Rhodium Catalyzed Allene Amidation: A Facile Entry into 2-Amidoallylcations for Unusual [3+3] Annulation Reactions.

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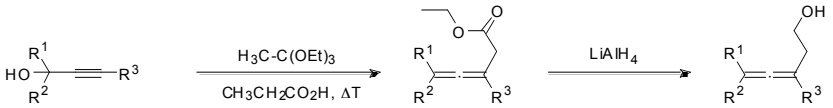
Materials and Methods: General Information. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 600 spectrometer (600 MHz ^{1}H, 150 MHz ^{13}C), a Varian Unity plus 600 (600 MHz ^{1}H, 150 MHz ^{13}C) or a Varian Inova 400 spectrometer (400 MHz ^{1}H, 100 MHz ^{13}C) at room temperature in $CDCl_3$ with internal $CHCl_3$ as the reference (7.25 ppm for ^{1}H and 77.00 ppm for ^{13}C). Chemical shifts (δ values) were reported in parts per million (ppm) and coupling constants (*J* values) in Hz. Multiplicity is indicated using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, hep = heptet, m = multiplet, b = broad signal). Infrared (IR) spectra were recorded using Thermo Electron Corporation Nicolet 380 FT-IR spectrometer. High resolution mass spectra were obtained using a Thermo Electron Corporation Finigan LTQFTMS (at the Mass Spectrometry Facility, Emory University). High performance liquid chromatography (HPLC) was carried out on an Agilent 1100 series, HPLC equipped with a Chiracel OD-H column (UV detection at 210 nm). Optical rotation was measured on a Perkin-Elmer Polarimeter 341. We acknowledge the use of shared instrumentation provided by grants from the NIH and the NSF. Melting points (mp) were taken using a Fisher-Johns melting point apparatus and are not corrected. Analytical thin layer chromatography (TLC) was performed on precoated glass backed EMD 0.25 mm silica gel 60 plates. Visualization was accomplished with UV light, ethanolic anisaldehyde, phosphomolybdic acid or CAM stain (Verghn's), followed by heating. Flash column chromatography was carried out using EMD Geduran® silica gel 60 (40-63 μm).

All reactions were conducted with anhydrous solvents in oven dried or flame-dried and argon-charged glassware. Anhydrous solvents were purified by passage through activated alumina using a *Glass Contours* solvent purification system unless otherwise noted. Solvents used in workup, extraction and column chromatography were used as received from commercial suppliers without prior purification. All reagents were purchased from Sigma-Aldrich and used as received unless otherwise noted. Bis*(tert*-butylcarbonyloxy)-iodobenzene was dried at 98°C under vacuum (0.02 mmHg) for 12 hours prior to use. 2,6-Lutidine was dried over KOH and

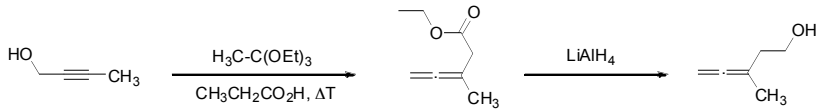
N,*N*-Dimethylacatamide (DMA) over 4Å molecular sieves prior to use. $Rh_2(esp)_2$ was purchased from Strem chemical company and used as received. (*Z*)-*N*-benzylideneaniline oxide (**2**) and (*Z*)-*N*-benzylidene-2-methylpropan-2-amine oxide (**14**) are commercially available from Alfa Aesar. (*Z*)-*N*-benzylidenemethanamine oxide (**18**)[1] and (Z)-N-(naphthalen-2-ylmethylene)aniline oxide[1] were prepared from *N*-methylhydroxylamine hydrochloride or N-phenylhydroxylamine[2] as described in the literature.

General Procedure (A) for the preparation of allenols.[3]



To an oven dried three-neck flask equipped with a Dean-Stark trap were added triethyl orthoacetate (3.4 eq.), the corresponding alkynyl-alcohol (1.0 eq.) and propionic acid (0.17 eq.) under an argon atmosphere. The reaction mixture was then heated to 150 °C (oil bath) and stirred for 2.5 h after reaching this temperature. Additional propionic acid (0.12 eq.) was added and the reaction mixture was stirred for a further 2.5 h under these conditions. After cooling to room temperature all volatile compounds were carefully removed under vacuum. After a short flash chromatographic purification the resulting ester was used directly without any further purification or characterization in the next step.
A solution of the ester (ca. 0.5 M in THF) was added dropwise to a suspension of $LiAlH_4$ (2.0 eq.) in THF at 0 °C. After the addition was completed, the reaction mixture was stirred for 1 h at room temperature, cooled to 0 °C and carefully diluted with aq. potassium sodium tartrate (0.5 M). The mixture was extracted with Et_2O and the combined organic extracts were dried over Na_2SO_4. Evaporation and purification by flash chromatography provided the corresponding allenol.

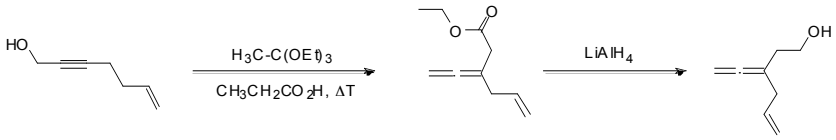
3-Methylpenta-3,4-dien-1-ol



Prepared according to general procedure A using but-2-yn-1-ol (3.28 mL, 43.8 mmol), triethyl orthoacetate (27.4 mL, 148.9 mmol) and propionic acid (0.56 mL, 7.45 mmol; 0.39 mL, 5.3 mmol). After removal of all volatile compounds the ester was obtained after a short flash chromatographic purification (20:1 hexanes/EtOAc, $R_f = 0.35$) as a pale yellow oil (2.54 g, 18.10 mmol) and used without any further purification and characterization.
The ester derivative was dissolved in THF (30 mL) and added dropwise to a suspension of $LiAlH_4$ (36.0 mL, 36.0 mmol, 1.0 M in THF) diluted with additional THF (7 mL) at 0 °C. The reaction mixture was diluted with aq. potassium sodium tartrate (0.5 M, 80 mL) followed by extraction with Et_2O (3 x 100 mL). Flash chromatographic purification (1:1 pentane/ Et_2O, R_f = 0.35) afforded 3-methylpenta-3,4-dien-1-ol (1.41 g, 33% (2 steps)) as a colorless oil.
IR (thin film, cm^{-1}) 3313, 2897, 1959, 1443, 1427, 1371, 1045, 1024, 1005, 845, 611; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.65 – 4.60 (m, 2H), 3.71 (t, 2H, *J* = 6.6 Hz), 2.21 – 2.15 (m, 2H), 1.87 (s,

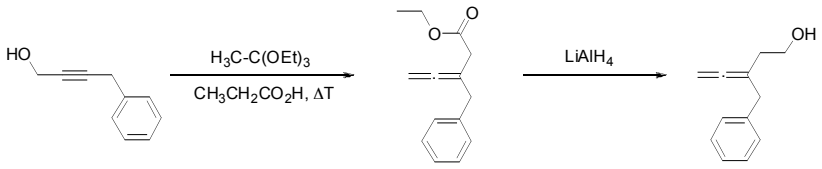
1H), 1.69 (t, 3H, *J* = 3.2 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 206.0, 95.4, 74.7, 60.5, 36.5, 18.8; **HRMS** (+ APCI) calculated for $C_6H_{11}O$ 99.0810, found 99.0804 $[M+H]^+$.

3-Vinylidenehex-5-en-1-ol



Prepared according to general procedure A using hex-5-en-2-yn-1-ol[4] (4.71 g, 49.0 mmol), triethyl orthoacetate (30.6 mL, 166.6 mmol) and propionic acid (0.62 mL, 8.33 mmol; 0.44 mL, 5.88 mmol). After removal of all volatile compounds the ester was obtained after a short flash chromatographic purification (20:1 hexanes/EtOAc, R_f = 0.40) as a pale yellow oil (5.02 g, 30.20 mmol) and used without any further purification and characterization.
The ester derivative was dissolved in THF (60 mL) and added dropwise to a suspension of $LiAlH_4$ (30.2 mL, 60.4 mmol, 2.0 M in THF) diluted with additional THF (50 mL) at 0 °C. The reaction mixture was diluted with aq. potassium sodium tartrate (0.5 M, 80 mL) followed by extraction with Et_2O (3 x 100 mL). Flash chromatography (1:1 pentane/ Et_2O, R_f = 0.50) afforded 3-vinylidenehex-5-en-1-ol (2.77 g, 46% (2 steps)) as a colorless oil.
IR (thin film, cm^{-1}) 3327, 2891, 1957, 1639, 1429, 1045, 1016, 991, 914, 847; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.76 (dddd, 1H, *J* = 16.8 Hz, 10.2 Hz, 7.0 Hz, 3.8 Hz), 5.07 – 5.01 (m, 1H), 5.03 – 4.99 (m, 1H), 4.73 – 4.69 (m, 2H), 3.69 (t, 2H, *J* = 6.4 Hz), 2.72 – 2.67 (m, 2H), 2.20 – 2.12 (m, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 205.7, 135.3, 116.2, 98.5, 76.2, 60.5, 37.2, 34.6; **HRMS** (+ APCI) calculated for $C_8H_{13}O$ 125.0966, found 125.0960 $[M+H]^+$.

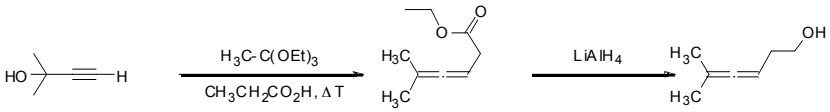
3-Benzylpenta-3,4-dien-1-ol



Prepared according to general procedure A using 4-phenylbut-2-yn-1-ol[5] (4.24 g, 49.0 mmol), triethyl orthoacetate (30.6 mL, 166.6 mmol) and propionic acid (0.62 mL, 8.33 mmol; 0.44 mL, 5.88 mmol). After removal of all volatile compounds the ester was obtained after a short flash chromatographic purification (7:3 pentane/Et_2O, R_f = 0.70) as a pale yellow oil (4.82 g, 22.28 mmol) and used without any further purification and characterization.
The ester derivative was dissolved in THF (45 mL) and added dropwise to a suspension of $LiAlH_4$ (22.3 mL, 44.60 mmol, 2.0 M in THF) diluted with additional THF (30 mL) at 0 °C. The reaction mixture was diluted with aq. potassium sodium tartrate (0.5 M, 80 mL) followed by extraction with Et_2O (3 x 100 mL). Flash chromatography (1:1 pentane/ Et_2O, R_f = 0.50) afforded 3-benzylpenta-3,4-dien-1-ol (2.39 g, 47% (2 steps)) as a pale yellow oil.
IR (thin film, cm^{-1}) 3336, 2901, 1957, 1495, 1443, 1051, 1014, 847, 696; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.32 – 7.26 (m, 2H), 7.24 – 7.19 (m, 3H), 4.79 – 4.74 (m, 2H), 3.70 (q, 2H, *J* = 6.0 Hz), 3.33 (t, 2H, *J* = 2.5 Hz), 2.20 – 2.14 (m, 2H), 1.74 (t, 1H, *J* = 5.7 Hz); **^{13}C NMR** ($CDCl_3$, 100

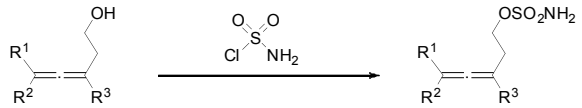
MHz) δ 206.3, 139.0, 128.8, 128.3, 126.3, 99.7, 76.0, 60.7, 39.6, 34.3; **HRMS** (+ APCI) calculated for $C_8H_{13}O$ 175.1123, found 175.1117 $[M+H]^+$.

5-Methylhexa-3,4-dien-1-ol



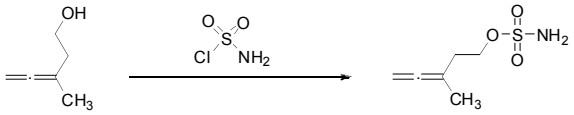
Prepared according to general procedure A using 2-methylbut-3-yn-2-ol (4.85 mL, 50.0 mmol), triethyl orthoacetate (31.2 mL, 170.0 mmol) and propionic acid (0.63 mL, 8.50 mmol; 0.45 mL, 6.0 mmol). After removal of all volatile compounds the ester was obtained after a short flash column chromatographic purification (20:1 hexanes/EtOAc, R_f = 0.44) as a pale yellow oil (4.53 g, 29.36 mmol) and used without any further purification and characterization.
The ester derivative was dissolved in 60 mL THF and added dropwise to a suspension of $LiALH_4$ (58.7 mL, 58.7 mmol, 1.0 molar solution in THF) diluted with additional 14 mL THF at 0 °C. The reaction mixture was diluted with aq. potassium sodium tartrate (0.5 M, 80 mL) followed by extraction with Et_2O (3 x 100 mL). Flash chromatography (1:1 pentane/ Et_2O, R_f = 0.45) afforded 5-methylhexa-3,4-dien-1-ol (2.87 g, 51% (2 steps)) as a colourless oil.
IR (thin film, cm^{-1}) 3309, 2980, 2933, 2908, 2854, 1445, 1230, 1190, 1045, 797, 573; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.96 – 4.87 (m, 1H), 3.64 (t, 2H, *J* = 6.0 Hz), 2.17 (q, 2H, *J* = 6.4 Hz), 1.89 (s, 1H), 1.66 (s, 3H), 1.65 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 202.5, 95.6, 85.0, 62.0, 32.4, 20.6; **HRMS** (+ APCI) calculated for $C_7H_{13}O$ 113.0966, found 113.0961 $[M+H]^+$.

General Procedure (B) for the preparation of sulfamate esters[6]



To an oven dried roundbottom flask equipped with stirring bar and a septum was added neat $ClSO_2NCO$ (2.5 eq.) under an argon atmosphere. The flask was cooled to 0 °C followed by the dropwise addition of formic acid (2.5 eq.). To the resulting white mass was added CH_3CN (0.8 mL/ mmol alcohol) and the contents were then warmed to 21 °C. After stirring for 12 h, the mixture was cooled to -5 °C and a solution of alcohol (1.0 eq.) in DMA (1.7 mL/ mmol alcohol) and 2,6-lutidine (2.7 eq.) was added dropwise. Transfer of the alcohol was made quantitative with an additional 0.5 mL of DMA. The resulting white suspension was stirred for 2 h keeping the temperature between -5 °C and 0 °C. After that time TLC indicated usually complete consumption of the starting material. The reaction mixture was then diluted with a saturated aq. $NaHCO_3$ at 0 °C (dropwise, slowly) and extracted with EtOAc (3 x). The combined organic extracts were washed with saturated aq. $CuSO_4$ (2 x), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatographic provided the desired sulfamate ester.

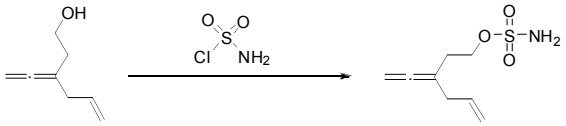
3-Methylpenta-3,4-dienyl sulfamate



Prepared according to general procedure B using 3-methylpenta-3,4-dien-1-ol (687 mg, 7.0 mmol), $ClSO_2NCO$ (1.52 mL, 17.5 mmol), formic acid (0.67 mL, 17.5 mmol), DMA (11.9 mL + 0.5 mL) and 2,6-lutidine (2.19 mL, 18.9 mmol). Flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.3) afforded 3-methylpenta-3,4-dienyl sulfamate (1.0 g, 81%) as a white solid.

Mp 34.9 – 35.5 °C; **IR** (thin film, cm^{-1}) 3375, 3284, 1961, 1541, 1340, 1171, 964, 914, 899, 868, 777; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.91 (s, 2H), 4.70 – 4.65 (m, 2H), 4.28 (t, 2H, *J* = 6.8 Hz), 2.40 – 2.34 (m, 2H), 1.72 (t, 3H, *J* = 3.2 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 206.0, 93.9, 75.6, 69.3, 32.2, 18.9; **HRMS** (+ APCI) calculated for $C_6H_{12}NO_3S$ 178.0538, found 178.0535 $[M+H]^+$.

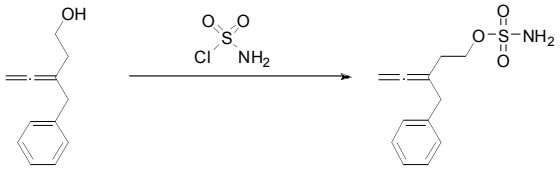
3-Vinylidenehex-5-enyl sulfamate



Prepared according to general procedure B using 3-vinylidenehex-5-en-1-ol (0.87 g, 7.0 mmol), $ClSO_2NCO$ (1.52 mL, 17.5 mmol), formic acid (0.67 mL, 17.5 mmol), DMA (11.9 mL + 0.5 mL) and 2,6-lutidine (2.19 mL, 18.9 mmol). Flash chromatographic purification (5:4 pentane/Et_2O, R_f = 0.3) afforded 3-vinylidenehex-5-enyl sulfamate (1.27 g, 82%) as a pale yellow oil.

IR (thin film, cm^{-1}) 3383, 3286, 2980, 1957, 1554, 1358, 1176, 980, 910, 773, 550; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.83 – 5.71 (m, 1H), 5.11 -5.05 (m, 1H), 5.07 – 5.03 (m, 1H), 4.98 (s, 2H), 4.79 – 4.75 (m, 2H), 4.27 (t, 2H, *J* = 7.0 Hz), 2.76 – 2.71 (m, 2H), 2.41 – 2.34 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 205.6, 134.8, 116.5, 96.9, 76.6, 69.1, 37.1, 30.2; **HRMS** (- APCI) calculated for $C_8H_{12}NO_3S$ 202.0538, found 202.0544 $[M-H]^+$.

3-Benzylpenta-3,4-dienyl sulfamate

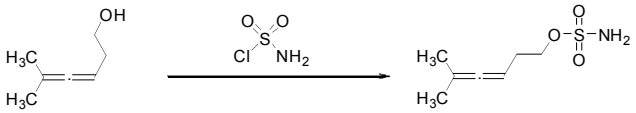


Prepared according to general procedure B using 3-benzylpenta-3,4-dien-1-ol (1.22 g, 7.0 mmol), $ClSO_2NCO$ (1.52 mL, 17.5 mmol), formic acid (0.67 mL, 17.5 mmol), DMA (11.9 mL + 0.5 mL) and 2,6-lutidine (2.19 mL, 18.9 mmol). Flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.3) afforded 3-benzylpenta-3,4-dienyl sulfamate (1.34 g, 76%) as a white solid.

Mp 41.0 – 41.5 °C; **IR** (thin film, cm^{-1}) 3383, 3286, 2978, 1957, 1554, 1495, 1454, 1360, 1178, 976, 916, 849, 777, 698; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.32 – 7.27 (m, 2H), 7.24 – 7.19 (m,

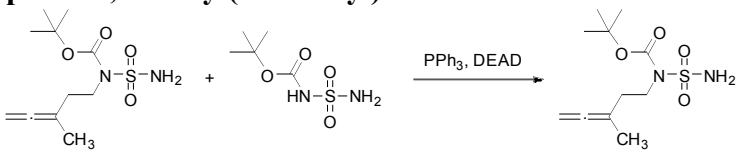
3H), 4.83 – 4.76 (m, 4H), 4.22 (t, 2H, *J* = 7.0 Hz), 3.33 (t, 2H, *J* = 2.6 Hz), 2.35 – 2.29 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 206.3, 138.7, 128.9, 128.4, 126.5, 98.0, 76.8, 69.3, 39.6, 30.0; **HRMS** (- APCI) calculated for $C_{12}H_{14}NO_3S$ 252.0694, found 252.0700 $[M-H]^+$.

5-Methylhexa-3,4-dienyl sulfamate



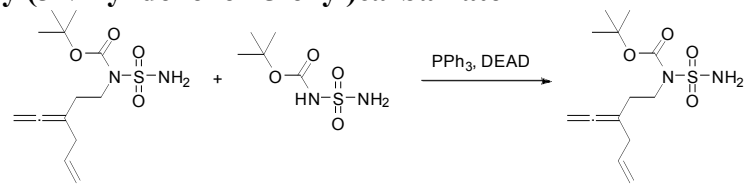
Prepared according to general procedure B using 5-methylhexa-3,4-dien-1-ol (0.79 g, 7.0 mmol), $ClSO_2NCO$ (1.52 mL, 17.5 mmol), formic acid (0.67 mL, 17.5 mmol), DMA (11.9 mL + 0.5 mL) and 2,6-lutidine (2.19 mL, 18.9 mmol). Flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.35) afforded 5-methylhexa-3,4-dienyl sulfamate (1.23 g, 92%) as a white solid.
Mp 39.5 – 39.9 °C; **IR** (thin film, cm^{-1}) 3358, 3259, 2914, 1547, 1346, 1335, 1186, 1163, 993, 916, 764; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.97 – 4.86 (m, 3H), 4.22 (t, 2H, *J* = 7.0 Hz), 2.38 (q, 2H, J = 6.7 Hz), 1.68 (s, 3H), 1.67 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 202.6, 96.6, 83.3, 70.6, 28.6, 20.5; **HRMS** (+ APCI) calculated for $C_7H_{14}NO_3S$ 192.0694, found 192.0692 $[M+H]^+$.

