

Iridium(III)-bis(imidazoliny)phenyl Catalysts for Enantioselective C–H Functionalization with
Ethyl Diazoacetate

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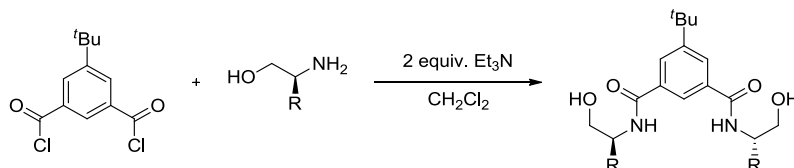
I. General Considerations

^1H and ^{13}C NMR spectra were recorded on a Varian Inova 600 spectrometer (600 MHz ^1H , 150 MHz ^{13}C) and a Varian Inova 400 spectrometer (400 MHz ^1H , 100 MHz ^{13}C) at room temperature in CDCl_3 (neutralized and dried with anhydrous K_2CO_3) with internal CHCl_3 as the reference (7.27 ppm for ^1H and 77.23 ppm for ^{13}C) or $(\text{CD}_3)_2\text{SO}$ with internal $(\text{CH}_3)_2\text{SO}$ as the reference (2.50 ppm for ^1H and 39.51 ppm for ^{13}C). Chemical shifts (δ values) were reported in parts per million (ppm) and coupling constants (J values) in Hz. Multiplicity is indicated using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, m = multiplet, br = broad signal.). Infrared (IR) spectra were recorded using Thermo Electron Corporation Nicolet 380 FT-IR spectrometer. High-resolution mass spectra were obtained using a Thermo Electron Corporation Finigan LTQFTMS (at the Mass Spectrometry Facility, Emory University). X-ray diffraction studies were carried out in the X-ray Crystallography Laboratory at Emory University on a Bruker Smart 1000 CCD diffractometer. Gas chromatography (GC) was carried out on an Agilent 6850 Network GC System equipped with a CHIRASIL-DEX CB column. High performance liquid chromatography (HPLC) was carried out on an Agilent 1100 Series equipped with Chirasil Chiralpak OJ-H and OD-H columns and a variable wavelength detector. We acknowledge the use of shared instrumentation provided by grants from the NIH and the NSF. Analytical thin layer chromatography (TLC) was performed on precoated glass backed EMD 0.25 mm silica gel 60 plates. Visualization was accomplished with UV light or ethanolic anisaldehyde, followed by heating. Flash column chromatography was carried out using Silicycle® silica gel 60 (40-63 μm).

All reactions were conducted with anhydrous solvents in oven-dried and nitrogen-charged glassware. Anhydrous solvents were purified by passage through activated alumina using a *Glass Contours* solvent purification system unless otherwise noted. PhCF_3 was dried over activated 4 Å molecular sieves and deoxygenated by bubbling through N_2 . Solvents for workup, extraction and column chromatography were used as received from commercial suppliers. All reagents used were purchased from commercial vendors and used as received unless otherwise noted. Phthalan was obtained from Alfa Aesar or Sigma Aldrich and distilled before use. Ethyl diazoacetate (EDA) was obtained from Sigma Aldrich containing 14 % (w/w %) dichloromethane and used without further purification. 4 Å powdered molecular sieves were activated by heating to 100 ° C under reduced pressure (0.2 torr) for 12 hours. Pyridine and Et_3N were purified by distillation from calcium hydride. $\text{IrCl}_3 \cdot 3\text{H}_2\text{O}$ and $\text{IrBr}_3 \cdot 4\text{H}_2\text{O}$ were purchased from Strem. Amino alcohols were purchased from Sigma Aldrich or Combi-Blocks. Full crystallographic data (CIF) is available as a separate file.

II. Procedures and Characterization Data

a) Catalyst Synthesis

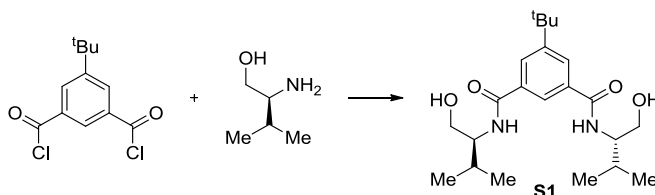


General Procedure A

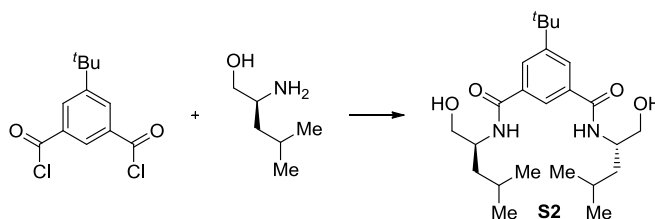
A procedure was adapted from the literature as follows:¹ A 0.5 M solution of 5-*tert*-butylisophthaloyl chloride (1.0 equiv.) in CH₂Cl₂ was added dropwise to a 0 °C mixture of amino alcohol (2.0 equiv.) and Et₃N (2.0 equiv.) in CH₂Cl₂ (0.29 M). The reaction mixture was warmed to ambient temperature and stirred approximately 20 h. Water was added (5 mL/1 mmol acyl chloride), and the mixture was stirred for 10 minutes. The phases were separated and the organic phase was dried over Na₂SO₄ and concentrated *in vacuo*. The resulting solid was purified as indicated to give the title amide.

General Procedure B

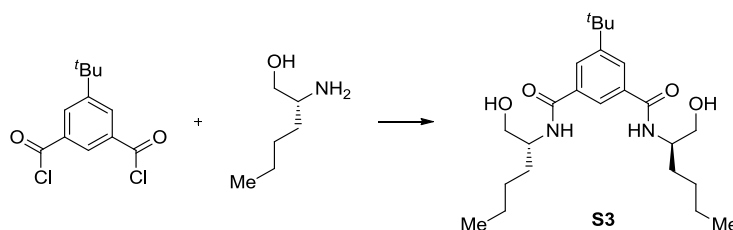
A procedure was adapted from the literature as follows:² A round bottom flask was charged with amino alcohol or amino alcohol·TFA salt (2.0 equiv) in isopropyl acetate (0.13 M in acyl chloride). The mixture was heated to 65 °C with vigorous stirring, and aqueous 1.5 M KHCO₃ (10 equiv.) was added. 5-*tert*-Butyl isophthaloyl dichloride (1.0 equiv) was added as a solid in three equal portions over the course of 30 minutes, and the mixture was aged at 65 °C for 12 h. The mixture was cooled to room temperature and poured into a separatory funnel. The phases were separated, and the aqueous phase was extracted with isopropyl acetate (3 x). The organics were combined, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting solid was purified as indicated to give the title amide.



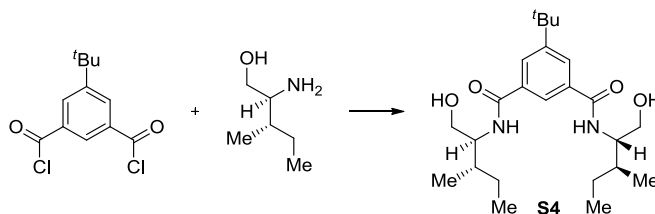
5-(*tert*-butyl)-N1,N3-bis((*S*)-1-hydroxy-3-methylbutan-2-yl)isophthalamide (S1). Prepared by general procedure A using 5-*tert*-butylisophthaloyl chloride (518 mg, 2.0 mmol) in CH₂Cl₂ (4 mL), L-valinol (413 mg, 4.0 mmol), and Et₃N (0.55 mL, 4.0 mmol) in CH₂Cl₂ (7 mL). Recrystallization from boiling Et₂O/CH₂Cl₂ afforded the title amide as a white flaky solid (582 mg, 74 %); **mp** 132-134 ° C; **IR** (thin film, cm⁻¹) 3303, 2963, 1636, 1537, 1214, 749; **¹H NMR** (400 MHz, CDCl₃) δ 7.84 (s, 1H), 7.72 (s, 2H), 7.18 (d, *J* = 9.8 Hz, 2H), 3.93 (dd, *J* = 9.2, 5.2 Hz, 2H), 3.84 (dd, *J* = 11.6, 3.1 Hz, 2H), 3.75 (dd, *J* = 7.3, 11.3 Hz, 2H), 1.94 (dq, *J* = 13.7, 6.8 Hz, 2H), 1.19 (s, 9H), 0.96 (t, *J* = 6.6 Hz, 12H); **¹³C NMR** (100 MHz, CDCl₃) δ 168.9, 152.1, 134.8, 127.5, 63.3, 58.0, 35.0, 31.3, 29.7, 19.7, 19.5; **HRMS** [+APCI] calculated for C₂₂H₃₇N₂O₄ 393.2748, found 393.2743 [M+H]⁺; [α]_D²⁰ -47.5 ° (*c* 1.0, CHCl₃).



5-(*tert*-butyl)-N1,N3-bis((*S*)-1-hydroxy-4-methylpentan-2-yl)isophthalamide (S2). Prepared by general procedure **A** using 5-*tert*-butylisophthaloyl chloride (1.04 g, 4.0 mmol) in CH₂Cl₂ (8 mL), (*S*)-leucinol (943 mg, 1.03 mL, 8.0 mmol), and Et₃N (1.16 mL, 8.0 mmol) in CH₂Cl₂ (14 mL). Recrystallization from boiling CH₂Cl₂ afforded the title amide as a white solid (1.36 g, 80 %); **mp** 161-164 ° C; **IR** (thin film, cm⁻¹) 3291, 2957, 2870, 1637, 1543; **¹H NMR** (400 MHz, CDCl₃) δ 7.85 (bs, 1H), 7.77 (bs, 2H), 6.93 (bs, 2H), 4.28 (bs, 2H), 3.82 (dd, *J* = 11.3, 3.2 Hz, 2H), 3.66 (dd, *J* = 11.0, 6.5 Hz, 2H), 3.08-3.05 (m, 2H), 1.67 (dq, *J* = 13.6, 6.7 Hz, 2H), 1.59-1.52 (m, 2H), 1.43-1.37 (m, 2H), 1.23 (s, 9H), 0.94 (d, *J* = 6.5 Hz, 12H); **¹³C NMR** (100 MHz, CDCl₃) δ 168.6, 154.9, 134.6, 127.1, 121.6, 65.5, 50.6, 40.2, 30.9, 25.0, 22.9, 22.4; **HRMS** [+APCI] calculated for C₂₄H₄₁N₂O₄ 421.3061, found 421.3060 [M+H]⁺; [α]_D²⁰ -43.7 ° (*c* 1.0, CHCl₃).

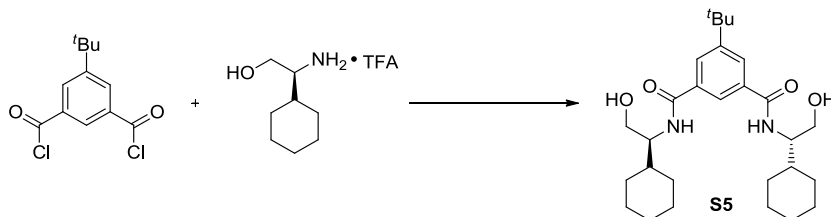


5-(*tert*-butyl)-N1,N3-bis((*R*)-1-hydroxyhexan-2-yl)isophthalamide (S3). Prepared by general procedure **B** using 5-*tert*-butylisophthaloyl dichloride (504 mg, 2.0 mmol), (*R*)-2-amino-1-hexanol (509 mg, 4.3 mmol), KHCO₃ (13 mL, 19.4 mmol). Mixed solvent recrystallization (EtOAc/hexanes) afforded the title compound as a white amorphous solid (463 mg, 57 %); **IR** (thin film, cm⁻¹) 3294, 2957, 2871, 1633, 1537, 1460, 1260, 1063; **¹H NMR** (400 MHz, CDCl₃) δ 7.86-7.69 (m, 3H), 7.43 (d, *J* = 7.9 Hz, 2H), 4.78 (br s, 2H), 4.11 (br s, 2H), 3.78-3.76 (m, 2H), 3.70-3.62 (m, 2H), 1.56-1.49 (m, 4H), 1.30-1.23 (m, 10H), 1.14 (s, 9H), 0.84 (t, *J* = 6.9 Hz, 6H); **¹³C NMR** (100 MHz, CDCl₃) δ 206.3, 168.8, 134.7, 127.5, 67.7, 64.9, 52.7, 35.0, 31.3, 28.6, 22.8, 14.2; **HRMS** (+APCI) calculated for C₂₄H₄₀N₂O₄Na 443.2880, found 443.2880 [M+Na]⁺. [α]_D²⁰ +68.4 ° (*c* 1.0, CHCl₃).

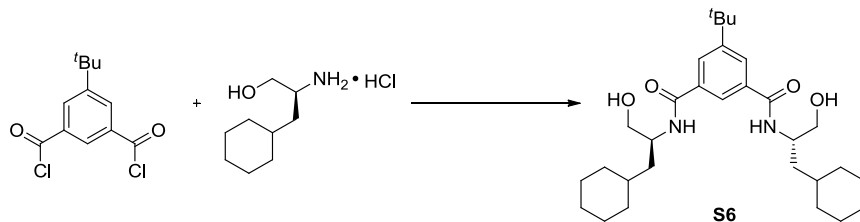


5-(*tert*-butyl)-N1,N3-bis((2*S*,3*S*)-1-hydroxy-3-methylpentan-2-yl)isophthalamide (S4). Prepared by general procedure **A** using 5-*tert*-butylisophthaloyl chloride (518 mg, 2.0 mmol) in CH₂Cl₂ (4 mL), (*S*)-isoleucinol (472 mg, 4.0 mmol), and Et₃N (0.55 mL, 4.0 mmol) in CH₂Cl₂ (7 mL). Recrystallization from boiling Et₂O/CH₂Cl₂ furnished the title amide as a white flaky

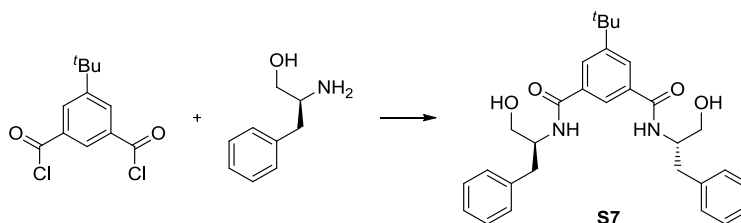
solid (454 mg, 54 %); **mp** 94-97 ° C; **IR** (thin film, cm^{-1}) 3304, 2963, 2341, 2145, 1636, 1539, 1214, 751; **^1H NMR** (400 MHz, CDCl_3) δ 7.96 (s, 1H), 7.81 (d, $J = 1.4$ Hz, 2H), 7.79 (d, $J = 1.5$ Hz, 2H), 7.31 (d, $J = 8.5$ Hz, 2H), 4.04-3.97 (m, 2H), 3.84-3.74 (m, 4H), 3.06 (q, $J = 7.3$ Hz, 2H), 1.80-1.70 (m, 2H), 1.57-1.47 (m, 2H), 1.29 (t, $J = 7.3$ Hz, 2H), 1.2 (s, 9H), 0.93 (d, $J = 6.7$ Hz, 6H), 0.88 (t, $J = 7.0$ Hz, 6H); **^{13}C NMR** (100 MHz, CDCl_3) δ 168.7, 152.0, 134.7, 127.8, 122.0, 62.8, 56.7, 46.4, 36.1, 35.0, 31.3, 26.2, 15.6, 11.6, 8.8; **HRMS** [+APCI] calculated for $\text{C}_{24}\text{H}_{41}\text{N}_2\text{O}_4$ 421.3061, found 421.3060 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} -62.0^\circ$ (c 1.0, CHCl_3).



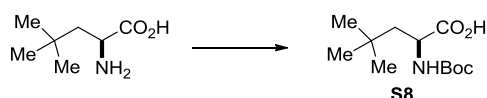
5-(tert-butyl)-N1,N3-bis((S)-1-cyclohexyl-2-hydroxyethyl)isophthalamide (S5). Prepared by general procedure **B** using (S)-2-amino-2-cyclohexylethanol·TFA salt (2.57 g, 10 mmol), in isopropyl acetate (40 mL, 0.13 M in acyl chloride), aqueous 1.5 M KHCO_3 (35 mL, 50 mmol, 10 equiv.), and 5-tert-Butyl isophthaloyl dichloride (1.3 g, 5.0 mmol). The resulting amide was obtained as a white solid (2.34 g, 99 %); **mp** 115-117 ° C; **IR** (thin film, cm^{-1}) 3289, 2927, 2853, 1706, 1640, 1535, 1157, 916; **^1H NMR** (600 MHz, CDCl_3) δ 7.85 (br s, 1H), 7.83 (br s, 2H), 6.69 (d, $J = 6.7$ Hz, 2H), 4.30 (br s, 2H), 3.82 (d, $J = 10.0$ Hz, 2H), 3.67-3.64 (m, 2H), 3.46 (dd, $J = 6.0, 3.6$ Hz, 2H), 3.18 (br s, 2H), 1.82 (d, $J = 12.4$ Hz, 2H), 1.73-1.62 (m, 8H), 1.28 (s, 9H), 1.21-1.12 (m, 6H), 1.00-0.87 (m, 4H); **^{13}C NMR** (100 MHz, CDCl_3) δ 168.4, 134.6, 127.2, 62.9, 61.7, 56.8, 56.4, 38.9, 38.1, 31.0, 29.2, 26.0, 25.8; **HRMS** [+NSI] calculated for $\text{C}_{28}\text{H}_{45}\text{N}_2\text{O}_4$ 473.3379, found 473.3374 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} -28.5^\circ$ (c 1.0, CHCl_3).



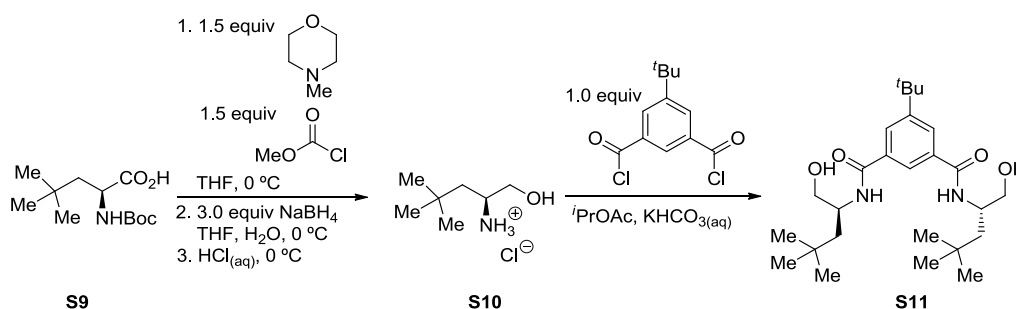
5-(tert-butyl)-N1,N3-bis((S)-1-cyclohexyl-3-hydroxypropan-2-yl)isophthalamide (S6). Prepared by general procedure **B** using (S)-2-amino-3-cyclohexylpropanol hydrochloride (1.08 g, 5.2 mmol, 2.0 equiv) in isopropyl acetate (20 mL, 0.13 M in acyl chloride), 1.5 M KHCO_3 (17 mL, 26 mmol, 10 equiv.), and 5-tert-Butyl isophthaloyl dichloride (671 mg, 2.6 mmol, 1.0 equiv). Diethyl ether (40 mL) was added to the crude solid with stirring, and the solid was collected by vacuum filtration to give the title amide as a white solid (1.25 g, 96 %); **mp** 88-90 ° C; **IR** (thin film, cm^{-1}) 3253, 2918, 2848, 1628, 1547, 1029, 902; **^1H NMR** (600 MHz, CDCl_3) δ 7.91 (d, $J = 15.7$ Hz, 2H), 7.25 (s, 1H), 6.29 (d, $J = 7.6$ Hz, 2H), 4.33-4.28 (m, 2H), 3.8 (dd, $J = 11.0, 2.9$ Hz, 2H), 3.66 (dd, $J = 11.0, 5.7$ Hz, 2H), 1.75-1.62 (m, 6H), 1.54-1.46 (m, 8H), 1.35 (s, 9H), 1.23-1.13 (m, 8H), 1.01-0.88 (m, 4H); **^{13}C NMR** (150 MHz, $(\text{CD}_3)_2\text{SO}$) δ 166.4, 151.1, 135.2, 126.9, 124.2, 64.3, 49.3, 35.2, 34.4, 34.0, 32.6, 31.5, 26.6, 26.2; **HRMS** [+APCI] calculated for $\text{C}_{30}\text{H}_{49}\text{N}_2\text{O}_4$ 501.3687, found 501.3685 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} -15.5^\circ$ (c 0.5, CHCl_3).



5-(tert-butyl)-N1,N3-bis((S)-1-hydroxy-3-phenylpropan-2-yl)isophthalamide (S7). Prepared by general procedure **B** using 5-tert-butylisophthaloyl dichloride (500 mg, 1.9 mmol) in isopropyl acetate (1.5 mL, 0.13 M in acyl chloride), (S)-2-amino-3-phenyl-1-propanol (590 mg, 3.9 mmol), 1.5 M KHCO₃ (13 mL, 19.4 mmol). Mixed solvent recrystallization (EtOAc/hexanes) afforded the title compound as a white solid (703 mg, 74 %); **mp** 76-79 ° C; **IR** (thin film, cm⁻¹) 3283, 2964, 1636, 1542, 1041; **¹H NMR** (400 MHz, CDCl₃) δ 7.73 (s, 1H), 7.61 (s, 2H), 7.28-7.19 (m, 10H), 7.08 (d, *J* = 12.8 Hz, 2H), 4.31 (br s, 2H), 3.76 (dd, *J* = 11.1, 2.9 Hz, 2H), 3.64 (dd, *J* = 11.6, 6.1 Hz, 2H), 2.96-2.86 (m, 4H), 1.15 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 172.5, 168.2, 151.9, 137.7, 134.4, 129.3, 128.6, 127.2, 126.6, 122.1, 63.6, 53.7, 37.1, 34.8, 30.9; **HMRS** (+NSI) calculated for C₃₀H₃₆N₂O₄ 489.2748, found 489.2743 [M+H]⁺; [α]_D²⁰ -84.6 ° (c 1.0, CHCl₃).



(S)-2-(((tert-butoxycarbonyl)amino)-4,4-dimethylpentanoic acid (S8). Adapting a procedure from Christoffers and Schuster,³ a 25 mL round bottom flask equipped with a stir bar was charged with (S)-2-amino-4,4-dimethylpentanoic acid (500 mg, 3.5 mmol, 1.0 equiv), H₂O (4 mL), MeOH (5 mL) and cooled to 0 ° C with stirring. Na₂CO₃ (376 mg, 3.6 mmol, 1.0 equiv) was added slowly, followed by a solution of Boc₂O (799 mg, 3.7 mmol, 1.1 equiv) in MeOH (1.25 mL). The suspension became mostly clear, after which a white precipitate formed. The mixture was permitted to come to 23 ° C and then stirred overnight. Water (5 mL) and then citric acid were added slowly at 23 ° C until approximately pH 3 was achieved. The resulting solution was extracted with CH₂Cl₂, and the combined organic layers were dried with Na₂SO₄ and concentrated *in vacuo* to afford a white sticky solid (769 mg, 91 % yield) which was used without further purification; **mp** 96-98 ° C; **IR** (neat, cm⁻¹) 3245, 3117, 2955, 1731, 1652, 1387, 1366, 1241, 1165, 902; **¹H NMR** (400 MHz, CDCl₃) δ 4.84 (d, *J* = 12 Hz, 1H), 4.34 (dt, *J* = 4, 8 Hz, 1H), 1.81 (dd, *J* = 4, 12 Hz, 1H), 1.44 (s, 9H), 0.98 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 178.9, 155.4, 80.8, 51.3, 45.9, 30.7, 29.5, 28.3; **HRMS** (+NSI) calculated for C₁₂H₂₄O₄N 246.1699, found 246.1699 [M+H]⁺; [α]_D²⁰ -21.6 ° (c 1.1, CHCl₃).

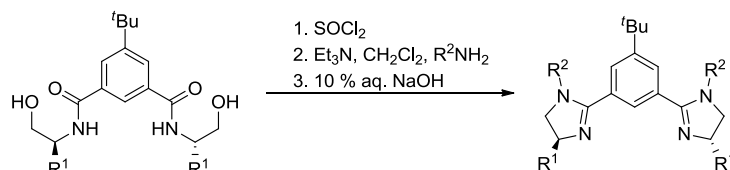


5-(*tert*-butyl)-*N*¹,*N*³-bis((*S*)-1-hydroxy-4,4-dimethylpentan-2-yl)isophthalamide (S11).

Adapting a procedure from Guaragna and coworkers,⁴ a 100 mL round bottom flask equipped with a stir bar was flame dried and placed under N₂. The flask was charged with **S9** (340 mg, 1.4 mmol, 1.0 equiv) and THF (12 mL). The solution was stirred and cooled to 0 °C. *N*-methylmorpholine (230 μL, 2.1 mmol, 1.5 equiv) was then added dropwise, followed by methyl chloroformate (160 μL, 2.1 mmol, 1.5 equiv) also dropwise. The reaction was allowed to come to 23 °C, at which time a white precipitate was observed to have formed. After 2 h at 23 °C, the reaction was filtered through Celite and recooled to 0 °C. NaBH₄ (158 mg, 4.2 mmol, 3.0 equiv) in H₂O (0.80 mL) was then added to the solution dropwise with stirring. Vigorous bubbling was observed. The reaction was permitted to stir another 30 min at 23 °C. Saturated NH₄Cl (aq) was then added, the mixture was extracted with Et₂O, and the organic layers were washed with saturated CuSO₄ (aq) and finally dried with Na₂SO₄. Concentration *in vacuo* afforded a clear oil (355 mg) which was used without further purification; **HRMS** (+NSI) calculated for C₁₂H₂₆O₃N 232.1907, found 232.1908 [M+H]⁺.

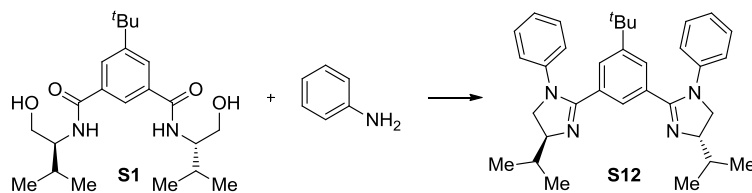
A 25 mL round bottom flask equipped with a stir bar was charged with the oil (355 mg, 1.0 mmol) and cooled to 0 °C. Concentrated HCl (aq) (2 mL) was added and the mixture was vigorously stirred. Significant bubbling was observed. The reaction was then concentrated *in vacuo* after bubbling ceased to afford a white powder (226 mg) which was used without further purification; **HRMS** (+NSI) calculated for C₇H₁₈ON 132.1383, found 132.1382[M+H]⁺.

A 25 mL round bottom flask equipped with a stir bar and a condenser was flame dried and placed under N₂ atmosphere. The flask was charged with **S10** (226 mg, 2.3 equiv) and *i*PrOAc (8 mL) and vigorously stirred. KHCO₃ (4 mL, 1.5 M in H₂O, 6.0 mmol, 10.2 equiv) was added dropwise and the mixture was heated to 65 °C. Once reaching 65 °C, 5-(*tert*-butyl)-isophthaloyl dichloride (152 mg, 0.59 mmol, 1.0 equiv) was added slowly over 5 min. The mixture was then heated at 65 °C with stirring for 4 h under N₂. The reaction was then cooled to 23 °C, extracted with *i*PrOAc, dried with Na₂SO₄, concentrated *in vacuo*, and purified by flash chromatography (7:3 → 1:1 hexanes:EtOAc) to yield the title compound as a white solid (238 mg, 38% yield over 3 steps); **R_f** 0.08 (75:25 EtOAc:hexanes); **mp** 136–140 °C; **IR** (neat, cm⁻¹) 3243, 2952, 2867, 1630, 1550, 1466, 1365, 1261, 1047, 908; **¹H NMR** (400 MHz, CDCl₃) δ 7.87 (t, *J* = 1.6 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 4.32 (m, 2H), 3.74 (dd, *J* = 4.0, 11.2 Hz, 2H), 3.60 (dd, *J* = 6.8, 11.2 Hz, 2H), 1.55 (dd, *J* = 8.4, 14.4 Hz, 2H), 1.43 (dd, *J* = 3.2, 14.4 Hz, 2H), 1.18 (s, 9H), 0.94 (s, 18H); **¹³C NMR** (100 MHz, CDCl₃) δ 168.1, 151.8, 134.7, 127.1, 121.9, 66.8, 49.5, 44.8, 34.8, 31.0, 30.4, 29.8; **HRMS** (+NSI) calculated for C₂₆H₄₄ N₂O₄Na 471.3199, found 471.3187 [M+Na]⁺; [**α**]_D²⁰ -38.3 ° (c 1.2, CHCl₃).

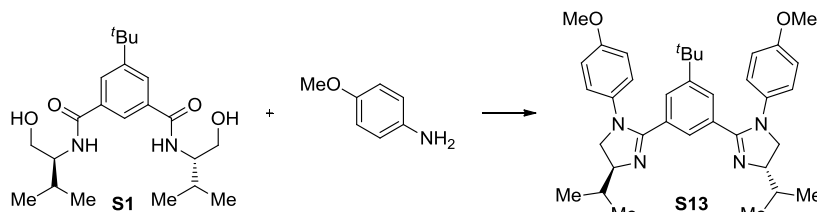


General Procedure C

A procedure was adapted from the literature as follows:⁵ A 10 mL flask was charged with amide (1.0 equiv) fitted with a reflux condenser, and evacuated and backfilled with dry nitrogen. SOCl₂ (16 equiv) was added via syringe, and the mixture was refluxed for approximately 7 h. Excess SOCl₂ was removed directly under high vacuum. The residue was dissolved in dry CH₂Cl₂ (0.18 M) and cooled to 0 °C. Et₃N (6.0 equiv) and the primary aniline (2.2 equiv) were added sequentially, and the mixture was stirred overnight at ambient temperature. 10 % aqueous NaOH (15 equiv) was added and stirred for 30 minutes. The phases were separated, and the aqueous phase was extracted with CH₂Cl₂ (3 x). The combined organics were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel as indicated to give the title compound.

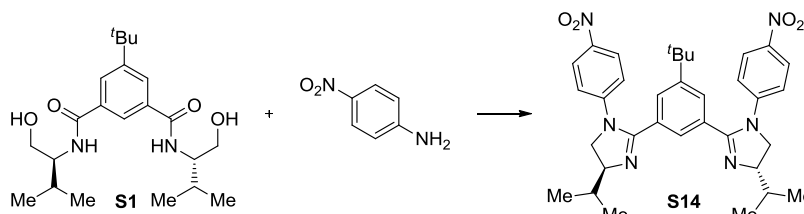


(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-phenyl-4,5-dihydro-1*H*-imidazole) (S12). Prepared by general procedure C using amide S1 (200 mg, 0.51 mmol), SOCl₂ (0.6 mL), Et₃N (0.43 mL, 3.1 mmol), CH₂Cl₂ (2.8 mL), aniline (104 mg, 1.1 mmol), and 10 % aq. NaOH (3 mL). Flash chromatography (EtOAc → 9:1 EtOAc:MeOH) afforded the title ligand as a light brown amorphous solid (230 mg, 89 %); **R_f** 0.08 (9:1 EtOAc:MeOH); **IR** (thin film, cm⁻¹) 2957, 2871, 1577, 1495, 1253, 730, 695; **¹H NMR** (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.23 (d, *J* = 1.5 Hz, 2H), 7.12 (t, *J* = 7.9 Hz, 4H), 6.96 (t, *J* = 7.3 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 4H), 4.20-4.07 (m, 4H), 3.62 (dd, *J* = 8.8, 7.0 Hz, 2H), 1.97-1.91 (m, 2H), 0.99 (d, *J* = 6.7 Hz, 6H), 0.92 (d, *J* = 7.0 Hz, 6H), 0.88 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 161.8, 150.7, 142.2, 128.9, 128.4, 124.3, 123.5, 69.0, 56.0, 34.6, 33.0, 30.8, 18.9, 17.8; **HRMS** [+APCI] calculated for C₃₄H₄₃N₄ 507.3482, found 507.3479 [M+H]⁺; [α]²⁰_D +42.7 ° (*c* 1.0, CHCl₃).

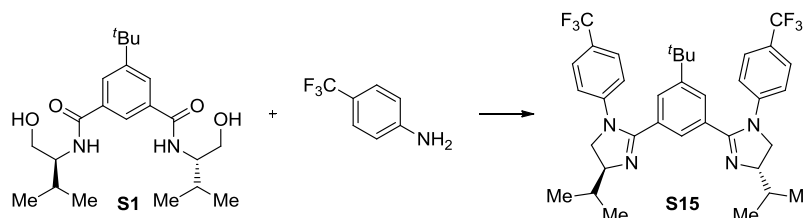


(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-(4-methoxyphenyl)-4,5-dihydro-1*H*-imidazole) (S13). Prepared by general procedure C using amide S1 (200 mg, 0.51 mmol), SOCl₂ (0.6 mL), Et₃N (0.43 mL, 3.1 mmol), CH₂Cl₂ (2.8 mL), 4-methoxyaniline (138 mg, 1.1 mmol), and 10 % aq. NaOH (3 mL). Flash chromatography (9:1 → 4:1 → 7:3 acetone:MeOH) afforded the title ligand as a white amorphous solid (229 mg, 79 %); **R_f** 0.13

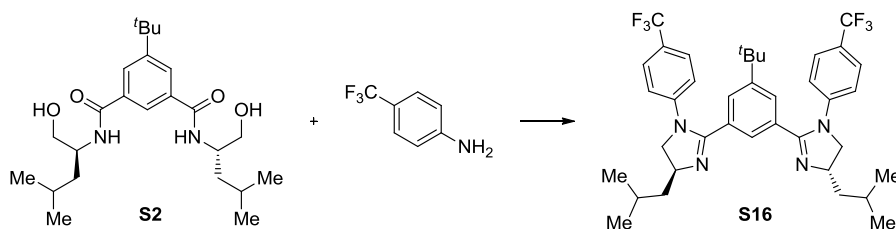
(8:2 acetone:MeOH); **IR** (thin film, cm^{-1}) 2957, 1510, 1244; **^1H NMR** (400 MHz, CDCl_3) δ 7.77 (s, 1H), 7.25 (s, 2H), 6.73 (d, $J = 8.9$ Hz, 4H), 6.67 (d, $J = 8.9$ Hz, 4H), 4.12-4.01 (m, 4H), 3.69 (s, 6H), 3.49 (t, $J = 7.1$ Hz, 2H), 1.94 (dd, $J = 12.3, 6.1$ Hz, 2H), 1.00 (d, $J = 7.0$ Hz, 6H), 0.92 (d, $J = 7.0$ Hz, 6H), 0.90 (s, 9H); **^{13}C NMR** (100 MHz, CDCl_3) δ 162.2, 156.9, 128.3, 127.4, 125.8, 114.3, 77.4, 56.9, 55.7, 34.6, 33.1, 30.9, 19.0, 17.8; **HRMS** [+APCI] calculated for $\text{C}_{36}\text{H}_{47}\text{N}_4\text{O}_2$ 567.3694, found 567.3689 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} +77.8^\circ$ (c 1.0, CHCl_3).



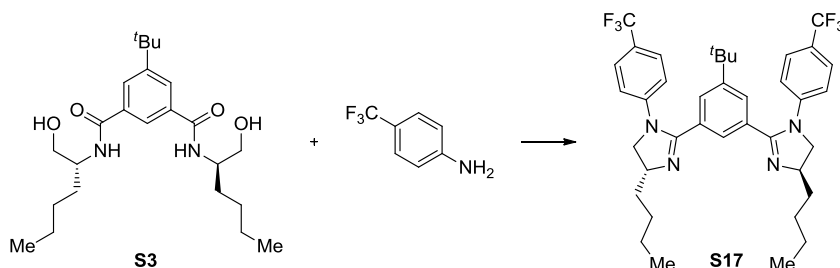
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-(4-nitrophenyl)-4,5-dihydro-1H-imidazole) (S14). Prepared by general procedure C using amide **S1** (200 mg, 0.51 mmol), SOCl_2 (0.6 mL), Et_3N (0.43 mL, 3.1 mmol), CH_2Cl_2 (3 mL), 4-nitroaniline (155 mg, 1.1 mmol), and 10 % aq. NaOH (3 mL). Flash chromatography ($\text{EtOAc} \rightarrow 95:5 \rightarrow 93:7$ $\text{EtOAc}:\text{MeOH}$) afforded the title ligand as a yellow solid (238 mg, 78 %); R_f 0.55 (95:5 $\text{EtOAc}:\text{MeOH}$); **mp** 120-122 $^\circ\text{C}$; **IR** (thin film, cm^{-1}) 2960, 1590, 1504, 1327; **^1H NMR** (400 MHz, CDCl_3) δ 7.98 (d, $J = 8.6$ Hz, 4H), 7.73 (s, 1H), 7.38 (s, 2H), 6.69 (d, $J = 9.0$ Hz, 4H), 4.19 (t, $J = 9.8$ Hz, 2H), 4.13-4.07 (m, 2H), 3.76 (dd, $J = 8.6, 7.0$ Hz, 2H), 1.92 (dd, $J = 13.1, 6.8$ Hz, 2H), 1.03 (s, 9H), 1.01 (d, $J = 7.0$ Hz, 6H), 0.91 (d, $J = 6.7$ Hz, 6H); **^{13}C NMR** (100 MHz, CDCl_3) δ 159.0, 152.1, 147.5, 141.8, 131.3, 128.1, 124.7, 119.8, 70.5, 55.4, 34.9, 33.0, 31.0, 19.1, 18.2; **HRMS** [+NSI] calculated for $\text{C}_{34}\text{H}_{41}\text{N}_6\text{O}_4$ 597.3184, found 597.3182 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} -9.8^\circ$ (c 0.3, CHCl_3).



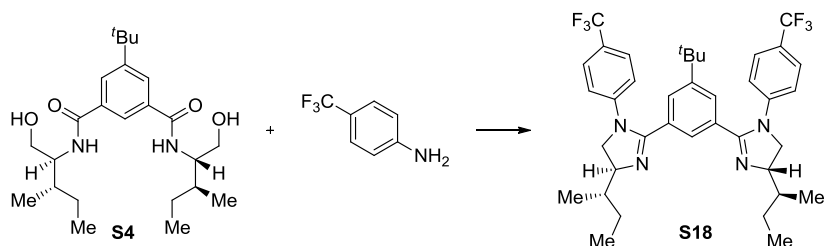
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole) (S15). Prepared according to general procedure C using amide **S1** (200 mg, 0.51 mmol), SOCl_2 (0.6 mL), Et_3N (0.43 mL, 3.1 mmol), CH_2Cl_2 (3 mL), 4-trifluoromethylaniline (180 mg, 1.1 mmol), and 10 % aq. NaOH (3 mL). Flash chromatography (95:5 $\rightarrow$ 9:1 $\text{EtOAc}:\text{MeOH}$) afforded the title ligand as a light yellow amorphous solid (274 mg, 84 %); R_f 0.50 (9:1 $\text{EtOAc}:\text{MeOH}$); **IR** (thin film) 2960, 1613, 1324, 1121, 1072; **^1H NMR** (400 MHz, CDCl_3) δ 7.75 (s, 1H), 7.33 (d, $J = 8.6$ Hz, 4H), 7.29 (d, $J = 1.2$ Hz, 2H), 6.72 (d, $J = 8.6$ Hz, 4H), 4.17 (t, $J = 9.8$ Hz, 2H), 4.06 (dt, $J = 10.6, 6.3$ Hz, 2H), 3.66 (dd, $J = 8.8, 6.8$ Hz, 2H), 1.89 (dq, $J = 13.0, 6.5$ Hz, 2H), 1.00 (d, $J = 6.7$ Hz, 6H), 0.95 (s, 9H), 0.90 (d, $J = 6.7$ Hz, 6H); **^{13}C NMR** (100 MHz, CDCl_3) δ 160.1, 151.3, 145.4, 131.0, 128.1, 126.6, 125.9, 124.7, 122.9, 121.5, 70.3, 55.5, 34.7, 33.1, 30.8, 19.0, 17.9; **HRMS** [+NSI] calculated for $\text{C}_{36}\text{H}_{41}\text{F}_6\text{N}_4$ 643.3229, found 643.3211 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} +10.6^\circ$ (c 0.4, CHCl_3).



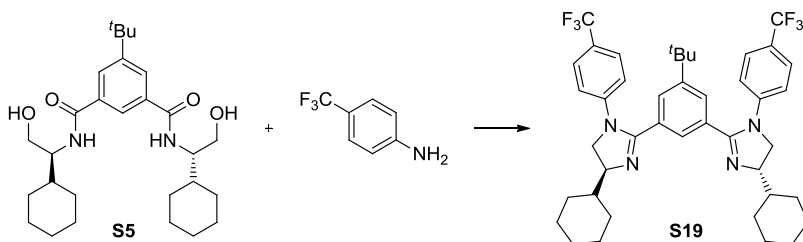
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isobutyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S16). Prepared by general procedure **C** using amide **S2** (950 mg, 2.3 mmol), SOCl₂ (2.8 mL), Et₃N (2.0 mL, 14.3 mmol), CH₂Cl₂ (13 mL), 4-trifluoromethylaniline (180 mg, 1.12 mmol), and 10 % aq. NaOH (14 mL). Flash chromatography (4:5 EtOAc:hexanes) afforded the title ligand as a colorless oil (793 mg, 52 %); **R_f** 0.66 (1:1 hexanes:EtOAc); **IR** (thin film) 2959, 2158, 2009, 1613, 1324, 1122, 750; **¹H NMR** (400 MHz, CDCl₃) δ 7.76 (s, 1H), 7.33 (d, *J* = 8.6 Hz, 4H), 7.24 (s, 2H), 6.71 (d, *J* = 8.6 Hz, 4H), 4.31-4.23 (m, 2H), 4.17 (t, *J* = 9.2 Hz, 2H), 3.63 (t, *J* = 8.2 Hz, 2H), 1.83 (dt, *J* = 13.3, 6.7 Hz, 2H), 1.74 (dt, *J* = 13.3, 6.7 Hz, 2H), 1.43-1.41 (m, 2H), 0.98-0.94 (m, 21H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.8, 151.2, 145.4, 131.1, 128.1, 126.7, 125.9, 121.1, 63.1, 58.8, 46.1, 34.7, 30.8, 25.5, 23.2, 22.8; **HRMS** [+NSI] calculated for C₃₈H₄₅N₄F₆ 671.3543, found 671.3523 [M+H]⁺; [α]_D²⁰ -31.1 ° (*c* 1.0, CHCl₃).



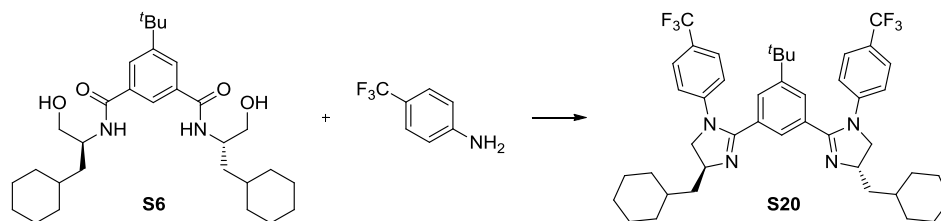
(4*R*,4'*R*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-butyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S17). Prepared according to general procedure **C** using amide **S3** (193 mg, 0.43 mmol), SOCl₂ (0.7 mL), Et₃N (0.4 mL, 2.9 mmol), CH₂Cl₂ (2.3 mL), 4-trifluoromethylaniline (0.12 mL, 0.96 mmol), and 10 % aq. NaOH (2.5 mL). Flash chromatography (EtOAc → 9:1 EtOAc:methanol) afforded the title ligand as an oil (110 mg, 38 %); **R_f** 0.32 (9:1 EtOAc:methanol); **IR** (thin film, cm⁻¹) 2962, 2933, 2873, 1612, 1522, 1323, 1123, 1070; **¹H NMR** (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.33 (d, *J* = 8.5 Hz, 4H), 7.24 (s, 2H), 6.72 (d, *J* = 8.2 Hz, 4H), 4.24-4.14 (m, 4H), 3.66 (t, *J* = 7.3 Hz, 2H), 1.83-1.77 (m, 2H), 1.59-1.52 (m, 2H), 1.43-1.33 (m, 8H), 0.94 (t, *J* = 4.9 Hz, 9H), 0.91 (t, *J* = 6.9 Hz, 6H); **¹³C NMR** (150 MHz, CDCl₃) δ 159.6, 156.2, 151.0, 145.1, 130.9, 127.8, 126.4, 125.6, 121.0, 64.5, 58.0, 36.0, 34.5, 30.6, 30.5, 27.9, 22.7, 13.9; **HMRS** (+NSI) calculated for C₃₈H₄₅N₄F₆ 671.3554, found 671.3550 [M+H]⁺; [α]_D²⁰ +8.1 ° (*c* 1.0, CHCl₃).



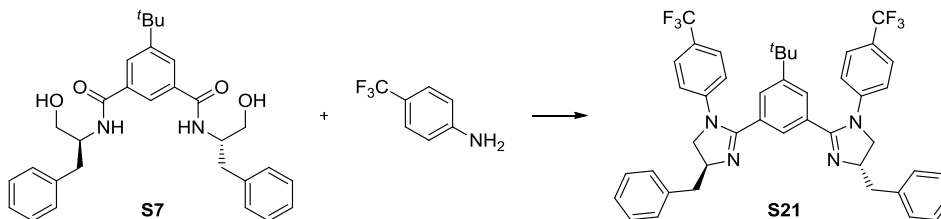
(S)-4-((S)-sec-butyl)-2-(3-(tert-butyl)-5-((S)-4-((S)-sec-butyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazol-2-yl)phenyl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole. (S18). Prepared by general procedure C using amide S4 (215 mg, 0.51 mmol), SOCl₂ (0.6 mL), Et₃N (0.43 mL, 3.1 mmol), CH₂Cl₂ (3 mL), 4-trifluoromethylaniline (180 mg, 1.1 mmol), and 10 % aq. NaOH (3 mL). Flash chromatography (EtOAc → 95:5 → 9:1 EtOAc:MeOH) afforded the title ligand as a white amorphous solid (220 mg, 64 %); *R_f* 0.61 (95:5 EtOAc:MeOH); **IR** (thin film) 2965, 1614, 1537, 1325, 1130, 751; **¹H NMR** (600 MHz, CDCl₃) δ 8.10 (s, 1H), 7.45 (d, *J* = 8.1 Hz, 4H), 7.17 (s, 2H), 7.06 (d, *J* = 5.7 Hz, 4H), 4.40-4.37 (m, 2H), 4.32 (t, *J* = 10.0 Hz, 2H), 3.85 (t, *J* = 8.3 Hz, 2H), 1.93 (s, 2H), 1.59-1.52 (m, 2H), 1.27-1.22 (m, 2H), 0.93 (t, *J* = 7.6 Hz, 12H), 0.81 (s, 9H); **¹³C NMR** (150 MHz, CDCl₃) δ 173.6, 161.9, 151.6, 142.4, 129.5, 126.4, 124.4, 123.7, 122.6, 64.9, 54.9, 38.3, 34.4, 30.2, 25.5, 21.4, 13.6, 11.4; **HRMS** [+APCI] calculated for C₃₈H₄₅N₄F₆ 671.3543, found 671.3540 [M+H]⁺; [α]_D²⁰ +30.2 ° (*c* 1.0, CHCl₃).



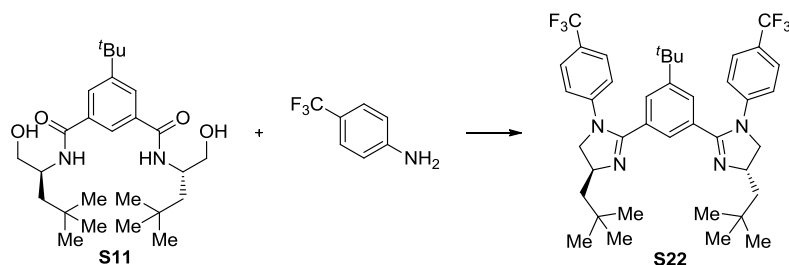
(4S,4'S)-2,2'-(5-(tert-butyl)-1,3-phenylene)bis(4-cyclohexyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole) (S19). Prepared by general procedure C using amide S5 (482 mg, 1.0 mmol), SOCl₂ (1.2 mL), Et₃N (0.86 mL, 6.2 mmol), CH₂Cl₂ (6 mL), 4-trifluoromethylaniline (362 mg, 2.2 mmol), and 10 % aq. NaOH (6 mL). Flash chromatography (EtOAc → 98:2 → 95:5 EtOAc:MeOH) afforded the title ligand as a light brown amorphous solid (155 mg, 21 %); *R_f* 0.13 (EtOAc); **IR** (thin film) 2929, 2855, 2366, 2043, 1709, 1613, 1325, 753; **¹H NMR** (600 MHz, CDCl₃) δ 7.78 (s, 1H), 7.32 (d, *J* = 8.6 Hz, 4H), 7.25 (d, *J* = 4.8 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 4H), 4.15 (t, *J* = 10.0 Hz, 2H), 4.05 (dt, *J* = 10.0, 6.7 Hz, 2H), 3.69 (dd, *J* = 8.8, 7.4 Hz, 2H), 1.90 (d, *J* = 12.4 Hz, 2H), 1.76 (t, *J* = 11.2 Hz, 4H), 1.66 (d, *J* = 11.9 Hz, 4H), 1.59 (dtd, *J* = 14.8, 7.4, 3.1 Hz, 2H), 1.30-1.20 (m, 4H), 1.15 (tt, *J* = 12.8, 2.9 Hz, 2H), 1.05 (dq, *J* = 24.2, 12.1, 3.2 Hz, 4H), 0.93 (s, 9H); **¹³C NMR** (150 MHz, CDCl₃) δ 160.0, 151.2, 145.4, 131.0, 128.1, 126.6, 125.8, 125.2, 123.4, 121.4, 69.6, 55.7, 43.1, 34.7, 30.8, 29.6, 28.5, 26.7, 26.3; **HRMS** [+APCI] calculated for C₄₂H₄₉F₆N₄ 723.3861, found 723.3864 [M+H]⁺; [α]_D²⁰ -11.8 ° (*c* 0.3, CHCl₃).



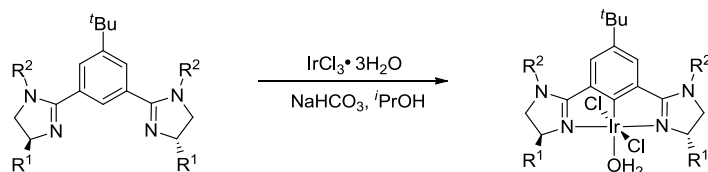
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-(cyclohexylmethyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S20). Prepared by general procedure C using amide **S6** (130 mg, 0.26 mmol), SOCl₂ (0.31 mL), Et₃N (0.4 mL, 2.9 mmol), CH₂Cl₂ (1.4 mL), 4-trifluoromethylaniline (51 μ L, 0.56 mmol), and 10 % aq. NaOH (1.5 mL). Flash chromatography (1:1 hexanes:EtOAc $\rightarrow$ 3:7 hexanes:EtOAc $\rightarrow$ EtOAc) afforded the title ligand as a white amorphous solid (123 mg, 63 %); *R_f* 0.57 (3:7 hexanes/EtOAc); **IR** (thin film) 3843, 3019, 2344, 2147, 1710, 1214, 744; **¹H NMR** (600 MHz, CDCl₃) δ 7.80 (s, 1H), 7.32 (d, *J* = 8.6 Hz, 4H), 7.23 (t, *J* = 1.4 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 4H), 4.31 (dt, *J* = 15.9, 7.8 Hz, 2H), 4.17 (t, *J* = 9.3 Hz, 2H), 3.62 (t, *J* = 8.3 Hz, 2H), 1.82-1.73 (m, 6H), 1.72-1.63 (m, 8H), 1.50 (ddd, *J* = 10.6, 7.0, 3.8 Hz, 2H), 1.38 (dt, *J* = 13.6, 7.0 Hz, 2H), 1.28-1.23 (m, 4H), 1.19-1.15 (m, 2H) 1.00-0.96 (m, 4H), 0.93 (s, 9H); **¹³C NMR** (150 MHz, CDCl₃) δ 159.7, 145.5, 131.3, 128.0, 126.7, 125.8, 121.1, 62.5, 58.9, 44.8, 34.9, 33.9, 33.5, 30.8, 26.8, 26.5; **HRMS** [+APCI] calculated for C₄₄H₅₃F₆N₄ 751.4169, found 751.4172 [M+H]⁺; [α]_D²⁰ - 26.3 ° (*c* 1.0, CHCl₃).



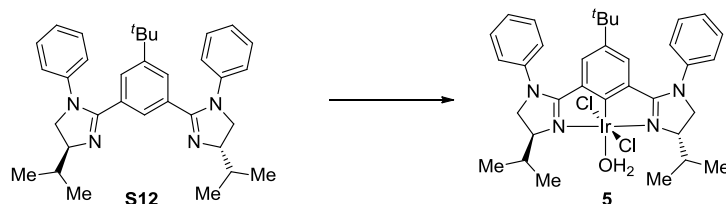
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-benzyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S21). Prepared according to general procedure C, using amide **S7** (420 mg, 0.86 mmol), SOCl₂ (1.1 mL), Et₃N (0.73 mL, 5.2 mmol), CH₂Cl₂ (4.7 mL), 4-trifluoromethylaniline (0.25 mL, 2.0 mmol), and 10 % aq. NaOH (5 mL). Flash chromatography (EtOAc $\rightarrow$ 9:1 EtOAc:MeOH) afforded the title compound as a yellow amorphous solid (303 mg, 48 %); *R_f* 0.24 (9:1 EtOAc:methanol); **IR** (thin film, cm⁻¹) 2969, 2195, 1611, 1521, 1376, 1321, 1163; **¹H NMR** (400 MHz, CDCl₃) δ 7.72 (t, *J* = 1.5 Hz, 1H), 7.29 (dd, *J* = 4.9, 3.4 Hz, 6H), 7.21-7.15 (m, 10H), 6.54 (d, *J* = 8.5 Hz, 4H), 4.58-4.51 (m, 2H), 4.11 (t, *J* = 9.6 Hz, 2H), 3.70 (dd, *J* = 9.5, 6.1 Hz, 2H), 3.16 (dd, *J* = 13.7, 4.6 Hz, 2H), 2.81 (dd, *J* = 13.6, 8.1 Hz, 2H), 0.98 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 160.6, 151.5, 145.3, 137.9, 131.1, 129.7, 128.6, 128.1, 128.06, 126.7, 126.5, 125.8, 124.8, 124.5, 123.0, 121.3, 65.5, 57.3, 42.0, 34.8, 30.8; **HRMS** (+NSI) calculated for C₄₄H₄₁N₄F₆ 739.3229, found 739.3227 [M+H]⁺; [α]_D²⁰ +164.4 ° (*c* 1.0, CHCl₃).



(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-neopentyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S22). Prepared according to general procedure C, using amide **S11** (95 mg, 0.21 mmol, 1.0 equiv), SOCl₂ (1.0 mL), Et₃N (200 μ L, 1.43 mmol, 6.8 equiv), CH₂Cl₂ (2.0 mL), 4-trifluoromethylaniline (75 μ L, 0.598, 2.8 equiv), and 10 % aq. NaOH (3 mL). Flash chromatography (8:2 hexanes:EtOAc $\rightarrow$ EtOAc) afforded the title compound as an amorphous off-white solid (99 mg, 67% yield); **R_f** 0.05 (very streaky, 100% EtOAc). **IR** (neat, cm⁻¹) 2955, 2902, 1612, 1521, 1321, 1117, 1070, 834, 731; **¹H NMR** (400 MHz, CDCl₃) δ 7.76 (t, *J* = 1.6 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 4H), 7.26 (d, *J* = 1.6 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 4H), 4.25 (dd, *J* = 8.0, 14.0 Hz, 4H), 3.66 (m, 2H), 1.94 (dd, *J* = 4.0, 14.0 Hz, 2H), 1.46 (dd, *J* = 8.0, 14.0 Hz, 2H), 1.00 (s, 18H), 0.96 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 159.1, 150.9, 145.2, 130.8, 127.7, 126.4, 125.6 (q, *J* = 4 Hz), 124.0 (q, *J* = 33 Hz), 122.7, 120.8, 62.0, 60.4, 51.0, 34.5, 30.6, 30.4, 30.0; **¹⁹F NMR** (375 MHz, CDCl₃) δ -65.2 (s, 6F); (-164.9, C₆F₆); **HRMS** (+NSI) calculated for C₄₀H₄₉N₄F₆ 699.3856, found 699.3850 [M+H]⁺; [α]_D²⁰ -100.8 ° (c 1.1, CHCl₃).

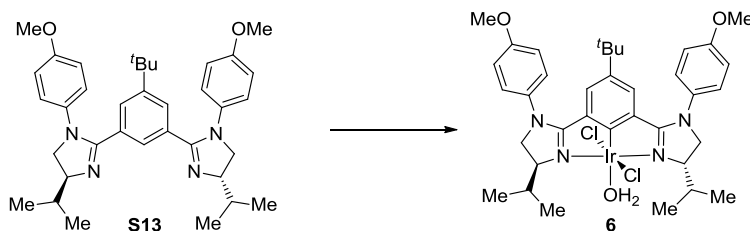


General procedure D. A dry round bottom flask was charged with ligand (1.0 equiv.), IrCl₃·3H₂O or IrBr₃·4H₂O (1.1 equiv.), and NaHCO₃ (1.1 equiv.). The flask was fitted with a reflux condenser and evacuated and backfilled with nitrogen. *i*PrOH (0.03 M) was added, and the mixture was refluxed until the ligand was consumed as judged by thin-layer chromatography. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The crude solid was purified by flash column chromatography on silica gel or by preparative thin layer chromatography as indicated to give the iridium(III) phebim complex.

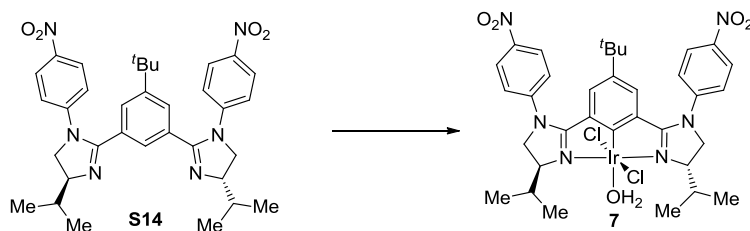


[(*S*, *S*)-*t*-ButylPhebim-Ph-*i*-Pr]IrCl₂(H₂O) (5). Prepared by general procedure **D** using ligand **S12** (139 mg, 0.27 mmol), IrCl₃·3H₂O (106 mg, 0.30 mmol), and NaHCO₃ (25 mg, 0.30 mmol). The reaction was refluxed in *i*PrOH (9 mL) for 5.5 h. Flash chromatography (1:1 hexanes:EtOAc) afforded iridium(III) phebim **5** as a dark red solid (59 mg, 27 %); **R_f** 0.67 (1:1 hexanes:EtOAc); **mp** 192 ° C; **IR** (thin film, cm⁻¹) 3353, 2954, 1493, 1288, 730, 696; **¹H NMR** (600 MHz, CDCl₃) δ 7.40 (t, *J* = 7.9 Hz, 4H), 7.31-7.27 (m, 6H), 6.52 (s, 2H), 4.41 (dd, *J* = 11.1,

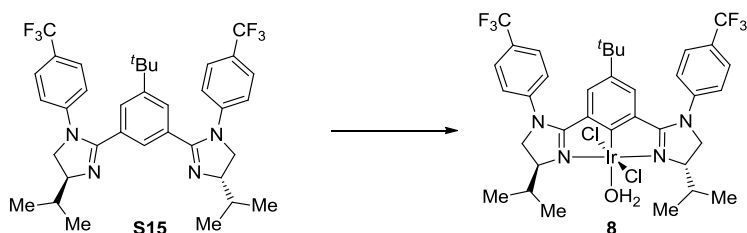
9.4 Hz, 2H), 4.30-4.27 (m, 2H), 4.05 (dd, $J = 9.3, 5.6$ Hz, 2H), 2.94 (br s, 2H), 2.54-2.50 (m, 2H), 0.98 (dd, $J = 14.8, 6.9$ Hz, 12H), 0.79 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 170.5, 141.3, 132.2, 129.4, 127.3, 126.4, 125.4, 68.0, 54.9, 34.4, 29.7, 19.4, 15.4; HRMS [+NSI] calculated for $\text{C}_{34}\text{H}_{41}\text{Cl}_2\text{IrN}_4$ 768.23320, found 768.23158 $[\text{M}-\text{H}_2\text{O}]^+$; $[\alpha]^{20}_{\text{D}} +24.9^\circ$ (c 0.1, CHCl_3).



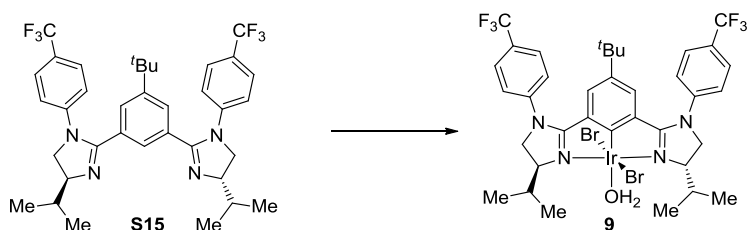
[(*S,S*)-*t*-ButylPhebim-4-OMe-Ph-*i*-Pr]IrCl₂(H₂O) (6). Prepared by general procedure **D** using ligand **S13** (35 mg, 0.062 mmol), IrCl₃·3H₂O (24 mg, 0.068 mmol), and NaHCO₃ (6 mg, 0.068 mmol). The reaction was refluxed in *i*PrOH (2 mL) for 12 h. Preparative thin layer chromatography (2:3 hexanes:EtOAc) afforded iridium(III) phebim **6** as a dark red solid (20 mg, 38 %); R_f 0.67 (2:3 hexanes:EtOAc); mp 190 °C; IR (thin film, cm^{-1}) 3353, 2956, 1510, 1244, 1033, 749; ^1H NMR (600 MHz, CDCl_3) δ 7.21 (d, $J = 8.6$ Hz, 4H), 6.91 (d, $J = 9.1$ Hz, 4H), 6.39 (s, 2H), 4.31-4.28 (m, 2H), 4.26-4.24 (m, 2H), 3.99 (dd, $J = 8.8, 5.5$ Hz, 2H), 3.81 (s, 6H), 2.50-2.48 (m, 2H), 2.32 (br s, 2H), 1.00 (d, $J = 6.2$ Hz, 6H), 0.95 (d, $J = 6.7$ Hz, 6H), 0.79 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 170.8, 159.0, 142.7, 134.1, 132.3, 128.4, 125.3, 114.7, 68.0, 55.9, 55.2, 34.4, 31.4, 29.9, 19.4, 15.5; HRMS [+APCI] calculated for $\text{C}_{36}\text{H}_{43}\text{N}_4\text{Cl}_2\text{Ir}$ 826.2387, found 826.2397 $[\text{M}-\text{H}_2\text{O}]^+$; $[\alpha]^{20}_{\text{D}} +41.8^\circ$ (c 0.1, CHCl_3).



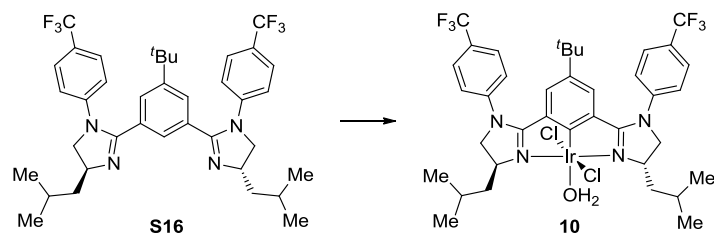
[(*S,S*)-*t*-ButylPhebim-4-NO₂-Ph-*i*-Pr]IrCl₂(H₂O) (7). Prepared by general procedure **D** using ligand **S14** (44 mg, 0.074 mmol), IrCl₃·3H₂O (29 mg, 0.081 mmol), and NaHCO₃ (7 mg, 0.081 mmol). The reaction was refluxed in *i*PrOH (2.5 mL) for 24 h. Preparative thin layer chromatography (1:1 hexanes:EtOAc) afforded iridium(III) phebim **7** as a dark red solid (10 mg, 15 %); R_f 0.48 (2:3 hexanes:EtOAc); mp 210 °C; IR (thin film, cm^{-1}) 3357, 2957, 1595, 1519, 1323, 1111, 752; ^1H NMR (600 MHz, CDCl_3) δ 8.29 (d, 4H, $J = 9.1$ Hz), 7.34 (d, $J = 9.1$ Hz, 4H), 7.01 (s, 2H), 4.58 (t, $J = 10.2$ Hz, 3H), 4.32 (br s, 2H), 4.09 (dd, $J = 9.8, 6.0$ Hz, 2H), 2.50 (br s, 2H), 1.01-0.95 (m, 15H), 0.89 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 195.5, 187.4, 146.7, 144.7, 132.2, 125.9, 125.0, 123.4, 68.4, 54.6, 34.9, 31.7, 29.9, 29.4, 19.5, 15.3; HRMS [+APCI] calculated for $\text{C}_{34}\text{H}_{38}\text{O}_4\text{N}_6\text{Ir}$ 787.2578, found 787.2578 $[\text{M}-\text{H}_2\text{O}-\text{Cl}-\text{HCl}]^+$; $[\alpha]^{20}_{\text{D}} +8.1^\circ$ (c 0.1, CHCl_3).



[(*S,S*)-*t*-ButylPhebim-4-CF₃-Ph-*i*-Pr]IrCl₂(H₂O) (8**).** Prepared by general procedure **D** using ligand **S15** (177 mg, 0.28 mmol), IrCl₃·3H₂O (109 mg, 0.31 mmol), and NaHCO₃ (26 mg, 0.31). The reaction was refluxed in *i*PrOH (9 mL) for 4.5 h. Flash chromatography (7:3 → 1:1 hexanes:EtOAc) afforded iridium(III) phebim **8** as a dark red solid (157 mg, 61 %); **R_f** 0.64 (1:1 hexanes:EtOAc); **mp** 222 ° C; **IR** (thin film, cm⁻¹) 2959, 2424, 2133, 1539, 1455, 1228, 782; **¹H NMR** (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.3 Hz, 4H), 7.38 (d, *J* = 8.3 Hz, 4H), 6.73 (s, 2H), 4.49 (t, *J* = 10.1 Hz, 2H), 4.35 (br s, 2H), 4.11-4.04 (m, 2H), 3.10 (br s, 2H), 2.54-2.51 (m, 2H), 0.98-0.93 (m, 12H), 0.89 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 170.3, 144.5, 143.0, 132.4, 128.6, 128.3, 126.5, 125.6, 125.2, 122.7, 68.3, 54.6, 34.6, 31.4, 29.6, 19.6, 15.5; **¹⁹F NMR** (375 MHz, CDCl₃) δ -65.5 (s, 6F); (-164.9, C₆F₆); **HRMS** [+APCI] calculated for C₃₆H₃₉Cl₂F₆N₄Ir 904.2080, found 904.2089 [M-H₂O]⁺; [**α**]_D²⁰ +22.6 ° (c 0.3, CHCl₃).

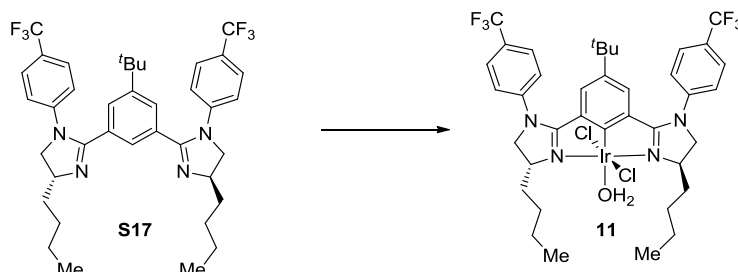


[(*S,S*)-*t*-ButylPhebim-4-CF₃-Ph-*i*-Pr]IrBr₂(H₂O) (9**).** Prepared by general procedure **D** using ligand **S15** (54 mg, 0.084 mmol), IrBr₃·4H₂O (47 mg, 0.092 mmol), and NaHCO₃ (8 mg, 0.092 mmol). The reaction was refluxed in *i*PrOH (3 mL) for 7.5 h. Flash chromatography (7:3 → 1:1 hexanes:EtOAc) afforded iridium(III) phebim **9** as a dark red solid (45 mg, 53 %); **R_f** 0.30 (7:3 hexanes:EtOAc); **mp** 186 ° C; **IR** (thin film, cm⁻¹) 3374, 2959, 1321, 1614, 1484, 1125, 1068, 845, 733; **¹H NMR** (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.2 Hz, 4H), 7.37 (d, *J* = 8.2 Hz, 4H), 6.75 (s, 2H), 4.52 (t, *J* = 10.1 Hz, 2H), 4.33 (br s, 2H), 4.08-4.05 (m, 2H), 2.52 (br s, 2H), 0.98 (app t, *J* = 7.6 Hz, 12H), 0.90 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 169.9, 144.5, 143.1, 132.2, 128.5, 126.5, 125.5, 125.0, 122.6, 68.5, 54.8, 34.5, 31.4, 29.3, 19.6, 15.7; **¹⁹F NMR** (375 MHz, CDCl₃) δ -65.5 (s, 6F); (-164.9, C₆F₆); **HRMS** [+NSI] calculated for C₃₆H₄₀BrF₆IrN₄O 930.1919, found 930.2139 [M-HBr]⁺; [**α**]_D²⁰ +25.2 ° (c 0.1, CHCl₃).

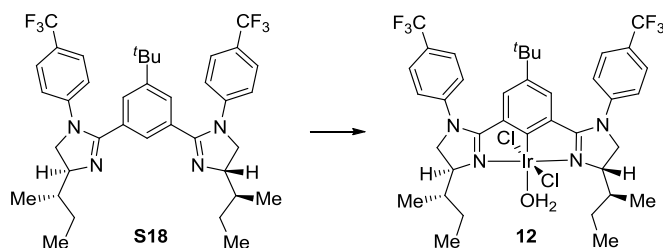


[(*S,S*)-*t*-ButylPhebim-4-CF₃-Ph-*i*-Bu]IrCl₂(H₂O) (10**).** Prepared by general procedure **D** using ligand **S16** (749 mg, 1.12 mmol), IrCl₃·3H₂O (445 mg, 1.23 mmol), and NaHCO₃ (103 mg,

1.23 mmol). The reaction was refluxed in *i*PrOH (37 mL) for 4.5 h. Flash chromatography (7:3 hexanes:EtOAc) afforded iridium(III) phebim **10** as a dark red solid (545 mg, 51 %); **R_f** 0.56 (7:3 hexanes:EtOAc); **mp** 218 ° C; **IR** (thin film, cm⁻¹) 3734, 3045, 2357, 2024, 1699, 1558, 1226, 782, 694; **¹H NMR** (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.6 Hz, 4H), 7.39 (d, *J* = 8.2 Hz, 4H), 6.65 (s, 2H), 4.53 (t, *J* = 10.6 Hz, 2H), 4.41-4.34 (m, 2H), 4.07 (dd, *J* = 9.2, 6.8 Hz, 2H), 2.77 (s, 2H), 2.20-2.13 (m, 2H), 1.74-1.65 (m, 4H), 1.02 (t, *J* = 6.5 Hz, 12H), 0.86 (s, 9H); **¹³C NMR** (150 MHz, CDCl₃) δ 169.7, 144.4, 142.9, 132.2, 128.6, 126.4, 125.44, 125.31, 62.3, 60.0, 43.7, 34.4, 31.3, 25.7, 24.1, 21.8, 18.6; **¹⁹F NMR** (375 MHz, CDCl₃) δ -65.6 (s, 6F); (-164.9, C₆F₆); **HRMS** [+APCI] calculated for C₃₈H₄₃N₄Cl₂F₆Ir 932.2393, found 932.2400 [M-H₂O]⁺; [**α**]_D²⁰ +15.9 ° (c 0.1, CHCl₃).

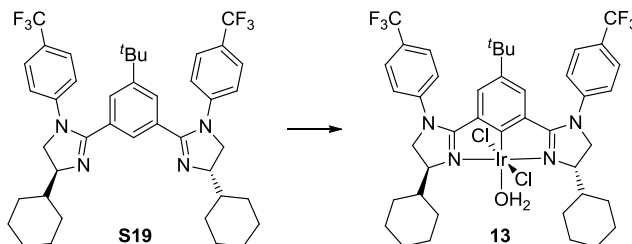


[(*R,R*)-*t*-ButylPhebim-4-CF₃Ph-*n*-Bu]IrCl₂(H₂O) (11**).** Prepared by general procedure **D** using **S17** (110 mg, 0.16 mmol), IrCl₃·3H₂O (65 mg, 0.18 mmol), and NaHCO₃ (17 mg, 0.20 mmol). The reaction was refluxed in *i*PrOH (5 mL) for 5 h. Preparative thin layer chromatography (7:3 hexanes:EtOAc) afforded iridium(III) phebim **11** as an orange solid (83 mg, 55 %); **R_f** 0.45 (7:3 hexanes:EtOAc); **mp** 230 ° C; **IR** (thin film, cm⁻¹) 3334, 2959, 2049, 1614, 1526, 1453, 1323, 1127, 1069; **¹H NMR** (400 MHz, CDCl₃) δ 7.60 (d, *J* = 9.2 Hz, 4H), 7.41 (d, *J* = 7.9 Hz, 4H), 6.68 (s, 2H), 4.54 (t, *J* = 9.8 Hz, 2H), 4.35 (br s, 2H), 4.07 (dd, *J* = 9.1, 6.7 Hz, 2H), 2.15 (br s, 2H), 1.82-1.74 (m, 2H), 1.47-1.24 (m, 9H) 0.91-0.82 (m, 14H); **¹³C NMR** (100 MHz, CDCl₃) δ 171.7, 145.9, 143.2, 131.9, 126.5, 126.4, 126.1, 126.0, 64.7, 59.0, 34.2, 30.9, 26.9, 22.5, 13.9; **HMRS** (+APCI) calculated for C₃₈H₄₃Cl₂F₆N₄Ir 932.2393, found 932.2388 [M-H₂O]⁺; [**α**]_D²⁰ -18.9 ° (c 0.1, CHCl₃).

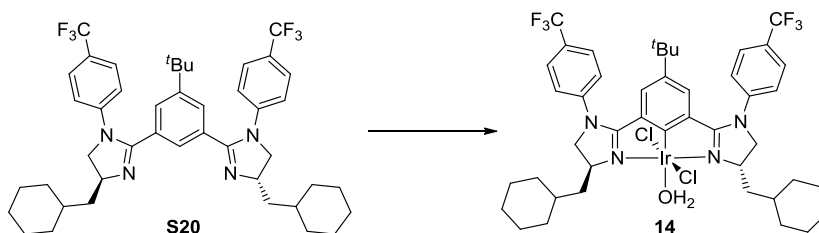


[(*S,S*)-*t*-ButylPhebim-4-CF₃Ph-*s*-Bu]IrCl₂(H₂O) (12**).** Prepared by general procedure **D** using ligand **S18** (100 mg, 0.15 mmol), IrCl₃·3H₂O (60 mg, 0.17 mmol), and NaHCO₃ (15 mg, 0.17 mmol). The reaction was refluxed in *i*PrOH (5 mL) for 7.5 h. Flash chromatography (1:1 → 3:7 hexanes:EtOAc) afforded iridium(III) phebim complex **12** as a dark red solid (50 mg, 35 %); **R_f** 0.36 (1:1 hexanes:EtOAc); **mp** 190 ° C; **IR** (thin film, cm⁻¹) 3853, 3019, 2361, 1714, 1540, 1214, 745, 668; **¹H NMR** (600 MHz, CDCl₃) δ 7.67 (d, *J* = 8.2 Hz, 4H), 7.37 (d, *J* = 8.2 Hz, 4H), 6.71 (s, 2H), 4.47 (t, *J* = 10.1 Hz, 2H), 4.40 (br s, 2H), 4.10-4.04 (m, 2H), 2.62 (br s, 2H), 2.25 (s, 2H), 1.41-1.35 (m, 2H), 1.31-1.27 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 6H), 0.94 (d, *J* = 6.3 Hz,

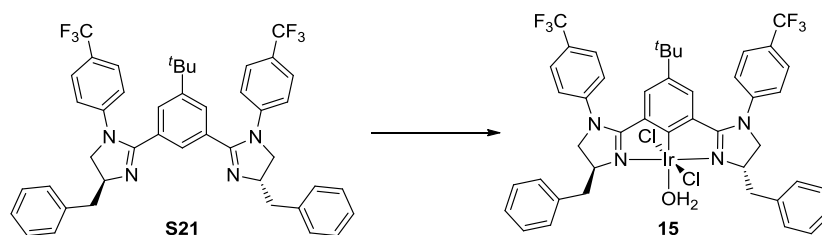
6H), 0.88 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 187.4, 144.4, 126.4, 125.5, 125.2, 66.9, 54.6, 36.4, 34.5, 31.3, 26.9, 14.4, 12.3; ^{19}F NMR (375 MHz, CDCl_3) δ -65.6 (s, 6F); (-164.9, C_6F_6); HRMS [+APCI] calculated for $\text{C}_{38}\text{H}_{43}\text{N}_4\text{Cl}_2\text{F}_6\text{Ir}$ 932.2393, found 932.2403 $[\text{M}-\text{H}_2\text{O}]^+$; $[\alpha]^{20}_{\text{D}} +26.5^\circ$ (c 0.1, CHCl_3).



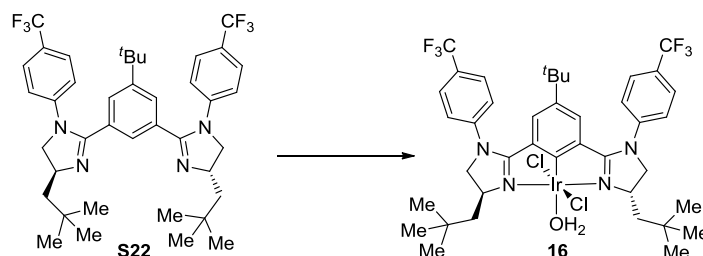
[(*S,S*)-*t*-ButylPhebim-4- CF_3Ph - ^cHex] $\text{IrCl}_2(\text{H}_2\text{O})$ (13**).** Prepared by general procedure **D** using ligand **S19** (139 mg, 0.19 mmol), $\text{IrCl}_3 \cdot 3\text{H}_2\text{O}$ (75 mg, 0.21 mmol), and NaHCO_3 (18 mg, 0.21 mmol). The reaction was refluxed in $i\text{PrOH}$ (6.5 mL) for 4.5 h. Preparative thin layer chromatography (7:3 hexanes:EtOAc) gave iridium(III) phebim **13** as a dark red solid (80 mg, 42 %); R_f 0.29 (7:3 hexanes:EtOAc); mp 216 $^\circ\text{C}$; IR (thin film, cm^{-1}) 3675, 2924, 2365, 1558, 1226, 781, 656; ^1H NMR (600 MHz, CDCl_3) δ 7.67 (d, $J = 8.5$ Hz, 4H), 7.36 (d, $J = 8.5$ Hz, 4H), 6.71 (s, 2H), 4.49 (t, $J = 10.2$ Hz, 2H), 4.23-4.20 (m, 2H), 4.14-4.10 (m, 2H), 2.15 (td, $J = 12.0, 2.4$ Hz, 2H), 1.95 (d, $J = 11.7$ Hz, 2H), 1.80 (d, $J = 12.9$ Hz, 2H), 1.70-1.65 (m, 6H), 1.35 (q, $J = 12.9$ Hz, 2H), 1.27-1.22 (m, 4H), 1.14-1.02 (m, 4H), 0.88 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 171.4, 169.7, 144.4, 143.2, 132.1, 128.2 (q, $^2J_{\text{C-F}} = 33.0$) 126.4, 125.4, 125.1, 123.1, 68.1, 60.6, 55.3, 39.7, 34.5, 31.3, 30.1, 26.7 (dd, $^1J_{\text{C-F}} = 178$, $^2J_{\text{C-F}} = 33.0$), 21.2, 18.7, 14.4; ^{19}F NMR (375 MHz, CDCl_3) δ -65.5 (s, 6F); (-164.9, C_6F_6); HRMS [+APCI] calculated for $\text{C}_{42}\text{H}_{47}\text{N}_4\text{Cl}_2\text{F}_6\text{Ir}$ 984.2706, found 984.2724 $[\text{M}-\text{H}_2\text{O}]^+$; $[\alpha]^{20}_{\text{D}} +28.4^\circ$ (c 0.1, CHCl_3).



[(*S,S*)-*t*-ButylPhebim-4- $\text{CF}_3\text{Ph}-\text{CH}_2^c\text{Hex}$] $\text{IrCl}_2(\text{H}_2\text{O})$ (14**).** Prepared by general procedure **D** using ligand **S20** (595 mg, 0.79 mmol), $\text{IrCl}_3 \cdot 3\text{H}_2\text{O}$ (314 mg, 0.89 mmol), and NaHCO_3 (75 mg, 0.89 mmol). The reaction was refluxed in $i\text{PrOH}$ (26 mL) for 4.5 h. Flash chromatography (7:3 hexanes:EtOAc) afforded iridium(III) phebim **14** as a light orange solid (428 mg, 52 %); R_f 0.63 (7:3 hexanes:EtOAc); mp 236 $^\circ\text{C}$; IR (thin film, cm^{-1}) 3019, 2347, 2039, 1710, 1214, 745, 667; ^1H NMR (600 MHz, CDCl_3) δ 7.68 (d, $J = 8.4$ Hz, 4H), 7.40 (d, $J = 8.4$ Hz, 4H), 6.70 (s, 2H), 4.56 (t, $J = 9.7$ Hz, 2H), 4.42-4.37 (m, 2H), 4.06 (dd, $J = 9.0, 7.0$ Hz, 2H), 2.20 (ddd, $J = 13.6, 10.3, 2.7$ Hz, 2H), 1.95 (br s, 2H), 1.87 (d, $J = 12.8$ Hz, 2H), 1.77-1.67 (m, 8H), 1.40-1.34 (m, 2H), 1.25-1.13 (m, 8H), 1.12-1.00 (m, 4H), 0.88 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 187.1, 169.6, 144.5, 143.1, 132.2, 126.5, 125.5, 125.4, 124.9, 123.1, 61.9, 60.2, 42.6, 35.4, 34.7, 34.6, 32.7, 31.4, 26.6, 26.5; ^{19}F NMR (375 MHz, CDCl_3) δ -65.6 (s, 6F); (-164.9, C_6F_6); HRMS [+APCI] calculated for $\text{C}_{44}\text{H}_{51}\text{N}_4\text{Cl}_2\text{F}_6\text{Ir}$ 1012.3019, found 1012.3025 $[\text{M}-\text{H}_2\text{O}]^+$; $[\alpha]^{20}_{\text{D}} +24.2^\circ$ (c 0.1, CHCl_3).

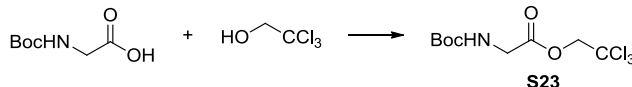


[(*S,S*)-*t*-ButylPhebim-*p*-CF₃Ph-Bn]IrCl₂(H₂O) (15**).** Prepared by general procedure **D** using ligand **S21** (140 mg, 0.19 mmol), IrCl₃·3H₂O (78 mg, 0.22 mmol), and NaHCO₃ (18 mg, 0.22 mmol). The reaction was refluxed in *i*PrOH (6 mL) for 6 h. Preparative thin layer chromatography (7:3 hexanes:EtOAc) afforded iridium(III) phebim **15** as an orange solid (104 mg, 54 %); **R_f** 0.41 (7:3 hexanes:EtOAc); **mp** 180 ° C; **IR** (thin film, cm⁻¹) 3338, 2962, 2231, 2046, 1525, 1452, 1321, 1125, 1068; **¹H NMR** (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.6 Hz, 4H), 7.39 (d, *J* = 8.2 Hz, 4H), 7.35-7.32 (m, 4H), 7.29-7.23 (m, 6H), 6.71 (s, 2H), 4.63 (tdd, *J* = 7.1, 3.9 Hz, 2H), 4.28 (t, *J* = 10.1 Hz, 2H), 4.04 (dd, *J* = 9.9, 7.2 Hz, 2H), 3.68 (dd, *J* = 14.0, 3.9 Hz, 2H), 2.96 (dd, *J* = 14.0, 10.5 Hz, 2H), 0.84 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 174.2, 172.2, 146.2, 136.5, 131.9, 129.3, 128.9, 126.9, 126.5, 126.4, 126.3, 126.2, 65.8, 58.7, 40.9, 34.6, 30.9; **¹⁹F NMR** (375 MHz, CDCl₃) δ -65.7 (s, 6F); (-164.9, C₆F₆); **HMRS** (+APCI) calculated for C₄₄H₃₈ClF₆N₄Ir 964.2313, found 964.2306 [M-H₂O-Cl-H]⁺; [**α**]_D²⁰ + 20.5 ° (c 0.1, CHCl₃).

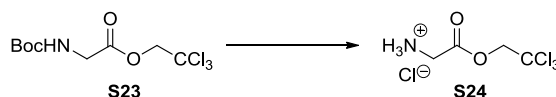


[(*S,S*)-*t*-ButylPhebim-*p*-CF₃Ph-CH₂^{*t*}Bu]IrCl₂(H₂O) (16**).** Prepared by general procedure **D** using ligand **S22** (99 mg, 0.14 mmol, 1.0 equiv), IrCl₃·3H₂O (60 mg, 0.17 mmol, 1.2 equiv), and NaHCO₃ (15 mg, 0.17 mmol, 1.2 equiv). The reaction was refluxed in *i*PrOH (5 mL) for 5 h. Preparative thin layer chromatography (8:2 hexanes:acetone) afforded iridium(III) phebim **16** as a red solid (43 mg, 31% yield); **R_f** 0.20 (8:2 hexanes:acetone); **mp** ≥ 250 ° C; **IR** (neat, cm⁻¹) 2955, 2835, 1613, 1558, 1474, 1321, 1291, 1124, 1068, 846, 599; **¹H NMR** (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.0 Hz, 4H), 7.41 (d, *J* = 8.0 Hz, 4H), 6.69 (s, 2H), 4.63 (t, *J* = 10.0 Hz, 2H), 4.34 (q, *J* = 10.0 Hz, 2H), 4.04 (t, *J* = 10.0 Hz, 2H), 2.86 (s, 4H), 2.46 (d, *J* = 16 Hz, 2H), 1.67 (dd, *J* = 10.0, 16.0 Hz, 2H), 1.04 (s, 18H), 0.87 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 169.6, 144.3, 142.6, 132.1, 127.9 (q, *J* = 33.0 Hz), 126.2 (q, *J* = 4.0 Hz), 125.3, 125.2, 122.4, 62.0, 60.8, 48.7, 34.3, 31.2, 31.1, 30.0, 30.2; **¹⁹F NMR** (375 MHz, CDCl₃) δ -65.6 (s, 6F); (-164.9, C₆F₆); **HRMS** (+NSI) calculated for C₄₀H₄₇Cl₂F₆N₄Ir 960.2706, found 960.2725 [M-H₂O]⁺; [**α**]_D²⁰ + 55.3 ° (c 0.4, CHCl₃).

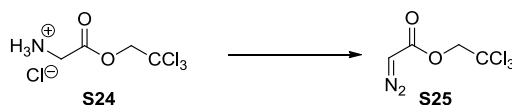
b) Diazoacetate Synthesis



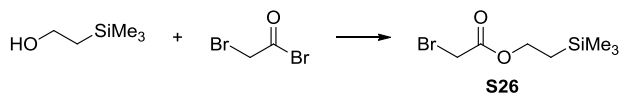
2,2,2-trichloroethyl 2-((tert-butoxycarbonyl)amino)acetate (S23). Prepared via the method of Veri.⁶ *N*-(*t*-butoxycarbonyl)glycine (3.3 g, 18.7 mmol) and 2,2,2-trichloroethanol (2.9 mL, 30.1 mmol) were stirred at 0 °C in CH₂Cl₂ (60 mL). DMAP (0.49 g, 4.0 mmol) and *N,N'*-dicyclohexylcarbodiimide (4.9 g, 23.6 mmol) were added and the resulting mixture was stirred at 0 °C for 3 h and then 23 °C overnight. The resulting solution was filtered and the filtrate was concentrated. The concentrate was then taken up in 50 mL each of EtOAc and water. The organic phase was then washed with two 30 mL portions of saturated NaHCO₃(aq) and brine. Following concentration, the residue was purified by flash chromatography (8:2 hexanes:EtOAc) to yield a white crystalline solid (2.04 g, 36 % yield); *R*_f 0.65 (EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 5.02 (s, 1H), 4.79 (s, 2H), 4.07 (d, *J* = 6.0 Hz, 2H), 1.46 (s, 9H). All spectral data matched those previously reported.^{6,7}



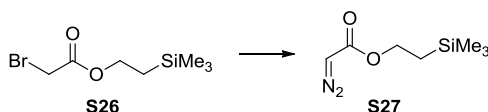
2-oxo-2-(2,2,2-trichloroethoxy)ethanaminium chloride (S24). A 4 M solution of HCl in EtOAc was cooled to 0 °C in a 50 mL round bottom flask equipped with a stir bar. **S23** (0.91 g, 3.0 mmol) was added in one portion and stirred at 0 °C for 90 min at which time the reaction was judged to be complete by TLC. The mixture was concentrated *in vacuo*, and the resulting solid was washed with dry Et₂O to yield a white crystalline solid in quantitative yield; *R*_f 0.55 (8:2 hexanes:EtOAc); ¹H NMR (400 MHz, D₂O) δ 5.00 (s, 2H), 4.10 (s, 2H). All spectral data matched those previously reported.⁶



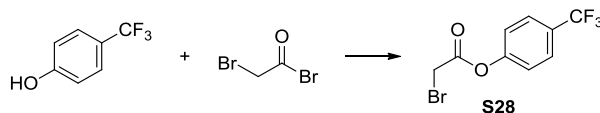
2,2,2-trichloroethyl 2-diazoacetate (S25). A 100 mL round bottom flask equipped with a stir bar was charged with **S24** (0.31 g, 1.3 mmol), CH₂Cl₂ (15 mL) and distilled water. The mixture was stirred and cooled to 0 °C. NaNO₂ (0.45 g, 6.6 mmol) was added, followed by 10% H₂SO₄ (aq) (3 mL). The mixture was stirred at 0 °C for 2 h at which time the reaction was judged to be complete by TLC. The organic layer was separated and washed with saturated NaHCO₃ (aq), dried with Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash chromatography (7:1 pentane:Et₂O) to afford a yellow oil (65.1 mg, 24 % yield); *R*_f 0.64 (7:3 hexanes:EtOAc). IR (neat, cm⁻¹) 2116, 1703, 1385, 1349, 1218, 1148, 1045, 796, 715, 572; ¹H NMR (400 MHz, CDCl₃) δ 4.79 (s, 2H), 4.90 (br s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 164.5, 95.0, 73.6, 46.6; HRMS (+NSI) calculated for C₄H₃Cl₃N₂O₂Na 238.9158, found 238.9164 [M+Na]⁺.



2-(trimethylsilyl)ethyl 2-bromoacetate (S26). Prepared via the method of Caprioli and coworkers.⁸ A 100 mL round bottom flask equipped with a stir bar was flame dried and placed under N₂ atmosphere. The flask was charged with 2-(trimethylsilyl)ethanol (1.7 mL, 11.5 mmol), pyridine (0.88 mL, 10.9 mmol), DMAP (124 mg, 1.0 mmol) and CH₂Cl₂ (20 mL). The mixture was stirred and cooled to 0 °C. Bromoacetyl bromide (0.97 mL, 11.1 mmol) was then added dropwise. The ice bath was removed and the resulting solution was allowed to stir for 2 h at 23 °C. The reaction was washed with two portions of 1 M HCl (aq) (15 mL each) followed by brine (15 mL). The organic layer was then dried with Na₂SO₄ and concentrated *in vacuo* to afford a brown oil (1.8 g, 68 % yield); *R*_f 0.68 (8:2 hexanes:Et₂O); ¹H NMR (400 MHz, CDCl₃) δ 4.29-4.24 (m, 2H), 3.81 (s, 2H), 1.06-1.01 (m, 2H), 0.05 (s, 9H). All spectral data matched those previously reported.⁸

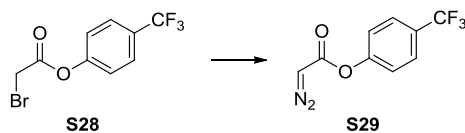


2-(trimethylsilyl)ethyl 2-diazoacetate (S27). A 100 mL round bottom flask equipped with a stir bar was flame dried and placed under N₂ atmosphere. The flask was then charged with **S26** (1.3 g, 5.4 mmol), THF (25 mL) and *N,N'*-ditosylhydrazine⁹ (3.5 g, 10.2 mmol). The mixture was stirred and cooled to 0 °C. DBU (3.7 mL, 24.7 mmol) was then added dropwise over 15 min. After stirring at 0 °C for another 20 min, starting material was judged to be completely consumed by TLC. Saturated NaHCO₃ (aq) (25 mL) was added, followed by extraction with Et₂O. The organic layer was further washed with water (25 mL) and brine (25 mL), dried with MgSO₄, and concentrated *in vacuo*. The residue was purified by flash chromatography (8:2 hexanes:Et₂O) to yield a yellow oil (0.5 g, 50 % yield); *R*_f 0.7 (8:2 hexanes:Et₂O); *IR* (neat, cm⁻¹) 2106, 1695, 1390, 1351, 1248, 1175, 1043, 858, 836, 742; ¹H NMR (400 MHz, CDCl₃) δ 4.69 (br s, 1H), 4.26-4.21 (m, 2H), 1.00-0.96 (m, 2H), 0.02 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ -1.5, 17.5, 46.1, 63.1, 166.9; *HRMS* (+NSI) calculated for C₇H₁₄N₂O₂SiNa 209.0722, found 209.0719 [M+Na]⁺.



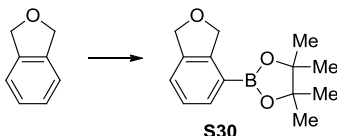
4-(trifluoromethyl)phenyl 2-bromoacetate (S28). Prepared by the method of Candish and Lupton.¹⁰ A 100 mL round bottom flask equipped with a stir bar was flame dried and placed under N₂ atmosphere. The flask was charged with CH₃CN (25 mL), pyridine (0.85 mL, 10.5 mmol, 2.1 equiv) and 4-(trifluoromethyl)phenol (800 mg, 4.9 mmol, 1.0 equiv). The mixture was then stirred and cooled to 0 °C. Bromoacetyl bromide (0.68 mL, 7.8 mmol, 1.6 equiv) was then added dropwise. The resulting solution was allowed to stir 15 min at 0 °C and then water (12 mL) was added. The mixture was extracted with CH₂Cl₂, dried with Na₂SO₄, concentrated *in vacuo*, and purified by flash chromatography (95:5 hexanes:EtOAc) to afford a slightly yellow oil (1.0 g, 72 % yield); *R*_f 0.57 (9:1 hexanes:EtOAc); *IR* (neat, cm⁻¹) 1766, 1611, 1320, 1259, 1203, 1101, 1062, 1017, 928, 853, 689, 586; ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d,

$J = 12$ Hz, 2H), 7.26 (d, $J = 12$ Hz, 2H); 4.07 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.3, 152.7, 129.6 (q, $J = 33$ Hz), 126.9 (q, $J = 4$ Hz), 125.0, 121.6, 25.2; ^{19}F NMR (375 MHz, CDCl_3) δ -65.5 (s, 3F), (-164.9, C_6F_6).

