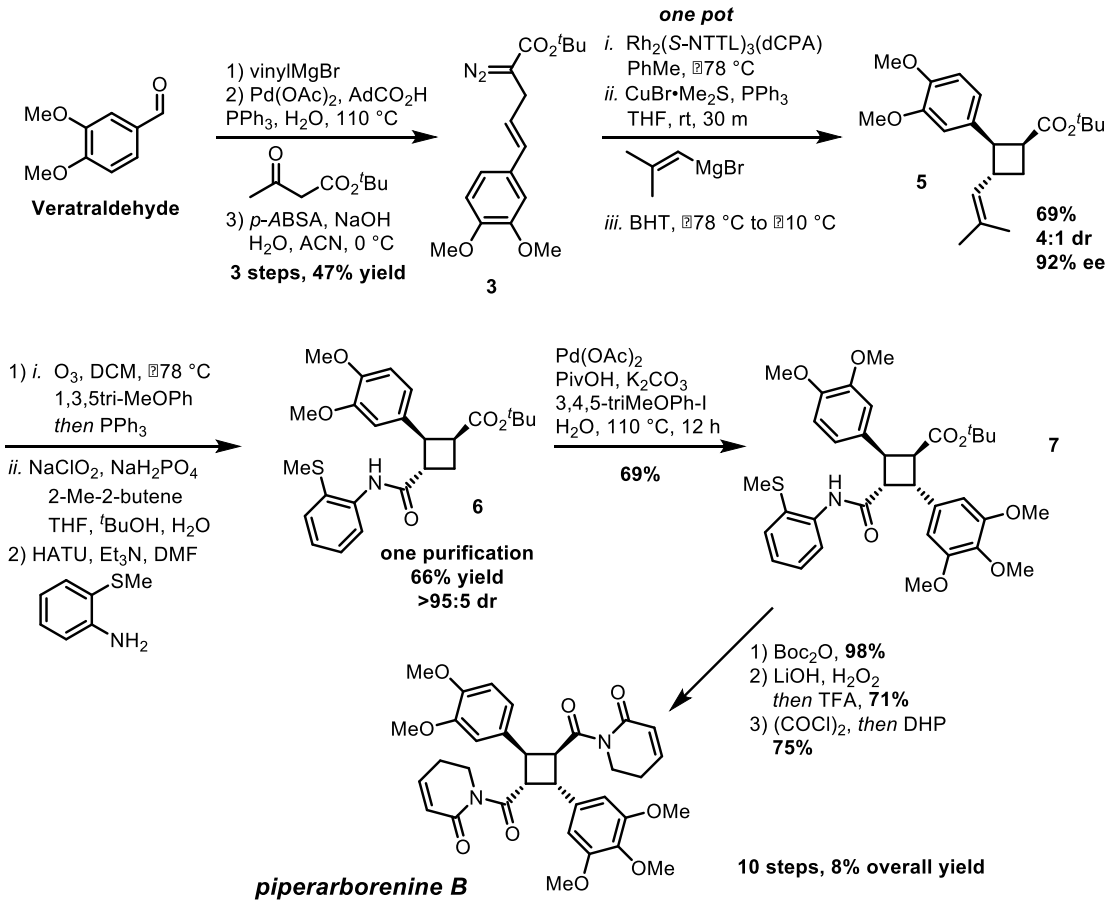
Supporting Information

Experimental Section

Experimental Section

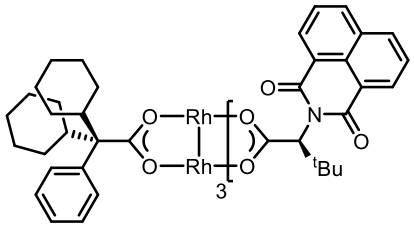
General Considerations. All reactions were carried out in glassware that was flame-dried under vacuum and cooled under N_2 unless otherwise noted. All commercially available reagents were used as received without further purification unless otherwise noted. Toluene and acetonitrile were dried with columns packed with activated neutral alumina. Tetrahydrofuran was freshly distilled from sodium/benzophenone. CuBr•Me_2S was freshly prepared according to literature procedure.[1] Chromatography was performed on silica gel (Silicycle 40-63D, 60Å). For ^{13}C NMR, multiplicities were distinguished using an ATP pulse sequence: typical quaternary and methylene carbons appear 'up' (C or CH_2); methine and methyl carbons appear 'down' (CH or CH_3). For the ^{13}C NMR spectra of the diazoester, the carbon attached to the diazo functionality could not be observed due to the quadrupolar coupling.[2] By FT-IR analysis, the newly synthesized diazoester compound displayed strong characteristic absorption at 2080 cm^{-1} which is attributable to diazo stretch. High-resolution mass spectrometry (HRMS) was performed using Liquid Injection Field Desorption Ionization (LIFDI) coupled with a time of flight (TOF) detector. As such, homogeneous solutions of all samples were directly transferred to an emitter inside the ion source via a fused silica capillary without breaking vacuum.

Enantioselective total synthesis of piperarborenine B



Experimental procedures

Rh_2(*S*-NTTL)$_3$(dCPA)



2,2-Dicyclohexyl-2-phenylacetic acid was prepared according to literature procedure.[3]

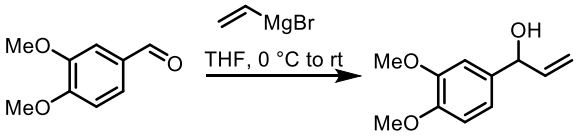
To an oven-dried round bottomed flask fitted with a reflux condenser was added dirhodium tetrakis[*N*-naphthaloyl-(*S*)-*tert*-leucinate] (250 mg, 0.17 mmol, 1.0 equiv), and 2,2-dicyclohexyl-2-phenylacetic acid (160 mg, 0.52 mmol, 3.0 equiv). The flask was evacuated and refilled with N_2 and chlorobenzene (25 mL, 0.007 M) was added. The reaction mixture was heated to 160 °C for 12 hours. A second batch of 2,2-dicyclohexyl-2-phenylacetic acid (52 mg, 0.17 mmol, 1.0 equiv) was added and heated at 160 °C for an additional 6 hours. The chlorobenzene was removed by distillation under N_2. The residue was dissolved in EtOAc and washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The green solid was purified by column chromatography (4% EtOAc:toluene) to provide the title compound as a green solid (154 mg, 62% yield). Crystals suitable for X-ray crystallography were grown from methanol by slow evaporation.

^{1}H NMR (400 MHz, 3:1 CD_2Cl_2:CD_3OD, referenced to CD_3OD) δ: 9.07 (d, *J* = 7.2 Hz, 1H), 8.62 (d, *J* = 7.2 Hz, 1H), 8.59 (br s, 2H), 8.48 (d, *J* = 7.2 Hz, 2H), 8.22 (dd, *J* = 7.9, 5.2 Hz, 2H), 8.15 (t, *J* = 7.6 Hz, 4H), 7.92 (t, *J* = 7.8 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 4H), 7.35 (br s, 2H), 7.15 (m, 3H), 6.03 (s, 1H), 5.71 (s, 2H), 2.26 – 2.06 (m, 2H), 1.86 – 1.77 (m, 1H), 1.74 – 1.62 (m, 3H), 1.58 – 1.40 (m, 5H), 1.40 – 1.10 (m, 28H), 1.10 – 0.97 (m, 3H), 0.92 – 0.62 (m, 4H), 0.55 – 0.22 (m, 3H). Peaks attributable to EtOAc were observed by ^{1}H NMR at 4.06, 1.99, and 1.20 ppm. ^{13}C NMR (101 MHz, 3:1 CD_2Cl_2:CD_3OD, referenced to CD_3OD) δ: 193.3 (C), 187.7 (C), 187.5 (C), 165.7 (C), 165.4 (C), 163.8 (C), 163.4 (C), 140.0 (C), 134.4 (CH), 134.3 (CH), 134.03 (CH), 133.96 (CH), 133.5 (CH), 132.4 (CH), 132.0 (C), 131.6 (CH), 131.4 (CH), 128.6 (C), 128.5 (C), 127.8 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 127.0 (CH), 126.0 (CH), 123.4 (C), 123.27 (C), 123.25 (C), 123.1 (C), 65.5 (C), 62.1 (CH), 61.7 (CH), 41.2 (CH), 41.0 (CH), 36.8 (C), 36.7 (C), 29.5 (CH_3), 29.3 (CH_3), 27.9 (CH_2), 27.8 (CH_2), 27.7 (CH_2), 27.6 (CH_2), 27.3 (CH_2), 27.1 (CH_2). Peaks attributable to EtOAc were observed by ^{13}C NMR at 172.4, 61.1, 21.1, and 14.2 ppm. A small peak at 30.2 ppm was attributed to an impurity.; FT-IR (NaCl, thin film): 2931, 1709, 1592, 1435, 1398, 1380, 1343, 1306, 1239, 1183,

906, 846, 788, 778, 710; UV-Vis (4.0×10^{-5} M, Et_2O) λ_{max}: 210, 236, 331, 343; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{74}H_{75}N_3O_{14}Rh_2^+$ 1435.3354; Found 1435.3345.

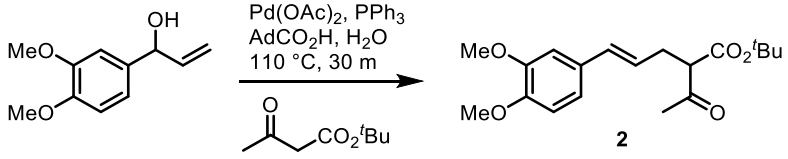
A circular dichroism spectrum was collected on a JASCO J-810 spectropolarimeter. Wavelength scans were recorded using a 2 nm date pitch, a 50 nm/min scan speed, and a 1 mm quartz cell. The spectrum of a solution of Rh_2(*S*-NTTL)$_3$(dCPA) (1.5×10^{-4} M in Et_2O) was collected at 21 °C.

1-(3,4-Dimethoxyphenyl)prop-2-en-1-ol



The experimental procedure was adapted from reported methods.[4]
To a flame-dried round bottomed flask equipped with a N_2 inlet adapter was added veratraldehyde (2.0 g, 12 mmol, 1.0 equiv) and the flask was evacuated and refilled with N_2 three times. THF (24 mL, 0.5 M) was added and the clear, homogeneous solution was chilled to 0 °C. Vinylmagnesium bromide (14 mL, 14 mmol, 1.2 equiv) was added and the reaction was stirred at 0 °C for one hour followed by one hour at room temperature. The reaction was judged complete by TLC analysis, quenched with saturated aqueous NH_4Cl, and diluted with ethyl acetate. The mixture was added to a separatory funnel and extracted three times with EtOAc. The collected organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The crude pale yellow oil was used in the next step without purification.

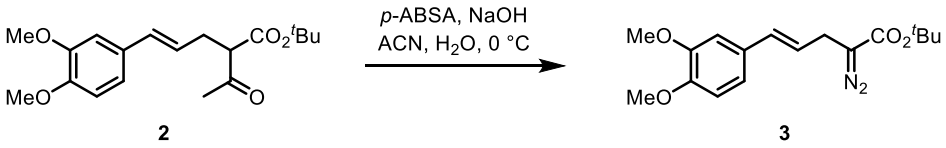
***tert*-Butyl (*E*)-2-acetyl-5-(3,4-dimethoxyphenyl)pent-4-enoate (2)**



The experimental procedure was adapted from reported methods.[5]
To a round bottomed flask containing crude vinyl alcohol was added *tert*-butyl acetoacetate (6.0 mL, 36 mmol, 3.0 equiv), $Pd(OAc)_2$ (54 mg, 0.24 mmol, 2 mol %), PPh_3 (320 mg, 1.2 mmol, 10 mol %), and 1-adamantanecarboxylic acid (220 mg, 1.2 mmol, 10 mol %). Distilled water was added (60 mL, 0.2 M), a reflux condenser was installed and the yellow suspension was heated to 110 °C. After reaching 110 °C, the reaction mixture was stirred 30 minutes before it was removed from the oil bath and allowed to cool to room temperature. Dichloromethane and

saturated aqueous $NaHCO_3$ were added. The mixture was added to a separatory funnel and extracted three times with DCM. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The crude yellow oil was diluted with Et_2O and treated with Silicycle SiliaMetS Thiol silica gel (250 mg). The mixture was triturated, filtered, and concentrated. The crude oil was passed through a plug of silica gel first using 1% EtOAc:Hex and then the product was collected using 20% EtOAc:hexanes. The ketoester **2** was obtained as a pale yellow oil (2.1 g) and used in the next step without further purification.

***tert*-Butyl (*E*)-2-diazo-5-(3,4-dimethoxyphenyl)pent-4-enoate (3)**



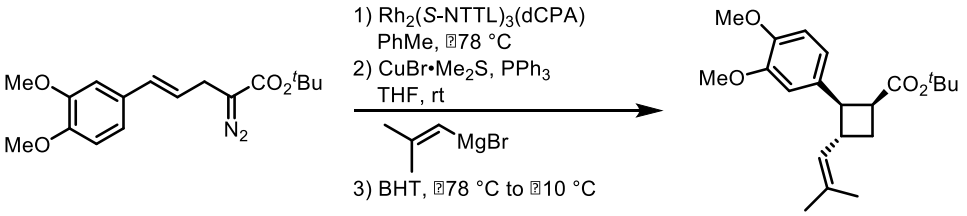
2 **3**

To a round bottomed flask was added *tert*-butyl (*E*)-2-acetyl-5-(3,4-dimethoxyphenyl)pent-4-enoate (2.1 g, 6.4 mmol, 1.0 equiv), acetonitrile (32 mL, 0.2 M), and 4-acetamidobenzenesulfonyl azide (3.1 g, 13 mmol, 2.0 equiv). The solution was cooled to 0 °C and a solution of sodium hydroxide (0.77 g, 19 mmol, 3.0 equiv) in H_2O (11 mL, 0.6 M) was added dropwise. The reaction mixture was stirred at 0 °C for an additional 2.5 hours. The reaction was diluted with Et_2O and H_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. Purification by column chromatography (20% EtOAc:hexanes) provided the desired diazoester as a viscous yellow oil (1.8 g, 88% yield). The three step yield from veratraldehyde was 47%.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.92 – 6.86 (m, 2H), 6.81 (d, J = 8.2 Hz, 1H), 6.41 (d, J = 15.7 Hz, 1H), 6.06 (dt, J = 15.7, 6.9 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.14 (d, J = 6.9 Hz, 2H), 1.49 (s, 9H); ^{13}C NMR* (101 MHz, $CDCl_3$) δ: 166.6 (C), 149.1 (C), 148.9 (C), 132.3 (CH), 130.0 (C), 122.5 (CH), 119.5 (CH), 111.1 (CH), 108.7 (CH), 81.5 (C), 56.0 (CH_3), 55.9 (CH_3), 28.5 (CH_3), 26.9 (CH_2); FT-IR (NaCl, thin film): 2977, 2935, 2835, 2080, 1685, 1515, 1456, 1341, 1265, 1159, 1114, 1028, 966, 740; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{17}H_{22}N_2O_4^+$ 318.1575; Found 318.1580.