***tert*-Butyl 3-methylpenta-3,4-dienyl(sulfamoyl)carbamate**



Diethyazodicarboxylate (0.41 mL, 2.60 mmol), was added dropwise to an ice cold mixture of 3-methylpenta-3,4-dien-1-ol (196 mg, 2.00 mmol), PPh_3 (0.68 g, 2.60mmol) and $BocNHSO_2NH_2$[7] (0.51 g, 2.60 mmol) in THF (10 mL) under an argon atmosphere. After completed addition the reaction mixture was warmed to 21 °C and stirred for 9 h, where TLC showed full conversion of the starting material. All volatile materials were removed under reduced pressure and the oily residue suspended in 15 mL of hexanes and concentrated again. The crude product was absorbed on silica gel and purified by flash chromatography (5:4 pentane/Et_2O, (R_f = 0.7, 9:1, CH_2Cl_2/EtOAc)) yielding *tert*-butyl 3-methylpenta-3,4-dienyl(sulfamoyl)carbamate (0.29 g, 53%) as a white solid.
Mp 68.5 – 69.0 °C; **IR** (thin film, cm^{-1}) 3379, 3267, 2980, 2933, 1960, 1701, 1551, 1454, 1370, 1342, 1288, 1256, 1142, 847, 719; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.29 (s, 2H), 4.62 -4.57 (m, 2H), 3.79 (dt, 2H, *J* = 7.3 Hz, *J* = 1.6 Hz), 2.29 – 2.21 (m, 2H), 1.71 (dt, 3 H, *J* = 3.2 Hz, *J* = 1.6 Hz), 1.51 (d, 9H, *J* = 1.6 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 206.7, 152.2, 95.1, 84.3, 74.3, 45.6, 33.5, 28.0, 18.5; **HRMS** (+ ESI) calculated for $C_{11}H_{20}N_{2Na}O_4S$ 299.1041, found 299.1036 $[M+Na]^+$.

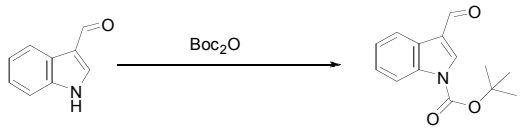
tert-Butyl sulfamoyl(3-vinylidenehex-5-enyl)carbamate



Diethyazodicarboxylate (0.31 mL, 1.95 mmol), was added dropwise to an ice cold mixture of 3-vinylidenehex-5-en-1-ol (186 mg, 1.50 mmol), PPh_3 (0.51 g, 1.95mmol) and $BocNHSO_2NH_2$[7] (0.38 g, 1.95 mmol) in THF (7.5 mL) under an argon atmosphere. After completed addition the reaction mixture was warmed to 21 °C and stirred for 5 h, where TLC showed full conversion of the starting material. All volatile materials were removed under reduced pressure and the oily residue suspended in 15 mL of hexanes and concentrated again. The crude product was absorbed on silica gel and purified by flash chromatography (5:4 pentane/Et_2O, R_f = 0.48) yielding *tert*-butyl sulfamoyl(3-vinylidenehex-5-enyl)carbamate (0.37 g, 82%) as a white solid.
Mp 45.5 – 46.8 °C; **IR** (thin film, cm^{-1}) 3375, 3280, 2980, 2116, 1691, 1552, 1363, 1340, 1176, 1138, 920, 714; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.83 – 5.72 (m 1H), 5.28 (s, 2H), 5.11 – 5.05 (m, 1H), 5.07 – 5.03 (m, 1H), 4.71 - 4.67 (m, 2H), 3.81 – 3.76 (m, 2H), 2.76 – 2.71 (m, 2H), 2.30 – 2.24 (m, 2H), 1.52 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 206.5, 152.2, 135.2, 116.5, 98.3, 84.3, 76.0, 45.8, 36.7, 31.4, 28.0; **HRMS** (+ ESI) calculated for $C_{13}H_{26}N_3O_4S$ 320.1644, found 320.1645 $[M+NH_4]^+$.

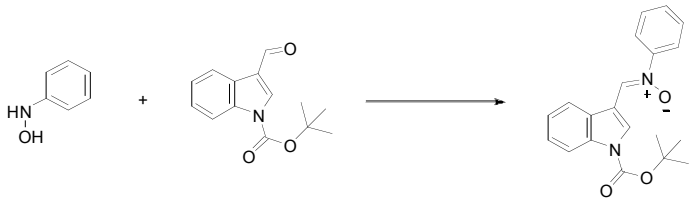
Preparation of Nitrones.

tert-Butyl 3-formyl-1H-indole-1-carboxylate



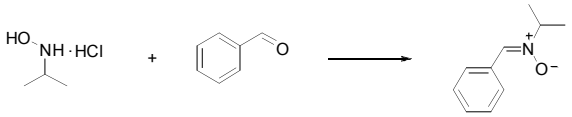
1H-Indole-3-carbaldehyde (2.90 g, 20.0 mmol) was dissolved in THF (200 mL) followed by the addition of 4(dimethylamino)pyridine (0.24 g, 2.0 mmol) and di-*tert*-butyl dicarbonate (5.51 mL, 24.0 mmol). The reaction mixture was stirred for 12 h at 21 °C, diluted with H_2O (50 mL) and extracted with Et_2O (3 x 100 mL). After concentration *in vacuo* the crude product was recrystallized from heptanes: EtOAc affording *tert*-butyl 3-formyl-1H-indole-1-carboxylate (4.22 g, 86%) as a white solid.
Mp 127.0 °C; **IR** (thin film, cm^{-1}) 3142, 2991, 2814, 1740, 1674, 1556, 1450, 1396, 1356, 1275, 1240, 1132, 837, 758, 748; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 10, 09 (s, 1H), 8.30 – 8.26 (m, 1H), 8.22 (s, 1H), 8.16 – 8.12 (m, 1H), 7.43 – 7.38 (m, 1H), 7.38 – 7.33 (m, 1H), 1.70 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 185.7, 148.7, 136.5, 135.9, 126.1, 126.0, 124.6, 122.1, 121.5, 115.1, 85.6, 28.0; **HRMS** (+ APCI) calculated for $C_{14}H_{16}NO_3$ 246.1130, found 246.1124 $[M+H]^+$.

(*Z*)-*N*-((1-(*tert*-Butoxycarbonyl)-1H-indol-3-yl)methylene)aniline oxide



tert-Butyl 3-formyl-1H-indole-1-carboxylate (2.45 g, 10.0 mmol) was mixed with *N*-phenylhydroxylamine[2] (1.31 g, 12.0 mmol) and $MgSO_4$ (2.0 g, 16.6 mmol). After the addition of CH_2Cl_2 (40 mL) the reaction mixture was stirred for 2 days at 21°C, filtered and concentrated *in vacuo*. Flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.25) afforded (*Z*)-*N*-((1-(*tert*-butoxycarbonyl)-1H-indol-3-yl)methylene)aniline oxide (3.0 g, 89%) as a pale yellow solid. **Mp** 69.5 – 71.5 °C; **IR** (thin film, cm^{-1}) 3182, 3057, 2978, 1732, 1529, 1452, 1362, 1257, 1225, 1142, 1068, 752, 687, 596; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.47 (s, 1H), 8.33 – 8.30 (m, 1H), 8.30 – 8.29 (m, 1H), 7.86 – 7.83 (m, 1H), 7.83 – 7.82 (m, 1H), 7.68 – 7.65 (m, 1H), 7.53 – 7.45 (m, 3H), 7.43 – 7.38 (m, 1H), 7.34 – 7.30 (m, 1H), 1.67 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 149.2, 147.8, 135.2, 129.7, 129.5, 129.2, 128.1, 126.2, 125.4, 123.3, 121.3, 117.7, 115.7, 111.5, 84.6, 28.1; **HRMS** (+ APCI) calculated for $C_{20}H_{21}N_2O_3$ 337.1552, found 337.1546 $[M+H]^+$.

(*Z*)-*N*-benzylidenepropan-2-amine oxide



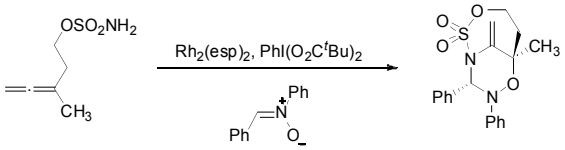
N-Isopropylhydroxylamine hydrochloride (1.34 g, 12.0 mmol) was dissolved in CH_2Cl_2 (40 mL) and mixed with benzaldehyde (1.01 mL, 10.0 mmol), Et_3N (1.95 mL, 14.0 mmol) and $MgSO_4$ (3.97 g, 33.0 mmol). The reaction mixture was stirred for 3 days at 21 °C. After filtration, the clear organic solution was washed with H_2O (50 mL) and brine (3 x 50 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The resulting yellow oil was mixed with heptanes and sonicated for a few minutes. After separation of the layers, the solvent was removed by decantation and the procedure repeated (if necessary). (*Z*)-*N*-Benzylidenepropan-2-amine oxide (1.07 g, 65%) was isolated as a yellow oil.
IR (thin film, cm^{-1}) 3066, 2978, 2933, 1580, 1560, 1450, 1363, 1300, 1175, 1146, 1088, 752, 690; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.27 – 8.21 (m, 2H), 7.43 (s, 1H), 7.42 – 7.37 (m, 3H), 4.21 (hep, 1H, *J* = 6.4 Hz), 1.50 (d, 6H, *J* = 6.4 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 131.9, 130.7, 130.1, 128.5, 128.4, 67.8, 20.9; **HRMS** (+ APCI) calculated for $C_{10}H_{14}NO$ 164.1075, found 164.1070 $[M+H]^+$.

General Procedure (C) for the preparation and reaction of 2-amidoallylcations with nitrones

Sulfamate ester or sulfamide (0.3 mmol, 1.0 eq.), the corresponding nitrone (1.5 - 5 eq.) and $Rh_2(esp)_2$ (11.4 mg, 5 mol %) were combined in a 2 dram reaction vial and capped with a teflon lined septum. The vial was evaporated two times and flushed with argon before a suspension of $PhI(O_2C^tBu)_2$ (195 mg, 0.48 mmol) in CF_3-C_6H_5 (2 mL) was added with a syringe in one portion.

The reaction mixture was stirred at 21 °C until TLC indicated no further reaction progress (1.5 – 20 h). The resulting dark blue green mixture was diluted with H_2O (5-10 mL) and extracted with EtOAc (3 x 20 mL). After drying with Na_2SO_4 and concentration *in vacuo*, the residue was purified by flash chromatography on silica gel as indicated. Mixed fractions were collected and purified again by flash chromatography to maximize the yield.

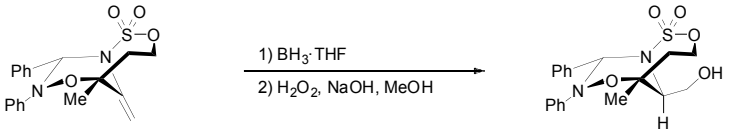
6-Methyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (**6**)



Prepared according to general procedure C using 3-methylpenta-3,4-dienyl sulfamate (53 mg, 0.30 mmol) and (*Z*)-*N*-benzylideneaniline oxide (237 mg ,1.20 mmol). After 20 h the reaction mixture was worked up, affording 6-methyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (73 mg, 65%) after flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.45) as a light brown solid. The relative stereochemistry of **6** was obtained by X-ray crystallography after derivatization to crystalline compound **8** (see below).

Mp 125.0 – 126.0 °C (decomposition); **IR** (thin film, cm^{-1}) 2983, 1734, 1657, 1597, 1491, 1454, 1373, 1358, 1182, 966, 903, 773, 692, 581; **^{1}H NMR** ($CDCl_3$, 600 MHz) δ 7.38 – 7.29 (m, 2H), 7.27 – 7.22 (m, 3H), 7.22 – 7.14 (m, 2H), 7.13 – 6.98 (m, 3H), 6.25 (s, 1H), 5.68 (s, 1H), 5.49 (s, 1H), 4.98 (t, 1H, *J* = 12.7 Hz), 4.27(dt, 1H, *J* = 13.0 Hz, *J* = 3.8 Hz), 2.20 – 2.05 (m, 2H), 1.67 (s, 3H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 145.5, 142.9, 137.3, 129.1, 128.6, 128.4, 127.7, 126.7, 123.6, 116.5, 86.3, 66.3, 41.0, 29.7, 24.1; **HRMS** (+ APCI) calculated for $C_{19}H_{21}N_2O_4S$ 373.1222, found 373.1223 $[M+H]^+$.

(6-Methyl-2,2-dioxido-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]dec-10-yl)methanol (8)

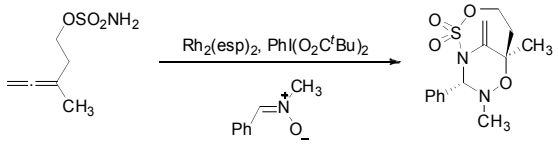


6-Methyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (60 mg, 0.16 mmol) was dissolved in THF (0.3 mL) and cooled to 0 °C. $BH_3 \cdot THF$ (0.64 mL, 0.64 mmol, 1 M in THF) was then added dropwise. After completed addition the green reaction mixture was warmed to room temperature and stirred for 20 h. After that time TLC indicated full consumption of the starting material and the mixture was cooled again to 0 °C, followed by the addition of MeOH (2.1 mL). After stirring at room temperature for 1 h, solid NaOH (140 mg, 3.50 mmol) and H_2O_2 (0.21 mL, 30 wt %) were added successively at 0 °C. The resulting milky suspension was warmed to room temperature and quenched after 1 h of stirring with saturated aq. NH_4Cl (30 mL). Extraction with EtOAc (3 x 30 mL), drying with Na_2SO_4 and concentration *in vacuo*, furnished (6-methyl-2,2-dioxido-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]dec-10-yl)methanol (35 mg, 56%) after flash chromatograpy (1:1 pentane/

Et_2O, R_f = 0.28) as a white solid. The relative stereochemistry was obtained by X-ray crystallography (see page S46).

Mp 55.0 – 56.0 °C; **IR** (thin film, cm^{-1}) 3508, 3423, 2972, 2960, 2910, 1715, 1495, 1454, 1379, 1346, 1242, 1228, 1194, 1178, 1043, 999, 949, 785, 756, 700, 692, 662, 590; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.40 – 7.35 (m, 2H), 7.29 – 7.22 (m, 5H), 7.04 – 7.00 (m, 2H), 6.99 – 6.94 (m, 1H), 6.68 (s, 1H), 5.28 (t, 1H, *J* = 12.1 Hz), 4.42 (m, 1H), 4.21 (ddd, 1H, *J* = 13.0 Hz, 4.5 Hz, 2.5 Hz), 3.88 (s, 1H), 3.78 – 3.72 (m, 1H), 2.89 (dd, 1H, *J* = 11.3 Hz, 4.1 Hz), 2.20 – 2.07 (m, 2H), 1.32 (s, 3H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 145.8; 134.7, 129.2, 128.6, 128.6, 128.1, 122.7, 115.6, 79.4, 77.9, 67.6, 62.6, 58.4, 38.0, 24.9; **HRMS** (+ APCI) calculated for $C_{19}H_{23}N_2O_5S$ 391.1328, found 391.1324 $[M+H]^+$.

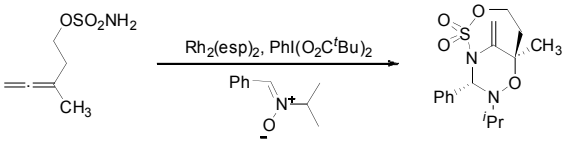
6,8-Dimethyl-10-methylene-9-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide



Prepared according to general procedure C using 3-methylpenta-3,4-dienyl sulfamate (53 mg, 0.30 mmol) and (*Z*)-*N*-benzylidenemethanamine oxide (61 mg , 0.45 mmol). After 2.5 h the reaction mixture was worked up, affording 6,8-dimethyl-10-methylene-9-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (63 mg, 68%) after flash chromatographic purification (2:1 pentane/Et_2O, R_f = 0.3) as a white solid.

Mp 135.1 – 136.0 °C (decomposition); **IR** (thin film, cm^{-1}) 2985, 2928, 2875, 1653, 1460, 1371, 1356, 1188, 1095, 1034, 959, 899, 756, 604; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.42 – 7.37 (m, 2H), 7.36 – 7.31 (m, 3H), 5.60 (d, 1H, *J* = 1.3 Hz), 5.41 (s, 1H), 5.36 (s, 1H), 4.20 – 4.12 (m, 1H), 4.16 (dt, 1H, *J* = 13.0 Hz, *J* = 3.6 Hz), 2.42 (s, 3H), 2.12 – 2.01 (m, 1H), 1.95 -1.88 (m, 1H), 1.57 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.3, 137.9, 129.5, 128.8, 127.5, 115.2, 88.9, 82.8, 65.7, 41.7, 41.1, 24.1; **HRMS** (+ APCI) calculated for $C_{14}H_{19}N_2O_4S$ 311.1066, found 311.1065 $[M+H]^+$.

8-*Iso*-propyl-6-methyl-10-methylene-9-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo [4.3.1]decane 2,2-dioxide

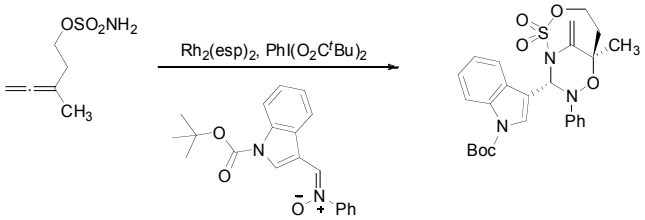


Prepared according to general procedure C using 3-methylpenta-3,4-dienyl sulfamate (53 mg, 0.30 mmol) and (*Z*)-*N*-benzylidenepropan-2-amine oxide (147 mg , 0.90 mmol). After 20 h the reaction mixture was worked up, affording 8-isopropyl-6-methyl-10-methylene-9-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (32 mg, 32%) after flash chromatographic purification (7:3 pentane/Et_2O, R_f = 0.5) as a white solid.

Mp 154.0 – 157.0 °C (decomposition); **IR** (thin film, cm^{-1}) 2978, 2935, 1778, 1655, 1458, 1375, 1352, 1182, 1082, 1043, 1036, 962, 905, 816, 712, 696, 609; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.57 – 7.24 (m, 5H), 5.82 s, 1H), 5.53 (s, 1H), 5.31 (s, 1H), 4.88 – 4.73 (m, 1H), 4.18 – 4.05 (m, 1H), 2.75 – 2.60 (m, 1H), 2.13 – 2.00 (m, 1H), 1.99 - 1.85 (m, 1H), 1.53 (s, 3H), 1.08 (d, 3H, J =

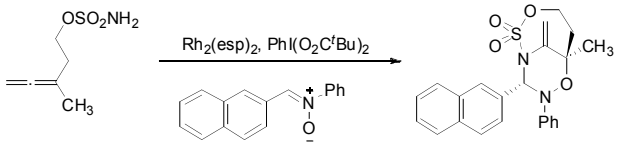
6.3 Hz), 1.01 (d, 3H, J = 6.3 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 129.3, 128.7, 127.4, 114.8, 84.2, 82.6, 65.6, 49.9, 41.1, 26.8, 23.7, 21.1, 13.2; **HRMS** (+ APCI) calculated for $C_{16}H_{23}N_2O_4S$ 339.1379, found 339.1377 $[M+H]^+$.

***tert*-Butyl 3-(8-isopropyl-6-methyl-10-methylene-2,2-dioxido-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]dec-9-yl)-1*H*-indole-1-carboxylate**



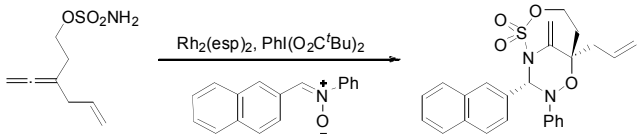
Prepared according to general procedure C using 3-methylpenta-3,4-dienyl sulfamate (53 mg, 0.30 mmol) and (*Z*)-*N*-((1-(*tert*-butoxycarbonyl)-1H-indol-3-yl)methylene)aniline oxide (403 mg , 1.20 mmol). After 20 h the reaction mixture was worked up, affording *tert*-butyl 3-(8-*iso*-propyl-6-methyl-10-methylene-2,2-dioxido-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]dec-9-yl)-1*H*-indole-1-carboxylate (71 mg, 46%) after flash chromatographic purification (7:3 pentane/Et_2O, (R_f in pentane/Et_2O = 0.5)) as a brown very viscous oil.
IR (thin film, cm^{-1}) 2978, 2928, 1732, 1597, 1493, 1450, 1367, 1309, 1254, 1225, 1184, 1148, 1088, 966, 899, 746; **^{1}H NMR** ($CDCl_3$, 600 MHz) δ 8.09 – 7.98 (m, 1H), 7.86 – 7.75 (m, 1H), 7.57 (s, 1H), 7.32 – 7.27 (m, 1H), 7.26 – 7.13 (m, 5H), 7.05 (s, 1H), 6.62 (b, 1H), 5.56 (s, 1H), 5.48 (s, 1H), 5.16 – 4.96 (m, 1H), 4.30 (d, 1H, *J* = 12.4 Hz), 2.31 – 2.10 (m, 2H), 1.68 (s, 3H), 1.61 (s, 9H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 149.4, 145.7, 135.3, 129.5, 128.8, 128.8, 128.1, 125.9, 125.9, 124.6, 124.6, 122.8, 120.7, 117.0, 115.1, 84.1, 66.7, 41.3, 29.7, 28.1,27.0, 24.3; **HRMS** (+ APCI) calculated for $C_{26}H_{30}N_3O_6S$ 512.1855, found 512.1846 $[M+H]^+$.

