Total synthesis based on the originally claimed structure of mucosin

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Supporting Information

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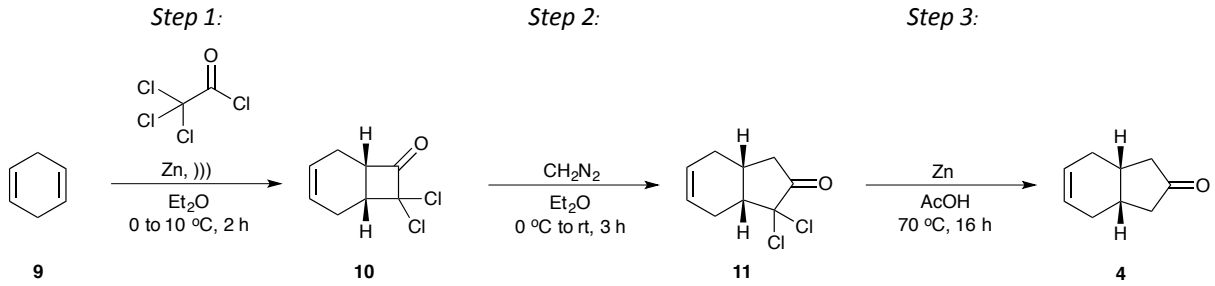
General Information

All commercially available reagents and solvents were used in the form they were supplied without any further purification. (+)-Bis[(*R*)-1-phenylethyl]amine hydrochloride (optical purity ≥ 99% *ee* by GLC) was purchased from Sigma-Aldrich. The stated yields are based on isolated material. The melting points are uncorrected. Thin layer chromatography was performed on silica gel 60 F_{254} aluminum-backed plates fabricated by Merck. Flash column chromatography was performed on silica gel 60 (40-63 µm) fabricated by Merck. NMR spectra were recorded on a Bruker Ascend^{TM} 400 at 400 MHz for ^{1}H NMR and at 100 MHz for ^{13}C NMR. Coupling constants (*J*) are reported in hertz and chemical shifts are reported in parts per million (δ) relative to the central residual protium solvent resonance in ^{1}H NMR ($CDCl_3$ = δ 7.27) and the central carbon solvent resonance in ^{13}C NMR ($CDCl_3$ = δ 77.00 ppm). Mass spectra were recorded at 70 eV on Waters Prospec Q spectrometer using EI as the method of ionization. IR spectra (4000–600 cm^{-1}) were recorded on a Perkin-Elmer Spectrum BX series FT-IR spectrophotometer using a reflectance cell (HATR). Optical rotations were measured using a 1 mL cell with a 1.0 dm path length on a Perkin Elmer 341 polarimeter using the stated solvents. Determination of enantiomeric excess was performed by GLC on an Agilent Technologies 7820A GC instrument with split (1:30) injection, FID

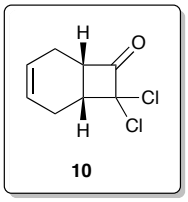
detector and equipped with a chiral stationary phase (Agilent J&W GC columns, CP-Chirasil-DEX CB, 25 m, 0.25 mm, 0.25 µm) applying the conditions stated. X-ray crystallography was performed on a Bruker D8 Venture diffractometer with InCoatec ImuS Microfocus radiation source and Photon 100 CMOS detector. Data collection with Apex2,[1] data integration and cell refinement with SAINT,[1] absorption correction by SADABS,[1] structure solution with SHELXT,[2] structure refinement with SHELXL.[3] Molecular graphics from Mercury.[4]

Preparation of *meso*-ketone (4):



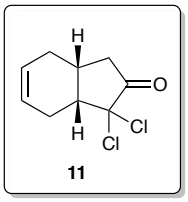
Scheme S-1 Synthetic route to *meso*-ketone **4**.

***rac*-(1*R*,6*S*)-8,8-Dichlorobicyclo[4.2.0]oct-3-en-7-one (10).[5]**



1,4-Cyclohexadiene **9** (5 g, 62.5 mmol, 1.0 equiv.) was added to a suspension of zinc powder (8.2 g, 125 mmol, 2.0 equiv.) in dry Et_2O (100 mL) and sonicated at 0 °C for 15 min. Then trichloroacetylchloride (22.8 g, 125 mmol, 2.0 equiv.) in dry Et_2O (100 mL) was added dropwise over 2 h while the reaction mixture was still sonicating. After complete addition the reaction mixture was sonicated for a further 2 h at 0-10 °C. The colour changed from colourless to dark yellow. The sonication was then stopped and the reaction mixture filtered and concentrated *in vacuo*. The resulting orange slurry was diluted in Et_2O (400 mL) and washed with H_2O (2 x 400 mL) and sat. aq. $NaHCO_3$ (1 x 400 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The resulting crude dark yellow oil was purified by column chromatography on silica (hexane/EtOAc 99:1) to afford the title compound as a colourless oil. All spectroscopic and physical data were in full agreement with those reported in the literature.[5] Yield: 2.25 g (47%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90-5.81 (m, 2H), 4.07-4.01 (m, 1H), 3.32 (ddt, *J* = 2.0, 7.9, 10.4 Hz, 1H), 2.63-2.50 (m, 2H), 2.39-2.32 (m, 1H), 2.17-2.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 127.3, 126.3, 88.5, 53.7, 45.2, 23.1, 21.3; IR (neat, cm^{-1}) 3041 (w), 2939 (w), 2895 (w), 2841 (w) 1799 (s), 1644 (w), 1433 (m); HRMS (EI+): Exact mass calculated for $C_8H_8OCl_2$ $[M]^+$: 189.9952, found 189.9953; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.65.

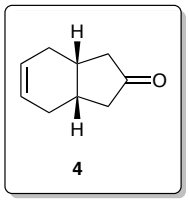
***rac*-(1*R*,6*R*)-7,7-Dichlorobicyclo[4.3.0]oct-3-en-7-one (11).**



To a stirring solution of *rac*-(1*R*,6*S*)-8,8-dichlorobicyclo[4.2.0]oct-3-en-7-one **10** (2.0 g, 10.5 mmol, 1.0 equiv.) in dry Et_2O (50 mL), at 0 °C, was added diazomethane (2.5 g, 58.8 mmol, 5.6 equiv.) in dry Et_2O (50 mL) dropwise over 15 min. The reaction mixture bubbled and turned a deep golden yellow colour. After 30 min the reaction was warmed to room temperature and left to stir for 2 h. The reaction was then quenched with glacial AcOH (5 mL) dropwise until there was no more gas evolution and the colour changed from golden yellow to almost colourless. The resulting mixture was then washed with H_2O (2 x 300 mL), sat. aq. $NaHCO_3$ (1 x 300 mL), brine (1 x 300 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The resulting dark yellow oil was purified by column chromatography on silica (hexane/EtOAc 9:1) to afford the title compound as a colourless oil. Yield: 1.6 g (75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ; 5.64-5.57 (m, 2H), 2.86-2.80 (m, 1H), 2.74-2.69 (m, 1H), 2.54 (dd, *J* = 7.5, 19.2 Hz, 1H), 2.38-2.29 (m, 2H), 2.07-2.00 (m, 2H), 1.72-1.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.7, 123.9, 123.1, 89.5, 46.7, 36.6, 28.1, 25.8, 23.5; IR (neat, cm^{-1}) 3033 (m), 2916 (m), 2842 (m), 1764 (s) 1662 (w) 1434

(m), 1402 (m); HRMS (EI+): Exact mass calculated for $C_9H_{10}OCl_2$ $[M]^+$: 204.0109, found 204.0103; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.60.

***meso*-(1*S*,6*R*)-Bicyclo[4.3.0]non-3-ene-8-one (4).[6]**



4

To a stirring suspension of zinc powder (1.71 g, 26.3 mmol, 2.0 equiv.) in glacial AcOH (50 mL) was added *rac*-(1*R*,6*R*)-7,7-dichlorobicyclo[4.2.0]oct-3-en-7-one (**11**) (2.7 g, 13.2 mmol, 1.0 equiv.) in glacial AcOH (30 mL) dropwise. The resulting reaction mixture was stirred for 16 h at 70 °C. The reaction mixture was then cooled to room temperature and filtered to remove the resulting solid. The filtrate was diluted with CH_2Cl_2 (200 mL) and washed with H_2O (2 x 300 mL), sat. aq. $NaHCO_3$ (1 x 300 mL), brine (1 x 300 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude pale yellow oil was purified by column chromatography on silica (hexane/EtOAc 95:5) to give the *meso* compound as a colourless oil. All spectroscopic and physical data were in full agreement with those reported in the literature.[6] Yield: 2.45 g (72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70-5.69 (m, 2H), 2.46-2.41 (m, 2H), 2.34-2.25 (m, 4H), 2.10 (dd, *J* = 6.4, 18.6 Hz, 2H) 1.89-1.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.6 124.6 (2C), 44.6 (2C), 32.3 (2C), 26.2 (2C); IR (neat, cm^{-1}) 3024 (m), 2834 (m), 2901 (s), 1744 (s), 1655 (w), 1439 (m), 1407 (s); HRMS (EI+): Exact mass calculated for $C_9H_{12}O$ $[M]^+$: 136.0888, found 136.0983; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.51.

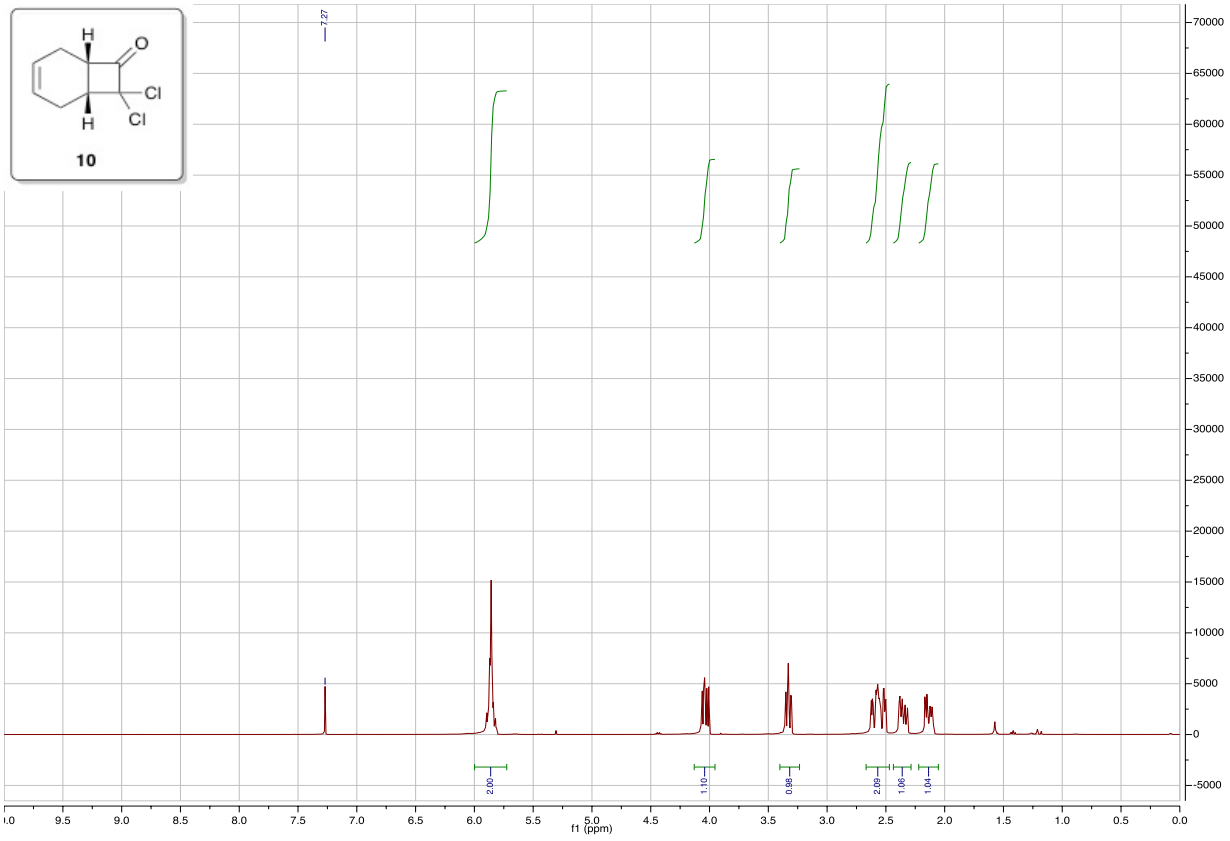


Figure S-1 ^{1}H-NMR spectrum of compound **10**.

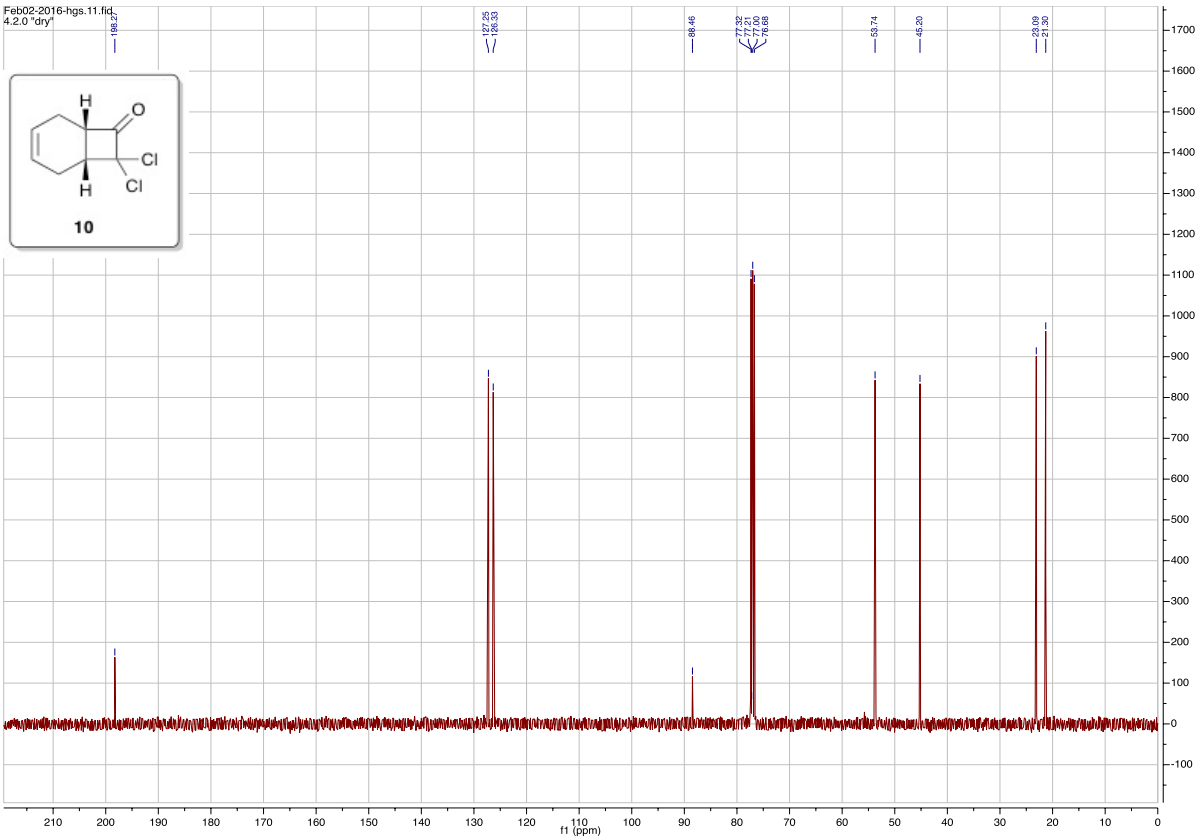


Figure S-2 ^{13}C-NMR spectrum of compound **10**.

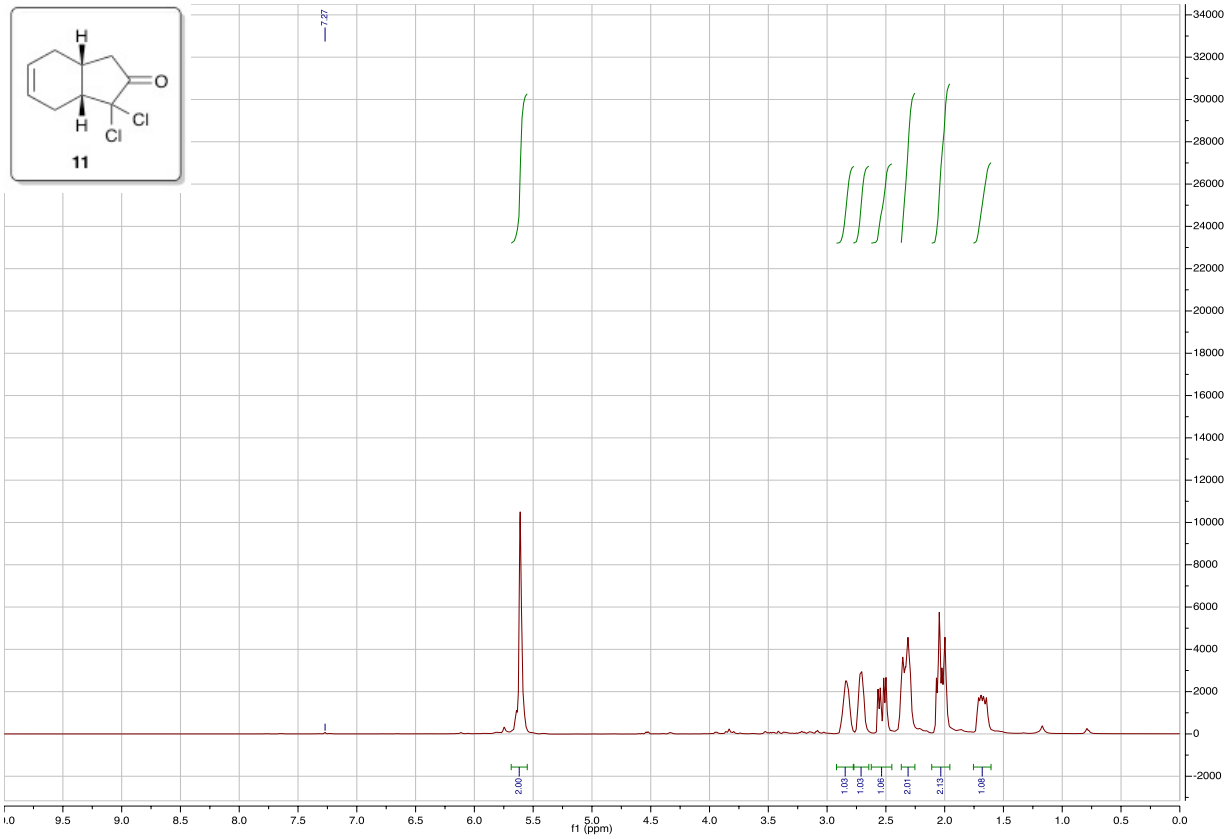


Figure S-3 ^{1}H-NMR spectrum of compound **11**.

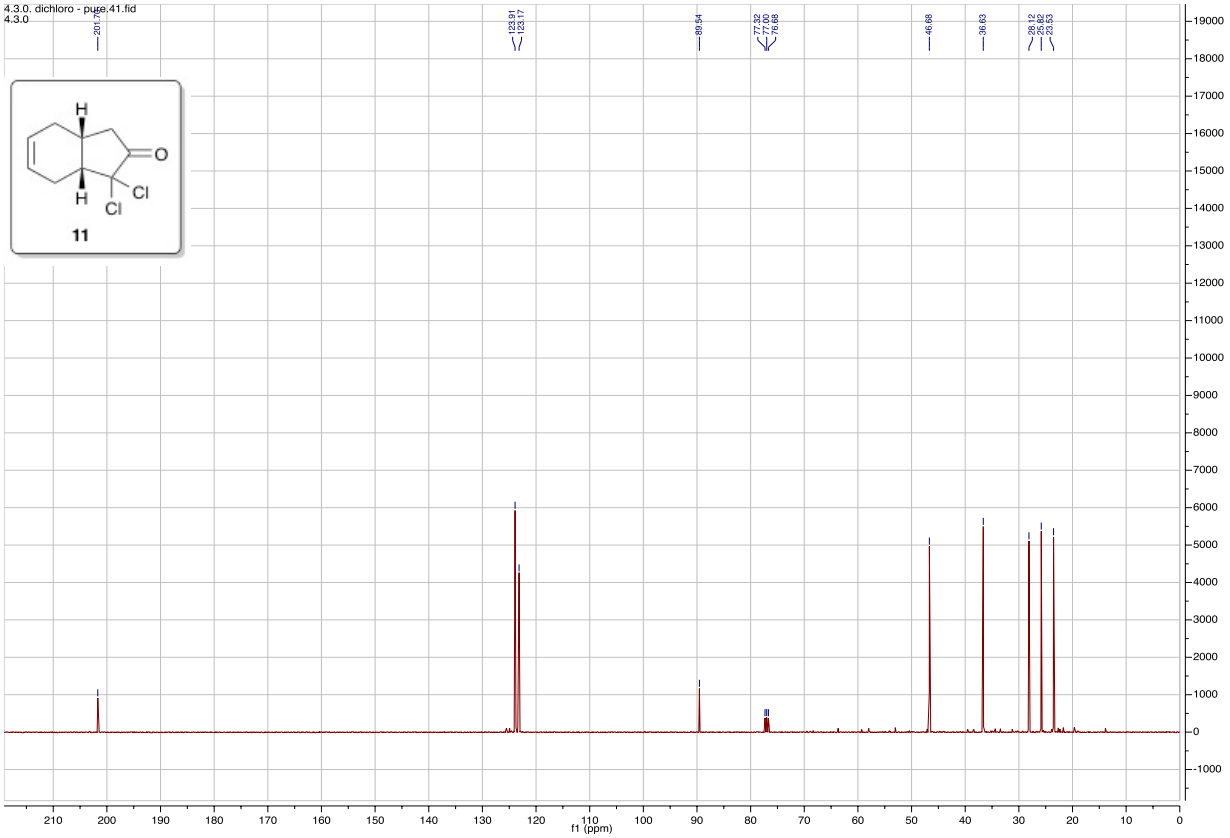


Figure S-4 ^{13}C-NMR spectrum of compound **11**.

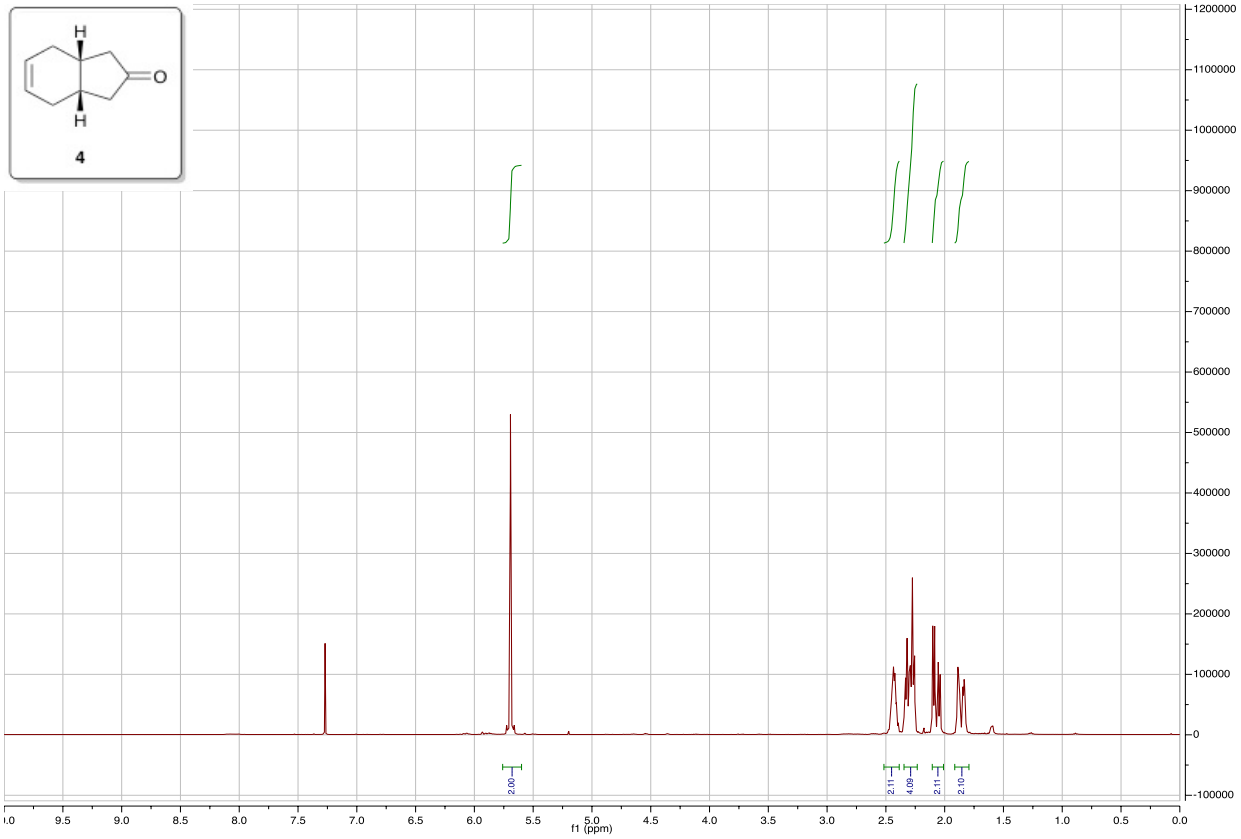


Figure S-5 ^{1}H-NMR spectrum of compound **4**.

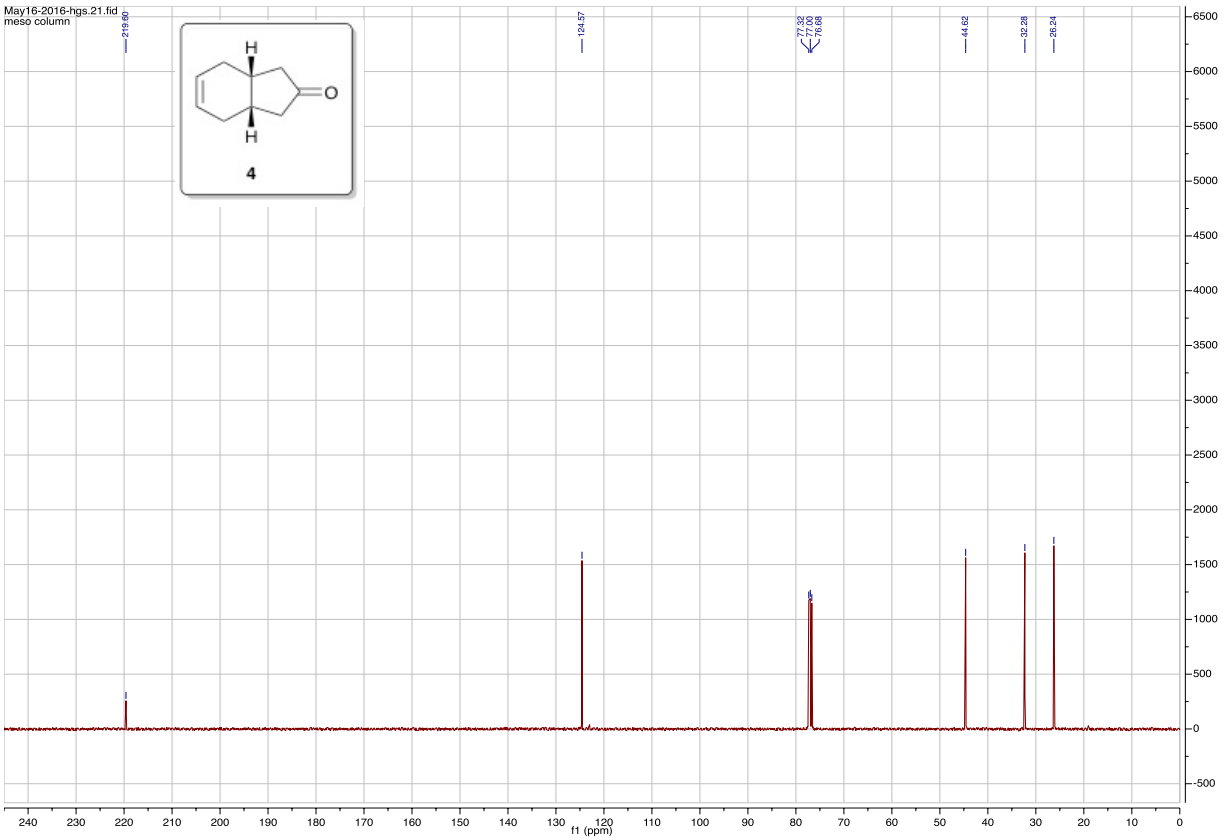


Figure S-6 ^{13}C-NMR spectrum of compound **4**.

Elemental Composition Report Page 1

Single Mass Analysis
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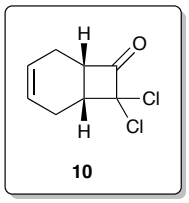
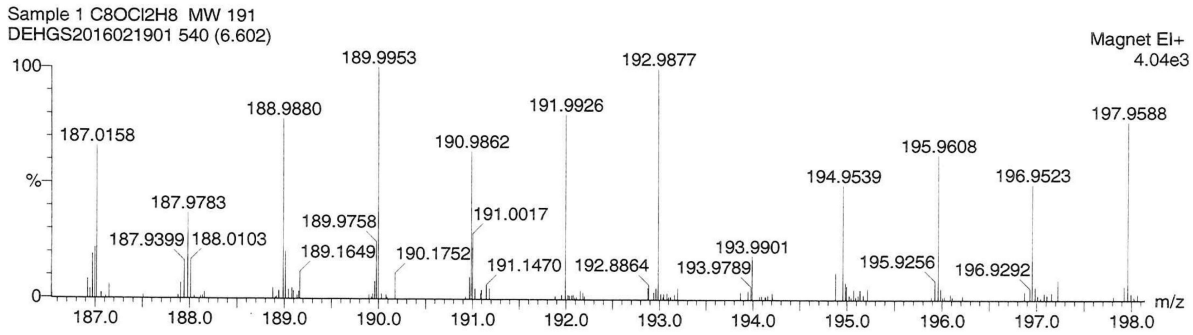
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%



10

Monoisotopic Mass, Odd and Even Electron Ions
44 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
189.9953	189.9952	0.1	0.4	4.0	1	C8 H8 O Cl2

Figure S-7 HRMS of compound **10**.

Elemental Composition Report Page 1

Single Mass Analysis
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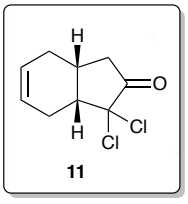
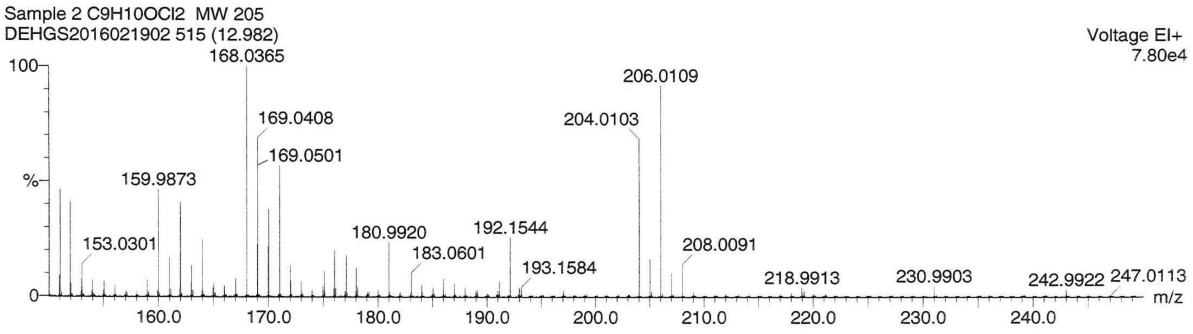
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%



11

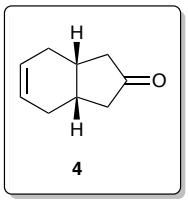
Monoisotopic Mass, Odd and Even Electron Ions
48 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
204.0103	204.0109	-0.6	-2.8	4.0	1	C9 H10 O Cl2

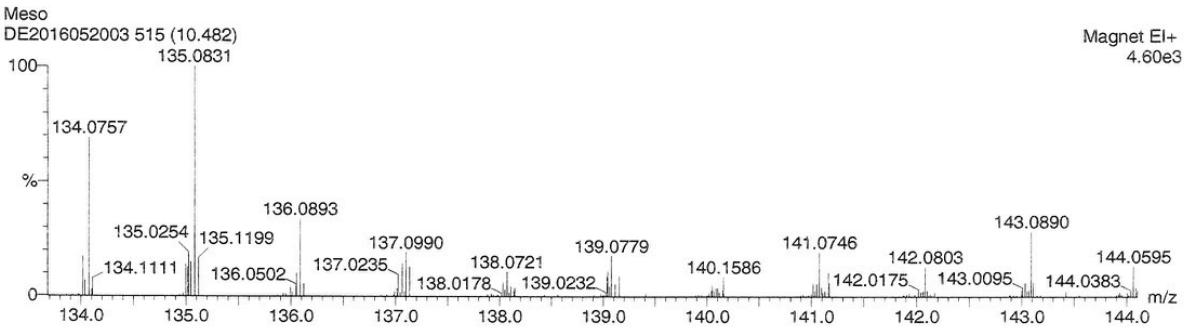
Figure S-8 HRMS of compound **11**.

