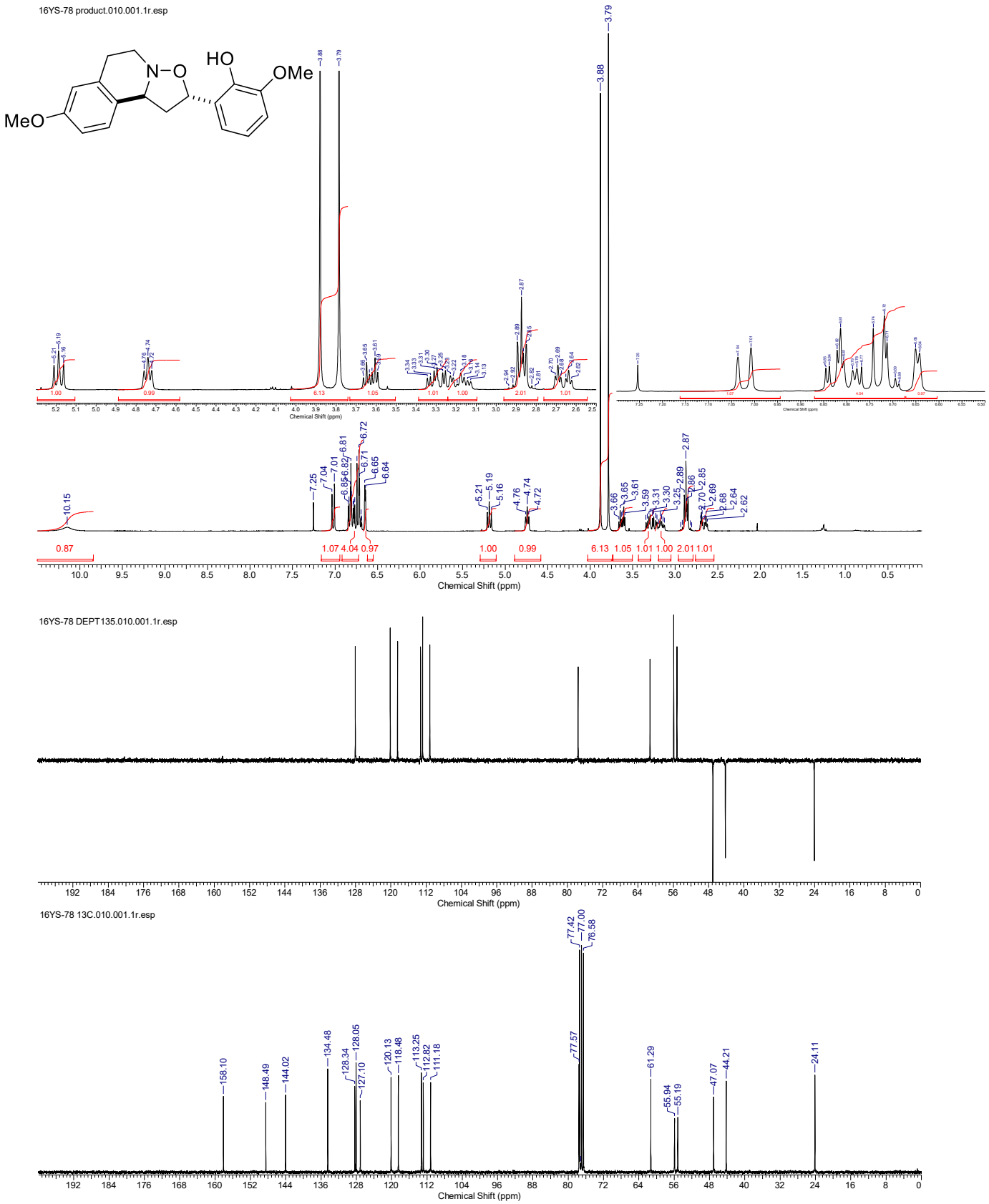




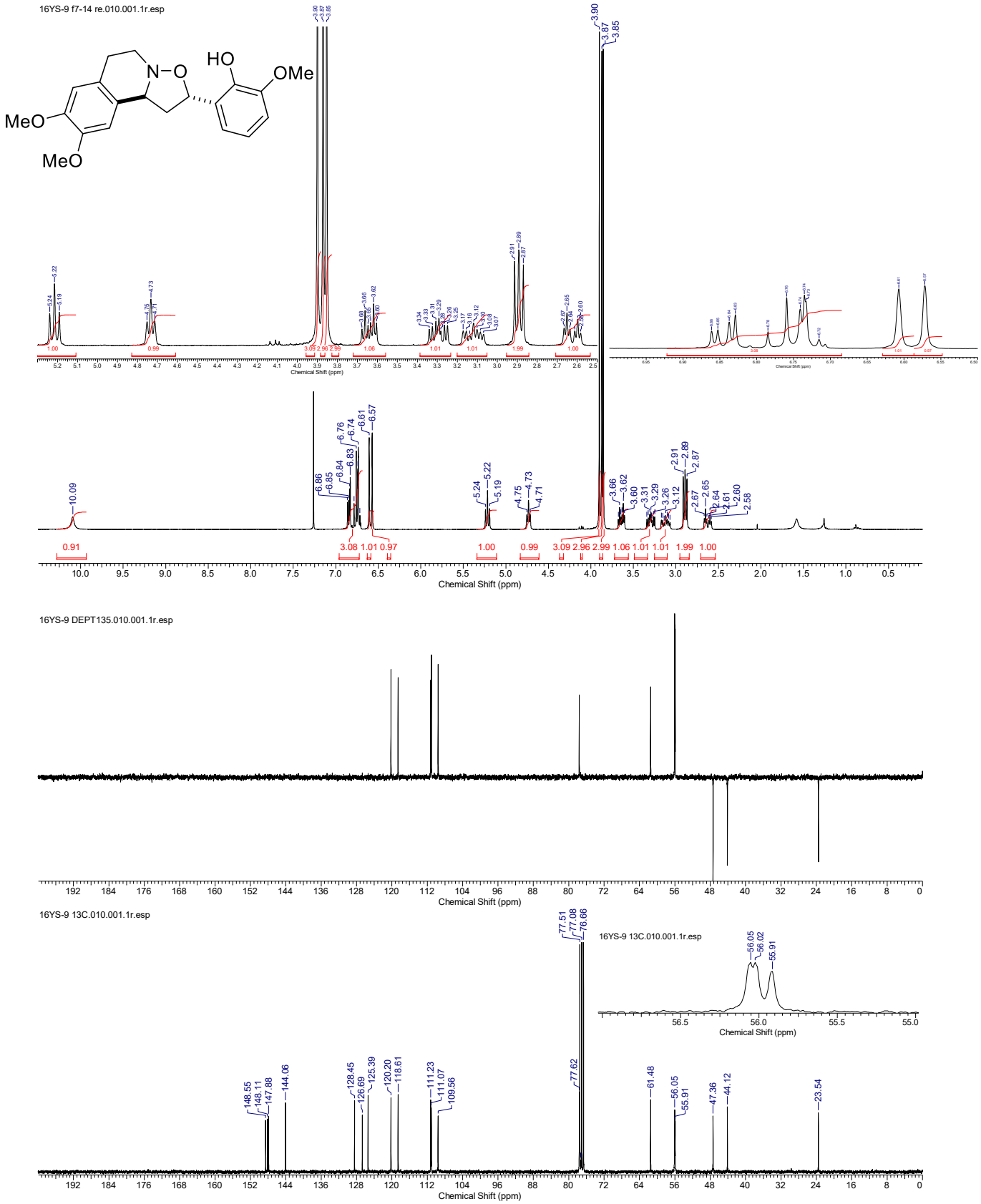
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3q**



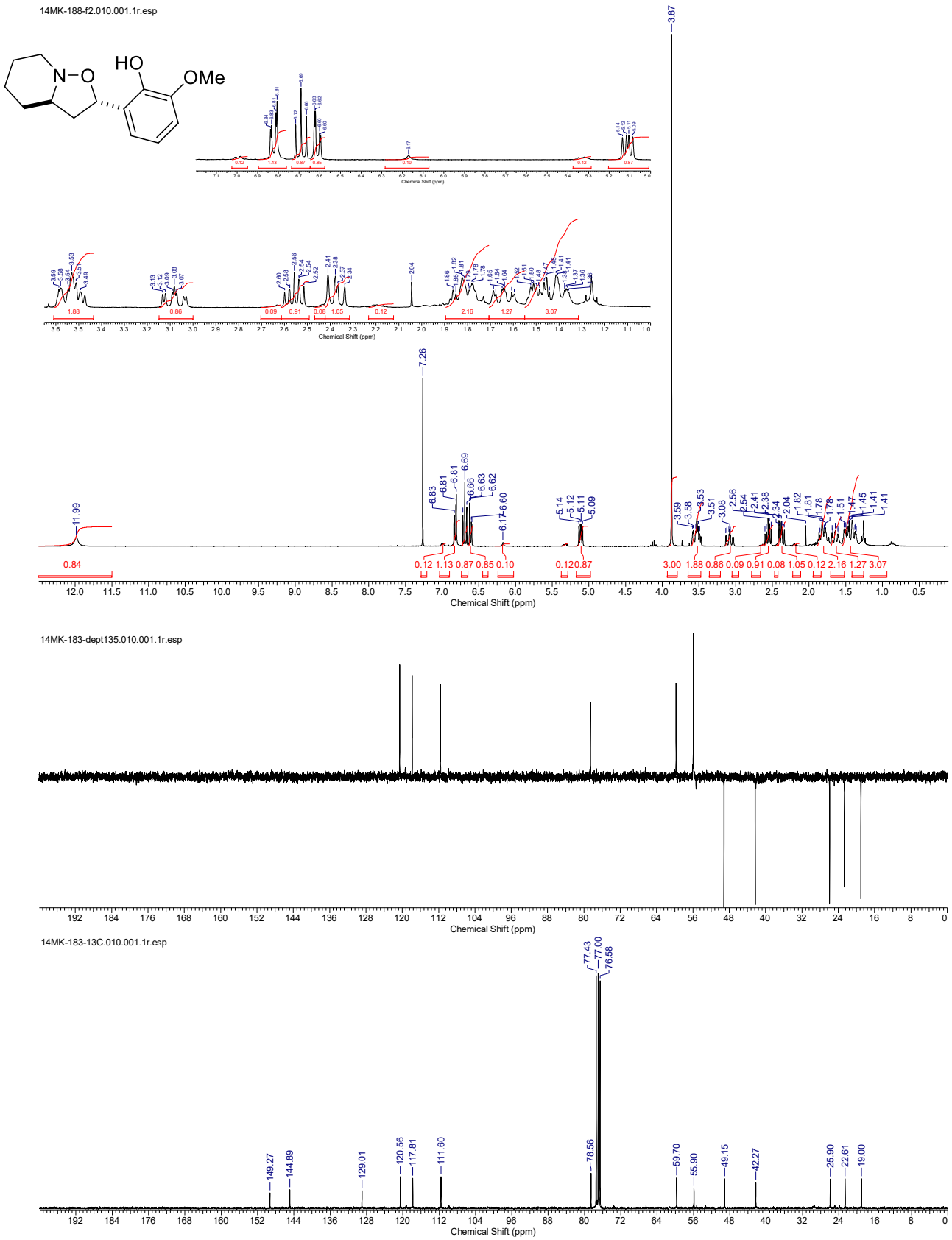
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3r**



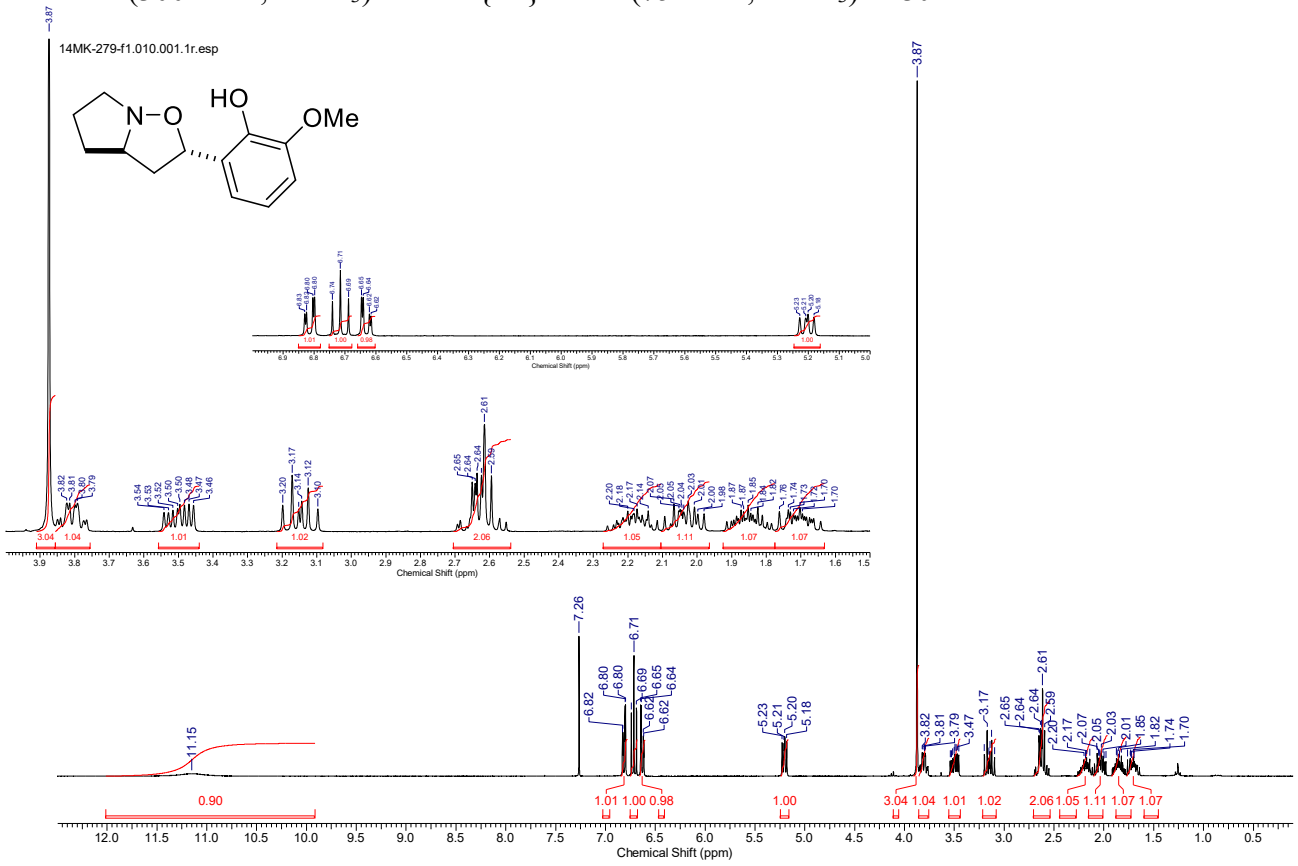
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3s**