6-Methyl-10-methylene-9-(2-naphthyl)-8-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1] decane 2,2-dioxide



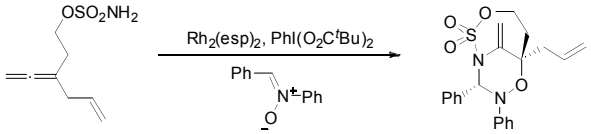
Prepared according to general procedure C using 3-methylpenta-3,4-dienyl sulfamate (53 mg, 0.30 mmol) and (Z)-N-(naphthalen-2-ylmethylene)aniline oxide (297 mg, 1.20 mmol). After 20 h the reaction mixture was worked up, affording 6-methyl-10-methylene-9-(2-naphthyl)-8-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (79 mg, 62%) after flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.37) as a light brown solid.
Mp 161.0 – 161.8 °C (decomposition); **IR** (thin film, cm^{-1}) 3059, 2972, 1657, 1599, 1493, 1358, 1313, 1230, 1184, 1092, 1051, 771, 581; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.81 – 7.70 (m, 4H), 7.57 – 7.51 (m, 1H), 7.50 – 7.42 (m, 2H), 7.19 – 7.09 (m, 4H), 7.07 – 7.02 (m, 1H), 6.44 (s, 1H), 5.70 (s, 1H), 5.51 (s, 1H), 5.01 (t, 1H, *J* = 12.4 Hz), 4.28 (dt, 1H, *J* = 12.8 Hz, *J* = 3.7 Hz), 2.24 – 2.02 (m, 2H), 1.71 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 145.4, 142.8, 134.8, 133.6, 132.8, 128.7, 128.7, 128.5, 128.3, 127.6, 127.6, 126.5, 126.1, 124.6, 123.6, 116.6, 86.1, 83.7, 66.4, 41.0, 24.2; **HRMS** (+ APCI) calculated for $C_{23}H_{23}N_2O_4S$ 423.1379, found 423.1373 $[M+H]^+$.

6-Allyl-10-methylene-9-(2-naphthyl)-8-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1] decane 2,2-dioxide



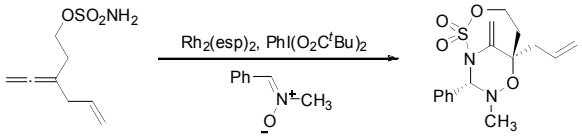
Prepared according to general procedure C using 3-vinylidenehex-5-enyl sulfamate (61 mg, 0.30 mmol) and (*Z*)-*N*-(naphthalen-2-ylmethylene)aniline oxide (297 mg, 1.20 mmol). After 20 h the reaction mixture was worked up, affording 6-allyl-10-methylene-9-(2-naphthyl)-8-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (81 mg, 60%) after flash chromatographic purification (7:3 pentane/Et_2O, $R_f = 0.34$) as a brown very viscous oil.
IR (thin film, cm^{-1}) 3061, 2968, 2918, 2852, 1655, 1597, 1491, 1377, 1362, 1184, 1086, 1018, 908, 729, 567; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.80 – 7.71 (m, 3H), 7.69 (s, 1H), 7.55 – 7.48 (m, 1H), 7.48 – 7.39 (m, 2H), 7.17 – 7.02 (m, 5H), 6.38 (s, 1H), 5.97 – 5.84 (m, 1H), 5.77 (s, 1H), 5.53 (s, 1H), 5.16 (s, 1H), 5.14 – 5.10 (m, 1H), 5.03 – 4.93 (m, 1H), 4.31 (dt, 1H, *J* = 13.1 Hz, *J* = 3.8 Hz), 3.13 – 3.03 (m, 1H), 2.54 dd, 1H, *J* = 14.4 Hz, *J* = 8.9 Hz), 2.17 (m, 2H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 145.2, 142.3, 134.6, 133.6, 132.8, 132.0, 128.6, 128.5, 128.3, 127.8, 127.6, 126.6, 126.1, 124.7, 123.6, 119.2, 116.6, 86.4, 85.2, 66.4, 41.0, 39.1, 29.7; **HRMS** (+ APCI) calculated for $C_{25}H_{25}N_2O_4S$ 449.1535, found 449.1529 $[M+H]^+$.

6-Allyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide



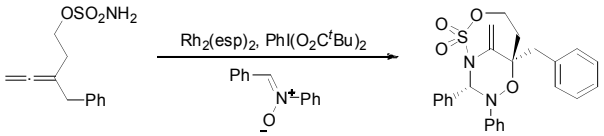
Prepared according to general procedure C using 3-vinylidenehex-5-enyl sulfamate (61 mg, 0.30 mmol) and (*Z*)-*N*-benzylideneaniline oxide (237 mg ,1.20 mmol). After 20 h the reaction mixture was worked up, affording 6-allyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (82 mg, 69%) after flash chromatographic purification (3:2 pentane/Et_2O, $R_f = 0.4$) as a brown solid.
Mp 144.0 – 145.5 °C (decomposition); **IR** (thin film, cm^{-1}) 3068, 3030, 2972, 2924, 1491, 1452, 1375, 1356, 1182, 1138, 1092, 1020, 953, 920, 793, 735, 692, 665, 573, 561; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.31 – 7.26 (m, 2H), 7.25 – 7.19 (m, 3H), 7.19 – 7.13 (m, 2H), 7.12 – 7.06 (m, 1H), 7.05 – 7.00 (m, 2H), 6.19 (s, 1H), 5.93 – 5.81 (m, 1H), 5.74 (s, 1H), 5.49 (s, 1H), 5.13 (s, 1H), 5.10 (d, 1H, *J* = 5.4 Hz), 4.99 – 4.90 (m, 1H), 4.28 (dt, 1H, *J* = 13.0 Hz, *J* = 3.8 Hz), 3.09 – 2.97 (m, 1H), 2.49 (dd, 1H, *J* = 14.3 Hz, *J* = 8.6 Hz), 2.16 – 1.97 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 145.3, 142.3, 137.1, 132.0, 129.2, 128.5, 128.4, 127.9, 126.8, 123.8, 119.1, 116.4, 86.7, 85.1, 66.3, 40.9, 39.1; **HRMS** (+ APCI) calculated for $C_{21}H_{23}N_2O_4S$ 399.1379, found 399.1370 $[M+H]^+$.

6-Allyl-8-methyl-10-methylene-9-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide



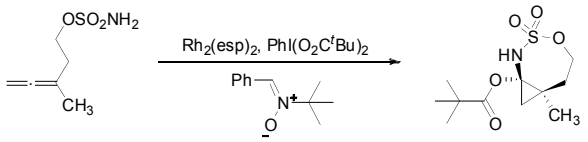
Prepared according to general procedure C using 3-vinylidenehex-5-enyl sulfamate (61 mg, 0.30 mmol) and (*Z*)-*N*-benzylidenemethanamine oxide (122 mg , 0.9 mmol). After 20 h the reaction mixture was worked up, affording 6-allyl-8-methyl-10-methylene-9-phenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (74 mg, 73%) after flash chromatographic purification (7:3 pentane/Et_2O, R_f = 0.4) as light brown viscous oil.
IR (thin film, cm^{-1}) 3072, 2972, 2916, 1647, 1456, 1377, 1362, 1184, 1092, 978, 916, 893, 824, 731, 698, 640, 582; **^{1}H NMR** ($CDCl_3$, 600 MHz) δ 7.40 – 7.37 (m, 2H), 7.36 – 7.32 (m, 3H), 5.99 – 5.91 (m, 1H), 5.63 (d, 1H, *J* = 1.0 Hz), 5.43 (s, 1H), 5.37 (d, 1H, *J* = 1.0 Hz), 5.19 (s, 1H), 5.18 – 5.15 (m, 1H), 4.82 – 4.76 (m, 1H), 4.18 (dt, 1H, *J* = 12.9 Hz, *J* = 3.8 Hz), 2.93 – 2.88 (m, 1H), 2.45 – 2.40 (m, 1H), 2.42 (s, 3H), 1.97 – 1.92 (m, 2H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 142.4, 137.8, 132.3, 132.2, 129.5, 128.7, 127.5, 115.4, 115.3, 88.7, 84.1, 65.9, 41.1, 39.1;
HRMS (+ APCI) calculated for $C_{16}H_{21}N_2O_4S$ 337.1222, found 337.1214 $[M+H]^+$.

6-Benzyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide



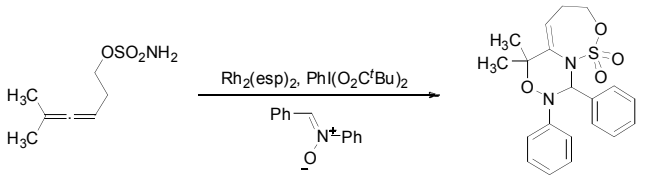
Prepared according to general procedure C using 3-benzylpenta-3,4-dienyl sulfamate (76 mg, 0.30 mmol) and (*Z*)-*N*-(naphthalen-2-ylmethylene)aniline oxide (297 mg, 1.20 mmol). After 20 h the reaction mixture was worked up, affording 6-benzyl-10-methylene-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]decane 2,2-dioxide (65 mg, 48%) after flash chromatographic purification (7:3 pentane/Et_2O, R_f = 0.34) as a white crystalline product.
Mp 184.5 – 185.5 °C (decomposition); **IR** (thin film, cm^{-1}) 3063, 3036, 2922, 2850, 1657, 1597, 1491, 1454, 1377, 1360, 1217, 1180, 1082, 1014, 960, 924, 764, 712, 689, 646, 575; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.31 – 7.23 (m, 5H), 7.21 – 7.10 (m, 6H), 7.05 – 7.00 (m, 2H), 7.00 – 6.94 (m, 2H), 6.10 (s, 1H), 5.87 (d, 1H, *J* = 1.0 Hz), 5.64 (d, 1H, *J* = 1.0 Hz), 4.93 – 4.82 (m, 1H), 4.20 (dt, 1H, *J* = 13.0 Hz, *J* = 3.5 Hz), 3.59 (d, 1H, *J* = 14.0 Hz), 2.96 (d, 1H, *J* = 13.7 Hz), 2,11 – 1.99 (m, 1H), 1.77 – 1.67 (m, 1H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 145.2, 136.9, 135.1, 130.9, 129.3, 128.4, 128.3, 128.2, 127.9, 126.7, 124.2, 116.0, 88.0, 85.3, 66.2, 41.5, 38.5, 29.7, 27.2;
HRMS (+ APCI) calculated for $C_{25}H_{25}N_2O_4S$ 449.1535, found 449.1529 $[M+H]^+$.

7-Methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl pivalate



Prepared according to general procedure C using 3-methylpenta-3,4-dienyl sulfamate (53 mg, 0.30 mmol) and (*Z*)-*N*-benzylidene-2-methylpropan-2-amine oxide (133 mg , 0.75 mmol). After 12 h the reaction mixture was worked up, affording 7-methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl pivalate (50 mg, 60%) after flash chromatographic purification (1:1 pentane/Et_2O, R_f = 0.3) as a white solid. The relative stereochemistry of **16** was obtained by X-ray crystallography (see page S46).
Mp 109.5 – 111.0 °C; **IR** (thin film, cm^{-1}) 3213, 2951, 2933, 2876, 1722, 1414, 1352, 1296, 1190, 1169, 1117, 1055, 1014, 959, 932, 885, 864, 760, 621; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.59 (s, 1H), 4.66 (t, 1H, *J* = 11.4 Hz), 4.23 (ddd, 1H, *J* = 12.5 Hz, *J* = 4.6 Hz, *J* = 1.9 Hz), 2.27 (dd, 1H, *J* = 16.0 Hz, *J* = 4.6 Hz), 1.92 (dd, 1H, *J* = 16.0 Hz, *J* = 11.4 Hz), 1.36 (d, 1H, *J* = 6.7 Hz), 1.32 (s, 3H), 1.19 (s, 9H), 0.95 (s, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 178.8, 69.2, 68.8, 38.9, 38.7, 33.0, 27.6, 26.6, 17.7; **HRMS** (+ APCI) calculated for $C_{11}H_{20}NO_5S$ 278.1062, found 278.1056 $[M+H]^+$.

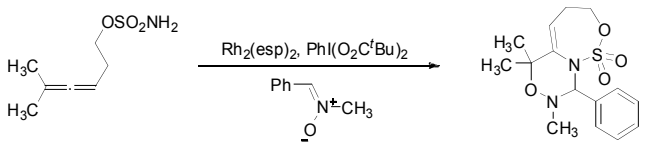
6,6-Dimethyl-8,9-diphenyl-4,6,8,9-tetrahydro-3*H*-[1,2,4]oxadiazino[4,5-*c*][1,2,3] oxathiazepine 1,1-dioxide



9:1 mixture of regioisomers

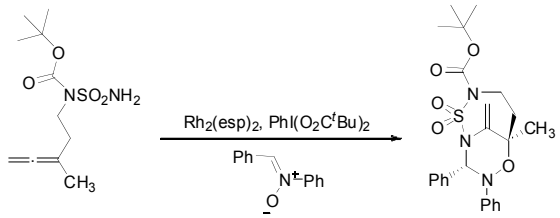
Prepared according to general procedure C using 5-methylhexa-3,4-dienyl sulfamate (57 mg, 0.30 mmol) and (*Z*)-*N*-benzylideneaniline oxide (296 mg , 1.50 mmol). After 20 h the reaction mixture was worked up, affording 6,6-dimethyl-8,9-diphenyl-4,6,8,9-tetrahydro-3*H*-[1,2,4]oxadiazino[4,5-*c*][1,2,3] oxathiazepine 1,1-dioxide (84 mg, 73%) after flash chromatographic purification (7:3 pentane/Et_2O, (R_f in pentane/Et_2O = 0.45)) as a brown solid.
IR (thin film, cm^{-1}) 3063, 3034, 2972, 2914, 1734, 1597, 1491, 1454, 1364, 1244, 1176, 1014, 908, 852, 793, 756, 694, 658; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.39 – 7.34 (m, 2H), 7.28 – 7.22 (m, 3H), 7.19 – 7.14 (m, 2H), 7.06 – 7.00 (m, 3H), 6.28 (s, 1H), 5.50 (s, 1H), 4.78 – 4.71 (m, 1H), 4.39 – 4.34 (m, 1H), 2.32 – 2.25 (m, 1H), 2.18 – 2.10 (m, 1H), 1.84 (s, 3H), 1.75 (s, 3H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 146.2, 146.1, 142.2, 138.5, 137.3, 131.6, 129.2, 128.9, 128.6, 128.5, 128.5, 128.4, 127.8, 127.7, 125.1, 122.4, 121.2, 116.6, 84.2, 73.0, 70.0, 67.4, 65.8, 32.4, 29.7, 27.6, 26.4, 25.7, 20.6, 19.0; **HRMS** (+ APCI) calculated for $C_{20}H_{23}N_2O_4S$ 387.1379, found 387.1379 $[M+H]^+$.

6,6,8-Trimethyl-9-phenyl-4,6,8,9-tetrahydro-3*H*-[1,2,4]oxadiazino[4,5-*c*][1,2,3]oxathiazepine 1,1-dioxide



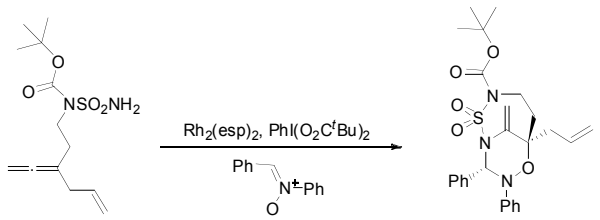
Prepared according to general procedure C using 5-methylhexa-3,4-dienyl sulfamate (57 mg, 0.30 mmol) and (*Z*)-*N*-benzylidenemethanamine oxide (61 mg , 0.45 mmol). After 1.5h the reaction mixture was worked up, affording 6,6,8-trimethyl-9-phenyl-4,6,8,9-tetrahydro-3*H*-[1,2,4]oxadiazino[4,5-*c*][1,2,3]oxathiazepine 1,1-dioxide (45 mg, 46%) after flash chromatographic purification (5:4 pentane/Et_2O, R_f = 0.45)) as a white solid.
Mp 119.8 – 120.6 °C (decomposition); **IR** (thin film, cm^{-1}) 3277, 3064, 3032, 2933, 2908, 2852, 1454, 1350, 1256, 1207, 1178, 1167, 1065, 1057, 1051, 1016, 935, 920, 860, 793, 725, 665; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.39 – 7.29 (m, 5H), 5.44 – 5.39 (m, 2H), 4.72 – 4.64 (m, 1H), 4.31 – 4.21 (m, 1H), 2.44 (s, 3H), 2.10 – 2.01 (m, 2H), 1.83 (s, 6H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 138.0, 137.3, 129.4, 128.7, 127.4, 123.3, 88.5, 76.9, 66.3, 41.6, 32.1, 20.7, 19.0; **HRMS** (+ APCI) calculated for $C_{15}H_{21}N_2O_4S$ 325.1222, found 325.1222 $[M+H]^+$.

***tert*-Butyl 6-methyl-10-methylene-8,9-diphenyl-7-oxa-2-thia-1,3,8-triazabicyclo[4.3.1]-decane-3-carboxylate 2,2-dioxide**



Prepared according to general procedure C using *tert*-butyl 3-methylpenta-3,4-dienyl(sulfamoyl)carbamate (83 mg, 0.30 mmol) and (*Z*)-*N*-benzylideneaniline oxide (237 mg ,1.20 mmol). After 20 h the reaction mixture was worked up, affording *tert*-butyl 6-methyl-10-methylene-8,9-diphenyl-7-oxa-2-thia-1,3,8-triazabicyclo[4.3.1]decane-3-carboxylate 2,2-dioxide (92 mg, 65%) after flash chromatographic purification (4:1 pentane/Et_2O, R_f = 0.35) as a white off solid.
Mp 153.2 - 154.0 °C; **IR 3**064, 3037, 2978, 2933, 1724, 1599, 1491, 1454, 1394, 1369, 1308, 1284, 1256, 1180, 1151, 1138, 1061, 910, 727, 696, 635, 598, **^{1}H NMR** ($CDCl_3$, 600 MHz) δ 7.40 – 7.36 (m, 2H), 7.27 – 7.22 (m, 3H), 7.16 – 7.12 (2H), 7.05 – 7.00 (m, 3H), 6.45 (s, 1H), 5.57 (s, 1H), 5.45 (s,1H), 4.10 – 3.94 (m, 2H), 2.33 – 2.20 (m, 1H), 1.87 – 1.79 (m, 1H), 1.71 (s, 3H), 1.41 (s, 9H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 151.7, 146.2, 143.2, 138.0, 129.3, 128.8, 128.7, 127.7, 125.9, 122.7, 118.4, 86.0, 83.9, 44.4, 38.5, 32.1, 28.1, 25.1; **HRMS** (+ APCI) calculated for $C_{24}H_{30}N_3O_5S$ 472.1905, found 498.1906 $[M+H]^+$.

tert-Butyl 6-allyl-10-methylene-8,9-diphenyl-7-oxa-2-thia-1,3,8-triazabicyclo[4.3.1]decane-3-carboxylate 2,2-dioxide



Prepared according to general procedure C using *tert*-butyl sulfamoyl(3-vinylidenehex-5-enyl)carbamate (91 mg, 0.30 mmol) and (*Z*)-*N*-benzylideneaniline oxide (237 mg ,1.20 mmol). After 20 h the reaction mixture was worked up, affording *tert*-butyl 6-allyl-10-methylene-8,9-diphenyl-7-oxa-2-thia-1,3,8-triazabicyclo[4.3.1]decane-3-carboxylate 2,2-dioxide (102 mg, 68%) after flash chromatographic purification (4:1 pentane/Et_2O, R_f = 0.45) as a white off solid.
Mp 139.2 – 142.0 °C; **IR** (thin film, cm^{-1}) 2982, 2966, 2930, 1778, 1709, 1678, 1595, 1493, 1400, 1367, 1294, 1180, 1146, 1001, 928, 750, 694, 665, 598; **^{1}H NMR** ($CDCl_3$, 600 MHz) δ 7.60 – 7.52 (m, 1H), 7.40 – 7.28 (m, 5H), 7.18 – 7.12 (m, 2H), 7.09 – 7.04 (m, 2H), 6.40 (s, 1H), 5.97 – 5.84 (m, 1H), 5.68 (s, 1H), 5.48 (s, 1H), 5.19 – 5.07 (m, 2H), 4.11 – 3.96 (m, 2H), 3.24 – 3.11 (m, 1H), 2.55 – 2.45 (m, 1H), 2.24 – 2.14 (m, 1H), 1.81 – 1.70 (m, 1H), 1.46 (s, 9H); **^{13}C NMR** ($CDCl_3$, 150 MHz) δ 175.3, 151.4, 145.7, 132.3, 130.8, 129.0, 128.5, 128.4, 128.3, 128.0, 127.7, 118.8, 117.8, 83.6, 43.8, 41.6, 38.2, 36.6, 27.90, 26.8; **HRMS** (+ APCI) calculated for $C_{26}H_{32}N_3O_5S$ 498.2063, found 498.2064 $[M+H]^+$.