Elemental Composition Report **Page 1**



Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
136.0893	136.0888	0.5	3.6	4.0	1	C9 H12 O

Figure S-9 HRMS of compound **4**.

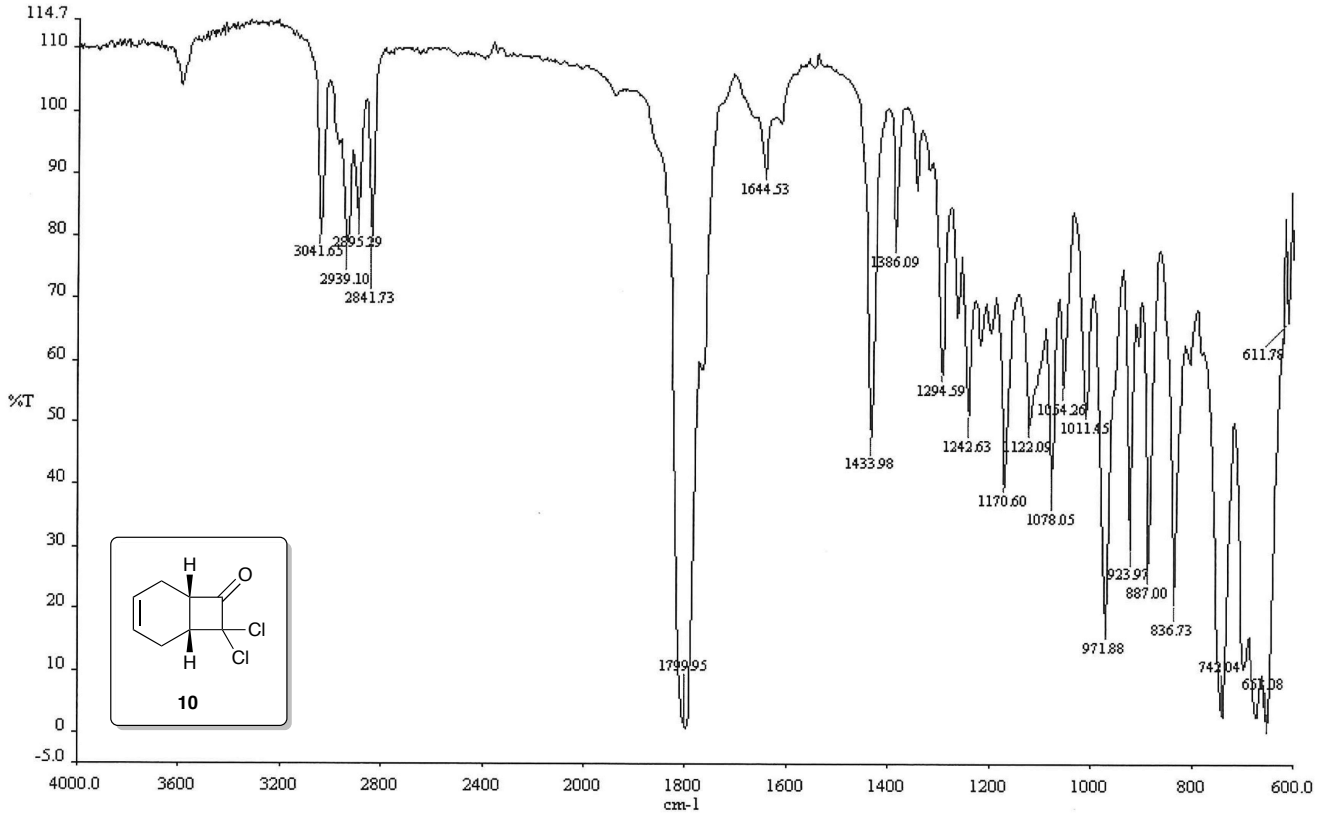


Figure S-10 IR of compound **10**.

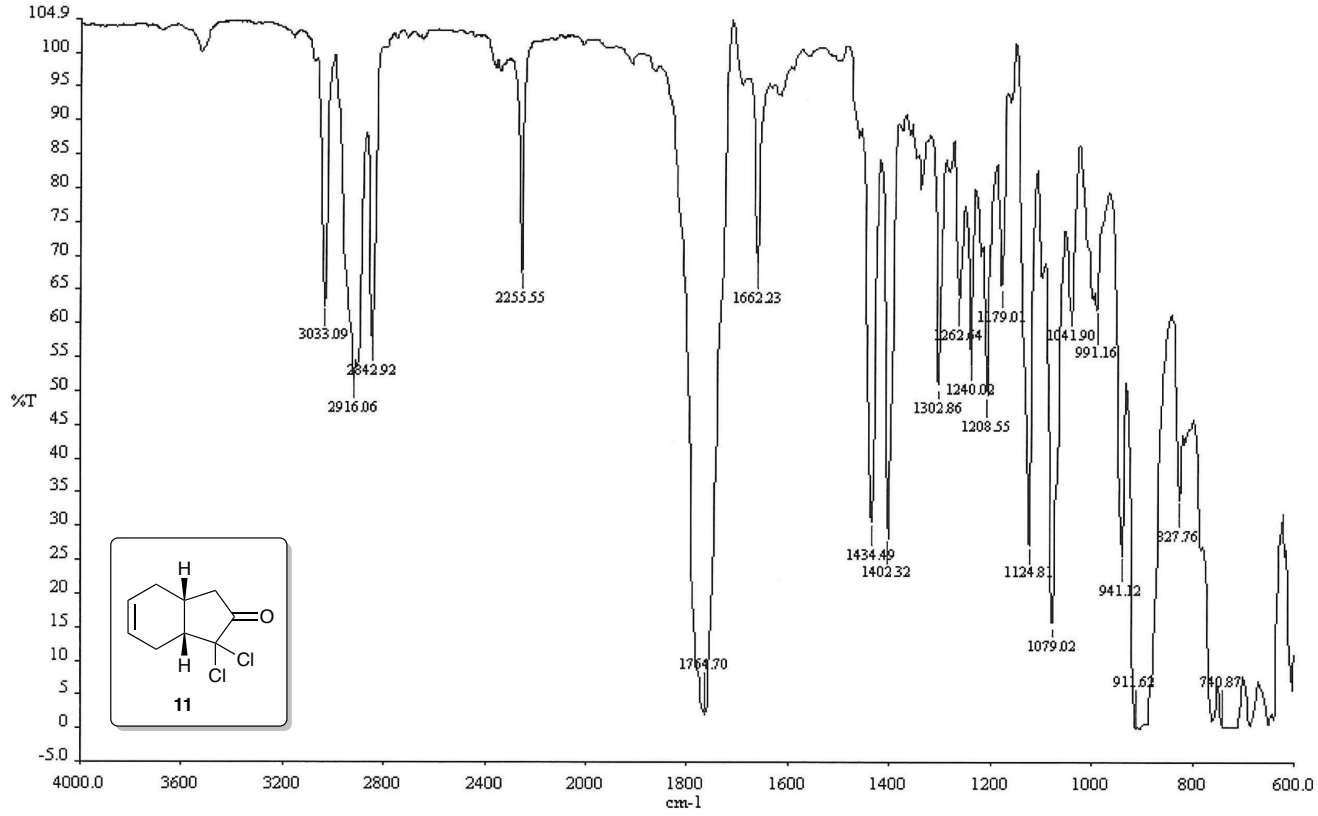


Figure S-11 IR of compound **11**.

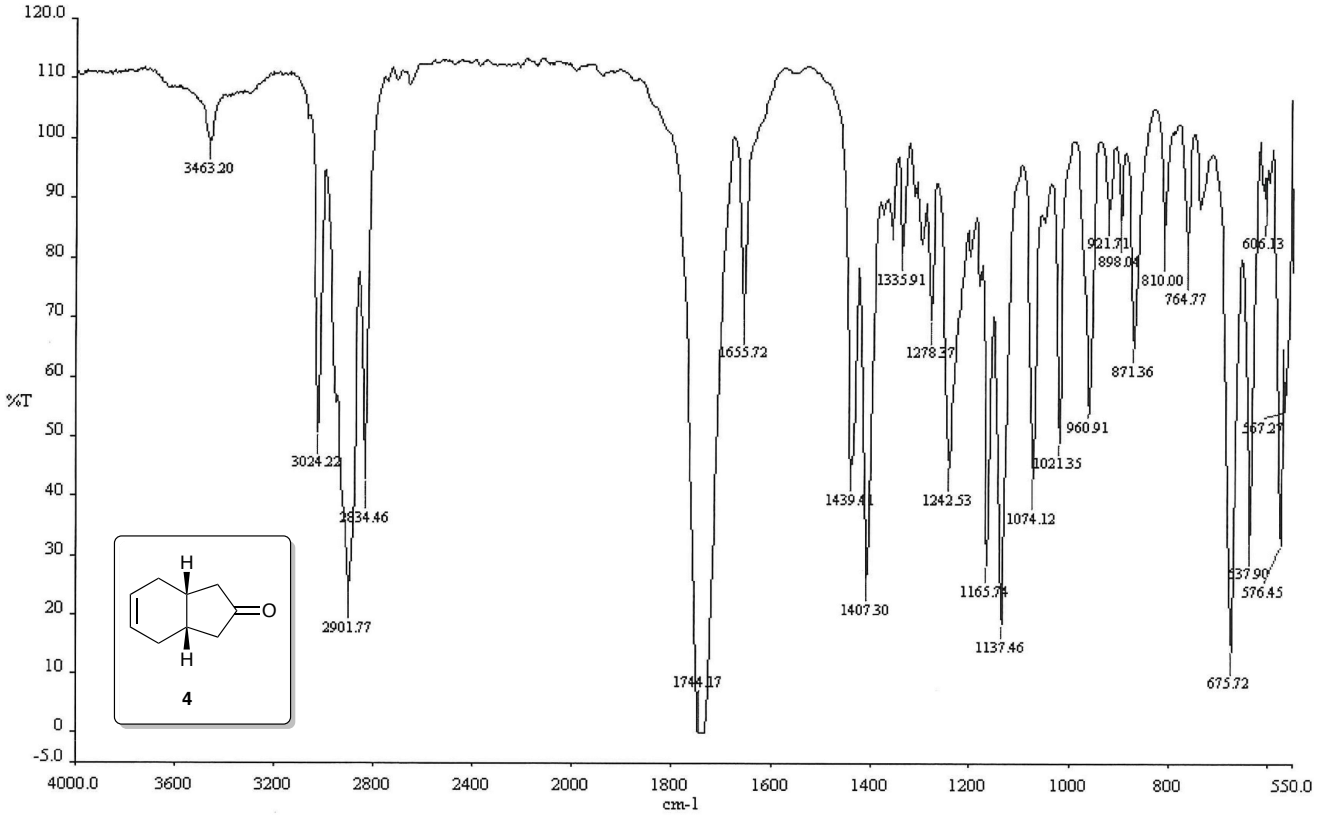
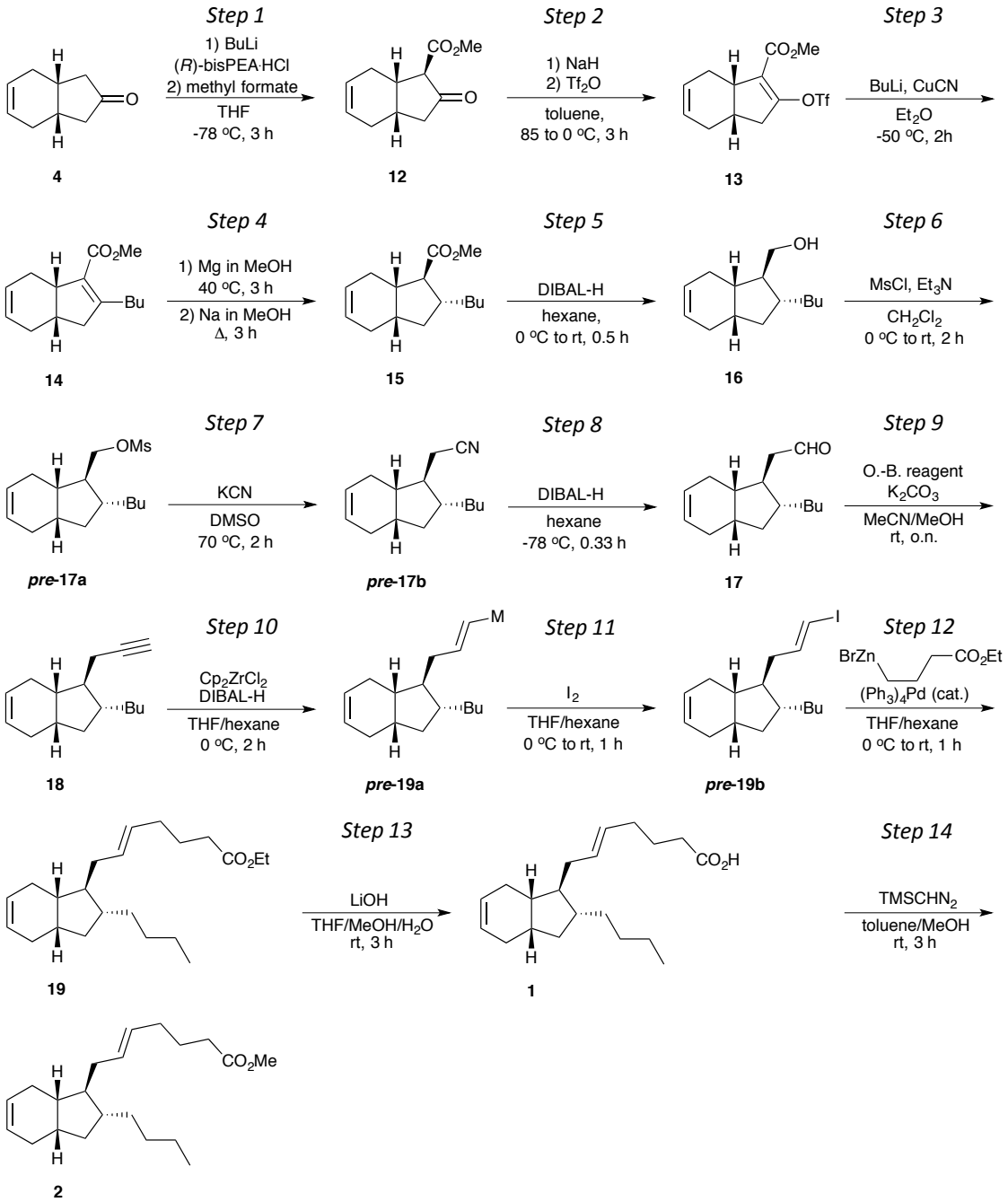


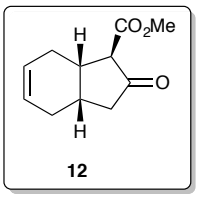
Figure S-12 IR of compound **4**.

Preparation of mucosin (1) and the methyl ester (2):



Scheme S-2 Synthetic route to mucosin (**1**) and its methyl ester **2**.

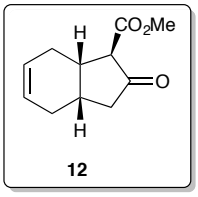
Methyl (1*S*,6*S*,7*R*)-8-oxobicyclo[4.3.0]non-3-ene-7-carboxylate (12).[7]



12

(+)-Bis[(*R*)-1-phenylethyl]amine hydrochloride (2.5 g, 9.60 mmol, 1.6 equiv.) was added in one portion to dry THF (10 mL) at room temperature and stirred for 5 min. The stirring suspension was then cooled to -78 °C and BuLi (2.5 M in hexane, 7.67 mL, 19.2 mmol, 3.2 equiv.) was added dropwise. The suspension changed colour from cloudy white to pale orange. After stirring at -78 °C for 15 min the suspension was warmed to room temperature whereby a transparent yellow solution was formed. This was then cooled to -78 °C again and *meso*-(1*S*,6*R*)-bicyclo[4.3.0]non-3-ene-8-one **4** (826 mg, 6.07 mmol, 1.0 equiv.) was added dropwise over 10 min in dry THF (10 mL). This mixture was then stirred for 45 min whereby a purple colour evolved. Methyl cyanoformate (0.96 mL, 12.1 mmol, 2.0 equiv.) was then added dropwise over 5 min. and the mixture immediately turned bright yellow in colour. This mixture was left stirring for 2.5 h and then quenched by addition of H_2O (2 mL) at -78 °C. The mixture was then warmed to room temperature and extracted with EtOAc (2 x 50 mL). The resulting organic layer was then washed with H_2O (2 x 100 mL), 0.5 M HCl (1 x 100 mL) and brine (1 x 100 mL). The organic layer was then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude keto-ester was purified by column chromatography (hexane/EtOAc 5:1) to form a colourless oil. This oil was then recrystallised from hexane at 0°C, filtered and air dried to obtain the title compound as white crystals. All spectroscopic and physical data were in full agreement with those reported in the literature.[7] Yield: 812 mg (69%); $[\alpha]_D^{26}$ -161.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73-5.66 (m, 2H), 3.76 (s, 3H), 3.04 (d, *J* = 11.1 Hz, 1H), 2.88-2.83 (m, 1H), 2.52-2.38 (m, 3H), 2.33-2.21 (m, 2H), 2.04 (dd, *J* = 1.9, 18.2 Hz, 1H), 1.67-1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 169.7, 124.9, 123.9, 57.7, 52.4, 46.6, 37.3, 29.7, 26.8, 25.3; IR (neat, cm^{-1}) 3034 (w), 2945 (m), 2908 (m), 2837 (w), 1751 (s), 1718 (s) 1656 (w) 1433 (s) 1404 (m); HRMS (EI+): Exact mass calculated for $C_{11}H_{14}O_3$ $[M]^+$: 194.9033, found 194.0943; m.p.: 59-61 °C; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.42.

***rac*-Methyl (1*S*,6*S*,7*R*)-8-oxobicyclo[4.3.0]non-3-ene-7-carboxylate (12).**

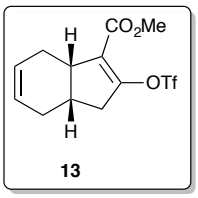


12

LDA (1M in THF/Hexanes, 1.65 mL, 1.65 mmol, 1.5 equiv.) was added dropwise to dry THF (5 mL) at -78 °C and stirred for 30 min. Then *meso*-(1*S*,6*R*)-bicyclo[4.3.0]non-3-ene-8-one **4** (150 mg, 1.10 mmol, 1.0 equiv.) was added dropwise in dry THF (5 mL) over 5 min and left to stir for 45 min. To the resulting yellow solution was added methyl cyanoformate (0.174 mL, 2.2 mmol, 2.0 equiv.) dropwise over 5 min and the reaction changed from yellow to colourless. After 30 min and monitoring the reaction via TLC the reaction was quenched at -78 °C by sat. aq. NH_4Cl (2 mL) and the reaction mixture was left to slowly warm to room temperature. The reaction mixture was then poured over H_2O (1 x 20 mL) and the organic phase separated. The aqueous phase was then extracted with EtOAc (2 x 20 mL). The organic phases were then combined, washed with H_2O (2 x 50 mL), brine (1 x 50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to from a crude yellow oil. This yellow oil was purified by column chromatography on silica (hexane/EtOAc, 5:1) to afford the racemic keto-ester. This was recrystallised in the same fashion as the optically active ketoester to afford pure white crystals. Yield: 166 mg, (78%).

The material was used in the preparation of racemic reference material for chiral GLC analysis.

Methyl (1*S*,6*S*)-8-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.3.0]non-3,7-diene-7-carboxylate (13).

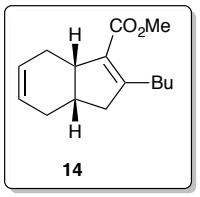


13

NaH (60% disp. in min. oil, 148 mg, 3.71 mmol, 1.8 equiv.) was added to dry toluene (10 mL). The suspension was stirred for 5 min and then methyl (1*S*,6*S,*7*R*)-8-oxobicyclo[4.3.0]non-3-ene-7-carboxylate **12** (400 mg, 2.06 mmol, 1.0 equiv.), dissolved in dry toluene (7 mL), was added dropwise over 10 min during which bubbling occurred. After the full addition of **12** the reaction mixture was heated to 85 °C for 1.5 h during which time the mixture turned to a brown colour. The reaction mixture was then cooled to 0 °C and the triflic anhydride (0.52 mL, 3.09 mmol, 1.5 equiv.), was added dropwise. The reaction mixture changed colour from brown to a pale yellow/white slurry. After stirring at 0 °C for 1 h and monitoring by TLC the reaction mixture was quenched carefully with H_2O (10 mL). The resulting mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with H_2O (1 x 150 mL), brine (1 x 150 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. This afforded a brown oil, which was purified by column chromatography on silica (hexane/EtOAc 95:5) to afford the unsaturated triflate as a colourless oil. Yield: 527 mg (83%); $[\alpha]_D^{26}$ +100.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95-5.89 (m, 1H), 5.86-5.81 (m, 1H), 3.81 (s, 3H), 3.10 (q, *J* = 6.7 Hz, 1H), 2.84-2.77 (m, 1H), 2.72-2.63 (m, 1H), 2.57-2.42 (m, 2H), 2.34-2.26 (m, 1H), 2.05-1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 153.9, 127.9, 127.3, 126.6, 118.3 (q, J_{CF} = 320 Hz), 51.8, 39.5, 38.9, 32.0, 27.3, 26.2; IR (neat, cm^{-1}) 3036 (w), 2953 (m), 2845 (w), 1723 (s), 1662 (m), 1425 (s); HRMS (EI+): Exact mass calculated for $C_{12}H_{13}O_5SF_3$ $[M]^+$: 326.0436, found 326.0438; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.75.

Following the same procedure as above, racemic synthesis was performed to obtain reference material for chiral GLC analysis.

Methyl (1*S*,6*S*)-8-butylbicyclo[4.3.0]non-3,7-diene-7-carboxylate (14).



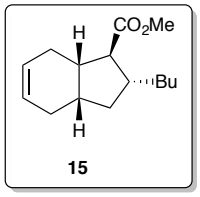
14

Solid Cu(I)CN (1.45 g, 16.18 mmol, 2.5 equiv.) was added to dry Et_2O (5 mL) at room temperature. This was stirred for 5 min, cooled to -50 °C and then BuLi (2.5 M in hexane, 6.47 mL, 16.18 mmol, 2.5 equiv.) was added dropwise over 5 min. This mixture was stirred for 1 h at -50 °C and a dark brown suspension occurred. Methyl (1*S*,6*S*)-8-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.3.0]non-3,7-diene-7-carboxylate **13** (1.98 g, 6.47 mmol, 1.0 equiv.) was then added via cannula at -50 °C in dry Et_2O (5 mL). The reaction changed from a dark brown suspension to black slurry and was left to stir for 1 h whilst monitoring by TLC. Once the reaction was finished sat. aq. NH_4Cl (5 mL) was added dropwise. The reaction turned from black to dark purple and was left to warm to room temperature. The subsequent ethereal slurry was filtered through celite and the celite filter washed with EtOAc (3 x 15 mL). The organic layer was then separated and the aqueous layer extracted with EtOAc (2 x 15 mL). The organic layers were then combined, washed with H_2O (1 x 100 mL), brine (1 x 100 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. This afforded a crude yellow oil, which was purified by column chromatography in silica (hexane/EtOAc 98:2) to afford the unsaturated butyl diene as a colourless oil. Yield: 1.33 g (88%); $[\alpha]_D^{26}$ +124.5 (c = 3.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88-5.83 (m, 1H), 5.79-5.73 (m, 1H), 3.72 (s, 3H), 2.94 (q, *J* = 7.6 Hz, 1H), 2.64-2.54 (m, 1H), 2.52-2.38 (m, 4H) 2.32-2.23 (m, 2H), 1.97-1.90 (m, 1H), 1.84-1.77 (m, 1H), 1.46-1.28 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 159.9, 132.5, 127.9, 126.4, 50.8, 43.7, 42.3, 34.2, 30.1, 29.8, 27.5, 27.2, 22.7, 13.9; IR (neat, cm^{-1}) 3025 (w), 2926 (s), 1709 (s), 1630

(w), 1433 (s); HRMS (EI+): Exact mass calculated for $C_{15}H_{22}O_2$ $[M]^+$: 234.1620, found 234.1628; TLC (hexane/EtOAc 9:1, $KMnO_4$ stain): R_f = 0.85.

Following the same procedure as above, racemic synthesis was performed to obtain reference material for chiral GLC analysis.

Methyl (1*S*,6*S*,7*S*,8*R*)-8-butylbicyclo[4.3.0]non-3-ene-7-carboxylate (15).



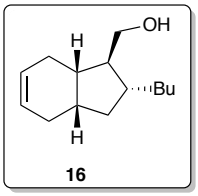
15

1) Methyl (1*S*,6*S*)-8-butylbicyclo[4.3.0]non-3,7-diene-7-carboxylate **14** (1.33 g, 5.68 mmol, 1.0 equiv.) was dissolved in MeOH (5 mL) at room temperature. This was stirred for 5 min then magnesium turnings (3.75 g, 156 mmol, 28 equiv.) were added in one portion. The turnings were stirred at room temperature for 10 min and then heated to 40 °C. A violent reaction occurs with lots of bubbling. After all the magnesium turnings had been consumed the addition of 27.5 equiv. of magnesium turnings in one portion was repeated at 40 °C. After 3 h the reaction was then cooled to room temperature to give a white cloudy mixture. Glacial AcOH (5mL) was added dropwise until the cloudy suspension had dissolved to leave a colourless solution. The reaction mixture was then concentrated *in vacuo* to leave a white slurry, which was poured over EtOAc/H_2O 1:1 (100 mL). The organic phase was separated and the aqueous layer was extracted again with EtOAc (2 x 50 mL). The organic phases were combined and washed with sat. aq. $NaHCO_3$ (1 x 100 mL), brine (1 x 100 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*, to give a crude product. This crude product was analysed by ^1H and ^{13}C NMR to show the reaction had gone to completion by the formation of two unconjugated diastereomeric esters in a 2:1 ratio, no further purification was carried out. The crude diastereomeric esters were then equilibrated with NaOMe as shown below.

2) To MeOH (10 mL) at room temperature was added sodium metal (760 mg, 33.1 mmol, 6.0 equiv.). This was left to stir until all the sodium metal had dissolved. The crude diastereomeric esters were then added dropwise in MeOH (5 mL) and the reaction mixture was heated to 70 °C and monitored by TLC. After 3 h the reaction had gone to completion, was cooled to room temperature and concentrated *in vacuo* but not to dryness. The crude mixture was then poured over Et_2O (50 mL) and H_2O (50 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (2 x 50 mL). The organic layers were then combined, washed with H_2O (1 x 50 mL), brine (1 x 50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to form a crude yellow oil. This crude yellow oil was purified by column chromatography on silica (hexane/EtOAc 98:2) to give the title compound as a colourless oil. Yield: 1.24 g (93%); $[\alpha]_D^{26}$ -4.32 (c = 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.73-5.66 (m, 2H), 3.69 (s, 3H), 2.32-2.22 (m, 1H) 2.22-2.14 (m, 5H), 2.09-2.02 (m, 1H), 1.91-1.77 (m, 2H), 1.54-1.49 (m, 1H), 1.36-1.21 (m, 5H), 1.15-1.09 (m, 1H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 126.3, 125.5, 55.5, 51.5, 42.7, 41.2, 38.3, 36.9, 35.4, 30.6, 28.0, 26.5, 22.8, 14.0; IR (neat, cm^{-1}) 3024 (m), 2927 (s), 2856 (s), 1726 (s), 1657 (w), 1628 (w), 1541 (w), 1520 (w), 1458 (m), 1434 (s); HRMS (EI+): Exact mass calculated for $C_{15}H_{24}O_2$ $[M]^+$: 236.1776, found 236.1783; TLC (hexanes/EtOAc 9:1, $KMnO_4$ stain): R_f = 0.85.

Following the same procedure as above, racemic synthesis was performed to obtain reference material for chiral GLC analysis.

(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-(hydroxymethyl)bicyclo[4.3.0]non-3-ene (16).

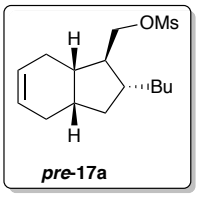


16

Methyl (1*S*,6*S*,7*S*,8*R*)-8-butylbicyclo[4.3.0]non-3-ene-7-carboxylate **15** (1.24 g, 5.25 mmol, 1.0 equiv.) was dissolved in hexane (20 mL) at room temperature and stirred for 5 min. The solution was then cooled to 0 °C and DIBAL-H (1 M in hexane, 10.5 mL, 10.51 mmol, 2.0 equiv.) was added dropwise over 5 min. The reaction was then left to warm to room temperature. After 30 min the reaction was cooled back to 0 °C and quenched with sat. aq. NH_4Cl (6 mL). The reaction mixture was allowed to warm to room temperature whereby a cloudy suspension occurred. This suspension was poured over sat. aq. NH_4Cl (30 mL) and the organic layer separated. The aqueous layer was extracted with EtOAc (2 x 25 mL) and the organic layers combined, washed with H_2O (1 x 100 mL), brine (1 x 100 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a crude cloudy oil. This was then purified by column chromatography on silica (hexane/EtOAc 95:5) to afford the title compound as a colourless oil. Yield: 1.01 g, (93%); $[\alpha]_D^{26}$ -10.33 (c = 8.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 5.70-5.64 (m, 2H), 3.61-3.52 (m, 2H), 2.24-2.03 (m, 3H), 1.92-1.81 (m, 4H), 1.57-1.42 (m, 4H), 1.33-1.22 (m, 5H), 1.18-1.11 (m, 1H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.0, 125.8, 65.7, 54.0, 41.0, 37.8, 37.7, 37.4, 35.0, 31.0, 27.7, 27.3, 22.9, 14.1; IR (neat, cm^{-1}) 3316 (br.), 3020 (m), 2918 (s), 1657 (m), 1464 (m), 1433 (m); HRMS (EI+): Exact mass calculated for $C_{14}H_{24}O$ [*M*-H_2O]$^+$: 190.1722, found 190.1723; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.35. The enantiomeric excess was determined by chiral GLC analysis (CP-Chirasil-DEX CB, using the following program: 80 ^{o}C (30 min) - 3 degrees/min to 150 ^{o}C - 150 ^{o}C (5 min)): t_r(*e*$_1$, major) = 38.97 min and t_r(*e*$_2$, minor) = 39.95 min; *ee*: > 99%.

Following the same procedure as above, racemic synthesis was made to obtain reference material for chiral GLC analysis.

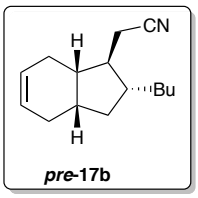
(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-((methylsulfonyl)oxymethyl)bicyclo[4.3.0]non-3-ene (pre-17a).



***pre*-17a**

To a stirring solution of (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-(hydroxymethyl)bicyclo[4.3.0]non-3-ene **16** (1.01 g, 4.81 mmol, 1.0 equiv.) in dry CH_2Cl_2 (10 mL) at room temperature, was added Et_3N (1.34 mL, 9.62 mmol, 2.0 equiv.) dropwise. This solution was left stirring for 5 min then cooled to 0 °C. Then methanesulfonyl chloride (1.12 mL, 14.43 mmol, 3.0 equiv.) was added dropwise and the reaction was left at 0 °C for 10 min then warmed to room temperature and left for 2 h. The reaction mixture turned colourless to yellow. After 2 h brine (5 mL) was added dropwise and the volatiles concentrated *in vacuo* to afford a yellow liquid. This was poured over EtOAc (50 mL) and sat. aq. $NaHCO_3$ (50 mL) was added. The organic layer was separated and the aqueous layer extracted with EtOAc (2 x 50 mL). The organic layers were combined and washed with brine (1 x 50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford a crude yellow oil. This was then purified by column chromatography on silica (hexane/EtOAc 95:5) to afford the title compound as a colourless oil. Yield: 1.30 g, (94%); $[\alpha]_D^{26}$ -11.65 (c = 8.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69-5.62 (m, 2H), 4.18-4.10 (m, 2H), 2.99 (s, 3H), 2.24-2.07 (m, 3H), 1.94-1.79 (m, 4H), 1.68-1.50 (m, 3H), 1.33-1.22 (m, 5H), 1.19-1.12 (m, 1H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.0, 125.2, 72.0, 50.3, 40.9, 38.0, 37.5, 37.2, 36.8, 34.9, 30.7, 27.2, 27.1, 22.7, 14.0; IR (neat, cm^{-1}) 3024 (w), 2926 (s), 1657 (w), 1464 (m) 1435 (w); HRMS (EI+): Exact mass calculated for $C_{15}H_{26}O_3S_2$ [*M*]$^+$: 286.1603, found 286.1606; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.45.