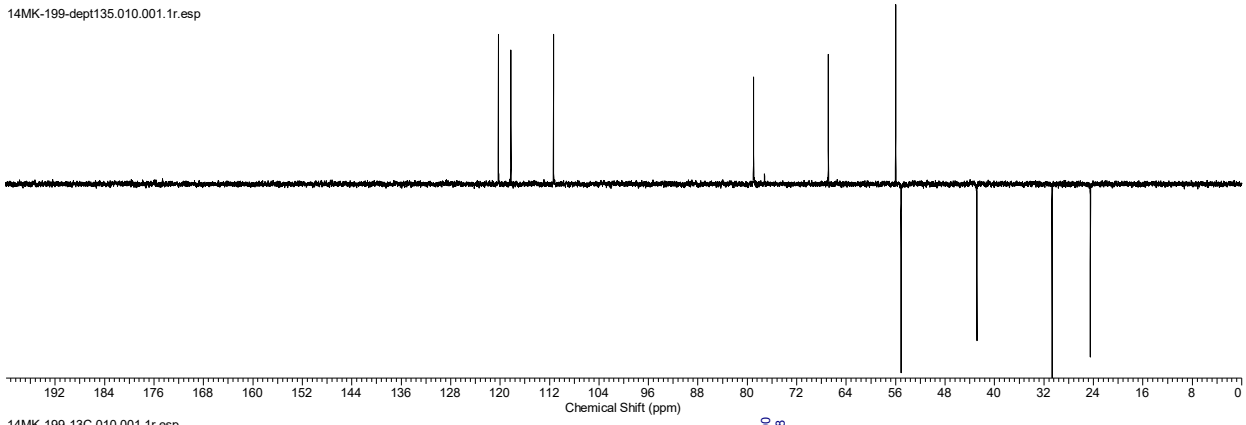


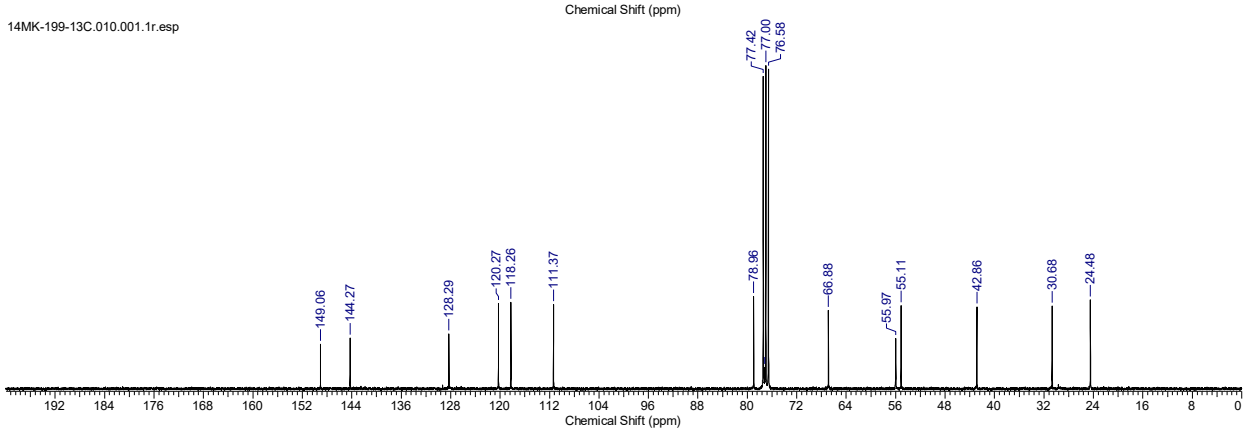
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3t**



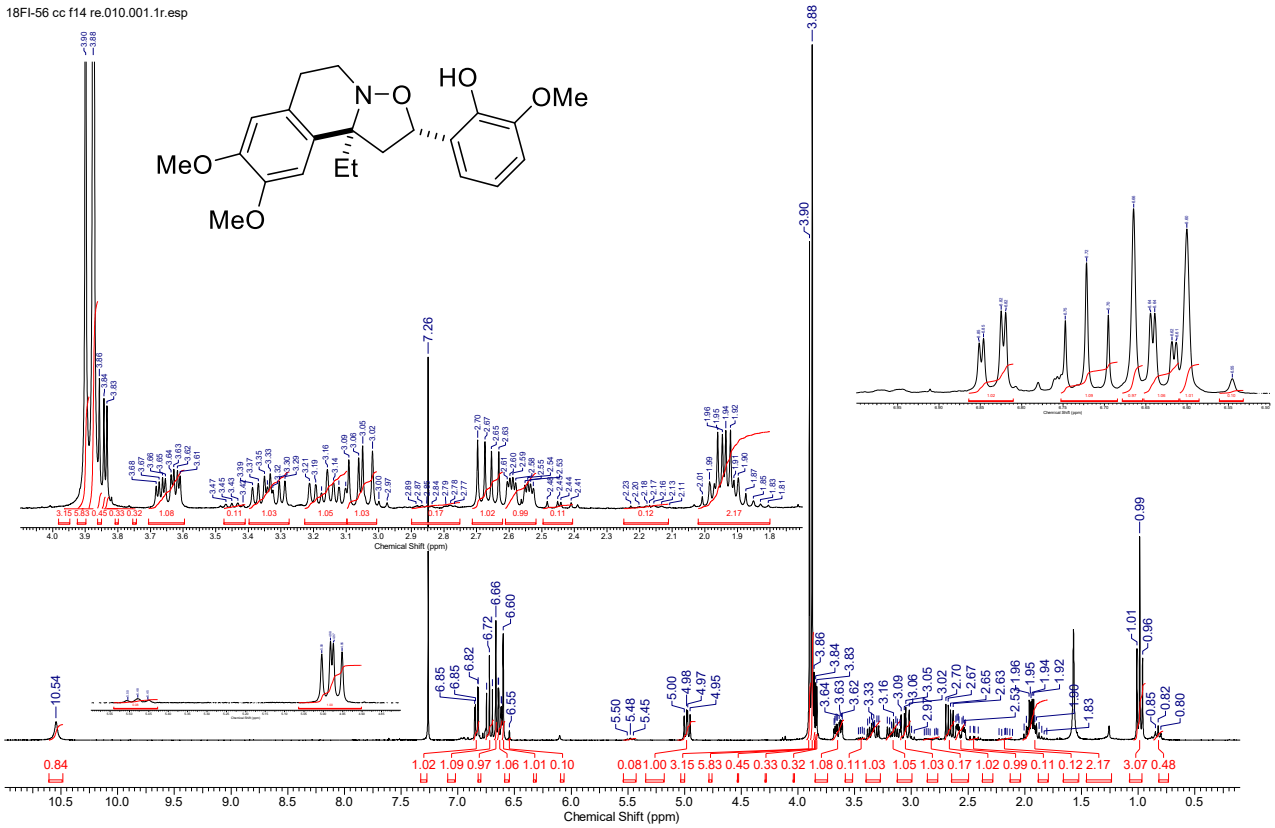
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3u**

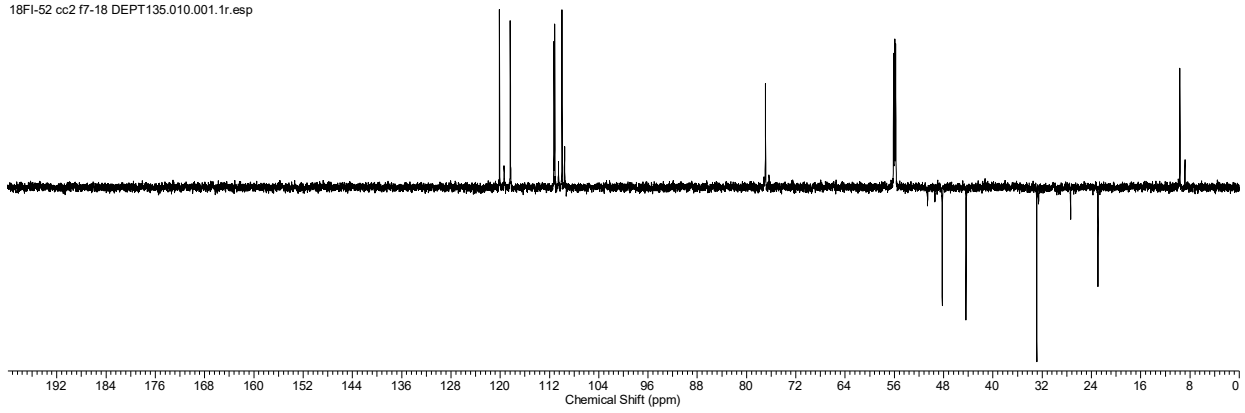


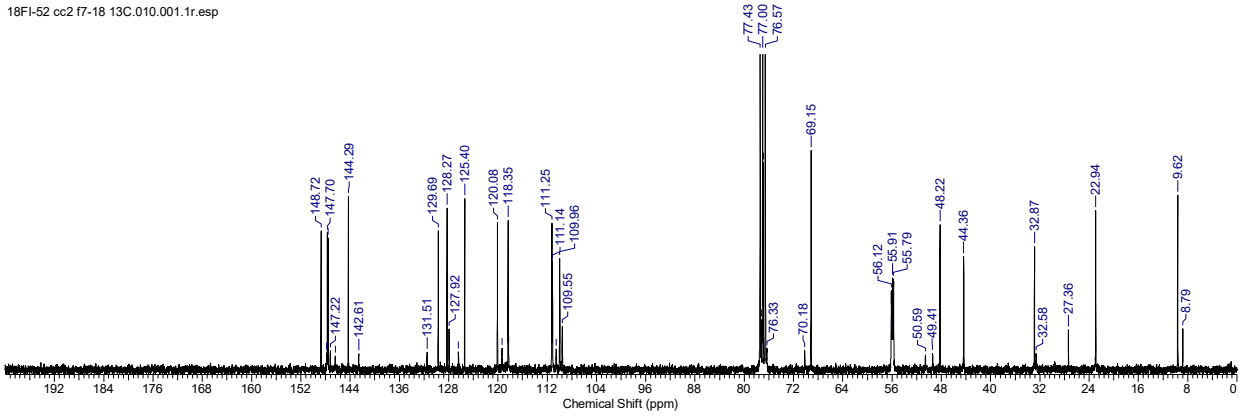




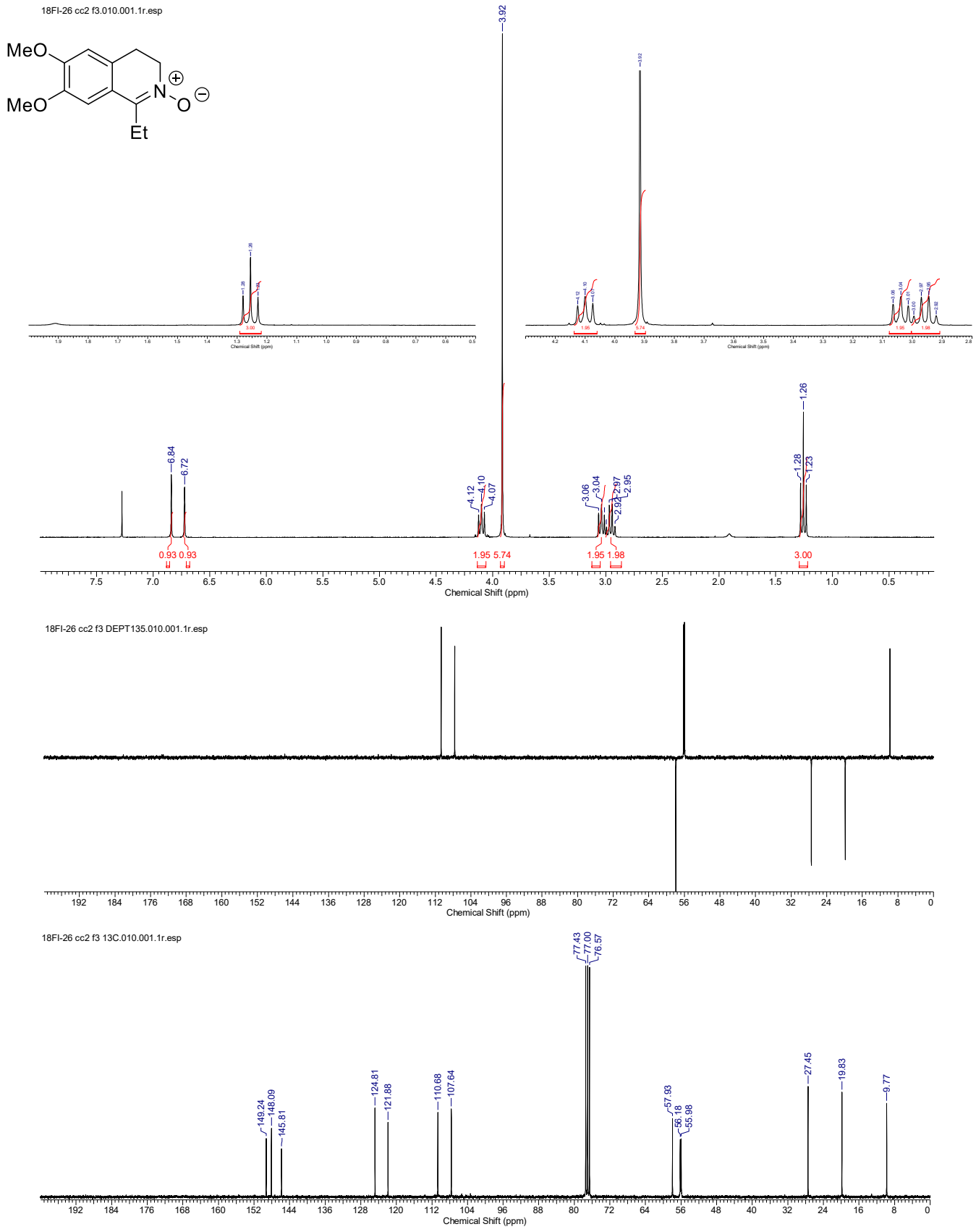
^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3v**