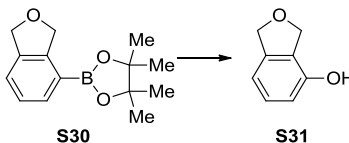


4-(trifluoromethyl)phenyl 2-diazoacetate (S29). A 100 mL round bottom flask equipped with a stir bar was flame dried and placed under N_2 atmosphere. The flask was charged with THF (25 mL), **S28** (1.1 g, 3.9 mmol) and N,N' -ditosylhydrazine⁹ (3.4 g, 10.0 mmol), stirred and cooled to 0 °C. DBU (3.7 mL, 24.7 mmol) was added dropwise over 15 min and the reaction was permitted to stir at 0 °C for another 15 min once addition was complete. Saturated NaHCO_3 (aq) (25 mL) was added, and the resulting mixture was extracted with Et_2O , washed with brine, and dried with Na_2SO_4 . Concentration *in vacuo* and purification by flash chromatography (hexanes $\rightarrow$ 95:5 hexanes:EtOAc) afforded a yellow oil (239 mg, 27 % yield); R_f 0.21 (9:1 hexanes:EtOAc); IR (neat, cm^{-1}) 3128, 2116, 1703, 1614, 1513, 1368, 1320, 1117, 1101, 1061, 1016, 725; ^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 5.04 (br s, 1H), ^{13}C NMR (100 MHz, CDCl_3) δ 152.9, 127.8, (q, $J = 30.0$ Hz), 126.7, (q, $J = 4.0$ Hz), 125.2, 122.5, 122.0, 47.0; ^{19}F NMR (375 MHz, CDCl_3) δ -65.4 (s, 3F), (-164.9, C_6F_6); HRMS (+NSI) calculated for $\text{C}_9\text{H}_5\text{N}_2\text{O}_2\text{F}_3\text{Na}$ 253.0195, found 253.0198 $[\text{M}+\text{Na}]^+$.

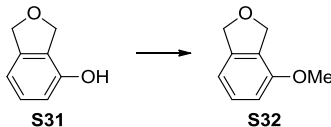
c) Substrate Synthesis



2-(1,3-dihydroisobenzofuran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S30). An oven-dried flask equipped with a reflux condenser was charged with phthalan (2.4 mL, 21.9 mmol, 1 equiv), $[\text{Ir}(\text{OMe})(\text{cod})]_2$ (39 mg, 0.06 mmol, 0.25 mol %), 3,4,7,8-tetramethyl-1,10-phenanthroline (62 mg, 0.26 mmol, 1 mol %), and bis(pinacolato)diboron (4.2 g, 16.7 mmol, 0.75 equiv) in tetrahydrofuran (108 mL). The mixture was heated to reflux for 22 h with vigorous stirring. The reaction mixture was cooled to room temperature and filtered through silica gel. The filtrate was concentrated *in vacuo* and flash chromatography (95:5 hexanes:EtOAc) afforded the title compound as a white solid (1.7 g, 32 %); R_f 0.55 (9:1 hexanes/EtOAc); mp 74–76 °C; IR (thin film, cm^{-1}) 2978, 2857, 1603, 1350, 1129, 1047, 967; ^1H NMR (400 MHz, CDCl_3) δ 7.68 (d, J = 7.0 Hz, 1H), 7.31 (d, J = 7.4 Hz, 1H), 7.27–7.23 (m, 1H), 5.23 (t, J = 2.0 Hz, 2H), 5.11–5.09 (m, 2H), 1.31 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 146.1, 138.2, 133.9, 126.5, 123.6, 83.8, 74.8, 73.2, 24.9; HRMS [+NSI] calculated for $\text{C}_{14}\text{H}_{19}\text{O}_3\text{BNa}$ 269.1319, found 269.1319 $[\text{M}+\text{Na}]^+$.

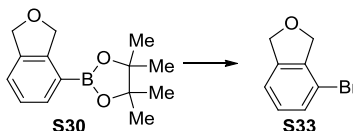


1,3-dihydroisobenzofuran-4-ol (S31). H_2O_2 (5 mL, 30 wt. % in H_2O) was added to a solution of S30 (1.7 g, 6.9 mmol, 1 equiv) in H_2O (5 mL) at room temperature. The reaction was stirred until thin layer chromatography indicated complete consumption of starting material (1 h). The mixture was transferred to a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (3 x). The combined organic extracts were washed with brine, dried over MgSO_4 and concentrated *in vacuo*. Flash chromatography (7:3 hexanes:EtOAc) afforded the title compound as a white solid (518 mg, 55 %); ^1H NMR (400 MHz, CDCl_3) δ 7.14–7.11 (m, 2H), 6.8 (d, J = 7.6 Hz, 1H), 6.63 (d, J = 8.2 Hz, 1H), 5.11 (d, J = 2.9 Hz, 4H). All spectral data matched those previously reported.¹¹

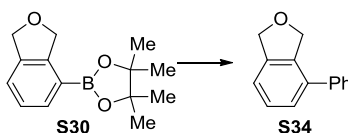


4-methoxy-1,3-dihydroisobenzofuran (S32). An oven-dried round bottom flask was charged with S31 (518 mg, 3.8 mmol, 1 equiv) and K_2CO_3 (1.06 g, 7.7 mmol, 2 equiv) in MeCN (15 mL). MeI (390 μL , 6.3 mmol, 1.6 equiv) was added via syringe. The reaction mixture was heated to 35 °C. Once thin layer chromatography indicated complete consumption of starting material (24 h), the reaction was quenched by the addition of NH_4Cl (aq). The biphasic mixture was transferred to a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (3 x). The combined organic extracts were washed with brine, dried over MgSO_4 and concentrated *in*

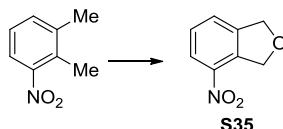
vacuo. Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a white solid (484 mg, 85 %); ¹H NMR (400 MHz, CDCl₃) δ 7.24-7.21 (m, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 8.3 Hz, 1H), 5.09 (s, 4H), 3.82-3.81 (m, 3H). All spectral data matched those previously reported.¹²



4-bromo-1,3-dihydroisobenzofuran (S33). Prepared according to literature procedure¹³ using **S30** (740 mg, 3.0 mmol), CuBr₂ (2 g, 9.0 mmol), MeOH (38 mL), and H₂O (38 mL). After heating for 6 h, flash chromatography (95:5 hexanes:EtOAc) afforded the title compound as a white amorphous solid (275 mg, 46 % yield); *R*_f 0.65 (9:1 hexanes:EtOAc); IR (thin film, cm⁻¹) 2852, 1720, 1574, 1447, 1128, 1045, 881; ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.34 (m, 1H), 7.15-7.08 (m, 2H), 5.15 (d, *J* = 7.8 Hz, 2H), 5.06 (d, *J* = 7.8 Hz, 2H), 4.18 (t, *J* = 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 141.0, 139.8, 130.2, 129.2, 119.7, 115.9, 74.7, 74.6; HRMS [+APCI] calculated for C₈H₈OBr 198.9753, found 198.9752 [M+H]⁺.

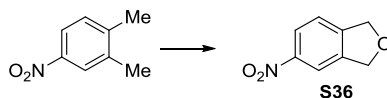


4-phenyl-1,3-dihydroisobenzofuran (S34). Prepared according to literature procedure¹⁴ using **S30** (50 mg, 0.20 mmol, 1 equiv), Pd(PPh₃)₄ (12 mg, 5 mol %), K₂CO₃ (56 mg, 0.41 mmol, 2 equiv), and PhI (50 μL, 0.45 mmol, 2 equiv) in DMF (0.6 mL). After heating for 19 h, flash chromatography (9:1 hexanes:EtOAc) afforded the title compound as a white solid (34 mg, 85 % yield); ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.30 (m, 7H), 7.22 (d, *J* = 7.4 Hz, 1H), 5.19 (d, *J* = 2.0 Hz, 2H), 5.17 (d, *J* = 2.0 Hz, 2H). All spectral data matched those previously reported.¹²

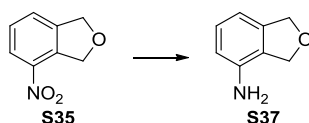


4-nitro-1,3-dihydroisobenzofuran (S35). Adapting a procedure by Favor and coworkers,¹⁵ a 250 mL round bottom flask equipped with a stir bar and condenser was charged with 1,2-dimethyl-3-nitrobenzene (7.9 mL, 59 mmol, 1.0 equiv) followed by *N*-bromosuccinimide (24 g, 135 mmol, 2.3 equiv) and CCl₄ (36 mL). The yellow suspension was stirred and benzoyl peroxide (150 mg, 0.01 equiv) was added. The suspension was stirred at reflux for 2 h, at which time another 500 mg (0.04 equiv) of benzoyl peroxide was added. The reaction was heated at reflux for another 2 h at which time it was cooled to room temperature, filtered to remove a white solid which was washed with additional CCl₄, and concentrated *in vacuo* to afford a yellow oil. The oil was immediately transferred to a clean 250 mL round bottom flask equipped with a condenser and stir bar. PhCH₃ (100 mL) was added, followed by neutral Al₂O₃ (75 g, Brockmann Activity I grade), and H₂O (5 mL) with vigorous stirring. The yellow suspension was heated to an external temperature of 120 °C for 40 h. The reaction was cooled to room temperature, filtered, and concentrated *in vacuo* to afford a yellow oil. Flash chromatography on

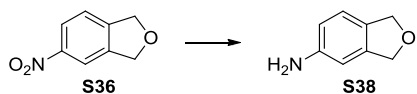
silica gel (95:5 → 93:7 hexanes:EtOAc) yielded a yellow powder (2.4 g, 25% yield over 2 steps); **R_f** 0.21 (9:1 hexanes:EtOAc); **mp** 106-108 ° C; **IR** (neat, cm⁻¹) 2916, 2863, 1518, 1338, 1045, 904, 818, 732; **¹H NMR** (400 MHz, CDCl₃) δ 8.14 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 5.53 (s, 2H), 5.20 (s, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 143.3, 143.1, 136.3, 129.0, 127.0, 122.7, 74.8, 73.2; **HRMS** (+APCI) calculated for C₈H₈O₃N 166.0499, found 166.0498 [M+H]⁺.



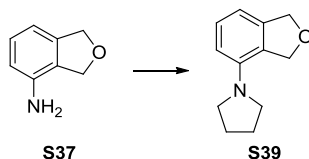
5-nitro-1,3-dihydroisobenzofuran (S36). Adapting a procedure by Favor and coworkers,¹⁵ a 250 mL round bottom flask equipped with a stir bar and condenser was charged with 1,2-dimethyl-4-nitrobenzene (8.0 g, 53 mmol, 1.0 equiv) followed by *N*-bromosuccinimide (24.6 g, 138 mmol, 2.6 equiv) and CCl₄ (40 mL). The yellow suspension was stirred and benzoyl peroxide (120 mg, 0.01 equiv) was added. The suspension was stirred at reflux for 2 h, at which time another 500 mg (0.04 equiv) of benzoyl peroxide was added. The reaction was heated at reflux for another 2 h at which time it was cooled to room temperature, filtered to remove a white solid which was washed with additional CCl₄, and concentrated *in vacuo* to afford a yellow oil. The oil was immediately transferred to a clean 250 mL round bottom flask equipped with a condenser and stir bar. PhCH₃ (100 mL) was added, followed by neutral Al₂O₃ (150 g, Brockmann Activity I grade), and H₂O (5 mL) with vigorous stirring. The now unstirrable yellow slurry was heated to an external temperature of 120 ° C for 4 h. The reaction was cooled to room temperature, filtered, and concentrated *in vacuo* to afford a yellow oil. Flash chromatography on silica gel (95:5 to 9:1 hexanes:EtOAc) yielded a yellow powder (2.04 g, 23% yield over 2 steps). **R_f** 0.24 (90:10 hexanes:EtOAc); **mp** 92-95 °C; **IR** (neat, cm⁻¹) 3105, 3036, 2859, 1519, 1343, 1321, 1043, 898, 736; **¹H NMR** (400 MHz, CDCl₃) δ 8.18 (dd, *J* = 2.0, 8.4 Hz, 1H), 8.11 (d, *J* = 1.6 Hz 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 5.18 (s, 4H); **¹³C NMR** (100 MHz, CDCl₃) δ 148.0, 146.4, 141.0, 123.3, 121.7, 116.6, 73.2, 73.0; **HRMS** (+APCI) calculated for C₈H₈O₃N 166.0499, found 166.0498 [M+H]⁺.



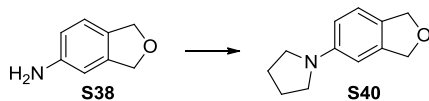
1,3-dihydroisobenzofuran-4-amine (S37). Adapting a procedure by Favor and coworkers,¹⁵ a 100 mL round bottom flask was equipped with a stir bar and charged with 4-nitro-1,3-dihydroisobenzofuran **S35** (2.4 g, 14.8 mmol) followed by THF (50 mL). The yellow suspension was vigorously stirred and 2 disposable glass pipettes' volumes of Raney[®] Ni (2800, slurry in H₂O) were added. The suspension was vigorously stirred at 23 °C for 19 h under a balloon of H₂. Filtration through Celite followed by concentration *in vacuo* afforded a yellow powder (1.8 g, 89% yield); **R_f** 0.16 (8:2 hexanes:EtOAc); **mp** 86-88 ° C; **IR** (neat, cm⁻¹) 3375, 3216, 3039, 2853, 1601, 1488, 1305, 1032, 995, 894, 757; **¹H NMR** (400 MHz, CDCl₃) δ 7.10 (t, *J* = 8.0 Hz, 1H), 6.67 (dd, *J* = 0.8, 8.0 Hz, 1H), 6.57 (dd, *J* = 0.8, 8.0 Hz, 1H), 5.12-5.10 (m, 2H), 5.04-5.02 (m, 2H), 3.54 (s, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 140.3, 140.2, 128.7, 123.8, 113.4, 110.8, 74.2, 71.7; **HRMS** (+NSI) calculated for C₈H₁₀ON 136.0757, found 136.0756 [M+H]⁺.



1,3-dihydroisobenzofuran-5-amine (S38). Adapting a procedure by Favor and coworkers,¹⁵ a 100 mL round bottom flask equipped with a stir bar and charged with 5-nitro-1,3-dihydroisobenzofuran **S36** (2.0 g, 12.2 mmol) followed by THF (40 mL). The yellow suspension was vigorously stirred and 2 disposable glass pipettes' volumes of Raney[®] Ni (2800, slurry in H₂O) were added. The suspension was vigorously stirred at 23 ° C for 24 h under a balloon of H₂. Filtration through Celite followed by concentration afforded a yellow powder (1.6 g, 11.9 mmol, 98% yield); **R_f** 0.16 (8:2 hexanes:EtOAc); **mp** 104-106 ° C; **IR** (neat, cm⁻¹) 3330, 3233, 3021, 2850, 1607, 1491, 1367, 1295, 1026, 818; **¹H NMR** (400 MHz, CDCl₃) δ 7.00 (d, *J* = 8.0 Hz, 1H), 6.60 (dd, *J* = 2.0 Hz, 8.0 Hz, 1H), 6.55 (d, *J* = 2.0 Hz, 1H), 5.01 (s, 4H), 3.70 (s, 2H), **¹³C NMR** (100 MHz, CDCl₃) δ 145.9, 140.5, 128.9, 121.5, 114.4, 107.3, 73.4, 73.3; **HRMS** (+NSI) calculated for C₈H₁₀ON 136.0757, found 136.0756[M+H]⁺.

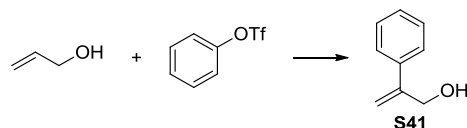


1-(1,3-dihydroisobenzofuran-4-yl)pyrrolidine (S39). Adapting a procedure by Xiong, Chen and coworkers,¹⁶ a 25 mL round bottom flask equipped with a stir bar and reflux condenser was flame dried and placed under N₂ atmosphere. The flask was then charged with **S37** (399 mg, 3.0 mmol, 1.0 equiv), K₂CO (1.3 g, 9.4 mmol, 3 equiv), CH₃CN (10 mL), and 1,4-dibromobutane (0.4 mL, 3.4 mmol, 1.1 equiv). The reaction mixture was stirred and heated to a vigorous reflux for 22 h at which times another 0.1 mL of 1,4-dibromobutane was added. After 45 h total of vigorous reflux, the orange mixture was cooled to 23 ° C, filtered, and concentrated *in vacuo* to give a yellow oil. Flash chromatography on silica gel yielded a slightly yellow oil (305 mg, 55 % yield); **R_f** 0.44 (9:1 hexanes:EtOAc); **IR** (neat, cm⁻¹) 2963, 2842, 1593, 1482, 1458, 1359, 1048, 1024, 911, 758, 730, 703; **¹H NMR** (400 MHz, CDCl₃) δ 7.16 (t, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 8.0 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 5.34 (m, 2H), 5.07 (m, 2H), 3.35 (m, 4H), 1.97 (m, 4H); **¹³C NMR** (100 MHz, CDCl₃) δ 144.0, 140.8, 128.6, 123.1, 111.2, 109.1, 74.1, 73.7, 49.0, 25.3; **HRMS** (+NSI) calculated for C₁₂H₁₆ON 190.1226, found 190.1227 [M+H]⁺.

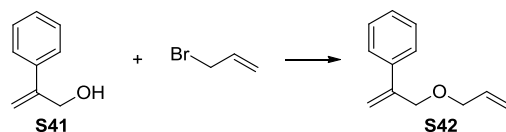


1-(1,3-dihydroisobenzofuran-5-yl)pyrrolidine (S40). Adapting a procedure by Xiong, Chen and coworkers,¹⁶ a 25 mL round bottom flask equipped with a stir bar and reflux condenser was flame dried and placed under N₂ atmosphere. The flask was then charged with **S38** (402 mg, 3.0 mmol, 1.0 equiv), K₂CO (1.3 g, 9.4 mmol, 3 equiv), CH₃CN (10 mL), and 1,4-dibromobutane (0.4 mL, 3.4 mmol, 1.1 equiv). The reaction mixture was stirred and heated to a vigorous reflux for 30 h at which time another 0.1 mL of 1,4-dibromobutane was added. After 45 h total of vigorous reflux, the orange mixture was cooled to 23 ° C, filtered, and concentrated *in vacuo* to an orange oil. Flash chromatography on silica gel yielded a light pink solid (241 mg, 43 % yield); **R_f** 0.44 (9:1 hexanes:EtOAc); **mp** 80-82 ° C; **IR** (neat, cm⁻¹) 2953, 2884, 2836, 1627,

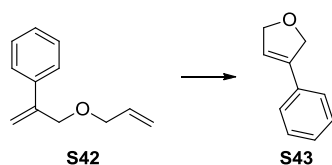
1573, 1504, 1366, 1185, 1036, 892, 796; **¹H NMR** (400 MHz, CDCl₃) δ 7.10 (d, *J* = 8.0 Hz, 1H), 6.51 (dd, *J* = 2.0 Hz, 8.0 Hz, 1H), 6.45 (s, 1H), 5.10 (d, *J* = 2.0 Hz, 2H), 5.08 (d, *J* = 2.0 Hz, 2H), 3.30 (m, 4H), 2.03 (m, 4H); **¹³C NMR** (100 MHz, CDCl₃) δ 147.7, 140.2, 125.5, 121.2, 111.0, 103.4, 73.6, 73.2, 47.8, 25.3; **HRMS** (+NSI) calculated for C₁₂H₁₆ON 190.1226, found 190.1229 [M+H]⁺.



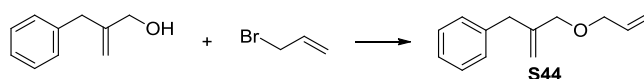
2-phenylprop-2-en-1-ol (S41). Prepared by the method of Glorius and coworkers.¹⁷ A 100 mL 2-necked round bottom flask equipped with a stir bar was flame dried and placed under N₂ atmosphere. The flask was charged with PhOTf (2.5 g, 9.4 mmol) followed by anhydrous DMF (15 mL), allyl alcohol (3.0 mL, 44.1 mmol), 1,3-bis(diphenylphosphino)propane (DPPP, 557 mg, 1.4 mmol) and Pd(OAc)₂ (215 mg, 0.96 mmol). DMF (15 mL) and Et₃N (4.6 mL, 33.0 mmol) were then added with stirring. The clear, light yellow solution was heated to 100 °C with stirring for 90 min and then cooled to 23 °C. C₆H₆ and water were added to the mixture. The organic portion was extracted twice more with water and lastly washed with 5 wt % LiCl (aq) solution. The organic layer was then dried with Na₂SO₄, concentrated *in vacuo*, and purified by flash chromatography (9:1 → 7:3 hexanes:Et₂O) to yield a clear oil (541 mg, 43 % yield); *R*_f 0.38 (2:1 hexanes:Et₂O); **IR** (neat, cm⁻¹) 3331, 3062, 3055, 3010, 1686, 1631, 1599, 1573, 1494, 1044, 1023, 901, 778, 703; **¹H NMR** (400 MHz, CDCl₃) δ 7.46-7.45 (m, 2H), 7.38-7.35 (m, 2H), 7.32-7.30 (m, 1H), 5.48 (d, *J* = 0.8 Hz, 1H), 5.38 (d, *J* = 0.8 Hz, 1H), 4.55 (s, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 147.2, 138.4, 128.5, 127.9, 126.1, 112.6, 65.0; **HRMS** (+NSI) calculated for C₉H₁₁O 135.0810, found 135.0805[M+H]⁺.



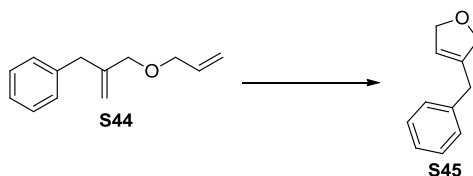
(3-(allyloxy)prop-1-en-2-yl)benzene (S42). Prepared by a procedure adapted from Mioskowski and coworkers.¹⁸ A 100 mL round bottom flask was equipped with a stir bar, flame dried and placed under N₂ atmosphere. The flask was charged with NaH (60% in oil, 209 mg, 5.2 mmol) and anhydrous THF (5 mL). The flask was then cooled to 0 °C and a solution of **S41** (526 mg, 3.9 mmol) in THF (5 mL) was added dropwise with stirring. After addition was complete, the flask was allowed to come to 23 °C and stirred for an additional 1 h. The flask was cooled to 0 °C again and a solution of allyl bromide (1.0 mL, 11.6 mmol) in THF (5 mL) was added dropwise. The flask was then stirred at 23 °C overnight to yield a cloudy white mixture. The flask was cooled to 0 °C and saturated NH₄Cl (aq) was added slowly. The mixture was extracted with Et₂O, and the organic portion was dried with Na₂SO₄, concentrated *in vacuo* and purified by flash chromatography (100 % hexanes) to afford a slightly yellow oil (530 mg, 77 % yield); *R*_f 0.9 (9:1 hexanes:CH₂Cl₂); **¹H NMR** (400 MHz, CDCl₃) δ 7.49-7.47 (m, 2H), 7.37-7.34 (m, 2H), 7.31-7.28 (m, 1H), 5.95 (ddt, *J* = 5.6, 10.3, 17.2 Hz, 1H), 5.54 (d, *J* = 0.6 Hz, 1H), 5.36 (d, *J* = 0.6 Hz, 1H), 5.38-5.17 (m, 2H), 4.39 (s, 2H), 4.06 (dt, *J* = 5.6, 1.3 Hz, 2H). All spectral data matched those previously reported.¹⁸



3-phenyl-2,5-dihydrofuran (S43). Adapting a procedure by Mioskowski and coworkers,¹⁸ a 250 mL round bottom flask equipped with a stir bar was flame dried and placed under N₂ atmosphere. The flask was charged with **S42** (601 mg, 3.45 mmol), CH₂Cl₂ (170 mL), and Grubbs' II catalyst (142 mg, 0.17 mmol) to afford a clear, maroon solution. The solution was then heated to reflux for 6 h. The light brown solution was then cooled to 23 °C, concentrated *in vacuo*, and then immediately purified by flash chromatography (95:5 $\rightarrow$ 9:1 hexanes:Et₂O) to afford a white crystalline solid (451 mg, 89 % yield); R_f 0.25 (9:1 hexanes:Et₂O); ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.28 (m, 5H), 6.24 (qn, *J* = 2.1 Hz, 1H), 5.02 (td, *J* = 4.8, 2.4 Hz, 2H), 4.86 (td, *J* = 4.8, 2.4 Hz, 2H). All spectral data matched those previously reported.¹⁸



(2-((allyloxy)methyl)allyl)benzene (S44). A 100 mL round bottom flask was equipped with a stir bar, flame dried and placed under N₂ atmosphere. The flask was charged with NaH (60% in oil, 502 mg, 12.6 mmol) and anhydrous THF (12 mL). The flask was then cooled to 0 °C and a solution of 2-benzylprop-2-en-1-ol¹⁹ (1.2 g, 8.2 mmol) in THF (12 mL) was added dropwise with stirring. After addition was complete, the flask was allowed to come to 23 °C and stirred for an additional 1 h. The flask was cooled to 0 °C again and a solution of allyl bromide (2.4 mL, 27.3 mmol) in THF (12 mL) was added dropwise. The flask was then stirred at 23 °C overnight to yield a cloudy white mixture. The flask was cooled to 0 °C and saturated NH₄Cl (aq) was added slowly. The mixture was extracted with Et₂O, and the organic portion was dried with Na₂SO₄, concentrated *in vacuo* and purified by flash chromatography (hexanes $\rightarrow$ 3:1 hexanes:CH₂Cl₂) to afford a clear oil (959 mg, 62 % yield); R_f 0.45 (1:1 hexanes:CH₂Cl₂); IR (neat, cm⁻¹) 3081, 3027, 2847, 1649, 1494, 1452, 1084, 905, 740, 698; ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.27 (m, 2H), 7.23-7.19 (m, 3H), 5.91 (ddt, *J* = 6, 10, 17.8 Hz, 1H), 5.28 (dq, *J* = 1.6, 17.2 Hz, 1H), 5.18 (m, 1H), 5.11 (m, 1H), 4.92 (m, 1H), 3.94 (dt, *J* = 1.6, 5.6 Hz, 2H), 3.87 (m, 2H), 3.40, (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 145.5, 139.1, 134.7, 129.0, 128.3, 126.1, 116.9, 113.3, 72.2, 70.9, 39.9; HRMS (+APCI) calculated for C₁₃H₁₇O 189.1279, found 189.1273 [M+H]⁺.



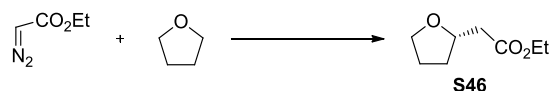
3-benzyl-2,5-dihydrofuran (S45). Adapting a procedure by Mioskowski and coworkers,¹⁸ a 250 mL round bottom flask equipped with a stir bar was flame dried and placed under N₂ atmosphere. The flask was charged with **S44** (600 mg, 3.2 mmol), CH₂Cl₂ (150 mL), and Grubbs' II catalyst (113 mg, 0.13 mmol) to afford a clear, maroon solution. The solution was then heated to reflux for 6 h. The light brown solution was then cooled to 23 °C, concentrated *in vacuo*, and then immediately purified by flash chromatography (95:5 $\rightarrow$ 9:1 hexanes:Et₂O) to

afford a clear oil (438 mg, 2.7 mmol, 86 % yield); **R_f** 0.31 (9:1 hexanes:Et₂O). Note: Product only slightly observable under UV light; anisaldehyde stain (dark green upon heating) required for adequate visualization. **IR** (neat, cm⁻¹) 3027, 2840, 1662, 1602, 1495, 1453, 1067, 1006, 897, 731, 689, 645; **¹H NMR** (400 MHz, CDCl₃) δ 7.30-7.27 (m, 2H), 7.21-7.17 (m, 3H), 5.44 (m, 1H), 4.62 (m, 2H), 4.49 (m, 2H), 3.41 (s, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 138.4, 128.7, 128.5, 126.4, 121.0, 100.7, 76.7, 76.0, 33.9; **HRMS** (+NSI) calculated for C₁₁H₁₃O 161.0966, found 161.0961 [M+H]⁺.

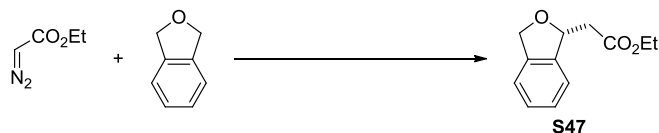
d) Preliminary Results Described in Equation 1 and Scheme 1

General procedure E.

A round bottom flask was charged with iridium phebim catalyst (0.5 mol % or 2 mol %, as indicated), 4 Å molecular sieves and a stir bar, then evacuated and backfilled with N₂. Substrate (4 equiv) and anhydrous PhCF₃ (1.7 M in substrate) were added via syringe, and the reaction mixture was cooled to -10 ° C in an ice/salt bath. A solution of ethyl diazoacetate (1 equiv, 13 % wt. CH₂Cl₂) in anhydrous PhCF₃ (0.29 M in diazoacetate) was added over 5 h via syringe pump. The temperature of the reaction mixture was maintained between -10 ° C and -5 ° C. After addition, once ethyl diazoacetate was completely consumed as judged by TLC, the mixture was concentrated *in vacuo*. The residue was purified as indicated to give the insertion product.



(S)-ethyl 2-(tetrahydrofuran-2-yl)acetate (S46). Prepared by general procedure **E** using ethyl diazoacetate (100 mg, 0.75 mmol) in PhCF₃ (3 mL), THF (285 μL, 3.52 mmol) in PhCF₃ (2 mL), [(*S,S*)-^{*t*}BuPhebox-^{*i*}Pr]IrCl₂(H₂O) **1**²⁰ (2.8 mg, 0.5 mol %), and 4 Å MS (176 mg). Flash chromatography (8:2 → 7:3 pentane:Et₂O) afforded the title compound as a colorless oil (60 mg, 51 % yield, 81:19 er); **R_f** 0.45 (7:3 pentane:Et₂O); **IR** (thin film, cm⁻¹) 2979, 1734, 1065; **¹H NMR** (400 MHz, CDCl₃) δ 4.21 (q, *J* = 7.0 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 3.85-3.80 (m, 1H), 3.70 (q, *J* = 7.4 Hz, 1H), 2.53 (dd, *J* = 15.3, 7.4 Hz, 1H), 2.41 (dd, *J* = 15.3, 5.9 Hz, 1H), 2.08-2.00 (m, 1H), 1.92-1.80 (m, 2H), 1.55-1.46 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 171.5, 75.4, 68.1, 60.6, 40.8, 31.4, 25.7, 14.3; **HRMS** [+APCI] calculated for C₈H₁₅O₃ 159.1016, found 159.1015 [M+H]⁺; [**α**]_D²⁰ -2.0 (*c* 1.0, CHCl₃); **HPLC** (Daicel OD-H, 1 % IPA:HEX, 1 mL/min), λ 230 nm, t_R(maj) = 6.43 min, t_R(min) = 7.58 min.



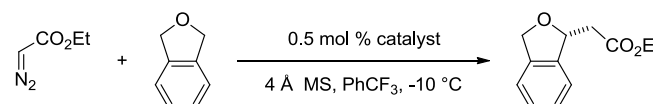
(R)-ethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S47). Prepared by general procedure **E** using ethyl diazoacetate (100 mg, 0.75 mmol) in PhCF₃ (3 mL), phthalan (380 μL, 3.52 mmol) in PhCF₃ (2 mL), [(*S,S*)-^{*t*}BuPhebox-^{*i*}Pr]IrCl₂(H₂O) **1**²⁰ (2.8 mg, 0.5 mol %), and 4 Å MS (176 mg). Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a colorless oil (125 mg, 81 % yield, 88:12 er); **R_f** 0.26 (8:2 pentane:Et₂O); **IR** (thin film, cm⁻¹) 2980, 2858, 1729, 1158, 1036, 750; **¹H NMR** (400 MHz, CDCl₃) δ 7.29-7.16 (m, 4H), 5.65 (dd, *J* = 6.9, 2.6 Hz, 1H), 5.10

(qd, J = 12.2, 2.1 Hz, 2H), 4.18 (qd, J = 7.1, 1.5 Hz, 2H), 2.74 (qd, J = 14.5, 6.4 Hz, 2H), 1.25 (td, J = 7.1, 0.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.9, 140.8, 139.3, 128.0, 127.5, 121.3, 121.2, 80.4, 72.8, 60.8, 41.8, 14.3; HRMS [+NSI] calculated for $\text{C}_{12}\text{H}_{15}\text{O}_3$ 207.1016, found 207.1019 $[\text{M}+\text{H}]^+$; $[\alpha]_D^{20}$ +39.1 $^\circ$ (c 1.0, CHCl_3); HPLC (Daicel OJ-H, 1 % IPA:HEX, 1 mL/min), λ 254 nm, $t_R(\text{min})$ = 17.5 min, $t_R(\text{maj})$ = 24.9 min.

e) Catalyst Optimization

Catalyst Optimization. Prepared by general procedure E using ethyl diazoacetate (100 mg, 0.75 mmol) in PhCF_3 (3 mL), phthalan (380 μL , 3.52 mmol) in PhCF_3 (2 mL), Ir(III) phehim catalyst (0.5 mol %), and 4 Å MS (176 mg). Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a colorless oil in the yield and enantioselectivity indicated. Compound was confirmed by ^1H NMR identical to above.

Table S1. Ir(III)-Phehim Optimization for C–H Insertion of Ethyl Diazoacetate into Phthalan

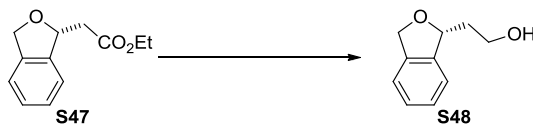


entry	catalyst	yield (%) ^b	er ^c
1	5	85	88:12
2	6	26	89:11
3	7	70	90:10
4	8	73	90:10
5	9	83	88:12
6	10	95	95:5
7	11	54	13:87 ^d
8	12	81	92:8
9	13	83	90:10
10	14	80	95:5
11	15	36	86:14

^aGeneral conditions: 0.29 M solution of ethyl diazoacetate in PhCF_3 was added over 5 h to a mixture of catalyst, phthalan (4 equiv), and 4 Å MS in PhCF_3 at $-10\text{ }^\circ\text{C}$. ^bIsolated yields.

^cDetermined by chiral HPLC. ^dCatalyst **11** is a member of the opposite enantio-series.

f) Acceptor-Only Diazoacetate Scope



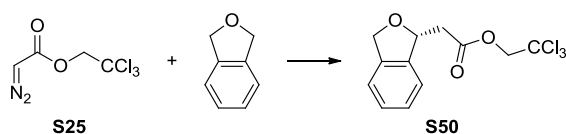
(R)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol (S48) A solution of **S47** (0.44 mmol, 1.0 equiv) in THF (2 mL, 0.2 M) was cooled to $0\text{ }^\circ\text{C}$. LAH (1.3 mL, 1 M in Et₂O, 3 equiv) was added dropwise. The reaction was warmed to room temperature. Once thin layer chromatography indicated complete consumption of starting material (1 h), the reaction mixture was poured into a vigorously stirring solution of Et₂O and a saturated aqueous Rochelle's salt solution. Et₂O was added and the resulting biphasic mixture was stirred vigorously for 3 h. The organic layer was separated, washed with brine, dried over MgSO_4 and concentrated *in vacuo*. Preparative thin layer chromatography (7:3 hexanes:EtOAc) afforded the title compound as a light yellow oil

(62 mg, 86 %); R_f 0.26 (7:3 hexanes:EtOAc); **IR** (thin film, cm^{-1}) 3398, 2855, 1461, 1046, 725; **^1H NMR** (600 MHz, CDCl_3) δ 7.28-7.21 (m, 3H), 7.15-7.12 (m, 1H), 5.41 (dd, $J = 8.8, 1.8$ Hz, 1H), 5.13 (dd, $J = 12.3, 2.3$ Hz, 1H), 5.05 (dd, $J = 12.3, 1.2$ Hz, 1H), 3.88-3.82 (m, 2H), 2.76 (br s, 1H), 2.17-2.12 (m, 1H), 1.94-1.89 (m, 1H); **^{13}C NMR** (150 MHz, CDCl_3) δ 141.4, 138.9, 127.6, 127.4, 121.0, 120.9, 83.7, 72.5, 60.8, 37.8; **HRMS** [+NSI] calculated for $\text{C}_{10}\text{H}_{13}\text{O}_2$ 165.0910, found 165.0909 $[\text{M}+\text{H}]^+$; **HPLC** (Daicel OJ-H, 5 % IPA:HEX, 1 mL/min), λ 210 nm, $t_R(\text{maj}) = 14.2$ min, $t_R(\text{min}) = 15.9$ min.



(*R*)-methyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S49). Prepared by general procedure E using methyl diazoacetate²¹ (57 mg, 0.57 mmol) in PhCF_3 (2 mL), phthalan (255 μL , 2.3 mmol) in PhCF_3 (1.3 mL), **10** (2.7 mg, 0.5 mol %), and 4 Å MS (118 mg). Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a colorless oil (79 mg, 72 % yield, 92:8 er). The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis. R_f 0.6 (7:3 pentane:Et₂O); **IR** (thin film, cm^{-1}) 2951, 2859, 1733, 1436, 1365, 1161, 1036, 750; **^1H NMR** (400 MHz, CDCl_3) δ 7.28-7.16 (m, 4H), 5.67-5.64 (m, 1H), 5.16-5.05 (m, 2H), 3.73 (d, $J = 0.8$ Hz, 3H), 2.83-2.69 (m, 2H); **^{13}C NMR** (150 MHz, CDCl_3) δ 171.3, 140.6, 139.1, 127.9, 127.4, 121.1, 80.3, 72.7, 51.8, 41.4; **HRMS** [+NSI] calculated for $\text{C}_{11}\text{H}_{13}\text{O}_3$ 193.0859, found 193.0858 $[\text{M}+\text{H}]^+$; $[\alpha]_D^{20} +45.8^\circ$ (*c* 1.0, CHCl_3).

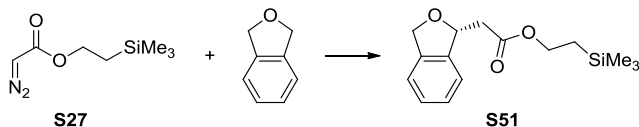
(*R*)-methyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S49). Prepared by general procedure E using methyl diazoacetate²¹ (56 mg, 0.55 mmol) in PhCF_3 (2 mL), phthalan (255 μL , 2.3 mmol) in PhCF_3 (1.3 mL), **14** (3 mg, 0.5 mol %), and 4 Å MS (118 mg). Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a colorless oil (73 mg, 69 % yield, 94:6 er). Compound was confirmed by ^1H NMR identical to above. The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis.



(*R*)-2,2,2-trichloroethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S50). Prepared by general procedure E using trichloroethyl diazoacetate **S25** (76 mg, 0.35 mmol) in PhCF_3 (1.2 mL), phthalan (155 μL , 1.57 mmol) in PhCF_3 (0.8 mL), **10** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (95:5 pentane:Et₂O) afforded the title compound as a colorless oil (90 mg, 84 % yield, 94:6 er). The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis. R_f 0.28 (95:5 pentane:Et₂O); **IR** (thin film, cm^{-1}) 3019, 2361, 1754, 1148, 1039, 749; **^1H NMR** (400 MHz, CDCl_3) δ 7.30-7.20 (m, 4H), 5.7 (td, $J = 5.1, 2.3$ Hz, 1H), 5.17 (dd, $J = 12.1, 2.0$ Hz, 1H), 5.08 (dd, $J = 12.1, 1.6$ Hz, 1H), 4.83 (dd, $J = 12.1, 2.4$ Hz, 1H), 4.75 (dd, $J = 11.7, 2.4$ Hz, 1H), 2.97 (dd, $J = 16.0, 4.7$ Hz, 1H), 2.88 (dd, $J = 16.0, 8.2$ Hz, 1H); **^{13}C NMR** (150 MHz, CDCl_3) δ

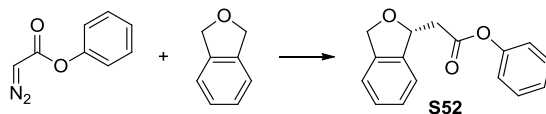
169.2, 140.1, 139.1, 128.0, 127.5, 121.2, 121.1, 94.7, 79.7, 74.1, 72.8, 41.2; **HRMS** [+NSI] calculated for $C_{12}H_{12}O_3Cl_3$ 308.9847, found 308.9848 $[M+H]^+$; $[\alpha]^{20}_D +35.2^\circ$ (c 1.0, $CHCl_3$).

(R)-2,2,2-trichloroethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S50). Prepared by general procedure **E** using trichloroethyl diazoacetate **S25** (76 mg, 0.35 mmol) in $PhCF_3$ (1.2 mL), phthalan (155 μ L, 1.57 mmol) in $PhCF_3$ (0.8 mL), **14** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (95:5 pentane:Et₂O) afforded the title compound as a colorless oil (77 mg, 71 % yield, 95:5 er). Compound was confirmed by ¹H NMR identical to above. The title compound was subjected to the LAH reduction procedure above to give (R)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis.



(R)-2-(trimethylsilyl)ethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S51). Prepared by general procedure **E** using trimethylsilyl ethyl diazoacetate **S27** (66 mg, 0.35 mmol) in $PhCF_3$ (1.2 mL), phthalan (155 μ L, 1.57 mmol) in $PhCF_3$ (0.8 mL), **10** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (95:5 pentane:Et₂O) afforded the title compound as a colorless oil (60 mg, 62 % yield, 93:7 er). The title compound was subjected to the LAH reduction procedure above to give (R)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis. **R_f** 0.24 (95:5 pentane:Et₂O); **IR** (thin film, cm^{-1}) 2953, 2897, 1729, 1248, 1158, 1038, 833, 749; **¹H NMR** (600 MHz, $CDCl_3$) δ 7.28-7.17 (m, 4H), 5.67-5.64 (m, 1H), 5.16-5.04 (m, 2H), 4.22 (td, J = 8.6, 2.3 Hz, 2H), 2.77 (dd, J = 15.7, 4.7 Hz, 1H), 2.71 (dd, J = 15.7, 7.8 Hz, 1H), 1.01-0.97 (m, 2H) 0.03 (s, 9H); **¹³C NMR** (150 MHz, $CDCl_3$) δ 170.9, 140.7, 139.2, 127.8, 127.4, 121.1, 121.0, 80.3, 72.7, 62.9, 41.8, 17.3, -1.5; **HRMS** [+NSI] calculated for $C_{15}H_{23}O_3Si$ 279.1411, found 279.1414 $[M+H]^+$; $[\alpha]^{20}_D +39.3^\circ$ (c 1.0, $CHCl_3$).

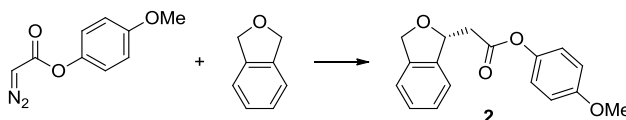
(R)-2-(trimethylsilyl)ethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S51). Prepared by general procedure **E** using trimethylsilyl ethyl diazoacetate **S27** (66 mg, 0.35 mmol) in $PhCF_3$ (1.2 mL), phthalan (154 μ L, 1.57 mmol) in $PhCF_3$ (0.8 mL), **14** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (95:5 pentane:Et₂O) afforded the title compound as a colorless oil (66 mg, 67 % yield, 94:6 er). Compound was confirmed by ¹H NMR identical to above. The title compound was subjected to the LAH reduction procedure above to give (R)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis.



(R)-phenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S52). Prepared by general procedure **E** using phenyl diazoacetate⁹ (57 mg, 0.35 mmol) in $PhCF_3$ (1.2 mL), phthalan (154 μ L, 1.57 mmol) in $PhCF_3$ (0.8 mL), **10** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a white solid (58 mg, 65 % yield, 91:9 er). The title compound was subjected to the LAH reduction procedure above to give (R)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis. **R_f** 0.35 (8:2 hexanes:EtOAc); **mp** 46-48 °C; **IR** (thin film, cm^{-1}) 3019, 2362, 1753, 1592, 1492, 1214, 1140, 919, 750; **¹H NMR** (600 MHz, $CDCl_3$) δ 7.39-7.19 (m, 7H), 7.07-7.04 (m, 2H), 5.78-5.75 (m,

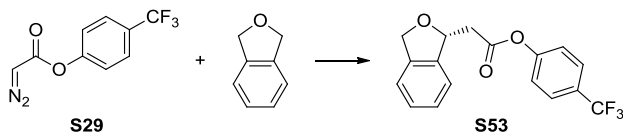
1H), 5.22-5.09 (m, 2H), 3.06 (dd, $J = 15.7, 4.7$ Hz, 1H), 2.98 (dd, $J = 15.7, 7.4$ Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 172.5, 169.3, 158.3, 150.5, 140.4, 139.2, 129.4, 128.0, 127.5, 128.9, 121.5, 121.2, 121.1, 80.3, 72.9, 41.7; HRMS [+NSI] calculated for $\text{C}_{16}\text{H}_{15}\text{O}_3$ 255.1016, found 255.1014 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} + 34.0^\circ$ (c 1.0, CHCl_3).

(*R*)-phenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S52). Prepared by general procedure E using phenyl diazoacetate⁹ (57 mg, 0.35 mmol) in PhCF_3 (1.2 mL), phthalan (154 μL , 1.57 mmol) in PhCF_3 (0.8 mL), **14** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (8:2 pentane: Et_2O) afforded the title compound as a white solid (61 mg, 68 % yield, 93:7 er). Compound was confirmed by ^1H NMR identical to above. The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis.



(*R*)-4-methoxyphenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (2). Prepared by general procedure E using 4-methoxy-phenyl diazoacetate¹⁰ (68 mg, 0.35 mmol) in PhCF_3 (1.2 mL), phthalan (154 μL , 1.57 mmol) in PhCF_3 (0.8 mL), **10** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (8:2 pentane: Et_2O) afforded the title compound as a white solid (57 mg, 57 % yield, 91:9 er). The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis. R_f 0.45 (7:3 hexanes: EtOAc); mp 44-47 ° C; IR (thin film, cm^{-1}) 3019, 2361, 1751, 1506, 1214, 920, 748; ^1H NMR (600 MHz, CDCl_3) δ 7.31-7.26 (m, 4H), 6.98-6.95 (m, 2H), 6.87-6.84 (m, 2H), 5.76-5.74 (m, 1H), 5.19 (dd, $J = 11.9, 2.6$ Hz, 1H), 5.1 (d, $J = 11.9$ Hz, 1H), 3.78 (s, 3H), 3.02 (dd, $J = 15.4, 4.8$ Hz, 1H), 2.95 (dd, $J = 15.4, 7.5$ Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 172.5, 169.6, 157.2, 144.0, 140.4, 139.2, 128.0, 127.5, 122.3, 121.2, 121.1, 114.4, 80.3, 72.8, 55.6, 41.6; HRMS [+NSI] calculated for $\text{C}_{17}\text{H}_{17}\text{O}_4$ 285.1121, found 285.1118 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} + 36.1^\circ$ (c 1.0, CHCl_3).

(*R*)-4-methoxyphenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (2). Prepared by general procedure E using 4-methoxy-phenyl diazoacetate¹⁰ (68 mg, 0.35 mmol) in PhCF_3 (1.2 mL), phthalan (154 μL , 1.57 mmol) in PhCF_3 (0.8 mL), **14** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (8:2 pentane: Et_2O) afforded the title compound as a white solid (70 mg, 70 % yield, 92:8 er). Compound was confirmed by ^1H NMR identical to above. The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis.

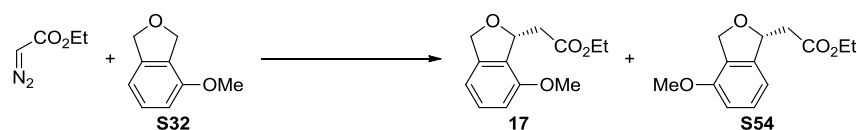


(*R*)-4-(trifluoromethyl)phenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S53). Prepared by general procedure E using 4-trifluoromethyl-phenyl diazoacetate **S29** (81 mg, 0.35 mmol) in PhCF_3 (1.2 mL), phthalan (154 μL , 1.57 mmol) in PhCF_3 (0.8 mL), **10** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (9:1 pentane: Et_2O) afforded the title compound as a white solid (88 mg, 78 % yield, 90:10 er). The title compound was subjected to the LAH reduction

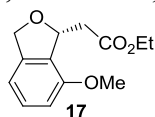
procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis. **R_f** 0.5 (8:2 hexanes:EtOAc); **mp** 70-72 ° C; **IR** (thin film, cm⁻¹) 3019, 2925, 2363, 1710, 1362, 1214, 922, 754; **¹H NMR** (600 MHz, CDCl₃) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.33-7.28 (m, 2H), 7.27-7.25 (m, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 5.77-5.74 (m, 1H), 5.19 (dd, *J* = 12.3, 2.9 Hz, 1H), 5.11 (d, *J* = 12.3 Hz, 1H), 3.08 (dd, *J* = 15.2, 4.1 Hz, 1H), 2.98 (dd, *J* = 15.2, 8.2 Hz, 1H); **¹³C NMR** (150 MHz, CDCl₃) δ 168.8, 156.4, 153.0, 140.0, 139.2, 128.1, 127.6, 126.8, 122.1, 121.2, 121.1, 115.4, 80.2, 72.9, 41.6, 29.7; **HRMS** [+NSI] calculated for C₁₇H₁₄O₃F₃ 323.0890, found 323.0890 [M+H]⁺; [α]_D²⁰ + 7.7 ° (*c* 1.0, CHCl₃).

(*R*)-4-(trifluoromethyl)phenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S53). Prepared by general procedure E using 4-trifluoromethyl-phenyl diazoacetate **S29** (81 mg, 0.35 mmol) in PhCF₃ (1.2 mL), phthalan (154 μL, 1.57 mmol) in PhCF₃ (0.8 mL), **14** (7 mg, 2 mol %), and 4 Å MS (80 mg). Flash chromatography (9:1 pentane:Et₂O) afforded the title compound as a white solid (78 mg, 69 % yield, 92:8 er). Compound was confirmed by ¹H NMR identical to above. The title compound was subjected to the LAH reduction procedure above to give (*R*)-2-(1,3-dihydroisobenzofuran-1-yl)ethanol for HPLC analysis.

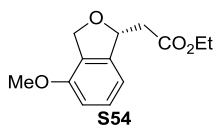
g) Substrate Scope



Prepared by general procedure E using ethyl diazoacetate (44 mg, 0.33 mmol) in PhCF₃ (1.1 mL), **S32** (200 mg, 1.3 mmol) in PhCF₃(0.75), **14** (7 mg, 2 mol %), and 4 Å MS (66 mg). Flash chromatography (9:1 → 8:2 pentane:Et₂O) afforded the title compounds as a mixture of separable regioisomers (49 mg, 63 % yield, 98:2 er **17**; 15 mg, 19 % yield, 94:6 er **S54**);

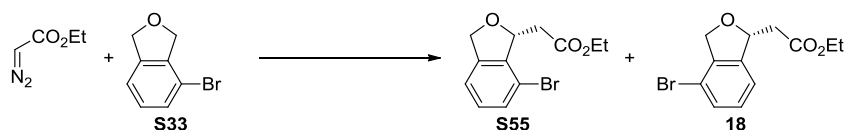


(*R*)-ethyl 2-(7-methoxy-1,3-dihydroisobenzofuran-1-yl)acetate (17). The title compound was isolated as 49 mg of a white amorphous solid (63 % yield, 98:2 er); **R_f** 0.28 (9:1 pentane: Et₂O); **IR** (thin film, cm⁻¹) 3019, 2032, 1730, 1614, 1485, 1270, 922, 749, 667; **¹H NMR** (600 MHz, CDCl₃) δ 7.26-7.24 (m, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 5.72 (d, *J* = 9.2 Hz, 1H), 5.15 (dd, *J* = 12.3, 2.6 Hz, 1H), 5.04 (d, *J* = 12.3 Hz, 1H), 4.16 (q, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 3.1 (dd, *J* = 15.6, 2.9 Hz, 1H), 2.57 (dd, *J* = 15.6, 9.0 Hz, 1H), 1.23 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 172.5, 171.3, 154.3, 141.2, 129.7, 113.2, 108.9, 79.9, 73.2, 60.5, 55.1, 39.9, 14.2; **HRMS** [+NSI] calculated for C₁₃H₁₇O₄ 237.1121, found 237.1119 [M+H]⁺; [α]_D²⁰ + 69.5 ° (*c* 1.0, CHCl₃); **HPLC** (Daicel OJ-H, 0.5 % IPA:HEX, 1 mL/min), λ 230 nm, t_R(min) = 25.8 min, t_R(maj) = 33.2 min.

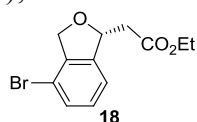


(*R*)-ethyl 2-(4-methoxy-1,3-dihydroisobenzofuran-1-yl)acetate (S54). The title compound was isolated as 15 mg of a white amorphous solid (19 % yield, 94:6 er); **R_f** 0.30 (9:1 pentane:Et₂O);

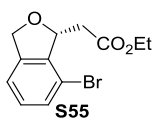
IR (thin film, cm^{-1}) 3019, 2342, 1731, 1599, 1487, 1267, 1038, 924, 889, 751; **^1H NMR** (600 MHz, CDCl_3) δ 7.25-7.24 (m, 1H), 6.75 (t, $J = 7.5$ Hz, 2H), 5.66-5.64 (m, 1H), 5.12 (dd, $J = 12.7, 2.6$ Hz, 1H), 5.04 (d, $J = 12.3$ Hz, 1H), 4.18, (q, $J = 7.0$ Hz, 2H), 3.81 (s, 3H), 2.76 (dd, $J = 15.8, 4.4$ Hz, 1H), 2.7 (dd, $J = 15.8, 8.3$ Hz, 1H), 1.25 (t, $J = 7.2$ Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3) δ 172.5, 129.3, 113.2, 110.0, 109.3, 80.9, 71.3, 60.7, 55.2, 41.7, 14.2; **HRMS** [+NSI] calculated for $\text{C}_{13}\text{H}_{17}\text{O}_4$ 237.1121, found 237.1119 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} + 31.0^\circ$ (c 1.0, CHCl_3); **HPLC** (Daicel OJ-H, 0.5 % IPA:HEX, 1 mL/min), λ 210 nm, $t_{\text{R}}(\text{min}) = 24.3$ min, $t_{\text{R}}(\text{maj}) = 31.8$ min.



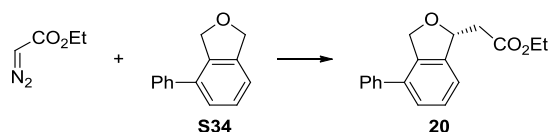
(NEM-vi-25-top, NEM-vi-25-bottom). Prepared by general procedure E using ethyl diazoacetate (45 mg, 0.34 mmol) in PhCF_3 (1.2 mL), **S33** (272 mg, 1.37 mmol) in PhCF_3 (0.8 mL), **14** (8 mg, 2 mol %), and 4 Å MS (68 mg). Flash chromatography (100:0 $\rightarrow$ 95:5 pentane:Et₂O) afforded the title compounds as a mixture of separable regioisomers (28 mg, 29 % yield, 94:6 er **18**; 9.5 mg, 10 % yield **S55**);



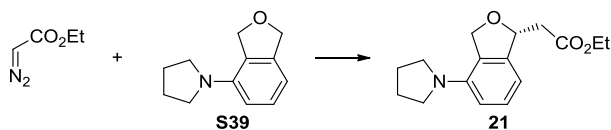
(R)-ethyl 2-(4-bromo-1,3-dihydroisobenzofuran-1-yl)acetate (18). The title compound was isolated as 28 mg of a white amorphous solid (29 % yield, 94:6 er); R_f 0.28 (9:1 hexanes:EtOAc); **IR** (thin film, cm^{-1}) 3019, 2359, 1733, 1361, 1214, 1042, 923, 750, 668; **^1H NMR** (400 MHz, CDCl_3) δ 7.39 (d, $J = 6.6$ Hz, 1H), 7.17-7.10 (m, 2H), 5.73 (t, $J = 7.4$ Hz, 1H), 5.10 (dd, $J = 12.9, 2.7$ Hz, 1H), 5.02 (dd, $J = 12.9, 1.6$ Hz, 1H), 2.76-2.74 (m, 2H), 1.25 (t, $J = 7.2$ Hz, 3H); **^{13}C NMR** (150 MHz, CDCl_3) δ 170.5, 142.6, 139.9, 130.8, 129.5, 120.0, 115.9, 81.5, 73.8, 60.8, 41.5, 29.7, 14.1; **HRMS** [+NSI] calculated for $\text{C}_{12}\text{H}_{14}\text{O}_3\text{Br}$ 285.0121, found 285.0120 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} + 12.8^\circ$ (c 1.0, CHCl_3); **HPLC** (Daicel OJ-H, 1 % IPA:HEX, 1 mL/min), λ 210 nm, $t_{\text{R}}(\text{min}) = 10.8$ min, $t_{\text{R}}(\text{maj}) = 17.0$ min.



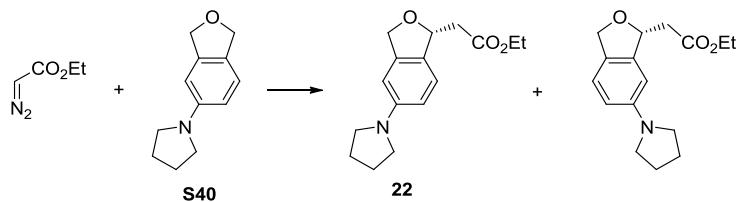
(R)-ethyl 2-(7-bromo-1,3-dihydroisobenzofuran-1-yl)acetate (S55). The title compound was isolated as 9.5 mg of a white amorphous solid (10 % yield); R_f 0.26 (9:1 hexanes:EtOAc); **IR** (thin film, cm^{-1}) 3019, 2357, 2196, 1733, 1214, 920, 889, 753, 665; **^1H NMR** (400 MHz, CDCl_3) δ 7.40-7.38 (m, 1H), 7.16-7.15 (m, 2H), 5.67 (dt, $J = 8.9, 2.4$ Hz, 1H), 5.22 (dd, $J = 12.5, 2.7$ Hz, 1H), 5.08 (dd, $J = 12.5, 0.8$ Hz, 1H), 4.16 (q, $J = 7.0$ Hz, 2H), 3.18 (dd, $J = 15.6, 2.7$ Hz, 1H), 2.66 (dd, $J = 15.6, 9.0$ Hz, 1H), 1.24 (t, $J = 7.0$ Hz, 3H); **^{13}C NMR** (150 MHz, CDCl_3) δ 170.7, 141.6, 140.0, 131.0, 129.8, 120.0, 116.3, 81.7, 73.0, 60.7, 39.3, 14.1; **HRMS** [+NSI] calculated for $\text{C}_{12}\text{H}_{14}\text{O}_3\text{Br}$ 285.0121, found 285.0118 $[\text{M}+\text{H}]^+$; $[\alpha]^{20}_{\text{D}} + 56.6^\circ$ (c 0.5, CHCl_3).



(R)-ethyl 2-(4-phenyl-1,3-dihydroisobenzofuran-1-yl)acetate (20). Prepared by general procedure E using **S34** (102 mg, 0.51 mmol), ethyl diazoacetate (17 mg, 0.13 mmol), **14** (2.6 mg, 2 mol %), and 4 Å MS (27 mg). Flash chromatography (100 % pentane → 95:5 pentane:Et₂O) afforded the title compound as a colorless oil (20 mg, 56 % yield, 96:4 er); **R_f** 0.28 (9:1 pentane:Et₂O); **IR** (thin film, cm⁻¹) 3020, 2007, 1732, 1214, 920, 756; **¹H NMR** (400 MHz, CDCl₃) δ 7.44-7.32 (m, 7H), 7.17 (d, *J* = 7.0 Hz, 1H), 5.71 (t, *J* = 5.3 Hz, 1H), 5.21 (dd, *J* = 12.5, 2.3 Hz, 1H), 5.15 (dd, *J* = 12.9, 2.0 Hz, 1H), 4.20 (q, *J* = 7.3 Hz, 2H), 2.86-2.74 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 170.8, 141.5, 139.8, 137.1, 136.1, 128.7, 128.2, 128.0, 127.8, 127.5, 120.0, 80.4, 72.5, 60.7, 41.6, 24.9, 14.2; **HRMS** [+NSI] calculated for C₁₈H₁₉O₃ 283.1329, found 283.1326 [M+H]⁺; [α]_D²⁰ +6.9 ° (*c* 1.0, CHCl₃); **HPLC** (Daicel OJ-H, 1 % IPA:HEX, 1 mL/min), λ 254 nm, t_R(min) = 21.9 min, t_R(maj) = 24.9 min.



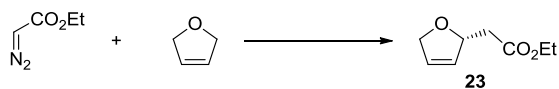
(R)-ethyl 2-(4-(pyrrolidin-1-yl)-1,3-dihydroisobenzofuran-1-yl)acetate (21). Prepared by general procedure E using **S39** (220 mg, 0.92 mmol) in PhCF₃ (0.5 mL), ethyl diazoacetate (30 μL, 0.25 mmol) in PhCF₃ (0.7 mL), **14** (6.1 mg, 2 mol %), and 4 Å MS (75 mg). Flash chromatography (95:5 → 93:7 hexanes:EtOAc) afforded the title compound as a light yellow oil (45.3 mg, 56% yield, 95:5 er); **R_f** 0.41 (8:2 hexanes:EtOAc); **IR** (neat, cm⁻¹) 2969, 2871, 1729, 1594, 1486, 1458, 1367, 1152, 1030, 770; **¹H NMR** (400 MHz, CDCl₃) δ 7.15 (t, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 5.60 (m, 1H), 5.37 (dd, *J* = 2.8, 11.2, 1H); 5.28 (dd, *J* = 1.6, 11.2 Hz, 1H); 4.21 (q, *J* = 7.2 Hz, 2H); 3.33 (m, 4H); 2.80 (dd, *J* = 4.0, 16.0 Hz, 1H), 2.68 (dd, *J* = 8.4, 15.2 Hz, 1H), 1.95 (m, 4H), 1.28 (t, *J* = 8.0 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 171.1, 144.0, 142.4, 128.8, 123.0, 111.8, 109.2, 80.3, 73.3, 60.6, 49.0, 41.8, 25.3, 14.2; **HRMS** (+NSI) calculated for C₁₆H₂₁NO₃ 275.1516, found 275.1510 [M]⁺; [α]_D²⁰ +9.0 ° (*c* 0.7, CHCl₃); **HPLC** (Daicel OJ-H, 10 % IPA:HEX, 1 mL/min), λ 254 nm, t_R(min) = 14.1 min, t_R(maj) = 31.3 min.



(R)-ethyl 2-(5-(pyrrolidin-1-yl)-1,3-dihydroisobenzofuran-1-yl)acetate, mix of regioisomers (22). Prepared by general procedure E using **S40** (407 mg, 2.15 mmol) in PhCF₃ (1.2 mL), ethyl diazoacetate (65 μL, 0.54 mmol) in PhCF₃ (1.4 mL), **14** (8.6 mg, 2 mol %), and 4 Å MS (165 mg). Flash chromatography (95:5 → 90:10 hexanes:EtOAc) afforded the title compound as a light pink oil (67.8 mg, 0.246 mmol, 45% yield, 4:1 mix of regioisomers); **R_f** 0.5 (8:2 hexanes:EtOAc); **IR** (neat, cm⁻¹) 2968, 2840, 1729, 1620, 1577, 1506, 1447, 1369, 1156, 1038,

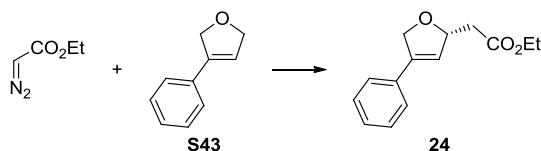
800; **¹H NMR** of major regioisomer (400 MHz, CDCl₃) δ 7.02 (d, *J* = 8.0 Hz, 1H); 6.48 (dd, *J* = 8.0, 4.0 Hz, 1H); 6.38 (d, *J* = 4.0 Hz, 1H); 5.60 (m, 1H); 5.10 (dd, *J* = 12.0, 2.4, Hz, 1H); 5.02 (d, *J* = 12.0 Hz, 1H); 4.20 (q, *J* = 8.0 Hz, 2H); 3.27 (m, 4H); 2.74 (dd, *J* = 12.0, 4.0 Hz, 1H); 2.69 (dd, *J* = 16.0, 8.0 Hz, 1H); 2.00 (m, 4H); 1.28 (t, *J* = 8.0 Hz, 3H); **¹H NMR** of minor regioisomer (400 MHz, CDCl₃) δ 7.06 (d, *J* = 8.0 Hz, 0.25H); 6.50 (dd, *J* = 8.0, 4.0 Hz, 0.25H); 6.34 (d, *J* = 4.0 Hz, 0.25H); 5.63 (m, 0.25H); 5.00 (d, *J* = 8.0 Hz, 0.25H); 4.21 (q, *J* = 8.0 Hz, 0.5H); 3.27 (m, 1H); 2.80 (dd, *J* = 16.0, 4.0 Hz, 0.25H); 2.00 (m, 1H); 1.29 (t, *J* = 8.0 Hz, 0.75H); **¹³C NMR** (signals presumed to correspond to the major regioisomer, 100 MHz, CDCl₃) δ 171.1 148.0, 140.5, 127.3, 121.5, 111.0, 103.3, 80.1, 72.8, 60.5, 47.8, 42.1, 25.4, 14.2; **HRMS** (+NSI) calculated for C₁₆H₂₂NO₃ 276.1594, found 276.1587 [M+H]⁺.

The title compound was subjected to the LAH reduction procedure above to give crude 2-(5-(pyrrolidin-1-yl)-1,3-dihydroisobenzofuran-1-yl)ethanol which was then derivatized as the *tert*-butyl-diphenylsilyl ether for HPLC analysis. The crude alcohol was dissolved in CH₂Cl₂ (3.0 mL) in an 8 mL screw cap vial. The mixture was stirred and recrystallized imidazole (22.6 mg, 0.331 mmol, 1.3 equiv) was added followed by TBDPSCl (80 μL, 0.308 mmol, 1.3 equiv) dropwise over 15 seconds at room temperature. Almost immediately, a white precipitate was observed. After 30 min, the reaction was filtered through celite, concentrated, and purified via column chromatography on silica gel (2.5:5:92.5 EtOAc:PhCH₃:hexanes) to afford the individual major (40.3 mg, 90:10 er) and minor (8.5 mg, 91:9 er) regioisomers. Major regioisomer: **R_f** 0.32 (5:10:85 EtOAc:PhCH₃:hexanes); **IR** (neat, cm⁻¹) 3070, 2929, 2855, 1662, 1506, 1371, 1107, 731, 700, 613; **¹H NMR** (400 MHz, CDCl₃) δ 7.71-7.68 (m, 4H), 7.44-7.36 (m, 6H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.45 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.38 (d, *J* = 2.0 Hz, 1H), 5.34 (m, 1H), 5.02 (dd, *J* = 2.0, 12.0, 1H), 4.97 (d, *J* = 12.0 Hz, 1H), 3.90 (m, 2H), 3.27 (m, 4H), 2.06 (m, 1H), 2.00 (m, 4H), 1.90 (m, 1H), 1.06 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 147.8, 140.6, 135.6, 135.6, 134.1, 134.0, 129.5, 129.0, 127.6, 121.6, 110.9, 103.5, 80.5, 72.4, 60.9, 47.9, 39.7, 26.9, 25.4, 19.2; **HRMS** (+NSI) calculated for C₃₀H₃₇NO₂Si 471.2594, found 471.2593 [M]⁺; [**α**]_D²⁰ + 8.0 ° (*c* 0.5, CHCl₃); **HPLC** (Daicel OJ-H, 15 % IPA:HEX, 0.3 mL/min), λ 254 nm, t_R(min) = 26.0 min, t_R(maj) = 40.8 min. Minor regioisomer: **R_f** 0.39 (5:10:85 EtOAc:PhCH₃:hexanes); **IR** (neat, cm⁻¹) 2928, 2854, 1621, 1505, 1372, 1108, 732, 701, 613; **¹H NMR** (400 MHz, CDCl₃) δ 7.72-7.67 (m, 4H), 7.44-7.35 (m, 6H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.47 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.32 (d, *J* = 8.0 Hz, 1H), 5.36 (m, 1H), 4.99 (dd, *J* = 2.0, 10.0 Hz, 1H), 4.95 (d, *J* = 10.0 Hz, 1H), 3.93 (m, 2H); 3.26 (m, 4H), 2.08 (m, 1H), 2.02 (m, 4H), 1.94 (m, 1H), 1.06 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ 135.6, 135.5, 134.1, 133.9, 129.5, 129.5, 127.6, 127.6, 121.4, 110.0, 86.6, 80.8, 72.1, 60.9, 56.9, 47.9, 39.3, 26.9, 25.4, 19.2; **HRMS** (+NSI) calculated for C₃₀H₃₇NO₂Si 471.2594, found 471.2593 [M]⁺; [**α**]_D²⁰ + 5.1 ° (*c* 0.4, CHCl₃); **HPLC** (Daicel OJ-H, 15 % IPA:HEX, 0.1 mL/min), λ 254 nm, t_R(min) = 51.8 min, t_R(maj) = 45.7 min.

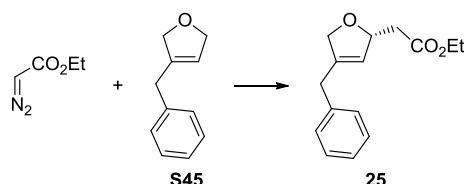


(R)-ethyl 2-(2,5-dihydrofuran-2-yl)acetate (23). Prepared according to general procedure E using ethyl diazoacetate (100 mg, 0.75 mmol) in PhCF₃ (3 mL), 2,5-dihydrofuran (226 μL, 3 mmol) in PhCF₃ (2 mL), **14** (6 mg, 0.5 mol %), and 4 Å MS (176 mg). Flash chromatography (8:2 pentane:Et₂O) afforded the title compound as a colorless oil (91 mg, 77 %, 88:12 er); **R_f** 0.31 (8:2 pentane:Et₂O); **IR** (thin film, cm⁻¹) 2983, 1731, 1179, 1028; **¹H NMR** (400 MHz,

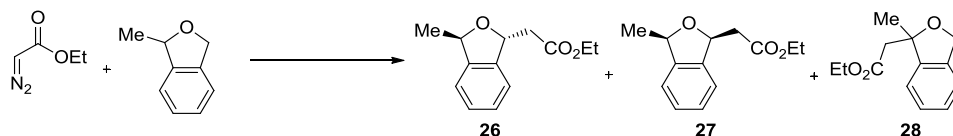
CDCl₃) δ 5.88 (dd, J = 6.3, 2.0 Hz, 1H), 5.80-5.78 (m, 1H), 5.16-5.10 (m, 1H), 4.65-4.52 (m, 2H), 4.09 (q, J = 7.2 Hz, 2H), 2.54-2.43 (m, 2H), 1.2 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.0, 128.8, 127.5, 82.4, 75.3, 60.6, 41.3, 14.3; HRMS [+NSI] calculated for C₈H₁₃O₃ 157.0865, found 157.0861 [M+H]⁺; [α]_D²⁰ -10.9° (c 0.25, CHCl₃); HPLC (Daicel OJ-H, 1 % IPA:HEX, 0.7 mL/min), λ 210 nm, t_R(min) = 14.6 min, t_R(maj) = 15.9 min.



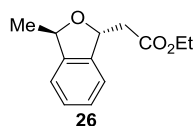
(R)-ethyl 2-(4-phenyl-2,5-dihydrofuran-2-yl)acetate (24). Prepared according to general procedure E using ethyl diazoacetate (55 μ L, 0.46 mmol) in PhCF₃ (1.8 mL), S43 (304 mg, 2.0 mmol) in PhCF₃ (1.2 mL), 14 (11 mg, 2.0 mol %), and 4 Å MS (103 mg). Flash chromatography (95:5 $\rightarrow$ 85:15 hexanes:Et₂O) afforded the title compound as a clear oil (61 mg, 57 %, 85:15 er); R_f 0.23 (4:1 hexanes:Et₂O); IR (neat, cm⁻¹) 2980, 2850, 1727, 1372, 1159, 1078, 1033, 750, 691; ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.28 (m, 5H), 6.21 (app q, J = 2.2 Hz, 1H), 5.39 (m, 1H), 5.06 (ddd, J = 2.0, 5.6, 12.0 Hz, 1H), 4.98 (ddd, J = 2.4, 3.6, 12.0 Hz, 1H), 4.18 (q, J = 8.0 Hz, 2H), 3.41 (s, 2H), 2.69 (dd, J = 7.0, 16.0 Hz, 1H), 2.61 (dd, J = 6.0, 16.0 Hz, 1H), 1.28 (t, J = 8.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 139.4, 132.0, 128.6, 128.3, 125.8, 122.6, 83.5, 75.0, 60.6, 41.3, 14.2; HRMS (+NSI) calculated for C₁₄H₁₇O₃ 233.1178, found 233.1170 [M+H]⁺. [α]_D²⁰ -34.3° (c 1.0, CHCl₃); HPLC (Daicel OJ-H, 10 % IPA:HEX, 1.0 mL/min), λ 254 nm, t_R(min) = 16.2 min, t_R(maj) = 29.1 min.



(R)-ethyl 2-(4-benzyl-2,5-dihydrofuran-2-yl)acetate (25). Prepared according to general procedure E using ethyl diazoacetate (65 μ L, 0.54 mmol) in PhCF₃ (2.1 mL), S45 (410 mg, 2.6 mmol) in PhCF₃ (1.4 mL), 14 (13 mg, 2.0 mol %), and 4 Å MS (126 mg). Flash chromatography (95:5 $\rightarrow$ 85:15 hexanes:Et₂O) afforded the title compound as a clear oil (41.5 mg, 31% yield, 81:19 er); R_f 0.28 (8:2 hexanes:Et₂O); Note: Product only slightly observable under UV light; anisaldehyde stain (dark green upon heating) required for adequate visualization; IR (neat, cm⁻¹) 3027, 2980, 2845, 1729, 1494, 1262, 1153, 1065, 1027, 758, 700; ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.28 (m, 2H), 7.25-7.17 (m, 3H), 5.45 (m, 1H), 5.20 (m, 1H), 4.57-4.46 (m, 2H), 4.14 (q, J = 8.0 Hz, 2H), 3.42 (s, 2H), 2.56 (dd, J = 7.2, 15.2 Hz, 1H), 2.50 (dd, J = 5.6, 15.2 Hz, 1H), 1.25 (t, J = 8.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.1, 141.0, 138.1, 128.6, 128.5, 126.4, 123.6, 82.8, 76.5, 60.5, 41.4, 33.8, 14.2; HRMS (+NSI) calculated for C₁₅H₁₈O₃Na 269.1154, found 269.1146 [M+Na]⁺. [α]_D²⁰ -31.6° (c 1.1, CHCl₃); HPLC (Daicel OJ-H 10 % IPA:HEX, 1.0 mL/min), λ 210 nm, t_R(min) = 12.9 min, t_R(maj) = 14.3 min.



ethyl 2-((1*R*,3*R*)-3-methyl-1,3-dihydroisobenzofuran-1-yl)acetate (26, 27, 28). Prepared by general procedure **E** using ethyl diazoacetate (117 mg, 0.88 mmol) in PhCF₃ (3 mL), 1,3-dihydro-1-methylisobenzofuran²² (472 mg, 3.5 mmol) in PhCF₃ (2 mL), **14** (4.5 mg, 0.5 mol %), and 4 Å MS (176 mg). Ethyl diazoacetate solution was added to the substrate solution at -10 °C and warmed to room temperature overnight. Flash chromatography (97:3 → 95:5 → 9:1 pentane:Et₂O) afforded the title compounds as a 85:5:10 mixture of **26**:**27**:**28** by GC and crude ¹H NMR. (116 mg, 60 % yield). **GC** (CHIRASIL DEX, 120 → 140 °C, 1 °C/min) t_r(**28**) = 18.596 min, t_r(**26**) = 21.839 min, t_r(**27**) = 23.556 min. Major product **26** was characterized as follows (88:12 er).

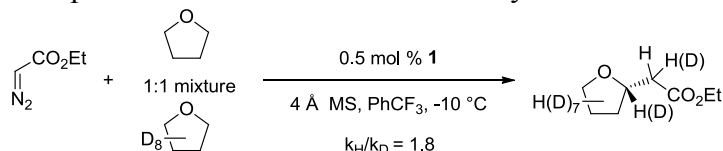


ethyl 2-((1*R*,3*R*)-3-methyl-1,3-dihydroisobenzofuran-1-yl)acetate (26). **R_f** 0.41 (9:1 pentane:Et₂O); **IR** (thin film, cm⁻¹) 3019, 2162, 2010, 1731, 1214, 1033, 920, 752, 668; **¹H NMR** (400 MHz, CDCl₃) δ 7.33-7.25 (m, 2H), 7.20-7.14 (m, 2H), 5.70 (td, *J* = 6.4, 2.9 Hz, 1H), 5.39 (qd, *J* = 6.3, 2.6 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 2.72 (d, *J* = 6.4 Hz, 2H), 1.48 (d, *J* = 6.4 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 170.9, 143.4, 140.7, 127.9, 127.5, 121.2, 121.0, 79.1, 79.0, 60.6, 41.8, 22.0, 14.2; **HRMS** [+NSI] calculated for C₁₃H₁₇O₃ 221.1172, found 221.1170 [M+H]⁺; **[α]_D²⁰** + 10.2 ° (*c* 1.0, CHCl₃); **HPLC** (Daicel OJ-H, 1 % IPA:HEX, 1 mL/min), λ 254 nm, t_R(min) = 8.4 min, t_R(maj) = 9.7 min.

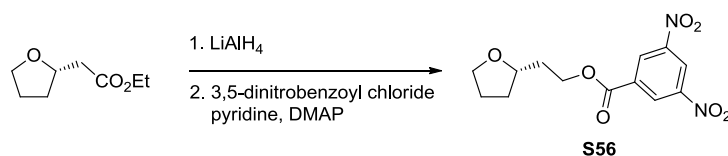
III. Kinetic Isotope Effect

For mechanistic insight, a 1:1 mixture of tetrahydrofuran and its fully deuterated analogue was subjected to C–H insertion conditions with ethyl diazoacetate and Ir(III) phebox **1** in order to calculate a kinetic isotope effect of 1.8 (Scheme S1). This value is very close to those previously reported for Rh-mediated donor/acceptor C–H into cyclohexane (2.0) and tetrahydrofuran (3.0),²³ indicating consistency with a concerted C–H insertion mechanism.

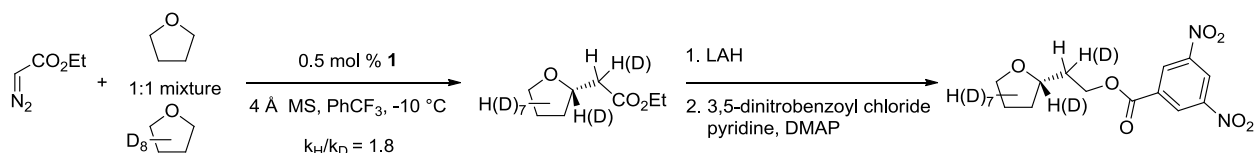
Scheme S1. Kinetic Isotope Effect for C–H Insertion of Ethyl Diazoacetate into Tetrahydrofuran



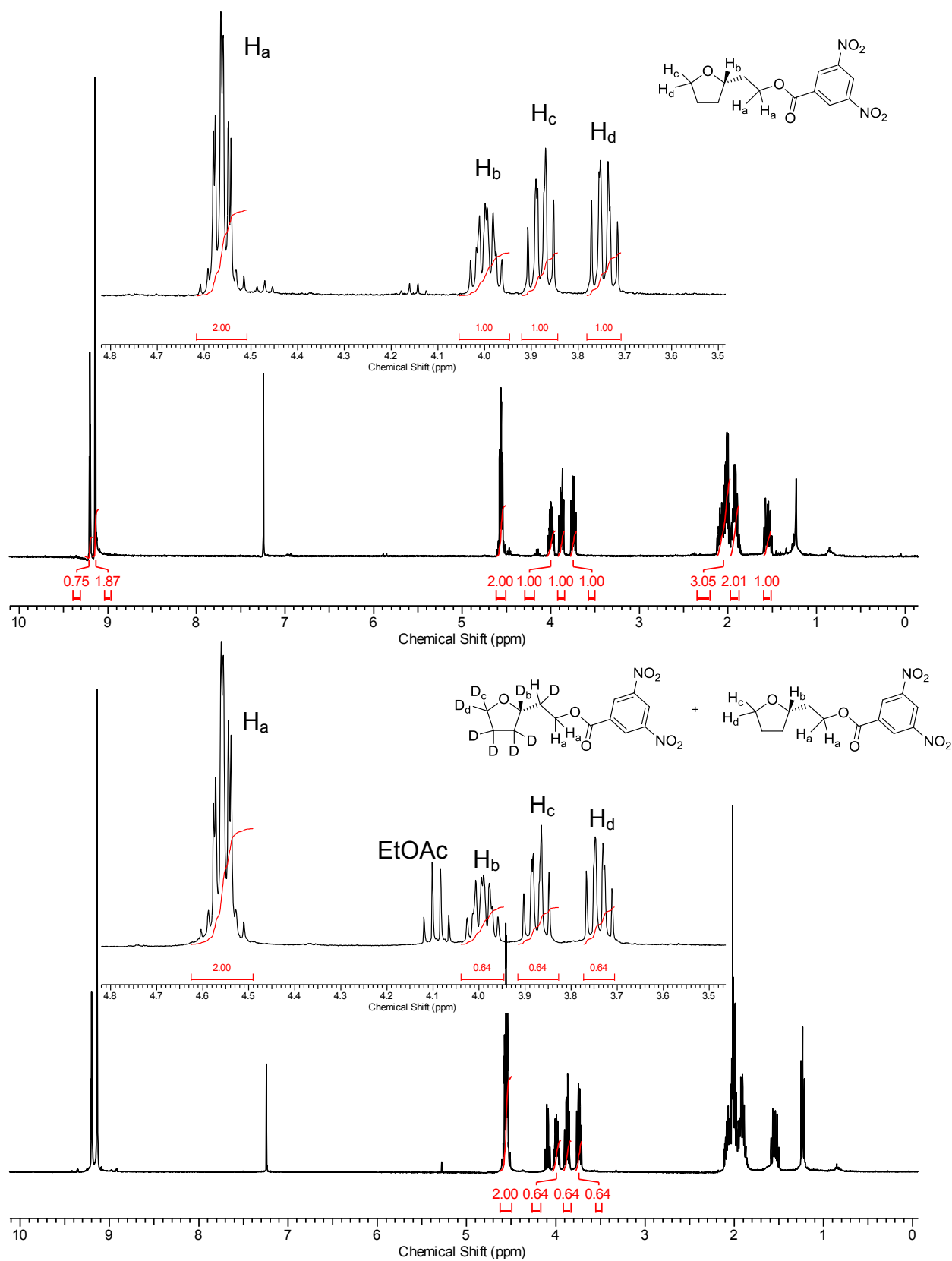
a) Kinetic Isotope Effect by ¹H NMR



(S)-2-(tetrahydrofuran-2-yl)ethyl 3,5-dinitrobenzoate (S56). A dry round bottom flask was charged with (S)-ethyl 2-(tetrahydrofuran-2-yl)acetate (48 mg, 0.30 mmol, 1.0 equiv) in THF (2 mL). The reaction mixture was cooled to 0 °C. LiAlH₄ (0.9 mL, 1 M in Et₂O, 3.0 equiv) was added dropwise, and the reaction was stirred overnight. Once thin layer chromatography indicated complete consumption of starting material, the reaction mixture was poured into a vigorously stirring solution of Et₂O (10 mL) and a saturated aqueous Rochelle's salt solution (5 mL). Et₂O (20 mL) was added and the resulting biphasic mixture was stirred vigorously for approximately 3 h. The organic layer was separated, washed with brine, dried over MgSO₄ and concentrated in vacuo. The crude product was dissolved in CH₂Cl₂ (1.2 mL). Et₃N (0.12 mL, 0.9 mmol, 3.0 equiv) and DMAP (1 mg, 5.5 μmol, 20 mol %) were added to the solution under N₂ and stirred for 10 min. 3,5-dinitrobenzoyl chloride (138 mg, 0.6 mmol, 2.0 equiv) was added in one portion, and the mixture was stirred for 1.5 h. NH₄Cl (aq) was added to the reaction mixture and extracted with CH₂Cl₂ (3 x). The combined organic layers were washed with NaHCO₃ (aq). The aqueous layer was extracted with CH₂Cl₂ (3 x). The combined organic layers were dried with MgSO₄, filtered, and concentrated *in vacuo*. Purification by preparative TLC (8:2 hexanes:EtOAc, 2 runs) afforded the title compound as a light yellow oil (55 mg, 59 % yield over 2 steps); **R_f** 0.21 (8:2 hexanes:EtOAc); **IR** (thin film, cm⁻¹) 3102, 2967, 2874, 1730, 1543, 1345, 1280, 1167, 722; **¹H NMR** (400 MHz, CDCl₃) 9.20 (t, *J* = 2.1 Hz, 1H), 9.14 (d, *J* = 2.1 Hz, 2H), 4.56 (td, *J* = 6.6, 1.8 Hz, 2H), 4.03-3.96 (m, 1H), 3.91-3.85 (m, 1H), 3.74 (td, *J* = 7.9, 6.4 Hz, 1H), 2.12-1.98 (m, 3H), 1.96-1.88 (m, 2H), 1.59-1.50 (m, 1H); **¹³C NMR** (150 MHz, CDCl₃) δ 162.7, 148.9, 134.3, 129.7, 129.6, 122.6, 122.5, 76.0, 68.1, 64.9, 34.8, 31.9, 25.8; **HRMS** [+NSI] calculated for C₁₃H₁₅N₂O₇ 311.0874, found 311.0871 [M+H]⁺.



(S)-2-(tetrahydrofuran-2-yl)ethyl 3,5-dinitrobenzoate. Prepared by general procedure **E** using ethyl diazoacetate (336 mg, 2.5 mmol) in PhCF₃ (8.6 mL), THF (408 μL, 5.0 mmol) and d⁸-THF (409 μL, 5.0 mmol) in PhCF₃ (5.7 mL), [(*S,S*)-*t*BuPhebox-*i*Pr]IrCl₂(H₂O) **1**²⁰ (8 mg, 0.5 mol %), and 4 Å MS (502 mg). The crude residue was taken forward without further purification. A dry round bottom flask was charged with the crude residue and dissolved in Et₂O (5 mL). The reaction mixture was cooled to 0 °C. LiAlH₄ (7.6 mL, 1 M in Et₂O, 3.0 equiv) was added dropwise, and the reaction was stirred overnight. Once thin layer chromatography indicated complete consumption of starting material, the reaction mixture was poured into a vigorously stirring solution of Et₂O (30 mL) and a saturated aqueous Rochelle's salt solution (15 mL). Et₂O (60 mL) was added and the resulting biphasic mixture was stirred vigorously for approximately 3 h. The organic layer was separated, washed with brine, dried over MgSO₄ and concentrated in vacuo. The crude product was dissolved in CH₂Cl₂ (8 mL). Pyridine (610 μL, 7.6 mmol, 3.0 equiv) and DMAP (31 mg, 0.26 mmol, 10 mol %) were added to the solution under N₂ and stirred for 10 min. 3,5-dinitrobenzoyl chloride (1.15 g, 5.0 mmol, 2.0 equiv) was added in one portion, and the mixture was stirred for 1.5 h. NH₄Cl (aq) was added to the reaction mixture and extracted with CH₂Cl₂ (3 x). The combined organic layers were washed with NaHCO₃ (aq). The aqueous layer was extracted with CH₂Cl₂ (3 x). The combined organic layers were dried with MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography (8:2 hexanes:EtOAc) afforded the title compound as a light yellow oil (192 mg, 25 % yield over 3 steps).



Calculations used for the determination of KIE value from ^1H NMR analysis:

$$H_a = 2.0$$

$$H_b = 0.64$$

$$D_b = 1 - 0.64 = 0.36$$

$$H_c = 0.64$$

$$D_c = 1 - 0.64 = 0.36$$

$$H_d = 0.64$$

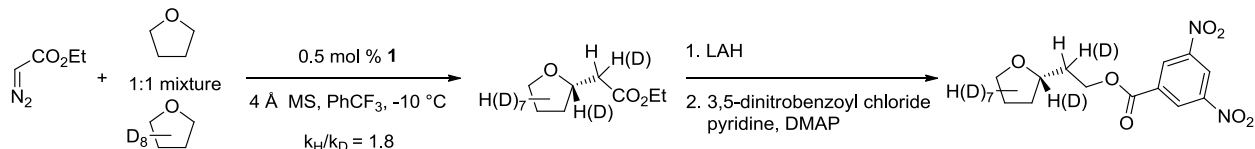
$$D_d = 1 - 0.64 = 0.36$$

$$\% \text{ H incorporated} = 0.64 / 1.0 = 64 \%$$

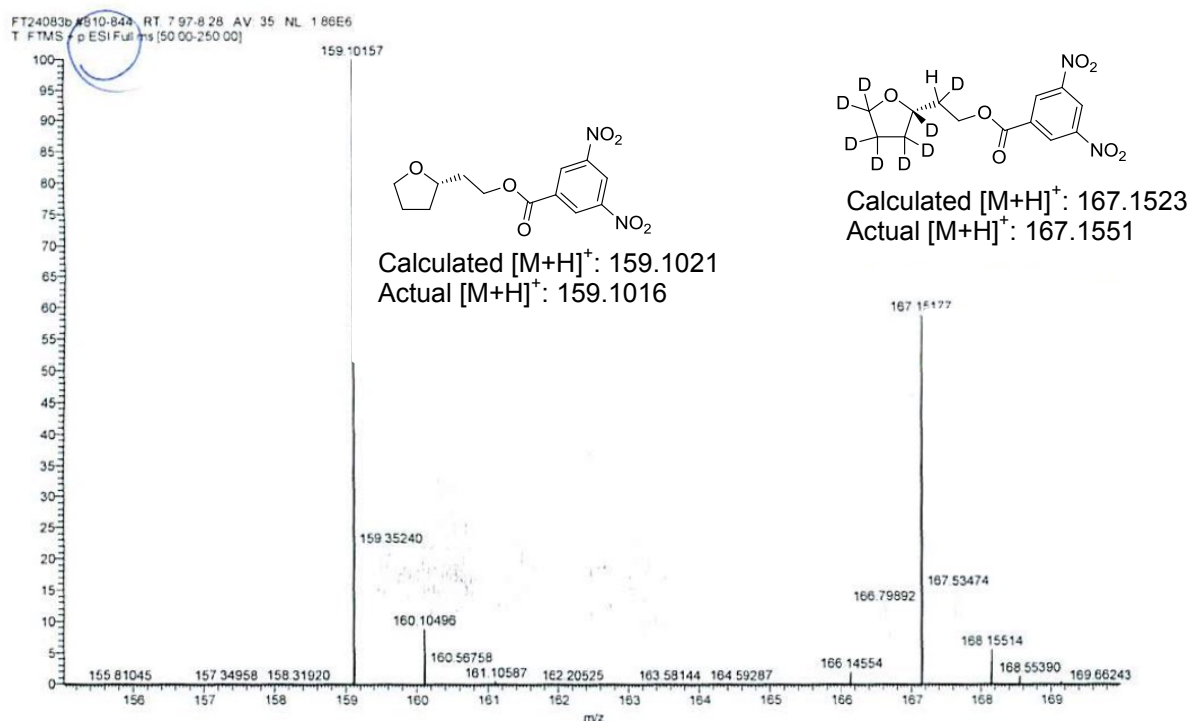
$$\% \text{ D incorporated} = 0.36 / 1.0 = 36 \%$$

$$\mathbf{KIE} = K_H / K_D = 0.64 / 0.36 = \mathbf{1.8}$$

b) Kinetic Isotope Effect by Mass Spectrometry



(S)-2-(tetrahydrofuran-2-yl)ethyl 3,5-dinitrobenzoate. Prepared by general procedure E using ethyl diazoacetate (100 mg, 0.88 mmol) in $PhCF_3$ (3 mL), THF (143 μL , 1.76 mmol) and d_8 -THF (142 μL , 1.76 mmol) in $PhCF_3$ (2 mL), [(*S,S*)-*t*BuPhebox-*i*Pr]IrCl₂(H₂O) **1**²⁰ (2.8 mg, 0.5 mol %), and 4 Å MS (176 mg). The crude residue was analyzed by ESI-MS.



m/z Intensity Relative

159.09913	130501.1	7.00
159.10157	1864901.6	100.00
160.10496	162675.2	8.72
167.15177	1101378.0	59.06
168.15514	102915.4	5.52

$$KIE = K_H / K_D = 100.00 / 59.06 = 1.7$$

IV. X-Ray Crystallographic Information

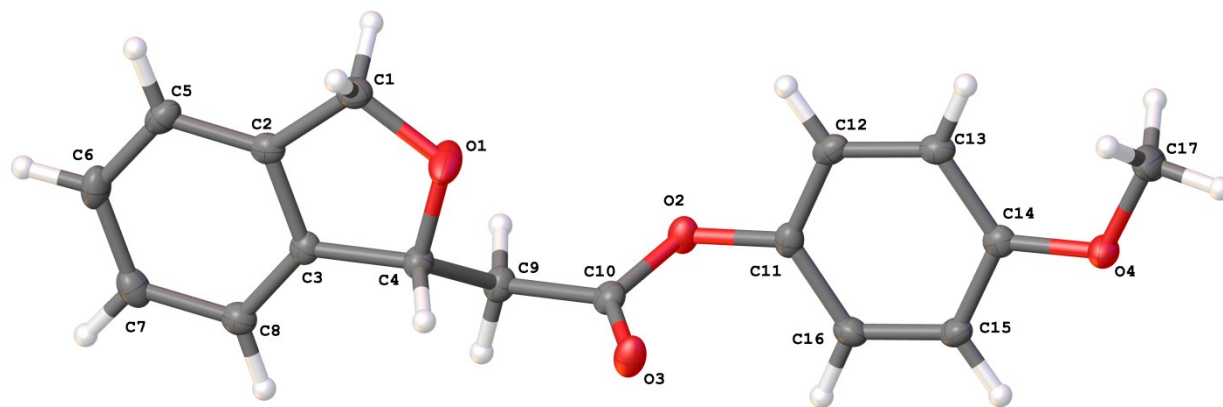
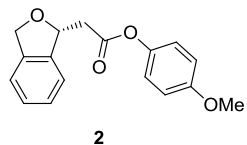


Table S2. Structural refinement data for (*R*)-4-methoxyphenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (**2**).