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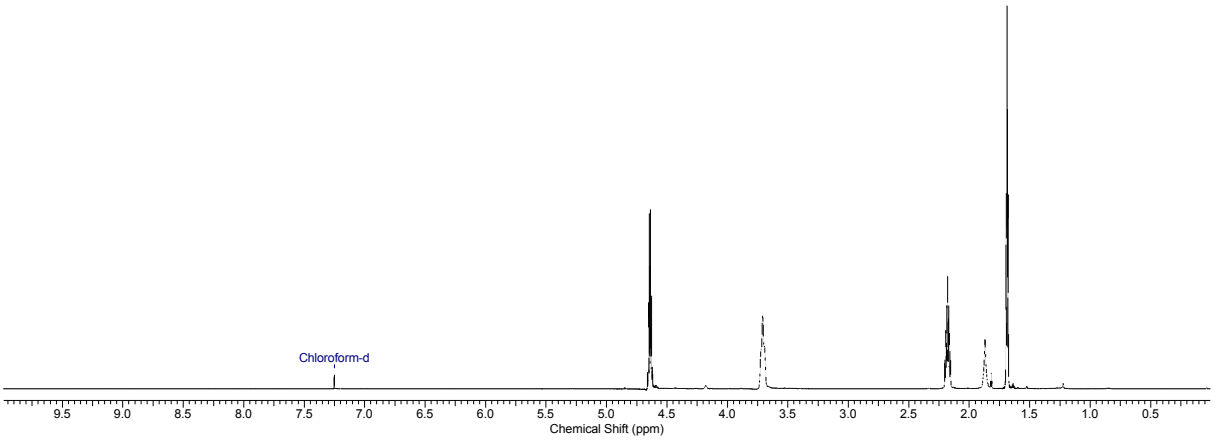
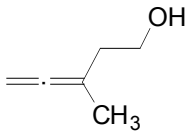
400 MHz $CDCl_3$





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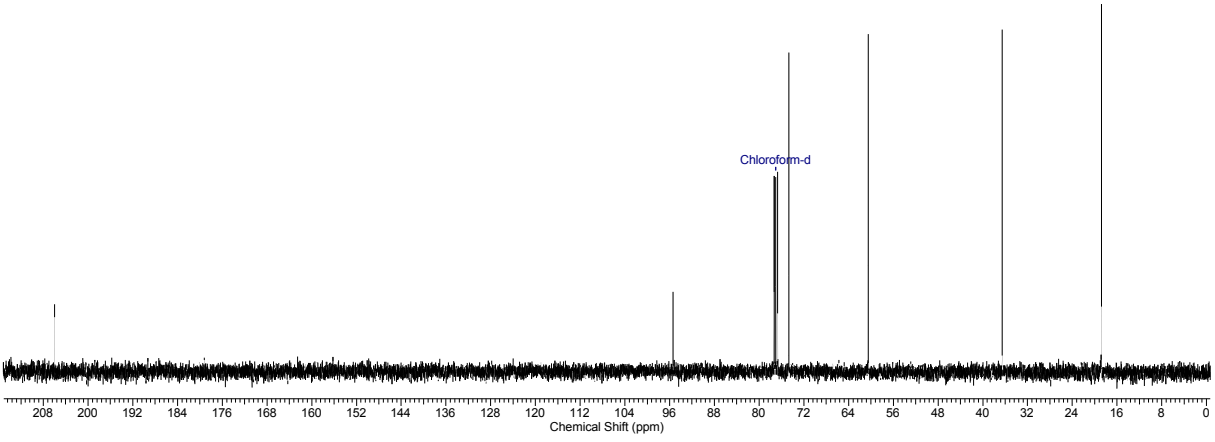

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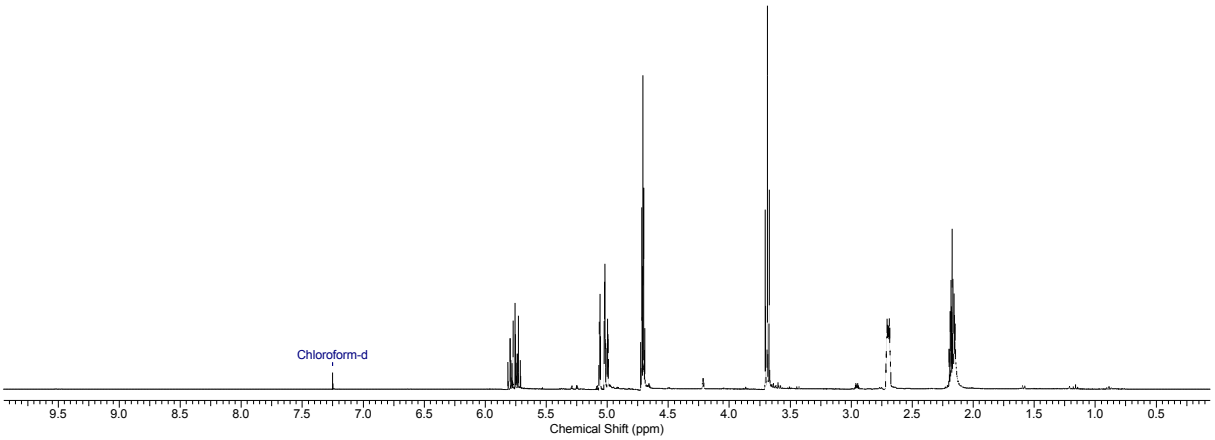

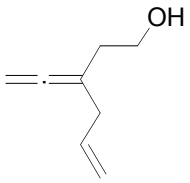

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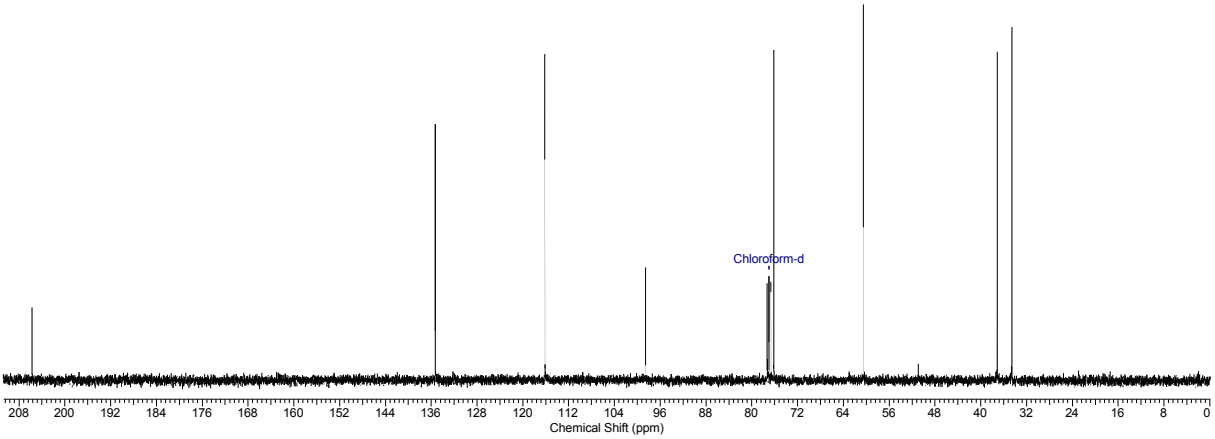

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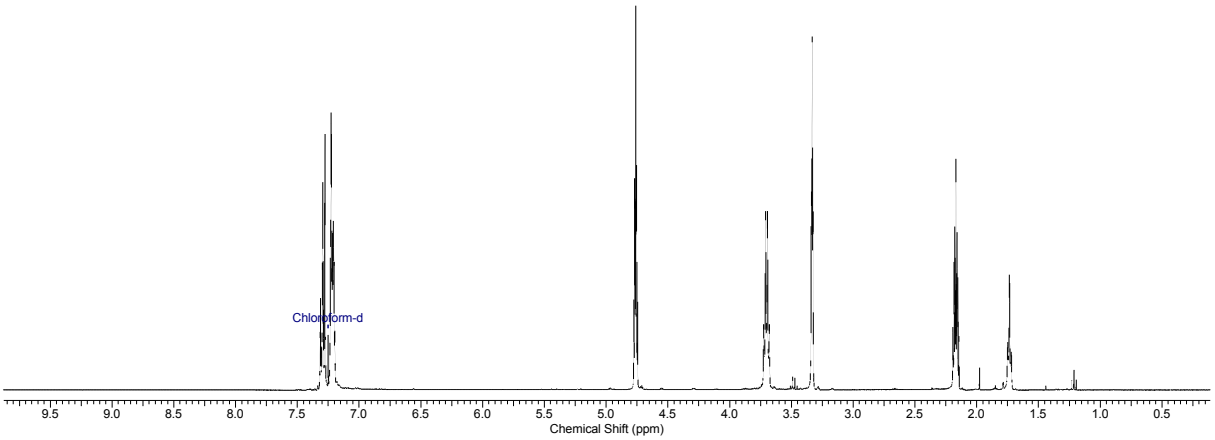

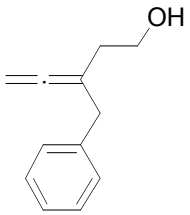

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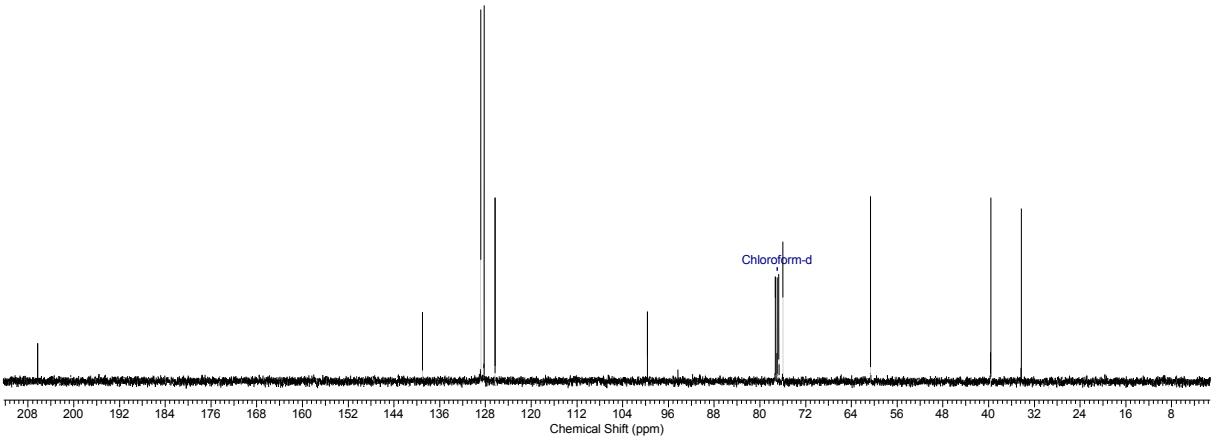

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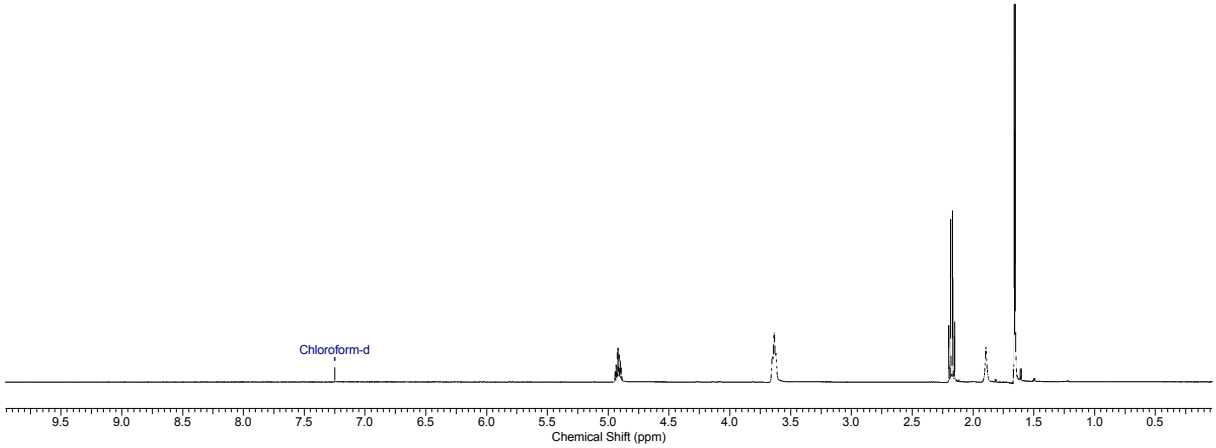

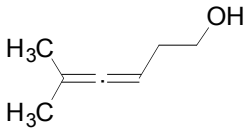

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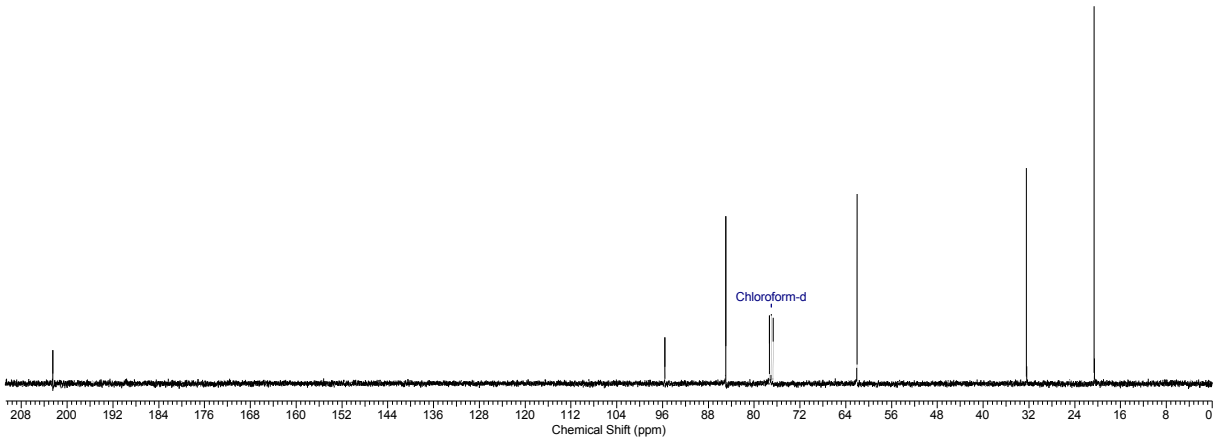

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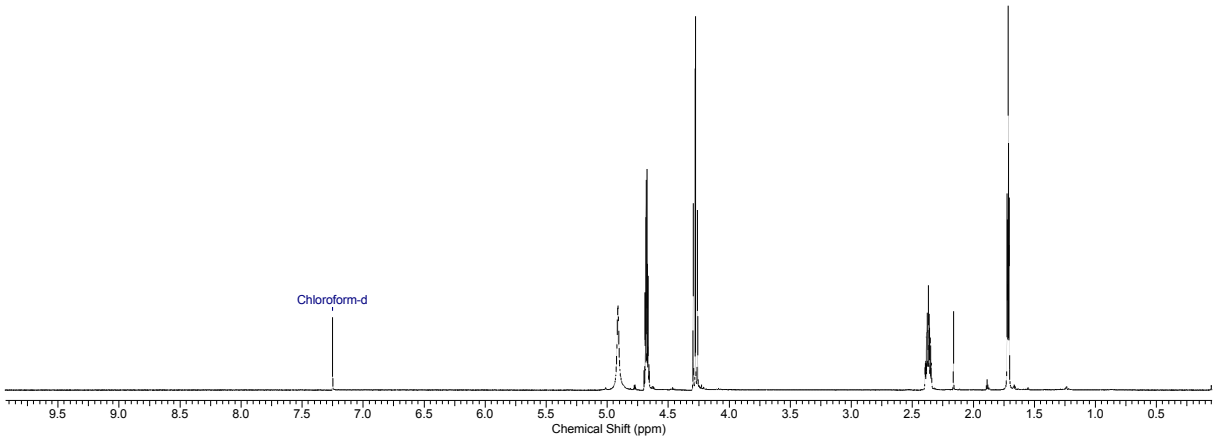
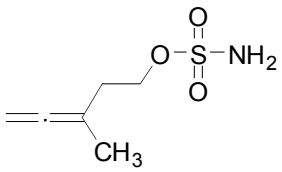
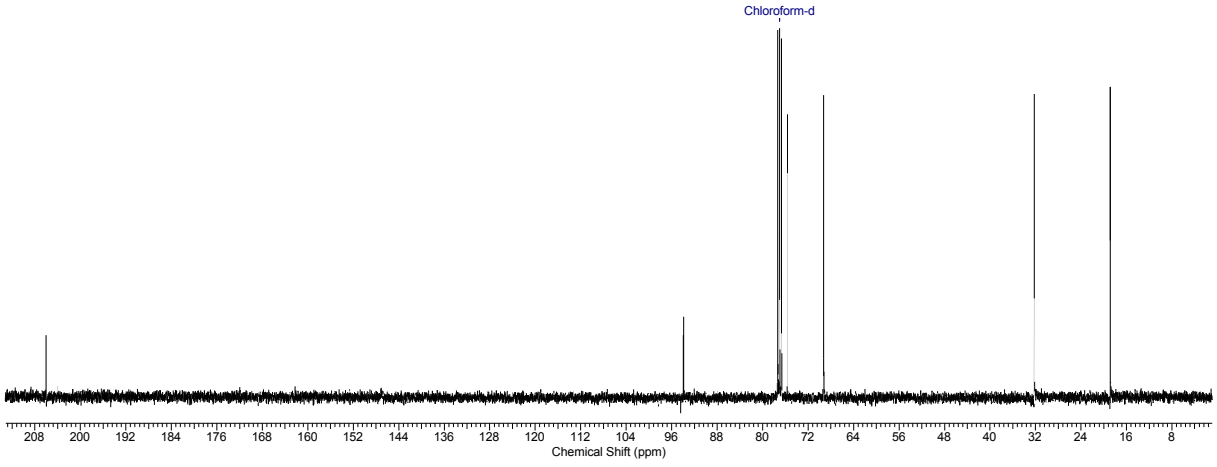




100 MHz, $CDCl_3$



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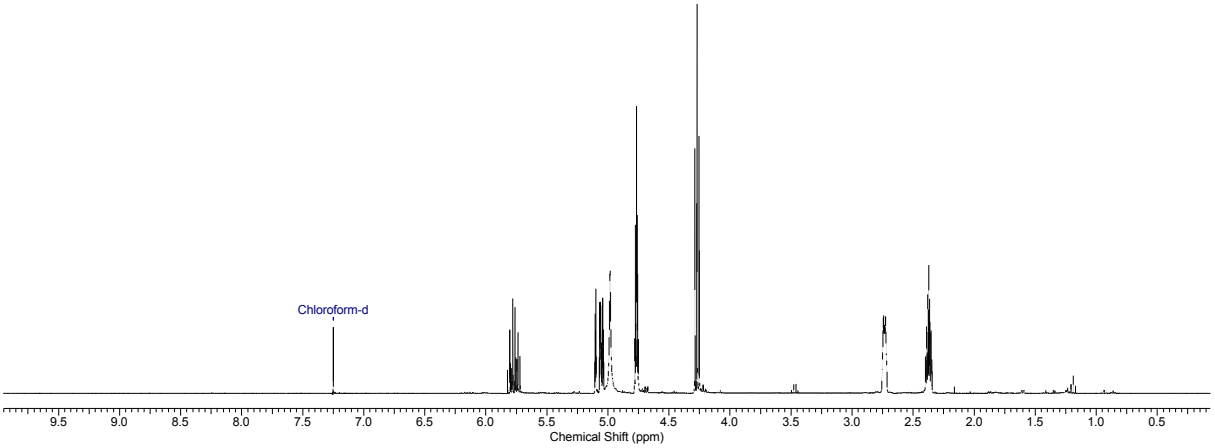

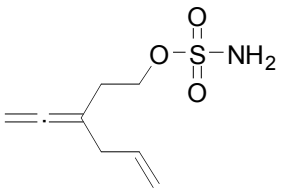

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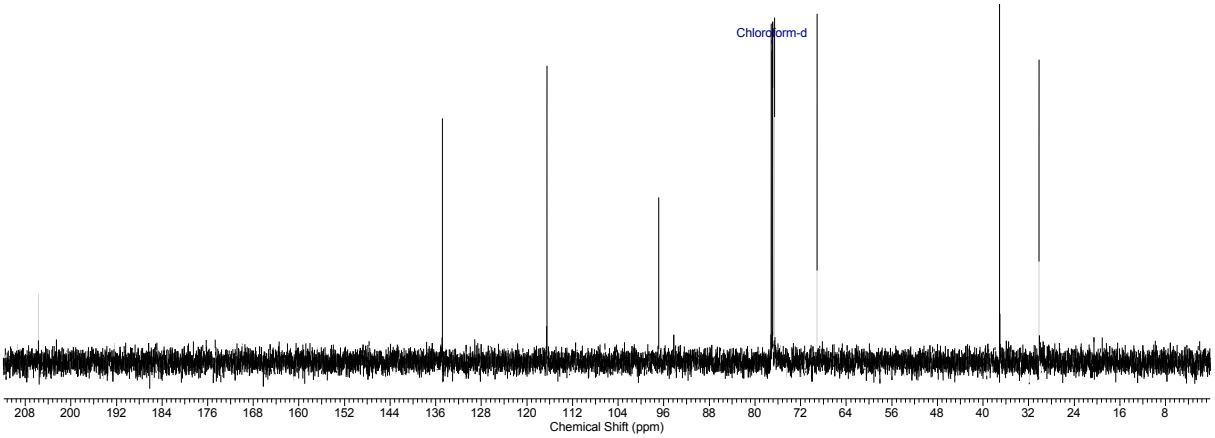

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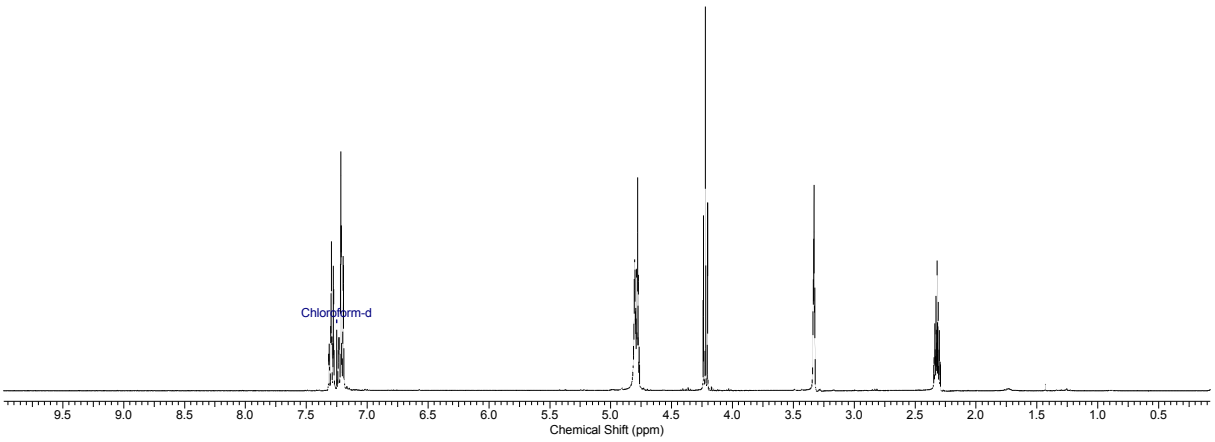