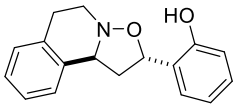


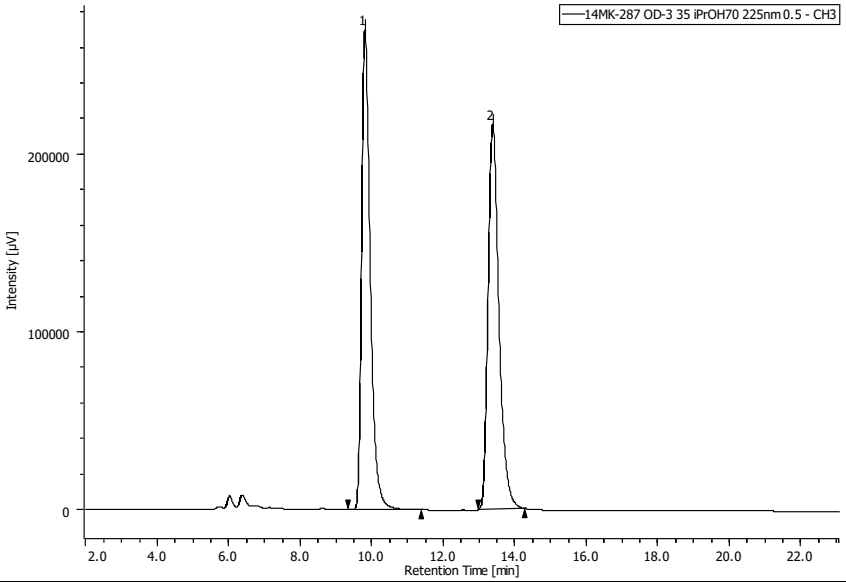


^{1}H NMR (300 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1i**



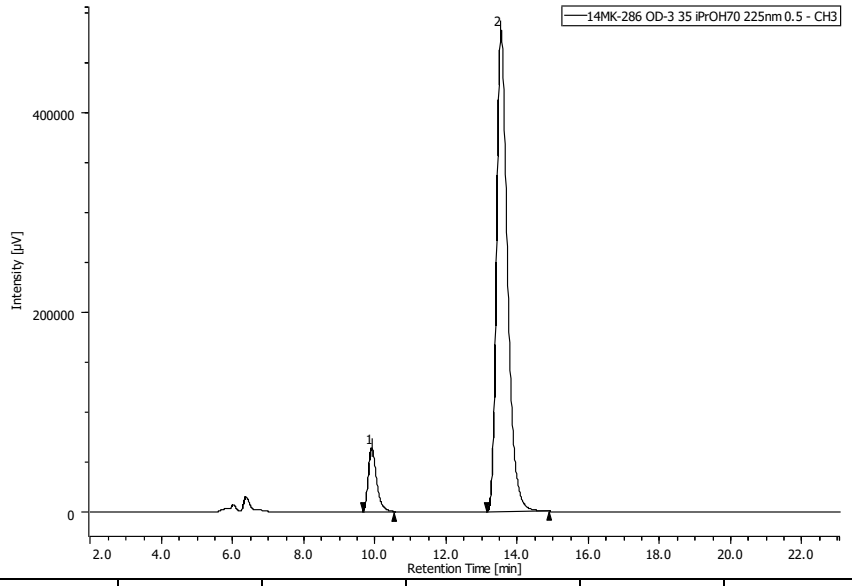
HPLC analyses HPLC analysis of **3a**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	9.800	4548545	270035	49.839
2	3	13.367	4577908	216398	50.161

Racemate

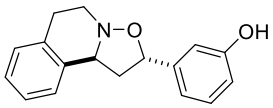


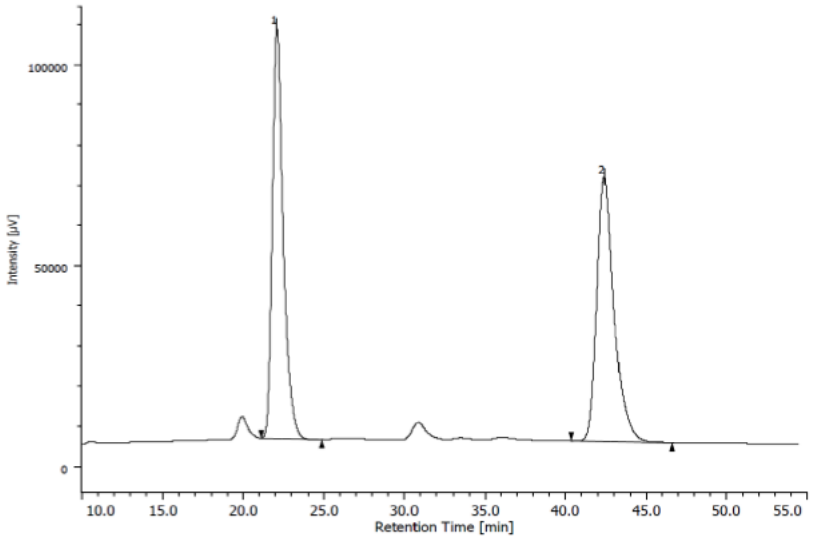
# Peak	CH	tR (min)	Area	Height	Area%
1	3	9.892	1032433	63623	9.092
2	3	13.525	10322775	480956	90.908

81% ee

Chiralcel OD-3, Hexane:^{i}PrOH = 30:70, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C

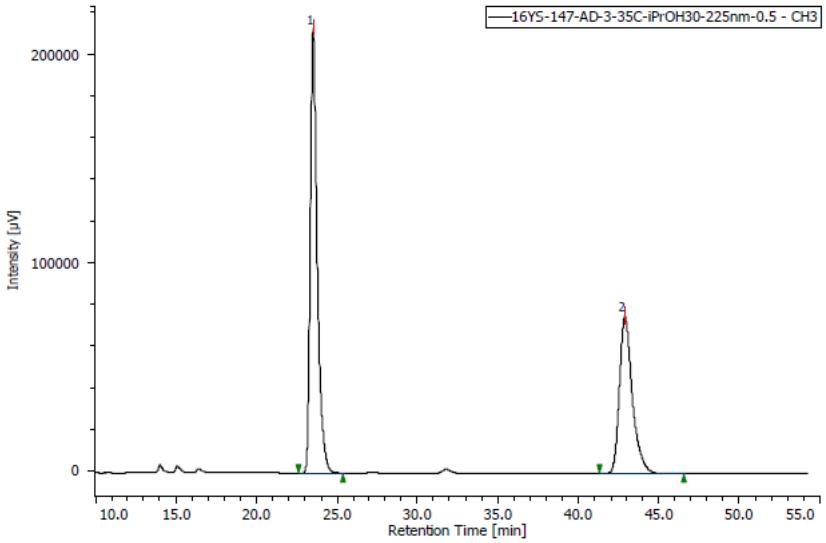
HPLC analysis of **4**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	22.1	3812987	102129	49.762
2	3	42.4	3849492	65723	50.238

Racemate

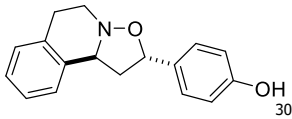


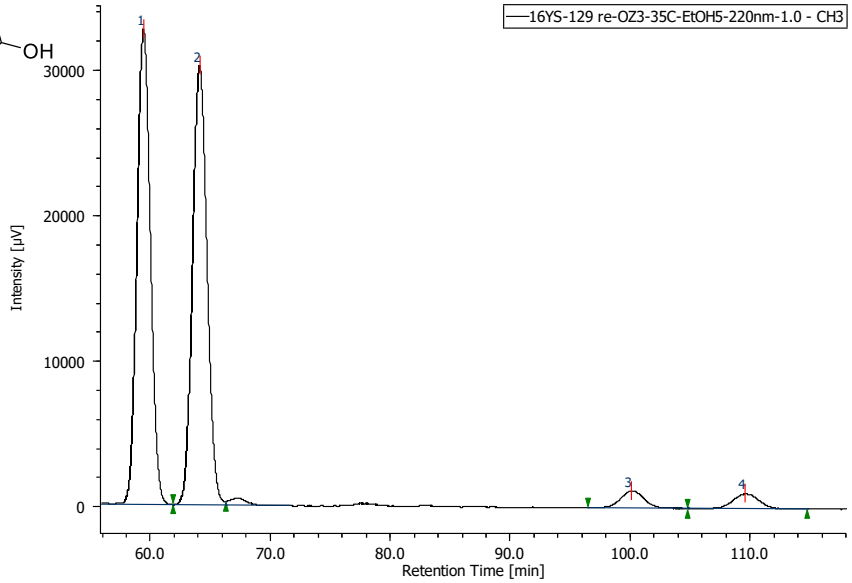
# Peak	CH	tR (min)	Area	Height	Area%
1	3	23.5	6441057	213374	60.563
2	3	42.9	4194182	75399	39.437

21% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 70:30, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C

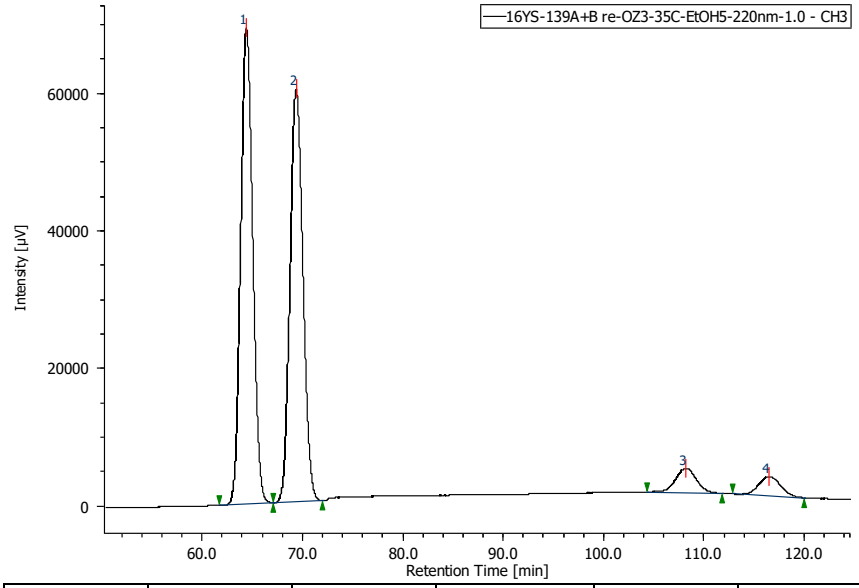
HPLC analysis of **5**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	59.442	2553736	32661	47.313
2	3	64.108	2541875	30167	47.093
3	3	100.075	150819	1159	2.794
4	3	109.5	151162	1004	2.801

Racemate

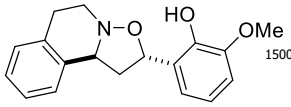


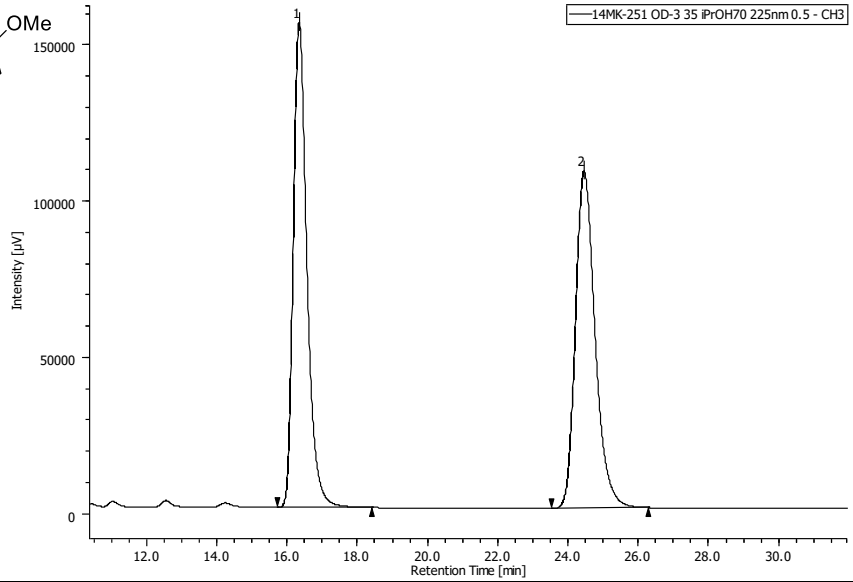
# Peak	CH	tR (min)	Area	Height	Area%
1	3	59.067	2095573	26929	49.008
2	3	64.475	1975185	23214	46.193
3	3	100.792	99724	817	2.332
4	3	111.583	105504	745	2.467

exo:*endo* = 92:8, 3% ee (*exo*), 3% ee (*endo*)

Chiralcel OZ-3, Hexane:EtOH = 95:5, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C

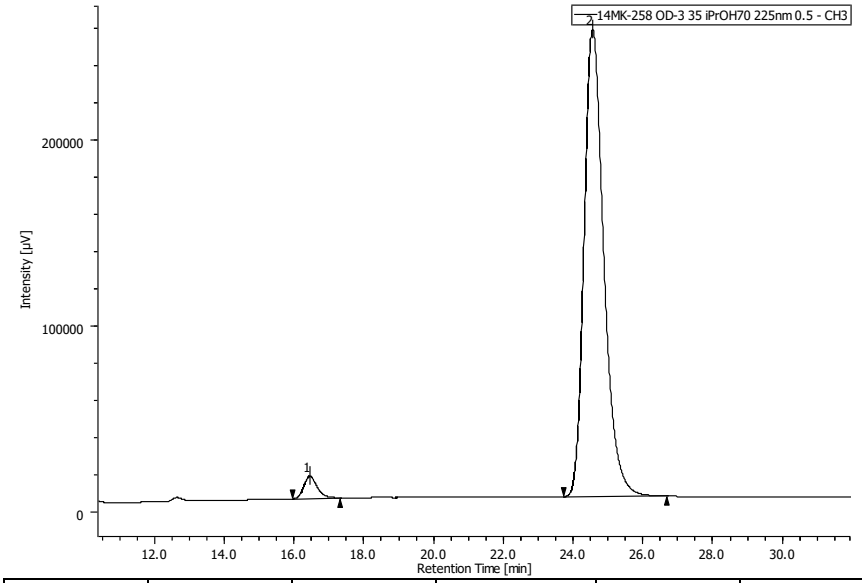
HPLC analysis of **3b**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	16.333	4127782	154788	49.924
2	3	24.442	4140287	107650	50.076