2	
Formula	C ₁₇ H ₁₆ O ₄
Form. Wt. (g/mol)	284.30
T (K)	100.02
Crystal system	Orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
<i>a</i> (Å)	7.47301(10)
<i>b</i> (Å)	12.08020(15)
<i>c</i> (Å)	15.6344(2)
α (°)	90
β (°)	90
γ (°)	90
<i>V</i> (Å³)	1411.40(3)
<i>Z</i>	4

ρ_{calc} (g/cm)	1.338
μ/mm^{-1}	0.781
F(000)	600.0
Crystal size (mm³)	$0.23 \times 0.185 \times 0.176$
Radiation	CuK α ($\lambda = 1.54178$)
2Θ range	9.252 to 146.698
Index ranges	$-9 \leq h \leq 8, -15 \leq k \leq 14, -19 \leq l \leq 19$
Reflns. Collected	24525
Unique reflns.	2805 [$R_{\text{int}} = 0.0236, R_{\text{sigma}} = 0.0108$]
Data/rest./par.	2805/36/242
GOF	1.101
Final R indexes [$I > 2\sigma(I)$]	$R_1 = 0.0270, wR_2 = 0.0668$
All data	$R_1 = 0.0273, wR_2 = 0.0670$
Largest diff. peak/hole / e Å⁻³	0.17/-0.26
Flack parameter	0.06(4)

V. Computational Details

All calculations were performed using the Gaussian 09 software package.²⁴ The geometries of molecules were optimized without symmetry constraints at the level of theory using M06 functional²⁵ and a combined basis set (denoted as BSS) consisting of LANL08(f) basis sets associated with the Hay-Wadt relativistic effective core potentials (RECPs)²⁶ for Ir atom, and 6-31G(d,p) basis sets for all other atoms. All transition states were confirmed to have one imaginary frequency associated with the reaction coordinate. The nature of transition states was confirmed by performing IRC (intrinsic reaction coordinate) calculations. Solvent effects were incorporated by using the CPCM method²⁷ with all geometries optimized in dichloromethane solvent at the M06/BSS level of theory. The reported enthalpies and Gibbs free energies (in kcal/mol) were calculated at the standard conditions (298.15 K and 1 atm).

Table S3: The calculated geometries (Cartesian coordinates, in Å) of the reported transition states.

TS1 pro-S

C	2.17840000	0.74113000	-0.07264100
C	2.88575000	0.98729100	1.20243400
O	3.47961000	-0.10226100	1.69671700
C	3.99517000	-0.02076900	3.03565600
Ir	0.16018400	0.20326200	-0.04858300
Cl	0.20107800	-0.18205600	2.33414400
C	-1.80189000	-0.12218600	-0.04625300
C	-2.68537600	0.92468800	0.20542900
C	-4.06477600	0.69923300	0.22479500
C	-4.57181400	-0.58520500	-0.02353000
C	-3.67189800	-1.63888800	-0.27607300
C	-2.29856800	-1.40573300	-0.28045700
C	-1.91636800	2.12538900	0.46932600
O	-2.43305900	3.28529400	0.85369400
C	-1.30661600	4.11480400	1.25566800
C	-0.06558700	3.39684500	0.70362500
N	-0.61524500	2.07759000	0.37055600
C	-1.18218700	-2.30723600	-0.49598100
O	-1.30116700	-3.60110000	-0.76371300
C	0.03768400	-4.07292500	-1.08193600
C	0.97634400	-2.95038600	-0.61398200
N	0.03459200	-1.83852200	-0.42777600
C	-6.07321100	-0.88029100	-0.03162900
C	1.77082300	-3.23808000	0.66575400
C	0.59071400	4.06548300	-0.50871900
Cl	0.14342100	0.59834200	-2.42792000
O	2.87286200	2.07141100	1.75474400
H	-4.05103400	-2.64311600	-0.46585100
H	-4.73923700	1.52673600	0.43450600
C	-6.39359600	-1.95999200	1.00782100
C	-6.48488600	-1.37565300	-1.42265100
C	-6.90766600	0.35473200	0.29921700
H	2.20470500	-2.27104800	0.97329800
H	-1.31523400	4.16286200	2.34937800
H	-1.46862600	5.11751700	0.84984100
H	0.07567300	-4.23080700	-2.16466000
H	0.18512000	-5.03066000	-0.57440000
H	1.67923400	-2.67922300	-1.41321100
H	0.69849800	3.26300500	1.48220600
H	1.34376100	3.34841500	-0.87175300
H	3.24673300	0.46551800	3.67201800
H	4.89643700	0.60563800	3.03474100
H	-7.56251000	-1.58702100	-1.44826200
H	-5.96001000	-2.29688400	-1.70415000
H	-6.26920600	-0.61939000	-2.18878600
H	-7.47039300	-2.17627600	1.00910000
H	-6.11265200	-1.63066500	2.01667800
H	-5.86901500	-2.90117900	0.80340100
H	-7.97256100	0.09029000	0.28875600
H	-6.76177400	1.15944500	-0.43296800

H	-6.67648700	0.75010300	1.29680100
C	1.31303100	5.33267800	-0.07427500
H	1.83319700	5.79546600	-0.92139100
H	0.61233100	6.08015500	0.32408200
H	2.05669500	5.12112600	0.70479400
C	-0.38798100	4.33047900	-1.64265700
H	0.14054600	4.73238600	-2.51552000
H	-0.89426200	3.41004700	-1.95906600
H	-1.15071300	5.06982800	-1.36062200
C	2.90600900	-4.20777400	0.36837700
H	3.51618300	-4.37935200	1.26384400
H	2.52353300	-5.18615900	0.04362000
H	3.56640000	-3.83193900	-0.42500000
C	0.89766200	-3.73855500	1.80704300
H	1.48813300	-3.82526600	2.72794000
H	0.07172700	-3.04809700	2.01470000
H	0.48265700	-4.73482800	1.59941400
C	4.27912300	-1.43146700	3.47277700
H	4.70620300	-1.44019200	4.48083600
H	3.35289400	-2.01945200	3.48705800
H	4.98906600	-1.91799100	2.79321400
H	2.70577400	-0.44135500	-3.92467200
H	2.45432600	1.50287100	-0.81535600
C	3.86899000	-0.80203500	-1.14202100
O	3.42368600	-1.42444600	-2.25411900
C	3.66518600	-0.59836600	-3.42129600
C	4.30282500	0.68187600	-2.90178200
C	4.85987100	0.25327700	-1.54473100
H	2.84495900	-0.26273500	-0.61738900
H	4.09885300	-1.50039300	-0.32812000
H	4.32895100	-1.17211100	-4.07871100
H	5.07227800	1.06278900	-3.57769300
H	3.54312600	1.46293900	-2.77551100
H	5.83895800	-0.23333000	-1.65419200
H	4.96421900	1.06547100	-0.81975300

TS2 pro-R

C	2.16899000	0.66208000	-0.11179700
C	2.92007500	0.85364800	1.14961600
O	3.45418100	-0.26934400	1.62776300
C	4.01983600	-0.21812100	2.94726700
Ir	0.14497000	0.18509900	-0.05895700
Cl	0.20586400	-0.24428200	2.31460100
C	-1.82537500	-0.09754400	-0.04516300
C	-2.68261400	0.96425500	0.23170900
C	-4.06721500	0.77425000	0.23991600
C	-4.60605300	-0.48973200	-0.04554500
C	-3.73234600	-1.55889900	-0.32209700
C	-2.35330900	-1.36028600	-0.31582600
C	-1.88292300	2.13823100	0.52378400
O	-2.36698500	3.29707600	0.94892900
C	-1.21741800	4.08573000	1.36849400
C	0.00321600	3.35196200	0.79100700
N	-0.58405800	2.06121800	0.41324600

C	-1.26192800	-2.28482000	-0.55470900
O	-1.42322400	-3.56891000	-0.84303700
C	-0.10180400	-4.08236800	-1.16191800
C	0.87149400	-3.00058300	-0.66959100
N	-0.02990100	-1.85436200	-0.48191400
C	-6.11448900	-0.74576500	-0.07097100
C	1.64513100	-3.34132500	0.60918700
C	0.67872800	4.04527500	-0.39616700
Cl	0.07485100	0.63887100	-2.42808200
O	2.96978700	1.93454400	1.70693200
H	-4.13617300	-2.54743700	-0.54080000
H	-4.72126300	1.61325500	0.46810200
C	-6.46995000	-1.83650600	0.94517500
C	-6.52872400	-1.20459500	-1.47394500
C	-6.91917000	0.50412000	0.27674300
H	2.14188000	-2.40652500	0.92129800
H	-1.22113200	4.10422200	2.46306900
H	-1.35551600	5.10284100	0.99083700
H	-0.06213800	-4.22562800	-2.24659700
H	0.00984800	-5.05148400	-0.66718000
H	1.59519900	-2.75712000	-1.46011100
H	0.76314400	3.16957500	1.56392500
H	1.42002100	3.32608100	-0.77854800
H	3.32481500	0.31159300	3.60920200
H	4.95584000	0.35391400	2.91194300
H	-7.61099600	-1.38879600	-1.50966400
H	-6.02524900	-2.13321000	-1.76987100
H	-6.28980100	-0.43975800	-2.22439000
H	-7.55177300	-2.02586400	0.93455100
H	-6.18856600	-1.53385200	1.96220100
H	-5.96720100	-2.78624700	0.72586100
H	-7.99055400	0.26885000	0.24946600
H	-6.74309300	1.31952800	-0.43672700
H	-6.68876800	0.87243500	1.28481600
C	1.42442900	5.28269200	0.08296200
H	1.95717400	5.76250400	-0.74663800
H	0.73761500	6.03085300	0.50358600
H	2.16055000	5.02964700	0.85660800
C	-0.29032300	4.36627300	-1.52381700
H	0.24853600	4.78953600	-2.38002300
H	-0.81064100	3.46592100	-1.87350000
H	-1.04197500	5.10796000	-1.21900200
C	2.71460300	-4.38244000	0.30816500
H	3.32773500	-4.57598600	1.19682300
H	2.26913900	-5.34092100	0.00545700
H	3.38497700	-4.06071500	-0.50090000
C	0.74039300	-3.79317900	1.74629300
H	1.32707200	-3.93873600	2.66198200
H	-0.03088700	-3.04678100	1.96915100
H	0.25259500	-4.75292300	1.52511300
C	4.23758900	-1.64214200	3.37874200
H	4.70284800	-1.67319700	4.36935500
H	3.28098800	-2.17678500	3.43152500
H	4.89187400	-2.16948300	2.67437100

H	2.48480700	1.40557500	-0.85894500
O	4.90915300	-0.10411900	-1.14342900
C	3.80822100	-0.88532400	-1.23808000
C	3.41165800	-1.01244800	-2.68564400
C	3.90311500	0.31913500	-3.24820400
C	5.11569600	0.61767500	-2.38189200
H	5.24352900	1.67763700	-2.14012100
H	2.81920500	-0.36673000	-0.68461500
H	6.04948800	0.24282800	-2.81956900
H	3.12683000	1.08338900	-3.11657000
H	4.15573900	0.26972200	-4.31032400
H	3.95176800	-1.86569600	-3.11990100
H	2.33557900	-1.16543700	-2.82371000
H	3.87932800	-1.77661700	-0.60141700

TS3 pro-S

C	1.82574200	0.43358100	0.17313000
C	2.48459500	0.59898700	1.48835900
O	2.93710900	-0.55303200	1.99212000
C	3.41799200	-0.53742200	3.34571500
Ir	-0.21099000	0.10735200	0.04687600
Cl	-0.36109100	-0.36597000	2.40965700
C	-2.19604400	-0.01943700	-0.10800200
C	-2.98912600	1.10577800	0.11631500
C	-4.37516400	1.02233700	0.00797900
C	-4.98866300	-0.19619900	-0.34237900
C	-4.18502600	-1.32340800	-0.56853600
C	-2.79545800	-1.23025000	-0.44397000
C	-2.12917100	2.21071100	0.49554700
O	-2.56269500	3.39870900	0.89172300
C	-1.40074300	4.10168600	1.41475400
C	-0.18996300	3.26951600	0.96156700
N	-0.83597200	2.03354500	0.50058000
C	-1.76051400	-2.22995600	-0.62048100
O	-1.98448300	-3.49080200	-0.96464200
C	-0.67857000	-4.08299500	-1.20664500
C	0.32648500	-3.08748300	-0.60712200
N	-0.51164500	-1.89289400	-0.43662700
C	-6.51343800	-0.24386400	-0.46181700
C	0.97725700	-3.51901400	0.71248700
C	0.67035200	3.91441900	-0.12817600
Cl	-0.04118700	0.58886900	-2.30918800
O	2.55524400	1.67132400	2.05687500
H	-4.63529200	-2.27631400	-0.83865400
H	-4.98748100	1.90407800	0.19722600
C	-6.97415700	0.75258900	-1.53139600
C	-7.14448000	0.12942300	0.88397700
C	-7.02070900	-1.62865100	-0.85540000
H	1.50645200	-2.62752000	1.09126900
H	-1.50829200	4.13773700	2.50334000
H	-1.42181200	5.12088200	1.01838300
H	-0.56848100	-4.19179600	-2.29044800
H	-0.66871700	-5.07350900	-0.74312700
H	1.11738400	-2.85812700	-1.33418100

H	0.46132400	3.02044500	1.81066700
H	1.40448500	3.14693800	-0.41990900
H	2.69797700	0.00382100	3.97061400
H	4.37134800	0.00736100	3.38046100
H	-8.24007700	0.10603700	0.80913100
H	-6.85647100	1.13651400	1.20924100
H	-6.84370500	-0.57620400	1.66923900
H	-8.06738200	0.72162600	-1.63307000
H	-6.53644300	0.51161300	-2.50881400
H	-6.69488700	1.78373800	-1.28303500
H	-8.11544000	-1.60974500	-0.92704600
H	-6.75309700	-2.39098100	-0.11230800
H	-6.63181600	-1.94683400	-1.83148200
C	1.43253500	5.09872300	0.44954400
H	2.09382100	5.54123700	-0.30466300
H	0.75074800	5.89141800	0.78888300
H	2.05059800	4.79935900	1.30560700
C	-0.12829600	4.30410400	-1.36241500
H	0.54038300	4.69391000	-2.13956200
H	-0.66058700	3.44351600	-1.78598000
H	-0.86015600	5.09458600	-1.14397800
C	2.00083300	-4.61719000	0.45682700
H	2.54763200	-4.85823800	1.37694500
H	1.51916900	-5.54306100	0.11132000
H	2.73515400	-4.32391600	-0.30606800
C	-0.03672500	-3.94120800	1.76535600
H	0.47023000	-4.16123100	2.71310600
H	-0.76629000	-3.14707700	1.96219500
H	-0.57594100	-4.85284100	1.47162100
C	3.56270000	-1.97532700	3.76155600
H	3.96695800	-2.04169800	4.77680900
H	2.58678900	-2.47605900	3.74528400
H	4.23906300	-2.51205800	3.08465300
H	2.65947200	-0.03095900	-3.29993600
H	2.25972800	1.12284300	-0.56776300
C	3.42206400	-1.28144400	-0.81382200
O	3.00849500	-1.65417400	-2.05940200
C	3.48976000	-0.70344600	-3.02786500
C	4.59730400	0.00547500	-2.32181200
C	4.56299200	-0.36518200	-0.97696700
H	2.45123900	-0.67541100	-0.30090200
H	3.47260000	-2.11858500	-0.10661800
H	3.79628200	-1.25952900	-3.92059000
C	5.55097400	0.90150500	-2.78259500
H	5.58683600	1.19637300	-3.82882700
C	5.47189000	0.14557600	-0.05650300
H	5.43424900	-0.15052200	0.99053600
C	6.43494800	1.03630900	-0.52066900
H	7.16807800	1.44560600	0.17006700
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H	7.23378600	2.10681600	-2.20669100

TS4 pro-R

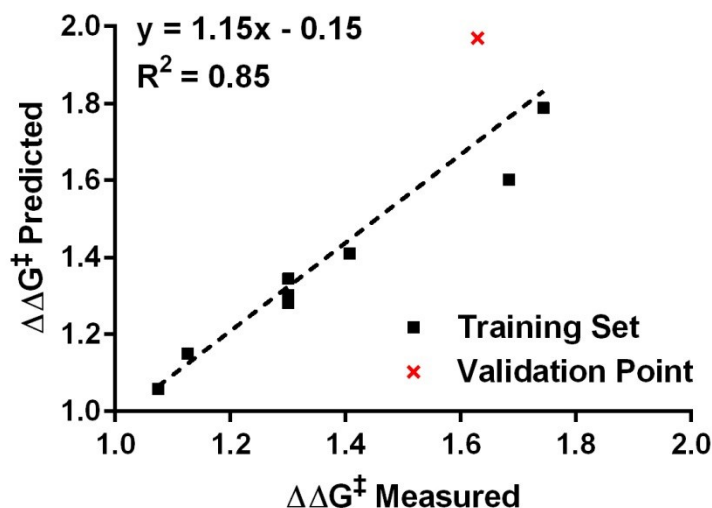
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C	2.05077700	-0.11826200	0.09508800
C	2.95649700	0.93922900	0.00848000
C	4.31589500	0.71674300	0.21182500
C	4.78692800	-0.57454200	0.52212900
C	3.86947700	-1.63104000	0.61592600
C	2.50788700	-1.39835500	0.39727600
C	2.22780400	2.14265000	-0.34922700
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C	1.73609700	4.14196800	-1.19426600
C	0.42693300	3.39957200	-0.87755200
N	0.92765800	2.08773000	-0.44943100
C	1.37736300	-2.30499700	0.42377500
O	1.46114400	-3.60493900	0.67526000
C	0.09188300	-4.08769800	0.75050200
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C	6.28653000	-0.77337000	0.75131200
C	-1.22396100	-3.25931700	-1.32670600
C	-0.45673000	4.05680500	0.18570000
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O	-2.48323400	2.06926400	-2.20695700
H	4.20941200	-2.63655400	0.85488800
H	5.01959300	1.54549200	0.13308900
C	6.74120000	0.10066600	1.92550800
C	7.05648600	-0.36901700	-0.51090300
C	6.63649700	-2.22352900	1.07633200
H	-1.63369300	-2.30591700	-1.70073600
H	1.92515900	4.22872400	-2.26884000
H	1.81807600	5.13081300	-0.73426600
H	-0.14435300	-4.23158800	1.81068800
H	0.04714600	-5.05103500	0.23534300
H	-1.63072900	-2.75899700	0.72101500
H	-0.17636900	3.25644300	-1.78540700
H	-1.26523100	3.33574700	0.38311400
H	-2.43971500	0.57624700	-4.24861000
H	-4.15808000	0.53749400	-3.80751100
H	8.13539100	-0.50569300	-0.35711300
H	6.89136800	0.68223000	-0.77624900
H	6.75638300	-0.98344800	-1.36973200
H	7.81565100	-0.03575100	2.10802900
H	6.20446600	-0.16646500	2.84524200
H	6.57062200	1.16730400	1.73510400
H	7.71937500	-2.31220100	1.22970200
H	6.36262100	-2.90591800	0.26125600
H	6.14543700	-2.56893500	1.99532900
C	-1.08391300	5.32535400	-0.37522000
H	-1.76565400	5.77786300	0.35457100

H	-0.32169800	6.07920100	-0.61800100
H	-1.65595200	5.11865600	-1.28877700
C	0.27948200	4.31757200	1.49074800
H	-0.41131800	4.71705900	2.24312000
H	0.71439600	3.39641700	1.89792600
H	1.08175500	5.05872600	1.36704900
C	-2.33882600	-4.29656500	-1.30505100
H	-2.72855100	-4.47025600	-2.31537300
H	-1.98109400	-5.26532100	-0.92741900
H	-3.17968800	-3.98572200	-0.66974200
C	-0.09675600	-3.68307600	-2.25691000
H	-0.47529300	-3.79503200	-3.28084000
H	0.70453700	-2.93561600	-2.28794900
H	0.33178400	-4.65215100	-1.96493700
C	-3.32104700	-1.40401600	-4.30405600
H	-3.62302000	-1.36455800	-5.35585200
H	-2.35483400	-1.91985000	-4.24227300
H	-4.06566800	-1.99185000	-3.75444900
H	-2.32382900	1.39367400	0.36372900
O	-4.78494300	-0.12732000	-0.11517200
C	-3.75022900	-0.85411200	0.39474200
C	-3.81900300	-0.76903400	1.86427200
C	-4.76157800	0.21248500	2.17413500
C	-5.33586600	0.73012600	0.89973000
H	-5.04861900	1.77142700	0.69164400
H	-2.63641900	-0.36251400	0.06143700
H	-6.42844000	0.66104500	0.83895700
H	-3.62254400	-1.81760500	-0.11627600
C	-5.02553900	0.55450100	3.49244700
H	-5.75940100	1.31843900	3.73880500
C	-3.11608200	-1.43384100	2.86426600
H	-2.36917900	-2.18885900	2.62704300
C	-4.32838800	-0.11474700	4.49590700
H	-4.52117000	0.13132600	5.53758700
C	-3.38656800	-1.09967200	4.18657800
H	-2.85677700	-1.60679500	4.98903600

VI. Linear Regression Mathematical Modeling Details

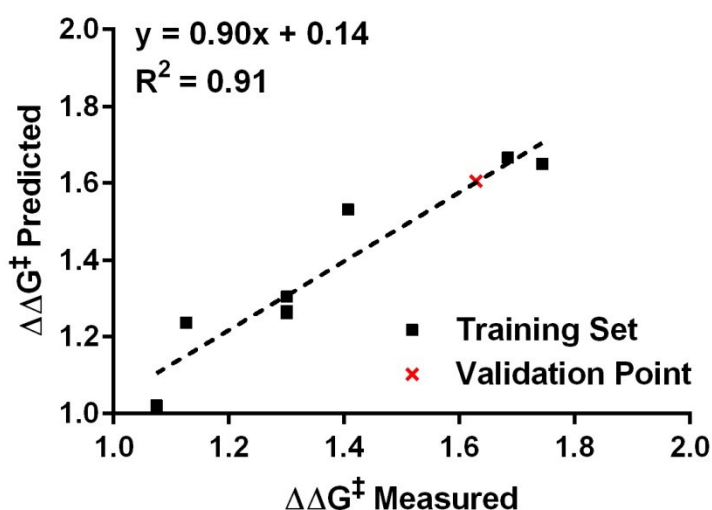
Modeling was performed using MATLAB²⁸ and a script similar to previous studies.²⁹ Initial modeling led to a model that incorporated Charton values and Sterimol B₅. Details of this model are:

$$y = 0.23 + 1.20 \text{ Charton} + 0.44 B_5 + 1.06 (\text{Charton} \times B_5)$$



This model predicted a $\Delta\Delta G^\ddagger$ of 1.97, equivalent to an enantiomeric ratio of 96.5 to 3.5. Because this model did not predict the measured ratio well, modeling was re-evaluated and a new model was found. This model is presented in the text, and the details repeated here:

$$y = 0.47 + 1.26(\text{Austel}) - 2.52(\text{Austel} \times E_s) - 2.54(E_s)^2$$



The values used to build these models are in Table S4. All values were collected from the same source.³⁰

Table S4. Ir(III)-Phebim catalyst steric parameters.

Group	<i>R</i>	<i>S</i>	Charton	B ₁	B ₅	L	Austel	E _s
Bn	86	14	0.7	1.52	6.02	4.62	4.00	-1.61
<i>n</i> Bu	87	13	0.68	1.52	4.54	6.17	3.00	-1.63
<i>i</i> Pr	90	10	0.76	1.9	3.17	4.11	3.00	-1.71
Et	90	10	0.56	1.52	3.17	4.11	2.00	-1.31
<i>c</i> Hex	90	10	0.87	1.91	3.49	6.17	3.00	-2.03
<i>s</i> Bu	91.5	8.5	1.02	1.9	3.49	4.92	4.00	-2.37
<i>i</i> Bu	94.5	5.5	0.98	1.52	4.45	4.92	4.00	-2.17
CH ₂ Hex	95	5	0.97	1.52	5.42	6.09	4.00	-2.22
CH ₂ <i>t</i> Bu	94	6	1.34	1.52	4.18	4.89	5.00	-2.98

The measured versus predicted values from both models are in Table S5. CH₂^{*t*}Bu was predicted after the model had been built with the initial eight groups.

Table S5. Comparison of measured and predicted $\Delta\Delta G^\ddagger$ values from the mathematical model.

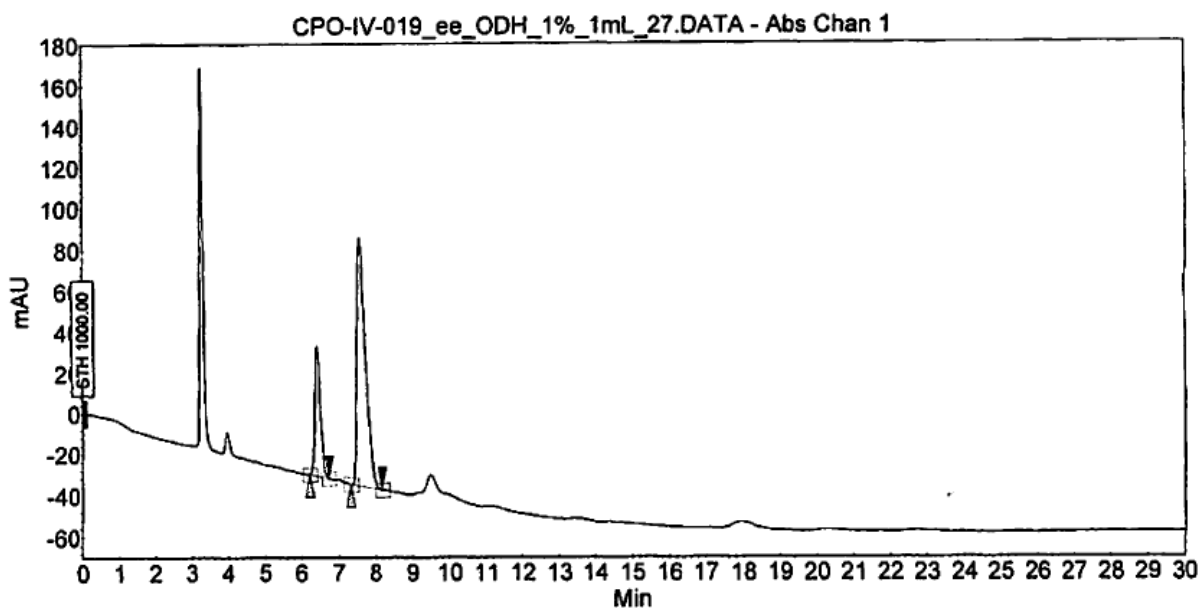
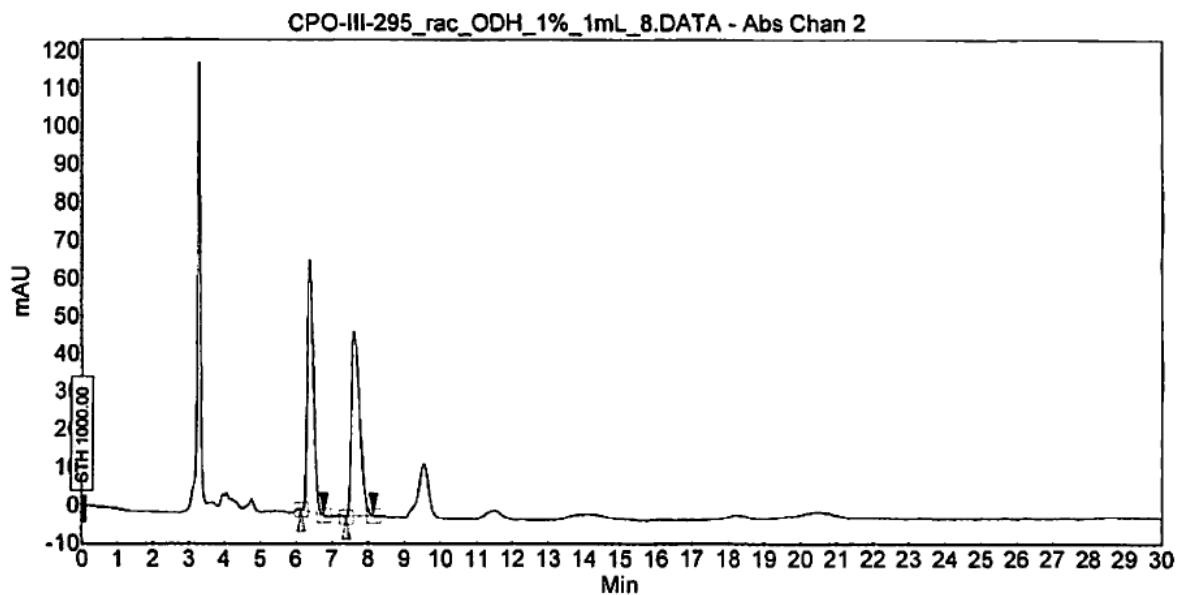
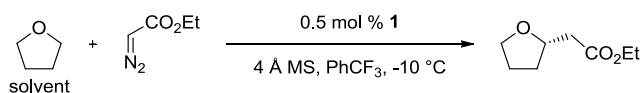
Group	Measured $\Delta\Delta G^\ddagger$ (kcal/mol)	Predicted $\Delta\Delta G^\ddagger$ (kcal/mol) Charton and Sterimol	Predicted $\Delta\Delta G^\ddagger$ (kcal/mol) Austel and E _s
Bn	1.07	1.06	1.02
<i>n</i> Bu	1.13	1.15	1.24
<i>i</i> Pr	1.30	1.30	1.30
Et	1.30	1.28	1.26
<i>c</i> Hex	1.30	1.34	1.27
<i>s</i> Bu	1.41	1.41	1.53
<i>i</i> Bu	1.68	1.60	1.67
CH ₂ Hex	1.74	1.79	1.65
CH ₂ <i>t</i> Bu	1.63	1.97	1.61

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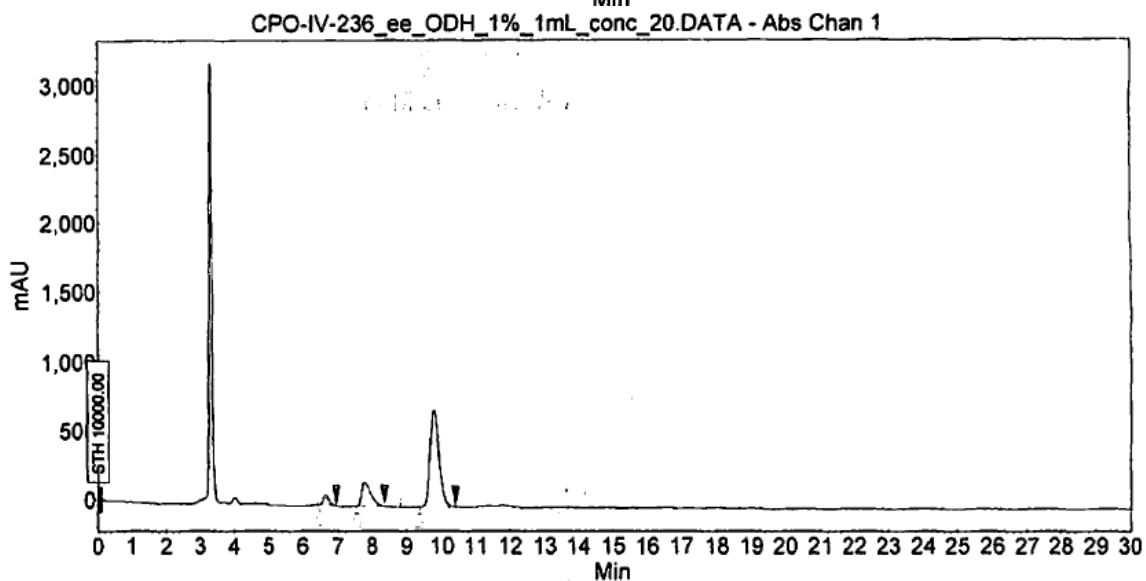
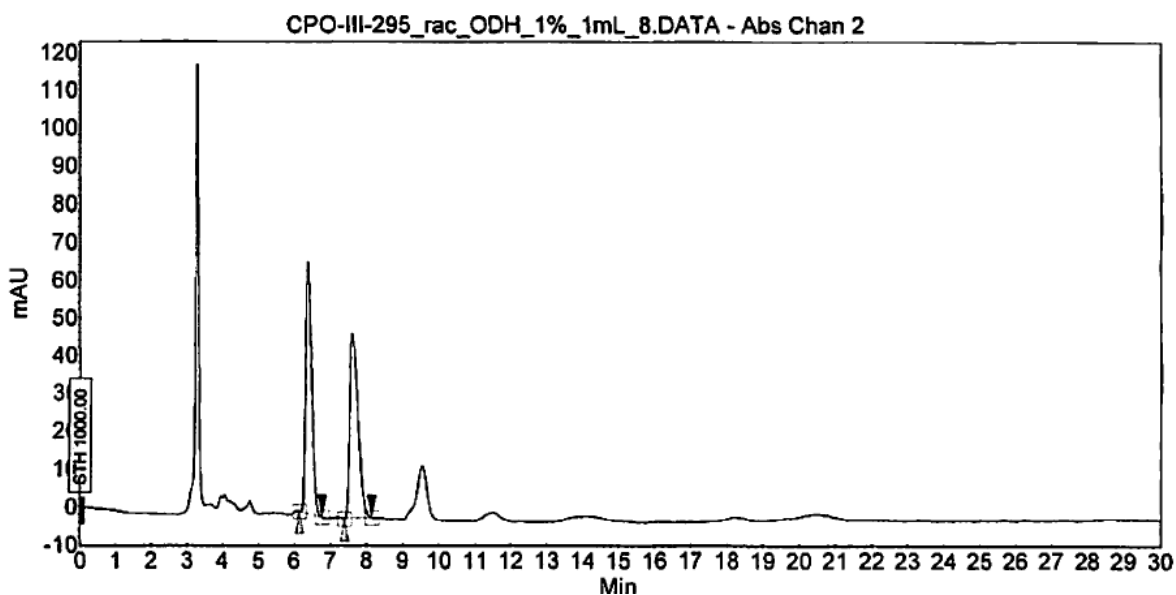
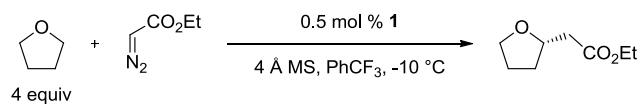
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VIII. HPLC Data



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	6.43	25.47	63.8	11.0	25.470
2	UNKNOWN	7.58	74.53	121.1	32.3	74.530
Total			100.00	184.9	43.3	100.000

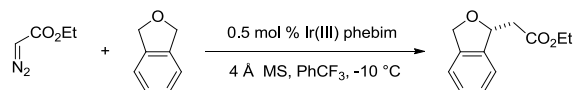


Peak results :

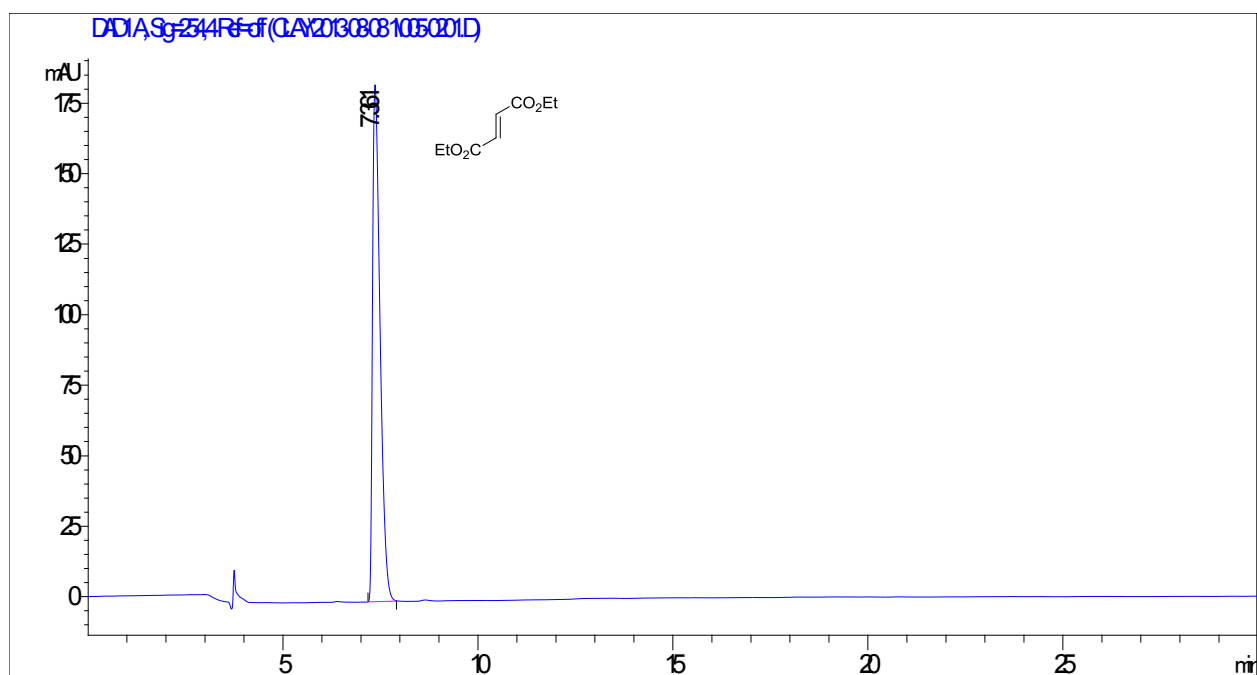
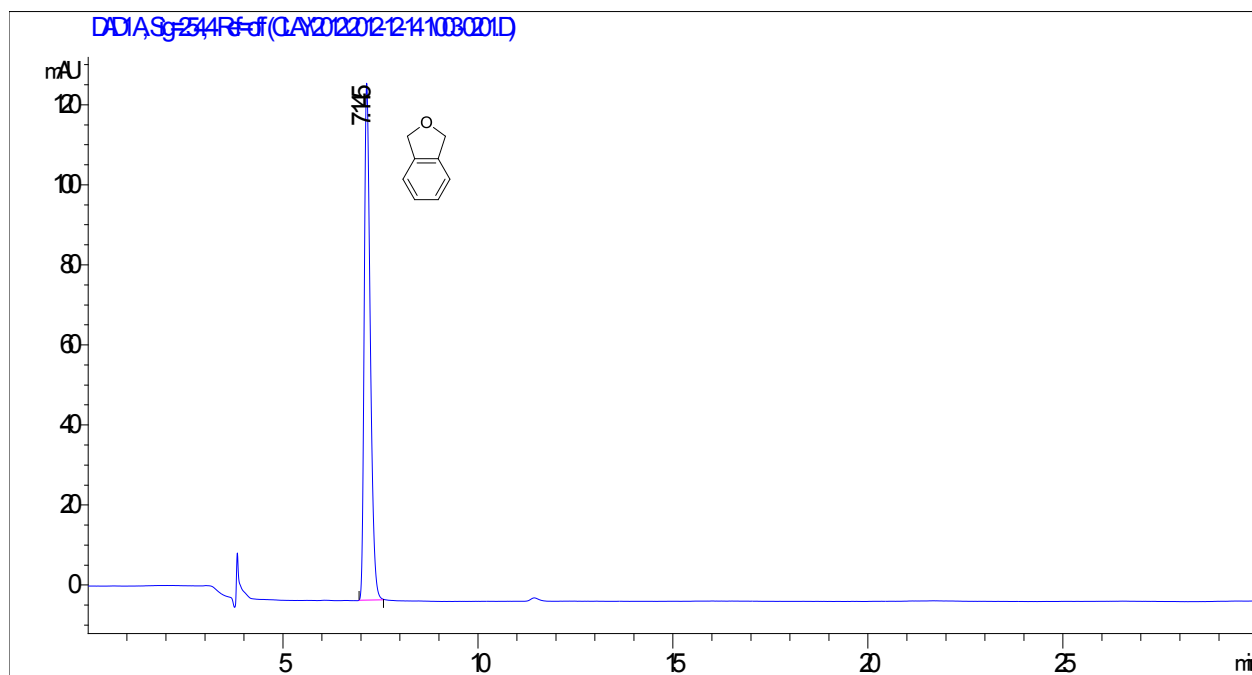
Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	6.64	4.77	73.7	13.2	4.772
2	UNKNOWN	7.75	19.86	174.6	54.8	19.865
3	UNKNOWN	9.78	75.36	705.8	207.8	75.363
Total			100.00	954.1	275.8	100.000

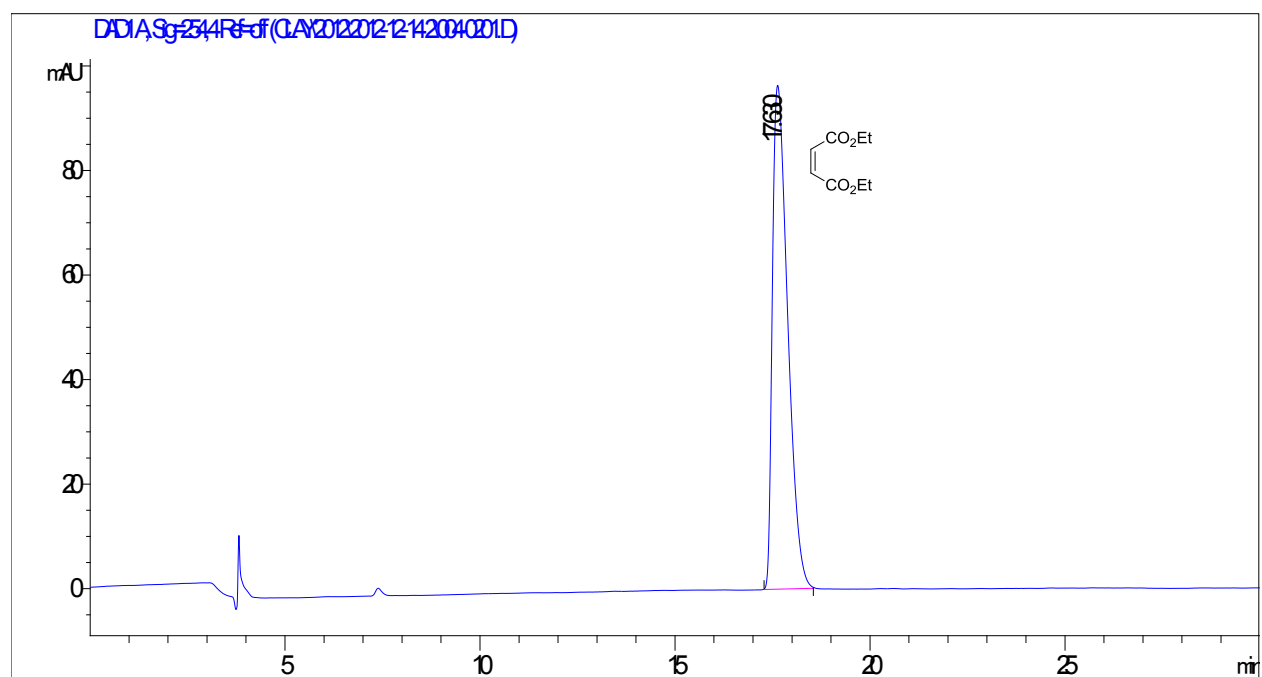
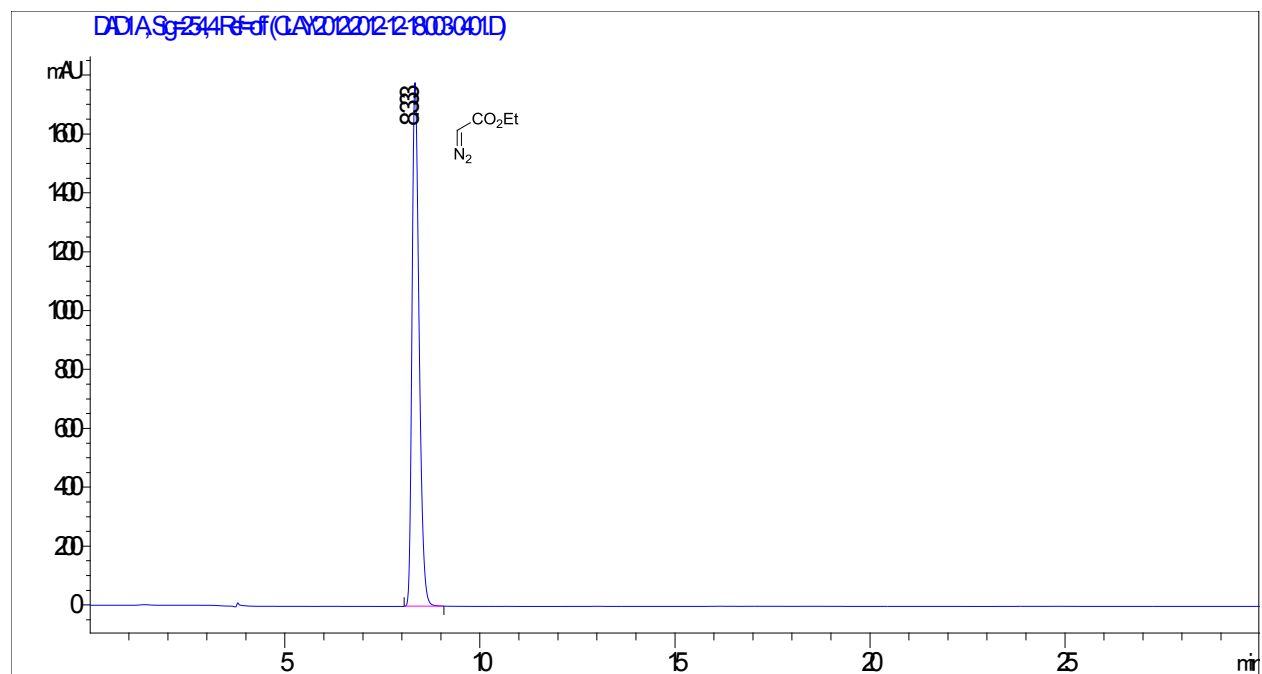


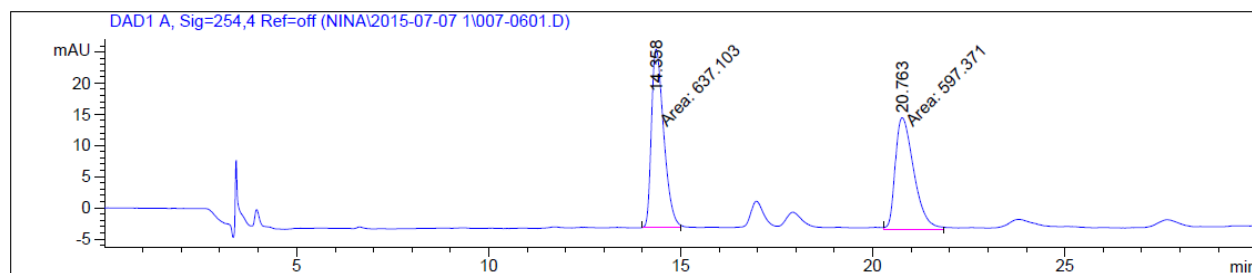
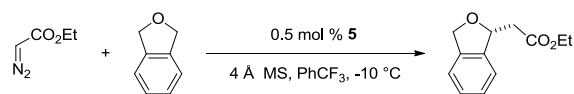
Catalyst Optimization Starting Materials and Side Products



HPLC (Daicel OJ-H, 1 % IPA:HEX, 1 mL/min), λ 254 nm, t_R (phthalan) = 7.15 min, t_R (diethyl fumarate) = 7.36 min, t_R (ethyl diazoacetate) = 8.33 min, t_R (diethyl maleate) = 17.63 min.



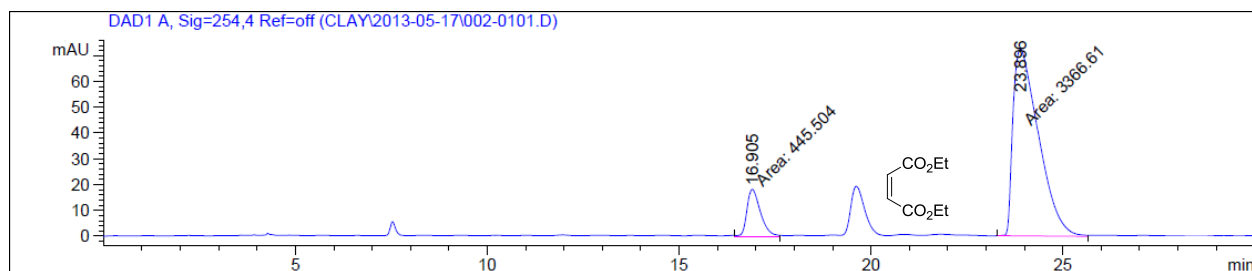




Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

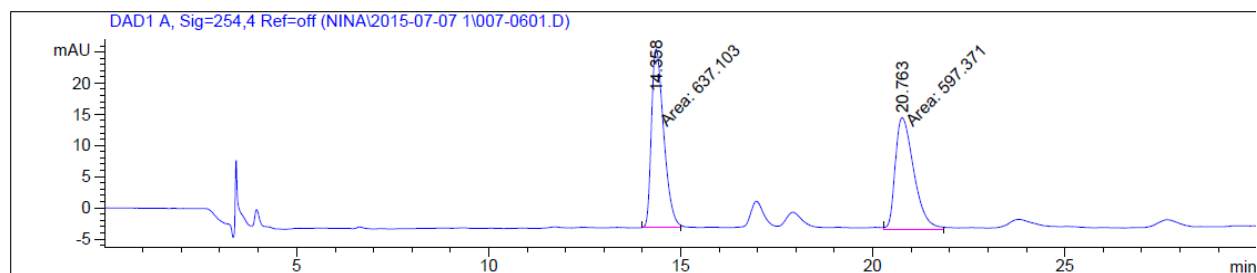
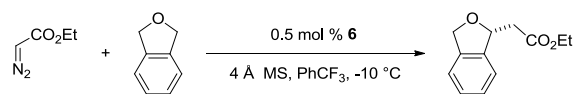
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

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1	16.905	MM	0.4060	445.50363	18.28667	11.6865
2	23.896	MM	0.7746	3366.60864	72.43604	88.3135

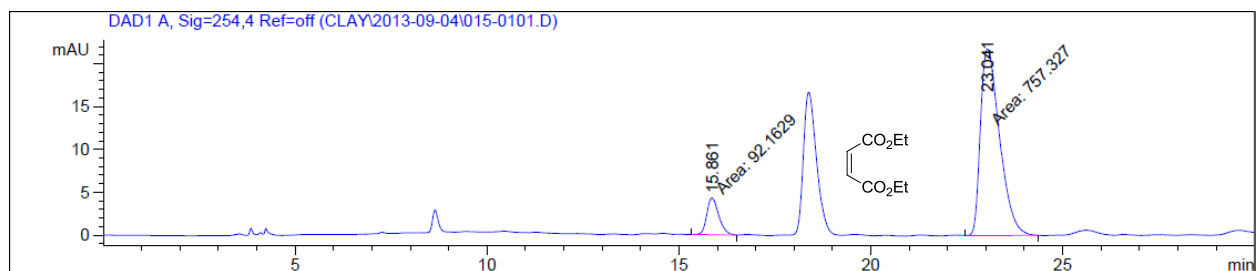
Totals : 3812.11227 90.72270



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

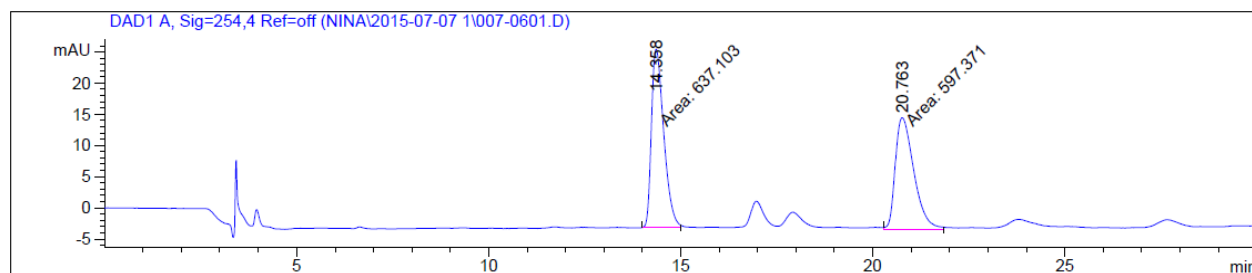
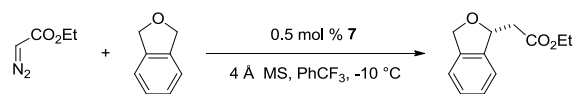
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.861	MM	0.3580	92.16287	4.29099	10.8492
2	23.041	MM	0.5801	757.32733	21.75729	89.1508

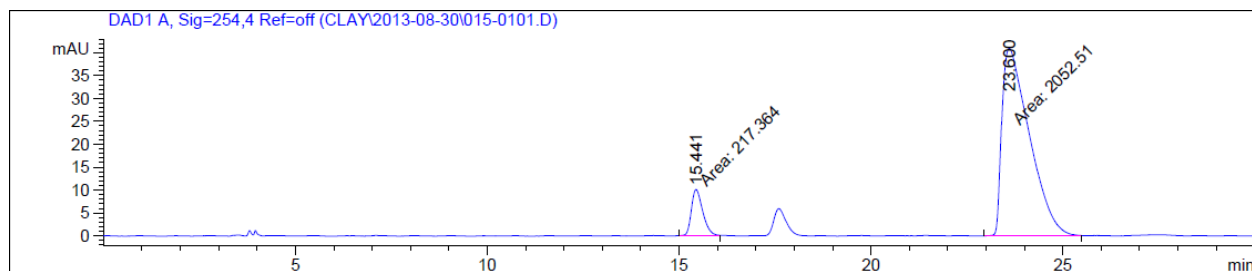
Totals : 849.49020 26.04827



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

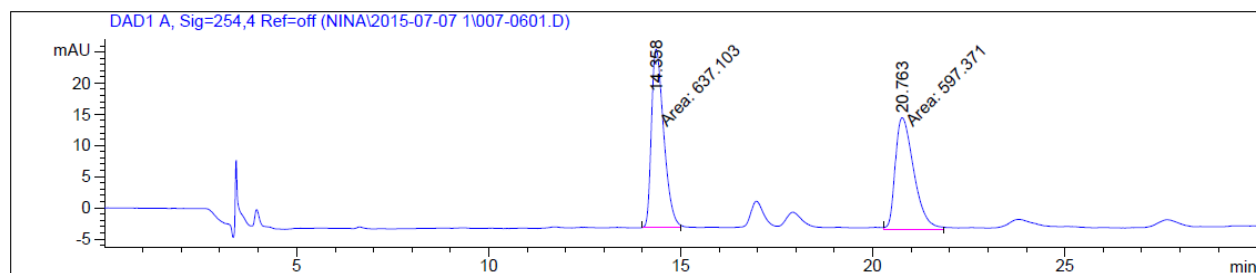
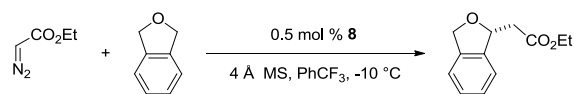
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.441	MM	0.3544	217.36377	10.22279	9.5760
2	23.600	MM	0.8321	2052.51318	41.11047	90.4240

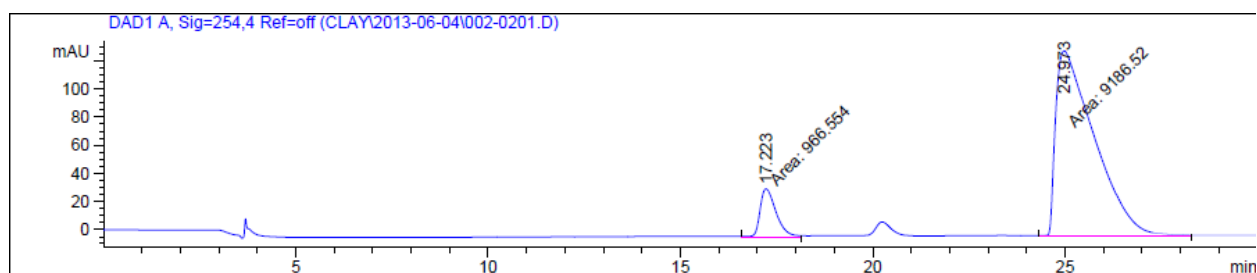
Totals : 2269.87695 51.33326



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

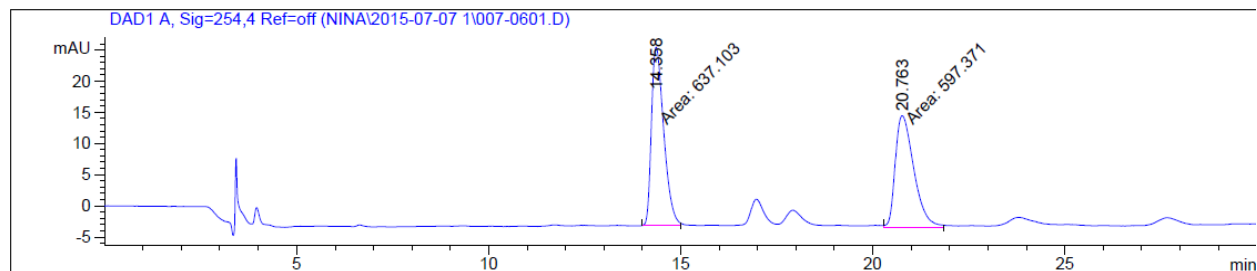
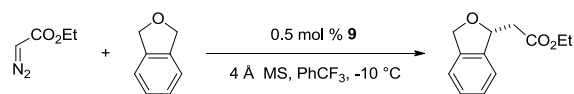
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.223	MM	0.4743	966.55438	33.96584	9.5198
2	24.973	MM	1.1657	9186.52148	131.34679	90.4802

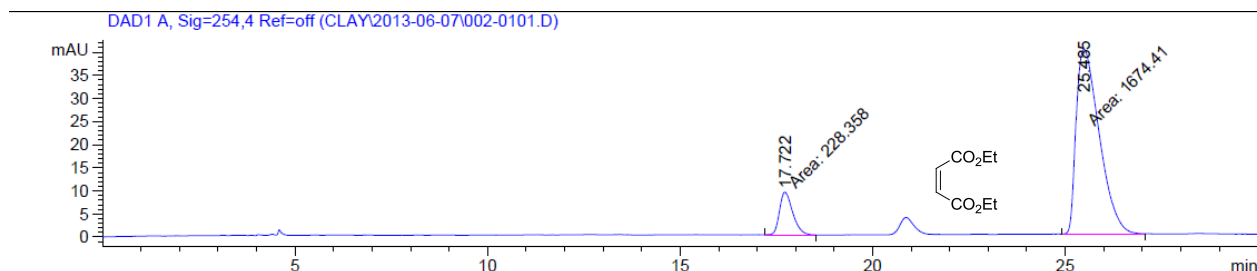
Totals : 1.01531e4 165.31262



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

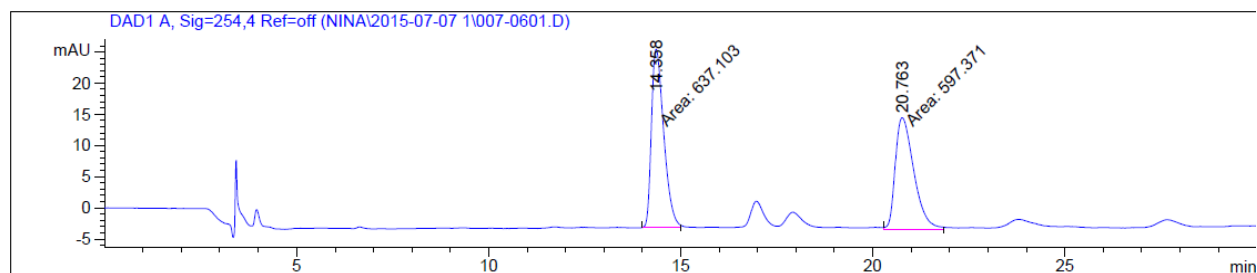
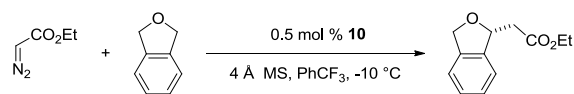
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.722	MM	0.4066	228.35831	9.35954	12.0014
2	25.485	MM	0.6976	1674.41211	40.00420	87.9986

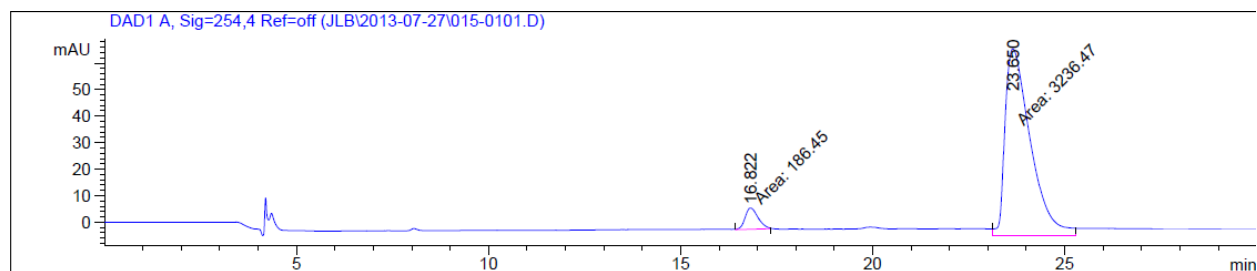
Totals : 1902.77042 49.36374



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

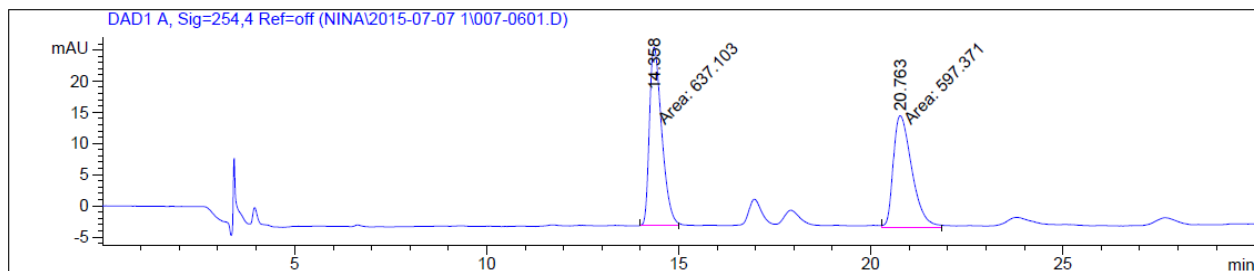
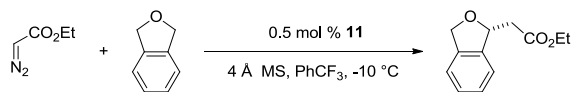
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.822	MM	0.3869	186.44960	8.03215	5.4471
2	23.650	MM	0.7660	3236.47241	70.42204	94.5529

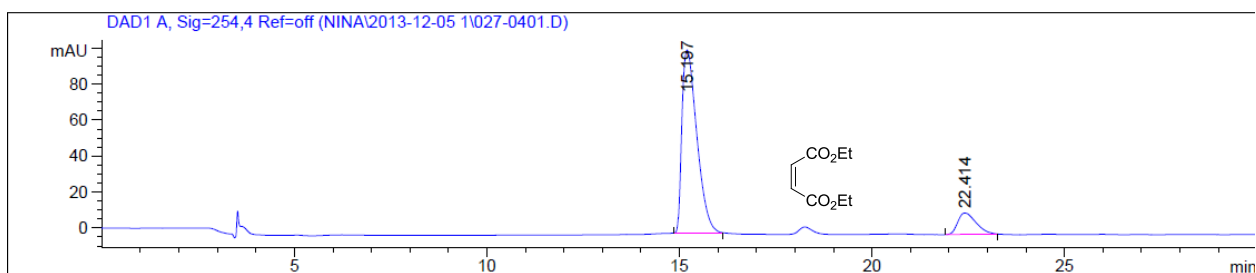
Totals : 3422.92201 78.45418



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

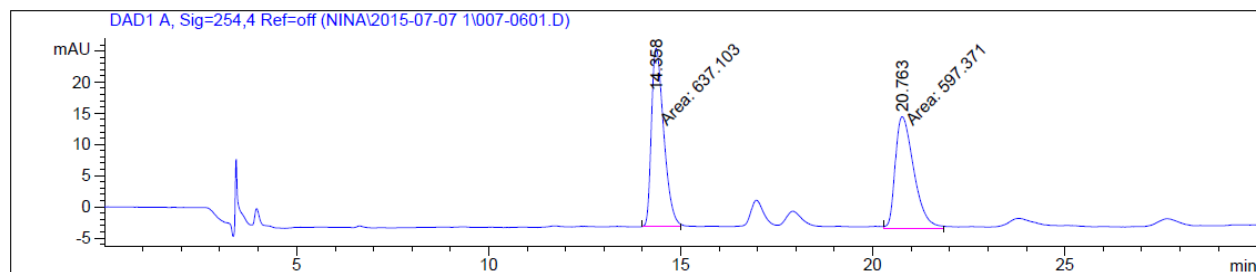
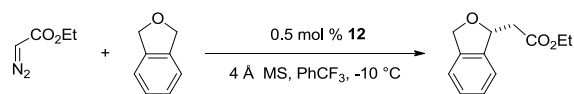
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.197	BB	0.4221	2761.57886	101.93052	87.5291
2	22.414	BB	0.4955	393.46213	11.97085	12.4709

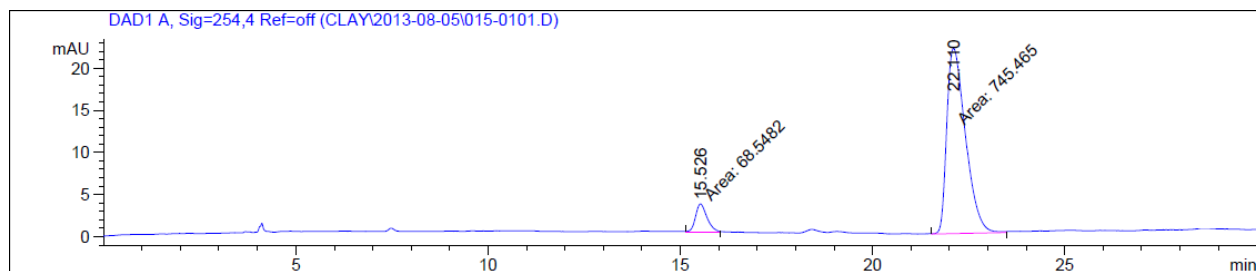
Totals : 3155.04099 113.90137



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

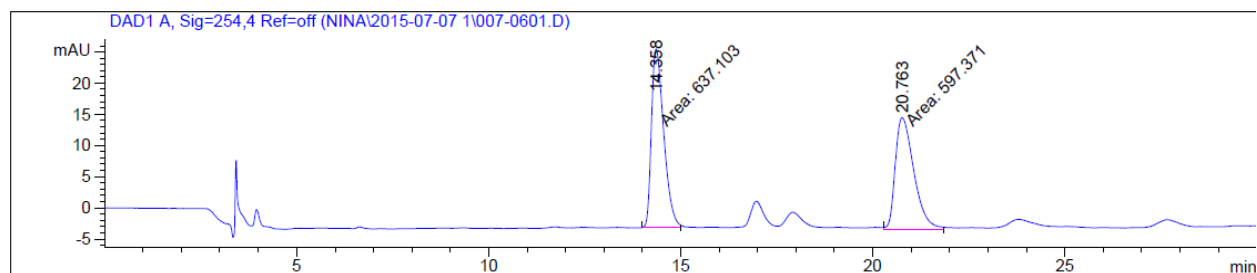
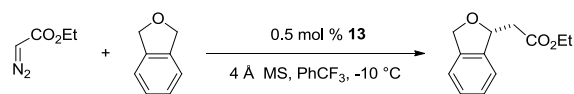
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.526	MM	0.3446	68.54819	3.31566	8.4210
2	22.110	MM	0.5640	745.46497	22.02788	91.5790

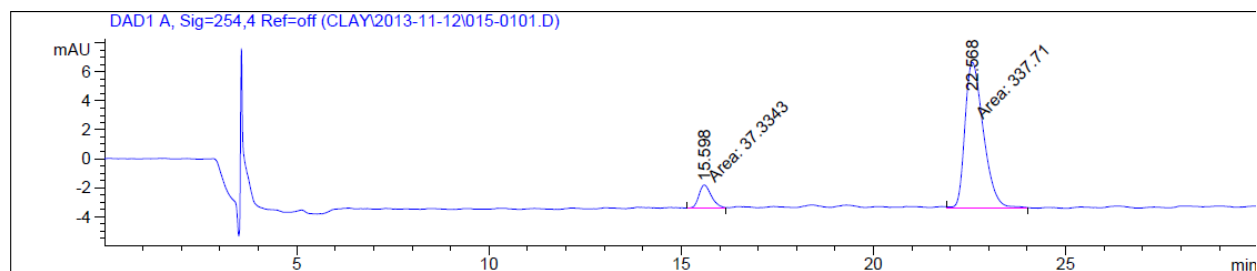
Totals : 814.01316 25.34354



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

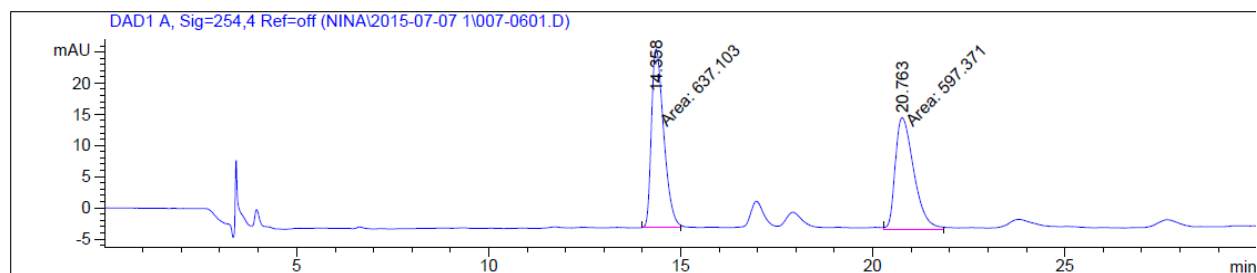
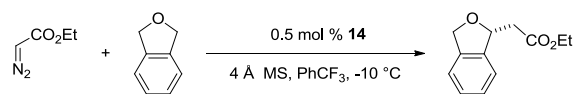
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.598	MM	0.3850	37.33426	1.61613	9.9546
2	22.568	MM	0.5569	337.71008	10.10624	90.0454

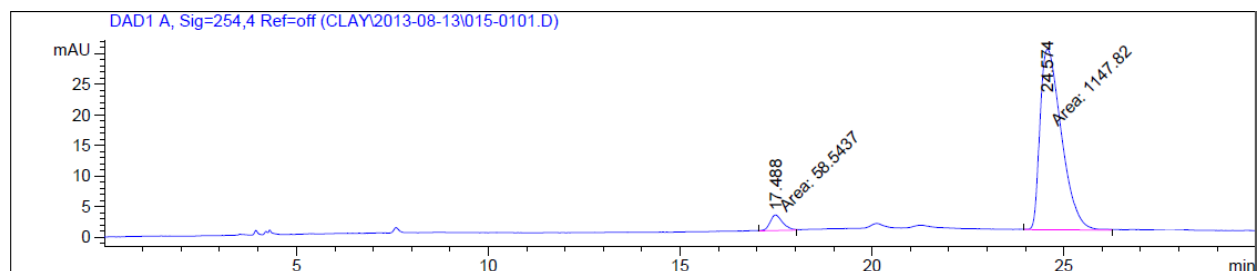
Totals : 375.04435 11.72237



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

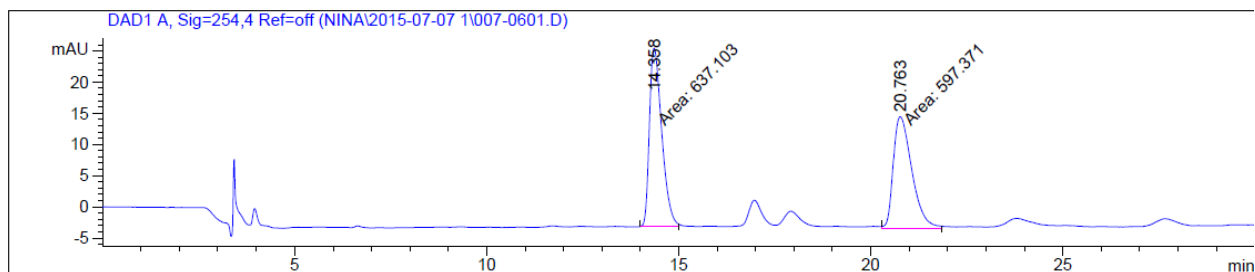
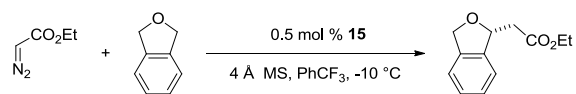
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.488	MM	0.3842	58.54367	2.53953	4.8529
2	24.574	MM	0.6471	1147.81519	29.56103	95.1471

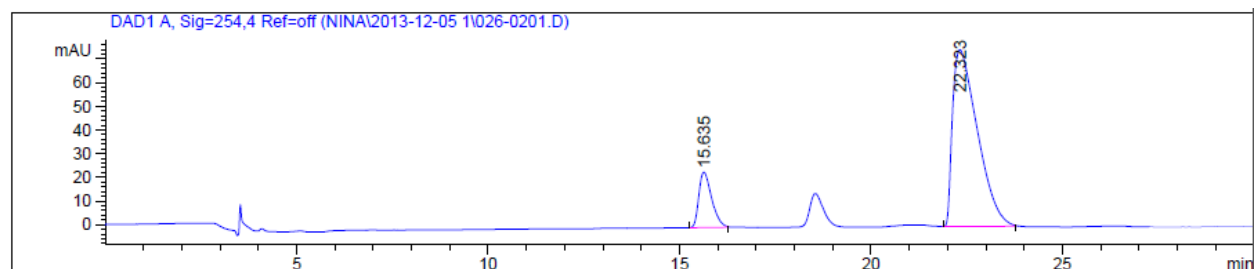
Totals : 1206.35886 32.10056



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.358	MM	0.3721	637.10333	28.53423	51.6093
2	20.763	MM	0.5573	597.37115	17.86541	48.3907

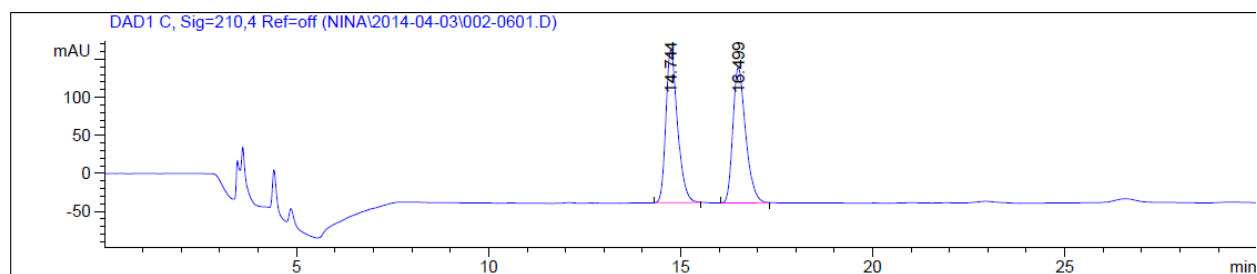
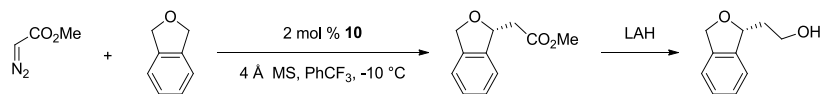
Totals : 1234.47449 46.39964



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.635	BB	0.3600	545.68378	23.40274	13.9467
2	22.323	BB	0.6835	3366.96680	74.75256	86.0533

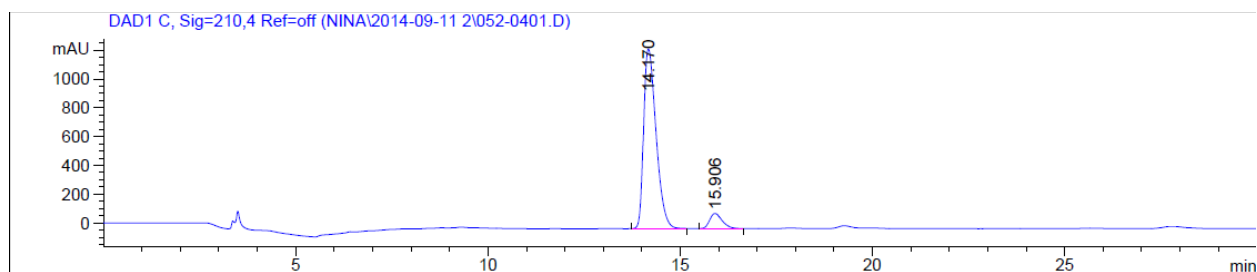
Totals : 3912.65057 98.15530



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

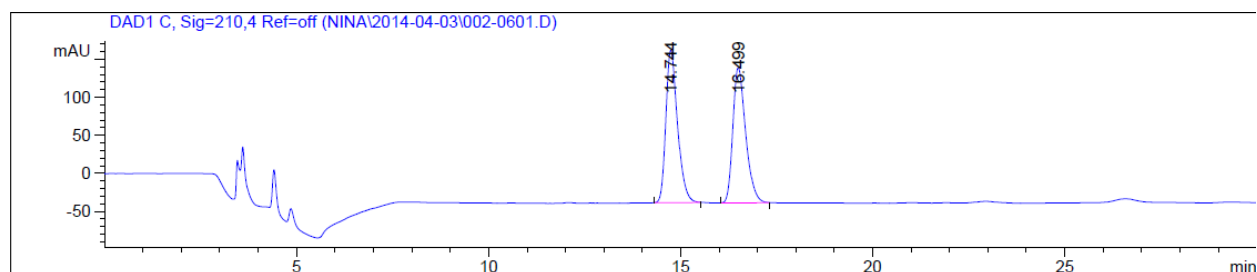
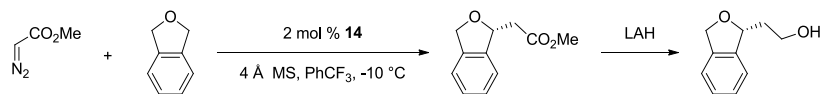
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.170	BB	0.3471	2.79630e4	1249.38208	92.1776
2	15.906	BB	0.3437	2372.99487	104.97583	7.8224

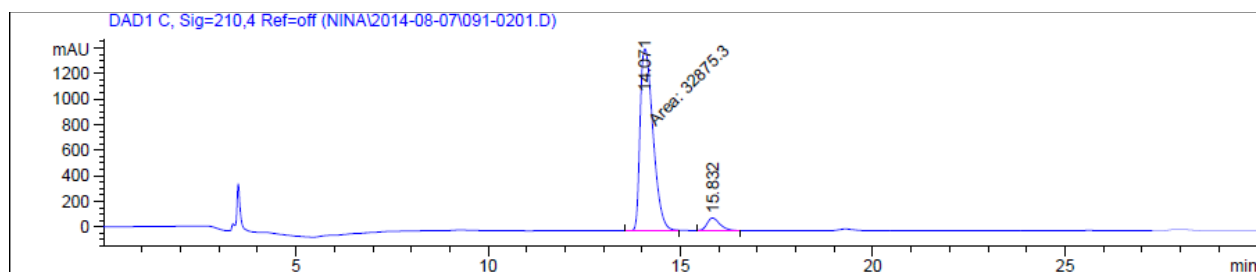
Totals : 3.03360e4 1354.35791



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

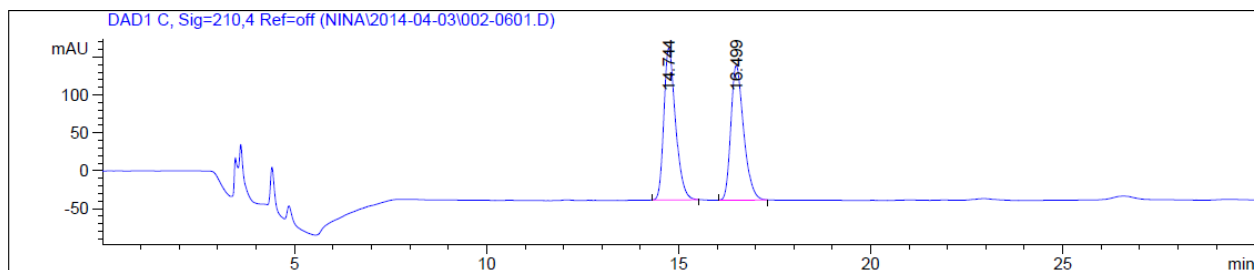
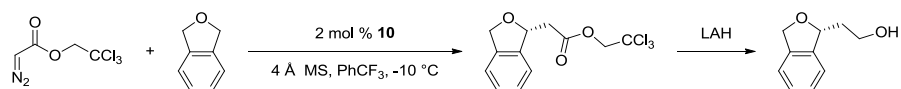
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.071	MM	0.3855	3.28753e4	1421.50244	93.6980
2	15.832	BB	0.3458	2211.15039	97.77789	6.3020

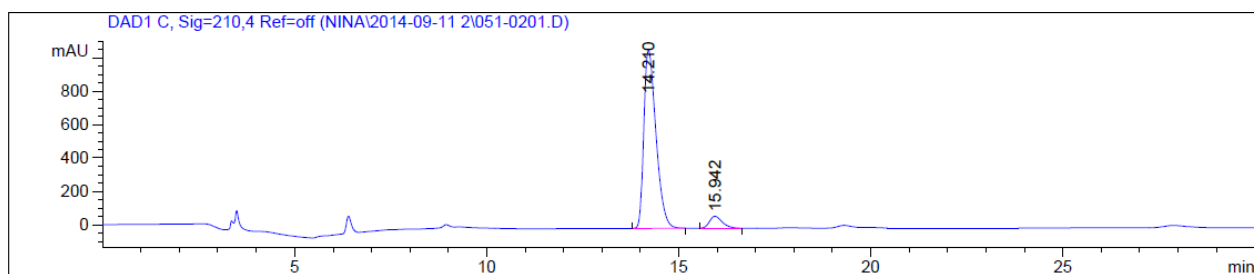
Totals : 3.50864e4 1519.28033



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

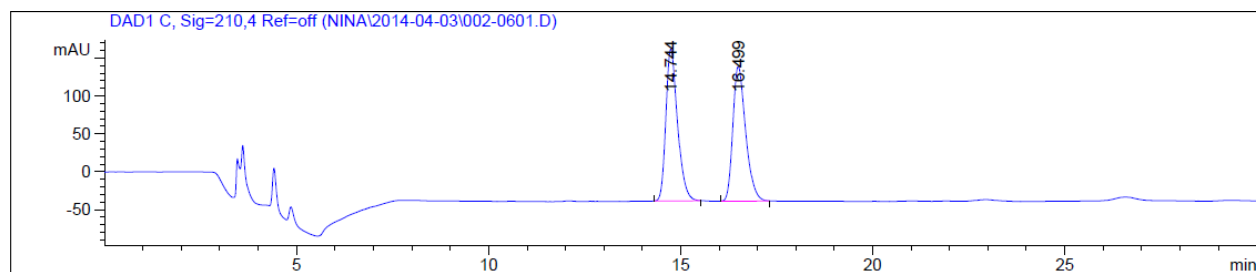
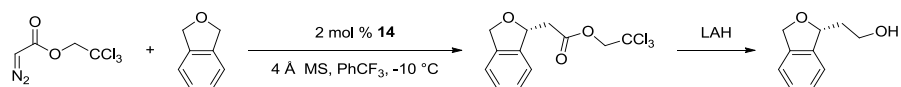
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.210	BB	0.3410	2.34825e4	1066.14734	93.5235
2	15.942	BB	0.3435	1626.15161	71.98818	6.4765

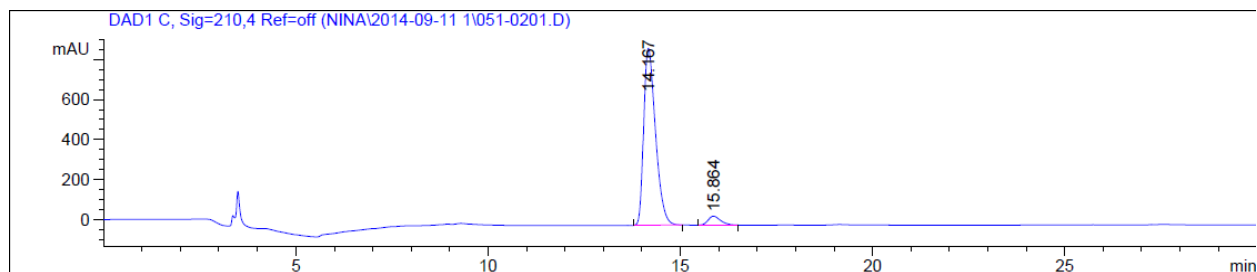
Totals : 2.51086e4 1138.13552



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

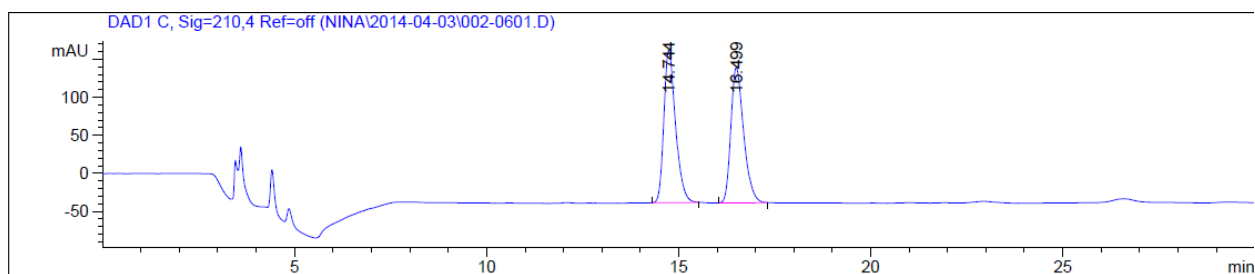
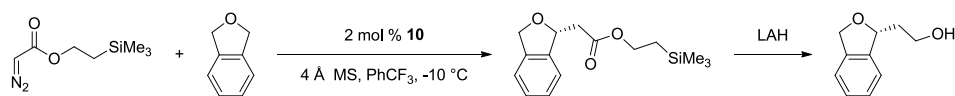
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.167	BB	0.3265	1.87930e4	882.12140	95.0652
2	15.864	BB	0.3343	975.53076	44.05865	4.9348

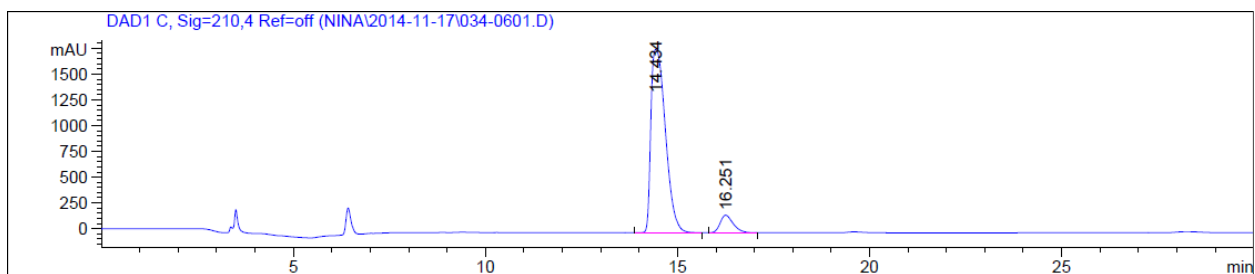
Totals : 1.97685e4 926.18005



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

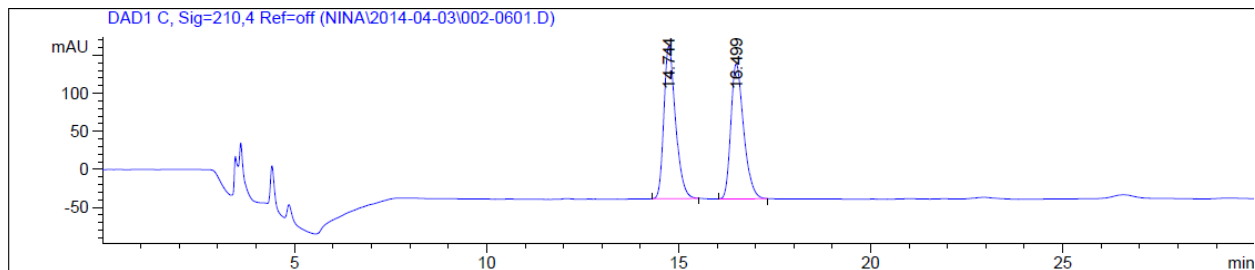
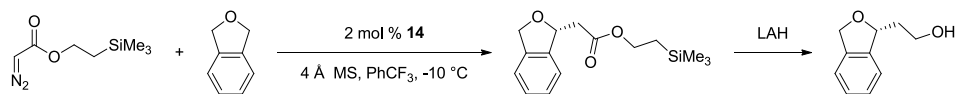
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.434	BB	0.4205	4.70203e4	1777.95764	92.1341
2	16.251	BB	0.3618	4014.33569	169.81734	7.8659

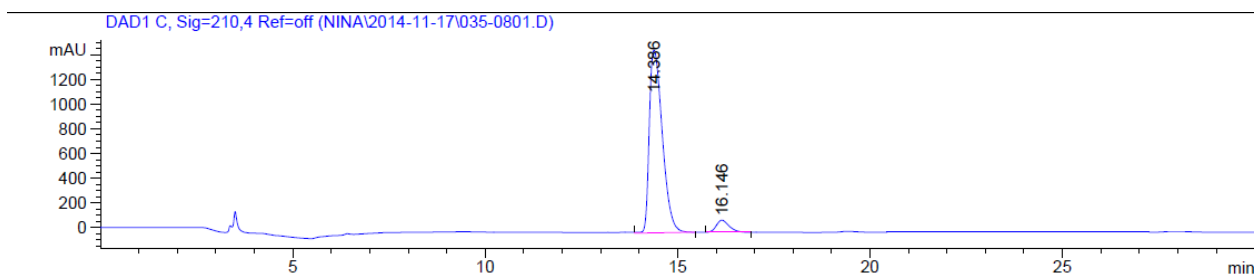
Totals : 5.10347e4 1947.77498



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

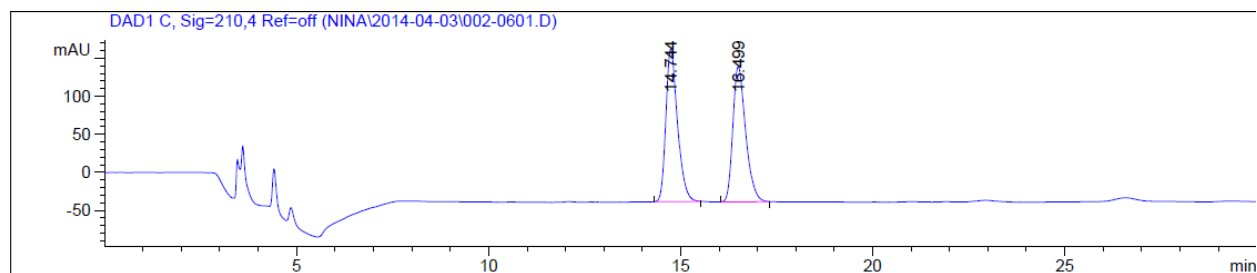
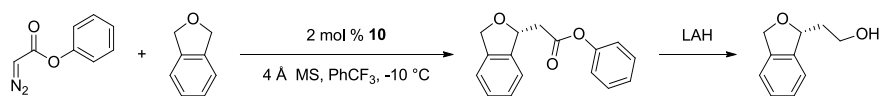
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.386	BB	0.3706	3.51173e4	1481.32349	94.0331
2	16.146	BB	0.3497	2228.39624	97.13264	5.9669

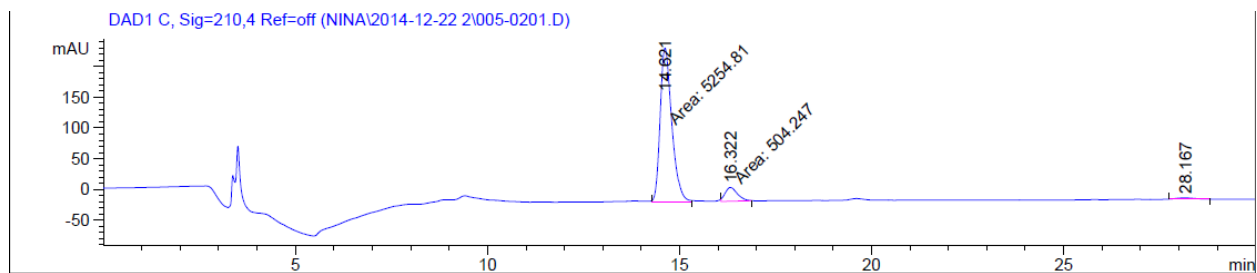
Totals : 3.73457e4 1578.45612



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

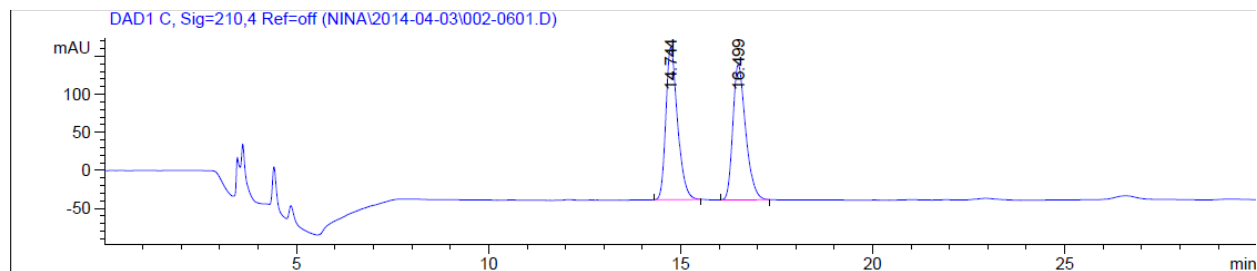
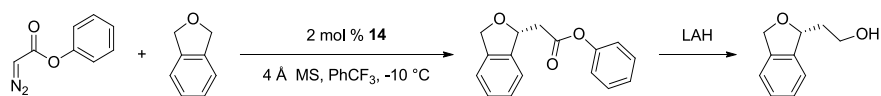
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.621	MM	0.3505	5254.80566	249.89125	90.2423
2	16.322	MM	0.3724	504.24701	22.56823	8.6596
3	28.167	BB	0.3989	63.94430	1.93806	1.0981

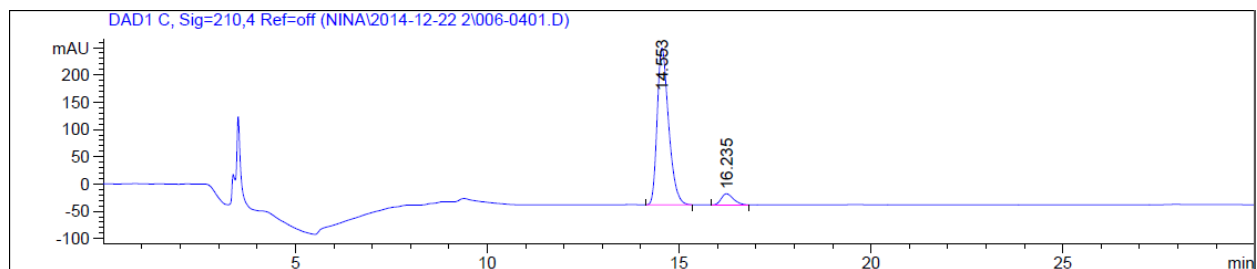
Totals : 5822.99697 274.39754



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

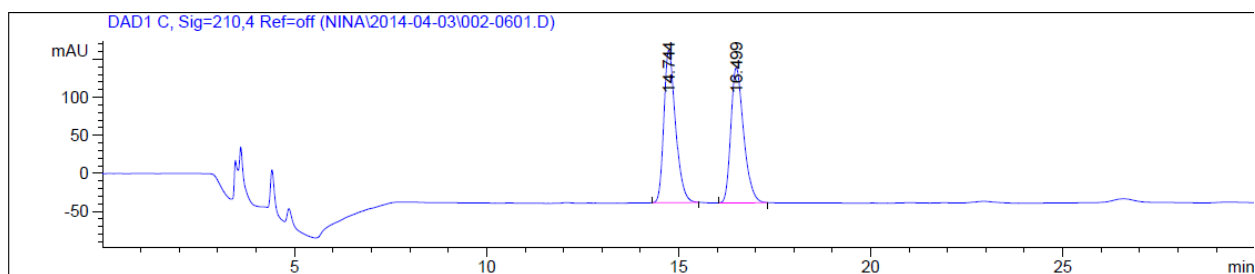
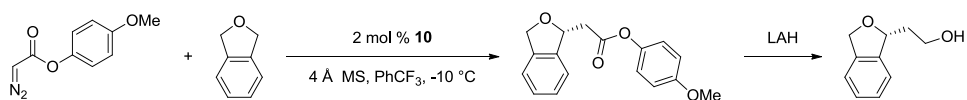
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.553	BB	0.3181	6015.99414	287.48108	92.9144
2	16.235	BB	0.3452	458.77490	20.48825	7.0856