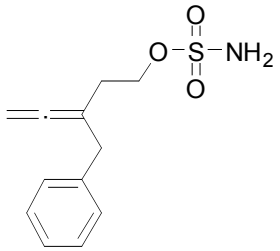

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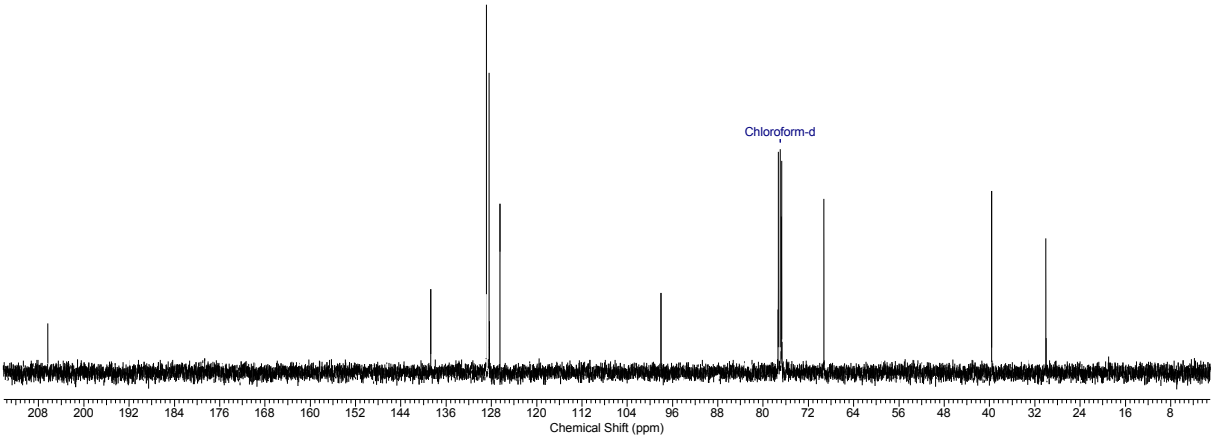

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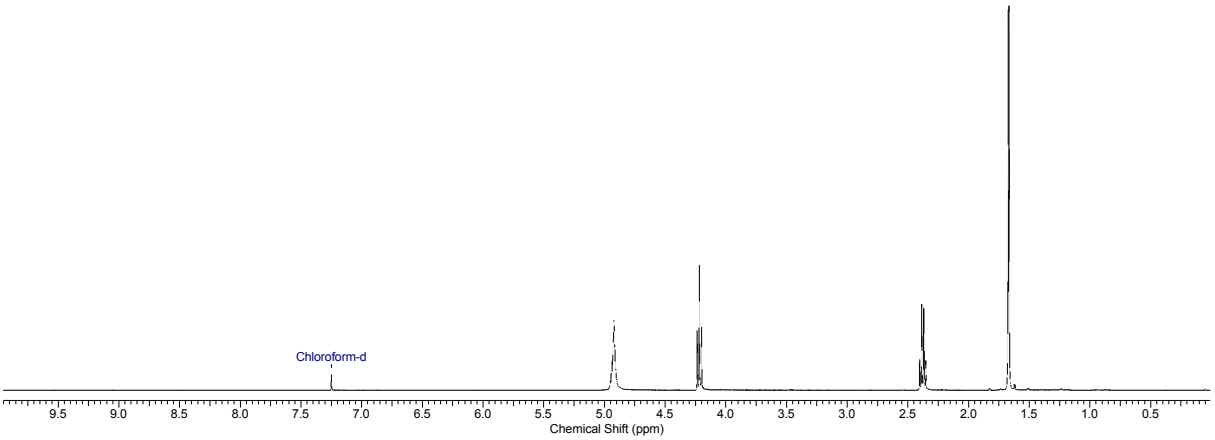

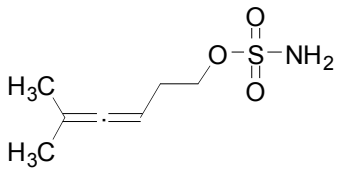

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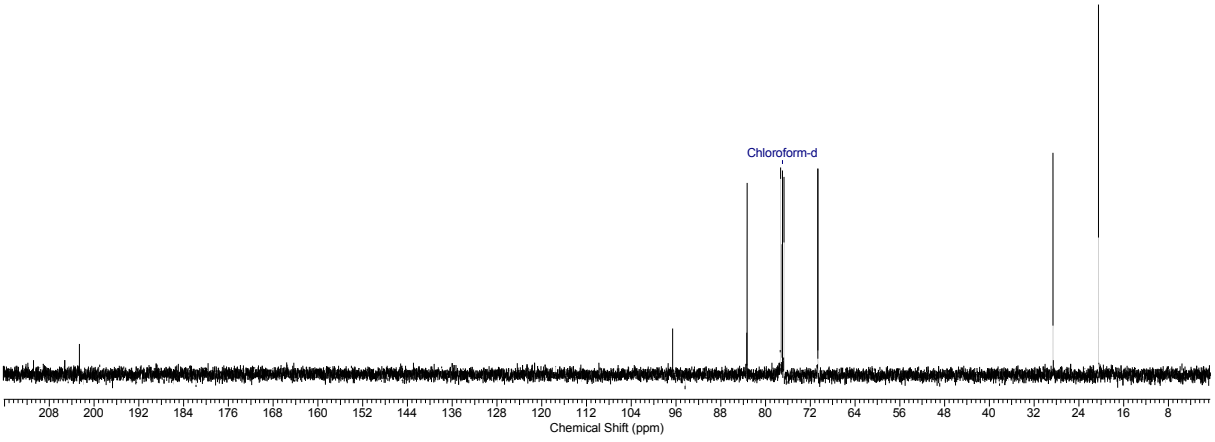

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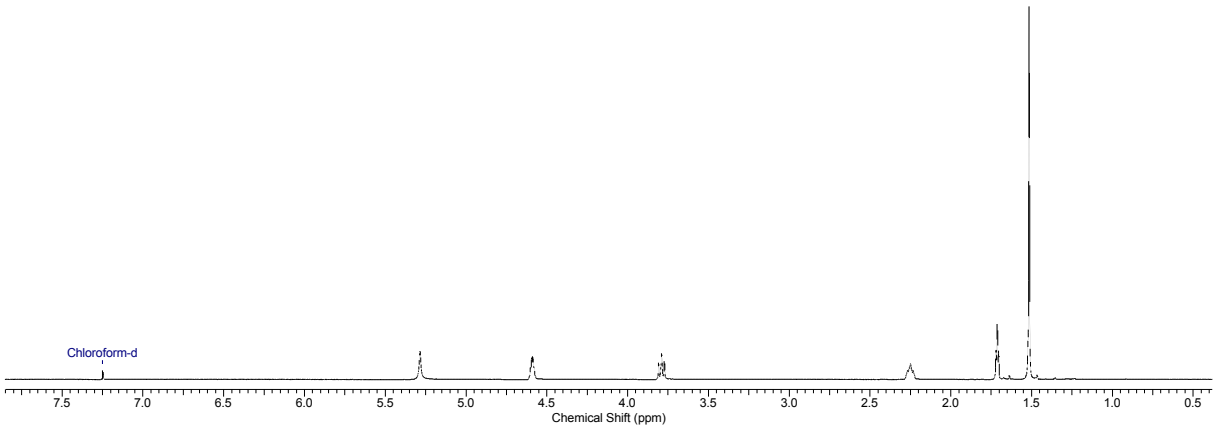

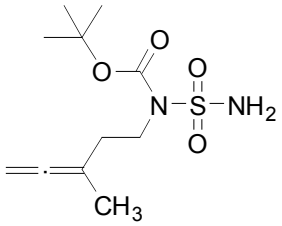

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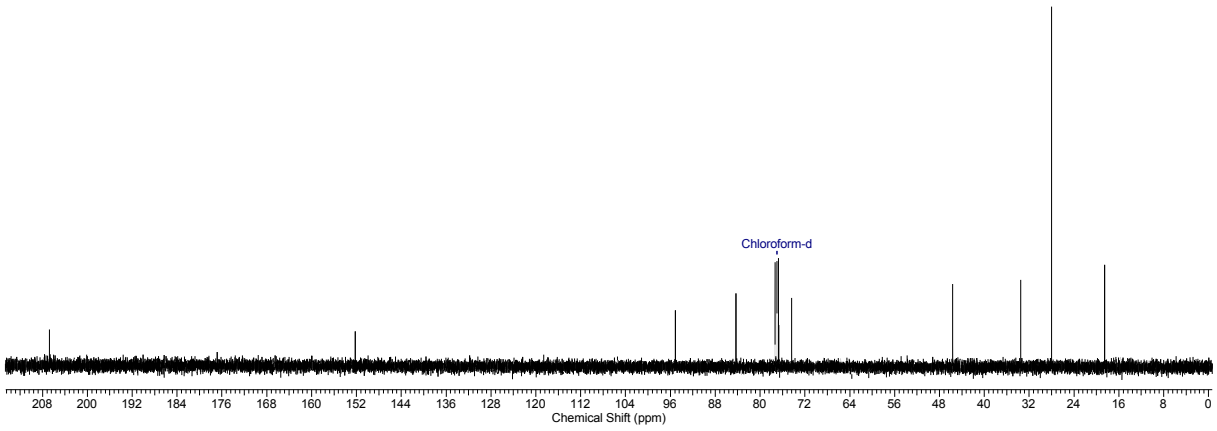

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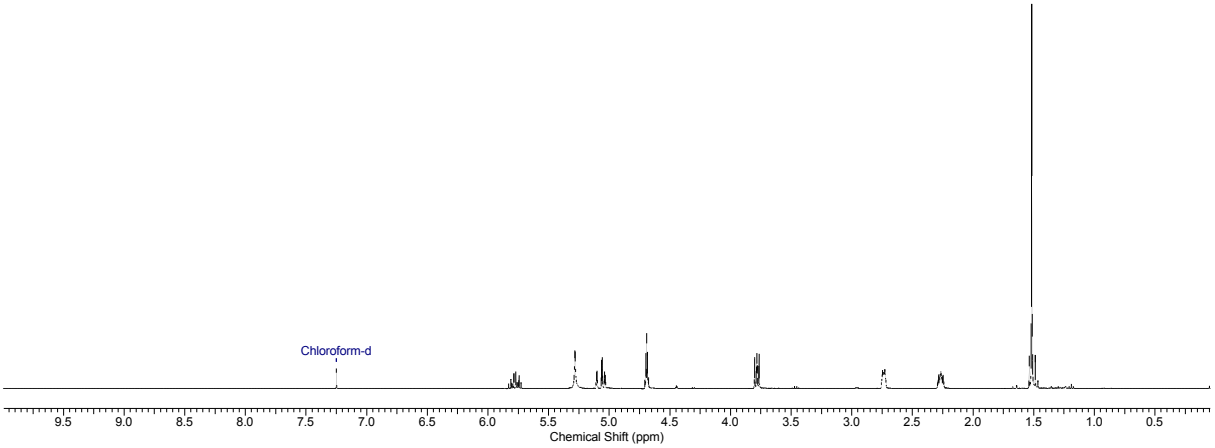

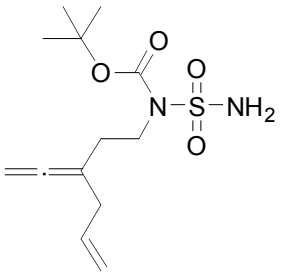

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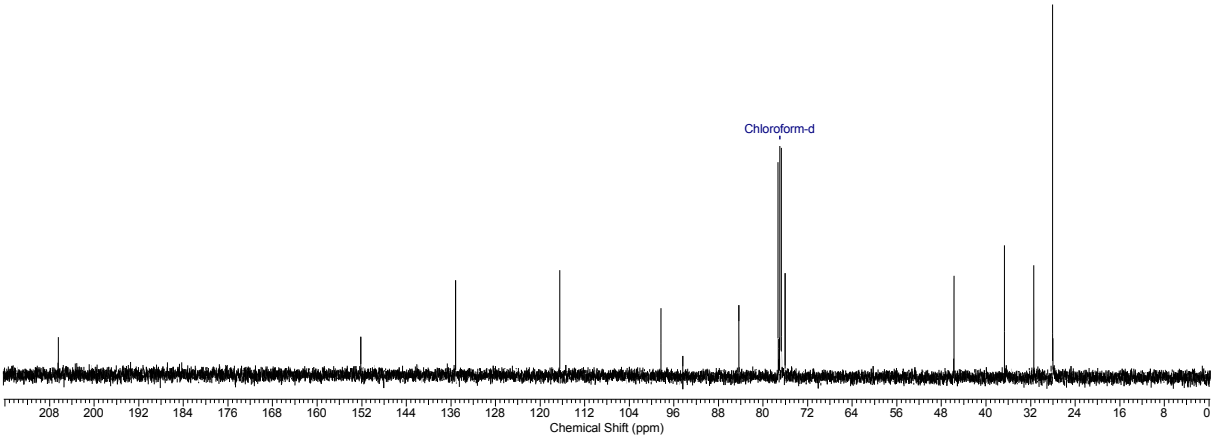

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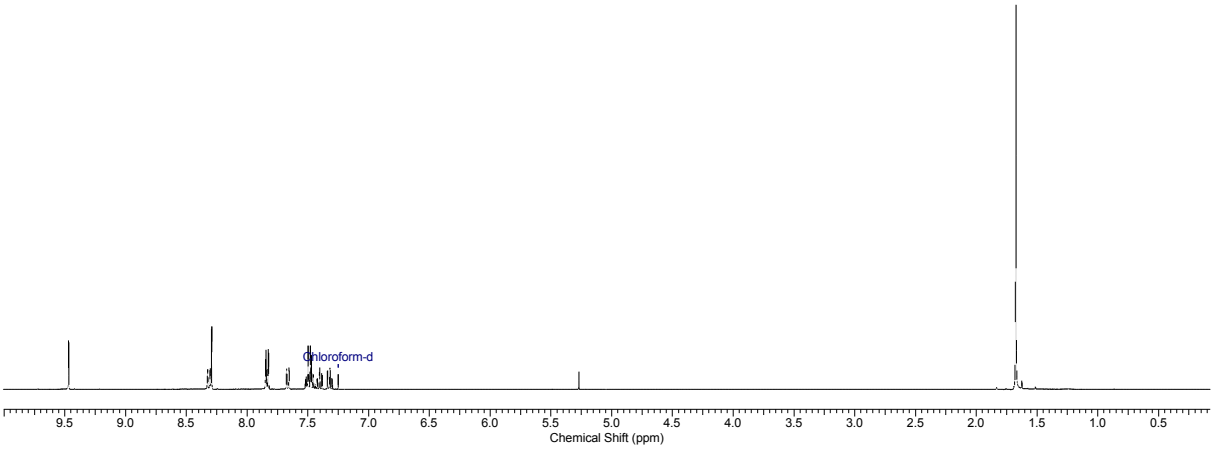

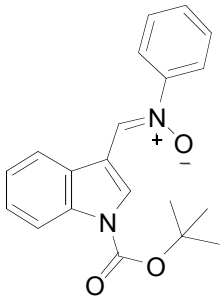

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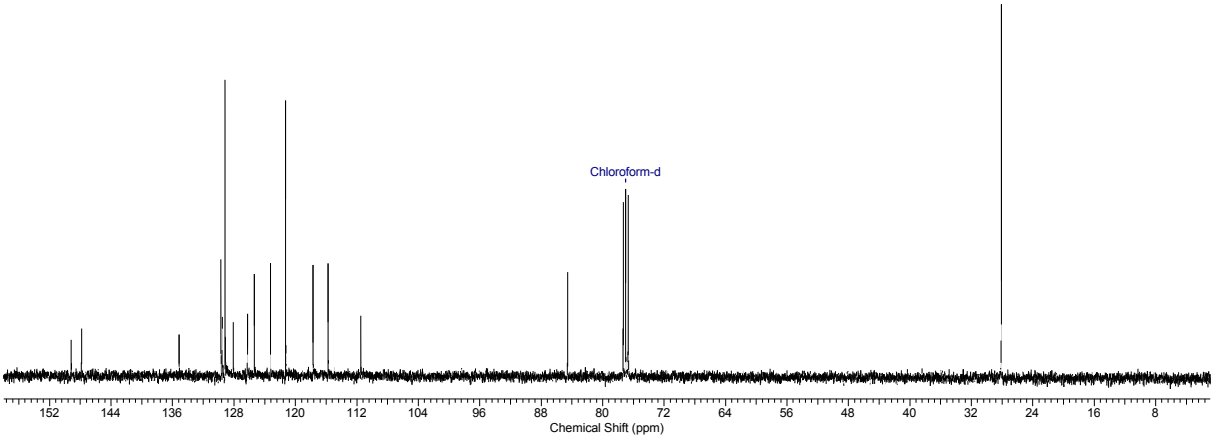

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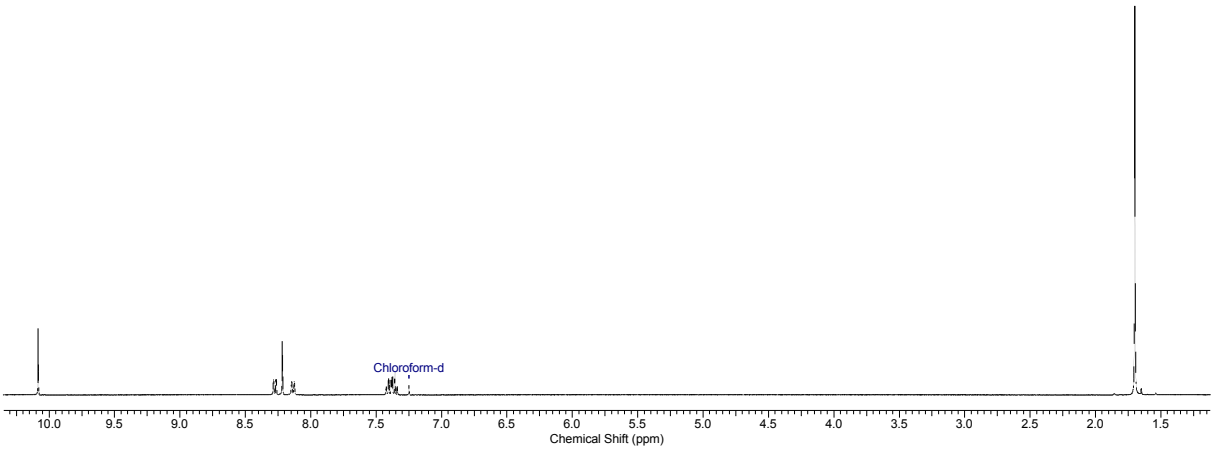

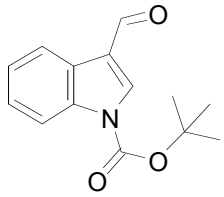

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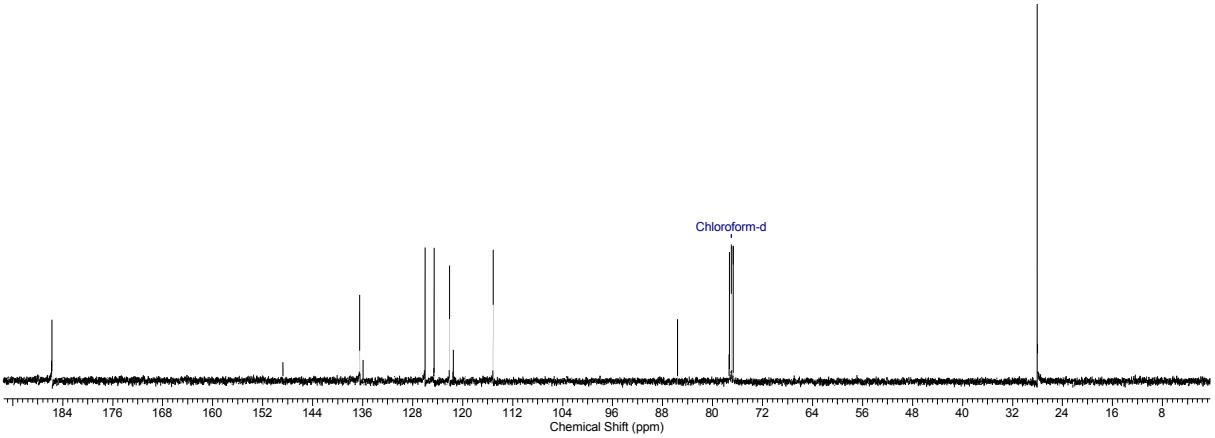