Racemate

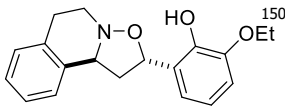


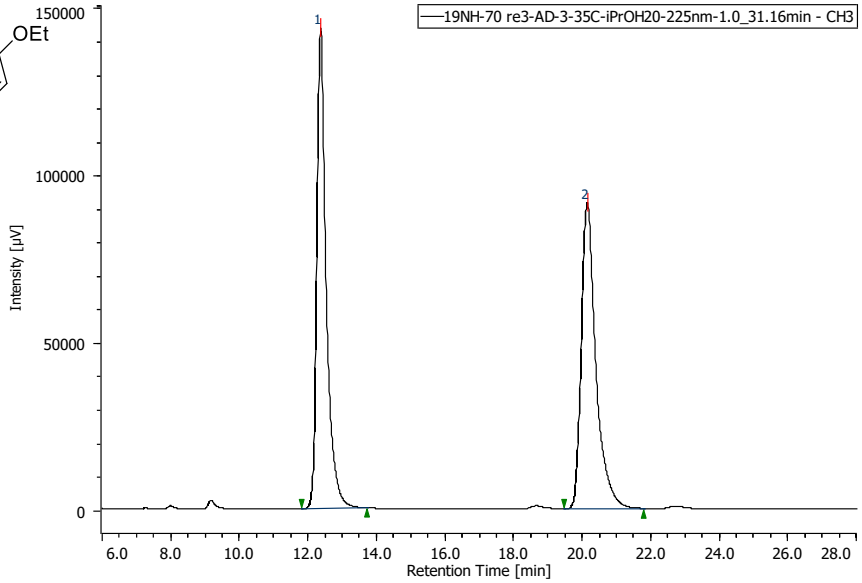
# Peak	CH	tR (min)	Area	Height	Area%
1	3	16.442	313459	11940	3.117
2	3	24.542	9741417	250528	96.883

94% ee

Chiralcel OD-3, Hexane:^{i}PrOH = 30:70, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C

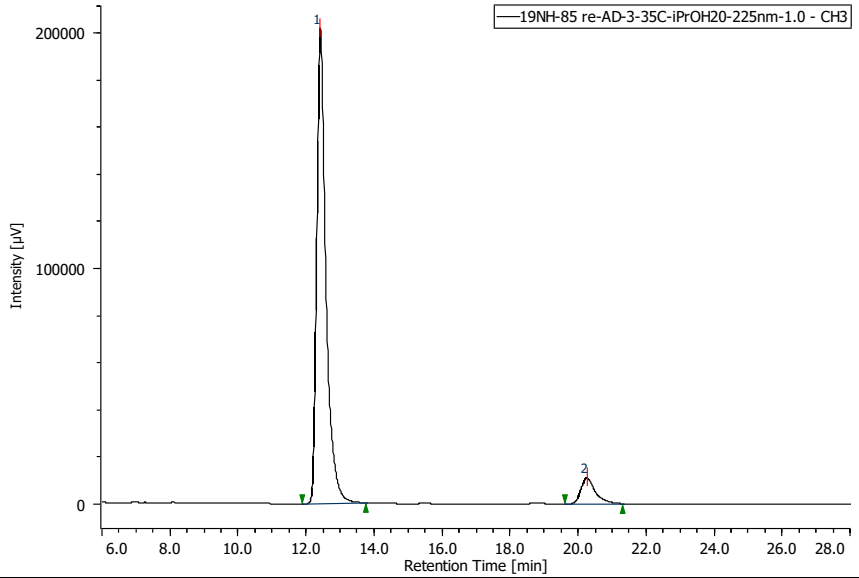
HPLC analysis of **3c**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	12.367	2732364	143046	50.404
2	3	20.133	2688591	91154	49.596

Racemate

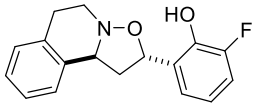


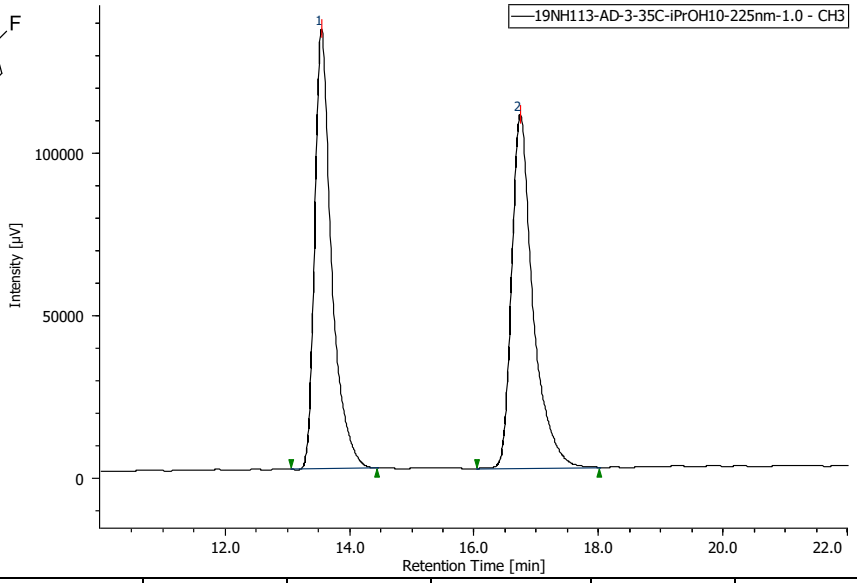
# Peak	CH	tR (min)	Area	Height	Area%
1	3	12.417	3781724	201129	92.082
2	3	20.242	325201	10989	7.918

84% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

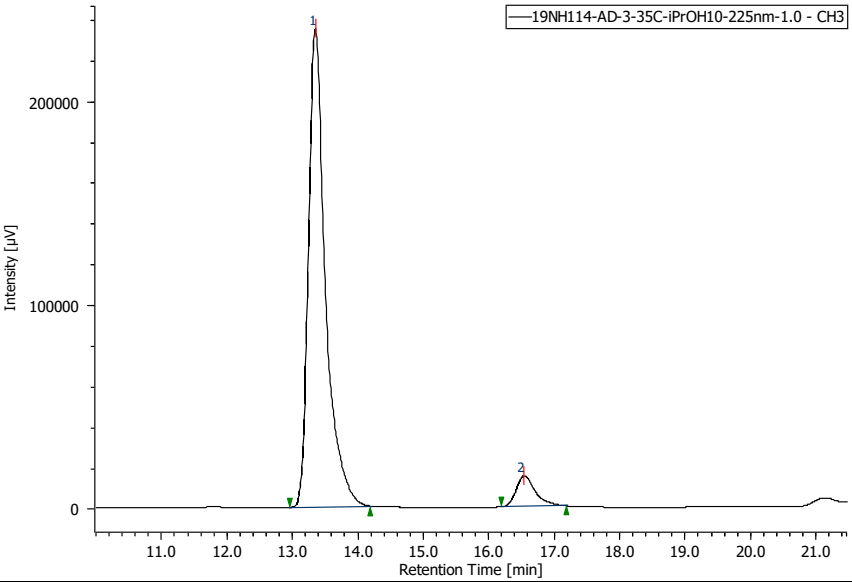
HPLC analysis of **3d**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	13.542	2552681	140904	50.07
2	3	16.733	2584970	90457	49.93

Racemate

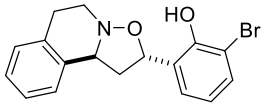


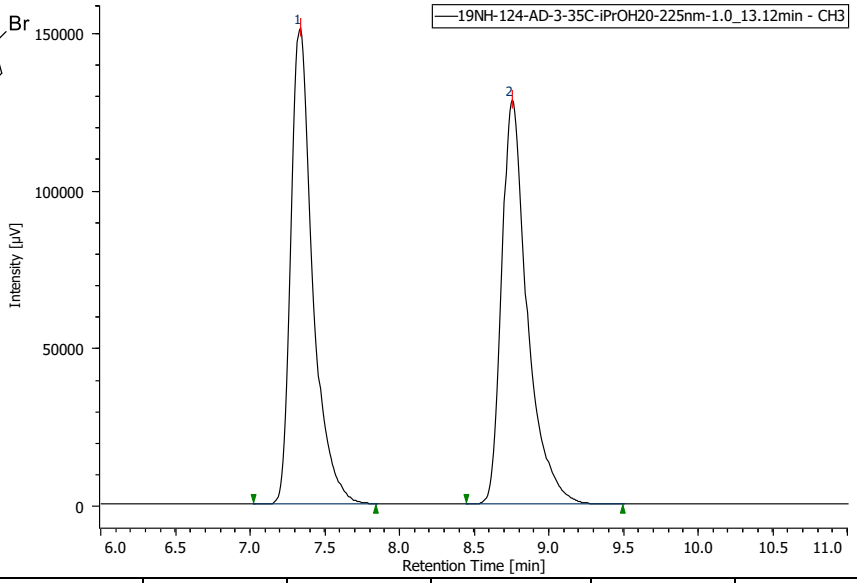
# Peak	CH	tR (min)	Area	Height	Area%
1	3	13.35	4193093	233908	93.175
2	3	16.533	307153	14989	6.825

86% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

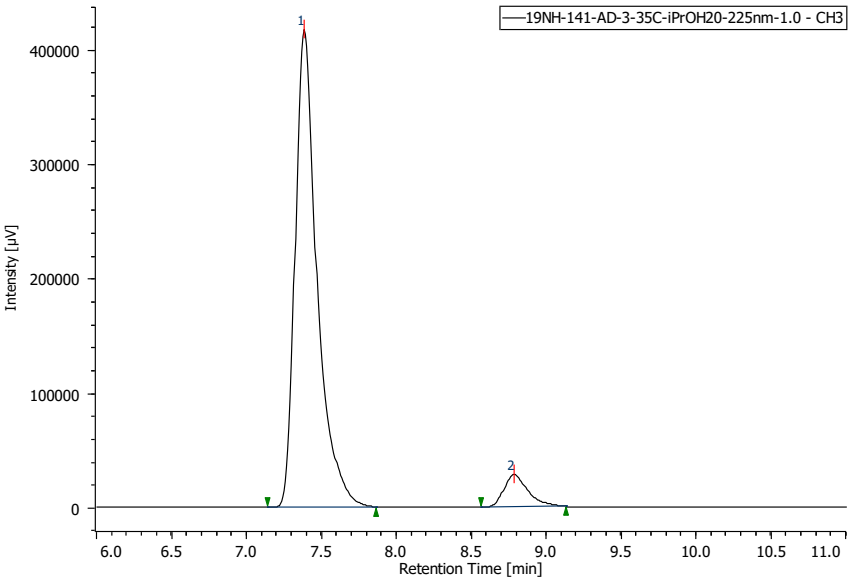
HPLC analysis of **3e**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	7.333	1521748	150397	49.942
2	3	8.75	1525307	127839	50.058

Racemate

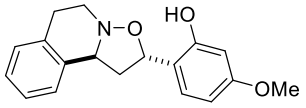


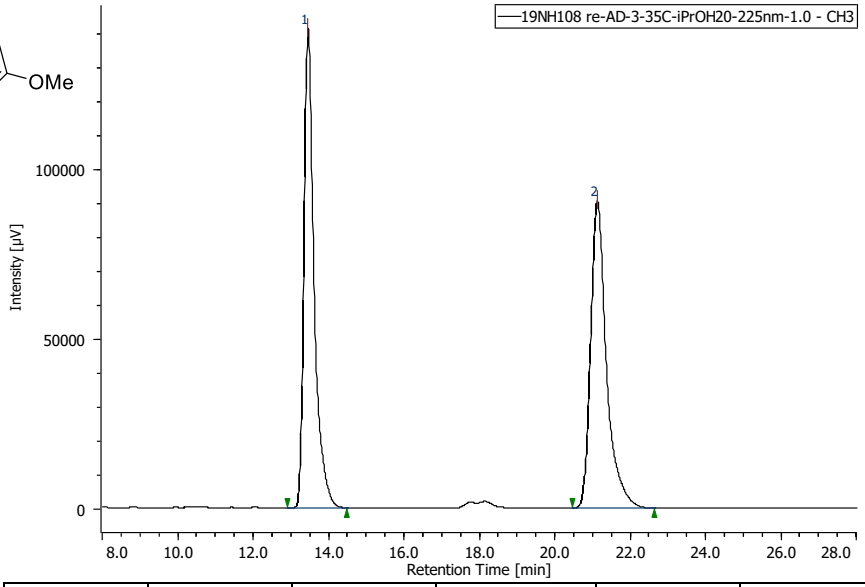
# Peak	CH	tR (min)	Area	Height	Area%
1	3	7.383	4233635	415614	93.036
2	3	8.783	316923	28127	6.964

86% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

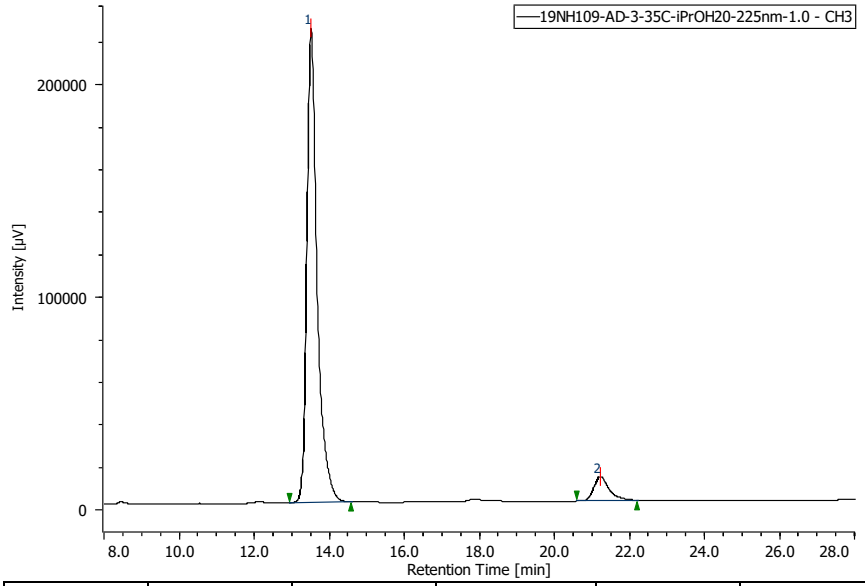
HPLC analysis of **3f**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	13.45	2637294	140904	50.07
2	3	21.117	2629917	90457	49.93