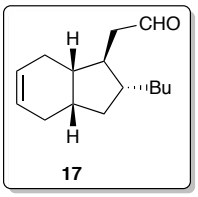
(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-(cyanomethyl)bicyclo[4.3.0]non-3-ene (pre-17b).



***pre*-17b**

To a stirring solution of (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-((methylsulfonyl)oxymethyl)bicyclo[4.3.0]non-3-ene **pre-17a** (1.30 g, 4.55 mmol, 1.0 equiv.) in dry DMSO (10 mL) was added solid KCN (1.77 g, 27.3 mmol, 6.0 equiv.) in one portion. The reaction mixture was then heated to 70 °C for 2 h. The reaction mixture changed from colourless to yellow. After 2 h the reaction was cooled to room temperature and H_2O (5 mL) was added dropwise. The reaction mixture turned from yellow to colourless. This was then poured over EtOAc (20 mL) and the organic layer separated. The aqueous layer was then extracted with EtOAc (2 x 20 mL) and the organic layers combined. They were then washed with brine (1 x 50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford a crude brown oil. This was then purified by column chromatography on silica (hexane/EtOAc 98:2) to give the title compound as a colourless oil. Yield: 906 mg, (92 %); $[\alpha]_D^{26}$ -19.15 (c = 8.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73-5.65 (m, 2H), 2.41 (d, *J* = 6.7 Hz, 2H), 2.27-2.14 (m, 3H), 2.04-1.96 (m, 1H), 1.93-1.76 (m, 3H), 1.67-1.49 (m, 3H), 1.36-1.19 (m, 5H), 1.15-1.08 (m, 1H), 0.90 (t, *J* = 6.8 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.5, 125.4, 119.0, 46.4, 43.9, 41.3, 37.9, 36.0, 34.6, 30.6, 27.9, 26.3, 22.8, 21.0, 14.0; IR (neat, cm^{-1}) 3024 (m), 2921 (s), 1658 (w), 1465 (m) 1436 (m); HRMS (EI+): Exact mass calculated for $C_{15}H_{23}N$ $[M]^+$: 217.1830, found 217.1827; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.82.

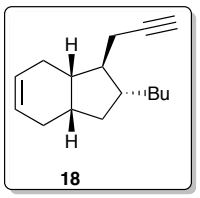
(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-(formylmethyl)bicyclo[4.3.0]non-3-ene (17).



17

A stirring solution of (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-(cyanomethyl)bicyclo[4.3.0]non-3-ene **pre-17b** (906 mg, 4.18 mmol, 1.0 equiv.) in hexane (10 mL) was cooled to -78 °C. Then DIBAL-H (1M in hexane, 6.26 mL, 6.26 mmol, 1.5 equiv.) was added dropwise over 5 min and the reaction left to stir for 20 min. Then sat. aq. Rochelle salt (5 mL) was added dropwise to the reaction mixture and then left to warm to room temperature. The resulting cloudy suspension was poured over EtOAc (20 mL) and sat. aq. Rochelle salt (20 mL). The organic layer was separated and the aqueous phase extracted with EtOAc (2 x 20 mL). The organic phases were combined and washed with brine (1 x 50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford a crude cloudy oil. This was then purified by column chromatography on silica (hexane/EtOAc, 95:5) to afford the aldehyde as a colourless oil. Yield: 813 mg, (88%); $[\alpha]_D^{26}$ -14.40 (c = 8.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (t, *J* = 2.5 Hz, 1H), 5.71-5.64 (m, 2H), 2.44 (dd, *J* = 2.5, 6.5 Hz, 2H), 2.22-2.08 (m, 3H), 1.96-1.91 (m, 1H), 1.89-1.67 (m, 4H), 1.55-1.49 (m, 2H), 1.33-1.15 (m, 5H), 1.13-1.08 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 126.3, 125.6, 49.5, 45.3, 45.0, 41.8, 37.9, 36.4, 34.9, 30.8, 27.7, 27.1, 22.8, 14.0; IR (neat, cm^{-1}) 3023 (m), 2923 (s), 2718 (m), 1720 (s), 1657 (w), 1465 (m), 1434 (m); HRMS (EI+): Exact mass calculated for $C_{15}H_{24}O$ $[M]^+$: 220.1827, found 220.1828; TLC (hexane/EtOAc 4:1, $KMnO_4$ stain): R_f = 0.82.

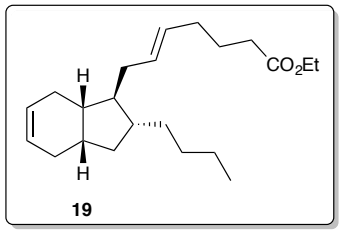
(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-(prop-2'-yn-1'-yl)bicyclo[4.3.0]non-3-ene (18).



18

To a stirring solution of (1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-(formylmethyl)bicyclo[4.3.0]non-3-ene **17** (300 mg, 1.36 mmol, 1.0 equiv.) in dry MeOH (15 mL) at 0 °C was added solid K_2CO_3 (451 mg, 3.27 mmol, 2.4 equiv.) in one portion and Ohira-Bestmann reagent (10% w/w in MeCN, 4.9 mL, 3.9 g, 2.05 mmol, 1.5 equiv.). The suspension was then warmed to room temperature and left stirring overnight. After analysis by TLC the mixture was treated with sat. aq. $NaHCO_3$ (20 mL), and the resulting mixture poured over CH_2Cl_2 (20 mL). The organic phase was separated and the aqueous phase was washed with CH_2Cl_2 (3 x 10 mL). The organic phases were then combined, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford a crude oil. This was purified by column chromatography on silica (hexane/EtOAc, 95:5) to afford title compound as a colourless oil. Yield: 253 mg, (86%); $[\alpha]_D^{26}$ -16.95 (c = 8.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73-5.66 (m, 2H), 2.28 (dd, *J* = 2.6, 5.9 Hz, 2H), 2.23-2.08 (m, 3H), 1.97-1.79 (m, 5H), 1.70-1.53 (m, 2H), 1.44-1.38 (m, 1H), 1.36-1.16 (m, 5H), 1.13-1.06 (m, 1H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ; 126.4, 126.0, 83.6, 68.6, 49.0, 43.5, 40.6, 38.2, 36.6, 34.8, 30.9, 28.1, 27.0, 22.9, 22.3, 14.1; IR (neat, cm^{-1}) 3310 (m), 3021 (m), 2954 (s), 2915 (s), 1657 (w), 1465 (m), 1435 (m); HRMS (EI+): Exact mass calculated for $C_{16}H_{24}$ $[M]^+$: 216.1878, found 216.1870; TLC (hexane, $KMnO_4$ stain and anisaldehyde dip): R_f = 0.24.

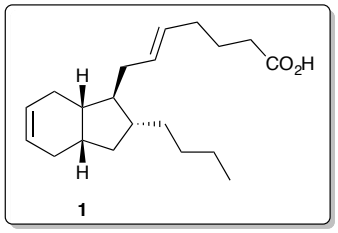
(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-((*E*)-7'-ethoxy-7'-oxohept-2'-enyl)bicyclo[4.3.0]non-3-ene (19).



19

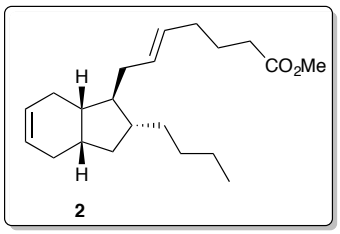
To a stirring solution of Cp_2ZrCl_2 (95 mg, 0.324 mmol, 2.0 equiv.) in dry THF (2 ml) at 0 °C was added DIBAL-H (1M in hexane, 0.32 mL, 0.324 mmol, 2.0 equiv.) via dropwise addition. The resulting homogenous mixture was then protected from light and stirred at 0 °C for 1 h after which time a colourless heterogeneous mixture formed. Then (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-(prop-2'-yn-1'-yl)bicyclo[4.3.0]non-3-ene **18** (35 mg, 0.162 mmol, 1.0 equiv.) dissolved in dry THF (2 mL) was added dropwise to the reaction mixture at 0 °C. After 1 h at 0 °C iodine (63 mg, 0.248 mmol, 1.5 equiv.) was added in one portion to the homogeneous yellow reaction mixture. The reaction mixture was then warmed to room temperature and stirred for 1 h. To the preformed vinyl iodide was successively added 4-ethoxy-4-oxobutylzinc bromide solution (0.5M in THF) (0.648 mL, 0.324 mmol, 2.0 equiv.) dropwise and $(Ph_3P)_4Pd$ (19 mg, 0.016 mmol, 0.01 equiv.) in one portion. The resulting tea brown mixture was stirred at room temperature for 1 h and monitored by TLC. Once the reaction had gone to completion 1M HCl (10 mL) was added dropwise and the reaction poured over Et_2O (15 mL). The aqueous phase was extracted with Et_2O (3 x 15 mL) and the organic phases combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to form a crude brown oily mixture. This oily mixture was purified by column chromatography on silica (hexane/EtOAc, 95:5) to afford the title compound as a colourless oil. Yield: 27 mg, (51%); $[\alpha]_D^{26}$ -11.15 (c = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70-5.64 (m, 2H), 5.47-5.33 (m, 2H), 4.13 (q, *J* = 7.1 Hz, 2 H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.22-2.15 (m, 1H), 2.12- 2.01 (m, 6H), 1.89-1.76 (m, 3H), 1.73-1.66 (m, 3H), 1.53-1.47 (m, 2H), 1.34-1.16 (m, 9H), 1.12-1.04 (m, 1H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 130.3, 129.9, 126.2, 126.1, 60.2, 51.0, 44.0, 40.3, 38.1, 37.7, 37.1, 34.9, 33.7, 31.9 31.0, 27.8, 27.7, 24.8, 22.9, 14.2, 14.1; IR (neat, cm^{-1}) 3021 (m), 2920 (s), 1734 (s), 1657 (w), 1438 (m); HRMS (EI+): Exact mass calculated for $C_{22}H_{36}O_2$ $[M]^+$: 332.2715, found 332.2722; TLC (hexane/EtOAc 95:5, $KMnO_4$ stain): R_f = 0.65.

(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-((*E*)-7'-hydroxy-7'-oxohept-2'-enyl)bicyclo[4.3.0]non-3-ene (1).



To a stirring solution of the (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-((*E*)-7'-ethoxy-7'-oxohept-2'-enyl)bicyclo[4.3.0]non-3-ene **18** (27 mg, 0.081 mmol, 1.0 equiv.) in THF/MeOH/H_2O (2:2:1) (5 mL) at room temperature was added lithium hydroxide monohydrate (119 mg, 2.84 mmol, 35.0 equiv.) in one portion. The reaction mixture was left stirring and monitored by TLC. After 3 h the reaction had gone to completion and was acidified to pH 2 by 1M HCl (5 mL). The reaction mixture was then poured over EtOAc (5 mL) and the aqueous phase extracted with EtOAc (3 x 5 mL). The organic phases were then combined and washed with brine (1 x 20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to form a colourless oil. This was then purified by column chromatography on silica (hexane/EtOAc, 3:2) to afford the title compound as a colourless oil. Yield: 24 mg, (97%); $[\alpha]_D^{26}$ -10.19 (c = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.24 (br, 1H), 5.71-5.64 (m, 2H), 5.48-5.33 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.23-2.14 (m, 1H), 2.13-2.02 (m, 6H), 1.89-1.75 (m, 3H), 1.73-1.65 (m, 3H), 1.55-1.44 (m, 2H), 1.36-1.15 (m, 6H), 1.12-1.05 (m, 1H), 0.89 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.3, 130.6, 129.7, 126.2, 126.0, 51.0, 44.0, 40.3, 38.1, 37.7, 37.1, 34.9, 33.3, 31.8, 31.0, 27.8, 27.7, 24.4, 22.9, 14.1; IR (neat, cm^{-1}) 3021 (m), 2920 (s), 1708 (s), 1457 (m), 1436 (m), 1412 (m); HRMS (EI+): Exact mass calculated for $C_{20}H_{32}O_2$ [*M*]$^+$: 304.2402, found 304.2391; TLC (hexane/EtOAc 3:2, $KMnO_4$ stain): R_f = 0.40.

(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-((*E*)-7'-methoxy-7'-oxohept-2'-enyl)bicyclo[4.3.0]non-3-ene (2).



To a stirring solution of (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-((*E*)-7'-hydroxy-7'-oxohept-2'-enyl)bicyclo[4.3.0]non-3-ene **1** (24 mg, 0.079 mmol, 1.0 equiv.) in toluene/MeOH (3:2) (5 mL) at room temperature was added TMS diazomethane solution (2M in hexane) (0.06 mL, 0.119 mmol, 1.5 equiv.) dropwise over 2 min. The reaction mixture bubbled and turned transparent yellow. The reaction was monitored by TLC and after 1 h had gone to completion. The reaction mixture was then concentrated *in vacuo* and directly purified by column chromatography on silica (hexane/EtOAc, 95:5) to afford the title compound as a colourless oil. Yield: 23 mg, (92%); $[\alpha]_D^{26}$ -9.8 (c = 0.8, hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70-5.64 (m, 2H), 5.46-5.33 (m, 2H), 3.67 (s, 3H), 2.31 (t, *J* = 7.6 Hz, 2H), 2.22-2.15 (m, 1H), 2.12-2.01 (m, 6H), 1.89-1.75 (m, 3H), 1.73-1.65 (m, 3H), 1.54-1.44 (m, 2H), 1.34-1.16 (m, 6H), 1.12-1.04 (m, 1H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ; 174.2, 130.4, 129.9, 126.3, 126.1, 51.4, 51.0, 44.0, 40.3, 38.1, 37.7, 37.1, 34.9, 33.4, 31.9, 31.0, 27.8, 27.7, 24.8, 22.9, 14.1; IR (neat, cm^{-1}) 3020 (w), 2952 (m), 2923 (s), 1741 (s), 1657 (w), 1603 (w), 1541 (w), 1508 (w), 1458 (m), 1436 (m); HRMS (EI+): Exact mass calculated for $C_{21}H_{34}O_2$ [*M*]$^+$: 318.2559, found 318.2544; TLC (hexane/EtOAc 95:5, $KMnO_4$ stain): R_f =0.65.

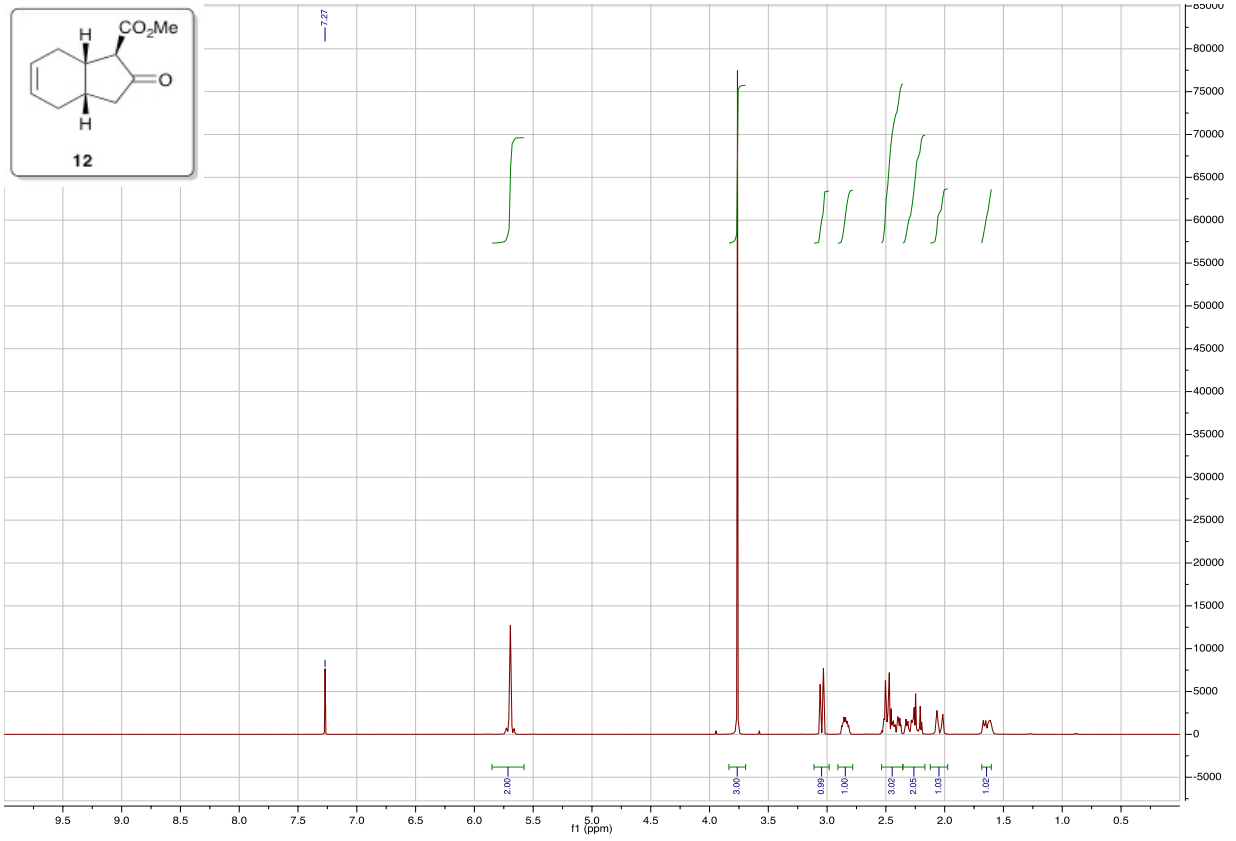


Figure S-13 ^{1}H-NMR spectrum of compound **12**.

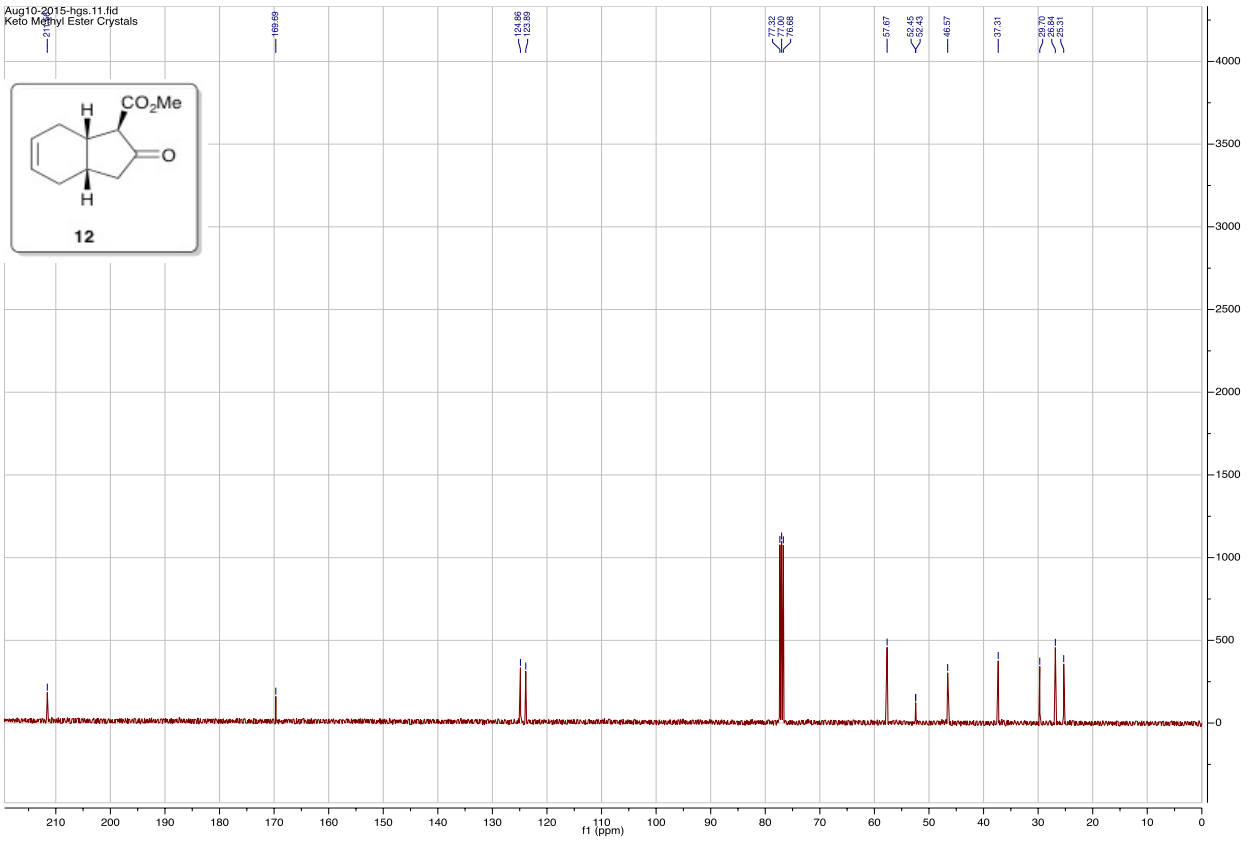


Figure S-14 ^{13}C-NMR spectrum of compound **12**.

Figure S-15 ^{1}H-NMR spectrum of compound **13**.

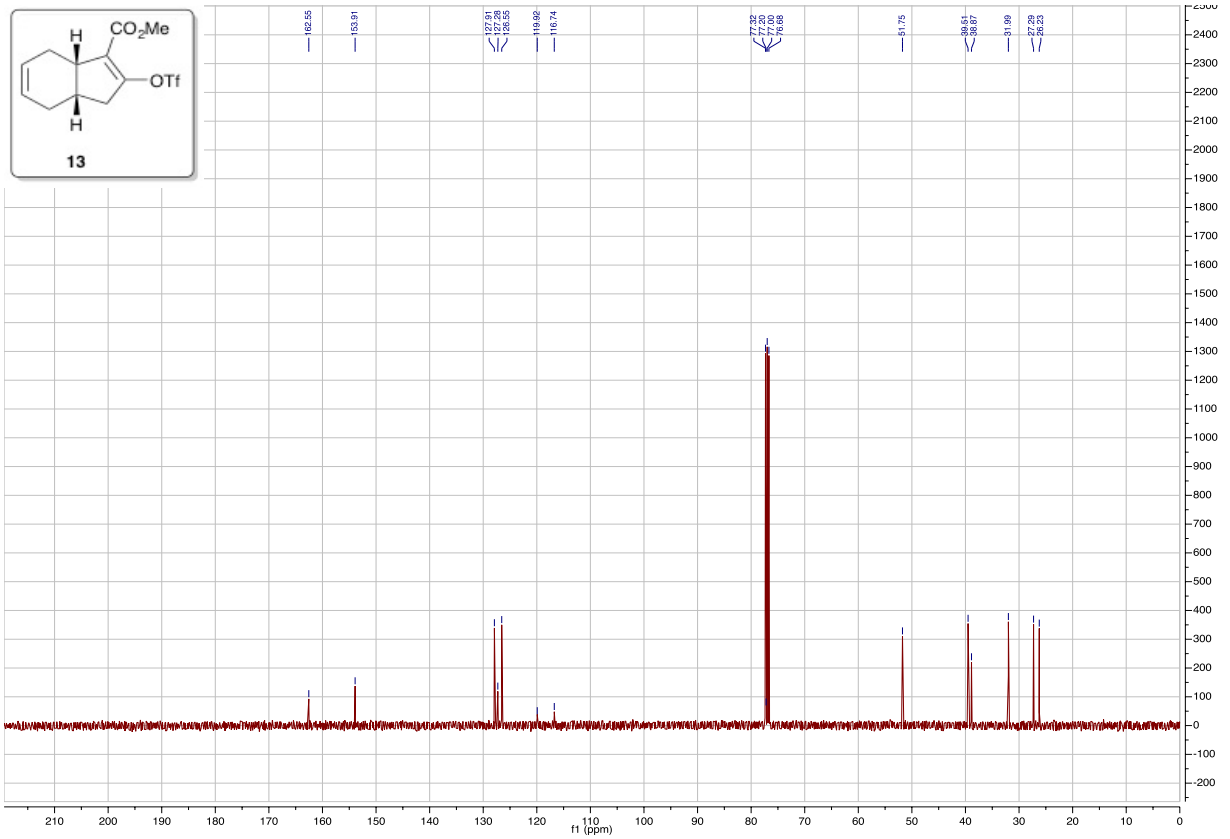


Figure S-16 ^{13}C-NMR spectrum of compound **13**.

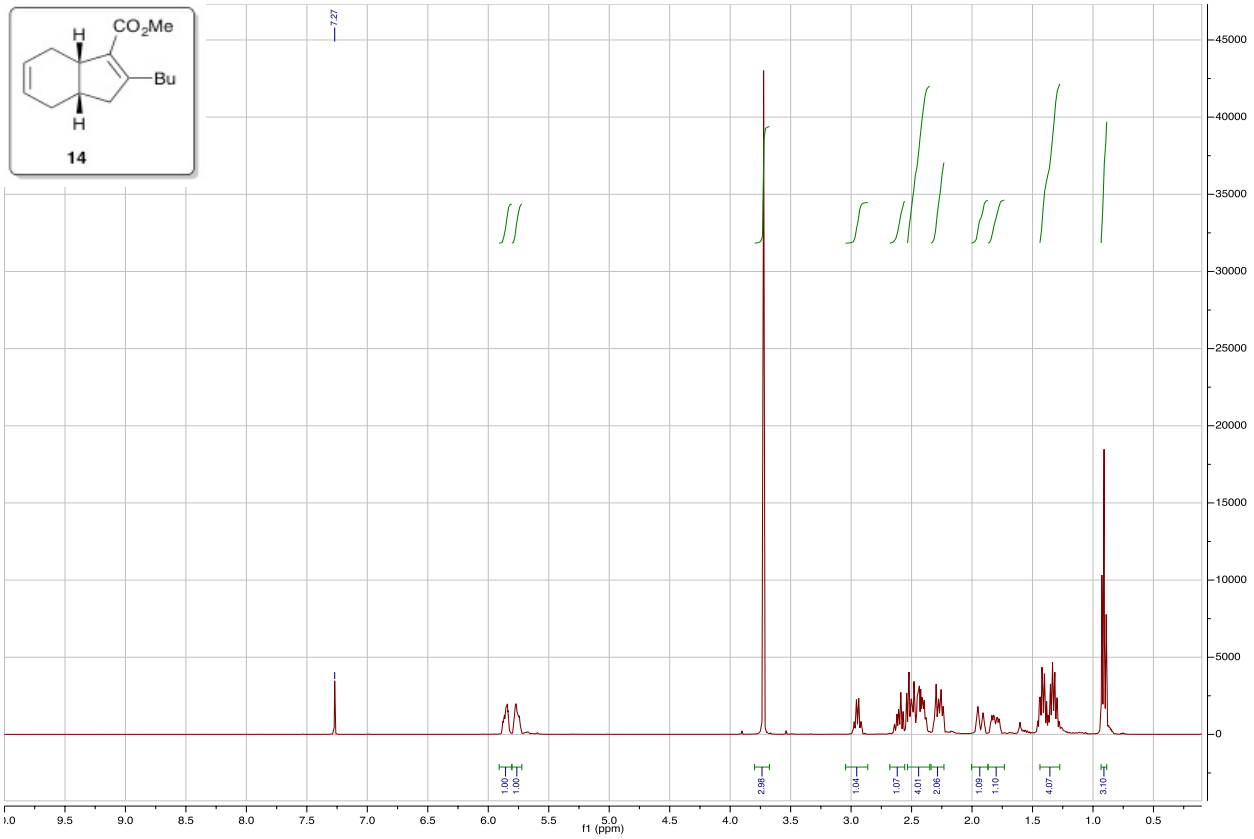


Figure S-17 ^{1}H-NMR spectrum of compound **14**.

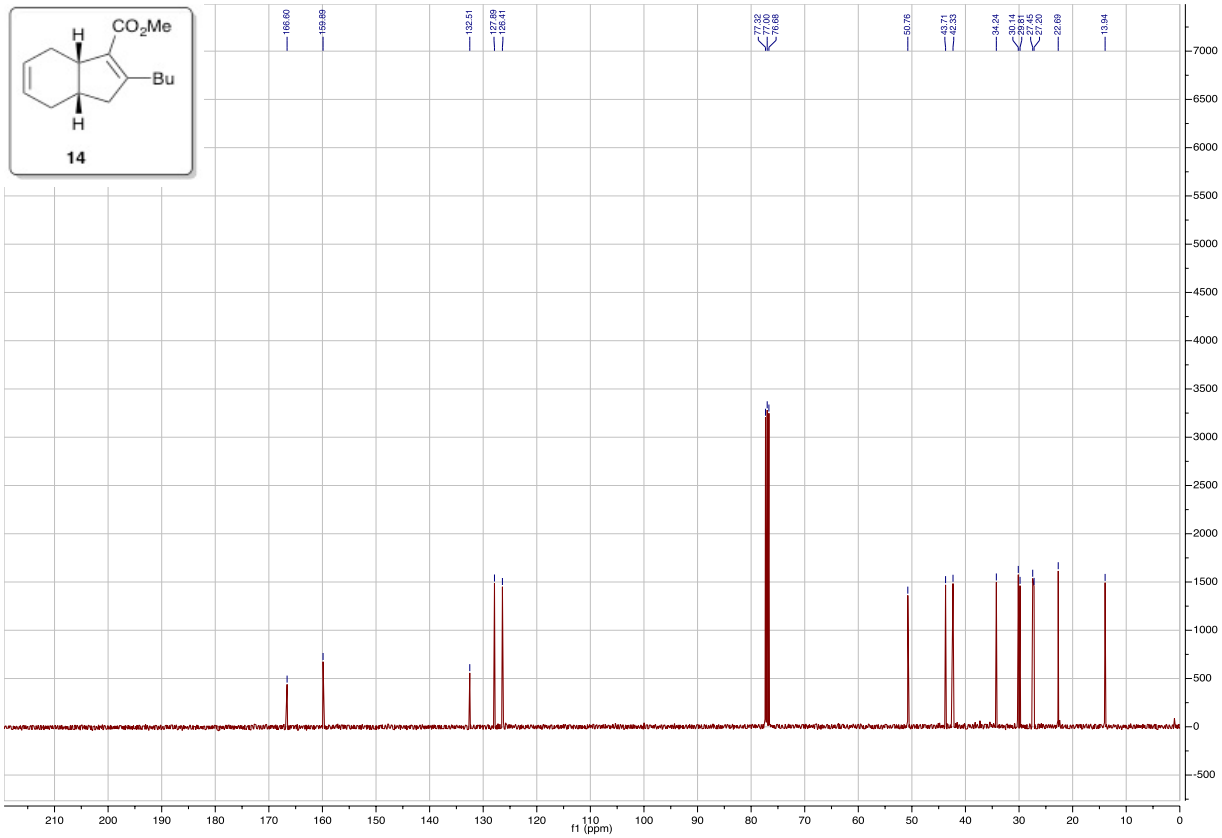


Figure S-18 ^{13}C-NMR spectrum of compound **14**.

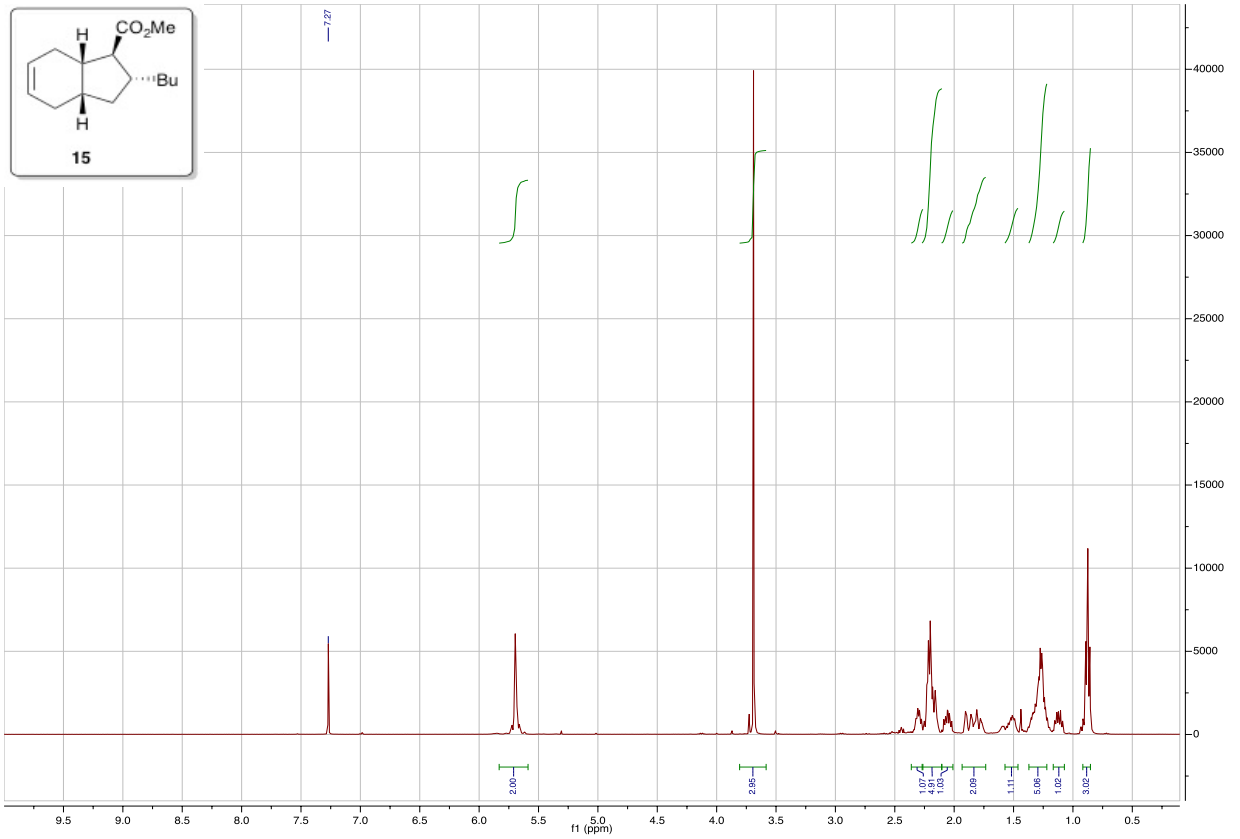


Figure S-19 ^{1}H-NMR spectrum of compound **15**.