*Note: For the ^{13}C NMR spectra of the diazoester, the carbon attached to the diazo functionality could not be observed due to the quadrupolar coupling.[2] By FT-IR analysis, the diazoester displayed strong characteristic absorption at ~2080 cm^{-1} which is attributable to diazo stretch.

***tert*-Butyl (1*S*,2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-3-(2-methylprop-1-en-1-yl)cyclobutane-1-carboxylate (5)**



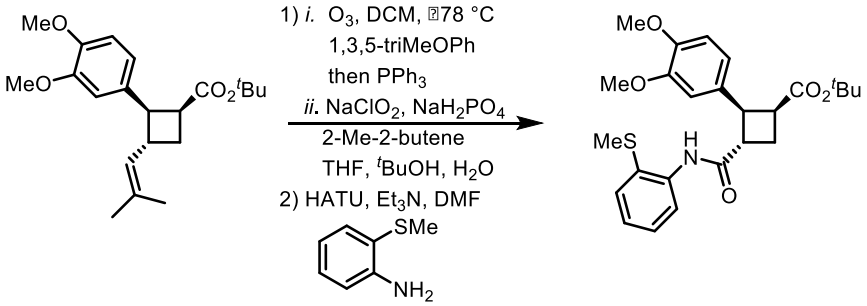
To flame-dried 300 mL round bottomed flask equipped with a septum-fitted, gas inlet adapter was added Rh_2(*S*-NTTL)$_3$(dCPA) (7.9 mg, 0.0055 mmol, 0.10 mol %). The flask was evacuated and refilled with N_2 three times. Anhydrous toluene (75 mL) was added, and the mixture was stirred under N_2 at room temperature until the catalyst had dissolved. The reaction was then cooled in a bath of dry ice/acetone (–78 °C). Diazoester **3** (1.75 g, 5.50 mmol, 1.00 equiv) was diluted with anhydrous toluene (35 mL) and then added to the reaction flask via syringe pump (15 mL/h) with stirring at –78 °C. After the addition was complete, the reaction was stirred for an additional 2 hours at –78 °C. Toluene was removed *in vacuo* and replaced with anhydrous THF (110 mL, 0.05 M). To the faint green solution in the same pot was added 'homemade' CuBr•Me_2S[1] (567 mg, 2.75 mmol, 50.0 mol %) and PPh_3 (1.73 g, 6.60 mmol, 1.20 equiv) with stirring at room temperature. To the pale orange solution was added 2-methyl-1-propenylmagnesium bromide (22.0 mL, 11.0 mmol, 2.00 eq, 0.5 M in THF). The solution quickly turned a dark green color and stirring was continued at room temperature for 25 minutes at which time full conversion was observed by analysis of a quenched aliquot by gas chromatography. The solution was chilled to –78 °C and 2,6-di(*tert*-butyl)-4-methylphenol (3.03 g, 13.8 mmol, 2.50 equiv) was added as a solid in one portion. The reaction was added to a brine/ice bath which warmed from –15 °C to –8 °C over 30 minutes. The reaction was quenched with 1 M HCl and extracted with EtOAc three times. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The crude oil was triturated with toluene and the resultant white solid was removed by filtration. Purification by column chromatography (10% toluene:hexanes then 5% EtOAc:hexanes) afforded the desired vinylcyclobutane as an oil (1.31 g, 69% yield, 4:1 dr, 92% ee). The diasteromeric ratio was determined to be 4:1 by gas chromatography analysis of the crude and purified material.

$[\alpha]_D^{20}$ +68.5 (*c* 1.0, $CHCl_3$). FT-IR (NaCl, thin film): 2975, 2933, 1719, 1517, 1460, 1366, 1241, 1151, 1030, 849; HRMS (CI-TOF) *m/z*: $[M]^+$ calcd for $C_{21}H_{30}O_4^+$ 346.2139; Found 346.2144. HPLC analysis: (CHIRALCEL OD column, 0.5% 2-propanol in hexanes, 1 mL/min, 220 nm), retention times at 9.436 min (minor enantiomer, major diastereomer) and 11.746 min (major enantiomer, major diastereomer), 92% ee. The enantiomers of the minor diastereomer eluted with retention times at 10.391 min (minor enantiomer, minor diastereomer) and 13.407 min (major enantiomer, minor diastereomer).

NMR spectral properties assigned to major diastereomer, *tert*-butyl (1*S*,2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-3-(2-methylprop-1-en-1-yl)cyclobutane-1-carboxylate: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.84 – 6.72 (m, 3H), 5.21 (dt, *J* = 8.9, 1.4 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.78 (app t, *J* = 9.2 Hz, 1H), 3.57 (app t, *J* = 9.7 Hz, 1H), 3.25 (m, 1H), 2.44 (ddd, *J* = 11.4, 8.7, 2.6 Hz, 1H), 1.85 (dt, *J* = 11.2, 8.7 Hz, 1H), 1.69 (s, 3H), 1.67 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.5 (C), 148.6 (C), 147.6 (C), 133.0 (C), 132.3 (C), 129.2 (CH), 119.6 (CH), 111.1 (CH), 110.9 (CH), 79.9 (C), 56.1 (CH_3), 55.8 (CH_3), 49.4 (CH), 43.2 (CH), 36.5 (CH), 28.0 (CH_2), 27.9 (CH_3), 25.8 (CH_3), 18.6 (CH_3).

NMR spectral properties assigned to minor diastereomer, *tert*-butyl (1*R*,2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-3-(2-methylprop-1-en-1-yl)cyclobutane-1-carboxylate: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.84 – 6.72 (m, 3H), 5.26 (dt, *J* = 9.0, 1.4 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.33 (t, *J* = 9.5 Hz, 1H), 3.10 – 2.98 (m, 1H), 2.89 (td, *J* = 9.8, 8.2 Hz, 1H), 2.31 (dt, *J* = 10.3, 8.0 Hz, 1H), 1.94 (q, *J* = 10.2 Hz, 1H), 1.69 (s, 3H), 1.67 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): 174.0 (C), 148.8 (C), 147.5 (C), 136.01 (C), 132.5 (C), 128.7 (CH), 118.3 (CH), 111.1 (CH), 109.8 (CH), 80.4 (C), 56.0 (CH_3), 55.8 (CH_3), 50.3 (CH), 43.4 (CH), 37.8 (CH), 29.3 (CH_2), 28.3 (CH_3), 25.9 (CH_3), 18.5 (CH_3).

***tert*-butyl (1*S*,2*R*,3*S*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl) cyclobutane-1-carboxylate (6)**



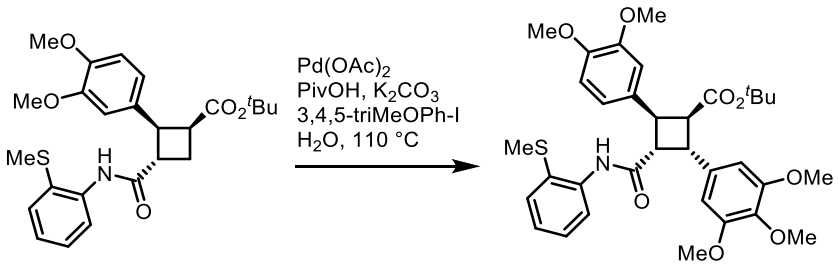
To a dry round bottomed flask was added vinylcyclobutane **5** (1.30 g, 3.75 mmol, 1.00 equiv), 1,3,5-trimethoxybenzene (631 mg, 3.75 mmol, 1.0 equiv), and DCM (38.0 mL, 0.1 M). The solution was chilled to –78 °C and O_3/O_2 was bubbled through for 30 minutes with vigorous stirring and TLC monitoring (1:1:3 Et_2O:DCM:hexanes). The introduction of ozone was ceased *before* the blue color of ozone was observed. (In runs that were allowed to proceed until the characteristic blue color of ozone was observed, significant decomposition was obtained.). The O_3 generator was switched off and O_2 was bubbled through the reaction for 5 minutes. PPh_3 (1.47 g, 5.63 mmol, 1.50 equiv) was added as a solid in one portion at –78 °C. The reaction mixture was allowed to warm to room temperature. After stirring at room temperature for 45 minutes, the solution was concentrated via rotary evaporation.

The resulting orange oil was dissolved in THF (19 mL, 0.2 M) and *tert*-butanol (19 mL, 0.2 M). The reaction was stirred at room temperature and 2-methyl-2-butene was added (7.5 mL, 15 mmol, 2.0 M in THF, 4.0 equiv). Monobasic sodium hydrogen phosphate (1.35 g, 11.3 mmol, 3.0 equiv) and sodium chlorite (1.36 g, 15 mmol, 4.0 equiv) were dissolved in H_2O (19 mL, 0.2 M) and the aqueous solution was added dropwise by pipette at room temperature. A bright yellow solution rapidly formed. The reaction mixture was stirred for 2 hours and full consumption of starting material was observed by TLC analysis (20% EtOAc:hexanes). The reaction was quenched with saturated aqueous NH_4Cl and extracted with EtOAc three times. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The pale yellow oil was used in the next step without further purification.

To a flame-dried round bottomed flask was added the crude carboxylic acid in DMF (38 mL, 0.10 M). Et_3N (1.05 mL, 7.50 mmol, 2.00 equiv) was added and the solution was chilled to 0 °C. HATU (1.71 g, 4.50 mmol, 1.10 equiv) was added as a solid in one portion and a golden-yellow solution was observed. The reaction was stirred for 15 minutes and then allowed to warm to room temperature for 10 minutes. After cooling to 0 °C, 2-(methylthio)aniline (0.940 mL, 7.50 mmol, 2.00 equiv) was added and the reaction was allowed to warm to room temperature. After 5 hours, TLC analysis revealed full consumption of the carboxylic acid and the reaction was subsequently quenched with saturated aqueous $NaHCO_3$ and diluted with EtOAc. The mixture was added to a separatory funnel and the aqueous layer was drained off. The organic layer was washed with 1 M HCl and brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. Purification by column chromatography (1:2:20 to 1:2:10 toluene:Et_2O:hexanes) provided the desired cyclobutane as an off-white solid (1.14 g, 66% yield, >95:5 dr). The diastereomeric ratio was determined by ^1H NMR analysis. A second band was collected containing 247 mg of the minor diastereomer (14% yield, >93:7 dr).

$[\alpha]_D^{20}$ +116 (*c* 1.0, $CHCl_3$); mp: 105 – 108 °C. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.37 (d, *J* = 8.3 Hz, 1H), 8.33 (s, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.25 (m, 1H), 7.07 – 6.98 (m, 1H), 6.92 – 6.83 (m, 1H), 6.85 – 6.79 (m, 2H), 4.17 (app t, *J* = 9.9 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.35 (dt, *J* = 10.5, 5.5 Hz, 1H), 2.58 – 2.45 (m, 2H), 2.14 (s, 3H), 1.12 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 172.8 (C), 171.9 (C), 148.9 (C), 148.3 (C), 138.7 (C), 133.7 (CH), 131.1 (C), 129.4 (CH), 124.8 (C), 124.4 (CH), 120.3 (CH), 119.8 (CH), 111.2 (CH), 111.1 (CH), 80.6 (C), 56.2 (CH_3), 56.0 (CH_3), 45.5 (CH), 43.4 (CH), 42.9 (CH), 27.9 (CH_3), 23.2 (CH_2), 19.0 (CH_3); FT-IR (NaCl, thin film): 3327, 2974, 2835, 1717, 1684, 1579, 1516, 1434, 1366, 1242, 1151, 1028, 761; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{25}H_{31}NO_5S^+$ 457.1918; Found 457.1937.

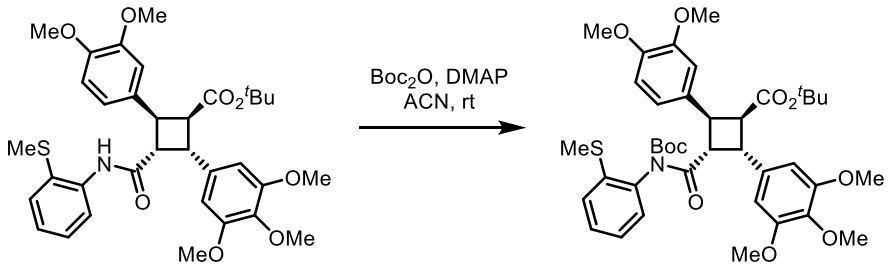
***tert*-Butyl (1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (7)**



A heavy-walled, 15 mL, cylindrical pressure vessel equipped with a stir bar was charged sequentially with *tert*-butyl (1*S*,2*R*,3*S*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl) cyclobutane-1-carboxylate **6** (1.09 g, 2.38 mmol, 1.00 equiv), K_2CO_3 (821 mg, 5.95 mmol, 2.50 equiv), pivalic acid (121 mg, 1.19 mmol, 50 mol %), 3,4,5-trimethoxy-1-iodobenzene (1.40 g, 4.76 mmol, 2.00 equiv), and $Pd(OAc)_2$ (107 mg, 0.476 mmol, 20 mol %). Water was added (8.0 mL, 0.30 M) and the vessel was sealed with a solid Teflon screw cap. The reaction vessel was placed in an oil bath preheated to 80 °C and heated to 110 °C with vigorous stirring. After 12 hours, the reaction mixture was allowed to cool to room temperature. Saturated aqueous $NaHCO_3$ was added followed by DCM. The mixture was transferred to a separatory funnel using DCM and additional saturated aqueous $NaHCO_3$ was added. The mixture was extracted three times with DCM. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. Purification by column chromatography (10:10:80 to 15:15:70 DCM:Et_2O:hexanes) afforded the desired product as an off-white solid (1.02 g, 69% yield).