Racemate

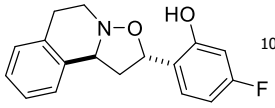


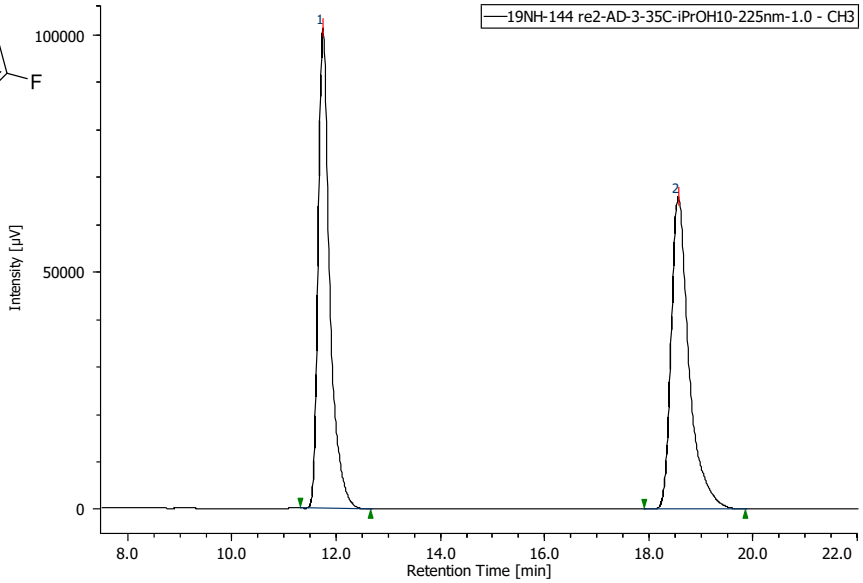
# Peak	CH	tR (min)	Area	Height	Area%
1	3	13.508	4236578	222156	92.927
2	3	21.208	322483	11326	7.073

86% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

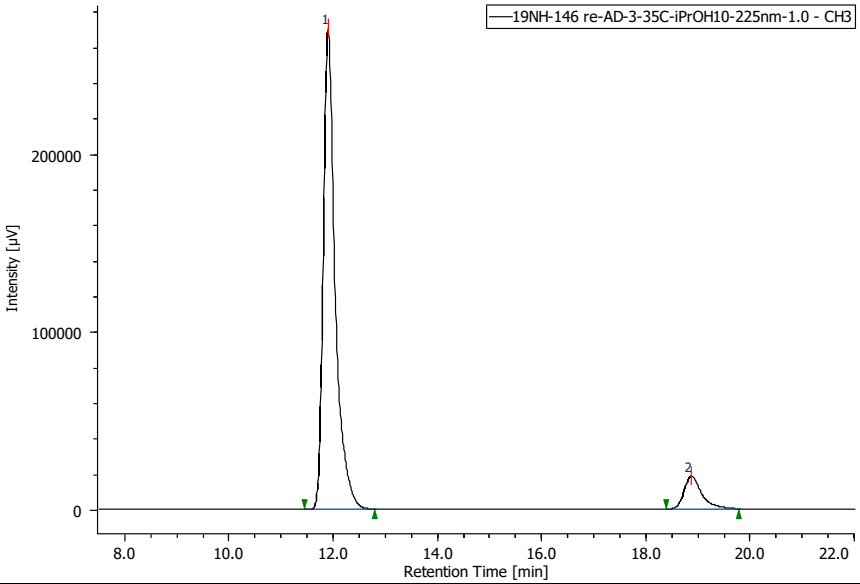
HPLC analysis of **3g**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	11.742	1560212	100922	49.923
2	3	18.55	1565024	65763	50.077

Racemate

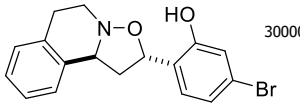


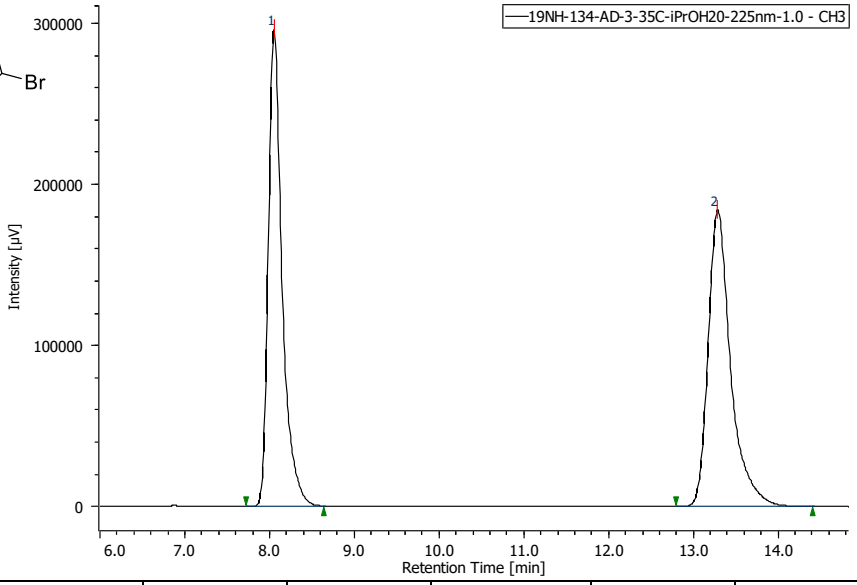
# Peak	CH	tR (min)	Area	Height	Area%
1	3	11.9	4264574	269060	90.784
2	3	18.858	432909	18458	9.216

82% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

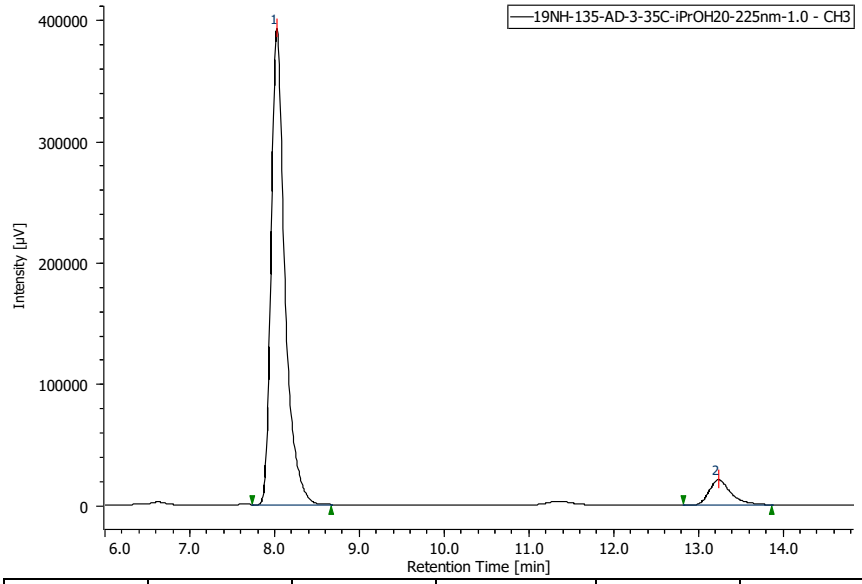
HPLC analysis of **3h**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	8.05	3335277	295649	49.875
2	3	13.275	3352037	183289	50.125

Racemate

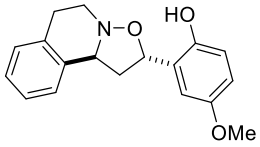


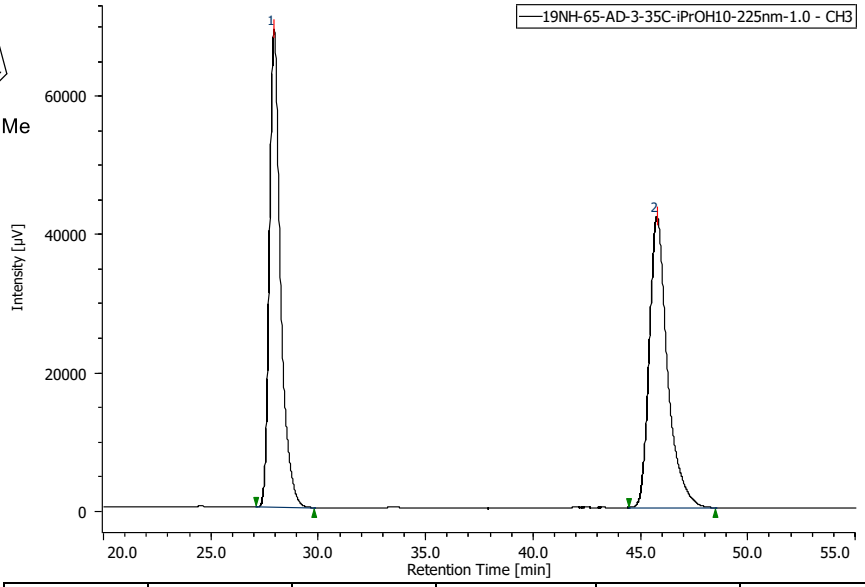
# Peak	CH	tR (min)	Area	Height	Area%
1	3	8.025	4395289	391007	92.241
2	3	13.225	369700	20827	7.759

84% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

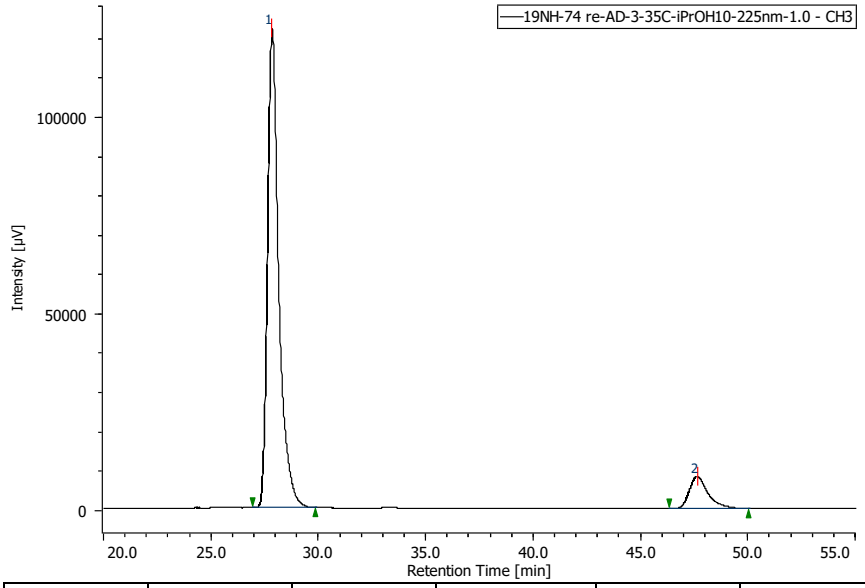
HPLC analysis of **3i**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	27.933	2470787	69018	50.023
2	3	45.733	2468510	41962	49.977

Racemate

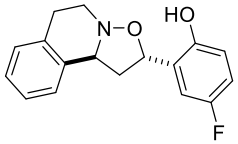


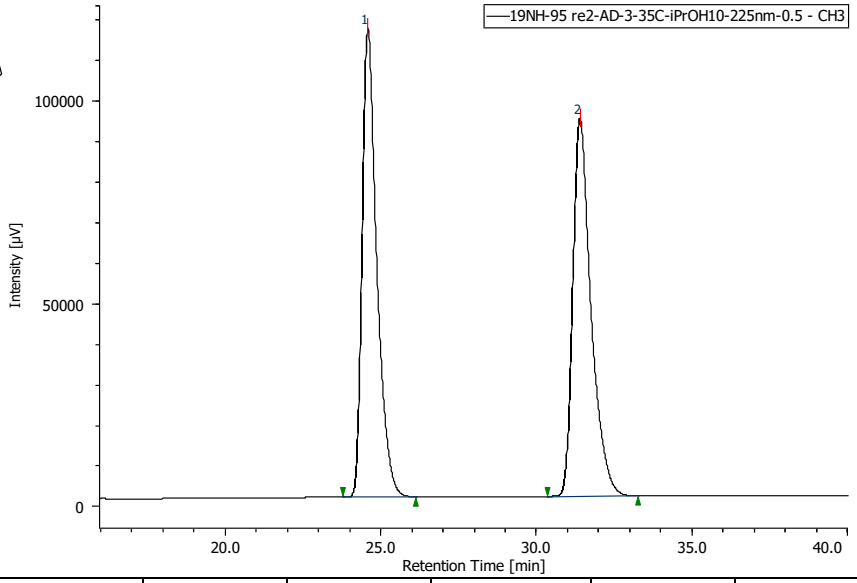
# Peak	CH	tR (min)	Area	Height	Area%
1	3	27.842	4410251	121528	89.596
2	3	47.6	512143	8280	10.404

79% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

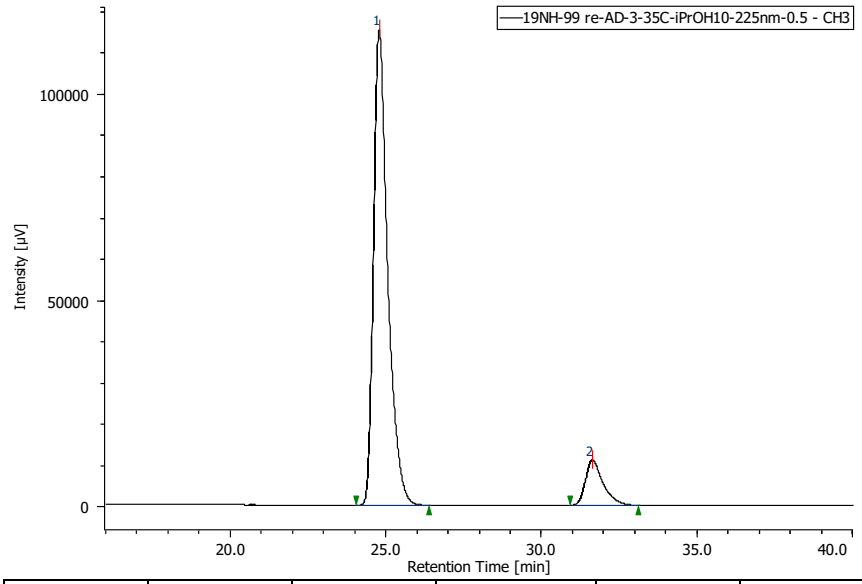
HPLC analysis of **3j**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	24.575	3760147	115373	49.96
2	3	31.383	3766129	92944	50.04