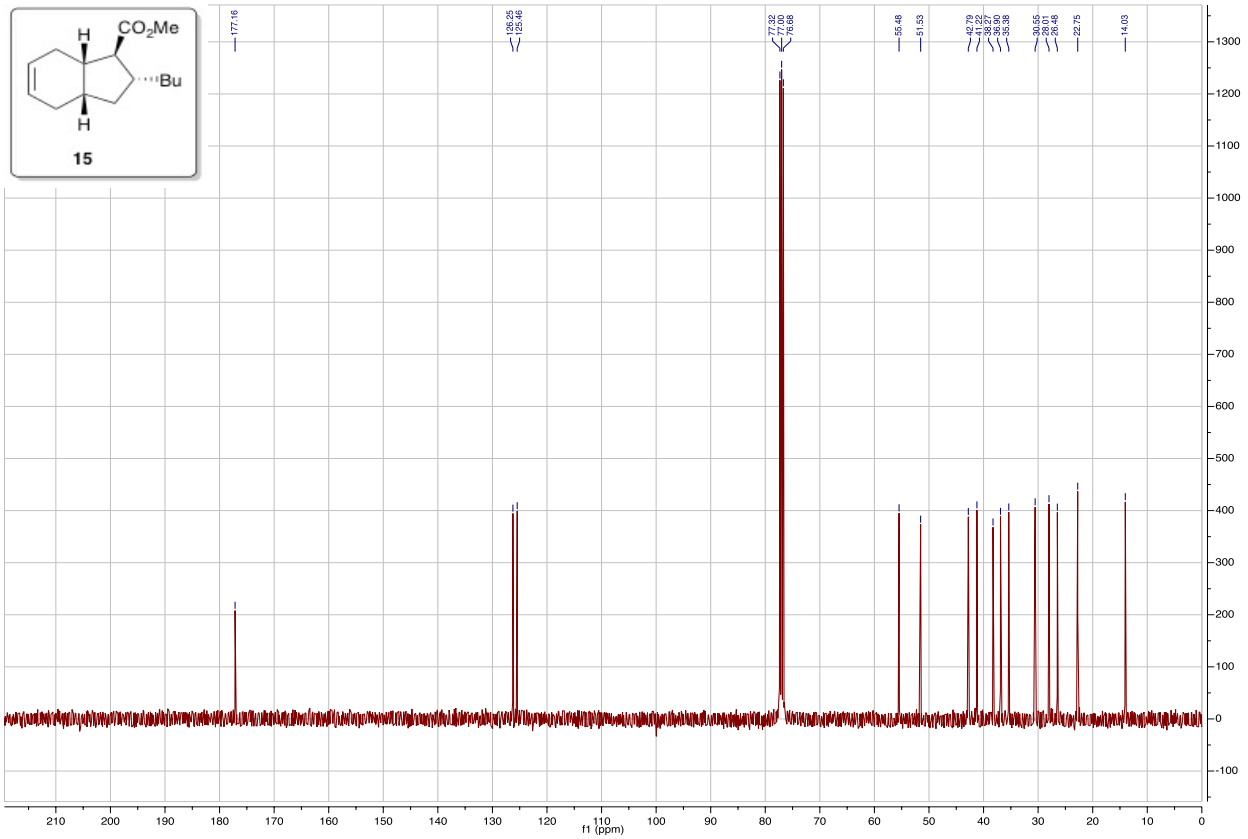


Figure S-20 ^{13}C-NMR spectrum of compound **15**.

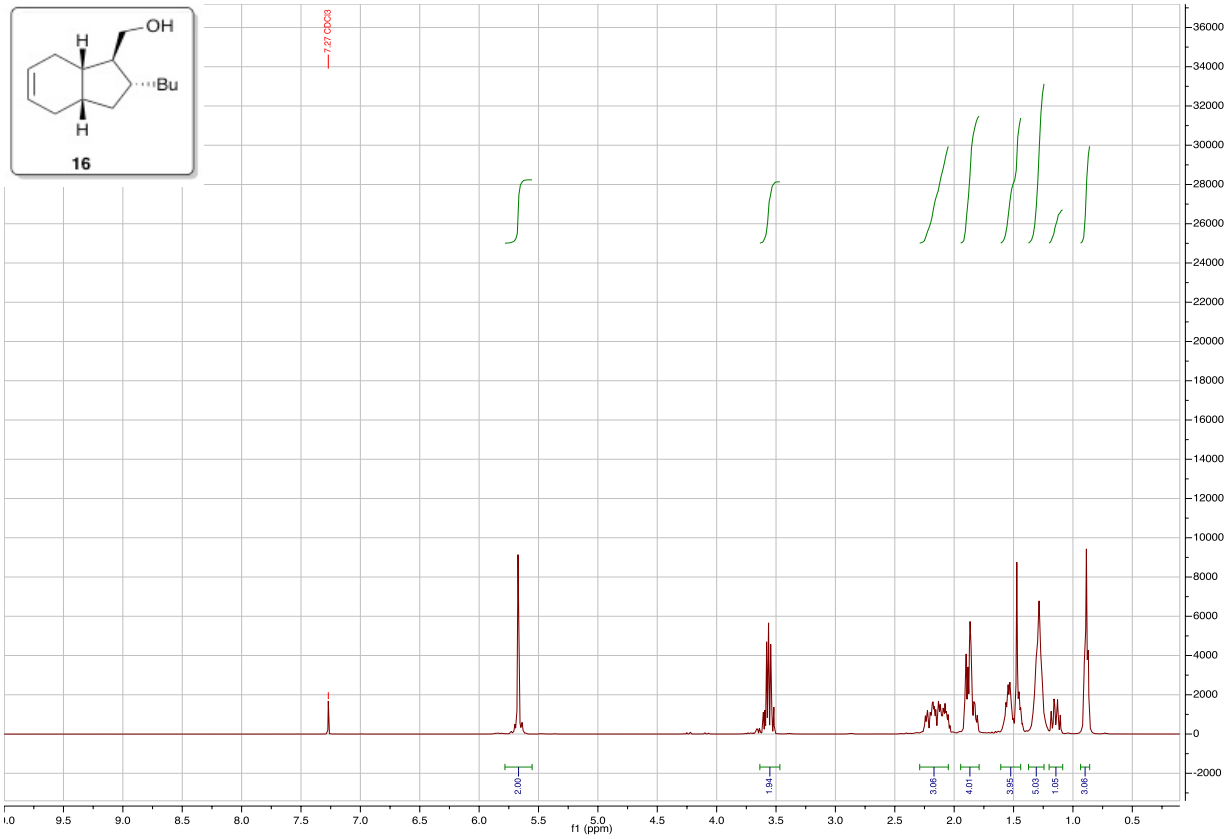


Figure S-21 ^{1}H-NMR spectrum of compound **16**.

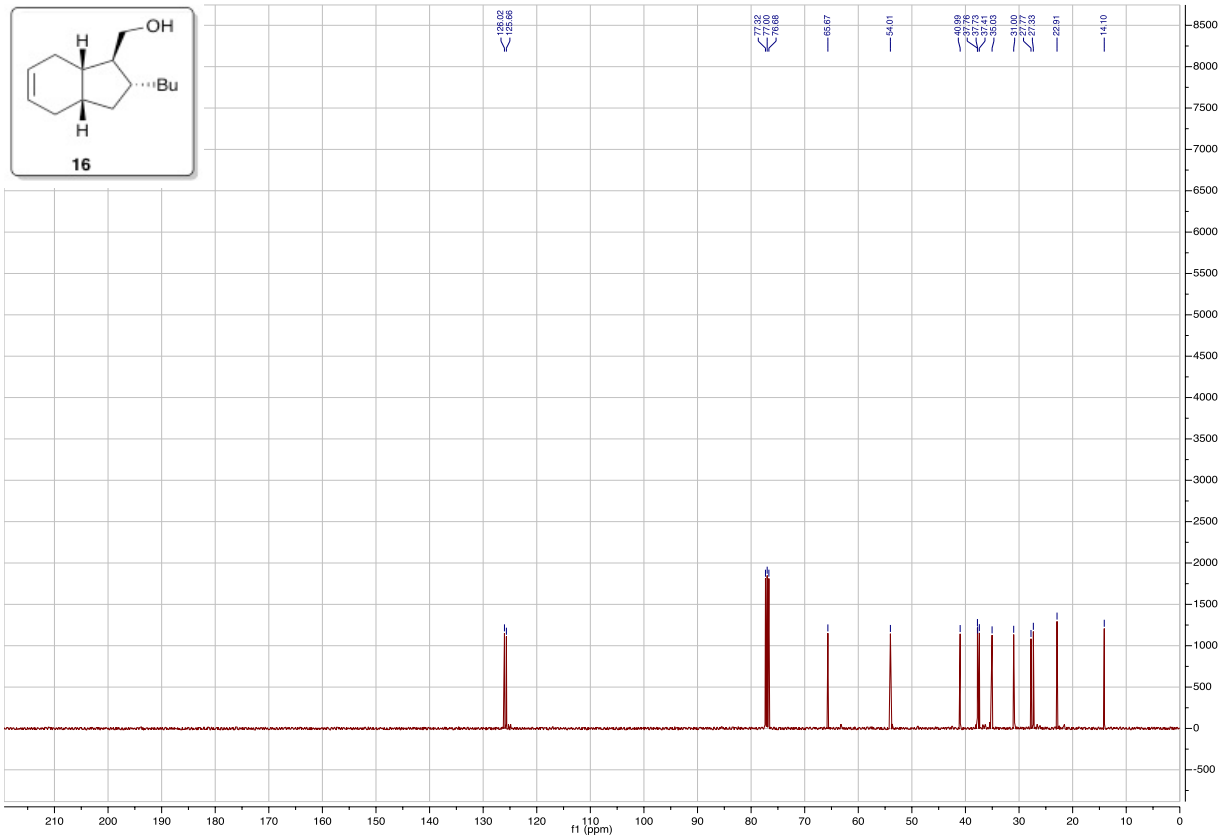


Figure S-16 ^{13}C-NMR spectrum of compound **22**.

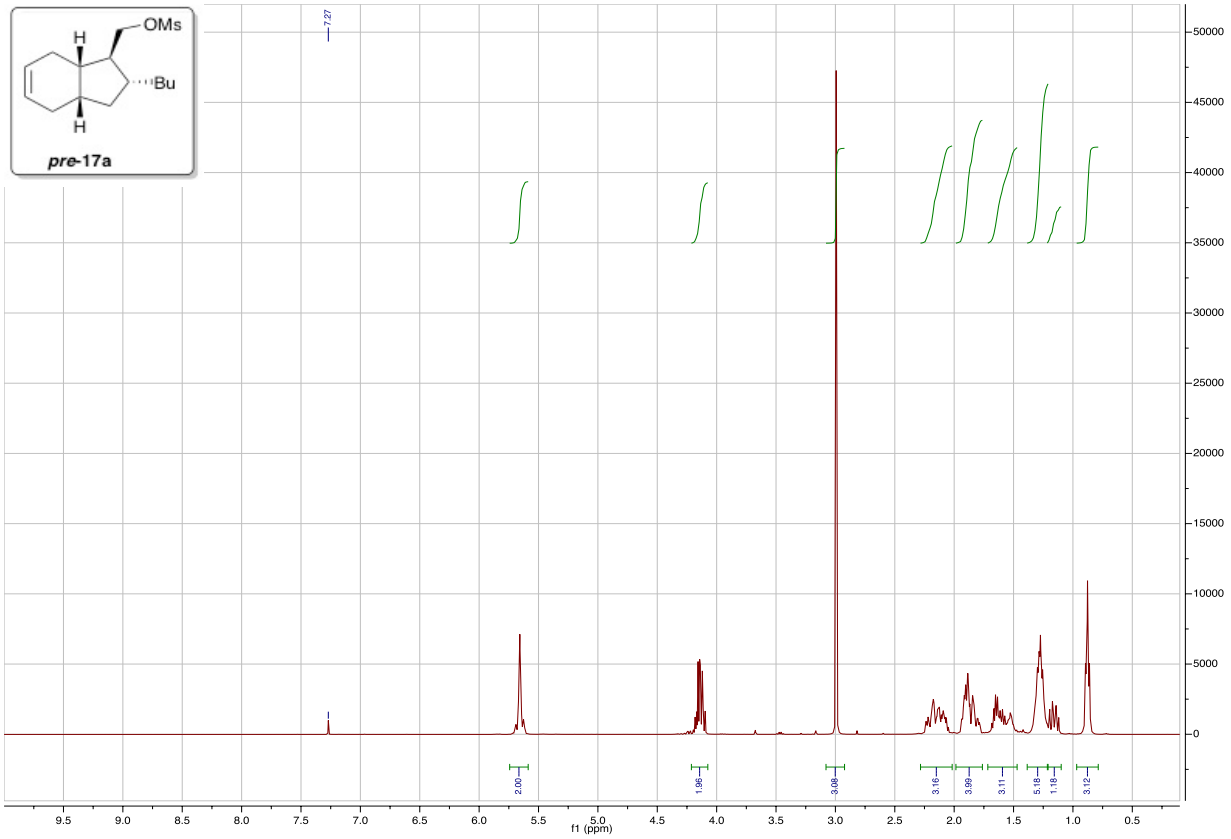


Figure S-23 ^{1}H-NMR spectrum of compound ***pre*-17a**.

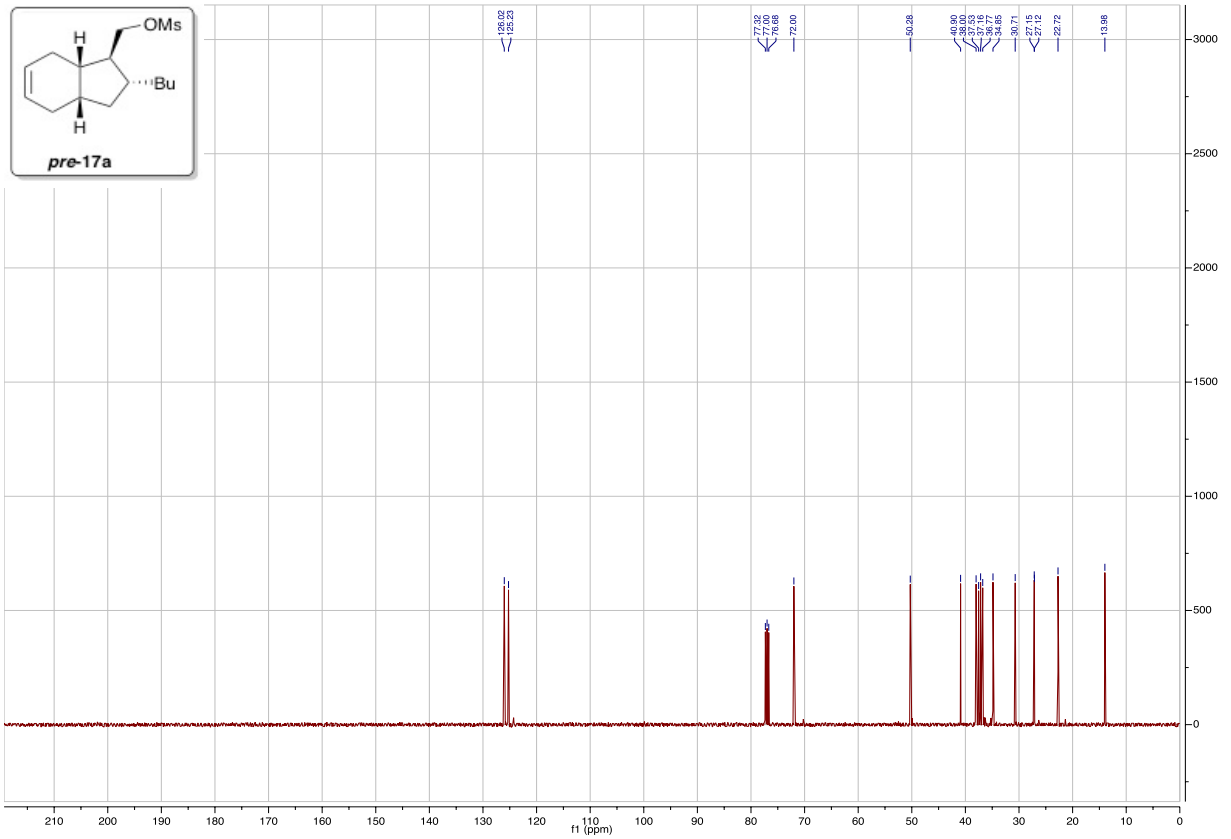


Figure S-24 ^{13}C-NMR spectrum of compound ***pre*-17a**.

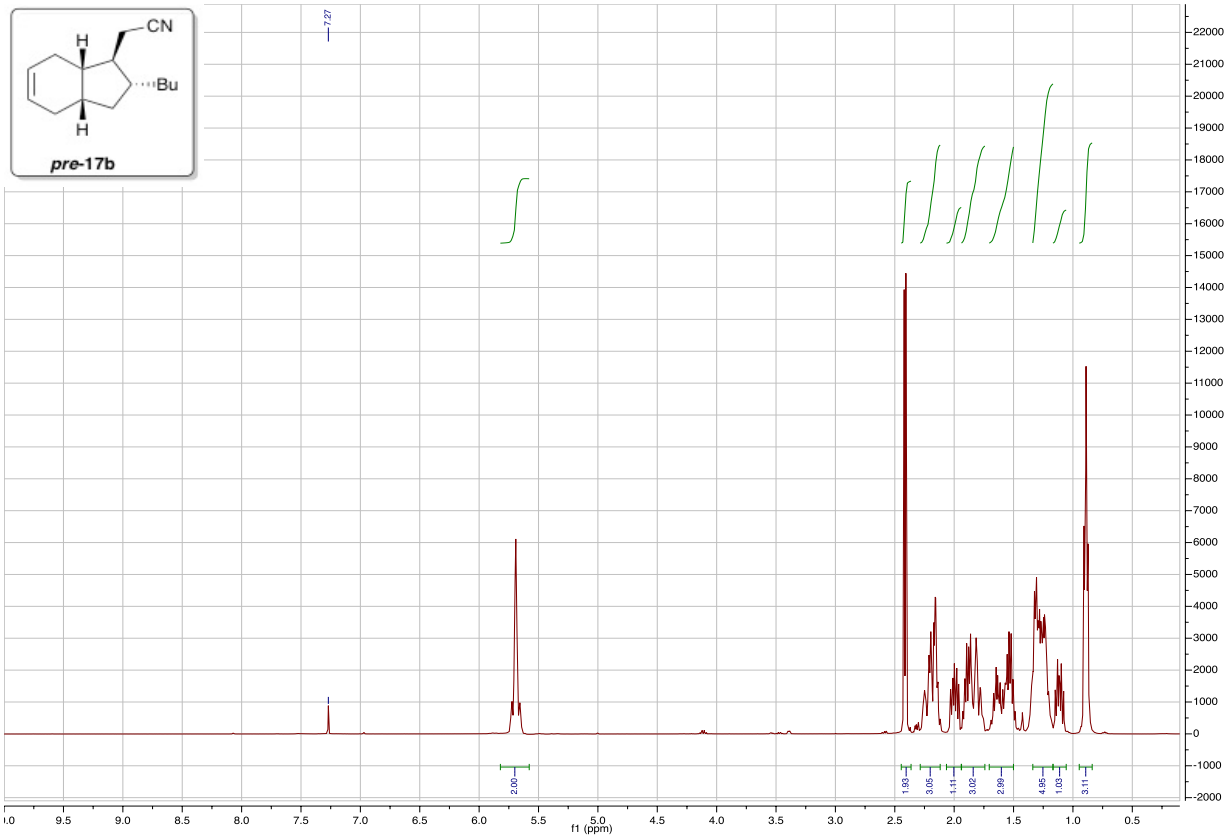


Figure S-25 ^{1}H-NMR spectrum of compound ***pre*-17b**.

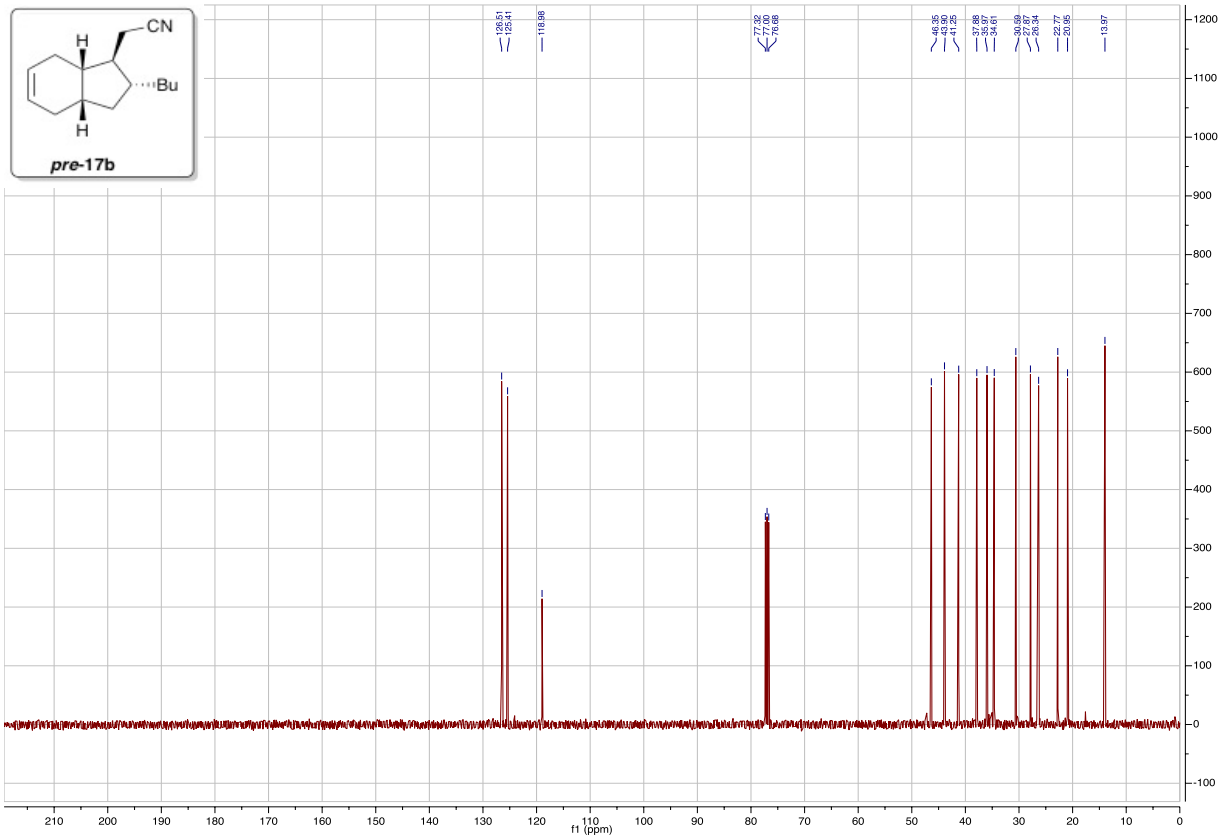


Figure S-26 ^{13}C-NMR spectrum of compound ***pre*-17b**.

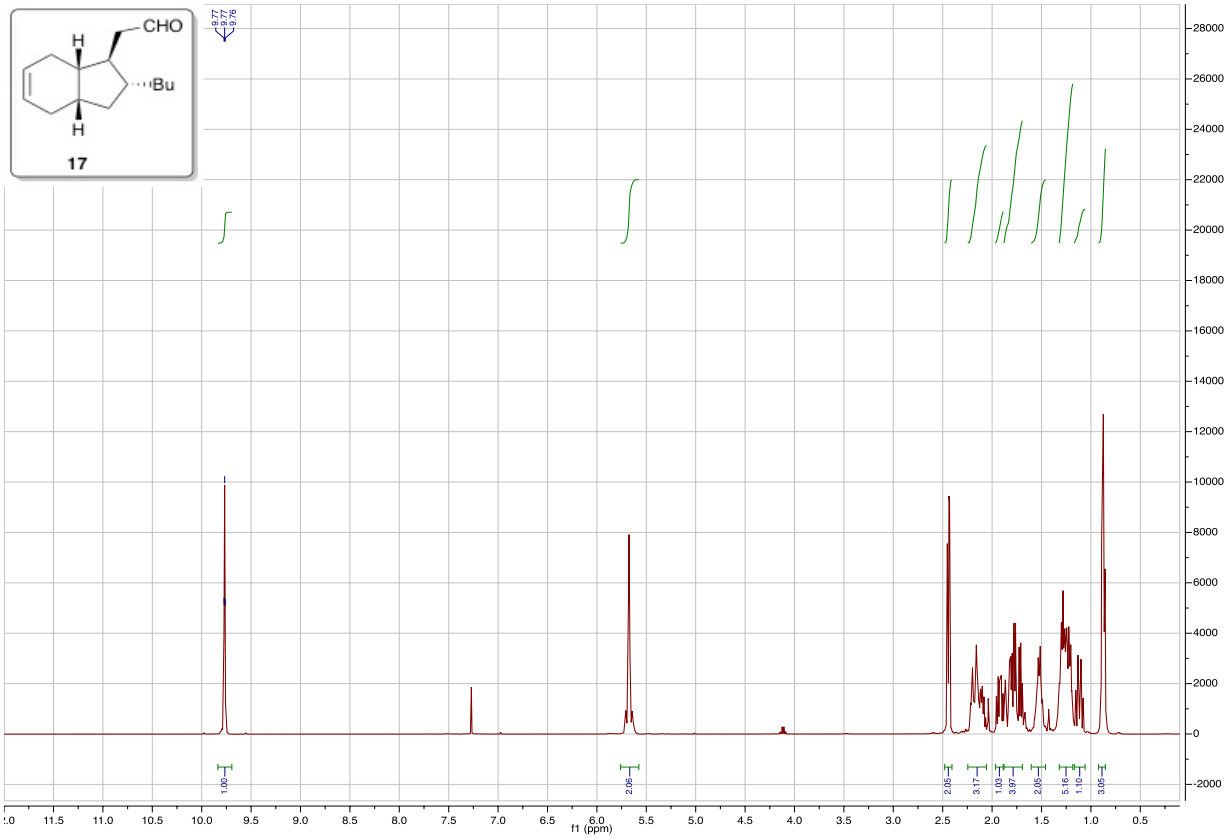


Figure S-27 ^{1}H-NMR spectrum of compound **17**.

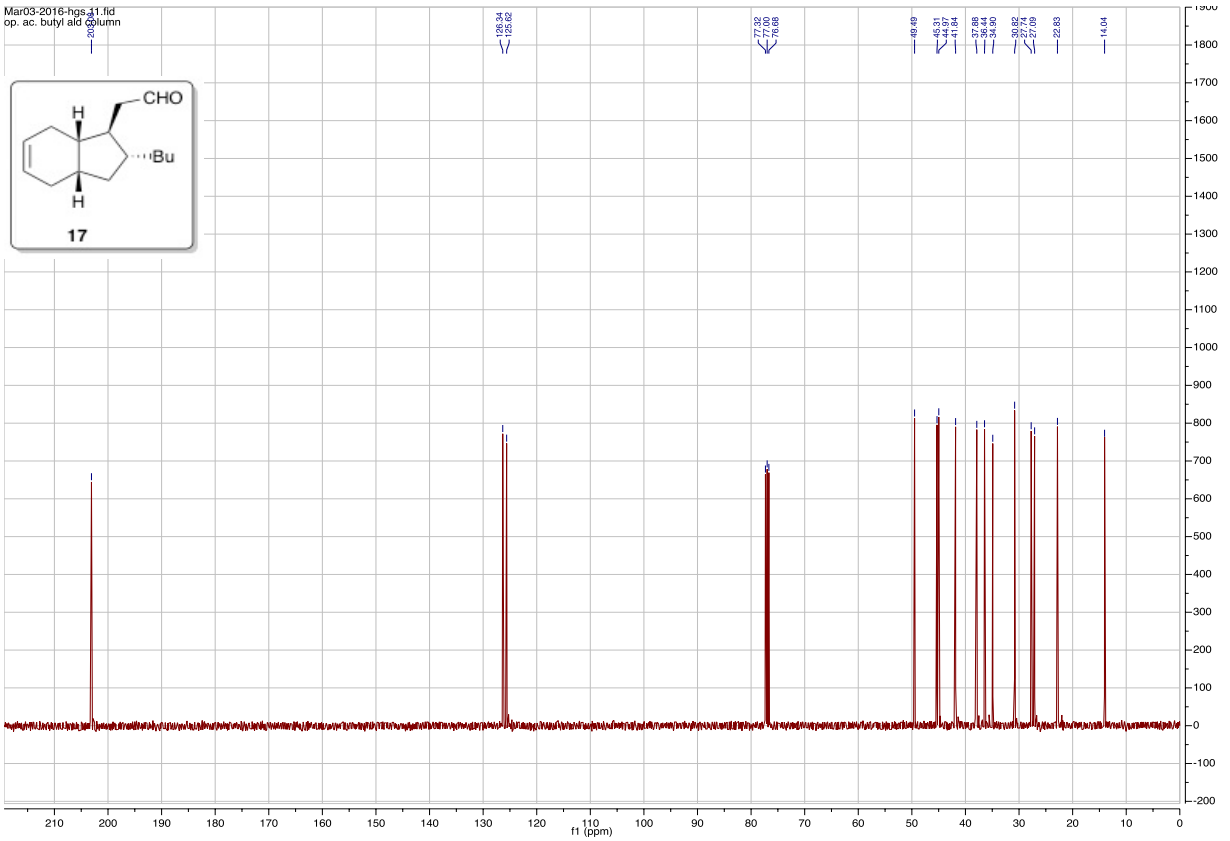


Figure S-28 ^{13}C-NMR spectrum of compound **17**.

Figure S-29 ^{1}H-NMR spectrum of compound **18**.

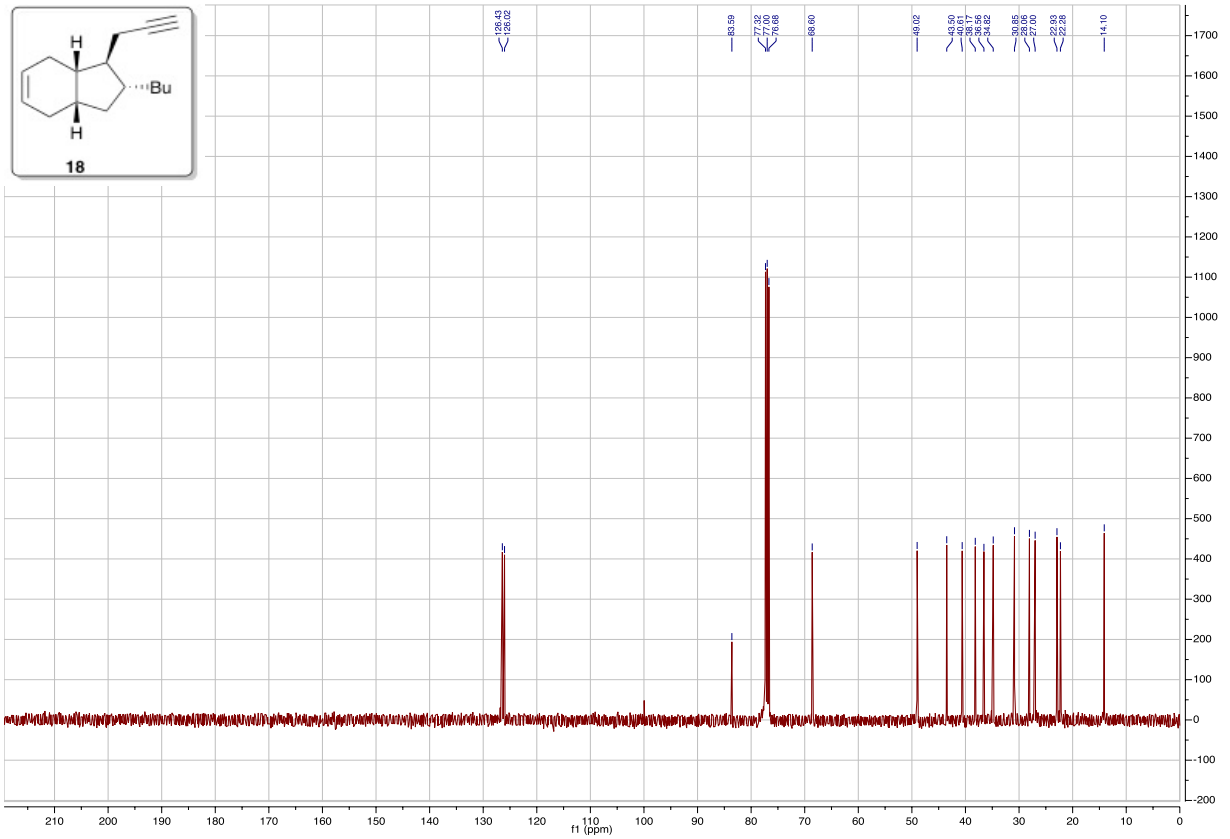


Figure S-30 ^{13}C-NMR spectrum of compound **18**.