$[\alpha]_D^{20}$ +15.3 (*c* 1.0, $CHCl_3$); mp: 135 – 137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.19 (d, *J* = 8.2 Hz, 1H), 7.95 (s, 1H), 7.35 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.01 – 6.94 (m, 2H), 6.93 (d, *J* = 2.0 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.60 (s, 2H), 4.53 (dd, *J* =11.1, 5.9 Hz, 1H), 4.43 (t, *J* = 9.5 Hz, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.87 – 3.79 (m, 2H), 3.78 (s, 6H), 3.67 (s, 3H), 2.09 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.2 (C), 169.7 (C), 153.2 (C), 148.8 (C), 148.3 (C), 138.3 (C), 137.2 (C), 134.7 (C), 133.3 (CH), 132.1 (C), 129.0 (CH), 124.6 (C), 124.3 (CH), 120.0 (CH), 119.8 (CH), 112.1 (CH), 111.2 (CH), 104.9 (CH), 80.8 (C), 60.8 (CH_3), 56.14 (CH_3, 2 peaks), 56.06 (CH_3), 50.1 (CH), 48.5 (CH), 42.9 (CH), 41.1 (CH), 27.8 (CH_3), 19.1 (CH_3); FT-IR (NaCl, thin film): 3327, 2973, 2933, 1719, 1684, 1589, 1513, 1463, 1251, 1126, 1028, 845, 765; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{34}H_{41}NO_8S^+$ 623.2548; Found 623.2575.

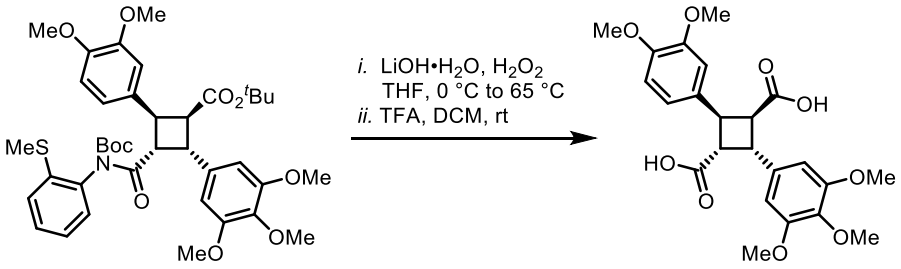
***tert*-Butyl (1*R*,2*R*,3*R*,4*R*)-3-((*tert*-butoxycarbonyl)(2-(methylthio)phenyl)carbamoyl)-2-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (7-Boc)**



To a flame-dried round bottomed flask was added *tert*-butyl (1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (**7**) (850 mg, 1.36 mmol, 1.00 equiv) and the flask was evacuated and refilled with N_2 three times. Dry acetonitrile (14 mL, 0.10 M) was added and the solution was stirred at room temperature. Boc_2O (450 mg, 2.04 mmol, 1.50 equiv) was added as a solid followed by DMAP (17 mg, 0.14 mmol, 0.10 equiv). The reaction mixture was stirred at room temperature for 12 hours, and subsequently concentrated via rotary evaporation. Purification by column chromatography (12.5:12.5:75 to 20:20:60 DCM:Et_2O:hexanes) provided the desired product as an off-white solid (969 mg, 98% yield). The NMR spectra indicate that the compound exists as a 4.3:1 mixture of rotamers.

$[\alpha]_D^{20}$ +42.4 (*c* 1.0, $CHCl_3$); mp: 139 – 142 °C. Spectral properties of the major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.23 – 7.13 (m, 2H), 7.03 – 6.92 (m, 2H), 6.90 (d, *J* = 1.5 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.63 (s, 2H), 5.88 (dd, *J* = 8.0, 1.4 Hz, 1H), 5.10 (ddd, *J* = 11.2, 8.2, 1.2 Hz, 1H), 4.67 (dd, *J* = 11.4, 8.1 Hz, 1H), 4.51 (dd, *J* = 11.1, 6.3 Hz, 1H), 3.92 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.84 (s, 6H), 2.30 (s, 3H), 1.29 (s, 9H), 1.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.3 (C), 171.6 (C), 153.1 (C), 151.1 (C), 148.7 (C), 148.0 (C), 137.2 (C), 137.01 (C), 136.95 (C), 136.1 (C), 132.7 (C), 128.5 (CH), 128.2 (CH), 126.4 (CH), 125.6 (CH), 120.1 (CH), 112.0 (CH), 111.1 (CH), 105.7 (CH), 82.7 (C), 80.7 (C), 61.1 (CH_3), 56.3 (CH_3), 56.2 (CH_3), 56.0 (CH_3), 49.9 (CH), 48.9 (CH), 43.3 (CH), 40.4 (CH), 27.9 (CH_3), 27.8 (CH_3), 15.5 (CH_3); FT-IR (NaCl, thin film): 2976, 1738, 1719, 1698, 1588, 1517, 1457, 1369, 1250, 1154, 1128, 1028, 845, 741; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{39}H_{49}NO_{10}S^+$ 723.3072; Found 723.3047.

(1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1,3-dicarboxylic acid (8)



To a 50 mL round bottomed flask equipped with a condenser was added **7-Boc** (960 mg, 1.3 mmol, 1.0 equiv) followed by THF (9.0 mL, 0.15 M). H_2O (4.4 mL, 0.3 M) was added and the mixture was cooled to 0 °C with vigorous stirring. Sequentially added were H_2O_2 (1.5 mL, 30% (w/w) in H_2O, 27 mmol, 20 equiv.) and $LiOH{\cdot}H_2O$ (670 mg, 16 mmol, 12 equiv). The reaction mixture was warmed to room temperature and stirred for 1 hour before heating to 50 °C. After 15 hours, incomplete conversion was observed by ^1H NMR analysis of an aliquot. H_2O_2 (2.5 mL, 30% w/w in H_2O), $LiOH{\cdot}H_2O$ (670 mg), and DMF[6] (1 mL) were added and the mixture was heated to 65 °C. The reaction was stirred an additional 15 hours and cooled to room temperature. The reaction mixture was diluted with EtOAc and saturated aqueous sodium sulfite was added and stirred for 20 minutes. The reaction mixture was acidified with 4 M HCl, diluted with H_2O and extracted with EtOAc three times. The organic layer was dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The crude oil was dissolved in DCM (5 mL, 0.26 M) and treated with trifluoroacetic acid (5 mL) at room temperature for 1 hour. Toluene (2 mL) was added and the reaction mixture was concentrated via rotary evaporation. Saturated aqueous K_2CO_3, and Et_2O were added. The aqueous layer was collected, acidified by dropwise addition of concentrated HCl, and extracted with a mixture of $CHCl_3$/^{i}PrOH (7:3) five times. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated via rotary evaporation to provide the diacid **8** as a white solid (420 mg, 71% yield).

$[\alpha]_D^{20}$ +8.2 (*c* 0.4, 1:1 MeOH:$CHCl_3$); mp: 265 – 268 °C. The spectral properties agreed with those described previously.[7] ^1H NMR (400 MHz, 1:1 CD_3OD:$CDCl_3$) δ: 6.93 – 6.88 (m, 2H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.59 (s, 2H), 4.34 (t, *J* = 11.6 Hz, 1H), 4.32 (t, *J* = 11.4 Hz, 1H), 3.92 – 3.79 (m, 2H), 3.87 (s, 3H), 3.85 (s, 6H), 3.83 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (101 MHz, 1:1 CD_3OD:$CDCl_3$) δ: 175.2 (C), 174.9 (C), 153.5 (C), 149.2 (C), 148.5 (C), 137.1 (C), 136.0 (C), 132.4 (C), 120.2 (CH), 111.9 (CH), 111.7 (CH), 105.2 (CH), 61.1 (CH_3), 56.3 (CH_3), 56.2 (CH_3), 56.2 (CH_3), 47.8 (CH), 47.8 (CH), 42.5(CH), 42.0 (CH); FT-IR (NaCl, thin film): 2941, 1686, 1587, 1522, 1512, 1465, 1433, 1267, 1242, 1128, 1027, 844; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{23}H_{26}O_9^+$ 446.1572; Found 446.1592.

Piperarborenine B (1)

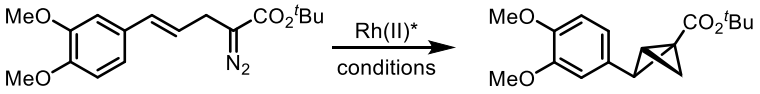
To a flame-dried round bottomed flask was added diacid **8** (400 mg, 0.896 mmol, 1.00 equiv) and the flask was evacuated and refilled with N_2 three times. THF (9 mL, 0.1 M) containing DMF (3.3 mg, 0.045 mmol, 0.050 equiv) was added. The heterogeneous mixture was chilled to 0 °C and oxalyl chloride (0.19 mL, 2.24 mmol, 2.50 equiv) was added dropwise. The homogeneous, yellow solution was allowed to warm to room temperature and stirred for 2 hours. The solution was concentrated via rotary evaporation resulting in a yellow foam. Toluene (3.6 mL, 0.25 M) was added to the crude acid chloride and the yellow solution was stirred at room temperature. Activated, powdered 4Å molecular sieves (900 mg) were added followed by a solution of 5,6-dihydropyridin-2(1H)-one (261 mg, 2.69 mmol, 3.00 equiv) in toluene (5.4 mL). After stirring at room temperature for 5 minutes, the reaction mixture was heated to 80 °C for 12 hours. The reaction mixture was cooled to room temperature, filtered through celite and rinsed with EtOAc. The solution was added to a separatory funnel, washed sequentially with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. Purification by column chromatography (1:1:1 DCM:Et_2O:hexanes) provided piperarborenine B as a white solid (409 mg, 75% yield).

$[\alpha]_D^{20}$ +5.7 (*c* 1.0, CH_2Cl_2); mp: 193 – 196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.88 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.82 – 6.75 (m, 2H), 6.69 – 6.60 (m, 2H), 6.51 (s, 2H), 5.79 – 5.72 (m, 2H), 4.95 – 4.85 (m, 2H), 4.79 – 4.70 (m, 2H), 3.93 – 3.84 (m, 1H), 3.86 (s, 3H), 3.85 (s, 6H), 3.84 (s, 3H), 3.77 – 3.72 (m, 1H), 3.78 (s, 3H), 3.49 – 3.30 (m, 2H), 2.11 – 1.99 (m, 2H), 1.71 – 1.57 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.3 (C), 174.2 (C), 164.58 (C), 164.56 (C), 152.8 (C), 148.3 (C), 147.8 (C), 145.3 (CH), 145.2 (CH), 136.56 (C), 136.55 (C), 133.2 (C),125.6 (CH), 125.5 (CH), 120.0 (CH), 112.0 (CH), 111.0 (CH), 105.1 (CH), 60.9 (CH_3), 56.3 (CH_3), 56.1 (CH_3), 56.0 (CH_3), 51.6 (CH), 51.5 (CH), 42.3 (CH), 41.7 (CH), 40.94 (CH_2), 40.90 (CH_2), 24.3 (CH_2), 24.3 (CH_2); FT-IR (NaCl, thin film): 2940, 2855, 1687, 1588, 1516, 1464, 1386, 1307, 1220, 1126, 1025, 814, 729; HRMS (LIFDI-TOF) *m/z*: $[M]^+$ calcd for $C_{33}H_{36}N_2O_9^+$ 604.2416; Found 604.2433.

Optimization table for enantioselective bicyclobutanation

To a dry 1-dram vial equipped with a stir bar was added the Rh(II) catalyst (0.00016 mmol, 0.5 mol %) and the vial was sealed with a Teflon-lined screw cap and wrapped with parafilm. The

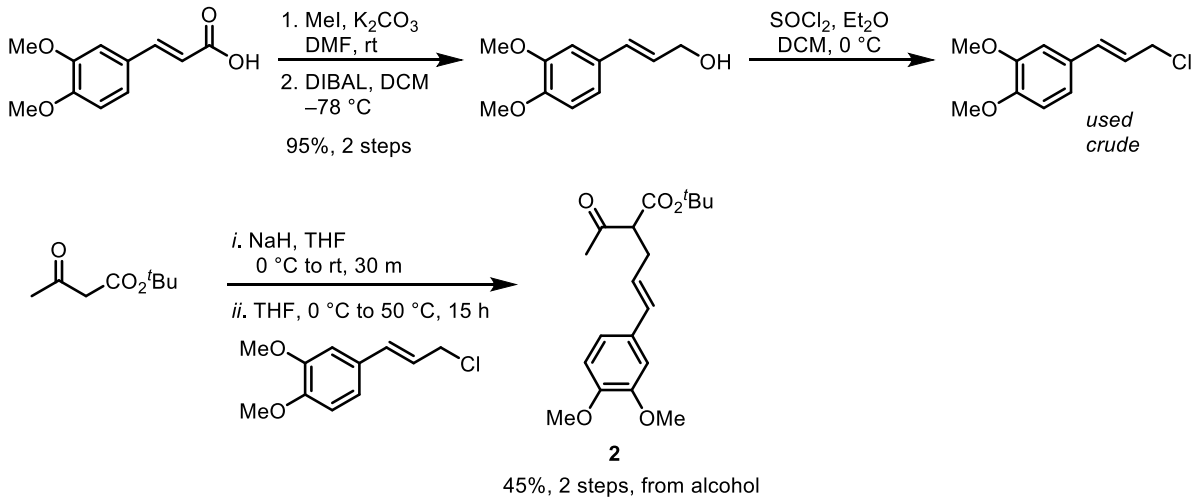
vial was evacuated and refilled with N_2 three times and solvent was added (0.42 mL). The solution was cooled to –78 °C with vigorous stirring. A solution of diazoester **3** (10 mg, 0.031 mmol) in toluene (0.2 mL) was added dropwise over 5 minutes. The solution was allowed to stir an additional 1 hour and warmed to room temperature. Analytical samples were prepared by preparatory TLC. HPLC analysis was performed using a CHIRALPAK IA column, 0.5% 2-propanol in hexanes, 1 mL/min at 220 nm.