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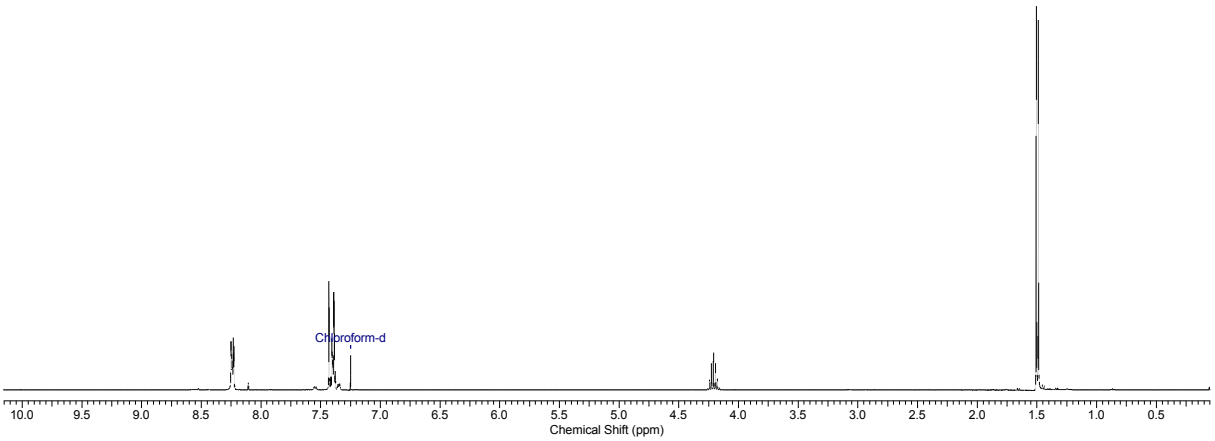

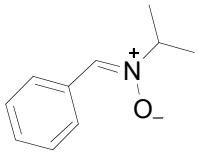

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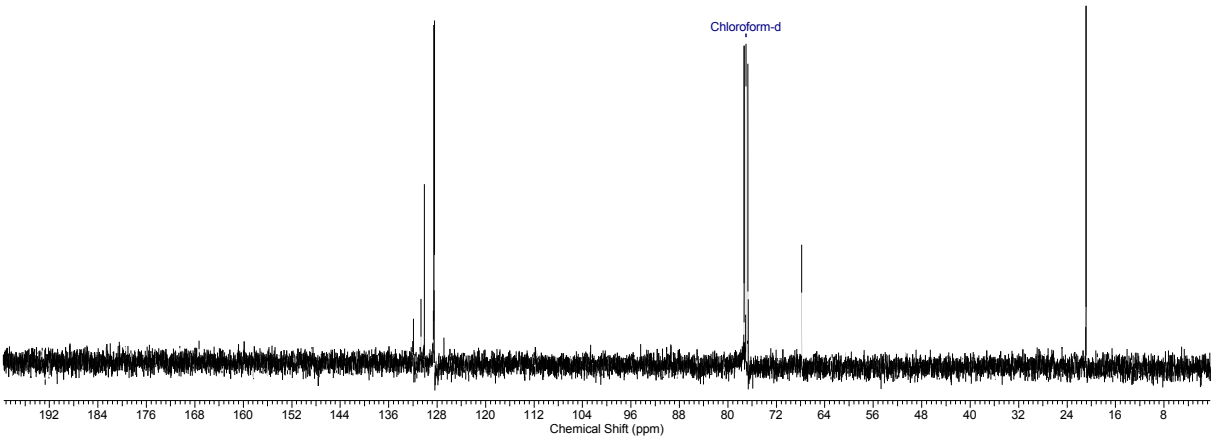
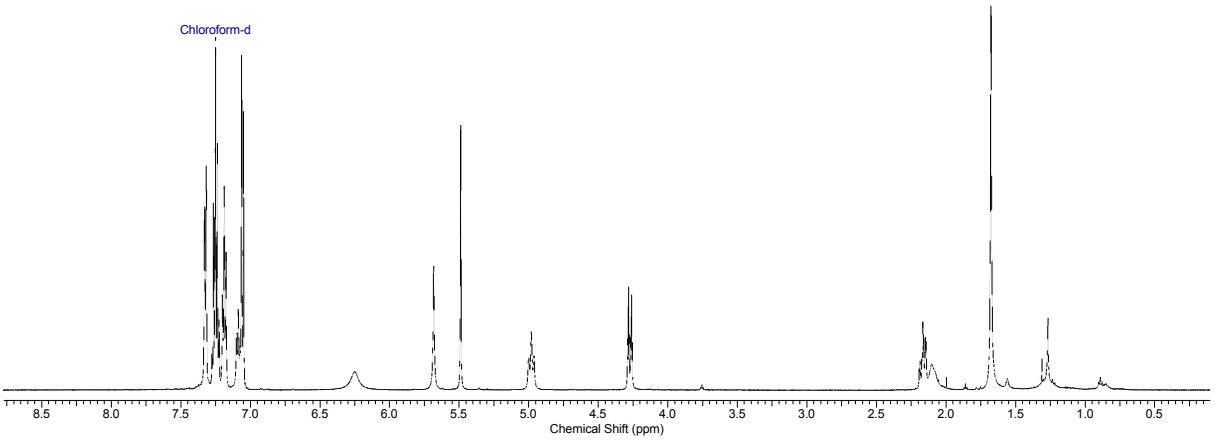
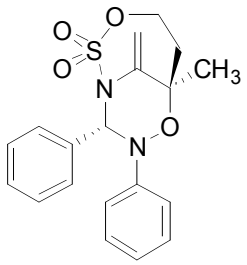
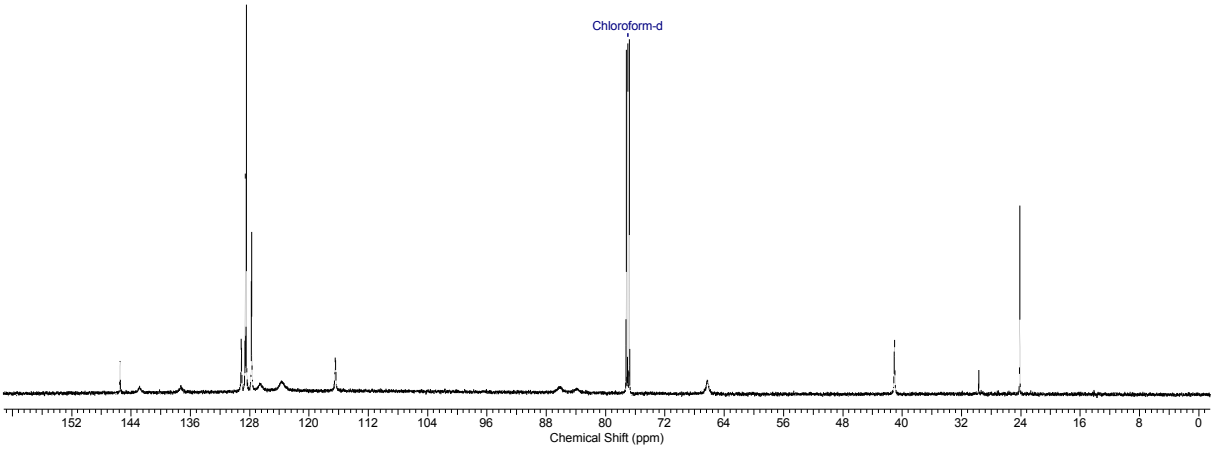