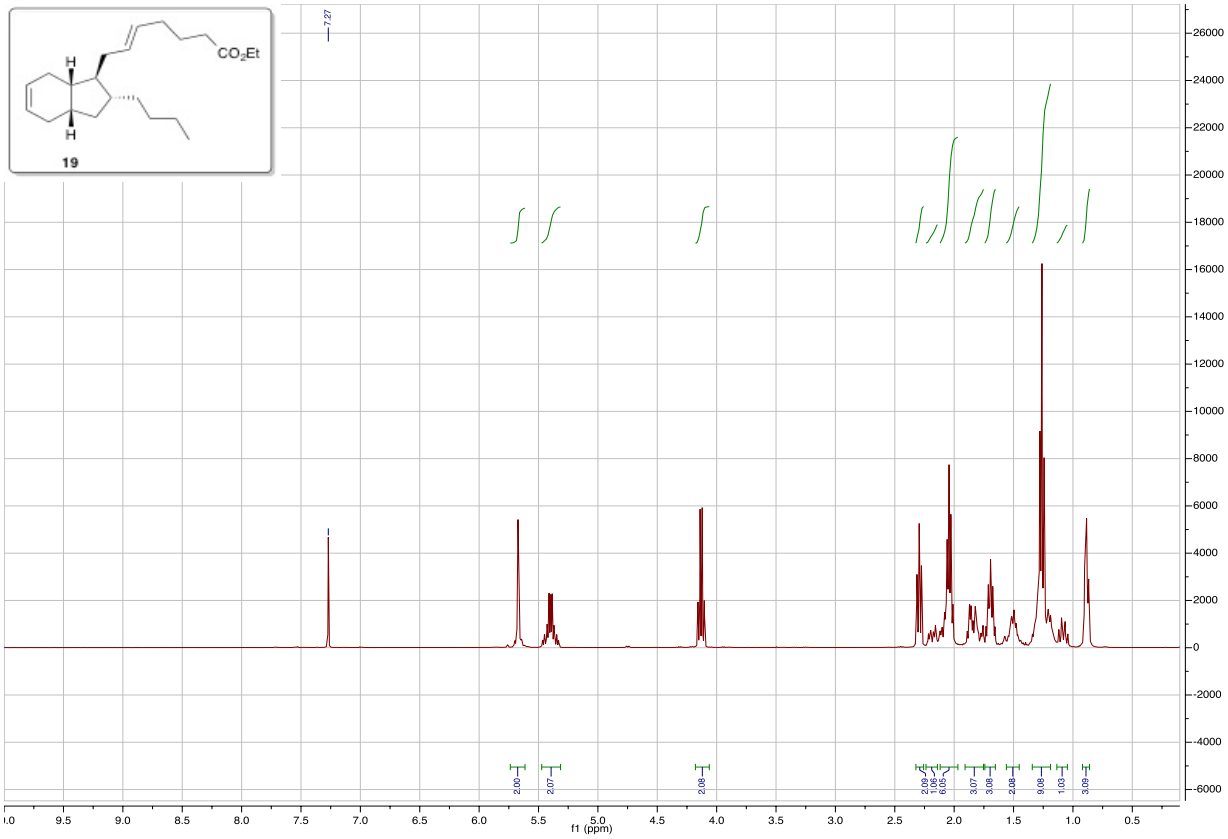


Figure S-31 ^{1}H-NMR spectrum of compound **19**.

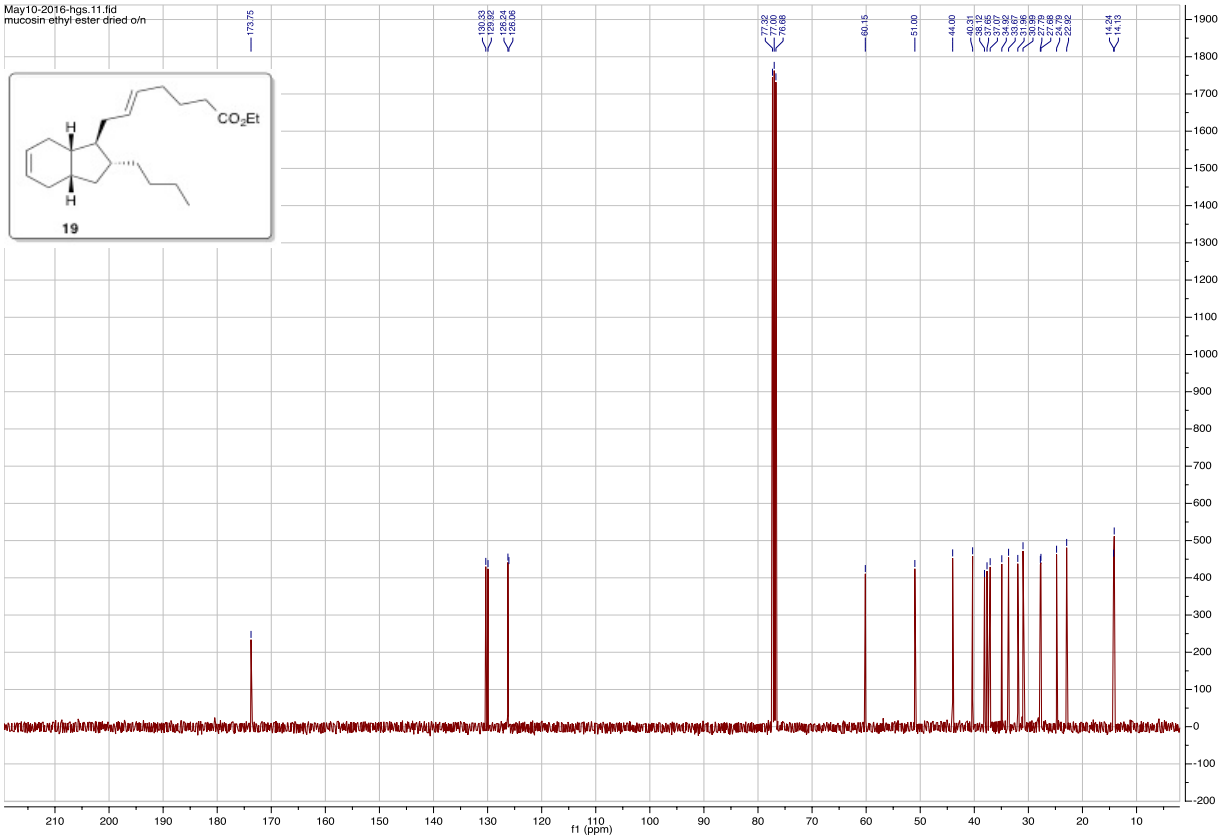


Figure S-32 ^{13}C-NMR spectrum of compound **19**.

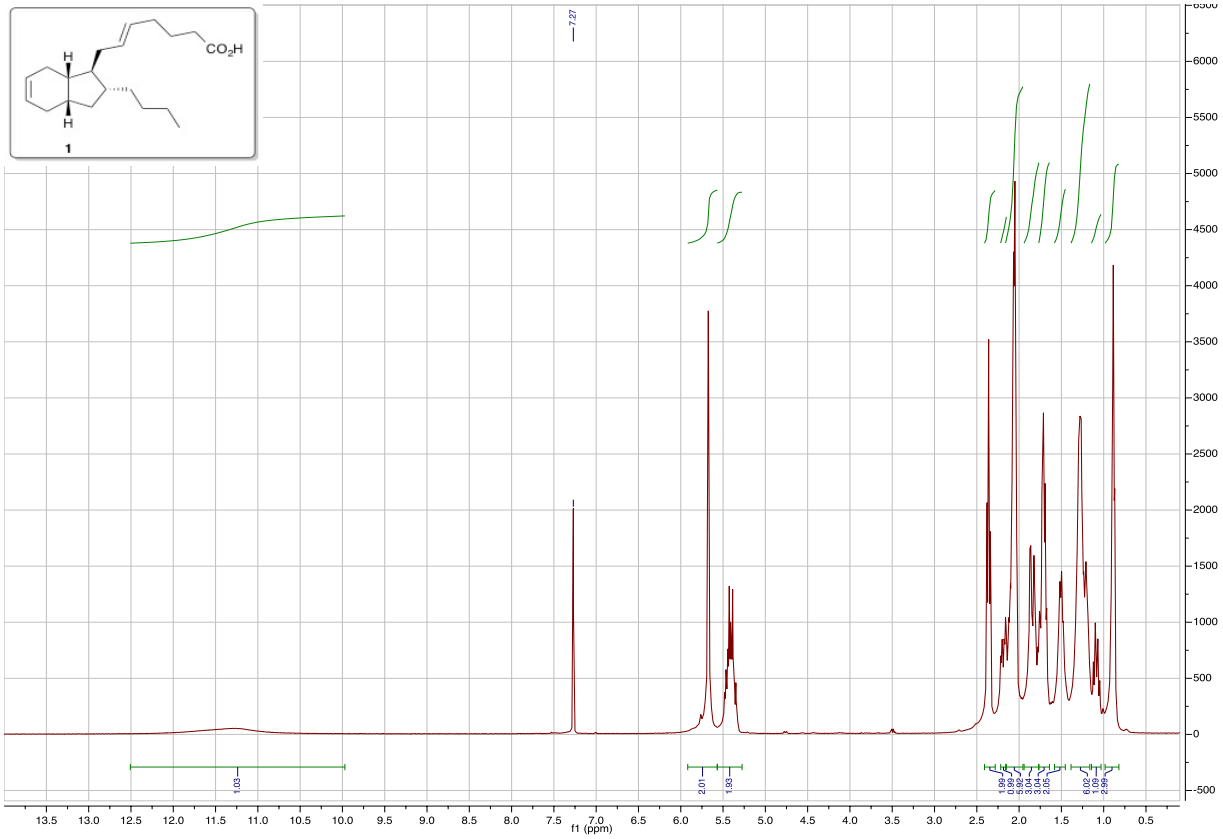


Figure S-33 ^{1}H-NMR spectrum of compound **1**.

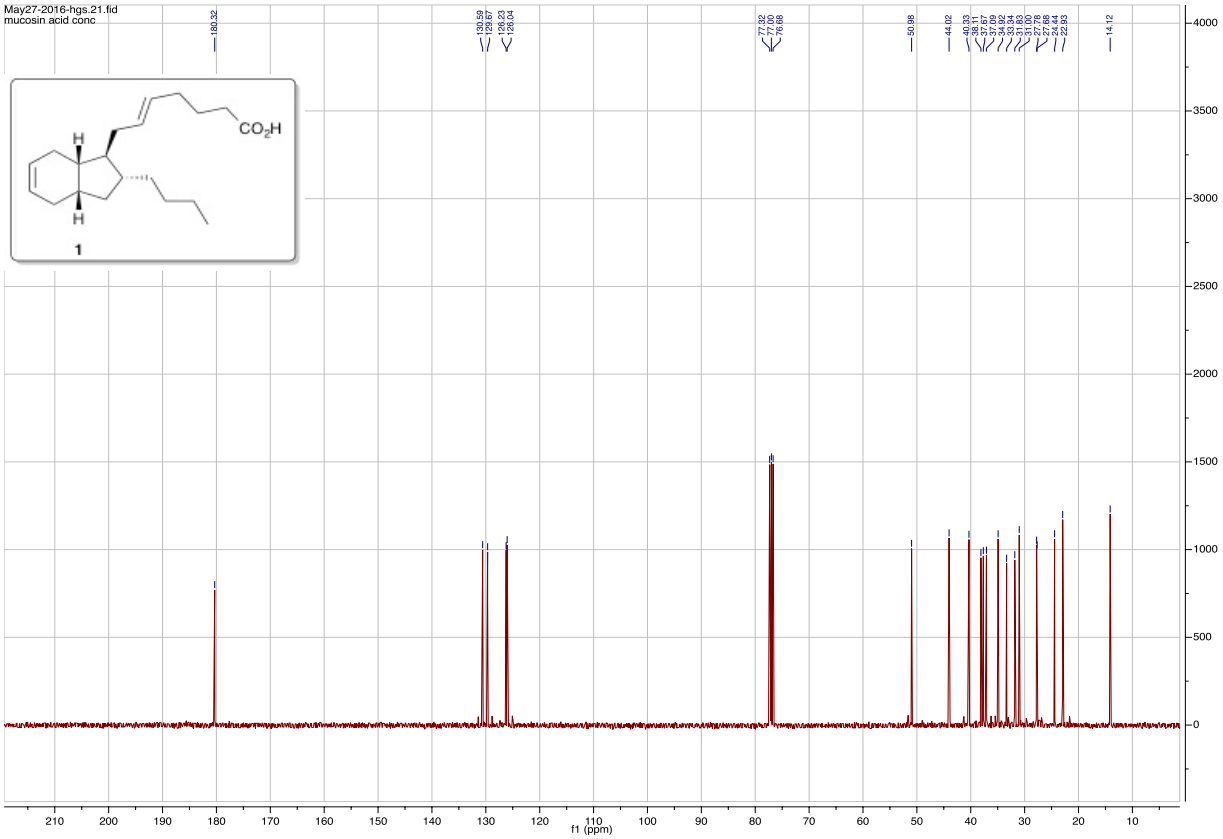


Figure S-34 ^{13}C-NMR spectrum of compound **1**.

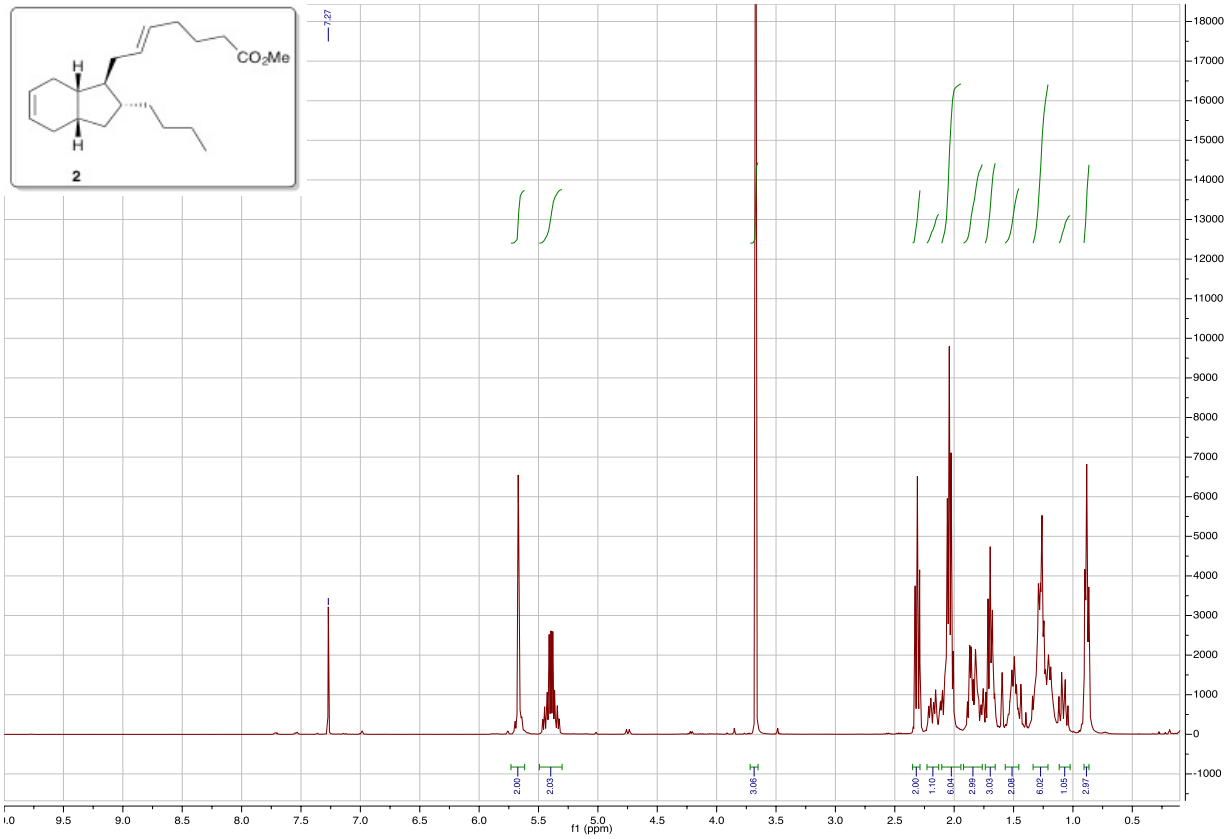


Figure S-35 ^{1}H-NMR spectrum of compound **2**.

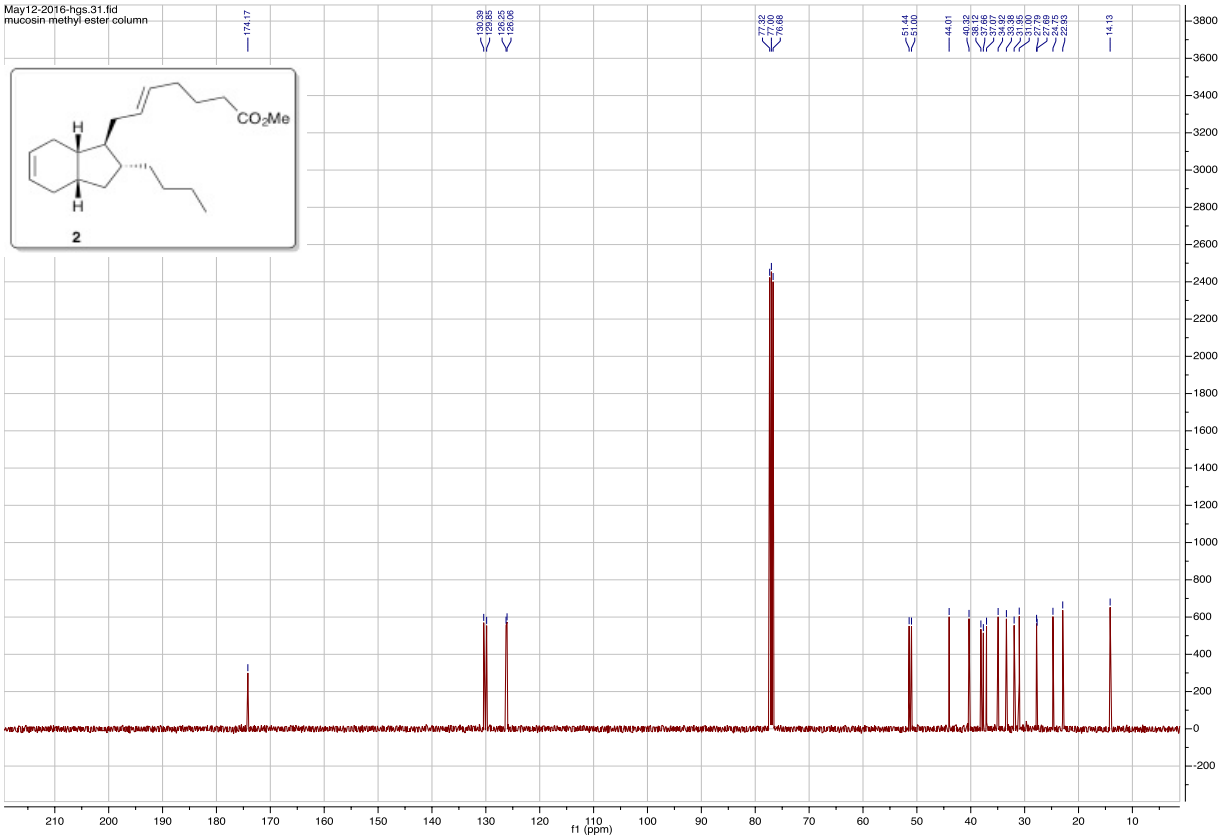


Figure S-36 ^{13}C-NMR spectrum of compound **2**.

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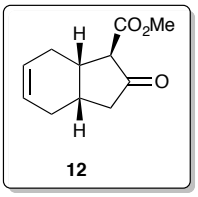
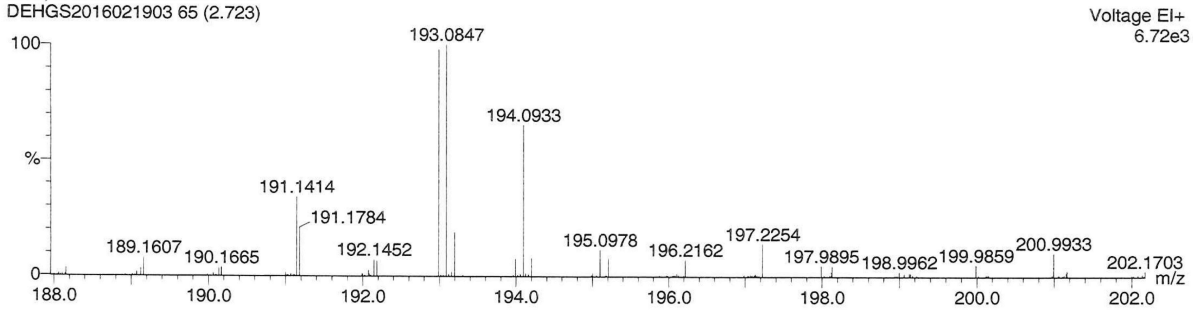


Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
47 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Sample 3 C11H14O3 MW 194
DEHGS2016021903 65 (2.723)

Voltage EI+
6.72e3



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
194.0933	194.0943	-1.0	-5.1	5.0	1	C11 H14 O3

Figure S-37 HRMS of compound **12**.

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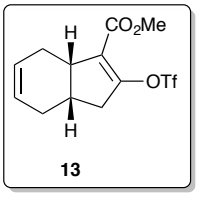
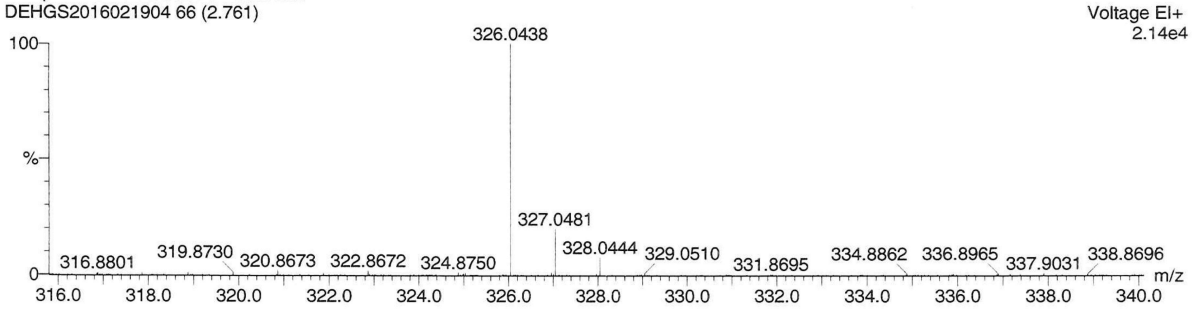


Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
287 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Sample 4 C12H13O5SF3 MW 326
DEHGS2016021904 66 (2.761)

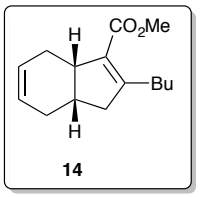
Voltage EI+
2.14e4



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
326.0438	326.0436	0.2	0.7	5.0	3	C12 H13 O5 S F3
	326.0424	1.4	4.2	9.0	2	C15 H12 O4 S F2
	326.0413	2.5	7.7	13.0	1	C18 H11 O3 S F

Figure S-38 HRMS of compound **13**.

Elemental Composition Report Page 1

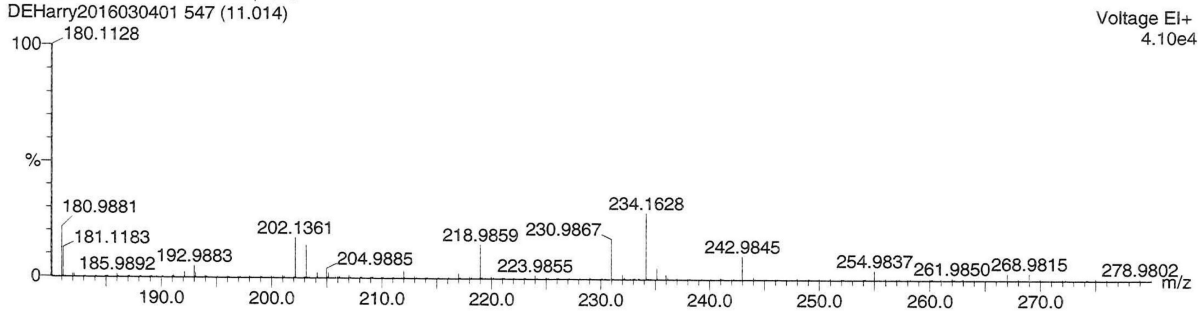


14

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
30 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

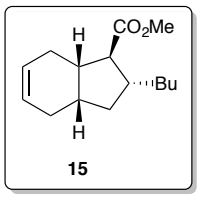
C15H22O2 HRMS MW 3234,1620
DEHarry2016030401 547 (11.014)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
234.1628	234.1620	0.8	3.5	5.0	1	C15 H22 O2

Figure S-39 HRMS of compound **14**.

Elemental Composition Report Page 1

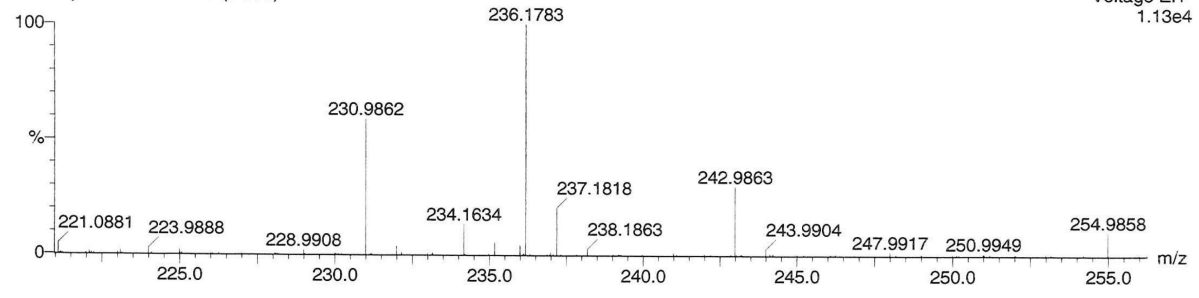


15

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
31 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

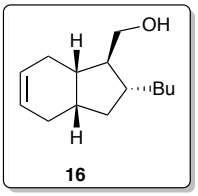
C15H24O2 HRMS MW 236,1776 pr 2
DEHarry2016030402 265 (5.336)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
236.1783	236.1776	0.7	2.8	4.0	1	C15 H24 O2

Figure S-40 HRMS of compound **15**.

Elemental Composition Report

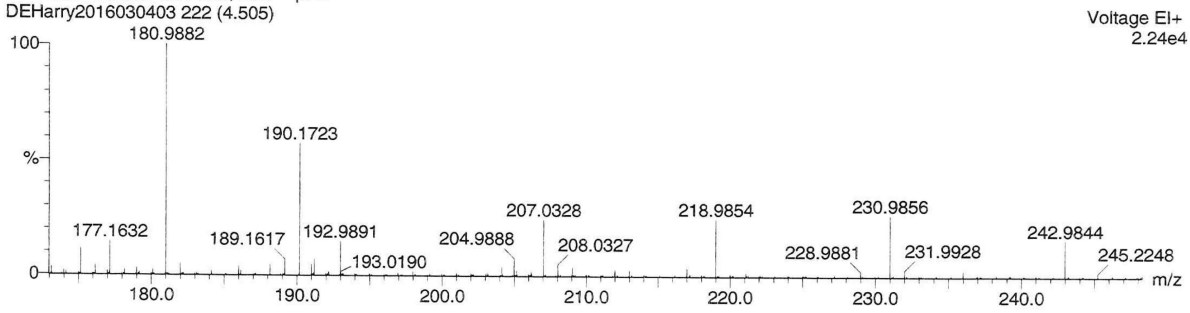


Page 1

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
21 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

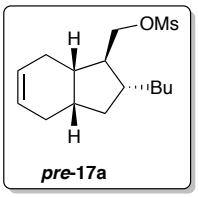
C14H24O HRMS MW 208,1827 pr 3
DEHarry2016030403 222 (4.505)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
190.1723	190.1722	0.1	0.8	4.0	1	C14 H22

Figure S-41 HRMS of compound **16**.

Elemental Composition Report

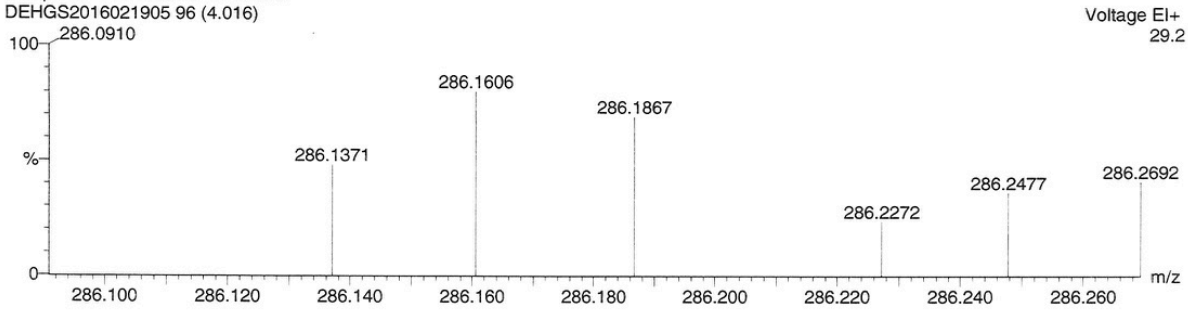


Page 1

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
234 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)

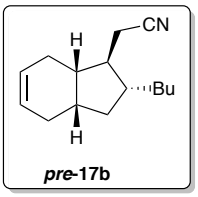
Sample 5 C15H26O3S MW 286
DEHGS2016021905 96 (4.016)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
286.1606	286.1603	0.3	1.2	3.0	5	C15 H26 O3 S
	286.1614	-0.8	-2.8	-1.0	2	C12 H27 O4 F S
	286.1592	1.4	5.0	0.0	1	C12 H24 O5 F2
	286.1580	2.6	9.0	4.0	4	C15 H23 O4 F
	286.1578	2.8	9.7	0.0	3	C13 H25 O F3 S

Figure S-42 HRMS of compound ***pre*-17a**.

Elemental Composition Report Page 1

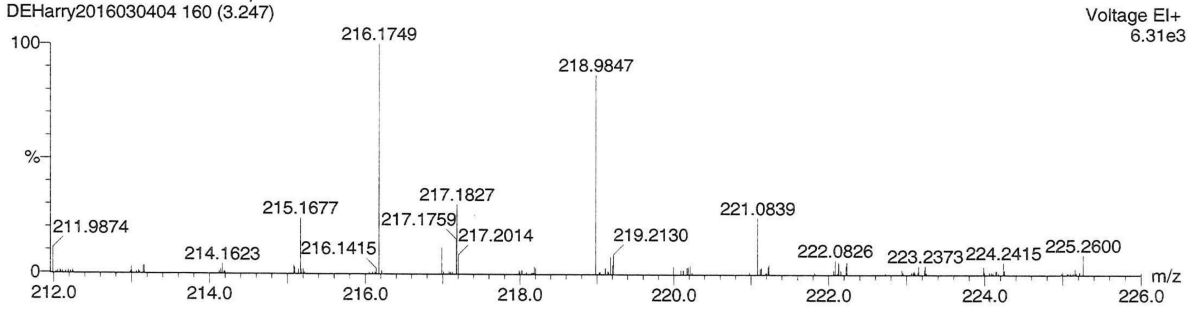


pre-17b

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
51 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

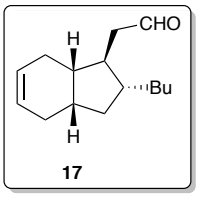
C15H23N HRMS MW 217 pr 4
DEHarry2016030404 160 (3.247)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
217.1827	217.1830	-0.3	-1.6	5.0	1	C15 H23 N

Figure S-43 HRMS of compound ***pre*-17b**.