Rh(II)*	Solvent	T (°C)	%ee
Rh_2(*S*-NTTL)$_4$	PhMe	–78	84
Rh_2(*S*-PTTL)$_4$	PhMe	–78	77
Rh_2(*S*-NTTL)$_3$(TPA)	PhMe	–78	63
Rh_2(*S*-PTTL)$_3$(TPA)	PhMe	–78	60
Rh_2(*S*-NTTL)$_3$(dCPA)	PhMe	–78	92
Rh_2(*S*-NTTL)$_4$	MTBE	–78	85
Rh_2(*S*-PTTL)$_4$	MTBE	–78	86
Rh_2(*S*-NTTL)$_3$(TPA)	MTBE	–78	72
Rh_2(*S*-PTTL)$_3$(TPA)	MTBE	–78	27
Rh_2(*S*-NTTL)$_3$(dCPA)	MTBE	–78	81
Rh_2(*S*-NTTL)$_4$	EtOAc	rt	88
Rh_2(*S*-PTTL)$_4$	EtOAc	rt	79
Rh_2(*S*-NTTL)$_3$(dCPA)	EtOAc	rt	50
Rh_2(*S*-TCPTTL)$_4$	EtOAc	rt	73
Rh_2(*R*-PTAD)$_4$	EtOAc	rt	–70
Rh_2(*S*-NTTL)$_3$(TPA)	EtOAc	rt	71
Rh_2(*S*-PTTL)$_3$(TPA)	EtOAc	rt	56

Alternate methods for synthesis of ketoester 2

1. **via 3,4-dimethoxycinnamyl chloride**



Methyl 3,4-dimethoxycinnamate. To a round bottomed flask was added 3,4-dimethoxycinnamic acid (15.4 g, 74.0 mmol, 1.0 equiv), K_2CO_3 (30.6 g, 222 mmol, 3.0 equiv),

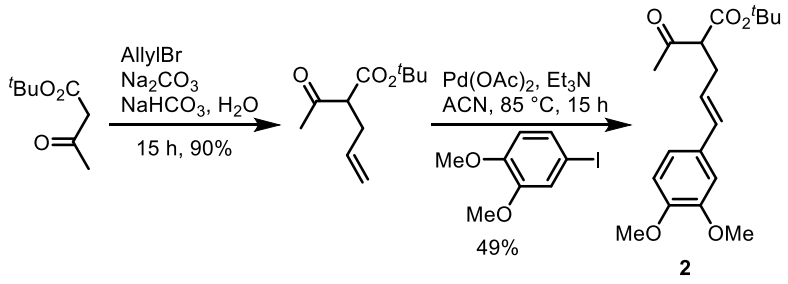
and DMF (100 mL, 0.7 M). To the vigorously stirring reaction mixture was added MeI (9.2 mL, 148 mmol, 2.0 equiv) at room temperature open to air. The reaction mixture was stirred for 3 hours at which time full consumption was observed by TLC analysis. The reaction mixture was diluted with H_2O and extracted three times with EtOAc. The combined organic extracts were washed two times with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. Methyl 3,4-dimethoxycinnamate was obtained as a white solid (16.2 g, 99%) and used in the next step without purification.

3,4-Dimethoxycinnamyl alcohol. To a flame-dried round bottomed flask was added methyl 3,4-dimethoxycinnamate (16.1 g, 72.5 mmol, 1.0 equiv) and DCM (180 mL, 0.4 M). The reaction mixture was cooled to –78 °C, and DIBAL-H was added dropwise via syringe (39 mL, 220 mmol, 3.0 equiv). The reaction mixture was stirred for 1 hour and was quenched with Glauber's salt at –78 °C and allowed to warm to room temperature with stirring for 4 hours. The reaction mixture was diluted with DCM, filtered through Celite and washed with DCM. The filtrate was concentrated and passed through a plug of silica gel (10 to 50 to 80% EtOAc:hexanes). The desired 3,4-dimethoxycinnamyl alcohol[8] was obtained as a white solid (13.5 g, 96% yield).

3,4-Dimethoxycinnamyl chloride. To a flame-dried round bottomed flask was added 3,4-dimethoxycinnamyl alcohol (5.85 g, 30.2 mmol, 1.0 equiv) and the flask was evacuated and refilled with N_2 three times. Et_2O (30 mL, 1 M) and DCM (3 mL) were added and the white suspension was cooled to 0 °C. Thionyl chloride (2.22 mL, 30.2 mmol, 1.0 equiv) was added over 1 minute and the reaction mixture became yellow and homogeneous. The reaction mixture was stirred for 1.5 hours, diluted with EtOAc and carefully added to ice cold saturated aqueous $NaHCO_3$ in an Erlenmyer flask. The mixture was stirred until bubbling ceased (about 15 minutes). The mixture was added to a separatory funnel and the aqueous layer was drained off. The organic layer was washed twice with $NaHCO_3$ and once with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The pale yellow oil was clean by ^1H NMR analysis and used in the next step immediately without purification.

Ketoester 2. To a flame-dried round bottomed flask was added NaH (1.33 g, 33.2 mmol, 1.1 equiv, 60% in mineral oil) and the flask was evacuated and refilled with N_2 three times. THF (40 mL) was added and *tert*-butyl acetoacetate (5.5 mL, 33.2 mmol, 1.1 equiv) was added at 0 °C and warmed to room temperature for 30 minutes. The reaction mixture was cooled to 0 °C and crude 3,4-dimethoxycinnamyl chloride was added in THF (20 mL) and the reaction mixture was heated to 50 °C for 14 hours. The reaction was cooled to room temperature and H_2O was added followed by 10 mL 4 M HCl. The mixture was extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The crude oil was passed through a plug of silica gel (5% then 30% EtOAc:hexanes) to provide 4.55 g of ketoester **2** (45% yield over 2 steps from 3,4-dimethoxycinnamyl alcohol).

2. **via Heck reaction of *tert*-butyl 2-allylacetoacetate:**

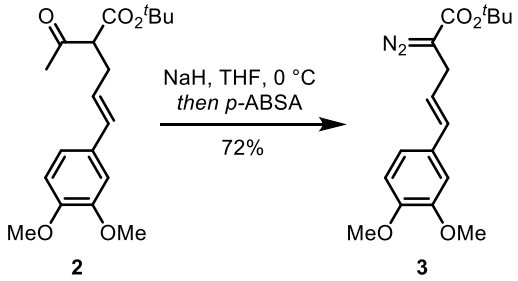


tert-Butyl 2-allylacetoacetate was prepared according to literature procedure.[9]

Ketoester 2. To an oven-dried round bottomed flask was added *tert*-butyl 2-allylacetoacetate (410 mg, 2.1 mmol, 1.5 equiv), 3,4-dimethoxyiodobenzene (360 mg, 1.4 mmol, 1.0 equiv), $Pd(OAc)_2$ (92 mg, 0.41 mmol, 30 mol %), acetonitrile (7 mL, 0.2 M) and Et_3N (0.6 mL, 4.1 mmol, 3.0 equiv). The reaction mixture was heated to 85 °C for 15 hours and subsequently cooled to room temperature. EtOAc and 1 M HCl were added and the mixture was extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. The crude oil was passed through a plug of silica gel (5% then 30% EtOAc:hexanes). The ketoester **2** was obtained as an oil (225 mg, 49% yield).

Alternate methods for synthesis of diazoester 3

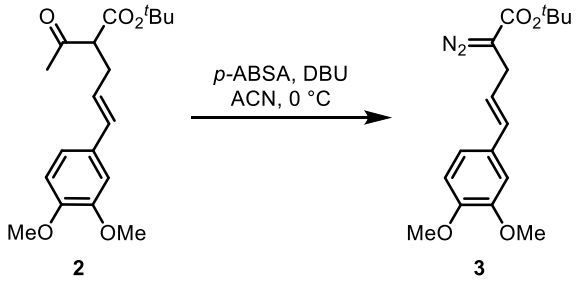
1. **NaH, *p*-ABSA, THF**



Diazoester 3. To a flame-dried round bottomed flask was added NaH (370 mg, 9.2 mmol, 1.5 equiv). The flask was evacuated and refilled with N_2 three times. THF (20 mL) was added and the reaction mixture was cooled to 0 °C. Ketoester **2** (2.05 g, 6.13 mmol, 1.0 equiv) was added in THF (10 mL) and the reaction mixture was allowed to warm to room temperature. After stirring for 30 minutes, the mixture was cooled to 0 °C, and *p*-acetamidobenzenesulfonyl azide (4.42 g, 18.4 mmol, 3.0 equiv) was added as a solid in one portion. The reaction mixture was stirred for an additional two hours before quenching with water. The reaction mixture was extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$,

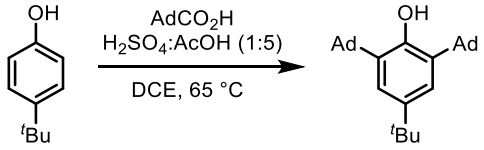
filtered, and concentrated via rotary evaporation. The crude yellow oil was purified by column chromatography (20% EtOAc:hexanes) to provide diazoester **3** (1.2 g, 61% yield).

2. DBU, *p*-ABSA, ACN



Diazoester 3. To a flame-dried round bottomed flask was added *p*-acetamidobenzenesulfonyl azide (1.4 g, 6.0 mmol, 2.0 equiv). The flask was evacuated and refilled with N_2 three times. *tert*-Butyl (*E*)-2-acetyl-5-(3,4-dimethoxyphenyl)pent-4-enoate (1.0 g, 3.0 mmol, 1.0 equiv) was added in acetonitrile (10 mL, 0.3 M). The reaction was cooled to 0 °C, and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.3 mL, 9.0 mmol, 3.0 equiv) was added via syringe. The reaction was stirred for 3 hours at 0 °C and acetonitrile was removed via rotary evaporation. The crude mixture was diluted with EtOAc and water and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated via rotary evaporation. Purification by column chromatography (20% EtOAc:hexanes) afforded the desired diazoester **3** (570 mg, 59% yield).

2,6-Di(adamantan-1-yl)-4-(*tert*-butyl)phenol (BDAP)



To a round bottomed flask was added 4-(*tert*-butyl)phenol (15 g, 100 mmol, 1.0 equiv), 1-adamantanecarboxylic acid (30 g, 200 mmol, 2.0 equiv), and 1,2-dichloroethane (100 mL, 1 M). To the solution at room temperature was added a mixture of H_2SO_4 (10 mL) and AcOH (50 mL) dropwise. The reaction mixture was heated to 65 °C for 15 hours. After cooling to room temperature the reaction mixture was diluted with DCM (300 mL) and H_2O (300 mL). The acidic aqueous layer was carefully extracted three times with DCM. The combined organic extracts were carefully added to a beaker containing saturated aqueous $NaHCO_3$ to neutralize residual acid. The mixture was extracted three times with DCM. The combined organic extracts were dried over $MgSO_4$, filtered, concentrated via rotary evaporation. The beige solid was dissolved in minimal DCM at room temperature. Excess MeOH was added and the white solids formed were

collected by filtration and washed with a cold mixture of MeOH:Et_2O (1:1). The desired product was obtained as a white solid (21 g, 50% yield). The compound was identical to that reported in the literature by ^{1}H NMR and ^{13}C NMR.[10]

*During some preparations, a white solid with a faint blue color was obtained which was otherwise pure by ^{1}H NMR analysis. While column chromatography did not remove the impurity, purification by sublimation at 210 °C under vacuum (300 mTorr) provided a pure white solid.

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9) King, J. F.; Rathore, R.; Lam, J. Y. L.; Guo, Z. R.; Klassen, D. F. *J. Am. Chem. Soc.* **1992**, *114*, 3028.
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Supporting Information

Spectra

Mixed-Ligand Chiral Rhodium(II) Catalyst Enables the Enantioselective Total Synthesis of Piperarborenine B

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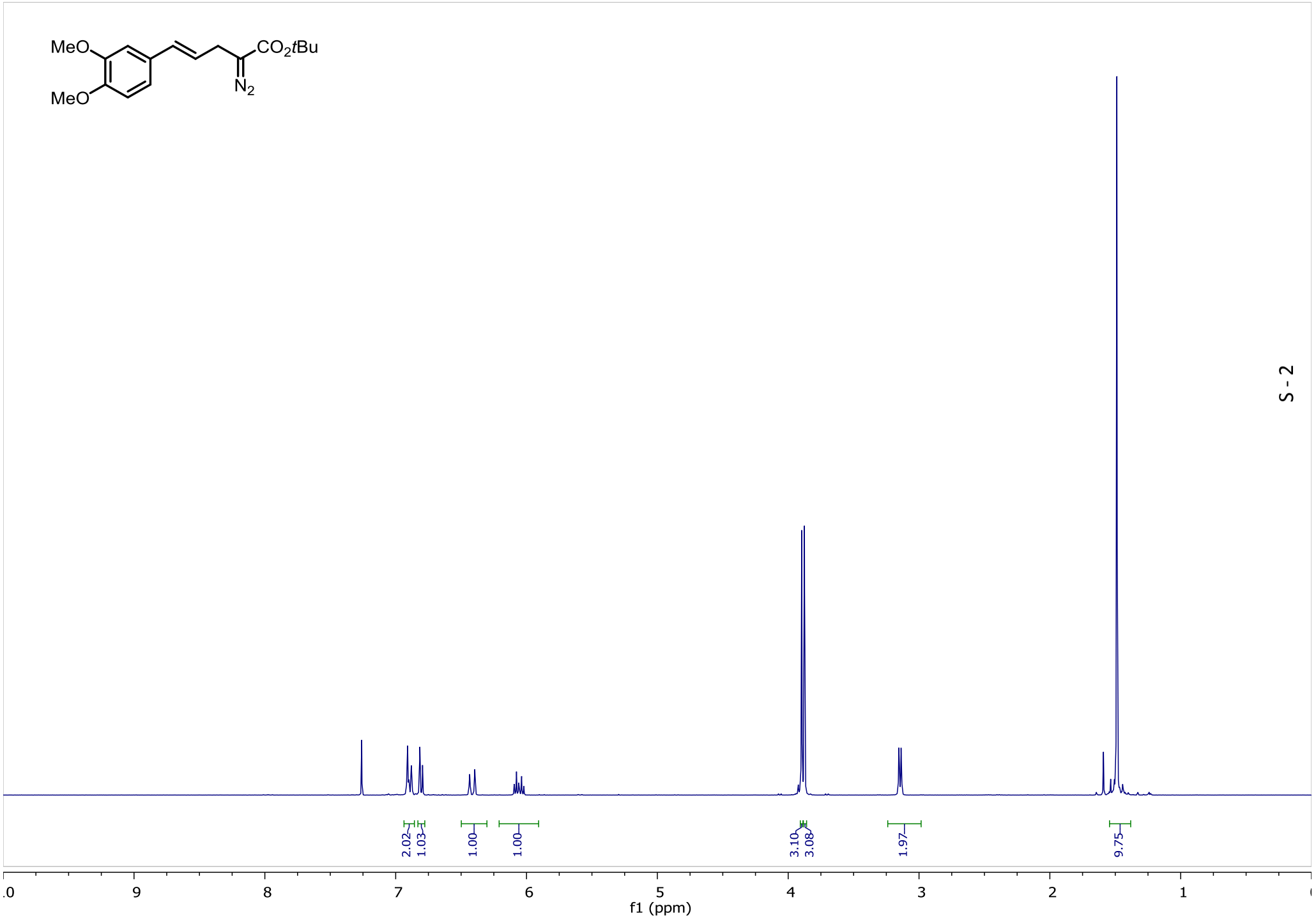
Brown Laboratory, Department of Chemistry and Biochemistry, University of Delaware, Newark, DE 19716, United States

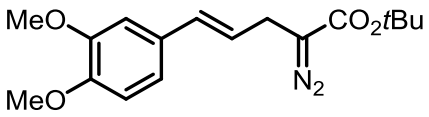
tert-butyl (*E*)-2-diazo-5-(3,4-dimethoxyphenyl)pent-4-enoate (**3**)

^{1}H NMR (400 MHz, $CDCl_3$)