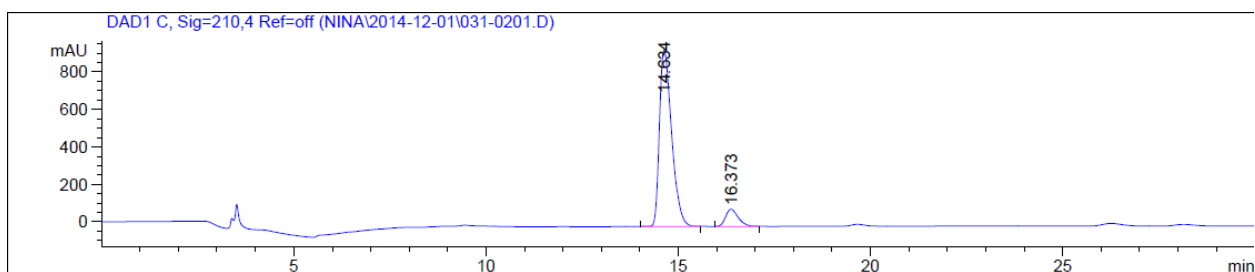
Totals : 6474.76904 307.96932



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

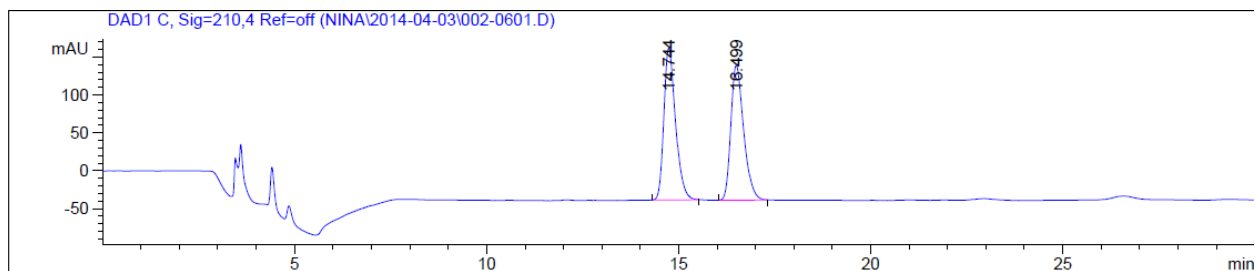
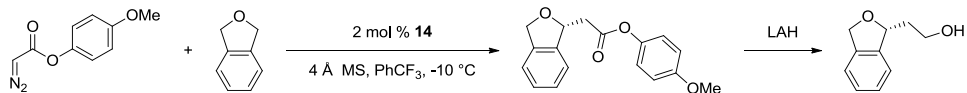
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.634	BB	0.3427	2.08809e4	941.80194	90.7960
2	16.373	BB	0.3516	2116.70166	92.26576	9.2040

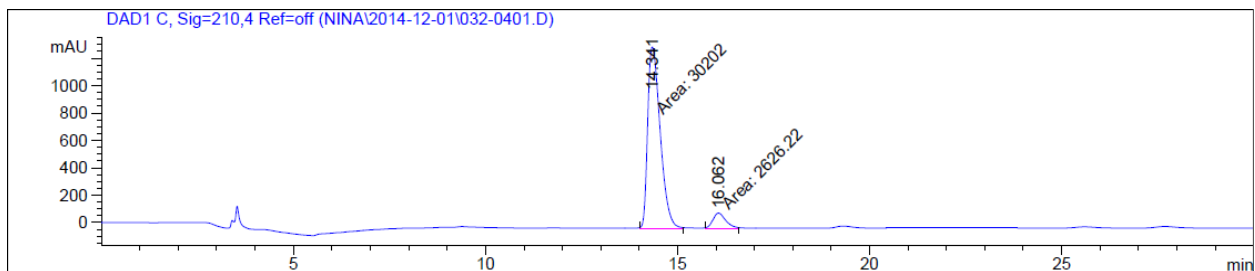
Totals : 2.29976e4 1034.06770



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

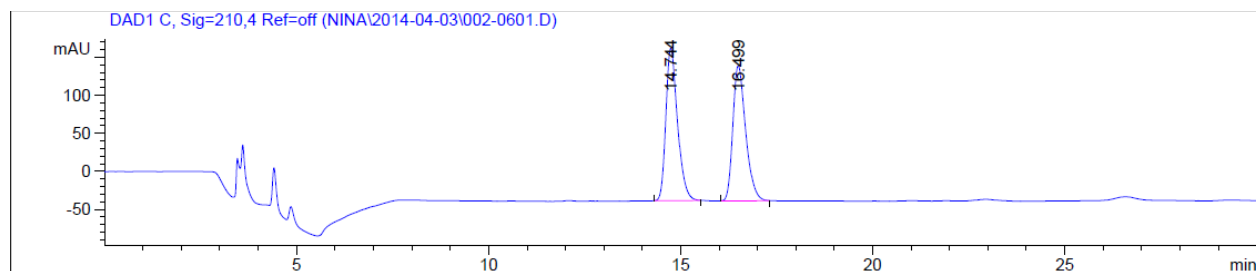
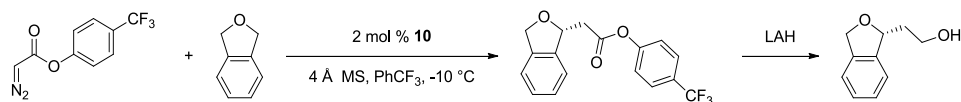
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.341	MM	0.3796	3.02020e4	1325.91382	92.0001
2	16.062	MM	0.3899	2626.21826	112.25780	7.9999

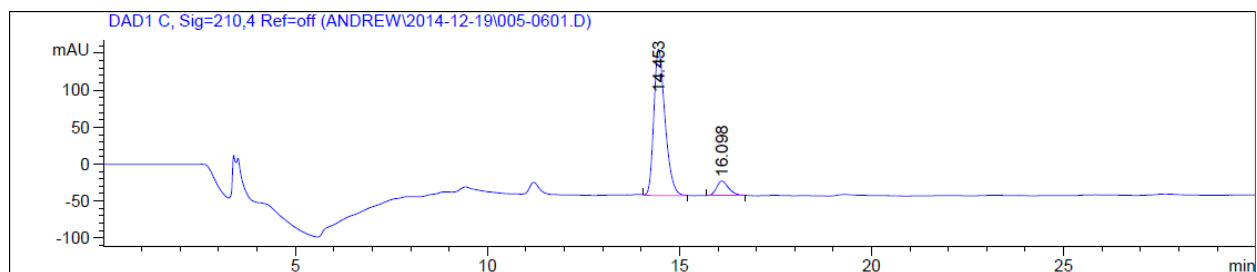
Totals : 3.28282e4 1438.17162



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

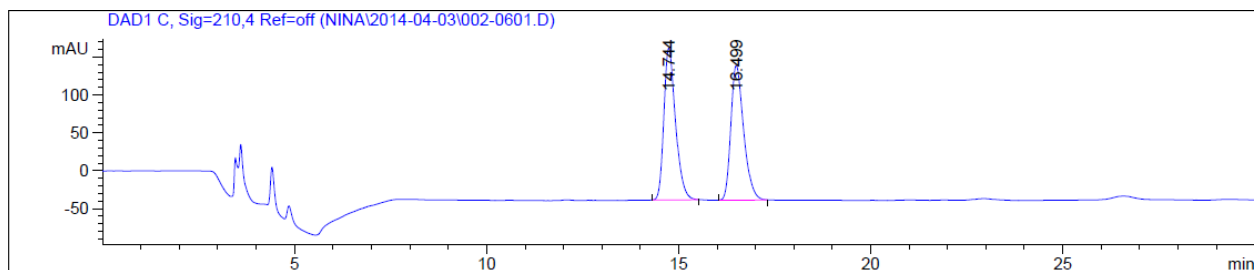
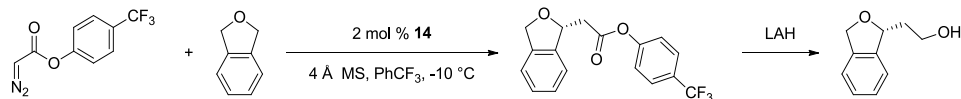
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.453	VB	0.3110	4052.43457	197.78882	90.1528
2	16.098	BB	0.3404	442.64069	19.82982	9.8472

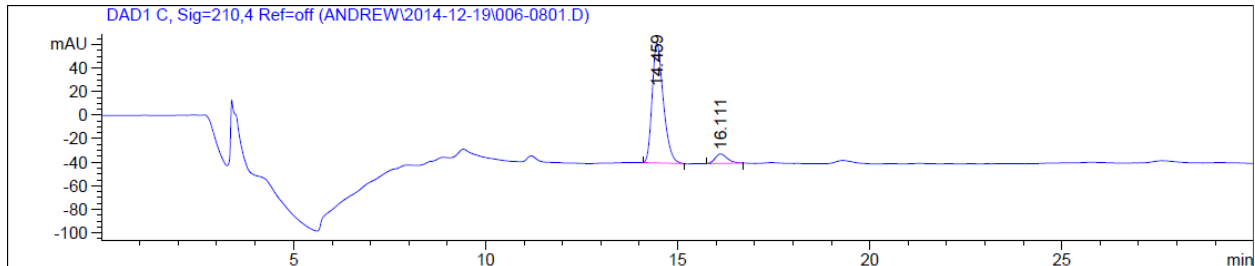
Totals : 4495.07526 217.61864



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	BB	0.3209	4235.80615	200.15521	50.6009
2	16.499	BB	0.3535	4135.21143	177.66600	49.3991

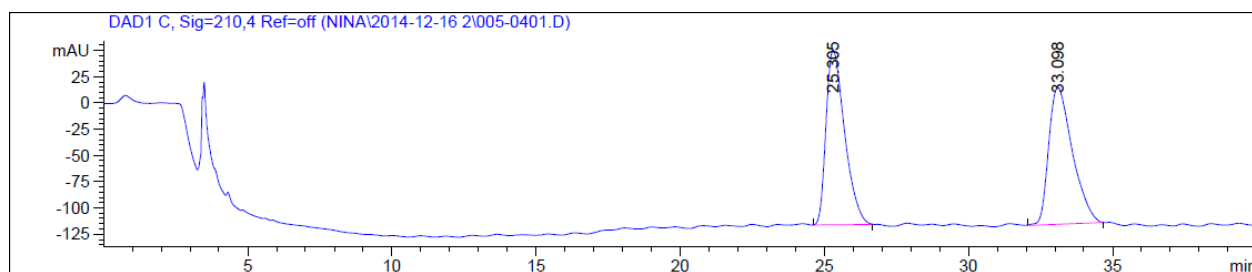
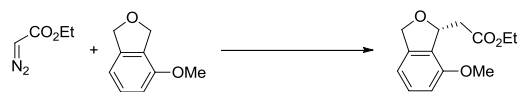
Totals : 8371.01758 377.82121



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.459	BB	0.3112	2089.42212	101.92041	92.0745
2	16.111	BB	0.3353	179.85083	8.09250	7.9255

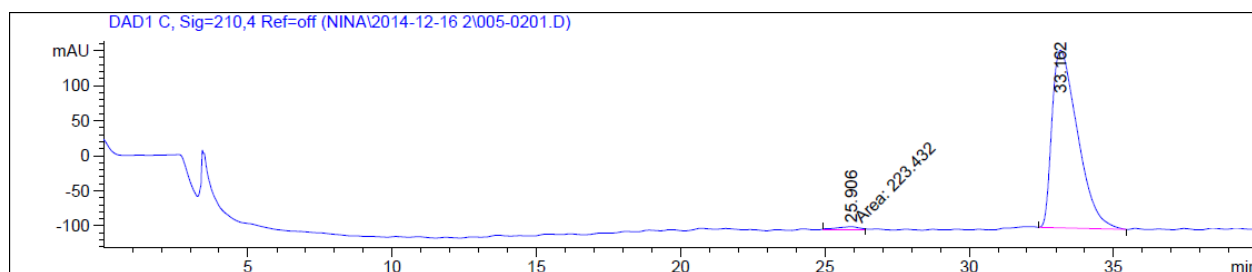
Totals : 2269.27295 110.01291



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.305	BB	0.6898	7471.09521	166.39967	50.0894
2	33.098	BB	0.8667	7444.43311	130.26862	49.9106

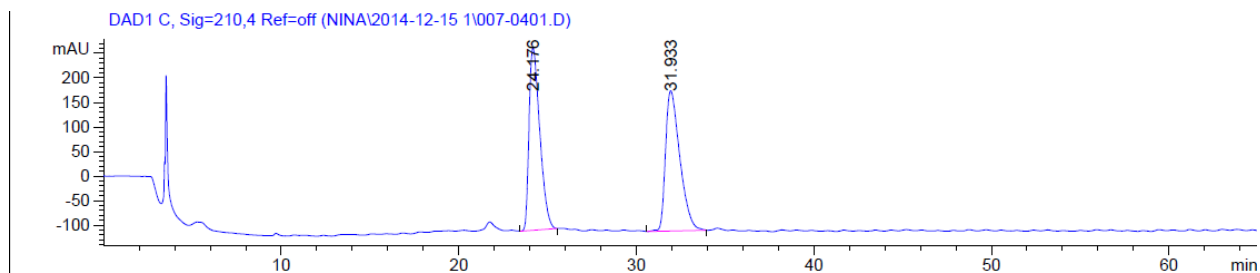
Totals : 1.49155e4 296.66829



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.906	MM	0.8960	223.43199	4.15602	1.4087
2	33.162	BB	0.9260	1.56370e4	253.36447	98.5913

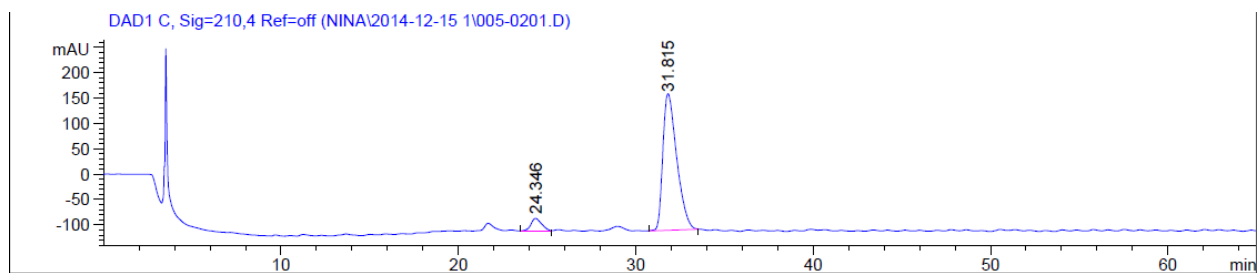
Totals : 1.58605e4 257.52049



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.176	VB	0.6499	1.56448e4	371.07114	49.4712
2	31.933	VB	0.8488	1.59792e4	285.59573	50.5288

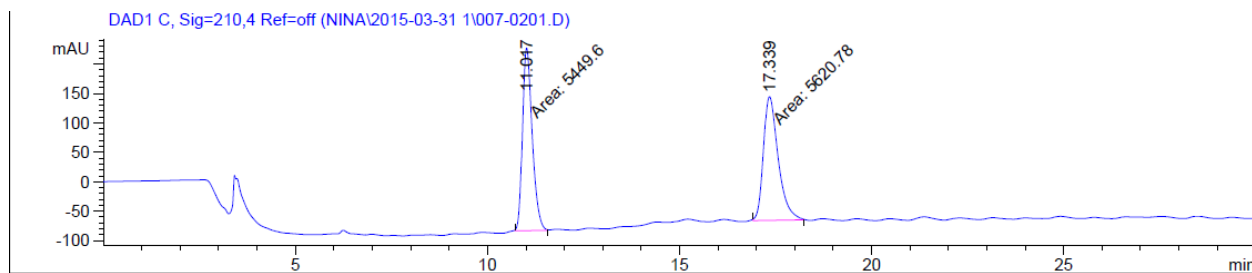
Totals : 3.16240e4 656.66687



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.346	VV	0.6209	1104.30969	25.31747	7.0068
2	31.815	BB	0.8269	1.46563e4	269.32123	92.9932

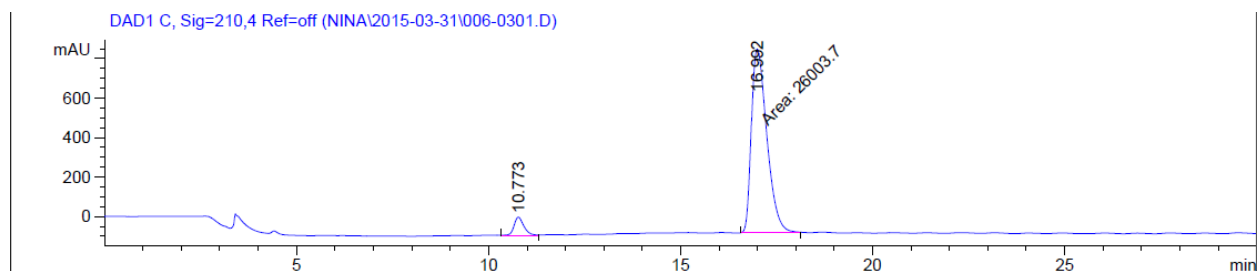
Totals : 1.57606e4 294.63870



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.017	MM	0.2929	5449.60352	310.11356	49.2269
2	17.339	MM	0.4460	5620.78320	210.05756	50.7731

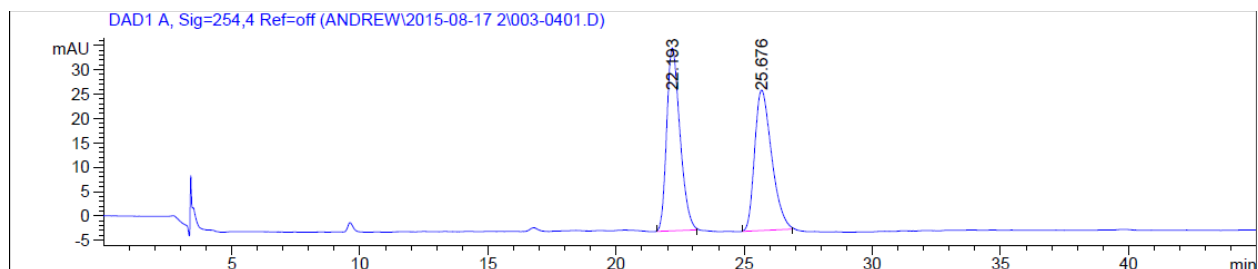
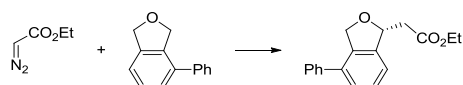
Totals : 1.10704e4 520.17111



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.773	BB	0.2783	1742.37476	93.96941	6.2797
2	16.992	MM	0.4654	2.60037e4	931.26843	93.7203

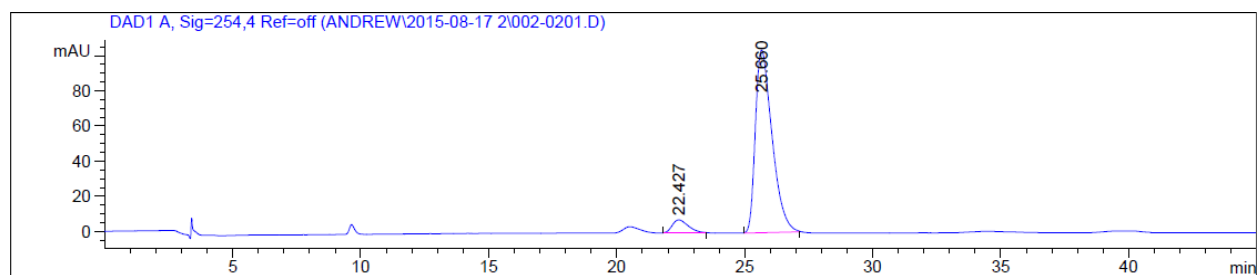
Totals : 2.77460e4 1025.23785



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.193	BB	0.5485	1352.74438	37.52847	50.4551
2	25.676	BB	0.6962	1328.34192	28.79670	49.5449

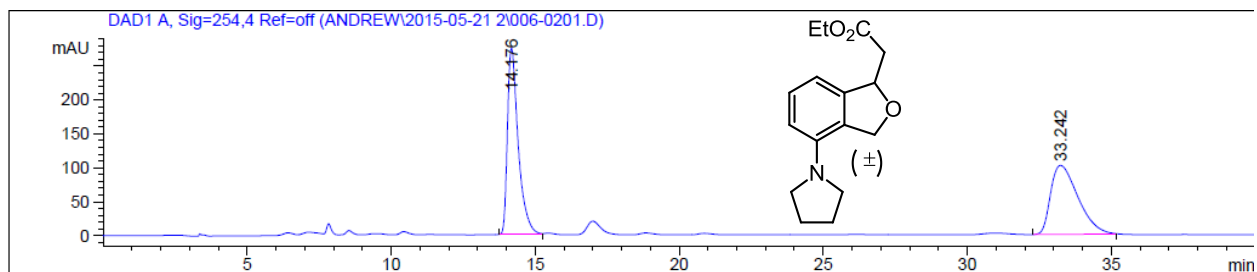
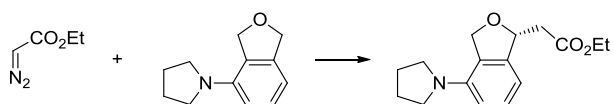
Totals : 2681.08630 66.32518



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.427	BB	0.6231	314.62387	7.32547	6.2630
2	25.660	BB	0.6894	4708.87305	103.77440	93.7370

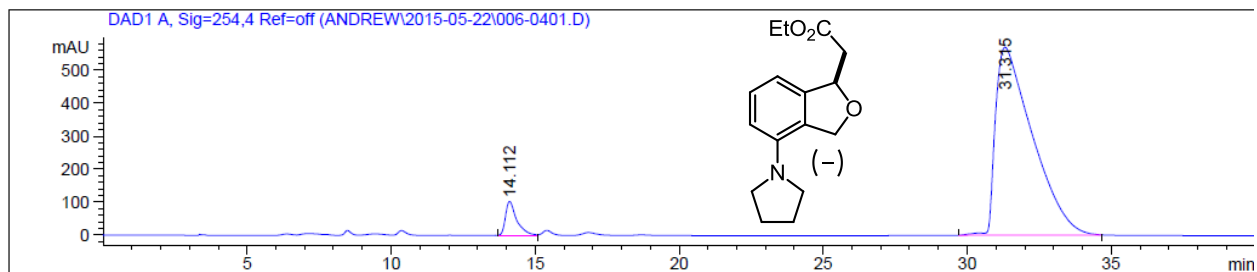
Totals : 5023.49692 111.09986



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.176	BB	0.3916	7146.29053	274.65466	51.6179
2	33.242	BB	1.0062	6698.31885	101.45926	48.3821

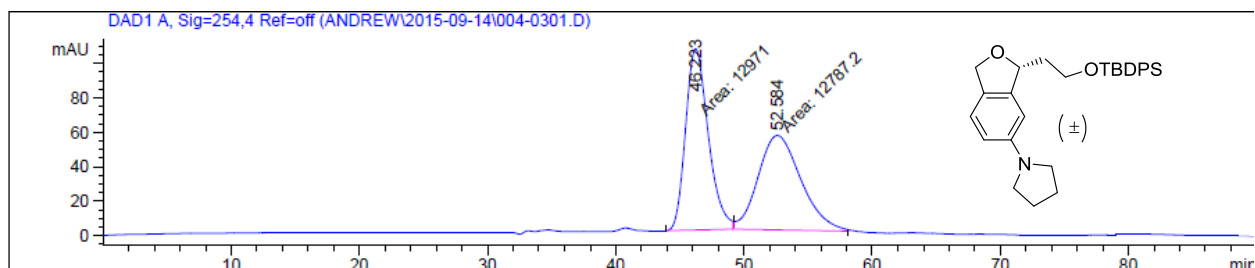
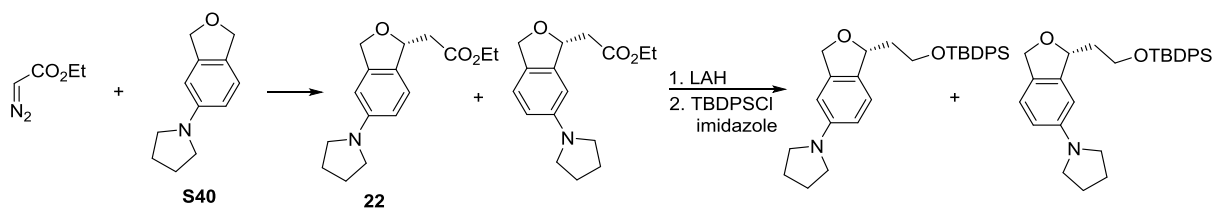
Totals : 1.38446e4 376.11392



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.112	BB	0.3956	2756.41089	102.55908	5.1337
2	31.315	BB	1.2708	5.09358e4	569.86713	94.8663

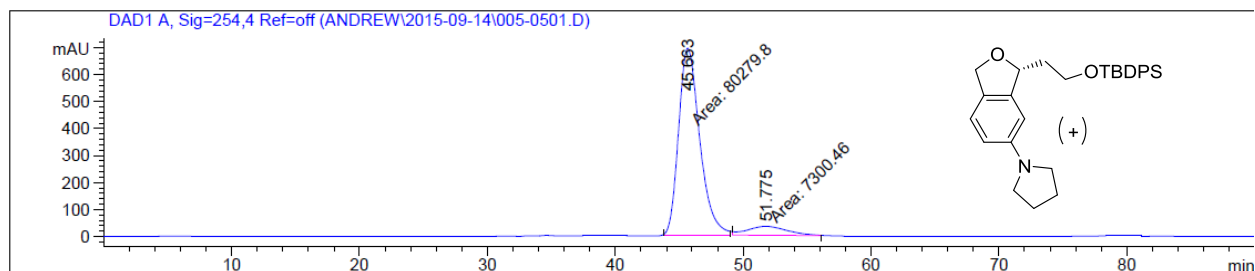
Totals : 5.36923e4 672.42621



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.223	MM	2.0558	1.29710e4	105.15704	50.3569
2	52.584	MM	3.8842	1.27872e4	54.86807	49.6431

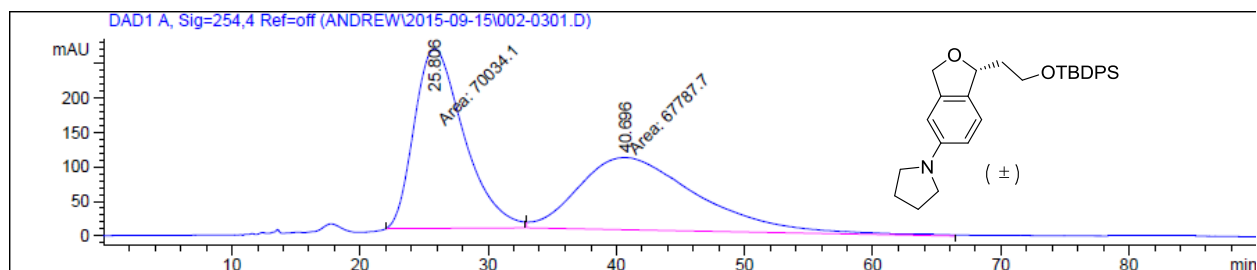
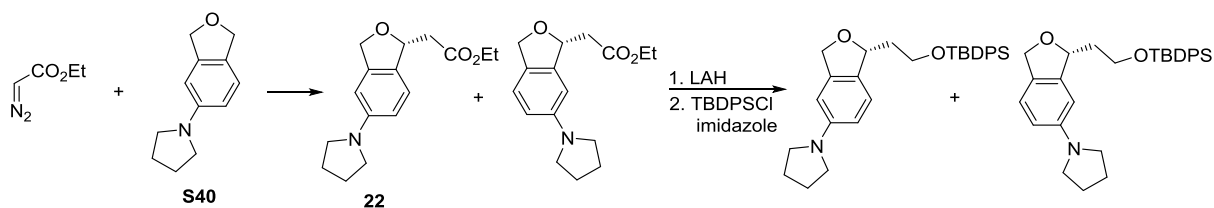
Totals : 2.57582e4 160.02512



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	45.663	MM	1.9242	8.02798e4	695.35242	91.6643
2	51.775	MM	3.6748	7300.46338	33.11041	8.3357

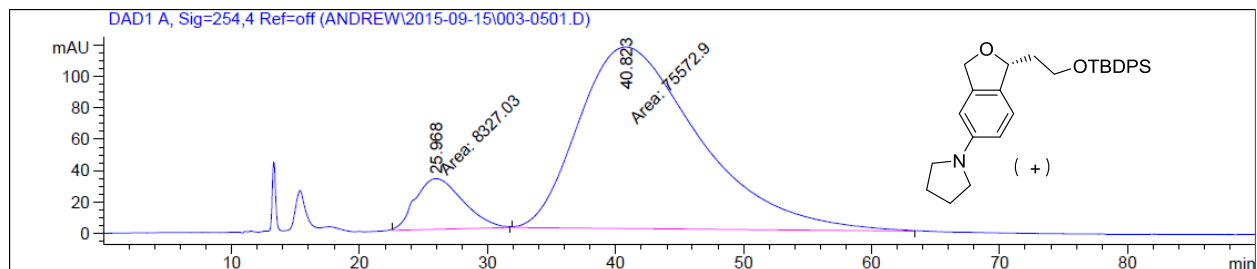
Totals : 8.75803e4 728.46283



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.806	MM	4.4932	7.00341e4	259.77750	50.8150
2	40.696	MM	10.8118	6.77877e4	104.49661	49.1850

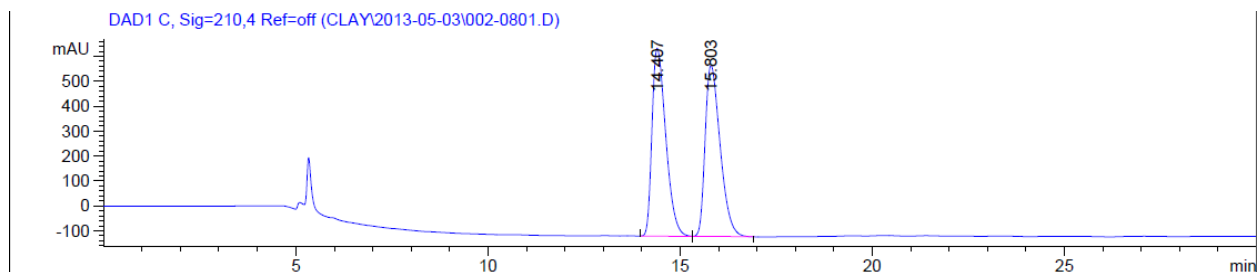
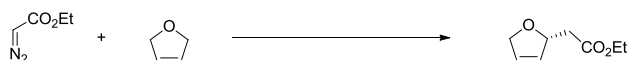
Totals : 1.37822e5 364.27411



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.968	MM	4.3103	8327.03418	32.19856	9.9250
2	40.823	MM	10.9090	7.55729e4	115.45967	90.0750

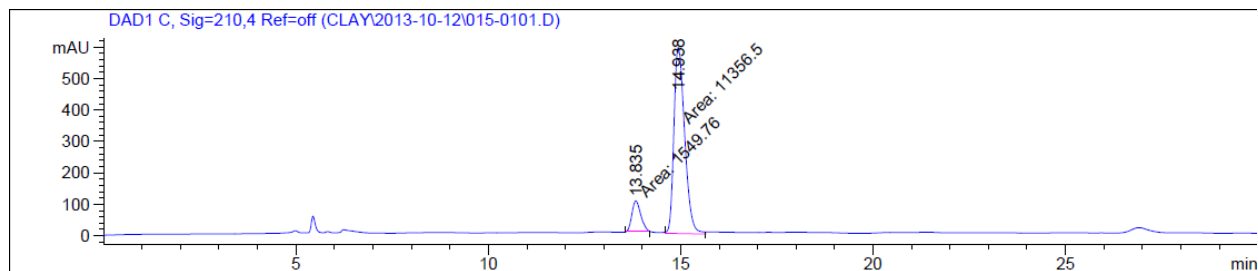
Totals : 8.39000e4 147.65823



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.407	BV	0.3824	1.86462e4	754.40552	49.8357
2	15.803	VB	0.4225	1.87691e4	687.53741	50.1643

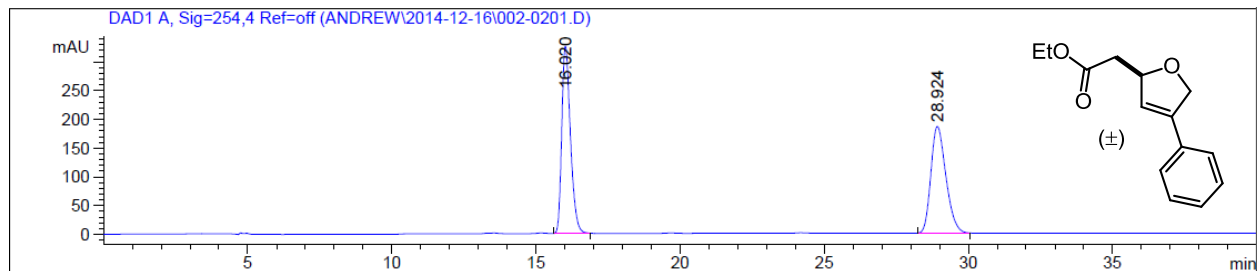
Totals : 3.74153e4 1441.94293



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.835	MM	0.2662	1549.76001	97.01272	12.0078
2	14.938	MM	0.3203	1.13565e4	590.91559	87.9922

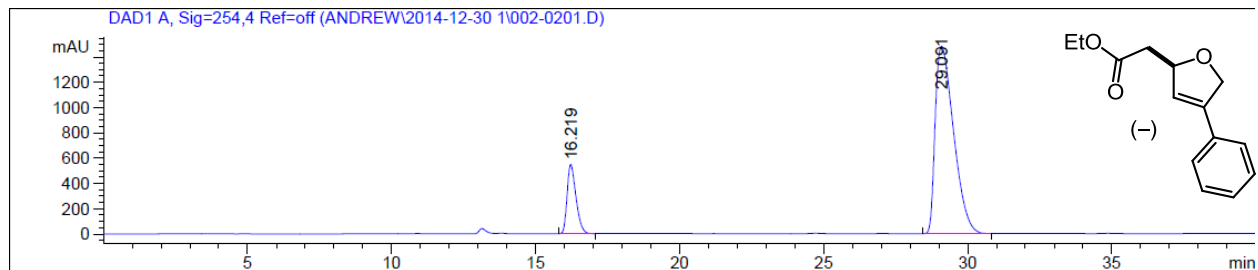
Totals : 1.29062e4 687.92831



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.020	BB	0.3194	6804.85840	326.16312	50.1674
2	28.924	BB	0.5601	6759.43701	185.95329	49.8326

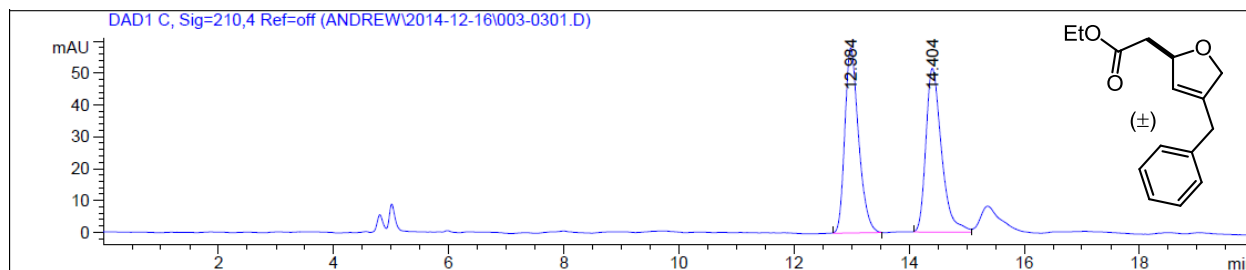
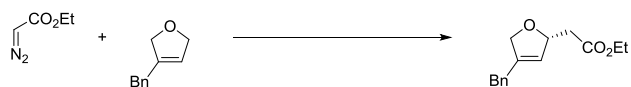
Totals : 1.35643e4 512.11641



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.219	BB	0.3288	1.17967e4	548.74457	15.1892
2	29.091	BB	0.6924	6.58683e4	1482.40454	84.8108

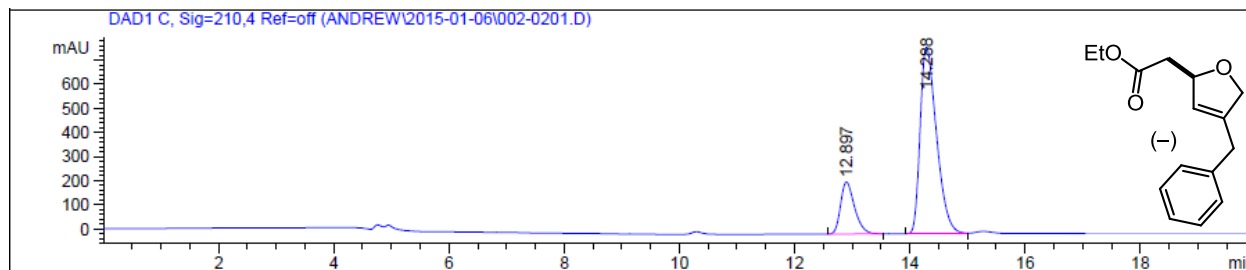
Totals : 7.76650e4 2031.14911



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.984	BB	0.2515	965.21252	58.19901	49.8551
2	14.404	BB	0.2840	970.82379	51.47895	50.1449

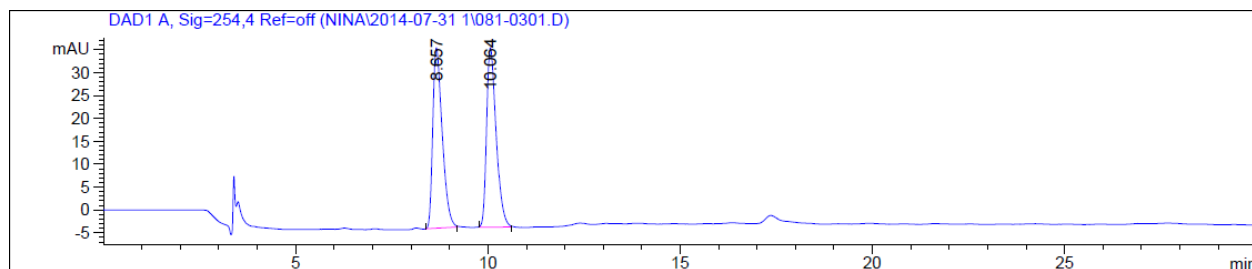
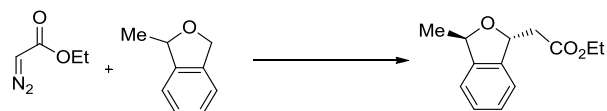
Totals : 1936.03632 109.67796



Signal 2: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.897	BB	0.2543	3629.76367	215.68619	19.1662
2	14.288	BV	0.3048	1.53086e4	773.81763	80.8338

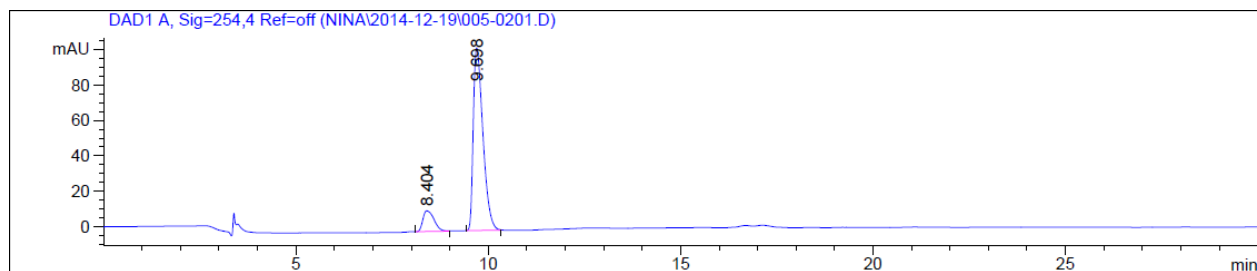
Totals : 1.89383e4 989.50381



Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.657	BB	0.2588	677.86847	39.39429	49.9453
2	10.064	BB	0.2643	679.35242	39.17409	50.0547

Totals : 1357.22089 78.56838



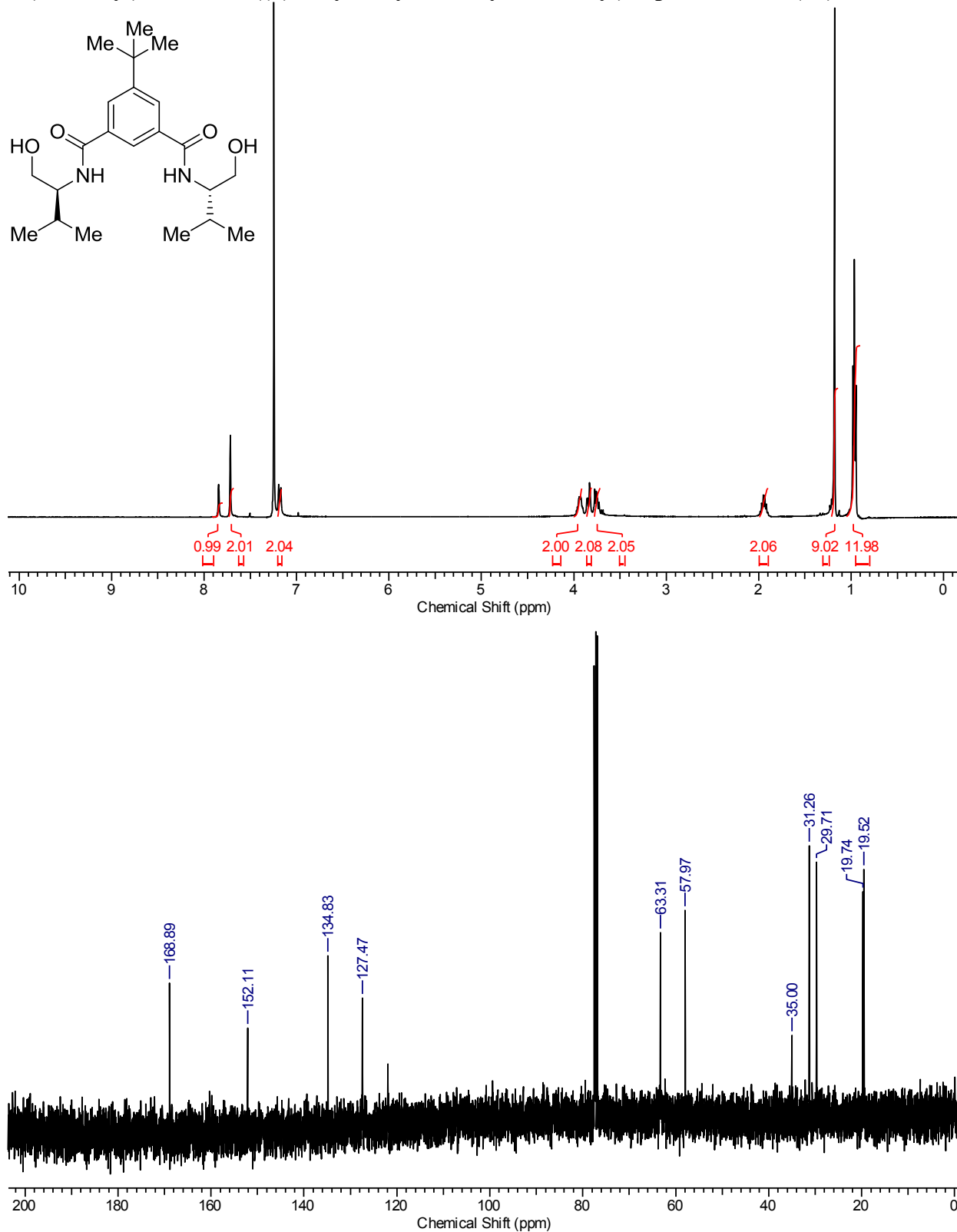
Signal 1: DAD1 A, Sig=254,4 Ref=off

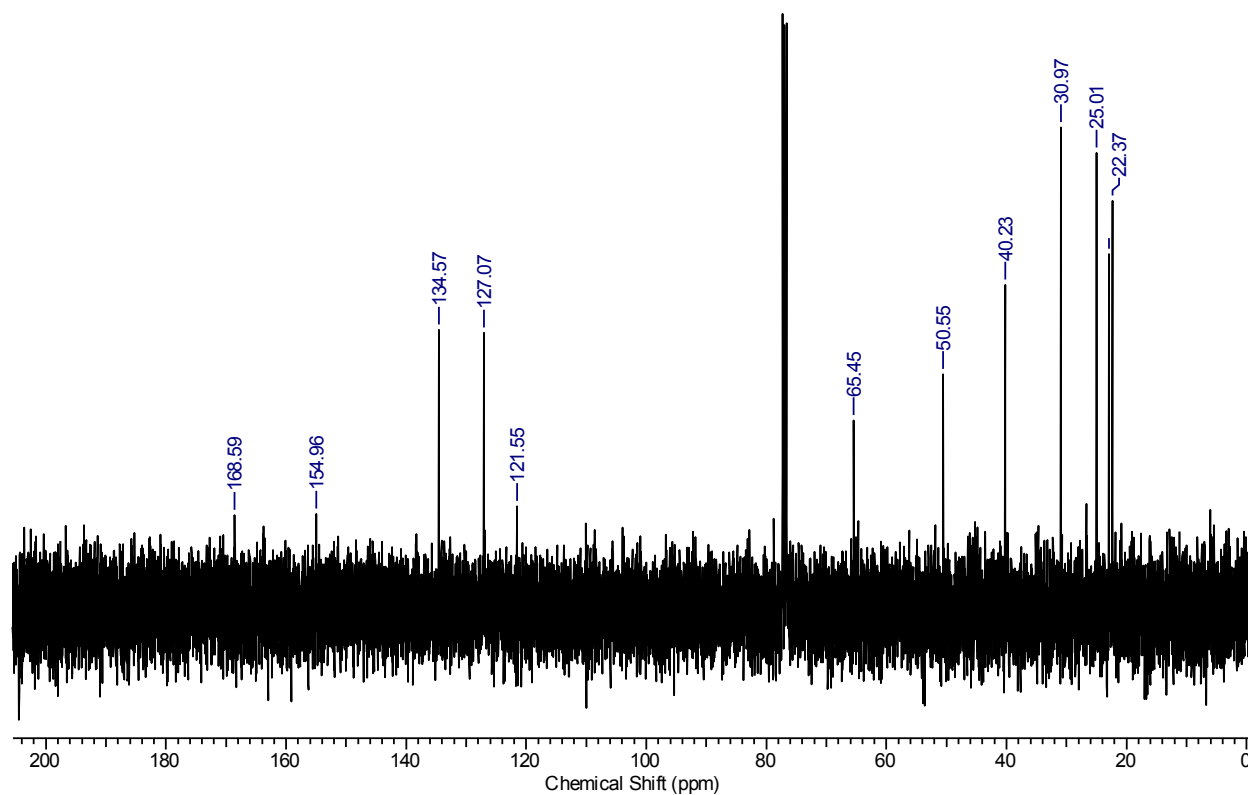
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.404	BB	0.3193	231.25298	11.66624	11.3630
2	9.698	BB	0.2706	1803.88025	102.84212	88.6370

Totals : 2035.13322 114.50836

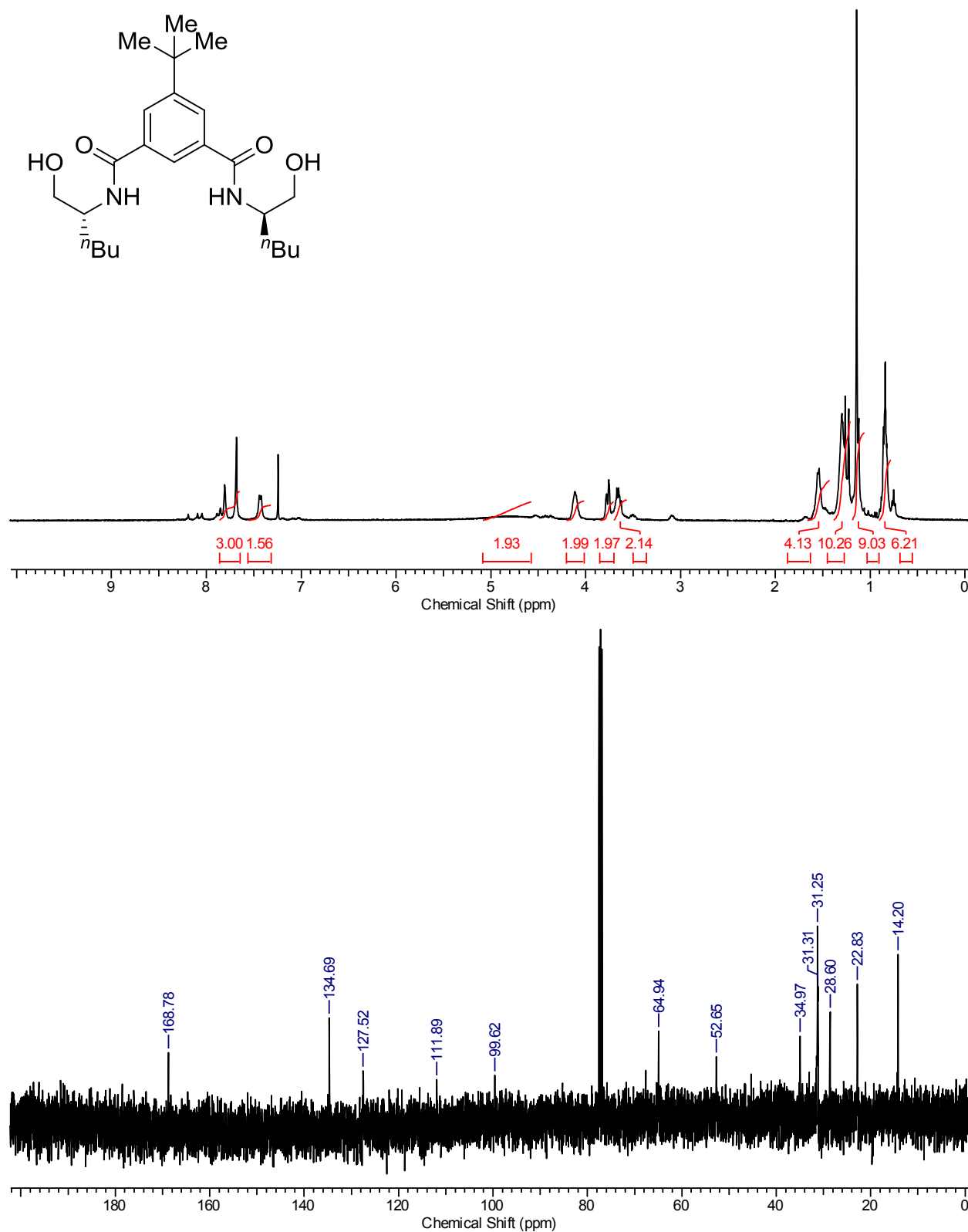
IX. NMR Spectra

5-(*tert*-butyl)-N1,N3-bis((*S*)-1-hydroxy-3-methylbutan-2-yl)isophthalamide (S1).

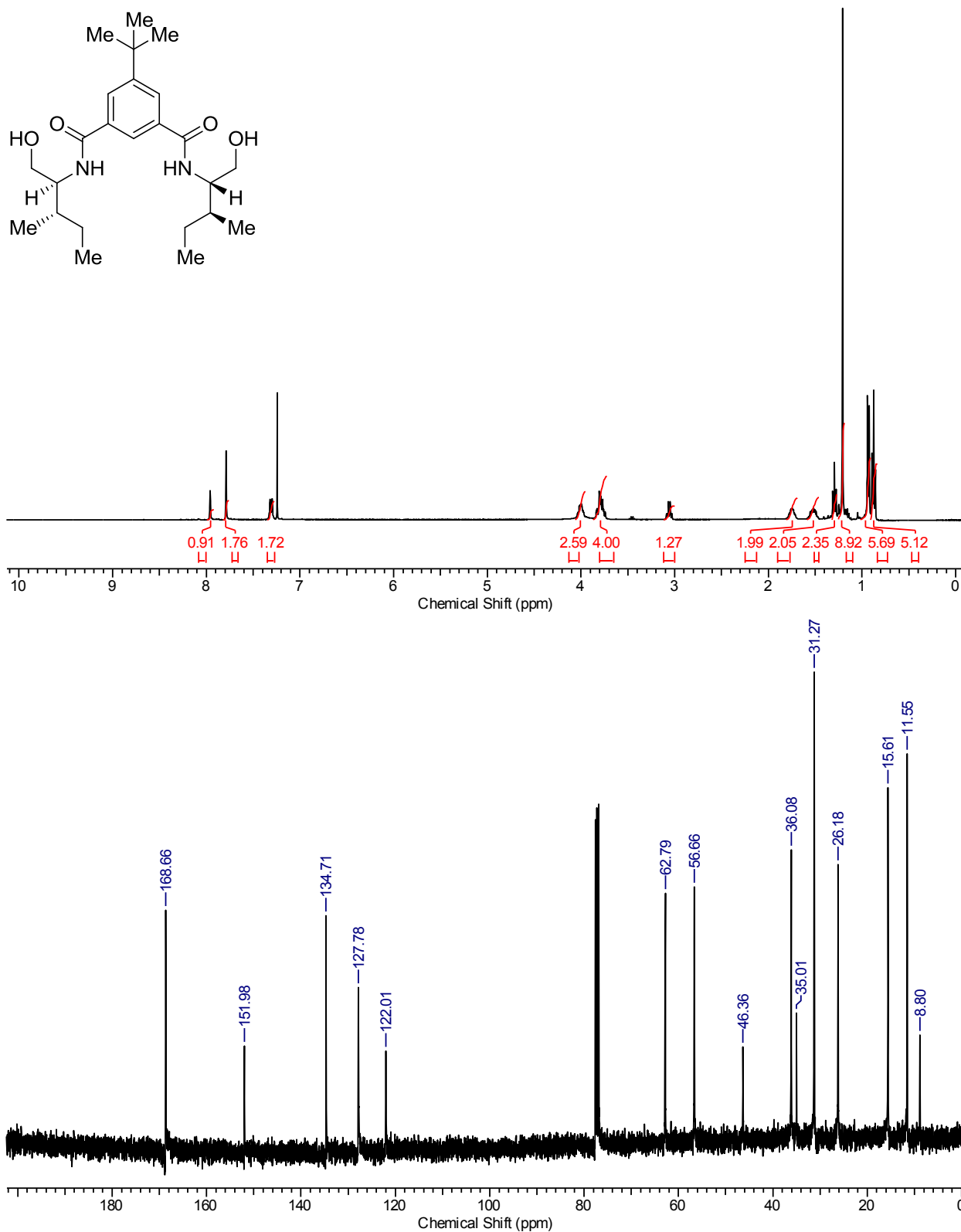


CC(C)C[C@H](NC(=O)c1ccc(cc1)C(=O)N[C@@H](C)C)C

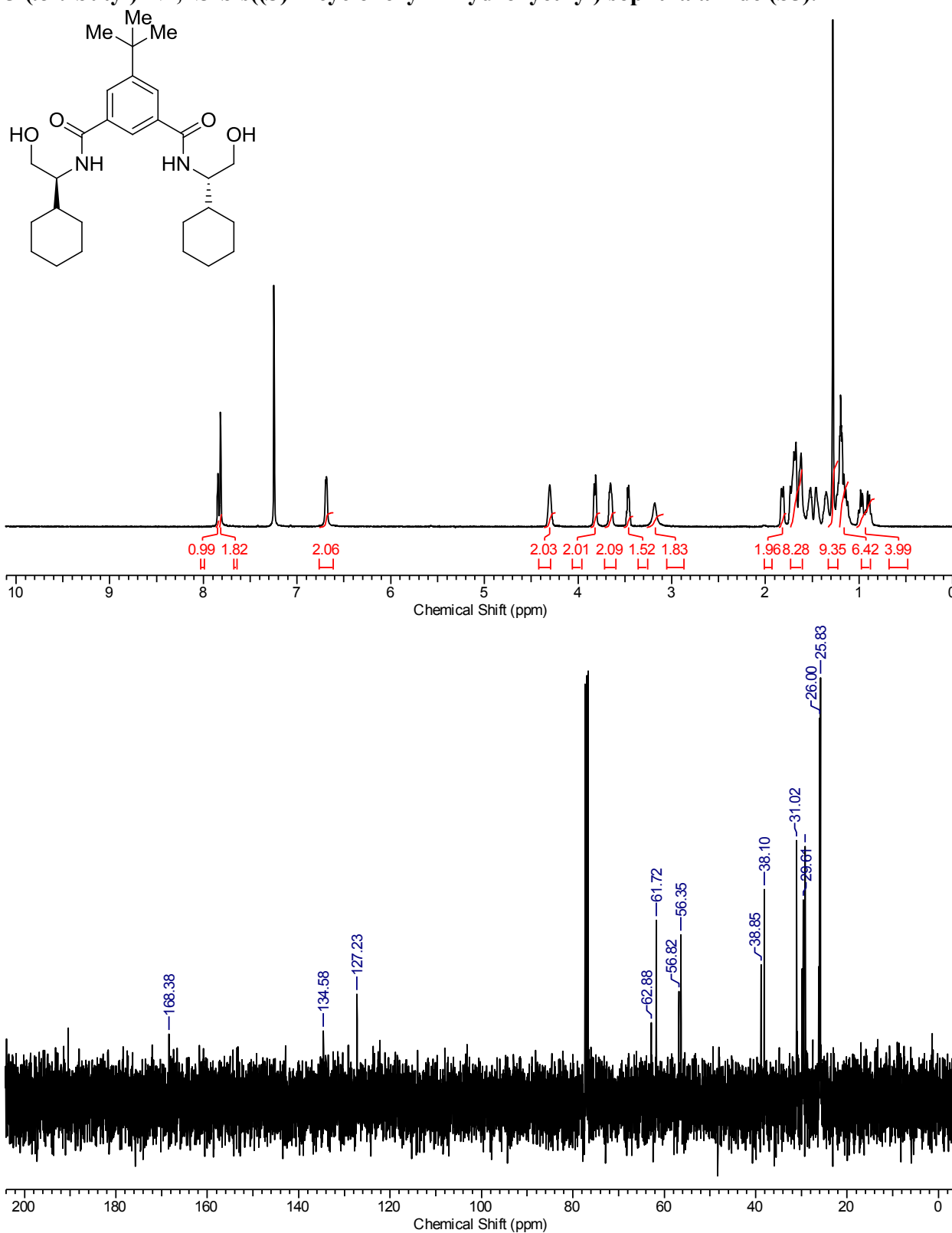
5-(*tert*-butyl)-*N*1,*N*3-bis((*R*)-1-hydroxyhexan-2-yl)isophthalamide (S3).



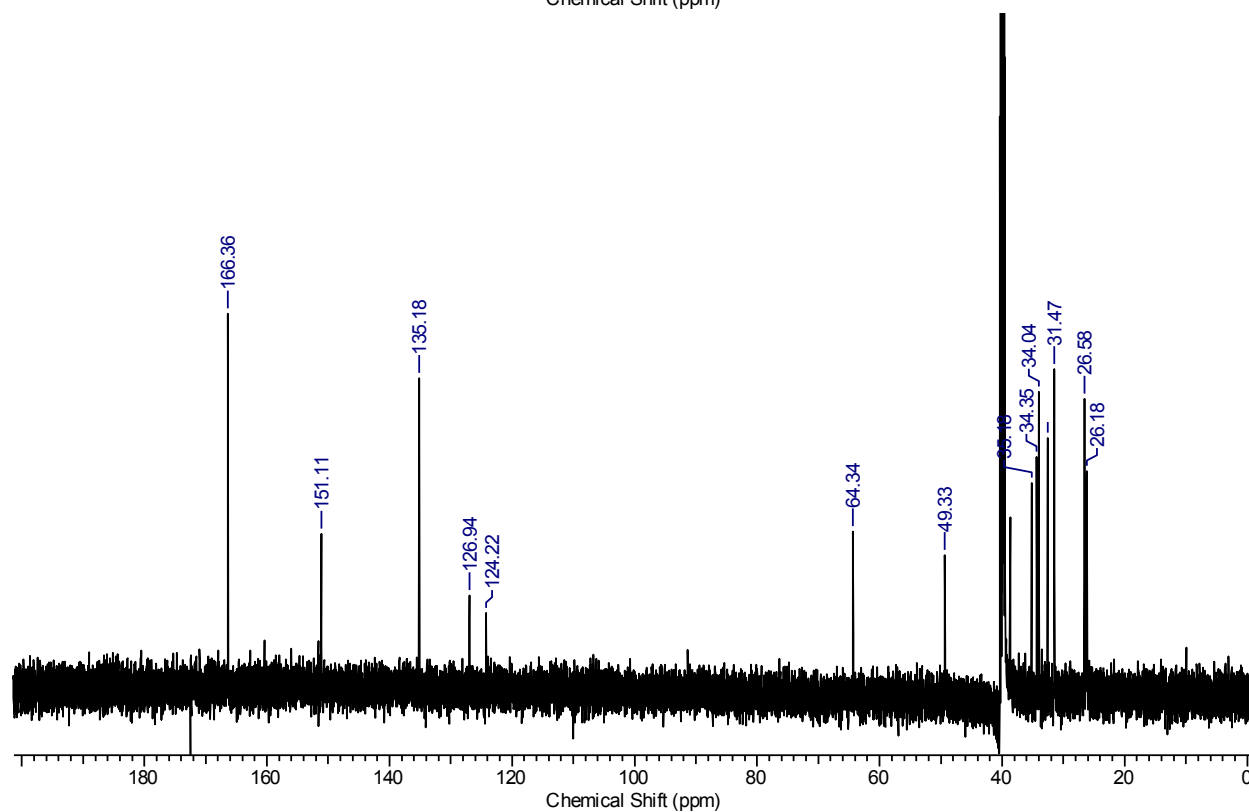
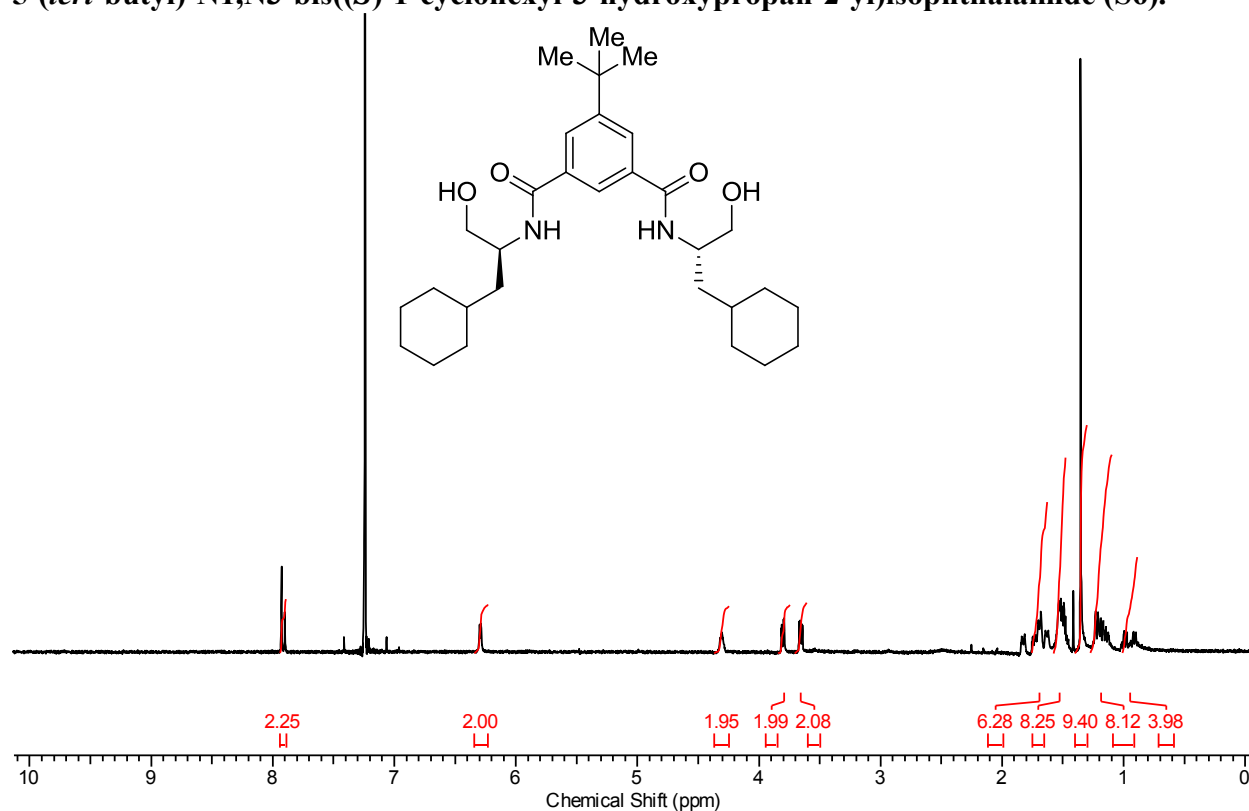
5-(*tert*-butyl)-N1,N3-bis((2*S*,3*S*)-1-hydroxy-3-methylpentan-2-yl)isophthalamide (S4).



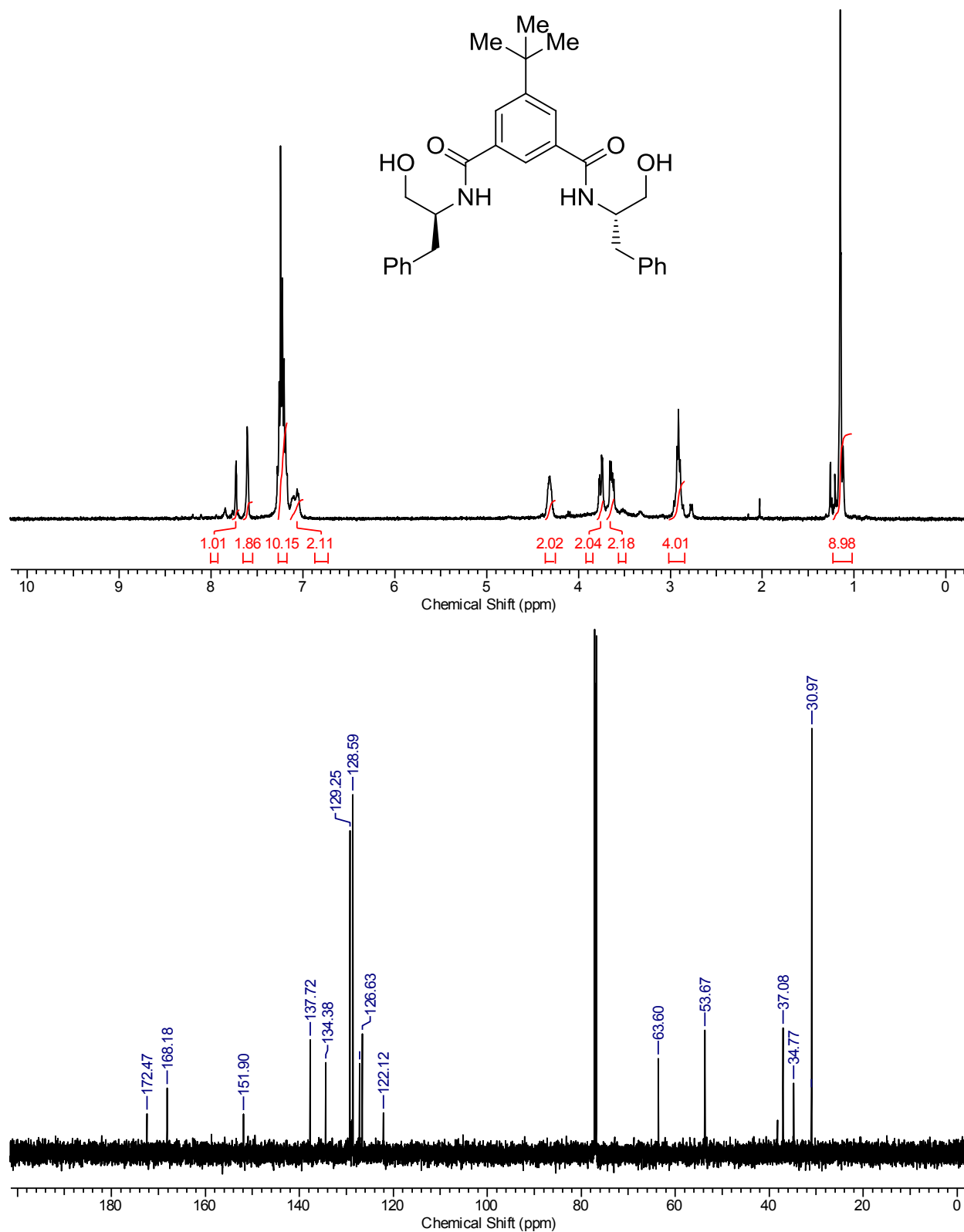
5-(*tert*-butyl)-N1,N3-bis((*S*)-1-cyclohexyl-2-hydroxyethyl)isophthalamide (S5).



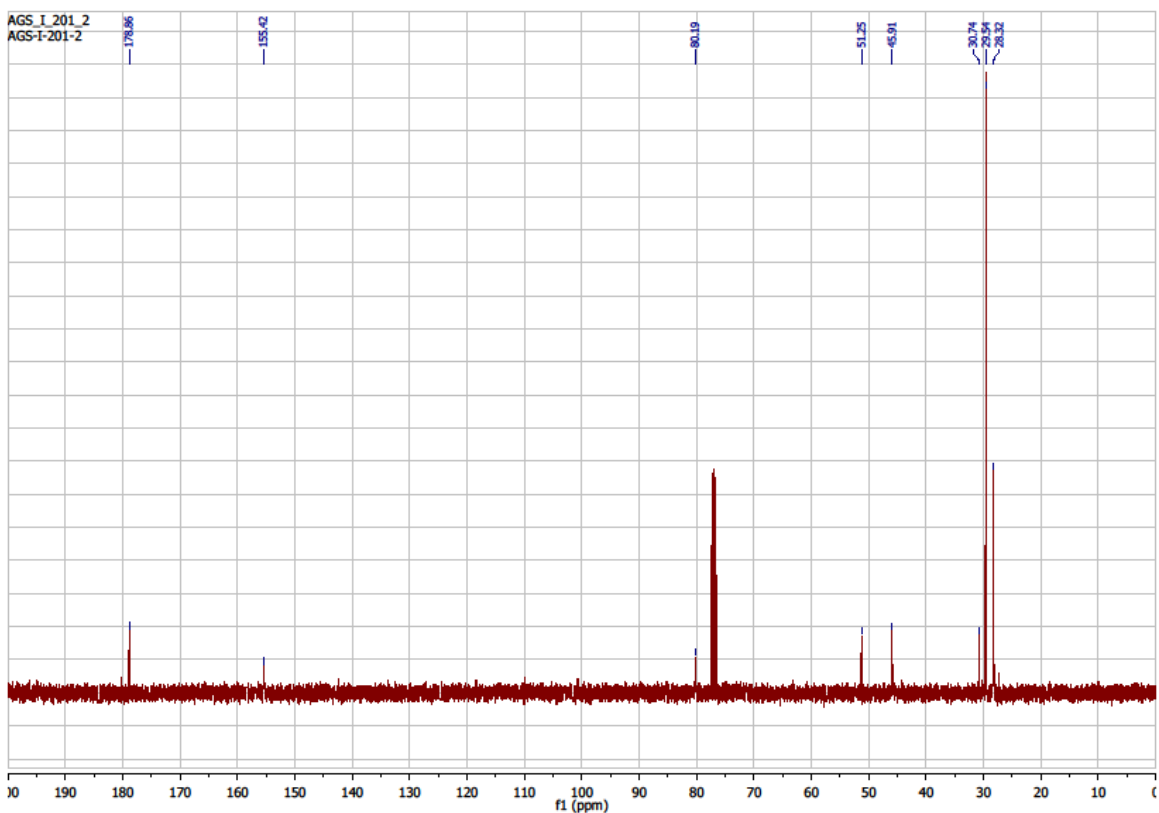
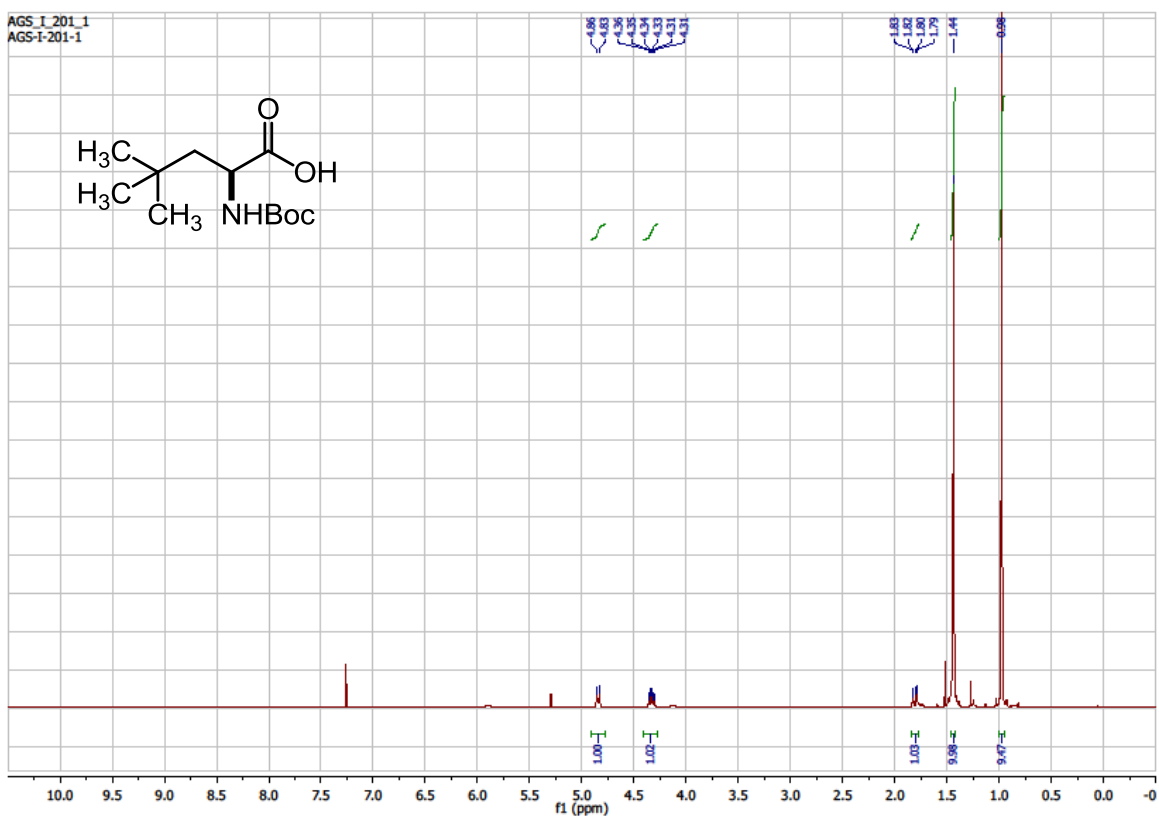
5-(*tert*-butyl)-N1,N3-bis((*S*)-1-cyclohexyl-3-hydroxypropan-2-yl)isophthalamide (S6).



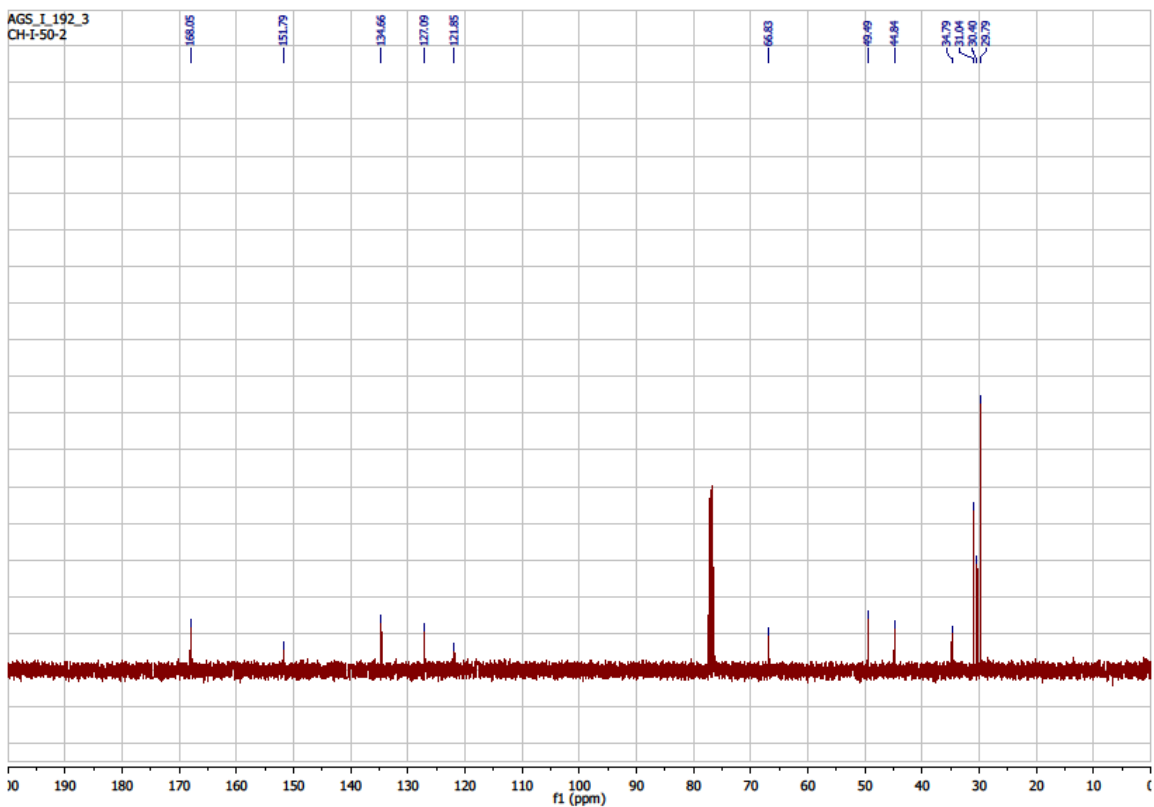
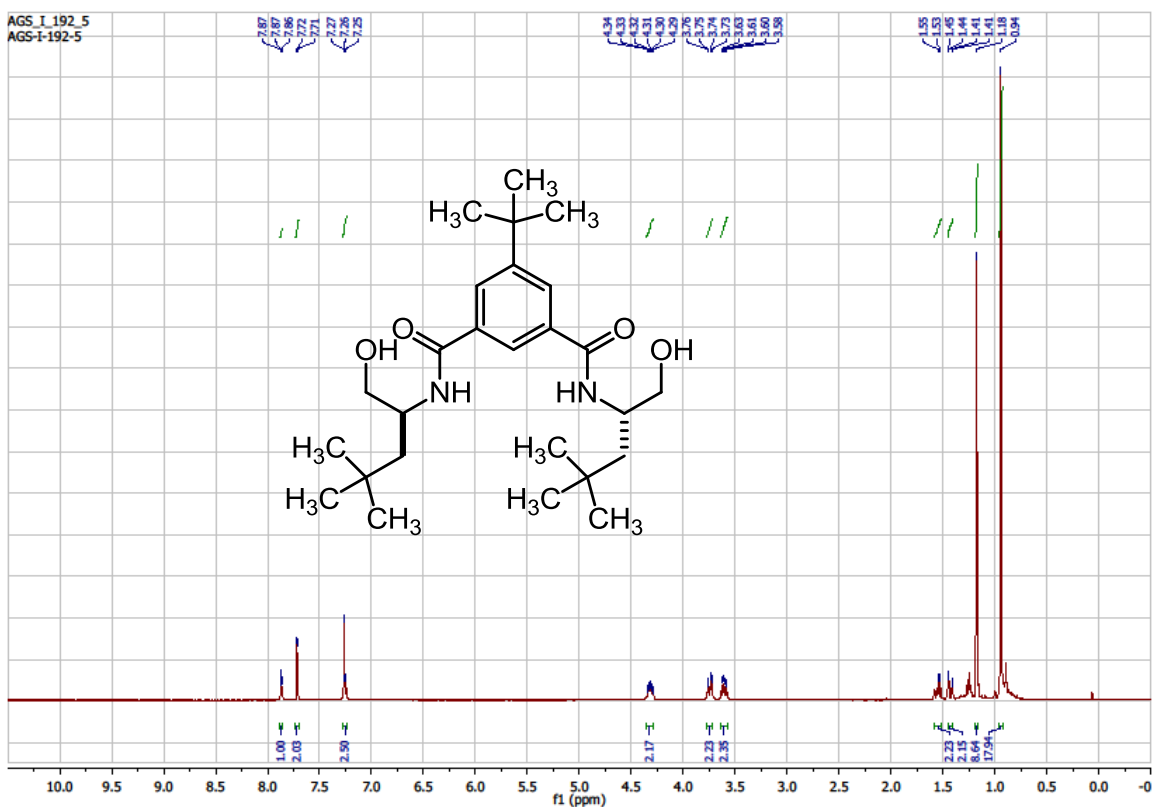
5-(*tert*-butyl)-*N*1,*N*3-bis((*S*)-1-hydroxy-3-phenylpropan-2-yl)isophthalamide (S7).



(S)-2-((*tert*-butoxycarbonyl)amino)-4,4-dimethylpentanoic acid (S8).



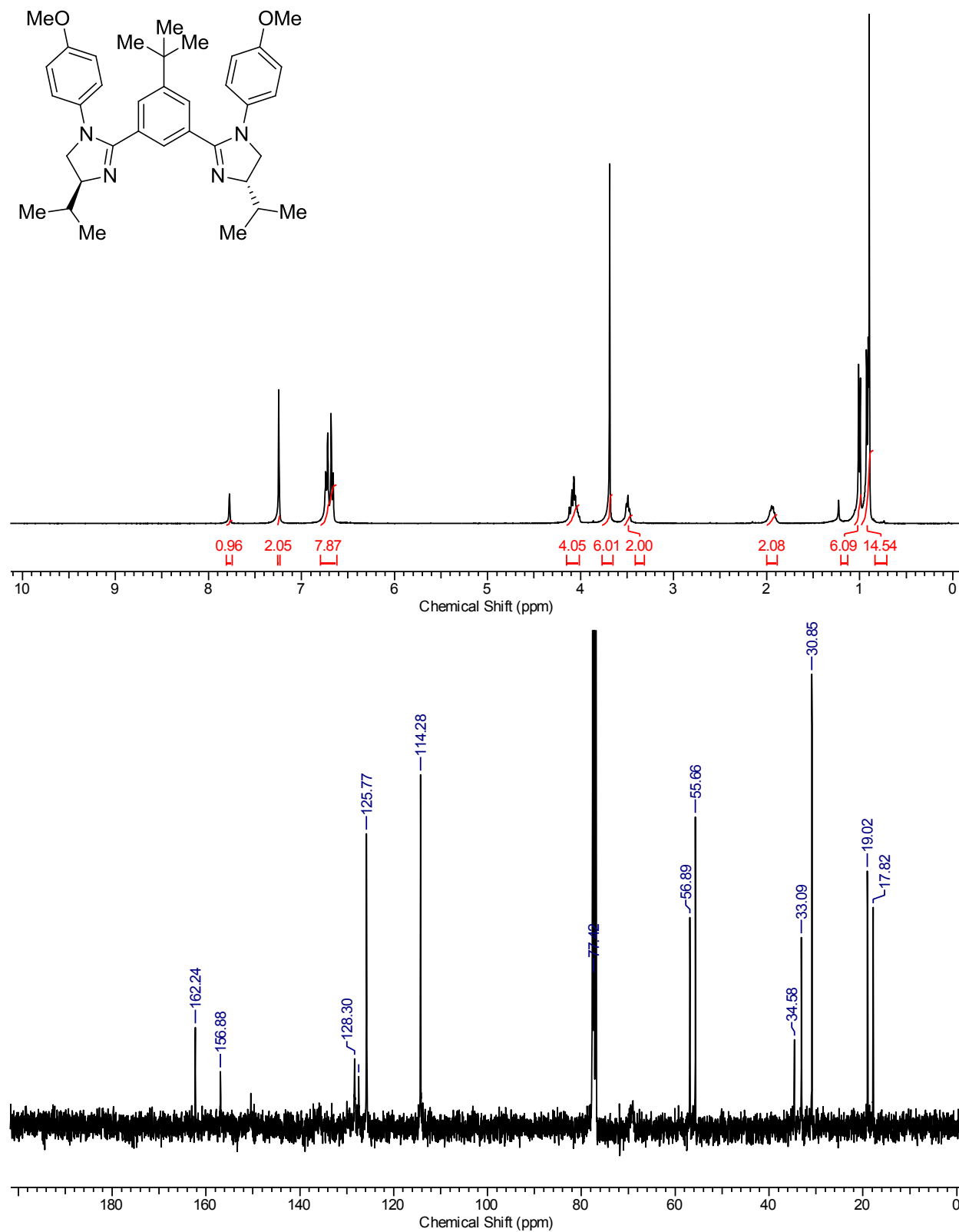
5-(*tert*-butyl)-*N*¹,*N*³-bis((*S*)-1-hydroxy-4,4-dimethylpentan-2-yl)isophthalamide (S11).



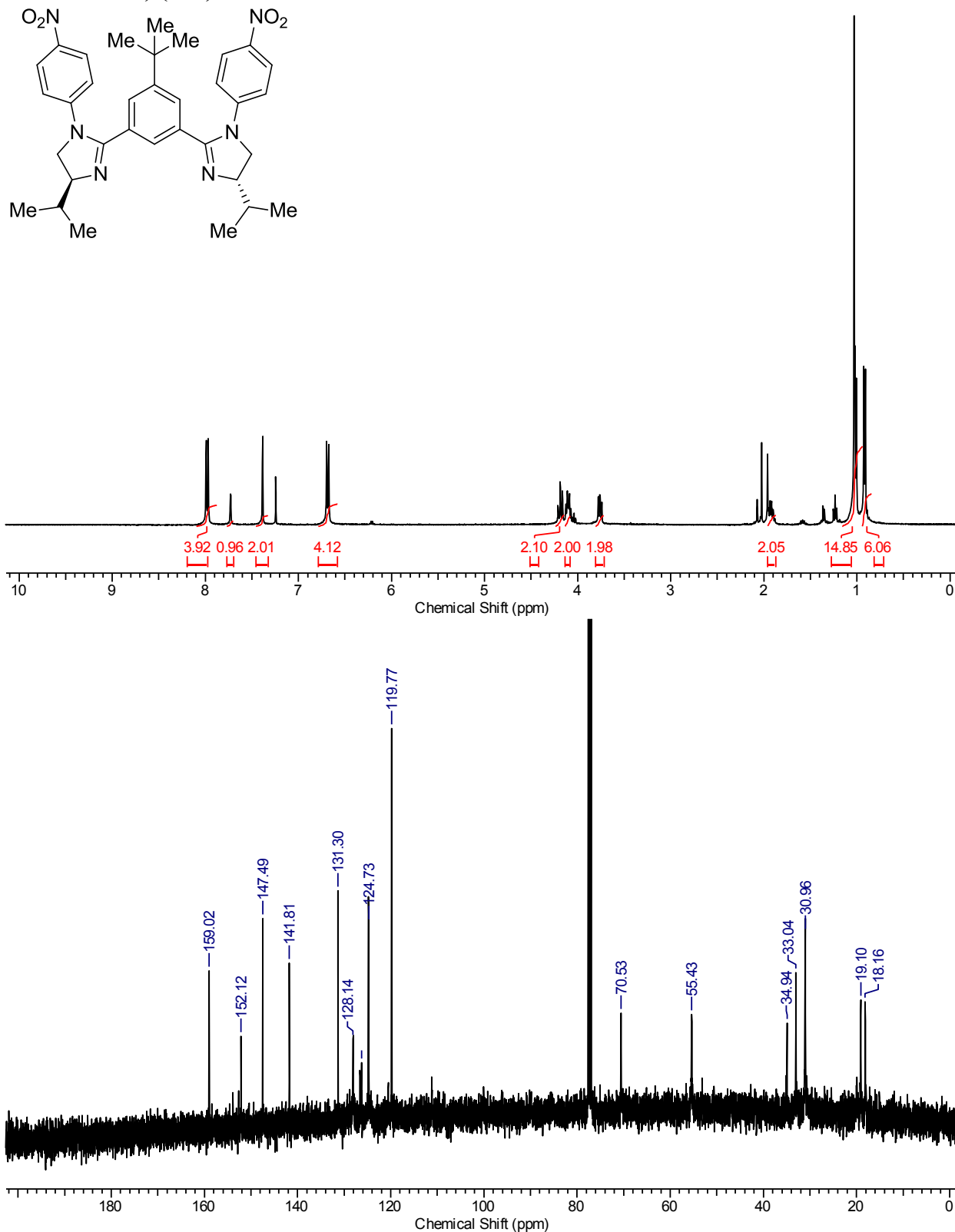
Chemical structure of compound 10: A central benzene ring substituted with a tert-butyl group and two 1-phenyl-2-methyl-1H-imidaz-2-yl groups. The left imidazole ring has a (1S,2S)-2,3-dimethylbutyl group at the 4-position, and the right imidazole ring has a (1R,2R)-2,3-dimethylbutyl group at the 4-position.



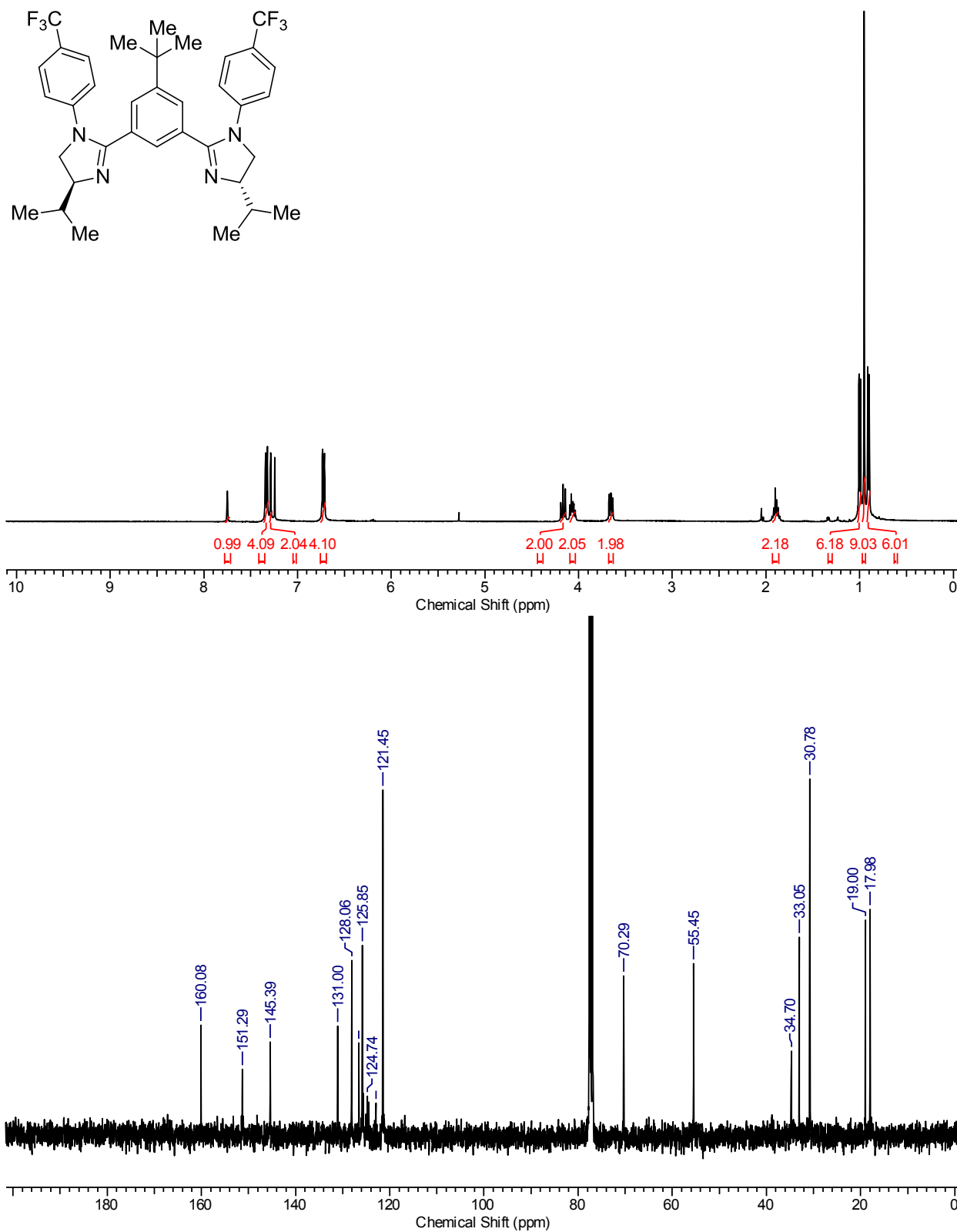
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-(4-methoxyphenyl)-4,5-dihydro-1*H*-imidazole) (S13).



