Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

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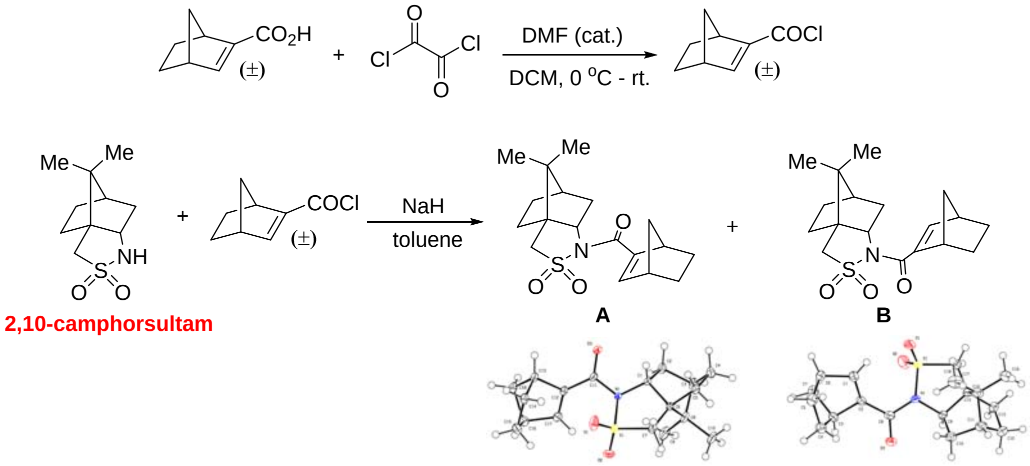
1. General Information

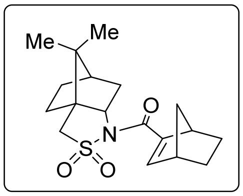
Unless noted otherwise, all solvents were dried by filtration through a Pure-Solv MD-5 Solvent Purification System (Innovative Technology). Dimethylformamide was then vacuum-distilled freshly over calcium hydride and carefully freeze-pump-thawed. Reaction temperatures were reported as the temperatures of the bather surrounding the flasks or vials. Sensitive reagents and solvents were transferred under nitrogen into a nitrogen-filled glovebox with standard techniques. Sodium acetate was purchased from STREM, stored and used directly in the glovebox. Analytical thin-layer chromatography (TLC) was carried out using 0.2 mm commercial silica gel plates (silica gel 60, F254, EMD chemical). Vials (15 x 45 mm 1 dram (4 mL) with PTFE lined cap attached) were purchased from Qorpak and flame-dried and cooled in a desiccator prior to usage. Mass spectra were recorded on an Agilent 6530 LC Q-TOF mass spectrometer using electrospray ionization with fragmentation voltage set at 115 V and processed with an Agilent MassHunter Operating System. X-ray diffraction data were collected at 100(2) K on a Bruker-Nonius Kappa CCD or Agilent SuperNova AtlasS2 CCD. Infrared spectra were recorded on a Nicolet 380 FTIR using neat thin film technique. Nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded with a Bruker (400 MHz, ^{1}H at 400 MHz, ^{13}C at 101 MHz) or Bruker Model DMX 500 (500 MHz, ^{1}H at 500 MHz, ^{13}C at 126 MHz). Chemical shifts were reported in parts per million (ppm, δ), downfield from tetramethylsilane (TMS, δ=0.00ppm) and were referenced to residual solvent ($CDCl_3$, δ=7.26 ppm (^{1}H) and 77.00 ppm (^{13}C)). All the ^{19}F chemical shifts were not referenced. Coupling constants were reported in Hertz (Hz). Data for ^{1}H NMR spectra were reported as follows: chemical shift (ppm, referenced to protium, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets, m = multiplet, coupling constant (Hz), and integration). All other materials were obtained from Aldrich Chemical Company or Combi-blocks and were used as received.

2. Experimental Procedures and Characterization Data

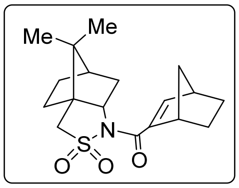
2.1 Chiral Resolution of Ester Substituted NBE



To a solution of NBE-CO_2H (700 mg, 5.1 mmol, 1.0 equiv) and 1 drop of DMF in DCM (5 mL) was added oxalyl chloride (648 mg, 5.1 mmol, 1.0 equiv) dropwise at 0 °C.[1] The reaction mixture was stirred at room temperature for another 1 h until the bubbling stopped. To another flame-dried round bottom flask was added sulfonamide (1.65g, 7.65 mmol, 1.5 equiv) and dry toluene (50 mL). Then NaH (3.06g, 76.5 mmol, 15 equiv) was added slowly to the flask and the reaction mixture was stirred at room temperature for another 30 min. After that, the generated acid chloride from the first flask was transferred into the second flask dropwise and the reaction mixture was stirred at room temperature until the reaction was completed. Then the reaction was quenched by 1M HCl and the aqueous lays was extracted by DCM for three times. The combined organic layers were dried over $MgSO_4$. Sulfonamide **A** and **B** were isolated via silica gel chromatography as a pair of diastereomers.

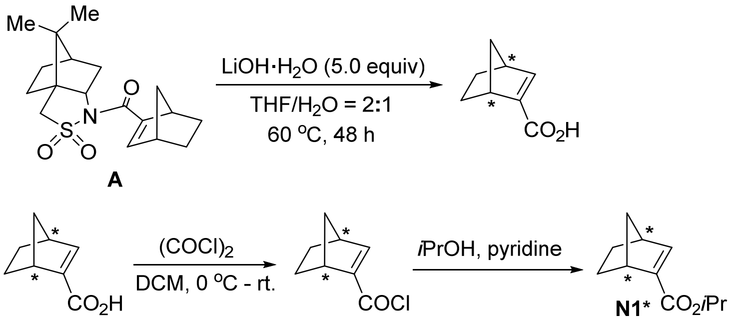


A: White solid (666 mg, 39%). R_f = 0.4 (hexane/ethyl acetate = 5:1). Mp = 125.7 – 127.1 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 3.4 Hz, 1H), 4.06 (dd, *J* = 7.7, 4.7 Hz, 1H), 3.47 (d, *J* = 13.6 Hz, 1H), 3.37 (d, *J* = 13.7 Hz, 2H), 3.03 (s, 1H), 2.03 (dd, *J* = 13.7, 7.7 Hz, 1H), 1.99 – 1.84 (m, 4H), 1.79 – 1.65 (m, 2H), 1.61 (dt, *J* = 8.6, 2.2 Hz, 1H), 1.45 – 1.24 (m, 5H), 1.21 (s, 3H), 0.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.30, 148.53, 141.13, 65.84, 53.81, 49.80, 47.96, 47.82, 45.28, 43.72, 43.08, 38.49, 33.34, 26.65, 24.21, 24.03, 21.36, 20.06. **IR** (KBr): υ 2960, 2874, 1671, 1590, 1332, 1286, 1172, 1140, 754, 536 cm^{-1}. **HRMS** (ESI): Calculated for $C_{18}H_{26}NO_3S$ (M+H$^+$): 336.1628, found: 336.1631.



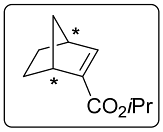
B: White solid (652 mg, 38%) R$_f$ = 0.3 (hexane/ethyl acetate = 5:1). Mp = 169.2 – 170.0 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.91 (d, *J* = 3.2 Hz, 1H), 4.04 (dd, *J* = 7.7, 4.7 Hz, 1H), 3.49 (d, *J* = 13.6 Hz, 1H), 3.39 (d, *J* = 13.6 Hz, 1H), 3.23 (s, 1H), 3.08 (s, 1H), 2.05 – 1.91 (m, 3H), 1.90 – 1.83 (m, 2H), 1.76 (ttd, *J* = 12.8, 9.4, 3.6 Hz, 2H), 1.56 (dt, *J* = 8.8, 2.2 Hz, 1H), 1.41 (ddd, *J* = 10.9, 9.1, 2.3 Hz, 1H), 1.37 (s, 1H), 1.21 (s, 4H), 1.19 – 1.12 (m, 1H), 1.11 – 1.05 (m, 1H), 0.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.12, 148.31, 142.38, 65.78, 53.74, 48.07, 47.81, 46.72, 45.36, 44.34, 43.99, 38.65, 33.34, 26.64, 25.24, 25.20, 21.44, 20.05. **IR** (KBr): υ 2962, 2876, 1668, 1586, 1334, 1288, 1139, 1054, 748, 536 cm^{-1}. **HRMS** (ESI): Calculated for $C_{18}H_{26}NO_3S$ (M+H$^+$): 336.1628, found: 336.1632.

2.2 General Procedure for Synthesis of Chiral NBEs



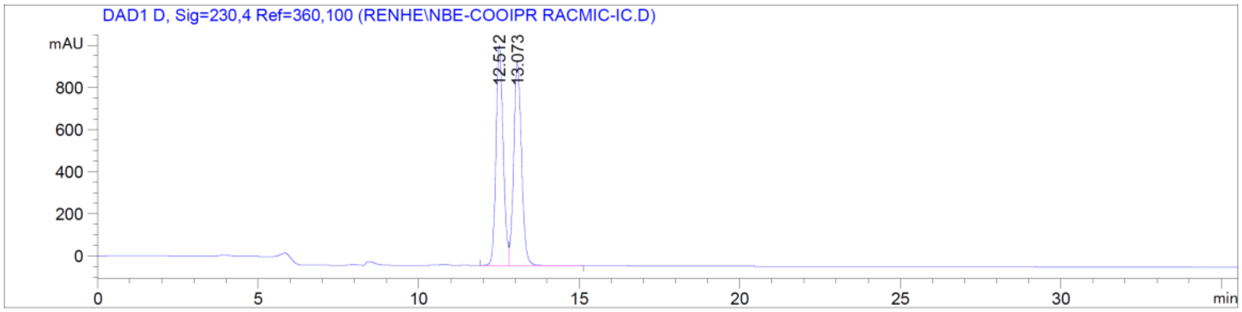
To a solution (18 mL, H_2O/THF = 1:2) of sulfonamide (565 mg, 1.69 mmol, 1.0 equiv) was added LiOH • H_2O (354 mg, 8.42 mmol, 5.0 equiv). The reaction was stirred at 60 °C for 48 h until the reaction mixture became clear. Then the aqueous layer was washed by diethyl ether for two times and then acidified by 1 M hydrochloric acid until pH < 7. Then the reaction mixture was extracted by dichloromethane for three times and the combined organic layers were dried over $MgSO_4$. The solvent was removed under vacuum to afford the chiral NBE-CO_2H as a colorless oil, which was used directly in the next step without further purification.

To a solution of NBE-CO_2H (276 mg, 2.0 mmol, 1.0 equiv) in DCM (2 mL) with 1 drop of DMF was added oxalyl chloride (254 mg, 2.0 mmol, 1.0 equiv) dropwise at 0 °C. The reaction mixture was stirred at room temperature for another 1 h until the bubbling stopped. Then a mixture of the corresponding alcohol (6.0 mmol, 3.0 equiv) and pyridine (949.2 mg, 12.0 mmol, 6.0 equiv) was added dropwise and the reaction mixture was stirred at room temperature for another 3 h until the reaction was completed. The organic layer was washed with 1 M hydrochloric acid and then concentrated under vacuum. The corresponding ester substituted NBE was isolated by silica gel chromatography (hexane/Et_2O = 20:1) as a colorless oil.



N1*: Colorless oil (151 mg, 42%). R_f = 0.6 (hexane/ethyl acetate = 20:1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.88 (d, *J* = 3.2 Hz, 1H), 5.05 (hept, *J* = 6.1 Hz, 1H), 3.24 (s, 1H), 3.00 (s, 1H), 1.74 (th, *J* = 13.0, 3.3 Hz, 2H), 1.52 – 1.43 (m, 1H), 1.26 (dd, *J* = 6.3, 4.1 Hz, 6H), 1.18 (d, *J* = 8.7 Hz, 1H), 1.07 (dt, *J* = 7.4, 2.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.7, 146.4, 141.6, 67.3, 48.3, 43.6, 42.0, 24.8, 24.7, 22.1. **IR** (KBr): υ 2978, 2874, 1707, 1279, 1259, 1163, 1110, 1076, 753 cm^{-1}. **HRMS** (ESI): Calculated for $C_{11}H_{17}O_2$ ($M+H^+$): 181.1223, found: 181.1219. **Chiral HPLC** (Chiralpak IC, hexane/isopropanol = 98:2, 0.5 mL/min, 230 nm): t_{minor} = 12.308 min, t_{major} = 12.778. $[\alpha]_D$ = -139.6 (c = 0.53, dichloromethane, 21.0 °C) at 98% ee.

Racemic N1



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Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  12.512 BV    0.2362 1.61599e4 1045.99609 49.6824
   2  13.073 VB    0.2588 1.63666e4  970.13281 50.3176

Totals :                  3.25265e4 2016.12891
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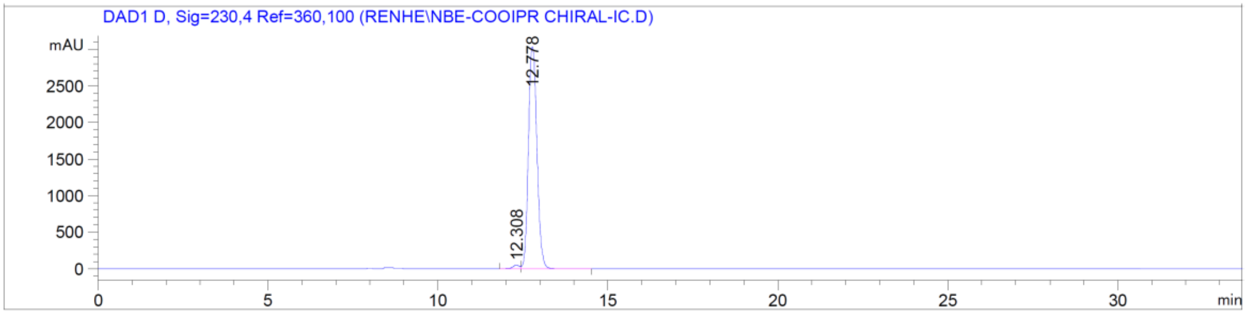
Enantiomeric N1*



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Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
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   2  12.778 VB    0.2705 5.26707e4 3034.12402  98.8046

Totals :                  5.33080e4 3081.94615
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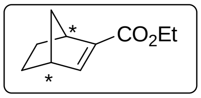
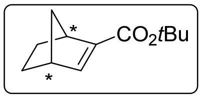
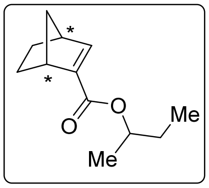


N2*: Colorless oil (47%). R_f = 0.5 (hexane/ethyl acetate = 20:1). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.26 (d, J = 3.1 Hz, 1H), 4.53 (q, J = 7.0 Hz, 2H), 3.61 (s, 1H), 3.36 (s, 1H), 2.09 (dtt, J = 15.1, 11.6, 7.6 Hz, 2H), 1.83 (d, J = 8.5 Hz, 1H), 1.64 (t, J = 7.1 Hz, 3H), 1.54 (d, J = 8.6 Hz, 1H), 1.44 (tdt, J = 7.6, 5.1, 2.3 Hz, 2H). **^{13}C NMR** (101 MHz,

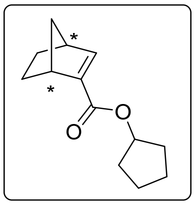
$CDCl_3$) δ 165.1, 146.8, 141.2, 60.2, 48.3, 43.6, 42.0, 24.8, 24.6, 14.5. **IR** (KBr): υ 2977, 2874, 1712, 1596, 1370, 1341, 1278, 1258, 1160, 1079, 753 cm^{-1}. **HRMS** (ESI): Calculated for $C_{10}H_{15}O_2$ ($M+H^+$): 167.1067, found: 167.1061. $[\alpha]_D$ = 155.6 (c = 0.32, dichloromethane, 22.0 °C).



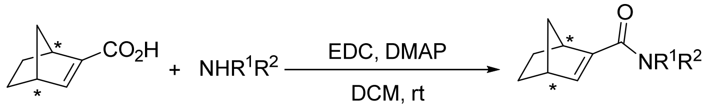
N3*: White solid (48%). R_f = 0.6 (hexane/ethyl acetate = 20:1). Mp = 52.0 – 54.0 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.79 (d, *J* = 3.1 Hz, 1H), 3.19 (s, 1H), 2.98 (s, 1H), 1.78 – 1.68 (m, 2H), 1.48 (s, 10H), 1.16 (d, *J* = 8.5 Hz, 1H), 1.07 (qd, *J* = 8.5, 2.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 145.6, 142.8, 80.0, 48.3, 43.5, 42.0, 28.4, 24.9, 24.7. **IR** (KBr): υ 2976, 2873, 1702, 1596, 1284, 1260, 1154, 1077, 756 cm^{-1}. **HRMS** (ESI): Calculated for $C_{12}H_{18}O_2Na$ ($M+Na^+$): 217.1199, found: 217.1184. $[\alpha]_D$ = 148.9 (c = 0.91, dichloromethane, 22.0 °C).



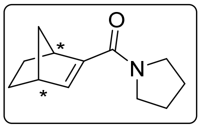
N4*: Colorless oil (50%, dr = 1:1). R_f = 0.5 (hexane/ethyl acetate = 20:1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.89 (dd, *J* = 6.6, 3.2 Hz, 1H), 4.88 (h, *J* = 6.1, 5.7 Hz, 1H), 3.24 (s, 1H), 3.00 (s, 1H), 1.74 (tt, *J* = 9.6, 1.9 Hz, 2H), 1.68 – 1.60 (m, 1H), 1.48 (d, *J* = 8.5 Hz, 1H), 1.23 (dd, *J* = 6.3, 5.2 Hz, 4H), 1.20 – 1.16 (m, 1H), 1.11 – 1.04 (m, 2H), 0.90 (td, *J* = 7.5, 5.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.86, 164.83, 146.45, 146.31, 141.64, 141.59, 71.85, 71.82, 48.28, 48.23, 43.57, 43.55, 42.04, 42.01, 29.08, 29.05, 24.83, 24.80, 24.67, 19.73, 19.67, 9.86, 9.85. **IR** (KBr): υ 2974, 1708, 1596, 1449, 1364, 1337, 1278, 1257, 1162, 933, 752 cm^{-1}. **HRMS** (ESI): Calculated for $C_{12}H_{19}O_2$ ($M+H^+$): 195.1380, found: 195.1370. $[\alpha]_D$ = -133.3 (c = 0.95, dichloromethane, 21.8 °C).



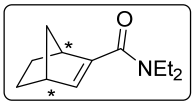
N5*: White solid (45%). R_f = 0.5 (hexane/ethyl acetate = 20:1). Mp = 60.2 – 60.8 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.79 (d, *J* = 3.2 Hz, 1H), 5.14 (dq, *J* = 6.0, 3.1 Hz, 1H), 3.16 (s, 1H), 2.92 (s, 1H), 1.80 (dtd, *J* = 12.5, 6.6, 6.0, 3.0 Hz, 2H), 1.71 – 1.60 (m, 6H), 1.58 – 1.47 (m, 2H), 1.40 (dt, *J* = 8.6, 2.1 Hz, 1H), 1.11 (d, *J* = 8.5 Hz, 1H), 1.04 – 0.96 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9, 146.3, 141.6, 76.6, 48.2, 43.5, 42.0, 32.9, 32.8, 24.8, 24.6, 23.91, 23.90. **IR** (KBr): υ 2871, 1703, 1593, 1449, 1369, 1341, 1277, 1217, 1116, 1078, 879, 753 cm^{-1}. **HRMS** (ESI): Calculated for $C_{13}H_{19}O_2$ ($M+H^+$): 207.1380, found: 207.1374. $[\alpha]_D$ = -130.1 (c = 0.99, dichloromethane, 22.0 °C).



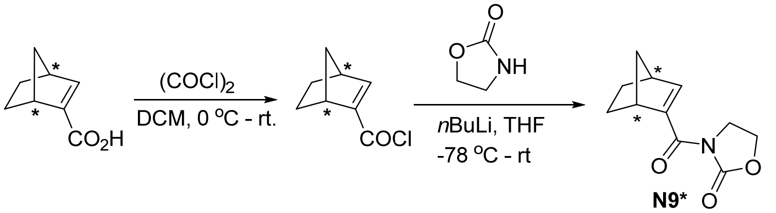
NBE-CO_2H (138 mg, 1.0 mmol, 1.0 equiv), amine (1.1 mmol, 1.1 equiv), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (230 mg, 1.2 mmol, 1.2 equiv) and 4-dimethylaminopyridine (12.2 mg, 0.1 mmol, 10 mol%) were dissolved in dichloromethane (5 mL). The reaction mixture was stirred at room temperature overnight. Then it was diluted with diethyl ether, washed with water and brine, dried over $MgSO_4$, and purified on silica gel chromatography (hexanes/ethyl acetate = 2:1) to afford the corresponding amide-derived norbornene **N7*** and **N8***.



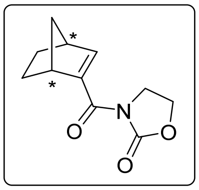
N7*: Colorless oil (49%). R_f = 0.3 (hexane/ethyl acetate = 2:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.30 (d, *J* = 3.1 Hz, 1H), 3.65 – 3.33 (m, 4H), 3.26 (s, 1H), 2.99 (s, 1H), 1.99 – 1.76 (m, 4H), 1.71 (d, *J* = 6.0 Hz, 2H), 1.37 (d, *J* = 8.3 Hz, 1H), 1.29 – 1.20 (m, 1H), 1.15 – 1.00 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.9, 144.4, 139.4, 48.4, 47.1, 46.3, 44.3, 43.8, 26.6, 25.3, 25.2, 24.2. **IR** (KBr): υ 2968, 2871, 1722, 1612, 1577, 1426, 1341, 1311, 1166, 875, 748 cm^{-1}. **HRMS** (ESI): Calculated for $C_{12}H_{18}NO$ ($M+H^+$): 192.1383, found: 192.1374. $[\alpha]_D$ = 76.9 (c = 1.27, dichloromethane, 21.6 °C).



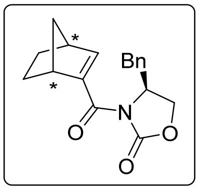
N8*: Colorless oil (50%). $R_f = 0.3$ (hexane/ethyl acetate = 2:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.10 (d, *J* = 3.1 Hz, 1H), 3.54 – 3.39 (m, 2H), 3.31 (dq, *J* = 14.1, 7.1 Hz, 2H), 3.12 (s, 1H), 2.97 (s, 1H), 1.76 – 1.66 (m, 2H), 1.44 – 1.33 (m, 2H), 1.13 (t, *J* = 7.1 Hz, 8H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.6, 143.2, 135.8, 47.4, 45.5, 43.5, 42.7, 39.4, 25.5, 25.4, 14.8, 13.0. **IR** (KBr): υ 2971, 2872, 1620, 1585, 1427, 1379, 1285, 1150, 1064, 812, 743 cm^{-1}. **HRMS** (ESI): Calculated for $C_{12}H_{20}NO$ (M+H$^+$): 194.1539, found: 194.1535. $[\alpha]_D = 125.7$ (c = 0.97, dichloromethane, 22.0 ^oC).