Elemental Composition Report Page 1

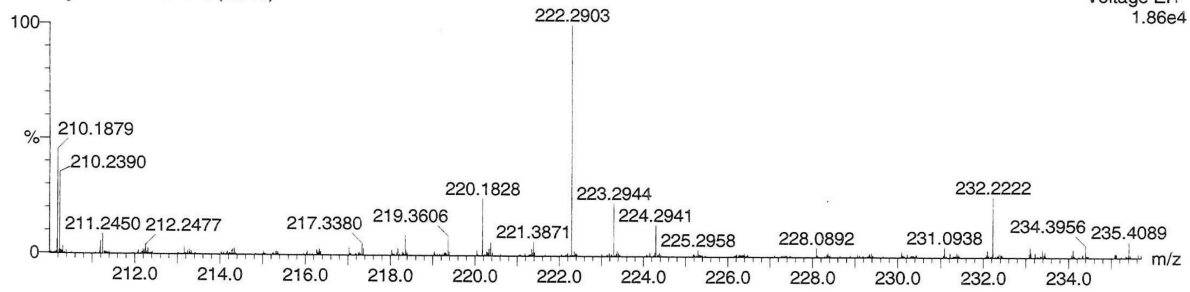


17

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
53 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

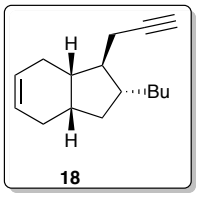
C15H24O HRMS MW 220 pr 5
DEHarry2016030405 276 (5.601)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
220.1828	220.1827	0.1	0.4	4.0	1	C15 H24 O

Figure S-44 HRMS of compound **17**.

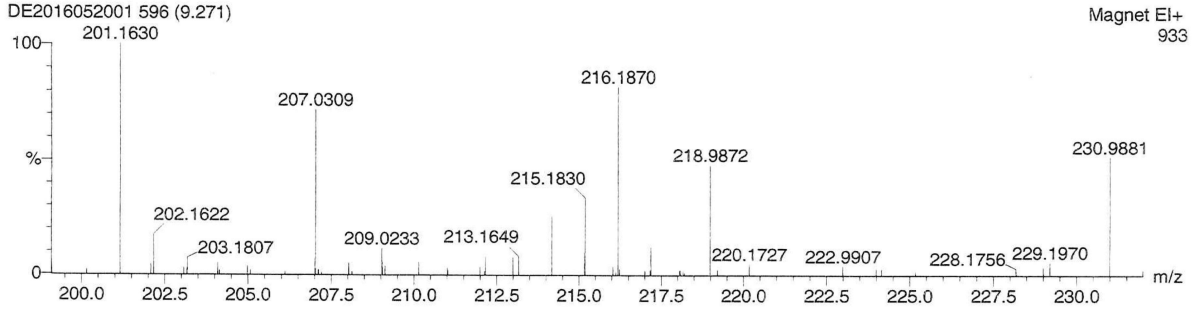
Elemental Composition Report Page 1



Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
6 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

A1K3
DE2016052001 596 (9.271)
Magnet EI+
933



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
216.1870	216.1878	-0.8	-3.7	5.0	1	C16 H24

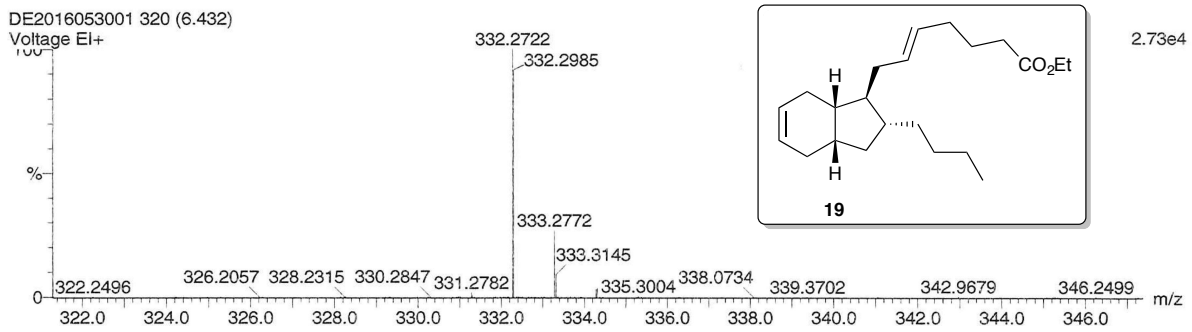
Figure S-45 HRMS of compound **18**.

Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
32 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

DE2016053001 320 (6.432)
Voltage EI+
2.73e4



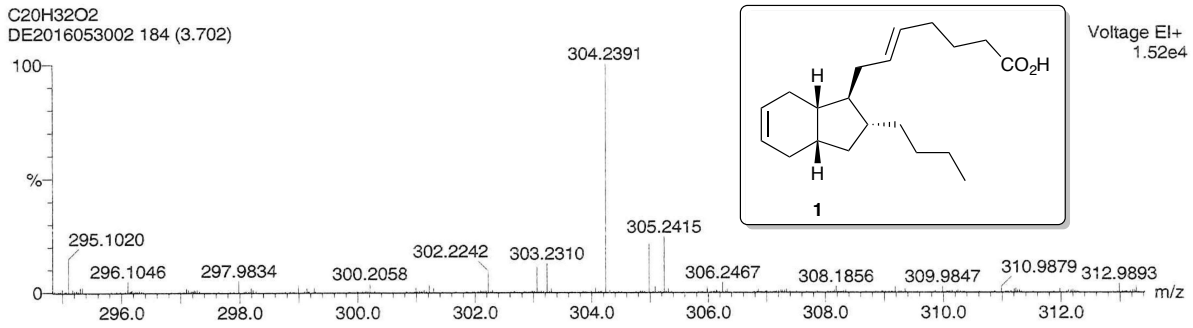
Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
332.2722	332.2715	0.7	2.0	5.0	1	C22 H36 O2

Figure S-46 HRMS of compound **19**.

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
29 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



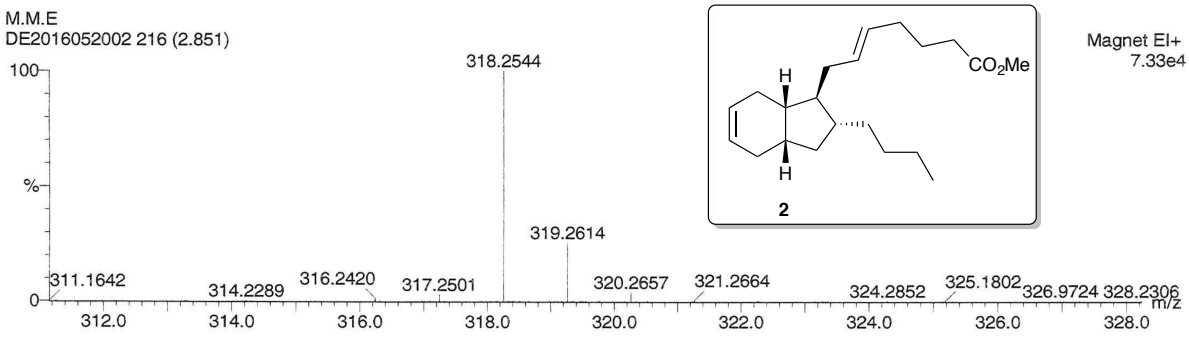
Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
304.2391	304.2402	-1.1	-3.7	5.0	1	C20 H32 O2

Figure S-47 HRMS of compound **1**.

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
31 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
318.2544	318.2559	-1.5	-4.7	5.0	1	C21 H34 O2

Figure S-48 HRMS of compound **2**.

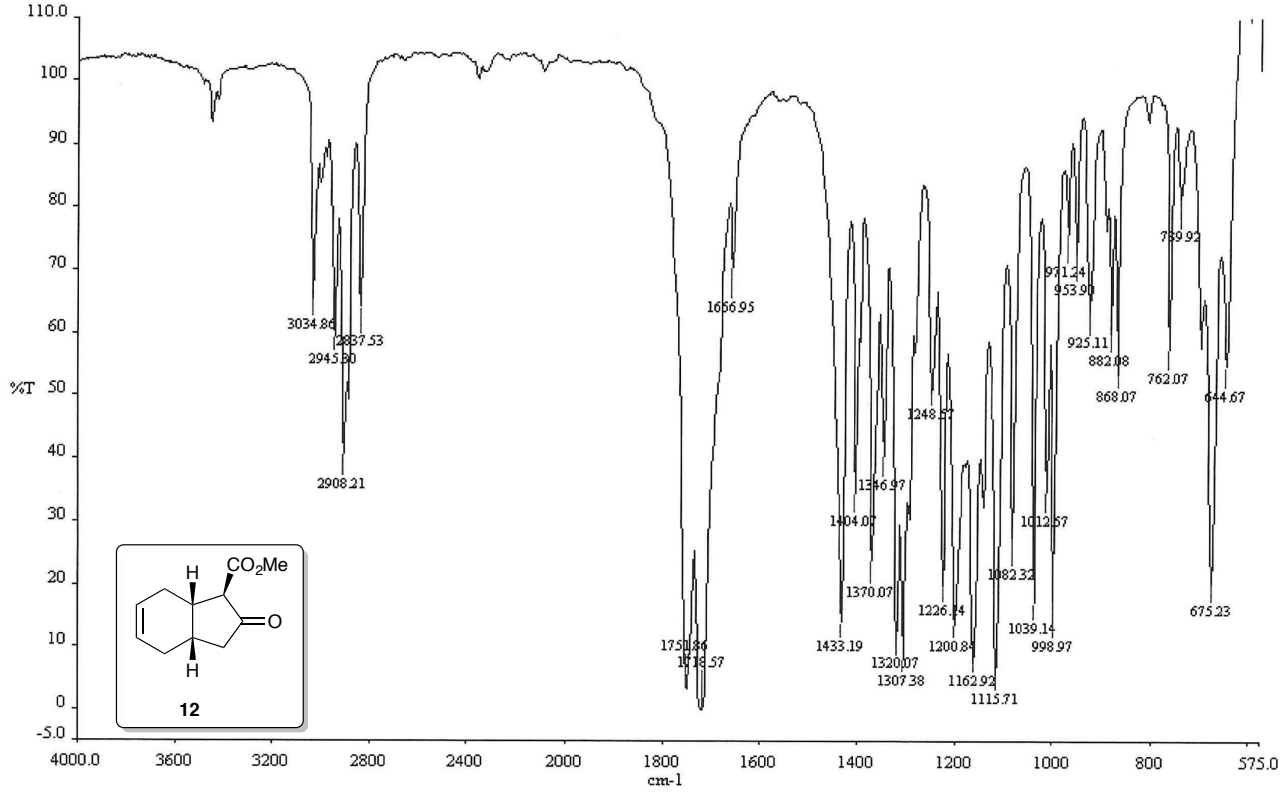


Figure S-49 IR of compound **12**.

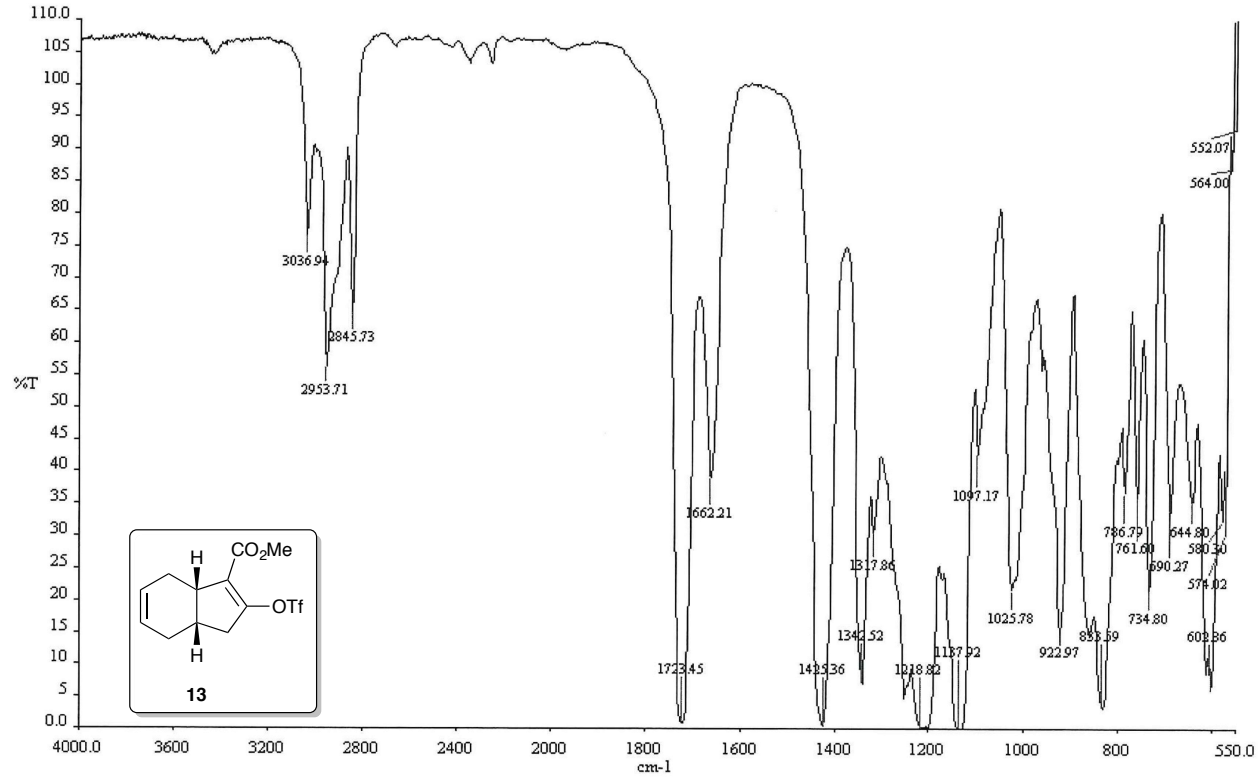


Figure S-50 IR of compound **13**.

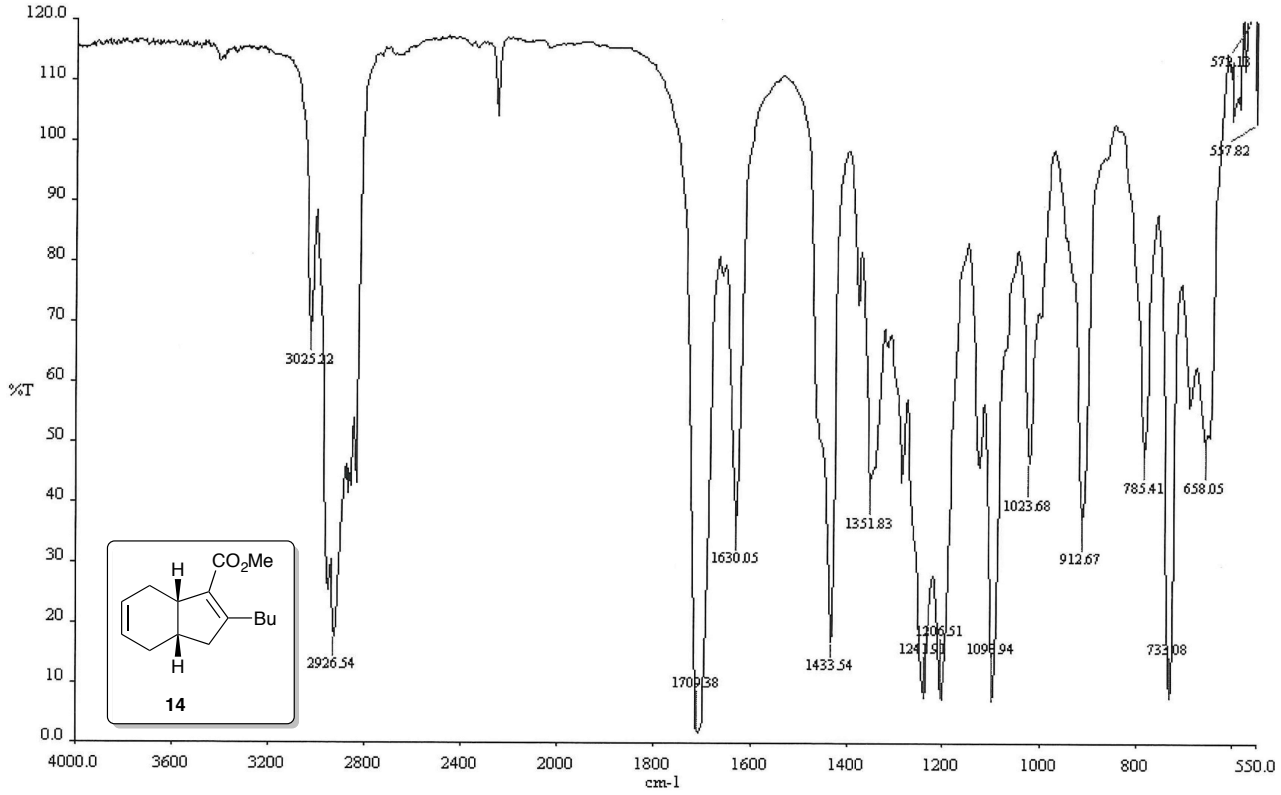


Figure S-51 IR of compound **14**.

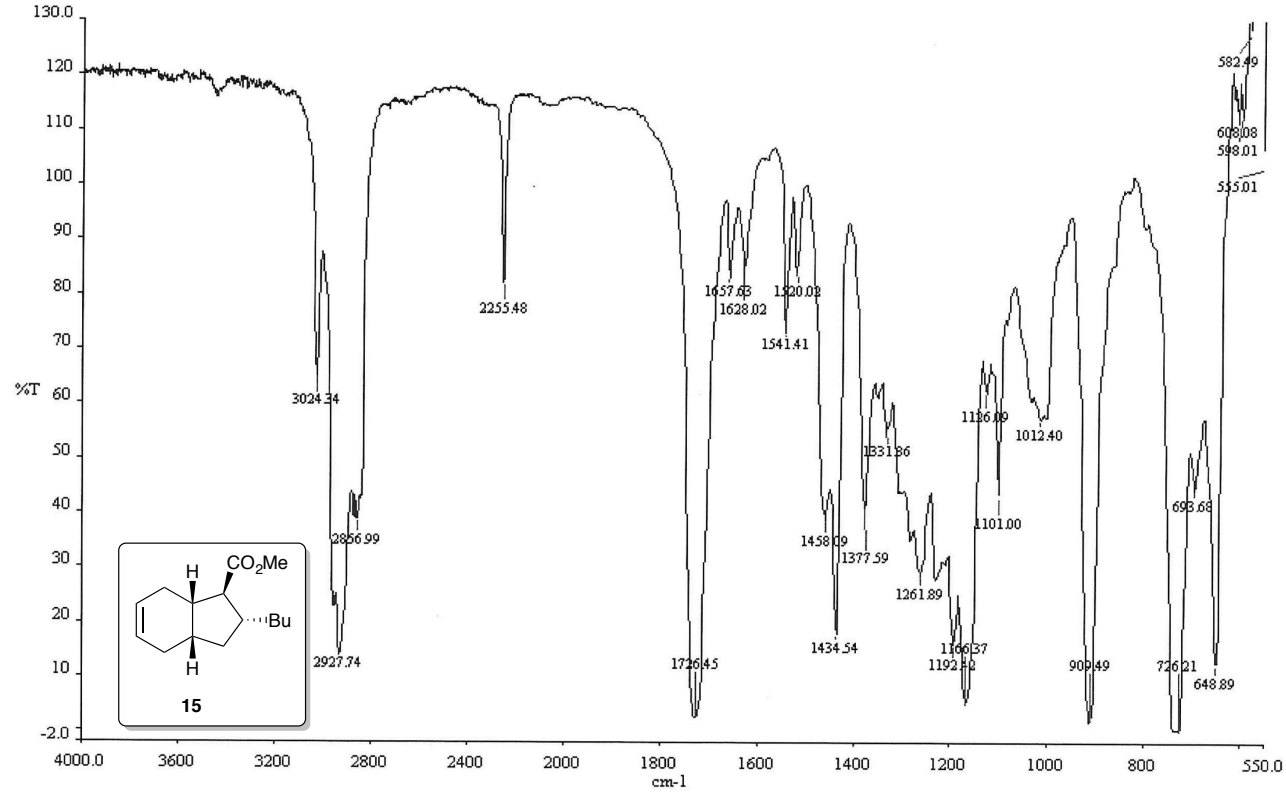


Figure S-52 IR of compound **15**.

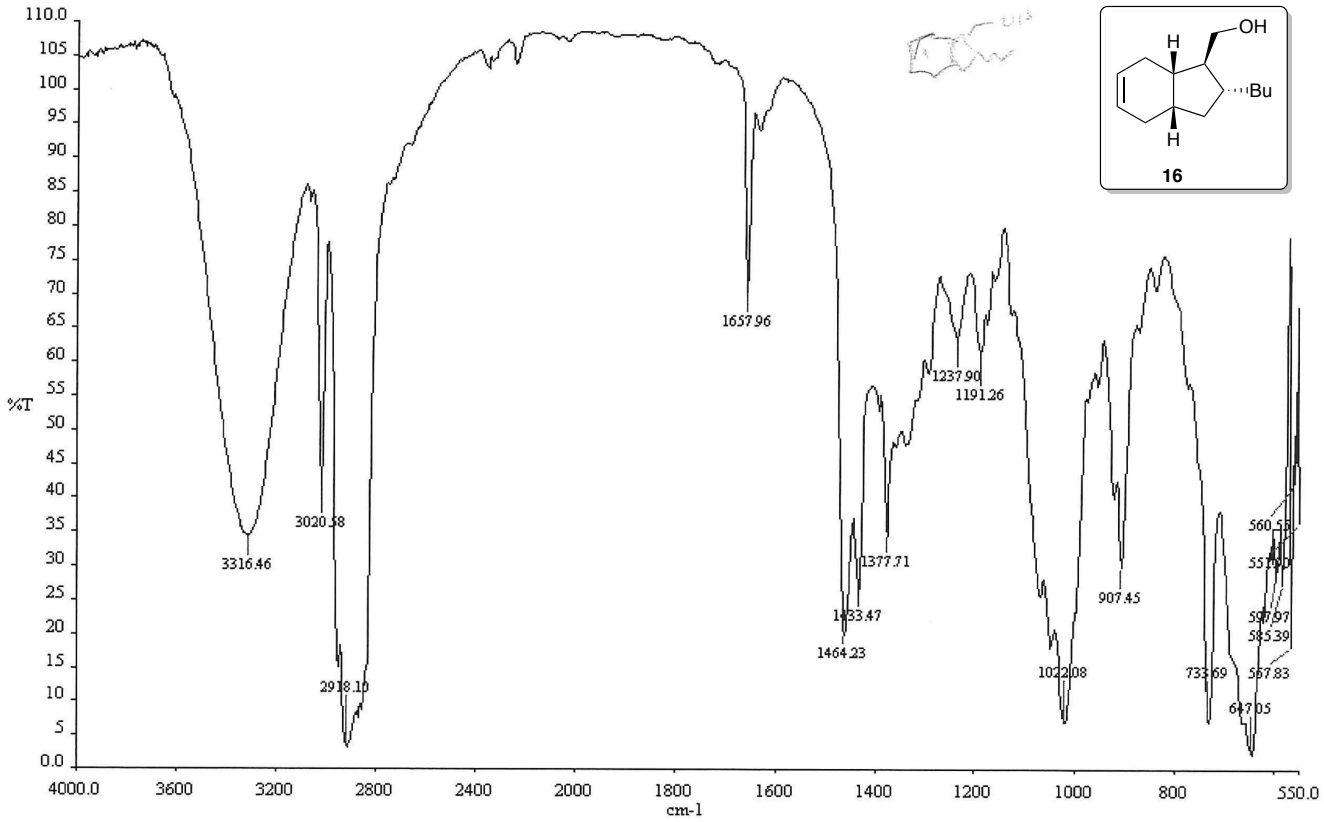


Figure S-53 IR of compound **16**.

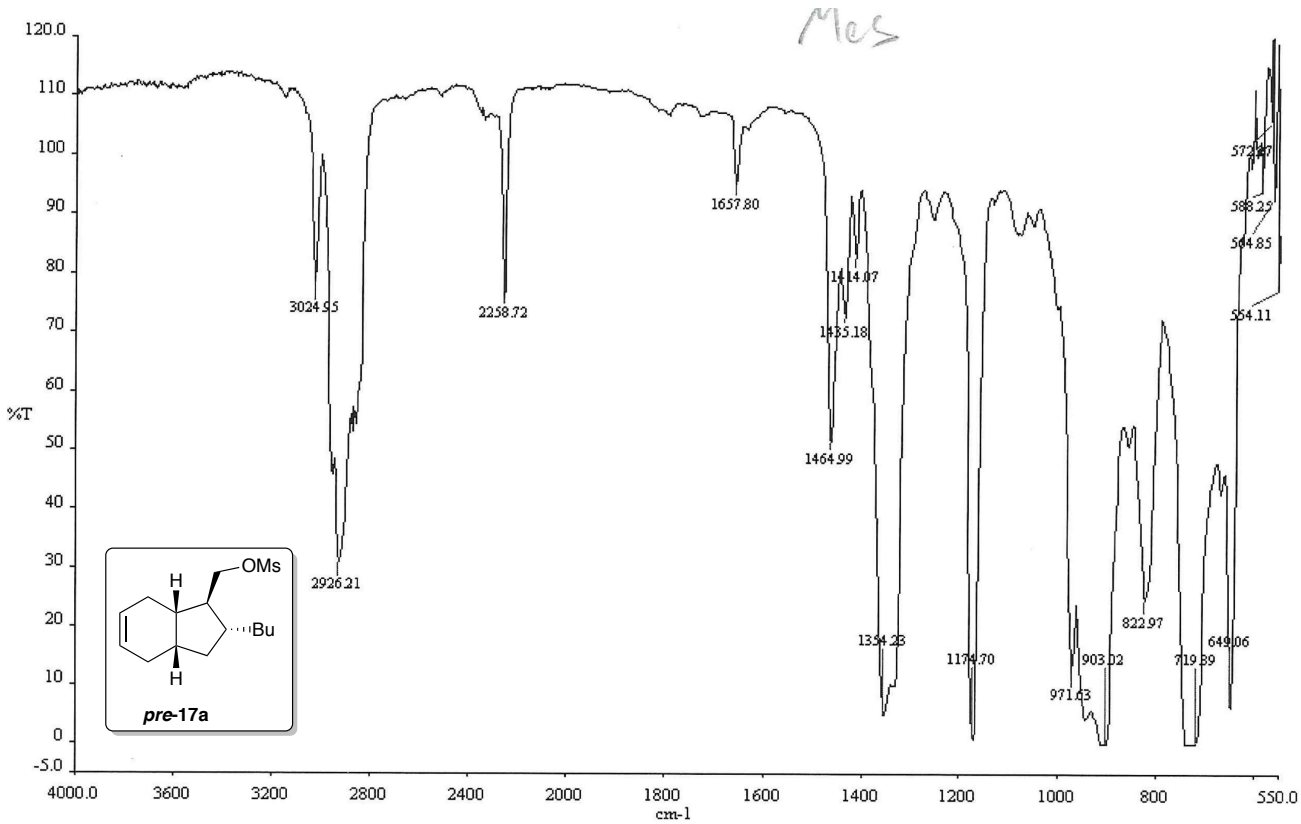


Figure S-54 IR of compound ***pre*-17a**.

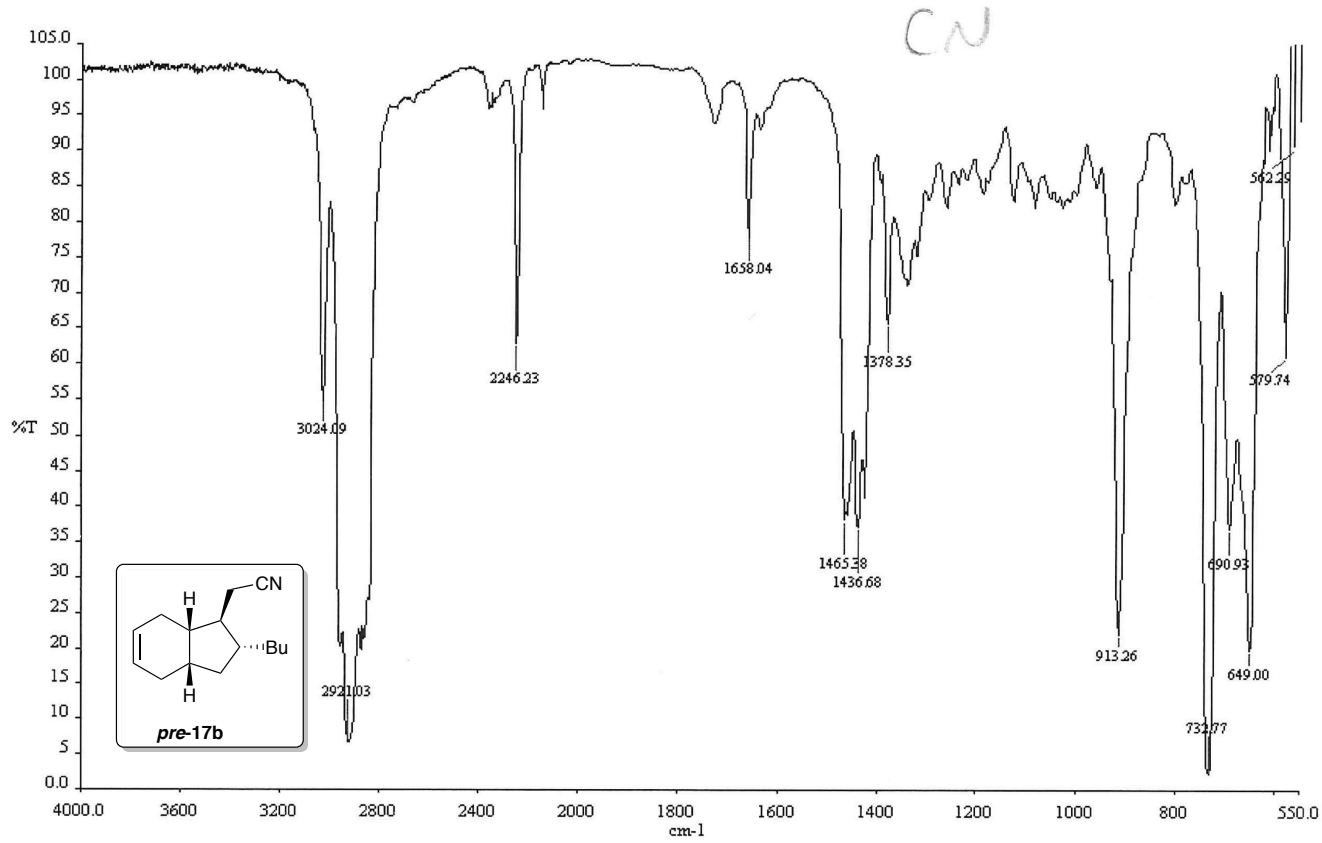


Figure S-55 IR of compound ***pre*-17b**.