600 MHz, $CDCl_3$

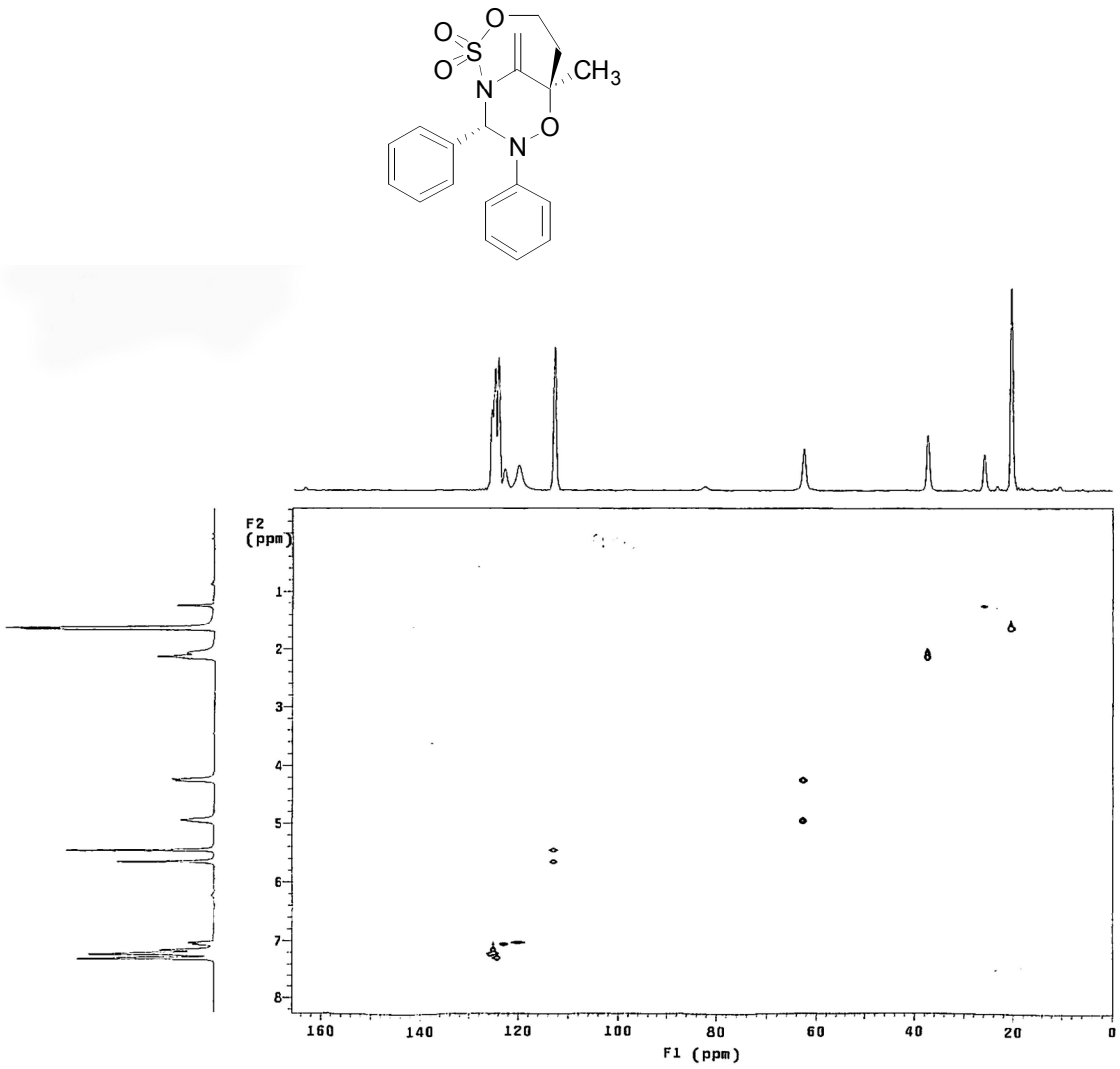




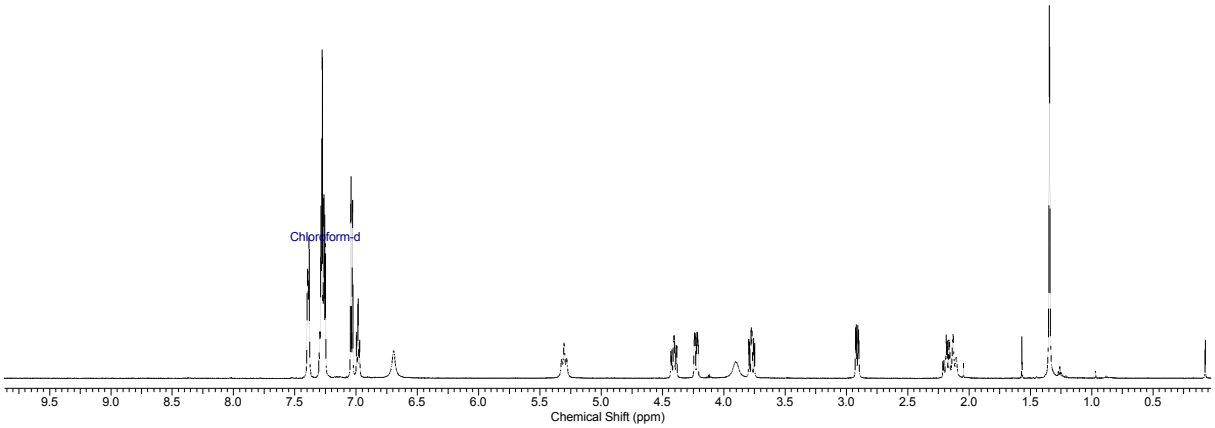
150 MHz, $CDCl_3$

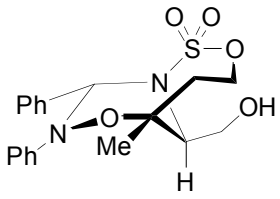


HMQC

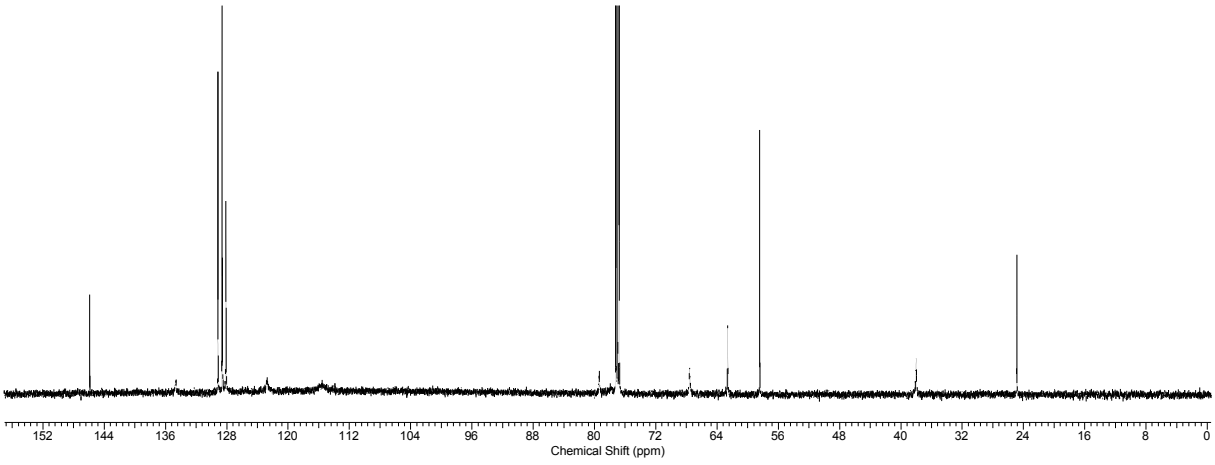


600 MHz $CDCl_3$

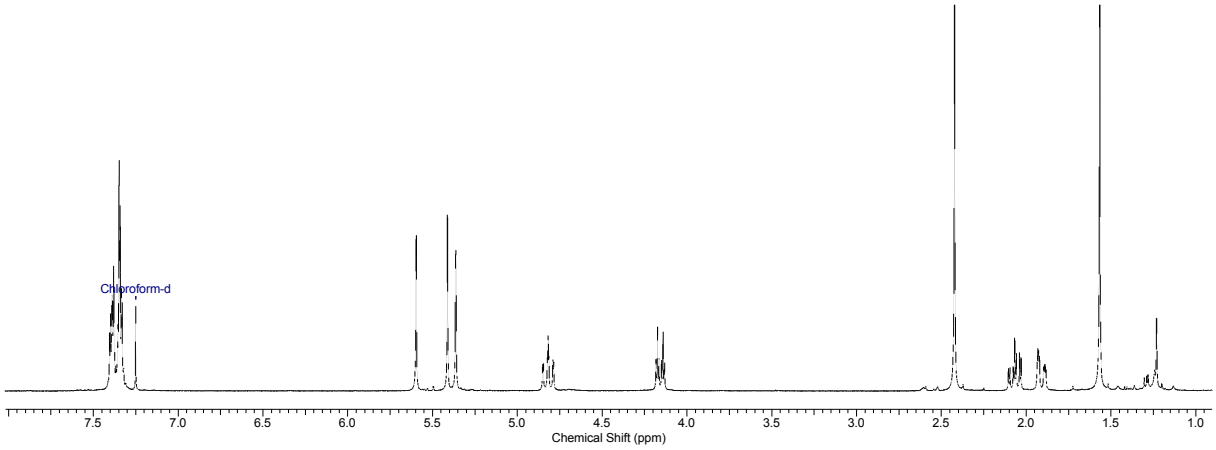


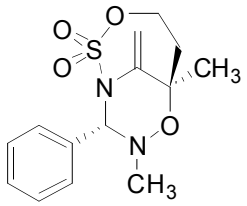


150 MHz $CDCl_3$

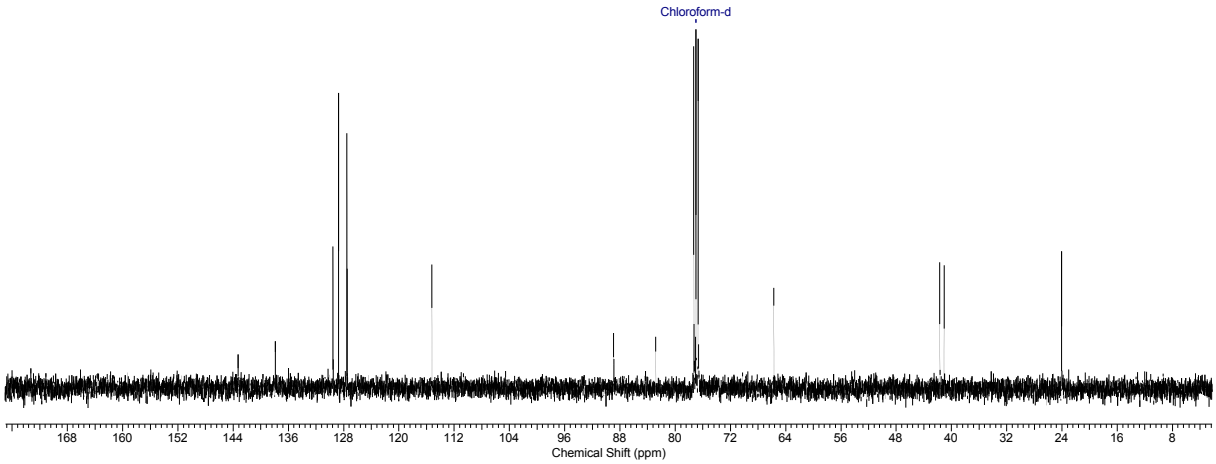


400 MHz, $CDCl_3$

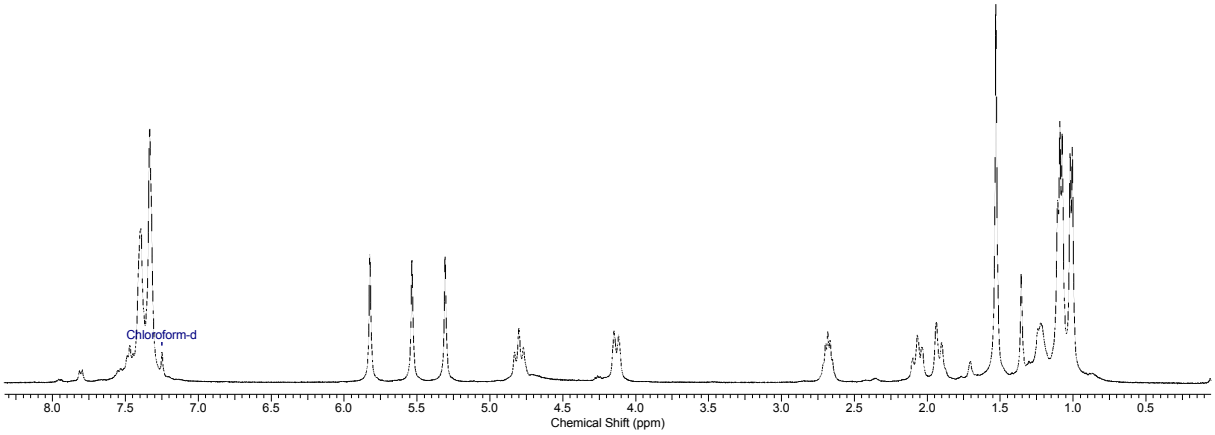


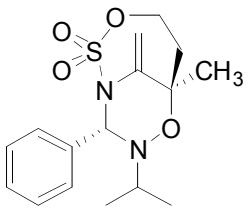


100 MHz, $CDCl_3$

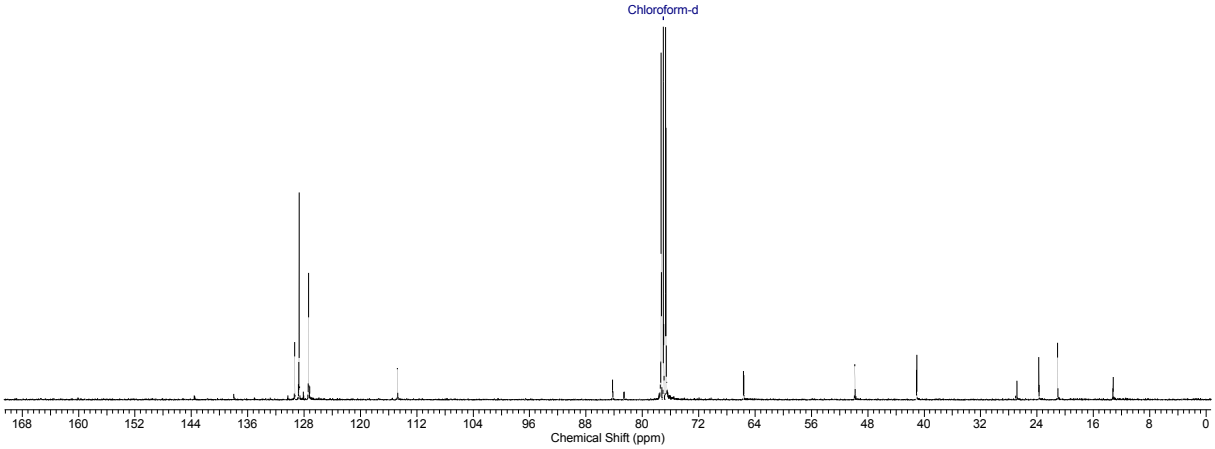


400 MHz, $CDCl_3$





100 MHz, $CDCl_3$



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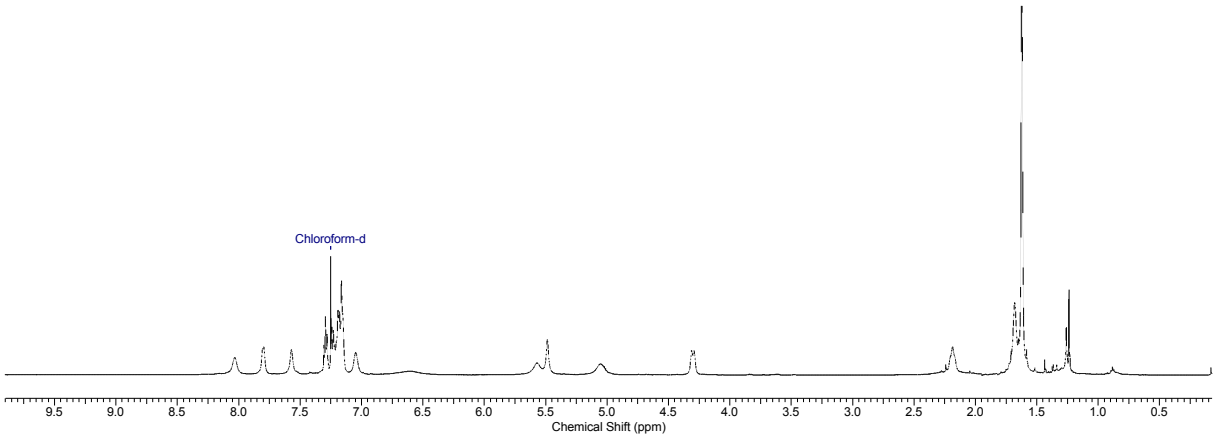
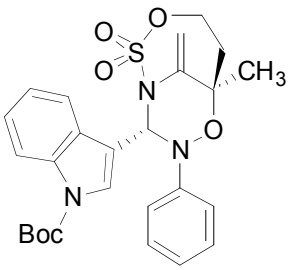
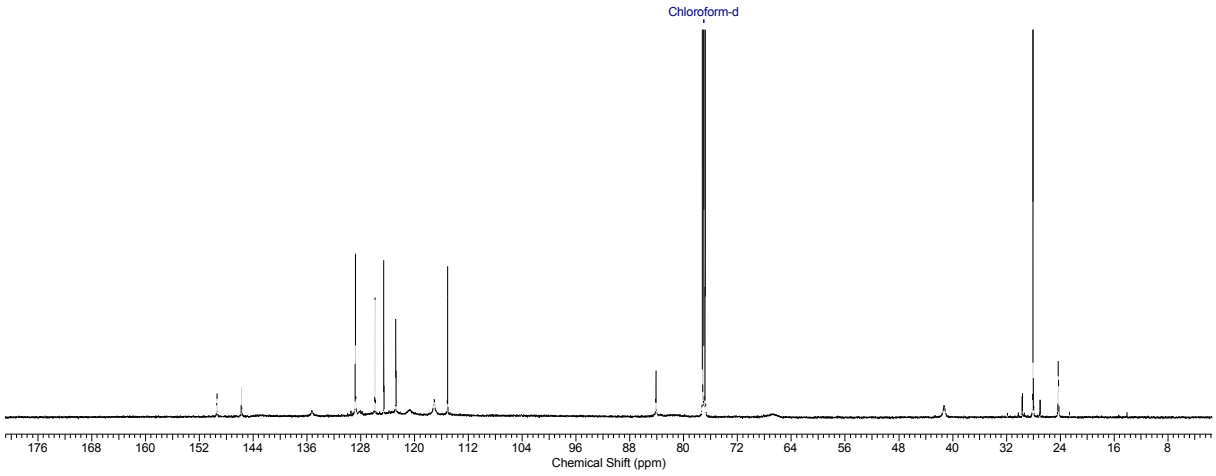
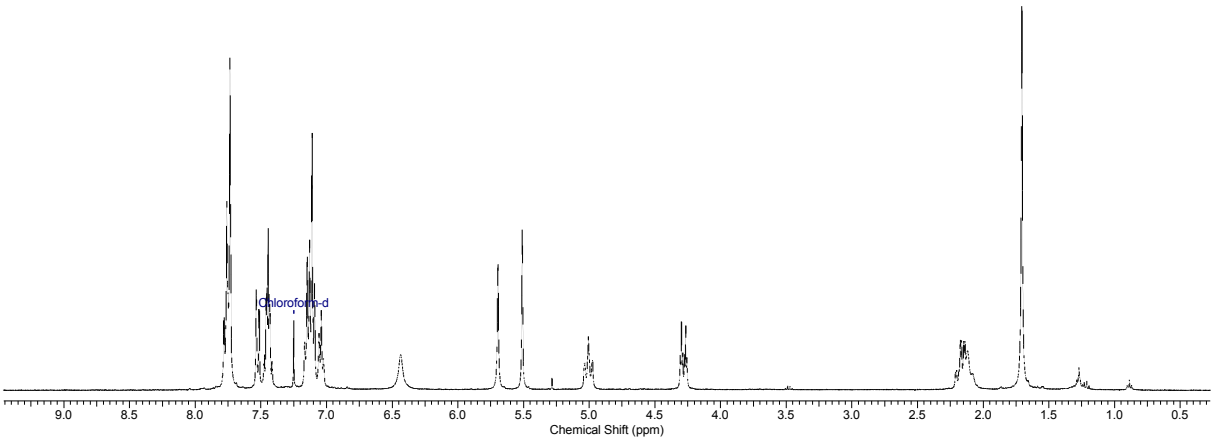


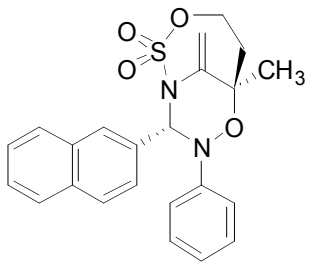


1500 MHz, $CDCl_3$

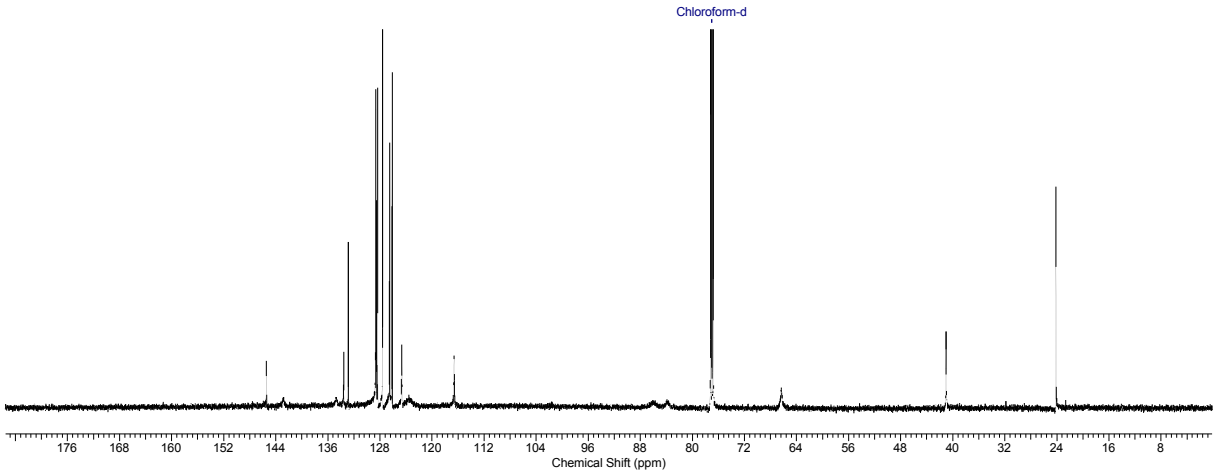


400 MHz, $CDCl_3$

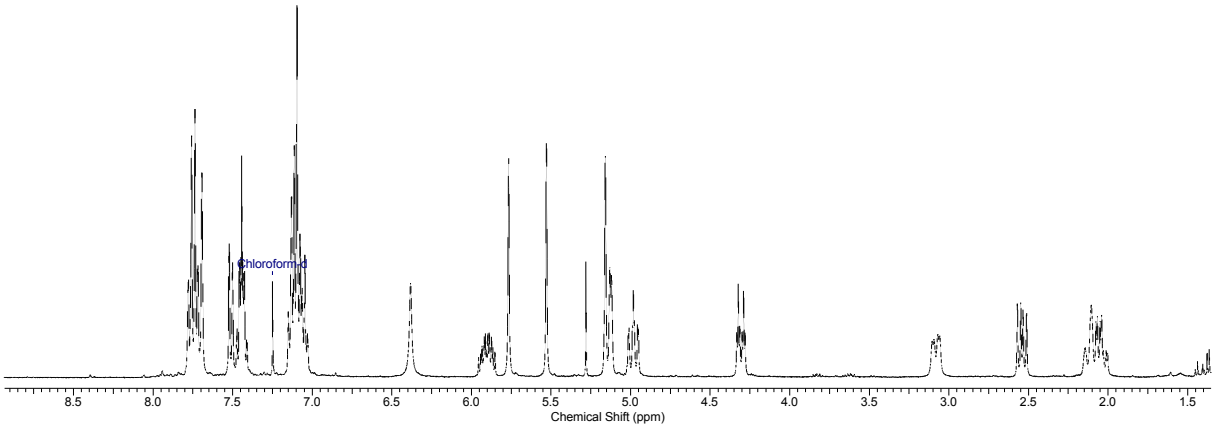


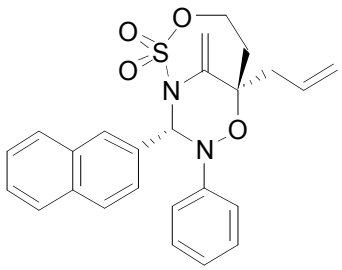


400 MHz, $CDCl_3$

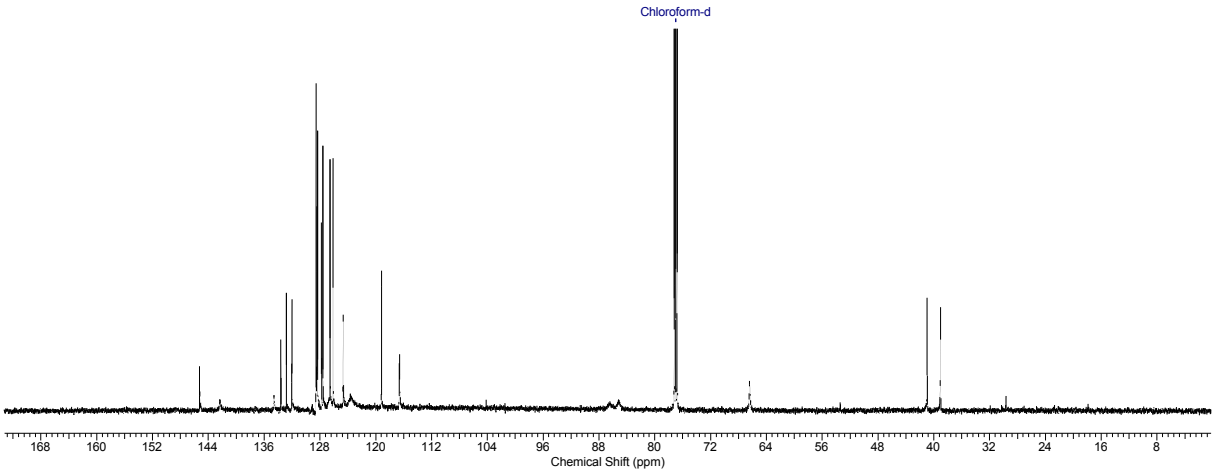


400 MHz, $CDCl_3$

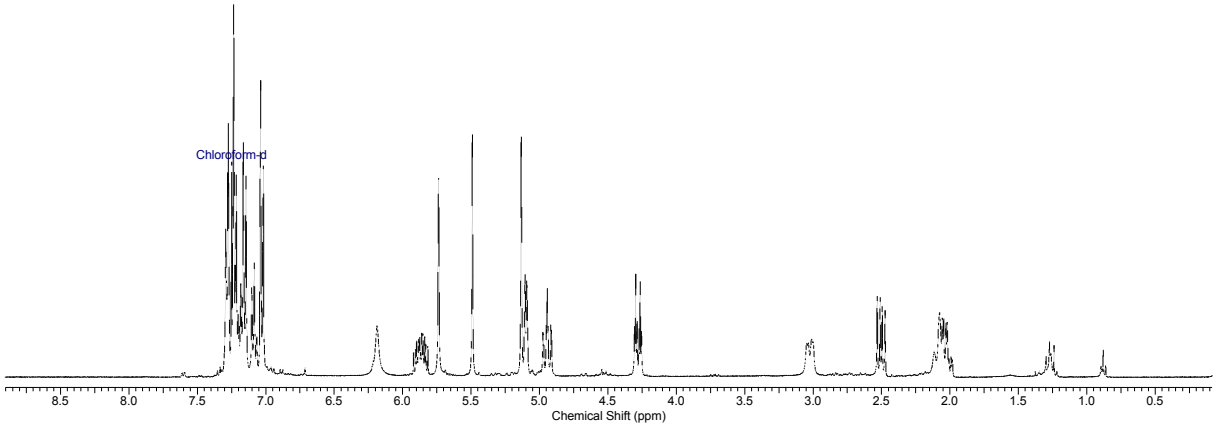


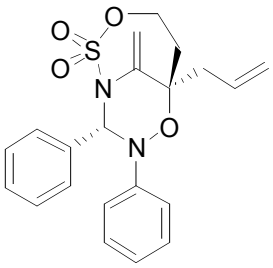


150 MHz, $CDCl_3$

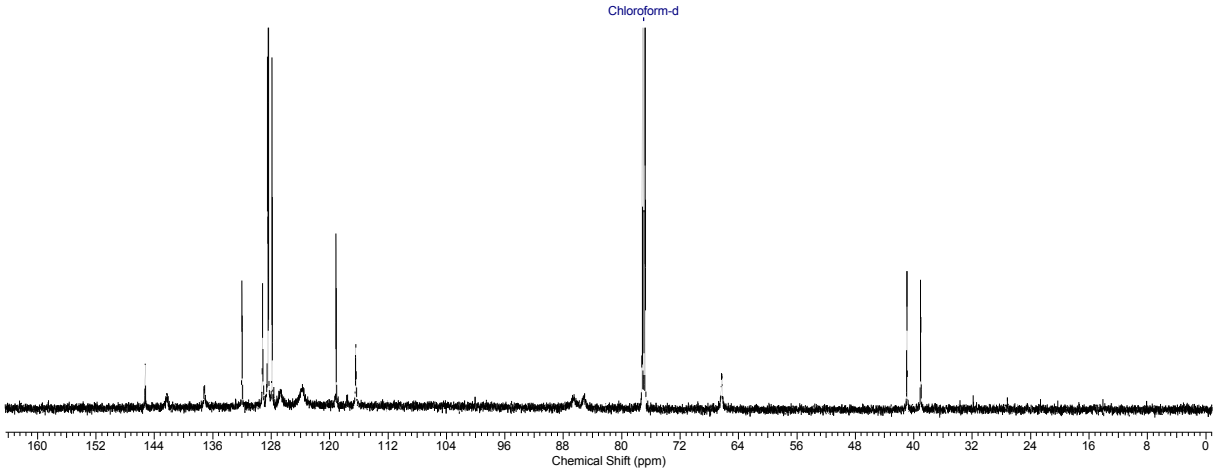


400 MHz, $CDCl_3$

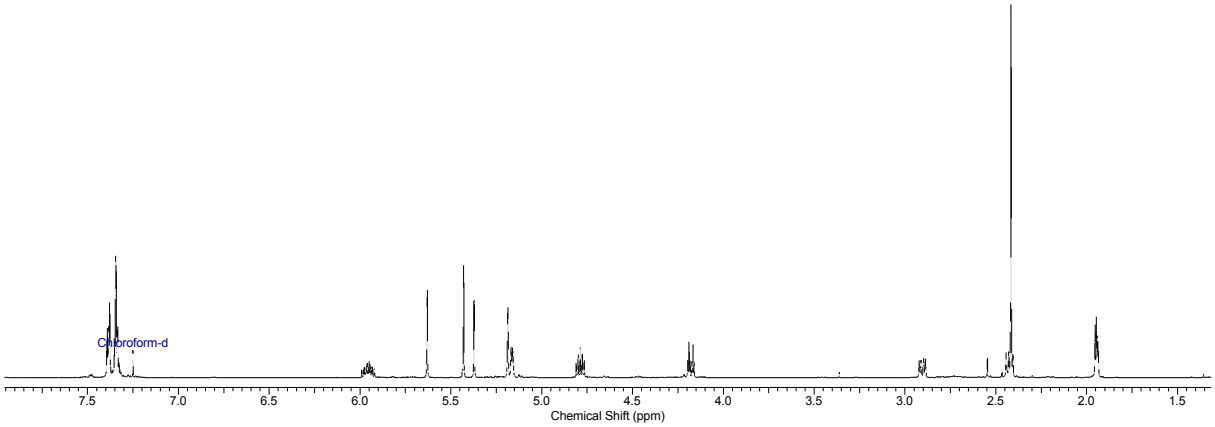


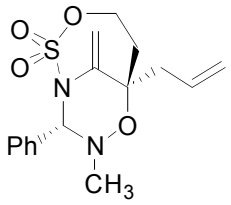


600 MHz, $CDCl_3$



600 MHz, $CDCl_3$





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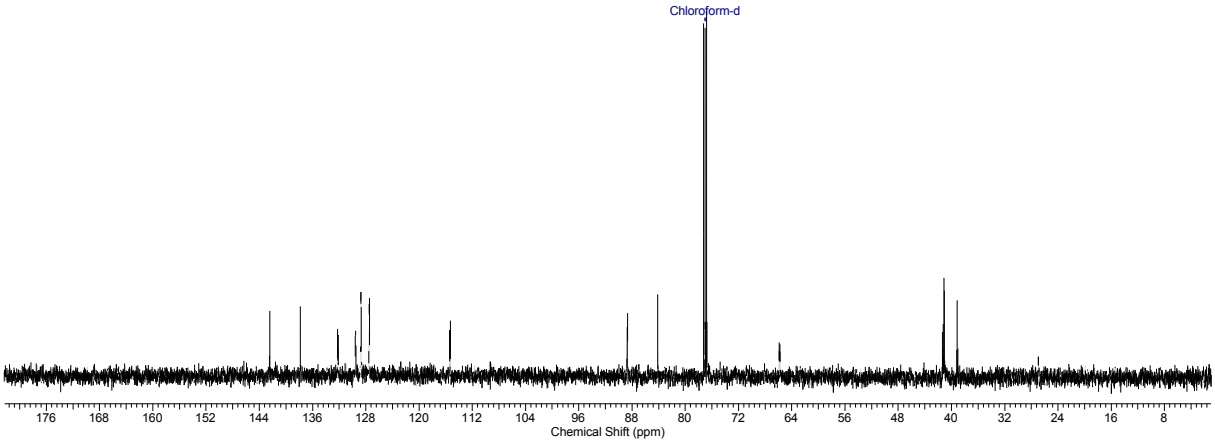
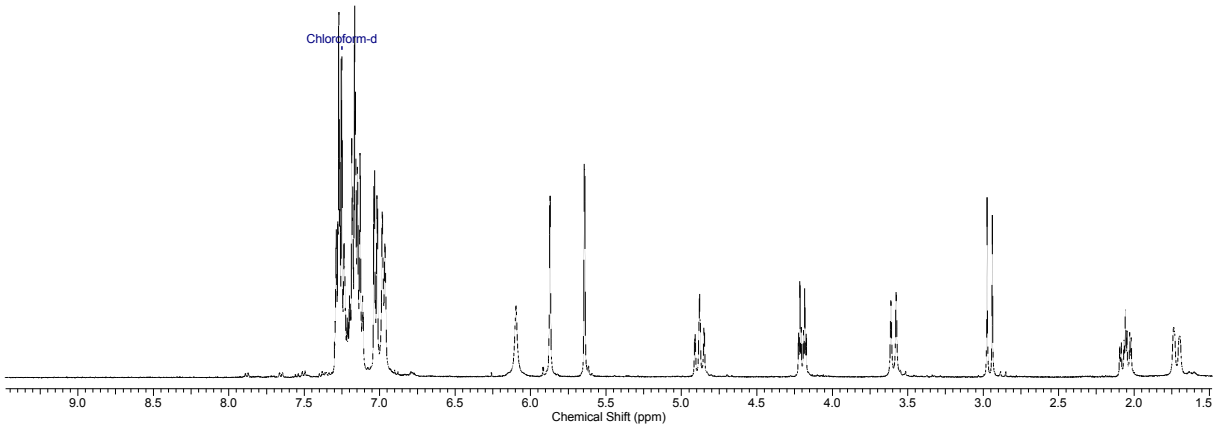
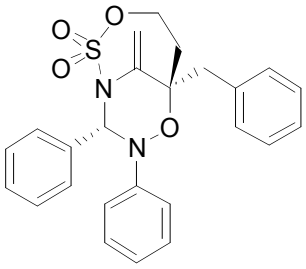
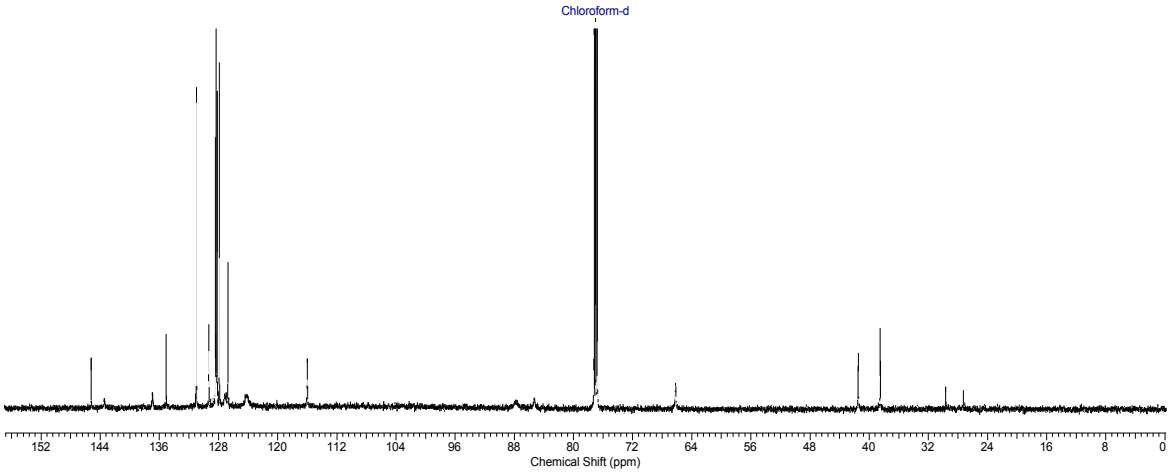