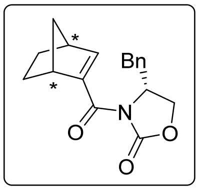
To a solution of NBE-CO_2H (138 mg, 1.0 mmol, 1.0 equiv) in DCM (1 mL) with1 drop of DMF was added oxalyl chloride (152 mg, 1.2 mmol, 1.2 equiv) dropwise at 0 ^oC. The reaction mixture was stirred at room temperature for another 1 h until the bubbling stopped. To another flame-dried round bottom flask was added 2-oxazolidinone (95.8 mg, 1.1 mmol, 1.1 equiv) and dry THF (10 mL). Then, *n*BuLi (0.81 mL, 1.6 M in hexane, 1.3 mmol, 1.3 equiv) was added dropwise to the flask at -78 ^oC and the reaction mixture was stirred at -78 ^oC for another 30 min. After that, the generated acyl chloride from the first flask was transferred into the second flask dropwise using dry THF. Then the reaction mixture was warmed to room temperature slowly and stirred for another 2 h. The reaction was quenched by 5 mL H_2O and the aqueous lays was extracted by ethyl acetate for three times. The combined organic layers were dried over $MgSO_4$ and then purified by silica gel chromatography to afford **N9***.



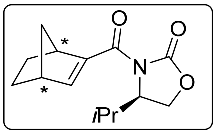
N9*: White solid (48%). $R_f = 0.2$ (hexane/ethyl acetate = 2:1). Mp = 85.4 – 87.9 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 3.3 Hz, 1H), 4.41 – 4.27 (m, 2H), 4.02 (ddd, *J* = 10.9, 9.0, 7.9 Hz, 1H), 3.91 (ddd, *J* = 10.8, 8.6, 5.9 Hz, 1H), 3.21 (s, 1H), 3.03 (s, 1H), 1.76 – 1.64 (m, 2H), 1.55 (dt, *J* = 8.6, 2.1 Hz, 1H), 1.20 – 1.00 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.7, 153.3, 148.3, 140.1, 62.2, 47.3, 44.2, 44.0, 43.6, 25.10, 25.06. **IR** (KBr): υ 2971, 2872, 1783, 1664, 1587, 1478, 1383, 1301, 1199, 1115, 1080, 1039, 987, 746, 698 cm^{-1}. **HRMS** (ESI): Calculated for $C_{11}H_{14}NO_3$ $(M+H^+)$: 208.0968, found: 208.0966. $[\alpha]_D$ = -65.9 (c = 0.97, dichloromethane, 22.0 °C).



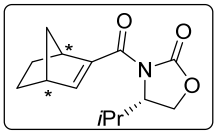
N10*: White solid (63%). $R_f = 0.2$ (hexane/ethyl acetate = 2:1). Mp = 105.9 – 107.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 3H), 7.19 – 7.13 (m, 2H), 6.89 (d, *J* = 3.0 Hz, 1H), 4.80 (tdd, *J* = 8.7, 5.1, 3.6 Hz, 1H), 4.25 (t, *J* = 8.6 Hz, 1H), 4.13 (dd, *J* = 8.9, 5.2 Hz, 1H), 3.32 – 3.21 (m, 2H), 3.11 (s, 1H), 2.83 (dd, *J* = 13.5, 8.9 Hz, 1H), 1.86 – 1.73 (m, 2H), 1.61 (dq, *J* = 6.4, 2.1 Hz, 1H), 1.28 – 1.18 (m, 2H), 1.17 – 1.10 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0, 153.4, 148.9, 140.7, 135.4, 129.6, 129.0, 127.4, 66.3, 55.5, 47.1, 44.3, 44.0, 38.0, 25.3, 25.3. **IR** (KBr): υ 2972, 2872, 1785, 1660, 1497, 1453, 1348, 1290, 1212, 1114, 746, 702 cm^{-1}. **HRMS** (ESI): Calculated for $C_{18}H_{20}NO_3$ $(M+H^+)$: 298.1438, found: 298.1439. $[\alpha]_D$ = -7.5 (c = 0.99, dichloromethane, 22.0 °C).



N11*: White solid (47%). $R_f = 0.2$ (hexane/ethyl acetate = 2:1). Mp = 92.4 – 93.1 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.30 – 7.25 (m, 1H), 7.24 – 7.20 (m, 2H), 6.86 (d, *J* = 3.2 Hz, 1H), 4.64 (ddt, *J* = 9.6, 7.3, 3.6 Hz, 1H), 4.24 – 4.11 (m, 2H), 3.40 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.32 (s, 1H), 3.09 (s, 1H), 2.80 (dd, *J* = 13.4, 9.6 Hz, 1H), 1.85 – 1.73 (m, 2H), 1.68 (dt, *J* = 8.6, 2.1 Hz, 1H), 1.28 – 1.10 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.7, 153.3, 147.6, 140.6, 135.6, 129.6, 129.0, 127.4, 66.3, 56.4, 47.7, 44.2, 44.1, 37.6, 25.1, 25.0. **IR** (KBr): υ 2973, 1785, 1659, 1453, 1350, 1293, 1211, 1114, 1084, 745, 702 cm^{-1}. **HRMS** (ESI): Calculated for $C_{18}H_{20}NO_3$ (M+H$^+$): 298.1438, found: 298.1441. $[\alpha]_D$ = -128.7 (c = 0.97, dichloromethane, 22.0 °C).

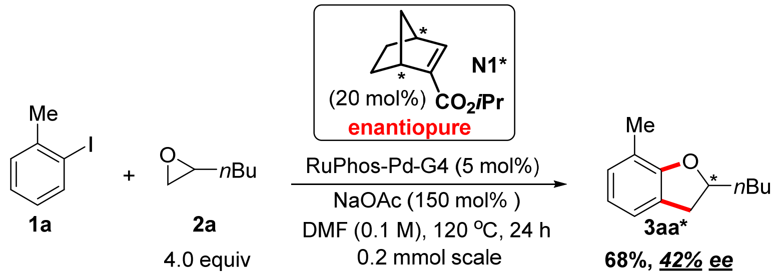


N12*: White solid (61%). R_f = 0.3 (hexane/ethyl acetate = 2:1). Mp = 84.1 – 86.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.88 (dt, *J* = 3.4, 1.0 Hz, 1H), 4.56 (dt, *J* = 9.0, 4.7 Hz, 1H), 4.30 (t, *J* = 8.9 Hz, 1H), 4.15 (dd, *J* = 9.0, 4.9 Hz, 1H), 3.24 (s, 1H), 3.09 (s, 1H), 2.27 (pd, *J* = 7.0, 4.4 Hz, 1H), 1.83 – 1.70 (m, 2H), 1.60 (dt, *J* = 8.6, 2.1 Hz, 1H), 1.22 – 1.15 (m, 2H), 1.12 – 1.05 (m, 1H), 0.87 (dd, *J* = 9.7, 7.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.1, 153.9, 148.6, 140.9, 63.5, 58.4, 46.9, 44.4, 44.0, 28.8, 25.4, 25.3, 17.9, 15.2. **IR** (KBr): υ 2965, 2873, 1783, 1665, 1587, 1485, 1388, 1363, 1289, 1203, 886, 764, 745 cm^{-1}. **HRMS** (ESI): Calculated for $C_{14}H_{20}NO_3$ (M+H$^+$): 250.1438, found: 250.1433. $[\alpha]_D$ = 37.2 (c = 1.13, dichloromethane, 22.0 °C).

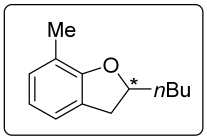


N13*: White solid (54%). R_f = 0.3 (hexane/ethyl acetate = 2:1). Mp = 85.5 – 89.4 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 3.3 Hz, 1H), 4.45 (dt, *J* = 8.6, 4.3 Hz, 1H), 4.28 (t, *J* = 8.7 Hz, 1H), 4.17 (dd, *J* = 8.9, 4.5 Hz, 1H), 3.28 (s, 1H), 3.05 (s, 1H), 2.42 (pd, *J* = 7.0, 4.1 Hz, 1H), 1.82 – 1.66 (m, 3H), 1.24 (dd, *J* = 8.6, 1.1 Hz, 1H), 1.19 – 1.11 (m, 2H), 0.90 (dd, *J* = 8.2, 7.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.6, 154.0, 146.8, 141.1, 63.5, 59.0, 48.3, 44.2, 43.8, 28.4, 24.9, 24.8, 18.0, 15.0. **IR** (KBr): υ 2965, 2672, 1783, 1672, 1589, 1465, 1387, 1341, 1293, 1201, 1079, 888, 766, 744 cm^{-1}. **HRMS** (ESI): Calculated for $C_{14}H_{20}NO_3$ (M+H$^+$): 250.1438, found: 250.1429. $[\alpha]_D$ = 132.5 (c = 1.02, dichloromethane, 22.0 °C).

2.3 Enantioselective Transformation Using Chiral NBE-CO_2*i*Pr (N1*)

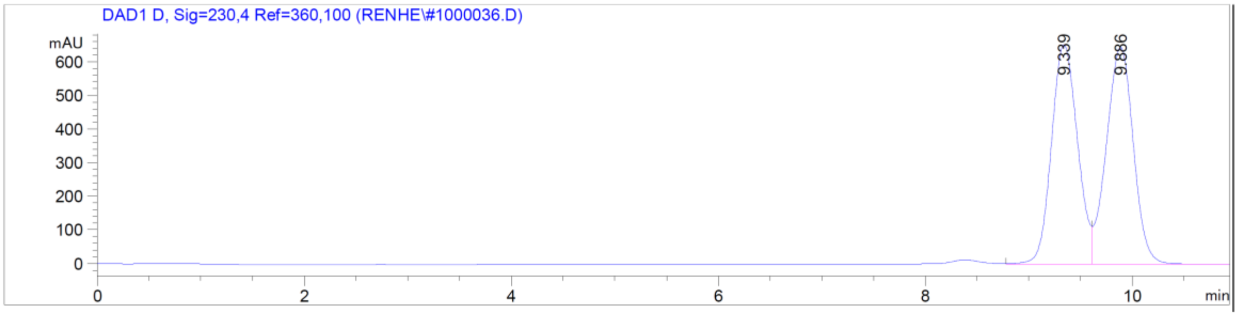


A flame-dried 4.0 mL vial was charged with aryl iodide **1a** (43.6 mg, 0.2 mmol, 1.0 equiv), NaOAc (24.6 mg, 0.3 mmol, 1.5 equiv) and RuPhos-Pd-G4 (8.5 mg, 0.01 mmol, 5 mol%). Then the vial was directly transferred into a nitrogen-filled glovebox without caps. After enantiomeric NBE-CO_2*i*Pr **N1*** (7.2 mg, 0.04 mmol, 20 mol%) and 1,2-epoxyhexane (80 mg, 0.8 mmol, 4.0 equiv) was added to the vial, 2 mL of degassed DMF was added. Then the vial was tightly sealed, transferred out of glovebox and stirred on a pie-block preheated to 120 °C for 24 hours. After completion of the reaction, the mixture was filtered through a thin pad of celite. The filter cake was washed with dichloromethane and diethyl ether, and the combined filtrate was concentrated. The residue was absorbed onto a small amount of silica gel and then purified by flash column chromatography on silica gel to give the desired product.



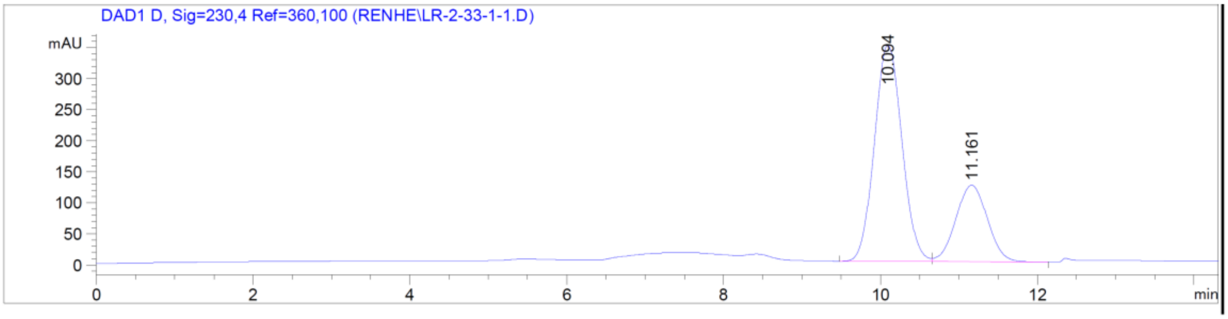
3aa*: Pale yellow oil (68%). $R_f = 0.4$ (hexane/ethyl acetate = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 (d, *J* = 6.9 Hz, 1H), 6.93 (ddq, *J* = 7.5, 1.5, 0.8 Hz, 1H), 6.74 (t, *J* = 7.4 Hz, 1H), 4.76 (dddd, *J* = 8.9, 7.8, 6.9, 6.2 Hz, 1H), 3.28 (dd, *J* = 15.4, 8.9 Hz, 1H), 2.86 (dd, *J* = 15.4, 7.8 Hz, 1H), 2.22 (s, 3H), 1.93 – 1.79 (m, 1H), 1.73 – 1.62 (m, 1H), 1.55 – 1.34 (m, 4H), 0.95 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.2, 129.2, 126.3, 122.4, 120.0, 119.6, 83.1, 36.0, 35.9, 27.7, 22.8, 15.4, 14.2. **IR** (KBr): υ 3025, 2956, 2931, 2859, 1599, 1467, 1260, 1186, 759 cm-1. **HRMS** (ESI): Calculated for $C_{13}H_{19}O$ ($M+H^+$): 191.1430, found: 191.1428. **Chiral HPLC** (Chiralpak OD-H, hexane/isopropanol = 99:1, 0.5 mL/min, 230 nm): t_{minor} = 11.161, t_{major} = 10.094. 42% ee.

Racemic 3aa

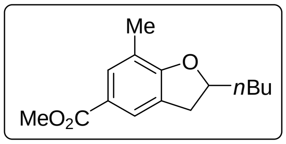


```
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.339 VV     0.2748 1.14719e4   653.63702  49.4863
   2   9.886 VBA    0.2817 1.17100e4   645.41187  50.5137

Totals :                   2.31819e4  1299.04889
```

Enantiomeric 3aa*

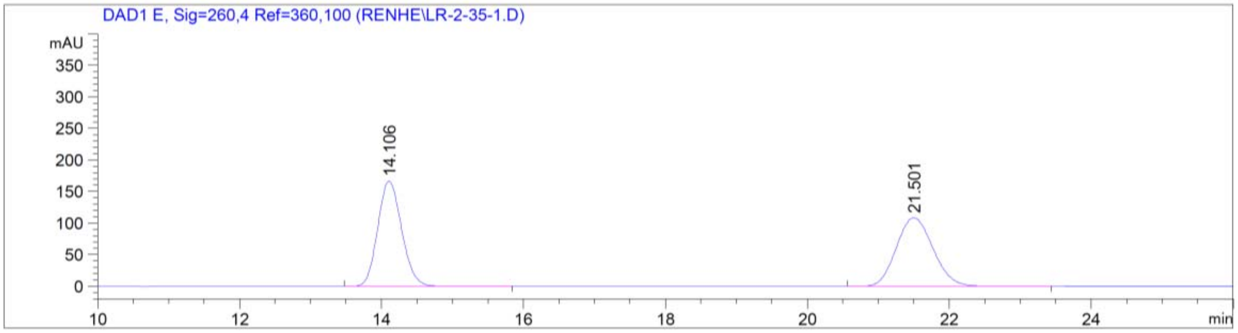


```
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.094 BV     0.3827 8513.32520  348.88733  71.0521
   2  11.161 VB     0.4418 3468.47949  123.45961  28.9479

Totals :                   1.19818e4   472.34694
```



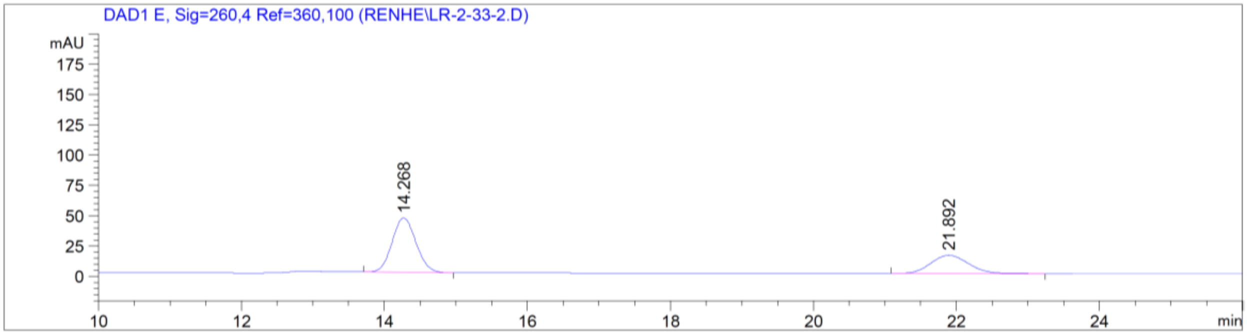
3ba*: Pale yellow oil (54%). R_f = 0.2 (hexane/ethyl acetate = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 7.65 (m, 2H), 4.89 – 4.78 (m, 1H), 3.85 (s, 3H), 3.28 (dd, *J* = 15.5, 9.0 Hz, 1H), 2.85 (dd, *J* = 15.5, 7.7 Hz, 1H), 2.21 (s, 3H), 1.90 – 1.78 (m, 1H), 1.74 – 1.62 (m, 1H), 1.54 – 1.32 (m, 4H), 0.93 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.4, 162.4, 131.9, 126.6, 124.4, 122.2, 119.3, 84.4, 51.8, 36.0, 35.3, 27.6, 22.7, 15.3, 14.1. **IR** (KBr): υ 2954, 2860, 1715, 1607, 1434, 1306, 1161, 954, 771 cm^{-1}. **HRMS** (ESI): Calculated for $C_{15}H_{21}O_3$ (M+H$^+$): 249.1485, found: 249.1492. **Chiral HPLC** (Chiralpak OD-H, hexane/isopropanol = 99:1, 0.5 mL/min, 260 nm): t_{minor} = 21.892, t_{major} = 14.268. 31% ee.

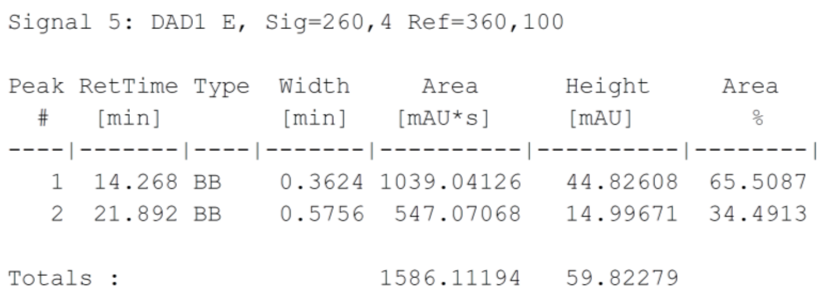
Racemic 3ba



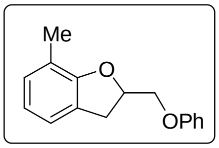
```
Signal 5: DAD1 E, Sig=260,4 Ref=360,100

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  14.106 BB    0.3649 3900.03076  166.73305  49.9833
   2  21.501 BB    0.5676 3902.63062  108.50792  50.0167

Totals :                  7802.66138  275.24097
```

Enantiomeric 3ba*



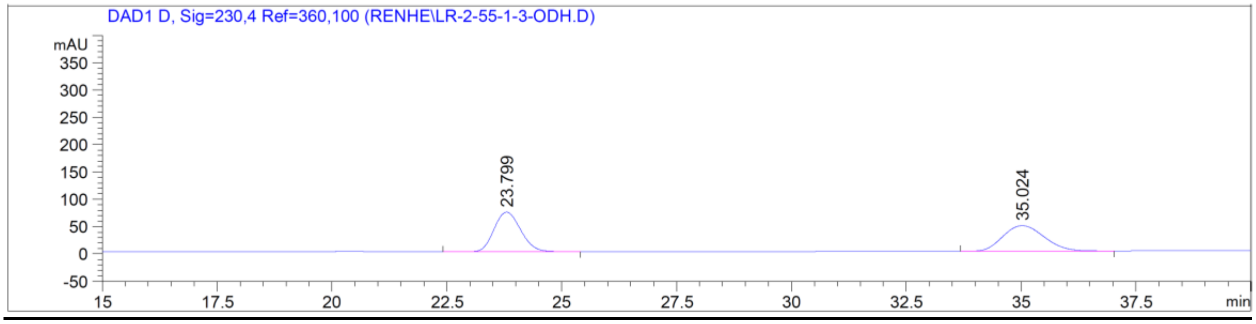


```
Signal 5: DAD1 E, Sig=260,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.268 BB    0.3624 1039.04126   44.82608  65.5087
   2  21.892 BB    0.5756  547.07068   14.99671  34.4913

Totals :                  1586.11194   59.82279
```



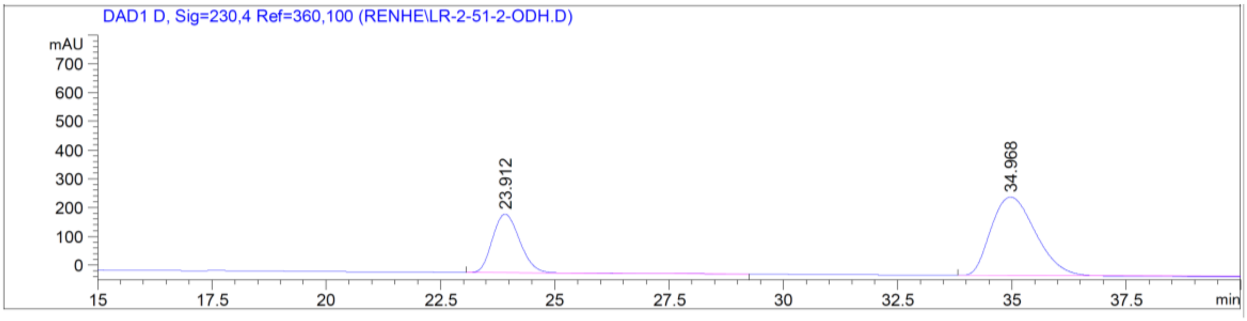
3ab*: White solid (92%). R_f = 0.3 (hexane/ethyl acetate = 40:1). Mp = 77.8 – 78.6 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 2H), 7.04 (ddd, *J* = 7.3, 1.4, 0.7 Hz, 1H), 7.03 – 6.91 (m, 4H), 6.79 (t, *J* = 7.4 Hz, 1H), 5.15 (dddd, *J* = 9.4, 7.0, 5.9, 5.3 Hz, 1H), 4.24 (dd, *J* = 9.9, 5.9 Hz, 1H), 4.10 (dd, *J* = 9.9, 5.3 Hz, 1H), 3.40 (dd, *J* = 15.7, 9.4 Hz, 1H), 3.17 (dd, *J* = 15.7, 7.1 Hz, 1H), 2.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.8, 157.9, 129.6, 129.5, 125.4, 122.5, 121.2, 120.6, 120.0, 114.8, 80.2, 69.9, 32.9, 15.4. **IR** (KBr): υ 3040, 2920, 2857, 1599, 1497, 1468, 1243, 1193, 1050, 754, 691 cm^{-1}. **HRMS** (ESI): Calculated for $C_{16}H_{17}O_2$ (M+H$^+$): 241.1223, found: 241.1221. **Chiral HPLC** (Chiralpak OD-H, hexane/isopropanol = 98:2, 0.5 mL/min, 230 nm): t_{minor} = 23.912, t_{major} = 34.968. 38% ee.