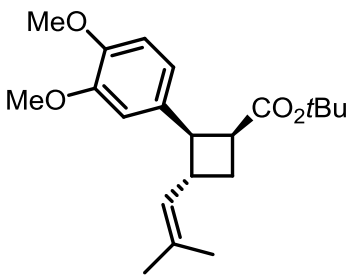


tert-butyl (*E*)-2-diazo-5-(3,4-dimethoxyphenyl)pent-4-enoate (**3**)

^{13}C NMR (101 MHz, $CDCl_3$)



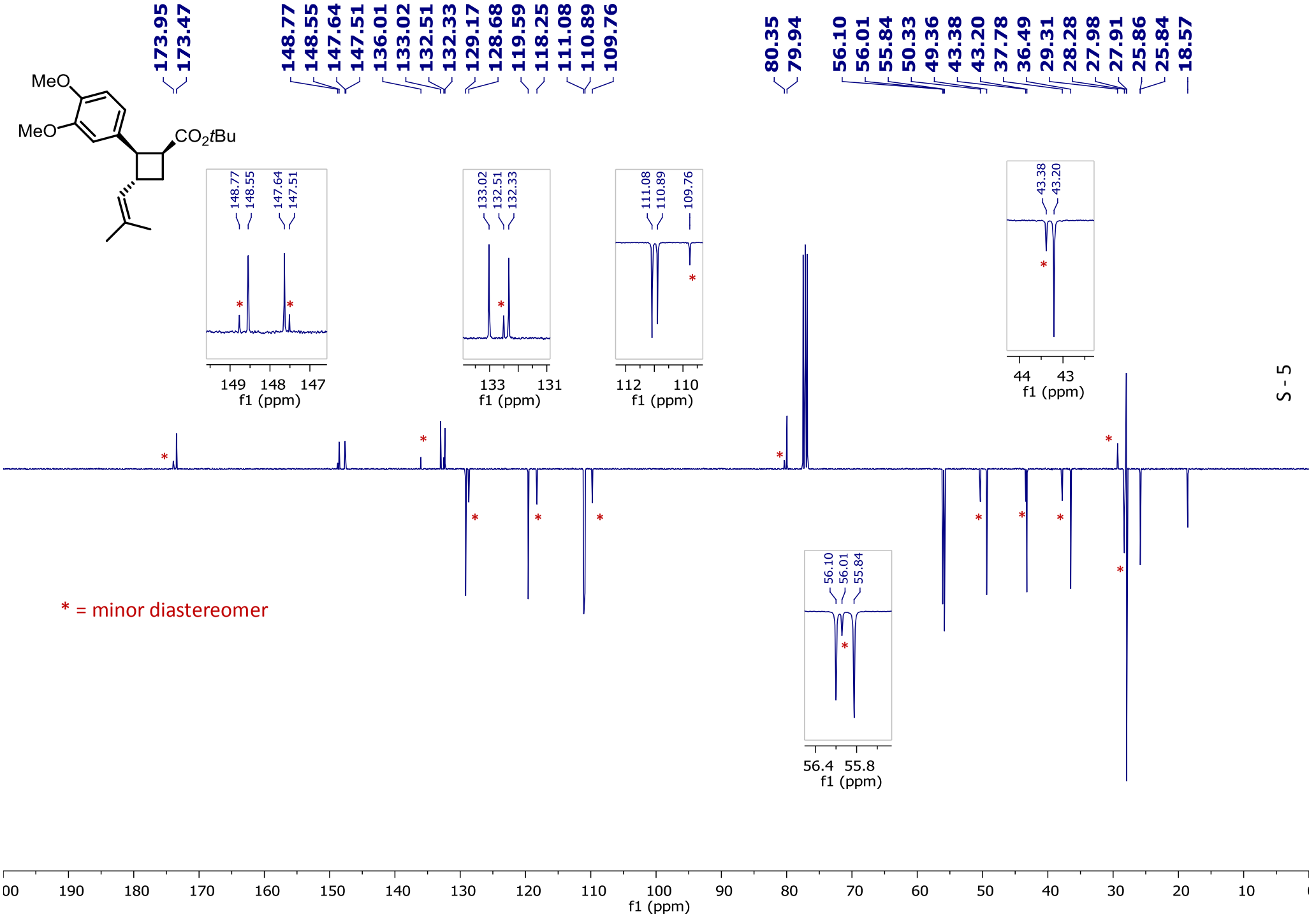
tert-butyl (1*S*,2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-3-(2-methylprop-1-en-1-yl)cyclobutane-1-carboxylate (**5**)
^{1}H NMR (400 MHz, $CDCl_3$)



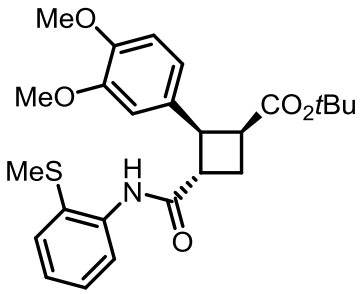
* = minor diastereomer

tert-butyl (1*S*,2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-3-(2-methylprop-1-en-1-yl)cyclobutane-1-carboxylate (**5**)

^{13}C NMR (101 MHz, $CDCl_3$)



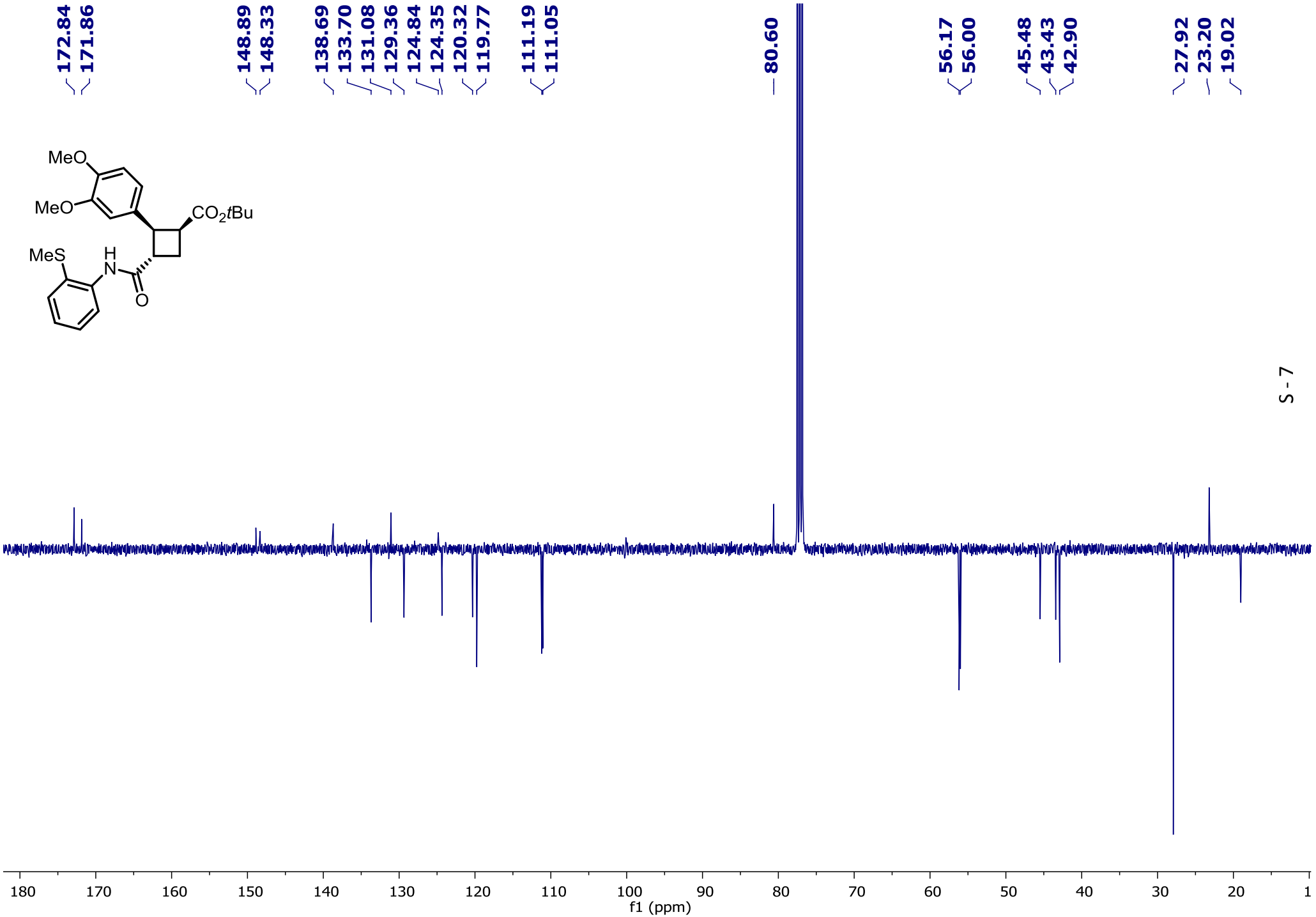
tert-butyl (1*S*,2*R*,3*S*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl)cyclobutane-1-carboxylate (**6**)
^{1}H NMR (400 MHz, $CDCl_3$)



* diethyl ether
**toluene

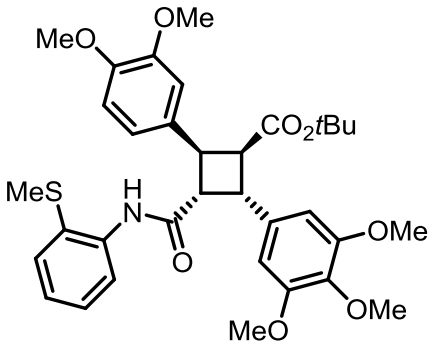
tert-butyl (1*S*,2*R*,3*S*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl)cyclobutane-1-carboxylate (**6**)

^{13}C NMR (101 MHz, $CDCl_3$)



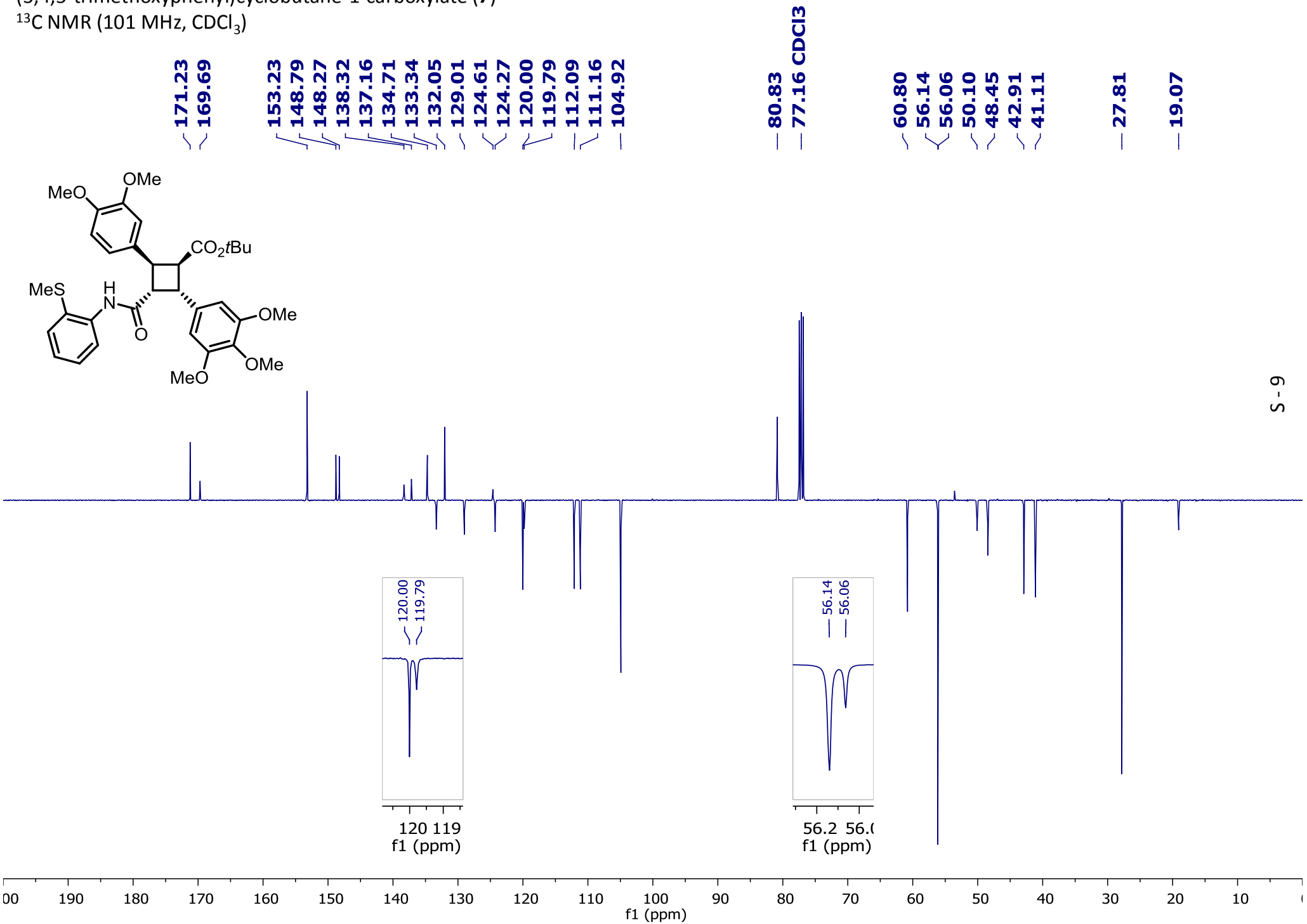
tert-butyl (1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (**7**)

^{1}H NMR (400 MHz, $CDCl_3$)



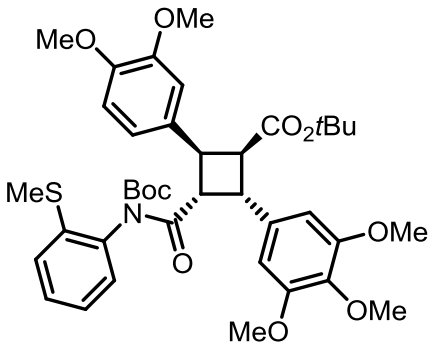
tert-butyl (1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-3-((2-(methylthio)phenyl)carbamoyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (**7**)

^{13}C NMR (101 MHz, $CDCl_3$)