400 MHz, $CDCl_3$,

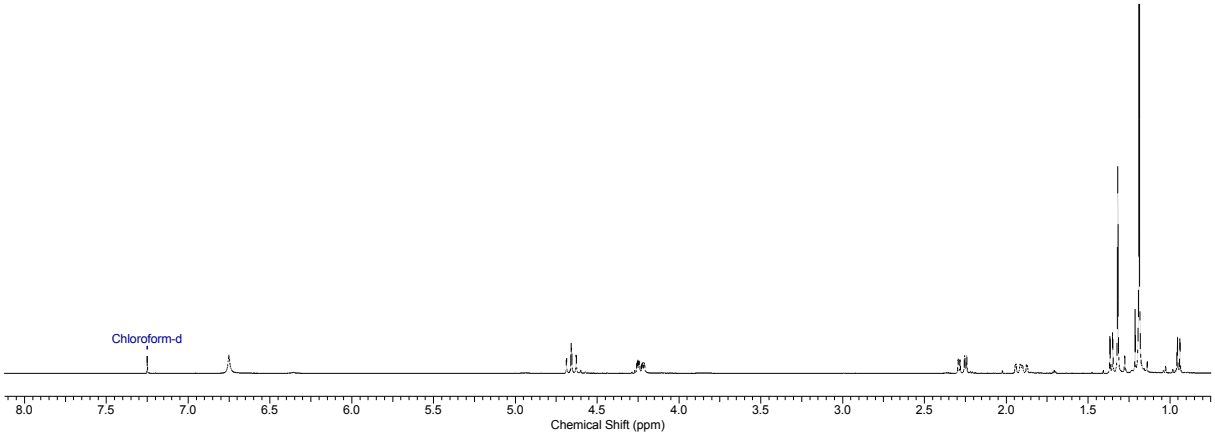


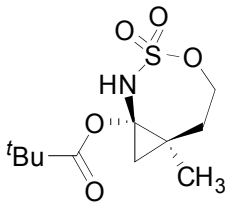


150 MHz, $CDCl_3$

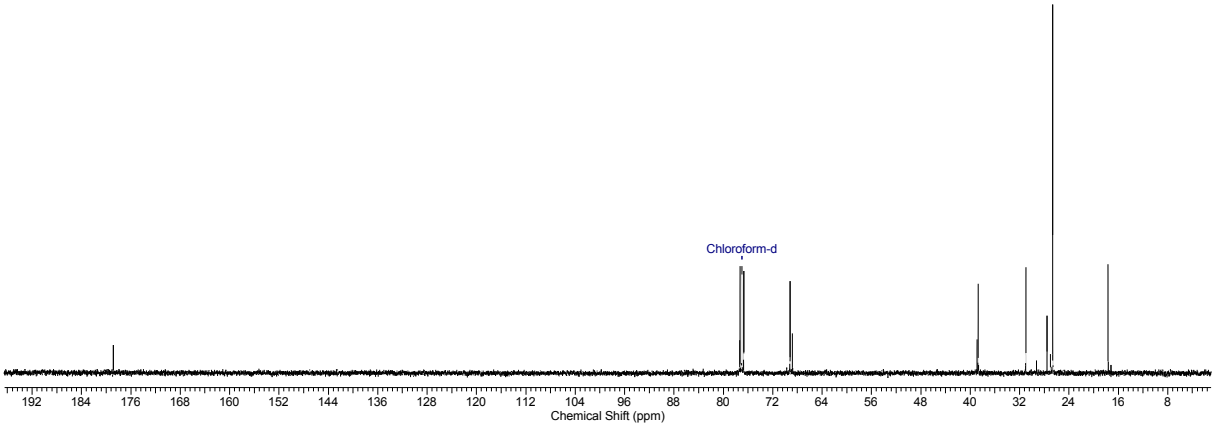


400 MHz, $CDCl_3$

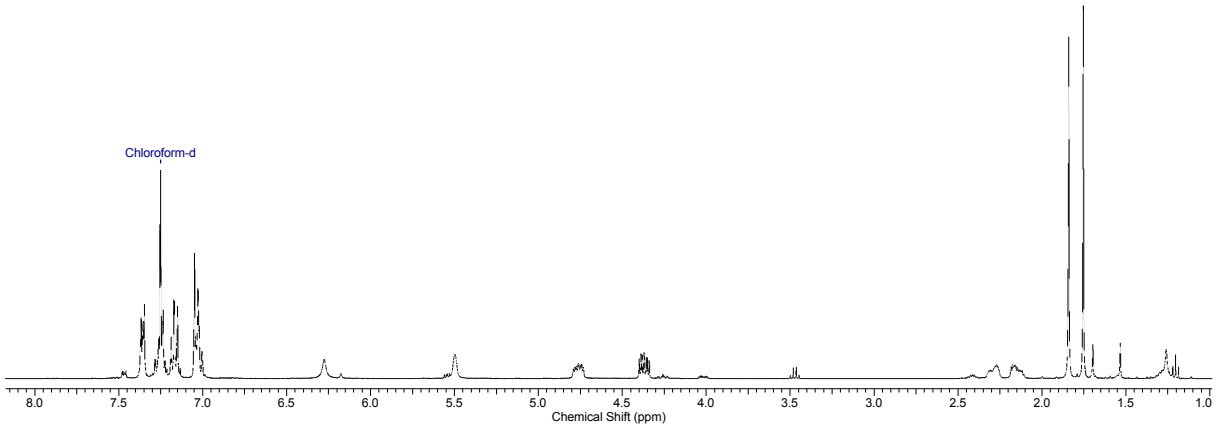


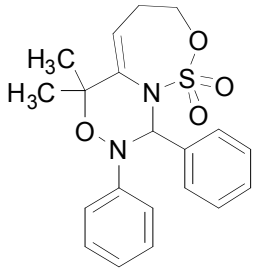


100 MHz, $CDCl_3$

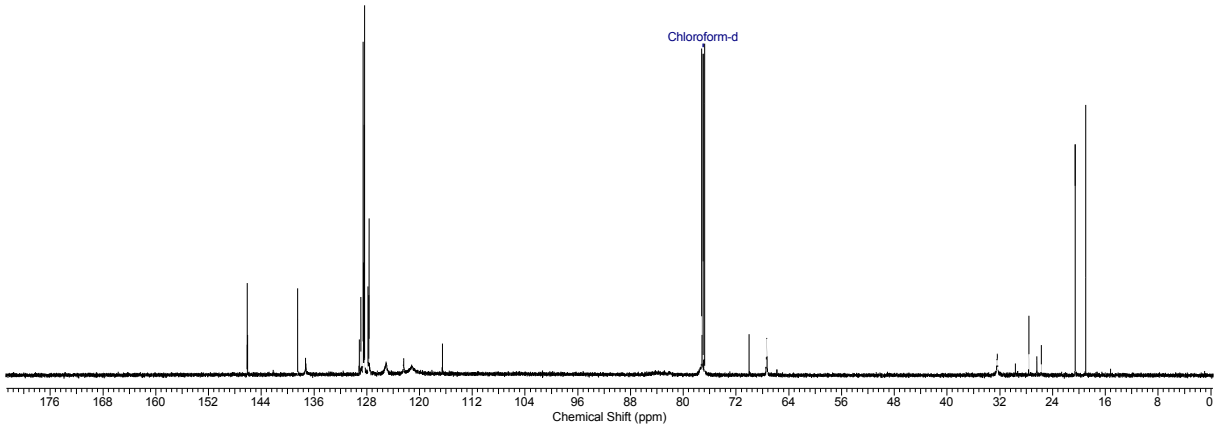


400 MHz, $CDCl_3$

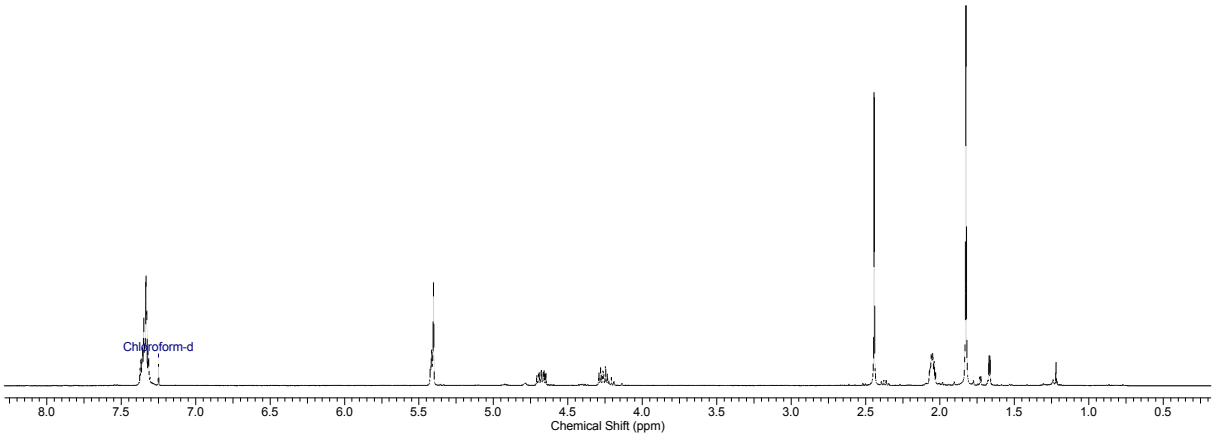


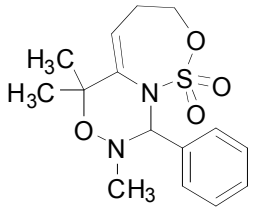


150 MHz , $CDCl_3$

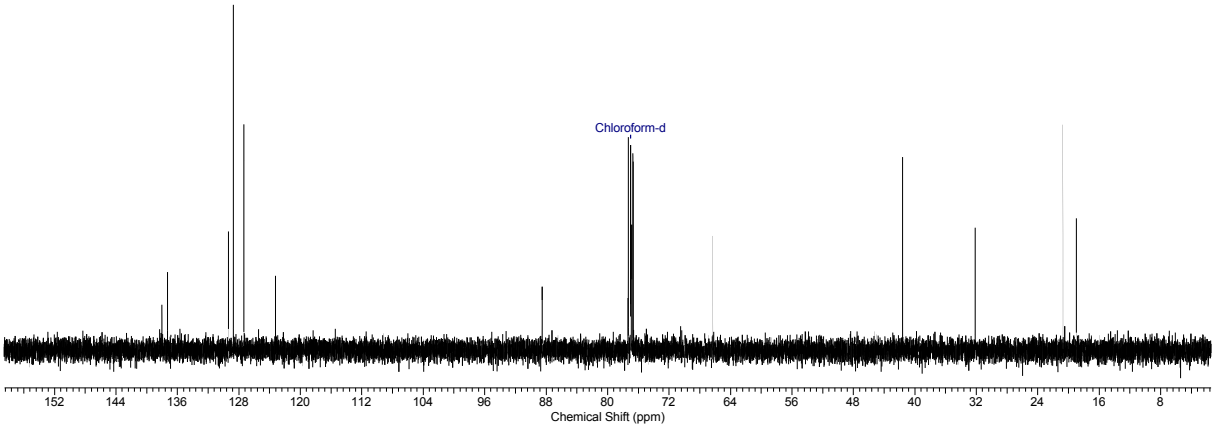


400 MHz, $CDCl_3$

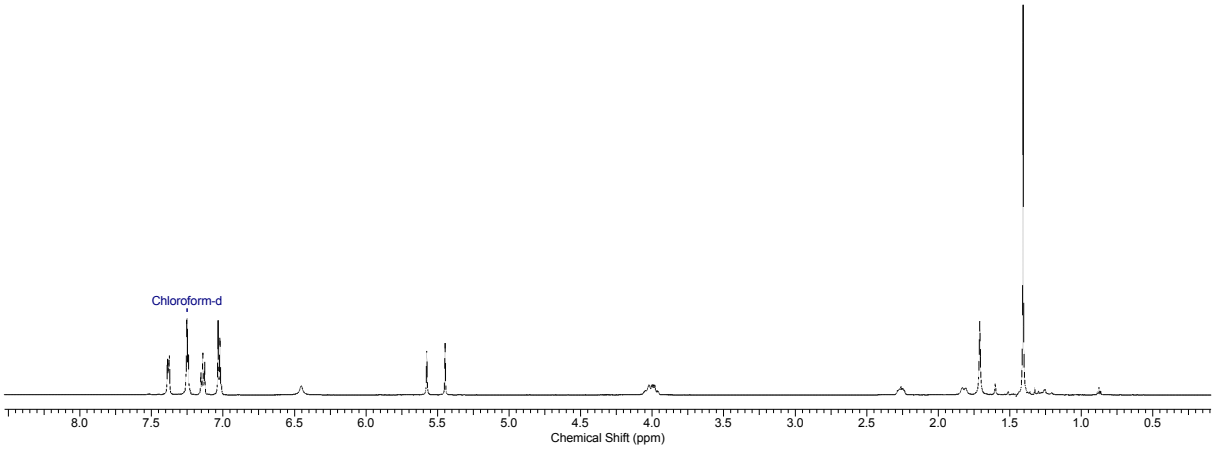


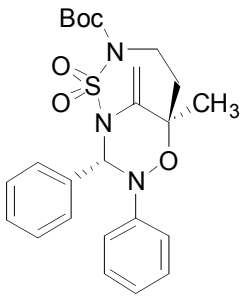


100 MHz , $CDCl_3$

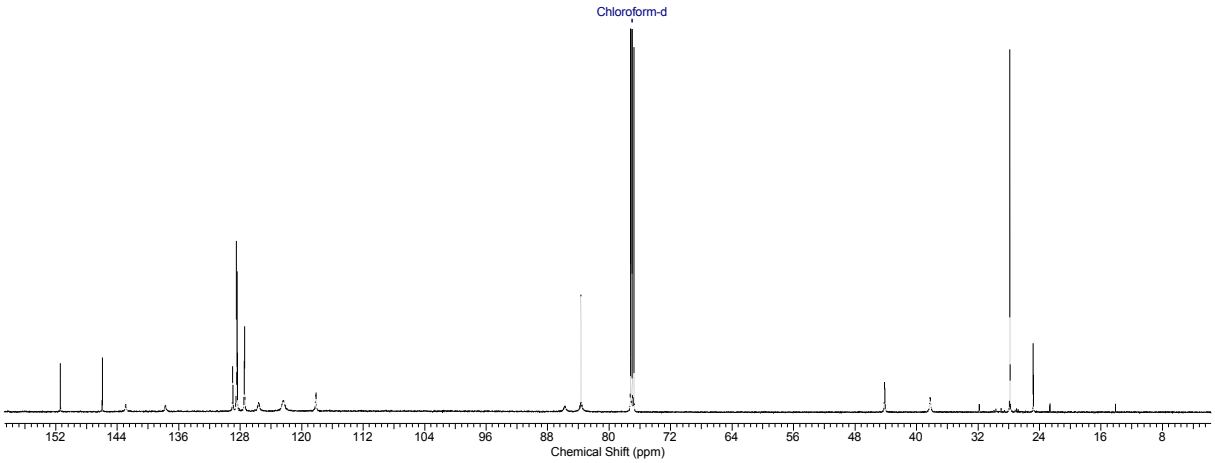


600 MHz, $CDCl_3$

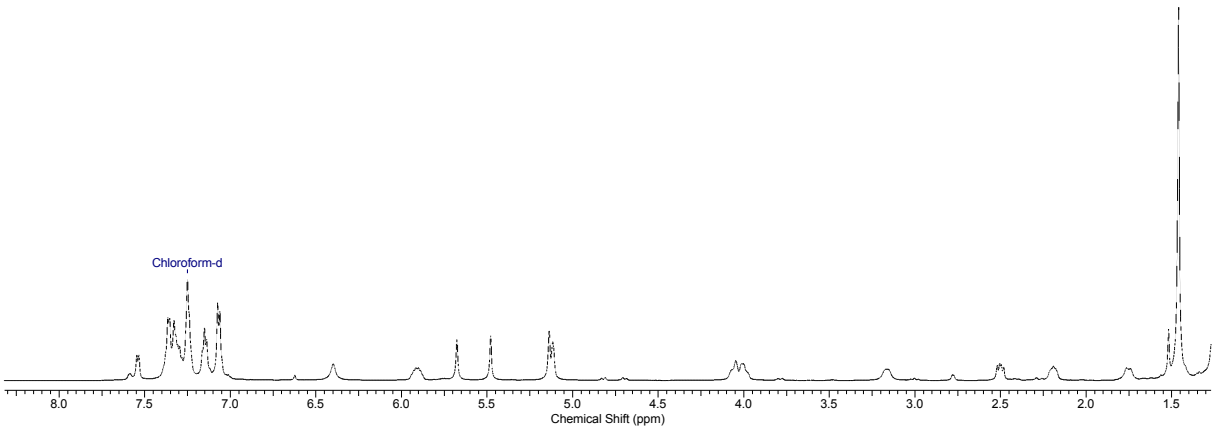


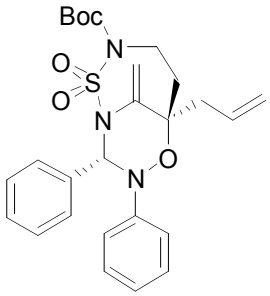


150 MHz, $CDCl_3$

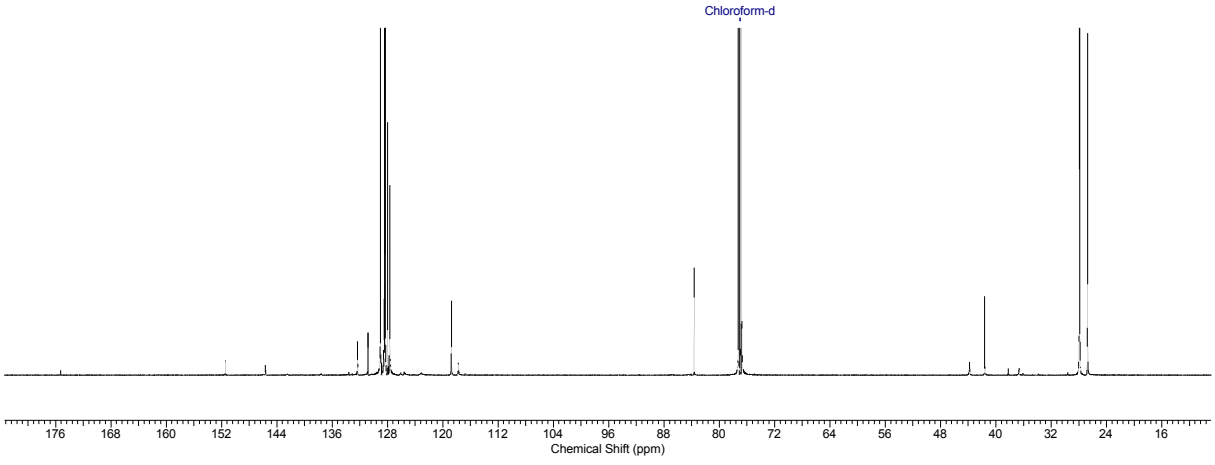


600 MHz, $CDCl_3$





150 MHz, $CDCl_3$

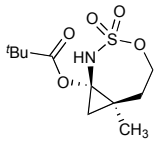


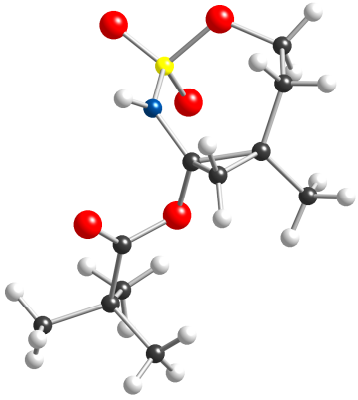
X-Ray structures

Structures were obtained of **10** and **8**. These data have been deposited in the Cambridge Crystallographic Data Centre and can be obtained free of charge via the internet: www.ccdc.cam.ac.uk/data_request/cif (CCDC 750090 and 750091 respectively). Crystallographic information files (cif format) are included in a separate file as supplementary information for this communication.

Graphical representations of these data are provided below.

7-Methyl-3,3-dioxido-4-oxa-3-thia-2-azabicyclo[5.1.0]oct-1-yl pivalate (**10**): CCDC 750090





(6-Methyl-2,2-dioxido-8,9-diphenyl-3,7-dioxa-2-thia-1,8-diazabicyclo[4.3.1]dec-10-yl)methanol (**8**): CCDC 750091