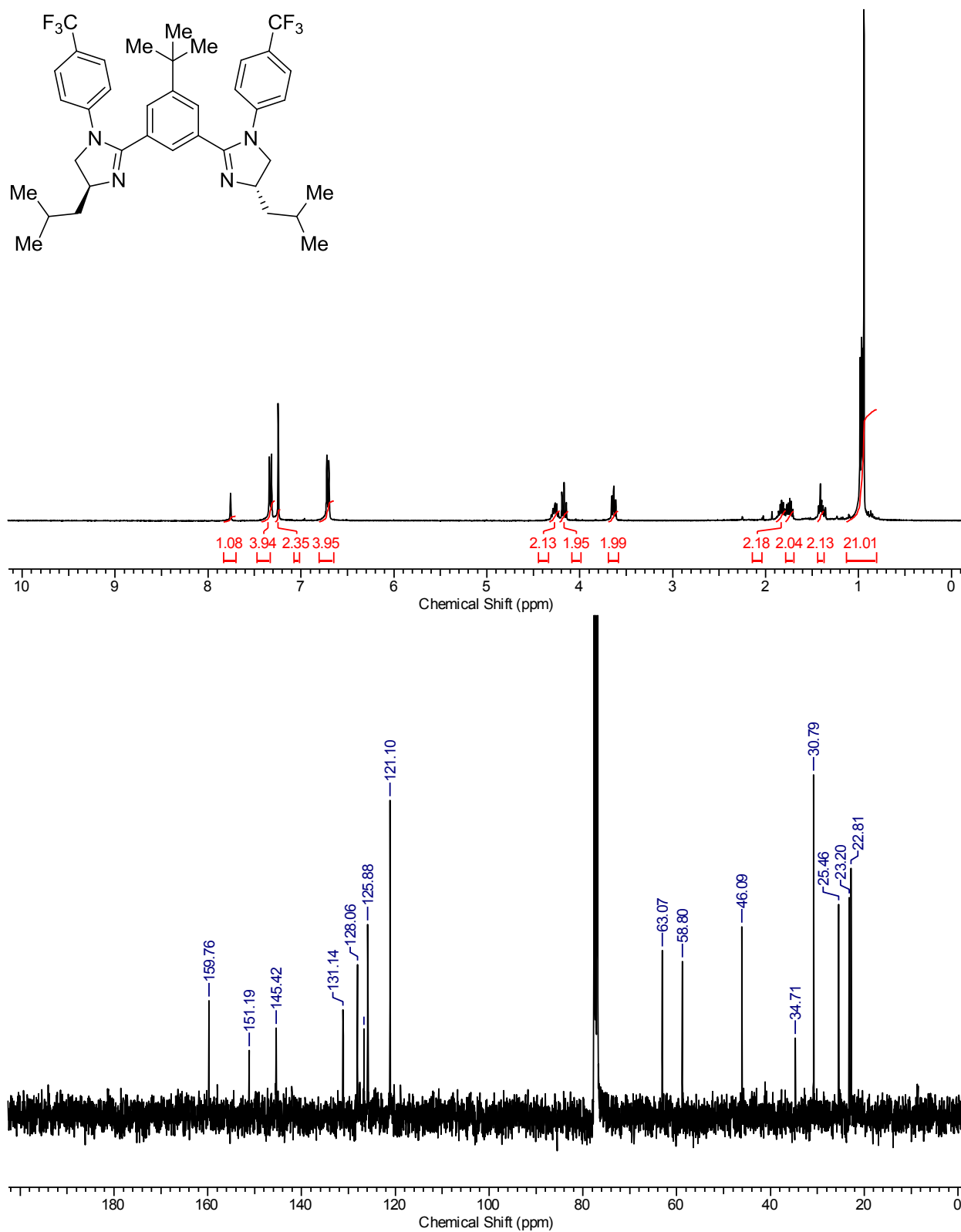
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-(4-nitrophenyl)-4,5-dihydro-1H-imidazole) (S14).



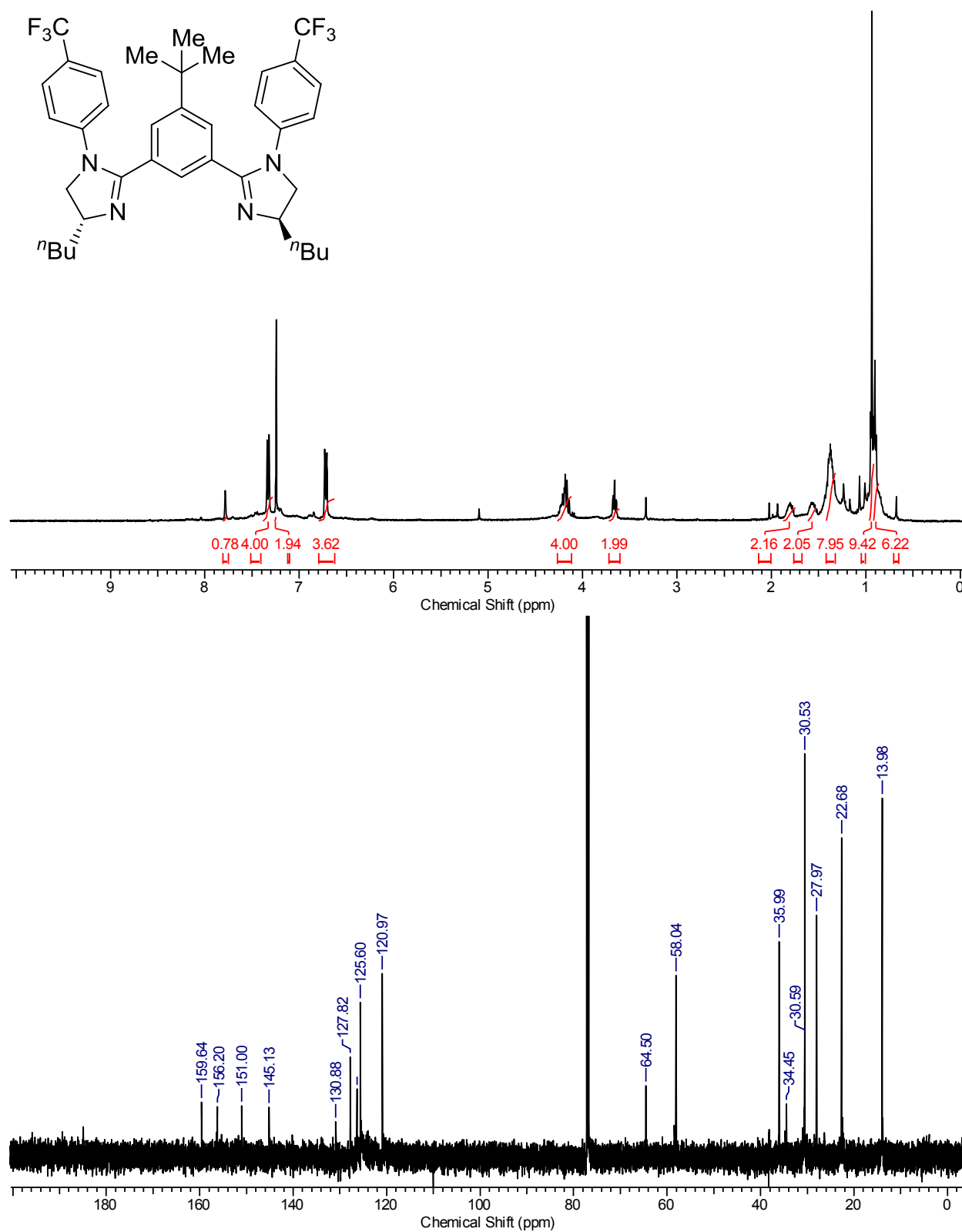
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isopropyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S15).



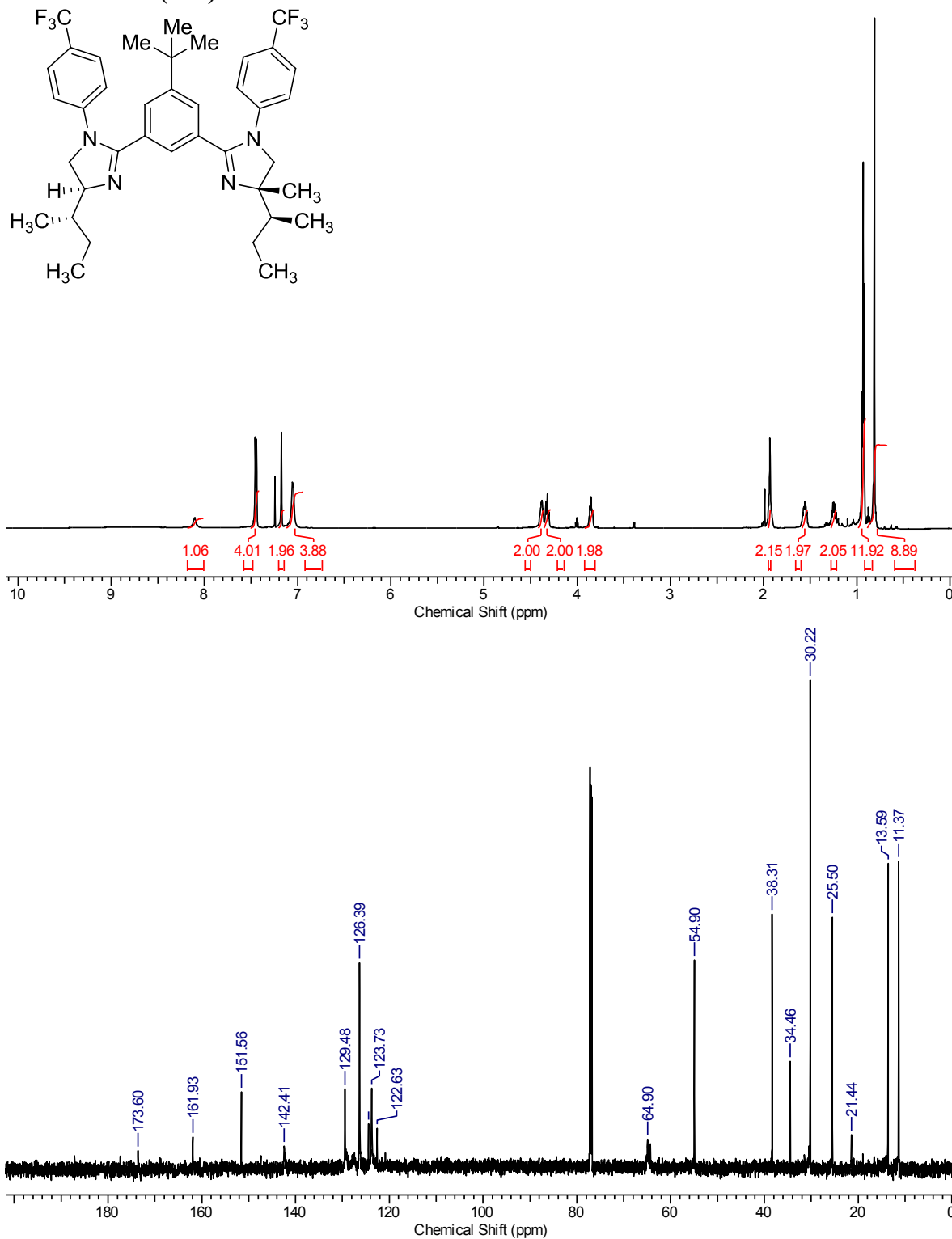
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-isobutyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S16).



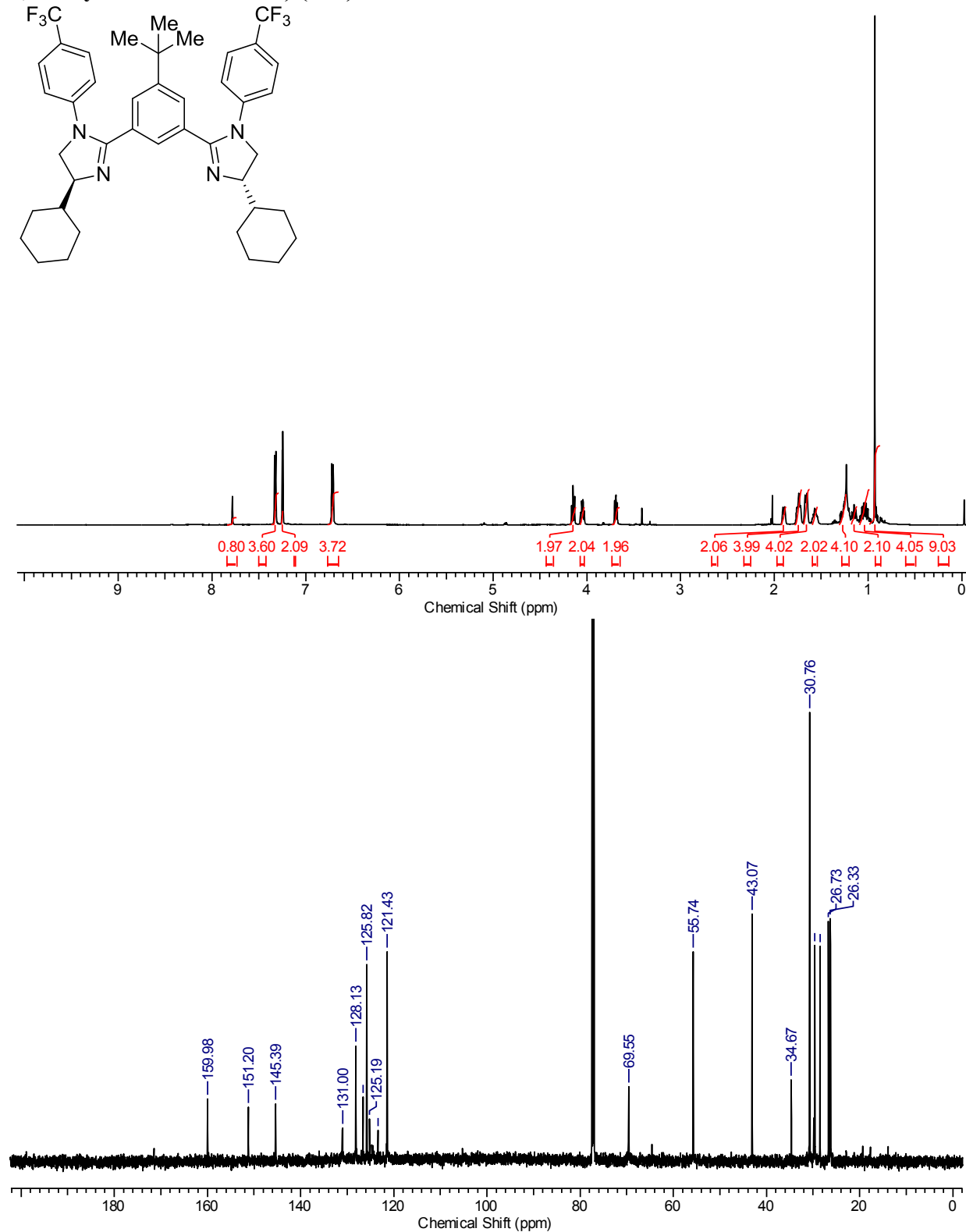
(4*R*,4'*R*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-butyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S17).



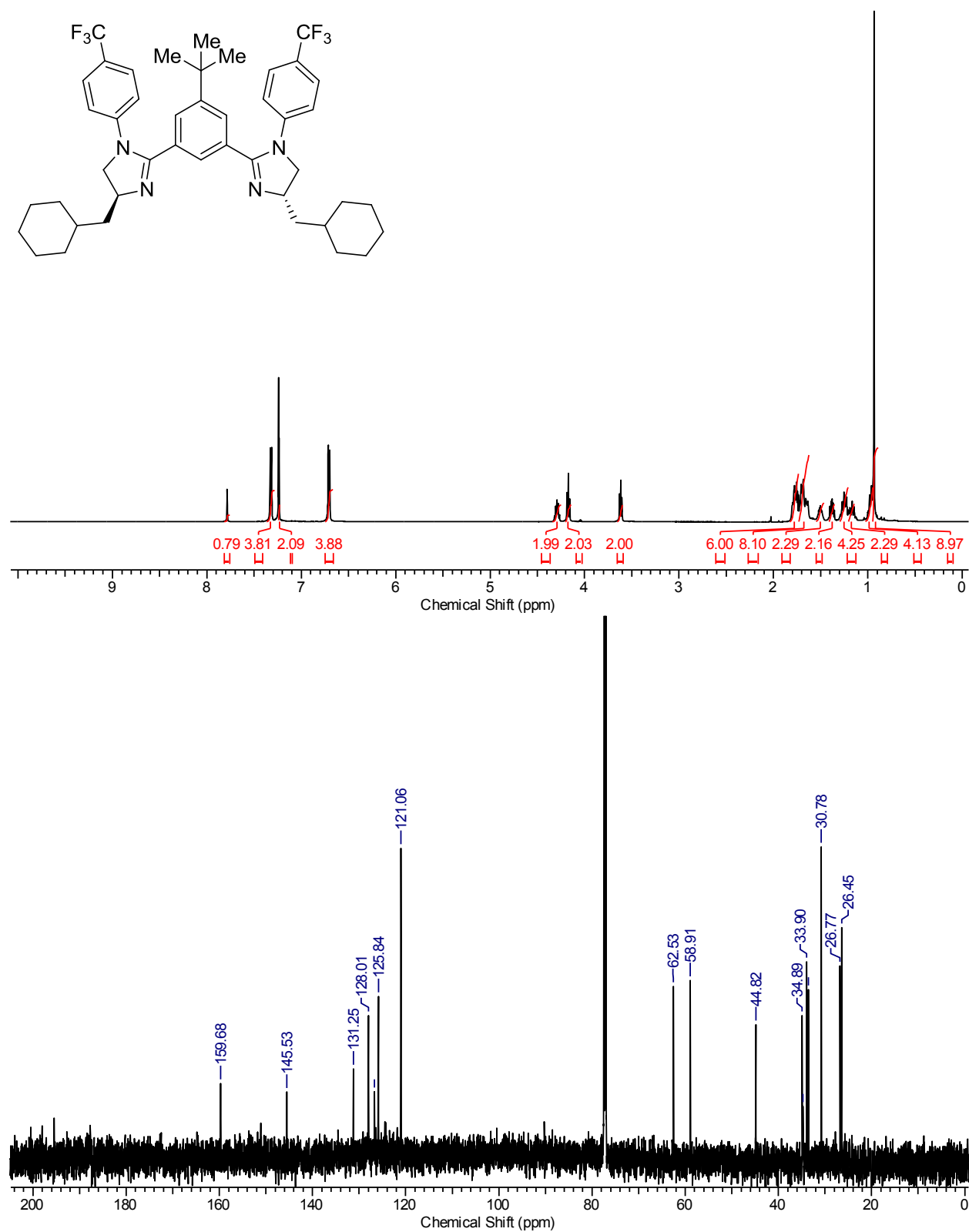
(S)-4-((S)-sec-butyl)-2-(3-(tert-butyl)-5-((S)-4-((S)-sec-butyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazol-2-yl)phenyl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole (S18).



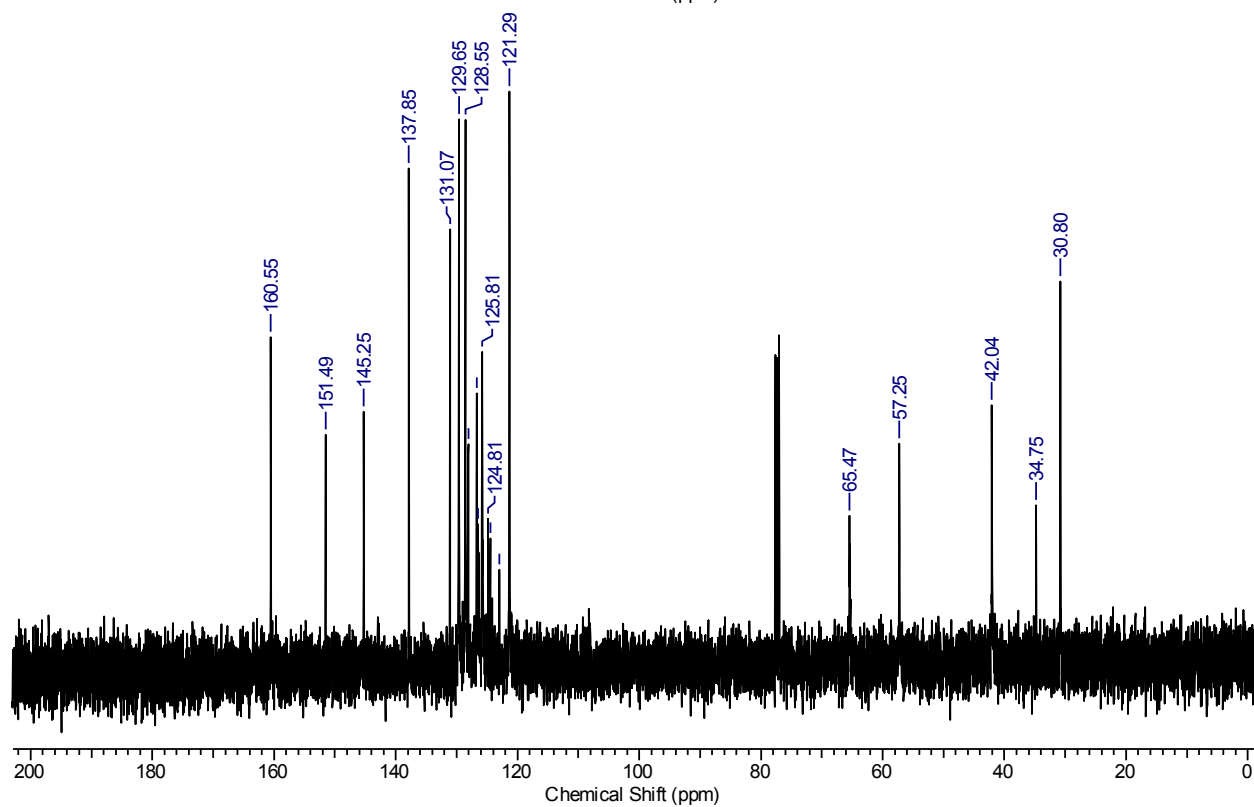
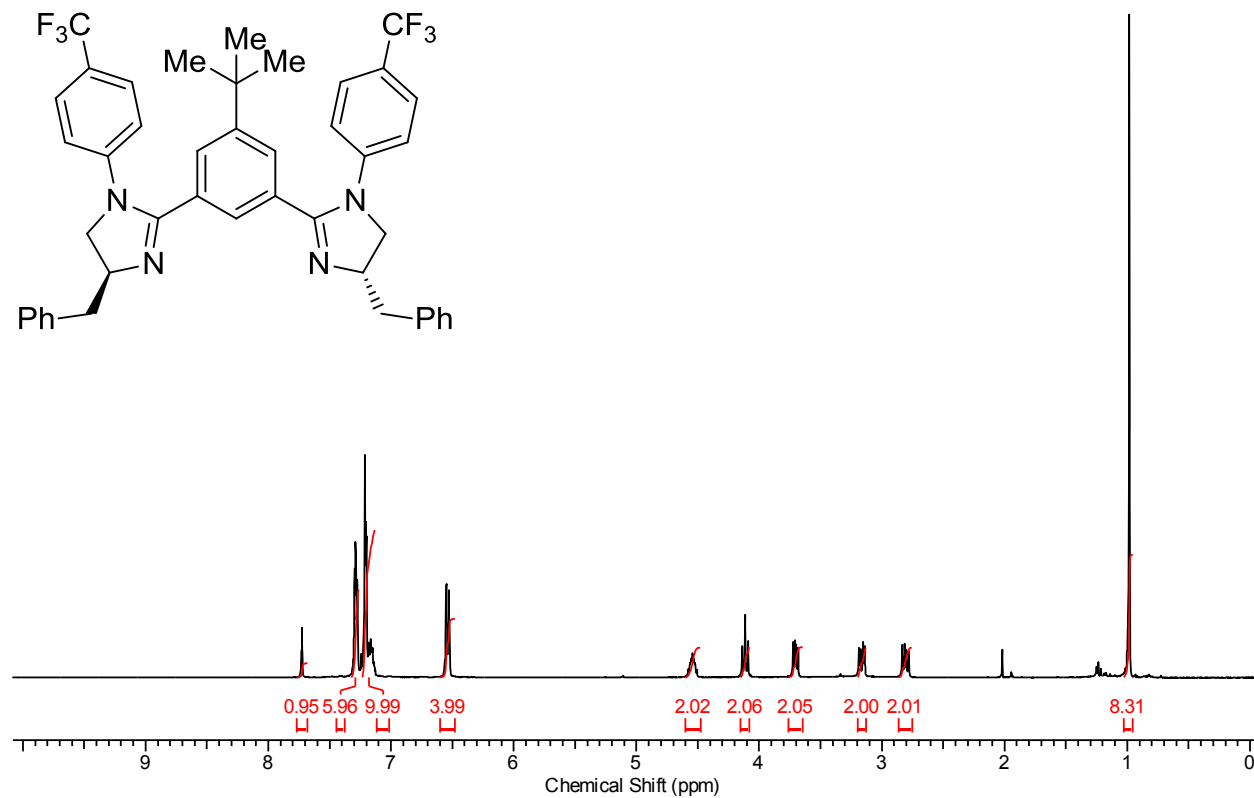
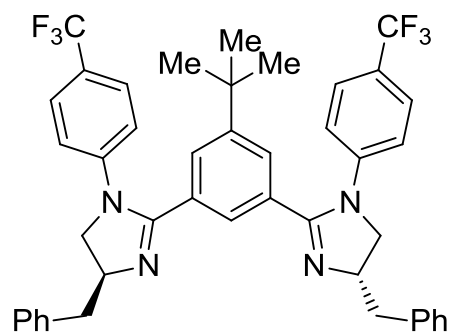
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-cyclohexyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S19).



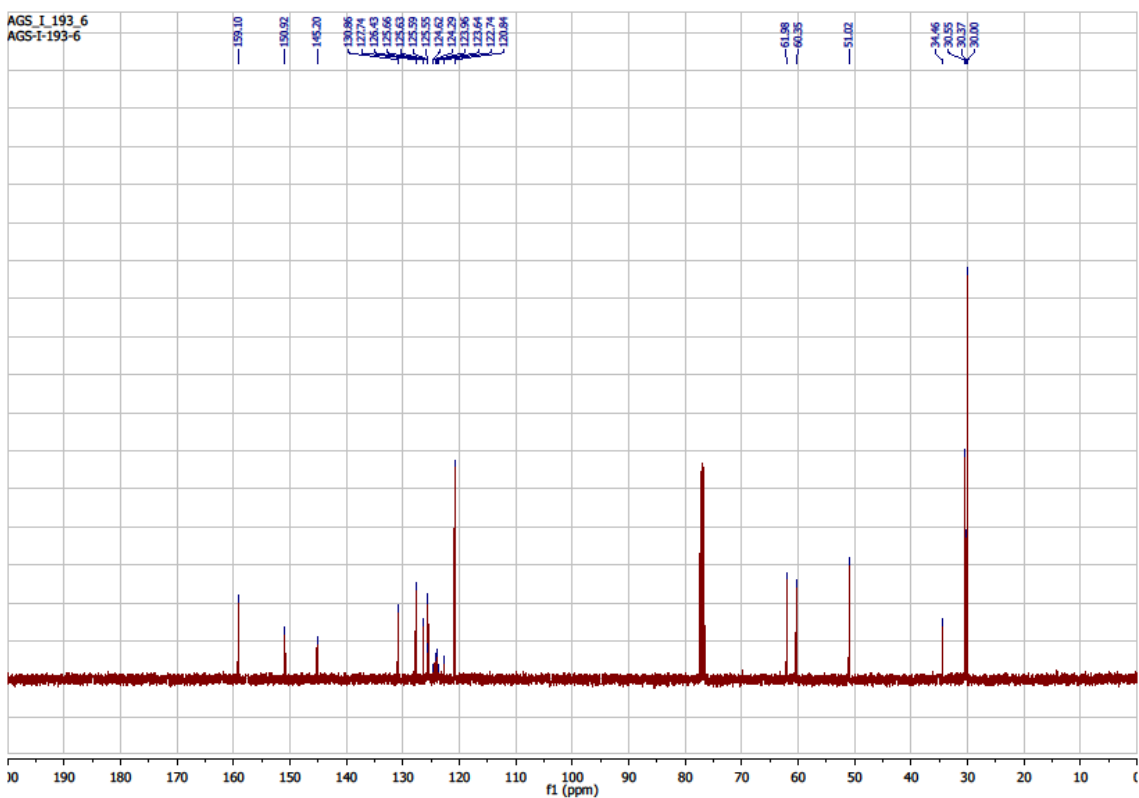
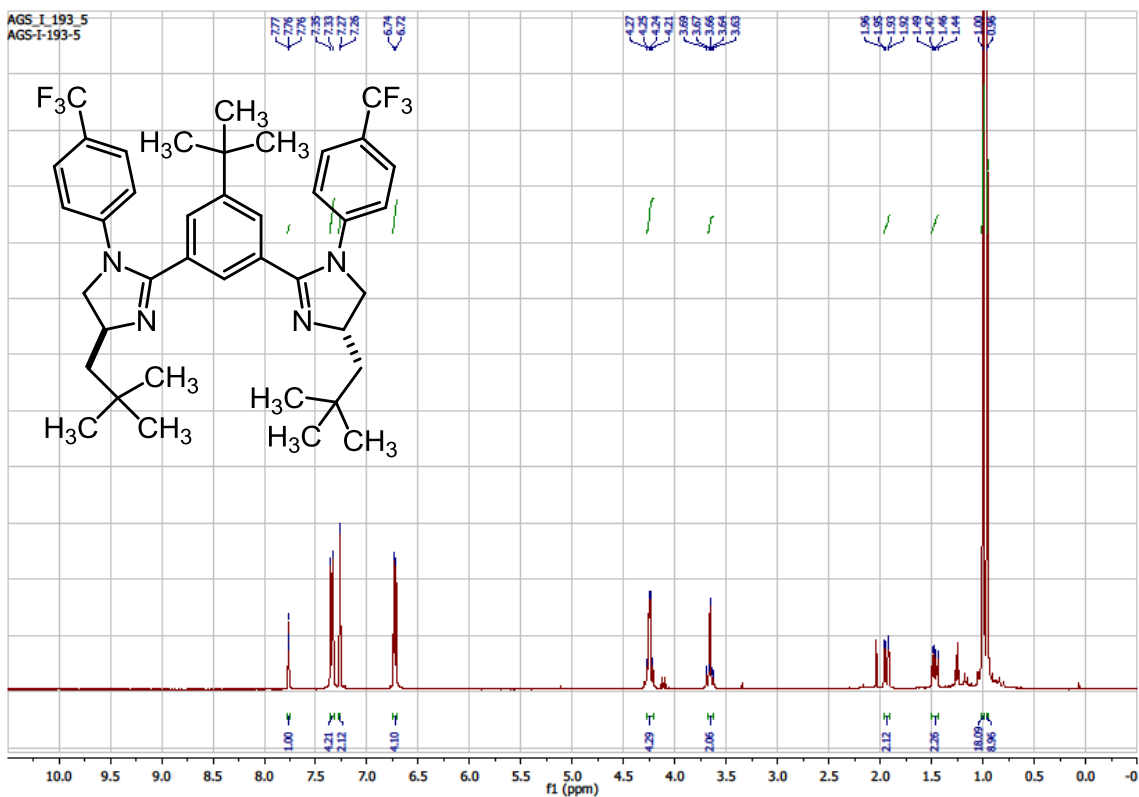
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-(cyclohexylmethyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S20).



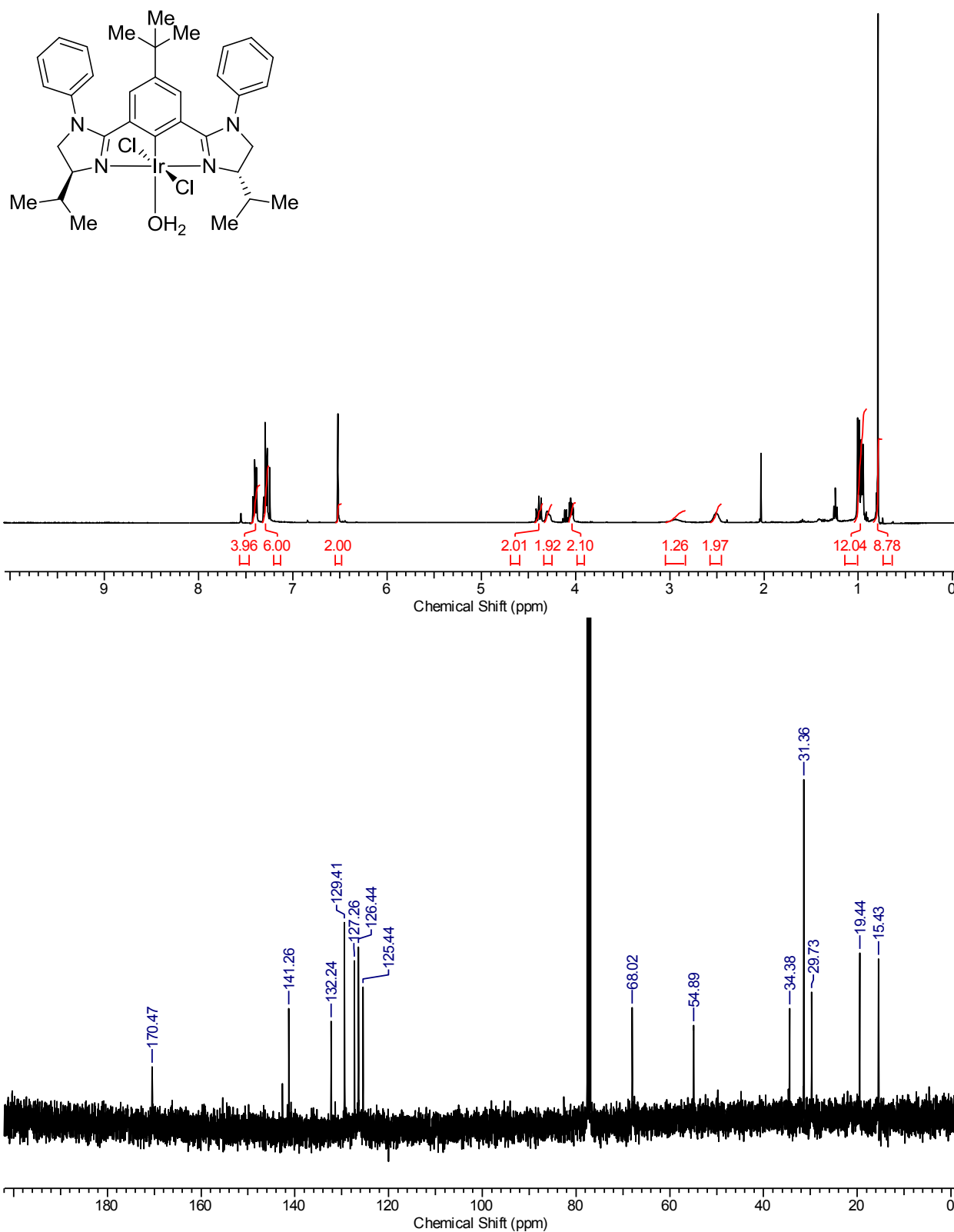
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-benzyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S21).



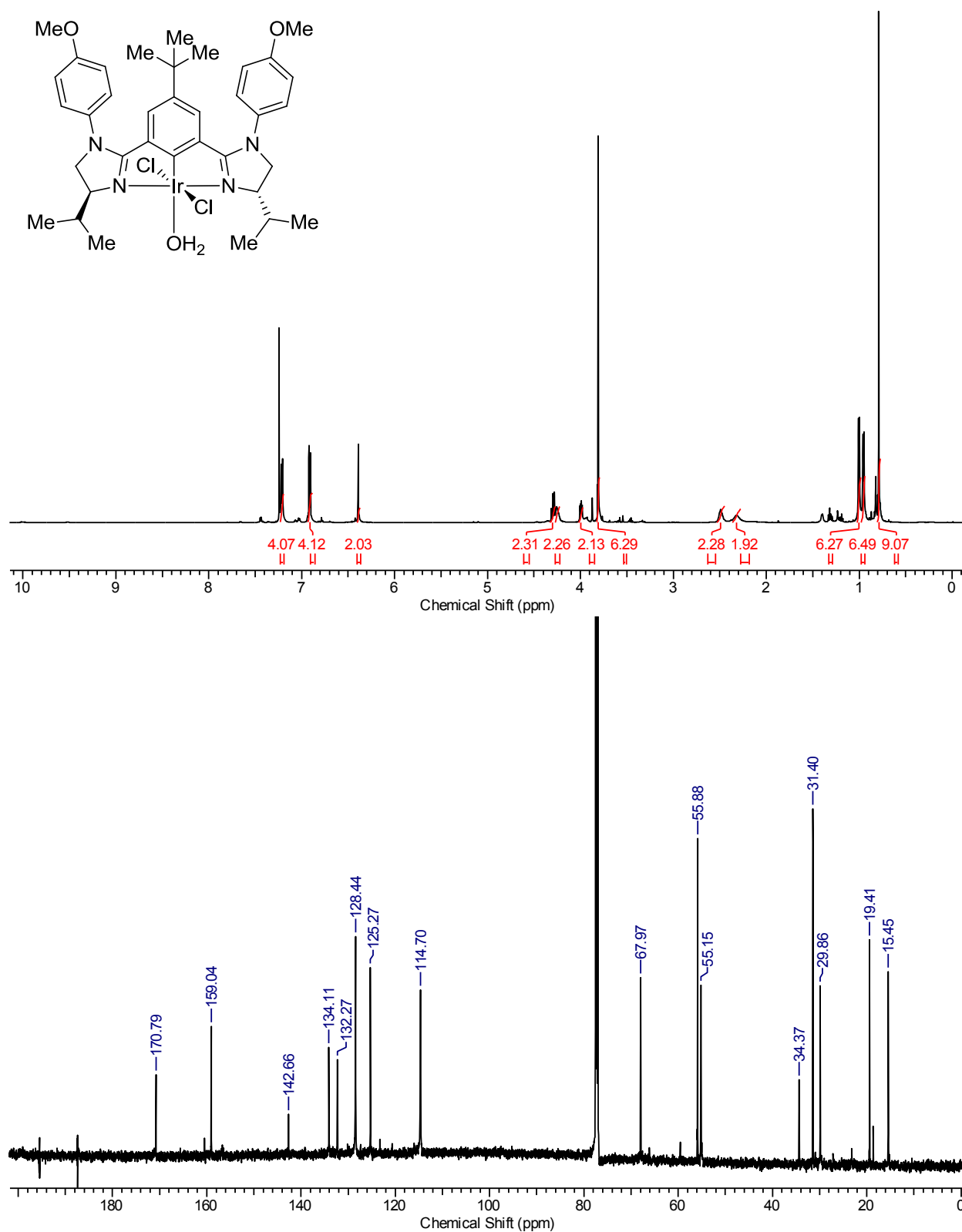
(4*S*,4'*S*)-2,2'-(5-(*tert*-butyl)-1,3-phenylene)bis(4-neopentyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazole) (S22).



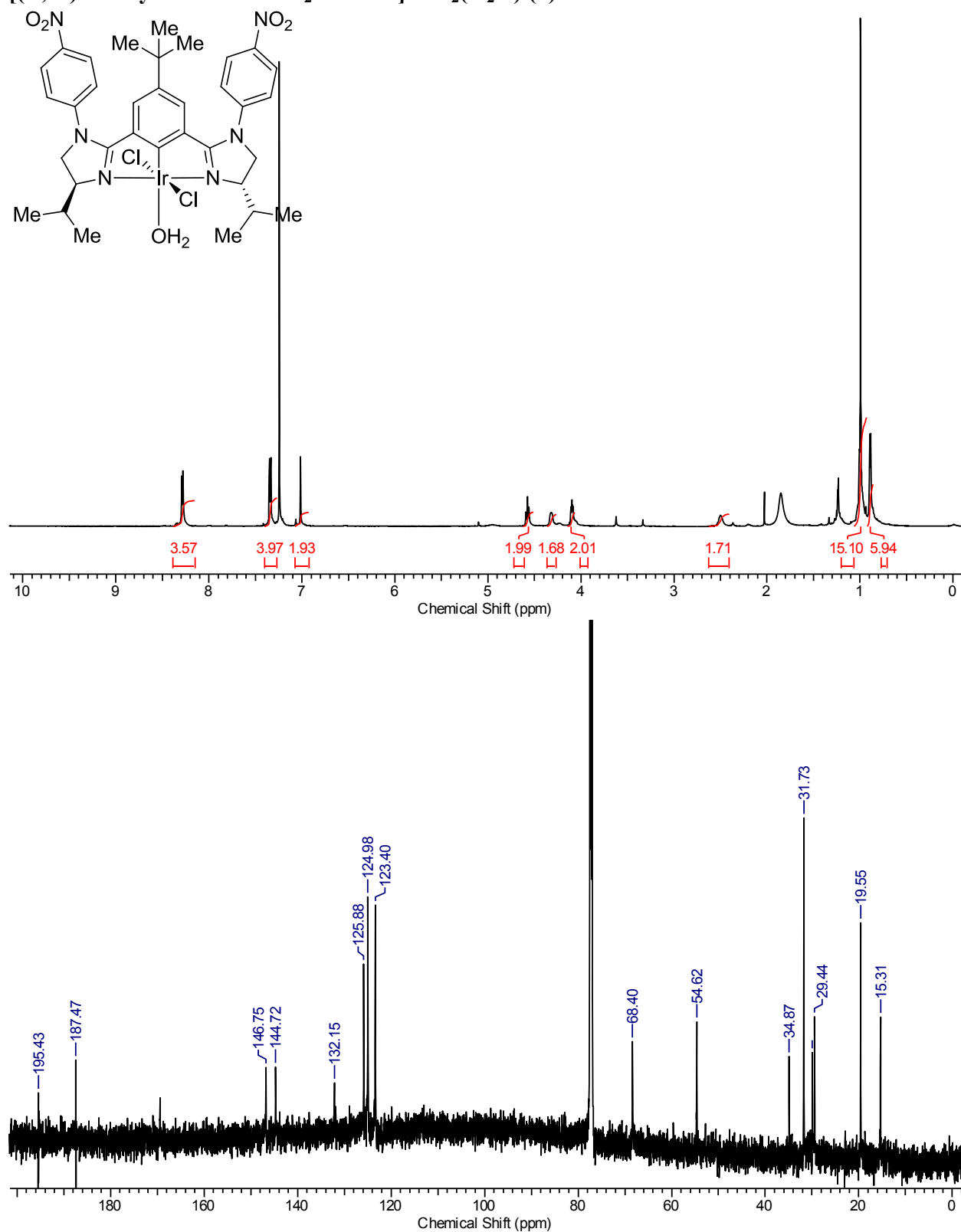
[(*R,R*)-*t*-ButylPhebim-Ph-*i*-Pr]IrCl₂(H₂O) (5).



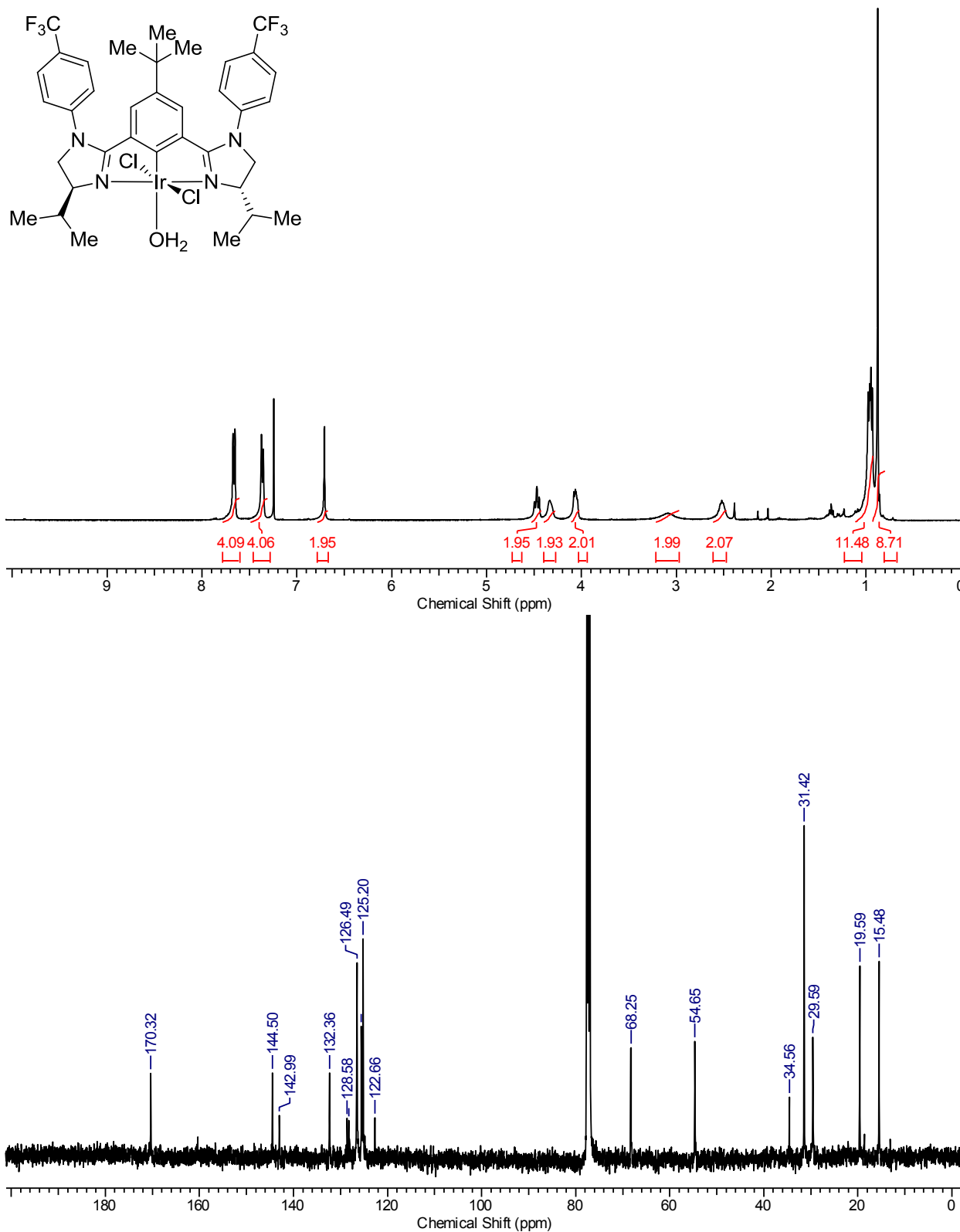
[(*R,R*)-*t*-ButylPhebim-4-OMe-Ph-*i*-Pr]IrCl₂(H₂O) (6).



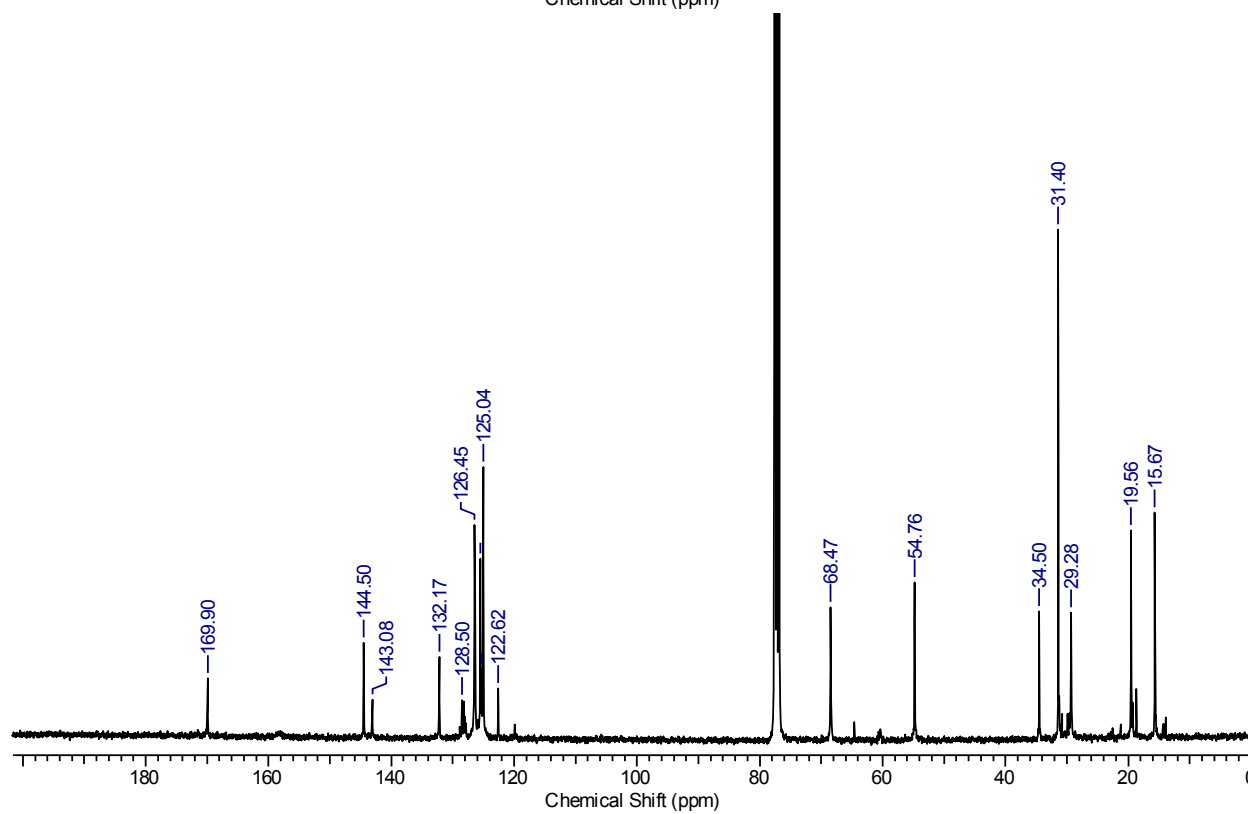
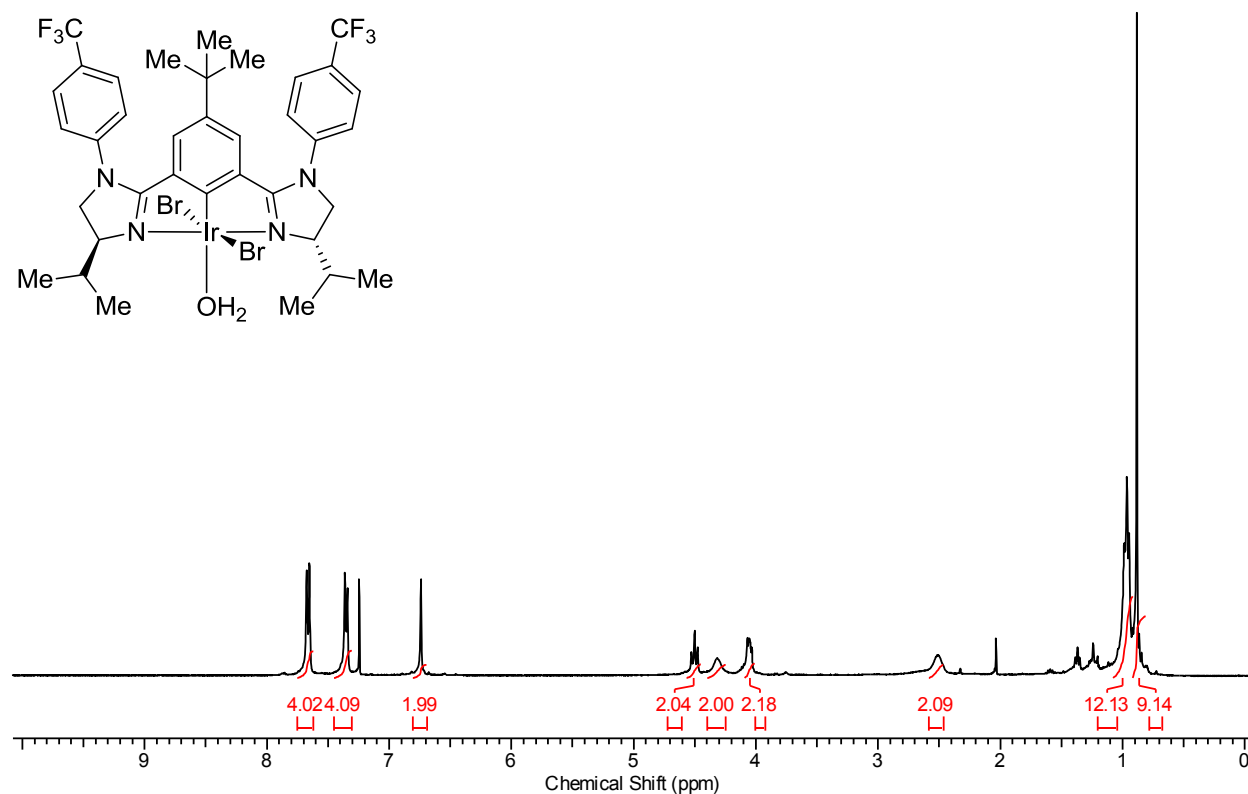
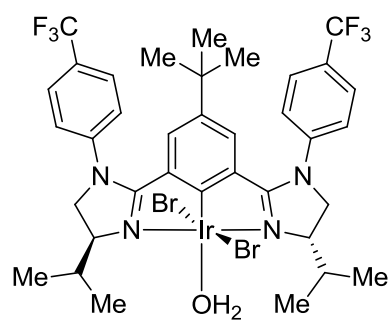
[(*R,R*)-*t*-ButylPhebim-4-NO₂-Ph-*i*-Pr]IrCl₂(H₂O) (7).



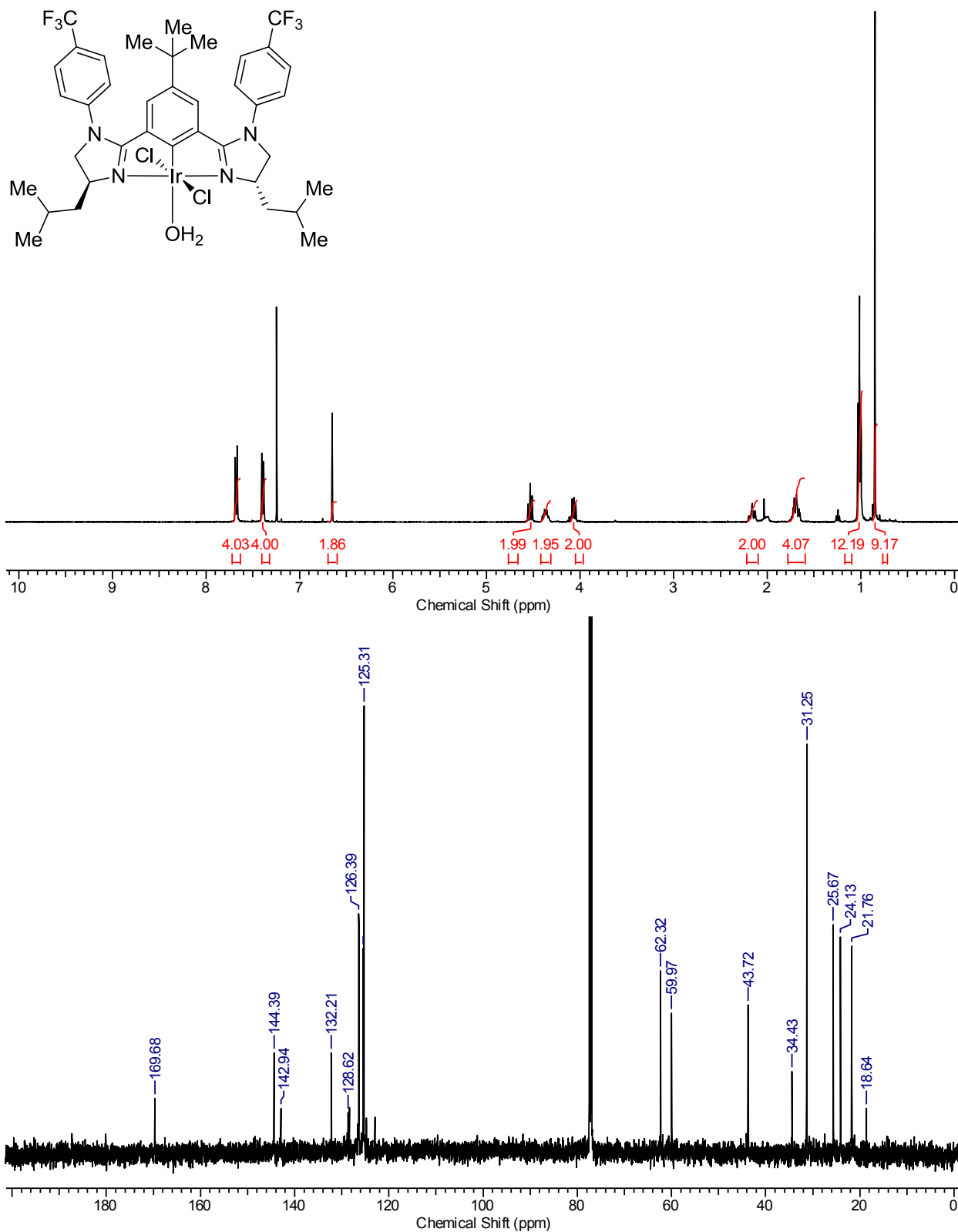
[(*R,R*)-*t*-ButylPhebim-4-CF₃-Ph-*i*-Pr]IrCl₂(H₂O) (8).



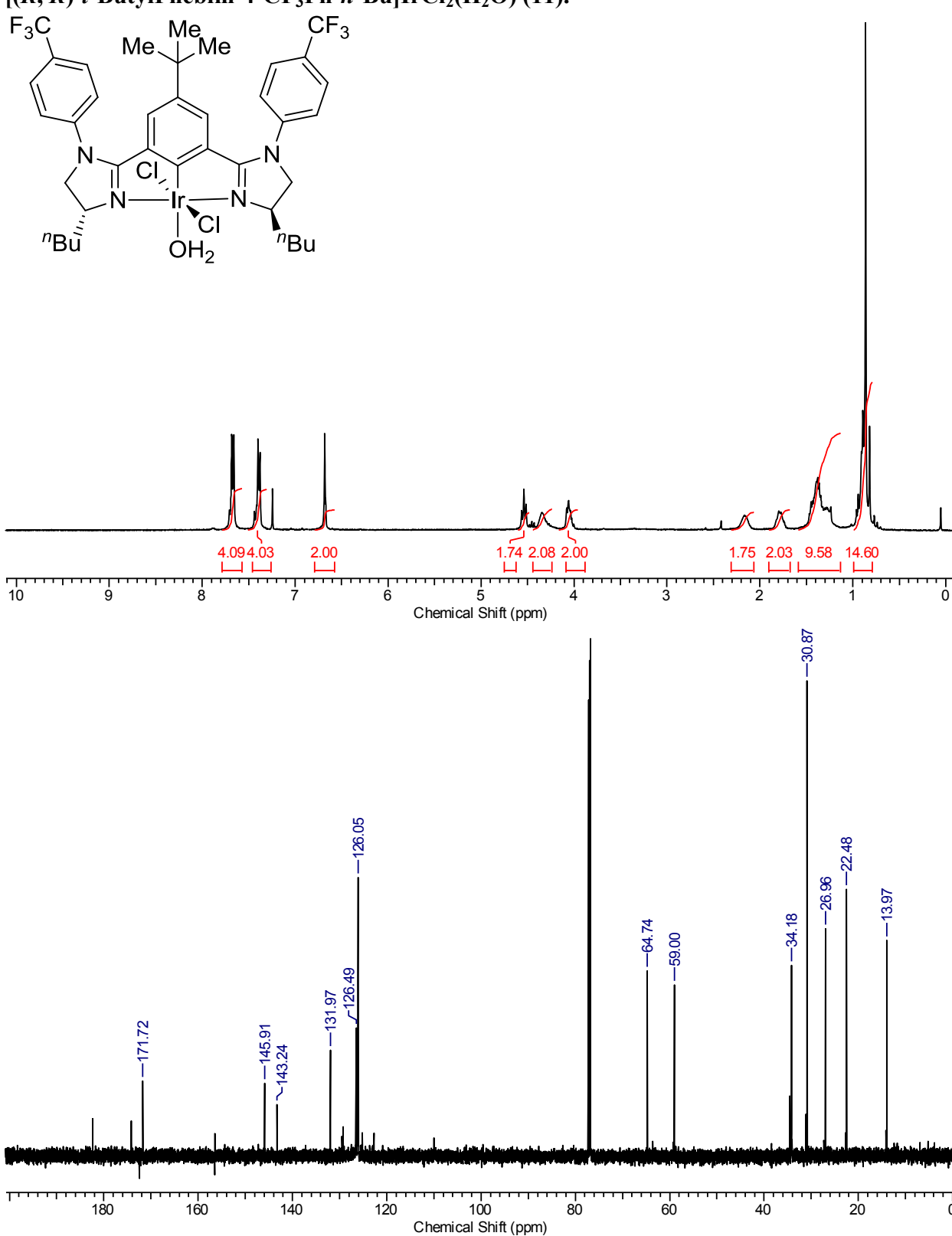
[(*R,R*)-*t*-ButylPhebim-4-CF₃-Ph-*i*-Pr]IrBr₂(H₂O) (9).



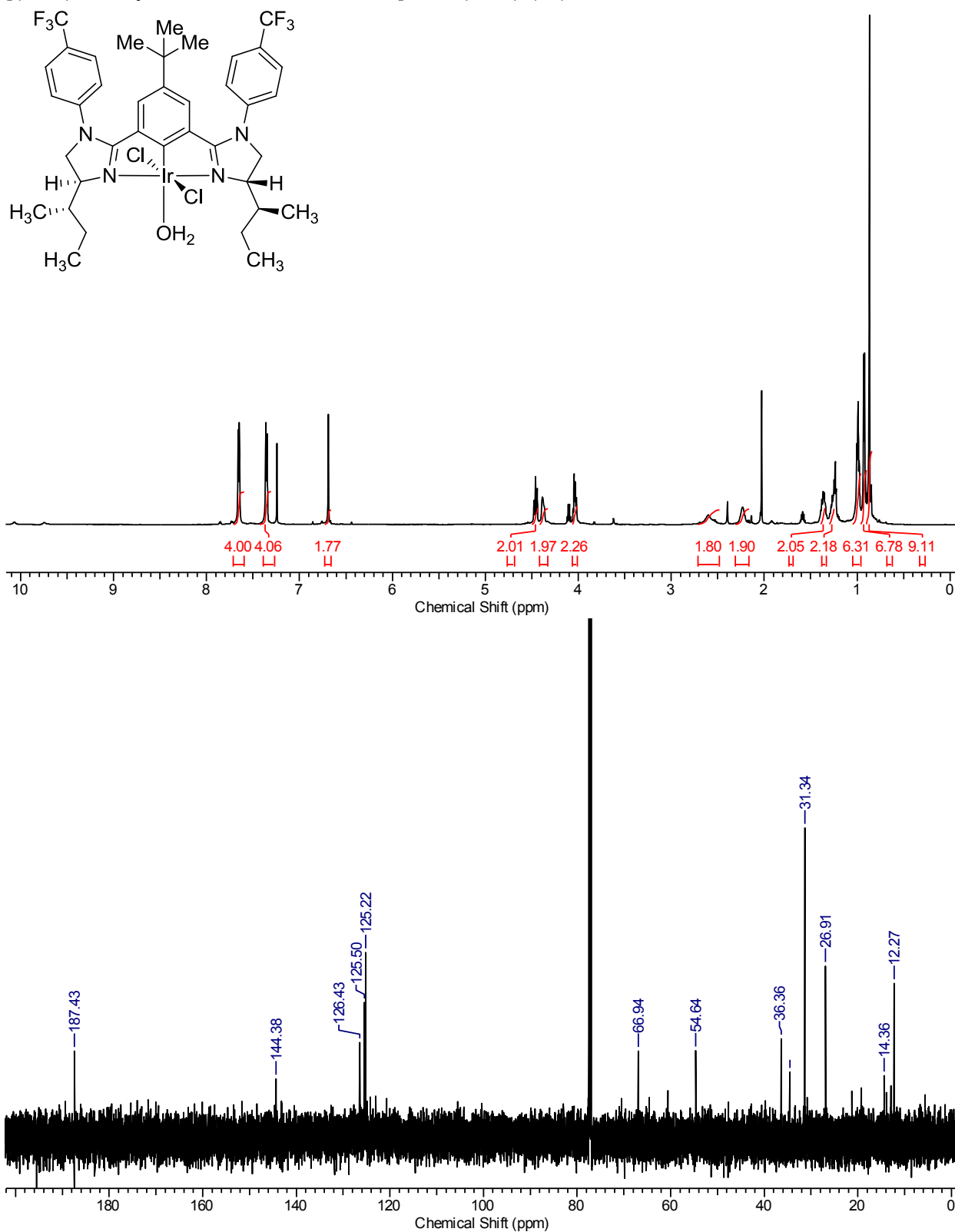
[(*R,R*)-*t*-ButylPhebim-4-CF₃-Ph-*i*-Bu]IrCl₂(H₂O) (10).



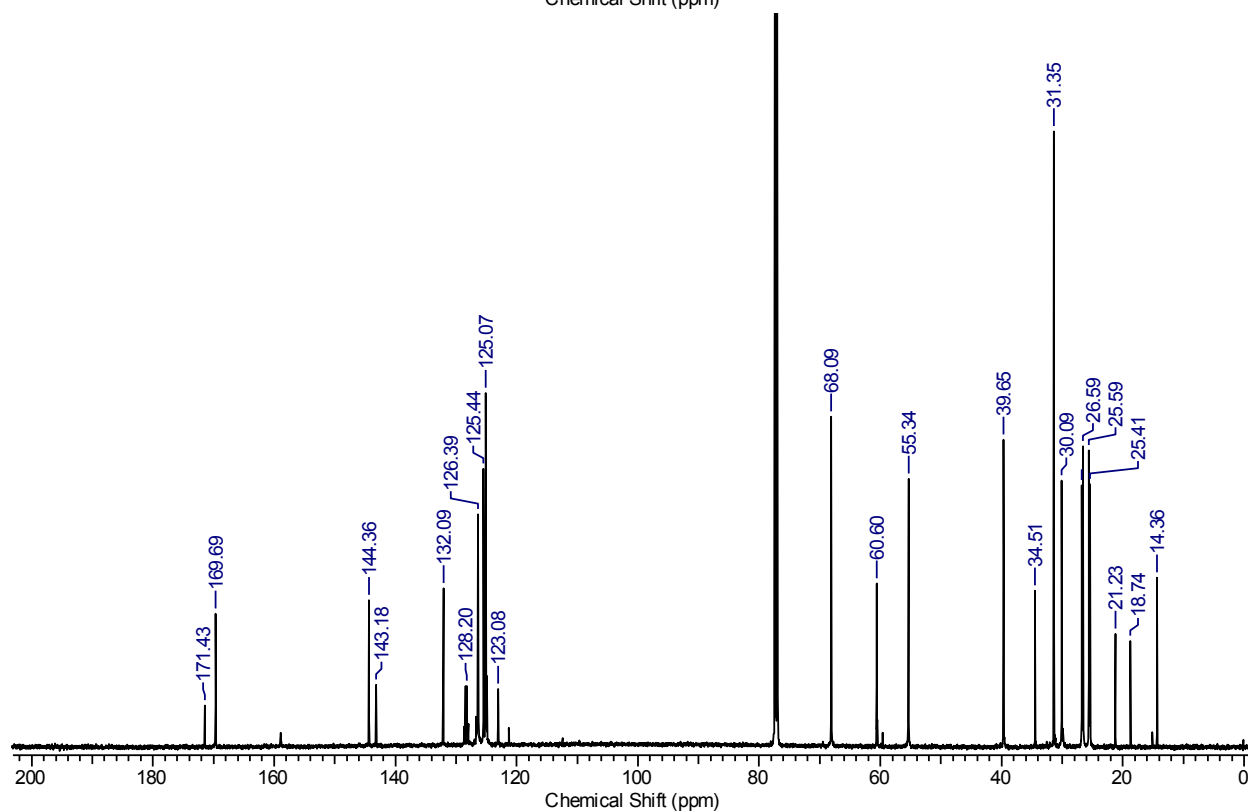
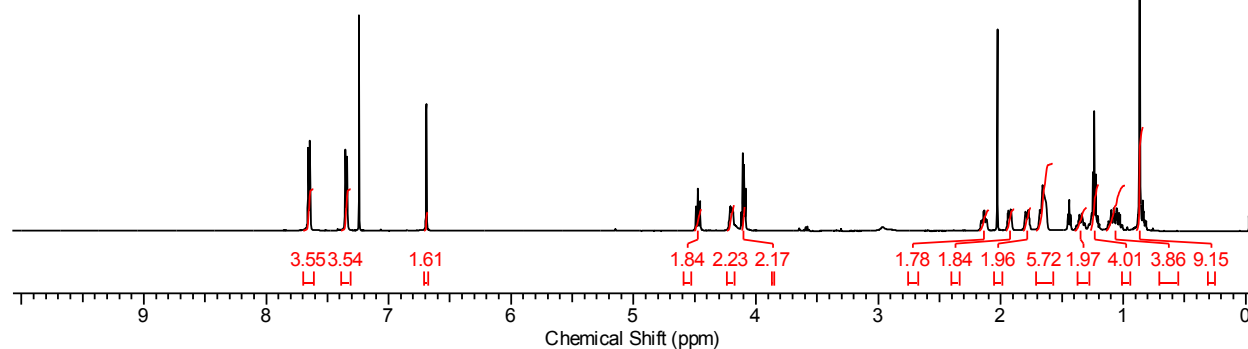
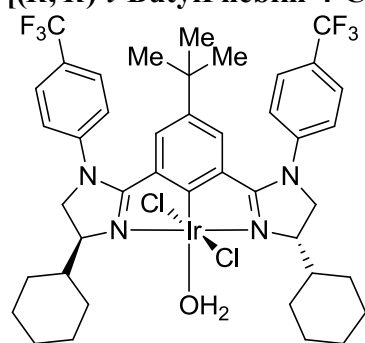
[(*R,R*)-*t*-ButylPhebim-4-CF₃Ph-*n*-Bu]IrCl₂(H₂O) (11).



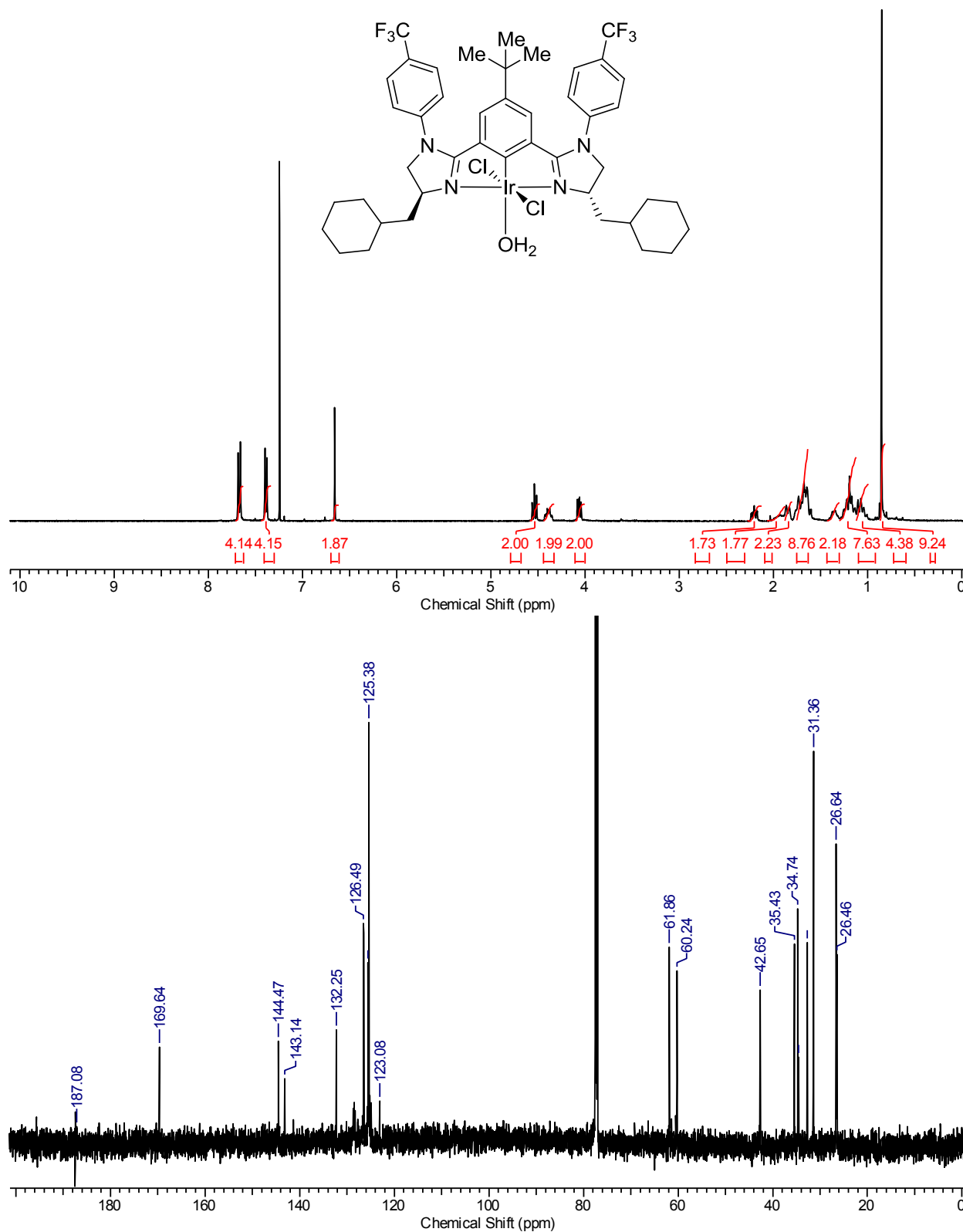
[(*R,R*)-*t*-ButylPhebim-4-CF₃-Ph-*s*-Bu]IrCl₂(H₂O) (12).



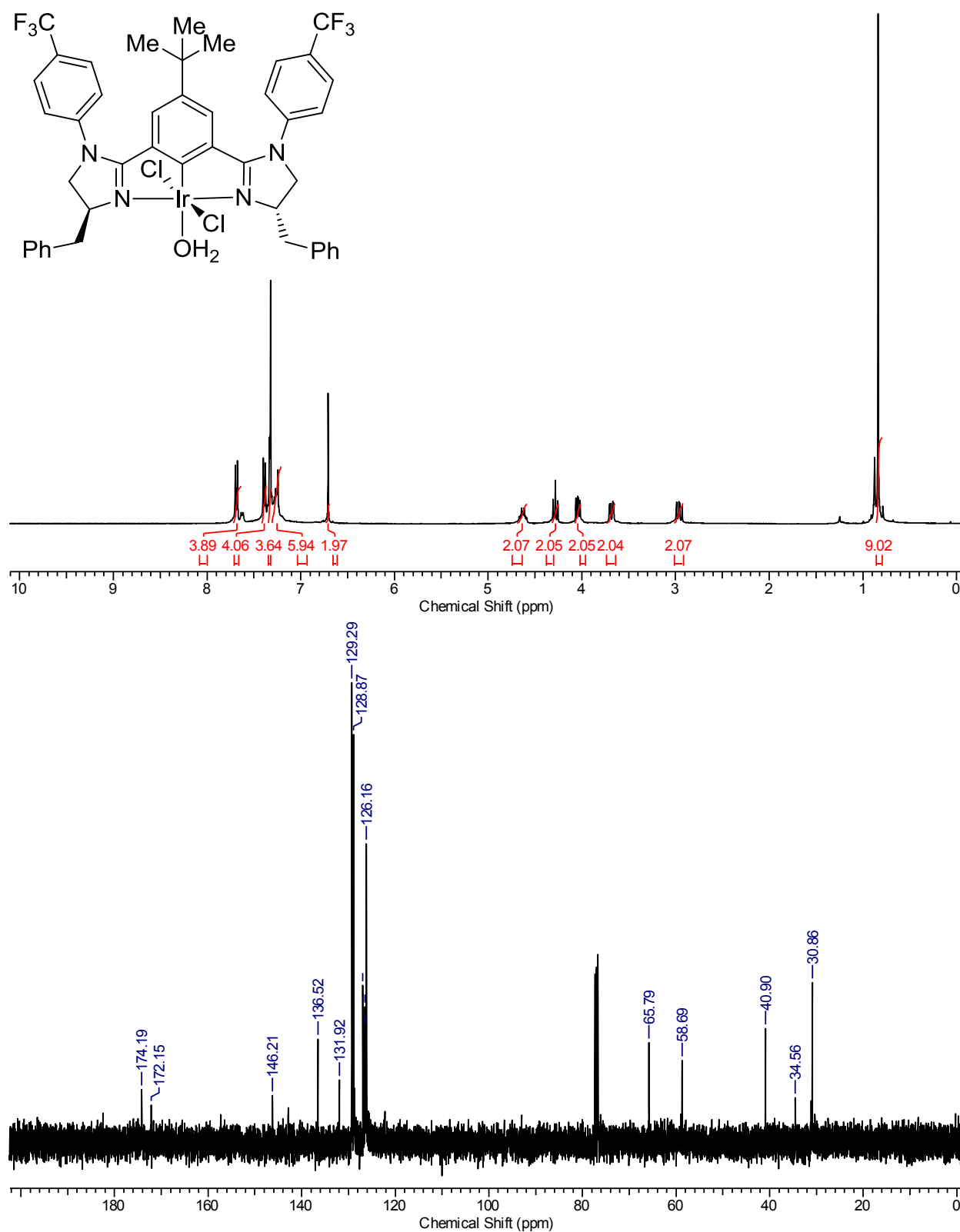
[(*R,R*)-*t*-ButylPhebim-4-CF₃Ph-^cHex]IrCl₂(H₂O) (13).



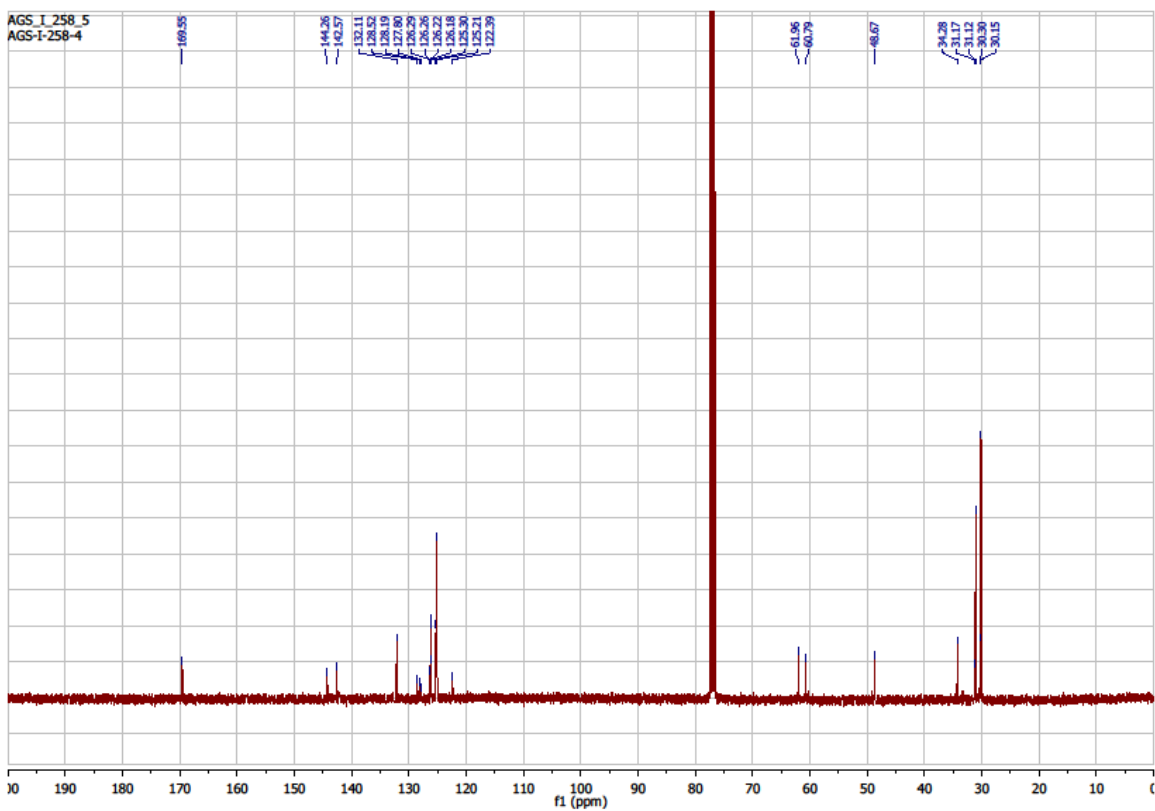
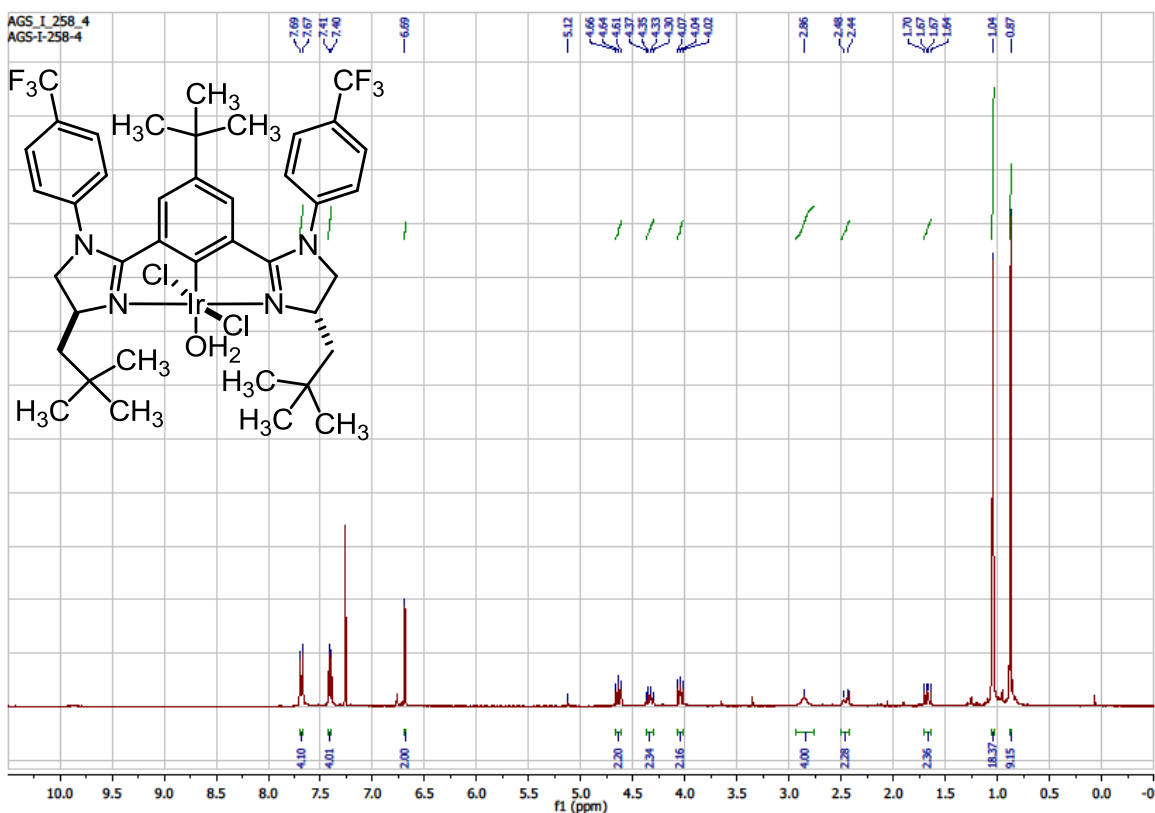
[(*R,R*)-*t*-ButylPhebim-4-CF₃Ph-CH₂^cHex]IrCl₂(H₂O) (14).



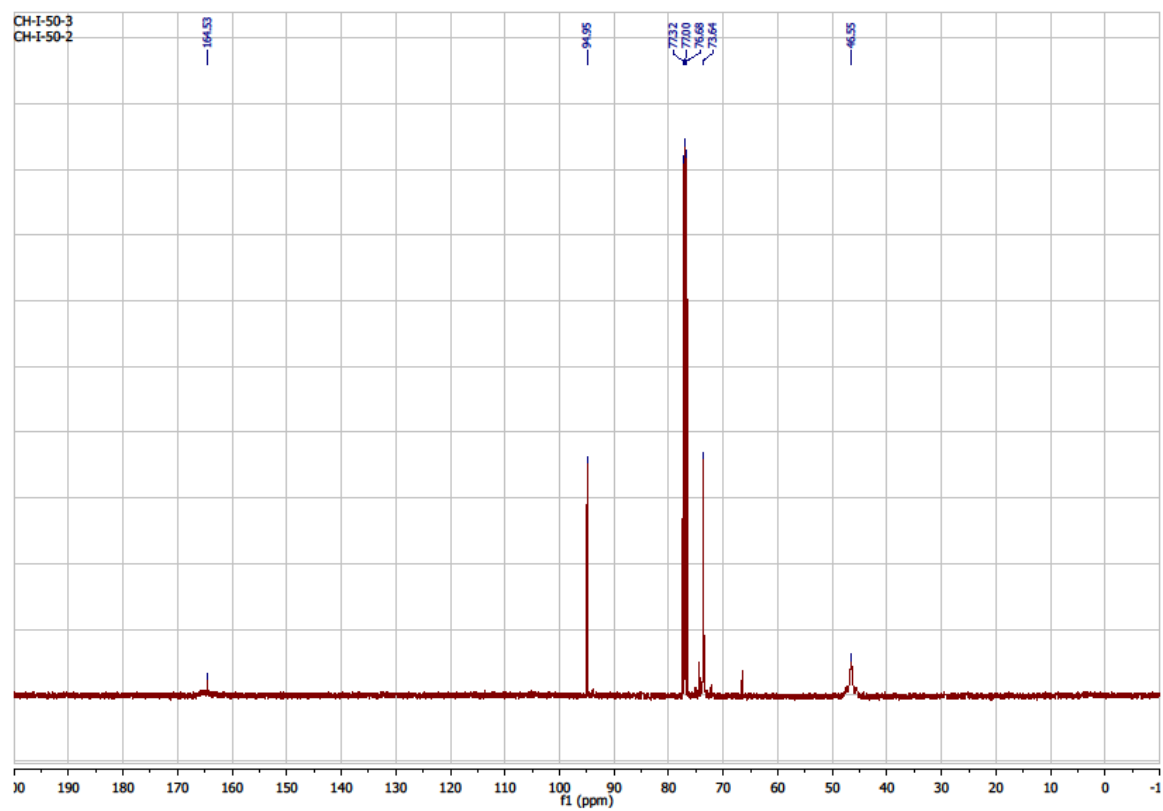
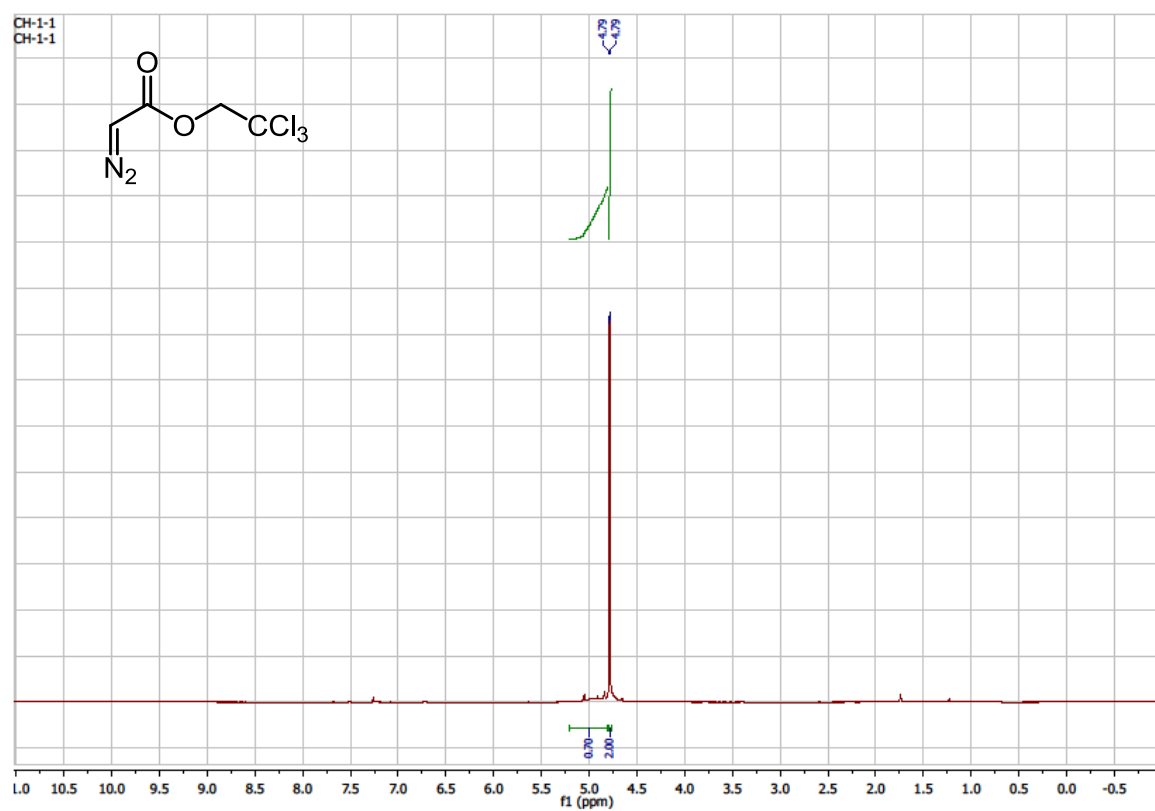
[(*S,S*)-*t*-ButylPhebim-*p*-CF₃Ph-Bn]IrCl₂(H₂O) (15).



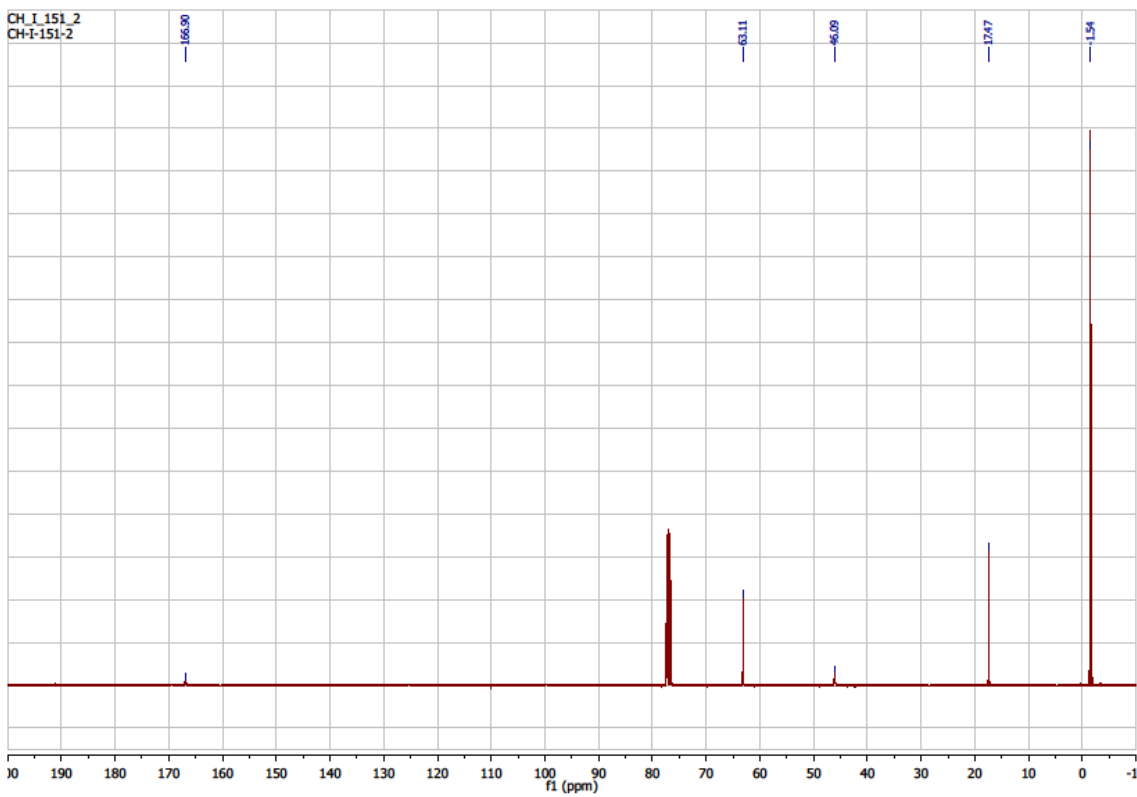
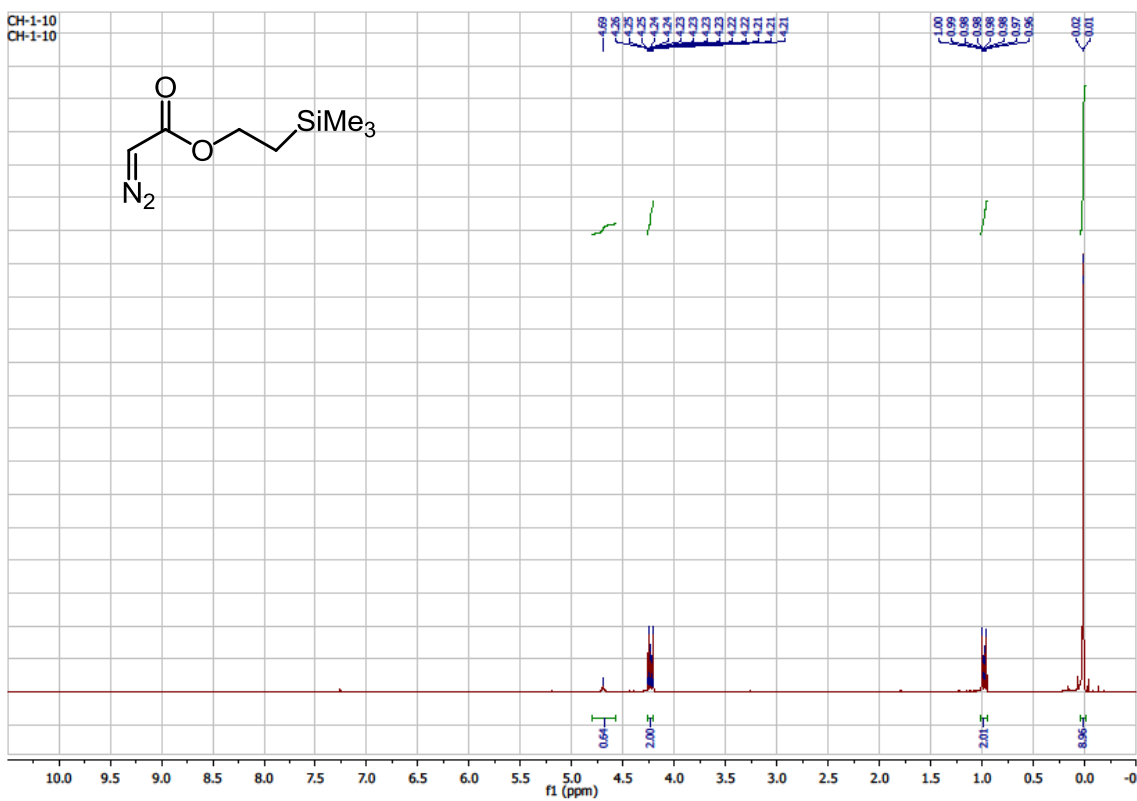
[(*S,S*)-*t*-ButylPhebim-*p*-CF₃Ph-CH₂^{*t*}Bu]IrCl₂(H₂O) (16).