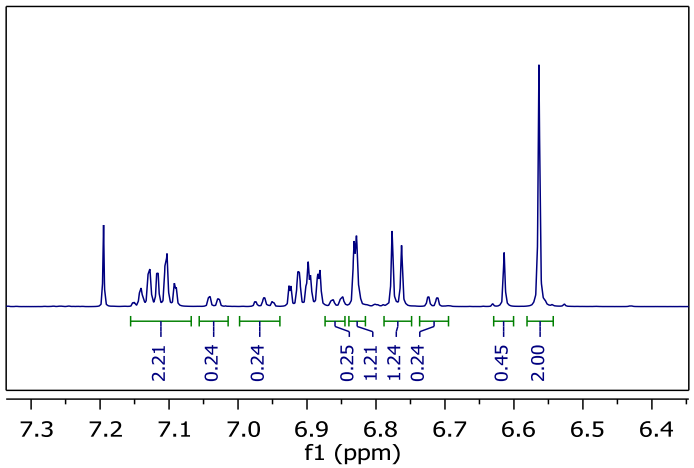


tert-butyl (1*R*,2*R*,3*R*,4*R*)-3-((*tert*-butoxycarbonyl)(2-(methylthio)phenyl)carbamoyl)-2-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (**7-Boc**)

^{1}H NMR (400 MHz, $CDCl_3$)

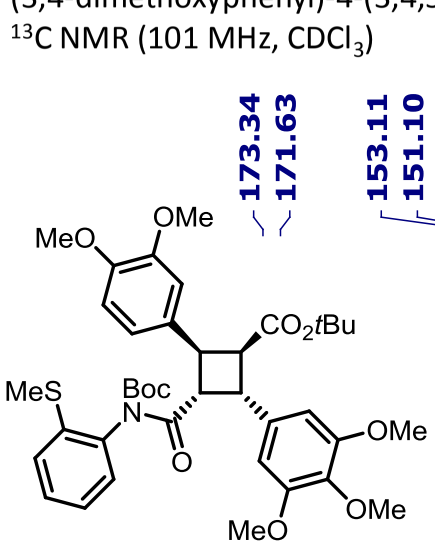


rotamers: 4.3:1



tert-butyl (1*R*,2*R*,3*R*,4*R*)-3-((*tert*-butoxycarbonyl)(2-(methylthio)phenyl)carbamoyl)-2-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1-carboxylate (**7-Boc**)

^{13}C NMR (101 MHz, $CDCl_3$)



rotamers: 4.3:1

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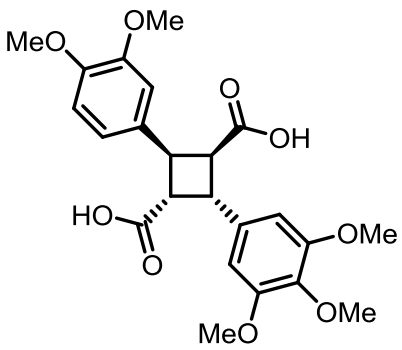
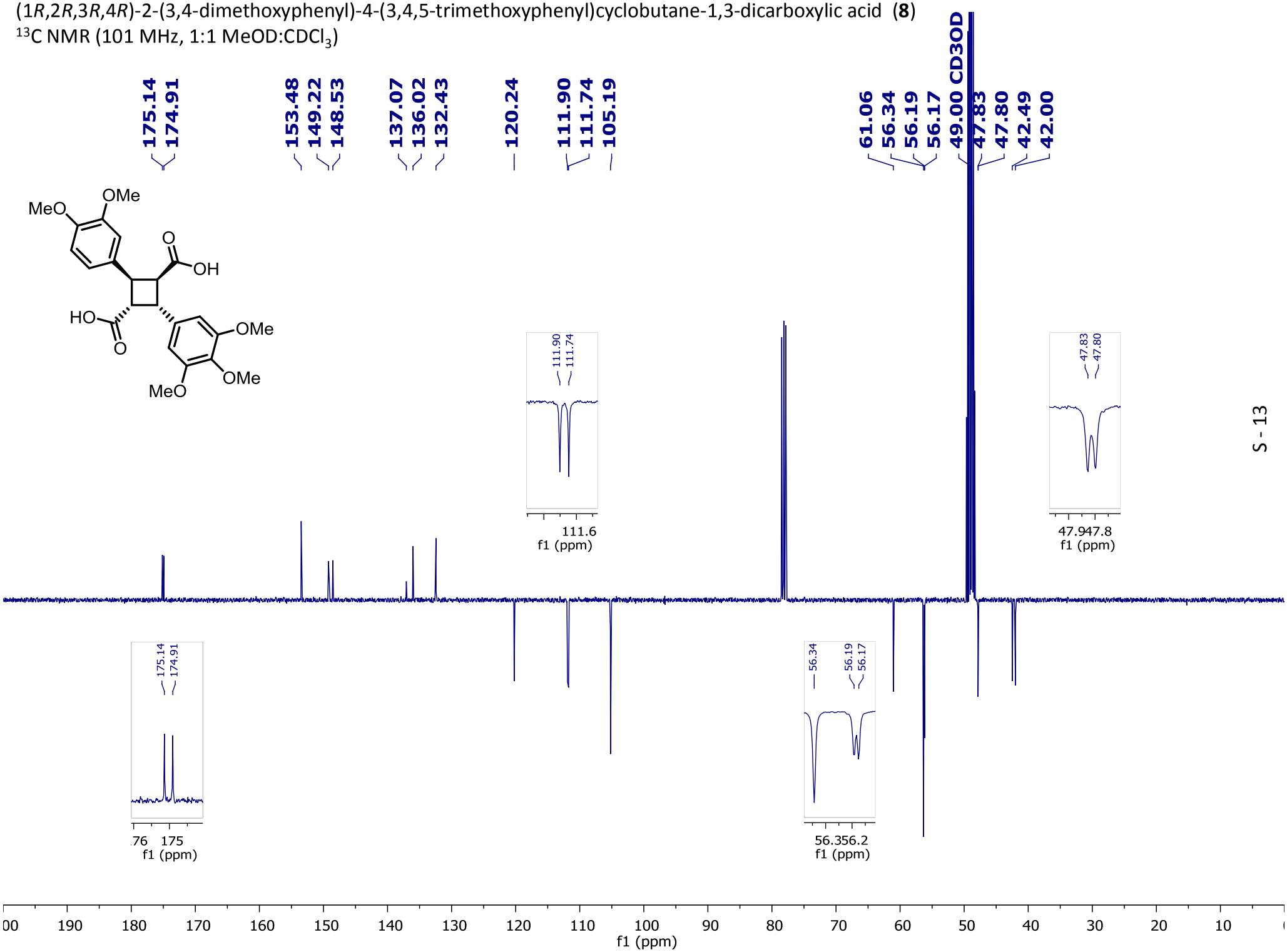
(1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1,3-dicarboxylic acid (**8**)

^{1}H NMR (400 MHz, 1:1 MeOD:$CDCl_3$)



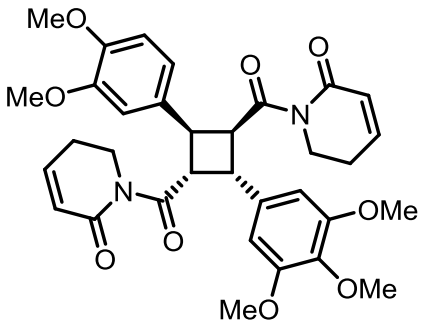
(1*R*,2*R*,3*R*,4*R*)-2-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)cyclobutane-1,3-dicarboxylic acid (**8**)

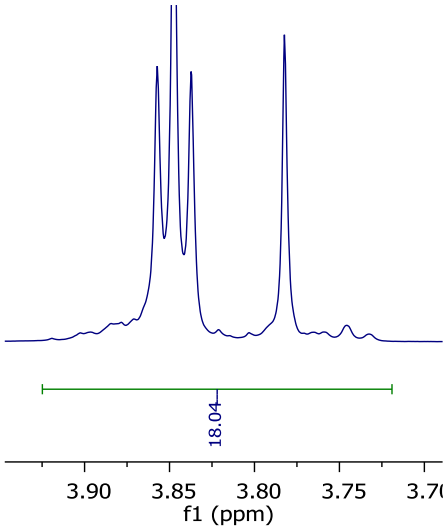
^{13}C NMR (101 MHz, 1:1 MeOD:$CDCl_3$)



Piperarborenine B (**1**)

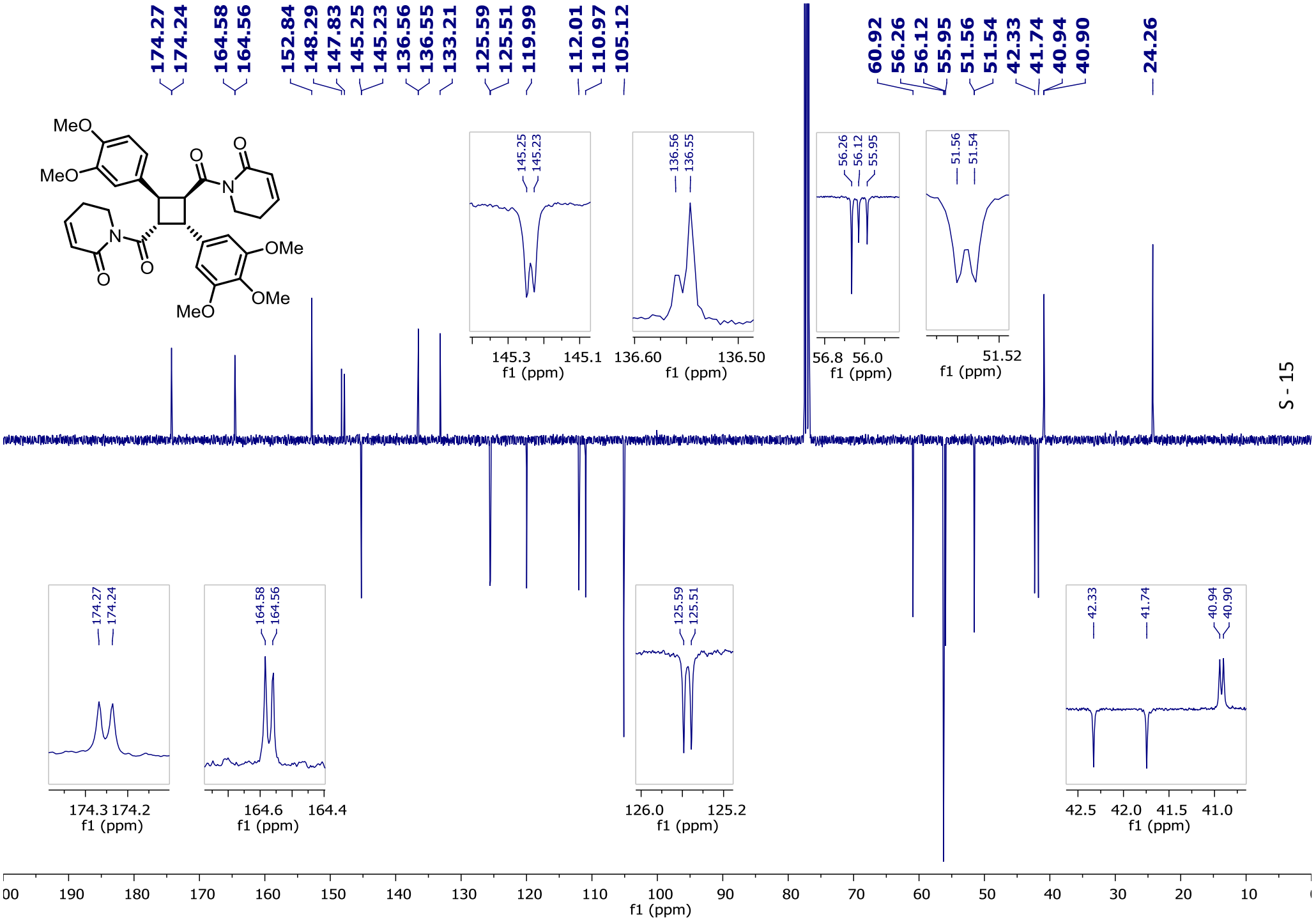
^{1}H NMR (400 MHz, $CDCl_3$)





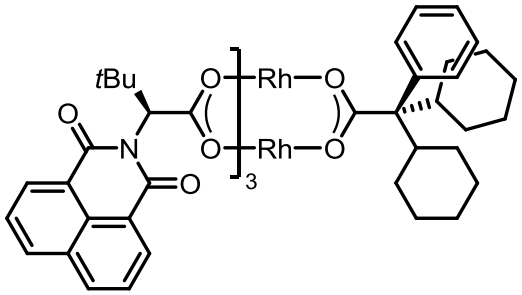
Piperarborenine B (**1**)

^{13}C NMR (101 MHz, $CDCl_3$)



Rh_2(*S*-NTTL)$_3$(dCPA)•2EtOAc

^{1}H NMR (400 MHz, 3:1 CD_2Cl_2:CD_3OD, referenced to CD_3OD)

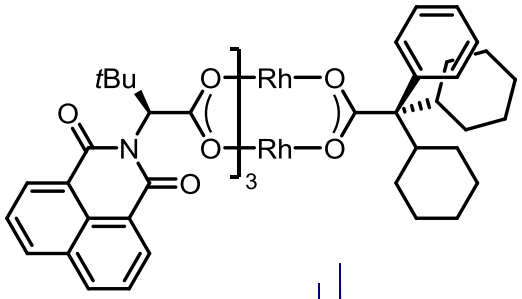


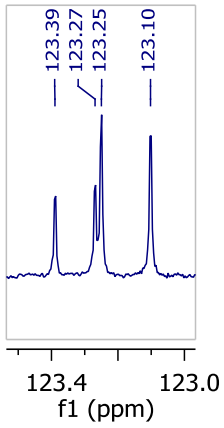
*EtOAc

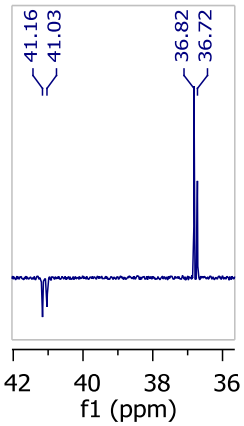
Rh_2(*S*-NTTL)$_3$(dCPA) •2EtOAc

^{13}C NMR (101 MHz, 3:1 CD_2Cl_2:CD_3OD, referenced to CD_3OD))

193.28 187.66 187.52 165.67 165.44 163.76 163.35 140.04 134.35 134.32 134.03 133.96 133.46 132.38 131.96 131.62 131.37 128.59 128.51 127.82 127.42 127.18 127.08 126.95 125.98 123.39 123.27 123.25 123.10 65.47 62.12 61.74 53.88 CD_2Cl_2 49.00 CD_3OD 41.16 41.03 36.82 36.72 30.15 29.49 29.25 27.85 27.82 27.74 27.61 27.28 27.08