Racemic 3ab

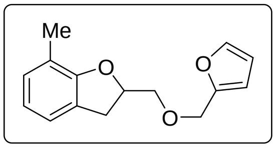


```
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.799 BB    0.6346 2908.75586   72.41602 49.9844
   2  35.024 BB    0.9928 2910.56860   46.59019 50.0156

Totals :                  5819.32446  119.00621
```

<u>Enantiomeric 3ab*</u>



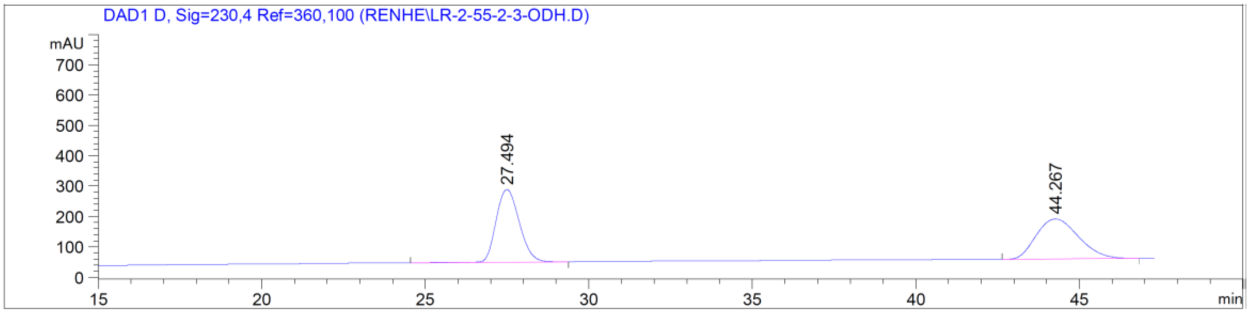
```
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.912 BB    0.6562 8405.07129  203.36694 31.2355
   2  34.968 BBA   1.0753 1.85036e4   272.80038 68.7645

Totals :                  2.69087e4   476.16733
```



3ac*: Yellow oil (78%). R_f = 0.2 (hexane/ethyl acetate = 40:1). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.43 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.00 (d, *J* = 7.0 Hz, 1H), 6.94 (ddq, *J* = 7.5, 1.5, 0.8 Hz, 1H), 6.76 (t, *J* = 7.4 Hz, 1H), 6.38 – 6.32 (m, 2H), 4.94 (dddd, *J* = 9.4, 7.5, 6.3, 4.8 Hz, 1H), 4.65 – 4.52 (m, 2H), 3.73 (dd, *J* = 10.4, 6.3 Hz, 1H), 3.64 (dd, *J* = 10.4, 4.8 Hz, 1H), 3.26 (dd, *J* = 15.6, 9.4 Hz, 1H), 3.00 (dd, *J* = 15.6, 7.5 Hz, 1H), 2.23 (d, *J* = 0.6 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 158.0, 151.7, 143.0, 129.3, 125.6, 122.4, 120.4, 119.8, 110.4, 109.6, 81.2, 72.1, 65.4, 32.8, 15.4. **IR** (KBr): υ 3119, 3049, 2919, 2857, 1599, 1468, 1261, 1194, 1151, 1073. 920, 758, 600 cm^{-1}. **HRMS** (ESI):

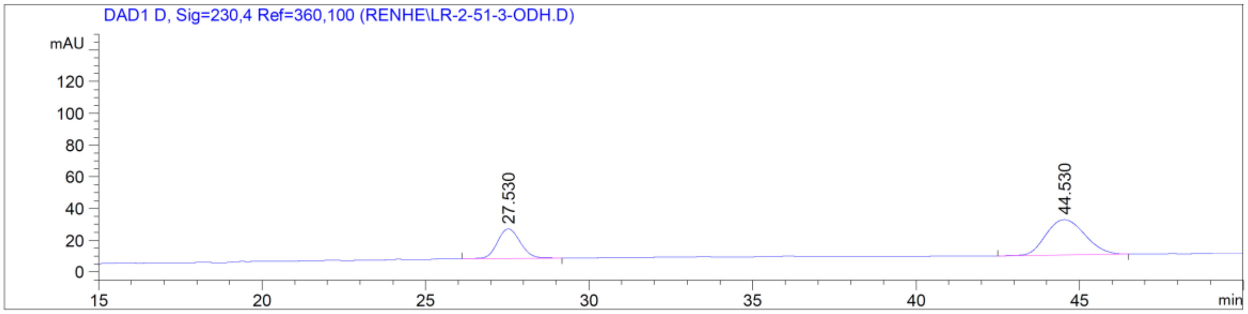
Calculated for $C_{15}H_{17}O_3$ ($M+H^+$): 245.1172, found: 245.1174. **Chiral HPLC** (Chiralpak OD-H, hexane/isopropanol = 95:5, 0.5 mL/min, 230 nm): t_{minor} = 27.530, t_{major} = 44.530. 34% ee.

Racemic 3ac



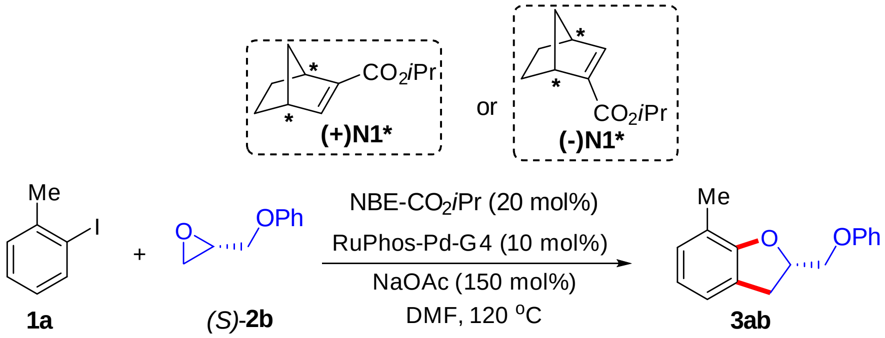
```
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  27.494 BB    0.7824 1.17421e4  239.31871  49.8019
   2  44.267 BB    1.4292 1.18355e4  131.60634  50.1981

Totals :                  2.35776e4  370.92505
```

Enantiomeric 3ac*



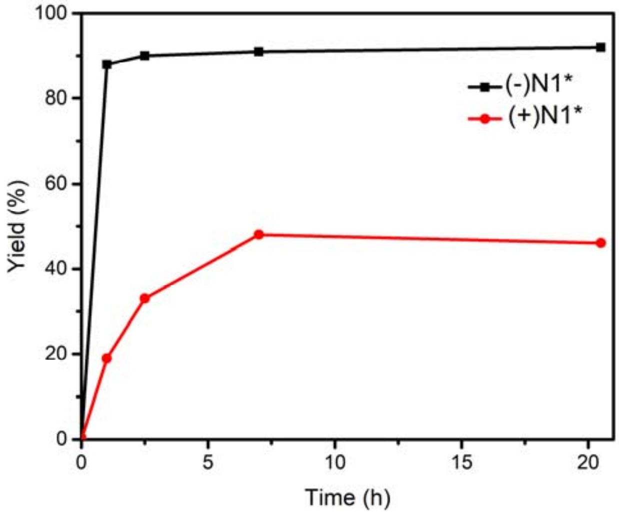
```
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  27.530 BB    0.7585  912.32776   18.72223  33.0027
   2  44.530 BB    1.2981 1852.07678   22.31998  66.9973

Totals :                  2764.40454   41.04220
```

2.4 Matched/Mismatched Experiments for the Stereochemistry of NBE and Epoxide

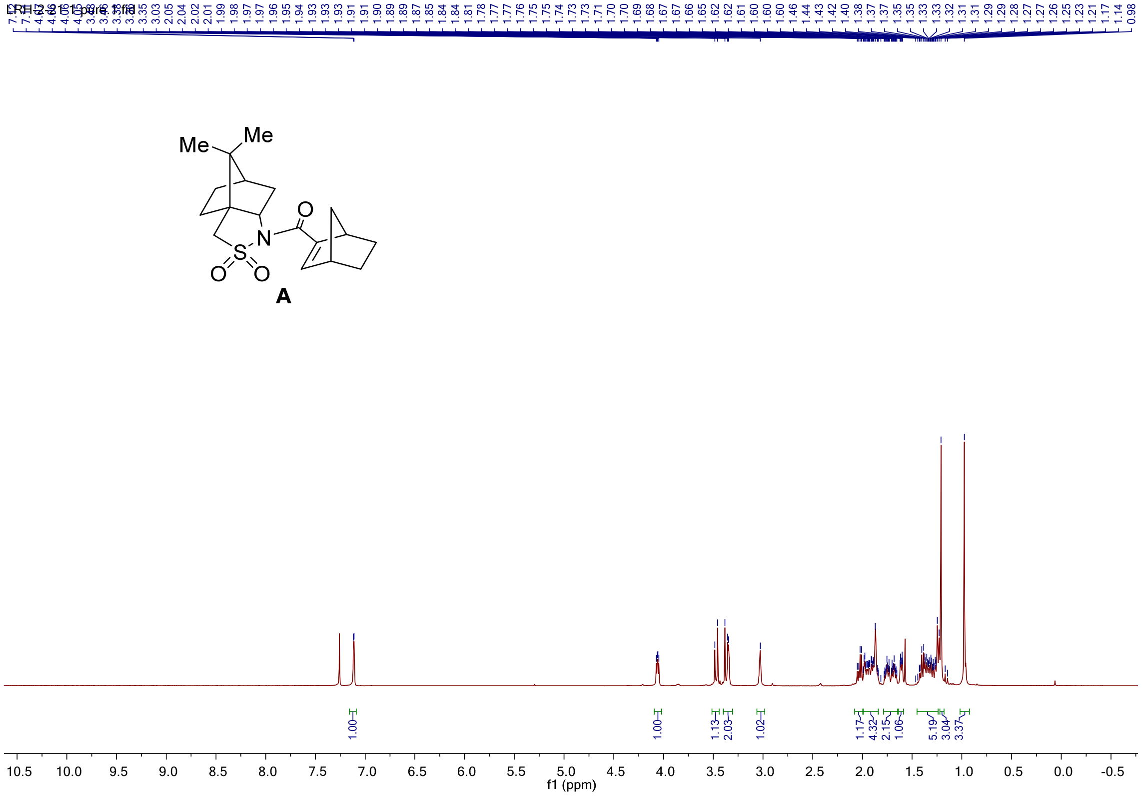


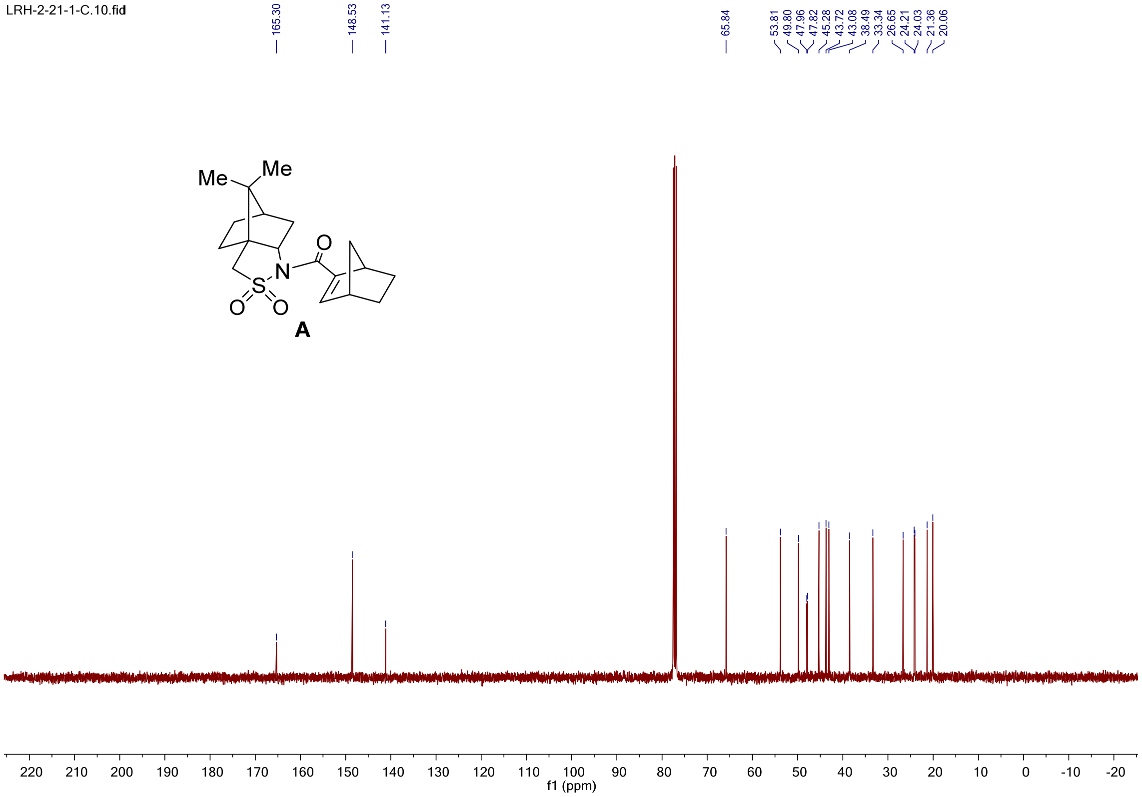
A flame-dried 4.0 mL vial was charged with aryl iodide **1a** (21.8 mg, 0.1 mmol, 1.0 equiv), NaOAc (12.3 mg, 0.15 mmol, 1.5 equiv) and RuPhos-Pd-G4 (8.5 mg, 0.01 mmol, 10 mol%). Then the vial was directly transferred into a nitrogen-filled glovebox without caps. After (+) or (−) NBE-CO_2*i*Pr **N1*** (3.6 mg, 0.02 mmol, 20 mol%) and chiral epoxide (*S*)-**2b** (60 mg, 0.4 mmol, 4.0 equiv) were transferred to the vial, 1 mL of degassed DMF was added. Then the vial was tightly sealed, transferred out of glovebox and stirred on a pie-block preheated to 120 °C. After completion of the reaction, the mixture was filtered through a thin pad of celite. The filter cake was washed with dichloromethane and diethyl ether, and the combined filtrate was concentrated. The residue was absorbed onto a small amount of silica gel and then purified by flash column chromatography on silica gel to give the desired product.

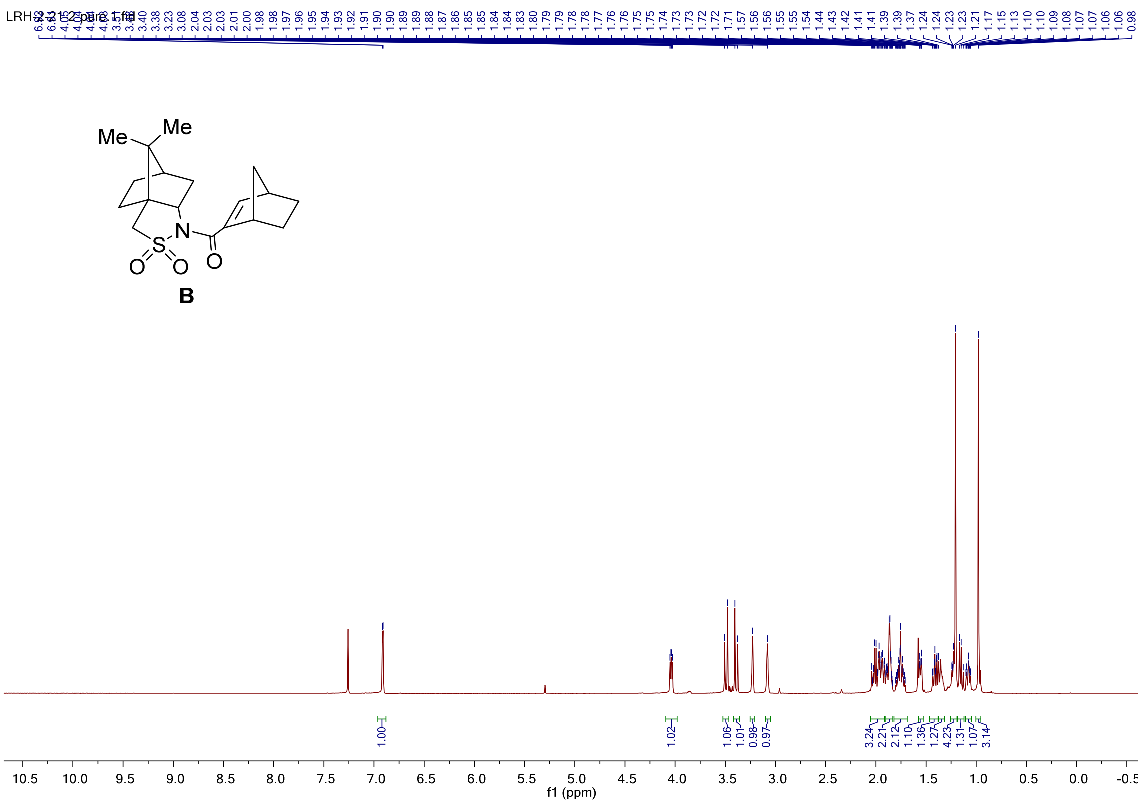
	1 h	2.5 h	7.0 h	20.5 h
Yield w/ **(−) N1***	88%	90%	91%	92%
Yield w/ **(+) N1***	19%	33%	48%	46%