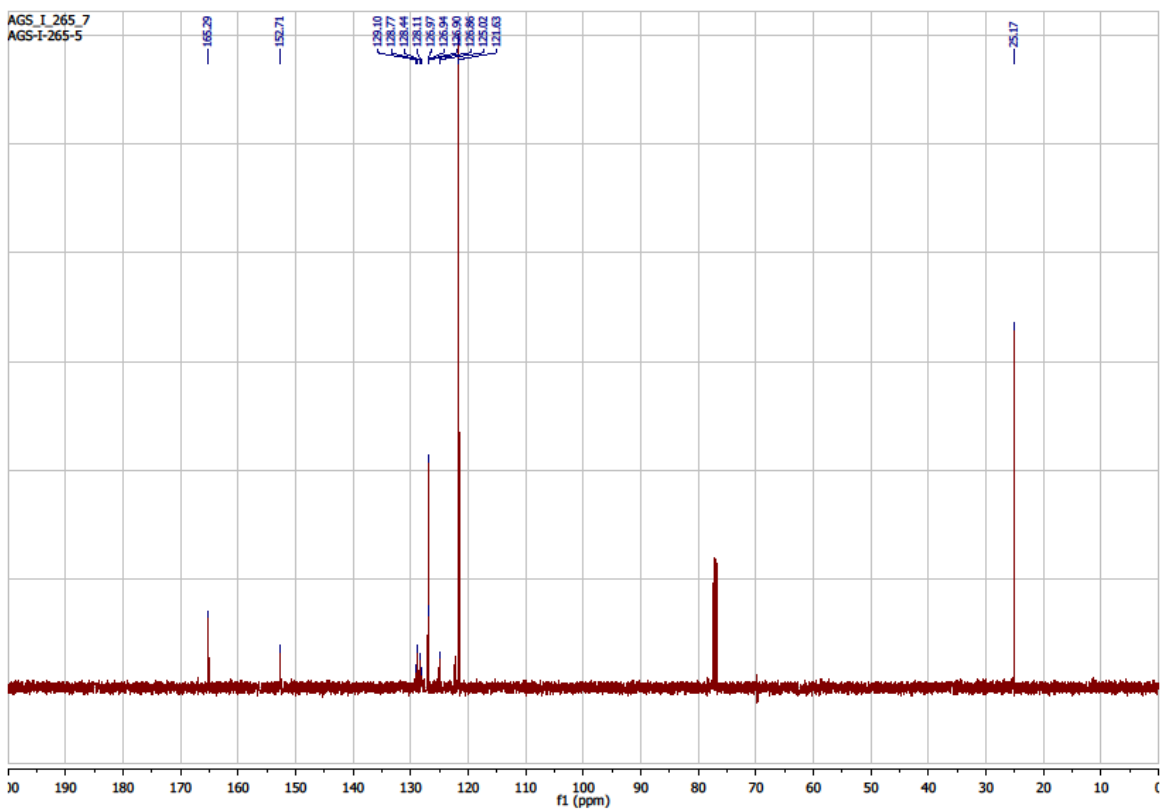
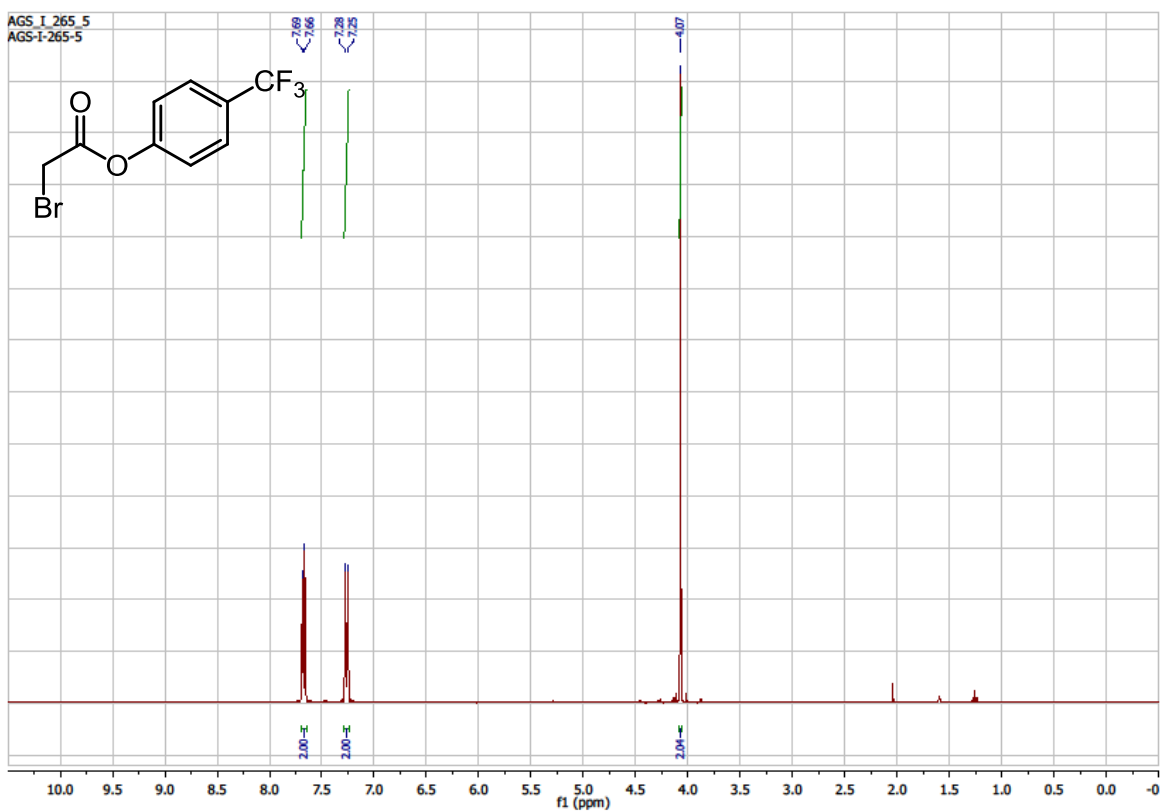
2,2,2-trichloroethyl 2-diazoacetate (S25).



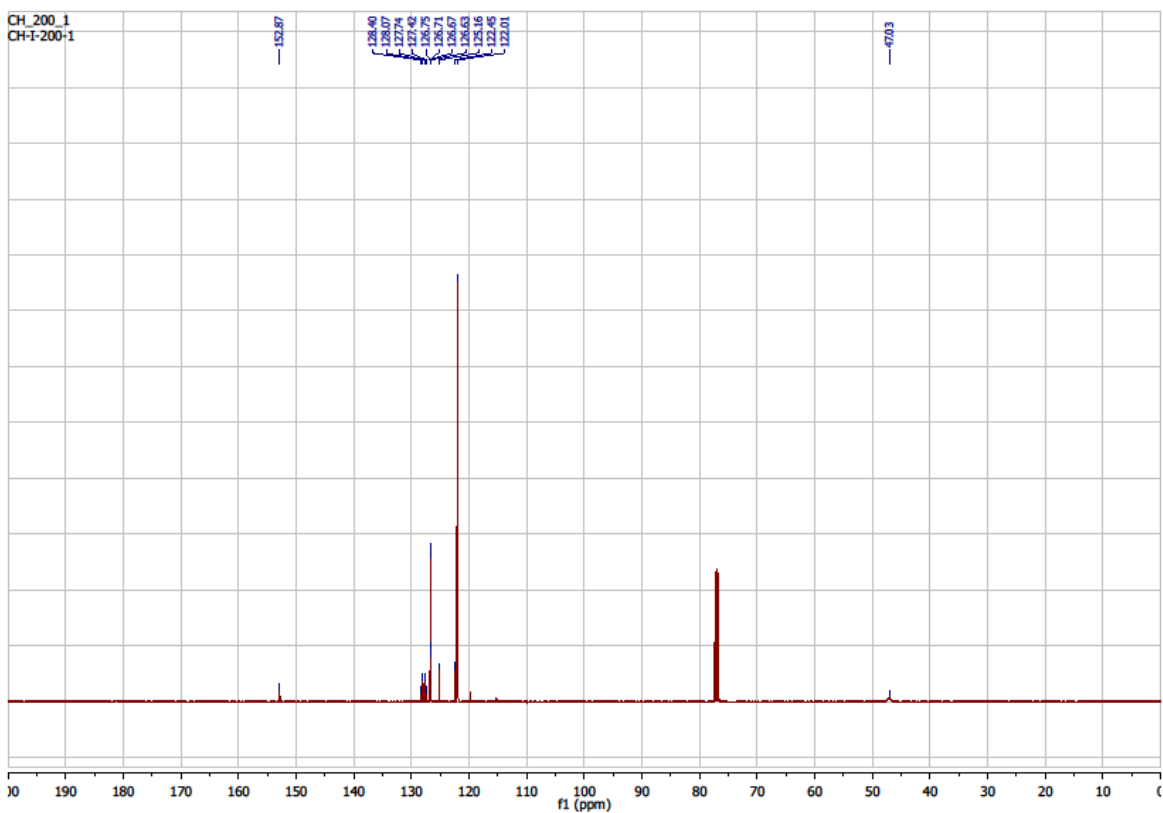
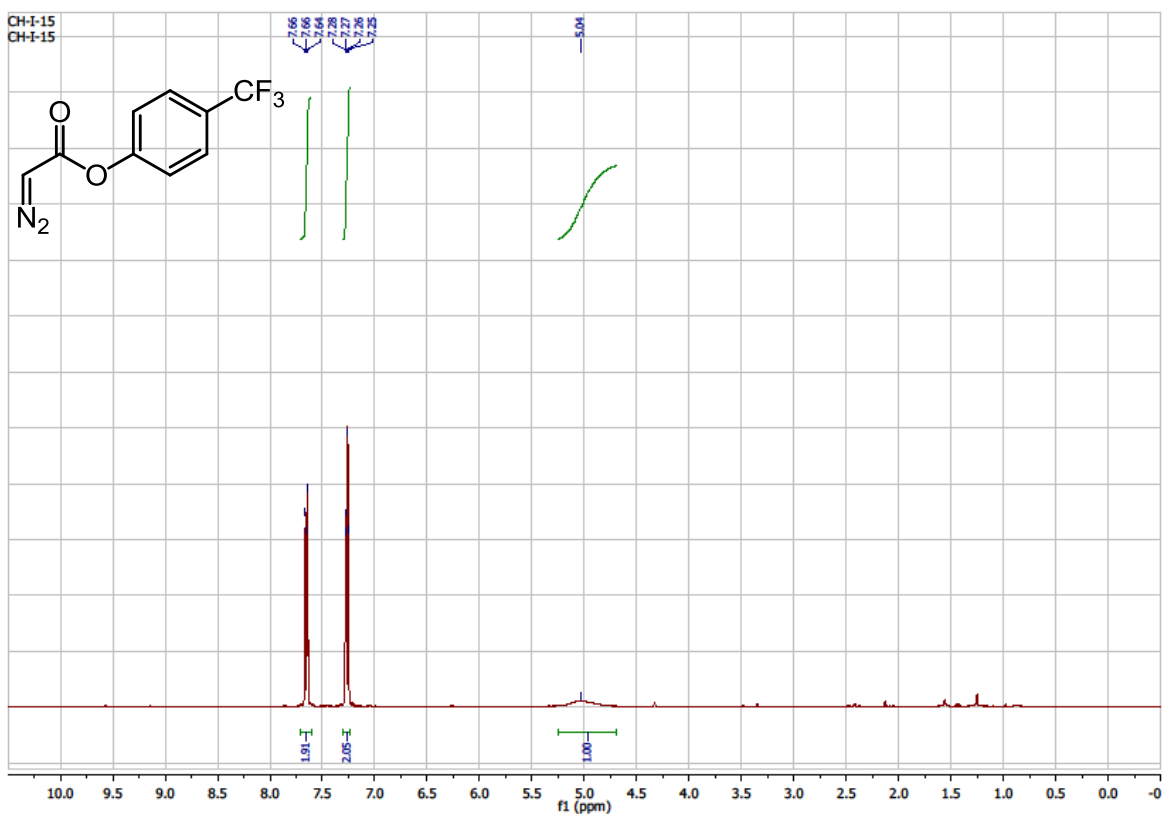
2-(trimethylsilyl)ethyl 2-diazoacetate (S27).



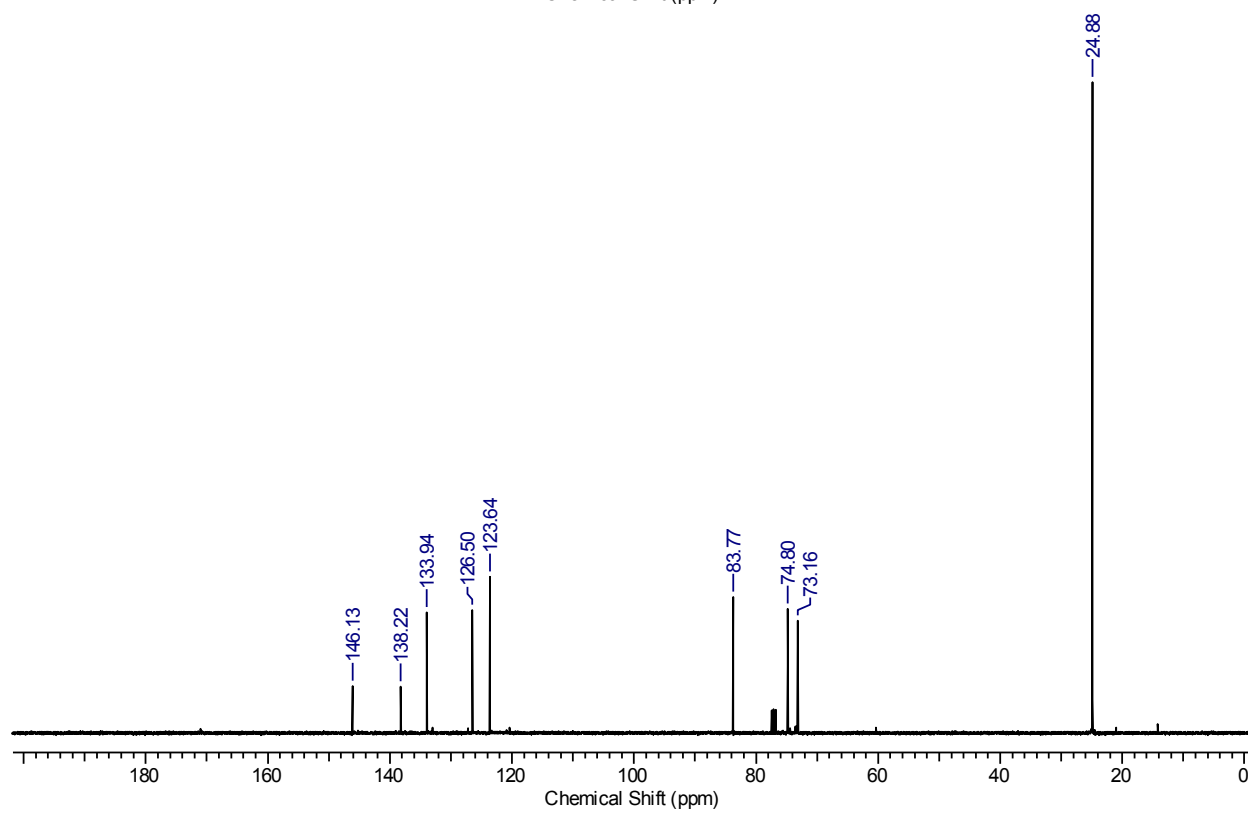
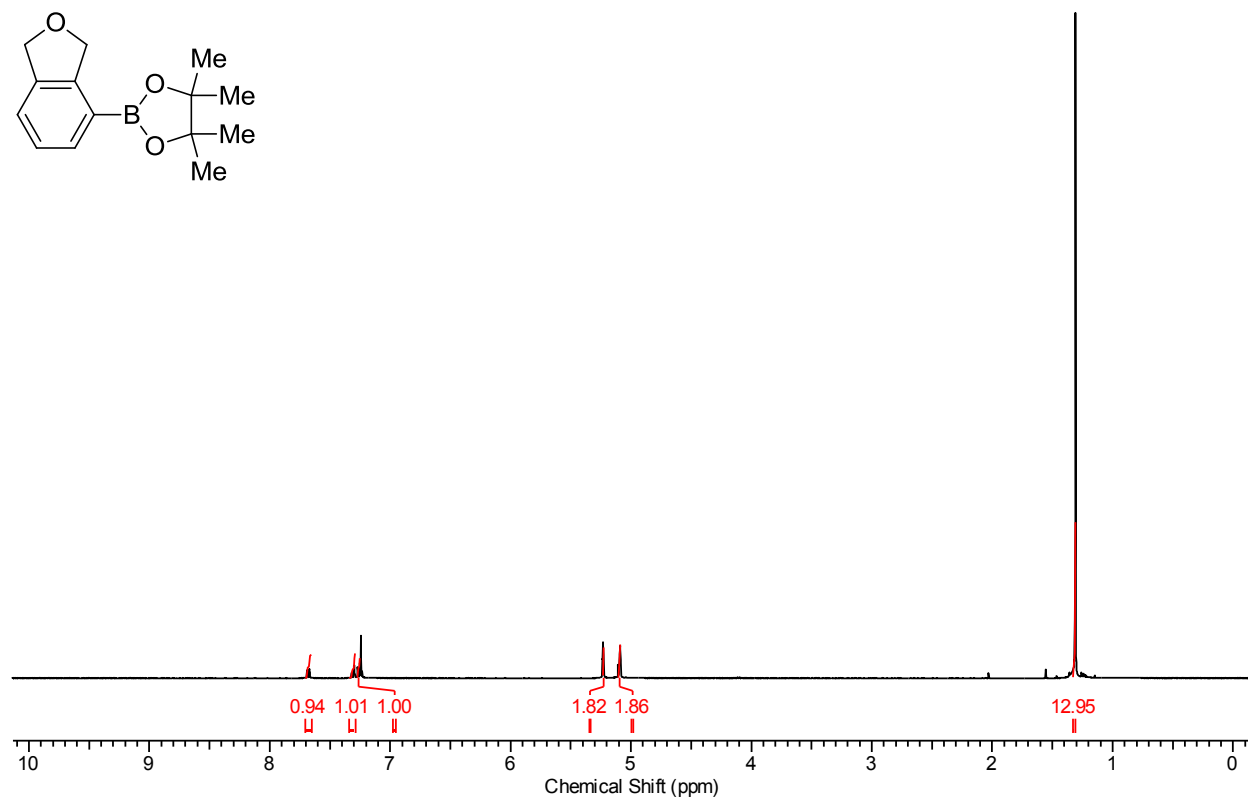
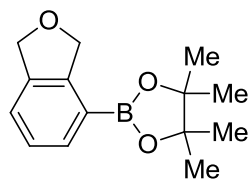
4-(trifluoromethyl)phenyl 2-bromoacetate (S28).



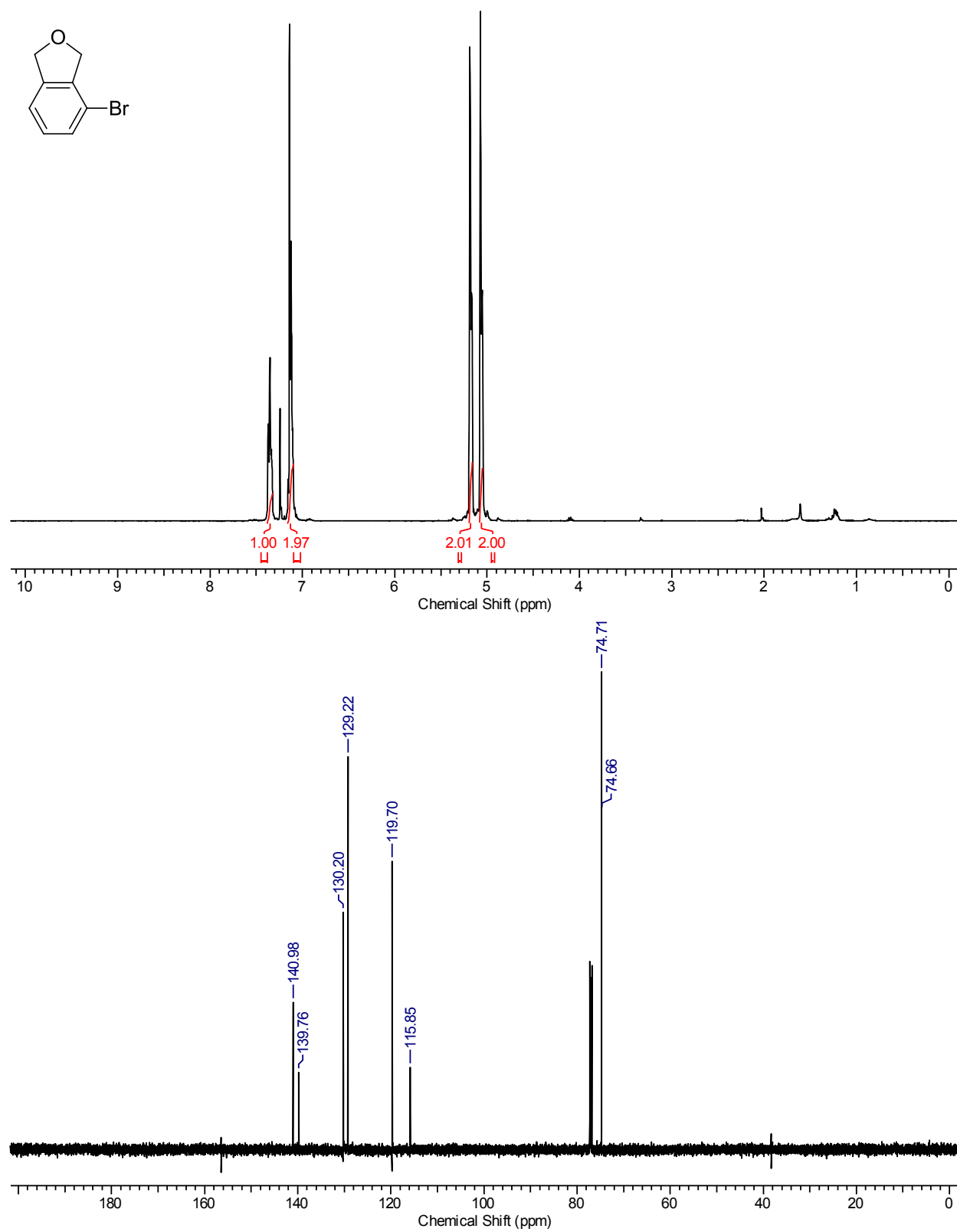
4-(trifluoromethyl)phenyl 2-diazoacetate (S29).



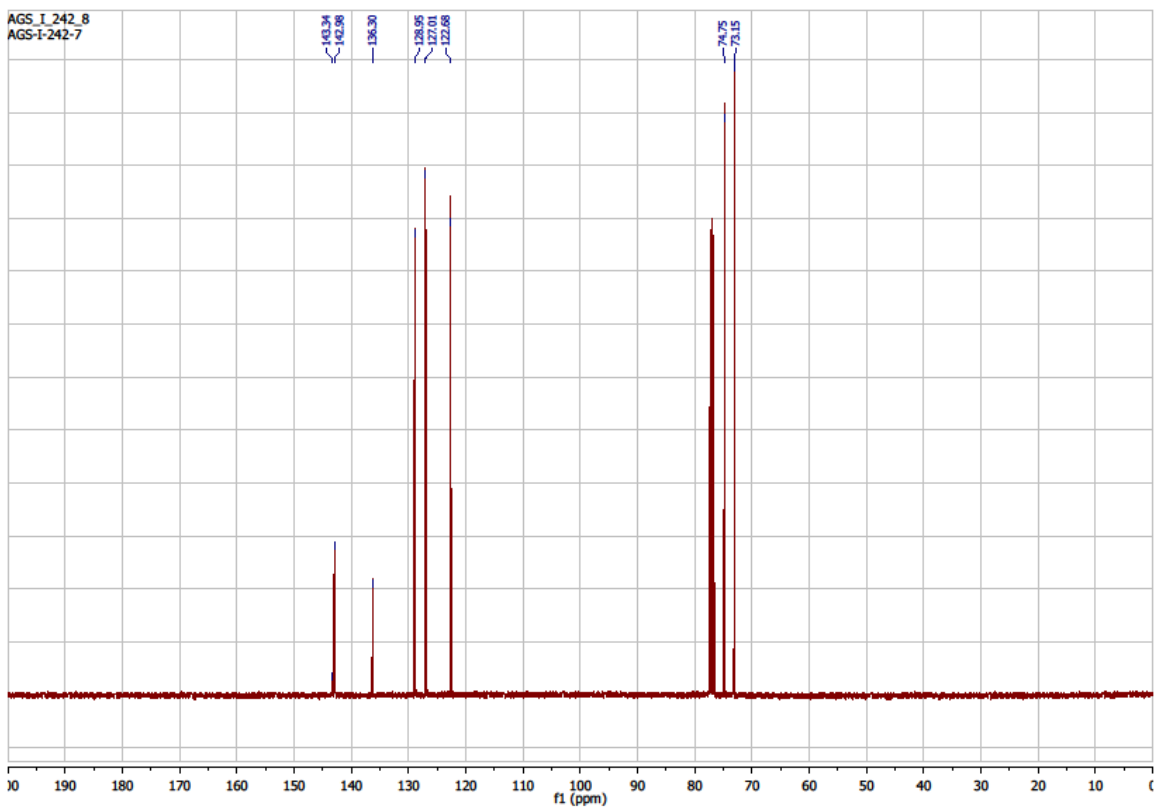
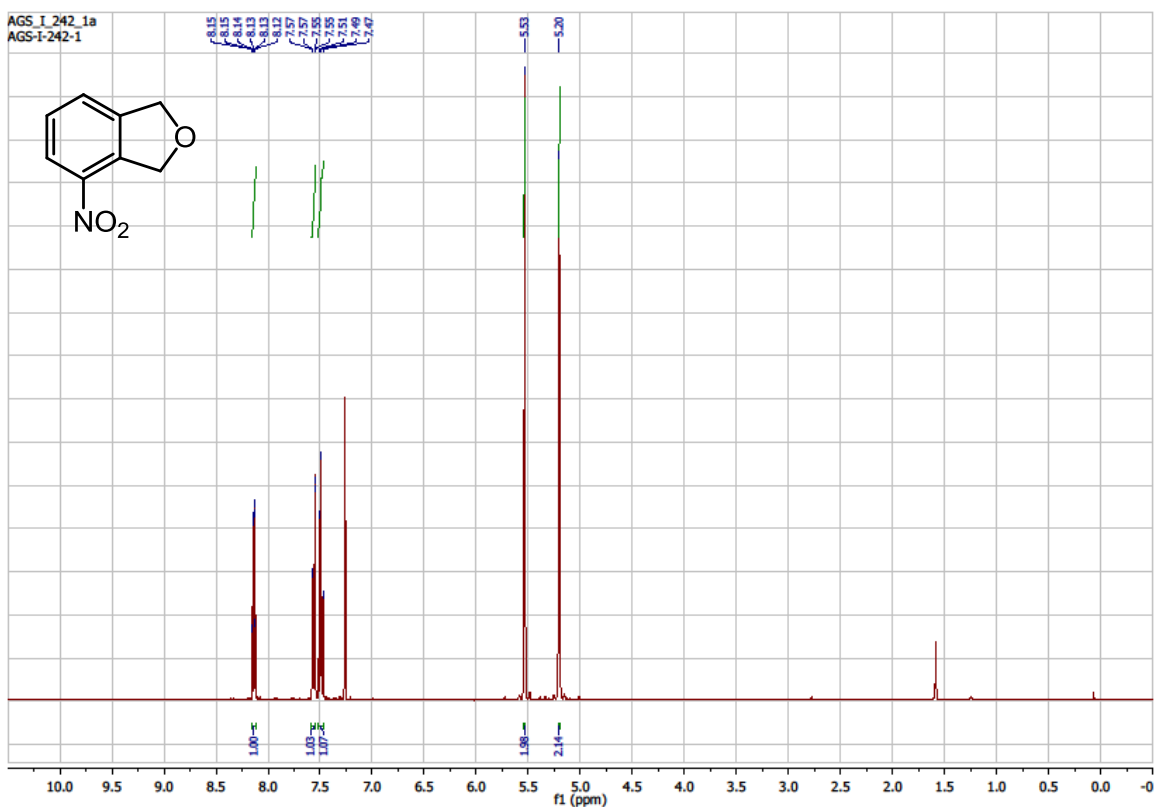
2-(1,3-dihydroisobenzofuran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S30).



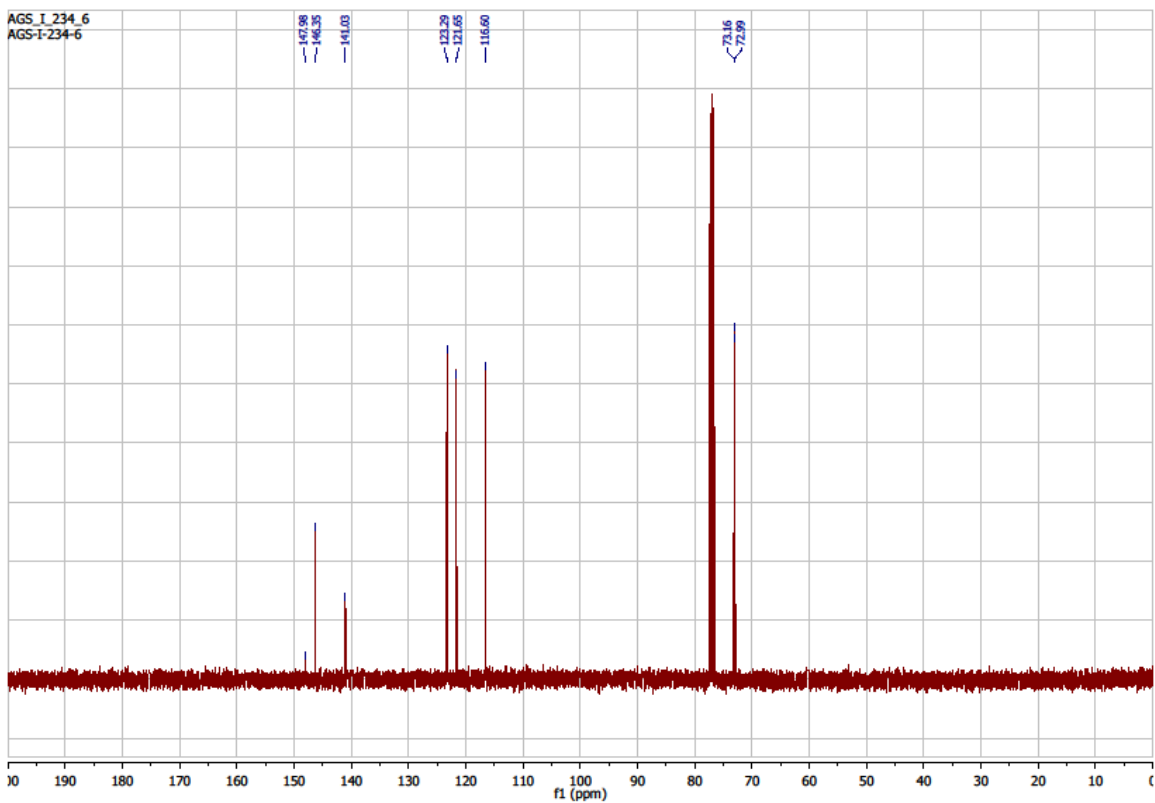
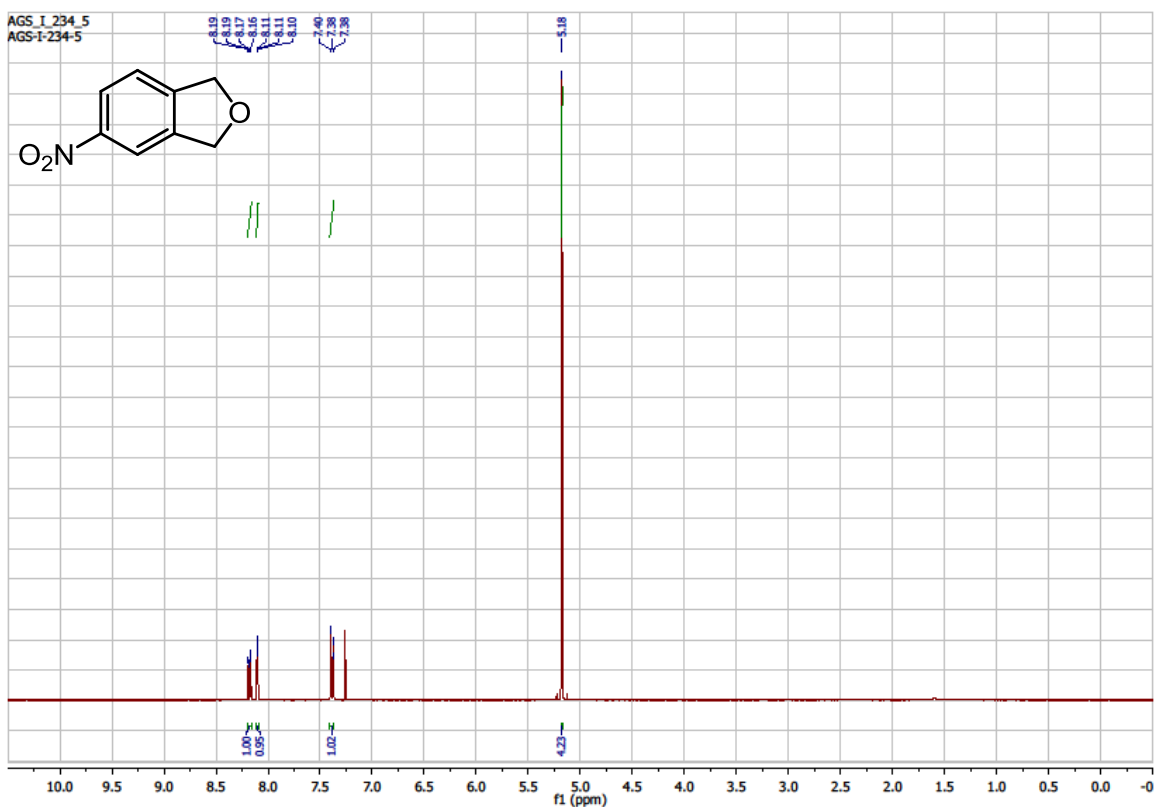
4-bromo-1,3-dihydroisobenzofuran (S33).



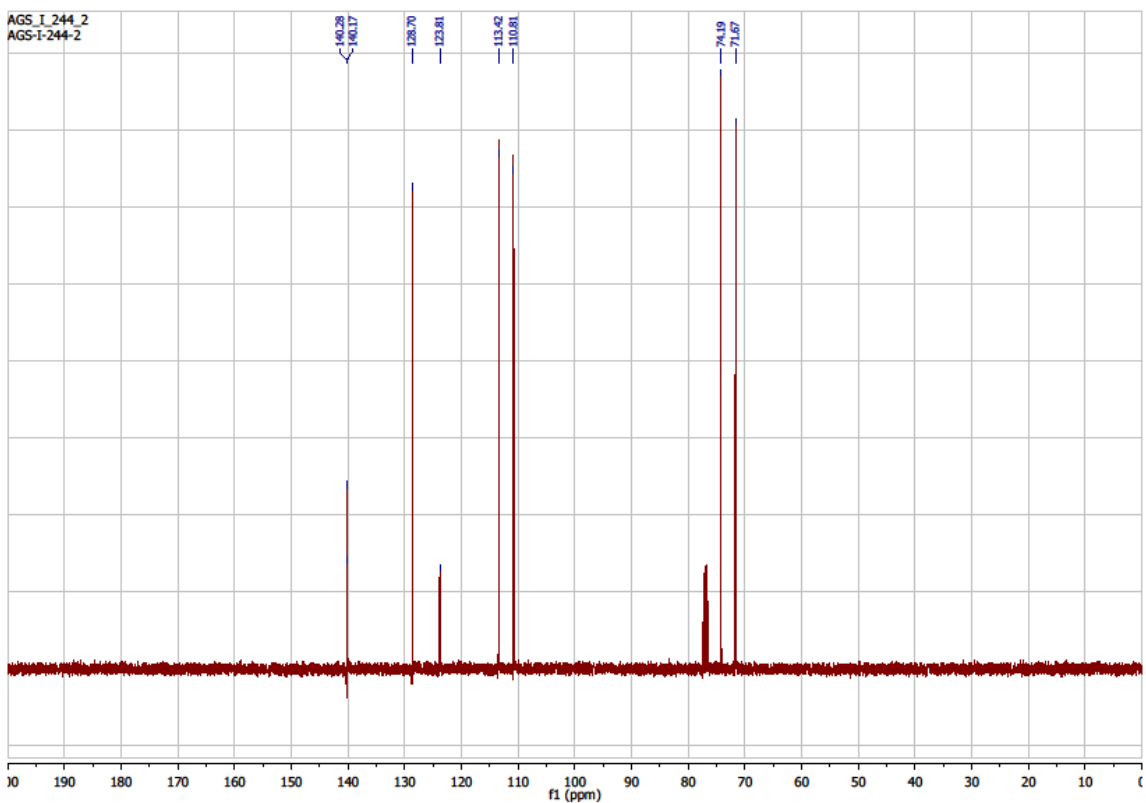
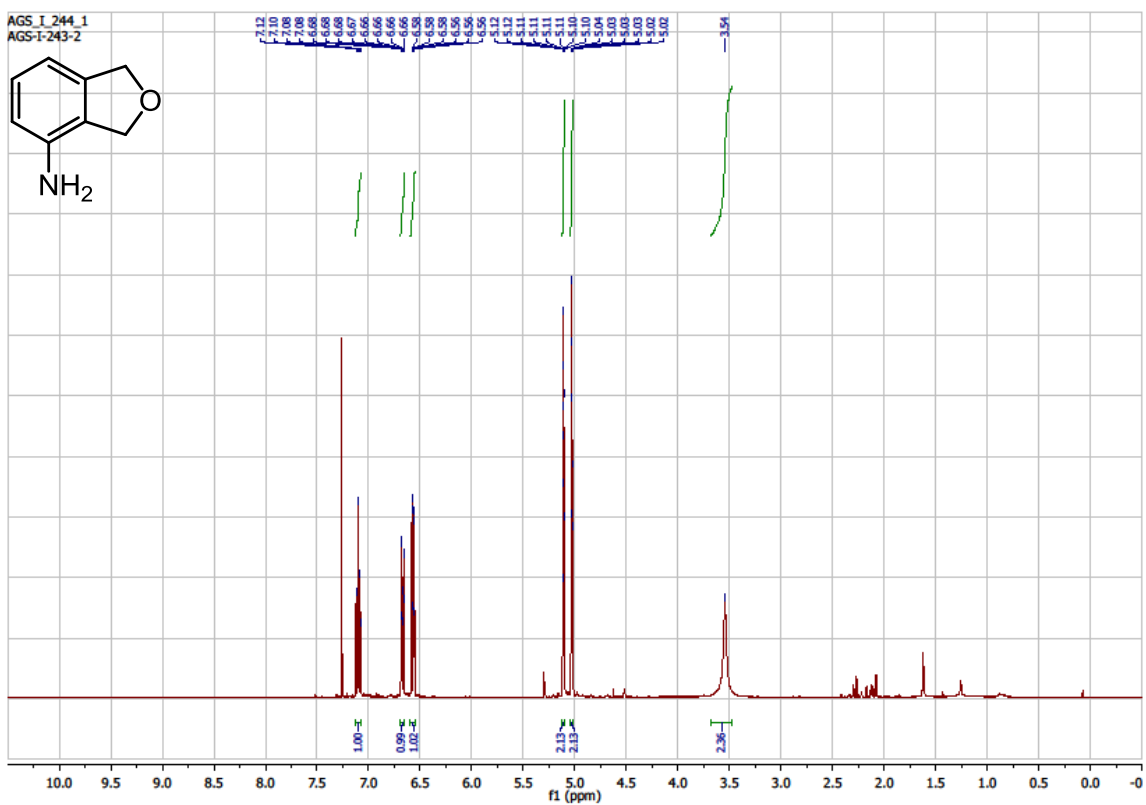
4-nitro-1,3-dihydroisobenzofuran (S35).



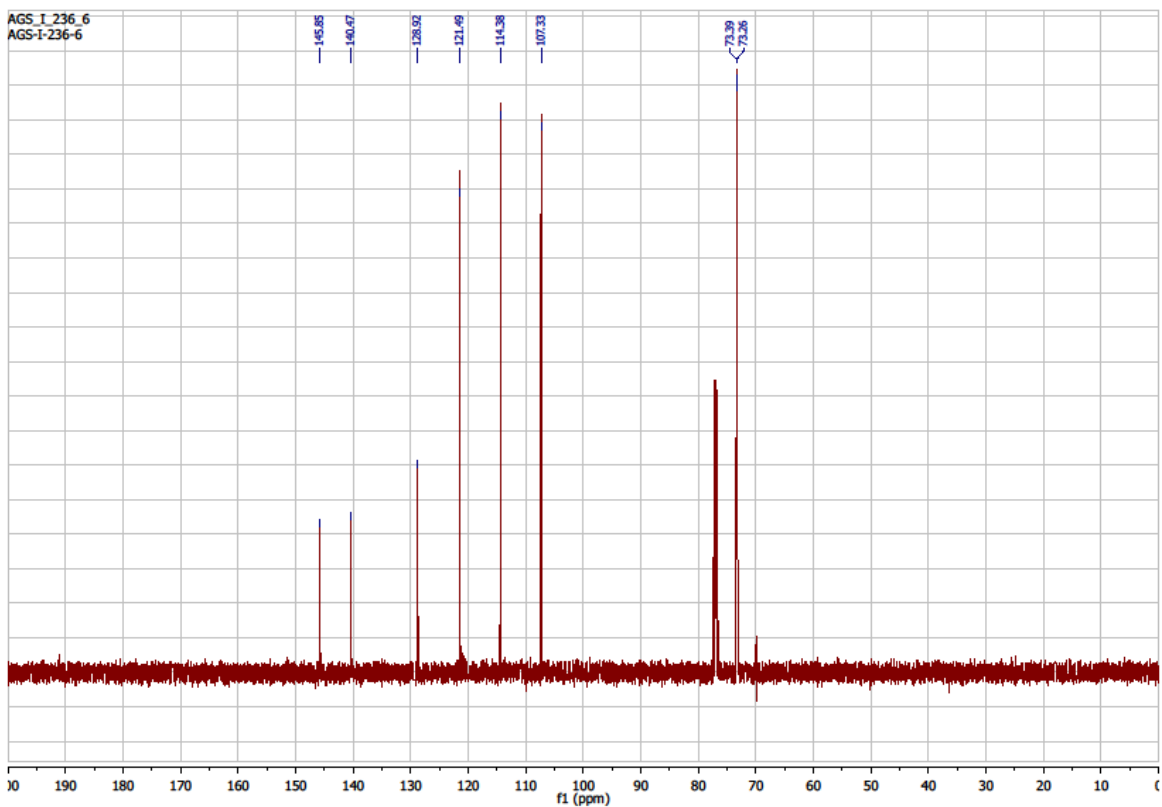
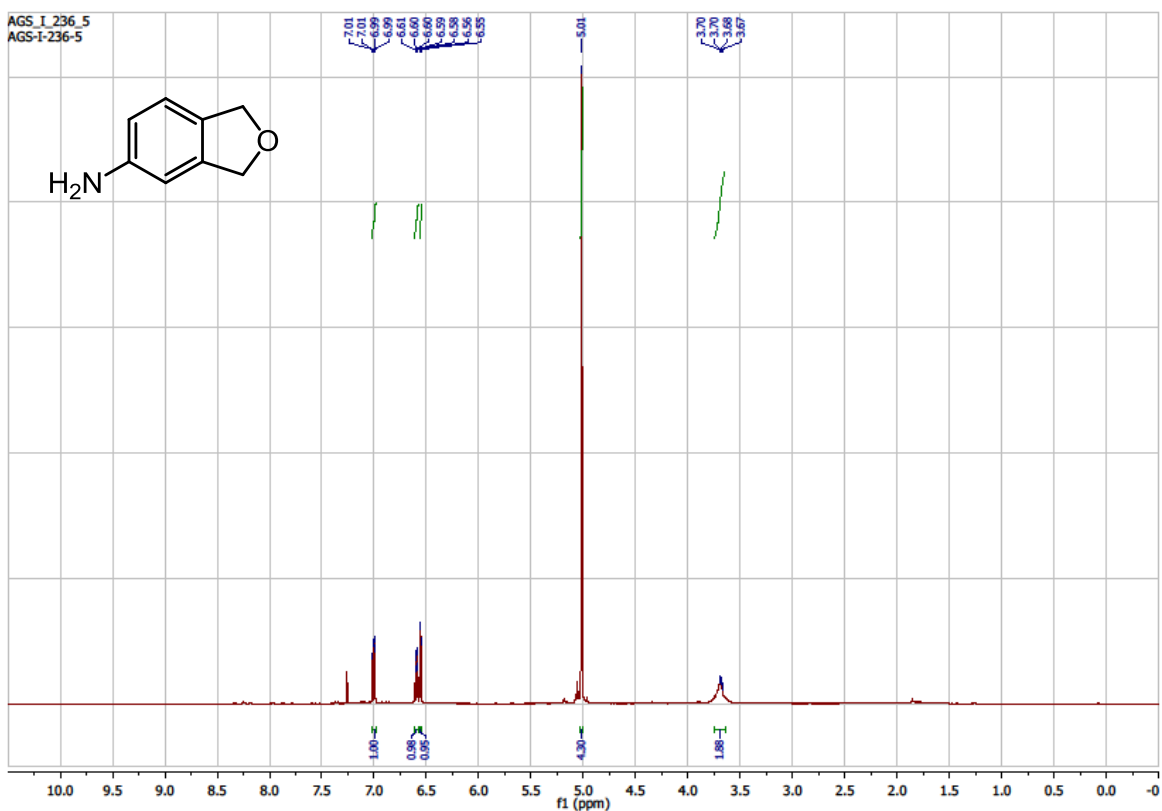
5-nitro-1,3-dihydroisobenzofuran (S36).



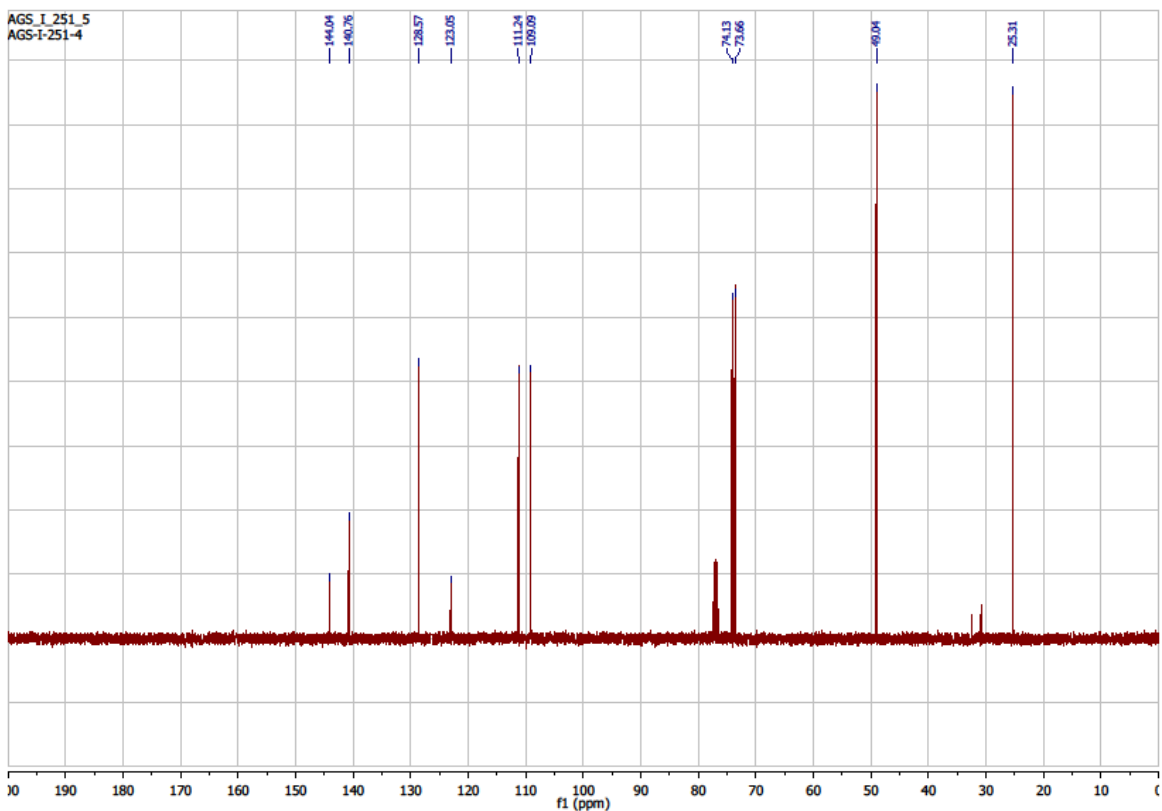
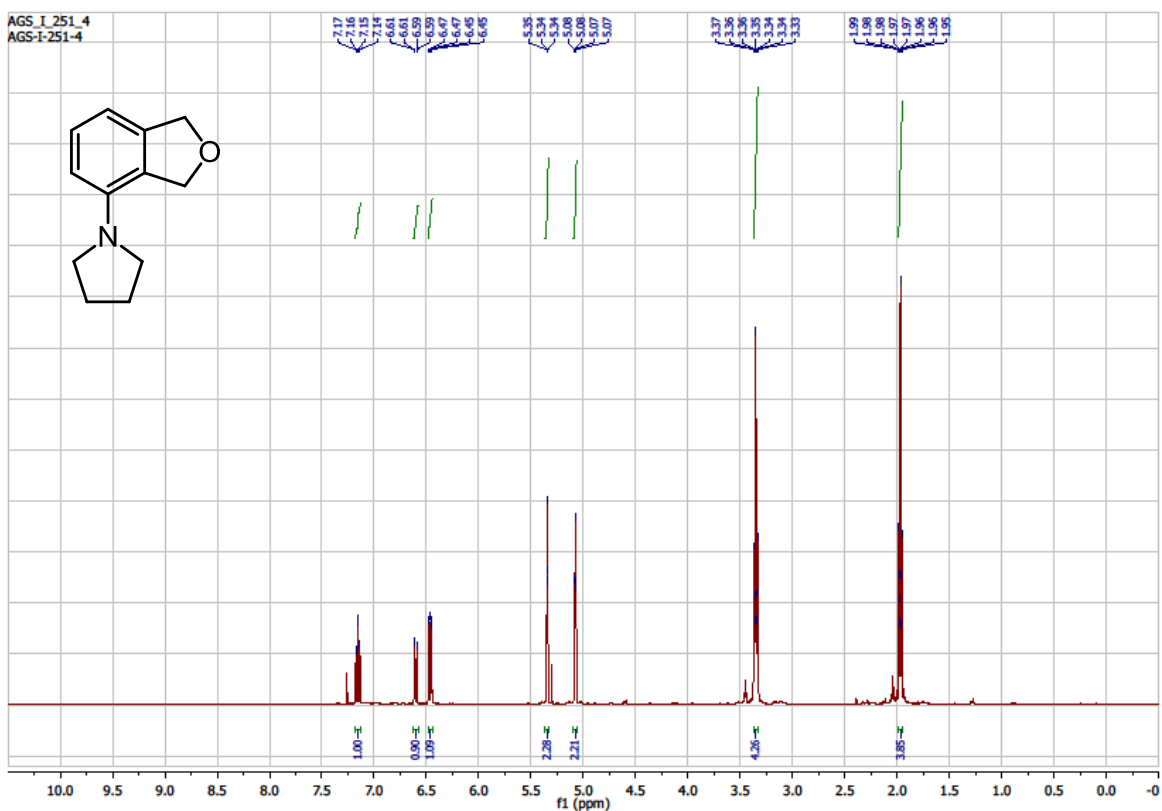
1,3-dihydroisobenzofuran-4-amine (S37).



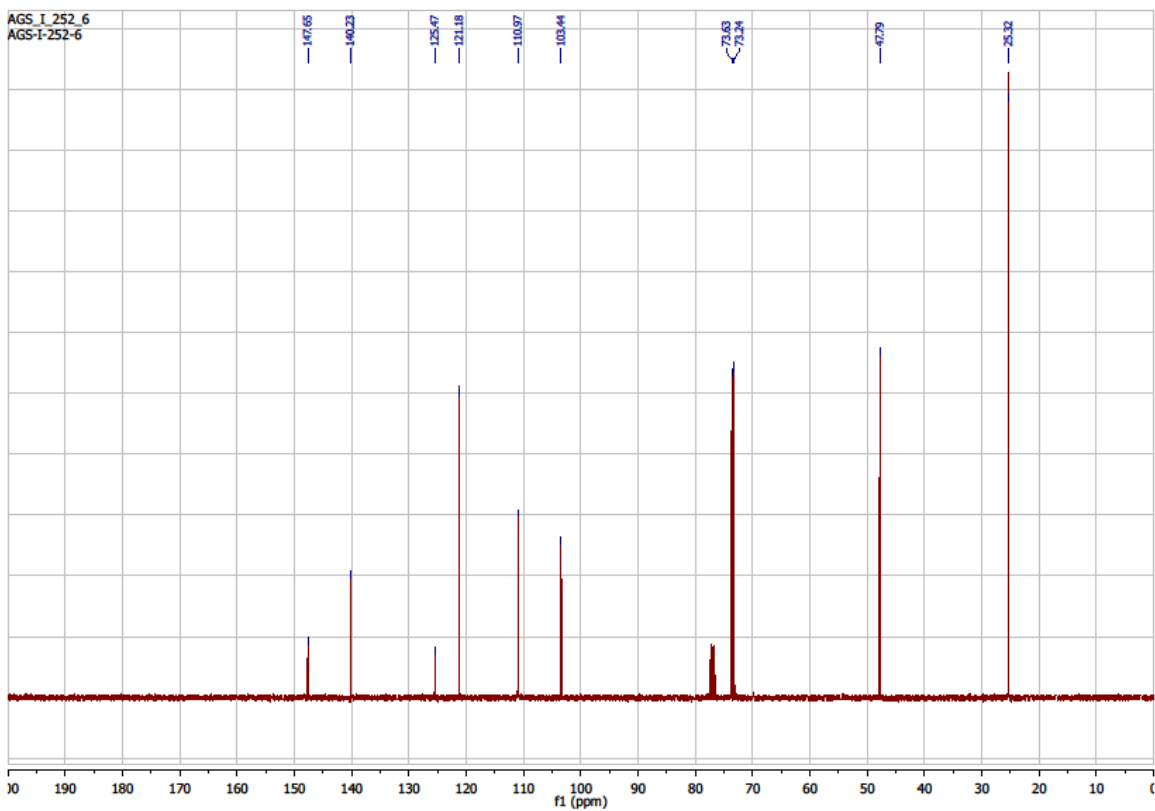
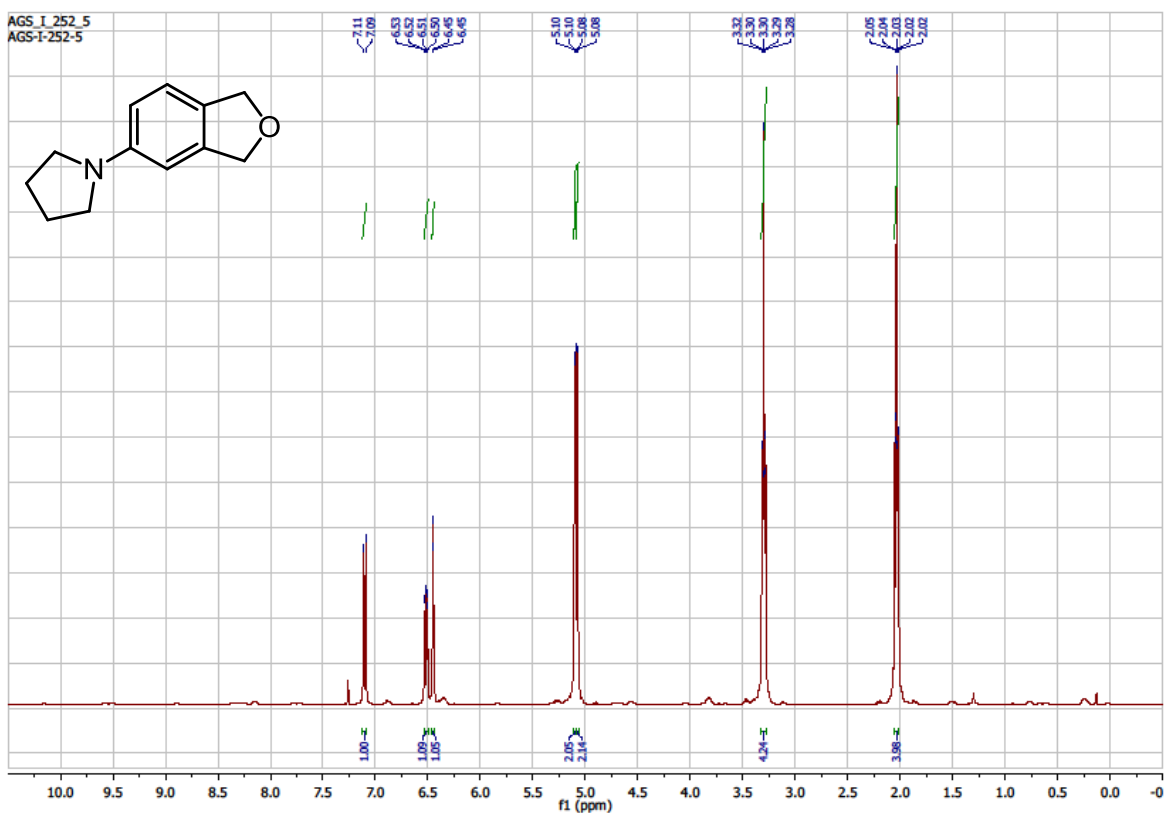
1,3-dihydroisobenzofuran-5-amine (S38).



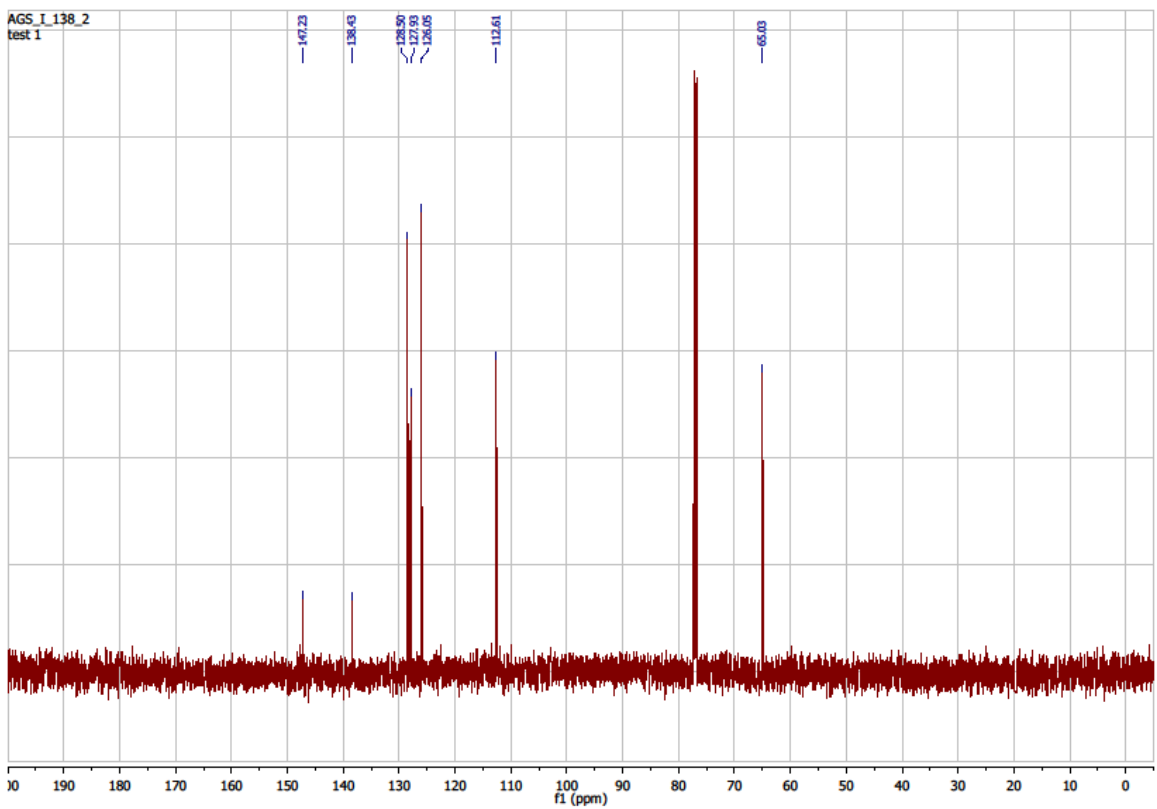
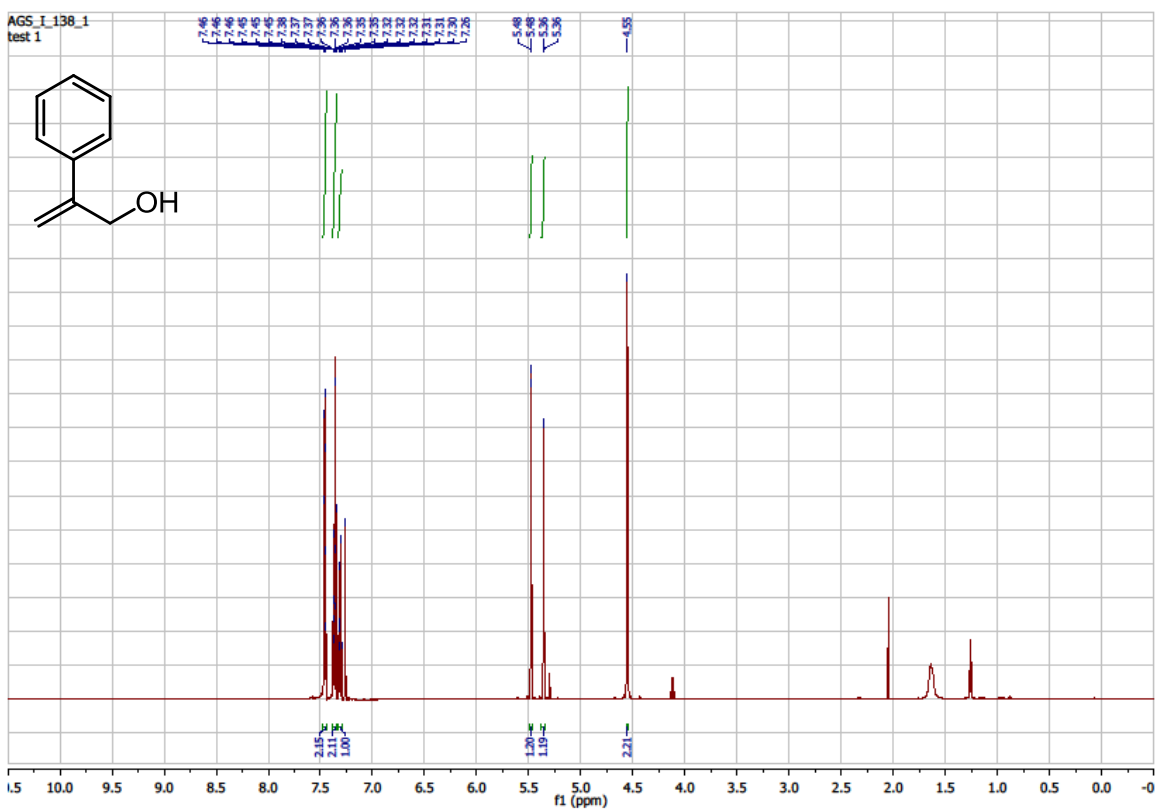
1-(1,3-dihydroisobenzofuran-4-yl)pyrrolidine (S39).



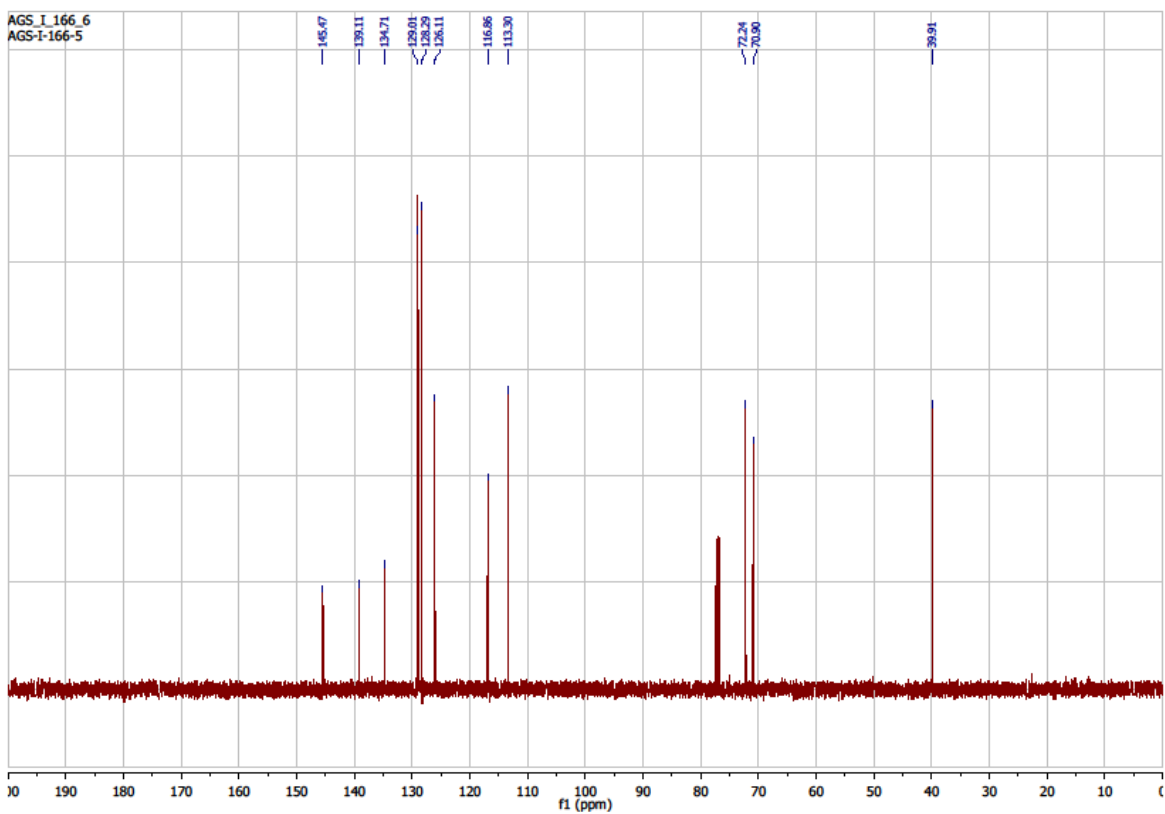
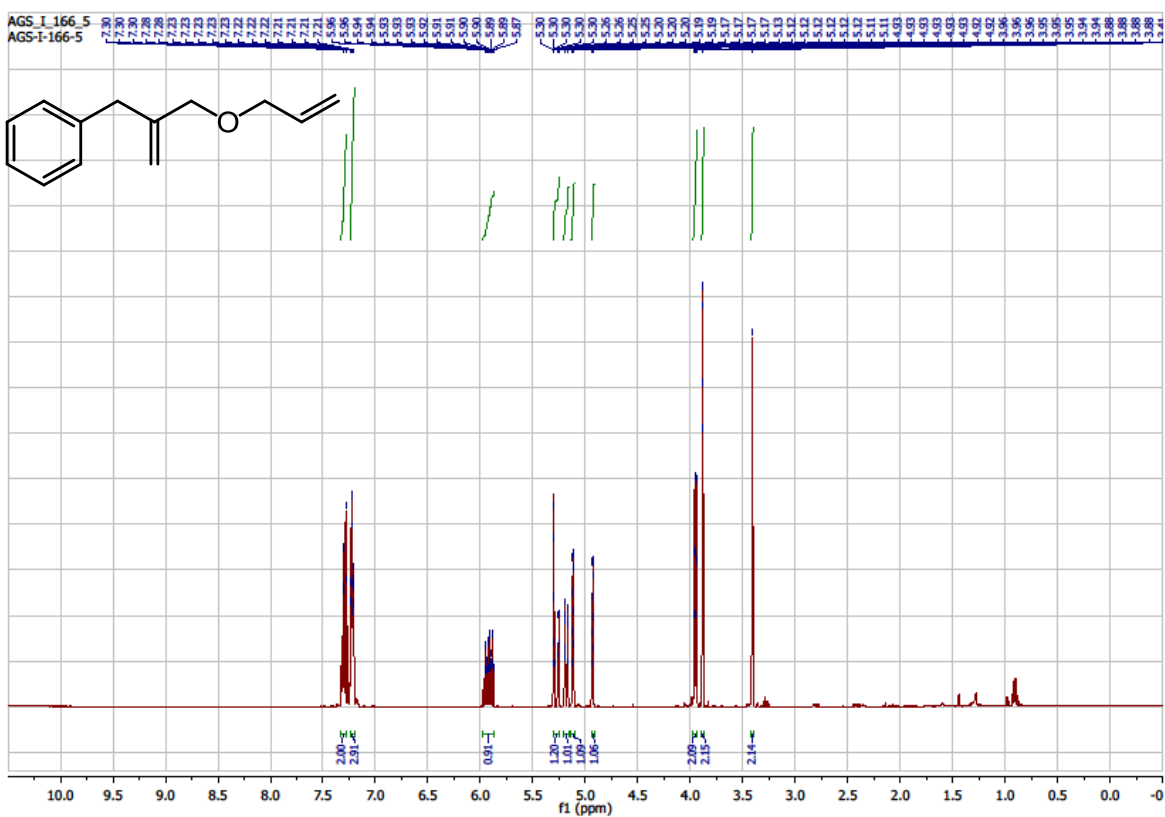
1-(1,3-dihydroisobenzofuran-5-yl)pyrrolidine (S40).



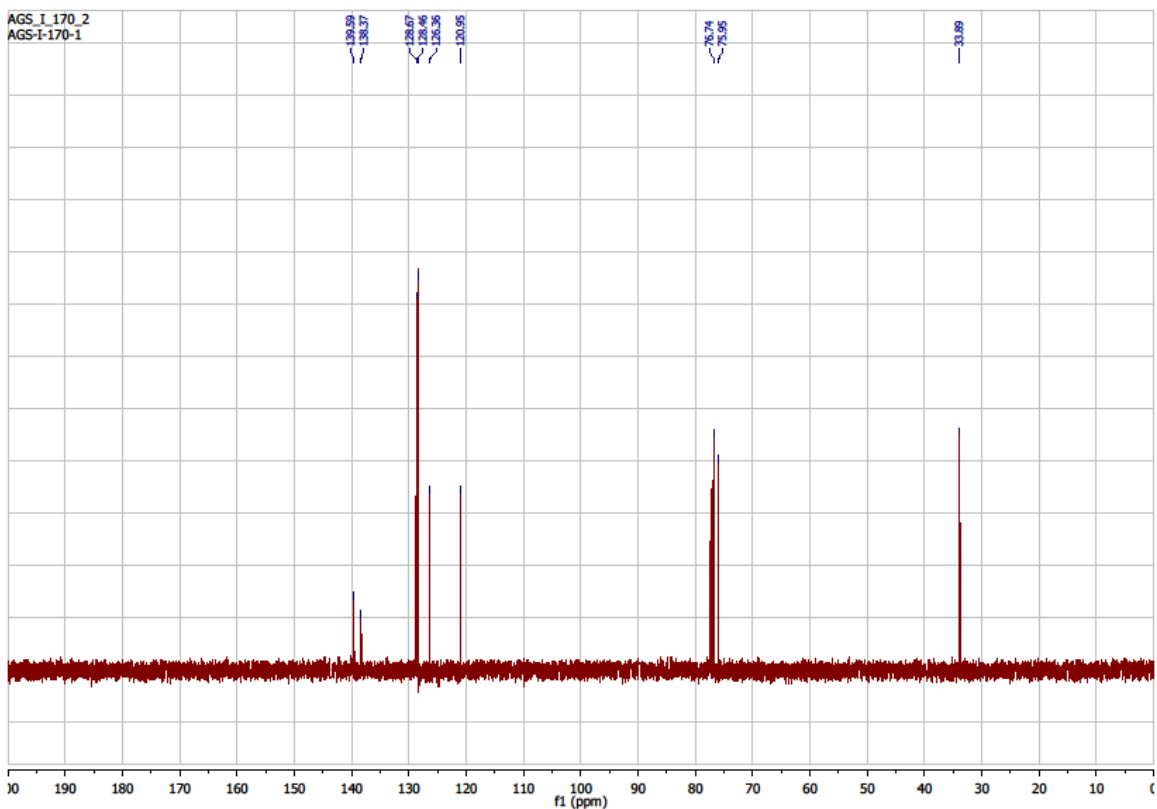
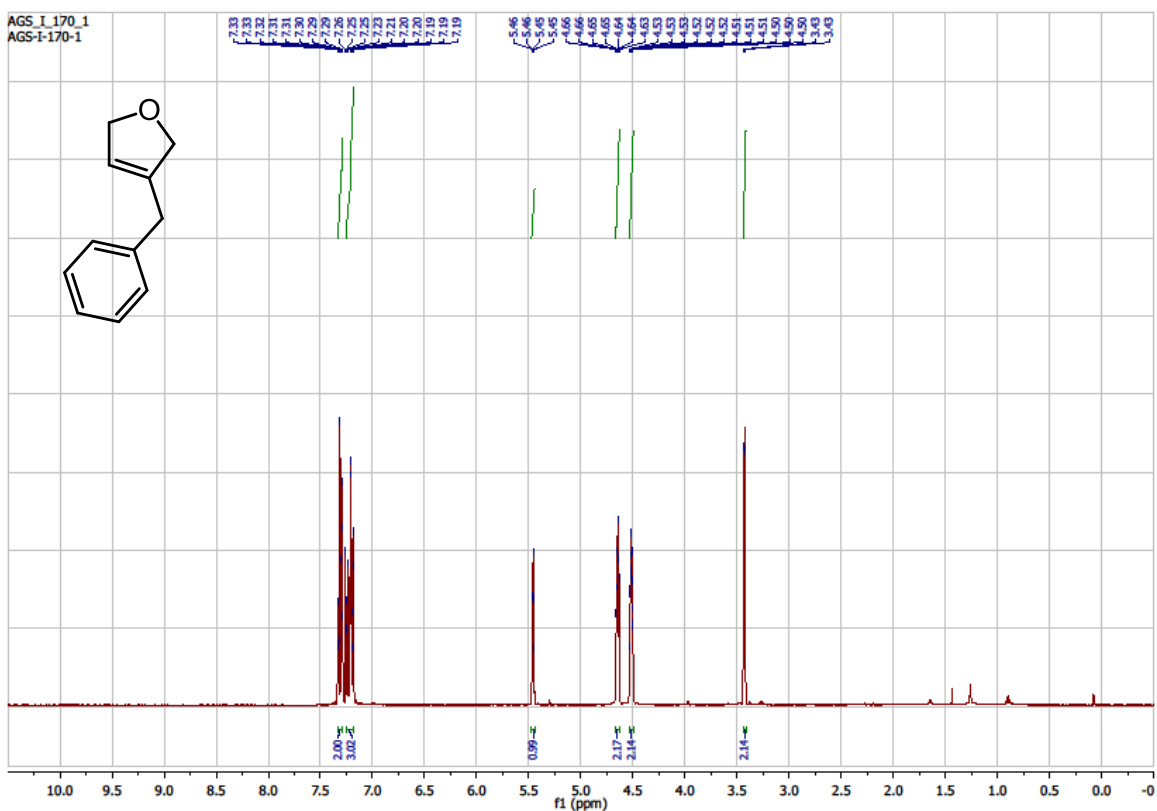
2-phenylprop-2-en-1-ol (S41).



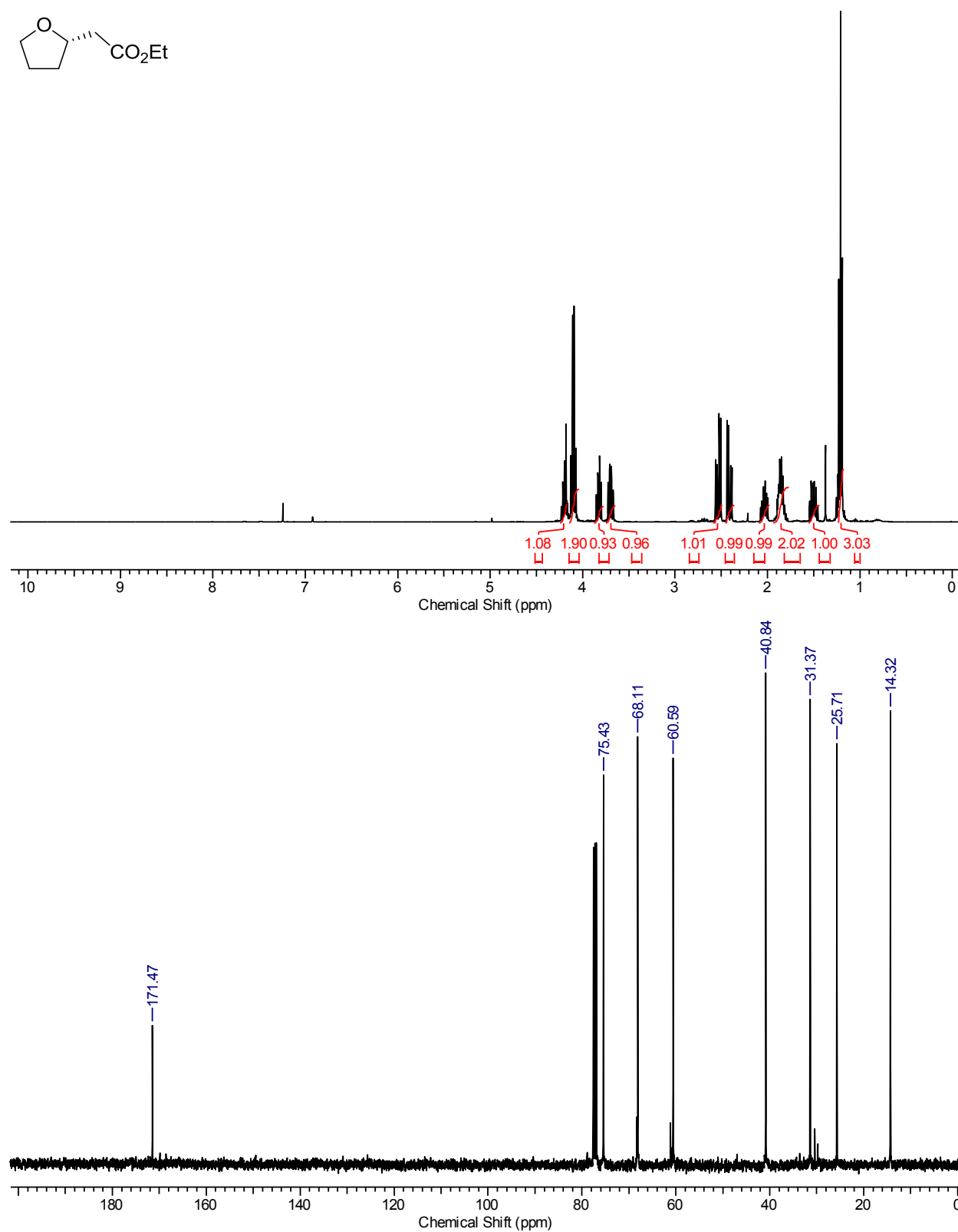
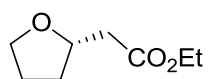
(2-((allyloxy)methyl)allyl)benzene (S44).



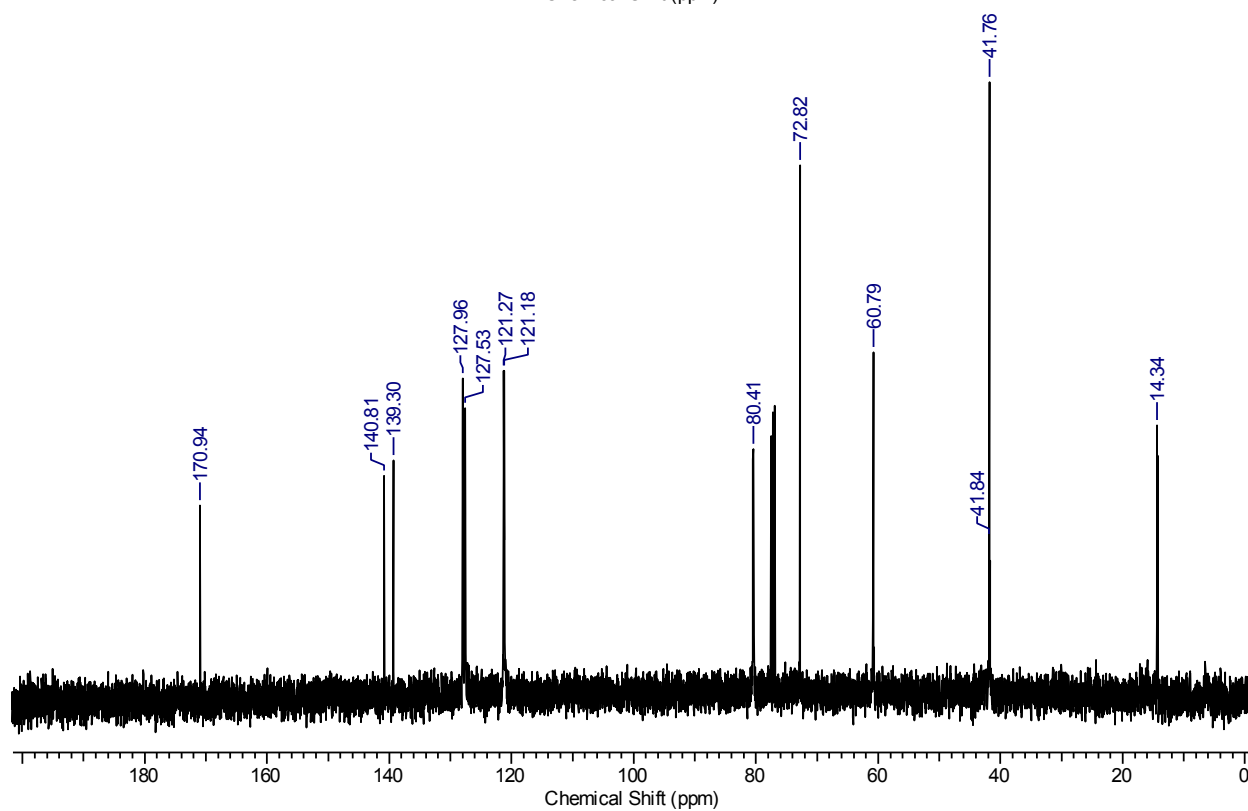
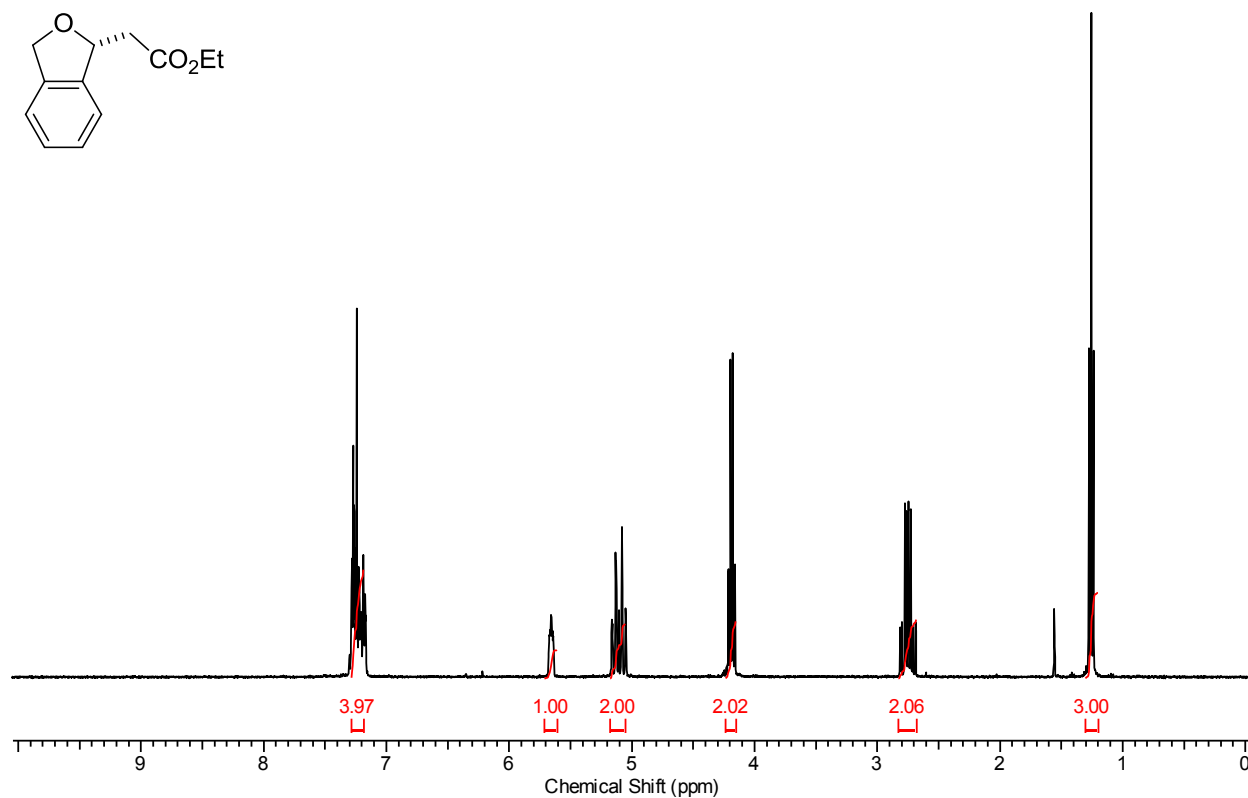
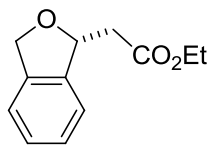
3-benzyl-2,5-dihydrofuran (S45).



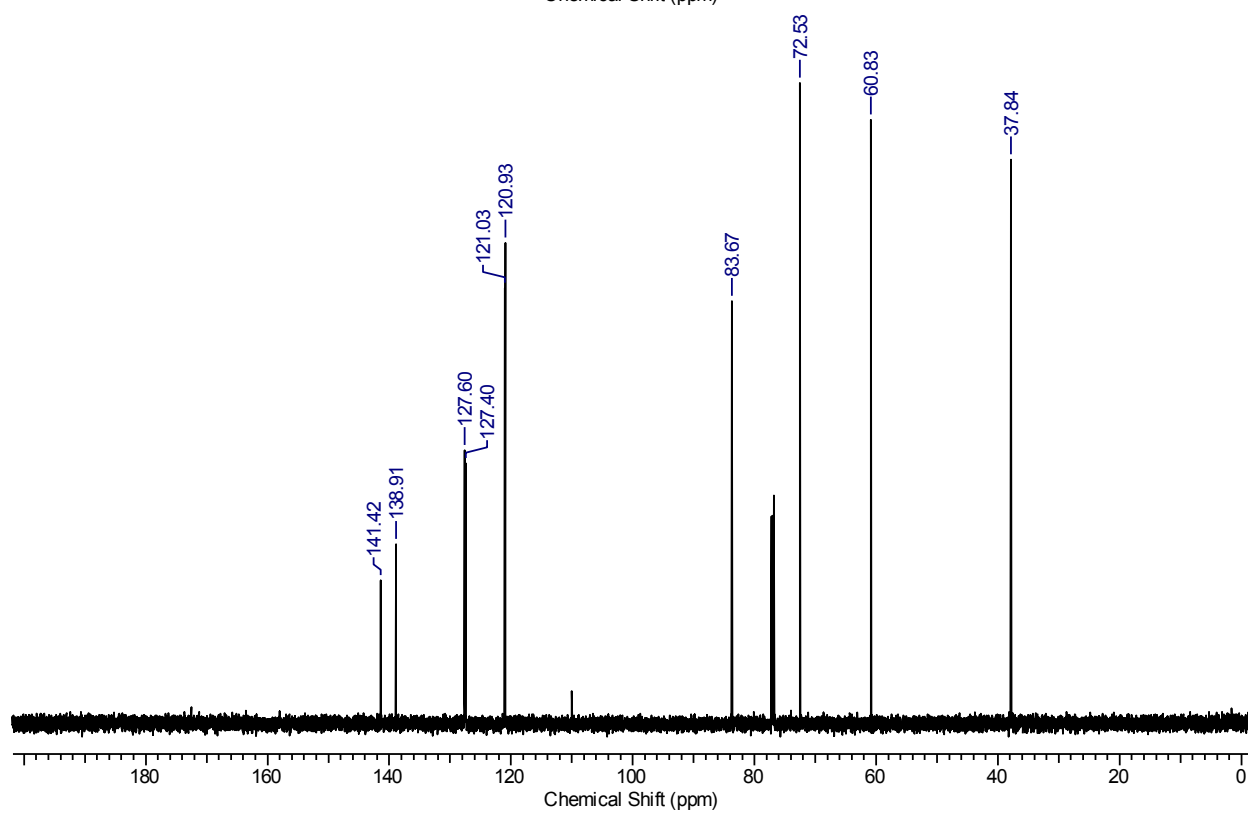
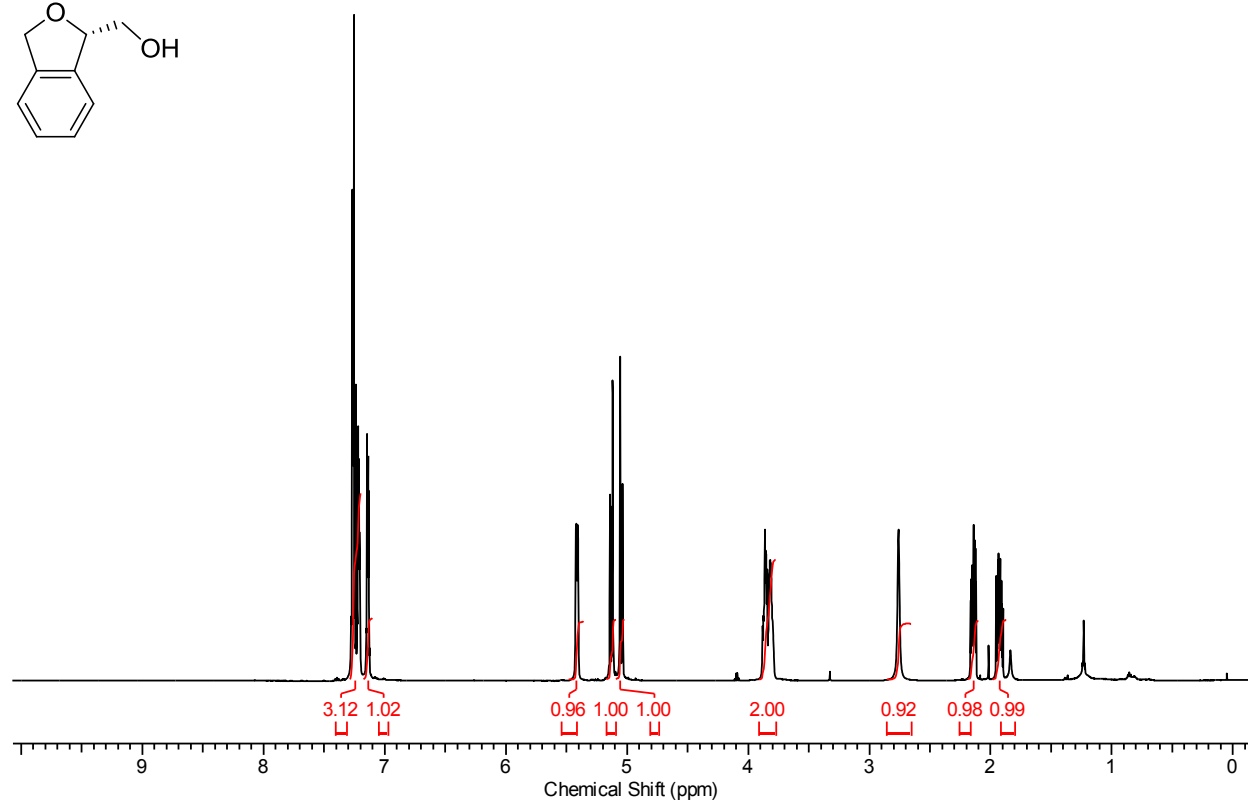
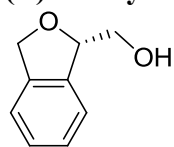
(S)-ethyl 2-(tetrahydrofuran-2-yl)acetate (S46).



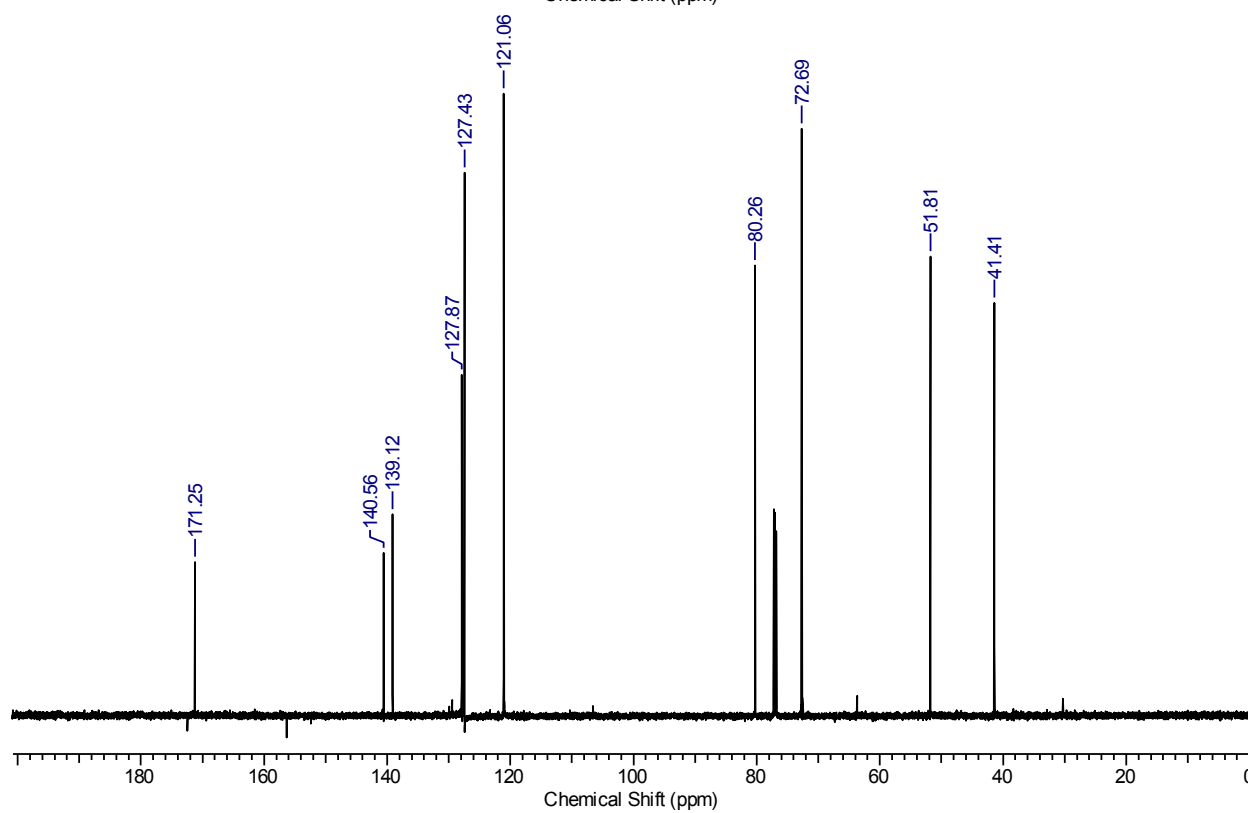
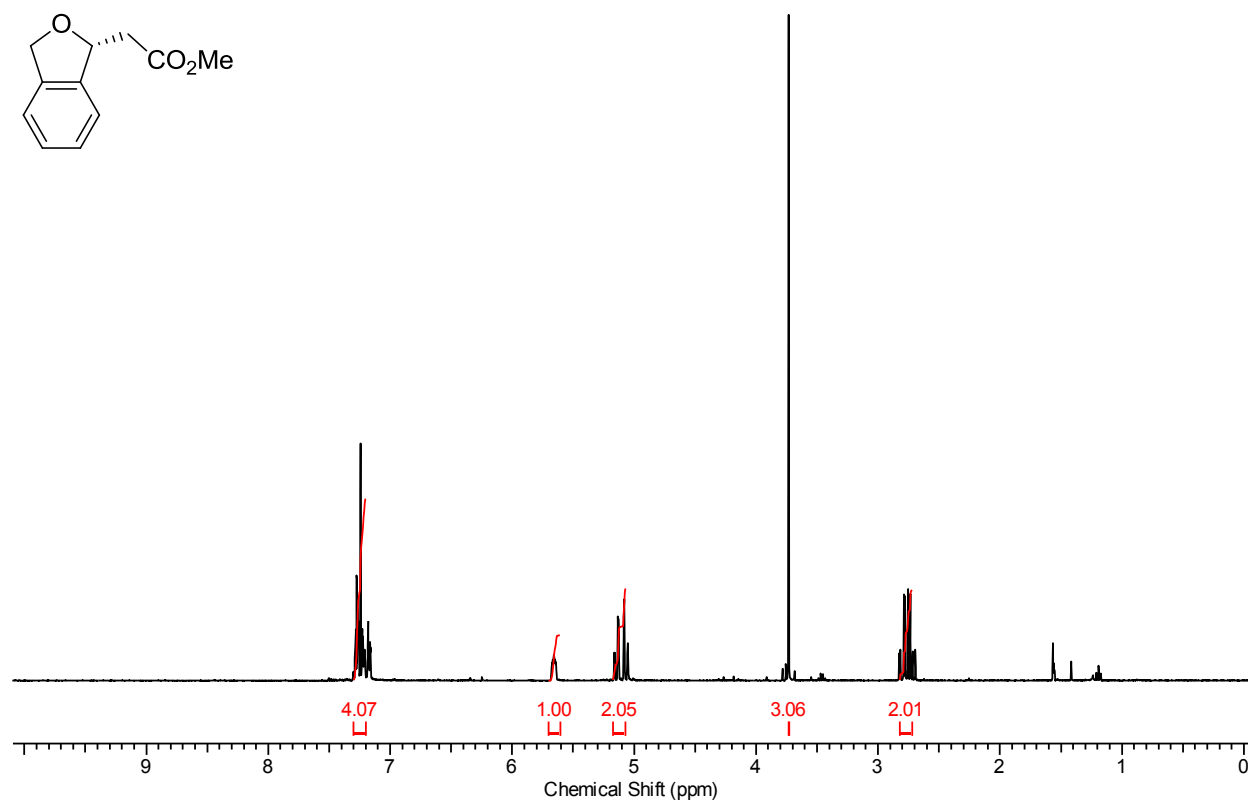
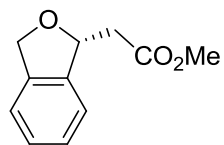
(R)-ethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S47).