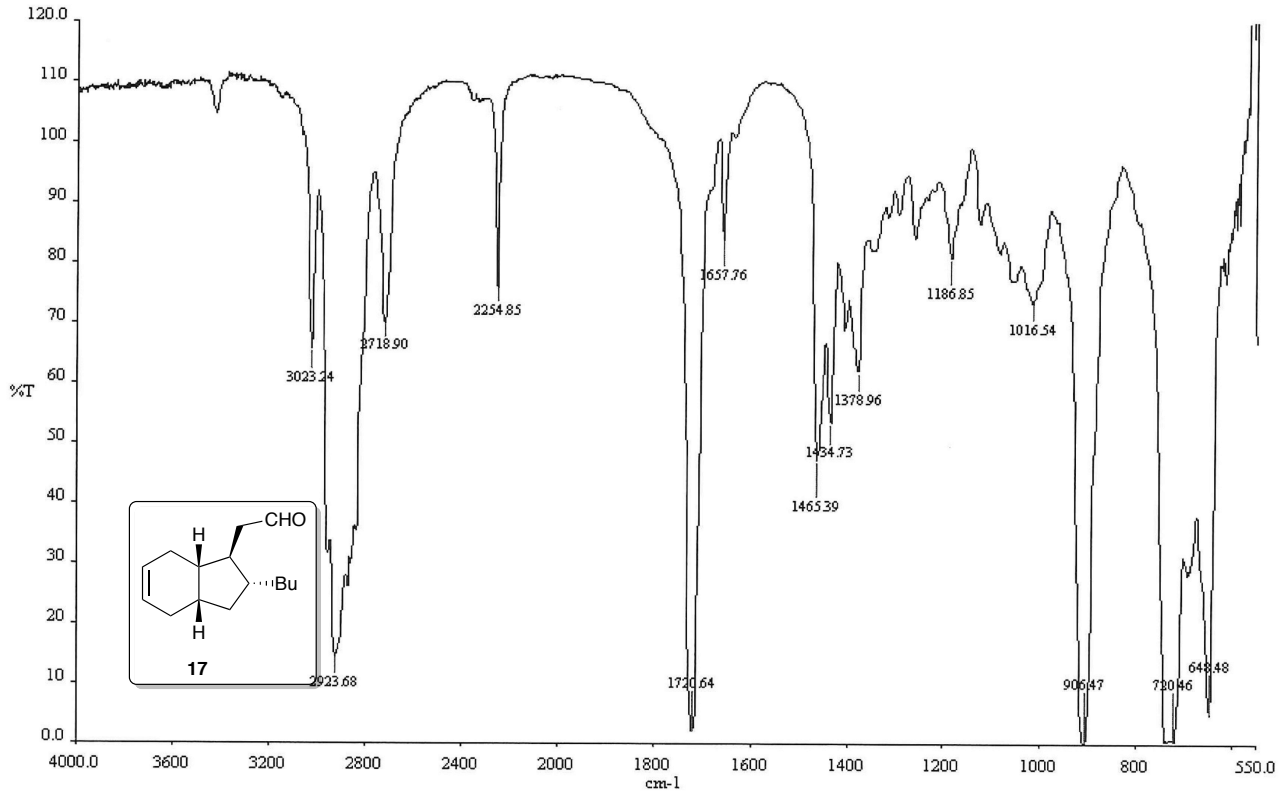


Figure S-56 IR of compound **17**.

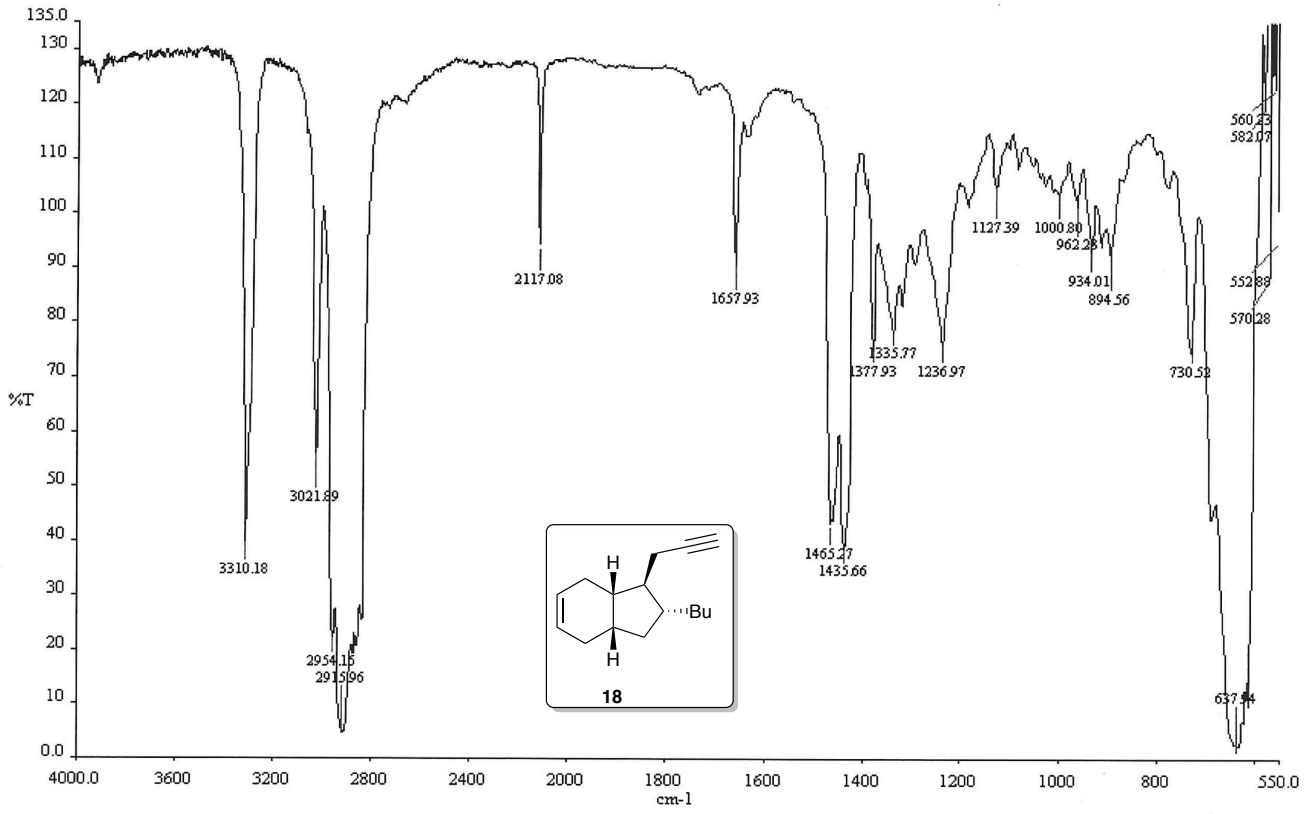


Figure S-57 IR of compound **18**.

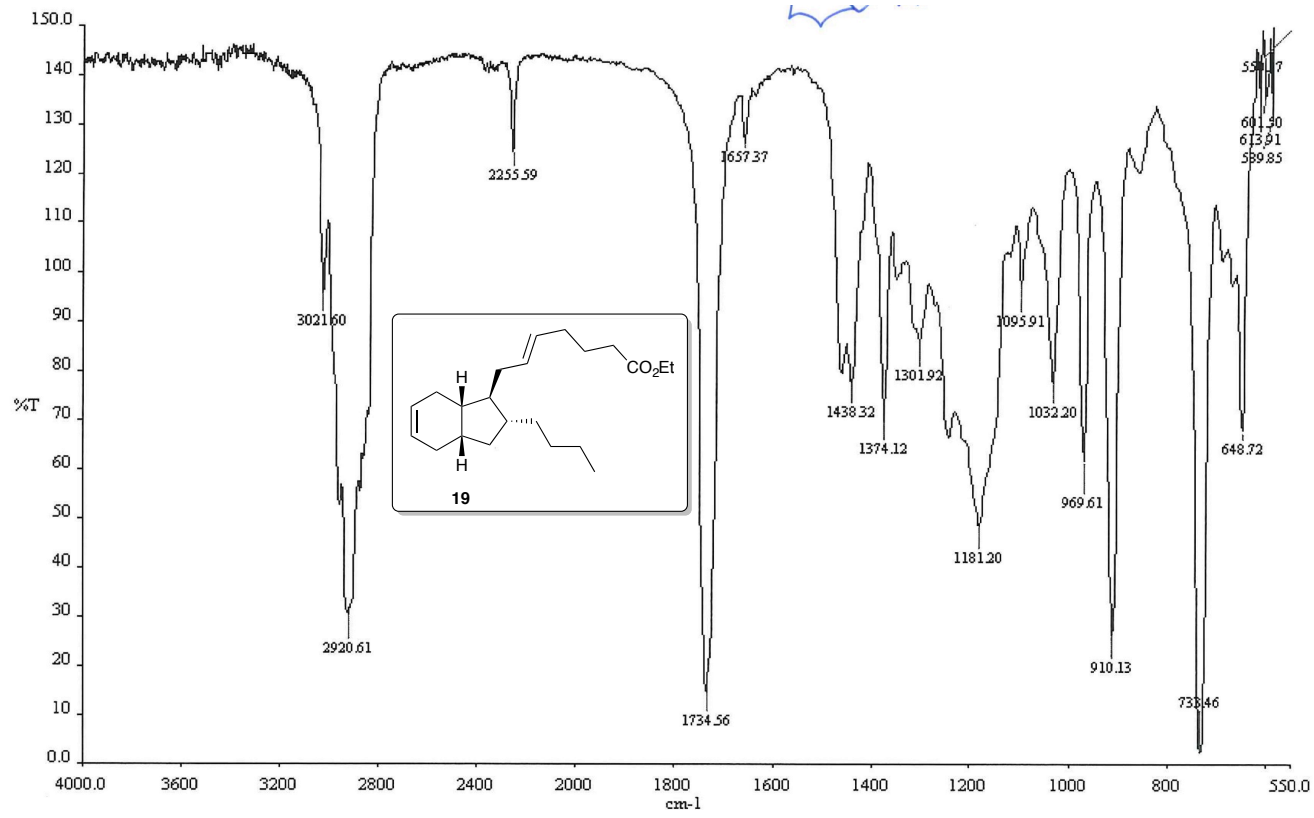


Figure S-58 IR of compound **19**.

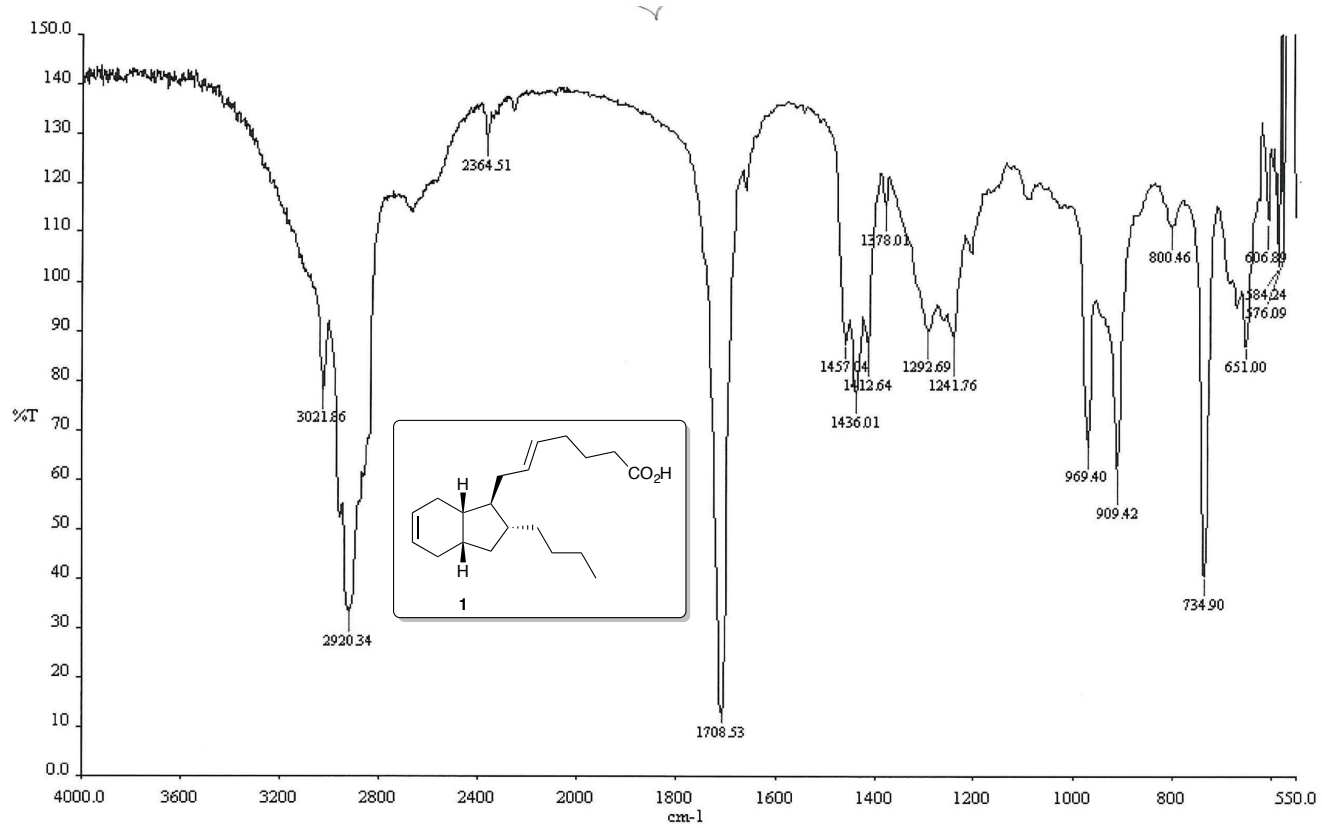


Figure S-59 IR of compound **1**.

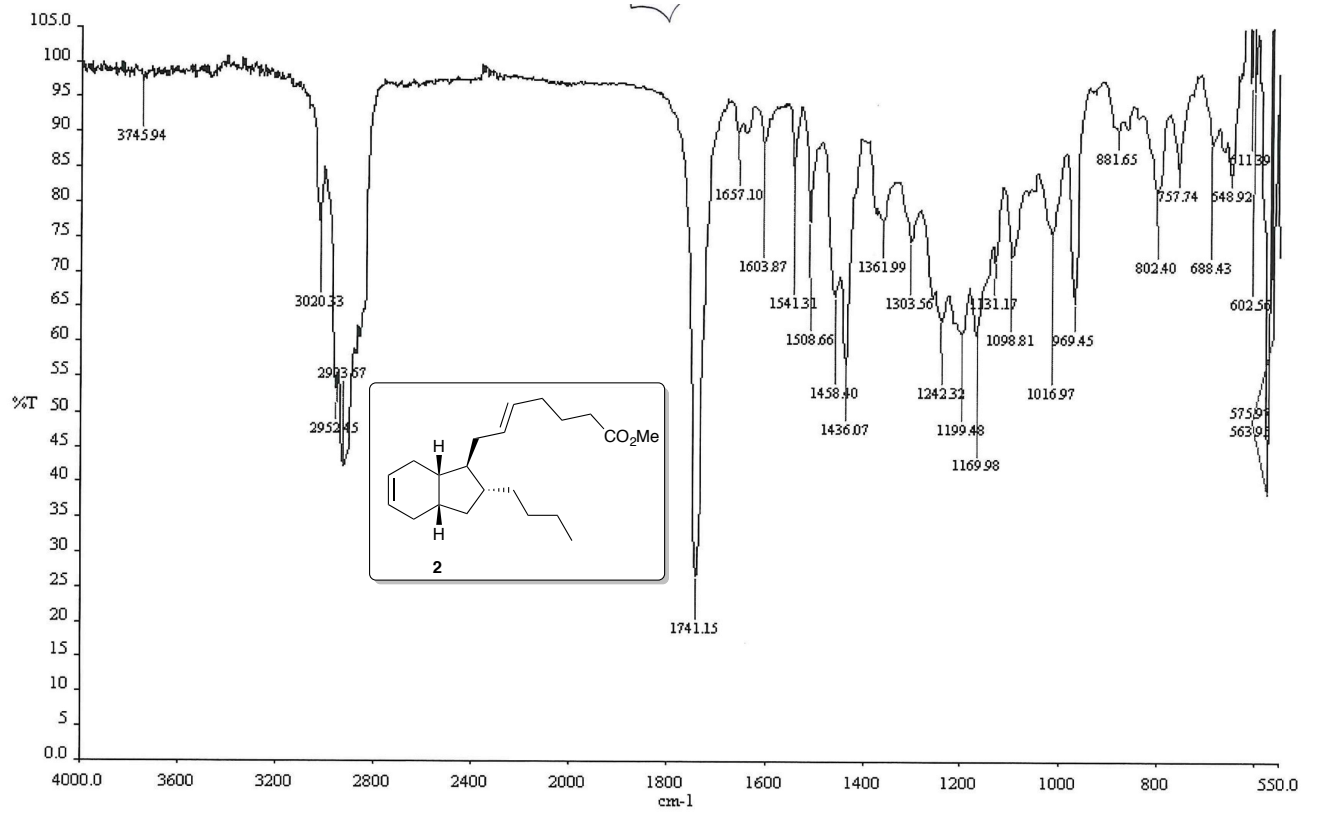
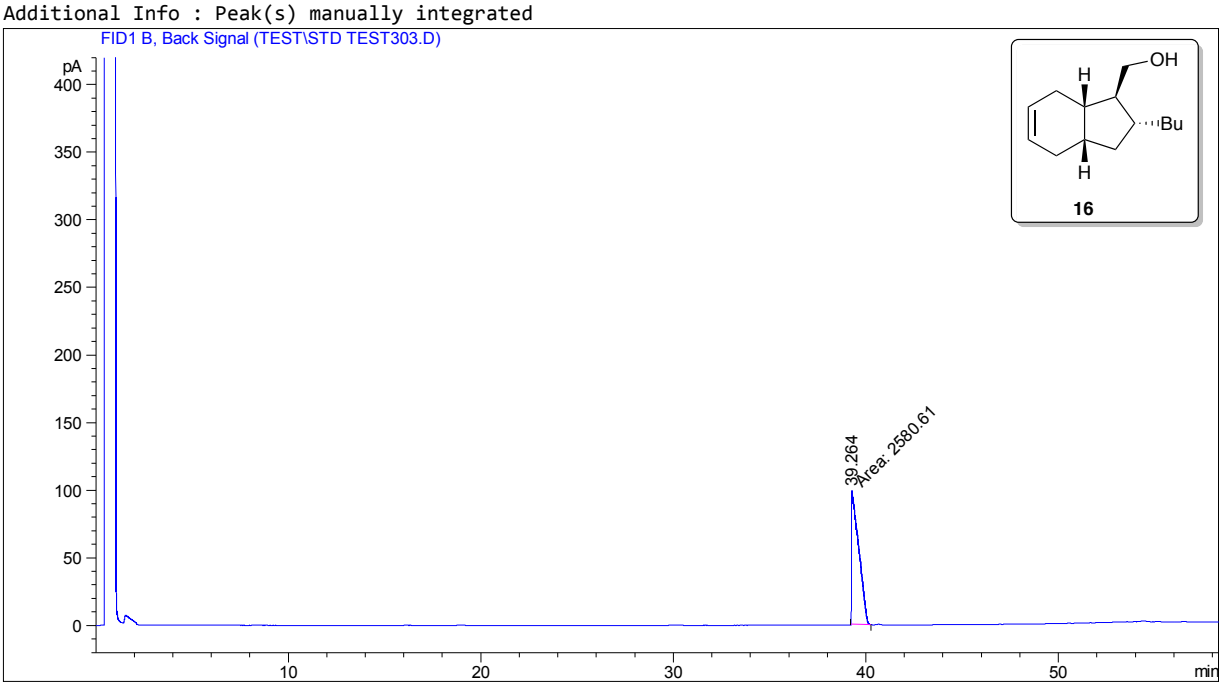


Figure S-60 IR of compound **2**.

Data File C:\CHEM32\1\DATA\TEST\STD TEST303.D
Sample Name: RAC

```
======================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : 7820 GC                       Location : Vial 1
Injection Date  : 5/2/2016 15:28:06
                                                Inj Volume : Manually
Method          : C:\CHEM32\1\METHODS\CP7502\CP7502.M
Last changed    : 5/2/2016 14:05:55 by SYSTEM
Sample Info     : 80 grader 30 min, 3 grader/min til 150 grader, 5 min hold time

Additional Info : Peak(s) manually integrated
```




```
======================================================================
                    External Standard Report
======================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Tuesday, August 20, 201311:04:49
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

RetTime  Type     Area     Amt/Area    Amount   Grp   Name
 [min]          [pA*s]               [ng/ul]
-------|------|----------|----------|----------|--|------------------
  3.710           -          -          -         tridekan
  4.351           -          -          -         tetradekan
  4.970           -          -          -         pentadekan
  5.557           -          -          -         hexadekan

Totals :                               0.00000
```


Figure S-61 Chiral GLC of compound **16**.

Data File C:\CHEM32\1\DATA\TEST\STD TEST303.D
Sample Name: RAC

1 Warnings or Errors :

Warning : Calibrated compound(s) not found

==========
==========
Area Percent Report
==========

Sorted By : Signal
Calib. Data Modified : Tuesday, August 20, 201311:04:49
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Area %	Name
1	3.710		0.0000	0.00000	0.00000	tridekan
2	4.351		0.0000	0.00000	0.00000	tetradekan
3	4.970		0.0000	0.00000	0.00000	pentadekan
4	5.557		0.0000	0.00000	0.00000	hexadekan
5	39.264	MM	0.4356	2580.60645	1.000e2	?

Totals : 2580.60645

1 Warnings or Errors :

Warning : Calibrated compound(s) not found

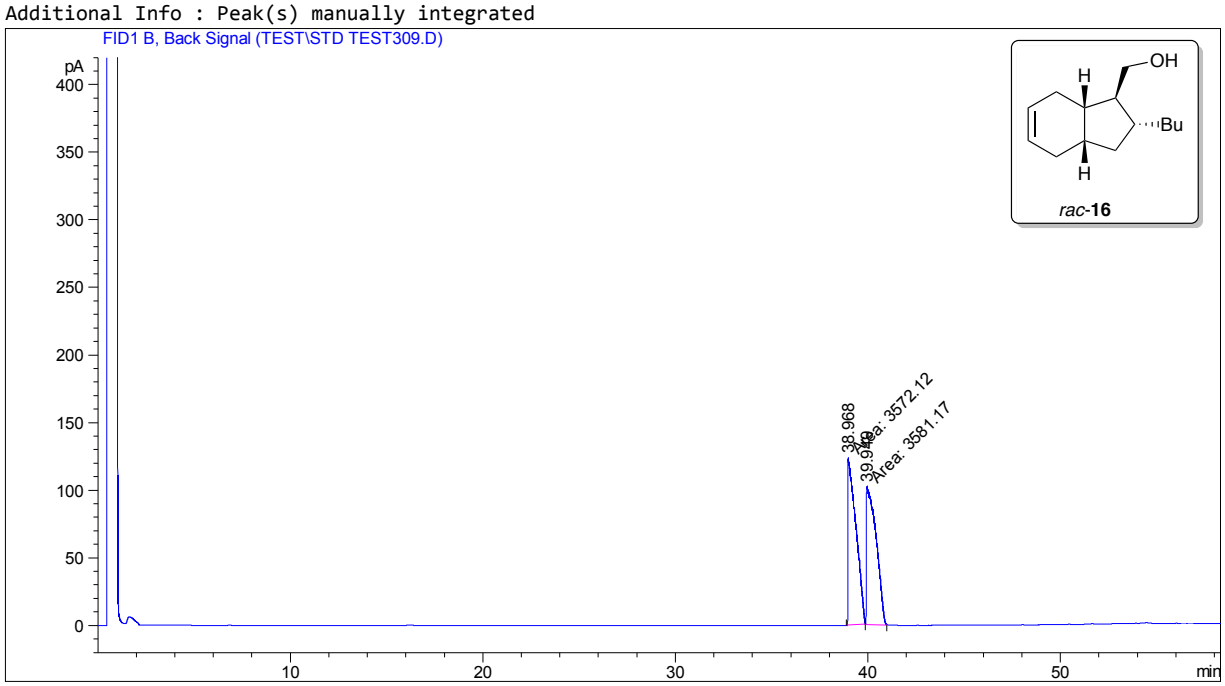
==========
*** End of Report ***

Figure S-62 Report from chiral GLC of compound **16**.

Data File C:\CHEM32\1\DATA\TEST\STD TEST309.D
Sample Name: Rac fort 1:5

```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : 7820 GC                        Location : Vial 1
Injection Date  : 5/10/2016 14:46:51
                                                 Inj Volume : Manually
Method          : C:\CHEM32\1\METHODS\CP7502\CP7502.M
Last changed    : 5/2/2016 14:05:55 by SYSTEM
Sample Info     : 80 grader 30 min, 3 grader/min til 150 grader, 5 min hold time

Additional Info : Peak(s) manually integrated
```




```
==========================================================================
                      External Standard Report
==========================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Tuesday, August 20, 201311:04:49
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

RetTime  Type     Area     Amt/Area    Amount   Grp   Name
 [min]          [pA*s]               [ng/ul]
-------|------|----------|----------|----------|--|------------------
  3.710           -          -          -         tridekan
  4.351           -          -          -         tetradekan
  4.970           -          -          -         pentadekan
  5.557           -          -          -         hexadekan

Totals :                               0.00000
```


Figure S-63 Chiral GLC of compound *rac*-**16**.

Data File C:\CHEM32\1\DATA\TEST\STD TEST309.D
Sample Name: Rac fort 1:5

1 Warnings or Errors :

Warning : Calibrated compound(s) not found

==========
==========
Area Percent Report
==========

Sorted By : Signal
Calib. Data Modified : Tuesday, August 20, 201311:04:49
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Area %	Name
1	3.710		0.0000	0.00000	0.00000	tridekan
2	4.351		0.0000	0.00000	0.00000	tetradekan
3	4.970		0.0000	0.00000	0.00000	pentadekan
4	5.557		0.0000	0.00000	0.00000	hexadekan
5	38.968	MM	0.4812	3572.11621	49.93671	?
6	39.949	MM	0.5835	3581.17065	50.06329	?

Totals : 7153.28687

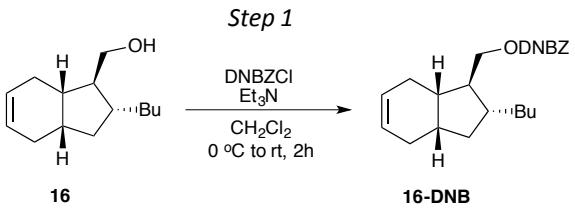
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

==========
*** End of Report ***

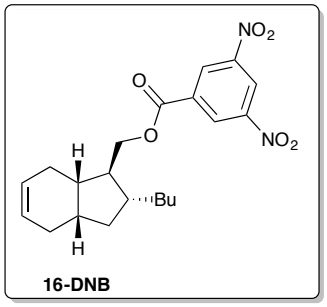
Figure S-64 Report from chiral GLC of compound *rac*-**16**.

Preparation 3,5-dinitrobenzoate derivative of (16).



Scheme S-3 Derivatization of advanced intermediate **16** to 2,5-dinitrobenzoate **16-DNB**.

(1*S*,6*S*,7*S*,8*R*)-8-Butyl-7-((3,5-dinitrobenzoyl)oxymethyl)bicyclo[4.3.0]non-3-ene (16-DNB).



A stirring solution of (1*S*,6*S*,7*S*,8*R*)-8-butyl-7-(hydroxymethyl)bicyclo[4.3.0]non-3-ene **16** (120 mg, 0.577 mmol, 1.0 equiv.) in dry DCM (10 mL) was added Et_3N (0.241 mL, 1.73 mmol, 3.0 equiv.) dropwise. The solution was then cooled to 0 °C and 3,5-dinitrobenzoyl chloride (173 mg, 0.75 mmol, 1.3 equiv.) was added in one portion. The reaction was slowly warmed to room temperature and monitored by TLC until completion. After 2h, the reaction mixture was poured over H_2O (10 mL) and the organic layer separated. The aqueous layer was then extracted with DCM (2 x 10 mL) and the organic layers combined. The organic layers were then washed with H_2O (1 x 30 mL), brine (1 x 30 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to form a crude orange oil. This was purified by column chromatography on silica (hexane/EtOAc, 95:5) to afford the title compound as a slightly off-white powder. Yield: 185 mg, (82%), $[\alpha]_D^{26}$ -3.67 (c = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25-9.24 (m, 1H), 9.16-9.15 (m, 2H), 5.74-5.67 (m, 2H), 4.45-4.37 (m, 2H), 2.27-2.14 (m, 3H), 2.01-1.90 (m, 4H), 1.85-1.79 (m, 1H), 1.74-1.68 (m, 1H), 1.66-1.60 (m, 1H), 1.42-1.19 (m, 6H), 0.89-0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 148.6, 134.1, 129.3 (2C), 126.2, 125.2, 122.3, 69.7, 50.0, 41.8, 38.7, 37.7, 37.2, 35.1, 30.9, 27.4, 27.3, 22.8, 14.0; IR (neat, cm^{-1}) 3012 (m), 3022 (m), 2922 (s), 1728 (s), 1628 (m), 1597 (w), 1540 (s), 1460 (m); HRMS (EI+): Exact mass calculated for $C_{21}H_{26}N_2O_6$ $[M]^+$: 402.1791, found 402.1788; m.p.: 45-47 °C; TLC (hexane/EtOAc 9:1, $KMnO_4$ stain): R_f =0.55.

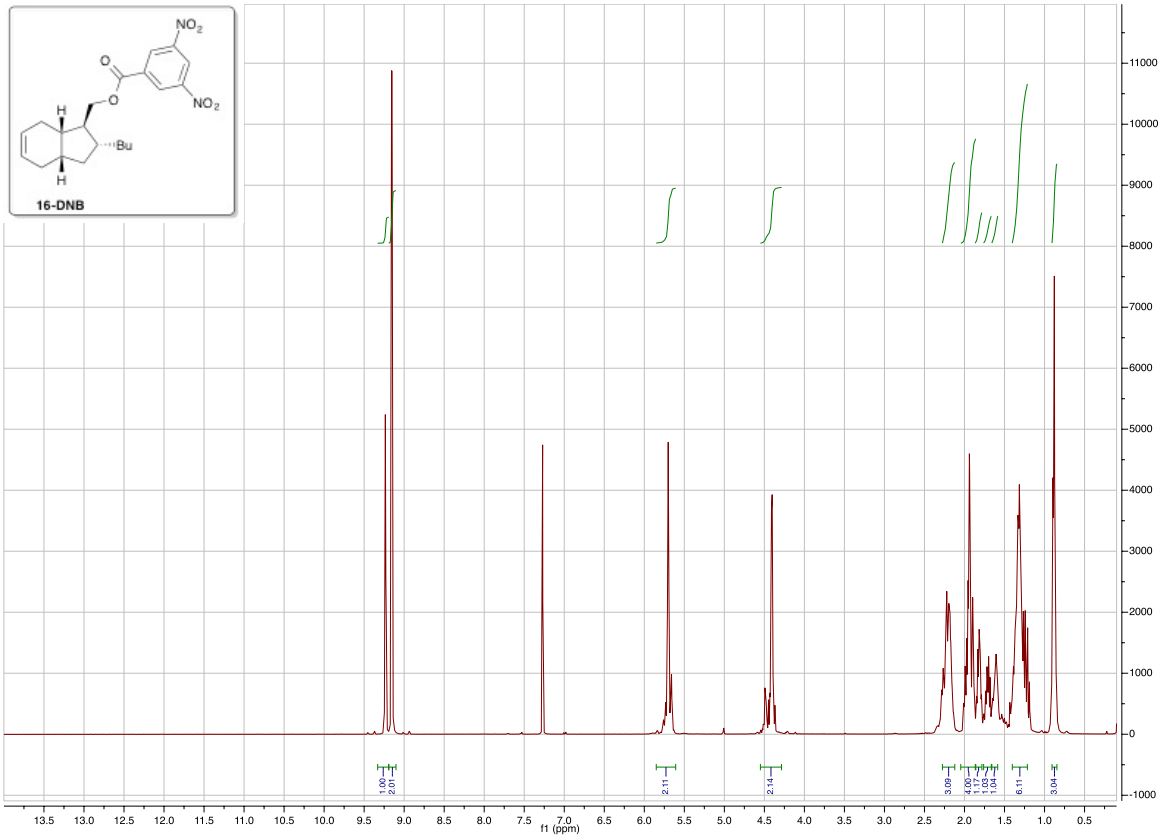


Figure S-65 ^{1}H-NMR spectrum of compound **16-DNB**.