100
80
60
40
20
0
Yield (%)
0
5
10
15
20
Time (h)
(-)N1*
(+)N1*

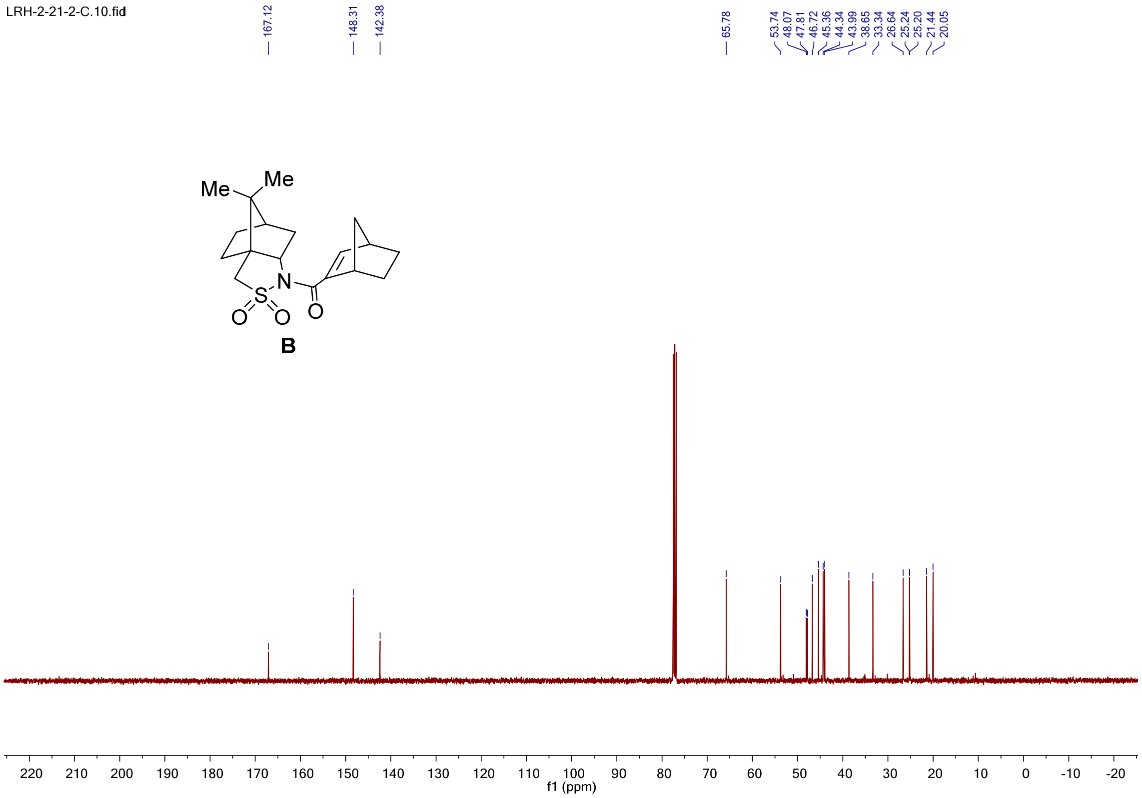
3. NMR Spectra



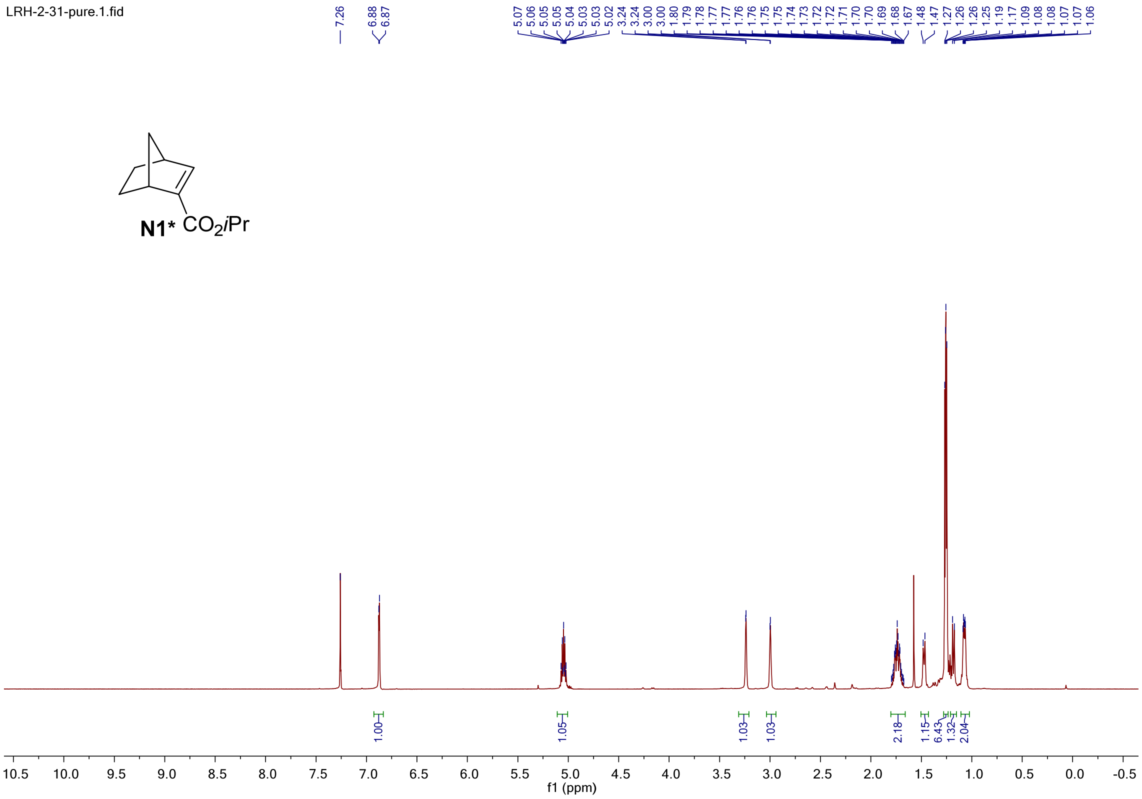


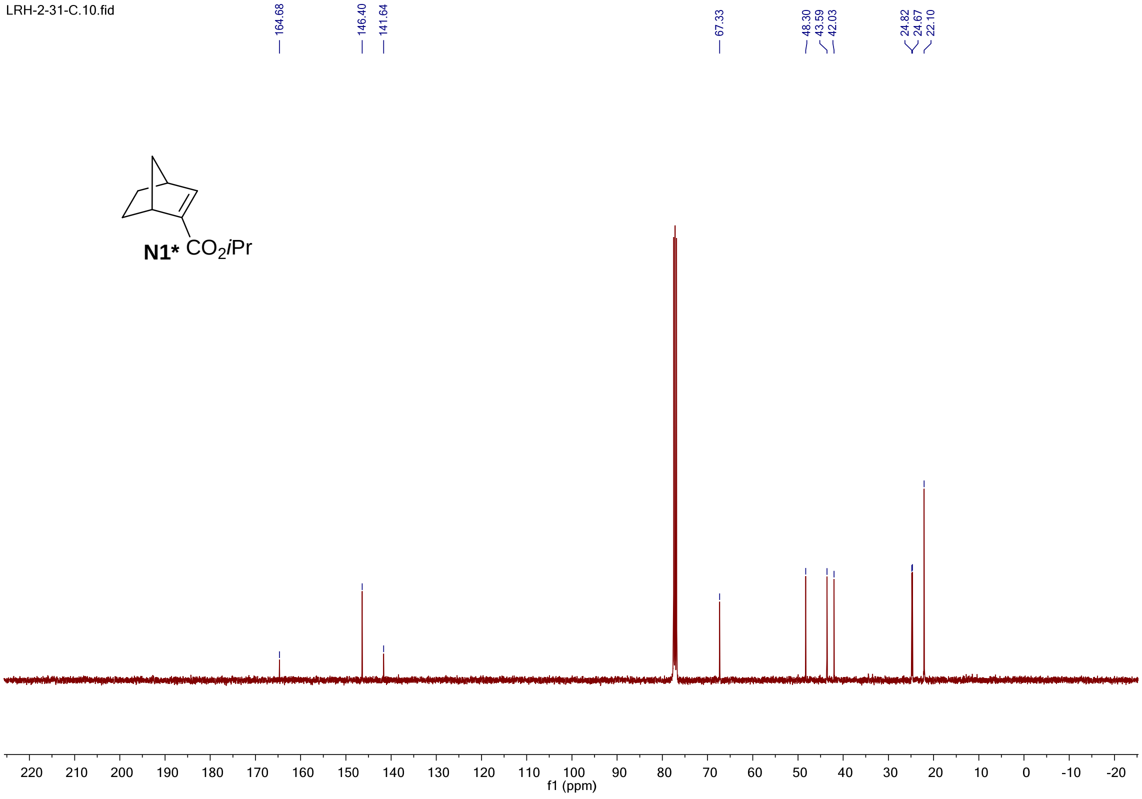

LRH-2-21-2 pure.1.fid
4.05
4.04
3.40
3.38
3.23
3.08
2.04
2.03
2.03
2.01
2.00
1.98
1.98
1.97
1.96
1.95
1.94
1.93
1.92
1.91
1.90
1.90
1.89
1.89
1.88
1.87
1.86
1.85
1.85
1.84
1.84
1.83
1.80
1.79
1.79
1.78
1.78
1.77
1.76
1.76
1.75
1.75
1.74
1.73
1.73
1.72
1.72
1.71
1.57
1.56
1.56
1.55
1.55
1.54
1.44
1.43
1.42
1.41
1.41
1.39
1.39
1.37
1.24
1.24
1.23
1.23
1.21
1.17
1.15
1.13
1.10
1.10
1.09
1.08
1.07
1.07
1.06
1.06
0.98
Me
Me
N
S
O
O
O
1.00
1.02
1.06
1.01
0.98
0.97
3.24
2.21
2.12
1.10
1.36
1.27
4.23
1.31
1.07
3.14
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

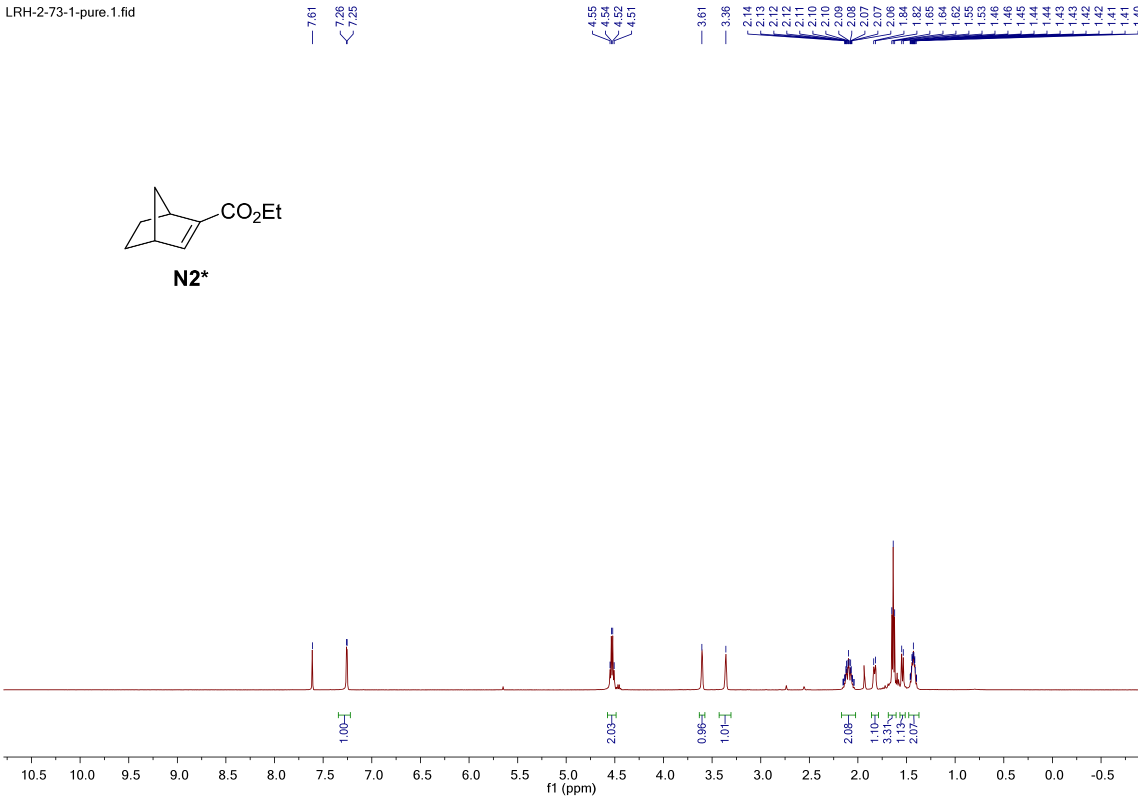
B

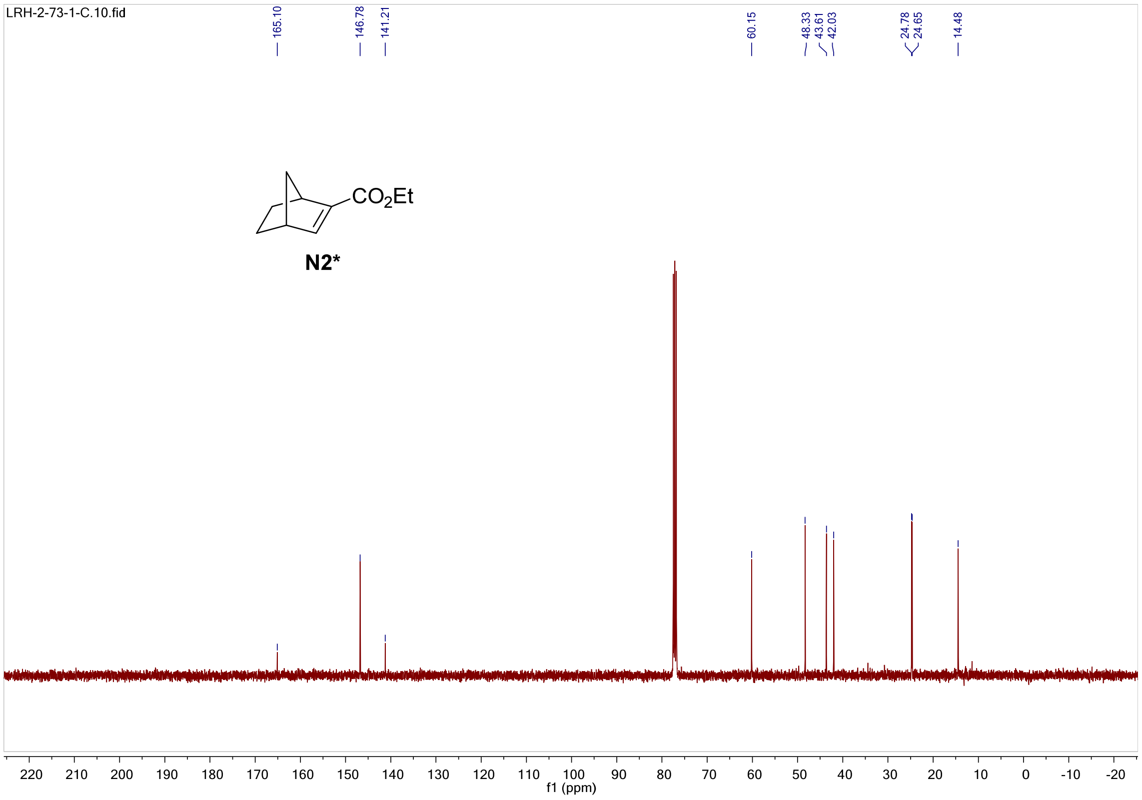

LRH-2-21-2-C.10.fid
167.12
148.31
142.38
65.78
53.74
48.07
47.81
46.72
45.36
44.34
43.99
38.65
33.34
26.64
25.24
25.20
21.44
20.05
Me
Me
N
S
O
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

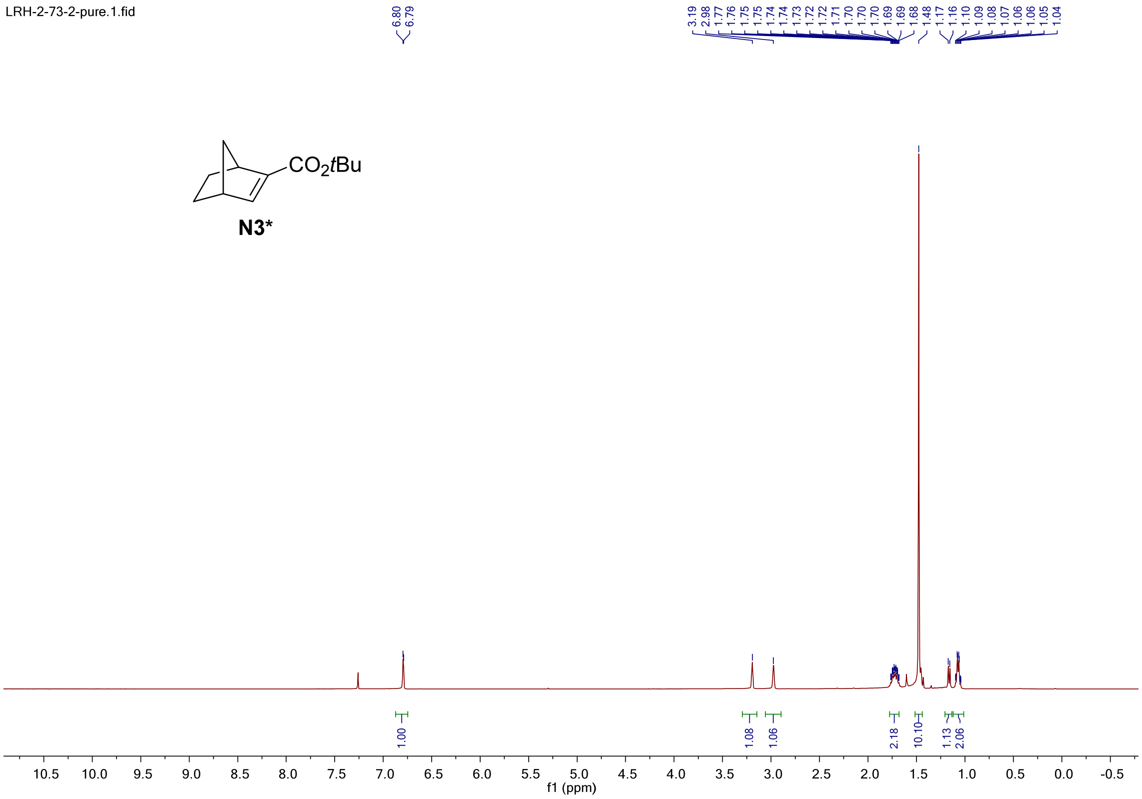
B

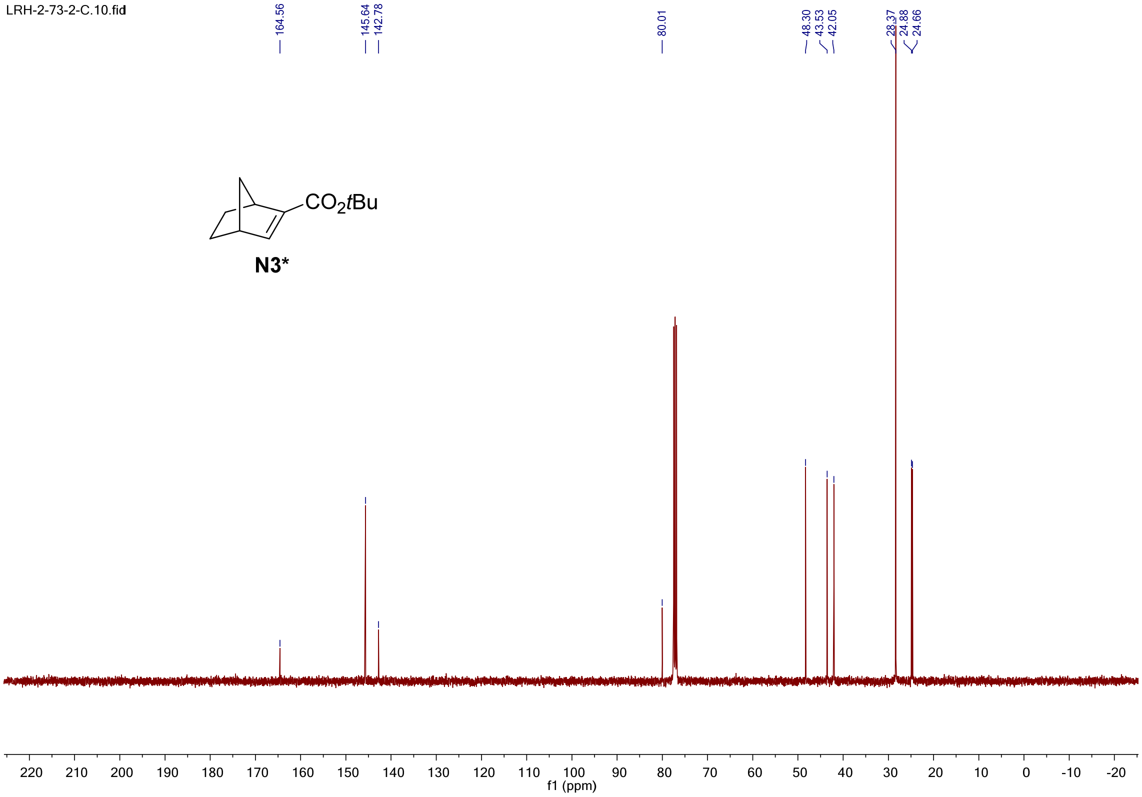

LRH-2-31-pure.1.fid
7.26
6.88
6.87
5.07
5.06
5.05
5.05
5.04
5.03
5.03
5.02
3.24
3.24
3.00
3.00
1.80
1.79
1.78
1.77
1.77
1.76
1.75
1.75
1.74
1.73
1.72
1.72
1.71
1.70
1.70
1.69
1.68
1.67
1.48
1.47
1.27
1.26
1.26
1.25
1.19
1.17
1.09
1.08
1.08
1.07
1.06
N1*
CO2iPr
1.00
1.05
1.03
1.03
2.18
1.15
6.43
1.32
2.04
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

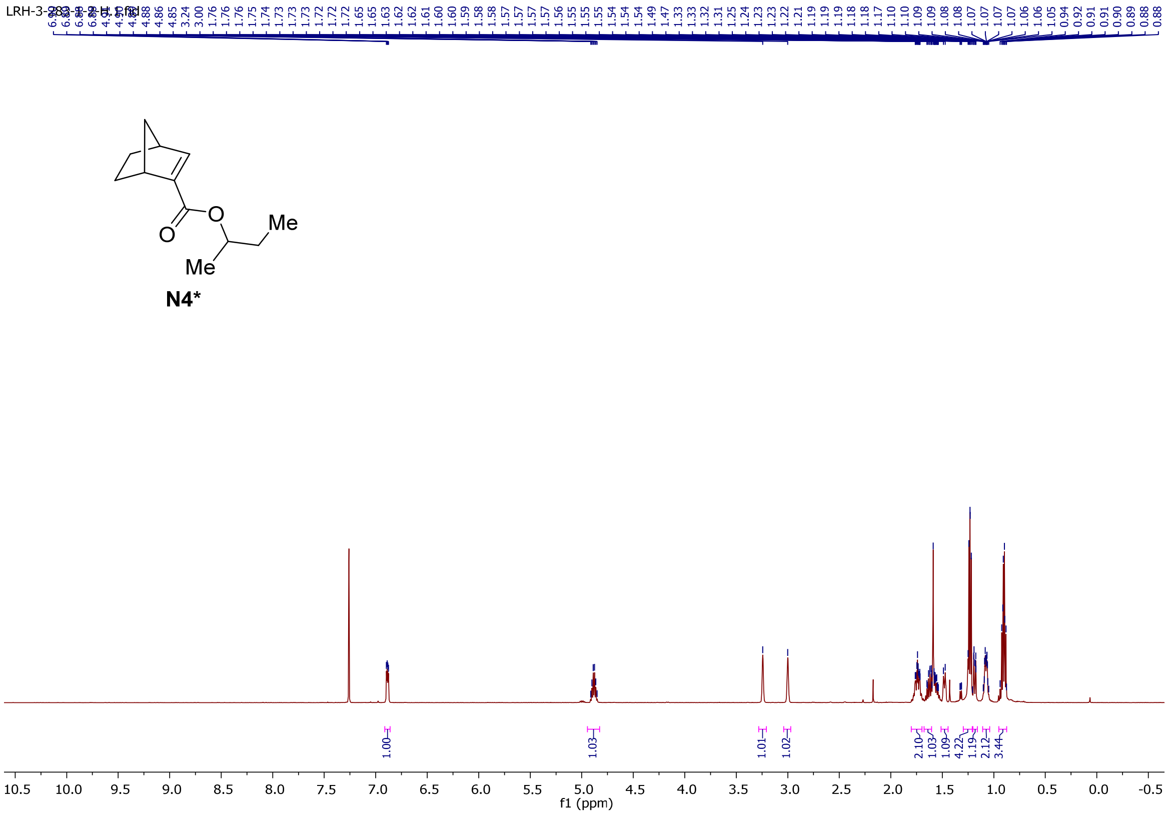

LRH-2-31-C.10.fid
164.68
146.40
141.64
67.33
48.30
43.59
42.03
24.82
24.67
22.10
N1*
CO2iPr
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

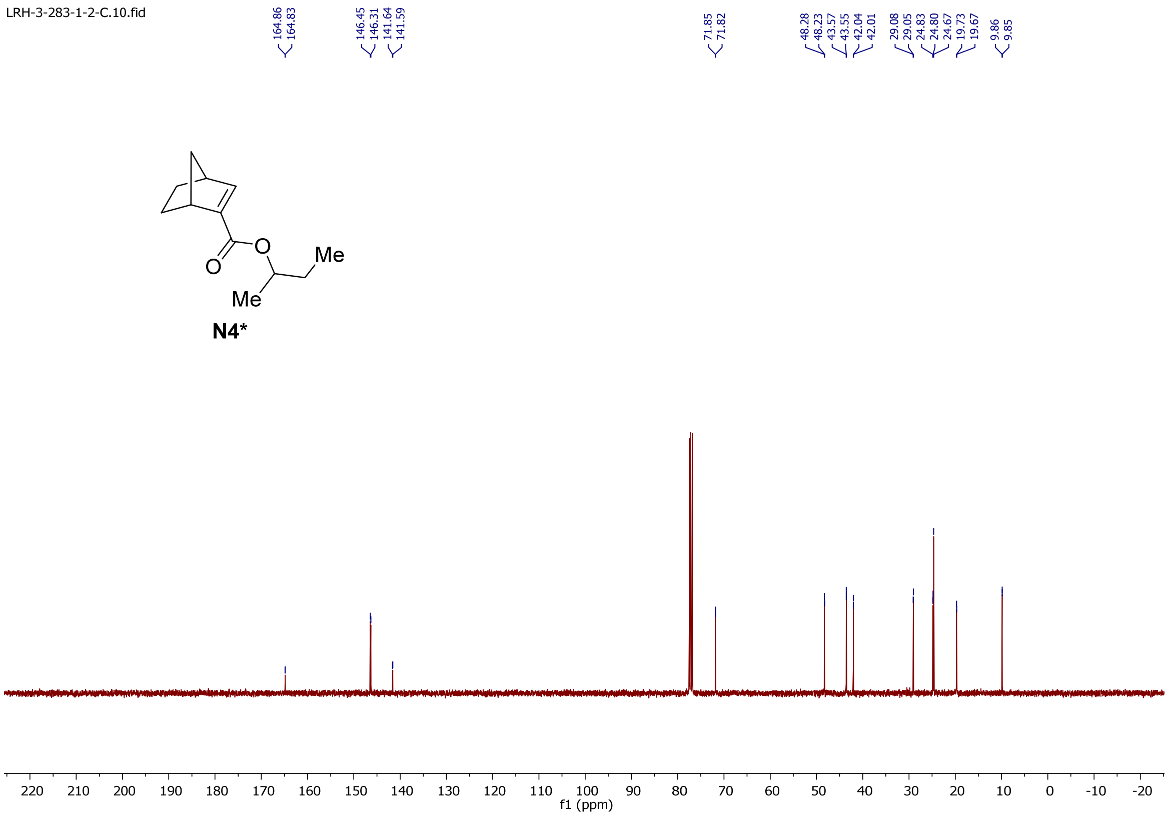

LRH-2-73-1-pure.1.fid
7.61
7.26
7.25
4.55
4.54
4.52
4.51
3.61
3.36
2.14
2.13
2.12
2.12
2.11
2.10
2.10
2.09
2.08
2.07
2.07
2.06
1.84
1.82
1.65
1.64
1.62
1.55
1.53
1.46
1.45
1.44
1.44
1.43
1.43
1.42
1.42
1.41
1.41
CO2Et
N2*
1.00
2.03
0.96
1.01
2.08
1.10
3.31
1.13
2.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