Racemate

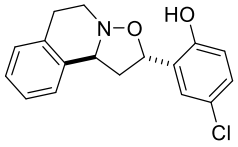


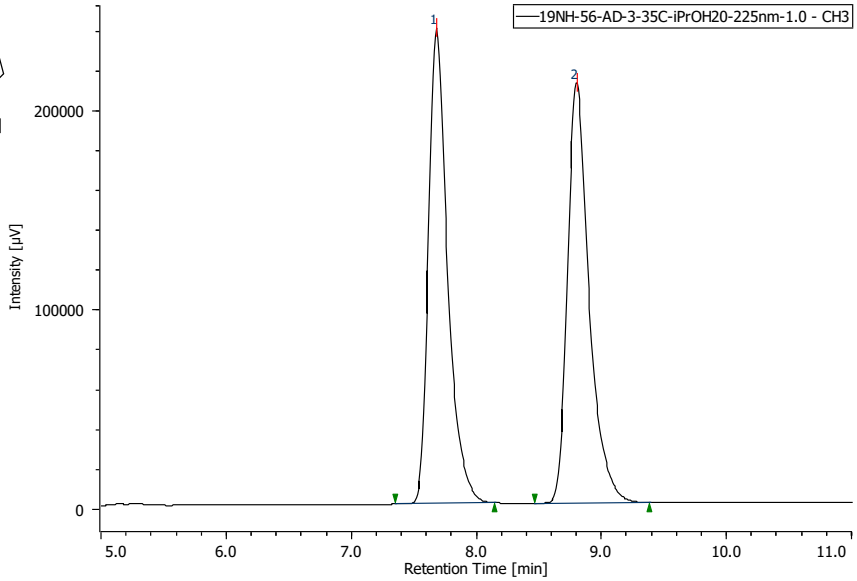
# Peak	CH	tR (min)	Area	Height	Area%
1	3	24.775	3619909	114826	89.423
2	3	31.625	428180	10948	10.577

79% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C

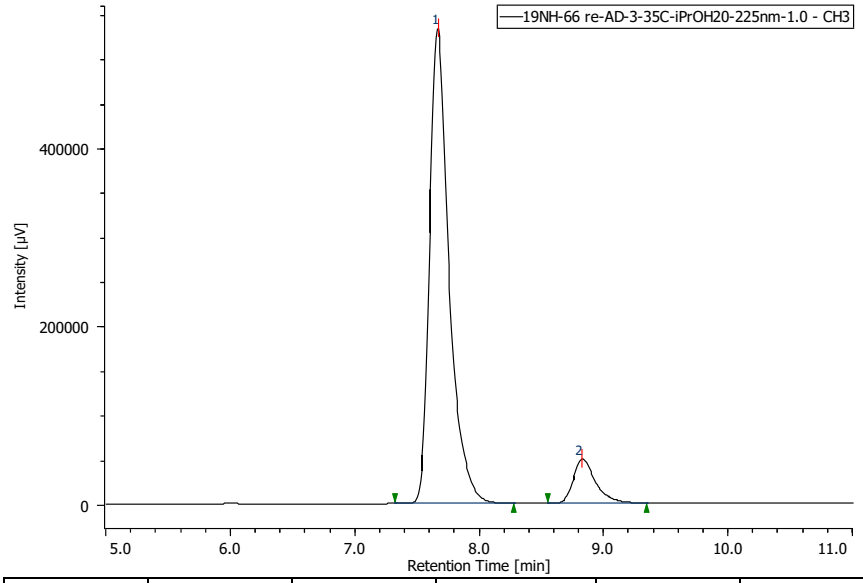
HPLC analysis of **3k**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	7.675	2518203	237804	49.928
2	3	8.8	2525465	210065	50.072

Racemate

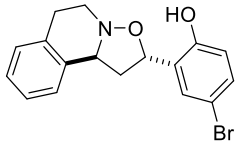


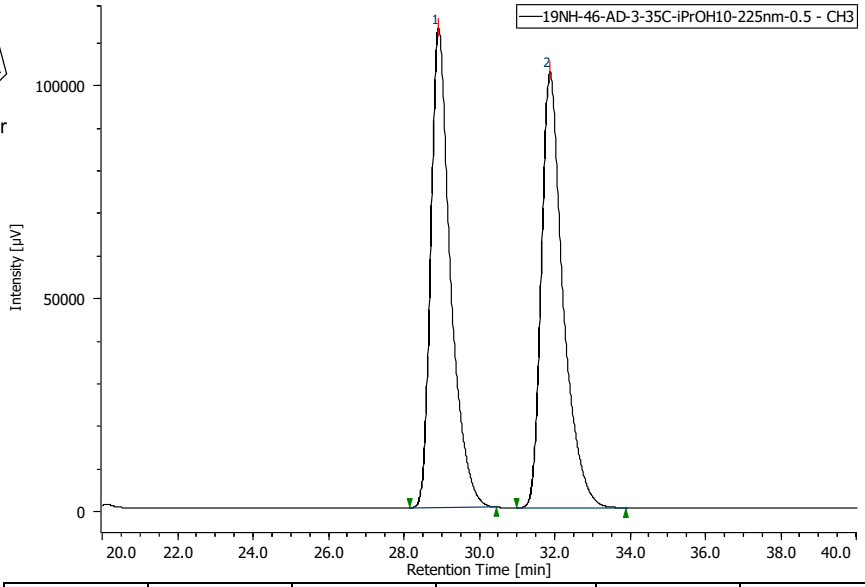
# Peak	CH	tR (min)	Area	Height	Area%
1	3	7.667	5750173	531355	90.417
2	3	8.825	609462	49939	9.583

81% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 80:20, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

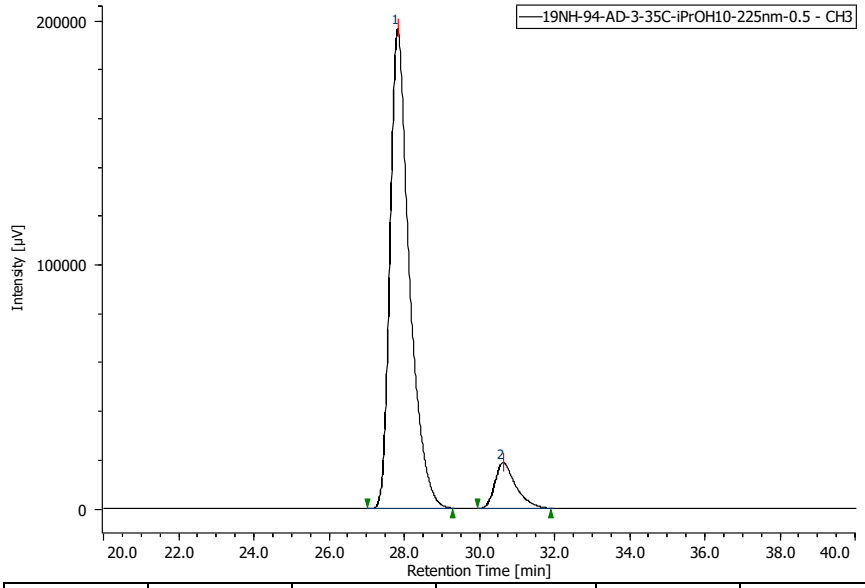
HPLC analysis of **3l**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	28.908	4071787	112167	49.968
2	3	31.858	4077036	102106	50.032

Racemate

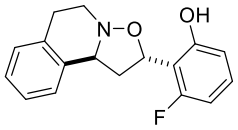


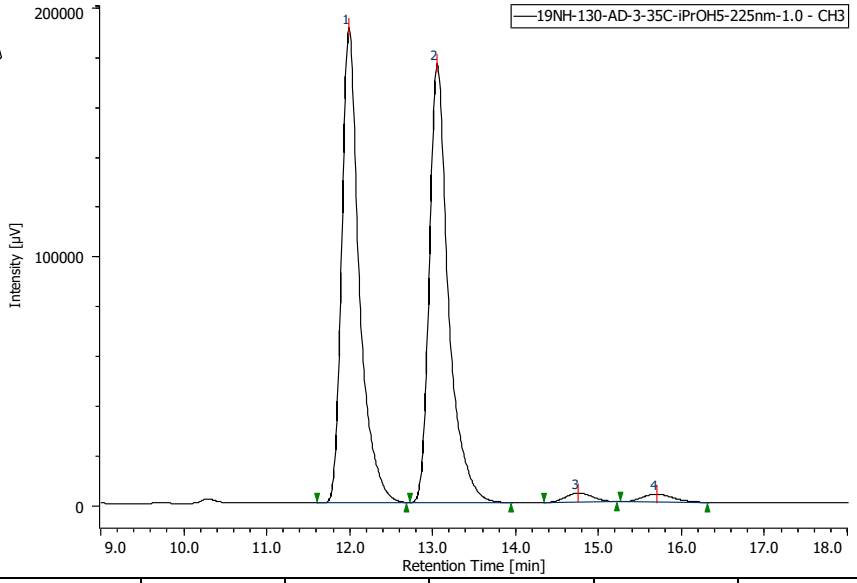
# Peak	CH	tR (min)	Area	Height	Area%
1	3	27.817	6991333	195988	90.605
2	3	30.625	724939	18752	9.395

81% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 90:10, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C

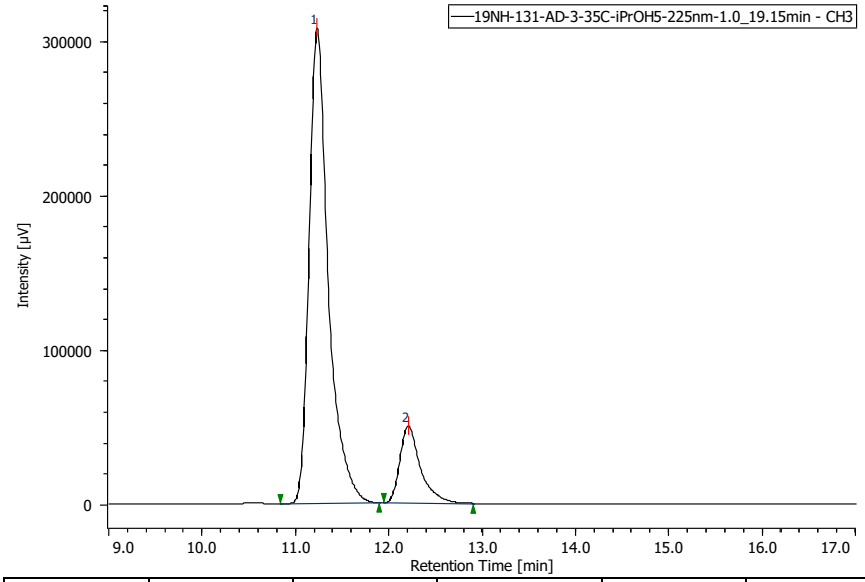
HPLC analysis of **3m**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	11.992	2807063	190216	48.541
2	3	13.05	2807212	175795	48.544
3	3	14.75	85353	3706	1.476
4	3	15.692	83235	3169	1.439

Racemate

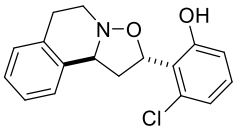


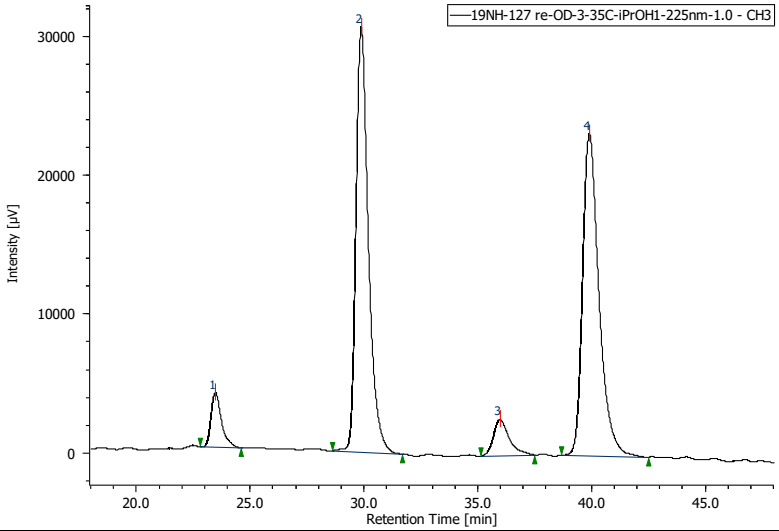
# Peak	CH	tR (min)	Area	Height	Area%
1	3	11.225	4384492	306708	85.204
2	3	12.208	761398	49933	14.796

70% ee

Chiralpak AD-3, Hexane:^{i}PrOH = 95:5, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

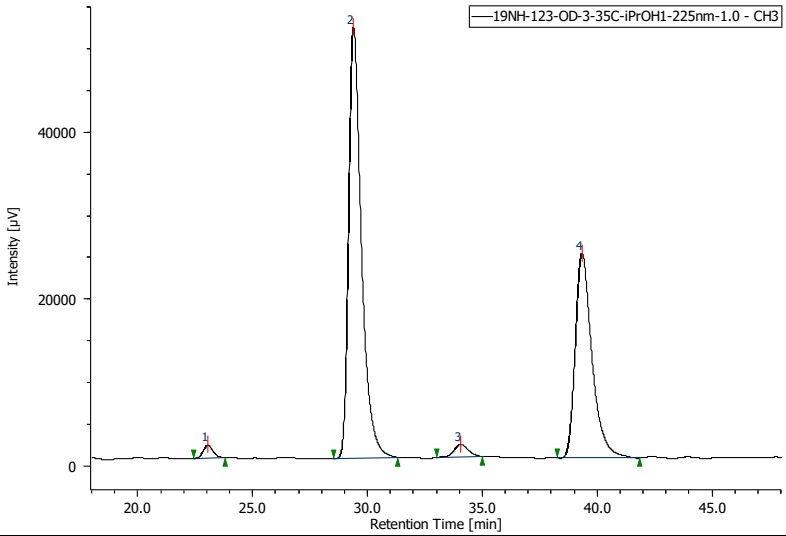
HPLC analysis of **3n**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	23.475	126905	3962	4.941
2	3	29.867	1155085	30654	44.97
3	3	35.95	124380	2593	4.842
4	3	39.883	1162200	23246	45.247