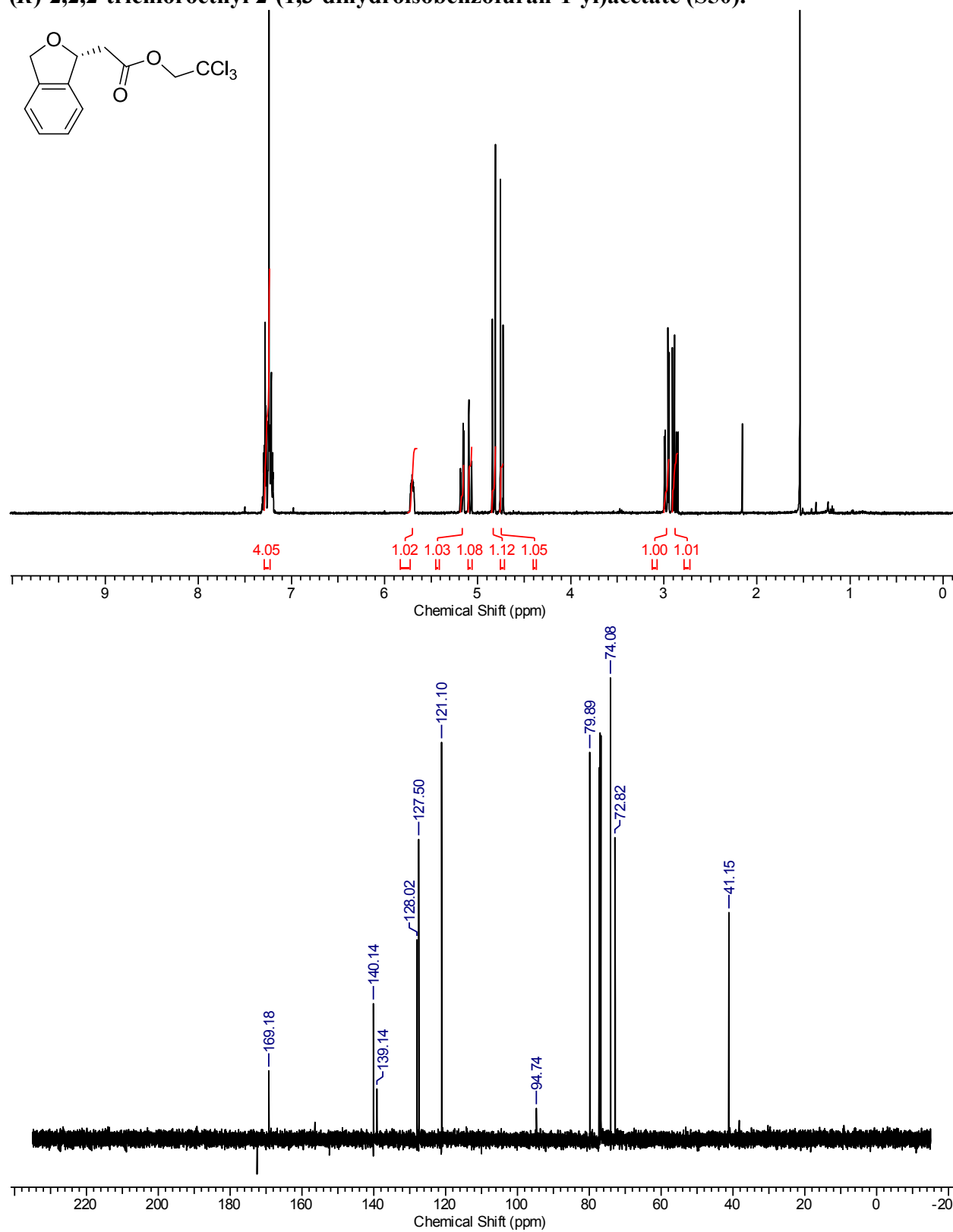
(R)-methyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S48).



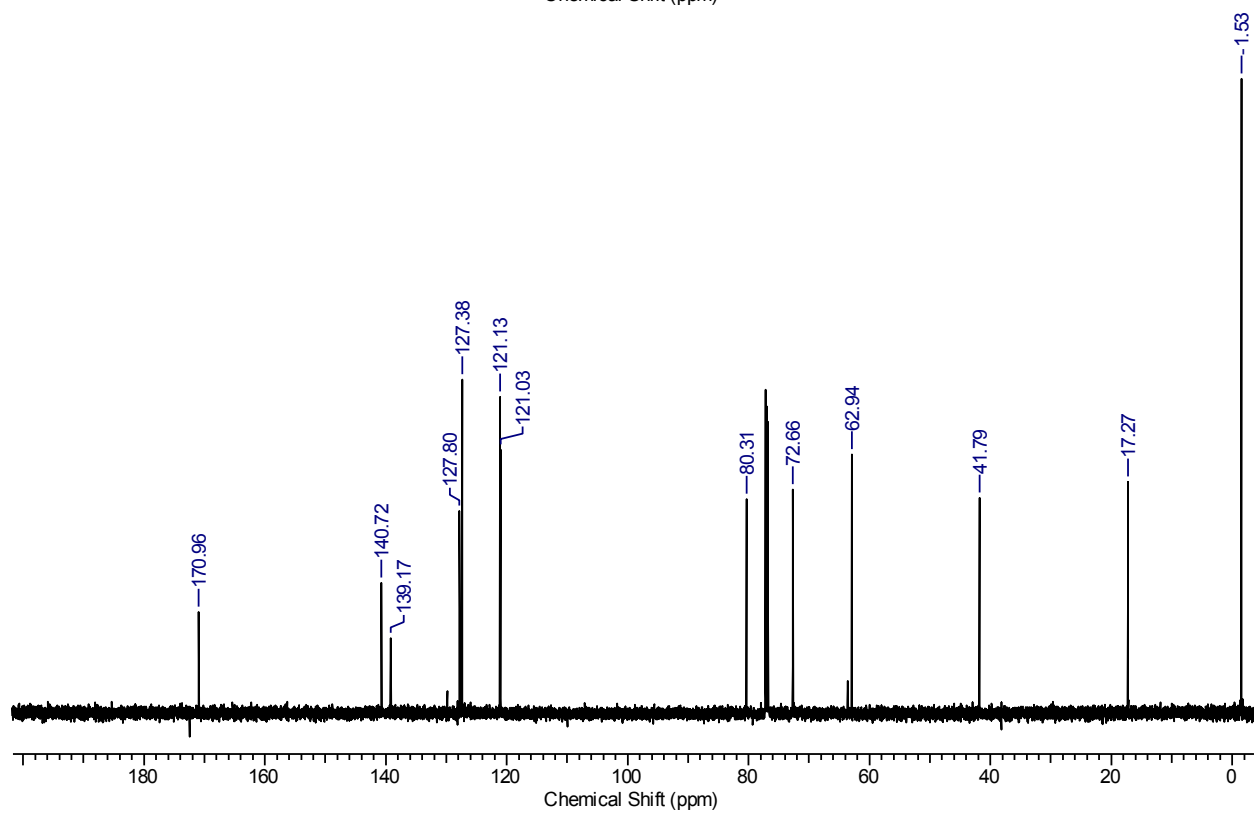
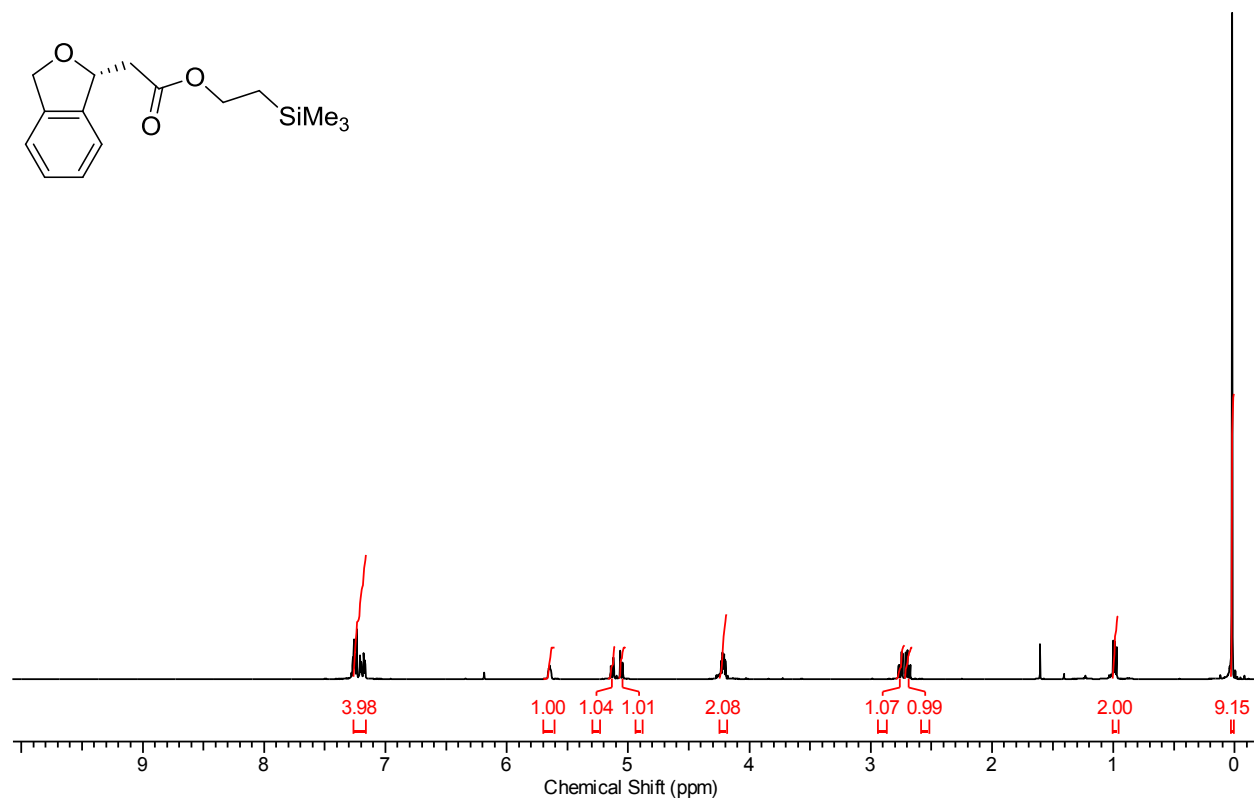
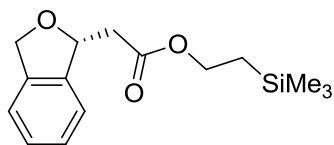
(R)-methyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S49).



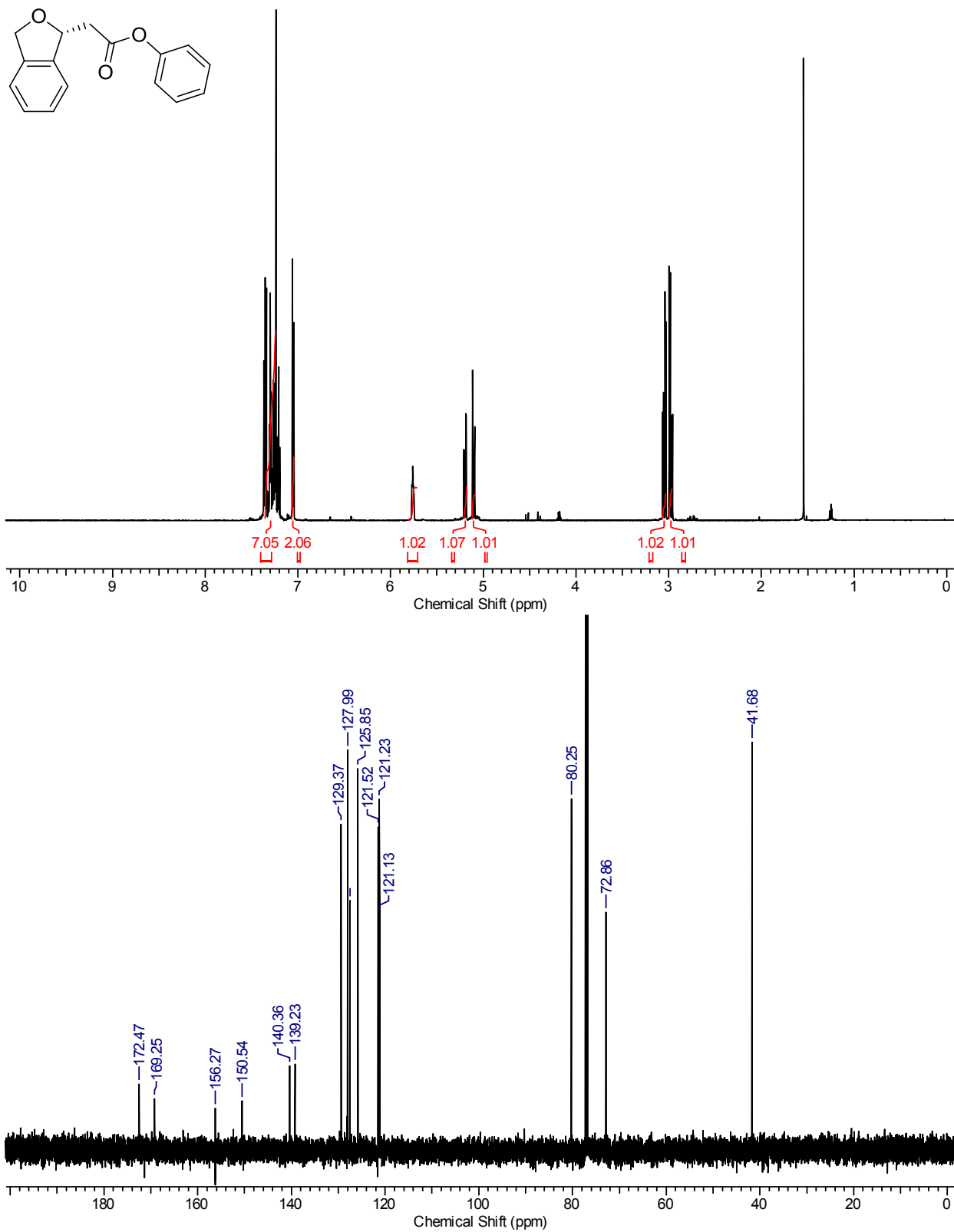
(R)-2,2,2-trichloroethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S50).



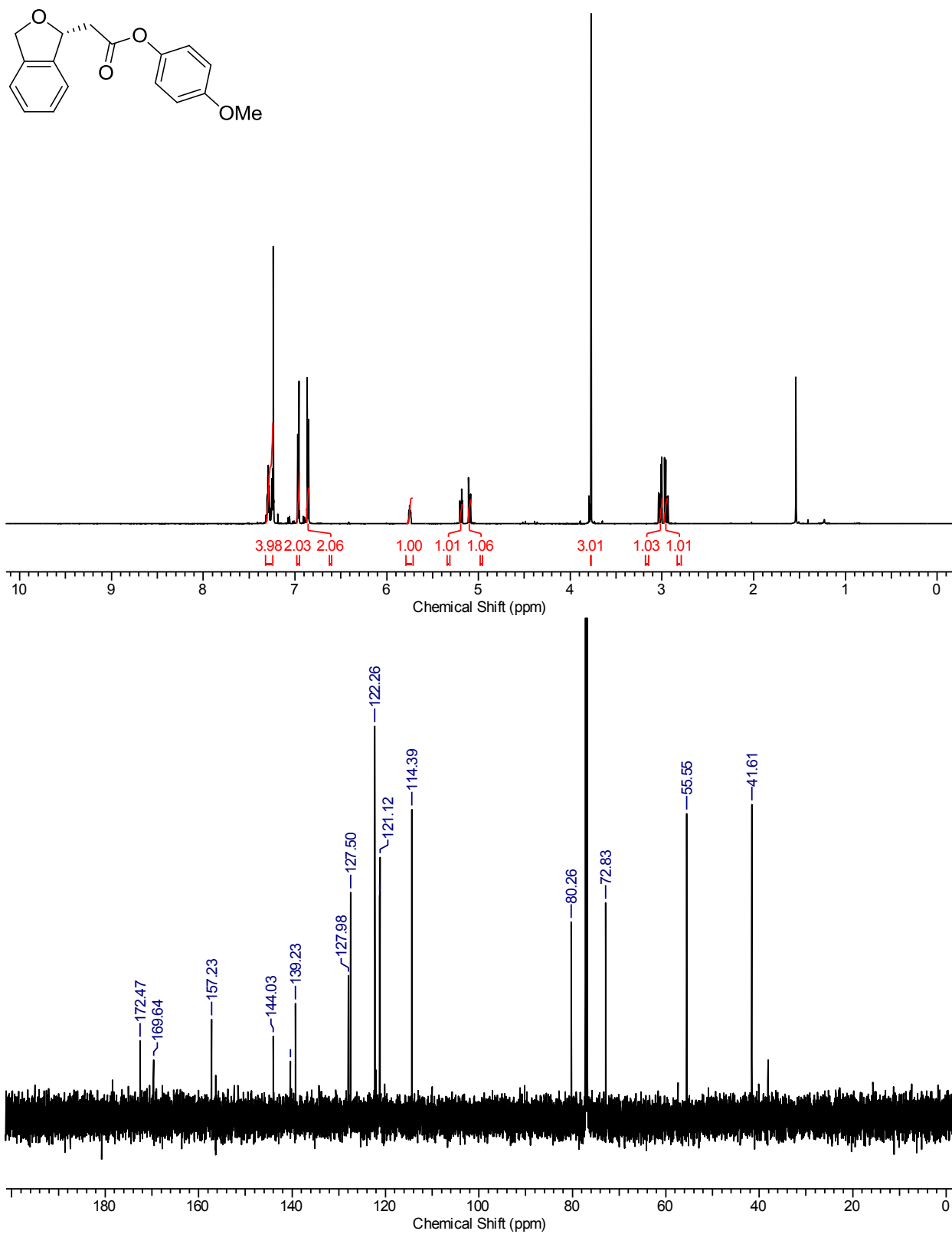
(R)-2-(trimethylsilyl)ethyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S51).



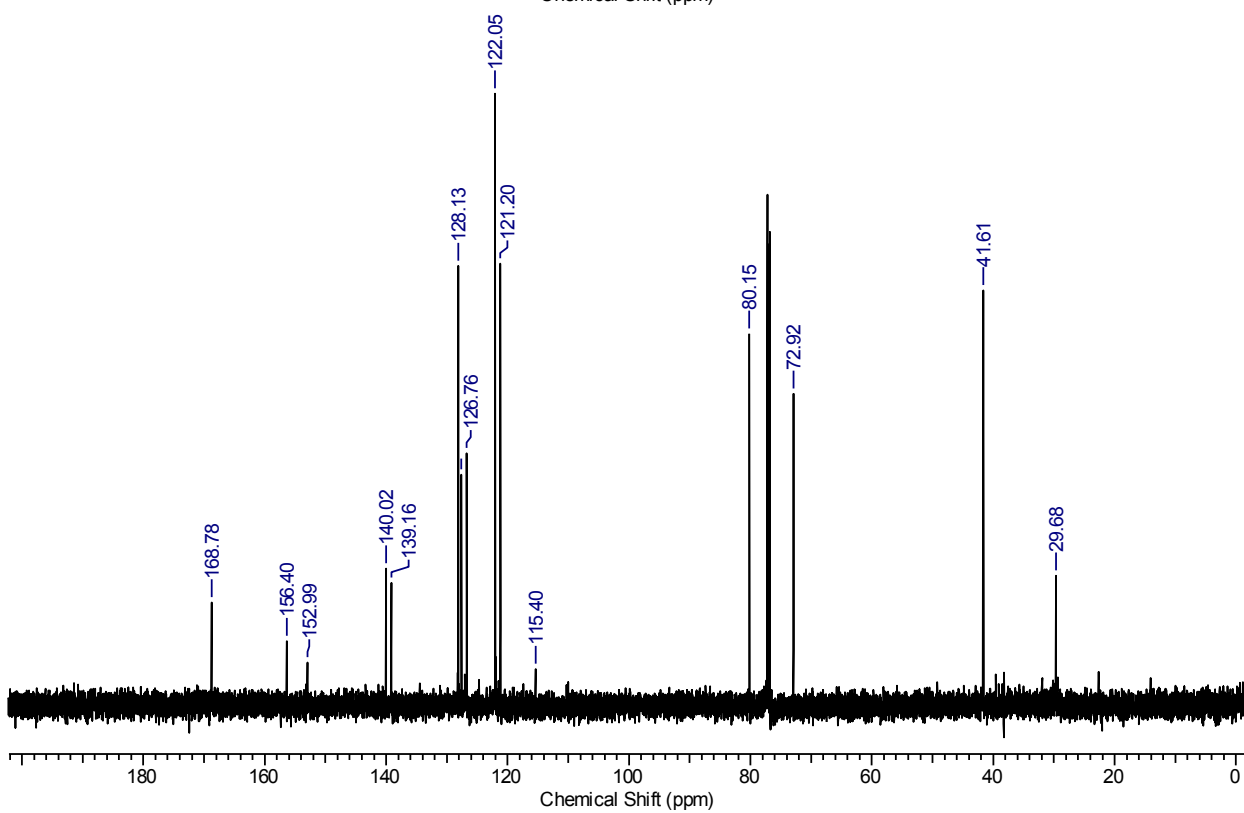
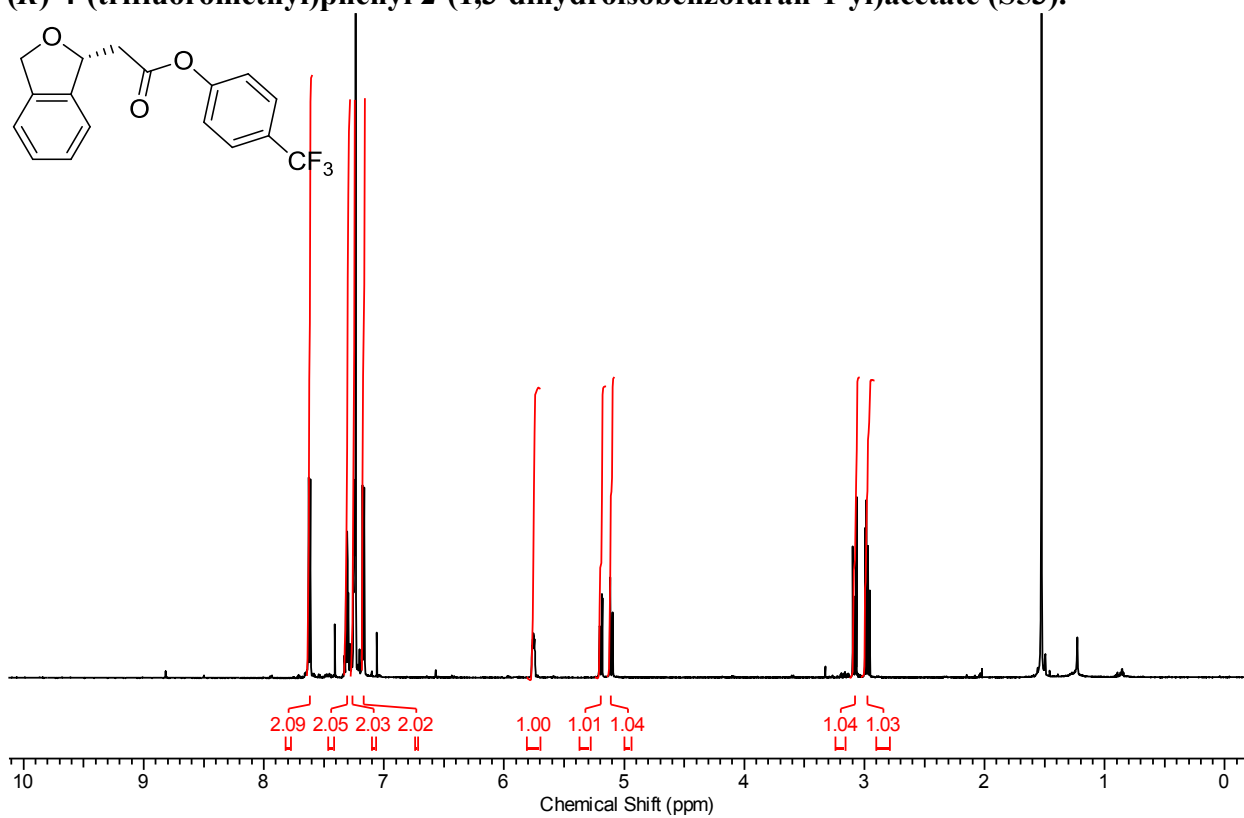
(R)-phenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S52).



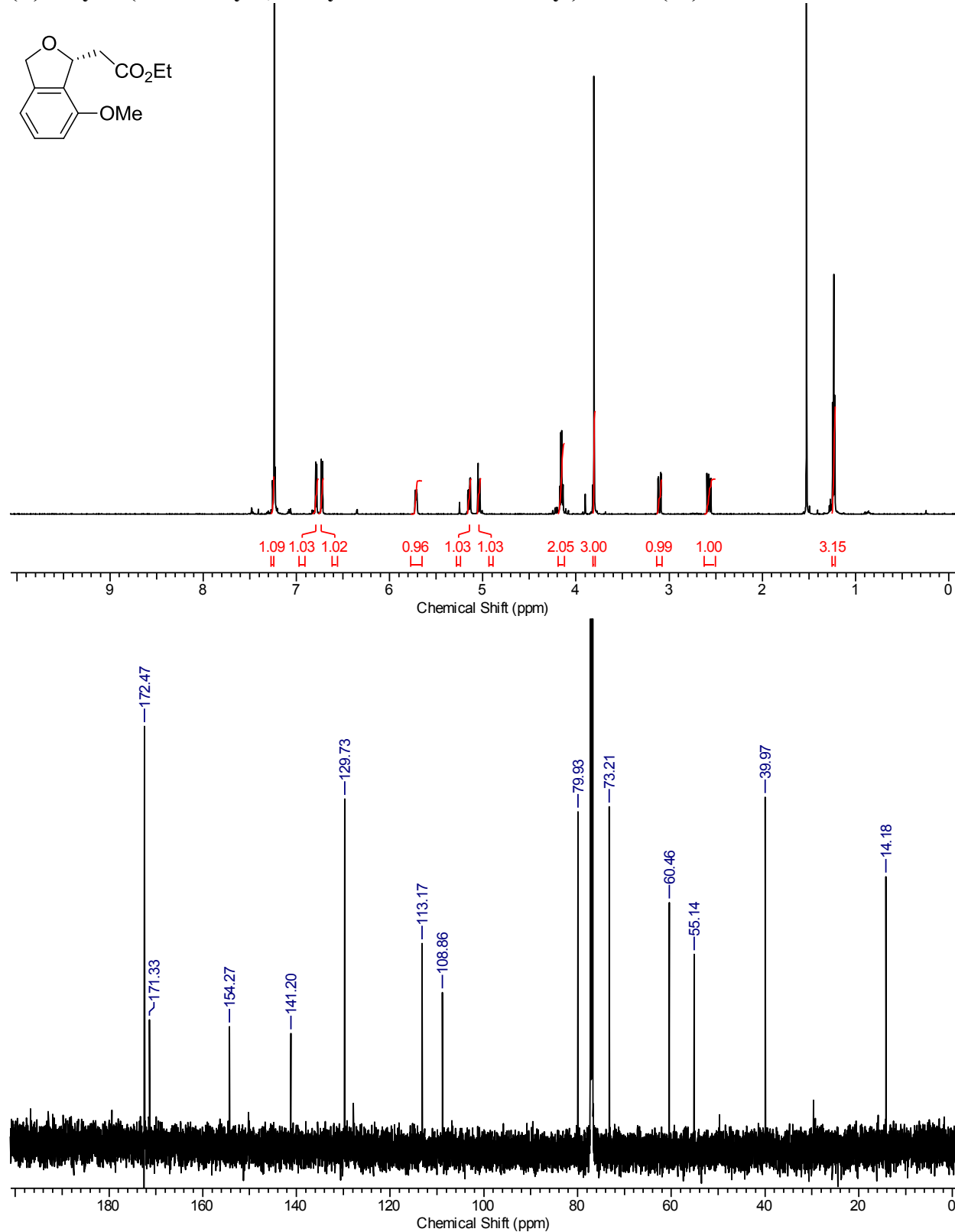
(R)-4-methoxyphenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (2).



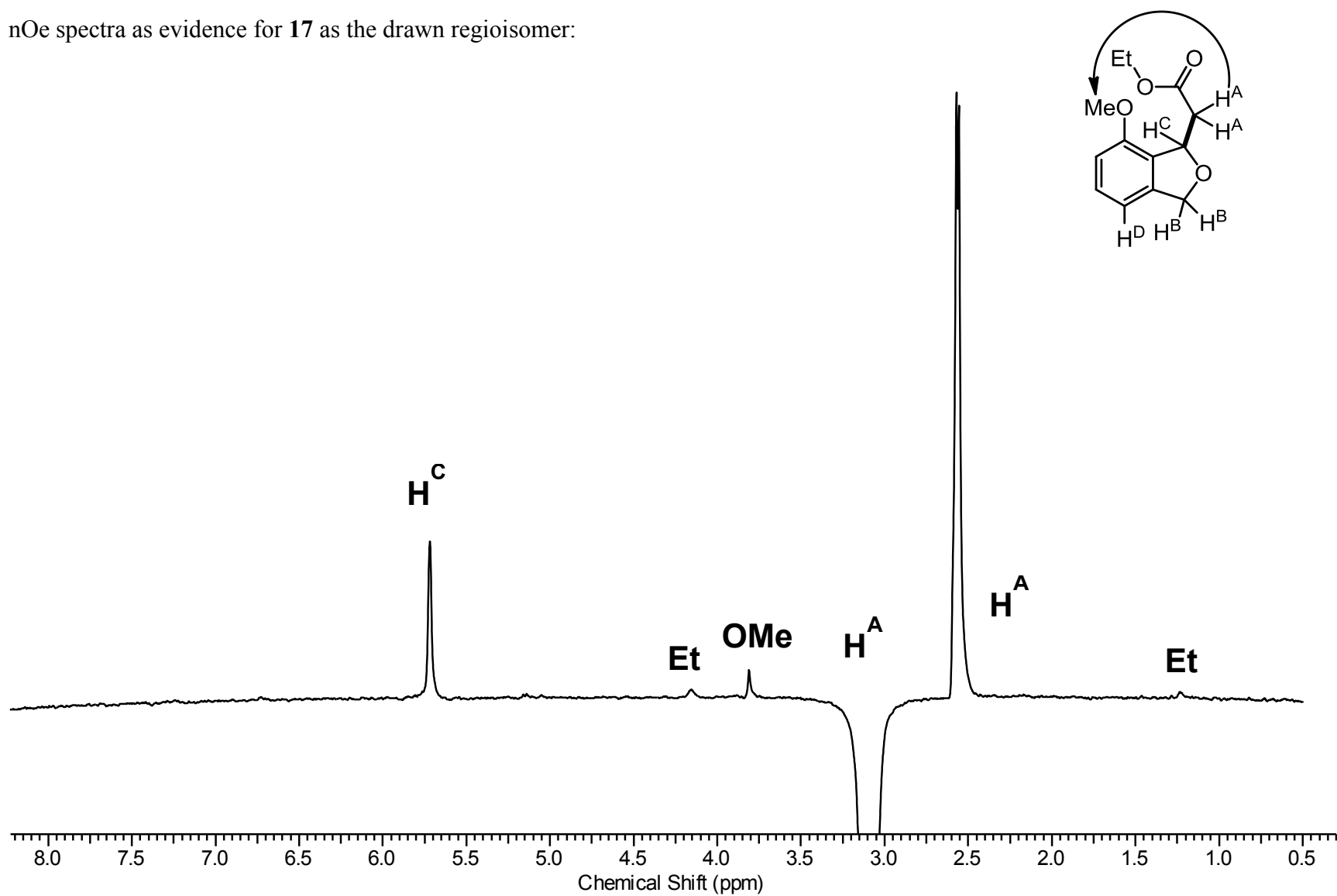
(R)-4-(trifluoromethyl)phenyl 2-(1,3-dihydroisobenzofuran-1-yl)acetate (S53).

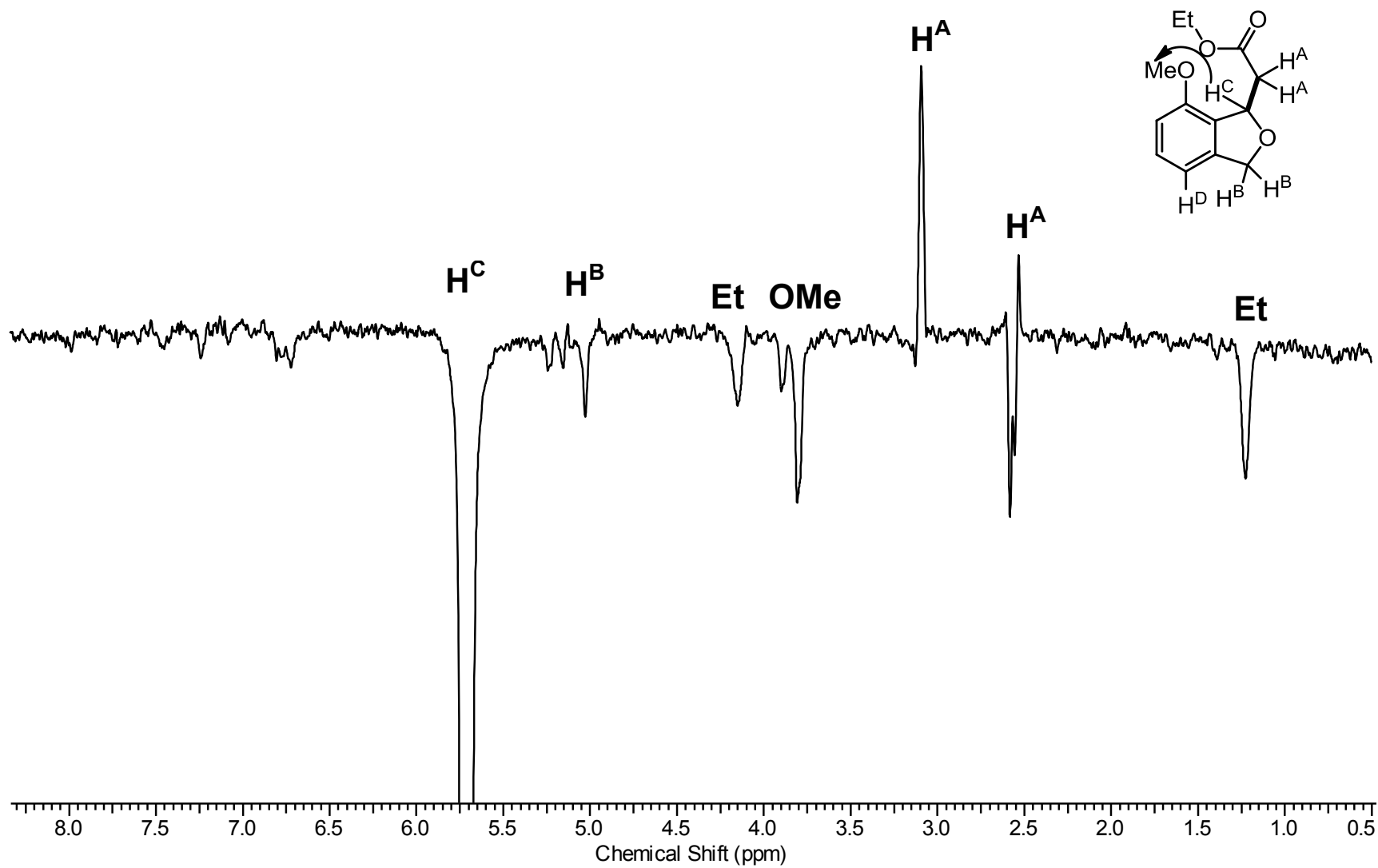


(R)-ethyl 2-(7-methoxy-1,3-dihydroisobenzofuran-1-yl)acetate (17).

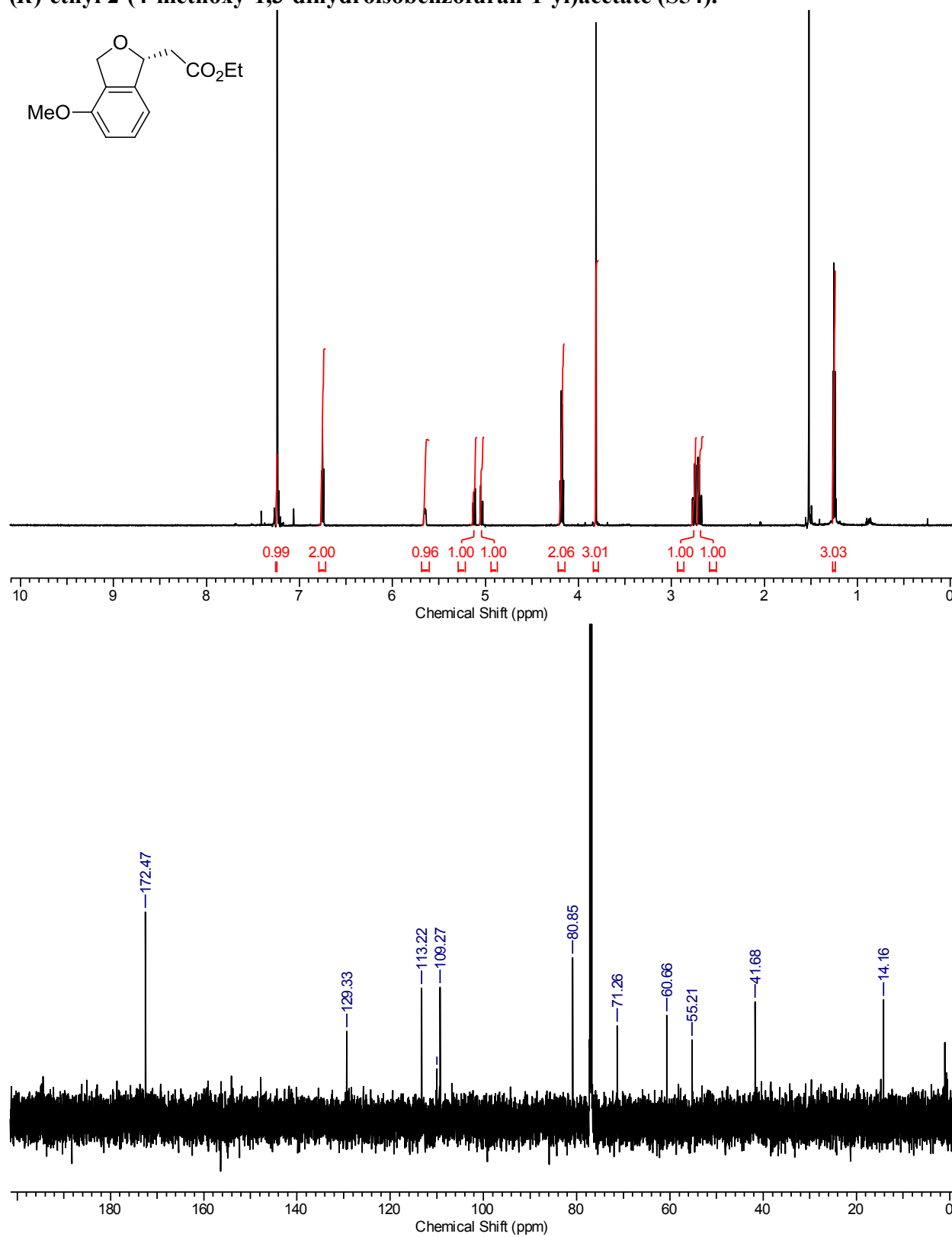


nOe spectra as evidence for **17** as the drawn regioisomer:

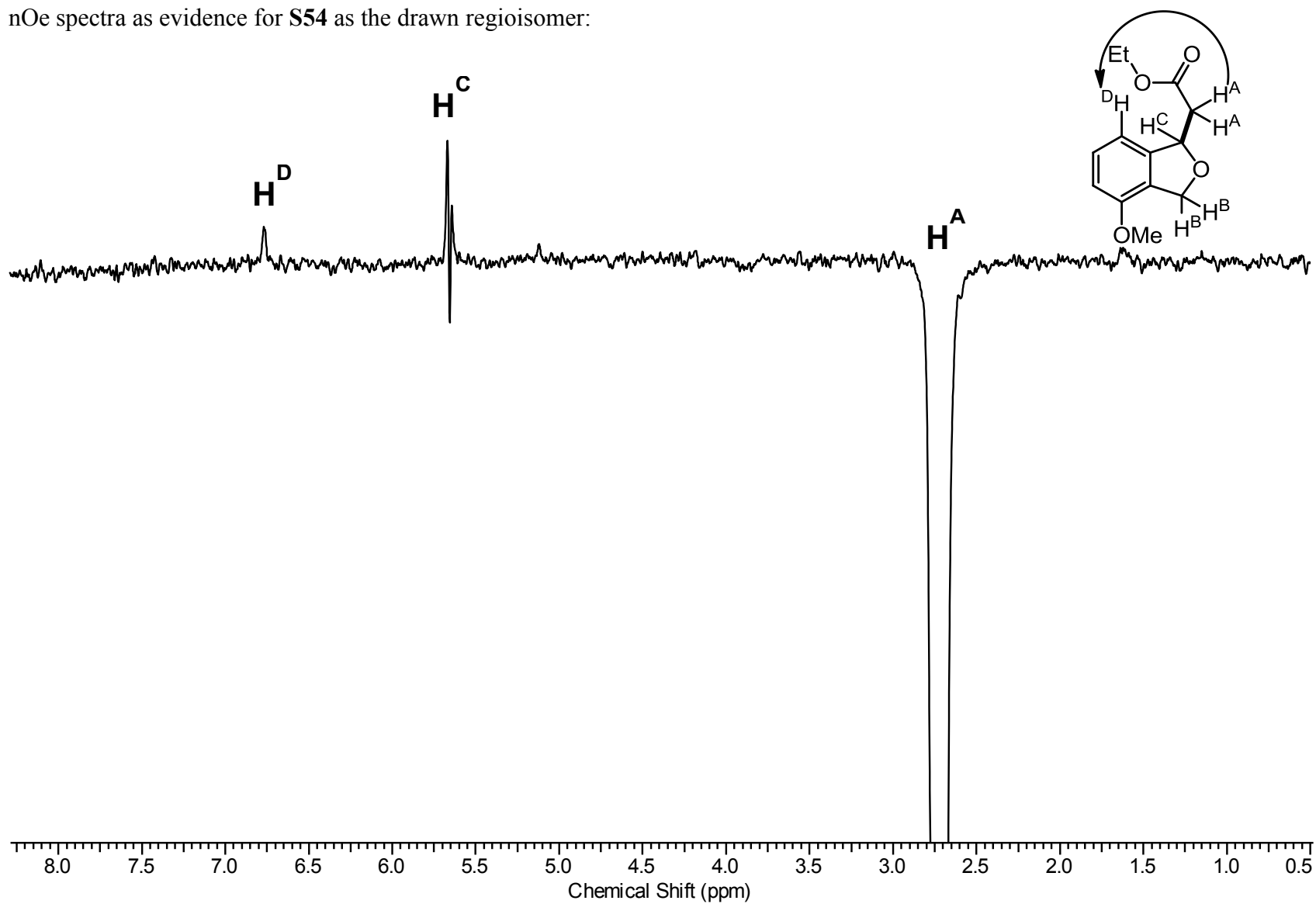




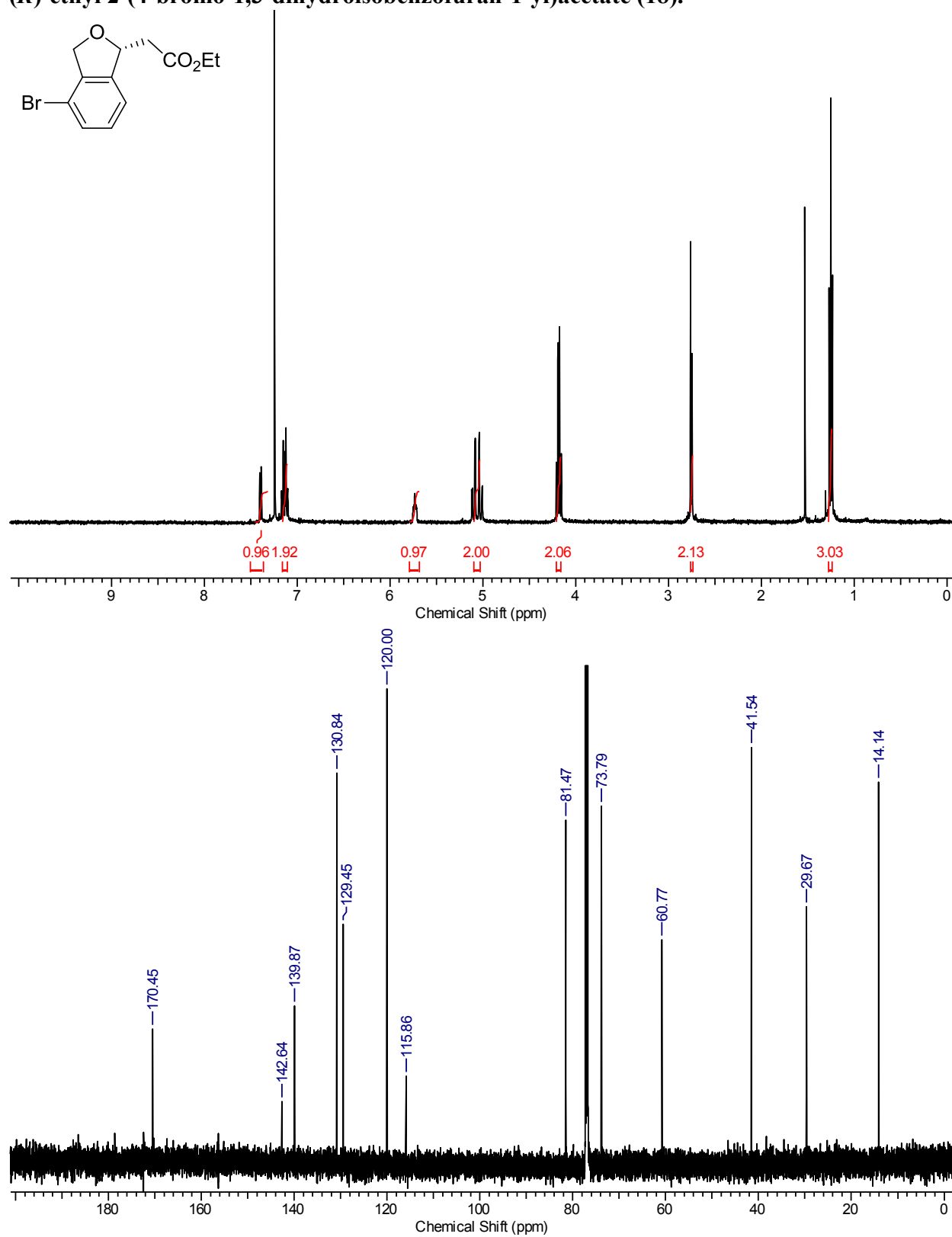
(R)-ethyl 2-(4-methoxy-1,3-dihydroisobenzofuran-1-yl)acetate (S54).



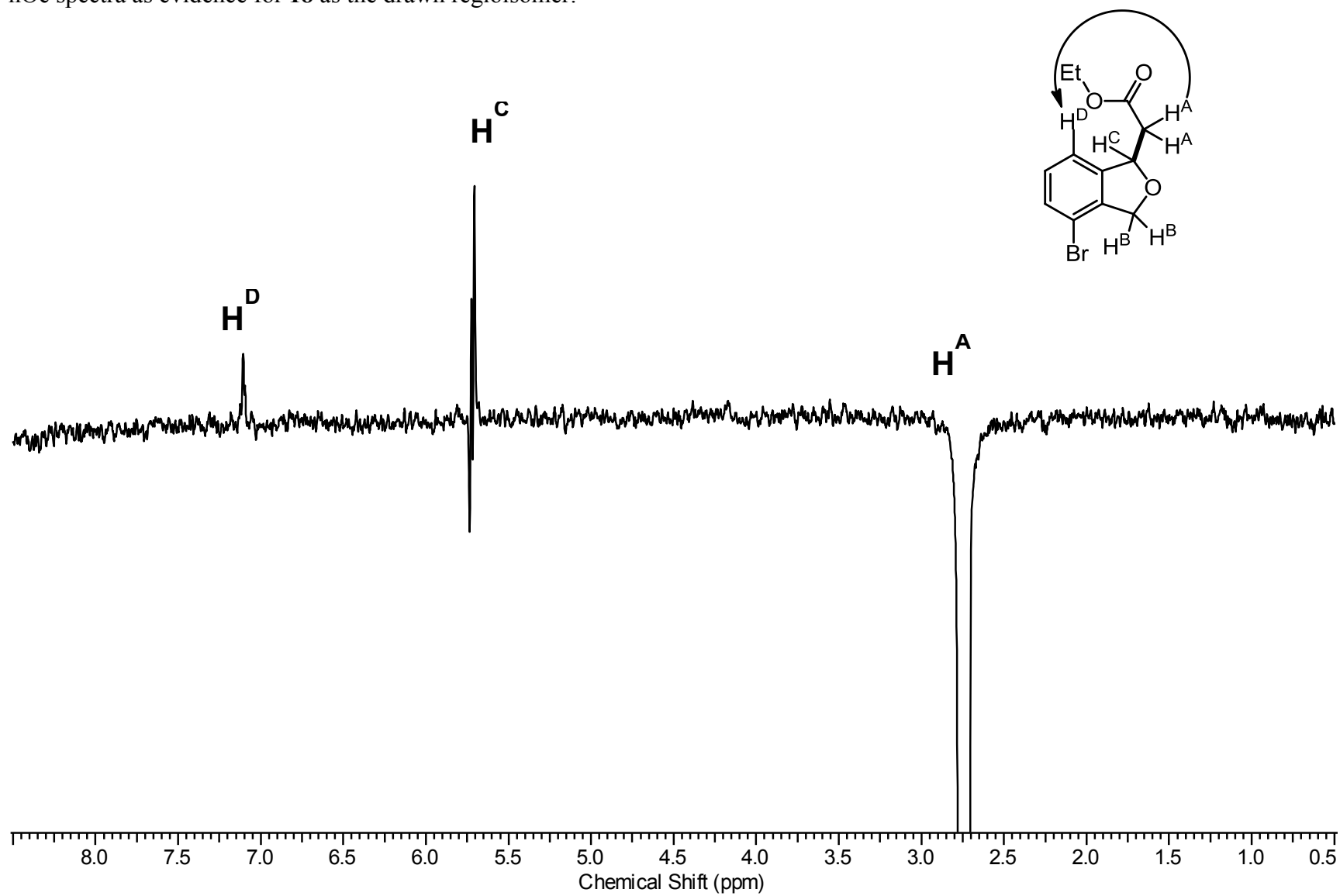
nOe spectra as evidence for **S54** as the drawn regioisomer:

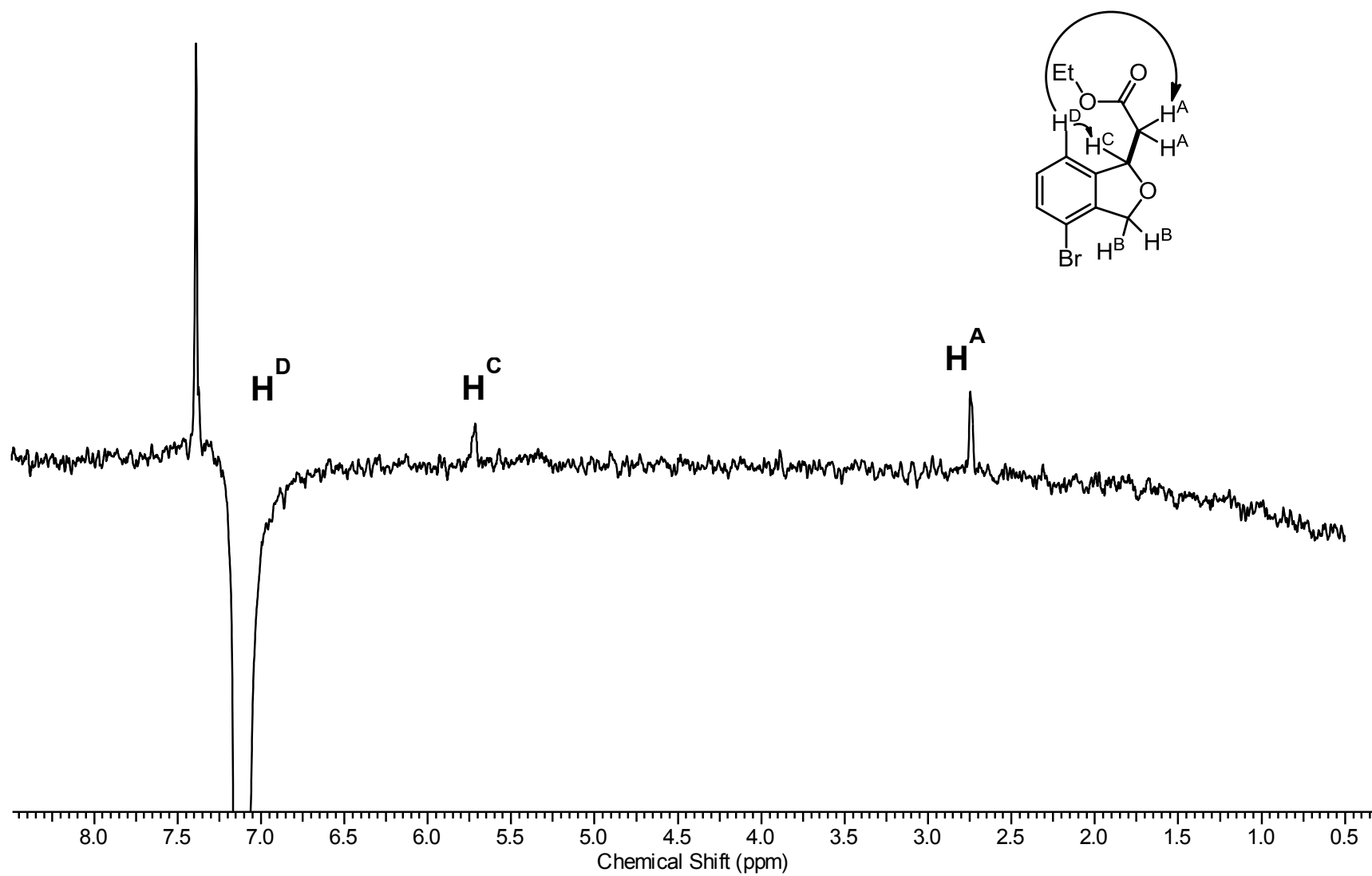


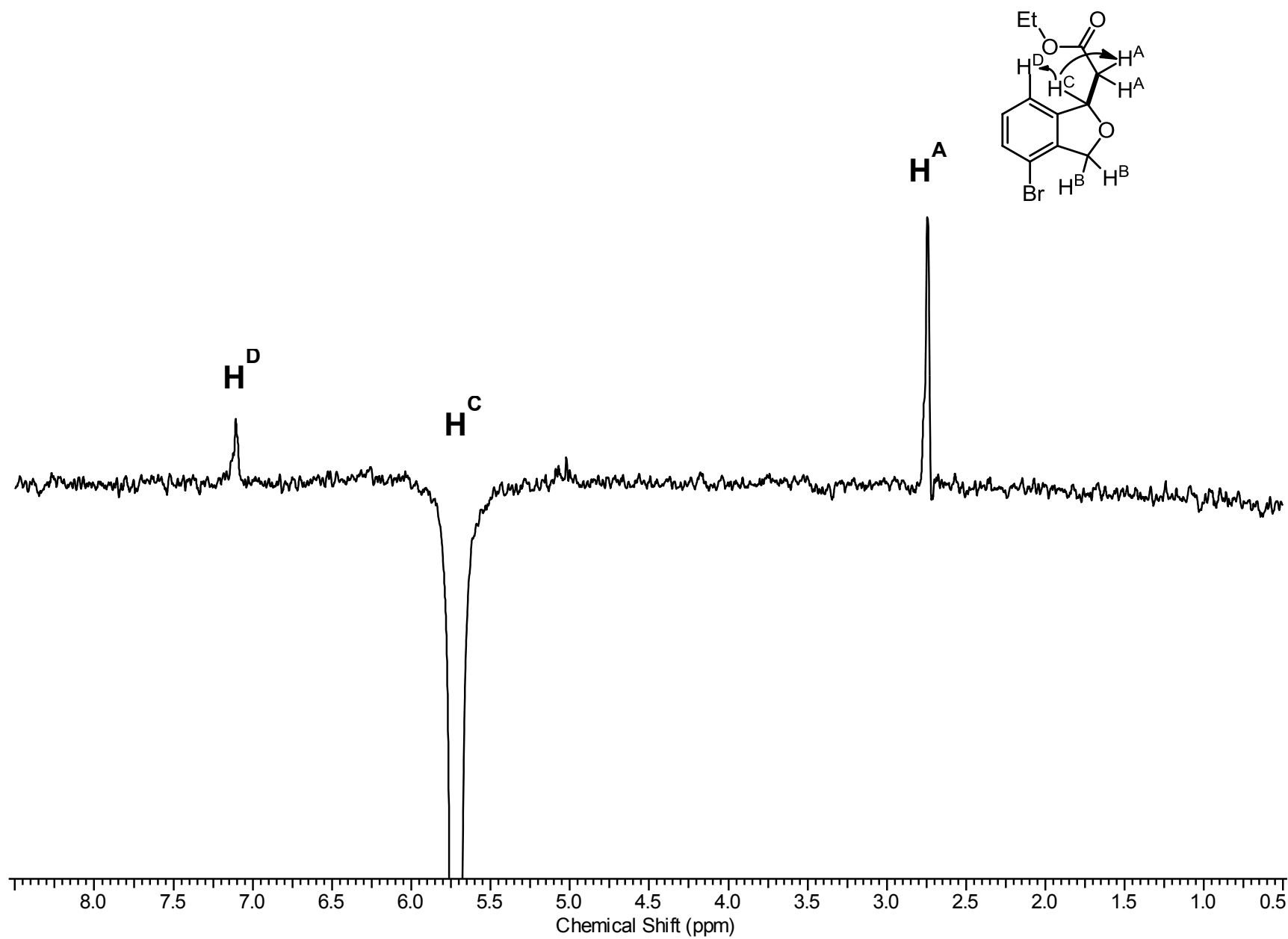
(R)-ethyl 2-(4-bromo-1,3-dihydroisobenzofuran-1-yl)acetate (18).



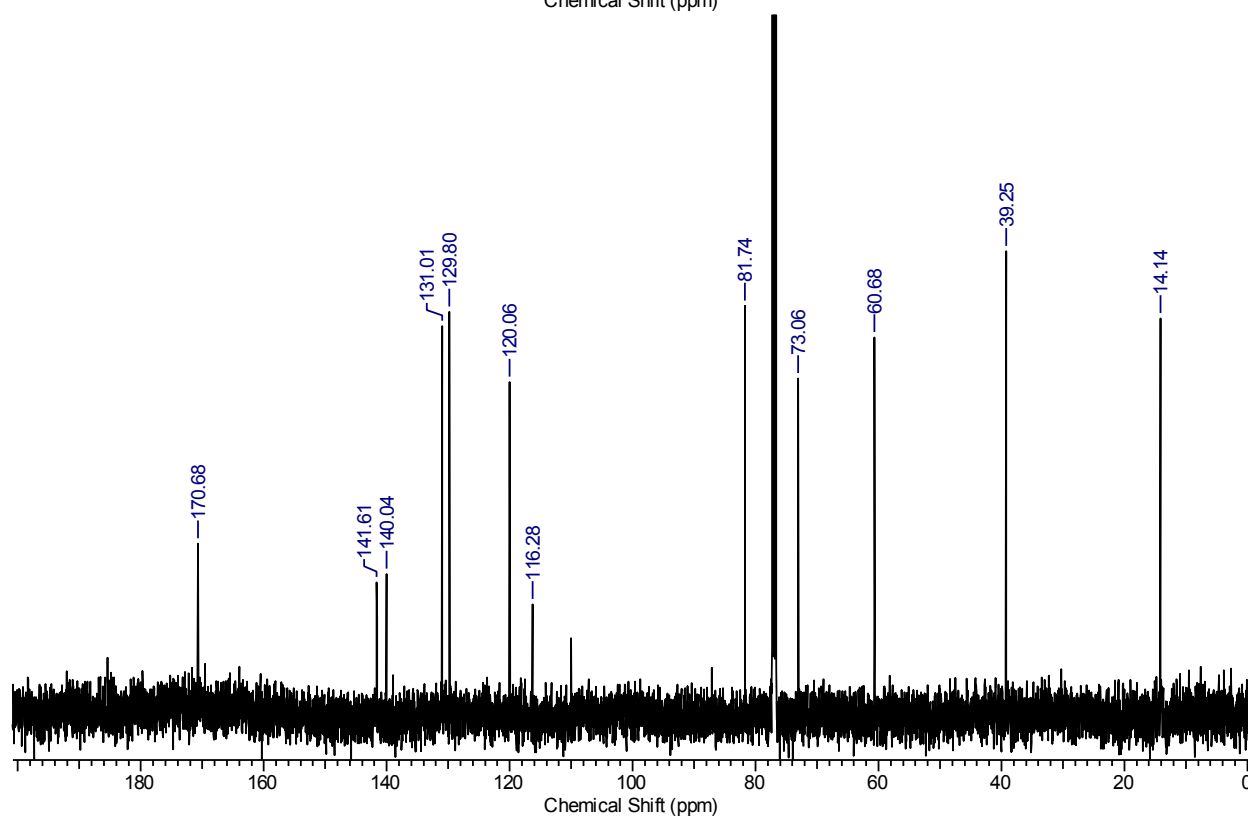
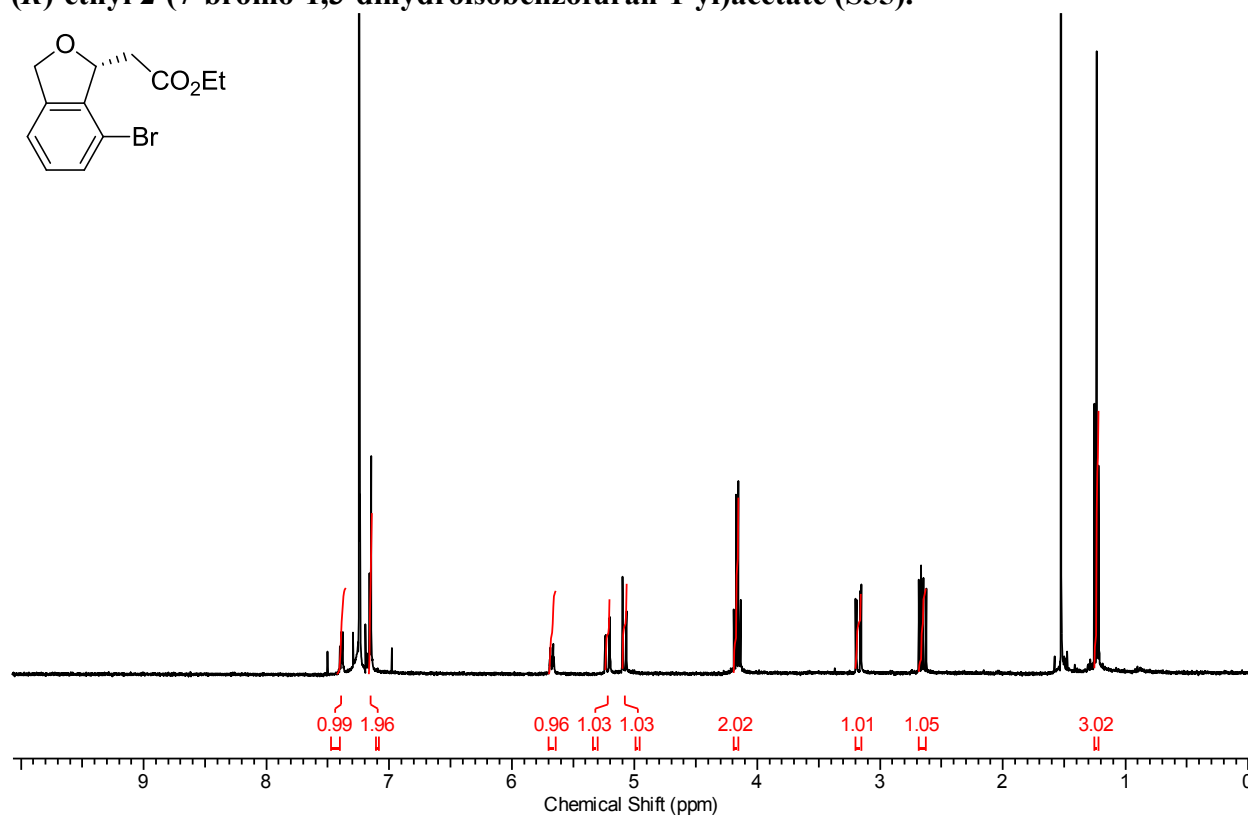
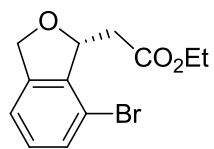
nOe spectra as evidence for **18** as the drawn regioisomer:



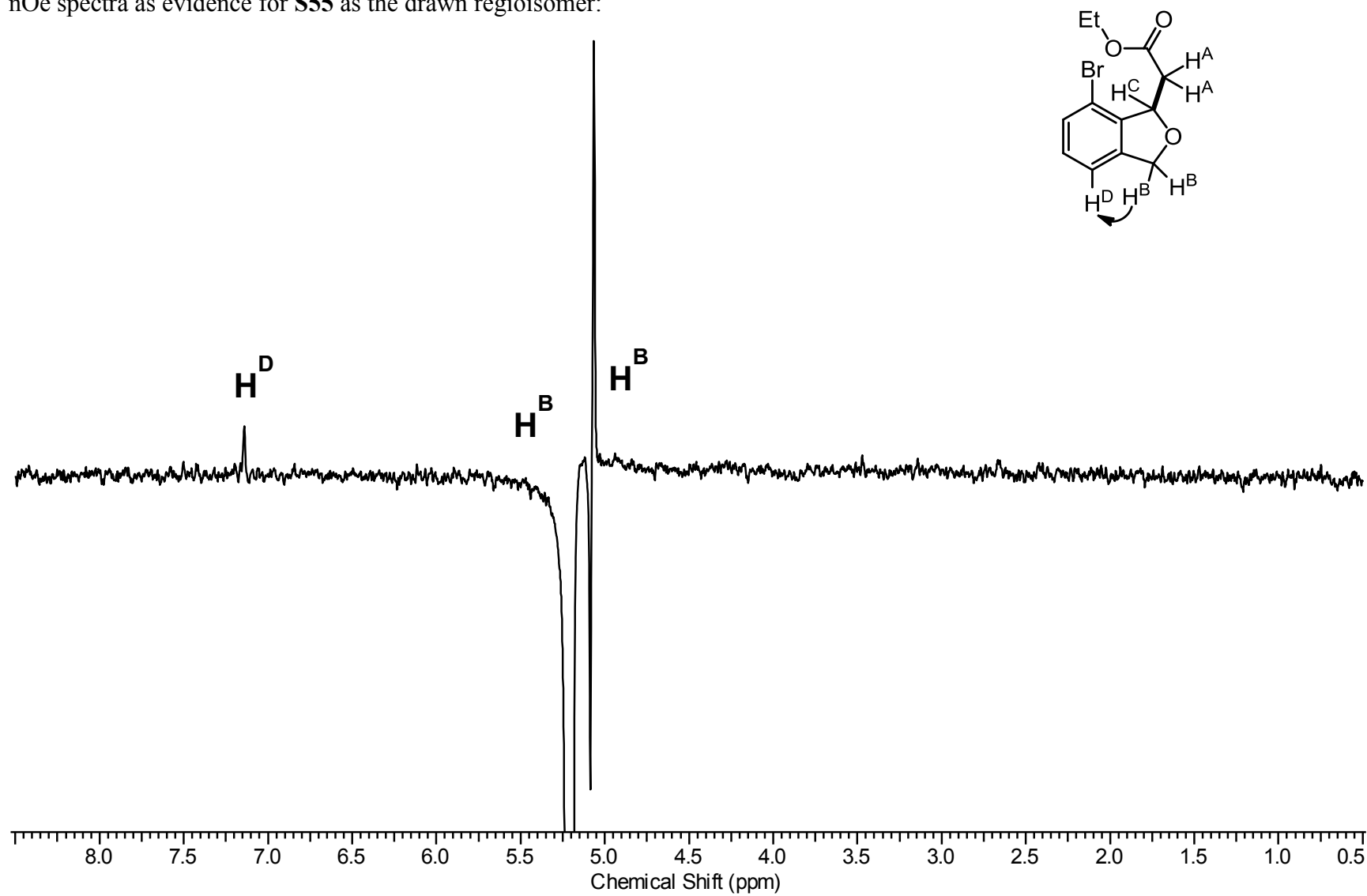


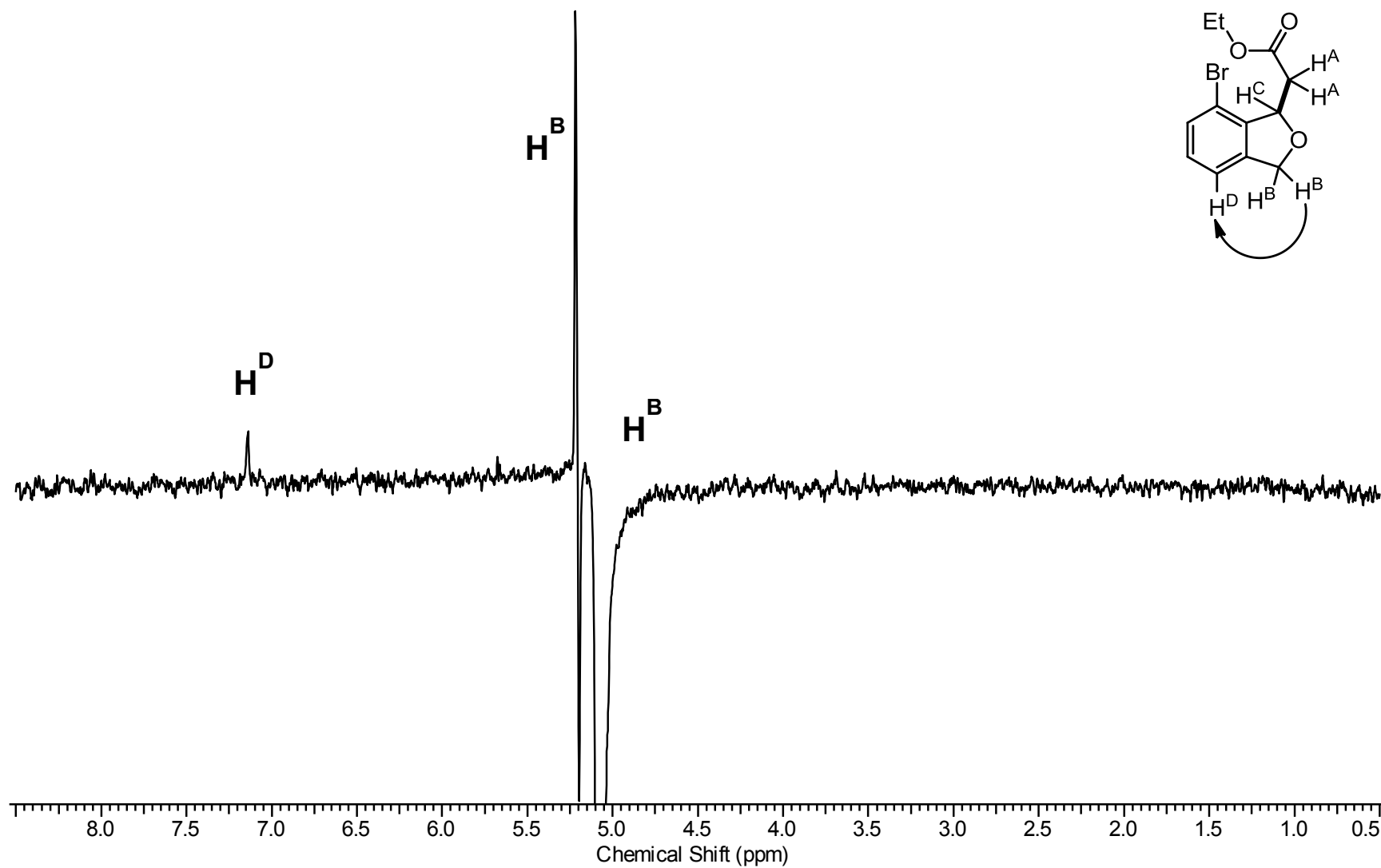


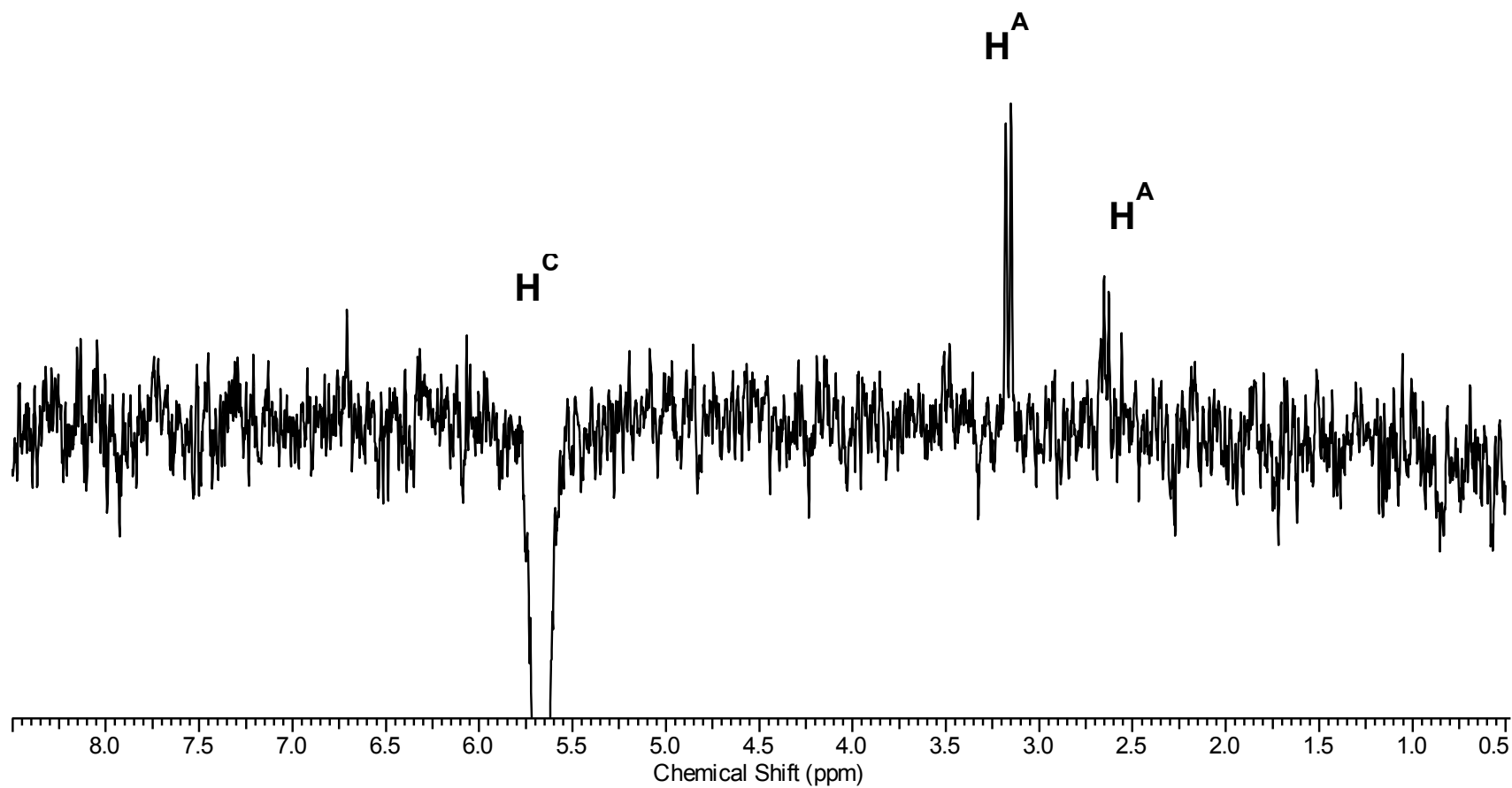
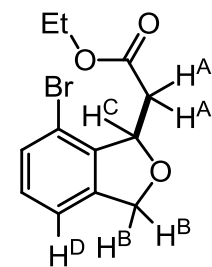
(R)-ethyl 2-(7-bromo-1,3-dihydroisobenzofuran-1-yl)acetate (S55).

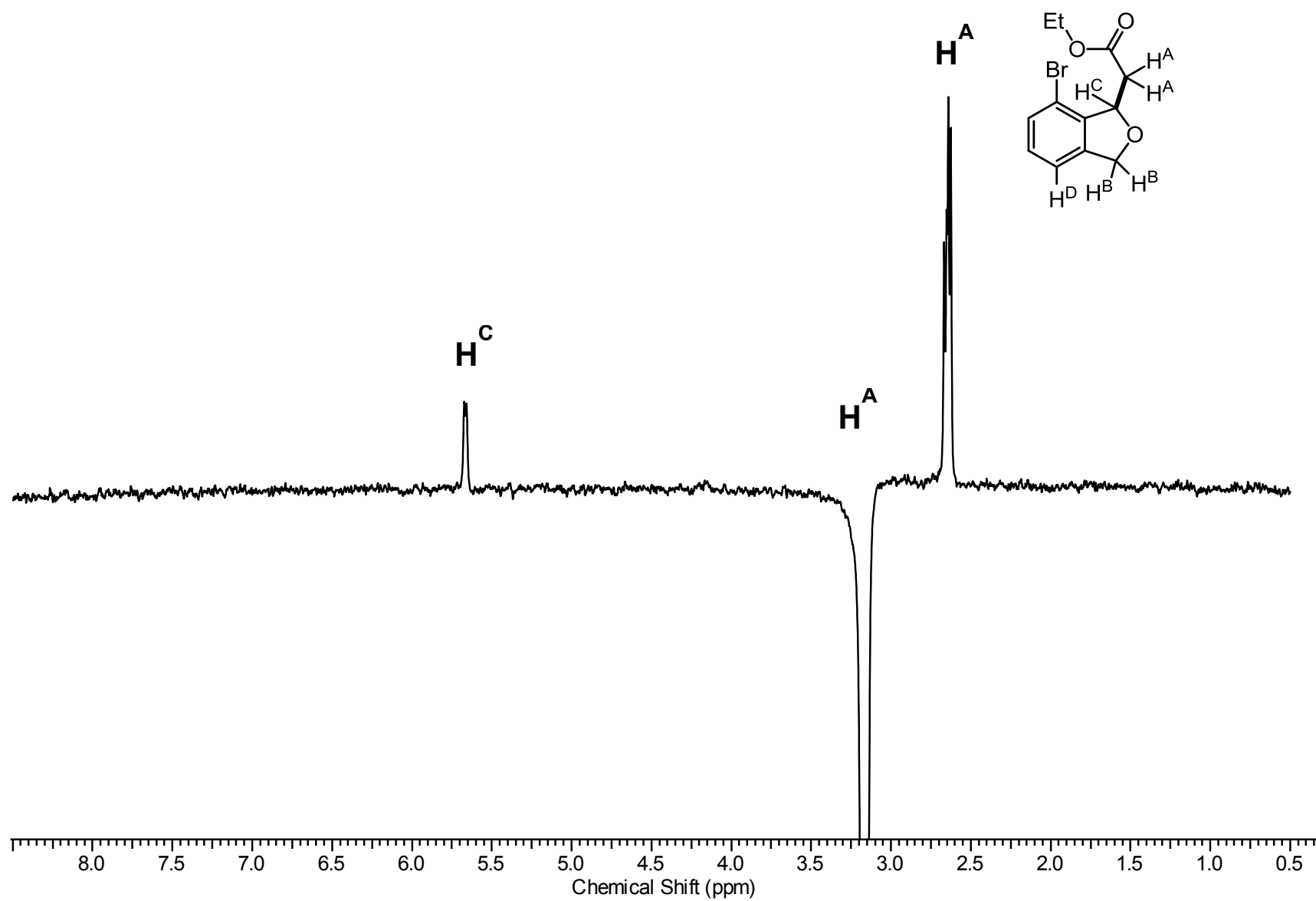


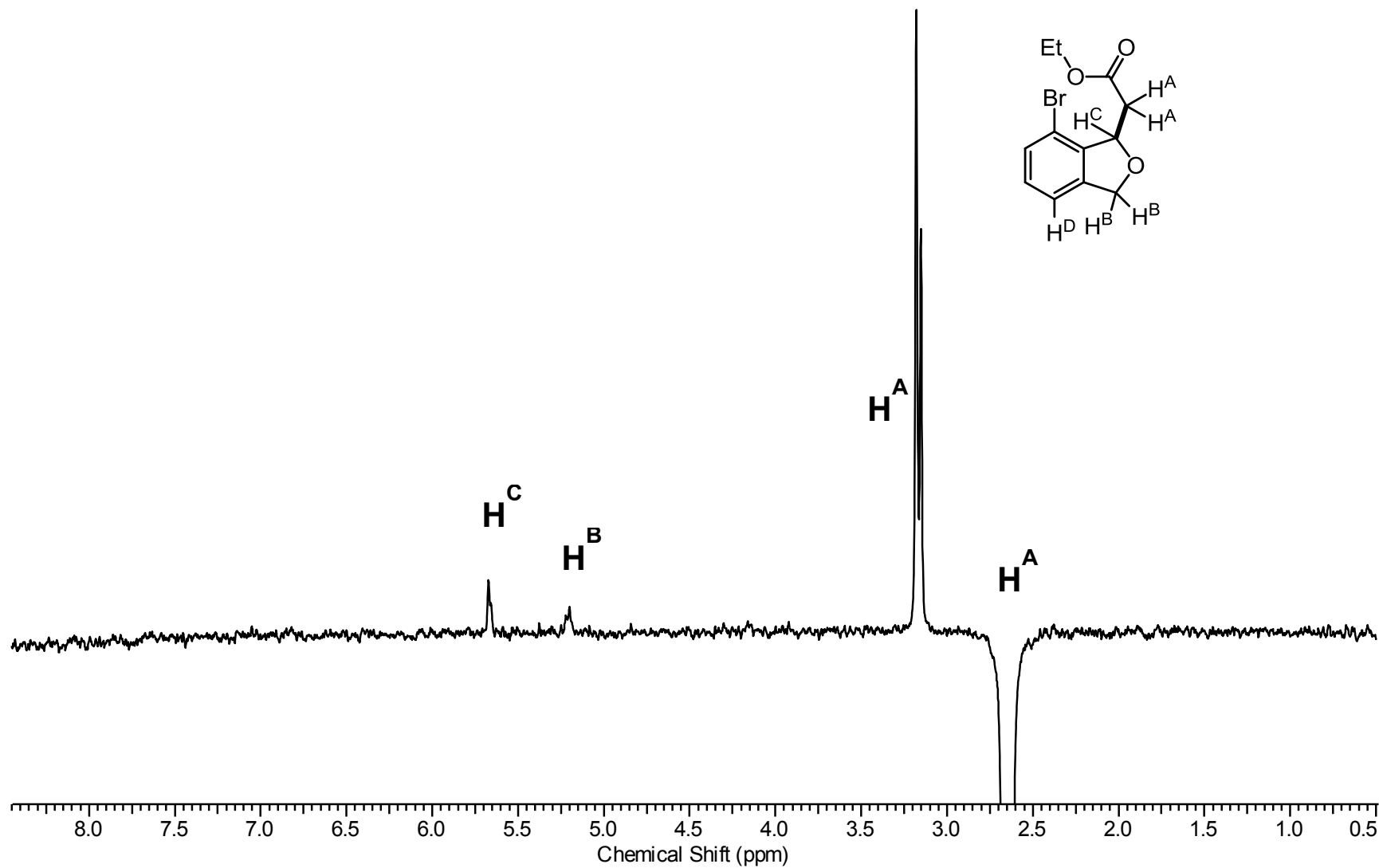
nOe spectra as evidence for **S55** as the drawn regioisomer:



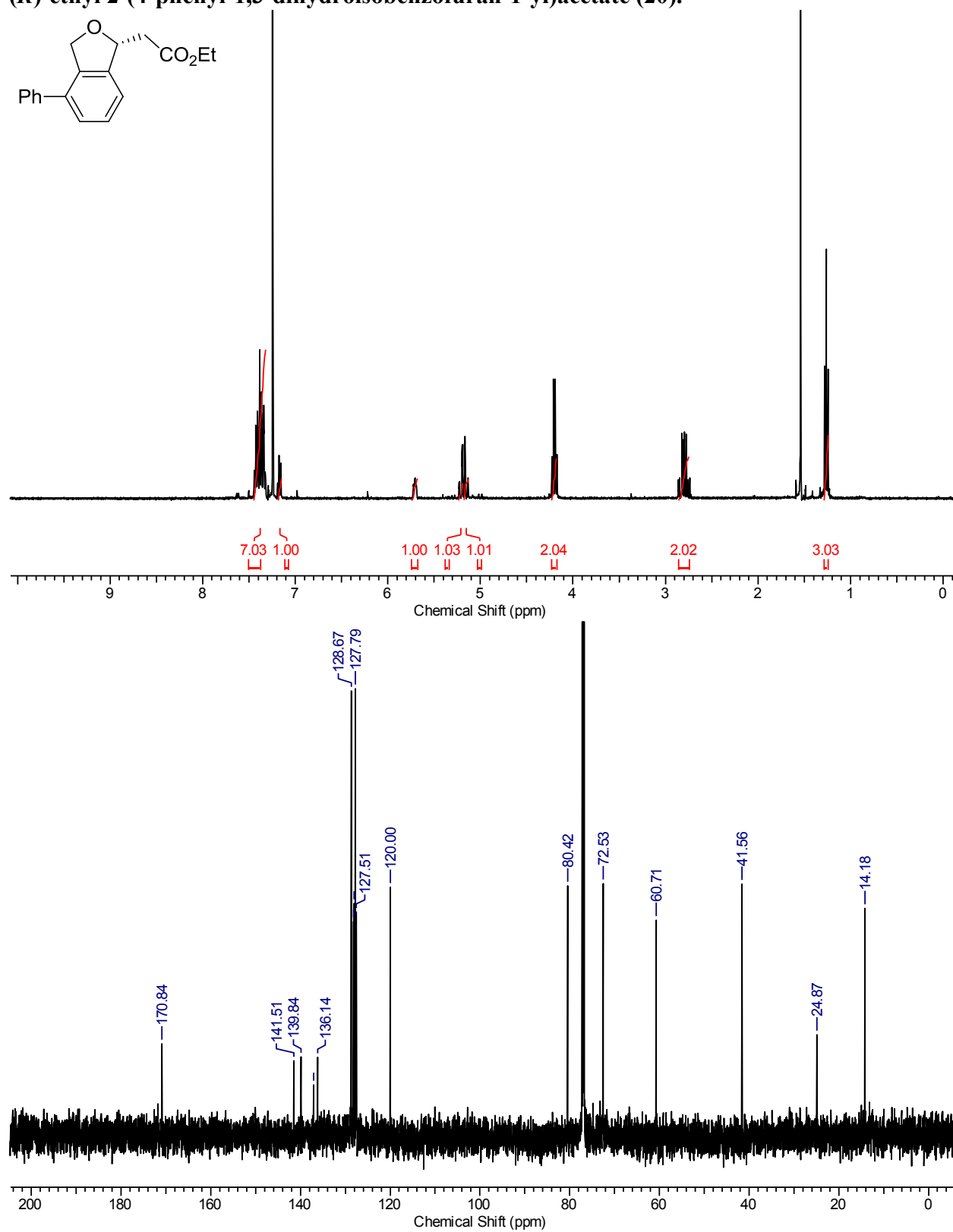




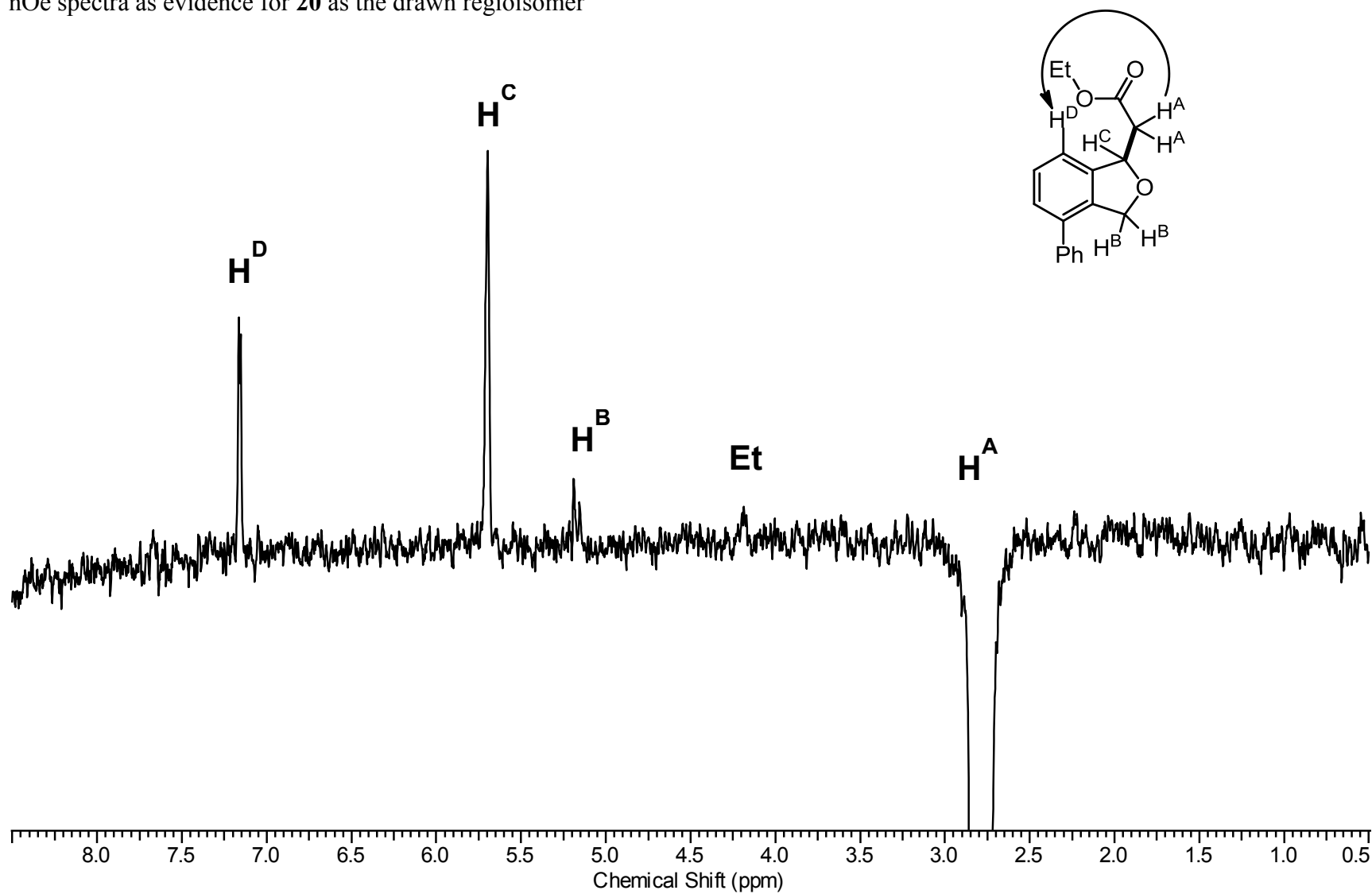


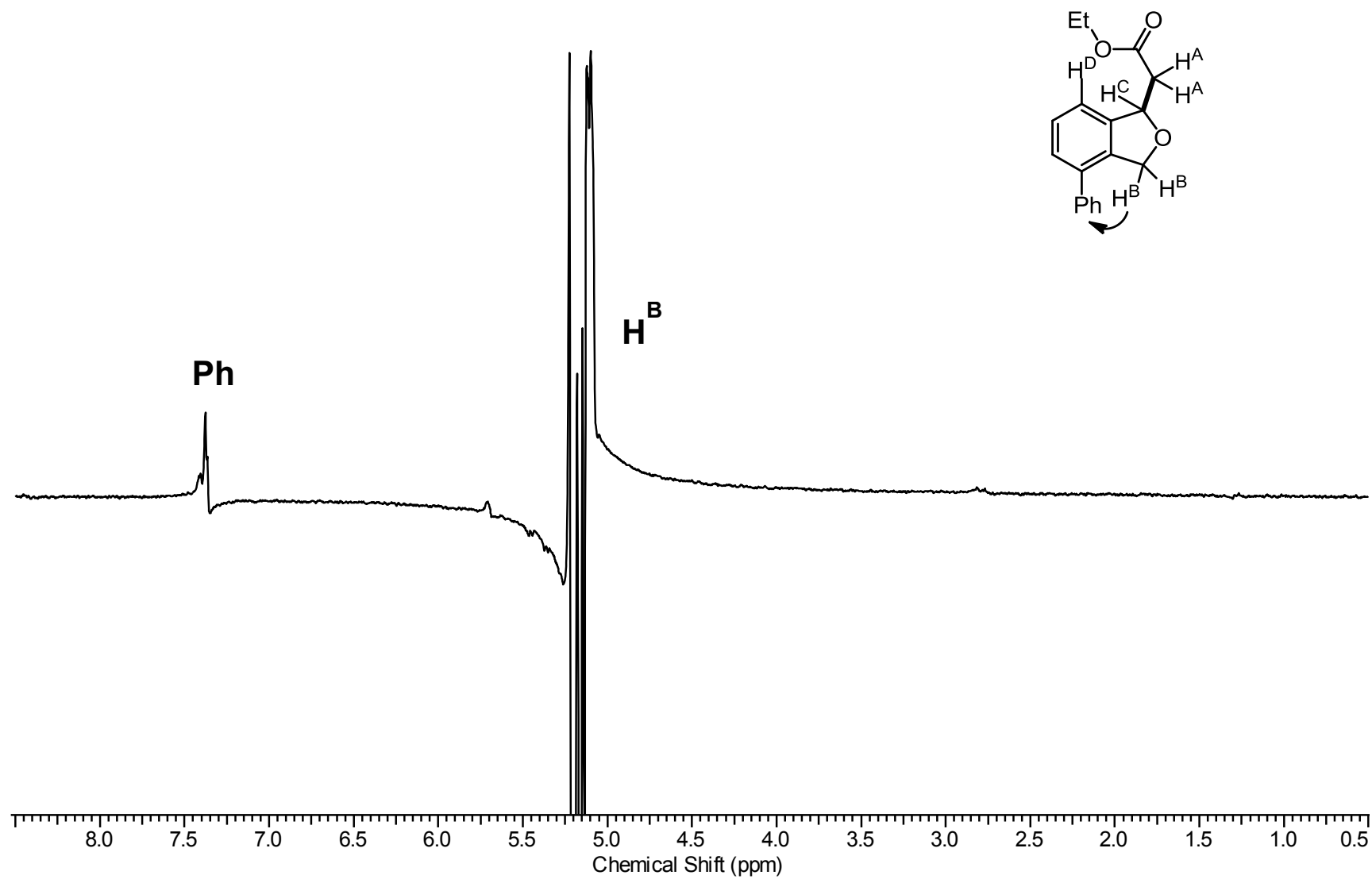


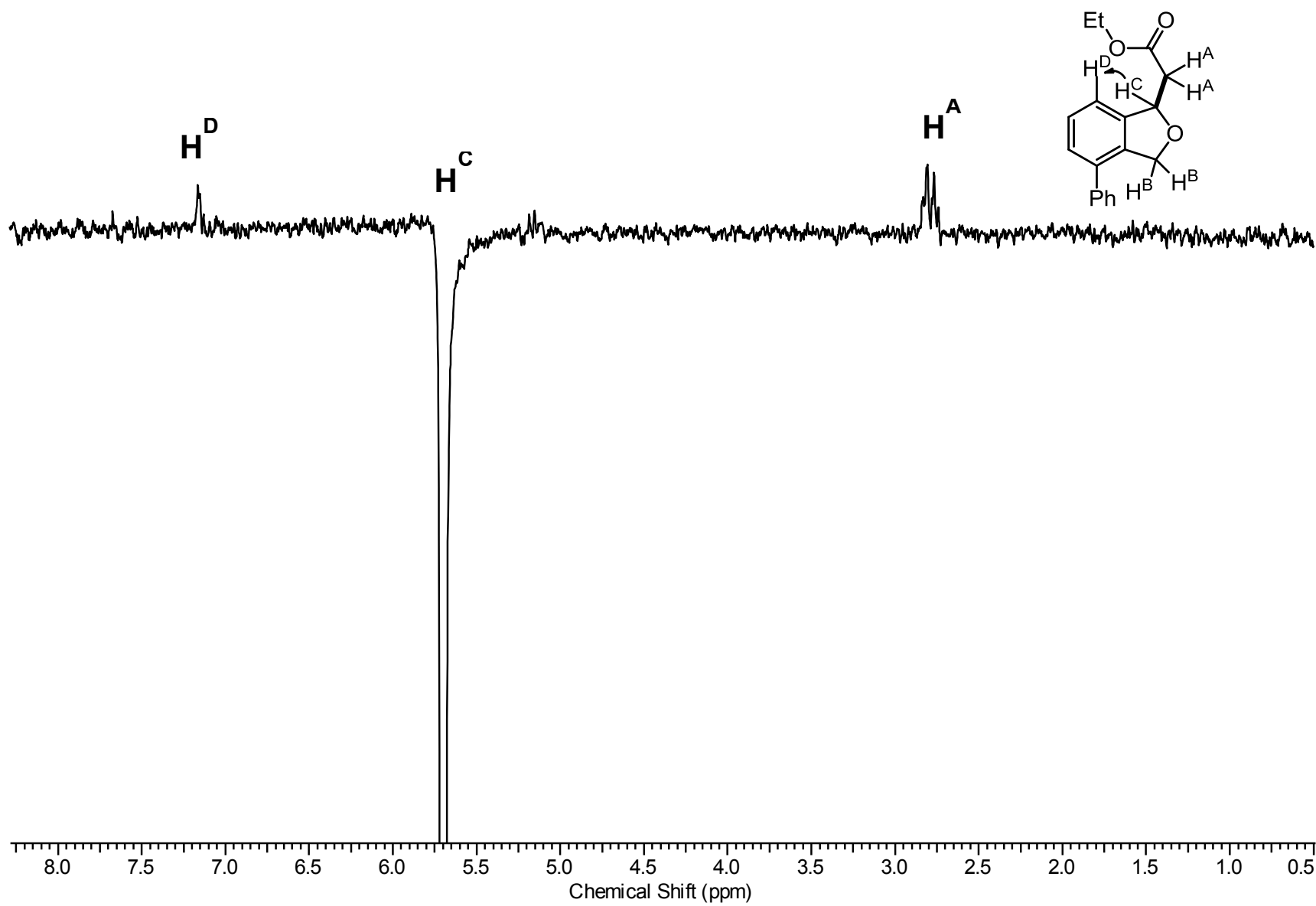
(R)-ethyl 2-(4-phenyl-1,3-dihydroisobenzofuran-1-yl)acetate (20).