*EtOAc

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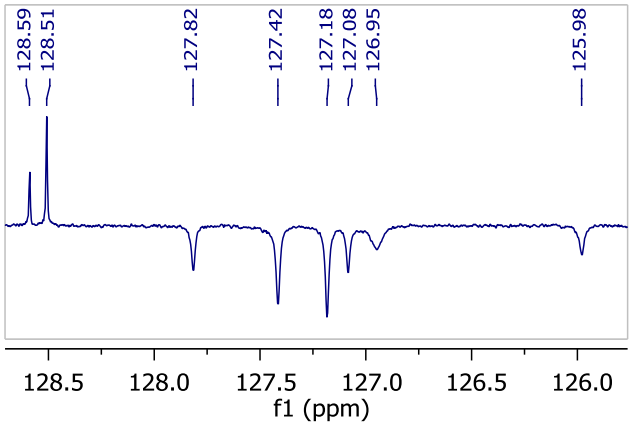
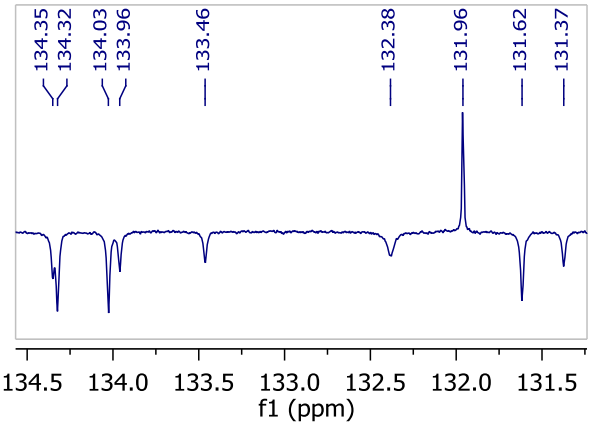
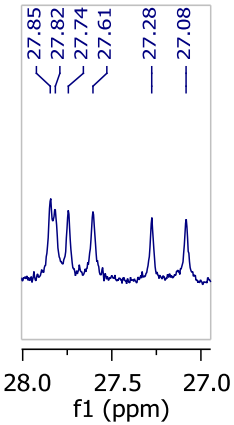
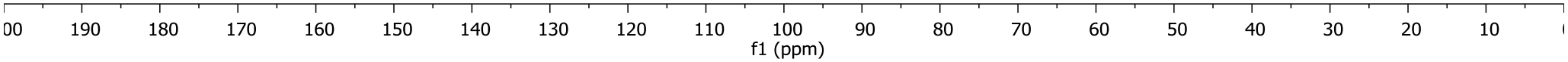
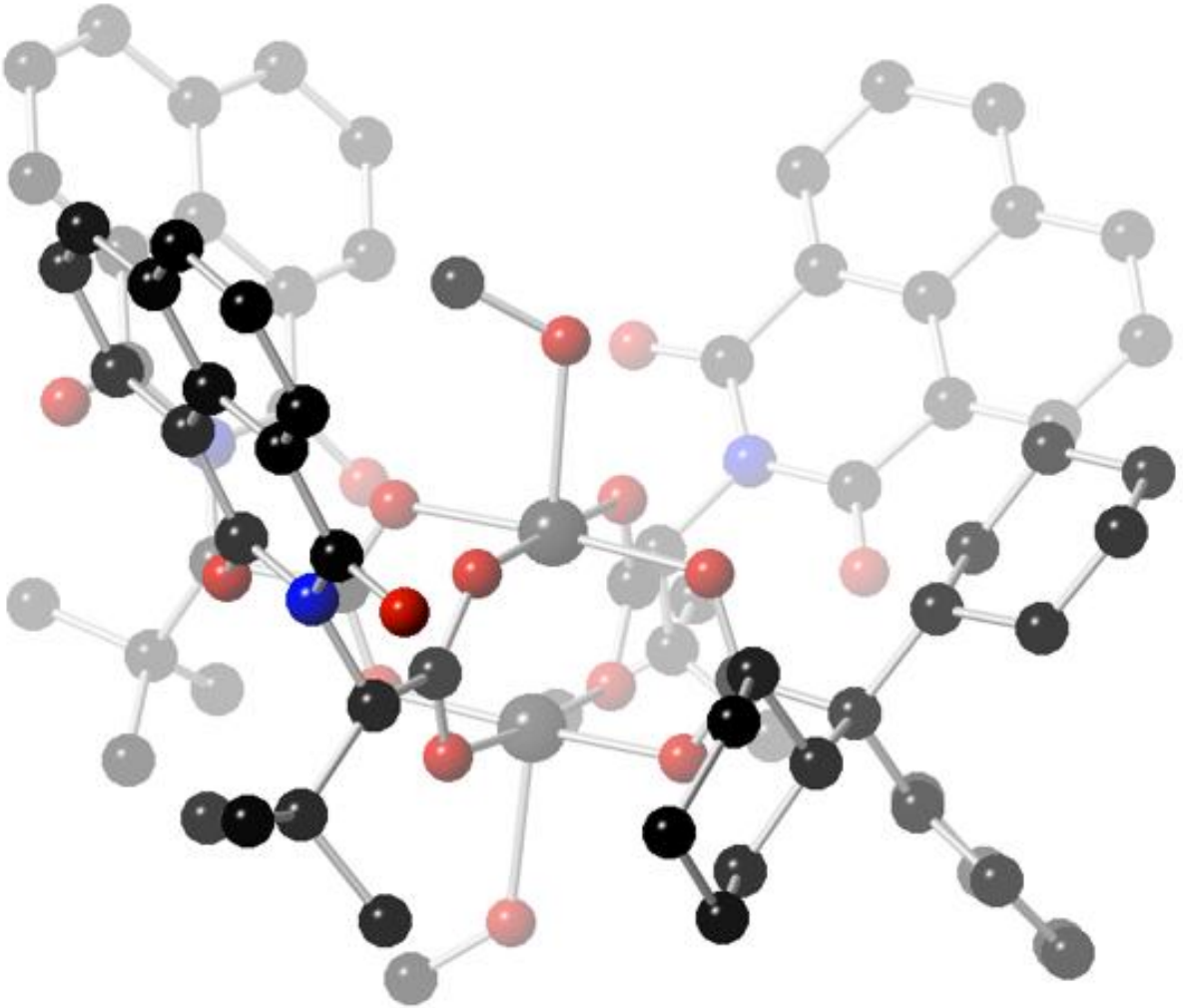




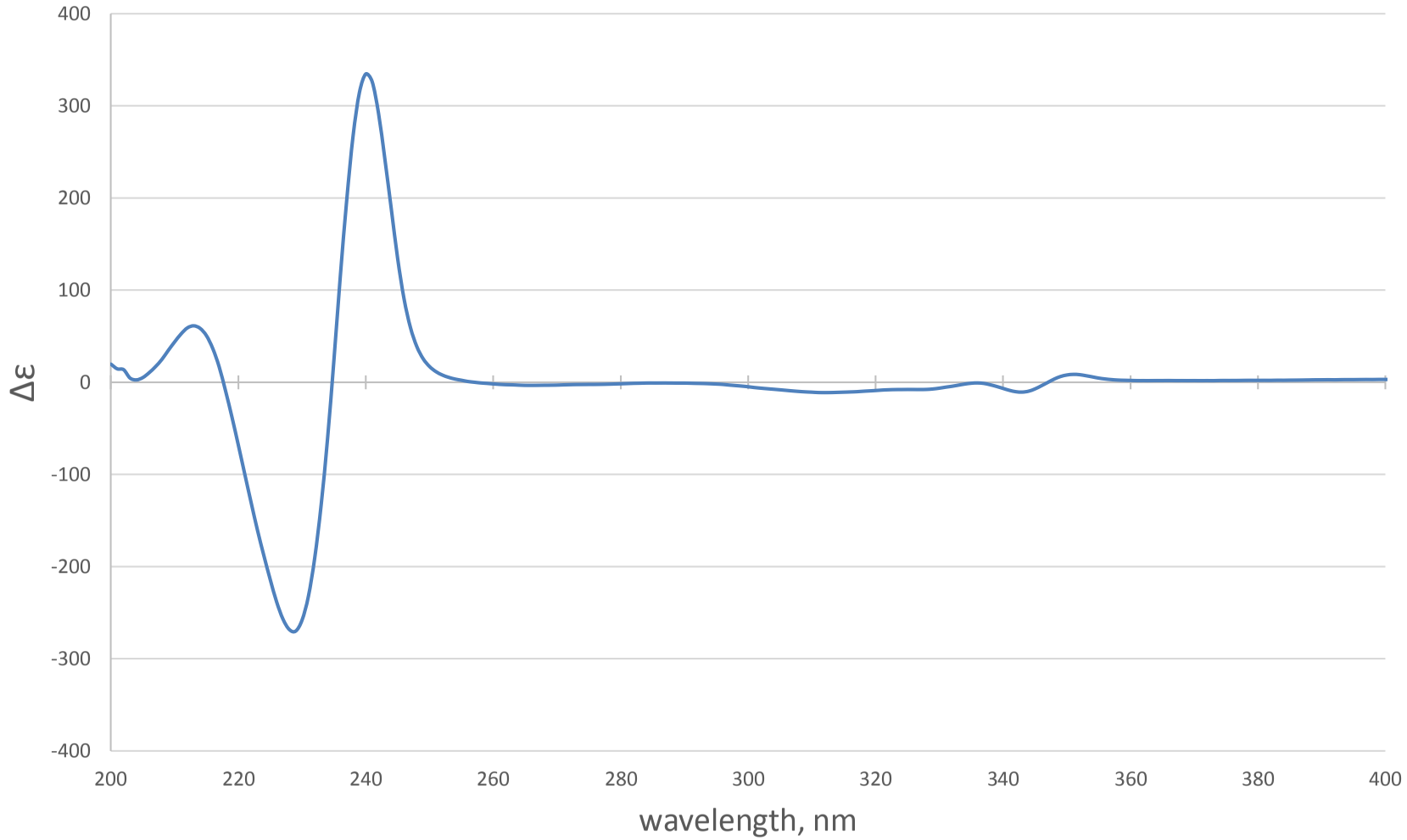




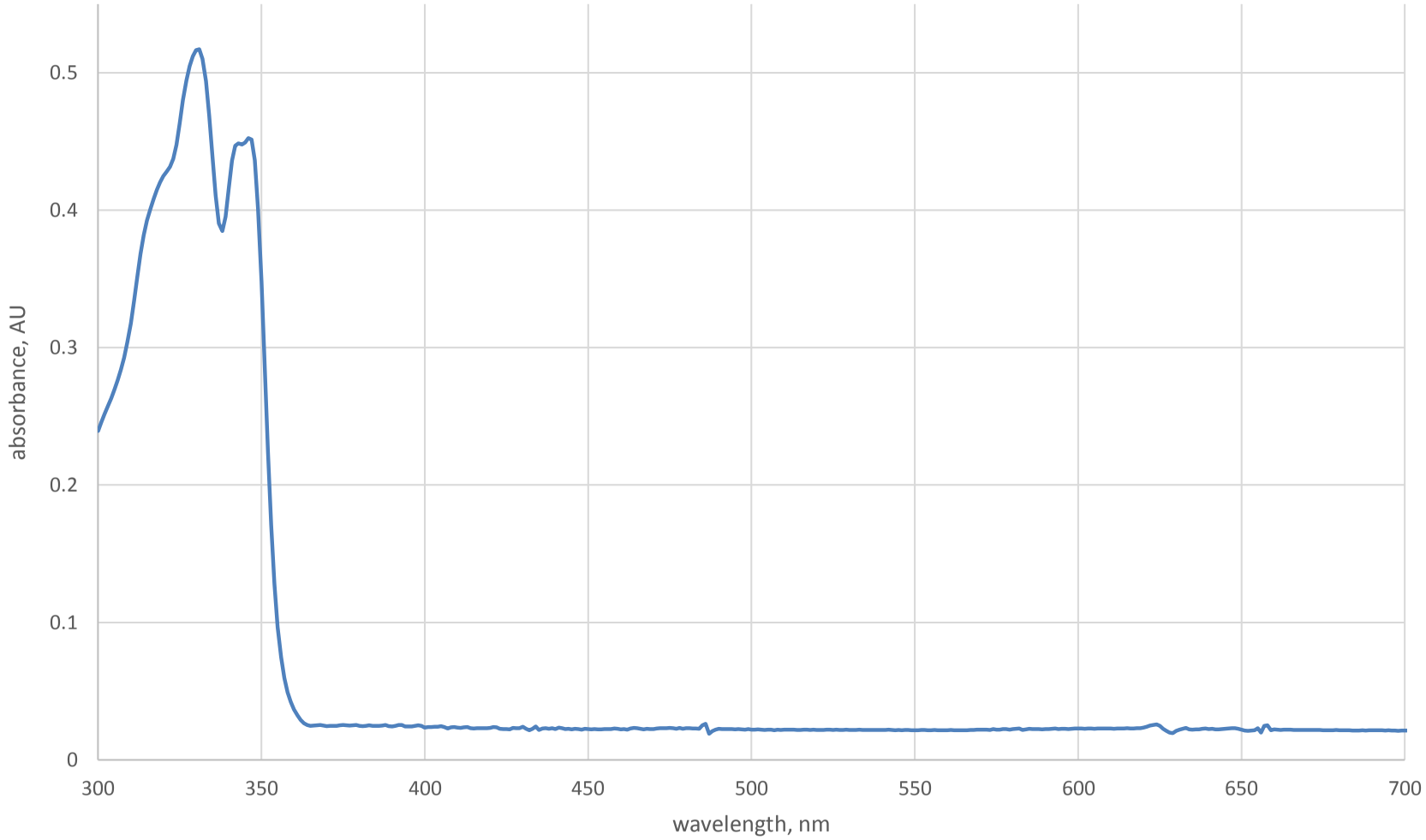
Rh_2(*S*-NTTL)$_3$(dCPA)
X-ray crystal structure



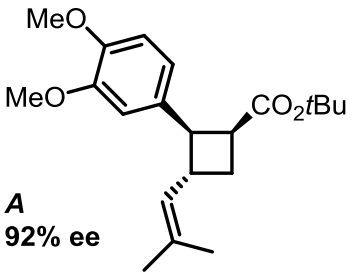
Rh_2(*S*-NTTL)$_3$(dCPA) (0.15 mM in Et_2O)
CD Spectrum at 21 °C



Rh_2(*S*-NTTL)$_3$(dCPA) (0.040 mM in Et_2O)
UV-Vis Spectrum at 25 °C

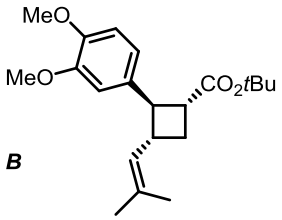


tert-butyl (1*S*,2*R*,3*R*)-2-(3,4-dimethoxyphenyl)-3-(2-methylprop-1-en-1-yl)cyclobutane-1-carboxylate (**5**)
HPLC Traces: ChiralCEL OD column, 0.5% 2-propanol in hexanes, 1mL/min, 220 nm