LRH-2-73-1-C.10.fid
165.10
146.78
141.21
60.15
48.33
43.61
42.03
24.78
24.65
14.48
CO2Et
N2*
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


LRH-2-73-2-pure.1.fid
6.80
6.79
3.19
2.98
1.77
1.76
1.75
1.75
1.74
1.74
1.73
1.72
1.72
1.71
1.70
1.70
1.70
1.69
1.69
1.68
1.48
1.17
1.16
1.10
1.09
1.08
1.07
1.06
1.06
1.05
1.04
CO2tBu
N3*
1.00
1.08
1.06
2.18
10.10
1.13
2.06
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


LRH-2-73-2-C.10.fid
164.56
145.64
142.78
80.01
48.30
43.53
42.05
28.37
24.88
24.66
CO2tBu
N3*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


LRH-3-283-1-2-H.1.fid
4.88
4.86
4.85
3.24
3.00
1.76
1.76
1.76
1.75
1.74
1.73
1.73
1.73
1.72
1.72
1.72
1.65
1.65
1.63
1.62
1.62
1.61
1.60
1.60
1.59
1.58
1.58
1.57
1.57
1.57
1.57
1.56
1.55
1.55
1.55
1.54
1.54
1.54
1.49
1.47
1.33
1.33
1.32
1.31
1.25
1.24
1.23
1.23
1.22
1.21
1.19
1.19
1.19
1.18
1.18
1.17
1.10
1.10
1.09
1.09
1.08
1.08
1.07
1.07
1.07
1.07
1.06
1.06
1.05
0.94
0.92
0.91
0.91
0.90
0.89
0.88
0.88
O
O
Me
Me
N4*
1.00
1.03
1.01
1.02
2.10
1.03
1.09
4.22
1.19
2.12
3.44
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


LRH-3-283-1-2-C.10.fid
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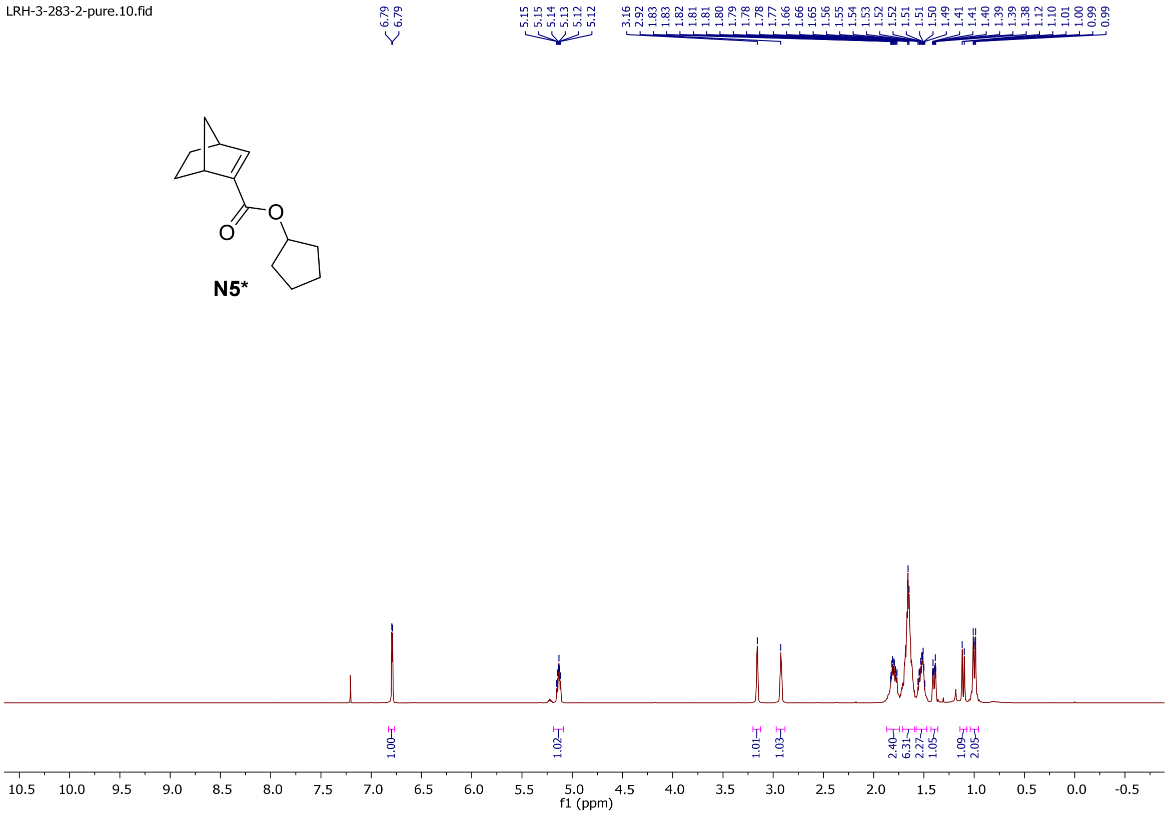
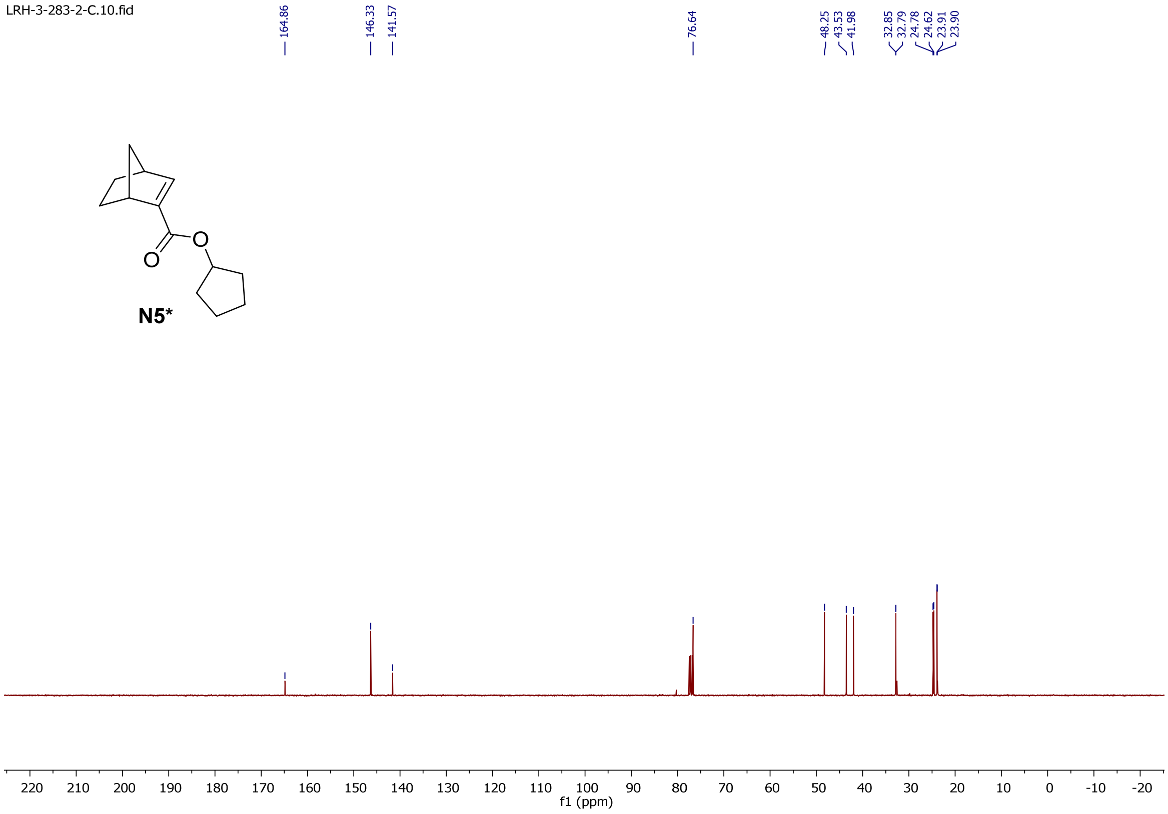
164.83
146.45
146.31
141.64
141.59
71.85
71.82
48.28
48.23
43.57
43.55
42.04
42.01
29.08
29.05
24.83
24.80
24.67
19.73
19.67
9.86
9.85
O
O
Me
Me
N4*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


LRH-3-283-2-pure.10.fid
6.79
6.79
5.15
5.15
5.14
5.13
5.12
5.12
3.16
2.92
1.83
1.83
1.82
1.81
1.81
1.80
1.79
1.78
1.78
1.77
1.66
1.66
1.65
1.56
1.55
1.55
1.54
1.53
1.52
1.52
1.51
1.51
1.50
1.49
1.41
1.41
1.40
1.39
1.39
1.38
1.12
1.10
1.01
1.00
0.99
0.99
O
O
N5*
1.00
1.02
1.01
1.03
2.40
6.31
2.27
1.05
1.09
2.05
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


LRH-3-283-2-C.10.fid
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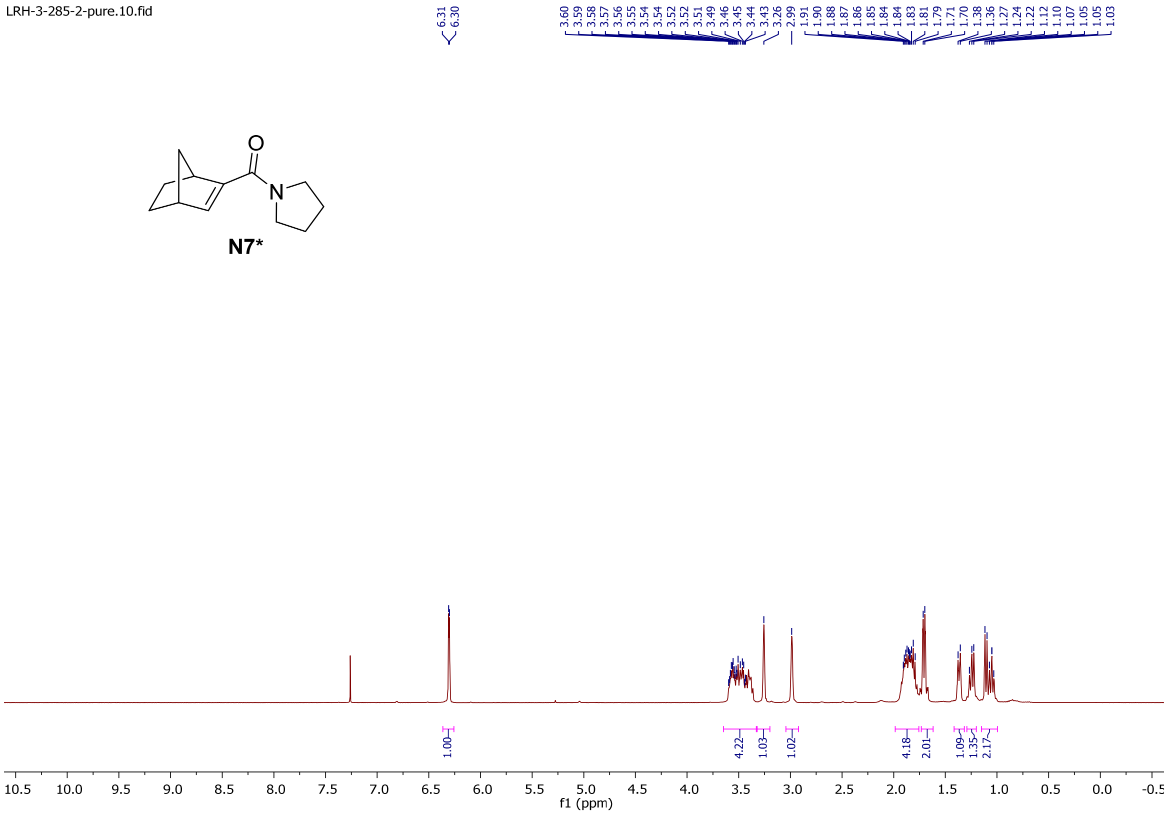
146.33
141.57
76.64
48.25
43.53
41.98
32.85
32.79
24.78
24.62
23.91
23.90
O
O
N5*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


LRH-3-285-2-pure.10.fid
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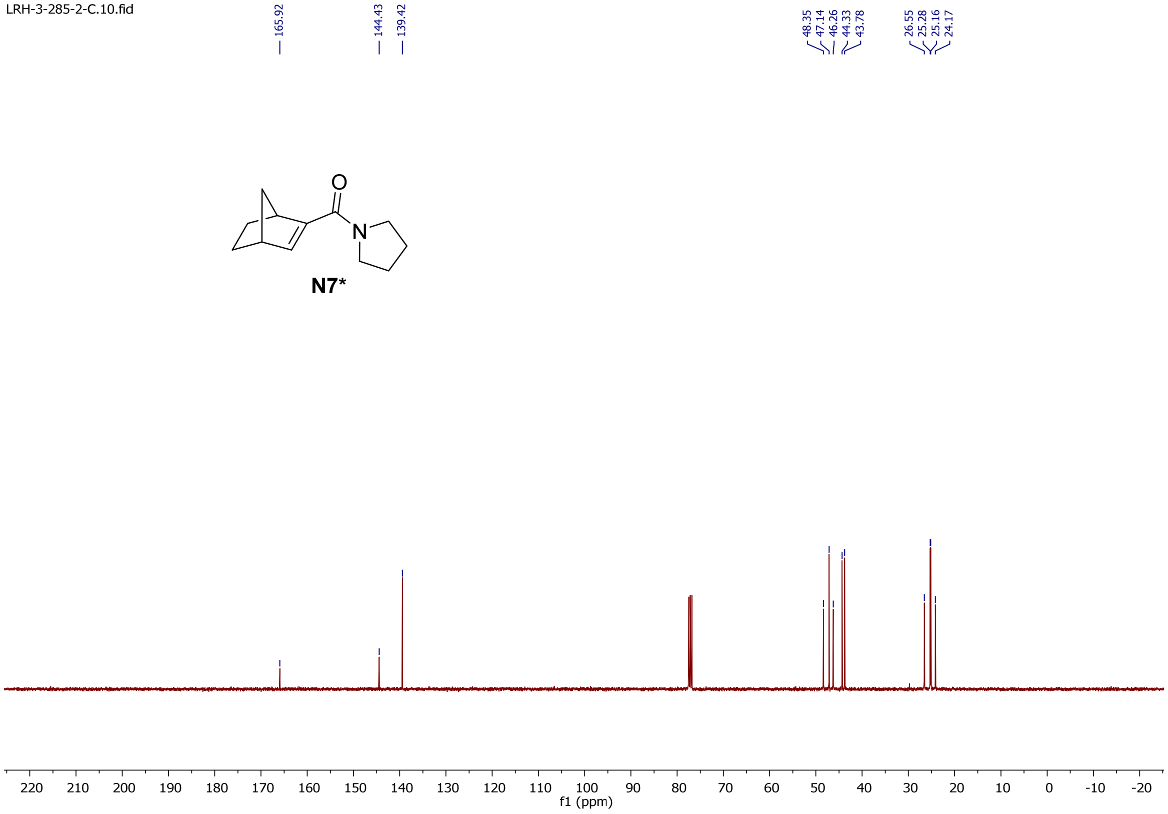
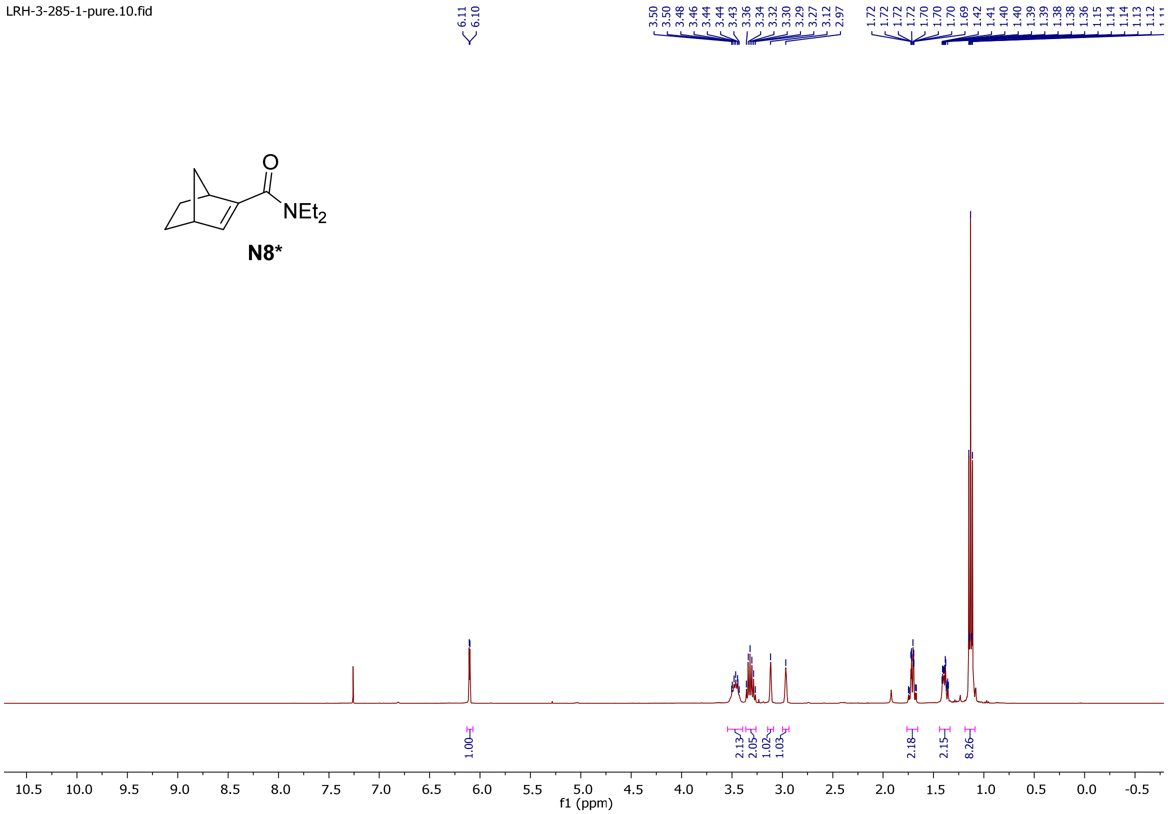
3.59
3.58
3.57
3.56
3.55
3.54
3.54
3.52
3.52
3.51
3.49
3.46
3.45
3.44
3.43
3.26
2.99
1.91
1.90
1.88
1.87
1.86
1.85
1.84
1.84
1.83
1.81
1.79
1.71
1.70
1.38
1.36
1.27
1.24
1.22
1.12
1.10
1.07
1.05
1.05
1.03
O
N
N7*
1.00
4.22
1.03
1.02
4.18
2.01
1.09
1.35
2.17
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


LRH-3-285-2-C.10.fid
165.92
144.43
139.42
48.35
47.14
46.26
44.33
43.78
26.55
25.28
25.16
24.17
O
N
N7*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