Racemate

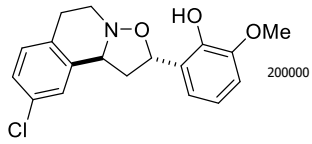


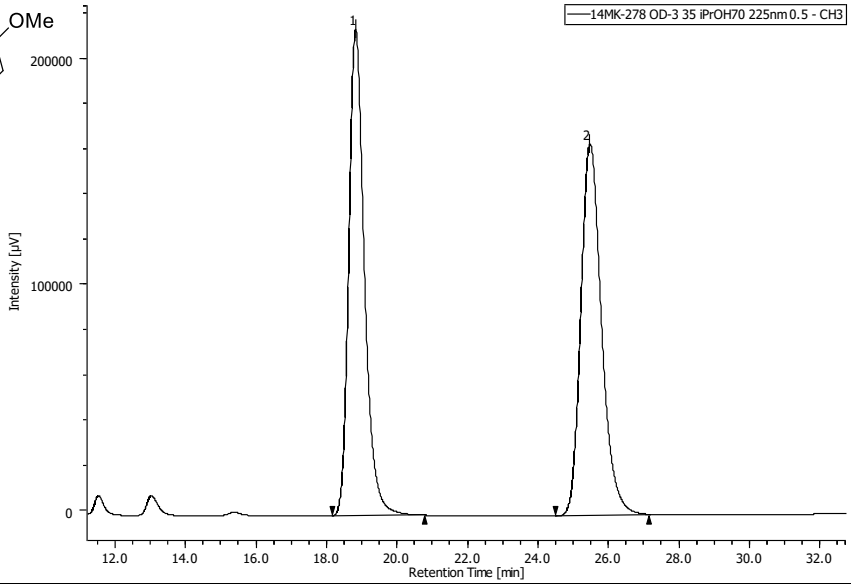
# Peak	CH	tR (min)	Area	Height	Area%
1	3	23.05	45625	1552	1.366
2	3	29.383	1992271	51534	59.668
3	3	34.05	62648	1505	1.876
4	3	39.317	1238385	24505	37.089

exo:*endo* = 97:3, 23% ee (*exo*), 16% ee (*endo*)

Chiralcel OD-3, Hexane:^{i}PrOH = 99:1, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

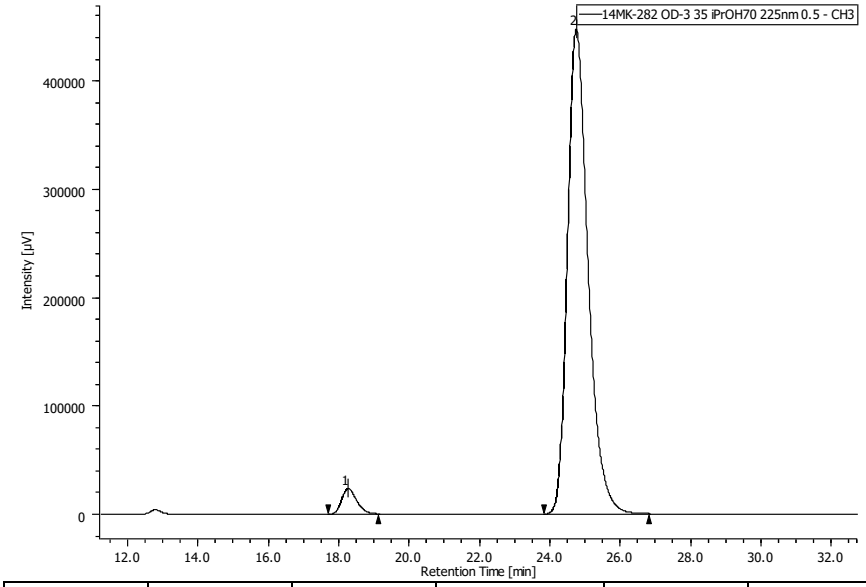
HPLC analysis of **3o**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	18.817	6642712	214735	50.027
2	3	25.458	6635584	163970	49.973

Racemate

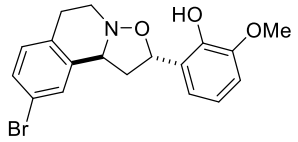


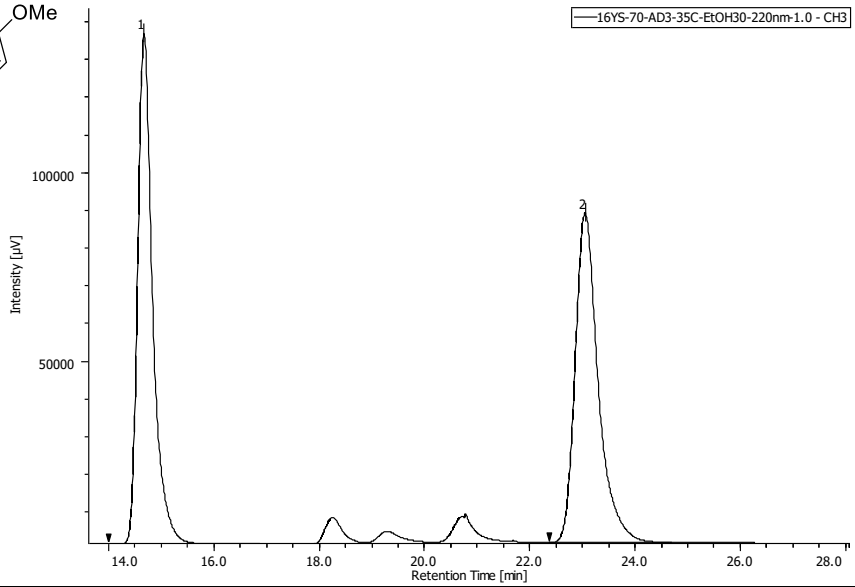
# Peak	CH	tR (min)	Area	Height	Area%
1	3	18.267	696296	23632	3.680
2	3	24.733	18223591	446587	96.320

93% ee

Chiralcel OD-3, Hexane:^{i}PrOH = 30:70, v/v, UV 225 nm, flow rate = 0.5 mL/min, 35 °C

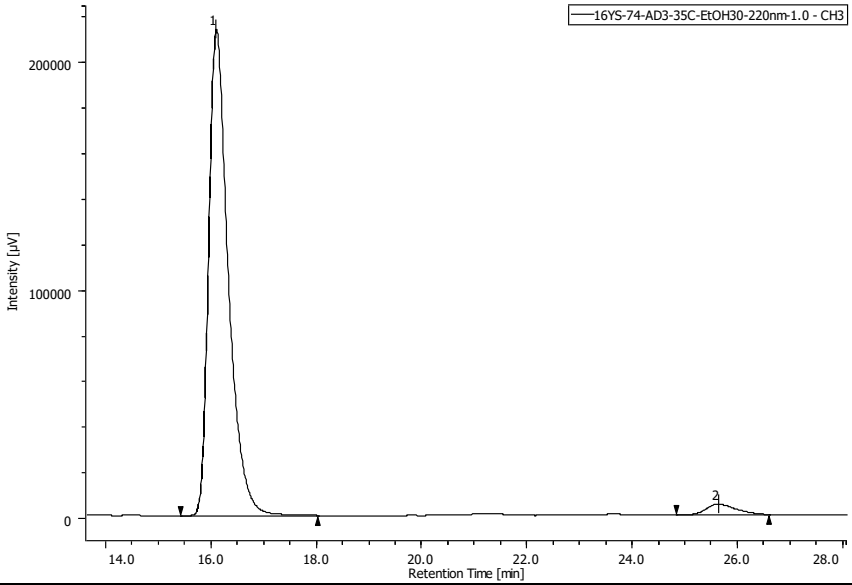
HPLC analysis of **3p**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	14.667	2657911	135169	50.182
2	3	23.042	2638642	87110	49.818

Racemate

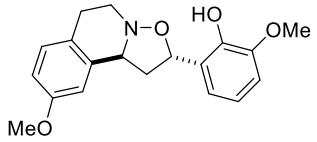


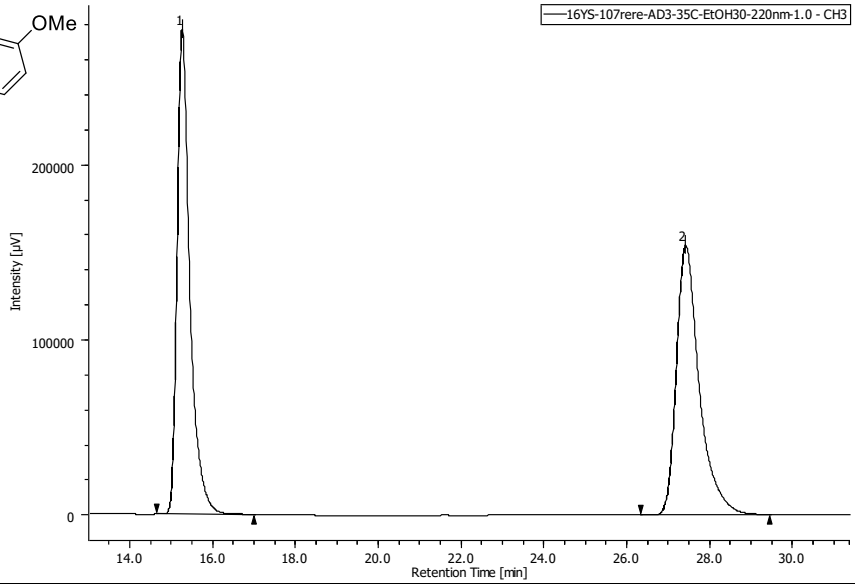
# Peak	CH	tR (min)	Area	Height	Area%
1	3	16.1	5491724	212923	96.787
2	3	25.617	182294	4576	3.213

94% ee

Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C

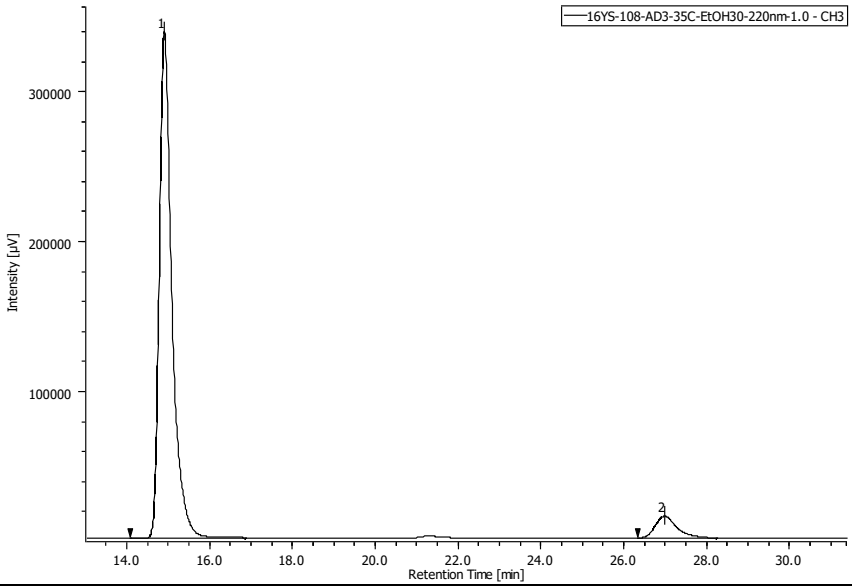
HPLC analysis of **3q**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	15.258	5904356	276478	50.063
2	3	27.408	5889575	153624	49.937

Racemate

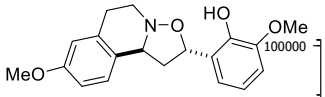


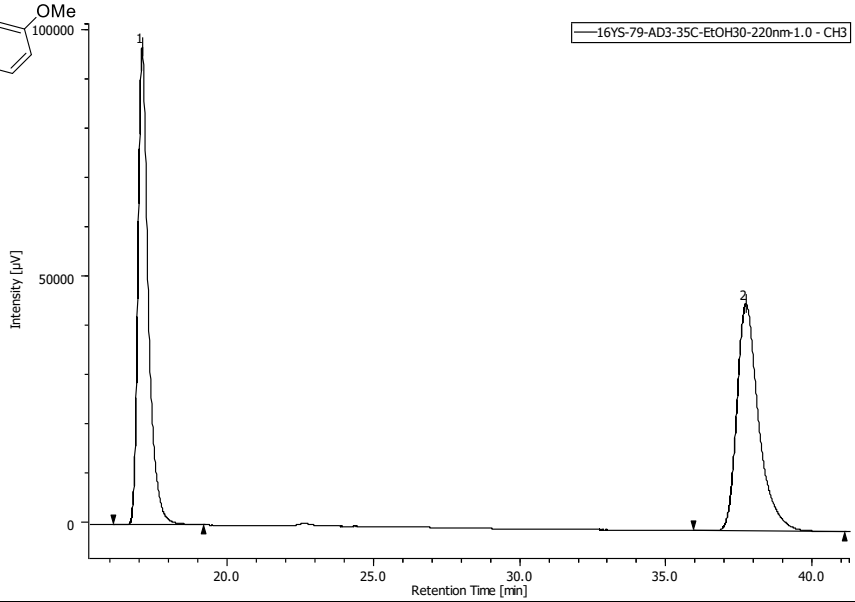
# Peak	CH	tR (min)	Area	Height	Area%
1	3	14.9	7080208	336840	92.991
2	3	26.967	533642	14506	7.009

86% ee

Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C

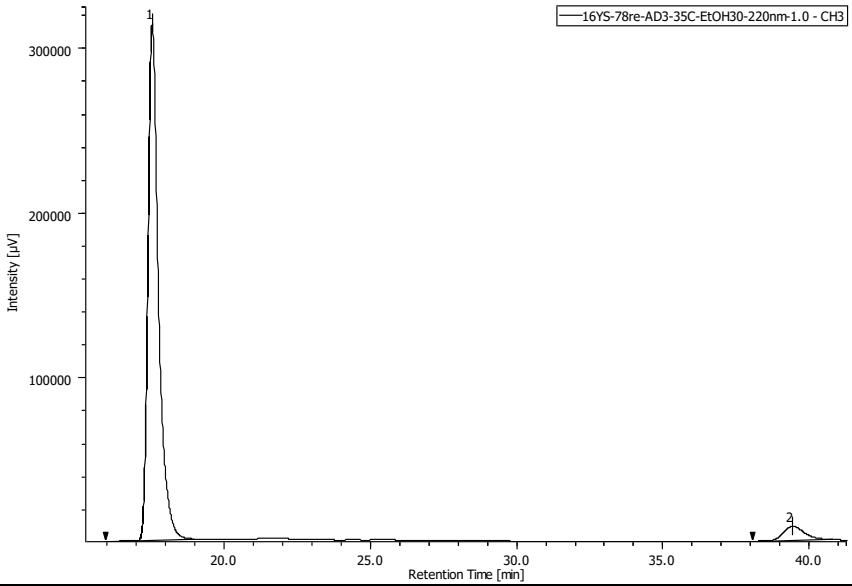
HPLC analysis of **3r**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	17.092	2375899	96790	49.968
2	3	37.708	2378982	46049	50.032