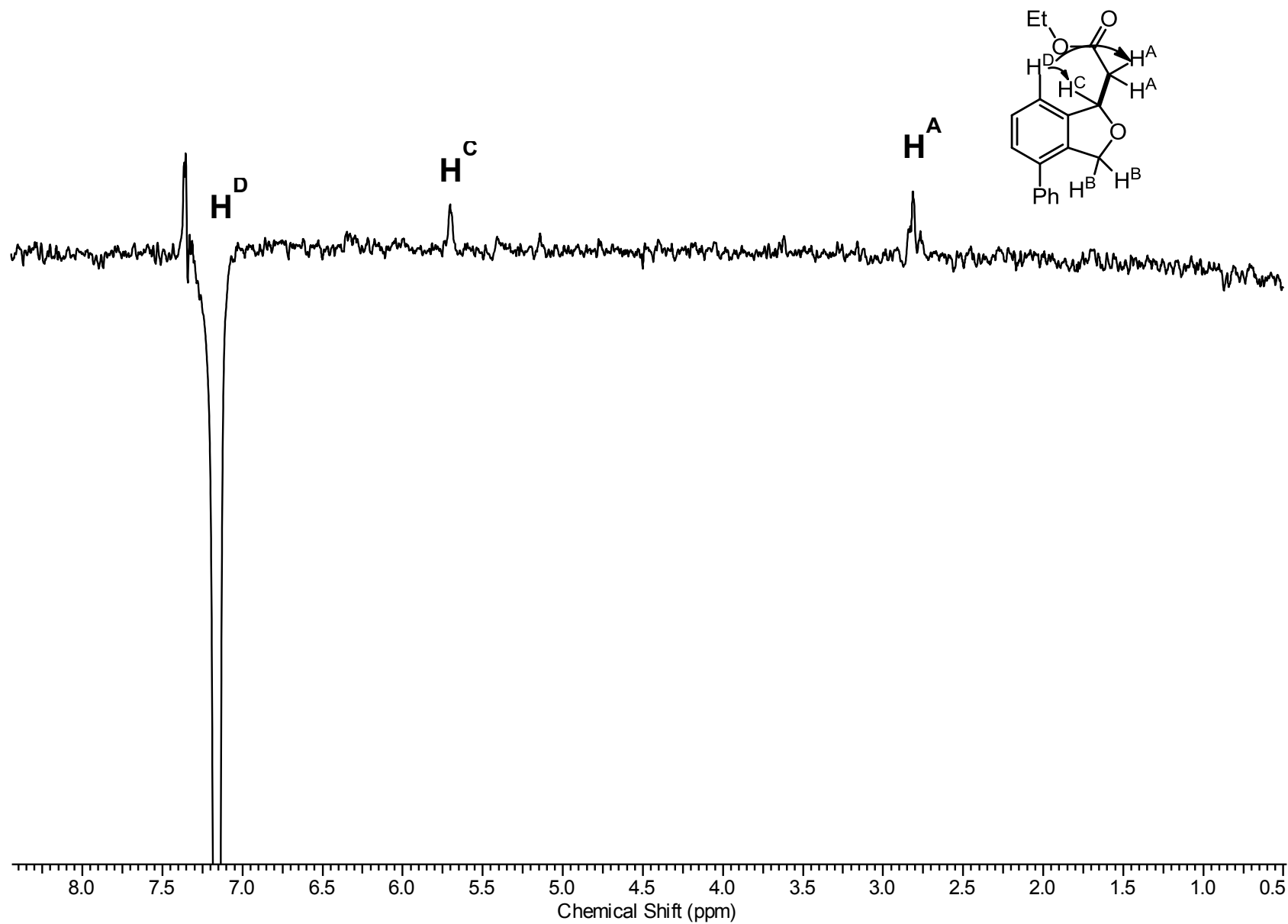


nOe spectra as evidence for **20** as the drawn regioisomer

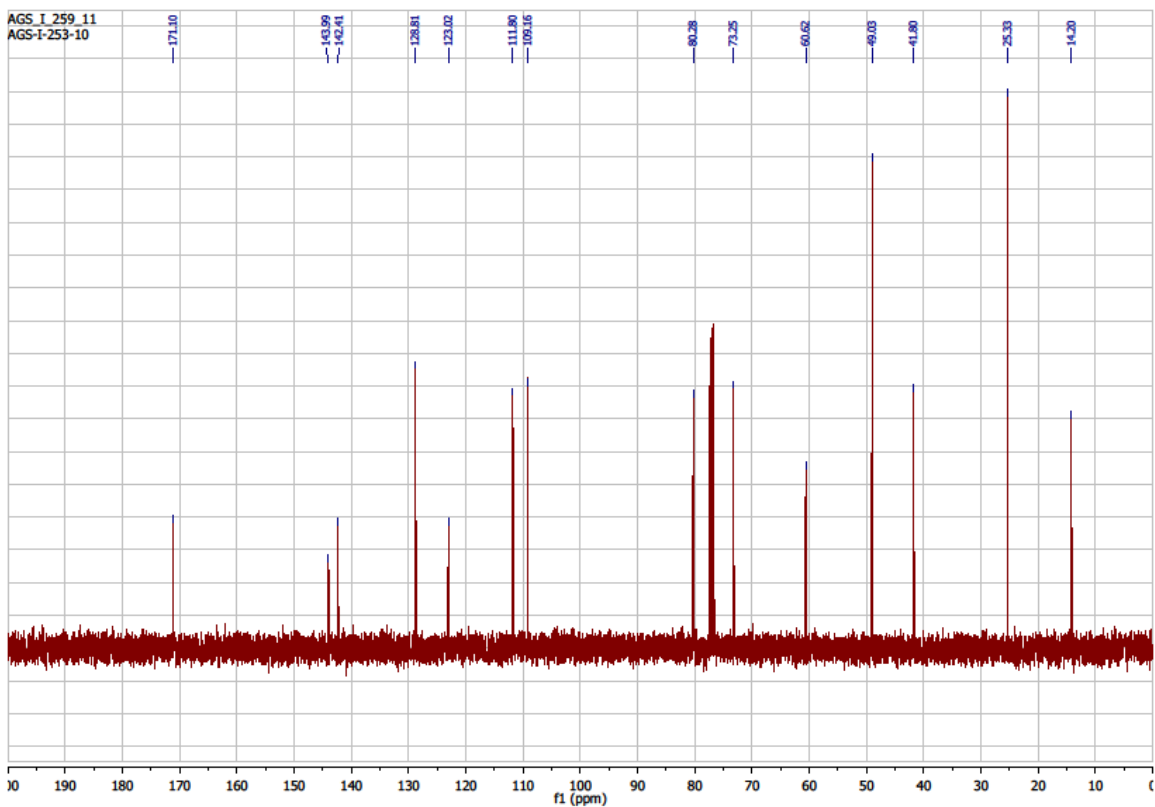
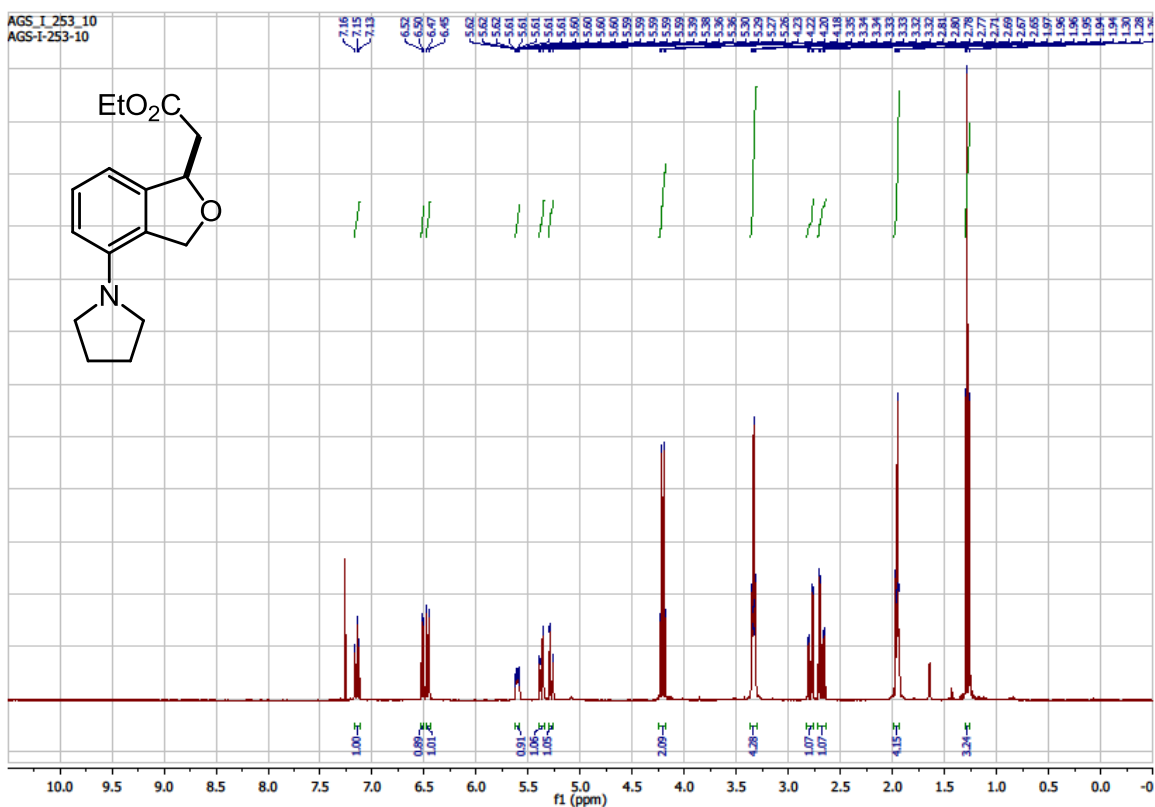




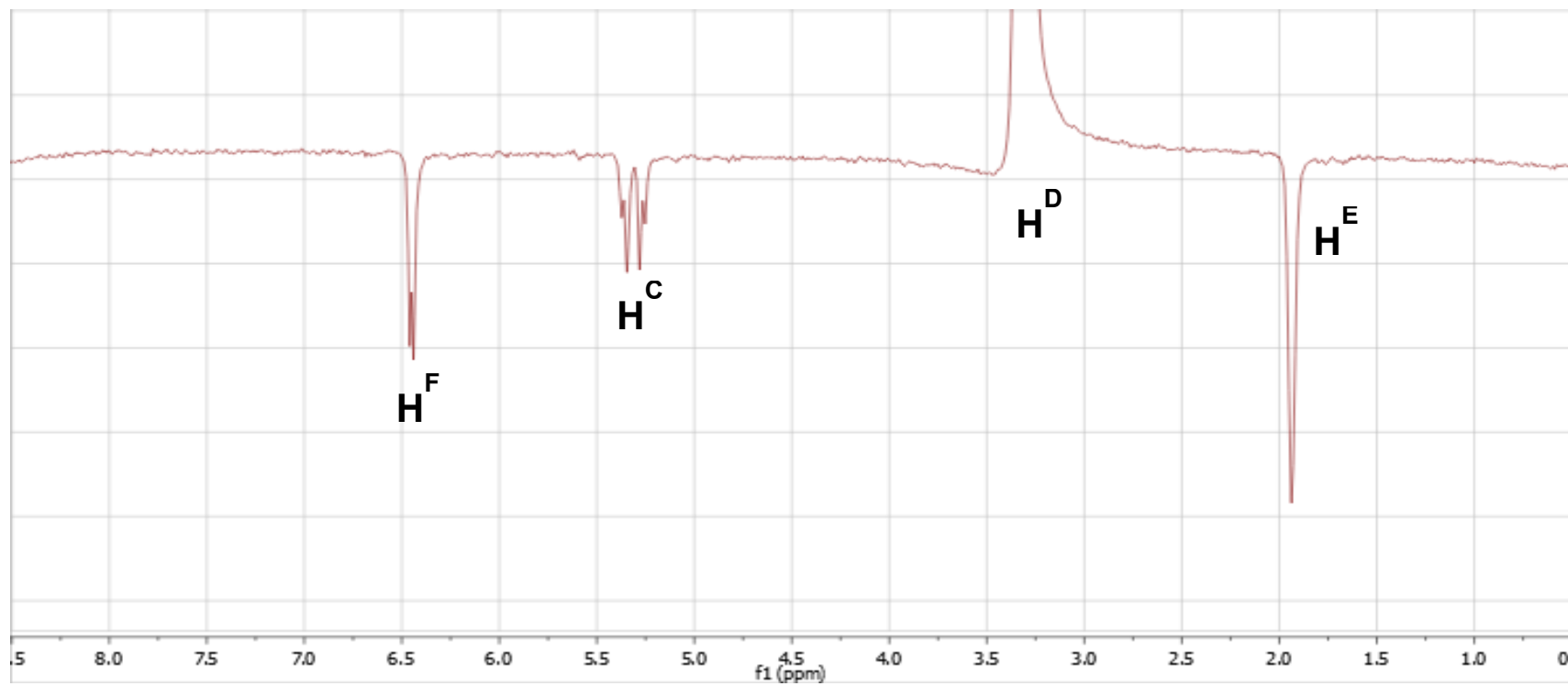
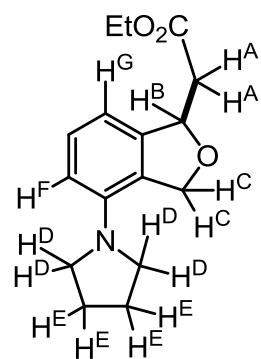




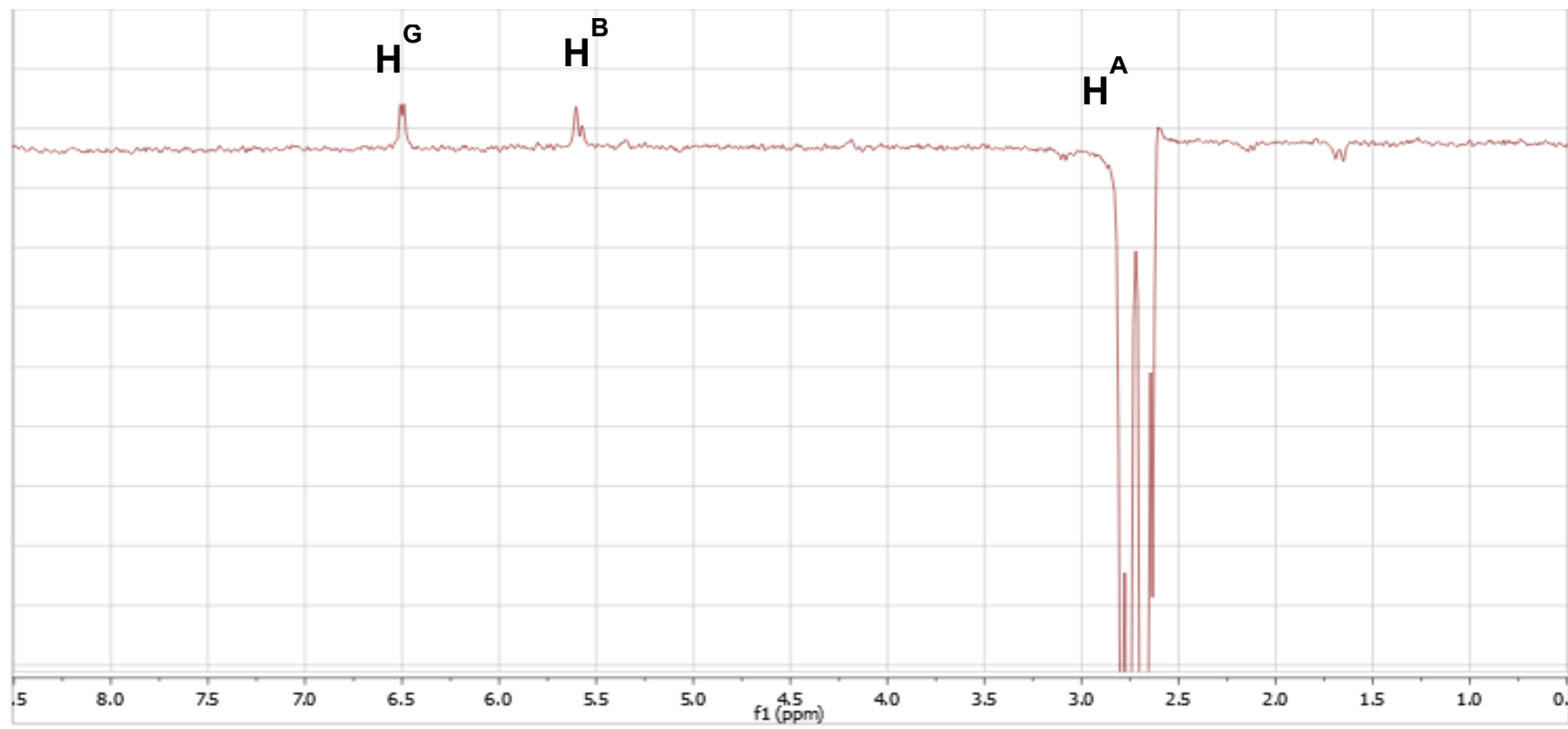
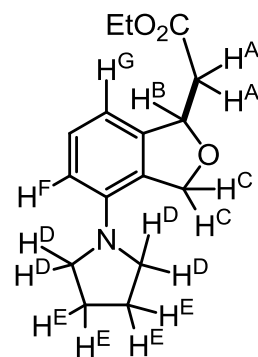
(R)-ethyl 2-(4-(pyrrolidin-1-yl)-1,3-dihydroisobenzofuran-1-yl)acetate (21).



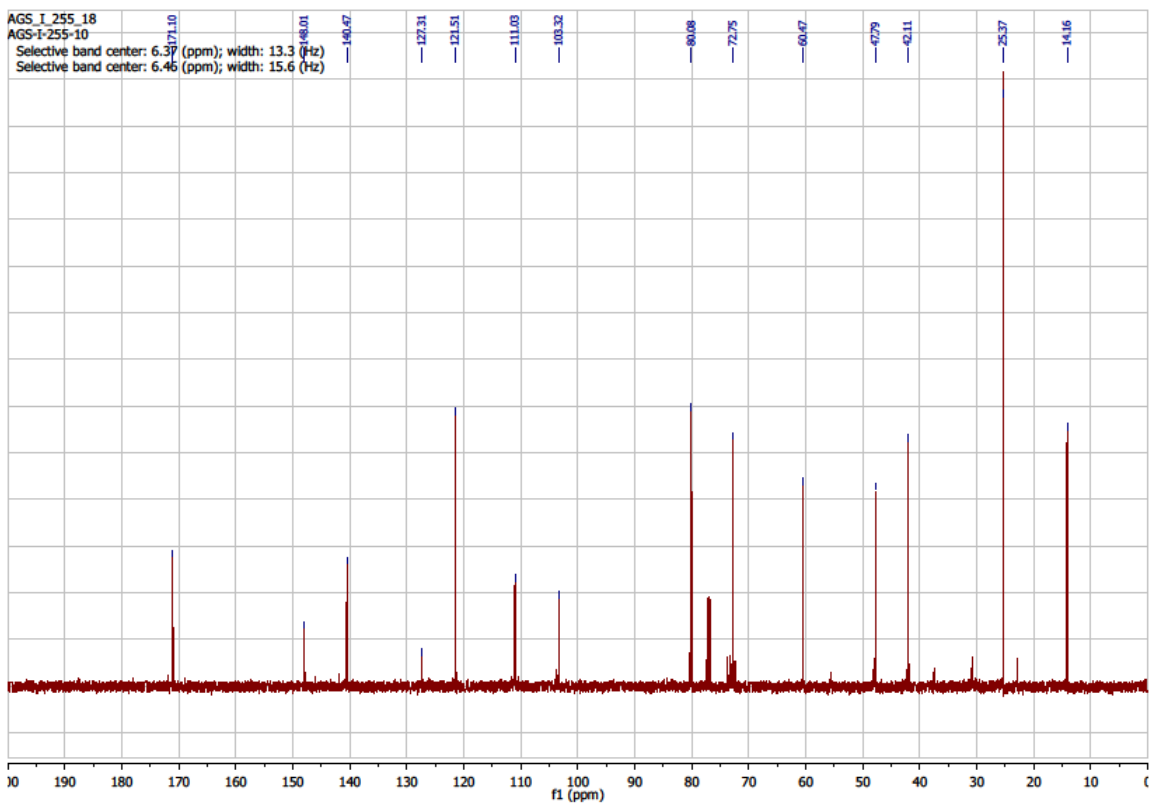
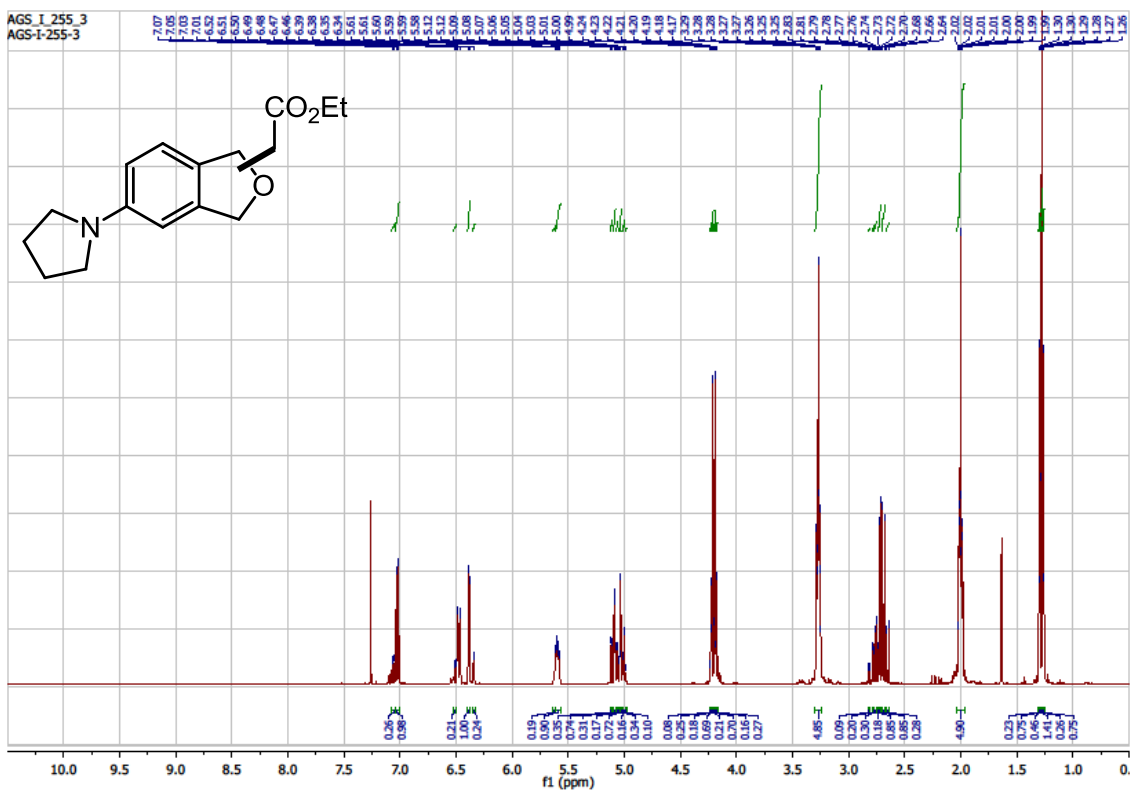
nOe spectra as evidence for **21** as the drawn regioisomer:



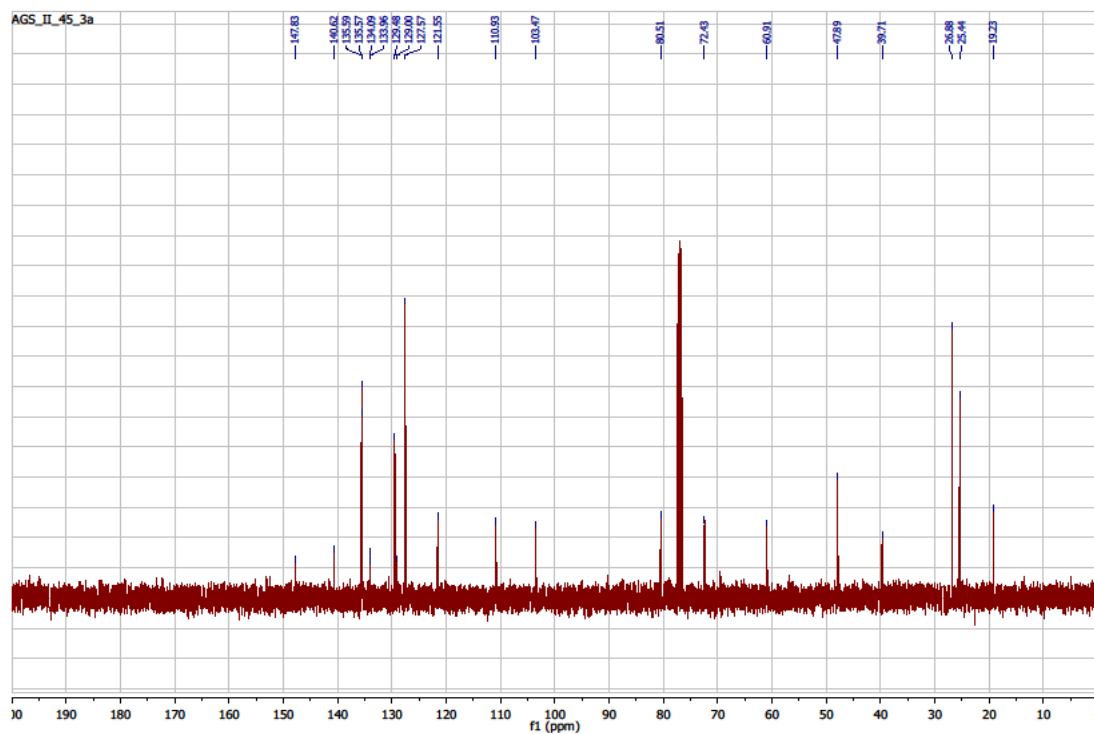
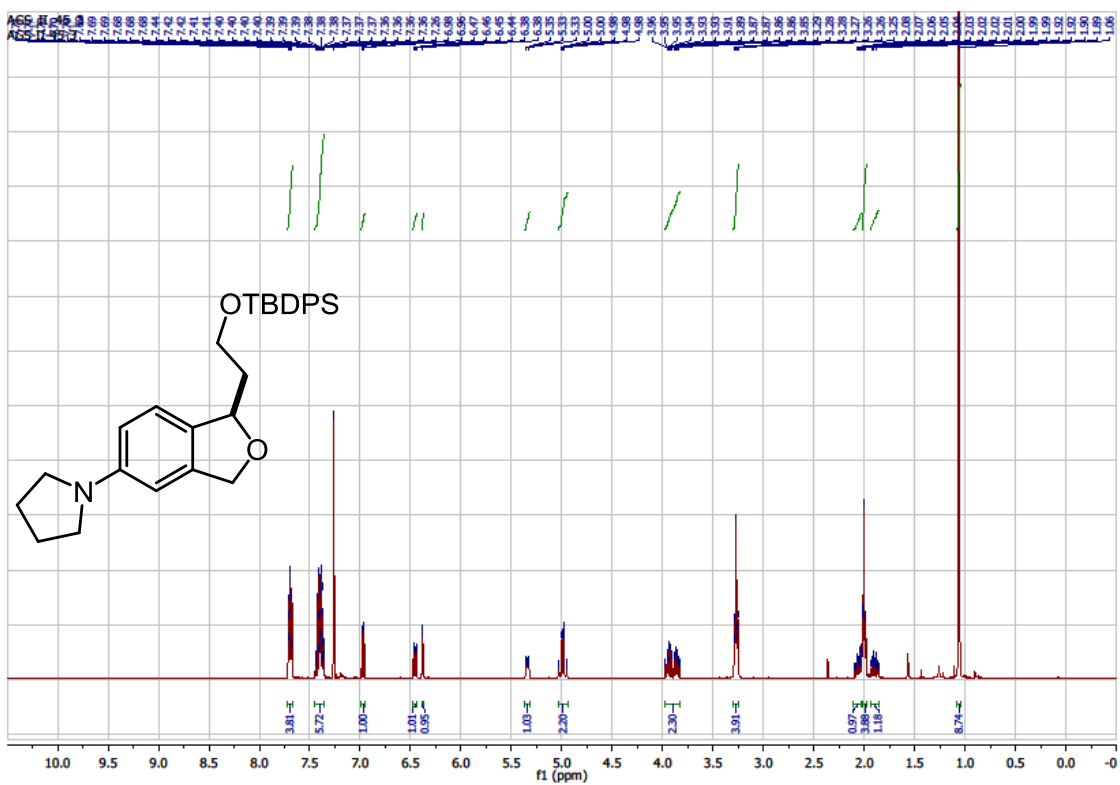
nOe spectra as evidence for **21** as the drawn regioisomer:



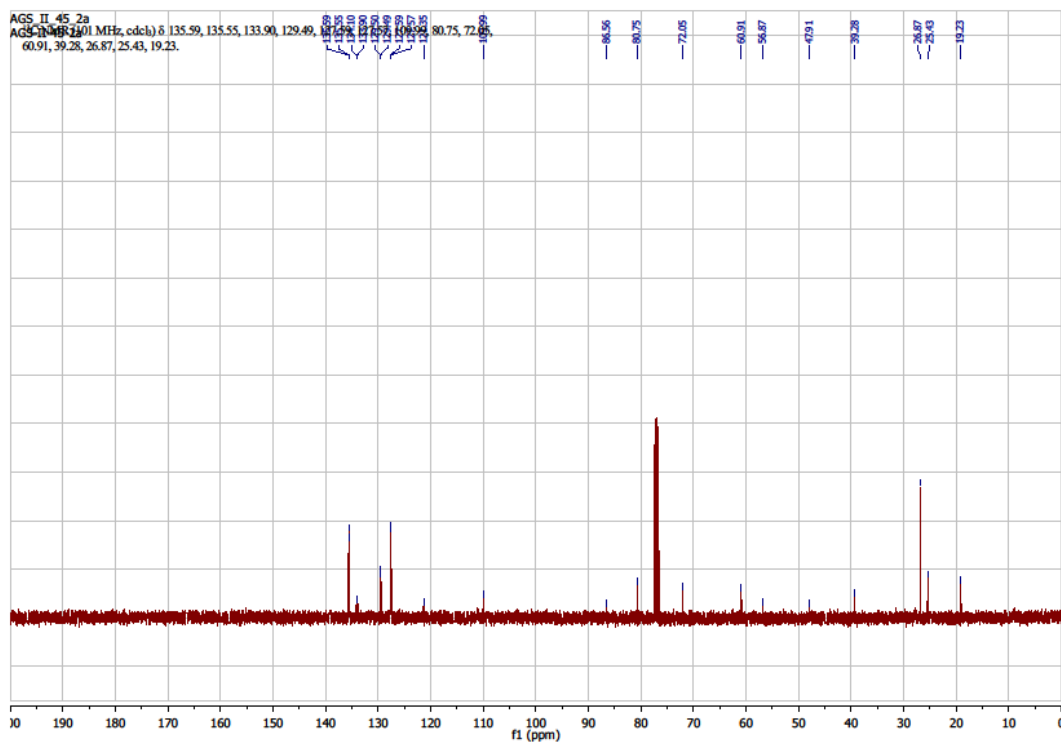
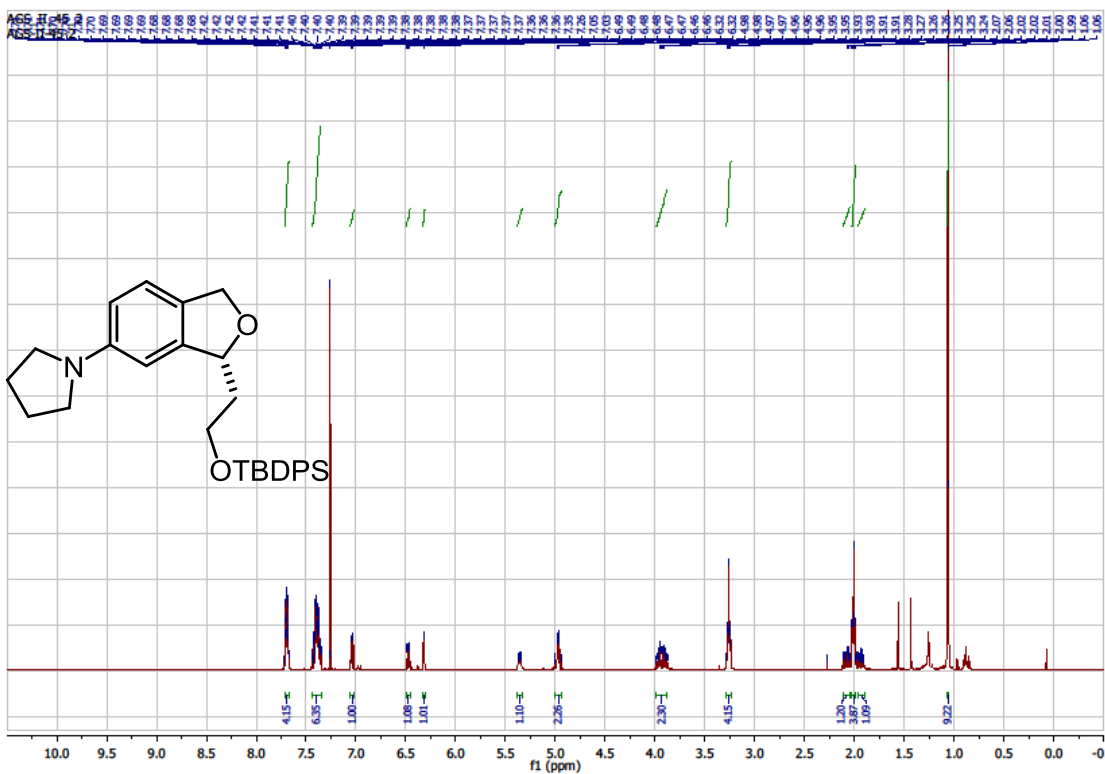
(R)-ethyl 2-(5-(pyrrolidin-1-yl)-1,3-dihydroisobenzofuran-1-yl)acetate, mix of regioisomers (22).



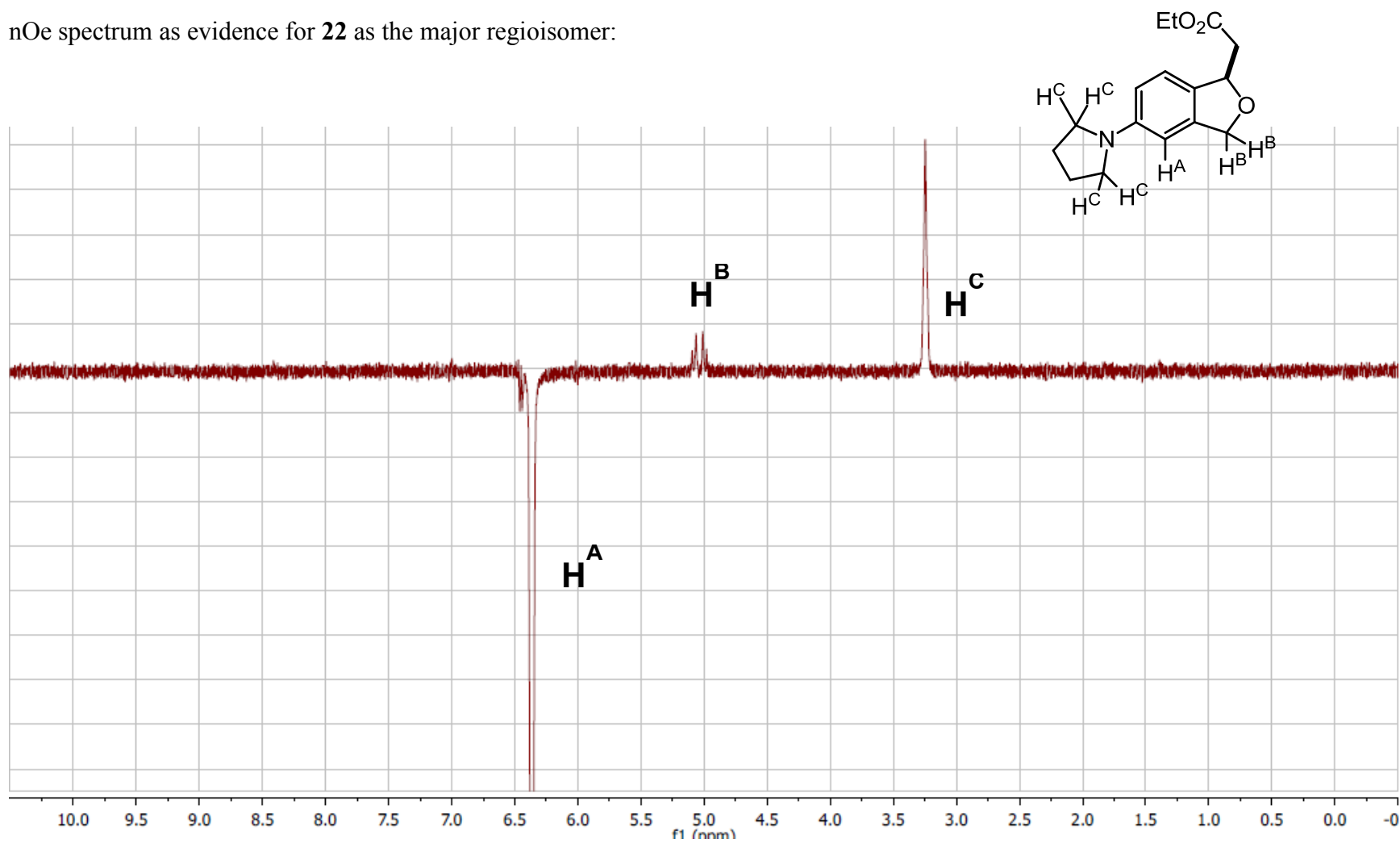
(R)-1-(1-(2-((*tert*-butyldiphenylsilyl)oxy)ethyl)-1,3-dihydroisobenzofuran-5-yl)pyrrolidine



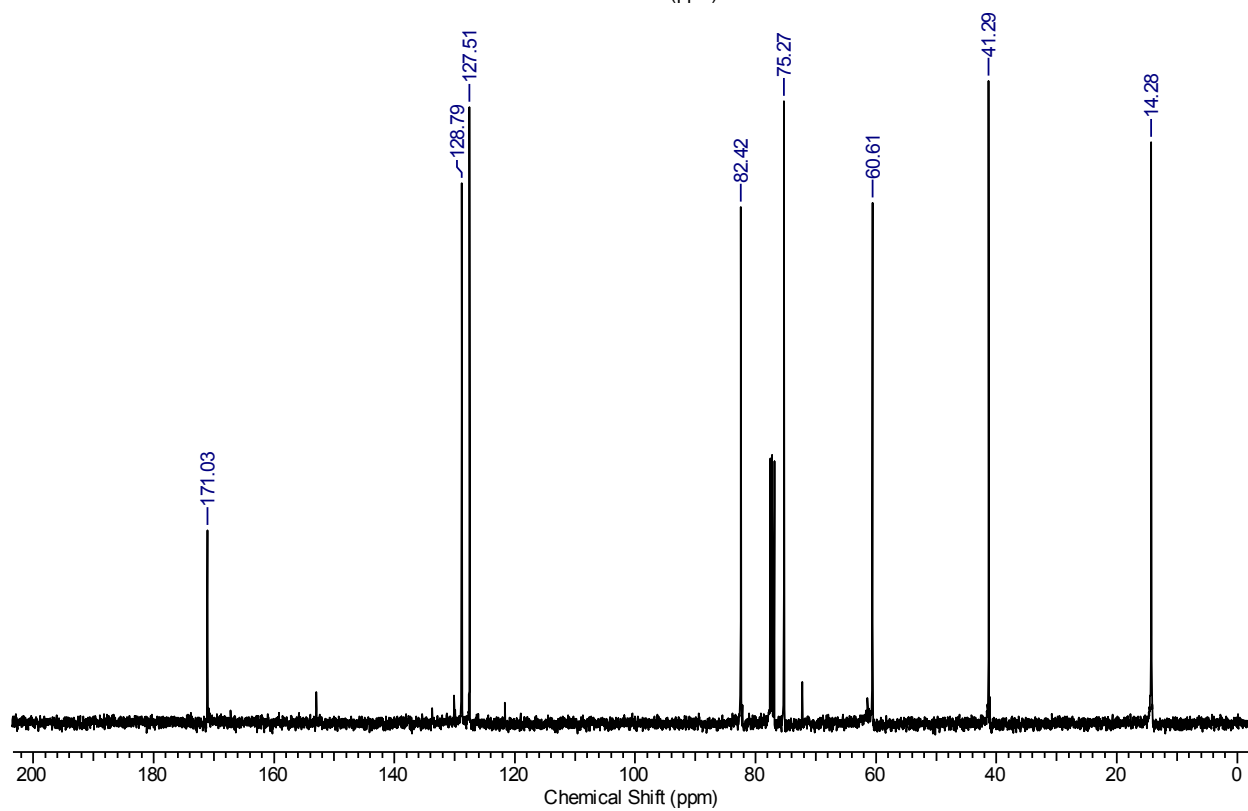
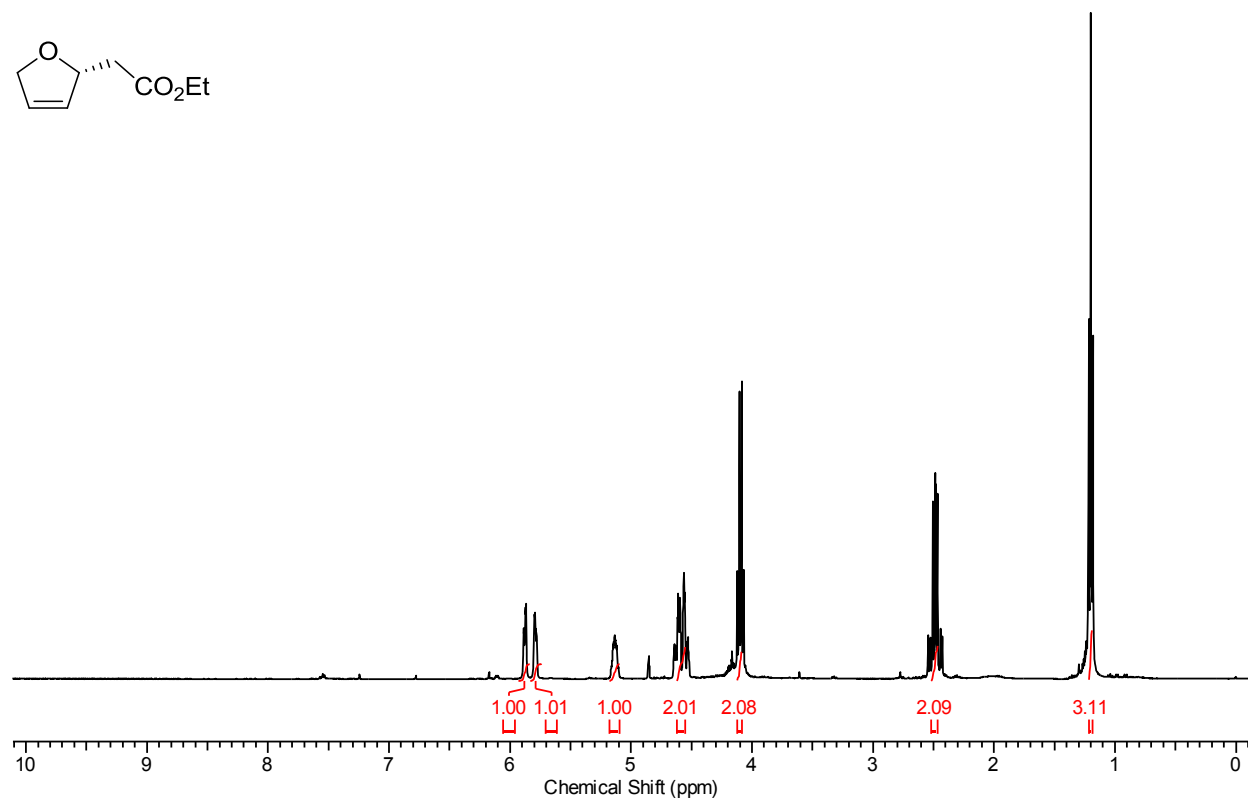
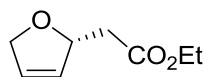
(*R*)-1-(3-(2-(((*tert*-butyldiphenylsilyl)oxy)ethyl)-1,3-dihydroisobenzofuran-5-yl)pyrrolidine



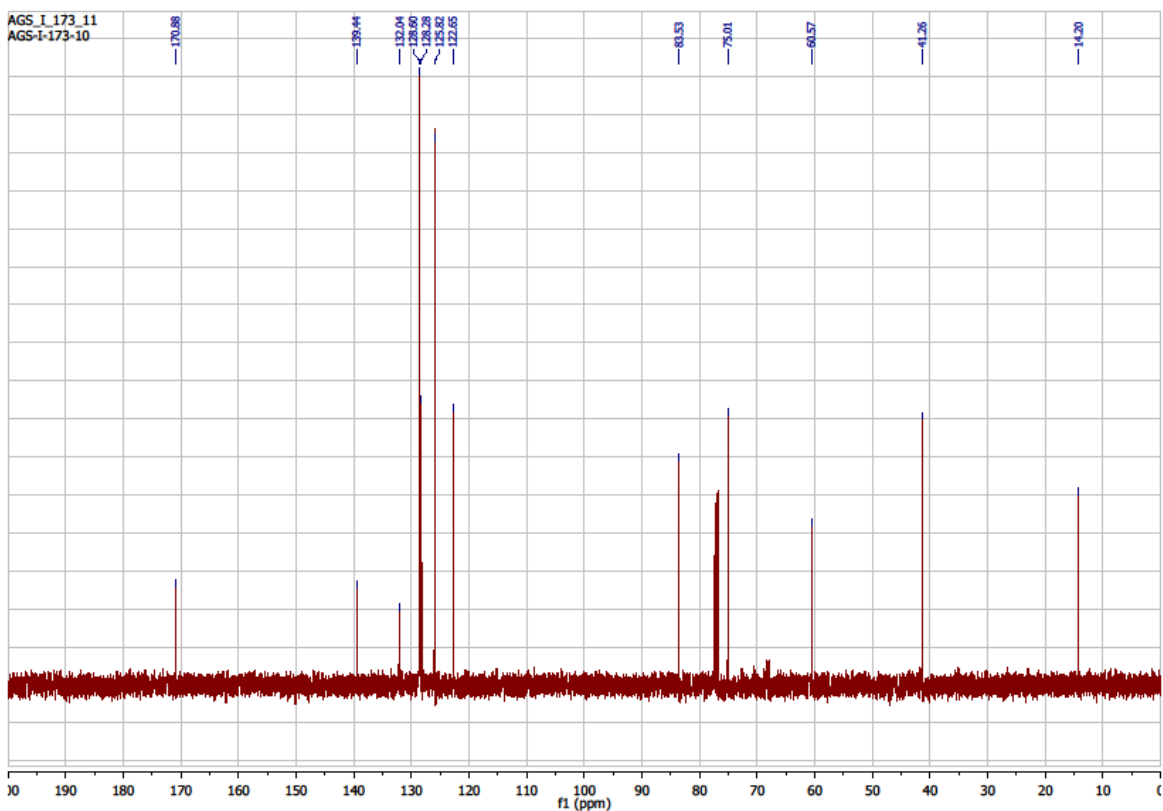
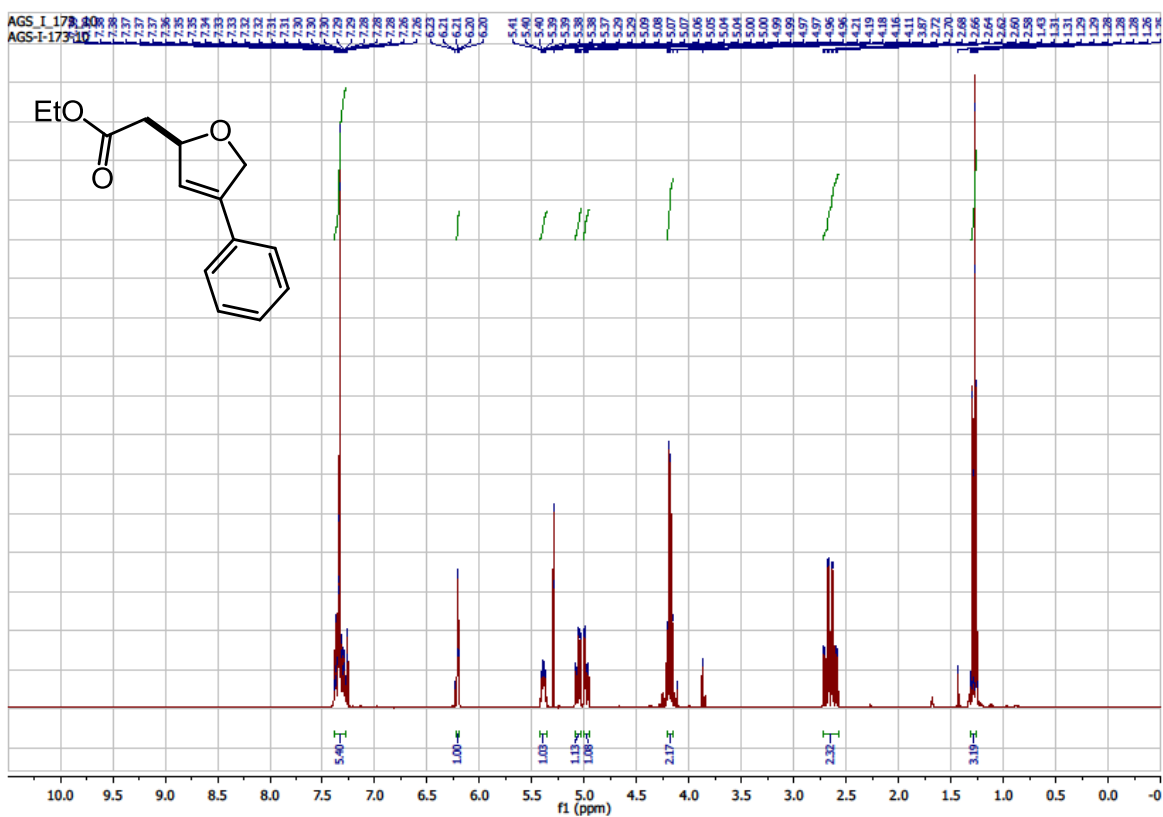
nOe spectrum as evidence for **22** as the major regioisomer:



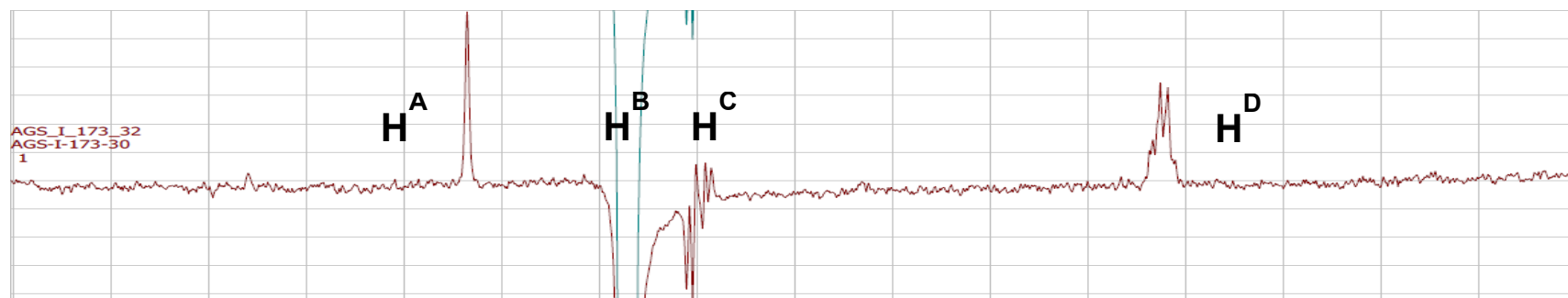
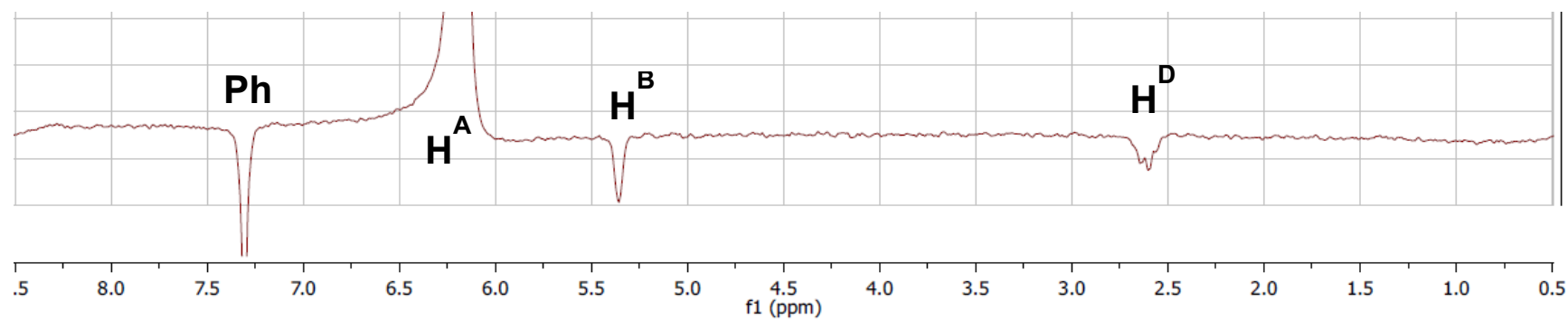
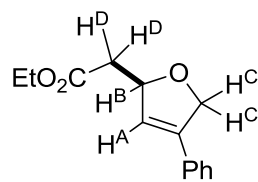
(*R*)-ethyl 2-(2,5-dihydrofuran-2-yl)acetate (23).



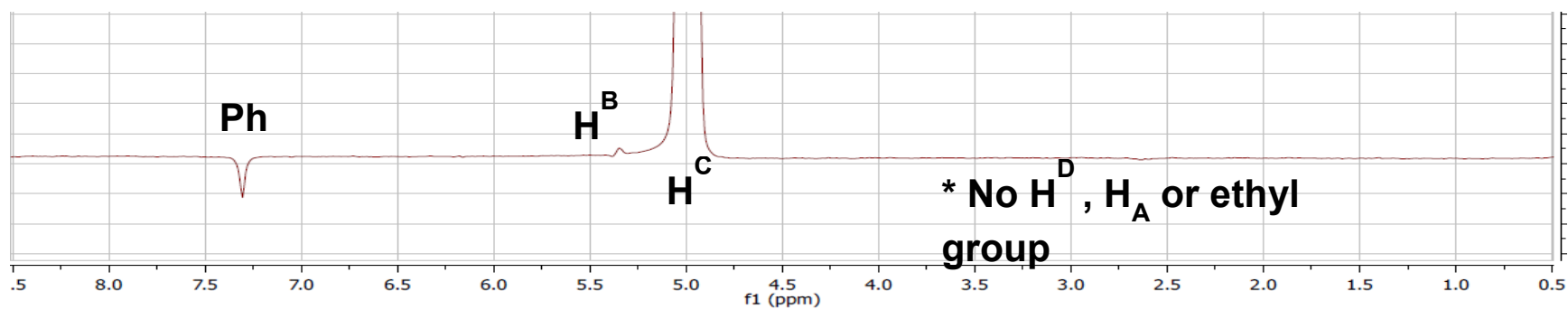
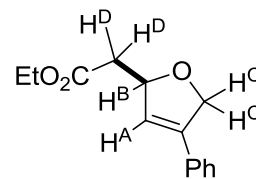
(R)-ethyl 2-(4-phenyl-2,5-dihydrofuran-2-yl)acetate (24).



nOe spectra as evidence for **24** as the drawn regioisomer:

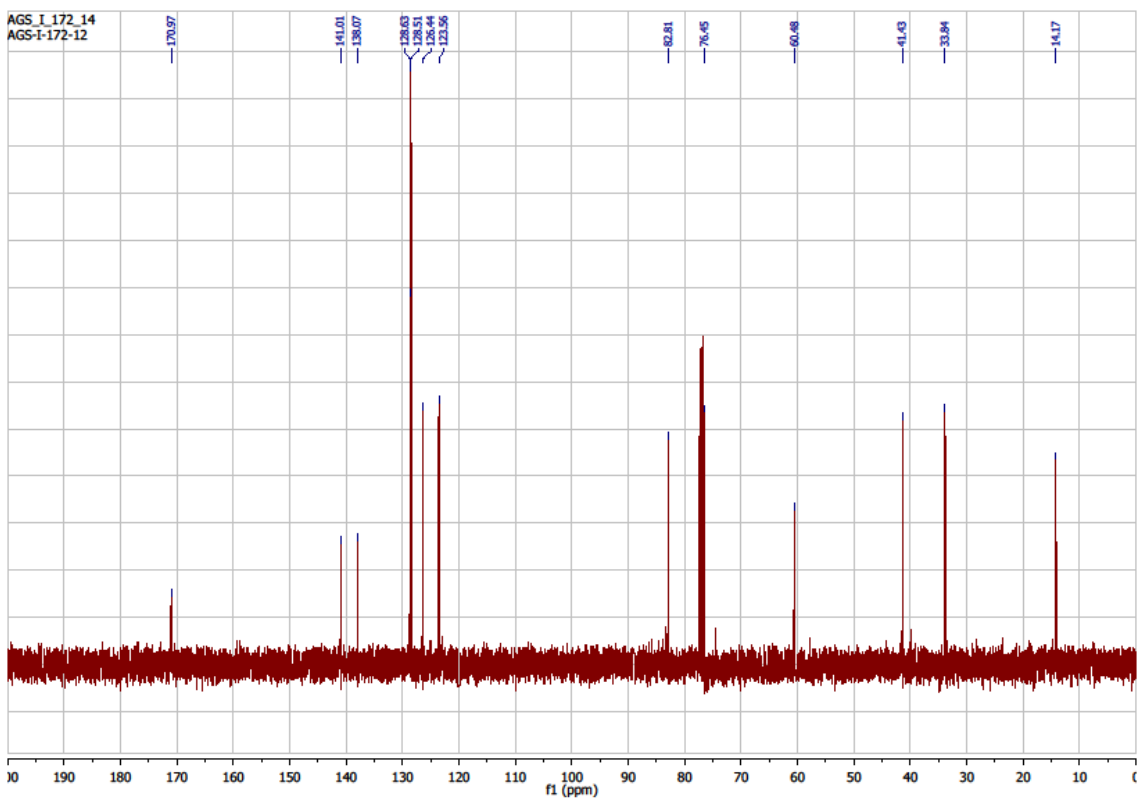
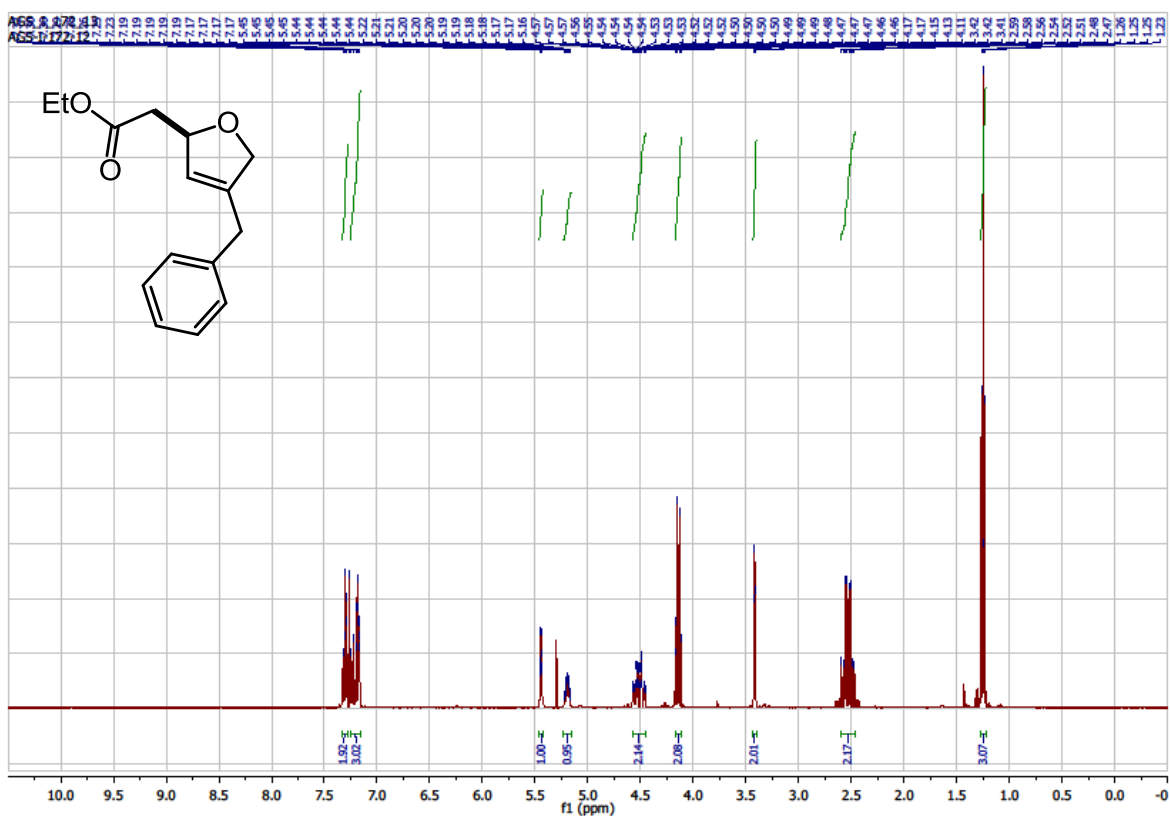


nOe spectra as evidence for **24** as the drawn regioisomer:

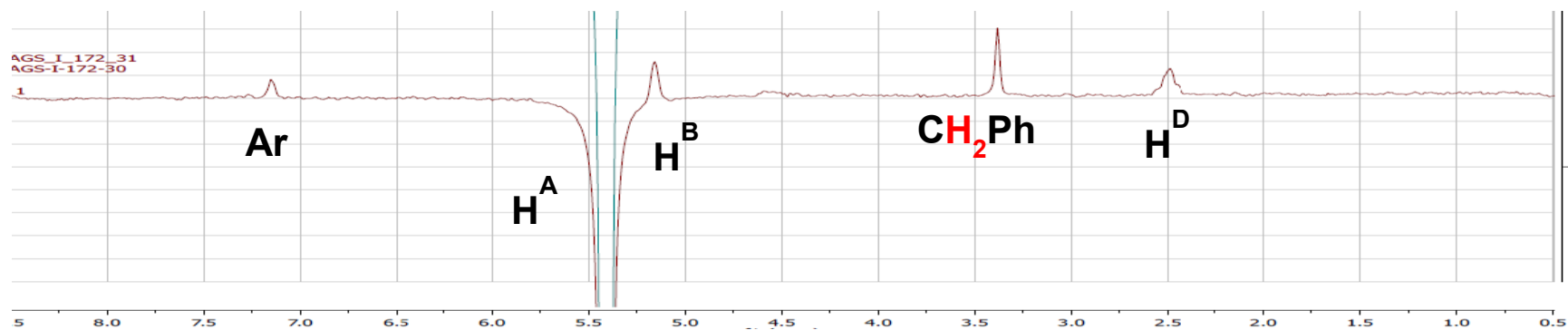
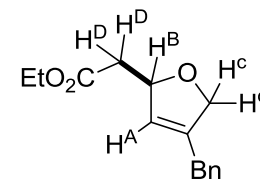


* No H^C or Ph

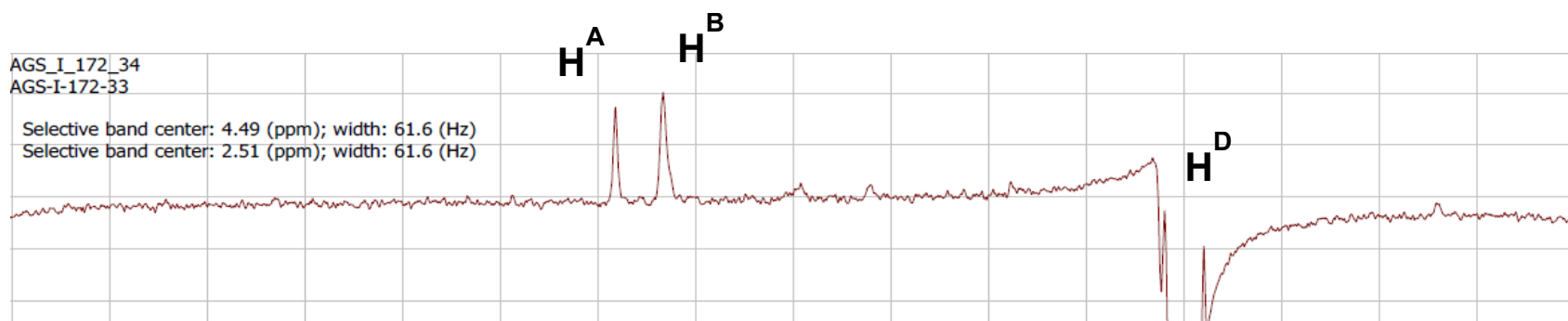
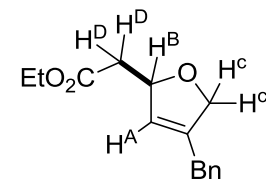
(*R*)-ethyl 2-(4-benzyl-2,5-dihydrofuran-2-yl)acetate (25).

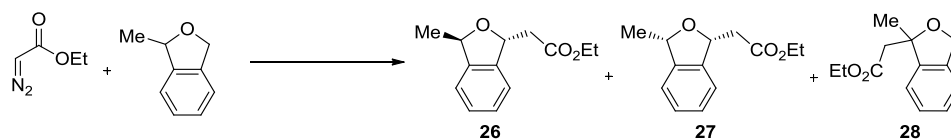


nOe spectra as evidence for drawn reg nOe spectra as evidence for **25** as the drawn regioisomer:



nOe spectra as evidence for drawn reg nOe spectra as evidence for **25** as the drawn regioisomer:

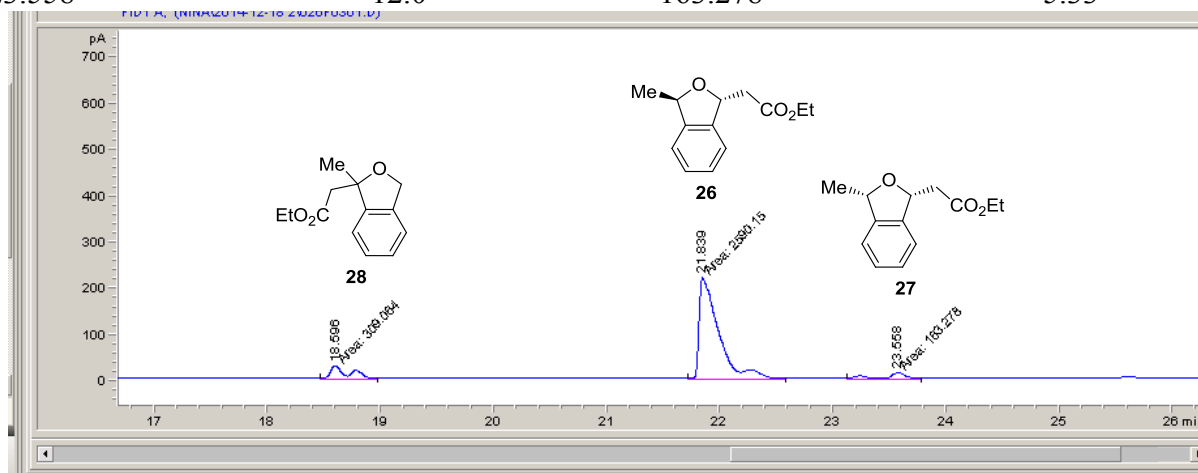




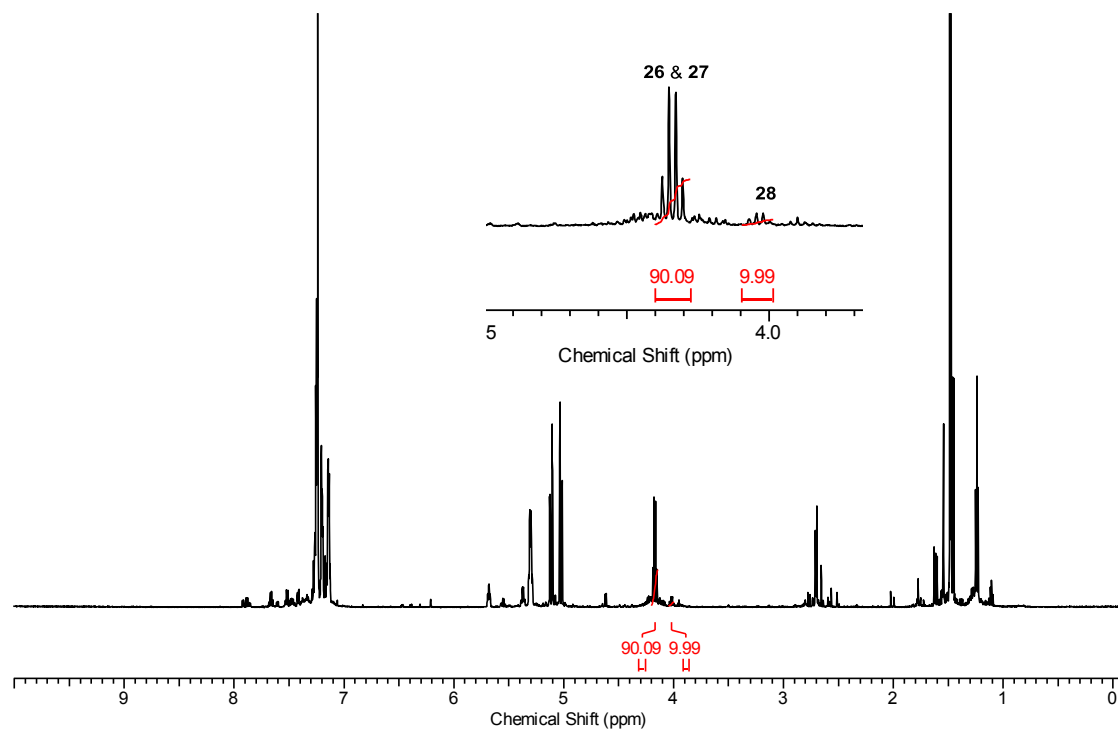
Chiral GC Traces

GC (CHIRASIL DEX, 120 $\rightarrow$ 140 $^{\circ}\text{C}$, 1 $^{\circ}\text{C}/\text{min}$) $t_{\text{r}}(\mathbf{28}) = 18.596 \text{ min}$, $t_{\text{r}}(\mathbf{26}) = 21.839 \text{ min}$, $t_{\text{r}}(\mathbf{27}) = 23.556 \text{ min}$

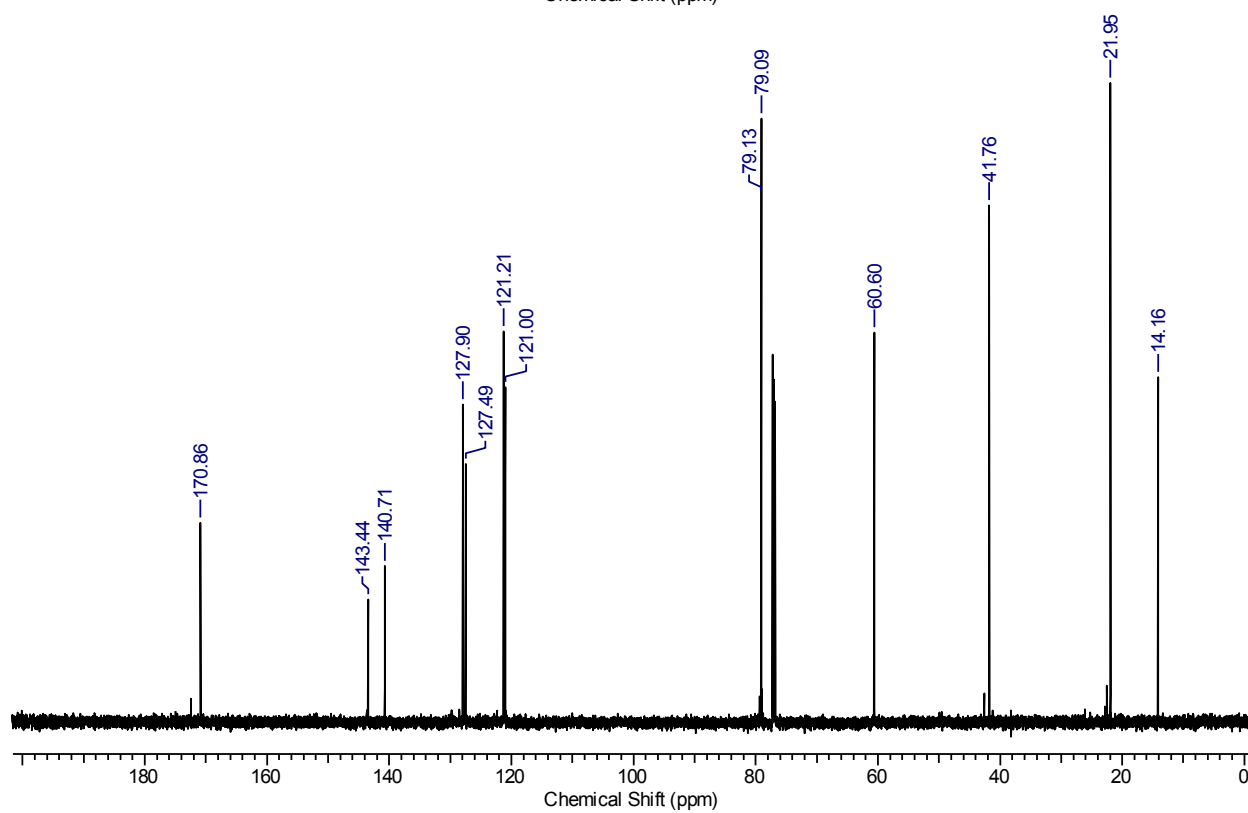
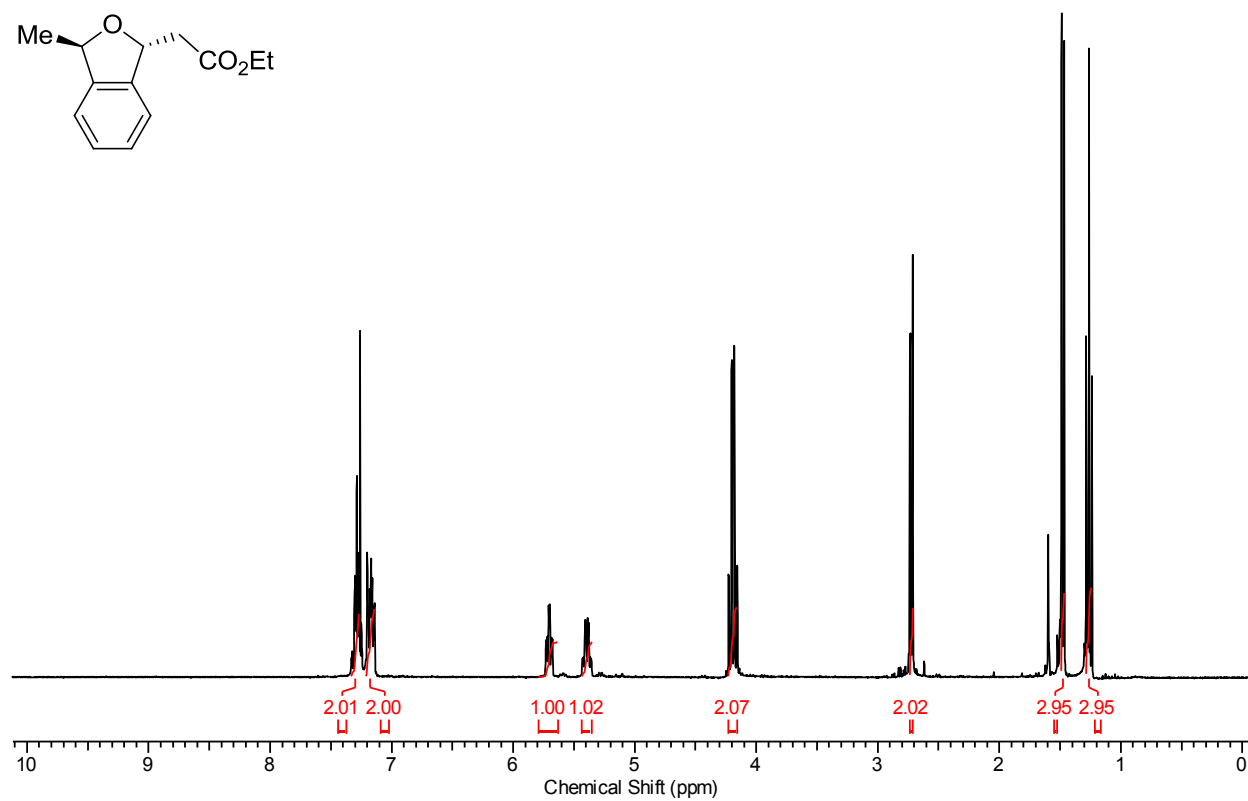
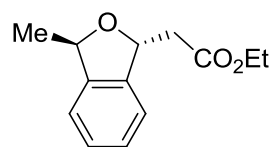
Time [Min]	Height [pA]	Area [pA.Min]	Area [%]
18.596	26.2	309.064	10.09
21.839	217.7	2590.15	84.58
23.558	12.0	163.278	5.33



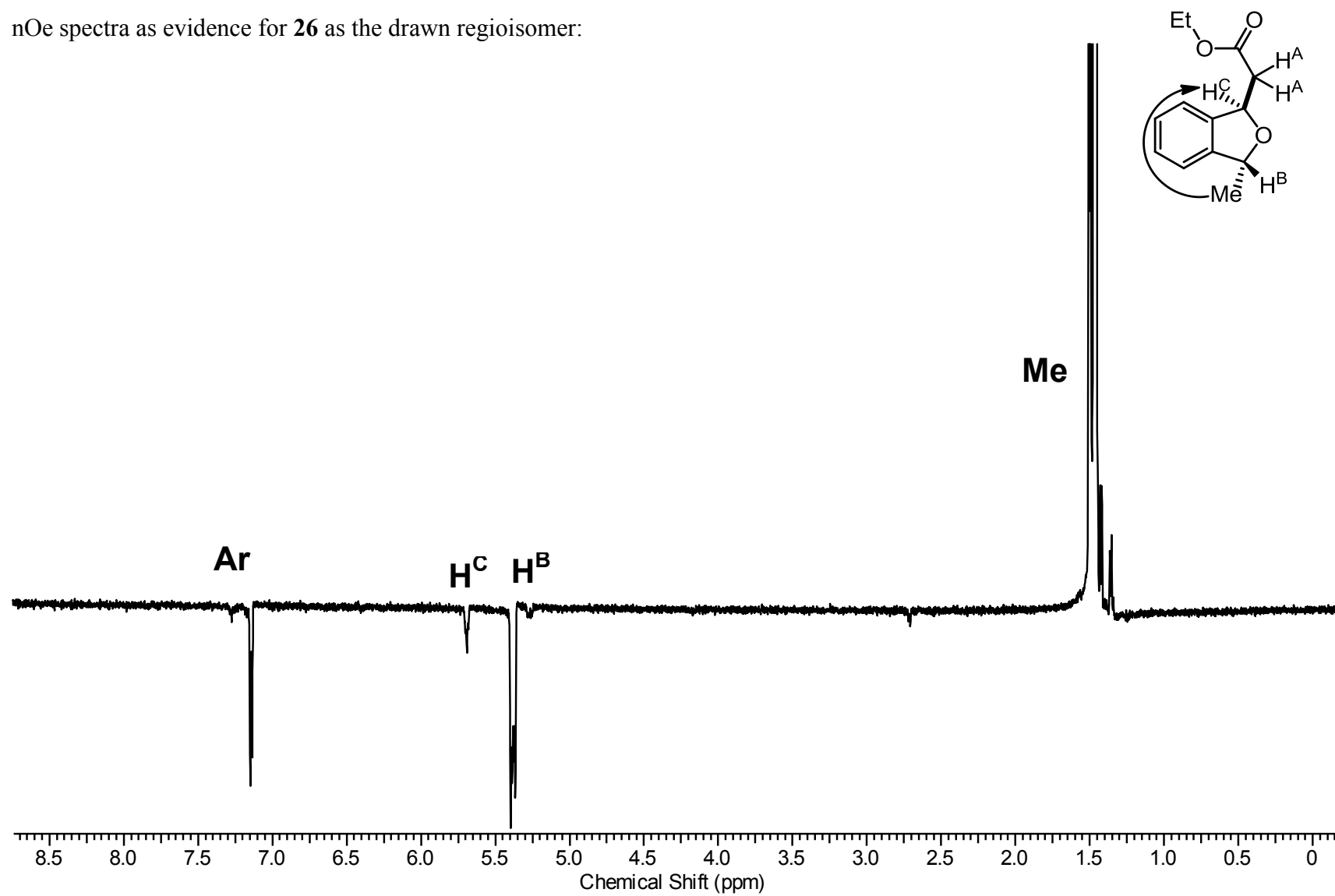
Crude ^1H NMR:

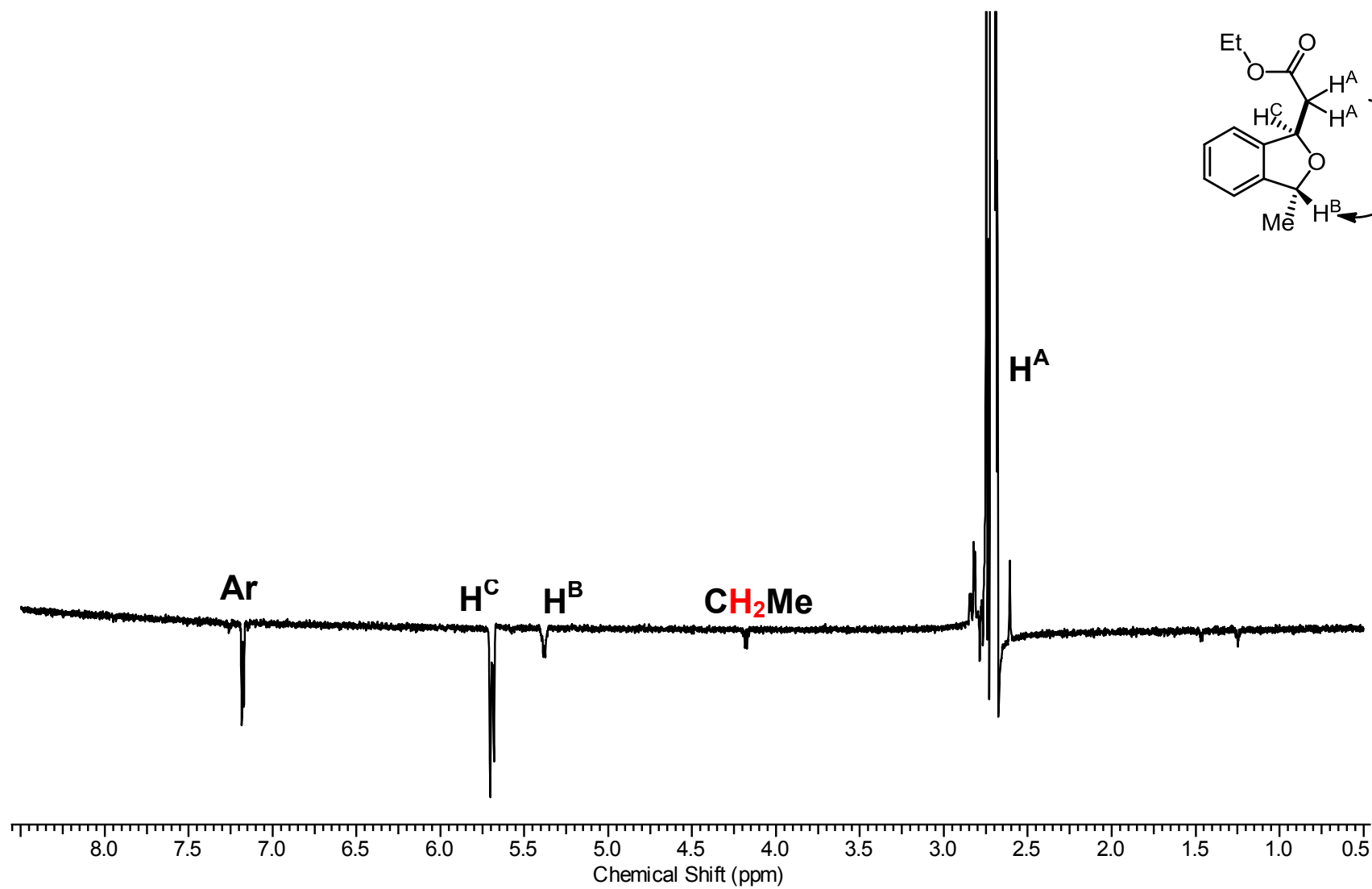


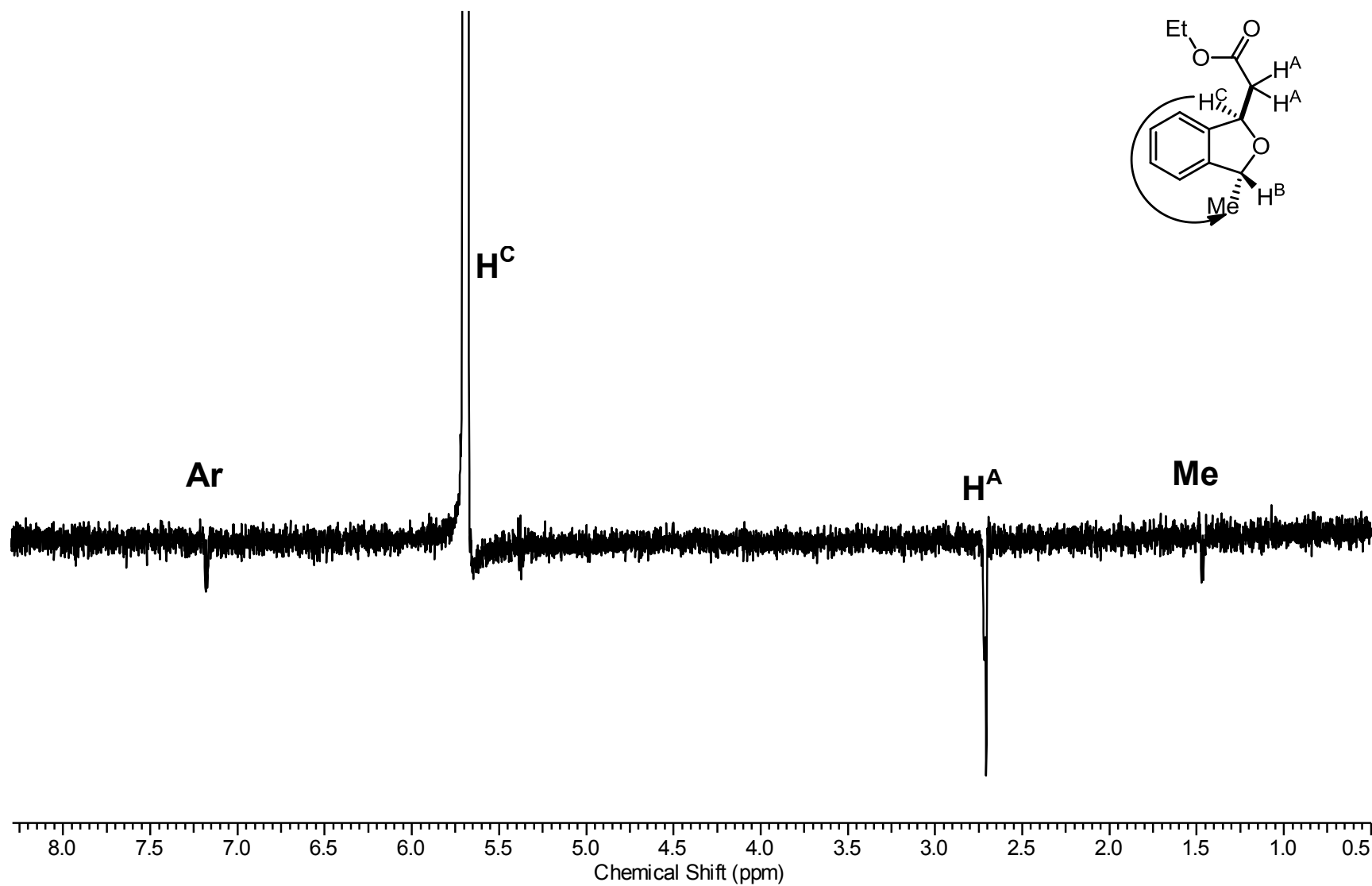
ethyl 2-((1*R*,3*R*)-3-methyl-1,3-dihydroisobenzofuran-1-yl)acetate (26).



nOe spectra as evidence for **26** as the drawn regioisomer:







(S)-2-(tetrahydrofuran-2-yl)ethyl 3,5-dinitrobenzoate (S56).