LRH-3-285-1-pure.10.fid
6.11
6.10
3.50
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3.48
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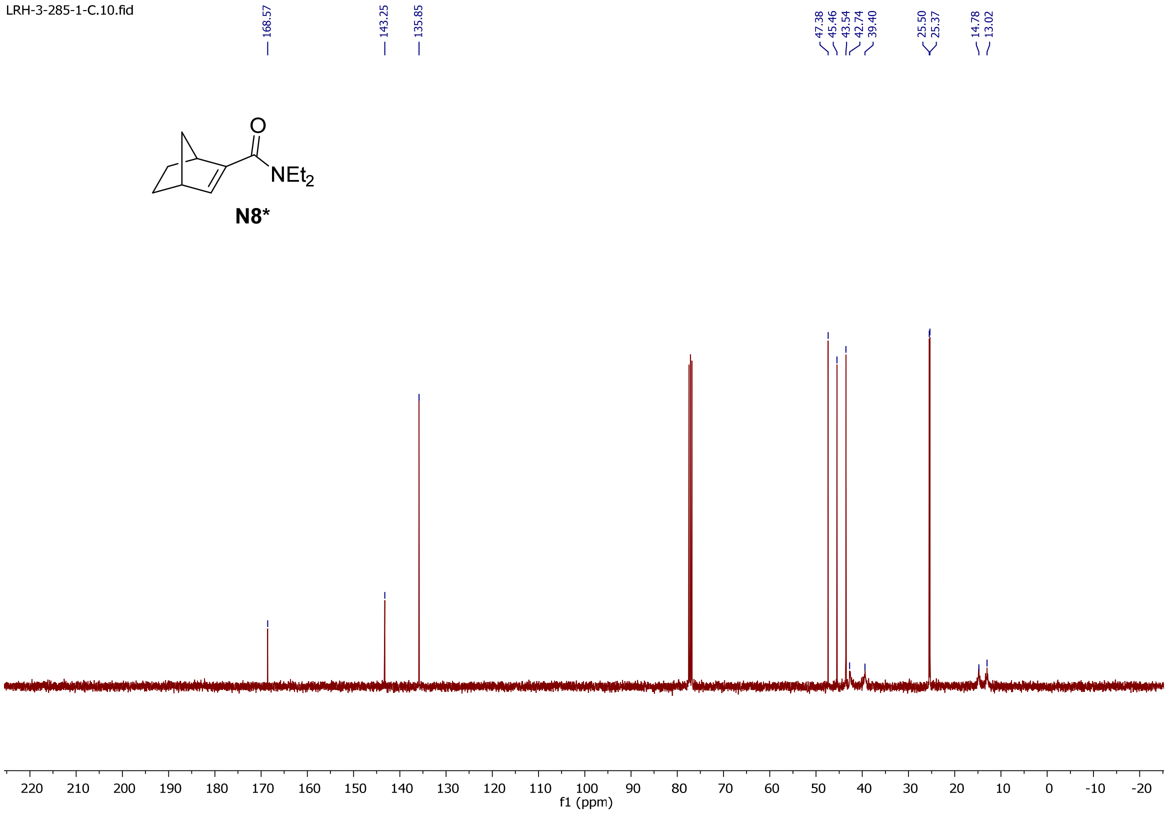
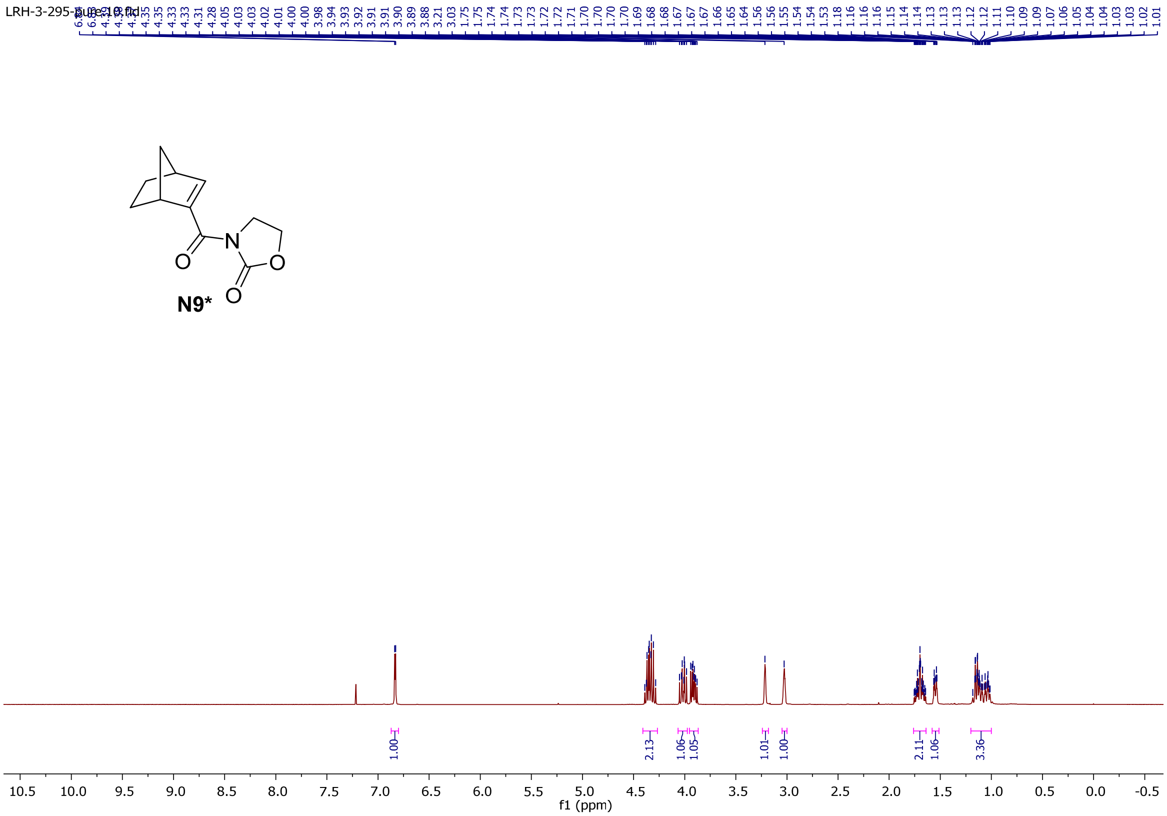
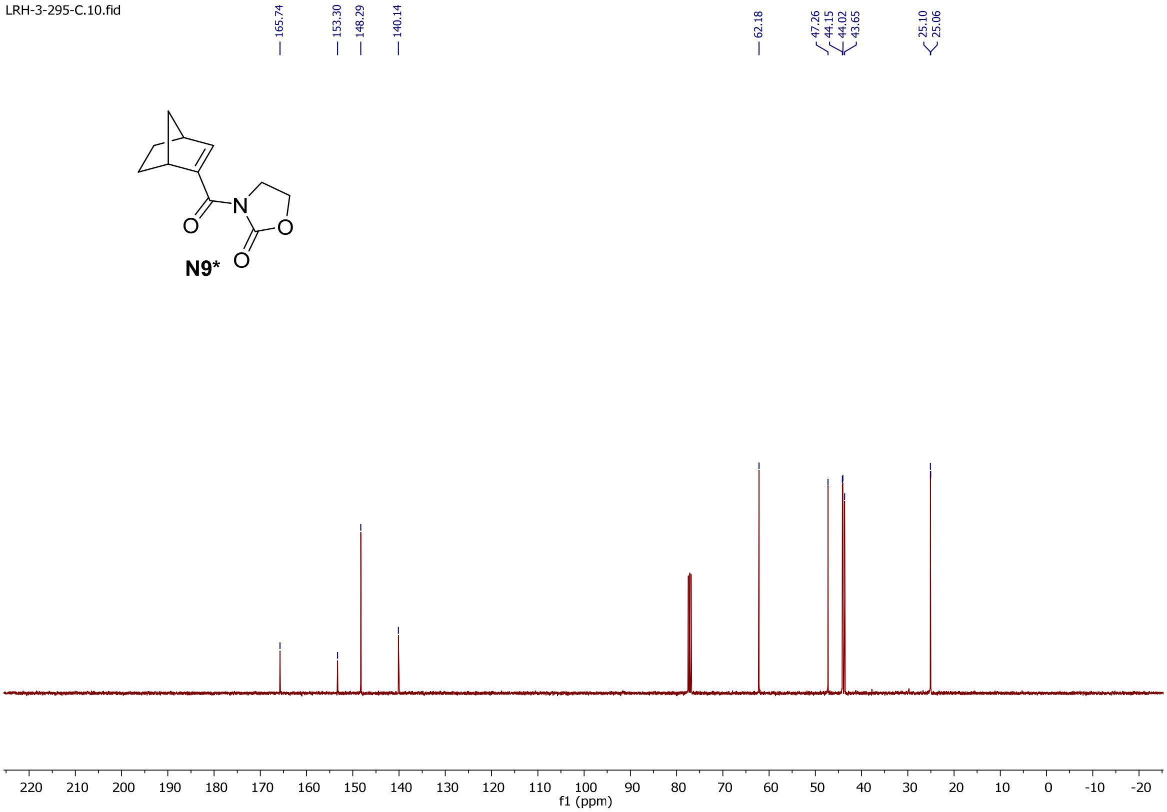
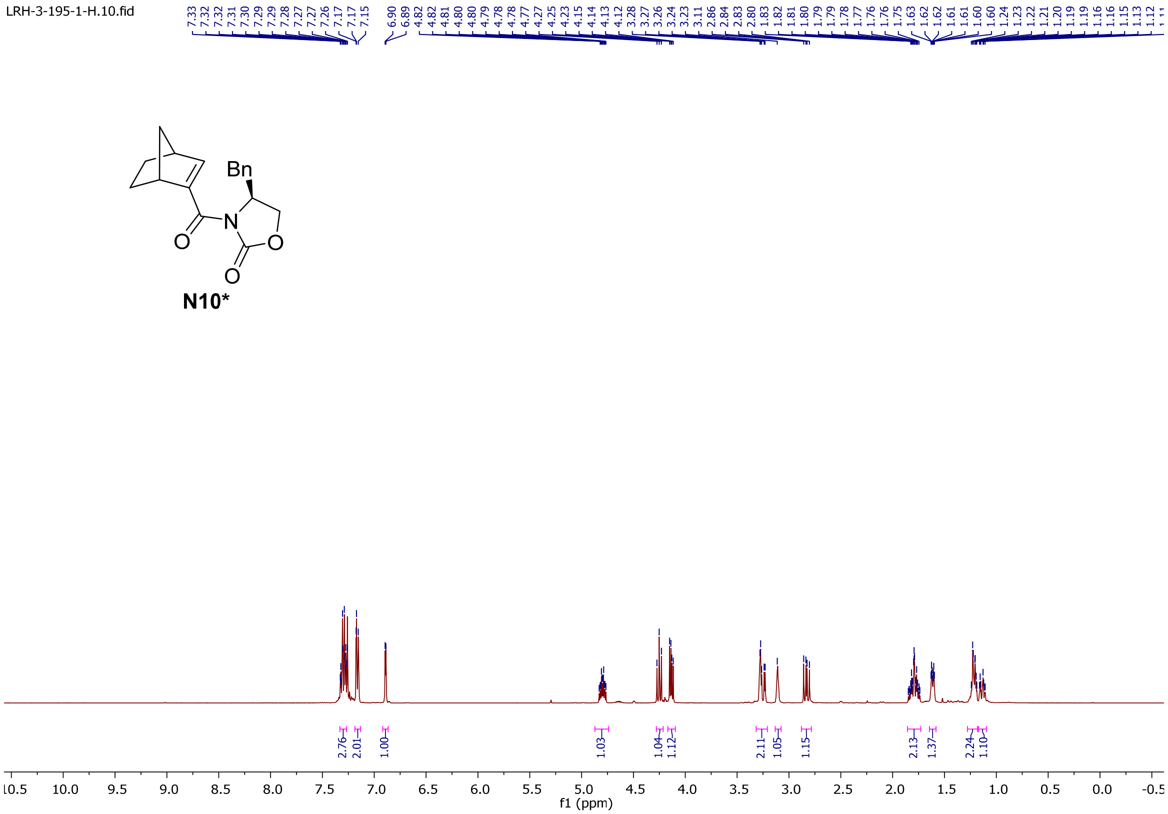
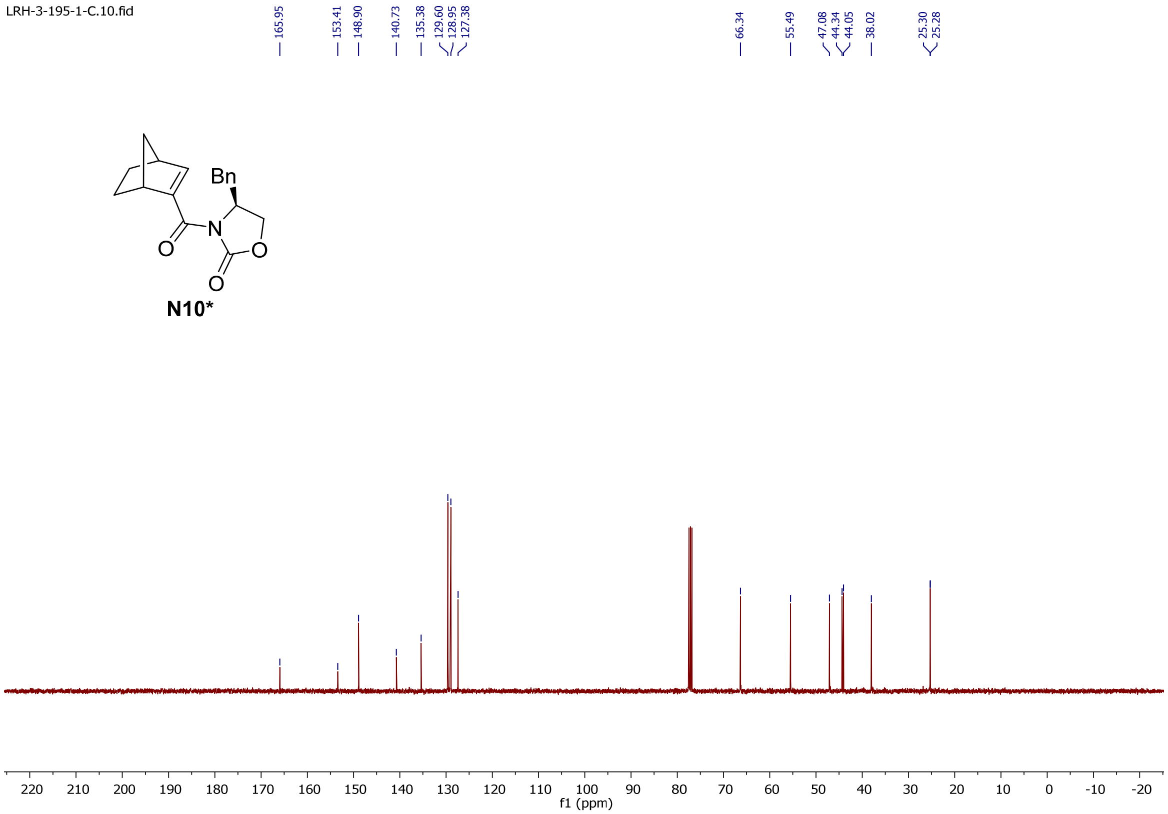
3.44
3.44
3.43
3.36
3.34
3.32
3.30
3.29
3.27
3.12
2.97
1.72
1.72
1.72
1.72
1.70
1.70
1.70
1.69
1.42
1.41
1.40
1.40
1.39
1.39
1.38
1.38
1.36
1.15
1.14
1.14
1.13
1.12
O
NEt2
N8*
1.00
2.13
2.05
1.02
1.03
2.18
2.15
8.26
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

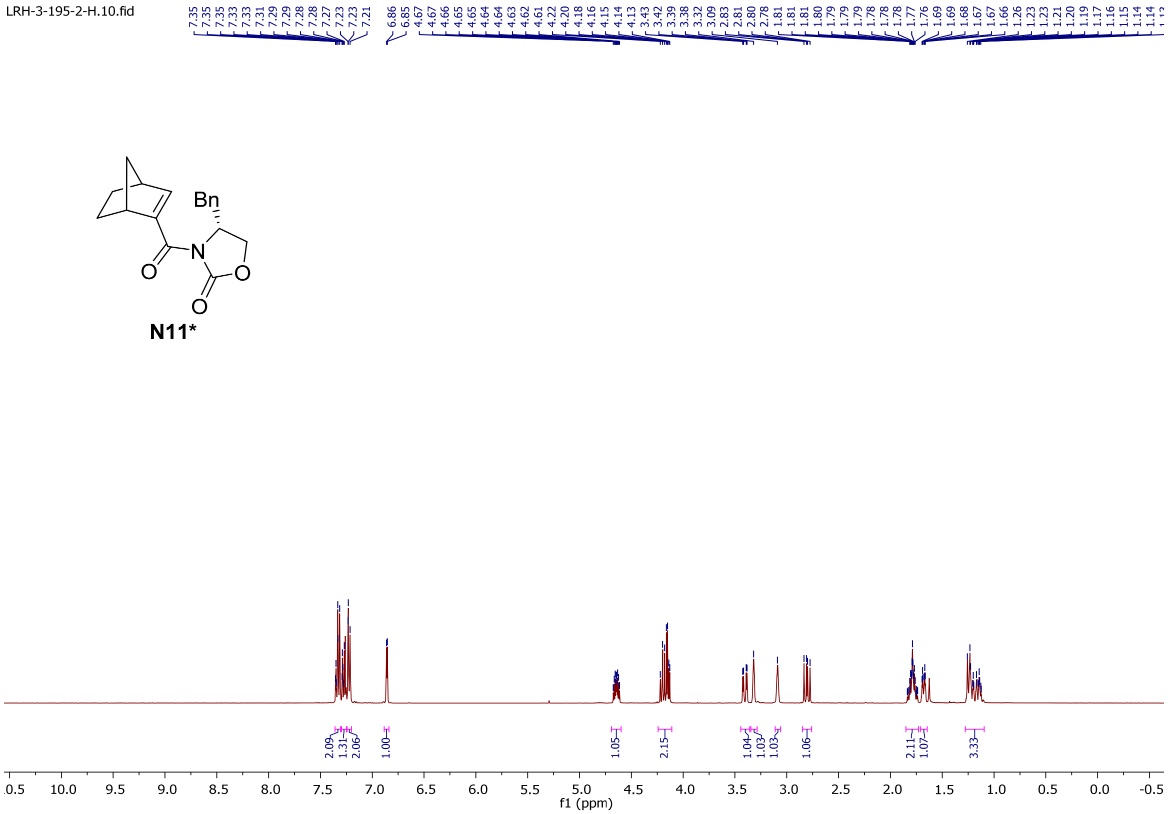

LRH-3-285-1-C.10.fid
168.57
143.25
135.85
47.38
45.46
43.54
42.74
39.40
25.50
25.37
14.78
13.02
O
NEt2
N8*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

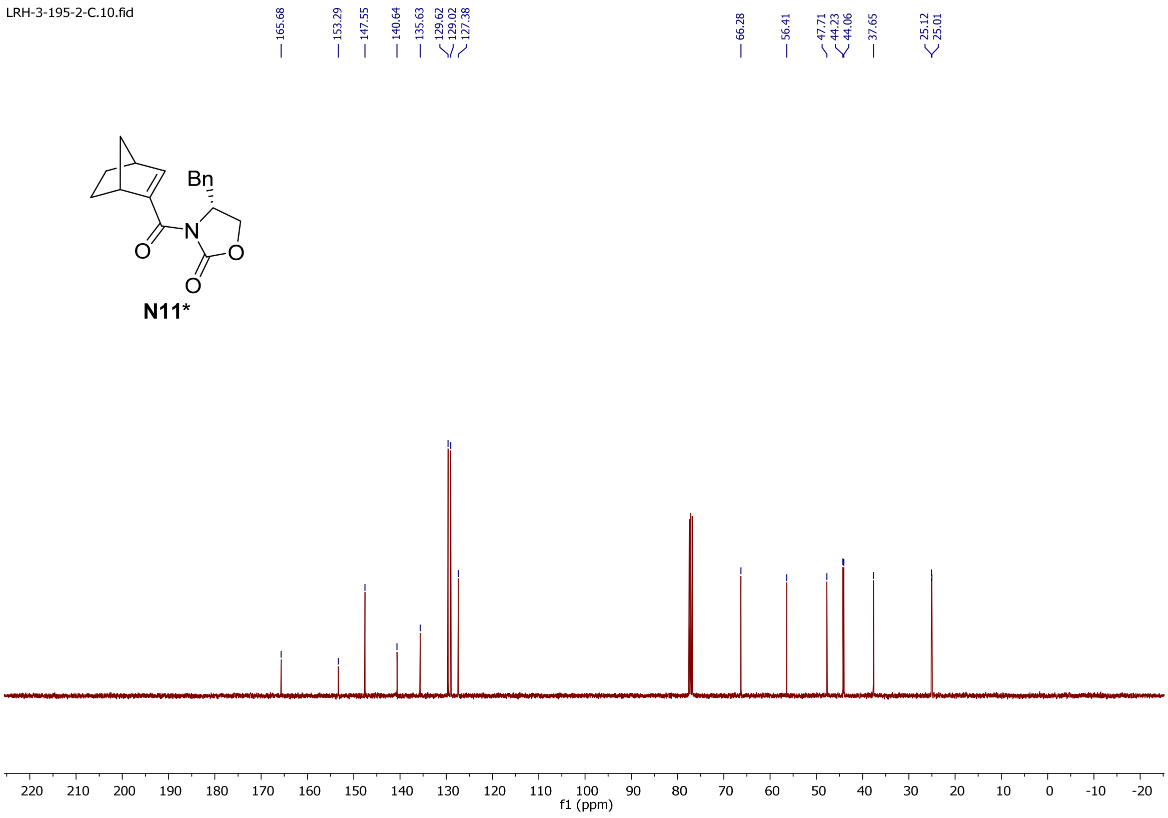

LRH-3-295-pure.10.fid
6.84
6.83
4.39
4.38
4.37
4.35
4.35
4.33
4.33
4.31
4.28
4.05
4.03
4.03
4.02
4.01
4.00
4.00
3.98
3.94
3.93
3.92
3.91
3.91
3.90
3.89
3.88
3.21
3.03
1.75
1.75
1.74
1.74
1.73
1.73
1.72
1.72
1.71
1.70
1.70
1.70
1.70
1.69
1.68
1.68
1.67
1.67
1.67
1.66
1.65
1.64
1.56
1.56
1.55
1.54
1.54
1.53
1.18
1.16
1.16
1.16
1.15
1.14
1.14
1.13
1.13
1.13
1.12
1.12
1.11
1.10
1.09
1.09
1.07
1.06
1.05
1.04
1.04
1.03
1.03
1.02
1.01
N
O
O
O
N9*
1.00
2.13
1.06
1.05
1.01
1.00
2.11
1.06
3.36
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


LRH-3-295-C.10.fid
165.74
153.30
148.29
140.14
62.18
47.26
44.15
44.02
43.65
25.10
25.06
N
O
O
O
N9*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


LRH-3-195-1-H.10.fid
7.33
7.32
7.32
7.31
7.30
7.29
7.29
7.28
7.27
7.27
7.26
7.17
7.17
7.15
6.90
6.89
4.82
4.81
4.80
4.80
4.79
4.78
4.78
4.77
4.27
4.25
4.23
4.15
4.14
4.13
4.12
3.28
3.27
3.26
3.24
3.23
3.11
2.86
2.84
2.83
2.80
1.83
1.82
1.81
1.80
1.79
1.79
1.78
1.77
1.76
1.75
1.63
1.62
1.62
1.61
1.61
1.60
1.60
1.24
1.23
1.22
1.21
1.20
1.19
1.19
1.16
1.15
1.13
1.12
Bn
N
O
O
O
N10*
2.76
2.01
1.00
1.03
1.04
1.12
2.11
1.05
1.15
2.13
1.37
2.24
1.10
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


LRH-3-195-1-C.10.fid
165.95
153.41
148.90
140.73
135.38
129.60
128.95
127.38
66.34
55.49
47.08
44.34
44.05
38.02
25.30
25.28
Bn
N
O
O
O
N10*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