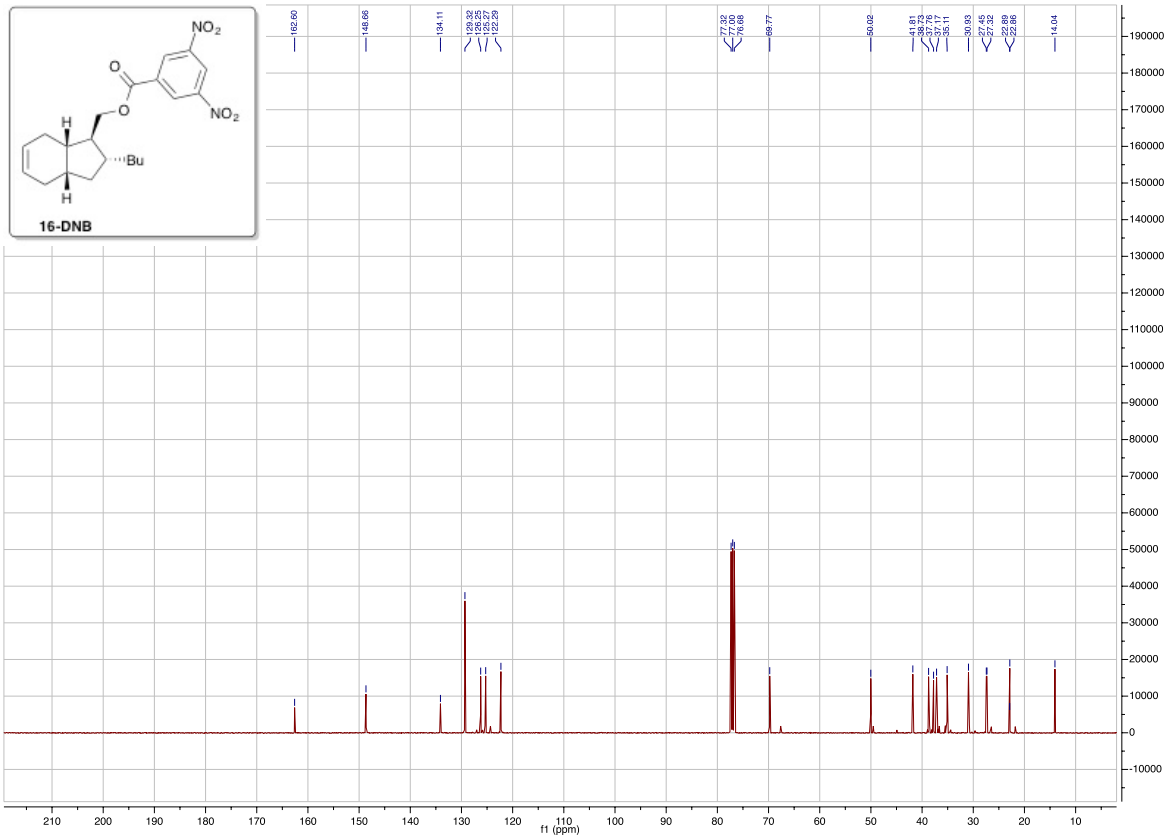
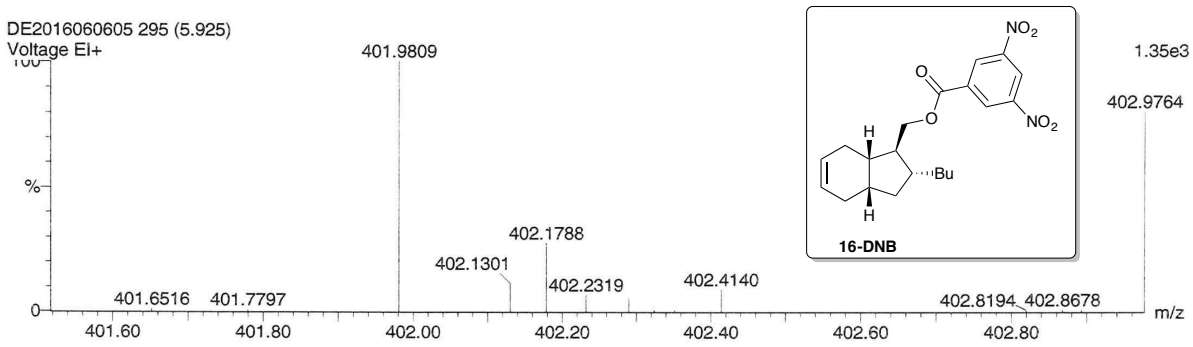


Figure S-66 ^{13}C-NMR spectrum of compound **16-DNB**.

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
23 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		200.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
402.1788	402.1791	-0.3	-0.7	10.0	1	C21 H26 N2 O6

Figure S-67 HRMS spectrum of compound **16-DNB**.

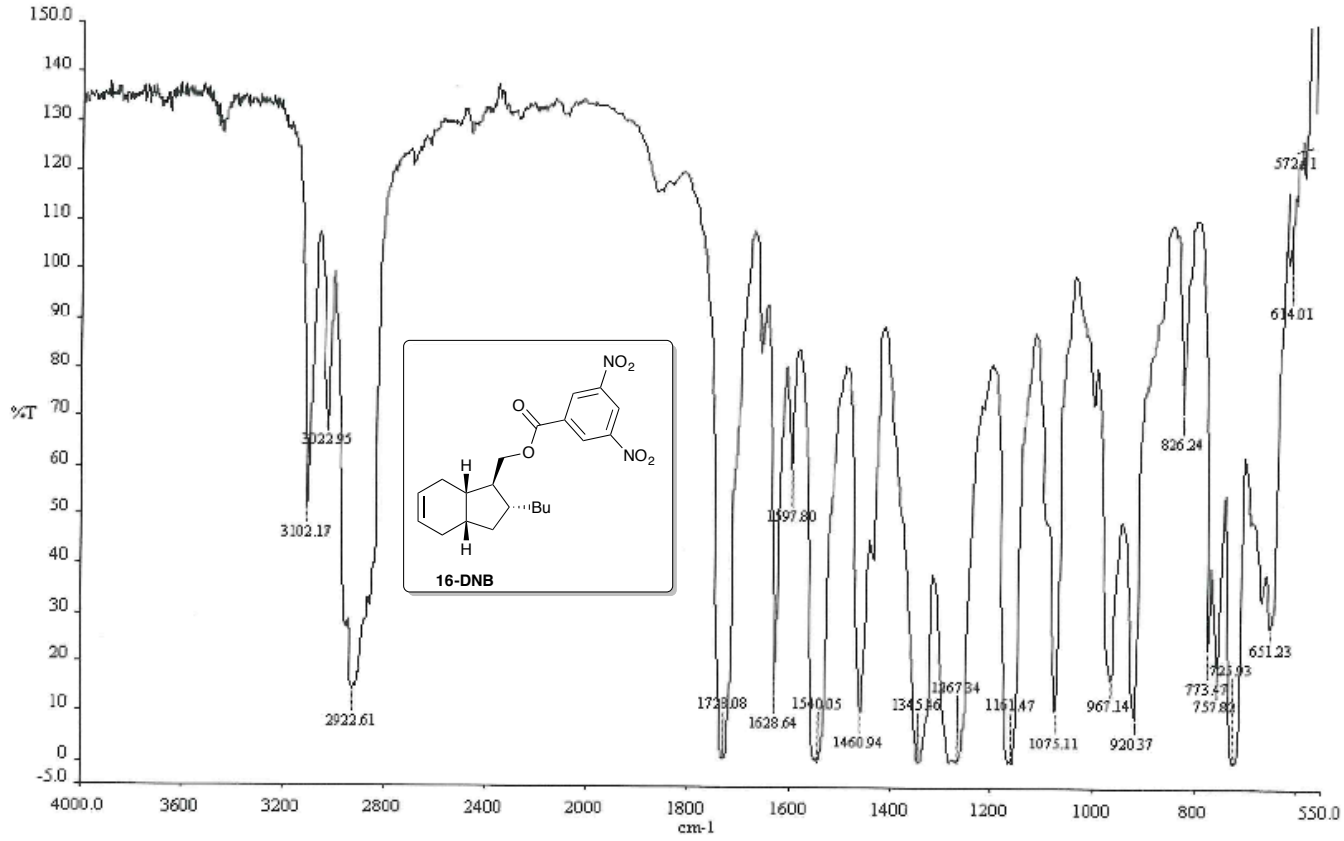


Figure S-68 IR spectrum of compound **16-DNB**.

X-ray crystallography on compound (16-DNB):

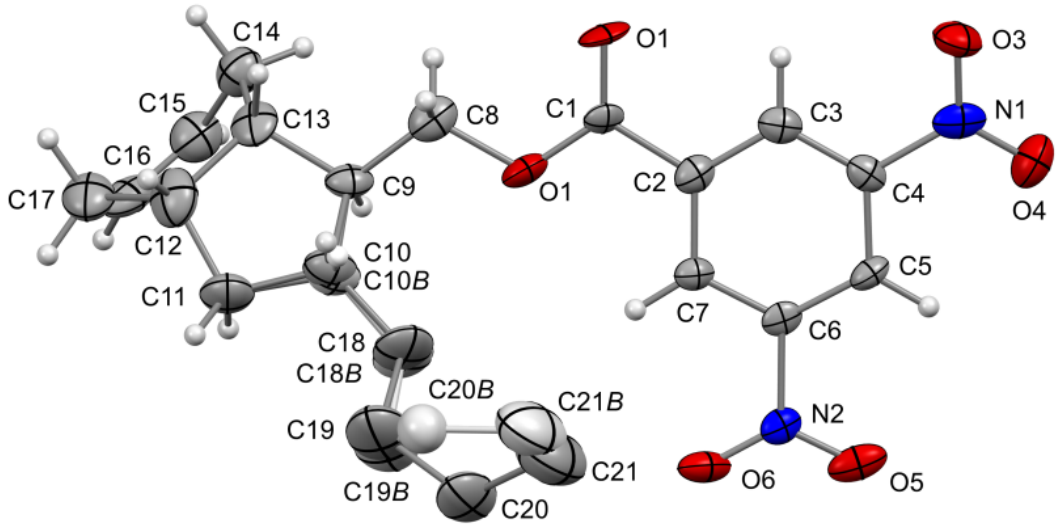


Figure S-69 Single crystal X-ray structure of the 3,5-dinitrobenzoate of alcohol **16** at 110 K. The disordered n-butyl group (H-atoms omitted) has a major orientation [occupancy 0.74(3)] with *trans,trans,gauche+* torsion angles along C9-C10-C18-C19-C20-C21, while the minor orientation (atoms in lighter tone) is *trans,gauche–,gauche–.*

Table S-1 Crystal data for 3,5-dinitrobenzoate of alcohol **16**.*

	(I)
Crystal data	
Chemical formula	$C_{21}H_{26}N_2O_6$
M_r	402.44
Crystal system, space group	Monoclinic, $P2_1$
a (Å)	10.866(5)
b (Å)	5.196(2)
c (Å)	18.617(10)
β (°)	106.703(11)
V (Å^3)	1006.8(9)
Z	2
Radiation	Mo Kα
Wavelength (Å)	0.71073
μ (mm^{-1})	0.098
Temperature (K)	110(2)
Crystal size (mm)	0.21 × 0.19 × 0.01
T_{min}, T_{max}	0.692, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	5899, 2089, 1718
R_{int}	0.140
θ_{max} (°)	20.86
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.085, 0.225, 1.03
No. of reflections	2089
No. of parameters	278
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.30, –0.28
CCDC	1484546

* Bruker D8 Venture diffractometer with InCoatec ImuS Microfocus radiation source and Photon 100 CMOS detector. Data collection with Apex2,[1] data integration and cell refinement with SAINT,[1] absorption correction by SADABS,[1] structure solution with SHELXT,[2] structure refinement with SHELXL.[3] Molecular graphics from Mercury.[4]

supporting information

First total synthesis of mucosin based on its structural assignment

Harrison C. Gallantree-Smith, Simen. G Antonsen, Carl Henrik Görbitz,* Trond V. Hansen, Jens M. J. Nolsøe and Yngve H. Stenstrøm

Experimental

Very fragile, small platelets were obtained by slow evaporation from a methanol/pentane mixture.

Refinement

Two disorder positions, with occupancies 0.74 (3) and 0.26 (3) were refined for the C18—C21 n-butyl group attached to C10. Their covalent geometries were restrained by a SHELXL SAME 0.004 0.008 command, additional restraints were imposed on the C—C bond lengthes in this substituent. Corresponmding atoms in the two conformations shared the same displacement parameteres, except that a fixed value was used for C20B, which is separted from C20 by 1.38 Å.

name

Crystal data

$C_{21}H_{26}N_2O_6$
M_r = 402.44
Monoclinic, $P2_1$
a = 10.866 (5) Å
b = 5.196 (2) Å
c = 18.617 (10) Å
β = 106.703 (11)°
V = 1006.8 (9) Å^3
Z = 2
$F(000)$ = 428
D_x = 1.327 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 2295 reflections
θ = 2.3–20.9°
μ = 0.10 mm^{-1}
T = 110 K
Plate, colourless
0.21 × 0.19 × 0.01 mm

Data collection

Bruker D8 Venture with Photon 100 CMOS detector diffractometer
Radiation source: InCoatec ImuS Microfocus
Graphite monochromator
Detector resolution: 8.3 pixels mm^{-1}
Sets of exposures each taken over 0.5° ω rotation scans
Absorption correction: multi-scan *SADABS* (Bruker, 2014)
T_{min} = 0.692, T_{max} = 1.000
5899 measured reflections
2089 independent reflections
1718 reflections with $I > 2\sigma(I)$
R_{int} = 0.214
θ_{max} = 20.9°, θ_{min} = 2.3°
h = −10→10
k = −5→5
l = −18→18

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.085
$wR(F^2)$ = 0.225
S = 1.03
2089 reflections
278 parameters
77 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0936P)^2 + 2.6032P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. Two disorder positions refined for n-butyl group attached to C10. Occupancies 0.74 (3) and 0.26 (3).

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
O1	0.4965 (7)	0.0115 (19)	0.3931 (4)	0.034 (2)	
N1	0.7700 (10)	0.288 (2)	0.6525 (7)	0.034 (3)	
C1	0.5467 (10)	0.212 (3)	0.3832 (7)	0.023 (3)	
O2	0.5244 (7)	0.3323 (19)	0.3180 (5)	0.032 (2)	
N2	0.8755 (9)	0.896 (2)	0.4771 (7)	0.025 (2)	
C2	0.6411 (11)	0.353 (3)	0.4451 (7)	0.028 (3)	
O3	0.7262 (8)	0.077 (2)	0.6594 (5)	0.040 (2)	
C3	0.6602 (11)	0.265 (2)	0.5163 (7)	0.028 (3)	
H31	0.6121	0.1220	0.5254	0.033*	
C4	0.7491 (10)	0.382 (3)	0.5752 (6)	0.025 (3)	
O4	0.8317 (8)	0.420 (2)	0.7046 (5)	0.044 (2)	
C5	0.8206 (10)	0.596 (2)	0.5648 (7)	0.024 (3)	
H51	0.8798	0.6815	0.6053	0.029*	
O5	0.9445 (7)	1.0018 (19)	0.5311 (5)	0.039 (2)	
C6	0.7990 (10)	0.672 (2)	0.4921 (7)	0.021 (3)	
O6	0.8619 (7)	0.9540 (18)	0.4128 (5)	0.036 (2)	
C7	0.7120 (10)	0.562 (2)	0.4316 (6)	0.023 (3)	
H71	0.7003	0.6265	0.3823	0.028*	
C8	0.4292 (12)	0.208 (3)	0.2553 (7)	0.036 (3)	
H81	0.3491	0.1772	0.2692	0.044*	
H82	0.4626	0.0397	0.2445	0.044*	
C12	0.3164 (15)	0.342 (3)	0.0499 (8)	0.055 (4)	
H121	0.3329	0.1800	0.0253	0.066*	
C13	0.2879 (13)	0.270 (3)	0.1245 (7)	0.041 (4)	
H131	0.2890	0.0776	0.1285	0.049*	
C14	0.1617 (12)	0.364 (3)	0.1326 (8)	0.046 (4)	
H141	0.0929	0.2417	0.1076	0.055*	
H142	0.1663	0.3703	0.1865	0.055*	
C15	0.1292 (13)	0.625 (3)	0.0990 (9)	0.050 (4)	
H151	0.0928	0.7505	0.1241	0.059*	
C16	0.1501 (12)	0.682 (3)	0.0365 (10)	0.049 (4)	
H161	0.1334	0.8508	0.0167	0.059*	
C17	0.2006 (14)	0.483 (3)	−0.0052 (8)	0.053 (4)	
H171	0.2286	0.5653	−0.0458	0.063*	
H172	0.1321	0.3573	−0.0281	0.063*	
C9	0.4010 (11)	0.375 (3)	0.1869 (7)	0.032 (3)	0.74 (3)
H91	0.3797	0.5522	0.2003	0.038*	0.74 (3)
C11	0.4409 (12)	0.494 (3)	0.0739 (8)	0.048 (4)	0.74 (3)
H111	0.4230	0.6802	0.0769	0.058*	0.74 (3)

H112	0.4911	0.4696	0.0377	0.058*	0.74 (3)
C10	0.5144 (12)	0.391 (4)	0.1509 (8)	0.044 (4)	0.74 (3)
H10	0.5419	0.2108	0.1440	0.053*	0.74 (3)
C18	0.6307 (14)	0.537 (6)	0.1938 (9)	0.060 (6)	0.74 (3)
H181	0.6668	0.4529	0.2431	0.072*	0.74 (3)
H182	0.6039	0.7130	0.2033	0.072*	0.74 (3)
C19	0.7354 (15)	0.558 (7)	0.1554 (11)	0.084 (7)	0.74 (3)
H191	0.7465	0.3889	0.1335	0.101*	0.74 (3)
H192	0.7092	0.6839	0.1139	0.101*	0.74 (3)
C20	0.8620 (16)	0.641 (4)	0.2089 (12)	0.067 (8)	0.74 (3)
H201	0.8470	0.8021	0.2333	0.081*	0.74 (3)
H202	0.9211	0.6827	0.1787	0.081*	0.74 (3)
C21	0.932 (4)	0.453 (7)	0.271 (2)	0.096 (13)	0.74 (3)
H211	1.0170	0.5212	0.2964	0.145*	0.74 (3)
H212	0.9403	0.2862	0.2482	0.145*	0.74 (3)
H213	0.8819	0.4328	0.3066	0.145*	0.74 (3)
C9B	0.4010 (11)	0.375 (3)	0.1869 (7)	0.032 (3)	0.26 (3)
H91B	0.3750	0.5474	0.2013	0.038*	0.26 (3)
C11B	0.4409 (12)	0.494 (3)	0.0739 (8)	0.048 (4)	0.26 (3)
H11B	0.4217	0.6809	0.0720	0.058*	0.26 (3)
H12B	0.4929	0.4588	0.0392	0.058*	0.26 (3)
C10B	0.5162 (13)	0.418 (5)	0.1535 (9)	0.044 (4)	0.26 (3)
H10B	0.5570	0.2473	0.1510	0.053*	0.26 (3)
C18B	0.619 (2)	0.598 (8)	0.1954 (11)	0.060 (6)	0.26 (3)
H18B	0.6533	0.5355	0.2476	0.072*	0.26 (3)
H19B	0.5803	0.7695	0.1975	0.072*	0.26 (3)
C19B	0.730 (3)	0.630 (9)	0.162 (3)	0.084 (7)	0.26 (3)
H20B	0.6960	0.6514	0.1073	0.101*	0.26 (3)
H21B	0.7786	0.7876	0.1829	0.101*	0.26 (3)
C20B	0.820 (3)	0.402 (9)	0.179 (3)	0.050*	0.26 (3)
H22B	0.8733	0.4081	0.1438	0.060*	0.26 (3)
H23B	0.7673	0.2438	0.1673	0.060*	0.26 (3)
C21B	0.911 (13)	0.37 (3)	0.258 (5)	0.096 (13)	0.26 (3)
H24B	0.9659	0.2227	0.2605	0.145*	0.26 (3)
H25B	0.8605	0.3521	0.2939	0.145*	0.26 (3)
H26B	0.9645	0.5281	0.2714	0.145*	0.26 (3)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.026 (4)	0.016 (5)	0.058 (6)	−0.013 (4)	0.011 (4)	−0.002 (4)
N1	0.017 (6)	0.025 (7)	0.061 (9)	0.008 (5)	0.014 (6)	0.009 (6)
C1	0.011 (5)	0.026 (5)	0.034 (6)	0.001 (5)	0.008 (4)	0.002 (5)
O2	0.020 (4)	0.027 (5)	0.047 (6)	−0.008 (4)	0.005 (4)	−0.005 (4)
N2	0.017 (4)	0.019 (5)	0.037 (5)	0.006 (4)	0.005 (4)	0.001 (5)
C2	0.021 (5)	0.023 (5)	0.037 (6)	0.004 (5)	0.005 (5)	0.000 (5)
O3	0.045 (5)	0.031 (6)	0.047 (6)	−0.004 (5)	0.017 (5)	0.012 (4)
C3	0.024 (5)	0.023 (5)	0.038 (6)	0.006 (4)	0.013 (5)	0.004 (5)
C4	0.022 (5)	0.025 (5)	0.030 (6)	0.009 (5)	0.011 (5)	0.007 (5)
O4	0.039 (5)	0.043 (6)	0.043 (6)	0.002 (5)	0.000 (5)	−0.012 (5)
C5	0.017 (5)	0.017 (5)	0.035 (6)	−0.001 (4)	0.003 (4)	−0.004 (5)

O5	0.023 (5)	0.024 (5)	0.073 (7)	0.001 (4)	0.019 (5)	−0.007 (5)
C6	0.011 (5)	0.019 (5)	0.034 (6)	0.007 (4)	0.007 (4)	0.000 (4)
O6	0.021 (4)	0.026 (5)	0.062 (7)	0.001 (4)	0.013 (4)	0.015 (4)
C7	0.018 (5)	0.019 (5)	0.033 (6)	0.003 (4)	0.008 (5)	0.003 (5)
C8	0.029 (7)	0.028 (7)	0.051 (9)	0.006 (6)	0.009 (7)	−0.006 (7)
C12	0.072 (12)	0.044 (9)	0.045 (9)	0.003 (9)	0.011 (9)	−0.014 (7)
C13	0.057 (10)	0.018 (7)	0.044 (8)	−0.005 (6)	0.009 (7)	−0.010 (6)
C14	0.040 (8)	0.052 (9)	0.046 (9)	−0.001 (7)	0.012 (7)	−0.007 (8)
C15	0.045 (9)	0.042 (10)	0.059 (11)	0.004 (7)	0.011 (9)	−0.001 (8)
C16	0.038 (9)	0.022 (8)	0.075 (12)	−0.005 (7)	−0.004 (8)	0.006 (8)
C17	0.067 (10)	0.029 (8)	0.057 (9)	−0.006 (7)	0.010 (8)	0.000 (8)
C9	0.029 (7)	0.021 (7)	0.047 (8)	0.001 (6)	0.014 (7)	0.005 (7)
C11	0.035 (8)	0.060 (9)	0.057 (10)	−0.008 (8)	0.023 (7)	0.002 (8)
C10	0.034 (8)	0.048 (9)	0.056 (10)	0.001 (7)	0.021 (8)	0.006 (8)
C18	0.029 (8)	0.089 (15)	0.071 (10)	−0.013 (9)	0.028 (8)	−0.007 (10)
C19	0.041 (10)	0.132 (19)	0.087 (13)	−0.005 (12)	0.031 (9)	0.019 (13)
C20	0.026 (12)	0.099 (19)	0.078 (17)	0.002 (12)	0.016 (11)	0.021 (14)
C21	0.09 (2)	0.10 (3)	0.104 (19)	0.00 (2)	0.029 (14)	0.045 (19)
C9B	0.029 (7)	0.021 (7)	0.047 (8)	0.001 (6)	0.014 (7)	0.005 (7)
C11B	0.035 (8)	0.060 (9)	0.057 (10)	−0.008 (8)	0.023 (7)	0.002 (8)
C10B	0.034 (8)	0.048 (9)	0.056 (10)	0.001 (7)	0.021 (8)	0.006 (8)
C18B	0.029 (8)	0.089 (15)	0.071 (10)	−0.013 (9)	0.028 (8)	−0.007 (10)
C19B	0.041 (10)	0.132 (19)	0.087 (13)	−0.005 (12)	0.031 (9)	0.019 (13)
C21B	0.09 (2)	0.10 (3)	0.104 (19)	0.00 (2)	0.029 (14)	0.045 (19)

Geometric parameters (Å, º) for (I)

O1—C1	1.213 (14)	C17—H171	0.9900
N1—O3	1.218 (13)	C17—H172	0.9900
N1—O4	1.219 (12)	C9—C10	1.565 (17)
N1—C4	1.474 (15)	C9—H91	1.0000
C1—O2	1.326 (14)	C11—C10	1.524 (18)
C1—C2	1.498 (16)	C11—H111	0.9900
O2—C8	1.467 (14)	C11—H112	0.9900
N2—O5	1.202 (11)	C10—C18	1.495 (19)
N2—O6	1.202 (11)	C10—H10	1.0000
N2—C6	1.502 (15)	C18—C19	1.512 (17)
C2—C3	1.361 (16)	C18—H181	0.9900
C2—C7	1.397 (16)	C18—H182	0.9900
C3—C4	1.377 (16)	C19—C20	1.51 (2)
C3—H31	0.9500	C19—H191	0.9900
C4—C5	1.403 (15)	C19—H192	0.9900
C5—C6	1.364 (16)	C20—C21	1.53 (2)
C5—H51	0.9500	C20—H201	0.9900
C6—C7	1.368 (15)	C20—H202	0.9900
C7—H71	0.9500	C21—H211	0.9800
C8—C9	1.497 (17)	C21—H212	0.9800
C8—H81	0.9900	C21—H213	0.9800
C8—H82	0.9900	C10B—C18B	1.50 (2)
C12—C11	1.52 (2)	C10B—H10B	1.0000
C12—C13	1.55 (2)	C18B—C19B	1.512 (18)

C12—C17	1.558 (19)	C18B—H18B	0.9900
C12—H121	1.0000	C18B—H19B	0.9900
C13—C14	1.504 (19)	C19B—C20B	1.51 (2)
C13—C9	1.530 (17)	C19B—H20B	0.9900
C13—H131	1.0000	C19B—H21B	0.9900
C14—C15	1.49 (2)	C20B—C21B	1.53 (2)
C14—H141	0.9900	C20B—H22B	0.9900
C14—H142	0.9900	C20B—H23B	0.9900
C15—C16	1.28 (2)	C21B—H24B	0.9800
C15—H151	0.9500	C21B—H25B	0.9800
C16—C17	1.49 (2)	C21B—H26B	0.9800
C16—H161	0.9500		

O3—N1—O4	124.5 (11)	C13—C9—C10	104.6 (10)
O3—N1—C4	116.4 (11)	C8—C9—H91	109.0
O4—N1—C4	119.0 (10)	C13—C9—H91	109.0
O1—C1—O2	125.0 (11)	C10—C9—H91	109.0
O1—C1—C2	122.8 (11)	C12—C11—C10	105.9 (11)
O2—C1—C2	112.2 (10)	C12—C11—H111	110.5
C1—O2—C8	114.9 (9)	C10—C11—H111	110.5
O5—N2—O6	125.9 (10)	C12—C11—H112	110.5
O5—N2—C6	116.5 (10)	C10—C11—H112	110.5
O6—N2—C6	117.7 (10)	H111—C11—H112	108.7
C3—C2—C7	120.0 (11)	C18—C10—C11	117.2 (12)
C3—C2—C1	117.6 (11)	C18—C10—C9	116.5 (11)
C7—C2—C1	122.3 (11)	C11—C10—C9	99.0 (10)
C2—C3—C4	120.2 (11)	C18—C10—H10	107.8
C2—C3—H31	119.9	C11—C10—H10	107.8
C4—C3—H31	119.9	C9—C10—H10	107.8
C3—C4—C5	122.0 (11)	C10—C18—C19	114.7 (13)
C3—C4—N1	120.6 (11)	C10—C18—H181	108.6
C5—C4—N1	117.5 (10)	C19—C18—H181	108.6
C6—C5—C4	115.0 (10)	C10—C18—H182	108.6
C6—C5—H51	122.5	C19—C18—H182	108.6
C4—C5—H51	122.5	H181—C18—H182	107.6
C5—C6—C7	125.3 (10)	C20—C19—C18	112.0 (14)
C5—C6—N2	117.5 (10)	C20—C19—H191	109.2
C7—C6—N2	117.2 (10)	C18—C19—H191	109.2
C6—C7—C2	117.5 (11)	C20—C19—H192	109.2
C6—C7—H71	121.2	C18—C19—H192	109.2
C2—C7—H71	121.2	H191—C19—H192	107.9
O2—C8—C9	110.3 (10)	C19—C20—C21	118 (2)
O2—C8—H81	109.6	C19—C20—H201	107.8
C9—C8—H81	109.6	C21—C20—H201	107.8
O2—C8—H82	109.6	C19—C20—H202	107.8
C9—C8—H82	109.6	C21—C20—H202	107.8
H81—C8—H82	108.1	H201—C20—H202	107.1
C11—C12—C13	104.7 (10)	C20—C21—H211	109.5
C11—C12—C17	115.6 (12)	C20—C21—H212	109.5
C13—C12—C17	111.8 (12)	H211—C21—H212	109.5
C11—C12—H121	108.2	C20—C21—H213	109.5

C13—C12—H121	108.2	H211—C21—H213	109.5
C17—C12—H121	108.2	H212—C21—H213	109.5
C14—C13—C9	111.3 (10)	C18B—C10B—H10B	107.8
C14—C13—C12	115.6 (11)	C10B—C18B—C19B	114.8 (15)
C9—C13—C12	105.6 (11)	C10B—C18B—H18B	108.6
C14—C13—H131	108.0	C19B—C18B—H18B	108.6
C9—C13—H131	108.0	C10B—C18B—H19B	108.6
C12—C13—H131	108.0	C19B—C18B—H19B	108.6
C15—C14—C13	111.5 (12)	H18B—C18B—H19B	107.5
C15—C14—H141	109.3	C20B—C19B—C18B	112.1 (16)
C13—C14—H141	109.3	C20B—C19B—H20B	109.2
C15—C14—H142	109.3	C18B—C19B—H20B	109.2
C13—C14—H142	109.3	C20B—C19B—H21B	109.2
H141—C14—H142	108.0	C18B—C19B—H21B	109.2
C16—C15—C14	120.3 (14)	H20B—C19B—H21B	107.9
C16—C15—H151	119.9	C19B—C20B—C21B	118 (2)
C14—C15—H151	119.9	C19B—C20B—H22B	107.8
C15—C16—C17	120.2 (13)	C21B—C20B—H22B	107.8
C15—C16—H161	119.9	C19B—C20B—H23B	107.8
C17—C16—H161	119.9	C21B—C20B—H23B	107.8
C16—C17—C12	109.4 (11)	H22B—C20B—H23B	107.1
C16—C17—H171	109.8	C20B—C21B—H24B	109.5
C12—C17—H171	109.8	C20B—C21B—H25B	109.5
C16—C17—H172	109.8	H24B—C21B—H25B	109.5
C12—C17—H172	109.8	C20B—C21B—H26B	109.5
H171—C17—H172	108.3	H24B—C21B—H26B	109.5
C8—C9—C13	111.3 (10)	H25B—C21B—H26B	109.5
C8—C9—C10	113.6 (10)		

O1—C1—O2—C8	1.1 (15)	C17—C12—C13—C9	−128.2 (11)
C2—C1—O2—C8	−178.0 (8)	C9—C13—C14—C15	83.5 (14)
O1—C1—C2—C3	−6.8 (16)	C12—C13—C14—C15	−37.0 (16)
O2—C1—C2—C3	172.3 (10)	C13—C14—C15—C16	40.9 (18)
O1—C1—C2—C7	170.7 (10)	C14—C15—C16—C17	3 (2)
O2—C1—C2—C7	−10.2 (14)	C15—C16—C17—C12	−47.5 (18)
C7—C2—C3—C4	0.2 (16)	C11—C12—C17—C16	−74.5 (15)
C1—C2—C3—C4	177.7 (10)	C13—C12—C17—C16	45.1 (15)
C2—C3—C4—C5	1.2 (16)	O2—C8—C9—C13	−171.4 (9)
C2—C3—C4—N1	179.8 (10)	O2—C8—C9—C10	70.8 (13)
O3—N1—C4—C3	14.6 (14)	C14—C13—C9—C8	86.1 (13)
O4—N1—C4—C3	−167.3 (10)	C12—C13—C9—C8	−147.7 (10)
O3—N1—C4—C5	−166.7 (9)	C14—C13—C9—C10	−150.8 (11)
O4—N1—C4—C5	11.4 (14)	C12—C13—C9—C10	−24.6 (13)
C3—C4—C5—C6	−2.4 (14)	C13—C12—C11—C10	29.4 (14)
N1—C4—C5—C6	179.0 (9)	C17—C12—C11—C10	152.9 (12)
C4—C5—C6—C7	2.5 (15)	C12—C11—C10—C18	−169.6 (13)
C4—C5—C6—N2	−178.4 (8)	C12—C11—C10—C9	−43.5 (14)
O5—N2—C6—C5	−4.6 (13)	C8—C9—C10—C18	−70.5 (16)
O6—N2—C6—C5	175.9 (9)	C13—C9—C10—C18	167.9 (14)
O5—N2—C6—C7	174.6 (9)	C8—C9—C10—C11	163.0 (11)
O6—N2—C6—C7	−4.8 (13)	C13—C9—C10—C11	41.4 (13)

C5—C6—C7—C2	−1.2 (15)	C11—C10—C18—C19	−60 (2)
N2—C6—C7—C2	179.6 (8)	C9—C10—C18—C19	−177.4 (19)
C3—C2—C7—C6	−0.2 (15)	C10—C18—C19—C20	−164 (2)
C1—C2—C7—C6	−177.7 (10)	C18—C19—C20—C21	68 (4)
C1—O2—C8—C9	173.8 (9)	C9B—C10B—C18B—C19B	178 (2)
C11—C12—C13—C14	121.2 (13)	C10B—C18B—C19B—C20B	−76 (4)
C17—C12—C13—C14	−4.7 (16)	C18B—C19B—C20B—C21B	−75 (10)
C11—C12—C13—C9	−2.3 (14)		

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