Racemate

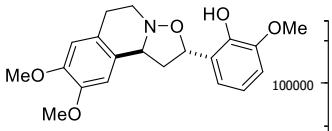


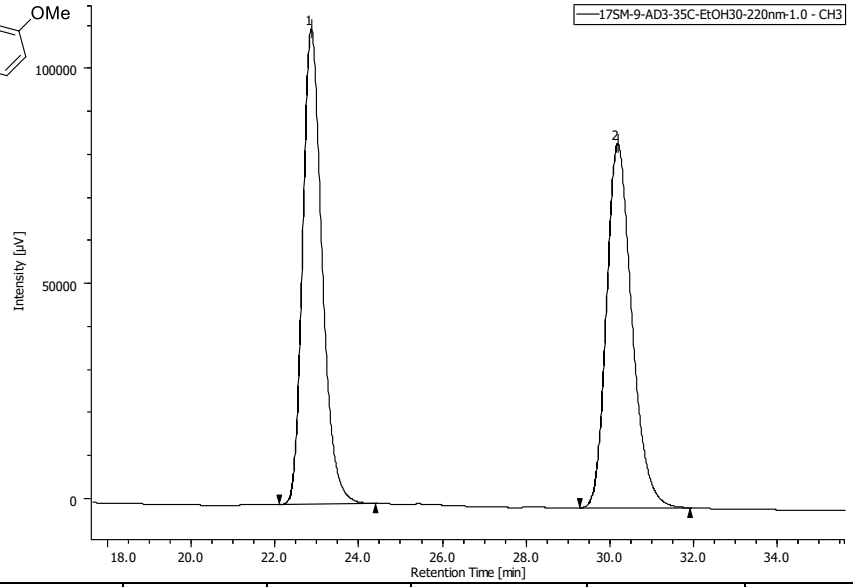
# Peak	CH	tR (min)	Area	Height	Area%
1	3	17.542	7795597	312452	94.796
2	3	39.417	427985	8496	5.204

90% ee

Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C

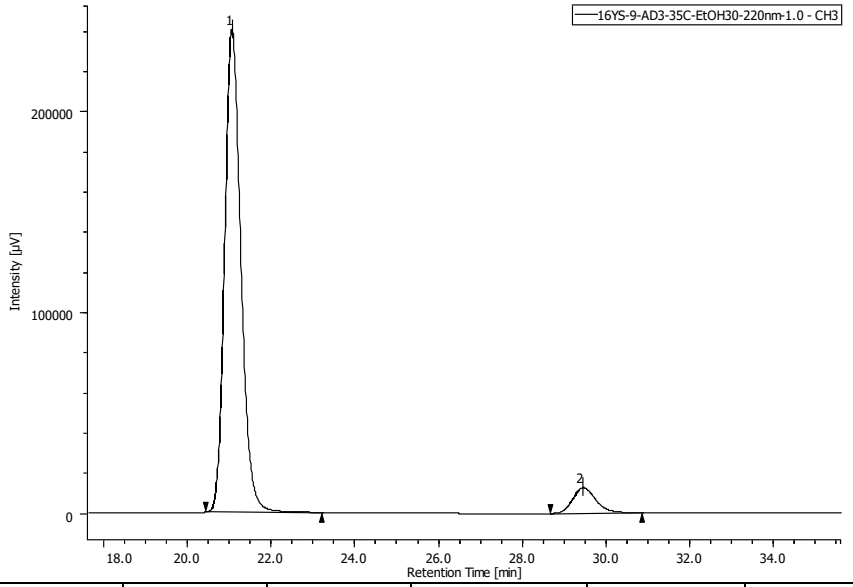
HPLC analysis of **3s**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	22.858	3552300	110178	49.874
2	3	30.175	3570312	84574	50.126

Racemate

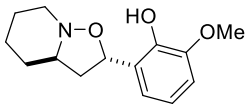


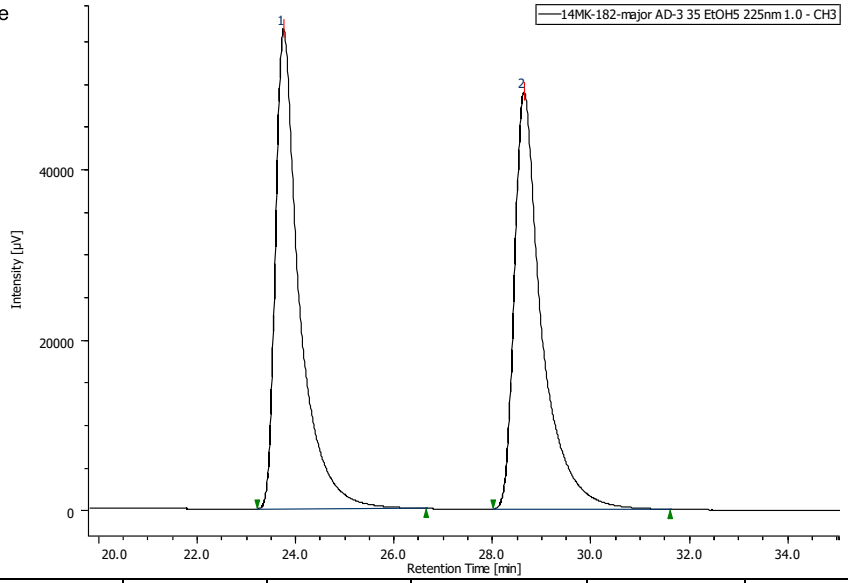
# Peak	CH	tR (min)	Area	Height	Area%
1	3	21.058	6464379	239810	92.913
2	3	29.45	493085	12767	7.087

86% ee

Chiralpak AD-3, Hexane:EtOH = 70:30, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C

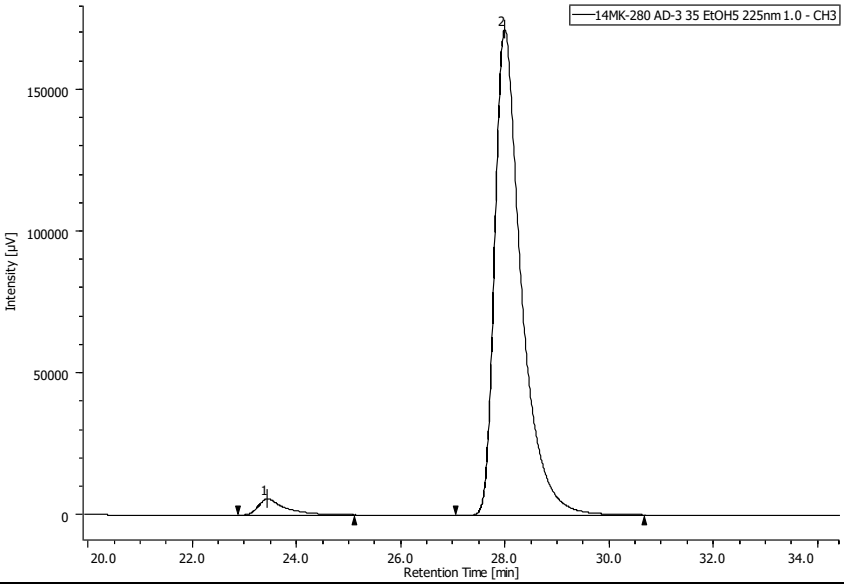
HPLC analysis of **3f**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	23.750	1900686	56193	50.240
2	3	28.633	1882505	48838	49.760

Racemate

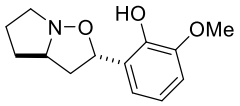


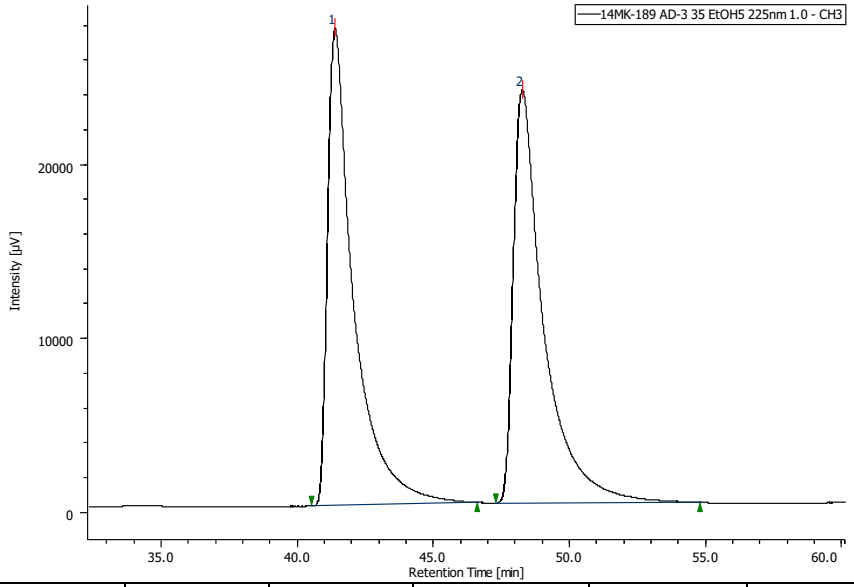
# Peak	CH	tR (min)	Area	Height	Area%
1	3	23.442	202827	5644	3.251
2	3	27.983	6035803	170833	96.749

93% ee

Chiralpak AD-3, Hexane:EtOH = 95:5, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

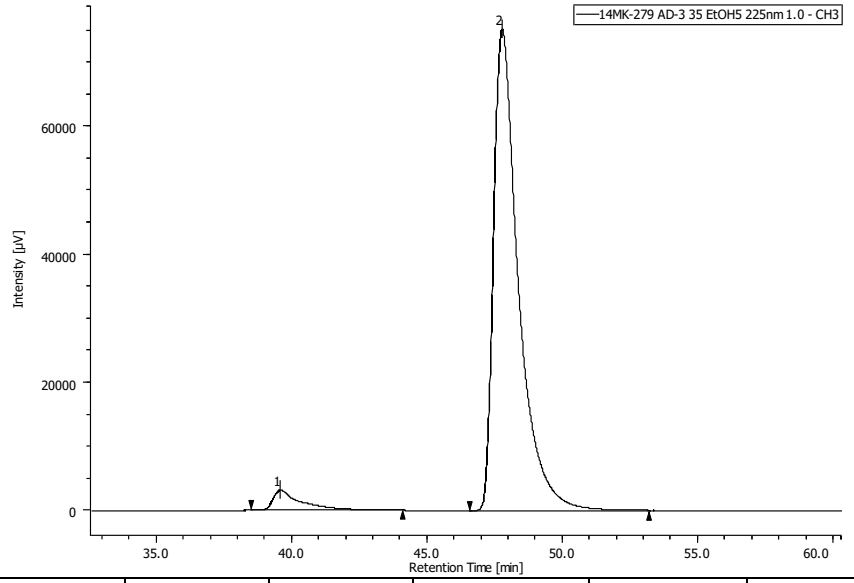
HPLC analysis of **3u**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	41.383	1830040	27401	49.954
2	3	48.258	1833399	23694	50.046

Racemate

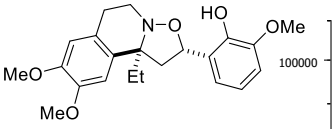


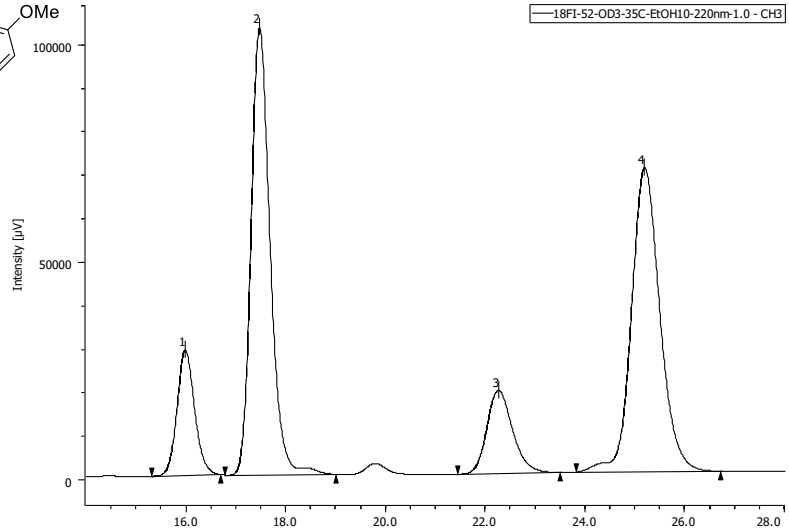
# Peak	CH	tR (min)	Area	Height	Area%
1	3	39.592	229263	3153	4.572
2	3	47.767	4784857	75073	95.428

91% ee

Chiralpak AD-3, Hexane:EtOH = 95:5, v/v, UV 225 nm, flow rate = 1.0 mL/min, 35 °C

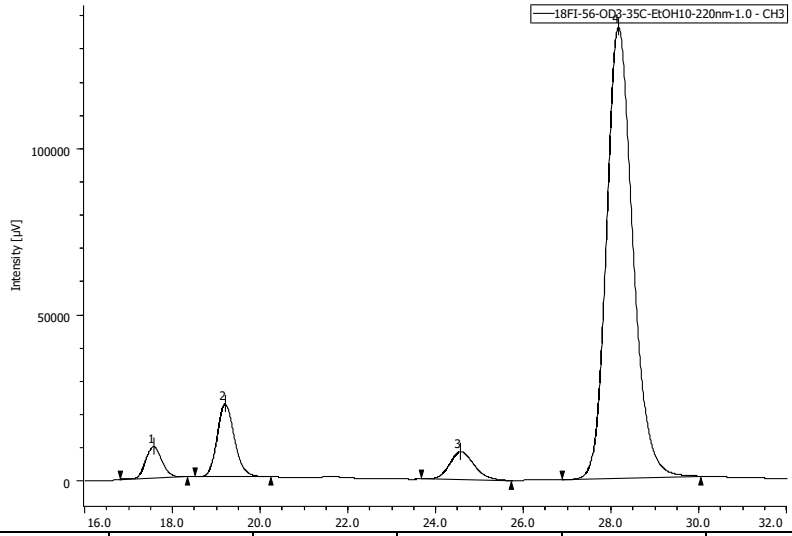
HPLC analysis of **3v**





# Peak	CH	tR (min)	Area	Height	Area%
1	3	15.983	703145	28777	10.236
2	3	17.475	2720558	102674	39.605
3	3	22.258	683572	19155	9.951
4	3	25.183	2761912	69697	40.207

Racemate



# Peak	CH	tR (min)	Area	Height	Area%
1	3	17.567	241589	9451	3.557
2	3	19.200	600031	21778	8.834
3	3	24.567	327578	8343	4.823
4	3	28.150	5623142	135318	82.787

exo:*endo* = 93:7, 81% ee (*exo*) , 15% ee (*endo*)

Chiralcel OD-3, Hexane:EtOH = 90:10, v/v, UV 220 nm, flow rate = 1.0 mL/min, 35 °C