LRH-3-195-2-H.10.fid
7.35 7.35 7.35 7.33 7.33 7.31 7.29 7.29 7.28 7.28 7.27 7.23 7.23 7.21 6.86 6.85 4.67 4.66 4.65 4.65 4.64 4.64 4.63 4.62 4.61 4.22 4.20 4.18 4.16 4.15 4.14 4.13 3.43 3.42 3.39 3.38 3.32 3.09 2.83 2.81 2.80 2.78 1.81 1.81 1.81 1.80 1.79 1.79 1.79 1.78 1.78 1.78 1.77 1.76 1.69 1.69 1.68 1.67 1.67 1.66 1.26 1.23 1.23 1.21 1.20 1.19 1.17 1.16 1.15 1.14 1.14
Bn
N
O
O
O
N11*
2.09 1.31 2.06 1.00 1.05 2.15 1.04 1.03 1.03 1.06 2.11 1.07 3.33
.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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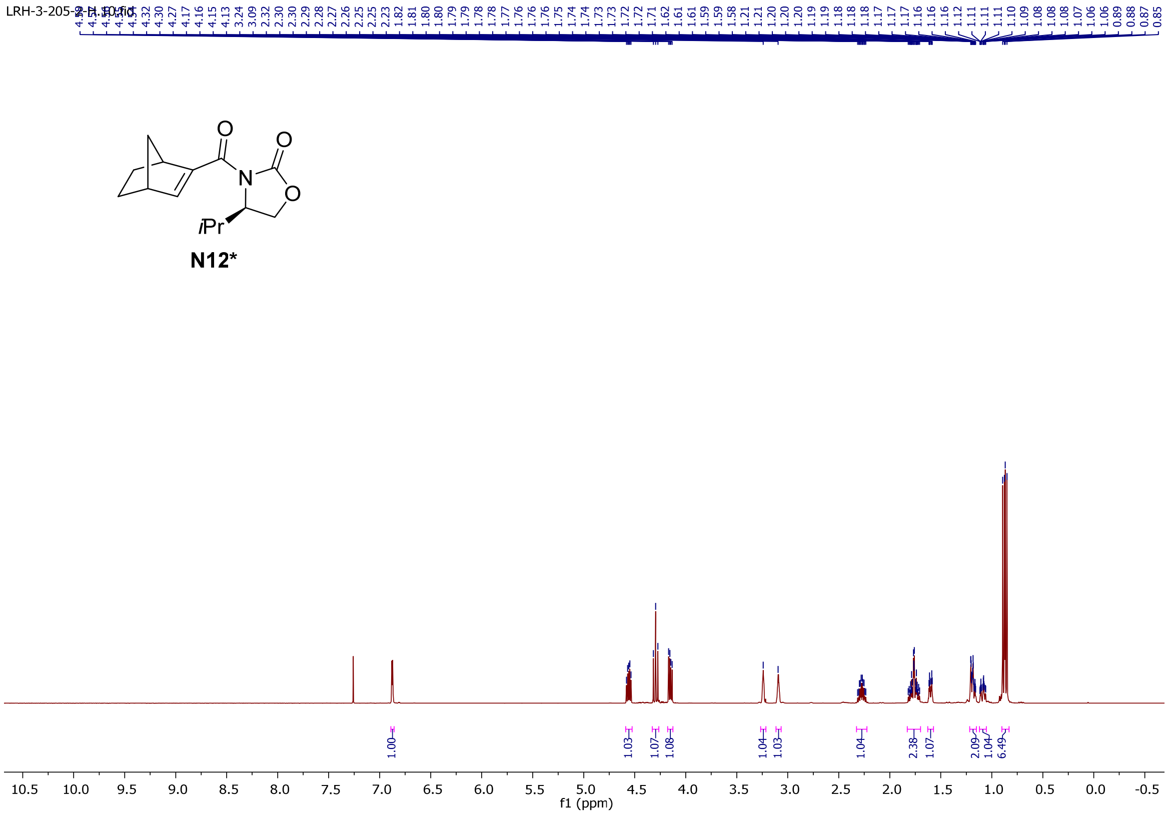
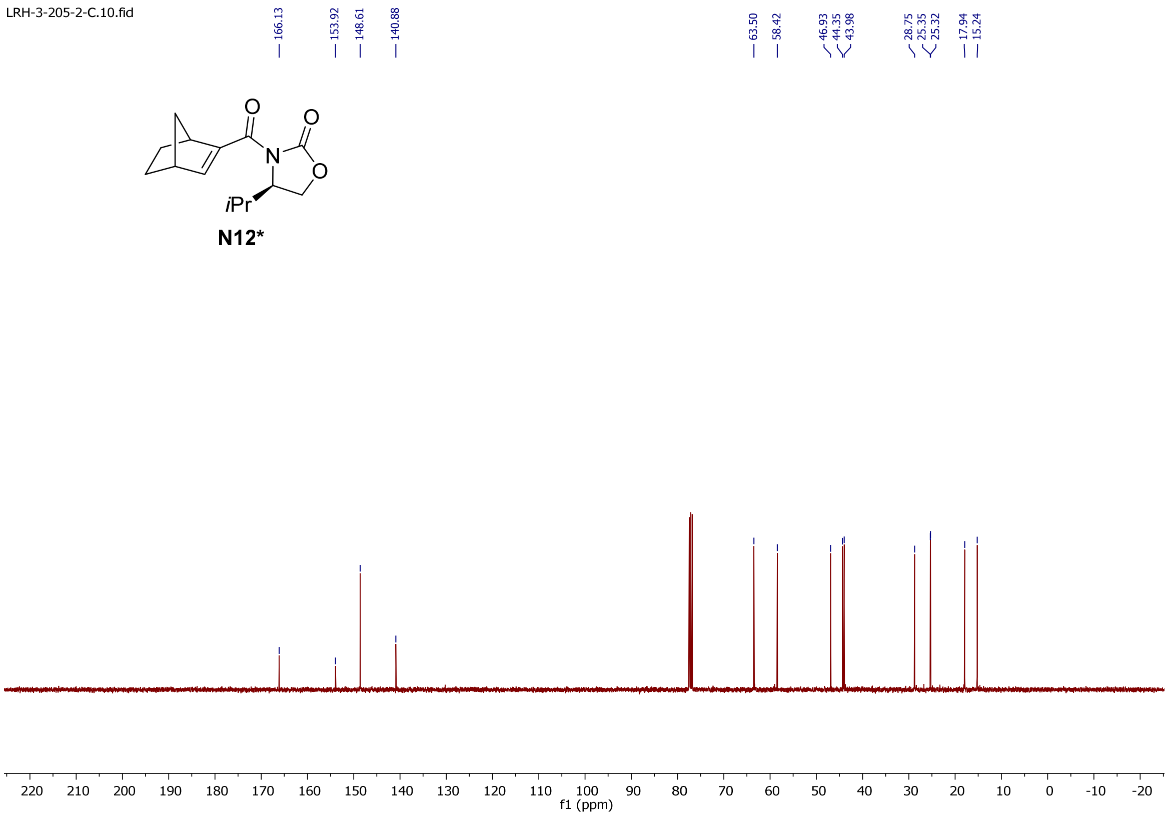
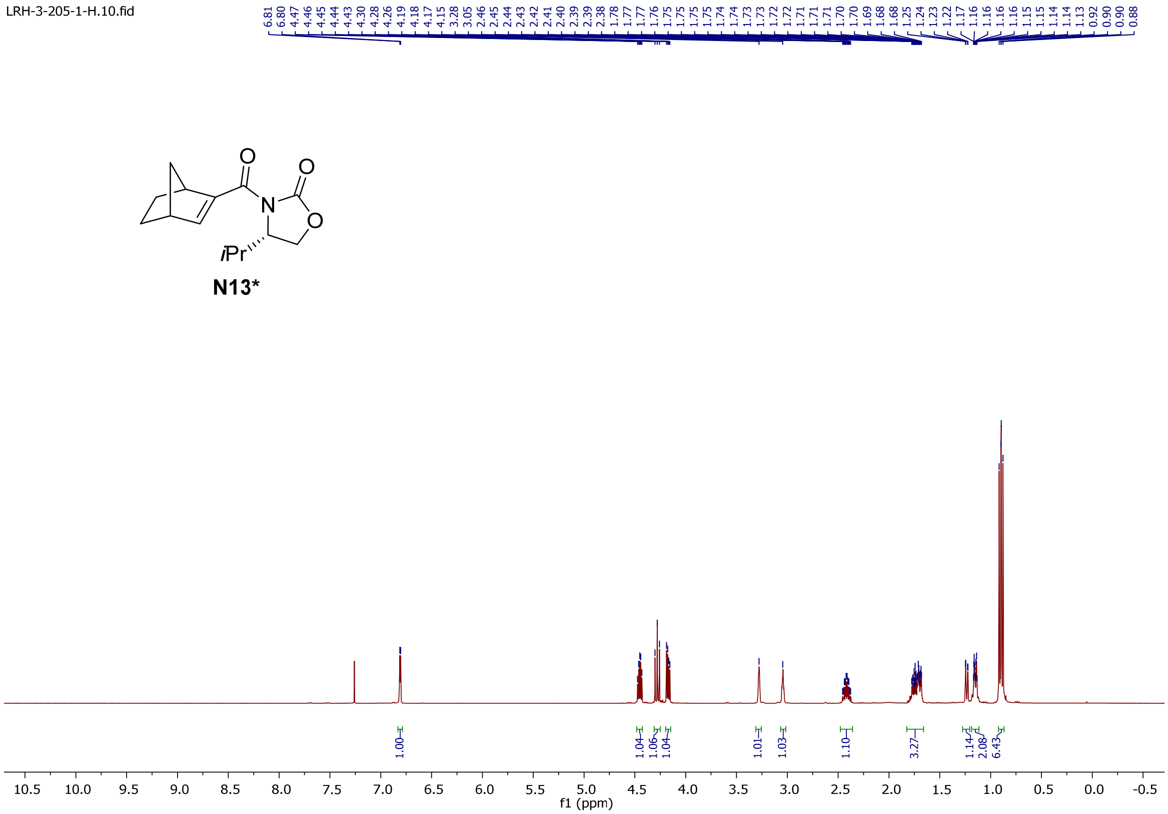
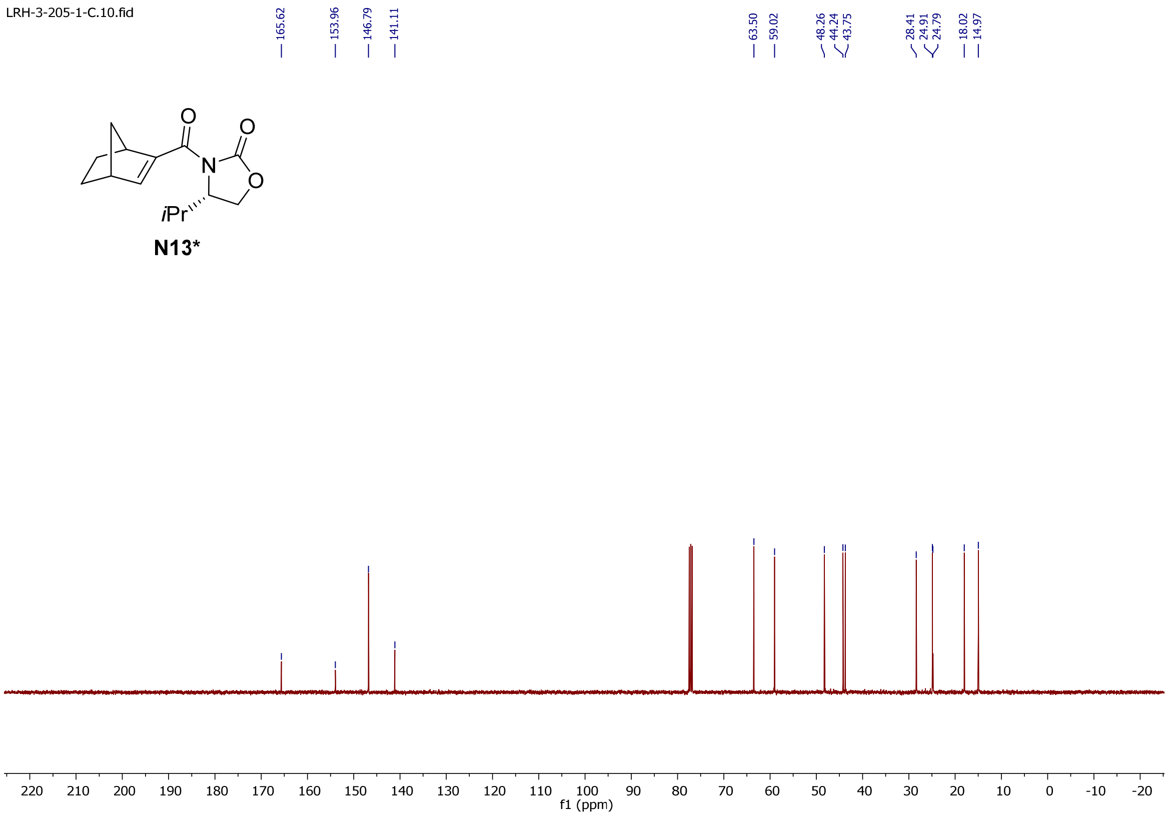
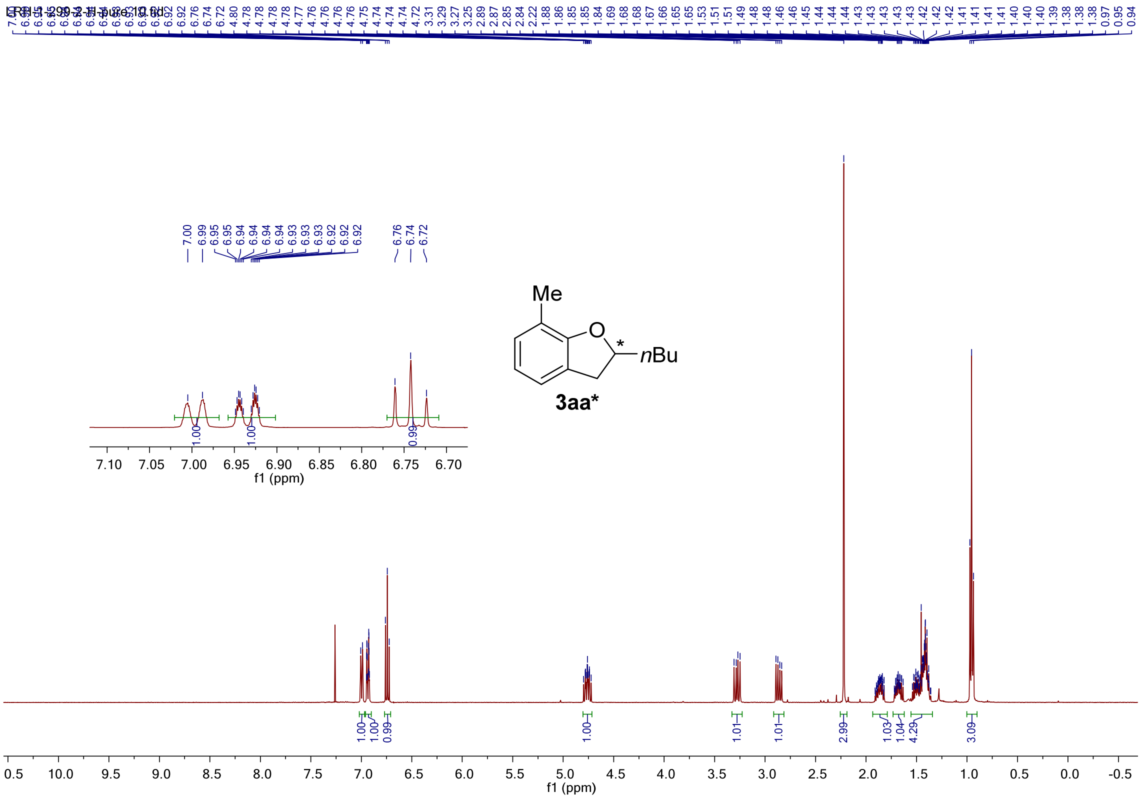
165.68 153.29 147.55 140.64 135.63 129.62 129.02 127.38 66.28 56.41 47.71 44.23 44.06 37.65 25.12 25.01
Bn
N
O
O
O
N11*
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

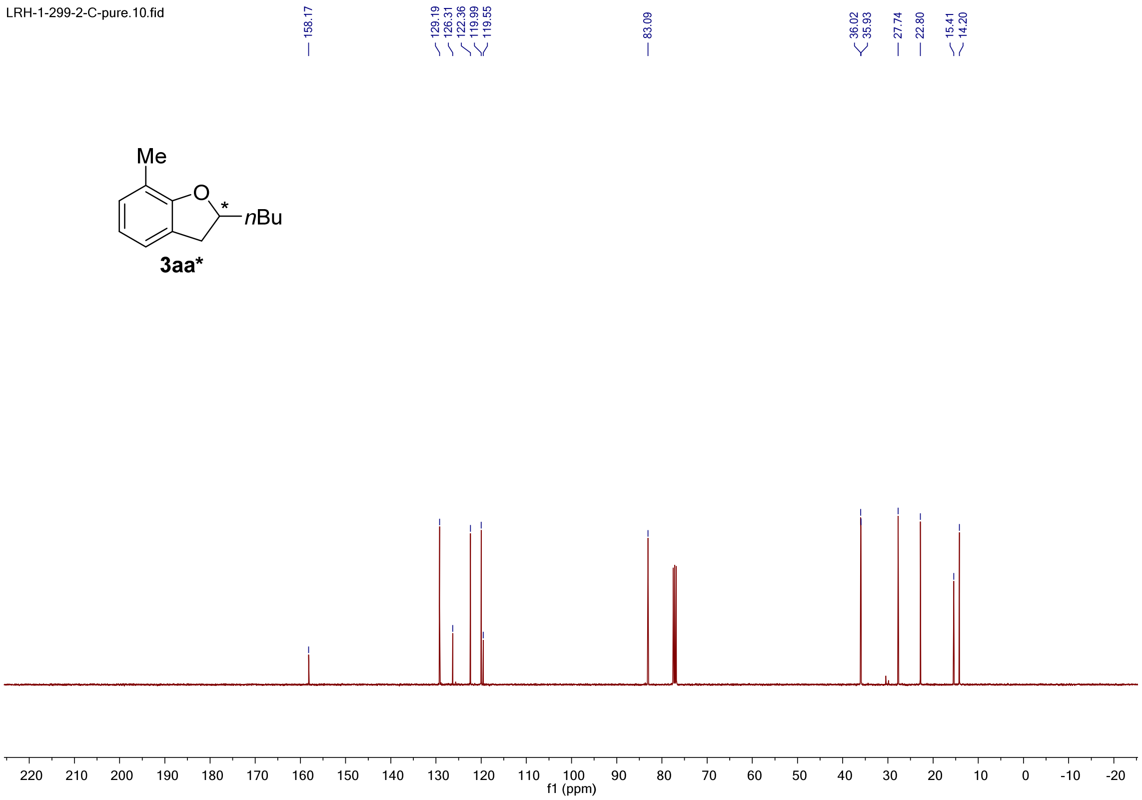

N12*
LRH-3-205-2-H.10.fid
4.32
4.30
4.27
4.17
4.16
4.15
4.13
3.24
3.09
2.32
2.30
2.30
2.29
2.28
2.27
2.26
2.25
2.25
2.23
1.82
1.81
1.80
1.80
1.79
1.79
1.78
1.78
1.77
1.76
1.76
1.76
1.75
1.74
1.74
1.73
1.73
1.72
1.72
1.71
1.62
1.61
1.61
1.59
1.59
1.58
1.21
1.21
1.20
1.20
1.20
1.19
1.19
1.18
1.18
1.18
1.17
1.17
1.17
1.16
1.16
1.16
1.12
1.11
1.11
1.11
1.10
1.09
1.08
1.08
1.08
1.07
1.06
1.06
0.89
0.88
0.87
0.85
O
O
N
O
iPr
1.00
1.03
1.07
1.08
1.04
1.03
1.04
2.38
1.07
2.09
1.04
6.49
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

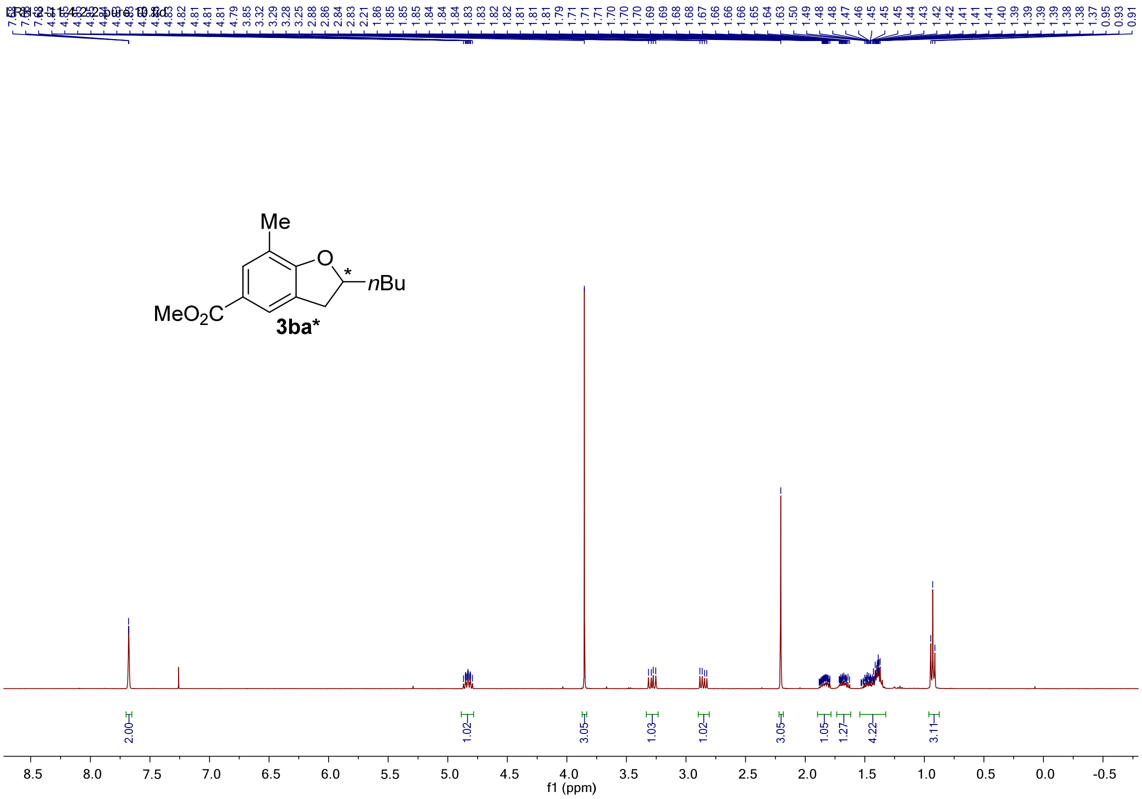

N12*
LRH-3-205-2-C.10.fid
166.13
153.92
148.61
140.88
63.50
58.42
46.93
44.35
43.98
28.75
25.35
25.32
17.94
15.24
O
O
N
O
iPr
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