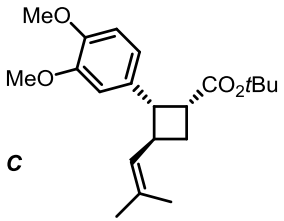
A
92% ee

major diastereomer
major enantiomer



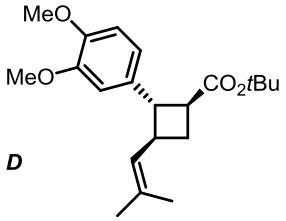
B

minor diastereomer
major enantiomer



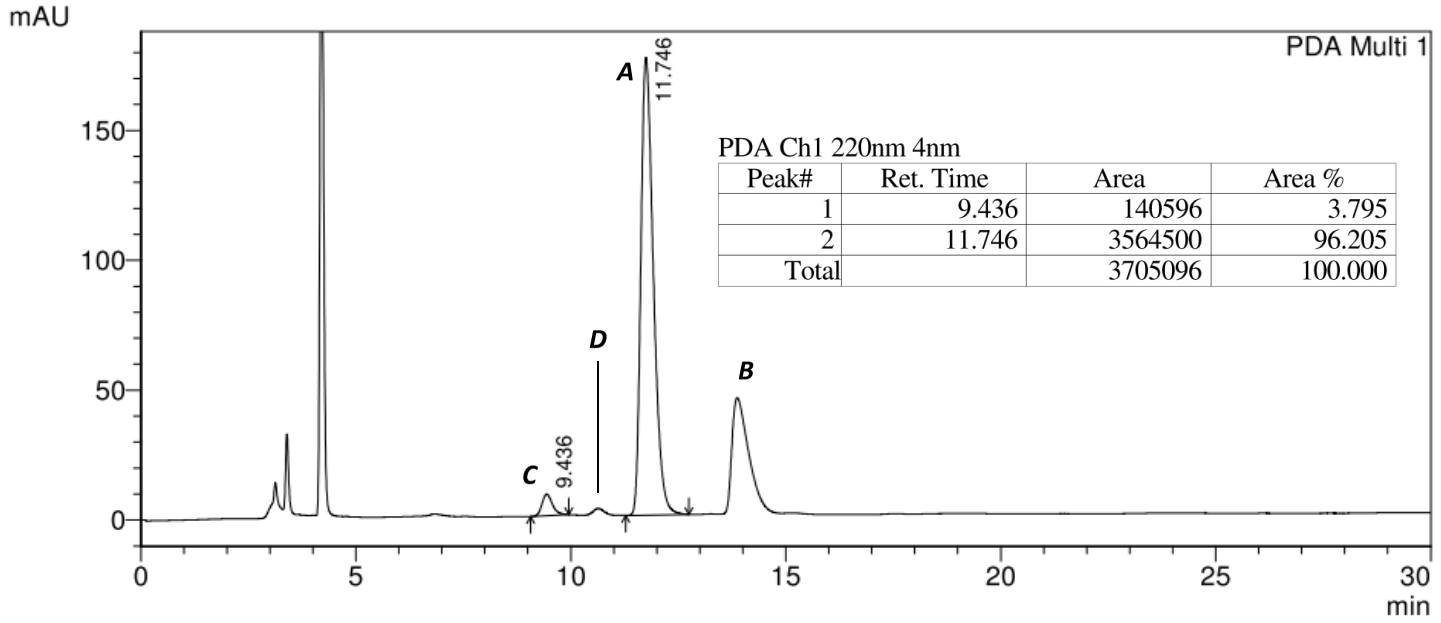
C

major diastereomer
minor enantiomer



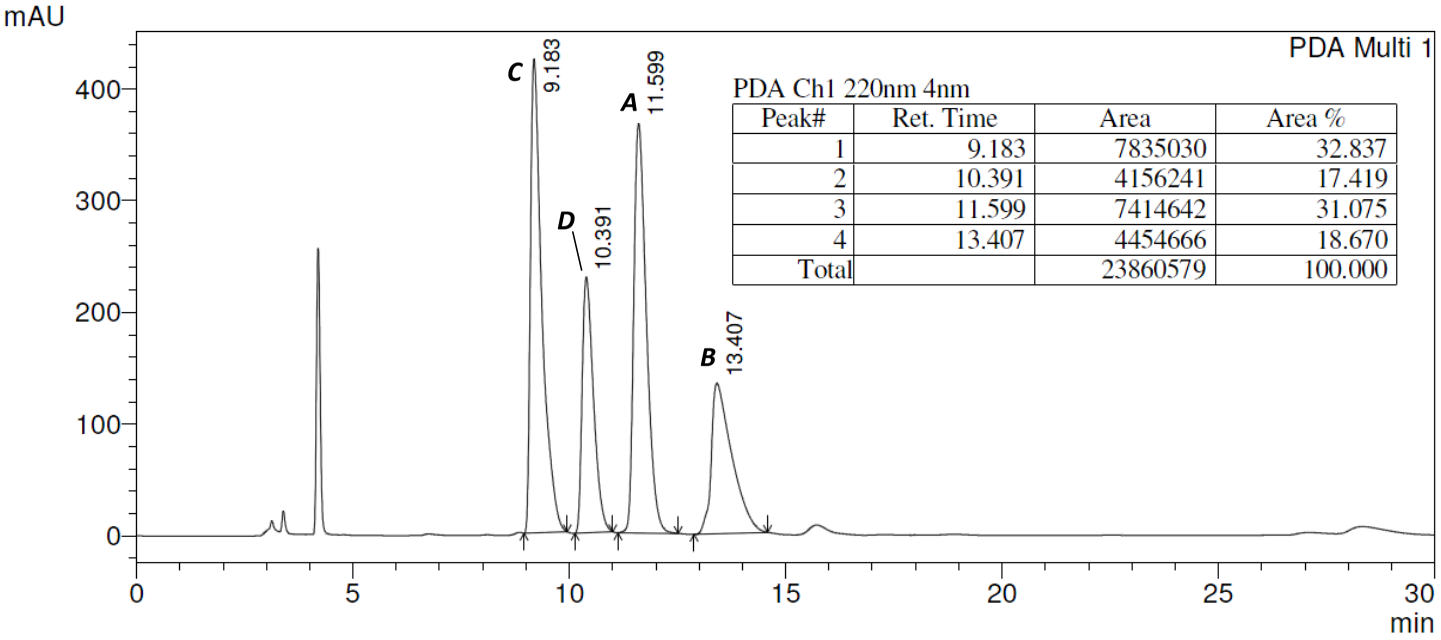
D

minor diastereomer
minor enantiomer



PDA Ch1 220nm 4nm

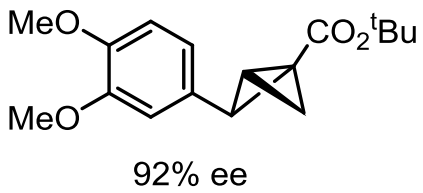
Peak#	Ret. Time	Area	Area %
1	9.436	140596	3.795
2	11.746	3564500	96.205
Total		3705096	100.000



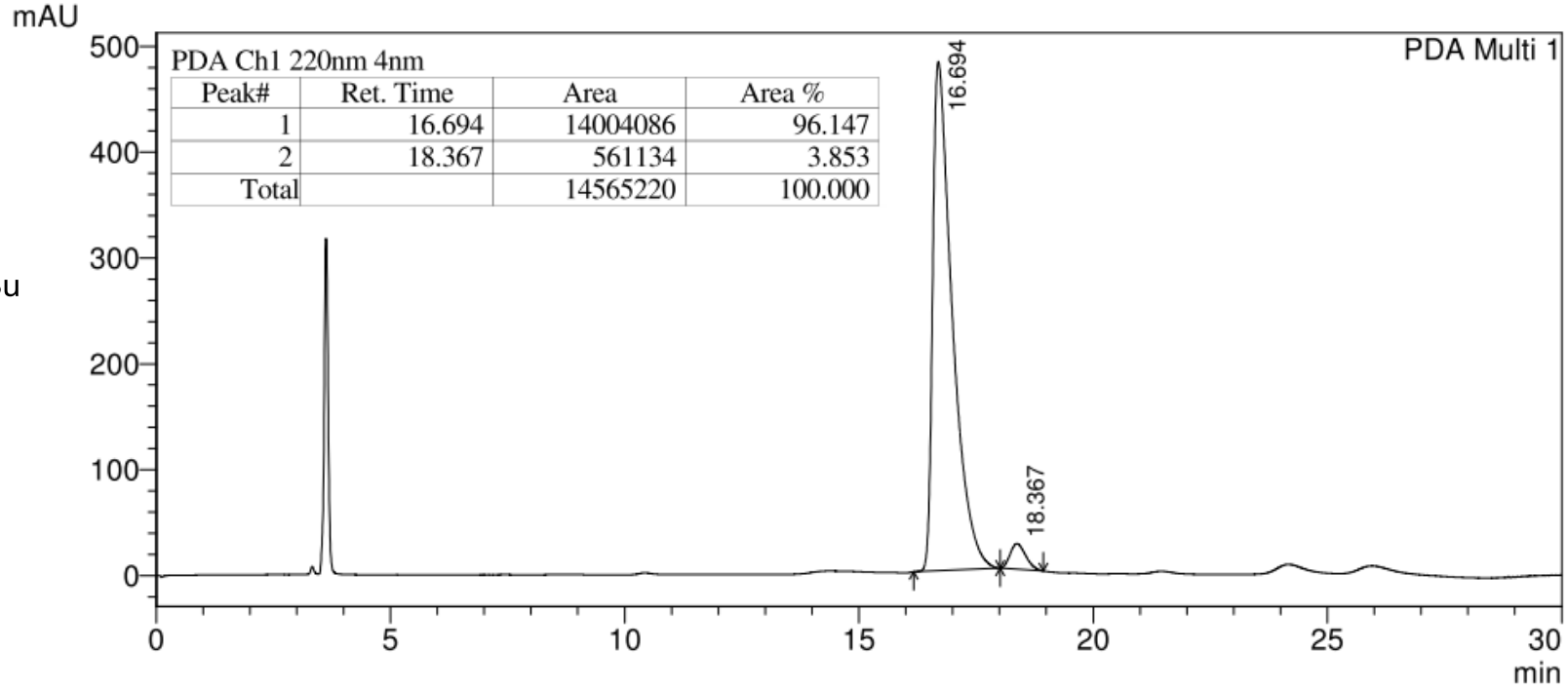
PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Area %
1	9.183	7835030	32.837
2	10.391	4156241	17.419
3	11.599	7414642	31.075
4	13.407	4454666	18.670
Total		23860579	100.000

tert-butyl (3*S*)-2-(3,4-dimethoxyphenyl)bicyclo[1.1.0]butane-1-carboxylate (**4**)
HPLC Traces: ChiralPAK IA column, 0.5% 2-propanol in hexanes, 1mL/min, 220 nm



92% ee



Peak#	Ret. Time	Area	Area %
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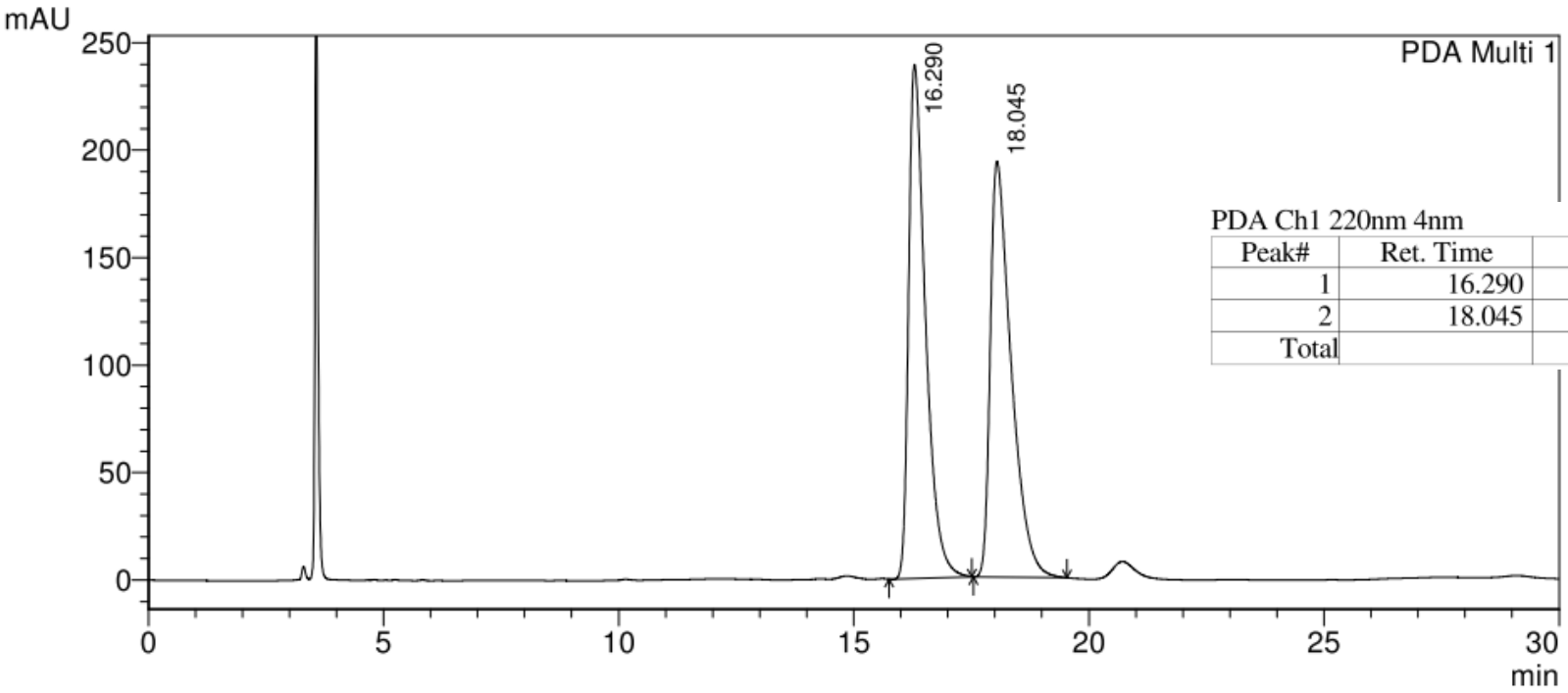
2	18.367	561134	3.853
Total		14565220	100.000



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Area %
1	16.290	5963478	49.899
2	18.045	5987607	50.101
Total		11951085	100.000