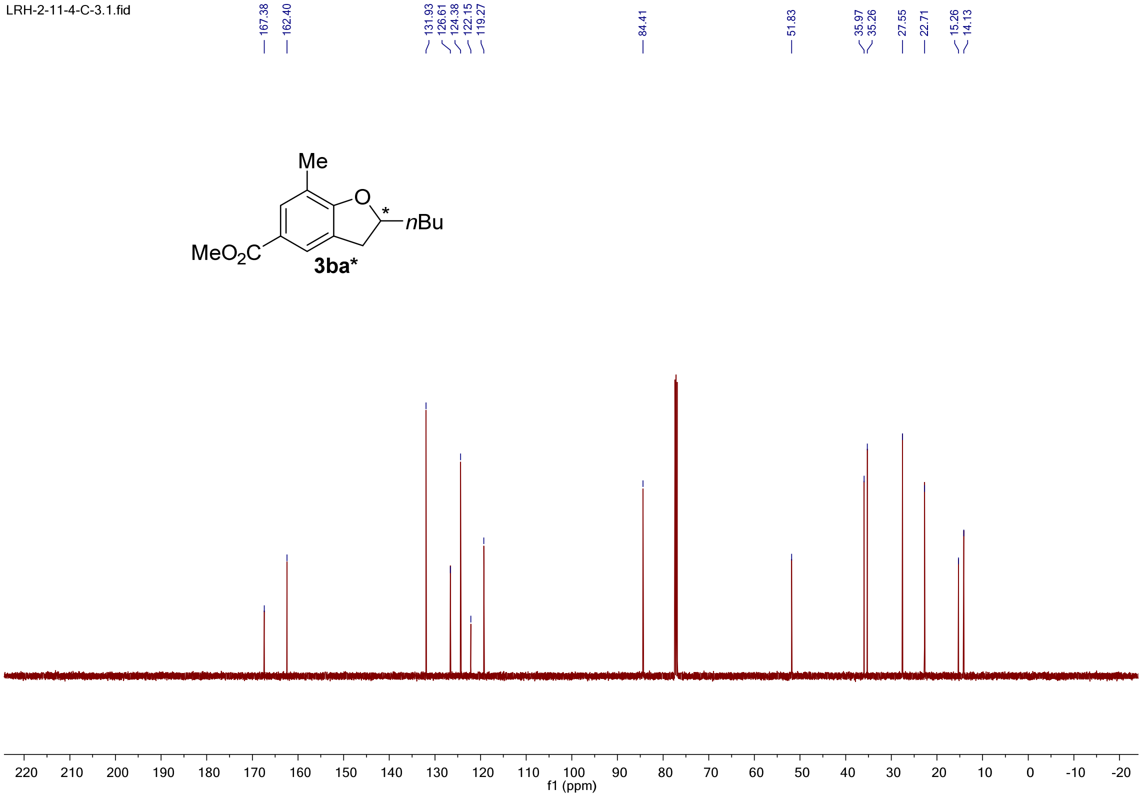

LRH-3-205-1-H.10.fid
6.81 6.80 4.47 4.46 4.45 4.44 4.43 4.30 4.28 4.26 4.19 4.18 4.17 4.15 3.28 3.05 2.46 2.45 2.44 2.43 2.42 2.41 2.40 2.39 2.39 2.38 1.78 1.77 1.77 1.76 1.75 1.75 1.75 1.74 1.74 1.73 1.73 1.72 1.72 1.71 1.71 1.71 1.70 1.70 1.69 1.68 1.68 1.25 1.24 1.23 1.22 1.17 1.16 1.16 1.16 1.15 1.15 1.14 1.13 0.92 0.90 0.90 0.88
O
O
N
O
iPr
N13*
1.00
1.04
1.06
1.04
1.01
1.03
1.10
3.27
1.14
2.08
6.43
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

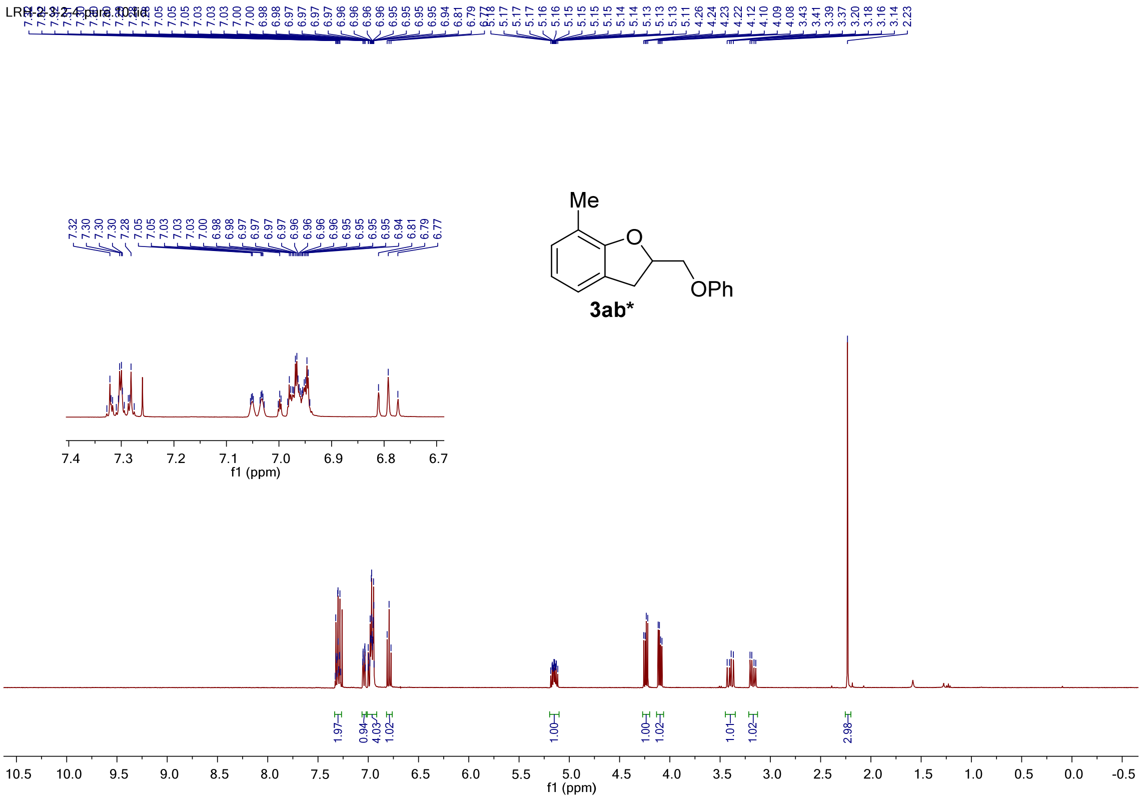

LRH-3-205-1-C.10.fid
165.62
153.96
146.79
141.11
63.50
59.02
48.26
44.24
43.75
28.41
24.91
24.79
18.02
14.97
O
O
N
O
iPr
N13*
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

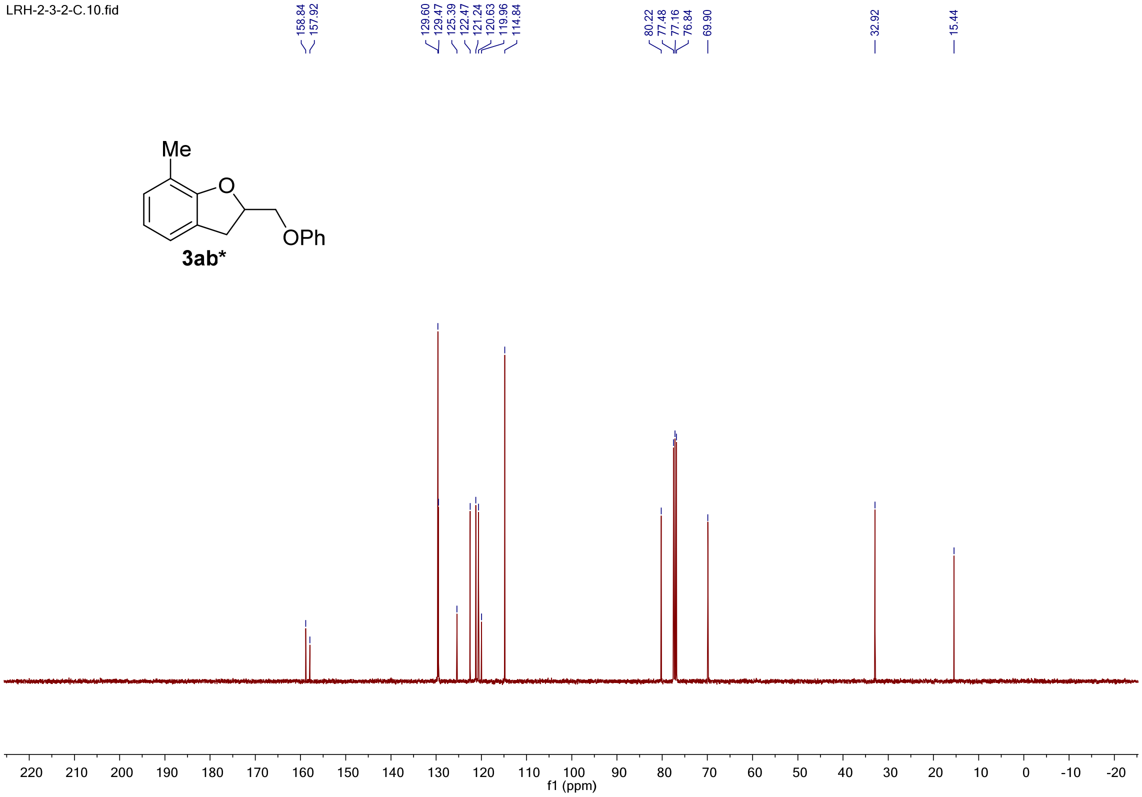

LRH-1-299-2-H-pure.10.fid
7.00 6.99 6.95 6.94 6.94 6.94 6.94 6.93 6.93 6.93 6.92 6.92 6.92 6.76 6.74 6.72 4.80 4.78 4.78 4.78 4.78 4.77 4.76 4.76 4.76 4.76 4.75 4.74 4.74 4.72 3.31 3.29 3.27 3.25 2.89 2.87 2.85 2.84 2.22 1.88 1.86 1.85 1.85 1.84 1.69 1.68 1.67 1.66 1.65 1.65 1.53 1.51 1.49 1.48 1.48 1.46 1.46 1.45 1.44 1.44 1.44 1.43 1.43 1.43 1.43 1.42 1.42 1.42 1.41 1.41 1.41 1.40 1.40 1.40 1.39 1.38 1.38 1.38 0.97 0.95 0.94
7.00 6.99 6.95 6.94 6.94 6.94 6.94 6.93 6.93 6.93 6.92 6.92 6.92
6.76 6.74 6.72
1.00 1.00 0.99
7.10 7.05 7.00 6.95 6.90 6.85 6.80 6.75 6.70
f1 (ppm)
Me
O
*
nBu
3aa*
1.00 1.00 0.99 1.00 1.01 1.01 2.99 1.03 1.04 4.29 3.09
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

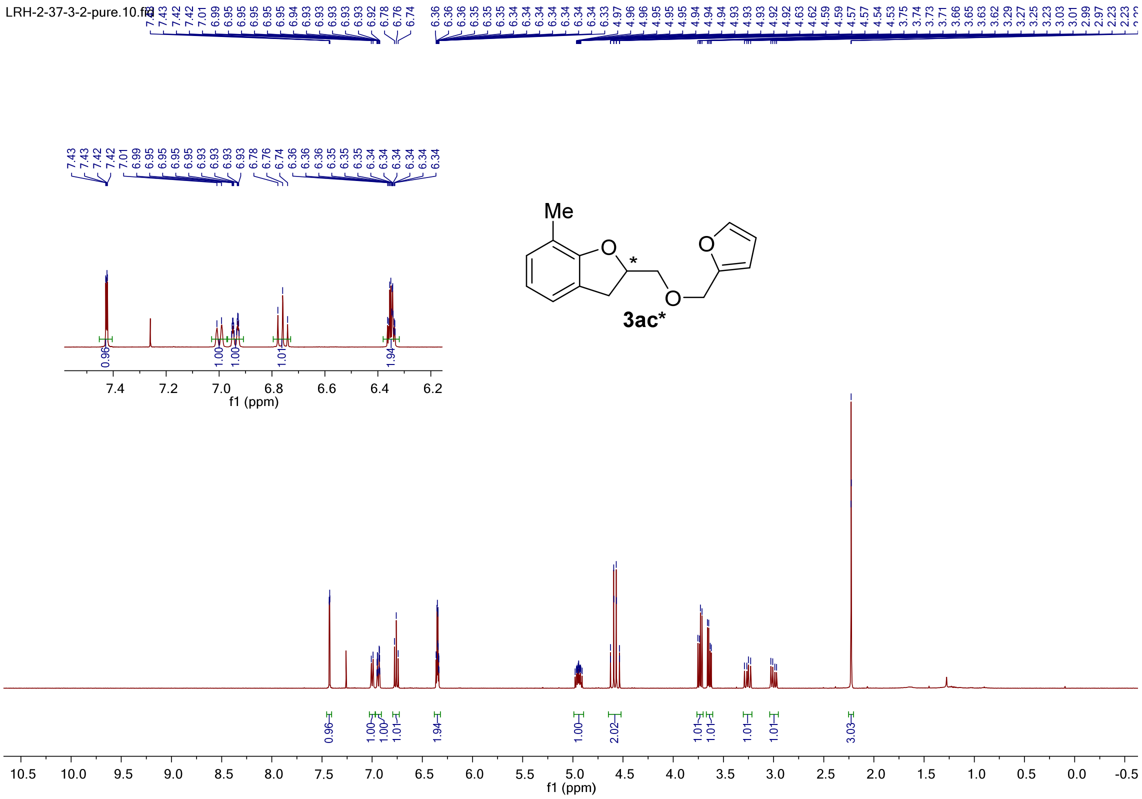

LRH-1-299-2-C-pure.10.fid
158.17
129.19 126.31 122.36 119.99 119.55
83.09
36.02 35.93
27.74
22.80
15.41 14.20
Me
O
*
nBu
3aa*
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


LRH-2-11-4-2-2-pure.10.fid
7.68 7.68 7.68 4.87 4.85 4.85 4.84 4.83 4.83 4.83 4.83 4.83 4.82 4.81 4.81 4.81 4.79 3.85 3.32 3.29 3.28 3.25 2.88 2.86 2.84 2.83 2.21 1.86 1.85 1.85 1.85 1.84 1.84 1.84 1.83 1.83 1.82 1.82 1.81 1.81 1.81 1.79 1.71 1.71 1.71 1.70 1.70 1.69 1.69 1.68 1.68 1.67 1.66 1.66 1.66 1.65 1.64 1.63 1.50 1.49 1.48 1.48 1.47 1.46 1.45 1.45 1.45 1.44 1.43 1.42 1.42 1.41 1.41 1.41 1.40 1.39 1.39 1.39 1.39 1.38 1.38 1.37 0.95 0.93 0.91
Me
O
*
nBu
MeO2C
3ba*
2.00
1.02
3.05
1.03
1.02
3.05
1.05
1.27
4.22
3.11
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


LRH-2-11-4-C-3.1.fid
167.38 162.40 131.93 126.61 124.38 122.15 119.27 84.41 51.83 35.97 35.26 27.55 22.71 15.26 14.13
Me
O
*
nBu
MeO2C
3ba*
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


LRH-2-3-2-4-pure.10.fid
7.05 7.05 7.05 7.03 7.03 7.03 7.00 7.00 6.98 6.98 6.97 6.97 6.97 6.97 6.96 6.96 6.96 6.96 6.95 6.95 6.95 6.95 6.94 6.81 6.79 6.77 5.18 5.17 5.17 5.17 5.16 5.16 5.15 5.15 5.15 5.15 5.14 5.14 5.13 5.13 5.13 5.11 4.26 4.24 4.23 4.22 4.12 4.10 4.09 4.08 3.43 3.41 3.39 3.37 3.20 3.18 3.16 3.14 2.23
7.32 7.30 7.30 7.30 7.28 7.05 7.05 7.03 7.03 7.03 7.00 6.98 6.98 6.97 6.97 6.97 6.96 6.96 6.96 6.96 6.95 6.95 6.95 6.95 6.94 6.81 6.79 6.77
Me
O
OPh
3ab*
7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
1.97 0.94 4.03 1.02 1.00 1.00 1.02 1.01 1.02 2.98
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


LRH-2-3-2-C.10.fid
158.84 157.92 129.60 129.47 125.39 122.47 121.24 120.63 119.96 114.84 80.22 77.48 77.16 76.84 69.90 32.92 15.44
Me
O
OPh
3ab*
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


LRH-2-37-3-2-pure.10.fid
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7.42
7.42
7.01
6.99
6.95
6.95
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6.95
6.94
6.93
6.93
6.93
6.93
6.92
6.78
6.76
6.74
6.36
6.36
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6.35
6.35
6.34
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4.96
4.95
4.95
4.95
4.94
4.94
4.94
4.93
4.93
4.93
4.92
4.92
4.63
4.62
4.59
4.59
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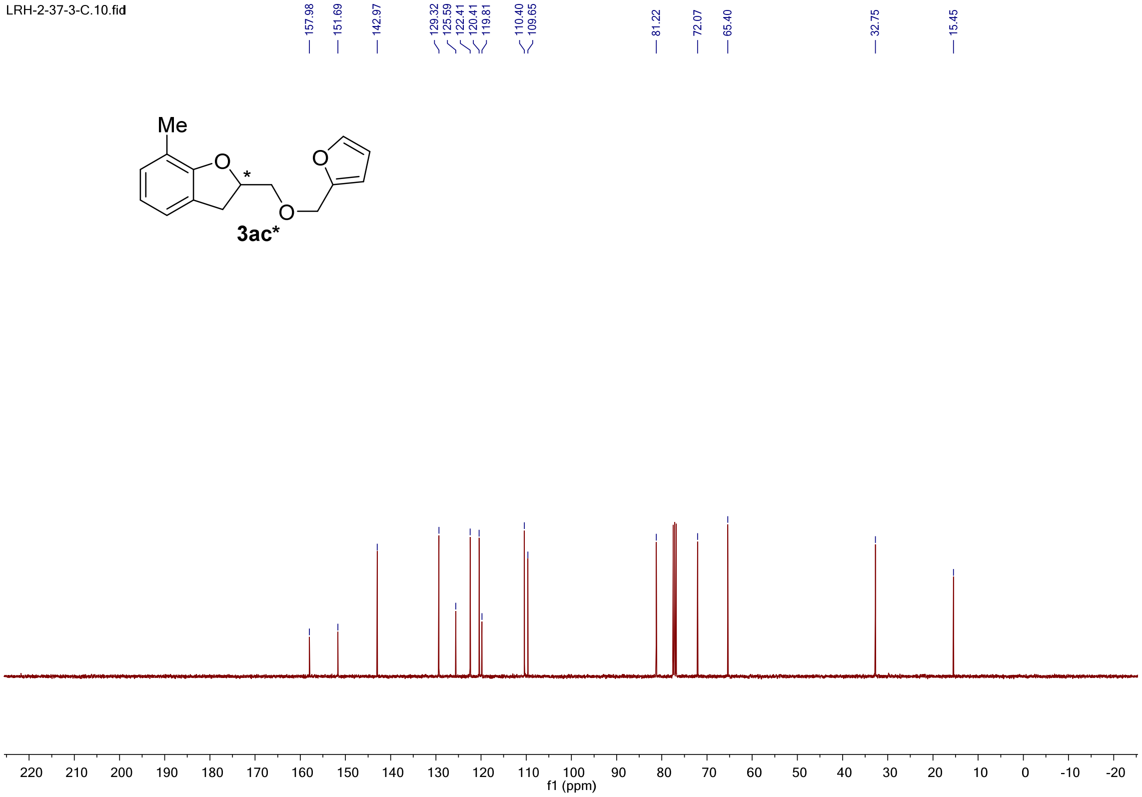
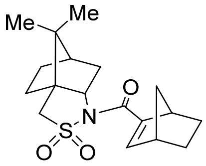
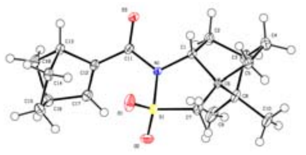
4.57
4.54
4.53
3.75
3.74
3.73
3.71
3.66
3.65
3.63
3.62
3.29
3.27
3.25
3.23
3.03
3.01
2.99
2.97
2.23
2.23
0.96
1.00
1.00
1.01
1.94
7.4
7.2
7.0
6.8
6.6
6.4
6.2
f1 (ppm)
Me
O
*
O
O
3ac*
0.96
1.00
1.00
1.01
1.94
1.00
2.02
1.01
1.01
1.01
1.01
3.03
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

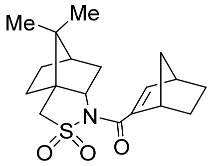

LRH-2-37-3-C.10.fid
157.98
151.69
142.97
129.32
125.59
122.41
120.41
119.81
110.40
109.65
81.22
72.07
65.40
32.75
15.45
Me
O
*
O
O
3ac*
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

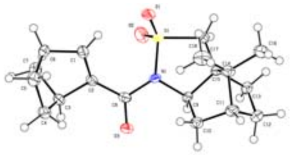
4. Crystallographic Data





Empirical formula	$C_{18}H_{25}NO_3S$	
Formula weight	335.45	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.8259(6) Å	α= 90°.
	b = 9.5135(8) Å	β= 90°.
	c = 22.6470(18) Å	γ = 90°.
Volume	1686.1(2) $Å^3$	
Z	4	
Density (calculated)	1.321 Mg/m^3	
Absorption coefficient	0.207 mm^{-1}	
F(000)	720	
Crystal size	0.510 x 0.380 x 0.320 mm^3	
Theta range for data collection	2.754 to 30.819°.	
Index ranges	-11<=h<=11, -13<=k<=13, -32<=l<=32	
Reflections collected	60626	
Independent reflections	5259 [R(int) = 0.0409]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.912	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5259 / 0 / 214	
Goodness-of-fit on F^2	1.044	
Final R indices [I>2sigma(I)]	R1 = 0.0304, wR2 = 0.0758	
R indices (all data)	R1 = 0.0350, wR2 = 0.0771	
Absolute structure parameter	0.039(12)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.295 and -0.406 e.$Å^{-3}$	





Identification code	LRH 2-21-2
Empirical formula	$C_{18}H_{25}NO_3S$
Formula weight	335.45
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.9608(8)
b/Å	9.0050(9)
c/Å	11.9856(12)
α/°	90
β/°	105.827(2)
γ/°	90
Volume/Å^3	826.64(14)
Z	2
ρ_{calc}g/cm^3	1.348
μ/mm^{-1}	0.211
F(000)	360.0
Crystal size/mm^3	0.1 × 0.06 × 0.05
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.318 to 54.998
Index ranges	$-10 \le h \le 10$, $-11 \le k \le 11$, $-15 \le l \le 14$
Reflections collected	12941
Independent reflections	3792 [R_{int} = 0.0422, R_{sigma} = 0.0432]
Data/restraints/parameters	3792/1/210
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0393, wR_2 = 0.0827
Final R indexes [all data]	R_1 = 0.0478, wR_2 = 0.0864
Largest diff. peak/hole / e Å^{-3}	0.30/-0.27
Flack parameter	0.02(3)

5. Reference

[1] M. Inai, T. Nishii, A. Tanaka, H. Kaku, M. Horikawa, T. Tsunoda, *Eur. J. Org. Chem.* **2011**, *2011*, 2719-2729.